Volume 20 (1973)

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CHAPTER 1

CYCLOPROPANES FROM UNSATURATED COMPOUNDS, METHYLENE IODIDE, AND ZINC-COPPER COUPLE

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INTRODUCTION

The reaction of the organozinc reagent prepared from methylene iodide and zinc-copper couple with substituted unsaturated compounds has proved to be a versatile and convenient method for the synthesis of cyclopropanes (Simmons and Smith, 1958¹).

$$\begin{array}{c} \overset{}{\overset{}}_{\mathbb{C}} \overset{}{\overset{}} + \mathrm{CH}_{2}\mathrm{I}_{2} + \mathrm{Zn}(\mathrm{Cu}) \xrightarrow{}{\overset{}} \overset{}{\overset{}} \overset{}{\overset{}} \overset{}{\overset{}} \mathrm{CH}_{2} + \mathrm{Zn}\mathrm{I}_{2} + (\mathrm{Cu}) \end{array}$$

The synthesis is stereospecific with regard to the stereochemistry of the unsaturated compound and is usually free from serious side reactions; it can be carried out under mild conditions in diethyl ether and affords cyclopropanes, often in good yields, that are dimculty accessible otherwise. A further advantage of the method is that it can be adapted easily to large-scale preparations. The structure of the organozinc intermediate,

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¹ H. E. Simmons and R. D. Smith, J. Amer. Chem. Soc., 80, 5323 (1958).

like that of the Grignard reagent, is not yet known with certainty, and it will be referred to in the text simply as "the zinc reagent" unless otherwise noted. This chapter reviews the reactions of the zinc reagent with carboncarbon double bonds and includes other of its reactions only incidentally.

Two useful variations of the cyclopropanation reaction have subsequently appeared which involve the same or a similar organozinc intermediate: (1) diazomethane reacts with zinc iodide in ether to form a reagent which converts unsaturated compounds to cyclopropanes (Wittig and Schwarzenbach, 1959²), and (2) methylene iodide and diethylzinc react in ether in the presence of unsaturated compounds to yield the corresponding cyclopropanes (Furukawa, Kawabata, and Nishimura, 1966³). The latter modification is particularly useful when the methylene iodide carries a substituent (alkyl, aryl) for the substituted cyclopropanes are formed in good yields, whereas the reaction of substituted methylene iodides with zinc-copper couple generally gives only low yields of products. The alkylidene iodide-diethylzinc reagents also attack alkylbenzenes to form 7-methylcyclohepta-1,3,5-trienes.

Processes are known in which a divalent carbon fragment adds to carbon-carbon double bonds either as a free carbene or as an organometallic complex. When the intermediacy of the organometallic complex can be demonstrated in the rate-determining step of cyclopropane formation, the process has been distinguished as a "methylene-transfer reaction."⁴ The formation of cyclopropanes with the zinc reagent was the first example of a methylene-transfer reaction in which the intervention of a free carbene could be excluded. A brief review of the cyclopropanation reaction has appeared.^{4a}

THE CYCLOPROPANATION REACTION

Nature of the Zinc Reagent. The reaction of methylene iodide with zinc-copper couple was first described by Emschwiller in 1929.⁵ It was suggested that the initial product was iodomethylzinc iodide (1a),

- ³ J. Furukawa, N. Kawabata, and J. Nishimura, Tetrahedron Lett., 1966, 3353.
- ⁴ E. P. Blanchard and H. E. Simmons, J. Amer. Chem. Soc., 86, 1337 (1964).
- 48 O. Kaltenberg, Wiad. Chem.. 26, 285 (1972) [C.A., 77, 74316u (1972)].

² G. Wittig and K. Schwarzenbach, Angew. Chem., 71, 652 (1959).

⁵ G. Emschwiller, C. R. Acad. Sci., Paris, 188, 1555 (1929).

because the resulting solution reacted with iodine to regenerate methylene iodide and zinc iodide, reacted with water to give methyl iodide and zinc hydroxide, and evolved ethylene slowly when heated. Subsequently it

$$CH_2I_2 + Zn(Cu) \longrightarrow ICH_2ZnI + (Cu)$$

was shown that 1 mol of methylene iodide consumes 1 g-atom of zine (from a 9:1 zinc-copper couple) to give, after filtration under nitrogen, a colorless homogeneous solution which yields eyclopropanes on addition of olefins;⁶ thus a soluble organozinc intermediate of limited stability was indicated as the significant species in the cyclopropane-forming reaction. It was proposed that 1a might be better represented as a complex of methylene and zinc iodide (1b) or as a structure with some donation of electrons from the carbon-bound iodine to the zinc atom (1c).⁶



Various zinc-copper couples have been employed, and it is known that the copper plays no role other than activating the zinc surface for reaction.⁶ In fact, in ether solvents such as 1,2-dimethoxyethane zinc metal alone is effective in the cyclopropane-forming reaction.⁷ Zinc reagents capable of methylene transfer have also been produced from chloroiodomethane⁴ and methylene bromide.⁸

The nature of the zinc reagent was clarified by studies of the organozinc compounds produced from diazomethane and zinc halides, whose solutions behave similarly to those prepared from the appropriate methylene halides and zinc-copper couple.^{2. 4. 9-12} There is evidence that, when ethereal diazomethane is added slowly to ethereal zinc iodide, reaction proceeds in a stepwise fashion.⁹ Although neither 1a nor bis(iodomethyl)-zinc (2a) can be isolated other than as unstable oils,^{6. 9} their solutions react with cyclohexene to produce bicyclo[4.1.0]heptane (3) in 20 and 22 % yields, respectively. Methylene iodide and zinc-copper couple react with cyclohexene under similar conditions to give 3 in 58 % yield.¹³

- ¹⁰ G. Wittig and F. Wingler, Justus Liebigs Ann. Chem., 656, 18 (1962).
- ¹¹ G. Wittig and F. Wingler, Chem. Ber., 97, 2139 (1964).
- ¹² G. Wittig and F. Wingler, Chem. Ber., 97, 2146 (1964).
- ¹³ R. D. Smith and H. E. Simmons, Org. Syntheses, 41, 72 (1961).

⁶ H. E. Simmons and R. D. Smith, J. Amer. Chem. Soc., 81, 4256 (1959).

⁷ D. B. Richardson, L. R. Durrett, J. M. Martin, Jr., W. E. Putnam, S. C. Slaymaker, and I. Dvoretzky, J. Amer. Chem. Soc., 87, 2763 (1965).

⁸ E. LeGoff, J. Org. Chem., 29, 2048 (1964).

⁹ G. Wittig and K. Schwarzenbach, Justus Liebigs Ann. Chem., 656, 1 (1961).

It is not yet known if 1a or 2a, or both, are formed in the primary reaction of methylene iodide and zinc-copper couple. The zinc reagent



prepared from 1 mol of methylene iodide and 1 g-atom of zinc is stoichiometrically equivalent (and presumably identical) with that prepared from 1 mol of diazomethane and 1 mol of zinc iodide. These solutions, however, are clearly different from that containing pure $2a.^9$ The zinc iodide complex 2b of 2a is another possible species that must be considered and is formally connected to 1a by the Schlenk equilibrium.

$$2 \operatorname{ICH}_{2}\operatorname{ZnI} \xrightarrow{} (\operatorname{ICH}_{2})_{2}\operatorname{Zn} \cdot \operatorname{ZnI}_{2}$$

$$1a \qquad 2b$$

The reactions undergone by the zinc reagent and carbonyl groups have provided some evidence that still other organozinc species, $CH_2(ZnI)_2$ and $Zn(CH_2ZnI)_2$, may be present in low concentrations in stoichiometrically prepared solutions of iodomethylzinc iodide.¹⁴ Such dizinc species are formed when iodomethylzinc iodide is subjected to prolonged heating in ether or is treated with excess zinc (see p. 68).

Schlenk equilibria have been clarified recently for organozinc compounds. Ethylzinc chloride and bromide occur as discrete tetramers in the solid state and in nonpolar solvents such as benzene,¹⁵ but crystalline ethylzinc iodide exists as a polymer of $[C_2H_5ZnI]$ units, and no structural elements resembling $[(C_2H_5)_2Zn\cdot ZnI_2]$ were detected.¹⁶ Ethylzinc iodide is unstable in hydrocarbon solvents in which zinc iodide precipitates, but all three ethylzinc halides are stable in ether, where they

¹⁴ I. T. Harrison, R. J. Rawson, R. Turnbull, and J. H. Fried, J. Org. Chem., **36**, 3515 (1971).

¹⁵ J. Boersma and J. G. Noltes, Tetrahedron Lett., 1966, 1521.

¹⁶ P. T. Moseley and H. M. M. Shearer, Chem. Commun., 1966, 876.

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exist as solvated monomers.^{15, 17, 18} Furthermore the Schlenk equilibria of ethylzinc halide monomers are established slowly in ether solvents and strongly favor the C₂H₅ZnX structure.^{17, 19} The structures of the tetramers mentioned above are believed to be analogous to that of methylzinc methoxide, in which the zinc and oxygen atoms occur alternately at the corners of a slightly distorted cube.²⁰ Finally, dialkylzincs are monomeric in ether and form mono- and di-etherates.^{21, 22}

From these considerations it might be expected that the reagent prepared from methylene iodide and zinc would exist as monomeric ICH_2ZnI rather than monomeric $(ICH_2)_2Zn\cdot ZnI_2$ in ether, if its behavior is similar to that of ethylzinc iodide. The presence of α -halogen, however, is the unique structural feature which gives rise to the special chemistry of the zinc reagent, and this feature may reverse Schlenk equilibria expectations. For example, monomeric ethylzinc iodide presumably carries two strongly bound ether molecules of solvation (tetrahedral coordination being assumed), and diethylzinc is solvated to the same extent. Iodomethylzinc iodide may require only one strongly bound ether if structure 1c adequately represents the species, whereas bis(iodomethyl)zinc may require no strongly bound ether of solvation if structure 2c is



meaningful. The presence of α -halogen may also disturb the expectation that iodomethylzinc iodide and bis(iodomethyl)zinc are monomeric in ether solution.

Although iodomethylzinc iodide is probably monomeric in ether solvents, it is interesting to consider an alternative view. There is some evidence that bis(chloromethyl)zinc exists as a tetramer in ether, but a polymeric structure (4) has been proposed.⁹ If tetramers of α -halozinc



- ¹⁷ M. H. Abraham and P. H. Rolfe, Chem. Commun., 1965, 325.
- ¹⁸ D. F. Evans and I. Wharf, J. Organometal. Chem., 5, 108 (1966).
- ¹⁹ R. E. Dessy and G. R. Coe, J. Org. Chem., 28, 3592 (1963).
- ²⁰ H. M. M. Shearer and C. B. Spencer, Chem. Commun., 1966, 194.
- ²¹ G. Allen, J. M. Bruce, and F. G. Hutchinson, J. Chem. Soc., 1965, 5476.
- ³² K.-H. Thiele, Z. Anorg. Allg. Chem., 319, 183 (1962); 322, 71 (1963).

species do occur in ether solvents, it might be supposed that they have structures analogous to that of methylzinc methoxide,²⁰ e.g., structure 5 for bis(iodomethyl)zinc. Similarly, iodomethylzinc iodide could be represented by 6 or a structural isomer. The presence of an α -halogen atom is supposed to induce methylene bridging, so that each zinc is hexacoordinate in 5 and pentacoordinate in 6 (the sixth site being occupied by solvent).



Zinc is normally tetracoordinate but hexacoordinate complexes of octahedral geometry are well known,^{23, 24} and qualitative studies have suggested that the zinc reagent is at least a monoetherate.²⁵ It is also known, however, that methylene transfer proceeds normally from a related species, $C_2H_5ZnCH_2I$, even in hydrocarbon solvents (p. 9), so that solvation may not be an important feature of the chemistry of α -halozinc species. In structures such as 6 there are two nonequivalent sets of four iodines, and it is noteworthy that the reagent prepared from chloroiodomethane and zinc is hydrolyzed by water to give methyl iodide and not methyl chloride.⁴ Such a result could be understood if iodide ions occupied

$$ClCH_2I + Zn(Cu) \longrightarrow [ClCH_2ZnI] \xrightarrow{+H_2O} CH_3I$$

sites in the cube, and the chloride ions projected externally. Furthermore, bridging of the methylenes is expected to induce some trigonal character in the carbon atoms and helps explain their unusual reactivity. Inspection of molecular models of 5 and 6 shows that the methylenes are accessible to the approach of double bonds in a substrate, but that such approach would have considerable steric requirements. Methylene-transfer transition states are, in fact, very sensitive to steric effects.

²³ L. Orgel, Transition Metal Chemistry, Methuen and Co., Ltd., London, 1960, pp. 76, 83.

²⁴ F. Basolo and R. G. Pearson, *Mechanisms of Inorganic Reactions*, John Wiley and Sons, Inc., New York, 1958, p. 82.

²⁵ H. E. Simmons, unpublished results.

The side reactions undergone by the zinc reagent and an ether solvent throw more light on the questions of solvation and nature of the reagent. When a diethyl ether solution of the zinc reagent is heated at reflux for several hours, the major product (80-90%) is ethylene, and small quantities of propylene, cyclopropane, methyl iodide, ethyl isopropyl ether, and methyl ethyl ether are concurrently produced. On aqueous hydrolysis of the reaction mixture small amounts of methane and ethanol are formed. These results can be rationalized in terms of attack of a bridged methylene group in structures such as 1c or 6 on an ether molecule coordinated to the zinc atom.⁴ Methyl iodide is formed in this process that involves an



ylid-like intermediate, which subsequently reacts with methyl iodide or methylene iodide to form ethyl isopropyl ether and 2-ethoxy-l-iodopropane, respectively. The latter compound gives propylene on reaction with zinc. Labeling experiments support this interpretation.⁴ These side reactions become important in synthetic applications only when the unsaturated compound reacts slowly because of steric or electronic reasons and when more basic ether solvents such as tetrahydrofuran and dimethoxyethane are used.

Finally, it is not unlikely that ICH_2CH_2ZnI and $ICH_2CH_2CH_2ZnI$ are formed transiently under some conditions when 1,2-diiodoethane and 1,3-diiodopropane are treated with zinc, and these intermediates are rapidly transformed to ethylene and cyclopropane, respectively. The higher homologs, $X(CH_2)_n ZnX$ (X = Br, I; n = 4, 5), have been prepared, but little is yet known of their chemistry.²⁶

Mechanism. It was originally suggested that the cyclopropaneforming reaction occurs by a one-step methylene-transfer mechanism in which the quasi-trigonal methylene group of iodomethylzinc iodide

²⁶ K.-H. Thiele and I. Benthin, Z. Chem., 8 (9), 344 (1968).

adds to an olefin π -bond such that both new carbon-carbon bonds are formed essentially simultaneously.^{1, 6} Subsequent research bolstered this



proposal,^{4, 27} and other workers have provided additional support.^{9, 11, 12} Mechanisms involving carbonium ions, carbanions, or radicals were considered unlikely,⁶ but it has been argued that the additions of the zinc reagent are a two-step reaction and analogous to those of chloromethyl-diethylaluminum with olefins.^{28, 29} Counterarguments have been provided;^{9, 11, 12, 27} this question is discussed below. Other zinc intermediates, such as $CH_2(ZnI)_2$, have been suggested as the active methylene-transfer species.³⁰ There is evidence, however, that $CH_2(ZnI)_2$ and $Zn(CH_2ZnI)_2$ are not active methylene-transfer reagents for carbon-carbon double bonds but rather undergo Wittig reactions with carbon-oxygen double bonds³¹ (see p. 66). Interesting speculative discussions of the mechanism of methylene-transfer reactions have been given.^{32, 33}

Although no detailed study of the mechanism of the cyclopropaneforming reaction has been made, several experimental observations have suggested the methylene-transfer interpretation. For simplicity of discussion, the active zinc reagent in cyclopropanation reactions is taken to be 1a, and "usual" conditions means the *in situ* reaction of an unsaturated compound, methylene iodide, and zinc-copper couple in ether.

1. The reaction of 1a with olefins occurs with discrimination in that only double bonds are attacked.⁴ No isomeric hydrocarbons, which would be expected had free methylene been an intermediate, have been detected among the products. Occasionally small amounts of isomerized olefins (double bond position isomers) and the corresponding cyclopropanes are detected, but this isomerization has been traced to the zinc metal and to the zinc iodide formed in the reaction and is not inherent in the cyclopropane synthesis.⁴ 1-Alkenes are sometimes prone to this kind of isomerization.³⁴ An early report³⁵ implying that gross insertion products accompany cyclopropane formation could not be verified.¹

- ²⁸ H. Hoberg, Justus Liebigs Ann. Chem., 656, 1 (1962).
- ²⁹ H. Hoberg, Justus Liebigs Ann. Chem., 656, 15 (1962).
- ³⁰ C. Fauveau, Y. Gault, and F. G. Gault, Tetrahedron Lett., 1967, 3149.
- ³¹ P. Turnbull, K. Syhora, and J. H. Fried, J. Amer. Chem. Soc., 88, 4764 (1966).
- 82 J. Villiéras, Bull. Soc. Chim. Fr., 1967, 1520.
- 33 B. Castro, Bull. Soc. Chim. Fr., 1967, 1533.
- ³⁴ R. Huisgen, personal communication.
- ³⁵ W. von E. Doering and P. M. LaFlamme, Tetrahedron, 2, 75 (1958).

²⁷ H. E. Simmons, E. P. Blanchard, and R. D. Smith, J. Amer. Chem. Soc., 86, 1347 (1964).

2. The reaction of 1a with olefins follows second-order kinetics (first-order in olefin and in 1a) which is in accord with a bimolecular process, but no conclusion can be drawn concerning a one- or two-step addition process.⁴

3. Cyclopropane formation occurs stereospecifically.^{1. 6} Thus *cis*- and *trans*-3-hexene react under the usual conditions to yield pure *cis*- and *trans*-1,2-diethylcyclopropane, respectively. The unreacted olefins were recovered pure, suggesting that no reversible and isomerizing coordination or addition of **1a** to olefin occurred before methylene transfer. It should be pointed out, however, that coordination of the olefin with the zinc atom in the reagent before methylene transfer cannot be dismissed, although attempts to demonstrate such coordination with ethylzinc iodide and diethylzinc failed. In this regard, partial asymmetric syntheses with the zinc reagent have been rationalized without specifically considering the olefin as a ligand during cyclopropanation (see p. **31**).

4. Competition studies with olefin mixtures show that the zinc reagent behaves as a weak electrophile toward double bonds in that reactivity of the olefin increases with increased alkyl substitution on the double bond, but this effect is offset by a concurrently increasing steric effect (Table I).^{4. 36} A definitive study³⁶ showed that there exists a delicate balance between electronic and steric factors, and interesting comparisons have been made with diimide reductions³⁷ and peracid epoxidations.³⁸ Similar competitions with dichlorocarbene³⁹ and dibromocarbene⁴⁰ are given in Table I for comparison, and it is evident that the zinc reagent more nearly parallels dibromocarbene in its relative rates of addition. If the methylene group is transferred from the zinc reagent in a one-step process analogous to that of singlet methylenes, then it is expected that the transition state for such a transfer will resemble that of the more bulky dibromocarbene.⁴

A later study employed the two double bonds of 4-vinylcyclohexene as an intramolecular competition system with both the zinc reagent prepared from methylene iodide/zinc-copper couple and that from diazomethane/zinc iodide.⁴¹ The ratio of the products, 4-cyclopropylcyclohexene: 3-vinylbicyclo[4.1.0]heptane, was ca. 0.50 for both reagents. The earlier studies^{4.36} had shown that the competition rate ratio is independent of the total concentration of olefins; however, the later

³⁶ B. Rickborn and J. H.-H. Chan, J. Org. Chem., 32, 3576 (1967).

³⁷ E. W. Garbisch, Jr., S. M. Schildcrout, D. B. Patterson, and C. M. Sprecher, J. Amer. Chem. Soc., 87, 2932 (1965).

³⁸ D. Swern, J. Amer. Chem. Soc., 69, 1692 (1947).

³⁹ W. von E. Doering and W. A. Henderson, J. Amer. Chem. Soc., 80, 5274 (1958).

⁴⁰ P. S. Skell and A. Y. Garner, J. Amer. Chem. Soc., 78, 5430 (1956).

⁴¹ U. Burger and R. Huisgen, Tetrahedron Lett., 1970, 3057.

		k _{olefin}	$ k_{\rm oyclohe} $	xene	<u> </u>
Olefin	ICH ₂ ZnI ^a	CCl_2^b	CBr_2^c	$N_2H_2^d$	RCO ₃ He
λ_{-}	(0.14)				
	0.30				
$\sim \sim \sim$	(0.36)	0.186	0.167		
$\sim \sim \sim$	(0.39)				
$\overset{+}{\checkmark}$	0.40				
\sim	(0.42)	·			
\checkmark		2.14		2.59	
$\overline{\bigcirc}$	0.44				
Ì	0.48				
\sum	0.55				
$\overline{\bigcirc}$	0.58				
	0.68				
~	(0.83)				
~~~		1.62		2.65	

TABLE I. RELATIVE REACTIVITIES OF OLEFINS

		$k_{olefin}/k_{cyclohexene}$						
Olefin	ICH ₂ ZnI ^a		$\operatorname{CBr}_2^c$	$N_2H_2^d$	RCO3H			
$\sum$	0.84							
$\bigcirc$	0.91							
×	0.92							
$\mathbf{i}$	0.94 (0.58)							
	0. <b>94</b>							
$\widehat{}$	0.95							
	0.95							
$\bigcirc$	1.00 (1.00)	1.00	1.00					
$\bigcirc$	1.18			12.1	1.36			
$\succ$	(1.29)	53.7	6.92					
	1.60			15.5	1.51			

TABLE I.	Relative	REACTIVITIES	OF	OLEFINS	(Continued)
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		kolet	$k_{eyclob}$	lexene	
Olefin	ICH2ZnIª	$\mathrm{CCl}_2^b$	$CBr_2^c$	$\mathrm{N_2H_2^d}$	RCO₃H¢
$\bigcirc$	1.70				
$\bigcirc$	2.14				
$\geq$	(2.18)	23.4	7.41		
	(2.53)	5.50		2.05'	
	3.84			3.27	
(	5.14				

TABLE I. RELATIVE REACTIVITIES OF OLEFINS (Continued)

^a Values in parentheses are from ref. 4, others from ref. 36. Values were determined for olefin pairs in ether solution when the zinc reagent was generated *in situ*. Experimental conditions were not identical in the two references quoted. Note the discrepancy for 1,2-dimethylcyclohexene.

study⁴¹ showed that the constant was not independent of the ratio of olefins in some cases, *e.g.*, the competition constant for 1-methylcyclopentene/cyclohexene mixtures varied from 4.9 to 2.8 when the olefin ratio changed from 1.4 to 0.34. On the other hand, 3,4-dihydropyran/cyclohexene mixtures showed little variation of the competition constant with the reagent from methylene iodide/zinc-copper couple ( $k_{\rm rel} = 7.3-7.7$ ) when the olefin ratio varied from 0.11 to 1.1, but the competition constant varied considerably in the diazomethane/zinc iodide system as a function of the relative concentration of olefins. The significance of these findings is not clear, but it may mean that the zinc reagents are not homogeneous.

^b Ref. 39. ^c Ref. 40. ^d Ref. 37. ^e Ref. 38.

^f This is the value for 2-methyl-1-pentene.

At any rate, the data in Table I were obtained largely with equal concentrations of olefins when feasible and so are reasonably comparable.

5. The suggestion that the zinc reagent adds to double bonds by a two-step mechanism^{28. 29} can account for the second-order kinetics and



stereospecificity of cyclopropane formation if the addition is *cis*. It has been argued that an aluminum intermediate analogous to 7 intervenes in the rapid cyclopropane-forming reaction of iodomethyldiethylaluminum and propylene, because interruption of the reaction by alcoholysis produced small amounts of n-butyl iodide.^{28, 29} Similar interception experiments with cis-3-hexene and the zinc reagent from chloroiodomethane²⁷ and with cyclobutene and bis(iodomethyl)zinc (2a)¹² failed to detect any trace of hydrolysis products of 7. An experiment by Wittig and Wingler¹² provided strong evidence against the two-step mechanism: trans-1,6-dichloro-3-hexene was allowed to react with bis(chloromethyl)zinc, and the only product isolated was trans-1,2-bis-(2-chloroethyl)cyclopropane (8) (95%). No trace was detected of the isomeric cyclopropane 9, which very likely would have formed had 10 been an intermediate. The corresponding reaction with iodomethyldiethylaluminum has not been reported. Additional evidence against the two-step mechanism is given (p. 21).



It has also been observed that zinc chloride catalyzes methylene transfer from bis(chloromethyl)zinc to cyclohexene.¹² It was suggested that zinc chloride functions by assisting the elimination of chloride ion during the transfer reaction as shown in the equation



It should be noted, however, that zinc chloride may also act to drive the Schlenk equilibrium toward chloromethylzinc chloride  $(ZnCl_2 + Zn(CH_2Cl)_2 \rightleftharpoons 2 ClCH_2ZnCl)$ , but unfortunately quantitative data on the relative reactivity of bis(chloromethyl)zinc and chloromethylzinc chloride are not available.

6. Good leaving groups other than halogen can function in appropriate derivatives to cause methylene transfer. Bis(benzoyloxymethyl)zinc,  $(C_6H_5CO_2CH_2)_2Zn$ , prepared from zinc benzoate and diazomethane, reacted with cyclohexene to give norcarane in 6% yield.⁴² In the presence of zinc iodide, magnesium iodide, and lithium iodide the yields were 91, 78, and 48%, respectively, and it seems likely the active species are of the type  $C_6H_5CO_2CH_2MX$ . The zinc reagent, made directly from iodomethyl benzoate and zinc-copper couple, reacted with cyclohexene to give norcarane in 73% yield. The reagent prepared from 1-iodoethyl

$$C_{6}H_{5}CO_{2}CH_{2}I + Zn(Cu) \longrightarrow C_{6}H_{5}CO_{2}CH_{2}ZnI \longrightarrow$$
$$\longrightarrow + IZnOCOC_{6}H_{5}$$

benzoate and zinc-copper couple similarly was active in ethylidene transfer (p. 46). The ability of other anions to replace halide ions in methylene-transfer transition states is consistent with the role assigned to halide ion.

7. Finally it should be pointed out that, although the methylenetransfer reaction of iodomethylzinc iodide to a double bond does not proceed by a radical mechanism, free radicals capable of attacking double bonds may be formed during the *in situ* generation and use of the zinc reagent. It is not unlikely that the mildly exothermic reaction of methylene iodide with bright zinc-copper couple surface involves transient iodomethyl radicals (ICH₂). The attack of these radicals (which must be

⁴² G. Wittig and M. Jautelat, Justus Liebigs Ann. Chem., 702, 24 (1967).

generated in the special environment of the metal surface) on double bonds does not lead to a significant fraction of the observed cyclopropane product. It is not impossible, however, that alkenes whose double bonds are unreactive toward methylene transfer from iodomethylzinc iodide, could form cyclopropanes as shown in the accompanying equation.



There is precedent for the radical addition and for the closure of such  $\beta$ -iodopropyl radicals to give cyclopropanes. In particular, methylene iodide reacts with t-butoxy and benzoyloxy radicals in the presence of olefins to yield cyclopropanes.⁴³ For example, when a mixture of methylene iodide, t-butyl peroxide, and an olefin was heated at 166°, 1-octene gave n-hexylcyclopropane (38%), cyclohexene gave norcarane (<1%), and cis- and trans-stilbene gave 1,2-diphenylcyclopropanes (54-58%). It should be noted that cyclohexene is more reactive than 1-octene toward iodomethylzinc iodide generated in situ, and that the zinc reagent gives low yields of products with trans-stilbene. The peroxide-induced formation of cyclopropanes, which most likely involves the generation and addition of iodomethyl radicals to the olefins, bears little resemblance to cyclopropanation by iodomethylzinc iodide.

It has been reported that the rate of cyclopropanation of olefins with iodomethylethylzinc (diethylzinc and methylene iodide³) is accelerated by molecular oxygen.^{43a} The yields are high and this modification is claimed to have synthetic advantages. The significance of this observation is not yet clear.

A molecular orbital treatment of the reaction of iodomethylzinc iodide with carbon-carbon and carbon-oxygen double bonds (p. 66) has been given.⁴⁴ Second-order perturbation calculations on the interaction of the  $\sigma$  and  $\sigma^*$  orbitals of the carbon-zinc single bond with the  $\pi$  and  $\pi^*$  orbitals of the double bond lead to the conclusion that the zinc reagent will behave as an electrophile toward C=C but as a nucleophile toward C=O. The reactivity of carbonyl compounds will be determined by their relative superdelocalizabilities, and the reactivity of carbon-carbon double bonds by their total electrophilic delocalizabilities. Relative reactivities based on these conclusions are in general accord with experiment, and the duality of the reactions of the zinc reagent can be thus understood.

⁴³ L. Kaplan, J. Amer. Chem. Soc., 89, 4566 (1967).

⁴³⁸ S. Miyano and H. Hashimoto, Chem. Commun., 1971, 1418.

⁴⁴ M. Hida, Bull. Chem. Soc. Jap., 40, 2497 (1967).

In conclusion, the reaction of iodomethylzinc iodide with a double bond can be characterized as a nucleophilic displacement at carbon of a molecule of zinc halide by the  $\pi$ -electrons in the double bond. The two carbon-carbon bonds are formed essentially synchronously, and with alkenes no sensible intermediate is involved. The intermediacy of a coordination complex with the olefin as ligand prior to methylene transfer has not yet been demonstrated or ruled out. A review of related  $\alpha$ elimination mechanisms has been given.⁴⁵

Substituted zinc reagents, RCHI(Zn1) but not R₂CI(ZnI), also undergo methylene-transfer reactions. The monosubstituted alkylidene reagents, however, react primarily by paths other than methylene transfer to double bonds when generated by the reaction of gem-diiodides with zinc metal.^{27. 46. 47} A careful study of the reaction of gem-diiodides with sodium, lithium, magnesium, zinc, and copper metals in ether solution has been reported,⁴⁸ and evidence has been presented that the zinc species, RCHI(Zn1), undergo decomposition in ether principally to olefins of rearranged structures. Thus 1,1-diiodo-2,2-dimethylbutane gave 1-ethyl-1-methylcyclopropane (0.8%), 1,1,2-trimethylcyclopropane (1.7%), cisand trans-3-methyl-2-pentene (90%), and 2-methyl-2-pentene (7.5%). It was suggested that bulky electron-donating groups facilitate ionization of the zinc reagent to  $\alpha$ -metallocarbonium ions which subsequently undergo typical carbonium ion rearrangements as shown in the accom-

$$CH_{3}CH_{2}C(CH_{3})_{2}CHI(ZnI) \longrightarrow CH_{3}CH_{2}C(CH_{3})_{2}C^{+}I^{-} \longrightarrow$$

$$CH_{3}CH_{2}C(CH_{3})_{2}C^{+}I^{-} \longrightarrow CH_{3}CH_{2}C(CH_{3})=CHCH_{3}$$

$$CH_{3}CH_{2}C^{+}I^{-} \longrightarrow CH_{3}CH_{2}C(CH_{3})=CHCH_{3}$$

panying equation. Similarly, 1,1-diiodo-2-methylpropane reacted with zinc-copper couple in ether, but the intermediate did not undergo significant methylene transfer to cyclohexene.⁴⁶ The products were isobutylene (91%), isobutane (7.8%), trans-2-butene (0.6%), cis-2-butene (0.3%), and methylcyclopropane (0.3%). It has been suggested that the small amounts of cyclopropanes formed in these reactions may arise from a 1,3-hydride shift to the zinc-bound carbon accompanied by elimination of zinc iodide as shown in the equation on p. 19.⁴⁶

- 48 W. Kirmse, Angew. Chem., Int. Ed. Engl., 4, 1 (1965).
- 48 R. C. Neuman, Tetrahedron Lett., 1964, 2541.
- ⁴⁷ W. Kirmse, Angew. Chem., Int. Ed. Engl., 4, 891 (1965).
- 48 W. Kirmse and G. Wachterhauser, Tetrahedron, 22, 73 (1966).



Independent evidence that  $\alpha$ -metallocarbonium ions may be easily generated in these systems comes from the behavior of the reagent prepared from diethylzinc and ethylidene iodide. This species, which is believed to be CH₃CHI(ZnC₂H₅), reacts with alkenes to form methylcyclopropanes by ethylidene transfer. The reagent also reacts with benzene to give 7-methylcyclohepta-1,3,5-triene, and relative reactivity studies with a series of alkylbenzenes showed partial rate factors similar to those observed in Friedel-Crafts alkylations.^{49, 50} This reaction might be depicted by the accompanying equation, in which the resemblance to an



alkylation mechanism is evident. Since iodomethylzinc iodide and, apparently, the reagent prepared from diethylzinc and methylene iodide do not attack benzene, the reactivity of the ethylidene reagent in this respect may be due to facile formation of an  $\alpha$ -metallocarbonium ion which is stabilized by the methyl group.

The intermediates and mechanism involved in the variation of the cyclopropane synthesis using diethylzinc and methylene iodide³ are not known with certainty. It seems likely, however, that this reaction proceeds by an initial exchange to form iodomethylethylzinc (11), which has the  $\alpha$ -halogen requisite for back-bonding and activation of the methylene group and which undergoes methylene-transfer reactions in good yields.

$$(C_2H_5)_2Zn + CH_2I_2 \longrightarrow C_2H_5Zn - CH_2 + C_2H_5I$$

An important feature of this system is that methylene transfer has been demonstrated in solvents such as *n*-pentane, cyclohexane, and benzene, as well as ether. It is therefore clear that strong solvation of iodomethylethylzinc by ether is not a prerequisite for methylene transfer to double bonds. It seems likely that iodomethylzinc iodide prepared from methylene iodide and zinc-copper couple would function similarly in nonpolar

⁴⁹ J. Nishimura, J. Furukawa, N. Kawabata, and T. Fujita, Tetrahedron, 28, 2229 (1970).

⁵⁰ J. Nishimura, J. Furukawa, and N. Kawabata, Bull. Soc. Chem. Jap., 43, 2195 (1970).

solvents, but the reagent has not yet been successfully generated in hydrocarbon solvents. Competition studies in ether show that this reagent discriminates more effectively than iodomethylzinc iodide between alkyl-substituted olefins. The relative reactivities^{50a} of tetramethylethylene, cyclohexene, and 1-heptene in ether are 8.82, 1.00, and 0.15, respectively, compared to 1.29, 1.00, and 0.39 for iodomethylzinc iodide. The spread of relative reactivities with iodomethylethylzinc is even larger in benzene and pentane. A Hammett  $\rho$ -value of -1.61 was found for a series of substituted styrenes, and it was suggested that inductive effects are particularly important in determining rates of methylene transfer from iodomethylethylzinc.

 $\alpha$ -Halobenzylzinc halides (C₆H₅CHXZnX) prepared from aryldiazomethanes and zinc halides undergo benzylidene transfer to olefins to give phenylcyclopropanes accompanied by the formation of stilbenes and insertion into the  $\alpha$  position of solvent ethers.^{51, 52} Such behavior is quite analogous to that exhibited by the halomethylzinc halides. Stop-flow kinetic studies, however, gave estimates of the half-lives of C₆H₅CHCl-(ZnCl) and *p*-CH₃C₆H₄CHCl(ZnCl) as 10 and 0.2 sec, respectively, and these species are clearly much less stable than iodomethylzinc iodide. The reagent prepared from *p*-tolyldiazomethane and zinc halides reacted with *cis*-2-butene to give the results shown in the accompanying equation.



In all cases the thermodynamically less stable syn isomer was formed predominantly, and the syn:anti ratio increased with the size of the halogen. These results can be understood in terms of steric requirements in a transition state like that discussed for iodomethylzinc iodide additions.^{1.6}

⁵¹ S. H. Goh, L. E. Closs, and G. L. Closs, J. Org. Chem., 34, 25 (1969).

⁵⁰⁸ J. Nishimura, J. Furukawa, N. Kawabata, and M. Kitayama, *Tetrahedron*, 27, 1799 (1971).

⁵² L. Y. Goh and S. H. Goh, J. Organometal. Chem., 23, 5 (1970).

Disubstituted reagents  $R_2CI(ZnI)$  are unstable and undergo elimination and coupling reactions when generated either by the reaction of gem-diiodides with zinc metal or from diazoalkanes and zinc halides. Methylene transfer to alkenes has not been observed with these species.⁵³

**Relative Rates and Stereoselectivity.** The methylene group of the solvated zinc reagent, whether monomeric or associated, is small compared to the surrounding zinc and iodine atoms, and the transition state during methylene transfer is thus considerably cluttered. The data in Table I show that the steric requirements of the cyclopropanation reaction can often be assessed by considering the methylene-transfer transition state; for example, it is readily understood that the rate of cyclopropanation of cyclohexene is reduced by only 9% on introduction of a 4-methyl group, but by 42% for a 3-methyl group. On the other hand, the relative rates for the monocycles (cyclopentene > cycloheptene > cyclohexene) are less obviously rationalized. Methylene-transfer rates, however, also reflect electronic and relief of strain effects, so that predictions are not always easily made. It was pointed out previously that alkyl substitution on a double bond mildly facilitates methylene transfer, but that the accumulative effect is soon swamped by rate-retarding steric effects. The strained rings in cyclopentene and bicyclo[2.2.1]heptene are especially reactive, but it is not known whether this is a consequence of ring strain or of sterically favorable transition states. Styrene might be expected to be especially reactive from the conjugative standpoint, but it reacts at a rate comparable to that of cyclohexene. Furthermore, indene is even less reactive than styrene. It is clear that more information is needed before methylene-transfer transition states can be understood.

Some methylene transfers to sterically inaccessible double bonds fail or give low yields because of the competing decomposition of the zinc reagent to ethylene and attack of the reagent on solvent. This is shown by the accompanying tabulation, where the methyl iodide arises from attack on solvent.⁴

	Reactivity	Cyclopropane Product, %	Ethylene, %	Methyl Iodide, %
3,3-Dimethyl- 1-butene	0.14	38.7	21.8	16.3
2-Methyl-1- butene	2.53	79.6	7.0	1.5

The methylene-transfer process often shows high stereoselectivity, and this is readily understood on the basis of the crowded transition

53 D. E. Applequist and H. Babad, J. Org. Chem., 27, 288 (1962).

state. Rationalization and prediction can often be made from simple model considerations, and the literature records several such instances. The following examples as well as many in the Scope and Limitations section exemplify the highly stereoselective nature of the cyclopropanation reaction. 1,4-Cyclohexadiene reacts with excess zinc reagent to yield the *cis*- and *trans*-tricyclooctanes 12 and 13 in the ratio 1:3.3,²⁷ but the related hydrocarbon 14 gave only *trans*-pentaeyclo[7.3.1.1^{3.7}.0.0^{3.7}]-tetradecane (15) (>99.5% trans).⁵⁴ cis,cis,cis-1,4,7-Cyclononatriene



afforded, remarkably, a 90 % yield of *cis*-tetracyclo[9.1.0.0^{3.5}.0^{7.9}]dodecane (16) with excess zinc reactant,⁵⁵ and *trans,trans,cis*-1,5,9-cyclododecatriene under these conditions gave a single tetracyclo[12.1.0.0^{4.6}.0^{9.11}]pentadecane (17) in 54% yield whose stereochemistry is unknown.⁵⁶



Bicycloheptenes undergo methylene transfer from the exo direction, e.g., bicyclo[2.2.1]heptene gave only exo-tricyclo[ $3.2.1.0^{2.4}$ ]octane (18).^{6. 27, 57} The example provided by the Diels-Alder adduct (19) of

- ⁵⁴ L. Birladeanu, T. Hanafusa, and S. Winstein, J. Amer. Chem. Soc., 88, 2315 (1966).
- ⁵⁵ R. S. Boikess and S. Winstein, J. Amer. Chem. Soo., 85, 343 (1963).
- ⁵⁵ H. Nozaki, M. Kawanisi, and R. Noyori, J. Org. Chem., 30, 2216 (1965).
- ⁵⁷ R. T. LaLonde, J.-Y. Ding, and M. A. Tobias, J. Amer. Chem. Soc., 89, 6651 (1967).



bicyclo[4.2.0]octa-2,4,7-triene and dimethyl acetylenedicarboxylate demonstrates the high stereoselectivity derived from ring strain and steric effects.⁵⁸ Cyclopropanation gave the adduct (20) which incidentally



confirmed the structure assignment of the *cis*-bicyclo[6.1.0]nona-2,4,6-triene and acetylenic ester adduct.

Coordination with Oxygen Functions. It was pointed out early that coordination of the zinc reagent with ether oxygen functions may facilitate and direct methylene-transfer reactions, e.g., 1-(o-methoxyphenyl)propene gave a higher yield of the corresponding cyclopropane than the m- or p-isomer, although the double bond of the o-isomer is more sterically hindered.⁶ The discovery by Winstein, Sonnenberg, and DeVries in 1959^{59, 60} that the hydroxyl group of 3-cyclopenten-1-ol can control methylene-transfer stereochemistry was of high importance, and this finding has been used widely in synthesis.

cis-3-Hydroxybicyclo[3.1.0]hexane (21) is formed in 79% yield and none (<0.5%) of the trans isomer was detected.⁵⁹⁻⁶¹ In contrast, the



acetate of the unsaturated alcohol gave the corresponding *cis* acetate in lower yield (18%) accompanied by some *trans* acetate (<10%). In

- 58 J. E. Baldwin and R. K. Pinschmidt, Chem. Commun., 1971, 820.
- 59 S. Winstein, J. Sonnenberg, and L. de Vries, J. Amer. Chem. Soc., 81, 6523 (1959).
- ⁶⁰ S. Winstein and J. Sonnenberg, J. Amer. Chem. Soc., 83, 3235 (1961).
- ⁶¹ E. J. Corey and R. L. Dawson, J. Amer. Chem. Soc., 85, 1782 (1963).

both cases, coordination of the zinc reagent with the ether oxygen function is thought to direct methylene transfer to the syn face of the double bond with respect to the oxygen. Although  $ester^{54.62.63}$  and  $ether^{64.65}$ functions exhibit such directive effects, the bare hydroxyl group generally gives higher yields and greater stereochemical control. When an appropriately positioned hydroxyl group assists the cyclopropanation reaction, the rate is normally greatly accelerated relative to the corresponding unsubstituted alkene. Three studies are particularly noteworthy (Dauben and Berezin, 1963⁶⁴; Chan and Rickborn, 1968⁶⁶; Poulter, Friedrich, and Winstein, 1969⁶⁷), and some results of the Chan and Rickborn study are given in Table II.

It is evident that in six-membered rings methylene transfer occurs with very high stereochemical control in allylic and homoallylic alcohols but, when the hydroxyl group is three carbons removed from the double bond, control is largely lost. The results for the allylic 2-cyclohexen-1-ols have been rationalized by a complex of partial formula 22, in which the quasiequatorial hydroxyl is bound to the dimer  $(ICH_2)_2ZnI \cdot ZnI_2$ , for it was suggested that a complex of  $ICH_2ZnI$  is neither sufficiently flexible nor large enough to allow facile centrosymmetric transfer of methylene.⁶⁶



Competitive kinetic studies of a series of homoallylic cyclohexenols suggested that these types react preferentially through a complex of the axial hydroxyl conformer, in contrast to the allylic cyclohexenols.^{66a}

The nature of the complex is not fully understood, and it may be that some reactions involve simple coordination complexes of the hydroxyl group, whereas others may involve formation of an intermediate zincate. It has been reported that for each mole of cyclopropane one mole of

⁶⁶ J. H.-H. Chan and B. Rickborn, J. Amer. Chem. Soc., **90**, 6406 (1968).
 ⁶⁶ J. A. Staroscik and B. Rickborn, J. Org. Chem., **37**, 738 (1972).
 ⁶⁷ C. D. Poulter, E. C. Friedrich, and S. Winstein, J. Amer. Chem. Soc., **91**, 6892 (1969).

⁶² J. J. Sims, J. Amer. Chem. Soc., 87, 3511 (1965).

⁶³ S. Sawada, K. Takehana, and Y. Inouye, J. Org. Chem., 33, 1767 (1968.)

⁴⁴ W. G. Dauben and G. H. Berezin, J. Amer. Chem. Soc., 85, 468 (1963).

⁶⁶ G. W. Klumpp, A. H. Veefkind, W. L. de Graaf, and F. Bickelhaupt, Justus Liebigs Ann. Chem., 706, 47 (1967).

Unsaturated Compound	$k_{ m rel}$	Stereochemistry, % cis
он	1.00	100
OCH ₃		
$\bigcirc$	0.50	100
CH ₂ OH	0.46	_
OH CH ₃	1.54	100
OH CH ₃	0.46	100
OH OH	0.091	100
OCH ₃	0.059	
CH ₂ OH	Very slow	<b>4</b> 5

TABLE II. RELATIVE RATES AND STEREOCHEMISTRY OF METHYL-ENE-TRANSFER REACTIONS WITH UNSATURATED ALCOHOLS AND ETHERS^a

^a The relative rates were determined by competition studies.⁶⁶

methyl iodide is formed from 3-cyclopenten-l-ol (suggesting an intermediate zincate),⁴ and that an iodimetrically equivalent amount of the zinc reagent and 2-cyclopenten-l-ol gave the cyclopropane product in ca. 80% yield (suggesting an intermediate hydroxyl complex).⁶⁴ More detailed studies of the complex have not resolved this question,⁶⁶ but it is not unlikely that prior complexation is followed by the slower formation of a zincate and that both species are capable of methylene transfer. The overall rate of transfer is greatly accelerated by complexation with suitably positioned hydroxyl groups for, when an equimolar mixture of cyclohexene and 2-cyclohexen-1-ol competes for one mole of the zinc reagent, the only product is cis-2-hydroxybicyclo[4.1.0]heptane.⁶⁴

The study by Poulter, Friedrich, and Winstein⁶⁷ conclusively showed that the methylene-transfer reaction in cyclic allylic alcohols occurs via a complex to the more accessible face of the double bond. These authors, furthermore, considered that a complex involving iodomethylzinc iodide suffices to explain the observed stereoselectivity (compare dimer complex 22).⁶⁶ The data in the accompanying equation show that a striking change in stereoselectivity occurs between the cycloheptenol and the cyclooctenol. A scale model of 2-cycloocten-1-ol (in the preferred chair-boat



conformation of cyclooctene) with the complexed hydroxyl group in an equatorial orientation suggests that methylene transfer should occur to the *anti* face of the double bond to form a product in which the cyclopropane ring and hydroxyl group bear a *trans* relationship. Addition to the *syn* face of the double bond is possible only in the smaller rings.⁶⁸⁻⁷⁰ The control of stereoselectivity in this manner has been used in a remarkable manner by the Winstein group to accomplish several unusual syntheses, examples of which are discussed under Scope and Limitations.

The juxtaposition of the double bond and hydroxyl group, even when close by in a homoallylic alcohol, may depend on the geometry in a sensitive way. Although 3-cyclopenten-1-ol gave exclusively addition to the syn face, this specificity was lost in a lower homolog. The reaction of 1,2-dimethylcyclopropene-3-carbinol with the reagent prepared from methylene iodide and diethylzinc gave a mixture of endo- (23) and exo-1,3-dimethylbicyclo[1.1.0]butylcarbinol (24).⁷¹ The endo isomer was

⁶⁸ C. D. Poulter, E. C. Friedrich, and S. Winstein, J. Amer. Chem. Soc., 92, 4274 (1970).

⁶⁹ C. H. De Puy and J. L. Mitchell, J. Org. Chem., 33, 3326 (1968).

⁷⁰ C. D. Poulter and S. Winstein, J. Amer. Chem. Soc., 92, 4282 (1970).

⁷¹ R. Breslow, H. Bozimo, and P. Wolf, Tetrahedron Lett., 1970, 2395.

formed predominantly but not exclusively (endo/exo = 2.57), and models suggest that the transition state for the expected assisted addition is unfavorable owing to the nearness and symmetrical relationship of the double bond.



As a final point, the cyclopropanation of *trans*-cyclooctene is seriously impaired by adventitious isomerization to the *cis* olefin under the reaction conditions, so that a mixture of the epimeric bicyclo[6.1.0]nonanes is obtained (p. 34). However, under similar conditions *trans*-2-cycloocten-1-ol gave the *cis*-cyclopropyl carbinol **26** (80%) stereospecifically,⁶⁹ and *cis*-2-cycloocten-1-ol was converted to *trans*-alcohol **25** (74%, containing <0.5% **26**).⁶⁷ Evidently complexation and intramolecular methylene transfer compete very effectively with the undesirable *cis*-trans isomerization of the double bond.



Ether functions also induce high stereoselectivity and increase the rate of methylene transfer, presumably by initial complexation. For example, under identical conditions 2-cyclohexen-1-ol and its methyl ether reacted rapidly to give good yields⁶⁴ of the *cis*-cyclopropanes 27 (60%) and 28 (70%).*⁶⁶ In a similar study of 2-cyclopenten-1-ol and its methyl ether, the allylic alcohol afforded pure *cis*-bicyclo[3.1.0]hexan-2-ol (47%), whereas the methyl ether gave slightly impure *cis* adduct (37%,

^{*} There is an earlier report that a mixture of *cis* and *trans* adducts is formed in the former reaction.⁷²

⁷² A. C. Cope, C. H. Park, and P. Scheiner, J. Amer. Chem. Soc., 84, 4862 (1962).



contaminated by 0.5-1% of the *trans* adduct).⁷³ It is likely that the small amount of *trans* adduct arises in a bimolecular methylene transfer by uncomplexed zinc reagent, since the geometry of the ether complex makes transfer to the *anti* face of the double bond energetically unfavorable in this almost rigid ring.

The cyclic homoallylic 3,4-diphenyl-3-cyclopenten-1-ol reacted rapidly with high stereoselectivity to produce the *cis*-cyclopropane 29 in 61%yield, whereas the ethylene ketal of the corresponding ketone reacted sluggishly and gave the cyclopropane 30 in 14% yield.⁷⁴ Presumably the rigid ketal forms a complex with the zinc reagent which cannot readily



undergo methylene transfer for geometric reasons. On the other hand, the acetal methyl 4,6-O-benzylidene-2,3-dideoxy- $\alpha$ -D-erythro-hex-2-enopyranoside gave a single product 31 which was assigned the stereochemistry shown, assuming that O-1 and O-3 dictate addition to the syn face of the double bond.⁷⁵

- 78 M. Hanack and H. Allmendinger, Chem. Ber., 97, 1669 (1964).
- 74 E. J. Corey and H. Uda, J. Amer. Chem. Soc., 85, 1788 (1963).
- ⁷⁵ E. L. Albano, D. Horton, and J. H. Lauterbach, Chem. Commun., 1968, 357.



The complicated interplay of steric effects and the directive effects of oxygen atoms is seen in the addition of bis(iodomethyl)zinc to syn.7.t-butoxybicyclo[2.2.1]heptadiene (32), which gave the *exo*- and *endo*-cyclopropanes 33 and 34, respectively, in the ratio 1.8:1, whereas *anti-7-t*-butoxybicyclo[2.2.1]heptene (35) gave only the *exo*-cyclopropane  $36^{65}$  (cf. the formation of  $18^6$ ). The free alcohol *anti-7*-hydroxybicyclo[2.2.1]heptene also gave only the *exo*-cyclopropane analogous to  $36^{76}$  (see also p. 49).



The carbonyl group in unsaturated ketones is potentially capable of coordinating the zinc reagent and thus influencing the rate and stereochemistry of methylene transfer. There are not yet many data to support the view that stereoselective additions occur through the intermediacy of such complexes, but there is evidence that the electron-withdrawing carbonyl group in certain  $\alpha,\beta$ -unsaturated ketones also accelerates the rate of methylene transfer. Competition studies with cyclohexene and 2-cyclohexen-1-one showed that the relative rate ratio was  $k_{\text{enone}}/k_{\text{ene}} = 1.8$ , and an intermediate carbonyl complex of the zinc reagent was postulated.⁷⁷ Similarly, the reaction of 2-methyl-5-isopropenyl-2-cyclohexen-1-one (**37**) with the zinc reagent gave the two possible mono-adducts shown, and the rate of attack at the conjugated double bond was

 ⁷⁶ A. C. Cope, S. Moon, C. H. Park, and G. L. Woo, J. Amer. Chem. Soc., 84, 4865 (1962).
 ⁷⁷ J.-C. Limasset, P. Amice, and J.-M. Conia, Bull. Soc. Chim. Fr., 1969, 3981.

2.9 times that at the unconjugated double bond.⁷⁷ The data in Table I



suggest that both double bonds would be attacked at comparable rates in the absence of the carbonyl group, which might be expected to deactivate the ring double bond on the basis of electronic effects. The observed acceleration must be due, in part, to an intermediate complex.

Ester groups also orient the incoming zinc reagent, as originally shown for 2-cyclohepten-1-yl acetate, which yielded only cis-2-acetoxybicyclo-[5.1.0]octane.^{6.78} Although 1,4-cyclohexadiene gave a mixture of predominantly *trans*-13 along with cis-12 (p. 22), the carbomethoxy group in 38 induced both cyclopropane rings to be cis-oriented in the products 39 and 40 (4:1) (epimer 40 arose from an unrelated isomerization).⁶² The



ester 41 corresponding to 14 also gave only the *cis*-cyclopropane 42 of high stereochemical purity in better than 45 % yield (only one epimer formed).⁷⁹



Allenic carbinols such as 43 undergo methylene transfer first to the  $\alpha,\beta$ -double bond (44), followed by a second addition to yield a spiropentane.^{80, 81} The alcohol corresponding to 44 was isolated along with the spiropentanes 45 and 46 which were formed in the ratio 3:1. This suggests that an intermediate zincate 44, which is incapable of complexing more zinc reagent, is formed whose bulky substituent directs the second

79 T. Hanafusa, L. Birladeanu, and S. Winstein, J. Amer. Chem. Soc., 87, 3510 (1965).

⁷⁸ A. C. Cope, S. Moon, and P. E. Peterson, J. Amer. Chem. Soc., 84, 1935 (1962).

⁸⁰ M. Bertrand and R. Maurin, Bull. Soc. Chim. Fr., 1967, 2779.

⁸¹ R. Maurin and M. Bertrand, Bull. Soc. Chim. Fr., 1970, 2261.

methylene transfer to the less hindered face of the double bond. In a study of four primary and secondary allenic carbinols, no monoadduct was detected in which addition had occurred to the  $\beta$ ,y-double bond.⁸⁰



It is interesting to note that the carbon-oxygen double bond in hydroxy ketones undergoes an analogous hydroxy-assisted Wittig reaction with related zinc species,  $CH_2(ZnI)_2$  or  $Zn(CH_2ZnI)_2$  (p. 68).

Partial Asymmetric Synthesis. Methylene transfer does not disturb optical centers adjacent to a double bond in hydrocarbons, as shown by the cyclopropanation of D-limonene.⁸ This property along with the ability of the reagent to form coordination complexes with oxygencontaining functions and with the high stereoselectivity of methylene transfers from such complexes has been used to induce optical activity through cyclopropanation. When the zinc reagent is complexed with an ester function of an optically active acid, methylene transfer to nearby double bonds in appropriate molecules induces optical activity in the cyclopropane carboxylic acid that results after hydrolysis. (-)-Menthyl esters of most  $\alpha,\beta$ - and  $\beta,\gamma$ -unsaturated carboxylic acids afford dextrorotatory cyclopropane carboxylic acids.⁸² The synthetic yield, optical yield, and absolute configuration, respectively, were determined in the cyclopropanation of the (-)-menthyl esters of the following acids: crotonic (21%, 2.8%, 18:28), trans-3-pentenoic (54.5%, -, 18:28), 3-methyl-2-butenoic (16.5%, --, S), fumaric (14%, 6.4%, 18:2S), trans-4phenyl-3-butenoic (35%, 1.4%, 1R:2S), and cinnamic (33%, 9.3%, 1R:2R). These results are considered to be in accord with a methylenetransfer mechanism and exclude a two-step mechanism^{28, 29} for the following reasons. Examination of models of the zinc reagent complex, partial structure 47, reveals that a twisted cisoidal conformation of the double bond is required to attain a transition state resembling a bicyclo-[3.1.0] structure. Therefore it is expected and observed that products



with (+)-(1S:2S) and (+)-(1R:2S) configurations should predominate over their respective enantiomers. It is interesting to note that a two-step mechanism for methylene transfer via an intermediate like 7 would eventually lead to the (1R:2R) configuration in the resulting cyclopropane. Extension of these arguments⁶³ explains the apparent anomaly in the cinnamate ester.

In another study the (-)-menthyl esters of the *trans*-cinnamic acids, p-XC₆H₄CH=CHCO₂-menthyl-(-) (X = H, CH₃, CH₃O, Br, Cl, F, (CH₃)₂N, NO₂), were submitted to the cyclopropanation reaction.^{82a} The resulting cyclopropanes were formed in the following yields: X = H (26%), CH₃ (14.5%), CH₃O (6%), Br (16.6%), Cl (22.4%). The corresponding products were not isolated when X = F, (CH₃)₂N, NO₂. Chemical structure determinations showed that the cyclopropanes were of absolute configuration (-)-1R:2R, and when X = H the optical yield was 10.9%.

Partial asymmetric syntheses have also been demonstrated by carrying out the cyclopropanation reaction in the presence of (-)-menthol.⁸² In this case the zinc reagent reacts first to form a complex or a zincate 48 with (-)-menthol, from which methylene transfer to a variety of olefins,  $\alpha,\beta$ -unsaturated ketones, and  $\alpha,\beta$ -unsaturated esters all give levorotatory cyclopropanes of R and R: R configurations, although in low



synthetic and optical yields. Since the absolute configuration of the inducing alcohol is (-)-(3R)-menthol, this observation may provide a useful method for determining the absolute configuration of cyclopropanes. The use of (-)-menthyl methyl ether failed to induce optical

activity, and this suggests that (-)-menthol may function via a zincate rather than a complex of the free alcohol.

Partial asymmetric synthesis has also been observed employing the zinc reagent 11 obtained from diethylzinc and methylene iodide^{3.83} in the presence of L-leucine,⁸⁴ and methylene transfer probably occurs from the complex of 11 with L-leucine. For example, *cis*-1-ethoxy-1-butene and *cis*-1-ethoxy-3-methyl-1-butene afforded the corresponding cyclopropanes stereospecifically in 56 and 61 % yields, respectively. The former is dextrorotatory and the latter levorotatory, and the small rotations observed imply low optical yields. Nothing is yet known of the absolute configurations of these products.

#### SCOPE AND LIMITATIONS

The zinc reagents¹⁻³ have been used primarily in the synthesis of cyclopropanes from alkenes and hydrocarbons containing a plurality of double bonds, substituted alkenes including hydroxyl-substituted alkenes and allenes. These reactions are discussed separately. The synthesis of cyclopropanes by transfer of a substituted methylene group to double bonds, which has not been extensively studied, is discussed (see p. 46). Cyclopropanation of unsaturated organometallic compounds is in a separate section, and the reactions of the zinc reagent with acetylenes and with carbon-oxygen double bonds, which do not yield cyclopropanes, are discussed briefly. Since the cyclopropane synthesis has been the basis for several methods of introducing angular methyl groups, this topic is also discussed. Finally, a brief survey is made of some other  $\alpha$ -haloorganometallic compounds which are capable of methylene transfer.

It is often convenient and advantageous to use excess zinc reagent, and this practice has usually been followed in the literature. The yields quoted in this chapter, therefore, are not generally directly comparable and are those reported in the literature, which should be consulted for the actual reaction conditions.

Alkenes. In general, the cyclopropane synthesis proceeds smoothly with unsubstituted alkenes and unconjugated polyenes to give cyclopropanes stereospecifically and without rearrangement in yields up to 80%, based on 1 mol each of methylene iodide and zinc.^{4, 6, 13, 85} Ethylene reacted with the zinc reagent in a closed system to form cyclopropane,⁶ and *trans*-ethylene-d₂ gave *trans*-cyclopropane-d₂, although an unrelated

⁸³ J. Furukawa, N. Kawabata, and J. Nishimura, Tetrahedron, 24, 53 (1968).

⁸⁴ J. Furukawa, N. Kawabata, and J. Nishimura, Tetrahedron Lett., 1968, 3495.

⁸⁵ H. E. Simmons, U.S. Pat. 3,074,984 (1963) [C.A., 58, 13819h (1963)].

isomerization caused apparent nonstereospecific addition under some conditions.⁸⁶ Similar difficulties were experienced in the reaction of this olefin with ethylidene iodide.⁸⁶ Alkyl groups facilitate methylene transfer to the double bond with respect to rate and yield, which generally increase in the order ethylene <1 < 1, 2-<1, 2, 3, 4-<1, 2, 3-<1, 1- when the indicated substituents are small alkyl groups. Electron-donating groups accelerate transfer from the mildly electrophilic reagent, but the observed order is determined by an overlying deceleration caused by steric effects from the accumulating alkyl groups (Table I).

The cyclic olefins react readily with the zinc reagent to form the bicyclo[n.1.0]alkanes in the following yields: cyclobutene  $(47\%)^{12}$  cyclopentene  $(53\%)^{12}$  cyclohexene  $(57\%)^{13}$  cyclooctene  $(74\%)^{12}$  and cyclododecene  $(79\%)^{.87}$  These are typical values from the literature, but under appropriate conditions all of these yields are expected to be at least 80% (see Experimental Conditions).

Although acyclic *cis*-1,2-disubstituted alkenes react faster than the corresponding *trans* isomers, this order is often reversed in cyclic alkenes, *e.g.*, *cis*,*trans*-1,5-cyclodecadiene and *cis*,*trans*,*trans*-1,5,9-cyclododeca-triene gave principally  $49^{88}$  and 50 (50/51 = 32),⁸⁹ respectively. When the



trans double bond is in a strained ring, cyclopropanation can be preceded by undesirable isomerization, apparently caused by the Lewis acid zinc iodide; thus trans-cyclooctene gave cis-bicyclo[6.1.0]nonane (80%) and trans-bicyclo[6.1.0]nonane (20%) under the usual conditions.⁹⁰ Larger rings with trans double bonds, such as trans-cyclodecene,^{91, 92} react normally.

- 86 D. W. Setser and B. S. Rabinovitch, J. Org. Chem., 26, 2985 (1961).
- 87 R. J. Rawson and I. T. Harrison, J. Org. Chem., 35, 2057 (1970).
- ⁸⁸ J. G. Traynham, G. R. Franzen, G. A. Knesel, and D. J. Northington, Jr., J. Org. Chem., **32**, 3285 (1967).
  - 88 H. Nozaki, S. Kato, and R. Noyori, Can. J. Chem., 44, 1021 (1966).
  - ⁹⁰ A. C. Cope and J. K. Hecht, J. Amer. Chem. Soc., 85, 1780 (1963).
  - ⁹¹ J. Graefe and M. Mühlstädt, Tetrahedron Lett., 1989, 3431.
  - ⁹² J. G. Traynham, J. S. Dehn, and E. E. Green, J. Org. Chem., 33, 2587 (1968).

Cyclic systems containing internal double bonds which are tetrasubstituted often undergo cyclopropanation with special ease. Thus isotetralin gave principally 52 in 50% yield (cf.  $14 \rightarrow 15$ , p. 22).⁹³ It is interesting to note that none of the other possible monoadduct was detected, although a diadduct 53 was formed in appreciable quantity.



A hexahydroanthracene similarly showed propensity for attack at a tetrasubstituted double bond and gave 54 in 23% yield.⁹⁴

Bicycloheptenes react readily with the zinc reagent, but the products are sometimes sensitive to degradation by zinc iodide. Bicyclo[2.2.1]heptene reacted rapidly to give good yields of *exo*-18, whereas the equally facile addition to bicyclo[2.2.1]heptadiene gave only low yields of tricyclo[3.2.1.0^{2, 4}]oct-6-ene (55) (*exo/endo* = 5.7:1) accompanied by a mixture of diadducts 56.^{6, 27} The major diadduct was shown to be the *exo, exo* isomer.^{95, 96} 3,3-Dideuterio-*exo*-55 has been prepared using dideuteriomethylene iodide.⁹⁷



The synthesis has been used widely to prepare hydrocarbons containing a plurality of cyclopropyl groups, e.g., the previously mentioned cistetracyclo[9.1.0.0^{3, 5}.0^{7, 9}]dodecane (16) from cis, cis, cis, 1, 4, 7-cyclononatriene.⁵⁵ 1,1-Dicyclopropylcyclopropane (57)⁹⁸ and 1,2-dicyclopropylcyclopropanes (58)⁹⁹ have been synthesized from vinylcyclopropanes,

⁹³ P. H. Nelson and K. G. Untch, Tetrahedron Lett., 1969, 4475.

⁹⁴ E. Vogel, U. Haberland, and J. Ick, Angew. Chem., Int. Ed. Engl., 9, 517 (1970).

⁹⁵ H. C. Volger, H. Hogeveen, and M. M. P. Gaasbeek, J. Amer. Chem. Soc., 91, 218 (1969).

⁹⁶ H. C. Volger, H. Hogeveen, and M. M. P. Gaasbeek, J. Amer. Chem. Soc., 91, 2137 (1969).

⁹⁷ T. J. Katz and S. Cerefice, J. Amer. Chem. Soc., 91, 2405 (1969); 93, 1049 (1971).

⁹⁸ F. Effenberger and W. Podszun, Angew. Chem., Int. Ed. Engl., 8, 976 (1969).

⁹⁹ A. Maercker, Angew. Chem., Int. Ed. Engl., 6, 557 (1967).
and the highly strained dispiro[2.1.2.0]heptane (60) has been prepared from the methylenecyclopropane 59.¹⁰⁰



The cyclopropane synthesis has been used advantageously to synthesize many *spiro* hydrocarbons. Spirohexane has been obtained in 20-25%yields from methylenecyclobutane,¹⁰¹ and bicyclohexylidene gave an 87% yield of the spirohydrocarbon  $61.^{102}$  The rotanes  $62,^{103}$   $63,^{104}$  and  $64^{105}$  were prepared in good yields, and these syntheses afforded the first entry to this class of hydrocarbons.



¹⁰⁰ W. R. Dolbier, Jr., K. Akiba, J. M. Riemann, C. A. Harmon, M. Bertrand, A. Bezaguet, and M. Santelli, J. Amer. Chem. Soc., **93**, 3933 (1971).

¹⁰¹ D. E. Applequist and J. A. Landgrebe, J. Amer. Chem. Soc., 86, 1543 (1964).

¹⁰² S. D. Koch, R. M. Kliss, D. V. Lopiekes, and R. J. Wineman, J. Org. Chem., 26, 3122 (1961).

¹⁰³ A. P. Krapcho and D. E. Horn, Tetrahedron Lett., 1969, 4537.

¹⁰⁴ J.-M. Conia and J. M. Denis, Tetrahedron Lett., 1969, 3545.

¹⁰⁵ J. L. Ripoll and J.-M. Conia, Tetrahedron Lett., 1969, 979.



Terpenes have been synthesized (also see p. 47) and modified by the methylene-transfer reaction. D-Limonene gave principally 65 with no evidence of loss of optical activity,⁶ and  $\beta$ -pinene afforded the tricyclic hydrocarbon 66 in 84% yield.¹⁰²



A general method for introduction of quaternary carbon atoms has been suggested on the basis of the accompanying sequence.¹⁰⁶ This technique



has been applied with success for the introduction of *t*-butyl and *gem*dimethyl groups in adamantane, for example, using methyleneadamantane.¹⁰⁷ The cyclopropanation reaction has been applied to the heptacyclic dimer of cyclooctatetraene to form a complicated saturated hydrocarbon  $C_{18}H_{20}$ , whose two cyclopropane rings were subsequently opened by reductive cleavage¹⁰⁶ to yield a hydrocarbon  $C_{18}H_{24}$  that could be finally rearranged to the difficulty accessible triamantane.¹⁰⁸

Conjugated dienes react readily with the zinc reagent to form monoand di-adducts whose proportions can often be controlled. No trace of products resulting from 1.4-addition has been detected. Butadiene gave vinvlcvclopropane and dicvclopropyl with the zinc reagent^{12, 109, 110} and the corresponding aryl derivatives with aryldiazomethanes and zinc halides.⁵¹ When isoprene was allowed to react with one-half mole of iodomethylzinc iodide, attack at the disubstituted double bond predominated to give 1-methyl-1-vinylcyclopropane (64.4%), isopropenylcyclopropane (3.6%), and 1-methyl-1-cyclopropylcyclopropane (32%).¹¹¹ Cyclopentadiene afforded the expected mono- and di-adducts, bicyclo-[3.1.0]hex-2-ene (43%) and tricyclo $[4.1.0.0^{2,4}]$ heptane (30%), and the cis/trans ratio of the diadducts was 92:1.12, 112 Similar results were observed with 1,3-cyclohexadiene.¹² 1,3,5-Cyclooctatriene reacted with the dideuterio zinc reagent at a terminal double bond to give a bicyclo[6.1.0]nona-2,4-diene.^{113, 114} Cyclooctatetraene gave the monoadduct bicyclo-[6.1.0]nona-2,4,6-triene.¹¹⁵ A novel example was provided by the dimethylenecyclopropane 67 which afforded the spirohydrocarbon 68.116



A single example of the methylene-transfer reaction has been reported that employs ethyl diiodoacetate and zinc-copper couple; under these conditions the diene 1,1,4,4-tetramethyl-1,3-butadiene gave the ester **69**, which was subsequently hydrolyzed to DL-chrysanthemumic acid.¹¹⁷

¹⁰⁸ V. Z. Williams, Jr., P. von R. Schleyer, G. J. Gleicher, and L. B. Rodewald, J. Amer. Chem. Soc., **89**, 3862 (1966).

¹⁰⁹ J. A. Landgrebe and L. W. Becker, J. Amer. Chem. Soc., 90, 395 (1968).

¹¹⁰ C. G. Overberger and G. W. Halek, J. Org. Chem., 28, 867 (1963).

¹¹¹ L. A. Nakhapetyan, I. L. Safonova, and B. A. Kazanskii, *Izv. Akad. Nauk SSSR*, Otd. Khim. Nauk, **1962**, 902 [C.A., **57**, 12333c (1962)].

- ¹¹² W. Kirmse and K. Pöhlmann, Chem. Ber., 100, 3564 (1967).
- ¹¹³ M. Ogliaruso and S. Winstein, J. Amer. Chem. Soc., 89, 5290 (1967).
- ¹¹⁴ P. Radlick and S. Winstein, J. Amer. Chem. Soc., 85, 344 (1963).
- ¹¹⁵ E. Vogel, Angew. Chem., 73, 548 (1961).
- ¹¹⁶ (a) J. K. Crandall, D. R. Paulson, and C. A. Bunnell, Tetrahedron Lett., 1969, 4217;
- (b) D. R. Paulson, J. K. Crandall, and C. A. Bunnell, J. Org. Chem., 35, 3708 (1970).
   ¹¹⁷ K.-H. Büchel and F. Korte, Z. Naturforsch. B, 17, 349 (1962).



Benzene does not react with iodomethylzinc iodide under normal conditions,^{6, 118} and benzenoid aromatics are generally unreactive. The 9,10 bond in phenanthrene is, however, sufficiently reactive to undergo cyclopropanation with iodomethylzinc iodide, and the hydrocarbon 70 could be isolated in 25% yield.⁷ Acenaphthylene similarly afforded the hydrocarbon 71 in 60% yield on treatment with bis(iodomethyl)zinc.⁹



The reagent prepared from diethylzinc and methylene iodide³ is similarly unreactive toward benzene; however, the corresponding reagent prepared from ethylidene iodide reacted with benzene and alkylbenzenes to form mixtures of alkyl-substituted 7-methylcyclohepta-1,3,5-trienes in 11-44 % yields. For example, toluene gave a mixture of 1,7-, 2,7-, and 3,7-dimethylcyclohepta-1,3,5-triene in a distribution of 22, 32, and 46 %, respectively.⁴⁹

Styrene and its phenyl-substituted derivatives gave the corresponding phenylcyclopropanes.^{6. 119} Even severely crowded vinylmesitylene gave (2,4,6-trimethylphenyl)cyclopropane in 37% yield.¹²⁰ Alkyl substitution on the vinyl group of styrene does not interfere with cyclopropane

¹¹⁸ E. Müller and H. Fricke, Justus Liebigs Ann. Chem., 661, 38 (1963).

¹¹⁹ S. Nishida, I. Moritani, and T. Sato, J. Amer. Chem. Soc., 89, 6885 (1967).

¹²⁰ R. Ya. Levina, V. N. Kostin, P. A. Gembitskii, S. M. Shostakovskii, and E. G. Treshchova, Zh. Obshch. Khim., **32**, 1377 (1962); J. Gen. Chem. (USSR), Engl. Transl., **32**, 1363 (1962).

formation, as exemplified by trans-1-phenylpropene  $(54\%)^{6.121}$ , although 1-phenyl-2-methylpropene gave useful yields of product only when treated with the reagent prepared from diethylzinc and methylene iodide.¹²² Indene gave the expected tricyclic adduct.^{36.123} trans-Stilbene has been converted to trans-1,2-diphenylcyclopropane in 48% yield.^{82.124}

The novel reaction of benzocyclobutadiene and iodomethylzinc iodide, both generated *in situ*, has been reported to yield a mixture of indene and its cyclopropanation product, and it has been proposed that pseudoindene **72** is an intermediate.¹²⁵



Substituted Alkenes. Alkenes substituted with the usual functional groups at sites remote from the double bond generally undergo cyclopropanation without difficulty unless the substituent bears strongly acidic protons. Examples are known in which the groups F, Cl, Br, I, OH, OR, OCOR, NH₂, NR₂, NHCHO, C=O, ketal, CO₂R, SO₂R and various heteroatoms do not interfere with cyclopropane formation.

Hydroxyalkenes are discussed separately below. Aminoalkenes react readily to give high yields of cyclopropanes, but few examples of this potentially important reaction have been recorded. Allylamine, when added to the preformed zinc reagent in ether, has been converted to cyclopropylcarbinylamine (73) in 65 % yield; this represents perhaps the most convenient synthesis of this amine.¹²⁶ Similarly, 2-methyl-3-aminopropene gave 1-aminomethyl-1-methylcyclopropane.¹²⁷ It is likely that

$$CH_2 = CHCH_2NH_2 \longrightarrow \bigcirc CH_2NH_2$$
  
73

these reactions proceed via a complex of the zinc reagent and amine, analogous to that formed by alcohols.

- ¹²¹ M. Comtet, J. Amer. Chem. Soc., 91, 7761 (1969).
- 122 P. H. Mazzocchi, R. S. Lustig, and G. W. Craig, J. Amer. Chem. Soc., 92, 2169 (1970).
- 123 A. L. Goodman and R. H. Eastman, J. Amer. Chem. Soc., 86, 908 (1964).
- ¹²⁴ S. Sawada and Y. Inouye, Bull. Chem. Soc. Jap., 42, 2669 (1969).
- 126 H. Tanida and S. Teratake, Tetrahedron Lett., 1967, 2811.
- 128 E. Ciganek, personal communication.
- 127 R. Perraud and P. Arnaud, Bull. Soc. Chim. Fr., 1968, 1540.

The unconjugated ketone 2-methyl-2-hepten-6-one gave the expected cyclopropanation product in 50% yield,¹²⁸ and ketals of such ketones reacted normally with the zinc reagent (cf. 30).⁷⁴ The typical unconjugated ester methyl 4-methyl-3-pentenoate also reacted normally.¹²⁹ A one-step synthesis of DL-cis-9,10-methyleneoctadecanoic acid (dihydrosterculic acid) has been achieved in 51% yield from methyl oleate.⁶ Subsequently, many long-chain unsaturated fatty acids were cyclopropanated in yields in excess of 90%, e.g., methyl elaidate,¹³⁰ methyl palmitoleate,¹³¹ methyl vaccenate,¹³¹ methyl linoleate,¹³¹ and others.¹³²⁻¹³⁴ In a study of note, all sixteen methyl cis-octadecenoates were converted in yields of 70-80% to the corresponding cyclopropane esters

$$H(CH_2)_mCH \longrightarrow CH(CH_2)_nCO_2CH_3 (m + n = 15)$$

which were obtained pure.¹³⁵ Ethyl spiropentanecarboxylate (74) has been obtained in yields up to 76% from ethyl 2-methylenecyclopropane-carboxylate.^{136, 137}



Alkenes substituted on the double bond with the usual functional groups are activated toward cyclopropanation by electron-donating groups and deactivated by electron-withdrawing groups; however, if the functional group can coordinate the zinc reagent, methylene transfer may be accelerated even by electron-withdrawing groups, *e.g.*, carbonyl (see p. 30).

- 130 R. Wood and R. Reiser, J. Amer. Oil Chem. Soc., 42, 315 (1965).
- ¹³¹ W. W. Christie and R. T. Holman, Lipids, 1, 176 (1966).
- ¹³² D. Blanchet, J. Gregoire, M. Heintz, D. Lefort, A. Pourchez, and J. Sorba, *Oleagineux*, **21**, 749 (1966) [*C.A.*, **66**, 67021 p (1967)].
  - ¹³³ D. Lefort, C. R. Acad. Sci., Paris, Ser. C, 263, 432 (1966).
  - 134 J.-C. Promé and C. Asselineau, Bull. Soc. Chim. Fr., 1966, 2114.
- ¹³⁵ W. W. Christie, F. D. Gunstone, I. A. Ismail, and L. Wade, *Chem. Phys. Lipids*, 2, 196 (1968).
  - ¹³⁶ E. F. Ullman and W. J. Fanshawe, J. Amer. Chem. Soc., 83, 2379 (1961).
  - 137 L. M. Konzelman and R. T. Conley, J. Org. Chem., 33, 3828 (1968).

¹²⁸ Y. Armand, R. Perraud, J.-L. Pierre, and P. Arnaud, *Bull. Soc. Chim. Fr.*, **1965**, 1893. ¹²⁹ W. C. Agosta, A. B. Smith, III, A. S. Kende, R. G. Eilerman, and J. Benham, *Tetrahedron Lett.*, **1969**, **45**17.

cis- and trans-1-Chloro-1-butene gave the corresponding cyclopropanes stereospecifically,^{138, 139} but chloromethylenecyclopentane was reported to give no adduct.¹⁴⁰ The exocyclic chloromethylene group in the conjugated diene **75** is similarly unreactive, and cyclopropanation occurs only at the isopropylidene group to yield **76**.¹⁴¹ Alkyl vinyl ethers, *e.g.*, dihydropyran,⁶ and aryl vinyl ethers, *e.g.*, phenyl vinyl ether,^{142, 143} react



rapidly to form the corresponding cyclopropanes. From furan the diadduct 5-oxotricyclo[ $4.1.0.0^{2}$ , ⁴]heptane was obtained in 19% yield.¹² *cis*-1,2-Bis(trimethylsiloxy)-2-butene (77) is cyclopropanated stereospecifically to give 78 under the usual conditions, and several other 1,2-bis(trimethylsiloxy) alkenes behave similarly.¹⁴⁴ A valuable means of



mono- $\alpha$ -methylation of aldehydes and ketones involves cyclopropanation of trimethylsilyl vinyl ethers followed by basic hydrolysis directly to the  $\alpha$ -methyl carbonyl compound in high yields.^{144 $\alpha$} Vinyl esters afford the expected cyclopropyl esters in low yields,^{6. 145-147} and the reactions are often accompanied by extensive polymerization of the vinyl ester.

- 188 G. L. Closs, R. A. Moss, and J. J. Coyle, J. Amer. Chem. Soc., 84, 4985 (1962).
- 189 G. L. Closs and J. J. Coyle, J. Amer. Chem. Soc., 87, 4270 (1965).
- 140 J. A. Landgrebe and D. E. Applequist, J. Amer. Chem. Soc., 86, 1536 (1964).
- 141 M. Bertrand and R. Maurin, Bull. Soc. Chim. Fr., 1967, 3549.

¹⁴² S. M. Shostakovskii, A. I. L'vov, and Ya. M. Kimel'fel'd, *Izv. Akad. Nauk SSSR*, Ser. *Khim.*, **1966**, 1754 [C.A., **66**, 37558b (1967)].

¹⁴³ A. A. Retinskii and S. M. Shostakovskii, *Izv. Akad. Nauk SSSR*, Ser. Khim., 1967, 413 [C.A., 67, 21464c (1967)].

¹⁴⁴ M. Audibrand, R. Le Goaller, and P. Arnaud, C. R. Acad. Sci., Paris, Ser. C, **268**, 2322 (1969).

144a J.-M. Conia and C. Girard, Tetrahedron Lett., in press.

¹⁴⁵ C. H. De Puy, L. R. Mahoney, and K. L. Eilers, J. Org. Chem., 26, 3616 (1961).

148 C. H. De Puy and L. R. Mahoney, J. Amer. Chem. Soc., 86, 2653 (1964).

¹⁴⁷ C. H. De Puy, G. M. Dappen, K. L. Eilers, and R. A. Klein, J. Org. Chem., 29, 2813 (1964).

On the other hand, 1-ethoxyvinyl acetate gave 1-ethoxycyclopropyl acetate in 35 % yield.¹⁴⁸

 $\alpha,\beta$ -Unsaturated ketones undergo cyclopropanation to form cyclopropyl ketones, but these reactions are very dependent on the structure of the initial ketone.^{128, 149} Cyclopropanation apparently fails with acrolein, crotonaldehyde, mesityl oxide, isophorone, and cinnamaldehyde, but cyclopropyl ketones are often formed in good yields from other  $\alpha,\beta$ unsaturated ketones.¹⁴⁹ It has been suggested that enolizable hydrogen atoms in the  $\gamma$ -position interfere with the reaction. Cyclic unsubstituted  $\alpha,\beta$ -unsaturated ketones, however, usually give good yields of cyclopropyl ketones.

It is claimed that the best method of preparation of methyl cyclopropyl ketone is from methyl vinyl ketone and the zinc reagent (50%).^{77, 149} A careful study of a large number of  $\alpha,\beta$ -unsaturated ketones has been reported, and several cyclopropyl ketones have been synthesized in one step in high yields; for example, 2-cyclopenten-1-one to bicyclo[3.1.0]-hexan-2-one (80\%), 2-cyclohexen-1-one to bicyclo[4.1.0]heptan-2-on (2-norcaranone) (90\%), and 2-methylenebornan-3-one to its spiro derivative **79** (100\%).⁷⁷ Other examples are provided by 3-methylene-2-norbornanone (40\%),¹⁵⁰ 2-isopropylidenecyclobutanone (37\%),⁷⁷ 3,4-



dimethyl-3-hexen-2-one (15%),¹²⁸ and *trans*-1-phenylbuten-3-one (40%).^{77, 151} The doubly  $\alpha,\beta$ -unsaturated ketone 2,6-dimethyl-2,5-heptadien-4-one (phorone) gave an 80% yield of a mixture of DL- and *meso*isomers **80**,¹⁵¹ and several other examples of this type are known.⁷⁷ The



linear dienone system in  $17\beta$ -acetoxyandrosta-4,6-dien-3-one reacted predominantly at the terminal double bond to give a mixture of  $6\beta$ , $7\beta$  and  $6\alpha$ , $7\alpha$  derivatives 81.¹⁴

- 148 H. H. Wasserman and D. C. Clagett, Tetrahedron Lett., 1964, 341.
- ¹⁴⁹ J.-M. Conia, Angew. Chem., Int. Ed. Engl., 7, 570 (1968).
- ¹⁵⁰ C. F. Wilcox, Jr., and R. G. Jesaitis, J. Org. Chem., 33, 2154 (1968).
- ¹⁵¹ J.-M. Conia and J.-C. Limasset, Tetrahedron Lett., 1965, 3151.



trans-Chromindogenide gave the spiro compound 82; the *cis* isomer gave the same product, and it was shown that the starting materials were isomerized both by light and by zinc-copper couple.¹⁵²



It has been suggested that a preferred method for the cyclopropanation of  $\alpha,\beta$ -unsaturated ketones is to carry out the methylene-transfer reaction on the corresponding ethylene ketal, followed by hydrolysis. In this way several vinyl acetylenes were converted to cyclopropyl ketones as shown in the accompanying equation.¹⁵³

$$R_{1}CH = CR_{2}C \equiv CH \xrightarrow{HocH_{2}CH_{2}OH} R_{1}CH = CR_{2} \xrightarrow{O} C \xrightarrow{O} CH_{3} \longrightarrow$$

$$R_{1}CH \xrightarrow{CH_{2}} CR_{2} \xrightarrow{O} C \xrightarrow{O} CH_{3} \longrightarrow R_{1}CH \xrightarrow{CH_{2}} CR_{2} \xrightarrow{O} CH_{3}$$

 $\alpha,\beta$ -Unsaturated esters undergo cyclopropanation, but the yields are very dependent on the specific ester. Methyl crotonate and ethyl *trans-p*methoxycinnamate were early shown to give the corresponding cyclopropanes stereospecifically.⁶ Similarly, *n*-butyl *cis*- and *trans*-2-methyl-2butenoate gave the corresponding cyclopropyl esters.¹⁵⁴ Dimethyl fumarate has been reported to afford dimethyl *trans*-1,2-cyclopropanedicarboxylate,¹⁵⁵ and 1-carbomethoxybicyclo[2.1.0]pentane (83) has been prepared from 1-carbomethoxycyclobutene.¹⁵⁶ An example provided by

¹⁵² J. A. Donnelly, D. D. Keane, K. G. Marathe, D. C. Meaney, and E. M. Philbin, *Chem.* Ind. (London), 1967, 1402.

¹⁵³ H. Monti, C. R. Acad. Sci., Paris, Ser. C, 265, 522 (1967).

¹⁵⁴ M. Bertrand and H. Monti, Tetrahedron Lett., 1968, 1069.

¹⁵⁵ J. F. McCarthy, J. G. Cannon, J. P. Buckley, and W. J. Kinnard, J. Med. Chem., 7, 72 (1964).

¹⁵⁶ P. G. Gassman and K. T. Mansfield, J. Org. Chem., 32, 915 (1967).



 $\alpha$ -(2-methyl-5-methoxy-3-indolyl)acrylate, which gave 84 with the zinc reagent in tetrahydrofuran, demonstrates that the synthesis often succeeds in the face of complex functionality.¹⁵⁷

Ketene acetals react readily and in good yield with the zinc reagent (cf. 1-ethoxyvinyl acetate¹⁴⁸). Dimethylketene dimethyl acetal was converted to 1,1-dimethyl-2,2-dimethoxycyclopropane (85) in 51 %



yield.¹⁵⁸ The cyclopropanone ketal 86 was prepared in 70% yield and was catalytically reduced to cyclopropanone hydrate.¹⁵⁹ The highly hindered



di-t-butylketene failed to react with iodomethylzinc iodide and was recovered unchanged.¹⁶⁰

Enamines, like vinyl ethers, are highly reactive toward the zinc reagent, and their cyclopropanation proceeds best by adding the enamine to an ether solution of the preformed reagent. In this way dimethylaminol-cyclopentene gave the bridgehead amine 87 in 36 % yield.¹⁶¹



¹⁵⁷ T.-Y. Shen, U.S. Pat. 3,328,423 (1967) [C.A., 67, 108559m (1967)].

¹⁵⁶ E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sattre, D. J. Scharf, and G. Tosi, J. Amer. Chem. Soc., **92**, 7428 (1970).

¹⁵⁹ R. Grewe and A. Struve, Chem. Ber., 96, 2819 (1963).

¹⁶⁰ M. S. Newman and A. Leegwater, J. Org. Chem., 33, 2144 (1968).

¹⁶¹ E. P. Blanchard, H. E. Simmons, and J. S. Taylor, J. Org. Chem., 30, 4321 (1965).

Cyclopropanation of a vinyl sulfone is demonstrated by the reaction of phenyl vinyl sulfone with the zinc reagent prepared from iodomethyl benzoate and zinc-copper couple, which yielded cyclopropyl phenyl sulfone (88).⁴²

$$C_{6}H_{5}SO_{2}CH = CH_{2} + C_{6}H_{5}CO_{2}CH_{2}ZnI \longrightarrow C_{6}H_{5}SO_{2} \longrightarrow$$
88

Alkylidene-Transfer Reactions. The zinc reagents RCHI(ZnI)and ArCHI(ZnI) can be generated and they undergo methylene-transfer reactions; however, the disubstituted reagents  $R_2CI(ZnI)$  and  $Ar_2CI(ZnI)$ are apparently too unstable to find use in synthesis. Some aspects of these reagents have been discussed under Mechanism, where it was pointed out that the reaction of alkylidene iodides with zinc-copper couple produced zinc reagents under conditions that promote their decomposition. The method of choice for carrying out alkylidene-transfer reactions is the variation employing diethylzinc and alkylidene iodides.³

The reaction of cyclohexene, ethylidene iodide, and zinc-copper couple gave a low yield (3.6%) of exo-7-methylbicyclo[4.1.0]heptane (89).27 None of the endo isomer was detected, and models of the anticipated transition state predict this result on the basis of steric considerations. The stereochemical outcome is sensitive, however, to the nature of the anions in the zinc complex as the following examples show. With benzoate ion as leaving group, the zinc reagent prepared from 1-iodoethyl benzoate and zinc-copper couple [C₆H₅CO₂CH(CH₃)ZnI] afforded with cyclohexene a 29% yield of a mixture of both endo-89 and exo-90 in the ratio 1.9:1.42The zinc reagent prepared from diethylzinc and ethylidene iodide  $[CH_3CHI(ZnC_2H_5)]$ , however, gave a 66% yield of a mixture of 89 and 90 in the ratio 1.5:1.83.84 When the latter variation was used, vinyl isobutyl ether formed a mixture of the cyclopropanes 91 and 92 (cis/trans =2.3) in 96% yield, and similarly benzylidene was transferred to cyclohexane in 64 % yield to form endo-93 and exo-94 in the ratio 17:1.84 Clearly, the transition state for transfer from the latter zinc reagents is quite different sterically from that of iodomethylzinc iodide.

A study has been made of the utility of the ethylidene reagent in synthesis.¹⁶² Yields of methylcyclopropanes ranged from 23 to 96% in the solvents diethyl ether, diisopropyl ether, and low-boiling petroleum ether. The ethylidene reagent  $CH_3CHI(ZnC_2H_5)$  is similar chemically in its reactions to  $CH_3CHI(ZnI)$ , but the transition states for ethylidene transfer seem to be less sterically crowded with the former and its reactions



are less stereoselective. Even iodomethylzinc iodide is more stereoselective, since bicyclo[2.2.1]heptene gave only *exo* adduct with iodomethylzinc iodide, whereas reaction with the ethylidene reagent gave a mixture of *exo*.95 and *endo*.96 in the ratio 2.2:1. The methyl group of the



exo adduct is trans to the ring junction as expected on steric grounds, but the stereochemistry of the endo adduct was not determined.¹⁶² The ethylidene reagent also undergoes hydroxyl-assisted transfer reactions as shown by the conversion of 3-cyclopenten-1-ol exclusively to a cis-3-



hydroxybicyclo[3.1.0]hexane 97. The reaction shows a further stereoselective feature in that the methyl group at  $C_6$  is *exo*-oriented.¹⁶²

It has been mentioned previously that the ethylidene iodide/diethylzinc reagent reacts with alkylbenzenes to give alkyl-substituted tropylidenes. The initial products are presumably norcaradienes, but the mechanism probably does not involve methylene transfer in the usual sense.

Hydroxyalkenes. The importance and some mechanistic aspects of the methylene-transfer reaction applied to hydroxyalkenes were stressed on p. 23. The ability of hydroxyl and alkoxyl groups to coordinate

## ORGANIC REACTIONS

iodomethylzinc iodide and so direct the stereochemistry of methylene transfer has added a valuable dimension to the cyclopropanation reaction. This stereochemical control has been used with particular effectiveness in steroid chemistry.

Acyclic hydroxyalkenes undergo stereospecific cyclopropanation in the normal manner. Studies of the influence of the position of the double bond relative to the hydroxyl group suggested that the yields of cyclopropanes were lower in homoallylic  $(\beta,\gamma)$  cases,^{127, 128} but it is likely that this generalization will have exceptions. Some typical examples include *trans*-4-hydroxy-2-pentene  $(\alpha,\beta; 60\%)$ , 4-hydroxy-1-butene  $(\beta,\gamma; 25\%)$ , and 6-hydroxy-2-methyl-2-heptene  $(\gamma,\delta; 65\%)$ .¹²⁷ In a case of internal competition, only the  $\alpha,\beta$ -double bond in the alcohol **98** underwent cyclopropanation with excess zinc reagent.¹⁶³ Curiously, allyl alcohol gave poor yields of cyclopropylcarbinol, and the major product was the formal, dicyclopropylcarbinoxymethane **(99)**, which can be made in good



yield in this manner.¹⁶⁴ The formal synthesis is less effective with larger

$$\mathrm{CH}_{2}=\mathrm{CHCH}_{2}\mathrm{OH} \longrightarrow (\bigcirc -\mathrm{CH}_{2}\mathrm{O})_{2}\mathrm{CH}_{2}$$

allylic alcohols, e.g., trans-2-buten-1-ol gave 45% formal/20% carbinol and methallyl alcohol gave 10% formal/70% carbinol. The cyclopropanation reaction has also been used to prepare selectively the hexadeuterio cyclopropyl carbinol 100.¹⁶⁵ A divinylcarbinol, 1,4-pentadien-3-ol,



has been converted to the monoadduct, cyclopropyl vinyl carbinol.¹⁶⁶

It has been pointed out that, according to conformational principles, the intramolecular transfer of a methylene group in the complex of a

¹⁶³ E. J. Corey, H. Yamamoto, D. K. Herron, and K. Achiwa, J. Amer. Chem. Soc., 92, 6635 (1970).

¹⁶⁴ Z. Majerski and P. von R. Schleyer, J. Org. Chem., 34, 3215 (1969).

¹⁶⁵ Z. Majerski and P. von R. Schleyer, J. Amer. Chem. Soc., 93, 665 (1971).

¹⁶⁶ K. B. Wiberg and A. J. Ashe, III, J. Amer. Chem. Soc., 90, 63 (1968).

cyclic hydroxyalkene with the zinc reagent occurs to the more accessible face of the double bond. When the complex geometry precludes intramolecular addition, reaction may occur intermolecularly and stereoselectivity is changed or lost. Thus the complex with *exo-7*-methylene-bicyclo[3.3.1]nonan-3-ol probably cannot react intramolecularly, but cyclopropanation still proceeds in 40% yield to give  $101.^{167}$  Similarly,



exo-5-hydroxybicyclo[2.2.1]heptene (102) adds a methylene group from the exo direction in a reaction that cannot involve the complexed reagent.¹⁶⁸⁻¹⁷⁰ It might have been expected that syn-7-hydroxybicyclo-[2.2.1]heptene derivatives would undergo facile exo addition, but the reports are somewhat conflicting. syn-7-Hydroxybicyclo[2.2.1]heptene



 $(103)^{168.171}$  and its benzo derivative  $105^{172}$  apparently failed to give adducts. These results are unexpected since *anti*-7-hydroxybicyclo-[2.2.1]heptene (104) and the *t*-butyl ether of 7-hydroxybicyclo-[2.2.1]heptadiene (32) were reported to give *exo* adduct⁷⁶ and predominantly *exo-syn*-33,⁶⁵ respectively, neither of which could have formed by an intramolecular complex. On the other hand, a mixture of the *syn*- and *anti*-7-hydroxyl derivatives 106 and 107 reacted with excess reagent to give *syn-exo* adduct 108, and 107 was recovered unchanged.¹⁷³ The explanation of these curious results probably lies in reaction variables such as whether the zinc reagent was preformed or not and the ratio of reagent to unsaturated alcohol.

- ¹⁶⁷ M. A. Eakin, J. Martin, and W. Parker, Chem. Commun., 1967, 955.
- 168 R. R. Sauers and J. A. Beisler, Tetrahedron Lett., 1964, 2181.
- ¹⁶⁹ A. K. Colter and R. C. Musso, J. Org. Chem., 30, 2462 (1965).
- ¹⁷⁰ R. R. Sauers, J. A. Beisler, and H. Freilich, J. Org. Chem., 33, 569 (1967).
- ¹⁷¹ R. E. Pincock and J. I. Wells, J. Org. Chem., 29, 965 (1964).
- ¹⁷² M. A. Battiste and M. E. Brennan, Tetrahedron Lett., 1966, 5857.
- ¹⁷³ S. C. Clarke, K. J. Frayne, and B. L. Johnson, Tetrahedron, 25, 1265 (1969).



The stereoselectivity exhibited in hydroxyl-assisted cyclopropanations can usually be understood on simple steric grounds, but this is not always the case. In the rigid methylene hydroxycyclobutane 109, addition occurs to the face of the double bond closer to the hydroxyl group, and the sole product is 110.¹⁷⁴ Even when bulky substituents elsewhere in the



molecule hinder intramolecular transfer, this mode often prevails; for example, both cis- and trans-3,4-diphenyl-2-cyclopenten-l-ol (111 and 112)



174 M. Bertrand and R. Maurin, Tetrahedron Lett., 1988, 4585.

underwent cyclopropanation on the same face of the double bond relative to the hydroxyl group.¹⁷⁵ The epimeric alcohols 113 and 114 behaved similarly, even though the transition state for intramolecular transfer in 114 is sterically unfavorable.¹⁷⁶ When there are two double bonds in the molecule, only one of which can react readily by an intramolecular mechanism, addition occurs exclusively to that double bond in a stereoselective fashion. For example, both 115 and 116¹⁷⁸ react in 60% and ca. 100% yields, respectively, by exclusive addition to the tetrasubstituted double bond from the syn face relative to the hydroxyl group. It is interest-



ing to note that the acetate of 115 gave a mixture of four major products, which were not identified, under the same reaction conditions.¹⁷⁷ Several examples of this type occur in the steroids.

A single hydroxyl group can apparently control the stereochemistry of successive methylene transfers in a diene, e.g., 1,4-cyclooctadien-7-ol gave the diadduct 117 in 90% yield.¹⁷⁹ Under the same conditions, 1,4-cyclooctadiene gave a 66:34 mixture of the *cis* and *trans* diadducts.



In this case the presence of the second double bond changes the ring geometry so that addition to the syn face is favored. The geometrical situation is changed again, however, in the nine-membered ring trienes, where cis, cis, cis. 2, 5, 7-cyclononatrien-1-ol and cis, cis, cis. 2, 4, 7-cyclonon-atrien-1-ol gave the adducts 118^{180. 181} and 119, respectively.

There are several examples in which cyclopropanations of rigid allylic

- 177 P. Radlick and W. Rosen, J. Amer. Chem. Soc., 88, 3461 (1966).
- ¹⁷⁸ J. J. Sims, J. Org. Chem., 32, 1751 (1967).

¹⁷⁵ J. S. Swenton, A. R. Crumrine, and T. J. Walker, J. Amer. Chem. Soc., 92, 1406 (1970).

¹⁷⁶ L. A. Paquette and O. Cox, J. Amer. Chem. Soc., 89, 5633 (1967).

¹⁷⁹ P. Radlick and S. Winstein, J. Amer. Chem. Soc., 86, 1866 (1964).

¹⁶⁰ M. Gasic, D. Whalen, B. Johnson, and S. Winstein, J. Amer. Chem. Soc., **89**, 6382 (1967).

¹⁸¹ D. Whalen, M. Gasic, B. Johnson, H. Jones, and S. Winstein, J. Amer. Chem. Soc., 89, 6384 (1967).



and homoallylic alcohols have given high yields of cyclopropyl carbinols, e.g., the methyleneadamantol 120 formed 121 in better than 80% yield.^{182, 183}



The cyclopropanation reaction has been used to great advantage in the stereospecific synthesis of highly cyclopropanated medium ring compounds.^{181a,b} The basic scheme is illustrated with *cis,cis,cis-2,5,8*-cyclo-decatrien-1-ol (A), which gives the *anti* adduct **B**. Oxidation of **B** with chromic anhydride to the ketone **C** is followed by stereospecific lithium aluminum hydride reduction to the *syn* epimer **D** which undergoes stereospecific homoallylic ring expansion to **E** with perchloric acid in dioxane. The di- and tri-adducts corresponding to **B** could also be



obtained selectively, and they were carried through a similar scheme. Finally, another cyclopropanation was performed on these products of a second ring expansion, and in this way pure samples of six epimeric tetracyclo[11.1.0.0^{3, 5}.0^{7, 9}]tetradecan-ll-ols of known stereochemistry were obtained.

^{181a} R. W. Thies, M. Gasic, D. Whalen, J. B. Grutzner, M. Sakai, B. Johnson, and S. Winstein, J. Amer. Chem. Soc., 94, 2262 (1972).

¹⁸¹^b R. W. Thies, M. Sakai, D. Whalen, and S. Winstein, J. Amer. Chem. Soc., **94**, 2270 (1972).

182 P. von R. Schleyer and V. Buss, J. Amer. Chem. Soc., 91, 5880 (1969).

183 J. C. Martin and B. R. Ree, J. Amer. Chem. Soc., 91, 5882 (1969).

Examples of the cyclopropanation reaction applied in the terpene area will be found throughout the text and in the Tabular Survey. A study of the cyclopropanation of  $\alpha$ -pinene, myrtenol, nopol,  $\beta$ -pinene, and pinocarveol clearly showed that complexes of the zinc reagent with allylic alcohols promote successful methylene transfer compared to complexes with homoallylic alcohols, judged by yield data.^{163a} The stereochemistry of the products was not determined, although it can be inferred. Verbenene was cyclopropanated in two steps but yields were not recorded.



1884 C. Filliatre and C. Guéraud, C.R. Acad. Sci., Paris, Ser. C, 273, 1186 (1971).



The key step in the total synthesis of DL-thujopsene was the stereoselective reaction of the zinc reagent with *cis*-7-hydroxy-4,4,10-trimethyl-



 $\Delta^5$ -octalin to give the cyclopropyl carbinol 122.¹⁸⁴ In the total synthesis of DL-sabinene an important step was the conversion of 3-isopropyl-2-cyclopenten-1-ol to the appropriate bicyclo[3.1.0]hexane skeleton 123.¹⁸⁵



The cyclopropanation has also been used in syntheses leading to determination of the absolute configuration of thujane.¹⁸⁶ During the synthesis of the sesquiterpene DL- $\beta$ -himachalene, a cyclopropane ring was introduced to give the intermediate **124** and later cleaved to generate a geminal dimethyl function.¹⁸⁷



184 W. G. Dauben and A. C. Ashcraft, J. Amer. Chem. Soc., 85, 3673 (1963).

- ¹⁸⁵ W. I. Fanta and W. Erman, J. Org. Chem., 33, 1656 (1968).
- 186 G. Ohloff, G. Uhde, A. F. Thomas, and E. sz. Kováts, Tetrahedron, 22, 309 (1966).
- 187 B. D. Challand, G. Kornis, G. L. Lange, and P. de Mayo, Chem. Commun., 1967, 704.

The control of stereospecificity of cyclopropanations by taking advantage of selectively placed hydroxyl groups has been widely exploited in steroid synthesis. Some special applications that involve cyclopropanation as the crucial step include introduction of  $19\alpha$ -methyl groups and synthesis of 5,7-cyclosteroids from B-norsteroids.

When a steroid possesses a hydroxyl group located at great distance from a double bond, cyclopropanation proceeds normally as in the case of the 1-methylenedihydrotestosterone ketals, which gave the spiro steroids 125.¹⁸⁸ Cyclopropanes have been introduced by hydroxyl-assisted reactions in the 17 $\alpha$  position of testosterone and 19-nortestosterone as shown in the products 126.¹⁸⁸ In the latter reaction the unprotected



 $\alpha,\beta$ -unsaturated ketone function does not interfere with addition to the remote allylic alcohol; this suggests that complexation by hydroxyl is more important than by carbonyl groups. The allylic alcohol in 3-(hydroxymethyl)androst-2-en-17 $\beta$ -ol 17-acetate underwent reaction via a complex to give the  $2\alpha,3\alpha$ -cyclopropane 127¹⁸⁹ presumably because of steric interference of the angular 10 $\beta$  methyl group. The corresponding diol also underwent exclusive  $\alpha$ -face cyclopropanation.^{189a}

Many conventional unsaturated steroid alcohols undergo stereoselective additions. Some of these types are exemplified by the partial formulas 128-140, which are identified specifically in Table III along with the direction of addition. Interestingly, cholesterol, cholesteryl acetate, and

¹⁸⁸ H.-G. Lehmann, H. Müller, and R. Wiechert, Chem. Ber., 98, 1470 (1965).

¹⁸⁹ P. Bourguignon, J. C. Jacquesy, R. Jacquesy, J. Levisalles, and J. Wagnon, *Chem. Commun.*, **1970**, 349.

^{189a} P. Bourguignon, J. C. Jacquesy, R. Jacquesy, J. Levisalles, and J. Wagnon, Bull. Soc. Chim. Fr., 1971, 269.



Type	Compound	Yield, ⁰∕	Orientation of Cyclopropage	Refs
		/0		
128	$3\beta$ , $17\beta$ -Dihydroxy-5 $\alpha$ -androst- 1-ene 17-acetate	60	β	190
128	3β,17β-Dihydroxy-19-nor-5α- androst-1-ene 17-acetate	43	β	190
128	3β-Hydroxy-5α-androst-1- en-17-one	39	β	190
128	3β,17β-Dihydroxy-1-methyl-5α- androst-1-ene 17-acetate	35	β	190
128	3β,17β-Dihydroxy-17α-ethynyl- 5α-androst-1-ene 17-acetate		β	190
128	3β,20-Dihydroxy-5α- pregn-1-ene		β	190
129	3β-Hydroxy-17α,20; 20,21- bismethylenedioxy-5α- pregn-1-ene	36	β	190
129	3β-Hydroxy-17α,20; 20,21- bismethylenedioxypregna- 1,5-dien-11-one	25	β	190
129	3β,17β-Dihydroxy-17α- methyl-1,5-androstadiene	52	β	191
130	3β,11β-Dihydroxy-17α,20; 20,21-bismethylenedioxy- pregna-1,5-diene	49, 40	β	190, 191
131	$17\beta$ ·Acetoxy-1 $\alpha$ -hydroxy-5 $\alpha$ - androst-2-ene	36	α	192
132	$3eta edot{Hydroxy}-\Delta^4$ -cholestene	62	β	193
133	$3lpha$ -Hydroxy- $\Delta^4$ -cholestene	65	α	193
134	$17\beta$ -Acetoxy- $\Delta^{4.6}$ -andro- stadien- $3\beta$ -ol		β	194
135	Estr-5(10)-ene- $3\beta$ , 17 $\beta$ -diol	·	β	195
135	3β-Hydroxy-8α-estr-5(10)-ene- 17-one 17-ethylene ketal		β	196
135	$8\alpha$ -Estr-5(10)-ene- $3\beta$ , 17 $\beta$ -diol		β	196
136	Estr-5(10)-ene-3 $\alpha$ , 17 $\beta$ -diol	85	α	195
137	3β,6β-Dihydroxy-19-nor- androst-5(10)-en-17-one 3-tetrahydropyranyl ether	·	β	197
138	3β,6α-Dihydroxy-19-nor- androst-5(10)-en-17-one 3-tetrahydropyranyl ether		α	197
139	Estr-5(10)-ene- $3\alpha$ , $11\beta$ , $17\beta$ - triol 3, 17-diacetate		β	31
140	$3\beta$ , $17\beta$ -Dibenzoyloxy- $\Delta^7$ - androstadie- $6\alpha$ -ol		α	194
140	Cholest-7-ene- $3\beta$ , $6\alpha$ -diol		α	198

## TABLE III. Cyclopropanation of Steroids

cholest-5-en-3-one are resistant to cyclopropanation under the usual conditions^{189b} and even under the forcing conditions²⁰⁰ of 75° and 18 hours. In the  $\Delta^5$ -series, *epi*-cholesterol, however, underwent cyclopropanation under mild conditions at the  $\alpha$ -face exclusively, but *epi*-cholesteryl acetate and  $3\alpha$ -methoxy-5-cholestene were unreactive even under forcing conditions. The complex of the zinc reagent with the equatorial hydroxyl group in cholesterol leaves the methylene moiety spatially removed from the  $\Delta^5$ -double bond and the addition reaction is frustrated. Furthermore, the 19-methyl group severely hinders intra- or intermolecular addition to the  $\beta$ -face. The axial hydroxyl group in *epi*-cholesterol, however, can orient and facilitate addition to the unhindered  $\alpha$ -face of the C₅-C₆ double bond. In earlier work, attempts to cyclopropanate 2-cholestene, 3-methyl-2-cholestene, and 3-phenyl-2-cholestene-2 failed to give products.^{189c}

As the examples in Table III show, the cyclopropane ring can be fused to most positions in steroid nuclei, and many types of functional groups do not interfere with the additions. Another interesting application has been the conversion of B-norsteroids to 5,7-cyclosteroids. The reaction of B-norcholesterol acetate 141b with the zinc reagent resulted in the isolation of both 142b (45%) and the epimeric  $5\alpha$ ,7 $\alpha$ -cyclosteroid 143b (2%).^{199, 200} When the  $3\alpha$ -acetoxy epimer corresponding to 141b was



1896 J. F. Templeton and C. W. Wie, Can. J. Chem., 49, 3636 (1971).

189c R. C. Cookson, D. P. G. Hamon and J. Hudee, J. Chem. Soc., 1963, 5782.

¹⁹⁰ R. Wiechert, O. Engelfried, U. Kerb, H. Laurent, H. Müller, and G. Schulz, *Chem. Ber.*, **99**, 1118 (1966).

- ¹⁹¹ M. Tanabe and D. F. Crowe, Tetrahedron, 23, 2115 (1967).
- ¹⁹² D. E. Evans, G. S. Lewis, P. J. Palmer, and D. J. Weyell, J. Chem. Soc., C, 1968, 1197.
- 193 W. G. Dauben, P. Laug, and G. H. Berezin, J. Org. Chem., 31, 3869 (1966).
- ¹⁹⁴ H. Laurent, H. Müller, and R. Wiechert, Chem. Ber., 99, 3836 (1966).
- ¹⁹⁵ R. Ginsig and A. D. Cross, J. Amer. Chem. Soc., 87, 4629 (1965).
- ¹⁹⁶ A. J. Birch and G. S. R. Subba Rao, J. Chem. Soc., **1965**, 5139.
- ¹⁹⁷ R. Ginsig and A. D. Cross, J. Org. Chem., **31**, 1761 (1966).
- ¹⁹⁸ F. T. Bond and R. H. Cornelia, Chem. Commun., 1968, 1189.
- 199 P. G. Gassman and W. E. Hymans, Chem. Commun., 1967, 795.
- 200 J. Joska, J. Fajkoš, and F. Šorm, Collect. Czech. Chem. Commun., 33, 2049 (1968).

subjected to the same conditions, the product was the  $3\alpha$ -acetoxy epimer corresponding to 142b. Furthermore, when either the alcohol 141a or its corresponding  $3\alpha$ -hydroxy epimer was treated with the zinc reagent, only 142a and its  $3\alpha$ -hydroxy epimer were formed, respectively, in low yields. It is clear that the directive influence of the hydroxyl group is lost in this series. Most likely, the complex of 141a and the zinc reagent is incapable of intramolecular addition, and intermolecular addition occurs from the  $\alpha$ -face, analogous to epoxidation. No conclusions can be drawn about the nature of the addition in the case of the  $3\alpha$ -hydroxy epimer related to 141a, which may occur intramolecularly.

An important application of the cyclopropanation reaction has been the introduction of the unnatural 19 $\alpha$ -methyl group. This has been accomplished by stereoselective control of methylene transfer to the  $\alpha$ face of steroids of type 136, as shown in the conversion of estr-5(10)-ene- $3\alpha$ ,17 $\beta$ -diol (144) to  $5\alpha$ ,19-cyclo-10 $\alpha$ -androstane- $3\alpha$ ,17 $\beta$ -diol (145) in 85% yield. Subsequent oxidation and isomerization of 145 were the basis of a facile synthesis of 10 $\alpha$ -androst-4-en-3-ones of type 146.¹⁹⁵ DL-18-Methyltestosterone (19 $\beta$ -methyls) have also been synthesized by this strategy.²⁰¹



The cyclopropanation has been used advantageously in the total synthesis of DL-alnusenone (149). At the stage of the allylic alcohol 147 the cyclopropyl group was introduced to give 148, and the three-membered ring was subsequently converted to the angular methyl at the starred position.²⁰²

²⁰² R. E. Ireland and S. C. Welch, J. Amer. Chem. Soc., 92, 7232 (1970).



Allenes. The cumulated double bonds of allenes are capable of undergoing stepwise cyclopropanation in the normal manner, and substituent effects are similar to those observed in alkenes. Stereoselectivity of methylene transfers in hydroxyallenes is also observed, and products can be predicted on the basis of the lowest energy conformation of the intermediate zinc reagent complex (cf. 43).

Although allene itself has not given useful yields of products, its alkyl derivatives afford both methylenecyelopropanes and spiropentanes, but in most cases no attempt has been made to optimize the yield of monoadducts. The double bonds of monoalkyl allenes sometimes show little selectivity toward the zinc reagent; for example, when 1,2-heptadiene was treated with 1 mol of zinc reagent, the monoadducts 150 and 151 were



formed in 10.5 and 11% yields, respectively, along with 12% of the diadduct 152.²⁰³ With 6 mol of reagent, the yields of these products were 1, 0, and 68%, respectively. Di- and tri-alkylsubstituted allenes give spiropentanes, but little information is available on the relative reactivity

²⁰³ Y. Vo-Quang, L. Vo-Quang, G. Emptoz, and P. Savignat, C. R. Acad. Sci., Paris, Ser. C, **262**, 220 (1966).

of the double bonds. 2,4-Dimethyl-2,3-pentadiene (tetramethylallene) gave largely monoadduct even with a large excess of zinc reagent.²⁰⁴⁻²⁰⁶

The cyclic allene, 1,2-cyclononadiene, afforded the monoadduct bicyclo[7.1.0]dec-1-ene (153).²⁰⁷ Other interesting applications include the conversion of vinylidenecyclopropane to the parent bicyclopropylidene (154),²⁰⁸ and the synthesis of the highly substituted hexamethylbicyclopropylidene from hexamethylvinylidenecyclopropane.¹¹⁶ The cyclopro-



panation reaction has provided a three-step synthesis of hypoglycin A (157), the key step of which was conversion of the allene 155 to the methylenecyclopropane 156 in 71% yield.²⁰⁹ Here methylene transfer



occurred to the more highly substituted double bond, and it is not known whether an intermediate complex was involved.

Acetylenes. No unequivocal evidence has been offered that alkynes react with the zinc reagent to yield cyclopropenes. 3-Hexyne reacted with the zinc reagent in ether to give three major products: 2-ethyl-1,3pentadiene and *cis*- and *trans*-l-ethyl-2-propenylcyclopropane.^{25, 210} A revealing example of the limits of methylene-transfer reactions is provided by the reaction of the strained acetylene cyclooctyne with iodomethylzinc

²⁰⁴ P. Battioni-Savignat, Y. Vo-Quang, and L. Vo-Quang, Bull. Soc. Chim. Fr., 1967, 249.

²⁰⁵ P. Battioni-Savignat, Y. Vo-Quang, and L. Vo-Quang, Bull. Soc. Chim. Fr., 1967, 3929.

²⁰⁶ P. Battioni-Savignat, L. Vo-Quang, and Y. Vo-Quang, Bull. Soc. Chim. Fr., 1970, 3942.

²⁰⁷ K. L. Erickson and J. Wolinsky, J. Amer. Chem. Soc., 87, 1142 (1965).

²⁰⁸ P. Le Perchec and J.-M. Conia, Tetrahedron Lett., 1970, 1587.

²⁰⁹ D. K. Black and S. R. Landor, Tetrahedron Lett., 1963, 1065.

²¹⁰ S. D. Andrews and J. C. Smith, Chem. Ind. (London), 1966, 1636.

²¹¹ G. Wittig and J. J. Hutchison, Justus Liebigs. Ann. Chem., 741, 79 (1970).

iodide.²¹¹ The products formed in 50% yield were 2-methylenebicyclo-[3.3.0]octane (158) and its spiro derivative 159 produced by subsequent cyclopropanation. The nature of the primary product suggests that methylene transfer may lead to a free carbene (or its complex with zinc



iodide), which undergoes transannular carbon-hydrogen insertion in the expected manner to form a pentalane.

An early report²¹² of the synthesis of sterculic acid from stearolic acid and the zinc reagent could not be repeated by later workers who employed stearolic acid or its methyl and ethyl esters.^{210, 213, 213a}

The reaction of 1-methoxy-1-butyne with the zinc reagent was carefully investigated, and five products were isolated, none of which was a cyclopropene.²¹⁴ These five products and their yields were *cis*-160 (5%), *trans*-160 (7%), 161 (8.5%), *cis*- and *trans*-162 (5.3%), and 163 (3.2%). The nature of the products strongly implicates 1-ethyl-2-methoxycyclo-propene (164) as their progenitor. Further reaction of 164 with the zinc



reagent could give the bicyclobutane 165, which would be expected to isomerize to 2-ethyl-3-methoxy-1,3-butadiene (166). Stepwise methylene transfer to 166 would produce 161 and 163. The remaining products can be accounted for by invoking Lewis acid-catalyzed  $(Znl_2)$  isomerization

²¹² N. T. Castelluci and C. E. Griffin, J. Amer. Chem. Soc., 82, 4107 (1960).

²¹³ W. J. Gensler, M. B. Floyd, R. Yanase, and K. Pober, J. Amer. Chem. Soc., **81**, 2397 (1969).

^{213a} W. J. Gensler, M. B. Floyd, R. Yanasc, and K. W. Pober, J. Amer. Chem. Soc., **92**, 2472 (1970).

²¹⁴ M. Jautelat and V. Schwarz, Tetrahedron Lett., 1986, 5101.



of cyclopropene 164 to *cis*- and *trans*-2-methoxy-1,3-pentadiene (167) which can undergo cyclopropanation at the  $C_1, C_2$  double bond to yield the observed *cis*- and *trans*-160. Finally, cyclopropanation of *cis*- and *trans*-160 would give the observed *cis*- and *trans*-162.

Acetylenic carbinols react with the zinc reagent to give in low yield a mixture of a cyclopropylcarbinyl ketone and an  $\alpha,\beta$ -unsaturated ketone.²¹⁵ The mechanism of this interesting transformation is unknown, but it is possible that a cyclopropene intermediate **169** is involved as shown in the accompanying equation. It is anticipated that the cyclopropene would be



formed via a complex, 168, and be subsequently isomerized by zinc iodide to an enolate butadiene, 170, in exactly the same manner proposed

²¹⁵ M. Vidal, C. Dumont, and P. Arnaud, Tetrahedron Lett., 1966, 5081.

for  $164 \rightarrow 167$ . Cyclopropanation of the tautomerized  $\beta,\gamma$ -unsaturated ketone 171 would be expected to yield the observed cyclopropylcarbinyl ketone 172. Further acid-catalyzed rearrangement of the butadiene or its tautomer could give the  $\alpha,\beta$ -unsaturated ketone 173.

Terminal acetylenes undergo an apparent insertion reaction at the acetylenic carbon-hydrogen bond  $(174\rightarrow 175)$ , but the mechanism of the

$$\begin{array}{ccc} \mathrm{RC} \equiv \mathrm{CH} & \longrightarrow & \mathrm{RC} \equiv \mathrm{CCH}_3 \\ 174 & 175 \end{array}$$

transformation is not yet clear.²¹⁶ The yields from alkynes are usually low but are moderate from phenylacetylenes,^{216. 217} e.g., p-methoxyphenylacetylene gave 1-(p-methoxyphenyl)propyne in 52.5% yield. The insertion product is often accompanied by small amounts of the corresponding terminal allene. Terminal diacetylenes similarly undergo the insertion reaction, exemplified by 1,3-pentadiyne which gave 2,4hexadiyne in 21% yield.²¹⁷ Enynes react at the terminal acetylenic carbon-hydrogen bond and at the double bond in the normal manner, e.g., 2-t-butyl-1-buten-3-yne gave 176 (56.5%), 177 (4.3%), and 178 (15%), from which it is clear that the terminal insertion reaction competes very effectively with the methylene-transfer reaction.²¹⁷ Unconjugated terminal diynes have also been studied.^{218, 219}

$$CH_2 = CC \equiv CH \longrightarrow CH_2 = CC \equiv CCH_3 + \bigcirc C \equiv CH_3 - CC \equiv CCH_3 + \bigcirc C \equiv CCH_3 + \sub C \equiv CCH_3 + \fbox C = CCH_3 + \sqsubset C = CCH_3 + \fbox C = CCH_3 + \sqsubset C = CCH_3 + \fbox C = C$$

Unsaturated Organometallic Compounds. The cyclopropanation of several organometallic compounds containing carbon-carbon double bonds has been carried out successfully with iodomethylzinc iodide. An early demonstration was the conversion of divinylmercury to dicyclopropylmercury (179) by the zinc reagent prepared *in situ* in tetrahydrofuran.²²⁰ Group IV metal compounds containing a vinyl group bonded to

- L. Vo-Quang and P. Cadiot, and A. Willemart, C. R. Acad. Sci., Paris, 255, 950 (1962).
   L. Vo-Quang and P. Cadiot, Bull. Soc. Chim. Fr., 1965, 1525.
- ²¹⁸ Y. Vo-Quang, L. Vo-Quang, and G. Emptoz, C. R. Acad. Sci., Paris, 258, 4586 (1964).
- ²¹⁹ G. Emptoz, L. Vo-Quang, and Y. Vo-Quang, Bull. Soc. Chim. Fr., 1965, 2653.
- ²²⁰ E. Tobler and D. J. Foster, Z. Naturforsch., B, 17, 135 (1962).

the metal react normally with the zinc reagent. Thus trimethylvinylsilane, trimethylvinylgermane, and trimethylvinylstannane gave the cyclopropyl derivatives 180 in yields of 50, 29, and 19%, respectively.²²¹ The lower yield of the stannane is caused by an unrelated redistribution reaction of tin compounds induced by zinc iodide formed in the reaction. Allyltrimethylgermane and other Group IV derivatives have afforded the corresponding cyclopropanes.²²²

A technique for the stereospecific preparation of cyclopropanes from 1-alkynes has been reported which involves addition of bromomethylzinc bromide to an intermediate 1-alkenylalane. An example is provided by 1-hexyne which is converted to the *trans*-1-alkenylalane 181 with diisobutylaluminum hydride followed by reaction with methylene bromide and zinc-copper couple. The resulting cyclopropylaluminum derivative 182 can be transformed to various cyclopropanes, *e.g.*, the hydrocarbon (62%) and the bromide (58%).²²³



An apparent insertion reaction by the zinc reagent into the siliconhydrogen bond has been observed. When iodomethylzinc iodide or bromomethylzinc bromide was allowed to react with triethysilane, methyltriethylsilane was formed in 64 and 55% yields, respectively.²²⁴

²²¹ D. Seyferth and H. M. Cohen, Inorg. Chem., 1, 913 (1962).

²²² I. E. Dolgii, A. P. Meshcheryakov, and G. K. Gaivoronskaya, *Izv. Akad. Nauk SSSR*, Otd. Khim. Nauk, **1963**, 1111 [C.A., **59**, 7551f (1963)].

²²³ G. Zweifel, G. M. Clark, and C. C. Whitney, J. Amer. Chem. Soc., 93, 1305 (1971).

²²⁴ D. Seyferth, H. Dertouzos, and L. J. Todd, J. Organometal. Chem., 4, 18 (1965).

The insertion reaction whose mechanism is unknown was shown by competition experiments to occur much more rapidly than addition of

$$(C_2H_5)_3SiH + XCH_2ZnX \rightarrow (C_2H_5)_3SiCH_3 + ZnX_2$$
  
(X = Br, I)

the zinc reagent to alkenes. The zinc reagents prepared from methylene iodide or ethylidene iodide and diethylzinc have also been shown to undergo insertion reactions into silicon-hydrogen bonds and tin-hydrogen bonds (see Table IV).²²⁵

$$R_3MH + R'CHI_2 + (C_2H_5)_2Zn \rightarrow R_3MCH_2R'$$

It might be mentioned here that halomethylzinc halides undergo the following reactions with tin and lead chlorides.²²⁶ Similarly,  $(CH_3)_2$ Sn-

$$\begin{split} \mathrm{XCH_2ZnX} &+ (\mathrm{CH_3})_3\mathrm{SnCl} \rightarrow (\mathrm{CH_3})_3\mathrm{SnCH_2X} + \mathrm{ZnXCl} \\ & \mathrm{X=Br, 86\%; X=1, 84\%} \\ \mathrm{ICH_2ZnI} &+ (\mathrm{CH_3})_2\mathrm{SnCl_2} \rightarrow (\mathrm{CH_3})_2\mathrm{Sn}(\mathrm{CH_2I})_2 \\ & \mathrm{ICH_2ZnI} + (\mathrm{CH_3})_2\mathrm{PbCl_2} \rightarrow (\mathrm{CH_3})_2\mathrm{Pb}(\mathrm{CH_2I})_2 \\ & \mathrm{31\%} \end{split}$$

 $(CH_2Br)_2$ ,  $C_6H_5(CH_3)_2SnCH_2I$ ,  $(C_6H_5)_3SnCH_2I$ ,  $Sn(CH_2I)_4$ ,  $(C_6H_5)_3PbCH_2I$ ,  $(CH_3)_3GeCH_2I$ , and  $(CH_3)_3GeCH_2Ge(CH_3)_3$  were prepared.^{226a}

**Carbon-Oxygen Double Bonds.** The carbonyl group of aldehydes and ketones reacts with the zinc reagent under special conditions to give terminal olefins in a transformation reminiscent of the Wittig reaction. Under the usual conditions, iodomethylzinc iodide gives normal cyclopropanation of unsaturated ketones (p. 43).

It was initially observed that  $17\beta$ -acetoxy- $11\beta$ -hydroxyestr-5(10)-en-3one (183) reacted with the preformed zinc reagent, prepared using a large excess of zinc-copper couple relative to methylene iodide, to give the 3methylene compound  $184.^{31}$  When the preparation of the reagent was interrupted after an intermediate time and the reaction then carried out, the *spiro*-steroid 185 could also be isolated. The influence of the  $11\beta$ hydroxyl group is vital, since the saturated 3-and 17-keto steroids and the 11-deoxy analog of 183 failed to react with the zinc reagent under these conditions. In contrast to these results, when ketone 183 was treated with

J. Nishimura, J. Furukawa, N. Kawabata, J. Organometal. Chem., 29, 237 (1971).
 D. Seyferth and S. B. Andrews, J. Organometal. Chem., 18, P21 (1969).

^{226a} D. Seyferth and S. B. Andrews, J. Organometal. Chem., 30, 151 (1971).



the zinc reagent prepared in situ using a 1:1 molar ratio of zinc and methylene iodide, a product 186 of angular methylation at  $C_{10}$  was



observed. The formation of 186 can be explained by  $ll\beta$ -hydroxylassisted cyclopropanation followed by alkoxide-catalyzed ring opening or directly by reaction of the complex with a  $\Delta^{3.5(10)}$ -dienolate formed by Lewis acids present.

These unusual observations have been clarified by a more detailed study which has provided a convenient alternative to the Wittig reaction for the transfer of a methylene group to aldehydes and ketones.¹⁴

The zinc reagent prepared *in situ* or by refluxing methylene iodide and zinc-copper couple in ether for up to 1 hour reacts with saturated ketones to give low yields of a mixture of the corresponding terminal olefin and its cyclopropanation product. Thus  $5\alpha$ -androstan-3-one gave 3,3-methylene- $5\alpha$ -androstane (187) and 3,3-ethano- $5\alpha$ -androstane (188).¹⁴ When the saturated ketone contains a hydroxyl group that can form a complex



with the reagent and orient the addition to the carbonyl group, good yields are obtained of the ethano derivative, e.g.,  $17\alpha$ -hydroxypregn-4ene-3,20-dione gave only 190 in 89% yield. This case makes it clear that



the hydroxyl-assisted reaction with carbonyl groups competes effectively with cyclopropanation of an  $\alpha,\beta$ -unsaturated ketone.  $\alpha$ -Hydroxy groups are particularly potent in facilitating the addition to the carbonyl group.

The zinc reagent preformed by heating methylene iodide with zinccopper couple under reflux for 2-4 hours or by employing a large excess of zinc-copper couple reacts with  $\alpha$ -hydroxy ketones to give good yields of the terminal olefin, *e.g.*, the pregnenedione gave 189 in 93% yield.¹⁴

These results can be rationalized by the intermediacy of zinc reagents containing the function  $-(ZnCH_2Zn)$  as shown in the accompanying equation. The usual zinc reagent prepared stoichiometrically in short

$$ICH_2ZnI + Zn \rightleftharpoons CH_2(ZnI)_2 \rightleftharpoons \frac{1}{2}Zn(CH_2ZnI)_2 + \frac{1}{2}ZnI_2$$

reaction times consists largely of iodomethylzinc iodide but may contain some bis(iodozinc)methylene  $[CH_2(ZnI)_2]$  and bis(iodozincmethylene)zinc  $[Zn(CH_2ZnI)_2]$ . It has been suggested that the two latter species react with hydroxy ketones in a manner somewhat analogous to that of hydroxy olefins, involving an intermediate complex or zincate 191 which reacts intramolecularly by addition/elimination (192 $\rightarrow$ 193). Under the usual



conditions, iodomethylzinc iodide is present and the intermediate hydroxy methylene compound 193 is converted further to the cyclopropane derivative 194. Long reaction times during preparation of the reagent or the presence of excess zinc reduces the concentration of iodomethylzinc iodide and allows isolation of 193. Thus the ROZnCH₂ZnI complex at C-11 in ketone 183 is of the proper size and configuration to react at the C-3 carbonyl group in Wittig fashion.

The olefination of carbonyl groups by gem-dimetallic reagents appears to be general^{227, 228} and lends support to the postulated  $-(ZnCH_2Zn)$ species. Other ketones such as hydroxymethyl (6-methoxy-2-naphthyl) ketone and  $\omega$ -hydroxyacetophenone have given the corresponding ethano



derivatives 195 and 196, respectively.¹⁴ In other work, the carbonyl group of acetophenone, benzophenone, diethyl ketone, and methyl benzoate failed to react usefully with the zinc reagent.²²⁹

Aliphatic and aromatic aldehydes react with iodomethylzinc iodide, prepared in tetrahydrofuran using excess zinc, to produce the corresponding olefins in 40-70% yields.²²⁹⁻²³¹ 2-Naphthaldehyde gave 2-vinylnaphthalene in 55% yield, and cinnamaldehyde gave 1-phenyl-1,3-butadiene but no subsequent cyclopropane derivative was formed, showing that the reaction with aldehyde groups must be facile.

It has been observed that benzoyl chloride and iodomethylzinc iodide react in dioxane to form benzoic anhydride in 60% yield.²³² In tetrahydrofuran the products were 4-iodobutyl benzoate (50%) and 4-chlorobutyl benzoate (29%), and in ether the major product was ethyl benzoate. Similarly, bis(chloromethyl)zinc reacted with acetyl chloride in ether to

- ²³⁰ H. Hashimoto, M. Hida, and S. Miyano, J. Organometal. Chem., 10, 518 (1967).
- ²³¹ S. Miyano, M. Hida, and H. Hashimoto, J. Organometal. Chem., 12, 263 (1968).

²²⁷ G. Cainelli, F. Bertini, P. Grasselli, and G. Zubiani, Tetrahedron Lett., 1967, 5153.

²²⁸ F. Bertini, P. Grasselli, G. Zubiani, and G. Cainelli, Tetrahedron, 26, 1281 (1970).

²²⁹ S. Miyano, M. Hida, and H. Hashimoto, Kogyo Kagaku Zasshi, **69**, 2134 (1966) [C.A., **66**, 85547u (1967)].

²³² K. Torii, S. Miyano, M. Hida, and H. Hashimoto, Kogyo Kagaku Zasshi, 70, 1735 (1967) [C.A., 69, 10525p (1968)].

form ethyl acetate and 2-chloroethyl acetate, and the latter was the sole product in methylene chloride.²³³ The mechanisms of these transformations are not known with certainty, but extensions of these observations may have synthetic utility.

Carbon-Nitrogen Double Bonds. The zinc reagent has been reported not to undergo methylene transfer to the carbon-nitrogen double bond of simple imines such as benzalaniline, N-t-butylethylidenimine, and N-methyl-t-butylidenimine.^{233a} Somewhat unexpectedly, three-membered ring formation succeeds when the carbon atom of the imine bears an electron-withdrawing substituent (--CO₂R). Thus, ethyl t-butylimino-acetate reacted with iodomethylzinc iodide under the usual conditions to yield the corresponding aziridine ester in 40% yield.^{223a} This represents

$$(CH_3)_3CN = CHCO_2C_2H_5 \longrightarrow (CH_3)_3CN | CHCO_2C_2H_5 \cup CHCO_2C_2H_5 \cup CH_2 \cup$$

a new synthesis of aziridine esters which are difficultly accessible otherwise.

Angular Methylation. The introduction of angular methyl groups at positions of ring fusion has been achieved by four methods employing iodomethylzinc iodide. The cyclopropanation of the 5(10) bond of appropriate steroids, especially when the directive effects of hydroxyl groups to control stereochemistry of the methylene transfer are used, has been discussed previously. Acid-catalyzed ring opening of the  $\beta$ - or  $\alpha$ -cyclopropane gives rise to the natural or unnatural 19-methyl steroids.^{195, 201}

A second method takes advantage of the stereochemical control exerted by a carbomethoxy group in cyclohexenes by which methylene transfer is so directed that the carbomethoxy group and cyclopropane are *cis* oriented. The acids corresponding to the previously discussed *cis* diadducts 39 and  $40^{62}$  and  $42^{79}$  are smoothly decarboxylated and rearranged near their melting points to give 197 and 198, respectively, in which the cyclopropane ring and methyl group are *cis* oriented.

A third method of potential importance has made use of the stereochemical control afforded by a strategically placed hydroxyl group to orient methylene transfer to a vinyl ether at a ring junction. In this way the octalin 199 was cyclopropanated selectively to give 200 in 91%yield,²³⁴ and the synthesis was completed by cleavage of the cyclopropyl

²³³ V. J. Stenberg, K. Kubik, and J. D. Johnson, Abstracts, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964, No. N33.

^{233a} P. Baret, H. Buffet, and J.-L. Pierre, Bull. Soc. Chim. Fr., 1972, 825.

²³⁴ E. Wenkert and D. A. Berges, J. Amer. Chem. Soc., 89, 2507 (1967).



ether and isomerization of the intermediate cyclopropanol to 201. The method has been successfully employed subsequently.²³⁵

A fourth method makes use of iodomethylzinc iodide with a lithium enolate of an appropriate ketone and avoids isolation and further transformation of an intermediate cyclopropane.²³⁶ The ketone 202 was converted to the enol benzoate 203 which was cleaved to the lithium enolate 204. The enolate gave inseparable mixtures of mono-, di-, and tri-methylated ketones with methyl iodide, but reaction of 204 with iodomethylzinc iodide afforded 65-75% yields of a 3:1 mixture of *cis*and *trans*-205 directly and no polymethylated products were detected. The ketones 205 are apparently generated even before hydrolytic workup and, if the lithium salt of the expected cyclopropanol is an intermediate, the proton source is not yet clear.

71

 ²³⁵ R. E. Ireland, D. R. Marshall, and J. W. Tilley, J. Amer. Chem. Soc., 92, 4754 (1970).
 ²³⁶ H. W. Whitlock, Jr., and L. E. Overman, J. Org. Chem., 34, 1962 (1969).


Other Organometallic Methylene-Transfer Reagents. Several  $\alpha$ -haloorganometallic species are now known which apparently react with alkene double bonds by variants of the methylene-transfer mechanism. The transition group zinc, cadmium, and mercury compounds are particularly effective, and examples of lithium, magnesium, aluminum, and indium species have been reported. An interesting example of related zinc reagents has been provided by bis(dichloromethyl)zinc (206), which has been prepared by the reaction of diehloromethyllithium with zinc

LiCHCl₂ 
$$\xrightarrow{\text{ZnCl}_2}$$
 Zn(CHCl₂)₂  $\xrightarrow{\text{cyclohexene}}$  benzene  
206

chloride at low temperature.²³⁷ This reagent transfers a chloromethyl group to cyclohexene in benzene but not in tetrahydrofuran.

Cadmium³ and indium^{237a} effectively replace zinc in another variation of the cyclopropane synthesis. For example, diethylcadmium and methylene iodide react in ether presumably to form ethyliodomethylcadmium which transfers methylene to carbon-carbon double bonds in high yields.²³⁸ The reactions are stereospecific with respect to alkene substituents and no carbon-hydrogen insertion is detected, *e.g.*, *cis*-propenyl *n*-propyl ether gave **207** in 87% yield. The scope of this method appears to parallel



²³⁷ G. Kobrich and H. R. Merkle, Chem. Ber., 99, 1782 (1966).
 ^{237a} T. Maeda, H. Tada, K. Yasuda, and R. Okawara, J. Organometal. Chem., 27, 13 (1971).
 ²³⁸ J. Furukawa, N. Kawabata, and T. Fujita, Tetrahedron, 26, 243 (1970).

closely that of the corresponding zinc system. Ethylidene iodide and benzal iodide transfer ethylidene and benzylidene groups, and a comparison of the zinc and cadmium systems with benzal iodide in the accompanying equation suggests that the transition states for transfer reactions are similar for the two metals. Although the reagent from



ethylidene iodide and diethylzinc gave syn/anti = 1.5 with cyclohexene in *n*-pentane, the ratio is reversed (syn/anti = 0.9) with the cadmium reagent in cyclohexane. The cadmium reagent from methylene iodide reacts with terminal acetylenes²³⁸ to give mixtures of allenes (major product) and methylacetylenes in a manner analogous to the zinc reagent.²¹⁷

Bromomethylmercuric bromide and bis(bromomethyl)mercury transfer methylene to alkenes in a synthetically useful manner, especially when it is desirable to avoid the presence of strong Lewis acids in the reaction medium (Seyferth, Eisert and Todd, 1964²³⁹ and Seyferth, Turkel, Eisert and Todd, 1969²⁴⁰). Bis(bromomethyl)mercury (208) reacts slowly (8 days) with cyclohexene and gives bicyclo[4.1.0]heptane in 74% yield, whereas bromomethylmercuric bromide brings about cyclopropanation only in the presence of diphenylmercury (presumably via C_eH₅HgCH₂Br).



Iodomethylmercuric iodide²⁴¹ and bis(iodomethyl)mercury behave similarly.^{6. 9. 239} A definitive study of these reactions showed that cyclopropanation occurs most likely via a methylene-transfer transition state, but

³³⁹ D. Seyferth, M. A. Eisert, and L. J. Todd, J. Amer. Chem. Soc., 86, 121 (1964).

³⁴⁰ D. Seyferth, R. M. Turkel, M. A. Eisert, and L. J. Todd, J. Amer. Chem. Soc., **91**, 5027 (1969).

³⁴¹ E. P. Blanchard, D. C. Blomstrom, and H. E. Simmons, J. Organometal. Chem., **3**, 97 (1965).

relative rate studies suggested that electronic factors are more important than steric factors in the case of mercury.²⁴⁰ The synthetic importance of organomercurials lies mostly in the phenyltrihalomethylmercurys, which generate dihalocarbenes under mild conditions.

Bromomethyllithium,²⁴² iodomethyllithium,¹¹ iodomethylmagnesium iodide,¹¹ several other magnesium species,^{32, 33} tris(iodomethyl)indium,²⁴³ iodomethyldiethylaluminum,^{28, 244} and chloromethylethylaluminum chloride⁴¹ have been reported to give bicyclo[4.1.0]heptane from reaction with cyclohexene. It has also been found that a mixture of an alkene and methylene chloride reacts with a magnesium film at 20 mm pressure to give low yields of cyclopropanes which are formed stereospecifieally and are unaccompanied by insertion products.³⁰ Zinc films reacted analogously and, on the basis that hydrolysis of films that had been exposed to methylene chloride gave only methane as product, it was suggested the cyclopropane-forming species were  $CH_2(MgCl)_2$  and  $CH_2(ZnCl)_2$ . Other interpretations are possible, however, for the latter observations.

Many species that might be considered complexes of carbenes and metals are known which react with olefins to form cyclopropanes. The reaction of polyhalomethanes with chromous sulfate in aqueous dimethylformamide in the presence of olefins gives cyclopropanes, and a chromium carbenoid has been postulated.²⁴⁵ An iridium carbenoid, [(C₆H₅)₂P]₂Ir(Cl)(CO)CH₂, prepared from [(C₆H₅)₂P]₂Ir(Cl)CO and diazomethane, reacted with styrene to give a mixture of phenylcyclopropane and  $\alpha$ -methylstyrene but only traces of norcarane from cyclohexene.²⁴⁶ A copper carbenoid was implicated in the reaction of (ArO)₃PCuCl with ethyl diazoacetate in the presence of cyclohexene.²⁴⁷ Analysis of the mixture of exo- and endo-7-carbethoxynorcarane obtained and the nature of ligand effects demonstrates that methylene-transfer transition states were not involved. On the other hand, the half-sandwich cyclopentadienyl(chloromethyl)iron dicarbonyl, (C5H5)Fe(CO)2CH2Cl, gave cyclopentadienyliron dicarbonyl chloride and norcarane in 80% yield when heated with cyclohexene at 50°.248 It was suggested that cyclopropane formation occurred by methylene transfer. A review of transition metal-carbene complexes has appeared.^{248a}

- 242 W. T. Miller and C. S. Y. Kim, J. Amer. Chem. Soc., 81, 5008 (1959).
- 242 K. Schwarzenbach, Thesis, Zürich, 1961.
- ²⁴⁴ D. B. Miller, Tetrahedron Lett., 1964, 989
- 248 C. E. Castro and W. C. Kray, Jr., J. Amer. Chem. Soc., 88, 4447 (1966).
- 246 F. D. Mango and I. Dvoretzky, J. Amer. Chem. Soc., 88, 1654 (1966).
- 247 W. R. Moser, J. Amer. Chem. Soc., 91, 1141 (1969).
- 248 P. W. Jolly and R. Pettit, J. Amer. Chem. Soc., 88, 5044 (1966).
- 248a D. J. Cardin, B. Cetinkaya, and M. F. Lappert, Chem. Rev., 72, 545 (1972).

#### EXPERIMENTAL CONDITIONS

It is important to recognize that the cyclopropanation of unsaturated compounds by methylene iodide and zinc-copper couple or by its variants involves a reactive, yet discriminating, organometallic intermediate whose reactivity varies considerably with the substrate. Furthermore, the zinc reagent slowly attacks many of the solvents which are otherwise most useful in synthesis, and it undergoes other self-destructive decompositions as well.⁴ For these reasons the method by which iodomethylzinc iodide or its equivalent is generated, whether it is generated in situ or prepared before the substrate is added, the solvent used, and the reaction conditions employed determine the yields of product and often the success or failure of the synthesis. The cyclopropanation reaction has seen several minor and a few major variations in experimental conditions. some of which are significant, but it has not yet been practicable to normalize all these modifications. It is therefore important that the experimenter consult the original literature for analogous reactions listed in the Tabular Survey.

#### Variations of the Method

Three principal experimental techniques have been employed to generate  $\alpha$ -halomethylzinc species that are capable of methylene-transfer reactions: (A) reaction of methylene iodide with a zinc-copper couple in an ether solvent; (B) reaction of a diazoalkane with zinc halides in an ether solvent; and (C) reaction of methylene or an alkylidene iodide with diethylzinc in ether or hydrocarbon solvents. For synthetic purposes, method A has been used far more extensively because it is generally the simplest, most convenient, and most economical variation when applicable. More experimental information is available concerning this method, and important modifications are known. For these reasons, most attention has been given to method A in this section, but examples of all three methods are provided.

## Method A [Methylene Iodide/Zinc-Copper Couple]

Zinc-Copper Couple. The method of preparation of the zinc-copper couple is an important factor in determining its reactivity toward methylene iodide in ether solvents and in achieving reproducible yields of cyclopropanes. Although cyclopropanation has been demonstrated with many couples, only four have proved reliable. Couples I, II, and III have been used for the bulk of the cyclopropanations described thus far in the literature, and couples II and III offer the advantages of ease of preparation and of good reproducibility. Couple IV has been described recently, and preliminary results suggest that it will be valuable in the cyclopropanation reaction. The yields of cyclopropanes are comparable when couples I, II, and III are used in the cyclopropane synthesis, and limited studies indicate that couple IV may give the highest yields.

Couple I (Simmons and Smith) is prepared by reduction of a mixture of powdered zinc and cupric oxide at 500° in an atmosphere of hydrogen. A detailed procedure has been given for the preparation^{6. 13} based on an original method.²⁴⁹ The couple shows no loss in activity on storage, even when precautions are not taken to exclude oxygen and atmospheric moisture. This couple reacts with methylene and alkylidene iodides and chloroiodomethane in diethyl ether and other ether solvents at 35°,^{4. 6. 27} but it does not form a zinc reagent with methylene chloride or bromide under these conditions. Couple I was employed in some of the early cyclopropanation studies, but it was largely supplanted by couple II within two or three years of the first successful cyclopropane synthesis.¹ Reproducible yields of cyclopropanes can be obtained with couple I, but its major disadvantage is the tedious preparation compared with that required for other couples.

Couple II (Shank and Shechter) is prepared by precipitation of copper from cupric sulfate solution onto freshly acid-washed zinc powder.²⁵⁰ A detailed procedure has been given for the preparation in *Organic Syntheses.*¹³ This couple offers the advantages of ease and rapidity of preparation, good storage properties, and reproducibility of yields in cyclopropanation, and it shows the same reactivity toward gem-dihalides as couple I. Couple II has been the most widely used in the cyclopropane syntheses reported in the literature up to 1972.

Couple III (LeGoff) is prepared by treating zinc dust or granules with a hot solution of cupric acetate in acetic acid.⁸ This couple is highly active and forms zinc reagents in ether solution from methylene iodide and bromide but not chloride. The yields of cyclopropanes obtained using methylene iodide are generally higher than those obtained using methylene bromide. A subsequent study of the influence of copper content in couple III on the yield of cyclopropane products showed a rather sharp maximum at 0.5% copper when an unsaturated steroidal alcohol was the substrate.²⁰⁶ Couple III is widely employed currently in the literature, and it shows all of the advantages of couple II as well as being highly active toward gem-diiodides and dibromides.

Couple IV (Rawson and Harrison) is prepared by heating at reflux a suspension of zinc dust and cuprous chloride in ether under nitrogen.⁸⁷ Its preparation, unlike that of other couples, uses equivalent quantities of both zinc and cuprous chloride. The couple is formed rapidly, and methylene iodide and an olefinic substrate are added subsequently to the same vessel to effect the cyclopropanation reaction. When the olefin/zinc

²⁴⁹ F. L. Howard, J. Res. Nat. Bur. Stand., A, 24, 677 (1940).

²⁵⁰ R. S. Shank and H. Shechter, J. Org. Chem., 24, 1825 (1959).

ratio was 2.6, the following cycloalkenes gave the expected bicycloalkanes in the yields shown: cyclohexene, 92%; *cis*-cyclooctene, 94%; cyclododecene, 79%. Styrene gave phenylcyclopropane in 69% yield. Copper powder in place of the salt also serves in the preparation of a similar couple which gives slightly reduced yields (cyclohexene, 87%). The zinc reagent can be preformed and olefinic substrates added subsequently;⁸⁷ for example, the reaction of isotetralin with the preformed reagent using couple IV gave a 50% yield of **52** and no other monoadduct was formed.⁹³ Couple IV has been employed successfully in the first example of a methylene-transfer reaction to the carbon-nitrogen double bond of certain imines.^{233a} This couple has seen limited use at present, but the preliminary findings show considerable promise for its utility.

Couple V (Conia, Denis and Girard) is prepared by adding granular zinc to a hot solution of silver acetate in acetic acid.^{252a} Compared to Zn(Cu) couples, use of the Zn(Ag) couple often gives higher yields of cyclopropanes with olefins, requires only a small excess in practice, and allows shorter reaction times. A further modification of value involves addition of pyridine during workup to complex the zinc salts, thus insuring complete hydrolysis of intermediate complexes when functional groups such as esters, aldehydes, and ketones are present in the products. The use of Zn(Ag) couple appeared in the literature too late for examples to be included in the Tabular Survey. A general procedure is given on p. 93, and the primary source should be consulted.^{144a.252a}

The first zinc-copper couple used to effect a cyclopropanation reaction²⁵ was prepared by heating granulated zinc and copper powder over a free flame,²⁵¹ but different batches varied considerably in reactivity toward methylene iodide. Couples prepared by the thermal decomposition of cupric citrate in the presence of zinc dust²⁵² reacted sluggishly with methylene iodide. A commercial zinc-copper couple (Ventron/Alfa Inorganics, Inc.) has been used successfully in cyclopropanations.¹⁶⁴

**Reagents.** No special precautions associated with purity of reagents are generally necessary in order to carry out successful cyclopropanations. Methylene iodide, solvents, and substrates, however, must be dried and preferably anhydrous, for small quantities of water react with initially formed zinc reagent to foul the couple surface. Commercial methylene iodide often contains small amounts of iodoform, but this does not seem to affect overall yields of cyclopropanes appreciably. Chloroiodomethane and methylene bromide can be used in place of methylene iodide, but only couple III seems sufficiently active to react usefully with the bromide. Although few workers have taken the precaution of using ether solvents which have been purified to remove peroxides, it has been reported that

²⁵¹ E. Krause and A. von Grosse, Die Chemie der Metallorganischen Verbindungen, Borntraeger, Berlin, 1937, p. 63.

²⁵² R. C. Krug and P. J. C. Tang, J. Amer. Chem. Soc., 76, 2262 (1954).

^{252a} J. M. Denis, C. Girard, and J. M. Conia, Synthesis, 1972, 549.

high yields of cyclopropanes were obtained from methyl oleate and elaidate only after the removal of peroxide impurities from the starting materials.¹³⁴

1,1-Dideuteriocyclopropanes are readily synthesized from dideuteriomethylene iodide by method A.⁴ A very convenient synthesis of  $\rm CD_2Br_2$ and  $\rm CD_2I_2$  has been described.²⁵³

Solvents. A solvent must meet several requirements in method A: (1) it must support the heterogeneous reaction of methylene iodide and zinc metal; (2) it must stabilize iodomethylzinc iodide, bis(iodomethyl)zinc, or equivalent species capable of methylene transfer; (3) it must not be subject to rapid attack by the zinc reagent at temperatures between 25 and  $60^{\circ}$ ; (4) it must not accelerate self-destructive decompositions of the zinc reagent, e.g., to ethylene; and (5) it must not so strongly solvate the zinc reagent as to interfere with the methylene-transfer process. Ethers conform well to these requirements, and experience has confirmed the original finding that diethyl ether is the best all-around solvent for carrying out the cyclopropane synthesis.⁶ Ethers promote the reaction of methylene iodide and zinc-copper couple, and the order of effectiveness is dimethoxyethane > tetrahydrofuran > diethyl ether. The reaction in dimethoxyethane is exothermic and requires no initiation by a catalytic quantity of iodine. On the other hand, ethers are attacked by the zinc reagent, and the rate of this reaction occurs in the same order. Diethyl ether has proved to be the best compromise, but it does react slowly with iodomethylzinc iodide to form ethyl isopropyl ether, methyl iodide, and propylene.⁴ In one study, diethyl ether gave yields of cyclopropanes twice those obtained in other ethers.²⁷

A modification of the usual procedure has been found valuable when the starting olefinic compound or cyclopropane product is unstable to the Lewis acid zinc iodide. This variant employs diethyl ether containing one equivalent of dimethoxyethane as solvent. Zinc iodide is precipitated rapidly and quantitatively as it is formed as the crystalline, insoluble 1:1 dimethoxyethane complex.²⁷ This solvent system has been used successfully in several instances.^{148, 190, 218}

Dimethoxyethane has been employed alone as solvent with commercial zinc dust (containing <0.01 % Cu) and methylene iodide. Under these conditions the reaction occurs exothermically, and phenanthrene has been cyclopropanated in this manner.⁷

Reference is made to the following solvents in which cyclopropanations have been carried out: ethyl acetate,⁶ tetrahydrofuran,^{155, 191, 218, 220} dimethoxyethane,^{156, 215, 219} dioxane,¹¹⁰ and di-*n*-butyl ether.²²¹ Other

²⁵³ J. G. Atkinson, D. W. Cillis, and R. S. Stuart, Can. J. Chem., 47, 477 (1969).

mixed solvents, such as diethyl ether/tetrahydrofuran,¹⁹¹ have been used. Often cyclopropanation is successful only in diethyl ether; for example, methylenecyclobutane gave spirohexane in this solvent, but the reaction failed in tetrahydrofuran and in dioxane.¹⁰¹ On the other hand, divinylmercury is converted readily to dicyclopropylmercury in tetrahydrofuran, but the reaction is reported to fail in diethyl ether.²²⁰

Reaction Conditions. The cyclopropane synthesis is normally carried out by stirring under reflux a suspension of zinc-copper couple in a solution of methylene iodide, unsaturated substrate, and ether. It is sometimes advantageous to add a small crystal of iodine which promotes formation of the zinc reagent, perhaps by cleansing the surface of the couple. Yields of cyclopropanes are highest when the reaction is run in relatively concentrated solution. One study employing cyclohexene (an alkene of average reactivity), methylene iodide, couple II, and ether found that the yield of norcarane was highest with a molar ratio 1:1:3, respectively.^{13, 27} In order to ensure high conversion of unsaturated compound to cyclopropane, many workers employ a large excess of the zinc reagent, and this procedure is often effective. For example, ratios as high as 16:1 zinc reagent/unsaturated compound have been used with the allene, methyl 3,4-pentadienoate.¹³⁶ Similarly, 2-methylenebornan-3one is cyclopropanated in yields of 33, 56, and 100% using ratios of zinc reagent/olefin of 1.4:1, 2.4:1, and 22:1, respectively.⁷⁷ It has been reported in one instance that the cyclopropanation reaction takes a different course when the zinc reagent is generated in the presence of excess zinc-copper couple.³¹

Reaction times have varied from 1 hour to 2 days. The cyclopropanation has often been run with excess reagent for long reaction times in order to maximize conversion of substrate to product. When excess zinc reagent is employed and self-destructive losses can be tolerated, the cyclopropane synthesis has been carried out to advantage in ether at elevated temperatures (60–100°) in sealed tubes^{86, 196, 201} or Parr bombs.^{109, 110} A modification that has been used with unsaturated hydroxy steroids involves initiation of the reaction under normal conditions, subsequent removal of ether solvent to leave a highly concentrated solution, and finally heating of this residue in a sealed tube at *ca*. 90°; estr-5(10)-ene-3 $\alpha$ ,17 $\beta$ -diol undergoes  $\alpha$ -face cyclopropanation under these conditions.¹⁹⁵ On the other hand, steroids in the 5(10)-ene-6 $\alpha$ ,17 $\beta$  series can be cyclopropanated at the  $\alpha$ -face under normal conditions.¹⁹⁷

For various purposes it is often desirable to preform the zinc reagent and subsequently add the substrate. This procedure has been employed when the substrate is decomposed or polymerized readily by zinc iodide, e.g., bicyclo[2.2.1]-heptadiene,^{25. 27} bicyclo[2.2.1]heptene,²⁵⁴ vinyl ethers,¹⁴² various hydroxyalkenes,^{4. 255} allylamine,¹²⁶ and enamines.¹⁶¹

Other modifications on the normal conditions have been reported. The zinc reagent has been generated *in situ* at low concentration by adding methylene iodide gradually after reaction has been initiated. In this way the yield of cyclopropanation product from 4-methyl-1-hexen-4-ol was increased from 20 to 80% by adding methylene iodide slowly to a mixture of zinc-copper couple and the unsaturated alcohol in ether.¹²⁷ Yields have been increased by recycling an initial reaction product by adding fresh methylene iodide and zinc-copper couple.^{130, 137}

Reaction mixtures are normally worked up by washing the ethereal solution with saturated ammonium chloride solution to remove zinc salts, and the product is isolated by appropriate techniques. In one instance excess methylene iodide was removed from the reaction mixture by addition of an alkene of low molecular weight, 2-methyl-2-butene, and zinc-copper couple, and the resulting trimethylcyclopropane was easily separated from the primary product.¹⁰² It has been found that addition of pyridine directly to the cooled reaction mixture is a method that avoids aqueous hydrolysis.^{252a} The complexed zinc salts can then be removed by filtration.

## Method B (Diazoalkanes/Zinc Halides)

Diazomethane and zinc iodide react in ether solution to form iodomethylzinc iodide and bis(iodomethyl)zinc depending on stoichiometry, and zinc chloride and bromide behave similarly.^{2, 27} The zinc reagents prepared by this method generally react with unsaturated compounds in the same manner as the iodomethylzinc iodide prepared in method A. Method B offers no practical advantages since diazomethane must be generated and dried by distillation, zinc iodide must be specially dried, and the yields of cyclopropane derivatives are often lower than those by Method A unless excess diazomethane is added during the cyclopropanation reaction.⁹ Cyclohexene gave bicyclo[4.1.0]heptane in 30% yield, but styrene could be converted to phenylcyclopropane in 85% yield using the special technique of adding excess diazomethane during the reaction.⁹ Yields up to 73% of bicyclo[4.1.0]heptane have been obtained from bis(chloromethyl)zinc and bis(iodomethyl)zinc, and the bicyclo[2.2.1]heptane derivatives 33, 34, and 36 (p. 29) were prepared by this method.⁶⁵

Reproducible conditions have been given for carrying out method  $B^{10, 12}$ and this is the best technique for preparation of moderately clean solutions of  $XCH_2ZnX$  and  $(XCH_2)_2Zn$  when such solutions are needed for other than synthetic purposes.

²⁵⁴ R. C. DeSelms and C. M. Combs, J. Org. Chem., 28, 2206 (1963).

²⁵⁵ L. A. Paquette and R. F. Eizember. J. Amer. Chem. Soc., 91, 7108 (1969).

Method B is also valuable because some substituted diazomethanes can be employed, *e.g.*, phenyldiazomethane gives phenylcyclopropanes, and clear procedures for carrying out these reactions have been published.^{51, 52}

### Method C (Alkylidene Iodide/Diethylzinc)

An unsaturated compound, diethylzinc, and solvent are stirred under nitrogen (see note concerning precautions, p. 91), and methylene iodide is added dropwise, producing a mildly exothermic reaction. In this way, cyclopropanation occurs smoothly, and the yields of products are generally slightly higher on a mole basis than those by method  $A^{3, 83}$  The zinc species in method C is probably different from that involved in methods A and B, but it behaves similarly with respect to yields and rates of methylene transfer as a function of substrate. There is at least one instance reported in which cyclopropanation failed by method A but was successful by method C.¹²² From a practical standpoint, method C offers no advantages over method A since diethylzinc is not readily available and is flammable in air and precautions must be made to exclude the atmosphere during cyclopropanation. The reaction sometimes occurs explosively when diethylzinc is added to mixtures of unsaturated compound and methylene iodide in a solvent; this manner of addition should be avoided.

Unlike methods A and B, method C can be carried out in hydrocarbon solvents. In fact, the highest yields of cyclopropane products are obtained in hydrocarbons such as benzene.⁸³ Cyclopropanation yields are lower in ether solvents such as diethyl ether, tetrahydrofuran, dimethoxyethane, and diisopropyl ether, and yields generally decrease with an increase in solvent polarity.

Method C is, however, of particular value since the reaction has been extended successfully to ethylidene and benzylidene iodide.^{84.}¹⁶² Ethyland phenyl-cyclopropanes can be prepared in good yield in this manner, whereas the corresponding reactions by method A give poor yields. Phenylcyclopropanes are also conveniently prepared by method B. The reagent prepared from ethylidene iodide and diethylzinc reacts with alkylbenzenes to form mixtures of alkyl-substituted 7-methylcyclohepta-1,3,5-trienes,⁴⁹ and extensions of this method may prove valuable in the synthesis of tropylidenes.

An important modification of method C has been reported that involves generation of the reagent under conditions that avoid handling diethylzinc (Sawada and Inouye¹²⁴). A stock solution of ethylzinc iodide in ether is prepared and is stable to storage. When an aliquot of this solution is treated with methylene iodide, a mildly exothermic reaction occurs, presumably between the diethylzinc present in low concentration and methylene iodide. An olefin is then added, and after 0.5-5 hours at reflux the reaction is worked up in the usual manner.

Diethylcadmium can be used in place of diethylzinc in method C, and the cadmium methylene-transfer reagent behaves very similarly to the corresponding zinc reagent.²³⁸ Thus far, no synthetic advantages have been demonstrated using this variation.

#### EXPERIMENTAL PROCEDURES

#### Zinc-Copper Couples

Couple I (Simmons and Smith).^{6, 13} Mallinckrodt A. R. wire-form cupric oxide (30 g, 0.38 mol) is ground to a powder in a mortar and mixed with Mallinckrodt A. R. zinc dust (240 g, 3.68 g-atom). The mixture is placed in a Vycor combustion boat lined with copper foil, and a thermocouple is embedded in the powder. The boat is placed in a Vycor tube heated by a muffle furnace. A mixed gas (hydrogen, 65 liters per hour; nitrogen, 25 liters per hour) is passed through the tube while the temperature is raised to 500° during 4 hours. The mixture is kept at 500° for 0.5 hour, and the tube is then allowed to cool to room temperature in a hydrogen atmosphere. The zinc-copper couple is obtained as dark gray lumps, which are ground to a fine powder in a mortar before use. In some instances a small amount of material is found in the mixture which has apparently melted and agglomerated during heating. This shiny, metallic material is easily separated from the powdered couple and is not used in the preparation of cyclopropanes.

Couple II (Shank and Shechter).^{13. 250} In a 500-ml Erlenmeyer flask fitted with a magnetic stirrer are placed zinc powder (49.2 g, 0.75 g-atom) and 40 ml of 3% hydrochloric acid. The mixture is stirred rapidly for 1 minute, then the supernatant liquid is decanted. In a similar manner the zinc powder is washed successively with three additional 40-ml portions of 3% hydrochloric acid, five 100-ml portions of distilled water, two 75-ml portions of 2% aqueous copper sulfate solution, five 100-ml portions of distilled water, four 100-ml portions of absolute ethanol, and five 100-ml portions of absolute ether. The couple is finally transferred to a Büchner funnel, washed with additional anhydrous ether, covered tightly with a rubber dam, and suction-dried until it reaches room temperature. The zinc-copper couple is stored overnight in a vacuum desiccator over phosphorus pentoxide and is then ready for use.

Couple III (LeGoff).⁸ To a hot, rapidly stirred solution of cupric acetate monohydrate (2.0 g, 0.01 mol) in 50 ml of glacial acetic acid is added zinc dust (35 g, 0.54 g-atom). After about 0.5 minute all of the copper has deposited on the zinc. The couple is allowed to settle for 0.5-1 minute, then as much of the acetic acid as possible is decanted, care being

taken not to lose the siltlike couple. The dark reddish gray couple is then washed with one 50-ml portion of acetic acid followed by three 100-ml portions of ether. The moist couple is ready for use.

Couple IV (Rawson and Harrison).⁸⁷ A mixture of zinc dust (17.0 g, 0.26 g-atom) and cuprous chloride (2.58 g, 0.026 mol) in 40 ml of dry ether is stirred and heated to reflux in a nitrogen atmosphere for 30 minutes. The couple is not isolated but is used directly in the preparation of cyclopropanes. For example, cyclohexene (10.1 ml, 0.1 mol) and methylene iodide (10.5 ml, 0.13 mol) are added, and the mixture is maintained at reflux for 24 hours. In this manner, bicyclo[4.1.0]heptane is formed in 92% yield.

Couple V (Conia, Denis, and Girard).^{252a} To a hot stirred solution of silver acetate (100 mg) in acetic acid (100 ml), granular zinc (17 g, 0.26 g-atom) is added in one portion. The mixture is stirred for 30 sec, and the zinc-silver couple formed is isolated by decantation and is washed with ether (5  $\times$  100 ml). [N.B. The original prescription for washing the couple with acetic acid should be avoided, personal communication by Prof. J. M. Conia.] Anhydrous ether (150 ml) is then poured onto the product and 2 or 3 small pieces of silver wool are added. The couple is used directly in the cyclopropanation reaction.

#### Method A

Bicyclo[4.1.0]heptane (Norcarane).^{6.8.13} The procedure described in Organic Syntheses¹³ serves as a model for the general application of method A. A mixture of methylene iodide (190 g, 0.71 mol), zinc-copper couple II (46.8 g, 0.72 g-atom), cyclohexene (53.3 g, 0.65 mol), anhydrous ether (250 ml), and a crystal of iodine is heated under reflux for 15 hours. The decanted ether solution is washed with saturated ammonium chloride solution, sodium bicarbonate solution, and water. Distillation affords 35-36 g (56-58%) of norcarane, bp 116-117°,  $n^{25}$  D 1.4546.

Norcarane can also be prepared using methylene bromide in place of methylene iodide.⁸ Zinc-copper couple III (30.5 g, 0.47 g-atom) and dry ether (100 ml) are placed in a flask equipped with a dropping funnel, magnetic stirrer, and reflux condenser. A few milliliters of methylene bromide is added and, if reaction does not initiate spontaneously, the stirred mixture is warmed briefly. While the mixture is kept at reflux, a solution of methylene bromide (76.6 g, 0.44 mol total) and cyclohexene (23.8 g, 0.29 mol) is added over a period of roughly 1 hour. The mixture is stirred at reflux for 20-30 hours, cooled, and decanted into a separatory funnel containing a mixture of ice and 1 N hydrochloric acid. Care should be exercised because of gas evolution. The ethereal solution is separated, washed with a second portion of ice-hydrochloric acid, then three times with water, and dried over potassium carbonate. Distillation affords norcarane in 61 % yield.

cis- and trans-1,2-Diethylcyclopropane.⁶ A mixture of cis-3hexene (10.0 g, 0.12 mol), methylene iodide (31.6 g, 0.12 mol), zinc-copper couple II (9.8 g, 0.12 g-atom), and anhydrous ether (60 ml) is stirred and heated under reflux while maintaining anhydrous conditions. After 20 hours the mixture is cooled and decanted into a separatory funnel, and the solids are washed with 30 ml of ether. The combined ether solutions are washed with cold 5% hydrochloric acid, 5% aqueous sodium bicarbonate, and water, and dried over anhydrous magnesium sulfate. The ether is removed through an efficient packed column, and the residue is distilled through a semimicro spinning-band column. There is recovered 4.4 g of unreacted olefin, bp 66-67°,  $n^{25}$ D 1.3920. Pure cis-1,2-diethylcyclopropane is obtained as a colorless liquid, bp 93.5°,  $n^{25}$ D 1.4035. The yield is 4.0 g (34.5%).

Pure trans-1,2-diethylcyclopropane is synthesized in an entirely analogous manner from trans-3-hexene. The product, bp 86.5°,  $n^{25}$ D 1.3982, is obtained in 15.5% yield.

**Spirohexane.**¹⁰¹ This procedure has been reported to be the most convenient laboratory method for obtaining pure spirohexane. A mixture of methylene iodide (53.6 g, 0.20 mol), zinc-copper couple II (16.3 g, 0.25 g-atom), iodine (0.15 g, 0.0012 g-atom), and anhydrous ether (165 ml) is stirred and heated at reflux for 30 minutes. Methylenecyclobutane (27.2 g, 0.40 mol) is added dropwise over 30 minutes to maintain spontaneous refluxing. When addition is complete, the mixture is heated for an additional 20 hours. The cooled mixture is filtered through Super-Cel, and the resulting solution is extracted with 5% hydrochloric acid, saturated sodium bicarbonate solution, and saturated sodium chloride solution and then dried. Distillation through a 3-ft wire-spiral column gives 5.11 g (0.075 mol) of unreacted methylenecyclobutane. The residue is distilled through a Holzman column to yield 6 g (22.5%) of spirohexane, bp 68-70°,  $n^{25}$  D 1.4193 (97% purity by vapor-phase chromatography).

Cyclopropylcyclopropane.¹⁰⁹ The following procedure, although the yield is low, has been reported to be the most convenient one for obtaining cyclopropylcyclopropane, and it demonstrates the handling of a gaseous reactant. Methylene iodide (300.0 g, 1.12 mol) and anhydrous ether (400 ml) are placed in a 1-liter stainless-steel Parr pressure vessel equipped with an overhead stirrer. The vessel is sealed and cooled to 5°, at which time nitrogen is passed into the system. The bomb is opened and zinc-copper couple II (126 g, 1.93 g-atoms) is added followed by the rapid addition of 1,3-butadiene (30 g, 0.56 mol), which had been condensed in a test tube, and iodine (1.0 g, 0.0039 mol). The bomb is sealed, heated to  $50^\circ$ , and rapidly stirred. Heating is discontinued, and the temperature rises to  $130^\circ$  during 1 hour. The temperature is then maintained at  $65^\circ$  for 24 hours, and the bomb is cooled to room temperature and vented. The ethereal solution is filtered through Super-Cel and then washed with 5% hydrochloric acid, saturated aqueous sodium bicarbonate, and water. The dried solution is distilled to yield 7.3 g (16%) of pure cyclopropyl-cyclopropane, bp 70-74°.

exo-Tricyclo[3.2.1.0^{2.4}]oct-6-ene.²⁷ Zinc-copper couple II (37.5 g, 0.54 g-atom), methylene iodide (134 g, 0.5 mol), and bicyclo[2.2.1]heptadiene (46.0 g, 0.5 mol) are stirred and heated at reflux in ether (155 ml) for 19 hours. The slurry is treated with 200 ml of cold aqueous ammonium chloride, and the ether phase is separated and extracted with 150 ml of aqueous ammonium chloride, 200 ml of water, and 20 ml of 5 % aqueous sodium bicarbonate. The solution is dried, the ether is removed by distillation, and the residue is distilled under high vacuum into a dry ice-cooled receiver. Fractionation then gives 9.9 g (19%) of product, bp 125–130°, containing exo-tricyclo[ $3.2.1.0^{2.4}$ ]oct-6-ene (ca. 73%), endo-tricyclo[3.2.1.0^{2, 4}]oct-6-ene (ca. 18%), and an unknown (ca. 9%) by vapor-phase chromatographic analysis. The exo isomer is purified by dissolving the product in 50 ml of saturated aqueous silver nitrate, from which a crystalline adduct separates on standing. The cooled mixture is filtered, and the adduct decomposed by steam distillation from 65 ml of water. The exo isomer (3.47 g),  $n^{25}$ D 1.4875, obtained in this manner was of 96.3% purity by vapor-phase chromatographic analysis.

**Bicyclo[4.1.0]heptan-2-one.**⁷⁷ Zinc-copper couple III (prepared from zinc (2.8 g, 0.043 g-atom) and cupric acetate monohydrate (0.16 g, 0.08 mol)) in anhydrous ether (20 ml) is heated to gentle reflux, and a few drops of methylene iodide is added. After the mild exothermic reaction has been initiated, a mixture of cyclohex-2-en-1-one (0.96 g, 0.01 mol) and methylene iodide (7.5 g, 0.027 mol) is added dropwise over 30 minutes. The mixture is heated under reflux for 36 hours and then cooled. Water (2 ml) is added dropwise and the mixture stirred for 1 hour. The precipitated zinc hydroxide is removed by centrifugation, and the ether layer is washed with 10% hydrochloric acid and with water. Distillation affords 1.0 g (90%) of bicyclo[4.1.0]heptan-2-one, bp 91° (15 mm).

Ethyl Spiropentanecarboxylate.^{136, 137} A mixture of zinc-copper couple II (82.0 g, 1.25 g-atoms) and methylene iodide (230 g, 0.86 mol) in dry ether (250 ml) is stirred and heated under reflux for 30 minutes. Ethyl 2-methylenecyclopropane carboxylate (34.0 g, 0.28 mol) is added, and the mixture is heated under reflux for 60 hours. The mixture is cooled, filtered, and washed successively with several portions each of dilute hydrochloric acid, dilute ammonium hydroxide, and water. The dried solution is concentrated to give 39.5 g of a yellow oil which contains 27 % ethyl spiropentanecarboxylate and 73 % unreacted starting ester (vaporphase chromatography, Apiezon). The crude product is recycled twice with the same quantities of reagents to give 39.7 g of a mixture containing 76% ethyl spiropentanecarboxylate. Distillation affords product of 84% purity, bp 83-84° (43 mm), and  $n^{22}$ D 1.4406. Overall yields of 70% can be realized, and final purification of the product is best carried out by preparative vapor-phase chromatography.

Methyl (Z,Z)-2-([2-Pentylcyclopropyl]methyl)cyclopropanoctanoate.¹³¹ A mixture of zinc-copper couple III (2 g, 0.031 g-atom) and dry ether (10 ml) is stirred, and a solution of methylene iodide (13.3 g, 0.050 mol) and methyl (Z,Z)-9,12-octadienoate (methyl linoleate) (0.2 g, 0.00068 mol) in dry ether (5 ml) is added at a rate to maintain spontaneous refluxing. The mixture is heated under reflux overnight, decanted from unreacted couple, and washed three times with cold 1 N hydrochloric acid and three times with water. The solution is dried, and the ether and unreacted methylene iodide are removed under reduced pressure. Chromatography of the crude product on a column of Florisil (20 cm  $\times$ 1 cm) gives the desired product on elution with 100 ml of light petroleum ether/ether (70:30). The overall yield is approximately 75%.

**2-Oxabicyclo[4.1.0]heptane.**⁶ A solution of dihydropyran (10.1 g, 0.12 mol), methylene iodide (53.6 g, 0.20 mol), zinc-copper couple I (16.3 g, 0.25 g-atom), and iodine (0.25 g, 0.002 g-atom) in dry ether (100 ml) is heated under reflux for 16 hours. The cooled mixture is filtered, and the filtrate is washed successively with cold 5% hydrochloric acid, 5% aqueous sodium bicarbonate, and water. The ether solution is dried and concentrated and, on distillation, affords 6.9 g (65%) of 2-oxabicyclo-[4.1.0]heptane, bp 121°,  $n^{25}$ D 1.4488.

Cyclopropyltrimethylsilane.²²¹ A mixture of methylene iodide (53.5 g, 0.2 mol), zinc-copper couple II (16.1 g, 0.24 g-atom), and iodine (0.15 g, 0.0012 g-atom) in di-*n*-butyl ether (105 ml) is stirred and heated at 55–65° for 30 minutes. To this mixture is added trimethylvinylsilane (22 g, 0.22 mol) in an equal volume of di-*n*-butyl ether. The mixture is maintained at 60° for 26 hours, cooled, and filtered. The filtrate is washed with 5% hydrochloric acid, 5% aqueous sodium bicarbonate, and with saturated aqueous sodium chloride. The ether solution is dried, concentrated, and distilled. Analysis by vapor-phase chromatography showed that the yield of product was 50%. A pure sample of cyclopropyltrimethylsilane, bp 91°,  $n^{25}$  D 1.4095, was isolated by distillation through a spinning-band column.

1,5-Dihydrospiro[2,4-benzodioxepin-3,1'-cyclopropane].¹⁵⁹ Zinccopper couple II (3 g, 0.046 g-atom), methylene iodide (7.6 g, 0.028 mol), and iodine (0.24 g, 0.002 g-atom) in dry ether (50 ml) are stirred and heated until reaction begins. After 30 minutes, 1,5-dihydro-3-methylene-2,4-benzodioxepin (2.0 g, 0.011 mol) is added in a little ether, and the mixture is heated at the boiling point for 10 hours. The reaction is worked up in the usual manner, and distillation at 0.01 mm with a bath temperature of 90° affords 1.5 g (70%) of pure product, mp 78°, from cyclohexane.

cis-Bicyclo[3.1.0]hexan-3-ol.⁶⁰ Anhydrous ether (60 ml) is added to zinc-copper couple (24.8 g, 0.38 g-atom, prepared in a manner similar to that for couple II) and to the stirred slurry is added rapidly an intimate mixture of methylene iodide (53.4 g, 0.20 mol) and 3-cyclopenten-1-ol (7.8 g, 0.093 mol). Additional ether (40 ml) is added, and after 5 minutes an exothermic reaction occurs which lasts for several minutes. The mixture is then heated at reflux for 1 hour, cooled, and filtered through Super-Cel. Water is added to the cooled mixture, and the ether boils spontaneously for several minutes while precipitation occurs. The mixture is filtered by suction through Super-Cel and washed several times with water. The organic layer is separated, and the aqueous layer extracted with ether. The combined ether solution is washed successively with brine, sodium thiosulfate solution, and finally with brine. The dried solution is concentrated and distilled to give 7.5 g (79%) of crude product, bp  $65-66^{\circ}$ (15 mm). Redistillation through a Podbielniak column gives pure cisbicyclo[3.1.0]hexan-3-ol, bp 76° (27 mm), n²⁵D 1.4775 in 75% yield.

cis-Bicyclo[4.1.0]heptan-2-ol.⁶⁴ To a well-stirred mixture of dry ether (215 ml), zinc-copper couple II (36 g, 0.55 g-atom), and iodine (0.2 g, 0.0016 g-atom) is added methylene iodide (115 g, 0.43 mol). The mixture is warmed until a spontaneous reaction begins which is moderated by a water bath maintained at 35°. After 30 minutes a solution of 2cyclohexen-l-ol (20 g, 0.2 mol) in dry ether (40 ml) is added to the refluxing solution over 20 minutes. Reflux is maintained for an additional hour, the mixture is then cooled to room temperature, and saturated ammonium chloride solution (50 ml) is added. The ethereal slurry is decanted into a separatory funnel, and the precipitated salts are washed with two 150-ml portions of ether. The combined ether solution is extracted with four 100-ml portions of saturated aqueous potassium carbonate and two 100-ml portions of saturated aqueous sodium chloride. The dried solution is concentrated, the residual oil is added to 75 ml of a saturated methanolic solution of sodium methoxide, and the resulting mixture is allowed to stand for 24 hours. The methanolic solution is then added to 500 ml of ether, and the resulting solution is washed with saturated aqueous sodium chloride until the washings are no longer basic. The ether solution is dried, the ether and methanol are removed at reduced pressure, and the residual

oil is distilled to give 14 g (63%) of cis-bicyclo[4.1.0]heptan-2-ol, bp 76-77° (10 mm),  $n^{25}$ D 1.4886.

3β-Hydroxy-4β,5β-methanocholestane.¹⁹³ A mixture of zinccopper couple II (0.687 g, 0.0105 g-atom), methylene iodide (2.34 g, 0.00875 mol), and a small crystal of iodine in dry ether (12 ml) is heated at reflux for 30 minutes. A solution of  $3\beta$ -hydroxy- $\Delta^4$ -cholestene (0.967 g, 0.0025 mol) in dry ether (7 ml) is added over 20 minutes and the mixture is stirred for an additional hour at reflux. The ice-cooled mixture is treated with saturated aqueous ammonium chloride, the ether layer is decanted, and the precipitate is washed twice with ether. The combined ether solution is washed with saturated aqueous sodium chloride and dried. The ether is removed under reduced pressure, and the residue is chromatographed immediately on 50 g of alumina (activity III). Hexane elutes a small amount of methylene iodide and 22 mg of a dimeric by-product. Benzene elutes 622 mg (62%) of crystalline  $3\beta$ -hydroxy- $4\beta$ , $5\beta$ -methanocholestane, mp 94–95°, from acetone.

17β-Hydroxy-1β,2β-methylen-5α-androstan-3β-ol 17-Acetate.¹³¹ A mixture of  $17\beta$ -hydroxy- $\Delta^1$ -androsten-3β-ol 17-acetate (33.2 g, 0.10 mol), methylene iodide (161 g, 0.60 mol), and zinc-copper couple II (27 g, 0.90 g-atom) in dry ether (600 ml) containing about 25% ethylene glycol dimethyl ether is heated under reflux for 20 hours. The cooled mixture is filtered, and the organic phase is washed with saturated aqueous ammonium chloride and water. The dried ether solution is concentrated under reduced pressure, and the residue is recrystallized from pentane/ether to give  $17\beta$ -hydroxy- $1\beta$ ,  $2\beta$ -methylen-5α-androstan- $3\beta$ -ol 17-acetate, mp 173-174°,  $[\alpha]^{25}D + 49°$ , in 60% yield.

 $5\alpha$ , 19-Cyclo-10 $\alpha$ -androstane- $3\alpha$ , 17 $\beta$ -diol.¹⁹⁵ Estr-5(10)-ene- $3\alpha$ , 17 $\beta$ diol (10.0 g, 0.036 mol) is added during 1 hour to a refluxing solution of methylene iodide (180 g, 0.67 mol) and a zinc-copper couple²⁵⁶ (60 g, 0.92 g-atom) in dry ether (350 ml). After the addition is complete, half of the solvent is removed by distillation, and additional dry ether (200 ml) is added. The mixture is transferred to a stainless-steel tube and heated for 3 hours at 92° under autogenous pressure before being cooled in an ice bath and poured into saturated aqueous sodium bicarbonate (500 ml). Three extractions with ether followed by evaporation of the combined dried extracts yield a crude product which affords 8.45 g (85%) of 5 $\alpha$ , 19cyclo-10 $\alpha$ -androstane- $3\alpha$ , 17 $\beta$ -diol, mp 162–163°, [ $\alpha$ ]²⁵D +40°.

#### Method B

**Bis(iodomethyl)zinc.**¹⁰ In a 500-ml flask equipped with stirrer, dropping funnel, and gas outlet port is placed dry zinc iodide (24 g, 0.075 mol) in absolute ether (50 ml), and the system is arranged to maintain a nitrogen atmosphere. The mixture is stirred until solution is complete and then cooled with an ice bath. Three hundred and twenty milliliters of a 0.5 M absolute ether solution of diazomethane is added dropwise over 30 minutes. The slightly cloudy solution is assayed by adding 1 ml of solution to 5 ml of a 0.2 N absolute ether solution of bis(iodomethyl)zinc per milliliter, corresponding to a yield of 80% based on zinc iodide. The solution can be stored under nitrogen at  $-20^{\circ}$  for approximately 2 days.

Solutions of iodomethylzinc iodide can be prepared by the same method by using half the quantity of diazomethane.

**Bicyclo[3.1.0]hexane.**¹⁰ A solution of bis(iodomethyl)zinc (25 mmol, prepared as above) in dry ether (155 ml) is added under nitrogen from a graduated dropping funnel to a 25-ml, three-necked flask equipped with a magnetic stirrer. The flask is also connected to a rotary evaporator under a nitrogen atmosphere. The rotating flask is maintained in a bath at -5 to  $-10^{\circ}$  so that the ether can be evaporated under a water pump vacuum. Ether is removed in this manner until the residual volume is 30 ml, and cyclopentene (4.1 g, 0.060 mol) is added under nitrogen. The stirred mixture is warmed slowly to 20° and, after reaction has initiated, the contents of the flask are maintained at 20–30°. After 20 minutes the mixture is heated at 50° for 2–3 hours and then water is added followed by dilute aqueous ammonium hydroxide. The ether solution is concentrated and distilled through a spinning-band column to give 2.65 g (54 %) of bicyclo[3.1.0]hexane, bp 81°,  $n^{25}$  D 1.4365.

**Cyclopropa[a]acenaphthene.**⁹ Acenaphthylene (7.6 g, 0.050 mol) is treated with an ethereal solution of bis(iodomethyl)zinc, prepared from zinc iodide (17.9 g, 0.063 mol) and diazomethane (0.140 mol), and the mixture is heated under reflux for 60 hours. The cooled solution is worked up in the usual manner to give a crude solid product which is purified by chromatography on neutral alumina using petroleum ether as eluent. There is obtained 4.3 g (52%) of colorless crystalline cyclopropa[a]-acenaphthene, mp 116°.

**Bicyclo[2.1.0]pentane.**¹² Cyclobutene (1.6 g, 0.060 mol) is added to a concentrated ether solution of bis(iodomethyl)zinc (0.032 mol) contained in a flask under a nitrogen blanket and maintained at  $-20^{\circ}$ . The mixture is warmed to  $20^{\circ}$ , and a reaction occurs in 5 minutes with precipitation of zinc iodide. After 12 hours the reaction mixture is cooled to  $-10^{\circ}$ , and methylcyclohexane (20 ml) is added followed by sufficient 1 N hydrochloric acid to neutralize the mixture. The dried organic phase is concentrated, and the residue is distilled through a spinning-band column to give two fractions boiling at  $34-40^{\circ}$  (1.8 g) and  $40-45^{\circ}$  (1.1 g). The first fraction contains 0.13 g and the second, 0.85 g of bicyclo[2.1.0]pentane. The pure product is obtained in the indicated amounts by vapor-phase chromatography (yield  $47^{\circ}_{0}$ ).

trans-1,2-Bis( $\beta$ -chloroethyl)cyclopropane.¹² To a solution of bis(chloromethyl)zinc (0.030 mol) in dry ether (110 ml), prepared from zinc chloride and diazomethane in a manner analogous to that used for bis(iodomethyl)zinc, is added dropwise trans-1,6-dichloro-3-hexene (3.1 g, 0.020 mol) while the temperature is maintained at  $-10^{\circ}$ . The mixture is stirred for 12 hours at 15° and then warmed to 40° for 2 hours. Ether (25 ml) is added, the mixture is hydrolyzed and neutralized with 1 N hydrochloric acid, and the solution is finally washed with water and dried. The solution is concentrated and the residue distilled to give 2.88 g (86%) of trans-1,2-bis( $\beta$ -chloroethyl)cyclopropane, bp 94° (13 mm),  $n^{25}$ D 1.4780.

1-(p-Anisyl)-2-vinylcyclopropane.⁵¹ Zinc chloride (1.0 g, 0.010 mol) is heated in a three-necked flask under reduced pressure (0.1 mm) until the salt begins to fuse. After cooling, a dry ice condenser and an addition funnel are attached, and ether (10 ml) is introduced to dissolve the zinc chloride. 1,3-Butadiene (0.5 g, 0.010 mol) is distilled into the flask which is maintained at  $-10^{\circ}$ . p-Anisyldiazomethane (1.5 g, 0.010 mol) dissolved in anhydrous ether is added dropwise to the magnetically stirred solution. Nitrogen evolution and decoloration are instantaneous. After addition is complete (15 minutes), the solvents are removed under reduced pressure, and the residue is washed with water (5 ml) and extracted with pentane. A mixture of *cis*- and *trans*-1-(*p*-anisyl)-2-vinyl-cyclopropane is obtained in 50% yield. The stereoisomers are separated on a 6-ft SFXF-1150 gas-chromatography column with the *cis* isomer having the shorter retention time. The *cis/trans* ratio of isomers is 6.7.

#### Method C

*n*-Butyl Cyclopropyl Ether.⁸³ The reaction is carried out under a nitrogen atmosphere in a 300-ml flask equipped with a magnetic stirrer,

reflux condenser, dropping funnel, thermometer, and gas-inlet tube with a three-way stopcock. *n*-Butyl vinyl ether (20.0 g, 0.20 mol), diethylzine (15 ml, 0.15 mol), and dry ether (100 ml) are introduced into the flask by hypodermic syringes. To the stirred mixture, methylene iodide (70.6 g, 0.25 mol) is added dropwise. An exothermic reaction usually occurs after an induction period. The addition must be performed in this order because an explosive reaction sometimes occurs when diethylzinc is added to a mixture of olefin and methylene iodide in a solvent. The stirred mixture is maintained at reflux for 3 hours and then cooled. The mixture is poured into a large quantity of dilute hydrochloric acid with stirring; during this time ethane is evolved. The organic layer is separated and washed with dilute aqueous sodium bicarbonate and with water. The ethereal solution is dried, the solvent removed by distillation, and the residue is fractionated to give 21 g (92%) of n-butyl cyclopropyl ether, bp 122.4°.

anti-3-Methyl-exo-tricyclo[ $3.2.1.0^{2.4}$ ]octane.¹⁶² The procedure employed in the preceding preparation of *n*-butyl cyclopropyl ether is carried out using norbornene (18.8 g, 0.20 mol), diethylzinc (35 ml, 0.35 mol), and ethylidene iodide (56.4 ml, 0.60 mol) in light petroleum ether (200 ml). The product is worked up in the usual manner to obtain 17.1 g (70%) of a mixture of the exo and endo isomers of 3-methyltricyclo[ $3.2.1.0^{2.4}$ ]octane which is separated and purified by vapor-phase chromatography. The mixture consists of the two isomers in the ratio 2.2:1, and the isomer obtained in larger amount was identified as anti-3methyl-exo-tricyclo[ $3.2.1.0^{2.4}$ ]octane, bp  $153^{\circ}$ ,  $n^{25}$ D 1.4744. The isomer formed in smaller amount was tentatively identified as anti-3-methylendo-tricyclo[ $3.2.1.0^{2.4}$ ]octane, bp  $170^{\circ}$ ,  $n^{25}$ D 1.4824.

exo-6-Methyl-cis-bicyclo[3.1.0]hexan-3-ol.¹⁶² The general procedure of method C is carried out using 3-cyclopenten-1-ol (10.0 g, 0.12 mol), ethylidene iodide (19 ml, 0.2 mol), and diethylzine (25 ml, 0.25 mol) in diisopropyl ether (100 ml). There is obtained 5.9 g (45%) of pure exo-6-methyl-cis-bicyclo[3.1.0]hexan-3-ol, bp 71-72° (36 mm),  $n^{25}$ D 1.4711.

7-Methylcyclohepta-1,3,5-triene.⁴⁹ The general procedure of method C is followed employing benzene (100 ml), diethylzinc (14 ml, 0.14 mol), and ethylidene iodide (19 ml, 0.2 mol), the excess benzene serving as solvent. The mixture is worked up in the usual manner, and the product is distilled through a packed column. There is obtained 6.5 g (31%) of 7-methylcyclohepta-1,3,5-triene, bp 131-132°,  $n^{25}$ D 1.5030.

Phenylcyclopropane (Sawada and Inouye Modification).¹²⁴ A stock solution of ethylzinc iodide is prepared in the following manner.

Ethyl iodide (156 g, 1 mol) is allowed to react with zinc-copper couple II (70 g, 1 g-atom) in absolute ether (900 ml), and the mixture is stirred at room temperature overnight. The supernatant liquid is withdrawn free from sludge and stored in a stoppered flask carrying a drying tube. After storage at room temperature for 1 week no precipitate was formed, and the activity of the solution remained unchanged. The solution can be standardized by addition of iodine followed by back titration with sodium thiosulfate solution.

Methylene iodide (15 g, 0.056 mol) is added to an aliquot of the stock solution (100 ml) containing 2 equivalents of ethylzinc iodide, and the mixture is stirred at reflux for 1 hour. To the chilled solution, styrene (5.2 g, 0.05 mol) is added, and the mixture is stirred and heated under reflux. Over a 2-hour period 50 ml of ether is allowed to distil. The resulting mixture is decomposed with water and dilute hydrochloric acid, and the organic layer is separated, washed with water, aqueous sodium thiosulfate, again with water, and dried over anhydrous magnesium sulfate. Distillation affords 4.6 g (78%) of phenylcyclopropane, bp  $64-65^{\circ}$  (20 mm),  $n^{25}$ D 1.5308.

#### **Miscellaneous Procedures**

Ethyl 2,2-Dimethyl-3-isobutenylcyclopropane-1-carboxylate (Ethyl DL-Chrysanthemumate).¹¹⁷ A mixture of ethyl diiodoacetate (102 g, 0.30 mol) and zinc-copper couple II (21 g, 0.32 g-atom) in absolute tetrahydrofuran (300 ml) is stirred and heated at 40–50°. 2,5-Dimethyl-2,4-hexadiene (66 g, 0.6 mol) is added dropwise and the mixture is maintained at reflux for 14 days. The cooled mixture is diluted with ether and washed with 1N hydrochloric acid and twice with water (100 ml). Distillation affords 7 g (12%) of ethyl 2,2-dimethyl-3-isobutenylcyclopropane-1-carboxylate, bp 34–37° (0.05 mm), identical with an authentic sample.

Ethyl dichloroacetate can be used in place of the iodo ester, but the yield of product is only 3-5%. The reaction apparently fails with ethyl dibromoacetate. The long reaction time cited in the literature is probably unnecessary.

Partial Asymmetric Synthesis of (-)-(R)-1,1-Diphenyl-2methylcyclopropane.⁸² Zinc-copper couple II (13 g, 0.2 g-atom) and methylene iodide (27 g, 0.1 mol) in absolute ether (150 ml) are stirred for 30 minutes, and (-)-menthol (5 g, 0.03 mol) in ether (20 ml) is added to the preformed solution of the zinc reagent. After the mildly exothermic reaction is over, 1,1-diphenyl-1-propene (10 g, 0.05 mol) in ether (20 ml) is added together with a few drops of boron trifluoride etherate. The mixture is refluxed for 30 hours and then decomposed with dilute hydrochloric acid. The organic layer is separated, washed well with aqueous sodium thiosulfate, and dried. After removal of ether, the residue is ozonized in carbon tetrachloride to remove the unreacted olefin. After the usual workup of the ozonide, the neutral fraction is chromatographed on a neutral alumina column  $(3 \times 210 \text{ cm})$  to give pure (-)-(R)-1,1-diphenyl-2-methylcyclopropane, completely free from (-)-menthol and benzophenone as indicated by vapor-phase chromatographic analysis. There is obtained 1.2 g (12%) of product, bp 104-105° (0.1 mm),  $n^{25}$ D 1.5764,  $[\alpha]_D^{25}$  -0.28° (neat), corresponding to an optical yield of 0.3%.

20,20-Ethano-17 $\alpha$ -hydroxypregn-4-en-3-one.¹⁴ A stirred mixture of zinc-copper couple III (14.9 g, 0.23 g-atom) and methylene iodide (11.7 ml) in ether (90 ml) was heated at reflux under nitrogen for 1 hour. 17 $\alpha$ -Hydroxypregn-4-ene-3,20-dione (2 g) was added to the cooled mixture and stirring was continued at 25° for 24 hours. The resulting mixture was diluted with benzene, the solids were removed by filtration, and the ethereal solution was worked up with aqueous ammonium chloride and with aqueous sodium bisulfite. The product was isolated by chromatography on silica gel and recrystallized to give 1.84 g (89%) of 20,20ethano-17 $\alpha$ -hydroxypregn-4-en-3-one, mp 229–231°,  $[\alpha]_D^{25}$  +82° (CHCl₃). A minor product, 20-(2'-iodoethyl)pregna-4,17(20)-dien-3-one, mp 159– 161°, was also isolated.

17-Hydroxy-20-methylenepregn-4-en-3-one.¹⁴ The procedure for 20,20-ethano-17 $\alpha$ -hydroxypregn-4-en-3-one was followed exactly except that the preformed zinc reagent was heated under reflux for 4 hours before addition of the ketone. There was obtained 1.84 g (93%) of 17-hydroxy-20-methylenepregn-4-en-3-one, mp 239-241°,  $[\alpha]_{p}^{25}$  -113° (CHCl₃).

General Procedure for Use of Zinc-Silver Couple.^{252a} To an ethereal suspension of Couple V, prepared from zinc (17 g), methylene iodide (34 g, 0.13 mol) is added dropwise with stirring at a rate to maintain gentle reflux. Stirring is continued for 1 hour at room temperature. The unsaturated compound (0.10 mol) is added dropwise over 15 minutes, and the mixture is allowed to reflux for 2-24 hours, depending on the specific unsaturated compound. The mixture is then cooled to 0° (ice bath), ether (150 ml) is added, and pyridine (12.6 g, 0.16 mol) is added dropwise with vigorous stirring over 1 hour. The resultant precipitate is removed by filtration and washed with ether  $(3 \times 30 \text{ ml})$ . The filtrate and workup are combined and a little pyridine is added dropwise until no more precipitate is formed. After filtration, the ether is removed under reduced pressure and the residue is distilled or crystallized. A second modification involves adding the unsaturated compound in one portion to Couple V in ether followed by the dropwise addition of methylene iodide. The workup then follows the above procedure.

In this manner the following unsaturated compounds were converted to the corresponding cyclopropanes in the indicated yields: cyclohexene (95%), vinylidenecyclopropane (51%), vinyl acetate (30%), 2,3-bis(trimethylsiloxy)-1,3-butadiene (78%), tetrahydropyranyl ether of 8-methylene-bicyclo[4.2.0]octan-7-ol (85%), but-3-en-2-one (60%), acrolein (5%), crotonaldehyde (80%), methyl acrylate (80%), and acrylonitrile (0%).

#### TABULAR SURVEY

The information in the following table covers the literature through January, 1973. An attempt was made to include all useful references to the cyclopropanation of unsaturated compounds with methylene iodide/ zinc-copper couple. The related cyclopropanations employing diazomethane/zinc iodide and methylene iodide/diethylzinc are included, as are variations of all three methods using substituted reagents. The bulk of the reactions cited are in Table IV, which is arranged in classes primarily according to substituents on the double bond undergoing reaction, but this listing is not always unambiguous. For example, all steroids are listed under "Steroids," regardless of substitution. Within a class, substrates are listed by empirical formula. A few miscellaneous substrates whose reactions are discussed in the text are listed at the end of Table IV.

The format of Table IV includes substrate class, molecular formula, unsaturated compound, reagent, preparative method, yield, reaction conditions, and references. Preparative method is given as A, B, or C in accord with the description under Experimental Procedures, Variations of the Method. Product isomer ratios are given under yield when known. When there is more than one reference, experimental data are taken from the first reference, and the remaining references are arranged in numerical order.

Additional data, experimental and otherwise, are incorporated on abstract cards that were used in the preparation of the chapter. These cards appear in microfiche form as an insert on the inside back cover of this volume. In this way it is hoped that more information than usual will be transmitted to the reader.

It will be noticed that the abstract cards are more informal than is the custom for textural material in *Organic Reactions* chapters. Names of compounds and journals, for example, are not always cited in uniform fashion, but care has been taken to remove ambiguities. The justification for this less formal presentation is the desire to communicate more information in a fashion that will reduce both errors and expense. Comments by readers will be welcomed.

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUN	red Compouni	UNSATURATED	FROM U	Cyclopropanes	OF	Synthesis	IV.	ABLE	
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	Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions Couple, Solvent, Other	Refs.
	ALKENES					
	$C_2H_2D_2$	(E)-Ethylene-1,2-d ₂	$CH_2I_2$	A(7) cis/trans 0.33ª	I, $(C_2H_5)_2O$ , 35°	86
			$CH_2I_2$	$A(35)$ cis/trans $0.33^a$	I, $(C_2H_5)_2O$ , 60°	86
			CH ₂ I ₂	A(2-4)	I, $(C_2H_5)_2O$ , removal of excess metal from ICH ₂ ZnI	86
				A (10)a	t (CH) o	0.0
	сv	Pahadan a		A (12)*	$(0_2H_5)_2$	80 1 C OF
	C H D	Ethylene		A(29)	$(U_2H_5)_2U_1$	1, 0, 80
	U ₃ Π ₅ D	$(\mathbf{Z})$ - <b>Fropene</b> -1-d		A(05) cisitrans 1° A(05) sistema 16	$I_{1} (U_{2}H_{5})_{2}U$	80 80
	сu	(E)-Propene-1-d	CHDI ₂	A (65) cis/trans 1"	$(U_2H_5)_2U$	80
	C ₃ n ₆	Propene		A()	$(U_2H_5)_2U$ , $100^\circ$ , 25 atm	257
		Cyclobutene	CH ₂ N ₂	B(47)		12
	$C_4H_8$	2-Methylpropene	$CH_{2}I_{2}$	A()	$(C_2H_5)_2O$	4, 30, 258
			C ₆ H ₅ CHN ₂	B(70)	ZnBr ₂	51
		I-Butene	CH ₂ I ₂	$\mathbf{A}(-)$	1, $(C_2H_5)_2O$ , 100°, 25 atm	257
		(Z)-2-Butene	CH ₂ I ₂	A(-)	$1, (C_2H_5)_2O$	4, 30, 35
95			$C_6H_5CHN_2$	B(70) syn/anti 4.7	ZnBr ₂	51
			$p \cdot CH_3C_6H_4CHN_2$	B(60) syn/anti 21	Znl ₂	51
			p-CH ₃ OC ₆ H ₄ CHN ₂	B(37) syn/anti 53	ZnBr ₂	51
		(E)-2-Butene	$\mathbf{CH}_{2}\mathbf{I}_{2}$	A(-)	I, $(C_2H_5)_2O$	4, 30, 35
	С <b>5</b> Н8	Methylenecyclobutane	$CH_2I_2$	A (20–25)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	101
		Cyclopentene	$CH_2I_2$	A(27)	I, $(C_2H_5)_2O$	1, 4, 6, 36, 41, 85, 260, 347
			CH,N,	B(54)	ZnCl	10
			$CH_2N_2$	B(53)	ZnI,	12, 10, 41
			CH ₃ CHI ₉ /(C,H ₅ ) ₉ Zn	C(-)		259, 261
	C,H,	2-Methyl-1-butene	CH,I,	A()	I, $(C_{2}H_{5})_{2}O$	4
	0 10	2-Methyl-2-butene	CH.1.	A(41)	I, $(\mathbf{C}, \mathbf{H}, 0, \mathbf{O})$	263, 4, 30, 102
		-	p-CH ₃ C ₄ H ₄ CHN ₂	B(52) syn/anti 1.5	ZnBr.	51
			p-CH,OC, H,CHN,	B(40) syn/anti 4.4	ZnI,	51
			CH,I,/(C,H,),Zn	C(-)	(C, H,),O	50 <b>a</b>
		I-Pentene	CHI	$\mathbf{A}(-)$	1, (C,H,),O	4
		$(\mathbf{Z})$ -2-Pentene	CH.I.	$\mathbf{A}(-)$	I, (C,H,),O	4, 264
		• •	* *		· • 3'4	-

^a Additions were nonstereospecific because of adventitious isomerization of ethylene.
^b The Sawada modification was used. See p. 91.

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Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
ALKENES	(contd.)				
	(E)-2-Pentene	CH.I.	A()	$I_{\epsilon} (C_{a}H_{\epsilon})_{a}O$	4
C.H.	Methylenespiropentane	CH.I.	A()	$(C, H_{\epsilon}), O$	100
C ₆ H ₁₀	l-Methylcyclopentene		A(61)	I, $(C_2H_5)_2O$ , preformed reagent	161, 36, 265, 266
	3-Methylcyclopentene	CH,1,	A(31)	II, $(\tilde{C_{9}H_{s}})_{9}O$	265
	Cyclohexene	CH ₂ I ₂	A (92)	III, (Ĉ ₂ H ₅ ) ₂ O, preformed reagent	87, 1, 3, 4, 6, 13, 34, 36, 41, 64, 77, 85, 250, 26 269
		CH _a Br.	A(61)	TTI	8
		$CH_2N_2$	B(73)	$ZnI_{2}$ , $(C_{2}H_{5})_{2}O$	10, 2, 9, 11, 12, 34, 41
		CH-N-	B(91)	ZnI., C.H.,	42
		CH.N.	B(72)	ZnCl., (C.H.).O	10
		CH.N.	$\mathbf{B}(12)$	ZnCl., C.H.	42
		CH _a N _a	B(36)	ZnBr, C.H.	42
		CH_N_	B()	ZnF., C.H.	42
		CH.N.	B(6)	(C.H.CO.CH.) Zn. C.H.	42
		C.H.CHN.	B(90) synlanti 3	ZnCl.	51
		p.CH.OC.H.CHN.	B(37) syn/anti 34	ZnCl	51
		CH_I_/(C_H_).Zn	C(90)	C.H.	83, 43a, 50a
		CH.I./C.H.ZnI	C(92) ^b	(Č,H,),O	124
		CH.CHI./(C.H.).Zn	C(66) syn/anti 1.5	Petroleum ether or n-pentane	84, 162, 238
		C, H, CHI, /(C, H, ), Zn	C(69) syn/anti 17	$(C_{2}H_{2})_{2}O$	238
		C, H, CHI, (C, H, ), Zn	C(68) syn/anti 6.6	n-Pentane	238
		CH,I,/(C,H,),Cd	C(86)		238
		CH.CHI./(C.H.).Cd	C(-) syn/anti 0.9	C _a H _a	238
		CH CHI (C H.) Cd	C(19) syn/anti 0.4	C ₄ H ₁₂	238, 267, 270
		CH.I./(C.H.).In	C()		237a
C.H.,	2,3-Dimethyl-l-butene		A()		271
0 14	3,3-Dimethyl 1-butene	CH,I,	A(—)	I, $(C_2H_5)_2O$	4
	2,3-Dimethyl-2-butene	CH ₂ I ₂	A(42)	I, $(C_2H_5)_2O$	6, 4, 41, 85, 271
		CH ₂ N ₂	B(78)	ZnI ₂	12

TABLE IV. Sy	NTHESIS OF C	YCLOPROPANES FROM	UNSATURATED	Compounds (	Continued
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		$CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$	C()	$(C_2H_s)_2O$	50 <b>a</b>
	3-Methyl-1-pentene	CH,N,	B(82)	ZnI	12
	(E)-3-Methyl-2-pentene	CH,I.	A(21)	I, (Č,H,),O	263
	1-Hexene	CH.I.	$\mathbf{A}(-)$	I, $(C, H_{5})_{2}O$	4
	(Z)-3-Hexene	CH.I.	A(35.5)	I, (C,H,),O	1, 6, 4, 85
		CH.N.	B(20)	ZnI,	12
	(E)-3-Hexene	CH,I,	A(15.5)	I, (Č,H,),O	1, 6, 4, 85
		CH,N,	B(20)	ZnI,	12
C7H10	2-Norbornene	CH ₂ I ₂	A(47) endo/exo 0.77	I, (Č ₂ H ₅ ) ₂ O	1, 6, 27, 36, 57, 85, 162, 254
		$CH_{3}CHI_{2}/(C_{2}H_{5})_{2}Zn$	C(70) endo/exo 0.45	Petroleum ether	162
C,H,,	Methylenecyclohexane	CH,I	A(—)	I, $(C_{2}H_{2}),O$	36, 262
	1-Methylcyclohexene	CH ₂ I ₂	A(33)	III, $(C_2H_5)_2O$	266, 36, 41, 272
	3-Methylcyclohexene	CH,I,	A()	I, $(C_{2}H_{5})_{2}O$	36
	4-Methylcyclohexene	CH,I,	A ()	I, $(C_2H_5)_2O$	36
	Cycloheptene	CH ₂ I	A(—)	I, $(C_2H_5)_2O$	36, 273, 274
C.H.	4,4-Dimethyl-I-pentene	CH,I,	A()	I, $(C, H_{5}), O$	222
	1-Heptene	CH ₂ I ₂	A(47)	I, $(C_2H_5)_2O$	6, 4, 85, 262, 348
		$CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$	C(66)	C _s H _s	83, 43a, 50a
	2-Heptene	$\mathrm{CH}_{2}\mathrm{I}_{2}/(\mathrm{C}_{2}\mathrm{H}_{5})_{2}\mathrm{Zn}$	C(90) mixture of cis and trans isomers	C _g H _g	<b>43a</b>
C8H10	exo-Tricyclo[3.2.1.0 ^{2,4} ] 6- octene	CH ₃ CHI ₂	A(—)	I, $(C_2H_5)_2O$	27
	endo-Tricyclo[3.2.1.0 ^{2.4} ]-6- octene	CH ₃ CHI ₃	A(—)	I, $(C_2H_5)_2O$	27
CHI.	l, l. Dicyclopropylethylene	CH,I,	A(—)	$I_{,} (C_{2}H_{5})_{2}O$	98
C.H.	Vinylcyclohexane	CH.I.	A(56)	I, $(C, H_{s}), O$	275
	1,2-Dimethylcyclohexene	CH,I,	A()	I, $(\overline{C_2H_5})_2O$	4, 36
	4,4-Dimethylcyclohexene	CH,I,	A(—)	I, $(C_{2}H_{5})_{2}O$	36
	cis-4,5-Dimethylcyclohexene	CH ₂ I ₂	A(—)	I, $(\tilde{C_2H_5})_2O$	36

• The Sawada modification was used. See p. 91.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
ALKENES (	contd.)				
C _R H ₁₄ (contd.	) trans-4,5-Dimethylcyclohexene	CH ₂ I ₂	A()	I, $(C_2H_5)_2O^{-1}$	36
	1-Ethylcyclohexene	CH ₂ I,	A()		272
	4-Ethylcyclohexene	CH ₂ I ₂	A()	I, $(C_2H_5)_2O$	36
	1-Methylcyoloheptene	CH ₂ I ₂	A(55)	$(C_2H_5)_2O$	342
	(Z)-Cyclooctene	CH ₂ I ₂	A(94)	III, $(C_2H_5)_2O$ , preformed reagent	87, 8, 276
		CH.Br.	A(56)	III, (Č,H,),0	8
		CH.N.	B(74)	ZnI,	12, 270, 274
		CH.I./(C.H.).Zn	C(98)	C, H,	43a
	(E)-Cvclooctene	CH.I.	A(-) cis/trans 0.8		90
	(	CH.I./(C.H.).Zn	C(98)	C.H.	43a
C ₈ H ₁₆	2,4,4-Trimethyl-I-pentene (mixture with 2,4,4- trimethyl-2-pentene)	CH ₂ 1 ₂	A(68)	$\mathbf{I}, (\mathbf{C}_{2}\mathbf{H}_{5})_{2}\mathbf{O}$	6, 85
	2,4,4-Trimethyl-2-pentene (mixture with 2,4,4- trimethyl-1-pentene)	CH ₂ I ₂	A(68)	I, $(C_2H_5)_2O$	6, 85
	4-Methyl-3-heptene	_	()	_	277
	1-Octene	CH ₂ I ₂	A(70)	I, $(C_2H_5)_2O$	6, 41, 85, 127, 250
		$CH_{\bullet}I_{\bullet}/(C_{\bullet}H_{\bullet})_{\bullet}Zn$	C(66)	C.H.	83, <b>4</b> 3a
		CH.I./C.H.ZnI	C(77)*	(Č,H,).O	124
	2-Octene	CH.I.	A ()		278
C ₉ H ₁₀	Tetracyclo[4.3.0.0 ^{2,4} .0 ^{8,7} ]	CH ₂ I ₂	A (65)	I, $(C_2H_5)_2O$	279
C.H.	(+)-Pulegene	_	()	_	271
• 1•	1-Propylcyclohexene	CH.I.	A()	_	272
	4-Isopropylcyclohexene	CH.I.	A()	I. $(C_{\bullet}H_{\bullet})_{\bullet}O$	36
	(Z)-Cyclononene		(-)		270
C.H.	2.4.4.Trimethyl-2-hexene	CH.L.	A(31)	II. $(C_{0}H_{1})_{0}O$	280
C ₁₀ H ₆ D ₆	(2-Methyl-d ₃ -propenyl- 3.3.3-d ₂ )benzene	$CH_2I_2/(C_2H_5)_2Zn$	C(75)		122. 183 <b>a</b>
C.,H.,	2(10), 3-Pinadiene (Verbene)	CHAIA	A()	II, $(C_{\bullet}H_{\bullet})_{\bullet}O$	183a
C. H.	$2(10)$ -Pinene ( $\beta$ -Pinene)	CH.I.	A(84.3)	I. (C.H.).O	102, 18 <b>3a</b>
- 1416	2(2) Pinone (g. Pinene)	CH I	A (19)	U (CH) O	1836

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

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	$C_{10}H_{18}$	1-Butylcyclohexene	CH,I,	A()		272
	10 10	3-Butylcyclohexene	CH,I,	A(-)	I, $(C_{2}H_{z})_{2}O$	36
		4-Butylcyclohexene	СН,1,	A(-)	I, (C,H,),O	36
		(Z)-Cyclodecene		( <u>    )</u>		91, 270
		(E)-Cyclodecene	_	( <u>   )</u>	_	91, 92
		p-Menthene-1	CH.I.	A(50)	$(C_2H_5)_2O$	349
		trans-p-Menthene-2	CH ₂ I ₂	A(28) mixture of cis and trans isomers	$(C_2H_5)_2O$	349
		cis-p-Menthene-8	CH,I,	A(63)	(C,H,),O	349
		trans.p.Menthene-8	CH I.	A(63)	(C,H,),O	349
	C10H20	2,4,4,5-Tetramethyl-2-hexene	CH,I,	A(26.2)	II, (C, H, ),O	280
	10 10	2,4,4-Trimethyl-2-heptene	CH.I.	A(33.5)	II. (C.H.).O	280
		3,7-Dimethyl-1-octene	CH,I,	A()		278
		1-Decene	CH,I,	$\mathbf{A}(-)$	III	262
	$C_{11}H_{14}$	10-Methylenetrispiro- [2.0.2.0.2.1]decane	CH ₂ I ₂	A()	I, $(C_2H_5)_2O$	104
		Tetracyclo[5.3.1.0 ^{2,6(ezo)} . 0 ^{8,10(ezo)} ]undeeene-3	CH ₂ I ₂	A(high)	I, $(C_2H_5)_2O$	27
		Tetracyclo[5,3,1,0 ^{2,6(endo)} , 0 ^{8,10(ezo)} undecene-3	CH ₂ I ₂	A(high)	I, $(C_2H_5)_2O$	27
66		$Tetracyclo[6.2.1.0^{2,7(exo)}, 0^{3,5(endo)}]undecene.9$	$CH_2I_2$	A(high)	I, $(C_2H_5)_2O$	27
		Tetracyclo[ $6.2.1.0^{2,7(endo)}$ . $0^{3,5(exo)}$ lundecene-9	CH ₂ I ₂	A(high)	I, $(C_2H_5)_2O$	27
	$\mathrm{C}_{11}\mathrm{H}_{14}\mathrm{O}$	(E)-1-(p-Methoxyphenyl)- 1-butene	CH ₂ I ₂	A(70)	I, $(C_2H_5)_2O$	281
	$C_{11}H_{16}$	2-Methyleneadamantane	$CH_2I_2$	A()	II, $(C_2H_5)_2O$	106, 107
			$CH_2I_2/(C_2H_5)_2Zn$	C(57)	$(C_2H_5)_2O$	282
		2(10)-Methano-3-pinene	$CH_2I_2$	A()	II, $(C_2H_5)_2O$	183a
	$C_{12}H_{18}$	2-Ethylideneadamantane	$CH_2I_2/(C_2H_5)_2Zn$	C(76)	$(C_2H_5)_2O$	282
	$C_{12}H_{20}$	Bicyclohexylidene	CH ₂ I ₂	A(87)	I, $(C_2H_5)_2O$	102
	$C_{12}H_{22}$	(Z)-Cyelododecene	CH ₂ I ₂	A(79)	IV, (C ₂ H ₅ ) ₂ O, preformed reagent	87, 56, 274
	C, Han	1-Isopropenyladamantane	СН,І,	A(—)	II, $(\tilde{C_{2}H_{1}})_{2}O$	106
	10 20	2-Isopropenyladamantane	CII,I,	A(-)	11, $(C, H_{c}), O$	106
	$C_{13}H_{22}$	I, 1, 4a-Trimethyl-1, 2, 3, 4, 4a, 5, 6, 7-octahydronaphthalene	CH ₂ I ₂	A(0)		184

TABLE IV.	Synthesis	OF	Cyclopropanes	FROM	UNSATURATED	Compounds	(Continued)

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
ALKENES (c	contd.)				
C14H18	13-Methylenetetraspiro- [2.0.2.0.2.0.2.1]tridecane	$CH_2I_2$	A(50)	I, $(C_2H_5)_2O$	105
C14H26	3,5-Dibutylcyclohexene	CH ₂ I ₂	A()	I, (C,H,),O	36
C14H28	1-Tetradecene	CH ₂ I ₂	A()		278
C15H14	(Z)-I,3-Diphenylpropene	CH ₂ I ₂	A(47)	I, (C ₂ H ₅ ) ₂ O	283
C16H16	2-Methyl-1,1-diphenyl-1- propene	CH ₂ I ₂	A(66)	$(C_2H_5)_2O^2$	350
C, H.,	2-Methyl-2-pentadecene	CH,I,	A(-)	_	278
C,H.	Kaurene	CH.I.	A(10)	$H_{c}(C,H_{c})_{0}O$	351
30 34	iso-Kaurene	CH,I,	A(10)	II, (C,H,),O	351
C20H40	l-Methylenenonadecane	CH ₂ I ₂	A()		278
POLYENES					
C ₄ H ₆	1,3-Butadiene	$CH_{2}I_{2}$ $CH_{2}N_{2}$ $C_{5}H_{5}CHN_{2}$ $T_{5}CHN_{2}$	A(30) B(48) mono/bis 0.16 B(70) syn/anti 2.8	II, p-dioxane, Parr bomb ZnI ₂ ZnCl ₂	110, 348 12 51
$C_{5}H_{6}$	Cyclopentadiene	p-CH ₃ OC ₆ H ₄ CHN ₂ CH ₂ I ₂	B(50) syn/anti 6.7 A(93 bis, 1.5 mono) cis/ trans 0.01	$ZnCl_2$ I, $(C_2H_5)_2O$	51 112, 60, 61
		CH ₂ N ₂	B(73) mono/bis 0.59	ZnI,	12
C ₅ H ₈	2-Methyl-1,3-butadiene	CH ₂ I ₂	A()[1,2-64.4%; 3,4-3.6%; bis-32%]	I, $(\hat{C}_{2}H_{5})_{2}O$	111, 284, 285
C.H.	1,3-Cyclohexadiene	CH ₂ N,	B(83) mono/bis 0.65	ZnI,	12
•••	1,4-Cyclohexadiene	CH,I,	A(37, mono)	II, (C,H,),O	268, 60, 352
		CH ₂ I	A(55)	I, $(C, H_s), O$	27
		CD,I,	A()		55
C ₆ H ₁₀	1,5-Hexadiene	CH ₂ I,	A(54) mono/bis 0.33	$I_{1} (C_{2}H_{2})_{2}O$	6, 348
C ₇ H ₈	2,5-Norbornadiene	CH ₂ I ₂	A(80) mono/bis 0.5	I, $(C_2H_5)_2O$	102, 6, 27, 85, 286
		CD,I,	A(-, mono)		97, 95
C ₈ H ₈	1,3,5,7-Cyclooctatetraene	CH_I	A(5.4)	I, $(C_2H_5)_2O$	276, 115
C ₈ H ₁₀	5-Methylene-2-norbornene	CH ₂ I ₂	A(26, bis)	I, $(C_2H_5)_2O$	27
- 10	1,3,5-Cyclooctatriene	CH ₂ I ₂	A(-, mono)		114
	-	CD ₂ I ₂	A(, mono)		113

	1,3,6-Cyclooctatriene	CH,I,	A()	_	114
C ₈ H ₁₂	1,4-Dimethylenecyclohexane	CH ₂ I ₂	A(-, bis)	_	287
	4-Vinylcyclohexene	CH ₂ I ₂	A(87.4) mono/bis 0.3	I, $(C_2H_5)_2O$	102
		CH ₂ Br ₂	A(—)	$I_{1}(C_{2}H_{5})_{2}O$	41
		CH ₂ N ₂	B()	ZnI, and ZnBr,	41
	1,4-Cyclooctadiene	CH ₂ I ₂	A() cis/trans 0.66	I, $(\tilde{C}_{2}H_{5})_{2}O$	179
	1,5 Cyclooctadiene	CH ₂ I,	A(73) mono/bis 0.48	II, (C,H,),O	288, 102, 276
C ₁ H ₁₄	2,5-Dimethyl-2,4-hexadiene	I2CHCO2C2H2	A(12)	_	117
	-	CĨ ₂ CHCÕ ₂ Ĉ ₂ H ₅	A(3-5)	_	117
C ₁ H ₁₂	endo-5-Vinyl-2-norbornene	CH,I,	$\mathbf{A}(-)$	I, (C,H,),O	34
• ••		CH,N,	B()	ZnI,	34
	(Z,Z,Z)-1,4,7-Cyclononatriene	CH,I,	A(80-90)	I, (Ĉ,H,),O	55
		CD,I,	A()	(C,H,),O	352
C10H12	1,4,5,8-Tetrahydronaph-	CH,I,	A(50, mono)	IV, (O,H,),O, preformed	93
	thalene			reagent	
	exo-3a,4,7,7a-Tetrahydro-	CH ₂ I ₂	A(68.5)	I, (C,H,),O	27
	4,7-methanoindene				
	endo-3a,4,7,7a-Tetrahydro-	CH ₂ I ₂	A(86)	I, $(C_{9}H_{5})_{9}O$	27
	4,7-methanoindene				
C10H16	(+)-p-Mentha-1,8-diene	CH ₂ I ₂	A(51)	II, $(C_2H_5)_2O$	250, 6, 85
	(D-Limonene)				
	(E,Z)-1,5-Cyclodecadiene	CH ₂ I ₂	A(48)	I, $(C_2H_5)_2O$	88
C10H18	(Z)-2,6-Dimethyl-2,6-		(—)		277
	octadiene				
	Diisopropylidenedimethyl-	CH ₂ I ₂	A(—)	I, $(C_{\mathbf{a}}H_{\mathbf{s}})_{\mathbf{a}}O$	116
	cyclopropane				
C, H1	4,8-Dihydro-s-hydrindacene	_	(—)	—	54
C12H18	(E,E,E)-1,5,9-Cyclo-	CH ₂ I ₂	A(—)	I, $(C_2H_5)_2O$	289
	dodecatriene				
	(E,E,Z)-1,5,9-Cyclo-	CH ₂ I ₂	A(64)	$I_{s} (C_{2}H_{s})_{2}O$	56, 89
	dodecatriene				
C12H20	(E,Z)-Bicyclo[10.1.0]-	CH,I,	A()	$I_{\bullet}(C_{\bullet}H_{\bullet})_{\bullet}O$	56
	trideca-4,8-diene	••			
$C_{14}H_{16}$	1,4,5,8,9,10-Hexahydro-	CH,I	A(23)	$I_{,}(C_{2}H_{5})_{2}O$	94
	anthracene			· · • 0/*	
C16H16	Cyclooctatetraene dimer	_	(—)	_	108
C16H24	7,14-Dimethylenedispiro-	CH ₂ I ₂	A (75-80, bis)	I, $(C_2H_5)_2O$	103
	[5.1.5.1]tetradecane				

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ADDE IV. SINIMESIS OF CICLOPROPANES FROM UNSATURATED COMPOUNDS (COMM	TABLE IV.	SYNTHESIS C	OF CYCLOPROPANES	FROM UNSATURATED	Compounds	(Continue
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	Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
	ARYL- AND	BENZO-ALKENES				
	$C_8H_5$	Bicyelo[4.2.0]octa- 1,3,5,7-tetraene	CH ₂ I ₂	A()	_	125
	C ₈ H ₇ Br	p-Bromostyrene	$CH_2I_2$	A(9)	I, $(C_2H_{\delta})_2O$ , accompanied by polymerization	119
	C ₈ H ₇ Cl	p-Chlorostyrene	$CH_2I_2$	A(12)	I, $(C_2H_5)_2O$ , accompanied by polymerization	119
			$CH_2I_2/(C_2H_5)_2Zn$	C(16)	$(C_{2}H_{5})_{2}O$	50a
	C,H,F	p-Fluorostyrene	$CH_2I_2/(C_2H_5)_2Zn$	C(23)	$(C_2H_5)_2O$	50a
	C ₈ H ₈	Styrene	CH ₂ I ₂	A(32)	$\mathbf{I}, \mathbf{C}_{2}\mathbf{H}_{5}\mathbf{)}_{2}\mathbf{O}$	1, 6, 36, 41, 85, 119, 123, 290
			CH,N,	B(60)	ZnI,	9
			CH ₂ I ₂ /(C ₂ H ₂ ) ₂ Zn	C(76)	C, H,	83, 43a, 50a
5			CH.I./C.H.ZnI	C(78) ^b	(Č,H,),O	124
5	C.H.F.	<i>m</i> -Trifluoromethylstyrene	CH.I./(C.H.),Zn	C(6)	(C,H,),O	50a
	C.H.	Indene	CH.I.	A(30)	I, (C,H,),O	123, 36, 125
	C.H.	o-Methylstyrene	CH,I,	A(-)		290
	• 10	p-Methylstyrene	CH,I,/(C,H,),Zn	C(67)	(C,H,),O	50a
		g-Methylstyrene		()		41
		(E)-1-Phenylpropene	CH.I.	A(54)	I, (C,H,),O	6, 82, 121
			CH.I./C.H.ZnI	C(68) ^b	$(C_{a}H_{s})_{a}O$	124, 291
		3-Phenylpropene	CH.I.	A(49)	i, (C,H.),O	1,6
	C ₈ H ₁₀ O	p-Vinylanisole	CH ₂ I	A(2)	I, $(C_2H_5)_2O$ , accompanied by polymerization	119
	C ₁₀ H ₉ NO ₂	6-Nitro-1,2- dihydronaphthalene	$CH_2I_2$	A(9)		353
	C10H10	l-Methyleneindane	CH ₂ I ₂	A(40)	I, $(C_2H_5)_2O$	292, 123
		1,2-Dihydronaphthalene	CH ₂ I ₂	A(20)	III, $(C_2H_5)_2O$	292, 123
	C ₁₀ H ₁₁ Cl	(E)-l-(p-Chlorophenyl)- l-butene	$CH_2I_2$	A(—)	I, $(C_2H_5)_2O$	138
	с. н	2.6-Dimethylstyrene	CH.I.	A()	_	290
	-1012	3.5-Dimethylstyrene	$CH_{\bullet}I_{\bullet}/(C_{\bullet}H_{\star})_{\bullet}Zn$	C(65)	_	354
		(2-Methylpropenyl)benzene	$CH_{a}I_{a}/(C_{a}H_{a})_{a}Zn$	C(75)	<u>—</u>	122
		(E)-1-Phenyl-1-butene	CH.I.	A(30)	I. (C.H.).0	281, 138

	C ₁₀ H ₁₂ O	o-Propenylanisole	CH ₂ I ₂	A(70)	1, $(C_2H_5)_2O$	1, 6				
		<i>m</i> -Propenylanisole	CH ₂ I ₂	A(60)	I, $(C_2H_5)_2O$	6				
		p-Propenylanisole	CH ₂ l ₂	A(63)	I, $(C_2H_5)_2O$	6				
			CH ₂ N ₂	B(70)	Znl ₂	9				
		o-Allylanisole	CH ₂ I ₂	A(48)	I, $(\tilde{C}_{2}H_{5})_{2}O$	6				
	C ₁₁ H ₁₁ NO ₂	2-Nitro-6,7-dihydro-5H- benzocycloheptene	CH ₂ I ₂	A(4)	_	353				
		l-Methylene-7-nitro-1,2,3,4- tetrahydronaphthalene	CH ₂ I ₂	A(31)	_	353				
	С., Н.,	1-Cyclopentenvibenzene	CH.I.	A(56)	$\Pi I, (C, H_{r}), O$	266, 161				
		l-Methylene-1,2,3,4- tetrahydronaphthalene	CH ₂ I ₂	A(75)	II, $(C_2H_5)_2O$	292				
		6,7-Dihydro-5H-benzo- cycloheptene	CH ₂ I ₂	A(—)	II, $(C_2H_5)_2O$	292				
	C11H14	2, 4, 6 Trimethylstyrene	CH ₂ I ₂	A(37)	II, $(C_2H_5)_2O$	120				
		(E)-1-(p-Tolyl)-1-butene	CH ₂ I ₂	A(—)	I, $(\dot{C}_{2}\dot{H}_{5})_{2}\dot{O}$	138				
	C ₁₂ H ₁₃ NO ₂	3-Nitro-5-methylene-6,7,8,9- tetrahydro-5H-benzocyclo- heptene	CH ₂ I ₂	A(20)	$(C_2H_5)_2O$	353				
103	C12H14	5-Methylene-6,7,8,9- tetrahydro-5H- benzocycloheptene	CH ₂ I ₂	A(74)	$(C_{g}H_{g})_{g}O$	353				
		(35:65 mixture with 5-meth	yl-7,8,9-trihydro-7H-benze	ocycloheptene)						
		(1-Cyclohexen-1-yl)benzene	CH ₂ I ₃	A(66)	III, $(C_2H_5)_2O$	266, 36				
	C14H12	1,1-Diphenylethylene	CH.I.	A(24)	I, $(C_2 H_5)_2 O$	6				
		(E)-Stilbene	CH,I,	A(18)	I, $(C_2H_5)_2O$	82				
			CH ₂ I ₂ /C ₂ H ₅ ZnI	$C(13)^b$	$(C_2H_5)_2O$	124				
	$C_{15}H_{14}$	l,l-Diphenyl-l-propene	$CH_{2}I_{2}$ $CH_{2}I_{2}/C_{2}H_{5}ZnI$	A(12) C(45) ^b	I, $(C_2H_5)_2O$ $(C_2H_5)_2O$	82 124				
	$C_{21}H_{18}S$	cis-α-Benzylthiostilbene		A(0)		355				
		$trans-\alpha$ -Benzylthiostilbene		A (0)	-	355				
	SUBSTITUTED OLEFINS									
	Hydroxy Olefin	.8								
	C.H.D.O	Allyl 1, 1, 2, 3-d, alcohol	CD.I.	A(20.2)	(C,H,),O	165				
	C.H.D.O	(E)-Allyl-2,3-d, alcohol	CH.I.	A(40-45)	(C,H,),O	164				
	C.H.O	Allyl alcohol	CH.I.	A(40-45)	(C,H,),O	164				
	· · ·	· · · ·	$\mathrm{CH}_{3}^{2}\mathrm{CHI}_{2}/(\mathrm{C}_{2}\mathrm{H}_{5})_{2}\mathrm{Zn}$	C(23) cis/trans 0.185	<b>i</b> -(Ĉ ₃ Ĥ ₇ )₂O	162				

Note: References 257-369 are on pp. 129-131. • The Sawada modification was used. See p. 91.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions Couple, Solvent, Other	Refs.
SUBSTITUT	FED OLEFINS (contd.)				
Hydroxy Ole	fins (contd.)				
C.H.ONA	(E)-2-Buten-1-ol. sodium salt	CH-L/C-H-ZnI	C(60) ^b	(C.H.).O	124
С.н.о	2-Methyl-2-propen-1-ol	CH I.	A(50)	I. (C.H.).0	128, 127, 164
	3-Buten-l-ol	CH.I.	A(26)	1. (C.H.).O	128, 127
	(Z)-2-Buten-1-ol	CH.I.	A(88)	(C.H.).O	293
	(E)-2-Buten-1-ol	CH.I.	A(40-45)	I. (C.H.).O	164
	(_)	CH.I./C.H.Znl	C(27)	(C.H.).O	124
		CH.CHI./(C.H.).Zn	C(85) cis/trans 1.7	i-(C.H.).O	162, 294
C.H.O	2. Methylenecyclobutanol	CH.I.	A()	<u> </u>	174
0,	2-Cyclopenten-1-ol	CH.I.	A(75)	I. (C.H.).O. preformed	64, 61, 67, 73,
			(,	reagent	295, 296, 356
	3-Cyclopenten-1-ol	CH ₂ I ₂	A (75)	I, (C ₃ H ₅ ) ₃ O	4, 59, 60, 61, 295, 356
		CH,CHI,/(C,H,),Zn	C(45)	i-(C,H,),O	162
	1.4-Pentadien-3-ol	CH.I.	$\mathbf{A}(-)$	11, (C.H.),0	166
C.H.,O	3-Methyl-3-buten-1-ol	CH.I.	A(10)	I, (C,H,),O	127
5 10	2-Methyl-3-buten-2-ol	CH.I.	A(60)	I. (C.H.).O	127
	4-Penten-2-ol	_ 11	( <u>)</u>		297
	(E)-3-Penten-2-ol (mixture with (Z)-3-penten-2-ol)	CH ₂ I ₂	A(60)	I, $(C_2H_5)_2O$	127, 298, 299
	(Z)-3-Penten-2-ol (mixture	CH.I.	A(60)	I, (C,H,),O	127, 298, 299
	with $(E)$ -3-penten-2-ol)				
C ₆ H ₁₀ O	2,3-Dimethyl-2-cyelopropene- 1-methanol	$\mathrm{CH_2I_2}/(\mathrm{C_2H_5})_2\mathrm{Zn}$	C(72)	_	71
	2-Methylenecyclopentanol	CH ₂ I ₂	A(74)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	64, 296
	3-Methyl-2-cyclopenten-1-ol	CH ₁ I ₂	A(43)	III, $(\tilde{C}_2H_b)_2O$	300, 356
	2-Cyclohexen-1-ol	CH ₂ I ₂	A(71)	I, $(C_2H_5)_2O$	67, 63, 64, 66, 72, 296, 300 301 356
сно	2.2. Dimethyl-3. buten, Lol		()		302
<b>3</b> ¹¹ 12 ⁽⁾	4. Methyl. L. penten. 3.0	CHI		(CH).0	303
	(E).4.Methyl.2.nenten.1.ol	CHI	A(17)	$(C_1H_1)$	303
	(2) A Methyl-2-penten   ol	CHI	Δ(Δ)	(CH)	303
	A Methyl 3-penter l.ol	~11 <u>2</u> *2	()		245
	5 Haven-9-0		()	_	297
CHO	2.5-Norbornedien-7-ol		B(0)	_	172
CHO	2.5 Cyclobentedien_l_ol	CH I	$\Delta(-)$	_	304
C7H10	3,5-Cycloheptadien-1-ol	CH ₂ I ₂	A()	—	304

TABLE IV.	SYNTHESIS OF	CYCLOPROPANES FROM	UNSATURATED	COMPOUNDS	(Continued)
TUDUE IV.	DINIMBOLD OI	OTODOLIOIANDS FROM	CHOMICIMITI	001110011103	(00/00/0000)

	exo-Bicyclo[3.2.0]hept-	CH ₂ I ₂	A(—)	II, $(C_2H_{\delta})_2O$	176
	endo-Bicyclo[3.2.0]hept- 3-en-2-ol	CH ₂ I ₃	A(—)	II, $(C_2H_5)_2O$	176
	endo-5-Norbornen-2-ol	_	()	-	66
	exo-5-Norbornen-2-ol	CH ₂ I ₂	A(39)	$(C_2H_5)_2O$	169, 66, 168, 170
	anti-2-Norbornen-7-ol	CH,I,	A(17)	(C,H,),O	76, 171
C ₇ H ₁₂ O	(Z,Z)-4-Methyl-2,4- hexadien-1-ol	CH ₂ I ₂	A (90)	III, (C ₂ H ₅ ) ₂ Ο	163
	1-Cyclohexene-1-methanol	_	(—)		66
	3-Cyclohexene-1-methanol	_	( <u>    )</u>		66
	2-Methylenecyclohexanol	CH ₃ I ₂	A(68)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	64, 296
	4-Methylenecyclohexanol	СН.1.	A(51)		305
	2-Methyl-2-eyclohexen-1-ol	CH ₂ I ₂	A(50)	1, (C ₂ H ₅ ) ₂ O, preformed	64
	3-Methyl-2-oyclohexen-1-ol	CH ₂ I ₂	A(57)	I, $(C_2H_5)_2O$ , preformed	64
	t <b>rans-</b> 5-Methyl-2-cyclohexen- l-ol	—	(—)		66
	cis-5-Methyl-2-cyclohexen-1-ol	_	(—)	_	66
10	1-Methyl-3-cyclohexen-1-ol	CH ₁ I	Å(—)	_	66a
Cri	cis-6-Methyl-3-cyclohexen-1-ol	CH,I,	A(—)	_	66a
	trans-6-Methyl-3-cyclohexen- l-ol	CH ³ 1 ³	A()		66a
	2-Cyclohepten-1-ol	CH ₂ I ₂	A(82)	I, $(C_2H_5)_2O$	67, 64, 288, 356
	3-Cyelohepten-1-ol	CH I.	A(89-90)	$\Pi_{\epsilon} (C_{\bullet}H_{\epsilon})_{\bullet}O$	288
C.H.O	3-Methyl-5-hexen-3-ol	CHI	A(20)	I. (C.H.).O	127
C ₂ H ₁₀ O	endo-tricyclo[3.2.1.0 ^{2.4} ]- 6-octen-sun-2-ol	CH ₃ I ₂	A()		173
	endo-Tricyclo[3.2.1.0 ^{2.4} ]-	CH ₂ I ₃	A(—)	—	173
C.HO	3.6-Cyclooctadien-1-ol	CH.I.	A(90, bis, cis)		179
-8-18-	exe-5-Norbornene-2-methanol		( <u> </u>		66
	endo-5-Norbornene-2-methanol	_	( <u> </u>	_	66
	endo-Bicyclo[2.2.2]-	CH ₃ I ₂	À(—)	$(C_{3}H_{5})_{2}O$	306
C ₂ H ₁₂ O ₂	2,5-Dimethylene-cyclohexane-	CH ₂ I ₃	A(50 bis)	I, $(C_{g}H_{5})_{2}O$	357
C ₉ H ₁₃ DO	1-Deuterio-2-cyeloocten-1-ol	CH ₂ I ₂	A(—)	II, (C ₃ H ₅ ) ₃ O	345

Note: References 257-369 are on pp. 129-131. • The Sawada modification was used. See p. 91.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITUT	TED OLEFINS (contd.)				······································
Hydroxy Olef	fins (contd.)				
C ₉ H ₁₄ O	3-Isopropyl-2-cyclopenten-1-ol	CH ³ I ³	A(67)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	185
	2-Ethylidenecyclohexanol	CH ₂ I ₂	A(49)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	64
	4,4-Dimethyl-2-cyclohexen- l-ol	CH ₂ I ₂	A(77)	III, $(\tilde{C}_2H_5)_2O$	356
	5,5-Dimethyl-2-cyclohexen- l-ol	CH ₂ I ₂	A(71)	$(C_2H_5)_2O$	307
	2,3-Dimethyl-2-cyclohexen-	CH ₂ I ₂	A(47)	I, (C ₂ H ₅ ) ₂ O, preformed	64
	4-Cycloheptene-1-methanol	CH.I.	A(29) cis/trans 3		308
	(Z)-2-Cycloocten-1-ol	CH.I.	A(74, anti)	I. (C.H.).O	67.68.345
	(E)-2-Cycloocten-1-ol	CH.I.	A(80)	I. (C.H.).O	69. 346
$\mathbf{C_8H_{14}O_2}$	2. Methoxy-3-methyl-2- cyclohexen-1-ol	CH ₂ I ₂	A()	$(C_2H_5)_2O$	158
C.HO	6-Methyl-5-hepten-2-ol	CH.I.	A(65)	I. $(C_{\bullet}H_{\bullet})_{\bullet}O$	127, 128
-816-	(Z)-2-Octen-1-ol	CH ₂ I ₂	A()	II, $(C_2H_5)_2O$ , preformed	255
	(Z)-2-Octen-4-ol		()		299
C.H. O	8-Methylenedispiro-	CH.I.	A (50)	$I_{c} (C_{a}H_{c})_{a}O$	104
00120	[2.0.2.2]octan-7-ol		()	-, ( 1 5/2 -	
	4.7-Dihvdroindan-2-ol	CH.I.	A(60)	III. $(C_{\bullet}H_{\star})_{\bullet}O$	177, 356
	(Z,Z,Z)-2,5,8-Cyclo- nonatrien-1-ol	CH ₂ I ₂	A()		180, 181
	(Z,Z,Z)-2,4,7-Cyclonona- trien-1-ol	CH ₂ I ₂	A(66.5)	111, $(C_2H_5)_2O$	180, 181, 181 <b>a</b>
C.H.0	4,5,6,7-Tetrahydroindan-2-ol	CH,I,	A(42)	III, $(C, H_{\epsilon}), O$	309, 356
C H ₁₅ O	3,5,5-Trimethyl-2-cyclohexen- l-ol	CH ₁ I	A()	III, $(C_2H_5)_2O$	356
$C_{8}H_{18}O$	4-Isopropylidene-2,2- dimethylcyclobutanol	CH ₂ I ₂	A()	—	174, 358
	2,2,3,3-Tetramethyl-4- methylenecyclobutanol	CH ₂ I ₂	A()	$(C_2H_5)_2O$	358
	3-Isopropyl-1-methyl-2- cyclopenten-1-ol	—	A(0)	<u> </u>	185
	4-Cyclooctene-l-methanol	CH.I.	A(29) cis/trans 3	-	308
	2-Cvclononen-1-ol	CH.I.	A(66)	III, $(C, H_{\epsilon}) = 0$	67, 70, 310

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued
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C10H14O	1,2,3,4,5,8-Hexahydro-2- naphthol	CH ₂ I ₂	$A(\approx 100)$	I, $(C_2H_\delta)_2O$	178, 344
	Bicyclo[7.1.0]deca-4,6- dien-3-ol		(—)	_	181
	(Z,Z,Z)-2,5,8-Cyclo- decatrien-1-ol	CH ₂ I ₂	A(65)	III, $(C_2H_5)_2O$	180, 181a
C10H15O	1,2,3,4,5,6,7,8-Octahydro-2- naphthol	CH ₂ I ₂	A(61)	—	309
	2,3,4,4a,5,6,7,8-Octahydro-2- naphthol	CH ₂ I ₂	A()	I11, $(C_2H_5)_2O$	356
	(Z,Z,Z)-3,6,9-Cyclo- uudecatrien-1-ol	CH ₂ I ₂	A(58)	III, $(C_2H_5)_2O$	181a
	exo-7-Methylenebicyclo- [3.3.1]nonan-3-ol	CH ₂ I ₃	A(40)	_	167
	endo-7-Methylenebicyclo- [3.3.1]nonan-3-ol	CH ₂ I ₂	A()	_	167
	Bicyclo[4.4.0]dec-1-en-2-o1	CH ₂ I ₂	A(67)	Ill, glyme, 50°	359
	Bicyclo[5.3.0]dec-l-en-2-ol	CH ₂ I ₂	A(79)	III, glyme, 40°	359
	trans-Bicyclo[4.4.0]dec- 3-en-1-ol	CH ₂ I ₂	A(—)	_	66a
	cis-Umbellulol	$CH_2I_2$	A(68) cis/trans 1	$(C_2H_5)_2O$	360
	trans-Umbellulol	$CH_2I_2$	A(68) cis/trans 1	$(\mathbf{C}_{2}\mathbf{H}_{5})_{2}\mathbf{O}$	360
	10-Hydroxy-2(3)-pinene (Myrtenol)	CH ₂ I ₂	A(80)	$\mathbf{II}, \ (\mathbf{\tilde{C}_2H_5})_2\mathbf{O}$	183a
	3-Hydroxy-2(10)-pinene (Pinacarveol)	CH ₂ I ₂	A(62)	II, $(C_2H_5)_2O$	183a
C ₁₀ H ₁₈ O	3-Methyl-6-isopropyl-2- cyclohexen-1-ol	CH ₂ I ₂	A(60.5)	I, (C ₂ H ₅ ) ₂ O, preformed reagent	6 <b>4</b>
С ₁₁ Н ₁₀ О	anti-1,4-Dihydro-1,4- methanonaphthalen-9-ol	_	A(0)	_	172
C ₁₁ H ₁₆ O	2-Methyleneadamantan-l-ol	CH ₂ I ₂	A(83)	I, $(C_2H_5)_2O$	182, 183, 311, 107
C ₁₁ H ₁₈ O	4a-Methyl-2,3,4,4a,5,6- 7,8-octahydronaphthalen- 2-ol (mixture of $\alpha$ and $\beta$ isomers)	CH ₂ I ₂	A(—)	(C ₂ H ₅ ) ₂ O	193
	l-Methyl-2,3,4,4a,5,6,7,8- octahydro-2-naphthol	CH ₂ I ₂	A()	III, $(C_2H_5)_2O$	356
	10-Hydroxymethyl-2(3)-pinene (Nopol)	CH ₂ I ₂	A(18)	II, $(C_2H_{\delta})_2O$	183a
$C_{12}H_{20}O$	4-Cyclohexylidene-2,2- dimethylcyclobutanol	CH ₂ I ₂	A()	$(C_2H_5)_2O$	358
C ₁₂ H ₂₀ O ₂	5-Methoxy-8a $\beta$ -methyl- 1,2,3,4,6,7,8,8a-octahydro- $\alpha$ -naphthol	CH ₂ I ₂	A(—)	_	235

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITU	TED OLEFINS (contd.)			····	· · · · · · · · · · · ·
Hydroxy Old	efins (contd.)				
C ₁₃ H ₂₂ O	4a $\beta$ ,8,8-Trimethyl-2,3,4,4a,5,6, 7,8-octahydro-2 $\beta$ -naphthol (mixture with 4a $\beta$ -8,8- trimethyl-2,3,4,4a,5,6,7,8- octahydro-2 $\alpha$ -naphthol)	CH ₂ I ₂	A(23)	(C ₂ H ₅ ) ₂ O	184, 312
	4aβ,8,8-Trimethyl-2,3,4,4a,5, 6,7,8-octahydro-2α.naphthol (mixture with 4aβ,8,8- trimethyl-2,3,4,4a,5,6,7,8- octahydro-2β-naphthol)	CH ₂ I ₂	A(23)	(C _B H _b ) ₂ O	184, 312
	10,10-Dimethylbicyclo-	CH ₂ I ₂	A(—)	III, $(C_2H_5)_2O$	358
$C_{13}H_{22}O_{2}$	[7.2.0]undec-1-en-11-01 5-Methoxy-1β,8aβ-dimethyl- 1,2,3,4,6,7,8,8a-octahydro- lα-naphthol	CH ₂ I ₃	A()	-	235
C ₁₅ H ₂₄ O ₃	5β,9-Dimethyl-2,3,4,4aβ,5,6,7, 9ag.octahydrospiro- [1H-benzocycloheptene-1,2', [1,3]dioxolan]-5-ol	CH ₂ I ₂	A(—)		187
$\mathbf{C_{15}H_{26}O}$	Bicyclo[10.3.0]pentadec-1- en-13-ol	$\mathbf{CH_2I_2}/(\mathbf{C_2H_5})_{2}\mathbf{Zn}$	C(37)	C ₆ H ₆	359
C ₁₅ H ₃₆ O ₃	7β-Isopropyl-1-methoxy- 4aα-methyl-2,3,4,4a,5,6,7α, 8-octahydro-2α-naphthol	CH ₂ I ₂	A(91)		234
$\mathbf{C_{17}H_{16}O}$	3,4α-Diphenyl-2-cyclopenten-	CH ₂ I ₂	A(47)	$(C_2H_5)_2O$	313, 175
	$3,4\hat{\beta}$ -Diphenyl-2-cyclopenten- 1 $\beta$ -ol	CH ₂ I ₂	A(67)	$(\mathbf{C_2H_5})_{2}\mathbf{O}$	313, 175
	3,4-Diphenyl-3-cyclopenten-	CH ₂ I ₂	A(61)	<u>.</u>	74
	5-Hydroxy-5-vinyl-5H- dibenzo[a,d]-10,11- dihydrocycloheptene	CH ₂ I ₂	A (52)	$(\mathbf{C_2H_\delta})_{2}\mathbf{O}$	314

## TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

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	C18H30O8	meso-3,4-Di-(4-hydroxy- cyclohexenyl)hexene	CH ₂ I ₃	A()		315
	C ₂₆ H ₃₆ O ₂	$3\beta$ -Hydroxy-10-methoxy- $6a\beta$ , $12b\beta$ , $14a\alpha$ -trimethyl- $1,2,3\alpha$ -5, $6,6a$ , $6b\alpha$ , $7,8$ , $12b$ , $13,14,14a$ , $14b\beta$ -tetradeca- hydropioene	CH ₂ I ₂	A(—)	(C ₂ H ₅ ) ₂ O/ <b>THF</b>	202
	Alkoxy Olefins					
	Vinyl Ethers					
	C ₈ H ₄ O C ₄ H ₄ O	Methyl vinyl ether Furen	$\begin{array}{c} \mathrm{CH}_{2}\mathrm{I}_{2}/(\mathrm{C}_{2}\mathrm{H}_{5})_{2}\mathrm{Zn}\\ \mathrm{CH}_{2}\mathrm{N}_{2}\\ \mathrm{CH}_{3}\mathrm{CHI}_{2}/(\mathrm{C}_{2}\mathrm{H}_{5})_{2}\mathrm{Zn} \end{array}$	C() B(19) C(32) endo/exo 3.2	$(C_2H_5)_2O$ $ZnI_2$ $(C_2H_3)_2O$	50a 12 162
	C _s H ₈ O C ₅ H ₈ O	Ethyl vinyl ether 3,4-Dihydro-2H-pyran	$CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$ $CH_{2}I_{2}$ $CH_{2}I_{2}/C_{2}H_{5}ZnI$ $CH_{2}CH_{2}I_{2}/C_{2}H_{5}ZnI$	C() A(66) C(80) ^b C(57) endo/exo 1.4	$(C_2H_5)_2O$ II, $(C_2H_5)_2O$ $(C_2H_5)_2O$ Petroleum ether	50a 250, 6, 34, 41 124, 50a 162
	C ₅ H ₁₀ O	Isopropyl vinyl ether ( $Z$ )-Methyl 1-butenyl ether ( $E$ )-Methyl 1-butenyl ether	$CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$ $CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$ $CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$ $CH_{3}I_{3}/(C_{3}H_{5})_{2}Zn$	C() C() C()	$(C_2H_5)_2O$ $(C_2H_5)_2O$ $(C_4H_2)_3O$	50a. 316 316
109	$\substack{\mathrm{C_6H_{10}O}\\\mathrm{C_6H_{12}O}}$	1,3-Butadienyl ethyl ether n-Butyl vinyl ether	$\frac{CH_2I_2}{CH_2I_2}/(C_2H_5)_2Zn$ $CH_2I_2/(C_2H_5)_2Zn$ $CH_2I_2/(C_2H_5)_2Zn$ $CH_2I_2/C_3H_5ZnI$	C(42) C(92) C(14) ^b	$\begin{array}{c} C_{\mathbf{g}} H_{\mathbf{g}} \\ (C_{2} H_{\mathbf{g}})_{2} O \\ (C_{\mathbf{q}} H_{\mathbf{g}})_{\mathbf{q}} O \end{array}$	83 83 124
		Isobutyl vinyl ether	CH _s I _s /(Č ₂ H ₅ ) ₂ Zn CH ₃ CHI ₂ /(Č ₂ H ₅ ) ₂ Zn	C(84) C(96) syn/anti 2.3	$(C_2^{\dagger}H_5)_2^{\bullet}O$ $(C_2^{\dagger}H_5)_2^{\bullet}O$	83 84, 162, 50a
		t-Butyl vinyl ether (Z).Propenyl propyl ether (E).Propenyl propyl ether (Z).Propenyl isopropyl ether (E).Propenyl isopropyl ether (Z).1.Butenyl ethyl ether	$\begin{array}{c} {\rm CH}_{2}{\rm I}_{4}/({\rm C}_{2}{\rm H}_{5})_{2}Z{\rm n}^{-}\\ {\rm CH}_{2}{\rm I}_{2}/({\rm C}_{2}{\rm H}_{5})_{2}{\rm Cd}\\ {\rm CH}_{2}{\rm I}_{2}/({\rm C}_{2}{\rm H}_{5})_{2}{\rm Cd}\\ {\rm CH}_{3}{\rm CH}_{2}/({\rm C}_{2}{\rm H}_{5})_{2}{\rm Zn}\\ {\rm CH}_{3}{\rm CHI}_{2}/({\rm C}_{2}{\rm H}_{5})_{2}{\rm Zn}\\ {\rm CH}_{3}{\rm CHI}_{2}/({\rm C}_{2}{\rm H}_{5})_{2}{\rm Zn}\\ {\rm CH}_{3}{\rm L}_{3}{\rm L}_{2}{\rm L}_{$	C() C(87) C(79) C(90) cis/trans 9.2 C(77) cis/trans 3 C(56)	$\begin{array}{c} (C_2^-H_5)_2^-O\\ (C_3^-H_5)_2O\\ (C_3^-H_5)_2O\\ (C_2^-H_5)_2O\\ (C_2^-H_5)_2O\\ (C_3^-H_5)_2O\\ L-Leucine used as asymmetric\end{array}$	50a 238, 50a 238, 50a 162 162 84, 50a
	0 11 0				cocatalyst; xylene	<i>cc</i>
	$C_7H_{12}O$ $C_7H_{14}O$	1-cyclonexenyl methyl ether (Z)-Isobutyl propenyl ether (E)-Isobutyl propenyl ether Ethyl 3-methyl-1-butenyl ether	$\begin{array}{l}\\ CH_2I_2/(C_2H_5)_2Zn\\ CH_2I_2/(C_2H_5)_2Zn\\ CH_2I_2/(C_2H_5)_2Zn \end{array}$	C(80) C(80) C(61)	$\begin{array}{c}\\ (C_2H_5)_2O\\ (C_2H_5)_2O\\ L-Leucine used as asymmetric cocatalyst; xylene \end{array}$	00 83, 50a 83 84, 50a

• The Sawada modification was used. See p. 91.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITU	TED OLEFINS (contd.)	······································			
Alkoxy Olefi	ins (contd.)				
Vinyl Ether	es (contd.)				
C,H,CIO C,H,O	p-Chlorophenyl vinyl ether Phenyl vinyl ether	$\begin{array}{c} \mathrm{CH_2I_2/(C_2H_3)_2Zn}\\ \mathrm{CH_3I_3}\end{array}$	C(67) A(27)	C _s H _s Accompanied by polymerization	83 142
C ₈ H ₁₄ O	Cyclohexylidenemethyl methyl ether	CH ₂ I ₂	A()	$(C_2H_5)_2O$	158
С ₃ Н ₁₆ О С ₃ Н ₁₀ О	Isopentyl propenyl ether p-Tolyl vinyl ether	$\mathrm{CH_{2}I_{s}/(C_{2}H_{6})_{g}Zn}_{\mathrm{CH_{g}I_{g}}}$	C(70) A(19)	(C ₂ H ₃ ) ₂ O Accompanied by	83 142
C ₈ H ₁₈ O	2,6-Dimethyl-l-cyclohexen-	CH ₂ I ₂	A()	$(C_2H_5)_3O$	158
C11H14O	Mesityl vinyl ether	CH ₂ I ₃	A(37.5)		142
Ketene Ace	tels				
$\mathbf{C_6H_{12}O_2}$	Dimethylketene dimethyl acetal	CH ₃ I ₃	A()	$(C_2H_5)_2O$	158
$C_{10}H_{10}O_{2}$	3-Methylene-1,5-dihydro- 2,4-benzodioxepin	CH ₂ I ₂	A(70)		159
1-Alkoxyvin	yl Esters				
$C_{6}H_{10}O_{3}$ $C_{11}H_{12}O_{3}$	1-Ethoxyvinyl acetate 1-Ethoxyvinyl benzoate	CH ₂ I ₂ CH ₂ I ₂	A(35) A(19)	Glyme Glyme	148 148
Other Type	8				
С ₈ Н ₁₀ О	Diallyl ether 2-Cyclopentenyl methyl ether	p-CH ₃ OC ₂ H ₄ CHN ₂ CH ₂ I ₂	B(16) syn/anti 2.7 A(37, cis)	ZnCl ₂	51 73
C ₈ H ₁₀ O ₈	2.5-Dihydro-2.5-dimeth- oxyfuran	CH ₂ I ₂	A(0)	III	317
$C_7 H_{12} O \\ C_7 H_{12} O_8$	2-Cyclohexenyl methyl ether 2-Isopropenyl-2-methyl- 1,3-dioxolane	CH ₂ I ₃ CH ₂ I ₂	A(70) A()		64,66 153

# TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

	C7H14O	Allyl isobutyl ether t-Butyl allyl ether ()-(S)-[2-Methyl-1-buten- 3.vg ether]	$CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$ $CH_{2}I_{2}$ $CH_{2}I_{2}/(C_{2}H_{5})_{2}Zn$	C(80) A(65) C(90)	$\begin{array}{c} C_6H_6\\ III, (C_2H_5)_2O\\ (C_2H_5)_2O \end{array}$	83 318 319
	$C_7H_{14}O_2$ $C_8H_{14}O$ $C_8H_{14}O_2$	Acrolein diethyl acetal 2-Cycloheptenyl methyl ether (E)-2-Methyl-2-[1-methyl- propertyl] 1-2 diagologo	CH ₂ I ₂ CH ₂ I ₂ CH ₂ I ₂	A (12) A() A()	I, $(C_2H_5)_2O$ III, $(C_2H_5)_2O$ -	6 310 153, 154
		2-Methyl-2-[I-ethylvinyl]- 1,3-dioxolane	CH ₂ I ₂	A()	-	153
	C.H.O	2H-1-Benzopyran	CH.I.	A (22)	(C,H,),O	320
	$C_{10}H_{16}O_2$	2-[1-Cyclohexenyl]-2-methyl- 1,3-dioxolane	CH ₂ I ₂	A(—)		153
	$\mathbf{C_{11}H_{16}O}$	7-t-Butoxy-2,5-norbornadiene	CH ₂ N ₂	B(69 mono syn) endo/exo 0.56 (18 bis)	; ZnI ₂	65
	C., H., O	7-t-Butoxy-2-norbornene	CH.N.	B(28 antiexo)	ZnI,	65
	C ₁₂ H ₁₈ O	2-Methoxy-3,4,4a,5,6,7- hexahydro-4a- methylnaphthalene	CH ₂ I ₂ /(C ₂ H ₅ ) ₂ Zn	C(45) cis/trans mixture	C ⁶ H ⁰	361
111	$\mathrm{C_{14}H_{16}O_{4}}$	Methyl 4,6-O-benzylidene- 2,3-dideoxy- $\alpha$ -D-erythro- bex-2-enopyranoside	CH ₂ I ₂	A()	_	75
	$\mathrm{C_{19}H_{18}O_2}$	7,8-Diphenyl-1,4- dioxaspiro[4.4]-non-7-ene	CH ₂ I ₂	A()		74
	Acyloxy Olefins	,				
	C.H.O.	Vinvl acetate	CH.I.	A(31)	I, (C,H,),O	6, 1, 146
	C.H.O.	Isopropenvl acetate	CH.I.	A(2.5)	I, (C,H,),O	145, 147
	C.H.O.	3-Cyclopentenyl acetate	CH.I.	A(10-18)	$I_{,}(C_{2}H_{5})_{,0}O$	60
	C ₈ H ₁₀ O ₅	2,5-Dihydro-2,5- diacetoxyfuran	CH ₂ I ₂	A(0)	III, $(C_2H_5)_2O$	317
	C.H.O.	2-Cyclohexenyl acetate	CH,I,	A(23)	III, $(C_2H_5)_2O$	63
	C, H, O,	2,5-Norbornadien-7-yl acetate	CH ₂ I ₂	A(0)		171
	C.H.,O.	exo-5-Norbornen-2-yl acetate	CH ₂ I ₂	A(12)		169
	• • •	5-Norbornen-2-yl acetate (mixture of endo and exo isomers)	CH ₂ I ₂	A(16)	-	169

TABLE IV.	Synthesis	OF	CYCLOPROPANES	FROM	UNSATURATED	Compounds	(Continued)
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Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITU	TED OLEFINS (contd.)				
Acyloxy Olef	îns (contd.)				
$C_0H_{14}O_2$	2-Cycloheptenyl acetate 3-Cycloheptenyl acetate	CH ₂ I ₂ CH ₂ I ₂	A() A(10) endo/exo 0.63	I, (C ₂ H ₅ ) ₂ O	6,78 288
C ₁₀ H ₁₄ O ₂	endo-Bicyclo[2.2.2]oct-5- en-2-yl acetate	CH ₂ I ₂	A()	$(C_2H_5)_2O$	306
$C_{10}H_{16}O_{2}$	4.Cycloheptenyl-1-methyl acetate	CH ₂ I ₂	A(87)	_	308
C11H14O2	4,7-Dihydro-2-indanyl acetate	CH ₂ I ₂	A()	III, $(C_2H_5)_2O$	177
Olefinic Acid	l Esters ^b				
$C_5H_8O_2$	Methyl crotonate	CH ₂ I ₂ CH ₂ J ₂ /C ₂ H ₂ ZnI	A(9) C(24) ^b	I, $(C_2H_5)_2O$ $(C_2H_4)_2O$	6, 1, 82 124
$C_8H_8O_2$	Methyl 1-cyclobutene-1- carboxylate	CH ₂ I ₂	A(5.3)	Glyme	156
C ₀ H ₈ O ₄	Dimethyl fumarate	CH ₂ I ₂	A(5)	THF	155, 82
C ₆ H ₁₀ O ₂	Methyl 3 methylcrotonate (methyl senecioate)	$CH_2I_2$	A(18)	$(C_2H_6)_2O$ , preformed reagent	82
C7H10O2	$\begin{array}{c} \operatorname{Methyl} \Delta^{1,\beta} \cdot \operatorname{cyclopropane}_{propionate} \\ \end{array}$	CH ₂ I ₂	A()	_	136
	Ethyl 2-methylenecyclo- propanecarboxylate	CH ₂ I ₂	A(76)	$(C_2H_5)_2O$	137, 136
C7H12O2	Methyl 4-methyl-3- pentenoate (methyl pyroterebate)	CH ₂ I ₂	A(—)		129, 362
$\mathrm{C_8H_{10}O_2}$	Methyl 2,5-cyclohexadiene- 1-carboxylate	CH ₂ I ₂	A(80 bis)		62, 343
C ₈ H ₁₀ O ₄	Dimethyl 2-methylene- 1,1-cyclopropane- dicarboxylate	CH ₂ I ₂	<b>A</b> (—)		136
	Dimethyl 3-methylene-1,2- cyclopropanedicarboxylate	CH ₂ I ₂	A()	_	136

$C_{8}H_{12}O_{4}$ $C_{9}H_{16}O_{2}$ $C_{10}H_{10}O_{2}$ $C_{10}H_{10}O_{4}$	Dimethyl dimethylfumarate Butyl $(Z)$ -2-methylcrotonate Butyl $(E)$ -2-methylcrotonate Methyl cinnamate Dimethyl $(E)$ -4-octene-1,8-	CH ₂ I ₂ CH ₂ I ₂ CH ₂ I ₂ CH ₂ I ₂ CH ₄ I ₂ CH ₄ I ₄	A(12) A() A() A(7) A(8))	$(C_2H_5)_2O$ , preformed reagent $(C_2H_5)_2O$ , preformed reagent $(C_2H_5)_2O$ , preformed reagent	82 154 154 82 321, 322
- 10, 10 - 4	dioate		(0-)		•,
$C_{11}H_{20}O_2 C_{12}H_{14}O_2$	Methyl 3-decenoate Ethyl (E)-p-methoxy- cinnamate	CH ₂ I ₂ CH ₂ I ₂	A() A(29) 	<b>I</b> , (C ₂ H ₅ ) ₂ O	278 6
C12H22O2	Methyl 10-undecenoate	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131
C ₁₃ H ₁₈ O ₂	cis,cis,cis-3,6,9- Cycloundecatrien-l-yl acetate	$CD_2I_2$	A(—)	III	181b
$C_{13}H_{20}O_{2}$	Methyl 4 $\beta$ -methyl-1,2,3,4, 5,6,7,8-octahydro-1- naphthalenecarboxylate	CH ₂ I ₂	A(—)	-	323
	Methyl 4α-methyl-1,2,3,4, 5,6,7,8-octahydro-1- naphthalenecarboxylate	CH ₂ I ₂	A(—)	_	323
C13H34O2	Methyl $(Z)$ -3-dodecenoate	CH ₂ I ₂	A()		130
	Methyl 3-dodecenoate (mixture of 64% trans + 36% cis)	CH ₂ I ₂	A(—)	—	130
C ₁₄ H ₁₆ O ₄	Dimethyl tricyclo[4.2.2.0 ^{2,5} ]- 3,9-decadiene-7,8- dicarboxylate	CH ₂ I ₂	A(—)	_	58
$\mathbf{C_{14}H_{18}O_2}$	Methyl 4,8-dihydro-p- hydrindacene-4-carboxylate	CH ₂ I ₂	A(—)	_	79, 54
C14H,40,	(-)-Menthyl crotonate	CH ₂ I ₂	A()	(C,H,),O	63
C ₁₅ H ₁₇ NO ₃	Ethyl 5-methoxy-2-methyl- α-methyleneindole-3-acetate	CH ₂ I ₂	A()	THF	157
C ₁₄ H ₂₆ O ₂	(-)-Menthyl 3-methyl- crotonate [(-)-menthyl senecioate]	CH ₂ I ₂	A()	$(C_2H_5)_2O$	63
	(-)-Menthyl (E)-3- pentenoate	CH ₂ I ₂	A(—)	$(C_2H_5)_2O$	63

^b' This section includes a few olefinic acids as reactants although cyclopropanation has been generally carried out on the corresponding esters. ^b The Sawada modification was used. See p. 91.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITUT	TED OLEFINS (contd.)		· · · · · · · · · · · · · · · · · · ·		
Olefinic Acid	Esters (contd.)				
$\mathbf{C_{15}H_{30}O_{2}}$	(Z)-9-Hexadecenoic acid (palmitoleic acid)	CH ₂ I ₃	A()	<u> </u>	324
C ₁₇ H ₃₀ O ₈	Methyl 2-cyclopentene-I- undecanoate (methyl hydrocarpate)	CH ₂ I ₂	A(70-80)	III, $(C_2H_{\delta})_2O$	131
$C_{17}H_{32}O_{2}$	Methyl (Z)-9-hexadecenoate (methyl palmitoleate)	$CH_2I_2$	A(70-80)	III, $(C_2H_5)_2O$	131
C ₁₈ H ₃₄ O ₉	(E)-11-Octadecenoic acid (cis-vaccenic acid)	CH ₃ I ₃	A(—)		363
C1.H.O2	(+)-Bornyl cinnamate	-	-	<u> </u>	63, 325
C ₁₉ H ₂₅ BrO ₂	()-Menthyl p-bromo- cinnamate	CH3I3	A()	III, $(C_{g}H_{g})_{g}O$	82a
$\mathrm{C_{12}H_{25}ClO_5}$	(-)-Menthyl p-chloro- cinnamate	CH ₂ I ₂	A(—)	III, $(C_gH_g)_gO$	82a
C ₁₅ H ₂₅ FO ₂	(-)-Menthyl p-fluoro- cinnamate	CH ₂ I ₂	A(0)		82a
C ₁₂ H ₃₈ NO ₄	()-Menthyl p-nitro	CH ₂ I ₂	A(0)	<b>—</b> •	82a
C, H.O.	(-)-Menthyl cinnamate	CH,I,	A()	III, $(C_{\mathbf{s}}H_{\mathbf{s}})_{\mathbf{s}}O$	63, 325, 82a
C ₁₃ H ₃₈ O ₂	Methyl (Z,Z)-9,12- octadienoate (methyl linolenate)	CH ₂ I ₂	A(70-80)	<b>III</b> , $(C_{\mathbf{g}}H_{\mathbf{g}})_{\mathbf{g}}O$	131
C19H34O2	Methyl (Z,Z)-4,7-octa- decadienoate	CH ₃ I ₃	A(70-80)	III, $(C_{g}H_{g})_{g}O$	131
	Methyl (Z,Z)-5,8-octa- decadienoate	CH ₂ I ₂	A(70-80)	III, $(C_{\mathbf{g}}H_{\mathbf{g}})_{\mathbf{g}}O$	131
	Methyl(Z,Z)-5,12-octa- decadienoate	CH ₂ I ₂	A(—)	III, $(C_{\underline{s}}H_{\underline{s}})_{\underline{s}}O$	364
	Methyl (Z,Z)-6,9-octa- decadienoate	CH ₂ I ₂	A(—)	III, $(C_2H_5)_3O$	364
	Methyl (Z,Z)-6,10-octa- decadienoate	CH ₃ I ₃	A(—)	III, (C ₂ H ₅ ) ₂ O	364

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

	Methyl $(Z,Z)$ -6, 11-octa-	CH ₂ I ₂	A()	III, $(C_{g}H_{\delta})_{2}O$	364
	Methyl (Z,Z)-6,12,octa- decadienoate	CH ₂ I ₂	A()	III, $(C_{g}H_{5})_{2}O$	364
	Methyl $(Z, Z)$ -7,12-octa- decadienoate	CH ₂ I ₂	A()	III, $(C_2H_5)_2O$	364
	Methyl (Z,Z)-8,12-octa- decadienoate	CH ₂ I ₂	A()	III, $(C_2H_5)_2O$	364
	Methyl (E,E)-9,11-octa- decadienoate	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131
	Methyl $(Z,Z)$ -9,12-octa- decadienoate (Methyl linoleate)	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131, 278, 364
	Methyl $(E, E)$ -9,12-octa- decadienoate (Methyl linolelaidate)	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_3O$	131
	Methyl 10,13-octadeca- dienoate	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131
C ₁₉ H ₃₆ O ₂	Methyl (Z)-6-octadecenoate (Methyl petroselinate)	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131
	Methyl $(E)$ -6-octadecenoate (Methyl petroselaidate)	CH ₂ I ₂	A(70-80)	III, (C ₂ H ₅ ) ₂ O	131
	Methyl (E)-9-octadceenoate (Methyl elaidate)	CH ₂ I ₂	A(90)	III, $(C_2H_5)_2O$	130–134
	Methyl (Z)-9-octadecenoate (Methyl oleate)	CH ₂ I ₂	A(90)	III, $(C_2H_5)_2O$	130, 6, 85, 131-134, 295, 326, 327, 365
	Methyl (E)-11-octadecenoate (Methyl vaccenate)	CH ₂ I ₂	A(70-80)	III, $(C_2H_5)_2O$	131, 326
C ₂₀ H ₂₂ O ₃	(+)-Bornyl o-methoxy- cinnamate	_	(—)		325
	(+)-Bornyl p-methoxy cinnamate		()	<u> </u>	325
C ₂₀ H ₂₆ O ₂	(—)-Menthyi (E)-4-phenyl- 3-butenoate	CH ₂ I ₂	A()	$(C_2H_5)_2O$	63
	(-)-Menthyl p-methoxy- cinnamate	CH ₂ I ₂	A(—)	III, (C ₂ H ₅ ) ₂ O	82a

TABLE IV.	SYNTHESIS OF	Cyclopropanes	FROM	UNSATURATED	Compounds	(Continued)
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Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITU	TED OLEFINS (contd.)		<u></u>		
Olefinic Acid	Esters (contd.)				
C20H22O2	(-)-Menthyl o-methoxy- cinnamate	_	(—)	_	325
	(-)-Menthyl p-methoxy- cinnamate	CH ₂ I ₂	A()	III, $(C_2H_5)_2O$	325, 82 <b>a</b>
C ₂₁ H ₃₁ NO ₂	(-)-Menthyl p-dimethyl- aminocinnamate	CH ₃ I ₃	A(0)	—	82a
$C_{s_1}H_{s_4}O_s$	Methyl (Z,Z,Z,Z)-5,8,11,14- eicosatetraenoate (methyl arachidonate)	CH ₂ I ₃	A(70-80)	III, (C ₂ H ₅ ) ₂ O	131
C., H., O.	Methyl $(Z)$ -ll-eicosenoate	CH.I.	A(70-80)	III, $(C_{\bullet}H_{\bullet})_{\bullet}O$	131
C ₂₃ H ₂₆ O ₂	(+)-Bornyl 3-(α-naphthyl) acrylate		()		325
$C_{23}H_{28}O_{2}$	(-)-Menthyl 3-(α-naphthyl) acrylate	_	(—)	_	325
$C_{23}H_{44}O_{2}$	Methyl (Z)-13-docosenoate (methyl erucate)	CH ₃ I ₃	A(70-80)	III, $(C_2H_5)_2O$	131
C ₈₄ H ₃₆ O ₄	(-)-Menthyl fumarate	CH,I	A(—)	$(C_{s}H_{s})_{s}O$	63
$\mathrm{C}_{35}^{*}\mathrm{H}_{48}^{*}\mathrm{O}_{2}$	Methyl (Z)-15-tetracosenoate (methyl nervonate)	CH ₁ I ₂	A(70-80)	III, $(C_3H_5)_2O$	131
Olefinic Keto	nes				
С.н.о	3-Buten-2-one	CH.I.	A(50)	III, $(C_H_s)_2O$	151, 77
00 *	2-Cyclopenten-l-one	CH.I.	A(80)	$(C, H_s)_{2}O$	77
C _s H _s O	(Z)-3-Penten-2-one	CH I	A(20)	$(C_2H_5)_2O$	77
C,HO	3-Methyl-2-cyclopenten-1-one	CHI	A(0)	$(C_2H_5)_2O$	77
	2-Cyclohexen-l-one	CH ₂ I ₂	A(90)	$(C_2H_5)_2O$	77
C ₆ H ₁₀ O	4-Methyl-3-penten-2-one	CH ₂ I ₂	A(75)	$(C_2H_5)_2O$	77, 82, 127 128
C7H10O	2-Isopropylidenecyclo- butanone	CH ¹ I ³	A(37)	$(C_2H_5)_2O$	77

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	3-Methyl-2-cyclohexen-1-one	CH,I,	A(0)	_	77
C7H12O	3,4-Dimethyl-3-penten-2-one	CH ₂ I ₂	A(73)	$(C_2H_5)_2O$	77
C ₈ H ₁₀ O	3-Methylene-2-norbornanone	CH ₂ I ₂	A(40)	$(C_2H_5)_2O$	77, 150
C ₈ H ₁₂ O	2-Isopropylidenecyclo- pentanone	CH ₂ I ₂	A(0)	_	77
	3,4,4-Trimethyl-2- cyclopenten-1-one	CH ₂ I ₂	A(0)	—	77
C ₈ H ₁₄ O	3,4-Dimethyl-3-hexen-2-one	CH ₂ I ₂	A(15)	—	128
	6-Methyl-5-hepten-2-one	CH ₂ I ₂	A(50)		128
C ₃ H ₁₄ O	2,6-Dimethyl-2,5-heptadien- 4-one	CH ₂ I ₂	A(43)	$(C_2H_5)_2O$	77, 151
	4-Isopropylidene-2,2- dimethylcyclobutanone	CH ₂ I ₂	A(49)	$(C_{3}H_{5})_{2}O$	174, 358
	2,2,3,3-Tetramethyl-4- methylenecyclobutanone	CH ₂ I ₂	A(45)	(C ₂ H ₅ ) ₂ O	358
	3,5,5-Trimethyl-2- cyclohexen-1-one	CH ₂ I ₂	A(0)	—	77, 128
C10H10O	(E)-4-Phenyl-3-buten-2-one	CH ₂ I ₂	A(40)	$(C_2H_5)_2O$	77, 151
C ₁₀ H ₁₄ O	2,4-Diisopropylidene- cyclobutanone	CH ₂ I ₂	A(40 mono)	$(C_2H_5)_2O$	77
	5-Isopropenyl-2-methyl- 2-cyclohexen-1-one	CH ₂ I ₂	A(27)	$(C_2H_5)_{s}O$	77
	2,6,6-Trimethyl-2,4- cycloheptadien-1-one	CH ₂ I ₂	A(25 mono)	(C ₂ H ₆ ) ₂ O	77
$\mathrm{C_{10}H_{16}O}$	l-(2,2-Dimethylcyclopropyl)- 3-methyl-2-buten-l-one	CH ₂ I ₂	A(82)	$(C_2H_5)_2O$	77, 151
	2-Isopropylidene-5- methylcyclohexanone	CH ₂ I ₂	A(0)	—	77
C ₁₁ H ₁₆ O	5-Isopropylidene-2,2- dimethylspiro[2.3]- hexan-4-one	CH ₂ I ₂	A(20) cis/trans 2	$(C_2H_g)_2O$	77
	2-Methyl-5-(1-methyl- cyclopropyl)-2-cyclohexen- 1-one (mixture with 1-methyl-4-isopropenyl-2- norcaranone)	CH ₃ I ₂	A(16)	(C ₂ H ₅ ) ₂ O	77

TABLE IV.	SYNTHESIS (	or Cyc	LOPROPANES	FROM	UNSATURATED	Compounds	(Continued	)
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Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITU	TED OLEFINS (contd.)				
Olefinic Kete	ones (contd.)				
C ₁₁ H ₁₆ O (contd.)	l-Methyl-4-isopropenyl-2- norcaranone (mixture with 2-methyl-5-(1-methylcyclo- propyl)-2-cyclohexen-1-one)	CH ₃ I ₂	A(16)	(C ₂ H ₆ ) ₂ O	77
	4,7,7-Trimethyl-3-methylene- 2-norbornanone	CH ₂ I ₃	A(100)	$i - (C_3H_7)_2O$	77
C12H18O	4-Cyclohexylidene-2-2- dimethylcyclobutanone	CH ₂ I ₂	A(30)	$(C_2H_5)_3O$	358
C13II20O	Pseudoionone	CH ₂ I ₂	A(75-95)	(C ₂ H ₅ ) ₂ O	328
	4aβ,8,8-Trimethyl-2,3- 4,4a,5,6,7,8-octahydro- 2-naphthalenone	CH ₃ I ₂	A(50)	$(C_{g}H_{5})_{2}O$	312
	10,10-Dimethylbicyclo[7.2.0]- undec-l-en-11-one	CH ₃ I ₂	A(60)	$(C_2H_5)_3O$	358
$C_{16}H_{12}O_{2}$	(Z)-3-Benzylidene-4- chromanone (chromindogenide)	_	()	—	329
	(E)-3-Benzylidene-4- chromanone (chromindogenide)	_	()	—	329
C ₂₂ H ₁₆ O ₃	(Z)-3-Benzylidene-2-phenyl- 4-chromanone (flavindogenide)	OH ₂ I ₃	A()	—	152, 329
	(E)-3-Benzylidene-2-phenyl- 4-chromanone (flavindogenide)	CH ₂ I ₂	<b>A</b> ()		152, 329
Olefinic Ami	ines				
C _s H ₇ N	Allylamine	CH ₂ I ₂	A(60-65)	III, (C ₂ H ₅ ) ₂ O, preformed reagent	126

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C ₄ H ₂ N	2-Methylpropenylamine	CH I.	A(80)	_	127
C,H,N	2-Vinylpyridine	CH.I.	A(0)		330
C7H13N	N,N-Dimethyl-1-cyclopenten- ylamine	CH ₃ I ₃	A(35.8)	$(C_{2}H_{5})_{3}O$ , preformed reagent	161
$C_8H_{15}N$	N,N-Dimethyl-1-cyclo- hexenvlamine	CH ₁ I ₂	A(8.15)	$(C_{2}H_{5})_{3}O$ , preformed reagent	161
C ₁₀ H ₁₇ N	1-(1-Cyclohexenyl)-	CH ₃ I ₃	A(8)	$(C_{g}H_{5})_{g}O$ , preformed reagent	161
C., H., N	1-(1-Cyclohexenyl)piperidine	CH.I./C.H.ZnI	C(28) ^b	(C.H.).O	124
C ₁₄ H ₂₁ NO	2-(N-Morpholino)-3,4,4a,5,6,7- hexahydronaphthalene	$\operatorname{CH}_{2}^{\mathbf{I}}\mathbf{I}_{2}^{\prime}/(\operatorname{C}_{2}^{\mathbf{H}}\operatorname{H}_{\boldsymbol{5}})_{2}\operatorname{Zn}$	C(34 mono)	C _g H _g	361
С ₁₅ Н ₂₃ NO	2-(N-Morpholino)-3,4,4a,5,6,7- hexahydro-4a- methylnaphthalene	$CH_{g}I_{g}/(C_{g}H_{g})_{g}Zn$	C(34 mono)	C ₃ H ₃	361
Haloolefins	· 1				
C,H,CI	(Z)-1-Chloro-1-butene	CH.I.	A ()	$(\mathbf{C}_{\bullet}\mathbf{H}_{\bullet})_{\bullet}\mathbf{O}$	138, 139
• •	(E)-1-Chloro-1-butene	CH.I.	$\mathbf{A}(-)$	(C, H, ), O	138, 139
C ₃ H ₃ Cl	(Chloromethylene)cyclo- pentane	CH I	A(0)		140
C, H ₁₀ Cl,	(E)-1,6-Dichloro-3-hexene	CH ₂ N ₂	B(94)	ZnI	12
C ₃ H ₃ O ₃ Cl ₄	7,7-Dimethoxy-1,2,3,4- tetrachloro-2,5- norbornadiene		A (0)	_ `	173
C ₁₀ H ₁₅ Cl	(Z)-l-Isopropylidene-2- ehloromethylene-3,3- dimethylcyclobutane	CH ³ I ³	<b>A</b> (—)	(C ₃ H ₅ ) ₃ O	141, 361
Olefinic Sulfon	68				
C ₃ H ₃ O ₃ S	Phenyl vinyl sulfone	C ₂ H ₅ CO ₂ CH ₂ I	A(18)	$(C_{g}H_{5})_{g}O$	42
Organometallic	Olefins				
C.H.Hg	Divinylmercury	CH.I.	A(—)	THF	220
C.H. Ge	Trimethylvinylgermane	CH.I.	A(29)	(C.H.).O	221
C.H.Si	Trimethylvinylsilane	CH.I.	A (50)	n-(C.H.).O	221, 222
C.H.Sn	Trimethylvinylstannane	CH.I.	A (18.8)	(C.H.).O	221
C ₃ H ₁₄ Ge	Allyltrimethylgermane	CH ₂ I ₂	A(—)	(C ₂ H ₅ ) ₂ O	222

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^b The Sawada modification was used. See p. 91.

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS	(Continued)
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Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
SUBSTITUT	ED OLEFINS (contd.)				
Organometalli	c Olefins (contd.)				
C.H.Si	Triethylvinylsilane	CH,I,	A()	$(C_{s}H_{s})_{s}O$	222
C ₁₀ H ₈₈ O ₂ Si ₂	(Z)-2,2,4,5,7,7-Hexamethyl- 3,6-dioxa-2,7-disila-4- octene	CH.I.	A(20-55)	<u> </u>	144
	(E)-2,2,4,5,7,7-Hexamethyl- 3,6-dioxa-2,7-disila-4- octene	CH ₂ I ₂	A(20–55)	—	144
C ₁₂ H ₂₈ O ₈ Si ₈	(Z)-4,5-Diethyl-2,2,7,7- tetramethyl-3,6-dioxa-2,7- disila-4-octene	CH ₃ I ₃	A(20-55)	-	144
C14H22A1	(E)-l-Hexen-l-yl diisobutyl sluminum	CH ₂ Br ₃	A(—)	III, $(C_{g}H_{\delta})_{g}O$	223
C ₁₄ H ₂₅ O ₅ Si ₂	(Z)-4,5-Dipropyl-2,2,7,7- tetramethyl-3,6-dioxa- 2,7-disila-4-octene	CH ₂ I ₃	A (20–55)		144
	(Z)-4,5-Diisopropyl-2,2,7,7- tetramethyl-3,6-dioxa-2,7- disila-4-octene	CIIgIg	A(20–55)	_	144
	(E)-4,5-Disopropyl-2,2,7,7- tetramethyl-3,6-dioxa-2,7- disila-4-octene	CH _s I _s	A(20-55)	_	144
STEROIDS					
C18H28O2	$8\alpha$ -Estr-5(10)-ene- $3\alpha$ , 17 $\beta$ -diol	CH,I,	A(85)	$(C_{2}H_{s})_{2}O$	195
	$8\alpha$ -Estr-5(10)-ene-3 $\beta$ , 17 $\beta$ -diol	CH,I	A()	$(\mathbf{C}_{3}\mathbf{H}_{5})_{3}\mathbf{O}$	196
$\mathrm{C_{19}H_{54}O_2}$	3-Methoxy- $\Delta^{1,3,8(10),15}$ estratetraen-17 $\beta$ -ol	CH ₂ I ₂	A(12)	_	331
C15H28O8	3-Hydroxy-5 <b>a-a</b> ndrost-1-en- 17-one	CH ₂ I ₂	A(39)	$(C_{\mathfrak{g}}H_{\mathfrak{z}})_{\mathfrak{g}}O$	190
$C_{so}H_{ss}O_s$	17β-Hydroxy-19-nor-17α- pregna-4,20-dien-3-one	CH ₃ I ₃	A(18)	_	188
$\mathrm{C_{20}H_{28}O_4}$	3-Oxoestr-5(10)-ene-11 $\beta$ ,17 $\beta$ - diol 17-acetate	CH ₂ I ₂	A(—)		31
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C.H.O.	Estr-2-en-17-ol acetate	CH.I.	A()	$(\mathbf{C},\mathbf{H}_{*}),\mathbf{O}$	332
	$17\alpha$ -Methyl-1,5-androstadiene- $3\beta$ ,17 $\beta$ -diol	CH ₂ I ₂	A (52)	THF	191
C ₃₀ H ₃₀ O ₃	$5\alpha$ -Estr-l-ene- $3\beta$ , $17\beta$ -diol 17-acetate	CH ₂ I ₂	A(43)	$(C_2H_5)_2O$	190
	$8\alpha$ -Estr-5(10)-ene- $3\beta$ ,17 $\beta$ -diol 17-acetate	CH ₂ I ₃	A(90)	_	333
	3β-Hydroxy-8α-estr-5(10)-en- 17-one cyclic ethylene acetal	CH ₂ I ₂	A(—)	_	196
$C_{20}H_{33}O_{2}$	3-(Hydroxymethyl)-17β- hydroxy-5α-androst-2-ene	CH ₂ I ₃	A()	II, (C ₃ H ₅ ) ₂ O	189a
$\mathbf{C_{s1}H_{s8}O_{2}}$	3β-Methoxy-19-nor-17α- pregna-1,3,5(10),20- tetraen-17β-ol	CH ₂ I ₃	A(35)		188
	Androsta-4,6-dien-17β-ol- 3-one 17-acetate	CH ₂ I ₂	A(30)	III, $(C_2H_b)_2O$	14
C ₂₁ H ₃₀ O ₂	17β-Hydroxy-17α-pregna- 4,20-dien-3-one	CH ₂ I ₂	A(39)	-	188
≌ C ₂₁ H ₃₀ O ₃	$(\pm)$ -18-Methylestra-5(10),9- (11)-diene-3 $\alpha$ ,17 $\beta$ -diol 17-acetate	CH ₂ I ₂	A()	$(C_2H_b)_2O$	201
	$(\pm)$ -18-Methylestra-5(10), 9(11)-diene-3 $\beta$ ,17 $\beta$ -diol 17-acetate	CH ₂ I ₂	A()		201
	3-Methylenestra-5(10)-ene- 118.178-diol 17-acetate	CH ₂ I ₂	A()	-	31
	Androsta-4,6-diene- $3\beta$ ,17 $\beta$ - diol 17-acetate	CH ₂ I ₂	<b>A(</b> —)	-	194
C., H., O	5a-Pregnan-20-one	CH ₁ I ₂	A(30)	III, $(C_2H_5)_2O$	334
C21 H3202	$5\alpha$ -Androst-2-en-17 $\beta$ -ol acetate	CH ₂ I ₂	A(50)	• • •	335
	$5\alpha$ -Pregn-l-ene- $3\beta$ ,20 $\beta$ -diol	CH ₂ I ₂	A()	(C ₂ H ₅ ) ₂ O	190

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
STEROIDS	(contd.)				
C ₂₁ H ₃₂ O ₃	$5\alpha$ -Androst-1-ene- $3\beta$ , $17\beta$ - diol 17-acetate	CH ₂ I ₂	A(60)	$(C_{\mathbf{g}}H_{\delta})_{\mathbf{g}}O$	190
	5α-Androst-2-ene-lα,17β- diol 17-acetate	CH ₂ I ₂	A(36)	II, $(C_2H_5)_2O$	192, 336
	Androst-4-ene-3 $\beta$ , 17-diol 17-acetate	CH ₂ I ₂	A(10)	$(\mathbf{C_{g}H}_{5})_{\mathbf{g}}\mathbf{O}$	193
	$(\pm)$ -18-Methylestr-5(10)- ene-3 $\alpha$ ,17 $\beta$ -diol 17-acetate	CH ₂ I ₂	A()	$(C_{\mathbf{g}}H_{\mathbf{b}})_{\mathbf{g}}O$	201
	$(\pm)$ -18-Methylestr-5(10)-ene- 3 $\beta$ ,17 $\beta$ -diol 17-acetate	CH ₂ I ₂	A(90)	$(C_{\mathbf{s}}H_{\mathbf{s}})_{\mathbf{s}}\mathbf{O}$	333, 201
C ₂₂ H ₃₀ O ₃	19-Nor-5α,17α-pregn-1-en- 20-yne-3β,17β-diol 17-acetate	CH ₂ I ₂	A()	(C ₃ H ₅ ) ₃ O	190
C22H52O	20-Methylenepregn-4-en-3-one	CH.I.	A(43)	III, $(C,H_{\epsilon})$ ,O	334
C ₂₂ H ₃₂ O ₄	Estr-5(10)-ene-3 $\alpha$ , 17 $\beta$ -diol diacetate	CH ₂ I ₂	A(0)		195
C ₃₂ H ₃₃ O ₅	Estr-5(10)-ene- $3\alpha$ , 11 $\beta$ , 17 $\beta$ - triol 3, 17-diacetate	CH ₂ I ₃	A()		31
C ₅₂ H ₃₃ O ₃	3-(Hydroxymethyl)androst- 2-en-17 $\beta$ -ol 17-acetate	CH ₂ I ₂	A()		189
C22H34	20-Methylene-5α-pregnane	CH ₂ I ₂	A(43)	III, $(C_{2}H_{5})_{2}O$	334
C ₂₂ H ₃₄ O ₃	l-Methyl-5 $lpha$ -androst-l-ene- 3 $eta$ ,17 $eta$ -diol 17-acetate	CH ₂ I ₂	A(35)	$(C_2H_b)_2O$	190
	17-Methoxy-5α-androst-16- ene-3β,17β-diol 3-acetate	$\mathrm{CH}_{2}\mathrm{I}_{2}/(\mathrm{C}_{2}\mathrm{H}_{5})_{2}\mathrm{Zn}$	C()	$(n-C_4H_3)_2O$	366
	l-Methylene-17β-hydroxy-5α- androstan-3-one cyclic ethylene acetal	CH ₂ I ₂	A(25)	-	188
C ²³ H ³⁰ O ⁶	3β-Hydroxy-17α,20:20,21- bis(methylenedioxy)pregna- 1,5-dien-11-one	CH ₂ I ₂	A(25)	$(C_{\mathbf{g}}H_{\mathbf{\delta}})_{\mathbf{g}}O$	190
)33H32O2	17α,20:20,21-Bis(methylene- dioxy)pregna-1,5-dien-3β-ol	CH ₂ I ₂	A(36)	$(C_2H_5)_2O$	190

С ₂₃ Н ₃₈ О6	$17\alpha$ , 20: 20, 21-Bis(methylene- dioxy)pregna-1, 5-diene-3 $\beta$ , 11 $\beta$ -diol	CH ₁ I ₂	A(49)	$(C_2H_5)_2O$ , THF	190, 191
$C_{23}H_{33}O_{5}$	Androst-7-ene-3 $\beta$ ,6 $\alpha$ ,17 $\beta$ - triol 3 $\beta$ ,17 $\beta$ -diacetate	CH ₂ I ₂	A(63)	II, $(C_2H_5)_2O$	367
С ₃₃ Н ₃₄ О4	6β-Hydroxy-3β-[(tetrahydro- pyran-2-yl)oxy]estr-5(10)- en-17-one	CH ₂ I ₂	A(—)		197
$C_{23}H_{34}O_5$	$5\alpha$ -Androst-16-ene- $3\beta$ , 17 $\beta$ - diol 3, 17-diacetate	$\mathrm{CH_2I_2/(C_2H_5)_2Zn}$	C()	$(n \cdot C_4 H_g)_2 O$	366
$\mathrm{C_{23}H_{35}ClO_4}$	3-(2-Chloroethoxy)-5α- androst-2-ene 17β-acetate	CH ₂ I ₂	A(50-60)	$(C_2H_6)_2O$	368
$\mathrm{C_{23}H_{36}}$	3,20-Bismethylene-5α-	CH ₂ I ₂	A(25)	III, $(C_2H_5)_2O$	334
$C_{23}H_{36}O_3$	<ul> <li>17β-Hydroxy-17α-methyl-</li> <li>1-methylene-5α-androstan-</li> <li>3-one cyclic ethylene acetal</li> </ul>	-	()	_	188
	17-Ethoxy-5α-androst-16-ene- 3β.178-diol 3-acetate	$\mathrm{CH_2I_2/(C_2H_5)_2Zn}$	C()	$(n - C_4 H_9)_9 O$	366
	$\begin{array}{l} 17\beta : [(Tetrahydropyran-2-yl)- \\ oxy]estr-5(10)-en-3\alpha-ol \\ (mixture with 17\beta- \\ [(tetrahydropyran-2-yl)- \\ oxy]estr-5(10)-en-3\beta-ol] \end{array}$	CH ₂ I ₂	A (—)	(C ₂ H ₅ ) ₂ O	195
	$\begin{array}{l} 17\beta \cdot [(\mathrm{Tetrahydropyran} - 2 \cdot y]) \\ \text{oxy]estr-} 5(10) \cdot en \cdot 3\beta \cdot ol \\ (\text{mixture with } 17\beta \cdot [tetrahydropyran \cdot 2 \cdot y]) \\ \text{oxy]estr-} 5(10) \cdot en \cdot 3\alpha \cdot ol \end{array}$	CH ₂ I ₂	A (90)	_	333, 195
C ₂₃ H ₃₆ O ₄	3β-[(Tetrahydropyran-2- yl)oxy]estr-5(10)-ene-6α,17β- diol	CH ₂ I ₂	()	-	197
C ₂₄ H ₃₆ O ₃	3,3-Ethylenedioxy-20- hydroxy-19-methylene- pregn-5-ene	CH ₂ I ₂	A (0)	III, $(C_2H_5)_2O$	334
C ₂₄ H ₃₈ O ₃	$17\beta$ -[(Tetrahydropyran-2- yl)oxy]18-methylestr- 5(10)-ene-3 $\beta$ -ol	CH ₂ I ₂	A (90)		333

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

	Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
	STEROIDS	(contd.)				<u> </u>
	$C_{25}H_{32}O_3$	$9\beta$ -Estr-5(10)-ene- $3\beta$ , 17 $\beta$ - diol 17-benzoate	CH ₂ I ₂	A()	$(C_2H_5)_2O$	337
	$C_{26}H_{44}O$	B-Norcholest-5-en- $3\alpha$ -ol	CH ₂ I ₂	A(34) $\alpha$ cyclopropanation	III, $(C_2H_5)_2O$	200
		B-Norcholest-5-en-3 $\beta$ -ol	CH ₂ I ₂	A(28) α cyclopropanation	III, $(C_2H_5)_2O$	200
	C27H46	Cholest 2-ene	CH ₂ I ₂	A(0)		189c
	C27H48O	Cholest-4-en-3α-ol	CH,I,	A(65)	$(C_2H_5)_2O$	193
		Cholest-4-en-3 $\beta$ -ol	CH,I,	A(62)	$(C_2H_5)_2O$	193
		Cholesterol	CH,I,	A(0)		189a
		epi-Cholesterol	CH,I,	A(60)	III, $(C_2H_5)_2O$	189a
124	$\mathbf{C_{28}H_{46}O_2}$	B-Norcholest-5-en-3α-ol acetate	CH ₂ I ₂	$A(35) \alpha$ cyclopropanation	III, $(C_2H_5)_2O$	200
		B-Norcholest-5-en-3 $\beta$ -ol acetate	CH ₂ I ₂	A(45) $\alpha$ cyclopropanation	III, $(C_2H_5)_2O$	199, 200
			CH.I.	$A(2)\beta$ cyclopropanation	III, $(C_{\bullet}H_{\star})_{\bullet}O$	199, 200
	C.H.	3-Methylcholest-2-ene	CH.I.	A(0)		189c
	C29H48O3	Cholest-7-ene- $3\beta$ , $6\alpha$ -diol	CH ₂ I ₂	A(44)	II, $(C_2H_5)_2O$	198, 367
		3-acetate				
	$C_{32}H_{52}O_{2}$	Lanosterol acetate	CH ₂ I ₂	A (0)		338
	С ₃₃ Н ₃₈ О ₅	5α-Androst-7-ene-3β,6α,17β- triol 3,17-dibenzoate	CH ₂ I ₃	A()		194
	$C_{33}H_{50}$	3-Phenylcholest-2-ene	CH ₂ I ₂	A(0)		189c
	ALLENES					
	C.H.	Vinylidenecyclopropane	CH.I.	A()	(C,H,),O	208
	C,H	3-Methyl-1,2-butadiene	CH.I.	A(38 bis)	(C,H,),O	204, 205
		2,3-Pentadienø	CH.I.	()	_	339
	C,HO,	Methyl-3,4-pentadienoate	CH.I.	A(35) mono/bis 1	(C,H,),O	136
	C _a H ₁ a	2-Methyl-2,3-pentadiene	CH.I.	A(41 bis)		204, 205, 339
		1,2-Hexadiene	CH.I.	A(67)	(C,H,),O	203
	C ₂ H ₁₀ O	4-Methyl-2,3-pentadien-1-ol	CH,I,	A(63)		80
		3-Methyl-3,4-pentadien-2-ol	CH ₂ I ₂	A(65) mono/bis 1.6	II, $(C_2H_5)_2O$	81

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$C_6H_{11}N$	N,N-Dimethyl-2,3- butadienylamine	CH ₂ I ₂	A(60-65)	III, (C ₂ H ₅ ) ₂ O, preformed reagent	126
С.Н.,	2,4-Dimethyl-2,3-pentadiene	CH.I.	A(88)	$(C_2H_b)_2O$	204, 205, 206
1 14	2-Methyl-2,3-hexadiene	CH,I,	A(10)	II, $(C_2H_5)_2O$	206
	1,2-Heptadiene	CH.I.	A(69)	$(C_2H_5)_2O$	203, 206
C.H.,O	5-Methyl-3,4-hexadien-2-ol	CH.I.	A(51)		80, 206
/ 21	2-Methyl-4,5-hexadien-3-ol	CH.I.	A(70) mono/bis 1	II, $(C_2H_5)_2O$	206
	1,2-Heptadien-4-ol	CH.I.	A(61)		80, 206
C _a H ₁ O	2,5-Dimethyl-3,4-hexadien-	CH,I,	A(48)	_	80, 206
0 10	2-ol				
C _e H ₁₄	1,2-Cyclononadiene	CH,I,	A(—)		207
C11H18	l-(Tetramethylcyclo- propylidene)-2-methyl- l-propene	CH ₂ I ₂	A(good)		116,206
C ₁₃ H ₁₇ NO ₅	Diethyl 2,3-butadienyl- (formamido)malonate	$CH_2I_2$	A(71)	_	209
ACETYLEN	ES				
C.H.	1.3-Pentadivne	CH.I.	A(21)°	$(C_{2}H_{a})_{2}O$	217, 218
с.н.	2-Methyl-1-buten-3-yne	CH.I.	A(17.5) ^c		217, 216
C.H.	1-Pentvne	CH.I.	A(28.5) ^c	_	217, 216
C'H O	l-Butynyl methyl ether	CH.I.	A(29)°	$(C_2H_5)_2O$	214
	3-Pentyn-2-ol	CH.I.	$A(40)^{\circ}$	$(C_2H_5)_2O/glyme$	215
C.H.	1,3-Hexadiyne	CH,I,	$A(12)^c$		217, 218
C H	l-Hexyne	CH,1,	A(25)°		216 - 218
0 10	3-Hexyne	CH,I,	A(0)	Preformed reagent	210, 25
C _a H ₁₀ O	3 Hexyn-2-ol	CH,I,	$A(26)^c$	$(C_2H_5)_2O/glyme$	215
0 10	2-Hexyn-4-ol	CH.I.	$A(35)^c$	$(C_2H_5)_2O/glyne$	215
C,H.	1,3-Heptadiyne	CH.I.	A(19)°	_	218, 217
С, Н,	1-Heptyne	CH,I,	A(18)°		217
C,H,O	2-Methyl-4-hexyn-3-ol	CH.I.	$A(22)^c$	$(C_{2}H_{5})_{2}O/glyme$	215
C.H.Br	p-Bromoethynylbenzene	CH ₃ CHI ₂ /(C ₂ H ₅ ) ₂ Cd	C(25) ^c	$C_6H_{12}$	238
C,H,Cl	p-Chloroethynylbenzene	CH,I,	A (42.5)°		217
C,H,D	Phenylacetylene-1-d,	CH ₃ CHI ₂ /(C ₂ H ₅ ),Cd	C(25)°	$C_{9}H_{12}$	238
C,H	Ethynylbenzene	CH,I,	A (43)°		216-218
		$CH_{2}I_{2}/(C_{2}H_{5})_{2}Cd$	C(64)°	C ₉ H ₁₂	238
		CH ₃ CHI2/(C2H5)2Cd	C(60)°	$C_{6}H_{12}$	238

^c Abnormal products were formed; see original article.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions Couple, Solvent, Other	Refs.
ACETYLENE (contd.)	28				
C ₈ H ₁₀	1,7-Octadiyne	CH,I,	A(37)°	Glyme	219, 218
	l-Ethynylcyclohexene	CH,I,	A(22)°	_	216
C ₈ H ₁₂	2-t-Butyl-1-buten-3-yne	CH,I,	A(75.8) ^c		217
	Cyclooctyne	CH ₂ I ₂	A(50) ^c	$(C_2H_s)_2O$	211
C ₉ H ₈	p-Ethynyltoluene	CH ₂ I ₂	A(35)°		216, 217
		$CH_3CHI_2/(C_2H_5)_2Cd$	C(33)°	C ₉ H ₁₂	238
C ₉ H ₈ O	p-Ethynylanisole	CH ₂ I ₂	$A(52.5)^{c}$	_	217
C, H12	1,8-Nonadiyne	CH ₂ I ₂	A(61) ^c	Glyme	218, 219
C ₁₀ H ₆	Phenylbutadiyne	CH ₂ I ₂	A(28)°		217, 218
C ₁₁ H ₁₀	2-Methyl-4-phenyl-1-buten- 3-yne	CH ₂ I ₂	A(20)°		340
C18H32O2	9-Octadecynoic acid	CH ₂ I ₂	A(4) ^c	II, $(C_{\bullet}H_{s})_{\bullet}O$	212
C ₁₉ H ₃₄ O ₂	Methyl 9-octadecynoate	CH ₂ I ₂	A(0)		210, 212, 213 213a
C ₂₀ H ₃₆ O ₂	Ethyl 9-octadecynoate	CH ₂ I ₂	A(0)		210, 212
BENZENOID	AROMATICS				
с.н.	Benzene	CHAIA	A(0)	_	118
. 60		CH _a CHI _a /(C _a H _a ) _a Zn	C(11-44)	_	49
C,H.	Toluene	CH, CHI, /(C, H, ), Zn	C(11-44)		49
C.H.	Ethylbenzene	CH,CHI,/(C,H,),Zn	C(11-44)		49
0 10	o-Xylene	CH,CHI,/(C,H,),Zn	C(11-44)	_	49
	m-Xylene	CH,CHI,(C,H,),Zn	C(11-44)		49
	p-Xylene	CH,CHI,/(C,H,),Zn	C(11-44)	_	49
C ₉ H ₁₂	Isopropylbenzene	CH ₃ CHI ₂ /(C ₂ H ₅ ) ₂ Zn	C(11-44)		49
• •	Mesitylene	$CH_3CHI_2/(C_2H_5)_2Zn$	C(11-44)	_	49
C ₁₀ H ₈	Naphthalene	CH ₃ CHI,/(C,H,),Zn	C(11-44)	_	49
C ₁₀ H ₁₄	t-Butylbenzene	CH ₂ CHI ₂ /(C ₂ H ₅ ) ₂ Zn	C(11-44)		49
C ₁₂ H ₈	Acenaphthylene	CH,N,	B(60)	ZnI,	9
C14H10	Phenanthrene	CH ₂ I ₂	A(25)	III, glyme	7
MISCELLAN	EOUS REACTIONS*				
C.H.Cl.Sn	Dichlorodimethylstannane	CH.I.	$A(79)^i$	III. (C.H.).O	226a
C, H, ClSn	Chlorotrimethylstannane	CH.I.	$\mathbf{A}(82)^{i}$	III, $(C_0H_r)_0O$	226a
с.н.о	3-Pentanone	CH I	A(0)	, (-25/2- THF	230

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

$C_6H_{16}Si$	Triethylsilane	CH ₂ I ₂	$A(64)^d$	$(C_2H_5)_2O$	224
		CH ₂ Br ₂	A (55) ^d	$(C_2H_5)_2O$	224
C ₆ H ₁₆ Sn	Triethylstannane	CH ₂ I ₂	C(21) ^e	$(C_2H_3)_2O$	225
		CH ₃ CHI,	C(53)*	$(C_{2}H_{3})_{2}O$	
C7H,CIO	Benzoyl chloride	CH ₂ I ₂	$A(60)^{f}$	Dioxane	232
	p-Chlorobenzaldehyde	CH,1,	A (74)9	THF	229, 230, 341
$C_7H_6O$	Benzaldehyde	CH,I,	A(67)"	THF	229, 231, 341
C, H, 0	Heptanal	Сн,1,	A (73) ⁹	THF	230
C, H, O	Acetophenone	CH,I,	A(0)	—	230, 341
	p-Tolualdehyde	СН,1,	$\mathbf{A}(52)^{g}$	THF	230, 229
	p-Anisaldehyde	СН,І,	A(48) ⁹	THF	230, 229
C.H.O.	Methyl benzoate	CH.I.	A(0)	_	230, 341
	ω-Hydroxyacetophenone	CH,I,	A(49) ^h	$(C_{\bullet}H_{\epsilon})_{\bullet}O$	14
C ₈ H ₁₁ ClSi	(p-Chlorophenyl)-	$CH_2I_2/(C_2H_5)_2Zn$	$C(73)^d$	$(C_2H_5)_2O$	225
		CH_CHI_/(C_H_)_Zn	$C(63)^d$	$(C_{2}H_{2})_{2}O$	225
$C_8H_{11}FSi$	(p-Fluorophenyl)-	$CH_2I_2/(C_2H_5)_2Zn$	C(74) ^d	$(C_2H_5)_2O$	225
		CH_CHI_(C_H_)_Zn	C(82) ^d	$(C, H,)_{0}O$	225
C.H., ISn	Iododimethvlphenvlstannane	CH.I.	A (94)	$(12, 5)^{2}$	2268
C.H.Si	Dimethylphenylsilane	CH.I./(C.H.).Zn	C(83) ^d	(C.H.).O	225
0 12	51 5	CH CHI (C.H.).Zn	C(64) ^d	(C.H.).O	225
C.H.,NO.	Ethyl N-t-butylformimidoyl	CH.I.	$A(40)^{l}$	$IV_{\star}(C_{2}H_{\star})_{\bullet}O$	233a
6 13 4	formate (ethyl N-t-butyl- iminoacetate)	* *	× /	· · 2 d·2	
C,H,O	Cinnamaldehyde	СН,І,	A(29) ^g	THF	230
C ₉ H ₁₁ F ₃ Si	[(m-Trifluoromethyl)phenyl]- dimethylsilane	$CH_2I_2/(C_2H_5)_2Zn$	C(73) [₫]	$(\mathbf{C_2H_5})_{2}\mathbf{O}$	225

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* The reactions included under this heading are not cyclopropanations but are discussed in the text.
* Abnormal products were formed; see original article.
d The product of the reaction is the corresponding Si--CH₃ compound resulting from Si-H insertion.
* The product of the reaction is the corresponding Sn-CH₃ compound resulting from Sn-H insertion.
t The yield is given for the major product, benzoic anhydride.
g The major product is the olefin obtained by replacing C=O with C=CH₂.
* The major product is the olefin obtained by replacing C=O with C(CH₂)₂.
* The product of these reactions is the new organometallic R₂M(CH₂I)₂, formed by replacement of halogen in the reactant with the ICH₂ group.
The product of the reaction is the corresponding aziridine ester.

Formula	Unsaturated Compound	Reagent	Method: A, B, C (Yield, %)	Reaction Conditions, Couple, Solvent, Other	Refs.
MISCELLAN	EOUS REACTIONS* (contd.)		· · · · · · · · · · · · · · · · · · ·		
		CH_CHI_/(C_H_)_Zn	$C(58)^d$	(C,H.),O	<b>22</b> 5
C.H.Si	<i>p</i> -Tolyldimethylsilane	CH,I,/(C,H,),Zn	C(63) ^d	(C.H.).O	225
• 1•	1 5 5	CH,CHI,/(C,H,),Zn	C(70) ^d	(C.H.),0	225
C, H, O	di-t-Butylketene	CH,I,	$\mathbf{A}(0)$	<u> </u>	160
C. H.O	1-Naphthaldehyde	CH,I,	A(73) ⁹	THF	230
11 •	2-Naphthaldehyde	CH.I.	A(55) ⁹	THF	230
C.,H.O	Benzophenone	CH.I.	A(0)	-	230
C13H12O3	Hydroxymethyl (6-methoxy- 2-naphthyl) ketone	CH ₂ I ₂	A(76) ^A	$(C_2H_\delta)_2O$	14
C ₁ ,H ₁₀ O	9-Anthraldehyde	CH.I.	$A(40)^g$	THF	230
C ₁₅ H ₁₇ LiO	4a-Methyl-2,3,4,4a,9,10- hexahydro-I-phenanthrol, lithium salt	CH ₂ I ₂	A(67) ⁴	-	236
C ₁₆ H ₁₉ LiO ₂	7-Methoxy-4a-methyl- 2,3,4,4a,9,10-hexahydro- 1-phenanthrol, lithium salt	CH ₂ I ₃	A(72) ^j	_	236
C18H15ClPb	Chlorotriphenylplumbane	CH ₂ I ₂	$\mathbf{A}(31)^i$	III, $(C_2H_5)_2O$	226a
C ₁₈ H ₁₅ ClSn	Chlorotriphenylstannane	CH ₂ I ₂	A(66) ⁶	III, $(C_2H_5)_2O$	226a
C1.H.0	5a-Androstan-3-one	CH ₂ I ₂	$A(low)^{g,h}$	$(C_2H_5)_2O$	14
C20H28O3	19-Norandrost-5(10)-en-17 $\beta$ - ol-3-one acetate	CH ₂ I ₂	A(20) ^k	$(C_2H_5)_2O$	14
C, H, O,	Pregn-4-en-17a-ol-3,20-dione	CH ₂ I ₂	$A(93)^{p}$ (89) ^h	$(C_2H_5)_2O$	14
C25H38O6	Methyl bisnorcholestane- $3\beta,5\alpha$ -diol-6-on-21-oate 3-acetate	CH ₂ I ₂	A(96) ^o	$(C_2H_5)_2O$	14
HgI.	Mercuric iodide	CH ₂ I ₃	A(86) ⁴	III, $(C_2H_5)_2O$	226a
		CD.I.	A(76) ⁴	III, $(C_2H_5)_2O$	226a
SnCl	Tetrachlorostannane	CH ₂ I ₂	A(17) ⁴	III, $(C_2H_5)_2O$	226a

TABLE IV. SYNTHESIS OF CYCLOPROPANES FROM UNSATURATED COMPOUNDS (Continued)

Note: References 257-369 are on pp. 129-131.

* The reactions included under this heading are not cyclopropanations but are discussed in the text.

The reactions included under this heading are not cycloproparators but are discussed in the text.
The product of the reaction is the corresponding Si—CH₃ compound resulting from Si—H insertion.
The major product is the olefin obtained by replacing C=O with C=CH₂.
The major product is the olefin obtained by replacing C=O with C(CH₂)₂.
The product of these reactions is the new organometallic R₂M(CH₂1)_y, formed by replacement of halogen in the reactant with the ICH₂ group.

³ The product is formed by cyclopropanation followed by ring opening to generate a  $CH_3$  group ⁴ The product is a mixture which results from cyclopropanation and  $\alpha$ -methylation of the ketone.

# **REFERENCES TO TABLE IV**

²⁵⁷ E. Taeger and C. Fiedler, Justus Liebigs Ann. Chem., 698, 42 (1966).

²⁵⁸ T. L. Jacobs and R. D. Wilcox, J. Amer. Chem. Soc., 86, 2240 (1964).

²⁵⁹ R. T. LaLonde and A. D. Debboli, Jr., J. Org. Chem., 35, 2657 (1970).

260 G. A. Olah and M. Calin, J. Amer. Chem. Soc., 90, 933 (1968).

²⁸¹ J. W. Wilt and W. J. Wagner, J. Org. Chem., 29, 2788 (1964).

²⁸² B. Rickborn and S. E. Wood, J. Amer. Chem. Soc., 93, 3940 (1971).

283 C. N. Pillai and H. Pines, J. Amer. Chem. Soc., 83, 3274 (1961).

²⁸⁴ C. S. Elliot and H. M. Frey, J. Chem. Soc., 1964, 900.

²⁸⁵ L. Skattebol, J. Org. Chem., **31**, 2789 (1966).

²⁶⁶ Yu. S. Shabarov, T. P. Surikova, V. S. Svirina, R. Ya. Levina, *Zh. Org. Khim.*, **1** 1895 (1965).

²⁴⁷ H. Nozaki, T. Aratani, and R. Noyori, Tetrahedron, 23, 3645 (1967).

²⁸⁸ W. D. Krumler, R. Boikess, P. Bruck. and S. Winstein, J. Amer. Chem. Soc., 86, 3126 (1964).

²⁸⁹ R. E. Winters and J. H. Collins, J. Amer. Chem. Soc., 90, 1235 (1968).

²⁷⁰ J. G. Traynham and J. S. Dehn, J. Amer. Chem. Soc., 89, 2139 (1967).

²⁷¹ W. Kirmse and G. Wächterhäuser, Tetrahedron, 22, 63 (1968).

²⁷² S. I. Khromov, G. P. Kochnova, O. I. Guseva, and E. S. Balenkova, Neftekhimiya, **6** (6), 809 (1966) [C.A., **66**, 104733v (1967)].

²⁷³ R. T. LaLonde and L. S. Forney, J. Org. Chem., 29, 2911 (1964).

²⁷⁴ C. Pinazzi, J.-C. Brosse, J. Brossas, and A. Pleurdeau, C. R. Acad. Sci., Paris, Ser. C, **266**, 443 (1968).

²⁷⁵ R. Ya. Levina, V. N. Kostin, P. A. Gembitskii, and E. G. Treshchova, Zh. Obshch. Khim., **31**, 829 (1961).

²⁷⁶ C. L. Osborn, T. C. Shields, B. A. Shoulders, J. F. Krause, H. V. Cortez, and P. D. Gardner, J. Amer. Chem. Soc., 87, 3158 (1965).

²⁷⁷ C. Pinazzi, G. Levesque, and D. Reyx, C. R. Acad. Sci., Paris, Ser. C., 263, 859 (1966).

²⁷⁸ C. Asselineau, H. Montrozier, and J.-C. Promé, Bull. Soc. Chim. Fr., 1969, 1911.

²⁷⁹ E. Wiskott and P. von R. Schleyer, Angew. Chem., Int. Ed. Engl., 6, 694 (1967).

²⁸⁰ R. Ya. Levina, V. N. Kostin, M. G. Gal'pern, and E. G. Treshchova, J. Gen. Chem, USSR, **35**, 788 (1965).

²⁸¹ G. L. Closs and R. A. Moss, J. Amer. Chem. Soc., 86, 4042 (1964).

²⁸² J. Vais, J. Burkhard, and S. Landa, Z. Chem., 8, 303 (1968).

²⁸³ C. L. Bumgardner and H. Iwerks, J. Amer. Chem. Soc., 88, 5518 (1966).

²⁸⁴ T. Takahashi, J. Polym. Sci., Part A-1, 6, 403 (1968).

²⁸⁵ R. J. Ellis and H. M. Frey, J. Chem. Soc., 1964, 959.

²⁸⁶ K. B. Wiberg and G. R. Wenzinger, J. Org. Chem., 30, 2278 (1965).

²⁸⁷ J. B. Lambert, J. L. Gosnell. Jr., D. S. Bailey, and L. G. Greifenstein, *Chem. Commun.*, **1970.** 1004.

²⁸⁸ A. C. Cope, S. Moon, and C. H. Park, J. Amer. Chem. Soc., 84, 4843 (1962).

²⁸² A. J. Ashe, Tetrahedron Lett., 1969, 523.

²⁹⁰ H. C. Brown and J. D. Cleveland, J. Amer. Chem. Soc., 88, 2051 (1966).

²⁹¹ J. P. Freeman, J. Org. Chem., 29, 1379 (1964).

²⁹² R. C. Hahn, P. H. Howard, S.-M. Kong, G. A. Lorenzo, and N. L. Miller, J. Amer. Chem. Soc., **91**, 3558 (1969).

²⁹³ R. G. Bergman, J. Amer. Chem. Soc., **91**, 7405 (1969).

²⁹⁴ W. Kirmse, M. Kapps, and R. B. Hager, Chem. Ber., 99, 2855 (1966).

²⁹⁵ L. D. Hess and J. N. Pitts, Jr., J. Amer. Chem. Soc., 89, 1973 (1967).

²⁹⁸ D. H. Marr and J. B. Stothers, Can. J. Chem., 45, 225 (1967).

²⁹⁷ L. D. Hess, J. L. Jacobson, K. Schaffner, and J. N. Pitts, Jr., J. Amer. Chem. Soc., 89, 3684 (1967).

²⁹⁸ W. G. Dauben, L. Schutte, and R. E. Wolf, J. Org. Chem., 34, 1849 (1969).

²⁹⁹ W. G. Dauben and R. E. Wolf, J. Org. Chem., 35, 374 (1970).

300 W. G. Dauben, L. Schutte, R. E. Wolf, and E. J. Deviny, J. Org. Chem., 34, 2512 (1969).

³⁰¹ R. K. Hill and J. W. Morgan, J. Org. Chem., 33, 927 (1968).

³⁰² Y. E. Rhodes and T. Takino, J. Amer. Chem. Soc., 92, 5272 (1970).

⁸⁰³ I. Lillien and R. A. Doughty, J. Org. Chem., 33, 3841 (1968).

³⁰⁴ J. B. Lambert, J. W. Hamersma, A. P. Jovanovich, F. R. Koeng, S. A. Sweet, and P. J. Kucinski, J. Amer. Chem. Soc., **92**, 6372 (1970).

- 305 A. S. Orahovats, V. S. Dimitrov, and S. L. Spassov, J. Mol. Struct., 6, 405 (1970).
- ³⁰⁸ D. A. Lightner and W. A. Beavers, J. Amer. Chem. Soc., 93, 2677 (1971).
- 307 S. W. Staley and F. L. Wiseman, Jr., J. Org. Chem., 35, 3868 (1970).

⁸⁰⁸ M. Hanack, W. Kraus, W. Rothenwöhrer, W. Kaiser, and G. Wentrup, Justus Liebigs Ann Chem., 703, 44 (1967).

- 808 J. E. Starr and R. H. Eastman, J. Org. Chem., 31, 1393 (1966).
- ³¹⁰ D. Seyferth and V. A. Mai, J. Amer. Chem. Soc., 92, 7412 (1970).
- ³¹¹ B. R. Ree and J. C. Martin, J. Amer. Chem. Soc., 92, 1660 (1970).
- ³¹² P. Amice and J.-M. Conia, C.R. Acad. Sci., Paris, Ser. C, 271, 948 (1970).

⁸¹³ J. S. Swenton, J. A. Hyatt, T. J. Walker, and A. L. Crumrine, J. Amer. Chem. Soc., 93, 4808 (1971).

- ³¹⁴ R. D. Hoffsommer, D. Taub, and N. L. Wendler, J. Med. Chem., 7, 392 (1964).
- ³¹⁵ A. J. Birch and G. S. R. Subba Rao, J. Chem. Soc., C, 1966, 1213.

³¹⁸ N. J. Turro and D. M. McDaniel, J. Amer. Chem. Soc., 92, 5727 (1970).

³¹⁷ G. Maier and T. Sayrac, Chem. Ber., 101, 1354 (1968).

³¹⁸ R. A. Sheldon and J. K. Kochi, J. Amer. Chem. Soc., 92, 5175 (1970).

³¹⁹ J. Jacobus, Z. Majerski, K. Mislow, and P. von R. Schleyer, J. Amer. Chem. Soc., 91, 1998 (1969).

820 W. Kirmse and H. Dietrich, Chem. Ber., 100, 2710 (1967).

³²¹ P. G. Gassman, F. J. Williams, and J. Seter, J. Amer. Chem. Soc.. 90, 6893 (1968).

- ³²² P. G. Gassman, J. Seter, and F. J. Williams, J. Amer. Chem. Soc., 93, 1673 (1971).
- 323 J. J. Sims and L. H. Selman, Tetrahedron Lett., 1969, 561.
- ³²⁴ T. Kaneshiro and A. G. Marr, J. Biol. Chem., 236, 2615 (1961).
- 325 H. Nozaki, H. Itó, S. Tunemoto, and K. Kondô, Tetrahedron, 22, 441 (1966).
- ³²⁶ J. W. Polacheck, B. E. Tropp, J. H. Law, and J. A. McCloskey, J. Biol. Chem., 241, 3362 (1966).

³²⁷ D. L. Turner, M. J. Silver, E. Baczynski, R. R. Holburn, and S. F. Herb, *Lipids*, 5, 650 (1970).

- 328 D. Felix, M. Stoll, and A. Eschenmoser, Chimia, 18, 174 (1964).
- ³²⁹ J. A. Donnelly and P. O'Boyle, Chem. Commun., 1969, 1060.
- ³³⁰ R. P. Mariella and K. H. Brown, J. Org. Chem., 34, 3191 (1969).
- ³³¹ O. Schmidt, K. Prezewowsky, G. Schulz, and R. Wiechert, Chem. Ber., 101, 939 (1968).
- ³³² M. E. Wolff, S.-Y. Cheng, and W. Ho, J. Med. Chem., 11, 864 (1968).
- 333 H. D. Berndt and R. Wiechert, Angew. Chem., Int. Ed. Engl., 8, 376 (1969).
- 334 M. E. Wolff, W. Ho, and M. Honjoh, J. Med. Chem., 9, 682 (1966).
- 335 M. E. Wolff, W. Ho, and R. Kwok, J. Med. Chem., 7, 577 (1964).
- ³³⁶ P. J. Palmer, Brit. Pat. 1,065,466 (1967) [C.A., 67, 73759x (1967)].

³³⁷ K. Syhora, J. A. Edwards, and A. D. Cross, Collect. Czech. Chem. Commun., 34, 2459 (1969).

338 R. Toubiana and E. Lederer, Bull. Soc. Chim. Fr., 1965, 2563.

- ³³⁹ W. Rahman and H. G. Kuivila, J. Org. Chem., 31, 772 (1966).
- 340 L. Vo-Quang, C. R. Acad. Sci., Paris, Ser. C, 266, 642 (1968).
- ³⁴¹ H. Hashimoto, M. Hida, and S. Miyano, Kogyo Kagaku Zasshi, **69**, 174 (1966) [C.A., **65**, 3771h (1966)].
  - ³⁴² J. B. Hendrickson and R. K. Boeckman, Jr., J. Org. Chem., 36, 2315 (1971).
  - ³⁴³ J. B. Lambert, F. R. Koeng, and J. W. Hamersma, J. Org. Chem., 36, 2941 (1971).
  - ³⁴⁴ J. A. Marshall and R. A. Ruden, Tetrahedron Lett., 1971, 2875.
  - ³⁴⁵ K. B. Wiberg and T. Nakahira, J. Amer. Chem. Soc., 93, 5193 (1971).
  - ³⁴⁸ P. G. Gassman, E. A. Williams, and F. J. Williams, J. Amer. Chem. Soc., 93, 5199 (1971).
- ³⁴⁷ J. B. Lambert, R. D. H. Black, J. H. Shaw, and J. J. Papay, J. Org. Chem., **35**, 3214 (1970).

# CYCLOPROPANES FROM UNSATURATED COMPOUNDS 131

346 R. A. Sheldon and J. K. Kochi, J. Amer. Chem. Soc., 92, 4395 (1970).

349 C. Filliatre and A. Bonakdar, C. R. Acad. Sci., Paris, Ser. C, 273, 1001 (1971).

350 G. E. M. Moussa and N. F. Eweiss, J. Appl. Chem., 21, 93 (1971).

351 D. R. Robinson and C. A. West, Biochemistry, 9, 70 (1970).

352 C. D. Poulter, R. S. Boikess, J. I. Brauman, and S. Winstein, J. Amer. Chem. Soc., 94, 2291 (1972).

363 R. C. Hahn and P. H. Howard, J. Amer. Chem. Soc., 94, 3143 (1972).

³⁵⁴ I. B. Repinskaya, A. I. Rezvukhin, and V. A. Koptyug, Zh. Org. Khim., 7, 2143 (1971); J. Org. Chem. (USSR), 7, 2225 (1971).

³⁵⁵ R. M. Dodson, P. H. Hammen, E. H. Jancis, and G. Klose, J. Org. Chem., **36**, 2698 (1971).

³⁵⁶ G. A. Russell, J. J. McDonnell, P. R. Whittle, R. S. Givens, and R. G. Keske, J. Amer. Chem. Soc., **93**, 1452 (1971).

357 T. Tsuji and S. Nishida, Chem. Commun., 1972, 284.

356 R. Maurin and M. Bertrand, Bull. Soc. Chim. Fr., 1970, 998.

359 G. Ohloff and W. Pickenhagen, Helt. Chim. Acta, 54, 1789 (1971).

³⁶⁰ R. H. Chung, G. J. Lin, J. M. Nicholson, A. Tseng, O. Tucker, and J. W. Wheeler, J. Amer. Chem. Soc., 94, 2183 (1972).

361 M. E. Kuehne and G. DiVincenzo, J. Org. Chem., 37, 1023 (1972).

362 W. A. Agosta and A. B. Smith, III, J. Amer. Chem. Soc., 93, 5513 (1971).

383 H. Goldfine and C. Panos, J. Lipid Res., 12 214 (1971).

364 F. D. Gunstone, M. L. K. Jie, and R. T. Wall, Chem. Phys. Lipids, 6, 147 (1971).

385 R. D. Kornberg and H. M. McConnell, Proc. Nat. Acad. Sci. U.S.A., 68, 2564 (1971).

388 W. F. Johns and K. W. Salamon, J. Org. Chem., 36, 1952 (1971).

387 W. G. Dauben and D. S. Fullerton, J. Org. Chem., 36, 3277 (1971).

388 J. F. Templeton and C. W. Wie, Tetrahedron Lett., 1971, 3955.

## CHAPTER 2

# SENSITIZED PHOTOOXYGENATION OF OLEFINS

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#### INTRODUCTION

Sensitized photooxygenations of olefins have been extensively studied: they represent convenient methods for introduction of oxygen at specific sites.¹⁻⁴ When an aerated solution containing a monoolefin, diene, or polvene and a sensitizer is irradiated with light that can be absorbed by the sensitizer, oxygenated products are formed whose nature depends upon the structure of the substrate and the lability of the initial photoproducts under the reaction conditions. The equations in Scheme 1 illustrate typical transformations that can be brought about, often in high vields. In some instances external sensitizers need not be added because substrates with appropriate light absorption properties (e.g., polvaromatic hydrocarbons) can also function as sensitizers. The ready reducibility of hydroperoxides to alcohols enhances the synthetic usefulness of these photooxygenations. In this review, coverage is restricted to molecules with one or more carbon-carbon double bonds; photooxygenation of compounds containing carbon-heteroatom multiple bonds or carboncarbon triple bonds are beyond the scope of this chapter.

#### MECHANISTIC CONSIDERATIONS

#### Formation of the Active Oxygenating Species

Ordinarily, only light absorbed by the sensitizer can promote photooxygenations and, because the excited singlet states of most sensitizers

¹ K. Gollnick, Advan. Photochem., 6, 1 (1968).

² C. S. Foote, Accts. Chem. Res., 1, 104 (1968).

³ K. Gollnick and G. O. Schenck in 1,4 Cycloaddition Reactions, J. Hamer, Ed., Academic Press, New York, 1967, p. 255.

⁴ A. Schönberg, *Preparative Organic Photochemistry*, Springer Publishing Co., New York, 1968.

SCHEME 1.

SENSITIZED PHOTOOXYGENATION OF VARIOUS OLEFINS



are too short lived to interact efficiently with other species, the triplet states are usually required in the transfer of energy to oxygen. This view is supported by numerous experiments, and the events involving the sensitizer are summarized in Eqs. 1-3.^{1, 5, 6} Superscripts 1 and 3 on the sensitizer (abbreviated Sens) refer to the lowest excited singlet and triplet states, respectively, and superscript 3 on oxygen refers to its triplet

⁵ G. O. Schenck and K. Gollnick, Forschungsberichte des Landes Nordrhein-Westfalen, Nr. 1256, Westdeutscher Verlag, Köln and Opladen (1963).

⁶ K. Gollnick and G. O. Schenck, Pure Appl. Chem., 9, 507 (1964).

ground state. The term "active oxygenating species" is noncommittal and could mean oxygen alone or oxygen bound in some way to the sensitizer.

Sens 
$$\xrightarrow{h_{\nu}}$$
 ¹Sens (Eq. 1)

 1 Sens  $\longrightarrow$   3 Sens (Eq. 2)

$3$
Sens +  $^{3}O_{2} \longrightarrow$  Active oxygenating species (Eq. 3)

Using various substituted fluorescein dyes as sensitizers, Gollnick and Schenck have carefully characterized the kinetic paths involved in the formation and destruction of the active oxygenating species, as illustrated in Figure 1 and described in Table I.⁶

The identity of the active species in photooxygenations has been a subject of controversy for many years. Among others, suggestions have been made that this species is an excited acceptor molecule  $(A^*)$ ,⁷ a negatively charged oxygen molecule  $(O_2^-)$ ,⁸ a vibrationally excited oxygen molecule  $(O_2^- \text{ vib})$ ,⁹ a sensitizer-oxygen complex  $(\text{Sens} \cdots O_2)^{3.10}$  or oxygen in a singlet excited state  $(^{1}O_2)$ .¹¹⁻¹⁴ The singlet oxygen viewpoint, originally proposed by Kautsky,¹¹ has received abundant experimental support in recent years, and most workers currently accept singlet oxygen as the active species in sensitized photooxygenations of olefins.^{2, 12-16} Thus Eq. 3 is now more informatively replaced by Eq. 3a, which depicts triplet sensitizer interacting with ground-state oxygen  $(^{3}O_2)$  to give singlet oxygen and ground-state singlet sensitizer with net spin preservation. Equation 4 represents formation of product  $(AO_2)$  from an acceptor molecule A. Spectroscopic studies have identified

$3$
Sens +  3 O₂  $\rightarrow$   1 O₂ +  1 Sens (Eq. 3a)

$$^{1}O_{2} + A \rightarrow AO_{2}$$
 (Eq. 4)

⁷ H. Gaffron, Z. Phys. Chem., B37, 437 (1937).

⁸ J. Weiss, Trans. Faraday Soc., 42, 133 (1946).

⁹ J. L. Rosenberg and F. S. Humphries, Photochem. Photobiol., 4, 1185 (1965).

¹⁰ (a) A. Schönberg, Ann., **518**, 299 (1935); (b) M. Koizumi and Y. Usui, *Tetrahedron Lett.*, **1968**, 6011.

¹¹ H. Kautsky, Biochem. Z., 291, 271 (1937).

¹² C. S. Foote and S. Wexler, J. Amer. Chem. Soc., 86, 3879 (1964).

¹³ C. S. Foote and S. Wexler, J. Amer. Chem. Soc., 86, 3880 (1964).

¹⁴ E. J. Corey and W. C. Taylor, J. Amer. Chem. Soc., 86, 3881 (1964).

¹⁵ C. S. Foote, S. Wexler, and W. Ando, Tetrahedron Lett., 1965, 4111.

¹⁶ C. S. Foote, S. Wexler, W. Ando, and R. Higgins, J. Amer. Chem. Soc., 90, 975(1968).

		Value for	Value for
Rate	Process	$\mathbf{R}$ ose Bengal	${f Erythrosin}$
Constant	(Units)	in Methanol	in Methanol
k ₂	Fluorescence of singlet sensitizer (sec ^{$-1$} )	$1.8 \times 10^8$	$1.8 \times 10^8$
k ₃	Internal conversion to ground state of singlet sensitizer (sec ⁻¹ )	$3.6 \times 10^8$	$6.8 \times 10^8$
k4	Quenching of singlet sen- sitizer to ground state by quencher Q (l/mol sec)		
k 5	Intersystem crossing to trip- let state of sensitizer (sec ^{$-1$} )	$1.7 \times 10^9$	$1.4  imes 10^9$
k ₆	Energy transfer from singlet sensitizer to oxygen (l/mol sec)	<u> </u>	-
k ₇	Energy transfer from triplet sensitizer to oxygen (l/mol sec)	$1.2 \times 10^9$	$1.2 \times 10^9$
k ₈	Decay of active oxygenating species to ground state $(\sec^{-1});^a$ henceforth termed $k_d$	<b>~5.3</b> × 10 ⁴	$\sim$ 5.3 $ imes$ 10 ⁴
k 9	Reaction of active oxy- genating species with ac- ceptor A, e.g., 2,3-dimethyl- 2-butene (l/mol sec); ^a henceforth termed $k_A$	~1.8 × 107	~1.8 × 107
k ₁₀	Quenching of active oxy- genating species to ground state with quencher $Q$ , e.g., $\beta$ -carotene (l/mol sec); ^b henceforth termed $k_{\Omega}$	$\sim 5 \times 10^9$	~5 × 10 ⁹
<i>k</i> ₁₁	Phosphorescence and radia- tionless deactivation of triplet sensitizer to ground state (sec ⁻¹ )	$6.5 \times 10^3$	5.8 × 10 ³
<i>k</i> ₁₂	Quenching of triplet sensitizer by quencher Q, e.g., cyclo- octatetraene (1/mol sec)	$5 \times 10^8$	11 × 10 ⁸
$\Phi$ ( ³ Sens)	Quantum yield of triplet sensitizer	0.76	0.62
$\Phi$ (O ₂ )	Quantum yield of active oxygenating species	0.76	0.62

TABLE I. DESCRIPTION OF RATES ILLUSTRATED IN FIGURE 11, 17, 18

^a These values were calculated on the assumption that the quenching rate of singlet oxygen by  $\beta$ -carotene was 5 × 10⁹ l/mol sec. ^b The quenching rate was presumed equal to the diffusion controlled rate.



FIGURE 1. Kinetic scheme for production of the active oxygenating species.*

* Dark arrows indicate primary path for formation of the active oxygenating species under usual conditions, *i.e.*, no quenchers (Q) present,  $O_2 \geq 10^{-5}M$  for rose bengal or chlorophyll a. The vibrational levels are represented by thin horizontal lines above each electronic level. The olefin acceptor and the oxygenated product are labeled A and  $AO_2$ , respectively.

singlet oxygen in both of its two excited singlet states, which are symbolically described as in the accompanying tabulation.^{2. 19-21}

Oxygen Molecule	Configuration of Electrons in Highe Occupied Orbitals	st Energy above Ground State
Second excited state $({}^{1}\Sigma_{g}^{+})$		37.5 kcal/mol
First excited state $(^{1}\Delta_{g})$		22.5  kcal/mol
Ground state $({}^{3}\Sigma_{g}^{-})$		

The formation of  ${}^{1}\Delta_{\rho}$  O₂ during the gas-phase photooxygenation of naphthalene²² and diffuoronaphthalene²³ has recently been demonstrated by paramagnetic resonance; Snelling has detected phosphorescence of

¹⁹ K. Kawaoka, A. U. Khan, and D. R. Kearns, J. Chem. Phys., 46, 1842 (1967).

²⁰ A. U. Khan and D. R. Kearns, J. Chem. Phys., 48, 3272 (1968).

²¹ G. Herzberg, Spectra of Diatomic Molecules, 2nd ed., D. Van Nostrand Co., Princeton, N.J., 1950.

²² (a) D. R. Kearns, A. U. Khan, C. K. Duncan, and A. U. Maki, J. Amer. Chem. Soc., **91**, 1039 (1969); (b) D. R. Kearns, Chem. Rev., **71**, 395 (1971).

²³ E. Wasserman, V. J. Kuck, W. M. Delavan, and W. A. Yager, J. Amer. Chem. Soc., **91**, 1040 (1969).

 ${}^{1}\Delta_{g}$  O₂ during gas-phase photolysis of benzene and oxygen.²⁴ Using a chemical system (hypochlorite and hydrogen peroxide) known to produce singlet oxygen principally in its  ${}^{1}\Delta_{g}$  state,²⁵⁻²⁸ Foote and co-workers have demonstrated with various substrates that product distributions,^{2, 12-15, 29, 30} stereoselectivity,^{2, 15} and relative reactivities^{2, 16} are virtually identical with those brought about by the "active oxygenating species" in photosensitized reactions.

Although  ${}^{1}\Sigma_{g}^{+}$  O₂ has also been observed spectroscopically in the gas phase,^{2, 25, 26, 31} there appear to be no authenticated cases of olefin reactions that require involvement of this second excited singlet state of oxygen. Kearns and Khan have calculated that sensitizers with triplet state energies between 22 and 38 kcal/mol can generate only  ${}^{1}\Delta_{a}$  O₂, sensitizers with triplet energies from 38 to 45 kcal/mol can generate proportions of  ${}^{1}\Sigma_{\rho}^{+}$  O₂ that increase from 0 to 90%, respectively, and sensitizers with triplet energies above 45 kcal/mol should all produce roughly 10%  $^{1}\Delta_{a}$  $O_2$  and 90 %  ${}^1\Sigma_g^+ O_2$ .³² Nevertheless, no variation in product distributions or in relative reactivities in photosensitized oxygenations has been found with sensitizers having triplet energies that ranged from 34.0 to 66.5 kcal/mol.³¹ In addition, gaseous  ${}^{1}\Sigma_{g}^{+}$  O₂ is reported to be collisionally deactivated by water with a rate constant of  $6.0 \times 10^8$  l/mol sec,²⁶ whereas gaseous  ${}^{1}\Delta_{q}$  O₂ is collisionally deactivated by water with a rate constant of  $8 \times 10^3$  l/mol sec.³³ Therefore, at least in aqueous solution, in order to be competitive  ${}^{1}\Sigma_{a}^{+}$  O₂ would have to react with a substrate about 10⁵ times faster than does  ${}^{1}\Delta_{a}$  O₂. Ogryzlo proposed that, ordinarily, most of the  ${}^{1}\Sigma_{\sigma}^{+}$  O₂ is collisionally transformed to  ${}^{1}\Delta_{\sigma}$  O₂.²⁶ Thus  ${}^{1}\Delta_{\sigma}$  O₂ appears to be the "active oxygenating species," although the case against involvement of  ${}^{1}\Sigma_{g}^{+}$  O₂ admittedly rests heavily on negative evidence. On the basis of increased photooxygenation efficiencies in D₂O and in a 1:1 mixture of  $D_2O$  and  $CD_3OD$ , the lifetime of  ${}^1\Delta_{\sigma}O_2$  is thought to be about 10 times longer in these solvents than in the corresponding nondeuterated media. It has been suggested that such deuterium effects can provide a simple diagnostic test for singlet oxygen.^{34,38a}

- ²⁷ R. J. Browne and E. A. Ogryzlo, Can. J. Chem., 43, 2915 (1965).
- ²⁸ J. S. Arnold, R. J. Browne, and E. A. Ogryzlo, Photochem. Photobiol., 4, 963 (1965).
- ²⁹ H. H. Wasserman and J. R. Scheffer, J. Amer. Chem. Soc., 89, 3073 (1967).
- ³⁰ R. W. Murray and M. L. Kaplan, J. Amer. Chem. Soc., 90, 537 (1968).
- ³¹ K. Gollnick, T. Franken, G. Schade, and G. Dörhöfer, Ann. N.Y. Acad. Sci., **171**, 89 (1970).
  - ³² D. R. Kearns and A. U. Khan, Photochem. Photobiol., 10, 193 (1969).
  - 33 R. P. Wayne, Advan. Photochem., 7, 311 (1969).
  - 34 P. B. Merkel, R. Nilsson, and D. R. Kearns. J. Amer. Chem. Soc., 94, 1030 (1972).

²⁴ D. R. Snelling, Chem. Phys. Letters, 2, 346 (1968).

²⁵ A. U. Khan and M. Kasha, J. Amer. Chem. Soc., 88, 1574 (1966).

²⁶ S. J. Arnold, M. Kubo, and E. A. Ogryzlo, *Advan. Chem. Ser.*, No. 77, Amer. Chem. Soc., Washington D.C., 1968, p. 133.

#### The Product-Forming Step

#### Monoolefins

The Ene Reaction. Photosensitized oxygenation of alkyl-substituted olefins produces allylic hydroperoxides with a shifted double bond. The overall change is similar to that of other ene reactions^{35, 36} and involves oxygen attack at an olefinic carbon and abstraction of an allylic hydrogen, as illustrated with 2,3-dimethyl-2-butene. The ease of such reactions is influenced only slightly by the solvent, but depends critically on steric, electronic, and conformational factors in the substrate.

$$^{1}O_{2} + CH_{3} C = CH_{3} \xrightarrow{k_{A}} CH_{3} C + CH_{2} CH_{3} C + CH_{2} CH_{3} C + CH_{2} CH_{3} C + CH_{2} CH_{3} C + CH_{3} C$$

Solvent Effects. In Fig. 1,  $k_{9}$  (generally designated  $k_{A}$ ) represents the specific rate constant for the product-forming step, *i.e.*, for combination of singlet oxygen with an olefinic acceptor, and  $k_8$  (generally designated  $k_d$ ) represents the rate constant for decay of singlet oxygen to its groundstate triplet. Ideally, we should like to know how solvents affect these rate constants individually, but, unfortunately, only their ratio  $(k_d/k_A)$  is readily determined experimentally.^{36a} (The ratio  $k_d/k_A$  is referred to as the  $\beta$  value and, for a given solvent, becomes smaller as the reactivity of a substrate becomes greater.) For citronellol, the  $\beta$  value ranged from 0.16 M in methanol to 0.12 M in 1-butanol to 0.06 M in 3:7 watermethanol;^{1, 5} whereas, for 2-methyl-2-pentene in twelve solvents, the  $\beta$ value ranged from 0.022 M in carbon disulfide to 0.04 M in ethyl acetate to 0.16 M in methanol.^{17, 37, 38} In these cases therefore the  $\beta$  values are not much affected by solvent, but very likely this insensitivity reflects compensatory behavior in  $k_d$  and  $k_A$  because separate studies on the lifetime of singlet oxygen indicate that its decay rate can vary appreciably with solvent.34, 38, 38a

³⁷ (a) C. S. Foote, Y. C. Chang, and R. W. Denny, J. Amer. Chem. Soc., **92**, 5216, 5218 (1970). (b) C. S. Foote and R. W. Denny, *ibid.*, **93**, 5162, 5168 (1971).

³⁸ C. S. Foote, E. R. Petersen, and K.-W. Lee, J. Amer. Chem. Soc., 94, 1032 (1972).

^{38a} P. B. Merkel and D. R. Kearns, J. Amer. Chem. Soc., **94**, 1029 (1972); *ibid.*, **94**, 7244 (1972); D. R. Adams and F. Wilkinson, J. Chem. Soc., Faraday Trans., I, **1972**, 586; R. H. Young, D. Brewer, and R. A. Keller, J. Amer. Chem. Soc., **95**, 375 (1973).

³⁵ R. T. Arnold and J. Dowdall, J. Amer. Chem. Soc., 70, 2590 (1948).

³⁶ J. A. Berson, R. G. Wall, and H. D. Perlmutter, J. Amer. Chem. Soc., **88**, 187 (1966).

^{36a} R. H. Young, K. Wehrly, and R. L. Martin, *J. Amer. Chem. Soc*, **93**, 5774 (1971); R. H. Young, R. L. Martin, N. Chinh, C. Mallon, and R. H. Kayser, *Can. J. Chem.*, **50**, 932 (1972).

Steric Effects. Schenck and Schulte-Elte investigated trialkylated monoolefins containing an increasingly bulky substituent at one site.^{1, 39} They found (Table II) that as the alkyl group was changed from methyl to isopropyl there were a decrease in the total reactivity (*i.e.*,  $\beta$  increased) and an increase in regiospecificity³⁸ favoring tertiary hydroperoxide (*i.e.*, oxygen attack at the gem-dimethylated carbon). They concluded that dye-sensitized photooxygenations are notably sensitive to steric hindrance.^{1, 39} It should be recognized, however, that in these systems inductive, conformational, and statistical factors are not constant, and individual contributions are difficult to evaluate.

TABLE	II.	THE EFFEC	т ог Метну	L BRANCHING	ON TH	E ISOMER	DISTRI-
BUTION	AND	Relative	Reactivity	OF TRIALKYL	ATED	Ethylene	S1. 2, 39

Compound		Relative Reactivity	Proportions of Hydroperoxide (%)		
	p value (M) in Methanol		Secondary	Tertiary	
$\succ$	0.11	38	46	54	
$\geq$	0.18	23	45	55	
$\succ$	1.3	3.2	5	95	
$\succ$	4.2	1.0	100		

Ring structures, with their more readily defined geometries, nonetheless indicate clearly that excited oxygen prefers to approach the less congested face of the olefinic plane. For example, steroidal monoolefins with C-5 double bonds (e.g., 1) give virtually exclusively  $5\alpha$ -hydroperoxides;⁴⁰⁻⁴² and (+)- $\alpha$ -pinene (2)⁶ and (+)-3-carene (3)⁴³ produce hydroperoxides only on the side opposite the gem-dimethyl bridge.

³⁹ K. H. Schulte-Elte, Dissertation, University of Göttingen (1961); Jahresverzeichnis der Deutschen Hochschulschriften, **78**, 348 (1962).

⁴⁰ A. Nickon and J. F. Bagli, J. Amer. Chem. Soc., 83, 1498 (1961); 81, 6330 (1959).

⁴¹ G. O. Schenck, K. Gollnick, and O. A. Neumüller, Ann., 603, 46 (1957).

⁴² G. O. Schenck and O. A. Neumüller, Ann., 818, 194 (1958).

⁴³ K. Gollnick, S. Schroeter, G. Ohloff, G. Schade, and G. O. Schenck, Ann., 687, 14 (1965).



* The abbreviations used for sensitizers are: AcrO, acridine orange; Hemat, hematoporphyrin; MB, methylene blue; RB, rose bengal; ZP, zinc tetraphenylporphin.

Electronic Effects. Singlet oxygen appears to be mildly electrophilic and sensitive to the nucleophilicity of the olefinic bond, for alkyl substitution increases the reactivity (decreases  $\beta$ ) of olefins. If we ignore differences in steric factors and in the number of available allylic hydrogen atoms, tetraalkylated olefins are about 20 times more reactive than trialkylated olefins, which in turn are some 150 times more reactive than dialkylated olefins, which are about 15 times more reactive than monoalkylated olefins. Specific examples are given in Table III (p. 144).

In addition, qualitative studies with steroidal ring-A olefins indicate that an allylic hydroxyl group can, through electron withdrawal, deactivate a substrate at least fivefold, and that acetylation or benzoylation of the allylic hydroxyl group can further reduce the olefin reactivity. Thus esterification may be sufficient to protect the double bond of an allylic alcohol unit during photooxygenation.⁴⁴ A quantitative measure of electronic effects, presumably free of steric and conformational components, has been obtained by Foote and Denny by examination of a series of phenyl-substituted 2-methyl-3-phenyl-2-butenes (4).^{17, 37} The relative rates of reaction, obtained by a competition method, varied only by a factor of 8 over the range of substituents from *para* methoxy to *para* cyano and correlated with the Hammett  $\sigma$  constants with a  $\rho =$ -0.92. On the reasonable presumption that the aryl ring is not sterically

⁴⁴ A. Nickon and W. L. Mendelson, J. Amer. Chem. Soc., 87, 3921 (1965).

Compound	β Value (M, CH ₃ OH)	Relative Reactivity
$= \sqrt{C_6 H_{13} \cdot n}$	165	1.0
	57	2.8
	10	16.5
$\succ$	0.11	1,500
$\succ$	0.003	55,000

 TABLE III. THE EFFECT OF ALKYL SUBSTITUTION ON THE

 REACTIVITY OF ETHYLENES TOWARD SINGLET OXYGEN^{2, 39, 45}

prevented from exerting normal electronic effects, these findings indicate that singlet oxygen is only weakly electrophilic. Interestingly, the isomer distribution 5:6 was 73%:27% and, within 2%, was virtually independent



of R. This lack of a strong Markovnikov directing influence has also been observed with unhindered trialkylated olefins, e.g., 2-methyl-2-butene, which produces approximately equal amounts of secondary and tertiary hydroperoxides (Table II).² On simple statistical grounds for available hydrogens (6 vs. 3), 2-methyl-2-butene might have been expected to favor the secondary over the tertiary hydroperoxide.

Conformational Effects. Using cholesterols monodeuterated at the  $7\alpha$ (7a) and  $7\beta$  (7b) positions, Nickon and Bagli demonstrated that formation of the  $5\alpha$ -hydroperoxides 8a and 8b, respectively, involves abstraction of the C-7 hydrogen from the side on which the C—O bond is formed.⁴⁰ Since singlet oxygen probably approaches the  $\pi$  orbital roughly perpendicular to the olefinic plane, they postulated a *cis* cyclic (but not necessarily concerted) mechanism in which the most favorable orientation of the



FIGURE 2. Cis Cyclic mechanism for the reaction of singlet oxygen with mono-olefins.

allylic hydrogen is approximately orthogonal to the olefinic plane (Figure 2). For cyclohexenoid rings in half-chair conformations, quasi-axial allylic hydrogen atoms are more suitably oriented than are quasi-equatorial hydrogen atoms, and ordinarily the double-bond shift leads to a quasi-axial C-O bond.^{40, 46} In 7, the  $7\alpha$ -hydrogen is readily abstracted by singlet oxygen since this hydrogen in the substrate and the newly created C-O bond in the product 8 possess quasi-axial orientations. Neither the  $7\beta$ - nor the  $4\alpha$ -hydrogen is readily abstracted, because each is quasi-



equatorial. Although the  $4\beta$ -hydrogen is quasi-axial, and therefore suitably poised, it is shielded by the angular methyl group at C-10 and, more importantly, its involvement requires creation of a  $6\beta$  C—O bond, which is sterically congested by *syn*-axial interaction with the angular methyl group. This preference for quasi-axial hydrogen and the retardation

⁴⁶ A. Nickon, N. Schwartz, J. B. DiGiorgio, and D. A. Widdowson, J. Org. Chem., **30**, 1711 (1965).

imposed by a methyl group syn-axial to the C—O bond were supported by experiments with other steroids such as  $5\alpha$ - and  $5\beta$ -cholest-6-ene (**9a** and **9b**)⁴⁰ and with 3-methyl- and 2-methyl- $5\alpha$ -cholest-2-ene (**10** and **13**), respectively,⁴⁷ which were photooxygenated in pyridine with hematoporphyrin as sensitizer.

The olefin **9a** has two suitably oriented quasi-axial allylic hydrogen atoms, but nevertheless oxygen combines only at C-7. The  $8\beta$ -hydrogen remains intact partly because it is shielded but largely because  $\beta$ -attack at C-6 is inhibited by *syn*-axial hindrance with the C-10 angular methyl group. The corresponding A/B *cis* epimer **9b** with its two  $\beta$ -oriented allylic hydrogens was virtually inert to prolonged photooxygenation. Lack of oxygenation at C-6 is understandable for the reasons noted above, and failure to oxygenate at C-7 is attributed largely to the unfavorable (quasi-equatorial) orientation of the  $5\beta$ -hydrogen. Hindrance to  $\beta$ approach at C-7 by the C-10 methyl group may also be a contributing



factor, but results with steroidal ring-A olefins (such as 13 and 5 $\beta$ -cholest-3-ene⁴⁶) suggest that hindrance from the  $\beta$  face is not in itself enough to account for the inertness of 9b.

The trisubstituted olefins 10 and 13 give the products and ratios shown. These results are instructive because the allylic methyl hydrogens can readily adopt optimum orientation whether oxygen attacks the  $\alpha$ - or  $\beta$ -face, and therefore factors that influence creation of the C-O bond

⁴⁷ A. Nickon, V. T. Chuang, P. J. L. Daniels, R. W. Denny, J. B. DiGiorgio, J. Tsunetsugu, H. G. Vilhuber, and E. Werstiuk, J. Amer. Chem. Soc., **94**, 5517 (1972). See also ref. 203.

become more identifiable. Pertinent observations are these: (a) no products are formed that require abstraction of a quasi-equatorial ring



hydrogen or generation of a C-O bond syn-axial to the angular methyl at C-10; (b) the predominance of 12 over 11 shows that methyl hydrogen atoms are not always favored over ring hydrogen atoms;⁴⁸⁻⁵² (c) the absence of the epimer of 11 and especially the only slight preference for 14 (axial C-O) over 16 (equatorial C-O) reveal the relative unimportance of stereoelectronic influence in the creation of the C-O bond. Furthermore, since primary deuterium isotope effects determined by intramolecular competition in oxygenation of monoolefins are low ( $k_{\rm H}/k_{\rm D} \sim 1.1-2.4$ ), a transition state for the product-forming step that resembles starting olefin rather than the allylic hydroperoxide is indicated.^{47, 53, 53a} Frequent predominance of axial hydroperoxides as primary products is therefore largely a consequence of the *cis*, cyclic mechanism, in which abstraction of axial C-H is favored because of its better orientation for cyclic transfer. This behavior in photooxygenation contrasts with other reactions where

48 E. Klein and W. Rojahn, Tetrahedron, 21, 2173 (1965).

49 J. A. Marshall and A. R. Hochstetler, J. Org. Chem., 31, 1020 (1966).

⁵⁰ G. O. Schenck, H. Eggert, and W. Denk, Ann., 584, 177 (1953).

⁵¹ J. A. Marshall, N. Cohen, and A. R. Hochstetler, J. Amer. Chem. Soc., 88, 3408 (1966).

52 G. O. Schenck, S. Shroeter, and G. Ohloff, Chem. Ind. (London), 1962, 459.

⁵³ F. A. Litt and A. Nickon, Advan. Chem. Ser., No. 77, Amer. Chem. Soc., Washington D.C., 1968, p. 118.

538 K. R. Kopecky and J. H. van de Sande, Can. J. Chem., 50, 4034 (1972).

strong stereoelectronic preferences for axial have been observed in generation of allylic cyclohexenoid bonds.^{54, 55}

Cholest-4-ene (17) illustrates a type of behavior possible for polycyclic systems with a conformationally mobile cyclohexene ring.⁵⁶ Hematoporphyrin-sensitized oxygenation of 17 in pyridine gave a mixture of hydroperoxides (ca. 83%), cholest-4-en-3-one (ca. 6%), and starting olefin (ca. 11%). The hydroperoxides initially produced were 18, 19, 20 roughly in the ratio 79:11:10.* Cholest-4-ene can adopt two inter-



convertible half-chair forms (17a and 17b), both of which must be invoked to account for the three initial hydroperoxides. Thus only 18 is expected from 17a, whereas products 19 and 20 are readily accommodated by form 17b. Importantly, the angular methyl group in 17b is axial to ring B and quasi-equatorial to ring A and initially presents a *syn*-axial interaction to the  $6\beta$ -hydrogen atom but not to a developing C-O bond at C-4. Therefore formation of 20 illustrates that a 1,3-diaxial relationship

* During the reaction or during subsequent reduction with sodium iodide about half of **18** and the bulk of **19** rearranged to their more stable allylic isomers, cholest-4-en- $3\alpha$ -ol and cholest-4-en- $3\beta$ -ol, respectively, so that the isolated products were the five allylic alcohols. Allylic rearrangements of tertiary hydroperoxides to secondary hydroperoxides have analogy^{67, 58} and, for other steroids, have been shown to be intramolecular and stereo-specifically *cis.*⁵⁹

⁵⁴ G. Stork and S. D. Darling, J. Amer. Chem. Soc., 82, 1512 (1960).

⁵⁵ G. Subrahmanyam, S. K. Malhotra, and H. J. Ringold, J. Amer. Chem. Soc., 88, 1332 (1966).

⁵⁶ A. Nickon and W. L. Mendelson, J. Org. Chem., 30, 2087 (1965).

⁵⁷ W. F. Brill, J. Amer. Chem. Soc., 87, 3286 (1965).

⁵⁸ B. Lythgoe and S. Trippett, J. Chem. Soc., 1959, 471.

⁵⁹ G. O. Schenck, O. A. Neumüller, and W. Eisfeld, Ann., 618, 202 (1958).

between hydrogen and methyl is insufficient by itself to block the oxygenation and again stresses that steric congestion at the developing C—O bond is of greater importance than congestion at the allylie hydrogen.⁵⁶

With open-chain olefins the degree of regiospecificity seemingly also can reflect the availability of suitably oriented hydrogens. For example, when 2,4-dimethyl-2-pentene is photooxygenated in methanol/2-propanol, only 5% of tertiary hydroperoxide is formed, probably because the required hydrogen orientation 21 for the *cis*, cyclic process corresponds to an unfavorable ground-state conformation.¹ Open-chain olefins are



tacitly presumed to undergo the ene reaction only by a cis, cyclic (*i.e.*, suprafacial process), but possible competition by an antarafacial path has not been excluded experimentally, although it appears less favorable geometrically.

Proposed Mechanisms. The details of the *cis*, cyclic mechanism, which is required by the stereochemical findings with steroidal rings, center around whether the C-O formation and C-H cleavage occur concertedly by an ene-like process or sequentially with generation of discrete, shortlived intermediates.⁵³ Initial cleavage of C-H to produce a mesomeric allylic radical, cation, or anion is excluded by the ubiquitous double-bond shift, and by the electronic and stereochemical facets of the reaction, among other things.^{6, 17} Preliminary formation of a C-O bond to give the diradical, ionic, or neutral intermediates 22a-22f has been considered and discussed.^{2, 17, 53} The singlet and triplet diradical species 22a and 22b are reasonably excluded on the grounds that olefins undergo no cis-trans isomerization during sensitized photooxygenation.^{31, 53} The zwitterions 22c and 22d are not tenable because the former species would not account for the direction of the observed electronic effects and both would be expected to possess strong Markovnikov directing influence and high solvent sensitivity. Electronic criteria^{2, 17} also tended to exclude the 1,2-dioxetane (i.e., 1,2-peroxide) intermediate 22e and the perepoxide (also called peroxirane^{22b}) intermediate 22f, but evidence against the



latter species is largely negative, especially since its structure is novel and its behavior and properties are still matters of conjecture.

The one-step ene mechanism (Eq. 5) accommodated all the facts and was generally accepted, since no evidence for intermediates existed. However, in 1969 Fenical, Kearns, and Radlick reported findings that seemingly opposed this view.^{60. 61} Among other things, they photo-

oxygenated 2,3-dimethyl-2-butene with methylene blue in 40% aqueous methanol containing 1 M sodium azide and isolated a mixture containing 3% of the allylic hydroperoxide and 97% of an azidohydroperoxide, which they proposed arose by interception of an intermediate dioxetane or perepoxide (Eq. 6). Subsequently other workers prepared several dioxetanes, including tetramethyldioxetane,⁶² and showed that they break down exclusively to two carbonyl fragments and not to allylic hydroperoxides,⁶³⁻⁶⁸ and so Kearns and co-workers favored the

⁶⁰ W. Fenical, D. R. Kearns, and P. Radlick, J. Amer. Chem. Soc., 91, 3396 (1969).

⁸¹ W. Fenical, D. R. Kearns, and P. Radlick, J. Amer. Chem. Soc., 91, 7771 (1969).

⁶² C. Mumford, Ph.D. Dissertation, University of Alberta, 1969; information provided by Dr. K. Kopecky. See also ref. 69a.

⁶³ (a) K. R. Kopecky, J. H. Van de Sande, and C. Mumford, Can. J. Chem., 46, 25 (1968);
(b) W. H. Richardson and V. F. Hodge, Tetrahedron Lett., 1971, 749; J. Amer. Chem. Soc., 93, 3996 (1971).

⁶⁴ K. R. Kopecky and C. Mumford, Can. J. Chem., 47, 709 (1969).

⁶⁵ P. D. Bartlett and A. P. Schaap, J. Amer. Chem. Soc., 92, 3223 (1970).

⁶⁶ S. Mazur and C. S. Foote, J. Amer. Chem. Soc., 92, 3225 (1970).

⁶⁷ P. D. Bartlett, G. D. Mendenhall, and A. P. Schaap, Ann. N.Y. Acad. Sci., 171, 79 (1970).

⁶⁸ A. P. Schaap and P. D. Bartlett, J. Amer. Chem. Soc., 92, 6055 (1970).

⁶⁸⁸ A. P. Schaap, Tetrahedron Lett., 1971, 1757; A. P. Schaap and N. Tontapanish, J. Chem. Soc., Chem. Commun., 1972, 490.

^{66b} J. H. Wieringa, J. Strating, H. Wynberg, and W. Adam, Tetrahedron Lett., 1972, 169.

perepoxide.⁶⁹ However, several research groups have presented evidence that the azido products arise by separate processes unrelated to the one that produces allylic hydroperoxide and have therefore questioned the relevance of the trapping experiments with azide ion.^{69a-d} Furthermore it was found



that, whereas methylene blue-sensitized photooxygenation of 2,3-dimethyl-2-butene in methanol gave only the allylic hydroperoxide, other sensitizers (e.g., fluorene, benzophenone, benzil) produced the methanol adduct 23 in various proportions.⁷⁰ If this adduct were derived simply by competitive nucleophilic attack of methanol on a perepoxide or other intermediate, it would be surprising if the sensitizer could influence the extent of interception. Here, again, extraneous side reactions, perhaps involving radicals or epoxide intermediates, may be competing.^{70a} Although further work is necessary to determine how products like 23 arise, as yet no single intermediate has firm experimental support, nor can any intermediate account as satisfactorily for the vast body of experimental data as does the onestep, ene mechanism.⁵³

The Dioxetane Reaction. In numerous sensitized photooxygenations, carbonyl compounds have been produced in addition to the normal ene products. In the past, these carbonyl products were presumed to have resulted from cleavages of the initial allylic hydroperoxide. Such cleavages

- ^{69b} C. S. Foote, T. T. Fujimoto, and Y. C. Chang, Tetrahedron Lett., 1972, 45.
- 690 K. Gollnick, D. Haisch, and G. Schade, J. Amer. Chem. Soc., 94, 1747 (1972).
- ^{69d} N. Hasty, P. B. Merkel, P. Radlick, and D. R. Kearns, *Tetrahedron Lett.*, 1972, 49.
   ⁷⁰ V. T. Chuang, S. R. Funk, M. J. Spillett, and A. Nickon, unpublished results.
- ⁷⁰⁴ E. J. Reardon, Jr., and P. J. Kropp, J. Amer. Chem. Soc., **93**, 5593 (1971); G. Roussi and R. Beugelmans, Tetrahedron Lett., **1972**, 1333.

⁶⁹ D. R. Kearns, W. Fenical, and P. Radlick, Ann. N.Y. Acad. Sci., 171, 34 (1970).

⁶⁹⁸ K. R. Kopecky, J. H. Van de Sande, and C. Mumford, *Preprints Div. Petrol. Chem.*, Amer. Chem. Soc., **16** (4), A45 (1971).

were known to occur with some allylic hydroperoxides at elevated temperature or in the presence of a trace of acid, as illustrated in Eq.  $7.^{39.71}$ 



Recently, however, several chemists have demonstrated that, in certain cases, singlet oxygen can add to a double bond directly without abstraction of hydrogen.^{60. 65-68. 68a. 72} For example, the photooxygenation of indene was known to produce homophthalaldehyde 25. However, the allylic hydroperoxide 24, which was synthesized separately, is reported to be stable under photooxygenation conditions and therefore may not be the key precursor of this dialdehyde. When photooxygenation of indene was conducted in methanol, homophthalaldehyde (ca. 80%, including some ketal) was accompanied by two methanol adducts, which were isolated as alcohols after a reduction step. These two adducts were presumed to arise from reaction of methanol with a dioxetane intermediate (26) which also could produce dialdehyde 25 by carbon-carbon bond fission.⁶⁰



⁷¹ G. O. Schenck and K. H. Schulte-Elte, Ann., **618**, 185 (1958).
 ⁷² C. S. Foote and J. W.-P. Lin, Tetrahedron Lett., 1968, 3267.

Although other interpretations for these particular results can be advanced, the reality of dioxetanes as distinct primary products in some sensitized photooxygenations is now well documented. For example, a relatively stable ( $t_{1/4} = 102$  minutes at 56°) dioxetane was isolated from tetramethoxyethylene,⁶⁶ and individual dioxetanes have been prepared, each with retention of stereochemistry, from *cis*- and *trans*-diethoxy-ethylene^{65. 67. 68} and from *cis*- and *trans*-ethoxyphenoxyethylene.^{68a} At or near room temperature, all these dioxetanes broke down to their corresponding carbonyl fragments. Interestingly, the rigid hydrocarbon adamantylideneadamantane afforded a stable dioxetane which could be decomposed to adamantanone when heated above the melting point (164°).^{68b} Some of these transformations are shown in the accompanying equations.



Evidently, during photoxygenation, only monoolefins that are sufficiently activated by a vinyl heteroatom or aryl group and that lack readily abstractable hydrogen tend to undergo carbon-carbon cleavage to carbonyl compounds or to other products attributable to dioxetane intermediates. For example, although photooxygenation of indene (Eq. 8) is presumed to proceed largely via a dioxetane intermediate, 2,3-dimethylindene gives at least 68% of a normal ene product.⁶⁰ (None of the isomeric allylic hydroperoxides was isolated; the diketone, therefore, may not arise entirely from a dioxetane intermediate.) Photooxygenation of



styrene, which has no allylic hydrogen, gives benzaldehyde and formaldehyde, presumably by way of a dioxetane,⁷³ but photooxygenation of 2-methyl-3-phenyl-2-butene (4) produces ene products exclusively.^{17, 37}

Dihydropyran, which has an activated double bond as well as allylic hydrogen atoms, gives butan-4-al-l-ol formate, presumably via a dioxetane intermediate, and 5,6-dihydro-2-pyrone, presumably by dehydration of the expected allylic hydroperoxide.^{67, 68} Interestingly the relative proportions of these two products are sensitive to solvent (Table IV) and vary from 9:91 in benzene to 85:15 in acetonitrile. We noted earlier that the rates of allylic hydroperoxidations did not depend markedly upon solvent; hence the data in Table IV may imply that the dioxetane mode is somewhat more sensitive to the surrounding medium.^{67, 68} From a practical standpoint, provided an abstractable allylic hydrogen is available, it may be possible to favor one mode or the other by judicious choice of solvent.⁷⁶



TABLE IV. SOLVENT DEPENDENCE OF THE DIOXETANE: ENE REACTION MODES FOR DIHYDROPYRAN^{67, 68}

Solvent	Dielectric Constant (20°)	Relative Yields, %		
		Dioxetane Mode	Ene Mode	
Benzene	2.27	9	91	
Acetone	21.2	45	55	
Methylene chloride	9.08	73	27	
Acetonitrile	37.5	85	15	

73 G. Rio and J. Berthelot, Bull. Soc. Chim. Fr., 1969, 3609

Although this solvent dependence is suggestive of a stepwise mechanism for dioxetane formation,^{67. 68. 74. 74a} preservation of stereochemistry, mentioned earlier for *cis* and *trans* isomeric olefins, would support a one-step process.^{68a} If the reaction is a concerted 2 + 2 cycloaddition, orbital symmetry considerations require that the bonding be suprafacial in one component and antarafacial in the other (*i.e.*,  $\pi 2s + \pi 2a$ ).⁷⁵ For preservation of configuration in dioxetane formation the olefinic component must necessarily bond suprafacially. Consequently the four centers should approach one another in a tetrahedral-like orientation similar to that proposed for concerted cycloaddition of ketenes to olefins.^{76a} A top view of this transition state with a *cis* olefin is depicted by either of the two diagrams shown, which differ only in that one shows the highest occupied molecular orbital (HOMO) of the olefin combining with the lowest unoccupied molecular orbital (LUMO) of the singlet oxygen,



whereas the other reverses the orbital roles. Although collapse of a dioxetane to two carbonyl fragments is strongly exothermic, orbital symmetry considerations suggest that a *concerted* path must encounter one of two types of energy barriers. One is a severe geometric distortion of the four-membered ring to allow a suprafacial-antarafacial disengagement of the carbonyl units. The other is a suprafacial-suprafacial cleavage to produce one of the two carbonyl products in an electronically excited state. The generation of excited states on thermal breakdown of some dioxetanes has been confirmed by observance of chemiluminescence,  $^{62-68}$ and the energy of these excited products has been used to induce other photochemical reactions.  $^{22b, 76b}$ 

### Conjugated Olefins and Aromatic Compounds

When a solution containing a cyclic conjugated diene or a polynuclear aromatic hydrocarbon and a sensitizer is oxygenated and irradiated, a 1,4-epidioxide with a double bond at the 2,3 position may be formed (Eq. 9). The reaction is thought to involve a concerted 1,4 cycloaddition

⁷⁵ R. B. Woodward and R. Hoffmann, Angew. Chem., Int. Ed. Engl., 8, 781 (1969).

⁷⁴ D. R. Kearns, J. Amer. Chem. Soc., 91, 6554 (1969).

⁷⁴⁸ A. P. Schaap and G. R. Faler, J. Amer. Chem. Soc., 95, 3381 (1973).

⁷⁶ A. G. Schultz and R. H. Schlessinger, Tetrahedron Lett., 1970, 2731.

⁷⁶⁸ R. Huisgen, L. A. Feiler, and G. Binsch, Chem. Ber., 102, 3460 (1969).

^{76b} E. H. White, J. Wiecko, and D. F. Roswell, J. Amer. Chem. Soc., 91, 5194 (1969).

#### ORGANIC REACTIONS

analogous to a Diels-Alder process. Solvent effects, steric effects, electronic effects, and mechanism are discussed briefly in the following paragraphs. Open-chain conjugated dienes can give products from attack on the individual olefinic units as well as 1,4-cycloadducts (see Table XXIII).^{76c-f} s-cis and s-trans Conformational isomerism may be a pertinent factor in these cases. Conjugated trienes and polyenes have not been studied enough to draw valid generalizations, but they seem to respond to singlet oxygen as though they were comprised of diene and/or monoene subunits (see Table XXX).

$$(Eq. 9)$$

Appreciable solvent effects on the rates of photooxygenations have been noted for aromatic hydrocarbons⁷⁷⁻⁷⁹ and furans.^{36a, 80, 81} For example,  $\beta$  values  $(k_d/k_A)$  for anthracene have been reported to range from 0.002 *M* in carbon disulfide to 0.013 *M* in chloroform to 0.11 *M* in bromobenzene.^{77, 82, 83} The relative rates of photooxygenation of 2-*p*anisylfuran ranged from 1.00 in 1-butanol to 3.27 in water to 5.64 in 1,2-ethanediol (see Table XIII, p. 176). The reactivity of anthracene does not appear to parallel any obvious solvent property, whereas for 2-*p*-anisylfuran there may be some correlation with dielectric constant and viscosity of the solvent.^{80, 81}

The addition of singlet oxygen to conjugated dienes is sensitive to steric effects, and bulky substituents can often block attack from one face of the  $\pi$  system. For example, (+)-nopadiene (27),⁸⁴ dehydrocantharidin (28),⁸⁵ ergosterol (29),⁸⁶ and lumisteryl acetate (30)⁸⁷ produce epidioxides on the side away from *gem*-dimethyl bridges or nearby angular methyl groups.

^{76C} K. Kondo and M. Matsumoto, J. Chem. Soc., Chem. Commun., 1972, 1332.

^{76d} J. Rigaudy, P. Capdevielle, and M. Maumy, Tetrahedron Lett., 1972, 4997.

^{76e} G. Rio and J. Berthelot, Bull. Soc. Chim. Fr., 1971, 2938.

⁷⁶¹ N. M. Hasty and D. R. Kearns, J. Amer. Chem. Soc., 95, 3380 (1973).

⁷⁷ R. Livingston, in Autoxidation and Antioxidants, Vol. I, W. O. Lundberg, Ed., John Wiley & Sons, Inc., New York, 1961, p. 249.

⁷⁸ E. J. Bowen and D. W. Tanner, Trans. Faraday Soc., 51, 475 (1955).

⁷⁹ C. Dufraisse and M. Badoche, C.R. Acad. Sci., 200, 1103 (1935).

⁸⁰ R. H. Young, N. Chinh, and C. Mallon, Ann. N.Y. Acad. Sci., **171**, 130 (1970); and private communication from R. H. Young. See also ref. 36a for some more recent and additional data.

⁸¹ R. H. Young, R. Martin, K. Wehrly, and D. Feriozi, Preprints Div. Petrol. Chem. Amer. Chem. Soc., 16 (4), A89 (1971).

⁸² E. J. Bowen, Trans. Faraday Soc., 50, 97 (1954).

83 R. Livingston and V. S. Rao, J. Phys. Chem., 63, 794 (1959).

⁸⁴ G. Helms, Dissertation, University of Göttingen, 1961; Jahresverzeichnis der Deutschen Hochschulschriften, **77**, 324 (1961).

⁸⁵ G. O. Schenck and R. Wirtz, Naturwiss., 40, 581 (1953).

⁸⁶ A. Windaus and J. Brunken, Ann., 460, 225 (1928).

87 P. Bladon, J. Chem. Soc., 1955, 2176.



Electron-donating groups increase the reactivity of 1,3-dienes and aromatic hydrocarbons and, conversely, electron-withdrawing groups decrease their reactivity.^{2, 39, 77, 88-91} Table V reveals these trends for 1,3-cyclohexadiene, furan, and anthracene. Table VI illustrates how substitution can alter the site of oxygenation in an anthracene system.

Although detailed mechanistic information is lacking on the reaction between singlet oxygen and conjugated dienes and aromatics, the 1,4 cycloadditions appear closely related to thermal Diels-Alder reactions between singlet-state dienes and singlet-state dienophiles.^{1, 3, 90} A concerted combination of  ${}^{1}\Delta_{g}$  O₂ and 1,3-dienes is symmetry allowed⁷⁵ and is

⁸⁸ R. Higgins, C. S. Foote, and H. Cheng, *Advan. Chem. Ser.*, No. 77, Amer. Chem. Soc., Washington, D.C., 1968, p. 102.

⁸⁹ E. Koch, Tetrahedron, 24, 6295 (1968).

O. Chalvet, R. Daudel, C. Ponce, and J. Rigaudy, Int. J. Quantum Chem., 2, 521 (1968).
 H. H. Wasserman and D. L. Larsen, J. Chem. Soc. Chem. Commun., 1972, 253; H. Hart

and A. Oku, *ibid.*, **1972**, 254; H. H. Wasserman and P. M. Keehn, *J. Amer. Chem. Soc.*, **94**, 298 (1972).

	TABLE Site of	VI. EI Single: Diphe	lectronic Effi f Oxygen Att nylanthracene	ECTS ON THE PACK IN 9,10- S ⁹⁰
C	C ₆ H ₅ H	$\rightarrow$	C ₆ H ₅ R C ₆ H ₅ R C ₆ H ₅ R'	+ $C_6H_5R$ $C_6H_5R'$ $C_6H_5R'$
			Relative	Yield, %
	R	R'	9,10-Peroxide	1,4-Peroxide
	н	Н	100	0
	н	OCH ₃	50	50
	OCH3	OCH ₃	0	100

presumed to occur by way of a suprafacial (boatlike) six-membered transition state, as illustrated.^{69, 74} However, this mechanism would not be expected to have a large solvent effect, and more evidence is required before acceptance of any details of the 1,4 addition.



#### REARRANGEMENTS AND REDUCTION OF THE PRIMARY PHOTOPRODUCTS

#### Allylic Hydroperoxides

Allylic hydroperoxides undergo a variety of isomerizations and freeradical transformations rather easily and these can produce secondary products during photooxygenations. Three common transformations are: allylic isomerization (Eq. 10), dehydration to form carbonyl products (Eq. 11), and skeletal changes initiated by migration of groups to oxygen (Hock cleavage,^{39, 71} Eq. 12).



(Eq. 12)

Examples of these three transformations that have been investigated include the allylic rearrangements of 4-methyl-4-hydroperoxy-2-pentene (Table VII),⁵⁷ the rearrangement-dehydration of  $3\beta$ -hydroxy-5 $\alpha$ -hydroperoxycholest-6-ene (31),⁵⁹ and the Hock cleavage of 1-(1'-cyclohexenyl)-1-hydroperoxycyclohexane, which was illustrated earlier in Eq. 7.

TABLE VII. SOLVENT EFFECTS ON THE ALLYLIC INTERCONVERSION OF 4-METHYL-4-HYDROPEROXY-2-PENTENE AND 2-METHYL-4-HYDROPEROXY-2-PENTENE AT 40°57

OOH		<b>`</b>
$\rightarrow$	<u>k1</u>	
/ \	`k_1	/ >-00н

	4-Methyl isomer	2-Methyl isomer			
Solvent	Initial Molar Concentration of 4-Methyl	$t_{\frac{1}{2}}$ $(k_1 \min)$	Initial Molar Concentration of 2-Methyl	$(k_{-1}^{t_{1/2}})$	
70% Water: 30%					
acetone	_	Very large			
Acetone-d ₆	0.15	1400			
4-Methyl-2-					
pentene	0.22	920			
Hexane	0.21	110	0.15	80	
Carbon tetra-					
chloride	0.21	65	0.32	170	



Allylic alcohols can be stereospecifically converted to  $\alpha,\beta$ -epoxyketones, and these transformations are believed to proceed through the normal ene products followed by secondary reactions.^{44, 92} Thus the photooxygenation of cholest-4-en-3 $\beta$ -ol gives the epoxyketone, presumably via the expectedly unstable ene product 5 $\alpha$ -hydroperoxy-cholest-3-en-3-ol (32), which could lose water by cleavage of the O–O bond. A second product is the conjugated enone, which could arise by elimination of hydrogen peroxide from the same intermediate. However, since the proportion of enone varied with different sensitizers, it could also arise by radical abstraction processes on the original substrate.^{44, 92, 92a}



To minimize secondary transformations and radical reactions, photooxygenations are usually performed at or below room temperature in the

92 A. Nickon and W. L. Mendelson, J. Amer. Chem. Soc., 85, 1894 (1963).

⁹²⁸ C. S. Foote and S.-Y. Wong, Preprints Div. Petrol. Chem., Amer. Chem. Soc., 14 (2), A93 (1969). presence of radical inhibitors. In addition, derived allylic hydroperoxides are frequently reduced to the more stable allylic alcohols before isolation. Commonly used reducing agents are sodium borohydride, trimethyl phosphite, lithium aluminum hydride, triphenylphosphine, sodium sulfite, and potassium iodide in acetic acid; the reduction normally proceeds in high yield.

### 1,4-Epidioxides

In general, 1,4-epidioxides obtained from conjugated dienes or aromatic hydrocarbons are more stable than are allylic hydroperoxides, and they can be isolated and purified at room temperature. The 1,4-epidioxides are valuable intermediates in syntheses because they can be converted into a variety of functionalized derivatives. Scheme 2 illustrates transformations of the 1,4-epidioxide, ascaridole, under various conditions of

SCHEME 2. OXIDATION, REDUCTION, AND THERMAL REARRANGEMENT OF ASCARIDOLE³



93 O. Wallach, Ann., 392, 49 (1912).

- 94 G. O. Schenck, Angew. Chem., 64, 12 (1952).
- ⁹⁵ G. O. Schenck, K. G. Kinkel, and H.-J. Mertens, Ann., 584, 125 (1953).

96 H. Paget, J. Chem. Soc., 1938, 829.

⁹⁷ (a) L. Horner and W. Jurgeleit, Ann., **591**, 138 (1955); (b) G. O. Pierson and O. A. Runquist, J. Org. Chem., **34**, 3654 (1969).

98 M. Matic and D. A. J. Sutton, J. Chem. Soc., 1953, 349.
reduction and oxidation and on thermal treatment.³ Although not all epidioxides would be expected to exhibit parallel behavior, these various possibilities should be kept in mind.^{99a}

Equations 13-15 illustrate some additional reported conversions, in situ, of 1,4-epidioxides in alkaline,^{99b} acidic,¹⁰⁰ and neutral¹⁰¹ media. Equation 16 shows a thermally induced reversal of the original photoaddition. Because of spin conservation, the oxygen molecule liberated should be in the singlet state, and this expectation has been confirmed experimentally (see p. 169).²⁹



⁹⁹ (a) W. E. Barnett and L. L. Needham, Chem. Commun., **1970**, 1383; (b) R. N. Moore and R. V. Lawrence, J. Amer. Chem. Soc., **81**, 458 (1959).

¹⁰⁰ C. Dufraisse and M. Gérard, C.R. Acad. Sci., 202, 1859 (1936).

¹⁰¹ C. S. Foote, M. T. Wuesthoff, S. Wexler, I. G. Burstain, R. W. Denny, G. O. Schenck and K.-H. Schulte-Elte, *Tetrahedron*, 23, 2583 (1967).

## LIMITATIONS, REACTIONS WITH OTHER FUNCTIONAL GROUPS, AND QUENCHERS

Although most sensitized photooxygenations of olefins proceed conveniently and produce few side products, weakly nucleophilic or sterically hindered olefins are markedly more difficult to oxygenate. In general, 1,3-dienes, tetraalkylated monoolefins, and many trialkylated monoolefins have  $\beta$  values less than 1.0 and can be photooxygenated within several hours, whereas some tri- and most di-alkylated monoolefins have  $\beta$  values between 1 and 10 and may require 1 or 2 days of irradiation as well as addition of radical inhibitors such as 2,6-di-t-butylphenol or 2,4,6-tri-t-butylphenol. These phenols suppress formation and propagation of radicals that form products with ground-state oxygen, but their usefulness as inhibitors in mechanistic studies is diminished because phenols can also react with singlet oxygen. Mono- and some di-alkylated monoolefins have  $\beta$  values between 10 and 100, and photooxygenation may require several days or longer. From these sluggish olefins, significant amounts of products derived from radicals may be formed even at reduced temperatures with radical inhibitors.46

Work with steroids and other cyclic systems revealed that the ease of oxygenation can depend critically on the availability of suitably aligned allylic hydrogen atoms and on the ability of the system to undergo necessary conformational changes when the double bond shifts.^{40, 46, 102} Therefore three-dimensional representations of molecules should be used to assess the likelihood of successful photooxygenations in polycyclic and hindered systems.

Photooxygenations may not be feasible for olefins that contain lightsensitive functional groups or groups that react with ground-state oxygen (e.g., 9-aminoanthracene).¹⁰³ These difficulties may sometimes be overcome by use of light filters and radical inhibitors. Irradiation at low temperatures can inhibit secondary transformations and is recommended for thermally sensitive reactants or products.

Although sensitized photooxygenation of other functional units are beyond the scope of this review, the examples of the behavior of nonolefinic substrates shown in Scheme 3 illustrate what may be expected if one of these groups is present in the olefinic substrate.

Unexpectedly sluggish photooxygenations can result when quenchers of excited species are unknowingly present. Quenchers of sensitized photooxygenations can function by preferential absorption of the light or by annihilation of either triplet sensitizer or singlet oxygen. Complete

¹⁰⁸ J. Rigaudy and G. Izoret, C.R. Acad. Sci., 238, 824 (1954).



Sulfides and Sulfoxides1, 18, 104, 104a



Pyrroles, 10 11 nophenesta Purines, Pyrimidines, DNA, RNA, etc.^{114–117} Amino Acids: Cystine, histidine, methionine, tryptophan, tyrosine, various proteins^{117–120a}

¹⁰⁴ G. O. Schenck and C. H. Krauch, Chem. Ber., 96, 517 (1963).

^{104a} For vinylic sulfides see: W. Adam and J.-C. Liu, J. Chem. Soc. Chem. Commun., 1972, 73; W. Ando, J. Suzuki, T. Arai, and T. Migita, *ibid.*, 1972, 477.

- ¹⁰⁵ G. O. Schenck, Angew. Chem., **69**, 579 (1957).
  - ¹⁰⁸ F. C. Schaefer and W. D. Zimmermann, J. Org. Chem., 35, 2165 (1970).
  - ¹⁰⁷ R. F. Bartholomew and R. S. Davidson, Chem. Commun., 1970, 1174.
  - ¹⁰⁷⁸ W. F. Smith, Jr., J. Amer. Chem. Soc., 94, 186 (1972).
  - 107b K. Gollnick and J. H. E. Lindner, Tetrahedron Lett., 1973, 1903.
  - ¹⁰⁸ A. Lukton, R. Weisbrod, and J. Schlesinger, Photochem. Photobiol., 4, 277 (1965).
  - 109 H. H. Wasserman, K. Stiller, and M. B. Floyd, Tetrahedron Lett., 1968, 3277.
- ¹¹⁰ H. H. Wasserman, Ann. N.Y. Acad. Sci., 171, 108 (1970).
- ¹¹¹ H. H. Wasserman and M. B. Floyd, Tetrahedron Suppl., 7, 441 (1966).
- ¹¹² H. H. Wasserman and E. Druckrey, J. Amer. Chem. Soc., 90, 2440 (1968).

¹¹³ (a) L. K. Low and D. A. Lightner, J. Chem Soc. Chem. Commun., **1972**, 116; (b) D. A. Lightner and G. B. Quistad, Angew. Chem., **84**, 216 (1972); (c) R. Ramasseul and A. Rassat, *Tetrahedron Lett.*, **1972**, 1337; (d) G. Rio and A. Lecas-Nawrocka, Bull Soc, Chim. Fr., **1971**, 1723; (e) A. Ranjon, *ibid.*, **1971**, 2068: (f) R. W. Franck and J. Auerbach, J. Org. Chem., **36**, 31 (1971).

- ¹¹⁴ M. I. Simon and H. Van Vunakis, Arch. Biochem. Biophys., 105, 197 (1964).
- ¹¹⁵ T. Matsuura and I. Saito, Tetrahedron, 25, 557 (1969).
- ¹¹⁶ K. Zenda, M. Saneyoshi, and C. Chihara, Chem. Pharm. Bull. (Tokyo), 13, 1108 (1965).
- ¹¹⁷ J. D. Spikes and R. Straight, Ann. Rev. Phys. Chem., 18, 409 (1967).
- ¹¹⁸ L. Weil, W. G. Gordon, and A. R. Buchert, Arch. Biochem. Biophys., 33, 90 (1951).
- ¹¹⁹ M. Tomita, M. Irie, and T. Ukita, Biochem., 8, 5149 (1969).
- ¹²⁰ J. D. Spikes and M. L. MacKnight, Ann. N.Y. Acad. Sci., 171, 149 (1970).
- ¹²⁰⁴ R. Nilsson, P. B. Merkel, and D. R. Kearns, Photochem. Photobiol., 16, 117 (1972).

absorption of the relevant incident wavelengths by chromophoric substances in the solution can prevent excitation of the sensitizer and inhibit oxygenation unless the excited chromophores themselves can efficiently transfer energy to oxygen. Triplet quenchers, such as nitrous oxide,¹²¹  $\beta$ -carotene, all-*trans* retinol,^{17, 18} halogen anions, and metal ions of the first transition series¹²¹ compete with oxygen for removal of energy from the excited triplet sensitizer. However, since good sensitizers have very large molar absorptivities ( $\epsilon$ ) and also can transfer energy to oxygen nearly at a diffusion controlled rate, high concentrations of chromophoric substances or triplet quenchers are normally required to stop sensitized photooxygenations.

 $\beta$ -Carotene and other fully conjugated carotenoids efficiently deactivate singlet oxygen and those with 30 carbon atoms or more do so without chemical change.^{17, 18, 37} In contrast, carotenoids of lower molecular weight readily combine chemically with singlet oxygen.¹²²⁻¹²⁴ Table VIII lists examples of some other known quenchers of singlet oxygen and their efficiencies. Thus, in the presence of an equimolar amount of  $\beta$ -carotene, only one singlet oxygen molecule in 10,000 would react with 2-methyl-2-pentene and only 60 in 10,000 (or 1 in 167) would react with 2,3-dimethyl-2butene. Quenching efficiency is of obvious practical importance in the inhibition of singlet oxygen reactions^{124a} and can have special significance in biological^{125a-d} and atmospheric oxygenations.^{125e-h} For example,  $\beta$ -carotene has been used in the treatment of porphyria, a disease characterized by the presence of incompletely digested porphyrin compounds that are in the blood and that can sensitize a person to sunlight or strong visible light.¹²⁵ⁱ

¹²¹ J. G. Calvert and J. N. Pitts, Jr., *Photochemistry*, John Wiley & Sons, Inc., New York, 1966, p. 686ff.

122 M. Mousseron-Canet, D. Lerner, and J.-C. Mani, Bull. Soc. Chim. Fr., 1966, 2144.

¹²³ M. Mousseron-Canet, J. C. Mani, J.-L. Olivé, and J.-P. Dalle, C.R. Acad. Sci., Ser. C., **262**, 1397 (1966).

¹²⁴ J.-P. Dalle, M. Mousseron-Canet, and J.-C. Mani, Bull. Soc. Chim. Fr., 1969, 232.
 ¹²⁴⁸ J. P. Dalle, R. Magous, and M. Mousseron-Canet, Photochem. Photobiol., 15, 411 (1972); I. B. C. Matheson and J. Lee, J. Amer. Chem. Soc., 94, 3310 (1972); R. Nilsson and D. R. Kearns, Photochem. Photobiol., 17, 65 (1973).

¹²⁵ (a) T. Wilson and J. W. Hastings, Photophysiology, A. C. Giese, Ed., Academic Press, New York, Vol V, 1970, p. 49; (b) I. R. Politzer, G. W. Griffin, and J. L. Laseter, Chem. Biol. Interactions, 3, 73 (1971); (c) H. W.-S. Chan, J. Amer. Chem. Soc., 93, 4632 (1971); (d) R. A. Ackerman, J. N. Pitts, Jr., and I. Rosenthal, Preprints Div. Petrol. Chem., Amer. Chem. Soc., 16 (4), A25 (1971); (e) J. W. Coomber and J. N. Pitts, Jr., Environ. Sci. Technol., 4, 506 (1970); (f) R. A. Ackerman, J. N. Pitts, Jr., and R. P. Steer, J. Chem. Phys., 52, 1603 (1970); (g) R. H. Kummler and M. H. Bortner, Ann. N.Y. Acad. Sci., 171, 273 (1970); (h) R. H. Kummler and M. H. Bortner, Preprints Div. Petrol. Chem., Amer. Chem. Soc., 16 (4), A44 (1971); (i) M. M. Mathews-Roth, M. A. Pathok, T. B. Fitzpatrick, L. C. Harber, and E. H. Kass, New England J. Med., 282, 1231 (1970).

Structure	$k_d/k_Q \ ({ m mol}/l)^a$	Relative Reactivity toward ¹ O ₂ ^b	Refs.
$\left(\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	1.8 × 10 ⁻⁵	10,000	17, 18
	$3 \times 10^{-3}$	<b>60</b> (	37
$(CH_3)_2C=C(CH_3)_2$		60	1, 2
0=0	8 × 10 ⁻³	22	18, 126
N	$3.4 \times 10^{-2}$	5.3	18, 127
$(\mathbf{C_2H_5})_2\mathbf{S}$	$9 \times 10^{-2}$	2°	18
$(CH_3)_2C=CHC_2H_5$		1	1, 2

TABLE	VIII.	SINGLET	OXYGEN	QUENCHERS
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^a  $k_d/k_0 = k_8/k_{10}$  (see Fig. 1, p. 139; note that  $\beta = k_d/k_A$ ).

^b These values include quenching by chemical reaction.

^c Diethyl sulfide also reacts chemically with singlet oxygen ( $\beta = 1.8$ ).¹⁸

## ALTERNATIVE METHODS FOR SINGLET OXYGEN PRODUCTION

Generation of singlet oxygen by photosensitization is preferred for most synthetic work because of convenience, yield, and ease of product isolation. In this section we consider five major nonphotochemical methods of producing this reactive species and mention briefly some less important methods.

Sodium Hypochlorite-Hydrogen Peroxide. A convenient method for generating singlet oxygen is the reaction of sodium hypochlorite with hydrogen peroxide.^{12, 13, 15, 16} Chemiluminescence measurements of the

¹²⁶ P.-S. Song and T. A. Moore, J. Amer. Chem. Soc., 90, 6507 (1968).

¹²⁷ C. Ouannès and T. Wilson, J. Amer. Chem. Soc., 90, 6527 (1968).

oxygen bubbles liberated indicate that both  $\Delta_{\sigma} O_2$  and  ${}^{1}\Sigma_{\sigma}^{+} O_2$  are produced and the former species predominates.^{25, 26} Trapping experiments with reactive olefins in methanol showed that the efficiency of  ${}^{1}\Delta_{\sigma} O_2$  production can be as high as 80%.¹⁶

$$NaOCl + H_2O_2 \longrightarrow O_2 + H_2O + NaCl$$

However, this method has several disadvantages. The normal procedure is to dissolve an olefin in an alcohol such as methanol containing aqueous hydrogen peroxide (from commercially available 30% aqueous hydrogen peroxide) at 0° and to add aqueous sodium hypochlorite (typical commercial products usually contain 14% of sodium hypochlorite).¹²⁸ Unreactive olefins require large excesses of the reagent, and solubility problems frequently arise because of the high proportion of water being introduced. Furthermore, this chemical system produces radicals, and competing radical oxidations can occur, although inhibitors (e.g., 2,6-di-t-butylphenol) can suppress the propagation of radical chains. Functional groups that are sensitive to hydrogen peroxide at 0° should not be present. However, groups that are directly attacked by sodium hypochlorite can frequently be tolerated because at a pH above 7 the hypochlorite is usually consumed preferentially by reaction with the hydrogen peroxide which is present in excess.¹²⁸ Interestingly, the yield of singlet oxygen from the reaction in nonalcoholic solutions is very low,¹²⁸ although a 1:1:1 benzene-methanol-diglyme solution has been found satisfactory for reactive olefins that are insoluble in methanol alone.^{17, 129}

Alkaline Hydrogen Peroxide-Bromine. A variant of the method just described is the simultaneous addition of aqueous 30% hydrogen peroxide and bromine to an alkaline solution of an olefin in a solvent such as ethanol, or the addition of bromine to the bottom layer of a two-phase system in which the lower phase is aqueous potassium hydroxide and hydrogen peroxide and the upper phase is a chlorobenzene solution of the reactive olefin. Although this method allows some diversity in the

 $Br_2 + OOH^- + OH^- \longrightarrow {}^1O_2 + H_2O + 2 Br^-$ 

choice of solvents, it is not recommended for general synthetic use because of low yields caused by, among other things, competing radical and bromination reactions, and by secondary reactions of the peroxidic products in the strongly alkaline solutions.¹³⁰

Triphenyl Phosphite-Ozone Adduct. A 1:1 adduct of triphenyl phosphite and ozone can be generated by passage of ozone into a solution

¹²⁸ C. S. Foote, S. Wexler, W. Ando, and R. Higgins, J. Amer. Chem. Soc., 90, 975 (1968).

¹²⁹ C. S. Foote and G. Uhde, unpublished results.

¹³⁰ E. McKeown and W. A. Waters, J. Chem. Soc., B, 1966, 1040.

of triphenyl phosphite in methylene chloride at  $-70^{\circ}$  and removal of excess ozone by nitrogen purge. The adduct is unstable above  $-35^{\circ}$  and decomposes into singlet oxygen and triphenyl phosphate, as determined by chemical traps and esr measurements.^{30, 131, 132} The decomposition is free from significant side reactions and produces singlet oxygen in high yield. For example, an equimolar solution of the adduct and 2,3-dimethyl-2-butene in methylene chloride at  $-30^{\circ}$  gave 2,3-dimethyl-3-hydroperoxy-1-butene in 53 % yield.³⁰

$$(C_6H_5O)_3P + O_3 \xrightarrow[CH_2Cl_2]{-70^\circ} (C_6H_5O)_3P - O_3 \xrightarrow[CH_2Cl_2]{-35^\circ} O_2 + (C_6H_5O)_3P \rightarrow O_3$$

However, for synthetic work this method may be inconvenient. The by-product, triphenyl phosphate, is sometimes difficult to separate completely from the peroxide products, a situation greatly aggravated when large excesses of adduct are required for unreactive olefins. Furthermore, it has been reported that the adduct can react directly with monoolefins to give product distributions different from those obtained in typical singlet oxygen reactions, and also that the adduct does not react readily with 1,3-dienes.^{67, 68, 132a} Therefore this ozone-phosphite ester adduct may not be simply regarded as a source of singlet oxygen, and much more needs to be learned before its potential as a predictable oxygenating species can be evaluated. The ozone adduct of the bicyclic phosphite 4-ethyl-2,6,7-trioxa-l-phosphabicyclo[2.2.2]octane is reported to be over 160 times more stable than that from triphenyl phosphite (half-lives of 76.2 vs. 0.47 minutes at 10°).^{132b} Singlet oxygen-like reactions have been observed from other oxygen-rich intermediates (e.g., hydrotrioxides) produced by ozone treatment of various substrates, but their potential for synthetic work has not yet been explored.^{133, 133a}

Thermal Decomposition of Epidioxides. Thermal decomposition of 9,10-diphenyl-9,10-epidioxy-9,10-dihydroanthracene (Eq. 16) appears to produce singlet oxygen in greater than 50% yield (and presumably close to 100%). The oxygenation procedure usually involves heating an olefin and the epidioxide under reflux in an organic solvent for 2–4 days  $(k_{dec} = 2.5 \times 10^{-5} \text{ sec}^{-1} \text{ and } t_{1/2} = 8$  hours in methylene chloride at 90°).²⁹ Although the method is well suited for mechanistic investigations, one disadvantage is the long time and relatively high temperature needed

¹³¹ R. W. Murray and M. L. Kaplan, J. Amer. Chem. Soc., 90, 4161 (1968).

¹³² R. W. Murray, J. W.-P. Lin and M. L. Kaplan, Ann. N.Y. Acad. Sci., 171, 121 (1970).

^{132a} T. W. Sam and J. K. Sutherland, J. Chem. Soc. Chem. Commun., 1972, 424.

^{132b} M. E. Brennan, Chem. Commun., 1970, 956.

¹³³ R. W. Murray, J. W.-P. Lin, and W. C. Lumma, Jr., J. Amer. Chem. Soc., **92**, 3205 (1970).

¹³³⁸ P. R. Story, E. A. Whited, and J. A. Alford, J. Amer. Chem. Soc., 94, 2143 (1972).

to decompose the epidioxide. Another is the difficulty of separating the 9,10-diphenylanthracene from the reaction products, especially when large excesses of epidioxide are used with unreactive olefins. Recently the preparation of 2,5-diphenyl-2,5-epidioxy-2,5-dihydrofuran by sensitized photooxygenation of 2,5-diphenylfuran in diethyl ether at  $-78^{\circ}$  and its subsequent decomposition at room temperature to produce singlet oxygen in at least 70 % yield have been reported.¹³⁴

Microwave Discharge. Singlet oxygen can be generated in a stream of gaseous oxygen by microwave discharge and can be combined with a substrate in the solid,¹⁴ liquid,¹³⁵ or gaseous state.^{125d} Although precautions must be taken to remove atomic oxygen and ozone, this method is attractive for mechanistic studies because it avoids side reactions that may be brought about by irradiation or by the presence of sensitizers or other chemicals. For many laboratories the cost or unavailability of microwave generators may preclude consideration of this method in routine synthetic work.

Miscellaneous Methods. Singlet oxygen has been detected spectroscopically or chemically in chain termination of primary and secondary peroxy radicals,^{136, 137} in the reaction of nitriles or peracids with alkaline hydrogen peroxide,¹³⁰ in the reaction of various metal ions with hydrogen peroxide,¹³⁸ in alkaline hydrolysis of peroxyacetyl nitrate,^{138a} in the thermal decomposition of potassium tetraperoxochromate(V) in aqueous methanol,^{138b} in the reaction of potassium superoxide (KO₂) with water in dimethyl sulfoxide,^{139, 140} and by energy transfer from excited (triplet) iodine molecules in hydrocarbon solvent.^{140a} The yield of singlet oxygen in these transformations is generally low, and little or no research has been done to adapt them to preparative scale oxygenations. Claims for singlet oxygen production in the thermal decomposition of diperoxychromium(VI) oxide etherates,^{141a} and in the reaction of soybean lipoxidase with methyl linoleate^{141b} may be unwarranted.^{141c}

¹³⁴ A. M. Trozzolo and S. R. Fahrenholtz, Ann. N.Y. Acad. Sci., 171, 61 (1970).

135 J. R. Scheffer and M. D. Ouchi, Tetrahedron Lett., 1970, 223.

¹³⁶ J. A. Howard and K. U. Ingold, J. Amer. Chem. Soc., 90, 1056 (1968).

¹³⁷ R. E. Kellogg, J. Amer. Chem. Soc., **91**, 5433 (1969).

- ¹³⁸ J. Stauff, Photochem. Photobiol., 4, 1199 (1965).
- ¹³⁸⁸ R. P. Steer, K. R. Darnall, and J. N. Pitts, Jr., Tetrahedron Lett., 1969, 3765.

^{138b} J. W. Peters, J. N. Pitts, Jr., I. Rosenthal, and H. Fuhr, J. Amer. Chem. Soc., 94, 4348 (1972).

¹³⁹ M. Kasha and A. U. Khan, Ann. N.Y. Acad. Sci., 171, 5 (1970).

¹⁴⁰ A. U. Khan, Science, 168, 476 (1970).

1408 J. Olmsted III and G. Karal, J. Amer. Chem. Soc., 94, 3305 (1972).

¹⁴¹ (a) H. W.-S. Chan, Chem. Commun., **1970**, 1550; (b) H. W.-S. Chan, J. Amer. Chem. Soc., **93**, 2357 (1971); (c) J. E. Baldwin, J. C. Swallow, and H. W.-S. Chan, Chem. Commun., **1971**, 1407.

#### ALTERNATIVE METHODS OF OXIDATION

Autoxidation. Allylic hydroperoxides can be obtained by treatment of monoolefins with ground-state oxygen under conditions conductive to radical formation and propagation.¹⁴² The reaction involves abstraction of hydrogen to give a mesomeric allylic radical that can combine with oxygen at either end of the allylic system to produce hydroperoxides with rearranged and nonrearranged double bonds. Conditions that favor autoxidation also encourage breakdown of the allylic hydroperoxides, and complex mixtures can result. Two illustrations of the striking difference in selectivity between autoxidation and sensitized photooxygenation are given by cholesterol^{143, 144} and  $\alpha$ -pinene,⁶ whose products and approximate relative proportions are illustrated in Table IX (p. 172).

Selenium Dioxide. Many simple olefins that do not contain carbonyl or other reactive functional groups can be oxidized to allylic alcohols by selenium dioxide.¹⁴⁵ (The corresponding unsaturated carbonyl compounds can also be formed.) Moreover, since the double bond usually does not shift, the derived allylic alcohols are frequently isomeric with those obtained by sensitized photooxygenations (see Table IX, p. 172).¹⁴⁶

Dehydrohalogenation of  $\beta$ -Halohydroperoxides. Several tetraalkylated monoolefins have been converted to  $\beta$ -halohydroperoxides by treatment with hydrogen peroxide and a positive halogen source such as N-chloroacetamide or 1,3-dibromo-5,5-dimethylhydantoin. Dehydrohalogenation has furnished allylic hydroperoxides in good yield.^{63a} Less substituted olefins, *e.g.*, 2-methyl-2-butene, also gave good yields of  $\beta$ -halohydroperoxides, but in basic solution they underwent cleavage rather than formation of allylic hydroperoxides.^{63a, 64} The halohydroperoxide method has not been explored enough to reveal its scope or limitations, but clearly the substrate should not have functional groups that are attacked by hydrogen peroxide or positive halogens.



¹⁴² E. G. E. Hawkins, Organic Peroxides, D. Van Nostrand Co., Inc., Princeton, N.J. 1961.

¹⁴³ S. Bergström, and O. Wintersteiner, J. Biol. Chem., 141, 597 (1941).

¹⁴⁴ J. E. van Lier and L. L. Smith, *J. Org. Chem.*, **35**, 2627 (1970): J. I. Teng, M. J. Kulig, L. L. Smith, G. Kan, and J. E. van Lier, *ibid.*, **38**, 119 (1973); *ibid.*, **38**, 1763 (1973).

¹⁴⁵ E. N. Trachtenberg, Oxidation, Vol. 1, R. L. Augustine, Ed., Marcel Dekker, Inc., New York, 1969, p. 119.

¹⁴⁶ N. Rabjohn, Org. Reactions, 5, 331 (1949).

TABLE IX. PRODUCTS FROM CHOLESTEROL^{143, 144, 147-149} and from  $\alpha$ -Pinene^{6, 50} in Sensitized Photooxygenation, Autoxidation, and Selenium Dioxide Oxidation



^a Each product is the allylic alcohol.

**Miscellaneous Methods.** Allylic hydroperoxides (or allylic alcohols) have been produced by the reaction of olefins with N-bromosuccinimide, to form allylic bromides, followed by treatment with potassium hydroxide-hydrogen peroxide;^{142, 151} by the reaction of olefins with t-butyl perbenzoate in benzene in the presence of cuprous salts, to give allylic benzoates, followed by hydrolysis to the allylic alcohol;^{152, 153} by autoxidation of olefins in potassium t-butoxide-t-butyl alcohol;¹⁵⁴ by reaction of olefins with lead tetraacetate followed by hydrolysis;^{155–158} and by autoxidation of olefins accelerated by metals, light, or other means.¹⁵⁹ Frequently these methods do not exhibit sufficient selectivity, stereospecificity, or regiospecificity to be used predictably.

Alternative routes to 1,2-dioxetanes include alkaline treatment of appropriate  $\beta$ -halohydroperoxides⁶³ and ozonolysis of olefins in appropriate solvents.^{133a}

## EXPERIMENTAL CONDITIONS

# Solvents

Table X shows for sensitized photooxygenation of 2-methyl-2-pentene how the  $\beta$  values and  $k_t$  values vary in different solvents. (The  $\beta$  values, it will be recalled, are inversely proportional to reactivity with  ${}^{1}O_{2}$ , and the  $k_t$  values are inversely proportional to the quantum yield of  ${}^{1}O_{2}$ .) The  $\beta$  value varied by a factor of only about 7 and the quantum yield of singlet oxygen varied by a factor of only 2 (except for *m*-dimethoxybenzene). Thus, since the efficiency of this oxygenation is not markedly influenced by solvent, the choice of solvent in sensitized photooxygenation of a monoolefin has often been dictated by the solubility of substrate and sensitizer and by solvent properties that influence ease of workup.

¹⁴⁷ O. Rosenheim and W. W. Starling, J. Chem. Soc., 1937, 377.

¹⁴⁸ L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis*, Vol. 1, John Wiley & Sons, Inc., New York, 1967, p. 141.

¹⁴⁹ E. Urion, C.R. Acad. Sci., 199, 363 (1934).

¹⁵⁹ G. Dupont and W. Zacharewicz, Bull. Soc. Chim. Fr., 2, (5), 533 (1935).

¹⁵¹ J. Hoffman, J. Org. Chem., 22, 1747 (1957).

¹⁵² B. Cross and G. H. Whitham, J. Chem. Soc., 1961, 1650.

¹⁵³ M. S. Kharasch, G. Sosnovsky, and N. C. Yang, J. Amer. Chem. Soc., 81, 5819 (1959).

¹⁵⁴ J. E. Baldwin, D. H. R. Barton, and J. K. Sutherland, J. Chem. Soc., 1964, 3312.

¹⁵⁵ L. F. Fieser and M. Fieser, Steroids, Rheinhold Publishing Co., New York, 1959.

¹⁵⁶ R. Criegee, Ann., 481, 263 (1930).

¹⁵⁷ R. Criegee in Oxidation in Organic Chemistry, K. Wiberg, Ed., Academic Press, New York, 1965, p. 337.

¹⁵⁸ G. H. Whitham, J. Chem. Soc., 1961, 2232.

¹⁵⁹ R. B. Mesrobian and A. V. Tobolsky in *Autoxidation and Antioxidants*, W. O. Lundberg, Ed., John Wiley & Sons, Inc., New York, 1961, p. 107.

The relative lifetimes of singlet oxygen in a few of these solvents have been determined independently and, as shown in the last column of Table X, carbon disulfide is particularly favorable.^{38, 38a} Note, however, that the variation in lifetimes exceeds the variation in  $\beta$ ; therefore the rate constants that constitute  $\beta$  (*i.e.*,  $k_d/k_A$ ) change to compensate each other partially when the solvent is varied.

Solvent	$eta,\ 25^\circ~(M)$	$k_t^{b}$	Relative Lifetime, ${}^{1}\Delta_{g} O_{2}{}^{38a}$
Carbon disulfide	0.022		200
Ethyl acetate	0.04	293	
Pyridine	0.05	175	
Bromobenzene	0.05	177	
Cyclohexanol	0.07	222	
Dimethyl sulfoxide	0.07	204	10.14774.0
Acetone	0.08	156	26
Benzene	0.10	230	24
Iodoethane	0.11	192	
Anisole	0.13	213	
<i>m</i> -Dimethoxybenzene	0.15	2300	
Methanol	0.16	140	7
Water			2
Ethanol			12
Cyclohexane			17
Acetonitrile			30
Chloroform			60
Carbon tetrachloride			700

 TABLE X. SOLVENT EFFECTS ON THE SENSITIZED^a

 Photooxygenation of 2-Methyl-2-pentene^{17, 37, 38}

^a The sensitizer was tetraphenylporphin, rose bengal, or zinc tetraphenylporphin.

^b The  $k_t$  values were obtained by extrapolation and are only approximate (±20%);  $k_t = 1/\Phi \ ^1O_2$ .

With monoolefins that can also react to form a discrete dioxetane, which decomposes to two carbonyl products, it may be possible to favor either the ene mode or the dioxetane mode by appropriate choice of solvent. With dihydropyran the dioxetane mode was favored by solvents of high dielectric constant (Table IV, p. 154),^{67, 68} but the opposite behavior has been reported for 1,2-diphenylcyclobutene.⁷⁶

In contrast to the monoolefins, photooxygenations of aromatic hydrocarbons respond more dramatically to solvent. As illustrated in Table XI, the rate of direct photooxygenation of rubrene with no added sensitizer is greater by a factor of 90 in carbon disulfide than in nitrobenzene.⁷⁹ However, since the rubrene photooxygenations are autosensitized, the rate differences may be due to a combination of the solvent effect on singlet oxygen production as well as on destruction. With the addition of efficient sensitizers (e.g., rose bengal or chlorophyll a), which have intense

> TABLE XI. SOLVENT EFFECTS ON THE RATE OF PEROXIDE FORMATION IN PHOTOOXYGENATION OF RUBRENE⁷⁹



Solvent	Relative Rate
Carbon disulfide	90
Chloroform	30
Methyl iodide	10
Benzene	10
Acetone	10
Ethyl ether	5
Pyridine	2.5
Nitrobenzene	1

absorption maxima and high quantum yields of  ${}^{1}O_{2}$  production, the effect of solvent on  $\beta$  values is easier to evaluate.^{77, 82} Pertinent data are given for anthracene in Table XII. Therefore in the presence of efficient external

TABLE XII. THE QUANTUM YIELDS OF SINGLET OXYGEN PRODUCTION AND THE $\beta$ Values for Anthracene in Various Solvents ^{77, 82, 83}							
Solvents	Φ ¹ O ₂	β (M)					
Carbon disulfide	0.42	0.002					
Chloroform	0.61	0.013					
Bromobenzene	0.84	0.11					

sensitizers (which would have comparably high  $\Phi {}^{1}O_{2}$  in all three solvents) anthracene would be expected to react 6 times faster in carbon disulfide than in chloroform, and 50 times faster than in bromobenzene (*i.e.*, rates inversely proportional to  $\beta$  only). The efficiency of carbon disulfide is attributed largely to its ability to prolong the lifetime of singlet oxygen.^{38, 38a} The relative reactivities of 2-*p*-anisylfuran (a very reactive substrate) in four hydroxylic solvents have recently been measured (Table XIII).⁸⁰ The rates varied by a factor of about 5 and, although the Hammett  $\rho$  values show a trend with the dielectric constants, the  $\beta$  values are not entirely in line. It has been suggested that the enhanced reactivity in 1,2-ethanediol may be due to its high viscosity, which increases the duration that  ${}^{1}O_{2}$  can remain in a reaction cage.^{80, 81, 36a}

Solvent	$\beta$ (M)	Relative Rate	Dielectric Constant (e)	Viscosity (cp)	م Value ^a
1-Butanol	0.0021	1.00	17.1	2.6	-1.03
Methanol	0.0010	2.02	32.6	0.55	-0.84
1,2-Ethanediol	0.00037	5.64	37.7	17.7	-0.45
Water	0.00064	3.27	78.5	0.9	-0.15

TABLE	XIII.	Relative	RATES	OF	OXYGENATION	OF	2-p-ANISYLFU	JRAN
in Vario	ŪS HYDI	ROXYLIC SO	LVENTS	WIT	h Rose Bengal	AS	SENSITIZER ^{80, 8}	31, 36a

^a  $\rho$  values for each solvent were determined separately with the *p*-CH₃O-, *p*-CH₃-, H-, and *p*-Cl-substituted 2-phenylfurans.

#### Sensitizers

The sensitizer is critical to the success of any sensitized photooxygenation. A good sensitizer should have a large molar absorptivity  $(\epsilon)$ at the pertinent wavelength, a high quantum yield of triplet formation, a long triplet lifetime, a low tendency toward hydrogen abstraction and self-oxidation (reactions that can cause dye bleaching), and a triplet energy not far above the energy of  ${}^{1}\Delta_{a}$  O₂ (22.5 kcal/mol) or  ${}^{1}\Sigma_{a}^{+}$  O₂ (37.5 kcal/mol) to permit efficient energy transfer to oxygen. Fortunately several common dyes meet these requirements adequately. Typical classes of dyes that have been used successfully in photooxygenations are the xanthenes (rose bengal, erythrosin, eosin, fluorescein), the thiazines (methylene blue), the porphyrins (chlorophyll a and b, hematoporphyrin), the porphins (zinc tetraphenylporphin), the acridines (acridine orange*) and various aromatic compounds (pyrene, dinaphthaleneheterocoerdianthrone (1,2,7,8-dibenzoperylene-3,9-quinthiophene, one)).^{31, 160} The solubilities and spectral properties of several efficient sensitizers are summarized in Table XIV.

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^{*} Acridine orange has been reported to abstract hydrogen in many reactions.¹⁶¹

¹⁶⁰ G. Oster, J. S. Bellin, R. W. Kimball, and M. E. Schrader, J. Amer. Chem. Soc., **81**, 5095 (1959).

¹⁶¹ A. Kira, S. Kato, and M. Koizumi, Bull. Chem. Soc. Jap., 39, 1221 (1966).

In general,  $10^{-4}$  to  $10^{-3} M$  solutions of sensitizers such as rose bengal or methylene blue ( $\epsilon > 10^4$ ) are used. At lower concentrations, these sensitizers may not absorb all the available useful light. At higher concentrations, they absorb all the useful light within a short distance from its entrance to the solution and deplete the oxygen in that region of the reaction vessel. The result can be a decrease in the efficiency of the photooxygenation and an increase in side reactions such as sensitizer bleaching. If the sensitizer becomes bleached, more can be added in the form of a concentrated solution. However, since sensitizer bleaching is autocatalytic,^{165, 169} a reaction solution that has been recharged with sensitizer will bleach slightly more rapidly than the original solution.

# Irradiation Apparatus

A versatile and efficient apparatus for sensitized photooxygenations is illustrated in Figure 3. Oxygen is circulated by means of pump  $P_1$  through a glass frit, which is impervious to the solution, and through the solution containing the dissolved sensitizer and olefin. The oxygen circulation rate is adjusted by control valve  $V_2$  and oxygen uptake is measured volumetrically in the buret. An internal liquid coolant is circulated by pump  $P_2$  and the temperature is regulated by that of the outer cooling bath. The internal coolant can be water or a solution chosen to serve also as a light filter.



FIGURE 3.

Cylindrical glass filters may also be placed within the lamp well around the light source, and a stream of cool air can be directed inside the lamp well to provide additional cooling, if desired. Presumably the efficiency of the apparatus could be enhanced with mirrors placed around the outer wall of the solution chamber; alternatively this wall could be silvered.

A simpler irradiation setup illustrated in Figure 4 is sufficient for most synthetic applications. The oxygen can be recirculated and the oxygen uptake measured in a buret, as described before, or the oxygen may simply be vented after passage through the solution and the reaction monitored by spectroscopic or chromatographic examination of aliquots. The light source illustrated in Figure 4 is a high-silica, halogen lamp (650 W-DWY or 1000 W-DXN; see p. 181), which is enclosed by a large Pyrex test tube suspended in the Dewar flask (5 liters). Tap water flowing through the Dewar flask and leaving by a siphon-type exit can keep the reaction solution near or even below room temperature (to help minimize side reactions), and the silvered wall of the Dewar flask greatly increases the efficiency of the photoxygenation, especially if aluminum foil is wrapped over the top of the flask.



FIGURE 4.

If reactants and products are not thermally sensitive, tubular fluorescent bulbs can be used as external light sources and, in such cases, the reaction vessel frequently need not be water-cooled. For example, many sensitized photooxygenations of steroids have been conducted with four 15-watt fluorescent bulbs (standard desk lamps) mounted vertically 2-3 inches from a cylindrical reaction vessel. The temperature of the reaction solution stays around  $40-45^{\circ}$ . A jet of air can be swept continuously over the reaction vessel to lower the temperature by a few degrees, if desired. However, this method, which usually requires longer irradiation times, is not practical for volatile reactants or solvents.

Low-temperature irradiations can be performed with either apparatus. The bath in Figure 3 can contain dry ice-acetone (or other coolant) with methanol (or other solvent) circulated through the inner jacket; or, preferably, the apparatus can be modified so that the bath also contains cold, recirculating methanol (Teflon tubing is preferable to pressure tubing for low temperatures). The immersion apparatus in Fig. 4 can readily be adapted by use of a half-silvered Dewar flask containing dry ice-isopropyl alcohol (or other transparent solvent) with the lamp unit mounted outside the Dewar flask.

#### Light Sources

For maximum efficiency a light source should strongly emit wavelengths corresponding to the  $\lambda_{max}$  of the sensitizer, but more frequently the choice of a lamp is dictated by its availability and ease of handling. The Sylvania or General Electric high-silica or quartz tungsten-halogen lamps, which are illustrated in Figures 4 and 5, are recommended. Both the DWY and the 500-Q are small, inexpensive, readily available photographic lamps, which emit a large amount of visible light (compare 20,000 lumens for the DWY lamp with 1750 lumens for a 100-watt incandescent light bulb; see Table XV) although some ultraviolet and a large amount of infrared light are also emitted. In addition, the rated lifetime of the DWY lamp (about 25 hours) can be increased to hundreds of hours when the lamp is operated at reduced voltages (50-80 volts). The lamp holder, illustrated in Fig. 4, can easily be made with 3-mm Pyrex tubing, copper wire, an electrical plug, and a block of wood.

# Light Filters

Some olefins contain functional groups or produce peroxidic products that are light-sensitive; in these cases, light filters may be useful to exclude undesired wavelengths. An example is the recent successful isolation of the 1,4-epidioxide of 1,4-dimethyl-9,10-diphenylanthracene. Earlier attempts to obtain this isomer had been thwarted by low yields evidently caused by secondary photochemical reactions induced at



FIGURE 5.

wavelengths below 350 nm as shown in the accompanying equation.¹⁷⁰



Solutions and commercially available glasses suitable for selective light filtration are listed by Calvert and Pitts.¹²¹ If necessary, light of any desired wavelength band can be transmitted to the reaction solution by judicious choice of tubular glass filters and/or filter solutions, such as aqueous potassium nitrite or copper sulfate, that circulate within the inner cooling jacket.

# Temperature Effects

Studies of the temperature dependence of sensitized photooxygenations with monoolefins and dienes revealed that the activation energies  $(E_A)$ are very low, usually between 1 and 5 kcal/mol and the entropies of activation ( $\Delta S^{\ddagger}$ ) are negative and high, usually -12 to -18 cal/degree

Substrate	<i>E₄</i> (kcal/mol)	$\Delta S^{\ddagger}$ (cal/degree mol)
2,5-Dimethylfuran	0.1	-14
Cyclopentadiene	0.3	-15
α-Terpinene	0.4	-15
2,3-Dimethyl-2-butene	0.5	-12
1,3-Cyclohexadiene	1.2	-18
2-Methyl-2-butene	1.6	-16
α-Pinene	4.5	-15
$\beta$ -Pinene	5.0	-15

TABLE XVI. ACTIVATION ENERGIES AND ACTIVATION ENTROPIES IN PHOTOSENSITIZED OXYGENATION OF VARIOUS OLEFINS^{89, 171}

mol (see Table XVI).^{89, 171} Therefore sensitized photooxygenations can be conducted at reduced temperatures without a large increase in reaction time. This feature can be useful for olefins sensitive to thermal autoxidations and for reactions whose products are thermally labile.

¹⁷¹ G. O. Schenck and E. Koch, Z. Elektrochem., 64, 170 (1960).

#### EXPERIMENTAL PROCEDURES

A larger number of preparative photochemical procedures is given by Schönberg.⁴ A safety shield is strongly recommended for distillation and manipulation of peroxides of low molecular weight.

2,3-Dimethyl-3-hydroperoxy-1-butene.⁷¹ A solution of 8.4 g (0.1 mol) of 2,3-dimethyl-2-butene and 0.05 g ( $5 \times 10^{-5}$  mol) of rose bengal in 80 ml of methanol was irradiated internally with a high-pressure mercury vapor lamp (Philips HP-125 W) in a water-cooled (18–20°) apparatus similar to the one in Fig. 3 through which oxygen was recirculated. After 50 minutes the oxygen uptake was 2.2 liters (>0.9 equivalent). After removal of the solvent at 12 mm (bath below 25°), distillation of the liquid residue under reduced pressure gave 9.5 g (82%) of 2,3-dimethyl-3-hydroperoxy-1-butene, bp 54–55° (12 mm).

 $3\beta$ -Hydroxy-5a-hydroperoxycholest-6-ene.⁴² A solution of 15 g (0.039 mol) of cholesterol and 0.05 g (8  $\times$  10⁻⁵ mol) of hematoporphyrin in 100 ml of pyridine was irradiated with an Osram HQA-500 lamp in a water-cooled (20°) apparatus through which oxygen was recirculated. After 0.043 mol (*ca.* 1.1 equivalents) of oxygen had been consumed, the solution was concentrated to 20 ml under reduced pressure, diluted with 20 ml of methanol, and heated brieffy with activated charcoal. After filtration of the hot solution, water was added dropwise until the solution became somewhat turbid. When cool, the solution deposited 11.8 g (73%) of  $3\beta$ -hydroxy-5a-hydroperoxycholest-6-ene; mp 148–149°, after recrystallization from aqueous methanol.

 $4\alpha,5$ -Epoxy- $5\alpha$ -cholestan-3-one.^{44, 92} Oxygen was continuously bubbled through a Pyrex tube containing a solution of 0.36 g ( $9.3 \times 10^{-4}$ mol) of cholest-4-en- $3\beta$ -ol and 0.005 g ( $8 \times 10^{-6}$  mol) of hematoporphyrin in 75 ml of pyridine while it was irradiated externally for 72 hours with four 15-watt fluorescent lamps without external cooling. After diethyl ether (200 ml) and activated charcoal were added, the mixture was swirled and filtered, and the filtrate was evaporated (bath temperature  $<40^{\circ}$ ). The residual oil was dissolved in petroleum ether (bp  $30-50^{\circ}$ ) and chromatographed on 18 g of alumina. Elution with benzene-petroleum ether (1:3) gave 0.18 g (49%) of crude  $4\alpha,5$ -epoxy- $5\alpha$ -cholestan-3-one, mp 105–110°; the melting point was raised to 123° after one crystallization from ethanol. Elution with benzene-petroleum ether (2:1-3:1) gave 0.045 g (13%) of cholest-4-en-3-one, mp 78.5–79° after crystallization from acetone-methanol; and elution with benzene-ether (5:1) gave 0.093 g (26%) of the starting allylic alcohol.

 $3\beta$ -Hydroxy-5,8 $\alpha$ -epidioxy-5 $\alpha$ -ergosta-6,22-diene.⁸⁶ A solution of 4 g (0.01 mol) of ergosterol and 0.006 g (1  $\times$  10⁻⁵ mol) of eosin in

1.2 liters of 95% ethanol at 60° was irradiated for 3 hours with a 200-watt Osram Nitralamp in an apparatus through which oxygen was circulated. The solution was concentrated at reduced pressure to a small volume, cooled, and crystals were collected to give 3 g (70%) of crude  $3\beta$ -hydroxy-5,8 $\alpha$ -epidioxy-5 $\alpha$ -ergosta-6,22-diene; mp 178°, after recrystallization from methanol.

2-Hydroperoxy-5-methoxy-2,5-dimethyl-2,5-dihydrofuran.¹⁰¹ A solution of 3.0 g (0.031 mol) of 2,5-dimethylfuran and 0.03 g ( $3 \times 10^{-5}$  mol) of rose bengal in 250 ml of methanol was irradiated internally with a Sylvania 625-watt Sun Gun lamp in a water-cooled immersion apparatus through which oxygen was recirculated. After 5 minutes, 686 ml (>0.9 equivalent) of oxygen had been taken up. The solvent was removed with a rotary evaporator, the residue was washed successively with cold diethyl ether and petroleum ether, and the solid residue was sublimed at 63° (0.15 mm) to give 3.6 g (72%) of 2-hydroperoxy-5-methoxy-2,5-dimethyl-dihydrofuran; mp 75-76°, after recrystallization from diethyl ether.

9,10-Diphenyl-9,10-epidioxy-9,10-dihydroanthracene.¹⁷² A solution of 9,10-diphenylanthracene in methylene chloride was passed through a column containing successive layers of neutral, basic, and neutral alumina. Methylene blue (25 mg,  $8 \times 10^{-5}$  mol) and 3.3 g (0.01 mol) of the purified 9,10-diphenylanthracene were dissolved in 125 ml of methylene chloride and the solution was irradiated at 15° with a 650-watt DWY lamp in a photooxygenation apparatus similar to that in Fig. 4 and through which oxygen was circulated. Within 30 minutes the dye became noticeably bleached, and the solution was poured through a similar alumina column, which was washed with additional methylene chloride. The pale-yellow eluent was concentrated to one-half volume at room temperature under reduced pressure, and an equal volume of ligroin was added. This solvent replacement process was repeated about three times and afforded 3.2 g (94%) of 9,10-diphenyl-9,10-epidioxy-9,10-dihydroanthracene; mp 180-181° dec.

This epidioxide has been obtained by sunlight irradiation of 9,10diphenylanthracene in carbon disulfide.⁴ However, for convenience, reliability, and high purity of product the procedure described above is recommended.

1,4-Dimethoxy-1,4-epidioxy-1,4-dihydro-9,10-diphenylanthracene.¹⁷³ A solution containing 2.0 g ( $5 \times 10^{-3}$  mol) of 1,4-dimethoxy-9,10-diphenylanthracene in 1 liter of diethyl ether was irradiated at

¹⁷² K. Cohen and A. Nickon, unpublished results.

¹⁷³ C. Dufraisse, J. Rigaudy, J.-J. Basselier, and N. K. Cuong, C.R. Acad. Sci., **260**, 5031 (1965).

 $-50^{\circ}$  with a Philips SP-500 mercury vapor lamp while oxygen was circulated. The product, which precipitated, was collected and washed with ether; weight 2.0 g (94 %), mp 180–185° dec.

1,1,2,2-Tetramethoxy-1,2-dioxetane.^{66,174} A photooxygenation apparatus containing a solution of 0.13 ml of 1,1,2,2-tetramethoxyethylene and ca. 0.4 mg (ca.  $6 \times 10^{-7}$  mol) of dinaphthalenethiophene in 4 ml of dry diethyl ether was placed in a half-silvered Dewar flask containing dry ice-isopropyl alcohol at  $-78^{\circ}$ . The solution was irradiated externally with a 650-watt DWY lamp for 1 hour. After evaporation of the solvent at  $-78^{\circ}$  under reduced pressure, evaporative distillation of the residue at 25° yielded 94% of crude 1,1,2,2-tetramethoxy-1,2-dioxetane, mp -8 to  $-9^{\circ}$  after low-temperature recrystallization from pentaneether. The dioxetane decomposes slowly at room temperature ( $t_{14} = 102$ minutes at 56°) to dimethyl carbonate (100%).

# TABULAR SURVEY¹⁷⁵

The following tables cover the literature through about March 1971, and references to pertinent developments in 1972 and early 1973 were added "in proof" to the text and tables wherever possible. The tables are restricted to compounds containing one or more carbon-carbon double bonds. Olefins are classified according to their greatest number of conjugated double bonds and subclassified by the number of fused rings. Within each subclassification, compounds are listed in order of increasing number of carbon atoms. In the column "Reaction Conditions and Reactivity  $(\beta)$ " are listed the solvent, sensitizer, solution temperature, light filters, reducing agents (when the allylic hydroperoxides were reduced) and, where available, the  $\beta$  values. The  $\beta$  value is the ratio of the rate of singlet oxygen decay to reaction of singlet oxygen with olefinic acceptor and, for a given solvent, provides an inverse measure of the reactivity of the olefin. If equipment is not available to simulate a reported set of conditions, the irradiation setup and experimental details for any other olefin of comparable reactivity (*i.e.*, similar  $\beta$  value) may be approximately applicable. The terms "solvent" and "sensitizer" designate experiments in which these agents were used but were not identified. The lamps and irradiation times described in the references are not tabulated, because photooxygenation efficiency depends markedly upon the geometry of the

¹⁷⁴ S. Mazur, Ph.D. Dissertation, University of California at Los Angeles, 1971.

 $^{^{175}}$  One of the authors (A. N.) is grateful to the National Institutes of Health (Grant No. GM-09693) for support of his work on photosensitized oxygenations including the unpublished research cited in refs. 70, 172, and 203. We are grateful to Stephen Funk for assistance and numerous helpful suggestions.

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irradiation apparatus and the efficiency of the light sources. Many lamps used and described were older models and inefficient compared to newer lamps and, therefore, reported photooxygenation conditions might be difficult to reproduce. The primary photoproducts and their relative yields are listed. Experiments in which the listed hydroperoxides were reduced to alcohols before assay or isolation are identified by reference to footnote b, and the yields and product distributions refer to the corresponding alcohols. The absence of specific stereochemical notations (e.g., heavy and dotted lines) for structures where geometric isomerism is possible implies that the stereochemistry was not determined. Primary photoproducts that presumably were formed but were unstable at room temperature are shown in brackets, and the secondary products are listed also. The column "Total Yield(s)" normally reflects the total yield of isolated products based on starting olefin, but in some cases refers to the extent of conversion as measured by oxygen uptake.

The abbreviation NR (no reaction) indicates that no singlet oxygen products were obtained *under the conditions of that particular experiment*. In these cases the reader should carefully evaluate the experimental details, because longer irradiation periods with more efficient lamps might produce significant conversion.

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Compound	β (M, ROH)	k _r a	Compound	β (M, MeOH)	$k_r^a$	Compound	β (M, CHCl ₃ )	$k_r^a$
$\bigcirc$	0.03	1.0	CHO CHO	0.6	0.05	Cl	0.024	1.2
$\sum_{i=1}^{n}$	0.01	3	$\langle 0 \rangle$	0.005	6		0.013	2.3
$\sum_{i=1}^{i}$	0.003	10	CH3 CH3	0.001	30	CH3	0.0012	25

TABLE V. ELECTRONIC EFFECTS ON THE REACTIVITY OF 1,3-CYCLOHEXADIENE,^{2, 39, 89} FURAN,^{88, 89} and Anthracene⁷⁷

^a All reactivities  $(k_{\tau})$  are relative to 1,3-cyclohexadiene taken as 1.0.

TABLE XIV. PROPERTIES OF SOME EFFICIENT SENSITIZERS

	Solubility ^a					Triplet
Sensitizer	CH3OH	C ₆ H ₆	$\lambda_{\max}$ (nm)	E	$\Phi$ ¹ O ₂	(kcal/mol)
Chlorophyll a ^{1, 162–164}	 +	+	666 (CH ₃ OH)	66,600	≥0.77	32
Methylene blue ^{31, 165, 166}	+	~~	669 $(n - C_4 H_0 OH)$	60,000	$\geq 0.23$	34 ^b
Zinc tetraphenylporphin ¹⁶⁷		+	425 $(C_{6}H_{6})$	630,000		
Hematoporphyrin ^{31, 166, 168}	+	+	405 (0.5 N HCl)	400,000		37°
Rose bengal ^{1, 31}	+		555 (CH ₃ OH)	104,000	0.76	39.5
Erythrosin ¹	+		530 (CH ₃ OH)	94,000	0.62	42.0

^a Plus (+) and minus (-) are relative to about  $10^{-4}$  M.

^b These values are probably 2-5 kcal/mol too high.

¹⁶² G. R. Seely and R. G. Jensen, Spectrochim. Acta, 21, 1835 (1965).

¹⁶³ G. R. Seely and R. G. Jensen, Spectrochim. Acta, 21, 1835 (1965).
 ¹⁶³ R. Livingston and K. E. Owens, J. Amer. Chem. Soc., 78, 3301 (1956).
 ¹⁶⁴ J. Franck, J. L. Rosenberg, and C. Weiss, Jr., in Luminescence of Organic and Inorganic Materials, H. P. Kalimann and G. M. Spruch, Eds., John Wiley & Sons, Inc., New York,

1962, p. 11. 165 N. Kosui, K. Uchida, and M. Koizumi, Bull. Chem. Soc. Jap., 38, 1958 (1965).

168 D. R. Kearns, R. A. Hollins, A. U. Khan, R. W. Chambers, and P. Radlick, J. Amer. Chem. Soc., 89, 5455 (1967).

187 G. R. Seely and M. Calvin, J. Chem. Phys., 23, 1068 (1955).

168 M. Legrand, Bull. Soc. Chim. Biol., 37, 133 (1955).

	Watts	Initial 220–32 Lumens nm	Spectral Energy Distribution (watts)						Total Visible Energy (watts)	
Lamp			220–320 nm	320360 nm	360–400 nm	400–500 nm	500-600 nm	600-700 nm	Per Lamp	Per Watt Input
Sodium vapor (LU-400)	400	42,000				10.30	55.30	39.60	105.20	0.263
Fluorescent (F-40, white)	40	3,250	0.058	0.016	0.227	2.10	4.54	2.30	8.95	0.224
Tungsten-halogen (DWY)	650	20,000	0.433	0.981	1.795	12.60	25.72	36.88	75.20	0.116
Medium pressure		,								
mercury (IJA-2)	250	6,800	17.55	1.260	7.530	6.640	10.60	0.470	17.71	0.071
Incandescent (100A)	100	1,750	0.008	0.039	0.103	0.843	2.24	3.86	6.94	0.069
Sunlamp (RS)	275	2,500	1.404	0.370	2.70	2.44	4.16	0.43	7.03	0.026

TABLE XV. Spectral Properties of Typical General Electric Lamps

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Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₄ H ₈	(CH ₃ ) ₂ C=CH ₂	$CH_3OH/methylene$ blue; 15° ( $\beta$ , 10°)	CH ₃ C(=CH ₂ )CH ₂ OOH		45
		$CH_3OH/rose bengal (\beta, 1.6)$	<b>3</b> )		89
	$trans-CH_3CH=CHCH_3$	$CH_{3}OH/rose$ bengal; $20^{\circ}$ ( $\beta$ , 12)	CH ₂ =CHCH(OOH)CH ₃		89
$C_5H_8O_2$	$trans-CH_3CH=CHCO_2CH_3$	1:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/ rose bengal; 20°		NR	39
C5H10	(CH ₃ ) ₂ C=CHCH ₃	1:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/ rose bengal; 20° ( $\beta$ , 0.055)	$(CH_3)_2C(OOH)CH=CH_2, CH_3C(=CH_2)CH(OOH)CH_3A (53) B (47)$	64	5, 39
		$CH_3OH/rose$ bengal A ( $\beta$ , 0.11)	, В		2
С <b>₆H₁₀O</b>	(CH ₃ ) ₂ C=CHCOCH ₃	1:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rose bengal; 20°		NR	39
C ₆ H ₁₂	$(CH_3)_2C=C(CH_3)_2$	$CH_3OH/rose$ bengal; $-25^\circ$ ; $P(C_eH_5)_2$ ( $\beta$ , 0.003)	$CH_3C(=CH_2)C(CH_3)_2OOH$	82°	1, 94
		$CH_3OH/rose$ bengal; NaBH ₄ ( $\beta$ , 0.003)	,,	86 ^b	1, 2

TABLE	XVII.	ACYCLIC	MONOOLEFINS

			6:4 $CH_3OH:H_2O/$ methylene blue; 1 <i>M</i> NeN-	$\begin{array}{lll} {\rm CH_3C(=CH_2)C(CH_3)_2OOH} & (3), \\ {\rm (CH_3)_2CN_3C(CH_3)_2OOH} & (97) \end{array}$		175
		$\mathit{trans}\text{-}\mathrm{CH}_{3}\mathrm{CH}{=}\mathrm{CHC}_{3}\mathrm{H}_{7}\text{-}n$	$CH_3OH/rose bengal;$ $15^{\circ}$ ( $\beta$ , 1.8 ^a )	_	_	<b>4</b> 5
		$(CH_3)_2C=CHC_2H_5$	1:1 $CH_3OH$ : ( $CH_3$ ) ₂ $CHOH/rose$ bengal; 20° ( $\beta$ , 0.18)	$(CH_3)_2C(OOH)CH=CHCH_3 A$ (55), $CH_3C(=CH_2)CH(OOH)C_2H_5 B$ (45)	89	5, 39
			$CH_3OH/rose$ bengal ( $\beta$ , 0.16)	A (51), B (49)		2, 17
		$cis\text{-}\mathrm{CH}_{3}\mathrm{CH}\text{=}\mathrm{C}(\mathrm{CH}_{3})\mathrm{C}_{2}\mathrm{H}_{5}$	$CH_3OH/rose$ bengal ( $\beta$ , 0.10)		-	2
		$trans\text{-}\mathrm{CH}_{3}\mathrm{CH}{=}\mathrm{C(CH}_{3})\mathrm{C}_{2}\mathrm{H}_{5}$	$CH_3OH/rose bengal$ ( $\beta$ , 0.07)			2
189		cis-CH ₃ CH=CHCH(CH ₃ ) ₂	$CH_3OH/rose bengal$ ( $\beta$ , 10)	$CH_2 = CHCH(OOH)CH(CH_3)_2  (96),$ $CH_2CH(OOH)CH = C(CH_2)_2  (4)$		2
		$trans-CH_3CH=CHCH(CH_3)_2$	$CH_3OH/rose bengal$ ( $\beta$ , 57)	$CH_2$ —CHCH(OOH)CH(CH_3) ₂ , CH_CH(OOH)CH=C(CH_3) ₂ ,		2
	C <b>7H19O</b>	(CH ₂ ) ₂ C=CHCH ₂ COCH ₂	Pyridine/rose bengal	(CH ₂ ) ₂ C(OOH)CH=CHCOCH	99°	176
	C ₇ H ₁₄	(CH ₃ ) ₂ C=CHCH(CH ₃ ) ₂	1:1 $CH_3OH$ : ( $CH_3$ ) ₂ $CHOH$ /rose bengal; 20° ( $\beta$ , 1.3)	$CH_{3}C(=CH_{2})CH(OOH)CH(CH_{3})_{2}$ (95), ( $CH_{3})_{2}C(OOH)CH=C(CH_{3})_{2}$ (5)	78	5, 39
	C ₈ H ₈	C ₆ H ₅ CH=CH ₂	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	C ₆ H ₅ CHO, CH ₂ O	78	73
	C ₈ H ₁₆	$(CH_3)_2C=C(CH_3)CH(CH_3)_2$	$CH_{3}OH/rose$ bengal	$\begin{array}{ll} (\mathrm{CH}_3)_2\mathrm{C}(\mathrm{OOH})\mathrm{C}(=\mathrm{CH}_2)\mathrm{CH}(\mathrm{CH}_3)_2 & (40),\\ \mathrm{CH}_3\mathrm{C}(=\mathrm{CH}_2)\mathrm{CCH}_3(\mathrm{OOH})\mathrm{CH}(\mathrm{CH}_3)_2 & (60) \end{array}$		2, 17

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₃ H ₁₆ (contd.	(CH ₃ ) ₂ C=CHC(CH ₃ ) ₃ .)	1:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rose bengal; 20° ( $\beta$ , 4.2)	$CH_3C (= CH_2)CH (OOH)C (CH_3)_3$	75	5, 39
	С ₉ Н ₁₀	$\mathrm{C_6H_5(CH_3)C}{=}\mathrm{CH_2}$	$CH_2Cl_2/methylene$ blue	C ₆ H ₅ COCH ₃ , CH ₂ O	—	69
		trans-C _e H ₅ CH=CHCH ₂	<u> </u>	C.H.CHO, CH.CHO	—	1, 5
190	С ₉ Н ₁₀ О	<i>p</i> -CH ₃ OC ₆ H ₄ CH=CH ₂	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	<i>р</i> [•] CH ₃ OC ₆ H ₄ CHO, CH ₂ O	74	73
Ĵ	C ₉ H ₁₈	CH ₂ =CHC ₇ H ₁₅ -n	$CH_3OH/methylene$ blue; $15^{\circ}$ $(\beta, 165^{a})$	$CH_2(OOH)CH=CHC_6H_{13}$ .n		45
	$\mathrm{C_{10}H_{10}O_2}$	$trans - (3, 4 - CH_2O_2C_6H_3) - CH = CHCH_2$	_	3,4-CH ₂ O ₂ C ₆ H ₃ CHO, CH ₃ CHO		5, 94
	C ₁₀ H ₁₂ O	$trans-C_6H_5CH = CHOC_2H_5$	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	C ₆ H ₅ CHO, C ₂ H ₅ OCHO	80	73
		$trans \cdot (p \cdot CH_3OC_6H_4) \cdot CH = CHCH_2$	<u> </u>	<i>p</i> -CH ₃ OC ₆ H ₄ CHO, CH ₃ CHO		1,5
	C ₁₀ H ₁₆	$(CH_3)_2C=CH(CH_2)_2C(=CH_2)-CH=CH_2$	Neat/chlorophyll; $20-25^{\circ}$	$\begin{array}{c} (\mathrm{CH}_3)_2\mathrm{C}(\mathrm{OOH})\mathrm{CH}=\mathrm{CHCH}_2\mathrm{C}(=\mathrm{CH}_2)\mathrm{CH}=\mathrm{CH}_2  (60),\\ \mathrm{CH}_3\mathrm{C}(=\mathrm{CH}_2)\mathrm{CH}(\mathrm{OOH})\mathrm{CH}_2\mathrm{CH}_2\mathrm{C}(=\mathrm{CH}_2)\mathrm{CH}=\mathrm{CH}_2 \\ \end{array} \tag{40}$	96 ^e	177
	C ₁₀ H ₁₈ O	$\begin{array}{c} (\mathrm{CH_3})_2\mathrm{C}{=}\mathrm{CH}(\mathrm{CH_2})_2\cdot\\ \mathrm{C}(\mathrm{CH_3})(\mathrm{OH})\mathrm{CH}{=}\mathrm{CH_2} \end{array}$	1:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rose	$(CH_{3})_{2}C(OOH)CH=CHCH_{2}C(CH_{3})(OH)CH=CH_{2}$ (60)	 ,	5, 39

# TABLE XVII. ACYCLIC MONOOLEFINS (Continued)

			bengal; $20^{\circ}$	$CH_3C(=CH_2)CH(OOH)(CH_2)_2CCH_3(OH)CH=CH_2$ (40)		
	$\mathrm{C_{10}H_{20}}$	$(CH_3)_2C=CH(CH_2)_2CH(CH_3)-C_2H_5$	(p, 0.10) 1:1 CH ₃ OH: (CH ₃ ) ₂ - CHOH/rose bengal; 20° ( $\beta$ , 0.18)	$(CH_3)_2C(OOH)CH=CHCH_2CH(CH_3)C_2H_5  (60), \\ CH_3C(=CH_2)CH(OOH)(CH_2)_2CH(CH_3)C_2H_5  (40)$		39
			Neat/chlorophyll		82	177
	$C_{10}H_{20}O$	$(CH_3)_2C=CH(CH_2)_2CH(CH_3)-CH_2CH_2OH$	$CH_3OH/rose$ bengal ( $\beta$ , 0.16)	$(CH_3)_2C(OOH)CH=CHCH_2CH(CH_3)CH_2CH_2OH $ (63),	95 ^b	5, 178
				$CH_{3}C(=CH_{2})CH(OOH)(CH_{2})_{2}CHCH_{3}CH_{2}CH_{2}OH$ (37)		
	C ₁₁ H ₁₃ Cl	$m \cdot \mathrm{ClC}_6\mathrm{H}_4(\mathrm{CH}_3)\mathrm{C} = \mathrm{C}(\mathrm{CH}_3)_2$	2:98 Pyridine: CH ₃ OH/rose bengal; 0–3°	$\begin{array}{l} m\text{-}\mathrm{ClC}_{6}\mathrm{H}_{4}\mathrm{C}(=\mathrm{CH}_{2})\mathrm{C}(\mathrm{CH}_{3})_{2}\mathrm{OOH}  (72),\\ m\text{-}\mathrm{ClC}_{5}\mathrm{H}_{4}(\mathrm{CH}_{3})\mathrm{C}(\mathrm{OOH})\mathrm{C}(=\mathrm{CH}_{2})\mathrm{CH}_{3}  (28) \end{array}$	b	2, 17
191		p-ClC ₆ H ₄ (CH ₃ )C=C(CH ₃ ) ₂	$(\beta, 0.07)$ 2:98 Pyridine: CH ₃ OH/rose	p-ClC ₆ H ₄ C(=CH ₂ )C(CH ₃ ) ₂ OOH (73),	Ъ	2, 17
			$(\beta, 0.06)$	$p \cdot \operatorname{ClC}_6 \operatorname{H}_4(\operatorname{CH}_3) \subset (\operatorname{UOH}) \subset (\operatorname{=CH}_2) \subset \operatorname{CH}_3  (27)$		
	C ₁₁ H ₁₄	$C_6H_5(CH_3)C=C(CH_3)_2$	2:98 Pyridine: CH ₃ OH/rose	$\begin{array}{ll} \mathrm{C_6H_5C(=CH_2)C(CH_3)_2OOH} & (71), \\ \mathrm{C_6H_5(CH_3)C(OOH)C(=CH_2)CH_3} & (29) \end{array}$	78 ¹	2, 17
		$\rm (CH_3)_2C{=}CHCH_2C_6H_5$	bengal $(\beta, 0.04)$ 1:1 CH ₃ OH: (CH ₃ ) ₆ CHOH/	$(CH_3)_2C(OOH)CH=CHC_6H_5$ (59),	95	5, 39
			rose bengal; $20^{\circ}$ ( $\beta$ , 0.13)	$CH_3C(=CH_2)CH(OOH)CH_2C_6H_5$ (41)		
	C ₁₁ H ₁₅ N	$p \cdot (CH_3)_2 NC_6 H_4 (CH_3) C = CH_2$	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	p-(CH ₃ ) ₂ NC ₆ H ₄ COCH ₃ , CH ₂ O ^d	67	73

Fo	rmula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₁₉	H ₁₉ N	m-NCC ₆ H ₄ (CH ₃ )C=C(CH ₃ ) ₂	2:98 Pyridine:	m-NCC ₆ H ₄ C(=CH ₂ )C(CH ₃ ) ₂ OOH (74),	b	2, 17
			CH ₃ OH/rose bengal; 0-3° (β. 0.12)	m-NCC ₆ H ₄ (CH ₃ )C(OOH)C(=CH ₂ )CH ₃ (26)		
			2:98 Pyridine: CH_OH/rose	$p-NCC_{6}H_{4}C(=CH_{2})C(CH_{3})_{2}OOH$ (74),	Ъ	2, 17
			bengal; $0-3^{\circ}$ ( $\beta$ , 0.16)	p·NCC ₆ H ₄ (CH ₃ )C(OOH)C(=CH ₂ )CH ₃ (26)		
=		OCH3				
C ₁₂	H ₁₄ O ₃	CH=CHCH ₃	CH ₃ OH/rose bengal; 20°	2-CH ₃ CO-3-CH ₃ OC ₆ H ₃ CHO, CH ₃ CHO		1, 5, 89
C ₁₂	H ₁₆	m-CH ₃ C ₈ H ₄ (CH ₃ )C=C(CH ₃ ) ₂	(p, 0.01) 2:98 Pyridine: CH_OH/rose	m-CH ₃ C ₉ H ₄ C(=CH ₂ )C(CH ₃ ) ₂ OOH (73),	8	2, 17
			bengal; $0-3^{\circ}$ ( $\beta$ , 0.04)	m-CH ₃ C ₆ H ₄ (CH ₃ )C(OOH)C(=CH ₂ )CH ₃ (27)		
		$p\text{-}\mathrm{CH_3C_6H_4(CH_3)C=C(CH_3)_2}$	2:98 Pyridine: CH_OH/rose	p-CH ₃ C ₆ H ₄ C(=CH ₂ )C(CH ₃ ) ₂ OOH (73),	ь	2, 17
			bengal; $0-3^{\circ}$ ( $\beta$ , $0.03$ )	$p \cdot \mathrm{CH}_3\mathrm{C}_6\mathrm{H}_4(\mathrm{CH}_3)\mathrm{C}(\mathrm{OOH})\mathrm{C}(=\mathrm{CH}_2)\mathrm{CH}_3$ (27)		
C ₁₂	H ₁₆ O	m-CH ₃ OC ₆ H ₄ (CH ₃ )C=C(CH ₃ ) ₂	2:98 Pyridine: CH_OH/rose	$m - CH_3OC_6H_4C (=CH_2)C (CH_3)_2OOH$ (71),	Ъ	2, 17
			bengal; $0-3^{\circ}$ ( $\beta$ , 0.04)	$m \cdot CH_3OC_6H_4(CH_3)C(OOH)C(=CH_2)CH_3$ (29)		

TABLE	XVII.	ACYCLIC	MONOOLEFINS	(Continued	)
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		p-CH ₃ OC ₆ H ₄ (CH ₃ )C=C(CH ₃ ) ₂	2:98 Pyridine: $CH_3OH/rose$ bengal; 0-3° ( $\beta$ 0.02)	p-CH ₃ OC ₆ H ₄ =C(CH ₂ )C(CH ₃ ) ₂ OOH (74), p-CH ₃ OC ₆ H ₄ (CH ₃ )C(OOH)C(=CH ₂ )CH ₃ (26)	Ъ	2, 17
	C ₁₃ H ₁₉ N	p-(CH ₃ ) ₂ NC ₆ H ₄ - (CH ₃ )C=C(CH ₃ ) ₂	(p, 0.02) 2:98 Pyridine: CH ₃ OH/rose bengal; 0-3° ( <i>β</i> 0.006 ^g )	<i>p</i> -(CH ₃ ) ₂ NC ₆ H ₄ C(=CH ₂ )C(CH ₃ ) ₂ OOH	Ъ	2, 17
	C ₁₄ H ₁₂	$(C_6H_6)_2C = CH_2$	$CHCl_3/methylene$ blue; $K_2CrO_4$ filter	$(C_{6}H_{5})_{2}CO, CH_{2}O^{d}$	79	73
		cis-C ₆ H ₅ CH=CHC ₆ H ₅	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	C ₆ H ₅ CHO	77	73
16		$\mathit{trans}\text{-}\mathrm{C}_{6}\mathrm{H}_{5}\mathrm{CH}{=}\mathrm{CHC}_{6}\mathrm{H}_{5}$	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	C ₆ H ₅ CHO	88	73
33	C ₁₅ H ₁₄	$(C_{6}H_{5})_{2}C=CHCH_{3}$ trans- $C_{6}H_{5}CH=C(CH_{3})C_{6}H_{5}$	 CHCl ₃ /methylene blue	$\begin{array}{l} (\mathrm{C_6H_5})_2\mathrm{CO}, \ \mathrm{CH_3CHO} \\ \mathrm{C_6H_5CHO} + \mathrm{C_6H_5COCH_3}  (10), \\ \mathrm{C_6H_5C(=CH_2)CH(C_6H_5)OOH}  (90) \end{array}$	. —	1 69
	C ₁₅ H ₂₄ (				_	180

	Formula Structure	Reaction Conditions and Reactivity. $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
_	C ₁₆ H ₁₆ O ₂	Cyclohexane/no sensitizer	О ООН	10	179
194	$C_{18}H_{22}N_2 [p-(CH_3)_2NC_6H_4]_2C=CH_2$	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	$[p \cdot (CH_3)_2 NC_6 H_4]_2 CO, CH_2 O^d$ $CO_2 CH_3$	71	73
	$C_{19}H_{32}O_2$ $C_2H_5$ $(CH_2)_7$	Neat/chlorophyll; 18°	$\begin{array}{c} C_2H_5 \\ \end{array} \\ HOO \end{array} $ (17),	36 ^ħ	181
			$\overbrace{OOH}^{CO_2CH_3}$		

TABLE XVII. ACYCLIC MONOOLEFINS (Continued)





TABLE XVII. ACYCLIC MONOOLEFINS (Continued)

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
			$n \cdot C_5 H_{11}$ $(CH_2)_3 CO_2 CH_3$ , HOO		
			$n \cdot C_5 H_{11}$ $(CH_2)_3 CO_2 CH_3$ , OOH		
			$\stackrel{n-\mathrm{C}_{5}\mathrm{H}_{\mathrm{II}}}{\longrightarrow} \stackrel{(\mathrm{CH}_{2})_{2}\mathrm{CO}_{2}\mathrm{CH}_{3}}{\longrightarrow}$		
			(The yield of each product was 12%.)		
$C_{22}H_{20}O_{2}$	$(p-CH_3OC_6H_4)_2C=CHC_6H_5$	CHCl ₂ /methylene blue; K ₂ CrO ₄ filter	$(p-CH_3OC_6H_4)_2CO$ (65), $C_6H_5CHO$ (62)	ĩ	73
$\mathrm{C}_{28}\mathrm{H}_{20}$	$(C_{6}H_{5})_{2}C=C(C_{6}H_{5})_{2}$	CHCl ₃ /methylene blue; K ₂ CrO ₄ filter	$(C_{g}H_{5})_{2}CO$	74	73

TABLE XVII. ACYCLIC MONOOLEFINS (Continued)



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	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₅ H ₈	$\bigcirc$	CH ₃ OH/methylene blue; 15° (β, 1.0 ^α )	ООН		45
			(β, 1.6)	"		1
	$C_{g}H_{g}$	$\bigcirc$		C ₆ H ₆ , H ₂ O ₂	<b></b>	1,184
200	C <b>₆H₁₀</b>	$\bigcirc$	$CH_{3}OH/rose$ bengal ( $\beta$ , 55) $CH_{3}OH/methylene$ blue; 15° ( $\beta$ , 16 ^a )	00Н		2 45
			CH ₃ OH/rose bengal; 20°		NR	48
		$\diamond$	$CH_3OH/rose$ bengal ( $\beta$ , 0.11 ^j )	(53), OOH (4), OOH (4),	OOH (43)	185
			$C_2H_5OH/methylene$ blue ( $\beta$ , 0.05)	_	95 ¹	1,50, 94
	C7H12	$\bigcirc$	$CH_3OH/rose bengal;$ 20° ( $\beta$ , 0.7)	ООН, ООН, ООН, ООН, С (44)	, , , , , , , , , , , , , , , , , , ,	2, 185

TABLE	XVIII.	MONOCYCLIC	MONOOLEFINS
TUDUU	~~ Y III.	MUNOUYCLIC	MONOOPELUP

		$(CH_3)_2CHOH/$ methylene blue $(\beta, 1.2)$	A (45), B (15), C (40)		50, 94 186
	$\bigcirc$	$CH_3OH/methylene$ blue; 15° ( $\beta$ , 25 ^a )			45
		CH ₃ OH/rose bengal; 20°		NR	48
$C_{g}H_{14}$	Č	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH; 18° ( $\beta$ , 0.03) CH OH/methylene	OOH (12), (12), (88),		1, 39, 94
		blue; $15^{\circ}$ ( $\beta$ , 0.006 ⁴ )			45
201		2:3 $H_2O:CH_3OH/$ fluorescein; 1 $M$ NaN ₃ ; Na ₂ SO ₃	Соон  N ₃	60 ⁵	187
	$\bigcirc$	$CH_3OH/rose$ bengal ( $\beta$ , 0.07 ^{<i>j</i>} )	(48), (48), (4),	_	185
			(48)		
		CH ₃ OH/rose bengal; 20°; Na ₂ SO ₃	CH ₂ OOH	170	48

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products and Relative Yield(s) (%)	Total Yield (%)	Refs.
	С ₉ Н ₁₆	$\bigcirc$	CH ₃ OH/rose bengal (β, 0.5 ^j )	ООН (31), ООН ⁽²⁷⁾ ,	_	185
				(42) 00H		
202	C ₁₀ H ₁₄ O ₄	CO ₂ H	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rose bengal; 18° ( $\beta$ , 0.04)	HOO $(O_2H)$ , HOO $(O_2H)$ $(O_2H)$	53	39
		CO ₂ H	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rose bengal; 18° ( $\beta$ , 0.06)	HOO $(O_2H)$ , HOO $(O_2H)$	_	39
	C ₁₀ H ₁₆	$\langle \rangle$	CH ₃ OH/rose bengal; 22 or -40°; Na ₂ SO ₃	$\begin{array}{c} & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$	86 ⁸	188
		¥	-40°; Na ₂ SO ₃	$\begin{array}{c c} (+) & (+) & (+) \\ A (34) & B (10) & C (20) \end{array}$		













Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₁₀ H ₁₈ (contd.)	$\sum_{k}$		CH200H		48, 190
° C ₁₂ H ₁₄	C ₆ H ₅	$CH_{3}OH/methylene$ blue ( $\beta$ , 2.5)	·		93
$C_{12}H_{18}O_4$	CO ₂ CH ₃	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/ rose bengal; 18° ( $\beta$ , 0.04)	$+OO \xrightarrow{CO_2CH_3}_{CO_2CH_3} (80), \qquad \qquad$	98	39
	CO ₂ CH ₃	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/ rose bengal; 18° (β, 0.06)	$HOO \xrightarrow{\text{CO}_2\text{CH}_3} (74), \xrightarrow{\text{CO}_2\text{CH}_3} (26)$	95	39
	CO ₂ H CO ₂ H	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/ rose bengal; 18° (β, 0.09)	$\begin{array}{c} \begin{array}{c} & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ $	_	39

TABLE XVIII. MONOCYCLIC MONOOLEFINS (Continued)



Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.


NR

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TABLE XIX. BICYCLIC MONOOLEFINS

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

CH₃OH/rose

bengal;  $40^{\circ}$ ( $\beta$ ,  $\geq 1500$ )

CN

 $\mathrm{C_{10}H_{13}N}$ 

		TABLE XIX. BIC	YCLIC MONOOLEFINS (Continued)		
Formula	1 Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) $(\%)$	Total Yield (%)	Refs.
C ₁₀ H ₁₆		$CH_{3}OH/rose$ bengal ( $\beta$ , 0.17)	(+) ООН		1,198
		CH ₃ OH/rose bengal	-	NR	198
210	(+)	$CH_3OH/rose$ bengal; 18–20° ( $\beta$ , 0.40)	(50), (50), (27),	841	1, 43
	(+)	CH ₃ OH/rose bengal (β, 0.21)	HOO. $(+)$ (18), HOO. $(+)$ (82)		1,198
		CH ₃ OH/rose bengal (β, 2.0)	$(25), \qquad (11)$		1, 198
		(CH ₃ ) ₂ CHOH/rose bengal; 20°; $P(C_{g}H_{5})_{3}$ ( $\beta$ , 0.15)		84 ^b	71
21		$(CH_3)_2CHOH/$ methylene blue $(\beta, 8.^{\circ})$	OOH (−) (≤ 99), (≤ 1)	70 ⁷	1, 50

CH₂OOH

30'

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NR

1, 50

89

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TABLE	XIX.	BICYCLIC	MONOOLEFINS	(Continued

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(CH₃)₂CHOH/ methylene blue

 $CH_3OH/rose$ bengal; 20° ( $\beta$ , 1)

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₁₀ H ₁₆ (contd.)	u.		CH₂OOH		
				—	1
		CH ₃ OH/rose bengal; 20°; Na ₂ SO ₃	(78), (78), (1+) (2), (2), (20)	72 ^b	199
C ₁₀ H ₁₆ O	OH	1:1 CH ₃ OH : (CH ₃ ) ₂ CHOH/rose bengal; 20°		NR	39
C ₁₁ H ₁₂		CH ₂ Cl ₂ /methylene blue; 0°; Na ₂ SO ₃	COCH ₃ (32), (32), (68)	95 ⁶	196
C ₁₁ H ₁₈		_	OOH	_	1

TABLE XIX. BICYCLIC MONOOLEFINS (Continued)







TABLE XIX. BICYCLIC MONOOLEFINS (Continued)







	Structure	Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Yield (%)	Refs.
Steroid-4-en	les ^m				
С ₂₇ Н44О		Pyridine/rose bengal; $18-20^{\circ}$ $(\beta, \geq 200)$		NR	204
C ₂₇ H ₄₆	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 34-40°; NaI/C ₂ H ₅ OH (β, 0.83)	HOO' (8) ¹ , HOO' (41) ¹ ,	80p	102, 204
	~~		(33), (2),		
			(9), 0 ⁽⁷⁾		

	C ₂₇ H ₄₆ O	HO.	Pyridine/hemato- porphyrin Pyridine/rose bengal; 18–20° (β, 5)	O ¹ A	A (83) (major),	٢,	0 B (17) ^{c.r} B (trace)	60	92 204
		HO C8H17	Pyridine/hemato- porphyrin or chlorin-e ₆ ; 40°	0	A (82)	×,	B (18) ^{c,r}	90	<b>44, 92</b> <b>44, 92</b>
219			Pyridine/ methylene blue; 40°	Α	(67),	в	(33)		44, 92
			Pyridine/ methylene blue; 40°	Α	(55),	B	(45)		44, 92
			Pyridine/ erythrosin B; 40°	Α	(38),	В	(62)		44, 92
			Pyridine/ sulforhodamine B; 40°	Α	(36),	В	(64)		44, 92
-			Pyridine/acridine orange; 40°	A (	(26),	B	(74)	 	44, 92

TABLE XX	. STEROIDAL	POLYCYCLIC	MONOOLEFINS	(Continued)
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	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₇ H ₄₆ O		Pyridine/eosin or	A (24), B (76)		44, 92
	(conta.)		4:1 Pyridine:	A (3), B (97)		44, 92
220		C ₈ H ₁₇	CH ₃ OH/ribonavin Pyridine/rose bengal; 18-20° $(\beta, 3.2)$	A (major), B (trace)		204
	C ₂₇ H ₄₆ O ₂	но он	Pyridine/rose bengal; 18-20° (β, 92)	0 0 0 0 0 0 H		204
	C ₂₈ H ₄₈ O	CH ₃ O	¹⁷ Pyridine/hemato- porphyrin; 40°		6	92
	$C_{29}H_{48}O$	$^{2} R_{1} \xrightarrow{C_{8}H_{11}}$	Pyridine/ hematoporphyrin; 40°	-	NR	92
	C ₃₁ H ₅₀ O,	$ \begin{array}{c} {}^{R_{2}}\\ A, R_{1} = CH_{3}CO_{2}, R_{2} = \\ A, R_{1} = R_{2} = CH_{3}CO_{2} \end{array} $	H 2 Pyridine/rose bengal; 18-20°		NR	204
	C ₃₄ H ₅₀ O ₅ Steroid-5	$ \begin{array}{l} \mathbf{A},  \mathbf{R_1} = \mathbf{C_6H_5CO_2}, \\ \mathbf{R_2} = \mathbf{H} \\ \textbf{-enes} \end{array} $	$(p, \geq 200)$ Pyridine/hemato- porphyrin; 40°		NR	<b>9</b> 2
221			R ₁ R ₂ R ₂	$ \begin{array}{c} R_5 \\ \hline \\ H \\ H$		
	Formula	Substit R ₁ R ₂ R ₃	R ₄ R ₅	ReactionConditions and $\operatorname{Product}(s)$ andReactivity ( $\beta$ ) $\operatorname{Yield}(s)$ (%)	Total I Relative Yield (%)	Refs.
	$\overline{C_{21}H_{30}O_{3}}$	CH ₃ CO ₂ H H	Н =0	Pyridine/hemato- A porphyrin		42, 105

TABLE XX. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)

	${ m Substituents}^n$					Reaction		Total	
Formula	R	R ₂	R ₃	R4	R ₅	Reactivity $(\beta)$	Yield(s) (%)	(%)	Refs.
$\overline{\mathrm{C}_{21}\mathrm{H}_{32}\mathrm{O}_2}$	но	Н	н	Н	СН ₃ СО	2:3 Pyridine: $C_{g}H_{g}/hemato-$ porphyrin; 20° ( $\beta$ , 1.8)	A	66 ^b	41, 42 105
С ₂₃ Н ₃₂ О2°	CH3CO ⁵	н	н	н	СН ₃ СО	1:9 Pyridine: $C_{6}H_{6}/hemato-$ porphyrin; 20° ( $\beta$ , 4.6)	A°	80 ⁴	41
°C ₂₇ H ₄₂ O ₃	но	н	Н	н	$C_8H_{14}O_2$	Pyridine/hemato- porphyrin	A 	70 ⁶	42, 105
C ₂₇ H ₄₄ O	-0	н	н	Н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 10-15°		—	56

II OCH , OL

III

							Pyridine/rose bengal	II		176
							Pyridine/hemato- porphyrin; dark ( ³ O ₂ )	I and II	-	56
	C ₂₇ H ₄₅ Br	Br	н	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 18-20° $(\beta, 4.6)$	Α	95 ⁷	204
	C ₂₇ H ₄₅ Cl	Cl	н	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 18–20° (β. 4.0)	Α	95 [†]	204
	$\mathrm{C_{27}H_{45}F}$	F	н	н	П	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 18–20° (8, 3.4)	Α	95 ⁷	204
22	$\mathrm{C_{27}H_{46}}$	н	Н	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 18–20° (8, 0.77)	Α	95	204
23	$\mathrm{C_{27}H_{46}O}$	но	Н	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 20° ( <i>B</i> . 0.9)	Α	75 ^b	40, 41, 42
							Pyridine/hemato- porphyrin ( $\beta$ , 1.2)	A (67),	90 ⁴	204
								HO B (33) ¹		
							CHCl ₃ /methylproto- porphyrin; RaNi/H ₂ ; 20°	A (0), B (100) ²	42 ⁸	59

		s	ubstituent	s ⁿ		Reaction		Total	
Formula	R ₁	R ₂	R ₃	R4	R ₅	Conditions and Reactivity $(\beta)$	Yield(s) (%)	(%)	Refs.
C ₂₇ H ₄₆ O (contd.)	Н	н	н	НО	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 40°		25	92
	Н	н	но	н	$C_8H_{17}$	Pyridine/hemato- porphyrin; 40°		20	92
$C_{27}H_{46}O_2$	но	Н	Н	но	C ₈ H ₁₇	Pyridine/hemato- porphyrin $(\beta > 200)$	~ ~ 0	NR	92, 204
	но	ОН	н	Н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 18–20° $(\beta, 21)$	Α	90 ⁴	204
	но	Н	но	Н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 40° (β, 10)	HO 0 (77),	73	92, 204

TABLE AA. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)	TABLE XX.	STEROIDAL	POLYCYCLIC	Monoolefins	(Continued)
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	$C_{27}H_{46}O_3$	но	Η	Н	Н00	C ₈ H ₁₇	Pyridine/hemato- porphyrin; $18-20^{\circ}$ $(\beta, >200)$		NR	204
	$\mathrm{C}_{28}\mathrm{H}_{48}\mathrm{O}$	СН ₃ О	Н	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; $18-20^{\circ}$ $(\beta, 1.5)$	Α	95 [†]	204
	$\mathrm{C_{29}H_{44}O_4}$	но	Н	Н	н	$\mathrm{C_{10}H_{15}O_3}$	Pyridine/hemato- porphyrin	Α		205
	$C_{29}H_{46}O_3$	CH ₃ CO ₂	Н	=0	0	C ₈ H ₁₇	Pyridine/hemato- porphyrin; $18-20^{\circ}$ $(\beta, \geq 200)$		NR	204
	$\mathrm{C}_{29}\mathrm{H}_{48}\mathrm{O}_{2}$	CH ₃ CO ₂	н	н	Н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; $18-20^{\circ}$ $(\beta, 2.4)$	Α	95 ^f	204
225	C ₃₁ H ₄₀ O ₂	$CH_3CO_2$	Н	Н	Η	С ₁₀ Н ₁₉	1:9 Pyridine: $C_6H_6/hemato-$ porphyrin; 20° ( $\beta$ , 4.1)	A	95 ^f	41, 42
	$C_{31}H_{50}O_4$	CH ₃ CO ₂	CH ₃ CO ₂	н	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin $(\beta, \geq 200)$		NR	204
		CH ₃ CO ₂	Н	н	CH ₃ CO ₂	$C_8H_{17}$	Pyridine/hemato- porphyrin ( $\beta$ , $\geq 200$ )	 )	NR	204
		CH ₃ CO ₂	Н	CH ₃ CO ₂	Н	C ₈ H ₁₇	Pyridine/hemato- porphyrin $(\beta, \geq 200)$		NR	92, 204
	$\mathrm{C_{31}H_{52}O_2}$	CH ₃ CO ₂	Н	Н	Н	C ₁₀ H ₂₁	1:9 Pyridine: $C_6H_6/hemato-$ porphyrin; 20° ( $\beta$ , 6.5)	Α	95 ^f	41

	Substituents			ubstituents"			Reaction		Total		
	Formula	R ₁	R ₂	R ₃	R4	R ₅	Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Yield (%)	Refs.	
	С ₃₄ Н ₅₀ О ₃	C ₆ H ₅ CO ₂	н	Н	Н	C ₈ H ₁₇	1:9 Pyridine: $C_{g}H_{g}/hemato-$ porphyrin; 20° ( $\beta$ , 4.0)	A	95 ⁷	41	
							Pyridine/hemato- porphyrin; $18-20^{\circ}$ ( $\beta$ , 2.8)	Α		204	
22		н	н	$C_6H_5CO_2$	н	$C_8H_{17}$	Pyridine/hemato- porphyrin; 40°		NR	92	
6	C ₄₁ H ₅₄ O ₄	C ₅ H ₅ CO ₂	н	$C_8H_5CO_2$	н	C ₈ H ₁₇	Pyridine/hemato- porphyrin; 40°		NR	92	
	Formula 8	Structure			Reacti Condit Reacti	on ions and vity (β)	Product(s) and Relati	ve Yield(s) (%)	Total Yield (%)	Refs.	
	Steroid-5(1	0)-enes	ò	H							
	C ₁₈ H ₂₆ O ₂				Pyridi benį	ne/rose gal	HOO		<b>4</b> 5°	176	
	,	0*~~~			CHCl ₃ (	( ⁸ O ₂ ); 45°	,,		40	206	
	Steroid-6	-enes		С.н.							
	C ₂₇ H ₄₄ O	0	Ŷ		Pyrid por	ine/hemato- phyrin			NR	40	
	$C_{27}H_{46}$			]	Pyrid por	ine/hemato- phyrin	ООН (70)	, (30)	44 ^b	40	
227				п ₁₇ ]	Pyrid por	ine/hem <b>at</b> o- phyrin			NR	40	
	C ₂₇ H ₄₆ O	$R_1 = H$	0. R. =	- H	Pyridi porp	ne/hemato- bhyrin	$R_1$ OOH B, $R_1 = HO$ (90)	$R_1 = HO  (10)$	64 ⁸	40	
	$C_{27}H_{46}O_2$	A, $R_1 = R_2$	$_2 = HO$		Pyridi porj	ine/hemato- phyrin			NR	40	

TABLE XX. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)

Formula Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
Steroid-5-enes (contd.) $C_{39}H_{43}O_3$ A, $R_1 = CH_3CO_2$ , $R_2 = H$ Steroid.7-enes	Pyridine/hemato- porphyrin	B, $R_1 = CH_3CO_2$	30 _p	40
$C_{21}H_{30}O_3$	1:9 Pyridine: $C_6H_6/hemato-$ porphyrin; 20° ( $\beta$ , 6.3)	CH CO	Þ	41
$C_{29}H_{46}O_2$ $R_1$ $R_2$	Pyridine/rose bengal; 18-20°; $P(C_{g}H_{5})_{3}$ ( $\beta$ , 1.9)	R ₁ R ₁ R ₁ R ₁ R ₁ R ₁ R ₁ R ₁	90 ⁵ . p	204
A, $R_1 = CH_3CO_2$ , $R_2 = H$ , $R_3 = C_8H_{17}$ $C_{30}H_{50}O_2$ A, $R_1 = CH_3CO_2$ , $R_2 = H$ , $R_3 = C_8H_{10}$	Pyridine/rose bengal; 18-20°; $P(C_8H_5)_3$ ( $\beta$ , 1.9)	B, $R_1 = CH_3CO_2$ , $R_3 = C_8H_{17}$ B, $R_1 = CH_3CO_2$ , $R_3 = C_9H_{19}$	P	204
$C_{30}H_{50}O_3$ A, $R_1 = CH_3CO_2$ , $R_2 = HO$ , $R_3 = C_9H_{19}$	Pyridine/rose bengal; 18-20°;		NR	204
Steroid-8-enes and Steroid-8(14)-enes R	$\frac{P(\bar{C_{6}H_{5}})_{3}}{(\beta, \geq 200)}$	R		
C ₂₇ H ₄₄ O ₅ HO	Pyridine/rose bengal	но оон	≥95°	176

TABLE XX. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)





TABLE XX. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)









	Formula Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	Steroid-17-enes (contd.)				
236	C ₂₁ H ₃₀ O ₂ HO	Pyridine/hemato- porphyrin	HO HO HO HO	-	209
	HOCH ₂ C ₂₁ H ₃₀ O ₃ HO	Pyridine/hemato- porphyrin	$HOCH_{2}$	≥68	209, 210
	$\begin{array}{c} HCO_2CH_2 \\ HO \\ C_{22}H_{28}O_4 \\ 0 \end{array}$	Pyridine/hemato- porphyrin	$\begin{bmatrix} 0 \\ HC0_2CH_2 \\ H \\ HO \\ HO \\ HO \\ HO \\ HO \\ HO \\ HO$	_	209
	$C_{22}H_{30}O_4$ HO	Pyridine/hemato- porphyrin	$\begin{array}{c} 0 \text{OOH} \\ \text{HCO}_2\text{CH}_2 & \text{H} \\ \text{HO} \\ H$		209
	$CH_{3}CO_{2}CH_{2}$ $HO$ $HO$ $O$	Pyridine/hemato- porphyrin	OOH CH ₃ CO ₂ CH ₂ H HO	_	20 <b>9</b>
237	$C_{23}H_{32}O_4$	Pyridine/hemato- porphyrin	OOH CH ₃ CO ₂ CH ₂ H HO	_	209
	C ₂₃ H ₃₈ O ₂	Pyridine/hemato- porphyrin	-	NR	209
	$\mathbf{A}, \mathbf{R_1} = \mathbf{CH_3}, \mathbf{R_2} = \mathbf{H}$				

TABLE XX. STEROIDAL POLYCYCLIC MONOOLEFINS (Continued)

Formula Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
Steroid-17-enes (contd.)	<u>, , , , , , , , , , , , , , , , , , , </u>			
$C_{23}H_{38}O_2$ (contd.) A, $R_1 = H, R_2 = CH_3$	Pyridine/hemato- porphyrin	$H \xrightarrow{OOH}_{CH_2OH}$ $R_2$ $R_2 = CH_2$	_	209
$C_{27}H_{44}O_4$ HO O HO HO HO HO HO HO	Pyridine/hemato- porphyrin		≥81	209
$ \begin{array}{c} \mathbf{A}, \ \mathbf{R_1} = \mathbf{CH_3} \\ \mathbf{C_{27}H_{44}O_5} \ \mathbf{A}, \ \mathbf{R_1} = \mathbf{HOCH_2} \end{array} $	Pyridine/hemato-	B, $R_1 = CH_3$ (88), C (12) B, $R_1 = HOCH_2$	—	209
$C_{29}H_{46}O_6$ A, $R_1 = CH_3CO_2CH_2$	Pyridine/hemato- porphyrin	$B, R_1 = CH_3CO_2CH_2$	—	209





	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₄ H ₂₀ O ₂		Pyridine/hemato- porphyrin; KI/CH ₃ CO ₂ H	о оон о (70), оон о (30)	70 ⁵	51
	C ₁₅ H ₂₄		_	.OOH	—	1, 211
40			CH ₃ OH/methylene blue; Na ₂ SO ₃	, , , , , , , , , , , , , , , , , , ,	878	212
		()		$\begin{array}{c} A^{-}(11) & D^{-}(20) \\ \hline \\ C^{-}(31) & D^{-}(17)^{l} \end{array}$		
				$\begin{array}{c} CHO & CO_2H \\ \hline \\ \hline \\ E & (9)^t & F & (6)^t \end{array}$		





	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₀ H ₂₄ O ₅	COCH ₃	Pyridine/hemato- porphyrin	_	NR	214b
242	C ₂₀ H ₂₈ O ₂	CO ₂ H	5:95 H ₂ O:C ₂ H ₅ OH/ methylene blue		NR	263
	C ₂₀ H ₃₀ O ₂	CO ₂ H	5:95 H ₂ O:C ₂ H ₅ OH methylene blue	I	NR	263
		CO ₂ H	5:95 H ₂ O:C ₂ H ₅ OH methylene blue	·	NR	263



Reaction<br/>Conditions and<br/>Reactivity ( $\beta$ )Total<br/>Yield<br/>Product(s) and Relative Yield(s) (%)Total<br/>Yield<br/>(%) $V_{29}H_{48}$  $C_{29}H_{48}$  $C_{29}H_{48}$  $C_{29}H_{17}$ <br/>Pyridine/hemato-<br/>porphyrin<br/>( $\beta$ ,  $\geq 200$ )NR 204

TABLE XXI. MISCELLANEOUS POLYCYCLIC MONOOLEFINS (Continued)

CH₃O₂C

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
$C_4H_6O_2$		$(CH_3)_2CO/rose$ bengal; 20° (6, 0, 63)	CHO O-CHO	95	67, 68
C4H8O	C ₂ H ₅ OCH=CH ₂	$(CH_3)_2CO/rose$ bengal ( $\beta$ , 2.4)	C ₂ H ₅ OCHO, CH ₂ O	Low	67
C₅H ₈ O		-	O OOH	_	94
		$C_6H_8$ /sensitizer; 20°			67
		$(CH_3)_2CO/rose$ bengal; 20° $(\beta 1 94)$	A (9) B (91) A (45), B (55)	_	67
		$CH_2Cl_2/sensitizer;$ 20°	A (73), B (27)	—	67
		CH ₃ CN/sensitizer; 20°	A (85), B (15)		67

TABLE XXII. MONOOLEFINS CONTAINING VINYL HETEROATOMS

TABLE XXII. MONOOLEFINS CONTAINING VINYL HETEROATOMS (Continued)

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₆ H ₈ O ₆	HO OH HO OH CH ₂ OH	Pyridine:CH ₃ OH/ rose bengal		44	1, 217
246			$CH_3OH/rose$ bengal; 20° ( $\beta$ , 0.01)			89
	C ₆ H ₁₂ O ₂	<i>сів-</i> С ₂ Н ₅ ОСН=СНОС ₂ Н ₅	$(CD_3)_2CO/rose$ bengal or $CFCl_3/$ tetraphenyl- porphin; -78° $(\beta, 0.004)$	$\begin{bmatrix} 0 - 0 \\ C_2 H_5 0 & OC_2 H_5 \end{bmatrix} \longrightarrow C_2 H_5 OCH 0$	90 C	65, 67, 68
		$trans-C_2H_5OCH=CHOC_2H_5$	$(CD_3)_2CO/rose$ bengal; -78° $(\beta, 0.014)$	$\begin{bmatrix} 0 - 0 \\ C_2 H_5 0 & O \\ & $	95 O	65, 67, 68
	$\mathrm{C_6H_{12}O_4}$	(CH ₃ O) ₂ C=C(OCH ₃ ) ₂	(C ₂ H ₅ ) ₂ O/zinc tetraphenyl- porphin	$\begin{bmatrix} O - O \\ (CH_3O)_2 \\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $	94 O	66



TABLE XXII. MONOOLEFINS CONTAINING VINYL HETEROATOMS (Continued)

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₁₃ H ₁₇ N	C ₆ H ₅	C ₆ H ₆ /zinc tetra- phenylporphin; 2,6-di- <i>t</i> -butyl- phenol	C ₆ H ₅ CHO, OHCN	48	72, 218
C ₁₄ H ₁₀ O	(C ₆ H ₅ ) ₂ C=C=O	CH ₂ Cl ₂ ^g	$(C_6H_5)_2CO, CO_2$		222
C ₁₄ H ₁₇ N	CH ₃	$(CH_3)_2CHOH/eosin$	(CH ₂ ) ₃ CHO	21	221
C ₁₄ H ₁₈ O	p-CH ₃ OC ₆ H ₄ -	Pyridine/hemato- porphyrin	$p \cdot \mathrm{CH_3OC_6H_4CO_2(CH_2)_2C(CH_3)_2CHO}$	70	220
$C_{15}H_{10}O_3$	OH OH	Pyridine/rose bengal; CH ₂ N ₂	$O_2CC_6H_3 (69), (69),$	64	223
	v		$OH \qquad (14), C_6H_5CO_2CH_3 (17) \qquad (14), C_6H_5CO_2CH_3 (17) \qquad (14), C_6H_5CO_2CH_3 (17) \qquad (17)$	)	



TABLE XXII. MONOOLEFINS CONTAINING VINYL HETEROATOMS (Continued)

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products and Rela	ative Yield(s) (%)	<u>.</u>	Tota Yield (%)	l d Refs.
	C ₁₆ H ₁₄ O ₂ (	contd)						
		C ₆ H ₅	$(CH_3)_2CO/r$ bengal; 2 $(\beta, 0.011)$	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array}\\ \end{array}\\ \end{array} \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \end{array} $ $ \end{array} $	,H _δ		90	67, 68
2		$\begin{array}{c} \mathit{trans}\text{-}\mathrm{C_6H_5(OCH_3)}\text{-}\\ \mathrm{C=\!C(OCH_3)C_6H_5} \end{array}$	(CH ₃ ) ₂ CO/ rose ben (β, 0.014	$C_6H_5CO_2$ gal; 20°	CH ₃		96	67, 6 <b>8</b>
5	C ₁₆ H ₁₈ O ₃	(p-CH ₃ OC ₆ H ₄ ) ₂ C=CHO	CH ₃ C ₆ H ₆ /dinag lenethiop 25°; (CH filter; div solution	ohtha- hene; ₃ ) ₂ CO ute CH ₃ O	$C_6H_4OCH_3-p$ OCH ₃ O-O		41	174, 405
			(CH ₃ ) ₂ CO/r bengal; -	OSE $-70^{\circ}$ $CH_{3}O$	COC ₆ H₄OCH₃·p OH			174, 405
	C ₁₉ H ₁₈ O ₇	CH ₃ O CH ₃ O CH ₃ O O O O O O O O O O O	g(OCH3)2·3,4 Pyridine/ros bengal; (	se CH ₂ N ₂ CH ₃ O CH ₃ O	O ₂ CC ₆ H ₃ (OCH ₃ ) ₂ -	3,4 (86),	, <b>9</b> 0	223



TABLE XXII. MONOOLEFINS CONTAINING VINYL HETEROATOMS (Continued)

Formula	R C Structure R	eaction onditions and ceactivity $(\beta)$	Products and Relative Yield(s) (%)	Total Yield (%)	Refs.
$C_{28}H_{22}N_2$	CH ₃ N N CH ₃ a c H ₃ a		O V N CH ₃		224
$\mathrm{C}_{28}\mathrm{H}_{30}\mathrm{N}_{2}$	(CH	3)2CHOH/eosin		21	221

F	ormula	Struc	eture			Reaction Conditions and Reactivity (β)	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.	
C C (0 (0	⁵ H ₆ 6H ₁₀ C ₇ H ₁₂ ) C ₁₂ H ₁₄ )	$\begin{array}{c} R_{I} \\ R_{1} \\ H \\ CH_{3} \\ H \\ H \\ H \\ H \end{array}$	$ \begin{array}{c} R_2 & R_2 \\ R_2 & CH_3 \\ H & CH_3 \\ CH_3 & CH_3 \\ C_6H_5 \end{array} $	3 ${}^{R_{4}}$ ${}^{R_{3}}$ H H ${}^{CH_{3}}$ ${}^{C_{6}H_{5}}$ ${}^{CH_{3}}$	R ₄ H CH ₃ CH ₃ CH ₃ CH ₃	Methylene blue or rose bengal; $0^{\circ}$ 98:2 CCl ₂ F ₂ :CH ₃ OH CH ₂ Cl ₂ CH ₂ Cl ₂	$\begin{array}{c} R_1 \\ R_2 \\ R_2 \end{array} \\ \begin{array}{c} O \\ R_4 \\ R_3 \\ R_3 \end{array}$	41-78	76c	
C C C	₈ H ₁₀ ₇ H ₁₀ O ₂ ₈ H ₁₄	$CH_2=CH_2=CH_2=CH_3C(CH_3)$	=C(CH ₂ =CHCH =C(CH ₂ CH==CH ) ₂ C==CH	3)C(CH ₃ I—CHC 3)CH—( ICH—C ICH—C	$ \begin{array}{l} \overset{()) \longrightarrow CH_2}{} \\ \overset{()) \longrightarrow CH_2}{} \\ \overset{()) \longrightarrow CH_3}{} \\ \overset{()) \longrightarrow CH_3}{} \\ \overset{()) \longrightarrow CH_3}{} \\ \overset{()) \longrightarrow CH_3}{} \\ \end{array} $	   CH ₃ OH/rose bengal	Hydroperoxides Hydroperoxides Hydroperoxides $CH_3CHO, OHCCH=CHCO_2CH_3$ $CH_3C(=CH_2)CH(OOH)CH=C(CH_3)_2,$ $(CH_3)_2C=CHCH_2OOH,$ $(CH_3)_2C(OCH_3)CH=CHC(CH_3)_2OOH$		225 225 225 1, 226 227	

TABLE XXIII. ACYCLIC CONJUGATED DIENES

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) ( $\%$ )	Total Yield (%)	Refs.
	C ₁₀ H ₁₆	Y	Neat/chlorophyll; 20–25°	H00 (60),	96¢	177
254				оон (40)		
	C16H14	C ₆ H ₅	3:5 CH ₃ OH:C ₆ H ₆ / rose bengal	$C_6H_5 \rightarrow C_6H_5$	55	227
			$ m CHCl_3/methylene$ blue; $ m K_2CrO_4$ filter	_	75	228
	C ₁₇ H ₁₄ O	C ₆ H ₅ C ₆ H ₅	CHCl ₃ /various sensi- tizers; K ₂ CrO ₄ or NaNO ₂ filter	$\begin{bmatrix} C_{6}H_{5} \\ 0 \\ 0 \\ COC_{6}H_{5} \end{bmatrix} \longrightarrow C_{2}H_{2}(38), C_{6}H_{5}CHO (14-C_{6}H_{5}CHO) (14-C_{6}H_{5}CHO$	 64),	76e

TABLE XXIII. ACYCLIC CONJUGATED DIENES (Continued)



Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
$C_5H_6$	$\bigcirc$	Neat/rose bengal; 100°	( <u>0-0</u> )	86	3, 230
		$CH_3OH/rose$ bengal ( $\beta$ , 0.002)	<b>3</b> 3		2
$C_{6}H_{8}$	$\bigcirc$	(CH ₃ ) ₂ CHOH/ methylene blue		19	4
	~	Neat/rose bengal	23	$\geq \! 75$	230
		$CH_3OH/rose bengal (\beta, 0.03)$	"		2
	$\hat{\mathbf{Q}}$		(0-0 <u>)</u>		225
C ₇ H ₁₀	$\bigcirc$	$C_2H_5OH/eosin; \leq 39^{\circ}$	0-0>	29	231
C ₈ H ₁₀ O	0 ×	$CH_3OH/rose$ bengal ( $\beta$ , 2)	_	_	89
C ₁₀ H ₁₀ O ₄	CO ₂ CH ₃	_	CO ₂ CH ₃		94



TABLE XXIV. MONOCYCLIC CONJUGATED DIENES

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.



TABLE XXIV. MONOCYCLIC CONJUGATED DIENES (Continued)

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₃ H ₂₂ O	СНОНСН3	_	CCCHOHCH ₃ (minor) ^b , V	=0 (majo	237a r) ⁱ
260	C ₁₃ H ₂₂ O ₂ HC	СНОНСН3	CH₃OH/rose bengal; OH	HO. CCCHOHCH ₃ , HO. C	o, —	237b
		O₂CCH ₃		HO. O2CCH3		
	C ₁₅ H ₂₄ O ₂	$\mathcal{A}$	$C_2H_5OH/eosin$			237c
	C ₁₇ H ₁₄	C ₆ H ₅	(C ₂ H ₅ ) ₂ O/di- naphthalene- thiophene	C ₆ H ₅ C ₆ H ₅		238
	C ₁₈ H ₁₄ O ₂	HO ₂ C C ₆ H ₅	CHCl _s /methylene blue	HO ₂ C C ₆ H ₅ C ₆ H ₅	_	238



Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
С ₃₅ Н ₂₆ О	A, $R_1 = HO$ , $R_2 = C_6 H_5$	(C ₂ H ₅ ) ₂ O/no sensitizer	$\mathbf{B}, \mathbf{R_1} = \mathbf{HO}, \mathbf{R_2} = \mathbf{C_6H_5}$		243, 245
³⁵ С ₃₆ Н ₂₈	$C_{6}H_{5}$ $C_{6}H_{5}$ $C_{6}H_{5}$ $C_{6}H_{5}$	$77:22:1 C_{g}H_{6}:$ $C_{2}H_{5}OH:H_{2}O/$ methylene blue	$\begin{array}{cccc} C_6H_5 & C_6H_5 & C_6H_5 \\ C_6H_5 & C_6H_5 & C_6H_5 \\ C_6H_5 & C_6H_5 & C_6H_5 \\ \end{array} $ (71), $\begin{array}{cccc} C_6H_5 & C_6H_5 \\ C_6H_5 & C_6H_5 \\ \end{array}$	(25) ¹ , ⁷⁶	246
C ₃₆ H ₂₈ O	$\begin{array}{c} CH_{3}O & C_{6}H_{5} \\ C_{6}H_{5} & & C_{6}H_{5} \\ C_{6}H_{5} & & C_{6}H_{5} \end{array}$	(C ₂ H ₅ ) ₂ O/no sensitizer	$C_{6}H_{5} \xrightarrow{C_{6}H_{5}} (4)^{i}$ $C_{6}H_{5} \xrightarrow{C_{6}H_{5}} (C_{6}H_{5})^{i}$ $C_{6}H_{2}O_{6} + \begin{bmatrix} C_{6}H_{5} & C_{6}H_{5} \\ C_{6}H_{5} & C_{6}H_{5} \end{bmatrix} \xrightarrow{i_{O_{2}}} C_{6}H_{5}$ $C_{6}H_{5} \xrightarrow{C_{6}H_{5}} C_{6}H_{5} \end{bmatrix} \xrightarrow{i_{O_{2}}} C_{6}H_{5}$		245 H5 5

IADLE AAIV. MONOCYCLIC CONJUGATED DIENES (COMM
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Form	ula Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₈ H ₈ (		_	Cl	λ	3, 248
C ₈ H ₉ I	NO CONH ₂	CH ₃ OH/methylene blue; 15°	CONH ₂	≥80 [%]	3, 24 <b>9</b>
C ₉ H ₁₀	O ₂ CO ₂ CH ₃	CH ₃ OH/methylene blue; 15°	CO ₂ CH ₃	≥80 ^ħ	3, 249
				50	85
	$\begin{array}{c} R_2 \\ R_3 \\ R_4 \end{array} \xrightarrow{R_1} CO_2 R_5 \end{array}$	CH ₃ OH/methylene blue; 15°	$\begin{array}{c} R_2 \\ R_2 \\ R_3 \\ R_4 \end{array} \xrightarrow{R_1} CO_2 R_5 \end{array}$	92	94
C ₁₀ H ₁	${}_{2}O_{2}$ A, $R_{1} = R_{2} = R_{3} = R_{4} = H$ , $R_{5} = C_{2}H_{5}$ A, $R_{1} = R_{3} = R_{4} = H$ , $R_{3} = R_{5} = CH_{3}$		B, $R_1 = R_2 = R_3 = R_4 = H$ , $R_5 = C_2H_5$ B, $R_1 = R_2 = R_4 = H$ , $R_3 = R_5 = CH_3$	À	225

	C ₁₁ H ₁₄ O ₂	$ \begin{array}{l} A, \ R_{1} \ = \ R_{3} \ = \ H, \\ R_{2} \ = \ R_{4} \ = \ R_{5} \ = \ CH_{3} \end{array} $		B, $R_1 = R_3 = H$ , $R_2 = R_4 = R_5 = CH_3$	λ	225
		A, $R_1 = R_4 = R_5 = CH_3$ , R, -R, -H	—	B, $R_1 = R_4 = R_5 = CH_3$ , $R_2 = R_3 = H$	ħ	225
		$ \begin{array}{l} R_{2} = R_{3} = R \\ A, R_{1} = R_{4} = H, \\ R_{2} = R_{3} = R_{5} = CH_{3} \end{array} $	_	B, $R_1 = R_4 = H$ , $R_2 = R_3 = R_5 = CH_3$	λ	225
26	C11H16		_	о , сн _з сно	_	3, 84
			Solvent/rose bengal	0, $0$ , $0$ , $0$ , $0$ , $0$ , $0$ , $0$ ,	55	3, 84
G		(+)	$CH_{3}OH/rose$ bengal ( $\beta$ , 2)	(64) (36)	-	8 <b>9</b>
	$\mathrm{C_{12}H_{14}O_4}$	O ₂ CCH ₃	_	O ₂ CCH ₃ O ₂ CCH ₃	h	225
	C ₁₂ H ₁₈	$\bigcirc - \bigcirc$	2:1 CH ₃ OH: (CH ₃ ) ₂ CHOH/rdse bengal; 20°		51	4, 39

TABLE XXV. BICYCLIC CONJUGATED DIENES

Formula	a Structure	Reaction Conditions and Reactive $f(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
² C ₁₃ H ₁₂ O	CH ₃ O OH O CH ₃ O	20:3:1 CS ₃ : CHCl ₃ :CH ₃ OH/ hematoporphyrin	$\begin{bmatrix} CH_{3}O & OH & O \\ CH_{3}O & & & \\ CH_{3}O & & \\ CH_{3}O$	55 D ₂ CH ₃	250
C13H18O	2 CO ₂ CH ₃		CO ₂ CH ₂	λ	225
C14H14O	$\begin{array}{c} \begin{array}{c} & & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ $	CS ₂ /no sensitizer	$\begin{bmatrix} & & & & \\ & & & & \\ & & & & \\ & & & & $	36 CO₂CH	250 3
	A, $R_1 = H$ , $R_2 = CH_3O$		B, $R_{I} =$	н	

TABLE XXV. BICYCLIC CONJUGATED DIENES (Continued)



	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
N	C ₁₉ H ₂₈ O ₂	R	5:95 H ₂ O: C ₂ H ₅ OH/eosin	HO	48	254
	C ₂₇ H ₄₂ O	$HU \sim V$ $A, R = HO$ $A, R = C_8H_{15}$ $C_8H_{17}$		B, R = HO B, R = $C_8H_{15}$	_	255
88	$C_{27}H_{44}$		$C_2H_5OH/eosin$		60	256
			Pyridine/rose bengal; 18–20° (β, 4.1)	ООН ООН	95 ^{1, h}	204
	C ₂₇ H ₄₄ O	HO	C ₂ H ₅ OH/eosin	HO		257
		Ç9H12				
	C ₂₈ H ₄₄ O		5:95 H ₂ O:C ₂ H ₅ OH/ eosin; 60°	HO	70	86
		HO [*] Ergosterol	Pyridine/hemato- porphyrin; 20° (β, 0.0045)	,,	95 ¹	41
			1:10 $CH_3OH:C_6H_6/$ eosin; $(CH_3CO)_2O$	$\star$	91	4, 258
2				CH ₃ CO ₂ (56), CH ₃ CO ₂		(25),

CH₃CO₂

HC

C₉H₁₇

(12),

(7)

259

38

TABLE XXVI.	STEROIDAL	POLYCYCLIC,	CONJUGATED	DIENES

269

 $\mathrm{C}_{\mathbf{28}}\mathrm{H}_{\mathbf{46}}\mathrm{O}$ 

но

 $C_2H_5OH/eosin$ 

C,H19

Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.



TABLE XXVI. STEROIDAL POLYCYCLIC, CONJUGATED DIENES (Continued)



Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.

Formu	ala Structure	Reaction Conditions and Reactivity $(\beta)$	Products(s) and Relative Yield(s) ( $\%$ )	Total Yield (%)	Refs.
C ₃₀ H ₄₆ (contd	CH ₃ CO ₂ R CH ₃ CO ₂	1:300 Pyridine: C ₂ H ₅ OH/eosin Y	CH ₃ CO ₂	77	261
	CH ₃ CO ₂	1:300 Pyridine: C ₂ H ₅ OH/eosin Y	CH ₃ CO ₂	72	261

TABLE XXVI STEROIDAL POLYCYCLIC, CONJUGATED DIENES (Continued)



TABLE XXVII. MISCELLANEOUS POLYCYCLIC, CONJUGATED DIENES

TABLE X	CXVII.	MISCELLANEOUS	POLYCYCLIC,	Conjugated	DIENES	(Continued)
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	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₀ H ₃₀ O ₂ (contd.)	CO ₂ H	5:95 H ₂ O:C ₂ H ₅ OH/ methylene blue		37	264
274	C ₂₂ H ₂₁ ClN ₂ O ₇	$\begin{array}{c} Cl & N(CH_3)_2 \\ OH & OH \\ OH & OH \\ OH \\ OH \\ OH \\ OH$	C ₆ H ₆ /3,4- benzpyrene	$\begin{array}{c} Cl & OOH \\ R_1 & OH & O \end{array}$	78	4, 265
	C ₃₈ H ₃₈ ClN ₂ O ₇	A, $R_1 = H$ , $R_2 = CONH_2$ A, $R_1 = H$ , $R_2 = CONHC(CH_3)_3$	4:1 Cyclo- hexane:C ₆ H ₆ /3,4- benzpyrene	B, $R_1 = H$ , $R_2 = CONH_2$ B, $R_1 = H$ , $R_2 = CONHC(CH_3)_3$	42	265
	C ₃₀ H ₃₈ ClN ₂ O ₇	A, $R_1 = C(CH_3)_3$ , $R_2 = CONHC(CH_3)_3$	Cyclohexane/ 3,4-benzpyrene	B, $\mathbf{R_1} = \mathbf{C}(\mathbf{CH_3})_3$ , $\mathbf{R_2} = \mathbf{CONHC}(\mathbf{CH_3})_3$	81	265



Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.
	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₄ H ₄ O	5 1 2 A	2:2:1 $CH_3OH:n-C_3H_7OH:(CH_3)_2CO$ rose bengal; $-90^{\circ}$	$\frac{D}{2} = \frac{1}{2} = \frac{1}$	95 ^f	267
			$CH_3OH/rose$ bengal ( $\beta$ , 0.005)	-	_	89
276	$\mathrm{C_5H_4O_2}$	А, 2-СНО	$C_2H_5OH/eosin$	$[B, 2 \text{ CHO}] \longrightarrow O_{3} O_{2} O_{2} H_{5}$	62	268
			$CH_3OH/rose$ bengal ( $\beta$ , 0.6)	,,, C ,,, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		89
	C5HO3	A, 2-CO ₂ H	C _o H _s OH/sensitizer	$[B, 2-CO_{\circ}H] \rightarrow C$		269
	C ₅ H ₅ O	A, 2-CH ₃	3:1 petroleum ether: $C_{g}H_{g}/di$ - naphthalenethio- phene; -20°	B, 2-CH ₃	—	39
			CH ₃ OH/rose bengal; 18–25°	$[B,2-CH_3] \longrightarrow HO0 \swarrow 0CH_3$	80	89, 101
		A, 3-CH ₃	5:95 $H_2O:C_2H_5OH/$ eosin: $V_2O_5$	$[B, 3-CH_3] \rightarrow C, 4-CH_3$	20	270
	C ₅ H ₆ O ₂	A, 2-CH,OH	$C_{o}H_{s}OH/eosin; 20^{\circ}$	$[B, 2-CH_OH] \rightarrow C$	74	269
		~	$CH_3OH/rose$ bengal ( $\beta$ , 0. 003)			89

	C ₅ H ₇ NO	A, 2-CH ₂ NH ₂	C ₂ H ₅ OH/sensitizer CH ₃ OH/rose	$[\mathbf{B}, 2\text{-}\mathbf{CH}_{2}\mathbf{NH}_{2}] \rightarrow \mathbf{C}$	_	94 89
			bengal; 20°			
	$C_6H_6O$	A, 2-CH=CH ₂	CH ₃ OH/rose bengal; 20°			89
	C ₆ H ₈ O	A, 2,4-(CH ₃ ) ₂	( $\beta$ , 0.002) CH ₃ OH/rose bengal; 20° ( $\beta$ , 0.002)			89
		A, 2,5-(CH ₃ ) ₂	$CH_3OH/rose$ bengal ( $\beta$ , 0.001)	$[B,2,5-(CH_3)_2] \longrightarrow HOO \swarrow O OCH_3$	72	88, 101
	$\mathbf{C_6H_8O_2}$	A, 2-CH ₂ OCH ₃	$C_2H_5OH/eosin;$ $V_2O_5$	$[\mathrm{B}, 2\text{-}\mathrm{CH}_2\mathrm{OCH}_3] \to \mathrm{C}$	24	225, 269
277			$CH_3OH/rose$ bengal; 20° ( $\beta$ , 0.003)		_	89
	C ₆ H ₉ NO	A, 2-CH ₂ NHCH ₃	$CH_3OH/rose$ bengal; 20°	_	—	89
	$C_7H_9NO_2$	A, 2-CH ₂ NHCOCH ₃	$C_2H_5OH/sensitizer$	$[B, 2 \cdot CH_2 NHCOCH_3] \rightarrow C,$ CH-CONH_2 CH_2(NHCOCH_2)	_	94
	$\mathrm{C_7H_{10}O_2}$	A, 2-CHOHC ₂ H ₅	$C_2H_5OH/eosin$	$[B, 2-CHOHC_2H_5] \rightarrow C, C_2H_5CHO^d$	—	3
	$C_8H_8O_5$	A, 3,4-(CO ₂ CH ₃ ) ₂	CH ₃ OH/rose bengal; 20°	_	_	89
	$C_{B}H_{12}O_{2}$	A, 2-CHOHC ₃ H ₇ - $i$ A $2$ -C(C-H_2)-OH	$(\rho, \sim 0.2)$ C ₂ H ₅ OH/eosin C H-OH/eosin	$[\mathbf{B}, 2\text{-}\mathbf{CHOHC}_{3}\mathbf{H}_{7}\cdot i] \to \mathbf{C}$ $[\mathbf{B}, 2\text{-}\mathbf{C}(\mathbf{C}, \mathbf{H}), \mathbf{OH}] \to \mathbf{C}$	_	3
	~9···14 ~2	11, 2-0102115/2011	2115011/008III	$[D, 2^{-}O(O_{2})_{2}O(D_{1}) \rightarrow O$	_	J

TABLE XXVIII. FURANS

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) ( $\%$ )	Total Yield (%)	Refs.
C ₉ H ₁₄ O ₃ C ₁₀ H ₇ BrO	A, 2-CH(OC ₂ H ₅ ) ₂ A, 2-C ₈ H ₄ Br-p	$\begin{array}{c} C_2H_6OH/cosin\\ CH_3OH/rose bengal;\\ h\nu: 550-750 nm\\ (\beta, 0.0033) \end{array}$	$[B, 2-CH(OC_2H_5)_2] \rightarrow C$ $[B, 2-C_6H_4Br \cdot p] \rightarrow p \cdot BrC_6H_4 = 0$ $(CH_3O) = 0$ $p \cdot BrC_6H_4 = 0$ $(CH_3O) = 0$	11 	271 80
C ₁₀ H ₇ ClO	A, 2-C ₆ H ₄ Cl- <i>p</i>	CH ₃ OH/rose bengal; <i>hν</i> : 550 750 nm (β, 0.0029)	$[B, 2-C_{6}H_{4}Cl \cdot p] \rightarrow p-ClC_{6}H_{4} \downarrow 0 \downarrow 0 , p-ClC_{6}H_{4}CO_{2}H$	62	80
		Dioxane/rose bengal; hv: 550-750 nm	(09) (31) p-ClC ₄ H ₄ CO ₂ H		80
		$H_2O/rose bengal;$ hv: 550-750 nm ( $\beta, 0.00071$ )		_	80
		n-C ₄ H ₈ OH/rose bengal; hv: 550- 750 pm (β. 0.0077)		—	80
		HO(CH ₂ ) ₂ OH/rose bengal; hv: 550- 750 nm (β. 0.00065)		—	80
C ₁₀ H ₈ O	A, 2-C ₆ H ₅	CH ₃ OH/rose bengal; <i>hv</i> : 550-750 nm (β, 0.0017)	$[B, 2 \cdot C_{6}H_{5}] \rightarrow \frac{C_{6}H_{5}}{CH_{3}O} \swarrow^{O}, C_{6}H_{5}CO_{2}H$		80





	Formula	Structure	ReactionConditions andReactivity $(\beta)$ Provide	oduct(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₁ H ₁₀ O (contd.)		<i>n</i> -C ₄ H ₈ OH/rose bengal; <i>hv</i> : 550– 750 nm ( <i>β</i> , 0.0038)			80
~	C ₁₁ H ₁₀ O ₂	A, 2-C ₆ H ₄ OCH ₃ -p	CH ₃ OH/rose bengal; $h\nu$ : 550– 750 nm ( $\beta$ , 0.0010)	$[B, 2 \cdot C_{g}H_{4}OCH_{g} \cdot p] \rightarrow$ $p \cdot CH_{3}OC_{g}H_{4} \longrightarrow 0$ $CH_{3}OC_{g}H_{4} \longrightarrow 0$ $p \cdot CH_{9}OC_{g}H_{4}CO_{2}H$		80
280			HO(CH ₂ ) ₂ OH/rose bengal; <i>hv</i> : 550– 750 nm ( <i>B</i> , 0,00037			80
			$H_2O/rose bengal;$ hv: 550-750 nm ( $\beta$ , 0.00064)	,	—	80
			$n - C_4 H_8 OH/rose$ bengal; $h\nu$ : 550– 750 nm ( $\beta$ , 0.0021)	_		80
		A, 2-CHOHC ₆ H ₅	$C_2H_5OH/eosin$	$[B, 2-CHOHC_6H_5] \longrightarrow C$	—	3
	C ₁₂ H ₁₁ NO	A, 2-CH ₂ NHCOC ₆ H ₅	$CH_{3}OH/methylene$ blue ( $\beta$ , 0.002)	_		1 <b>93</b>

TABLE XXVIII. FURANS (Continued)



	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₀ H ₁₄ O (contd.)		CH ₃ OH/rose bengal; 20° $(\beta, \sim 0.01)$	_		89
282	C ₂₀ H ₃₀ O		CH ₃ OH/eosin	0 0 0 0 CH3	50 ¹	402
	C ₂₈ H ₁₈ Br ₂ O	$\begin{array}{c} C_{6}H_{5} \\ p \cdot BrC_{6}H_{4} \end{array} \begin{array}{c} C_{6}H_{6} \\ C_{6}H_{4}B \end{array}$	(CH ₃ ) ₂ CO/ methylene blue r-p	$\begin{array}{c} C_{6}H_{5} \longrightarrow C_{6}H_{5} \\ p-BrC_{6}H_{4} \end{array} C_{6}H_{4}Br-p \end{array}$	-	278
	C ₂₃ H ₂₀ O	$\begin{array}{c} C_8H_5 \\ C_8H_5 \\ C_6H_5 \\ \end{array} \begin{array}{c} C_6H_5 \\ C_6H_5 \\ \end{array}$	CS ₂ /heterocoer- dianthrone	$\begin{bmatrix} C_{6}H_{5} & 0 & C_{6}H_{5} \\ C_{6}H_{5} & C_{6}H_{5} \end{bmatrix} \longrightarrow \begin{bmatrix} 0 & 0 & 0 \\ C_{6}H_{5}C & C_{6}H_{5} \\ C_{6}H_{5} & C_{6}H_{5} \end{bmatrix} \xrightarrow{A}$	94	27 <b>4</b> , 275

TABLE	XXVIII.	FURANS	(Continued)
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Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C4H4S	Thiophene	CH ₃ OH/rose bengal; 20° $(\beta, \ge 600)$		NR	89
C4H5N	Pyrrole	H ₂ O/eosin		321	281
C ₅ H ₇ N	l-Methylpyrrole	H ₂ O/eosin	0 √ ^N ^{OH}	48 ¹	281
C ₆ H ₈ S	2,5-Dimethyl- thiophene	CHCl ₃ /methylene blue	cis-CH ₃ COCH=CHC(CH ₃ )SO A (67), trans-CH ₃ COCH=CHCOCH ₃ B (33)	84 <i>1</i>	282
		CH ₃ OH/methylene blue	A (97), B (3)	72	282, 283a
C ₆ H ₉ N	2,5-Dimethylpyrrole	$CH_{s}OH/rose$ bengal; 20° ( $\beta$ , 0.16)	_		89
C ₁₀ H ₉ N	1-Phenylpyrrole	CH ₃ OH : H ₂ O : (CH ₃ ) ₃ COH ⁴		7	283b

TABLE XXIX.	THIOPHENES,	Pyrroles,	AND	MISCELLANEOUS	Conjugated	Dienes	Containing	VINYL
			H	ETEROATOMS				



	·		ILLEROAL	IOMS (Ourserrace)		
	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₄ H ₁₃ NO ₂ (contd.) (C ₁₇ H ₁₁ NO ₂ )	$\begin{array}{ccc} CH_3 & C_2H_5 & H \\ H & C_2H_5 & CH_3 \\ H & C_6H_5 & H \end{array}$				
	C ₁₆ H ₁₃ N	2,5-Diphenylpyrrole	CS ₂ /heterocoer- dianthrone; 0°	$\begin{array}{c} \mathbf{HOO} \\ \mathbf{C_6H_5} \\ \end{array} \\ \begin{array}{c} \mathbf{N} \\ \mathbf{C_6H_5} \\ \end{array} \\ \begin{array}{c} \mathbf{C_6H_5} \\ C_$	50	285
28(	C ₂₀ H ₁₆ S	S C ₆ H ₅	C ₆ H ₆	COC ₆ H ₅	ı	3, 286
ű	C ₂₁ H ₁₇ N	$ \begin{array}{c}                                     $	Aqueous n-C ₄ H ₉ OH	COC ₆ H ₅	2	287
	C ₂₃ H ₁₉ N	C ₆ H ₅ C ₆ H ₅ C ₆ H ₅	CH ₂ Cl ₂ /methylene blue	$C_{6}H_{5}C_{6}C_{6}H_{5} \qquad (65), C_{6}H_{5}CO_{2}H \qquad (12)$ $C_{6}H_{5}O$	<b>i, I</b>	288
	C ₂₆ H ₁₉ N	C ₆ H ₅ N-C ₆ H ₅	CS ₂	$ \begin{array}{c} C_{6}H_{5} \\ \hline O \\ O \\$	96 ^x	287
	$\mathbf{C_{28}H_{20}S}$	2,3,4,5-Tetraphenyl- thiophene	CS ₂	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	NR	274

TABLE XXIX.	Thiophenes,	PYRROLES,	AND	MISCELLANEOUS	CONJUGATED	DIENES	Containing	VINYL
		HE	TERO	ATOMS (Continue	d)			

	C ₂₈ H ₂₁ N	1,2,3,5-Tetraphenyl- pyrrole	CH ₂ Cl ₂ /methylene blue	$C_{6}H_{5}C_{6}H_{5} \xrightarrow{C_{6}H_{5}} C_{6}H_{5}$ $C_{6}H_{5}C_{6}H_{5} \xrightarrow{C_{6}H_{5}} C_{6}H_{5}$ $C_{6}H_{5}O$ $C_{6}H_{5}O$	70 ¹	288
		2,3,4,5-Tetraphenyl- pyrrole	CH _s OH/methylene blue	$\begin{array}{c} HOO \\ C_6H_5 \\ C_6H_5 \\ C_6H_5 \\ C_6H_5 \end{array} \\ C_6H_5 \end{array}$	80	289
			CH ₃ OH/methylene blue	$\begin{array}{c} CH_3O\\C_6H_5\\C_6H_5\\C_8H_5\\O\\C_6H_5\end{array} \xrightarrow{C_6H_5} (65), \begin{array}{c} C_6H_5CONH\\C_6H_5\\C_6H_5\end{array} \xrightarrow{C_6H_5} (35)\\C_6H_5\end{array} \xrightarrow{C_6H_5} (35)$	) ⁸⁵¹	279, 290
287			CH ₃ OH/methylene blue; KOH	$\begin{array}{c} H \\ \downarrow \\ C_6H_5 \\ C_6H_5 \\ C_6H_5 \end{array}$	35 ¹	279, 290
	C ₂₈ H ₂₁ NO		-	$\begin{array}{c} 0 \\ HOO \\ C_6H_5 \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} 0 \\ H_5 \\ \end{array} \\ $	-	291
	C ₃₄ H ₂₅ N	C ₆ H ₅ C ₆ H ₅ Pentaphenylpyrrole	(C ₂ H ₅ ) ₂ O/hetero- coerdianthrone; -65°; NH ₄ I/ CH ₃ CO ₂ H	$C_{6}H_{5} \xrightarrow{C_{6}H_{5}} C_{6}H_{5}$	67 ¹	292
			CHCl ₂ /methylene blue	$\begin{array}{c} \begin{array}{c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & \\ & & & \\ & & & & \\ & & & & \\ & & & \\ & & & & \\ & & & \\ & & & & \\ & & & & \\ & & & & \\ & $	72 ¹	292

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₇ H ₈ O		(CH ₃ ) ₂ CO/hemato- porphyrin		90	293
C ₇ H ₈	$\bigcirc$	CH ₃ OH/rose bengal; H ⁺		25	1, 105, 294
		CH ₃ OH/methylene blue	(10), (12),	b	294
			O, OH (56), HO (22)		
$C_8H_8O_2$	OCH3	9:3:1 $CS_2$ : $(C_2H_5)_2$ CH ₈ OH/hemato- porphyrin-dimeth	$ \begin{array}{c} D: & O \\ \text{and} & O \\ \text{charge} & O \\ $	88	295
		ester; -40 to -2 CS ₂ /hematopor- phyrin-dimethyl ester	$[A] \rightarrow \bigcirc $	29 ¹	295

TABLE XXX. TRIENES AND POLYENES





Note: Footnotes a-u are on p. 331. References 176-407 are on pp. 331-336.



TABLE XXX. TRIENES AND POLYENES (Continued)





## TABLE XXX. TRIENES AND POLYENES (Continued)

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) $(\%)$	Total Yield (%)	Refs.
C ₃₀ H ₂₂	C ₆ H ₅ C ₆ H ₅ C ₆ H ₅	2:1 (C ₂ H ₅ ) ₂ O: C ₂ H ₅ OH/eosin	$\begin{array}{c} C_{6}H_{5} \\ \hline \\ C_{6}H_{5} \\ \hline \\$	Н ₅ (6)	305, 306
C ₃₀ H ₄₂ O	Yah	sharper	Сн ₂ он		
		$\begin{array}{c} {\rm CH_{g}OH/methylene}\\ {\rm blue} \ (\beta,\leq 0.01)\\ {\rm C_9H_{17}}\end{array}$			17, 18
C ₃₀ H ₄₂ O ₂	CH ₃ CO ₂	$\frac{1:1 C_6 H_6: (C_2 H_5)_2 O}{(trace pyridine)/eosin}$	CH ₃ CO ₂	≥47	307, 308
C ₃₀ H ₄₄ O ₂	CH,CO,	1:1 C ₆ H ₆ : (C ₂ H ₅ ) ₂ O (trace pyridine)/ eosin	CH ₃ CO ₂ (80),	22	307, 308
	$R = CH(CH_s)CH=C$	CHCH (CH3)CH (CH3),			











	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₈ H ₈ I ₂ O ₃	HO-CH2CH2CO2H	H ₂ O (pH 7.6)/ erythrosin		18	313
	$C_9H_{12}O_3$	I' 1,2,4-Trimethoxybenzene	CH ₃ OH/rose			316,
	C ₁₀ H ₁₄ O ₄	1,2,3,5-Tetramethoxy- benzene	CH ₃ OH/rose bengal			316, 401
300		1,2,4,5-Tetramethoxy- benzene	CH ₃ OH/rose bengal	CH ₃ O OCH ₃ (20),	25	316, 401
				$CH_{3O} OCH_{3} (80)$ $CH_{3O} OCH_{3} (80)$		
	C ₁₁ H ₁₆ O ₅	Pentamethoxybenzene	CH ₃ OH/rose bengal	CH ₃ O CH ₃ O CH ₃ O O CH ₃ O O CH ₃ O O CH ₃ O	57	316, 401
	$\mathrm{C_{12}H_{18}O_{6}}$	Hexamethoxybenzene	CH ₃ OH/rose bengal	— —		316, 401









	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₆ H ₂₆ O ₂ (contd.)	(CH ₃ ) ₃ C OCH ₃ OCH ₃	CH3OH/rose bengal		NR	318
304	C ₁₈ H ₃₀ O	(CH ₃ ) ₃ C C(CH ₃ ) ₃ C C(CH ₃ ) ₃	CH3OH/eosin	$(CH_3)_3C$ $C(CH_3)_3$ ,	14	315
				A (93) $(CH_3)_3C$ C $(CH_3)_3$ $(CH_3)_3C$ OOH		
			CH ₂ OH/rose bengal	B (7) B		402

TABLE XXXI. MONOCYCLIC AROMATIC COMPOUNDS (Continued)

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	$C_{11}H_8O_8P_2Na_4$	OPO ₃ Na ₂ OPO ₃ Na ₂	CH3CO2H/riboflavin	$\begin{bmatrix} 0 \text{PO}_3\text{Na}_2 \\ 0 \text{PO}_3\text{Na}_2 \\ 0 \text{PO}_3\text{Na}_2 \end{bmatrix} \rightarrow \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$	80	319, 320
305	$C_{12}H_{12}O_2$	OCH ₃	(C ₂ H ₅ ) ₂ O/benzan- throne	OCH ₃ OCH ₃ A	80	170, 321
			(C ₂ H ₅ ) ₂ O	$[A] \longrightarrow \bigcup_{\substack{\text{CH}_30\\0\\0\\\text{OCH}_3}}^{\text{CH}_30}$	55–60	170, 321
			$C_gH_g$	$[A] \longrightarrow \underbrace{CO_2CH_3}_{OCH_3}$	30–50	170, 321

TABLE XXXII. NAPHTHALENES AND PHENANTHRENES

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Products(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₂ H ₁₆	C ₆ H ₅	Many solvents		NR	268
306	$C_{24}H_{20}O_2$	$C_6H_5 OCH_3$	$(C_2H_5)_2O; -50^{\circ}$	$C_6H_5$ OCH ₃ $C_6H_5$ OCH ₃	80	170, 322
			C ₆ H ₆	$[A] \longrightarrow \begin{array}{c} C_6H_5 \\ \hline CO_2CH_3 \\ \hline C_6H_5 \\ \hline CHO \\ C_6H_5 \\ OCH_3 \end{array}$	<b>3</b> 0–50	170
	C ₂₆ H ₁₈	C ₆ H ₅	Many solvents	_	NR	268

TABLE XXXII. NAPHTHALENES AND PHENANTHRENES (Continued)

TABLE XXXIII. ANTHRACENES



Formula	Substituent(s) in	Reaction Conditions and Reactivity $(B)$	Correspondingly Substituted Product(s) and Belative Vield(s) (%)	Total Yield	Refe
Tormula		(p)		( /0/	1015.
C ₁₄ H _e Cl ₂	9,10-Dichloro	$CS_2$ ( $\beta$ , 0.02)	Α		77, 82
		$CCl_{4}$ ( $\beta$ , 0.01)	Α		77, 82
		$CHCl_{3}$ ( $\beta$ , 0.06)	Α		77, 82
C14H2N2O4	9,10-Dinitro	CS,			323
C, H, NO,	9-Hydroxy-10-nitroso	CH ₃ CO ₂ H	9,10-Anthraquinone		<b>3</b> 2 <b>4</b>
	9-Nitro	CS.	A .	h	323
C, H Cl	1-Chloro	$CS_{0}(\beta, 0.005)$	Α		77, 82
		CHCl, $(\beta, 0.01)$	Α		77, 82
		$CCl_{a}$ ( $\beta$ , 0.005)	Α		77, 82
	9-Chloro	$CS_{2}(\beta, 0.003)$	Α		77, 82
		$CC1_{1}(\beta, 0.003)$	Α		77, 82
		CHCl, $(\beta, 0.02)$	Α		77, 82
C1.H.	None	$CS_{0}(\beta, 0.002)$	Α		77, 82
14 10		<b>2</b> · · · · ·			325
		$C_{\mathbf{s}}\mathbf{H}_{\mathbf{s}}$ ( $\beta$ , 0.5)	Α		78, 83
		$C_{e}H_{5}(\beta, 0.04)$	Α		77, 82
		$C_{s}H_{5}Br(\beta, 0.1)$	Α		77, 82, 83
		CHCl ₃ (β, 0.01)	Α		77, 82,
C ₁₄ H ₁₀ O ₂	9,10-Dihydroxy	CS ₂	$[A] \rightarrow 9,10 \cdot Anthraquinone$	3	170 326

	Formula	Substituent (s) in Anthracene	Reaction Conditions and Reactivity (β)	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₄ H ₁₁ N	9-Amino	$(C_2H_5)_2O$	NH VIII	35*	103
	C ₁₅ H ₁₂	9-Methyl	$\begin{array}{c} \mathrm{CHCl}_3\left(\beta,0.003\right)\\ \mathrm{CCl}_4\left(\beta,0.001\right)\\ \mathrm{CS}_2 \end{array}$	ÓOH A A A	 16	77, 82 77, 82 327
308	C ₁₅ H ₁₂ O	9-Hydroxy-10-methyl	$(C_2H_\delta)_2O$		<b>80</b> %	324, 328
		2-Methoxy 9-Methoxy	CS ₂ CS ₂	A [A] $\rightarrow 9,10$ ·Anthraquinone	<del>6</del> 0	329 329
	C ₁₆ H ₁₂ O	9-Hydroxy-10-vinyl	$(C_2H_5)_2O$		91 <b>*</b>	<b>328, 33</b> 0
	C ₁₆ H ₁₄	1,4-Dimethyl 9,10-Dimethyl	CS ₂ Pyridine/methylene	/ OOH A (35), B (65) A A	<u>66</u>	212 327 277
		9-Ethyl	blue (β, 0.003) CS ₂	Α		327

				Q		
	C ₁₆ H ₁₄ O	9-Hydroxy-10-ethyl	$(C_2H_5)_2O$		67*	324, 328
	C ₁₆ H ₁₄ O ₂	1,4-Dimethoxy 2,6-Dimethoxy 9,10-Dimethoxy	$(C_2H_5)_2O; -50^\circ$ CHCl ₃ ; 20° CS ₂	A OOH	 NR 67	173 331 173, 326
	C17H14O	9-Hydroxy-10-(1- propenyl)	$(C_2H_5)_2O$	ООН	91*	<b>3</b> 28, 330
309	$\mathrm{C_{17}H_{16}}$	9-Methyl-10-ethyl	CS ₂	A 0	58	327
	C ₁₇ H ₁₆ O	9-Hydroxy-10-propyl	(CH ₃ ) ₂ CO		8	<b>33</b> 2
	$C_{17}H_{16}O_{3}$	2,6,9-Trimethoxy	CHCl ₃ ; 20°	$n \cdot C_3 H_7$ OOH [A] $\rightarrow 2,6$ -Dimethoxy-9,10-anthraquinone	>99	331
	C ₁₈ H ₁₆ O	9-Hydroxy-10-(1- butenyl)	$(C_2H_5)_2O$		8	<b>3</b> 30
	C ₁₈ H ₁₆ O ₄	2,6-Dimethoxy-9-acetoxy	CHCl ₃ ; 20°		NR	331

TABLE XXXIII. ANTHRACENES (Continued)

	Formula	Substituent(s) in Anthracene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₁₈ H ₁₈ O ₂	1,4-Diethoxy 1,4-Dimethoxy-9,10- dimethyl	$(C_2H_5)_2O; -50^\circ$ $(C_2H_5)_2O$	B A ^t	30	90, 333 329
	$C_{18}H_{18}O_4$	1,4,9,10-Tetramethoxy	$(C_2H_5)_2O$	A O	$\geq \! 30$	173, 329
310	С ₁₉ Н ₁₈ О	9-Hydroxy-10-(3- methyl-1-butenyl)	$(C_2H_5)_2O$	ООН		330
	C ₂₀ H ₁₃ Br C ₂₀ H ₁₂ I C ₂₀ H ₁₄	9-Bromo-10-phenyl 9-Iodo-10-phenyl 9-Phenyl	$\begin{array}{c} \mathrm{CS}_{2} \\ \mathrm{CS}_{2} \\ \mathrm{CHCl}_{3} \left(\beta,  0.007\right) \end{array}$			334 334 77, 82
			$CS_2$ ( $\beta$ , 0.0008)	Α	36	77, 82, 334
	C ₂₀ H ₁₄ O	9-Hydroxy-10-phenyl	CH₃OH + KOH	C ₆ H ₅ OOH	80 ^s	328, 335

				ŅН		
	$\mathrm{C_{20}H_{15}N}$	9-Amino-10-phenyl	$(C_2H_5)_2O$		80"	103
	CarHar	9-Cvclobexvl	CS.	A	14	337
	C., H. O.	9-Carboxy-10-phenyl	CS.	Outcome vague		338
	$C_{21}$ H ₁₄ $C_{2}$	9-Methyl-10-phenyl	CS.	A	63	339
	211116	o szoniji zo pilonji			00	000
	$\mathrm{C_{21}H_{16}O}$	9-Benzyl-10-hydroxy	(CH ₃ ) ₂ CO		≥67*	332
		9. Methoxy. 10. phenyl	CS	$C_6H_5CH_2$ OOH	80	335
	сня	9 10-Di(2-thienvl)	CS ₂	A	80	340
3	C H O	9-Carbomethoxy, 10-	CS ₂	<u></u>	50	224
-	C22 ¹¹ 16 ^C 2	phenyl	0.02	A	50	334
	$C_{22}H_{18}$	9-Ethyl-10-phenyl	$CS_2$	Α		339
	$C_{22}H_{18}O_{2}$	l,4-Dimethoxy-9-phenyl	$(C_2H_5)_2O; -50^\circ$	В	75	173
	$C_{23}H_{20}O_{2}$	1,4-Dimethoxy-9-methyl- 10-phenyl	$(C_2H_5)_2O$	$\mathbf{A}^t$	30	329
	C.H.N.	9.10-Di-(2-pyridyl)	CS.	А	60	329. 341
	C.H.S	9-Phenyl-10-(2-thienyl)	CS.	Α	69	340
	$C_{a}H_{a}O_{a}$	1.4-Diethoxy-9-phenyl	CHCl ₂ ; -50°: filter	B		170
	C.H.N	9-Phenyl-10-(2-pyridyl)	CS.	Ā	60	329. 341
	Co.H.Br.	9.10-Di- $(p$ -bromophenvl)	CS.	A	90	336
	Co.H. Cl.	1.4-Dichloro-9.10-	CS _o	A		342
	- 2016 - 2	diphenyl				
			Tetrahydrofuran; —50°; filter	Α	75	170

	Formula	Substituent(s) in Anthracene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	C ₂₆ H ₁₆ Cl ₂ (contd.)	1,5-Dichloro-9,10- diphenyl	CS ₂	A	30	343
	C ₂₆ H ₁₇ Br	2-Bromo-9,10-diphenyl	CS ₂	Α	38	344
1	$C_{26}H_{17}Cl$	l-Chloro-9,10-diphenyl	$CS_2$	Α	45	343
	C26H18	1,4-Diphenyl	$CS_2$	Α		342
		9,10-Diphenyl	$CS_{2}(\beta, 0.003)$	Α	>99	4, 77, 82
			$C_{6}\bar{H}_{6}$ ( $\beta$ , 0.05)		_	78, 83
			$CHCl_{3}$ ( $\beta$ , 0.004)		—	77, 82
			Pyridine ( $\beta$ , 0.02 ^{<i>a</i>} )			277
312	$C_{28}H_{20}N_2O_2$	l,4-Dimethoxy-9,10-di- (2-pyridyl)	$(C_2H_5)_2O$	A ^{h. t}	60	329, 341
	C., H.,	9-Cyclohexyl-10-phenyl	CS ₂	Α		337
	C,,H,O,	2-Carboxy-9,10-diphenyl	CS,	Α	30	344
(	C ₂₇ H ₁₉ Cl	1-Chloro-4-methyl-9,10- diphenyl	CS ₂	Ať	20	343
(	C ₂₇ H ₁₉ ClO	l-Chloro-4-methoxy-9,10- diphenyl	$(C_2H_5)_2O$	A ^{h. t}	—	345
			Tetrahydrofuran; - 50°; filter	A (50), B (50)	—	170
	C.,H.,	l-Methyl-9,10-diphenyl	CS,	$\mathbf{A}^{t}$	35	343
	21 20	2-Methyl-9,10-diphenyl	CS,	Α	12	346
(	C ₂₇ H ₂₀ O	1-Methoxy-9,10-diphenyl	Tetrahydrofuran; $-50^{\circ}$ ; filter	A (50), B (50)	—	170
			(C,H,),O	$A^{h.t}$		345
		2-Methoxy-9,10-diphenyl	CS ₂	Α	80	347

TABLE XXXIII. ANTHRACENES (Continued)

	$C_{27}H_{20}OS$	1-Methylsulfinyl-9,10- diphenyl	$CS_2$	Α	25-30	347
		2-Methylsulfinyl-9,10- diphenyl	$CS_2$	Α	20-30	347
	$\mathrm{C}_{27}\mathbf{H}_{20}\mathbf{O}_{2}\mathbf{S}$	l-Methylsulfonyl-9,10- diphenyl	$CS_2$	Α	25	347
		2-Methylsulfonyl-9,10- diphenyl	$CS_2$	Α	70	347
	$C_{27}H_{20}S$	1-Methylthio-9,10- diphenyl	$CS_2$	Α	30-35	347
		2-Methylthio-9,10- diphenyl	$CS_2$	Α	80	347
	$\mathrm{C}_{28}\mathbf{H}_{20}$	9-Phenyl-10-(p-vinyl- phenyl)		Α	99	348
	C28H20O	2-Acetyl-9,10-diphenyl	CS,	Α	70	349
313	C ₂₈ H ₂₀ OS	2-Acetylthio-9,10- diphenyl	$CS_2$	Α	55	347
	C28H20O2	2-Acetoxy-9,10-diphenyl	CS ₂	Α	75	347
		2-Carbomethoxy-9,10- diphenyl	$CS_2$	A	65	344
	$\mathrm{C}_{28}\mathrm{H}_{21}\mathbf{NO}$	2-Acetyl-9,10-diphenyl oxime	$CS_2$	A	<b>6</b> 0	349
	$\mathrm{C}_{28}\mathbf{H}_{22}$	1,4-Dimethyl-9,10- diphenyl	$CHCl_3$ ; $-50^\circ$ and +50°; KNO ₂ filter	A (30), B (70)		170, 400
		-	CS ₂	$A^{h,t}$	30	343
		2,3-Dimethyl-9,10- diphenyl	$CS_2$	Α	90	343
		9,10-Di(o-tolyl)	$CS_2$	Α	90	350
		9,10-Di $(m$ -tolyl)	$CS_2$	Α	80	350
		9,10-Di $(p$ -tolyl)	$CS_2$	Α	74	350

TABLE XXXIII.	ANTHRACENES	(Continued)	ŧ
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Formula	Substituent(s) in Anthracene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₂₈ H ₂₂ O	1-Methoxy-4-methyl-	CS ₂	B ^{h,t}	30	343
$C_{28}H_{22}O_{2}$	1,2-Dimethoxy-9,10- diphenyl	$(C_2H_5)_2O$	A ^{h.t}		351
	1,4-Dibenzyloxy	(C ₂ H ₅ ) ₂ O; -50°; KNO ₂ filter	B		90, 170, 333
		$(C_2H_5)_2O; -50^{\circ}$	$[B] \longrightarrow \bigcup_{\substack{0 \\ OCH_{9}C_{8}H_{5}}}^{O}$		170, 333
	1,4-Dimethoxy-9,10- diphenyl	(C ₂ H ₅ ) ₂ O; -50°	В	94	4, 173, 352
		$(C_2H_\delta)_2O + HCl$	$[B] \begin{array}{c} C_6H_5 O \\ C_6H_5 OCH_3 \\ \hline C_6H_5 OCH_3 \\ \hline C_6H_5 CHO \\ \hline C_6H_5 CHO \\ \hline C_6H_5 \\ \hline CHO \\ \hline CHO \\ \hline C_6H_5 \\ \hline CHO \\ \hline CHO \\ \hline C_6H_5 \\ \hline CHO \\ \hline CHO \\ \hline C_6H_5 \\ \hline CHO $	_	353

	1,5-Dimethoxy-9,10- diphenyl	$(C_2H_5)_2O$		NR	354
	1,8-Dimethoxy-9,10- diphenyl	$(C_2H_5)_2O$	A ^{<i>h</i>.<i>t</i>}		354
	2,3-Dimethoxy-9,10- diphenyl	$(C_2H_5)_2O$	A ^t		351
	2,6-Dimethoxy-9,10- diphenyl	$9:1 \text{ CS}_2:(\text{C}_2\text{H}_5)_2\text{O}$	Α	50	354
$\mathrm{C}_{29}\mathrm{H}_{22}\mathrm{O}$	2-Methyl-3-acetyl-9,10- diphenyl	$CS_2$	Α		349
ω	2-Propionyl-9,10- diphenyl	$CS_2$	Α	70	349
$\overline{\mathbf{a}}  \mathrm{C}_{29} \mathrm{H}_{24} \mathrm{O}_{3}$	1,2,6.Trimethoxy-9,10- diphenyl	$(C_2H_5)_2O$	A ^t	25	355
$\mathrm{C}_{30}\mathrm{H}_{24}$	1,2-Tetramethylene-9,10- diphenyl	CS ₂			356
	2,3-Tetramethylene-9,10- diphenyl		Α	—	357
$\mathrm{C}_{30}\mathrm{H}_{24}\mathrm{Br}_{2}$	l,4-Di-(2-bromoethyl)- 9,10-diphenyl	$(C_2H_5)_2O$	B ^{h. t}	70- 80	352
$\mathrm{C}_{30}\mathrm{H}_{24}\mathrm{Cl}_{2}$	1,4-Di-(2-chloroethyl)- 9,10-diphenyl	$(C_2H_5)_2O$	$\mathbf{B}^{\mathbf{\lambda},t}$	70- 80	352

TABLE XXXIII. ANTHRACENES (Continued)

Formula	Substituent(s) in Anthracene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
$C_{30}H_{26}O_2$	1,4-Diethoxy-9,10- diphenyl	$(C_2H_5)_2O$	By''	70– 80	352
$C_{30}H_{26}O_4$	1,2,5,6-Tetramethoxy- 9,10-diphenyl	$(C_2H_5)_2O$	A ^t	40	355
$\mathrm{C_{32}H_{25}NO_4}$	l Diacetylamino-2- acetoxy-9,10-diphenyl	$CS_2$	Α	50	355
$C_{32}H_{30}O_2$	1,4-Di-(1-methylethoxy)- 9,10-diphenyl	$(C_2H_5)_2O$	B ^{h,t}	75	352
	1,4-Dipropoxy-9,10- diphenyl	$(C_2H_5)_2O$	$\mathbf{B}^{h,t}$	75	352
C33H22O	2-Benzoyl-9,10-diphenyl	CS ₂	Α	80	349
C34H22	9,10-Di-(1-naphthyl)	CS ₂	Α	—	358
-1 -12	9,10-Di-(2-naphthyl)	CS,	Α		358
CasHas	1,2,9,10-Tetraphenyl	CS,	Α		359
••• ••	1,4,9,10-Tetraphenyl	CS,	Α		342
	9,10-Bis-(p-biphenyl)	CS,	Α	31	346
$\mathrm{C}_{38}\mathbf{H_{26}O_{2}}$	1,4-Diphenoxy-9,10- diphenyl	$(\mathbf{C_2H_5})_2\mathbf{O}$	$\mathbf{B}^{h,t}$	50	352
$\mathbf{C_{38}H_{26}S_2}$	1,4-Di(phenylthio)-9,10- diphenyl	CS ₂	A ^{<i>h</i>. <i>t</i>}	40	347
C40H30O2	1,4-Dibenzyloxy-9,10- diphenyl	$CS_2$	B _{<i>h</i>.<i>t</i>}	70- 80	352



TABLE	XXXIV.	<b>TETRACENES</b>	(Continued)	)
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Formula	Substituent(s) in Naphthacene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
		Pyridine $(\beta, 0.001)$	<u> </u>	<u> </u>	277
		$C_6H_6$ ( $\beta$ , 0.002 ^a )		-	78
$C_{44}H_{28}O_{4}$	5,11-Di.(p-carboxyphenyl)- 6,12-diphenyl		Α	—	3, 373
$\mathrm{C}_{44}\mathrm{H}_{32}$	2,8-Dimethyl-5,6,11,12- tetraphenyl	_	Α	—	374
	2-Methyl-5,6,12-triphenyl- 11-p-tolyl	_	A, B ^{<i>h</i>}	—	374
	5,11-Diphenyl- $6,12$ -di- $(p$ -tolyl)	—	Α	—	374
$C_{44}H_{32}O_2$	5,11-Di-(p-methoxyphenyl)- 6,12-diphenyl		Α	-	375
$C_{46}H_{36}$	2,8-Dimethyl-5,11-di-(p-tolyl)- 6,12-diphenyl	$C_{6}H_{6}$	Α	-	365, 376
$\mathrm{C}_{50}\mathbf{H}_{32}$	5,11-Di-(1-naphthyl)-6,12- diphenyl	$CS_2$	Α	<b>9</b> 0	377
	5,11-Di-(2-naphthyl)-6,12- diphenyl	$C_6H_6$	Α	—	3, 378
$C_{54}H_{36}$	5,11-Bis-(biphenyl)-6,12-diphenyl	C ₆ H ₆	Α	—	379
C ₆₆ H ₄₄	2,6,8,12-Tetraphenyl-5,11- bis-(biphenyl)	C ₆ H ₆	Α	—	379

## TABLE XXXV. 1,2-BENZANTHRACENES



Formula	Substituent(s) in Benzanthracene	Reaction Conditions and Reactivity $(\beta)$	Correspondingly Substituted Product(s) and Relative Yield(s) (%)	Total Yield (%)	Ref.
C18H19	None	CS ₂	Α		380
C ₁₉ H ₁₄	7-Methyl	$CS_2$	Α	h	380
	12-Methyl	CS ₂	Α	h	380
C ₂₀ H ₁₆	7,12-Dimethyl	$C_{6}H_{6}$	Α	h	380
C ₂₁ H ₁	7-(1-Methylethyl)	ĊŠ,	Α	h	380
0	7,8,12-Trimethyl	CS,	Α	h	380
	7,9,12-Trimethyl	CS,	Α	h	380
C,,H,,	7,8,9,12-Tetramethyl	CS,	Α	h	380
C30H20	7,12 Diphenyl	CS,	Α	20	380

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	$C_{18}H_{12}Cl_4O_2$	$\begin{array}{c} OCH_3 & Cl \\ \hline \\ OCH_3 & Cl \\ \hline \\ OCH_3 & Cl \end{array}$	C ₆ H ₆	$\begin{array}{c} CO_2CH_3 \\ Cl \\ C$	 /-	381
320	$C_{20}H_{12}$		C ₆ H ₆			382
	C ₂₀ H ₁₂ S	S S	CS ₂			347
	C ₂₁ H ₁₆		CS ₂		NR	383, 384







TABLE XXXVI. MISCELLANEOUS AROMATIC COMPOUNDS (Continued)





TABLE XXXVI. MISCELLANEOUS AROMATIC COMPOUNDS (Continued)

	Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
	$C_{36}H_{22}$	C ₆ H ₅ C ₆ H ₅	CS ₂	C ₆ H ₅ C ₆ H ₅	60 ⁿ	343
328	$\mathrm{C}_{40}\mathrm{H}_{22}$	C ₆ H ₅	$CS_2$	_		394
	$C_{40}H_{24}$	$C_{6}H_{5}$ $C_{6}H_{5}$ $C_{6}H_{5}$ $C_{6}H_{5}$	CS ₂	$ \begin{array}{c} C_6H_5 \\ \hline 0 \\ \hline$	85 ⁿ	394
	C ₄₀ H ₂₆	$C_6H_5$	CS2		NR	395
329	$C_{42}H_{22}O_4$	$O_2CC_6H_5$	CS2	$O_2CC_6H_5$	54 ^h	397
	C46H30	$\overbrace{C_6H_5}^{C_6H_5}, \overbrace{C_6H_5}^{C_6H_5}$	] CS ₂	$C_6H_5 C_6H_5$ $C_6H_5 C_6H_5$ $C_6H_5 C_6H_5$		3, 360
	$\mathrm{C}_{50}\mathrm{H}_{32}$	$C_{6}H_{5} C_{6}H_{5}$	$CS_2 + Na_2CO_3$	$C_{6}H_{5} C_{6}H_{5}$	75	377

TABLE XXXVI. MISCELLANEOUS AROMATIC COMPOUNDS (Continued)

Formula	Structure	Reaction Conditions and Reactivity $(\beta)$	Product(s) and Relative Yield(s) (%)	Total Yield (%)	Refs.
C ₅₂ H ₃₄		$C_6H_5$ $CS_2$	$C_{e}H_{5}$ $C_{e}H_{5}$ $C_{e}H_{5}$ $C_{e}H_{5}$ $C_{e}H_{5}$	70	394
с ₅₄ Н ₃₄	C ₆ H ₅ C ₆ H	CS ₂	$C_{6}H_{5} C_{6}H_{5}$ $C_{6}H_{5}$ $C_{6}H_{5}$ $(67),$	75	377
			$C_{6}H_{5} C_{6}H_{5}$ $C_{6}H_{5}$		

## TABLE XXXVI. MISCELLANEOUS AROMATIC COMPOUNDS (Continued)

## FOOTNOTES TO TABLES XVII-XXVI

^a The values were obtained by comparison and are based on a  $\beta$  value of 0.003 M for 2,3dimethyl-2-butene.

^b The products were isolated or assayed after reduction of the peroxidic mixture.

^c The product(s) may have arisen by reaction with ground-state oxygen  $({}^{3}O_{2})$ .

^d This product is presumed to have been formed but was not isolated or characterized.

• The products were analyzed by spectroscopic means.

^f The yield was based upon oxygen uptake and a presumed 1:1 stoichiometry for  ${}^{1}O_{2}$  and the substrate.

⁹ The actual oxygen uptake was very slow because of triplet sensitizer quenching.

^h The structure of the product(s) is presumed; characterization was not complete.

ⁱ See column 4 for the absolute yields of these products.

ⁱ The  $\beta$  values were obtained by comparison and are based on a  $\beta$  value of 0.7 M for 1-methylcyclohexene.

* Two additional azide products were detected but not isolated.

¹ The product was formed from a secondary reaction.

^m In addition to the normal steroid-x-enes, where the double bond is located between carbon atoms x and x + 1, exocyclic methylene groups at carbon x are also included.

ⁿ A ketone function at a particular site is represented by replacement of the R group by =0.

^o A double bond is also present at C-16.

^p The primary product reacts with a second mole of singlet oxygen.

^q Singlet oxygen was produced by chemical means.

^r This product may be formed by reactions initiated by abstraction of hydrogen by excited sensitizer molecules.

⁵ The olefin reacts with ground-state oxygen. If an epidioxide is formed, it decomposes to the products shown.^{328, 335}

^{*} See ref. 170 for reasons why the original identification of the products might be suspect.

" The structure of the product was not determined and is unknown.

## **REFERENCES TO TABLES XVII-XXXVI**

¹⁷⁶ N. Furutachi, Y. Nakadaira, and K. Nakanishi, Chem. Commun., 1968, 1625.

¹⁷⁷ R. L. Kenney and G. S. Fisher, J. Amer. Chem. Soc., 81, 4288 (1959).

¹⁷⁸ G. Ohloff, E. Klein, and G. O. Schenck, Angew. Chem., 73, 578 (1961).

¹⁷⁹ C. D. Snyder and H. Rapoport, J. Amer. Chem. Soc., 91, 731 (1969).

¹⁸⁰ G. W. K. Cavill and I. M. Coggiola, Aust. J. Chem., 24, 135 (1971).

¹⁸¹ D. Cobern, J. S. Hobbs, R. A. Lucas, and D. J. Mackenzie, J. Chem. Soc., C, 1966, 1897.

¹⁸² G. E. Hall and D. G. Roberts, J. Chem. Soc., B, **1966**, 1109.

¹⁸³ H. Morimoto, I. Imada, and G. Goto, Ann., 735, 65 (1970).

¹⁸⁴ H. Köller, Diplomarbeit, University of Göttingen, 1958.

¹⁸⁵ N. Dirlam, M.S. Dissertation, University of California at Los Angeles, 1969.

¹⁸⁸ K. Gollnick, Advan. Chem. Ser., No. 77, Amer. Chem. Soc., Washington, D.C., 1968, p. 78.

¹⁸⁷ W. Fenical, D. R. Kearns, and P. Radlick, J. Amer. Chem. Soc., 91, 7771 (1969).

¹⁸⁸ G. O. Schenck, K. Gollnick, G. Buchwald, S. Schroeter, and G. Ohloff, Ann., 674, 93 (1964).

189 C. S. Foote, S. Wexler, and W. Ando, Tetrahedron Lett., 1966, 4111.

¹⁹⁰ E. Klein and W. Rojahn, Dragoco Rept., 11, 123 (1964) [C.A. 61, 8344e (1964)].

¹⁹¹ R. L. Kenney and G. S. Fisher, J. Org. Chem., 28, 3509 (1963).

¹⁹² G. Ohloff and G. Unde, Helv. Chim. Acta, 48, 10 (1965).

¹⁹³ G. O. Schenck, H. Mertens, W. Müller, E. Koch, and G. P. Schiemenz, Angew. Chem., 68, 303 (1956).

¹⁹⁴ M. Mousseron-Canet, J.-P. Dalle, and J.-C. Mani, Tetrahedron Lett., 1968, 6037.

¹⁹⁵ W. Schänzer, Dissertation, University of Göttingen, 1952; Jahresverzeichnis der Deutschen Hochschulschriften, **69**, 281 (1953).

¹⁹⁶ For recent product studies see W. Skorianetz, K. H. Schulte-Elte, and G. Ohloff, *Helv. Chim. Acta*, 54, 1913 (1971).

¹⁹⁷ T. T. Fujimoto, Ph.D. Dissertation, University of California at Los Angeles, 1971; Diss. Abstr., 32 (12), 6910-B (1972).

¹⁹⁸ K. Gollnick and G. Schade, Tetrahedron Lett., 1966, 2335.

¹⁹⁹ E. Klein and W. Rojahn, Chem. Ber., 98, 3045 (1965).

²⁰⁰ J. A. Marshall and W. I. Fanta, J. Org. Chem., 29, 2501 (1964).

²⁰¹ K. H. Schulte-Elte and G. Ohloff, Helv. Chim. Acta, 51, 494 (1968).

²⁰² K. Gollnick and G. Schade, Tetrahedron Lett., 1968, 689.

²⁰³ A. Nickon, J. B. DiGiorgio, and P. J. L. Daniels, J. Org. Chem., 38, 533 (1973).

²⁰⁴ W. Eisfeld, Ph.D. Dissertation, University of Göttingen, 1958.

²⁰⁵ J. A. Edwards, J. S. Mills, J. Sundeen, and J. H. Fried, J. Amer. Chem. Soc., **91**, 1248 (1969).

²⁰⁶ E. L. Shapiro, T. Legatt, and E. P. Oliveto, Tetrahedron Lett., 1964, 663.

²⁰⁷ J. E. Fox, A. I. Scott, and D. W. Young, Chem. Commun., 1967, 1105.

²⁰⁸ W. P. Schneider and J. C. Babcock, U.S. Pat. 3,281,415.

²⁰⁹ W. P. Schneider and D. E. Ayer, *Proc. 2nd Int. Congr. Hormonal Studies*, L. Martini, F. Franschini, and M. Motta, Eds., Int. Congress Series 132, Excerpta Medica Foundation, Amsterdam, 1967, p. 254.

²¹⁰ W. P. Schneider and D. E. Ayer, Proc. 2nd Int. Congr. Hormonal Studies, Milan, 1966, p. 254.

²¹¹ K. Gollnick and G. Schade, unpublished results, quoted in ref. 1.

²¹² S. Itô, H. Takeshita, T. Muroi, M. Ito, and K. Abe, Tetrahedron Lett., 1969, 3091.

²¹³ G. Ohloff, H. Strickler, B. Willhalm, C. Borer, and M. Hinder, *Helv. Chim. Acta*, 53, 623 (1970).

²¹⁴ (a) H. Takeshita, T. Sato, T. Muroi, and S. Ito, *Tetrahedron Lett.*, **1969**, 3095; (b) J. MacMillan (Univ. of Bristol), personal communication.

²¹⁵ (a) R. A. Bell and R. E. Ireland, *Tetrahedron Lett.*, **1963**, 269; (b) R. A. Bell, R. E. Ireland, and L. N. Mander, J. Org. Chem. **31**, 2536 (1966).

²¹⁶ S. Masamune, J. Amer. Chem. Soc., 86, 290 (1964).

²¹⁷ G. O. Schenck, Z. Elektrochem., 64, 997 (1960).

²¹⁸ J. W.-P. Lin, Ph.D. Dissertation, University of California at Los Angeles, 1969; Diss. Abstr., **30** (6), 2609-B (1969).

²¹⁹ J. E. Huber, Tetrahedron Lett., 1968, 3271.

²²⁰ R. S. Atkinson, Chem. Commun., 1970, 177.

²²¹ K. Pfoertner and K. Bernauer, Helv. Chim. Acta, 51, 1787 (1968).

²²² L. J. Bollyky, J. Amer. Chem. Soc., 92, 3230 (1970).

²²³ T. Matsuura, N. Matsushima, and R. Nakashima, Tetrahedron, 26, 435 (1970).

²²⁴ F. McCapra and R. A. Hann, Chem. Commun., 1969, 442.

²²⁵ G. O. Schenck, Z. Elektrochem., 56, 855 (1952).

²²⁶ H. E. Heyke, Diplomarbeit, University of Göttingen, 1951.

²²⁷ M. Brenner, Ph.D. Dissertation, University of California at Los Angeles, 1969; *Diss.* Abstr., **30** (4), 1582-B (1969).

²²⁸ G. Rio and J. Berthelot, Bull. Soc. Chim. Fr., 1969, 1664.

²²⁹ G. Rio and J. Berthelot, Bull. Soc. Chim. Fr., 1970, 1509.

²³⁰ G. O. Schenck and D. E. Dunlap, Angew. Chem., 68, 248 (1956).

²³¹ A. C. Cope, T. A. Liss, and G. W. Wood, J. Amer. Chem. Soc., 79, 6287 (1957).

²³² G. Buchwald, Diplomarbeit, University of Göttingen, 1954.

²³³ C. H. Krauch, Diplomarbeit, University of Göttingen, 1958.

²³⁴ M. Mousseron-Canet, J.-C. Mani, J.-P. Dalle, and J.-L. Olivé, Bull. Soc. Chim. Fr., 1966, 3874.

²³⁵ M. Mousseron-Canet, J.-C. Mani, and J.-L. Olivé, C.R. Acad. Sci., Ser. C, **262**, 1725 (1966).

236 M. Mousseron-Canet, J.-C. Mani, and J.-P. Dalle, Bull. Soc. Chim. Fr., 1967, 608.

²³⁷ (a) S. Isoe, S. B. Hyeon, H. Ichikawa, S. Katsumura, and T. Sakan, Tetrahedron

Lett., 1968, 5561; (b) S. Isoe, S. Katsumura. S. B. Hyeon, and T. Sakan, *ibid.*, 1971, 1089; (c) A. Sato and H. Mishima, *ibid.*, 1969, 1803.

²³⁸ G. Rio and M. Charifi, C.R. Acad. Sci., Ser. C, **268**, 1960 (1969); G. Rio and M. Charifi, Bull. Soc. Chim. Fr., **1970**, 3585.

²³⁹ H. J. Kuhn, Diplomarbeit, University of Göttingen, 1959.

²⁴⁰ J. Rigaudy and P. Courtot, Tetrahedron Lett., 1961, 95.

²⁴¹ N. M. Bikales and E. I. Becker, J. Org. Chem., 21, 1405 (1956).

²⁴² C. Dufraisse, G. Rio, and J.-J. Basselier, C.R. Acad. Sci., 246, 1640 (1958).

²⁴³ C. Dufraisse. A. Etienne, and J. Aubry, C.R. Acad. Sci., 239, 1170 (1954).

²⁴⁴ J.-J. Basselier and J.-P. Le Roux, C.R. Acad. Sci., Ser. C, 268, 970 (1969).

²⁴⁵ C. Dufraisse, G. Rio, and A. Liberles, C.R. Acad. Sci., 256, 1873 (1963).

246 G. R. Evanega, W. Bergmann, and J. English, Jr., J. Org. Chem., 27, 13 (1962).

²⁴⁷ G. Rio and A. Ranjon, C.R. Acad. Sci., 248, 111 (1959).

²⁴⁸ G. Grebe, Dissertation, University of Göttingen, 1952; Jahresverzeichnis der Deutschen Hochschulschriften, **68**, 283 (1952).

²⁴⁶ G. O. Schenck and H. Ziegler, Naturwiss., 38, 356 (1951).

²⁵⁰ E. J. Forbes and J. Griffiths, J. Chem. Soc., C, 1967, 601.

²⁵¹ H. C. Barrett and G. Büchi, J. Amer. Chem. Soc., 89, 5665 (1967).

²⁵² R. Criegee, W.-D. Wirth, W. Engel, and H. A. Brune, Chem. Ber., 96, 2230 (1963).

²⁵³ T. G. Halsall, W. J. Rodewald, and D. Willis, Proc. Chem. Soc., 1958, 231.

²⁵⁴ A. Butenandt and J. Paland, Chem. Ber., 72, 424 (1939).

²⁵⁵ D. Dvornik, M. Kraml, and J. F. Bagli, J. Amer. Chem. Soc., 86, 2739 (1964).

²⁵⁶ E. L. Skau and W. L. Bergmann, J. Org. Chem., 3, 166 (1938).

²⁵⁷ F. Schenck, K. Buchholz, and O. Wiese, Chem. Ber., 69, 2696 (1936).

²⁵⁸ S. Iwasaki and K. Tsuda, Chem. Pharm. Bull. (Tokyo), 11, 1034 (1963).

²⁵⁹ A. Windaus and R. Langer, Ann., 508, 105 (1933).

²⁶⁰ D. H. R. Barton and G. F. Laws, J. Chem. Soc., 1954, 52.

²⁶¹ W. G. Dauben and G. J. Fonken, J. Amer. Chem. Soc., 81, 4060 (1959).

²⁸² R. N. Moore and R. V. Lawrence, J. Amer. Chem. Soc., 80, 1438 (1958).

²⁶³ W. H. Schuller and R. V. Lawrence, J. Amer. Chem. Soc., 83, 2563 (1961).

²⁴⁴ W. H. Schuller, R. N. Moore, and R. V. Lawrence, J. Amer. Chem. Soc., 82, 1734 (1960).

²⁶⁵ M. Schach von Wittenau, J. Org. Chem., 29, 2746 (1964).

²⁶⁶ M. Mousseron-Canet and J.-P. Chabaud, Bull. Soc. Chim. Fr., 1969, 245.

²⁶⁷ E. Koch and G. O. Schenck, Chem. Ber., 99, 1984 (1966).

²⁶⁸ H. Hanecka in *Methoden der Organischen Chemie*, Vol. 8, part 3, E. Müller, Ed., G. Thieme, Stuttgart, 1952, p. 402.

²⁶⁹ G. O. Schenck, Ann., 584, 156 (1953).

²⁷⁰ J. P. van der Merwe and C. F. Garbers, J. S. African Chem. Inst., **17**, 149 (1964) [C.A. **62**, 9088e (1965)].

²⁷¹ I. Shopov, A. Obreshkov, and I. Paniaotov, J. Prakt. Chem., [4] 33, 309 (1966).

²⁷² H. H. Wasserman and A. R. Doumaux, Jr., J. Amer. Chem. Soc., 84, 4611 (1962).

²⁷³ H. H. Wasserman and R. Kitzing, Tetrahedron Lett., 1969, 5315.

²⁷⁴ J. Martel, C.R. Acad. Sci., 244, 626 (1957).

²⁷⁵ C. Dufraisse, G. Rio, and A. Ranjon, C.R. Acad. Sci., Ser. C, 264, 516 (1967).

²⁷⁶ C. Dufraisse and S. Ecary, C.R. Acad. Sci., **223**, 735 (1946). For recent papers on these types of compounds see F. Nahavandi, F. Razmara, and M. P. Stevens, *Tetrahedron Lett.*, **1973**, 301.

²⁷⁷ T. Wilson, J. Amer. Chem. Soc., 88, 2898 (1966).

²⁷⁸ R. E. Lutz, W. J. Welstead, Jr., R. G. Bass, and J. I. Dale, J. Org. Chem., 27, 1111 (1962).

²⁷⁹ H. H. Wasserman and A. Liberles, J. Amer. Chem. Soc., 82, 2086 (1960).

²⁶⁰ J.-J. Basselier and J.-P. Le Roux, C.R. Acad. Sci., Ser. C, 270, 1366 (1970).

²⁸¹ P. de Mayo and S. T. Reid, Chem. Ind. (London), 1962, 1576.

²⁶² C. N. Skold and R. H. Schlessinger, Tetrahedron Lett., 1970, 791.

²⁸³ (a) H. H. Wasserman and W. Strehlow, *Tetrahedron Lett.*, **1970**, 795; (b) R. W. Franck and J. Auerbach, J. Org. Chem. **36**, 31 (1971).

- ²⁸⁴ C. S. Foote, I. G. Burstain, and R. W. Denny, unpublished results.
- 285 G. Rio, A. Ranjon, O. Pouchot, and M.-J. Scholl, Bull. Soc. Chim. Fr., 1969, 1667.
- 286 A. Mustafa, J. Chem. Soc., 1949, 256.
- ²⁸⁷ W. Theilacker and W. Schmidt, Ann., 605, 43 (1957).
- ²⁸⁸ H. H. Wasserman and A. H. Miller, Chem. Commun., 1969, 199.
- ²⁸⁹ C. Dufraisse, G. Rio, A. Ranjon, and O. Pouchot, C.R. Acad. Sci., 261, 3133 (1965).
- ²⁹⁰ G. Rio, A. Ranjon, and O. Pouchot, C.R. Acad. Sci., Ser. C, 263, 634 (1966).
- ²⁹¹ G. Rio, A. Ranjon, and O. Pouchot, Bull. Soc. Chim. Fr., 1968, 4679.
- 292 C. Dufraisse, G. Rio, and A. Ranjon, C.R. Acad. Sci., Ser. C, 265, 310 (1967).
- ²⁹³ M. Oda and Y. Kitahara, Tetrahedron Lett., 1969, 3295.
- ²⁹⁴ A. S. Kende and J. Y.-C. Chu, Tetrahedron Lett., 1970, 4837.
- ²⁹⁵ E. J. Forbes and J. Griffiths, J. Chem. Soc., C, 1968, 575.
- 298 M. Oda and Y. Kitahara, Angew. Chem., Int. Ed. Engl., 8, 673 (1969).
- 297 E. Koerner von Gustorf, F.-W. Grevels, and G. O. Schenck, Ann., 719, 1 (1968).
- 298 C. S. Foote and M. Brenner, Tetrahedron Lett., 1968, 6041.
- ²⁹⁹ M. Mousseron-Canet, J.-P. Dalle, and J.-C. Mani, Bull. Soc. Chim. Fr., 1968, 1561.
- ³⁰⁰ M. Mousseron-Canet, J.-P. Dalle, and J.-C. Mani, Photochem. Photobiol., 9, 91 (1969).
- 301 J.-L. Olivé and M. Mousseron-Canet, Bull. Soc. Chim. Fr., 1969, 3252.
- ³⁰² D.-A. Lerner, J.-C. Mani, and M. Mousseron-Canet, Bull. Soc. Chim. Fr., 1970, 1968.
- 303 H. B. Henbest and R. A. L. Wilson, Chem. Ind. (London), 1956, 86.
- ³⁰⁴ G. O. Schenck and O. A. Neumüller, unpublished results.
- 305 C. Dufraisse, A. Etienne, and J.-J. Basselier, C.R. Acad. Sci., 224, 2209 (1957).
- ³⁰⁶ J.-J. Basselier, C.R. Acad. Sci., 258, 2851 (1964).
- ³⁰⁷ P. Bladon and T. Sleigh, Proc. Chem. Soc., 1962, 183.
- ³⁰⁸ P. Bladon and T. Sleigh, J. Chem. Soc., **1965**, 6991.
- ³⁰⁹ P. Bladon, R. B. Clayton, C. W. Greenhalgh, H. B. Henbest, E. R. H. Jones, B. J. Lovell, G. Silverstone, G. W. Wood, and G. F. Woods, J. Chem. Soc., **1952**, 4883.
- ³¹⁰ G. D. Laubach, E. C. Schreiber, E. J. Agnello, and K. J. Brunings, J. Amer. Chem. Soc., 78, 4746 (1956).
- ³¹¹ K. Hasegawa, J. D. Macmillan, W. A. Maxwell, and C. O. Chichester, *Photochem. Photobiol.*, 9, 165 (1969).
  - ³¹² S. Isoe, S. B. Hyeon, and T. Sakan, Tetrahedron Lett., 1969, 279.
- ³¹³ T. Matsuura, A. Nishinaga, K. Matsuo, K. Omura, and Y. Oishi, J. Org. Chem., 32, 3457 (1967).
  - ³¹⁴ T. Matsuura, N. Yoshimura, A. Nishinaga, and I. Saito, Tetrahedron Lett., 1969, 1669.
  - ³¹⁵ T. Matsuura, K. Omura, and R. Nakashima, Bull. Chem. Soc. Jap., 38, 1358 (1965).
  - ³¹⁶ I. Saito and T. Matsuura, Tetrahedron Lett., 1070, 4987.
- ³¹⁷ T. Matsuura, A. Nishinaga, N. Yoshimura, T. Arai, K. Omura, H. Matsushima, S. Kato, and I. Saito, *Tetrahedron Lett.*, **1969**, 1673.
  - ³¹⁸ I. Saito, S. Kato, and T. Matsuura, Tetrahedron Lett., 1970, 239.
- ^{318a} For recent papers on these and related compounds see T. Matsuura, N. Yoshimura,
- A. Nishinaga, and I. Saito, Tetrahedron, 28, 4933 (1972); T. Matsuura, H. Matsushima,
- S. Kato, and I. Saito, *ibid.*, 28, 5119 (1972); I. Saito, N. Yoshimura, T. Arai, K. Omura, A. Nishinaga, and T. Matsuura, *ibid.*, 28, 5131 (1972).
- ³¹⁹ P.-S. Song and T. A. Moore, Photochem. Photobiol., 7, 113 (1968).
- ³²⁰ P.-S. Song and T. A. Moore, J. Amer. Chem. Soc., 90, 6507 (1968).
- ³²¹ J. Rigaudy, C. Deletang, and J.-J. Basselier, C.R. Acad. Sci., Ser. C, 268, 344 (1969).
- 322 J. Rigaudy, C. Deletang, and J.-J. Basselier, C.R. Acad. Sci., Ser. C, 263, 1435 (1966).
- ³²³ C. Dufraisse and R. Priou, C.R. Acad. Sci., 212, 906 (1941).
- ³²⁴ P. L. Julian, W. Cole, and G. Diemer, J. Amer. Chem. Soc., 67, 1721 (1945).
- 325 C. Dufraisse and M. Gérard, C.R. Acad. Sci., 201, 428 (1935).
- 328 C. Dufraisse and R. Priou, Bull. Soc. Chim. Fr., [5] 6, 1649 (1939).
- 327 A. Willemart, Bull. Soc. Chim. Fr., [5] 5, 556 (1938).
- 328 A. G. Davies, Organic Peroxides, Butterworths, London, 1961.

- 329 Y. Lepage, Ann. Chim. (Paris), [13] 4, 1137 (1959).
- 330 P. L. Julian, W. Cole, and E. W. Meyer, J. Amer Chem. Soc., 67, 1724 (1945).
- 331 D. W. Cameron and P. E. Schütz, J. Chem. Soc., C. 1967, 2121.
- 332 P. L. Julian and W. Cole, J. Amer. Chem. Soc., 57, 1607 (1935).
- 333 J. Rigaudy, N. C. Cohen, N. K. Cuong, C.R. Acad. Sci., Ser. C, 264, 1851 (1967).
- 334 C. Dufraisse, L. Velluz, and L. Velluz, Bull. Soc. Chim. Fr., [5] 4, 1260 (1937).
- 335 C. Dufraisse, A. Etienne, and J. Rigaudy, Bull. Soc. Chim. Fr., 1948, 804.
- 334 C. Dufraisse and J. Morgoulis-Molho, Bull. Soc. Chim. Fr., [5] 7, 928 (1940).
- 337 A. Willemart, Bull. Soc. Chim. Fr., [5] 6, 204 (1939).
- 338 C. Dufraisse, L. Velluz, and L. Velluz, C.R. Acad. Sci., 203, 327 (1936).
- 338 A. Willemart, Bull. Soc. Chim. Fr., [5] 4, 1447 (1937).
- 340 A. Étienne, Bull. Soc. Chim. Fr., 1947, 634.
- 341 A. Étienne and Y. Lepage, C.R. Acad. Sci., 236, 1498 (1953).
- 342 C. Dufraisse and L. Velluz, C.R. Acad. Sci., 211, 790 (1940).
- 343 M.- T. Mellier, Ann. Chim. (Paris), [12] 10, 666 (1955).
- 344 L. Velluz and L. Velluz, Bull. Soc. Chim. Fr., [5] 5, 192 (1938).
- 345 C. Dufraisse, L. Velluz, and R. Dumuynek, C.R. Acad. Sci., 215, 111 (1942).
- 346 D. Duveen and A. Willemart, J. Chem. Soc., 1939, 116.
- ³⁴⁷ R. Panico, Ann. Chim. (Paris), [12] 10, 695 (1955).
- 343 G. Meyer, Bull. Soc. Chim. Fr., 1970, 702.
- 348 P. de Bruyn, Ann. Chim. (Paris), [11] 20, 551 (1945).
- 350 A. Willemart, Bull. Soc. Chim. Fr., [5] 4, 510 (1937).
- 351 C. Dufraisse, C. Pinazzi, and J. Baget, C.R. Acad. Sci., 217, 375 (1943).
- 382 G. Bichet, Ann. Chim. (Paris), [12] 7, 234 (1952).
- 353 J. E. Baldwin, H. H. Basson, and H. Krauss, Jr., Chem. Commun., 1968, 984.
- 354 C. Dufraisse and L. Velluz, Bull. Soc. Chim. Fr., [5] 9, 171 (1942).
- 355 A. Étienne and J. Salmon, Bull. Soc. Chim. Fr., 1954, 1133.
- 356 L. Velluz, Bull. Soc. Chim. Fr., [5] 6, 1541 (1939).
- 357 C. Dufraisse and R. Horclois, Bull. Soc. Chim. Fr., [5] 3, 1894 (1936).
- 358 A. Willemart, Bull. Soc. Chim. Fr., [5] 4, 357 (1937).
- 350 A. Étienne and J. Weill-Raynal, Bull. Soc. Chim. Fr., 1953, 1136.
- 360 A. Étienne and C. Beauvois, C.R. Acad. Sci., 239, 64 (1954).
- 361 C. Dufraisse and R. Horclois, Bull. Soc. Chim. Fr., [5] 3, 1880 (1936).
- 362 E. J. Bowen and A. H. Williams, Trans. Faraday Soc., 35, 765 (1939).
- 383 C. Dufraisse, A. Étienne, and C. Winnick, C.R. Acad. Sci., 236, 2133 (1953).
- 384 C. Dufraisse, A. Étienne, and J. Jolly, C.R. Acad. Sci., 233, 1243 (1951).
- 385 M. Loury, Ann. Chim. (Paris), [12] 10, 807 (1955).
- 368 C. Dufraisse and R. Horclois, Bull. Soc. Chim. Fr., [5] 3, 1894 (1936).
- 387 M. Badoche, Bull. Soc. Chim. Fr., [5] 9, 393 (1942).
- 388 M. Badoche, Bull. Soc. Chim. Fr., [5] 3, 2040 (1936).
- 388 M. Badoche, C.R. Acad. Sci., 198, 1515 (1934).
- 370 C. Dufraisse and L. Velluz, Bull. Soc. Chim. Fr., [5] 3, 254 (1936).
- 371 C. Dufraisse and H. Rocher, Bull. Soc. Chim. Fr., [5] 2, 2235 (1935).
- 372 C. Dufraisse and N. Drisch, C.R. Acad. Sci., 191, 619 (1930).
- 373 C. Dufraisse and N. Drisch, C.R. Acad. Sci., 194, 99 (1932).
- 374 C. Dufraisse and M. Loury, C.R. Acad. Sci., 194, 1664 (1932).
- 375 C. Dufraisse and R. Buret, C.R. Acad. Sci., 192, 1389 (1931).
- 378 C. Dufraisse and J.-A. Monier, Jr., C.R. Acad. Sci., 196, 1327 (1933).
- 377 D. Bertin, Ann. Chim. (Paris), [12] 8, 296 (1953).
- 378 A. Willemart, Ann. Chim. (Paris), [10] 12, 345 (1929).
- 378 D. Duveen and A. Willemart, Bull. Soc. Chim. Fr., [5] 6, 1334 (1939).
- 380 J. W. Cook and R. H. Martin, J. Chem. Soc., 1940, 1125.
- 381 J. Font, F. Serratosa, and L. Vilarrasa, Tetrahedron Lett., 1970, 4105.
- 362 C. B. Allsopp, Nature, 145, 303 (1940).
- 383 L. Velluz, C.R. Acad. Sci., 206, 1514 (1938).
- 384 W. Bergmann and M. J. McLean, Chem. Rev., 28, 367 (1941).

## **ORGANIC REACTIONS**

- 385 C. F. H. Allen and J. A. van Allan, J. Org. Chem., 18, 882 (1953).
- ³⁸⁶ E. Clar and F. John, Chem. Ber., 63, 2967 (1930).
- ³⁸⁷ A. Étienne and C. Beauvois, C.R. Acad. Sci., 239, 64 (1954).
- 388 H. H. Wasserman and P. M. Keehn, J. Amer. Chem. Soc., 88, 4522 (1966).
- ³⁸⁹ W. H. Richardson and V. Hodge, J. Org. Chem., 35, 1216 (1970).
- ³⁹⁰ C. Dufraisse and J. Baget, C.R. Acad. Sci., 220, 47 (1945).
- ³⁹¹ W. Dilthey, S. Henkels, and M. Leonhard, J. Prakt. Chem. (2), 151, 97 (1938).
- 392 Y. A. Arbuzov, Russ. Chem. Rev. (Engl. Transl.), 34, 558 (1965).
- ³⁹³ A. F. A. Ismail and Z. M. El-Shafei, J. Chem. Soc., 1957, 3393.
- 394 G. Sauvage, Ann. Chim. (Paris), [12] 2, 844 (1947).
- 395 C. Dufraisse, L. Velluz, and L. Velluz, Bull. Soc. Chim. Fr., [5] 5, 600 (1938).
- ³⁹⁶ C. E. Clar, Chem. Ber., 76, 257 (1943).
- ³⁹⁷ H. Brockmann and R. Mühlmann, Chem. Ber., 81, 467 (1948).
- 398 C. F. H. Allen and A. Bell, J. Amer. Chem. Soc., 64, 1253 (1942).
- 399 T. Oritani and K. Yamashita, Agr. Biol. Chem., 34, 1821 (1970).
- 400 J. Rigaudy, J. Guillaume, and D. Maurette, Bull. Soc. Chim. Fr., 1971, 144.

⁴⁰¹ For some more recent papers on alkoxybenzenes see I. Saito, M. Imuta, and T. Matsuura, *Tetrahedron*, **28**, 5307, 5313 (1972).

⁴⁰² C. S. Foote and M. Thomas, unpublished results.

403 J. Rokach, D. McNeill, and C. S. Rooney, Chem. Commun., 1971, 1085.

⁴⁰⁴ W. R. Adams and D. J. Trecker, *Tetrahedron*, **28**, 2361 (1972). For other norbornyl olefins see E. F. J. Duynstee and M. E. A. H. Mevis, *European Polymer Journal*, **8**, 1375 (1972); C. W. Jefford, M. H. Laffer, and A. F. Boschung, J. Amer. Chem. Soc., **94**, 8904 (1972).

- 405 C. S. Foote, S. Mazur, P. A. Burns, and D. Lerdal, J. Amer. Chem. Soc., 95, 586 (1973).
- For related behavior see G. Rio, D. Bricout, and L. Lacombe, Tetrahedron Lett., 1972, 3583. 408 G. Rio and M. Charifi, Bull. Soc. Chim. Fr., 1970, 3598. The related ketone 3,4-diphenyl-
- 3-cyclopentenone reacts similarly in 80% yield.

407 R. H. Young and H. Hart, Chem. Commun., 1967, 827.

#### CHAPTER 3

# THE SYNTHESIS OF 5-HYDROXYINDOLES BY THE NENITZESCU REACTION

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## **INTRODUCTION**

The preparation of 5-hydroxyindole derivatives by the reaction of p-benzoquinones with certain enamines was suggested by the work of Nenitzescu who reported in 1929 that the parent quinone, p-benzoquinone, reacts with ethyl 3-aminocrotonate in boiling acetone to yield ethyl 5-hydroxy-2-methylindole-3-carboxylate (Eq. 1).¹ The procedure was largely ignored until the 1950s, when interest in melanin-related substances and recognition of serotonin as a 5-hydroxyindole derivative stimulated an exploration of the scope of the reaction. These investigations confirmed the mild conditions under which the reaction occurs and indicated that mono-, di-, and tri-substituted quinones react with equal facility. Most frequently the enamine component is an alkyl  $\beta$ -aminoacrylate that must have a  $\beta$ -substituent. However,  $\beta$ -aminoacrylonitriles,  $\beta$ -aminoacrylamides, and  $\beta$ -amino- $\alpha$ , $\beta$ -unsaturated ketones can also be used. Although the method is reported to give indoles in yields varying

¹ C. D. Nenitzescu, Bull. Soc. Chim. Romania, 11, 37 (1929) [C.A., 24, 110 (1930)].

from 5 to 90 %, the ease with which the reaction occurs and the availability of the reactants render it attractive even in those instances where the yield of product is low.



This particular synthetic method is now commonly known as the Nenitzescu indole synthesis. However, it should be noted that the construction of the indole nucleus by the reduction of  $o,\omega$ -dinitrostyrenes is also the discovery of the same investigator.² In this chapter the scope and limitations of the former preparative route is critically evaluated as part of a general survey of the reactions of quinones with enamines, but indole synthesis by reduction of  $o,\omega$ -dinitrostyrenes is not.

## **MECHANISM**

The formation of a 5-hydroxyindole by reaction of a p-quinone with an enamine requires the formation of a carbon-to-carbon and a nitrogen-to-carbon bond. Two mechanisms (A and B), differing in the sequence of the required bond formations, have been proposed for the Nenitzescu indole synthesis, and recent evidence indicates that the carbon-carbon bond is formed first. Inasmuch as the details of the mechanism have intrinsic value in predicting the scope and limitations of a process, examination of the evidence is warranted.

**Mechanism A.** The mechanism favored by the majority of investigators suggests initial carbon-to-carbon condensation between reactants to give hydroquinones of type  $1.^{3-5}$  The isolation of the geometric isomers 2 from typical Nenitzescu condensations is the subject of

- ³ R. J. S. Beer, H. F. Davenport, and A. Robertson, J. Chem. Soc., 1953, 1262.
- 4 G. Domschke and H. Furst, Chem. Ber., 92, 3244 (1959).
- ⁵ E. D. Bergmann, D. Ginsburg, and R. Pappo, Org. Reactions, 10, 226 (1959).

^{*} The stereochemistry about the unsaturated center in ethyl 3-aminocrotonate and its congeners is depicted as shown to maintain the spatial relationship of principal reactants and products. However, spectroscopic evidence indicates that the enamines possess the reverse geometry [G. O. Dudek and G. P. Volpp, J. Amer. Chem. Soc., 85, 2697 (1963)].

⁸ C. D. Nenitzescu, Chem. Ber., 58, 1063 (1925).

several reports,^{3, 6-14} and no less than three groups of investigators have noted the conversion of this type of hydroquinone to 5-hydroxyindoles.^{7-10, 12-14} Despite apparent unanimity of opinion about the ability of hydroquinones like 1 to function as intermediates for the 5-hydroxyindoles, disagreement exists about the manner by which the transformation occurs. (See Chart 1, p. 339.)

Only one direct conversion of a hydroquinone of type 1 to a 5-hydroxyindole has been reported.¹⁵ The transformation proceeds in about 10% yield at room temperature, and the investigators interpreted the formation of 5-hydroxyindole as evidence for a Bucherer-type reaction  $(1 \rightarrow 3 \rightarrow 4)$ . However, other workers, aware of the potential pathway, could not demonstrate its intervention with other hydroquinones of this type.⁸⁻¹¹

When the geometrical isomers 2 are treated with an oxidizing agent, e.g., a quinone, under isomerizing conditions (acetic acid), 5-hydroxyindoles result.^{8-10.12-14} Isomerizing conditions, per se, are not adequate to effect this conversion; instead 5-hydroxybenzofurans^{3.7.8} or other nonindolic products result.^{6.12} An oxidant cannot convert 2 to an indole when the medium is incapable of effecting this isomerization. Thus injection of hydroquinones 2 into competitive Nenitzescu reactions in which a quinone is available as oxidant and ethanol is the solvent does not result in the formation of the corresponding indoles.^{9.10}

These observations implicate quinones of structure 5 as more advanced intermediates in the preparation of 5-hydroxyindoles. This is supported by the isolation of the geometric isomers of such quinones from typical Nenitzescu condensations,^{9-11, 15} and their subsequent conversion into 5-hydroxyindoles.^{7, 10, 15a} Grinev and his collaborators describe the isomerization of one such geometric isomer into that of proper stereochemistry, *e.g.*, 5, by exposure to ethanol. Catalytic hydrogenation of the resulting substance then afforded the 5-hydroxyindole.⁷ A later

⁶ A. N. Grinev, V. N. Ermakova, I. A. Mel'nikova, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **31**, 2303 (1961) [*C.4.*, **56**, 10075c (1962)].

⁷ A. N. Grinev, V. N. Ermakova, and A. P. Terent'ev, Zh. Obshch. Khim., **32**, 1948 (1962) [C.A., **58**, 4498g (1963)].

⁸ D. Raileanu and C. D. Nenitzescu, *Rev. Roum. Chim.*, **10**, 339 (1965) [*C.A.*, **63**, 9903f (1965)].

88 D. Raileanu, M. Palaghita, and C. D. Nenitzescu, Tetrahedron, 27, 5031 (1971).

⁹ G. R. Allen, Jr., and M. J. Weiss, Chem. Ind. (London), 1966, 117.

¹⁰ G. R. Allen, Jr., C. Pidacks, and M. J. Weiss, J. Amer. Chem. Soc., 88, 2536 (1966).

¹¹ S. A. Monti, J. Org. Chem., 31, 2669 (1966).

¹² G. R. Allen, Jr., and M. J. Weiss, J. Org. Chem., 33, 198 (1968).

¹³ R. Littell and G. R. Allen, Jr., J. Org. Chem., 33, 2064 (1968).

¹⁴ Y. Yamada and M. Matsui, Agr. Biol. Chem., 35, 282 (1971).

¹⁵ Y. Yamada and M. Matsui, Agr. Biol. Chem., 34, 724 (1970).

^{15a} U. Kücklander, Tetrahedron, 28, 5251 (1972).



investigation confirmed this facile isomerization and demonstrated that quinone 5 rapidly cyclizes to give a carbinolamine (Chart 1).^{15a} Reduction of this intermediate by hydroquinone or the primary adduct 2 in acetic acid proceeds via the quinonimmonium cation 6 to give the 5-hydroxy-indole.^{15a} Moreover, the reduction (sodium hydrosulfite) of an equilibrated mixture derived from the geometric isomers of quinones 5 and their conjugate acids gives 5-hydroxyindoles.¹⁰

In summary, the Nenitzescu synthesis proceeds by the paths outlined in Chart 1 which involve the following stages: (1) Michael addition of the carbon terminal of the enamine triad to the quinone, (2) oxidation of the resulting hydroquinone to the quinone either by the starting quinone or the quinonimmonium intermediate 6, which is generated at a later stage, (3) cyclization of the quinone adduct 5, if in the *cis* configuration, to the quinonimmonium intermediate 6, and (4) reduction of this last intermediate to the 5-hydroxyindole by the initial hydroquinone adduct. Alternatively, the initial Michael adduct 1 may be transformed into the 5-hydroxyindole by way of a Bucherer reaction on intermediate 3. However, the evidence for this process is not compelling.

It may be noted that the initial formation of the hydroquinone is fully consistent with the chemistry of the enamines as delineated by Stork and his co-workers.¹⁶ Moreover, the elaboration of the 5-hydroxyindole from the initial adduct by an oxidation-reduction sequence parallels the mechanisms believed to be operative in the Harley-Mason synthesis of indoles from 2,5-dihydroxyphenethylamines,¹⁷⁻²¹ in the conversion of 2hydroxyphenethylamines to 5-hydroxyindoles by treatment with potassium nitrosodisulfonate,²² and in 'he conversion of 2'-aminophenylhydroquinone to carbazole by a catalytic amount of ferric chloride.²³

Mechanism B. The alternative mechanism proposed for the Nenitzescu procedure requires initial nitrogen-to-carbon condensation of the enamine and quinone.²⁴ The mechanism is compatible with certain aspects of quinone chemistry,²⁵ including the reversible nucleophilic 1,2 addition of bisulfite and hydroxide ions²⁶ and the irreversible 1,2 addition of an unsaturated oxyphosphorane to the carbonyl group of *p*-quinones.²⁷ Interception of adducts of type 8, formally derived from initial 1,2 condensation of enamine with benzoquinone or by oxidation of 3 was reported recently.^{28, 29} Submission of the carbinolamines 8 to the conditions of a typical Nenitzescu reaction failed to yield a 5-hydroxyindole derivative. However, treatment with a catalytic amount of quinone in acetic acid did afford the indole. The intermediacy of the carbinolamines in the

- 17 R. J. T. Cromartie and J. Harley-Mason, J. Chem. Soc., 1952, 2525.
- ¹⁸ J. Harley-Mason, J. Chem. Soc., 1953, 200.
- ¹⁹ J. Harley-Mason and A. H. Jackson, J. Chem. Soc., 1954, 1165.
- ²⁰ J. A. Moore and M. Rahm, J. Org. Chem., 26, 1109 (1961).
- ²¹ J. A. Moore and E. C. Capaldi, J. Org. Chem., 29, 2860 (1964).
- ²² H.-J. Teuber and O. Glosauer, Chem. Ber., 98, 2648 (1965).
- ²³ H. Stetter and M. Schwarz, Ann., 617, 54 (1958).
- ²⁴ E. A. Steck, R. P. Brundage, and L. T. Fletcher, J. Org. Chem., 24, 1750 (1959).

²⁵ Z. E. Jolles in *Chemistry of Carbon Compounds*, E. H. Rodd, Ed., Vol. III, Elsevier Publishing Co., New York, 1956, p. 714.

²⁶ (a) C. A. Bishop, R. F. Porter, and L. K. J. Long, J. Amer. Chem. Soc., 85, 3991 (1963);
(b) C. A. Bishop and L. K. J. Long, Tetrahedron Lett., 1964, 3043.

27 F. Ramirez, H. J. Kugler, and C. P. Smith, Tetrahedron Lett., 1965, 261.

28 R. Littell, G. O. Morton, and G. R. Allen, Jr., Chem. Commun., 1969, 1144.

29 R. Littell, G. O. Morton, and G. R. Allen, Jr., J. Amer. Chem. Soc., 92, 3740 (1970).

¹⁶ G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, J. Amer. Chem. Soc., 85, 207 (1963).

Nenitzescu procedure, as suggested by this experiment, proved untenable, for omission of the oxidizing agent merely afforded the hydroquinone 1. This evidence precludes mechanisms proceeding through intermediates such as 8 since these are transformed into 5-hydroxyindoles only after conversion to the hydroquinones that arise from initial carbon-carbon condensation.



SCOPE AND LIMITATIONS

The Nenitzescu synthesis has proved useful for the preparation of a variety of 5-hydroxyindole derivatives. Among them are compounds substituted variously on nitrogen, at  $C_2$ , and in the benzene ring. The 3-substituent is most often carbalkoxy but can be acyl, cyano, or carbox-amido. The 3-carbalkoxy derivatives are particularly useful because decarbalkoxylation under alkaline or acid conditions is achieved easily. The resulting 5-hydroxyindoles constitute intermediates for the biologically important tryptamines and other 3-substituted indoles. Moreover, the 5-hydroxy function of the primary product serves as an entry into a variety of 4,5-indoloquinones and 5-oxygenated 4,7-indoloquinones. The latter class is of interest because of its relation to certain derivatives of the mitomycin antibiotics.

Other nitrogen-containing heterocyclic systems, e.g., isoquinoline and tetrahydrocarbazole, may be synthesized by Nenitzescu-like reactions. A variety of oxygen-containing heterocyclic systems result from reaction of quinones with the appropriate enamine. In ensuing sections the influence exerted on the reaction by the structures of the quinone and the enamine, by the stoichiometry of the reactants, as well as the influence of solvent and certain Lewis acid catalysts is examined. Related reaction systems are also discussed.

The recent thorough study of the reaction of benzoquinone with ethyl 3-aminocrotonate (Eq. 1) constitutes a useful reference for the ensuing discussion.¹¹ Reaction of these substances gives 30% of ethyl 5-hydroxy-2-methylindole-3-carboxylate, as first noted by Nenitzescu.¹ In addition, four other products are formed: hydroquinone (25%), 1:1 and 1:2 hydroquinone-enamine adducts 9 and 11, and an oxidized 1:1 adduct, quinone 10. The 1:2 adduct (11) apparently is derived by reaction of the initial enamine with the quinone 10. Interestingly, the preceding products account for 91% of the quinone and 76% of the enamine.



Structure of the Quinone. Only p-quinones have been used in the Nenitzescu indole synthesis, and the utility of 1,4-benzoquinone and 1,4-naphthoquinone in this procedure is well documented in the literature. Moreover, the usefulness of mono-, di-, and tri-substituted benzoquinones also has been demonstrated.

The formation of three isomeric 5-hydroxyindole-3-carboxylates is possible from a monosubstituted quinone. Such a result is compatible with the mechanism presented above, and, indeed, the isolation of 4-, 6and 7-substituted 5-hydroxyindole-3-carboxylates has been reported. The circumstance in which the three possible isomers result from a single reaction has yet to be described. Nevertheless, the formation of two isomers in a given condensation is encountered frequently and, although the nature of the nitrogen substituent of the enamine has significance (see p. 353), the course of reaction largely depends upon the nature of the quinone substituent. The steric requirements and electronic character of the latter determine its influence. Toluquinone (12a) reacts with ethyl 3-aminocrotonate to give essentially a 1:1 ratio of the 6-methyl- and 7-methyl-5hydroxyindole-3-carboxylates 13a and 14a.^{10, 11, 30} However, the next higher homolog, 12b, reacts with the enamine to give the 6-isomer 13b exclusively. This result reflects the greater steric requirement of the ethyl group, which is most likely exerted at the nitrogen-to-carbon cyclization step of the reaction. In neither instance is the formation of the 4-alkyl isomer noted. Apparently the steric requirement of the quinone alkyl substituent mitigates against the condensation at C-3 necessary for the formation of this isomer. The isolation of the adduct hydroquinones 15a and 16a as the only side products in the reaction of toluquinone with the enamine supports this conclusion.^{10, 11}

When the quinone substituent is methoxy, the 7-isomer is not formed even if the condensation is conducted with ethyl 3-aminocrotonate which, from steric considerations, is most favorable to formation of the 7-isomer.



The exclusive formation of the 6-isomer from methoxybenzoquinone (Eq. 2) could reflect substituent steric requirements but is more probably the result of the strong directive influence on the site of nucleophilic addition to the quinone system, a well-established effect in quinone chemistry.³¹ This conclusion is also supported by the sole formation of the 6-isomer from 2-hydroxy-1,4-benzoquinone and ethyl 3-aminocrotonate.³² The apparently exclusive formation of the 6-isomer from the reaction of the N-methyl-substituted crotonate with benzylthioquinone (Eq. 3) appears to be the consequence of similar effects.²⁴



The haloquinones present contradictory substituent effects. Although the inductive effect of halogen would suggest formation of 4-haloindoles

³¹ H. S. Wilgus, III, E. Frauenglass, E. T. Jones, R. F. Porter, and J. W. Gates, Jr., J. Org. Chem., 29, 594 (1964).

32 R. J. S. Beer, K. Clarke, H. F. Davenport, and A. Robertson, J. Chem. Soc., 1951, 2029.

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none has been isolated. Steric requirements and mesomeric properties of the substituent favor formation of the 6-haloindoles, with the 7isomer a secondary possibility. 2-Fluoro-1,4-benzoquinone reacts with ethyl 3-aminocrotonate to form 12% of the 6-fluoro-5-hydroxyindole-3carboxylate, whereas the other haloquinones give 7-24% of mixtures of the 6- and 7-isomers.¹³ Despite a report to the contrary,³³ 2-phenyl-1,4benzoquinone also affords in low yield a mixture of the 6- and 7-phenyl isomers, the former product predominating.³⁴





The mechanism of the Nenitzescu indole synthesis predicts that the reaction could yield 4-substituted 5-hydroxyindoles by use of quinones in which electron-withdrawing substituents activate the ortho site. Indeed, initial Michael addition of ethyl 3-aminocrotonate at the ortho position has been realized with quinones monosubstituted by acetyl, carbomethoxy, or trifluoromethyl. However, the initial hydroquinone adduct from 2-acetylbenzoquinone undergoes cyclization via the acetyl group to yield an isoquinoline (see p. 368).

The hydroquinone adduct 18 is the primary reaction product from 2carbomethoxy-1,4-benzoquinone.¹² Inasmuch as it is formed under nonequilibrating conditions (boiling ethanol), the *trans* stereochemistry of the product precludes completion of the indole synthesis. However, when the adduct was treated with a catalytic amount of the initial quinone under equilibrating conditions (acetic acid), the Nenitzescu reaction to give the 4-carbomethoxyindole was completed. The apparently exclusive formation of *trans* adduct 18 under nonequilibrating conditions deserves

³³ A. N. Grinev, G. M. Borodina, G. V. Yaroslavtseva, and L. M. Alekseeva, *Khim. Geterotsikl.-Soedin.*, **1970**, 1634 [C.A., **74**, 53398v (1971)].

³⁴ J. F. Poletto and M. J. Weiss, unpublished results, cited in M. J. Weiss, G. R. Allen, Jr., G. Gibs, C. Pidacks, J. F. Poletto, and W. A. Remers, *Topics in Heterocyclic Chemistry*, R. N. Castle, Ed., John Wiley and Sons, 1969, p. 190.

comment. Presumably the stereochemistry of the Michael adduct is determined in the deprotonation of an intermediate such as 17. Although exclusive formation of the *trans* adduct is unusual, deprotonation to the isomer of stereochemistry the reverse of that required for indole synthesis is a fairly general phenomenon. Since the geometry of adducts such as 18 permits intramolecular hydrogen bonding between the carbonyl oxygen of the ester and the amino group, these adducts are probably the thermodynamically favored isomers.



The trifluoromethyl substituent exerts a strong negative inductive effect without the opposing mesomeric forces characteristic of the halogens. The former effect dominates any steric requirements that mitigate against condensation at  $C_3$  (cf. toluquinone), and the group does not offer an alternative site for nitrogen-to-carbon condensation as do the acyl and carbalkoxy groups. These features are illustrated in the reaction of 2trifluoromethyl-1,4-benzoquinone with ethyl or t-butyl 3-aminocrotonate and ethyl 3-ethylaminocrotonate (Chart 2).¹³ In each reaction the initial carbon-carbon condensation occurs at the 3 position of the quinone. The first two esters afford directly the 4-trifluoromethyl-5-hydroxyindoles in 54-62% yield. Yet, the reaction of the third ester is another example of the previously noted phenomenon whereby the hydroquinone adduct formed in a nonisomerizing medium (acetone) apparently assumes stereochemistry improper for completion of indole synthesis, for this adduct is the only isolated product (41%). However, its conversion to the indole by oxidation under equilibrating conditions (acetic acid) is extremely efficient (86%).

Certain properties of the trifluoromethyl group render it particularly useful in broadening the scope of the Nenitzescu indole synthesis. The group may be converted smoothly to methyl by reduction with lithium





CHART 2

aluminum hydride.¹³ This reduction permits the synthesis of certain 5-hydroxy-4-methylindole derivatives that are not available by a direct Nenitzescu reaction. Moreover, the directive influence of the trifluoromethyl group in conjunction with the ability to replace it by hydrogen on hydrolytic treatment provides access to 7-substituted 5-hydroxyindoles (see p. 350).

Quinones with two like substituents react as anticipated in the Nenitzescu synthesis. In particular, treatment of 2,5-dimethyl-³⁵ and 2,5dichloro-1,4-benzoquinone³⁶ with ethyl 3-aminocrotonate affords the corresponding 4,7-disubstituted 5-hydroxyindoles (Eq. 4). Similar behavior is shown by the corresponding 2,3-disubstituted quinones, which yield the 6,7-disubstituted derivatives (Eq. 5).³⁶⁻³⁸ 2,3-Dimethoxybenzoquinone gives significant amounts (24-28%) of the *trans* Michael adduct 18a as well as 23-36% of the expected 5-hydroxy-6,7-dimethoxyindole-3carboxylate.^{8a} Utilization of the 2,6-disubstituted quinones has not been

³⁵ G. R. Allen, Jr., unpublished observations.

³⁶ A. N. Grinev, I. A. Zaitsev, V. I. Shvedov, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **28**, **447** (1958) [*C.A.*, **52**, 14585c (1958)].

³⁷ H.-J. Teuber and G. Thaler, Chem. Ber., 91, 2253 (1958).

³⁶ A. N. Grinev, V. I. Shvedov, and A. P. Terent'ev, Zh. Obshch. Khim., 26, 1452 (1956) [C.A., 50, 14711b (1956)].

reported, but the formation of 4,6-disubstituted 5-hydroxyindoles is likely with these substrates.



The more interesting situation exists in quinones possessing two dissimilar substituents. The site of initial carbon-to-carbon condensation is explicable in terms of the relative electronic effects, and transformations of the 5-hydroxyindoles give indoles not readily available by other procedures. In this context, 2-chloro-5-methyl-1,4-benzoquinone (**19a**) is a noteworthy example, for, although neither substituent alone directs condensation to the adjacent position in the monosubstituted quinones, the disubstituted quinone and t-butyl 3-aminocrotonate give, in 51 % yield, only the 5-hydroxyindole-3-carboxylate **20a**.³⁹ The conversion of this indole ester to 5-methoxy-2,7-dimethylindole by methylation, acidcatalyzed decarbalkoxylation, and reductive removal of the chlorine establishes the location of the substituents and suggests a useful synthesis of 7-alkylindole derivatives.

More recent work has shown that the same quinone, 19a, behaves similarly with ethyl 3-aminopentenoate (Eq. 6) and that the homologous



ethyl quinone 19b reacts in parallel fashion with *t*-butyl 3-aminocrotonate to form the indole 20b.⁴⁰

The usefulness of certain substituted trifluoromethyl-1,4-benzoquinones in the Nenitzescu procedure has also been studied.¹³ The results indicate the dominant role of the trifluoromethyl group in determining the course of the reaction. Moreover, as indicated above, the reaction products serve as starting materials for the preparation of other 5-hydroxyindoles which are not readily available by alternative procedures. 2-Chloro-5-trifluoromethylbenzoquinone clearly illustrates these features, for with ethyl 3-aminocrotonate it gives the 7-chloro-4-trifluoromethyl derivative 21 in 74% yield. Acid treatment of this last substance affords 7-chloro-5hydroxy-2-methylindole, which is not accessible by conventional indole syntheses.



⁴⁰ J. F. Poletto, G. R. Allen, Jr., A. E. Sloboda, and M. J. Weiss, *J. Med. Chem.*, **16**, 757 (1973).

The control by the trifluoromethyl group on the course of the reaction is also shown by the isomeric 2-chloro-3-trifluoromethylbenzoquinone which furnishes the 6-chloro-7-trifluoromethylindole 22 in 78% yield. Acid treatment of this indole gives 6-chloro-5-hydroxy-2-methylindole; however, this substance is available more conveniently by reaction of 2-chlorobenzoquinone and ethyl 3-aminocrotonate.¹³ The directive influence of the trifluoromethyl group also competes with the strongly electron-donating methoxyl group. Thus 2-methoxy-5-trifluoromethyl-1,4-benzoquinone and ethyl 3-aminocrotonate give 25% each of the two possible isomeric indoles (Eq. 7).



The behavior of 2-bromo-5-methoxybenzoquinone toward t-butyl 3aminocrotonate also reflects the strong directive influence that the methoxy group exerts on the site of nucleophilic addition to the quinone. The product is a bromine-free t-butyl  $\alpha$ -hydroquinonyl- $\beta$ -aminocrotonate in low yield, and it is accompanied by significant quantities of 2-bromo-5-methoxyhydroquinone.⁴¹ The former product arises from addition of the aminocrotonate at the 2 position and loss of bromide ion in the ensuing aromatization process.



Quinones having three substituents have attracted little study. However, a report on the reaction of the hydroxyquinone 23 with ethyl 3aminocrotonate suggests orthodox behavior inasmuch as the completely substituted indole resulted.³² 1,4-Naphthoquinone reacts with ethyl 3-



⁴¹ J. F. Poletto, unpublished observations.

aminocrotonate to give the benz[g]indole-3-carboxylate.⁴² Numerous related reactions have been described in the literature, and the yields (50-60%) recorded for reactions of ethyl 3-aminocrotonate and its congeners with naphthoquinone are usually superior to those reported with benzoquinone. This observation is understandable within the context of the mechanism of the Nenitzescu procedure. Fusion of the benzo ring onto *p*-quinone eliminates the possibility for certain competing reactions available in the benzoquinone series, the most obvious of which is the interception of a quinone adduct such as 10 by a second molecule of ester to form a hydroquinone such as 11 (see p. 344).



The reaction of ethyl 3-aminocrotonate with o-quinones has been investigated only in a limited sense. The tetrahalo-o-quinones 24 give relatively unstable 1:1 adducts.⁴³ When treated with hydrogen chloride, these adducts are transformed into the indole-3-carboxylates 25, presumably via the intermediate shown. It is clear that, despite the formal similarity of reactants and products, the usual Nenitzescu mechanism is not operative.



⁴² A. N. Grinev, N. K. Kul'bovskaya, and A. P. Terent'ov, *Zh. Obshch. Khim.*, **25**, 135 (1955) [*C.A.*, **50**, 4903g (1956)].

43 W. Ried and P. Weidemann, Chem. Ber., 102, 2684 (1969).

The parent o-benzoquinone presents more interesting possibilities. In addition to the mode of reaction observed with the tetrahaloquinones, the possibility for competitive 1,4 and 1,6 Michael additions exists. Although 1,4 addition would presumably terminate in the mono adduct, 1,6 addition could result in the formation of the interesting 7-hydroxyindole-3-carboxylate. Experiments with o-quinone to distinguish between the possibilities have yet to be performed.



Structure of the Enamine. The general utility of  $\beta$ -aminoacrylates, acrylamides, and acrylonitriles for indole synthesis by the Nenitzescu procedure was indicated in the Introduction. However, these substances also require a  $\beta$ -substituent (alkyl, phenyl, alkoxy, or carbalkoxy).  $\beta$ -Amino- $\alpha$ , $\beta$ -unsaturated ketones react with *p*-quinones to give 3-acyl-5-hydroxyindoles. Substitution on the terminal carbon of the enamine triad by an electron-withdrawing group seems required, for enamines lacking this feature give nonindolic products on reaction with quinones. The dominant role of the structure of the quinone in determining the site(s) of initial carbon-to-carbon condensation and, as a consequence, the location of the substituents in the 5-hydroxyindoles was discussed earlier. It was noted that the structure of the enamine ester can exert a secondary effect in determining the course of the Nenitzescu procedure. In this section the dependence of the structure of the product upon that of the enamine is discussed.

The reaction of toluquinone (12a) with ethyl 3-aminocrotonate and a series of ethyl 3-alkylaminocrotonates clearly illustrates the influence of the N-alkyl substituent upon the formation of isomeric 5-hydroxyindoles. Although toluquinone and the unsubstituted aminocrotonate give 6-methyl- and 7-methyl-5-hydroxyindole-3-carboxylate, 13a and 14a, in essentially equal amounts,^{10,11,30} replacement of an amino hydrogen atom with a methyl group increases the ratio of 6-isomer/7-isomer to 2.^{i0,30}

Lengthening the nitrogen alkyl group to ethyl, *n*-propyl, and *n*-butyl results in a precipitous decline of the 7-isomer, the ratio of 6-isomer/7-isomer rising to 10-20 to  $1.^{10, 30}$  This influence is steric, and evidence indicates that the effect is exerted in the second stage of the Nenitzescu synthesis, *i.e.*, the cyclization of the quinone adduct, which involves the condensation of the nitrogen onto the quinone carbonyl group.



The reaction of toluquinone with ethyl 3-isopropylaminocrotonate is a specific illustration of this effect. The products are ethyl 1-isopropyl-2,6dimethyl-5-hydroxyindole-3-carboxylate and the *trans* isomer 26 of the hydroquinone adduct that would serve as the precursor of the 7-methyl isomer 28.¹⁰ However, isomerization of the *trans* isomer under oxidizing conditions fails to give 28. The excessive spatial requirements of the adjacent alkyl groups, including the bulky isopropyl chain, in the indole 28 apparently preclude its formation by cyclization of 27.



Numerous alkyl 3-aminocrotonates possessing other substituents on nitrogen have been used in the Nenitzescu synthesis. In general, the reaction of these enamines with benzoquinone parallels that of the parent substance. For example, aminocrotonates possessing N-alkyl groups substituted by carbethoxy,¹ dimethylamino,²⁴ cyano,⁴⁴ and hydroxy⁴⁵⁻⁴⁷ afford the corresponding 1-substituted alkyl-5-hydroxyindoles. The anticipated behavior also is observed when the nitrogen substituent is cyclohexyl,³⁶ phenyl,^{45, 48} substituted phenyl^{45, 46, 48, 49} (including certain *ortho*-substituted derivatives),^{45, 46, 48} benzyl,^{4, 24, 45, 46, 50-52} and phenethyl.⁵¹ The reaction of ethyl 3-(*p*-chloroanilino)crotonate with 1,4-naphthoquinone constitutes an interesting exception. 5-Acetoxy-4-hydroxybenz[g]indole (30).⁵³ Products similar to the 4,5-dioxygenated derivative 29 have been isolated in the indole series (see p. 384). The pathway postulated for the formation of these substances suggests that 29 should possibly be reformulated as a 4-acetoxy-5-hydroxybenz[g]indole.



In addition to the 3-aminocrotonates, other  $\beta$ -amino- $\beta$ -substituted acrylates can be used as the enamine component in the Nenitzescu procedure. Examples are the  $\beta$ -aminoacrylates containing  $\beta$ -ethyl,^{10,40}

⁴⁴ A. N. Grinev, N. E. Rodzevich, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **27**, 1690 (1957) [*C.A.*, **52**, 3762b (1958)].

⁴⁵ A. N. Grinev, V. N. Ermakova, E. Vrotek, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **29**, 2777 (1959) [*C.A.*, **54**, 10992d (1960)].

⁴⁴ A. N. Grinev, V. I. Shvedov, and I. P. Sugrobova, Zh. Obshch. Khim., **31**, 2298 (1961) [C.A., **56**, 4710d (1962)].

47 G. R. Allen, Jr., and M. J. Weiss, J. Med. Chem., 10, 23 (1967).

⁴⁸ A. N. Grinev, V. I. Shvedov, and E. K. Panisheva, *Zh. Org. Khim.*, **1**, 2051 (1965) [*C.A.*, **64**, 9669e (1966)].

49 F. Eiden and U. Kücklander, Arch. Pharm., 304, 57 (1971).

⁵⁰ W. Werner, Arch. Pharmaz., 305, 350 (1972).

⁵¹ F. A. Trofimov, V. I. Nozdrich, A. N. Grinev, and V. I. Shvedov, *Khim. Farm. Zh.*, 1 22 (1967) [*C.A.*, **68**, 59396r (1968)].

52 S. N. Betkerur and S. Siddappa, J. Chem. Soc., C, 1967, 296.

53 U. Kücklander, Tetrahedron Lett., 1971, 157.

 $\beta$ -n-propyl,⁵⁴ or  $\beta$ -n-heptadecyl⁵⁴ substituents, all of which furnish the corresponding 2-alkyl-5-hydroxyindole-3-carboxylates (Eq. 8). Moreover, crotonates possessing a carbalkoxy substituent on the terminal carbon give the usual product (see p. 358).⁵¹ Similarly, ethyl  $\beta$ -amino- $\beta$ -ethoxy-acrylate reacts with benzoquinone to yield 26% of a 2-ethoxyindole.³ This reaction constitutes the first stage of a potentially useful oxindole synthesis, for treatment of the ethoxyindole with mineral acid affords 5-hydroxyoxindole.



Limited studies with alkyl  $\beta$ -aminocinnamates suggest their general utility for the preparation of 2-phenylindole derivatives.^{8, 55} The reaction of ethyl  $\beta$ -aminocinnamate with benzoquinone also has significance with respect to the mechanism of the Nenitzescu reaction. If the reaction is conducted in chloroform or benzene, the products are the 1:1-hydroquinoid 31 and the 2:1-quinoid 33 adducts, as well as hydroquinone.⁸ The oxidized adduct, quinone 33, apparently results from oxidation of 31 to the quinone adduct 32, reaction of this last substance with ethyl  $\beta$ aminocinnamate and oxidation. The isolation of an approximate double equivalence of hydroquinone suggests that benzoquinone serves as the required oxidant and that its redox potential is appreciably greater than

⁵⁴ A. N. Grinev, V. N. Ermakova, and A. P. Terent'ev, Zh. Obshch. Khim., **31**, 490 (1961) [C.A., **55**, 22286b (1961)].

⁵⁵ S. N. Betkerur and S. Siddappa, J. Chem. Soc., C, 1968, 1795.

those of quinone 32 or 33. Treatment of the adduct 31 with a catalytic quantity of benzoquinone in acetic acid gives the 2-phenylindole 34 as predicted by the mechanism. However, the preparation of the phenylindole is achieved more conveniently by mixing the original reactants in acetic acid. Interestingly, thermolysis of the hydroquinoid adduct 31 gives 89% of the lactone 35.



Another study indicates that substituted aminofumarates react with benzoquinone to afford 21-90% of N-substituted 5-hydroxyindole-2,3-dicarboxylates (Eq. 9).⁵⁶ Saponification and decarboxylation furnish the 2,3-unsubstituted indoles and illustrate an indirect preparation of such derivatives by the Nenitzescu procedure.

Ethyl 3-amino-4,4,4-trifluorocrotonate fails to react with benzoquinone and 2-trifluoromethyl-1,4-benzoquinone.³⁵ However, it does react with 2-carbomethoxy-1,4-benzoquinone, the initial Michael adduct cyclizing to give the 2-aminodihydrobenzofuran  $36.^{35}$  This reaction appears to be more rapid than the oxidation of the Michael adduct that is required for indole formation. Studies with related alkyl  $\beta$ -substituted



 $\beta$ -aminoacrylates R'C(NH₂)=CO₂R where R' = CCl₃ or S-alkyl have yet to be reported.



The indirect preparation of 2-unsubstituted indoles by the Nenitzescu reaction was noted above (Eq. 9). The reaction of benzoquinone with 4anilino-3-buten-2-one constitutes an interesting example of the attempted direct preparation of such a derivative. Although three reaction paths are available, only the product of path a is isolated.⁵⁷ The reaction of ethyl  $\beta$ -(n-butylamino)acrylate, which is available from n-butylamine and ethyl propiolate,⁵⁸ with benzoquinone and its derivatives apparently has not been studied.

The reaction of alkyl  $\alpha$ -substituted- $\beta$ -aminoacrylates with benzoquinones is significant despite their inherent inability to produce 5hydroxyindoles. The reported isolation of the Michael adduct 37 from the interaction of benzoquinone and ethyl 3-amino-2-methylcrotonate constituted the earliest key to the mechanism of the Nenitzescu reaction.³ However, a subsequent investigation of the reaction of this enamine with 2,3-dimethoxybenzoquinone suggests that assignment of structure 37 to the product derived from benzoquinone is probably erroneous. Spectroscopic evidence indicates that the material resulting in 46% yield from

⁵⁷ G. Domschke, personal communication.

⁵⁸ R. Huisgen, K. Herbig, A. Siegl, and H. Huber, Chem. Ber., 99, 2526 (1966).



interaction of ethyl 3-amino-2-methylcrotonate and the dimethoxybenzoquinone is a mixture of isomeric dihydrobenzofuranols.^{8a} In the absence of similar experimental data for 37, the alternative dihydrobenzofuranol structure appears more reasonable. Interestingly, diethyl aminomethylenemalonate,  $H_2NCH=C(CO_2Et)_2$ , and ethyl 3-acetamidocrotonate,  $AcNHC(Me)=CHCO_2Et$ , do not react with benzoquinone.³



The previous discussion has emphasized the preparation of alkyl indole-3-carboxylates. However, the Nenitzescu procedure also may be adapted to the preparation of indolyl-3-carbonitriles,⁸ carboxamides,⁶ and

ketones.^{38, 44, 48, 59-62} Benzoquinone reacts with 3-aminocinnamonitrile to give 5-hydroxy-2-phenylindole-3-carbonitrile.⁸



The preparation of indole-3-carboxamides is illustrated by the reaction of benzoquinone with 3-methylaminocrotonanilide, which gives 5hydroxy-1,2-dimethylindole-3-carboxanilide.⁶ The attempt to extend this reaction to 3-amino-, 3-ethylamino-, and 3-benzylamino-crotonanilide was unsuccessful. The process stops at the hydroquinones formed by Michael addition of the enamines to benzoquinone.⁶ These products have significance with respect to the mechanism of the procedure, for acid treatment purportedly gives the 3-acyloxindoles (Eq. 10). Evidence for the oxindole structure is not convincing, however, and formulation as the isomeric 5hydroxybenzofuran is more reasonable. In any event, these experiments again illustrate the inadequacy of isomerizing conditions alone for the conversion of the initial Michael adducts to the 5-hydroxyindoles that is characteristic of the Nenitzescu procedure, and they also emphasize the necessity for an oxidant.

The preparation of 5-hydroxyindolyl-3-ketones by reaction of quinones with enamines of acetylacetone has been studied extensively by Grinev and his collaborators.⁶⁰⁻⁶³ The procedure is complicated by the appearance of benzofuranyl-3-ketones either as co-products or as the exclusive product. The Russian workers have correlated the structure of the product with the basicity of the amine from which the enamine is derived. Those enamines obtained from highly basic amines ( $pK_b$  3-3.4) react with benzoquinone to give benzofurans. Enamines derived from amines of medium basicity ( $pK_b$  4.6-5) give mixtures of the indole and benzofuran ketones, whereas those prepared from less basic arylamines ( $pK_b$  8-10) furnish the indole derivative only. The enamines of acetylacetone derived from *p*-bromo- and *p*-nitro-aniline fail to react with benzoquinone.

⁶³ A. N. Grinev, L. A. Bukhtenko, and A. P. Terent'ev, Zh. Obshch. Khim., **29**, 945 (1959) [C.A., **54**, 1482b (1960)].

⁵⁹ G. Domschke and H. Olemann, J. Prakt. Chem., 311, 786 (1969).

⁴⁰ A. N. Grinev, V. I. Shvedov, and A. P. Terent'ev, Zh. Obshch. Khim., **26**, 1449 (1956) [C.A., **50**, 14710i (1956)].

⁴¹ A. N. Grinev, V. L. Florent'ev, V. I. Shevdov, and A. P. Terent'ev; Zh. Obshch. Khim., **30**, 2311 (1960) [C.A., **55**, 8430c (1961)].

⁶² A. N. Grinev, V. I. Shevdov, and I. P. Sugrobova, Zh. Obshch. Khim., **31**, 2298 (1961) [C.A., **56**, 4710d (1962)].



It appears that the nature of the quinone also influences the reaction path. Benzoquinone reacts with 4-amino-3-penten-2-one and its N-phenyl derivative to furnish significant quantities of the indolic product, but 2,3-dichloro-1,4-benzoquinone reacts with these enamines to give only the 6,7-dichlorobenzofuran. 2,3-Dimethyl-1,4-benzoquinone and 4-methylamino-3-penten-2-one react to form only the indolic product, whereas this enamine reacts with benzoquinone and 2,3-dichloro-1,4-benzoquinone to give only the benzofuran and 6,7-dichlorobenzofuran, respectively.



Reaction of benzoquinones and the enamines derived from cyclohexane-1,3-diones provides access to 6-hydroxy-4-ketotetrahydrocarbazoles.²⁹ The scope of this procedure has not been investigated thoroughly, but the preparation of the 6-hydroxy-4-keto-7-methoxytetrahydrocarbazoles by reaction of 2-methoxy-1,4-benzoquinone with the enamines derived from cyclohexane-1,3-dione and dimedone (5,5-dimethylcyclohexane-1,3-dione) illustrates its potential. Moreover, 2-carbomethoxy-1,4benzoquinone and the dimedone derivative react to give the tetrahydrocarbazolecarboxylic ester as one principal product. An important distinction exists between the reaction of this quinone with ethyl 3-aminocrotonate (p. 347) and the cyclic enamine. The initially formed Michael adduct assumes the improper geometry with the former substance, thus precluding completion of indole synthesis. The Nenitzescu process is completed only after isomerization of the initial adduct under oxidizing conditions.¹² In contrast, the initial adduct from the enamine of the cyclohexane-1,3-dione must assume the proper geometry, a consequence of which is the observed formation of the heterocycle.



The reaction of the trifluoromethylbenzoquinones with the cyclic enamines is complex in that the choice of solvent and, to some degree, temperature and length of reaction determine the product structure. The



 $\mathbf{R} = \mathbf{H}, \mathbf{C}\mathbf{I}; \ \mathbf{R} = \mathbf{H}, \mathbf{M}\mathbf{e}$ 

effect of these experimental parameters is examined more extensively in a subsequent section (see p. 383), but it may be indicated that selection of appropriate conditions with trifluoromethylbenzoquinone gives either the tetrahydrocarbazolecarboxylic acid or the trifluoromethyltetrahydrocarbazole.²⁹ The formation of the former substance apparently involves the intermediacy of the latter.

The reaction of the 3-amino-2-cyclohexenones with benzoquinone or toluquinone apparently has little preparative value, since several products result.²⁹ The complexity of the reaction profile in these examples may derive in part from the formation of 3,4-dihydro-8-hydroxy-1(2H)-dibenzofuranones, *e.g.*, 38, since concomitant formation of a 5-hydroxy-benzofuran and a 5-hydroxyindole was noted in the reaction of benzo-quinone with the enamine of acetylacetone (p. 361).⁶⁰ The possibility of isomer formation is an added complication with toluquinone.



A 3-indolyl phenyl ketone has been prepared by the reaction of benzoquinone and the  $\alpha$ -aminoacrylate 39 derived from ethyl benzoylpyruvate.⁵⁹



The preparation of 4-ketotetrahydrocarbazoles above represents a special situation in which the 2- and 3-substituents of the enamine component are joined to form a carbocycle. Utilization of the Nenitzescu procedure for the preparation of 2,3-dihydropyrrolo[1,2-a]indoles, which have importance because of their relation to the mitomycin antibiotics, illustrates the preparation of indoles from enamines wherein the substituent on nitrogen and the  $\beta$ -substituent form a heterocycle.^{14.15}

Reaction of 2-carbethoxymethylenepyrrolidine (40) with 2 equivalents of benzoquinone in the presence of acetic acid gives ethyl 7-hydroxy-2,3dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate in 44% yield. The similar reaction with 2 equivalents of toluquinone gives a mixture of the 5- and 6-methyl derivatives in 30% total yield. Surprisingly, the 5-methyl product predominates in a 3:1 ratio in the latter reaction. This observation constitutes an apparent contradiction to the isomer ratios seen when a series of 3-alkylaminocrotonates react with toluquinone (p. 353). In particular, reaction of this quinone with those alkylaminocrotonates in which the alkyl group is ethyl, *n*-propyl, isopropyl, and *n*-butyl gives only minute quantities of that isomer in which the methyl group is situated *peri* to the N-alkyl group.

In this connection it is noteworthy that the mechanism of the Nenitzescu synthesis suggests that the initial carbon-to-carbon condensations leading to the 5- and 6-methylpyrrolo[1,2-a] indoles should proceed with equal facility, and no factors detrimental to the completion of the synthesis of the 6-methyl derivative are evident.



The mechanism of the Nenitzescu synthesis has also been studied by utilizing the reactants of Eq. 11. Molar equivalents of 40 and toluquinone react in methanol containing acetic acid to give the isomeric hydroquinones (Chart 3). Addition of an equivalent of benzoquinone effects oxidation of these hydroquinones to the corresponding quinones, which give the pyrrolo[1,2-a]indole derivatives, apparently by reduction of the intermediate quinonimmonium species. Reaction of 2 molar equivalents of toluquinone with the enamine in methanol (no acetic acid present) stops at the quinone adduct; toluhydroquinone also results. This observation suggests that the geometry about the double bond in the quinone adduct is improper for completion of pyrrolo[1,2-a] indole synthesis and indicates that equilibration to the isomer with the necessary stereochemistry cannot be effected in the usual organic solvents. If acetic acid is added to such a reaction solution, the pyrrolo[1,2-a] indoles and toluquinone result. This experiment indicates that acetic acid isomerizes the guinone adduct by protonation at the terminal carbon of the enamine triad and subsequent deprotonation.^{58, 64, 65} Cyclization of the quinone having proper stereochemistry about the unsaturated center then leads to the quinonimmonium species whose reduction affords the products. The appearance of toluquinone at the end of the reaction indicates that toluhydroquinone can serve as reductant in the final stage.

⁶⁴ K. Herbig, R. Huisgen, and H. Huber, Chem. Ber., 99, 2546 (1966).

⁶⁵ S. Toppet, E. van Loock, G. L'abbé, and S. Smets, Chem. Ind. (London). 1971, 703.



Chart 3

The reaction of 2-cyanomethylenepyrrolidine with toluquinone also has been studied as an entry into the pyrrolo[1,2-a]indole system. This enamine and 2 molar equivalents of the quinone in methanol containing acetic acid give 70% of the isomeric Michael adducts in the quinone oxidation state (Chart 4).¹⁴ This result contrasts sharply with the direct formation of the pyrrolo[1,2-a]indole system when 2-carbethoxymethylenepyrrolidine is the enamine component, and an explanation for this divergent behavior has not been advanced.

The original investigators found that the pyrrolo[1,2-a]indoles could be prepared in low yield by treatment of the isolated quinones with aluminum amalgam (up to 30 hours at  $50-60^{\circ}$ ), sodium borohydride, or lithium in liquid ammonia for 1 hour at  $-35^{\circ}$ .¹⁴ Under these conditions the quinones are transformed first into the corresponding hydroquinones. Inasmuch as small quantities of the pyrrolo[1,2-a]indoles ultimately result, intervention of a Bucherer reaction was invoked to explain this result.¹⁴



## PREPARATION OF OTHER HETEROCYCLIC SYSTEMS

Although the most widely documented use of the Nenitzescu procedure is in the preparation of 5-hydroxyindoles, other heterocyclic systems can be prepared by the method, as shown by the formation of benzofurans in several reactions. The preparation of this and other heterocyclic systems is examined in this section. The nature of the heterocyclic product is largely determined by the structure of the enamine and, to a lesser extent, that of the quinone. Dialkylaminocrotonates^{66, 67} and  $\beta$ -(diethylamino)vinyl ketones⁶⁷ react with benzoquinone to give the corresponding benzofurans. A rigorous comparison of the efficiency of this procedure with the Lewis acid-catalyzed reaction of quinones with 1,3dicarbonyl systems for the preparation of such benzofurans apparently

⁶⁶ G. Domschke, J. Prakt. Chem., 32, 140 (1966).

⁶⁷ F. A. Trofimov, T. I. Mukhanova, A. N. Grinev, and V. I. Shvedov, *Zh. Org. Khim.*, **3**, 2185 (1967) [C.A., **68**, 68809e (1968)].

has not been made.⁶⁸ However, it appears that the enamine process offers some advantage in that it permits the preparation of the 2-unsubstituted derivatives of benzofuran, a result not realized with the former procedure.



 $\mathbf{R} = \mathbf{H}$ , alkyl;  $\mathbf{R}' = \mathbf{a}$ lkoxy, alkyl, aryl

Enamines derived from secondary amines and aldehydes or alicyclic ketones react with quinones to furnish 2-amino-2,3-dihydro-5-hydroxybenzofurans.⁶⁹⁻⁷¹ These condensations apparently are sensitive to the same substituent effects in the quinone that determine isomer formation in the Nenitzescu indole synthesis.⁷² Strong electron-donating substituents in the quinone favor formation of the 6-substituted isomer, whereas electron-withdrawing groups give predominantly the 7-substituted isomer. In the latter instance excessive steric requirements apparently preclude the formation of the 4-isomer.



The preparation of 5-hydroxyindole-2,3-dicarboxylates by the reaction of N-substituted aminofumarates with benzoquinone was noted earlier (Eq. 9, p. 358). Surprisingly, the reaction of this quinone with diethyl aminofumarate proceeds uniquely to give the coumarin.⁷³ The formation

- ⁷¹ K. Ley and R. Nast, Angew. Chem., Int. Ed. Engl., 6, 174 (1967).
- 78 G. R. Allen, Jr., J. Org. Chem., 33, 3346 (1968).
- ⁷³ G. Domschke, Chem. Ber., 98, 2920 (1965).

⁶⁸ C. A. Giza and R. L. Hinman, J. Org. Chem., 29, 1453 (1964), and references cited therein.

^{**} K. C. Brannock, R. D. Burpitt, H. E. Davis, H. S. Pridgen. and J. G. Thweatt, J. Org. Chem., 29, 2579 (1964).

⁷⁰ G. Domschke, J. Prakt. Chem., [4] 32, 144 (1966).

of the 7- and 8-methyl homologs of this coumarin in the reaction of toluquinone with diethyl aminofumarate indicates that the behavior of this enamine toward benzoquinones is general.⁷⁴



Isoquinoline derivatives can also be prepared by the Nenitzescu procedure. For example, 2-acetyl-1,4-benzoquinone reacts with the ethyl and t-butyl esters of 3-aminocrotonic acid to give the 4-isoquinolinecarboxylates.¹² Reaction of the ethyl ester with 2-carbomethoxy-1,4-benzoquinone constitutes an indirect preparation of an isoquinoline derivative, because the primary product 18 cyclizes in acetic acid to give the isoquinolone



(Eq. 12). If an oxidant, such as the starting quinone, is present, the isoquinoline is accompanied by an equivalent yield of the indole derivative (p. 347).¹² Each example shows that for isoquinoline synthesis to take place the substituent in the quinone must direct the initial Michael condensation to the adjacent carbon atom and must offer a site for the intramolecular cyclization that can compete with the Nenitzescu cyclization.

⁷⁴ G. R. Allen, Jr., and J. F. Poletto, unpublished results.

The preparation of a tetrahydrocarbazolecarboxylic ester by reaction of 2-carbomethoxy-1,4-benzoquinone with 3-amino-5,5-dimethyl-2-cyclohexenone was noted on p. 362. Although the carbazole derivative is a significant product, a phenanthridinedione, possibly 41 which could arise from cyclization of the amino group in the Michael adduct onto the quinone substituent, is the major product.



Tetrasubstituted o-quinones, e.g., tetrabromo- and tetrachloro-oquinone, 9,10-phenanthrenedione, and chrysoquinone, react with the enamines of aldehydes and alicyclic ketones to give 2,3-benzo-1,4dioxenes of partial formula 42.^{75.76} These products are the formal result of a 4 + 2 cycloaddition; the reactions of o-quinones with olefins⁷⁷⁻⁸¹ and ketenes^{82.83} constitute earlier precedents for this reaction path.



## **RELATED REACTION SYSTEMS**

Quinone Imides and Enamines. Quinone imides are analogs of benzoquinones, and their electrophilic character suggests that reaction with enamines would constitute a potentially general synthesis of 5aminoindoles, 6-amino-1,2,3,4-tetrahydrocarbazoles, and related compounds. This possibility was first recognized by Kuehne, who found that 1-pyrrolidino- and 1-hexamethyleneimino-cyclohexene react exothermically with quinonedibenzenesulfonimide.⁸⁴ After addition of mineral

- ⁷⁵ W. Ried and E. Torok, Naturwiss., 51, 265 (1964).
- ⁷⁶ W. Ried and E. Torok, Ann., 687, 187 (1965).
- 77 A. Schönberg and A. Mustafa, J. Chem. Soc., 1944, 387.
- 78 A. Schönberg and A. Mustafa, J. Chem. Soc., 1945, 551.
- 79 A. Schönberg and A. Mustafa, J. Chem. Soc., 1947, 997.
- ⁸⁰ A. Schönberg, N. Latif, P. Moubasher, and W. I. Awad, J. Chem. Soc., 1950, 374.
- ⁸¹ L. Horner and H. Merz, Ann., 570, 89 (1950).
- ⁸² W. Reid and W. Radt, Ann., 676, 110 (1964).
- ⁸³ W. Reid and W. Radt, Ann., 688, 170 (1965).
- ⁸⁴ M. E. Kuehne, J. Amer. Chem. Soc., 84, 837 (1962).

acid the 6,9-bis-benzenesulfonyl derivative of 6-amino-1,2,3,4-tetrahydrocarbazole results. These transformations and the suggested mechanism are shown in Chart 5.



The preparation of 5-aminoindoles by this procedure has only a formal resemblance to the Nenitzescu reaction. The enamine triad does not require the usual electron-withdrawing group on the terminal carbon, and ring closure occurs by simple nucleophilic addition to yield a 2-aminoindoline which undergoes loss of the amino group derived from the enamine on treatment with acid. These features of the 5-aminoindole synthesis are comparable to the preparation of 2-aminodihydrobenzofurans (p. 367), which can be converted to benzofurans on acid treatment.

Domschke and his co-workers extended the initial observations of Kuehne to include the reaction of benzoquinone-bisdimethylsulfamoylimide with a variety of enamines.⁸⁵ In each example the quinone imide reacts with the enamine to give a 2-aminoindoline which is difficult to isolate (Chart 6). Acid treatment furnishes the corresponding indole.

⁸⁵ G. Domschke, G. Heller, and U. Natzeck, Chem. Ber., 99, 939 (1966).



The utility of benzoquinone-bisdimethylsulfamoylimide for the preparation of the 6,9-bisdimethylsulfamoyl derivative of 6-amino-1,2,3,4-tetrahydrocarbazole and certain congeners was also illustrated. The results suggest that the bisdimethylsulfamoylimide is superior to the dibenzenesulfonimide for synthetic purposes, since the yield of tricyclic derivatives (50-70%) is clearly greater with the former reagent.

Quinone Imides and Active Methylene Compounds. The preparation above of indoles by reaction of enamines with quinone imides was suggested by the earlier studies on the chemistry of these electrophilic species by Adams and his co-workers.⁸⁶⁻⁹² The reaction of quinone imides with active methylene compounds, part of this study, closely parallels the first stage of the Nenitzescu procedure. Cyclization of the resulting substituted p-phenylenediamine, followed by aromatization with loss of water, gives derivatives of 5-aminoindoles.



Benzoquinonedibenzimide (R = COPh),^{86.91} benzoquinonedimethanesulfonimide  $(R = SO_2Me)$ ⁸⁹ benzoquinonedibenzenesulfonimide (R =benzoquinone-bisdimethylsulfamoylimide SO₂Ph),^{87,91} and  $(\mathbf{R} =$ SO₂NMe₂)⁸⁹ have been used in such reactions. The reported reactions of these quinone imides with active methylene compounds proceed quite efficiently and seem to provide little basis for selection from among the group. However, the original investigators indicate that complex side reactions are normally not observed with benzoquinonedibenzimide (R = COPh).⁹¹ The ease of removal of the substituents on nitrogen in the final product is also an important consideration for synthetic purposes in the selection of the appropriate quinone imide. The dibenzimide ( $\mathbf{R} =$ COPh) and bisdimethylsulfamoylimide ( $R = SO_2NMe_2$ ) are clearly superior in this regard as the discussion on p. 371 illustrates. Thus the dibenzimide appears to be the preferred reactant, with the bisdimethylsulfamoylimide an attractive alternative.

A variety of active methylene compounds has been used. Acetylacetone, benzoylacetone, diethyl malonate, ethyl acetoacetate, ethyl benzoylacetate, dibenzoylmethane, 2-carbethoxycyclopentanone, 2-carbethoxycyclohexanone, 2-carbethoxy-5-methylcyclohexanone, and 5,5dimethyl-1,3-cyclohexanedione are illustrative. In general, a catalytic

- 87 R. Adams and D. C. Blomstrom, J. Amer. Chem. Soc., 75, 3403 (1953).
- 88 R. Adams and W. P. Samuels, Jr., J. Amer. Chem. Soc., 77, 5375 (1955).
- 89 R. Adams and W. P. Samuels, Jr., J. Amer. Chem. Soc., 77, 5383 (1955).
- ⁹⁰ R. Adams and L. Whitaker, J. Amer. Chem. Soc., 78, 658 (1956).
- ⁹¹ R. Adams, L. M. Werbel, and M. D. Nair, J. Amer. Chem. Soc., 80, 3291 (1958).
- 98 R. Adams and W. Reifschneider, Bull. Soc. Chim. Fr., 1958, 23.

⁸⁶ R. Adams and D. S. Acker, J. Amer. Chem. Soc., 74, 5872 (1952).

amount of sodium methoxide or triethylamine is added to generate the enolate anion.

Cyclization of the primary reaction products can be effected thermally or by treatment with an acid selected from 5% or constant-boiling hydrochloric acid, 48% hydrobromic acid and cold, concentrated sulfuric acid. The earliest cyclization, which suggested the general utility of the present procedure for the preparation of 5-aminoindoles, was observed on melting the adduct derived from 2-methylbenzoquinonedibenzenesulfonimide and ethyl acetoacetate; the 3-acetyloxindole resulted (Eq. 13).⁸⁷ Acid-



catalyzed cyclization of the initial products can be effected with complete or partial removal of the nitrogen-protecting groups. Proper choice of the quinone imide and cyclization conditions allows the preparation of a specifically protected 5-aminoindole. The selections available are listed in the accompanying tabulation.

Substituent on Quinonediimide	Position of Remaining Substituents after Cyclization with				
	5% HCl	22 % HCl	48% HBr	Concd H ₂ SO ₄	
PhCO	·	None		1,5	
MeSO,		1,5	1,5	_	
PhSO,		1,5		5	
$Me_2NSO_2$	1,5	None	None	5	

Exceptions to these generalizations exist,^{85,88} and it should be noted that 3-acetyl, 3-benzoyl, and 3-carbethoxyl groups are cleaved under the usual conditions of the cyclization reaction when 22% hydrochloric acid or 48% hydrobromic acid is used.^{88,91}

In addition to the acidic reagents mentioned above, lithium in liquid ammonia or lithium aluminum hydride can be used to remove certain groups on the heterocyclic nitrogen. The dimethylsulfamoyl group on the 5-amino substituent is stable to both of these reagents.^{85,93} Thus the lithium-ammonia system selectively cleaves the 1-dimethylsulfamoyl group,⁸⁵ whereas the hydride removes 1-arylsulfonyl residues.⁹³
The reaction of active methylene compounds with benzoquinone diimides having nuclear substituents has been studied to a limited degree only. Representative additions to toluquinonedibenzenesulfonimide, 2chlorobenzoquinonedibenzenesulfonimide, and 2-chlorobenzoquinone-bisdimethylsulfamoylimide have been reported.^{87,88} In each instance the formation of isomeric *p*-phenylenediamines is possible. However, the products appeared to be isomerically pure in contrast to the indoles derived by reaction of the corresponding quinones with ethyl 3-aminocrotonate. The position of the entering group was not established rigorously, but it is most likely *para* to the ring substituent.



2-Phenylsulfonylbenzoquinone-bisdimethylsulfamoylimide reacts with acetylacetone to give a single isomer.⁸⁸ The electronic character of the sulfonyl group and its steric requirements suggest that the condensation occurs *meta* to this substituent, rather than *para* as the authors postulated.



Acetylacetone reacts with 2-azidobenzoquinone-bisdimethylsulfamoylimide to give a mixture of isomers of unknown constitution.⁸⁸

Ethyl benzoylacetate and acetylacetone react with 2,3-dichlorobenzoquinone-bisdimethylsulfamoylimide to give the expected adducts in high yield; the formation of isomers is not possible. Despite the demonstrated ability of the 2,3-dichloroquinone diimide to condense with active methylene compounds, the corresponding 2,5-dichloroquinone diimide failed to give adducts.⁸⁸

Naphthoquinonedibenzenesulfonimide and naphthoquinone-bisdimethylsulfamoylimide react with active methylene compounds, including nitroethane.^{88,94} The conversion of the initial products to benz[g]indole derivatives has been studied in only a limited manner. The product of reaction of the bisdimethylsulfamoylimide and acetylacetone gives the benz[g]indole when treated with cold, concentrated sulfuric acid. Yet constant-boiling hydrochloric acid converts the adduct to an unidentified high-melting, highly colored material.



Cyclic compounds containing active methylene groups have been used in reactions with quinone diimides to prepare 6-amino-1,2,3,4-tetrahydrocarbazoles and a  $\beta$ -carboline derivative. For example, cyclization of the products derived from benzoquinone-bisdimethylsulfamoylimide and cyclohexanone-2-carboxylic ester or 5-methylcyclohexanone-2carboxylic ester with 22% hydrochloric acid gives 6-amino-1,2,3,4tetrahydrocarbazole and its 3-methyl derivative, respectively.⁸⁶ The



products derived from reaction of benzoquinonedibenzimide with 5,5dimethylcyclohexane-1,3-dione and benzoquinonedibenzenesulfonimide with 4-carbethoxy-1-methyl-3-piperidone cyclize under the influence of constant-boiling hydrochloric acid to furnish a 6-aminocarbazolone and a  $\beta$ -carboline derivative, respectively.⁹¹





 $R = Me, CH_2CO_2Et$ 





 $R = Me, CH_2CO_2Et$ 



Similarly, cyclohexane-1,3-dione and benzoquinonedibenzenesulfonimide give an adduct which on treatment with acetic acid furnishes the 6,9-dibenzenesulfonyl derivative of 6-amino-1,2,3,4-tetrahydrocarbazol-4one.⁹⁵ 2-Methylcyclohexane-1,3-dione and 2-carbethoxymethylcyclohexane-1,3-dione also add to benzoquinonedibenzenesulfonimide in the expected manner. However, cyclization of initial adducts 43 with glacial acetic acid is accompanied by cleavage of the 3-acyl substituent, giving  $\gamma$ -(2-indolyl)butyric acids as the sole product.⁹⁵ These results constitute further examples of substituent cleavage in the 3H-indole system.⁹⁶ Use of pyridine and acetic anhydride affords the angular-substituted tetrahydrocarbazole when applied to the adduct of 2-methylcyclohexane-1,3dione. Not surprisingly, submission of the product derived from 2carbethoxymethylcyclohexane-1,3-dione to these cyclization conditions gives the 4,4-spirodihydro-2-quinolone.

Quinone monoimides also react with active methylene compounds to give 1:1 adducts.⁹⁷ The monobenzenesulfonimide and monomethanesulfonimide of benzoquinone as well as naphthoquinonemonobenzenesulfonimide have been used in this way. The high yields of benzofurans formed on acid-catalyzed cyclization of the addition products and the absence of 5-hydroxyindoles in the cyclization products attest to the specificity of the site of attack by the nucleophiles.



Quinones and Ynamines. The reaction of benzoquinones with ynamines has received only limited study. However, products resulting from both 1,2 and 1,4 addition of the ynamine to the electrophilic quinone have been isolated. For example, 2-diethylamino-l-phenylacetylene reacts with benzoquinone at room temperature to give a quinonemethide, the product of 1,2 addition.⁹⁸

95 R. R. Holmes, K. G. Untch, and H. D. Benson, J. Org. Chem., 26, 439 (1961).

- 97 R. Adams and L. Whitaker, J. Amer. Chem. Soc., 78, 658 (1956).
- 98 J. Ficini and A. Krief, Tetrahedron Lett., 1967, 2497.

⁹⁸ J. C. Powers, Tetrahedron Lett., 1965, 655.



Dual behavior is observed in the reaction of N-methyl-N-phenyl-1amino-1-hexyne with benzoquinone. This ynamine is a poorer nucleophile than the diethyl ynamine, and reasonable reactivity is observed only after addition of boron trifluoride etherate. Under these conditions the highly electrophilic quinone-boron trifluoride complex reacts with the





ynamine in a 1,2 manner to give the *p*-alkylated phenol.⁹⁸ This product presumably arises from a prototropic shift in an intermediate quinonemethide. In the absence of boron trifluoride the reaction is sluggish, and a 2-aminobenzofuran results in low yield. The latter substance apparently arises from an initial Michael reaction to give an intermediate which then undergoes direct ring closure similar to that postulated in the preparation of dihydrobenzofurans (p. 367).

2-Diethylamino-1-phenylacetylene and N-phenylbenzoquinone imine give only the product of 1,2 addition to the carbonyl group.⁹⁸



Quinones and Dienamines. The reaction of dienamines and quinones proceeds in the normal Diels-Alder sense giving products arising from a 4 + 2 cycloaddition.⁹⁹ Thus benzoquinone and 1-piperidino-1,3butadiene afford naphthoquinone in low yield. Products arising from a 1,3-dipolar species were not detected, but this investigation preceded recognition of the essential features of the chemistry of enamines.¹⁶ Naphthoquinone and naphthazarin furnish the corresponding anthraquinones when treated with 1-diethylamino-1,3-butadiene.



#### EXPERIMENTAL CONDITIONS

The choice of experimental conditions can exert a major influence on the course of the Nenitzescu procedure and thereby determine the structure of the major product. The mechanism demonstrated to be operative for the method explains the genesis of certain anomalous products and suggests ways to avoid them, thus increasing the efficiency of the synthesis of 5-hydroxyindoles. In this section, attention is directed to the selection of experimental conditions that most influence the structure of the product.

Ratio of Reactants. Best yields of 5-hydroxyindole derivatives result when equimolar amounts of the quinone and enamine are used. An excess of enamine frequently gives nonindolic products derived from two enamine units and one quinone unit, *e.g.*, 11, or the product resulting from the initial Michael addition of the enamine to the quinone. A product of the former type was observed in Nenitzescu's initial investigation, although the oxidation state of the product remains uncertain.¹



The 2,5-dichloro derivative of 11 results from the reaction of 2,5dichlorobenzoquinone with a 50 % molar excess of ethyl 3-aminocrotonate.^{36, 40} Yet equimolar quantities of these reactants give the expected 4,7-dichloro-5-hydroxyindole-3-carboxylate.⁴⁰ Reaction of a 50 % molar excess of the aminocrotonate with 2-methoxybenzoquinone in ethanol gives the Michael adduct in excellent yield.³⁵ This adduct can be transformed efficiently into the 5-hydroxy-6-methoxyindole on treatment with a catalytic amount of methoxybenzoquinone in acetic acid. Acetic acid presumably isomerizes the hydroquinone about the olefinic center to the



proper stereochemistry for cyclization. The direct preparation of the 5hydroxy-6-methoxyindole from equimolar quantities of 2-methoxybenzoquinone and ethyl 3-aminocrotonate was noted earlier (p. 345). Use of excess quinone has been recorded infrequently, but the limited studies indicate no advantage. Thus 2 equivalents of toluquinone react with 2-cyanomethylene- and 2-carbethoxymethylene-pyrrolidine to give the Michael adducts in the quinone oxidation state.^{14, 15} The appearance



of toluhydroquinone as a co-product suggests that the second equivalent of quinone is used to oxidize the initially formed hydroquinone adduct to give the observed product.

Effect of Solvent. Acetic acid is the most effective solvent for the Nenitzescu reaction. However, acetone, methanol, ethanol, benzene, methylene chloride, chloroform, and ethylene dichloride have often been used, particularly before the superiority of acetic acid was recognized. The greater utility of acetic acid is most likely the result of its ability to isomerize the olefinic intermediates to those isomers capable of giving derivatives of 5-hydroxyindole. The reaction of benzoquinone with ethyl 3-aminocinnamate dramatically illustrates this effect.⁸ The expected ethyl 5-hydroxy-2-phenylindole-3-carboxylate is formed in 46% yield



in acetic acid. Yet the 1:1 hydroquinone (24%) and 1:2 quinone (3%) adducts result when benzene or chloroform is the solvent; none of the 5-hydroxyindole is isolated. Moreover, acetic acid is reputedly superior to ethanol for the preparation of the 1-alkyl derivatives from ethyl 3-alkyl-aminocinnamates and quinones.⁵⁵

The reaction of 2,5-dichloro-1,4-benzoquinone with t-butyl 3-aminocrotonate to give the expected 5-hydroxyindole-3-carboxylate proceeds poorly in ethanol, but the indole derivative is formed in 60% yield in acetic acid.⁴⁰ The reaction of toluquinone with 2-carbethoxymethylenepyrrolidine illustrates further the usefulness of acetic acid in promoting



the indole synthesis. Reaction of 2 equivalents of the quinone with 1 equivalent of the enamine, using methanol as the reaction medium, gives the isomeric quinoid adducts. However, if acetic acid is added to the reaction medium, the Nenitzescu synthesis culminating in the pyrrolo-indoles is completed.¹⁴



These examples illustrate the advantage of using a reaction medium capable of isomerizing intermediate Michael adducts, thus allowing the cyclization to occur. Acetic acid has repeatedly demonstrated this capability, particularly when the usual solvents are ineffective in this regard. The reaction of 3-amino-2-cyclohexen-1-one with 2-trifluoromethyl-1,4benzoquinone constitutes still another striking example of the role that the solvent can exercise. In boiling ethanol these materials give the carbinolamine, whereas the 6-hydroxy-5-trifluoromethylcarbazole results in acetic acid under comparable conditions.²⁹



Although these results suggest the general superiority of acetic acid as the reaction medium, a recent study emphasizes the existence of exceptions. Werner reported that benzoquinone reacts with ethyl 3-methylamino-, 3-benzylamino-, and 3-amino-crotonate to give largely (18-25%)ethyl 5-hydroxy-2-methylbenzofuran-3-carboxylate and little (0-5%)5-hydroxyindole in this solvent.⁵⁰



However, Kücklander isolated four products from the reaction of benzoquinone with ethyl 3-methylaminocrotonate in acetic acid.^{15a} In addition to an unspecified amount of the expected ethyl 5-hydroxy-1,2-dimethylindole-3-carboxylate, the acetoxy derivative (15%), the 4,4'-diindolyl (5%), and the 4,6'-diindolyl (7%) substances result.



The unusual 5-acetoxy-4-hydroxyindole-3-carboxylates are also formed when benzoquinone reacts in acetic acid with ethyl anilino-, p-methoxyanilino-, and p-nitroanilinocrotonate.¹⁰⁰ The 5-acetoxy-4-hydroxyindole reportedly becomes more significant in the reaction of benzoquinone with 4-anilino-3-penten-2-one in this medium.



The formation of these products has been interpreted as proceeding by addition of acetic acid to the quinonimmonium species which is postulated as a latter-stage intermediate in the usual Nenitzescu process. This postulate is supported by preparation of an acetoxyhydroxyindolecarboxylate by treatment of the intermediate carbinolamine 45 with acetic acid.^{15a}



A subsequent acetyl migration is required to account for the observed products. There is no reliable evidence for such a migration and the possibility remains that these products should be formulated as 4-acetoxy-5-hydroxyindoles.

The formation of a 4,4'-diindolyl derivative in unspecified yield has also been observed in the reaction of benzoquinone with ethyl 3-benzylaminocrotonate in acetic acid. The dimer is apparently a minor product which accompanies the expected 5-hydroxyindole.¹⁰¹



The origin of the 4,4'-diindolyl and 4,6'-diindolyl substances has been projected as the result of reaction of the "normal" 5-hydroxyindole-3carboxylate with the carbonium ions that are mesomeric with the quinoniminonium intermediate.^{15a} This postulate is reinforced by the isolation of such dimers from reaction of the carbinolamine 45 (p. 385) with ethyl 5-hydroxy-1,2-dimethylindole-3-carboxylate in acetic acid. Alternatively such products could represent dimerization of two phenoxy radicals derived from the initially formed 5-hydroxyindole derivative.

One other side reaction deleterious to the usual 5-hydroxyindole synthesis has been observed in this medium. The reaction of benzoquinone with ethyl 3-(p-chloroanilino)crotonate illustrates this process. The anticipated 5-hydroxyindole-3-carboxylate is formed when ethanol is the solvent.^{45, 102} However, a 6-hydroxyindole-3-carboxylate results in acetic acid. The yields in each instance do not preclude formation of the isomeric product. Nevertheless, the product isolated from the acetic acid medium constitutes the first experimental verification of a reaction path recognized to be available to quinones and enamino esters and ketones.¹⁰ Presumably the 6-hydroxyindole-3-carboxylate synthesis derives from the initial 1,2 addition of the carbon terminal of the enamine triad onto the quinone carbonyl, and an analogy for this reaction path is to be found in the products derived from benzoquinones and ynamines.⁹⁸



The variability of the isolated product with changes in the solvent also is evident in the interaction of benzoquinone with 1-(4-morpholino)-1phenylethylene. 5-Hydroxy-2-phenylbenzofuran is formed in ethanol.⁷⁰ Yet, the benzo[1,2-b;4,5-b']difuran nucleus is formed from these

¹⁰⁸ U. Kuckländer, Tetrahedron Lett., 1971, 2093.

reactants in methylene chloride or benzene.¹⁰³ In this instance, hydroquinone also is isolated. If acetic acid is added to methylene chloride, a



third reaction, resulting in the formation of 1;3,5,7-tetraphenylanthraquinone, occurs.¹⁰⁴ The isolation of 1,3,6,8-tetraphenylanthraquinone from treatment of 1-(4-morpholino)-2-phenylethylene with benzoquinone in the same medium suggests that this behavior is general.



¹⁰³ G. Domschke, Chem. Ber., 99, 930 (1966).
¹⁰⁴ G. Domschke, Chem. Ber., 99, 934 (1966).

The results in acetic acid have been interpreted as proceeding by the dimerization of the enamine, which is accelerated in acidic media by the formation of the immonium salt.^{105,106} The dimerization culminates in the formation of a dienamine, which then reacts with benzoquinone in a normal Diels-Alder sense. It is apparent that benzoquinone is expended in the oxidation of the cycloaddition product to the anthraquinone, and this fact accounts, in part, for the low yields recorded.



The preparation of benzofurans by the reaction of dialkylaminocrotonates with benzoquinone was noted on p. 366. The medium in this transformation was methylene chloride containing a small quantity of acetic acid.⁶⁶ The benzofuran is accompanied by an unspecified amount of diethyl 2,6-dimethylbenzo[1,2-b;4,5-b']difuran-3,7-dicarboxylate. However, the latter material is the major product if the reaction is conducted in acetic acid alone.



¹⁰⁵ C. Mannich and E. Kniss, *Chem. Ber.*, **74**, 1629 (1941).
 ¹⁰⁶ G. Opitz and W. Merz, *Ann.*, **652**, 139 (1962).

Effect of Temperature. Little information is available concerning the effects of varying the temperature. The Nenitzescu reaction is usually exothermic, and most of the results discussed previously were realized at the boiling temperature (56–118°) of the reaction medium. However, the product derived from 2-trifluoromethyl-1,4-benzoquinone and 3-amino-2-cyclohexen-1-one does vary with the reaction temperature.²⁹ In acetic acid at the maximum temperature reached during the spontaneous exothermic reaction, a carbinolamine results. In boiling acetic acid the tetrahydroketocarbazole is formed. These results indicate that temperature can play a role in determining the products of the Nenitzescu reaction, but delineation of its importance requires further experiments.



EXPERIMENTAL PROCEDURES

Ethyl 2,6-Dimethyl-5-hydroxyindole-3-carboxylate and Ethyl 2,7-Dimethyl-5-hydroxyindole-3-carboxylate. (Use of Acetone as the Solvent and Separation of Isomeric Indoles).^{40,107} A solution of 3.71 kg (30.4 mol) of toluquinone (practical grade) and 3.92 kg (30.4 mol) of ethyl 3-aminocrotonate in 8.4 liters of acetone was heated on the steam bath with stirring. When reflux temperature was attained, there occurred a vigorous exothermic reaction which sustained boiling for 2 hours despite the application of external cooling. The solution was maintained at reflux temperature for an additional 3 hours, then 3 liters of acetone was removed by distillation. The concentrate was stored at 3-5° for 16 hours and filtered; the pink-gray filter cake was washed thoroughly with ether and dried to give 3.425 kg of solid. This material was stirred for 5 minutes with three successive 8-liter portions of acetone and collected by filtration. The

¹⁰⁷ Unpublished results of George R. Allen, Jr., and J. Nocera.

combined filtrates from the three acetone washes were concentrated to a volume of approximately 4 liters and cooled to give 1.11 kg (15.5%) of ethyl 2,6-dimethyl-5-hydroxyindole-3-carboxylate, mp 225–228°.

The dry filter cake (1.85 kg) remaining from the acetone extractions was then extracted with 5 liters of boiling acetone for 5 minutes, and the mixture was filtered hot to give 0.81 kg (11.5 %) of ethyl 2,7-dimethyl-5hydroxyindole-3-carboxylate, mp 192–196°.

t-Butyl 4-Chloro-5-hydroxy-2,7-dimethylindole-3-carboxylate (Use of Acetic Acid).³⁹ To a hot solution of 3.12 g (19.9 mmol) of 2chloro-5-methyl-1,4-benzoquinone¹⁰⁸ in 15 ml of glacial acetic acid was added 3.14 g (20 mmol) of t-butyl 3-aminocrotonate.¹³ The solution was allowed to stand for 30 minutes without the application of heat and was then cooled. The solid was collected, washed with chilled acetic acid, and dried to give 2.99 g (51 %) of t-butyl 4-chloro-5-hydroxy-2,7-dimethylindole-3-carboxylate, mp 178–180° dec.

Ethyl trans-3-Amino-2-(2-carbomethoxy-3,6-dihydroxyphenyl)crotonate (Formation of a Michael Adduct as the Principal Product).¹² A solution of 830 mg (5 mmol) of 2-carbomethoxy-1,4-benzoquinone¹⁰⁹ and 645 mg (5 mmol) of ethyl 3-aminocrotonate in 10 ml of ethanol was heated under reflux for 2 hours. The solvent was removed. Trituration of the residue with ether gave 871 mg (59%) of ethyl trans-3-amino-2-(2-carbomethoxy-3,6-dihydroxyphenyl)crotonate as crystals, mp 132.5-134.5°.

Ethyl 4-Carbomethoxy-5-hydroxy-2-methylindole-3-carboxylate (Isomerization of a Michael-type Hydroquinone and Conversion into an Indole).¹² A solution of 1.96 g (6.65 mmol) of ethyl *trans*-3amino-2-(2-carbomethoxy-3,6-dihydroxyphenyl)crotonate and 200 mg (1.2 mmol) of 2-carbomethoxy-1,4-benzoquinone in 30 ml of glacial acetic acid was heated on the steam bath for 15 hours and evaporated. Trituration of the residue with 25 ml of methylene chloride gave 383 mg (23%) of ethyl 5,8-dihydroxy-3-methylisocarbostyril-4-carboxylate, mp 253-254° dec.

The methylene chloride filtrate was chromatographed on a magnesiasilica absorbent. The material eluted by methylene chloride-acetone (95:5) was recrystallized from acetone-hexane to give 550 mg (30%) of ethyl 4-carbomethoxy-5-hydroxy-2-methylindole-3-carboxylate, mp 141– 143°.

Ethyl 5-Hydroxy-2-methylbenzofuran-3-carboxylate.⁶⁶ Ethyl  $\beta$ -piperidinocrotonate¹¹⁰ (13.8 g, 0.07 mol) in 100 ml of methylene

¹⁰⁸ H. H. Hodgson and F. H. Moore, J. Chem. Soc., 1926, 2036.

¹⁰⁹ J. Cason, Org. Reactions, 4, 354 (1948).

¹¹⁰ E. Knoevenagel, Chem. Ber., 31, 738 (1898).

chloride was treated with 9 g (0.15 mol) of acetic acid. A solution of 5.4 g (0.05 mol) of benzoquinone in 50 ml of methylene chloride was added dropwise with stirring in the course of 5 hours. The reaction was allowed to stand overnight; then the solvent was removed under reduced pressure. The residue was dissolved in ether and filtered; the filtrate was washed with water and evaporated. Crystallization of the residue from benzene gave 4.8 g (40%) of ethyl 5-hydroxy-2-methylbenzofuran-3-carboxylate, mp 144°.

2,3-Dihydro-5-hydroxy-6-methoxy-3,3-dimethyl-2-(4-morpholinyl)furan (Formation of a 2-Amino-2,3-dihydrobenzofuran).⁷² A solution of 1.38 g (10 mmol) of 2-methoxy-1,4-benzoquinone¹¹¹ and 1.49 g (10 mmol) of isobutenylmorpholine¹¹² in methylene chloride was stirred at room temperature for 1 hour. Removal of the solvent and trituration of the residue with ether gave 2.44 g (87%) of 2,3-dihydro-5-hydroxy-6-methoxy-3,3-dimethyl-2-(4-morpholinyl)benzofuran as crystals, mp 157–161°. A sample recrystallized from methanol had mp 168–169°.

Ethyl 5,8-Dihydroxy-1,3-dimethylisoquinoline-4-carboxylate.¹² A solution of 870 mg (5.8 mmol) of 2-acetyl-1,4-benzoquinone¹¹³ and 750 mg (5.8 mmol) of ethyl 3-aminocrotonate in 10 ml of chloroform was heated at reflux temperature for 2 hours. Removal of the solvent and crystallization of the residue from acetone-hexane gave 1.07 g (71%) of ethyl 5,8-dihydroxy-1,3-dimethylisoquinoline-4-carboxylate as crystals which decomposed slowly above 267°.

Ethyl 3-Amino-6-hydroxycoumarin-4-carboxylate.⁷³ A solution of 4.7 g (25 mmol) of diethyl aminofumarate⁷³ and 2.7 g (25 mmol) of benzoquinone in 20 ml of glacial acetic acid was allowed to stand overnight. Filtration, washing the collected solid with chloroform, and recrystallization from dilute ethanol gave 4.9 g (79%) of ethyl 3-amino-6-hydroxyeoumarin-4-carboxylate, mp 172°.

5-Dimethylsulfamoylamino-1-dimethylsulfamoyl-3-methylindole (Interaction of a Quinone Diimide and an Enamine).⁸⁵ A solution of 3.2 g (10 mmol) of 1,4-benzoquinone-bisdimethylsulfamimide¹¹⁴ in 100 ml of chloroform was treated with a solution of 1-propenylpiperidine¹¹⁵ in 30 ml of chloroform and allowed to stand overnight. The precipitated N,N'-bisdimethylsulfamoyl-p-phenylenediamine was collected by filtration, and the solvent was removed from the filtrate. The residue was

¹¹¹ H. G. H. Erdtman, Proc. Roy. Soc. (London), A143, 177 (1933).

¹¹² E. Benzing, Angew. Chem., 71, 521 (1959).

¹¹³ M. C. Kloetzel, R. P. Dayton, and B. Y. Abadir, J. Org. Chem., 20, 38 (1955).

¹¹⁴ R. Adams and P. Shafer, J. Amer. Chem. Soc., 75, 667 (1953).

¹¹⁵ C. Mannich and H. Davidsen, Chem. Ber., 69, 2106 (1936).

heated at reflux temperature with 30 ml of 5% hydrochloric acid for 1 hour. Filtration of the cooled mixture and recrystallization of the solid from ethanol gave 2.6 g (72%) of 5-dimethylsulfamoylamino-1-dimethyl-sulfamoyl-3-methylindole, mp 167°.

Ethyl 2-{2,5-bis-[(Dimethylsulfamoyl)amino]phenyl}acetoacetate (Addition of an Active Methylene Compound to a Quinone Diimide).⁸⁸ To a solution of 1.0 g (0.31 mmol) of 1,4-benzoquinone-bisdimethylsulfamimide¹¹⁴ in the minimum quantity of anhydrous dioxane at room temperature was added 1.1 molar equivalents of redistilled ethyl acetoacetate and about 40 mg of sodium methoxide. After discharge of the orange color, 6 drops of glacial acetic acid were added, and the solution was concentrated by evaporation in a stream of dry air to a volume of about 15 ml. Addition of 100 ml of petroleum ether (bp 30-60°) precipitated an oil that crystallized on intermittent scratching to give a quantitative yield of product. Recrystallization of the product from chloroform-cyclohexane gave crystals having mp 149.5-151.5°.

5-Amino-2-methylindole (Cyclization of an Adduct from a Quinone Diimide and Active Methylene Compound).⁸⁸ A suspension of 0.5-1.0 g (1.1-2 mmol) of ethyl 2-{2,5-bis[(dimethylsulfamoyl)amino]phenyl}aceto-acetate in 40 ml of 22 % hydrochloric acid was heated at reflux temperature for 24 hours. The reaction mixture was filtered, and the ice-cooled filtrate was rendered alkaline with 15% aqueous sodium hydroxide and extracted with ether. The dried ethereal solution was evaporated in a stream of dry nitrogen to give 87% of 5-amino-2-methylindole, which was purified by sublimation to give crystals, mp 157-159°.

### TABULAR SURVEY

The literature up to January 1973 has been reviewed. Coverage of the Russian and Romanian literature is restricted to articles abstracted by *Chemical Abstracts*, whereas the review of other cited literature is based on primary sources. The tables are arranged in terms of the structure of the major product. In examples where two or more products of different structure result in essentially equivalent yield, the entry is repeated in the appropriate table(s). For example, if the reaction gives a 5-hydroxyindole-3-carboxylate and a Michael adduct as products, an entry giving both products will be found in Tables I and IV. Certain minor products are frequently observed in the Nenitzescu synthesis; these substances have been designated A, B, C, and D in the tables. The gross structure is shown below for each class; the substituents in the ring are designated in the tables, whereas those on nitrogen are apparent from the enamine component of the reaction.



Internally, the tables are organized by increasing complexity of (1) the quinone and (2) the enamine. The order is apparent in the instance of the former component. The tabulation is based on an NOCHXY order of the elements in the enamine. Thus for a given quinone the products arising from reaction with  $NO_2C_nH_{2n-1}$  appear before those derived from  $NO_3C_nH_{2n-1}$ .

#### TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES



Formulas A, B, C, and D are displayed above.

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) ( $\%$ )	Refs.
C ₆ H ₂ Cl ₂ O ₂	2,3-Dichloro-1,4-		
	Ethyl 3-amino- crotonate	Ethyl 6,7-dichloro-5-hydroxy-2- meth' dole-3-carboxylate (43)	36
	Ethyl 3-methylamino- crotonate	Ethyl ( ichloro-5-hydroxy-1,2- dimet ndole-3-carboxylate (7), 5,6-dichloro-A (63)	116

### TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES



Formulas A, B, C, and D are displayed above.

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
C ₆ H ₂ Cl ₂ O ₂	2,3-Dichloro-1,4- benzoguinone and		
	Ethyl 3-amino- crotonate	Ethyl 6,7-dichloro-5-hydroxy-2- meth dole-3-carboxylate (43)	36
	Ethyl 3-methylamino- crotonate	Ethyl ( ichloro-5-hydroxy-1,2- dimet ndole-3-carboxylate (7), 5,6-dichloro-A (63)	116

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
$C_{6}H_{2}Cl_{2}O_{2}$ (contd.)	2,3-Dichloro-1,4- benzoquinone and		<u>,</u>
	Ethyl 3-ethylamino- crotonate	Ethyl 6,7-dichloro-1-ethyl-5- hydroxy-2-methylindole-3- carboxylate (55)	38
	Ethyl 3-n-propyl- aminocrotonate	Ethyl 6,7-dichloro-5-hydroxy-2- methyl-1-n-propylindole-3- carboxylate (7), 5,6-dichloro-A (57)	116
	Ethyl 3-n-butyl- aminocrotonate	Ethyl 1-n-butyl-6,7-dichloro-5- hydroxy-2-methylindole-3- carboxylate (5), 5,6-dichloro- A (71)	116
	Ethyl 3-anilino- crotonate	Ethyl 6,7-dichloro-5-hydroxy-2- methyl-1-phenylindole-3- carboxylate (13)	116
	Ethyl 3-benzylamino- crotonate	Ethyl 1-benzyl-6,7-dichloro-5- hydroxy-2-methylindole-3- carboxylate (9), 5,6-dichloro-A (50)	116
	Ethyl 3-( <i>p</i> -toluidino)- crotonate	Ethyl 6,7-dichloro-5-hydroxy-2- methyl-1-p-tolylindole-3- carboxylate (17)	116
	Ethyl 3-( <i>p</i> -anisidino)- crotonate	Ethyl 6,7-dichloro-5-hydroxy-1- ( <i>p</i> -methoxyphenyl)-2-methyl- indole-3-carboxylate (12)	116
	2,5-Dichloro-1,4-	• • • •	
	Ethyl 3-amino- crotonate	Ethyl 4,7-dichloro-5-hydroxy-2- methylindole-3-carboxylate (27)	40
	t-Butyl 3-amino- crotonate	t-Butyl 4,7-dichloro-5-hydroxy-2- methylindole-3-carboxylate (60)	<b>4</b> 0
	Ethyl 3-ethylamino- crotonate	Ethyl 4,7-dichloro-1-ethyl-5- hydroxy-2-methylindole-3- carboxylate (30)	36
C ₆ H ₃ BrO ₂	2-Bromo-1,4- benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 6-bromo-5-hydroxy-2- methylindole-3-carboxylate (5), ethyl 7-bromo-5-bydroxy-2-	13
		methylindole-3-carboxylate (2)	

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
C ₃ H ₃ ClO ₃	2-Chloro-1,4-		
	benzoquinone and		
	Ethyl 3-amino-	Ethyl 6-chloro-5-hydroxy-2-	13, 42
	crotonate	methylindole-3-carboxylate (16-	
		20), ethyl 7-chloro-5-hydroxy-2-	
		methylindole-3-carboxylate (4)	
C ₆ H ₃ FO ₂	2-Fluoro-1,4-		
	benzoquinone and		
	Ethyl 3-amino-	Ethyl 6-fluoro-5-hydroxy-2-	13
	crotonate	methylindole-3-carboxylate (12)	
$C_{6}H_{3}IO_{2}$	2-Iodo-1,4-		
	benzoquinone and		
	Ethyl 3-amino-	Ethyl 5-hydroxy-7-iodo-2-methyl-	13
	crotonate	indole-3-carboxylate (7), ethyl	
		5-hydroxy-6-iodo-2-methylindole-	
	14 Democratic and	3-carboxylate (1)	
$C_4H_4O_2$	1,4-Benzoquinone and	Februl & budgering 9 methodis data 9	1 4 11
	Etnyl 3-amino-	Etny: 5-nydroxy-2-metnylindole-3-	1, 4, 11, 94 49 45
	crotonate	$\begin{array}{c} \textbf{B}  (10), \textbf{C}  (13) \end{array}$	24, 42, 40
	Ethyl 3-methylamino-	Ethyl 5-hydroxy-1,2-dimethylindole-	7, 24,
	crotonate	3-carboxylate (32–60), A (6)	42, 45
	Ethyl 3-ethylamino-	Ethyl l-ethyl-5-hydroxy-2-methyl-	44
	crotonate	indole-3-carboxylate (75)	
	Ethyl 3-amino-2-	Ethyl 5-hydroxy-2-n-propylindole-3-	54
	hexenoate	carboxylate (20)	
	Ethyl 3-n-butylamino-	Ethyl I-n-butyl-5-hydroxy-2-methyl-	52, 54
	crotonate	indole-3-carboxylate $(27-30)$	0
	cinnamate	carboxylate (46)	0
	Ethyl 3-n-hexylamino-	Ethyl 1-n-hexyl-5-hydroxy-2-	24
	crotonate	methylindole-3-carboxylate (22)	
	Ethyl 3-(cyclohexyl-	Ethyl 1-cyclohexyl-5-hydroxy-2-	36
	amino)crotonate	methylindole-3-carboxylate (33)	-
	Ethyl 3-anilino-	Ethyl 5-hydroxy-2-methyl-1-	1, 45,
	crotonate	phenylindole-3-carboxylate (27-	48
		53)	
	Ethyl 3-(o-toluidino)-	Ethyl 5-hydroxy-2-methyl-1-	36, 45
	crotonate	(o-tolyl)indole-3-carboxylate	
		(27-54)	
	Ethyl 3-(p-toluidino)-	Ethyl 5-hydroxy-2-methyl-1-(p-tolyl)	)- <b>4</b> 8
	crotonate	indole-3-carboxylate (25)	

## TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES (Continued)Formulas A, B, C, and D are displayed on p. 393.

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) ( $\%$ )	Refs.
С.Н.О.	1 4-Benzoquinone and		
(contd.)	Ethyl 3- (benzylamino)- crotonate	Ethyl l-benzyl-5-hydroxy-2- methylindole-3-carboxylate (22- 58)	4, 24, 45, 52, 117
	Ethyl 3- <i>n</i> -propyl- aminocinnamate	Ethyl 5-hydroxy-2-phenyl-1-n- propylindole-3-carboxylate (28)	55
	Ethyl 3-(p-methyl- , benzylamino)- crotonate	Ethyl 5-hydroxy-2-methyl-1- (p-methylbenzyl)indole-3- carboxylate (22)	118
	Ethyl 3-isobutyl- aminocinnamate	Ethyl 5-hydroxy-1-isobutyl-2- phenylindole-3-carboxylate (23)	55
	Ethyl 3-(2,4-dimethyl- benzylamino)- crotonate	Ethyl 5-hydroxy-2-methyl-1- (2,4-dimethylbenzyl)indole-3- carboxylate (26)	118
	Ethyl 3-amino-2- eicosenate	Ethyl 2-n-heptadecyl-5-hydroxy- indole-3-carboxylate (26)	54
	Ethyl 3-amino-3- ethoxyacrylate	Ethyl 5-hydroxy-2-ethoxyindole-3- carboxylate (26)	3
	Ethyl 3-(2-hydroxy- ethylamino)- crotonate	Ethyl 5-hydroxy-1-hydroxyethyl-2- methylindole-3-carboxylate (46)	45
	Ethyl 3-(o-methoxy- anilino)crotonate	Ethyl 5-hydroxy-l-(o-methoxy- phenyl)-2-methylindole-3- carboxylate (6)	48
	Ethyl 3-(m-methoxy- anilino)crotonate	Ethyl 5-hydroxy-l-( <i>m</i> -methoxy- phenyl)-2-methylindole-3- carboxylate (22)	48
	Ethyl 3-(p-methoxy- anilino)crotonate	Ethyl 5-hydroxy-l-(p-methoxy- phenyl)-2-methylindole-3- carboxylate (35)	48
	Ethyl 3-(o-methoxy- benzylamino)- crotonate	Ethyl 5-hydroxy-l-(o-methoxy- benzyl)-2-methylindole-3- carboxylate (21)	118
	Ethyl 3-(p-methoxy- benzylamino)- crotonate	Ethyl 5-hydroxy-l-(p-methoxy- benzyl)-2-methylindole-3- carboxylate (29)	118
	Dimethyl 2-methyl- aminofumarate	Dimethyl 5-hydroxy-1-methylindole- 2,3-dicarboxylate (82)	56
	Dimethyl 2-ethyl- aminofumarate	Dimethyl 5-hydroxy-1-ethylindole- 2,3-dicarboxylate (90)	56

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
$C_{6}H_{4}O_{3}$	1,4-Benzoquinone and	······································	
(contd.)	<ul> <li>Dimethyl 2-n-propyl- aminofumarate</li> </ul>	Dimethyl 5-hydroxy-1- <i>n</i> -propylin- dole-2,3-dicarboxylate (88)	56
	Dimethyl 2-isopropyl- aminofumarate	Dimethyl 5-hydroxy-l-isopropyl- indole-2,3-dicarboxylate (50)	56
	Dimethyl 2- <i>n</i> -butyl- aminofumarate	Dimethyl 1-n-butyl-5-hydroxy- indole-2,3-dicarboxylate (44)	56
	Dimethyl 2- <i>t</i> -butyl- aminofumarate	Dimethyl 1-t-butyl-5-hydroxy- indole-2,3-dicarboxylate (21)	56
	Diethyl 3-methyl- aminoglutaconate	Ethyl 3-carbethoxy-5-hydroxy-1- methylindolyl-2-acetate (19)	51
	Ethyl 3-(carbethoxy- methylamino)- crotonate	Ethyl 3-carbethoxy-5-hydroxy-2- methylindolyl-1-acetate ()	1
	Diethyl 3-ethyl- aminoglutaconate	Ethyl 3-carbethoxy-1-ethyl-5- hydroxyindolyl-2-acetate (31)	51
	Dimethyl 2-cyclo- hexylamino- fumarate	Dimethyl 1-cyclohexyl-5-hydroxy- indole-2,3-dicarboxylate (71)	56
	Dimethyl 2-n-hexyl- aminofumarate	Dimethyl 1-n-hexyl-5-hydroxy- indole-2,3-dicarboxylate (36)	56
	Dimethyl 2-phenyl- aminofumarate	Dimethyl 5-hydroxy-1-phenylindole- 2,3-dicarboxylate (63)	56
	Dimethyl 2-benzyl- aminofumarate	Dimethyl 1-benzyl-5-hydroxyindole- 2,3-dicarboxylate (90)	56
	Dimethyl 2-(p-tolyl- amino)fumarate	Dimethyl 5-hydroxy-l-( <i>p</i> -tolyl)- indole-2,3-dicarboxylate (43)	56
	Ethyl 3-(3,4-dimeth- oxybenzylamino)- crotonate	Ethyl 5-hydroxy-1-(3,4-dimethoxy- benzyl)-2-methylindole-3-car- boxylate (18)	118
	Diethyl 3-benzyl- aminoglutaconate	Ethyl 1-benzyl-3-carbethoxy-5- hydroxyindolyl-2-acetate (22)	51
	Diethyl 3-phenethyl- aminoglutaconate	Ethyl 3-carbethoxy-5-hydroxy-1- phenethylindolyl-2-acetate (25)	51
	Dimethyl 2-(p- methoxyphenyl- amino)fumarate	Dimethyl 5-hydroxy-l-(p-methoxy- phenyl)indole-2,3-dicarboxylate (62)	56
	Ethyl 3-(2-cyano- ethylamino)- crotonate	Ethyl 1-(2-cyanoethyl)-5-hydroxy-2- methylindole-3-carboxylate (48)	44

Molecular Formula of	<b>D</b>		<b>.</b>
Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
C ₆ H ₄ O ₂	1,4-Benzoquinone and		
(contd.)	Ethyl 3-(3-dimethyl- aminopropylamino)- crotonate	Ethyl 1-(3-dimethylaminopropyl-5- hydroxy-2-methylindole-3- carboxylate (10)	24
	Ethyl 3-( <i>p</i> -dimethyl- aminoanilino)- crotonate	Ethyl 1-( <i>p</i> -dimethylaminophenyl)- 5-hydroxy-2-methylindole-3- carboxylate (43)	48
	Ethyl 3-(o-acetamido- anilino)crotonate	Ethyl 1-(o-acetamidophenyl)-5- hydroxy-2-methylindole-3- carboxylate (6)	48
	Ethyl 3-(m-aceta- midoanilino)- crotonate	Ethyl 1-( <i>m</i> -acetamidophenyl)-5- hydroxy-2-methylindole-3- carboxylate (38)	48
	Ethyl 3-(p-aceta- midoanilino)- crotonate	Ethyl 1-( <i>p</i> -acetamidophenyl)-5- hydroxy-2-methylindole-3- carboxylate (40)	48
	Ethyl 3-(p-nitrobenz- ylamino)crotonate	Ethyl 5-hydroxy-2-methyl-1-( <i>p</i> - nitrobenzyl)indole-3-carboxylate (23)	118
	Ethyl 3-(m-chloro- anilino)crotonate	Ethyl 1-(m-chlorophenyl)-5- hydroxy-2-methylindole-3- carboxylate (23)	48
	Ethyl 3-(p-chloro- anilino)crotonate	Ethyl 1-( <i>p</i> -chlorophenyl)-5-hydroxy- 2-methylindole-3-carboxylate (20-24)	48, 100
~	Ethyl 3-(p-bromobenz- ylamino)crotonate	Ethyl 1-(p-bromobenzyl)-5-hydroxy- 2-methylindole-3-carboxylate (16)	118
$C_6H_4O_3$	2-Hydroxy-1,4-		
	Ethyl 3-amino- crotonate	Ethyl 5,6-dihydroxy-2-methyl- indole-3-carboxylate (—)	3
C ₇ H ₂ ClF ₃ O ₂	2-Chloro-3-tri- fluoromethyl-1,4- benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 6-chloro-5-hydroxy-2-methyl- 7-trifluoromethylindole-3- carboxylate (78)	13
	2-Chloro-5-trl- fluoromethyl-1,4- benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 7-chloro-5-hydroxy-2-methyl- 4-trifluoromethylindole-3- carboxylate (74)	13

Molecular Formula of Ouinone	Beactanta	Product(s) and Vield(s) (%)	Refe
			14010.
C ₇ H ₂ F ₃ O ₂	2-Trifluoromethyl-1, 4-benzoquinone and		
	Ethyl 3- <b>a</b> mino- crotonate	Ethyl 5-hydroxy-2-methyl-4- trifluoromethylindole-3- carboxylate (54)	13
	t-Butyl 3-amino- crotonate	t-Butyl 5-hydroxy-2-methyl-4- trifluoromethylindole-3- carboxylate (62)	13
C,H ₅ ClO ₅	2-Chloro-5-methyl- 1,4-benzoquinone and		
	t-Butyl 3-amino- crotonate	t-Butyl 4-chloro-5-hydroxy-2,7- dimethylindole-3-carboxylate (51)	39
	Ethyl 3-amino-2- pentenoate	Ethyl 4-chloro-2-ethyl-5-hydroxy- 7-methylindole-3-carboxylate (41)	40
C,H ₆ O ₂	2-Methyl-1,4-		
	benzoquinone and Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-2,6-dimethylindole- 3-carboxylate (9-12), ethyl 5- hydroxy-2,7-dimethylindole-3- carboxylate (6-14), 5-methyl-A (5), 6-methyl-A (1)	<b>3, 1</b> 0, 11
	Ethyl 3-methylamino- crotonate	Ethyl 5-hydroxy-1,2,6-trimethyl- indole-3-carboxylate (22), ethyl 5-hydroxy-1,2,7-trimethylindole-3- carboxylate (10)	10
	Ethyl 3-ethylamino- crotonate	Ethyl 1-ethyl-5-hydroxy-2,6- dimethylindole-3-carboxylate (24), ethyl 1-ethyl-5-hydroxy-2,7- dimethylindole-3-carboxylate (5)	10
	Ethyl 3-n-propyl- aminocrotonate	Ethyl 5-hydroxy-2,6-dimethyl-1-n- propylindole-3-carboxylate (21), ethyl 5-hydroxy-2,7-dimethyl-1- n-propyl-3-carboxylate (1)	10
	Ethyl 3-isopropyl- aminocrotonate	Ethyl 5-hydroxy-1-isopropyl-2,6- dimethylindole-3-carboxylate (18), 6-methyl-A (18)	10
	Ethyl 3-n-butyl- aminocrotonate	Ethyl 1-n-butyl-5-hydroxy-2,6- dimethylindole-3-carboxylate (18-23), ethyl 1-n-butyl-5- hydroxy-2,7-dimethylindole-3- carboxylate (2)	10, 52

## TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES (Continued)Formulas A, B, C, and D are displayed on p. 393.

Molecular Formula of Quino <b>ne</b>	Reactants	Product(s) and Yield(s) (%)	Refs.
C ₇ H ₆ O ₂ (contd.)	2-Methyl-1,4- benzoquinone and Ethyl 3-ethylamino- 2-pentenoate	Ethyl 1,2-diethyl-5-hydroxy-6- methylindole-3-carboxylate (20), ethyl 1,2-diethyl-5-hydroxy-7- methylindole-3-carboxylate (1.5)	10
	Ethyl 3-benzylamino- crotonate	Ethyl 1-benzyl-5-hydroxy-2,6- dimethylindole-3-carboxylate (25)	52
	Ethyl 3-n-propyl- aminocinnamate	Ethyl 5-hydroxy-2-phenyl-1- <i>n</i> - propylindole-3-carboxylate (18)	55
	Ethyl 3-isobutyl- aminocinnamate	Ethyl 5-hydroxy-1-isobutyl-2- phenylindole-3-carboxylate (17)	55
	Ethyl 3-(2-hydroxy- ethylamino)- crotonate	Ethyl 5-hydroxy-1-hydroxyethyl- 2,6-dimethylindole-3-carboxylate (14), ethyl 5-hydroxy-1-hydroxy- ethyl-2,7-dimethylindole-3- carboxylate (1)	47
C7H8O3	2-Methoxy-1,4-		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-6-methoxy-2- methylindole-3-carboxylate (38- 49) 5-methoxy-B (10)	3, 10, 34
	Ethyl 3-ethylamino- crotonate	Ethyl 1-ethyl-5-hydroxy-6- methoxy-2-methylindole-3- carboxylate (63)	10
	Ethyl 3-amino-3- ethoxyacrylate	Ethyl 2-ethoxy-5-hydroxy-6- methoxyindole-3- carboxylate (51)	3
C ₈ H ₅ F ₃ O ₃	2-Methoxy-5-tri- fluoromethyl-1,4- benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-4-methoxy-2- methyl-7-trifluoromethylindole-3- carboxylate (25), ethyl 5- hydroxy-7-methoxy-2-methyl-4- trifluoromethylindole-3- carboxylate (25)	13
C ₈ H,ClO ₂	2-Chloro-5-ethyl-1,4- benzoquinone and		40
	t-Butyl-3-amino- crotonate	2-methylindole-3-carboxylate (60)	40

# TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES (Continued)Formulas A, B, C, and D are displayed on p. 393.

Molecular Formula of Quinone	Reactants	Product(s) and Yield(s) (%)	Refs.
C ₈ H ₈ O ₃	2-Ethyl-1,4-		
	benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 6-ethyl-5-hydroxy-2- methylindole-3-carboxylate (30), 6-ethyl-A (0.3)	10
	Ethyl 3-ethylamino- crotonate	Ethyl 1,6-diethyl-5-hydroxy-2- methylindole-3-carboxylate (14), ethyl 1,7-diethyl-5-hydroxy-2- methylindole-3-carboxylate (0.2)	10
	2,3-Dimethyl-1,4-		
	benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-2,6,7-trimethyl- indole-3-carboxylate (61)	37
	2,5-Dimethyl-1,4-		
	benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-2,4,7-trimethyl- indole-3-carboxylate ()	35
C ₈ H ₈ O ₈	2-Hydroxy-3,6-		
	dimethyl-1,4-		
	benzoquinone and		_
	Ethyl 3-amino- crotonate	Ethyl 5,6-dihydroxy-2,4,7-trimethyl- indole-3-carboxylate (46)	3
$C_8H_8O_4$	2,3-Dimethoxy-1,4-		
	benzoquinone and		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-6,7-dimethoxy-2- methylindole-3-carboxylate (23- 36), 5,6-dimethoxy-A (24-28)	8a
C ₁₂ H ₄ Cl ₂ O ₂	2-(2,4-Dichloro-	· · · · · · · ·	
	phenyl)-1,4-		
	benzoquinone and		
	Ethyl 3-methyl <b>a</b> mino- crotonate	Ethyl 6-(2,4-dichlorophenyl)-5- hydroxy-1,2-dimethylindole-3- carboxylate (16)	33
C12H,ClO2	2-(4-Chlorophenyl)-		
	1,4-benzoquinone		
	and		
	Ethyl 3-amino- crotonate	Ethyl 6-(4-chlorophenyl)-5-hydroxy- 2-methylindole-3-carboxylate (17)	33
	Ethyl 3-methylamino- crotonate	Ethyl 6-(4-chlorophenyl)-5-hydroxy- 1,2-dimethylindole-3-carboxyl- ate (15)	33

Molecular Formula of Quinone	Reactant	Product(s) and Yield(s) (%)	Refs.
C ₁₈ H ₇ NO ₄	2-(4-Nitrophenyl)-1,4- benzoquinone and Ethyl 3-methylamino- crotonate	Ethyl 5-hydroxy-1,2-dimethyl-6-(4- nitrophenyl)indole-3-carboxyl- ate (14)	33
$C_{12}H_8O_2$	2-Phenyl-1,4-benzo- guinone and		
	Ethyl 3-amino- crotonate	Ethyl 5-hydroxy-2-methyl-6- phenylindole-3-carboxylate (), ethyl 5-hydroxy-2-methyl-7- phenylindole-3-carboxylate ()	33, 34
	Ethyl 3-methylamino-	Ethyl 5-hydroxy-1,2-dimethyl-6-	33
	crotonate Ethyl 3-benzylamino- crotonate	phenylindole-3-carboxylate (16) Ethyl 1-benzyl-5-hydroxy-2- methyl-6-phenylindole-3- carboxylate (16)	33
C ₁₂ H ₉ NO ₂	2-Anilino-1,4-benzo-		
	quinone and Ethyl 3-methylamino- crotonate	Ethyl 6-anilino-5-hydroxy- 1,2-dimethylindole-3- carboxylate (29)	119
C13H1002S	2-Benzylthio-1,4-		
	benzoquinone and Ethyl 3-methylamino- crotonate	Ethyl 6-benzylthio-5-hydroxy-1,2- dimethylindole-3-carboxylate (38)	24
$C_{13}H_{11}NO_2$	2-(p-Toluidino)-1,4-		
	Ethyl 3-methyl- aminocrotonate	Ethyl 5-hydroxy-1,2-dimethyl-6- (p-toluidino)indole-3-carboxylate (80)	119
	2-(N-Methylanilino)-		
	1,4-benzoquinone an		
	Ethyl 3-methyl- aminocrotonate	Ethyl 5-hydroxy-1,2-dimethyl-6- (N-methylanilino)indole-3- carboxylate (54)	119
C ₁₃ H ₁₁ NO ₃	2-(p-Methoxyanilino)		
	1,4-benzoquinone ar	nd	
	Ethyl 3-methyl- aminocrotonate	Ethyl 5-hydroxy-1,2-dimethyl-6- ( <i>p</i> -methoxyanilino)indole-3- carboxylate (59)	119



Note: References 116-124 are on p. 454.



# TABLE I. SYNTHESIS OF ALKYL 5-HYDROXYINDOLE-3-CARBOXYLATES (Continued)Formulas A, B, C, and D are displayed on p. 393.

Note: References 116-124 are on p. 454.

## TABLE II. 5-Hydroxy-1H-benz[g]indoles Prepared from 1,4-Naphthoquinone and Enamines



Enamine	Product(s) and Yield(s) (%)	Refs.
Ethyl 3-aminocrotonate	Ethyl 5-hydroxy-2-methyl-1H-benz[g]- indole-3-carboxylate (56)	42
Ethyl 3-methylaminocrotonate	Ethyl 5-hydroxy-1,2-dimethyl- $1H$ -benz[g]- indole-3-carboxylate (51)	42
Ethyl 3-ethylaminocrotonate	Ethyl 1-ethyl-5-hydroxy-2-methyl-1H- benz[g]indole-3-carboxylate (57)	52
Ethyl 3-n-butylaminocrotonate	Ethyl 1-n-butyl-5-hydroxy-2-methyl-1H- benz[g]indole-3-carboxylate ()	36, 45
Ethyl 3-anilinocrotonate	Ethyl 5-hydroxy-2-methyl-1-phenyl-1H- benz[g]indole-3-carboxylate (51)	36, 45
Ethyl 3-(p-chlorophenyl- amino)crotonate	Ethyl 1-(p-chlorophenyl)-5-hydroxy-2- methyl·1H-benz[g]indole-3-carboxylate (), ethyl 5-acetoxy-1-(p-chlorophenyl)- 4-hydroxy-2-methyl-1H-benz[g]indole- 3-carboxylate ()	5 <b>3</b>
Ethyl 3-benzylaminocrotonate	Ethyl 1-benzyl-5-hydroxy-2-methyl-1H- benz[a]indole-3-carboxylate (37)	52
Ethyl 3-n-propylamino- cinnamate	Ethyl 5-hydroxy-2-phenyl-1- <i>n</i> -propyl- 1 <i>H</i> -benz[ <i>q</i> ]indole-3-carboxylate (56)	55
Ethyl 3-isobutylamino- cinnamate	Ethyl 5.hydroxy-1-isobutyl-2-phenyl-1H- benz[q]indole-3-carboxylate (50)	55
Dimethyl 2-phenylamino- fumarate	Dimethyl 5-hydroxy-l-phenyl-l $H$ - benz[q]indole-2,3-dicarboxylate (32)	56
Diethyl 3-aminoglutaconate	Ethyl 3-carbethoxy-5-hydroxy- $1H$ - benz[g]indolyl-2-acetate (50)	51
4-Methylamino-3-penten-2-one	3. Acety]-5-hydroxy-1,2-dimethyl-1H- benz[g]indole, 3-acetyl-5-hydroxy-2- methylnaphtho[1,2-b]furan (total, 74) ^a	61
4-Anilino-3-penten-2-one	<b>3</b> -Acetyl-5-hydroxy-2-methyl-1-phenyl- 1H-benz[g]indole (69)	61

Note: References 116-124 are on p. 454.

^a The mixture was separated by fractional crystallization.

### TABLE III. 5-Hydroxyindole-3-carbonitriles, -carboxamides, and -ketones from Benzoquinones and Enamines

Molecular Formula of	Framina	Product(s) and Vield(s) $(9/)$	Bofs
$C_6H_4O_2$	3-Aminocinnamonitrile	5-Hydroxy-2-phenylindole-3-carbonitrile (32)	8
	3-Methylaminocrotonanilide	5-Hydroxy-1,2-dimethylindole-3- carboxanilide (64)	6
	4-Amino-3-penten-2-one	3-Acetyl-5-hydroxy-2-methylindole (38), 3-acetyl-5-hydroxy-2-methyl- benzofuran (29)	60
	4-(2-Hydroxyethylamino)- 3-penten-2-one	3-Acetyl-5-hydroxy-1-hydroxyethyl-2- methylindole, 3-acetyl-5-hydroxy-2- methylbenzofuran (total, 20) ^a	62
	4-Anilino-3-penten-2-one	3-Acetyl-5-hydroxy-2-methyl-1- phenylindole (32-53)	38, 48, 61
	4-(o-Toluidino)-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methyl-1- (o-tolyl)indole (34)	48
	4-(p-Toluidino)-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methyl-1- (p-tolyl)indole (37)	48, 62
	4-Benzylamino-3-penten- 2-one	3-Acetyl-1-benzyl-5-hydroxy-2- methylindole, 3-acetyl-5-hydroxy-2- methylbenzofuran (total, 49) ^b	62
	4-(Carbethoxymethylamino)- 3-penten-2-one	Ethyl 3-acetyl-5-hydroxy-2-methyl-1- indolyl acetate, 3-acetyl-5-hydroxy- 2-methylbenzofuran (total, 42) ^b	62
	4-(o-Anisidino)- 3-penten-2-one	3-Acetyl-5-hydroxy-2-methyl-1- (o-methoxyphenyl)indole (34)	48, 62
	4-( <i>m</i> -Anisidino)-3- penten-2-one	3-Acetyl-5-hydroxy-2-methyl-1- ( <i>m</i> -methoxyphenyl)indole (30)	48
	4-( <i>p</i> -Anisidino)-3- penten-2-one	3-Acetyl-5-hydroxy-2-methyl-1- ( <i>p</i> -methoxyphenyl)indole (38-50)	48,62
	Ethyl 2-amino-3-benzoyl- acrylate	Ethyl 3-benzoyl-5-hydroxyindole-2- carboxylate (45)	59, 120
	Ethyl 2-benzylamino-3- acetylacrylate	Ethyl 3-acetyl-1-benzyl-5-hydroxy- indole-2-carboxylate ()	120
	4-(p-Dimethylaminophenyl- amino)-3-penten-2-one	3-Acetyl-1-(p-dimethylaminophenyl)-5- hydroxy-2-methylindole (38-58)	48, 62
	4-(m-Acetamidophenyl- amino)-3-penten-2-one	l-(m-Acetamidophenyl)-3-acetyl-5- hydroxy-2-methylindole (48)	48
	4-(p-Acetamidophenyl- amino)-3-penten-2-one	l-(p-Acetamidophenyl)-3-acetyl-5- hydroxy-2-methylindole (57)	48,62
	4-(m-Chlorophenylamino)- 3-penten-2-one	3-Acetyl-l-( <i>m</i> -chlorophenyl)-5- hydroxy-2-methylindole (26)	48
	4-(p-Chlorophenylamino)- 3-penten-2-one	3-Acetyl-l-(p-chlorophenyl)-5- hydroxy-2-methylindole (26)	48
$C_8H_8O_2$	4-(Methylamino)-3-penten- 2-one ^c	3-Acetyl-5-hydroxy-1,2,6,7-tetra- methylindole (28)	61
	4-Anilino-3-penten- 2-one ^c	3-Acetyl-5-hydroxy-2,6,7-trimethyl-1- phenylindole (45)	61

The quinone was 1,4-benzoquinone unless otherwise indicated.

Note: References 116-124 are on p. 454.

^a The mixture was separated by fractional crystallization from acetic acid.

^b The compounds were separated by fractional crystallization from methanol.

^c The quinone was 2,3-dimethyl-1,4-benzoquinone.

TABLE IV. MICHAEL ADDUCTS ISOLATED AS MAJOR PRODUCTS FROM THE REACTION OF QUINONES AND ENAMINES



The substituents in the Michael adducts are listed under  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$ . The indole derivative, when formed, is named. Formulas B, C and D are displayed on p. 393.

407	Molecular Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s) (%)	Refs.
	$\overline{C_6H_2Cl_2O_2}$	2,3-Dichloro-1,4- benzoquinone	Ethyl 3-methylamino- crotonate	$ \begin{array}{llllllllllllllllllllllllllllllllllll$	116
			Ethyl 3-n-propyl- aminocrotonate	$R_1 = n \cdot Pr, R_2 = Me, R_3 = OEt, R_4 = 3.4 \cdot Cl_2$ (57), ethyl 6,7-dichloro-5-hydroxy-2-methyl- l-n-propylindole-3-carboxylate (7)	116
			Ethyl 3-n-butylamino- crotonate	$R_1 = n \cdot Bu$ , $R_2 = Me$ , $R_3 = OEt$ , $R_4 = 3,4 \cdot Cl_2$ (71), ethyl l-n-butyl-6,7-dichloro-5-hydroxy- 2-methylindole-3-carboxylate (5)	116
			Ethyl 3-benzylamino- crotonate	$ \begin{array}{l} \mathbf{R_1} = \mathbf{PhCH_2}, \mathbf{R_2} = \mathbf{Me}, \mathbf{R_3} = \mathbf{OEt}, \mathbf{R_4} = \mathbf{3,4\text{-}Cl_2} \\ (50), \ \text{ethyl $1$-benzyl-6,7-dichloro-5-hydroxy-} \\ \textbf{2-methylindole-3-carboxylate}  (9) \end{array} $	116

Note: References 116-124 are on p. 454.

TABLE IV.	MICHAEL ADDUCTS ISOLATED AS MAJOR PRODUCTS FROM THE REACTIONS OF
	QUINONES AND ENAMINES (Continued)

	Molecular Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s) (%)	Refs.
	$\overline{\mathrm{C_6H_4O_2}}$	1,4-Benzoquinone	Ethyl 3-aminocrotonate	$R_1 = H, R_2 = Me, R_3 = OEt, R_4 = H$ (16), B (10), C (10), ethyl 5-hydroxy-2-methyl- indole-3-carboxylate (30)	11
			Ethyl 3-aminocinnamate	$R_1 = H, R_2 = Ph, R_3 = OEt, R_4 = H$ (24), D (3.5)	8
			3-Aminocrotonanilide	$R_1 = H, R_2 = Me, R_3 = NHPh, R_4 = H$ (48)	6
			3-Ethylaminocroton- anilide	$\mathbf{R}_{1} = \mathbf{Et}, \ \mathbf{R}_{2} = \mathbf{Me}, \ \mathbf{R}_{3} = \mathbf{NHPh}, \ \mathbf{R}_{4} = \mathbf{H}$ (62)	6
408			3-Benzylaminocroton- anilide	$R_1 = PhCH_2, R_2 = Me, R_3 = NHPh, R_4 = H$ (32)	6
	$\mathrm{C_7H_5BrO}_{3}$	2-Bromo-5-methoxy- 1,4-benzoquinone	t-Butyl 3-aminocro- tonate	$R_1 = H, R_2 = Me, R_3 = OBu \cdot t, R_4 = 4 \cdot OMe$ (5)	41
	$C_7H_6O_2$	2-Methyl-1,4- benzoquinone	Ethyl 3-isopropylamino- crotonate	$R_1 = i$ -Pr, $R_2 = Me$ , $R_3 = OEt$ , $R_4 = 3$ -Me (18), ethyl 5-hydroxy-1-isopropyl-2,6-dimethyl- indole-3-carboxylate (18)	10
	$C_8H_6O_4$	2-Carbomethoxy- 1,4-benzoquinone	Ethyl 3-aminocrotonate	$R_1 = H, R_2 = Me, R_3 = OEt, R_4 = 6 \cdot CO_2 Me$ (59)	12
	$\mathbf{C_8H_8O_2}$	2,5-Dimethyl-1,4- benzoquinone	Ethyl 3-ethylamino- crotonate	$R_1 = Et, R_2 = Me, R_3 = OEt, R_4 = 3.6 \cdot (Me)_2$ (23)	35
	$C_8H_8O_4$	2,3-Dimethoxy-1,4- benzoquinone	Ethyl 3-aminocrotonate	$\begin{array}{l} R_1 = H, \ R_2 = Me, \ R_3 = OEt, \ R_4 = 3,4 \cdot (OMe)_2 \\ (24-28), \ ethyl \ 5-hydroxy-6,7-dimethoxy-2- \\ methylindole-3-carboxylate  (23-36) \end{array}$	8a



Molecul <b>ar</b> Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s) (%)	Refs.
$\mathbf{C_6H_2Cl_2O_2}$	2,3-Dichloro-1,4- benzoquinone	4-Amino-3-penten-2-one 3-Acetyl-6,7-dichloro-5-hydroxy-2-methylbenzo furan (74)		63
	-	4-Methylamino-3-penten- 2-one	3-Acetyl-6,7-dichloro-5-hydroxy-2-methylbenzo- furan (74)	61
		4-Anilino-3-penten-2-one	3-Acetyl-6,7-dichloro-5-hydroxy-2-methylbenzo- furan (99)	61
		5-Anilino-4-hexen-3-one	3-Propionyl-6,7-dichloro-5-hydroxy-2-methyl- benzofuran (—)	121
$C_6H_4O_2$	1,4-Benzoquinone	4-Amino-3-penten-2-one	3-Acetyl-5-hydroxy-2-methylbenzofuran (29), 3-acetyl-5-hydroxy-2-methylindole (38)	60
		4-Methylamino-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methylbenzofuran (35)	44
		4-Ethylamino-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methylbenzofuran (33)	44
		1-Diethylamino-1-buten- 3-one	3-Acetyl-5-hydroxybenzofuran (57)	67
		4-Butylamino-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methylbenzofuran (39)	62
		4-Diethylamino-3-penten- 2-one	3-Acetyl-5-hydroxy-2-methylbenzofuran (29)	67

Note: References 116-124 are on p. 454.

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TABLE V.	5-Hydroxybenzofurans	FROM THE CONDENSATION	OF QUINONES	WITH ENAMINES	(Continued)

	Molecular Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s) (%)	Refs.
410	$C_{\bullet}H_{\bullet}O_{2}$ 1 (contd.)	I,4-Benzoquinone (contd.)	4-Anilino-3-buten-2-one	5-Hydroxy-2-methylbenzofuran-3-carbox- aldehyde (40)	120
			3-Diethylaminoacrylo- phenone	5-Hydroxy-3-benzofuranyl phenyl ketone (68)	67
			3-Diethylamino-4'- methylacrylophenone	5-Hydroxy-3-benzofuranyl p-tolyl ketone (36)	67
			3-Diethylamino-2',4'- dimethylacrylophenone	5-Hydroxy-3-benzofuranyl 2,4-dimethylphenyl ketone (36)	67
			3-Diethylamino-4'-chloro- acrylophenone	5-Hydroxy-3-benzofuranyl <i>p</i> -chlorophenyl ketone (54)	67
			Ethyl 3-dimethylamino- crotonate	Ethyl 5-hydroxy-2-methylbenzofuran-3- carboxylate (40)	66
			Ethyl 3-diethylamino- crotonate	Ethyl 5-hydroxy-2-methylbenzofuran-3- carboxylate (23)	67
			Ethyl 3-piperidino- crotonate	Ethyl 5-hydroxy-2-methylbenzofuran-3- carboxylate (40)	66
			3-Diethylamino-3',4'-di- methoxyacrylophenone	5-Hydroxy-3-benzofuranyl 3,4-dimethoxyphenyl ketone (33)	67
	$\mathrm{C_{10}H_6O_2}$	1,4-Naphthoquinone	4-Methylamino-3-penten- 2-one	<ul> <li>3-Acetyl-5-hydroxy-2-methylnaphtho[1,2-b]furan,</li> <li>3-acetyl-5-hydroxy-1,2-dimethyl-1H-benz[g]- indole (total, 74)^a</li> </ul>	61

Note: References 116-124 are on p. 454.

^a The mixture was separated by fractional crystallization.


	Molecular Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s) (%)	Refs.
	$C_6H_4O_2$	Benzoquinone	Dimethylaminoiso- butylene	2-Dimethylamino-2,3-dihydro-3,3-dimethyl- 5-benzofuranol (48)	69
41			Ethyl 3-amino-2-methyl- crotonate	Ethyl 2-amino-2,3-dihydro-5-hydroxy-2- methylbenzofuran-3-carboxylate (30)	3
1			1-Piperidinopropene	2,3-Dihydro-3-methyl-2-(1-piperidino)-5- benzofuranol (69)	70
			1-Diethylaminobutylene	2-Diethylamino-2,3-dihydro-3-ethyl-5- benzofuranol (60)	69
			1-Morpholinocyclopentene	2,3-Dihydro-2-morpholino-2,3-trimethylene-5- benzofuranol (87)	70
			1-Piperidinoisobutylene	2,3-Dihydro-3,3-dimethyl-2-(1-piperidino)- 5-benzofuranol (49)	69
			1-Piperidinobutylene	2,3-Dihydro-3-ethyl-2-(1-piperidino)-5-benzo- furanol (85-87)	69, 70
			1-Morpholinocyclo- hexene	2,3-Dihydro-2-morpholino-2,3-tetramethylene- 5-benzofuranol (69)	70

Molecular Formula of Quinone	Quinone	Enamine	Product(s) and Yield(s)(%)	Refs.
$C_6H_4O_2$ (contd.)	Benzoquinone (contd.)	5-Methyl-1-morpholino- cyclohexene	5a,6,7,8,9,9a-Hexahydro-7-methyl-5a- morpholino-2-dibenzofuranol (84)	122
		1 Mombolin oavelo	9.2 Dihudna 9 mamhalina 9.2 nantamathulana	70

TABLE VI.	PREPARATION OF	2-SUBSTITUTED	Amino-2,3-Dihydro	5-BENZOFURANOLS
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		I-Morpholinocyclo-	2,3-Dihydro-2-morpholino-2,3-pentamethylene-	70
		heptene	5-benzoturanol (97)	
		4-(1-Heptenyl)morpholine	2,3-Dihydro-2-morpholino-3-pentyl-5-	69
			Denzoluranol (96)	
		l-Piperidino-4-methyl- pentene	2,3-Dihydro-3-isobutyl-2-piperidino-5-benzo- furanol (87)	70
		1-Piperidino-2-phenyl- ethylene	2,3-Dihydro-3-phenyl-2-piperidino-5-benzo- furanol (68)	70
$C_7H_6O_2$	Toluquinone	1-Morpholinocyclohexene	2,3-Dihydro-6-methyl-2-morpholino-2,3- tetramethylene-5-benzofuranol (94)	122
$C_7H_6O_3$	2-Methoxy-1,4- benzoquinone	Ethyl 3-amino-2-methyl- crotonate	Ethyl 2-amino-2,3-dihydro-5-hydroxy-2- methylbenzofuran-3-carboxylate (70)	3
		4-Isobutenylmorpholine	2,3-Dihydro-6-methoxy-3,3-dimethyl-2- morpholino-5-benzofuranol (87)	72
C ₈ H ₆ O ₄	2-Carbomethoxy-1,4- benzoquinone	Ethyl 3-amino-4,4,4-tri- fluorocrotonate	Ethyl 2-amino-4-carbomethoxy-2,3-dihydro- 5-hydroxy-2-trifluoromethylbenzofuran- 3-carboxylate (23)	35

	$C_8H_8O_4$	2,3-Dimethoxy-1,4- benzoquinone	Ethyl 3-amino-2-methyl- crotonate	Ethyl 2-amino-2,3-dihydro-5-hydroxy-6,7- dimethoxy-2-methylbenzofuran-3- carboxylate (46)	8a
	$\mathrm{C_{10}H_6O_2}$	Naphthoquinone	4-Isobutenylmorpholine	2,3-Dihydro-3,3-dimethyl-2-morpholino- naphtho[1,2-b]furan-5-ol (73)	71
	$\mathrm{C_{12}H_8O_2}$	2-Phenyl-1,4- benzoquinone	1-Piperidinopropene	2,3-Dihydro-3-methyl-7-phenyl-2-piperidino- 5-benzofuranol (62)	72
		-	4-Isobutenylmorpholine	2,3-Dihydro-3,3-dimethyl-2-morpholino-7- phenyl-5-benzofuranol (70), 2,3-dihydro- 3,3-dimethyl-2-morpholino-6-phenyl-5- benzofuranol (7)	72
			1-Morpholinocyclohexene	2,3-Dihydro-2-morpholino-2,3-tetramethylene-6- phenyl-5-benzofuranol (74)	122
41	$\mathbf{C_{12}H_8O_4S}$	2-Phenylsulfonyl-1,4- benzoquinone	Ethyl 3-aminocrotonate	Ethyl 2-amino-2,3-dihydro-5-hydroxy-2-methyl 4-phenylsulfonylbenzofuran-3-carboxylate (58)	123
13		·	Ethyl 3-methylamino- crotonate	Ethyl 2,3-dihydro-5-hydroxy-2-methyl-2- methylamino-4-phenylsulfonylbenzofuran-3- carboxylate (53)	123
			Ethyl 3-diethylamino- crotonate	Ethyl 2-diethylamino-2,3-dihydro-5-hydroxy- 2-methyl-4-phenylsulfonylbenzofuran-3- carboxylate (35)	123
			Ethyl 3-anilinocrotonate	Ethyl 2-anilino-2,3-dihydro-5-hydroxy-2- methyl-4-phenylsulfonylbenzofuran-3- carboxylate (67)	123

	Molecular Formula of				
	Quinone	Quinone	Enamine	Products and Yields (%)	Refs.
			A. Isoquinoline-4-carboxylates		
	C ₈ H ₆ O ₃	2-Acetyl-1,4-benzoquinone	Ethyl 3-aminocrotonate	HO $CO_2Et$ Me N (71) HO $Me$	12
41			t-Butyl 3-aminocrotonate	HO $CO_2Bu-t$ Mc $Mc$ HO $Me$ (67)	12
-	C _s H _s O _s	2-Carbomethoxy-1,4-benzoquinone	Ethyl 3-aminocrotonate	HO $CO_2Et$ Me NH HO $O(25)^a$	12
	······································	B	6-Hydroxycoumarin-4-carboxylates		
	C ₈ H ₄ O ₂	1,4-Benzoquinone	Ethyl aminofumarate	$HO \underbrace{CO_2Et}_{O O O} NH_2 $ (48)	7 <b>3</b> , 124
	C,HO,	2-Methyl-1,4-benzoquinone	Ethyl aminofumarate	$\begin{array}{c} \text{HO} \\ \text{HO} \\ \text{Me} \end{array} \begin{array}{c} \text{CO}_2 \text{Et} \\ \text{NH}_2 \\ \text{O} \\ \text{O} \end{array} (17), \end{array}$	74
				HO Me Me Me Me Me Me Me Me Me $MH_2$ (9)	
	<u> </u>	C. 2	2,3-Dihydro-6-hydroxy-4(1H)-carbazolones		
	C,H <b>\$F\$</b> 0 <b>\$</b>	2-Trifluoromethyl-1,4-benzoquinone	3-Amino-2-cyclohexen-1-one	$HO \qquad CO_2H O \qquad (23)$	29
415			3-Amino-5,5-dimethyl-2- cyclohexen-1-one	$H \rightarrow H \rightarrow$	29
				но о"	

TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES

2-Methoxy-1,4-benzoquinone

C,H,O3

• The yield is an overall figure for two stages, the last of which is treatment of the initial hydroquinone with acetic acid.

3-Amino-5,5-dimethyl-2-

cyelohexen-l-one

3-Amino-2-cyclohexen-1-one

(45)

Мe

Мe

Ń | Н (40)

MeO

HQ

MeO

29

29

Note: References 116-124 are on p. 454.



TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES (Continued)

	Molecular Formula of Quinone	Quinone	Enamine	Products and Yields (%)	Refs.
			E. 2,3-Benzo-1,4-dioxenes (con	tinued)	
	$C_4Br_4O_2$ (contd.)	Tetrabromo-1,2-benzoquinone (contd.)	l-(4-Morpholino)cyclopentene	$Br_{4} \xrightarrow{(1)}_{(N)} (3)$	76
418			I-Piperidinoisobutylene	$\mathbf{Br}_{4} \underbrace{\bigcirc \mathbf{Me}}_{\mathbf{N}} \underbrace{\bigcirc \mathbf{Me}}_{\mathbf{N}} \underbrace{(19)}_{\mathbf{N}}$	76
			1-Pyrrolidinocyclohexene		76
			l-(4-Morpholino)cyclohexene	$\mathbf{Br}_{\mathbf{t}} \underbrace{(80)}_{\mathbf{t}}$	76

TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES (Continued)



	Molecular Formula of Quinone	Quinone	Enamine	Products and Yields (%)	Refs.
			E. 2,3-Benzo-1,4-dioxenes (con	stinued)	
420	$C_{e}Cl_{4}O_{2}$ (contd.)	Tetrachloro-1,2-benzoquinone (contd.)	l-(4-Morpholino)cyclohexene		76
			l-Piperidinocyclohexene	$Cl_{4} \qquad \qquad$	76
	$\mathrm{C_{13}H_6N_3O_3}$	Phenanthrolinquinone ^b	l - (4-Morpholino)cyclohexene l - (4-Morpholino)cycloheptene	? (18) ? (15)	76 76
	$C_{14}H_6O_2$	Phenanthraquinone	1-Pyrrolidinoisobutylene	Me O Me (33) N	76

TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES (Continued)



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Note: References 116-124 are on p. 454.

^b This nomenclature is that used in the original paper, but it is insufficient to permit distinction between the possible isomers.

	Molecular Formula of Quinone	Quinone	Enamine	Products and Yields (%)	Refs.
			E. 2,3-Benzo-1,4-dioxenes (continued	()	
422	C ₁₄ H ₈ O ₂ (contd.)	Phenanthraquinone (contd.)	l-(4-Morpholino)cyclohexene		76
			1-Piperidinocyclohexene		76
			1-(4-Morpholino)cycloheptene		76





TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES (Continued)



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	Molecul <b>a</b> r Formula of Quinone	Quinone	Enamine	Products and Yields (%)	Refs.
			E. 2,3-Benzo-1,4-dioxenes (continued)		
	C ₁₈ H ₁₀ O ₂ (conid.)	Chrysoquinone (contd.)	l-(4-Morpholino)cycloheptene		76
-			F. Pyrrolo[1,2-a]indoles		
.26	C ₆ H ₆ O ₆	1,4-Benzoquinone	2-Carbethoxymethylene pyrrolidine	HO CO ₃ Et (14)	14
	C7H6O3	2-Methyl-1,4-benzoquinone	2-Carbethoxymethylene pyrrolidine	HO Me (Total. 30)	14
				HO Me	

TABLE VII. PREPARATION OF OTHER HETEROCYCLIC SYSTEMS FROM QUINONES AND ENAMINES (Continued)



TABLE VIII. 5-AMINOINDOLE DERIVATIVES FROM QUINONE DIIMIDES AND ENAMINES

TABLE VIII. 5-AMINOINDOLE DERIVATIVES FROM QUINONE DIIMIDES AND ENAMINES (Continued)

	Molecular Formula of Quinone Diimide	Quinone Diimide	Enamine	Product and Yield (%)	Refs.
	C ₁₀ H ₁₆ N ₄ O ₄ S ₂ (contd.)	l,4-Benzoquinonedimethyl- sulfamoyldiimide (contd.)	l-(4-Morpholino)- cycloheptene	Me ₂ NSO ₂ NH (51) SO ₂ NMe ₂	85
428	$\mathrm{C_{18}H_{14}N_2O_4S_2}$	l,4-Benzoquinonedibenzene- sulfonimide	l-Pyrrolidino- cyclohexene	$\begin{array}{c} PhSO_2NH \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	84
			l-Hexamethyleneimino- cyclohexene	PhSO ₂ NH N SO ₂ Ph (10)	84



TABLE IX. 1,4-DIACYLAMINOBENZENES DERIVED FROM QUINONE DIIMIDES AND ACTIVE METHYLENE COMPOUNDS

"The product is a mixture of isomers.

TABLE IX.	1,4-DIACYLAMINOBENZENES DERIVED FROM QUINONE DIIMIDES AND	
	ACTIVE METHYLENE COMPOUNDS (Continued)	

	Molecular Formula of Quinone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
	C ₁₀ H ₁₅ ClN ₄ O ₄ S ₂	2-Chloro-1,4-benzoquinone- bisdimethylsulfamimide	Acetylacetone	Cl Cl (98) CH(COMe) ₂ NHSO ₂ NMe ₂	88
43(			Ethyl 2-oxocyclo- pentanecarboxylate	$Me_2NSO_2HN \qquad CO_2Et \qquad (97) \\ Me_2NSO_2HN \qquad O$	88
0			Ethyl 2-oxocyclo- hexanecarboxylate	$Me_2NSO_2HN \qquad CO_2Et \qquad (98)$ $Me_2NSO_2HN \qquad O$	88
			Ethyl 4-methyl-2-oxo- cyclohexanecarboxylate	Me ₂ NSO ₂ HN Cl- Me ₂ NSO ₂ HN O (95)	88
			Ethyl benzoyl- acetate	Cl CH(COPh)CO ₂ Et NHSO ₂ NMe ₂ (74)	88



Note: References 116-124 are on p. 454.

^a The product is a mixture of isomers.

TABLE IX.	1,4-DIACYLAMINOBENZENES DERIVED FROM QUINONE DIIMIDES ANI
	ACTIVE METHYLENE COMPOUNDS (Continued)

	Molecular Formula of Quínone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
	$C_{10}H_{16}N_4O_4S_2$ (contd.)	l,4-Benzoquinone-bis- dimethylsulfamimide (contd.)	Ethyl 2-oxocyclo- hexanecarboxylate	$Me_2NSO_2NH \qquad CO_2Et \qquad (98)$ $Me_2NSO_2HN \qquad O$	88
432			Ethyl 4-methyl-2-oxo- cyclohexanecarboxylate	Me ₂ NSO ₂ NH CO ₂ Et Me NSO ₂ HN 0	98
			Benzoylacetone	NHSO ₂ NMe ₂ (100) CH(COMe)('OPh NHSO ₂ NMe ₂	88
			Ethyl benzoylacetate	NHSO ₂ NMe ₂ (100) CH(COPh)CO ₂ Et NHSO ₂ NMe ₂	88



TABLE IX.	1,4-DIACYLAMINOBENZENES DERIVED FROM QUINONE DIIMIDES AND
	ACTIVE METHYLENE COMPOUNDS (Continued)

	Molecular Formula of Quinone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
	C ₁₈ H ₁₄ N ₈ O ₃	l,4-Benzoquinone- dibenzimide	Acetylacetone	NHCOPh (76) CH (COMe) ₂ NHCOPh	86
434			Diethyl malonate	NHCOPh (75) C'H/(CO ₂ Et) ₂	86
			5,5-Dimethylcyclo- hexane-1,3-dione	PhCONH O Mc (88) PhCOHN O	91
			Ethyl 2-oxonipecotate	$\begin{array}{c} \mathbf{PhCONH} & \mathbf{CO_{p}Et} \\ & & & \\ & & & \\ & & & \\ & & & \\ \mathbf{PhCOHN} & \mathbf{O} \end{array} $ (100)	91



TABLE IX.	1,4-DIACYLAMINOBENZENES DERIVED FROM QUINONE DIIMIDES AND	,
	ACTIVE METHYLENE COMPOUNDS (Continued)	

	Molecular Formula of Quinone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
	$\begin{array}{c} \mathrm{C_{18}H_{14}N_{2}O_{4}S_{2}}\\ (contd.) \end{array}$	1,4-Benzoquinonedibenzene- sulfonimide (contd.)	2-Methylcyclohexane- 1,3-dione	PhSO ₂ NH Me PhSO ₂ HN O (94)	95
436			5,5-Dimethylcyclo- hexane-1,3-dione	PhSO ₂ NH O Me (76) PhSO ₂ HN O	87
			Ethyl 2-oxocyclo- pentanecarboxylate	$\begin{array}{c} PhSO_2NH \\ & \bigcirc \\ PhSO_2HN \end{array} (97) \\ \end{array}$	87
			Ethyl 2,6-dioxo- cyclohexylacetate	$\begin{array}{c} PhSO_2NH & O \\ & & & \\ & & & \\ PhSO_2HN & (H_2CO_2Et \end{array} $ (89)	95



 

 TABLE IX.
 1,4-Diacylaminobenzenes
 Derived from Quinone Diimides and Active Methylene Compounds (Continued)

	Molecular Formula of Quinone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
438	C ₁₈ H ₁₄ N ₈ O ₄ S ₃ (contd.)	l,4-Benzoquinonedibenzene- sulfonimide (contd.)	Ethyl l-methyl-3- oxopyrrolidinyl- 4-carboxylate	PhSO ₂ NH CO ₂ Et NMe (82)	91
			Ethyl l-methyl-3- oxopiperidinyl- 4-carboxylate	PhSO ₂ HN O PhSO ₂ NH CO ₂ Et NMe (95)	91
			3-Acetyl-1-ethyl- oxindole	PhSO ₂ HN O PhSO ₂ NH (OMe CO-NH (56) PhSO ₂ HN	91



	Molecul <b>a</b> r Formula of Quinone Diimide	Quinone Diimide	Active Methylene Compound	Product and Yield (%)	Refs.
440	C ₁₂ H ₁₃ N ₄ O ₄ S ₂	1,4-Naphthoquinone-bis- dimethylsulfamimide	Acetylacetone	$(100)$ $(100)$ $CH(COMe)_2$ $NHSO_2NMc_2$	88
			Ethyl acetoacetate	$(79)$ $(HSO_2NMe_2$ $(79)$ $(HSO_3NMe_2$	88
			Ethyl benzoylacetate	NHSO ₂ NMe ₂ (99) CH(COPh)CO ₂ Et NHSO ₂ NMe ₂	88

# TABLE X. 1,4-Diacylaminonaphthalenes Derived from Naphthoquinone Diimides and Active Methylene Compounds



	Molecular Formula of Quinone Imide	Quinone Imide	Active Methylene Compound	Product and Yield (%)	Refs.
442	C13H3NO3S	1,4-Benzoquinonemono- benzenesulfonimide	Acetylacetone	NHSO ₂ Ph CH(COMe) ₂ (94)	90
			Ethyl acetoacetate	NHSO ₂ Ph CH(COMe)CO ₂ Et (94)	90
			Diethyl malonate	$ \begin{array}{c} \mathbf{N}\mathbf{HSO_2Ph} \\ \mathbf{O}\mathbf{H} \\ (\mathbf{I}\mathbf{B}) \\ \mathbf{O}\mathbf{H} \\ \end{array} $ (18)	90

## TABLE XI. 4-BENZENESULFONAMIDO-PHENOLS AND -1-NAPHTHOLS FROM QUINONE MONOIMIDES AND ACTIVE METHYLENE COMPOUNDS



	Starting Material	Reaction Conditions	Product and Yield (%)	Refs.
	NHSO ₂ Me CH(COMe) ₂ NHSO ₂ Me	22% HCl, reflux, 12 hr	$MeSO_2NH$ $MeSO_2NH$ $Me$ $Me$ $Me$ $Me$ $SO_2Me$ $Me$ $Me$ $Me$ $Me$ $Me$ $Me$ $Me$	89
		Coned $H_2SO_4$ , room temp, 24 hr	$MeSO_2NH \qquad \qquad COMe \qquad \qquad Me \qquad (48) \qquad \qquad$	89
444	NHSO ₂ NMe ₂ Cl ('H(COMe) ₂ NHSO ₂ NMe ₂	22% HCl, reflux, 4 hr	$H_{2}N$ $H$	88
	CI CI CI NHSO ₂ NMe ₂ CI CH(COPh)CO ₂ Et NHSO ₂ NMe ₂	22% HCl, reflux, 89 hr	$H_{2}N$ $(55)$ $Cl$ $Cl$ $H$	88
	Cl CH(COMe) ₂ NHSO ₂ NMe ₂	22% HCl, reflux, 12 hr	$H_2N$ $H_2N$ $H$ $H$ $H$ $H$ $H$ $H$ $H$	88

TABLE XII. SYNTHESIS OF 5-AMINOINDOLES AND CONGENERS FROM 1,4-DIACYLAMINOBENZENES







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Note: References 116-124 are on p. 454.

CH(COMe)1

Me₂NSO₂NH

PhO₂S

Me2NSO2HN Ó NHSO2NMe2

NHSO2NMe2

NHSO2NMe2

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	Starting Material	Reaction Conditions	Product and Yield (%)	Refs.
	NHNO2Ph CH(COMe)2 NHSO2Ph	22% HCl, reflux, 12 hr	PhSO ₂ NH COMe Me (80) SO ₂ Ph	91
448		Concd $H_2SO_4$ , room temp, 24 hr	PhSO ₂ NH Me (30)	91
	PhSO ₂ NH O PhSO ₂ HN O	HOAc, reflux, 1.5 hr	PhSO ₂ NH (98)	95
	PhSO ₂ NH O Me PhSO ₂ HN O	HOAc, reflux, 2.5 hr	PhSO ₂ NH Me N $-CH_2CH_2CH_2CO_2H$ (80) SO ₂ Ph	95

 TABLE XII.
 Synthesis of 5-Aminoindoles and Congeners from 1,4-Diacylaminobenzenes (Continued)



	Starting Material	Reaction Conditions	Product and Yield (%)	Refs.
450	PhSO ₂ NH ('O ₂ Et PhSO ₂ HN O	22% HCl, reflux, 16 hr	PhSO ₂ NH NMe (56) SO ₂ Ph	91
	PhSO ₂ NH O PhSO ₂ HN CH ₂ CO ₂ Et	HOAc, reflux, 3 hr	PhSO ₂ NH (H ₂ CO ₂ H) $(H_2CO_2H)$ (98) $(H_2CH_2CH_2CO_2H)$ (98) $(SO_2Ph)$	95
	PhCONH O Me PhCOHN O	22% HCl, reflux, 17 hr	$H_2N$ $Me$ (60)	91
			**	

## TABLE XII. Synthesis of 5-Aminoindoles and Congeners from 1,4-Diacylaminobenzenes (Continued)



Note: References 116-124 are on p. 454.

Starting Material	Reaction Conditions	Product and Yield (%)	Refs.
NHSO ₂ Me ('H(('OMe) ₂ )	Dioxane-37% HCl, reflux, 12 hr	MeSO ₂ NH COMe Me (35)	90
NHSO ₂ Ph CH(COMe)a OH	20% HCl, reflux, 5.5 hr	PhSO ₂ HN O Me (77)	90
NHSO ₂ Ph CH(('OMe)CO ₂ Et OH	20% HCl, reflux, 3 hr	$PhSO_2HN \underbrace{CO_2Et}_{O}Me  (96)$	90
PhSO₂NH	70% $H_2SO_4$ , room temp, 48 hr	PhSO ₂ HN	90
$\begin{array}{c} & (O_2Et) \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ $	37% HCl, reflux, 18 hr	PhSO ₂ NH (33) ⁴	90

 TABLE XIII.
 5-Aminobenzofuran and 5-Aminonaphtho[1,2-b]furan Derivatives Prepared from

 4-Substituted Sulfamido-phenols and -I-naphthols



^a The original investigators formulated this product as the isomeric 2-benzenesulfamido-7,8,9,9a-tetrahydrodibenzofuran. However, the indicated 6,7,8,9-tetrahydrodibenzofuran is the more likely structure.

## **ORGANIC REACTIONS**

## **REFERENCES TO TABLES**

¹¹⁶ A. N. Grinev, G. Y. Uretskaya, and S. F. Liberman, *Khim. Geterotsikl. Soedin.*, 7, 335 (1971) [C.A., 76, 14241k (1972)].

¹¹⁷ A. N. Grinev, V. N. Ermakova, and A. P. Terent'ev, *Doklady Akad. Nauk S.S.S.R.*, **121**, 862 (1958) [*C.A.*, **53**, 1167e (1959)].

¹¹⁸ A. N. Grinev and K. A. Sklobovskii, *Khim. Geterotsikl.-Soedin.*, 5, 100 (1969) [C.A., 70, 114930d (1969)].

¹¹⁹ A. N. Grinev, V. I. Shvedov, E. K. Panisheva, N. S. Bogdanova, I. S. Nikolaeva, and G. N. Pershin, *Khim.-Farm. Zh.*, **5**, 3 (1971) [*C.A.*, **75**, 88435c (1971)].

¹²⁰ G. Domschke, East German Patent 61,800 [C.A., 70, 47295k (1969)].

¹²¹ A. N. Grinev and V. I. Shvedov, Zhur. Obshchei Khim., **32**, 2614 (1962) [C.A., **58**, 7896b (1963)].

¹²² A. N. Grinev and S. A. Zotova, *Khim. Geterotsikl. Soedin.*, 7, 443 (1971) [C.A., 76, 249892 (1972)].

¹²³ F. A. Trofimov, N. G. Tsyshkova, V. I. Nozdrich, and A. N. Grinev, *Khim.-Farm.* Zh., 5, 30 (1971) [C.A., 75, 35567r (1971)].

¹²⁴ G. Domschke and H. Oelmann, J. Prakt. Chem., 311, 800 (1969).

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### CHAPTER 4

## THE ZININ REDUCTION OF NITROARENES

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#### INTRODUCTION

The Zinin reduction is a method for the reduction of nitroarenes by negative divalent sulfur (sulfide, sulfhydrate, and polysulfides). This versatile reaction can be carried out in standard laboratory equipment and has been used for plant-scale manufacture of aromatic amines when other reduction media are destructive to sensitive compounds or result in undesired side reactions.

The reaction, first used by Zinin in 1842 to prepare aniline from nitrobenzene,¹ has since been of great importance in the preparation of aromatic amines. With the advent of catalytic reduction procedures, Zinin's method has seen less use in the laboratory as a preparative technique. Recently published laboratory texts of organic chemistry often fail to mention this rather simple procedure for the preparation of a host of ordinary or rare amines. Economically, in most instances it has not proved so attractive as the iron reduction method in commercial applications,² but it is used with more sensitive compounds that would not be compatible with acid media or would be reduced farther than desired by the iron or catalytic hydrogenation process.

Refinements in technique³ and a better understanding of the reaction mechanism (see below) should make the method attractive for the preparation of a variety of amines. A closer look at the technology may lead to the development of processes which offer advantages over many current catalytic and iron reduction methods. For instance, a recent article describes a continuous process for reducing 1-nitronaphthalene with aqueous sodium disulfide.⁴ Several reactions discussed on pp. 460– 464 produce products other than the expected amines and should lead to general preparative methods for materials not readily obtainable by other reduction methods.

#### MECHANISM

The stoichiometry of the Zinin reduction is illustrated by Zinin's original reduction of nitrobenzene by aqueous ammonium sulfide.

$$4 \text{ C}_6 \text{H}_5 \text{NO}_2 + 6 \text{ S}^{2-} + 7 \text{ H}_2 \text{O} \rightarrow 4 \text{ C}_6 \text{H}_5 \text{NH}_2 + 3 \text{ S}_2 \text{O}_3^{2-} + 6 \text{ OH}^{-}$$

¹ N. Zinin, J. Prakt. Chem., [1] 27, 149 (1842).

² P. H. Groggins, Unit Processes in Organic Synthesis, McGraw-Hill, New York, 1958, pp. 186-190.

³ H. I. Stryker, U.S. Pat. 3,223,727 (1965) [C.A., 64, 4051 (1966)].

⁴ G. M. Tomokkin and B. I. Kissin, Khim. Prom., 3, 79 (1960) [C.A., 55, 469 (1961)].

If the reductant is disulfide, the equation is analogous.

$$C_{6}H_{5}NO_{2} + S_{2}^{2-} + H_{2}O \rightarrow C_{6}H_{5}NH_{2} + S_{2}O_{3}^{2-}$$

Although earlier studies,⁵⁻⁷ particularly those by Hodgson,^{8.9} provide insight into the mechanism, the kinetic work of Hojo and co-workers is the most helpful.¹⁰ They worked mostly with disulfide, which reduced nitrobenzene much more rapidly than did sulfide. The medium they used was aqueous methanol, and the rate increased rapidly with increasing concentration of water. They showed that when sufficient alkali is present to keep the equilibrium

$$S_2^{2-} + H_2O \rightleftharpoons HS_2^- + OH^-$$

far on the side of disulfide ion, the rate of reaction is first-order in disulfide ion and first-order in nitroarene. Electron-withdrawing substituents speeded up the reaction considerably; the relative rates fitted the Hammett equation well, with  $\rho = -3.55$ . Azoxybenzene is reduced very slowly compared to nitrobenzene. These observations suggest that the rate-determining step is attack of disulfide ion on the nitro group. Probably the first product is a nitroso compound, which is rapidly reduced to a hydroxylamine and then an amine.

$$ArNO_2 + S_2^{2-} \rightarrow ArNO \rightarrow ArNHOH \rightarrow ArNH_2$$

These kinetic studies suggest to the experimenter that disulfide ion rather than sulfide ion be used; that as high a concentration of water be used as is consistent with complete or partial solution of the nitroarene in the reaction mixture; that enough excess alkali be used to have almost all the reductant present as sulfide ion or disulfide ion; and that excess reductant be used to ensure a rapid reduction that does not stop at an intermediate stage, thus minimizing condensations of intermediates to give azoxy or azo compounds.

The uniqueness of the Zinin reduction of nitroarenes, as compared to reduction by iron or catalytic hydrogenation, lies in its lower reduction potential and its narrow useful range of electromotive force. This means that functional groups other than nitro are less likely to be reduced. Moreover, selective reduction of one nitro group in a dinitro- or trinitroarene is often possible. Some useful generalizations (pp. 458–459) often enable

⁵ H. Goldschmidt and H. Larsen, Z. Phys. Chem. (Leipzig), 71, 437 (1910).

⁶ K. Brand, J. Prakt. Chem., [2] 74, 449 (1906).

⁷ I. M. Kogan and A. I. Kizber, J. Gen. Chem., 5, 1762 (1935).

⁸ H. H. Hodgson, J. Soc. Dyers Colour., 59, 246 (1943).

⁹ H. H. Hodgson, J. Chem. Soc., 1944, 75.

¹⁰ M. Hojo, Y. Takagi and Y. Ogata, J. Amer. Chem. Soc., 82, 2459 (1960).

one to predict which isomer will be obtained, but the detailed mechanistic knowledge necessary for more comprehensive generalization is lacking. Steric hindrance and the relative reduction potentials of the different nitro groups may be factors. Hodgson has invoked resonance⁹ and hyperconjugation¹¹ to explain relative ease of detachment of oxygen from different nitro groups. Studies on the sulfur-sulfide electrode¹² may be used to explain the limits of the reduction medium.

It is evident that much remains to be learned about the mechanism and that studies using modern techniques and instruments would be desirable.

### SCOPE AND LIMITATIONS

While the reaction may be called the sulfide reduction method, the hydrosulfide method, or the polysulfide method, the term Zinin reduction which credits the discoverer is more general in implication and would properly include the many related procedures generated from Zinin's initial research. Generally, the reaction is applied to the reduction of mono- and poly-nitroarenes to the corresponding amines and nitro-amines, but has found application in the conversion of some nitroso and azo compounds to amines. It can also be used for the preparation of some hydroxylamines and benzotriazoles starting with the proper nitro compounds (see pp. 461, 462).

Generally the reagents used are ammonium, sodium, or potassium sulfides, hydrosulfides, or polysulfides. Manganous sulfide¹³ and ferrous sulfide¹⁴ are also used. An improvement in reductions with alkali sulfides by the addition of selenium has been suggested.¹⁵ The tables show that the method is applicable to practically any type of nitroarene. The presence of a wide variety of substituents on the aromatic nucleus can be tolerated without seriously reducing the effectiveness of the sulfur reagent.

The positions of the substituents play an important role in the progress of the reaction. For example, they affect the ease of reduction of mononitroarenes. In polynitro compounds the relative positions of the groups determine whether reduction gives monoamino or polyamino derivatives and determine the isomer distribution of the monoamino products. One of the advantages of the Zinin reduction is that it often stops at the nitroamine stage to give a particular isomer in high yield. Consideration of the

¹¹ H. H. Hodgson, J. Soc. Dyers Colour., 62, 114 (1946).

¹² P. L. Allen and A. Hickling, Chem. Ind. (London), 1954, 1558.

¹³ General Aniline and Film Co., U.S. Pat. 1,765,660 (1930) [C.A., 24, 4051 (1930)].

¹⁴ R. E. Kirk and D. F. Othmer, *Encyclopedia of Chemical Technology*, Vol. I, Interscience Encyclopedia, New York, 1947, p. 701.

¹⁵ F. Feigl and P. W. West, Anal. Chem., 19, 351 (1947).

tables suggests some useful generalizations. For example, in substituted dinitro- and trinitro-benzenes (Tables II and III) the least hindered nitro group is preferentially reduced.



No simple generalization can be made about dinitronaphthalenes (Table II). In dinitro- and trinitro-phenols and their ethers (Table IV), a nitro group ortho to hydroxy or alkoxy is preferentially reduced.



As a convenient laboratory procedure for converting nitroarenes to arylamines, the Zinin reduction is rarely surpassed by any other method. Catalytic hydrogenation requires more expensive equipment, and the techniques are considerably more difficult if one takes into account catalyst preparation, catalyst poisoning hazards, and the risk of reducing other groups. Reduction by iron is not generally a convenient laboratory method, being reserved for large-scale commercial applications. Moreover, it cannot be used for reduction of a single nitro group on a polynitro compound, nor can it be used on substrates harmed by acid media (e.g., some ethers and thioethers). Although there are some exceptions, lithium aluminum hydride and lithium borohydride generally convert nitro compounds to mixtures of azoxy and azo compounds.

#### Side Reactions

The reduction of a nitroarene does not always give the corresponding arylamine. The reduction may stop at the intermediate hydroxylamine stage, or another group in the molecule may undergo reduction or other reaction. Generally these reactions are unwanted and should be avoided as much as possible. Occasionally the reaction is useful, as in the conversion of o-nitroazobenzenes to benzotriazoles or the conversion of pnitrotoluene to p-aminobenzaldehyde. The principal side reactions are briefly described below.

**Dehalogenation** (ArHal  $\rightarrow$  ArH). Dehalogenations are rare. Only two occurrences were found in the literature: the conversion of 4,5-dichloro-3-iodonitrobenzene to 3,4-dichloroaniline¹⁶ and the reduction of 2-chloro-1,3-dinitrobenzene to *m*-nitroaniline.¹⁷

Formation of Sulfonic Acid (ArNO₂  $\rightarrow$  ArSO₃H). Three examples of the replacement of a nitro group by a sulfonic acid group are known. Each involves a trinitrobenzene with electron-releasing groups. The mechanism of this reaction is not known, but an oxygen exchange from the displaced nitro group to the entering sulfur species probably takes place. A Piria reaction^{*} would be a possible explanation if excessive exposure to oxygen occurred.³ 1,2,4-Trimethyl-3,5,6-trinitrobenzene is reduced to 1,2,4-trimethyl-5-amino-3-nitrobenzene-6-sulfonic acid in 40% yield.¹⁸



Similarly, 2,3,5-trinitro-1,4-xylene is converted to 3-amino-5-nitro-1,4-xylene-2-sulfonic acid¹⁹ and 2,5-dimethyl-3,4,6-trinitroanisole to 2,5-dimethyl-4-amino-6-nitroanisole-3-sulfonic acid.²⁰

* The formation of aminosulfonic acids from nitroarenes and metal sulfites; R. Piria, Ann., 78, 31 (1851).

¹⁶ G. Koerner and A. Contardi, Atti Acad. Lincei, [5] **22**, 835 (1914); F. Beilstein, Handbuch der Organischen Chemie, Vol. XI-XII, 4th Ed., First Supplement, Julius Springer, Berlin (1933), p. 301.

¹⁷ W. Borsche and D. Rantscheff, Ann., 379, 160 (1911).

¹⁸ J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 34, 17 (1915).

¹⁹ J. J. Blanksma, Rec. Trav. Chim. Pays Bas, 24, 49 (1905).

²⁰ J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 24, 50 (1905).

Replacement of Halogen by the Mercapto Group (ArHal  $\rightarrow$  ArSH). In the large number of Zinin reactions that have been studied, each involving sulfhydryl, sulfide, or polysulfide reagents, it is surprising that only one example of a halogen atom being replaced by a mercapto group was found: 3-bromo-9-nitro-7H-benz[de]anthracen-7-one was converted to 9-amino-3-mercapto-7H-benz[de]anthracen-7-one.²¹ The bromine was activated by conjugation to a carbonyl group, which helps explain this unique replacement.



**Hydroxylation** (ArH  $\rightarrow$  ArOH). Two examples of hydroxylation were found. In both, the hydroxyl group entered *ortho* to an acid group and a *meta* nitro group was reduced to amino. 3-Nitrobenzoic acid was converted to 3-amino-6-hydroxybenzoic acid.⁵ 3-Nitrobenzenesulfonic acid was similarly converted to 3-amino-6-hydroxybenzenesulfonic acid.²²

Hydroxylamine Formation (ArNO₂  $\rightarrow$  ArNHOH). Hydroxylamines are thought to be intermediates in the Zinin reaction, but they have been isolated in only four instances. In none did the authors explain why further reduction did not occur. The reason may be that there was insufficient Zinin reagent to complete the reduction, or complexes resistant to reduction may have formed. Further study of these reactions using modern techniques should be made. The four examples are: dimethyl nitroterephthalate to dimethyl (hydroxyamino)terephthalate;²⁴ N-(onitrobenzyl)-o-toluamide to N-(o-hydroxyaminobenzyl)-o-toluamide;²⁵ Nmethyl-3'-nitro-p-toluenesulfonanilide to N-methyl-3'-hydroxyamino-ptoluenesulfonanilide;²⁵ and dimethyl 5-nitroisophthalate to dimethyl 5-(hydroxyamino)isophthalate.²³ (Equation on p. 462.)

Thiosulfonic Acid Formation  $(ArSO_3 \rightarrow ArSO_2SH)$ . Thiosulfonic acid derivatives were formed by the reduction of nitrobenzenesulfonic acids in two instances. In both, ammonium sulfide was the reducing agent.

²¹ E. Holzapfel, O. Braunsdorf, and P. Nawiasky, Ger. Pat. 443,022 (1927) [Frdldr., 15, 725 (1928)]. Here and elsewhere Frdldr. means P. Friedlaender, Fortschritte der Teerfarben-fabrikation, Julius Springer, Berlin.

²² H. Goldschmidt and H. Larsen, Z. Phys. Chem. (Leipzig), 71, 440 (1910).

²³ J. B. Cohen and D. McCandlish, J. Chem. Soc., 87, 1269 (1905).

²⁴ K. Auwers and E. Frese, Ann., 450, 302 (1926).

²⁵ O. Baudisch, H. Gurewitsch, and S. Rothschild, Ber., 49, 200 (1916).



5-Nitro-o-toluenesulfonic acid was converted to 5-amino-o-toluenethiosulfonic acid.²⁶ Similarly, 3,5-dinitro-p-toluenesulfonic acid gave 3,5diamino-p-toluenethiosulfonic acid.²⁷



Reduction of Azido Groups  $(ArN_3 \rightarrow ArNH_2)$ . In the reduction of nitro compounds containing an azido group the azido group is reduced to amino. Examples of this reaction are the reduction of 2-azido-1-nitro-anthraquinone to 1,2-diaminoanthraquinone²⁸ and of 2,6-diazido-1,5-dinitroanthraquinone to 1,2,5,6-tetraaminoanthraquinone.²⁸

Elimination of a Sulfonic Acid Group ( $ArSO_3H \rightarrow ArH$ ). There are two instances of hydrolysis of a sulfonic acid group from an aromatic ring during a Zinin reduction. Both involve disulfonic acids in which one group is hydrolyzed. The systems are both aqueous, sodium sulfide being utilized in the first reaction and sodium disulfide in the second. 1,8-Dihydroxy-4,5-dinitro-2,7-anthraquinonedisulfonic acid is reduced to



²⁶ H. Limpricht and A. Hefster, Ann., 221, 345 (1883).

²⁷ J. J. Blanksma, Chem. Weekbl., 10, 136 (1913).

²⁸ Bayer and Co., Ger. Pat. 337,734 (1921) [Frdldr., 13, 400 (1921)].

4,5-diamino-1,8-dihydroxy-2-anthraquinonesulfonic acid²⁹ and 1,5-dihydroxy-4,8-dinitro-2,7-anthraquinonedisulfonic acid to 4,8-diamino-1,5-dihydroxy-2-anthraquinonesulfonic acid.²⁹

**Decarbonylation** (ArCOCOAr  $\rightarrow$  ArCOAr). 2,7-Dinitrophenanthraquinone is converted to 2,7-diaminofluorenone by boiling with aqueous ammonium sulfide.³⁰ The decarbonylation probably results from a benzilic acid rearrangement followed by loss of carbon dioxide from the intermediate diphenyleneglycolic acid.





**Benzotriazole Formation.** An elegant method for preparing benzotriazoles is afforded by Zinin reduction of o-nitrophenylazo compounds. In the four reported examples, the yields are good. The reactions take place in alcoholic media using either ammonium sulfide or sodium sulfide. The structure required is a nitro group ortho to the azo group in a phenylazo compound. For example, 3-nitro-4-phenylazoaniline is converted to 5-amino-2-phenyl-2H-benzotriazole.³¹ The other examples are p-(onitrophenylazo)aniline to 2-(p-aminophenyl)-2H-benzotriazole,³² 4-(1naphthylzzo).3-nitroaniline to 5-amino-2-(1-naphthyl)-2H-benzotriazole,³¹ and p-(4-amino-2-nitrophenylazo)benzenesulfonic acid to p-(5-amino-2Hbenzotriazol-2-yl)-benzenesulfonic acid.³²



- ²⁹ Bayer and Co., Ger. Pat. 119,228 (1901) [Frdldr., 6, 1353 (1901)].
- ³⁰ G. Schultz and R. Anschutz, Ber., 10, 325 (1877).
- ³¹ B. Chakrabarty and K. K. Barat, J. Indian Chem. Soc., 5, 585 (1928).
- 32 B. Chakrabarty and K. K. Barat, J. Indian Chem. Soc., 5, 558 (1928).

Oxidation of Methyl or Methylene. An unusual reaction was extensively studied by Hodgson wherein *p*-nitrotoluene was reduced with sodium polysulfide in an alcoholic medium to give a 75% yield of *p*aminobenzaldehyde;³³ detailed directions are given in Organic Syntheses.³⁴ Excess sodium hydroxide leads to a 10% yield with correspondingly higher *p*-toluidine production. In a similar reaction, 4,4'-dinitrodiphenylmethane is converted to a mixture of 4,4'-diaminobenzophenone and 4amino-4'-nitrobenzophenone.³⁵

#### Zinin Reduction of Compounds without a Nitro Group

A few kinds of compounds other than nitroarenes have been reduced under conditions of the Zinin reduction. Except for reduction of nitrosobenzenes to arylamines, the reductions have found little use. New applications could probably be found.

Reduction of Nitrosoarenes to Arylamines (Table XI). When reduced under the same conditions as the corresponding nitro compounds, nitrosoarenes produce the corresponding amines. Two N-nitrosoanilines have given the corresponding arylhydrazines.

Cleavage of Azo Groups (ArN=NAr  $\rightarrow$  ArNH₂). Two azo compounds substituted with hydroxy and ethoxy groups have been reduced with cleavage of the azo group: p-(3-hydroxy-4-methoxyphenylazo)-benzenesulfonic acid to 5-aminoguaicol³⁶ and p-(2-ethoxy-4-hydroxy-phenylazo)benzenesulfonic acid to 4-amino-3-ethoxyphenol.³⁷

Reduction of Azobenzenes to Hydrazobenzenes. The only example of hydrazobenzene formation from an azo compound, the conversion of 4,4'-dinitroazobenzene to 4,4'-diaminohydrazobenzene by ammonium sulfide in alcoholic solution, is in the 1850 literature and probably should be reinvestigated.³⁸

#### EXPERIMENTAL CONDITIONS AND PROCEDURES

The experimental procedures given by no means cover all the modifications that have been employed during the more than one hundred years

³³ H. H. Hodgson, R. R. Davies, and H. G. Beard, J. Chem. Soc., 1944, 4.

³⁴ E. Campaigne, W. M. Budde, and G. F. Schaefer, Org. Syntheses, Coll. Vol. 4, 31 (1963).

³⁵ L. M. Litvinenko, N. F. Levchenko, and S. U. Tsukerman, *Zh. Obshch. Khim.*, 29, 1470 (1959) [*C.A.*, 54, 8721 (1960)].

³⁶ M. Heidelberger and W. A. Jacobs, J. Amer. Chem. Soc., 41, 1459 (1919)

³⁷ M. Heidelberger and W. A. Jacobs, J. Amer. Chem. Soc., 41, 1467 (1919).

³⁸ A. Laurent and C. Gehrhardt, Ann., 75, 74 (1850).

this method has been used. It is hoped that the examples given will furnish the chemist with sufficient information that he may tailor the reagents or conditions to favor the reduction he requires. The large number of references should give ample background for the reduction of the particular type of compound that may be under investigation. In the tables eight reducing methods (based on the reduction system) are catalogued (see p. 467), and three of the methods are exemplified below. The reaction need not be limited to these systems, since other alkali sulfides or polysulfides may prove adequate. While the reaction mechanisms that have been presented indicate the involvement of water in the reaction, it may prove advantageous to use systems containing other solvents with reduced amounts of water.

5-Nitro-*m*-phenylenediamine (Method II).³⁹ An ammonium sulphide solution is prepared by passing hydrogen sulfide into a solution of 54 ml of concentrated aqueous ammonia and 100 ml of 95% ethyl alcohol. The solution is cooled during the addition, which continues until approximately 10.5 g (0.30 mol) of hydrogen sulfide is absorbed.

3,5-Dinitroaniline (5 g, 0.027 mol) is dissolved in 50 ml of 95% ethyl alcohol in a 150-200 ml flask provided with a reflux condenser and a dropping funnel. The solution is brought to a boil and 41 ml of the ammonium sulfide solution is added dropwise to the refluxing solution over a 3-hr period. The hydrogen sulfide content of the solution is approximately 2.8 g (0.082 mol).

After the addition the mixture is cooled and made strongly acid by the addition of 6 N hydrochloric acid. (Care should be taken to safely neutralize or otherwise remove the toxic hydrogen sulfide that may be evolved during the acidification). The hot reaction mixture is filtered to removesulfur, and the filtrate is concentrated to about 200 ml. The solution is treated with aqueous ammonia to a blue test on litmus paper and cooled to precipitate 3.35 g (0.022 mol) of 5-nitro-*m*-phenylenediamine. The product is collected by filtration and the filtrate is saved for the recovery of an additional 0.2 g (0.0013 mol) of product by treatment with aqueous sodium carbonate and extraction with ether. The total yield is 85%, mp 140–141°; mp of N,N-diacetyl derivative, 270° (dec).

Metanilic Acid (Method VII).³ A solution of 49.2 g (1.23 mol) of aqueous 30% sodium hydroxide and 67.4 g (1.14 mol) of sodium hydrosulfide (sodium sulfhydrate) in 211 ml of water is placed in a suitable Pyrex flask equipped with a stirrer, a reflux condenser, and a Glascol

³⁹ B. Flurscheim, J. Prakt. Chem., [2] 71, 538 (1905).

heating mantle. To the reducing solution is added 300 g of a 41.7% aqueous solution of the sodium salt of *m*-nitrobenzenesulfonic acid (0.556 mol). The mixture is agitated under reflux for 12 hours and then cooled to room temperature. Sulfur dioxide is passed into the stirred solution until the solution is acidic as indicated by pH test paper or other conventional methods. The resulting suspension is cooled to 20° and the colorless crystals of metanilic acid are removed by filtration. A second crop may be obtained by further cooling of the filtrate. The total yield is 110 g (99%).

The purity of the material is determined by a standard nitrite titration. Positive identification may be obtained by conversion to the sulfonamide derivative (mp  $142^{\circ})^{40}$  or by comparison of the infrared or ultraviolet spectrum with authentic spectra (*e.g.*, Sadtler Ref. No. 17193 and No. 5427, respectively).⁴¹

Sodium Picramate (Method IV).⁴² Picric acid (10 g, 0.044 mol) is dissolved in 100 ml of methanol by heating the mixture to 55° with agitation. Enough aqueous sodium hydroxide or ammonium hydroxide is added to just neutralize the picric acid, using pH test papers or other conventional methods. The reducing agent (24 g of Na₂S·9 H₂O, 0.10 mol, and 8.4 g, 0.10 mol, of sodium bicarbonate in 40 ml of water; equivalent to 5.6 g, 0.10 mol, of sodium hydrosulfide) is added evenly to the sodium picrate slurry during 10–15 minutes at 55–60°. The mixture should be tested with ferrous sulfate test paper until a positive black test, indicating the presence of excess sodium hydrosulfide, is obtained. Additional sodium hydrosulfide solution should be added if the test is not obtained. The mixture is cooled to 10°, and 150 ml of chilled water is added. Sodium picramate is filtered from the resulting slurry and washed with chilled salt solution. The yield is 8.37 g as picramic acid (96%).

The purity of the material is obtained by a standard nitrite titration. The melting point of the free acid isolated by acidification from the aqueous solution should be 169°. Further identification may be obtained by comparing the infrared or ultraviolet spectrum with authentic spectra (e.g., Sadtler Ref. No. 5982 or No. 1685, respectively).⁴¹ The authors note that with water alone as solvent a yield of 83% was obtained. With ethanol instead of methanol, the yield was only 55% even though twice the amount of reducing agent was used.

⁴⁰ R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 2nd Ed., Wiley, New York, 1946, p. 176.

 ⁴¹ "Sadtler Standard Spectra," Sadtler Research Laboratory, Inc., Philadelphia, Pa.
 ⁴² H. H. Hodgson and E. R. Ward, J. Chem. Soc., 1945, 663.
#### TABULAR SURVEY

The tables include reactions reported before January 1973.

Space does not allow a complete description of the reactions listed. Reaction times and conditions are necessarily omitted. The tables do provide a key to the reducing media.

There was very little yield information in the older literature. Any yields reported are given in the tables; the absence of a yield means that none was reported.

The reduction methods are identified under the following designations: Method I, alcoholic ammonium sulfide; Method II, aqueous ammonium sulfide; Method III, alcoholic sodium sulfide; Method IV, aqueous sodium sulfide; Method V, alcoholic sodium polysulfide; Method VI, aqueous sodium polysulfide; Method VII, alcoholic sodium hydrosulfide; Method VIII, aqueous sodium hydrosulfide.

Number Carbon	of	Mathad	Braduct (Vield %)	Pofe
Atoms		Method		14010.
C,	Nitrobenzene	Ι	Aniline	1
-		v	·· (71)	77
	1-Chloro-2-nitrobenzene	v	o-Chloroaniline	43a
	1-Chloro-3-nitrobenzene	v	m-Chloroaniline (70)	78
	1-Bromo-3-nitrobenzene	v	m-Bromoaniline (Good)	43a, 52
	1-Bromo-4-nitrobenzene	I	p-Bromoaniline	48
	l-Iodo-3-nitrobenzene	Ι	<i>m</i> -Iodo <b>a</b> niline	48
	l-Iodo-4-nitrobenzene	I	p-Iodoaniline	48
	1,2-Dichloro-3-iodo-5-nitro- benzene	Ι	3,4-Dichloroaniline	16
С,	o-Nitrotoluene	v	o-Toluidine (65)	43a
•	<i>m</i> -Nitrotoluene	v	<i>m</i> -Toluidine (60)	43a
	p-Nitrotoluene	I	p-Toluidine	44a
	-	v	p-Aminobenzaldehyde (75)	33, 34
	4-Chloro-2-nitrotoluene	v	5-Chloro-o-toluidine (100)	49
	2-Chloro-4-nitrotoluene	III	3-Chloro-p-toluidine	43a
		v	•••	43a, 22,
				23, 50
	2-Bromo-4-nitrotoluene	Ι	3-Bromo-p-toluidine (85)	51
		v	**	43a
	2-Iodo-4-nitrotoluene	v	3-Iodo-p-toluidine	43a
C.	p-(Isopropyl)nitrobenzene	I	p-(Isopropyl)aniline	45, 66
C,	1-Nitronaphthalene	Ι	1-Naphthylamine	1
	-	VIII		46
	2-Nitronaphthalene	VII	2-Naphthylamine	43b
C,,	3-Methyl-l-nitronaphthalene	VII	3-Methyl-l-naphthylamine	44b
••	6-Methyl-2-nitronaphthalene	VII	6-Methyl-2-naphthylamine	44b
	7.Methyl-1-nitronaphthalene	VII	7-Methyl-l-naphthylamine	44b
C,,	5 Nitroacenaphthene	Ι'	5-Aminoacenaphthene	66
C14	4-Nitrophenanthrene	Ι	4-Phenanthrylamine	47

TABLE I. REDUCTION OF MONONITROARENES AND THEIR HALOGEN DERIVATIVES

Number	of			
Atoms	Nitro Compound	Method	Product (Yield %)	Refs.
<u> </u>	a Dinitrobenzene	T	e-Nitroaniline	53, 87
0		ÎTT		43a
		VII	.,	88
	m.Dinitrohenzene	H.S.	m-Nitroaniline (67)	54
		pyridin	0	
		I	••	55
		VII	••	6
	p-Dinitrobenzene	Ι	<i>p</i> -Nitroaniline	56
	2-Chloro-1,3-dinitrobenzene	I	m-Nitroaniline	17
	5-Chloro-1,3-dinitrobenzene	Ι	5-Chloro-3-nitroaniline	23
	4-Chloro-2,6-dinitrotoluene	Ι	2-Amino-4-chloro-6-nitrotoluene	23
C,	2,3-Dinitrotoluene	I	2-Nitro-m-toluidine (Low)	57, 58
•	2,4-Dinitrotoluene	I	3-Nitro- <i>p</i> -toluidine	59
	,	VII	(80)	62
	3.5-Dinitrotoluene	II	5-Nitro-m-toluidine	67
	-,	I	(86)	61
	2,6-Dinitrotoluene	Ī	3-Nitro-o-toluidine (Good), (96), (80)	63, 64, 65
C.	1-Ethyl-2.4-dinitrobenzene	II	4-Ethyl-3-nitroaniline (Low)	60
	3.5-Dinitro-o-xylene	II	5-Nitro-3,4-xylidine	68
	2.4-Dinitro- <i>m</i> -xylene	I	3-Nitro-2,4-xylidine	69
	4.6-Dinitro- <i>m</i> -xylene	I	5-Nitro-2,4-xylidine	70
	2.5-Dinitro-p-xylene	I	4-Nitro-2,5-xylidine	71
	2.6-Dinitro-p-xylene	I	3-Nitro-2,5-xylidine	70
C.	3.5-Dinitro-1.2.4-trimethyl-	I	2,4,5-Trimethyl-3-nitroaniline	72
0	benzene	III	2-Amino-4-nitro-3,5,6-trimethyl- benzenesulfonic acid (40)	73
	3,6-Dinitro-1,2,4-trimethyl- benzene	I	2,3,5-Trimethyl-4-nitroaniline	72
	2,6-Dinitromesitylene	I	2,4,6-Trimethyl-3-nitroaniline (40)	89
C ₁₀	1,3-Dinitronaphthalene	II	3-Nitro-1-naphthylamine	75
	1,5-Dinitronaphthalene	I	5-Nitro-l-naphthylamine (63)	76, 77
	1,6-Dinitronaphthalene	I	5-Nitro-2-naphthylamine (40)	75
	1,7-Dinitronaphthalene	I	8-Nitro-2-naphthylamine	75
	1,8-Dinitronaphthalene	$(\mathbf{NH}_4)_2\mathbf{S}$ in	1,8-Diaminonaphthalene (77)	86
~	2,3-Dinitronaphthalene		3-Nitro-2-naphthylamine	11
C ₁₁	1,5-Dinitro-2-methyl- naphthalene	1	6-Methyl-5-nitro-1-naphthyl- amine	79
C ₁₁	5-t-Butyl-2,4-dinitro-m-xylene	IV	4-t-Butyl-3-nitro-2,6-xylidine	74
	2,4'-Dinitrobiphenyl	I	4-Amino-2'-nitrobiphenyl	84
	4,4'-Dinitrobiphenyl	I	4-Amino-4'-nitrobiphenyl	80
		VIII	Benzidine	81, 82
C ₁₃	4,4'.Dinitrodiphenylmethane	v	4,4'-Diaminobenzophenone, 4-amino-4'-nitrobenzophenone	35
C ₁₄	2,4-Dinitrostilbene	I, IV	4-Amino-2-nitrostilbene (Good)	17, 83
	4,4'-Dinitrostilbene	IV	4,4'-Diaminostilbene (Good)	17
	4,4'-Dinitro-3,3'-dimethyl- biphenyl	VI	4-Amino-3,3'-dimethyl-4'- nitrobinhenyl	85
	Bis-(2-nitro-p-tolyl) disulfide	VI	6-(2-Nitro-p-tolyldithio)- m-toluidine	250

Number o Carbon Atoms	of Trinitro Compound	Method	Product (Yield %)	Ref.
C	1,3,5-Trinitrobenzene	v	3,5-Dinitroaniline	90
•		Ι,	••	91
		VII	··	43a
С,	2,4,6-Trinitrotoluene	I	3,5-Dinitro- <i>p</i> -toluidine	92
1		I	N-(2,4-Dinitro-o-tolyl) hydroxylamine	93
C.	l-Ethyl-2,4,6-trinitrobenzene	I	4-Ethyl-3,5-dinitroaniline	94
•	2,4,6-Trinitro- <i>m</i> -xylene	I	3,5-Dinitro-2,4-xylidine	95
	2,3,5-Trinitro-p-xylene	I	6-Amino-4-nitro-2,5-xylene- sulfonic acid	19
C ₉	2,4,6-Trinitromesitylene	I	2,4,6-Trimethyl-3,5-dinitro- aniline	96
		I	2,4,6-Trimethyl-5-nitro-m- phenylenediamine	97
	1,2,4-Trimethyl-3,5,6-trinitro- benzene	I	2-Amino-3,5,6-trimethyl-4- nitrobenzenesulfonic acid (40)	18
C,1	3-t-Butyl-2,4,6-trinitrotoluene	I	4.t-Butyl-3,5-dinitro-o-toluidine	99
C12	5-t-Butyl-2,4,6-trinitro-m-xylene	Ι	4-4-Butyl-3,5-dinitro-2,6-xylidine	98

TABLE III. REDUCTION OF TRINITROARENES

Number of Carbon Atoms	Nitro Compound	Method	Product (Yield %)	Ref.
C.	o-Nitrophenol	I	o.Aminophenol	100
·	2,4-Dinitrophenol	Ι	2-Amino-4-nitrophenol (32)	103
	2-Chloro-4,6-dinitrophenol	Ι	6-Amino-2-chloro-4-nitrophenol	104
	2-Bromo-4,6-dinitrophenol	Ι	6-Amino-2-bromo-4-nitrophenol	105
	4-Bromo-2,6-dinitrophenol	II	2-Amino-4-bromo-6-nitrophenol	106
	Pierie acid	Ι	2-Amino-4,6-dinitrophenol (84)	111
		VIII	·· (84)	112
		IV	•• (96)	40
C,	o-Nitroanisole	Ι	o-Anisidine	18
·	<i>p</i> -Nitroanisole	I	<i>p</i> -Anisidine	101
	2,4-Dinitroanisole	V	5-Nitro-o-anisidine	43a
Ca	2-Methyl-5-nitroanisole	V	4-Methyl-m-anisidine	102
U	2,4-Dinitrophenetole	Ι	5-Nitro-o-phenetidine	43a
C ₉	2,3-Dimethoxy-5,6-dinitro- toluene	Ι	4,5-Dimethoxy-2-nitro-m- toluidine	107
	2,3-Dimethoxy-4,6-dinitro- toluene	VIII	2,3-Dimethoxy-5-nitro-p-toluidine (Excellent)	• 1 <b>08</b>
	l,2,4-Trimethoxy-5,6-dinitro- benzene	I .	3,4,6-(or 3,5,6)-Trimethoxy-2- nitroaniline	109
	2,5-Dimethyl-3,4,6-trinitro- anisole	VII	6-Amino-3-methoxy-4-nitro-2,5- xylenesulfonic acid	20
C15	2,4-Dinitro-4'-methoxystilbene	Ι	4-Amino-4'-methoxy-2-nitro- stilbene	110

## TABLE IV. REDUCTION OF NITROPHENOLS AND ETHERS

Note: References 43-271 are on pp. 477-481.

Number of Carbon Atoms	Nitro Compound	Method	Product (Yield %)	Ref.
C.	p-Nitrobenzaldehyde	v	p-Aminobenzaldehyde	43a
0	5-Bromo-3-nitrobenzaldehyde	v	3-Amino-5-bromobenzaldehyde	113
C ₇	4-Nitro-o-anisaldehyde	V	4-Amino-o-anisaldehyde	102
·	4-Nitro-m-anisaldehyde	V	4.Amino-m-anisaldehyde	114
C12	3,5-Dinitrobenzophenone	Ι	3-Amino-5-nitrobenzophenone	116
C ₁₃	2-Nitrofluorenone	ш	2-Aminofluorenone (77)	115
13	3-Nitrofluorenone	IV	3-Aminofluorenone	115
	3,5-Dinitro-4-methylbenzo- phenone	I	3-Amino-4-methyl-5-nitrobenzo- phenone	117
	2,7-Dinitrofluorenone	V	2,7-Diaminofluorenone	117
	4-Methyl-3,4',5-trinitrobenzo- phenone	Ι	4',5-Diamino-4-methyl-3-nitro- benzophenone	117
C14	2-Methoxy-7-nitrofluorenone	III	7-Amino-2-methoxyfluorenone	115
	3-Nitro-7H-benz[de]anthracen-7-one	VI	3-Amino-7H-benz[de]anthracen-7- one (83)	121
	3-Bromo-9-nitro-7H-benz[de]- anthracen-7-one	I	9-Amino-3-mercapto-7H-benz[de]- anthracen-7-one, 3,3'-thiobis(9- amino-7H-benz[de]anthracen- 7-one	21
C15	N-(4,5-Dimethoxy-2-nitrobenz- ylidene)aniline	III	N-(2-Amino-4,5-dimethoxybenz- ylidene)aniline (80)	120
C ₁₇	N-(5-Ethoxy-2-nitrobenzylidene)- p-phenetidine	III	N-(2-Amino-5-ethoxybenz- ylidene)-p-phenetidine	118
C ₁₈	6- <i>t</i> -Butyl-2,4-dimethyl-3,3',5- trinitrobenzophenone	II	3-Amino-6- <i>t</i> -butyl-2,4-dimethyl- 3′,5-dinitrobenzophenone	118

Number Carbon Atoms	of Nitro Compound	Method	Product (Yield %)	Ref.
<u>с.</u>	m-Nitrobenzoic acid	II	5-Amino-2-hydroxybenzoic acid	5
- 1	2-Chloro-3-nitrobenzoic acid	II	3-Amino-2-chlorobenzoic acid (60)	122
	p-Nitrobenzoic acid	II	p-Aminobenzoic acid	123
	p-Nitrobenzamide	II	<i>p</i> -Aminobenzamide	125
	3-Nitrosalicylio acid	II	3-Aminosalicylic acid	132
	3,5-Dinitrobenzoic acid	Ι	3-Amino-5-nitrobenzoio acid	137
		Ι	3,5-Diaminobenzoio acid	138
	3,5-Dinitrobenzamide	II	3,5-Diaminobenzamide	139
	3,5-Dinitrosalicylic acid	II	3-Amino-5-nitrosalicylic acid	142
C ₈	p-Nitrophenylacetic acid	II	p-Aminophenylacetic acid (84)	129
-	3-Nitrophthalic acid	IV	3-Aminophthalic acid	131
	4-Nitrophthalic acid	IV	4-Aminophthalic acid	131
	p-Nitrobenzoylurea	I	<i>p</i> -Aminobenzoylurea	134
	5-Bromo-3-nitroanisic acid	II	3-Amino-5-bromoanisic acid	135
С,	4-Nitrohippuric acid	II	4-Aminohippuric acid (45)	126
	2,4-Dimethyl-6-nitrobenzoic acid	IV	2-Amino-4,6-dimethylbenzoic acid	128
	2,4-Dimethyl-3,5-dinitrobeazoic acid	Ι	5-Amino-2,4-dimethyl-3-nitro- benzoic acid (95)	140

TABLE VI. REDUCTION OF NITROARENE CARBOXYLIC ACIDS, ESTERS, AND AMIDES

Number of Carbon Atoms	Nitro Compound	Method	Product (Yield %)	Ref.
Cia	3-Nitro-4-isopropylbenzoic acid	TT	3. Amino. 4. isopropylbenzoic scid	127
~10	2-(p-Nitrophenyl)butyric acid	ÎÎ	2-(p-Aminophenyl)butyric acid	130
	Dimethyl 5-nitroisophthalate	II	Dimethyl 5-(hydroxyamino)isoph- thalate	23
	Dimethyl nitroterephthalate	Ι	Dimethyl (hydroxyamino)tereph- thalate	24
	N.(p.Nitrophenacyl)glycine	I	N-(p-Aminophenylacetyl)glycine	133
	2. (2,4-Dinitrophenyl) isobutyric acid	II	2-(4-Amino-2-nitrophenyl)iso- butyric acid	141
C ₁₄	o-Methoxyphenyl p-nitrobenzoate	II	o-Methoxyphenyl p-aminobenzo- ate	124
	5.5'-Dinitrodiphenic acid	IV	5.5'-Diaminodiphenic acid	143
C ₁₅	N-(o-Nitrobenzyl)-o-toluamide	Ι	N-(o-Hydroxyaminobenzyl-o- toluamide (80)	25

# TABLE VI. REDUCTION OF NITROARENE CARBOXYLIC ACIDS, ESTERS, AND AMIDES (Continued)

Number o Carbon Atoms	of Nitro Compound	Method	Product (Yield %)	Refs.
C.	o-Nitrobenzenesulfonic acid	I	o-Aminobenzenesulfonic acid	144
•	m-Nitrobenzenesulfonic acid	I	Metanilic acid	145
		VII	••	5
		VII	·· (99)	3
		IV	4-Amino-l-phenol-2-sulfonic acid	22, 146
	p-Nitrobenzenesulfonic <b>a</b> cid	I	Sulfanilic acid	144
	4-Bromo-3-nitrobenzenesulfonic acid	II	4-Bromometanilic acid	147
	5-Bromo-2-nitrobenzenesulfonic acid	II	2-Amino-5-bromobenzenesulfonic acid	148
	6-Nitro-l-phenol-2,4-disulfonic acid	IV	6-Amino-1-phenol-2,4-disulfonic acid	166
	2-Hydrazino-4-nitrobenzene- sulfonic acid	I	2-Hydrazinosulfanilic acid	167
	2,6-Dinitro-l-phenol-4-sulfonic acid	IV	2-Amino-6-nitro-1-phenol-4- sulfonic acid	173
C,	2-Nitro-m-toluenesulfonic acid	I	2-Amino-m-toluenesulfonic acid	149
•	2-Nitro-p-toluenesulfonic acid	I	2-Amino-p-toluenesulfonic acid	59
	4-Nitro-o-toluenesulfonic acid	I	4-Amino-o-toluenesulfonic acid	150
	3(or 5)-Bromo-2-nitro- <i>p</i> -toluene- sulfonic <b>s</b> cid	I	2-Amino-3(or 5)-bromo- <i>p</i> -toluene- sulfonic acid	151
	5-Nitro-o-toluenesulfonic acid	I	5-Amino-o-toluenesulfonic acid	<b>59</b>
	5-Nitro-o-toluenesulfonic acid	I	5-Amino-o-toluenethiosulfonic acid	26
	6-Nitro-m-toluenesulfonic acid	Ι	6-Amino-m-toluenesulfonic acid	152
	m-Nitro-a-toluenesulfonic acid	Ι	m-Amino-α-toluenesulfonic acid	156
	2-Nitro-4-sulfobenzoic acid	Ι	4-Sulfoanthranilic acid	161
		II	(55)	162
	3.Nitro-4-sulfobenzoic acid	1	3-Amino-4-sulfobenzoic acid	163
	4-Nitrotoluene-2,6-disulfonic acid	Ι	4-Aminotoluene-2,6-disulfonic acid	164

TABLE VII. REDUCTION OF NITROARENESULFONIC ACIDS

Note: References 43-271 are on pp. 477-481.

Number o Carbon Atoms	Mitro Compound	Method	Product (Yield %)	Refs.
C ₇ (contd.)	3,5-Dinitro-p-toluenesulfonic acid	1	3-Amino-5-nitro- <i>p</i> -toluene- sulfonic acid	168-170
			3,5-Diamino-p-toluenethio- sulfonio acid	27
	2,4-Dinitro-a-toluenesulfonic acid	II	2(or 4)-Amino-4(or 2)-nitro-α- toluenesulfonic acid	171
Ca	5-Nitro-2,4-xylenesulfonic acid	I	5-Amino-2,4-xylenesulfonic acid	153
C ₉	3-Nitro-2,4,6-trimethylbenzene- sulfonic acid	II	3-Amino-2,4,6-trimethylbenzene- sulfonic acid	155
C ₁₀	4-Nitro-1-naphthalenesulfonic acid	Ι	4-Amino-1-naphthalenesulfonic acid	157
	5-Nitro-l-naphthalenesulfonic acid	I	5-Amino-l-naphthalenesulfonic acid	158
	5-Nitro-2-naphthalenesulfonic acid	I	5-Amino-2-naphthalenesulfonic acid	159
	8-Nitro-2-naphthalenesulfonic acid	Ι	8-Amino-2-naphthalenesulfonic acid	160
	4-Nitro-2,6-naphthalene- disulfonic acid	Ι	4-Amino-2,6-naphthalene- disulfonic acid	165
	4-Nitro-2,7-naphthalene- disulfonic acid	Ι	4-Amino-2,7-naphthalene- disulfonic acid	165
	8-Hydroxy-5,7-dinitro-2- naphthalenesulfonic acid	IV	2-Amino-4-nitro-1-naphthol-7- sulfonic acid	172
	4,5-Dinitro-2,7-naphthalene- disulfonic acid	Ι	4,5-Diamino-2,7-naphthalene- disulfonic acid	167
C ₁₁	5-Isobutyl-3-nitro- <i>o</i> -toluene- sulfonic <b>a</b> cid	Ι	3-Amino-5-isobutyl-c-toluene- sulfonic acid	154
C ₁₄	4,4'-Dinitro-2,2'-stilbene- disulfonic acid	IV	4-Amino-4'-nitro-2,2'-stilbene- disulfonic acid (80)	174

## TABLE VII. REDUCTION OF NITROARENESULFONIC ACIDS (Continued)

Number of Carbon Atoms	Nitro Compound	Method	Product (Yield %)	Ref.
<u> </u>	1. Nitroanthrequinone	IV	1. A minoenthrequinone	175
-14	2-Chloro-5-nitroanthraquinone	īv	1-Amino-6-chloroanthraquinone (90-95)	176
	8-Nitro-2-anthraquinonesulfonic acid	Lead salt H.S	8-Amino-2-anthraquinonesulfonic acid	187
	2-Nitrophenanthrenequinone	IV	2-Aminophenanthrenequinone (89)	180
	1-Hydroxy-4-nitroanthraquinone	IV	1-Amino-4-hydroxyanthraquinone	183
	2-Azido-1-nitroanthraquinone	IV	1,2-Diaminoanthraquinone	28
	2,6-Diazido-1,5-dinitroanthra- quinone	IV	1,2,5,6-Tetraminoanthraquinone	193
	2-Amino-1-nitroanthraquinone	IV	1,2-Diaminoanthraquinone (88)	211
	l-Amino-4-chloro-2-nitro- anthraquinone	IV	1,2-Diamino-4-chloroanthra- quinone	212
	1,5-Dinitroanthraquinone	II	1,5-Diaminoanthraquinone (90)	194
	1,6-Dinitroanthraquinone	II	1,6-Diaminoanthraquinone	195

TABLE VIII. REDUCTION OF NITROQUINONES AND DERIVATIVES

Number of Carbon	ſ.			<u> </u>
Atoms	Nitro Compound	Method	Product (Yield %)	Refs.
C ₁₄ (contd.)	2,7-Dinitrophenanthrenequinone	VIII	2-Amino-7-nitrophenanthrene- quinone	199
		I	2,7-Diaminofluorenone	30
	1,5-Dinitro-2,6-dihydroxyanthra- quinone	III	1,5-Diamino-2,6-dihydroxyanthra- guinone	202
	1,8-Dinitro-5,7,12,14-pentacene- tetrone	VIII	1,8-Diamino-5,7,12,14-pentacene- tetrone (95)	197
	1,2,4,5,6,8-Hexahydroxy-3,7- dinitroanthraquinone	IV	3,7-Diamino-1,2,4,5,6,8-hexa- hydroxyanthraquinone	203
	7-Bromo-1,8-dihydroxy-4,5- dinitro-2-anthraquinonesulfonic acid	IV	4,5-Diamino-7-bromo-1,8- dihydroxy-2-anthraquinone- sulfonic acid	204
	6-Bromo-1,5-dihydroxy-4,8- dinitro-2-anthraquinonesulfonic acid	IV	4,8-Diamino-6-bromo-1,5- dihydroxy-2-anthraquinone- sulfonic acid	204
	l,8-Dihydroxy-4,5-dinitro-2,7- anthraquinonedisulfonic acid	IV	4,5-Diamino-1,8-dihydroxy-2- anthraquinonesulfonic acid	29
	1,5-Dihydroxy-4,8-dinitro-2,6- anthraquinonedisulfonic acid	VIII	4,8-Diamino-1,5-dihydroxy-2,6- anthraquinonedisulfonic acid (100)	206
	1,5-Dihydroxy-4,8-dinitro-2,7- anthraquinonedisulfonic acid	IV	4,8-Diamino-1,5-dihydroxy-2- anthraquinonesulfonic acid	29
	2,6-Dihydroxy-1,5-dinitro-3,7-	VIII	1,5-Diamino-2,6-dihydroxy-3,7-	207
C ₁₅	2-Methyl-1-nitroanthraquinone	IV	l-Amino-2-methylanthraquinone (97)	177
	2-Methoxy-l-nitroanthraquinone	IV	1-Amino-2-methoxyanthraquinone	181
	1-Nitro-2-anthraquinone- carboxamide	II	1-Amino-2-anthraquinonecarbox- amide	184
	l-Amino-2-methyl-4-nitro-	IV	1,4-Diamino-2-methyl-	212
	1-Hydroxy-3-methyl-2-nitro- anthraquinone	IV	2-Amino-1-hydroxy-3-methyl- anthraquinone	182
	1-Nitro-2-anthraquinone-	IV	1-Amino-2-anthraquinone-	184
	5-Nitro-1-anthraquinonesulfonic	II	5-Amino-1-anthraquinonesulfonic acid	185
	8-Nitro-1-anthraquinone- sulfonic acid	II	8-Amino-1-anthraquinone- sulfonic acid	185
	5-Nitro-2-anthraquinone- sulfonic acid	VI	5-Amino-2-anthraquinone- sulfonic acid	186
	2-Methyl-1,5-dinitroanthra-	IV	1,5-Diamino-2-methylanthra-	196
	2-Methyl-1,8-dinitroanthra-	IV	1,8-Diamino-2-methylanthra-	196
	1-Hydroxy-3-methyl-2,4- dinitroanthraquinone	IV	2,4-Diamino-1-hydroxy-3- methylanthraquinone	201
C.	2-Amino-3-nitrofluorenone	III	2,3-Diaminofluorenone	117
10	1,2-Dimethoxy-3-nitroanthra- quinone	IV	3-Amino-1,2-dimethoxyanthra- quinone (100)	188
	1,2-Dimethoxy-4-nitroanthra- quinone	II	4-Amino-1,2-dimethoxyanthra- quinone (67)	189
	1,3-Dimethyl-2,4-dinitroanthra- quinone	IV	1,3-Dimethyl-2,4-diaminoanthra- guinone	179
C ₁₈	4-Nitrobenz[a]anthracen-7,12- dione	IV	4-Aminobenz[a]anthracen-7,12- dione	190
	3-Methoxy-2-nitro-7-H-	III	2-Amino-3-methoxy-7-H-	191
C ₃₂	4,10-Dinitrodibenzo[de,jk]pyrene- 6,12-dione	IV	4,10-Diaminodibenzo[de,jk]- pyrene-6,12-dione	200

## TABLE VIII. REDUCTION OF NITROQUINONES AND DERIVATIVES (Continued)

Number	Tumber of					
Carbon	Nites Company	Mathad	Deadward (Mintal 04)	DC		
Atoms		Method	Product (1 leid %)	Kei.		
C.	o-Nitroaniline	IV	o-Phenylenediamine	208		
	2,4-Dinitroaniline	VII	4-Nitro-o-phenylenediamine (80)	216		
	2,6-Dinitroaniline	I	3-Nitro-o-phenylenediamine	119		
	3,5-Dinitroaniline	II	5-Nitro- <i>m</i> -phenylenediamine (86)	39		
C,	4,6-Dinitro-o-toluidine	I	2,3-Diamino-5-nitrotoluene	217		
	4,6-Dinitro-o-anisidine	II	3-Methoxy-5-nitro-o-phenylene- diamine	226		
	4-Amino-3,5-dinitrobenzoic acid	I	3,4-Diamino-5-nitrobenzoic acid	227		
	N-Methyl-2,4-dinitroaniline	VIII	N ¹ -Methyl-4-nitro-o-phenylene- diamine (60)	239		
	2-Anilino-3,5-dinitrobenzoic acid	II	2-Anilino-2,5-diaminobenzoic acid	246		
C.	2'-Nitro-p-acetotoluidide	I	2'-Amino-p-acetotoluidide	209		
•	3,5-Dinitro-2,4-xylidine	I	2,4-Dimethyl-5-nitro-m- phenylenediamine	218		
	4,6-Dinitro-2,5-xylidine	III	3,6-Dimethyl-4-nitro-o-phenylene- diamine (81)	219		
	N-Ethyl-2,4-dinitroaniline	II	N ¹ -Ethyl-4-nitro-o-phenylene- diamine	234		
	2,5-Dinitro-N-methyl- <i>p</i> - toluidine	I	2-Amino-5-nitro-N ⁴ -methyl-p- toluidine	229		
	3,5-Dinitro-N-methyl- <i>p</i> - toluidine	I	3-Amino-5-nitro-N ⁴ -methyl- <i>p</i> - toluidine	235		
C,	2,4,6-Trimethyl-3,5-dinitro- aniline	I	2,4,6-Trimethyl-5-nitro- <i>m</i> -	222		
C ₁₀	2,3,5,6-Tetramethyl-4-nitro-	I	2,3,5,6-Tetramethyl- <i>p</i> -phenylene-	210		
	4-Amino-7-nitro-1-naphthalene-	I	4,7-Diamino-l-naphthalene-	215		
	4-t-Butyl-2,6-dinitroaniline	I	4-t-Butyl-6-nitro-o-phenylene-	220		
C ₁₁	4-4-Amy)-2,6-dinitroaniline	I	4-t-Amyl-6-nitro-o-phenylene- diamine	221		
C.	3.5-Dinitro-o-phenylenediamine	I	5-Nitro-1.2.3-benzenetriamine	214		
14	3.4'-Dinitrobiphenylamine	I	3-Nitrobenzidine	223		
	2.4-Dinitrodiphenvlamine	Ī	2-Amino-4-nitrodiphenylamine	224		
	2.4'-Dinitrodiphenylamine	I	2-Amino-4'-nitrodiphenylamine	236		
	4.4'-Dinitrodiphenylamine	ĪV	4-Amino-4'-nitrodiphenylamine	237		
	2'-Chloro-2,4-dinitrodiphenyl-	V	2-Amino-4-nitro-2'-chlorodi- phenylamine	238		
	4-Amino-2',4'-dinitro- diphenylamine	I	2,2'-Diamino-4'-nitro- diphenylamine	242		
C.,	2-Amino-3-nitro-9-fluorenone	III	2.3-Diamino-9-fluorenone	117		
19	2-Methyl-2',4'-dinitrodiphenyl-	III	2-Methyl-2'-amino-4'-nitro- diphenylamine	228		
	4-Methyl-2',4'-dinitrodiphenyl-	I	4-Methyl-2'-amino-4'-nitro- diphenylamine	224		
	N-Methyl-2,4-dinitrodiphenyl- amine	III	N-Methyl-2-amino-4-nitrodi- phenylamine	240		
	4-Anilino-3,5-dinitrobenzoic acid	VI	3-Amino-4-anilino-5-nitrobenzoic acid (93)	245		
	N-Methyl-2,2',4,4'-tetranitro- diphenylamine	I	N-Methyl-2-amino-2',4,4'-tri- nitrodiphenylamine	251		

Number o Carbon Atoms	of Nitro Compound	Method	Product (Yield %)	Ref.
<u> </u>	2-Amino-l-nitroanthraquinone	IV	1.2-Diaminoanthraquinone (88)	211
-14	l-Amino-4-chloro-2-nitro- anthraquinone	IV	l,2-Diamino-4-chloroanthra- quinone	212
	l-Amino-2,4-dinitroanthra- quinone	Ι	1,2,4-Triaminoanthraquinone	225
	3-Nitro-4- $p$ -toluidinobenzoic acid	VI	3-Amino-4- <i>p</i> -toluidinobenzoic acid (33)	230
	4'-(2,4-Dinitroanilino) acetanilide	Ι	4'-(2-Amino-4-nitroanilino) acetanilide	241
	2',6'-Dinitro- <i>p</i> -toluobenz <b>a</b> mide	II	2'-Amino-6'-nitro-p-toluobenz- amide	247
C ₁₅	l-Amino-2-methyl-4-nitro- anthraquinone	IV	l,4-Diamino-2-methylanthra- quinone	212
C ₁₆	l-Amino-2-ethoxy-4-nitro- anthraquinone	IV	l,4-Diamino-2-ethoxyanthra- quinone	213
	N-(2,4-Dinitrophenyl)-1- naphthylamine	Ι	N-(2-Amino-4-nitrophenyl)-1- naphthylamine (60)	243
	N·(2,4-Dinitrophenyl)-2- naphthylamine	IV	N-(2-Amino-4-nitrophenyl)-2- naphthylamine	244
C17	4-(1-Naphthylamino)-3- nitrobenzoic acid	Ι	3-Amino-4-(1-naphthylamino)- benzoic acid	231
C ₁₈	N-Methyl-3'-nitro-p- toluenesulfonanilide	III	N.Methyl-3'-hydroxyamino-p- toluenesulfonanilide	25
	N-(2,4-Dinitrophenyl)-2- diphenylamine	III	N-(2-Amino-4-nitrophenyl)- 2-diphenylamine	252
C ₂₁	2. (1. Anthraquinonylamino)- 5. nitrobenzoic acid	III	5-Amino-2-(1-anthraquinonyl- amino)benzoic acid	232
	l-Benzamido-4-nitroanthra- quinone	Iĭ	l-Benzamido-4-amino- anthraquinone	248
C ₂₈	1,5-Dibenzamido-4,8-dinitro- anthraquinone	II	l,5-Dibenzamido-4,8-diamino- anthraquinone	249

TABLE X. REDUCTION OF NITROARYL AZO COMPOUNDS

Number of Carbon Atoms	Nitro Compound	Method	Product (Yield %)	Ref.
C.,	3-Nitroazobenzene	v	<i>m</i> -Phenylazoaniline (90)	253
	4-Nitroazobenzene	v	p-Phenylazoaniline (90)	253
	p-(p-Nitrophenylazo)phenol	I	p-(p-Aminophenylazo)phenol	255
	4-(p-Nitrophenylazo)resorcinol	II	4 (p-Aminophenylazo)resorcinol	256
	4. (p-Nitrophenylazo)benzene- sulfonic acid	II	4-(p-Aminophenylazo)benzene- sulfonic acid	257
	3-Nitro-4-phenylazoaniline	Ι	5-Amino-2-phenyl-2H-benzo- tri <b>s</b> zole	31
	p-(o-Nitrophenylazo)aniline	Ι	2-(p-Aminophenyl)-2H-benzotria- zole	32
	<i>p</i> -( <i>p</i> -Nitrophenylazo)aniline	Ι	4,4'-Diaminoazobenzene	261
		III	4,4'-[Azobis(p-phenyleneazo)]- dianiline	26 <b>2</b>
	4-( <i>p</i> -Nitrophenylazo)- <i>m</i> - phenylenediamine	IV	4-(p-Aminophenylazo)-m- phenylenediamine	265

Number o Carbon	umber of arbon				
Atoms	Nitro Compound	Method	Product (Yield %)	Ref.	
C ₁₂ (contd.)	p-(4-Amino-2-nitrophenylazo)- benzenesulfonic acid	I	p-(5-Amino-2H-benzotriazol-2-yl)- benzenesulfonic acid (Good)	32	
	4,4'-Dinitroazobenzene	Ι	4,4'-Diaminohydrazobenzene	38	
	4,4'-Azobis-(2-nitrophenol)	I	4,4'-Azobis-(2-aminophenol)  (30)	270	
	3,3'-Azobis-(6-nitrobenzene- sulfonic acid)	II	3,3'-Azobis-(6-aminobenzene- sulfonic acid)	269	
C ₁₃	5-(p-Nitrophenylazo)salicylic acid	II	5-(p-Aminophenylazo)salicylic acid	256	
C ₁₄	N,N-Dimethyl- <i>p</i> -(o-nitro- phenylazo)aniline	V	p-(o-Aminophenylazo)-N,N-di- methylaniline	254	
	4-(p-Nitrophenylazo)-2,5- xylidine	IV	4-( <i>p</i> -Aminophenylazo)-2,5- xylidine	258	
C18	4-(p-Nitrophenylazo)-l- naphthol	II	4-(p-Aminophenylazo)-1- naphthol	256	
	2-(p-Nitrophenylazo)-1- naphthol	Ι	2-(p-Aminophenylazo)-1- naphthol	256	
	4-(p-Nitrophenylazo)-1- naphthylamine	II	4. (p-Aminophenylazo)-l-naphthyl- amine	263	
	4-(l-Naphthylazo)-3-nitroaniline	Ι	5-Amino-2-(1-naphthyl)-2H- benzotriazole (Good)	31	
	4-(2-Naphthylazo)-3-nitroaniline	Ι	5-Amino-2-(2-naphthyl)-2H- benzotriazole (Good)	260	
	2,3-Dimethyl-4'-(p-nitro- phenylazo)acotanilide	IV	4-(p-Aminophenylazo)-2',3'- dimethylacetanilide	266	
	4-Amino-5-hydroxy-6-{p-nitro- phenylazo)-l-naphthalene- sulfonic acid	VI	4-Amino-6-(p-aminophenylazo)-5- hydroxy-l-naphthalenesulfonic acid	267	
	4,5-Dihydroxy-3-(p-nitro- phenylazo)-2,7-naphthalene- disulfonic acid	VI	3-(p-Aminophenylazo)-4,5-di- hydroxy-2,7-naphthalene- disulfonic acid	268	
	N-(2,4-Dinitrophenyl)-l-m- tolylazo-2-naphthylamine	v	N-(2-Amino-4-nitrophenyl)-1-m- tolylazo-2-naphthylamine	271	
	7-Amino-1-hydroxy-2-(p-nitro- phenylazo)-3,6-naphthalene- disulfonic acid	IV	7-Amino-2-(p-aminophenylazo)- l-hydroxy-3,6-naphthalene- disulfonic acid	260	
C ₁₇	l-(2-Methoxy-4-nitrophenylazo)- 2-naphthol	I	l-(4-Amino-2-methoxyphenyl- azo)-2-naphthol	255	
C ₁₈	N-Ethyl-4-(p-nitrophenylazo)-1- naphthylamine	IV	4-(p-Aminophenylazo)-N-ethyl-1- naphthylamine	264	
	2,4.Dinitro-2'-phenylazo- diphenylamine	v	2-Amino-4-nitro-2'-phenyl- azodiphenylamine	271	
	2,4-Dinitro-4'-phenylazo- diphenylamine	v	2-Amino-4-nitro-4'-phenyl- azodiphenylamine	271	
C ₂₀	2,4-Dinitro-2'-methyl-4'- o-tolylazodiphenylamine	v	2-Amino-4-nitro-2'-methyl-4'- o-tolylazodiphenylamine	271	
	2,4-Dinitro-4'-methyl-2-p- tolylazodiphenylamine	v	2-Amino-4-nitro-4'-methyl-2-p- tolylazodiphenylamine	271	
C ₂₂	N-(2,4-Dinitrophenyl).l. phenylazo-2-naphthylamine	v	N-(2-Amino-4-nitrophenyl)-1- phenylazo-2-naphthylamine	271	
	N ¹ -[(p-2-Naphthylamino)phenyl]- 2,4-dinitro-m-phenylene- diamine	v	N ¹ -[(p-Naphthylamino)phenyl]-4- nitro-1,2,3-benzenetriamine	271	
C ₂₃	N-(2,4-Dinitrophenyl)-l-p- tolylazo-2-naphthylamine	V .	N-(2-Amino-4-nitrophenyl)-1-p- tolylazo-2-naphthylamine	271	
	N-(2,4-Dinitrophenyl)-4-p- tolylazo-l-naphthylamine	V	N-(2-Amino-4-nitrophenyl)-4-p- tolylazo-1-naphthylamine	271	

Number o Carbon Atoms	f Nitroso Compound	Method	Product (Yield %)	Ref.
C,	3-(Methylthio)-4-nitrosophenol	II	4-Amino-3-(methylthio)phenol	233
	N-Methyl-o-nitro-N-nitrosoaniline	I	o-(l-Methylhydrazino)aniline	205
C ₈	N-Ethyl-o-nitro-N-nitrosoaniline	Ι	o.(l.Ethylhydrazino)aniline	205
	4-(N-Methyl-N-nitrosoamino)-2- nitrotoluene	Ι	5-(N-Methyl-N-nitrosoamino)-o- toluidine (60)	192
C10	2-Nitroso-l-naphthylamine	II	1,2-Naphthalenediamine	193
C18	2,6-Diallyl-4-nitrosophenol	II	4-Amino-2,6-diallylphenol	259

TABLE XI. REDUCTION OF NITROSOARENES AND N-NITROSOANILINES

#### **REFERENCES TO TABLES**

- ^{43a} J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 28, 107 (1909).
- 43b V. Veseley and L. K. Chudzilov, Rec. Trav. Chim. Pays-Bas, 44, 356 (1925).
- 44a A. W. Hoffmann and J. S. Musprat, Ann., 54, 12 (1845).
- 44b V. Veseley and L. K. Chudzilov, Rec. Trav. Chim. Pays Bas, 44, 364 (1925).
- 45 E. J. Constani and H. Goldschmidt, Ber., 21, 1157 (1888).
- ⁴⁶ R. D. Haworth and A. Lapworth, J. Chem. Soc., 119, 774 (1921).
- ⁴⁷ E. Schmidt, Ber., 12, 1158 (1879).
- ⁴⁶ P. Griess, J. Chem. Soc., **19**, 56 (1866).
- 49 H. H. Hodgson and P. Anderson, J. Chem. Soc., 125, 2195 (1924).
- ⁵⁰ C. Van de Bunt, Rec. Trav. Chim. Pays-Bas, 48, 141 (1929).
- ⁵¹ H. J. Lucas and N. F. Scudder, J. Am. Chem. Soc., 50, 245 (1925).
- ⁵² H. H. Hodgson and J. H. Wilson, J. Chem. Soc., 125, 127 (1924).
- 53 A. Rinne and T. Zincke, Ber., 7, 1374 (1874).
- 54 O. L. Brady, J. N. E. Day, and C. V. Reynolds, J. Chem. Soc., 1929, 2266.
- 55 J. S. Muspratt and A. W. Hoffman, Ann., 57, 215 (1846).
- ⁵⁶ A. Rinne and T. Zincke, Ber., 7, 871 (1874).
- ⁵⁷ H. Limpricht, Ber., 18, 1402 (1885).
- ⁵⁸ J. Kenner and M. Parkin, J. Chem. Soc., 117, 857 (1920).
- ⁵⁹ F. Beilstein and A. Kuhlberg, Ann., 155, 11 (1870).
- ⁶⁰ E. L. Cline and E. E. Reid, J. Amer. Chem. Soc., 49, 3152 (1927).
- ⁶¹ W. Staedel, Ann., 217, 199 (1883).
- 58 O. L. Brady, J. N. E. Day, and W. J. W. Rolt, J. Chem. Soc., 121, 529 (1922).
- ⁶³ E. Noelting, J. Prakt. Chem., [2] 74, 470 (1906).
- ⁶⁴ A. S. Wheeler, J. Amer. Chem. Soc., 44, 136 (1922).
- ⁶⁵ O. L. Brady and A. Taylor, J. Chem. Soc., 117, 877 (1920).
- 66 F. Quincke, Ber., 21, 1456 (1888).
- ⁶⁷ G. Schultz and A. A. Sander, Ber., 42, 2634 (1909).
- ⁶⁶ E. Nootting, Ber., 35, 632 (1902).
- 69 J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 28, 94 (1909).
- ¹⁰ R. Fittig, W. Ahrens, and L. Matcheider, Ann., 147, 18 (1868).
- ⁷¹ S. Von Kostanecki, Ber., 19, 2319 (1886).
- ⁷² A. Huender, Rec. Trav. Chim. Pays-Bas, 34, 17 (1915).
- ⁷³ J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 24, 47 (1905).
- ⁷⁴ H. Baur, Ber., 33, 2565 (1900).
- ⁷⁵ V. Veseley and K. Dvorak, Bull. Soc. Chim. Fr., [4] 33, 327 (1923).
- ⁷⁶ F. Beilstein and A. Kuhlberg, Ber., 6, 87 (1873).
- ⁷⁷ N. Zinin, Ann., 85, 329 (1853).
- ⁷⁶ P. Ferrero and C. Caflisch, Helv. Chim. Acta, 11, 806 (1928).

- 79 V. Veseley and J. Kapp, Rec. Trav. Chim. Pays-Bas, 44, 366 (1925).
- ⁸⁰ G. Schultz, H. Schmidt, and H. Strasser, Ann., 207, 350 (1881).
- ⁸¹ R. Fittig, Ann., 124, 278 (1862).
- ⁸² G. Schultz, Ann., 174, 223 (1874).
- ** J. Thiele and R. Escales, Ber., 34, 2846 (1901).
- 84 M. Freund and P. Niderhofheim, Ger. Pat. 115,287 (1899) [Frdldr., 6, 96 (1901)].
- ⁸⁸ G. Schultz, G. Rohde, and F. Vicari, Ann., **352**, 121 (1907).
- 66 N. N. Vorozhtsov and V. V. Kozlov, J. Gen. Chem., 7, 739 (1937) [C.A., 31, 5348 (1937)].
- 87 J. J. Blanksma, Rec. Trav. Chim. Pays. Bas, 20, 126 (1901).
- 88 A. Laubenheimer, Ber., 11, 1156 (1878).
- ** E. Knecht, Ann., 215, 98 (1882).
- ⁹⁰ B. Flurscheim, J. Prakt. Chem., [2] 71, 537 (1903).
- ⁹¹ M. A. C. De Koch, Rec. Trav. Chim. Pays-Bas, 20, 112 (1901).
- ** R. Anschutz and W. Zimmerman, Ber., 48, 154 (1915).
- 93 D. McCandlish, J. Chem. Soc., 87, 1265 (1905).
- 94 O. L. Brady, J. N. E. Day, and P. S. Allison, J. Chem. Soc., 1928, 979.
- ⁹⁵ Bussenius and Eisenstuck, Ann., 113, 165 (1860).
- •• R. Fittig, Ann., 141, 139 (1867).
- 97 R. Anschutz, Ann., 235, 183 (1886).
- 98 Thann et Mulhous, Cie., Ger. Pat. 90,291 (1895) [Frdldr., 4, 1300 (1894-1897)].
- •• J. J Blanksma, Ber., 24, 2839 (1891).
- ¹⁰⁰ J. Hofmann, Ann., 103, 351 (1857).
- ¹⁰¹ A. Cobenzl, Chem. Ztg., 39, 860 (1915).
- 102 J. J. Blanksma, Rec. Trav. Chim. Pays-Bas, 29, 407 (1910).
- ¹⁰⁸ K. Auwers and H. Rohrig, Ber., 30, 995 (1895).
- ¹⁰⁴ A. Faust and H. Muller, Ann., 173, (1874).
- ¹⁰⁵ R. Meldola, G. H. Woolcott, and E. Wray, J. Chem. Soc., 09, 1326 (1896).
- ¹⁰⁶ R. Meldola and F. H. Stratfield, J. Chem. Soc., 73, 687 (1898).
- ¹⁰⁷ R. Majima and T. Okazski, Ber., 49, 1493 (1916).
- 108 J. C. Cain and J. L. Simonsen, J. Chem. Soc., 105, 161 (1914).
- 109 R. Jones and T. G. H. Robinson, J. Chem. Soc., 111, 926 (1917).
- ¹¹⁰ P. Pfeiffer, Ber., 48, 1805 (1915).
- ¹¹¹ K. Brand, J. Prakt. Chem., [2] 74, 491 (1906).
- ¹¹² G. Egerer, J. Biol. Chem., 35, 565 (1918).
- 113 J. J. Blanksma, Chem. Weekbl., 6, 899 (1911).
- 114 H. H. Hodgson and H. G. Beard, J. Chem. Soc., 127, 878 (1925).
- ¹¹⁵ A. Echert and E. Langecker, J. Prakt. Chem., [2] 118, 268 (1928).
- ¹¹⁶ W. A. Waters, J. Chem. Soc., 1929, 2110.
- ¹¹⁷ W. Blakey and H. A. Scarborough, J. Chem. Soc., 1928, 2493.
- ¹¹⁸ E. Noelting, Chim. Ind. (Paris), 6, 731 (1921).
- ¹¹⁹ W. Borsche and D. Rantscheff, Ann., 379, 163 (1911).
- 120 A. Rilliet, Helv. Chim. Acta, 5, 548 (1922).
- 121 A. Luttringhaus and H. Neresheimer, Ann., 473, 285 (1929).
- 122 A. F. Holleman and G. L. Voerman, Rec. Trav. Chim. Pays-Bas, 21, 57 (1902).
- ¹²³ G. Fischer, Ann., **127**, 142 (1863).
- 194 J. D. Reidel, Ger. Pat. 67,923 (1891) [Frdldr., 3, 868 (1890-1894)].
- 125 F. Beilstein and E. Reichenbach, Ann., 132, 144 (1864).
- 126 J. B. Muenzen, L. R. Cerecedo, and C. R. Sherwin, J. Biol. Chem., 87, 473 (1926).
- 127 A. Cahours, Ann. Chim. Phys., [3] 53, 334 (1858).
- ¹²⁸ K. Schirmacher and A. Brunner, Ger. Pat. 239,092 [Frdldr., 10, 488 (1910-1912)].
- 129 G. R. Robertson, Org. Syntheses, Coll. Vol. 1, 2nd Ed., 52. (1941).
- ¹³⁰ G. Schroeter, Ber., 40, 1596 (1907).
- ¹³¹ H. Seidel, Ber., 34, 4352 (1901).
- ¹³² A. Deninger, J. Prakt. Chem., [2] 42, 551 (1890).
- ¹³³ E. Hotter, J. Prakt. Chem., [2] 38, 113 (1888).
- 134 W. A. Jacobs and M. Heidelberger, Am. Chem. J., 39, 2431 (1917).

- 135 L. Balbiano, Gazz. Chim. Ital., 14, 1245 (1884) [Chem. Zentr., 1886, II, 38].
- ¹⁸⁸ K. van Auwers and E. Frese, Ann., 450, 302 (1926).
- ¹⁶⁷ H. Hubner, Ann., 228, 81 (1884).
- ¹⁸⁸ C. Voit, Ann., 99, 106 (1856).
- 139 D. Muretow, Z. Angew. Chem., 1870, 652 [Chem. Zentr. 1871, II, 19].
- 140 H. L. Wheeler and C. Hoffman, J. Amer. Chem. Soc., 45, 1440 (1911).
- 141 L. Edeleanu, J. Chem. Soc., 53, 560 (1888).
- 149 R. Meldola and R. Brightman, J. Chem. Soc., 111, 540 (1917).
- 148 F. Pufahl, Ber., 62, 2120 (1929).
- 144 H. Limpricht, Ann., 177, 79 (1875).
- 145 H. Limpricht, Ann., 177, 73 (1875).
- 146 H. Goldschmidt and H. Larsen, Z. Phys. Chem. (Leipzig), 71, 1440 (1910).
- 147 C. Goslic, Ann., 180, 100 (1876).
- 148 A. Thomas, Ann., 186, 126 (1877).
- 149 H. Pechmann, Ann., 173, 215 (1874).
- ¹⁵⁰ E. Wechwarth, Ann., 172, 193 (1874).
- ¹⁵¹ M. Hayduck, Ann., 174, 350 (1874).
- ¹⁵² G. Foth, Ann., 230, 306 (1885).
- 153 O. Jacobsen and H. Ledderbogge, Ber., 16, 193 (1883).
- 154 G. Errera, Gazz. Chim. Ital., 19, 537 (1889) [Chem. Zentr., 1891, II, 535].
- ¹⁵⁵ H. Rose, Ann., 164, 70 (1872).
- ¹⁵⁸ A. Purgotti and C. Monti, Gazz. Chim. Ital., 30 II, 254 (1900) [Chem. Zentr., 1900 II,

960].

- 157 P. T. Cleve, Ber., 23, 960 (1890).
- ¹⁵⁸ E. Schmidt and B. Schaal, Ber., 7, 1367 (1874).
- ¹⁵⁹ P. T. Cleve, Bull. Soc. Chim. Fr., [2], 26, 447 (1876).
- 189 P. T. Cleve, Ber., 21, 3264 (1888).
- 181 O. Keller and G. Schulze, Arch. der Pharm., 263, 499 (1925).
- ¹⁶² E. Hart, Am. Chem. J., 1, 411 (1879).
- 183 E. Hart, Am. Chem. J., 1, 347 (1879).
- ¹⁸⁴ O. Kornatzki, Ann., 221, 198 (1883).
- 185 J. E. Alen, Ber. (Ref.), 17, 437 (1884).
- 188 W. Markwald, Ann., 274, 350 (1893).
- ¹⁸⁷ H. Limpricht, Ber., 18, 2194 (1885).

188 H. E. Fierz-David and L. Blangey, Fundamental Processes of Dye Chemistry, 5th Ed., Interscience, New York, 1949, p. 153.

- ¹⁸⁹ J. Perl, Ber., 18, 2194 (1885).
- ¹⁷⁰ H. Schwanert, Ann., 186, 360 (1903).
- ¹⁷¹ G. Mohr, Ann., **221**, 225 (1883).
- 179 T. Krober, Ger. Pat. 189,513 (1905) [Frdldr., 9, 361 (1911)].
- 173 P. Julius, Ger. Pat. 121,427 (1901) [Frdldr., 6, 877 (1901)].
- 174 A. Wahl, Bull. Soc. Chim. Fr., [3], 29, 347 (1903).
- ¹⁷⁵ I. G. Farben., Ger. Pat. 492,446 (1930) [Frdldr., 16, 1419 (1913)].
- 178 H. E. Fierz David, Helv. Chim. Acta, 10, 214 (1927).

177 H. E. Fierz-David and L. Blangey, Fundamental Processes of Dye Chemistry, 5th Ed., Interscience, New York, 1949, p. 228.

- 178 R. Scholl, J. Potschiwauscheg, and J. Lenko, Monatsh. Chem., 32, 695 (1911).
- ¹⁷⁹ R. Scholl, Ber., 43, 354 (1910).
- ¹⁸⁰ K. Brass and E. Ferber, Ber., 55, 544-551 (1922).
- ¹⁸¹ E. Benesch, Monatsh. Chem., 32, 450 (1911).
- 182 R. Eder and O. Manoukian, Helv. Chim. Acta, 9, 58 (1926).
- ¹⁶³ L. Gattermann, Ann., 393, 163 (1912).
- ¹⁸⁴ E. Terres, Ber., 46, 1639 (1913).
- 185 O. Schmidt, Ber., 37, 71 (1904).
- ¹⁸⁸ Badische. Ger. Pat. 114,262 (1900) [Frdldr., 6, 324 (1901)].
- ¹⁸⁷ A. Claus, Ber., 15, 1520 (1882).

## ORGANIC REACTIONS

- 188 A. G. Perkin and R. C. Storey, J. Chem. Soc., 1929, 1416.
- 189 C. Seer and E. Karl, Monatsh. Chem., 34, 640 (1913).
- ¹⁹⁰ R. Scholl, Ber., 44, 2375 (1911).
- ¹⁹¹ P. Nawiasky and J. Muller, Ger. Pat. 486,021 (1929) [Frdldr., 16, 1497 (1931)].
- ¹⁹² J. Pinnow, Ber., **31**, 2928 (1898).
- ¹⁹³ A. Harden, Ann., 255, 155 (1889).
- 194 H. E. Fierz-David and L. Blangey, Fundamental Processes of Dye Chemistry, 5th Ed.,
- Interscience, New York, 1949, p. 237.
  - ¹⁹⁵ A. Echert, Monatsh. Chem., 35, 296 (1914).
  - 186 A. Schaarschmidt and A Stahlschmidt, Ber., 45, 3454 (1912).
  - ¹⁹⁷ G. Machek, Monatsh. Chem., 53/54, 663 (1929).
  - 188 G. Schultz and R. Anschutz, Ber., 10, 325 (1877).
  - 199 K. Brass and G. Nickel, Ber., 58, 207 (1925).
  - ²⁰⁰ M. A. Kunz and E. Berthold, Ger. Pat. 495,367 (1928) [Frdldr., 16, 1414 (1931)].
  - ²⁰¹ R. Eder and O. Manoukian, Helv. Chim. Acta, 9, 55 (1926).
  - ²⁰² G. Heller, Z. Angew. Chem., 42, 173 (1929).
  - ²⁰³ G. Heller, E. Mertz, and A. Siller, Ber., 62, 936 (1929).
  - ²⁰⁴ Bayer and Co., Ger. Pat. 114,200 (1900) [Frdldr., 6, 352 (1901)].
  - ²⁰⁵ A. Hempel, J. Prakt. Chem., [2], 41, 170 (1890).

²⁰⁶ H. E. Fierz-David and L. Blangey, Fundamental Processes of Dye Chemistry, 5th Ed., Interscience, New York, 1949, p. 320.

- ²⁰⁷ G. Heller, Z. Angew. Chem., 42, 173 (1929)
- ²⁰⁸ FIAT Report No. 1313, Vol. I (1948), p. 229.
- ²⁰⁹ Z. Bankiewicz, Ber., 22, 1399 (1889).
- ²¹⁰ J. C. Cain, Ber., 28, 968 (1895).
- ²¹¹ F. Ullmann and R. Medenwald, Ber., 46, 1806 (1913).
- ²¹² Badische, Ger. Pat. 279,866 (1914) [Frdldr., 12, 419 (1917)].
- ²¹³ P. Nawiasky, Ger. Pat. 485,275 (1929) [Frdldr., 16, 1245 (1931)].
- ²¹⁴ L. M. Norton and J. F. Elliott, Ber., 11, 327 (1878).
- ²¹⁵ P. Friedlaender and J. Weisberg, Ber., 28, 1842 (1895).
- ²¹⁶ J. Pinnow and F. Wiskott, Ber., 32, 900 (1899).
- ²¹⁷ O. Kym and M. Ringer, Ber., 48, 1674 (1915).
- ²¹⁸ E. Noelting and G. Thismar, Ber., 35, 630 (1902).
- ²¹⁹ K. Fries and K. Noll, Ann., 389, 374 (1912).
- ²²⁰ K. Jedlicka, J. Prakt. Chem., [2], 48, 104 (1893).
- 221 R. Anschutz and G. Rauff, Ann., 327, 215 (1903).
- ²²² R. Fittig, Ann., 141, 139 (1867).
- ²²⁸ R. J. W. LeFevre and E. E. Turner, J. Chem. Soc., **1928**, 246.
- ²²⁴ K. Brand and E. Wild, Ber., 56, 110 (1923).
- ²²⁵ E. Terres, Monatsh. Chem., 41, 608 (1920).
- ²²⁸ W. Borsche, Ber., 50, 1348 (1917).
- ²²⁷ W. Kellner and F. Beilstein, Ann., 128, 173 (1863).
- ²²⁸ Meister, Lucius & Bruning, Ger. Pat. 85,388 (1869) [Frdldr., 4, 77 (1899)].
- 229 J. Pinnow, J. Prakt. Chem., [2], 62, 508 (1900).
- ²⁸⁰ K. Ullmann and E. Deletra, Ann., 332, 85 (1904).
- ²³¹ E. Heidensleber, Ber., 28, 3458 (1890).
- ²³² F. Ullmann and P. Dootson, Ber., 51, 16 (1918).
- 233 T. Zincke and J. Muller, Ber., 46, 1779 (1913).
- ²³⁴ K. Streitwolf and A. Fehle, Ger. Pat, 489,459 (1929) [Frdldr., 16, 2319 (1931)].
- 235 J. Pinnow, J Prakt. Chem., [2], 63, 359 (1901).
- 238 R. Nietzki and Baur, Ber., 28, 2977 (1895).
- ²³⁷ E. Wirth, Ger. Pat. 139,568 (1903) [Frdldr., 7, 71 (1905)].
- ²⁸⁸ K. Fries, Ann., 454, 206 (1927).
- 289 O. L. Brady, J. N. E. Day, and C. V. Reynolds, J. Chem. Soc., 1929, 2265.
- 240 H. Lindemann, Ber., 57, 1559 (1924).
- 241 P. Kehrmann, F. Rademacher, and O. Feder, Ber., 31, 3084 (1898).

### THE ZININ REDUCTION OF NITROARENES

- ²⁴² O. Kym, Ber., 37, 1072 (1904).
- ²⁴³ E. Heim, Ber., 21, 2302 (1888).
- ²⁴⁴ M. Battegay and J. Vechot, Bull. Soc. Chim. Fr., [4] 37, 1286 (1925).
- ²⁴⁵ A. Lindemann and W. Wessel, Ber., 58, 1229 (1925).
- ²⁴⁶ F. Ullmann, Ann., 386, 84 (1909).
- ²⁴⁷ H. Hubner, Ann., 208, 317 (1881).
- ²⁴⁸ M. Battegay and J. Bernhardt, Bull. Soc. Chim. Fr., [4] 33, 1516 (1923).
- ²⁴⁹ Bayer and Co., Ger. Pat. 220,581 (1910) [Frdldr., 9, 764 (1911)].
- ²⁵⁰ T. Zincke and H. Rose, Ann., 406, 109 (1914).
- ²⁵¹ R. Nietzki and A. Raillord, Ber., **31**, 1461 (1898).
- ²⁵² G. Banus and J. Guteros, An. Real Soc. Espan., 20, 481 (1922) [C.A., 17, 2574 (1923)].
- ²⁵³ G. Charrier and A. Beretta, Gazz. Chim. Ital., 54, 981 (1924).
- ²⁵⁴ K. Elbs, J. Prakt. Chem., [2] 108, 223 (1924).
- ²⁵⁵ R. Meldola and J. V. Eyre, Chemical News of Industrial Science, 83, 286 [F. Beilstein, Handbuch der Organischen Chemie, Vol. 16, 4th Ed., Springer, Berlin, 1933, p. 170].

  - ²⁵⁶ R. Meldola, J. Chem. Soc., 47, 662 (1885).
  - ²⁵⁷ J. V. Janovsky, Ber., 16, 1488 (1883).
  - ²⁵⁶ Anilin-Fabrik., Ger. Pat. 72,392 (1893) [Frdldr., 3, 734 (1894)].
  - ²⁵⁹ L. Claisen, Ann., 418, 103 (1919).
  - ²⁶⁰ Badische, Ger. Pat. 275,040 (1914) [Frdldr., 11, 421 (1912-1914)].
  - ²⁶¹ E. Noelting and F. Binder, Ber., 20, 3016 (1887).
  - ²⁶² O. N. Witt and E. Kopetschni, Ber., 45, 1153 (1912).
  - ²⁶³ R. Meldola, J. Chem. Soc., 43, 432 (1883).
  - ²⁶⁴ Anilin-Fabrik., Ger. Pat. 293,186 (1916) [Frdldr., 13, 572 (1916-1921)].
  - ²⁶⁵ Anilin-Fabrik., Ger. Pat. 64,434 (1892) [Frdldr., 3, 742 (1890-1894)].
  - ²⁶⁶ Meister, Lucius & Bruning, Ger. Pat, 88,013 (1896) [Frdldr., 4, 1021 (1894-1897)].
  - ²⁶⁷ A. Blank and M. Latten, Ger. Pat. 243,685 (1912) [Frdldr., 10, 895 (1910-1912)].
  - ²⁶⁶ Meister, Lucius & Bruning, Ger. Pat. 70,885 (1893) [Frdldr., 3, 599 (1890-1894)].
  - ²⁶⁹ W. Lewcock, J. Soc. Chem. Ind. (London), 44, 1537 (1925).
  - ²⁷⁰ W. G. Christiansen, J. Amer. Chem. Soc., 46, 499 (1924).
  - ²⁷¹ G. Charrier and A. Beretta, Gazz. Chim. Ital., 53, 733 (1923).