THE REACTIONS OF MESITYL OXIDE

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I. INTRODUCTION

Mesityl oxide (I) is a tri-functional intermediate of considerable utility in the synthesis of a number of different types of organic compounds.

$$(CH_3)_2C{=}CH{-}CO{-}CH_3$$

I

The possibility of effecting reaction at the double bond, the carbonyl group, the α-methyl group or several of these sites simultaneously is the key to the versatility of this material.

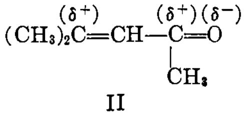
The chemistry of mesityl oxide has not previously been reviewed and this article will attempt to cover the literature through 1960. Where possible, significant post-1960 references have been included. Emphasis has been given to more recent work in the area since such work is, in general, more complete and offers better description of the experimental procedures.

Mesityl oxide is actually 4-methyl-3-pentene-2-one, but the name mesityl oxide is so well-established that it will be used throughout this review. All other nomenclature conforms to "Chemical Abstracts" systems.

The poly-functionality of mesityl oxide provides the logical basis for this review of its reactions. For purposes of brevity, preparations of mesityl oxide and the well-known preparations of mesitylene and phorone from mesityl oxide have been omitted.

II. THE REACTIVITY OF MESITYL OXIDE

The majority of the reactions of mesityl oxide are those of either an α,β-unsaturated carbonyl compound or those of a methyl ketone. From structure II, it can be seen that both the carbonyl carbon atom and the β-ethylenic carbon atom are activated for nucleophilic attack.



$$(CH_3)_2\overset{(\delta^+)}{C}{=}CH{-}\underset{\displaystyle |\atop CH_3}{\overset{(\delta^+)}{C}}{=}\overset{(\delta^-)}{O}$$

II

Accordingly, mesityl oxide may undergo 1,2- or 1,4-

addition. The general tendency for nucleophilic reagents to add at the end of a conjugated system (β-carbon) is partially balanced by the greater charge on the carbonyl carbon closer to the electronegative oxygen atom which initiates the electronic shift. Due to these opposing factors, quantitative prediction of the site of reaction is difficult. However, as will be seen, the β-carbon atom appears more favored for nucleophilic addition.

The further description of mesityl oxide as a methyl ketone leads immediately to its reactivity in aldol- and Claisen-type condensations. The methyl group, rendered electron-deficient by the carbonyl oxygen, readily loses a proton to form the carbanion which is the attacking species in these reactions. The combination of the high electrophilicity of the β-carbon with this reactivity of the α-methyl group is an important factor in many of the cyclization reactions of mesityl oxide.

Some of the reactions of mesityl oxide are also complicated by the several tautomeric forms possible for the molecule. At equilibrium, at room temperature, mesityl oxide is a nine-to-one mixture (142) of I and 4-methyl-4-pentene-2-one (III, isomesityl oxide). Freshly prepared, mesityl oxide is primarily I and equilibrates with III very slowly unless base is present.

$$CH_2{=}C(CH_3){-}CH_2{-}CO{-}CH_3$$

III

When base-catalyzed equilibration is combined with an attacking species which is a good hydrogen acceptor, the major reaction product may be derived from III rather than I. This will be illustrated later.

One further structural tautomer of mesityl oxide, the enol form IV, is possible. However, enolic reactions of mesityl oxide are very limited.

$$(CH_3)_2C{=}CH{-}C(OH){=}CH_2$$

IV

III. REACTIONS AT THE DOUBLE BOND

A. SIMPLE ADDITIONS

Mesityl oxide undergoes a variety of simple nucleophilic additions at the double bond. These reactions all proceed by Markownikoff addition as would be expected from the polarization of the molecule (structure II). Furthermore, the activating influence of the carbonyl oxygen makes addition facile and rapid. In only a few cases is a small amount of the counter-Markownikoff product isolated.

Mesityl oxide readily adds halogens, hydrohalic acids and hypohalic acids. The results of these reactions are summarized in Table I. Often, the reaction product is unstable and yields have either been omitted or refer to crude products.

TABLE I

REACTIONS OF MESITYL OXIDE WITH HALOGENS, HYDROHALIC ACIDS AND HYPOHALIC ACIDS

Reagent	Product: $(CH_3)_2CXCHYCOCH_3$		Yield, %	References
	X	Y		
Cl_2	Cl	Cl	30	(41)
Br_2	Br	Br	..	(117, 48)
I_2	I	I	..	(49)
HCl	Cl	H	..	(128)
HBr	Br	H	..	(131)
HI	I	H	..	(118)
HOCl	OH	Cl	60	(115, 139)
HOBr	OH	Br	25	(115)
HOI	OH	I	..	(115)

This instability often allows secondary reactions to be performed directly in solution. For example, chlorination of mesityl oxide in the presence of sodium bicarbonate (145) gives 60–70% of 3-chloro-4-methyl-3-pentene-2-one (V), formed by dehydrochlorination of the original dichloro-adduct.

$$(CH_3)_2C{=}CCl{-}CO{-}CH_3$$

V

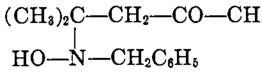
The addition of ammonia and simple amines to mesityl oxide is straightforward and requires no catalyst. However, the 4-amino-4-methyl-2-pentanones (VI) obtained as products are again unstable and are usually isolated as salts.

$$(CH_3)_2C(NR_1R_2){-}CH_2{-}CO{-}CH_3$$

VI

R_1	R_2	Yield, %	Reference
H	H	69	(67)
Me	H	"Quantitative"	(71)
Me	Me	"Good"	(71)

"Good" yields of 4-(N-benzyl-N-hydroxylamino)-4-methyl-2-pentanone (VII) have been reported in a similar reaction of mesityl oxide and N-benzyl-hydroxylamine (134). The yield of the corresponding reaction with N-phenylhydroxylamine is described as very poor.



$$\begin{array}{l}(CH_3)_2C{-}CH_2{-}CO{-}CH_3\\ \qquad\;\;|\\ HO{-}N{-}CH_2C_6H_5\end{array}$$

VII

The addition of alcohols to mesityl oxide to give 4-alkoxy-4-methyl-2-pentanones (VIII) may be acid- (73) or base-catalyzed (144). In general, basic catalysis appears to produce better yields. Some typical reactions are listed in Table II.

TABLE II

REACTIONS OF MESITYL OXIDE WITH ALCOHOLS

ROH, R =	Yield of $(CH_3)_2C(OR)CH_2$-$COCH_3$ (VIII), %	Reference
Me	[a]	(144)
Et	21	(73)
Et	82	(144)
Pr	..	(73)
Bu	25	(73)
Bu	[b]	(144)
iso-Bu	..	(73)
iso-Amyl	..	(73)
Benzyl	..	(73)

[a] "High" yield based on 45–50% conversion. "High" yield based on 32% conversion.

More recently (101), anion exchange resins have been used to catalyze the additions. A yield of 90–95% (40–60% conversion) is obtained with methanol and 82% (27% conversion) with ethanol.

Hydrogen sulfide adds to mesityl oxide with triethylamine as catalyst (53) to yield 80% of 4-mercapto-4-methyl-2-pentanone (IX). With a potassium hydroxide catalyst (7), an unspecified amount of the bis-compound X is formed as by-product.

$(CH_3)_2C(SH)—CH_2—CO—CH_3$ IX

$S(C(CH_3)_2—CH_2—CO—CH_3)_2$ X

The reaction of mesityl oxide and thiocyanic acid (24) results in a 72% yield of 4-methyl-4-thiocyanato-2-pentanone (XI). Similarly, mesityl oxide adds sulfuric acid (86) to give 2-methyl-4-oxo-2-pentane-sulfonic acid (XII, as the sodium salt). The identical product is obtained by direct addition of sodium bisulfite (61).

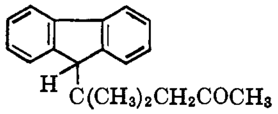
$(CH_3)_2C(SCN)—CH_2—CO—CH_3$
XI

$(CH_3)_2C(SO_3Na)—CH_2—CO—CH_3$
XII

The addition of aromatic compounds to mesityl oxide is illustrated by aluminum chloride-catalyzed reactions with benzene (74) and chlorobenzene (40). The products are, respectively, 4-methyl-4-phenyl-2-pentanone (XIII, 72–89% yield) and 4-(*p*-chlorophenyl)-4-methyl-2-pentanone (XIV, 62% yield). Fluorene adds to mesityl oxide in 15–20% yield using a potassium hydroxide catalyst (54). The product, 4-(9-fluorenyl)-4-methyl-2-pentanone (XV), may be obtained in 55% yield by the use of 9-fluorenylsodium.

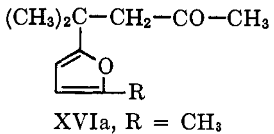
$(CH_3)_2C(C_6H_5)—CH_2—CO—CH_3$
XIII

$(CH_3)_2C(C_6H_4—Cl\text{-}p)—CH_2—CO—CH_3$
XIV



XV

The heterocyclic 2-methylfuran (97, 165) and 2-ethylfuran (165) undergo acid-catalyzed additions to give XVIa (50%) and XVIb, respectively.



XVIa, R = CH_3
b, R = C_2H_5

A variety of phosphorus- and/or sulfur-containing organic acids, including dialkyl phosphites (124), dialkyl dithiophosphates (72), thiolacetic acid (23, 150) and ethyl alkylphosphonites (125), have been allowed to react with mesityl oxide. High yields of the simple addition products are generally obtained. These reactions may be uncatalyzed, base-catalyzed or free radical-catalyzed and are summarized in Table III.

TABLE III

REACTIONS OF MESITYL OXIDE WITH PHOSPHORUS AND/OR SULFUR-CONTAINING ORGANIC ACIDS

Reagent	Catalyst	Product yield, %	Reference
$(RO)_2POH$, R =	$(CH_3)_2C(P(O)(OR)_2)CH_2COCH_3$		
Me	NaOMe	70	(124)
Bu	NaOBu	77	(124)
iso-Bu	NaOBu-iso	69	(124)
$(RO)_2PS_2H$	$(CH_3)_2C(SP(S)(OR)_2)CH_2COCH_3$		
Et	...	88	(72)
2-ClEt	...	86	(72)
iso-Pr	...	76	(72)
sec-Bu	...	99	(72)
4-Me-2-pentyl	...	85	(72)
n-tetradecyl	...	81	(72)
C_6H_5	...	74	(72)
CH_3COSH	$(CH_3)_2C(SCOCH_3)CH_2COCH_3$		
CH_3COSH	Piperidine	64	(150)
CH_3COSH	Benzoyl peroxide	92	(23)
$EtP(O)(OR)H$	$(CH_3)_2C(P(O)(OR)Et)CH_2COCH_3$		
Et	NaOEt	46	(125)
Bu	NaOBu	36	(125)

Treatment of mesityl oxide with phosphorus trichloride and acetic anhydride (42), followed by hydrolysis, gives 33% of the phosphite XVIIa. The butyl ester XVIIb is obtained in 20% yield when the intermediate is treated with butyl alcohol and sodium rather than hydrolyzed. By direct action of butyldichlorophosphine–acetic anhydride and diphenoxychlorophosphine–acetic anhydride on mesityl oxide, the addition products XVIIc (74%) and XVIId (41%) are obtained.

$(CH_3)_2CX—CH_2—CO—CH_3$
XVII

XVIIa, X = PO_3H_2; c, X = $PO_2HC_4H_9$
b, X = $PO_2H(OC_4H_9)$; d, X = $PO(OC_6H_5)_2$

The Ritter reaction of nitriles and mesityl oxide using a sulfuric acid catalyst (135) results in fair yields of the substituted amides. These reactions along with several other miscellaneous simple additions are listed in Table IV.

TABLE IV

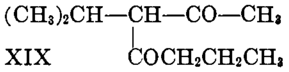
Reagent	Catalyst	Product $(CH_3)_2C(R)$-CH_2COCH_3, R =	Yield, %	Reference
C_6H_5CN	H_2SO_4	$NHCOC_6H_5$	45–55	(135)
CH_3CN	H_2SO_4	$NHCOCH_3$	25	(135)
$CH(NO_2)_3$	...	$C(NO_2)_3$	...	(153)
NaN_3	...	N_3	38	(18)
CH_3NO_2	Et_2NH	CH_2NO_2	65	(88)

The peroxide-catalyzed addition of simple aldehydes to mesityl oxide (116) gives fair to good yields of diketones XVIII, although conversions are rather low.

$ROC—C(CH_3)_2—CH_2—CO—CH_3$
XVIII

R	Conversion, %	Yield, %
CH_3	10	31
n-C_3H_7	41	97
n-C_6H_{13}	..	37–61

In the case of butyraldehyde, a small amount (about one part in ten) of the counter-Markownikoff product XIX is isolated from the reaction.



$$(CH_3)_2CH—\underset{\displaystyle COCH_2CH_2CH_3}{\underset{|}{CH}}—CO—CH_3$$

XIX

B. ADDITION ACCOMPANIED BY SECONDARY REACTIONS

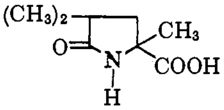
Several other addition reactions of mesityl oxide have been described but these are somewhat complicated by side-reactions or reactions at other sites. Potassium cyanide adds to mesityl oxide (99) giving the nitrile XX (mesitonitrile) in good yields. Compound XX may then react, *in situ*, to give the cyanohydrin XXI which cyclizes to the pyrrolidone XXII (mesitylic acid).

$$(CH_3)_2C(CN)—CH_2—CO—CH_3$$

XX

$$(CH_3)_2C(CN)—CH_2—C(OH)(CN)—CH_3$$

XXI



XXII

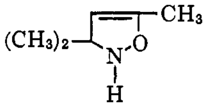
A similar situation exists with hydroxylamine. The hydroxamic acid XXIII is formed by addition of mesityl oxide, but this is accompanied by formation of mesityl oxide oxime (XXIV) and the cyclized product XXV, arising from an internal condensation of XXIII (64).

$$(CH_3)_2C(NHOH)—CH_2—CO—CH_3$$

XXIII

$$(CH_3)_2C═CH—C(CH_3)═NHOH$$

XXIV



XXV

The reaction of elemental sulfur, hydrogen and mesityl oxide, catalyzed by cobalt polysulfide–acetic acid (50), gives 15% of 4-mercapto-2-methyl-2-pentene (XXVI) and 20% of 2,4-dimercapto-2-methylpentane (XXVII), formed by addition and oxygen replacement. The reaction of ethanethiol with mesityl oxide (123) may result in counter-Markownikoff addition yielding 2,2,3-tris-(ethylmercapto)-4-methylpentane (XXVIII), but no evidence exists that the "abnormal" adduct is actually the product.

$$(CH_3)_2C═CHCHSHCH_3$$

XXVI

$$(CH_3)_2C(SH)CH_2CHSHCH_3$$

XXVII

$$(CH_3)_2CHCH(SEt)C(SEt)_2CH_3$$

XXVIII

C. HYDROGEN SUBSTITUTION AND MISCELLANEOUS REACTIONS

Several reactions involving substitution of the hydrogen on the α-ethylenic carbon atom have been reported. Treatment of mesityl oxide with dimethyl sulfate using sodium *tert*-amylate as catalyst (34) yields 41% of 3,4-dimethyl-3-pentene-2-one (XXIX). The similar reaction using benzyl bromide gives an unspecified amount of the 3-benzyl analog of XXIX. The reaction of ethylene with mesityl oxide (75) results in a 7% yield of 3-ethyl-4-methyl-3-pentene-2-one (XXX).

$$(CH_3)_2C═C(CH_3)—CO—CH_3$$

XXIX

$$(CH_3)_2C═C(C_2H_5)—CO—CH_3$$

XXX

The base-catalyzed cyanoethylation of mesityl oxide with acrylonitrile (25) gives 10–15% of XXXI and 74% of XXXII. The formation of XXXII illustrates the double bond shift which may occur in the presence of strong base and a good hydrogen acceptor.

$$(CH_3)_2C═C(CH_2CH_2CN)—CO—CH_3$$

XXXI

$$CH_2═C(CH_3)—C(CH_2CH_2CN)_2—CO—CH_3$$

XXXII

IV. REACTIONS AT THE CARBONYL GROUP

A. GRIGNARD REACTIONS

The majority of reactions at the carbonyl group of mesityl oxide are Grignard or Grignard-type. As opposed to simple addition reactions at the double bond which are generally based on 1,4-addition, these may be considered as 1,2-additions across the carbonyl double bond. There is a wise range of yields in mesityl oxide–Grignard reactions and a number of low yield syntheses have been included because of the unusual products obtainable from them. Table V summarizes some of these reactions.

The mode of dehydration of the product alcohols can be changed by variation in the reaction conditions. For example, with ethyl Grignard reagents dehydration

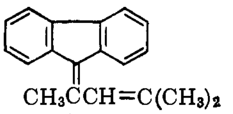
TABLE V

GRIGNARD REACTIONS OF MESITYL OXIDE

Reagent	Product	Yield, %	Reference
MeMgI	$Me_2C═CHC(OH)Me_2$	29	(51)
MeMgI	$Me_2C═CHCMe═CH_2$	..	(56)
EtMgBr	$Me_2C═CHC(Et)═CH_2$	12	(83)
EtMgBr	$Me_2C═CHC(Me)═CHMe$	51	(47)
EtMgI	$Me_2C═CHC(Me)═CHMe$	53	(141)
tert-BuMgCl	$Me_2C═CHC(CMe_3)═CH_2$ + $CH_2═CMeCH═CMeCMe_3$	35	(154)
isoamylMgBr	$CH_2═CMeCH_2CMe═CHCH_2$-$CHMe_2$	...	(84)
C_6H_5MgBr	$Me_2C═CHC(C_6H_5)═CH_2$	"Low"	(83)
C_6H_5MgBr	$Me_2C═C═C(C_6H_5)Me$	44	(87)
$C_6H_5CH_2MgCl$	$Me_2C═CHCMe(OH)CH_2C_6H_5$	26	(52)
$CH_2═CHCH_2MgBr$	$Me_2C═CHCMe(OH)CH_2CH═CH_2$	90	(109)
$Me_2C═CHLi$	$Me_2C═CHCMe(OH)CH═CMe_2$	8	(20)
$Me_2C═CMeLi$	$Me_2C═CHCMe(OH)CMe═CMe_2$	67	(21)
$CH_2═CMeLi$	$Me_2C═CHCMe(OH)CMe═CH_2$	74	(21)
C_2H_2-Ca	$Me_2C═CHCMe(OH)C≡CH$	75	(114)

may occur between the hydroxyl and ethyl or methyl groups (47, 83, 141); with phenyl Grignards, dehydration occurs with the α-methyl group or internally with the α-ethylenic carbon giving an allene (83, 87). In the case of *tert*-butyl magnesium chloride (154) one of the products obtained is that from a double-bond shift and internal dehydration, while with isoamylmagnesium bromide (84) the double bond shift also occurs but the product is still formed by external dehydration with the amyl group. No systematic investigation of the various reactions of mesityl oxide with Grignard reagents has as yet been made and this appears a fertile field for investigation.

The reaction of 9-fluorenylmagnesium bromide and mesityl oxide has also been reported (147) and gives 30% of the hydrocarbon XXXIII. Here, the dehydration involves the 9-hydrogen of fluorene.



XXXIII

B. MISCELLANEOUS REACTIONS

In addition to Grignard-type reactions, mesityl oxide undergoes a few other miscellaneous reactions at the carbonyl. Halogenolysis with phosphorus pentachloride (10) gives 4,4-dichloro-2-methyl-2-pentene (XXXIV). The acid-catalyzed reaction with ketene (58) yields 47% of the enol acetate of mesityl oxide (XXXV). This is one of the very few enolic reactions of mesityl oxide described in the literature. Cyanoacetic acid adds to mesityl oxide at the carbonyl group under the influence of piperidine hydrochloride (90) ultimately to give XXXVI. Finally, the reaction of mesityl oxide with potassium cyanide, followed by treatment with ammonia and hydrogen sulfide, results in an over-all yield of 14% of the thioamide XXXVII (1).

$(CH_3)_2C{=}CH{-}CCl_2{-}CH_3$
XXXIV

$(CH_3)_2C{=}CH{-}C(OCOCH_3){=}CH_2$
XXXV

$(CH_3)_2C{=}CH{-}C(CH_3){=}C(CN){-}COOH$
XXXVI

$(CH_3)_2C{=}CH{-}C(CH_3)(NH_2){-}CSNH_2$
XXXVII

V. REACTIONS AT THE α-METHYL GROUP

Aldol-type reactions of mesityl oxide and various carbonyl compounds have been reported and comprise the bulk of the material on simple reactions at the α-methyl group. In the presence of aniline-N-magnesium bromide, mesityl oxide undergoes self-condensation to give 67% of a seven to one mixture of XXXVIII and its dehydration product XXXIX (28). Similar catalysis of the reaction of mesityl oxide and acetophenone yields 31% of XL if mesityl oxide is added to the catalyst solution first and 33% of XLI if acetophenone is added first.

$(CH_3)_2C{=}CHC(CH_3)(OH)CH_2COCH{=}C(CH_3)_2$
XXXVIII

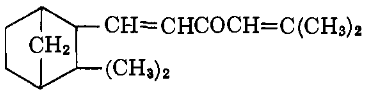
$(CH_3)_2C{=}CHC(CH_3){=}CHCOCH{=}C(CH_3)_2$
XXXIX

$(CH_3)_2C{=}CH{-}C(CH_3)(OH){-}CH_2{-}CO{-}C_6H_5$
XL

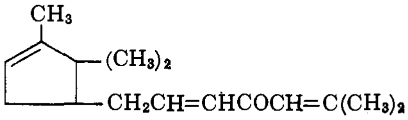
$(CH_3)_2C{=}CH{-}CO{-}CH_2{-}C(CH_3)(OH)C_6H_5$
XLI

Aldol condensations of mesityl oxide with benzaldehyde (acid catalyzed) (31), camphenaldehyde (base catalyzed, 43% yield) (5) and 4-(2,3,3-trimethylcyclopentenyl)-acetaldehyde (base catalyzed, 35%) (6) have also been reported and give compounds XLII, XLIII and XLIV, respectively.

$(CH_3)_2C{=}CH{-}CO{-}CH{=}CH{-}C_6H_5$
XLII



XLIII



XLIV

Ethyl oxalate undergoes a base-catalyzed Claisen condensation with mesityl oxide (30) to give a 100% yield (70% conversion) of the diketone XLV. When trioxymethylene is condensed with mesityl oxide using an anion exchange resin (160) there is obtained at an early stage of the reaction 10% of the condensation product XLVI and 30% of XLVII, formed by a double bond shift. On prolonged heating with magnesia, the mixture isolated consists of 25% XLVI and 20% XLVII. Some of the bis-hydroxymethyl compound XLVIII is also isolated.

$(CH_3)_2C{=}CH{-}CO{-}CH_2{-}CO{-}CO_2Et$
XLV

$(CH_3)_2C{=}CH{-}CO{-}CH_2{-}CH_2OH$
XLVI

$CH_2{-}C(CH_3){-}CH(CH_2OH){-}CO{-}CH_3$
XLVII

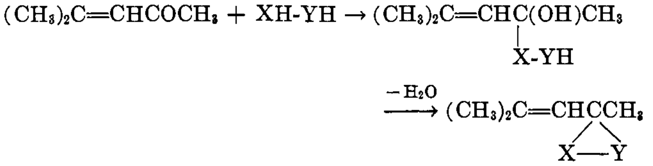
$CH_2{=}C(CH_3){-}C(CH_2OH)_2{-}CO{-}CH_3$
XLVIII

VI. REACTIONS AT SEVERAL SITES—CYCLIZATIONS

The outstanding utility of mesityl oxide lies in its ability to undergo a variety of condensation reactions leading to carbocyclic and heterocyclic compounds. This ability is a direct result of the polyfunctionality of the molecule and the fact that any of five different sites, the α-methyl group, the carbonyl group, the α-ethylenic carbon, the β-ethylenic carbon and either of the terminal *gem*-dimethyl groups, may participate in cyclization reactions.

Mesityl oxide may contribute one to five carbon atoms to formation of a ring. The resulting cyclic compounds have a three- to seven-membered ring depending upon the mode of condensation of mesityl oxide and the structure of the other reagent. The following discussion summarizes the major types of cyclization reactions on the basis of the number of carbon atoms from mesityl oxide in the product ring system.

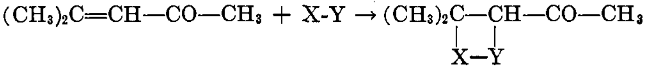
Condensation Type 1. In the majority of reactions in which mesityl oxide donates a single carbon atom to the formation of a ring, it is the carbonyl carbon which is involved. The product may be formulated as arising from a 1,2-addition to the carbonyl group and a secondary internal attack on the carbonyl carbon involving dehydration of the intermediate alcohol. The formula XH–YH represents the terminal atoms of a two- to five-membered homo- or hetero-linear chain.



$$(CH_3)_2C{=}CHCOCH_3 + XH\text{-}YH \rightarrow (CH_3)_2C{=}CH\underset{\substack{|\\ X\text{-}YH}}{C}(OH)CH_3 \xrightarrow{-H_2O} (CH_3)_2C{=}CH\underset{\substack{/\ \backslash\\ X—Y}}{C}CH_3$$

Type 1

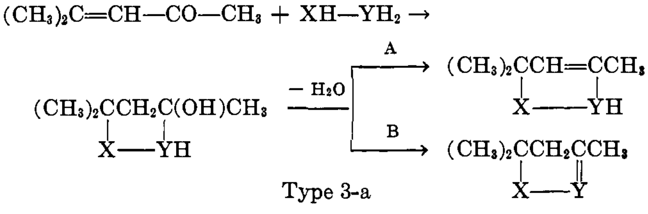
Condensation Type 2.—Those cyclization reactions in which two carbon atoms from mesityl oxide take part can be generally formulated as additions to the carbon–carbon double bond and require no further comment.



$$(CH_3)_2C{=}CH{-}CO{-}CH_3 + X\text{-}Y \rightarrow (CH_3)_2\underset{|}{C}{-}\underset{|}{CH}{-}CO{-}CH_3 \quad \underset{X{-}Y}{}$$

Type 2

Condensation Type 3-a.—By far the greatest number of ring-forming reactions of mesityl oxide involve the donation of three carbon atoms. The most common mechanism for these condensations is a combination of 1,4-addition and 1,2-addition. The order of these reactions is a function of the other material used. The cyclic alcohol formed may then dehydrate with either the α-ethylenic carbon (A) or the second reagent (B) supplying a hydrogen.

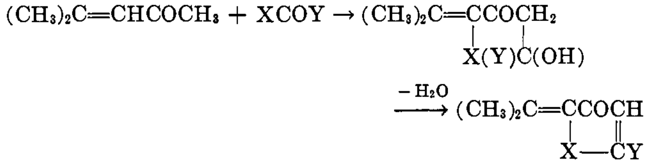


$$(CH_3)_2C{=}CH{-}CO{-}CH_3 + XH{-}YH_2 \rightarrow$$

$$\underset{\substack{|\quad\ \ |\\ X—YH}}{(CH_3)_2CCH_2C(OH)CH_3} \xrightarrow{-H_2O} \begin{cases} \xrightarrow{A} \underset{\substack{|\quad\ \ |\\ X—YH}}{(CH_3)_2CCH{=}CCH_3} \\ \xrightarrow{B} \underset{\substack{|\quad\ \ \|\\ X—Y}}{(CH_3)_2CCH_2CCH_3} \end{cases}$$

Type 3-a

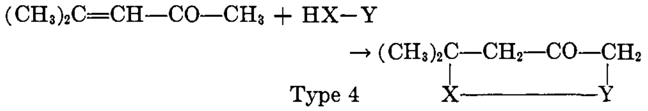
Condensation Type 3-b.—A second form of three-carbon donation by mesityl oxide is a combination of substitution at the α-ethylenic carbon and an aldol reaction at the α-methyl group. The cyclic β-keto alcohol initially formed is usually isolated in the dehydrated form.



$$(CH_3)_2C{=}CHCOCH_3 + XCOY \rightarrow (CH_3)_2C{=}\underset{\substack{|\qquad\ \ |\\ X(Y)C(OH)}}{CCOCH_2} \xrightarrow{-H_2O} (CH_3)_2C{=}\underset{\substack{|\quad\ \ \|\\ X—CY}}{CCOCH}$$

Type 3-b

Condensation Type 4.—Generally, mesityl oxide supplies a four-carbon segment for a ring-forming reaction by reaction at the β-ethylenic carbon (1,4-addition) and at the α-methyl group. The type of reaction at the α-methyl varies and will be described with specific examples during the review.

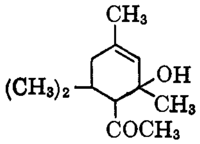


$$(CH_3)_2C{=}CH{-}CO{-}CH_3 + HX{-}Y \rightarrow \underset{\substack{|\qquad\qquad\qquad |\\ X—————Y}}{(CH_3)_2C{-}CH_2{-}CO{-}CH_2}$$

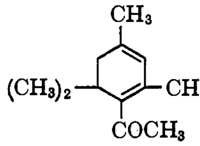
Type 4

A. SELF-CONDENSATION

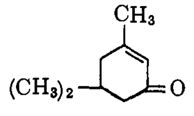
The dimerization of mesityl oxide with lithium (22) gives a 10% yield of 6-acetyl-1,3,5,5-tetramethyl-2-cyclohexenol (XLIX). The ring forms through a Type 2 condensation of one molecule and a Type 4 condensation of the other. By use of barium or calcium oxide as catalyst (158), a 30% yield of L, the dehydrated form of XLIX, is obtained. This is accompanied by a 10% yield of 3,5,5-trimethyl-2-cyclohexenone (LI, isophorone).



XLIX



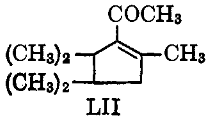
L



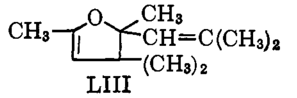
LI

A further report on dimerization with lithium (9) indicates a yield of 13% of XLIX, some L, but also 5% of 2-acetyl-1,3,3,4,4-pentamethylcyclopentene (LII) and 4% of 5-(2-methyl-1-propenyl)-2,4,4,5-tetramethyldihydrofuran (LIII). The formation of LII is formulated simply as standard Type 2 and Type 3 condensations. In the case of LIII, Type 1 and 3 reactions appear to occur, but, additionally, one of the two molecules supplies an oxygen to form the furan ring.

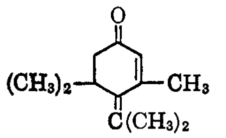
The self-condensation of mesityl oxide on an anion-



LII



LIII



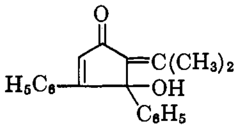
LIV

exchange resin (161) yields 16% of LI along with some 4-isopropylidene-3,5,5-trimethyl-2-cyclohexenone (LIV). Compound LIV is formed through Type 4 condensation of one molecule and an unusual two carbon reaction of the other molecule. This can be formulated as substitution at the α-ethylenic carbon and an aldol reaction and dehydration at the carbonyl group.

B. CONDENSATIONS GIVING CARBOCYCLIC COMPOUNDS

1. *Cyclopentane Derivatives*

The condensation of mesityl oxide and benzil (base-catalyzed) (82) gives 16% of 3,4-diphenyl-4-hydroxy-5-isopropylidene-2-cyclopentenone (LV). This is the only five-membered carbocyclic compound derived from mesityl oxide (except by self-condensation) and is formed by a Type 3b reaction.



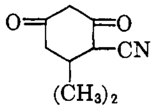
LV

2. *Cyclohexane Derivatives*

The majority of carbocyclic compounds obtained from mesityl oxide are six-membered and the formation of a number of these materials serve as excellent examples of several condensation types. Type 4 condensation is illustrated by the sodium-catalyzed reaction of ethyl or methyl cyanoacetate with mesityl oxide (133), yielding a mixture of the open-chain adduct LVI and the cyclohexadione LVII. LVI, when separated, is readily cyclized to LVII, establishing the probable mechanism.

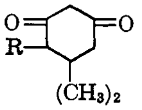
$CH_3—CO—CH_2—C(CH_3)_2—CH(CN)—CO_2R$

LVI



LVII

A group of similar reactions is summarized below.

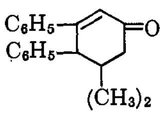


Reactant	Catalyst	Product, R =	Yield, %	Reference
$C_6H_5CH_2CO_2Et$	NaOEt	C_6H_5	57	(17)
$CH_2(CO_2Et)_2$	NaOEt	H	70	(95)
$CH_2(CO_2Et(Me))_2$	Na or KOH	$CO_2Et(Me)$	..	(152)

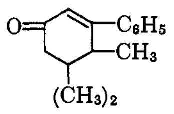
Benzyl phenyl ketone (desoxybenzoin) also undergoes a Type 4 reaction with mesityl oxide (78). The final product LVIII (52% yield) arises through dehydration of the intermediate β-keto alcohol. The linear intermediate LIX may also be isolated in 25–50% yield by use of milder conditions. A similar base-catalyzed reaction of mesityl oxide and ethyl phenyl ketone (27) yields 20% of the cyclohexenone LX.

$C_6H_5—CO—CH(C_6H_5)—C(CH_3)_2—CH_2—CO—CH_3$

LIX

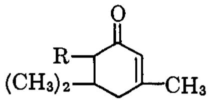


LVIII



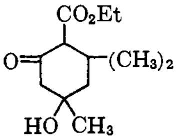
LX

The base-catalyzed reaction of N,N-diethylacetoacetamide with mesityl oxide (149) illustrates a Type 3a condensation giving a cyclohexane derivative. The product, N,N-diethyl 4,6,6-trimethyl-3-cyclohexen-2-one carboxamide (LXIa), is obtained in 61% yield. The corresponding reaction with N-ethyl-N-(2-methylphenyl)-acetoacetamide (148) yields the carboxamide LXIb. Mesityl oxide also reacts with methyl ethyl ketone and benzyl methyl ketone (27) in a like manner, the products isolated being LXIc (10% yield) and LXId (73% yield), respectively.

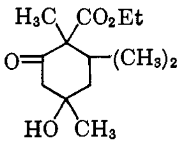


LXIa, R = $CON(C_2H_5)_2$;
b, R = $CON(C_2H_5)C_6H_4CH_3$-*o*;
c, R = CH_3
d, R = C_6H_5

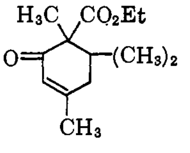
Mesityl oxide and ethyl acetoacetate condense in the presence of sodium (102) to give a low yield of ethyl 4-hydroxy-4,6,6-trimethyl-2-cyclohexanone carboxylate (LXII). More rigorous conditions (89) result in dehydration and decarboxylation of LXII so that isophorone (LI) is eventually obtained. A similar reaction with ethyl 3-methylacetoacetate yields 44% of the 1-methyl analog of LXII (LXIII), 7% of the dehydrated compound LXIV and 8% of the isophorone analog LXV.



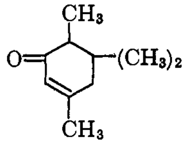
LXII



LXIII

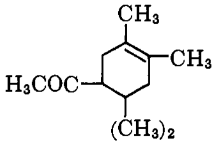


LXIV

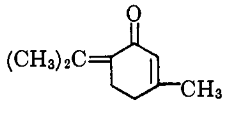


LXV

The condensation of mesityl oxide with 2,3-dimethylbutadiene (55) proceeds by a Diels–Alder reaction (Type 2) to give 5-acetyl-1,2,4,4-tetramethylcyclohexene (LXVI). The reaction of mesityl oxide and methyl vinyl ketone, catalyzed by sodium *tert*-amylate, has been surrounded by some controversy as to the actual products (15, 16, 35, 108). It now seems that the material isolated from this condensation is a mixture of 3-methyl-6-isopropylidene-2-cyclohexenone (LXVII, piperetinone) and isoxylitone (LV). Compound LXVII arises from a Type 3b reaction, while LV arises from self-condensation of two molecules of mesityl oxide. The combined yield is about 40%.



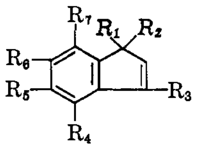
LXVI



LXVII

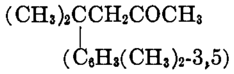
3. *Polycyclic Derivatives*

The ring-fusion of mesityl oxide with pseudocumene (1,2,4-trimethylbenzene) (140) is catalyzed by aluminum chloride and yields 25% of 1,1,3,4,5,7-hexamethylindene (LXVIIIa). The reactions of *m*-and *p*-xylene (32) give 27% of 1,1,3,4,6-pentamethylindene (LXVIIIb) and 28% of 1,1,3,4,7-pentamethylindene (LXVIIIc), respectively.



LXVIIIa, $R_1 = R_2 = R_3 = R_4 = R_5 = R_7 = CH_3$; $R_6 = H$
b, $R_1 = R_2 = R_3 = R_4 = R_6 = CH_3$; $R_5 = R_7 = H$
c, $R_1 = R_2 = R_3 = R_4 = R_7 = CH_3$; $R_5 = R_6 = H$

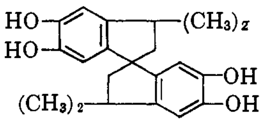
The probable mechanism of these Type 3a condensations is demonstrated by isolation of 4-(3,5-dimethylphenyl)-4-methyl-2-pentanone (LXIX) from the reaction giving LXVIIIb.



$$\underset{\displaystyle (C_6H_3(CH_3)_2\text{-}3,5)}{(CH_3)_2\overset{}{C}CH_2COCH_3}$$

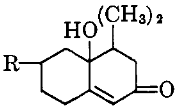
LXIX

Mesityl oxide also reacts with catechol (1,2-dihydroxybenzene) (11). In this case, however, a rather complicated secondary reaction ensues and the product finally isolated is the bis-spirohydrindene LXX (17% yield).



LXX

The base-catalyzed reaction of mesityl oxide with 2-hydroxy-cyclohexanone (33) proceeds by a Type 4 condensation and dehydration of the intermediate alcohol to yield 46% of LXXIa. A similar reaction with 4-methyl-2-hydroxycyclohexanone gives a 35–40% yield of LXXIb.

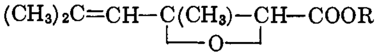


LXXIa, R = H
b, R = CH_3

C. CONDENSATIONS GIVING HETEROCYCLIC COMPOUNDS

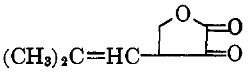
1. *Five-membered or Smaller Rings—One Hetero Atom*

The methoxide-catalyzed reaction of mesityl oxide with ethyl chloroacetate (69) yields 55% of the oxetane LXXII (R = CH_2CH_3). A small amount of the methyl analog LXXII (R = CH_3) is also formed by preliminary alcoholysis of ethyl chloroacetate by methoxide. The reaction appears to proceed by an initial 1,2-addition and subsequent cyclization by dehydrohalogenation. Formaldehyde and ethyl oxalate condense with mesityl oxide in the presence of methoxide (126) to give 53% of 2,3-diketo-4-isobutenyltetrahydrofuran (LXXIII). The reaction involves a rather unusual donation of the carbonyl carbon atom and α-methyl group as a two-carbon fragment by mesityl oxide.



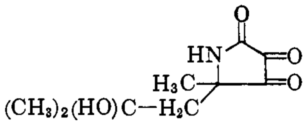
$$(CH_3)_2C{=}CH{-}\underbrace{C(CH_3){-}CH}_{O}{-}COOR$$

LXXII

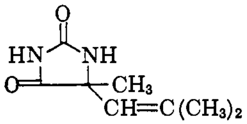


LXXIII

Low yields of both 2-(2-hydroxyisobutyl)-2-methyl-3,4,5-triketopyrrole (LXXIV) and 5-methyl-5-(2-methyl-1-propenyl)-hydantoin (LXXV) may be obtained by the reaction of mesityl oxide with potassium cyanide and ammonium carbonate (68). The formation of both of these materials illustrates Type 1 condensation except that LXXIV also contains a hydroxylic function arising from the addition of the elements of water to the carbon–carbon double bond.



LXXIV

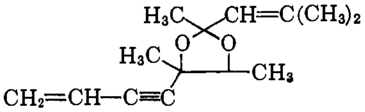


LXXV

2. *Five-membered or Smaller Rings—Two Hetero Atoms*

The reaction of mesityl oxide with 1,2-glycols and similar compounds leads to formation of 1,3-dioxolanes by condensation at the carbonyl (Type 1). The general reaction and some specific examples are listed in Table VI.

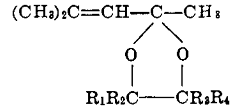
The condensation of mesityl oxide with 2,3-epoxy-3-methyl-6-heptene-4-yne (120) also yields 23% of a substituted dioxolane LXXVI.



LXXVI

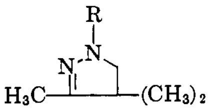
TABLE VI

FORMATION OF 1,3-DIOXOLANES

Reagent $\begin{array}{l}R_1R_2C(OH)\\ \vert\\ R_3R_4C(OH)\end{array}$	Product 	Yield, %	Reference
$R_1 = R_2 = R_3 = R_4 = H$		70–90	(132)
$R_1 = R_2 = R_3 = H;\ R_4 = CH_3$		70–90	(132)
$R_1 = R_3 = H;\ R_2 = R_4 = C_6H_5$		. . .	(85)
$R_1 = R_2 = R_3 = R_4 = CH_3$		. . .	(85)
$R_1 = R_3 = CH_3;\ R_2 = R_4 = C_6H_5$		. . .	(85)

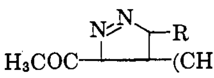
The condensation of mesityl oxide with some of the common "carbonyl" reagents provides an excellent route to the formation of the pyrazole nucleus. The initially formed carbonyl derivative readily cyclizes, with the over-all reaction being of Type 3a. However, as contrasted to previously mentioned condensations of this type, the primary reaction is a 1,2-addition rather than a 1,4-addition.

The reaction of mesityl oxide and hydrazine (38) gives 48% of 3,5,5-trimethyl-Δ^2-pyrazoline (LXXVIIa). In the corresponding reaction with phenylhydrazine (8), the phenylhydrazone may be isolated or the reaction may be carried directly to 1-phenyl-3,5,5-trimethyl-Δ^2-pyrazoline (LXXVIIb). The over-all yield is 60%. A similar reaction series has been described for *p*-nitrophenylhydrazine; however, by use of *p*-nitrophenylhydrazine hydrochloride, a direct quantitative yield of the pyrazoline LXXVIIc may be obtained. The analogous reaction with semicarbazide (65) can give either mesityl oxide semicarbazone or the pyrazoline carboxamide LXXVIId.



LXXVIIa, $R = H$; b, $R = C_6H_5$; c, $R = C_6H_4NO_2$-*p* d, $R = CONH_2$

The condensation of mesityl oxide with diazomethane and diazoethane (2) also leads to pyrazolines, 3-acetyl-4,4-dimethyl-Δ^1-pyrazoline (LXXVIII, R = H, 44% yield) and 3-acetyl-4,4,5-trimethyl-Δ^1-pyrazoline (LXXVIII, $R = CH_3$), respectively. In these cases, ring formation is of Type 2.



LXXVIII

A recent report (76) describes the reaction of mesityl oxide with diazomethane in the presence of boron trifluoride etherate. The products isolated are the ketones LXXIX and LXXX, rather than the pyrazoline.

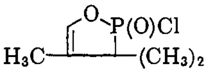
$(CH_3)_2C{=}CH{-}CH_2{-}CO{-}CH_3$

LXXIX

$(CH_3)_2C{=}CH{-}CO{-}CH_2{-}CH_3$

LXXX

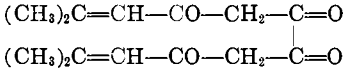
Mesityl oxide condenses with phosphorus trichloride—acetic anhydride to give 22% of the oxaphosphole oxide LXXXI (4).



LXXXI

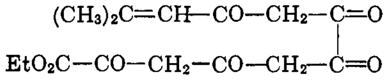
3. *Six-membered Rings—One Hetero Atom*

The reaction of diethyl oxalate and two moles of mesityl oxide (137) gives an 18% yield of compound LXXXII formed by two Claisen-type condensations. This product, in the presence of acid, undergoes cyclization to the bis-pyrone LXXXIII in 80% yield. The over-all process illustrates a Type 4 reaction. A similar reaction of two moles of ethyl oxalate with one mole of mesityl oxide and one mole of acetone yields 17% of the adduct LXXXIV which also undergoes acid-catalyzed cyclization (50%) to the pyrone LXXXV.



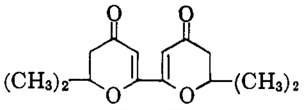
$$\begin{array}{l}(CH_3)_2C{=}CH{-}CO{-}CH_2{-}C{=}O\\ \qquad\qquad\qquad\qquad\quad\ \vert\\ (CH_3)_2C{=}CH{-}CO{-}CH_2{-}C{=}O\end{array}$$

LXXXII

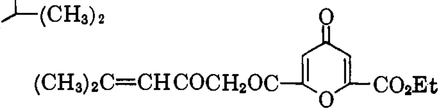


$$\begin{array}{r}(CH_3)_2C{=}CH{-}CO{-}CH_2{-}C{=}O\\ \vert\ \ \ \\ EtO_2C{-}CO{-}CH_2{-}CO{-}CH_2{-}C{=}O\end{array}$$

LXXXIV

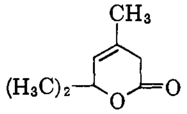


LXXXIII



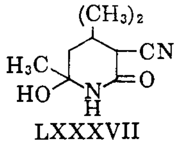
LXXXV

A pyrone, LXXXVI, is also formed in the boron trifluoride-catalyzed Type 3a condensation of mesityl oxide with ketene (164). The yield is 80%.



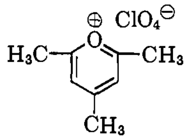
LXXXVI

The single six-membered mononitrogen heterocycle reported (127) from mesityl oxide is 6-hydroxy-4,4,6-trimethyl-2-piperidone-3-carbonitrile (LXXXVII), prepared in quantitative yield by a base-catalyzed reaction with cyanoacetamide. This is also a Type 3a condensation, but here, dehydration of the alcohol has not occurred.

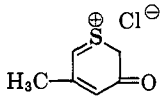


LXXXVII

When mesityl oxide is treated with sulfuric acid hydrate and acetic anhydride (138), a 22% yield of the pyrillium salt (LXXXVIII, as the perchlorate) is obtained. By treatment of mesityl oxide with thionyl chloride (121) a compound tentatively identified as the thiopyrillium salt LXXXIX is obtained. This is the one example of possible Type 5 condensation in the literature.



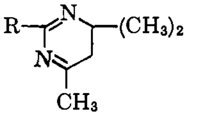
LXXXVIII



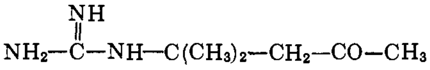
LXXXIX

4. *Six-membered Rings—Two Hetero Atoms*

The condensation of mesityl oxide and ammonium thiocyanate (70) gives 84% of 2-thio-4,4,6-trimethyldihydropyrimidine (XCa), while the base-catalyzed condensation of guanidine and mesityl oxide (146) yields 85–91% of 2-amino-4,4,6-trimethyldihydropyrimidine (XCb). Both these reactions illustrate Type 3a condensation with dehydration of the intermediate. Initial 1,4-addition of guanidine is shown by isolation of an 80% yield of the cyclizable linear intermediate XCI using guanidine thiocyanate. A similar reaction with benzamidine gives the 2-phenyl analog (XCc).



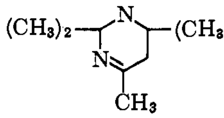
XCa, R = SH
b, R = NH_2
c, R = C_6H_5



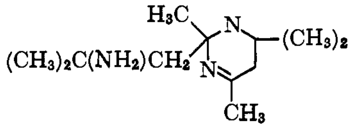
$NH_2—\overset{NH}{\overset{\|}{C}}—NH—C(CH_3)_2—CH_2—CO—CH_3$

XCI

Tetrahydropyrimidines may be obtained by the action of ammonia and acetone on mesityl oxide (19). If mesityl oxide is treated with ammonia and acetone and additional ammonia then added, a 66% yield of 2,2,4,4,6-pentamethyltetrahydropyrimidine (XCII) is isolated. By the initial reaction of ammonia and mesityl oxide, followed by treatment with more mesityl oxide and ammonia (omitting acetone), 11% of pyrimidine XCIII is obtained.

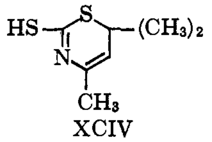


XCII

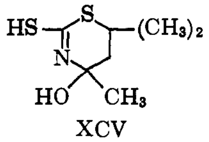


XCIII

The reaction of mesityl oxide and dithiocarbamic acid, using an acid catalyst (81), yields 91% of 2-mercapto-4,6,6-trimethylthiazine (XCIV). Less rigorous reaction conditions allow isolation of the 4-hydroxydihydro compound XCV. This is another example of Type 3a condensation.

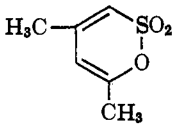


XCIV



XCV

The sulfone of mesityl oxide (XCVI) is formed in 41% yield by the action of chlorosulfonic acid–acetic anhydride (43) (Type 4). An equivalent yield is reported (105) by the use of sulfuric acid–acetic anhydride.



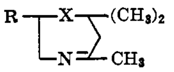
XCVI

5. *Seven-membered Rings*

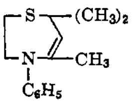
Mesityl oxide undergoes Type 3a condensations with four-membered diamines and aminothiols to give diazepines and thiazepines. These reactions are summarized in Table VII. As can be seen, dehydration of the intermediate cyclic alcohol occurs preferentially with the ring nitrogen, but can occur with the α-ethylenic carbon when the nitrogen is substituted.

TABLE VII
FORMATION OF DIAZEPINES AND THIAZEPINES

Product



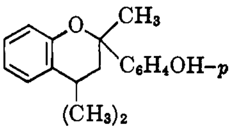
Reagent	X	R	Yield, %	Reference
$NH_2CH_2CH_2NH_2$	NH	H	56	(107)
$NH_2CH_2CH_2SH$	S	H	68	(106)
$NH_2CH_2CHSHCH_3$	S	CH_3	41	(107)
$C_6H_5NHCH_2CH_2SH$			..	(107)

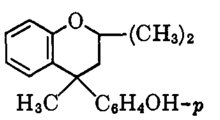


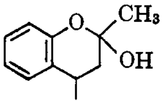
6. *Polycyclic Compounds*

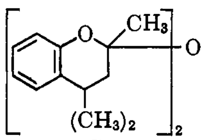
A considerable amount of work has been devoted to the reaction of mesityl oxide with different mole ratios of phenol. The acid-catalyzed condensation of mesityl oxide with two or four moles of phenol (39) was originally claimed to give 2-(*p*-hydroxyphenyl)-2,4,4-trimethylchromane (XCVII). However, it has recently been shown (12) that this Type 3a reaction proceeds counter-wise and the product is 4-(*p*-hydroxyphenyl)-2,2,4-trimethylchromane (XCVIII). The equimolar, acid-catalyzed reaction of mesityl oxide and phenol (or substituted phenols such as *m*- and *p*- nitrophenol, the cresols, trinitro-*m*-cresol, 6-chloro-*m*-cresol, carvacrol and thymol) is described (110) as giving mixtures of the chromanol XCIX and the dichromanyl ether C, but this mode of condensation must also be open to some question.

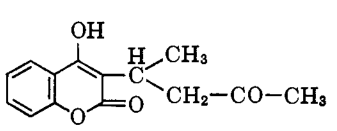
A similar condensation of mesityl oxide and 4-hydroxycoumarin (77) gives about 13% of 4-methyl-4-(3-(4-hydroxy-2-chromenone))-2-pentanone (CI) and 32% of 2-hydroxy-2,4,4-trimethyl-3H,5H-pyrano(3,2c)-(1)benzopyran (CII).

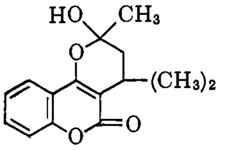

XCVII


XCVIII

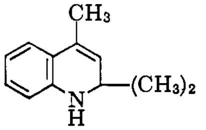

XCIX

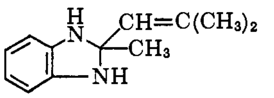

C


CI

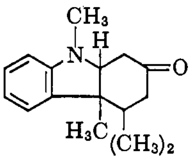

CII

The fusion of mesityl oxide and aniline using an iodine catalyst (91) and subsequent addition of acid yields 65% of 2,2,4-trimethyldihydroquinoline (CIII) by a Type 3a condensation. The acid-catalyzed reaction of mesityl oxide and *o*-phenylenediamine (44) was originally thought to give a 1,4-dihydroquinoxaline. This material has now been proved (122) to be 2-isobutenyl-2-methylbenzimidazoline (CIV), formed in a Type 1 reaction. This is confirmed by pyrolysis to the known 2-methylbenzimidazole. The over-all yield is 33%.

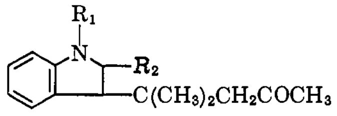

CIII


CIV

1,3-Dimethylindole also undergoes an acid-catalyzed fusion with mesityl oxide (130) to give 57% of the carbazole CV. This ring closure involves a Type 4 condensation.

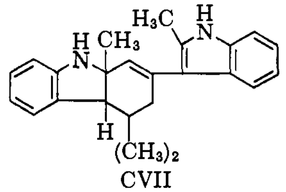

CV

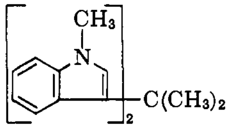
This work has been extended to other simple mono- and dimethylindoles and to indole itself (111, 112). By use of equimolar quantities of mesityl oxide and the indole or excess mesityl oxide, the 4-methyl-4-(3-indolyl)-2-pentanone intermediates (CVI) are isolated. Isolation of CVI demonstrates an initial 1,4-addition in the reaction. These reactions are listed below.


CVI

R_1	R_2	Yield, %
H	H	6
CH_3	H	28
H	CH_3	70
CH_3	CH_3	5

With a molar excess of four parts of 2-methylindole to three parts of mesityl oxide, a 67% yield of the indolylcarbazole CVII is isolated. With a two-to-one excess of 1-methylindole over mesityl oxide, 36% of 1,1′-dimethyl-3,3′-isopropylidene-bis-indole (CVIII) is the product.


CVII


CVIII

VII. REDUCTION, OXIDATION, AND PYROLYSIS

The literature contains a considerable body of material relating to these processes as applied to mesityl oxide. However, the discussion in this section will be limited to direct synthetic applications rather than a generalized survey of the area. The references cited have been chosen to give a combination of the best yields and procedures.

A. REDUCTION

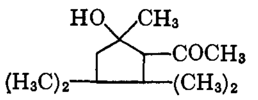
Both the double bond and the carbonyl group of mesityl oxide are readily reduced. By proper choice of reducing agent and/or catalyst, reduction to the saturated ketone, alcohol or hydrocarbon or reduction to the unsaturated alcohol may be accomplished. A few typical procedures are summarized in Table VIII.

TABLE VIII
REDUCTIONS OF MESITYL OXIDE

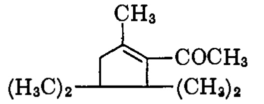
Product	Reducing agent	Catalyst	Yield, %	Reference
Me_2CHCH_2COMe	H_2	Ni	95–100	(36)
	H_2	Pd	94–97	(96)
$Me_2CHCH_2CHOHMe$	H_2	Copper chromite	100	(3)
	H_2	Raney Cu	95	(80)
$Me_2CHCH_2CH_2CH_3$	H_2	WS_2-$(NH_4)_2WS_4$	...	(98)
$Me_2C{=}CHCHOHMe$	H_2	Al(iso-Pr)$_3$	80	(79)
	$NaBH_4$	...	77	(26)

A number of reductive condensations of mesityl oxide leading to cyclic compounds has also been reported. The reduction of mesityl oxide with aluminum amalgam (151) or electrolytically (93) gives 1,3,3,4,4-pentamethyl-5-acetylcyclopentanol (CIX). A direct yield of 60–70% of the dehydrated cyclopentene CX is obtained using sodium amalgam or aluminum amalgam (63). The postulated intermediate of this reaction CXI has not been isolated.

A second cyclization to the tetrahydrofuran CXII or its dehydration product CXIII can occur using



CIX

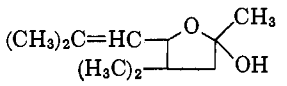


CX

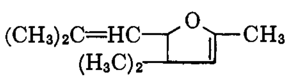
$(CH_3)_2C{=}CH{-}C(OH)(CH_3){-}C(COCH_3){=}C(CH_3)_2$

CXI

sodium amalgam (159), magnesium- or zinc-acetic acid (156), or electrolytic reduction (157). The intermediate CXIV has also been isolated using electrolytic techniques. The best reported yields are 55% for CXII and 35% for CXIII. By use of magnesium-acetic acid at −25 to −30° "good" yields of both CXII and CXIII are simultaneously obtained (92).



CXII



CXIII

$((CH_3)_2C{=}CH{-}C(CH_3)(OH){-})_2$

CXIV

B. OXIDATION

The oxidation of mesityl oxide may proceed in a variety of ways depending upon the oxidizing agent and reaction conditions. The action of dilute permanganate in acetone (66) or hydrogen peroxide-osmium tetroxide (104) gives low yields of the glycol CXV. The only other oxidation of mesityl oxide proceeding without cleavage of the molecule is that with cobalt acetate-cupric acetate-acetic acid (45) which yields the acid CXVI.

$(CH_3)_2COH{-}CHOH{-}CO{-}CH_3$

CXV

$CH_3C(COOH){=}CH{-}CO{-}CH_3$

CXVI

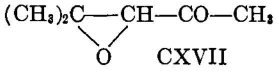
A number of oxidative cleavages are listed in Table IX.

TABLE IX

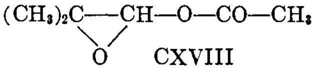
OXIDATIONS OF MESITYL OXIDE

Reagent	Products	Yield, %	Reference
Dil. HNO_3	$MeCOOH + (COOH)_2$	...	(29)
Dil. $KMnO_4$	$MeCOOH + Me_2COHCOOH$	...	(122)
2.5% $KMnO_4$	$Me_2CO + MeCOCOOH$	...	(143)
NaOCl	$CHCl_3 + Me_2C{=}CHCOOH$	75 (acid)	(14)
NaOBr	$CHBr_3 + Me_2C{=}CHCOOH$	44 (acid)	(94)
NaOI	$CHI_3 + Me_2C{=}CHCOOH$	75 (acid)	(37)

Epoxidation of mesityl oxide to give 3,4-epoxy-4-methyl-2-pentanone (CXVII) can be performed with *tert*-butyl peroxide-Triton B (163) (44% yield), N-bromosuccinimide (57) (56%) or hydrogen peroxide-sodium hydroxide-magnesium sulfate (162) (87%). When peroxyacetic acid (119) is used for epoxidation, only 20% of CXVII is obtained but this is accompanied by a 53% yield of the epoxy ester CXVIII.

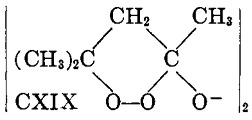


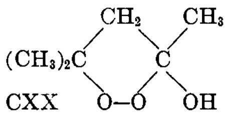
CXVII



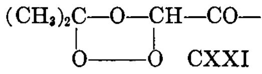
CXVIII

In the presence of sulfuric acid (129), mesityl oxide and hydrogen peroxide afford 46% of bis-(3,5,5-trimethyl-1,2-dioxolanyl)-3-peroxide (CXIX). The sodium hydroxide-catalyzed reaction of mesityl oxide and hydrogen peroxide at 0 to −5° gives 45% of CXVII, but also 34% of 3-hydroxy-3,5,5-trimethyl-1,2-dioxolane (CXX). The dioxolane CXX on treatment with excess peroxide gives CXIX.





Treatment of mesityl oxide with ozone (62) gives an almost quantitative yield of the explosive, unstable ozonide CXXI. However, when the reaction is run as a heterogeneous system with water (60), the ozonide decomposes, *in situ*, into acetone and pyruvaldehyde (CXXII).



CXXI

$CH_3{-}CO{-}CHO$

CXXII

C. PYROLYSIS

The direct pyrolysis of mesityl oxide on activated alumina (100) or phosphoric acid-silica (103) gives acetic acid and isobutylene as major products. The reaction is, however, not clean-cut and a number of other materials are obtained.

In addition to this homo-pyrolysis, a number of mixed pyrolyses have been described and are briefly summarized in Table X.

TABLE X

PYROLYSES OF MESITYL OXIDE

Reagent	Catalyst	Products	Yield, %	Reference
$CO{-}H_2O$	H_3PO_4	$MeCOOH + Me_3CCOOH$	..	(59)
Benzene	$ZnCl_2{-}Al_2O_3$	$C_6H_5CMe_3$	26	(136)
iso-PrOH	$ZnO{-}Al_2O_3$	Methylpentadienes	62	(13)
iso-PrOH	$CrO_3{-}Al_2O_3$	Methylpentadienes	75	(113)

VIII. REFERENCES

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