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The Synthesis of Phenanthrenes

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I. Introduction

Since the discovery of phenanthrene in coal tar and the elucidation of its structure,[2] many synthetic schemes have been investigated for the preparation of it and its derivatives. Stimulation for these studies has been provided by the fact that many naturally occurring compounds of biological and therapeutic interest contain a phenanthrene or reduced phenanthrene nucleus (e.g., steroids, resin acids, morphine, and aporphine alkaloids). A considerable number of synthetic routes is now available; Clar[3] has included a short review of the synthesis of phenanthrene in his treatise, while some of the earlier routes to the ring system are given by Fieser.[4] In addition, some of the individual methods have been separately reviewed[5,6] or have been included with other material in reviews.[7–10] A recent Japanese paper[11] includes a survey of the preparation of monosubstituted phenanthrenes.

The main aim of this review is to survey all the important methods by which the fully aromatic phenanthrene ring system may be synthesized. Where a specific method has already been reviewed in a readily accessible journal, our intention is simply to update the review with references from the more recent literature. To this effect, we have covered the literature to December 1974. It is, of course, necessary to include the formation of many reduced phenanthrene systems, which can usually be readily dehydrogenated to phenanthrenes. Syntheses, which would require the breaking of carbon–carbon bonds during this aromatization step, are usually omitted, unless they provide the only examples of an interesting method, anticipated to be of more general application. In this way the size of the review was limited, mainly by omitting reference to the synthesis of steroids, and of di- and triterpenoids, which have been subject to earlier review.[12,13]

The reaction sequences used in the synthesis of phenanthrenes are often lengthy, so we have concentrated our attention on the stage at which the phenanthrene or reduced phenanthrene ring system is completed. This stage has been broadly classified into three types: carbocyclic ring expansion, intramolecular cyclization, and intermolecular cycloaddition. These main groups have been subdivided according to the ring system or the ring assembly utilized, and the reaction type (e.g., cycloalkylation, cycloacylation, etc.) of this stage.

II. Carbocyclic Ring Expansion Reactions

A. Wagner–Meerwein and Related Rearrangements of Fluorenyl Derivatives

Under suitable conditions, fluorenyl methane derivatives **1** give rise to carbonium ions **2**, which lead to **3** by Wagner–

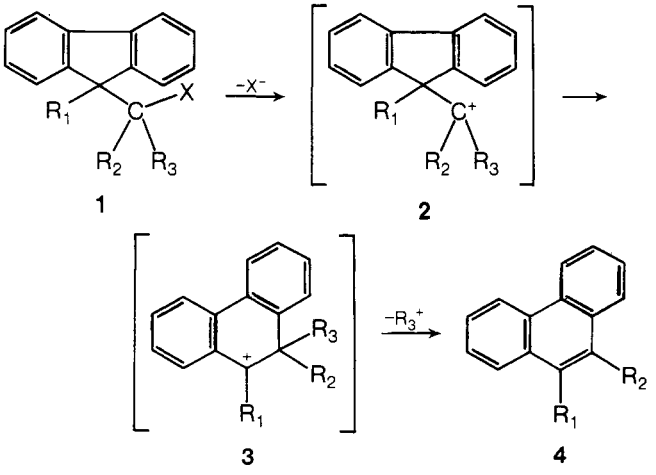
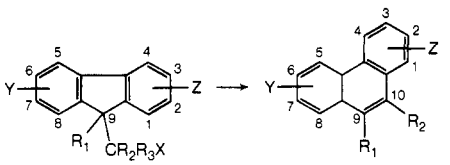


TABLE I. Phenanthrenes from Fluorene Derivatives

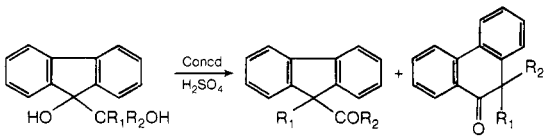


X	R_1	R_2	R_3	Y	Z	Reaction conditions	% yield	Ref
OH	H	H	H	H	H	P_2O_5	90–100	14
OH	H	H	H	H	1-Me	P_2O_5	100	19
OH	H	H	H	H	3-Me	P_2O_5	88	20
OH	H	H	H	H	3-OMe	P_2O_5	93	20
OH	H	H	H	H	2-F	PPA	64	21
OH	H	H	H	H	4-Br	P_2O_5	47	22
OH	H	H	H	H	2-NO_2	PPA	45	17
OH	H	H	H	7-Me	2-Me	P_2O_5	75	359
OH	H	H	H	7-Br	2-Br	P_2O_5	10	16
OH	H	Me	H	H	H	P_2O_5	20[a]	25
OH	Me	H	H	H	H	PPA	65	25, 26
						$SOCl_2$/AgOAc/AcOH	61	*d*
						Al_2O_3/350°	75	25
OH	Me	Me	H	H	H	P_2O_5	90	25
						Al_2O_3/350°	75	25
OH	Me	Me	Me	H	H	PPA	30–50	*e*
OH	Me	Ph	H	H	H	P_2O_5	100	*f*
OH	Et	H	H	H	H	PPA	66	26
OH	Et	Me	H	H	H	Al_2O_3/350°	65	25
OH	Et	Et	Et	H	H	PPA	30–50	*e*
OH	*t*-Bu	H	H	H	H	PPA	Low[b]	26
OH	$CH_2CH{=}CH_2$	Ph	H	H	H	P_2O_5	82[c]	*g*
OH	$PhCH_2$	H	H	H	H	PBr_3/100°	75	*h*
OH	Ph	Ph	H	H	H	I_2/AcOH	100	*i*
OH	9-Fluorenyl	H	H	H	H	P_2O_5	65	*j*
OH	2-Naphthylmethyl	H	H	H	H	P_2O_5	80	*k*
OH	9-Phenanthrylmethyl	H	H	H	H	P_2O_5	75	*k*
OAc	H	H	H	H	2-NO_2	PPA	89	18
$OCOCF_3$	CO_2Me	H	H	H	H	HCO_2H	82	*l*
$OCOCF_3$	CO_2Me	CO_2Me	H	H	H	HCO_2H	62	*l*
OTs	Me	H	H	H	H	HCO_2H	99	26, *m*
OTs	Me	Me	H	H	H	HCO_2H	99	*m*
OTs	Me	Me	H	H	2-NO_2	HCO_2H	74	17
OTs	Et	H	H	H	H	HCO_2H	99	26, *m*
OTs	*i*-Pr	H	H	H	H	HCO_2H	99	26, *m*
OTs	*t*-Bu	H	H	H	H	HCO_2H	99	26, *m*
OTs	$PhCH_2$	H	H	H	H	HCO_2H	99	26, *m*
Cl	Me	Ph	H	H	H	HCO_2H	100	*f*
Cl	Et	H	H	H	H	KOH/MeOH/150°	60	24
Cl	Et	Me	H	H	H	KOH/MeOH/150°	70	24
Cl	OH	Cl	H	H	H	*n*-BuLi/piperidine	44	*n*
Br	Me	H	H	H	H	$AgClO_4$/AcOH	77	*l*
						Quinoline	70	*l*
Br	Ph	H	H	H	H	$AgClO_4$/AcOH	66	*l*
						Quinoline	74	*l*
Br	$CONMe_2$	H	H	H	H	CF_3CO_2Ag/HCO_2H	53	*l*
Br	OH	Me	H	H	H	R MgX/C_6H_6	62	27
Br	Br	*p*-$MeOC_6H_4$	H	H	H	KOAc/AcOH	90	*o*
NH_2	H	H	H	6, 7-$(OMe)_2$	2,3-$(OMe)_2$	HNO_2		23

[a] Plus 9-ethylidenefluorene. [b] Plus 9-methylenefluorene and phenanthrene. [c] Plus 9-phenyl-10-prop-1-enylphenanthrene. [d] P. M. G. Bavin, *Can. J. Chem.*, **38**, 1099 (1960). [e] F. A. L. Anet and P. M. G. Bavin, *ibid.*, **36**, 763 (1958). [f] P. M. G. Bavin, *ibid.*, **37**, 2023 (1959). [g] A. H. A. Tinnemans and W. H. Laarhoven, *J. Am. Chem. Soc.*, **96**, 4617 (1974). [h] G. Wittig, P. Davis, and G. Koenig, *Chem. Ber.*, **84**, 627 (1951). [i] W. E. Bachmann, *J. Am. Chem. Soc.*, **55**, 3857 (1933). [j] S. Wawzonek and E. J. Dufek, *ibid.*, **78**, 3530 (1956). [k] M. Matzner, S. Glazer-Tarasiejska, and R. H. Martin, *Bull. Soc. Chim. Belg.*, **69**, 551 (1960). [l] P. M. G. Bavin, *Can. J. Chem.*, **42**, 1409 (1964). [m] F. A. L. Anet and P. M. G. Bavin, *ibid.*, **43**, 2465 (1965). [n] G. Koebrich and J. Grosser, *Tetrahedron Lett.*, 4117 (1972). [o] Z. Rappoport and A. Gal, *J. Org. Chem.*, **37**, 1174 (1972).

Meerwein shift; at this stage, elimination gives 9- and 9,10-substituted phenanthrenes **4** in good yield.[8,14] Many of the substituted fluorenes **1** required for this rearrangement can readily be prepared (e.g., from fluorenyl-9-carbocyclic acids by alkylation and reduction), so the method is of wide potential application to phenanthrene synthesis. The conversion of a fluorene to a phenanthrene was first reported in 1904,[15] but not until the work of Brown and Bluestein[14,16] were the synthetic possibilities examined. A variety of leaving groups (X) have been utilized (see Table I), although the majority of reactions have involved fluorenylcarbinols **1** (X = OH), using dehydrating agents such as phosphorus pentoxide or polyphosphoric acid (PPA). Formolysis

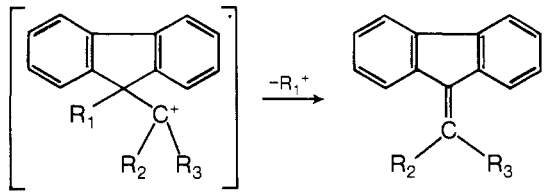
TABLE II. Rearrangement[29] of Some 9-Fluorenols



R_1	R_2	% fluorene	% phenanthrone
Ph	Ph	5	75
Me	Ph	60	Trace
Me	Me	65	Nil

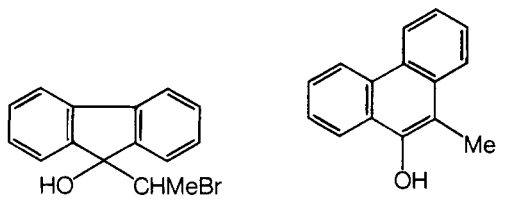
of either tosyl esters **1** (X = $OSO_2C_6H_4$-*p*-Me) or trifluoroacetate esters **1** (X = $OCOCF_3$), diazotization of 9-aminomethylfluorenes **1** (X = NH_2), and treatment of 9-halomethylfluorenes **1** (X = Cl or Br), with various acidic or basic reagents have also been successful. Further variations can be introduced by using fluorenes substituted in one or both of the aromatic rings.[8] Thus 2-nitro-,[17,18] 1-methyl-,[19] 3-methyl-,[20] 3-methoxy-,[20] 2-fluoro-,[21] 4-bromo-,[22] 2,7-dibromo-,[16] 9,10-dimethyl-2-nitro-,[17] and 2,3,6,7-tetramethoxyphenanthrene[23] have been prepared.

The nature of the groups R_1, R_2, and R_3 in **1** influence the outcome of the rearrangement. If R_1 = H, then a proton may be lost from **2** before rearrangement, resulting in the formation of

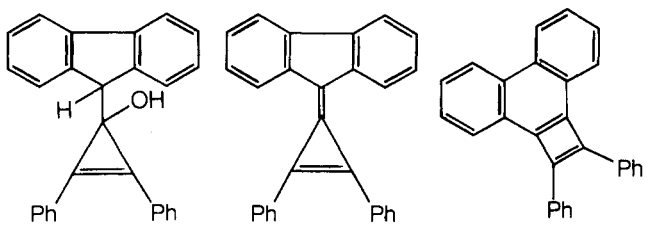


2 **5**

a derivative of 9-methylenefluorene **5** in place of,[24] or as well as,[25] phenanthrenes. Indeed, the stable *tert*-butyl carbonium ion can be expelled[26] from **2** (R_1 = *t*-Bu, R_2 = R_3 = H) yielding **5** (R_2 = R_3 = H). Compounds of type **5** have themselves been converted to phenanthrenes;[27] thus **5** (R_2 = Me, R_3 = H) treated with *N*-bromosuccinimide gives **6**, which yields 10-methyl-9-phenanthrol (**7**) on reaction with a Grignard reagent. An exceptional case was observed[28] with **8**, which on dehydration with phosphoryl chloride in pyridine gave no **9**, presumably due to steric effects. Instead, the phenanthrene derivative **10** was obtained

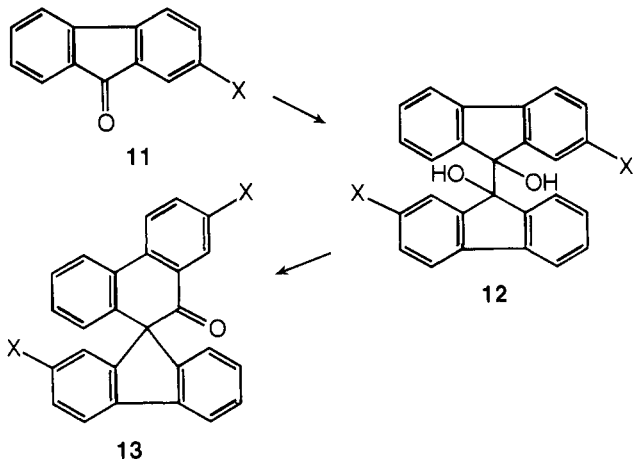


6 **7**



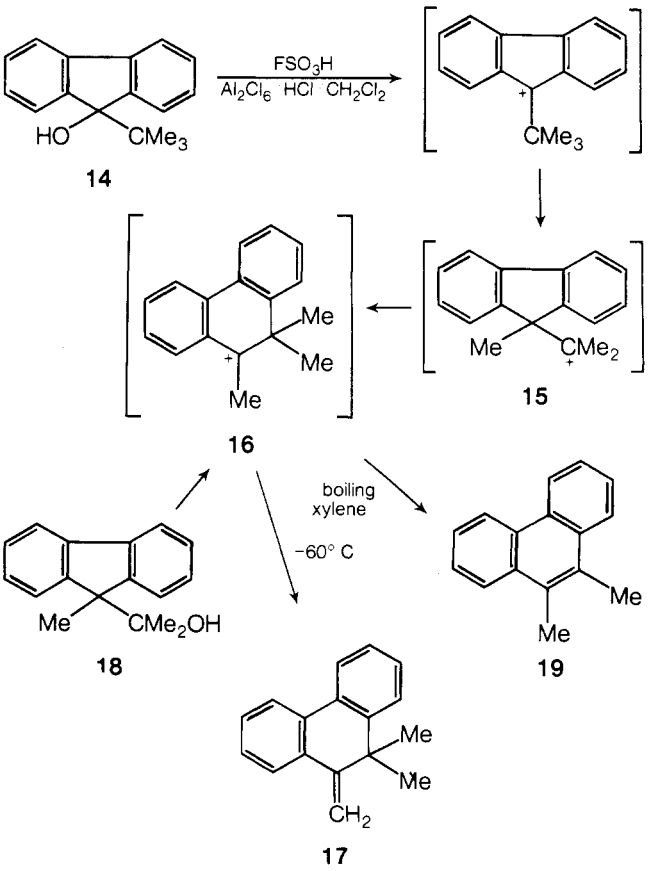
8 **9** **10**

in 72% yield. When R_1 = OH, then the course of the pinacol–pinacolone rearrangement of **1** depends upon the identity of R_2 and R_3 (see Table II),[29] since an alternative carbonium ion may now be generated at the 9 position of the fluorene ring. The formation of **13** (X = H) by the zinc dust fusion[30] of fluorenone **11** (X = H) similarly involves a pinacol–pinacolone rearrangement of the intermediate **12** (X = H). The reduction of **11** (X = Br) using zinc–amalgam and hydrochloric acid leads to the isolation of **12** (X = Br), which can be converted[31] in low yield to **13** (X = Br) by heating with sulfuric acid in acetic acid solution.



11 **12** **13**

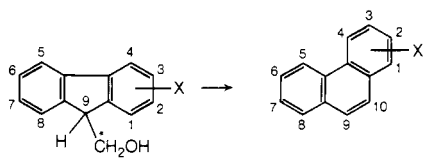
The intermediate carbonium **2** has been generated by a number of alternative routes. Thus **2** is presumably intermediate in the formation of 9-methyl-, 9-ethyl-, and 9-ethyl-10-methylphenanthrene, by the treatment of 9-vinyl-, 9-allyl-, and 9-allyl-9-methylfluorene, respectively, with phosphorus pentoxide.[24] Dehydration of 9-*tert*-butylfluorenol (**14**) using strong acids at −60 °C proceeds[32] with rearrangement, via carbonium ions **15** and **16** giving **17**. Treatment of **18** with formic acid[33] at 40 °C



14 **15** **16** **18** **19** **17**

likewise gives a 10% yield of **17**; however, under more drastic conditions (PPA in boiling xylene) a methyl group is eliminated to yield **19**. Good yields of **21** may be obtained by either the dehydration[25] of **20** (X = OH) or by the elimination[24] of hydrogen chloride from **20** (X = Cl). However, **24** results in poor yield,

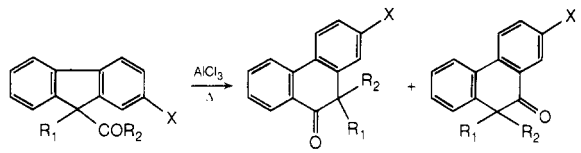
TABLE III. Migratory Aptitudes in 9-Hydroxymethylfluorenes



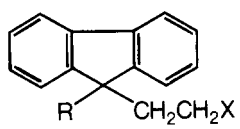
*14C label

X	% 14C at C-9	% 14C at C-10	Ref
1-Methyl	50	50	19
3-Methyl	27	73	20
3-Methoxy	2	98	20

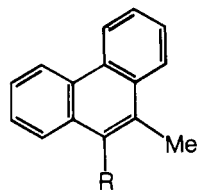
TABLE IV. Rearrangements of 9-Acylfluorenes



R_1	R_2	X	Combined % yield of phenanthrones	Ref
Me	Me	H	36	37
Me	Me	NO_2	Nil	37
Me	Et	H	57	37
Me	Et	Me	60	37
Me	Et	NO_2	Nil	37
Me	Ph	H	Low	38
Et	Et	H	63	37
Et	Et	Me	66	37
Et	Ph	H	45	38
i-Pr	Ph	H	Nil	38
Ph	Me	H	85	38
Ph	Et	H	10	38
Ph	*i*-Pr	H	Nil	38
Ph	Ph	H	85	38

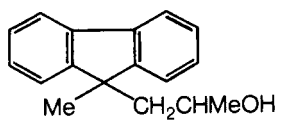


20

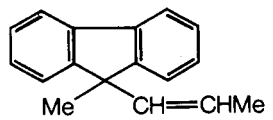


21

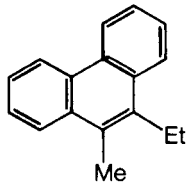
when either **22** or the derived **23** is treated[33] with phosphorus tribromide or hydrogen bromide, respectively. Attempts to obtain chlorofluorocarbene insertion reactions with fluorene, by treatment with dichlorofluoromethane and tetraethylammonium bromide in the presence of ethylene oxide,[34] resulted mainly in



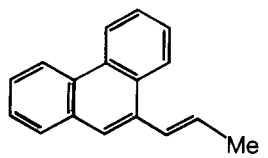
22



23

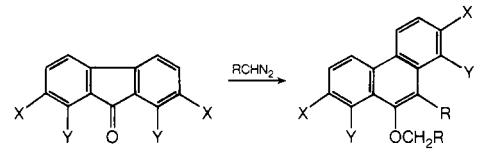


24



25

TABLE V. Ring Expansion of Fluorenones



X	Y	R	% yield	Ref
H	H	H	30–90	43, 44, *b*
H	H	Me	66	44
H	Cl	H	Nil[a]	44
H	Cl	H	25	44
Cl	H	H	41	*b*
Br	H	H	34–75	44, *b*
Br	H	Me	85	44
$Et_2NCH_2CH_2O$–	H	H		*c*

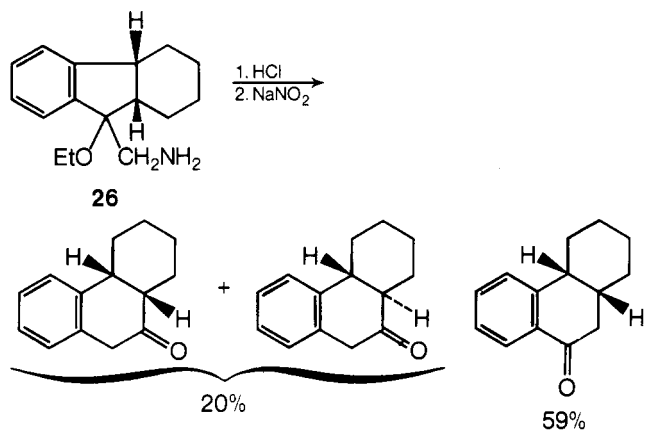
[a] 50% 1,8-dichlorospiro[fluorene-9,2'-oxirane] isolated. [b] L. C. Washburn and D. E. Pearson, *J. Med. Chem.*, 17, 676 (1974). [c] D. R. Meyer, A. D. Sill, and P. L. Tiernan, Germany Offen. 2,362,577; *Chem. Abstr.*, 82, 4064 (1975).

reaction with the ethylene oxide. The major product, 9-ethylidenefluorene (**5**, R_2 = Me; R_3 = H) was accompanied by 5% of the rearranged product **25**.

The mechanism of the rearrangement and the migratory aptitude of the benzo and substituted benzo groups of fluorenes have been investigated[19,20,35,36] (see Table III). The electronic effects of the 3-methyl and 3-methoxy groups, especially the latter, predictably favor the migration of the substituted benzo group. The 1-methyl group has no effect, possibly because of the steric and electronic effects of the methyl cancelling each other in this position.[19]

9-Acylfluorenes rearrange[37,38] to a mixture of the corresponding phenanthrenes, when heated with aluminum trichloride (see Table IV).

The 1,2,3,4-tetrahydrofluorene **26** may also undergo rearrangement on diazotization, with the formation of reduced phenanthrone products.[39] Interestingly alkyl migration predominates, a somewhat unexpected result, which was explained on steric grounds.[39]



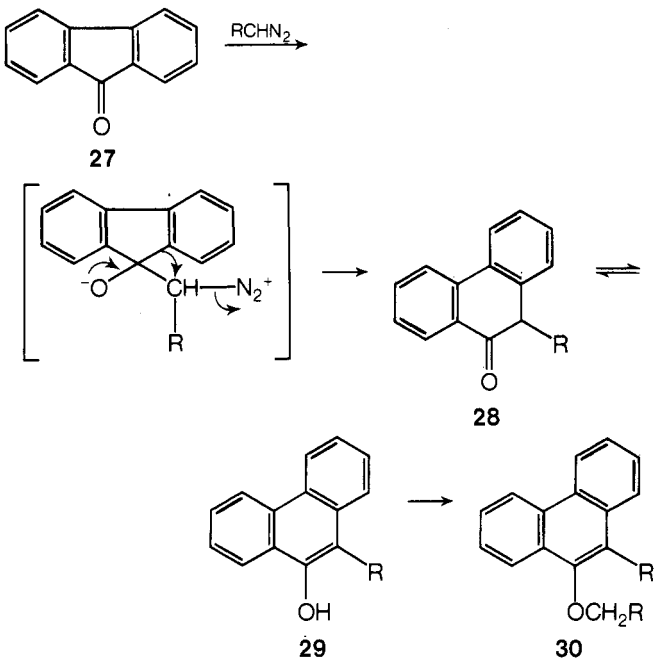
26

20%

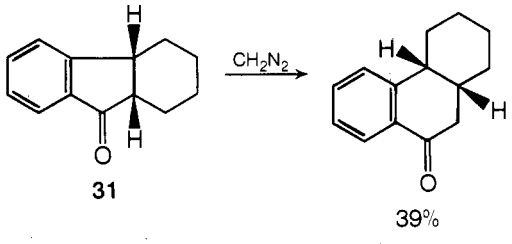
59%

B. Ring Expansion of Fluorenones with Diazoalkanes

The well-known[40–42] ring expansion of cyclic ketones using diazoalkanes may be applied[43,44] to fluorenone **27**. The expected product **28** can tautomerize to **29**, which is then alkylated by an excess of diazoalkane to yield **30**. The reaction has also been applied successfully with a number of other examples (see Table V), while 2,3,4,7-tetramethoxyfluorenone yields either 2,3,4,7,9- or 2,3,4,7,10-pentamethoxyphenanthrene on treatment with diazomethane.[45] It is important[44] to use pure distilled diazoalkane



in ether solution for good yields. The ring expansion method has also been used[43] with the hexahydrofluorenone **31**. Once again, the product resulted from alkyl migration with retention of configuration (see **26** above).



Since fluorenones are quite readily accessible compounds, this particular ring expansion merits more attention.

C. Radical-Induced Rearrangements of Fluorenyl Derivatives

The rearrangement of 9-fluorenylacetaldehydes **32** to yield phenanthrenes has been reported.[46,47] The reactions are similar to the ionic rearrangements discussed in section II.A, but involve radical intermediates. Radical **33** undergoes disproportionation and competitive hydrogen radical abstraction leading to a mixture of **34** and **35**, with the latter predominating.

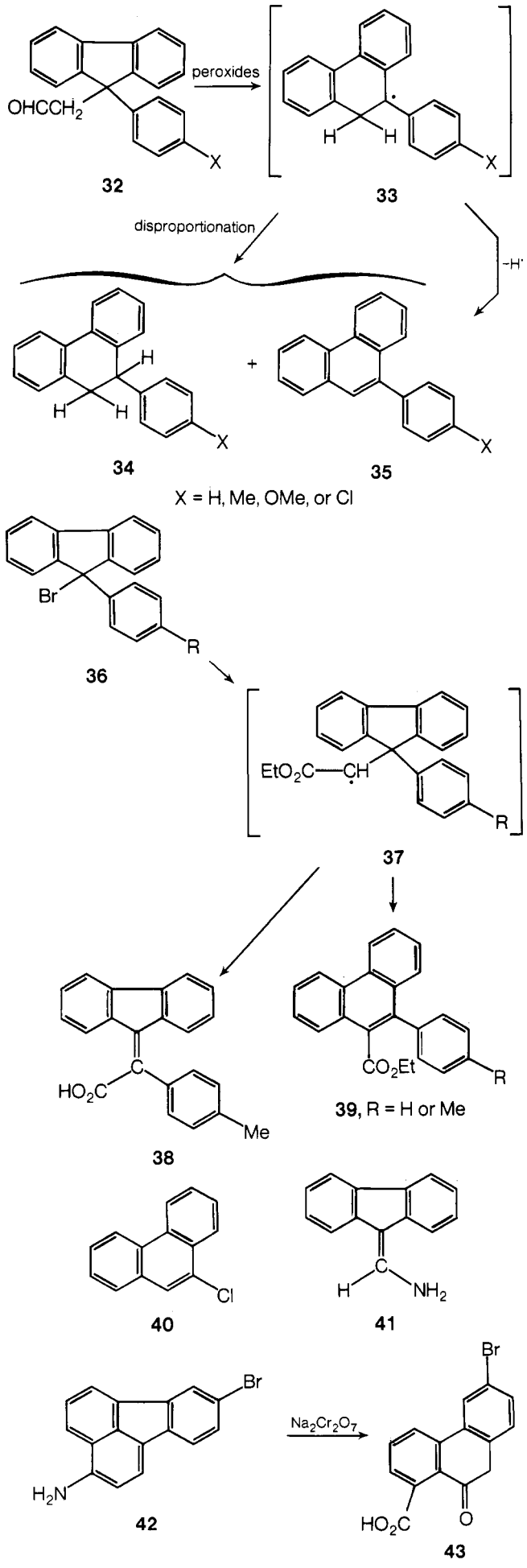
The formation of phenanthrene derivatives **39**, when 9-bromo-9-arylfluorenes **36** are treated with ethyl diazoacetate and copper sulfate in cyclohexane,[48] probably involves radical intermediates. The formation of **38** (in 22% yield) arises[48] presumably by migration of the 9-aryl group in the intermediate radical **37** (R = Me).

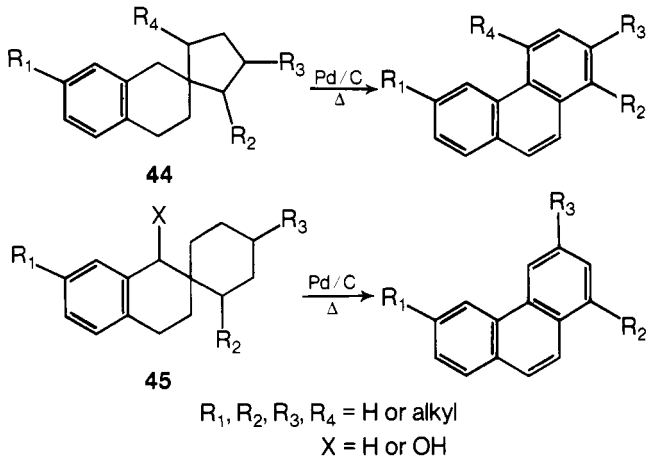
D. Miscellaneous Rearrangements of Fluorene Derivatives

9-Chlorophenanthrene (**40**) is reported[49] as a minor product of the reaction of nitrosyl chloride with **41**. 3-Bromo-9-phenanthrone-8-carboxylic acid (**43**), formed[50] by the oxidation of **42** with sodium dichromate, presumably involves rearrangement of a fluorene intermediate, formed by an oxidative opening of the amino-substituted ring.

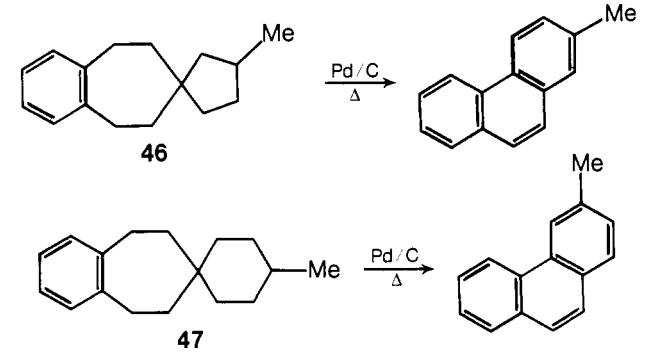
E. Rearrangement of Spiro Compounds

Both rearrangement and ring enlargement of spiro compounds yielding phenanthrenes are known. Thus various spiro-tetralins

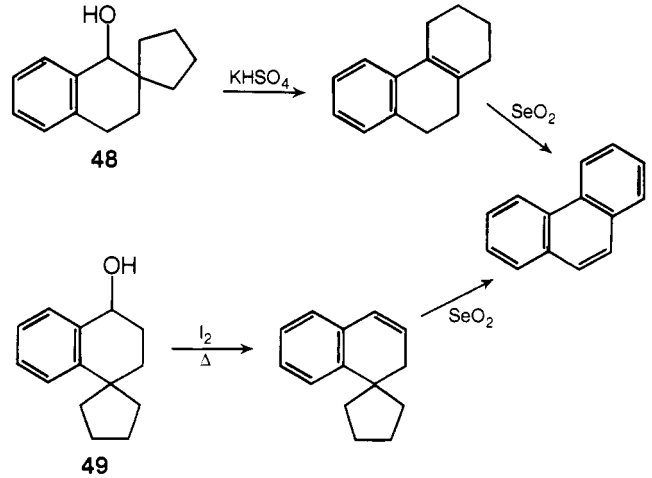




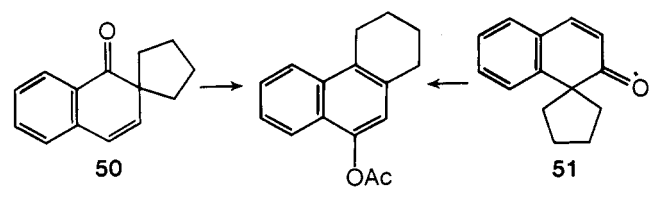
44 and **45** give rise to phenanthrenes on catalytic dehydrogenation[51,52] at 320–350 °C. Similarly, the benzospiro[6.4]undecane **46** and benzospiro[6.5]dodecane **47** give small yields of 2-methyl- and 3-methylphenanthrene, respectively, on catalytic dehydrogenation[53,54] at 380–400 °C. The spiro-tetralins



48 and **49** have been converted[55] to phenanthrene by dehydration followed by dehydrogenation with selenium dioxide. The



eneones **50** and **51** both yield 1,2,3,4-tetrahydro-9-phenanthryl acetate in good yield, when treated with sulfuric acid in acetic anhydride.[56]



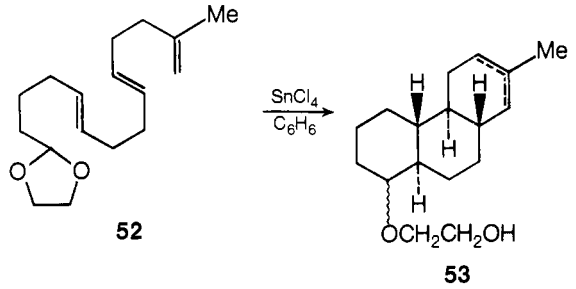
Although many of these spiro compounds are readily prepared, the use of these methods as a general procedure for phenanthrene synthesis is limited by uncertainty regarding the orientation of substituents in the products.

III. Intramolecular Cyclization Reactions

The majority of phenanthrene syntheses involve intramolecular cyclizations of variously substituted aromatic and hydroaromatic compounds. These reactions have been classified into four main groups, according to the nature of the parent aromatic system (or its reduced equivalent): benzenoid, naphthalenoid, stilbenoid, and biphenyloid. Additionally a small section on the cyclization of tetradecane derivatives is included. These main groups are then further subdivided according to the reaction type of the cyclization stage (e.g., cycloalkylation, cycloacylation, condensation, etc.).

A. Cyclization of Tetradecane Derivatives

The triple cyclization of tetradecane derivatives to yield perhydrophenanthrenes has in general been aimed at the production of diterpenoids, with angular alkyl and *gem*-dialkyl substituents. However, *trans,trans*-13-methyl-5,9,13-tetradecatrienal, as its cyclic acetal **52**, has been cyclized[57] to a dodecahydrophenanthrene **53** in 89% yield. The position of the double bond was uncertain. It seems unlikely that this method will find wide application to the synthesis of phenanthrenes.



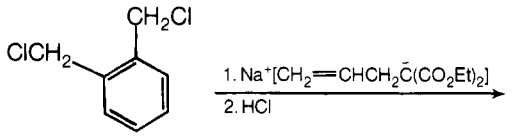
B. Cyclization of Benzenoid Compounds

The reactions in this group are of little general importance, although they have been used to synthesize specific alkyl- and polyalkylphenanthrenes. All of these methods necessarily involve a double cyclization. When the intermediates formed by a single cyclization have been isolated, then their further cyclization is discussed under the group (naphthalenoid, stilbenoid, or biphenyloid) appropriate to that intermediate. Similar procedures separated in this manner are cross-referenced.

1. Intramolecular Cycloalkylation

The ortho-disubstituted benzene **55**, readily prepared from **54**, undergoes[58] double cyclization on treatment with aluminum trichloride, yielding **56**. A similar procedure[58b] using the meta-disubstituted benzene **57** (R = H) gave only the octahydroanthracene **58** (R = H), although **57** (R = Me) gave a mixture of **58** (R = Me) and **59**. The octahydrophenanthrenes **56** and **59** were converted by standard procedures[58] into 1,3,6,8-tetramethyl- and 1,3,5,7,10-pentamethylphenanthrene, respectively. Since the ortho-disubstituted starting materials are readily available and the cyclization occurs in good yield (ca. 70%), this is a promising, though little exploited, route to phenanthrene derivatives.

The direct Friedel–Crafts alkylation of benzene derivatives with excess reagent may lead to octahydrophenanthrenes. Thus benzene alkylated[59] with excess of 2,5-dichlorohexane in the presence of aluminum trichloride gives a 4:1 mixture of **60** and **61**, while *o*-cresol yields[60] **62** along with several isomeric tetralins. Similarly **63** (R = Me) is formed in 39% yield among other



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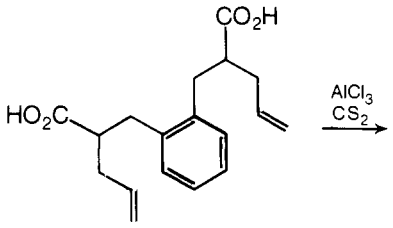

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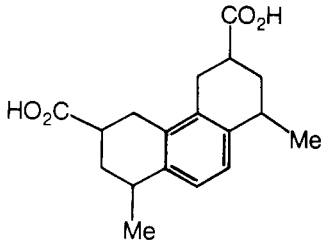
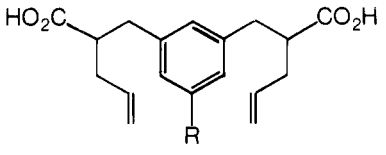


56



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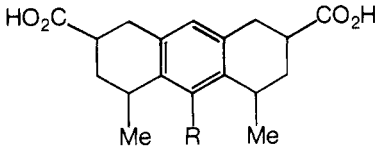

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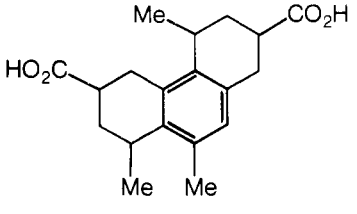

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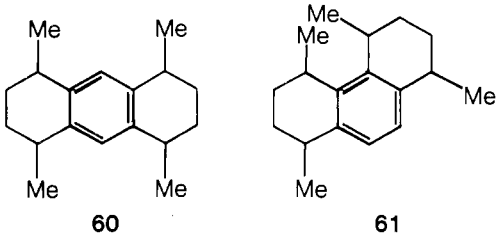
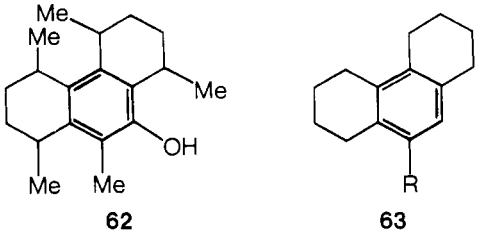


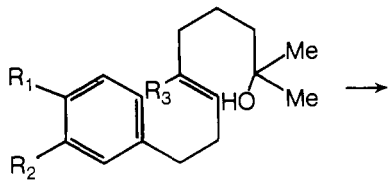
60 61



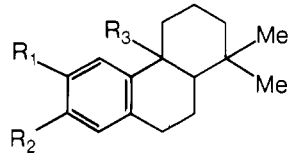
62 63

products when toluene is alkylated[61] using 1,4-dichlorobutane. Among the products from the alkylation[62] of benzene and toluene with tetrahydrofuran and aluminum trichloride were **63** (R = H) and **63** (R = Me), respectively. Similar procedures have been applied to naphthalenoid precursors (see section III.C.1). The value of this method is limited by the need to separate product mixtures.

Suitable monosubstituted benzenes may undergo double cyclization to give octahydrophenanthrenes. For example, the alcohols **64** have been cyclized[63] in about 25% yield, using either PPA or cold concentrated sulfuric acid. The starting materials are readily available.[63,64] Numerous similar cyclizations



64

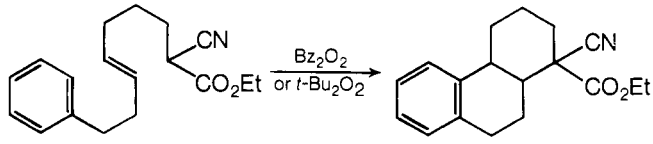


65

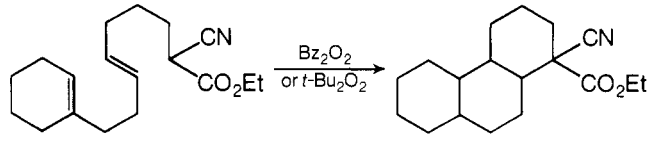
R_1 = H	R_2 = H	R_3 = H
i-Pr	Me	H
H	Me	OMe

have been investigated, but the products, as in the case of **65**, have always included angular or *gem*-dialkyl substituents.

Radical-induced cycloalkylations have been reported; thus **66** and **68** are converted into phenanthrene derivatives **67** and **69**, respectively, on treatment[65-67] with peroxides. The products **67** and **69** yield the corresponding 1-carboxy derivatives by hydrolysis and decarboxylation.



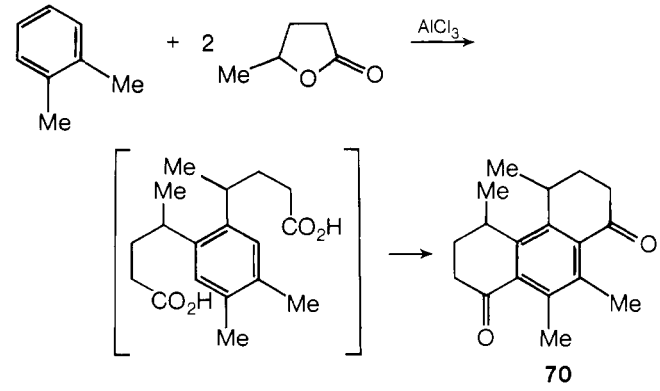
66 67



68 69

2. *Intramolecular Cycloacylation*

The Friedel–Crafts cycloacylation of suitable benzene derivatives may also result in the formation of hydrophenanthrenes. Thus the treatment of *o*-xylene with γ-valerolactone and alu-

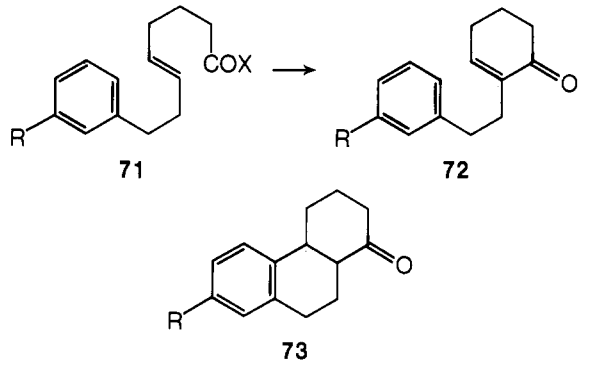


70

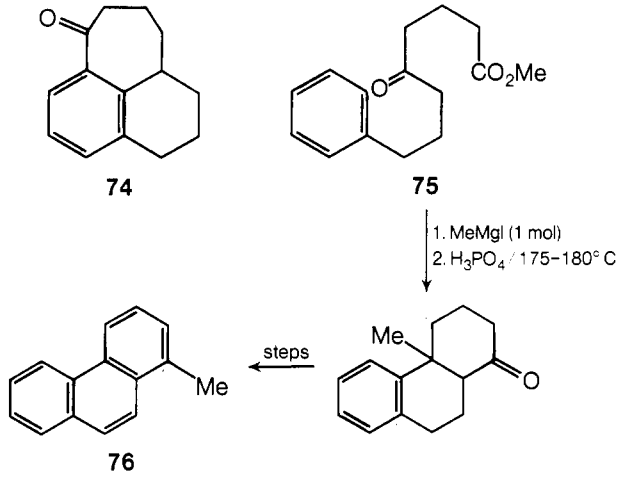
minum trichloride results[68] in dialkylation followed by a double cycloacylation, giving a 15% yield of **70**. 4,5,9,10-Tetramethylphenanthrene may be prepared[68] from **70**, although in poor yield due to steric overcrowding.

3. *Intramolecular Cycloalkylation and Cycloacylation*

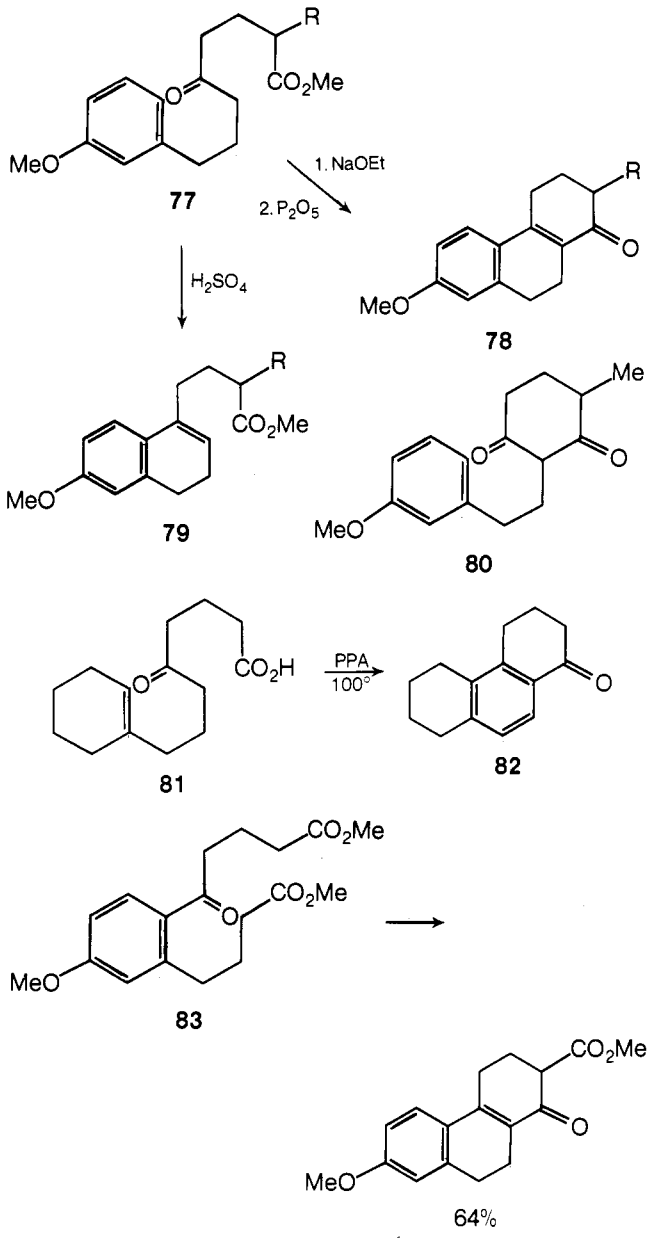
Frequently, in the double cyclization of benzene derivatives, one cyclization may be regarded as an acylation, while the other is an alkylation. The cyclization[69,70] of suitably constituted alkenoic acids or their derived acid chlorides, e.g., **71** (X = OH or Cl), provides such an example. However, since the intermediates **72** have frequently been isolated, this process is discussed as



a cyclization of stilbenoid systems (see section III.D). Aldehyde **71** (R = X = H) has been cyclized[65] by a radical-induced process using peroxides; the product **73** is believed to have a trans ring junction. Interestingly cyclization of acid **71** (R = H, X = OH) using PPA[69] gave only **74**. However, in the conversion of methyl 8-phenyl-5-oxo-octanoate (**75**) to 1-methylphenanthrene (**76**), the desired cyclization was effected[71] in low yield (10%) using phosphoric acid.

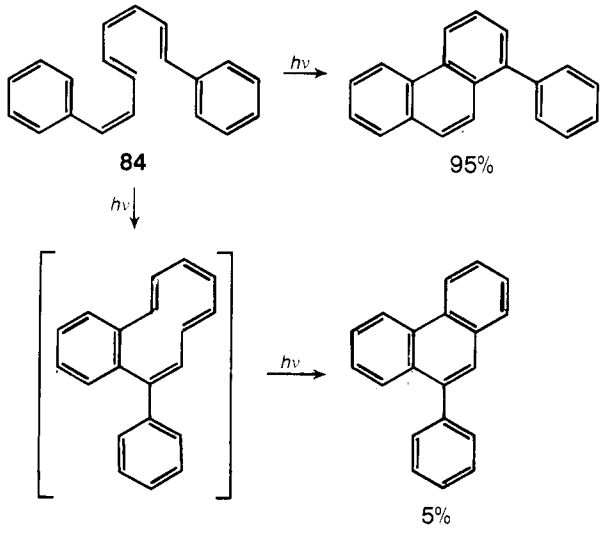


8-Aryl-5-oxooctanoates (**77**) may undergo direct double cyclization to phenanthrene derivatives **78**. Treatment[72] of **77** (R = H or R = Me) with cold concentrated sulfuric acid leads to the isolation of the corresponding intermediate dihydronaphthalene **79** (R = H or R = Me), the cyclization of which is discussed in section III.C.2. However, **77** (R = Me) was converted[72a] to **78**, by treatment with sodium ethoxide, followed by phosphorus pentoxide, without isolation of the intermediate **80**. The cyclization of compounds such as **80** is an example of the Robinson and Schlittler method[73] discussed in section III.D.2. The cyclization of a related hydrobenzenoid system has been observed; thus **81** yields[74] **82** on treatment with PPA. The cyclization[72b] of **83**, although involving condensation reactions is included here for convenience.



4. *Photocyclization*

Few examples of this reaction type are known. However, ultraviolet irradiation[75] converts **84** into 1-phenylphenanthrene, together with a small amount of 9-phenylphenanthrene.



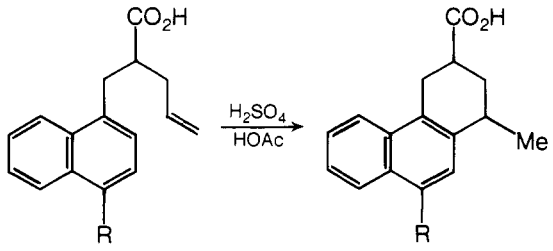
C. Cyclization of Naphthalenoid Compounds

Suitable naphthylalkenes, -alkanols, -alkanals, -alkanones,

-alkanoic acids, and -alkenoic acids have all been cyclized to tetrahydrophenanthrenes, which may be dehydrogenated to phenanthrenes. Naphthalene derivatives are in fact among the most important intermediates in the synthesis of phenanthrenes.

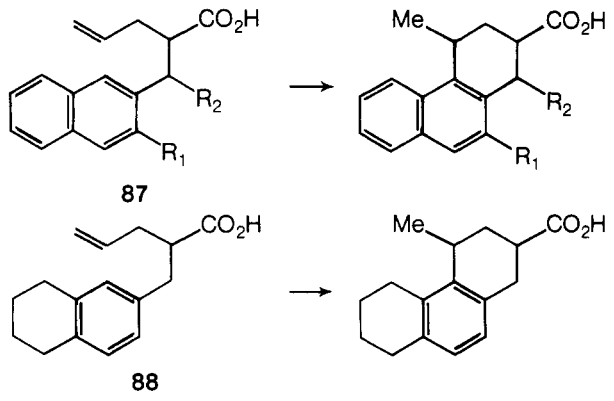
1. Intramolecular Cycloalkylation

Both 1- and 2-naphthylalkenes have been cyclized using acidic reagents. Thus, **85** (R = H or Me) on treatment[76,77] with sulfuric



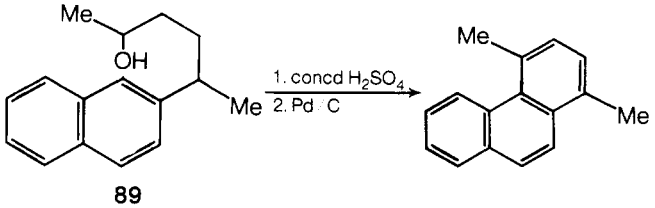
85 **86**

acid gave **86**, and the 2-naphthyl derivatives **87** and **88** have been similarly cyclized.[58b,78] Since the starting materials **85**, **87**, and **88** are readily prepared,[58b,76-78] this method constitutes a useful route to various alkyl- and carboxy-substituted phenanthrenes.



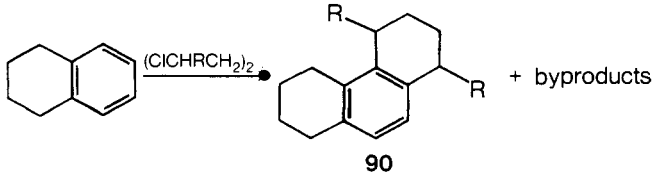
87 **88**

A number of 1- and 2-naphthylalkanols have likewise been cyclized by acid treatment. The majority of these have been concerned with terpene synthesis (see Table VI). A simple example involves the 2-naphthylalkanol **89**, which is cyclized[79] using sulfuric acid. Once again this presents a potentially useful method for the synthesis of alkylphenanthrenes.



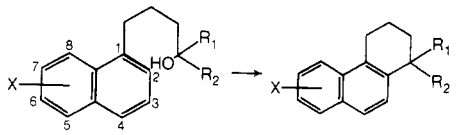
89

The Friedel–Crafts cycloalkylation of tetralin and naphthalene derivatives may lead to phenanthrenes. Thus tetralin treated with



90

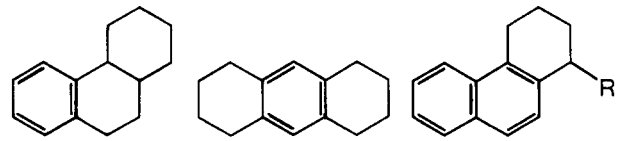
TABLE VI. Cyclization of 1-Naphthylalkanols



R_1	R_2	X	Reaction conditions	% yield	Ref
Me	Me	H	85% H_2SO_4		*a*
Me	Et	H	85% H_2SO_4		*a*
Et	Et	H	85% H_2SO_4		*a*
$-(CH_2)_5-$		H	85% H_2SO_4		*a*
Me	Me	6-Me	PPA	64	*b*
Me	Me	6-Me, 7-OMe	PPA		*b*
Me	Me	6-*i*-Pr, 7-OMe	PPA	60	*c*
Me	Me	5,7-$(OMe)_2$	H_2SO_4	34	*d*

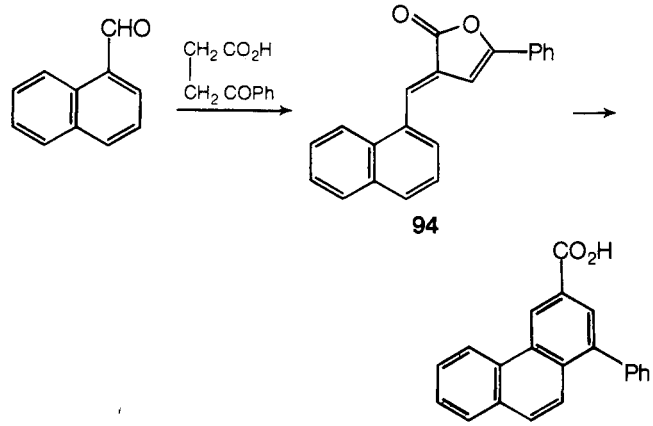
[a] H. Adkins and D. C. England, *J. Am. Chem. Soc.*, **71**, 2958 (1949). [b] D. Nasipuri and D. N. Roy, *J. Indian Chem. Soc.*, **40**, 327 (1963). [c] D. Nasipuri and A. K. Mitra, *J. Chem. Soc., Perkin Trans. 1*, 285 (1973). [d] M. Tateishi, T. Kusumi, and H. Kakisawa, *Tetrahedron*, **27**, 237 (1971).

1,4-dichlorobutane[80] or 2,5-dichlorohexane[59] in the presence of aluminum trichloride gives the octahydrophenanthrenes **90** (R = H and R = Me) in 20 and 38% yield, respectively, among other products (see also section III.B.1). The reaction of 1,4-dichlorobutane with tetralin at higher temperature (60–70 °C) is reported[81] to yield octahydrophenanthrene **91** in addition to **90** (R = H) and **92**. In a related process, the sodio derivative of



91 **92** **93**

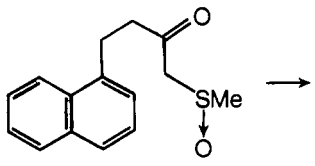
naphthalene reacts[82] with 1,4-dichlorobutane or 1,4-dichloropentane to give **93**, R = H or R = Me, respectively, along with other products. The synthetic utility of these methods is limited



94

by the production of by-products. The formation[83] of 1-phenylphenanthrene-3-carboxylic acid from **94** under Friedel–Crafts conditions provides an interesting phenanthrene synthesis; however, the overall yield from 1-naphthaldehyde was only 7%. More promising is the formation of **97**, when **95** is treated[84] with trifluoroacetic anhydride, this reaction is believed to involve cycloalkylation in the intermediate **96**.

Cyclization of the 1- and 2-naphthylbutyl radicals has been observed.[85,86] The 4-(1-naphthyl)butyl radical, prepared[85] from bis-5-(1-naphthyl)valeroyl peroxide, 5-(1-naphthyl)valeric acid/lead tetraacetate, or 5-(1-naphthyl)butane/tributyltin, yields **98**. The isomeric 4-(2-naphthyl)butyl radical, prepared[86] from 5-(2-naphthyl)valeric acid/lead tetraacetate yields a little **99** along with **98** (44%).



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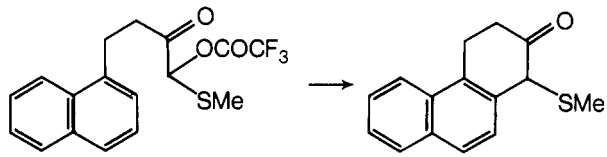
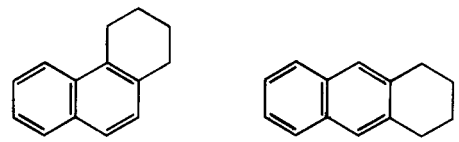


96 97

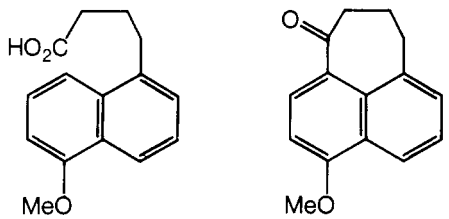


98 99

1- or 2-*n*-butyl- and higher alkylnaphthalenes may be converted[87-89] to phenanthrenes by high-temperature dehydrogenation over platinum/carbon, chromic oxide/alumina, iridium/alumina, or palladium/gumbrine catalysts. The 2-alkylnaphthalenes, which additionally give rise to anthracenes, give the best yields[87,88] of phenanthrenes at higher temperature (ca. 450 °C) over chromic oxide/alumina. 4-Alkyl substituents may be lost from the resultant phenanthrene.[88] This method is of limited value as a laboratory procedure, although it could be useful on an industrial scale.

2. *Intramolecular Cycloacylation*

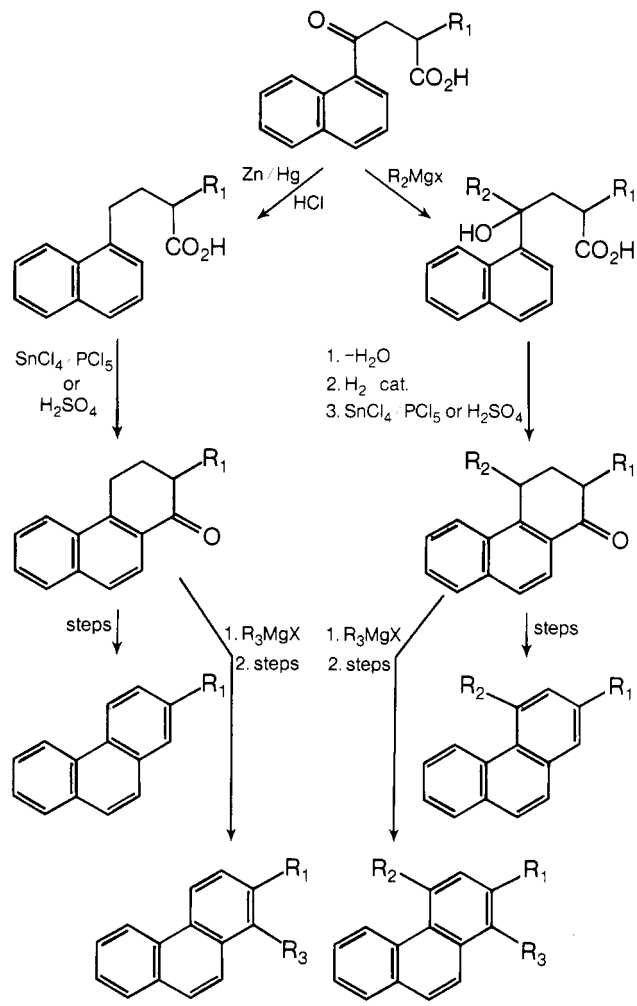
Among the most important routes to phenanthrenes, from naphthalenoid intermediates, is the acid-catalyzed cyclization[10] of the readily available 1- and 2-naphthylbutyric acids. The yields of 1- and 4-oxo-1,2,3,4-tetrahydrophenanthrenes are usually high, although products other than phenanthrenes may be formed on occasion. Thus **100**, in which the 8 position of the naphthalene ring is activated, yields[90] preferentially **101**. 4-(2-Naphthyl)butyric acids may lead to the formation of small amounts of anthracene by-products,[91] or in even larger proportion if the directive influence of the 1-naphthyl position is lost, e.g., **103**.[92] The conversion into fully aromatic phenanthrenes occurs in variable yield; however, many routes are available (see Scheme I), which permit the introduction of additional alkyl groups. Further variation may be achieved, for example, by formation[93] of the oxime from the 4-oxo group, leading in turn to 4-amino- and 4-halophenanthrenes. This results in a very flexible phenanthrene synthesis, which has been widely used.



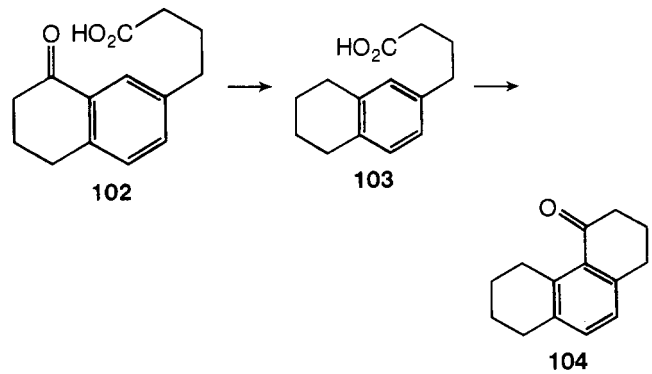
100 101

The most commonly used method for the preparation of the 3-(naphthoyl)propionic and 4-(naphthyl)butyric acids was introduced by Haworth[94] and involves[10] the Friedel–Crafts acylation of naphthalene or substituted naphthalenes by succinic anhydride or its mono- or symmetrical dialkyl derivatives. The half acid chloride of succinic acid, or its esters, have been used[95,96] for succinoylation. Succinoylation may produce mixtures of isomers; thus naphthalene yields[94,97] both 1- and 2-naphthoylpropionic acids, which were separated by fractional crystallization. Substituted naphthalenes frequently lead to only one naphthoylpropionic acid derivative, owing to the directive influence of the substituents. The scope of the Haworth method is illustrated by the examples in Table VII. The keto acid **102**, obtained by the double succinoylation of benzene followed by reduction and cyclization, failed[92] to cyclize further, although **103** could be cyclized, yielding **104** and the corresponding octahydroanthracene.

SCHEME I[a]



[a] 3-(2-Naphthoyl)propionic acids may be treated similarly.



102 103 104

Numerous other methods have been used for the preparation of 4-(naphthyl)butyric acids, thus allowing the side chain to be attached at positions unavailable by the Haworth synthesis. The reaction of naphthylmagnesium bromides, for example, with ethylene oxide provides naphthylethanols converted to naphthylbutyric acids via their halides and diethyl malonate. In this way have been obtained 8- and 9-methoxy-1,2,3,4-tetra-

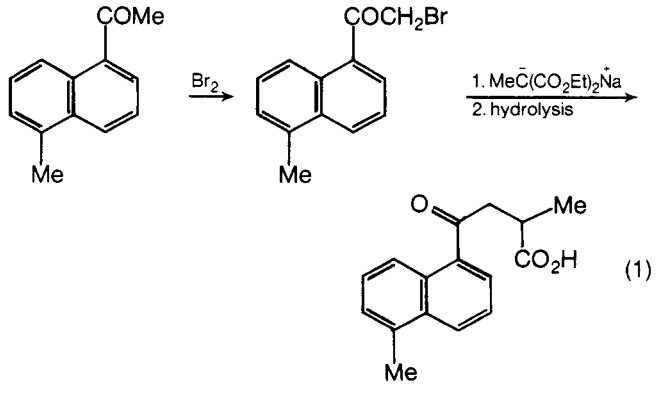
TABLE VII. Phenanthrenes from the Haworth Synthesis

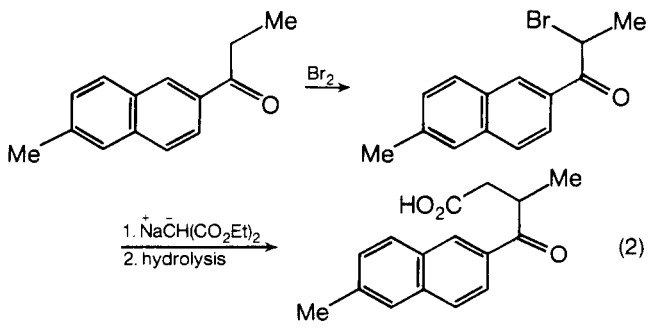
Naphthalene substituents	RCH–CO / O / CH_2–CO R =	Position of succinoylation	Phenanthrenes prepared	Ref
Unsubstd	H	1 and 2	1-Me; 4-Me; 1-Ph; 1-$CH(OH)CH_2NR_2$; 4-$CH(OH)CH_2NR_2$; 1,4-$(Me)_2$	94, *d*, *e*
Unsubstd	Me	1 and 2	2-Me; 3-Me; 1,2-$(Me)_2$; 1,3-$(Me)_2$; 2,4-$(Me)_2$; 3,4-$(Me)_2$; 1,3,4-$(Me)_3$	94, 104, 195
1-Me	H	4	9-Me; 1,9-$(Me)_2$	104
1-Me	CH_2CO_2H	4	2,9-$(Me)_2$	*f*
2-Me	H	6	1,7-$(Me)_2$; 1-Et-7-Me	*g*, *h*
2-Me	CH_3	6	1,3,7-$(Me)_3$	105
2-Me	CH_2CO_2H	6	3,7-$(Me)_2$	*f*
2-*i*-Pr	H	6	1-Me-7-*i*-Pr; 1-Et-7-*i*-Pr; 1,4-$(Me)_2$-7-*i*-Pr	*h*
2-*i*-Pr	CH_3	6	1-Me-7-*i*-Pr	*i*
1-$CH_2CH_2CO_2H$	H	4	*b*	*j*
2-$CH_2CH_2CO_2H$	H	6	*b*	*k*
2-$CH_2CH_2CH_2CO_2H$	H	6	*b*	*l*
1-OH	H	4	*c*	*m*
2-OMe	H	1, 6 and 8[a]	2-OMe; 2-Me-6-OMe	*n*, *o*
1,2-$(Me)_2$	H	4	9,10-$(Me)_2$	*p*
1,6-$(Me)_2$	H	4	3,10-$(Me)_2$; 1,6,9-$(Me)_3$	*q*
1,7-$(Me)_2$	H	4	2,10-$(Me)_2$; 1,7,9-$(Me)_3$	*q*
1-Me-7-*i*-Pr	H	4	2-*i*-Pr-10-Me; 2,9-$(Me)_2$-7-*i*-Pr	*r*
1,8-$(Me)_2$	Me	4	1,6,10-$(Me)_3$; 1,7,10-$(Me)_3$	*s*
2,3-$(Me)_2$	H	7	1,6,7-$(Me)_3$	105
1,7-$(OMe)_2$	H	4	*b*	*t*
2,3$(OMe)_2$	H	7	6,7-$(OMe)_2$-1,2,3,4-$(H)_4$	*u*
2,7-$(OMe)_2$	H	3	7,10-$(OMe)_2$-1,2,3,4-$(H)_4$	*v*
1-CO_2H,8-NH_2 lactam	H	5	8-CO_2H-9-NO_2-1,2,3,4-$(H)_4$	*w*
2-F,8-Ph	H	5	1,9-$(Ph)_2$-7-F	*x*
2,3,6-$(Me)_3$	H	7 and 8	2,3,9-$(Me)_3$; 2,3,5,9-$(Me)_4$; 2,3,8,9-$(Me)_4$	*y*

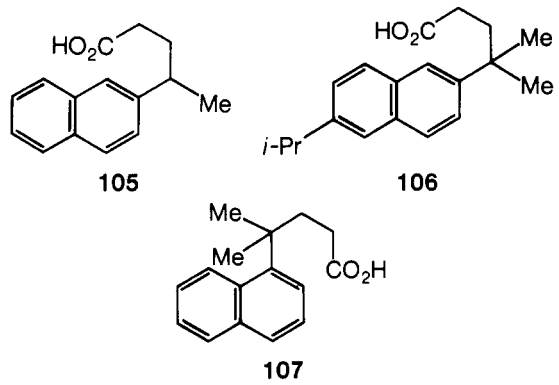
[a] The author in footnote *o* suggests that this is due to impurity. [b] Phenanthrenes not prepared, but cyclized to the corresponding phenanthrones. [c] Converted into 4-methyl-4′-oxocyclohexeno[5′,6′:5,6]benzo[*h*]coumarin via a Von Pechmann reaction and cyclization. [d] A. L. J. Beckwith and M. J. Thompson, *J. Chem. Soc.*, 73 (1961). [e] L. O. Krbechek, R. R. Riter, R. G. Wagner, and C. W. Huffman, *J. Med. Chem.*, **13**, 234 (1970). [f] K. R. Tatta and J. C. Bardhan, *J. Chem. Soc., C*, 893 (1968). [g] R. D. Haworth, B. M. Letsky, and C. R. Mavin, *J. Chem. Soc.*, 1784 (1932). [h] R. D. Haworth, *ibid.*, 2717 (1932). [i] L. V. Thoi and H. N. Bich, *Ann. Fac. Sci., Univ. Saigon*, 31 (1963–4); *Chem. Abstr.*, **65**, 2188 (1966). [j] A. U. Rahman, B. M. Vuano, and N. M. Rodriguez, *Aust. J. Chem.*, **25**, 1521 (1972). [k] A. U. Rahman and N. M. Rodriguez, *Chem. Ber.*, **104**, 2651 (1971). [l] A. U. Rahman and A. A. Khan, *ibid.*, **95**, 1786 (1962). [m] M. G. Parekh and K. N. Trivedi, *J. Indian Chem. Soc.*, **46**, 815 (1969). [n] W. E. Bachmann and W. J. Horton, *J. Am. Chem. Soc.*, **69**, 58 (1947). [o] M. Ghosal, *J. Org. Chem.*, **25**, 1856 (1960). [p] N. P. Buu-Hoi and G. Saint-Ruf, *C. R. Acad. Sci., Ser. C*, **254**, 2366 (1962). [q] N. P. Buu-Hoi and G. Saint-Ruf, *Bull. Soc. Chim. Fr.*, 2307 (1963). [r] H. Kobayashi, *Bull. Chem. Soc. Jpn.*, **35**, 1970 (1962); *Chem. Abstr.*, **58**, 8995 (1963). [s] J. A. Corran and W. B. Whalley, *J. Chem. Soc.*, 4719 (1958). [t] N. P. Buu-Hoi and G. Saint-Ruf, *Bull. Soc. Chim. Fr.*, 624 (1966). [u] N. P. Buu-Hoi and G. Saint-Ruf, *C. R. Acad. Sci., Ser. C*, **260**, 593 (1965). [v] G. Saint-Ruf and N. P. Buu-Hoi, *Bull. Soc. Chim. Fr.*, 2225 (1970). [w] S. M. Kupchan and M. Mokotoff, *J. Med. Chem.*, **10**, 977 (1967). [x] M. Sy and G. A. Thiault, *Bull. Soc. Chim. Fr.*, 1308 (1965). [y] W. Carruthers and J. D. Gray, *J. Chem. Soc.*, 2422 (1957).

hydro-1-phenanthrone,[98] 1-, 2-, and 4-*n*-decylphenanthrene,[99] and 7-methoxyphenanthrene-1,2-dicarboxylic acid anhydride.[100] 1-Naphthylmagnesium bromide may be reacted with succinic anhydride[101] or 2,3-dimethylsuccinic anhydride,[102] and 5-methyl-1-naphthylmagnesium bromide with *R*-(−)-$ClCOCH_2C$-$MeEtCO_2Me$,[103] to yield 3-(1-naphthoyl)propionic acids and by reduction 4-(1-naphthyl)butyric acids. Another variation involves bromination of 1-[104] or 2-acylnaphthalenes[105] followed by reaction with diethyl malonate to yield 1- or 2-naphthoylpropionic acids (see eq 1 and 2).

Naphthalene may be alkylated under Friedel–Crafts conditions using 4-pentenoic acid[79] giving rise directly to 4-(2-naphthyl)-4-methylbutyric acid (**105**); similarly, **106** may be obtained[106] from 2-isopropylnaphthalene and 4-methyl-3-pentenoic acid, and **107** from naphthalene and either 4-methyl-3-pentenoic or







105 106 107

4-methyl-2-pentenoic acid.[107] The Stobbe condensation[108] between 2-acetylnaphthalene and diethyl succinate forms the basis of another route to 4-(2-naphthyl)butyric acids and thus phenanthrenes. The method developed by Johnson and his coworkers[109-111] is summarized in Scheme II. The overall yield was 54% (for R = Me), so although the reaction sequence is lengthy, it provides an efficient phenanthrene synthesis. The direct cyclization of the mixed products of condensation, **108** (R = Me) and **109** (R = Me) leads[109] to lower yields of phenanthrenes, since only **108** (R = Me) is suitable for cyclization. Reduction of the double bond in **108** and **109** prior to cyclization via the derived acid anhydride **110** was successful[112] with R = Ph, X = H. Similarly **110** (R = H, X = OMe) gave[113] **111** in 95% yield, although when **110** (R = Et, X = OMe) was cyclized[114] **112** predominated. The direct cyclization of the Stobbe condensation products using sodium acetate in acetic anhydride has been used to convert[115] the aldehydes **113** (R = H), **114** (R = H), and **115** (R = H) and the ketones **113** (R = Ph),[116] **114** (R = Ph),[117] and **115** (R = Ph)[118] into the phenanthrenes **116** (R = H), **117** (R = H, X = H), **118** (R = H), **116** (R = Ph), **117** (R = Ph, X = Me), and **118** (R = Ph), respectively.

The Reformatskii reaction has been used to make 4-(naphthyl)butyric acid derivatives from tetralones. In a direct manner, alkyl 4-(1-naphthyl)butyrates are formed from 1-tetralones by reaction with alkyl 4-bromocrotonates, followed by double bond migration under the influence of palladium catalysts at 300 °C (see Table VIII). A less direct approach using alkyl bromoacetates leads to the formation of **119**, followed by reaction with a sodiomalonic ester yielding **120**, which may be cyclized (see Scheme III).

The product **121** of the Reformatskii reaction between 5,8-

SCHEME II

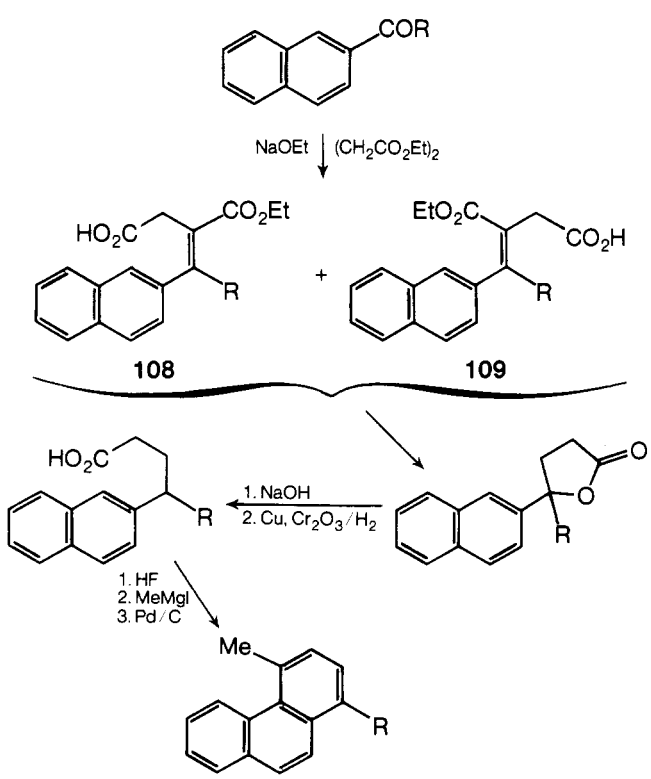
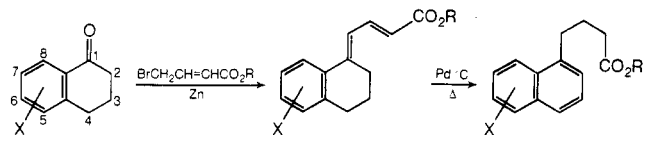
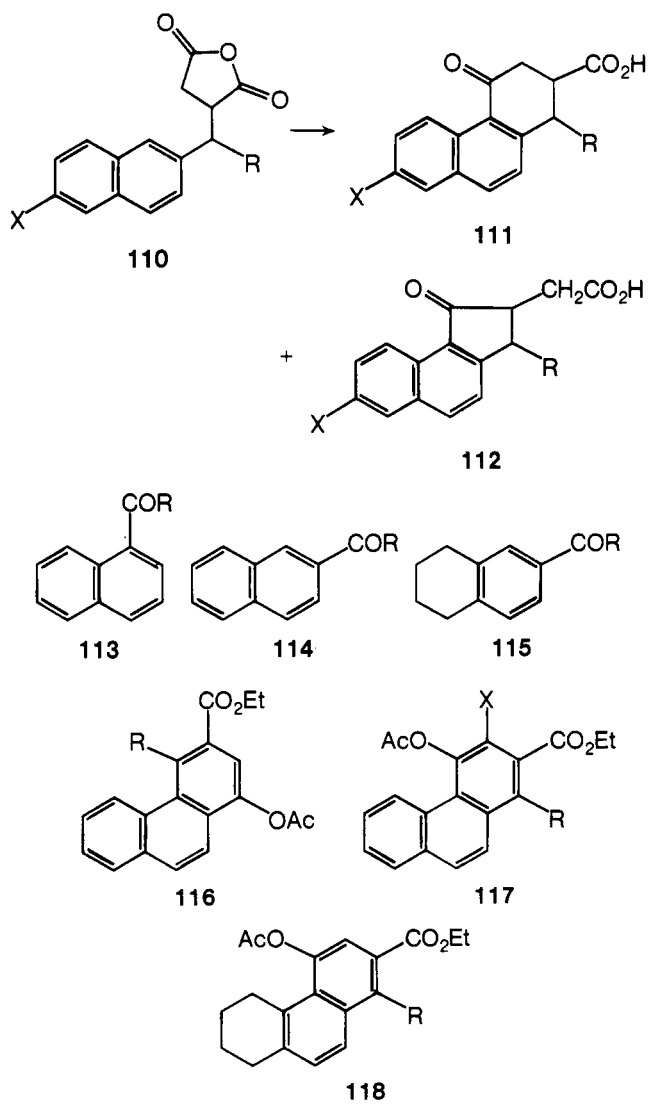


TABLE VIII. Reformatskii Reaction of 1-Tetralones and 4-Bromocrotonates



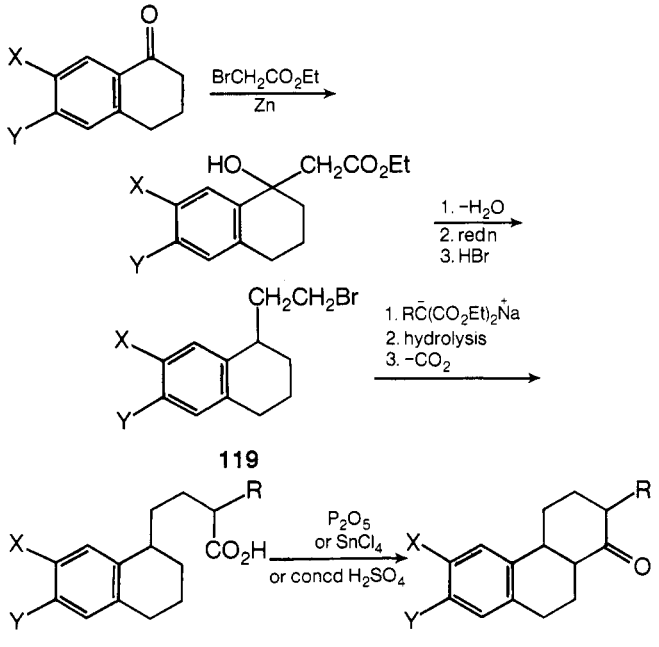
X	R	% yield overall	Ref
6-Me	Me	25	*b*
6-Me,7-OMe	Me		*b*
6-*i*-Pr,7-OMe	Me	40	*c*
6-OMe	Me	68	*d*
6-OMe	Et	26	*e*
6,8-$(OMe)_2$	Me		159a
5,7,8-$(OMe)_3$[a]	Et		*f*

[a] The 8-OMe group is replaced by H during the Reformatskii reaction. [b] D. Nasipuri and D. N. Roy, *J. Indian Chem. Soc.*, **40**, 327 (1963). [c] D. Nasjpuri and A. K. Mitra, *J. Chem. Soc., Perkins Trans. 1*, 285 (1973). [d] G. Stork, *J. Am. Chem. Soc.*, **69**, 2936 (1947). [e] J. G. Morgan, K. D. Berlin, N. N. Durham, and R. W. Chesnut, *J. Heterocycl. Chem.*, **8**, 61 (1971). [f] M. Tateishi, T. Kusumi, and H. Kakisawa, *Tetrahedron*, **27**, 237 (1971).



110 111 112 113 114 115 116 117 118

SCHEME III

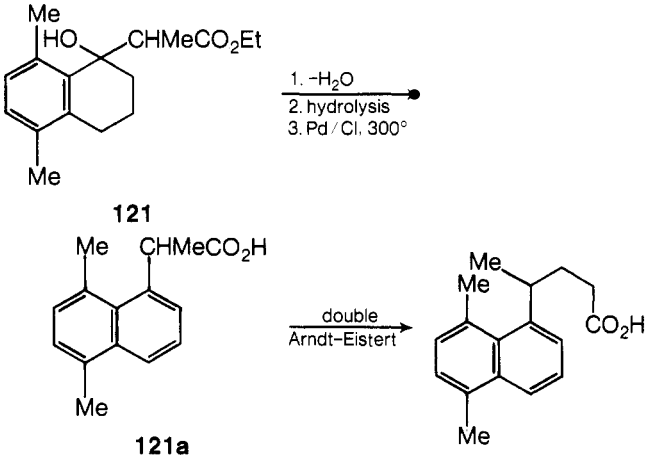


119

120

X = H, Y = OMe, R = H[119]
X = H, Y = OMe, R = Me[120]
X = H, Y = *i*-Pr, R = H[121]
X = OMe, Y = H, R = H[122]

dimethyl-1-tetralone and ethyl 2-bromopropionate has been converted[123] into **122**, by a double application of the Arndt–Eisert procedure on the intermediate **121a**. Only a single Arndt–Eisert

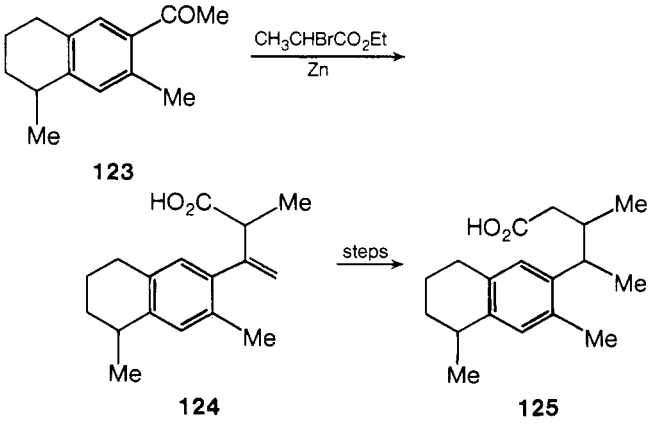


121

121a

122

procedure was required during the conversion[124] of **124**, the Reformatskii product of **123** and ethyl 2-bromopropionate, into **125**.

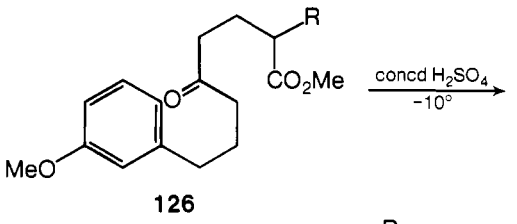


123

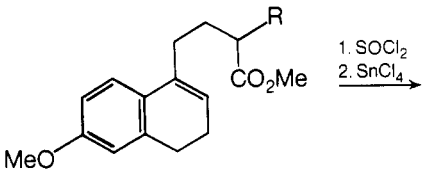
124

125

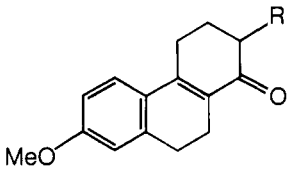
The cyclization of **126** (R = H or Me) (see also section III.B.3) using[72] cold concentrated sulfuric acid leads to good yields of **127**, which were ring closed to phenanthrene derivatives **128**.



126

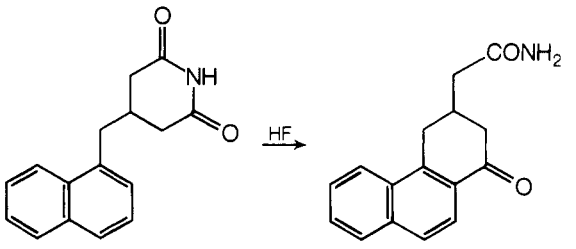


127



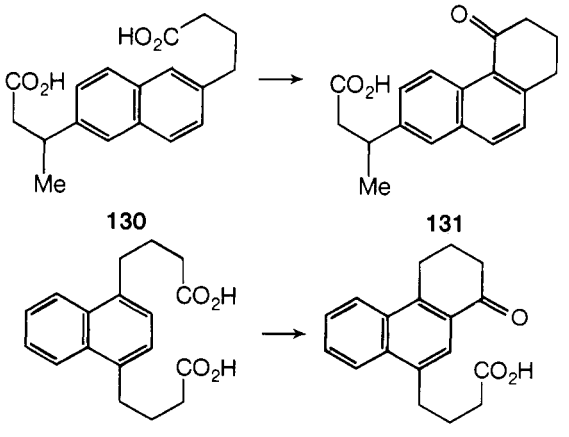
128

The Michael addition has been used[125-127] to prepare a number of naphthylaliphatic dibasic acids suitable for cyclization[90b,125,127,128] to phenanthrene derivatives (see Scheme IV). This procedure has in general given good yields. An unusual method for the cyclization of this type of dibasic acid, as their cyclic imides **129**, has been described.[129] Those dibasic acids



129

with 2-carboxyalkyl side chains are especially useful in the synthesis of tetracyclic compounds by further intramolecular cyclization. Thus, **130** and **132** were intended for the synthesis of tetracyclic compounds; however, the tetrahydrophenanthrones **131** and **133** were prepared[130] as intermediates.

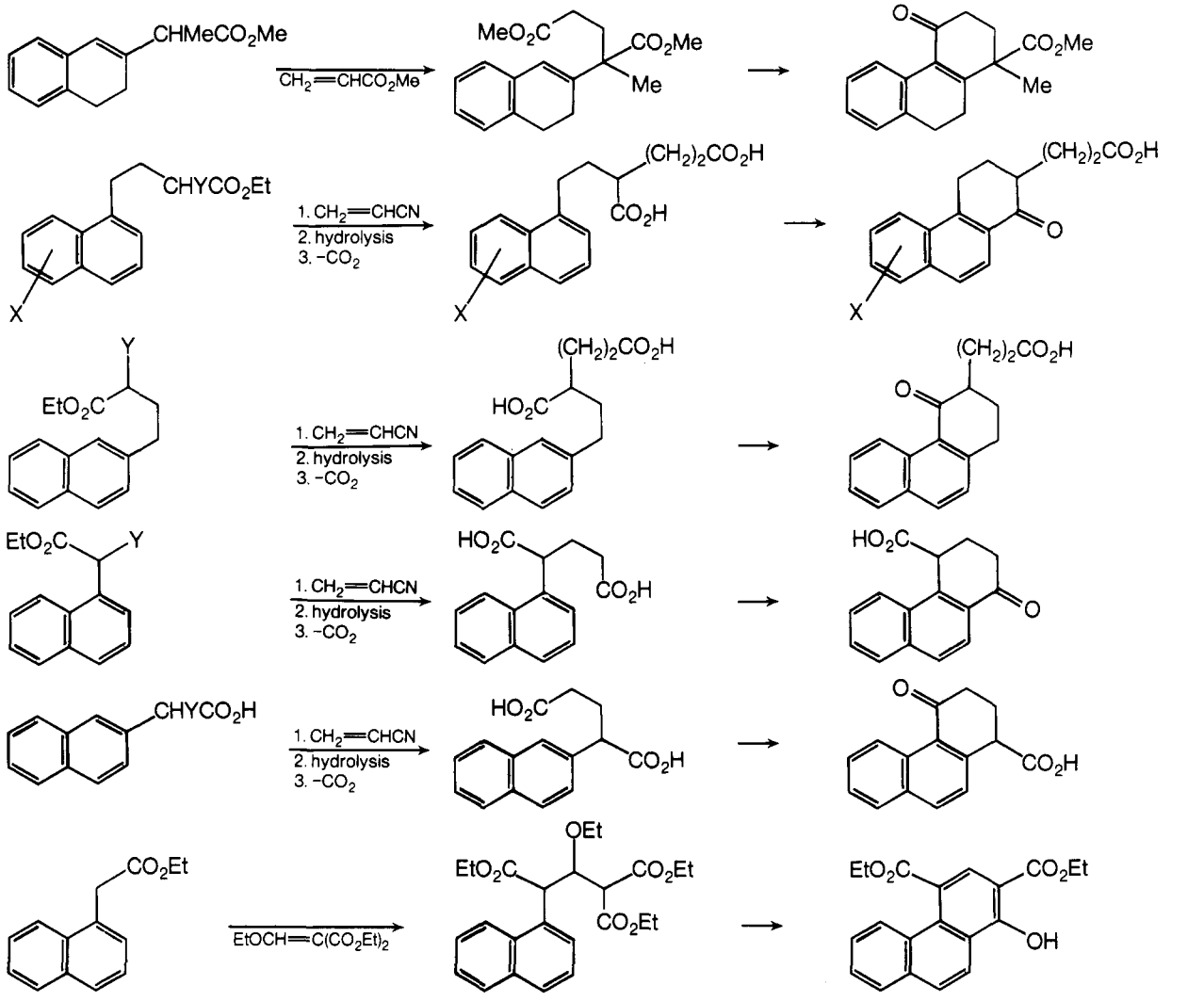


130 131

132 133

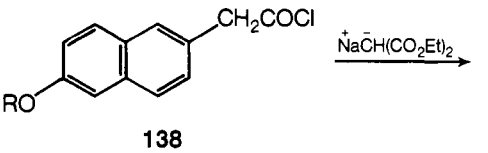
Another approach to naphthylbutyric acids makes use of 1-halomethylnaphthalenes. Thus **134** gives **135** on treatment with sodiomalonate esters; the side chain is then stepped up, either by means[131] of an Arndt–Eisert process yielding **136**, or by re-

SCHEME IV

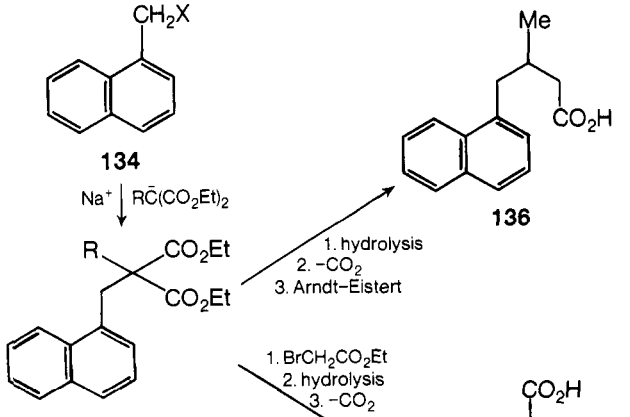


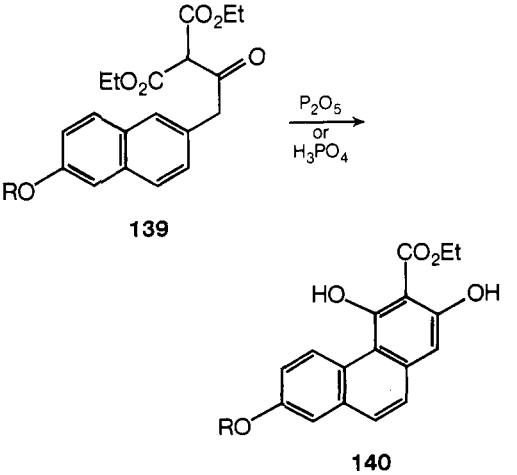
X = H, 4-OMe, 5-OMe, 6-OMe, or 7-OMe (in naphthalenes)
Y = CO_2Et or CN

action[132] with ethyl bromoacetate yielding **137**. A related procedure makes use[133] of 2-naphthylacetyl chloride **138**, which with diethyl sodiomalonate yields **139**, readily cyclized to the phenanthrene **140**.



138

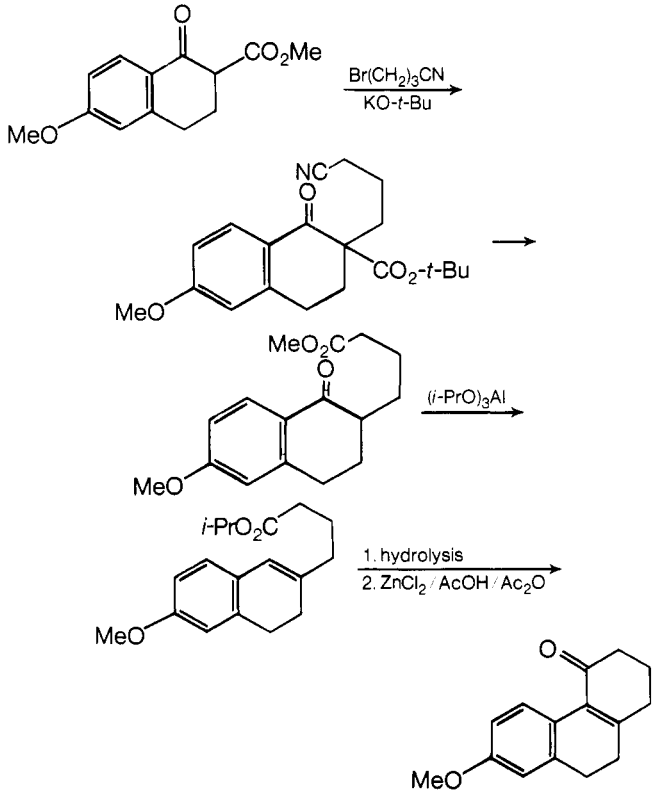




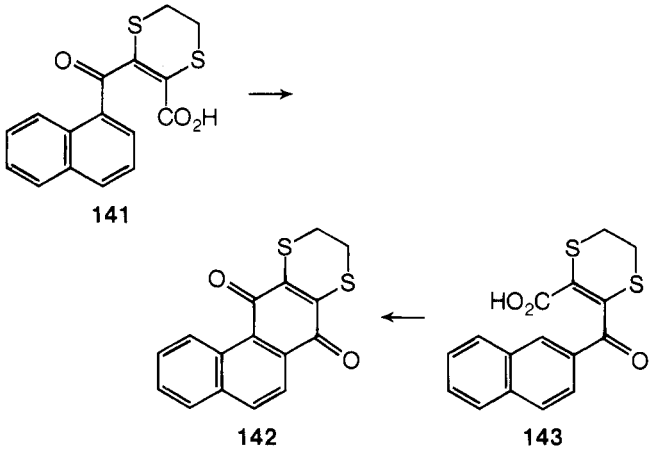
R = Me or CH_2Ph

Use has also been made[134] of the nucleophilic reactivity of 2-alkoxycarbonyl-1-tetralones (see Scheme V).

SCHEME V



An unusual cycloacylation procedure involves[135] **141** or the isomeric **143**, which yields **142** on treatment with sulfuric acid.



3. *Intramolecular Condensation*

The cyclodehydration of suitably constituted 1-naphthylalkanones or alkanals provides a route to phenanthrene derivatives, e.g., **144** → **145**[136,137] and **146** → **147**.[138] The starting materials are generally prepared from 4-(naphthyl)butyric acids by Claisen condensation, e.g., **148** → **149** → **150**.[139] 2-Naphthylalkanones or alkanals may also be cyclized, e.g., **151** → **152**;[140] however, anthracenes as well as phenanthrenes are now possible. The suggestion, that phenanthrene formation is inhibited[141] by substitution at the 4 position, does not always seem to hold[142] (see Table IX).

The Diekmann cyclization of suitable naphthalenoid diesters has been used for phenanthrene synthesis. The commonest intermediates have been **153**, often aromatized to **154** before cyclization. The cyclization[143] of **155** has also been reported. The preparation of **153** has generally involved cyclization of **156** with cold concentrated sulfuric acid. The Diekmann cyclization and decarboxylation of **153** then yields **157** (X = H, R = H;[144] X = 8-Me, R = H;[144] X = H, R = Me;[145] X = 8-Me, R = Me;[145] X = 6-OMe, 7-*i*-Pr, R = H;[146] X = 7-OMe, 8-*i*-Pr, R = H[147]). A

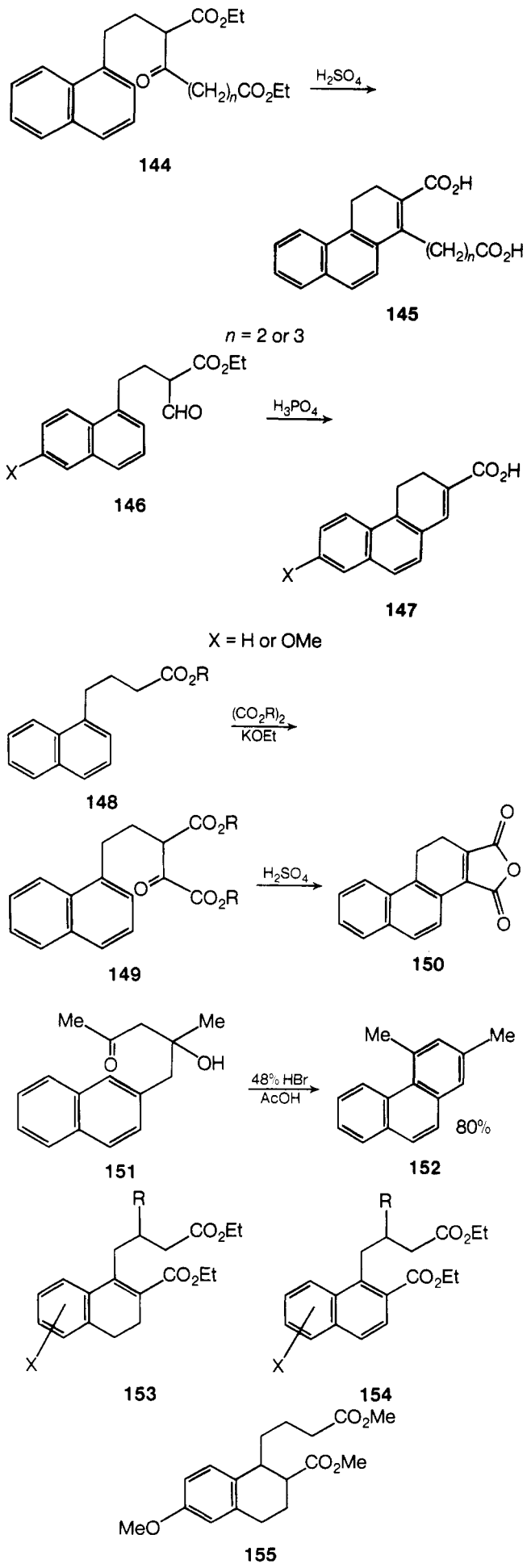
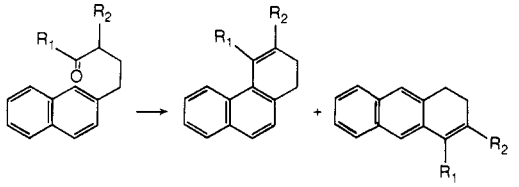
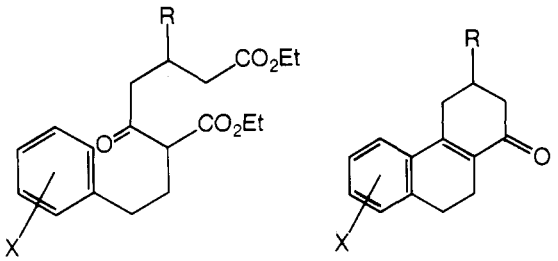


TABLE IX. Cyclodehydration of Some 2-Naphthylalkanones

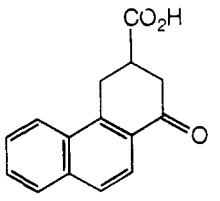


R_1	R_2	Product	Ref
H	H	Phenanthrene only	141
Me	H	Phenanthrene + anthracene	141
Et	H	Anthracene only	141
$-CH_2CH_2CH_2CH_2-$		Anthracene only	141
CO_2Et	CO_2Et	Phenanthrene only[a]	142

[a] Using 80% H_2SO_4, R_1,R_2 = —COOCO—; using 20% H_2SO_4, hydrolysis and decarboxylation occur, $R_1 = CO_2H$, $R_2 = H$.

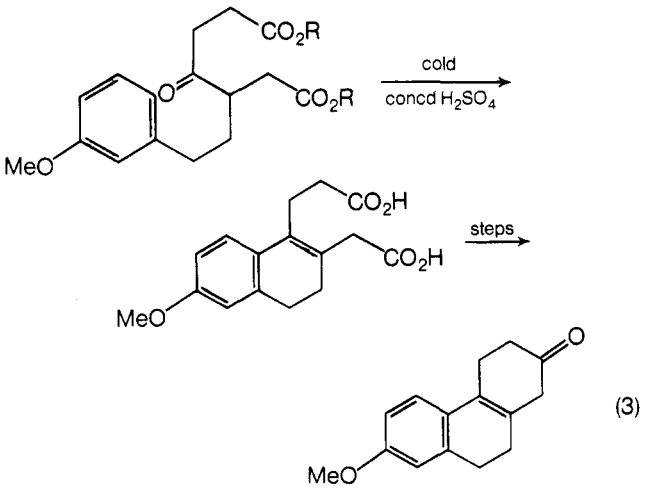


156 157



158

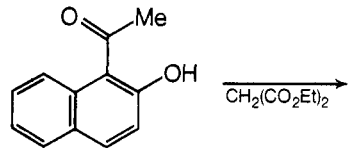
different route was used to obtain **154** (X = H, R = CO_2Et), which was cyclized[132] to yield **158**. A related approach[148] is summarized in eq 3.



(3)

A rather unexpected result (only *Chemical Abstracts* consulted) has been reported,[149] in which **159** is condensed with diethyl malonate yielding **160**, rather than the more readily explicable **161**.

A promising route to 9,10-dihydrophenanthrenes, which has received little attention, involves the base catalyzed condensation[150] of 1-dimethylamino-2-nitroethene with **162** (X = CN or CO_2Et) leading to **163** and **164** in 45 and 38% yield, respectively. There would seem to be scope for further exploitation of this reaction.



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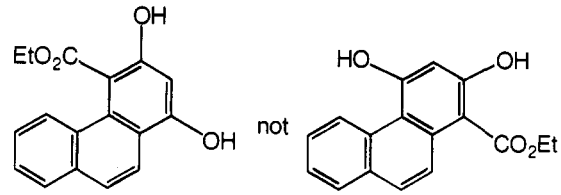
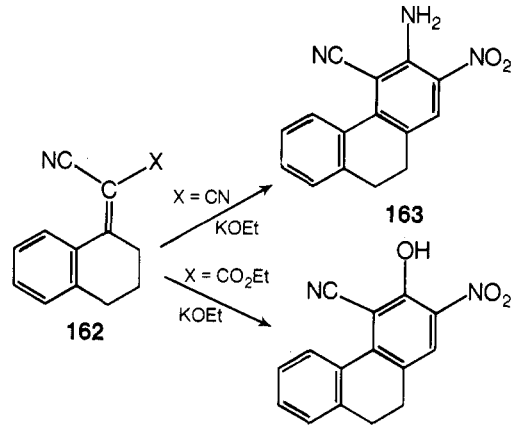


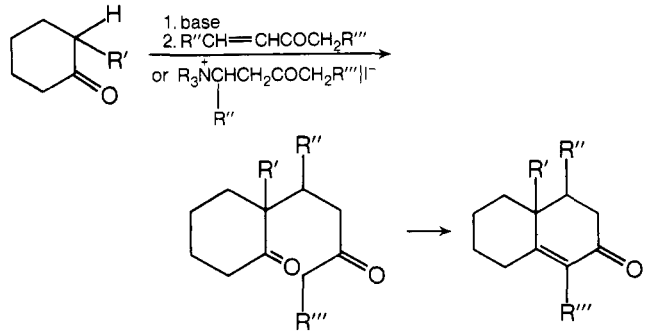
160 161



162 163 164

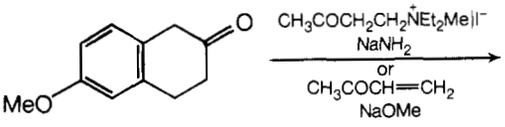
The ring annelation method devised by Robinson[151] is among the more important condensation processes by which phenanthrene may be synthesized. The process involves the Michael addition of an enolate anion to an α,β-unsaturated ketone, followed by cyclization involving an aldol-type condensation (Scheme VI).[152] The corresponding Mannich base methiodide may be used with advantage in place of the α,β-unsaturated ketone. This, and related annelations, has been used extensively in steroid syntheses[153] and is beyond the scope of this review, which in the main is confined to the formation of hydrophenanthrones having no angular alkyl groups. Since many simple derivatives of 1- and 2-tetralones are quite readily prepared, the Robinson method offers considerable scope in the synthesis of such phenanthrones, although the method has been little explored in this direction.

SCHEME VI

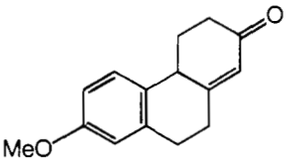


When 1- or 2-tetralones are used, the method yields hydrophenanthrones. Thus the ketone **165** condensed with 4-diethylaminobutan-2-one methiodide in the presence of sodamide[138] or methyl vinyl ketone in the presence of sodium methoxide[154] gave the hexahydrophenanthrone **166**.

1-Diethylaminopentan-3-one methiodide has also been condensed with 6-methoxy-2-tetralone (**165**),[155] 5-methoxy-2-tetralone,[156] and 6-isopropyl-2-tetralone[157] to give good yields



165



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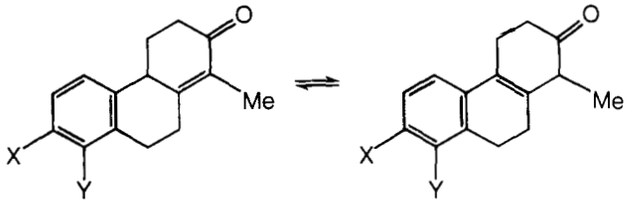
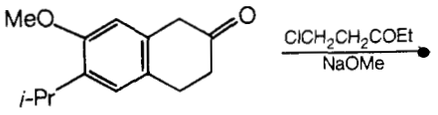


167 168

of the corresponding 1-methylphenanthrone derivatives **167** and **168** (X = OMe, Y = H; X = H, Y = OMe; X = *i*-Pr, Y = H) in tautomeric equilibrium. 1-Chloropentan-3-one has also been used as a precursor of ethyl vinyl ketone; thus **169** → **170** although in poor yield.[158]



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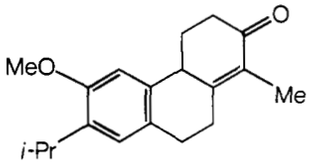
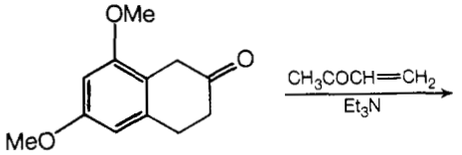


170

The formation of 2,4-dimethoxy-7-hydroxy-9,10-dihydrophenanthrene (**173**), as a minor side-product in the Robinson annelation of **171** with methyl vinyl ketone, was attributed[159] to the presence of **172** as impurity. When substantiated, this could prove a useful route to 9,10-dihydrophenanthrols, not otherwise readily prepared.



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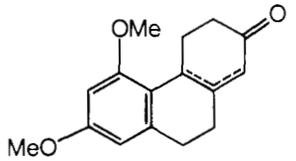

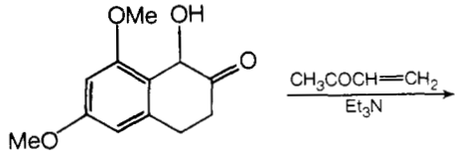

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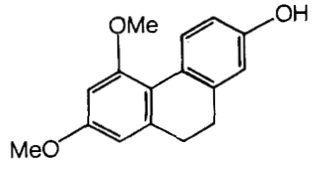
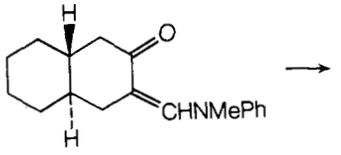


173

The direct condensation[160] of either *cis*- or *trans*-2-decalones as their enamines with methyl vinyl ketone leads to a mixture of anthracene and phenanthrene products. These arise owing to competition between positions 1 and 3 of the decalone in the Michael addition process. When the 3 position is first protected, using the method of Birch and Robinson,[161] then the resultant *trans*-decalone **174** may be converted[162] by the Robinson procedure to the phenanthrene derivative **175**.



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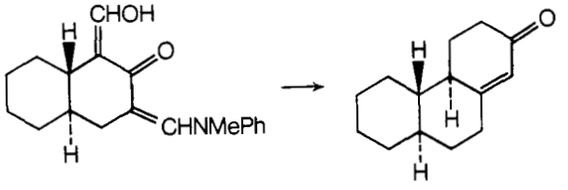
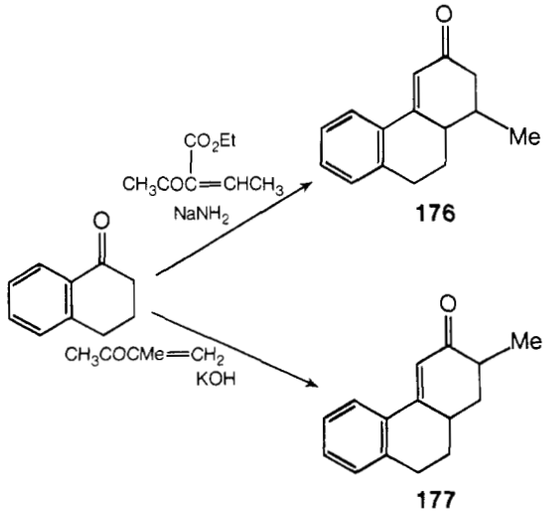


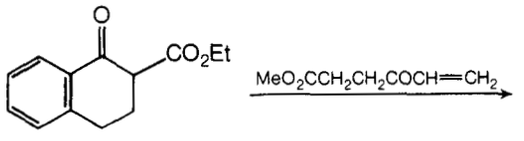
175

1-Tetralones may also be used as starting materials in the synthesis of phenanthrenes. Thus 1-tetralone may be condensed with either ethyl 2-acetylcrotonate[163] or methyl 2-propenyl ketone[164] to yield **176** and **177**, respectively. More commonly the 2 position of the 1-tetralone is activated by preliminary formylation using ethyl formate, before application of the Robinson annelation procedure (see Table X).



176 177

Similarly 2-alkoxycarbonyl-1-tetralones undergo ring annelation; thus **178** and **180** may be converted into the corre-



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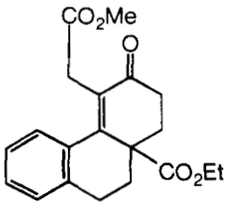
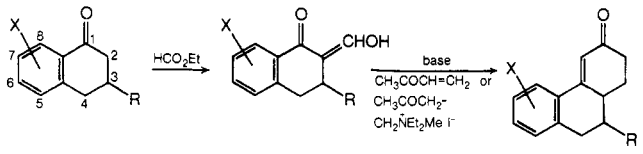


179

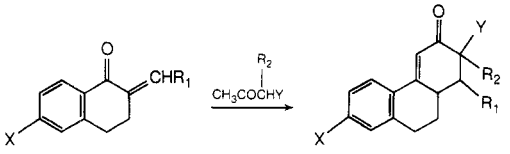
TABLE X. The Robinson Annelation of 1-Tetralones



1-Tetralone X	R	Base	% yield overall	Ref
6-OMe	H	Et_3N	78	*a*
7-OMe	H	Et_3N	51	*b*
6,8-$(OMe)_2$	H	Et_3N	73	*c*
7-OMe,6-*i*-Pr	H	KO-*t*-Bu	15	*d*
5,7,8-$(OMe)_3$	Me	Et_3N		159a

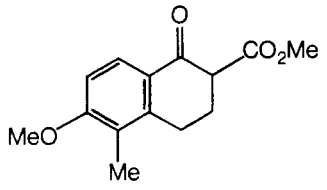
[a] A. A. Akhrem and I. G. Zavel'skaya, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1637 (1960); *Chem. Abstr.*, **55**, 8365 (1961). [b] R. B. Turner, D. E. Nettleton, Jr., and R. Ferebee, *J. Am. Chem. Soc.*, **78**, 5923 (1956). [c] E. Hardegger, N. Rigassi, J. Seres, C. Egli, P. Mueller, and K. O. Fitzi, *Helv. Chim. Acta*, **46**, 2543 (1963). [d] S. K. Sengupta, R. N. Biswas, and B. K. Bhattacharyya, *J. Indian Chem. Soc.*, **36**, 659 (1959).

TABLE XI. Cyclization of 1-Tetralones with Ethyl Acetoacetate or 2-Methylacetonitrile

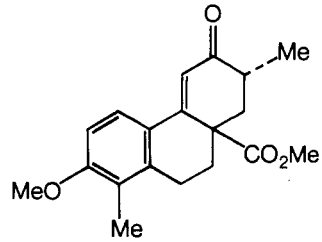


X	R_1	Y	R_2	% yield	Ref
H	Ph	CO_2Et	H	45	*a, b*
OMe	CO_2Me	CN	Me		*c*
OMe	$CH_2CH_2CO_2H$	CN	Me		*c*

[a] D. M. W. Anderson, N. Campbell, D. Leaver, and W. H. Stafford, *J. Chem. Soc.*, 3992 (1959). [b] D. M. W. Anderson and D. Leaver, *ibid.*, 450 (1962). [c] D. K. Banerjee, S. R. Ramadas, G. Ramani, and S. N. Mahapatra, *Indian J. Chem.*, **9**, 1 (1971).



180



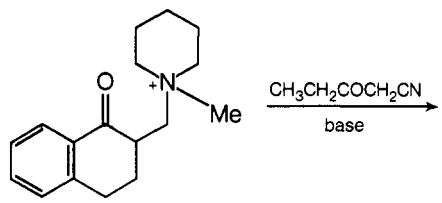
181

sponding **179** and **181** by treatment with 2-methoxycarbonylethyl vinyl ketone[165] and methyl 2-propenyl ketone,[166] respectively.

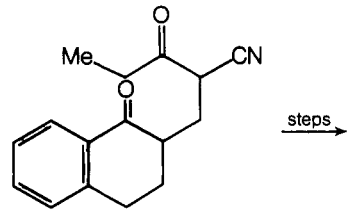
An interesting alternative to the Robinson ring extension involves condensation of a 1-tetralone with an aldehyde, followed by the Michael addition of either ethyl acetoacetate or 2-methylacetoacetonitrile and an aldol-type cyclization (see Table XI).

Closely related to this procedure is the method of Brown and Ragault,[167] which involves the Mannich reaction of 1-tetralone, followed by condensation of the product methiodide **182** with propioacetonitrile to yield **183**. Cyclization, dehydration, hydrolysis, and decarboxylation of **183** in concentrated hydrochloric acid gives a separable mixture of the hydrophenanthrones **184** and **185**.

The ring annelation method of Stork[168] has been applied[169]



182



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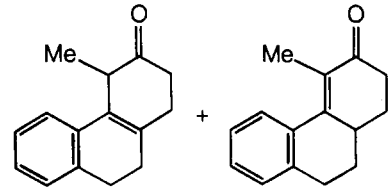
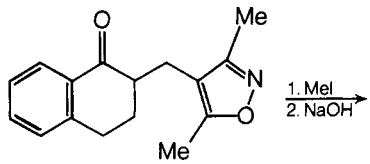
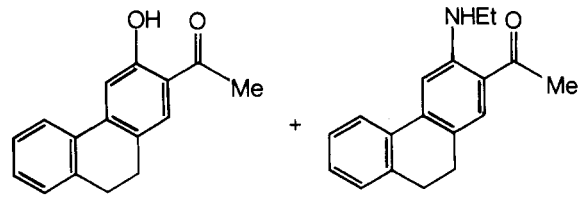


184 185

to the formation of the 9,10-dihydrophenanthrenes **186** and **187** in 40% overall yield. There appears to be some confusion in this paper, in that if the reagent used was methyl iodide, then the product **187** should have an *N*-methyl substituent. However, the method is an interesting one, which could be further exploited for the synthesis of simple 9,10-dihydrophenanthrenes.





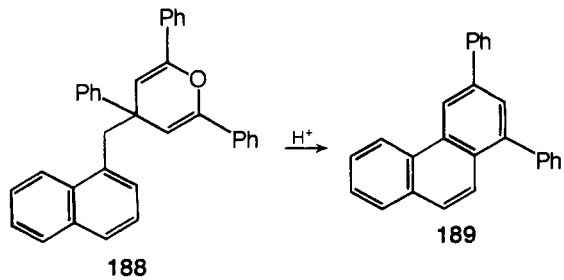
186 187

4. Photocyclization

This method is rather limited in scope as suitable naphthalenoid precursors are not readily available. An example is provided by the work of Tinnemans and Laarhoven[170] (see Scheme VII).

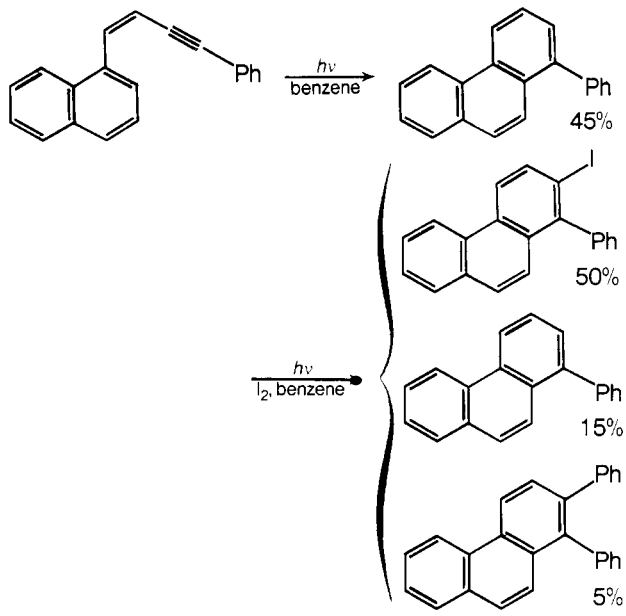
5. Miscellaneous Methods

The cyclization of certain dihydropyran derivatives with perchloric acid has led to phenanthrene derivatives. Thus **188** → **189** and **190** → **191** in 94 and 58% yield,[171] respectively. Since

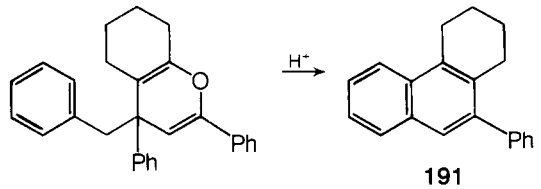


188 189

SCHEME VII

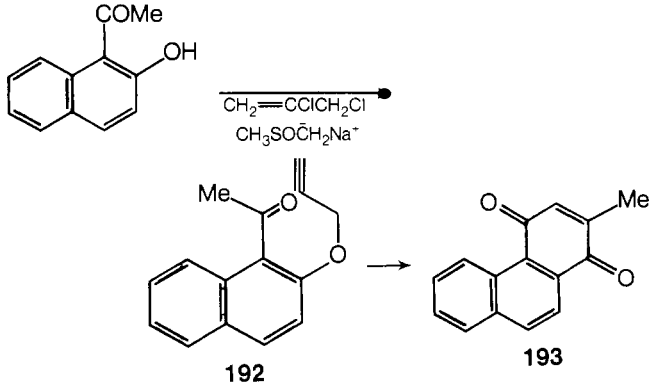


the starting materials are quite readily available,[172] this method seems an attractive one for the synthesis of specific phenanthrenes.



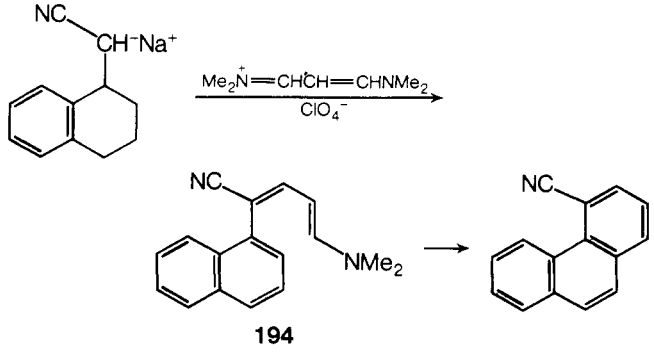
190 191

The base-catalyzed reaction of 1-acetyl-2-naphthol with 2,3-dichloropropene leads to the formation first of the propargyl ether **192** and then somewhat unexpectedly to the 1,4-phenanthraquinone **193** in 60% yield. A mechanism has been proposed[173] for this interesting rearrangement.



192 193

3-Dimethylaminopropenylidenedimethylammonium perchlorate is an interesting synthetic reagent capable of further exploitation. Its reaction[174] with the sodio derivative of 1-naphthylacetonitrile leads to **194**, which undergoes a thermal electrocyclic rearrangement, followed by elimination to yield 4-phenanthronitrile (91%). Clearly this reaction could be of considerable value in phenanthrene synthesis. 2-Phenyl-4-phenanthronitrile was similarly prepared[174] using 3-dimethylamino-2-phenylpropenylidenedimethylammonium perchlorate.

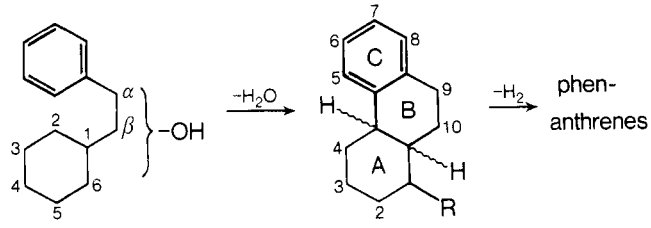


194

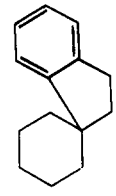
D. Cyclization of Stilbenoid Compounds

1. *Intramolecular Cycloalkylation*

Phenethylcyclohexanols **195** that possess the hydroxyl function at the 1, 2, 3, or β position have been cyclized to octahydrophenanthrenes **196** in the presence of acid catalysts such as phosphorus pentoxide, phosphoric acid, PPA, aluminum chloride, hydrogen halides, or sulfuric acid. The products can be dehydrogenated to the fully aromatic phenanthrenes, and since the starting materials are readily accessible in a number of cases, the process does constitute an attractive method for synthesizing phenanthrenes. The ring-closure reaction often proceeds in high yield (~80%), but is sometimes accompanied by spiran **197** formation. The octahydrophenanthrene **196** may have a cis or trans A/B ring junction, but in the context of aromatic phenanthrene synthesis this geometry is unimportant. The method has been extensively used for the synthesis of terpenes, steroids, and morphine derivatives. A thorough study of the mechanism has been made.[8] These topics will not be further considered here.

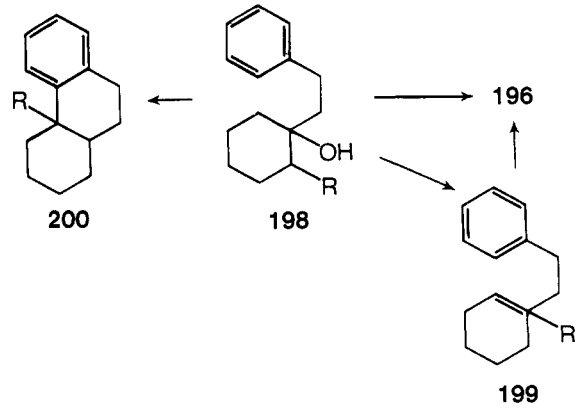


195 196



197

In the Bogart–Cook synthesis a β-phenethylcyclohexan-1-ol **198** (R = H) can be cyclodehydrated to the octahydrophenanthrene **196** (R = H) by concentrated sulfuric acid.[175] Alternatively,[176] milder dehydrating agents (e.g., iodine, potassium hydrogen sulfate, 50% sulfuric acid) convert **198** (R = H) into the olefin **199** (R = H), which can be ring-closed to **196** (R = H)



200 198 199

TABLE XII. Cyclization of β-Phenethylcyclohexanols

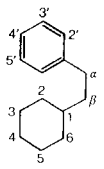
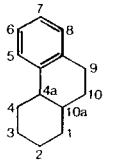
Cyclohexanol									Hydrophenanthrene									
1	2	3	6	2′	3′	4′	5′	Other	2	4a	5	6	7	8	10a	Other	Reagent	% yield	Ref
H	H	H	H	H	H	H	H	β-OH	H	H	H	H	H	H	H		H_2SO_4	65	182
OH	H	H	H	H	H	H	H		H	H	H	H	H	H	H		H_2SO_4		182
																	H_2SO_4	60	176
																	H_2SO_4	80	188
																	P_2O_5	90	*a*
																	hν	70	177
OH	Me	H	H	H	H	H	H		H	Me	H	H	H	H	H		H_2SO_4	92	182
																	$AlCl_3$		122
OH	H	Me	H	H	H	H	H		Me	H	H	H	H	H	H		H_2SO_4		181
OH	Me	H	H	Me	H	H	Me		H	Me	Me	H	H	Me	H		P_2O_5	86	178
OH	H	H	H	Me	H	H	Me		H	H	Me	H	H	Me	H		P_2O_5	82	178
OH	Me	H	Me	H	Pr*i*	H	H		H	Me	H	H	Pr*i*	H	H	1-Me	H_2SO_4	82	*b*
OH	Me	H	Me	Me	H	Pr*i*	H		H	Me	H	Pr*i*	H	Me	H	1-Me			183
OH	H	H	H	Me	H	H	OMe		H	H	OMe	H	H	Me	H		$AlCl_3$	2	179
OH	H	H	H	H	OMe	H	H		H	H	H	H	OMe	H	H		H_2SO_4	95	191, 187
OH	H	H	H	H	OMe	H	H		H	H	OMe	H	H	H	H		H_2SO_4		187
OH	H	H	H	OMe	H	H	H		H	H	H	H	H	OMe	H		H_2SO_4	95	188
OH	H	H	H	H	H	OMe	H		H	H	H	OMe	H	H	H		H_2SO_4	5	188
																	H_2SO_4	75	*c, d*
OH	Me	H	H	Cl	H	H	H		H	Me	H	H	H	Cl	H		H_2SO_4	96	*e*
OH	Me	H	H	Cl	H	H	OMe		H	Me	OMe	H	H	Cl	H		H_2SO_4	45	*f*
OH	$(CH_2)_2NMe_2$	H	H	H	H	H	H		H	$(CH_2)_2$-H NMe_2	H	H	H	H	H		H_3PO_4	60	183a
OH	CH_2CO_2H	H	H	H	H	H	H		H	H	H	H	H	H	H	1-CH_2CO_2H	H_3PO_4	80	*g, h*
H	OH	H	H	H	H	H	H		H	H	H	H	H	H	H		P_2O_5	70	*i*, 197
																	P_2O_5	100	194
H	OH	H	H	H	H	H	H	5-Me	Me	H	H	H	H	H	H		H_2SO_4	63	194
H	OH	H	H	Me	H	H	Me	α-Me	H	H	Me	H	H	Me	H	9-Me	H_2SO_4	50	*k*
Me	OH	H	H	H	H	H	H		H	H	H	H	H	H	Me		P_2O_5		*l*, 194
CO_2Et	OH	H	H	Me	H	H	Me		H	H	Me	H	H	Me	CO_2Et		P_2O_5		194
CO_2Et	OH	H	H	Me	H	H	Me	5-Pr*i*	Pr*i*	H	H	H	H	Me	CO_2Et		P_2O_5		*j*
H	OH, Me	H	H	H	H	Pr*i*	H		H	Me	H	Pr*i*	H	H	H		P_2O_5	80	189
H	OH, Me	H	H	H	H	H	H		H	Me	H	H	H	H	H		P_2O_5		*l*
H	OH	H	H	H	H	H	H	α-Me	H	H	H	H	H	H	H	10-Me	H_2SO_4		*k*
H	OH, Me	H	H	OMe	H	H	H	5-OMe	OMe	Me	H	H	H	OMe	H		HF	83	*m*
H	OH, Me	H	H	Br	H	H	OMe		H	Me	OMe	H	H	Br	H		H_2SO_4	78	*f*
H	OH, Me	H	H	Cl	H	H	H		H	Me	H	H	H	Cl	H		H_2SO_4	82	*e*
CO_2Et	OH, Me	H	H	H	H	H	OMe	5-OMe	OMe	Me	OMe	H	H	H	CO_2Et		H_2SO_4		*n*
H	OH, Et	H	H	H	H	H	H		H	Et	H	H	H	H	H		$AlCl_3$		*o*
H	H	OH	H	H	H	H	H		H	H	H	H	H	H	H		P_2O_5	60	197
																	P_2O_5	82	196
																	P_2O_5	74	*p*

TABLE XII (continued)

H	H																	P_2O_5	50	189	
H	H	OH	H	H	H	H	H	4-Pr^i	H	H	H	H	H	H	H	H	3-Pr^i	P_2O_5		198	
		OH	H	H	H	H	H	5-Me	Me	H	H	H	H	H	H	H					

[a] J. van de Kamp and E. Mosettig, *J. Am. Chem. Soc.*, **58**, 1062 (1936). [b] S. N. Slater, *J. Chem. Soc.*, 68 (1941). [c] M. Mousseron-Canet and J. C. Guilleux, *Bull. Soc. Chem. Fr.*, 3858 (1966). [d] H. Christol, Y. Pietrasarta, and J. L. Vernet, *C. R. Acad. Sci., Ser. C*, **270**, 1477 (1970). [e] R. A. Barnes and M. D. Konort, *J. Am. Chem. Soc.*, **75**, 303 (1953). [f] R. A. Barnes, H. P. Hirschler, and B. R. Bluestein, *ibid.*, **74**, 4091 (1952). [g] J. O. Jilek and M. Protiva, *Chem. Listy*, **51**, 643 (1951); *Chem. Abstr.*, **51**, 11306 (1957). [h] M. Proyita, J. O. Jilek, E. Adlerova, and L. Novak, *Experientia*, **13**, 71 (1957). [i] R. A. Barnes and A. D. Olin, *J. Am. Chem. Soc.*, **78**, 3830 (1956). [j] J. C. Bardhan and S. C. Sengupta, *J. Chem. Soc.*, 2798 (1932). [k] J. Colonge and F. Collomb, *Bull. Soc. Chim. Fr.*, **18**, 285 (1951). [l] G. A. R. Kon, *J. Chem. Soc.*, 1081 (1933). [m] W. B. Renfrow, A. Renfrow, E. Shoun, and C. A. Sears, *J. Am. Chem. Soc.*, **73**, 317 (1951). [n] R. A. Barnes, H. P. Hirschler, and B. R. Bluestein, *ibid.*, **74**, 32 (1952). [o] J. D. Fulton and R. Robinson, *J. Chem. Soc.*, 1463 (1933). [p] J. C. Bardhan, R. N. Adhya, and K. C. Bhattacharyya, *ibid.*, 1346 (1956).

TABLE XIII. Cyclization of Ketones and Diketones

1	3	4	5	6	α	2′	3′	5′	1	2	3	4	5	7	8	10	Ref
CO_2Et	H	H	Pr^i	H	H	Me	H	H	H	Pr^i	H	H	H	H	Me	H	*a*
H	H	H	H	H	Me	H	H	H	H	H	H	H	H	H	H	Me	*b*
H	H	Me	H	H	Me	H	H	H	H	H	Me	H	H	H	H	Me	*b*
H	Me	H	H	Me	Me	H	H	H	Me	H	H	Me	H	H	H	Me	*b*
H	Me	H	H	=O	H	H	H	H	=O	H	H	Me	H	H	H	H	72a
H	H	H	H	=O	H	H	OMe	H	=O	H	H	H	H	OMe	H	H	73, 205
H	H	H	H	=O	H	H	H	H	=O	H	H	H	H	H	H	H	206
H	H	H	H	=O	H	OMe	H	OMe	=O	H	H	H	OMe	H	OMe	H	*c*
H	H	H	H	=O	H	H	OMe	H	=O	H	H	H	H	OMe	H	H	*d*

[a] J. C. Bardhan and S. C. Sengupta, *J. Chem. Soc.*, 2798 (1932). [b] J. Colonge and F. Collomb, *C. R. Acad. Sci., Ser. C*, **237**, 547 (1950). [c] S. Imai, *J. Sci. Hiroshima Univ., Ser. A*, **33** (1969); *Chem. Abstr.*, **73**, 109568 (1970). [d] A. J. Birch, H. Smith, and R. E. Thornton, *J. Chem. Soc.*, 1339 (1957).

with stannic chloride. The olefin **199** (R = H) has also been[177] photocyclized to **196** (R = H) in good yield. The required alcohol **198** (R = H) is usually prepared by the interaction of the Grignard reagent derived from a β-phenethyl bromide and a cyclohexanone. If a substituted cyclohexanone is used, the alcohol, e.g., **198** (R = alkyl) may be cyclized to either **196** (R = alkyl) or **200** (R = alkyl).[122,178,179] Thus with **198** (R = CH_2CO_2H) only **196** (R = CH_2CO_2H) was isolated,[180] whereas with **198** (R = Me, $CH_2CH{=}CH_2$, or $CH_2CH_2NMe_2$) the 4a-substituted octahydrophenanthrene **200** is formed.[181-185] When an alkyl or alkoxyl group is at the position meta to the side chain in the phenyl ring, cyclization can proceed to yield the 5- or the 7-substituted phenanthrene derivative.[181,184-187] The nature and position of substituents in the aromatic ring can also influence the proportions of spiran formed. Thus, when **201** is treated[188] with concentrated sulfuric acid a 95:5 mixture of octahydrophenanthrene and spiro compound **202** is formed, whereas when the isomeric *m*-methoxyphenethylcyclohexan-1-ol is similarly treated, the ratio of phenanthrene to spiran is reversed.

201

202

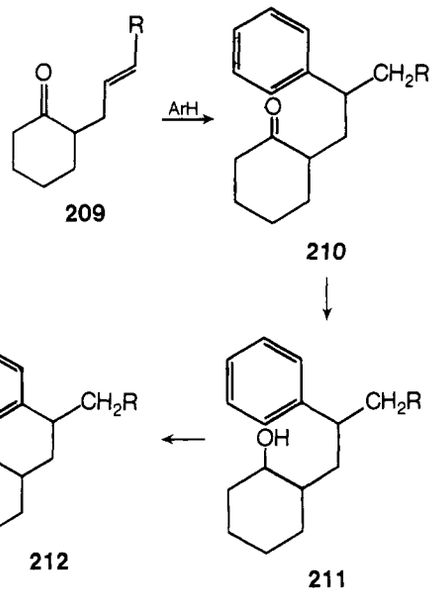
The assumption has been made[182,189] that the mechanism of the cyclization reaction to octahydrophenanthrenes, using concentrated sulfuric acid, involves initial dehydration followed by cyclization of the olefin produced. This assumption is now known to be erroneous,[8] although it is known that olefins can be cyclized to octahydrophenanthrenes.[190]

A modification to this general approach involves[191] the treatment of, for example, **203** with mercuric acetate and perchloric acid when a mixture of **204** + **205** (R = H) is produced in a total yield of 55%. The isomeric cyclohexene **206** is cyclized to **207** (R = H) in 40% yield with mercuric perchlorate in acetic acid.[192] Similarly the olefins **208** (R = H or OMe) can be converted[193] into **207** (R = H or OMe) and **205** (R = H or OMe).

203 **204** **205**

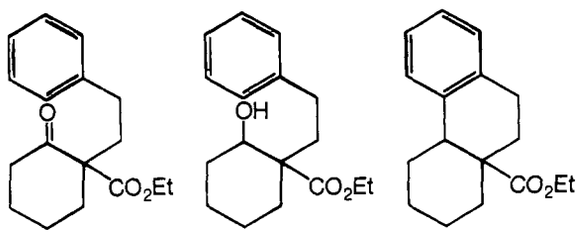
206 **207** **208**

A 2-(β-phenethyl)cyclohexanol can also be cyclodehydrated to a phenanthrene derivative[194] under acid conditions. The required alcohol can be obtained[79] by the interaction of 2-allylcyclohexanone derivatives with an aromatic ring (the Colonge–Mukherji reaction), followed by reduction of the intermediate

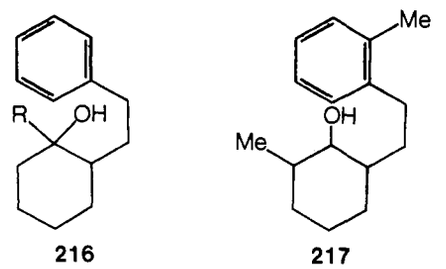


ketone, i.e., **209** → **210** → **211** → **212**. This method has been used quite extensively.

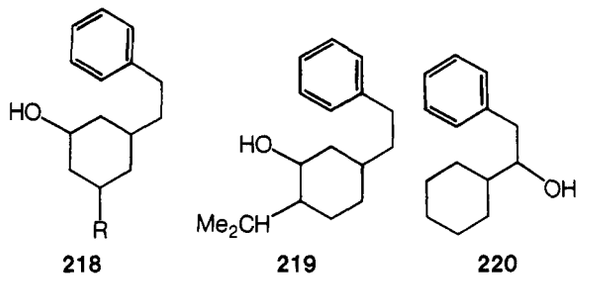
Alternatively, the potassium salt of a derivative of ethyl cyclohexanone-2-carboxylate is alkylated by a β-phenethyl halide. The keto ester **213** is then hydrolyzed, decarboxylated, and reduced to the required alcohol.[194] In those derivatives of **213** where removal of the ethoxycarbonyl group is difficult, reduction to **214**, followed by cyclization yields **215** from which the bridgehead substituent is removed upon dehydrogenation.[194]



In a further variation a 2-(β-phenethyl)cyclohexanone is allowed to react with a Grignard reagent to form a tertiary alcohol **216**, which is then cyclized to a 4a-substituted octahydrophenanthrene.[189] Although overall yields are low, the methods outlined above are suitable[194] for the preparation of those phenanthrenes with an unsubstituted C-ring since β-arylethyl halides are readily available. Dehydrogenation of the intermediate octahydrophenanthrenes is usually easily accomplished. However, it has been reported[195] that cyclization of **217**, followed by dehydrogenation, yields 1,8-dimethylphenanthrene.



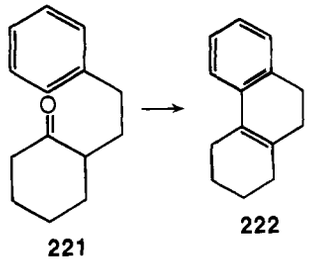
The cyclodehydration of 3-(β-phenethyl)cyclohexanol **218** (R = H) was found by Pal[196] and by Ray[197] to produce 1,2,3,4,4a,9,10,10a-octahydrophenanthrene. The process has not been generally applied to the synthesis of phenanthrenes since the required cyclohexanols are not readily accessible. However, 2-methyl-[198] and 3-isopropylphenanthrene[189] have been prepared from **218** (R = Me) and **219**, respectively.



The cyclization of alcohols of the type **220** was first reported by Bogart,[182] but overall yields are low and the reaction appears to be an unattractive one (see Table XII).

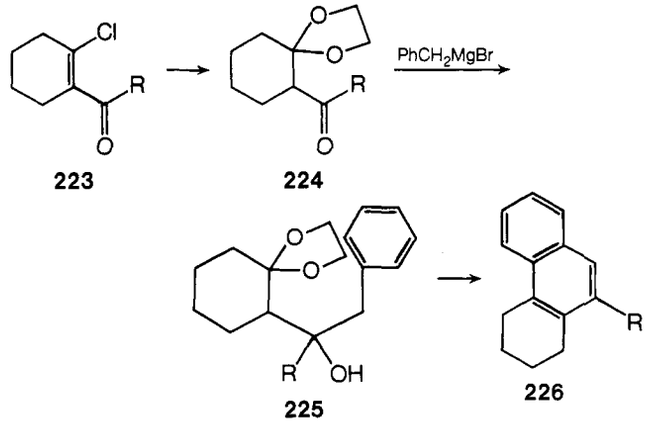
2. Intramolecular Condensation

In this process a suitable β-phenethylcyclohexanone (**221**) is cyclized, under acid conditions, to a hexahydrophenanthrene (**222**). The earlier literature has been reviewed by Fieser and Fieser[4] and by Popp and McEwen.[199] Some more recent examples are summarized in Table XIII.

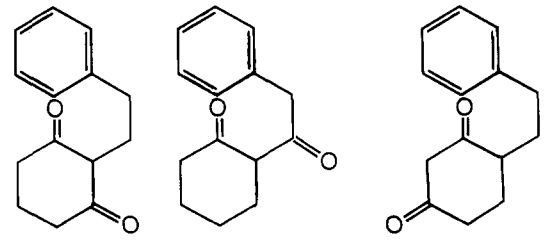


A modified Colonge–Mukherji reaction has been used in which the cyclohexanone derivative, formed by the interaction of 2-allylcyclohexanone with the aromatic compound, is cyclized (sulfuric acid or hydrogen bromide in acetic acid). If the aromatic ring is activated to electrophilic attack, the cyclization reaction can be accomplished in one step.[200,201] Generally C_{10}-substituted hexahydrophenanthrenes are formed, although the method has also been used[202] for compounds unsubstituted at C_{10}. When 2-β-phenethylcyclohexanone itself is treated with PPA[203] a mixture of 1,2,3,4-tetrahydro- and 1,2,3,4,4a,9,10,10a-octahydrophenanthrenes is produced.

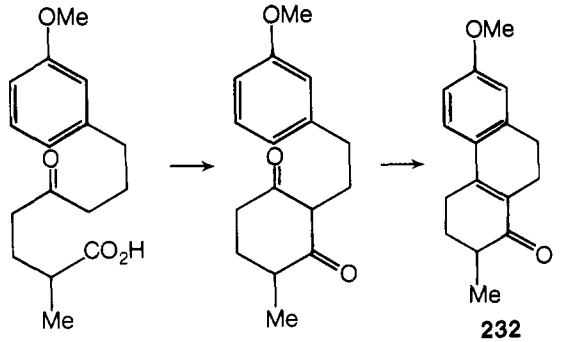
2-Acyl-1-chlorocyclohexenes **223** (R = Me, Et, or Pr^i), obtained by the reaction between cyclohexanone and the acyl chloride, have been converted via the ketals **224** and **225** into the phenanthrenes **226**, R = Me, Et, or Pr^i, respectively.[204]



Hydrophenanthrones can be prepared from cyclohexane-1,3-dione derivatives of the types **227**, **228**, and **229**. Compounds of the type **227** have been prepared[72a,73,205] by the cyclization of appropriate 5-oxo-8-aryloctanoic acids (see also sections III.B and III.C), for example, **230** → **231** → **232**. The octanoic acids themselves are available from the reaction of a 4-phenylbutyroyl chloride with ethyl sodio-α-acetylglutarate.[72a,73,122,205]

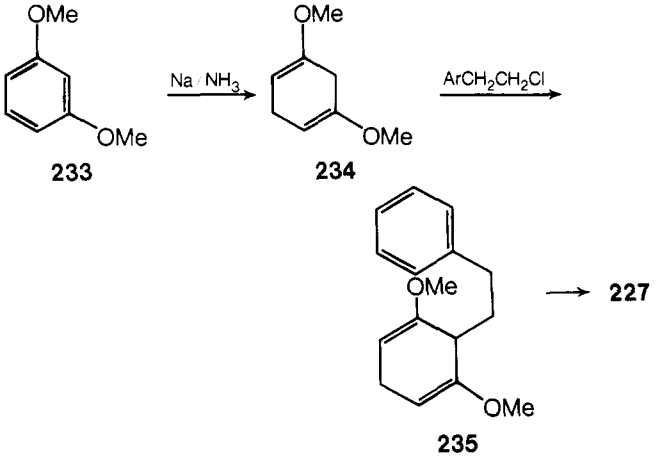


227 228 229



230 231 232

The diketones **227** can also be obtained[205] by alkylation of dihydroresorcinols with β-arylethyl halides or by use[206] of the Birch reduction, for example, **233** → **234** → **235** → **227**. 1,3-



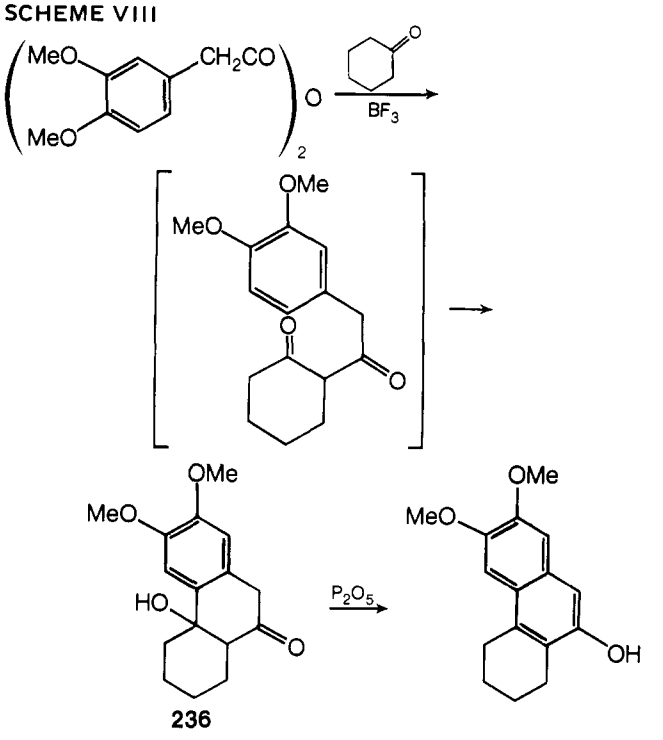
233 234 235 227

Diketones of the type **228** may be involved[207] when an arylacetic acid anhydride is condensed with cyclohexanone in the presence of boron trifluoride. Acylation and cyclization occurred to provide **236** in 68% yield from homoveratric acid (Scheme VIII). Substituted cyclohexanones have been used but only those arylacetic acids carrying electron-releasing substituents and not sterically hindered by ortho substitution have been successfully reacted.[207]

Syntheses of phenanthrenes involving diketones of the type **229** were devised by Walker[208,209] and are summarized in Scheme IX. The phenylacetic acids must possess one or more methoxyl (or hydroxyl) group, but 2,4-dihydroxybenzaldehyde can be replaced by 2,5-dihydroxy- or 2,4,6-trihydroxybenzaldehyde or by phloroacetophenone.

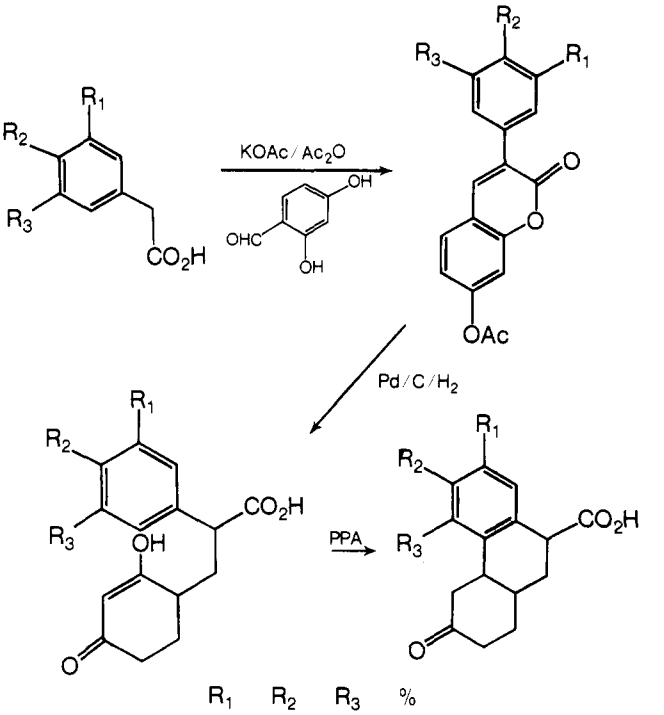
β-Phenethylcyclohexenones are[210] cyclized by PPA to provide 1-ketooctahydrophenanthrenes in good yield (see Table XIV). The required starting materials have been obtained by the cyclization of suitable alkenoic acids (see section III.B). Thus if **237** (R = H or Cl) is treated[69] with PPA, the phenanthrene derivative **239** (R = H or Cl) is produced in 17–45% yield. Good yields of **239** are realized if the acid chloride of **237** is allowed to react with acetyl tetrafluoroborate or silver tetrafluoroborate; with the latter reagent, the intermediate **238** can be isolated. When **237** (R = OMe) is similarly treated,[70] the phenanthrone **239** (R = OMe) is produced in 15% yield only. Cyclization of **240** with aluminum trichloride results[211,212] in **243** in only 5% yield, but when a mixture of phenylacetyl chloride and cyclohexene is treated with aluminum trichloride, **243** is produced[213] in 55% yield; presumably **240** is an intermediate. However, when **241** is cyclized[214] with PPA, the yield of **242** is 90%. Photocyclization of **240** was more successful;[215] the cis/trans mixture **243** was formed in 87% yield when a benzene solution of **240** containing boron trifluoride etherate was irradiated.

SCHEME VIII



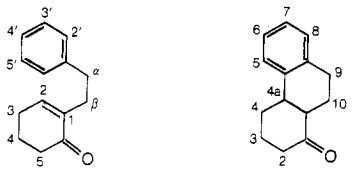
236

SCHEME IX



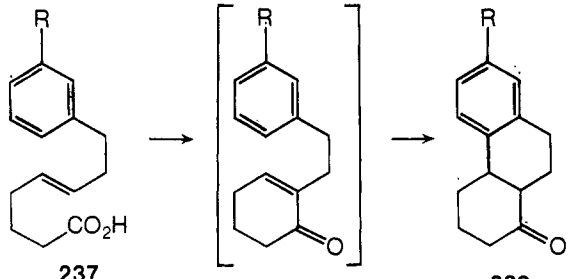
R_1	R_2	R_3	%
H	H	H	Nil
OMe	H	H	95
OMe	OMe	H	52
OMe	OMe	OMe	28
OH	H	H	71

TABLE XIV. Cyclization of Cyclohexenones

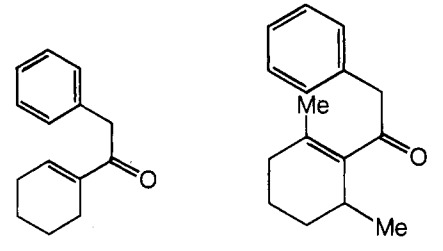


2	2^1	3^1	4^1	4a	6	7	8	%	Ref
Me	H	H	H	Me	H	H	H		*a*
Me	H	H	H	Me	H	H	H	66	210
Me	H	H	H	Me	H	H	H	70	*b*
Me	H	OMe	H	Me	H	OMe	H	89	210
Me	H	OMe	H	Me	H	OMe	H	65	*b*
Me	H	Pr^i	H	Me	H	Pr^i	H	65	*b*
Me	H	Pr^i	H	Me	H	Pr^i	H	65	*c*
H	OMe	H	OMe	H	OMe	H	OMe		*d*

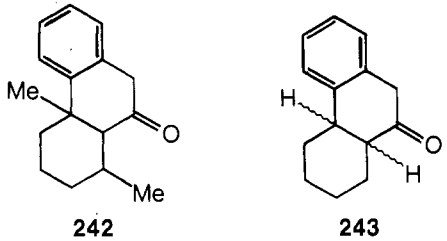
[a] J. A. Barltrop and A. C. Day, *Chem. Ind. (London)*, 1450 (1959). [b] G. Stork and A. Burgstahler, *J. Am. Chem. Soc.*, **73**, 3544 (1951). [c] M. Sharma, U. R. Ghatak, and P. C. Dutta, *Tetrahedron*, **19**, 985 (1963). [d] S. Imai, *J. Sci. Hiroshima Univ., Ser. A-2*, **35**, 161 (1971); *Chem. Abstr.*, **77**, 61657 (1972).



237 238 239



240 241

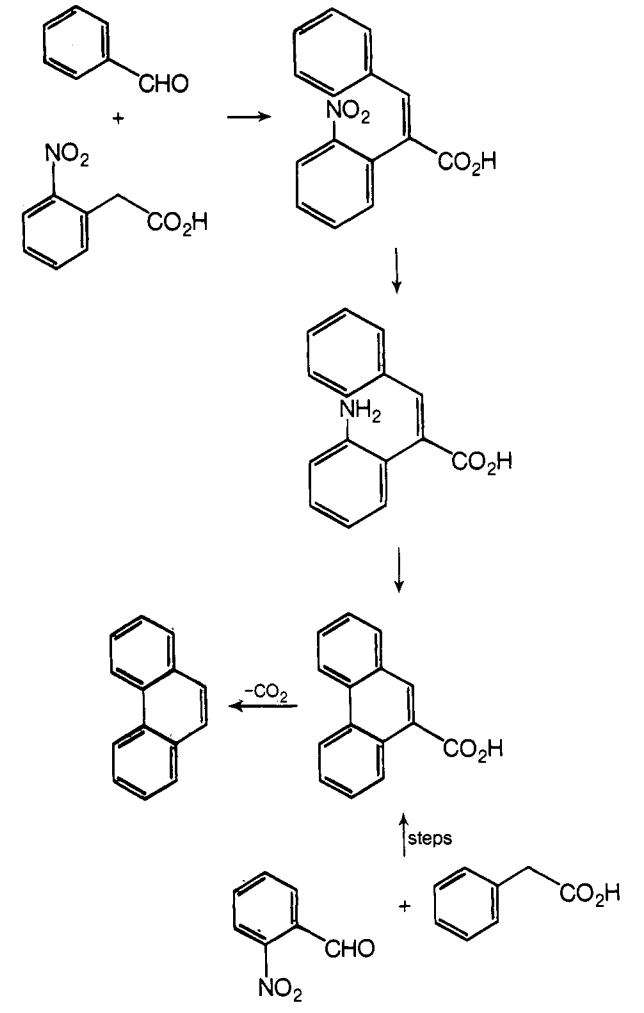


242 243

3. *The Pschorr Synthesis*

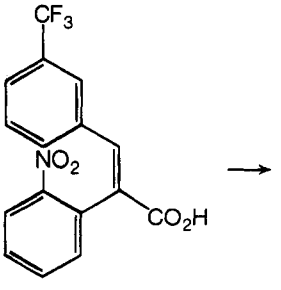
The Pschorr reaction is the name given to a group of related procedures whereby polycyclic systems are formed by the union of two aryl nuclei, effected by the decomposition of an appropriate diazonium salt. Pschorr himself[216] was concerned with the production of phenanthrenes (Scheme X), and the method constituted the first route for the preparation of substituted phenanthrenes with substituents in known orientations. The method, which is still used extensively for phenanthrenes, has also been used in the preparation of polycyclic systems and for the synthesis of certain alkaloids.[5d] Two previous reviews[5a,b] have surveyed the scope of the reaction, and a tabular summary of all reactions reported up to 1956 has been included in one of them.[5a] A description has also been given[5a] of all of the stages of the synthesis (preparation of the α-(*o*-nitroaryl)-*trans*-cinnamic

SCHEME X

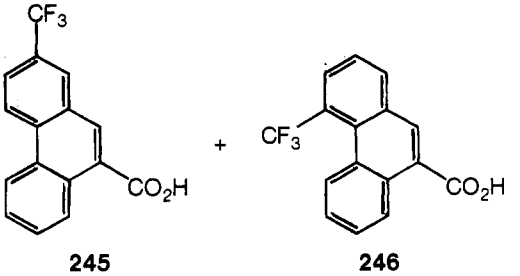


acid, reduction to the amine, diazotization and ring closure, and decarboxylation of the phenanthrene-9-carboxylic acid formed). Although the reaction sequences are still widely used, there are certain limitations. Thus, *o*-nitrobenzaldehydes and substituted phenylacetic acids are often difficult to obtain so that the α-aryl-*trans*-cinnamic acids are inaccessible. Overall yields in the five-stage synthesis are often low.

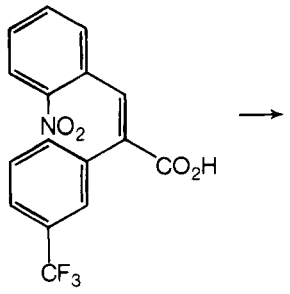
Cyclization to phenanthrenes has been achieved with α-arylcinnamic acids carrying one or more halogen, alkyl, alkoxy,



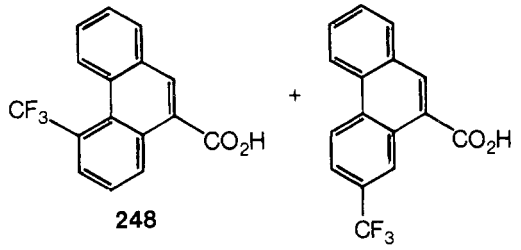
244



245 246



247



248 249

nitro, amino, cyano, ester, or hydroxyl functions in most positions around the ring system. Although 4,5-dialkoxy substituted phenanthrenes have been prepared by the Pschorr route, 4,5-dialkyl substitution is much more difficult to achieve, presumably owing to steric hindrance. When the substituents in the rings of the cinnamic acid are unsymmetrically placed, cyclization can result in a mixture of two products. Recent examples[217] are **244** → **245** + **246** and **247** → **248** + **249**. Blocking one of the sites of cyclization with Br (which can be removed subsequently by reduction) has been used frequently to obtain isometrically pure phenanthrenes.

A summary of the literature from 1957 to date on phenanthrenes prepared by the Pschorr reaction appears as Table XV.

A number of sets of conditions has been used[218] to decompose the diazonium salt to effect the cyclization, and these are the following:

A. Copper-catalyzed decomposition in aqueous sulfuric acid solution (Pschorr's original method).

B. Thermal decomposition in aqueous acid solution in the absence of copper.

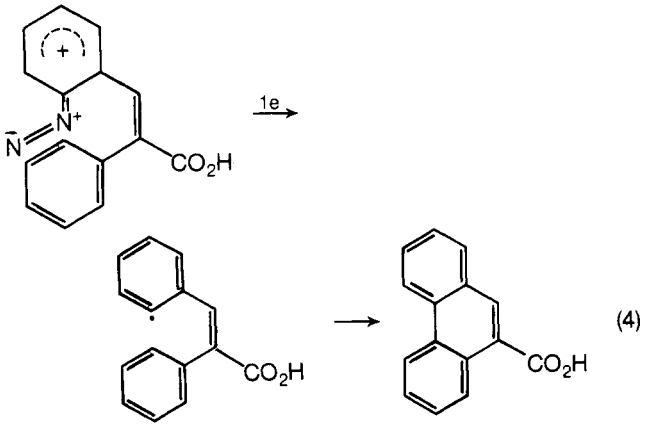
C. Copper-catalyzed decomposition in aqueous alkaline solution.

D. Thermal decomposition of a suspension of the diazonium fluoroborate in acetone in the presence of copper.

The mechanism of the Pschorr reaction has been the subject of considerable investigation in recent years, and this work has been reviewed by Williams[218] and by Abramovitch.[5c,219] Both homolytic and heterolytic pathways have been considered; it is now generally accepted that the precise mechanism operative will depend very largely upon the conditions of the reaction, which also affect the yield considerably.

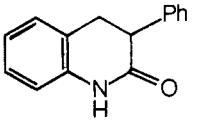
Gellert and Chauncy[220,221] found that yields of cyclized product can be improved substantially by diazotizing the amine with amyl nitrite in acetone, followed by the addition of sodium iodide; very little 2-iodo-α-phenylcinnamic acid is formed. The iodide ion may be[222] responsible for the production of a redox system involving aryl and iodine radicals. In the copper-catalyzed reaction it is postulated[222] that a redox system is involved with the generation of aryl radicals which are not free, but which are held on the copper surface. When the 2-diazonium α-arylcinnamic acids are treated with pyridine,[223] or reduced electrochemically in aprotic solvents,[222] free radicals are formed which then cyclize to phenanthrenes in high yield (eq 4).

Various modifications of the Pschorr cyclization have been examined; a popular one involves[224] the condensation of a benzaldehyde with a phenylacetonitrile, followed by cyclization, hydrolysis of the resulting 9-phenanthronitrile, and decarboxyl-

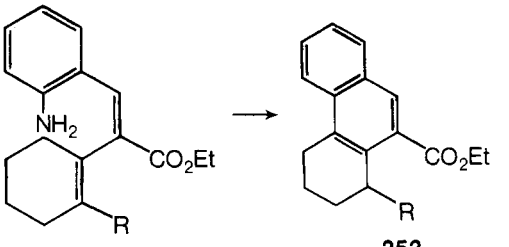


(4)

ation. It seems, however, to offer very little advantage. 9,10-Dihydrophenanthrenes can[225] be obtained from dihydrocinnamic acids via 3-phenyl-3,4-dihydrocarbostyrils **250**. An interesting variation involves[226,227] the cyclization of **251** (R = H or Me), when a tetrahydrophenanthrene **252** (R = H or Me) results in about 30% yield.

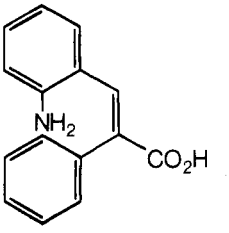


250



251 252

An intriguing reaction was reported by Sieper[228] who found that when **253** is treated with *N*-nitrosodiphenylamine, phenanthrene-9-carboxylic acid is the product.



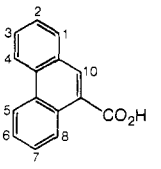
253

4. *Photocyclization of Stilbenes*

Stilbenes may undergo one or more different types of photochemical reactions, depending upon conditions.[229,230] The more important ones are isomerization, dimerization, and cyclodehydrogenation. This section of the review is concerned with the latter reaction, and will be confined to a survey of the conversion of simple stilbenes to phenanthrenes, although interesting and useful applications of the photocyclodehydrogenation reaction have also been made to polynuclear aromatic structures[6,231] and to heterocyclic compounds.[232] This discussion will concentrate upon work that has been published since the review by Stermitz,[6a] although, for the sake of completeness, Table XVI contains the material summarized previously.

The photochemical transformation of stilbenes to phenanthrenes was established in the early 1950's.[233,234] In the last 10–15 years, the reaction has been shown[6a,231] to provide a valuable synthetic route to certain types of substituted phenanthrenes (Table XVI), especially since stilbenes themselves

TABLE XV. Phenanthrenes by Pschorr Reaction



R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	Conditions	Yield	Ref
H	H	H	H	H	$O-CH_2CH_2-O$		H	HNO_2, H_2SO_4, Cu	8.2	*a*
H	H	H	H	$O-CH_2CH_2-O$		H	H	HNO_2, H_2SO_4, Cu	3.1	*a*
H	$O-CH_2-O$		H	H	$O-CH_2-O$		H		21	*b*
H	$O-CH_2-O$		H	$O-CH_2-O$		H	H		8	*b*
H	$O-CH_2-O$		H	$O-CH_2-O$		H	Br			*b*
OMe	H	H	H	H	$O-CH_2-O$		H	H_2SO_4/MeOH, $NaNO_2$, Cu	10	*c*
H	H	OMe	OEt	H	H	H	H	H_2SO_4/MeOH, $NaNO_2$, Cu	65	*d*
H	H	OEt	OMe	H	H	H	H	H_2SO_4/MeOH, $NaNO_2$; Cu	63	*d*
H	H	H	H	H	H	H	H	AmONO/acetone, $\Delta + I_2$	70	220
H	OMe	OMe	H	H	H	H	H	AmONO/acetone, $\Delta + I_2$	72	221
H	OMe	OMe	H	H	OMe	H	H	AmONO/acetone, $\Delta + I_2$	60	221
H	OMe	OMe	H	OMe	OMe	H	H	AmONO/acetone, $\Delta + I_2$	45	221
H	OMe	OMe	H	H	OMe	OMe	H	AmONO/acetone, $\Delta + I_2$	45	221
H	OMe	OMe	H	H	Me	H	H	AmONO/acetone, $\Delta + I_2$	55	221
H	H	H	H	H	H	H	Me	AmONO/acetone, $\Delta + I_2$	65	221
H	OMe	H	OMe	H	H	OAc	H		10	*e*
H	$O-CH_2-O$		H	OMe	OMe	OMe	H			*f*
H	OMe	OMe	H	OMe	OMe	H	H	BuONO/acetone		*g*
H	H	OMe	OMe	OMe	OMe	H	Br	AmONO, NaH_2PO_2, Cu	10	*h*
H	H	OMe	OMe	OMe	OMe	H	H	AmONO, NaH_2PO_2, Cu	20	*h*
H	OMe	OMe	H	H	OMe	H	H	$NaNO_2$, Cu-bronze	56	*i*
H	OMe	OMe	H	H	OMe	OMe	H		4.5	*j*
H	OMe	OMe	H	OMe	OMe	H	H		3.5	*j*
H	H	OMe	H	H	OMe	OMe	H	BuONO, acetone, Cu	41	*k*
H	OMe	$O-CH_2-O$		H	OMe	OMe	H	PentylONO/Cu	42	*l*
H	OMe	OMe	H	H	OMe	H	H			*m*
H	OMe	OMe	H	OMe	H	OMe	H	AmONO, Cu	31	*n*
H	OMe	OMe	H	OMe	OMe	OMe	H	AmONO, Cu	30	*n*
H	H	OMe	OEt	H	H	OMe	OEt			*o*
H	H	OMe	OEt	H	H	OEt	OMe			*o*
H	H	OMe	OMe	H	H	OEt	OEt			*o*
H	OMe	H	H	H	$O-CH_2-O$		H	HNO_2/MeOH, Na_2HPO_4, Cu	25	*p*
H	OMe	H	H	$O-CH_2-O$		H	Br	HNO_2/MeOH, Na_2HPO_4, Cu		*p*
H	H	OMe	OMe	H	OMe	H	OEt			*q*
H	H	OMe	OEt	H	OMe	H	OMe			*q*
H	H	OMe	OMe	H	OEt	H	OMe			*q*
OMe	H	OMe	H	$O-CH_2-O$		H	Br			*r*
H	H	OMe	H	$O-CH_2-O$		H	Br	AmONO		*s*
H	H	NO_2	H	OMe	H	OMe	H	HNO_2/H_2SO_4	47	*t*
H	H	F	H	H	H	H	H	AmONO, NaH_2PO_2, Cu	67	*u*
H	H	CF_3	H	H	H	H	H	AmONO, NaH_2PO_2, Cu	37	*u*
H	H	H	H	H	F	H	H	AmONO, NaH_2PO_2, Cu	34	*u*
H	H	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	30	*u*
H	H	H	H	H	CF_3O	H	H	AmONO, NaH_2PO_2, Cu	57	*u*
H	H	Br	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	67	*u*
H	H	Cl	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	61	*u*
H	H	I	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	54	*u*
H	H	CF_3	H	H	Br	H	H	AmONO, NaH_2PO_2, Cu	69	*u*
H	H	CF_3	H	H	Cl	H	H	AmONO, NaH_2PO_2, Cu	52	*u*
H	H	CF_3	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	42	*u*
H	CF_3	H	H	H	H	H	H	AmONO, NaH_2PO_2, Cu	31	217
H	H	H	CF_3	H	H	H	H	AmONO, NaH_2PO_2, Cu	6	217
H	H	H	H	CF_3	H	H	H	AmONO, NaH_2PO_2, Cu	12	217
H	H	H	H	H	H	CF_3	H	AmONO, NaH_2PO_2, Cu	12	217
Br	H	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	36	217
H	Cl	H	H	CF_3	H	H	H	AmONO, NaH_2PO_2, Cu	20	217
H	Cl	H	H	H	H	CF_3	H	AmONO, NaH_2PO_2, Cu	20	217
H	CF_3	H	H	H	H	Cl	H	AmONO, NaH_2PO_2, Cu		217
H	H	H	CF_3	H	H	Cl	H	AmONO, NaH_2PO_2, Cu		217
H	Br	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	51	217
H	H	H	Br	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	65	217
H	Cl	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	79	217
H	CF_3	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	20	217
H	H	H	CF_3	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	40	217

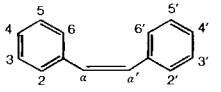
TABLE XV (continued)

H	H	Me	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	40	217
H	H	SO_2Me	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	40	217
H	H	CF_3	H	H	H	Cl	H	AmONO, NaH_2PO_2, Cu	58	217
Cl	Cl	H	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	45	217
Cl	H	Cl	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	37	217
Me	H	Me	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	43	217
Br	H	Br	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	71	217
H	Cl	Cl	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	31	217
H	Br	Br	H	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	33	217
H	Cl	H	Cl	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	69	217
H	Br	H	Br	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	35	217
H	CF_3	H	CF_3	H	Cl	H	H	AmONO, NaH_2PO_2, Cu	60	217
H	CF_3	H	CF_3	H	H	Cl	H	AmONO, NaH_2PO_2, Cu	72	217
H	CF_3	H	CF_3	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	52	217
H	H	CF_3	H	Cl	H	Cl	H	AmONO, NaH_2PO_2, Cu	17	217
H	H	CF_3	H	H	Cl	Cl	H	AmONO, NaH_2PO_2, Cu	45	217
H	CF_3	H	CF_3	H	Cl	Cl	H	AmONO, NaH_2PO_2, Cu	45	217
H	Br	Br	Br	H	CF_3	H	H	AmONO, NaH_2PO_2, Cu	43	217
H	H	OBz	H	H	OMe	OMe	H			217
H	H	OBz	H	OMe	OMe	H	H			*v*
H	H	OMe	H	H	$O-CH_2-O$		H	AmONO/DMF	68	*w*
H	H	H	Me	H	H	H	H	Electrochem. redn of diazonium salt	90	*w*
H	OMe	H	H	H	H	H	H	Electrochem. redn of diazonium salt	80	*w*
H	H	OMe	H	H	H	H	H	Electrochem. redn of diazonium salt	94	*w*
H	H	H	OMe	H	H	H	H	Electrochem. redn of diazonium salt	93	*w*
H	Br	H	H	H	H	H	H	Electrochem. redn of diazonium salt	94	*w*
H	H	H	Br	H	H	H	H	Electrochem. redn of diazonium salt	96	*w*
H	H	H	H	H	$O-CH_2-O$		H	$NaNO_2$, H_2SO_4, Cu	43	*x*
H	H	H	H	$O-CH_2-O$		H	H	$NaNO_2$, H_2SO_4, Cu	36	*x*
H	H	OMe	H	H	$O-CH_2-O$		H	$NaNO_2$, H_2SO_4, Cu	31	*y*
H	H	OMe	H	$O-CH_2-O$		H	H	$NaNO_2$, H_2SO_4, Cu	5	*y*
H	H	OMe	H	$O-CH_2-O$		H	Br	$NaNO_2$, H_2SO_4, Cu	32	*y*
H	H	H	H	OMe	OMe	H	Br			*z*
H	H	OMe	H	OMe	OMe	H	Br			*z*
H	H	H	H	H	C_6H_5	H	H	AmONO, Cu		*aa*
H	H	H	H	Cl	OMe	OMe	Cl		65	*bb*

[a] M. Sasamoto, *Chem. Pharm. Bull.*, **8**, 324 (1960); *Chem. Abstr.*, **55**, 10448 (1961). [b] H. Shirai and N. Oda, *ibid.*, **10**, 31 (1962); *Chem. Abstr.*, **58**, 3368 (1963). [c] H. Shirai and N. Oda, *J. Pharm. Sci. Jpn.*, **76**, 1287 (1956); *Chem Abstr.*, **51**, 9646 (1951). [d] M. Tomita, Y. Watanabe, and H. Furukawa, *Yakugaku Zasshi*, **81**, 942 (1961); *Chem Abstr.*, **55**, 27393 (1961). [e] M. R. Letcher and L. R. M. Nhamo, *J. Chem. Soc. Perkin Trans. 1*, 1263 (1973). [f] R. M. Letcher and L. R. M. Nhamo, *ibid.*, 2941 (1972). [g] E. Gellert, T. R. Govindachari, M. V. Lakshmikantham, I. S. Ragadi, R. Rudzats, and N. Viswanathan, *J. Chem. Soc.*, 1008 (1962). [h] D. M. Hall, J. E. Ladbury, M. S. Lesslie, and E. E. Turner, *ibid.*, 3475 (1956). [i] P. Marchini and B. Belleau, *Can. J. Chem.*, **36**, 581 (1958). [j] T. R. Govindachari, M. V. Lakshmikantham, K. Nagarajan, and B. R. Pai, *Tetrahedron*, **4**, 311 (1958). [k] T. R. Govindachari, B. R. Pai, S. Prabhakar, and T. S. Savitri, *ibid.*, **21**, 2573 (1965). [l] G. Y. Moltrasio, D. Giacopello, and M. J. Vernengo, *Aust. J. Chem.*, **26**, 2035 (1973). [m] C. K. Bradsher and H. Berger, *J. Am. Chem. Soc.*, **79**, 3287 (1957). [n] R. M. Letcher and L. R. M. Nhamo, *J. Chem. Soc. C.*, 3070 (1971). [o] T. Ibuka, *Yakugaku Zasshi*, **85**, 579 (1965); *Chem. Abstr.*, **63**, 11629 (1965). [p] H. Shirai and N. Oda, *Chem. Pharm. Bull.*, **8**, 727 (1960); *Chem. Abstr.*, **55**, 15441 (1961). [q] Y. Watanabe and M. Matsumura, *Yakugaku Zasshi*, **83**, 991 (1963); *Chem. Abstr.*, **60**, 4201 (1964). [r] M. Pailer and P. Bergthaller, *Monatsh. Chem.*, **98**, 579 (1967). [s] M. Pailer and P. Bergthaller, *ibid.*, **97**, 484 (1966). [t] E. Hardegger, H. R. Biland, and H. Corrodi, *Helv. Chim. Acta*, **46**, 1354 (1963). [u] E. A. Nodiff, K. Tanabe, C. Seyfried, S. Matsuura, Y. Kondo, E. H. Chen, and M. P. Tyagi, *J. Med. Chem.*, **14**, 921 (1971). [v] W. Wiegrebe, L. Faber and H. Budzikiewcz, *Justus Liebigs Ann., Chem.* **733**, 125 (1970). [w] M. Pailer, W. Streicher, G. Widermann, and M. Rotter, *Monatsh. Chem.*, **103**, 659 (1972). [x] H. Shirai and N. Oda, *Yakugaku Zasshi*, **79**, 241, 259 (1959); *Chem. Abstr.*, **53**, 13, 123d (1959). [y] H. Shirai and N. Oda, *Yakugaku Zasshi*, **79**, 245 (1959); *Chem. Abstr.*, **53**, 13, 124b (1959). [z] R. Crohare, H. A. Priestap, M. Farina, M. Cedola, and E. A. Ruveda, *Phytochemistry*, **13**, 1957 (1974). [aa] A. L. J. Beckwith and M. J. Thompson, *J. Chem. Soc.*, 73 (1961). [bb] C. K. Bradsher, F. C. Brown, and P. H. Leake, *J. Am. Chem. Soc.*, **79**, 1468 (1957).

are readily available compounds.[235-239] Cyclization occurs[6b,240,241] from the *cis*-stilbene; a *trans*-stilbene is first photoisomerized to its geometric isomer (Scheme XI), which then cyclizes, reversibly, to a 4a,4b-dihydrophenanthrene. The latter, which is now believed to be the trans isomer **254**, then loses hydrogen to some acceptor molecule to give, in a dark reaction, the aromatic phenanthrene.[6b,242-245] Summaries of the early work on the mechanism of this reaction have been provided by Stermitz[6a] and by Blackburn and Timmons.[6b] When the stilbene **255** is photolyzed,[246-248] the product **256** is stable and can be isolated. The geometry at the 4a,4b positions has been established as trans by oxidation[249] of **256** to *rac*-butane-1,2,3,4-tetracarboxylic acid (**257**). Controversy remains as to whether the *cis*-stilbene cyclizes to **254** from an excited singlet state or from a vibrationally excited ground state. Calculations based upon the HMO method suggest[250] that a higher vibrational ground state is involved. It can be predicted[251] from orbital symmetry considerations that an excited singlet state of *cis*-stilbene should give *trans*-4a,4b-dihydrophenanthrene (**254**) by conrotatory closure, whereas the cis isomer of **254** should result from a "hot" ground state. Scholz et al.[252] used simple HMO to calculate free valence indexes in the first excited state of a large number of compounds containing the stilbene-like moiety, and it was concluded[253] that if the sum of the free va-

TABLE XVI. The Photocyclodehydrogenation of Stilbenes



R_2	R_3	R_4	R_5	R_6	R_2'	R_3'	R_4'	R_5'	R_α	R_α'	Conditions[a]	% yield	Ref
H	H	H	H	H	H	H	H	H	H	H	I	60–90	*f*
H	H	H	H	H	H	H	H	H	H	H	I	58	*g*
H	H	H	H	H	H	H	H	H	H	H	I		257
H	H	H	H	H	H	H	H	H	H	H	I	73	235
H	H	H	H	H	H	H	H	H	H	H	Air/Ph_2Se_2	86	262
H	H	H	H	H	H	H	H	H	H	H	I	82	241
H	OMe	H	H	H	H	OMe	H	H	H	H	Pentane	73	*g*
H	H	F	H	H	H	H	H	H	H	H	I	76	235
H	H	Cl	H	H	H	H	H	H	H	H	I	76	235
H	H	Br	H	H	H	H	H	H	H	H	I	76	235
H	H	OMe	H	H	H	H	H	H	H	H	I	38	257
H	H	OMe	H	H	H	H	H	H	H	H	I	42	235
H	H	Me	H	H	H	H	H	H	H	H	I	67	235
H	H	CF_3	H	H	H	H	H	H	H	H	I	60	235
Cl	H	H	H	H	H	H	H	H	H	H	I	57	235
OMe	H	H	H	H	H	H	H	H	H	H	I	46	235
Me	H	H	H	H	H	H	H	H	H	H	I	57	235
H	CF_3	H	H	H	H	H	H	H	H	H	I	89	235
CF_3	H	CF_3	H	H	H	H	H	H	H	H	I	89	235
H	H	OMe	H	H	H	H	OMe	H	H	H	I		257
H	H	NO_2	H	H	H	H	OMe	H	H	H	I	Nil	257
H	H	NO_2	H	H	H	H	NMe_2	H	H	H	I	Nil	257
H	OAc	OAc	H	H	H	OMe	H	OMe	H	H	III	15	*h*
H	OMe	H	OMe	H	Me	H	H	H	H	H	I	33	*i*
OAc	OMe	H	H	H	H	H	H	H	H	H	I	65	*j*
H	H	Pr*i*	H	H	H	H	Pr*i*	H	H	H	I	69	*k*
H	Me	H	H	H	H	H	H	H	H	H	I	. .[b]	255
H	Cl	H	H	H	H	H	H	H	H	H	I	. .[b]	255
H	CF_3	H	H	H	H	H	H	H	H	H	I	. .[b]	255
Me	Me	H	H	H	Me	Me	H	H	H	H	Petrol/I_2	50	258
Me[c]	Me	H	H	H	Me	Me	H	H	H	H	Petrol/I_2		258
OMe	H	H	H	OMe[c]	H	H	H	H	H	H	I	90	261
OMe	H	H	H	OMe[c]	OMe	H	H	H	H	H	I	91	261
OMe	H	OMe	H	OMe[c]	H	H	H	H	H	H	I	85	261
OMe	H	OMe	H	OMe[c]	OMe	H	H	H	H	H	I	74	261
Me	H	OMe	H	OMe[c]	H	H	H	H	H	H	I	38	261
Me	H	OMe	H	OMe[c]	OMe	H	H	H	H	H	I	63	261
OMe	H	H	H	OMe[c]	H	H	Cl	H	H	H	I	56	261
OMe	H	H	H	OMe[c]	H	H	CO_2Me	H	H	H	I	48	261
OMe	H	H	H	OMe[c]	H	H	Pr*i*	H	H	H	I	87	261

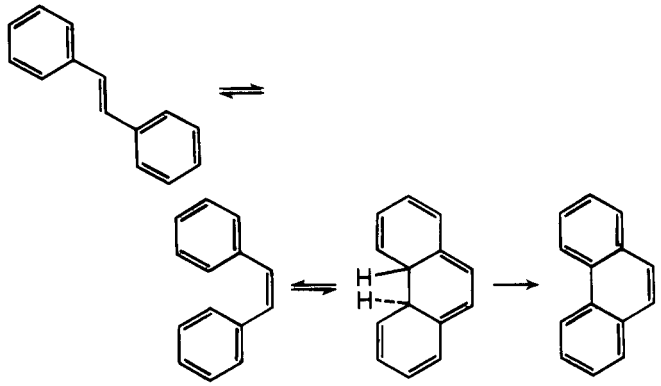
H	H	OH	H	H	H	H	OH	H	Et	Et	HOAc/N_2	14	*g*
H	H	OH	H	H	H	H	OH	H	Et	Et			247–249
													246
H	H	OMe	H	H	H	H	OMe	H	Et	Et	HOAc/N_2	54	264, *g*
H	H	H	H	H	H	H	H	H	CO_2H	H	I	72	235
H	H	H	H	H	H	H	H	H	Ph	H	I	85	235
H	H	H	H	H	H	H	H	H	$-CH_2CH_2CH_2-$		I	71	235
H	OMe	OMe	H	H	H	OMe	OMe	H	CO_2Me	H	I	31	*l*
H	H	OMe	H	H	H	H	OMe	H	Me	Me		11	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	Et	I	16	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	Me	III	0.6	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	Me	IV	47	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	Et	IV	55	263, 264
H	H	OMe	H	H	H	H	OMe	H	Et	Et	IV	63	263, 264
H	H	H	H	H	H	H	H	H	Me	Me	I	28	263, 264
H	H	H	H	H	H	H	H	H	Me	Me	IV	55	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	H	I	32	263, 264
H	H	OMe	H	H	H	H	OMe	H	Me	H	IV	33	263, 264
H	H	OMe	H	H	H	H	H	H	H	H	I	31	263, 264
H	H	OMe	H	H	H	H	H	H	H	H	IV	39	263, 264
Me	H	H	F	H	Me	H	H	F	H	H	I	49	259
H	H	Br	H	H	H	H	Br	H	H	H	I	40	260
H	H	CN	H	H	H	H	CN	H	H	H	I	40	260
H	Me	H	Me	H	H	Me	H	Me	H	H	I	60	260
Me[c]	H	H	F	H	Me	H	H	F	H	H	I	13	259
Me[c]	H	Me	H	Me	H	H	H	H	H	H	I	3	260
I[c]	H	H	H	H	H	H	H	H	H	H	V	90	265, 270
I[c]	H	H	H	H	Me	H	H	H	H	H	V	96	265, 270
I[c]	H	H	H	H	H	H	H	H	H	CO_2Me	V	71	265, 270
I[c]	H	H	H	H	Me	H	H	H	H	CO_2Me	V	62	265, 270
I[c]	H	H	H	H	H	H	H	H	H	NO_2	V	40	265, 270
I[c]	H	H	H	H	CO_2R	H	O–CH_2–O		H	NO_2	V	26	265, 270
I[c]	H	H	H	OMe	CO_2Me	H	O–CH_2–O		H	NO_2	V	54	265, 270
I[c]	H	H	H	H	CO_2Me	H	H	H	H	NO_2	V	50	265
I[c]	H	OMe	H	OMe	CO_2Me	H	O–CH_2–O		H	NO_2	V		269
H	H	H	H	H	H	H	H	H	CN	CN	C_6H_6	23	*m*
H	H	H	H	H	H	H	H	H	OMe	H	MeOH		281
H	H	H	H	H	H	H	H	H	OAc	H	HOAc		281
H	H	H	H	H	H	H	H	H	CN	CN	II	60[d]	271
H	H	H	H	H	H	H	H	H	H	CN	II	3	271
H	H	H	H	H	H	H	H	H	H	$CONH_2$	II	41[d]	271
H	H	H	H	H	H	H	H	H	H	Me	II	39[d]	271

TABLE XVI (continued)

R_2	R_3	R_4	R_5	R_6	R_2'	R_3'	R_4'	R_5'	R_α	R_α'	Conditions[a]	% yield	Ref
H	H	H	H	H	H	H	H	H	Me	Me	II	50[d]	271
H	H	H	H	H	H	H	H	H	H	Ph	II	57[d]	271
H	H	H	H	H	H	H	H	H	Ph	Ph	II	70[d]	271
H	H	H	H	H	H	H	H	H	CO–O–CO		II	43[d]	271
H	H	H	H	H	H	H	H	H	CN	CN	II	85[d]	271
H	H	H	H	H	H	H	H	H	CN	CN		22[d]	272
H	H	H	H	H	H	H	H	H	CN	CN		60[d]	272
H	H	H	H	H	H	H	H	H	CO_2Me	H	$CHCl_3$/No O_2	72[d]	273, 276
H	H	H	H	H	H	H	H	H	COPh	CO_2H	C_6H_6/O_2		*n*
H	H	H	H	H	H	H	H	H	CN	OMe			277
H	H	H	H	H	H	H	H	H	CN	CN	$CHCl_3$	7[d]	*o*
H	H	H	H	H	H	H	H	H	OC–NH–CO		EtOH	4[d]	*o*
Me	H	Me	OMe	H	Me	H	Me	OMe	H	H	I_2	20[e]	256
H	OAc	H	H	H	H	OMe	H	OMe	H	H	EtOH	33	*p*
Me	H	Me	OMe	H	Me	H	Me	OMe	H	H	I_2/O_2		*q*
H	OMe	H	OMe	H	H	OAc	OMe	H	H	H	III	35–40	*r*
H	OMe	OMe	OMe	H	H	OAc	OMe	H	H	H	III	35–40	*r*
C_6H_5	H	H	H	H	H	H	H	H	H	H	c-$C_6H_{12}/C_6H_6/I_2$	64	*s*
H	H	C_6H_5	H	H	H	H	H	H	H	H	I_2	57	*s*
H	C_6H_5	H	H	H	H	H	H	H	H	H	I_2	86	*s*
H	OMe	H	OMe	H	H	OH	H	H	H	H			*t*
H	OMe	H	OMe	H	H	OMe	OBz	H	H	H			*u*
H	H	Br	H	H	H	H	H	H	CO_2Me	H	I_2/O_2		*v*
OMe	Me	CO_2Me	H	H	OMe	H	H	H	H	H	I		*w*
H	H	CHO	H	H	H	H	CHO	H	H	H	C_6H_6	40	*x*, *y*
H	OMe	H	OMe	H	H	OH	OMe	H	H	H			*z*
D[c]	H	D	H	D	D	H	D	H	H	H	I	39	*aa*
D[c]	H	D	H	D	H	H	H	H	H	H	I	27	*aa*
H	D	H	D	H	H	D	H	D	H	H	I	25	*aa*
H	D	H	D	H	H	H	H	H	H	H	I	33	*aa*
D	D	D	D	D	H	H	H	H	H	H	I	48	*aa*
H	Me	H	Me	H	H	H	CO_2Me	H	H	H	C_6H_6/I_2	68	*bb*

[a] Conditions: I, cyclohexane/I_2/air; II, cyclohexane/I_2/N_2; III, ethanol/I_2/air; IV, ethanol/I_2/CuX_2; V, cyclohexane. [b] About 1:1 mixture of 2- and 4-substituted phenanthrenes. [c] This group is lost in the cyclization. [d] As 9,10-dihydrophenanthrene. [e] As 1,3,6,8-tetramethyl-4,5-dimethoxyphenanthrene (4.5%) + 1,3,6-trimethyl-4,6-dimethoxyphenanthrene (15.5%). [f] F. B. Mallory, C. S. Wood, J. T. Gordon, L. C. Lindquist, and M. L. Savitz, *J. Am. Chem. Soc.*, **84**, 4361 (1962). [g] P. Hugelshofer, J. Kalvoda, and K. Schnaffner, *Helv. Chim. Acta*, **43**, 1322 (1960). [h] R. M. Letcher, L. R. M. Nhamo, and I. T. Gumiro, *J. Chem. Soc. Perkin Trans. 1*, 206 (1972). [i] M. V. Sargent and D. O'N. Smith, *J. Chem. Soc. C*, 329 (1970). [j] H. D. Becker, *J. Org. Chem.*, **34**, 2026 (1969). [k] A. P. Bindra, J. A. Elix, and M. V. Sargent, *Aust. J. Chem.*, **24**, 1721 (1971). [l] R. B. Herbert and C. J. Moody, *J. Chem. Soc. D*, 121 (1970). [m] J. H. Boyer and R. Selvarajan, *J. Am. Chem. Soc.*, **91**, 6122 (1969). [n] G. Rio and J. C. Hardy, *Bull. Soc. Chim. Fr.*, 2642 (1967). [o] M. V. Sargent and C. J. Timmons, *J. Am. Chem. Soc.*, **85**, 2186 (1963). [p] R. M. Letcher and L. R. M. Nhamo, *J. Chem. Soc. Perkin Trans. 1*, 1263 (1973). [q] M. S. Newman and H. M. Chung, *J. Org. Chem.*, **39**, 1036 (1974). [r] R. M. Letcher and L. R. M. Nhamo, *J. Chem. Soc. Perkin Trans. 1*, 2941 (1972). [s] S. C. Dickerman and I. Zimmerman, *J. Org. Chem.*, **39**, 3429 (1974). [t] A. Stoessl, G. L. Rock, and M. H. Fisch, *Chem. Ind. (London)*, 703 (1974). [u] T. Hashimoto, K. Hasegawe, H. Yamaguchi, M. Saito, and S. Ishimoto, *Phytochemistry*, **13**, 2849 (1974). [v] T. Lin, R. E. Harmon, W. Pierantoni, and J. C. W. Su, *Org. Prep. Proced. Int.*, **6**, 185 (1974). [w] I. M. Cresp, R. G. F. Giles, and M. V. Sargent, *Chem. Commun.*, 11 (1974). [x] J. Y. Wong, C. Manning, and C. C. Leznoff, *Angew. Chem.*, **86**, 734 (1974). [y] J. Y. Wong, C. Manning, and C. C. Leznoff, *Angew. Chem., Int. Ed. Engl.*, **13**, 666 (1974). [z] R. M. Letcher, *Phytochemistry*, **12**, 2789 (1973). [aa] J. L. Charlton, B. Kostyk, and H. K. Lai, *Can. J. Chem.*, **52**, 3577 (1974). [bb] A. H. A. Tinnemans and W. H. Laarhoven, *J. Am. Chem. Soc.*, **96**, 4611 (1974).

SCHEME XI



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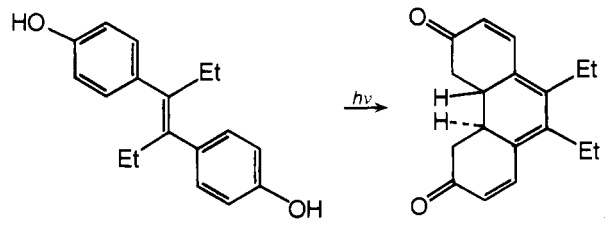
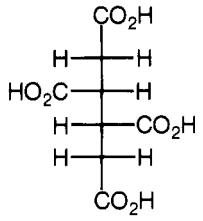
lence indexes of the terminal atoms concerned in the photocyclization exceeds a certain value, cyclization to the phenanthrene will occur. In those cases where cyclization may proceed in more than one way, it was possible to predict the orientation by these calculations. It has been pointed out,[254] however, that this is not the only factor affecting the ability of a given stilbene derivative to undergo cyclization.



255 256



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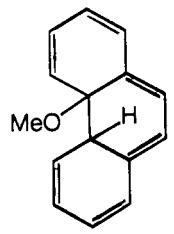
The general procedure for effecting photocyclization involves[235] the irradiation of a solution of the stilbene (0.01 mol) in cyclohexane (1 l.) containing iodine (0.0005 mol) in an atmosphere of air, using a 100-W medium-pressure mercury lamp. At higher stilbene concentrations, side reactions occur,[235] mainly dimerization to tetraarylcyclobutanes. In the absence of air yields of phenanthrenes are reduced, and in the absence of both air and iodine very little phenanthrene is formed.

Phenanthrenes have been obtained (Table XVI) in good yields from stilbenes substituted in the α, ortho, and/or para positions with methyl, methoxyl, halogen, cyano, phenyl, carboxyl, alkoxycarbonyl, and trifluoromethyl groups. Meta-substituted stilbenes may give rise to mixtures of 2- and 4-substituted phenanthrenes which are not always easy to separate. It has been found[255] that these two modes of cyclization can occur at comparable rates despite the steric hindrance to the formation of the 4-substituted phenanthrene. Yields of the highly sterically hindered 4,5-disubstituted phenanthrenes are usually low under the normal conditions.[256] The cyclization fails if the stilbene carries acetyl,[235] dimethylamino,[235,257] or nitro[235,257] substituents. The carbon–iodine bond is very easily broken photochemically so that this substituent is frequently lost from any position in the stilbene. Loss of methyl, chloro, bromo, methoxyl, or carboxyl groups from the ortho positions, especially of poly-ortho-substituted stilbenes, has been observed.[256,258-261] Even with *o*-methoxystilbene, photolysis under nitrogen results[261] in a 58% yield of phenanthrene itself; presumably the intermediate is **258**, which readily loses methanol. When a choice exists between methyl and methoxyl loss, only the latter was observed.[261]

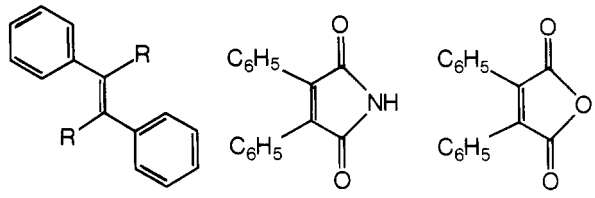


258

Recent modifications to the photolysis reaction have included the use of selenium radicals, generated from diphenyl selenide, as the dehydrogenating agent.[262] Good yields of highly sterically hindered phenanthrenes have been achieved in this way. The presence of cupric ions was found[263,264] to increase yields of phenanthrenes from α,α^1-disubstituted stilbenes, but to have little or no effect upon stilbenes with one or no α substituents.

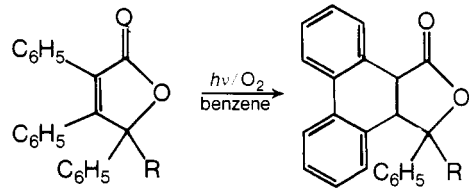
An important modification of the original photocyclization reaction, which was first described by Kupchan and Wormser,[265] involves the photolysis of *o*-iodostilbene.[266] The C–I bond is broken during the course of the reaction, which proceeds via free-radical intermediates rather than through the formation of **254**. A number of compounds has been studied[208,209,265,267-270] by this method which is particularly effective for the preparation of nitrophenanthrenes.[265,271]

Irradiation of **259** (R = CN), **260**, and **261** in solution exposed to air gave[272,273] mainly the expected phenanthrenes, but small amounts of the corresponding 9,10-disubstituted-9,10-dihydrophenanthrenes were also produced. However, when the same



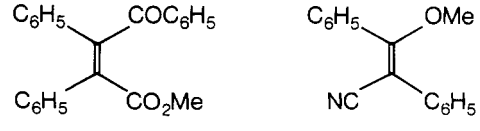
259 260 261

compounds were irradiated in degassed ethanol, only the 9,10-dihydrophenanthrenes were formed. Subsequent work showed that the 9,10-dihydrophenanthrenes are the products only when *two* strongly electron-withdrawing groups are present at the α,α^1 positions in the stilbene. The reaction, which is of some synthetic value, probably involves a radical reaction, and does not proceed via the 4a,4b-dihydrophenanthrene.[274] However, evidence has been presented[275,272] for ionic rather than radical behavior when diphenylfumarodinitrile (**259**, R = CN) is photocyclized. The irradiation of **262** is reported[276] to give the



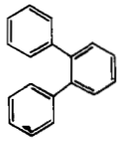
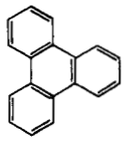
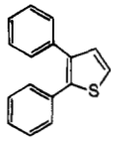
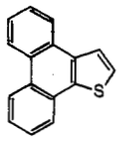
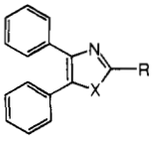
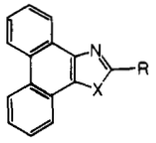
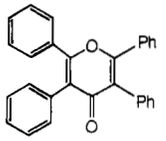
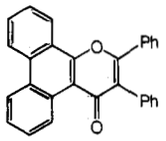
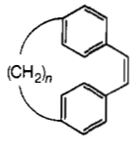
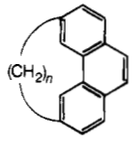
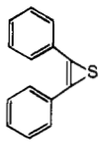
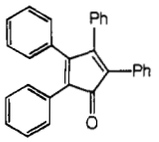
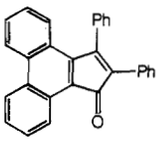
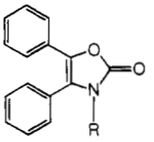
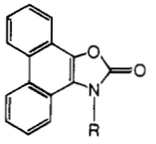
262 263

9,10-dihydrophenanthrene **263** when R = OMe or OH, but the corresponding phenanthrene is isolated when R = H or $OCOCH_3$. The photolysis of **264** is also reported[276] to yield the aromatic



264 265

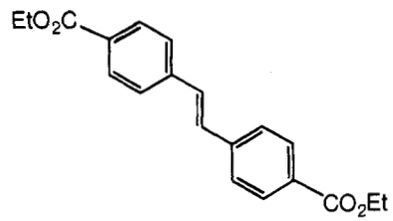
TABLE XVII. Cyclization of Substituted Stilbenes

Stilbene derivative	Product	% yield	Ref
			*a*
		70	*b*
			*c*
	X R		
	O Me	55	
	S Me	87	
	NH H	75	
	NH Ph	40	
	NPh Ph	90	
		7	*d*
			*e*
	n = 7–10		
	Phenanthrene		*f*
			*g*
			*h*
	R = H	39	
	R = Me	70	

[a] T. Sato, Y. Goto, and K. Hata, *Bull. Chem. Soc., Jpn.*, **40**, 1994 (1967); *Chem. Abstr.*, **67**, 108 482 (1967). [b] H. Wynberg, H. van Driel, R. M. Kellogg, and J. Butler, *J. Am. Chem. Soc.*, **89**, 3487 (1967). [c] J. L. Cooper and H. H. Wasserman, *Chem. Commun.*, 200 (1969). [d] N. Ishibe, M. Odani, and M. Sunami, *ibid.*, 1034 (1971). [e] S. E. Potter and I. O. Sutherland, *ibid.*, 520 (1973). [f] T. Sato, Y. Goto, T. Tohyama, S. Hayashi, and K. Hata, *Bull. Chem. Soc. Jpn.*, **40**, 2975 (1967); *Chem. Abstr.*, **68**, 77 447 (1968). [g] E. J. McNelis, U.S. Patent 3,123,649 (1964); *Chem. Abstr.*, **60**, 144545 (1964). [h] A. S. Dey and J. L. Neumeyer, *J. Med. Chem.*, **17**, 1095 (1974).

phenanthrene; photocyclization of **265** gives[277] 9-cyano-10-methoxyphenanthrene in 65% yield. When **266** was irradiated,[278] the expected phenanthrene was accompanied by the anthracene derivative **267**; this was thought to arise from the triplet state of **266**.

Although this review is concerned essentially with simple



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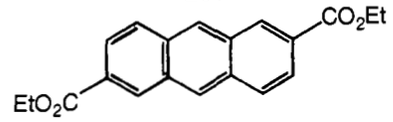
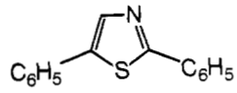


267

stilbene derivatives, the compounds in Table XVII represent potentially interesting extensions to the photocyclization reaction. This extension does not always give unambiguous results; rearrangement of the heterocyclic precursor may occur before cyclization, e.g.,[279] **268** → **269** + **270** → **271**.



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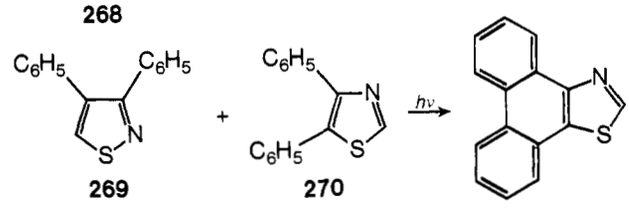
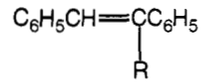


269 **270** **271**

When diphenylacetylene is irradiated in ethanol,[280] a 10% yield of phenanthrene is realized. It was later found[281] that in methanol as solvent the major product is **272**, whereas in acetic acid solution the products are **273** and 9-acetoxyphenanthrene.

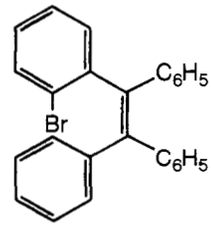


272, R = OMe
273, R = OAc

5. *Miscellaneous*

Treatment of **274** with butyllithium, followed by carbon dioxide, gives the expected acid, but with dimethyl carbonate a 25% yield of 9,10-diphenyl-9,10-dihydrophenanthrene can be isolated.[282]

A very interesting and potentially important method is due to



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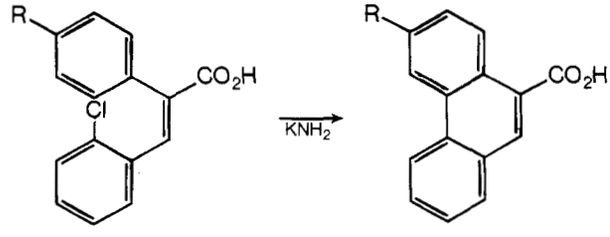
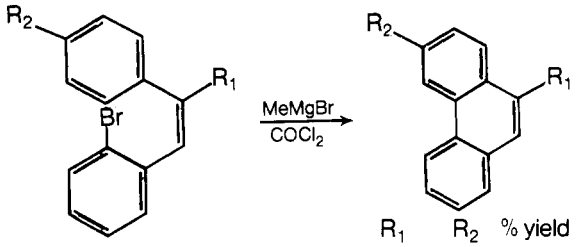


275 **276**

Kessar et al.,[283] in which chloro acids of the type **275** (R = H or OMe), undergo cyclodehydrohalogenation when reacted with potassium amide in liquid ammonia. The phenanthrene-9-carboxylic acids **276** (R = H or OMe) are formed in 46 and 55% yield, respectively. The reaction was originally thought to involve a benzyne intermediate, but this is now[284] known not to be so. The full scope of the reaction is not yet known.

When stilbenes such as **277** are treated[285,286] with methylmagnesium bromide and cobalt chloride, high yields of phenanthrenes can be obtained (Scheme XII). It is believed that

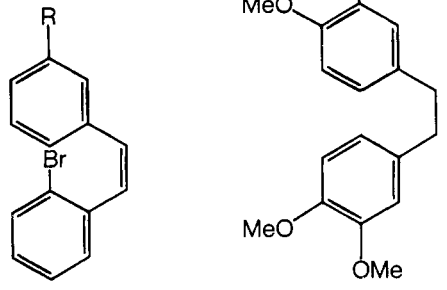
SCHEME XII



277

R_1	R_2	% yield
H	H	75
H	Me	78
H	OMe	85
C_6H_5	H	75

homolytic cleavage of the carbon–halogen bond occurs to give a radical which then reacts in an intramolecular substitution reaction with the second aryl nucleus. When cyclization can occur in two possible ways, for example, from **278**, a mixture of the 2- and 4-substituted phenanthrenes results.[287,288] Treatment of tetraphenylethylene with chromyl chloride gives[289] 9,10-diphenyl-9,10-dihydrophenanthrene in high yield. Tetraphenylethylene can[290] be oxidized electrolytically to 9,10-diphenylphenanthrene. The diarylethane **279** has been cyclized



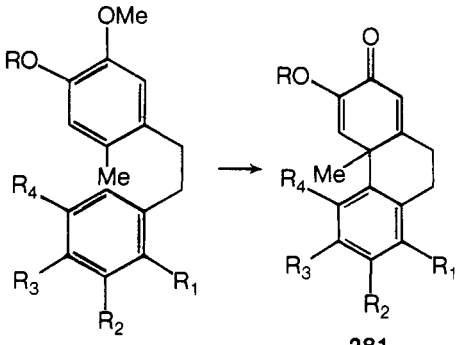
278 279

electrolytically[291,292] to the 9,10-dihydrophenanthrene in almost quantitative yield, and this type of reaction has been extended by Stermitz et al. to give **281** from **280** (Scheme XIII). When the diarylethane **282** is allowed to react with a HF/SbF_5 mixture at 0°, three products are formed[294] in ratios that vary with time (Scheme XIV).

An unexpected cyclization to **284** occurred[295] when **283** was allowed to react with potassium permanganate in acetic acid. When **279** is treated with tris(*p*-bromophenyl)ammoniumyl hexachloroantiminate ($(p\text{-}BrC_6H_4)_3N^+SbCl_6^-$), 2,3,6,7-tetramethoxyphenanthrene is formed via a cation radical.[296] Phenol oxidation techniques have been applied[297] with the treatment of **285** with ferric chloride or ceric ammonium sulfate, but the yield of the 9,10-dihydrophenanthrene was not given. An interesting phenanthrene ring formation occurs (70% yield) when **286** is treated[298,299] with iodine and mercuric acetate, followed by heating to 230–290° with copper bronze.

9,10-Diphenylphenanthrene is formed[300] when **287** is treated with aluminum trichloride.

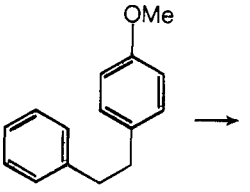
SCHEME XIII



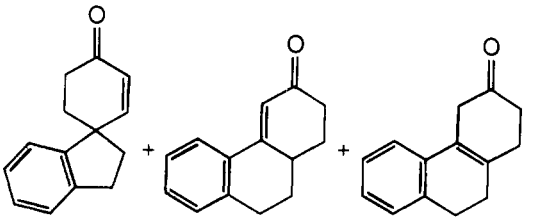
280 281

R	R_1	R_2	R_3	R_4	%
Me	H	OMe	OMe	H	98
Me	OMe	H	H	OMe	88
Et	H	OMe	OMe	H	"high"

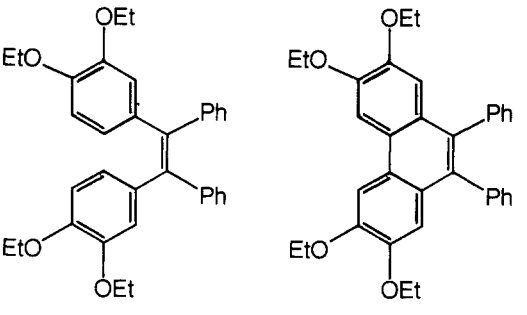
SCHEME XIV



282



Time (min)	%	%	%
20	24	23	5
70	4	66	4
120	0	56	44



283 284

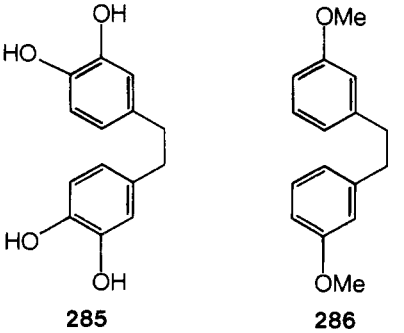


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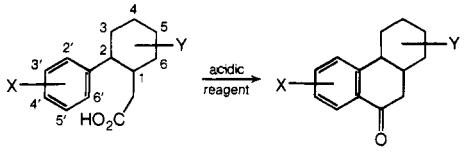
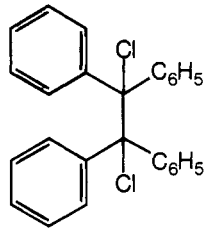
TABLE XVIII. Cyclization of 2-Phenylcyclohexylacetic Acid Derivatives



2-Arylcyclohexylacetic acids					
	X	Y	Acidic reagent	% yield	Ref
trans	H	H	H_2SO_4	65–79	306–309, 311
			HF	88–92	211, 310, 312
trans	H	4-Me	PPA	82	318
trans	3'-Me	H	HF	85	*c*
trans	3'-OMe	H	HF	87	*c*
trans	2'-Me	4-Me	PPA	8	318
trans	4'-Me	4-Me	PPA	25	318
trans	4'-Cl	H	PPA		317
cis	4'-Cl	H	PPA		317
trans	2',5'-$(Me)_2$	H	HF	90	*d*
cis	2',5'-$(Me)_2$	H	HF		314
	2',5'-$(Me)_2$	4-Me			*e*
trans	2',3'-$(OMe)_2$	H	$ZnCl_2/Ac_2O/AcOH$	75	309
trans	2',3'-$(OMe)_2$	3-OH	$ZnCl_2/Ac_2O/AcOH$	35	309
trans	H	3-Oxo	H_2SO_4	40	*f*
trans	H	5-Oxo	H_2SO_4	60	303
	H	6-Oxo	PPA	100	316
			HF		*g*
trans	2'-Me	3-Oxo	HF	100	304
trans	3'-Me	3-Oxo	HF	89	*c*
trans	3'-OMe	3-Oxo	HF	98 crude	*c, h*
trans	2',5'-$(Me)_2$	3-Oxo	HF	82[b]	*d*
trans	2',5'-$(OMe)_2$	3-Oxo	HF	86	*d*
trans	2',3'-$(OMe)_2$	3-Oxo[a]	$ZnCl/Ac_2O/AcOH$	65	309

[a] As its ethylene glycol ketal. [b] Accompanied by a small % of the unexpected *cis* isomer, shown to be the thermodynamically more stable in base-catalyzed equilibrium, probably due to base-catalyzed isomerization during workup. [c] S. Bien and M. Boazi, *J. Chem. Soc.*, 1727 (1959). [d] S. Bien, L. Cohen, and K. Scheinmann, *ibid.*, 1495 (1965). [e] D. N. Chatterjee and S. P. Bhattacharjee, *Indian J. Chem.*, 12, 958 (1974). [f] C. F. Koelsch, *J. Am. Chem. Soc.*, 73, 2951 (1951). [g] L. E. Coles, V. S. Gandhi, and D. W. Mathieson, *J. Pharm. Pharmacol.*, 12, 518 (1960). [h] S. Bien and D. Ginsburg, *J. Chem. Soc.*, 2065 (1963).



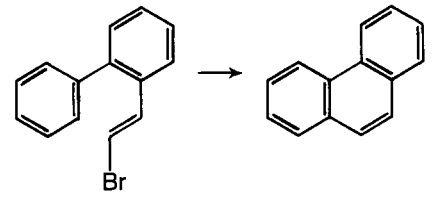
287

E. Cyclization of Biphenyloid Compounds

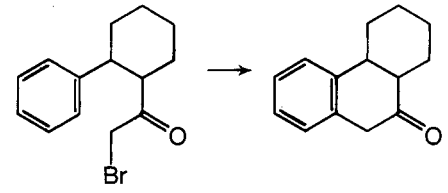
Biphenyls and phenylcyclohexanes, suitably substituted in the 2 position, are converted by a variety of alkylation, acylation and condensation procedures into phenanthrene derivatives. A number of 2,2'-disubstituted biphenyls may be cyclized, mainly by reductive methods or the Wurtz reaction, leading to the formation of phenanthrenes. These methods provide valuable synthetic routes to a number of phenanthrenes, especially those containing 9- and 10-substituents.

1. Intramolecular Cycloalkylation

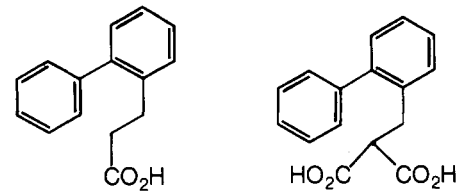
Few examples of this type have been examined. However, β-bromo-2-phenylstyrene is cyclized (see eq 5) by treatment[301] with either zinc chloride (73% yield) or aluminum trichloride (39% yield) and bromomethyl 2-phenylcyclohexyl ketone by aluminum trichloride[211] (11% yield, see eq 6). Radical-induced cycloalkylations leading to phenanthrenes are also known. Thus, **288** and **289** give 9,10-dihydrophenanthrene and phenanthrene respectively, when oxidized[302] either electrolytically or with lead tetraacetate.



(5)



(6)

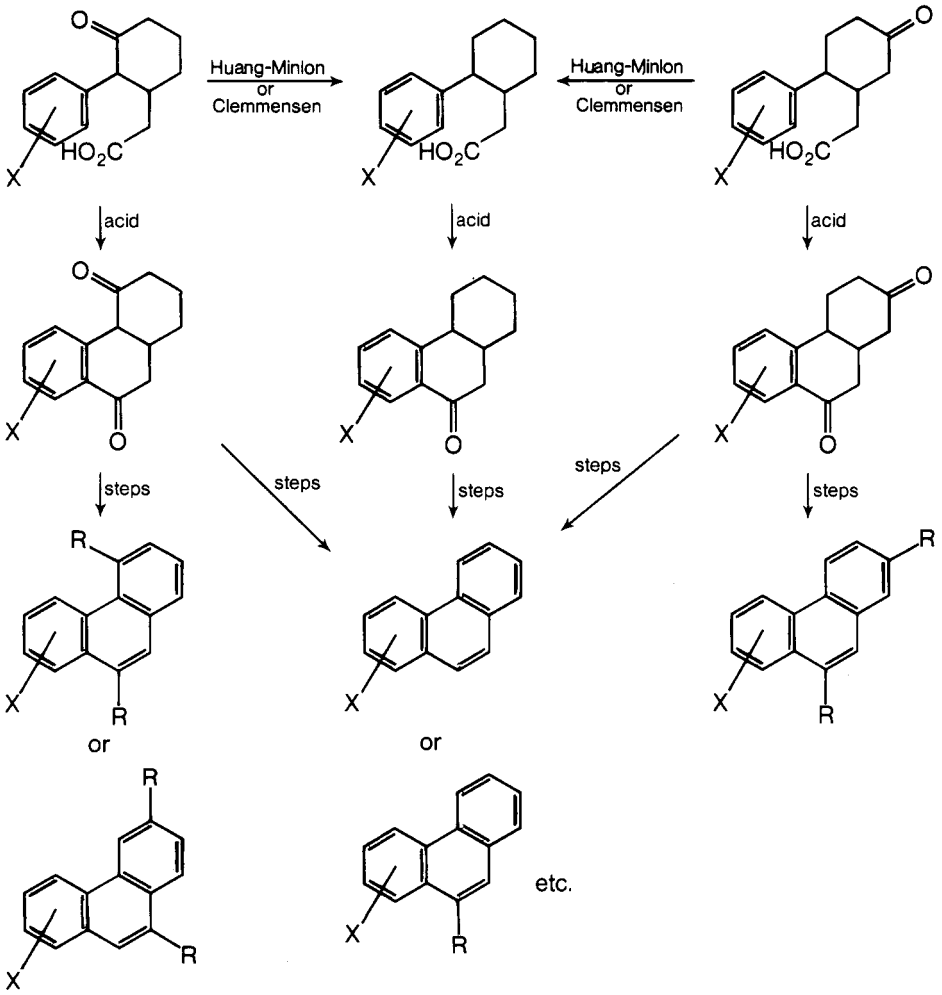


288 289

2. Intramolecular Cycloacylation

The cyclization of 2-arylcyclohexylacetic acids in the presence of acidic reagents to give 1,2,3,4,4a,9,10,10a-octahydro-9-phenanthrones often occurs in high yield (>80%). These phenanthrones have been aromatized by standard procedures, when additional alkyl or aryl substituents may be introduced by Grignard reactions of the carbonyl group. The 2-arylcyclohex-

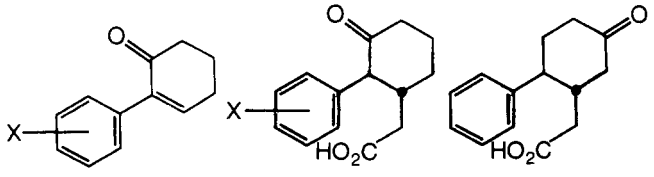
SCHEME XV



ylacetic acids can be prepared by reduction of the corresponding 2-aryl-3-oxo- or 6-aryl-3-oxocyclohexylacetic acids. These compounds, when cyclized before reduction, provide further sites for the introduction of substituents by the Grignard reaction[303] or by base-catalyzed alkylation.[304] This method provides an extremely valuable route to a wide range of phenanthrenes, which is illustrated in Scheme XV. Terpenoids have been obtained[305] in this manner.

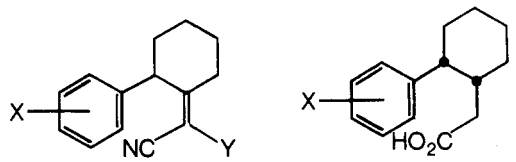
The cyclization of the parent compound, 2-phenylcyclohexylacetic acid, has been reported by several authors,[211,306-312] the confusion in the earlier literature being settled by Gutsche and Johnson.[211] The ring closure has been catalyzed by a variety of acidic reagents and applied to a number of 2-arylcyclohexyl- and 2-aryloxocyclohexylacetic acids (see Table XVIII).

The starting materials for this route are readily available. The commonest preparation utilizes a 2-arylcyclohex-2-enone,[313] **290**, which undergoes Michael addition with a malonic or a cy-

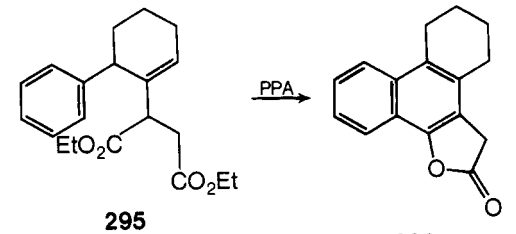


290 **291** **292**

anoacetic ester. The product on hydrolysis and decarboxylation was found[309] to yield a *trans*-2-aryl-3-oxocyclohexylacetic acid, **291**. 4-Phenylcyclohex-3-enone has similarly been converted[303] into *trans*-6-phenyl-3-oxocyclohexylacetic acid (**292**). A variation involves condensation of cyanoacetic ester[308] or malononitrile[314] with 2-arylcyclohexanones. The products **293** (Y = CO_2R or CN) catalytically reduced, followed by hydrolysis and decarboxylation, yield *cis*-2-arylcyclohexylacetic acids (**294**). A similar process involves the Stobbe condensation of 2-phenylcyclohexanone with diethyl succinate; the product **295** has been cyclized[315] to **296** in 80% yield. A different approach was used

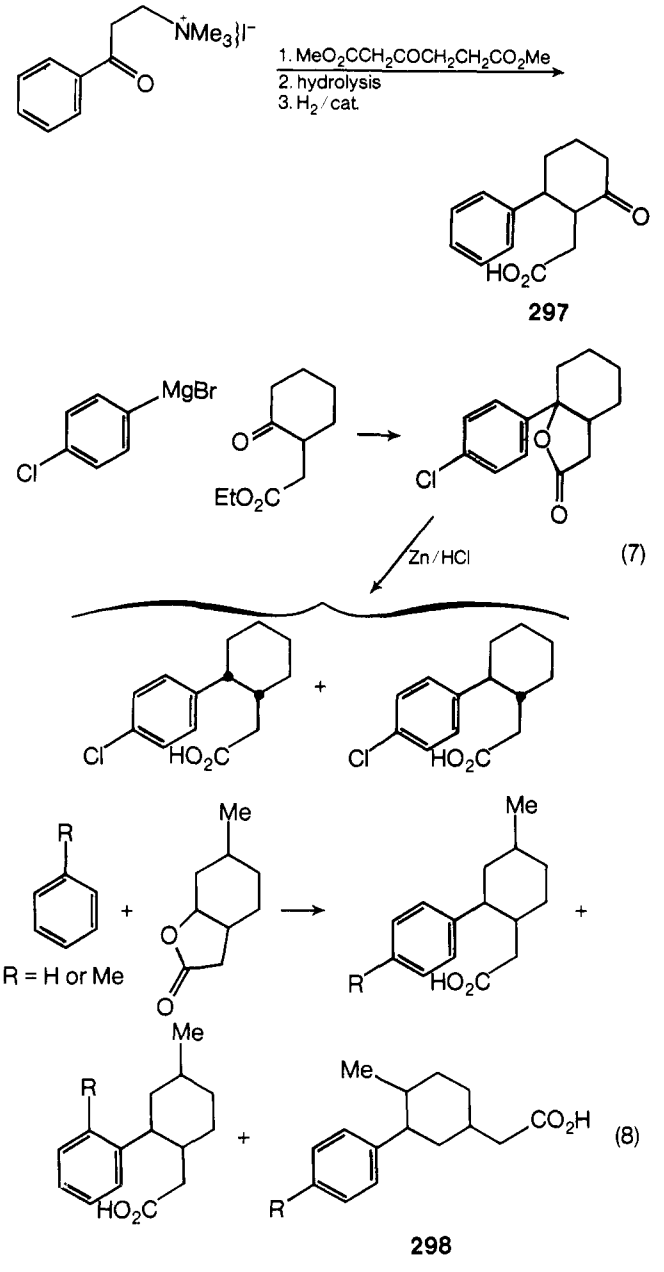


293 **294**

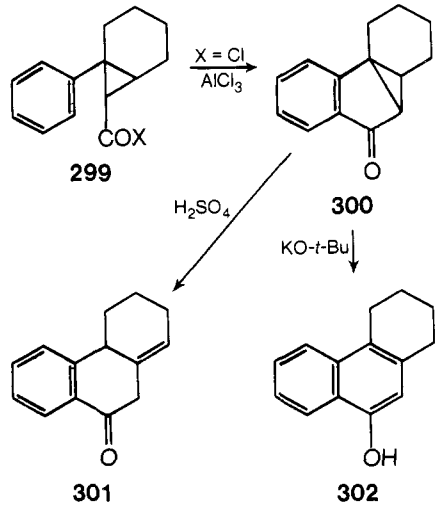


295 **296**

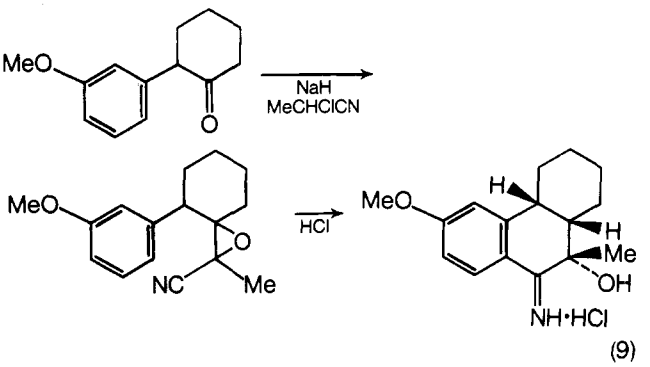
by Nasipuri and Roy,[316] in which β-dimethylaminopropiophenone methiodide was condensed with the potassium derivative of dimethyl 3-oxoadipate, followed by hydrolysis and reduction to yield **297** of unspecified configuration. 2-Arylcyclohexylacetic acids have also been prepared by the action[317] of a Grignard reagent with ethyl 2-oxocyclohexylacetate (see eq 7) and by an abnormal Friedel–Crafts reaction[318] of 2-hydroxy-4-methylcyclohexylacetic acid lactone (see eq 8), in which **298** was an unexpected by-product.

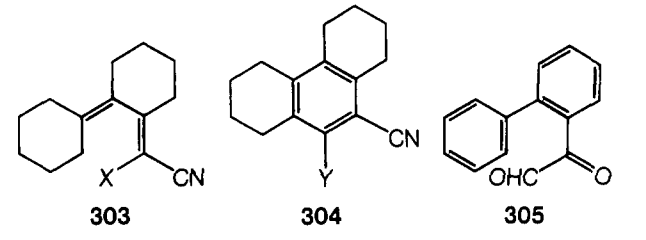


Besinet et al.[319] have described a process, which is related to the cyclization of 2-arylcyclohexylacetic acids. 1-Phenylcyclohexene was converted into **299** (X = OEt) by treatment with ethyl diazoacetate, and the derived acid chloride **299** (X = Cl) was cyclized with aluminum trichloride. The product **300** was rearranged, in unstated yield, to **301** and **302** by the action of acid or base, respectively. The method would appear to be of little general synthetic utility.



The cyclization[320] of 2-arylcyclohexylacetonitriles is also known for one example (see eq 9). The related dinitrile **303** (X = CN) gives a quantitative yield of 9-amino-10-cyano-1,2,3,4,5,6,7,8-octahydrophenanthrene (**304**, Y = NH_2) by treatment[321] with acids, while **303** (X = CO_2Et) gives the corresponding 9-hydroxy compound **304** (Y = OH).





Intramolecular cycloacylation reactions of the fully aromatic biphenyls are of little importance in phenanthrene synthesis. However, ethyl 2-biphenylylacetate[322] and 2-biphenylylacetonitrile[323] have been cyclized by sulfuric acid treatment, to yield 9-hydroxy- and 9-aminophenanthrene, respectively. The action[324] of a zinc chloride, acetic anhydride, and acetic acid mixture on 2-biphenylylacetic acid produces 9-acetoxyphenanthrene in 55% yield. Selenium dioxide converts[325] 2-acetylbiphenyl into 9,10-phenanthraquinone, either directly in dioxane (15% yield) or indirectly in ethanol via **305**, which was cyclized by treatment with aluminum trichloride/anisole (overall yield 11%). An attempt to extend this procedure to 5-chloro-2-acetylbiphenyl gave[325] only a 0.4% yield of 3-chloro-9,10-phenanthraquinone.

3. Intramolecular Condensation

The cyclization of 2-biphenylylaldehydes, e.g., **306** (R_1 = H, R_2 = Me) in the presence of acid was found[326] to be accompa-

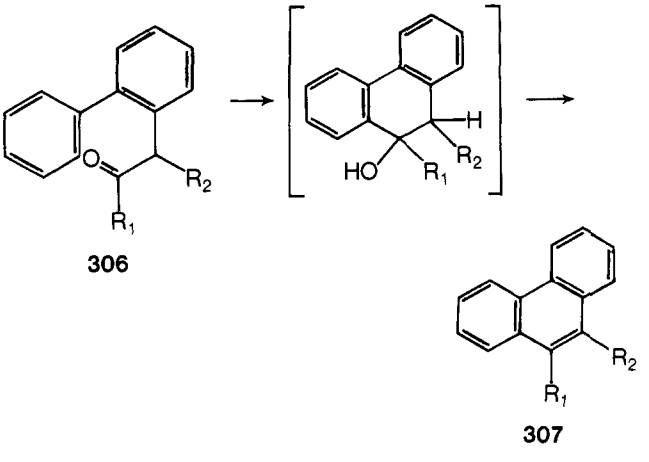
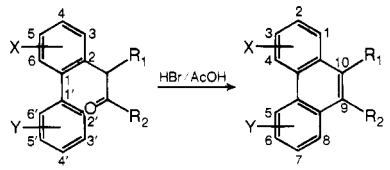


TABLE XIX. Aromatic Cyclodehydration[a] of 2-Biphenylylmethylcarbonyl Compounds



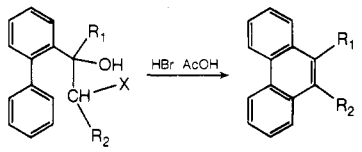
Starting material				Phenanthrene					
R_1	R_2	X	Y	R_1	R_2	X	Y	% yield	Ref
H	H	H	H	H	H	H	H	78	326
H	Me	H	H	H	Me	H	H	80	326
H	*i*-Bu	H	H	H	*i*-Bu	H	H	35	326
H	4-MeOPh[b]	H	H	H	4-HOPh	H	H	45	*i*
Me	H	H	H	Me	H	H	H	93	326
Me	Me	H	H	Me	Me	H	H	87	328
Me	Et	H	H	Me	Et	H	H	86	328
Me	*n*-Pr	H	H	Me	*n*-Pr	H	H	100	328
Me	*i*-Pr[c]	H	H	Me	H	H	H	71	328
Me	*i*-Pr[c]	5-OMe[b]	H	Me	H	3-OH	H	72	328
Me	*n*-Bu	H	H	Me	*n*-Bu	H	H	92	328
Me	Ph	4-Br	4'-Br	Me	Ph	2-Br	7-Br	84[d]	332
Me	4-MeOPh[b]	H	H	Me	4-HOPh	H	H	82	*j*
Me	OH	H	H	Me	OH	H	H	75	326
Et	H	H	H	Et	H	H	H	100	326
Et	Et	H	H	Et	Et	H	H	91	328
Et	*i*-Pr[c]	H	H	Et	H	H	H	25	328
Et	4-MeOPh[b]	H	H	Et	4-HOPh	H	H	82	*j*
Et	4-MeOPh[b]	5-OMe[b]	H	Et	4-HOPh	3-OH	H	51	*k*
Et	4-MeOPh	4-OMe	4'-OMe	Et	4-MeOPh	2-OMe	7-OMe	66[e]	332
n-Pr	Me	H	H	*n*-Pr	Me	H	H	100	328
n-Pr	*n*-Pr	H	H	*n*-Pr	*n*-Pr	H	H	89	328
i-Pr[c]	Me	H	H	H	Me	H	H	56	328
i-Pr[c]	Et	H	H	H	Et	H	H	52	328
n-C_9H_{19}	*n*-C_9H_{19}	H	H	*n*-C_9H_{19}	*n*-C_9H_{19}	H	H	70	329
n-C_9H_{19}	*n*-$C_{14}H_{29}$	H	H	*n*-C_9H_{19}	*n*-$C_{14}H_{29}$	H	H	34	329
n-$C_{14}H_{29}$	*n*-$C_{14}H_{29}$	H	H	*n*-$C_{14}H_{29}$	*n*-$C_{14}H_{29}$	H	H	23	329
CO_2Et[c]	Me	3,4-$(NO_2)_2$	H	H	Me	1,3-$(NO_2)_2$	H	54	331
				CO_2Et	Me	1,3-$(NO_2)_2$	H	60[d]	331
CO_2Et[c]	CO_2Et	H	H	H	CO_2H	H	H	67	*l*
				CO–O–CO		H	H	63[d]	324
CO_2Et	CO_2Et	H	3'-OMe	CO–O–CO		H	6-OMe	73[d,f]	330
				CO–O–CO		H	8-OMe		
CO_2Et[c]	CO_2Et	H	4'-OMe	H	CO_2H	H	7-OMe	36	330
				CO–O–CO		H	7-OMe	16	330
CN[g]	Me	H	H	CN	Me	H	H	56	326
				$CONH_2$	Me	H	H	22[h]	326
				H	Me	H	H	22[h]	326
CN[g]	Et	H	H	$CONH_2$	Et	H	H	24	326
				H	Et	H	H	73[h]	326
CN[g]	Ph	H	H	CN	Ph	H	H	27[d]	*m*
				H	Ph	H	H	29	*m*
CN[g]	4-MeOPh[b]	H	H	$CONH_2$	4-MeOPh	H	H	23[d]	*m*
				H	4-HOPh	H	H	96	*m*

[a] The acidic reagent is HBr/AcOH unless otherwise stated. [b] Demethylated during cyclodehydration. [c] This group is eliminated during cyclodehydration. [d] Acidic reagent cold concentrated sulfuric acid. [e] Acidic reagent PPA. [f] Mixture of isomers difficult to separate. [g] May be modified during cyclodehydration. [h] Reaction prolonged. [i] F. P. Palopoli, V. J. Feil, D. E. Holtkamp, and A. Richardson Jr., *J. Med. Chem.*, **17**, 1333 (1974). [j] C. K. Bradsher and W. J. Jackson Jr., *J. Am. Chem. Soc.*, **73**, 3235 (1951). [k] C. K. Bradsher and W. J. Jackson Jr., *ibid.*, **74**, 4880 (1952). [l] T. A. Geissmann and R. W. Tess, *ibid.*, **62**, 514 (1940). [m] C. K. Bradsher and R. S. Kittila, *ibid.*, **72**, 277 (1950).

nied by dehydration to phenanthrenes, e.g., **307** (R_1 = H, R_2 = Me). This type of reaction has been termed[327] an "aromatic cyclodehydration". The reaction occurs under the influence of many acidic reagents, e.g., PPA, 85% sulfuric acid, or hydrobromic acid–acetic acid mixture. The reaction is particularly valuable because it gives rise to phenanthrenes directly, in good yields, under conditions much milder than those used for dehydrogenation. The biphenylyl starting materials may be synthesized in good yields by well-established methods,[328-334] so aromatic cyclodehydration provides an attractive route to phenanthrenes, especially those with 9,10-substituents. The method has been the subject of earlier review,[7] the most recent[7b] in 1974, but in a little known journal. The discussion will therefore be limited, although the majority of the experimental data will be summarized in the form of tables.

The cyclization of the aldehydes and ketones of the type **306** has been widely studied and good yields of phenanthrenes obtained, where R_1 and R_2 = aryl, alkyl, CO_2R, CN. Phenanthrenes **307**, where R_1 or R_2 = *i*-Pr, cannot be obtained by this method, the *i*-Pr group being eliminated[328] during cyclodehydration. Nevertheless, phenanthrenes bearing large substituents at the 9 and 10 positions have been formed,[329] e.g., **307** (R_1 = R_2 =

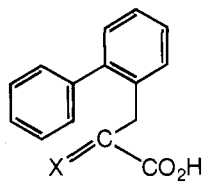
TABLE XX. Aromatic Cyclodehydration of 2-Biphenylylethene Glycols and Their Ethers and Related Compounds



R_1	R_2	X	% yield	Ref
Ph	Ph	OH	29[a]	*d*
			low[b]	*e*
4-MeOPh	4-MeOPh	OH	28[a,c]	*d*
H	H	OMe	46	327
Me	H	OMe	50	*f*
Et	H	OMe	54	*g*
n-Pr	H	OMe	51	*g*
n-Bu	H	OMe	40	*g*
$PhCH_2$	H	OMe	70	*g*
Ph	H	OMe		*h*
4-MePh	H	OMe		*h*
Me	H	OPh	32[a]	*f*
Ph	H	OPh	84	*h*
Ph	Me	OPh	72[a]	*i*
Ph	Et	OPh	70	*i*
Ph	Ph	OPh	62[a]	*i*
Me	H	O-2-naph	23	*f*
Me	H	NEt_2	10	*f*
Me	H	Cl	<1	*f*

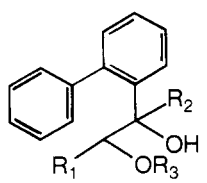
[a] These yields are overall yields; the intermediate glycol derivative was not isolated. [b] I_2/AcOH acidic reagent in this case. [c] The product was 9,10-bis(4-hydroxyphenyl)phenanthrene. [d] C. K. Bradsher and L. J. Wissow, *J. Am. Chem. Soc.*, **65**, 2304 (1943). [e] P. T. Lansbury, J. R. Rogozinski, and F. L. Coblentz, *J. Org. Chem.*, **26**, 2277 (1961). [f] C. K. Bradsher and R. W. H. Tess, *J. Am. Chem. Soc.*, **61**, 2184 (1939). [g] C. K. Bradsher and S. T. Amore, *ibid.*, **63**, 493 (1941). [h] C. K. Bradsher and A. K. Schneider, *ibid.*, **60**, 2960 (1938). [i] C. K. Bradsher and R. Rosher, *ibid.*, **61**, 1524 (1939).

n-C_9H_{19} and n-$C_{14}H_{29}$). The results of this type of cyclization are summarized in Table XIX. Treatment of the related **308** (X = NOH or S) with acids gives[335] 9-phenanthrenecarboxylic acid.

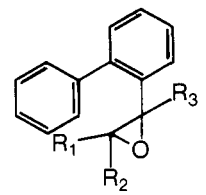


308

Compounds, which may undergo acid-catalyzed rearrangement of the pinacol–pinacolone type to give **306** or its derivatives, have also been investigated. Thus 2-biphenylylglycols **309** (R_3 = H), their ethers **309** (R_3 = alkyl), or aryl and olefin oxides **310** all undergo aromatic cyclodehydration to yield phenanthrenes. In the case of **310**, when R_1 and R_2 are both alkyl, elimination of an alkyl group is observed.[334] The results of these reactions are summarized in Tables XX and XXI.



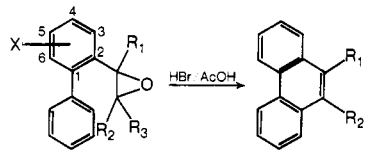
309



310

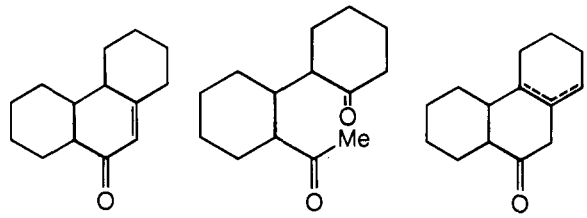
Condensation reactions leading to perhydrophenanthrenes have been described. Thus 1-acetylcyclohexene condenses[336] with cyclohexanone in the presence of sodamide yielding **311**,

TABLE XXI. Aromatic Cyclodehydrations of 2-Biphenylylethene Oxides



R_1	R_2	R_3	X	% yield	Ref
H	H	H	H	2	327
H	Et	H	H	43	*b*
H	*n*-Pr	H	H	66	*b*
H	*i*-Pr	H	H	69	*b*
H	*n*-Bu	H	H	34	*b*
H	*n*-C_5H_{11}	H	H	53	*b*
Me	H	H	H	40	*c*
Me	Me	H	H	39	*d*
Me	Me	Me	H	8	334
Et	Me	H	H	54	*c*
n-Pr	Et	H	H	44	*c*
n-Bu	*n*-Pr	H	H	67	*c*
i-Bu	*i*-Pr	H	H	*a*	328
n-C_5H_{11}	H	H	H	31	*d*
Ph	Me	H	4,5-$(Me)_2$	32	333
Ph	Me	Me	H	56	334
Ph	Et	H	4,5-$(Me)_2$	44	333
Ph	Et	Et	H	60	334
Ph	*n*-Pr	H	H	64	*d*
Ph	*n*-$C_{10}H_{21}$	H	H	39	*d*

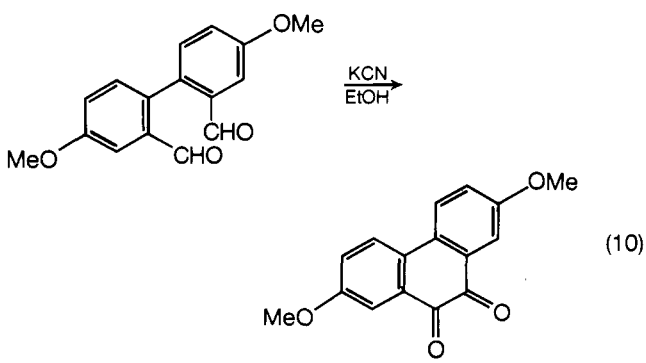
[a] Product was 9-isobutylphenanthrene, *i*-Pr eliminated during cyclodehydration. [b] C. K. Bradsher and S. T. Amore, *J. Am. Chem. Soc.*, **63**, 493 (1941). [c] C. K. Bradsher and S. T. Amore, *ibid.*, **65**, 2016 (1943). [d] C. K. Bradsher and S. T. Amore, *ibid.*, **66**, 1280 (1944).



311 **312** **313**

presumably via **312**. In a similar reaction the pyrrolidine enamine of cyclohexanone condenses[337] with 1-acetylcyclohexene to give **313**, in which the position of the double bond is uncertain.

The cyclization, by condensation, of some 2,2′-disubstituted biphenyls has been described. A benzoin-type condensation has led to the formation of phenanthraquinones from both 2,2′-dialdehydo-[338] and also 2-aldehydo-2′-carbalkoxybiphenyls[339] (see eq 10 and 11). The acyloin condensation has been used to cyclize[340] a 2,2′-dicarbethoxybiphenyl (see eq 12); again a phenanthraquinone results. Dieckmann-type condensations have also been used. Thus **314** is cyclized[341] by treatment with sodium



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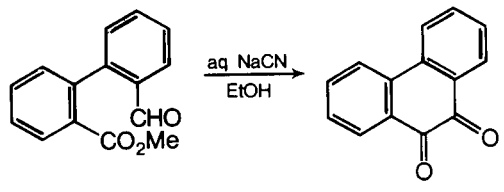
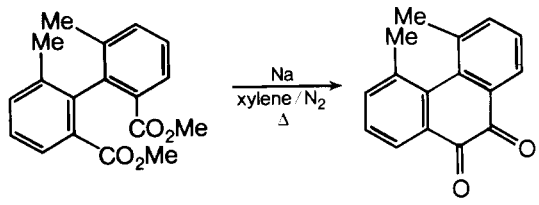
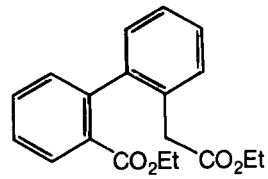


(11)

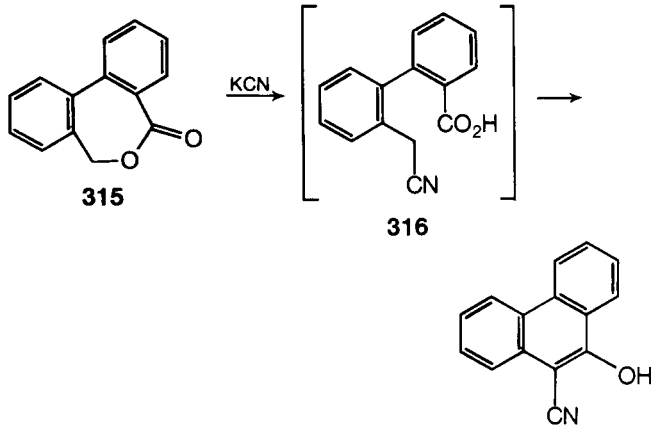


(12)



314

ethoxide yielding ethyl 10-hydroxy-9-phenanthrenecarboxylate (45% yield). The formation of 9-cyano-10-hydroxyphenanthrene from **315**, involves[342] ring closure in the intermediate **316**. The base-catalyzed cyclization of **317** occurs[341] in 85% yield; the product **318** may be converted into phenanthrenes by a number of methods (see Scheme XVI).



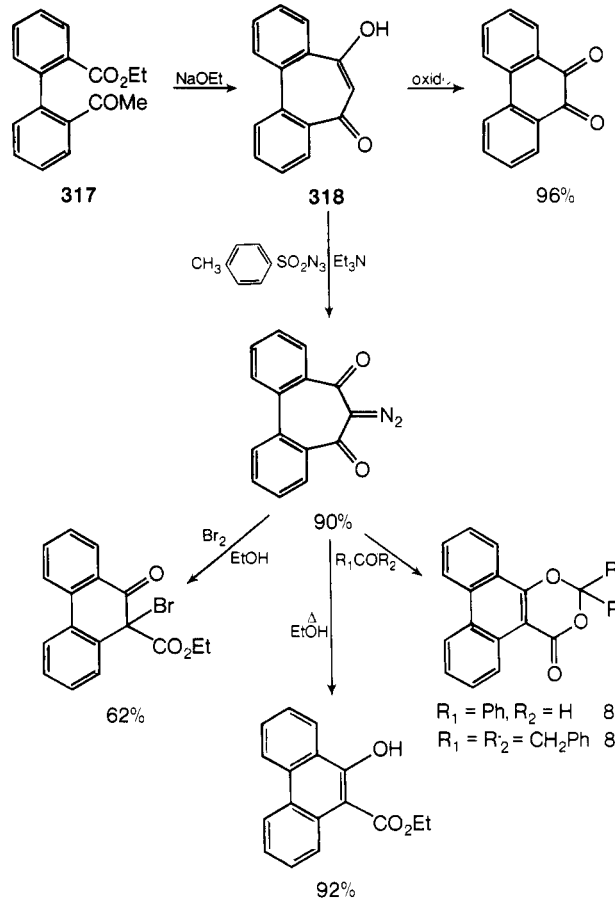
315 **316**

4. Reductive Cyclization

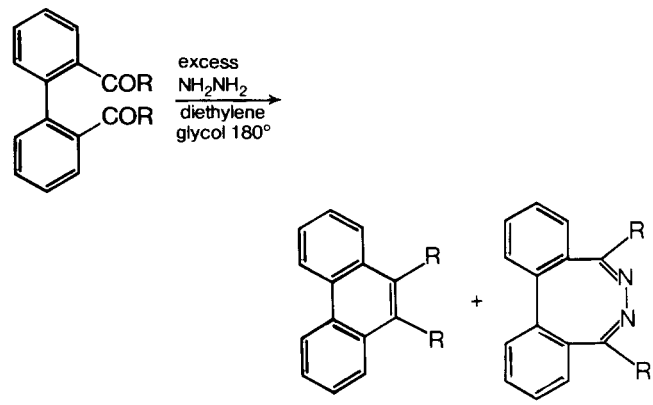
The cyclization of a number of 2,2′-disubstituted biphenyls to phenanthrenes is known and the subject was reviewed[343] in 1968. Most of these methods are not particularly attractive as general methods of phenanthrene synthesis. However, reductive cyclization of 2,2′-diacylbiphenyls is a useful route to some 9,10-substituted phenanthrenes.

2,2′-Diacylbiphenyls yield phenanthrenes on treatment with hydrazines. 2,2′-Biphenyldicarboxaldehyde gives[344] an almost quantitative yield of phenanthrene, on heating with excess hydrazine in acetic acid. 3,6-Dinitrophenanthrene (88% yield) was obtained in an analogous manner, although the reaction failed to produce 4,5-dialkylphenanthrenes.[344] When 2,2′-diacylbiphenyls react with hydrazine a mixture of a phenanthrene and a diazocine results[345] (see Scheme XVII). The yield of phenanthrene is optimized by using a large excess of anhydrous hydrazine in boiling diethylene glycol. Hydrazine may also be used[344] to reduce 2,2′-bis(dibromomethyl)biphenyl, when a 60% yield of phenanthrene is obtained. The use of arylhydrazines has led[346] to the formation of **319** (X = H, 2-Me, 4-Me, 2-OMe, 4-Cl, 4-Br, 2-NO_2, and 3-NO_2) from 2,2′-biphenyldicarboxaldehyde. The Clemmensen reduction also converts 2,2′-diacetylbiphenyls into phenanthrenes. Thus **320** (X = H[347] or OMe[348]) reduced by

SCHEME XVI



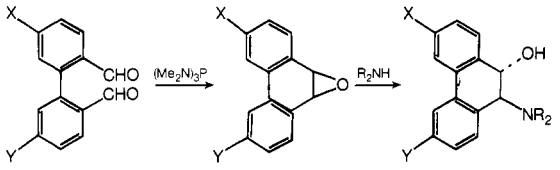
SCHEME XVII



R	Excess of NH_2NH_2	%	%
Me	30×	25	30
Et	16×	31	48
Ph	30×	26	60
	45×	86	nil

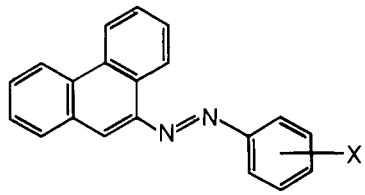
zinc and hydrochloric acid gave the corresponding 9,10-dimethylphenanthrenes. Reduction using magnesium, zinc–alkali, or sodium amalgam leads to 9,10-dihydroxyphenanthrenes. Reductions of **321** (R = CH_2CH_2Ph,[349] phenyl,[350] 4-methylphenyl,[350,351] 4-biphenyl,[349] 2,4-dimethylphenyl,[349,351] 4-chlorophenyl,[349] 4-fluorophenyl,[349] 2,4,6-trimethylphenyl,[351] 2,3,5,6-tetramethylphenyl,[351] and 1-naphthyl[349,351]) have been carried out (see eq 13). The reductive coupling of mesityl 2-methoxyphenyl ketone occurred[352] on reduction with magnesium yielding 9,10-dimesitylphenanthrene, with elimination of the methoxy group. A similar reaction has been observed[353] with duryl 2-methoxy- and 2,6-dimethoxyphenyl ketones.

TABLE XXII. Reduction of 2,2′-Biphenyldicarboxaldehydes with Tris(dimethylamino)phosphine

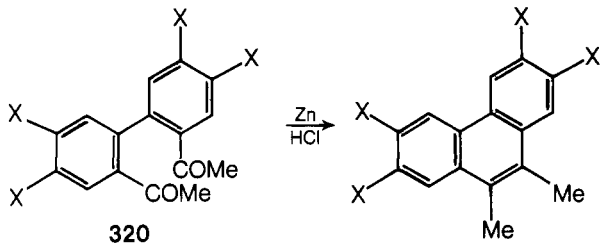


X	Y	% yield	Ref
H	H	84–89	354, *a*
Br	Br	74	*a*
CF_3	CF_3	64	*a*
Br	H	Not stated	*a*

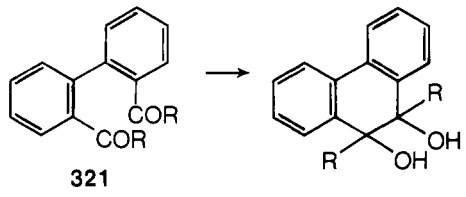
[a] A. S. Dey and J. L. Neumeyer, *J. Med. Chem.*, **17**, 1095 (1974).



319



320

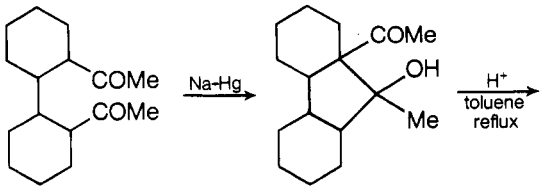


321

(13)

An interesting reducing agent, tris(dimethylamino)phosphine, has been introduced by Newman and Blum,[354] which converts 2,2′-biphenyldicarboxaldehyde into 9,10-epoxyphenanthrene. Applications of the use of this reagent are summarized in Table XXII.

The reduction[355] of 2,2′-diacetylbicyclohexyl using sodium amalgam does not lead directly to a perhydrophenanthrene; instead **322** was isolated. However, acid-catalyzed rearrangement of **322** leads to 9,10-dimethyl-1,2,3,4,5,6,7,8-octahydrophenanthrene in 16% yield.



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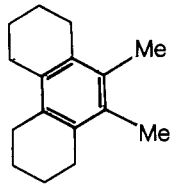
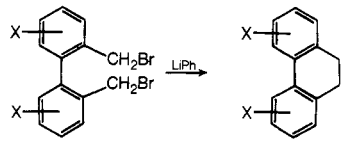


TABLE XXIII. Wurtz Reactions[a] of 2,2′-Bis(bromomethyl)biphenyls

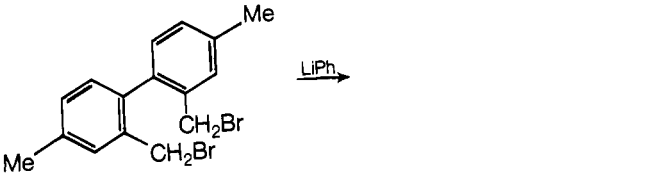


X	% yield	Ref
H	86	356
	79[b]	*d*
4-Me	87	359
6-Me	80, 39, 30	357, 340, *e*
$6\text{-}CD_3$	100[c]	*f*
5-OMe	38	358
6-OMe	55, low	*g*, *h*
$4,6\text{-}(Me)_2$	76	*i*
$5,6\text{-}(Me)_2$	84	*i*
$4,5,6\text{-}(OMe)_3$		*j*

[a] In the presence of phenyllithium unless otherwise stated. [b] Disodio-1,1,2,2-tetraphenylethane used. [c] Yield improved by adding the bis(bromomethyl)biphenyl to the phenyllithium. [d] E. Mueller and G. Roescheisen, *Chem. Ber.*, **90**, 543 (1957). [e] K. Mislow and H. B. Hopps, *J. Am. Chem. Soc.*, **84**, 3018 (1962). [f] K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, *ibid.*, **86**, 1733 (1964). [g] M. S. Newman and R. L. Childers, *J. Org. Chem.*, **32**, 62 (1967). [h] D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 3072 (1951). [i] H. A. Karnes, B. D. Kybett, M. H. Wilson, J. L. Margrave, and M. S. Newman, *J. Am. Chem. Soc.*, **87**, 5554 (1965). [j] N. K. Kochetkov, A. Y. Khorlin, and O. S. Chizhov, *Izv. Akad. Nauk SSR, Otd. Khim. Nauk*, 856 (1962); *Chem. Abstr.*, **57**, 13704 (1962).

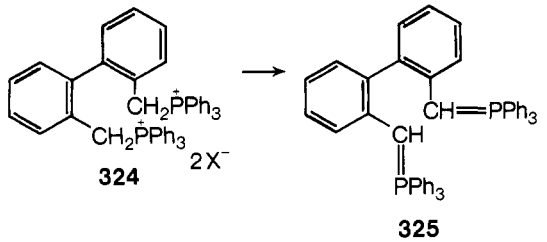
5. *Wurtz Cyclization and Related Procedures*

The Wurtz-type cyclization of 2,2′-bis(halomethyl)biphenyls was another procedure reviewed by Buntrock and Taylor.[343] The starting materials are readily prepared, by standard methods, from 2,2′-biphenylcarboxylic acids[356] or substituted anthranilic acids[357] and 2-iodoalkylbenzenes.[358] Typically the reaction involves treatment of a 2,2′-bis(bromomethyl)biphenyl, e.g., **323**,[359] with phenyllithium in ethereal solution, resulting in excellent yields of the corresponding 9,10-dihydrophenanthrene. The method provides an attractive route to a number of 9,10-dihydrophenanthrenes, and its applications are summarized in Table XXIII. A closely allied reaction has been used[360] to synthesize phenanthrene, 1,4-dimethylphenanthrene, and 2,7-dinitrophenanthrene (see eq 14). Similarly, the bis(triphenylphosphonium methyl)biphenyl salt **324** is converted into phen-



323

87%



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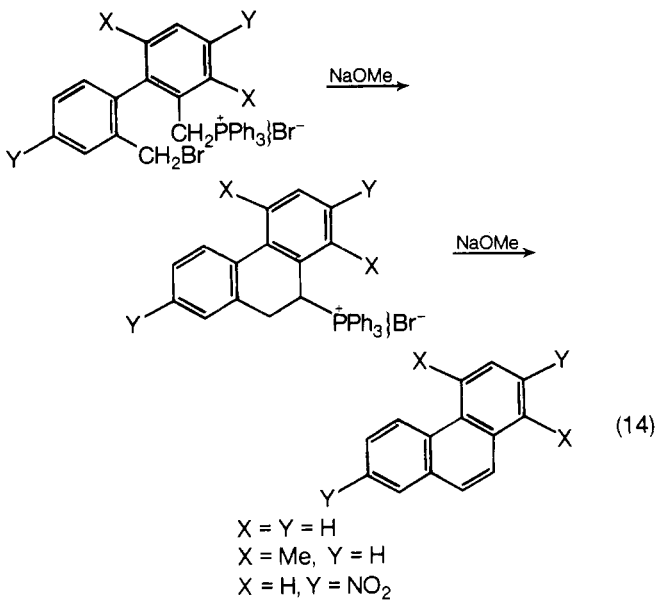
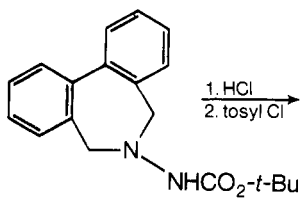
325



(14)

anthrene when treated with sodium hydride. This may occur either directly[361] with the periodate salt **324** (X = IO_4) or indirectly with the bromide salt **324** (X = Br), which first forms[362] the ylide **325**, converted into phenanthrene by atmospheric oxidation.

Carpino[363] has introduced a variation of the general method, which avoids the need to use phenyllithium. The bis(halomethyl)biphenyl is treated with *tert*-butyl carbazate (NH_2NHCOO-*t*-Bu); the product **326** when hydrolyzed and treated



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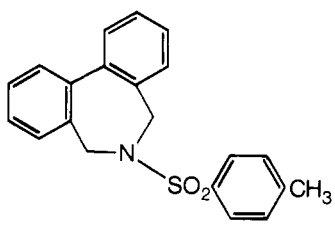
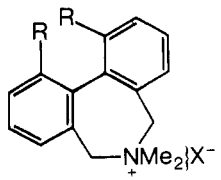


327

with *p*-toluenesulfonyl chloride yields **327**, which forms 9,10-dihydrophenanthrene (95% yield) on warming with aqueous sodium hydroxide for 2–3 min. The azepinium salts **328** may also be converted into phenanthrene derivatives. Thus **328** (R = H, X = Cl) subjected[364] to Hofmann elimination conditions gives an unstated yield of phenanthrene, while **328** (R = Me, X = Br)



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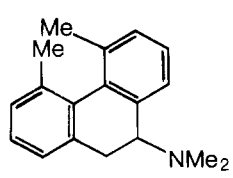
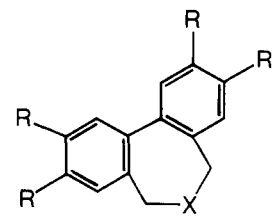


329

treated[340,365] with potassium amide in liquid ammonia yields 4,5-dimethylphenanthrene, gradually reduced to its 9,10-dihydro derivative on prolonged reaction. The use of phenyllithium in the latter process allows the isolation of the intermediate **329** (85% yield). The dibenzooxepin **330** (R = H, X = O) is converted[366] into 9-hydroxy-9,10-dihydrophenanthrene in 90% yield by potassium amide in liquid ammonia or in 25% yield using[367] *tert*-butyl peroxide. The tetramethoxy derivative **330** (R = OMe, X



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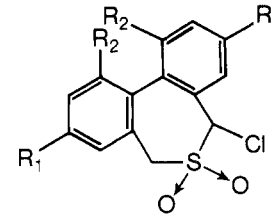


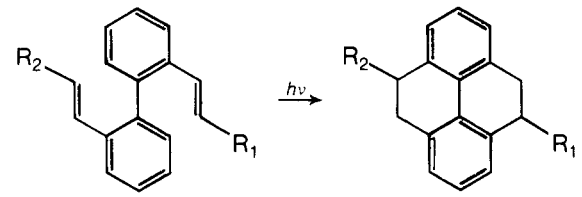
331

= O) gives[368] the corresponding phenanthraquinone on sodium dichromate oxidation. Thiepins too have yielded phenanthrenes. Thus **330** (R = H, X = S) desulfurized[369] by Raney nickel results in a 25% yield of phenanthrene. Paquette[370] has introduced an elegant method, by which 2,7-dihydro-3,4,5,6-dibenzothiepins are converted into phenanthrenes. The thiepin chlorinated by sulfuryl chloride and oxidized by *m*-chloroperbenzoic acid yields **331** (R_1 = R_2 = H or R_1 = Me, R_2 = H) which undergoes base-catalyzed rearrangement to phenanthrene (96% yield) or 2,7-dimethylphenanthrene (92% yield), respectively; however, the rearrangement fails to proceed for **331** (R_1 = H, R_2 = Me).

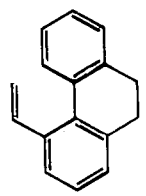
6. Photocyclizations

The photocyclization of biphenyloid derivatives has not so far provided any important general methods for the synthesis of phenanthrenes.

The photocyclization of biphenylylethenes is known. Thus the photolysis[371] of 2-biphenylylethene itself, in benzene in the presence of oxygen, gives a 100% conversion to 9,10-dihydrophenanthrene. Ultraviolet irradiation, under anaerobic conditions, of **332** leads[372,373] to the formation of 4,5,9,10-tetrahydropyrenes **333** for a variety of substituents, e.g., R_1 = R_2



332 **333**

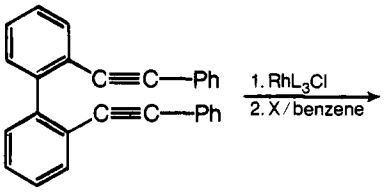


334

= H, CN, CO_2Et, and Ph; R_1 = H, R_2 = Ph. In the case where R_1 = R_2 = H, then a little of the intermediate 9,10-dihydrophenanthrene **334** was also isolated.[373] Padwa and Mazzu[372] have shown that **334** can be obtained in good yield in a short-term irradiation. A useful photocyclization of the sodium enolate of diethyl 2-biphenylylmalonate yields[374] ethyl 9-hydroxyphenanthrenecarboxylate in 70% yield. The photochemical oxidation of 2,2′-biphenyldicarboxaldehyde yields[375] phenanthraquinone.

7. Miscellaneous Methods

Tris(triphenylphosphine)rhodium(I) chloride forms[376] a 1:1 complex with **335**, which, when treated with oxygen, gave 51% of 9,10-dibenzoylphenanthrene and 10% **336** (X = O). Treatment of the complex with carbon monoxide, sulfur, or selenium gave **336** (X = CO, S or Se) in 63, 60, or 11% yield, respectively.



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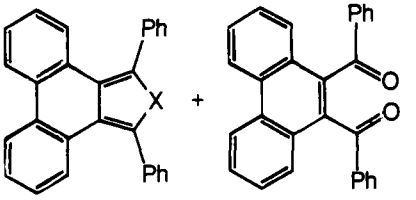


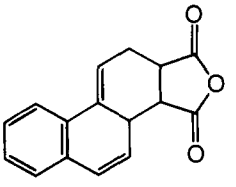
336 only when X = O

IV. Intermolecular Cycloaddition Reactions

A. From Naphthalenes

1. Naphthalene Derivatives as Dienes

1- and 2- vinylnaphthalene derivatives have sufficient diene activity to undergo the Diels–Alder reaction with typical dienophiles.[377-379] In some cases the expected adduct, for example, **337** from 1-vinylnaphthalene and maleic anhydride, can be isolated, although more usually this initial structure is isomerized under the reaction conditions to the aromatic system (e.g., **338**).



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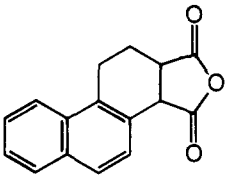
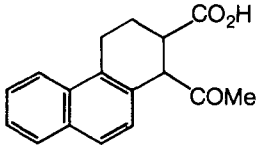


338

The conversion of **337** into **338** can also be accomplished easily in a separate step. Structures such as **337** and **338** are readily dehydrogenated to the fully aromatic phenanthrenes, so that the Diels–Alder reaction constitutes a useful method for the synthesis of phenanthrenes. One of the major interests in the reported work in this area has been in the synthesis of steroid skeleta, when the geometry of the adducts has been a central issue. In this review the configurations of the adducts have been ignored, since the adducts are regarded only as intermediates in the preparation of the aromatic phenanthrenes. Certain diene additions have been excluded from consideration because the main objective of the reported work has been the aquisition of derivatives containing angular alkyl groups.

With unsymmetrical dienophiles two structural isomers are possible, and in many cases a mixture is obtained. Addition of β-acetylacrylic acid to 1-vinylnaphthalene gives[380] a mixture of **339** and **340** in the ratio of 4:1. In other cases only one of the



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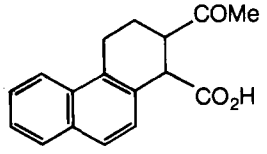

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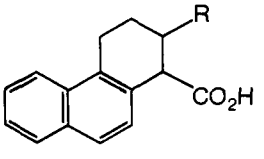
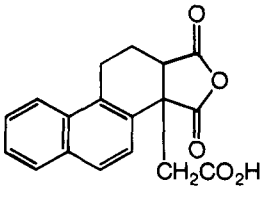
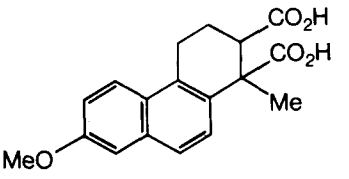


341, R = alkyl



342

two possible isomers has been reported, for example,[381] the adduct of β-alkylacrylic acid and 1-vinylnaphthalene is **341**, and with aconitic acid[381] the product is **342**. The addition of citraconic anhydride to 1-vinyl-6-methoxynaphthalene yields[382] the dicarboxylic acid **343**. An adduct between 1-vinylnaphthalene and cinnamaldehyde has been reported,[383] but the orientation was not proved. In most cases the orientation of addition has been established by modifying the side chain, then dehydrogenating to phenanthrenes. Thus, 1-methylphenanthrene has been obtained[381] from **342**. In certain cases, when the addition reaction is carried out under more severe conditions, only the aromatic phenanthrene is isolated. Thus, when 1-vinylnaphthalene is fused with fumanonitrile, the product is[383] phenanthrene-1,2-dicarboxylic anhydride. The same product is available[383]



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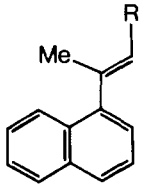
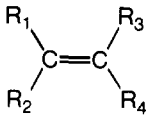


344

by adding acetylenedicarboxylic acid to 1-vinylnaphthalene. It has been concluded[384] that the reaction of **344** (R = H or Me) with maleic anhydride gave such poor yields of adducts that the Diels–Alder reaction does not constitute a satisfactory method for the preparation of certain alkylphenanthrenes. The dienophiles **345** and **346** have been reported[380,381] not to react with



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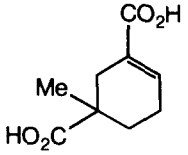


346

R_1	R_2	R_3	R_4
H	H	H	CHO
Et	H	Me	CHO
Et	H	H	CO_2Et
Me	Me	H	CO_2H
Et	H	Me	CO_2H
CH_3CO	H	Me	CO_2H

1-vinylnaphthalene. A summary of successful cycloadditions to 1-vinylnaphthalenes appears in Table XXIV.

An interesting variant on the reactions considered above involves[385] the addition of **347** to 1-vinylnaphthalene. The adduct, **348**, obtained in 75% yield, can be converted via **349** to 1-phenylphenanthrene **350** (Scheme XVIII).

SCHEME XVIII

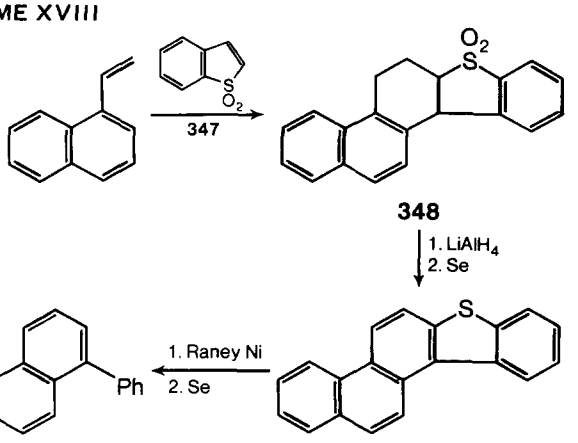
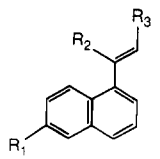


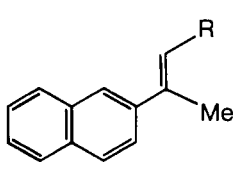
TABLE XXIV. Diene Additions of 1-Vinylnaphthalenes



R_1	R_2	R_3	Dienophile	% yield of adduct	Ref
H	H	H	MA[a]	32	386
H	H	H	MA	35	*b*
OMe	H	H	MA	Low	386
OMe	H	H	MA	30	*c*
H	H	H	$CH_3COCH{=}CHCO_2H$	36	380
H	H	H	$MeCH{=}CHCO_2H$	26	381
H	H	H	$EtCH{=}CHCO_2H$	18	381
H	H	H	$CH_2{=}CHCO_2H$	12	381
H	H	H	$CH_2{=}CBrCO_2H$	18	381
H	H	H	$CH_2{=}CHCOMe$	5	381
H	H	H	$Me(CN)C{=}CHCO_2Et$	19	381
H	H	H	Aconitic acid	14	381
H	H	H	Chloromaleic anhydride	40	381
H	H	H	MA	57	382
OMe	H	H	MA	30	382
H	H	H	Diethyl maleate	89	382
OMe	H	H	Fumaric acid	72	382
OMe	H	H	Citraconic anhydride	60	382
OMe	H	H	Mesaconic anhydride	72	382
H	H	H	PhCH=CHCHO		383
H	H	H	Cyclopentene-1,2-dicarboxylic anhydride		*d*
H	Me	H	MA	8	384
H	Me	Me	MA	4	384
H	H	Me	MA	77	*e*
H	H	H	$(NC)_2C{=}C(CN)_2$		*f*

[a] MA = maleic anhydride. [b] V. R. Skvarchenko, W-L. Lin, and R. Ya. Levina, *Zh. Obshch. Khim.*, **31**, 383 (1961); *Chem. Abstr.*, **55**, 22259 (1961). [c] W. E. Bachmann and M. C. Kloetzel, *J. Am. Chem. Soc.*, **60**, 2204 (1938). [d] S. C. Gupta and A. Bahattacharyya, *J. Indian Chem. Soc.*, **31**, 897 (1954); *Sci. Cult.*, **18**, 439 (1953). [e] L. F. Fieser and W. H. Daude, *J. Am. Chem. Soc.*, **63**, 782 (1941). [f] W. H. Cherry, J. T. Craig, Q. N. Porter, H. G. Upstill, and S. Sternhell, *Tetrahedron Lett.*, 4727 (1972).

Although adducts with 2-vinylnaphthalenes can be obtained, the reaction has not been studied so widely as the corresponding additions to 1-vinylnaphthalene. 2-Vinylnaphthalene itself forms[386] an adduct (6%) with maleic anhydride, and **351** (R = H or Me) also reacts.[384] By using nitrobenzene as solvent, the fully aromatic phenanthrene can be formed directly. A more reactive dienophile, tetracyanoethylene, enables the adducts **352** to be formed[387-389] in high yields from 2-vinylnaphthalenes. Maleic anhydride adds[387] to the more reactive 6-methoxy-2-vinylnaphthalene to give the expected adduct in 75% yield.



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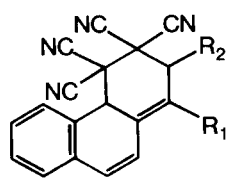
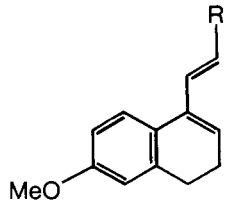


352

R_1	R_2	% yield
H	H	95
Me	H	83
Et	H	93
n-Pr	H	91
i-Pr	H	97
t-Bu	H	39

1-Vinyl- and 2-vinyl-3,4-dihydronaphthalenes have also been used as dienes (Table XXV). Once again the incentive has been to develop methods for steroid synthesis, but some adducts have been dehydrogenated to phenanthrene derivatives.

The addition of citraconic anhydride to 6-methoxy-1-vinyl-3,4-dihydronaphthalene (**353**, R = H) was originally[390] believed to give the adduct **354** only, but later workers[391,392] reported the



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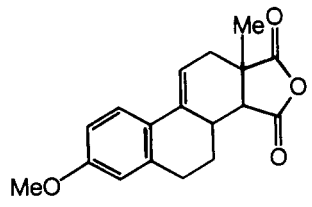

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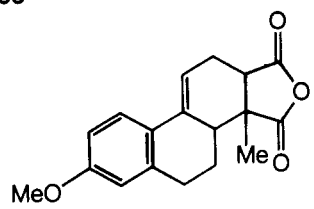
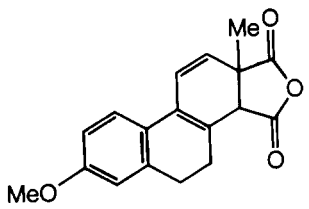
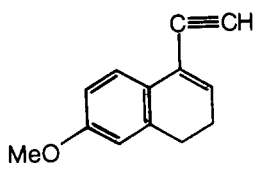


355

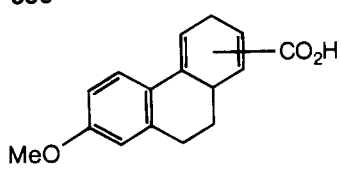
formation of both **354** and **355**. Dienophiles such as methyl vinyl ketone also provide[393,394] mixtures resulting from both modes of addition. However, the addition of citraconic anhydride to **353** (R = OAc) is claimed[395] to give only the adduct **356**. An interesting variation of potential significance is summarized in Scheme XIX.



356



357



358

SCHEME XIX

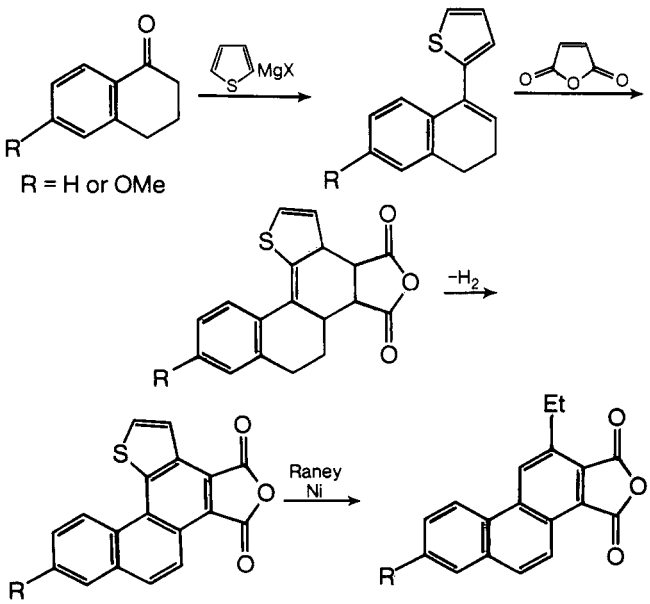
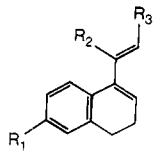


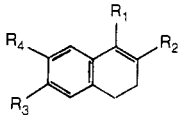
TABLE XXV. Diene Additions to 1-Vinyl-3,4-dihydronaphthalenes



R_1	R_2	R_3	Other	Dienophile	% adduct	Ref
H	H	H		MA		*a*
MeO	H	H		MA	49	*a*, *b*
					65	*c*
					70	*d*
OMe	H	H	7-OMe	MA	41	*e*
H	AcO	H		MA	50	*f*
H	OMe	H		CH_2=$CHCO_2Me$	80	*g*
OMe	H	H		CH_2=$CHCO_2Et$	32	394, *h*
OMe	H	H	5,7-$(OMe)_2$	CH_2=$CHCO_2Me$	88	*i*
OMe	H	H		CH_2=$C(Me)CO_2Me$	43	*j*
OMe	H	H		CH_2=CHCOMe	32	393, 394
OMe	H	OAc		CH_2=$C(Me)CO_2Me$	47	*k*
OMe	H	H		EtCH=$C(Me)CO_2H$		*l*
OMe	H	H		Citraconic anhydride	70	380, 390–392
OMe	H	OAc		Citraconic anhydride	51	395
OMe	H	H		MeCOCH=CHCOMe	30	*m*
OMe	H	H		CH_2=$CHCO_2H$		*n*
OMe	H	H		CH_2=$C(Me)CO_2H$		*n*

[a] E. Dane, O. Hoss, A. W. Bendsell, and J. Schmitt, *Justus Liebigs Ann. Chem.*, **532**, 39 (1937); **536**, 183 (1938). [b] V. M. Andreev, S. M. Segal, and V. F. Kucherov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1475 (1961); *Chem. Abstr.*, **56**, 428 (1962). [c] V. F. Kucherov, V. M. Andreev, and L. K. Lysauchuk, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1796 (1960); *Chem. Abstr.*, **55**, 1795 (1961). [d] I. N. Nazarov, I. V. Torgov, and G. P. Verkholetova, *Dokl. Akad. Nauk SSSR*, **112**, 1067 (1957); *Chem. Abstr.*, **51**, 14647 (1957). [e] V. Askam, H. Williams, and D. Jones, British Patent 1 281 466; *Chem. Abstr.*, **77**, 101293 (1972). [f] M. F. Ansell and G. T. Brooks, *J. Chem. Soc.*, 201 (1961). [g] Z. G. Hajos, K. J. Doebel, and M. W. Goldberg, *J. Org. Chem.*, **29**, 2527 (1964). [h] F. Hoffmann-La Roche and Co., British Patent 825 907; *Chem. Abstr.*, **54**, 15346 (1960). [i] P. N. Rao, B. E. Edwards, and L. R. Axelrod, *J. Chem. Soc. C*, 2863 (1971). [j] M. W. Goldberg, L. M. Jampolsky, and R. W. Kierstead, French Patent 1 377 005; *Chem. Abstr.*, **62**, 14601 (1965). [k] T. I. Sorokina, I. I. Zaretskaya, and I. V. Torgov, *Dokl. Akad. Nauk SSSR*, **129**, 345 (1959); *Chem. Abstr.*, **54**, 7659 (1960). [l] E. Buchta and H. Bayer, *Chem. Ber.*, **90**, 1647 (1957). [m] M. Goldberg and P. Muller, *Helv. Chim. Acta*, **23**, 831 (1940). [n] T. R. Klose and L. N. Mander, *Aust. J. Chem.*, **27**, 1287 (1974).

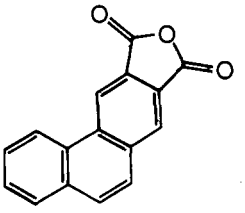
TABLE XXVI. Dihydronaphthalenes as Dienophiles



R_1	R_2	R_3	R_4	Other	Diene	Yield, %	Ref
CO_2Et	H	H	H		Butadiene	27	*a*
CO_2Et	H	H	OMe		Butadiene	13	*a*
CO_2Et	H	H	H		2,3-Dimethylbutadiene	21	*a*
CO_2H	H	H	H		Butadiene	23	*b*
CO_2H	H	H	H		2,3-Dimethylbutadiene	74	*b*
CO_2H	H	OMe	H		Butadiene	31	*b*
CO_2H	H	OMe	H		2,3-Dimethylbutadiene	85	*b*
CO_2Et	H	Br	OMe	C(8)-OMe	2,3-Dimethylbutadiene	54	*b*
					Butadiene	9	*b*
H	CO_2H	Br	H		Butadiene	13	*c*
H	CO_2H	Br	H		2,3-Dimethylbutadiene	31	*c*
H	CO_2H	OMe	OMe		2,3-Dimethylbutadiene	11	*c*
CO–O–CO		H	H		Butadiene	63	*d*
						40	*e*
						72	*e*
CO–O–CO		H	H		2,3-Dimethylbutadiene	97	*d*
CO–O–CO		OMe	H		Butadiene	75	*d*
CO–O–CO		H	OMe		Butadiene	75	*d*
CO–O–CO		OMe	OMe		Butadiene	75	*d*
CO–O–CO		OH	OH		Butadiene	75	*d*
CO–O–CO		Me	OMe		Butadiene	75	*d*
CO–O–CO		H	Bu^t		Butadiene	75	*d*
CO–O–CO		H	H		2-Methylbutadiene	80	*e*

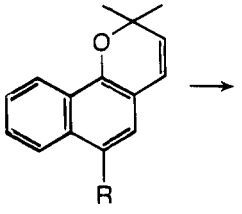
[a] L. F. Fieser and H. L. Holmes, *J. Am. Chem. Soc.*, **58**, 2319 (1936). [b] L. F. Fieser and H. L. Holmes, *ibid.*, **60**, 2548 (1938). [c] H. L. Holmes and L. W. Trevoy, *Can. J. Res.*, **B22**, 56 (1944). [d] L. F. Fieser and E. B. Hershberg, *J. Am. Chem. Soc.*, **57**, 2192 (1935). [e] V. R. Skvarchenko, L. A. Chervoneva, V. A. Puchnova, and R. Ya. Levina, *Zh. Obshch. Khim.*, **30**, 54 (1960); *Chem. Abstr.*, **54**, 21017h (1960).

The acetylenic derivative **357** also behaves as a diene[396,397] toward maleic anhydride, *p*-benzoquinone, and propiolic acid. With the latter, the mixture of the two possible isomers **358**, obtained in 45% yield, contains a 4:1 ratio of the C-2 and the C-1 acids. Propiolic acid also adds[398] to 1- and to 2-naphthylpropiolic acids to give the same adduct **359**.



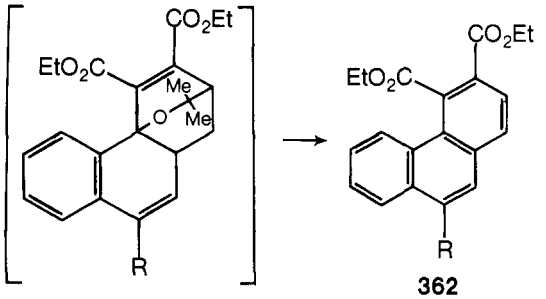
359

A variation which has not been extensively studied involves[399] the addition of diethyl acetylenedicarboxylate to **360**, when the phenanthrene **362** can be isolated. Presumably the reaction involves the initial (4 + 2) adduct **361**.



R = H or OMe

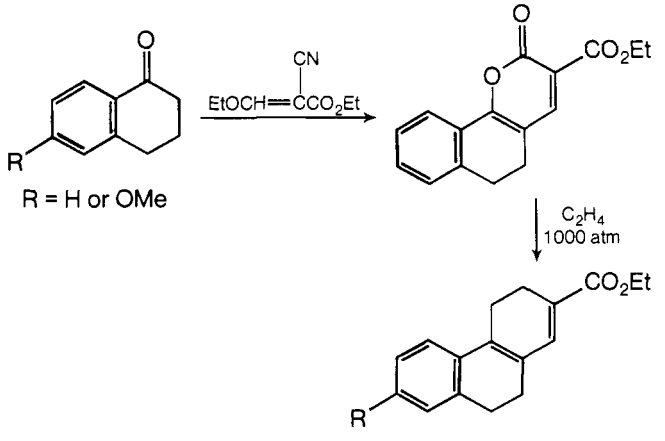
360



361 **362**

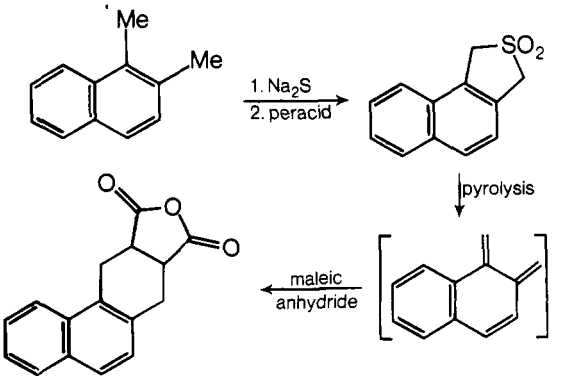
A new phenanthrene synthesis[400] is summarized in Scheme XX, and a preparation[401] of the 1,2,3,4-tetrahydrophenanthrene **363** is summarized in Scheme XXI. These methods have been insufficiently studied to establish their scope.

SCHEME XX



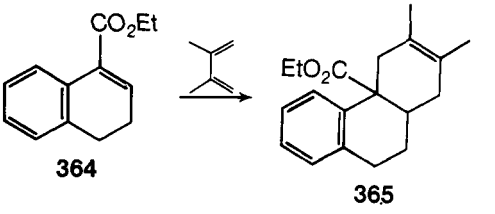
R = H or OMe

SCHEME XXI

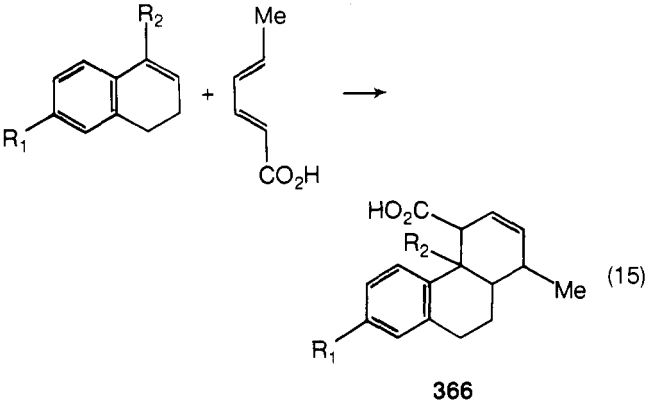


363

Dihydronaphthalenes have also been[402,403] added to sorbic acid to give phenanthrene derivatives **366** (eq 15).



364 **365**

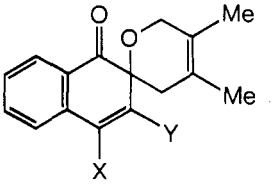


(15)

366

R_1	R_2	% yield
H	H	18
H	Me	12
OMe	H	12

The first report that 1,2-naphthoquinones add to dienes was made in 1934,[404] and in recent years the scope of this reaction has been more closely defined. Simple adducts have been obtained in a number of cases (Table XXVII), although with 4-chloro-, 4-bromo- and 3,4-dichloro-1,2-naphthoquinones addition of 2,3-dimethylbutadiene leads[405] to the spiro compound **367**, rather than to the expected (4 + 2) cycloadduct.



367

X = Cl, Br, or Cl

Y = H, H, or Cl

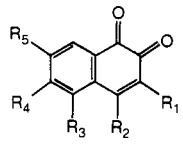
2. Naphthalenes as Dienophiles

3,4-Dihydronaphthalenes that possess ethoxycarbonyl or carboxylic acid groups at C-1 and/or C-2 react with butadiene or 2,3-dimethylbutadiene to give varying amounts of the expected adducts, for example, **364** → **365** (Table XXVI). 3,4-

B. From Styrenes

Dienophiles such as *p*-benzoquinones will add to certain styrenes to give phenanthrene derivatives (Table XXVIII). Hydrophenanthrenes have also resulted from the addition of maleic

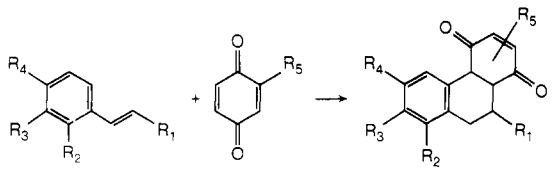
TABLE XXVII. 1,2-Naphthoquinones as Dienophiles



R_1	R_2	R_3	R_4	R_5	Diene	% adduct	Ref
H	H	H	H	H	2,3-Dimethylbutadiene	69	405
H	CH_2Ph	H	H	H	2,3-Dimethylbutadiene	65	*b*
H	$CH(CO_2Et)_2$	H	H	H	2,3-Dimethylbutadiene		*b*
H	CH_2CN	H	H	H	Butadiene	56	*c, d*
H	CH_2CN	H	OMe	H	Butadiene	60	*e*
H	CH_2CN	H	OMe	H	2,3-Dimethylbutadiene	71	*e*
H	CH_2CN	OMe	OMe	H	Butadiene		*d*
H	CN	H	H	H	2,3-Dimethylbutadiene	83	405
H	Cl	H	H	H	2,3-Dimethylbutadiene	*a*	*f*
Me	H	H	H	Me	2,3-Dimethylbutadiene		404
CO_2Me	H	H	H	H	2,3-Dimethylbutadiene	84	405
OMe	H	H	H	H	2,3-Dimethylbutadiene	75	405
Cl	H	H	H	H	2,3-Dimethylbutadiene	84, 70	405, *f*
Br	H	H	H	H	2,3-Dimethylbutadiene	76	*f*
NO_2	H	H	H	H	2,3-Dimethylbutadiene	85	405

[a] Adduct eliminates HCl leading to 2,3-dimethylphenanthraquinone (15% yield). [b] L. F. Fieser and C. K. Bradsher, *J. Am. Chem. Soc.*, **61**, 417 (1939). [c] M. Gates and W. F. Newhall, *ibid.*, **70**, 2261 (1948). [d] M. D. Gates, U.S. Patent 2 766 245 (1956); *Chem. Abstr.*, **51**, 6710 (1957). [e] M. Gates and W. G. Webb, *J. Am. Chem. Soc.*, **80**, 1186 (1958). [f] L. F. Fieser and J. T. Dunn, *ibid.*, **59**, 1016 (1937).

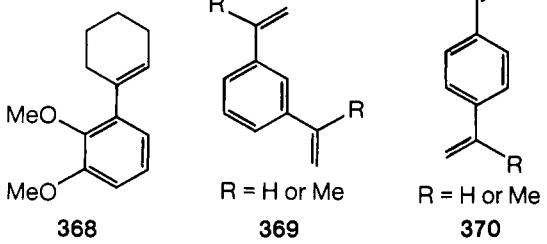
TABLE XXVIII. Addition of *p*-Benzoquinone to Styrenes



R_1	R_2	R_3	R_4	R_5	Ref
H	H	H	H	Me	*a, b*
H	H	H	H	OMe	*a–c*
H	H	H	OMe	Me	*b*
H	Me	H	H	Me	*a, b*
H	Me	H	H	OMe	*a–c*
H	OMe	H	H	Me	*b*
Me	H	OMe	OH	H	*d*

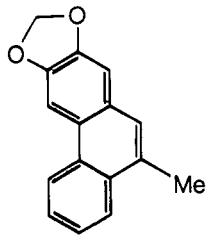
[a] M. Lora-Tamayo, *Tetrahedron*, **4**, 17 (1958). [b] M. Lora-Tamayo, A. Alberola, and C. Corral, *An. Real Soc. Espan. Fis. Quim., Ser. B*, **53**, 63 (1957); *Chem. Abstr.*, **51**, 12057 (1957). [c] Y. Inouye and H. Kakisawa, *Bull. Soc. Chem. Jpn.*, **44**, 563 (1971); *Chem. Abstr.*, **74**, 99700 (1971). [d] M. Lora-Tamayo, *Mem. Acad. Cienc. Artes Barcelona*, **28**, 197 (1946); *Chem. Abstr.*, **41**, 4468 (1947).

anhydride to **368**[406] and by "double additions" to **369** and **370**.[407,408]

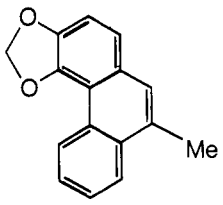


368 **369** **370**

One of the more interesting developments occurred when it was found[409] that arynes will add to styrenes yielding either 9,10-dihydrophenanthrenes or phenanthrenes. Although yields are usually modest, the reaction has the great merit that target molecules are available in one step from readily available starting materials. The reaction is typified by the addition of benzyne to isosafrole when[410,411] a mixture of **371** and **372** and the corresponding 9,10-dihydrophenanthrenes was formed. The



371



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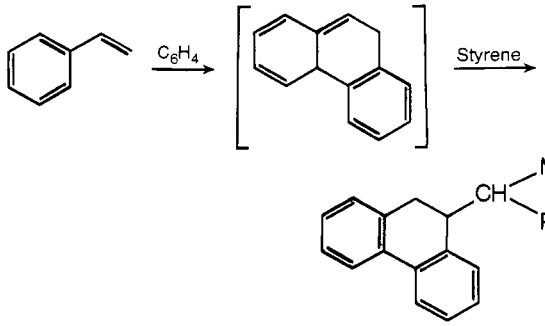
reaction mixture can become very complex when an unsymmetrical benzyne is used, thus limiting the scope of the reaction sequence. For example,[412] 4-chlorobenzyne adds to isosafrole to give an inseparable mixture of the 6- and 7-chloro derivatives of **371** and **372**. Wolthuis[413] isolated three products from the reaction of benzyne with α-methylstyrene, viz., 9-methylphenanthrene (4%), 2,3-diphenylpropene (32%), and 9-benzylphenanthrene (18%). The reaction of benzyne with styrene itself has been studied by a number of workers. In the first investigation[414] benzyne was generated by reacting *o*-fluorobromobenzene with magnesium, but a pure product could not be isolated; later it was found[415] to react with a fivefold excess of styrene to provide 9-phenyl-9,10-dihydrophenanthrene in 87% yield. By using benzyne formed by the aprotic diazotization of anthranilic acid and a 50-fold excess of styrene, a mixture of the diastereoisomers of **373** has[416] been isolated (26% yield). The product is believed to arise from an ene reaction between styrene and the initial adduct (see eq 16).



(16)

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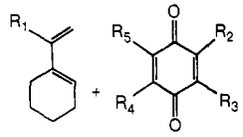
TABLE XXIX. Additions to 1-Vinylcyclohexenes



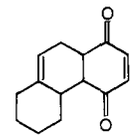
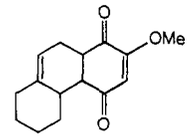
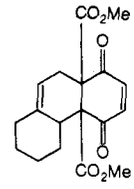
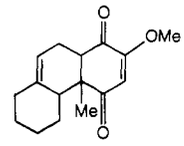
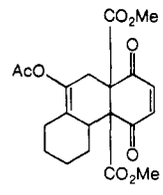
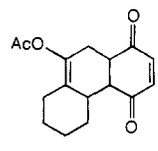
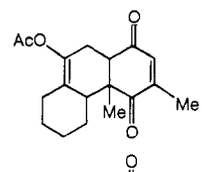
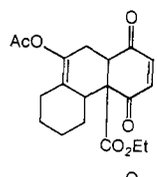
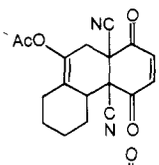
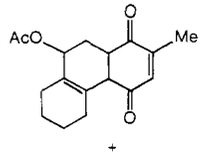
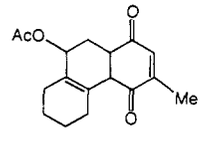
R_1	R_2	R_3	R_4	R_5	Other	Adduct	%	Ref
H	H	H	H	H				*a–d*
H	OMe	H	H	H			63	*e*
H	CO_2Me	CO_2Me	H	H			38	*f*
H	H	OMe	H	Me			5	*g*
OAc	CO_2Me	CO_2Me	H	H			30	*f, h*
OAc	H	H	H	H			62 67 48	*i* *j* *k* *m*
OAc	Me	H	H	Me			45	*m*
OAc	CO_2Et	H	H	H				*h*
OAc	CN	CN	H	H				*h*
OAc	Me	H	H	H		 + 	35 10	*i* *i*

TABLE XXIX (continued)

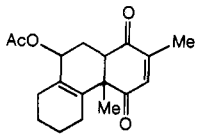
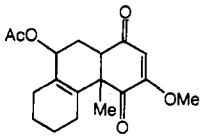
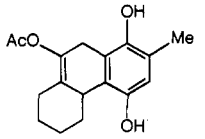
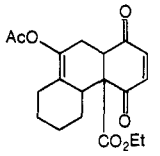
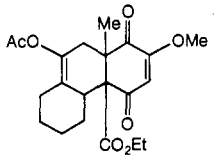
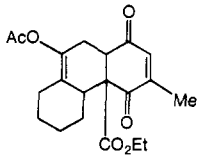
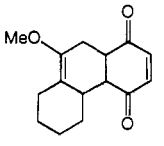
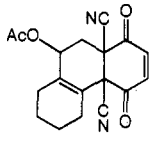
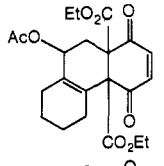
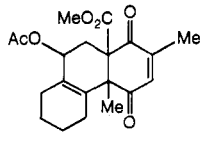
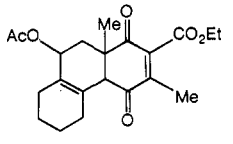
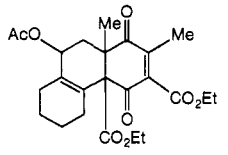
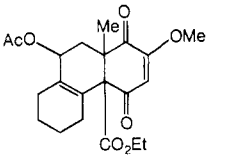
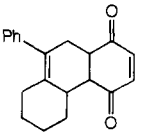
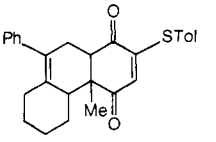
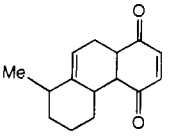
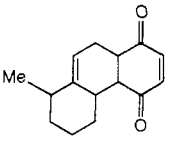
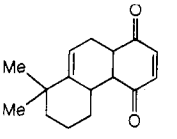
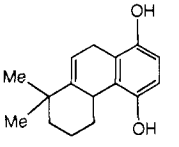
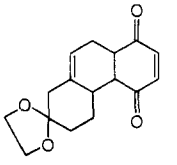
R_1	R_2	R_3	R_4	R_5	Other	Adduct	%	Ref
OAc	Me	H	Me	H			46	*i*
OAc	Me	H	H	OMe			82	*i*
OAc	Me	H	H	H			27	*i*
OAc	CO_2Et	H	H	H			97	*i*
OAc	CO_2Et	Me	OMe	H			39	*i*
OAc	CO_2Et	H	H	Me			63	*i*
OMe	H	H	H	H			72	*n*
OAc	CN	CN	H	H			50	*o*
OAc	CO_2Et	CO_2Et	H	H			30	*o*
OAc	CO_2Me	Me	H	Me			11	*o*
OAc	Me	H	Me	CO_2Et			56	*o*
OAc	Me	CO_2Me	CO_2Me	Me			43	*o*

TABLE XXIX (continued)

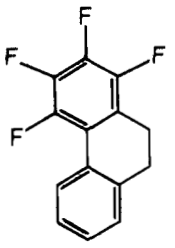
R_1	R_2	R_3	R_4	R_5	Other	Adduct	%	Ref
OAc	Me	CO_2Me	H	OMe			11	*o*
Ph	H	H	H	H			13	*p*
Ph	H	Me	H	*p*-TolS			25	*p*
H	H	H	H	H	2-Me or 6-Me		25	*q*
H	H	H	H	H	6-Me		25	*q, r*
H	H	H	H	H	$6,6\text{-}(Me)_2$	 + 		*s*
H	H	H	H	H			87	*t, u*

[a] S. Sugasawa and K. Kodama, *Chem. Ber.*, **72**, 675 (1939). [b] I. N. Nazarov, G. P. Verkholetova, and I. V. Torgov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 283 (1959); *Chem. Abstr.*, **53**, 22082 (1959). [c] H. Christol, F. Pietrasanta, Y. Pietrasanta, and J. C. Rousselou, *Bull. Soc. Chim. Fr.*, 2770 (1972). [d] G. Ohloff, H. Farnow, and G. Schade, *Chem. Ber.*, **89**, 1549 (1956). [e] A. Alberola, M. Lora-Tamayo, A. del Rey, J. L. Soto, and M. Soto, *An. Real. Soc. Espan. Fis. Quim., Ser. B*, **59**, 151 (1963); *Chem. Abstr.*, **59**, 9927 (1963). [f] M. F. Ansell, B. W. Nash, and D. A. Wilson, *J. Chem. Soc.*, 3012 (1963). [g] A. Alberola, F. Amat, M. Lora-Tamayo, and J. L. Soto, *An. Real. Soc. Espan. Fis. Quim., Ser. B*, **62**, 699 (1966); *Chem. Abstr.*, **66**, 28431 (1967). [h] M. F. Ansell, G. C. Culling, B. W. Nash, D. A. Wilson, and J. W. Lown, *Proc. Chem. Soc.*, 405 (1960). [i] M. F. Ansell and B. A. Knights, *J. Chem. Soc.*, 2903 (1961); M. F. Ansell and G. C. Culling, *ibid.*, 2908 (1961). [j] I. N. Nazarov, V. F. Kucherov, V. M. Andreev, and G. M. Segal, *Dokl. Akad. Nauk SSSR*, **104**, 729 (1955); *Chem. Abstr.*, **50**, 11304 (1956). [k] M. Mousseron, F. Winternitz, and C. Balmossiere, *C. R. Acad. Sci., Ser. C*, **243**, 1328 (1956). [m] M. F. Ansell and G. T. Brooks, *J. Chem. Soc.*, 4518 (1956). [n] I. A. Favorskaya and L. V. Fedorova, *Zh. Obshch. Khim.*, **24**, 242 (1954); *Chem. Abstr.*, **49**, 4538 (1955). [o] M. F. Ansell, B. W. Nash, and D. A. Wilson, *J. Chem. Soc.*, 3006 (1963). [p] V. Georgian and J. Lepe, *J. Org. Chem.*, **29**, 45 (1964). [q] P. A. Robens and J. Walker, *J. Chem. Soc.*, 1610 (1952). [r] T. J. King and G. Read, *ibid.*, 5090 (1961). [s] H. Kakisawa and M. Ikeda, *Nippon Kaguku Zasshi.*, **88**, 476 (1967); *Chem. Abstr.*, **69**, 2740 (1968). [t] K. K. Pivnitskii and I. V. Torgov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1080 (1961); *Chem. Abstr.*, **55**, 27238 (1961). [u] I. V. Torgov, *Tr. Konf. Vop. Str. Reakts. Sposobn. Atsetalei, Akad. Nauk Kirg. SSR, Inst. Organ. Khim.*, 3 (1961); *Chem. Abstr.*, **60**, 7963 (1964).

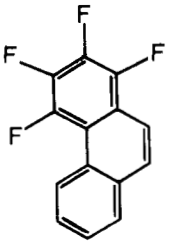
The more electrophilic tetrahalogenobenzynes have also been employed,[417-420] and a number of different types of products have been isolated, depending upon conditions. Thus, tetrachlorobenzyne (from pentachlorophenyllithium) reacted with styrene to give 1,2,3,4-tetrachloro-9,10-dihydrophenanthrene in 34% yield, whereas the corresponding phenanthrene resulted (75% yield) when the aryne was generated from anthranilic acid.[417,421] Tetrafluorobenzyne has also been formed by a variety of methods and reacted with styrene; the compounds **374**, **375**, and **376** have been identified among the products. 2-Methyl-, 3-methyl-, 4-methyl-, and 2,4-dimethylstyrene react with tetrafluorobenzyne in an analogous way.[417-420]

The method used to generate the aryne can be very important, as can the solvent and temperature at which the reaction is conducted.[411] Probably the best method used so far is the aprotic diazotization of anthranilic acids.[422,423] When benzenediazonium-2-carboxylate hydrochloride is used[424] to form benzyne in the presence of isosafrole, the major product is *trans*-3-(3′,4′-methylenedioxyphenyl)-4-methyl-3,4-dihydroisocoumarin (**377**), presumably derived by formation of **378**, followed by its attack at the double bond of isosafrole.

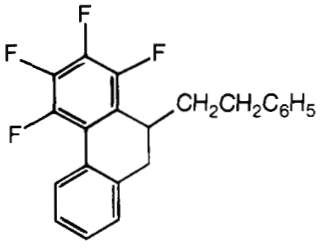
Phenylacetylene reacts with benzyne (from benzenediazon-



374

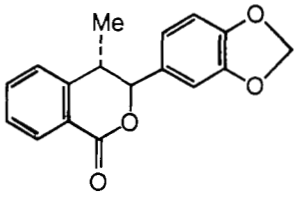


375

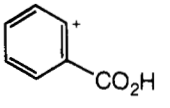


376

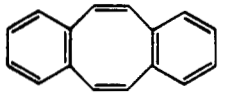
ium-2-carboxylate) to form[425] a hydrocarbon mixture from which phenanthrene and **379** can be isolated. When the benzyne was generated from benzenediazonium-2-carboxylate hydrochloride or by the aprotic diazotization of anthranilic acid, 9-phenylphenanthrene, as well as phenanthrene and **379**, was isolated. The reaction between 3,4-dimethoxyphenylacetylene and benzyne gives[411] a 40% yield of 2,3-dimethoxyphenanthrene together[426] with some 3,4-dimethoxyphenanthrene and the cyclooctatetraene **380.** When the benzyne was[426] generated from ben-



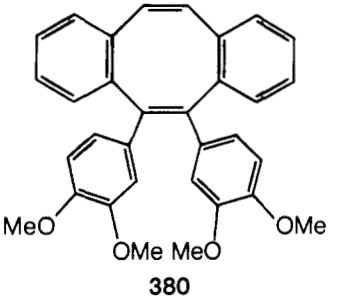
377



378



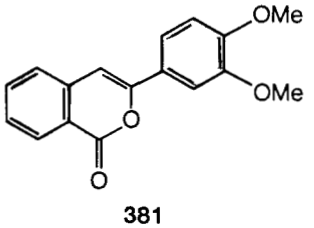
379



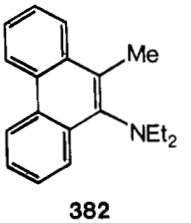
380

zenediazonium-2-carboxylate hydrochloride and reacted with 3,4-dimethoxyphenylacetylene, the above three compounds were again isolated, together with the isocoumarin **381.**

An interesting preparation of phenanthrenes involves[427] the treatment of *o*-chlorophenylmagnesium bromide sequentially



381

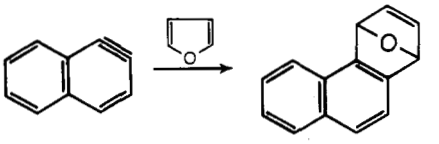


382

with chromic chloride (to form $(o\text{-}ClC_6H_4)_3Cr$) and methylphenylacetylene when 9-phenyl-10-methylphenanthrene is produced in almost 60% yield; a benzyne intermediate is implicated.

The phenanthrene **382** is formed[428] in 10% yield when benzyne (from *o*-fluorobromobenzene) reacts with *N,N*-diethylaminopropyne.

An alternative route to phenanthrenes involving an aryne was reported by Wittig and Benz[429-431] and involves the Diels–Alder reaction between 1,2-naphthyne and furan (eq 17).

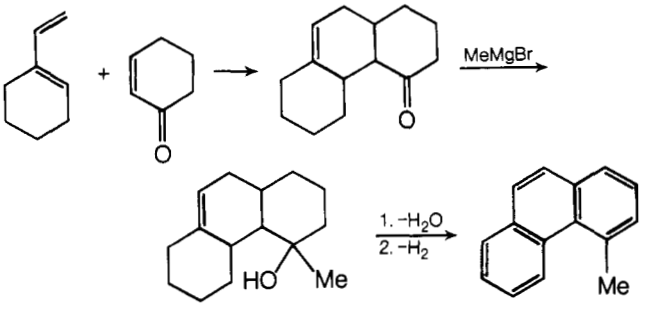


(17)

C. Miscellaneous Methods

1-Vinylcyclohexenes behave as dienes toward typical dienophiles, and since the dienes are readily accessible and the adducts can be dehydrogenated to phenanthrenes, these reactions do provide a useful route to phenanthrenes. Almost all of the reactions reported have utilized *p*-benzoquinones as dienophiles (Table XXIX). α,β-Unsaturated ketones have also been used[432] (Scheme XXII).

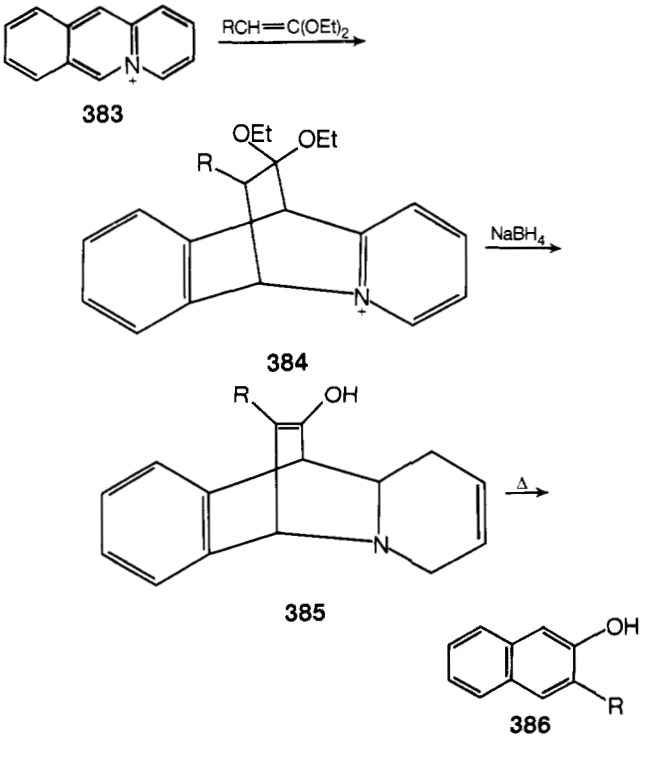
SCHEME XXII



Reduced phenanthrenes have been prepared[433-445] by adding, e.g., maleic anhydride to 1,1′-bicyclohexenyl (eq 18), but since these structures are far removed from the aromatic phenanthrene state of oxidation, they are of limited importance.

A recent paper[446] contains a description of the cycloadducts

SCHEME XXIII



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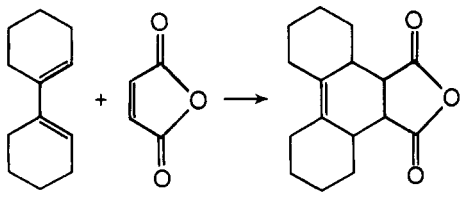
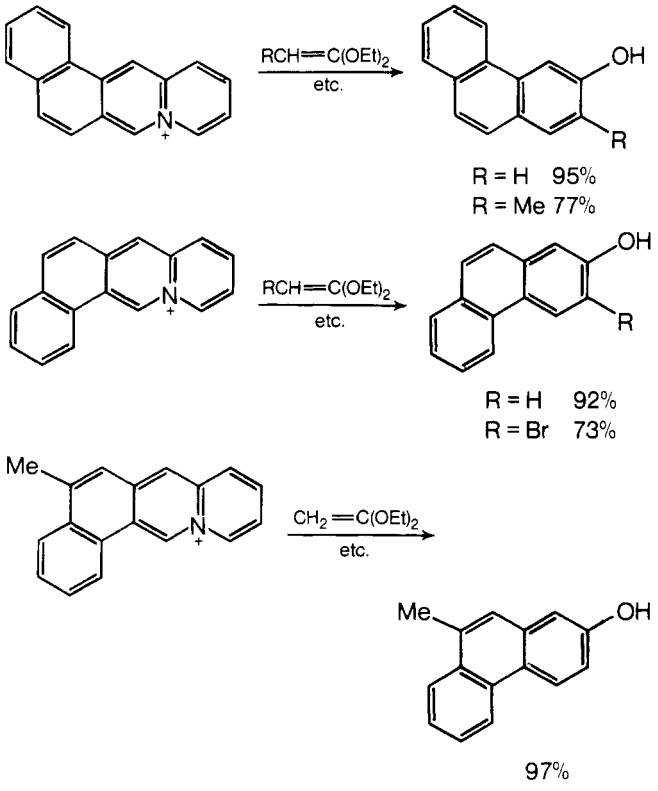


(18)

384, derived from quaternary salts such as **383** and ketone acetals. Reduction of **384** with sodium borohydride gives **385**, which upon thermolysis undergoes a retro-Diels–Alder reaction to yield **386** (Scheme XXIII). When this sequence is applied[446] to the appropriate quaternary salts, it constitutes a method for the preparation of phenanthrenes (Scheme XXIV).

SCHEME XXIV



Acknowledgment. It is a pleasure to acknowledge the help of Mr. P. R. Mills of the Library Staff of Bath University for his assistance with the literature survey.

V. References

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