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Dehydrogenation of Polycyclic Hydroaromatic Compounds

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I. Introduction

Dehydrogenation reactions are of broad synthetic utility. By definition, dehydrogenation involves removal of one or more pairs of hydrogen atoms to provide an unsaturated bond or bonds. In order to limit this article to manageable dimensions, coverage will be restricted to dehydrogenation of fused carbocyclic ring systems to afford cyclic olefinic and aromatic molecules. Thus, the analogous reactions of heterocyclic compounds and reactions such as the oxidation of alcohols to aldehydes and ketones, or oxidation of hydrazo to azo compounds, will not be covered. Also excluded is the dehydrocyclization reaction which has been reviewed elsewhere.[1]

Dehydrogenation is frequently the last step in the synthesis of polycyclic aromatic hydrocarbons and their derivatives.[2] The principal methods employed in the older literature involve the use of sulfur, selenium, or the platinum metals. Although these reagents still find useful application, particularly in the synthesis of unsubstituted polycyclic aromatic ring systems, they require relatively drastic conditions unsuitable for the synthesis of the more sensitive compounds currently of greatest interest, such as the oxidized metabolites of carcinogenic hydrocarbons. An additional limitation of these traditional methods is the impracticality of controlling the extent of reaction to obtain intermediate olefinic products, themselves often potentially valuable synthetic intermediates.

New milder methods of dehydrogenation, less hampered by these limitations, are gradually supplanting the conventional methods. The best known of these is the use of high oxidation potential quinones, such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and chloranil. Others include trityl salts, alkyllithium–*N,N,N′,N′*-tetramethylethylenediamine complexes, and bromination–dehydrobromination with *N*-bromosuccinimide, in addition to various miscellaneous methods. While none of these procedures approach the high selectivity and efficiency of enzymatic transformations, progress toward this ultimate goal has been encouraging in recent years. It is hoped that this review will stimulate chemists to devise still more efficient procedures.

II. Scope of the Review

Despite the rather extensive literature on dehydrogenation, no comprehensive review of this topic is available. The use of sulfur, selenium, and the platinum metals were summarized by Plattner in 1948[3] in a review oriented toward identification of natural product ring systems through aromatization. Numerous examples of the use of the same reagents for the synthesis of polycyclic hydrocarbons are dispersed throughout the comprehensive two-volume survey of hydrocarbon chemistry published by Clar in 1964.[2] Quinone dehydrogenations of all types were reviewed for the first time by Jackman in 1960.[4] More recently reactions of the most commonly employed quinone, DDQ, were surveyed by Walker and Hiebert in 1967,[5] and the use of quinones as oxidants was reviewed by Becker in 1974.[6] The newer methods of dehydrogenation have not to our knowledge been reviewed.

We have striven for complete literature coverage through mid-1977. However, this has proven an impossible task, since many dehydrogenation reactions are buried in the experimental sections of papers on other subjects and not indexed under this topic. We, therefore, offer our apologies in advance for any such inadvertent omissions.

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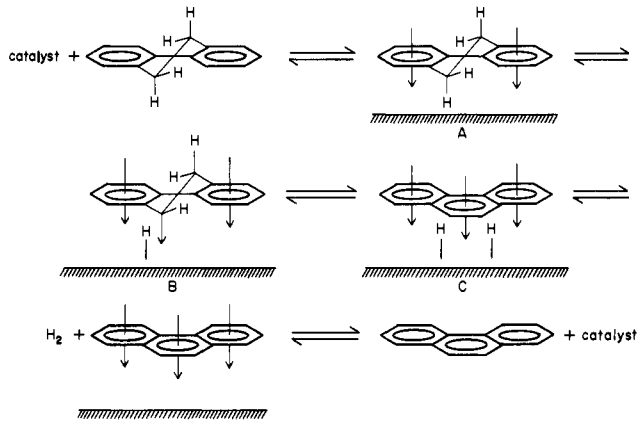


Figure 1. Proposed mechanism of catalytic dehydrogenation of hydroaromatic compounds.

III. Nomenclature

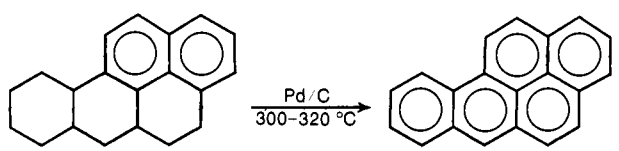
Several competing nomenclature systems have been employed in the past to designate the structures of polycyclic hydrocarbon compounds. The IUPAC 1957 Rules which will be employed throughout this article are now the currently accepted standard on both sides of the Atlantic, having been officially adopted by *Chemical Abstracts* and foreign chemical societies. Unfortunately, some of the confusion persists, and the reader will encounter the older nomenclatures in Clar's otherwise excellent treatise on polycyclic hydrocarbon chemistry[2] and in the older literature.

IV. Catalytic Dehydrogenation

A. Selection of Catalysts and Conditions

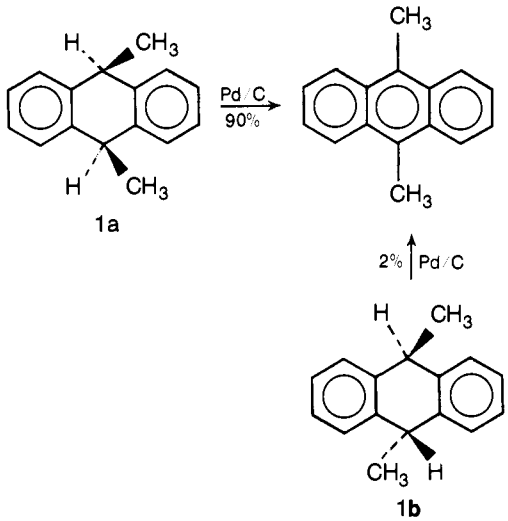
Catalytic dehydrogenation of hydroaromatic compounds is one of the classic methods of synthesis of polycyclic aromatic molecules. The most generally satisfactory catalysts are platinum and palladium employed as the finely divided free metals or supported on activated charcoal.[7] Nickel and copper catalysts have proven less satisfactory, since they require higher reaction temperatures which lead to thermal decomposition, skeletal rearrangement, and other side reactions.

Optimum temperatures vary widely, dependent principally upon the structure of the hydroaromatic compound and the nature of the catalysts. Tetralin has been smoothly dehydrogenated at temperatures as low as 185 °C while decalin and 9-methyldecalin require temperatures exceeding 300 °C.[8,9] In general, dehydrogenation proceeds more readily and in better yield the closer the starting material is to being fully aromatic. Solvents may or may not be employed. In the absence of solvent, reaction temperatures in the range of 300–340 °C are commonly utilized. In cases where the polycyclic aromatic product sublimes readily, it may be convenient to sublime it directly from the reaction mixture. For example, catalytic dehydrogenation of decahydrobenzo[*a*]pyrene over Pd/C at 300–320 °C afforded benzo[*a*]pyrene collected as a sublimate from an air condenser.[10]



Reactions in solution are generally conducted at reflux in relatively high-boiling solvents, such as cumene (bp 153 °C), *p*-cymene (bp 176 °C), decalin (bp ~185 °C), nitrobenzene (bp 211 °C), naphthalene (bp 218 °C), quinoline (bp 238 °C), or 1-methylnaphthalene (bp 244 °C). The recently introduced polyglycol ethers[11] (e.g., diglyme, bp 162 °C; triglyme, bp 216 °C) offer the advantages of a wide range of boiling points and convenience of removal during workup by virtue of their miscibility with water. Vigorous boiling or passage of a stream of inert gas through the solution is frequently employed both to stir the mixture and to sweep hydrogen from the system as it is liberated. If carbon dioxide is used, the exit gas may be passed through aqueous potassium hydroxide to remove the carbon dioxide, and the remaining hydrogen may be collected in a gas buret to follow the progress of the dehydrogenation.[12]

Alkyl substitution appears to influence minimally the overall rate or the temperature required, except where the substituent interferes with adsorption on the catalyst surface. As might be anticipated, bulky groups tend to retard the rate of reaction. However, even methyl groups may dramatically inhibit reaction in cases where they sterically block association with the catalyst. Thus, the rate of dehydrogenation of *cis*-9,10-dimethyl-9,10-dihydroanthracene (**1a**) to 9,10-dimethylanthracene over 10% Pd/C in refluxing diglyme greatly exceeded that of the corresponding trans stereoisomer (**1b**) as measured by the percentage conversion (90 and 2%, respectively) in the same time period (12 h).[11] Similar results were obtained with the monoethyl and diethyl homologs of **1**.[11]



1a

1b

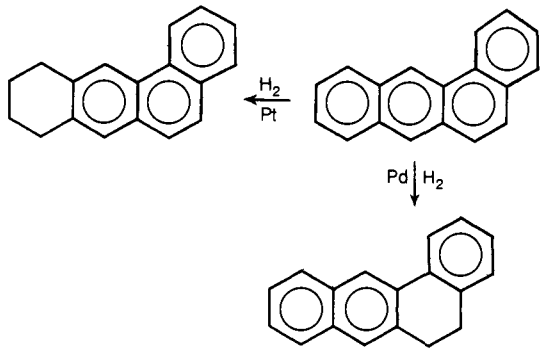
B. Mechanism

Catalytic dehydrogenation is in essence the reverse of catalytic hydrogenation. The two processes, therefore, involve the same mechanism(s) viewed from opposite viewpoints. While hydrogenation has been the subject of numerous investigations,[12-14] dehydrogenation of hydroaromatic compounds has been employed mainly for preparative purposes and has received little systematic study. Considerable weight of experimental evidence supports the generalization that hydrogenation involves cis addition of two hydrogen atoms from the less hindered side of the double bond or polycyclic ring system.[12-17] Conversely, dehydrogenation appears to involve predominantly cis hydrogen abstraction.[7-9,11,13] Competing secondary processes, including olefin isomerization, hydrogen exchange, and epimerization, may occur simultaneously on the catalyst surface, complicating attempts to study the mechanism of the hydrogenation–dehydrogenation process. Despite these difficulties, it is now reasonably well established that hydrogenation occurs by stepwise transfer of hydrogen atoms to the adsorbed molecule, rather than by concerted cis addition.

A mechanism based on that postulated originally by Horiuti and Polanyi[18] to explain hydrogenation provides the simplest explanation of the essential facts concerning dehydrogenation of hydroaromatic compounds. According to this scheme (Figure 1), dehydrogenation of a dihydroarene, such as dihydrophenanthrene, may be depicted as a series of equilibria involving π-bonded and σ-bonded intermediates. The substrate is initially

adsorbed on the catalyst surface by π bonds to one or more aromatic rings. The number of rings associated in this manner will be dependent in individual cases upon the ease of adoption of a favorable planar conformation and steric factors, such as the presence of bulky substituents. Transfer of an axially oriented hydrogen atom from the partially saturated central ring of the π-bonded intermediate A to the catalyst leads to a σ-bonded intermediate B. Loss of a second hydrogen provides a fully aromatic polycyclic ring system C still closely associated with the catalyst surface by π bonds. Alternatively, an intermediate having two σ bonds to the ring undergoing reaction is also conceivable. Desorption of molecular hydrogen from the catalyst surface and its loss from solution shift the equilibria to favor formation of the fully aromatic molecule, e.g., phenanthrene. Desorption of the aromatic product into solution frees the catalyst for repetition of the cycle. However, competition for active sites on the catalyst surface between the fully aromatic product and the partially saturated starting material is likely to favor preferential association of the product as a consequence of the greater extent of π-bonding possible. This may result in slowing down the reaction rate as the reaction proceeds. No clearcut evidence concerning this effect has been reported.

Marked differences in the regioselectivity of Pd and Pt catalysts in the low-pressure hydrogenation of polycyclic hydrocarbons have recently been reported.[19,20] Palladium catalysts under mild conditions catalyze hydrogen addition to the relatively olefinic electron rich K-region bonds,[19] while hydrogenation of the same compounds over platinum tends to take place on terminal rings.[20] For example, hydrogenation of benz[*a*]anthracene over Pd/C at ambient temperature affords 5,6-dihydrobenz[*a*]-anthracene, while similar reaction over a Pt catalyst furnishes 8,9,10,11-tetrahydrobenz[*a*]anthracene. The molecular basis

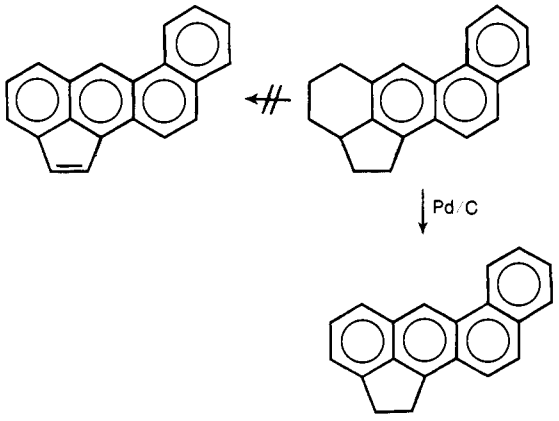


of this metal effect is not understood. It may be a consequence of the relative spacing of the metal atoms on the catalyst surface in relation to the bond distances in the hydrocarbon molecule. In any case, it appears likely that similar regioselectivity may be possible under appropriately controlled conditions during dehydrogenation (e.g., in the partial dehydrogenation of 5,6,8,9,10,11-hexahydrobenz[*a*]anthracene). This, however, remains to be established.

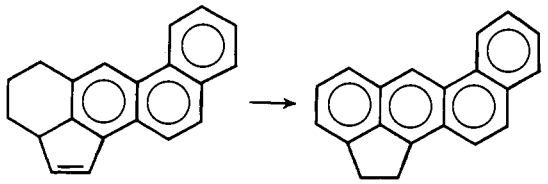
C. Dehydrogenation Reactions

1. *Aromatization of Unsubstituted Polycyclic Hydrocarbons*

In Table I are summarized published examples of catalytic dehydrogenation of unsubstituted polycyclic hydrocarbons. The catalyst employed with few exceptions is Pd/C. Yields are generally good. Since these studies were oriented virtually exclusively toward synthesis, the nature of secondary products is largely unknown. It is generally observed that five-membered fused rings fail to undergo dehydrogenation. For example, 2a,3,4,5-tetrahydrocholanthrene affords cholanthrene[29] rather than cholanthrylene. If an olefinic bond is initially present in a

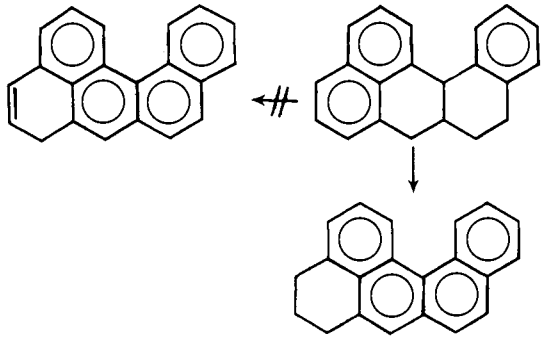


five-membered ring, as in **2**,[38] it is lost during reaction. Similarly,

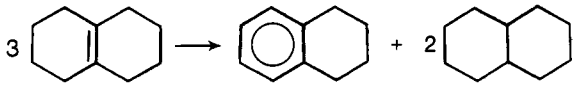


2

dehydrogenation of a fused six-membered ring system incapable of formation of a fully aromatic arene stops short of formation of a partially olefinic arene.[31]



Disproportionation is frequently the initial stage preceding full aromatization. Linstead et al.[9] observed that reaction of refluxing octalin over Pd/C slowed down after an initial period of hydrogen evolution. The product at this stage consisted of decalin and tetralin in 2:1 ratio. Reaction of decalin is considerably slower



than that of tetralin or octalin. The tendency toward disproportionation may be utilized to synthetic advantage. For example, 9,10-dihydroanthracene on heating over Pd/C at 225 °C for 15 h disproportionated to anthracene and 1,2,3,4-tetrahydroanthracene.[43] This represents a relatively convenient synthesis of the latter otherwise not readily accessible hydrocarbon.

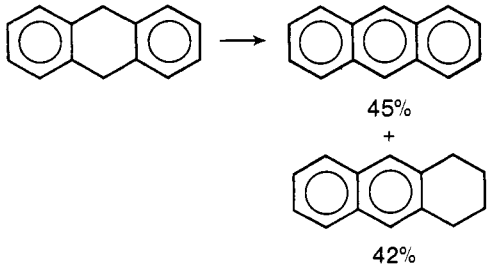


TABLE I. Catalytic Dehydrogenation of Unsubstituted Polycyclic Hydrocarbons

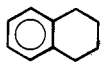
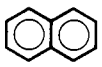
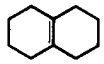
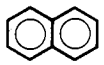
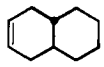
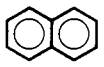
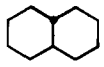
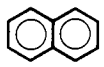
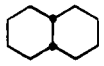
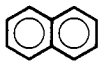
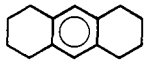
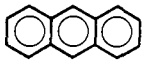
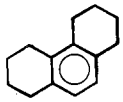
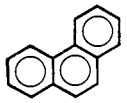
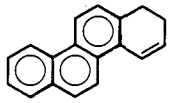
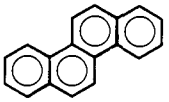
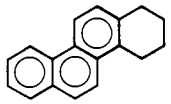
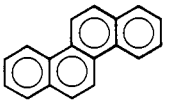
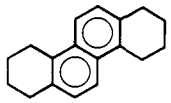
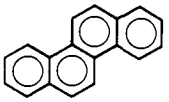
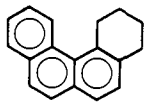
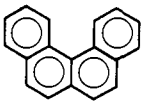
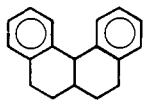
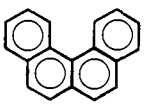
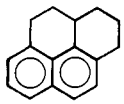
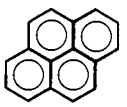
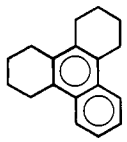
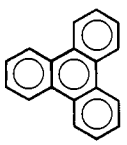
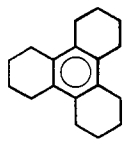
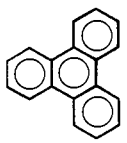
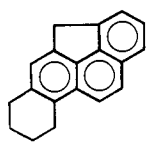
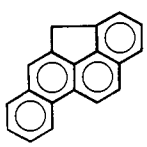
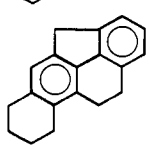
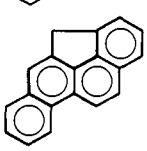
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd/C	Reflux, 1 h	37	9
		Pd/C	Reflux, 6 h	87	9
		Pd/C	Reflux, 22 h	97	9
		Pt/C	Reflux, 21 h	78	9
		Pd/C	Reflux, 23 h	37	9
		Pd/C	300 °C	82	9
		Pt/C	Reflux, 21 h	12	9
		Pd/C	Reflux, 21 h	6.5	9
		Pt/C	300 °C	95	9
		Pd/C	Reflux, 1 h	100	9
		Pd/C	Reflux, 1 h	100	9
		Pd/C	300–320 °C, 1 h	93	21
		Pd/C	300–320 °C, 1 h	87	21
		Pt	270 °C		22
		Pd/C	310–320 °C, 15 min	61	23
		Pt	310–320 °C, 7 h, CO_2	60	24
		Pd/C	300–320 °C, 45 min	51	25
		Pd/C	300 °C, 2 h	~100	26
		Cu	450–500 °C		27
		Pd/C	250–265 °C, 1 h	54.5	28
		Pd/C	265 °C, 1 h	64	28
			265–270 °C, 50 min	64	28

TABLE I (*Continued*)

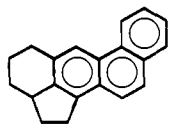
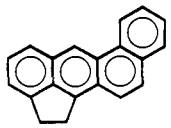
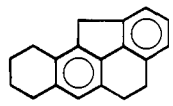
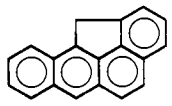
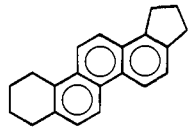
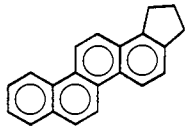
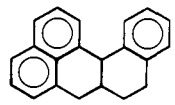
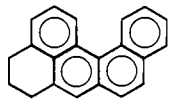
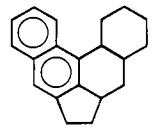
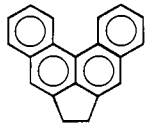
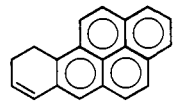
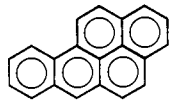
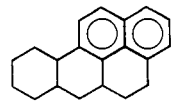
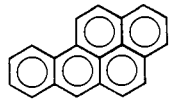
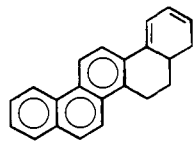
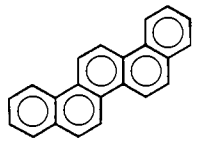
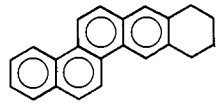
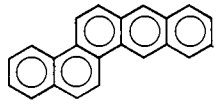
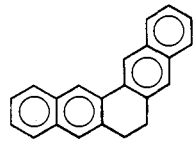
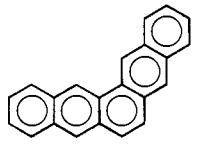
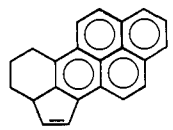
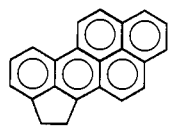
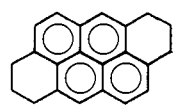
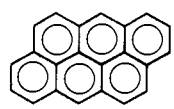
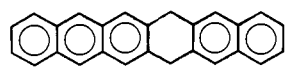
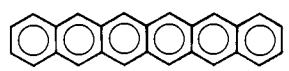
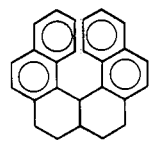
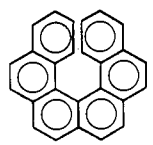
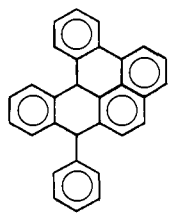
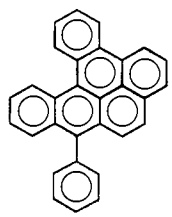
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd/C	300 °C, 30 min	80	29
		Pd/C	220–265 °C, 30 min 265–300 °C, 30 min 300–320 °C, 10 min		28
		Pd/C	270 °C, 1 h	48	30
		Pd/C	290–300 °C, 45 min	91	31
		Pd/C	300–310 °C, 30 min	10	32
		Pd/C	*p*-Cymene, reflux, 3 h	74	33
		Pd/C	300–320 °C, 2 h	73	10
		Pd/C	340 °C, 1 h	~35	34
		Pd	300 °C, 3 h		35
		Pd/C Pd/C	*p*-Cymene, reflux, 4 h 350 °C, 4 h	67 90	36 37
		Pd/C	310–330 °C, N_2	71	38
		Pd/C	290–300 °C, 1 h	~100	31
		Pd/C	Trichlorobenzene 200 °C		39
		Rh/Al	300 °C	64	40
		Pt/C			41

TABLE I (*Continued*)

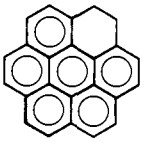
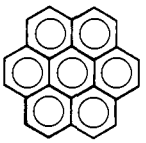
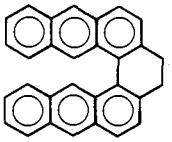
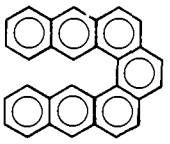
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd		87	42
		Pd/C	*p*-Cumene, reflux, 4 h	80	36

TABLE II. Catalytic Dehydrogenation of Substituted Polycyclic Hydrocarbons

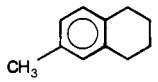
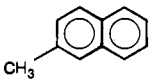
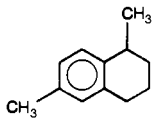
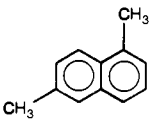
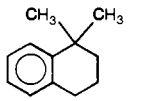
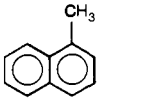
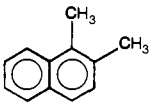
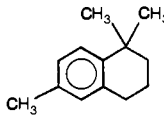
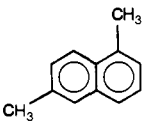
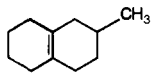
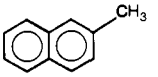
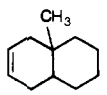
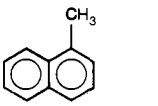
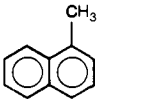
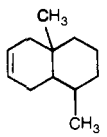
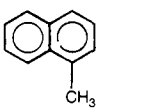
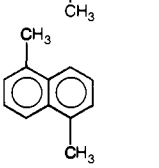
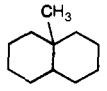
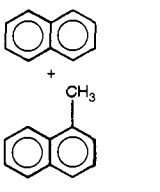
Substrate	Product	Catalyst	Conditions[a]	Yield %	Ref
		Pd/C	Reflux	80	7
		Pd/C	Reflux	87	7
		Pd/C	320°, 31 h	Major	7
				Minor	
		Pd/C			7
		Pt/C			7
		Pt/C	300°	50	9
		Pt/C	355°	70	9
		Pd/C	300°	80	9
		Pd/C	Reflux		7
		Pt/C	Reflux		7
		Pd/C	Reflux		7
		Pt/C	Reflux		7
		Pt/C	330°	40	9

TABLE II (*Continued*)

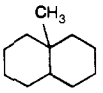
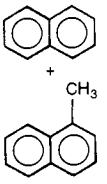
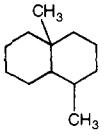
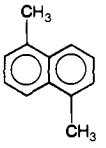
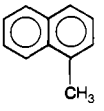
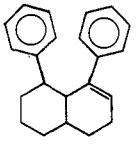
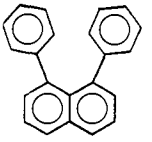
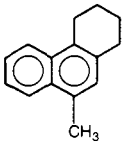
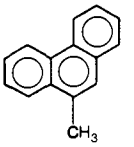
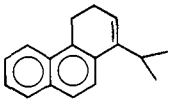
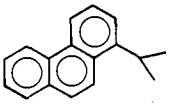
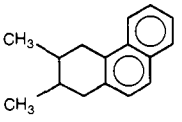
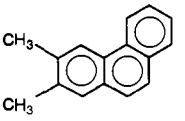
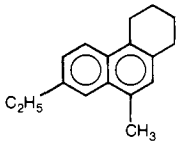
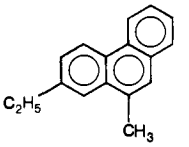
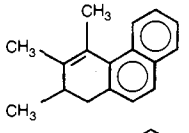
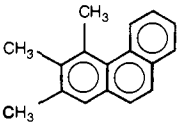
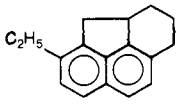
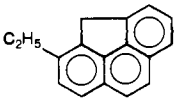
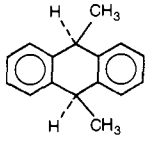
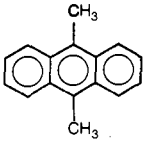
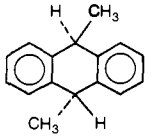
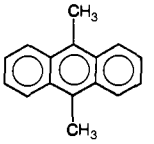
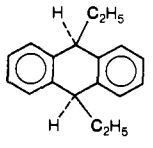
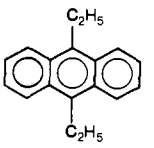
Substrate	Product	Catalyst	Conditions[a]	Yield, %	Ref
		Pd/C	330°	50	9
		Pt/C	330°		9
		Pd/C	330°		9
		Pd/C	Cumene, reflux, 42.5 h	54	44
		Pd/C	300–320°, 1 h	83	45
		Pd/C		65	46
		Pd/C	300–330°, 1.5 h		47
		Pd/C	300–320°, 1 h	93	45
		Pd/C		>17	47
		Pd/C		74	48
		Pd/C	Diglyme reflux, 6 h	91	11
		Pd/C Pd/C	Diglyme, reflux, 6 h Diglyme, reflux, 12 h	11 24	11 11
		Pd/C	Diglyme, reflux, 12 h	90	11

TABLE II (*Continued*)

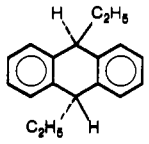
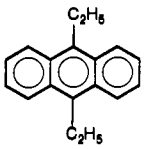
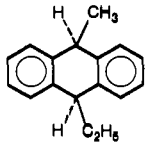
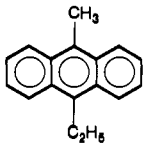
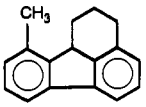
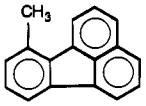
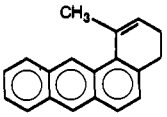
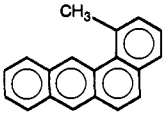
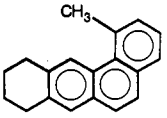
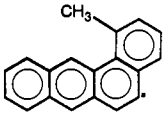
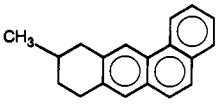
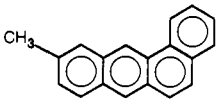
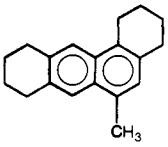
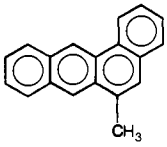
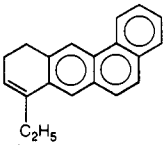
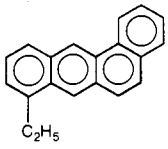
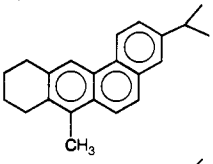
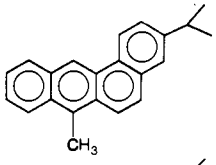
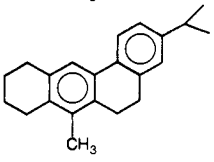
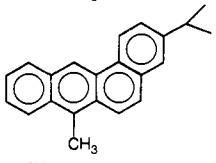
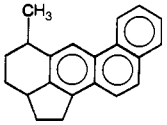
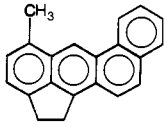
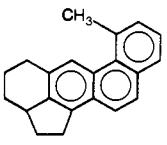
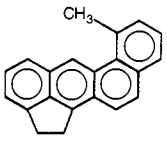
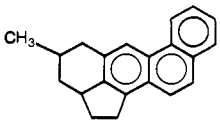
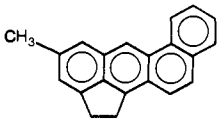
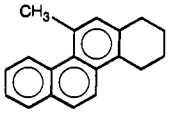
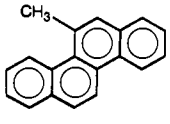
Substrate	Product	Catalyst	Conditions[a]	Yield, %	Ref
		Pd/C	Diglyme, reflux, 12 h	2	11
		Pd/C	Diglyme, reflux, 24 h		11
		$Pd/BaSO_4$	200–290°	81	49
		Pt	CO_2, Δ		50
		Pd/C	300–320°, 30 min	75	51
		Pd/C	300–320°, N_2	77	52
		Pd/C	300–320°, 1 h	87	45
		Pd/C	330–340°, 1 h	70	53
		Pd/C	265°, 1 h 265–276°, 1.5 h 295–300°, 20 min	>62	54
		Pd/C	295°, 1 h 265–275°, 1.5 h 295–300°, 30 min	87	54
		Pd/C	300–315°, 20 min	>70	55
		Pd/C	310°, 30 min	93	56
		Pd/C	300–310°, 25 min	86	55
		Pd/C	300–320°, 45 min	85	51

TABLE II (*Continued*)

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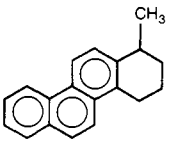
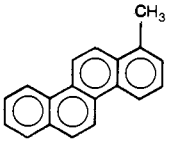
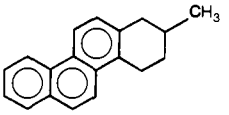
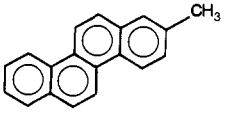
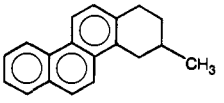
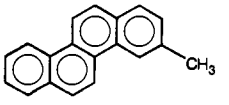
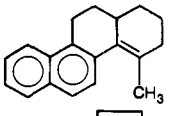
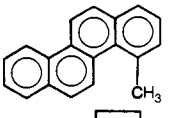
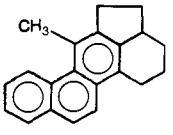
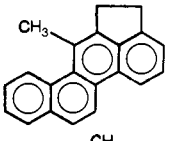
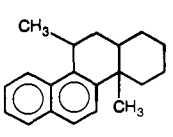
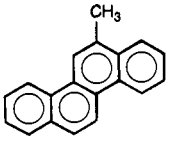
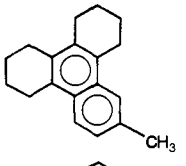
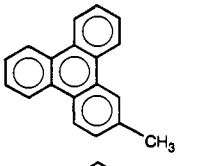
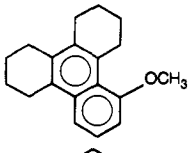
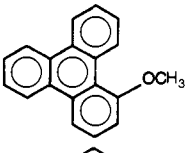
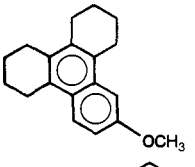
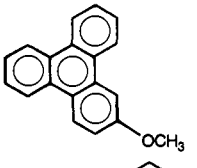
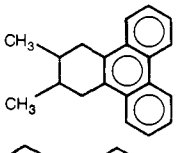
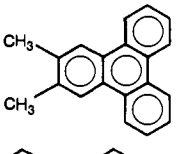
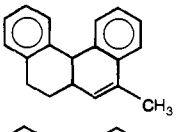
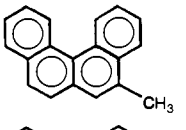
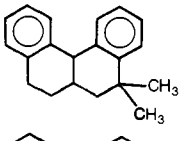
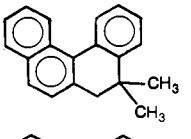
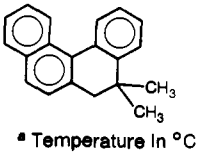
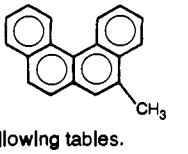
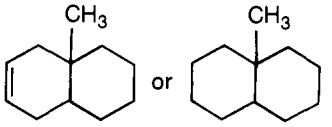
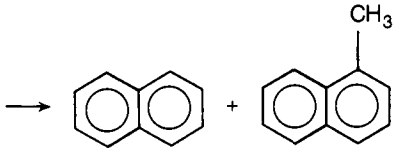
		Pd/C	300–320°, 1 h	94	57
		Pd/C	300–320°, 1 h	90	21
		Pd/C	300–320°, 1 h	92	57
		Pd/C	300–320°, 1 h	78	58
		Pd/C	310°, 45 min	>44	59
		Pd/C	310°, 16 h	4	60
		Pd/C	300°, 2 h		26
		Pd/C	300°, 2 h	~100	26
		Pd/C	300°, 3 h		26
		Pd/C	300–325°, 1.5 h	62	47
		Pt	310–320°, CO_2		24
		Pd/C	300°, 4 h	70	61
		Pd/C	360°, 2 h	80	61

[a] Temperature in °C in this and the following tables.

2. Aromatization of Substituted Polycyclic Hydrocarbons

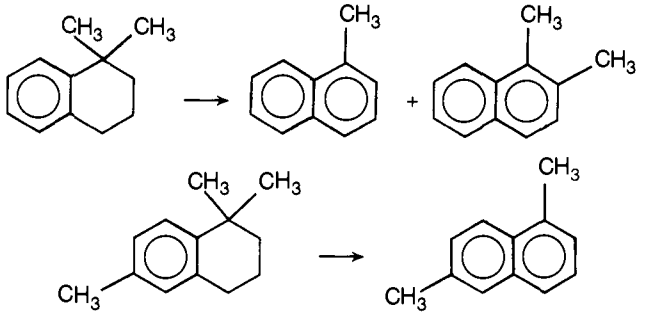
Numerous examples of catalytic dehydrogenation of substituted arenes have been reported (Table II). Although loss or rearrangement of substituents may occur, these are generally not major pathways, at least for alkyl substituents. The only systematic studies were conducted by Linstead et al.[7,9] who investigated the action of metallic catalysts on methylated tetralins, octalins, and decalins. Despite the semiquantitative nature of this older data, a number of conclusions are evident. Most significantly, methyl groups on aromatic rings or tertiary methyl groups are relatively unaffected during reactions over Pd/C or Pt/C catalysts under the usual conditions. Thus, 1- and 2-methyloctalin,[9] 1-methyldecalin,[9] 6-methyltetralin,[7] and 1,6-dimethyltetralin[7] furnish 1- and 2-methylnaphthalene, 6-methylnaphthalene, and 1,6-dimethylnaphthalene, respectively, as the major products. On the other hand, quaternary methyl groups, either bridgehead or geminal, tend to undergo elimination and to lesser extent migration to adjacent ring positions. Thus, 9-methyldecalin and 9-methyloctalin undergo conversion in the vapor phase over Pd/C at 320 °C to afford naphthalene, while similar reactions over Pt/C furnish both naphthalene and 1-



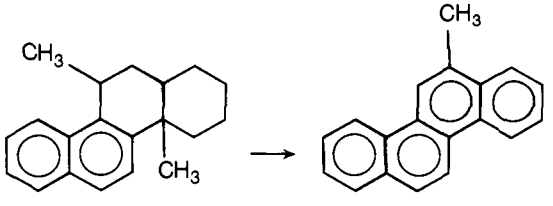


methylnaphthalene.[7] The extent of migration becomes almost equal to that of elimination when asbestos is employed as the catalyst support.[9] Analogous reactions of the corresponding 4,9-dimethyldecalin and octalin gave analogous results.

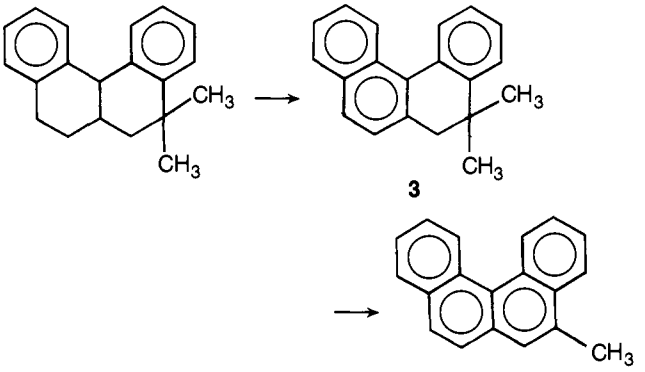
1,1-Dimethyltetralin on treatment with Pd/C at reflux gave 1-methylnaphthalene accompanied by a small amount of 1,2-dimethylnaphthalene; similar reaction over Pt/C provided only 1-methylnaphthalene.[7] 1,1,6-Trimethyltetralin over platinized asbestos or palladized charcoal afforded only the eliminated product, 1,6-dimethylnaphthalene.[7]



With larger polycyclic ring systems essentially similar results are obtained. Loss or migration of alkyl groups is rare. However, both are exhibited by 4a,11-dimethyl-1,2,3,4,4a,11,12,12a-octahydrochrysene which undergoes conversion to 6-methylchrysene over Pd/C.[60] Part of the driving force for the rearrangement is the bay region steric interaction between the



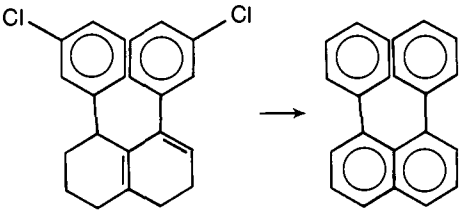
11-methyl group and the 10-proton. 5,5-Dimethyl-5,6,6a,7,8,12b-hexahydrobenzo[*c*]phenanthrene on treatment with Pd/C at 300 °C for 4 h underwent transformation to the dihydro derivative **3**, retaining the geminal dimethyl function.[61] At higher temperature (360 °C) **3** lost a methyl group to provide the fully aromatic 5-methylbenzo[*c*]phenanthrene.



3

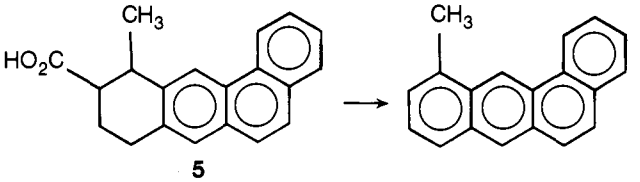
As observed for unsubstituted polycyclic arenes, five-membered fused rings fail to undergo hydrogen loss. Also, dehydrogenation of alkyl side chains (e.g., isopropyl to isopropenyl) is generally not detected.

Halogen atoms are generally lost during catalytic dehydrogenation. For example, the dichloronaphthalene derivative **4** is dehydrogenated to 1,8-diphenylnaphthalene.[44] Hydrogenolysis of aryl halides is, of course, well known.[62]



4

Decarboxylation can also occur during dehydrogenation, dependent upon temperature, catalyst, and other factors. For example, the carboxylic acid derivative of benz[*a*]anthracene **5** on heating at 300–310 °C over Pt/C underwent decarboxylation and dehydrogenation to furnish 11-methylbenz[*a*]anthracene.[50] The bis-anhydride **6** underwent multiple decarboxylation



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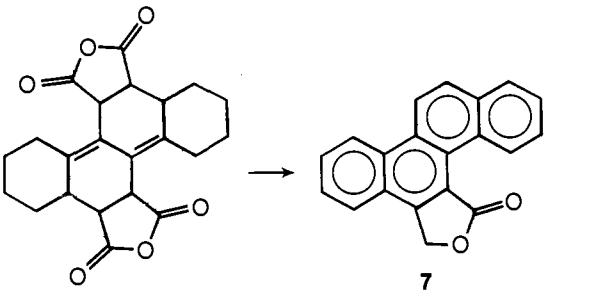

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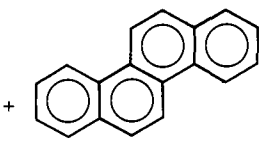
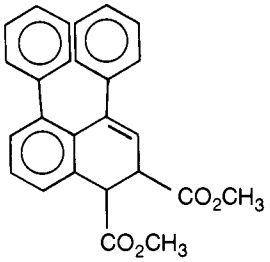


over 30% Pt/C at 280–350 °C to provide chrysene and the chrysene derivative **7**.[63] In contrast, the naphthalene diester derivative **8** was smoothly transformed over Pd/C in refluxing cumene to the fully aromatic compound **9** with retention of both carbomethoxy groups.[44]



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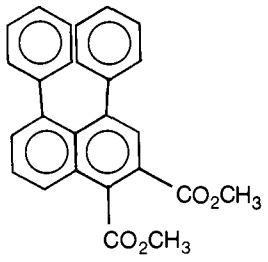
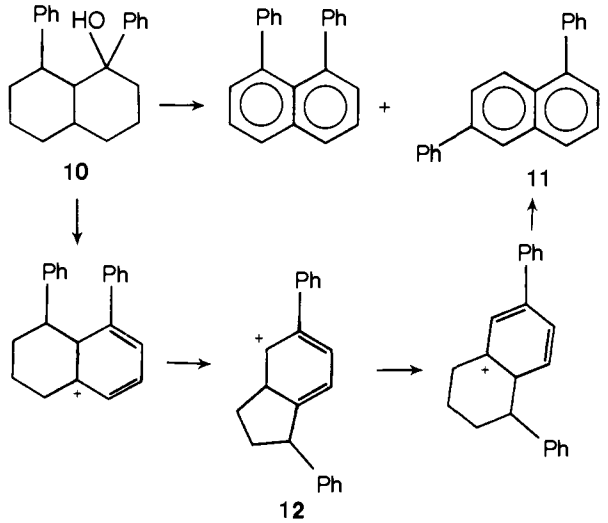


9

3. *Dehydrogenation and Dehydration of Polycyclic Hydrocarbon Alcohols*

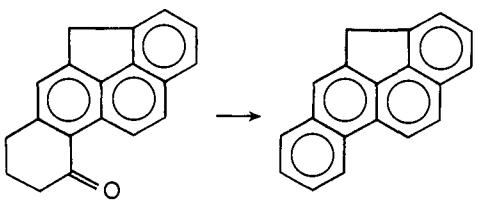
Alcohols are frequently intermediates in the synthesis of polycyclic arenes. Most commonly they arise through either (a) reduction, or (b) reaction with Grignard or organolithium reagents of ketonic precursors formed by cyclization. It is convenient to carry out dehydration and dehydrogenation simultaneously. Published examples of reactions of this type are summarized in Table III. Palladium on charcoal has been the the overwhelming choice as catalyst for such reactions. Yields are generally good. Although rearrangement is seldom a significant complication, it may occur when steric crowding is severe, as in **10**, reaction of which affords 1,6-diphenylnaphthalene (**11**) as well as 1,8-diphenylnaphthalene.[64] It is likely that this apparent migration of the phenyl group may involve ring opening and a spiro intermediate such as **12**.



10 **11** **12**

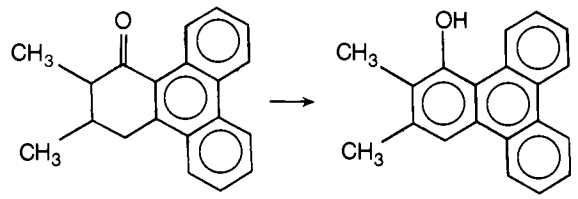
4. *Aromatization of Polycyclic Aromatic Ketones*

Direct dehydrogenation of polycyclic aromatic ketones is the most commonly employed synthetic route to polycyclic phenols (Table IV). Although yields are generally satisfactory, deoxygenation may occur as a secondary pathway. Loss of oxygen



13

probably involves reduction of the carbonyl function to the alcohol followed by hydrogenolysis or dehydration. The ketone **13** on heating in a sealed tube in the presence of Pd/C at 275–285 °C gave the corresponding deoxygenated polycyclic hydrocarbon as the sole identifiable product.[28] The 2,3-dimethyltriphenylene derivative **14** on heating over Pd/C afforded the corresponding phenol and 2,3-dimethyltriphenylene in somewhat greater than 2:1 ratio.[47]



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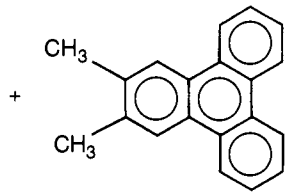


5. *Homogenous Catalytic Dehydrogenation*

The use of soluble hydrogenation catalysts such as tris(triphenylphosphine)rhodium(I) chloride for dehydrogenation has been investigated by Blum and Biger.[43] They compared the activity of several catalysts for the dehydrogenation of 9,10-dihydroanthracene, dibenzo[*a*,e]cyclooctadiene, and 1,2,3,4,7,12-hexahydrobenz[*a*]anthracene (Table V). From this study it appears that the rates of homogeneous dehydrogenation reactions are approximately of the same order as those of the related heterogenous processes with Pd/C. The relative order of catalyst activity is on this basis $IrCl(CO)(PPh_3)_2 > RhCl(PPh_3)_3 > RuCl_2(PPh_3)_3$. The relatively greater efficiency of these soluble iridium and rhodium catalysts in the conversion of hexahydrobenz[*a*]anthracene to benz[*a*]anthracene and dihydroanthracene to anthracene in comparison with Pd/C suggests they may be deserving of more serious investigation than they have been accorded to date.

V. Dehydrogenation with Sulfur and Selenium

A. General Aspects and Mechanism

Elemental sulfur and selenium, like the platinum metals, are classical dehydrogenation reagents. Sulfur exists in a large number of molecular forms including a stable eight-membered ring in a crown conformation[85] and linear chains of widely variable length.[86] Selenium also exists in various forms, including a cyclic Se_8 structure; however, the latter, in contrast to sulfur, is less stable than the infinite chain form.[87] The outer electronic configurations of sulfur and selenium are $[Ne]3s^23p^4$ and $[Ar]3d^{10}4s^24p^4$, respectively. Their facility as dehydrogenation reagents is a consequence of their tendency to complete the inert gas configuration by acquisition of two electrons with formation of the respective hydrides, H_2S and H_2Se. *Since both H_2S and H_2Se have disagreeable odors and are toxic, all operations must be conducted in a well-ventilated hood.*

The mechanism of dehydrogenation of hydroaromatic compounds by means of sulfur and selenium is not well established. The evidence is consistent with radical mechanisms involving abstraction of hydrogen atoms from allylic or benzylic positions, although other possibilities are not conclusively ruled out.[86] The following mechanistic scheme provides the simplest explanation of the essential facts. According to this scheme illustrated for

TABLE III. Catalytic Dehydrogenation and Dehydration of Polycyclic Hydrocarbon Alcohols

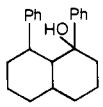
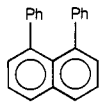
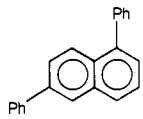
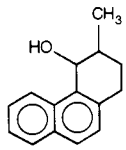
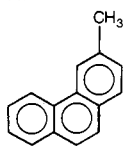
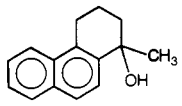
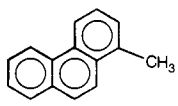
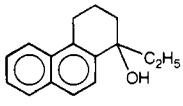
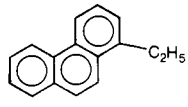
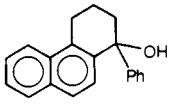
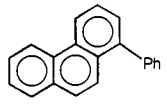
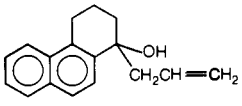
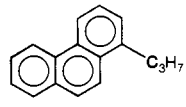
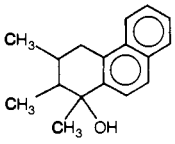
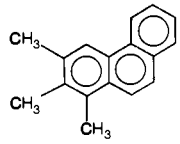
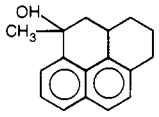
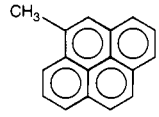
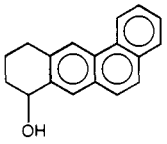
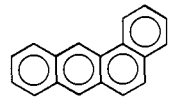
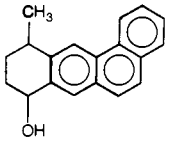
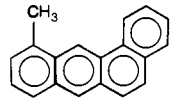
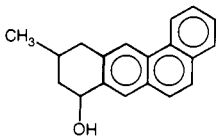
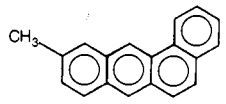
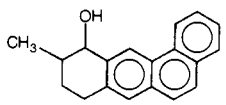
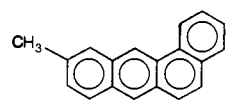
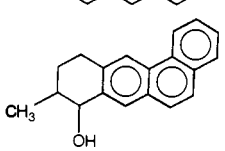
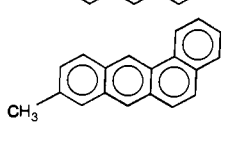
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
	 + 	Pd/C	340°	28 13	64
		Pd/C	300–310°, 30 min	95	65
		Pd/C	310–320°, N_2, 30 min	90	46
		Pd/C	310–320°, N_2	90	46
		Pd/C	310–320°, N_2	94	46
		Pd/C	215–220°, N_2	80	45
		Pd/C	300–350°, 1 h	>42.5	46
		Pd/C	300–320°, 1 h	52	23
		Pd/C	310°, 45 min	70	29
		Pd/C	230–250° 300–310°, N_2	79	52
		Pd/C	300–310°, N_2	74	52
		Pd/C	300–310°, N_2	89	52
		Pd/C	300–310°, N_2	90	52

TABLE III (*Continued*)

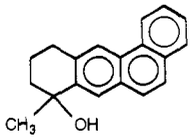
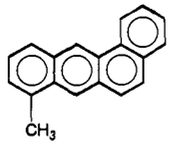
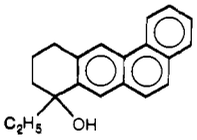
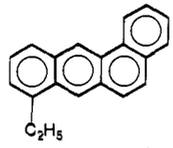
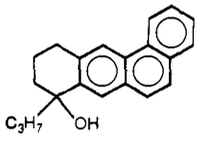
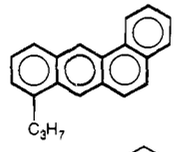
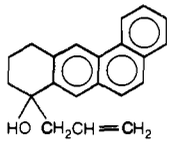
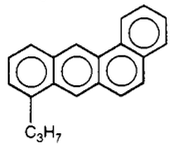
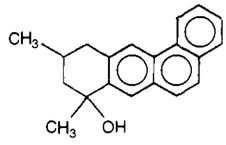
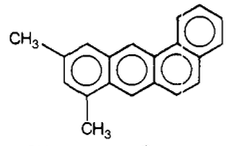
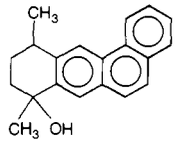
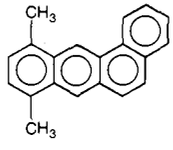
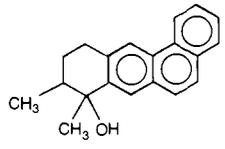
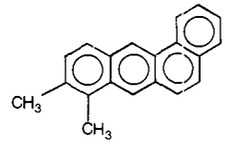
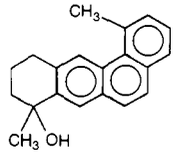
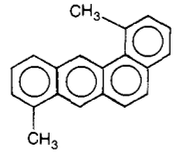
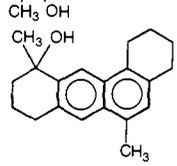
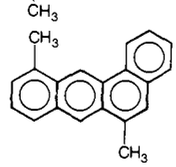
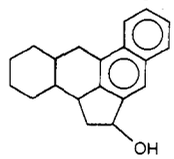
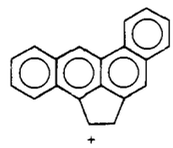
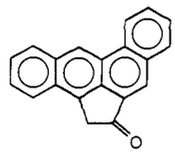
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd/C	310–320°	78	46
		Pd/C	310–320°, 30 min	>65	53
		Pd/C		69	53
		Pd/C	300, 30 min	73	53
		Pd/C	300–310°, N_2	74	52
		Pd/C	300–310°. N_2	82	52
		Pd/C	300–310°. N_2	63	52
		Pd/C	310°. 20 min		56
		Pd/C	300–320°, 1 h	90	45
		Pd/C	1-MN[a] reflux, 10.25 h	60 8.6	66
		Pd/C	300–320°, 1 h	>67	59

TABLE III (*Continued*)

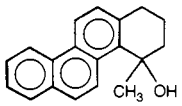
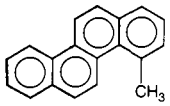
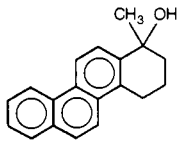
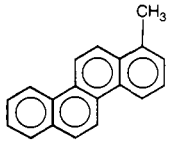
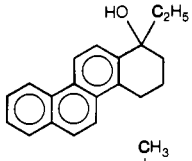
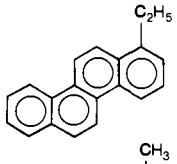
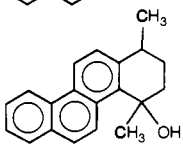
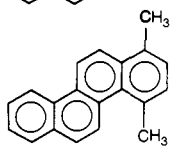
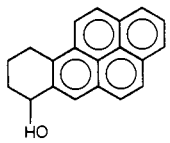
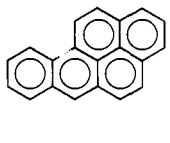
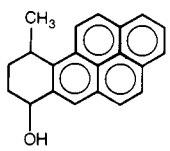
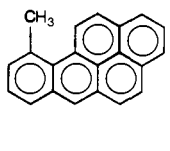
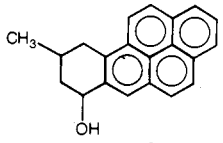
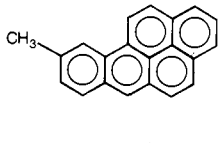
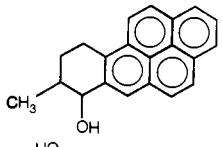
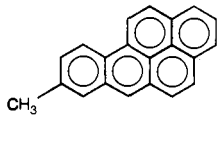
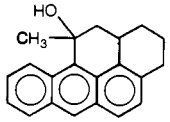
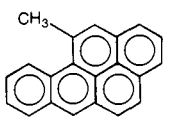
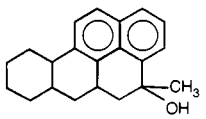
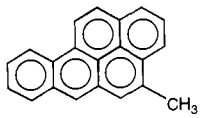
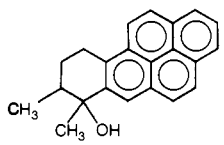
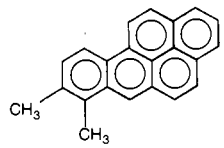
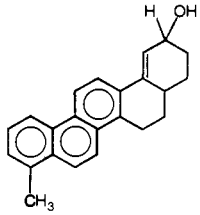
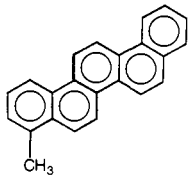
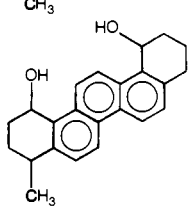
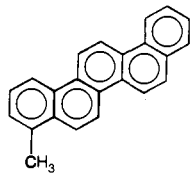
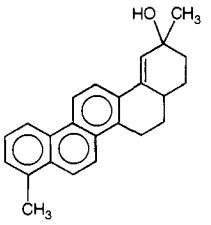
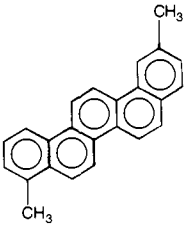
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd/C	300–320°, 1 h	92	21
		Pd/C	300–320°, 1 h	>61	57
		Pd/C	Δ, 1 h	>86	57
		Pd/C	300–320°, 1 h	>73	57
		Pd/C	300–320°, 1 h	>79	57
		Pd/C	310–320°, N_2 1.5 h	>80	67
		Pd/C	300–320°, 20 min	50	68
		Pd/C	300–320°, 20 min	>32	68
		Pd/C	300–320°, 20 min	>42	68
		Pt/C	1-MN, reflux	23	69
		Pd/C	300°, 1 h	>54	10
		Pd/C	300–320°, 30 min	91	68
		Pd/C	340°, 1 h	>40	34
		Pd/C	280–290°, 45 min	40	70

TABLE III (*Continued*)

Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd/C	340°, 1 h	>47	34

[a] 1-MN denotes 1-methylnaphthalene.

TABLE IV. Catalytic Dehydrogenation of Polycyclic Aromatic Ketones

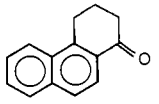
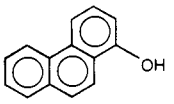
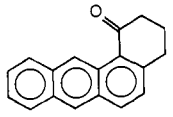
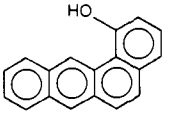
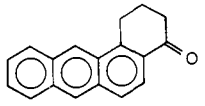
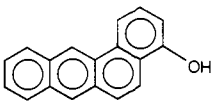
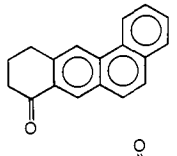
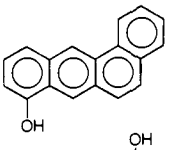
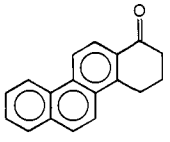
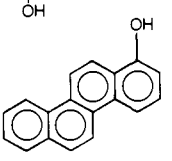
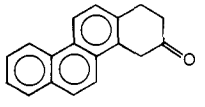
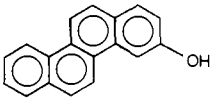
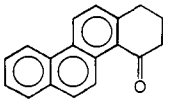
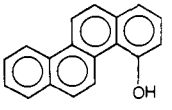
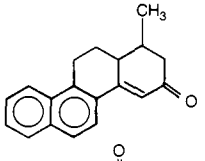
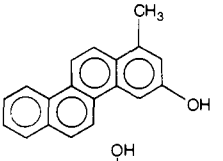
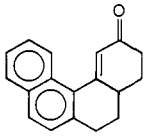
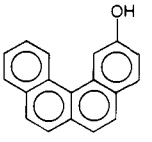
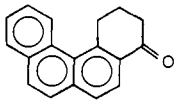
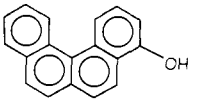
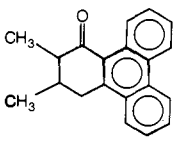
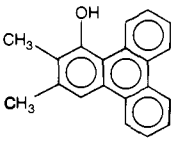
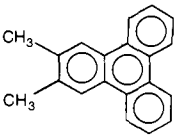
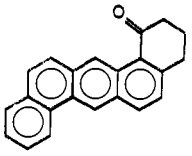
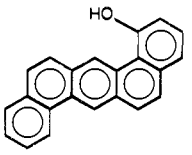
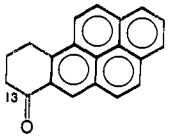
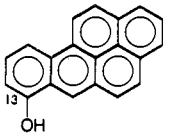
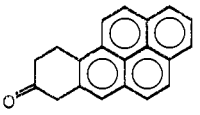
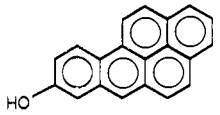
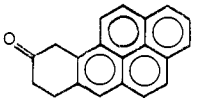
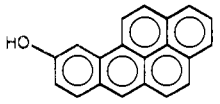
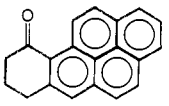
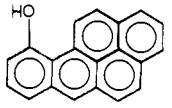
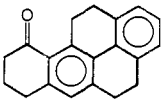
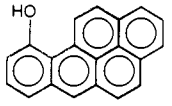
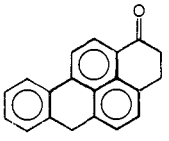
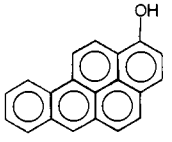
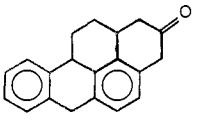
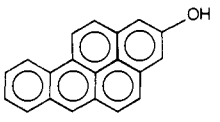
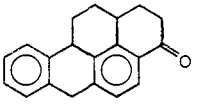
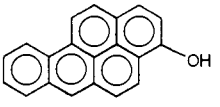
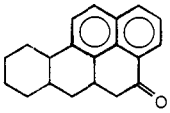
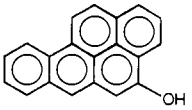
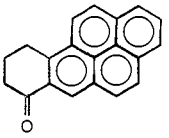
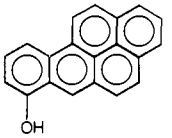
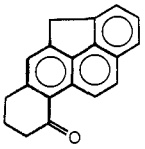
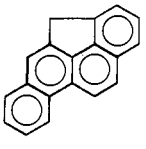
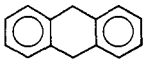
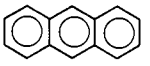
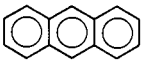
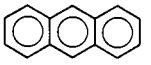
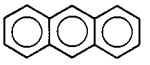
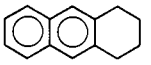
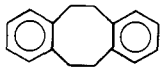
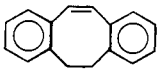
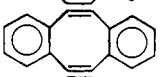
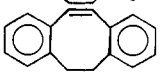
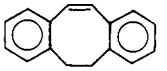
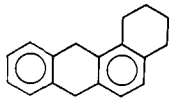
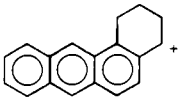
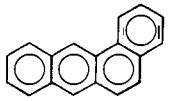
Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd	Naphthalene, reflux	86	71
		Pd	1-MN, reflux, 18 h		72
		Pd	1-MN, reflux, 16 h		72
		Pd	1-MN, reflux, 12 h		73
		Pd	1-MN, reflux, 30 h		74
		Pd Pd	1-MN, reflux, 20 h Xylene, reflux, 3 days	83	74 75
		Pd	Mesitylene, reflux, 20 h	80	74
		Pd/C	*p*-Cymeme, reflux, 70 h	77	76
		Pd/C	200–300°, 20 min 320°, ~40 min	73	77
		Pd/C	*p*-Cymene, reflux, 2 h	71	78
				26	
	+	Pd/C	300–310°; 7 h		47
				11	

TABLE IV (*Continued*)

Substrate	Product	Catalyst	Conditions	Yield, %	Ref
		Pd	1-MN, reflux, 12 h		73
		Pd/C	1-MN, reflux, 18 h	50	79
		Pd	1-MN, reflux, 64 h		80
		Pd	1-MN, Ar, >240°, 10 h	67	81
		Pd	1-MN, N_2, reflux, 18 h		80
		Pd	1-MN, Ar, >240, 10 h	80	81
		Pd	1-MN, Ar, >240°, 10 h	70	81
		Pd	1-MN, reflux, 24 h	74	82
		Pd	1-MN, Ar, >240°, 27 h	90	81
		Pd	1-MN, Ar, >240°, 15 h	61	81
		Pd/C	1-MN, N_2, reflux		83
		Pd	1-MN, Ar, >240°, 7 h	95	81
		Pd	1-MN, Ar, >240°, 20 h	48	81
		Pd	Δ		84
		Pd	1-MN, Ar, >240°, 4 h	62	81
		Pd/C	275–285°, 6 h (sealed tube)	19.5	28

dihydrophenanthrene (Figure 2), a sulfenyl (or selenyl) radical initially abstracts hydrogen from a benzylic position to afford a hydroarene radical, such as II. These dehydrogenation reactions occur at temperatures at which rupture of sulfur–sulfur bonds to form sulfenyl radicals is known to take place.[88] The resulting radical intermediate may decompose via any of the expected pathways for radical decomposition (e.g., dimerization), or it may combine with a second sulfur radical to produce an adduct, such as III. Thermal decomposition of the latter (or reaction with a sulfenyl radical) will produce the hydrocarbon sulfenyl intermediate IV. The latter may (a) dimerize to a disulfide, (b) abstract hydrogen from the starting hydrocarbon, regenerating II and the thiol V, or (c) undergo internal hydrogen transfer to VI. Loss of H_2S from V via ionic (analogous to dehydration) or radical mechanism affords phenanthrene. Dehydrogenations by sulfur or selenium are catalyzed by various polar substances (e.g., silicates, amines, oleic acid)[88,89] which may catalyze this elimination, although this is not established. Decomposition of

TABLE V. Homogeneous Catalytic Dehydrogenation[43]

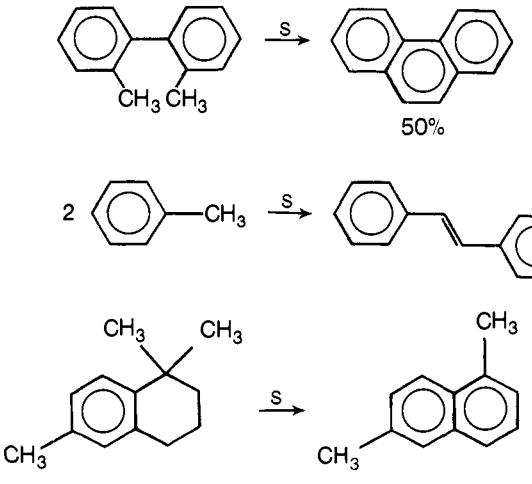
Substrate	Catalyst	Product	Conditions	Yield, %	Ref
	$RhCl(PPh_3)_3$		225°, 15 h	97	
	$RhCl_3(AsPh_3)_3$		225°, 15 h	47	
	$RuCl_2(PPh_3)_3$		225°, 15 h	58	
	10% Pd/C	 + 	225°, 15 h	45 42	
	$RhCl(PPh_3)_3$	 	265°, 5 h	17 1	
	$RuCl_2(PPh_3)_3$		265°, 15 h	2	
	10% Pd/C		265°, 15 h	2	
				 + 	
	$RhCl(PPh_3)_3$[a]		225°, 12 h	17	75
	$IrCl(CO)(PPh_3)_2$[a]		225°, 12 h	0	92
	$RuCl(PPh_3)_3$[a]		225°, 12 h	45	42
	10% Pd/C[a]		225°, 12 h	21	58

[a] Complete transformation to benz[*a*]anthracene was achieved by these catalysts in the order listed after 15, 21, 12, and 16 h, respectively.

VI with loss of the thioyl radical is an alternative route to phenanthrene.

B. Choice of Reagent and Secondary Reactions

Since sulfur is considerably cheaper and less toxic than selenium, it is usually the first choice for preliminary exploratory studies. On the other hand, selenium is a milder reagent, and reactions are often cleaner with fewer side products. Sulfur-containing side products are sometimes difficult to separate from the products of sulfur dehydrogenation. Among the secondary processes which may occur with sulfur are cyclodehydrogenation (e.g., 2,2′-dimethylbiphenyl to phenanthrene[90]), dimerization (e.g., toluene to stilbene[86]), elimination of methyl groups on tertiary carbon atoms (e.g., 1,1,6-trimethyltetralin to 1,6-dimethylnaphthalene[91]), and condensation (e.g., acenaphthene to dinaphthalenethiophene (**15**) and decacylene (**16**)[92]). All of these processes are consistent with free-radical intermediates.



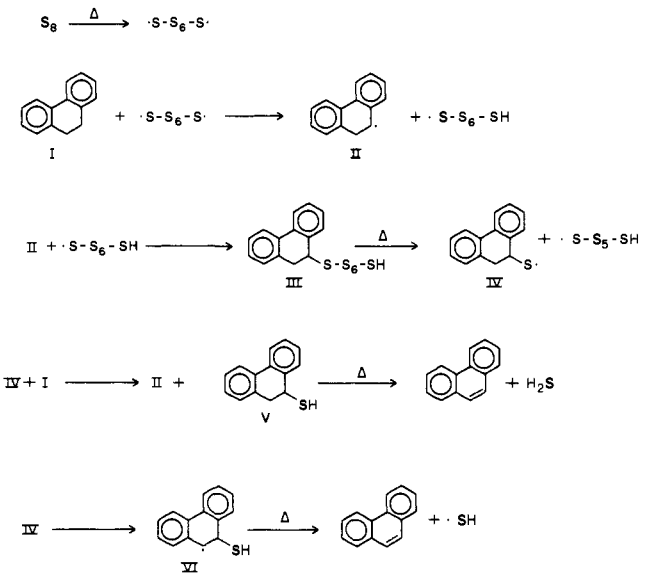
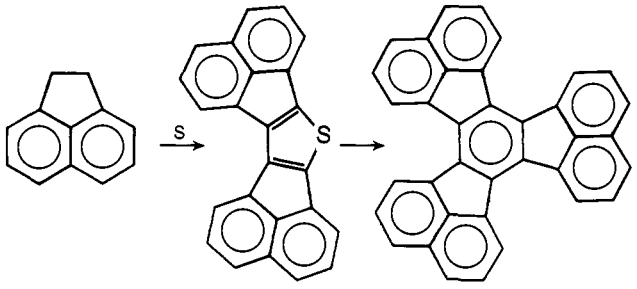


Figure 2. Proposed mechanism of dehydrogenation of hydroaromatic compounds by sulfur and selenium (modified from that proposed by Silverwood and Orchin for selenium dehydrogenation).[89]

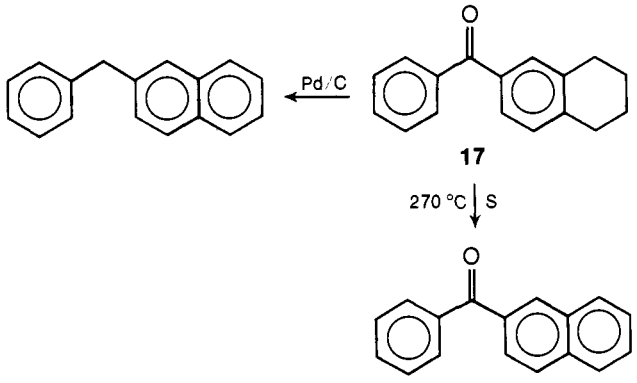


15 16

C. Dehydrogenation Reactions

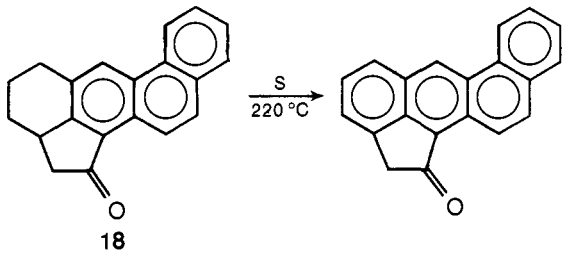
Examples of dehydrogenation of polycyclic hydroaromatic compounds by sulfur and selenium are listed in Tables VI and VII, respectively.

Although ketone functions often survive dehydrogenation by sulfur, if the carbonyl function is part of a six-membered ring a phenol is generally the product. Thus, reaction of the ketone **17**



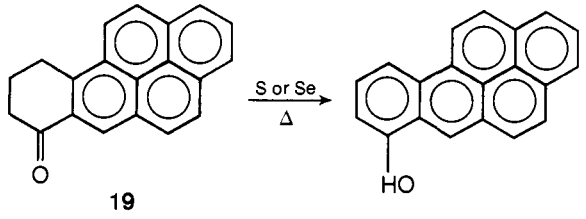
17

gave 2-naphthyl phenyl ketone (58%), whereas reaction of the same compound over Pd/C gave the reduced hydrocarbon 2-benzylnaphthalene as the principal product.[123] Reaction of the five-membered ring ketone **18** with sulfur gave the corresponding



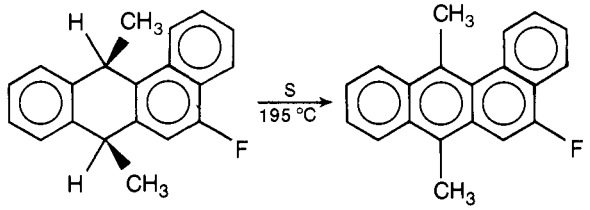
18

dehydrogenated ketone,[29] whereas reaction of the six-membered ring ketone **19** furnished the corresponding phenol.[124]



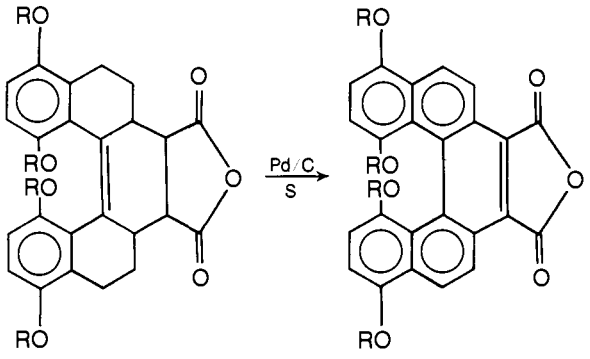
19

Carboxylic acid, anhydride, and ester functions are also generally retained unless they are located on fully substituted saturated carbon atoms. Arylhalogen atoms are also retained, in contrast to catalytic dehydrogenation. This fact has been utilized by Newman to synthesize the 5-fluoro analog **20** of the highly potent carcinogenic hydrocarbon 7,12-dimethylbenz[*a*]anthracene.[101] Numerous other analogs of 7,12-dimethylbenz[*a*]anthracene have also been synthesized through dehydrogenation with sulfur (Table VI).



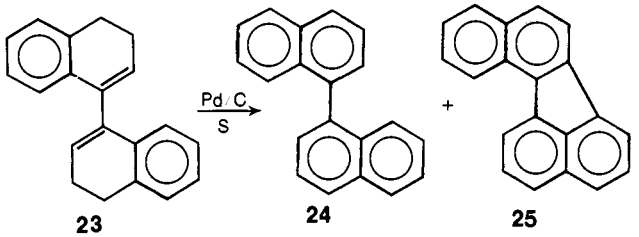
20

Crawford and co-workers[125,126] discovered a surprising combination for effecting dehydrogenation: Pd/C plus sulfur. Attempts to dehydrogenate **21** with Pd/C or sulfur alone were unsuccessful. However, when an intimate mixture of **21**, 30% Pd/C, and sulfur was heated at 300 °C for 5 min, hydrogen sulfide was evolved, and **22** was obtained.



21 **22**

Sulfur or Pd/C alone dehydrogenates **23** to **24** at 300–310 °C, but at this temperature the combination of the two affords a mixture of equal parts 1,1′-binaphthyl (**24**) and **25.** Since **24** is not dehydrogenated to **25** under the conditions of the experiment, cyclodehydrogenation to **25** must occur prior to complete aromatization.



23 **24** **25**

VI. Dehydrogenation with Quinone Reagents

A. General Aspects and Mechanism

Although the dehydrogenation of hydroaromatic compounds by quinones was reported first by Clar and John in 1930,[127] it failed to gain general acceptance until the more extensive investigations of Braude, Jackman, Linstead, and coworkers[128–131] more than 20 years later. These studies established the advantage of quinone dehydrogenation as a method of selective abstraction of hydrogen from hydroaromatic compounds under mild conditions. In contrast to the older methods using the platinum metals, sulfur, and selenium, reactions can frequently be conducted stepwise, removing hydrogen atoms in pairs and stopping at intermediate stages as desired. Also the method is applicable to a wider range of compounds, including natural products,[4–6] and carcinogenic hydrocarbon metabolites,[20,132–134] compounds incapable of survival under the drastic conditions required by older methods. The literature on quinone dehydrogenation has expanded rapidly, and various aspects have been treated in reviews by Jackman,[4] Walker and Hiebert,[5] and Becker.[6]

TABLE VI. Dehydrogenation with Sulfur

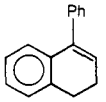
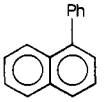
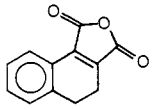
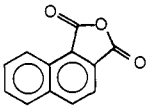
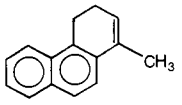
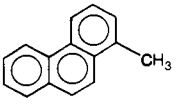
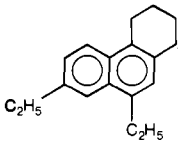
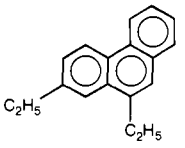
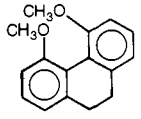
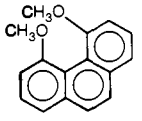
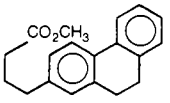
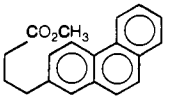
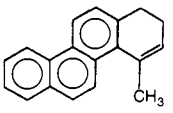
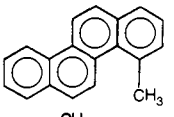
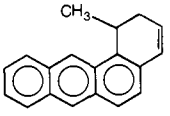
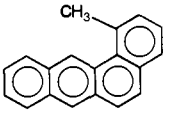
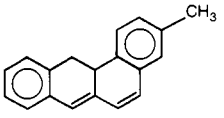
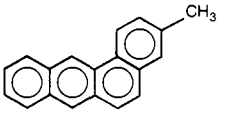
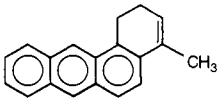
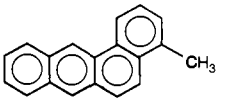
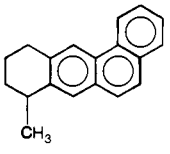
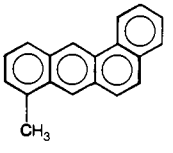
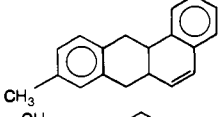
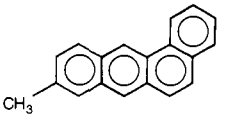
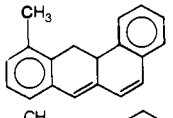
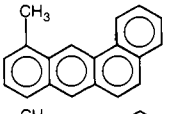
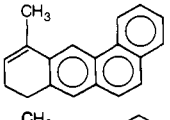
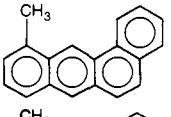
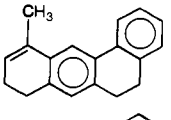
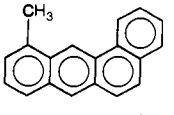
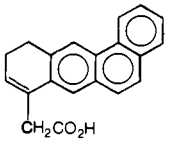
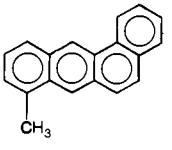
Substrate	Product	Conditions	Yield, %	Ref
		250–270°	91–94	93
		230–235°	76–91	94
		260°, 30 min	25	46
		200–220°, 1 h	80	45
		225°, 2 h 225°, 2 h	61	95 96
		232–255°	53	97
		215–240°	50	97
		220–240°, 10 min[a]	60	98
		230–250°, 1 h	61	99
		220–240°, 10 min[a]	75	98
		200–255°	50	97
		250°	54	99
		240–250°	51	99
		205–245°	95	97
		230–240°	56	100
		210°, 1 h	20	29

TABLE VI (*Continued*)

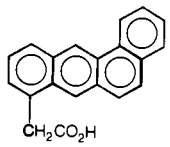
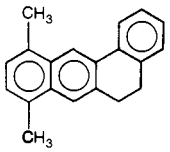
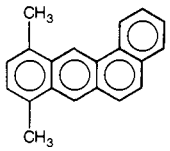
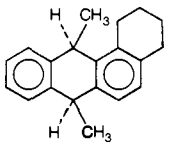
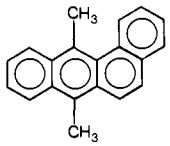
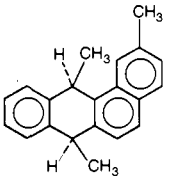
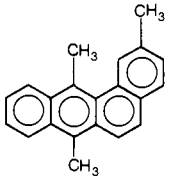
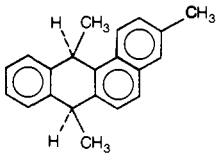
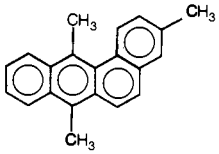
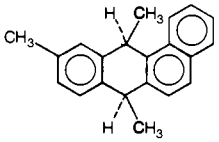
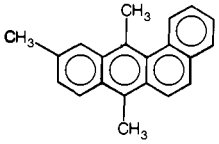
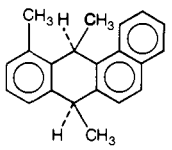
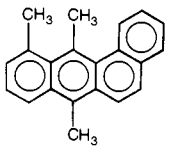
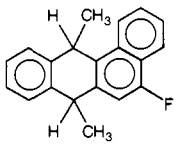
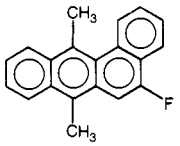
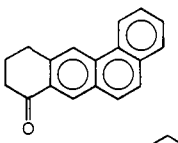
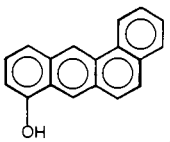
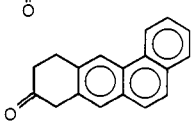
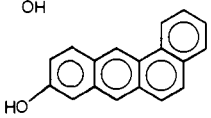
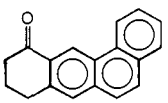
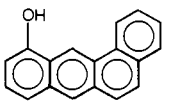
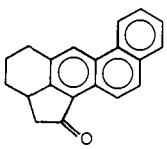
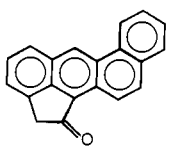
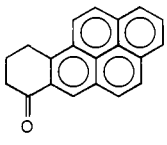
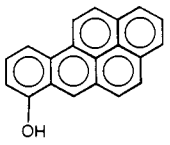
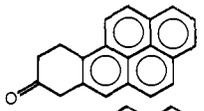
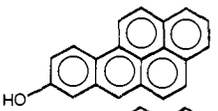
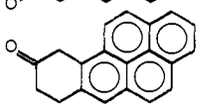
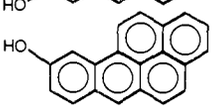
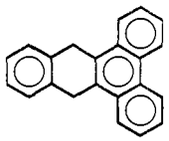
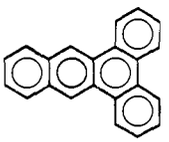
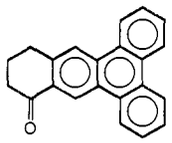
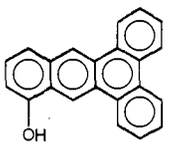
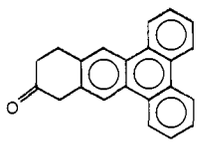
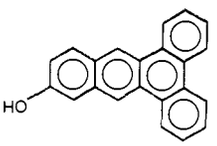
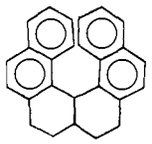
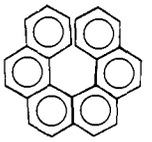
Substrate	Product	Conditions	Yield, %	Ref
			10	
		210–215°	40	97
		170°, 15 min	90	101
		270°. 15 min	72	102
		270°. 15 min		102
		270°. 15 min	70	102
		270°, 15 min		102
		195°, 3 h 260°. 5 min	75	101
		212–215°		103
		220°, 30 min	26	103
		230–255°	45	99
		220°, 30 min	61	29
		210–215°, 70–80 min 220–230°. 75 min	30 19	84 104

TABLE VI (*Continued*)

Substrate	Product	Conditions	Yield, %	Ref
		220°, 30 min	20	80
		220°, 30 min	28	80
		200–230°, 1 h	78	105
				106
				106
		225°, 20 min	66	40

[a] Zn was then added and the mixture heated another 10 min at 200–230°.

TABLE VII. Dehydrogenation with Selenium

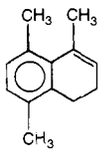
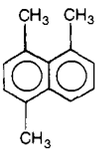
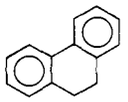
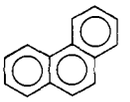
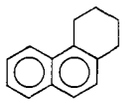
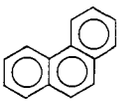
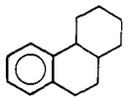
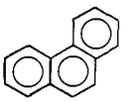
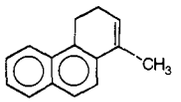
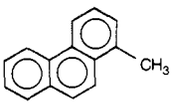
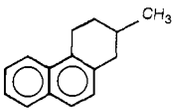
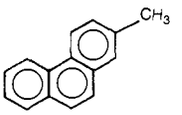
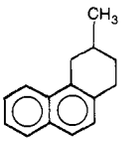
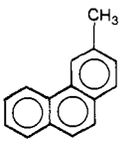
Substrate	Product	Conditions	Yield, %	Ref
		295°, 16 h	66	89
		260°, 1 h	46	89
		300–340°, 24 h		107
		320–340°		108
		300–340°, 24 h	50	107
		300–340°, 24 h		107
		300–340°, 24 h		107

TABLE VII (*Continued*)

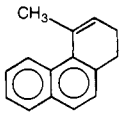
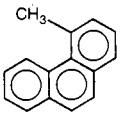
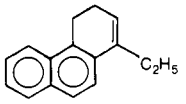
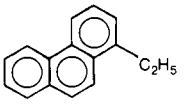
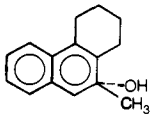
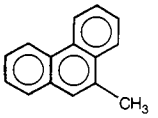
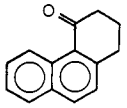
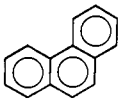
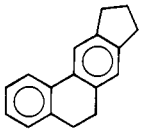
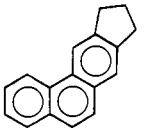
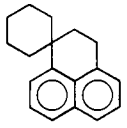
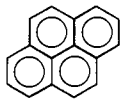
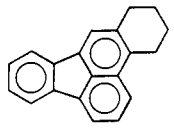
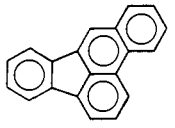
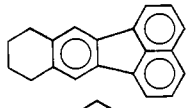
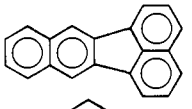
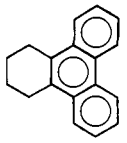
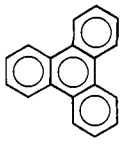
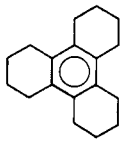
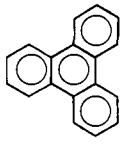
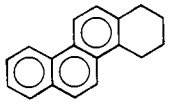
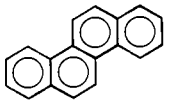
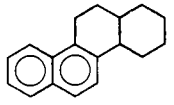
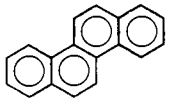
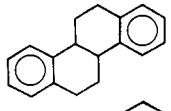
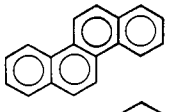
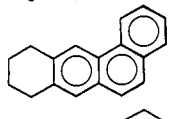
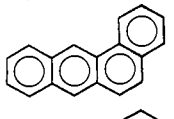
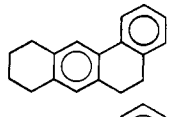
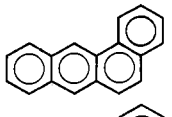
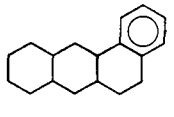
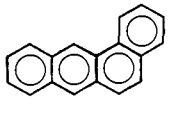
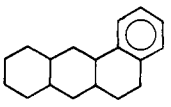
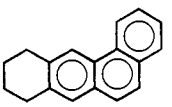
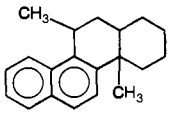
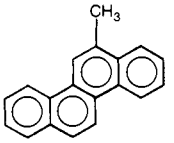
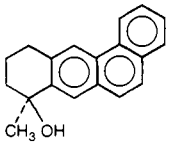
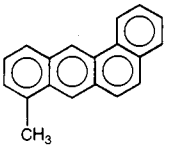
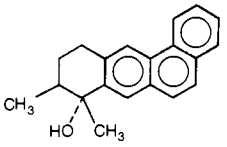
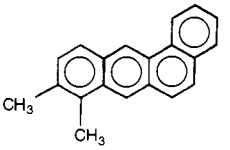
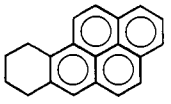
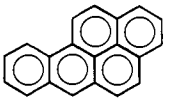
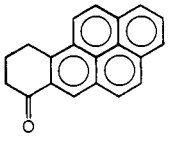
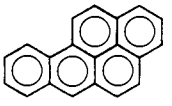
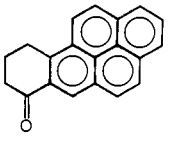
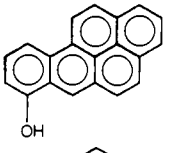
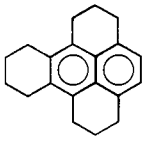
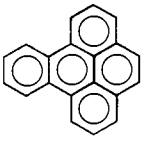
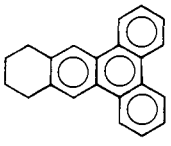
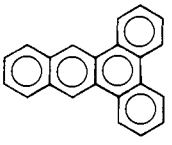
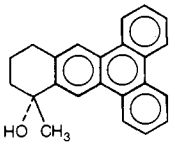
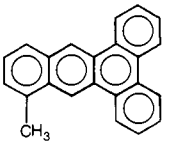
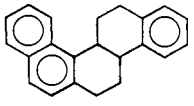
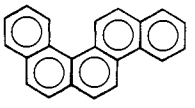
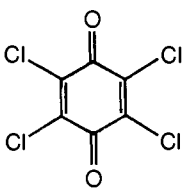
Substrate	Product	Conditions	Yield, %	Ref
		300–340°, 24 h		107
		340°	25	46
				107
		200°		109
		300–310°, 16 h		110
		320–340°, 33 h	50	111
		350°, 3 h	89	112
		340°, 5 h	85	112
		320°, 10 h		113
				113, 114
		290–310°, 24 h		115
		300–310°, 14 h (sealed tube)	19	111
		300°, 20 h	60	116
		280–290°, 15 h 305–315°, 10 h		115
		290–315°	100	110
		320–330°	50	117

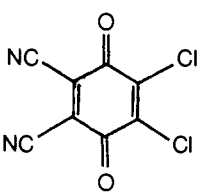
TABLE VII (*Continued*)

Substrate	Product	Conditions	Yield, %	Ref
		320–340°, 24 h		118
		320°, 24 h	9	60
		300–320°, 20 h	75	119
		300–310°, 10 h	73	120
		320–340°, 16 h	34	109
		320–340°, 6 h	17	109
		310–320°, 2 h	Trace	104
		320–340°, 20 h	20	109
		350°, 2.5 h	53	112
		330°, 2 h	42	112
		325–330° 325–330°, 24 h	 2	121 122

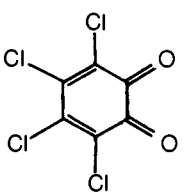
The quinones most generally employed as reagents are 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), *p*-chloranil, and *o*-chloranil. 9,10-Phenanthraquinone and its nitro derivatives are frequently used in the dehydrogenation of steroids. The diphenoquinones, such as 3,3′,5,5′-tetrachloro-4,4′-diphenoquinone, have seen more limited use, although their fairly high oxidation potential and their ready availability suggests broader applicability.



p-chloranil



DDQ



o-chloranil

The ionic mechanism put forward by Braude, Jackman, and Linstead[130] accounts most satisfactorily for the experimental observations. According to this scheme, the initial rate-determining step involves transfer of a hydride ion from the hydrocarbon to the quinone (eq 2). Rapid proton transfer from the

resulting conjugate acid to the hydroquinone anion then leads to the dehydrogenated product and the hydroquinone (eq 3). It is possible, and even probable in many cases, that charge-transfer complex formation[5] (eq 1) precedes initial transfer, since

$$AH_2 + Q \rightarrow [AH_2 \cdot Q] \quad (1)$$

$$AH_2 + Q \xrightarrow{\text{slow}} AH^+ + QH^- \quad (2)$$

$$AH^+ + QH^- \xrightarrow{\text{fast}} A + QH_2 \quad (3)$$

the effective quinones are also known to be efficient acceptors for such complexes.[135] Consistent with this mechanism, the reactions studied were found to be (1) first order in both reactants; (2) faster in polar solvents, such as dimethylformamide, than in nonpolar solvents, such as benzene; (3) unaffected by radical initiators; (4) faster with quinones of higher oxidation potential; and (5) acid catalyzed in the case of quinones of low potential ($E_0 < 600$ mV). Moreover, when the hydrogen undergoing transfer is isotopically labeled, large isotope effects are observed.[138,137] In the acid-catalyzed reaction the protonated quinone QH^+ presumably acts as an efficient hydride acceptor (eq 4-6).

$$Q + H^+ \rightarrow QH^+ \quad (4)$$

$$AH_2 + QH^+ \rightarrow AH^+ + QH_2 \quad (5)$$

$$AH^+ \rightarrow A + H^+ \quad (6)$$

Further clarification of mechanistic details is provided by a more recent study of the dehydrogenation of *cis*-1,2-dideuterioacenaphthene by DDQ and *o*-chloranil.[138] Reaction in benzene solution proceeds with predominantly cis elimination. Initial ion-pair formation and partial collapse of the ion pairs to products before dissociation accounts for the net cis elimination. The amount of cis elimination decreases as solvent polarity increases, in agreement with the ion-pair hypothesis.

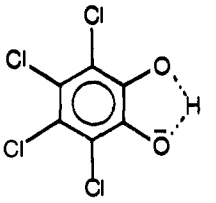
Harvey and Fu[33] observed that dehydrogenation of *trans*-9,10-diisopropyl-9,10-dihydroanthracene by DDQ in refluxing benzene is much slower than that of the cis isomer, in further support of the cis-elimination mechanism.

Several cases have been described which do not accord entirely with an ionic bimolecular mechanism. Thus, Hashish and Hoodless[139] report that dehydrogenation of 1,4-dihydronaphthalene by *p*-chloranil in phenetole appears to follow second-order kinetics only in the later stages of reaction. They suggest that electron transfer within an initially formed charge-transfer complex may be the rate-determining step in this reaction. More recently evidence has been obtained which suggests that reaction of 1,4-cyclohexadiene with DDQ may involve simultaneous rather than stepwise hydrogen transfer.[140,141]

B. Selection of Reagent and Conditions

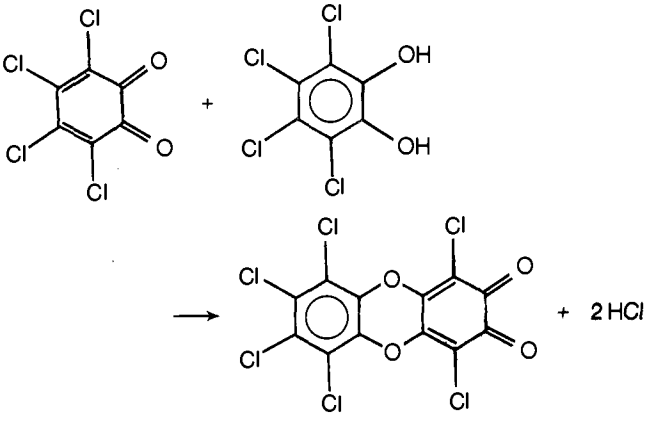
The choice of quinone reagent is dictated by the oxidation potential of the quinone, the anticipated ease of dehydrogenation of the substrate, and the probability of side reactions.

Quinones of high oxidation potential are more powerful electron or anion acceptors than are those of low oxidation potential, and the rates of dehydrogenation reactions reflect these differences. Electron-withdrawing groups enhance the potential of a quinone, while electron-donating groups decrease it. For example, DDQ, the most powerful quinone reagent in routine use, dehydrogenates 1,2-dihydronaphthalene 5500 times faster than *p*-chloranil at 100 °C, while *o*-chloranil reacts 4200 times faster than *p*-chloranil under the same conditions.[4] The generally greater reactivity of the *o*-quinones compared to the *p*-quinones is presumed to be a consequence of strong hydrogen bonding in the transition state leading to a catecholate monoanion.[128]



The ease of dehydrogenation is dependent upon the degree of stabilization of the incipient carbonium ion in the transition state. An olefinic bond or a benzene ring is sufficient for hydride abstraction to occur. Thus, decalin is inert to quinone dehydrogenation, whereas octalins and tetralin are converted to naphthalene. In general, the greater the resonance energy of the carbonium ion intermediate, the more facile its formation. According to Braude et al.,[129] the ease of dehydrogenation of hydroaromatic compounds follows the sequence 1,4-dihydrobenzene > 1,4-dihydronaphthalene > 9,10-dihydroanthracene > 1,2-dihydronaphthalene. The relative rates at 80 °C are in the approximate ratio 100:50:10:1 independent of the quinone (benzoquinone, chloranil, or thymoquinone). This sequence is explicable as a consequence of the differences in the additional resonance stabilization which accompany the aromatization of the donor.

The most common side reactions are Diels-Alder reaction and nucleophilic substitution. DDQ is a powerful dienophile which forms an adduct with anthracene even in the cold. On the other hand, both *p*- and *o*-chloranil are relatively weak dienophiles for which Diels-Alder reactions are generally not seriously competitive with dehydrogenation (except with polyacenes). The dicyanoquinones, such as DDQ, are known to be sensitive to hydrolysis with evolution of hydrogen cyanide;[4] therefore anhydrous reaction conditions are essential. The side reaction most commonly encountered with *o*-chloranil involves interaction of the quinone with its hydroquinone leading to formation of a new quinone and hydrogen chloride. This reaction is relatively slow and is only significant in dehydrogenations which proceed with difficulty.

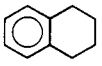
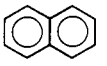
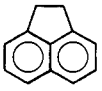
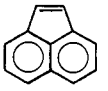
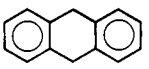
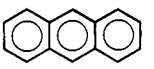
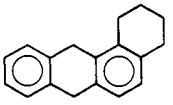
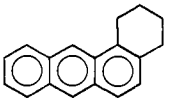
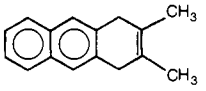
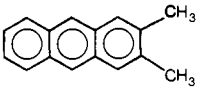
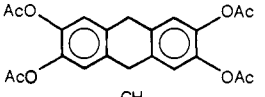
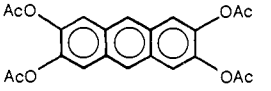
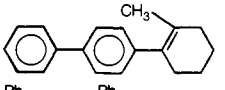
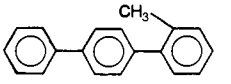
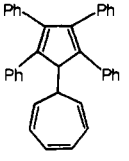
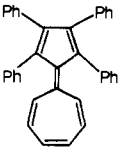


In general, reactions are conducted at reflux temperature in an inert solvent such as benzene (bp 80 °C), dioxane (bp 101 °C), toluene (bp 110 °C), chlorobenzene (bp 121 °C), or xylene (bp 138-144 °C) selected according to the desired operating temperature. *It is important that these solvents be rigorously dried before use.* It is convenient to follow the course of dehydrogenation of hydroaromatic compounds by TLC on silica gel impregnated with 2,4,7-trinitrofluorenone (TNF). This adsorbant efficiently separates hydroaromatic and aromatic compounds inseparable on silica gel alone.[20,142]

C. Quinone Dehydrogenations

Examples of dehydrogenation of hydroaromatic compounds by *p*-chloranil, *o*-chloranil, and DDQ are summarized in Tables

TABLE VIII. Dehydrogenation with *p*-Chloranil

Substrate	Product	Conditions (solvent,[a] time)	Yield, %	Ref
		A, 20 h	>100[b]	128
		A, 20 h	59[b]	128
		A, 1 day	70[b]	143
		A, 2 h	95	33
		B	~100	144
		B	72	145
		B	71	146
		C	64	147

[a] Solvent: A, benzene; B, xylene; C, CCl_4. [b] Yield based on recovered substrate.

TABLE IX. Dehydrogenation with *o*-Chloranil

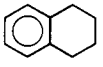
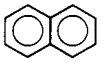
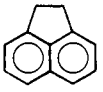
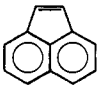
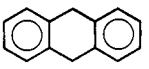
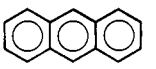
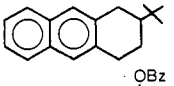
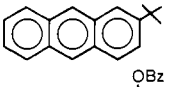
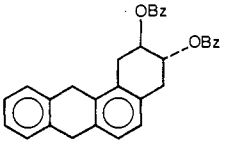
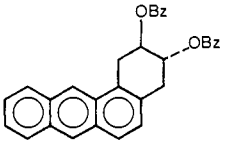
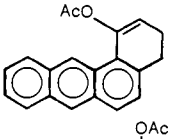
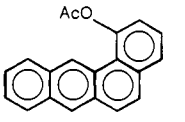
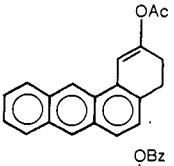
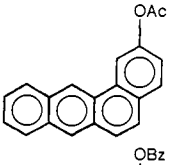
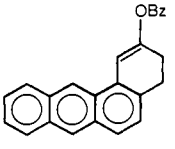
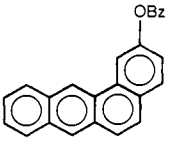
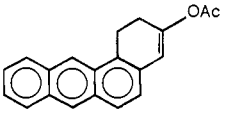
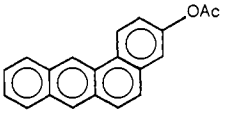
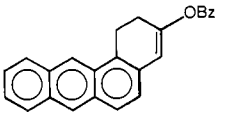
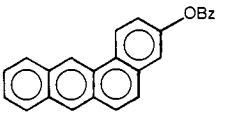
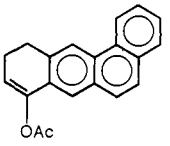
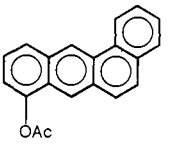
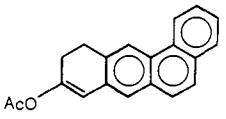
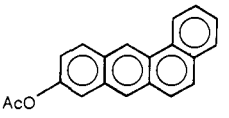
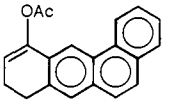
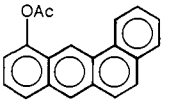
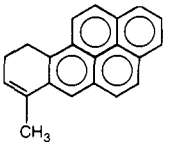
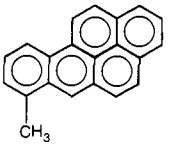
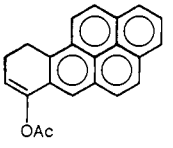
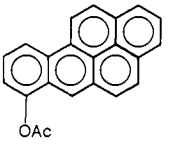
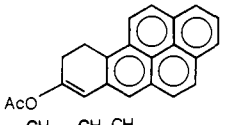
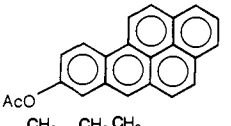
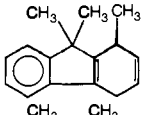
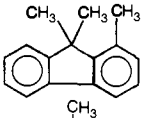
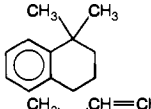
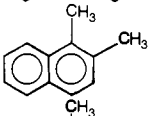
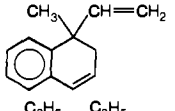
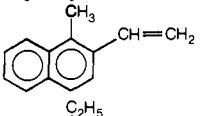
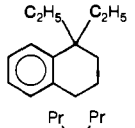
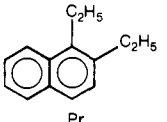
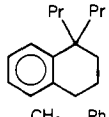
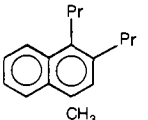
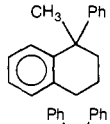
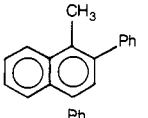
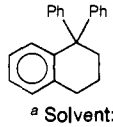
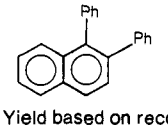
Substrate	Product	Conditions (solvent,[a] time)	Yield, %	Ref
		A, 2 h	~100[a]	128
		A, 20 h	60[a]	128
		A, 1 day	~100	143
		A, 50 min	84	148
		A, 1 day	85	143
		A, 3 h	89	149
		A, 1.5 h	91	149
		A, 2.5 h	84	149
		A, 3 h	89	149

TABLE IX (*Continued*)

Substrate	Product	Conditions (solvent,[a] time)	Yield, %	Ref
		A, 3 h	86	149
		A, 1 h	99	33
		A, 1 day	70	33
		A, 2 h	80	33
		A, 1 h	78	33
		A, 1 h	97.5	33
		A, 2 h	85	33
		A, 1 h	~100	150
		A, 20 h	84[b,c]	152
		B	27	151
		A, 20 h	40[b,d]	152
		A, 20 h	57[b,e]	152
		A, 20 h	56[b,f]	152
		A, 20 h	47[b,g]	152

[a] Solvent: A, benzene; B, toluene. [b] Yield based on recovered substrate. [c] 78% hydrocarbon recovered. [d] 85% hydrocarbon recovered. [e] 93% hydrocarbon recovered. [f] 90% hydrocarbon recovered. [g] 95% hydrocarbon recovered.

TABLE X. Dehydrogenation with DDQ

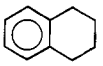
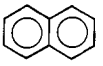
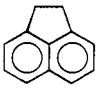
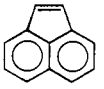
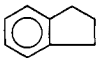
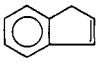
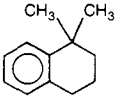
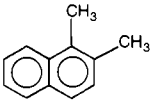
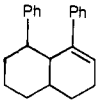
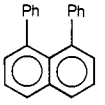
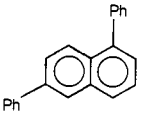
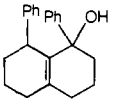
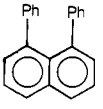
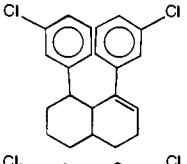
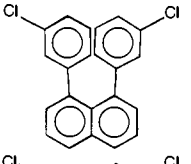
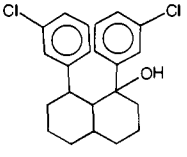
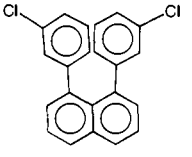
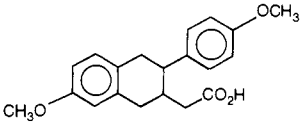
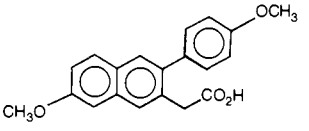
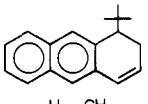
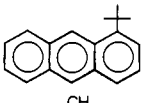
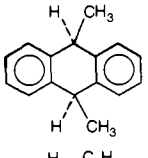
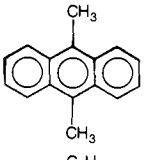
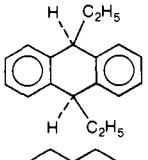
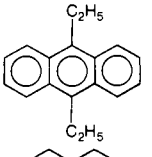
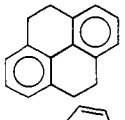
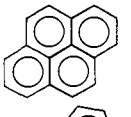
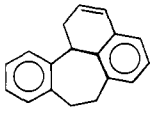
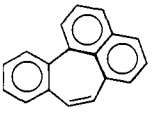
Substrate	Product	Conditions	Yield, %	Ref
		A, 2 h	100[b]	128
		A, 20 h	79[b]	128
		A, 4 h	76[b]	152
		A	76	146
			56	
		B, 40 h		64
			44	
		A, 11.5 h A, 19.5 h	45 51	95 64
		B, 16 h	32	44
		B, 16 h	35	44
		A, 18.5 h	75	153
		A, 1 h	19	148
		A, 16 h	65	11
		A, 12 h	65	11
		A	~100	154
		A	65	155

TABLE X (*Continued*)

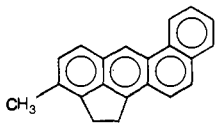
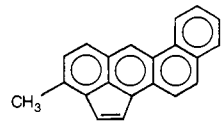
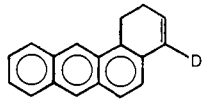
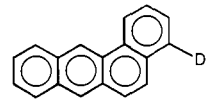
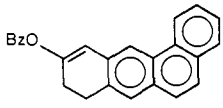
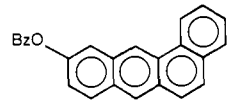
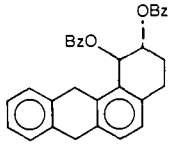
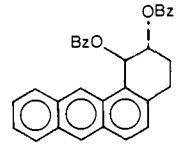
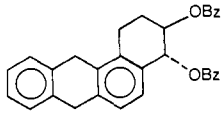
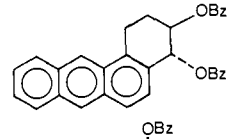
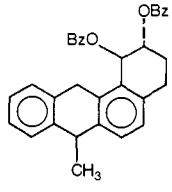
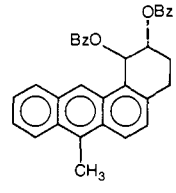
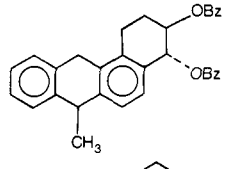
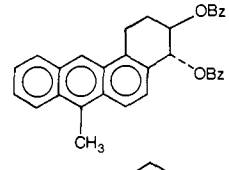
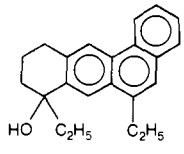
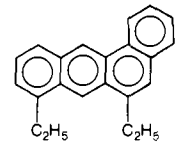
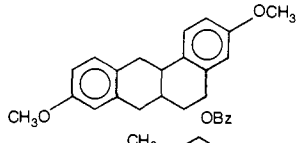
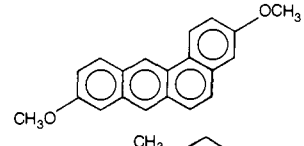
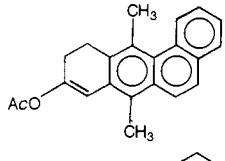
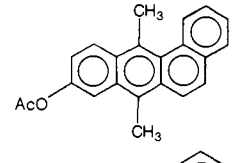
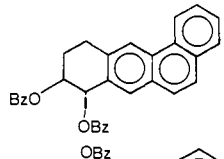
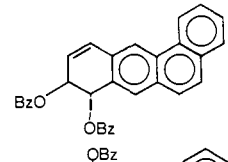
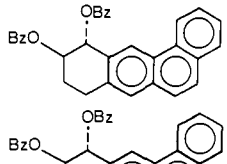
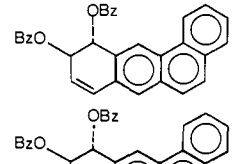
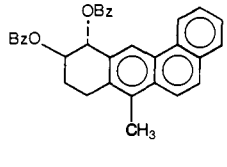
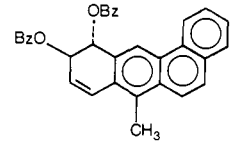
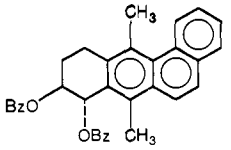
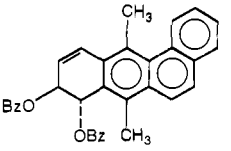
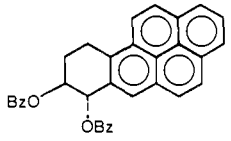
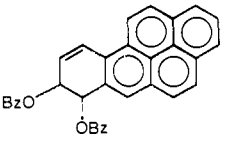
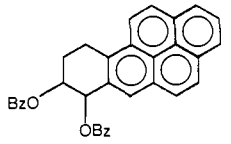
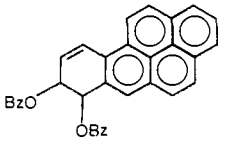
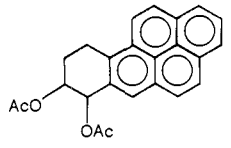
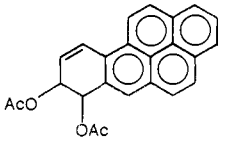
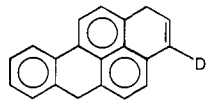
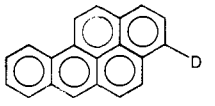
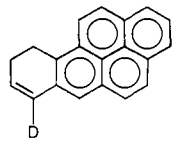
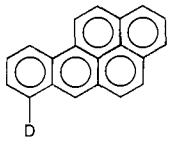
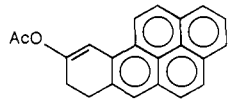
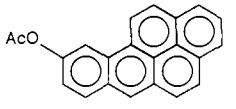
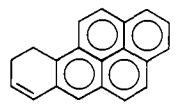
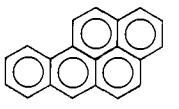
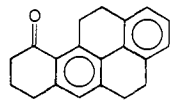
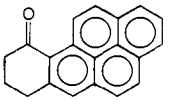
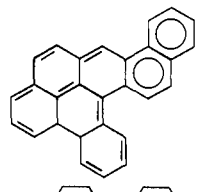
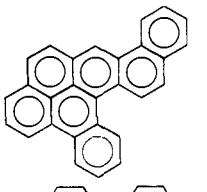
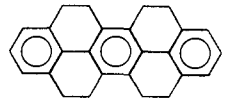
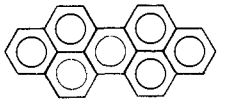
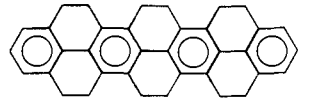
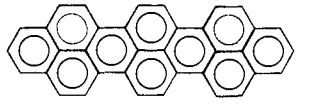
Substrate	Product	Conditions	Yield, %	Ref
		A, 2 h	65	156
		A, 1 h	62	33
		A, 6 h	84	33
		A, 1 h[d]	88	132
		A, 1 h[d]	88	132
		A, 2.5 h[d]	70	157
		A, 2.5 h[d]	70	157
		A, 3 h	35.5	158
		A, 16 h	95	153
		A, 1 h	70	159
		C, 24 h	88	133
		C, 48 h	90	133
		C, 48 h	82	133

TABLE X (*Continued*)

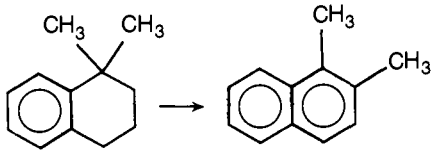
Substrate	Product	Conditions	Yield, %	Ref
		C, 6 days	65	159
		A, 2 h	80	133
		C, 16 h	93	133
		C, 3 h	87	133
		A, 3 h	72	160
		A, 1 h	88	33
		A, 5 h	74	33
		A, 1 h	90	33
		A	54	82
		A, 20 h	70	161
		A, 22 h	~100	154
		D	~100	154

[a] Solvent: A, benzene; B, chlorobenzene; C, dioxane; D, xylene. [b] Yield based on recovered substrate. [c] Isolated as its bromohydrin. [d] Reactions were carried out with the mixtures of 1,2- and 3,4-dioldibenzoates.

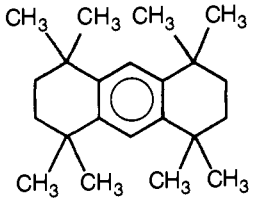
VIII, IX, and X, respectively. Yields are generally good. Five-membered rings, such as acenaphthene, which are resistant to catalytic or sulfur dehydrogenation undergo smooth transformation to the corresponding olefins with these quinone reagents. Although seven-membered rings and alkyl side chains are inert under conditions where the five- and six-membered rings are rapidly dehydrogenated, under more vigorous conditions they too undergo dehydrogenation. As a consequence, quinones may be utilized to selectively dehydrogenate specific rings or to aromatize rings without affecting side chains.

Another unique feature of quinone dehydrogenation compared to the traditional methods is the facility of aromatization of rings bearing quaternary carbon atoms. In contrast to the platinum metal catalyzed reactions, rearrangement rather than elimination

of one of the groups generally occurs, in keeping with the ionic mechanism. For example, 1,1-dimethyltetralin is converted to 1,2-dimethylnaphthalene. Migrations of ethyl, isopropyl, and

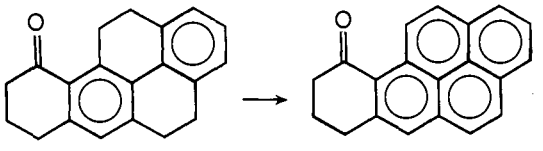


phenyl groups, as well as methyl groups, have been observed. In order for reactions of this type to take place, the ring to be dehydrogenated must contain at least one benzylic or allylic hydrogen atom. Therefore, it is not surprising that the octahydrooctamethylanthracene (**26**) fails to dehydrogenate with *o*-chloranil.[152]



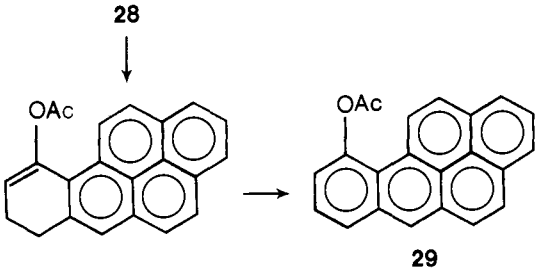
26

Relatively little is known concerning the fate of other functional groups. It appears that halide, alkoxy, acyloxy, and carboxyl groups on aromatic rings can generally survive quinone dehydrogenation unchanged. Saturated primary and secondary alcohols are also stable. In contrast, allylic, propagylic, and benzylic alcohols are oxidized to the corresponding aldehydes and ketones.[162,163] Tertiary alcohols tend to undergo dehydration. Ketonic groups appear to be unaffected; there are no recorded examples of the further transformation of cyclic ketones to phenols. Thus, 10-keto-4,5,7,8,9,10,11,12-octahydrobenzo[*a*]pyrene (**27**) is converted by DDQ only as far as **28**.[82] On



27 **28**

the other hand, the corresponding phenols (e.g., **29**) are con-

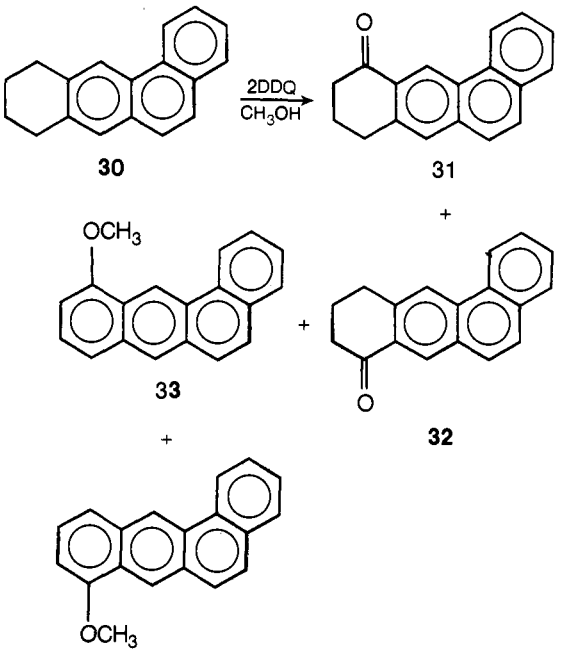


29

o-chloranil. This sequence has been employed extensively in the authors laboratory to synthesize the isomeric phenol derivatives of benz[*a*]anthracene, benzo[*a*]pyrene, 7,12-dimethylbenz[*a*]anthracene, and other polycyclic arenes.[33,149,157,159] The phenols are among the principal metabolites of the carcinogenic hydrocarbons,[164] and the phenolic derivatives of authentic structures are required for identification of the individual isomers produced.[165]

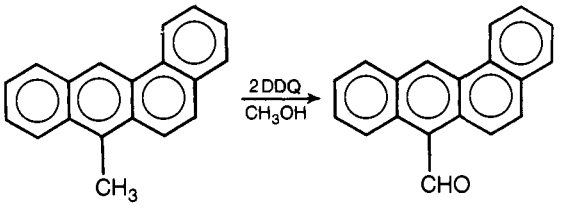
Reactions of hydroaromatic compounds with DDQ in methanol afford principally the oxidation products arising through reaction of the intermediate carbonium ions with the solvent. Reaction of 8,9,10,11-tetrahydrobenz[*a*]anthracene (**30**) with 2 equiv of

DDQ in methanol furnished the related ketones **31** and **32** in 4:1



30 **31** **33** **32** **34**

ratio as the major products; minor amounts of the related phenol methyl ethers **33** and **34** were also produced.[33] Similar reaction of 7-methylbenz[*a*]anthracene afforded 7-formylbenz[*a*]anthracene (**35**).[157]



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D. Stepwise Dehydrogenation and Theoretical Prediction of Product Structure

Partial dehydrogenation of hydroaromatic molecules in stepwise fashion (removing one pair of hydrogen atoms at a time) holds promise as a method of important synthetic utility. The essential advantage is the potential for the introduction of functional groups directly into the ring system at positions not normally prone to electrophilic or nucleophilic substitution in the fully aromatic molecule. The feasibility of stepwise dehydrogenation of tetrahydro aromatic rings has very recently been demonstrated in the authors laboratory[20] as a key step in the synthesis of the oxidized metabolites of carcinogenic hydrocarbons. For example, treatment of 7,8,9,10-tetrahydrobenzo[*a*]pyrene (**36**) and 8,9,10,11-tetrahydrobenz[*a*]anthracene (**30**) with 1 equiv of DDQ in refluxing benzene affords the corresponding dihydroarenes **37** and **38**, respectively, as the major products (Table XI); reaction of **30** also affords the isomeric 10,11-dihydrobenz[*a*]anthracene (**39**) as a minor product.[20,134] The site of initial hydride abstraction in these reactions is anticipated to be a function of the relative stability of the respective benzylic carbocations. This is calculable by MO orbital methods. The experimental findings are in agreement with prediction based on the perturbational MO method of Dewar.[186] Thus, the delocalization energies (expressed in β units) of the carbocations derived from **36** and **30** are highest in the 10 and 11 positions, respectively, the regions of observed preferential dehydrogenation. Subsequent experiments have shown the general applicability of this method (Table XI). Products are, with one exception, in accord with MO theoretical prediction. The exception

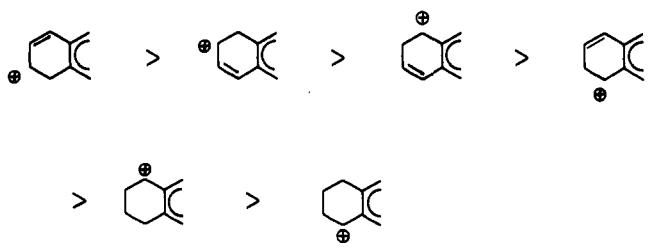
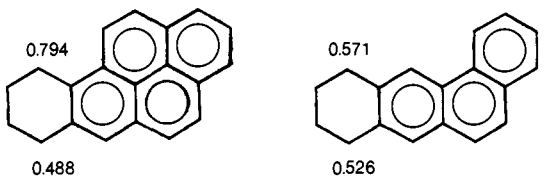
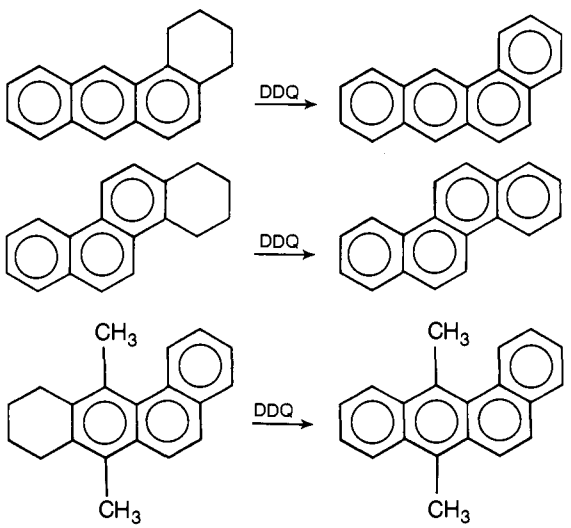


Figure 3. Relative ΔE_{deloc} of carbocations derived from **31**, **38**, and **39**.



is 12-methyl-8,9,10,11-tetrahydrobenz[*a*]anthracene which provides the corresponding 10,11-dihydroarene rather than the expected 8,9-dihydro isomer as the sole dihydro product. The reason appears to be steric interference by the 12-methyl group to attack at the 11 position directing reaction to the 8 position.

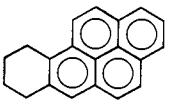
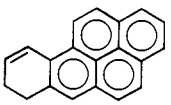
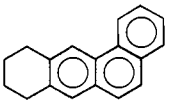
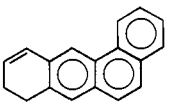
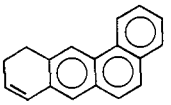
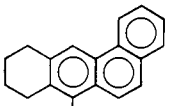
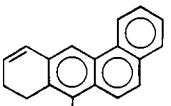
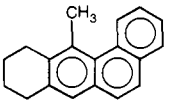
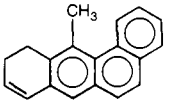
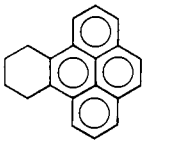
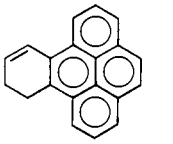
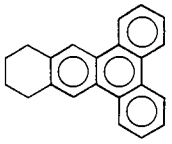
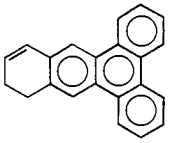
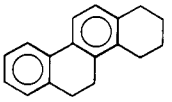
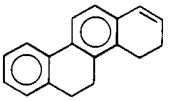
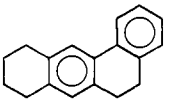
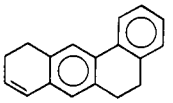
It is actually surprising that these reactions can be controlled to afford relatively high yields of the dihydroarenes, since the fully aromatic products arising through further dehydrogenation are anticipated to be thermodynamically more stable than the dihydroarene intermediates. MO theoretical calculations confirm this intuitive idea.[33] The delocalization energies (ΔE_{deloc}) of the individual carbocations derived from **37** and **38** (Figure 3) are all higher than those of the carbocations derived from **36** and **30**, respectively, leading to prediction that dehydrogenation of **37** and **38** should be more facile than **36** or **30**. This suggests that initial charge-transfer complex formation may be an important first step in these reactions; intermolecular orientation within such a complex may be more favorable for hydride abstraction from the tetrahydro than the dihydroarenes. With less reactive tetrahydroarenes (e.g., 1,2,3,4-tetrahydrobenz[*a*]anthracene, 1,2,3,4-tetrahydrochrysene, or 7,12-dimethyl-8,9,10,11-tetrahydrobenz[*a*]anthracene), the fully aromatic hydrocarbon is the only product detected.[33] In these cases, it would appear that the initial dehydrogenation is simply too slow to compete effectively with the second stage dehydrogenation step.



Since the fully aromatic side products can generally be recyclized by reconversion to the tetrahydroarene via catalytic hydrogenation,[20] high overall conversions are attainable.

Since the synthetic approach frequently affords only one of two possible isomeric olefins, a synthetic approach to olefinic compounds with a conjugated double bond in the alternative ring position would be desirable. A simple solution to this problem involves DDQ dehydrogenation of more saturated hydroaromatic homologs. Thus, dehydrogenation of 5,6,8,9,10,11-hexahydrobenz[*a*]anthracene (**40**) with DDQ affords 5,6,10,11-tetrahydrobenz[*a*]anthracene (**41**).[33] This is in accord with prediction since ΔE_{deloc} is maximum at the 8 position of **40**. Similarly, DDQ dehydrogenation of 1,2,3,4,5,6-hexahydrochrysene (**42**) provides 3,4,5,6-tetrahydrochrysene as the major product.[33] This finding is again in agreement with theoretical prediction. From a synthetic viewpoint, these findings are quite significant, since by altering the extent of hydrogenation of the starting material it is possible to direct the position of introduction of the double bond. Since the olefinic bond may be utilized to introduce diverse functional groups into the molecule, this general approach may be employed to synthesize substituted polycyclic

TABLE XI. Stepwise DDQ Dehydrogenation of Hydroaromatic Compounds[a]

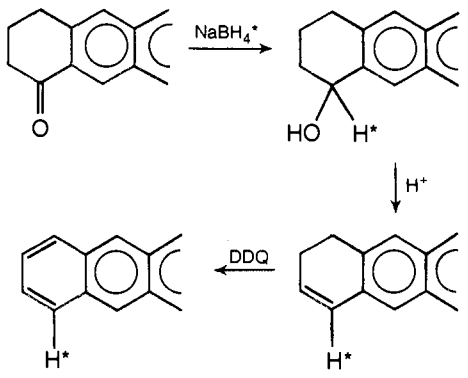
Hydrocarbon	Product	Yield, %[b]	Ref
 36	 37	90	20
 30	 38	52	20
	 39	13	
		70	20
		65	20
		56	20
		50	20
 42	 43	70	33
 40	 41	~15	33

[a] Reactions were carried out in refluxing benzene (5–15 min) with equimolar amounts of DDQ and the hydrocarbon. [b] Yields are based on percentage conversion.

hydrocarbons not accessible through direct substitution (generally limited to a few sites in the molecule).

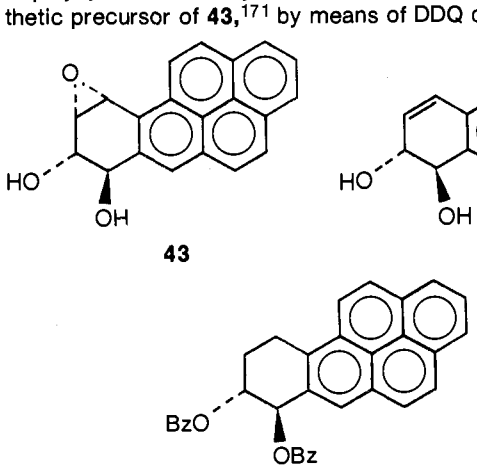
E. Synthesis of Isotopically Labeled Polycyclic Hydrocarbons

As a consequence of the recent discovery that carcinogenic hydrocarbons require metabolic activation to exert their biological activity,[134] high specific activity deuterium and tritium labeled hydrocarbon derivatives are required for metabolism studies. In the few cases where the appropriate aryl halide isomers are available, hydrogenolysis with deuterium or tritium gas provides a convenient synthetic route. [6-^2H]Benzo[*a*]pyrene and high specific activity [6-^3H]benzo[*a*]pyrene have been prepared by this route;[167] the specificity of labeling in the 6 position is supported by 270-MHz proton NMR and tritium NMR, respectively.[187,188] A serious drawback of this method is the scrambling of the isotopic label which may occur with the catalysts employed. Therefore, in the absence of direct experimental proof, specificity of labeling should never be assumed. In cases where the aryl halide is unavailable, a relatively simple and convenient method has recently been devised.[33,180] This approach involves reduction of the appropriate ketonic intermediate with labeled sodium borohydride, dehydration of the resulting alcohol, and DDQ dehydrogenation.[33,160] The use of DDQ or *o*-chloranil in the final step is crucial, since these reagents do not lead to scrambling and/or loss of the isotopic label. Compounds prepared via this sequence include 3- and 7-deuteriobenzo[*a*]pyrene and 4-deuteriobenz[*a*]anthracene.[33,160]



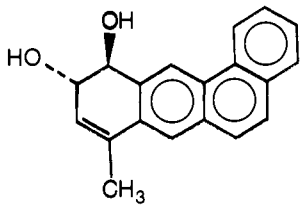
F. Synthesis of Metabolites of Carcinogenic Hydrocarbons

Identification of the diol epoxide derivative **43** as the probable biologically active form in humans[169] and other species[170] of the common environmental carcinogen benzo[*a*]pyrene has stimulated strong research interest in the oxidized metabolites of polycyclic arenes. Synthesis of the **7**,8-dihydrodiol **44**, synthetic precursor of **43**,[171] by means of DDQ dehydrogenation of the related tetrahydrodioldibenzoate **45** has recently been described.[133] Under the mild conditions employed elimination does not occur to significant extent. This synthetic method is general and is the method of choice for the synthesis of the analogous dihydrodiols of other polycyclic arenes[133,134] (Table X), particularly the methylated dihydrodiols, e.g., **46**, which could not be synthesized by the alternative bromination–dehydrobromination approach.



43 **44**

45



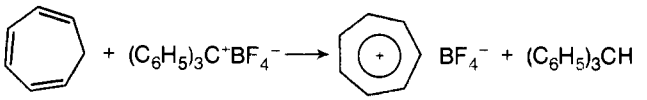
46

Quinone dehydrogenation has also proven useful in the synthesis of the phenol metabolites, dihydroarenes, and isotopically labeled carcinogenic hydrocarbons, as described in sections C, D, and E, respectively.

VII. Dehydrogenation with Trityl Salts

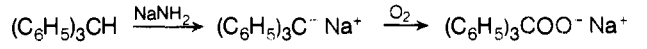
A. Trityl Perchlorate and Trityl Fluoroborate

The trityl (i.e., triphenylmethyl) carbocation was first employed by Dauben[172,173] to synthesize stable tropylium salts through abstraction of hydride from cycloheptatriene. Subsequently, in 1959 Bonthrone and Reid[174] reported the use of trityl perchlorate to dehydrogenate a series of hydroaromatic compounds, including

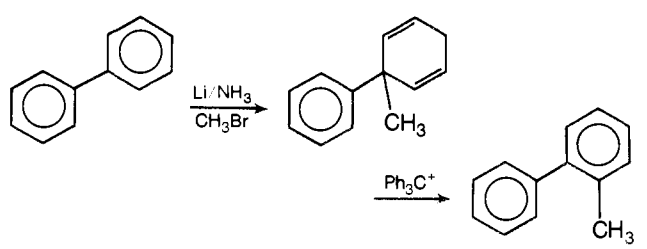


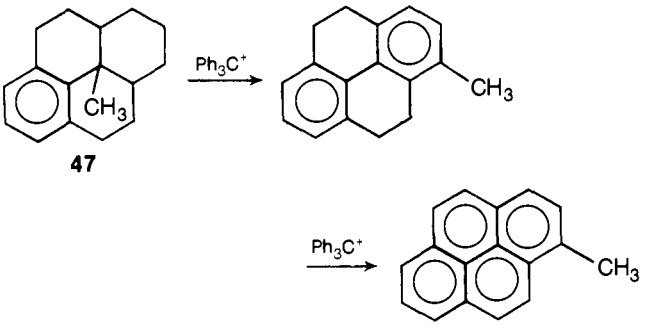
9,10-dihydroanthracene and 4,5,9,10-tetrahydropyrene, to fully aromatic products. Reactions were found to be complete in 15 min or less in boiling acetic acid. The accepted mechanism involves successive hydride abstraction and loss of a proton, the key step being removal of the hydride ion. Yields are generally high (Table XII).

Removal of the by-product triphenylmethane from the polycyclic hydrocarbon products is sometimes difficult. However, treatment of the crude product mixture with sodamide in liquid ammonia and bubbling air into the resulting solution of the trityl anion generates the corresponding hydroperoxide which can easily be separated by passage through a column of alumina.[175,176]



Rearrangement of quaternary alkyl groups may accompany dehydrogenation.[175] 1-Methyl-1,4-dihydrobiphenyl on treatment with trityl fluoroborate in dichloroethane underwent facile methyl migration and aromatization to 2-methylbiphenyl. Since the starting hydroaromatic compound is readily available from biphenyl through reductive methylation with lithium in ammonia and methyl bromide, the overall sequence represents a rather elegant method of regiospecific alkylation of biphenyl in the ortho position. The related hydrocarbons **47** and **48** underwent similar

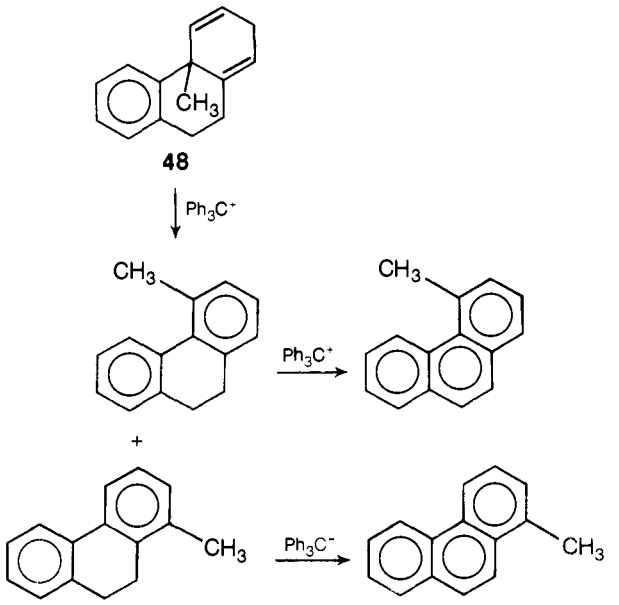




47

rearrangement and aromatization. Conversion of the partially saturated products to 1-methylpyrene and 1- and 4-methylphenanthrene was effected with excess trityl reagent.

However, there are no examples of stepwise dehydrogenation in which the second step is anticipated to be more favorable than the first. Attempted partial dehydrogenation of 1,2,3,4-tetrahydrobenz[*a*]anthracene with trityl fluoroborate furnished benz[*a*]anthracene as the sole detectable product.[33]



48

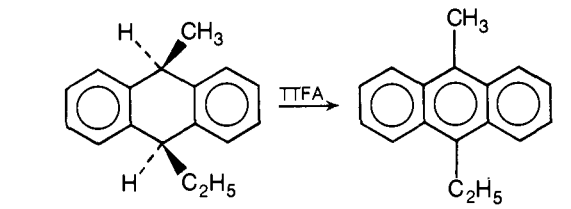
B. Trityl Trifluoroacetate

Recently Fu and Harvey demonstrated that trityl trifluoroacetate (TTFA) generated in situ from triphenylmethanol in trifluoroacetic acid (and a small amount of the acid anhydride to remove the water formed) is comparable in reactivity to trityl

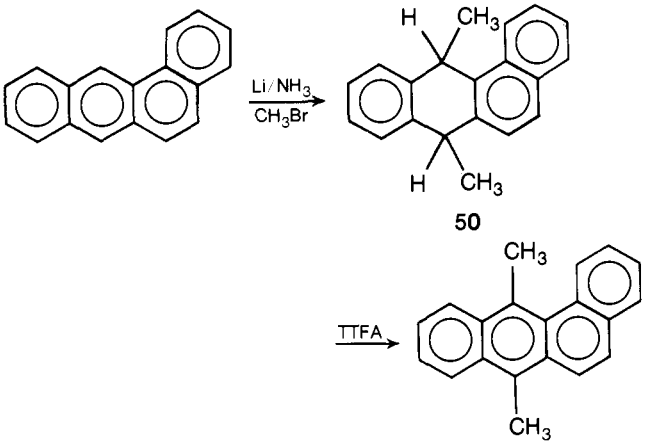
$$(C_6H_5)_3COH + CF_3CO_2H \rightleftarrows (C_6H_5)_3C^+CF_3CO_2^- + H_2O$$

perchlorate and fluoroborate.[177] TTFA is more convenient and more economical than the latter reagents and in certain cases provides higher yields (Table XII). In particular, 9- and 10-alkylated derivatives of 9,10-dihydroanthracene, which commonly provide relatively unsatisfactory results by other methods, were smoothly dehydrogenated by TTFA. For example, reactions of *cis*-9-ethyl-10-methyl-9,10-dihydroanthracene (**49**) with a wide range of other reagents (Pd/C, sulfur, $AlCl_3$, I_2, $FeCl_3$, $SbCl_5$, chloranil, DDQ, $Ph_3C^+ClO_4^-$, $Ce(NH_4)_2(NO_2)_6$, and $Pb(OAc)_4$) led generally to intractable mixtures from which only low yields of 9-ethyl-10-methylanthracene could be isolated.[178] However, dehydrogenation of **49** by TTFA provided the anthracene derivative in 85% yield.[177]

Analogous reaction of **50** provides 7,12-dimethylbenz[*a*]anthracene.[179] Since **50** is readily obtainable from benz[*a*]anthracene through reductive methylation,[180] the overall sequence constitutes a simple direct route to this potent carcinogenic hydrocarbon.

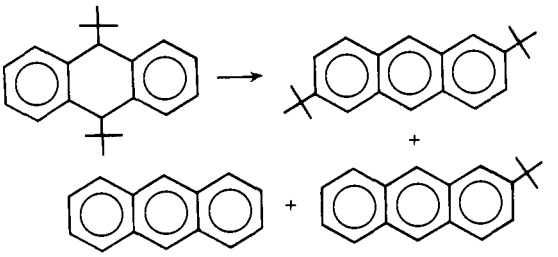


49



50

tert-Butyl groups tend to undergo facile intermolecular rearrangement when acidic conditions are employed. Thus, *trans*-9,10-di-*tert*-butyl-9,10-dihydroanthracene on treatment with TTFA in refluxing trifluoroacetic acid underwent disproportionation to 2,6-di-*tert*-butylanthracene, 2-*tert*-butylanthracene, and anthracene.[148] The same result ensued on similar reaction of 1,4-di-*tert*-butyl-1,4-dihydroanthracene or when 2-*tert*-butyl- or 9-*tert*-butylanthracene was refluxed in trifluoroacetic acid alone.



Tritylation, it should be noted, was not found to be a significant secondary reaction in any of the cases investigated. On the other hand, substitution of *tert*-butyl alcohol for trityl alcohol in the trifluoroacetic acid catalyzed reaction of 9,10-dihydrophenanthrene led to formation of substantial amounts of *tert*-butylated phenanthrenes.[33] Similarly, reaction of anthracene and 9,10-dimethylanthracene with *tert*-butyl trifluoroacetate generated in situ furnished 2,6-di-*tert*-butylanthracene and 2,6-di-*tert*-butyl-9,10-dimethylanthracene, respectively, in good yield.[148]

Virtually nothing is known concerning the fate of other functional groups in reactions with trityl salts. Ketonic groups appear to be unaffected. Although perinaphthanones can be dehydrogenated into perinaphthenones by trityl perchlorate,[174] neither β-tetralone nor the cyclic ketone **19** is aromatized into the corresponding phenols by this reagent.[33] Dehydration of tertiary alcohols occurs as expected with TTFA in trifluoroacetic acid. Attempted aromatization of 9-trimethylsilyl-9,10-dihydroanthracene with TTFA in trifluoroacetic acid furnished anthracene as the sole product.[182] Protodesilylation of arylsilanes is well known.

VIII. Dehydrogenation with Alkyllithium–TMEDA Complexes

The RLi–TMEDA method was devised by Harvey on the rational concept that if the dianions of dihydroarenes could be

TABLE XII. Dehydrogenation with Trityl Salts

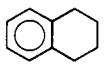
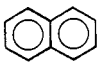
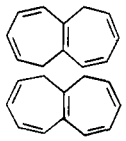
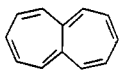
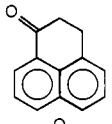
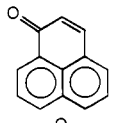
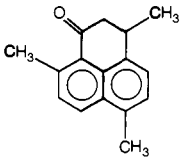
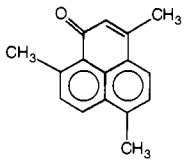
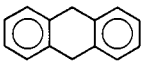
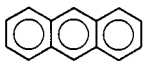
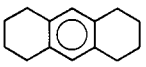
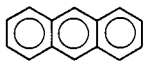
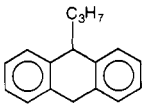
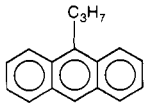
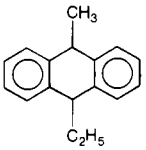
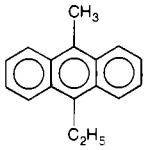
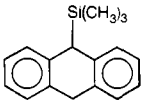
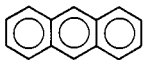
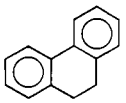
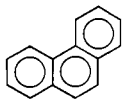
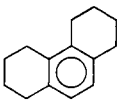
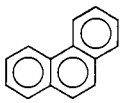
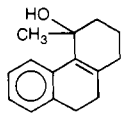
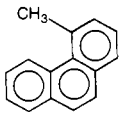
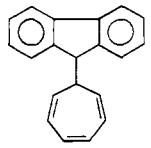
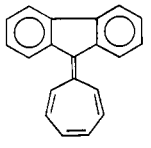
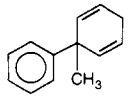
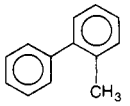
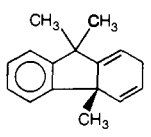
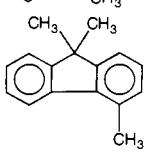
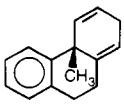
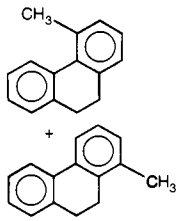
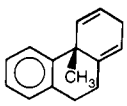
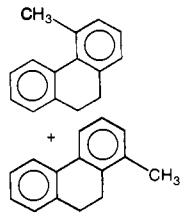
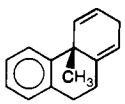
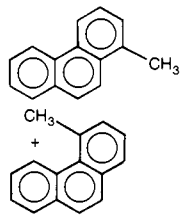
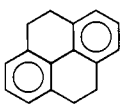
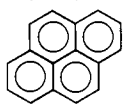
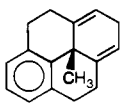
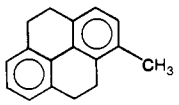
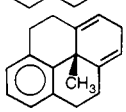
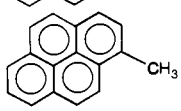
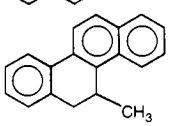
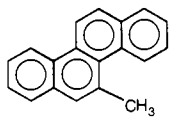
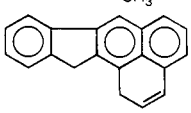
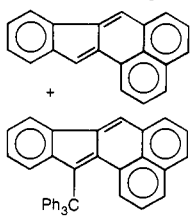
Substrate	Product	Reagent	Conditions	Yield, %	Ref
		A	15 h	100	177
		B	1. CH_2Cl_2 2. $(CH_3)_3N$, $CHCl_3$ 0°	36	173
		C	HOAc, reflux 10 min	80	174
		C	HOAc, reflux 15 min	81	174
		A C	6 h HOAc, reflux 4 min	100 90	177 174
		A	20 h	32	177
		A	6 h	65	177
		A	20 h	85	177
					182
		A	6 h 1 h 1 h	100 80 84[b]	177 177 177
		A	18 h	61	177
		A	3 h	77	177
		B		30–35	147
		B	$ClCH_2CH_2Cl$, reflux, 10 min	98	175
		B	HOAc, reflux, 1 h	70	150

TABLE XII (*Continued*)

Substrate	Product	Reagent	Conditions	Yield, %	Ref
		B	$ClCH_2CH_2Cl$, 3–4°, 1 h	58(62)[c] 37(38)[c]	175
		B (~2 equiv)	HOAc, 25°, 1 h	71 29	175
		B (2.4 equiv)	HOAc, reflux 1 h	64 28	175
		C	HOAc, reflux 5 min	93	174
		B	$ClCH_2CH_2Cl$, 3–4°, 1 h	100	175
		B	HOAc 20°, 1 h	100	175
		B (3 equiv)	HOAc, reflux, 5 min	80	175
		A	18 h	85	177
		B	HOAc, reflux		184
		C	HOAc, RT, 3 h	11 26	74

[a] A, a solution of trityl alcohol in trifluoroacetic acid (TFAA); B, Ph_3CBF_4; C, Ph_3CClO_4. [b] Containing acetic anhydride in 17%. [c] Yields in parentheses obtained after additional 5 min reflux.

TABLE XIII. Dehydrogenation with the RLi–TMEDA Complex

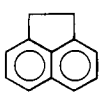
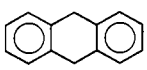
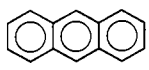
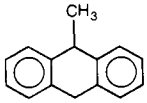
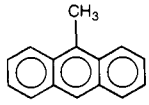
Substrate	Product	Yield, %	Ref
		98	183
		99	178, 183
		99	178, 183

TABLE XIII (*Continued*)

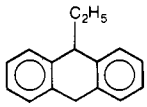
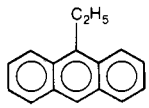
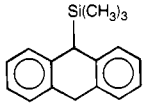
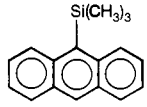
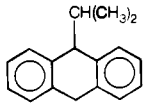
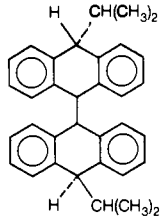
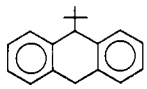
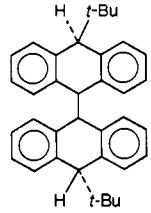
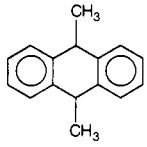
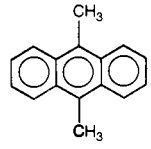
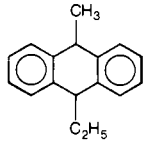
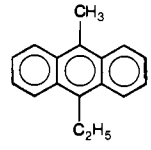
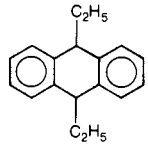
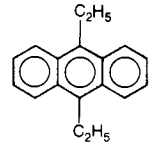
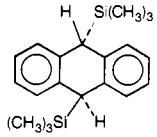
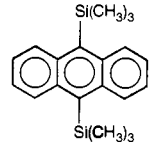
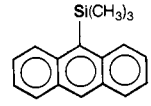
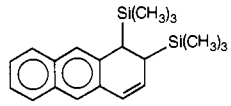
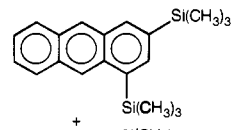
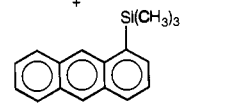
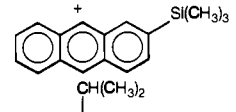
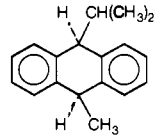
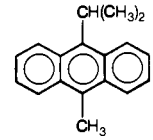
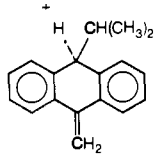
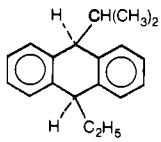
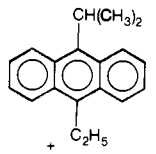
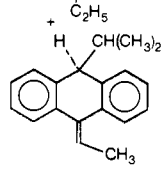
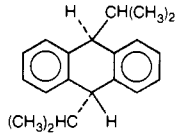
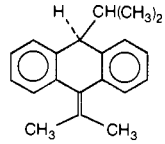
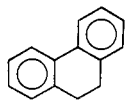
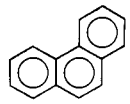
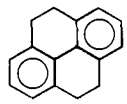
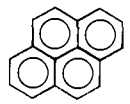
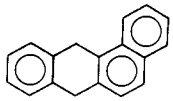
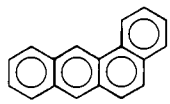
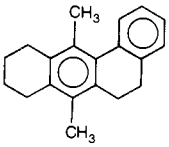
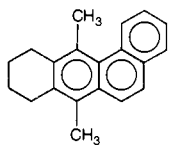
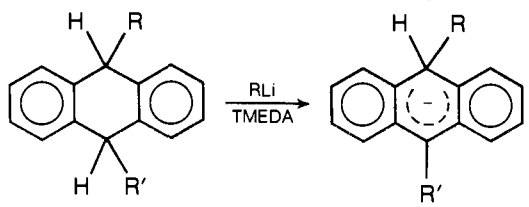
Substrate	Product	Yield, %	Ref
		99	178, 183
		95	182
		72	183
		90	183
		99	178, 183
		99	178, 183
		99	178, 183
		32	
		50	182
		15	
		30	182
		8	
		5	183

TABLE XIII (*Continued*)

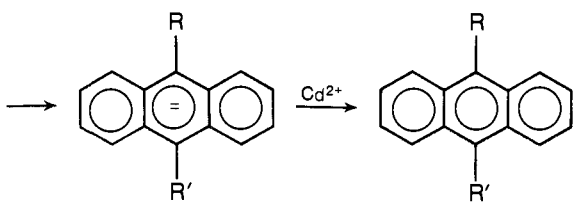
Substrate	Product	Yield, %	Ref
		63	
		10	183
		42	
		34	183
		100	183
		72[a] 94[b]	183
		97	183
		80	33

[a] In the absence of added metal salt. [b] In the presence of copper(II) iodide.

generated by double deprotonation, aromatization might be achieved through electron transfer to a suitable acceptor.[178,183] It was found that although alkyllithium reagents alone tended to form only monoanions of dihydroanthracenes, *n*-butyllithium and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) in a hydrocarbon solvent formed the corresponding dianions. Treatment of the latter with a metal salt, such as $CdCl_2$, afforded fully aromatic products in essentially quantitative yield. Other metal salts (e.g., $PbCl_2$, CuI_2, $CuBr_2$, $HgCl_2$, nickel(II) acetylacetonate) or other electron acceptors (e.g., I_2) also serve, though none quite so effectively. Analogous reactions of other hydroaromatic hydrocarbons proceeded similarly to provide the corresponding dehydrogenated compounds in high yield (Table XIII).

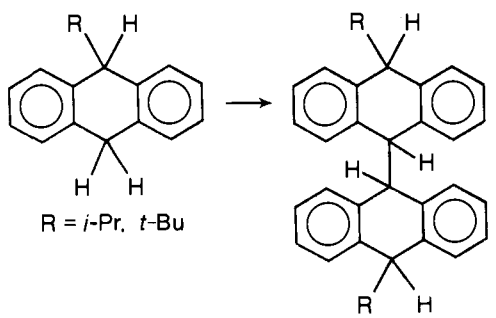


red



purple

The analogous reactions of 9-isopropyl- and 9-*tert*-butyl-9,10-dihydroanthracene followed a different course, providing instead the dimeric products arising through coupling in the unsubstituted positions.[183] In these cases only monoanionic intermediates are formed as a consequence of steric inhibition of dianion formation by the bulky tertiary and secondary alkyl groups.



The steric effect alone is not sufficient to inhibit dianion formation, since the analogous 9-trimethylsilyl-9,10-dihydroanthracene formed a dianion readily on treatment with RLi–

TABLE XIV. Dehydrogenation with NBS

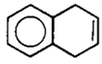
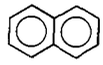
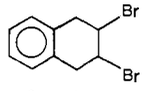
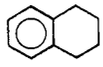
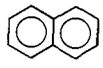
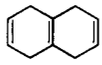
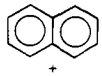
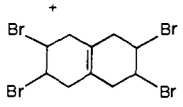
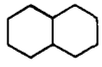
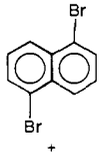
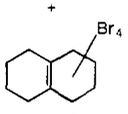
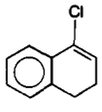
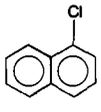
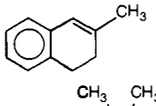
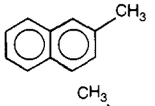
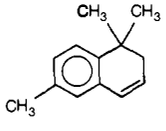
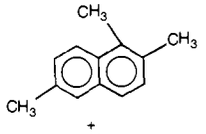
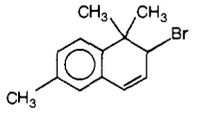
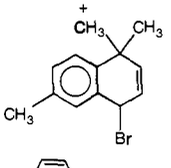
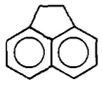
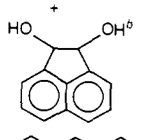
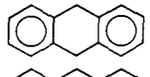
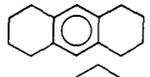
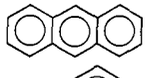
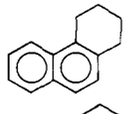
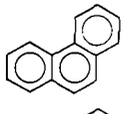
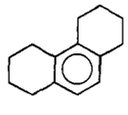
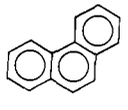
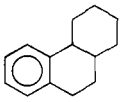
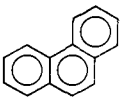
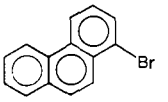
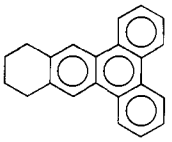
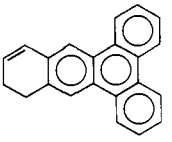
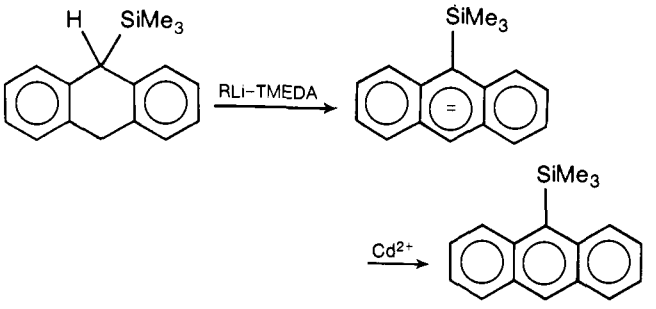
Substrate	Product	Conditions[a]	Yield, %	Ref
	 + 			185
		0.5 h	74	186
	 + 		(1:1)	187
			9	
	+ 	0.33 h	14	186
				188
				188
			14	
	+ 	4 h		189
	+ 		86	
			20	
	+ 		8	186
				185
			69	186
			79	186
			63	186

TABLE XIV (*Continued*)

Substrate	Product	Conditions[a]	Yield, %	Ref
	 + 	HOAc, KOAc, 4 h	21 12	186
		*c*	15	33

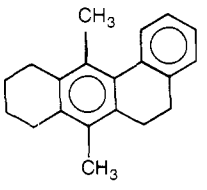
[a] All reactions were conducted in refluxing CCl_4 with dibenzoyl peroxide as catalyst. [b] This compound was assumed to arise from reaction of the dibromide with water and alkali.[186] [c] Dehydrobromination was achieved with DBN.



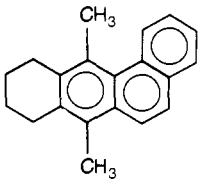
TMEDA.[182] Stabilization of the adjacent negative charge by the trimethylsilyl group apparently outweighs the contrary effect of peri interaction on the bulky group in the intermediate. The dianion on treatment with $CdCl_2$ is converted to 9-trimethylsilylanthracene. This constitutes the first successful synthesis of this compound. Analogous syntheses of a number of other mono- and bistrimethylsilyl derivatives of anthracene have also been reported.[182] It is likely that this synthetic approach will prove generally applicable to the preparation of other arylsilanes.

9,10-Dihydrophenanthrene underwent smooth dehydrogenation to phenanthrene with RLi–TMEDA alone, *in the absence of added metal salt!*[178,183] The mechanism of this transformation is uncertain. Tetralin, on treatment with even a large excess of the reagent for prolonged periods, underwent only modest conversion to naphthalene.[183]

As a consequence of the much greater facility of dehydrogenation of dihydro vs. tetrahydro rings by this reagent, regioselective dehydrogenation of the former is possible. Thus, the hydrocarbon **51** underwent regioselective dehydrogenation in the K region with RLi–TMEDA–Cd(II) to afford **52.**[33] In contrast,



51



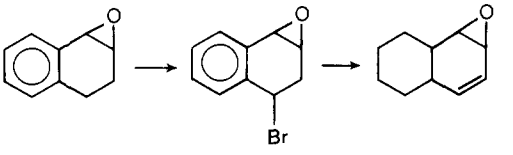
52

reaction of 5,6,8,9,10,11-hexahydrobenz[*a*]anthracene **40** with DDQ took place, as mentioned earlier, in the outer ring to provide 5,6,10,11-tetrahydrobenz[*a*]anthracene (**41**). Therefore, the two procedures are complementary in their action on this hydroaromatic ring system.

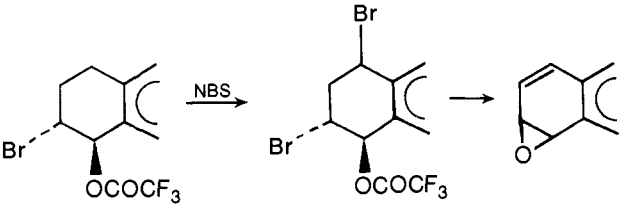
IX. NBS Bromination–Dehydrobromination

Benzylic bromination with *N*-bromosuccinimide followed by base-catalyzed elimination has been employed to dehydrogenate a number of hydroaromatic compounds (Table XIV) with variable success. Brominations are generally carried out in refluxing CCl_4 in the presence of benzoyl peroxide. Dehydrobrominations are commonly accomplished by treatment of the brominated products with a tertiary amine, such as pyridine or quinoline; other bases employed include potassium acetate, potassium carbonate, and lithium carbonate. Details of the mechanism and other aspects of NBS bromination have been surveyed in several review articles.[187b,190,191] The scope of this method is limited, however, by the tendency to furnish brominated side products (Table XIV).

NBS bromination–dehydrobromination has seen practical application in the synthesis of arene oxides and arene dihydrodiols.[134] This method was employed by Vogel in the first successful synthesis of naphthalene oxide.[192] The most satisfactory base for this purpose was found to be diazobicyclononane (DBN).



The non-K-region arene oxide derivatives of 1-methylnaphthalene, phenanthrene, benz[*a*]anthracene, benzo[*a*]pyrene, and dibenz[*a,h*]anthracene have subsequently been synthesized via this route (Table XV). A modification of this approach devised by Yagi and Jerina[194] involves bromination of the appropriate bromohydrin ester with NBS followed by base treatment to effect both elimination of HBr and generation of the epoxide ring. The trifluoroacetate ester group is found to be particularly advantageous as a blocking group during the bromination step because of its ease of removal in the final step. Polycyclic arene oxides derived from naphthalene, phenanthrene, anthracene, and benzo[*a*]pyrene have been synthesized via this synthetic route (Table XV).



The NBS method has also been utilized to synthesize the dihydrodiol metabolites of carcinogenic polycyclic hydrocarbons (Table XV).[134] Synthesis of *trans*-7,8-dihydroxy-7,8-dihydrobenzo[*a*]pyrene (**43**) through NBS bromination of the related tetrahydrodiol dibenzoate **45** followed by thermal or base-catalyzed elimination of HBr was described by McCaustland and Engel[200]

TABLE XV. Dehydrogenation with NBS: Arene Oxides

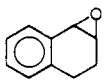
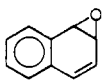
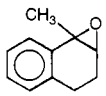
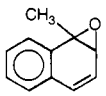
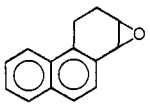
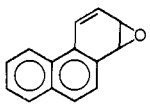
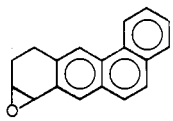
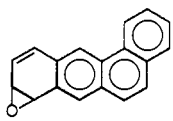
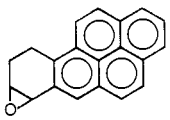
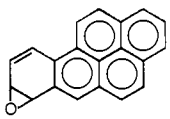
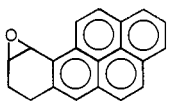
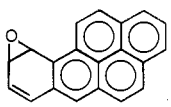
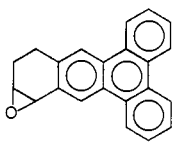
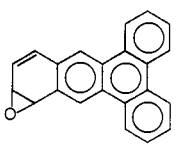
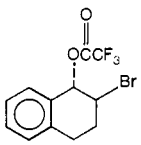
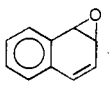
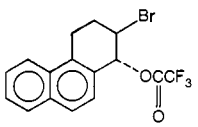
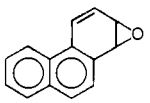
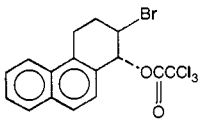
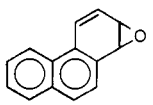
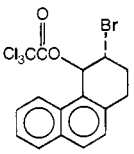
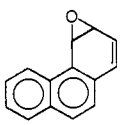
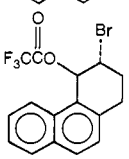
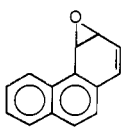
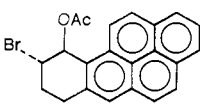
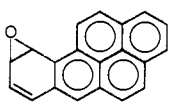
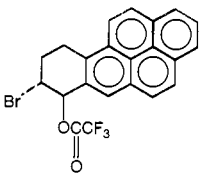
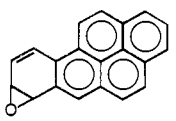
Substrate	Product	Conditions[a]	Yield, %	Ref
		*b*	19	192
				193
		*b*, 150–160°, light, *f*	61	194
		*b*, *e*	33	195
		*b*, *e*	24	196
		*b*, *e*	33	196
		*b*, *e*	37	197
		*b*, 50–60°, light *f*, *g*	76[h]	194
		*b*, 50–60°, light *f*, *g*	72[h]	194
		*b*, 50–60°, light *f*, *g*	49[h]	194
		*b*, 50–60°, light, *f*, *g*	70	194
		*b*, 50–60°, light *f*, *g*	77	194
		*b*, 50–60°, light *f*, *g*	60	194
		*b*, 50–60°, light *f*, *g*	57	194

TABLE XV (*Continued*)

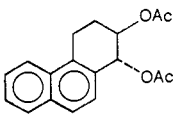
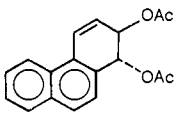
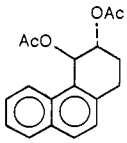
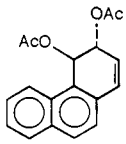
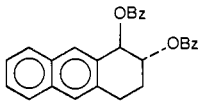
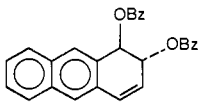
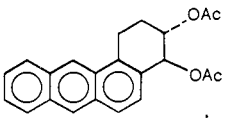
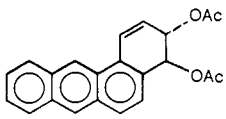
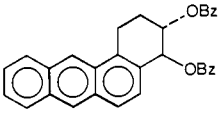
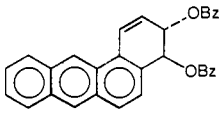
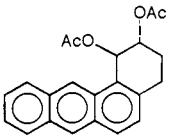
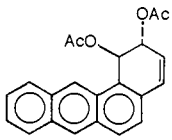
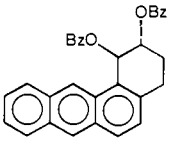
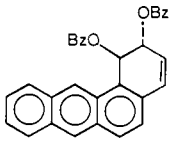
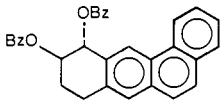
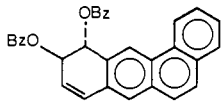
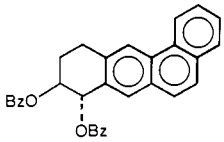
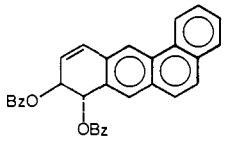
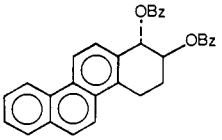
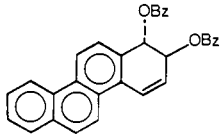
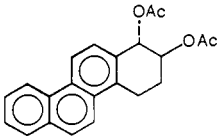
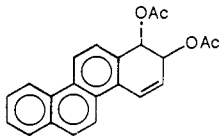
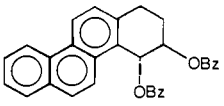
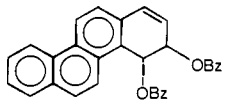
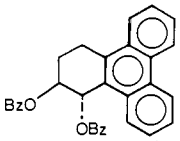
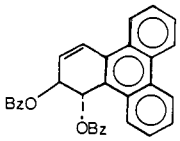
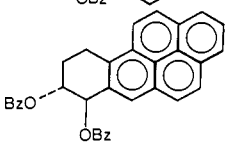
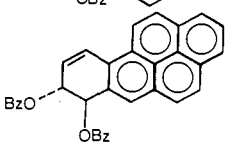
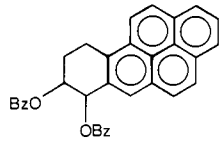
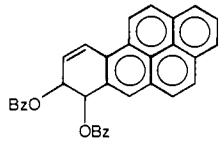
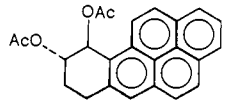
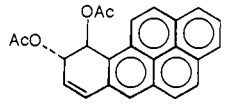
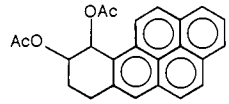
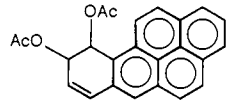
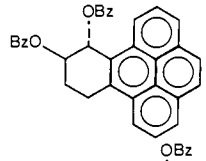
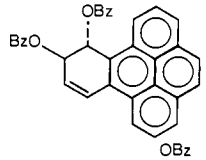
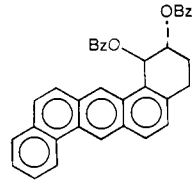
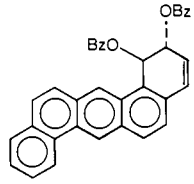
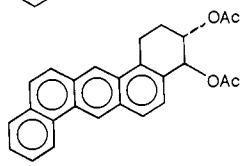
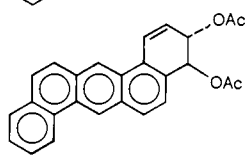
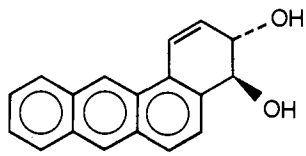
Substrate	Product	Conditions[a]	Yield, %	Ref
		*b, d*	35	198
		*b, d*	56	198
		*b, d*	20	198
		*b, d*	26	198
		*c, e*	44	132
		*b, d*	15	198
		*c, e*	45	132
		*b, d* *c, e*	41 45	198 133
		*b, d* *c, e*	46 68	198 133
		*c, e*	30	33
		-, *e*	24	199
		-, *e*	45	199
		*c, e*	50	156
		-, *d* -, *e*	68 50	200 133

TABLE XV (*Continued*)

Substrate	Product	Conditions[a]	Yield, %	Ref
		*c, e*	5	133
		*c, e*	26	33
				201
		*c, e*	50	157
		-, *e*	31	199
		-, *e*	22	199

[a] All reactions were conducted in refluxing CCl_4. [b] Azobisisobutyronitrile was employed as catalyst. [c] Dibenzoyl peroxide was used as catalyst. [d] Dehydrobromination was effected in boiling xylene alone or in the presence of an appropriate base, e.g., $NaHCO_3$. [e] Dehydrobromination was effected with DBN. [f] Dehydrobromination was effected with $NaOCH_3$ in dry tetrahydrofuran. [g] The epoxide ring was also generated on base treatment. [h] Yields are specified for the overall transformation of the bromohydrin ester to arene oxide.

and by Beland and Harvey.[171] Although the DDQ route has recently been found to be superior to the NBS method in the synthesis of **43** and many other dihydrodiols,[133,134] it is less satisfactory where the hydrogen to be removed as hydride is in a sterically crowded environment and loss is unassisted by electronic factors. In these cases, e.g., in the synthesis of *trans*-3,4-dihydroxy-3,4-dihydrobenz[*a*]anthracene (**53**), the NBS method is still the only effective synthetic approach. The ste-



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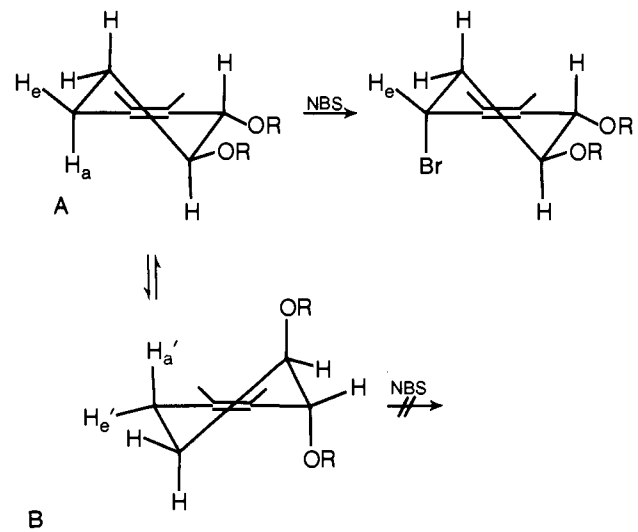
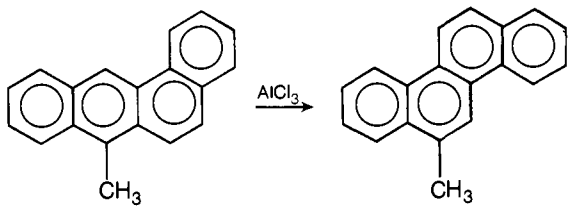
reochemistry of bromine substitution is an important factor in these reactions. Bromination has been found to occur stereoselectively on the axial benzylic position H_a of the less hindered diequatorial conformer A, since bromine attack on the diaxial conformer B is inhibited by 1,3-diaxial steric interaction.[171] In some cases a second stereoisomeric bromo diester has been detected as a minor product.[132,193]



X. Miscellaneous Methods

A. Lewis Acids

Among the most powerful dehydrogenating agents are Lewis acids such as aluminum chloride and antimony pentachloride. For example, treatment of 9,10-dihydroanthracene and 9,10-dihydro-9,10-diphenylanthracene with $AlCl_3$ affords anthracene[202] and 9,10-diphenylanthracene,[203] respectively. Similarly, reaction of dihydroanthracene and dihydrotetracene with $SbCl_5$ provides anthracene and tetracene, respectively.[204] However, these reagents are equally powerful catalysts for rearrangements, disproportionation, and other secondary reactions. In some cases profound rearrangement of the molecular ring structure may occur. For example, 7-methylbenz[*a*]anthracene on treatment with $AlCl_3$ in benzene rearranges to 6-methylchrysene.[205] For these reasons and because these reagents are incompatible with many functional groups, Lewis acids are seldom employed for dehydrogenation.



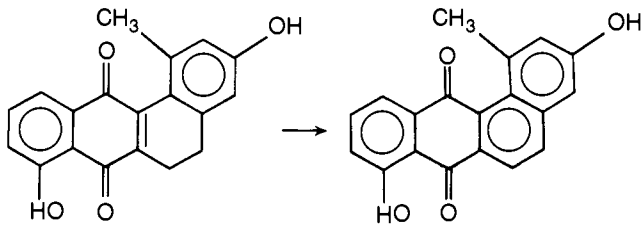
B. Alumina

Dehydrogenation has occasionally been observed during chromatographic separation of hydroaromatic compounds.[143] For example, treatment of a mixture of 1,4-dihydro-*p*-terphenyl (**54**) and *cis*- and *trans*-1′,4′-dihydro-*p*-terphenyl (**55**) with basic Al_2O_3 afforded *p*-terphenyl and recovered *trans*-**55**. The observed cis stereospecificity of this reaction is remarkable. Further investigation of dehydrogenation of hydroaromatic molecules over alumina would appear warranted.

54 **55**

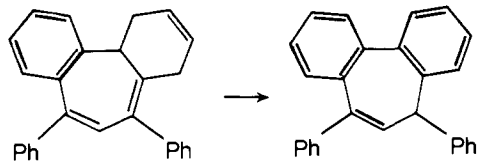
C. Nitrobenzene

Dehydrogenation of 5,6-dihydro-3,8-dihydroxy-1-methylbenz[*a*]anthracene-7,12-dione took place on heating in nitrobenzene and pyridine at reflux temperature.[206]



D. Diphenylpicrylhydrazyl

Dehydrogenation of **56** was effected by refluxing with diphenylpicrylhydrazyl in benzene for 72 h.[207]



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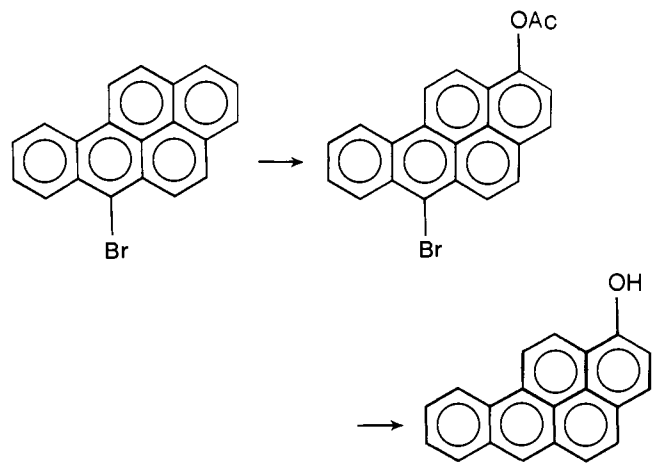
XI. Summary and Prospects

It is appropriate at this point to consider the current status of knowledge in this field from a broader perspective with a view to projection of possible future trends.

The level of research activity in dehydrogenation methods has historically paralleled the degree of interest in the chemistry of the polycyclic arenes. The number of papers published in polycyclic hydrocarbon chemistry reached a peak in the 1930s under the leadership of Fieser, Cook, Bachmann, Badger, and their associates. Their efforts were stimulated by the demonstration by Kennaway[208] of the carcinogenic activity of the pure hydrocarbon molecules dibenz[*a*,*h*]anthracene and benzo[*a*]pyrene. Following this lead, chemists undertook the synthesis of a vast array of polycyclic arenes in the hope that structure–activity correlations might provide some insight into the mechanism of causation of cancer. Synthetic approaches to diverse new polycyclic ring systems were devised. The last step in these synthetic sequences was commonly aromatization through dehydrogenation over sulfur, selenium, or the platinum metals. The relatively drastic conditions required by these methods were tolerated since the compounds synthesized were for the most part the fully aromatic hydrocarbon molecules unsubstituted except by alkyl groups. These investigations culminated in the development of quantum mechanical theories, notably the Pullman theory,[209] which attempted to correlate molecular electronic structural features with carcinogenic activity. However, it gradually became clear that the theories were inadequate to account for the biological observations, and the active carcinogens did not appear to be distinguished by any unique mode of chemical reactivity. As a consequence, interest declined and the chemistry of polycyclic hydrocarbons fell into neglect.

In contrast to the dramatic advances made in almost every other aspects of organic chemistry, the hydrocarbon field has remained virtually stagnant for over 30 years. While a few of the smaller polycyclic arenes such as anthracene, phenanthrene, pyrene, and cyrysene are available relatively cheaply, the larger polycyclic ring systems remain rare and expensive, synthetically available only through the same tedious multistep syntheses devised many years earlier. There is a great need for development of more convenient and direct synthetic approaches utilizing modern concepts in order to make these compounds available for research. Methods of mild selective dehydrogenation are likely to play an important role in any novel synthetic approaches.

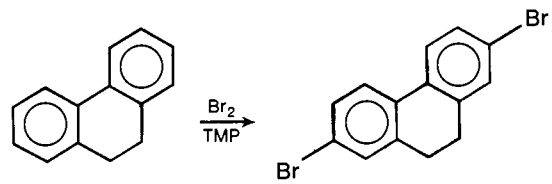
A second major problem lies in the deficiency of methods for regioselective introduction of functional groups into any desired ring position of a polycyclic arene. Electrophilic, nucleophilic, or radical substitution generally provides only a small fraction of the total number of possible isomeric structures. The traditional solution to this problem has been laborious total synthesis of each isomeric derivative from appropriately substituted smaller molecular units. For example, synthesis of all the isomeric phenols of benzo[*a*]pyrene via individual complex multistep synthesis has recently been described.[81] However, by this traditional approach, very few complete sets of isomeric derivatives of any polycyclic arene have ever been, or are ever likely to be, synthesized. Some preliminary approaches to development of methods for the introduction of functional groups into positions not normally prone to direct substitution have been explored in the authors' laboratory. One of these involves the use of blocking groups. For example, synthesis of 1-hydroxybenzo[*a*]pyrene has been achieved by initial bromination of benzo[*a*]pyrene in the 6 position, acetoxylation in the 1 position with $Pb(OAc)_4$, and removal of both the acetate function and bromine by treatment with *n*-butyllithium.[210] A second approach



involves regioselective hydrogenation in the K region[19] by Pd/C or in terminal rings[20] by Pt/C to afford polycyclic hydroaromatic intermediates. Mild dehydrogenation of the latter with DDQ furnishes the corresponding dihydroarenes[20] (e.g., **38**) which may

be employed as substrates for the synthesis of phenols, dihydrodiols, etc. Methods of mild dehydrogenation compatible with the functional groups present are required in these syntheses. While the methods of dehydrogenation currently in use (DDQ, NBS) are effective in many cases, it is hoped that mild methods of even wider general utility can be developed in the future.

The polycyclic hydroaromatic compounds obtained by hydrogenation may also be employed as substrates for direct aromatic substitution. Since the substitution pattern of the aromatic ring system remaining on partial hydrogenation generally differs from that of the parent arene, new substituted arenes may be obtained via the sequence: hydrogenation, substitution, dehydrogenation. For example, bromination of phenanthrene affords 9-bromophenanthrene, whereas bromination of 9,10-dihydrophenanthrene in trimethyl phosphate furnished the 2,7-dibromoderivative.[211] Dehydrogenation of the latter with DDQ would be expected to provide 2,7-dibromophenanthrene. This approach deserves to be exploited much more extensively than it has in the past.



Recent identification of the diol epoxide derivative **43** as the active form of the potent precarcinogen benzo[*a*]pyrene[169,170] provides strong stimulus for development of convenient synthetic approaches to the full range of oxidized hydrocarbon metabolites. The latter include phenols, quinones, dihydrodiols, oxides, diol epoxides, and their further oxidized derivatives and conjugates. This poses a major challenge to synthetic organic chemists, since the potential number of compounds and isomers is very large. The need for mild efficient methods of dehydrogenation will be correspondingly large, since a key step in all these syntheses must be dehydrogenation. The synthetic challenge must first be met before the comparative chemical reactivity and other properties of these molecules can be fully elucidated. It is hoped these efforts may open the door to a new modern chemistry of the polycyclic arenes.

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