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PART I

THE SCOPE AND MECHANISM OF BISANNELATION OF BISARYNE
EQUIVALENTS WITH FURANS

PART II

DEOXYGENATION OF ARENE-1,4-ENDOXIDES WITH LOW-VALENT
TRANSITION METALS

By

Godson Chukuemeka Nwokogu

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ABSTRACT

PART I

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In Part I of this thesis, optimal reaction procedures for bisannelation of furans to tetrabromoarenes (bisaryne equivalents) were developed by considering the nature and solubility of the bisaryne equivalents, solvent effects, reaction temperature, concentration of n-butyllithium (n-BuLi) and its rate of addition. The generality of the bisannelation process was demonstrated by its success with various *p*-disubstituted tetrabromoarenes. Bisaryne equivalents with electron-releasing substituents gave good yields of bisadducts while those with electron-withdrawing groups gave poor yields with all furans. Tetrabromoarenes with different 1,4-substituents, e.g. methyl tetrabromo-*p*-cresolate and tetrabromo-*p*-chlorotoluene gave poor yields due to a secondary reaction.

The syn/anti ratios of bisadducts showed very little dependence on the bisaryne equivalent structure and on the furan substituents. The isomer ratios for bisadducts of the same bisaryne equivalent with furan itself and methyl-substituted furans were not much different. These results are consistent with the intermediacy of a benzyne.

Investigation of the mechanism of bisannulation showed that it could occur through either monolithiation or dilithiation of the tetrabromoarenes. Whereas tetrabromoarenes with electron-releasing groups, e.g., tetrabromo-p-xylene, formed bisadducts by stepwise monolithiation/annulation, those with electron-withdrawing groups like tetrabromo-p-difluorobenzene formed dilithio-arenes, which then underwent aryne formation/annulation. The relative position of the lithium atoms in these dilithio-derivatives was exclusively para.

Treatment of most tetrabromoarenes with one equivalent of n-BuLi in the presence of furans resulted in mono-adducts in toluene only. Methyl tetrabromo-p-cresolate and tetrabromo-p-dimethoxybenzene gave monoannulation products also in THF due to their solubility in this solvent.

For tetrabromoarenes with different 1,4-substituents, e.g., methyl tetrabromo-p-cresolate 34 and tetrabromo-p-chlorotoluene, treatment with one equivalent of n-BuLi led to two isomeric monolithiation intermediates. One of these monolithiation derivatives formed benzyne only while the other

probably formed benzyne in competition with proton abstraction. For example, treatment of 34 with one equivalent of n-BuLi and excess 2,5-dimethylfuran gave a monoadduct and methyl 3,5,6,-tribromo-p-cresolate.

Polyolithiation of bisaryne equivalents stopped at the dilithio-derivative no matter how much excess of n-BuLi was employed.

In Part II of this thesis, an efficient new method for the direct deoxygenation of arene endoxides was developed. Low-valent forms of iron, titanium and tungsten were used to aromatize naphthalene-1,4-endoxides and anthracene-1,4:5,8-diendoxides, even when peri-interactions were severe. Hence, 1,4,5,8,9,10-hexamethylantracene was prepared from 1,4,5,8,9,10-hexamethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide using low-valent titanium. Adducts of furan and 2,5-dimethylfuran were effectively deoxygenated by the three metals. Adducts of tetramethylfuran underwent a 1,3-hydrogen migration under the influence of reduced iron whereas reduced titanium led either to partial deoxygenation or to a mixture of non-oxygen containing hydrocarbons. Reduced tungsten effected deoxygenation of only the endoxide functions of 9,10-dimethoxyanthracene diendoxides. Reduced iron and titanium, however, also effected the replacement of the methoxyl groups with hydrogen. Hence 1,4,5,8-tetramethyl-9,10-dimethoxy-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide gave 1,4,5,8-tetramethyl-9,

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10-dimethoxyanthracene when treated with reduced tungsten, but led to 1,4,5,8-tetramethylantracene on reaction with low-valent iron or titanium.

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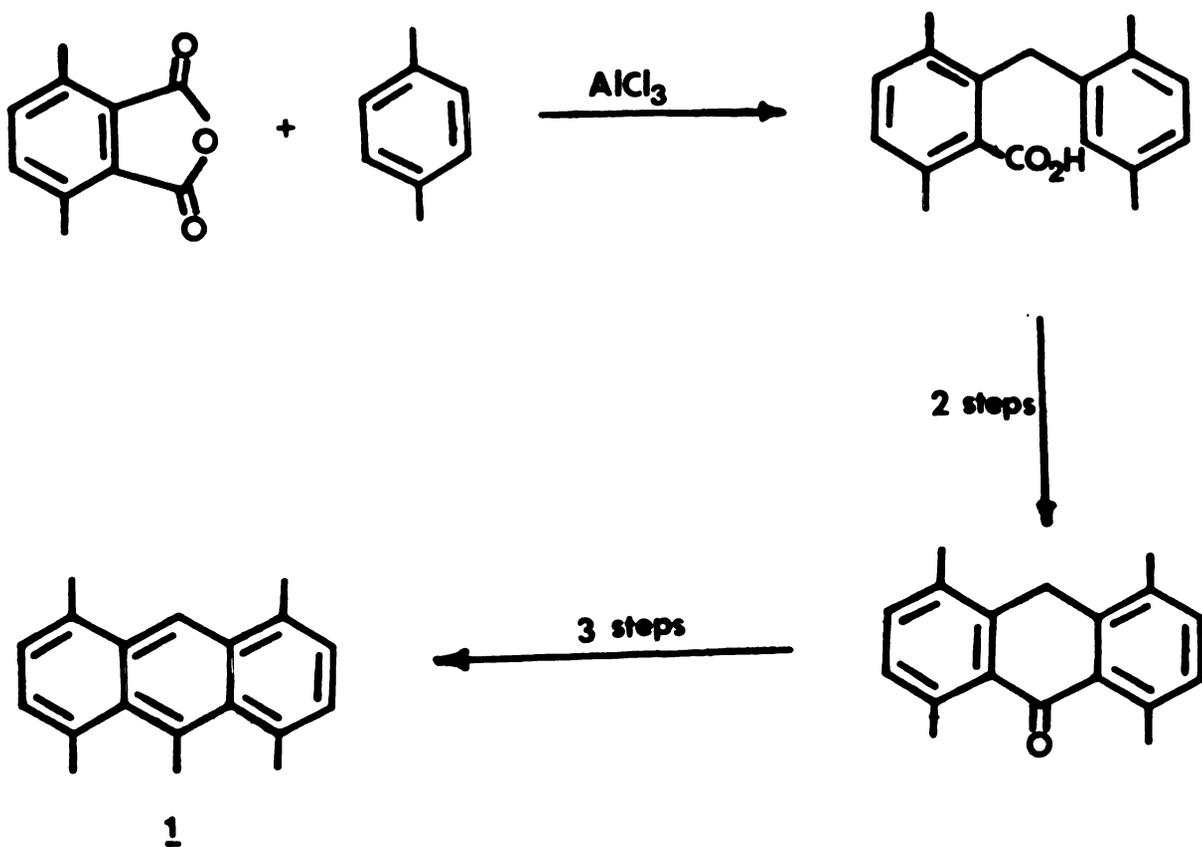
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PART I

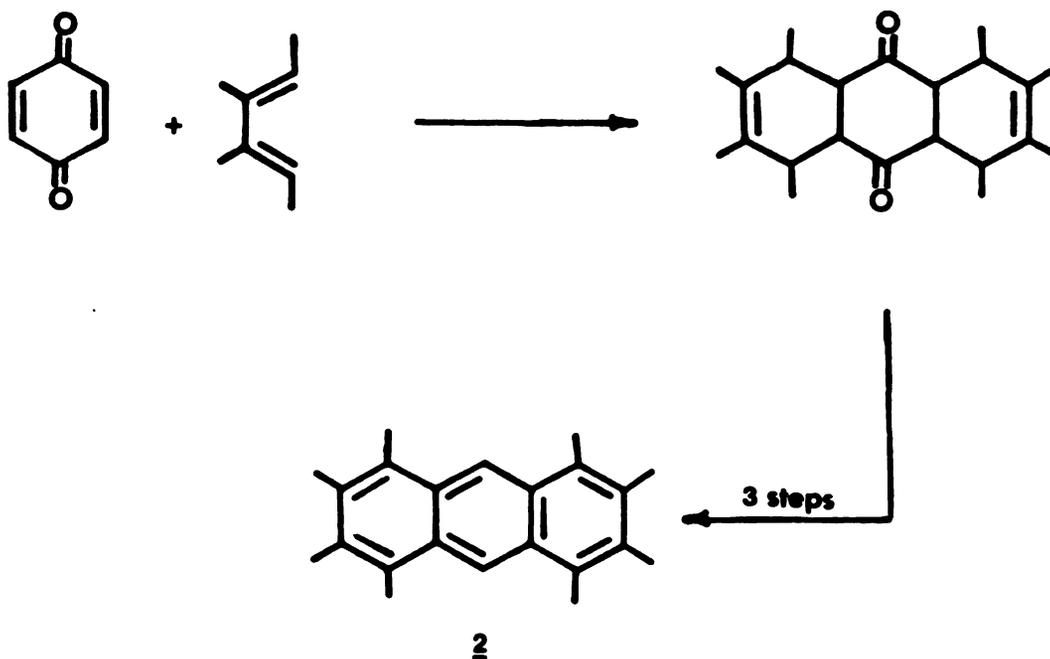
THE SCOPE AND MECHANISM OF BISANNELATION OF BISARYNE
EQUIVALENTS WITH FURANS

INTRODUCTION

The methods that have been used for the construction of fused aromatic rings can be classified into the Haworth (Scheme 1)¹ and the Diels-Alder (Scheme 2)² types of annelation to an existing benzene or six-membered ring.

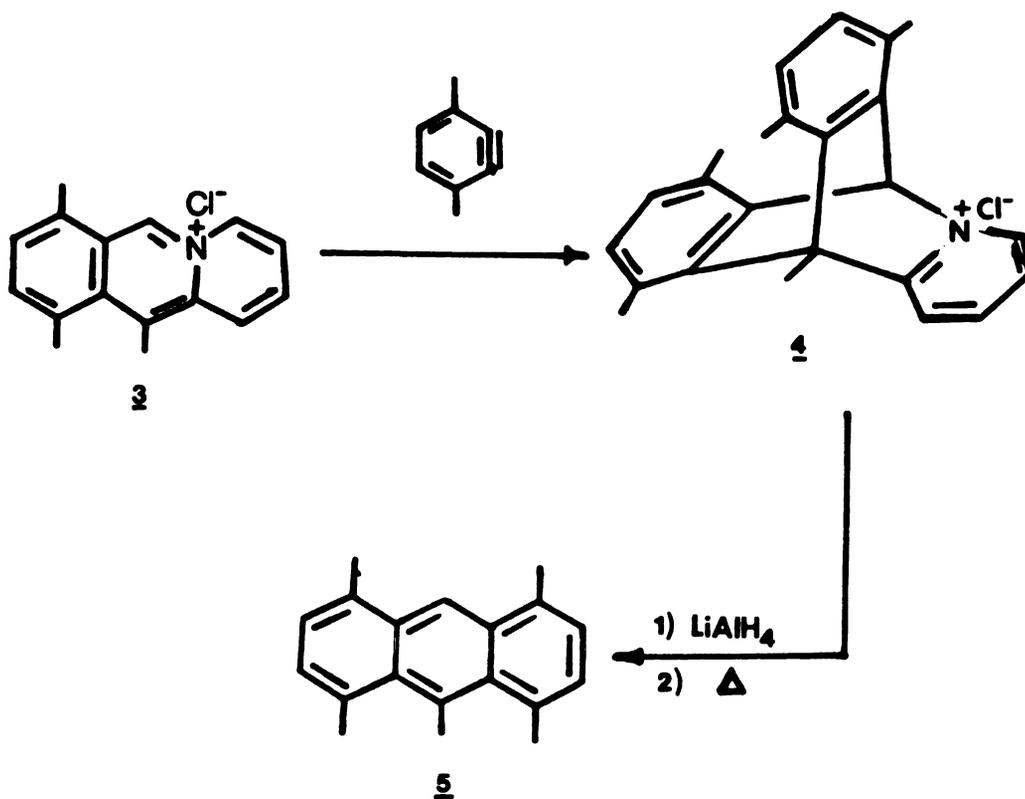


Scheme 1



Scheme 2

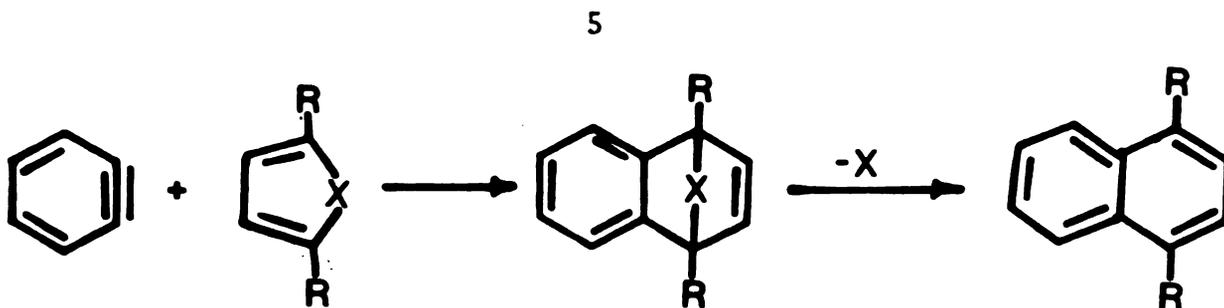
The Diels-Alder approach is especially suitable when the dienophile is an aryne. If a cyclic diene is used, at least two of the ring carbons of the adduct are sp^3 -hybridized through a 1,4- and/or 9,10-bridge. Aromatization, as a last step, involves cleavage of this bridge. This modification of the cycloaddition pathway to acenes has found effective application in the synthesis of aromatic compounds with severe peri-interactions (Scheme 3).³ The 4a-azoniaanthracene 3 formed the adduct 4 with 3,6-dimethylbenzyne generated from the appropriate diazonium carboxylate. Reduction of the pyridine bridge to a dihydropyridine allowed a retro Diels-Alder reaction to generate the anthracene 5.



Scheme 3

The introduction of steric strain in the last step is more than compensated for by the stabilization gained from aromatization.

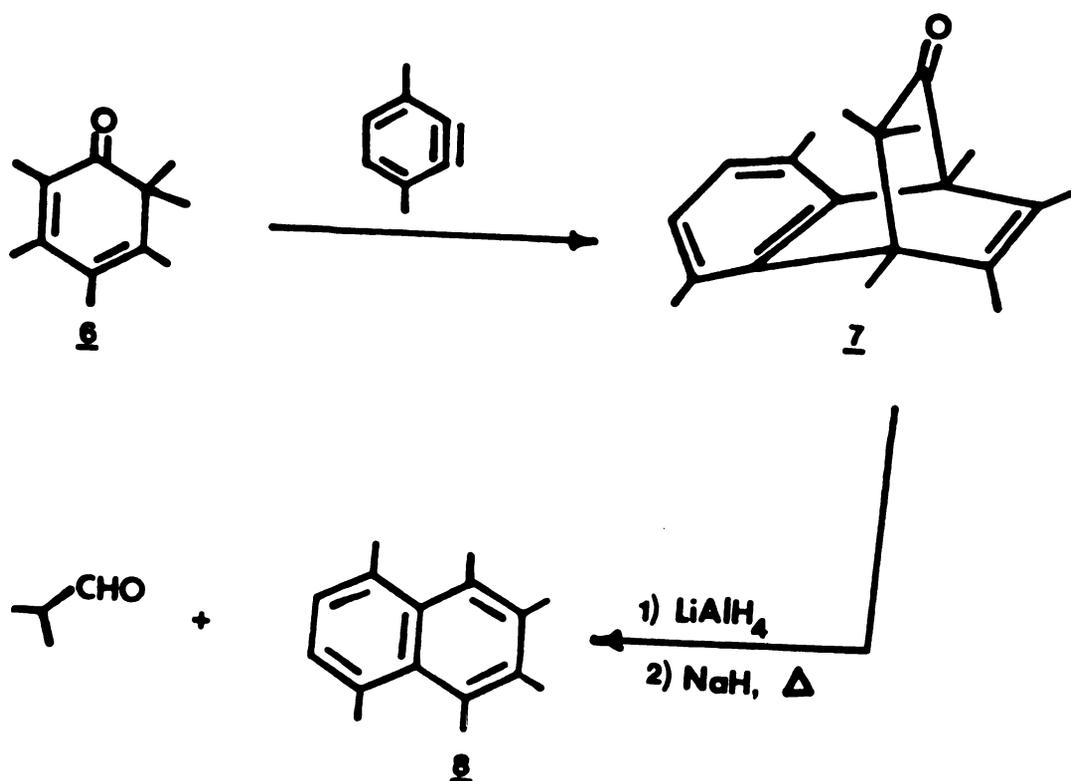
This two-step reaction sequence, involving a cycloaddition of an aryne to a cyclic diene followed by cleavage of the bridge from the resulting adduct,^{3,4} has become the most versatile method for the synthesis of simple and strained polynuclear aromatic compounds. Because of the reactivity of arynes, the first step is highly exothermic.⁵ As an approach to highly substituted acenes, the sp³-hybridization of some of the ring carbons in the adducts



allows accommodation of the steric strain due to the substituents at this stage in the assembly of the molecular framework. This makes it possible to have all the required substituents present in the diene and dienophile, thus reducing the number of necessary steps for the preparation of a specifically substituted acene. The second step involves as an important driving force, the formation of a new aromatic ring by the elimination of a small fragment X (the bridge).

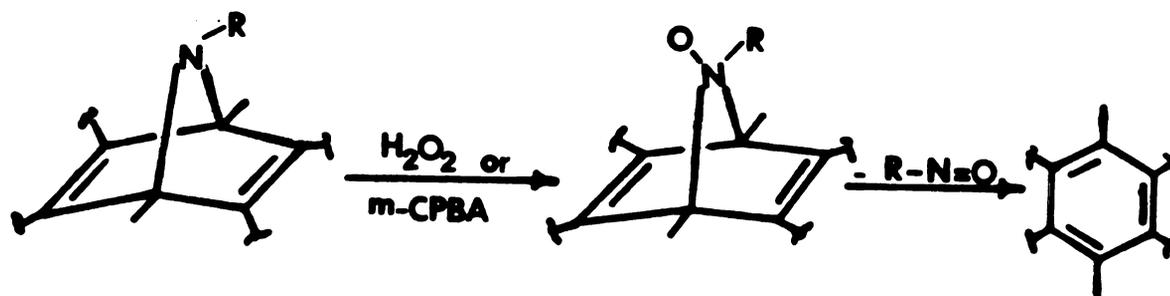
Various types of bridges (X) have been used in the described sequence and their eventual cleavage often is preceded by the reduction or oxidation of the bridging system. The application of a pyridine bridge and its cleavage is illustrated in Scheme 3.³ As shown in Scheme 4 the cyclohexadienone 6 reacted with 3,6-dimethylbenzyne to give the adduct 7 which has a two-carbon bridging system. Reduction of the keto-group to an alkoxide was done to facilitate the retro Diels-Alder cleavage of the bridge in the aromatization step leading to 8.⁶

Oxidation to N-oxides of the imino group of pyrrole adducts⁷ allows its loss as a nitroso group. Hart and co-workers have used this bridging system in short syntheses of

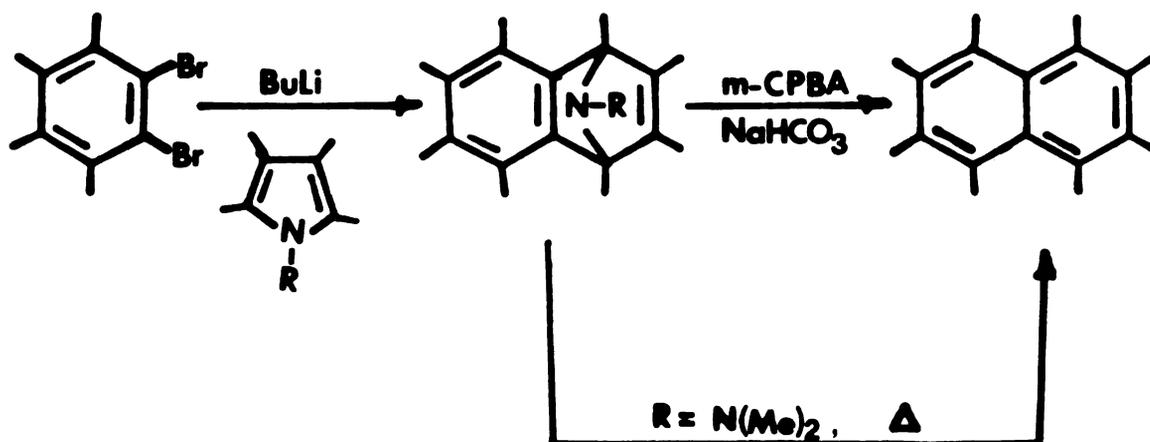


Scheme 4

octamethylnaphthalene,⁸ decamethylantracene **9**⁹ and dodecamethylnaphthacene.¹⁰ The introduction of the imino-N,N-dimethylamino bridge by Lai¹¹ led to marked improvements in

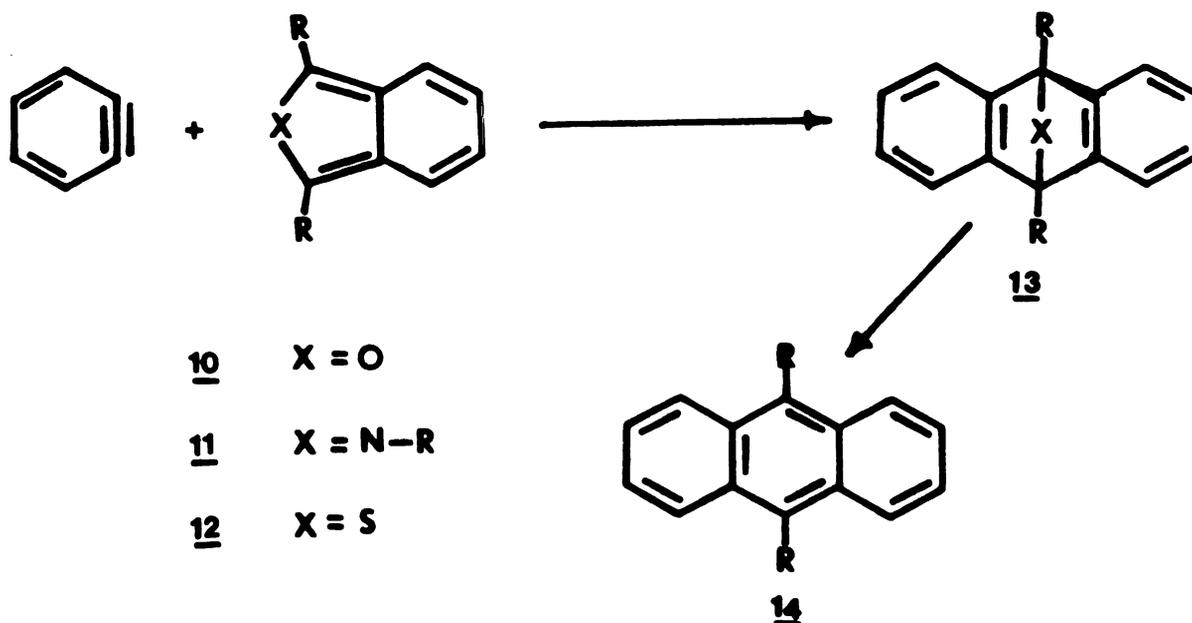


the overall yields of these strained aromatic hydrocarbons.



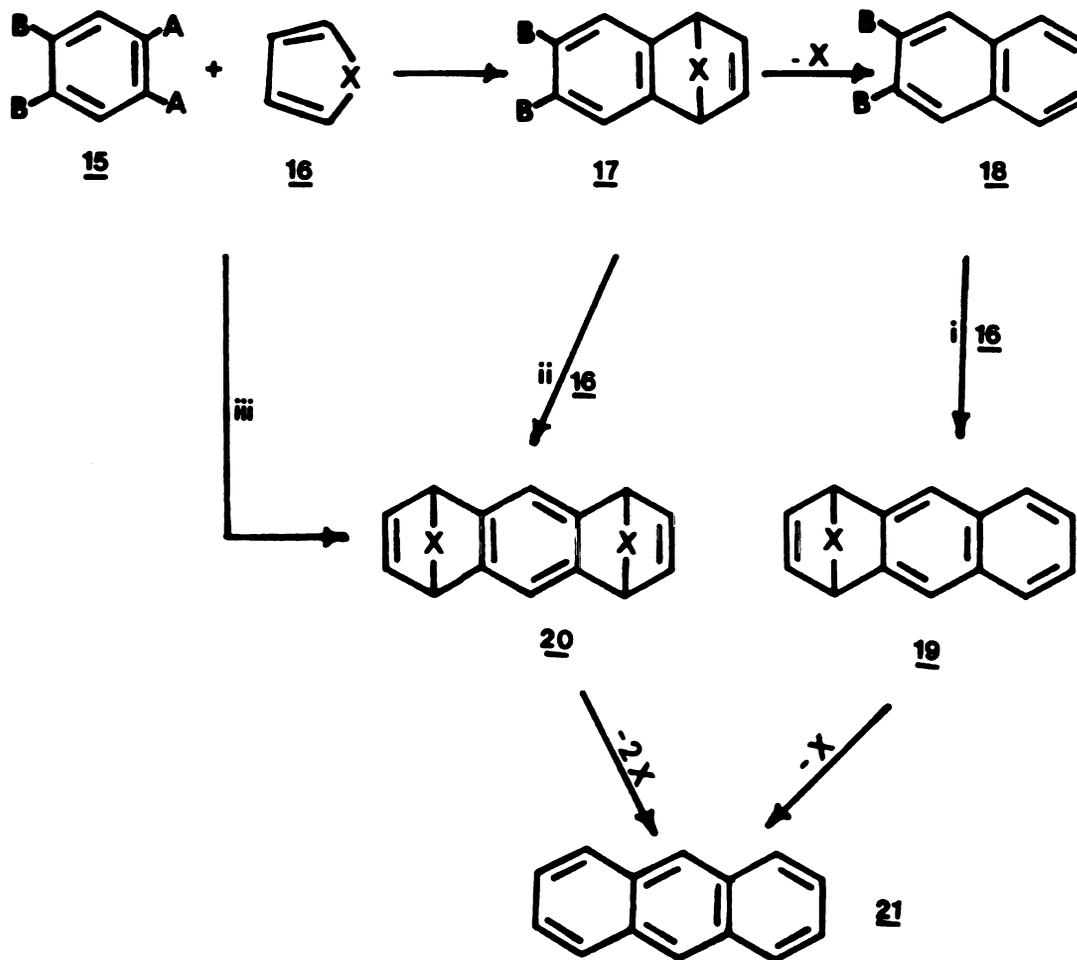
Oxygen and sulfur have also been used as bridges in the synthesis of simply substituted acenes.¹²

One can envision applying this two-step strategy to the synthesis of anthracenes in several ways. The central ring could originate from either the diene component or the aryne precursor. In the former case, the diene can be an isobenzofuran ($X = \text{O}$),¹² isoindole ($X = \text{N-R}$)¹³ or



isobenzothiophene ($X = S$).¹² For example, the reaction of 1,3-diphenylisobenzofuran 10 ($X = O$, $R = Ph$) with benzyne gave the adduct 13 ($X = O$, $R = Ph$) which was deoxygenated either by treatment with zinc in acetic acid or by heating in diglyme at 162°C.^{12,14} The low availability and stability of variously substituted isobenzofurans, isoindoles and isobenzothiophenes limits the versatility of this method.

If the central ring of the anthracene originates from the aryne component, sequential annelations or



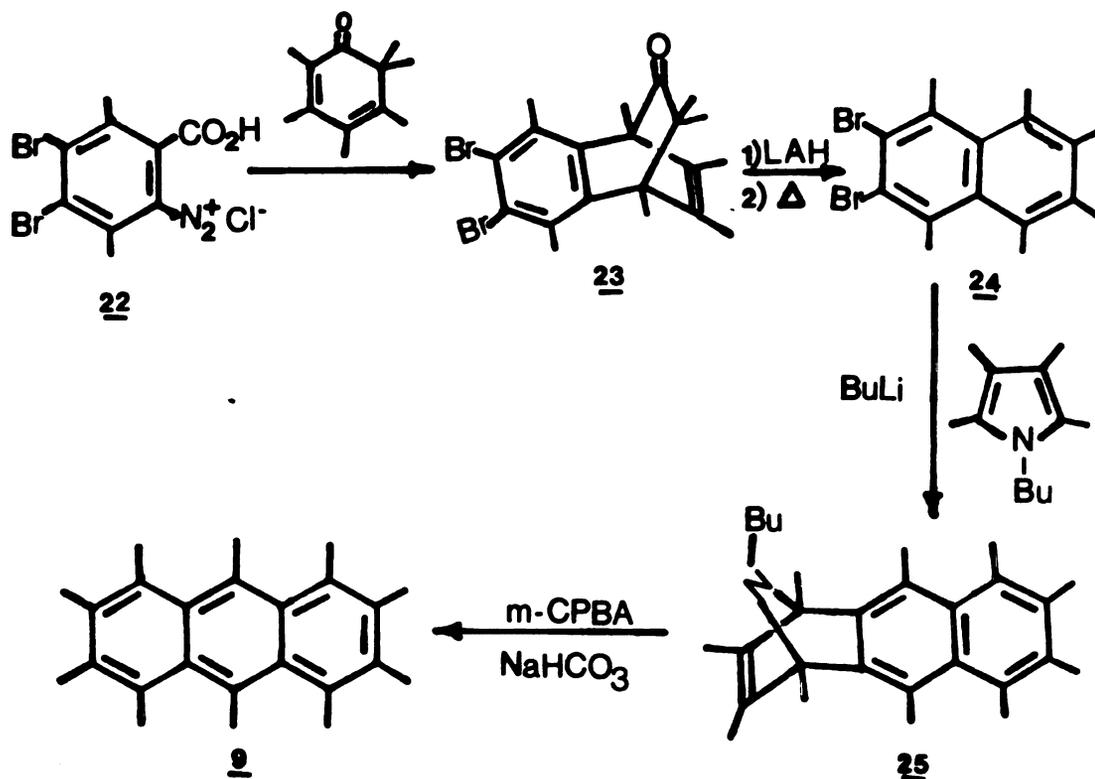
Scheme 5

bisannelation might be possible (Scheme 5). A monoaryne derived from 15 (A and B are groups capable of generating aryne) can undergo cycloaddition and the resulting monoadduct 17 can then be converted to the anthracene 21 by one of two sequences (i and ii). The bridge can be eliminated to give the naphthalene 18 which is set up, by the presence of groups B, to give another aryne leading to the anthracene 21 via the adduct 19 (sequence i). Alternately, monoadduct 17 can undergo a second aryne cycloaddition to give the bisadduct 20 from which both bridges could be eliminated (sequence ii). If the bridges (X) are different, they have to be cleaved by two different methods. Cleavage can be affected simultaneously, however, if the bridges are identical.

Another alternative would be the direct formation of the bisadduct 20 if the groups A and B are such that they could be converted to arynes by the same reagent (sequence iii). In this case, the reactant 15 serves as a bisaryne equivalent, although mechanistically, the formation of 20 may occur in a stepwise manner, i.e. via 17.

Examples of these different synthetic sequences have appeared in the chemical literature. Sequence (i) is exemplified by the synthesis of decamethylantracene 9 (Scheme 6).⁹ The initial aryne was generated from the diazonium carboxylate function of 22 and trapped with the cyclohexadienone 6 to form the adduct 23. Cleavage of the

bridge before the next cycloaddition was done to avoid reaction of the carbonyl group of 23 with *n*-BuLi which was used to generate a naphthyne from 24. Trapping of this

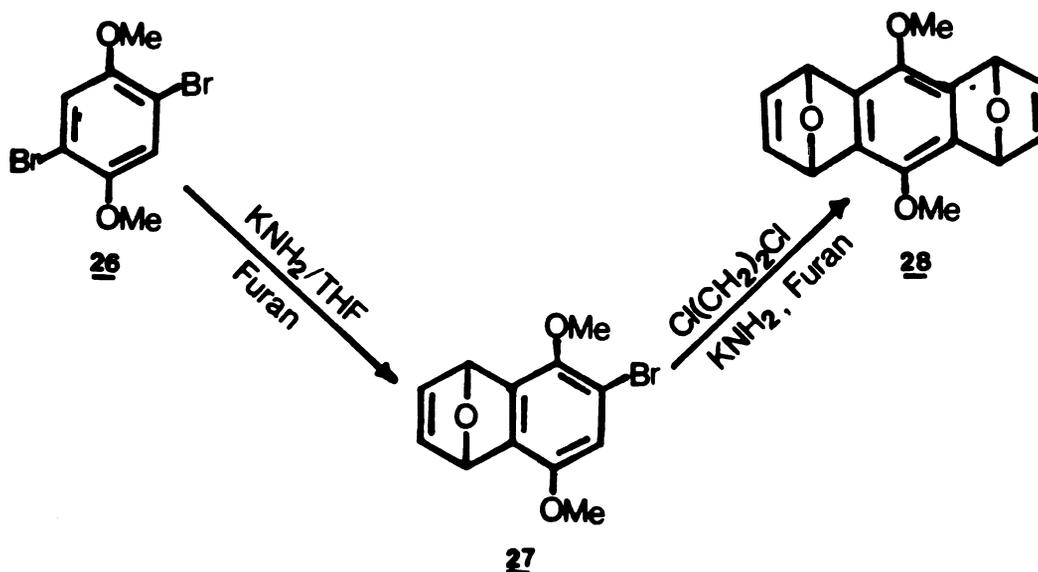


Scheme 6

aryne with *N*-butyl-tetramethylpyrrole resulted in the adduct 25 which was converted to 9 using *m*-chloroperbenzoic acid. The use of two methods of benzyne generation and bridge cleavage have less adverse consequence on the

utility of this scheme than the difficulty of preparing the bifunctional benzyne precursor 22.

The sequence (ii) was used in the preparation of the furan bisadduct 28.¹⁵ Metal-hydrogen exchange between potassium amide and 2,5-dibromo-p-dimethoxybenzene 26 in the presence of furan resulted in the monoadduct 27. After isolation, 27 was subjected to a second aryne cycloaddition



in the same manner but at a higher temperature to give the bisadduct 28. The special advantage of this sequence is the ease of preparation of the bifunctional aryne synthon 26.

Only one mention was made prior to the beginning of this work of the use of tetrahalobenzenes 29 as bisaryne

bisannulation that the first part of this thesis is concerned. In the second part, a new method for the removal of the bridge when $X = 0$ will be described.

RESULTS AND DISCUSSION

A. Choice and Preparation of Reactants:

The preparation of aromatic fluorides from the parent arenes involves nitration, reduction to the amine, diazotization and pyrolysis of the diazonium tetrafluoroborate salt.¹⁶ For each additional fluorine substituent, some or all of these steps have to be repeated. On the other hand, the polybromination of activated and slightly deactivated arenes is a facile one-pot and often high-yield process. Also, the bond strengths of the C-F and C-Br bonds (117 kcal/mol and 65 kcal/mol respectively) indicate that an o-lithiobromoarene will be more efficient in the generation of benzyne than an o-lithiofluoroarene.

Considering therefore the ease of polybromination of most arenes and the ease of loss of LiBr from o-lithiobromoarenes, it was anticipated that the more accessible tetrabromoarenes would be better bisaryne equivalents than tetrafluoro-, tetrachloro and mixed (especially those containing F and Cl) tetrahaloarenes. A precedent in favor of this expectation was the successful bisannulation of pyrroles to 2,3,6,7-tetrabromo-1,4,5,8-tetramethylnaphthalene.¹⁰ Tetraiodobenzenes would be expected to be better

than other bisaryne equivalents but the substitution of iodine on the ring is a cumbersome and costly process.

The tetrabromoarenes used in this work were prepared by standard methods. Activated arenes like p-xylene, p-cresol and p-chlorotoluene were brominated at below -5°C in the presence of catalytic amounts of iron filings and excess bromine without solvent.¹⁷ The less reactive arenes like p- and o-dichlorobenzene, p-difluorobenzene (Table 1)

TABLE 1
PREPARATION AND YIELD OF TETRABROMOARENES

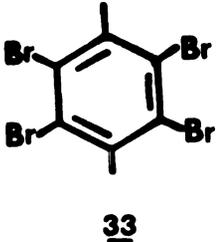
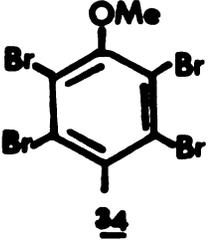
Entry	Precursor	Product	Yield	Reference
1		 <u>33</u>	73	17
2		 <u>24</u>	90	19, 20

TABLE 1 (Cont'd.)

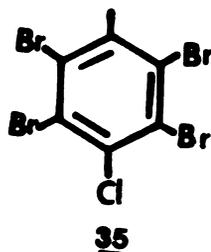
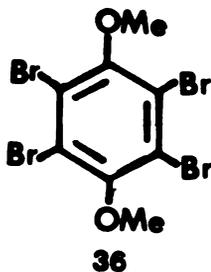
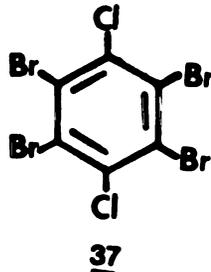
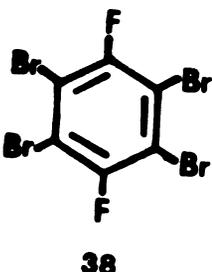
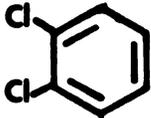
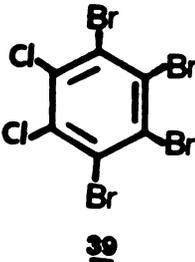
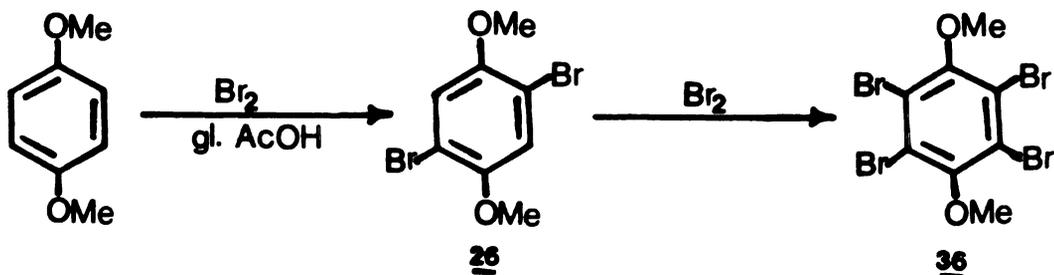
Entry	Precursor	Product	Yield	Reference
3		 <u>35</u>	72	--
4		 <u>36</u>	71	21
5		 <u>37</u>	94	18
6		 <u>38</u>	71	24

TABLE 1 (Cont'd.)

Entry	Precursor	Product	Yield	Reference
7			97	18

were refluxed in excess bromine with iron filings for about 6 h. Polybromination of p-dimethoxybenzene was accomplished in two steps. Initial bromination in glacial acetic acid gave the 2,5-dibromoarene 26.²¹ After isolation, 26 was then

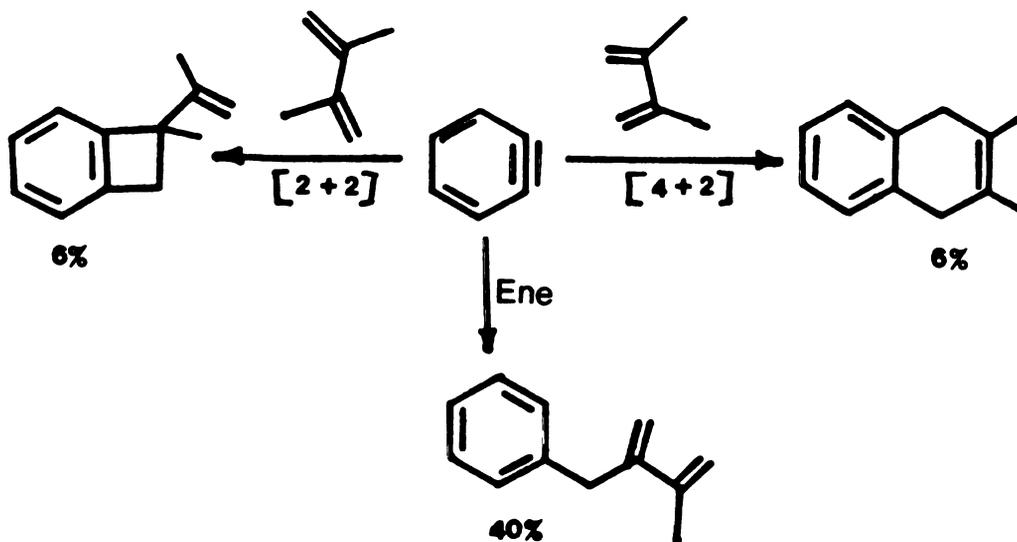


treated with excess bromine at room temperature without catalyst and solvent to give 36.

The choice of five-membered ring dienes--in this case furans--is a recognition of the conformational requirements of the Diels-Alder cycloaddition. In the transition state for the concerted reaction, the diene must have an

s-cis conformation. For acyclic dienes, the s-trans is usually the more stable and abundant conformer. Reactions of benzyne with acyclic 1,3-dienes therefore give low yields (often less than 20%) of [4 + 2] adducts. For example, when benzyne reacted with 2,3-dimethyl butadiene, the major product arose from the ene reaction of the s-trans isomer (Scheme 7).²²

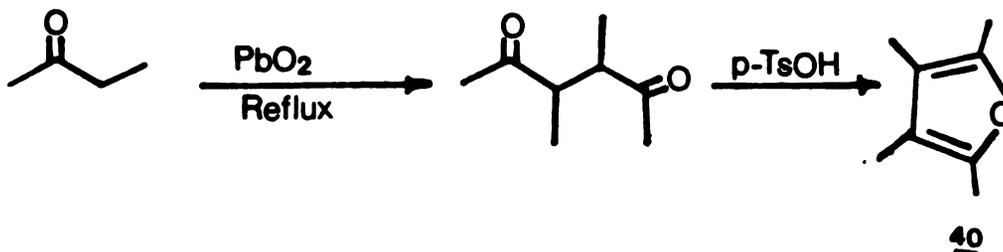
With the cyclic dienes--furans and pyrroles--the s-cis conformation is fixed for the diene, thus ensuring the right geometry for the transition state in the cycloaddition process. Furans were chosen in this work over



Scheme 7

pyrroles because they and their adducts are more stable to light and air.

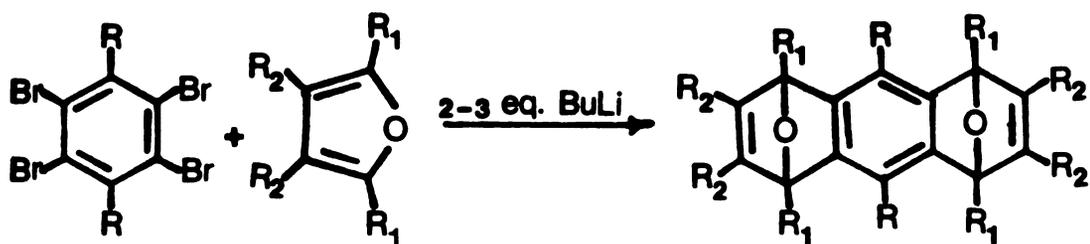
All the furans used were commercially available except tetramethylfuran 40²³ which was prepared by cyclizing 3,4-dimethylhexan-2,5-dione at reflux in benzene in the presence of catalytic amounts of p-toluenesulfonic acid



(p-TsOH). The dione was prepared by the radical coupling of 2-butanone with lead dioxide (PbO₂).

B. Development of Reaction Conditions for the Use of Tetrabromoarenes as Bisaryne Equivalents with Furans

We have found that tetrabromoarenes with 1,4-substituents function as better bisaryne equivalents than tetrafluoro-, tetrachloro- and mixed (F, Cl, Br) tetrahaloarenes thus allowing ready conversion of benzenes to acenes in two steps (the second step is the subject of the second part of this thesis). Treatment of the easily available tetrabromoarenes with two or more equivalents of n-BuLi in an anhydrous solvent (tetrahydrofuran, diethyl ether or toluene) at -78°C or 0°C in the presence of furans gave the bisadducts after quenching either at the reaction temperature or after allowing the mixture to warm to 25°C.



The yields of bisadducts depended on the reagents and reaction conditions and in general, represent a marked improvement over the results which Wittig¹⁶ obtained with 2,6-difluoro-3,5-dibromo-p-xylene 30. The success of this reaction with different para-disubstituted tetrabromoarenes shows that the method is broad in scope (Table 2). Our success in developing a new and effective method for the direct aromatization of the resulting endoxides, which is described in Part II of this thesis, demonstrates the general utility of this scheme (bisannelation with furans) for the synthesis of substituted, strained polynuclear aromatic compounds.

The yields given in Table 2 are for isolated products at optimized reaction conditions; the products consist of a mixture of syn and anti isomers. In the case of Entry 13, about 10% of the 9,10-dibromo analog of the adduct 54 was also present (observed from the mass spectrum of the product mixture).

The optimized procedure for bisannelation consisted of dissolution of 5 mmol of the tetrabromoarene in 300 mL

of the appropriate and anhydrous solvent containing up to ten molar equivalents of the appropriate furan. The bisaryne equivalents 34, 36 and 38 remained in solution, especially in THF, at this concentration even at -78°C . In the case of 33, 35, 37 and 39, some fraction of these reagents precipitated at the reaction temperature. After the slow addition of 2.5 to 3.0 molar equivalents of n-BuLi diluted with dry hexane under argon atmosphere (2 h), all reaction mixtures were either colored (reddish-brown or yellow) or milky white suspensions. The reaction mixture was stirred for a further 2 to 3 h at -78°C , quenched at the same temperature or allowed to warm to 25°C (6 h) before work up to isolate the product. Purification in most cases was achieved by chromatography and/or recrystallization.

TABLE 2

BISADDUCTS OF BISARYNE EQUIVALENTS

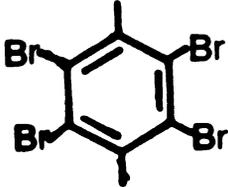
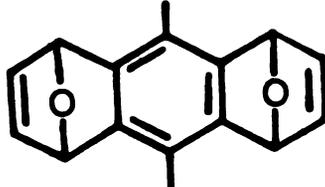
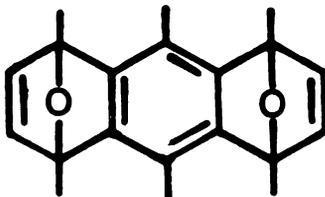
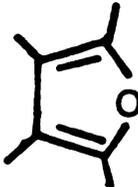
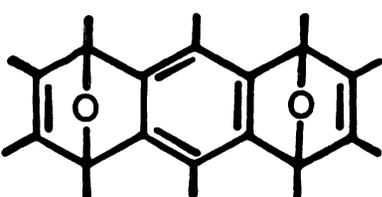
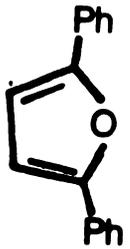
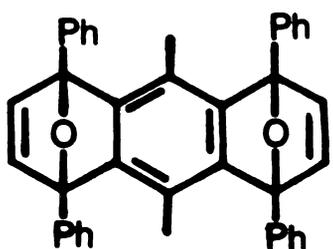
Entry	Bisaryne Equiv.	Diene	Bisadduct	Yield %
1	 <u>33</u>	 <u>16</u>	 <u>32</u> ¹⁶	89
2	<u>33</u>	 <u>41</u>	 <u>42</u>	76
3	<u>33</u>	 <u>40</u>	 <u>43</u>	78
4	<u>33</u>	 <u>44</u>	 <u>45</u>	5

TABLE 2 (Cont'd.)

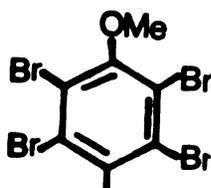
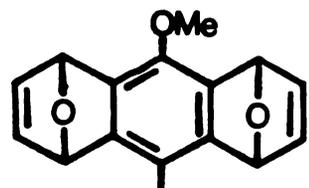
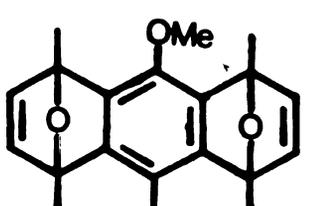
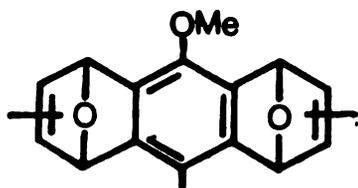
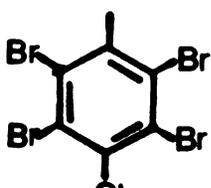
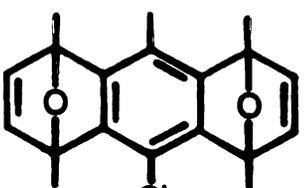
Entry	Bisaryne Equiv.	Diene	Bisadduct	Yield %
5	 <u>34</u>	<u>16</u>	 <u>46</u>	87
6	<u>34</u>	<u>41</u>	 <u>47</u>	71
7	<u>34</u>	 <u>48</u>	 <u>49</u>	73
8	 <u>35</u>	<u>41</u>	 <u>50</u>	16

TABLE 2 (Cont'd.)

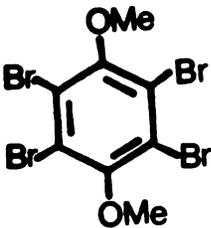
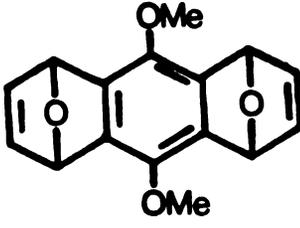
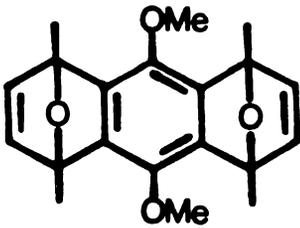
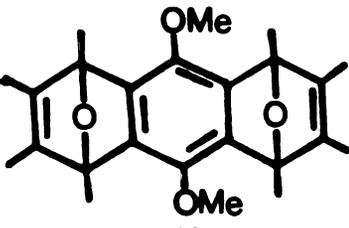
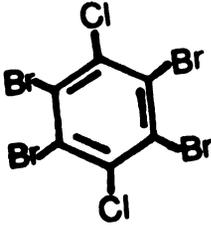
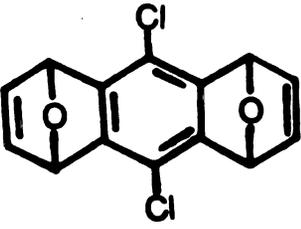
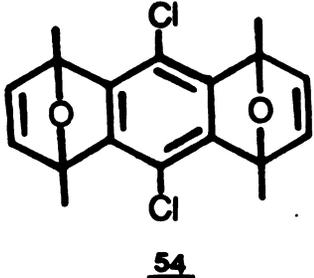
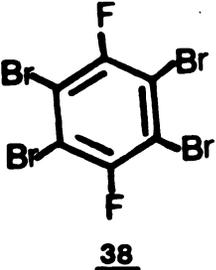
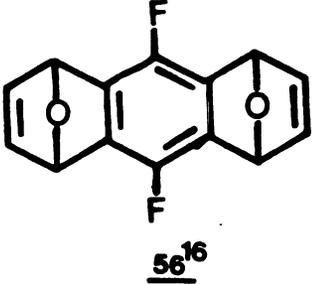
Entry	Bisaryne Equiv.	Diene	Bisadduct	Yield %
9	 <u>36</u>	<u>16</u>	 <u>28</u> ¹⁵	86
10	<u>36</u>	<u>41</u>	 <u>51</u>	73
11	<u>36</u>	<u>40</u>	 <u>52</u>	78
12	 <u>37</u>	<u>16</u>	 <u>53</u>	6

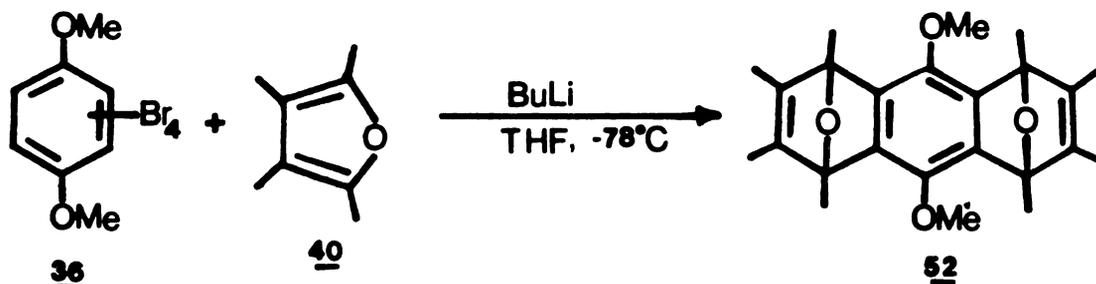
Table 2 (Cont'd.)

Entry	Bisaryne Equiv.	Diene	Bisadduct	Yield %
13	<u>37</u>	<u>41</u>		26
14		<u>16</u>		23

B(i). The Effect of Solubility of the Bisaryne Equivalent and Concentration of n -BuLi on Yields of Bisadducts

The solubility of the tetrabromoarenes and the concentration of n -BuLi have a marked influence on the yield and cleanness of the bisannulation reactions in all solvents. For example, when the volume of solvent and quantity of the bisaryne equivalent were such that the

tetrabromoarene precipitated to a large extent on cooling to -78°C , the product often contained some unreacted bisaryne equivalent even when excess $n\text{-BuLi}$ was used. This was particularly true when the reaction was quenched at -78°C after 2-3 h. The reaction of a 0.36 M slurry of 36 in dry THF containing three molar equivalents of tetramethylfuran 40 with two equivalents of undiluted $n\text{-BuLi}$ at -78°C gave 59% of the bisadduct 52 and about 20% of unreacted 36 was

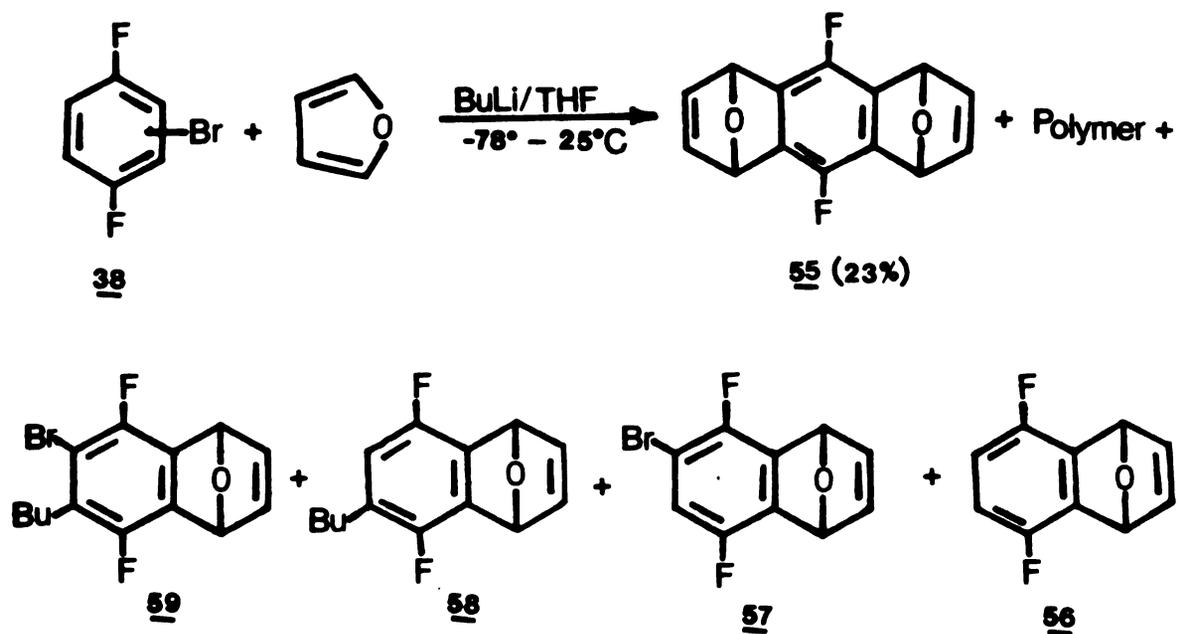


recovered. When the reaction was repeated using an 0.017 M solution of 36 in dry THF containing excess tetramethylfuran at -78°C with 2.5 equivalents of $n\text{-BuLi}$ diluted six times with hexane, the yield of 52 improved to 79%. In this case, the proton NMR spectrum of the crude product showed no trace of starting tetrabromoarene.

B(ii). Determination of the Best Solvent for Bisannulation with the Different Tetrabromoarenes

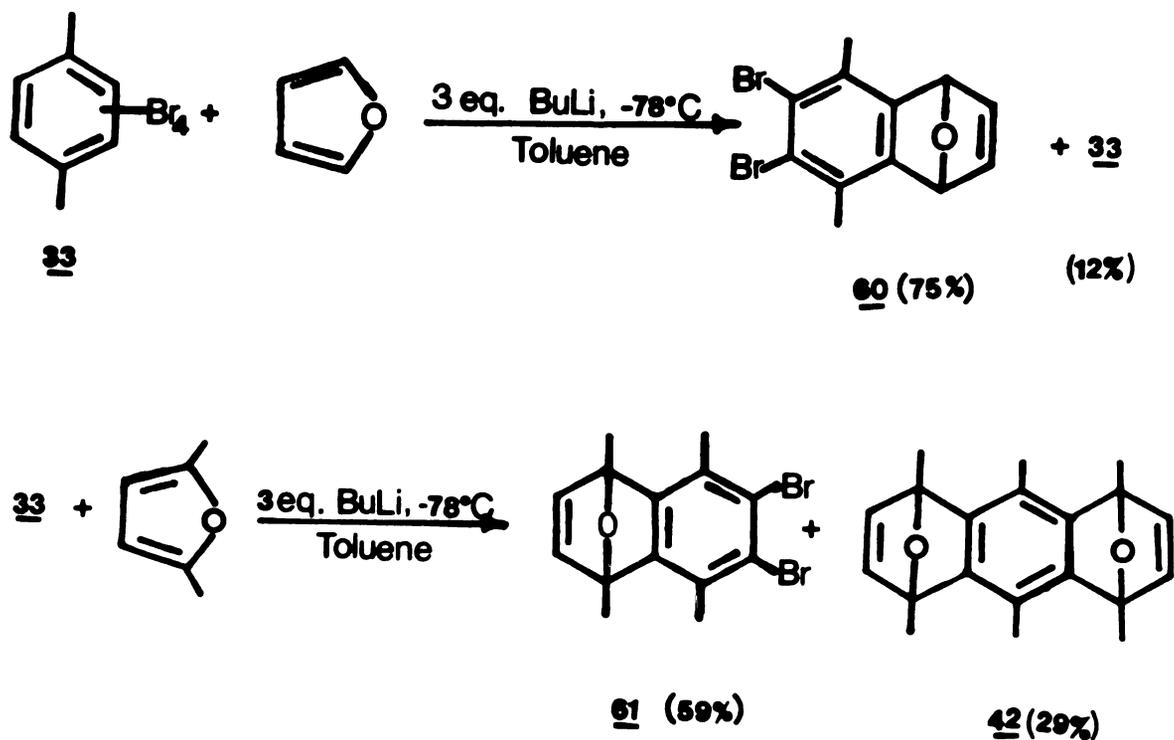
Tetrahydrofuran is often used as a solvent of choice for metalation and metal-halogen exchange reactions.²⁵ While

this may be so for this step of the bisannelation sequence, THF is not always the best solvent for the overall bisannelation. Reactions with different tetrabromoarenes in different solvents showed that THF worked well for bisannelations with 34 and 36. Even though the yields of bisadducts with 37 and 38 were low (cf. Table 2; Entries 12, 13 and 14), THF was the only solvent from which it was possible to isolate bisadducts of these bisaryne equivalents. Reactions with these tetrabromoarenes in ether and toluene, at various temperatures, gave oils and polymeric materials. The use of THF as reaction solvent is especially adequate if the bisannelation can be run effectively at -78°C , as is the case with 34 and 36. When reactions in THF have inevitably to be run at 0°C or allowed to warm to room temperature, as is the case with 37 and 38, the yield is often low due to reduction, butylation and polymerization. For example, when the tetrabromoarene 38 was reacted with n-BuLi in the presence of furan at -78°C and the reaction mixture was warmed to 25°C , the product consisted of the bisadduct 55, a mixture of monoadducts 56-59 (0.25 g) in the ratio 20 : 3 : 2 : 25 (gc determined) and polymeric substances (Scheme 8).



Scheme 8

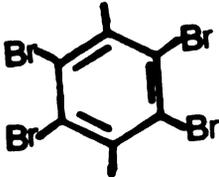
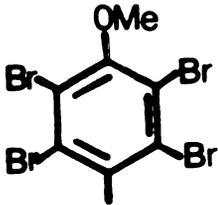
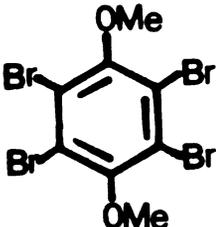
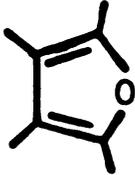
Toluene gave the best results for reactions with the bisaryne equivalent 33. The reaction mixture necessarily had to warm to room temperature for complete reaction but even then, these reactions were often clean. Stopping the reaction at -78°C after about 2 h or stirring led mainly to monoadduct. Even the use of three equivalents of *n*-BuLi at these conditions gave the monoadducts 60 and 61 as the major products in the attempted bisannelations of furan and 2,5-dimethylfuran to tetrabromo-*p*-xylene 33 (Scheme 9).



Scheme 9

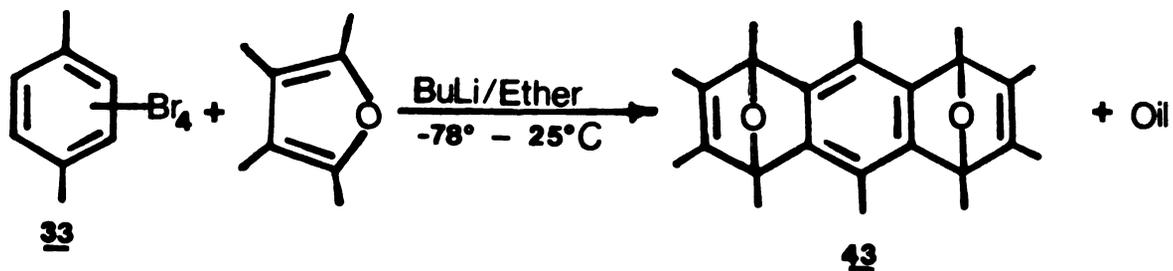
Table 3 summarizes the results of a comparative study on the influence of solvents on the yield of products which led to the identification of best solvents for bisannelations with the different tetrabromoarenes. The reaction conditions in each series differ only in the solvent. When a solvent is best for a specific bisaryne equivalent, this conclusion is valid independent of the furan used. This is illustrated by Series 1 and 2 in Table 3.

TABLE 3
 SOLVENT EFFECT ON THE YIELDS OF BISADDUCTS

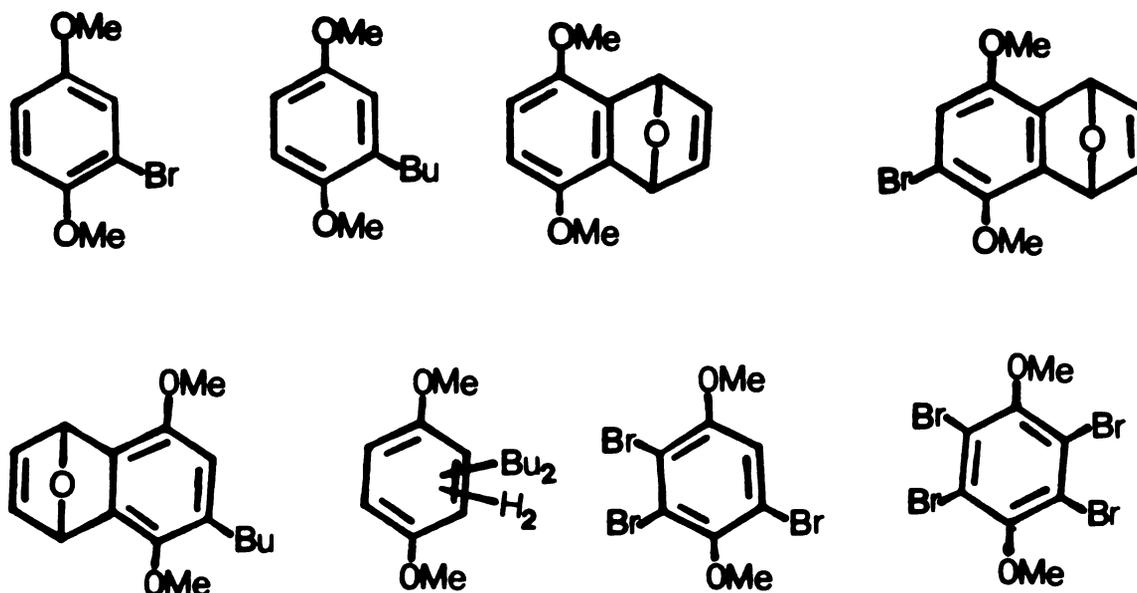
Series	Tetrabromoarene	Furan	Solvent	Bisadduct %
1	 <u>33</u>	 <u>16</u>	Toluene	72
			Ether	35
			THF	71
2	<u>33</u>	 <u>41</u>	Toluene	76
			Ether	63
			THF	68
3	 <u>34</u>	<u>16</u>	Toluene	0
			Ether	0
			THF	87
4	 <u>36</u>	 <u>40</u>	Ether	30
			THF	78

B(iii). Effect of Reaction Temperature on Bisadduct Yield

When some bisannellation reaction mixtures (especially the heterogeneous mixtures) were allowed to warm to room temperature before quenching, butylated monoadducts, butylated arenes, reduced monoadducts and reduced haloarenes were found as components of an oily fraction of the product mixture. In some cases, this oil accounted for a major fraction of the total weight of the products. For example, an 0.1 M slurry of 33 in dry ether containing two equivalents of tetramethyrfuran, when reacted with three equivalents of undiluted *n*-BuLi at -78°C followed by allowing to warm to 25°C ,



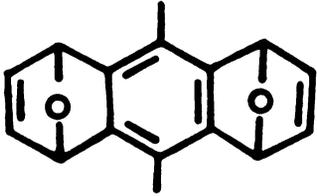
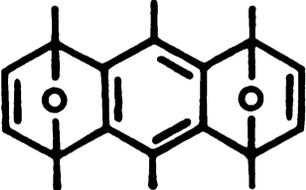
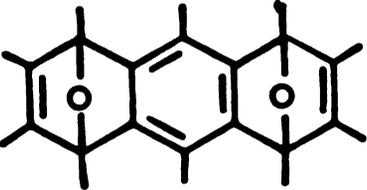
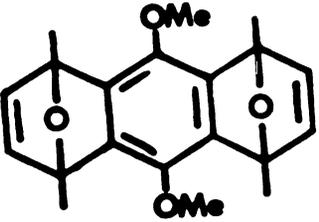
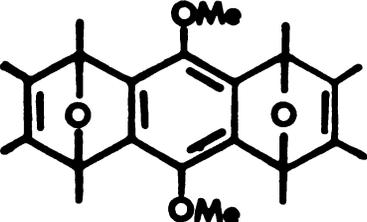
gave only 37% of 43. A large fraction of the product mixture was an oily mass. The GC-MS analysis of the oil from a similar preparation of the bisadduct 28 (cf. Table 2, Entry 9) led to the identification of the following components:



This result is similar to that obtained in the reaction of tetrabromo-*p*-difluorobenzene 38 with furan (cf. Scheme 8) when the reaction mixture was warmed to room temperature before workup. A much better yield and cleaner reaction is achieved, even with heterogeneous bisannellation reaction mixtures, if the reaction can be run effectively at -78°C . As an illustration, the bisannellation of tetrabromo-*p*-xylene 33 with tetramethylfuran gave a 78% yield of clean bisadduct 43 when the reaction was quenched at -78°C (the yield for the same reaction quenched at 25°C was 37%). Not all bisannellation reactions, however, can be run effectively at -78°C as illustrated by monoadduct formation in toluene (cf. Scheme 9) and formation of mainly 57 (cf. Scheme 8) when these reactions were run and quenched at that temperature. Most bisannellations can be effected in THF and diethyl ether at -78°C and Table 4

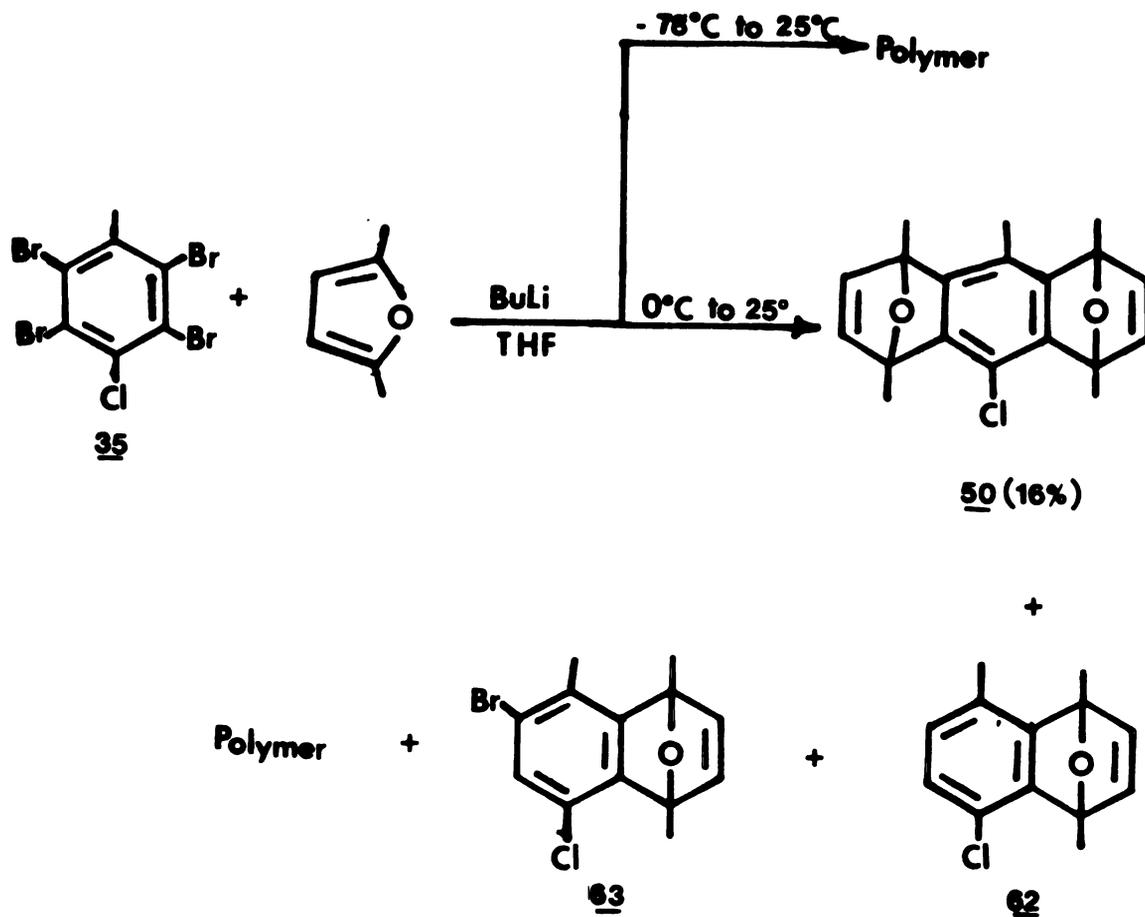
TABLE 4

YIELD OF BISADDUCTS AT DIFFERENT REACTION TEMPERATURES

Entry	Bisadduct	Solvent	Yield % at	
			-78°C	-78°C to 25°C
1	 <u>32</u>	THF	87	71
2	 <u>42</u>	Ether	72	63
3	 <u>43</u>	Ether	78	40
4	 <u>51</u>	THF	56	32
5	 <u>52</u>	Ether	30	22

illustrates the advantage of quenching the reactions at this temperature in these cases. All other factors except the reaction temperature were the same for the reactions in each entry in Table 4.

Some tetrabromoarenes did not give any adducts at all at -78°C . Tetrabromo-*p*-dimethoxybenzene 36 was totally recovered unreacted in toluene at this temperature. Bisaryne equivalents which contain additional electron-withdrawing groups on the aromatic ring such as 35 and 37 gave better yields (even though still low when compared to the yields obtained with the reactive tetrabromoarenes 33 and 36) when the reactions were run at 0°C . In these cases, the addition of *n*-BuLi at -78°C , followed by allowing the reaction mixture to warm to 25°C , led to intractable polymeric substances. For example, the tetrabromoarene 35, when reacted with *n*-BuLi in THF at -78°C in the presence of 2,5-dimethylfuran, followed by allowing the mixture to warm to room temperature, gave only polymer. The same reaction when run at 0°C and warmed to 25°C , gave the bisadduct 50 (16% isolated yield), a mixture of 50 and the monoadducts 62 and 63 (1 g) in the ratio 2 : 2 : 1 and some polymer (Scheme 10). Presumably, the lithio-derivative of 35 accumulated at -78°C because it could not decompose at this temperature to give benzyne. As the temperature rose to 25°C , benzyne was formed and reacted with the lithioarenes faster than it reacted with the diene.



Scheme 10

B(iv). Electronic Influence of Substituents on the Furans

Whereas furan and methyl-substituted furans gave good yields with the reactive tetrabromo-p-xylene 33 in toluene, 2,5-diphenylfuran 44 gave less than 5% of the bisadduct 45 and a lot of polymeric material. About 70% of the diene 44 was recovered unchanged. This poor result exemplifies the

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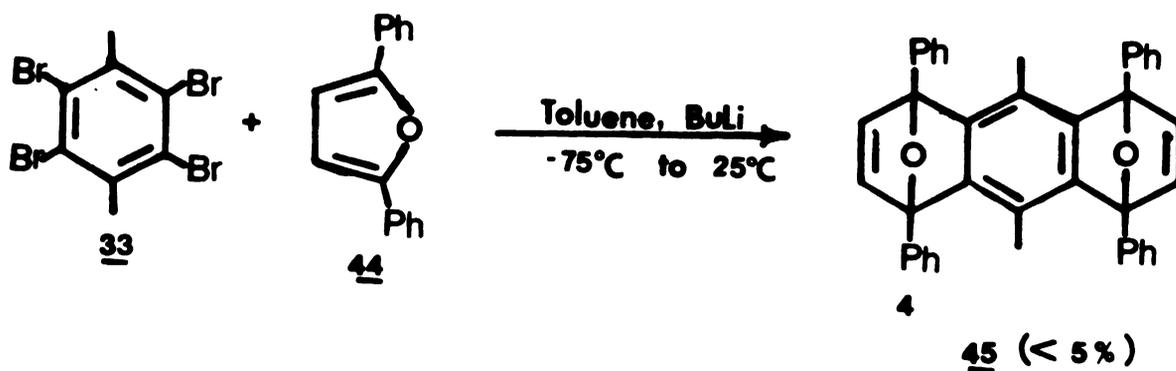
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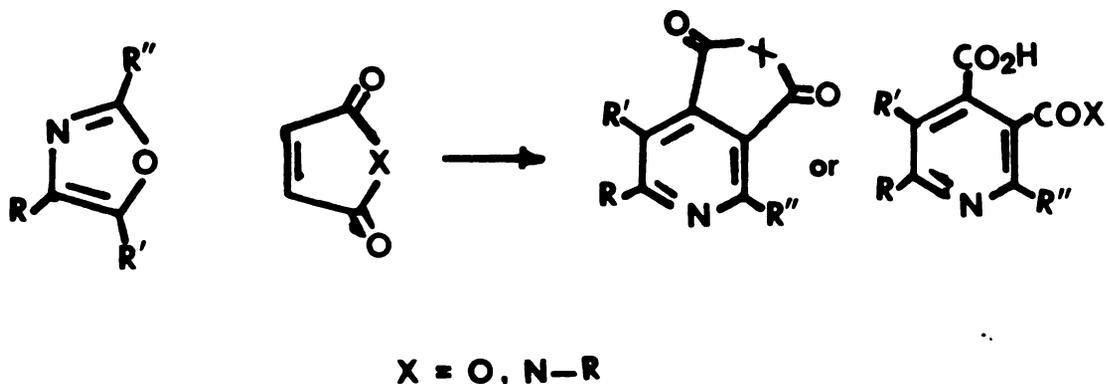
influence of substituents at the 2,5-positions of the furan ring on its reactivity as a diene. The reactive methyl-substituted furans trapped effectively the arynes generated from 33, resulting in the good yields, but with 44 the



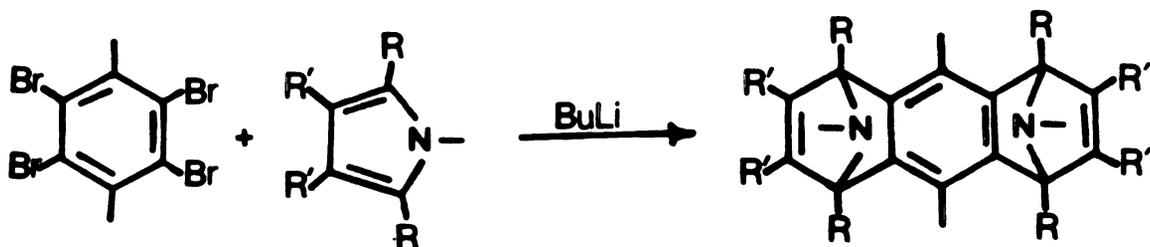
benzyne underwent other reactions faster than it could react with the diene. There is no doubt that this outcome was due to the reduced reactivity of the furan ring caused by the presence of the phenyl groups.

Similar results have been observed when similarly substituted pyrroles and oxazoles were used as dienes in cycloadditions.^{26,27} In fact, in these cases, no adducts were formed. Kondrat'eva and Khuan²⁶ found that the introduction of electron-withdrawing groups at the 2- and/or 5-positions of the oxazole ring did reduce the yield of adducts by more than 50% in the cycloaddition reaction of oxazoles with maleic anhydride or maleimide. They also showed that whereas oxazoles with one phenyl group at the 4-position and a methyl substituent at the 2- or 5-position gave good yields of adducts, the 2,5-diphenyl analog with no additional methyl substituents on the ring did not react. A steric

explanation for this failure was ruled out by the success of similar cycloadditions with the equally hindered 2-phenyl-5-ethoxyoxazole.



The results obtained by Lai²⁷ in bisannelations with phenyl-substituted pyrroles are also consistent with the findings of Kondrat'eva and Khuan. For example, he found that both 2,5-dimethyl-3,4-diphenyl-N-methylpyrrole and 2,5-diphenyl-3,4-dimethyl-N-methylpyrrole gave about the same yield of bisadducts with tetrabromo-p-xylene 33, but that the 2,5-diphenyl and tetraphenyl derivatives were completely unreactive.



$R = CH_3, R' = Ph; R = Ph, R' = CH_3$ Yield = 59%

$R = Ph, R' = H; R = R' = Ph$ Yield = 0%

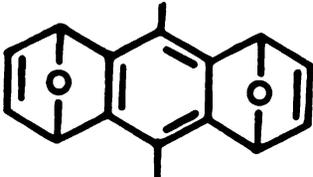
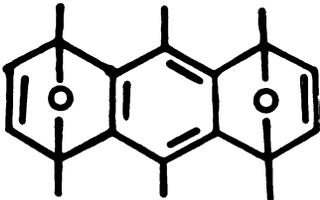
These results were interpreted to mean that electronic factors are more important than steric factors in cycloaddition reactions. Phenyl groups are electron-withdrawing and their effect at the 2- and/or 5-positions is to make the heterocycle more aromatic and less of a diene by inducing more delocalization of the lone pair of the hetero atom into the ring system. It appears from the work of Kondrat'eva²⁶ and Lai²⁷ that the presence of electron-releasing groups like methyl (by induction) and methoxyl (by resonance) compensates effectively for the delocalizing influence of an electron-withdrawing group like a phenyl substituent.

C. Factors Affecting the Distribution of the Syn and Anti Isomers of Bisadducts

The distribution of the syn and anti isomers of the bisadducts depended weakly, if at all, on the tetrabromoarenes and the furans. Nor did the solvent or reaction temperature affect the syn/anti ratios. These ratios were calculated from the 250 MHz proton NMR spectra of the crude product mixtures by integrating and averaging the ratios for all the clean signals (Table 5).

TABLE 5

EFFECT OF SOLVENT AND REACTION TEMPERATURE ON
THE RATIOS^{a,b} OF SYN AND ANTI ISOMERS

Series	Bisadduct	Solvent	Temperature	Ratio
1		Toluene	-78°C to 25°C	50 : 50
		THF	-78°C to 25°C	50 : 50
		THF	-78°C	47 : 53
		Ether	0°C	49 : 51
2		Toluene	-78°C to 25°C	42 : 58
		Ether	-78°C to 25°C	42 : 58
		THF	-78°C to 25°C	40 : 60
		Toluene	-78°C	44 : 56
		Ether	-78°C	41 : 59
		THF	-78°C	42 : 58

^aReactions were run at the same reagent concentrations.

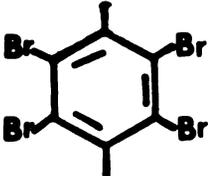
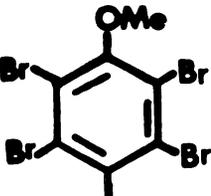
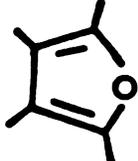
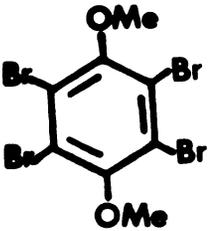
^bIt is not known which is the major isomer.

There did not seem to be any difference in the syn/anti ratios for 2,5-dimethylfuran and tetramethylfuran bisadducts (cf. Table 5, Series 2 and Table 6, Entries 3 and 4). This may be reasonable if steric and electronic effects of only the substituents at the 2,5-positions affect the geometry of the transition state and reactivity of the furan.

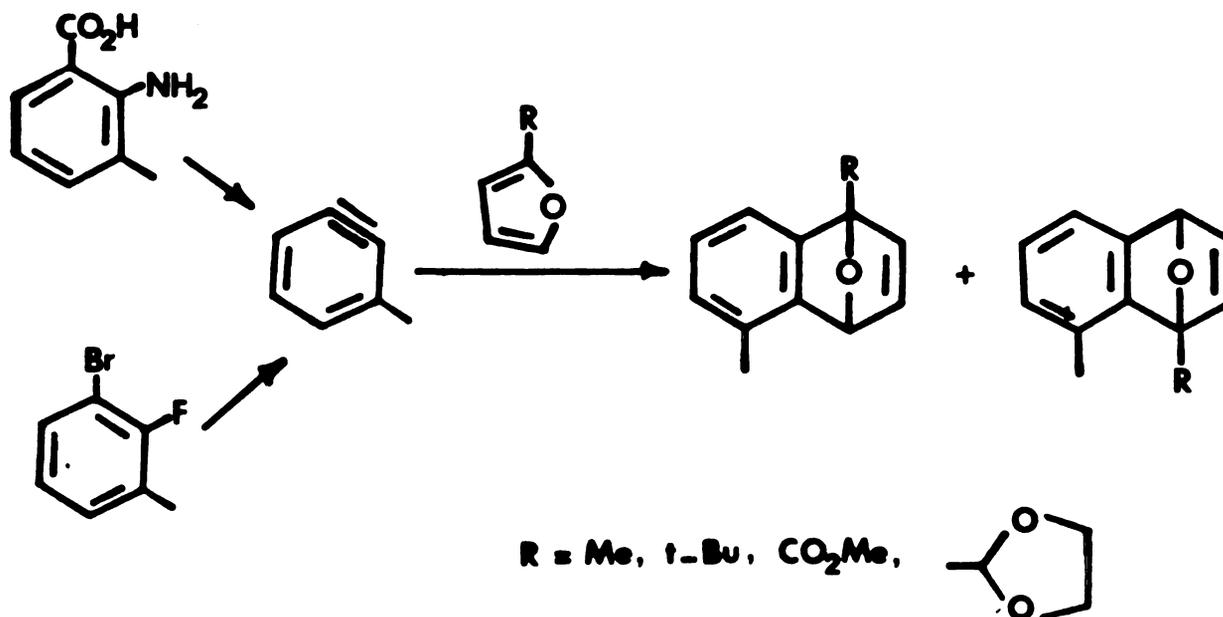
The ratios also depended more on the furan than on the bisaryne equivalent, because very similar ratios were obtained for the same furan with different tetrabromoarenes (Table 6). The reaction conditions leading to the results in Table 6 were the same for each type of furan.

TABLE 6

SYN/ANTI RATIOS OF BISADDDUCTS OF THE SAME FURAN
WITH DIFFERENT TETRABROMOARENES

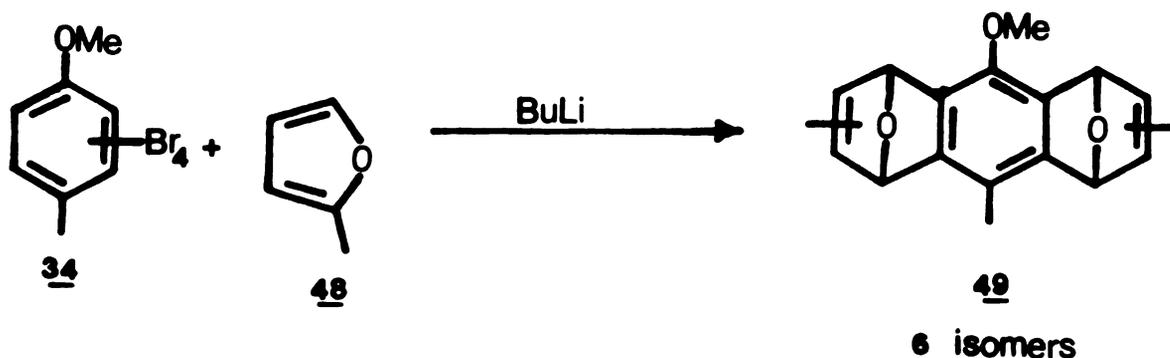
Entry	Tetrabromoarene	Furan	Isomer Ratio
1	 <u>33</u>	 <u>16</u>	50 : 50
2	 <u>34</u>	 <u>16</u>	50 : 50
3	 <u>33</u>	 <u>40</u>	36 : 64
4	 <u>36</u>	 <u>40</u>	40 : 60

Newman²⁸ has examined the steric effect on isomer ratios of the adducts formed from 2-substituted furans and 3-methylbenzyne. He found that the ratios varied from 42/58 for 2-methylfuran to 36/64 for 2-(1,3-dioxolan-2-yl)-



furan--a very small variation for such a change in steric bulk--and concluded that the ratios could be assumed to be the same within the limits of experimental error. The ratios of regio-isomers obtained by Newman are similar to the values in Table 5, Series 2 and in Table 6, Entries 4 and 4 for syn/anti isomers of bisadducts. These ratios, which also could be taken to be the same within the limits of experimental error, are consistent with the conclusion that steric constraints are only of minor consequence in determining isomer ratios. It also implies that the

annelations do in fact involve benzyne intermediates. In an attempt to confirm this conclusion further, the isomer ratio in the bisannelation of methyl tetrabromo-*p*-cresolate 34 with 2-methylfuran 48 was sought. Three regio-isomers with respect to the substituents, each having syn and anti

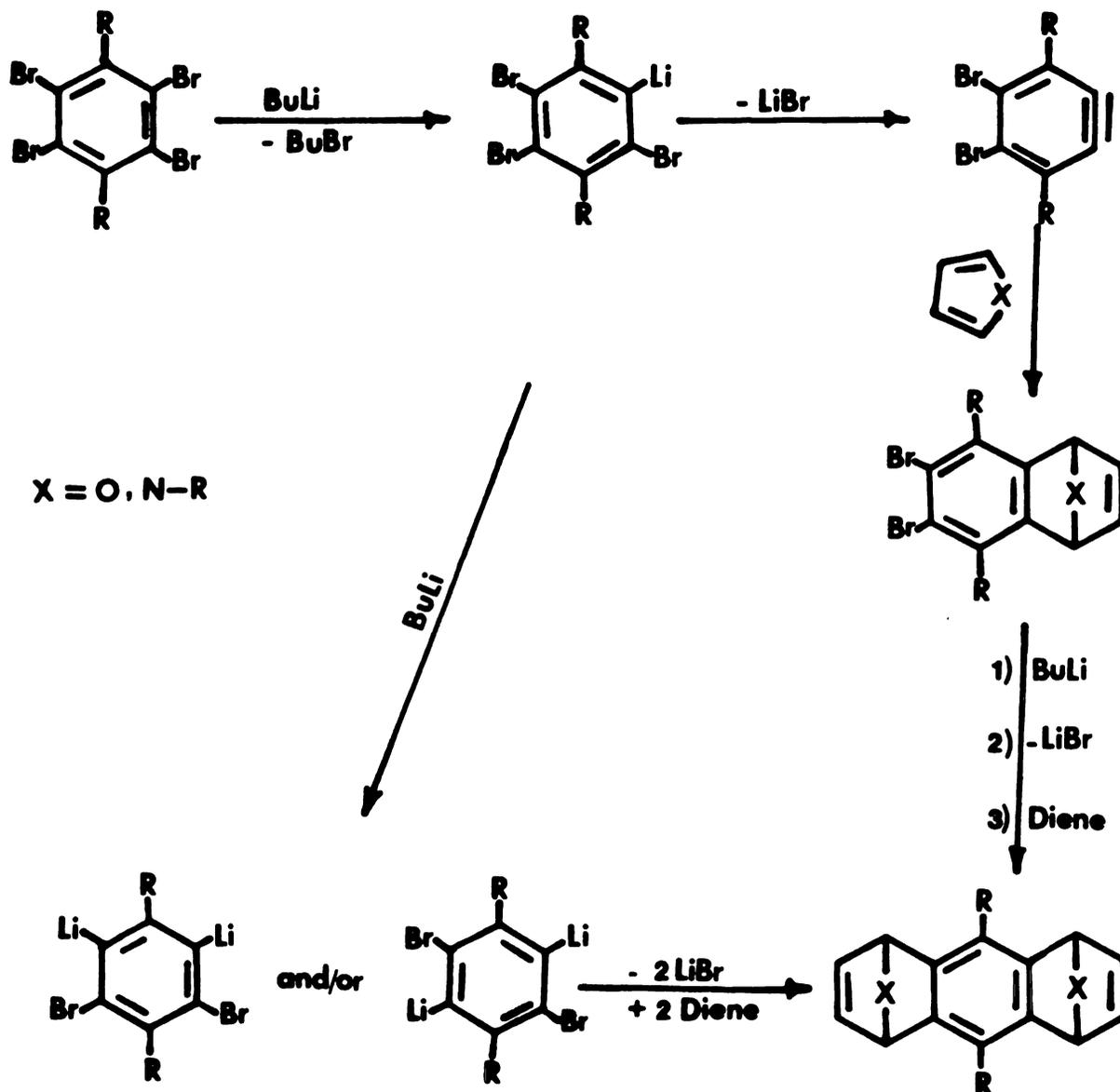


stereoisomers due to the orientation of the endoxide oxygens, were expected. Unfortunately, the crude product mixture did not give clean proton NMR signals to allow the identification of the number of isomers and their ratio. The small differences between the isomer ratios of the adducts of substituted furans and the small divergence of these values from the 50/50 ratio observed for furan itself may be primarily due to the small differences in the electronic effects of these substituents.

D. Mechanism of Bisannelation

Wittig¹⁶ concluded from the isolation of the mono-adduct 31 (cf. page 12) in the bisannelation of 2,6-difluoro-

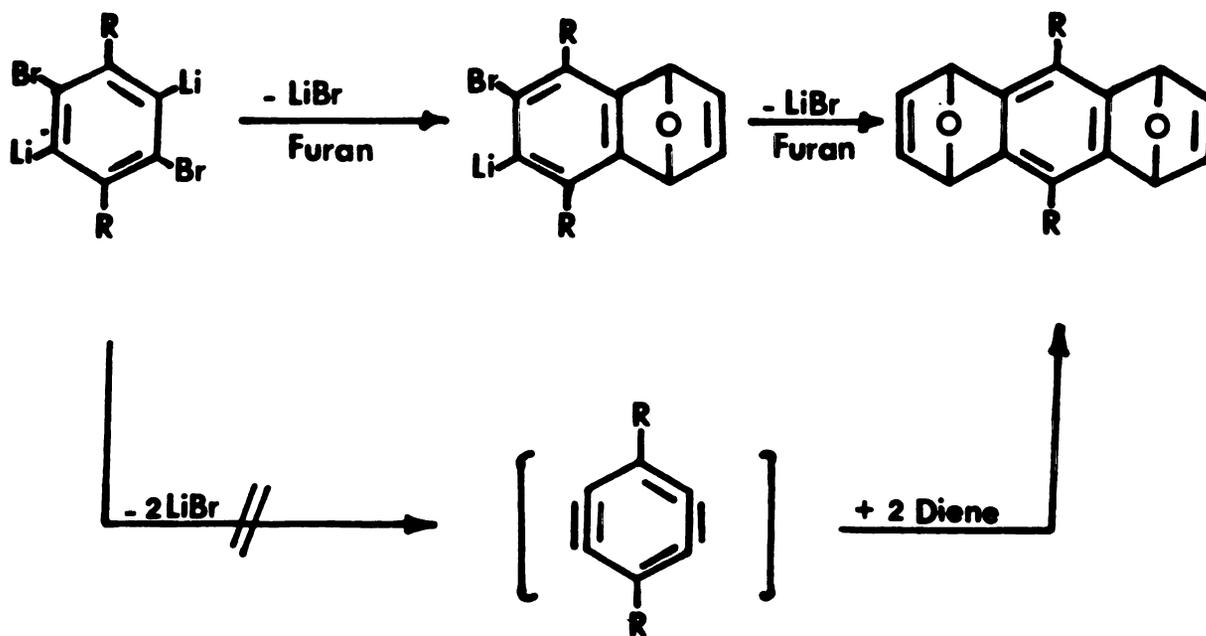
3,5-dibromo-p-xylene 30 with furan using magnesium, that the formation of the bisadduct 32 was a stepwise process. But the absence of the monoadduct when n-BuLi was substituted for magnesium requires that the possibility of bismetalation be considered. Therefore it was of interest, after realizing good yields and establishing the generality of this bisannelation reaction, to investigate the mechanism of the process. The possible reaction pathways under consideration are summarized in Scheme 11.



Scheme 11

Bisarynes have been postulated as intermediates in certain mass spectral fragmentations and also to rationalize

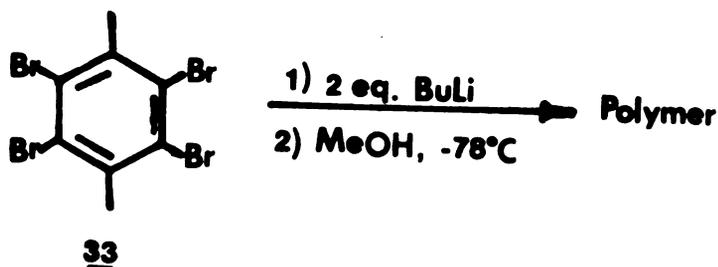
products from the copolyrolysis of benzene with pyromellitic dianhydride²⁹ but because of their high energy, they were not expected to be intermediates in bisannelation with tetrabromoarenes. Consequently, the inquiry was formulated in terms of determining whether monolithio-and/or dilithio-derivatives of the bisaryne equivalents were involved. If a dilithio-arene was formed, it was anticipated that benzyne would be generated from it one after the other and not



Scheme 12

simultaneously (Scheme 12), although the design of an experiment to test between these alternatives is exceedingly difficult.

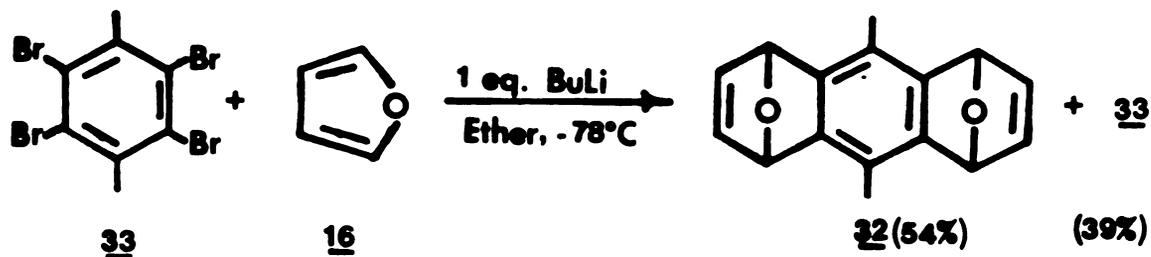
An attempt to intercept the dilithio-intermediate of the tetrabromoarene 33 at -78°C in THF was unsuccessful. The product was a high melting point polymer which was



presumably formed prior to quenching with methanol. We reasoned that the lithio-derivative might be so reactive at -78°C that it could not be intercepted by quenching. A similar problem was encountered by Wittig³⁰ in the lithiation of *o*-dihaloarenes and was overcome by Gilman³¹ by utilizing lower temperatures. We therefore lowered the reaction temperature to -100°C but recovered the tetrabromoarenes unchanged on quenching at the same temperature, probably due to their very low solubility at this temperature.

Monoadducts were observed in the GC-MS analysis of the oil from reactions of some bisaryne equivalents like tetrabromo-*p*-dimethoxybenzene 36, tetrabromo-*p*-difluorobenzene 38 and tetrabromo-*p*-chlorotoluene 35 with furan (cf. page 32, and Schemes 8 and 10). The formation of a monoadduct when only one molar equivalent of *n*-BuLi is used could furnish another strategy for verifying whether or not bisadducts are formed in a stepwise manner.

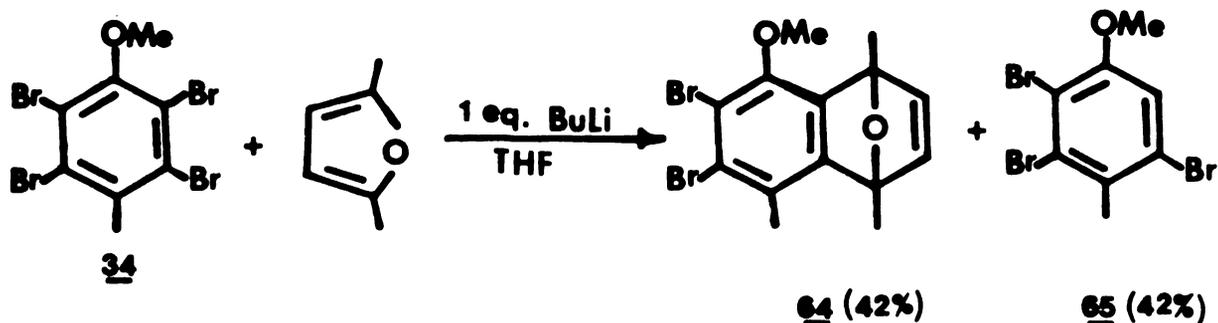
Treatment of the tetrabromoarene 33 in ether containing excess furan with one equivalent of n-BuLi at -78°C gave 54% of the bisadduct 32 and 39% of the starting 33



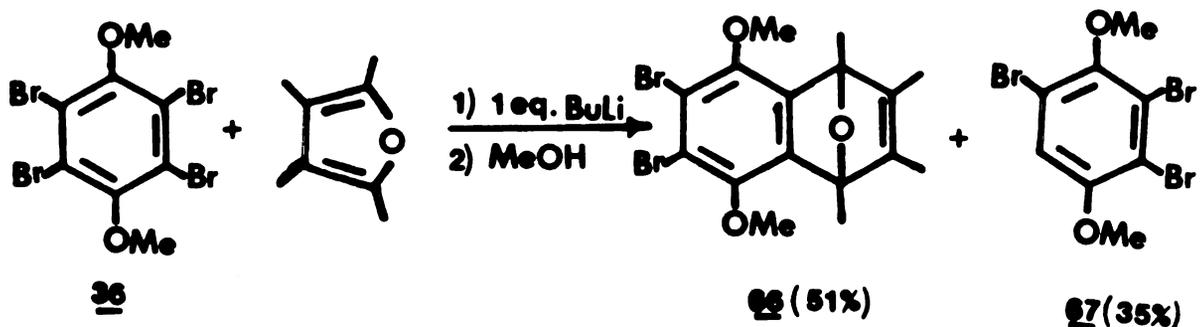
was recovered. These preliminary results might be interpreted as consistent with the intermediacy of dilithio-arenes but a stepwise metalation-cycloaddition is still a possible explanation of the observations if the monoadduct is metalated faster than the tetrabromoarene. The presumed faster metalation of the monoadduct may be related to its greater solubility. It was not, however, convenient to check this postulate on the influence of solubility because of the very low solubility of tetrabromo-p-xylene 33 in THF at -78°C (1.025 g, 2.4 mmol/L).

A more soluble tetrabromoarene was therefore sought and found in the methyl ether of tetrabromo-p-cresol 34. Ten mmoles (10 mmol) of this bisaryne equivalent remained in solution in 100 mL of THF at -78°C . Treatment of this tetrabromoarene with one equivalent of n-BuLi gave the first

isolated monoadduct (64) from a tetrahalo-bisaryne equivalent (Wittig¹⁶ prepared a monoadduct from a similar substrate using magnesium but found only the bisadduct with *n*-BuLi). This result confirmed the importance of solubility on the



formation and isolation of monoadducts. Later, it was also found that 5 mmol of 36 remained in solution in 300 mL of THF at -78°C . On treatment of this solution with one equivalent of *n*-BuLi at this temperature, 86% of monolithiation products (66 and 67) was obtained.



It follows therefore, that for tetrabromoarenes with electron donating groups like methyl (by induction) and

methoxyl (by resonance), the bisannelation process is stepwise. This conclusion was also proved by an independent method.³² For these bisaryne equivalents, the monolithio-derivatives are so reactive that they cannot be intercepted at -78°C by electrophiles that are not present in the reaction mixture before the metalation.

The change of solvent from the polar THF and diethyl ether to the less polar toluene ensured the successful preparation of monoadducts from most tetrabromoarenes, even when they precipitated from solution on cooling to -78°C. Although the bisaryne equivalents are still less soluble than the monoadducts in toluene, their solubility is slightly better (1.29 g, 3.06 mmol/L for tetrabromo-p-xylene 33) than in THF (1.025 g, 2.4 mmol/L for 33) and ether. This enhanced solubility, in conjunction with their higher reactivity towards metal-halogen exchange, favors the metalation of the tetrabromoarenes in the presence of the monoadducts. Table 7 shows that various monoadducts can be prepared in this way. The ability to prepare such monoadducts makes it possible to synthesize unsymmetrical bisadducts which could lead to unsymmetrically substituted acenes (Scheme 12). Hence the monoadduct 64 formed from the bisaryne equivalent 34 and 2,5-dimethylfuran may undergo a second aryne cycloaddition with a differently substituted cyclic diene to give the unsymmetrical bisadduct 68. Aromatization of this bisadduct would give the unsymmetrically substituted anthracene 69.

TABLE 7

MONOADDUCTS OF BISARYNE EQUIVALENTS (PREPARED IN TOLUENE)

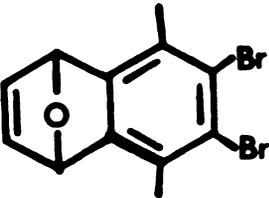
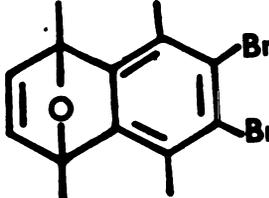
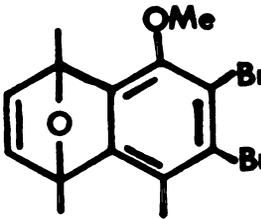
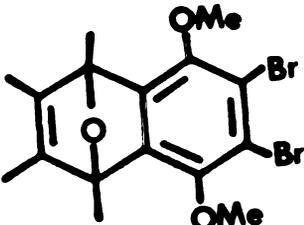
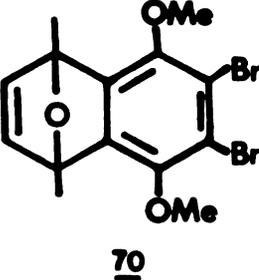
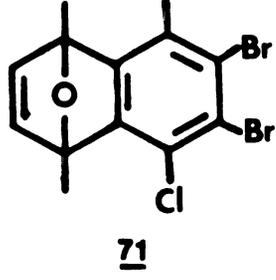
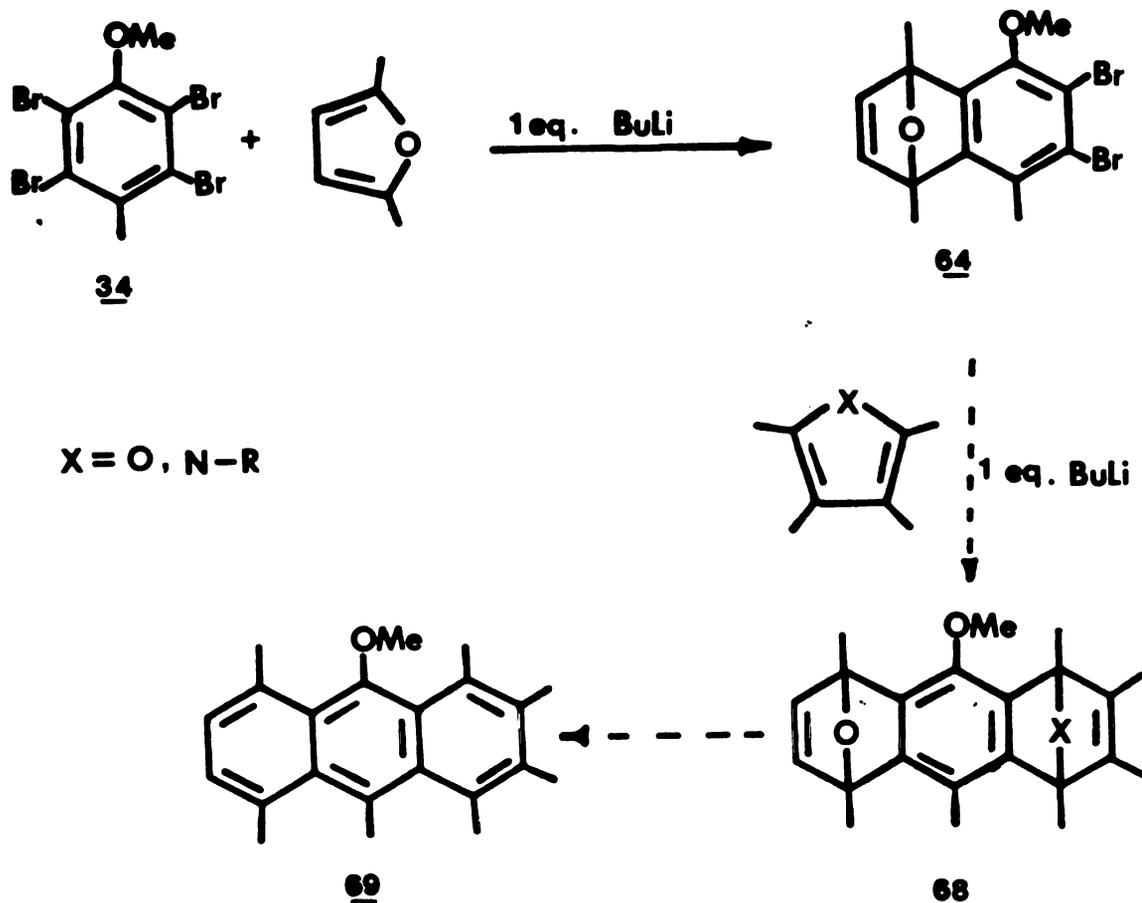
Entry	Monoadduct	Yield ^a %
1	 <u>60</u>	75
2	 <u>61</u>	59
3	 <u>64</u>	53
4	 <u>66</u>	51

TABLE 7 (Cont'd.)

Entry	Monoadduct	Yield ^a %
5	 <u>70</u>	44
6	 <u>71</u>	23

^anot optimized.

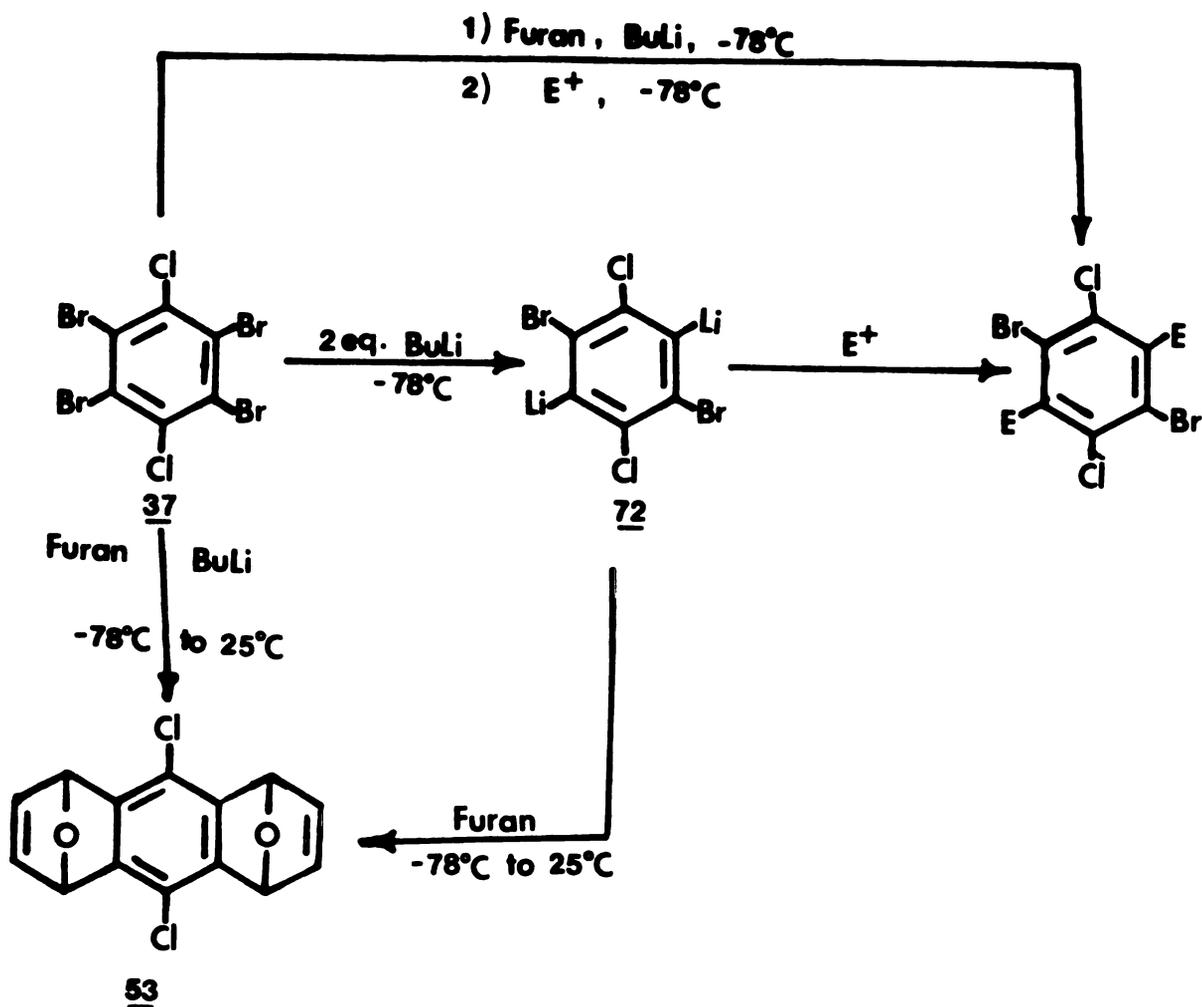


Scheme 12

The identification of the substituent types on the tetrabromoarenes that permit stepwise bisannellation does not rule out the alternative (bislithiation) pathway for other substituent types. Therefore an examination of bisadduct formation by bisaryne equivalents with 1,4-substituents which have the opposite electronic effect to those of methyl and methoxyl groups was undertaken. The inability to intercept the monolithio-intermediates of the tetrabromoarenes 33, 34 and 36 even at -78°C was due to their propensity to lose

LiBr. A bisaryne equivalent that could form a stable dilithio-arene must have substituents which stabilize the monolithio-derivative at -78°C . Earlier work on the metalation of o-dibromoarenes show that electron-withdrawing groups stabilize o-halolithio-arenes.³³

A study of the bisannelation of tetrabromo-p-dihalo-benzenes with furans showed that the formation of bisadduct in these cases occurred through dilithio-intermediates. For example, when tetrabromo-p-dichlorobenzene 37 was treated with two equivalents of n-BuLi at -78°C , the dilithio-derivative 72 was formed; it could be intercepted with different electrophiles. In the presence of furan, no adduct was obtained when the reaction mixture was quenched at -78°C with electrophile (E). The isolated product was due to electrophilic capture of the dilithio-arene 72. If the reaction mixture was warmed to room temperature before quenching, the bisadduct 53 was obtained. Bisadduct 53 was also formed if, after the addition of n-BuLi and stirring for a further 2 h at -78°C , furan was added and the mixture was then warmed to 25°C (Scheme 13). These observations indicate that the dilithio-arene 72 is long lived at -78°C .

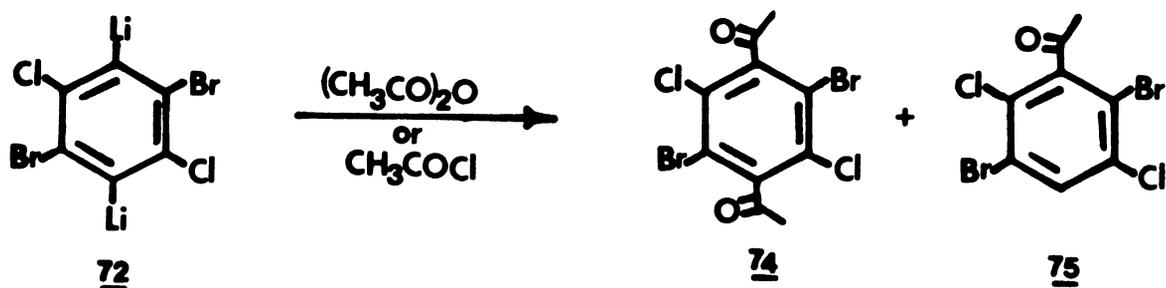


Scheme 13

It can be inferred at this point that the pathway to bisannelation preferred by a bisaryne equivalent depends on the substituents.

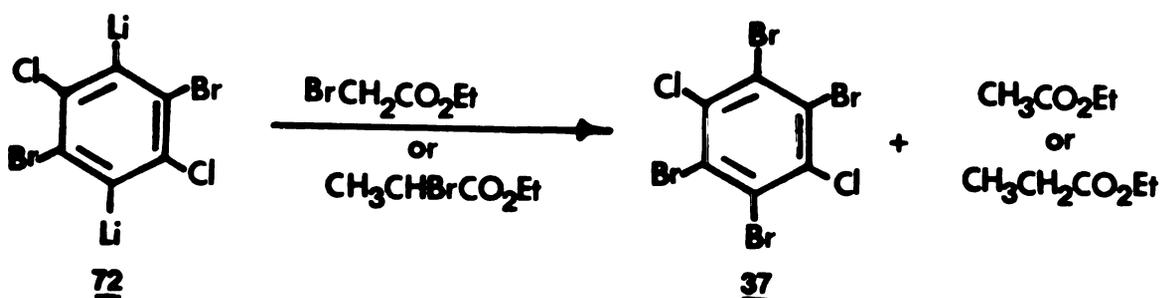
The interception of the stable dilithio-compounds of some tetrabromoarenes at low temperatures with different electrophiles turned out to provide an easy route for the

introduction of unusual substituents on the benzene ring (Table 8). In addition to the expected diacetyl product 74 1-acetyl-2,5-dibromo-3,6-dichlorobenzene 75 (12%) was obtained when acetic anhydride was used to intercept 72.



When acetyl chloride was used, 75 was the major product (24%) and 74 was a minor product (7%).

The use of α -bromoesters as electrophiles resulted in recovery of the starting material (tetrabromo-*p*-dichlorobenzene 37) because the esters afforded bromonium ion as the



electrophile (i.e., they reacted by displacement on bromine rather than on carbon).

Diethyl sulfate could not be used to replace the bromine atoms of tetrabromoarenes with ethyl groups in this

TABLE 8

REACTION OF DILITHIO-ARENES WITH ELECTROPHILES

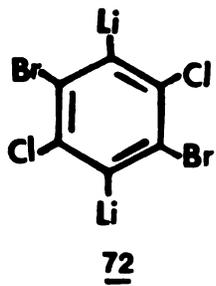
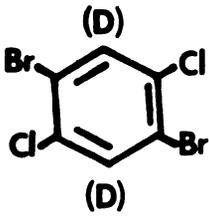
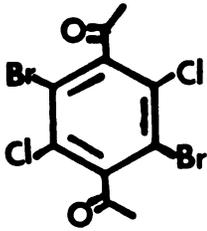
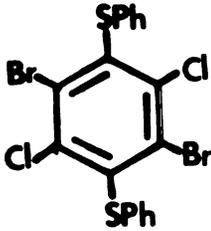
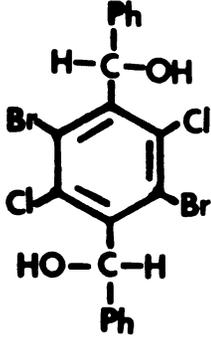
Entry	Dilithio-arene	Electrophile	Product (%)
1	 <p style="text-align: center;"><u>72</u></p>	MeOH (D)	 <p style="text-align: center;"><u>73</u> (61; 64)</p>
2	<u>72</u>	(CH ₃ CO) ₂ O or CH ₃ COCl	 <p style="text-align: center;"><u>74</u> (30)</p>
3	<u>72</u>	PhSSPh	 <p style="text-align: center;"><u>76</u> (39)</p>
4	<u>72</u>	PhCHO	 <p style="text-align: center;"><u>77</u> (33)</p>

TABLE 8 (Cont'd.)

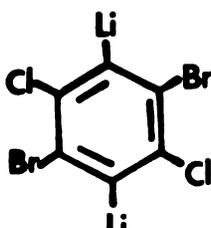
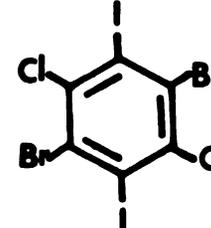
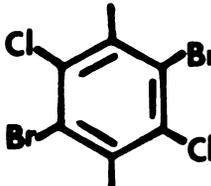
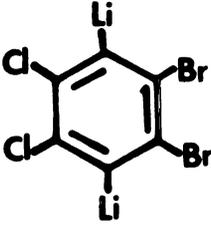
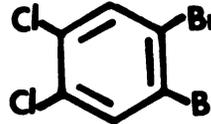
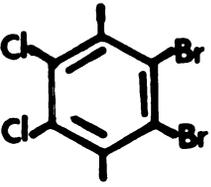
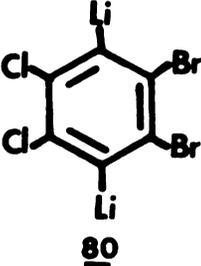
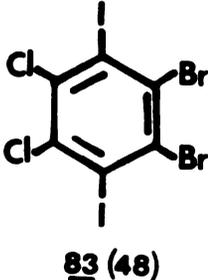
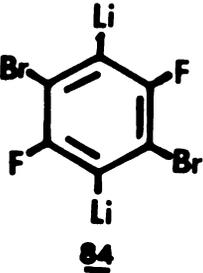
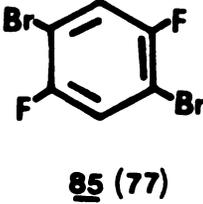
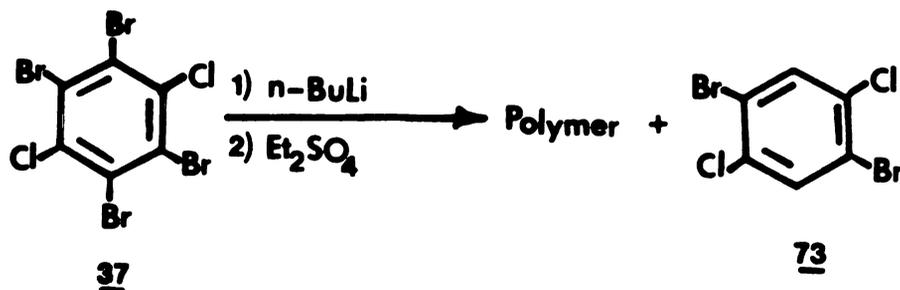
Entry	Dilithio-arene	Electrophile	Product (%)
5	 <u>72</u>	I_2	 <u>78</u> (72)
6	<u>72</u>	Me_2SO_4	 <u>79</u> (97)
7	 <u>80</u>	$MeOH$	 <u>81</u> (55)
8	<u>80</u>	Me_2SO_4	 <u>82</u> (93)

TABLE 8 (Cont'd.)

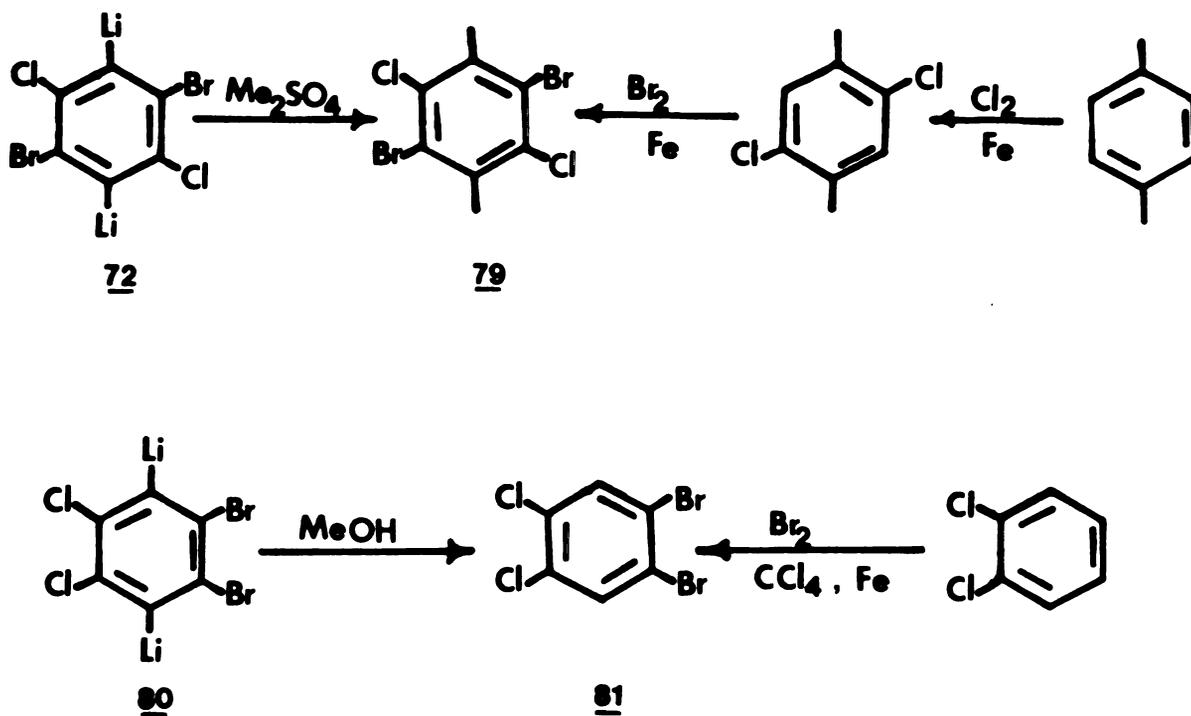
Entry	Dilithio-arene	Electrophile	Product (%)
9	 <u>80</u>	I ₂	 <u>83</u> (48)
10	 <u>84</u>	MeOH	 <u>85</u> (77)

way. For example, the attempted interception of the dilithio-derivative of 37 with diethyl sulfate led mainly to a polymer and trace of 73. Both ethyl iodide and ethyl



bromide were also ineffective for introducing ethyl groups on the aromatic ring by this method.

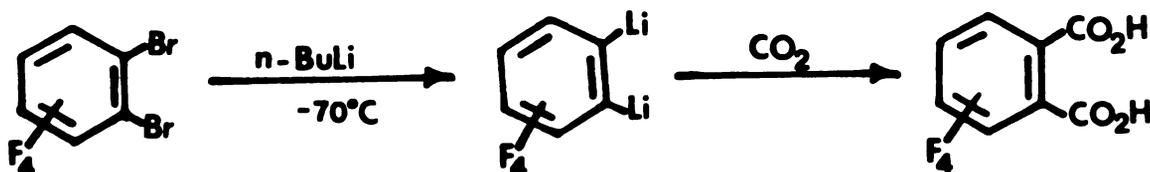
Bislithiation was exclusively para in all cases. Structural proof of this orientation was afforded by the identity of the methanol and dimethyl sulfate intercepted products of some of the dilithio-arenes with samples prepared by independent methods (Scheme 14a,b).



Scheme 14a,b

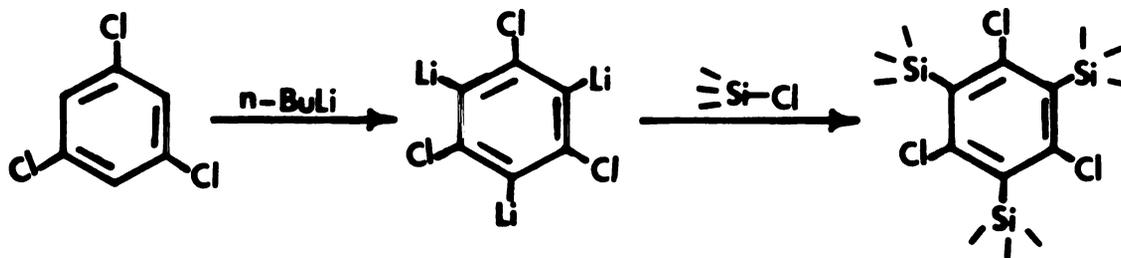
E. Attempts at Trilithiation of Tetrabromoarenes

Dilithiation and trilithiation of arenes have previously been realized with polyfluoro- and polychloro-benzenes only by either multiple metalations,^{37,38} metal-halogen exchange³⁹ or both.⁴⁰ The *o*-dilithio-derivative of *o*-dibromotetrafluorobenzene was intercepted in 90% yield by carboxylation at -70°C .³⁹ *o*-Dilithiation was obviously possible due to the stabilizing influence of the fluorine



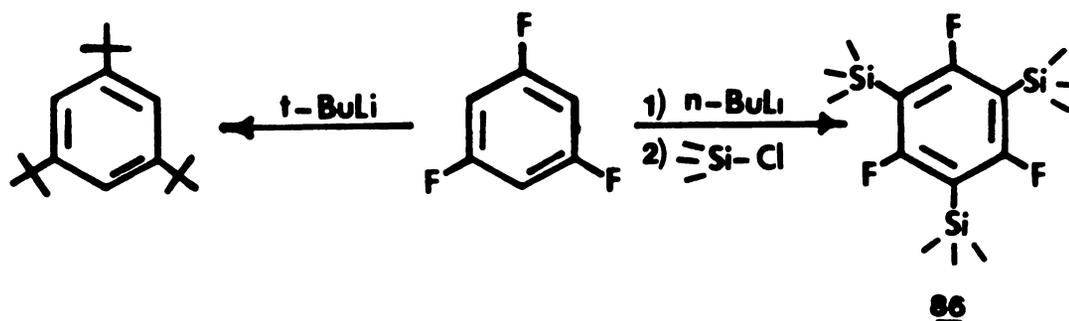
atoms on the anionic centers.

A trilithio-arene was prepared by metalation of 1,3,5-trichlorobenzene with three equivalents of $n\text{-BuLi}$. The



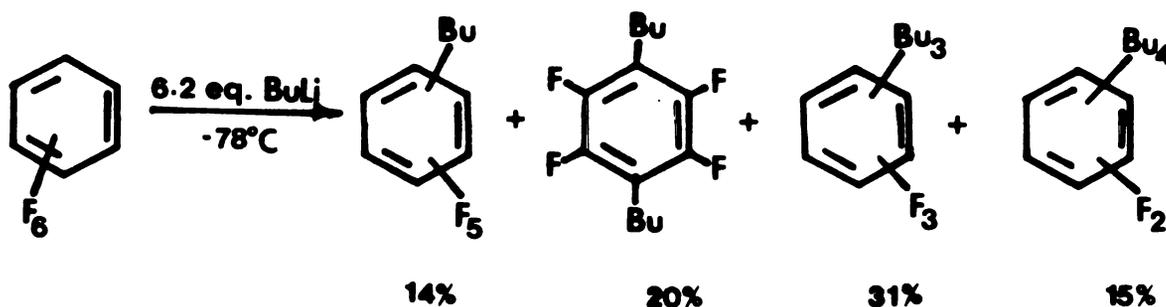
trilithio-derivative was intercepted with trimethylsilyl chloride.³⁷

With 1,3,5-trifluorobenzene, the product depended on the alkyl lithium used.⁴¹ Whereas *n*-BuLi effected metalations



leading to the tris-trimethylsilylbenzene **86**, *t*-BuLi caused substitution reactions, to give 1,3,5-tri-*t*-butylbenzene.

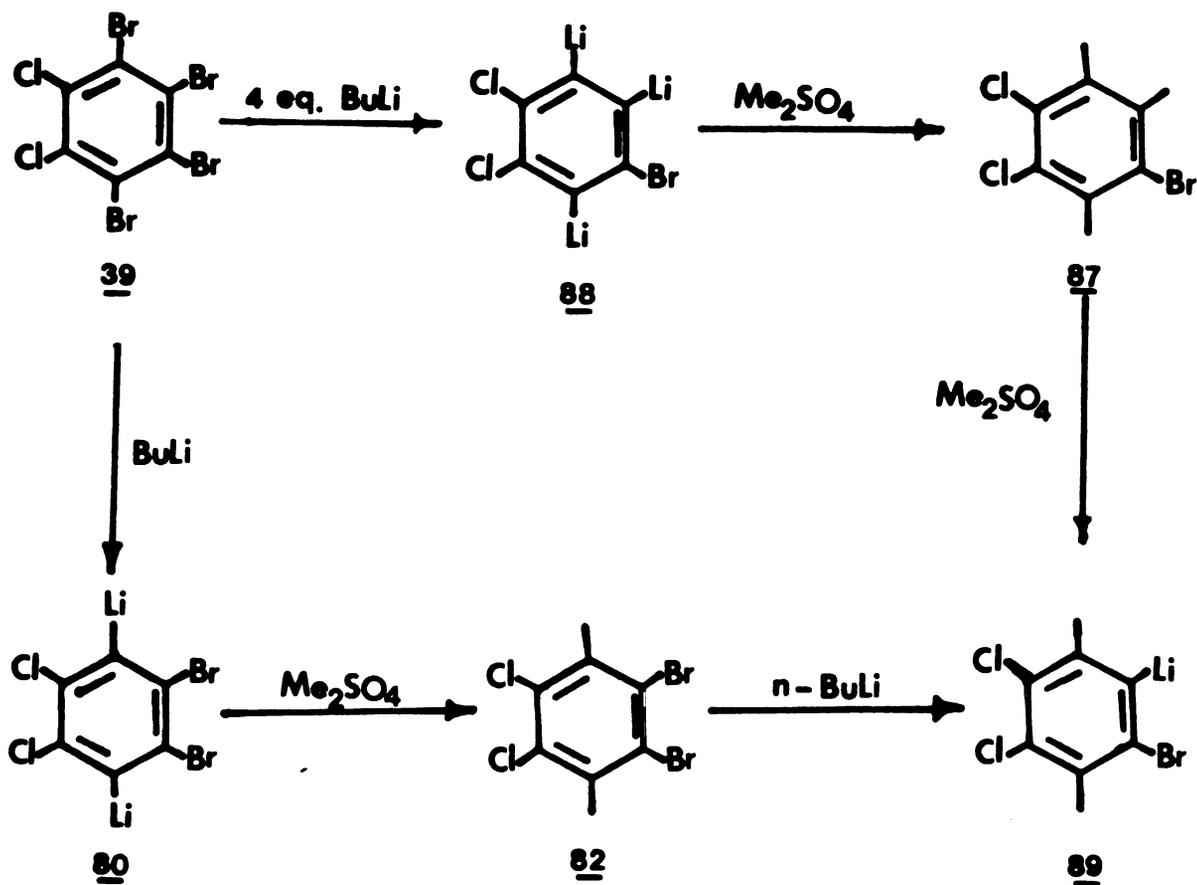
The formation of mono-, di-, tri- and tetra-*n*-butylbenzene in the attempted polymetalation of hexafluorobenzene with 6.2 equivalents of *n*-BuLi⁴² was not a case of



polylithiation but rather of nucleophilic aromatic substitution. With six strong electron-withdrawing groups like fluorine, the electron deficiency created on the ring is high enough to make substitution the preferred reaction.

We have shown that tetrabromoarenes with other electron withdrawing groups do give stable dilithio-derivatives by metal-halogen exchange (cf. Table 8, p. 57). There is no reported trilithiation of arenes by metal-halogen exchange. It was therefore of interest to attempt the introduction of more than two lithium groups on the same ring by this method, using tetrabromoarenes.

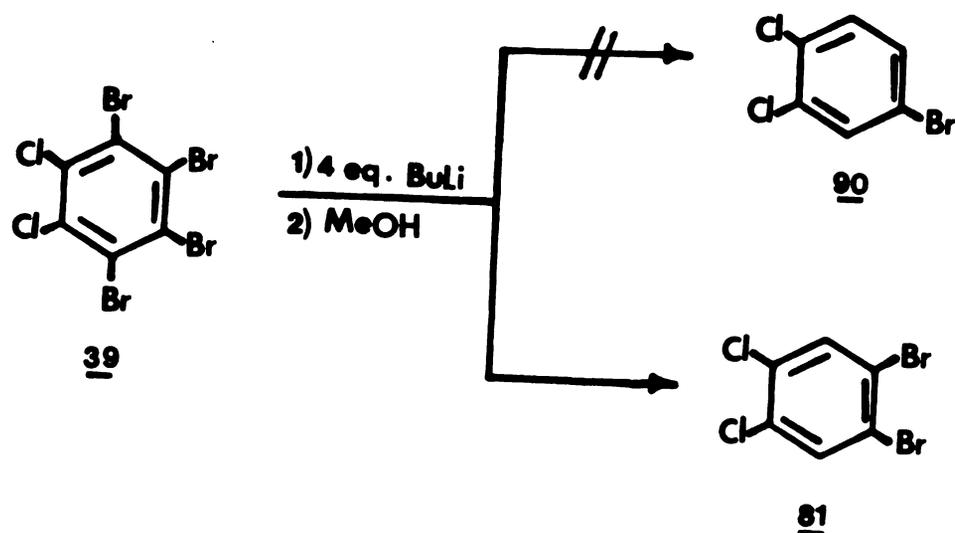
Reaction of the tetrabromoarene 39 with four equivalents of n-BuLi in toluene and interception of the lithiated species with dimethyl sulfate gave the pseudo-cumene 87 in 55% yield (Scheme 15). As proposed in the Scheme, this product could arise either from the trilithio-



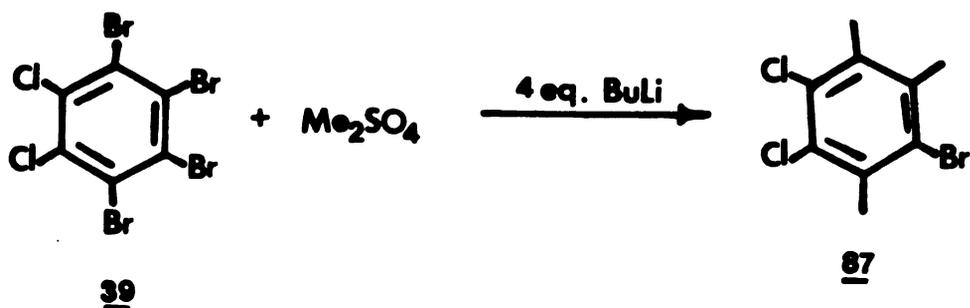
Scheme 15

derivative **88** or by stepwise process from an initially formed dilithio-compound **80**. An electrophilic attack on **80** by dimethyl sulfate would give the tetrahalo-p-xylene **82** whose monolithio-derivative **89** is then methylated to give the observed product.

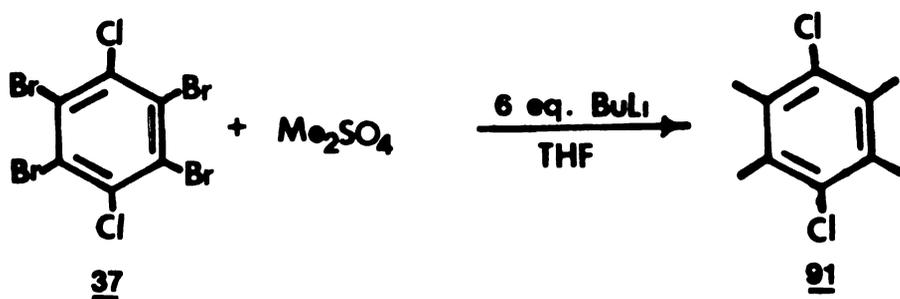
In order to differentiate between these pathways, the reaction of **39** with four equivalents of $n\text{-BuLi}$ was quenched with methanol. 2,3-Dibromo-5,6-dichlorobenzene **81** was formed, together with some polymeric substances. No product of trilithiation (**90**) was found.



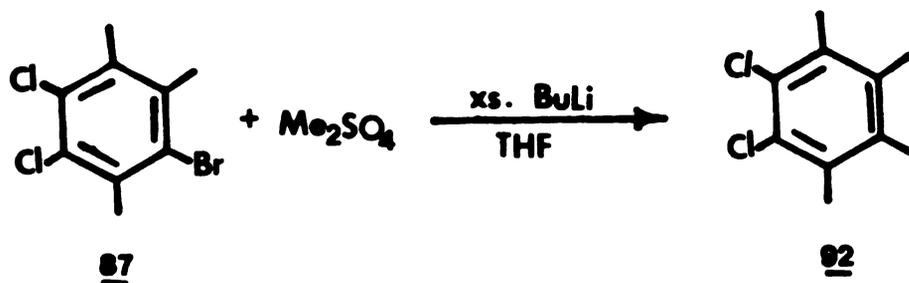
The above result meant that the formation of pseudocumene 87 when a similar reaction was quenched with dimethyl sulfate occurred by the stepwise pathway. Such an outcome would require either that (a) dimethyl sulfate be stable to n-BuLi at -78°C or (b) dibromo-*p*-xylene 82 metalate faster than n-BuLi reacts with Me_2SO_4 at this temperature. In order to determine whether any of these premises apply, dimethyl sulfate was added to a slurry of the tetrabromoarene 39 in toluene and n-BuLi was subsequently added to the mixture at -78°C . The amount of dimethyl sulfate initially present was more than enough to destroy all of the n-BuLi if the two substances reacted at this temperature. The isolation of 87 in 87% yield confirmed that dimethyl sulfate is in fact stable towards n-BuLi at low temperatures and that the formation of the pseudocumene 87 was a stepwise process.



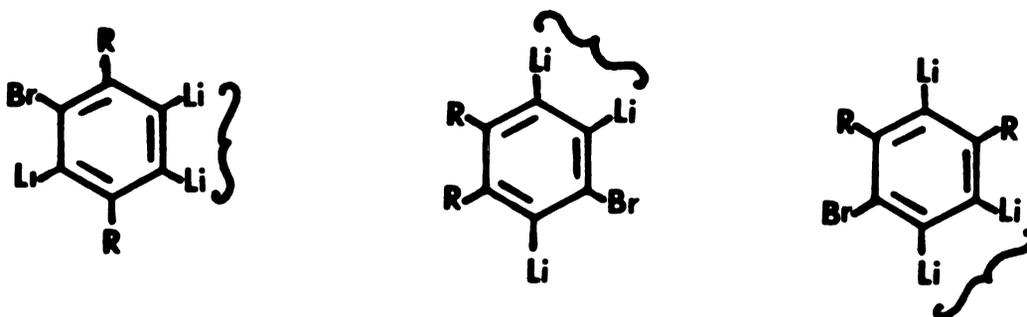
The use of six and nine equivalents of n-BuLi, in an attempt to replace all of the bromine atoms with methyl groups failed in toluene, even at 0°C. The product in these cases was 87, formed in high yield. Replacement of the remaining bromine atom in 87 by a methyl group, using toluene as solvent, was also unsuccessful. When the solvent was changed to THF, however, it was possible to replace all



of the bromine atoms in 37 to obtain p-dichlorodurene 91. Similarly, the replacement of the bromine atom in 87 leading to o-dichloroprehnitene 92 was successful in THF.

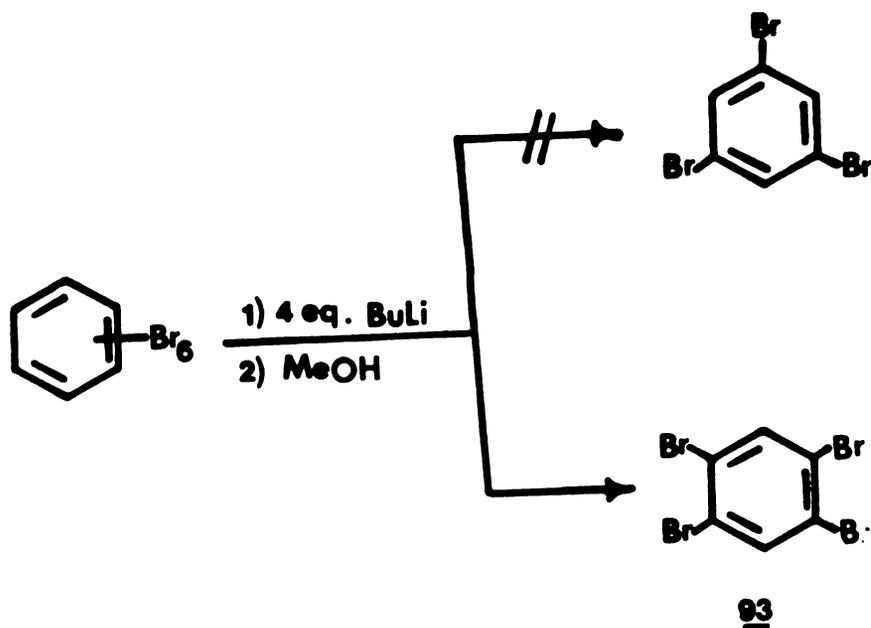


The preparation of a trilithio-arene from a tetrabromoarene requires that two of the lithium atoms be positioned ortho to one another. The absence of products of trilithio-intermediates in our attempts to polyolithiate tetrabromoarenes implies that the remaining substituents cannot sustain an o-dilithio-arrangement (four fluorine atoms on



the ring can sustain such arrangement, cf. p. 61). A symmetrical trilithio-arene was prepared from 1,3,5-trichlorobenzene³⁷ and we reasoned that if bromine atoms could be as effective as chlorine and fluorine⁴¹ in sustaining a symmetrical trilithio-arene, then hexabromobenzene would be a good precursor for its preparation by metal-halogen exchange. The attempted trilithiation of hexabromobenzene using excess n-BuLi and quenching with methanol gave only the tetrabromobenzene 93.

These investigations on polyolithiations establish that only the p-dilithio-haloarenes can be obtained from tetrabromoarenes and hexabromobenzene no matter how large an excess of n-BuLi is used. Dilution and slow addition of BuLi suppresses butylation of the lithio-arene intermediates. Application of this fact was instrumental in improving the



yields of bisadducts with dienes and in the isolation of addition products from carbonyl compounds. The use of exactly two equivalents of *n*-BuLi often led to incomplete reaction in bisannelations and unrecognizable products in the interception reactions with carbonyl compounds.

F. Electronic Effects of the Remaining Substituents on the Metalation of and Aryne Formation from Tetrabromoarenes

As a consequence of this study on the mechanism of bisannelation, it was possible to investigate the influence of inductive and mesomeric effects on the mono- and dilithiation of tetrabromoarenes and the generation of benzyne from these intermediates. The 1,4-substituents on the bisaryne equivalents are representative of most possible combinations of such electronic effects (Table 9).

TABLE 9

ELECTRONIC CHARACTER OF THE p-SUBSTITUENTS OF
TETRABROMOARENES

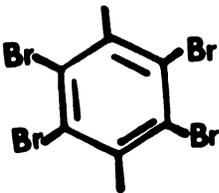
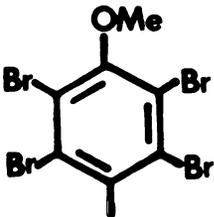
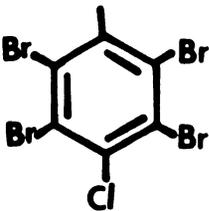
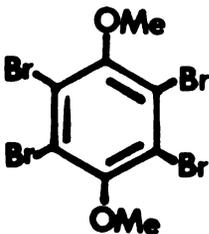
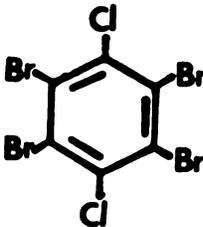
Entry	Tetrabromoarene	Electronic Character
1	 <p style="text-align: center;"><u>33</u></p>	+1 ; +1
2	 <p style="text-align: center;"><u>34</u></p>	-1, +M ; +1
3	 <p style="text-align: center;"><u>35</u></p>	+1 ; -1
4	 <p style="text-align: center;"><u>36</u></p>	-1, +M ; -1, +M

TABLE 9 (Cont'd.)

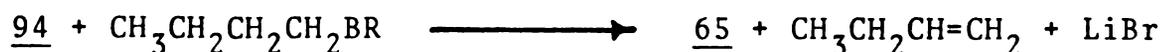
Entry	Tetrabromoarene	Electronic Character
5	 <p style="text-align: center;"><u>37</u></p>	-1 , -1

I = Inductive Effect; M = Mesomeric Effect; (+) = Electron-releasing to the ring; (-) = Electron-withdrawing from the ring.

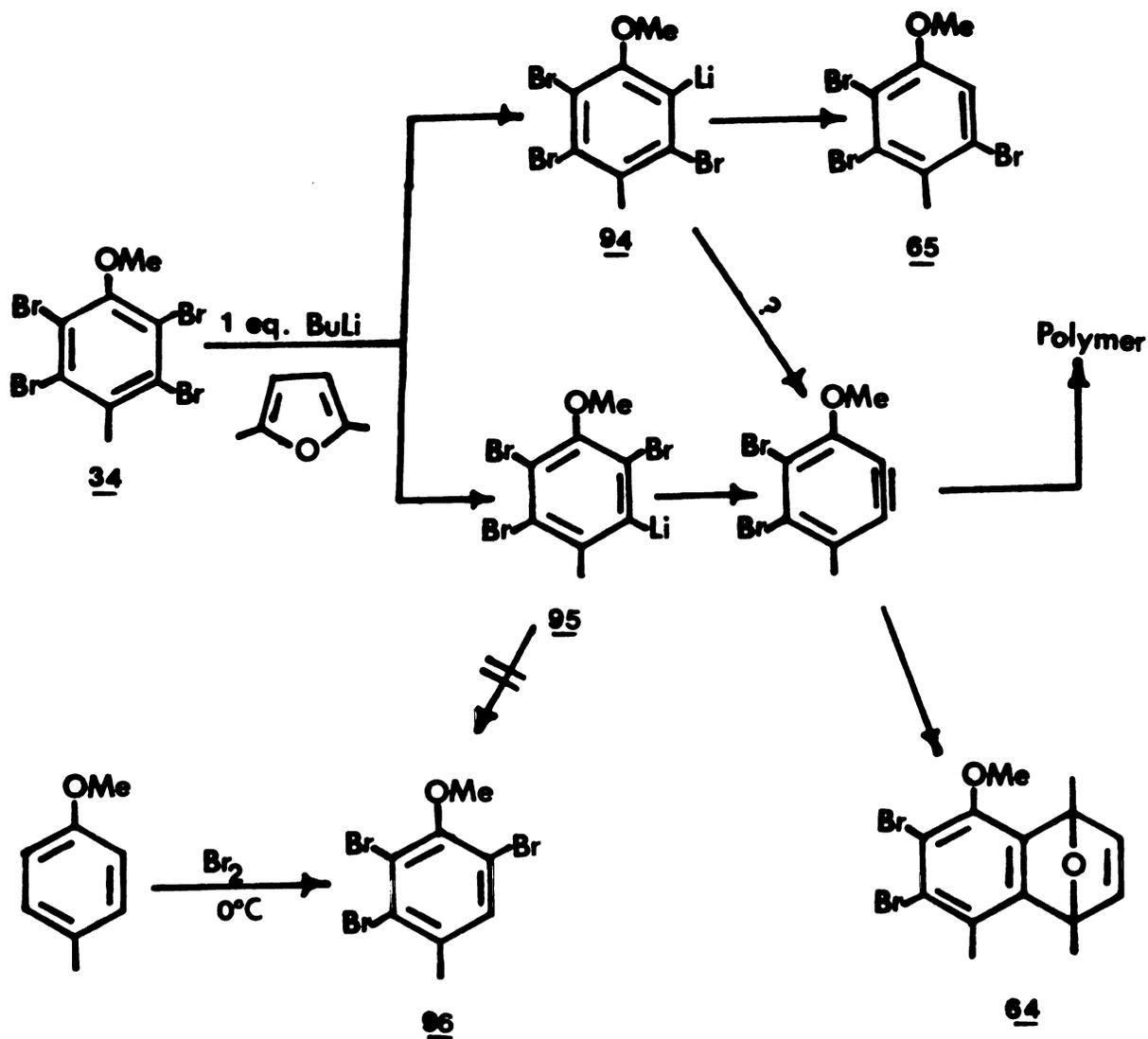
Entries 1, 2 and 4 formed monoadducts when suspended in toluene but it was not possible to intercept the monolithio derivatives even at -78°C (monolithio derivatives of 34 and 36 were intercepted in isolable yields only when they were totally in solution during the reaction, cf. p. 49). It is probable that under these heterogeneous reaction conditions, the monolithio-intermediate of these bisaryne equivalents eliminated LiBr spontaneously because in the absence of diene, these reactions in toluene resulted in polymers. The presence of the other two bromine atoms could not effectively compensate for the destabilizing effects of the electron-releasing methyl and methoxyl groups on the developing o-bromoarene anions. On the other hand, p-dihalo-substituents stabilize both the mono- and dilithio-derivatives of

tetrabromoarenes, making it possible to intercept these species at -78°C or higher temperatures with various electrophiles.

Between these two types of 1,4-substituents with identical electronic effects are those with mixed inductive and/or mesomeric effects. For the substrates with these substituents, the question arises of regioselectivity, relative ease of metalation and loss of LiBr. The products of the reaction of methyl tetrabromo-*p*-cresolate 34 with one equivalent of *n*-BuLi relate to this question of induction-biased metalation when two isomers are possible (Scheme 16). The isolation of the tribromoarene 65¹⁹ made it possible to discriminate between the two monolithio-intermediates 94 and 95 by their products. The intermediate 95 probably lost LiBr easily to form benzyne which was either trapped by diene to give the adduct 64 or reacted with the monolithio-arenes 94 and 95 to form polymeric substances. The other isomer 94 abstracts a proton from butyl bromide and probably also forms benzyne.



Evidence that 95 was not capable of proton abstraction like 94 came from the absence of the other isomer of methyl



Scheme 16

tribromo-p-cresolate **96** in the reaction product mixture (**96** was prepared by an independent method⁴³ for comparison). Quenching the reaction mixture with methanol-d₁ did not result in deuterium incorporation in **65**. This observation indicated that proton abstraction might be a fast process for **94**. Whereas it was possible to rule out proton abstraction

for 95, such a decision with respect to benzyne formation cannot be made for 94 from these results, as competition between these two processes is very possible.

In THF, the ratio of monoadduct 64 to methyl tribromo-p-cresolate 65 was 50/50 but as the solvent polarity decreased, the predominance of 64 increased (Table 10).

TABLE 10
INFLUENCE OF SOLVENT POLARITY ON THE DISTRIBUTION OF
MONOMETALATION PRODUCTS OF METHYL
TETRABROMO-p-CRESOLATE (34)

Solvent	64 (%)	65 (%)
THF	42 ^a	42 ^a
Ether	34	11
THF/Benzene (5 : 1)	55	13
THF/Toluene (5 : 7)	45	5
Toluene	48	0

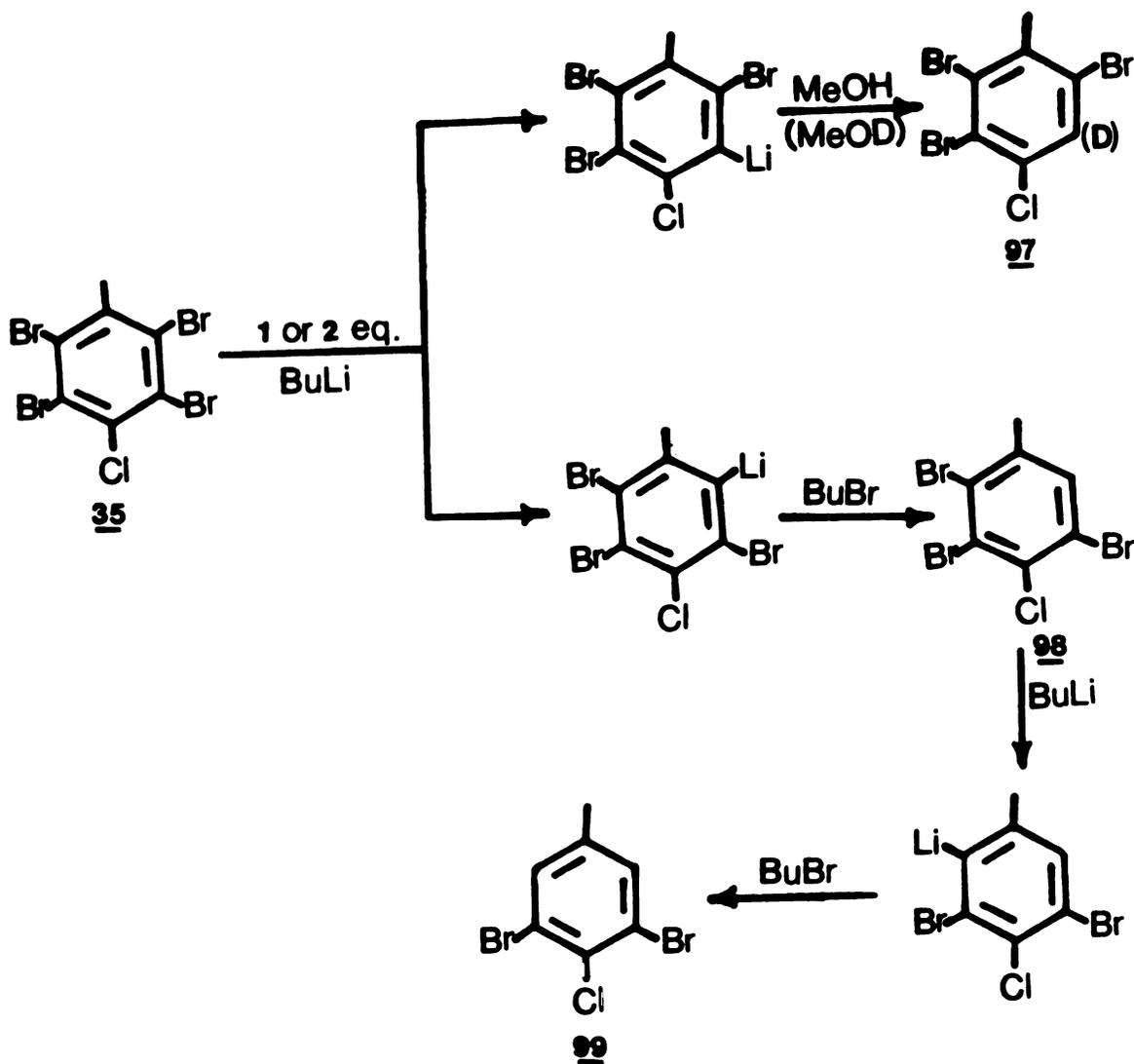
^arelative to recovered starting material.

Because of uncertainty about how the intermediates 94 and 95 contribute to the formation of the adduct 64 and the accompanying polymeric substances, the ratio of 64 and 65 may not be a measure of the competitive formation of the monolithio-intermediates 94 and 95. Nevertheless, the results in Table 10 definitely show that the ratio of products depends on the polarity of the solvent. This dependence may arise

from the loss of selectivity due to the greater reactivity of n-BuLi as the polarity of the solvent is increased. Also, solvation and ionization in polar solvents may render 94 more reactive for proton abstraction rather than for benzyne formation.

Two products were also isolated from the reaction of the tetrabromoarene 35 with one equivalent of n-BuLi when the reaction was quenched with MeOH (Scheme 17). The tribromo-compound 97 was the major product and the m-diprotio-arene 99 was present in trace quantity. The isomeric tribromoarene 98 was not detected. It was probably metalated immediately after it was formed to give the dibromoarene 99. The use of two equivalents of n-BuLi led to the same product mixture but in this case, the yield of 99 improved to 4%. No p-dilithiation product was observed in both instances. Quenching of the reactions with one or two equivalents of n-BuLi with methanol-d₁ resulted in deuterium incorporation in 97 but not in 99. These results from quenching the reactions with methanol and methanol-d₁ confirm that when the electronic effects of the p-substituents of the tetrabromoarene are different, metalation ortho to the stronger electron-releasing substituent leads to fast proton abstraction from any proton source in the reaction mixture.

The following conclusions can therefore be drawn about the inductive and mesomeric effects of 1,4-substituents on the effectiveness of tetrabromoarenes as benzyne precursors:



Scheme 17

(a) Better yields of bisadducts are obtained with tetrabromoarenes which have substituents of equal inductive and/or mesomeric effect. Those with electron-donating groups, e.g., tetrabromo-*p*-xylene **33** and tetrabromo-*p*-dimethoxybenzene **36**, are much more efficient bisaryne equivalents than those with electron-withdrawing groups like tetrabromo-*p*-dichlorobenzene **37**. A slight improvement in yield is achieved with bisaryne

equivalents of the second type if the metalation is carried out at a higher temperature (0°C - 25°C) at which condition the lithio-intermediates decompose on formation to give benzyne.

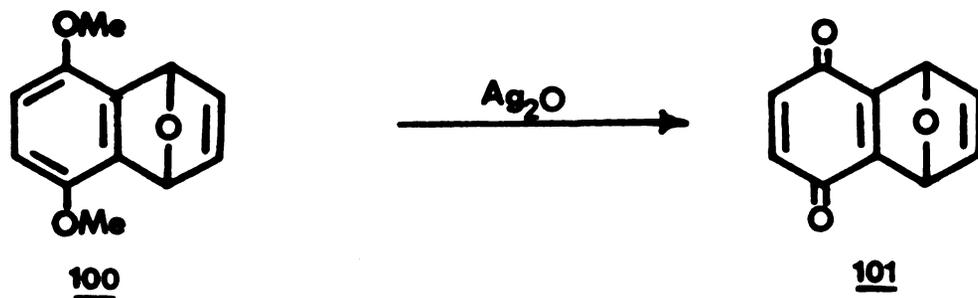
(b) If the electronic effects are similar but different in magnitude (e.g., methyl tetrabromo-p-cresolate 34), the effectiveness of the bisaryne equivalent is diminished. This is due to the fact that of the two monolithio-derivatives formed by such substrates, one forms benzyne mainly while for the other, proton abstraction is competitive with benzyne formation.

(c) The least efficient tetrabromoarenes are those whose substituents have opposing electronic effects as in tetrabromo-p-chlorotoluene 35. For these bisaryne equivalents, metalation is heavily biased towards the monolithio-arene which is more stable and therefore forms benzyne with difficulty. The minor monolithiation isomer in this case also abstracts a proton faster than it can form an aryne.

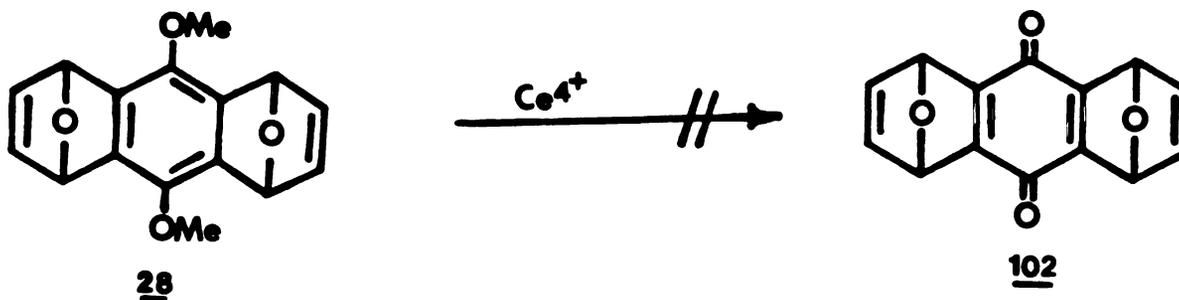
G. Some Transformations of the Bisadducts

All but three (28, 32 and 55) of the bisadducts prepared during this work (cf. Table 2) are novel compounds and probably have a rich chemistry. A few miscellaneous transformations were tried with some of them and the results are described here.

Cragg and coworkers¹⁵ effected the oxidative demethylation of the naphthalene endoxide 100 to the quinone 101 with Ag_2O but this reagent could not cause the same



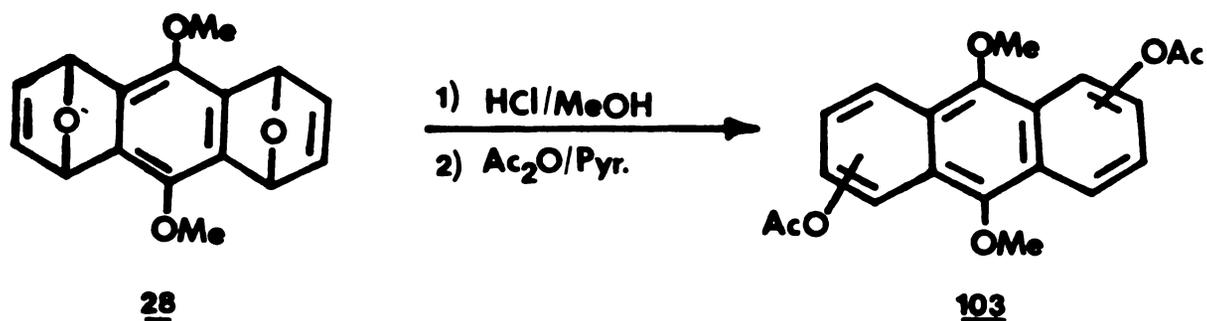
transformation in the bisadduct 28. We tried a stronger oxidant - ceric ammonium nitrate - without success. Acid-catalysed demethylation followed by oxidation was ruled out



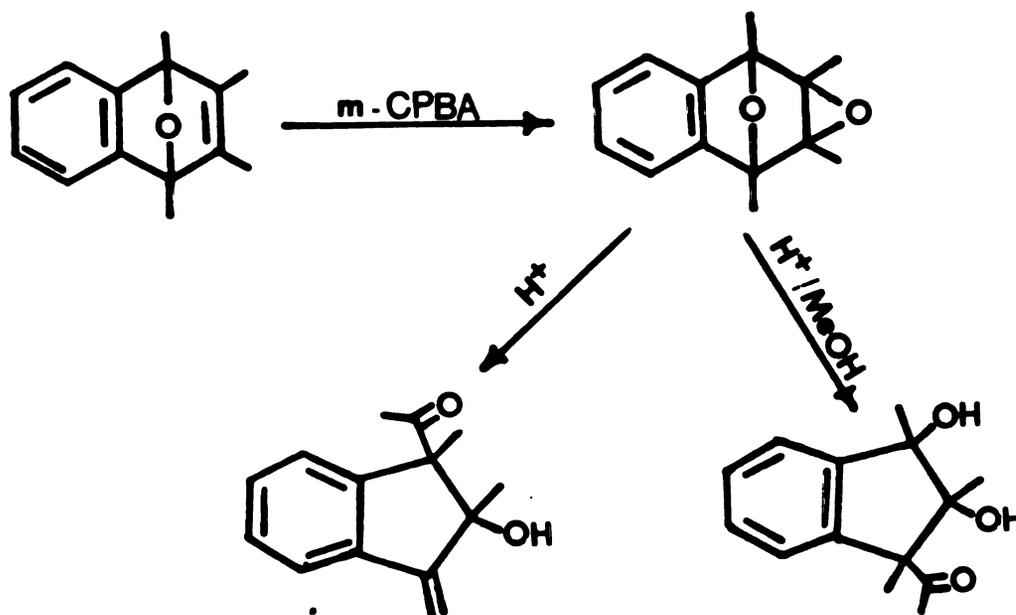
as an alternative route because of the facile hydrolytic ring opening of endoxides in acidic media.

It was anticipated that the acid-catalysed hydrolysis of bisadduct 28 would afford an intermediate for the eventual synthesis of anthracycline-like compounds but our preliminary results showed that this hydrolysis was not regioselective.

The free phenolic compound mixture had to be acetylated to stabilize the product (mixture of two isomers of 103).

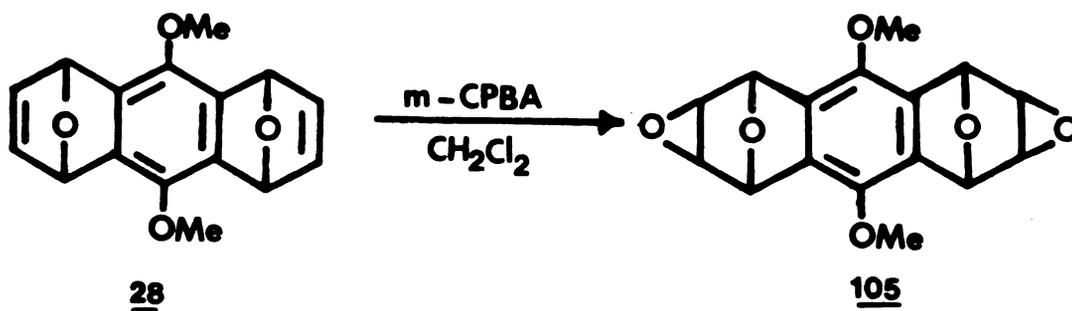
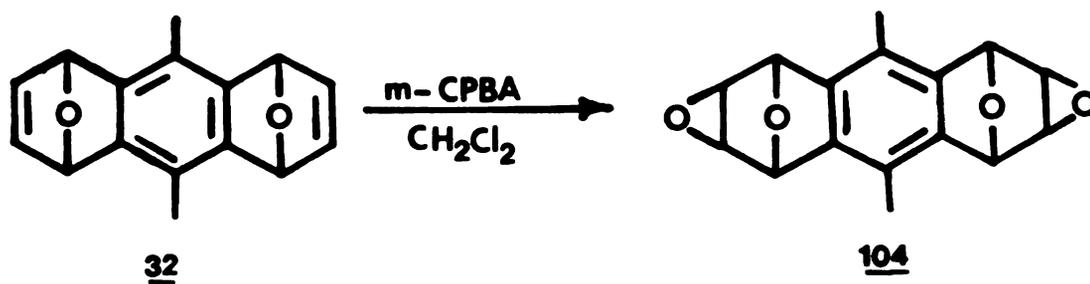


Naphthalene endoxides have been epoxidized and subjected to acid-catalysed transformations (Scheme 18).²³



Scheme 18

The anthracene diendoxides 28 and 32 were easily epoxidized by a similar method but the acid-catalyzed hydrolysis of the resulting bis-epoxides 104 and 105 gave intractable substances.



EXPERIMENTAL

1. General Procedures

^1H NMR spectra were measured in CDCl_3 or CCl_4 solution on a Varian T-60 (δ values given to two places after the decimal) or on a Bruker WM-250 (δ values given to three places after the decimal) spectrometer with chemical shifts reported in σ -units from tetramethylsilane (TMS) as an internal standard. The Bruker WM-180 spectrometer was used for recording the proton NMR spectra of 146 and 149. ^{13}C NMR spectra were determined on a Varian CFT-20 spectrometer. Ultraviolet (UV) spectra were recorded on a Unicam SP-800 spectrometer. Infrared (IR) spectra were obtained using a Perkin-Elmer 167 spectrophotometer. Mass spectra were determined with Finnigan 4000 employing the INCOS data system at 70 eV. High resolution mass spectra were obtained on a Varian CH5 spectrometer. Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan. Melting points were taken on a Thomas Hoover Unimelt apparatus and are uncorrected. Neutral alumina (Activity grade II) was used for column chromatography unless otherwise stated and gas chromatographic separations were run on a 13' x 1/4" column packed with 10% SE-30 on chromosorb W with DMCS. n-BuLi

in hexane was used and it was standardized using the titration method.⁴⁴

2. 9,10-Dimethoxy-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (28)

A suspension of the tetrabromoarene 36 (2.29 g, 5 mmol) in 300 mL of dry THF containing 4 g (58.82 mmol) of furan was cooled to -78°C under argon. n-Butyllithium (10 mL, 1.6 M) diluted with 30 mL of dry hexane was added dropwise at a constant rate over 1 h. After an additional 0.5 h, the reaction was stopped by adding 10 mL of methanol. THF was removed on a rotary evaporator and the solid residue was taken up in CH₂Cl₂ (100 mL). The solution was washed with water and dried (Na₂SO₄). Evaporation of the solution to dryness left a solid which after chromatography on alumina and elution first with a 50/50 mixture of hexane and CH₂Cl₂ followed by THF, gave 1.18 g (86%) of 28 as a mixture of syn and anti isomers: mp - the solid turned brownish-yellow at 240°C and melted to a brown liquid at 250°C (lit.¹⁵ 203°C-223°C). A pure isomer was obtained by chromatography of the product mixture on alumina with CH₂Cl₂; it melted at 203-5°C without decomposition. ¹H NMR (CDCl₃) δ 3.77 (s, 6 H), 5.72 (br s, 4 H), 6.87 (br s, 4 H); ¹³C NMR of mixture of the isomers (CDCl₃) δ 60.61 and 60.31, 80.77, 138.72, 142.97 and 143.15, 143.97 and 144.12; mass spectrum, m/e (relative intensity) 270 (M⁺, 43), 215 (100), 199 (77), 183 (25), 139 (30), 63 (23), 43 (3).

3. 9,10-Dimethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (32)

Tetrabromo-p-xylene 33¹⁷ (2.3 g, 5.5 mmol) was suspended in 300 mL of anhydrous toluene containing 3.8 g (55.88 mmol) of furan and the mixture was cooled to -78°C under argon. n-Butyllithium (6.5 mL, 2.4 M) diluted with 30 mL of dry hexane was added over 1.5 h and the reaction mixture was warmed to room temperature over 8 h. After quenching the reaction with 10 mL of methanol, toluene was removed on a rotary evaporator. The residue was redissolved in CH₂Cl₂ (100 mL), washed with water and dried (Na₂SO₄). Evaporation of the solution to dryness left 1.37 g of crude 32 which showed a syn/anti ratio of 50/50 (calculated by averaging the ratios of the integrals for the three proton signals in the 250 MHz proton NMR spectrum of this crude product mixture). Chromatography on alumina using a 50/50 mixture of hexane and CH₂Cl₂ removed traces of monoadduct. A second elution with CH₂Cl₂, followed by THF gave 0.95 g (72%) of 32 as a mixture of two isomers. The product was recrystallized from THF: mp - the solid turned yellow at 205°C and melted to a brown liquid at 265°C (lit.¹⁶ starts to melt at 210°C, decomposed at 300°C). ¹H NMR (CDCl₃) δ 2.239; 2.245 (2s, 6 H), 5.701; 5.704 (2s, 4 H), 7.022; 7.027 (2s, 4 H); ¹³C NMR (CDCl₃) δ 14.56, 81.15, 121.44 and 121.63, 143.39 and 143.25, 146.46; mass spectrum, m/e (relative intensity) 238 (M⁺, 28), 212 (11), 183 (100), 165 (51), 152 (24).

4. Methyl tetrabromo-p-cresolate (34)

p-Cresol (20 g, 0.185 mol) was dropped into 60 mL (1.156 mol) of bromine containing 1 g of iron filings at room temperature. Small portions of CHCl_3 were added from time to time to keep the reaction mixture stirrable. After 6 h, the evolution of HBr subsided and the resulting slurry was taken up in hot CHCl_3 . The solution was washed successively with aqueous NaHSO_3 and NaHCO_3 and evaporated to dryness on a rotary evaporator to give 73 g (93%) of tetrabromo-p-cresol as white needles: mp 195-6°C (lit.¹⁹ 196°C).

Potassium hydroxide (10 g) in 50 mL of water was added to 32.3 g (76.2 mmol) of tetrabromo-p-cresol and the hot suspension was treated with 20 g (0.159 mol) of dimethyl sulfate. A milky white cake formed which was rendered stirrable by adding 20 mL of CHCl_3 . Stirring for 6 h at room temperature was followed by refluxing for 4 h. The reaction mixture, after cooling to room temperature, was extracted with CHCl_3 and the extract was evaporated to dryness to give 32.5 g (97%) of 34 as white needles: mp 136-8°C (lit.²⁰ 135°C); ^1H NMR (CDCl_3) δ 2.72 (s, 3 H), 3.78 (s, 3 H).

5. Tetrabromo-p-chlorotoluene (35)

p-Chlorotoluene (10.5 g, 83.3 mmol) was added dropwise over 0.25 h into bromine (50 mL, 0.975 mol) containing 2 g of Fe at room temperature. After 6 h, during which time the

evolution of HBr subsided, excess bromine was destroyed by washing successively with aqueous NaHSO_3 and NaHCO_3 . The suspension was filtered and the solid was dissolved in CHCl_3 . Iron filings were removed from the solution by filtration and evaporation to dryness left 26.4 g (72%) of crystals of 35: mp 264-5°C; ^1H NMR (CCl_4) δ 2.77; mass spectrum, m/e (relative intensity) 442 (M^+ , 31), 363 (29), 203 (55), 122 (57), 87 (100). Anal. Calc'd. for $\text{C}_7\text{H}_3\text{Br}_4\text{Cl}$: C, 19.01; H, 0.68. Found: C, 19.05; H, 0.68.

6. Tetrabromo-p-dimethoxybenzene (36)

p-Dimethoxybenzene (65.4 g, 0.474 mol) was dissolved in 60 mL of glacial acetic acid by warming on a water bath. Bromine (50 mL, 0.975 mol) dissolved in 50 mL of glacial acetic acid was added slowly via a funnel until the red color of bromine did not discharge but deepened on further addition. Heating was continued for 1 h and the precipitated 2,5-dibromo-p-dimethoxybenzene 26 was filtered and washed with glacial acetic acid (120 g, 86%; mp 140-2°C, lit.²¹ 102-4°C).

The dibromo-arene 26 (40 g, 0.135 mol) was dissolved in 40 mL (0.780 mol) of bromine and the mixture was stirred at 25°C for 1.5 h, after which time the evolution of HBr subsided. The tetrabromoarene, suspended in excess bromine was dissolved in CHCl_3 and the solution was washed successively

with aqueous NaHSO_3 and NaHCO_3 . A yellow product was obtained on evaporation of the chloroform solution. The decolorization of this product was achieved by treating the solid with concentrated aqueous NaOH followed by recrystallization from CCl_4 to give 50 g (82%) of 36 as white needles: mp $193-5^\circ\text{C}$ (lit.²¹ 194°C); ^1H NMR (CDCl_3) δ 3.80.

7. Tetrabromo-p-difluorobenzene (38)

Bromine (100 mL, 1.926 mol) was stirred with 1 g of iron filings for 0.25 h and then p-difluorobenzene (6.5 g, 56.1 mmol) was added through a dropping funnel over 0.25 h. Stirring was continued at room temperature for 3 h and the reaction mixture was refluxed for 6 h. Excess bromine was destroyed after the mixture cooled to 25°C by washing successively with aqueous NaOH , NaHSO_3 and NaHCO_3 . The gray solid floating at the top of the aqueous workup was collected and dissolved in 500 mL of CCl_4 . Evaporation of the organic solution was stopped as crystallization was observed. After isolating the crystals by filtration, the mother liquor was concentrated again to yield more crystals: total yield of 38 was 18.4 g (71%): mp $162-4^\circ\text{C}$; mass spectrum, m/e (relative intensity) 430 (M^+ , 8), 351 (9), 270 (27), 191 (23), 110 (100), 79 (34).

Anal. Calc'd. for $\text{C}_6\text{Br}_4\text{F}_2$: C, 16.77. Found: C, 16.89.

8. Tetramethylfuran (40)²³

A vigorously stirred slurry of lead dioxide (100 g) in 300 mL of 2-butanone was refluxed until the purple color of PbO_2 was replaced by the bright yellow color of lead oxide (6 h). The lead oxide was filtered and 160 mL of unreacted 2-butanone was recovered on a rotary evaporator. Distillation of the yellow liquid residue at reduced pressure (15-20 Torr) gave 24 g (21%) of 3,4-dimethyl-hexan-2,5-dione as the fraction boiling between 90-100°C.

The 3,4-dimethylhexan-2,5-dione (11 g) in 100 mL of benzene containing 0.3 g of p-TsOH was heated under reflux using a water trap until the volume of water in the trap remained constant. After a total of about 75 mL of benzene and water had been distilled off through the trap, the dark liquid residue was transferred to a system for distillation at reduced pressure. Distillation was continued at atmospheric pressure in this set-up until the thermometer read 81°C and then a water aspirator was used to distill and collect the fraction boiling up to 100°C. This fraction represented 7 g (73%) of tetramethylfuran. A trace of benzene in the product was removed with agitation under a vacuum pump for several minutes.

9. 1,4,5,8,9,10-Hexamethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (42)

A heterogeneous mixture of the tetrabromoarene 33 (2.38 g, 5.6 mmol) and 5.4 g (56 mmol) of 2,5-dimethylfuran in 300 mL of anhydrous THF was cooled to -78°C under argon. After the addition of 10 mL of 2 M BuLi diluted with 30 mL of dry hexane (1.5 h), the reaction mixture was allowed to warm to room temperature during 8 h and 10 mL of water was added to destroy excess BuLi. The solvent was evaporated on a rotary evaporator, the residue was taken up in CH_2Cl_2 , washed with water and dried (Na_2SO_4). Removal of methylene chloride left 1.91 g of crude product mixture whose ^1H NMR (250 MHz) spectrum showed a syn/anti ratio of 42/58. Chromatography on alumina with a 50/50 mixture of hexane and CH_2Cl_2 gave 1.12 g (68%) of a mixture of isomers of 42 which was recrystallized from CHCl_3 : mp - the solid turned brownish-yellow at 200°C and melted to a brown liquid completely at 230°C ; ^1H NMR (CDCl_3) δ 1.936; 1.961 (2s, 12 H), 2.290; 2.344 (2s, 6 H), 6.789 (br s, 4 H); ^{13}C NMR (CDCl_3) δ 13.81 and 14.39, 18.69 and 19.00, 89.44 and 89.73, 121.72 and 122.09, 147.46, 149.74 and 150.09; mass spectrum, m/e (relative intensity) 294 (M^+ , 2), 251 (10), 225 (33), 209 (43), 43 (100); high resolution mass spectrum calculated for $\text{C}_{20}\text{H}_{22}\text{O}_2$: 294.16141. Found 294.16198.

10. Decamethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (43)

A suspension of 9.28 g (22 mmol) of 33 in 50 mL of dry ether containing 11 g (89 mmol) of tetramethylfuran was cooled to -78°C under argon and 22 mL of 2.1 M BuLi was added over 0.5 h using a syringe. The mixture was stirred at -78°C for 5 h and 6 mL of methanol was added. The reaction mixture was evaporated to dryness on a rotary evaporator and the residue was shaken with 200 mL of CHCl_3 . The solution was washed with water and dried (Na_2SO_4). Concentration of the solution on a rotary evaporator left an oil covered solid, which after trituration with cold hexane, led to the isolation of 4.4 g (57%) of bisadduct mixture whose proton NMR (60 MHz) spectrum (all three signals) showed an isomer ratio of 36/64. Recrystallization of the product mixture from a mixture of CH_2Cl_2 and MeOH gave shiny white needles: mp - the solid started to melt at 264°C and melted completely to a brown liquid at 274°C ; ^1H NMR (CDCl_3) δ 1.598; 1.667 (2s, 12 H), 1.865; 1.832 (2s, 12 H), 2.356; 2.302 (2s, 6 H); ^{13}C NMR (CDCl_3) δ 10.64 and 10.88, 14.21 and 15.14, 17.23 and 17.58, 89.46 and 89.89, 120.50 and 121.08, 145.40 and 145.60, 149.56 and 150.00; UV (CDCl_3) λ_{max} (Σ) 257 (993), 290 (978); mass spectrum, m/e (relative intensity) 350 (M^+ , 18) 308 (22), 296 (24), 264 (53), 253 (100), 43 (20).

Anal. Calc'd. for $\text{C}_{24}\text{H}_{30}\text{O}_2$: C, 82.24; H, 8.63. Found: C, 82.28; H, 8.53.

Repetition of this reaction with 2.32 g (5.5 mmol) of 33, 5.4 g (43.55 mmol) of tetramethylfuran in 300 mL of anhydrous ether and 8 mL of 2 M BuLi in 30 mL of hexane gave a crude product whose proton NMR spectrum also showed a syn/anti ratio of 36/64. The yield from this reaction, which was quenched at -78°C after a total of 5 h at this temperature, was 1.5 g (78%).

11. 1,4,5,8-Tetraphenyl-9,10-dimethyl-1,4,5,8-tetrahydro-anthracene-1,4:5,8-diendoxide (45)

In a similar procedure as for the preparation of the bisadduct 42, 1.04 g (2.5 mmol) of tetrabromo-p-xylene 33 in 140 mL of anhydrous toluene containing 1 g (4.5 mmol) of 2,5-diphenylfuran was treated with 6 mL of 2 M BuLi diluted with 20 mL of dry hexane to give a yellow gum. The gum was chromatographed on alumina by elution first with hexane to separate unreacted furan (0.7 g, 70%) and lastly with THF. The gummy substance which was eluted with THF was redissolved in CHCl_3 and after two days of standing, deposited some solid as thin plates (less than 5%): mp- the solid turned brown at 250°C and melted to a dark brown liquid at 268°C; ^1H NMR (CDCl_3) δ 1.40; 1.48 (2s, 6 H), 7.17-7.67 (complex m, 24 H); mass spectrum, m/e (relative intensity) 437 (M - Ph-C=O, 40), 332 (M - 2Ph-C=O, 9), 106 (6), 105 (Ph-C=O, 100), 77 (11). The quantity of product isolated precluded further purification in order to obtain

analytical grade sample and the absence of the parent peak in the mass spectrum ruled out the use of high resolution mass spectrum for further characterization of this compound.

12. 9-Methyl-10-methoxy-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (46)

A solution of the tetrabromoarene 34 (2.22 g, 5.1 mmol) and 4 g (58.82 mmol) of furan in 300 mL of anhydrous THF was cooled to -78°C under argon. The addition of 10 mL of 1.6 M BuLi diluted with 30 mL of dry hexane took 1 h after which time the reaction mixture was allowed to warm to room temperature during 6 h. Water (10 mL) was added and THF was removed on a rotary evaporator. The residue was redissolved in CH_2Cl_2 , the solution was washed with water and dried (Na_2SO_4). The crude product weighed 1.15 g and its proton NMR (250 MHz) spectrum showed a 50/50 ratio of syn/anti isomers (calculated from the methyl and methoxyl signals). Chromatography using a 30% mixture of hexane in CH_2Cl_2 on alumina eluted unwanted oily products. Final elution with THF gave 1.12 g (87%) of 46 as a mixture of syn and anti isomers. Recrystallization was done from a mixture of CH_2Cl_2 and MeOH: mp $220-2^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 2.214; 2.228 (2s, 3 H), 3.855; 3.865 (2s, 3 H), 5.673 (br s, 2 H), 5.888 (br s, 2 H), 7.016 (br s, 4 H); ^{13}C NMR (CDCl_3) δ 14.34, 59.74 and 60.03, 80.82, 81.11, 118.64 and 118.43, 135.64 and 135.52, 142.98 and 143.34, 143.17, 146.58,

149.39; mass spectrum, m/e (relative intensity) 254 (M^+ , 15), 228 (6), 199 (100), 183 (45), 167 (37), 152 (37).

Anal. Calc'd. for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55.

Found: C, 75.73; H, 5.48.

13. 10-Methoxy-1,4,5,8,9-pentamethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (47)

Methyl tetrabromo-p-cresolate 34 (2.23 g, 5.1 mmol) was dissolved in 300 mL of anhydrous ether, 5.4 g (56 mmol) of 2,5-dimethylfuran was added and the mixture was cooled to -78°C under argon. n-Butyllithium (10 mL, 1.6 M) diluted with 30 mL of dry hexane was added dropwise over 1 h. The reaction mixture turned red at the early stage of the addition but faded to yellow at the end. After one more hour at -78°C , 10 mL of methanol was added. On decantation of the ethereal solution, a red precipitate was left which was water soluble. The ether solution was washed with water and dried (Na_2SO_4). Removal of the ether was done on a rotary evaporator at room temperature. The faint brown oily residue crystallized to a yellow solid on evacuation with a vacuum pump. Chromatography on basic alumina and elution first by a 50/50 mixture of hexane and CH_2Cl_2 and followed by THF gave a transparent oil which solidified after further drying with a vacuum pump. The resulting solid was washed with hexane to give 0.9 g (56%) of the bisadduct 47. One pure isomer of 47 was obtained from this

product mixture by a second chromatography on basic alumina by using first CH_2Cl_2 followed by THF: mp 172-3°C. The mixture of isomers was recrystallized from $\text{CH}_2\text{Cl}_2/\text{MeOH}$: mp - the solid started to darken at 150°C and melted to a brown liquid at 200°C; ^1H NMR (CDCl_3) δ 1.955 (s, 6 H), 1.971 (s, 6 H), 2.310; 2.361 (2s, 3 H), 3.588; 3.672 (2s, 3 H), 6.835 (br s, 4 H); mass spectrum, m/e (relative intensity) 310 (M^+ , 8), 267 (33), 241 (84), 225 (100), 43 (6).

Anal. Calc'd. for $\text{C}_{20}\text{H}_{22}\text{O}_3$: C, 77.39; H, 7.14.

Found: C, 77.32; H, 7.17.

14. 9,?,?-Trimethyl-10-methoxy-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (49)

To a solution of 34 (4.31 g, 9.43 mmol) and 2-methylfuran (3.5 g, 43 mmol) in 100 mL of anhydrous ether at -78°C under argon was added 10 mL of 2.2 M BuLi diluted with 30 mL of dry hexane over 2 h. During the addition, the reaction mixture turned orange and then back to milky white. Three hours later at -78°C, 3 mL of methanol was added and the suspension was filtered while cold. The filter cake was washed with water and air dried. The filtrate was washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness on a rotary evaporator at room temperature left a colorless oil. On further drying with a vacuum pump (12 h), the oil deposited some crystals (total weight of oil and crystals was 1.66 g). The crystals were

filtered and combined with the solid collected earlier to give a total of 1.9 g (73%) of a complex mixture of isomers of the bisadduct 49. It was not possible to separate all the isomers by chromatography but one of them was obtained uncontaminated by the others through chromatography on alumina with CH_2Cl_2 . This isomer had the following characteristics: mp - the solid turned very dark at 150°C and melted to a black liquid at 170°C ; ^1H NMR (CDCl_3) δ 1.97 (s, 6 H), 2.17 (s, 3 H), 3.53 (s, 3 H) 5.47 (br d, 2 H), 6.73 (AB type q, 4 H); mass spectrum, m/e (relative intensity) 282 (M^+ , 6), 239 (25), 213 (63), 197 (100), 167 (23), 152 (20), 43 (16); high resolution mass spectrum calculated for $\text{C}_{18}\text{H}_{18}\text{O}_3$: 282.12436. Found: 282.12560.

The proton NMR spectrum of the isomer mixture showed three peaks each for the methyl and methoxyl groups. The product and its solution in CHCl_3 turned green after a few days.

15. 1,4,5,8,9-Pentamethyl-10-chloro-1,4,5,8-tetrahydro-anthracene-1,4:5,8-diendoxide (50)

Tetrabromo-p-chlorotoluene 35 (2.22 g, 5 mmol) and 10 g (0.104 mol) of 2,5-dimethylfuran were dissolved in 300 mL of anhydrous THF at 0°C under argon and BuLi (10 mL, 1.6 M) diluted with 30 mL of dry hexane was added over 1 h. After the mixture warmed to room temperature (2 h), 10 mL of water was added and THF was removed on a rotary

evaporator. The residue was taken up in CH_2Cl_2 , washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness left a brown oil which on washing down a column of alumina with 10% CH_2Cl_2 in hexane, gave a red viscuous oil. This oil was dispersed in methanol and hexane was then added until a cloudy consistency was obtained. On standing in the refrigerator for a few hours, 0.25 g (16%; the yield for this reaction in toluene was 15%) of the bisadduct 50 was deposited. The mother liquor was concentrated to give 1 g of a gummy oil which was found by GC-MS to be a mixture of the bisadduct and the monoadducts 63 and 62 (cf. p. 35, Scheme 10) in the ratio 2 : 2 : 1 respectively. Further purification of the bisadduct was achieved by washing with cold CCl_4 and recrystallization from the same solvent: mp 253-6°C; ^1H NMR (CDCl_3) δ 1.966 (s, 6 H), 2.015 (s, 6 H), 2.399 (s, 3 H), 6.769-6.824 (AB type q, 4 H); mass spectrum, m/e (relative intensity) 314 (M^+ , 7), 271 (22), 245 (90), 229 (96), 43 (100); high resolution mass spectrum calculated for $\text{C}_{19}\text{H}_{19}\text{ClO}_2$: 314.10622. Found: 314.10736.

16. 9,10-Dimethoxy-1,4,5,8-tetramethyl-1,4,5,8-tetrahydro-anthracene-1,4:5,8-diendoxide (51)

This compound was prepared according to the procedure used for the preparation of bisadduct 42. Hence 5.4 g (12 mmol) of 2,5-dimethylfuran and 2.30 g (5 mmol) of tetrabromo-p-dimethoxybenzene 36 were treated with 10 mL of

1.6 M BuLi. The isolated yield after work-up and chromatography on alumina with CH_2Cl_2 was 1.19 g (72%): mp the compound turned yellow at 270°C and melted completely to a brown liquid at 277°C ; ^1H NMR (CDCl_3) δ 1.981 (s, 12 H), 3.676 (s, 6 H), 6.840 (br s, 4 H); mass spectrum, m/e (relative intensity) 326 (M^+ , 8), 283 (47), 257 (100), 241 (92), 227 (26), 43 (60).

Anal. Calc'd. for $\text{C}_{20}\text{H}_{22}\text{O}_4$: C, 73.60; H, 6.79.

Found: C, 73.70; H, 6.82.

17. 9,10-Dimethoxy-1,2,3,4,5,6,7,8-octamethyl-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (52)

A mixture of the tetrabromoarene 36 (4.1 g, 9 mmol) and tetramethylfuran (3 g, 24 mmol) in 25 mL of anhydrous THF was cooled to -78°C under argon. n-Butyllithium (8 mL, 2.5 M) was added by syringe over 10 min and the stirred reaction mixture was allowed to warm to room temperature during 8 h. After evaporation of the THF, the residue was shaken with CH_2Cl_2 . About 0.8 g (20%) of unreacted 36 was recovered as insoluble material from the CH_2Cl_2 solution by filtration. The filtrate was washed with water and dried (Na_2SO_4). Removal of the solvent and trituration of the product with cold ether gave 2 g (59%) of the bisadduct 52. Further purification was realized by chromatography on alumina with CH_2Cl_2 followed by recrystallization from a mixture of methanol and CH_2Cl_2 : mp - the solid started to

turn brown at 280°C and melted to a brown liquid at 290°C; ^1H NMR (CDCl_3) δ 1.681; 1.728 (2s, 12 H), 1.882; 1.851 (2s, 12 H), 3.751; 3.696 (2s, 6 H); mass spectrum, m/e (relative intensity) 382 (M^+ , 6), 339 (22), 328 (15), 296 (58), 285 (100), 43 (24).

Anal. Calc'd. for $\text{C}_{24}\text{H}_{30}\text{O}_4$: C, 75.36; H, 7.91.

Found: C, 75.51; H, 7.87.

Repetition of this reaction with a solution of 2.32 g (5.31 mmol) of 36, 5 g (40.32 mmol) of tetramethylfuran in 300 mL of anhydrous THF and 10 mL of 1.92 M BuLi in 30 mL of dry hexane gave 1.5 g (78%) of 52 on quenching the reaction at -78°C. The crude product showed an isomer ratio of 40/60 (calculated by averaging the ratios of the integrals of all the signals).

18. 9,10-Dichloro-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (53)

Furan (5 g, 74 mmol) was added to a stirred, cooled (-78°C) suspension of tetrabromo-p-dichlorobenzene 37¹⁸ (2.30 g, 5 mmol) in 100 mL of anhydrous THF under argon. n-Butyllithium (8 mL, 1.6 M) diluted with 30 mL of dry hexane was added over 1 h. The dark blue mixture turned reddish-brown as it warmed to 25°C in 6 h. Methanol (10 mL) was added and the solvent was removed on a rotary evaporator. The reddish-brown oily residue was redissolved in ether, the solution was washed with water and dried (Na_2SO_4). On

passing this solution down a column of basic alumina and concentrating the eluate, a yellow solid was left which after trituration with cold hexane gave 0.08 g (6%) of the bisadduct 53. The product was recrystallized by dissolving in CHCl_3 and then adding methanol until the solution became cloudy. Fine crystals were deposited after standing in the refrigerator: mp 227-231°C with decomposition; $^1\text{H NMR}$ (CCl_4) δ 5.57 (br s, 4 H), 6.93 (br s, 4 H); mass spectrum, $\underline{m/e}$ (relative intensity) 278 (M^+ , 30), 252 (18), 223 (70), 189 (100), 152 (63).

Anal. Calc'd. for $\text{C}_{14}\text{H}_8\text{Cl}_2\text{O}_2$: C, 60.24; H, 2.89.

Found: C, 60.13; H, 2.90.

19. 9,10-Dichloro-1,4,5,8-tetramethyl-1,4,5,8-tetrahydro-anthracene-1,4:5,8-diendoxide (54)

To a suspension of the tetrabromoarene 37¹⁸ (3.67 g, 8 mmol) in 100 mL of anhydrous ether cooled to -78°C under argon was added 7 g (73 mmol) of 2,5-dimethylfuran. A solution of BuLi (9 mL, 2.2 M) diluted with 30 mL of dry hexane was added over 1 h and the brown reaction mixture was allowed to warm to 25°C in 6 h. After the addition of 10 mL of methanol, the mixture was concentrated on a rotary evaporator. The brown oily residue was redissolved in CH_2Cl_2 , washed with water and dried (Na_2SO_4). The brown oil left after evaporation to dryness was chromatographed on silica gel using CH_2Cl_2 to give 0.7 g (26%) of the

bisadduct 54 containing about 10% by weight of the dibromo-analog. Repeated chromatography and recrystallizations were not effective in separating the different compounds: mp of mixture; 240-3°C; ^1H NMR (CDCl_3) δ 1.90 (s, 12 H), 6.60 (s, 4 H); mass spectrum (CI): $(M + 1)^+ = 335$ for 54 and 423 for the dibromo-analog.

20. 9,10-Difluoro-1,4,5,8-tetrahydroanthracene-1,4:5,8-diendoxide (55)

p-Difluoro-tetrabromobenzene 38 (2.26 g, 5.3 mmol) was dissolved in 100 mL of anhydrous THF containing 5 g (74 mmol) of furan. The solution was placed under argon and cooled to -78°C. After the addition of 6 mL of BuLi (2.1 M) diluted with 30 mL of dry hexane (1 h), the reaction mixture was allowed to warm to 25°C in 6 h. Methanol (10 mL) was added and the solvent was removed on a rotary evaporator. The dark brown oily residue was taken up in CH_2Cl_2 , washed with water and dried (Na_2SO_4). Concentration of this solution gave a dark brown oil with crystals suspended in it. Chromatography on basic alumina with benzene gave 0.79 g of solid. A second chromatography using firstly hexane gave 0.25 g of a mixture of the monoadducts 56, 57, 58 and 59 in the ratio 20 : 3 : 2 : 25 (determined by GC-MS) respectively, as an oil which solidified on cooling. Second elution with a 50/50 mixture of hexane and methylene chloride gave 0.30 g (23%) of 55 as a mixture of syn/anti isomers. The

product turned brown at 260°C, decreased in volume and became darker as the temperature rose but did not melt completely even at 310°C (lit.¹⁶ decomposed at 265°C); ¹H NMR (CDCl₃) δ5.67 (br s, 4 H), 6.92 (br s, 4 H); mass spectrum, m/e (relative intensity) 246 (M⁺, 37), 220 (15), 191 (94), 189 (100), 188 (62), 164 (14).

21. 5,8-Difluoro-6-bromo-1,4-dihydronaphthalene-1,4-endoxide (57)

In a procedure similar to that for the preparation of bisadduct 55, 2.26 g (5.3 mmol) of tetrabromo-p-difluorobenzene 38 and 5 g (74 mmol) of furan in 100 mL of anhydrous THF were treated with 6 mL of 2.1 M BuLi and the reaction was quenched at -78°C to give a brown oil which was chromatographed on basic alumina with benzene as eluent to give 0.55 g (41%) of the monoadduct 57 as an oil. The product had a very strong odor and solidified on cooling in a dry-ice bath. It sublimed into thin needles at room temperature. Analytical sample of this compound was prepared by subliming at atmospheric pressure from the molten state (fluffy shiny sheets): mp 91-2°C; ¹H NMR (CCl₄) δ5.78 (br s, 2 H), 6.77 (m, 1 H), 6.95 (br s, 2 H); mass spectrum, m/e (relative intensity) 258 (M⁺, 3), 232 (15), 151 (100), 125 (10).

Anal. Calc'd. for C₁₀H₅BrF₂O: C, 46.37; H, 1.95.

Found: C, 46.39; H, 1.82.

22. Attempted Interception of a Dilithio-derivative of Tetrabromo-p-xylene 33

A slurry of 4.2 g (10 mmol) of tetrabromo-p-xylene 33 in 100 mL of anhydrous THF under argon at -78°C was treated with 10 mL of 2.4 M BuLi added by syringe over 5 min. The reaction mixture turned dark brown as the addition of BuLi progressed and 2 h after the end of addition of BuLi and at -78°C, 10 mL of methanol was added. Workup of the reaction mixture gave 2 g of a brown powder which was insoluble in chloroform and most other common solvents. The solid product did not melt even at 290°C.

23. Reaction of Tetrabromo-p-xylene 33 with One Equivalent of BuLi in THF. Attempted Preparation of the Mono-adduct 60

A suspension of 33 (2.29 g, 5.4 mmol) in 300 mL of anhydrous THF containing 4 g (59 mmol) of furan was cooled to -78°C. The dropwise addition of 5 mL of 1.6 M BuLi diluted with 30 mL of dry hexane took 1 h after which the mixture was stirred at this temperature for 2 h. The reaction was stopped with 10 mL of methanol and 0.9 g (39%) of unreacted 33 was recovered by filtration of the cold reaction mixture. The filtrate was washed with water, dried (Na_2SO_4) and evaporated to dryness to afford 0.7 g (54%) of the bisadduct 32. The identity of this product was shown by its proton NMR and mass spectra (see p. 82).

24. Reaction of Tetrabromo-p-xylene 33 with Three Equivalents of BuLi in the Presence of Furan at -78°C. The Preparation of the Monoadduct 60

The solution of tetrabromo-p-xylene 33 (2.26 g, 5.4 mmol) in 300 mL of dry toluene containing 4 g (59 mmol) of furan became a suspension on cooling to -78°C under argon. n-Butyllithium (10 mL, 1.6 M) diluted with 30 mL of dry hexane was added over 1 h and after two more hours at -78°C, unreacted organometallic species were destroyed with 10 mL of methanol. Toluene was removed on a rotary evaporator. The residue was dissolved in CH₂Cl₂, washed with water and dried (Na₂SO₄). The solution was concentrated and the residue was subjected to chromatography on alumina with a 5 : 3 mixture of hexane and CH₂Cl₂. The monoadduct 60 (6,7-dibromo-5,8-dimethyl-1,4-dihydronaphthalene-1,4-endoxide) was isolated in 75% yield (1.33 g) and 0.28 g (12%) of 33 was recovered: mp 155-7°C; ¹H NMR (CDCl₃) δ 2.37 (s, 6 H), 5.65 (br s, 2 H), 6.88 (br s, 2 H); mass spectrum, m/e (relative intensity) 330 (M⁺, 26), 304 (32), 223 (100), 141 (44), 115 (27). Anal. Calc'd. for C₁₂H₁₀Br₂O: C, 43.67; H, 3.05; Br, 48.42. Found: C, 43.75; H, 3.05; Br, 48.32.

25. Reaction of **33** with Three Equivalents of BuLi at -78°C in the Presence of 2,5-Dimethylfuran. 1,4,5,8-Tetramethyl-6,7-dibromo-1,4-dihydronaphthalene-1,4-endoxide (**61**)

By a similar procedure as for the preparation of the monoadduct **60**, 2.31 g (5.5 mmol) of tetrabromo-p-xylene **33**, 5.4 g (56 mmol) of 2,5-dimethylfuran and 10 mL of 1.6 M BuLi gave 0.95 g (59%) of the monoadduct **61** and 0.57 g (29%) of the bisadduct **42** which were separated by chromatography on alumina using a 5 : 3 mixture of hexane and CH₂Cl₂: mp of **61**; 143-5°C (CHCl₃); ¹H NMR (CDCl₃) δ 1.87 (s, 6 H), 2.42 (s, 6 H), 6.52 (s, 4 H); mass spectrum. m/e (relative intensity) 358 (M⁺, 1), 332 (3), 315 (6), 279 (3), 234 (3), 155 (6), 43 (100).

Anal. Calc'd. for C₁₄H₁₄Br₂O: C, 46.96; H, 3.94.

Found: C, 47.07; H, 4.04.

26. 1,4,5-Trimethyl-6,7-dibromo-8-methoxy-1,4-dihydronaphthalene-1,4-endoxide (**64**) and Tribromoarene **65**

A solution of methyl tetrabromo-p-cresolate **34** (4.5 g, 10.5 mmol) and 5.2 g (54 mmol) of 2,5-dimethylfuran in 100 mL of anhydrous THF was cooled to -78°C under argon. n-Butyllithium (5 mL, 2.2 M) diluted with 30 mL of dry hexane was added over 2 h and the solution was allowed to warm to 25°C during 6 h. Methanol (5 mL) was added and the solvent was removed on a rotary evaporator. The red oily residue

was taken up in CH_2Cl_2 (100 mL), washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness left a light brown oil which solidified on further drying with a vacuum pump. Chromatography on alumina with 10% CH_2Cl_2 in hexane gave a 2 g mixture of unreacted 34 and the methyl tribromo-p-cresolate 65.¹⁹ Proton NMR spectrum of this mixture and its weight were used to calculate the yield of 65 (0.9 g, 32%; 42% with respect to recovered starting 34, of Table 10, p. 73) and quantity of unreacted 34 (1.1 g, 24%). A pure sample of 65 was obtained from this mixture by gas chromatography at 250°C: mp of 65; 122-4°C (lit.¹⁹ 115°C); ^1H NMR (CDCl_3) δ 2.57 (s, 3 H), 3.83 (s, 3 H), 6.97 (s, 1 H). Final elution of the column with CH_2Cl_2 gave 1.226 g of an oil which solidified on standing. Washing of this solid with cold hexane gave 0.9 g (31%; 42% with respect to recovered 34) of the monoadduct 64: mp 149-151°C ($\text{CH}_2\text{Cl}_2/\text{MeOH}$); ^1H NMR (CDCl_3) δ 1.97 (s, 6 H), 2.43 (s, 3 H), 3.70 (s, 3 H), 6.63 (br s, 2 H); mass spectrum, m/e (relative intensity) 374 (M^+ , 2), 331 (62), 293 (34), 252 (13), 125 (17), 43 (100).
Anal. Calc'd. for $\text{C}_{14}\text{H}_{14}\text{Br}_2\text{O}_2$: C, 44.95; H, 3.77; Br, 42.72. Found: C, 44.97; H, 3.62; br, 42.61.

27. Attempted Deuterium Incorporation in 65

To a solution of 4.4 g (10 mmol) of 34 and 7 g (73 mmol) of 2,5-dimethylfuran in a mixture of 100 mL of anhydrous THF

and 20 mL of dry benzene at -78°C under argon was added 6.5 mL of 1.96 M BuLi diluted with 30 mL of dry hexane over 2 h. The reaction mixture was stirred for 8 h during which time the temperature rose to 25°C . Methanol- d_1 (10 mL) was added and the mixture was worked up as in experiment #26. A mixture of the tribromo-p-cresolate 65 (0.45 g, 13%) and unreacted 34 (0.18 g, 4%) was separated by chromatography on alumina with 10% CH_2Cl_2 in hexane. Pure 65 was obtained from this mixture by glc at 250°C . This compound had the same NMR spectrum as that obtained for 65 in experiment #26 when the reaction was quenched with methanol. In order to differentiate the tribromo-p-cresolate 65 from its isomer 96,⁴³ this isomer 96 was prepared by the bromination of p-cresol at 0°C without catalyst (mp of the free phenol of 96; $96-8^{\circ}\text{C}$, lit.¹⁹ 101°C) followed by methylation of the free phenol as in the preparation of methyl tetrabromo-p-cresolat 34; ^1H NMR of 96 (CCl_4) δ 2.03 (s, 3 H), 3.77 (s, 3 H), 7.23 (s, 1H). The aromatic proton of 65 appeared at σ 6.97. The monoadduct 64 (1.9 g, 53%) was isolated by the final elution of the column with CH_2Cl_2 .

28. 1,2,3,4-Tetramethyl-5,8-dimethoxy-6,7-dibromo-1,4-dihydronaphthalene-1,4-endoxide (66)

A solution of tetrabromo-p-dimethoxybenzene 36 (2.24 g, 4.9 mmol) in 300 mL of anhydrous THF containing 3 g (24 mmol) of tetramethylfuran was cooled to -78°C under argon.

n-Butyllithium (3 mL, 1.9 M) diluted with 20 mL of dry hexane was added over 1 h. Two hours later, the mixture was quenched with 10 mL of methanol at the same temperature. After the removal of THF on the rotary evaporator, the residue was redissolved in CH₂Cl₂, washed with water and dried (Na₂SO₄). The solid left after evaporation of the solvent was shaken in hexane (100 mL) leading to the recovery of 0.53 g of starting 36. The hexane solution was passed down a column of alumina to give 0.6 (35%) of the tribromoarene 67; mp 98-9°C (lit.²¹ 101-2°C); ¹H NMR (CCl₄) δ 3.73 (s, 3 H), 3.78 (s, 3H), 6.87 (s, 1 H). Final elution of the column with CH₂Cl₂ gave 0.8 g (51%) of the monoadduct 66 as an oil which solidified on standing in the refrigerator for a few hours: mp 94-6°C (MeOH); ¹H NMR (CDCl₃) δ 1.63 (s, 6 H), 1.77 (s, 6 H), 3.71 (s, 6 H); mass spectrum, m/e (relative intensity) 418 (M⁺, 4), 375 (35), 339 (42), 124 (24), 43 (100).

Anal. Calc'd. for C₁₆H₁₈Br₂O₃: C, 45.96; H, 4.33; Br, 38.22. Found: C, 46.03; H, 4.36; Br, 38.28.

29. 1,4-Dimethyl-5,8-dimethoxy-6,7-dibromo-1,4-dihydro-naphthalene-1,4-endoxide (70)

To a suspension of the tetrabromoarene 36 (4.55 g, 10 mmol) and 7 g (73 mmol) of 2,5-dimethylfuran in 100 mL of anhydrous toluene cooled to -78°C under argon was added 5.2 mL of 2.2 M BuLi diluted with 30 mL of dry hexane over

2 h. The mixture was allowed to warm to 25°C in 3 h and the toluene was removed on a rotary evaporator. The white solid residue was dissolved in CH₂Cl₂, washed with water and dried (Na₂SO₄). The resulting solid was triturated with hexane and weighed 3 g. Chromatography of this solid on alumina using first a 10% mixture of CH₂Cl₂ in hexane followed by pure CH₂Cl₂ gave 1.72 g (37%) of unreacted 36 and 1.1 g (44%) of the monoadduct 70: mp 162-5°C (CH₂Cl₂/MeOH); ¹H NMR (CDCl₃) δ 1.97 (s, 6 H), 3.73 (s, 6 H), 6.67 (s, 2 H); mass spectrum, m/e (relative intensity) 390 (M⁺, 6), 347 (64), 311 (42), 43 (100).

Anal. Calc'd. for C₁₄H₁₄Br₂O₃: C, 43.11; H, 3.62; Br, 40.97. Found: C, 43.00; H, 3.48; Br, 40.98.

30. 1,4,5-Trimethyl-6,7-dibromo-8-chloro-1,4-dihydronaphthalene-1,4-endoxide (71); 63 and 97

A suspension of tetrabromo-p-chlorotoluene 35 (2.25 g, 5 mmol) in 300 mL of anhydrous toluene containing 3 g (31 mmol) of 2,5-dimethylfuran was maintained at 0°C under argon while 6 mL of 1.06 M BuLi diluted with 30 mL of dry hexane was added over 1 h. The reaction mixture was stirred at this temperature for 2 h and then 10 mL of water was added. Workup by the usual procedure for reactions in toluene gave 1.82 g of crude product which was gradient eluted over alumina with hexane, 10%, 50% and finally pure methylene chloride. The following fractions were collected: 97 (0.71 g,

38%; for data on this compound, see p. 118); 71 (0.45 g, 23%) and 63 (0.17 g, 12%). Both 71 and 63 were contaminated with each other. For 71: $^1\text{H NMR}$ (CCl_4) δ 1.53 (s, 3 H), 1.95 (s, 3 H), 2.42 (s, 3 H), 6.60 (s, 2 H); mass spectrum, m/e (relative intensity) 352 (M - 26, 4), 335 (1), 256 (3), 139 (7), 43 (100); high resolution mass spectrum calculated for $\text{C}_{13}\text{H}_{11}\text{Br}_2\text{ClO}$:

Found:

For 63: $^1\text{H NMR}$ (CCl_4) δ 1.53 (s, 3 H), 1.95 (s, 3 H), 2.31 (s, 3 H), 6.60 (s, 2 H), 6.95 (s, 1 H); mass spectrum, m/e (relative intensity) 300 (M^+ , 5), 285 (5), 274 (47), 257 (31), 176 (21), 141 (16), 115 (8), 43 (100); high resolution mass spectrum calculated for $\text{C}_{13}\text{H}_{12}\text{BrClO}$: 299.97506. Found: 299.97409.

31. Interception of the Dilithio-arene 72 in the Presence of Furan. Preparation of 2,5-Dibromo-p-dichlorobenzene
73

To a stirred suspension of tetrabromo-p-dichlorobenzene 37 (2.32 g, 5 mmol) in 100 mL of anhydrous ether at -78°C under argon was added 5 g (73 mmol) of furan. n-Butyllithium (5 mL, 2.3 M) diluted with 30 mL of dry hexane was added over 1.5 h and 10 min later, 20 mL of methanol was added to the reaction mixture. After warming to 25°C , the ether solution was washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness on a rotary evaporator left a yellow

tinted solid which was chromatographed on silica gel with hexane to give 0.93 g (61%) of the arene 73: mp 147-9°C (lit.³⁴ 146-8°C); ¹H NMR (CCl₄) δ7.53. No furan adduct was detected. When a similar reaction mixture was allowed to warm to room temperature before quenching, furan bisadduct 53 was obtained. Bisadduct 53 was also isolated when furan was added to the dilithio-derivative and the mixture was warmed to 25°C before work up (see experiment #18 for work-up and data on 53).

The use of methanol-d₁ to quench this reaction at -78°C gave 64% of the dideuterio-analog of 73; mp 145-7°C; mass spectrum, m/e (relative intensity) 306 (M⁺, 22), 227 (13), 146 (27), 111 (40), 76 (100).

32. p-Diacetyl Derivative 74 and Monoacetyl Derivative 75 of Tetrabromo-p-dichlorobenzene

In a similar procedure as for the preparation of 77, 2.59 g (5.3 mmol) of tetrabromo-p-dichlorobenzene 37 was reacted with 9 mL of 2.4 M BuLi at -78°C and the resulting dilithio-intermediate was intercepted at the same temperature with 3 mL (32 mmol) of acetic anhydride. Work-up gave a suspension of crystals in oil from which 0.62 g (30%) of the diacetyl derivative 74 and 0.22 g (12%) of the monoacetyl derivative 75 were isolated by chromatography on silica gel using first hexane followed by THF. The monoacetyl compound was initially liquid but solidified on standing. Analytical

sample of 75 was obtained by glc at 250°C: ^1H NMR (CCl_4) δ 1.80 (s, 3 H), 7.55 (s, 1 H); mass spectrum, m/e (relative intensity) 346 (M^+ , 23), 331 (89), 224 (37), 143 (46), 108 (100).

Anal. Calc'd. for $\text{C}_8\text{H}_4\text{Br}_2\text{Cl}_2\text{O}$: C, 27.70; H, 1.16.

Found: C, 27.74; H, 1.13.

For the diacetyl compound 74: mp 241-3°C (CCl_4): ^1H NMR (CCl_4) δ 2.48; mass spectrum, m/e (relative intensity) 388 (M^+ , 25), 373 (100), 331 (33), 303 (16), 251 (20), 223 (19), 188 (24), 108 (14), 43 (73).

Anal. Calc'd. for $\text{C}_{10}\text{H}_6\text{Br}_2\text{Cl}_2\text{O}_2$: C, 30.87; H, 1.56.

Found: C, 30.68; H, 1.47.

With acetyl chloride in place of acetic anhydride, 24% of 75 and 7% of 74 were obtained.

33. p-Bisphenylthio-2,5-dibromo-3,6-dichlorobenzene (76)

Butyllithium (5 mL, 2.4 M) diluted with 30 mL of dry hexane was added over 1 h to a suspension of 2.51 g (5.4 mmol) of tetrabromo-p-dichlorobenzene 37 in 300 mL of anhydrous toluene at -78°C under argon. The reaction mixture was stirred for another 2 h and then 2.30 g (10.5 mmol) of diphenyldisulfide dissolved in 30 mL of dry hexane was added over 10 min. After warming to 25°C (6 h), organometallic species were destroyed with 10 mL of methanol. Toluene was removed on a rotary evaporator, the residual oily suspension

was taken up in CHCl_3 , washed and dried (Na_2SO_4). Evaporation of the solvent left an oily suspension which after shaking with hexane and filtering, gave 1.1 g (39%) of 76. A pure sample of 76 was prepared by washing down a column of silica gel first with hexane to remove diphenyldisulfide and finally with a 3 : 2 mixture of hexane and CCl_4 : mp 209-212°C (CCl_4); ^1H NMR (CCl_4) δ 7.12 (br s); mass spectrum, m/e (relative intensity) 522 (M^+ , 100), 290 (89), 145 (28), 109 (22).

Anal. Calc'd. for $\text{C}_{18}\text{H}_{10}\text{Br}_2\text{Cl}_2\text{S}_2$: C, 41.49; H, 1.93.

Found: C, 41.56; H, 1.98.

Quenching the reaction mixture at -78°C with methanol after the addition of diphenyldisulfide gave 73 in 89% yield.

34. Interception of p-Dilithio Derivative of Tetrabromo-p-dichlorobenzene with Benzaldehyde. Preparation of 77

To a stirred suspension of 2.59 g (5.6 mmol) of tetrabromo-p-dichlorobenzene 37 in 300 mL of anhydrous toluene at -78°C under argon was added 16 mL of 1.4 M BuLi diluted with 30 mL of dry hexane over 1 h. The yellowish-milky mixture was stirred for another 2 h at -78°C after which 5 mL (50 mmol) of benzaldehyde was added by syringe. The reaction mixture was allowed to warm to 25°C in 6 h and toluene was removed on a rotary evaporator. The transparent yellow gel was washed with water and extracted with 300 mL

of ether. Concentration of the dried (Na_2SO_4) solution left shiny crystalline grains in excess benzaldehyde. The crystals were isolated by shaking with cold hexane and filtering to give 0.94 g (33%) of 77 as shiny grains: mp $242-6^\circ\text{C}$; ^1H NMR ($\text{DMSO}-d_6$) δ 3.30 (br s, 2 H), 6.67 (br s, 2 H), 7.20 (br s, 10 H); mass spectrum, m/e (relative intensity) 516 (M^+ , 100), 439 (26), 313 (18), 105 (8).
Anal. Calc'd. for $\text{C}_{20}\text{H}_{14}\text{Br}_2\text{Cl}_2\text{O}_2$: C, 46.46; H, 2.73.
 Found: C, 46.52; H, 2.77.

35. 1,4-Dibromo-2,5-dichloro-3,6-diiodobenzene (78)

Anhydrous toluene (100 mL) containing 2.31 g (5 mmol) of tetrabromo-*p*-dichlorobenzene 37 was cooled to -78°C under argon and 5 mL of 2.4 M BuLi diluted with 30 mL of dry hexane was added over 1 h. Two hours later at the same temperature, 2.64 g (10 mmol) of iodine dissolved in 25 mL of dry toluene was added over 5 min and the reaction mixture was allowed to warm to room temperature in 4 h. The brown slurry was washed with concentrated aqueous NaOH until the brown color faded, then with water and the toluene solution was dried (Na_2SO_4). Removal of toluene on a rotary evaporator gave a white powder: 2 g (72%); mp $265-7^\circ\text{C}$ (CCl_4); mass spectrum, m/e (relative intensity) 556 (M^+ , 11), 429 (5), 302 (30), 188 (56), 142 (47), 127 (13), 107 (100).
Anal. Calc'd. for $\text{C}_6\text{Br}_2\text{Cl}_2\text{I}_2$: C, 12.95. Found:

36. 2,5-Dichloro-3,6-dibromo-p-xylene (79)

A suspension of tetrabromo-p-dichlorobenzene 37 (2.41 g, 5.2 mmol) in 300 mL of anhydrous toluene under argon at -78°C was treated with 5 mL of 2.4 M BuLi diluted with 30 mL of dry hexane over 1 h. After two hours of stirring at this temperature, 3 mL (32 mmol) of dimethyl sulfate was added through a syringe. Four hours later, 10 mL of MeOH was added and the toluene was removed on a rotary evaporator. The solid residue was taken up in CH_2Cl_2 , washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness left crystalline needles which, after trituration with cold hexane, weighed 1.7 g (97%). Further purification was achieved by glc at 250°C : mp $229-231^{\circ}\text{C}$ (lit.³⁵ 226°C). There was no depression in the melting point of a mixture of this product with an authentic sample which was prepared by first chlorinating p-xylene followed by the bromination of the resulting 2,5-dichloro-p-xylene. The use of diethyl sulfate, ethyl bromide and ethyl iodide in a similar reaction to introduce ethyl groups gave polymeric substances and trace of 73 in each case.

37. Reaction of Tetrabromo-o-dichlorobenzene with Four Equivalents of BuLi. Preparation of 2,3-Dichloro-5,6-dibromobenzene (81)

To a stirred suspension of tetrabromo-o-dichlorobenzene 39 (2.38 g, 5.1 mmol) in 300 mL of anhydrous toluene at

-78°C under argon was added over 1 h, BuLi (16 mL, 1.36 M) diluted with 30 mL of dry hexane. After another 2 h at this temperature, the reaction mixture was quenched with 20 mL of methanol. Toluene was removed on a rotary evaporator and the solid residue was taken up in hexane (the remaining solid was water soluble). The hexane solution was washed with water and dried (Na₂SO₄). After evaporation of the hexane, the product was chromatographed on alumina with hexane to give 0.7 g (45%) of 81. No mono- or trilithiation products were detected. Further purification was achieved by glc at 250°C: mp 150-2°C. Mixed melting point with a sample prepared by the bromination of o-dichlorobenzene in CCl₄ using iron filings as catalyst showed no depression; ¹H NMR (CCl₄) δ 7.53; mass spectrum, m/e (relative intensity) 304 (M⁺, 100), 225 (47), 144 (36), 109 (27), 74 (30).
Anal. Calc'd. for C₆H₂Br₂Cl₂: C, 23.64; H, 0.66.
 Found: C, 23.71; H, 0.70.

A similar reaction but with two equivalents of BuLi gave 55% yield of 81.

38. 2,3-Dibromo-5,6-dichloro-p-xylene (82)

A slurry of tetrabromo-o-dichlorobenzene 39 (1.81 g, 3.90 mmol) in 200 mL of anhydrous toluene at -78°C under argon was stirred with 3 mL (32 mmol) of dimethyl sulfate and BuLi (7 mL, 1.4 M) diluted with 30 mL of dry hexane was added over 1 h. At the beginning of the addition, the

reaction mixture turned blue, deepened with the addition and discharged to milky white in 4 h after the addition.

Quenching the reaction with 10 mL of methanol and work-up as in experiment # 36 gave 1.2 g (93%) of 82. The analytical sample was prepared by glc at 250°C: mp 236-8°C; $^1\text{H NMR } \delta$ (CCl_4) σ 2.63; mass spectrum, $\underline{m/e}$ (relative intensity) 332 (M^+ , 100), 297 (19), 253 (87), 218 (7), 172 (40), 136 (81), 102 (37).

Anal. Calc'd. for $\text{C}_8\text{H}_6\text{Br}_2\text{Cl}_2$: C, 28.87; H, 1.82.

Found: C, 28.91; H, 1.82.

39. 1,2-Dibromo-3,6-diiodo-4,5-dichlorobenzene (83)

This compound was prepared by a procedure similar to that for the preparation of 78 from 2.42 g (5.2 mmol) of the tetrabromoarene 39, 7 mL of 1.8 M BuLi and 3 g (12 mmol) of iodine. The yellow product was decolorized by dissolving in toluene and boiling the solution with decolorizing carbon. After filtration, the filtrate was evaporated to dryness and the faintly yellow solid was chromatographed on alumina (Activity grade I) with CCl_4 . The yield of 83 was 1.4 g (48%): mp 268-270°C (CCl_4); mass spectrum, $\underline{m/e}$ (relative intensity) 556 (M^+ , 46), 509 (26), 430 (17), 302 (56), 142 (78), 107 (100).

Anal. Calc'd. for $\text{C}_6\text{Br}_2\text{Cl}_2\text{I}_2$: C, 12.95. Found: C, 13.08.

40. 2,5-Dibromo-p-difluorobenzene (85)

This compound was obtained in 77% yield from 2.08 g (5 mmol) of tetrabromo-p-difluorobenzene 38 in 100 mL of ether in a procedure similar to that described in experiment #31 but without furan; mp 60-2°C (lit.³⁶ 65-6°C).

41. Attempted Interception of the Dilithio Derivative of Tetrabromo-p-dichlorobenzene with α -Bromoesters

In a procedure similar to that for experiment #34, 2.49 g (5.38 mmol) of tetrabromo-p-dichlorobenzene 37 was treated with 8 mL of 2.4 M BuLi and quenched with 2 g (12 mmol) of ethyl bromoacetate. Work-up gave 1.6 g (64%) of 37. The odor of ethyl acetate was strong during the aqueous work-up.

A similar result was obtained with ethyl α -bromopropionate.

42. Preparation of the Trihalo-pseudocumene 87

Dimethyl sulfate (3 mL, 32 mmol) was added to a suspension of 2.40 g (5.2 mmol) of tetrabromo-o-dichlorobenzene 39 in 300 mL of anhydrous toluene at -78°C under argon and 16 mL of 1.36 M BuLi diluted with 30 mL of dry hexane was added over 1.5 h. A blue color developed during the addition, deepened with further addition and faded towards the end. The reaction mixture was stirred for an additional 3 h after

which time the reaction mixture became milky white. Methanol (10 mL) was added and toluene was removed on a rotary evaporator. The white solid residue was shaken in hexane and the hexane extract was washed with water and dried (Na_2SO_4). Evaporation of the solution to dryness left white needles which after trituration with cold hexane and drying, weighed 1.21 g (87%). A sample of pure 87 was obtained by glc at 250°C: mp 215-7°C; ^1H NMR (CCl_4) δ 2.43 (s, 6 H), 2.55 (s, 3 H); mass spectrum, m/e (relative intensity) 268 (M^+ , 100), 233 (36), 187 (73), 115 (64). Anal. Calc'd. for $\text{C}_9\text{H}_9\text{BrCl}_2$: C, 40.34; H, 3.39. Found: C, 40.30; H, 3.27.

When dimethyl sulfate was added to the reaction mixture after metalation, the isolated yield of 87 was 55%. When six and nine equivalents of BuLi and 6 mL (64 mmol) of dimethyl sulfate were used as in the described procedure, the yields of 87 were 89% and 83% respectively.

43. p-Dichlorodurene (91)

A slurry of tetrabromo-p-dichlorobenzene 37 (2.36 g, 5.1 mmol) in 300 mL of anhydrous THF containing 6 mL (64 mmol) of dimethyl sulfate at -78°C under argon was treated with 25 mL of 2.4 M BuLi diluted with 30 mL of dry hexane. The reaction mixture was allowed to warm to room temperature in 8 h and then it was quenched with 30 mL of methanol.

Removal of THF, extraction of the solid residue with hexane, washing with water and drying (Na_2SO_4) led to 0.92 g (89%) of 91 as crystalline needles: mp $193-5^\circ\text{C}$ (lit.³⁵ $189-190^\circ\text{C}$); ^1H NMR (CCl_4) δ 2.33.

44. Dichloroprehnitene (92)

In a similar procedure as for experiment #43, a solution of pseudocumene 87 (0.96 g, 3.6 mmol) in 100 mL of anhydrous THF containing 2 mL (21 mmol) of dimethyl sulfate was treated with 4 mL of 2.4 M BuLi to give 0.6 g (95%) of 92: mp $194-6^\circ\text{C}$ (lit.³⁵ 195°C); ^1H NMR (CCl_4) δ 2.18 (s, 6 H), 2.35 (s, 6 H).

45. Attempted Trimetalation of Hexabromobenzene. Preparation of 2,3,5,6-Tetrabromobenzene (93)

In a procedure similar to that for the preparation of 81 (experiment #37), hexabromobenzene (3.17 g, 5.70 mmol) was reacted with 10 mL of 2.2 M BuLi and the reaction mixture was quenched with methanol. Unreacted hexabromobenzene (1 g) and 1.1 g (49%) of 93 were isolated: mp 175°C (lit.³⁵ 180°C); ^1H NMR(CDCl_3) δ 7.78.

46. Monolithiation of Tetrabromo-p-chlorotoluene. Preparation of the Tribromoarene 97

A slurry of tetrabromo-p-chlorotoluene 35 (2.21 g, 5 mmol) in 300 mL of anhydrous toluene at -78°C under argon was reacted with 5 mL of 1.2 M BuLi diluted with 30 mL of dry hexane. The mixture was stirred for 2 h after the addition of BuLi (1 h) and 10 mL of methanol was added. Work-up of the reaction mixture according to the procedure for reactions in toluene gave 1.5 g of a mixture of 97 and the starting 35 in the ratio of 3 : 1 (estimated from the proton NMR spectrum of the mixture) respectively. A trace of the m-diprotio-arene 99 was also observed from the crude. The yield of 97 was calculated from the proton NMR spectrum and total weight of product as 62%. Pure sample of 97 was obtained by glc at 250°C: mp 95-6°C; ^1H NMR (CCl_4) δ 2.63 (s, 3 H), 7.53 (s, 1 H); mass spectrum, m/e (relative intensity) 364 (M^+ , 100), 283 (87), 203 (33), 123 (26); high resolution mass spectrum calculated for $\text{C}_7\text{H}_4\text{Br}_3\text{Cl}$: Found:

When a similar reaction run with 2.36 g (5.3 mmol) of 35 was quenched with methanol- d_1 , 1.8 g of a 2 : 1 mixture of 97-d₁ and starting 35 was obtained. The signal at 7.53 was missing but the aromatic signal of the trace m-diprotio-arene could still be observed. For data on 97-d₁ and 99, see the next experiment.

47. Reaction of Tetrabromo-p-chlorotoluene with Two Equivalents of BuLi. Preparation of 97-d₁ and 99

In a similar procedure as for experiment #46, 2.33 g (5 mmol) of tetrabromo-p-chlorotoluene 35 was treated with 7 mL of 2.4 M BuLi. The reaction mixture was quenched with 10 mL of methanol-d₁ and work-up gave 1.62 g of a product mixture consisting of 72% of 97-d₁ and 4% of 99 (by proton NMR spectrum - methyl signals). Pure samples of 97-d₁ and 99 were obtained by glc at 250°C: for 97-d₁; mp 98-100°C; ¹H NMR (CCl₄) δ 2.62; mass spectrum, m/e (relative intensity) 365 (M⁺, 100); high resolution mass spectrum calculated for C₇H₃DBr₃Cl:

Found:

For 99: mp 95-7°C; ¹H NMR (CCl₄) δ 2.45 (s, 3 H), 7.28 (s, 2 H); mass spectrum, m/e (relative intensity) 284 (M⁺, 84), 205 (86), 123 (70), 89 (100) 63 (69); high resolution mass spectrum calculated for C₇H₅Br₂Cl:

Found:

48. Attempted Oxidative Demethylation of the Bisadduct 28

The bisadduct 28 (0.3 g, 1.1 mmol) was dissolved in 50 mL of acetonitrile and the stirred solution was cooled in an ice bath. Ceric ammonium nitrate (1.1 g, 2 mmol) dissolved in a mixture of 25 mL of water and 25 mL of acetonitrile was added dropwise in 0.5 h. After 2 h at 0°C, the reaction mixture was allowed to warm to 25°C in 15 min. Water (50 mL) was added and the mixture was extracted with

500 mL of CH_2Cl_2 in two portions of 250 mL. The extract was dried (Na_2SO_4) and removal of the solvent gave 0.2 g of 28.

49. Endoxide Ring Opening of the Bisadduct 28. Preparation of 103

To a 100-mL flask was added 20 mL of methanol, 0.42 g (1.6 mmol) of the bisadduct 28 and 2 mL of concentrated HCl. The suspension was gradually heated on a water bath for 2 h. On removal of the solvent from the yellowish-brown solution, a dark green powder was left. The solid was redissolved in 20 mL of pyridine giving a green solution. An exothermic reaction took place on the addition of 20 mL of acetic anhydride and the reaction mixture turned brown. After 6 h of gentle reflux, the solvent mixture was evaporated on a rotary evaporator. The brown solid residue was washed with water to give 0.44 g (78%) of 103 as a yellow powder. The product had low solubility in most common solvents and could not be purified any further. It was not possible to separate the isomers of 103 which were formed even when an isomer of 28 was used: mp - the solid started to sublime at 210°C and left a black residue at 220°C which melted at 235-8°C to a brown liquid; because of low solubility in CDCl_3 the proton NMR spectrum of 103 consisted of broad peaks at δ 2.4; 4.0; 7.4 and 8.3; mass spectrum, m/e (relative intensity) 354 (M^+ , 7), 326 (22), 312 (16), 284 (14), 270 (3), 269 (100), 255 (83), 239 (28), 139 (14); IR (CDCl_3): 3000, 1770, 1355,

1210, 1050 cm^{-1} ; high resolution mass spectrum calculated for $\text{C}_{20}\text{H}_{18}\text{O}_6$: 354.10921. Found: 354.11034.

50. Bisepoxidation of Bisadduct 32. Preparation of 104

To 25 mL of CH_2Cl_2 was added 0.3 g (1.25 mmol) of the bisadduct 32. The solution was cooled to 0°C and 0.5 g (2.96 mmol) of m-CPBA in 20 mL of CH_2Cl_2 was added over 20 min. Stirring was continued for 8 h during which time the temperature rose to 25°C and the reaction mixture became a milky suspension. Methylene chloride (300 mL) was added to dissolve much of the precipitate and the solution was washed successively with aqueous NaHSO_3 , NaHCO_3 and water. After drying (Na_2SO_4) and evaporation to dryness, 0.24 g (71%) of 104 was collected. The product had low solubility in most common solvents and could not be purified further; mp - a color change was observed at 206°C and the solid melted with bubbling at $220\text{-}3^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.293 (6 H), 3.508 (4 H), 5.219 (4 H); mass spectrum, m/e (relative intensity) 270 (M^+ , 10), 241 (100), 212 (67), 183 (36), 128 (9); high resolution mass spectrum calculated for $\text{C}_{16}\text{H}_{14}\text{O}_4$: 270.08931; Found: 270.08921.

51. Bisepoxidation of the Bisadduct 28. Preparation of 105

In a similar procedure as for experiment #50, 0.29 g (1.1 mmol) of bisadduct 28 gave 0.28 g (87%) of 105: mp -

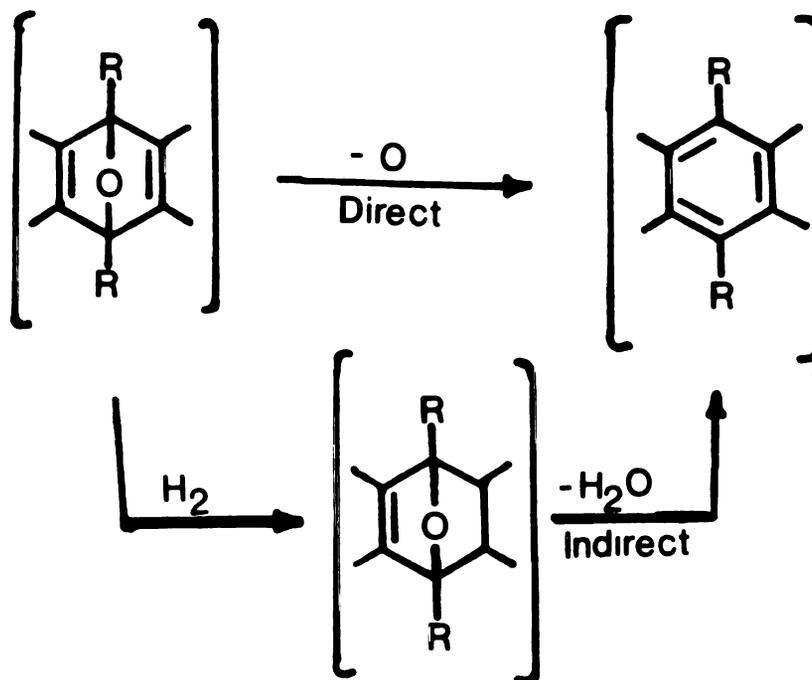
the solid started to darken at 210°C. Bubbling was observed as it started to melt at 223°C; ^1H NMR (CDCl_3) δ 3.50 (s, 4 H), 3.83 (unresolved, 6 H), 5.23 (2s, 4 H); mass spectrum, $\underline{m/e}$ (relative intensity) 302 (M^+ , 6), 273 (100), 229 (66), 214 (29), 115 (20); high resolution mass spectrum calculated for $\text{C}_{16}\text{H}_{14}\text{O}_6$: 302.07838; Found: 302.07904.

PART II

DEOXYGENATION OF ARENE-1,4-ENDOXIDES WITH LOW-VALENT
TRANSITION METALS

INTRODUCTION

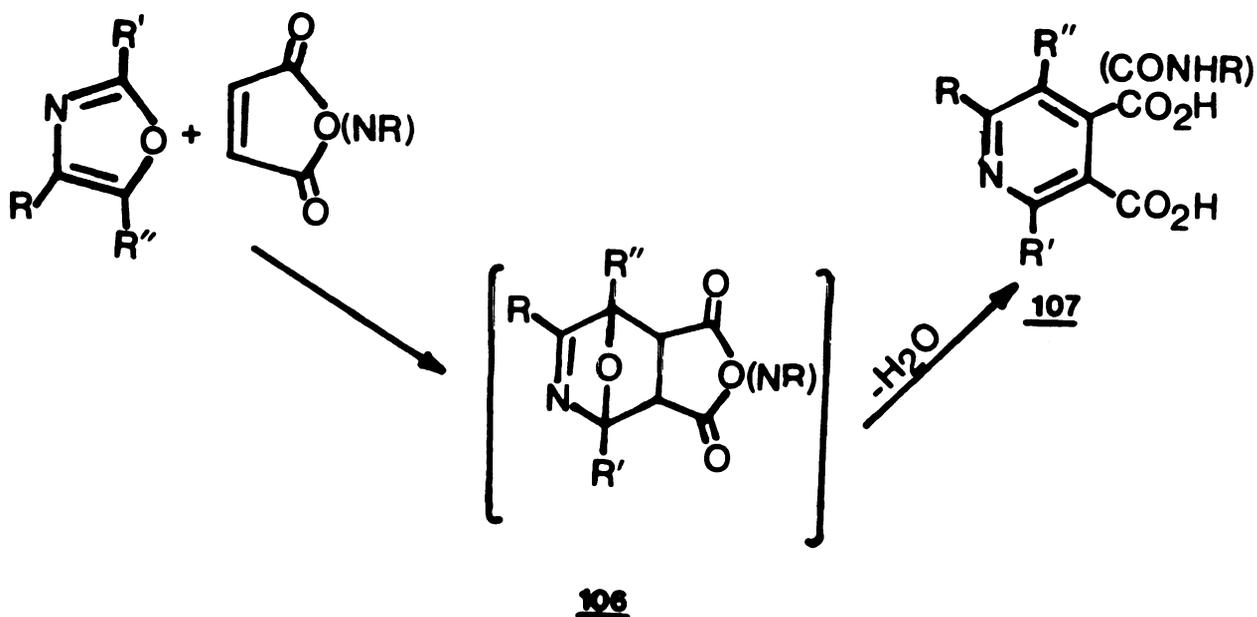
Arene-1,4-endoxides can function as useful synthetic precursors to acenes. Over the years, many methods which can be classified as (a) direct or (b) indirect have been developed for the aromatization step (Scheme 19).



Scheme 19

A. Direct Deoxygenation of Arene-1,4-endoxides

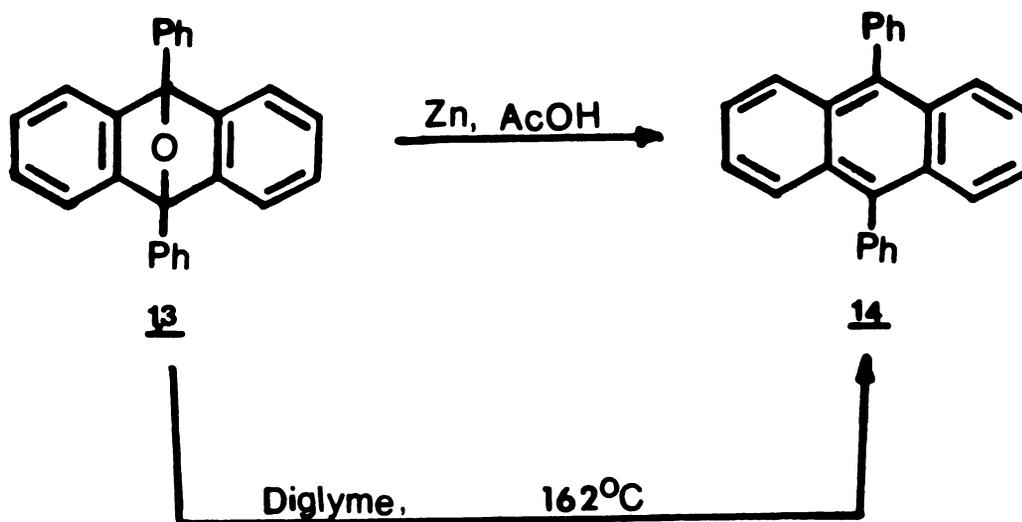
Reactions which proceed with the spontaneous loss of oxygen either in the elemental or in the combined form as water are uncommon. One such aromatization is the preparation of pyridine-3,4-dicarboxylic acids (cinchomeric acids) 107 or their imides by the reaction of maleic anhydride or maleimide with oxazoles.²⁶ The oxygen-bridged compound 106



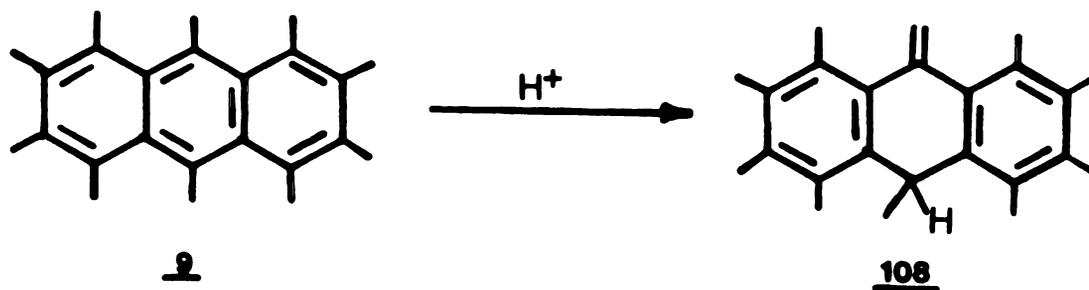
was not isolated but supposedly lost a molecule of water spontaneously to give the aromatic diacids or imides 107. This water was responsible for the hydrolysis of the anhydrides and imides into the isolated free acids and amides.

The deoxygenation of dibenzo-endoxide 13 was effected in high yield by treatment with zinc in acetic acid¹² and in a much poorer yield by heating in diglyme at 162°C for

2 h.¹⁴ Acidic conditions associated with the zinc/acetic acid method, however, cannot be used with highly strained



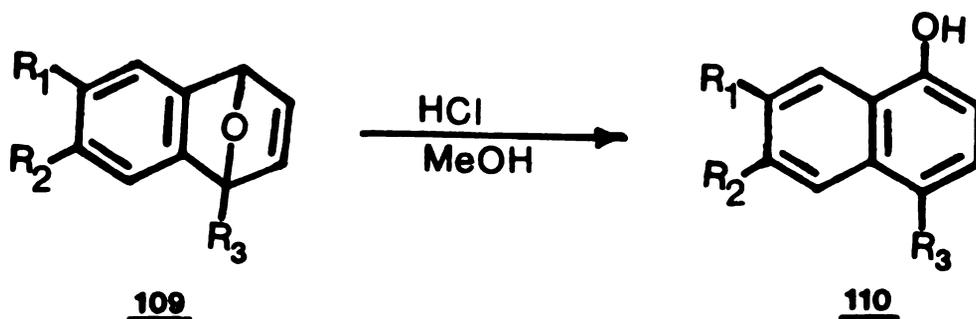
acenes because loss of aromaticity in one of the rings may



occur.⁹ The thermal method is not even general for variously substituted 9,10-dihydroanthracene-9,10-endoxides.

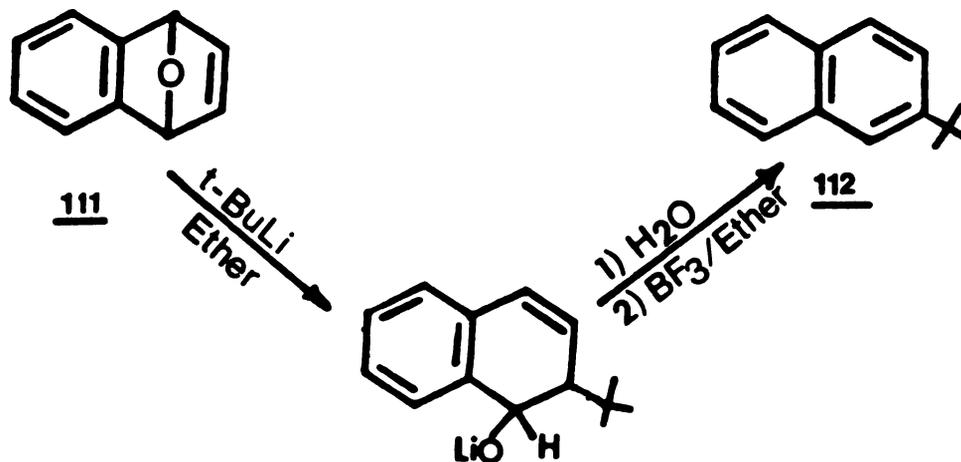
The direct treatment of arene endoxides with acids, usually HCl in methanol, leads to aromatization with the

retention of the oxygen as an α -substituent on the acene.⁴⁵ For example, the endoxide 109 ($R_1 = \text{CH}_3$, $R_2 = R_3 = \text{H}$) isomerized to the α -naphthol 110 ($R_1 = \text{CH}_3$, $R_2, R_3 = \text{H}$) on warming in MeOH containing a little hydrochloric acid.



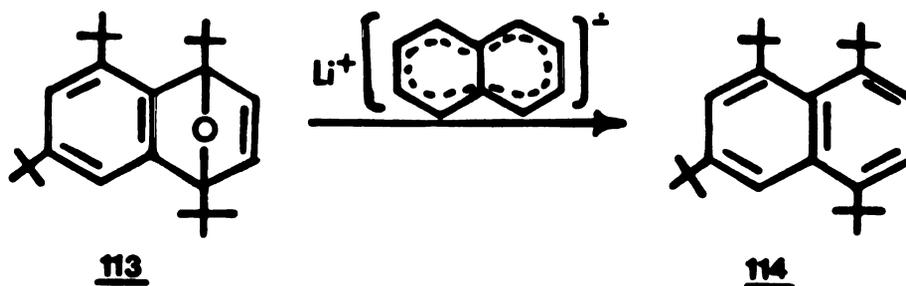
When both 1,4-positions are substituted, this aromatization reaction follows a complex pattern.²³ Even though this transformation leads to aromatization, it is not a deoxygenation.

In connection with the direct methods of deoxygenation involving acidic media, it is relevant to mention the work of Caple and co-workers⁴⁷ on the aromatization of the naphthalene-1,4-endoxide 111. The reaction of 111 with $t\text{-BuLi}$ in ether, followed by acidic work-up, gave 2- t -butylnaphthalene 112. This mode of dehydrative aromatization, however,



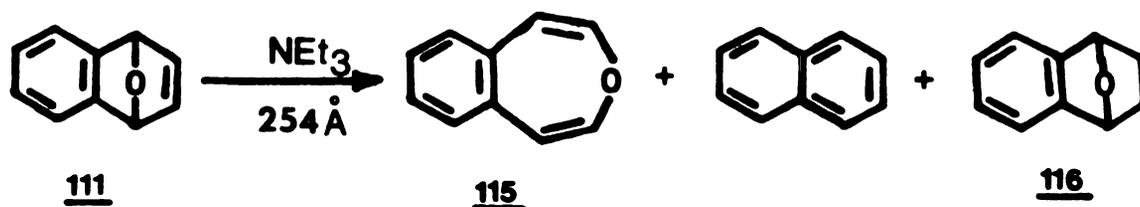
will not apply to endoxides blocked at the 2,3-positions with substituents.

Of all the non-acidic methods of deoxygenative aromatization, the use of naphthalenides⁴⁸ and amalgams⁴⁹ of group IA metals has shown the most promise for the preparation of strained acenes. Deoxygenation of the highly hindered endoxide 113 with lithium naphthalenide was achieved in high yield without the loss or migration of the strained



butyl groups in the resultant tetra-*t*-butylnaphthalene 114. A major disadvantage of this procedure is that equivalent amounts of naphthalene are produced during the reaction, and the naphthalene sometimes cannot be easily separated from the desired product.

The direct deoxygenation of arene endoxides could possibly occur as an extrusion reaction, i.e., as a cycloreversion. Such a reaction was anticipated by Woodward and Hoffman.⁵⁰ An examination of molecular models of naphthalene endoxide 111 for orbital symmetry considerations, by Polovsky,⁴⁸ indicated that a photochemical 'non-linear' disrotatory reaction might lead to oxygen extrusion. Previously, Ziegler and Hammond⁵¹ found oxepin 115 as the only low molecular weight product in this reaction but

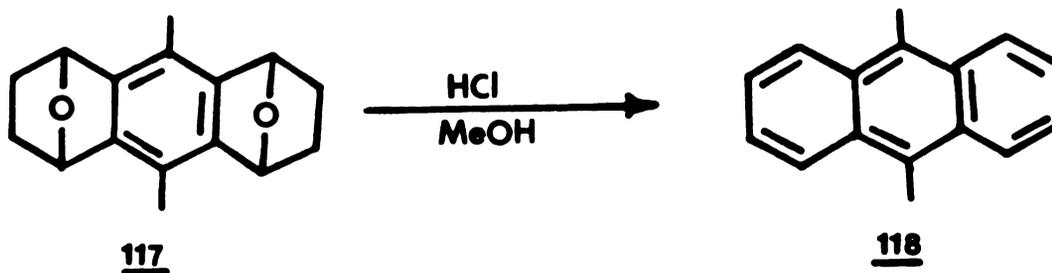


Polovsky was able to isolate and identify naphthalene and the tetrahydronaphthalene endoxide 116, both formed in very low yields under a variety of reaction conditions. Even

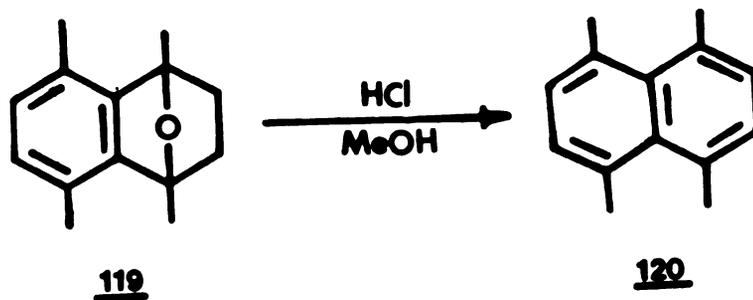
though the isolation of naphthalene implied that a deoxygenation had taken place, it was not clear from the results whether an extrusion reaction was responsible or whether some intermediate was involved. The low yield (less than 1%) and conversion (less than 18%) make this process inadequate for synthetic purposes.

B. Deoxygenation of Arene-1,4-endoxides by Indirect Methods

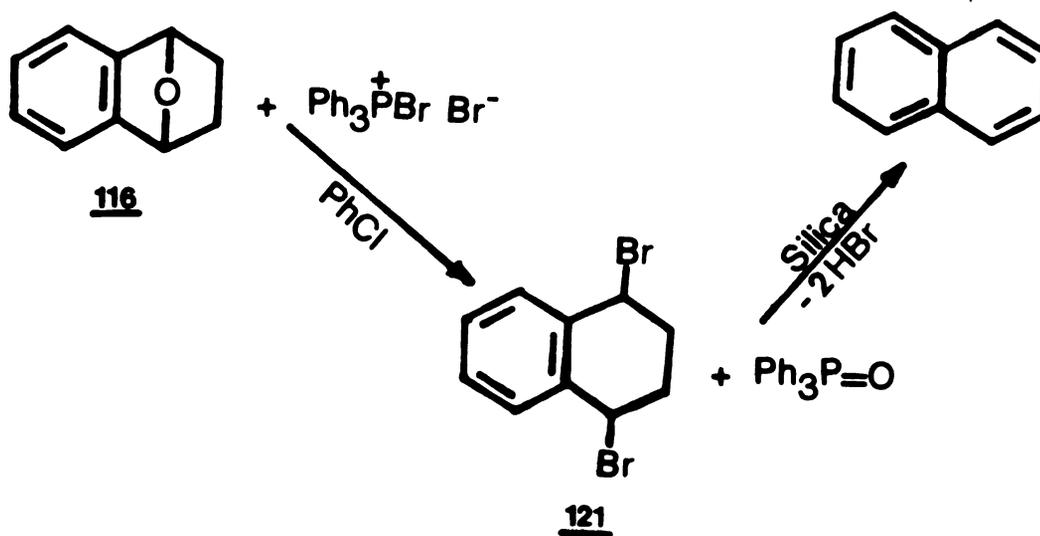
These methods have found wide use for simply substituted arene endoxides. They involve initial reduction of the unconjugated double bond followed by acid-catalyzed dehydration. The use of methanolic HCl for the dehydration step is illustrated in the synthesis of 9,10-dimethylantracene 118¹⁶ from the octahydroanthracene diendoxide 117



and 1,4,5,8-tetramethylnaphthalene 120¹⁰ from the tetrahydronaphthalene endoxide 119.

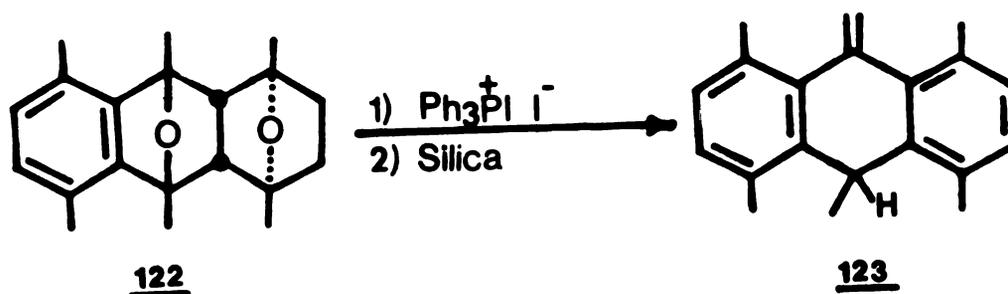


Bromotriphenylphosphonium bromide was introduced by DeWit and co-workers⁵² as a reagent for a two-step dehydration procedure (Scheme 20). The second step of this

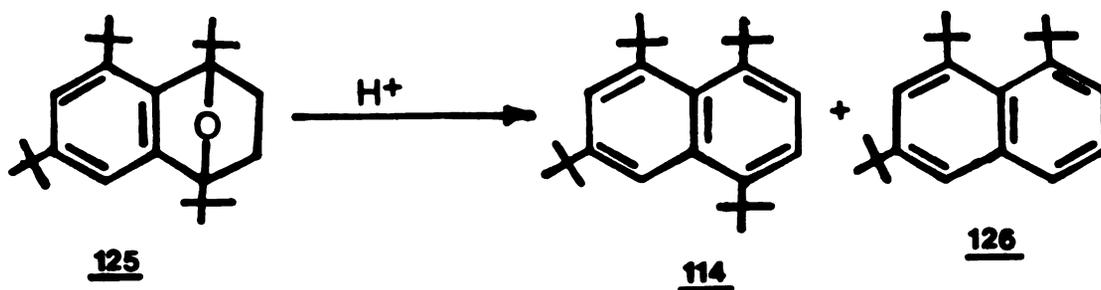


Scheme 20

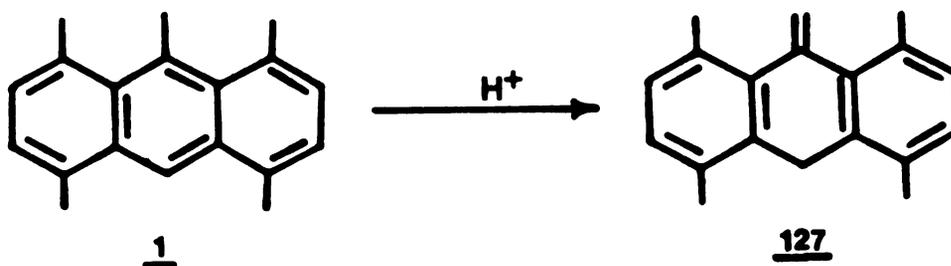
procedure is the dehydrobromination of 121 over silica gel. The first application of this method, even with a modified and presumably more effective reagent, to a peri-substituted substrate revealed that it engenders the same problem as with the acidic reagents. Thus refluxing a solution of 122 and iodotriphenylphosphonium iodide in dimethylformamide (DMF) and passing the reaction mixture through silica gel gave 123,⁵³ and not the desired hexamethylanthracene 136.



A variety of modern ether cleaving reagents⁵⁴⁻⁵⁷ have also been used for the dehydration of reduced arene endoxides. Aside from requiring at least two steps, the indirect process is not applicable to dibenzo-endoxides and acid-catalyzed dehydration often leads to substituent loss⁵⁸ as illustrated by the presence of the tri-*t*-butylnaphthalene 126 in the aromatization of 1,4,6,8-tetra-*t*-butyl-1,2,3,4-tetrahydronaphthalene-1,4-endoxide 125, by this method, to tetra-*t*-butylnaphthalene 114. Hydrogen migrations are inevitable in acidic media for strained aromatic hydrocarbons when benzylic protons are present.^{3,9,10}



Because of the problems associated with the use of



existing methods for the deoxygenation of arene-1,4-endoxides as presented in the above overview, it is apparent that the effective use of arene-1,4-endoxides as precursors for peri-substituted acenes requires the development of a new or modified reagent or method to effect the aromatization, preferably one which could be carried out in a neutral medium.

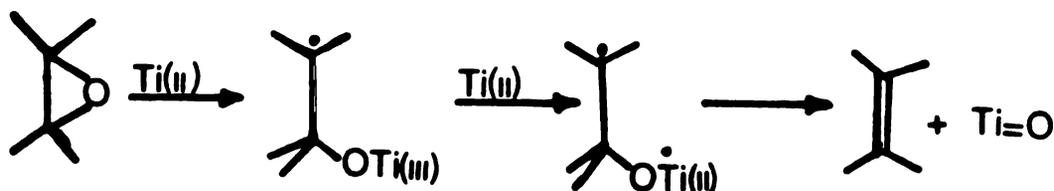
c. Low-valent Transition Metals in the Deoxygenation of Epoxides

During recent years, many reagent systems have been developed for converting epoxides to alkenes and the most successful of these are the low-valent forms of metals in the transition series, especially titanium,⁵⁸ chromium,⁵⁹ iron⁶⁰

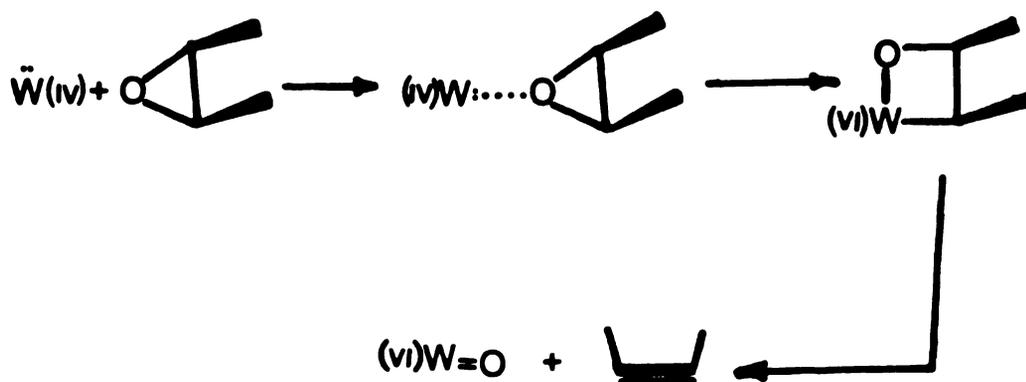
and tungsten.⁶¹ The low-valent species are prepared by treating the most available halide of the metals with reducing agents like LiAlH_4 and BuLi which have been shown to give better results than other hydride sources.⁶²



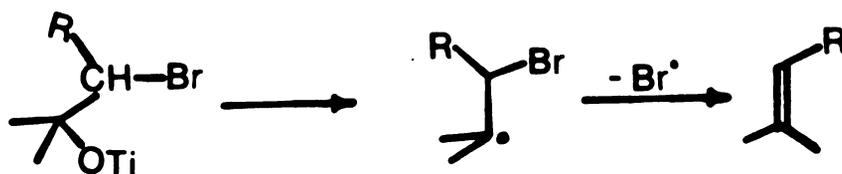
Deoxygenations were found to be stereospecific with tungsten but not with iron and titanium. This difference in the stereochemical outcome of the reaction depending on the metal used has been rationalized mechanistically.^{58,61} Whereas deoxygenation with low-valent iron and titanium go through



a radical pathway, the reaction with tungsten involves a metallocycle. The radical mechanism is especially favored



when the M-O bond is formed next to a group that can undergo further reaction (Scheme 21) or a group that can stabilize



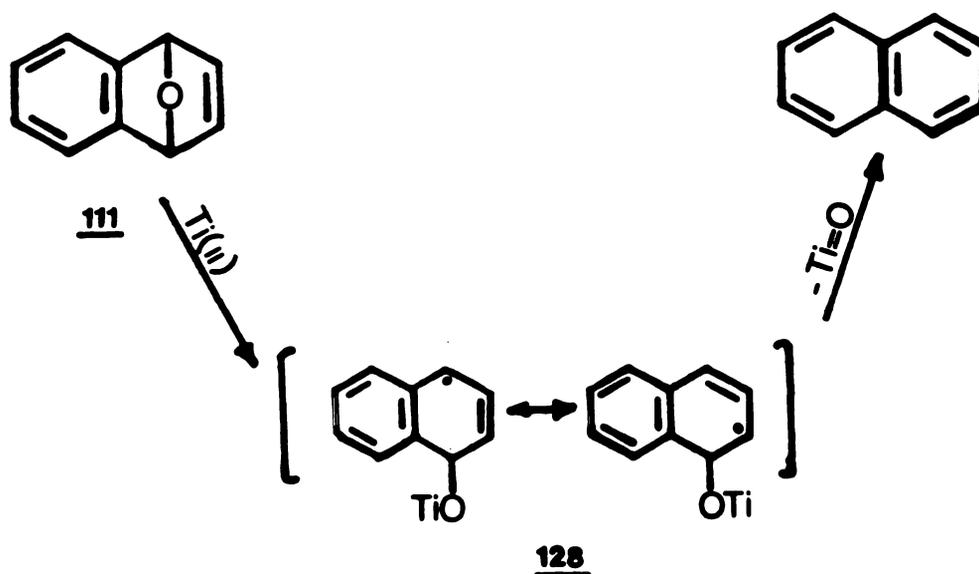
Scheme 21

a free radical center. For example, the greater reactivity of styrene oxide over cyclohexene oxide was rationalized by



the stabilizing influence of the phenyl group on the radical center.⁶⁰

The radical mechanism proposed for these deoxygenation processes appears to be compatible with application of these reagents to arene-1,4-endoxides (Scheme 22), especially as stereochemistry is irrelevant in the final products. Hence if this mechanism operated, the radical 128 would be expected



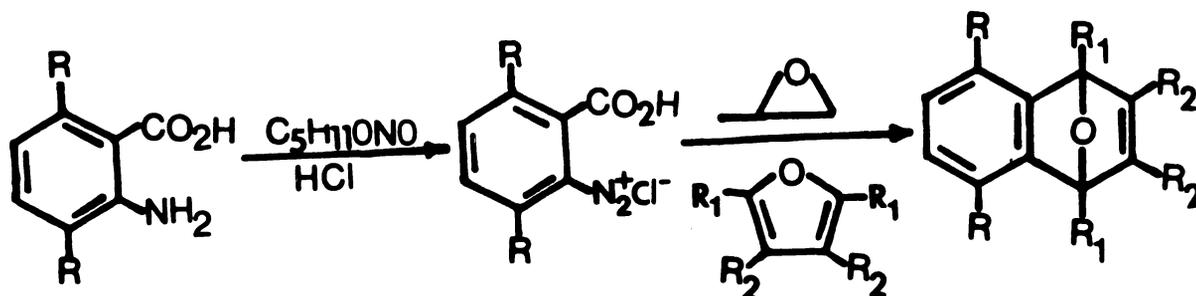
Scheme 22

to be stabilized by resonance with both the benzene ring and the isolated double bond. Loss of $M=O$ from this intermediate (128), as was the case for the alkene oxides, should lead to deoxygenation and give naphthalene.

In this part of the thesis, the exploration of this proposal, which led to the development of low-valent transition metals as effective reagents for the deoxygenative aromatization of arene endoxides, will be described.

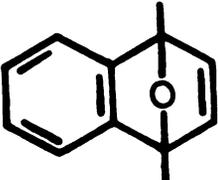
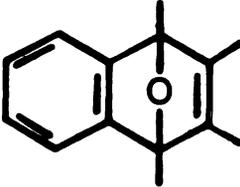
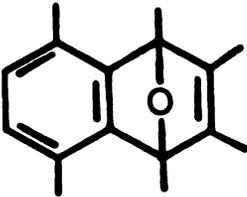
RESULTS AND DISCUSSION

In order to have a complete series of substrates for the investigation of the applicability of this reagent system to the deoxygenation of arene endoxides, the following naphthalene-1,4-endoxides were prepared by generating benzyne from the appropriate diazonium carboxylates in the presence of the appropriate furans (Table 11).



Of all the probable transition metals and their oxidation states that could be used in this way, titanium trichloride, tungsten hexachloride and ferric chloride were chosen on the basis of ease of handling and availability. Extensive exploratory studies were carried out with ferric chloride and the findings were then applied to the reactions with tungsten hexachloride and titanium trichloride.

TABLE 11
YIELDS OF NAPHTHALENE-1,4-ENDOXIDES

Entry	Endoxide	Yield (%)
1	 <u>129</u> ²³	66
2	 <u>133</u> ²³	35
3	 <u>135</u>	36

The preliminary experiments with reduced iron showed that the conditions of Fujisawa and co-workers⁶⁰ needed

to be modified for optimal and predominate yield of one product. For example, treatment of the tetramethylfuran bisadduct 43 (see Table 12 for structure) according to their procedure gave a mixture of two substances which could not be separated easily for identification. If the amount of n-BuLi was less than three molar equivalents per mole of ferric chloride, the endoxides were recovered unchanged. The most effective ratio of substrate to ferric chloride was found to be 1 : 3. When the ratio of substrate to ferric chloride was greater than the above, some endoxide and/or partially deoxygenated products resulted, especially with the anthracene diendoxides. The optimal ratio of substrate : metal chloride : n-BuLi was found to be 1 : 3 : 12 per mole-atom of oxygen in the substrate (this refers only to endoxide-type oxygen in the molecule).

Consequently, the general procedure for carrying out the deoxygenation of arene-1,4-endoxides using reduced iron, titanium and tungsten involves the addition of n-BuLi to a slurry or solution of the metal chloride in ether or THF at -78°C under argon or nitrogen. After one or two hours of stirring at this temperature, the mixture was allowed to warm to room temperature and then, a solution of the substrate in the appropriate solvent was added. The dark colored reaction mixture was stirred for the times given in Table 12. In some cases, the substrates were added prior to warm up to room temperature, but this generally

TABLE 12

DEOXYGENATION OF ARENE-1,4-ENDOXIDES WITH LOW-VALENT TRANSITION METALS

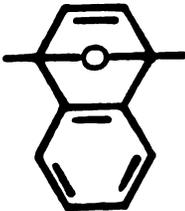
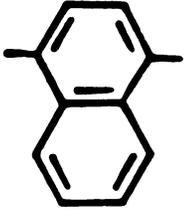
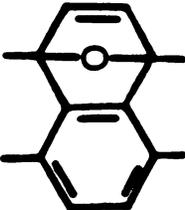
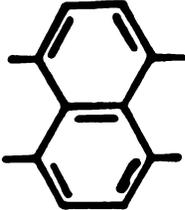
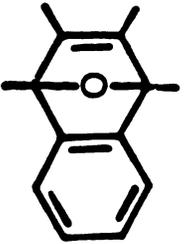
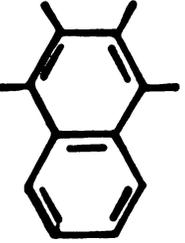
Entry	Substrate	Mol Ratio	Time (h)	Product	Yield %
1		1 : 3 : 12	6		81 ^a (81, 88) ^c
	<u>129⁴⁶</u>			<u>130⁶³</u>	
2		1 : 3 : 12	6		63 ^a
	<u>131¹⁰</u>			<u>132¹⁰</u>	
3		1 : 3 : 12	5		96 ^a 89 ^c , 55 ^b
	<u>133²³</u>			<u>134⁶⁴</u>	

TABLE 12 (Cont'd.)

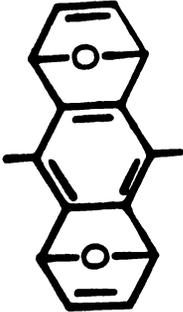
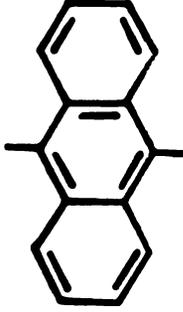
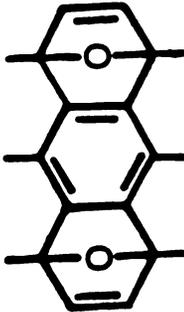
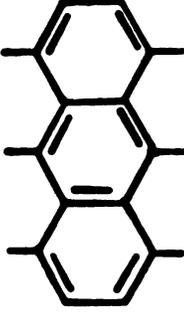
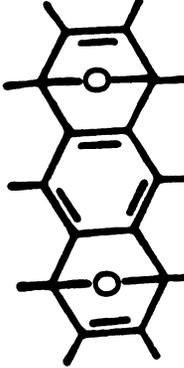
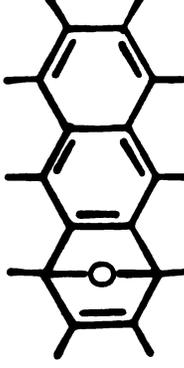
Entry	Substrate	Mol Ratio	Time (h)	Product	Yield %
4	 <u>32</u> ¹⁶	1 : 6 : 24	10	 <u>118</u> ¹⁶	56 ^a
5	 <u>42</u>	1 : 6 : 24	9	 <u>136</u>	40 ^a 16 ^c , 79 ^b
6	 <u>43</u>	1 : 6 : 24	10	 <u>137</u>	50 ^b

TABLE 11 (Cont'd)

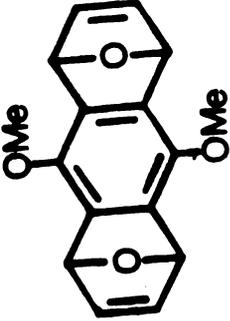
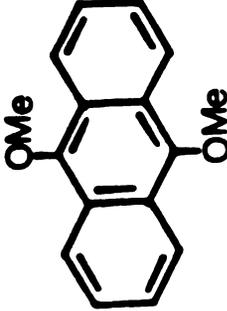
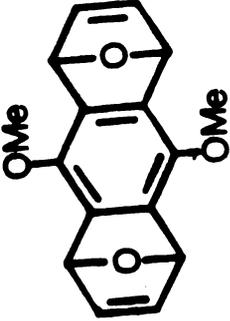
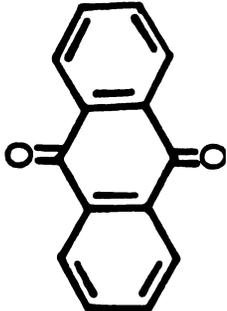
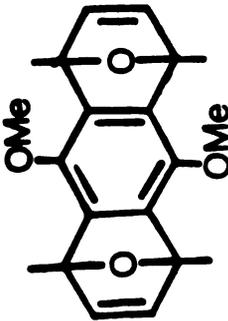
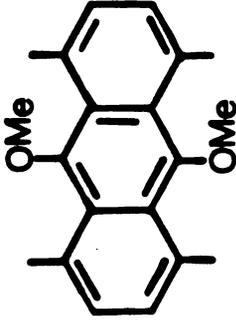
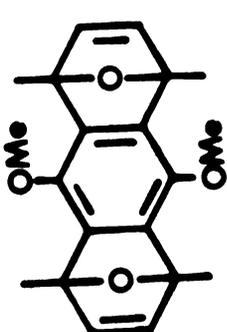
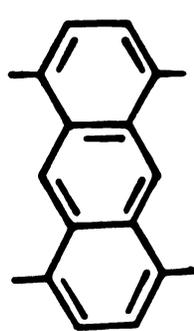
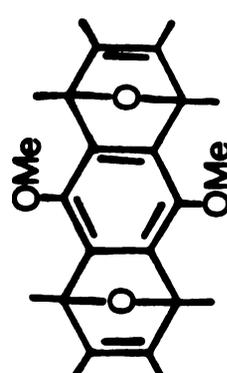
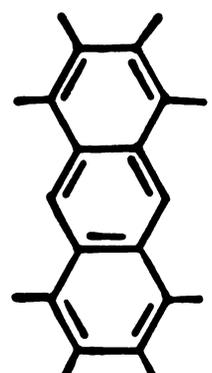
Entry	Substrate	Mol Ratio	Time (h)	Product	Yield %
7	 <chem>COC1=C(C2=CC=CC=C2)C(OC)=C3C=CC=CC=C31</chem> <u>28</u> ¹⁵	1 : 6 : 24	6	 <u>138</u> ⁶⁵	20 ^a 89 ^c
8	 <u>28</u>	1 : 6 : 24	48	 <u>139</u>	55 ^a
9	 <u>51</u>	1 : 6 : 24	24	 <u>140</u>	47 ^c

TABLE 11 (Cont'd)

Entry	Substrate	Mol Ratio	Time (h)	Product	Yield %
10	 <p style="text-align: center;"><u>51</u></p>	1 : 6 : 24	18	 <p style="text-align: center;"><u>141</u>^{1,66}</p>	60 ^a 54 ^b
11	 <p style="text-align: center;"><u>140</u></p>	1 : 6 : 24	12	 <p style="text-align: center;"><u>141</u></p>	97 ^b
12	 <p style="text-align: center;"><u>52</u></p>	1 : 6 : 24	90	 <p style="text-align: center;"><u>22,64</u></p>	63 ^a

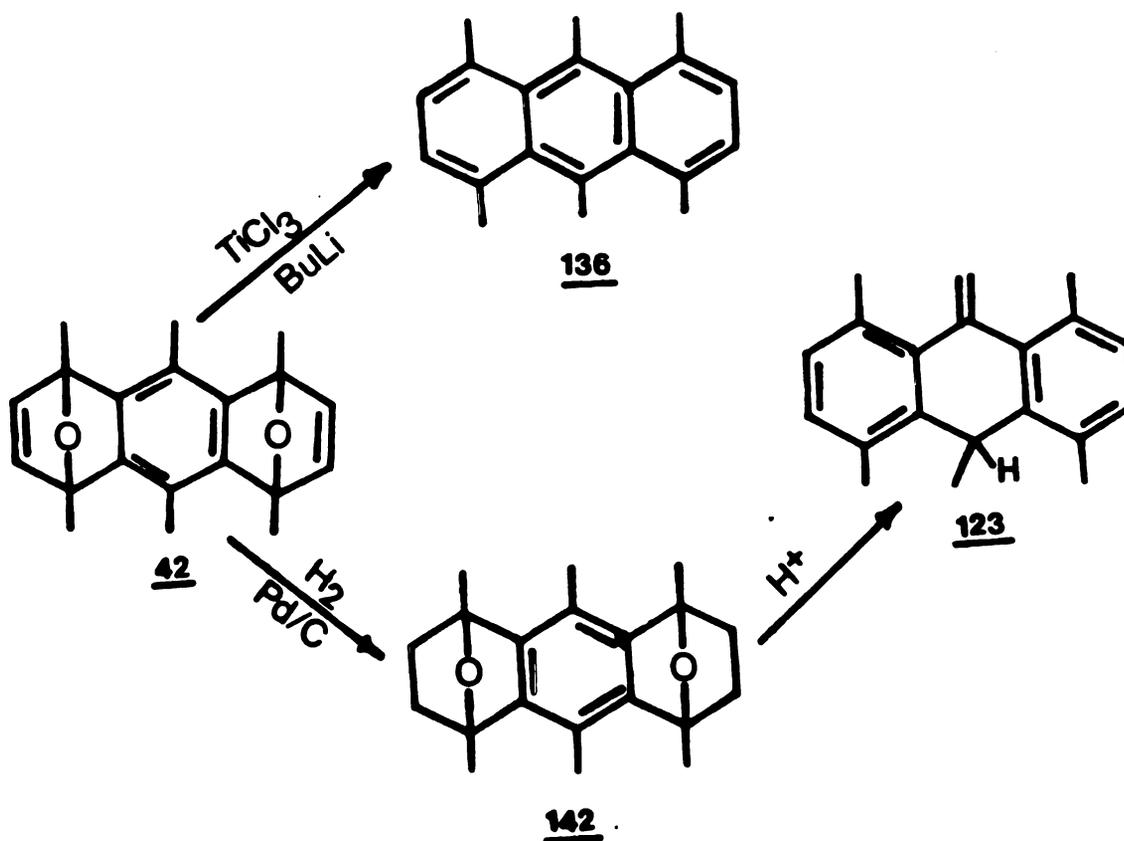
a. Yields with FeCl₃

b. Yields with TiCl₃

c. Yields with WCl₆

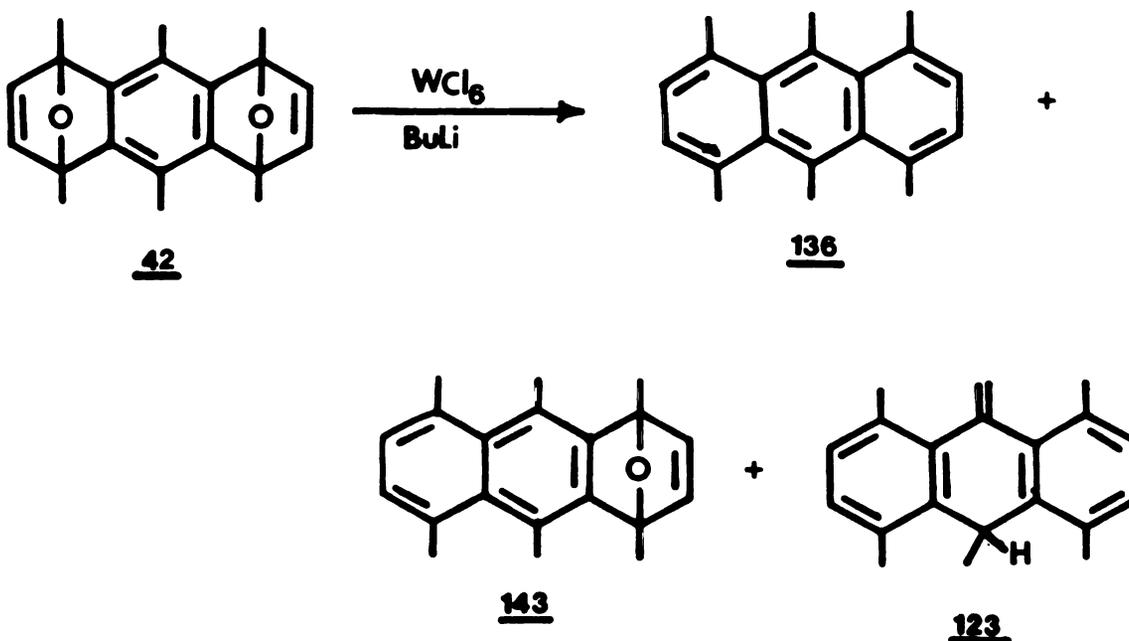
made no difference in the results. Work-up included suction filtration over a bed of neutral alumina (Activity grade II) to deactivate and remove the reduced metals, removal of the solvent and chromatography in most cases. The reactions leading to anthracenes were followed by thin layer chromatography (TLC) utilizing the blueish fluorescence of the products under ultraviolet (UV) light.

The examples in Table 12 illustrate that this method can be used effectively to aromatize naphthalene-1,4-endoxides and anthracene-1,4:5,8-diendoxides. Its special utility can be appreciated from the direct transformation of 42 into 136, a compound with multiple peri-interactions.



This hindered anthracene could not be prepared from 42 by the reduction-dehydration method, nor could it be obtained from other precursors such as 122⁵³ due to its easy rearrangement to 123 (see p. 132 for the structure of 122).

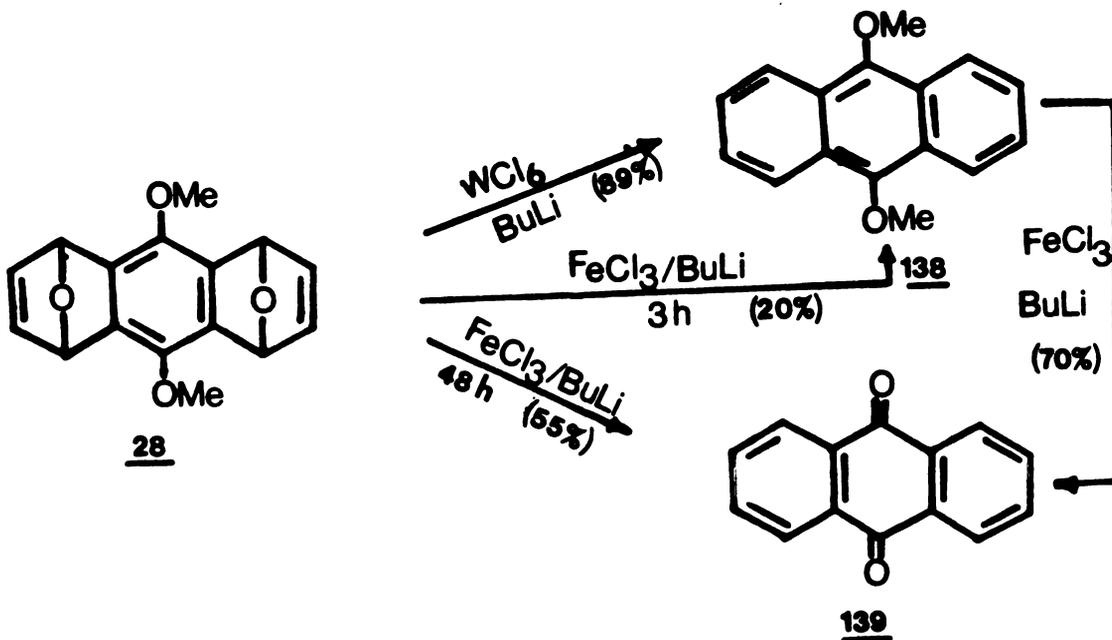
The particular metal used does not seem to matter in some cases. For example, 1,4-dimethyl-1,4-dihydronaphthalene-1,4-endoxide 129 was deoxygenated equally well with low-valent iron (81%) and tungsten (81-94%). In other instances, however, the metal makes an appreciable difference in the results. Thus hexamethylanthracene 136 was best prepared from 42 using reduced titanium. Reduced iron gave the same product cleanly but in lower yield and with tungsten, two other products were also formed (123 and



143). Tungsten was also more effective than iron in

converting bisadduct 28 to anthracene 138 (Scheme 23).

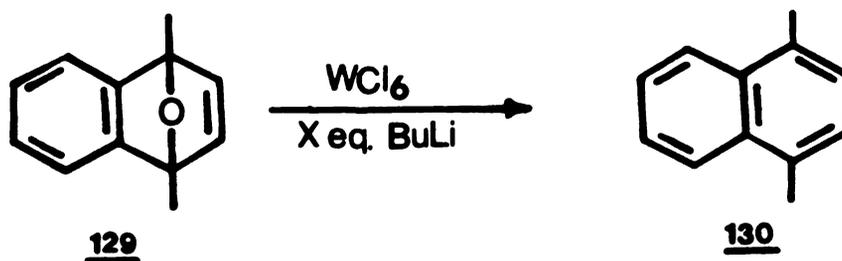
Attempts to increase the yield of 138 using a longer reaction time with iron gave instead, the anthraquinone 139.



Scheme 23

Even though the exact nature and oxidation state of the active metal species in these reactions is not known, the ratio of metal chloride to n -BuLi was crucial in the reactions with iron and titanium. The use of less than three molar equivalents, i.e., formally one mole of BuLi per mole-atom of halogen, led to recovery of the endoxide 135 at both -78°C , room temperature and at reflux in THF. This was not the case, however, with tungsten. Conditions

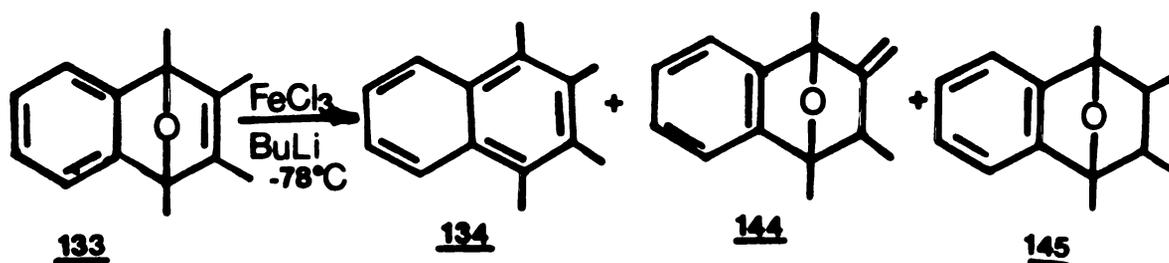
other than total 'replacement' of the halogens worked as well. For example, with the reagent ratios given below, the endoxide 129 was converted to the naphthalene 130 in the yields shown.



WCl ₆ : BuLi	Yield %
1 : 6	88
1 : 3	94

The reaction of the bisadduct 42 with tungsten to give hexamethylantracene 136, its rearranged form 123 and anthracene-1,4-endoxide 143 (cf. p. 146) is an example of the cases where the use of less than the optimal ratio of 1 : 6 : 24 between the substrate, metal halide and BuLi leads to partial deoxygenation. The actual ratio for this reaction was 1 : 2 : 6 respectively. When the ratio was changed to 1 : 3 : 9, only the rearranged hydrocarbon 143 was isolated, in 49% yield.

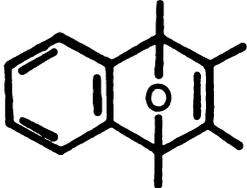
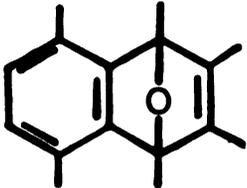
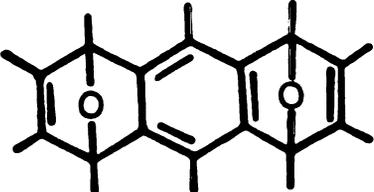
Of the three metals used, titanium and tungsten gave better results than iron in most cases. This may be either due to reduced iron being a weaker reagent or perhaps the mechanism for deoxygenation is different. An observation that may seem consistent with the latter rationale is the fact that with reduced iron, two reactions other than deoxygenation were encountered with certain polymethylarene endoxides. Although 133 could be converted to 134 in good yield with WCl_6 and TiCl_3 (cf. Table 12), reduced iron reacted differently at -78°C (if the reaction mixture was allowed to warm to 25°C before the removal of reduced iron species, deoxygenation was affected in 96% yield). For example, the endoxide 133, with a substrate to reagents ($\text{FeCl}_3/\text{BuLi}$) ratio of 1 : 3 : 12 at -78°C , gave only 7% of the desired naphthalene 134 and also 7% of the reduction product 145. The major product resulted from a



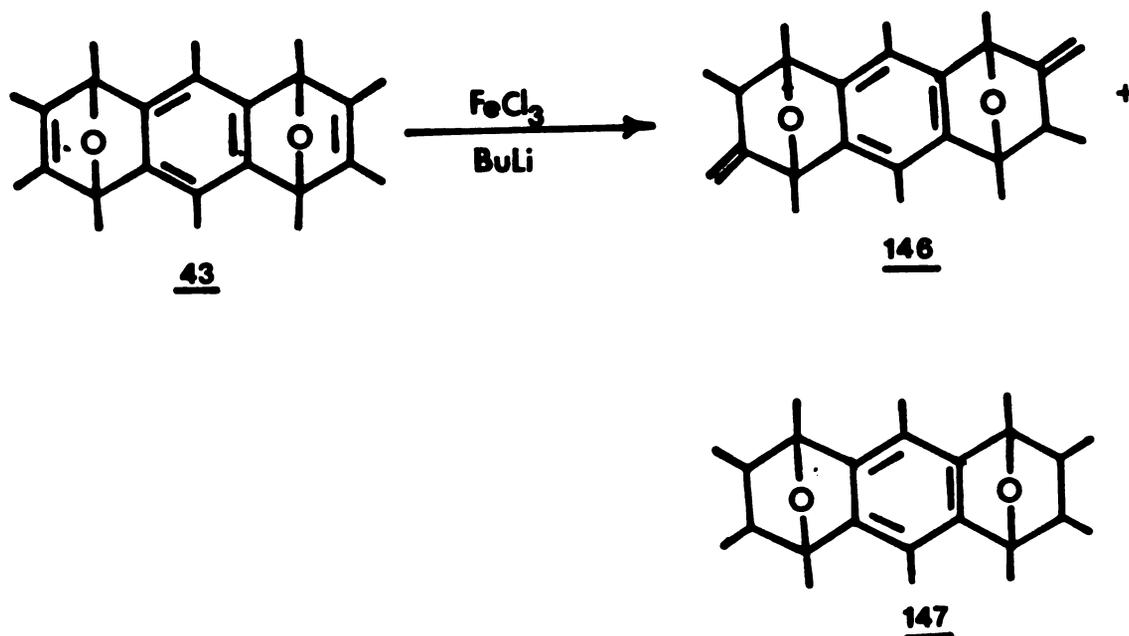
1,3-hydrogen migration (144, 59%). With the more substituted substrates (Table 13), reduced iron did not give any deoxygenation product under any of the reaction conditions

tried. The endoxides 43 and 135 gave the product of allylic rearrangement with reduced endoxides as minor products. When the reaction of diendoxide 43 with reduced iron was allowed to warm to room temperature before work-up, an equimolar mixture of the rearrangement and reduction products 146 and 147, which could not be separated easily was formed.

TABLE 13
 REACTION OF ADDUCTS OF TETRAMETHYLFURAN WITH
 REDUCED IRON AT -78°C

Substrate	Rearrangement (%)	Reduction (%)	Deoxygenation (%)
	59 (<u>144</u>)	7 (<u>145</u>)	7 (<u>134</u>)
<u>133</u>			
	70 (<u>148</u>)	30 (<u>149</u>)	--
<u>135</u>			
	78 (<u>146</u>)	--	--
<u>43</u>			

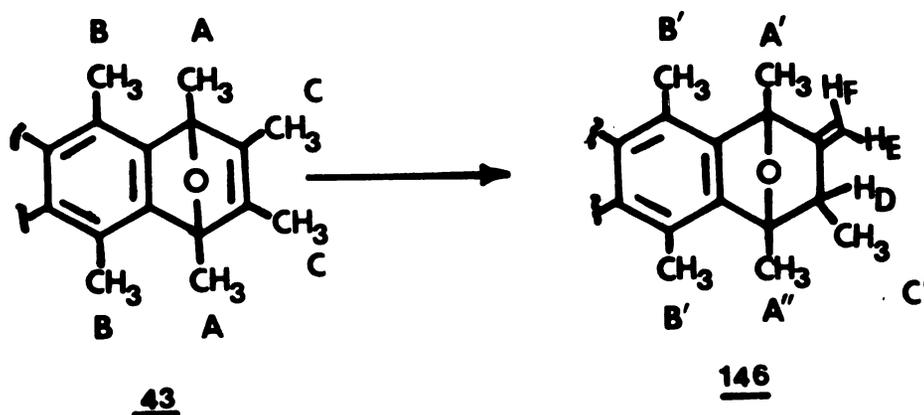
Separation of the reduced metals from the reaction mixture



at low temperatures gave mainly 146 and only trace of 147. The use of a mixture of syn and anti isomers of 43 led to a mixture of two isomeric rearrangement products. They were formed in the same ratio as the syn/anti ratio of the starting bisadduct mixture. The use of one isomer of 43 gave a single isomer of rearrangement product. These results indicate that this rearrangement is stereospecific.

Physical and chemical evidence were used to assign the structure of the novel rearrangement product 146. The parent peak in the mass spectrum of 146 was the same as the molecular weight of the starting bisadduct (M^+ , 350) and the proton NMR spectrum was very different from that of 43. The proton NMR spectrum also revealed an unusual symmetry

in the structure of the product. These preliminary observations implicated a molecular rearrangement. The new relationships between the protons in 146 were sorted out through double irradiation experiments performed at 180 MHz. The bridgehead and aromatic methyl groups in 146 (A', A'' and B') have almost the same chemical shifts as in the starting bisadduct (A and B, Scheme 24), but the vinyl

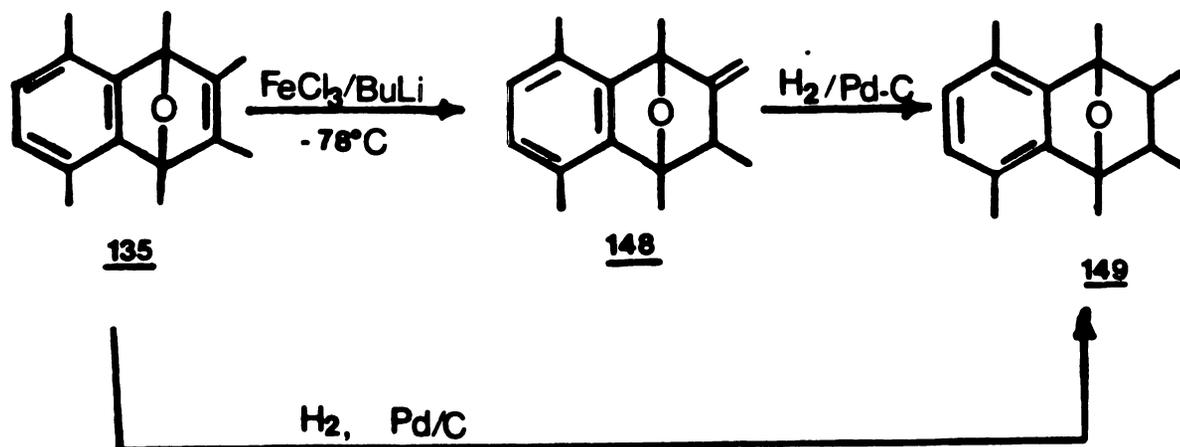


Scheme 24

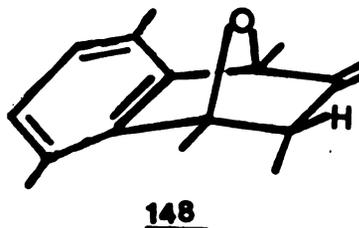
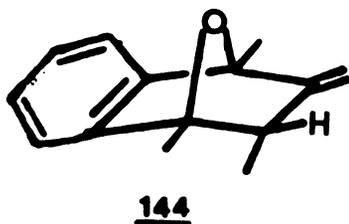
methyl groups C in 43 had disappeared from their former position giving rise to four new types of protons, H_{C'}, H_D, H_E and H_F in 146. It follows that it is this part of the molecule that has undergone rearrangement. A doublet appeared at δ 0.704 and 0.743 (6 H, $J = 7$ Hz) belonging to the protons of the C' methyl groups. A multiplet for the methine proton H_D was centered at δ 2.556 (2 H). The terminal

vinyl protons H_E and H_F appeared as doublets at δ 4.628/4.636 (2 H, $J = 1.34$ Hz) and 4.947/4.960 (2 H, $J = 2.29$ Hz). On double irradiation of H_D (δ 2.556), the doublet at δ 0.704/0.743 collapsed into a singlet and the doublets of H_E and H_F also became singlets, showing that the methine proton was situated so that it coupled with the upfield methyl groups (δ 0.704/0.743) and with the vinyl protons. Decoupling of H_C , simplified the multiplet at δ 2.556 into an unresolved triplet and no other signals were altered by this irradiation. Double irradiation of the vinyl proton at δ 4.947/4.960 defined the multiplet for H_D at δ 2.556 as a broad quartet whereas decoupling the proton at δ 4.628/4.636 resulted in H_D becoming a clean quartet ($J = 7$ Hz), with each of the four components split into doublets ($J = 2.3$ Hz). This coupling pattern uncovered by these irradiations is consistent for a product of an allylic hydrogen shift in 43 to give 146, whose partial structure is shown in Scheme 24. This proton NMR spectral pattern was similar for the rearrangement products of 133 and 135.

The structures of the 1,3-hydrogen shift products were also interrelated to the endoxides by catalytic

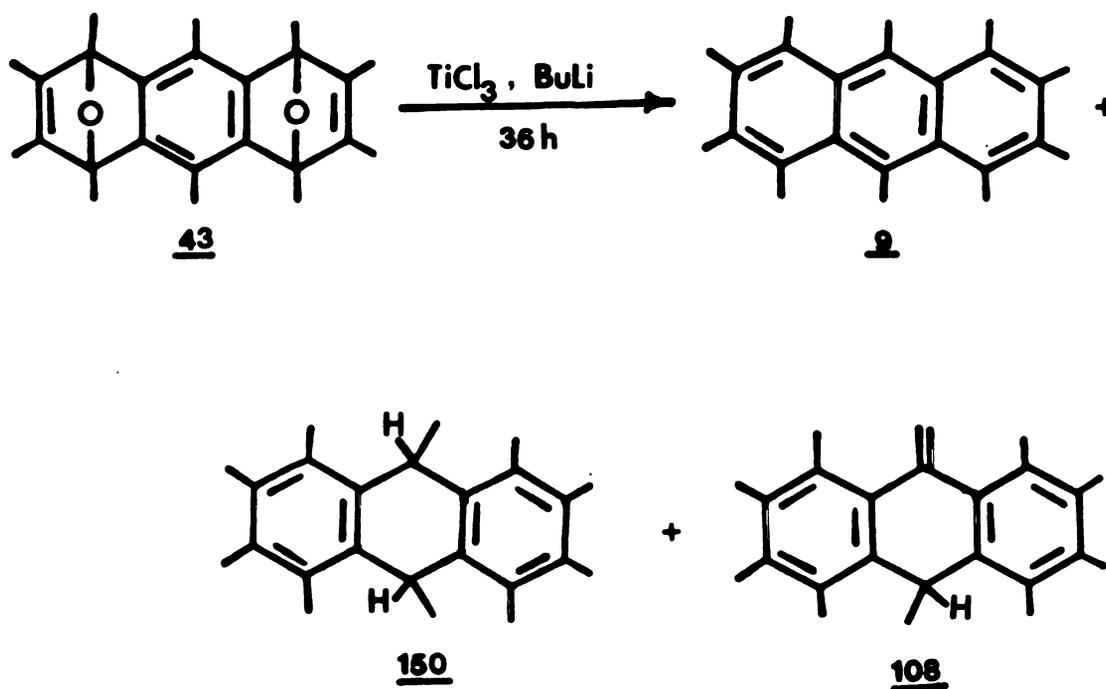


hydrogenation. Thus reduction of the adduct 135 and of its rearranged form 148 gave the same product 149. Similarly, reduction of 43 and its rearranged form 146 gave 147 in each case (see p. 152). The catalytic hydrogenation of 133, 135, 144 and 148 led to one isomer of reduced product in each instance. Single isomers of 43 and its rearranged form 146 gave a single isomer of 147 also. The reduction of the adducts and their rearranged forms is therefore stereospecific. The methine proton in the rearranged forms (144, 146 and 148) probably has an exo stereochemistry.



The methyl and methine protons at the 2,3-positions of the reduced endoxides 145, 147 and 149 have the same NMR pattern as meso-2,3-dibromobutane - an $X_3AA'X'_3$ system - which has been discussed in some detail by Anet.⁶⁷ Detailed analysis of the proton NMR spectra of these compounds would be required in order to determine the coupling constant between the methine protons. This value would, in turn, be used to determine the stereochemistry at the 2,3-positions of the reduced adducts.

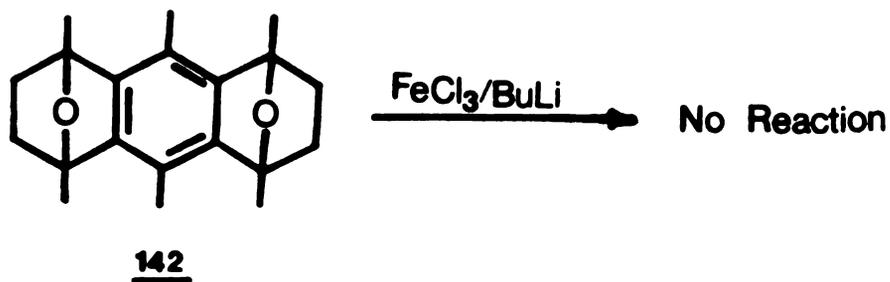
No rearrangement similar to that described above for the reaction of adducts of tetramethylfuran with reduced iron was observed with reduced titanium and tungsten. For example, bisadduct 43, when stirred with reduced titanium at 25°C for 10 h, gave the partially deoxygenated product 137 (cf. Table 12, Entry 6). Similar reaction with reduced iron gave the product of a 1,3-hydrogen migration 146. At very long reaction times, reduced titanium and tungsten could lead to the reduction and rearrangement of the deoxygenated product. Thus, when the deoxygenation of 43 with reduced titanium was run for 36 h, the desired



product 9 was further reduced to 150 and underwent rearrangement to 109. Whereas, therefore, reduced titanium and tungsten do not cause allylic rearrangement and reduction of

the endoxides, as reduced iron does, they may cause reduction and rearrangement of the resultant hydrocarbons if such compounds remain in contact for long periods with the low-valent metal species.

The presence of traces of reduced arene endoxides in the reactions with reduced iron led us to suspect that they might be intermediates in the deoxygenation process. An attempt to aromatize 142 by this procedure, however, was

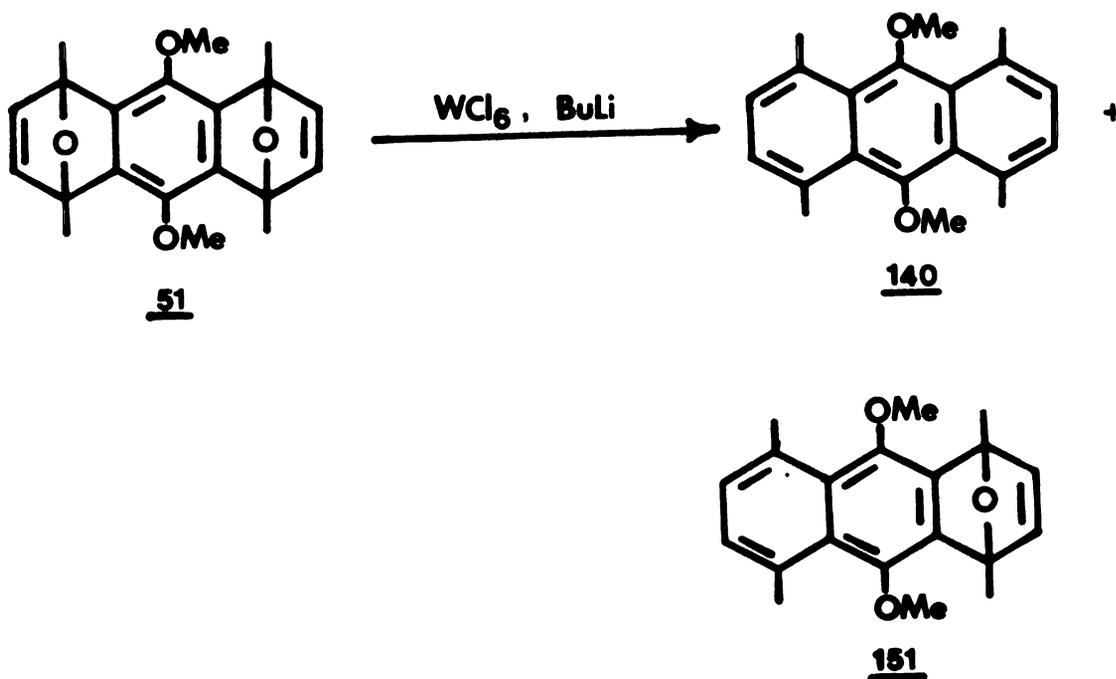


unsuccessful.

Surprisingly, aromatization of 9,10-dimethoxyanthracene diendoxides was accompanied by the simultaneous loss of the methoxyl groups to give aromatic hydrocarbons. The reduced metals were used in the same optimal reagent to substrate ratio which was developed for the 9,10-dimethyl analogs. For example, when 51 was stirred with low-valent iron, 1,4,5,8-tetramethylantracene 141^{1,66} was obtained.



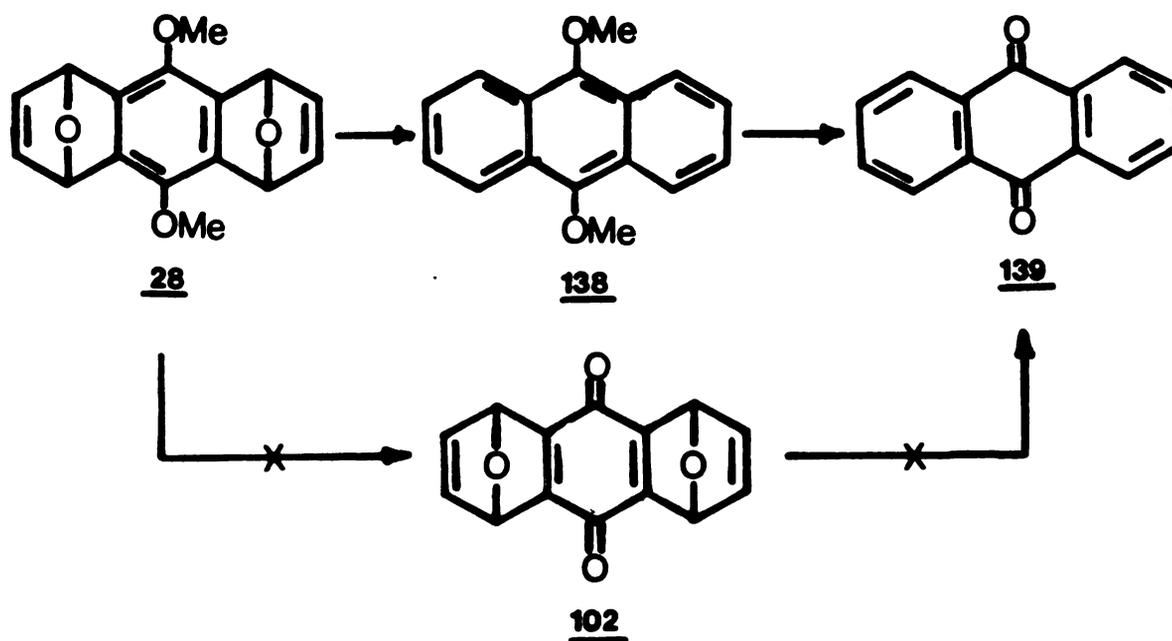
Similar treatment of the bisadduct 52 gave the octamethylanthracene 2^{2,64} (cf. Table 12). Only FeCl_3 and TiCl_3 affected the methoxyl groups in this manner. Reduced tungsten often gave the 9,10-dimethoxyanthracene as the ultimate product. For example, treatment of the bisadduct 51 with reduced tungsten led to an equimolar mixture of the



anthracene 140 and the partially deoxygenated compound 151.

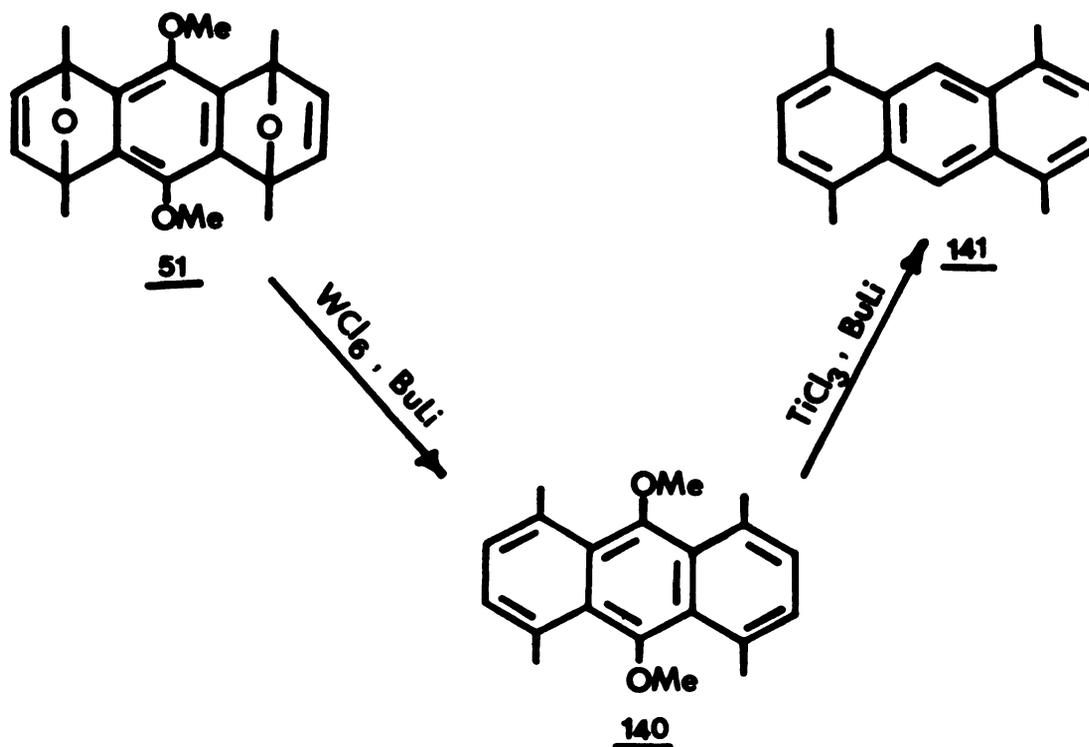
It appears that peri-interactions may be responsible for the replacement of the methoxyl groups with hydrogen because, with the furan bisadduct 28, only the quinone 139 could be obtained even after long reaction times (cf. Scheme 23).

Attempts were made to determine how and at which stage the methoxyl groups are lost. On page 77 it was reported that it was not possible to prepare the quinone 102 of the bisadduct 28. It follows then that demethoxylation cannot occur before deoxygenation of the endoxide function of the molecule. But 9,10-dimethoxyanthracene 138 was converted in 70% yield to the quinone 139 by



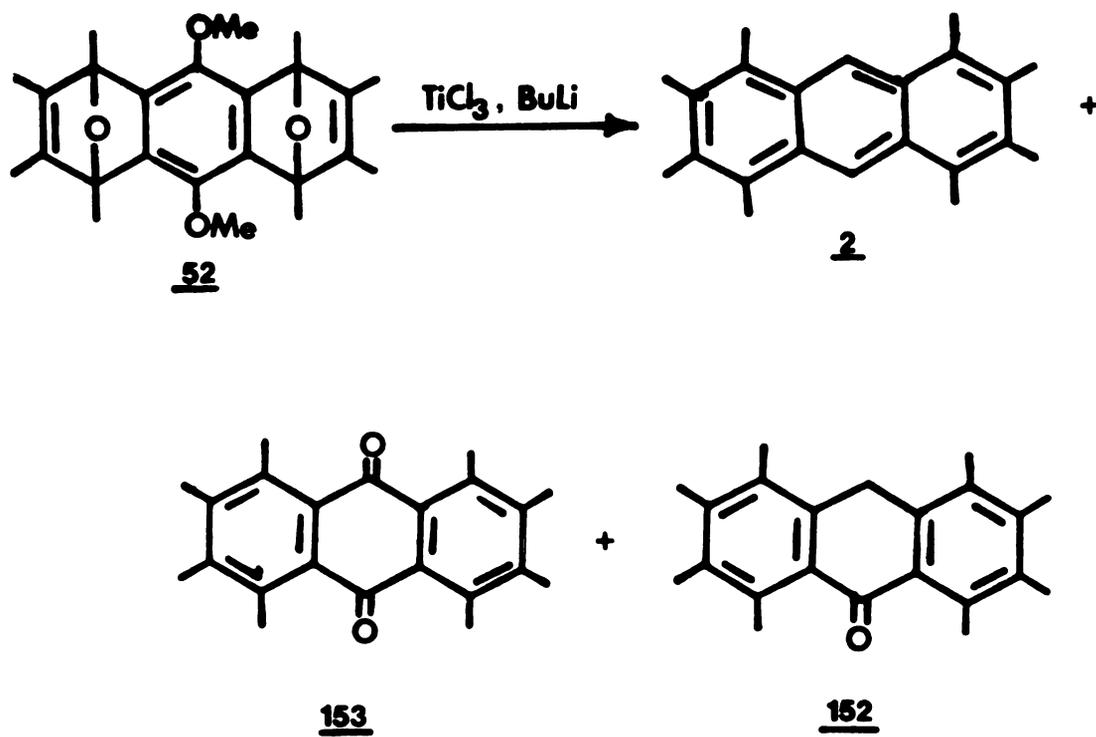
$\text{FeCl}_3/\text{BuLi}$, showing that this reagent system can effect demethylation of the 9- and 10-methoxyl groups. It is therefore probable that for the transformation of 28 to 139, deoxygenation of the endoxide function occurred first to give the anthracene 138 which was then demethylated and oxidized to anthraquinone 139.

The conversion of hindered 9,10-dimethoxyanthracene diendoxides to aromatic hydrocarbons with reduced iron and titanium might also involve initial deoxygenation of the endoxide functions to give the hindered 9,10-dimethoxyanthracenes. These intermediates could then be converted to the hydrocarbons probably through the intermediacy of quinones and other oxo-derivatives of the anthracenes. To verify whether hindered 9,10-dimethoxyanthracenes could be converted to aromatic hydrocarbons by reduced titanium and iron, diether 140, prepared from bisadduct 51 using reduced tungsten, was treated with reduced titanium and actually led to anthracene 141 in very high yield (Scheme 25).

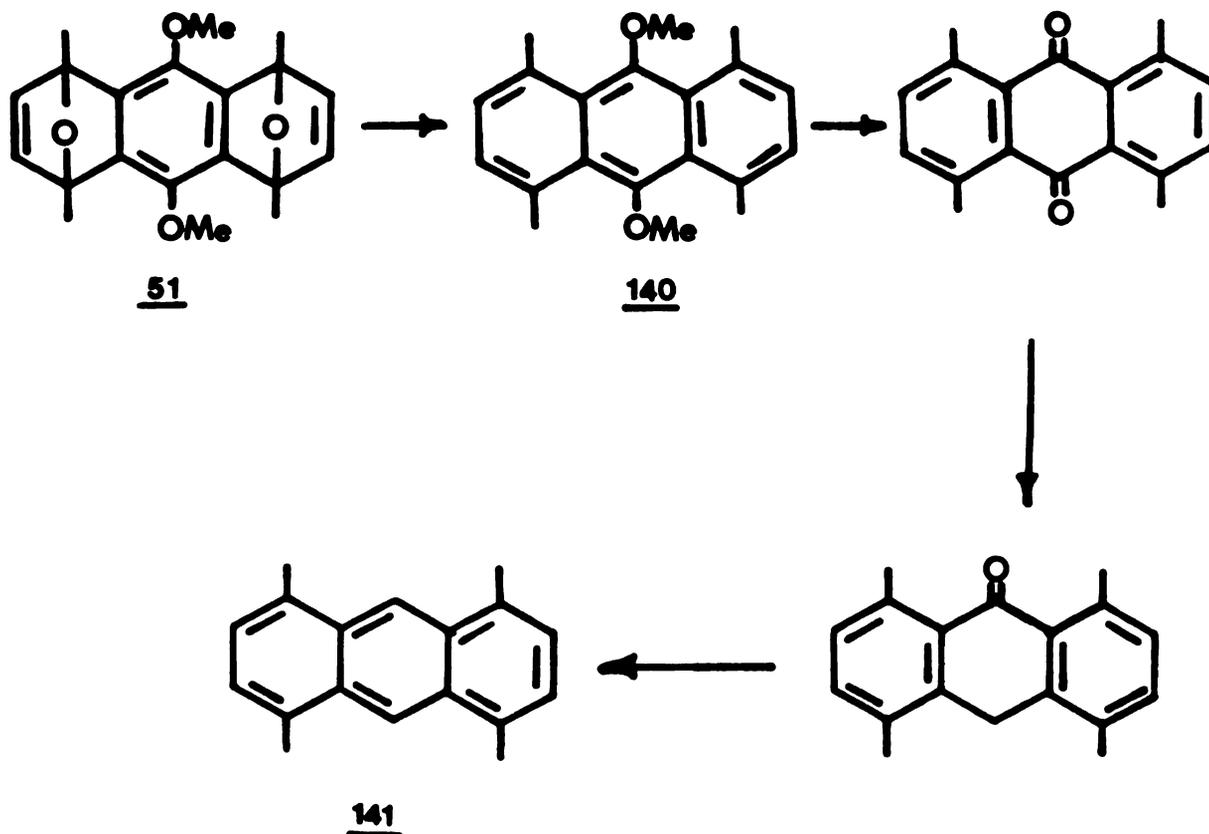


Scheme 25

An indication that quinones and other oxo-derivatives of anthracenes might be systematic intermediates in the loss of the methoxyl groups of hindered anthracene diendoxides and anthracenes (i.e., the 9,10-methoxyl groups) was provided by the identification of oxo-derivatives 152 and 153 in the reaction of the bisadduct 52 with reduced titanium. From these observations, the conversion of



9,10-dimethoxyanthracene diendoxides **51** and **52** to



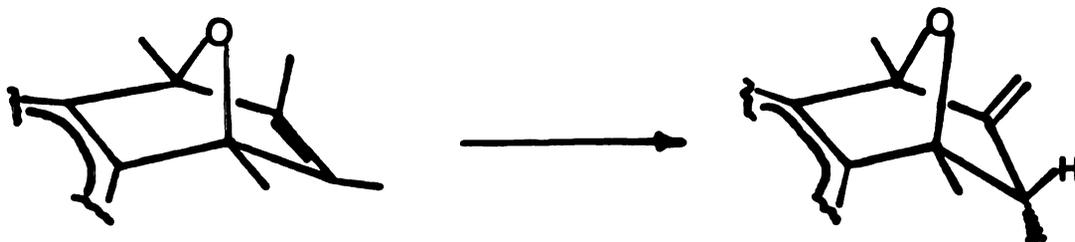
anthracenes 141 and 2 respectively, can be formulated as involving the steps illustrated with 51 above.

All the reactions effected with these reduced transition metal species represent new applications of these reagents. Even though deoxygenation was effected as was surmised by analogy with alkene oxides, there is not enough evidence from our results to confirm that the same mechanism operates here. Further investigation is required to ascertain the nature and oxidation state of the active metal species.

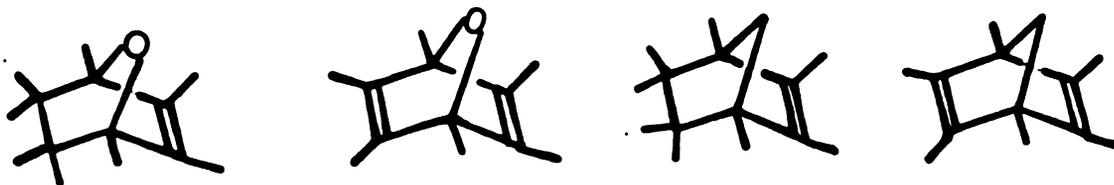
In conclusion, low-valent transition metals, especially Ti, W and Fe, are effective reagents for one-

step aromatization of arene endoxides even when multiple peri-interactions pose serious problems with the regular methods for aromatizing such compounds or their derivatives. The adducts of 2,5-dimethylfuran and furan itself are deoxygenated in good yields by all three metals. The adducts of tetramethylfuran can be aromatized with reduced titanium and tungsten but the reaction has to be monitored more closely with respect to time to avoid partial deoxygenation or reduction of the resulting aromatic hydrocarbon. Whereas tungsten will give the 9,10-dimethoxyanthracenes, iron and titanium will simultaneously replace the methoxyl groups with hydrogen in their reactions with the 9,10-dimethoxyanthracene diendoxides.

The 1,3-hydrogen shift observed in the reaction of tetramethylfuran adducts with reduced iron is unprecedented and interesting because a more substituted double bond isomerizes to a stable terminal double bond. This process would not be expected purely on thermodynamic considerations from the simple hydrocarbon analogs. The strain between the



C_1 and C_2 methyl groups does not seem to be high enough to account for this unusual rearrangement. It would be instructive to verify whether this process is also possible for the similarly substituted oxanorbornenes, oxanorbornadienes, norbornenes and norbornadienes.



EXPERIMENTAL

1. 1,2,3,4,5,6,7,8-Octamethylantracene (2)

To a slurry of 1.96 g (12.1 mmol) of anhydrous sublimed FeCl_3 in 50 mL of anhydrous THF at -78°C under argon was added 32 mL of 1.6 M BuLi. The mixture was stirred at this temperature for 2 h and 0.66 g (1.73 mmol) of the bisadduct 52, suspended in 100 mL of dry THF was run into the reaction mixture. After 90 h of stirring, during which time the temperature rose to 25°C , the fluorescence of the product reached a maximum (tlc, alumina/hexane). The reaction mixture was filtered through a layer of alumina and the layer was washed many times with THF. The combined filtrates were evaporated to dryness on a rotary evaporator. The yellow solid was triturated with cold hexane to remove oily matter and gave 0.31 g (62%) of anthracene 2: mp $290-2^\circ\text{C}$ with decomposition (lit.⁶⁴ $297-8^\circ\text{C}$); ^1H NMR (CDCl_3) δ 2.45 (s, 12 H), 2.73 (s, 12 H); mass spectrum, m/e (relative intensity) 291 ($\text{M} + 1$, 31), 290 (M^+ , 100), 275 (5).

2. 9,10-Dimethylantracene (118)

This compound was prepared according to the typical procedure for deoxygenations with FeCl_3 (experiment #6). Thus 1.93 g (11.8 mmol) of FeCl_3 , 27 mL of 1.7 M BuLi and 0.47 g (2 mmol) of the anthracene diendoxide 32 gave 0.23 g (56%) of 118: mp 179-180°C (lit.¹⁶ 180-1°C).

3. 1,4,5,8,9-Pentamethyl-10-methylene-9,10-dihydroanthracene (123)

In a similar procedure as for experiment #15, 2.44 g (6 mmol) of WCl_6 , 11 mL of 2.2 M BuLi and 0.57 g (2 mmol) of the diendoxide 42 gave 0.25 g (49%) of 123: mp 159°C-161°C; ^1H NMR (CCl_4) δ 1.27 (d, 3 H, $\underline{J} = 7$ Hz), 2.33 (s, 6 H), 2.47 (s, 6 H), 4.23 (q, 1 H, $\underline{J} = 7$ Hz), 5.43 (s, 2 H), 6.70 (s, 4 H); mass spectrum, $\underline{m/e}$ (relative intensity) 262 (M^+ , 23), 247 (100), 230 (5), 215 (9), 202 (6). Both the precursor to this compound (42) and the aromatic isomer--hexamethylantracene 136--showed correct elemental analyses (see p. 88 and 173).

4. 1,4-Dimethyl-1,4-dihydronaphthalene-1,4-endoxide (129)

The compound 129^{23,46} was prepared as in experiment #7 in 66% yield from benzene diazonium carboxylate and 2,5-dimethylfuran. The solvent for the annelation step was THF and propylene oxide was omitted: bp 97°C (2.5 torr);

^1H NMR (CDCl_3) δ 1.70 (s, 6 H), 6.40 (s, 2 H), 6.50-6.90 (m, 4 H); ^{13}C NMR (CDCl_3) δ 19.15, 92.45, 122.14, 128.54, 150.71, 156.79.

5. 1,4-Dimethylnaphthalene (130)

To 25 mL of anhydrous THF under argon at -78°C containing 1.62 g (4.1 mmol) of WCl_6 was added 5.6 mL of 2.2 M BuLi through a syringe. After 10 min., the reaction flask was removed from the bath and allowed to warm to room temperature in 1 h. A solution of 0.43 g (2.5 mmol) of the endoxide 129 in 10 mL of anhydrous THF was added to the reaction mixture through a syringe and the stirring was continued for 6 h. Removal of THF on a rotary evaporator left a black residue which was taken up in ether (50 mL). The blue solution was washed several times with aqueous NaOH until the organic layer was colorless. Subsequent washing of the solution with water and drying (Na_2SO_4) gave 0.37 g (94%) of 130⁶³ as an oil after evaporation to dryness: ^1H NMR (CCl_4) δ 2.60 (s, 6 H), 6.90 (s, 2 H), 7.10-7.40 (m, 2 H), 7.60-7.80 (m, 2 H); mass spectrum, $\underline{m/e}$ (relative intensity) 156 (M^+ , 100), 141 (93), 128 (13) 115 (18); UV (n-heptane) λ_{max} 235 ($\log \epsilon = 4.05$), 279 (3.8), 290 (3.89), 300 (3.68); Ir (CCl_4) 3000, 1660, 1460-1400, 1030 cm^{-1} .

6. Typical Deoxygenation Procedure with FeCl₃. Preparation of 1,4,5,8-Tetramethylnaphthalene (132)

Sublimed anhydrous FeCl₃ (0.98 g, 6.0 mmol) was added to 25 mL of anhydrous THF under argon at -78°C. *n*-Butyllithium (12 mL, 2 M) was added and the mixture was stirred for 2 h. A solution of the endoxide 131¹⁰ (0.43 g, 2.0 mmol) in 10 mL of anhydrous THF was added (syringe) and the mixture was left to warm to room temperature with stirring during 6 h. After the removal of THF on a rotary evaporator, the black residue was shaken with ether (100 mL) and the suspension was suction filtered. The ether extract was washed with water, dried (Na₂SO₄) and evaporated to dryness. The solid residue was chromatographed on alumina with chloroform. The product was recrystallized from CHCl₃ to give 0.25 g (63%) of 132 as thin needles: mp 129-131°C (lit.¹⁰ 131-2°C).

7. 1,2,3,4-Tetramethyl-1,4-dihydronaphthalene-1,4-endoxide (133)

Anthranilic acid (11.4 g, 8.3 mmol) was suspended in 150 mL of anhydrous THF containing a catalytic amount (0.18 g) of trichloroacetic acid. The reaction mixture was cooled to 0°C in an ice-salt bath and isoamyl nitrite (19 mL) was added at such a rate that the reaction temperature remained below 18°C. Stirring was continued until the

initially formed brick-red precipitate turned tan white. The precipitated diazonium carboxylate was filtered and washed with THF.

To a suspension of the diazonium carboxylate in dichloroethane was added 7.97 g (64 mmol) of tetramethylfuran, followed by 23 mL of propylene oxide. The mixture was brought to gentle reflux on a water bath. When gas evolution ceased, the reaction mixture was cooled to room temperature, washed many times with aqueous NaOH and finally with water until the washings had a light red color. The solution was dried (Na_2SO_4) and concentrated on a rotary evaporator to give a red oil. Vacuum distillation (89-95°C, 1.3 Torr) gave 4.5 g (35%) of 133: mp 41-3°C (lit.⁴⁶ 45.6-46°C); ^1H NMR (CDCl_3) δ 1.57 (s, 6 H), 1.60 (s, 6 H), 6.70 (m, 4 H); mass spectrum, m/e (relative intensity) 200 (M^+ , 90), 185 (100), 159 (89), 142 (42), 128 (23), 115 (29).

8. Typical Procedure for Deoxygenation with WCl_6 . Preparation of 1,2,3,4-Tetramethylnaphthalene (134)

To a suspension of 2.45 g (6.2 mmol) of WCl_6 in 25 mL of anhydrous THF under argon at -78°C was added 10 mL of 2.4 M BuLi. The mixture was stirred for 1 h and then allowed to warm to 25°C in 1 h. A solution of the endoxide 133 (0.41 g, 2.0 mmol) in 10 mL of anhydrous THF was added over 10 min. and the mixture was stirred for 5 h. The

solvent was removed on a rotary evaporator and the residue was extracted with ether (100 mL). The blue ether solution was washed several times with aqueous NaOH until the blue color discharged, then the organic layer was washed with water and dried (Na_2SO_4). The solution was concentrated until crystals of 134 deposited; the mixture was cooled and the crystals of 134 were collected by suction filtration as long white needles (0.34 g, 89%; mp 106-7°C, lit.⁶⁴ 106.5-107.5°C).

9. 1,2,3,4,5,8-Hexamethyl-1,4-dihydronaphthalene-1,4-endoxide (135)

3,6-Dimethylantranilic acid (8.4 g, 5.1 mmol) suspended in 140 mL of absolute ethanol was cooled in an ice-salt bath and 6 mL of concentrated HCl was added. Isoamyl nitrite (14 mL) was added to the reaction mixture at such a rate that the reaction temperature remained below -5°C. After 1 h of stirring, 140 mL of ether was added and stirring was continued below 10°C for another 1 h during which time the diazonium carboxylate dropped from the solution as a yellow solid.

The solid was isolated by filtration and suspended in 500 mL of dichloroethane. Tetramethylfuran (6.18 g, 50 mmol) and 21 mL of propylene oxide were added and the mixture was refluxed on a water bath until the evolution of gas subsided greatly. After cooling to 25°C, the dark brown

reaction mixture was washed several times with aqueous NaOH and water and then dried (Na_2SO_4). Evaporation of the solution to dryness on a rotary evaporator left a solid which, after recrystallization from methanol, gave 4.2 g (36%) of 135 as needles: mp 101-3°C; ^1H NMR (CCl_4) δ 1.50 (s, 6 H), 1.70 (s, 6 H), 2.20 (s, 6 H), 6.30 (s, 2 H); IR (CS_2) 3000, 1380, 1150, 800 cm^{-1} ; mass spectrum, m/e (relative intensity) 228 (M^+ , 6), 185 (100), 174 (42), 155 (19). A derivative of this compound (148, see p.185) showed correct elemental analysis.

10. Attempted Deoxygenation of Endoxide 135 with a 1 : 2 Ratio of FeCl_3 to $n\text{-BuLi}$

A slurry of anhydrous sublimed FeCl_3 (0.49 g, 3.01 mmol) in 20 mL of anhydrous THF cooled to -78°C under argon was stirred while 3 mL of 2.1 M BuLi was added through a syringe. After 1 h at this temperature, a solution of the endoxide 135 (0.23 g, 1.01 mmol) in 20 mL of anhydrous THF was added and stirring was continued for 4 h more at -78°C . The solvent was evaporated on a rotary evaporator and the black residue was shaken with 50 mL of ether. The ether solution was washed with water and dried (Na_2SO_4). Evaporation to dryness gave 0.23 g (100%) of the starting endoxide 135 and no other substance was isolated.

11. Typical Deoxygenation Procedure with TiCl_3 . Preparation of 1,4,5,8,9,10-Hexamethylanthracene (136)

To a stirred suspension of 1.3 g (8.4 mmol) of TiCl_3 in 25 mL of anhydrous ether under argon at -78°C was added 16 mL of 2 M BuLi in 10 min. After 1 h at this temperature, the mixture was warmed to room temperature, a suspension of the diendoxide 42 (0.42 g, 1.4 mmol) in 50 mL of anhydrous ether was added in 10 min and the reaction mixture was stirred for 9 h. Filtration of the black mixture through a bed of alumina and concentration of the ether solution gave 0.29 g (79%) of the anthracene 136: mp $196-8^\circ\text{C}$ (n-hexane); ^1H NMR (CCl_4) δ 2.70 (s, 12 H), 2.83 (s, 6 H), 6.87 (s, 4 H); mass spectrum, m/e (relative intensity) 262 (M^+ , 100), 247 (88), 232 (19); UV (n-heptane) λ_{max} 425 ($\log \epsilon = 3.71$), 404 (3.73), 276 (4.76), 224 (3.90).
Anal. Calc'd. for $\text{C}_{20}\text{H}_{22}$: C, 91.55; H, 8.45.
 Found: C, 91.71; H, 8.39.

12. Decamethyl-1,4-dihydroanthracene-1,4-endoxide (137)

To a suspension of TiCl_3 (1.26 g, 8.2 mmol) in 25 mL of anhydrous ether under argon at -78°C was added 16 mL of 2 M BuLi over 5 min. The mixture was stirred for 1 h and then allowed to warm to 25°C in 1 h. A suspension of the adduct 43 (0.48 g, 1.4 mmol) in 75 mL of anhydrous ether was added and the mixture was stirred for 10 h. Filtration

of the reaction mixture through a layer of alumina, removal of the solvent on a rotary evaporator and trituration of the residue with hexane gave 0.19 g of a white solid which was identified by its proton NMR spectrum to be unreacted bisadduct 43. The hexane solution was concentrated to give a yellow tinted solid which after recrystallization from hexane, weighed 0.23 g (50% yield of 137): mp 148-150°C; ^1H NMR (CCl_4) δ 1.63 (s, 6 H), 1.84 (s, 6 H), 2.27 (s, 6 H), 2.42 (s, 6 H), 2.45 (s, 6 H); mass spectrum, m/e (relative intensity) 334 (M^+ , 11), 291 (100), 276 (11), 261 (11); high resolution mass spectrum calculated for $\text{C}_{24}\text{H}_{30}\text{O}$: 334.22980. Found: 334.22967.

13. 9,10-Dimethoxyanthracene (138)

Tungsten hexachloride (1.62 g, 4.1 mmol) was added to 25 mL of anhydrous THF at -78°C under argon. n-Butyllithium (6 mL, 2.2 M) was added and the stirred mixture was maintained at this temperature for 2h. The addition of 0.51 g (2.0 mmol) of the bisadduct 28, dissolved in 50 mL of anhydrous THF took 15 min. and the reaction mixture was left to warm to 25°C in 6 h. Filtration through a layer of alumina and evaporation of THF on a rotary evaporator gave a solid which was chromatographed on alumina with hexane. Final elution of the column with THF gave 0.40 g (89%) of 138 as yellow granular crystals: mp 195-7°C (lit.⁶⁵ 202°C).

14. Mixture of the Deoxygenated Products of the Bisadduct 43 (9, 108 and 150)

To a suspension of 2.21 g (14 mmol) of TiCl_3 in 25 mL of anhydrous THF at -78°C under argon was added 24 mL of 2.4 M BuLi over 10 min. The reaction mixture was stirred for 1 h at -78°C and then allowed to warm to 25°C in 2 h. A solution of the bisadduct 43 (0.82 g, 2.34 mmol) in 75 mL of anhydrous THF was added in 15 min. and the reaction was followed by tlc (alumina/hexane) until the yellow spot, probably of decamethylantracene 9, predominated (36 h). The reaction mixture was filtered through a layer of alumina, the greenish-yellow solution was concentrated on a rotary evaporator and the residue was redissolved in 500 mL of hexane. The hexane solution was washed with water and dried (Na_2SO_4). After removing the solvent, the yellow solid residue was chromatographed on alumina using hexane. Evaporation of the eluate to dryness gave 0.6 g of a yellow solid. The proton NMR spectrum of this solid showed that it was a mixture of 9, 108 and 150. The peaks at δ 2.60 and 2.67 (ratio 1 : 2) correspond to the 9,10- and 1,4,5,8-methyl protons of decamethylantracene. The singlet at δ 5.17, the quartet centered at δ 4.30 and the doublet at δ 1.30 are characteristic of the rearranged form 108 of decamethylantracene. The signals at δ 4.30 and 1.30 are also characteristic of the 9,10-dihydrodecamethylantracene 150. On standing in the CCl_4 solution, the yellow color

disappeared totally in 1 h and the proton NMR spectrum of this solution showed that the peaks at δ 2.60 and 2.67 had moved from this position and merged with the methyl peaks originally at δ 2-2.5. The vinyl peak at δ 5.17 had intensified as did also the doublet at δ 1.30. The loss of color and the intensification of the peaks at δ 5.17 and 1.30 are characteristic of the rearrangement of 9 to 108. Mass spectrum of the mixture, m/e (relative intensity) 318 (M^+ , 14), 303 (100), 290 (28), 151 (25), 145 (33), 91 (29), 57 (32); by chemical ionization ($M + 1$) 319. Based on the parent peak in the mass spectrum of the mixture being 318, the total yield of deoxygenation product is 81% (0.6 g). It was not possible to separate the components by chromatography.

15. 1,4,5,8,9,10-Hexamethyl-1,4-dihydroanthracene-1,4-endoxide (143)

A suspension of WCl_6 (1.60 g, 4 mmol) in 25 mL of dry THF at $-78^\circ C$ under argon was stirred with 5.6 mL of 2.2 M BuLi for 10 min. and the mixture was allowed to warm to $25^\circ C$ in 1 h. A solution of the bisadduct 42 (0.55 g, 1.9 mmol) in 50 mL of anhydrous THF was added and the reaction mixture was stirred for 3 h more. Evaporation of the solvent left a dark residue which was extracted with ether. The extract was washed successively with aqueous NaOH and water and dried (Na_2SO_4). The dark yellow solid left after the

removal of ether on a rotary evaporator was chromatographed on alumina first with hexane to give 0.08 g (16%) of a 1 : 4 mixture of hexamethylanthracene 136 and its rearranged form 123 respectively. Further elution of the column with THF gave 0.24 g (46%) of 143 as a white solid: mp 155-7°C; ^1H NMR (CCl_4) δ 1.92 (s, 6 H), 2.52 (s, 6 H), 2.63 (s, 6 H), 6.47 (s, 2 H), 6.77 (s, 2 H); mass spectrum, m/e (relative intensity) 278 (M^+ , 10), 252 (22), 236 (20), 235 (100), 220 (21), 205 (12); high resolution mass spectrum calculated for $\text{C}_{20}\text{H}_{22}\text{O}$: 278.16712. Found: 278.16707.

16. Deoxygenation of Bisadduct 28 with FeCl_3 . Preparation of Anthraquinone (139)

Anhydrous THF (50 mL) containing 2 g (12 mmol) of FeCl_3 was cooled to -78°C under argon and 25 mL of 2 M BuLi was added. The mixture was stirred for 2 h and 0.56 g (2.06 mmol) of the bisadduct 28 dissolved in 100 mL of dry THF was run into the reaction mixture in 15 min. After 48 h, during which time the temperature of the mixture rose to 25°C , the reaction mixture was filtered through a layer of alumina. The filtrate was evaporated to give 0.24 g (55%) of anthraquinone 139 as a yellow powder. The melting point and proton NMR spectrum of this product were identical with those of an authentic sample.

When a similar reaction was worked up 3 h after the addition of the substrate 28, 9,10-dimethoxyanthracene 138 was obtained in 20%.

17. Conversion of 9,10-Dimethoxyanthracene to Anthraquinone (139)

To a suspension of 1.96 g (12 mmol) of sublimed anhydrous FeCl_3 in 50 mL of anhydrous THF at -78°C under argon was added 22 mL of 2.2 M BuLi in 5 min. Stirring was continued for 2 h and the mixture was allowed to warm to 25°C in 1 h. The anthracene 138 (0.50 g, 2.1 mmol) dissolved in 100 mL of anhydrous THF was added over 20 min and the reaction mixture was gently heated to reflux. The characteristic fluorescence of 138 disappeared after 20 min of reflux but the reaction was continued for 9 h. The black suspension was filtered through a layer of alumina, THF was removed on a rotary evaporator and the residue was redissolved in CH_2Cl_2 . The solution was washed with water and dried (Na_2SO_4). Evaporation to dryness and trituration of the residual faint yellow needles with hexane gave 0.31 g (70%) of 139.

18. 1,4,5,8-Tetramethyl-9,10-dimethoxyanthracene (140)

A suspension of tungsten hexachloride (1.37 g, 3.5 mmol) in 25 mL of anhydrous THF at -78°C under argon was

treated with 6 mL of 2.4 M BuLi; the mixture was stirred at this temperature for 1 h and then allowed to warm to 25°C in 1 h. The bisadduct 51 (0.16 g, 0.5 mmol) dissolved in 5 mL of anhydrous THF was added and the mixture was stirred for 24 h more. The solvent was removed on a rotary evaporator and the residue was extracted with ether. The extract was washed successively with 40% aqueous NaOH and water and dried (Na_2SO_4). Removal of the solvent left a yellow oil (0.149 g) which was chromatographed on alumina with hexane to give 0.069 g (47%) of the anthracene 140 as yellow shiny plates: mp 153-5°C (n-hexane); ^1H NMR (CDCl_3) δ 2.80 (s, 12 H), 3.45 (s, 6 H), 6.88 (s, 4 H); mass spectrum, m/e (relative intensity) 294 (M^+ , 31), 279 (100), 263 (9), 147 (35).
Anal. Calc'd. for $\text{C}_{20}\text{H}_{22}\text{O}_2$: C, 81.60; H, 7.53. Found: C, 81.52; H, 7.70.

Further elution of the column with chloroform gave 0.072 g (47%) of 1,4,5,8-tetramethyl-9,10-dimethoxy-1,4-dihydroanthracene-1,4-endoxide (151): mp 125-7°C (CHCl_3); ^1H NMR (CDCl_3) δ 2.05 (s, 2 H), 2.70 (s, 6 H), 3.53 (s, 6 H), 6.63 (s, 2 H), 6.92 (s, 2 H); mass spectrum, m/e (relative intensity) 310 (M^+ , 31), 267 (100), 237 (22), 165 (20); high resolution mass spectrum calculated for $\text{C}_{20}\text{H}_{22}\text{O}_3$: 310.15708. Found: 310.15690.

19. Demethoxylation of anthracene 140. Preparation of 1,4,5,8-Tetramethylantracene (141)

To a suspension of TiCl_3 (0.50 g, 3.2 mmol) in 10 mL of anhydrous THF at -78°C under argon was added 7 mL of 1.9 M BuLi. The mixture was stirred for 1 h at -78°C , left to warm to 25°C in 2 h and a solution of the anthracene 140 (0.10 g, 0.30 mmol) in 75 mL of anhydrous THF was added. After 16 h, the reaction mixture was filtered over a layer of alumina and the solvent was removed on a rotary evaporator. The residue was chromatographed on alumina (hexane eluent) to give 0.07 g (93%) of the anthracene 141 which was recrystallized from a 1 : 1 mixture of chloroform and n-heptane: mp $220-2^\circ\text{C}$ (lit.⁶⁶ $221-1.5^\circ\text{C}$); ^1H NMR (CCl_4) δ 2.37 (s, 12 H), 6.93 (s, 4 H), 8.30 (s, 2 H); mass spectrum, m/e (relative intensity) 234 (M^+ , 100), 219 (21), 203 (10), 189 (5), 117 (9), 102 (8).

20. Direct Preparation of anthracene 141 from Bisadduct 51

Sublimed anhydrous FeCl_3 (4.06 g, 25 mmol) was suspended in 50 mL of anhydrous THF at -78°C under argon. n-Butyllithium (50 mL, 2 M) was added in 20 min. and the mixture was stirred for 2 h. A solution of 1.41 g (4.3 mmol) of bisadduct 51 in 100 mL of anhydrous THF was added in 0.5 h and the mixture was stirred for 18 h during which time the temperature rose to 25°C . Filtration was carried

out over a layer of alumina which was washed with THF until the greenish-yellow color of the product was no longer noticeable in the filtrate. Concentration of the combined filtrate left a solid which was redissolved in CH_2Cl_2 . The solution was washed with water and dried (Na_2SO_4). A brown solid residue was left on evaporation of the solution to dryness. The residue was shaken with hexane and the extract was passed down a column of alumina. The eluate was evaporated to dryness on a rotary evaporator and the product was recrystallized from hexane to give 0.61 g (60%) of the anthracene 141 as pale yellow crystals: mp 222-3°C.

21. Attempted Deoxygenation of the Endoxide 133 with Reduced Iron. Preparation of 1,3,4-Trimethyl-2-methylene-1,2,3,4-tetrahydronaphthalene-1,4-endoxide (144)

To a slurry of 0.90 g (5.6 mmol) of anhydrous sublimed FeCl_3 in 25 mL of anhydrous ether at -78°C under argon was added 10 mL of 2.3 M BuLi. After 2 h of stirring at this temperature, a solution of the endoxide 133 (0.38 g, 2.0 mmol) in 10 mL of dry ether was added and the reaction was left for 1 h at -78°C . The cold reaction mixture was suction filtered over a layer of alumina and the filtrate was washed with water and dried (Na_2SO_4). Removal of the solvent on a rotary evaporator left 0.28 g of an oil whose proton NMR spectrum showed the presence of 1,2,3,4-tetramethylnaphthalene 134, the rearranged form of the adduct

133 (144) and the reduced derivative of the adduct 145 in the ratio 1 : 8 : 1 respectively. Chromatography of this mixture on alumina with a 1 : 9 mixture of hexane and chloroform led to the separation of 134 from the other two components: mp of 134; 106-7°C (lit.⁶⁴ 106.5-7.5°C). A sample of the pure rearranged adduct 144 was obtained as a liquid by glc at 200°C from its mixture with 145. ¹H NMR (CCl₄) δ 0.61 (d, 3 H, J = 7 Hz), 1.63 (s, 3 H), 1.70 (s, 3 H), 2.50 (m, 1 H), 4.47 (d, 1 H, J = 2.3 Hz), 4.77 (d, 1 H, J = 2.3 Hz), 6.88 (br s, 4 H); mass spectrum, m/e (relative intensity) 200 (M⁺, 23), 185 (10), 157 (72), 146 (100), 129 (23), 115 (36), 103 (16); high resolution mass spectrum calculated for C₁₄H₁₆O:

Found:

22. Hydrogenation of 133 and 144. Preparation of 1,2,3,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene-1,4-endoxide (145)

A solution of the endoxide 133 (0.35 g, 18 mmol) in 50 mL of absolute ethanol was hydrogenated at 70 psi of hydrogen for 6 h at room temperature over 0.3 g of 10% palladium on charcoal. The catalyst was removed by filtration, the solvent was removed on a rotary evaporator and the residue was purified by chromatography on alumina by first using hexane followed by chloroform as eluents. The liquid product 145 weighed 0.34 g (96%): ¹H NMR (CDCl₃) δ

0.32 (d, 6 H, $J = 7$ Hz), 1.57 (s, 6 H), 2.07 (m, 2 H), 6.87 (br s, 4 H); mass spectrum, m/e (relative intensity) 146 (100), 131 (38), 115 (17); with chemical ionization, $(M + 1)^+ = 203$.

Anal. Calc'd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97.

Found: C, 83.01; H, 9.07.

The proton NMR spectrum of 145 obtained from the deoxygenation of 133 with reduced iron (vide supra) was identical with that obtained from the hydrogenation of 133.

Hydrogenation of a mixture of 133 and 144 (1 : 1) obtained in a deoxygenation reaction of 133 gave 145 in 93% yield.

23. Attempted Deoxygenation of Diendoxide 43 with Reduced Iron. Preparation of 146

To 25 mL of anhydrous THF at -78°C under argon was added 0.93 g (5.7 mmol) of anhydrous sublimed FeCl_3 followed by 10 mL of 2.1 M BuLi. After 2 h of stirring at this temperature, a solution of the bisadduct 43 (0.32 g, 0.9 mmol) in 25 mL of dry THF was added in 15 min. and the reaction mixture was stirred at -78°C for 4 h. Filtration and evaporation of the solvent left a residue which was taken up in CH_2Cl_2 , washed with water and dried (Na_2SO_4). The yellow solid residue obtained after removal of the solvent was chromatographed on alumina and first eluted by hexane to remove the yellow coloring impurity. Further

elution with a 9 : 1 mixture of CH_2Cl_2 and hexane gave 0.25 g (78%) of 146: mp 233-5°C (ethanol); ^1H NMR (CDCl_3) δ 0.72 (d, 6 H, \underline{J} = 7 Hz), 1.86 (s, 6 H), 1.89 (s, 6 H), 2.33 (s, 6 H), 2.56 (m, 2 H), 4.63 (d, 2 H, \underline{J} = 2.3 Hz), 4.95 (d, 2 H, \underline{J} = 2.3 Hz); mass spectrum, $\underline{m/e}$ (relative intensity) 350 (M^+ , 63), 306 (48), 296 (77), 253 (100). The hydrogenation derivative of 146, which is described in experiment #24, and the starting bisadduct 43 gave correct elemental analyses.

24. Hydrogenation of 43 and 146. Preparation of Deca-
methyl-octahydroanthracene-1,4:5,8-diendoxide (147)

The bisadduct 43 (0.33 g, 0.9 mmol) dissolved in 40 mL of absolute ethanol was hydrogenated at atmospheric pressure and room temperature in 12 h over 0.3 g of 10% palladium on charcoal to give 0.31 g (93%) of 1,2,3,4,5,8,9,10-decamethyl-1,2,3,4,5,6,7,8-octahydroanthracene-1,4:5,8-diendoxide 147: mp 251-2°C (ethanol); ^1H NMR (CCl_4) δ 0.43 (d, 12 H, \underline{J} = 7 Hz), 1.67 (s, 12 H), 1.80-2.30 (m, 4 H), 2.20 (s, 6 H); mass spectrum, $\underline{m/e}$ (relative intensity) 298 (31), 242 (100), 122 (17); with chemical ionization, $(\text{M} + 1)^+ = 355$.

Anal. Calc'd. for $\text{C}_{24}\text{H}_{34}\text{O}_2$: C, 81.31; H, 9.67.

Found: C, 81.45; H, 9.61.

Similar hydrogenation of 146 gave the same product (147) in 98% yield.

25. Reaction of the Endoxide 135 with Low-Valent Iron
Preparation of 1,3,4,5,8-Pentamethyl-2-methylene-
1,2,3,4-tetrahydronaphthalene-1,4-endoxide (148)

To 25 mL of anhydrous ether at -78°C under argon was added 1.44 g (8.9 mmol) of anhydrous sublimed FeCl_3 , followed by 16 mL of 2.2 M BuLi. After 2 h of stirring at this temperature, a solution of the endoxide 135 (0.44 g, 2 mmol) in 20 mL of anhydrous ether was added and the reaction mixture was maintained at -78°C for 4 h. The cold mixture was filtered, the filtrate was washed with water, dried (Na_2SO_4) and evaporated to dryness on a rotary evaporator. The viscous oil (0.44 g) solidified after standing for several hours. The proton NMR spectrum of the product showed that it consisted of a 7 : 3 mixture of the rearranged adduct 148 and the reduced derivative 149 (i.e., 70% of 148 and 30% of 149). Pure 148 was obtained from this mixture by glc at 210°C : mp $55-7^{\circ}\text{C}$; ^1H NMR (CCl_4) δ 0.66 (d, 3 H, $\underline{J} = 7$ Hz), 1.76 (s, 3 H), 1.77 (s, 3 H), 2.27-2.28 (m, 6 H), 2.43-2.49 (m, 1 H), 4.53 (d, 1 H, $\underline{J} = 2.3$ Hz), 4.89 (d, 1 H, $\underline{J} = 2.3$ Hz), 6.67 (s, 2 H); ^{13}C NMR (CDCl_3) δ 12.97, 14.87, 16.42, 45.28, 84.42, 84.88, 99.13, 124.22, 124.43, 126.62, 127.03, 127.65, 140.63, 141.80, 155.88; mass spectrum, $\underline{m/e}$ (relative intensity) 228 (32), 185 (42), 174 (100).

Anal. Calc'd. for $\text{C}_{16}\text{H}_{20}\text{O}$: C, 84.16; H, 8.83.

Found: C, 84.24; H, 9.00.

26. Hydrogenation of 135 and 148. Preparation of 1,2,3,4,5,8-Hexamethyl-1,2,3,4-tetrahydronaphthalene-1,4-endoxide (149)

A solution of the endoxide 135 (0.21 g, 0.9 mmol) in 50 mL of absolute ethanol was hydrogenated at atmospheric pressure and room temperature over 0.3 g of 10% palladium on charcoal. Filtration of the reaction mixture and evaporation of the solution on a rotary evaporator gave an oil which was chromatographed on alumina (3 : 7 :: hexane : chloroform). The yield of 149 was 0.21 g (99%): mp 45-7°C; ^1H NMR (CCl_4) δ 0.43 (d, 6 H, $J = 7$ Hz), 1.72 (s, 6 H), 2.06-2.18 (m, 2 H), 2.27 (s, 6 H), 6.57 (s, 2 H); ^{13}C NMR (CDCl_3) δ 8.93, 16.62, 17.18, 42.38, 85.72, 126.31, 126.81, 141.71; mass spectrum, m/e (relative intensity) 174 (100), 159 (9); with chemical ionization, $(M + 1)^+ = 231$.

Anal. Calc'd. for $\text{C}_{16}\text{H}_{22}\text{O}$: C, 83.43; H, 9.63.

Found: C, 83.26; H, 9.55.

Similar hydrogenation of 148 gave a quantitative yield of 149. Also, 149 obtained from the deoxygenation of 135 with low-valent iron (vide supra) had the same proton NMR spectrum as the hydrogenation product.

27. Deoxygenation of Bisadduct 52 with Low-valent Titanium.
The Interception of 152 and 153

Using the typical procedure for deoxygenation with TiCl_3 (experiment #11), 2.14 g (13.88 mmol) of TiCl_3 , 23 mL

of 2.4 M BuLi and 0.83 g (2.17 mmol) of bisadduct 52 were reacted in 72 h to give a mixture of 2, 152 and 153 (0.3 g). It was difficult to separate the components effectively but small quantities of pure 2 and 153 were obtained by chromatography on alumina using 80% hexane in CH_2Cl_2 .

2: mp 290-2°C (lit.⁶⁴ 297-8°C); ^1H NMR (CDCl_3) δ 2.45 (s, 12 H), 2.73 (s, 12 H), 8.53 (s, 2 H); mass spectrum, m/e (relative intensity) 291 (M + 1, 31), 290 (M^+ , 100), 275 (5).

152:² This compound was contaminated with 153 and was not obtained in pure form for proton NMR spectrum. It was possible to record its mass spectrum because compound 153 with which it was contaminated did not show any peaks on electron impact mass spectral determination: mass spectrum for 152, m/e (relative intensity) 307 (M + 1, 12), 306 (M^+ , 48), 291 (100), 233 (9), 138 (7).

153: mp - sublimed completely at 280-5°C (lit.² 303°C); ^1H NMR (CDCl_3) δ 2.23 (s, 12 H), 2.47 (s, 12 H); mass spectrum - there were no peaks observed by electron impact on a pure sample of 153. Chemical ionization showed $(\text{M} + 1)^+ = 321$.

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