Concerning the Stereochemistry of Reductive Alkylation of Anthracene and Naphthalene

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A substantial amount of work has appeared which is concerned with alkylation of anions derived from the 9,10-dihydroanthracene system. A pattern has emerged which suggests that substituents on the opposite meso carbon can exert considerable stereochemical control by (a) dictating preferred conformations and/or (b) providing steric obstruction. Although closely related, naphthalene exhibits behavior reported herein which deviates considerably from that of anthracene. Although methylation of 1-methyl-4-sodio-1,4-dihydronaphthalene is stereospecific providing only the cis product, ethylation of 1-ethyl-4-sodio-1,4-dihydronaphthalene furnishes a nearly equal mixture of cis and trans products. In anthracene just the opposite is true, with methylation being rather unselective and ethylation providing mainly the cis product. Isopropylation of the ethyl- and isopropyl-substituted systems as well as methylation of the isopropyl derivative is also reported. An explanation for the observed stereochemical control is forwarded which suggests that with small substituents, 1,4-dihydronaphthalene resembles 1,4-cyclohexadiene more than 9,10-dihydroanthracene with only slight deviation from planarity, whereas large substituents cause "dihydroanthracene-like" behavior.

The reaction of alkali metals with polynuclear aromatic compounds in anhydrous ammonia has furnished an important method for the preparation of reduced ring systems.[1] Protonation of the anionic intermediates (Scheme I) results in the initial formation of dihydro products whereas the addition of alkylating agents produces reduced products containing a variable number of alkyl groups. Although the formation of dialkylated products had initially been attributed to the intermediacy of dianions,[2] it was later shown that biphenyl can be dialkylated by an amide extraction process (Scheme I, lower path).[3] More recently,[4] inverse alkylation procedures have indicated monoanions to be the primary intermediate with both naphthalene and anthracene.

In any event, it is clear that any stereochemistry associated with reduction or reductive alkylation must result from the protonation or alkylation of the final monoanion. Thus numerous papers have appeared in recent years concerning the stereochemical outcome of such reactions of 9-alkyl-10-metallo-9,10-dihydroanthracenes,[5] and, as recently pointed out by Bank et al.,[5f] with sometimes inconsistent results. The pattern that now emerges is that alkylation (R'X) of 9-alkyl-10-lithio-9,10-dihydroanthracenes provides cis products when R and R' are both primary but trans products when R and R' are large (with the exception of R = R' = Me which shows little stereoselectivity). This is particularly well demonstrated[5e] in the case of R = *i*-Pr or *t*-Bu which shows a steady increase in the trans/cis ratio as R' increases in size through the series Me < Et < *i*-Pr. On the other hand, protonation of 9,10-dialkyl-10-lithio-9,10-dihydroanthracene results in trans product[7] when R is primary and cis products when R is large (*i*-Pr, *t*-Bu) (Scheme II).[5e]

Earlier suggestions,[5e] which seem to be consistent with the recent kinetic data of Bank et al.,[5f] provide complex equilibria (Scheme III) involving ring inversion of the

Scheme I

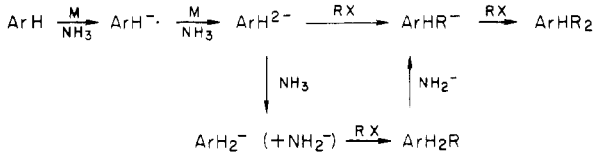


Table I. Alkylation of 1-Alkyl-1,4-dihydronaphthalene and 9-Alkyl-9,10-dihydroanthracene Anions with RX[a]

		cis/trans[b]	
R	RX	dihydronaphthalene	dihydroanthracene
Me	Me[c]	100/0	78/22
Et	Et[c]	43/57	85/15
i-Pr	*i*-Pr[c]	0/100	25/75 (ref 2a)
Me	*i*-Pr[d]	24/76	41/59[e] (ref 5b)
i-Pr	Me[d]	78/22	100/0[e] (ref 5b)

[a] Ammonia solutions unless otherwise noted. [b] From integrated NMR intensities. [c] Reductive dialkylations. [d] Alkylation of anion formed from monosubstituted hydrocarbon and base. [e] In THF. However, see ref 5b for similarities of stereochemistry in both THF and ammonia.

(1) (a) Birch, A. J.; Rao, G. Subba "Advances in Organic Chemistry, Methods and Results"; Taylor, E. C., Ed.; Wiley-Interscience: New York, 1972. (b) Smith, H. "Chemistry in Nonaqueous Ionizing Solvents"; Jander, G., Spandau, H., Addison, C. C., Eds.; Interscience: New York, 1963; Vol. I, Part 2. (c) Harvey, R. G. *Synthesis* **1970**, 161.

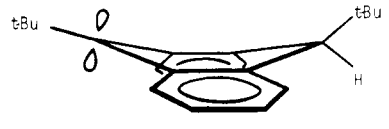
(2) (a) Harvey, R. G.; Arzadon, L. *Tetrahedron* **1969**, *25*, 4887. (b) Harvey, R. G.; Davis, C. C. *J. Org. Chem.* **1969**, *34*, 3607.

(3) Lindow, D. F.; Cortez, C. N.; Harvey, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 5406.

(4) Rabideau, P. W.; Burkholder, E. G. *J. Org. Chem.* **1978**, *43*, 4283.

(5) (a) Reference 2. (b) Zieger, M. E.; Gelbaum, L. T. *J. Org. Chem.* **1972**, *37*, 1012. (c) Daney, M.; Lapouyade, R.; Mary, M.; Bouas-Laurent, H. *J. Organomet. Chem.* **1975**, *92*, 267. (d) Fabre, C.; Salem, M. H. A.; Mazaleyrat, J. P; Tchaplo, A.; Welvart, Z. *Ibid.* **1975**, *87*, 9. (e) Fu, P. P.; Harvey, R. G.; Paschal, J. W.; Rabideau, P. W. *J. Am. Chem. Soc.* **1975**, *97*, 1145. (f) Bank, S.; Bank, J.; Davey, M.; Labrande, B.; Bouas-Laurent, H. *J. Org. Chem.* **1977**, *42*, 4058.

(6) Structures such as **1b** and **1c** are somewhat troublesome since models indicate a pseudoequatorial anion to be nearly orthogonal to the benzene rings. However, large substituents can cause a flattening of the dihydroanthracene ring,[5d,10] and perhaps it is only in these cases that equatorial alkylation is important. An additional example is the protonation of 9,10-di-*tert*-butyl-10-lithio-9,10-dihydroanthracene to afford a cis product which most certainly involves pseudoequatorial protonation. However, this structure is expected to be substantially "flattened", and one might also consider the possibility of sp^2 hybridization in this case (i.e., **2**), in view of the ready occurrence of 9-alkylidene-9,10-dihydroanthracenes (a completely planar structure seems less consistent with alkylation data; however, see ref 7a).



(7) (a) Panek, E. J.; Rodgers, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 6921. (b) Lapouyade, R.; Mary, M.; Bouas-Laurent, H.; Labandibar, P. *J. Organomet. Chem.* **1972**, *34*, C25. (c) Daney, M.; Lapouyade, R.; Bouas-Laurent, H.; *Tetrahedron Lett.* **1978**, 783.

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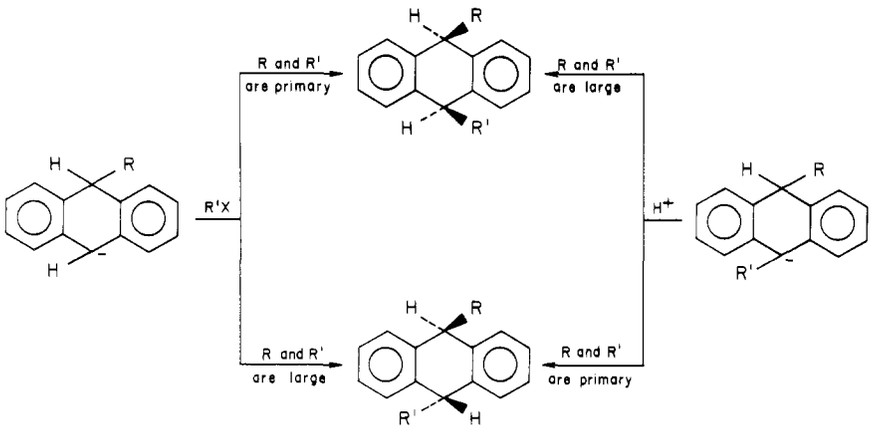
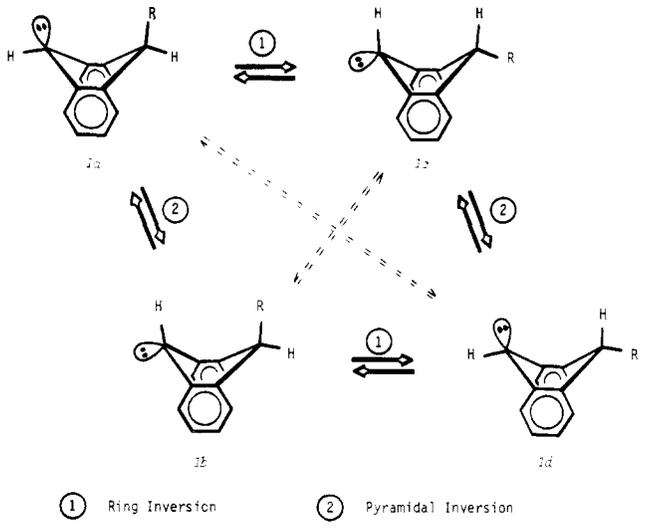
Scheme II



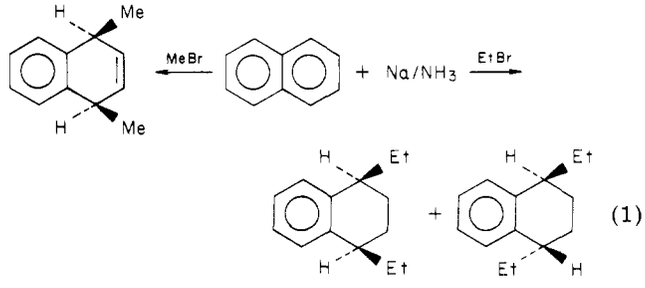
Scheme III



whole dihydroanthracene system as well as pyramidal inversion of the carbanion center. It is possible, of course, that both processes could occur simultaneously (broken lines). When the known pseudoaxial preference of substituents in this system[9] is considered together with the much more efficient overlap of a pseudoaxial carbanion, **1a** emerges as the most likely conformation. Furthermore, kinetic data[5f] seem to support the alkylation of **1a** as the major process with primary halides. As the substituent increases in size, trans products begin to predominate suggesting alkylation of **1b**[6] (this process is also favored by Bank et al., for large alkylating agents).[5f]

There have not been any reports concerned specifically with the stereochemical aspects of the reductive alkylation of naphthalene, perhaps due to the fact that the closely related anthracene system has been so well studied. Interestingly, the observation that reductive dimethylation of naphthalene provides only the cis isomer[11] must be regarded as strikingly different when compared to the case for anthracene. The major steric factor with dihydroanthracene is the "peri" interactions from the C-1 and C-8 positions. However, methyl is presumably not large enough to cause serious steric interactions of this type, since reductive methylation of anthracene is not very stereoselective, and, in addition, NMR indicates that 9-methyl-9,10-dihydroanthracene does not show a strong axial preference.[9] Thus, since one of these steric interactions is absent in 1,4-dihydronaphthalenes, *a reduction instead of an increase* in stereoselectivity is to be expected.

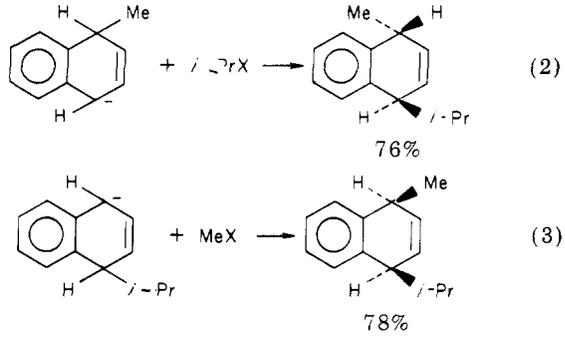
In order to investigate this problem in more detail, we carried out the reductive ethylation of naphthalene and discovered to our surprise that ethylation is in fact less selective than methylation resulting in a mixture of both cis and trans isomers (eq 1) (see Table I). Once again, this



(1)

is in contrast to anthracene which provides mainly the cis isomer. Reductive alkylation with isopropyl bromide, however, leads only to formation of the trans isomer, and this is, in fact, similar to the behavior of anthracene although more selective.

In an attempt to determine whether the size of the initial alkyl group incorporated or the second alkyl halide is determining stereochemistry, we examined both the isopropylation of a methylated dihydronaphthalene anion and the methylation of the monoisopropyl system (eq 2 and 3). Interestingly, both reactions were highly selective,



(2)

76%

(3)

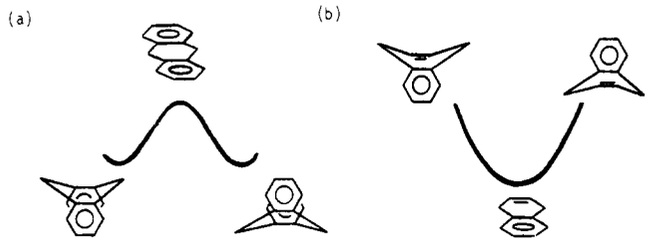
78%

favoring different isomers (see Table I). As one would expect, the NMR spectra of both of these isomers were quite similar in both pattern and chemical shift. However, the isomer resulting from the methylation reaction showed a singlet for the aromatic resonance but a somewhat more complex and broader vinyl signal than the other isomer. This is consistent with a cis assignment, since it has been shown by NOE experiments[5e] that in *trans*-9,10-dialkyl-

(8) Harvey, R. G.; Arzadon, L.; Grant, J.; Urberg, K. *J. Am. Chem. Soc.* **1969**, *91*, 4545.

(9) Brinkman, A. W.; Gordon, M.; Harvey, R. G.; Rabideau, P. W.; Stothers, J. B.; Ternay, A. L. *J. Am. Chem. Soc.* **1970**, *92*, 5912. See also: Lapouvade, R.; Labandibar, P. *Tetrahedron Lett.* **1970**, 1589.

Scheme IV



9,10-dihydroanthracenes, the trans alkyl groups cause a shift in the "ortho" aromatic protons causing a more complex aromatic region. Also, the cis geometry provides for significantly larger coupling between the allylic and vinyl protons providing the more complex pattern. However, in order to provide more evidence for this assignment, we subjected a mixture of these two isomers to dehydrogenation over Pd/C. The isomer we have assigned as cis aromatized more rapidly than the other isomer, and this is consistent with data that show that *cis*-9,10-dialkyl-9,10-dihydroanthracenes lose hydrogen faster than the corresponding trans isomers.[8]

Thus, a comparison of the alkylation behavior of 1,4-dihydronaphthalenes and 9,10-dihydroanthracenes (Table I) affords two seemingly contradictory observations. First, reductive methylation of naphthalene is stereospecific in providing only the cis isomer, and second, the dihydronaphthalene system has a greater tendency to afford trans products. These results signal some fundamental differences betweeen the two systems, and there must be some provisions made in Scheme III to account for the somewhat modified behavior of naphthalene.

In order to provide such an explanation, we must consider the basic stereochemical nature of the cyclohexadiene ring system.[10] As mentioned previously, it seems well accepted that 9,10-dihydroanthracene exists as rapidly equilibrating boat conformations (Scheme IV) with the planar form as an energy maximum. Derivatives of 1,4-cyclohexadiene, on the other hand, have been shown to be planar by NMR,[10] and Laane and Lord[12] suggested the pattern in Scheme IV for 1,4-cyclohexadiene itself, providing the planar form as an energy minimum. It now appears that 1,4-dihydronaphthalene lies somewhere in between, since large substituents cause "puckering" (presumably resulting in a boat-shaped ring similar to 9,10-dihydroanthracene), but the degree of puckering decreases sharply with a decrease in substituent size.[13] Thus, we would suggest that if the 1,4-dihydronaphthalene system resembles (b) in Scheme IV, a methyl substituent in the anion might provide only a slight folding (favoring pseudoaxial preference), which would result in greater access toward alkylation from the same side (this is in contrast to 9,10-dihydroanthracene wherein NMR results suggest little effect by a methyl substituent on the boat-to-boat inversion[9]). Hence, with a small alkylating agent like methyl halide, more rapid alkylation occurs cis to the methyl substituent resulting in the stereospecific production of the cis isomer. If the alkylating agent is larger (i.e., *i*-PrX), a steric effect with the methyl substituent results,[5f] reducing the rate of pseudoaxial attack and the trans product predominates (76/24).

In view of the cis stereospecificity discussed above for naphthalene in reductive dimethylation, it seems somewhat incongruous to note that naphthalene has in fact a greater tendency toward trans products than anthracene. However, the 1-methyl-4-sodio-1,4-dihydronaphthalene must be regarded as an exceptional case possessing a conformation which quickly gives way to a more folded structure with substituents larger than methyl (this sort of conformational continuum apparently does not exist for 9,10-dihydroanthracene). Since one "peri" interaction is missing from dihydronaphthalene as compared to dihydroanthracene, it is not at all surprising that 1-alkyl-4-sodio-1,4-dihydronaphthalenes with larger R groups (i.e., folded conformations like **1a** and **1b** in Scheme III) would provide more equatorial substitutions (trans products).

Experimental Section

General Procedures. The general procedure for reductive alkylation is as follows. The hydrocarbon in one part dry cosolvent (ether or THF) is added to two parts anhydrous ammonia at −78 °C (or at reflux, −33 °C) under helium. Lithium or sodium metal (1.25 equiv) is then added and stirring is continued for 20 min.

(1) Normal Quench. An excess of alkyl halide dissolved in dry cosolvent is added from a dropping funnel at a reasonable rate (frothing) until the deep color is discharged. Saturated ammonium chloride solution is immediately added, and the product isolated by ether extraction.

(2) Inverse Quench. The reaction mixture is pumped (helium pressure) through a glass tube which is immersed in a large excess of alkyl halide (under helium) cooled to −78 °C. **Caution**: frothing may occur.

1-Ethyl-1,4-dihydronaphthalene and *cis*- and *trans*-1,4-Diethyl-1,4-dihydronaphthalene. We have recently reported the preparation of these compounds.[4]

1-Isopropyl-1,4-dihydronaphthalene. Naphthalene (4 g) was reacted with sodium metal (2.1 g) according to the above procedure, using an inverse quench into isopropyl bromide. The reaction mixture (4.3 g) contained 93% of the monoisopropyl product (by NMR). Purification was accomplished by fractional distillation (bp 108–110 °C (5 mm)): NMR ($CDCl_3$) δ 7.1 (m, 4 H), 5.9 (complex d, 2), 3.25 (m, 3), 2.0 (m, 1), 0.75 (d of d, 6).

Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.23; H, 9.59.

***cis*-1-Methyl-4-isopropyl-1,4-dihydronaphthalene.** Sodium metal (1.2 g) was added to 80 mL of anhydrous ammonia containing 0.3 g of ferric chloride at −33 °C. After 20 min, 1-isopropyl-1,4-dihydronaphthalene (1.8 g) in 40 mL of ether was added and stirring was continued for 15 min. Inverse quenching (as above) into methyl iodide afforded 1.6 g of product after workup (shown by NMR to be 78% cis) which was purified by spinning-band distillation (bp 116–120 °C (5 mm)): NMR ($CDCl_3$) δ 7.1 (s, 4 H), 5.85 (m, 2), 3.3 (m, 2), 2.0 (b m, 1), 1.36 (d, 3), 1.0 (d, 3), 0.65 (d, 3).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.15; H, 9.49.[14]

***trans*-1-Methyl-4-isopropyl-1,4-dihydronaphthalene.** This compound was prepared by reacting 1-methyl-1,4-dihydronaphthalene (2.0 g) as above and quenching into isopropyl bromide affording 1.7 g of an isomer mixture (cis/trans ratio 24/76 by NMR). The trans isomer was isolated by spinning-band distillation[14b] (bp 116–120 °C (5 mm)): NMR ($CDCl_3$) δ 7.1 (m, 4 H), 5.85 (b s, 2), 3.3 (m, 2 H), 2.0 (b m, 1), 1.38 (d, 3), 0.95 (d, 3), 0.6 (d, 3).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.98; H, 9.61.

Dehydrogenation of *cis*- and *trans*-1-Methyl-4-isopropyl-1,4-dihydronaphthalene. An approximately equal mixture (1 g) of the two isomers was combined with 20 mg of 10% Pd/C in 25 mL of diglyme and the mixture was refluxed for 15 min. Filtration and ether/water workup produced 0.92 g of product in which one isomer (assigned as cis) was almost completely aromatized (by NMR).

(10) Rabideau, P. W. *Acc. Chem. Res.* **1978**, *11*, 141.
(11) Rabideau, P. W.; Harvey, R. G. *Tetrahedron Lett.* **1970**, 4139.
(12) Laane, J.; Lord, R. C. *J. Mol. Spectrosc.* **1971**, *39*, 340.
(13) Rabideau, P. W.; Burkholder, E. G.; Yates, M. J.; Paschal, J. W. *J. Am. Chem. Soc.* **1977**, *99*, 3596.

(14) (a) This compound was sensitive to air and repeated microanalyses were variable with carbon usually a bit low. (b) After purification, both cis and trans isomers contained some contamination from the other.

1,4-Diisopropyl-1,4-dihydronaphthalene. This compound was prepared from naphthalene (4 g) according to the above procedure, using a normal quench with isopropyl bromide. GLPC of the reaction mixture (5.2 g) indicated above 60% of the desired compound, with the remainder being 1-isopropyl-1,4-dihydronaphthalene. Fractional distillation provided an analytical sample (bp 120–124 °C (5 mm)): NMR ($CDCl_3$) δ 7.1 (b s, 4 H), 5.9 (b d, 2), 3.3 (m, 2), 2.0 (b m, 2), 0.95 (d, 6), 0.7 (d, 6).

Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.34. Found: C, 89.87; H, 10.07.

Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No. 1-Isopropyl-1,4-dihydronaphthalene, 70320-95-5; naphthalene, 91-20-3; isopropyl bromide, 75-26-3; *cis*-1-methyl-4-isopropyl-1,4-dihydronaphthalene, 70320-96-6; methyl iodide, 74-88-4; 1-methyl-1,4-dihydronaphthalene, 21564-70-5; *trans*-1-methyl-4-isopropyl-1,4-dihydronaphthalene, 70320-97-7; *trans*-1,4-diisopropyl-1,4-dihydronaphthalene, 70320-98-8; 1-ethyl-1,4-dihydronaphthalene, 36789-17-0; 9-methyl-9,10-dihydroanthracene, 17239-99-5; 9-ethyl-9,10-dihydroanthracene, 605-82-3; 9-isopropyl-9,10-dihydroanthracene, 17573-50-1; *cis*-1,4-dimethyl-1,4-dihydronaphthalene, 21947-40-0; *cis*-1,4-diethyl-1,4-dihydronaphthalene, 67542-20-5; *trans*-1,4-diethyl-1,4-dihydronaphthalene, 67542-21-6; *cis*-9,10-dimethyl-9,10-dihydroanthracene, 13417-34-0; *trans*-9,10-dimethyl-9,10-dihydroanthracene, 13417-35-1; *cis*-9,10-diethyl-9,10-dihydroanthracene, 20826-55-5; *trans*-9,10-diethyl-9,10-dihydroanthracene, 23660-32-4; 1-isopropyl-4-methylnaphthalene, 1680-53-1.

Oxidation of Sulfides and Phosphines by Aromatic Selenonic and Seleninic Acids[1]

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Both alkyl sulfides and triphenylphosphine are readily oxidized by *p*-chlorobenzeneselenonic acid to alkyl sulfoxides and triphenylphosphine oxide, the selenonic acid itself being reduced to *p*-chlorobenzeneseleninic acid. The seleninic acid, in an acid-catalyzed reaction, then even more rapidly oxidizes additional sulfide to sulfoxide (or Ph_3P to phosphine oxide) and is itself reduced to a diselenide. Study of the mechanism of this oxidation of sulfides by aromatic seleninic acids indicates that the rate-determining step is nucleophilic attack by the sulfide on the protonated seleninic acid, $ArSe(OH)_2^+$, to give the sulfoxide, a proton, and the selenenic acid, ArSeOH. The selenenic acid can then disproportionate to the diselenide, ArSeSeAr, and the seleninic acid. Despite the strong inherent oxidizing power of *p*-chlorobenzeneselenonic acid and its facile oxidation of alkyl sulfides and Ph_3P, it does not oxidize such other potentially oxidizable organic functionalities as alcohols, alkenes, or ketones.

The chemistry of aromatic selenonic acids ($ArSeO_3H$) has been explored previously in only a very limited way.[2] Like aromatic sulfonic acids ($ArSO_3H$) selenonic acids are strong acids.[2] However, quite unlike sulfonic acids, they are also apparently strong oxidizing agents,[2] strong enough reportedly to oxidize hydrogen chloride to chlorine.[3] This led us to wonder if selenonic acids might not be effective oxidizing agents for a variety of organic substrates and if their reactions with a number of compounds might not take an interesting course and be of potential synthetic value. For this reason we undertook a study of the reactions of a typical aromatic selenonic acid with a variety of different types of organic compounds.

This study revealed that, despite the ability of the selenonic acid to readily oxidize a halide ion such as bromide ion to Br_2, it is remarkably inert toward many organic functionalities that one might think it would oxidize.

We did find, however, two organic substrates that the selenonic acid would readily oxidize, alkyl sulfides and triphenylphosphine. In examining these two oxidations in more detail, we discovered, somewhat to our surprise, that, provided a strong acid is present as catalyst, the corresponding seleninic acid ($ArSeO_2H$) will actually oxidize either alkyl sulfides or triphenylphosphine faster than does the selenonic acid. The present paper describes what we have been able to learn about the character and mechanism of the oxidations of these two substrates by the two different types of organoselenium acids.

Results

p-Chlorobenzeneselenonic acid (1), which has been prepared and carefully characterized by Rebane,[4] was the aromatic selenonic acid selected for study. The corresponding seleninic acid, *p*-$ClC_6H_4SeO_2H$, and benzeneseleninic acid ($PhSeO_2H$) were the seleninic acids used. Because of the limited solubility of 1 in all common organic solvents except acetic acid and acetonitrile, acetonitrile was used as the solvent medium for most of the reactions.

Oxidation of Sulfides by *p*-Chlorobenzeneselenonic Acid. Treatment of dibenzyl sulfide with an equimolar amount of *p*-chlorobenzeneselenonic acid (1) in acetonitrile at room temperature resulted in quantitative oxidation of the sulfide to dibenzyl sulfoxide and in the formation of approximately 0.2 mol of bis(*p*-chlorophenyl) diselenide/mol of sulfide oxidized. Similar stoichiometry was observed in an oxidation carried out in acetic acid.

We also examined the oxidation of a diaryl sulfide, Ph_2S, by 1. In this case after a reaction time (18 h at room temperature in acetonitrile) far more than that sufficient for complete oxidation of dibenzyl sulfide to the sulfoxide

(1) This research was supported by the National Science Foundation, Grant CHE-76-13346.

(2) D. L. Klayman, "Organic Selenium Compounds: Their Chemistry and Biology", D. L. Klayman and W. H. H. Gunther, Eds., Wiley, New York, N.Y., 1973, pp 141–3.

(3) (a) H. W. Doughty, *Am. Chem. J.*, **41**, 326 (1909); (b) R. Lesser and R. Weiss, *Chem. Ber.*, **46**, 2640 (1913).

(4) E. Rebane, *Acta Chem. Scand.*, **23**, 1819 (1969).

0022-3263/79/1944-2357$01.00/0