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meso-Dihydroanthracene Chemistry: Synthesis and Mechanistic Information. 1,4 Conjugate Eliminations

STANLEY J. CRISTOL†

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

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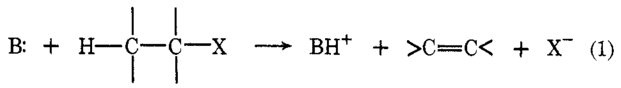
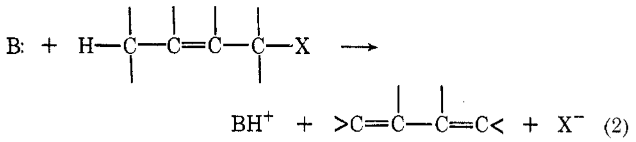
About 20 years ago our research group, then thoroughly involved with attempts to explore the consequences of dual mechanisms for bimolecular 1,2 or β elimination[1] (eq 1), began to think about plausible mech-



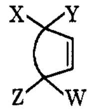
$$\mathrm{B{:}} + \mathrm{H{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X} \longrightarrow \mathrm{BH^+} + \mathrm{{>}C{=}C{<}} + \mathrm{X^-} \qquad (1)$$



$$\mathrm{B{:}} + \mathrm{H{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{C}{=}\overset{|}{C}{-}\overset{|}{\underset{|}{C}}{-}X} \longrightarrow \mathrm{BH^+} + \mathrm{{>}C{=}\overset{|}{C}{-}\overset{|}{C}{=}C{<}} + \mathrm{X^-} \qquad (2)$$

anisms for 1,4 conjugate elimination (eq 2). Interest in this area was piqued by the discovery[2] by Young at UCLA of the abnormal bimolecular allylic displacement (SN2′) reaction. It was thought that its stereochemistry[3] might be related to that of a concerted 1,4 conjujate elimination in the way that the preferred anti β elimination was related to inversion in bimolecular (SN2) displacement reactions.[1a]

In order to look at the question of stereochemistry in such reactions, we had to utilize systems in which groups to be eliminated could be fixed, *i.e.*, cis and trans to each other, and ring systems (**1**) offered such possibilities.



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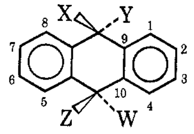

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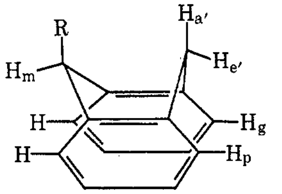

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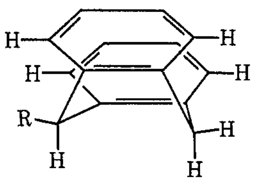

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Although there were a number of possible choices for **1**, we decided to work in the *meso*-dihydroanthracene system (**2**) for the simple reason that synthetic prospects appeared good. This turned out to be a fortunate choice, not only because synthetic procedures could be developed but also because the system (**2**) allowed us, as our sophistication grew, to look at conformational effects, not only on 1,4 conjugate elimination processes but also on reactions at the bow and stern of the boat-shaped cyclohexadiene ring system.[4]

Conformational Analysis

The flat projection (**2**) of the *meso*-dihydroanthracene system obscures the very interesting conformational situation which exists. Consideration of normal bond angles shows that structures **3** and/or **4** are to be anticipated, and that the two bonds at both C-9 and C-10 (the meso atoms) have quite different stereochemical positions. The "folded" structure was demonstrated by X-ray analysis[5] of 9,10-dihydroanthracene and discussed in detail by Beckett and coworkers.[6] They noted the possibility of conformational "isomers" and suggested that the barrier for interconversion of one "butterfly" form to the other should be small. This process, *i.e.*, **3** → **4**, we call "ring conversion." Thus substituents might choose (or be forced) to have either axial or equatorial positions.[7] We will discuss conforma-

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(1) See, for example: (a) S. J. Cristol, *J. Amer. Chem. Soc.*, **69**, 338 (1947); (b) S. J. Cristol, N. L. Hause, and J. S. Meek, *ibid.*, **73**, 674 (1951).

(2) R. E. Kepner, S. Winstein, and W. G. Young, *ibid.*, **71**, 115 (1949); W. G. Young, I. D. Webb, and H. L. Goering, *ibid.*, **73**, 1076 (1951).

(3) G. Stork and W. N. White, *ibid.*, **75**, 4119 (1953).

(4) The most common way to make a six-membered boat-shaped ring is to construct a short bridge across the C-1 and C-4 carbon atoms (*e.g.*, norbornane, norbornene, and norbornadiene). While a good deal of our knowledge of stereochemical preferences in organic reactions is derived from such systems, most of these are "gunwale" reactions of boats. As the bow and stern carbon atoms are bridgeheads, reactions at these positions are difficult and do not offer, in general, opportunity to look at stereochemical effects.

(5) W. G. Ferrier and J. Iball, *Chem. Ind.* (*London*), 1296 (1954).

(6) (a) A. H. Beckett and B. A. Mulley, *ibid.*, 146 (1955); (b) *J. Chem. Soc.*, 4159 (1955); (c) A. H. Beckett and J. Walker, *Tetrahedron*, **19**, 545 (1963).

(7) The terms axial (a) and equatorial (e) which we suggested[8] for describing the positions at the bow and stern of the central boat-form ring (in analogy with their use in other rings) seem now to be generally accepted. Perhaps acceptance of this usage, rather than that suggested by Beckett and Mulley as "perp" and "lin" as positions on a "barge" or the more colorful terms[9] "flagpole" and "bowsprit," was furthered by the whimsical Irish satire published[10] in a paper entitled "The Stereochemistry of Octahydrohexairon. A Molecular 'Raft'."

(8) S. J. Cristol, W. Barasch, and C. H. Tieman, *J. Amer. Chem. Soc.*, **77**, 583 (1955).

(9) C. J. Angyal and J. A. Mills, *Rev. Pure Appl. Chem. Aust.*, **2**, 185 (1952).

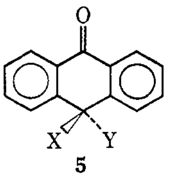
(10) A. S. Smith (pseud.), *Chem. Ind.* (*London*), 353 (1955).

tional preferences later, but it is clear that Beckett and Mulley recognized the problem in their first papers[6] and showed that results in the literature on dihydroanthracenes were consistent with the idea tht axial substituents suffer less from nonbonded interactions with peri substituents (*i.e.*, those at C-1, C-4, C-5, and C-8) than do equatorial substituents, so that **3** would be more stable than **4**.

Pmr studies on *meso*-dihydroanthracene itself show that, on the nmr time scale, the four meso protons are identical, at least down to −55°.[11,12c] This confirmed the suggestion of Beckett and Mulley that ring conversion has only a small energy barrier.[11]

Synthesis of Appropriate *meso*-Dihydroanthracenes

Three methods of synthesis suggest themselves as possible processes for the preparation of compounds useful for our studies. They are: (a) additions to anthracenes; (b) reduction of anthrones (**5**) or anthraquinones (**6**) to alcohols (**7**) or diols (**8**), possibly followed by esterification; and (c) replacement of an atom or group in a *meso*-dihydroanthracene by another.



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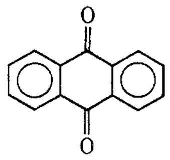

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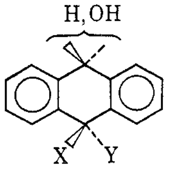

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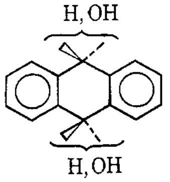

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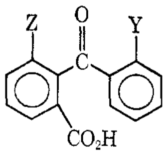
Although it is possible to prepare dihalides by the addition of halogens to a variety of anthracenes, and although some of these are cis and some are trans,[13] neither addition nor displacement has led to a cis–trans pair of dihalides in a given system, and our early efforts[8] in this area also were fruitless.[14] On the other hand solvolysis of dihalides had been shown[15] to lead to cis–trans mixtures of diols or diol esters of known configuration,[16] and a variety of reduction procedures on anthraquinones had been shown to lead to cis–trans mixtures of diols.[17] It was also known that diol derivatives suffered elimination reactions.[15] We therefore decided to put our efforts into preparative methods involving reductions of anthraquinones or anthrones.

A number of anthraquinones are available commercially (being dye intermediates), but our interest in having a number of substituents with greater steric demand than hydrogen at the peri positions made synthesis of others necessary. Syntheses *via* Diels–Alder reactions on *p*-benzoquinone followed by dehydrogenation were successul,[18] while preparation by acid-catalyzed ring closure of benzoylbenzoic acids (**9**, **11**) was complicated by attendent Hayashi rearrangements[19] of 3-substituted 2-aroylbenzoic acids (**9**) to 6-substituted compounds (**11**) so that preparations designed to lead to 1,8-disubstituted anthraquinones (**10**) often led instead largely to 1,5 compounds (**12**). Our studies,[18,20] which added to the mechanistic information and ideas adduced by Sandin[19c] and by Newman[19d] and their students, showed the effects of substitution and of acid concentration upon the rates of Hayashi rearrangements, which proceeds through intermediates like **13**, and anthraquinone formation, which involves intermediates like **14**. Unfortunately, the mechanisms of these reactions make the formation of mixtures unavoidable in many cases. However, we learned how to do a "reverse-Hayashi" rearrangement—that is, to go from 6-alkyl derivatives (**11**) to 3-alkyl derivatives (**9**) with change in acid concentration, which had not been done before. We thus had to live with the formation of mixtures of anthraquinones when we started with 3- or 6-substituted aroylbenzoic acids. On the other hand, cyclization of benzylbenzoic acids (**15**) proceeded in



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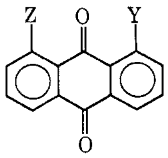

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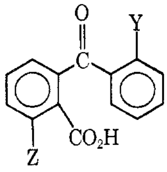

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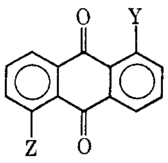

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(11) There has been a modest amount of discussion in the literature on the pmr spectra of *meso*-dihydroanthracenes.[12] Due to space limitations, this subject will not be included here. The use of pmr data for ring conversion rates on the 7,12-dihydropleiadenes represents an analogous problem.[12g]

(12) (a) M. L. Caspar, J. N. Seiber, and K. Matsumuto, Abstracts, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan 1964, p 30C; (b) R. Lepouyade and P. Labandibar, *Tetrahedron Lett.*, 1589 (1970), and references cited therein; (c) D. Nicholls and M. Szwarc, *J. Amer. Chem. Soc.*, **88**, 5757 (1966); (d) D. Y. Curtin, C. G. Carlson, and C. G. McCarty, *Can. J. Chem.*, **42**, 565 (1964); (e) R. G. Harvey, L. Arzador, J. Grant, and K. Urberg, *J. Amer. Chem. Soc.*, **91**, 4335 (1969); (f) A. W. Brinkman, M. Gordon, R. G. Harvey, P. W. Rabideau, J. B. Strothers, and A. L. Ternay, Jr., *ibid.*, **92**, 5912 (1970); (g) P. T. Lansbury, *Accounts Chem. Res.*, **2**, 210 (1969); (h) M. L. Caspar, unpublished work.

(13) See ref 8 for appropriate citations.

(14) It seems likely that, with more sophisticated methods of detection, analysis, and separation, and with clearer understanding of reaction course and the consequences of kinetic and thermodynamic control, this problem should yield to continued investigation.

(15) E. d. B. Barnett, M. A. Mathews, and J. W. Cook, *Recl. Trav. Chim. Pays-Bas*, **43**, 530 (1924); **44**, 217, 728, 818, 894 (1925); **45**, 68, 558 (1926).

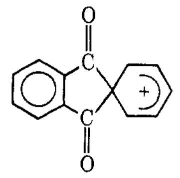
(16) E. Bergmann and A. Weizmann, *J. Amer. Chem. Soc.*, **60**, 1801 (1938).

(17) (a) E. Boyland and D. J. Manson, *J. Chem. Soc.*, 1837 (1951); (b) S. J. Coffey and V. Boyd, *ibid.*, 2468 (1954).

(18) S. J. Cristol and M. L. Caspar, *J. Org. Chem.*, **33**, 2020 (1968).

(19) (a) M. Hayashi, *J. Chem. Soc.*, 2516 (1927); 1513, 1520, 1524 (1930); (b) M. Hayashi, S. Tsuruoka, I. Morikawa, and H. Namikawa, *Bull. Soc. Chem. Jap.*, **11**, 184 (1936); (c) R. B. Sandin, R. Melby, R. Crawford, and D. G. McGreer, *J. Amer. Chem. Soc.*, **78**, 3817 (1956); (d) M. S. Newman and K. G. Ihrman, *ibid.*, **80**, 3652 (1958).

(20) S. J. Cristol, K. Schwarzenbach, and M. L. Caspar, Abstracts, 19th International Congress of Pure and Applied Chemistry, London, 1963, Part A, p 71.



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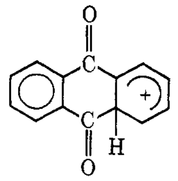

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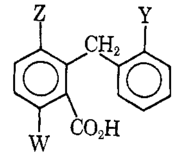

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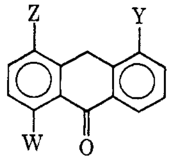

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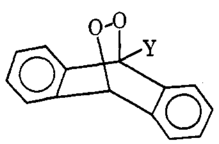
good yield and without rearrangement to the corresponding anthrones (**16**). The procedure which involves reduction of **9** (or **11**) to the corresponding **15**, cyclization to **16**, and oxidation to **10** (or **12**) thus is an alternative to the direct cyclization followed by mixture separation.

With a variety of anthraquinones in hand, we next looked at ethereal lithium aluminum hydride and methanolic sodium borohydride reductions to the diols.[21] With few exceptions, yields of diols with either reagent were close to quantitative, and stereochemical consequences were also very similar.[22] The stereochemistry of diols produced could be determined by independent preparation of the cis diol by hydride reduction of the corresponding anthracene photoperoxide (**17**) and/or



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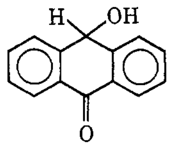

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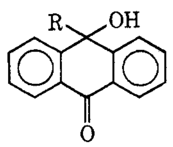

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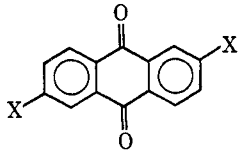
by noting the presence of intramolecular hydrogen bonding in the cis diol by infrared spectral studies. In a few cases, pmr correlations have been used.[12a,h]

As the reduction of the anthraquinones undoubtedly proceeds through the corresponding oxanthrones,[23] *e.g.*, **18**, or their aluminum or boron esters,[24] we decided to look at some of these. As work proceeded, it became clear that steric factors were significant in the stereochemistry of the reductions. For this reason, 10-alkyloxanthrones (**19**) were studied.

Our studies encompassed about 20 compounds and led to product mixtures ranging from stereoselectivity toward cis diol, no substantial stereoselectivity, to selectivity toward trans diol. Our results indicate that when there are no peri (1, 4, 5, and 8) substituents, the reaction is not highly stereoselective, with the cis diol the major product (with $NaBH_4$). This conclusion is based upon work with anthraquinone (**6**), 2,6-dimethylanthraquinone (**20**-CH_3), and 2,6-dichloroanthraquinone (**20**-Cl). The situation is quite different for the 1,5-disubstituted anthraquinones **21**-CH_3, **21**-Cl, and **21**-Br,



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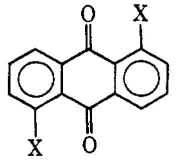

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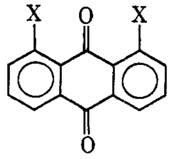

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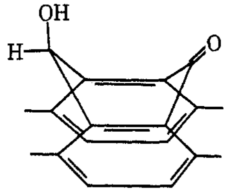
where 80–95% of the products were trans diols, or the 1,8 compounds **22**-CH_3 and **22**-Cl, where again the products were preponderantly trans. Thus the course of the reaction is markedly sensitive to peri substitution.

The stereochemical outcome of the reaction is determined, as mentioned above, by reduction of the intermediate boat-form oxanthrone, which may exist in two nonidentical conformations in which the hydroxyl group is axial, as in **23**, or equatorial, as in **24**. A model of anthrone (**25**) shows that the distance between the



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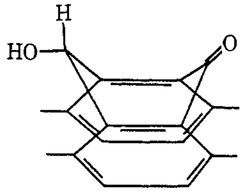

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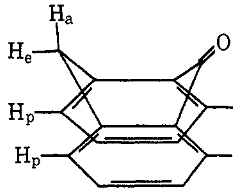

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equatorial and peri protons is about 2.4 Å, while the axial–peri proton distance is 3.1 Å. The equatorial–peri distance between centers is not markedly changed with oxygen substitution at C-10, or with methyl or chlorine substitution at C-4 or C-5 (or any combination of these), while such changes increase the axial–peri distance to 3.3 to 3.5 Å. Thus the nonbonded interactions between equatorial and peri substituents should approximate those between similar substituents located at 1,3-diaxial positions on a cyclohexane ring.[25] If one assumes that the van der Waals radii of the atoms con-

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(21) S. J. Cristol, M. L. Caspar, and M. Toji, Abstracts, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1967, No. S 67.

(22) Reductions of anthraquinones with borohydride to the diols require the presence of air to reoxidize any hydroquinone formed as a side reaction product. Reductions with $LiAlH_4$ apparently do not yield hydroquinones in notable amounts.

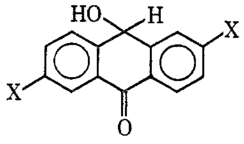
(23) This has been shown to be the case for aluminum isopropoxide reduction of anthraquinone, where **18** has been isolated, and we have isolated monoreduction products with $LiAlH_4$.

(24) The half-reduced product with $LiAlH_4$ will certainly be present as lithium alkoxyaluminum species, but in view of the facts that (a) we used a large excess of hydride reducing agent and (b) both isomers were always obtained, it seems safe to assume that the reduction of the second carbonyl group involved (or could involve) a second molecule of lithium aluminum hydride. Put another way, the reaction of each carbonyl group with the hydride appears in the main part to be intermolecular. An intramolecular process could lead only to trans diol (see below). The greater amounts of trans diols in certain reductions with lithium aluminum hydride over those with sodium borohydride may be due to intramolecular processes. With the sodium borohydride–methanol reductions the alkoxyborohydride intermediates can exchange with methanol so that it is possible that the oxanthrones themselves are intermediates. Support for this comes from the observation that some quinones and corresponding oxanthrones gave identical reaction mixtures.

(25) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1967.

cerned lead to an approximate measure of the interaction energy between groups,[26] one may estimate relative energies of the two conformations of oxanthrones. In oxanthrone itself, conformations **23** and **24** may not differ substantially in energy, but as groups larger than hydrogen are substituted peri to the carbinol carbon atom, the conformations analogous to **23** (axial hydroxyl) should become more stable than those with equatorial OH (**24**). All other things being equal, transition states for reduction of oxanthrones should similarly reflect such conformational stabilities.

Extension of the concept of "steric approach control" suggested for hydride reduction of cyclic ketones[28,29] to the anthrone model **25** leads to the obvious prediction that axial attack by hydride (to give equatorial alcohol) should be favored, even when there are no 1 or 8 substituents (peri to the keto group) in the anthrone, and that this preference should be enhanced when there are large peri substituents. Thus reductions of anthraquinone (**6**) and 2,6-disubstituted compounds **20** which proceed through oxanthrones **18** and **26**, respectively, in which equatorial OH is not markedly disfavored, give mixtures of diols containing substantial cis product, consistent with the conformational arguments. In a similar fashion, one can rationalize the predominant trans diol products from the 1,5 compounds **21**, which must proceed *via* the oxanthrone **27**, where preferences for axial OH and axial hydride transfer lead to trans diol. The situation with the 1,8 compounds **22** is confused by the fact that the first reduction may occur at the keto group flanked by the peri substituents (*e.g.*, to give **28**) or that remote from them (*e.g.*, to give **29**). Reduction of **28** (prepared by hydrolysis of 10-bromo-4,5-dimethylanthrone) gave almost pure trans diol, while reduction of the anthraquinone **22**-CH_3 gave about 25% cis diol, suggesting that a large part of this reaction proceeded *via* **29**.



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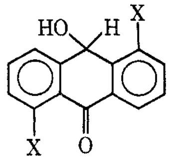

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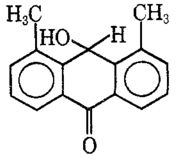

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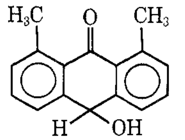

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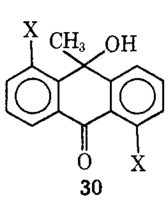
In order to prove that the principal effect of the C-10 hydroxyl group on reduction of the C-9 keto group was conformational, rather than due to an intramolecular process,[24] we looked at the reduction of some 10-methyloxanthrones. Here peri substituents should force the larger methyl group axial, with equatorial-OH resulting, so that axial hydride attack should give cis diol. This is observed with **30**-CH_3 which gave 67% cis diol (compare **27**-CH_3 with 88% trans diol) and **30**-Cl which gave 52% cis diol, each with one peri substituent, and **31**, where two peri substituents force the reaction toward 90% cis diol.



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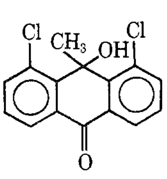

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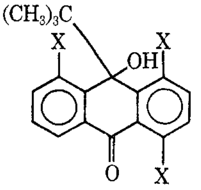
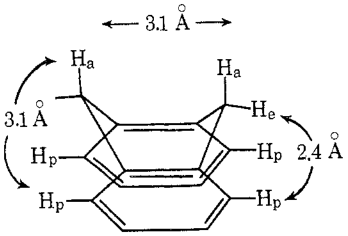


32

In most of the reductions both diols were formed, and it is not known whether the minor isomers are formed by axial hydride attack involving the less favored conformation or by equatorial attack with favored anthrone conformation. To show the possibility of the latter reaction, we prepared several 10-*tert*-butyl-10-oxanthrones (*e.g.*, **32**). The distance between axial protons in *meso*-dihydroanthracene (**33**) is 3.1 Å, and a similar distance between the axial proton in anthrone and the incoming axial hydride in reduction might be expected. Placing the bulky *tert*-butyl group at C-10 fixes the conformation with equatorial OH and also hinders axial attack. Under such circumstances, reduction by borohydride is much slower and gives almost completely trans diol, presumably the result of equatorial hydride attack on conformations related to **34**.



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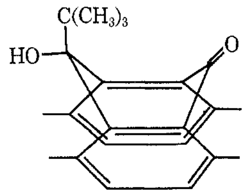

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The reductions described above often led (by kinetic control) to mixtures rich in one diol, from which it was difficult to isolate reasonable quantities of the minor diol. However, reduction is controlled, as discussed above, by "steric approach control," while the relative stabilities of cis and trans isomers are controlled (formula **33**) by the steric interactions between meso and peri substituents, generally to avoid large equatorial–peri interactions (distance between protons, 2.4 Å) and occasionally to avoid axial–axial interactions. As the ring conversion "butterfly flip" energy barrier is small,[6,11]

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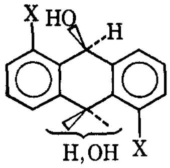
(26) We have chosen to discuss conformational analysis of anthrones and *meso*-dihydroanthracenes in terms of van der Waals radii rather than in more sophisticated fashion, as it is clear that free-energy differences in 1,3-cyclohexane systems[25] (axial–axial *vs.* axial–equatorial) will not be directly related to equilibrium values in our systems. Bond deformation energies are different in the two systems, as are the abilities of aliphatic and aromatic protons in hydrogen bonding. In addition, dipole–dipole interactions must be considered, and in certain cases axial–axial interactions in *meso*-dihydroanthracenes will be important. We recognize that this treatment does not accommodate the variation in size of atoms or groups with direction of approach. Nevertheless the conformational free-energy difference of *ca.* 1.5 kcal/mole for a methyl group in *meso*-dihydroanthracenes[12a] is very similar to that found for a cyclohexyl methyl group.[25] Pauling's[27] values for effective van der Waals radii were used: H, 1.20 Å; O, 1.40 Å; Cl, 1.80 Å; Br, 1.95 Å; CH_3, 2.0 Å.

(27) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p 189.

(28) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Amer. Chem. Soc.*, **78**, 2579 (1956).

(29) H. C. Brown and J. Muzzio, *ibid.*, **88**, 2811 (1966).

conformational preferences may be met, and equilibrium studies, where isomerization is possible, should reflect these, as has been shown in a number of 9,10-dihydro-9,10-anthracenecarboxylic acid derivatives.[6,30] Thus conformational arguments (avoidance of equatorial–peri interactions, except for hydrogen–hydrogen and hydrogen–oxygen which are approximately equal[31]) suggest the following relative stabilities. 9,10-Dihydro-9,10-anthradiol (**8**) should have cis–trans isomers of approximately equal stabilities, while *trans*-**35**-Cl, the principal reduction product of **21**-Cl, has one O–Cl equatorial–peri interaction and should be less stable than its cis isomer, in which both OH groups can assume axial positions. Similar arguments can be made for **35**-CH_3 and **35**-Br isomers. Conformational analysis predicts that **36** and **37** should have roughly equal cis–trans stabilities (only H–H and O–H equatorial–peri interactions are present at one position), so that reduction products from **22** (rich in *trans*-**36**) and from **31** (rich in *cis*-**37**) should isomerize to mixtures richer in the other isomers. A particularly interesting case is the trans isomer **38**, formed by equatorial hydride attack, which has the secondary hydroxyl axial. Due to the greater steric interference between the axial OH and the *tert*-butyl group, *trans*-**38** should isomerize more nearly completely to the cis diol, compared with *trans*-**37**, with the smaller methyl group.



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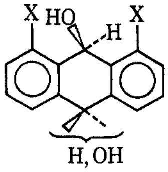

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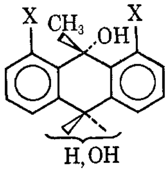

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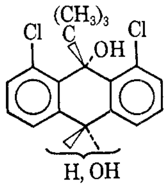
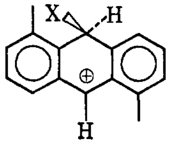


38

To test these predictions, experiments of two sorts were conducted. Equilibration of acetate esters in acetic acid, involving carbonium ion intermediates, and base-catalyzed epimerization of diols, with carbanion intermediates, were both studied.

As an example of the first type, when the diacetate of *trans*-**36**-Cl was allowed to stand at room temperature in acetic acid containing sodium acetate for 4 hr, a mixture of 80% trans and 20% cis diacetates resulted. A similar experiment with the cis diacetate (2 hr) gave about 20% trans. Attendant elimination reactions prevented us from carrying these reactions further, but clearly the equilibrium constant is close to unity. Predominant elimination reactions with the dimethyl derivatives precluded their study.

When the diacetate of the 1,5-substituted trans diol **35**-Cl was heated at reflux in acetic acid (sodium acetate present), the solution contained 60% of the cis diacetate in 15 min and 85% of cis diacetate in 30 min. Presumably complete equilibration would lead to substantially all-cis diacetate. The diacetate of the trans dimethyl diol **35**-CH_3 was converted completely to cis diacetate in 2.5 hr at 25°. The relative rates of the diacetate equilibrations (**35**-CH_3 much faster than **35**-Cl) make the assumption that a dihydroanthryl cation (**39**) is the intermediate in these reactions very reasonable (see below).



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When either isomer of 1,8-dichloro-9-methyl-9,10-dihydro-9,10-anthradiol (**37**-Cl) was treated with *ca.* 0.1 *M* NaOH in ethanol for 16 hr at 50°, a mixture containing approximately equal amounts of both diols resulted. On the other hand, the 9-*tert*-butyl trans diol **38** isomerizes under similar conditions completely to cis diol.

These isomerization studies (and others like them) thus fully confirm predictions made on the basis that the central ring in *meso*-dihydroanthracenes (a) is boat form, (b) is readily interconverted, and (c) is subject to serious steric interactions. Furthermore they permitted us to prepare a large number of cis–trans diols for the work described in the next sections.

1,4 Conjugate Eliminations[8,32]

In our first paper[8] on rates of base-promoted bimolecular elimination reactions with the 1,5-dichloro diol (**35**-Cl) isomers and with their benzoates, we noted that syn eliminations from trans compounds were significantly (>10^3) faster than anti eliminations. We proposed that a transition state such as **40** might be favorable in a concerted syn process. This process was formally analogous with the mechanism proposed[2,3] for the S_N2' displacement reaction and was therefore attractive. However, we noted a number of anti 1,4 conjugate eliminations described in the literature and withheld judgment.[33] We continued work on the diols whose syntheses we have described above in order to test this idea. Table I gives rate constants for 1,5-disubstituted compounds (**35**), for 2,6-disubstituted compounds (**41**), and for the 1,8-dichloro pair **36**-Cl. The data show that all of the syn eliminations proceed more rapidly than their anti counterparts, but that the rate ratios vary substantially. Without large peri substit-

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[30] J. Rigaudy and L. H. Danh, *C. R. Acad. Sci., Ser. A*, **256**, 5370 (1963).

[31] It would appear possible that the slightly larger van der Waals radii sum for O–H over H–H, which is destabilizing, is compensated for by the possibility of peri-H–equatorial-O bonding, which is stabilizing.

[32] S. J. Cristol, M. Toji, and M. L. Caspar, Abstracts, 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963, p 1M.

[33] de la Mare[34] has since shown that the case[35] in which anti 1,4 conjugate elimination was presumed to be faster than syn elimination is probably incorrect.

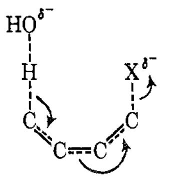
[34] P. B. D. de la Mare, R. Koenigsberger, and J. S. Lomas, *J. Chem. Soc. B*, 834 (1966).

[35] H. D. Orloff and A. J. Kolka, *J. Amer. Chem. Soc.*, **76**, 5484 (1954).

Table I
Rates of Elimination of Water from 9,10-Dihydro-9,10-anthradiols with Sodium Hydroxide in Ethanol at 50°

1,5 substituent (**35**)	$k_{\text{trans}}{}^{a}$	$k_{\text{cis}}{}^{a}$	$k_{\text{trans}}/k_{\text{cis}}{}^{b}$
Cl,Cl	2.8×10^{-2}	1.1×10^{-6}	2.6×10^{4}
H,H	3.3×10^{-4}	1.5×10^{-5}	22
CH_3,CH_3	3.9×10^{-5}	3.5×10^{-9}	1.1×10^{4}
2,6 substituent (**41**)			
Cl,Cl	6.0×10^{-2}	1.4×10^{-3}	43
H,H	3.3×10^{-4}	1.5×10^{-5}	22
CH_3,CH_3	7.8×10^{-5}	3.2×10^{-6}	24
1,8 substituent (**36**)			
Cl,Cl	9.2×10^{-2}	1.3×10^{-4}	7.1×10^{2}

[a] l. sec^{-1} $mole^{-1}$. [b] Ratio of the rate of syn elimination to that of anti elimination.



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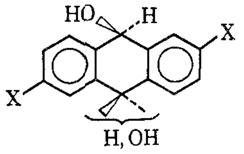

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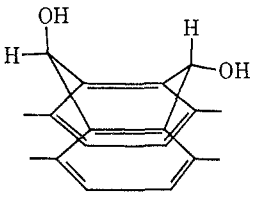

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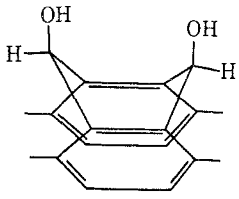

43

uents, the ratios are 20–40, and they are much greater (>10^4) with large groups at C-1 and C-5.

Closer inspection of the data suggests that the trans diols data are "normal," that is, for both series chlorine substitution activates for elimination compared with hydrogen, and methyl deactivates. The cis diol data, however, look "peculiar" in that both chlorine and methyl deactivate compared with hydrogen. The data are displayed in Figures 1 and 2 as Hammett plots[36] to show the same feature. Syn eliminations (from trans diols; Figure 1) proceed almost as rapidly with large peri substituents as without, and all the data are accommodated to a reaction constant ρ of 3.4. On the other hand, anti eliminations (Figure 2) are markedly inhibited by large peri substituents, although the unhindered reactions also have the rather high ρ value of 3.1.

Conformational ideas suggest that the trans diols may be reactive because they (**42**) must have one axial hydrogen, unhindered and exposed to attack by base. On the other hand, the preferred conformation (**43**) of the cis diol has only equatorial hydrogens, which are shielded from attack by base by the peri hydrogens and/or substituents. The alternative conformation has axial hydrogens suitable for attack, but the higher energy of equatorial–peri destabilizing interactions.

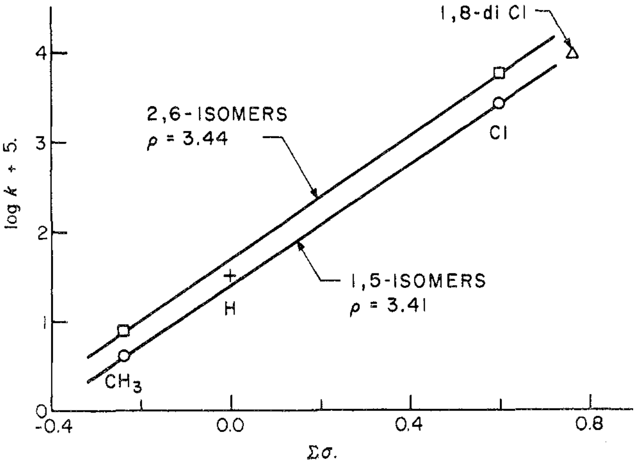

Figure 1. Hammett $\rho\sigma$ treatment of data of Table I for syn elimination from trans diols.

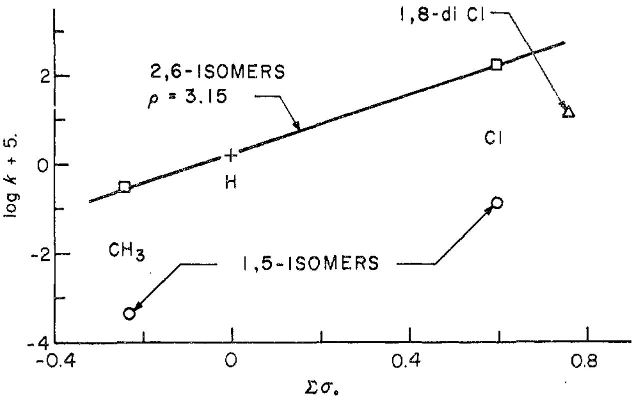

Figure 2. Hammett $\rho\sigma$ treatment of data of Table I for anti elimination from cis diols.

These ideas plus the high ρ values observed suggested consideration of an alternative process, one involving a carbanion intermediate, rather than a concerted process, for both syn and anti eliminations. The carbanion process would fit the high ρ values and would predict, in suitable cases, (a) D exchange, (b) base-catalyzed isomerizations, (c) small effects on rates of leaving anionoid group (nucleofuge), and (d) preference for axial protons, not for syn elimination. We decided to look at these possibilities.

For syn eliminations from 1,5-dichloro trans diol derivatives (**35**) we found the following relative rates: diol, 1.0; diacetate, 10; dibenzoate, 16; monobenzoate (loss of water), 32. The first three pieces of data are readily accommodated to the effect of these groups on the acid strengths of the protons involved. The fact that the monobenzoate loses water twice as fast as the dibenzoate loses benzoic acid (no statistical correction has been applied) is certainly consistent with a carbanion process and is not consistent with a concerted process.

We looked for deuterium exchange with **44** which ex-

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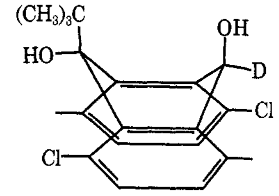
[36] We have chosen to plot log k *vs.* $\sigma_m + \sigma_p$, except for the 1,8 compound, where we used $2\sigma_p$.



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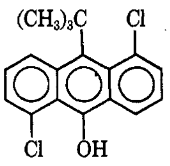

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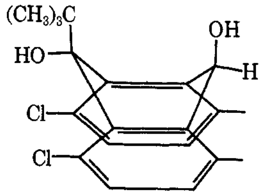

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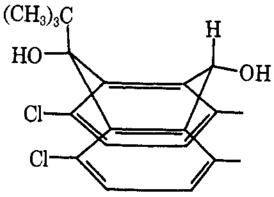

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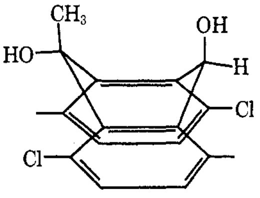
changes deuterium readily to ethanolic alkali ($k_{ex} \sim 10^{-5}$ l. sec^{-1} mole^{-1} at 73°). The rate of exchange was quite similar to that of elimination from the 1,5-dichloro cis diol **35**-Cl (see Table I). No elimination occurred with **44**, presumably because the aromatized product **45** would have serious steric interactions. Diol **46** also does not suffer elimination, but in ethanolic alkali isomerizes to **47**. Its rate constant for isomerization at 50° (1.7×10^{-4} l. sec^{-1} mole^{-1}) is very close to that for elimination from 1,8-dichloro cis diol (**36**-Cl), suggesting that both reactions involve attack at the equatorial proton peri to hydrogens to give carbanions.

With the less bulky methyl compounds **48** and **49** we find that cis–trans isomerization (**48** more stable than **49**) competes with elimination, and also that the cis diol **49** eliminates water (anti) more rapidly than does the trans isomer **48** (syn elimination).



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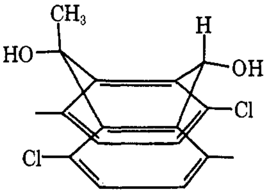

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These data, and others like them, suggest Scheme I as the path for various base-promoted reactions, with no evidence at hand at all for any concerted processes.

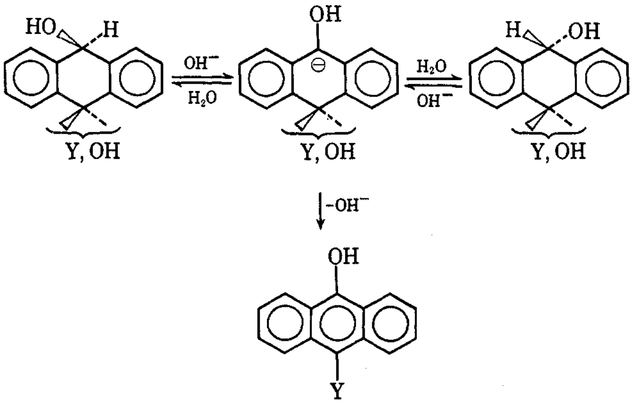
We are not in a position to comment upon whether the preference for attack at axial protons is entirely steric or partly stereoelectronic. Models suggest that orbital overlap of the benzene rings may be greater with the axial orbital than with the equatorial one.

The results of this portion of our studies were somewhat disappointing. Although we have done quite a bit of interesting chemistry, we have ended on an inconclusive note, and we are still left with our original problem—that is, what kind of transition state should be preferred in concerted 1,4 conjugate elimination?

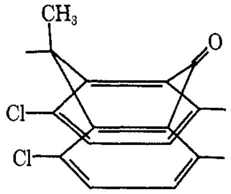
Meso Substitution Reactions

As noted above in the section on synthesis, displacement reactions at the meso positions have been known for some time, but little mechanistic information is derivable from early work. For example, it is not possible to know, from the description of these experiments, whether kinetic or thermodynamic control was involved. As described above, our own work on acid-catalyzed isomerization presumably gives examples of such reactions, involving carbonium ion intermediates, such as **39**. No examples of bimolecular displacements are known to us, although we have not investigated these at all.

Scheme I



Insight into conformational aspects of dihydroanthracenes now permits one to prepare molecules with "fixed" axial and equatorial substituents to begin to investigate stereochemical aspects of displacement reactions at the bow and stern of the center ring, and we have begun such an investigation. Reduction of the anthrone **50** with $LiAlH_4$ gives **51** and **52** in a ratio of 95:5, and this is converted to a 50:50 mixture in acidic aqueous dioxane. The peri chlorine atoms force the methyl group into the axial position, and therefore the hydroxyl groups in **51** and **52** can be confidently assigned the positions shown. Acetates and benzoates of both alcohols have been prepared. Both **51**- and **52**-benzoates solvolyze in aqueous dioxane, in acetic acid, and in methanol to give identical product mixtures of alcohols, acetates, and methyl ethers, indicating the intermediacy of a common species, **53**. In each case, the principal kinetic product is the derivative of the cis alcohol **52**, although measurable quantities of the epimer are also present. Equilibrium isomerizations have also been conducted and a study of solvolysis rates from derivatives of both isomers has been begun. Although we have not reached the state of being able to discuss these



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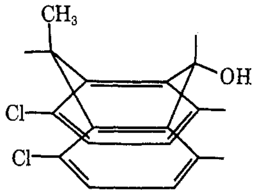

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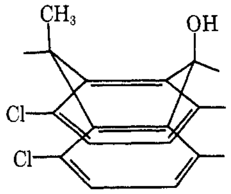

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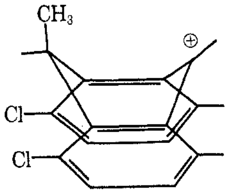


53

with any degree of sophistication, our initial results indicate that formation of the cation **53** from axial and equatorial progenitors and coordination of **53** with nucleophiles from either direction is not a highly discriminatory process and that differences will probably be found to have steric roots.

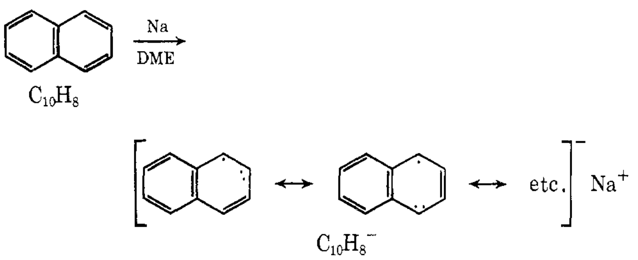
I am pleased to acknowledge my indebtedness to those of my colleagues who participated in this work. Portions of this were conducted as parts of the Ph.D. dissertation work of Werner Barasch, Myron L. Caspar, Leo E. Rademacher, Charles H. Tieman, and Masuo Toji and the postdoctoral work of Raymond P. Anderson and Kurt Schwarzenbach. We are also indebted to the National Science Foundation for generous support.

Electron Transfer, Naphthalene Radical Anion, and Alkyl Halides

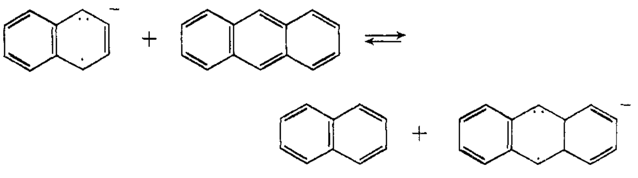
JOHN F. GARST
Department of Chemistry, The University of Georgia, Athens, Georgia 30601

Received October 19, 1970

In solvents like 1,2-dimethoxyethane (DME), naphthalene is readily reduced by alkali metals.[1] The resulting solutions of alkali naphthalenes are green, conducting, and paramagnetic. Consistent with these properties, alkali naphthalenes are formulated as ionic substances consisting of alkali cations and naphthalene radical anions.[2]



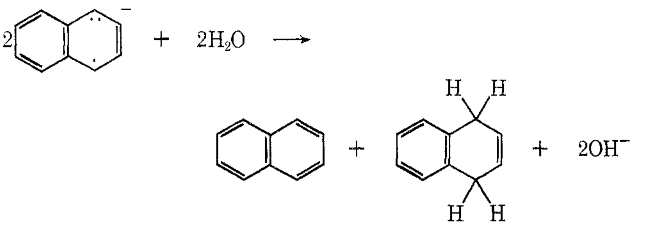
Sodium naphthalene is reactive toward oxygen, water, carbon dioxide, alkyl halides, aromatic hydrocarbons, and many other compounds. Its reactions with aromatic hydrocarbons are among the simplest.[2]



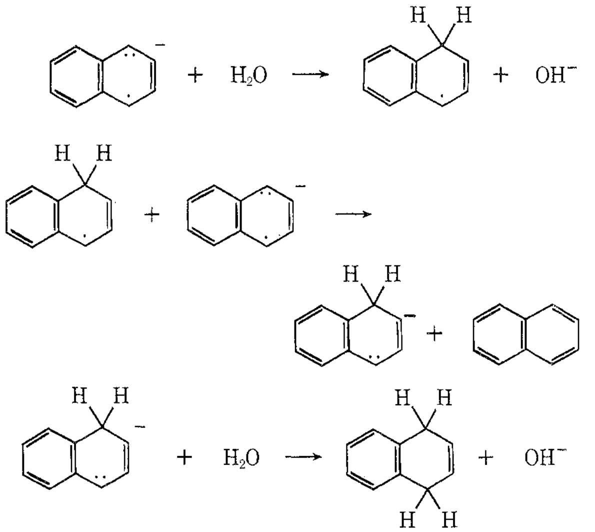
(metal counterions are omitted here and in many following equations)

Such reactions proceed to equilibrium positions which are determined largely by the relative electron affinities of the parent hydrocarbons. These are electron-transfer (ET) reactions, and many of the reactions of naphthalene radical anion fall into this class.

Alkali naphthalenes can also act as Lewis bases. Consider the reaction of sodium naphthalene with water:



Bank and Closson, and more recently Bank and Bockrath,[3] have verified the reaction mechanism proposed earlier by Paul, Lipkin, and Weissman (eq 1).[4] In the



(1)

initial step of this process, naphthalene radical anion acts as a proton acceptor. In other reactions it acts in parallel fashion, *i.e.* as a base or a nucleophile.

Reactions of alkyl halides with naphthalene radical anion recently attracted our attention,[5] and that of

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[1] N. D. Scott, J. F. Walker, and V. L. Hansley, *J. Amer. Chem. Soc.*, **58**, 2442 (1936).

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