more stable ketone, the cyclization of which gives nigericin.

Acid treatment of nigericin (same isolation procedure as for all antibiotics) give some epinigericin (≤1%). Thus it seems that nigericin was converted into epinigericin on isolation. But according to the proposed model for nigericin biosynthesis,[14] epinigericin may be a natural product.

By 2D NMR methods, we have completely assigned ^1H and ^{13}C NMR spectra and determined the structure of a new antibiotic, epinigericin, with only 0.1 mmol of material. We have shown that epinigericin and nigericin have closely related conformations. Epinigericin is half as toxic as nigericin (on the population dynamic in exponential growth of *Tetrahymena pyriformis*) and presents also half antimicrobial activity. NMR conformational studies of this new polyether carboxylic antibiotic and its complexes with various cations, in conjunction with studies of its biological properties are underway.

Experimental Section

General Methods. Infrared spectra were recorded with a Perkin-Elmer 327 spectrometer in KBr. Positive and negative FAB (fast atom bombardment) mass spectra were obtained with a ZAB 2F VG spectrometer (Manchester, G.B.). ^{13}C NMR spectra were run on a Bruker 300 MSL instrument in C_6D_6. The two-dimensional correlated ^1H NMR experiment "COSY" was also performed on the Bruker 300 MSL. The applied pulse sequence was $(\pi/2)$-(t1)-$(\pi/4)$-(FID,t2). The spectral width in F1 and F2 was 1272.265 Hz. The number of data points in F2 was 2048 and 128 increments were recorded. Before Fourier transformation, zero filling was applied in t1 (size × si_1 = 1024), and the data were multiplied with unshifted sine bell in two dimensions. Total acquisition was 10 h for nigericin and epinigericin.

Thin-layer chromatography (TLC) was carried out by using Merck precoated silica gel F-254 plates. Spots were visualized with H_2SO_4-H_2O (50/50 v/v).

Production of Epinigericin. The antibiotic epinigericin was produced and isolated from a strain of *Streptomyces hygroscopicus* NRRL B-1865.[2] The EtOAc extract was concentrated and the residue fractionally separated by chromatography column on silica gel (Merck silica gel 60, 0.063–0.200 mm). Elution with cyclohexane–ethyl acetate yielded crude epinigericin (400 mg from 15 L of culture broth). The purification of epinigericin-Na was achieved by a flash chromatography column[15] using MeOH–$CHCl_3$ with increasing amounts of MeOH as eluting solvent: TLC (MeOH–$CHCl_3$, 95:5) R_f 0.58 (0.70 for nigericin); IR (KBr) 3200, 2900, 1580, 1380, 1120, 1040, 950, 650 cm^{-1}. Anal. Calcd for $C_{40}H_{67}O_{11}Na$: C, 64.36; H, 8.98; O, 23.58. Found: C, 64.66; H, 9.43; O, 23.05.

Epinigericin was isolated from its sodium salt by running it through a flash chromatography column with the same solvents as above, acidified with 5% acetic acid: ^1H NMR (C_6D_6), see Table II; ^{13}C NMR (C_6D_6), see Table I.

Acknowledgment. Our thanks to Mrs. G. Kergomard and N. Grangemare for the antimicrobial tests.

(14) Cane, D. E.; Celmer, W. D.; Westley, J. W. *J. Am. Chem. Soc.* **1983**, *105*, 3594.

(15) Clark Still, W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *14*, 2923.

8a,9-Dihydro-8a-methyl-9-methyleneanthracene: A Hydrocarbon with Fused Blocked Aromatic Rings

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The title compound 1 was prepared from diketone 2 by a four-step synthesis. Photorearrangement of 1 proceeded slowly compared to that of the corresponding fused blocked aromatic ketone A to form 1,10-dimethylanthracene in variable yields. Thermolysis of 1 yielded the "double aromatization" product, 9-ethylanthracene. The thermal rearrangement was not affected by the addition of free radical chain inhibitors. An attempt to prepare 1 by reaction of hydrocarbon 3 with NBS and dibenzoyl peroxide yielded the vinyl bromide 5.

Blocked aromatic molecules, which contain unsaturated six-membered rings that can be aromatized by the migration or loss of a single substituent, exhibit a wide range of rapid and often unusual rearrangement processes.[1,2] Molecules with fused blocked aromatic rings, in which the migration of a single substituent might simultaneously convert two or more alicyclic rings to aromatic structures, should rearrange with even greater facility.

Our group recently reported the synthesis of the fused blocked aromatic ketone A[3] and provided evidence for the formation of ketone B as a short-lived intermediate.[4a] As expected, these compounds rearranged to form aromatic isomers, ketone B, at an immeasurably fast rate. However, both ketones rearranged by processes that resulted in aromatization of a single ring (eq 1 and 2), rather than by "double aromatization" processes.

Until the appearance of a preliminary communication about this work,[4b] no example of formation of a hydrocarbon with fused blocked aromatic rings had been reported. Since the isomerization of hydrocarbons to aromatic isomers is usually more exothermic than the corresponding processes with carbonyl compounds, we decided to prepare the fused blocked aromatic hydrocarbon 1 to see whether double aromatization processes or other novel reactions could be observed.

(1) E.g.: Miller, B. *Acc. Chem. Res.* **1975**, *8*, 245.
(2) (a) von Auwers, K.; Keil, G. *Chem. Ber.* **1903**, *36*, 1861. (b) von Auwers, K. *Liebigs Ann. Chem.* **1907**, *352*, 219. (c) von Auwers, K.; Jühlicher, W. *Chem. Ber.* **1922**, *55*, 2167. (d) Fuson, R. C.; Miller, T. G. *J. Org. Chem.* **1952**, *17*, 316. (e) Tse, R. L.; Newman, M. S. *Ibid.* **1956**, *21*, 638. (f) Bird, C. W.; Cookson, R. C. *Ibid.* **1959**, *24*, 441. (g) Hart, H.; DeVrieze, J. D. *Tetrahedron Lett.* **1968**, 4259. (h) Newman, M. S.; Layton, R. M. *J. Org. Chem.* **1968**, *33*, 2338. (i) Miller, B.; Lai, K.-H. *J. Am. Chem. Soc.* **1972**, *94*, 3472. (j) Miller, B.; Saidi, M. R. *Ibid.* **1976**, *98*, 2544.

(3) Miller, B.; Bhattacharya, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 3234.
(4) (a) Miller, B.; Baghdachi, J. *J. Chem. Soc., Chem. Commun.* **1986**, 511. (b) Miller, B.; Baghdachi, J. *Ibid.* **1986**, 1257.

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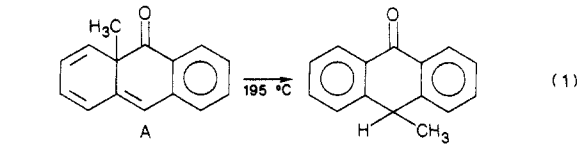
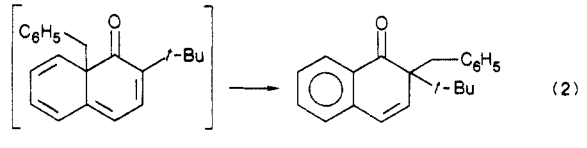
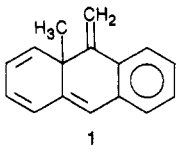


(1)

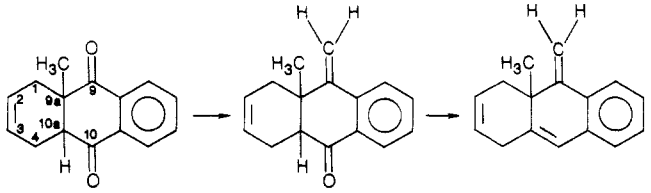


(2)



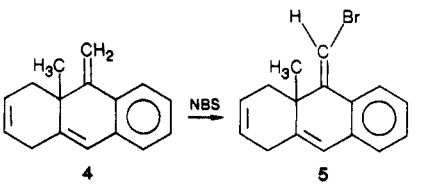
Synthesis

Miller and Bhattachrya[3] reported that reduction of diketone **2** with sodium borohydride proceeded by attack at C-9 adjacent to the quaternary center, the apparently more hindered of the two carbonyls. We therefore anticipated that a methylene group could be introduced at C-9 by reaction of **2** with carbanionoid reagents. However, no reaction was observed between **2** and Wittig or Wadsworth–Emmons reagents, while preliminary experiments suggested that, not unexpectedly, reaction with methyllithium followed by dehydration gave a complex mixture of products. However, reaction of **2** with the Corey–King reagent, $(C_6H_5)_3P{=}CHLi$,[5] proceeded smoothly to yield the desired methylene ketone **3** as a 3:2 mixture of two stereoisomers. Painstaking chromatography resulted in isolation of the major, faster moving isomer. By analogy with the corresponding diketones (**2** and its trans isomer) in whose spectra the methyl resonance of the cis isomer appears at lower field,[3] this isomer is tentatively assigned the cis geometry.



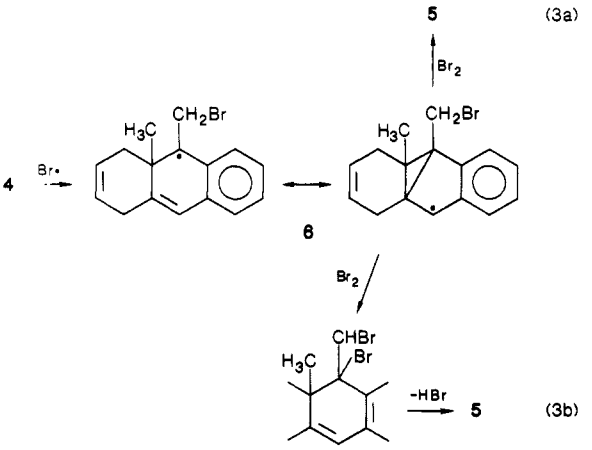
Separating the stereoisomers of **3** on a large scale would have been very inconvenient, but was unnecessary. The mixture of stereoisomers was reduced with lithium aluminum hydride and the resulting mixture of alcohols dehydrated with *p*-toluenesulfonyl chloride in pyridine to yield triene **4**.

Only the introduction of one more double bond was necessary to furnish the desired fused blocked aromatic hydrocarbon **1**. Reaction of **4** with NBS was expected to yield a mixture of allylic bromides, but dehydrobromination of each bromide should give the same elimination product, **1**. However, reaction of **4** with NBS and dibenzoyl peroxide provided no evidence for formation of allylic bromides, nor did attempted dehydrohalogenation of the crude product with DBU or potassium *tert*-butoxide appear to yield any of the desired **1**. Instead, a single product, the vinylic bromide **5**, was obtained in 78% yield from reaction with NBS. The *Z* geometry of the exocyclic double bond of **5** was assigned on the basis of the location



of the terminal vinyl proton resonance at δ 6.44, in comparison to singlets at δ 5.10 and 5.60 in **4**. Since a downfield shift of >1.3 ppm due to bromine substitution is close to the expected effect, while a shift of only 0.84 ppm is far smaller than anticipated,[6] it is concluded that the remaining vinyl proton must be the upfield hydrogen anti to the aromatic ring. This geometry is supported by the marked downfield shift (>0.5 ppm) of the signal for the aromatic proton at C-1 in **5** compared to **4**.

Formation of **5** from **4** appears to be quite an unusual reaction. We are not aware of any other example of displacement of a vinylic hydrogen by NBS. The spectrum of the product before chromatography was quite similar to that of **5**, so that **5** was not formed by loss of HBr during chromatography. Since the reaction does not occur in the absence of the initiating peroxide, it apparently proceeds by a radical chain mechanism. Two possible mechanisms are shown in eq 3a and 3b.[7] Presumably, the stability of



(3a)

(3b)

radical **6** (possibly enhanced by homoallylic resonance as shown) allows it to await the arrival of a bromine (or NBS) molecule rather than revert to the starting olefin. The crowded structure of **6** might then favor the novel reaction shown in eq 3a rather than formation of the dibromide. Alternatively, the very crowded dibromide, once formed, may rapidly lose HBr to form **5**.

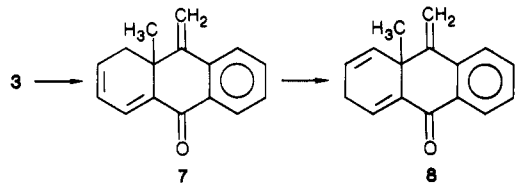
Since allylic bromination of **4** could not be achieved and since an attempt to add 1 mol of bromine to **4**, in the forlorn hope that addition to the exocyclic double bond would be appreciably faster than addition to the other double bonds, gave no useful products, we abandoned the attempt to prepare **1** from **4**. Instead, a double bond was introduced α to the carbonyl group of **3** by formation and oxidation of the α-phenylselenyl ketone.

Since the anion of the resulting unsaturated ketone **7** would itself have a fused blocked aromatic structure, the reaction of **7** with strong bases (potassium *tert*-butoxide or potassium hydride) was studied to determine whether aromatization products might be observed.[8] However, the

(5) Corey, E. J.; Kang, J. *J. Am. Chem. Soc.* **1982**, *104*, 4724.

(6) E.g.: *Sadtler Standard Spectra*: Proton NMR *Collection*; Sadtler Research Laboratories: Philadelphia. Compare spectra 6408 (styrene) and 10473 (β-bromostyrene).

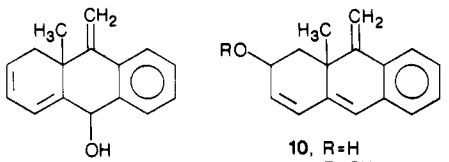
(7) For evidence that bromine atoms are chain carriers in NBS brominations, see: Incremona, J. H.; Martin, J. C. *J. Am. Chem. Soc.* **1970**, *92*, 627 and references therein.



7 8

only product obtained, even after long reaction times, was the partially deconjugated ketone **8**.

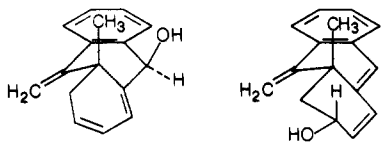
Reduction of ketone **7** with sodium borohydride and cerium(III) chloride[9] appeared to proceed smoothly, with no evidence for the feared conjugate reduction. The spectra of the crude product corresponded to that of the expected alcohol, **9**. However, attempts to purify **9** by chromatography on Florisil or silica gel invariably yielded only the rearranged alcohol **10**. In an early run in which the reaction, after reduction in methanol, was worked up by addition of 0.25 M hydrochloric acid, a mixture of **10** and its methyl ether **11** was obtained.



9 10, R=H 11, R=CH$_3$

Although alcohol **9** could not be purified, its spectra suggested that the crude product was of reasonable purity, and it seemed necessary only to dehydrate it to form hydrocarbon **1**. However, attempted dehydration of **9** by reaction with *p*-toluenesulfonyl chloride or thionyl chloride in pyridine again resulted in formation of alcohol **10**. That alcohol was recovered unchanged from prolonged reaction under the same conditions.

The great reactivity of alcohol **9** suggests that it has the cis geometry (**9a**) in which the hydroxy group occupies the

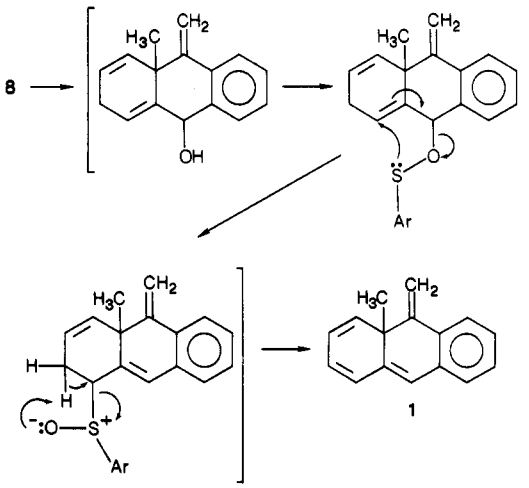


9a 10a

reactive pseudo-axial position.[10] The comparative lack of reactivity of **10**, in contrast, suggests that the hydroxy group is trans to the methyl, in the pseudo-equatorial position (structure **10a**). In each case, the products obtained are those that would result from the expected attack of the nucleophilic reagent from the direction anti to the methyl group.

Since our supplies of ketone **7** and alcohol **9** had run short at this point, we decided to attempt the formation of **1** from the available ketone **8**. Ketone **8** was reduced with sodium borohydride–cerium(III) chloride, and the resulting alcohol, which was not purified, was reacted directly with 2,4-dinitrobenzenesulfenyl chloride in triethylamine, according to the procedure of Reich and Wollowitz.[11] The fused blocked aromatic hydrocarbon **1** was thereby obtained in 22% yield.

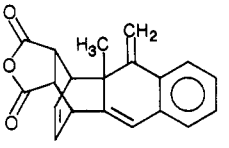
The yield in the process described above could undoubtedly be improved. However, work on this reaction



was stopped when it was found that on refluxing in benzene in the presence of small amounts of iodine **9** was dehydrated to **1** in ca. 65% yield. The use of zinc chloride in place of iodine resulted in somewhat lower yields. In either case, it was important to keep the reaction time to a minimum.

Properties of Hydrocarbon 1. Hydrocarbon **1** is a bright yellow oil, with an electronic spectrum whose long wavelength absorption (sh, 396 nm) appears at somewhat lower wavelengths than that of ketone A.[3] It decomposes on standing, even in the refrigerator, and within several days becomes a very viscous, difficultly soluble material. The NMR and UV spectra of the product lack clearly defined peaks, except for those apparently due to residual **1**. Attempts to isolate low molecular weight products from this apparent polymer were unavailing. Therefore, small quantities of **1** were prepared from alcohol **9** and purified by flash chromatography each day before use.

Hydrocarbon **1** forms a single Diels–Alder adduct on heating with maleic anhydride. It is assumed that addition occurs from the less hindered β-face of the diene to form adduct **12**, but clear proof of the geometry of the adduct is lacking.

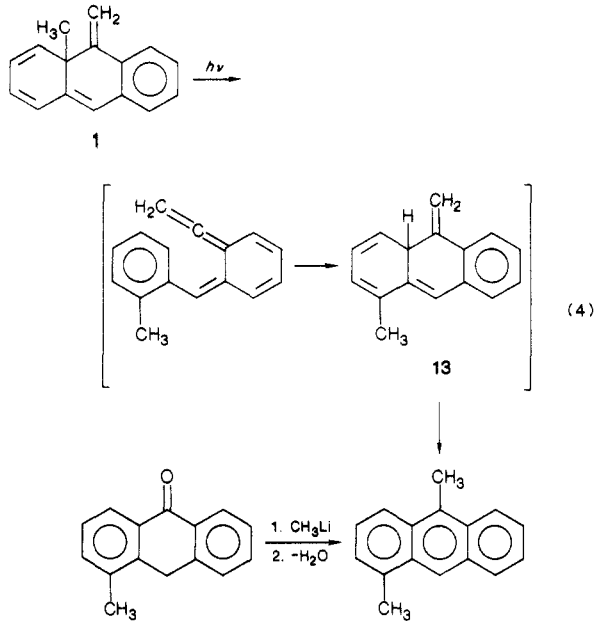


12

Unlike the fused blocked aromatic ketone A, which rearranged rapidly on irradiation through Pyrex (reaction was frequently complete in 20–30 min) to form 4-methylanthrone in quantitative yields,[3] hydrocarbon **1** reacted relatively slowly under the same conditions. Irradiation for ca. 20–24 h was necessary to achieve nearly complete disappearance of **1**, and the products consisted in large part of high molecular weight material, which did not appear (except as an upward drifting baseline) in GLPC analysis. A single low molecular weight product was obtained in variable yields (ca. 5–20%, GLPC analysis) and isolated by preparative GLPC. Its spectra showed it to be a dimethylanthracene, and comparison with a synthetic sample prepared by reaction of methyllithium with 4-methylanthrone showed it to be 1,10-dimethylanthracene.

Formation of 1,10-dimethylanthracene is assumed to proceed by a photochemical ring opening–ring closing sequence (eq 4) similar to that which occurs in photolysis of ketone A.[3] It is not clear whether the relatively slow reaction of **1** and low yield of 1,10-dimethylanthracene are due to an intrinsically slower ring opening in hydrocarbon

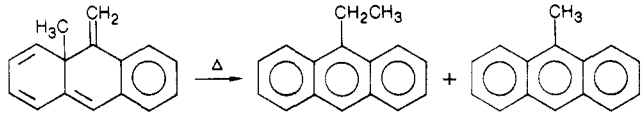
(8) Rearrangements of an anion with fused blocked aromatic rings have been reported: Miller, B.; Bhattacharya, A. K. *J. Org. Chem.* **1983**, *48* 2412.
(9) Gemal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5455.
(10) Bhattacharya, A. K.; Miller, B. *J. Am. Chem. Soc.* **1983**, *105*, 3242.
(11) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051.
(12) Bergmann, E. D.; Loewenthal, E. *Bull Soc. Chim. Fr.* **1952**, 66.



1 compared to ketone A or whether they are due to a comparatively slow rate of aromatization of the intermediate hydrocarbon **13**. Photoirradiation of **13** might result in reformation of **1** or in formation of high molecular weight materials directly from **13**.

We anticipated that reaction of **1** with acids would proceed by protonation of the exocyclic double bond, followed by methyl migration to yield the 10,10-dimethyl-9-anthracenium ion. However, reaction of **1** with sulfuric acid in acetic acid solution gave no isolable low molecular weight products. Only a dark colored viscous material, presumably formed by protonation of the polyene chain rather than the exocyclic methylene group, was obtained.

When hydrocarbon **1** was heated in benzene, toluene, or anisole solutions at temperatures up to 125 °C the rate of disappearance of **1** to form viscous materials increased, but no identifiable rearrangement products or other low molecular weight products were obtained. When **1** was heated in diphenyl ether solution at 154–155 °C, however, two low molecular weight products, totaling ca. 20% yield (GLPC analysis), were obtained in the ratio 5:95. Runs in diphenyl ether, tetralin, or *N,N*-dimethylaniline at temperatures up to ca. 190 °C gave similar results, except that yields increased (up to ca. 27%) with increasing temperature. The two products were identified by GC–MS and comparison with standard samples as 9-methylanthracene (the minor product) and 9-ethylanthracene.



Thermolysis of **1** was also carried out in the absence of solvents by dropping the hydrocarbon through a vertical tube containing Pyrex beads at 375 °C. Under these conditions the yields of 9-methylanthracene and 9-ethylanthracene increased to ca. 45%, while the ratio of 9-methylanthracene to 9-ethylanthracene rose to 17:83.

The formation of 9-ethylanthracene from **1** represents the first example of a molecular rearrangement in which migration of a single substituent results in aromatization of *two* alicyclic rings. The most obvious mechanism for this reaction is by a radical chain "semibenzene rearrangement" process. However, addition of radical chain inhibitors (including benzoquinone, α-naphthol, and hydroquinone) to solutions of **1** in diphenyl ether at 175 °C or to **1** heated at 375 °C did not significantly affect the yields of alkylanthracenes or the ratio of 9-ethyl- to 9-methylanthracene. The rates of disappearance of **1** in solution were also not noticeably changed. This evidence argues against free radical chain mechanisms for the formations of 9-ethylanthracene and 9-methylanthracene.

It is possible that 9-ethylanthracene is formed by a concerted (presumably antarafacial) [1,3]-migration. Alternatively, it may be formed by a free radical dissociation–recombination reaction occurring within a solvent cage. The latter process seems more likely, since it is consistent with the large temperature effect on the yields of the alkylanthracenes.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237B spectrometer. Only major peaks are reported. ^{1}H nuclear magnetic resonance spectra were recorded on Perkin-Elmer R12 or Varian XL 300 spectrometers. GC/MS analyses were obtained with a Perkin Elmer-Hitachi RMUGL instrument. Microanalyses were carried out by the University of Massachusetts Microanalytical Laboratory.

***cis*- and *trans*-10a-Methyl-10-methylene-5,8,8a,10a-tetrahydro-9(10*H*)-anthracenones 3.** A suspension of methyltriphenylphosphonium bromide (31.62 g, 0.0884 mol) in 300 mL of dry THF was stirred under an atmosphere of dry argon and cooled to −50 °C. A solution of *tert*-butyllithium (1.55 M, 117 mL, 0.18 mol) in hexane was added slowly. The resulting deep red solution was allowed to warm to −20 °C, and a solution of 8a-methyl-4,8,8a,10a-tetrahydro-9,10-anthracenedione (20.0 g, 0.0884 mol) in 70 mL of dry THF was added over a 45-min period. The resulting orange suspension was allowed to warm to room temperature. Excess *tert*-butyl alcohol was added and the mixture stirred for an additional 2 h. Water (200 mL) was added, the resulting layers were separated, and the organic layer was evaporated to afford a brown oil, which was extracted several times with hot hexane. The hexane extracts were combined, washed with water, dried over sodium sulfate, filtered, and evaporated to yield 24 g of a brown oil. The product was chromatographed on silica gel, eluting with 10% dichloromethane in hexane to yield 15.24 g (0.068 mol, 77%) of a mixture of the two stereoisomers.

Repeated chromatography of a 2.4-g sample of the mixture of stereoisomers on silica gel yielded 0.14 g of the faster moving isomer as a pale yellow oil: ^{1}H NMR δ 1.22 (s, 3 H), 1.7–2.7 (m, 4 H), 2.0–2.7 (m, 5 H), 5.22 (s, 1 H), 5.68 (m, 2 H), 5.75 (s, 1 H), 7.1–7.7 (m, 3 H), 8.05 (dd, J = 7 Hz, 1 Hz, 1 H); IR (neat) 1680, 1590, 1464, 1440, 1422, 1294, 1267, 1224, 897, 776, 771, 760 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.49; H, 7.06.

8a-Methyl-9-methylene-5,8,8a,9-tetrahydroanthracene (4). A suspension of lithium aluminum hydride (4.2 g, 0.0129 mol) in 100 mL of anhydrous ether was stirred under an atmosphere of argon, and a solution of a mixture of stereoisomers of ketone **3** (15.4 g, 0.069 mol) in 100 mL of anhydrous ether was added slowly over a 45-min period. The mixture was stirred for an additional 45 min, and 100 mL of ethyl acetate was added as rapidly as the rate of refluxing permitted. The resulting mixture was poured into ice and 0.05 M hydrochloric acid. The organic layer was separated and the aqueous layer extracted with four 100-mL portions of dichloromethane. The combined organic layers were washed with water and dried over magnesium sulfate, and the solvent was evaporated under vacuum to yield 14.7 g of a pale yellow oil.

A portion of the oil from reduction of ketone **3** (11.25 g, 0.050 mol) was dissolved in 60 mL of dry pyridine, cooled to 5 °C in an ice bath, and stirred. Freshly recrystallized *p*-toluenesulfonyl chloride (12.0 g, 0.063 mol) was added at a rate that kept the reaction temperature below 12 °C. The mixture was then stirred at room temperature for 4 days, poured into ice water, and extracted with dichloromethane. The dichloromethane extracts were washed with dilute sulfuric acid, with sodium bicarbonate solution, and with brine and dried over anhydrous sodium sulfate. The

mixture was filtered and the solvent evaporated under vacuum to yield a brown oil, which was subjected to chromatography on neutral alumina (activity III), eluting with 10% dichloromethane in hexane. Hydrocarbon **4** was obtained as a pale yellow oil (3.48 g, 0.017 mol, 34% based on amount of **3** employed): ^{1}H NMR δ 1.25 (s, 3 H), 2.3 (m, 2 H), 2.8–3.05 (m, 2 H), 5.10 (s, 1 H), 5.60 (s, 1 H), 5.65 (m, 2 H), 6.10 (br s, 1 H), 6.8–7.3 (m, 3 H), 7.48–7.65 (m, 1 H); IR (neat) 1621, 1488, 1460, 1422, 883, 772, 746 cm^{-1}; UV (methanol) λ_{max} 245 (ϵ = 16 024), 294 (3745) nm. Anal. Calcd for $C_{16}H_{16}$: C, 92.26; H, 7.74. Found: C, 92.04; H, 7.51.

9-(Bromomethylene)-8a-methyl-5,8,8a,9-tetrahydroanthracene (5). *N*-Bromosuccinimide (0.93 g, 5.2 mmol) (freshly recrystallized and dried) and benzoyl peroxide (0.1 g, 0.4 mmol) were added to a solution of hydrocarbon **4** (1.02 g, 4.9 mmol) in 10 mL of dry carbon tetrachloride. The mixture was heated under reflux for 1.5 h and filtered while hot. After being cooled to ca. 40 °C, the filtrate was washed with aqueous sodium bisulfite solution and with water and dried over anhydrous calcium chloride. Evaporation of the solvent under vacuum left 1.4 g of yellow oil. Part of this oil (0.90 g) was chromatographed on neutral alumina, eluting with 10% dichloromethane in hexane. Bromide **5** (0.71 g, 2.47 mmol, 78% based on amount of product chromatographed) was obtained as a yellow oil: ^{1}H NMR δ 1.21 (s, 3 H), 2.2–2.4 (m, 2 H), 2.95–3.12 (m, 2 H), 5.75–5.9 (m, 2 H), 6.17 (t, J = 1 Hz, 1 H), 6.44 (s, 1 H), 6.9–7.4 (m, 3 H), 8.05–8.25 (m, 1 H). Anal. Calcd for $C_{16}H_{15}Br$: C, 66.91; H, 5.26; Br, 27.82. Found: C, 66.61; H, 5.23; Br, 28.11.

10a-Methyl-10-methylene-5,10a-dihydro-9(10*H*)-anthracenone (7). A solution of 1.5 M *n*-butyllithium in hexane (8.55 mL, 12.8 mmol) was added to a stirred solution of dry dicyclohexylamine (2.32 g, 12.8 mmol) in 10 mL of dry THF, which had been cooled to −72 °C and kept under an atmosphere of nitrogen. The reaction mixture was stirred at −72 °C for 15 min, allowed to warm to room temperature for 30 min, and then again cooled to −72 °C. A solution of ketone **5** (2.96 g, 12.8 mmol) in 15 mL of dry THF was added over a 10-min period, and the resulting deep green solution was allowed to warm to −20 °C for 45 min and then again cooled to −72 °C. A solution of phenylselenium bromide (3.3 g, 14.08 mmol) in 15 mL of THF was added slowly over a 20-min period, and the reaction mixture was allowed to warm to room temperature and stirred for an additional 3 h. It was poured into a mixture of ice and 1 M hydrochloric acid and extracted with ether. The organic extracts were washed with dilute hydrochloric acid and with water and dried over anhydrous magnesium sulfate. The solvent was evaporated under vacuum to leave 5.48 g of light yellow oil, which was chromatographed on Florisil. Elution with 10% dichloromethane in petroleum ether yielded 3.5 g of a pale yellow oil, which was dissolved in 50 mL of 95% ethanol and added slowly to a solution of sodium periodate (13.8 g, 64.0 mmol) in 200 mL of water. The reaction temperature was maintained between 5 and 10 °C during the addition. After completion of the addition, the mixture was stirred at room temperature for 5.5 h and extracted with ether. The ether extracts were washed with water and dried over sodium sulfate, and the solvent was evaporated under vacuum. The residual yellow oil (1.84 g) was chromatographed on Florisil, eluting with 5% ethyl acetate in hexane to yield ketone **7** (1.2 g, 5.4 mmol, 42%) as a light yellow oil: ^{1}H NMR δ 1.05 (s, 3 H), 2.60–2.75 (m, 2 H), 5.17 (s, 1 H), 5.53 (s, 1 H), 6.25–6.37 (m, 2 H), 7.3–7.5 (m, 2 H), 7.55–7.7 (m, 2 H), 8.08–8.25 (m, 1 H); IR (neat) 1670, 1632, 1605, 1548, 1455, 1284, 1120, 1035, 890, 770, 701 cm^{-1}; UV (methanol) λ_{max} 245 (ϵ 21 600), 340 (11 882) nm. Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.34. Found: C, 86.43; H, 6.51.

10a-Methyl-10-methylene-7,10a-dihydro-9(10*H*)-anthracenone (8). Potassium *tert*-butoxide (0.25 g, 2.2 mmol) was added to a solution of ketone **7** (0.300 g, 1.34 mmol) in 5 mL of dry HMPA. The nearly black solution that resulted was shaken briefly and allowed to stand at room temperature for 2 h. Water and then 1 M hydrochloric acid were added, the mixture was extracted with dichloromethane, and the dichloromethane extracts were washed with water and then brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under vacuum to leave 290 mg of a light brown oil, which was chromatographed on Florisil, eluting with 10% ethyl acetate in hexane. Ketone **8** (0.180 g, 0.81 mmol, 61%) was obtained as a pale yellow oil: ^{1}H NMR δ 1.24 (s, 3 H), 2.9–3.0 (m, 2 H), 5.25 (s, 1 H), 5.55 (s, 1 H), 5.85–6.0 (m, 2 H), 6.95–7.05 (m, 1 H), 7.3–7.7 (m, 3 H), 8.1–8.25 (m, 1 H); IR (neat) 1655, 1595, 1450, 1340, 1030, 770, 720, 690 cm^{-1}; UV (methanol) λ_{max} 238 (ϵ 14 450), 265 (sh, 9080) nm. Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.34. Found: 86.17; H, 6.30.

Reduction of 7. Formation of 5,10a-Dihydro-6-hydroxy-10a-methyl-9(10*H*)-anthracenone and 6-Methoxy-10a-methyl-5,10a-dihydro-9(10*H*)-anthracenone. Cerium(III) chloride hydrate (1.0 g, 3.2 mmol) was added to a solution of ketone **7** (0.71 g, 3.19 mmol) in 5 mL of methanol, and the mixture was stirred at room temperature until a homogeneous solution was obtained. Sodium borohydride (0.12 g, 3.2 mmol) was added in portions over a 2-min period, and stirring was continued for an additional 5 min. Water was added and the mixture extracted with ether. The ether layer was washed with water and dried over sodium sulfate. Evaporation of the solvent left 0.70 g of **10a-methyl-10-methylene-5,9,10,10a-tetrahydro-9-anthracenol (9)** as a pale yellow oil: ^{1}H NMR δ 1.45 (s, 3 H), 2.0–2.35 (m, 2 H), 3.50 (s, 1 H, OH), 4.98 (s, 1 H, CHOH), 5.16 (s, 1 H), 5.47 (s, 1 H), 5.7–6.0 (m, 3 H), 3.18–7.6 (m, 4 H); IR (neat) 4350 (vs), 1640, 1615, 1495, 1468, 1385, 1302, 1037, 976, 892, 765, 750, 699 cm^{-1}; UV (methanol) λ_{max} 254, 262, 285 (sh) nm.

Attempted chromatography of **9** on Florisil, eluting with 5% ethyl acetate in petroleum ether, gave **8a-methyl-9-methylene-7,8,8a,9-tetrahydro-7-anthracenol (10)** (0.43 g, 1.9 mmol, 61% from **7**) as a yellow oil: ^{1}H NMR δ 1.27 (s, 3 H), 2.0–2.4 (m, 2 H), 4.45–4.70 (m, 1 H), 5.14 (s, 1 H), 5.43 (s, 1 H), 5.8–6.1 (m, 1 H), 6.24–6.45 (m, 2 H), 7.05–7.65 (m, 4 H); IR 3420 (vs), 1492, 1458, 1095, 1055, 988, 950, 890, 775, 745 cm^{-1}; UV (methanol) λ_{max} 251 (ϵ 24 300), 259 (24 200), 305 (sh, 6000), 322 (7100), 335 (sh, 5200) nm. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.38; H, 6.99.

In a second run employing 1.11 g (5.0 mmol) of ketone **7**, 0.25 M hydrochloric acid was added to the methanolic solution after reduction with sodium borohydride. Workup was continued as described above to yield after chromatography, **7-methoxy-8a-methyl-9-methylene-7,8,8a,9-tetrahydroanthracene (11)** (0.53 g, 2.25 mmol, 44%) as a yellow oil: ^{1}H NMR δ 1.23 (s, 3 H), 1.7–2.4 (m, 2 H), 3.39 (s, 3 H), 3.95–4.25 (m, 1 H), 5.14 (s, 1 H), 5.41 (s, 1 H), 5.6–5.8 (m, 1 H), 6.05–6.45 (m, 2 H), 7.05–7.7 (m, 4 H); IR (neat) 1605, 1450, 1080, 980, 770, 735 cm^{-1}; UV (ethanol) λ_{max} 248 (ϵ 22 450), 259 (23 700), 312 (6405), 321 (6200), 347 (sh, 3800). Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.29; H, 7.51.

Further elution yielded 0.125 g (11%) of alcohol **10**.

8a,9-Dihydro-8a-methyl-9-methyleneanthracene (1). a. By Dehydration with Iodine or Zinc Chloride in Benzene. Iodine (1.8 mg, 0.014 mmol) was added to a solution of alcohol **9** (0.154 g, 0.68 mmol) in 10 mL of dry benzene, and the mixture was heated to reflux for 20 min, at which point the purple color of the iodine had disappeared. (Overlong heating should be avoided.) The solvent was evaporated under vacuum, with the temperature kept below 30 °C. The residue was chromatographed on neutral alumina (activity III), eluting with 5% ethyl acetate in hexane, to yield hydrocarbon **1** (0.091 g, 0.44 mmol, 65%) as a bright yellow oil: ^{1}H NMR δ 1.10 (s, 3 H), 5.35 (s, 1 H), 5.65 (s, 1 H), 5.94 (m, 1 H), 6.12 (m, 1 H), 6.24 (m, 2 H), 6.40 (s, 1 H), 7.08 (m, 1 H), 7.22 (m, 2 H), 7.58 (m, 1 H); IR (neat) 3160, 3065, 3020, 2950, 1650, 1505, 1480, 1477, 1402, 1135, 900, 865, 780, 758, 721 cm^{-1}; UV (hexane) λ_{max} 238 (ϵ 29 820), 247 (28 670), 253 (sh, 22 935), 268 (sh, 16 055), 277 (21 330), 289 (16 742), 377 (16 350), 396 (sh, 9175); mass spectrum, m/Z (relative abundance) 206 (M^+, 100), 192 (52), 191 (95), 189 (33), 101 (22), 100 (31). Anal. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 92.95; H, 6.85.

Another run on a similar scale was carried out by the same procedure except that 15.0 mg of anhydrous zinc chloride was employed in place of iodine. Hydrocarbon **1** was obtained in 54% yield.

b. From Ketone 8. Sodium borohydride (0.066 g, 1.8 mmol) was added to a stirred solution of ketone **8** (0.38 g, 1.71 mmol) and cerium(III) chloride hydrate (0.52 g, 1.75 mmol) in 5 mL of methanol. Stirring was continued for 10 min, the mixture was then diluted with water and extracted with dichloromethane, and the organic layer was washed with brine and water and dried over anhydrous sodium sulfate. Evaporation of the solvent under vacuum left 0.375 g of pale yellow oil, which was dissolved in 10 mL of dry dichloromethane. Triethylamine (0.50 g) was added, and the solution was cooled to −35 °C. 2,4-Dinitrobenzenesulfenyl

chloride (0.90 g, 3.85 mmol) was added over a 0.5-h period. The resulting suspension was stirred at −35 °C for an additional half hour and then allowed to warm to room temperature and stirred for an additional 3 h. Hexane (50 mL) was added, the mixture cooled in ice and filtered. The solvents were evaporated under vacuum to leave 1.1 g of partially solid material, which was extracted with hexane, and the hexane was evaporated to leave 0.55 g of brown oil. Chromatography on neutral alumina (activity III) yielded hydrocarbon **1** (0.077 g, 0.38 mmol, 22%).

Reaction of 1 with Maleic Anhydride. A solution of hydrocarbon 1 (0.20 g, 0.97 mmol) and maleic anhydride (0.24 g, 2.4 mmol) in dry toluene was heated at reflux for 2.5 h. The solution was allowed to stand overnight at room temperature and the solvent evaporated under vacuum. The residue was heated at 105 °C at a pressure of 0.3 Torr until sublimation of excess maleic anhydride was complete. The dark brown oil remaining crystallized on standing in the refrigerator. Recrystallization from ether yielded adduct **12** (0.081 g, 0.27 mmol, 29%) as white needles: mp 178–180 °C; ^{1}H NMR δ 1.02 (s, 3 H), 3.23–3.50 (m, 2 H), 3.60–4.00 (m, 2 H), 5.30 (s, 1 H), 5.63 (s, 1 H), 6.32–6.50 (m, 3 H), 7.07–7.30 (m, 3 H), 7.40–7.65 (m, 1 H). Anal. Calcd for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.91; H, 5.29.

Photorearrangement of Hydrocarbon 1. A stream of argon was bubbled through a solution of 1 (0.224 g, 1.09 mmol) in 20 mL of benzene in a Pyrex flask for 10 min, and the solution was then irradiated by a GE 275-W sun lamp for 18 h. GLPC analysis by comparison with standard solutions on a 6-ft 3% SE-30 Chromosorb W column at 180 °C showed the solution to contain 0.15 mmol (14%) of 1,10-dimethylanthracene. Chromatography on alumina, eluting with petroleum ether, followed by recrystallization from benzene–hexane, yielded 7 mg (3.4 mmol, 3%) of pure 1,10-dimethylanthracene.

1,10-Dimethylanthracene. A solution of methyllithium in hexane (1.55 M, 5 mL, 7.75 mmol) was added to a stirred solution of 4-methylanthrone[12] (0.62 g, 3.0 mmol) in 25 mL of anhydrous ether. Water was added and the ether layer was washed with water and with brine and dried over magnesium sulfate. Evaporation of the solvent left a yellow powder, which was chromatographed on Florisil, eluting with 10% dichloromethane in petroleum ether, to yield 1,10-dimethylanthracene (0.405 g, 2.0 mmol, 67%) as yellow crystals: mp 127–128 °C; ^{1}H NMR δ 2.82 (s, 3 H), 3.05 (s, 3 H), 7.28–7.60 (m, 4 H), 7.95–8.44 (m, 3 H), 8.48 (s, 1 H); IR (mineral oil) 868, 831, 789, 722 cm^{-1}; UV (hexane) λ_{max} 342 (ϵ 4350), 358 (7550), 377 (12080), 398 (12090). Anal. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 92.95; H, 6.99.

Thermal Rearrangement of 1. a. In Diphenyl Ether Solution. Diphenyl ether (5 mL) was heated at 154–155 °C and degassed with a stream of argon. Hydrocarbon 1 (0.087 g, 0.42 mmol) was added and heating was continued under an argon atmosphere for 28 min. The solution was cooled in ice and analyzed by GLPC on a 6-ft, 3% OV 101 on Chromosorb W column at 170 °C. In addition to a peak for residual 1 (t_R 10.4 min), new peaks were present at retention times of 8.7 and 9.2 min. These components were identified by GC/MS as 9-methylanthracene and 9-ethylanthracene, respectively. Calibration aginst standard solutions showed that 9-methylanthracene and 9-ethylanthracene were obtained in 4% and 27% yields, respectively, together with 9% of recovered 1.

Reactions at higher temperatures or in tetralin solutions were carried out by the same procedure.

b. In *N,N*-Dimethylaniline Solution. A solution of hydrocarbon 1 (0.157 g, 0.76 mmol) in 5 mL of *N,N*-dimethylaniline was heated at reflux in the dark under an atmosphere of argon for 2.5 h. The solution was allowed to cool, and water and 1 M hydrochloric acid were added. The resulting mixture was extracted with ether and the ether layer was washed with water and with brine and dried over magnesium sulfate. Evaporation of the solvent left 0.150 g of a viscous red oil. GLPC analysis showed the absence of 1 and the presence of 9-methylanthracene (6%) and 9-ethylanthracene (31%).

c. In the Absence of Solvents. A Pyrex tube (15.0 × 0.8 cm) filled with Pyrex beads (ca. 0.4 cm in diameter) was heated to 375 °C by electrical heating tape. A stream of argon was passed through the tube and hydrocarbon 1 (0.20 g, 1.0 mmol) was dropped into the tube, which was then immediately cooled in dry ice. The reaction product was dissolved in dichloromethane and the solvent evaporated to give 0.2 g of a red oil, which was analyzed by GLPC.

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Stereochemistry of Hydride Reductions of 4,8-Dihalo-2-thiaadamantanes and Related Thiabicyclo[3.3.1]nonanes

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$LiAlD_4$ reductions of *anti*-4,8-dihalo-2-thiaadamantanes and *anti*-2,6-dihalo-9-thiabicyclo[3.3.1]nonanes in ether and THF solution occur with complete retention of configuration. Participation by sulfur to form intermediate thiiranium ions is the most likely explanation for this behavior. Reaction of the thiabicyclononanes with $LiEt_3BD$ involves chiefly elimination; single-electron transfer is a significant (20–25%) pathway in the reaction of $LiEt_3BD$ with the thiaadamantane.

Introduction

A neighboring heteroatom might affect the hydride reduction of an alkyl halide in several ways: (a) by nucleophilic participation to form an intermediate onium ion, leading to reduction with retention of configuration; (b) by formation of a monodentate complex with the reagent, delivering hydride intramolecularly (retention or inversion); (c) by formation of a bidentate complex of halide, neighboring group, and reagent, to be attacked by a second molecule of reductant (inversion); (d) by altering the reduction potential of the C–X bond so as to make single-electron-transfer (SET) reduction more or less likely (no stereoselectivity); or (e) by a steric effect.

The possibility of effecting a choice among these mechanisms by appropriate selection of heteroatom and reagent, and thereby controlling the stereoselectivity of the reduction, seems to us a goal of some importance, given the widespread use of such reductions in synthesis. We therefore have begun to examine a number of systems suitable for the observation of each kind of behavior.

In this paper, we report our examinations of the stereochemical course of $LiAlD_4$ and $LiEt_3BD$ reductions of

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