γ Elimination of a Sulfonyl Group to Form a Cyclopropane Ring

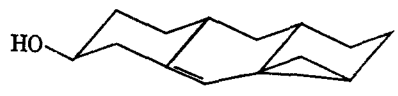
W. L. Parker[1] and R. B. Woodward

Chemistry Department, Harvard University, Cambridge, Massachusetts 02138

Received January 22, 1969

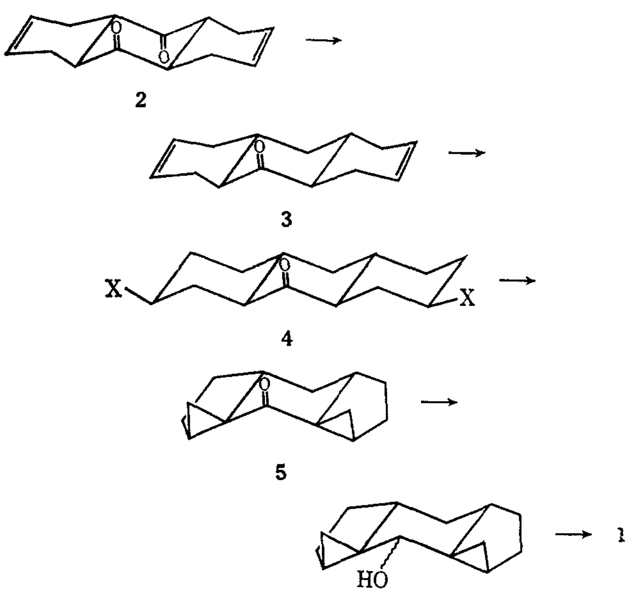
A model system, **1**, has been synthesized for a study of the isosterol rearrangement. A key step in this synthesis introduces a novel method for the formation of cyclopropane rings through base-catalyzed γ elimination of sulfinate ions from δ-keto sulfones; the method possesses special stereochemical advantages. The ketone, **5**, is of interest in possessing a dicyclopropyl ketone system of known fixed stereochemistry.

In the course of synthesizing **1** for a study of the isosterol rearrangement, an interesting and potentially versatile reaction for the formation of three-membered rings was developed. The synthesis was carried out on the broad outline in Scheme I. Two major problems in this route are regioselective addition to the double bonds of **3** to give leaving groups γ to the carbonyl group of **4**, and production of the stereochemistry shown for **4** in which the leaving groups are suitably disposed for γ elimination to form the cyclopropane rings.



1

Scheme I

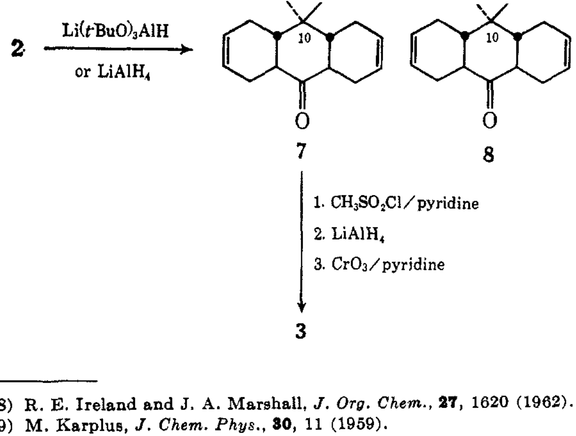


The starting material for this sequence (**2**) was reported by Alder and Stein[2] to result from the base-catalyzed isomerization of the Diels–Alder adduct of butadiene and quinone. The stereochemistry of the octahydroanthraquinones, perhydroanthracenes, and other related systems has been studied by several groups.[3-7]

For the conversions of **2** to **3**, the selective reduction of one of the ketone groups of **2** was necessary. This was accomplished as described by Ireland and Marshall for the partial reduction of Δ^6-octaline-1,4-dione using lithium tri-*t*-butoxyaluminohydride.[8] Treatment of **2** with 1 equiv of this reagent in tetrahydrofuran gave the equatorial monoalcohol, **7**, in 61% yield and a mixture of monoalcohols containing much of the axial alcohol, **8**, in 30% yield. The configurations of the hydroxyl groups were assigned on the basis of nuclear magnetic resonance spectra in trifluoroacetic acid. The spectrum of **7** showed a triplet at 3.89 ppm with $J = 8.5$ Hz, while the spectrum of **8** had a singlet at 4.17 ppm with width at half-height of about 4.5 Hz ($J < 2.3$ Hz). These peaks were assigned to the protons at C-10. The magnitudes of the splittings are a function of the dihedral angles between these protons and the protons at the ring junctions.[9] In **7**, the dihedral angle is about 180° and a large coupling constant (*ca.* 9.2 Hz) is expected, while, in **8**, the angle is about 60°, which should give a small (*ca.* 1.7 Hz) coupling constant. Reduction of **2** with lithium aluminum hydride also gave **7** and **8**, but the yields are very poor by this method. The fact that a mixture of axial and equatorial alcohols was obtained provides excellent additional chemical evidence[3] for the *trans,syn,trans* configuration of **2**. The *trans,anti,trans* configuration, which has recently been proposed for this substance,[7] would have resulted in the formation of a racemic but otherwise homogeneous monoalcohol.

Treatment of **7** with methanesulfonyl chloride in pyridine followed by reduction of the mesylate with lithium aluminum hydride in refluxing tetrahydrofuran gave an alcohol that was oxidized to **3** with chromium trioxide–pyridine complex[10] (Scheme II).

Scheme II



---

[1] To whom inquiries should be directed at the Squibb Institute for Medical Research, New Brunswick, N. J. 08903.

[2] K. Alder and G. Stein, *Ann.*, **501**, 283 (1933).

[3] R. K. Hill, J. G. Martin, and W. H. Stouch, *J. Amer. Chem. Soc.*, **83**, 4006 (1961).

[4] J. W. Cook, N. A. McGinnis, and S. Mitchell, *J. Chem. Soc.*, 286 (1944).

[5] W. S. Johnson, *Experientia*, **7**, 315 (1951).

[6] R. L. Clarke, *J. Amer. Chem. Soc.*, **83**, 965 (1961).

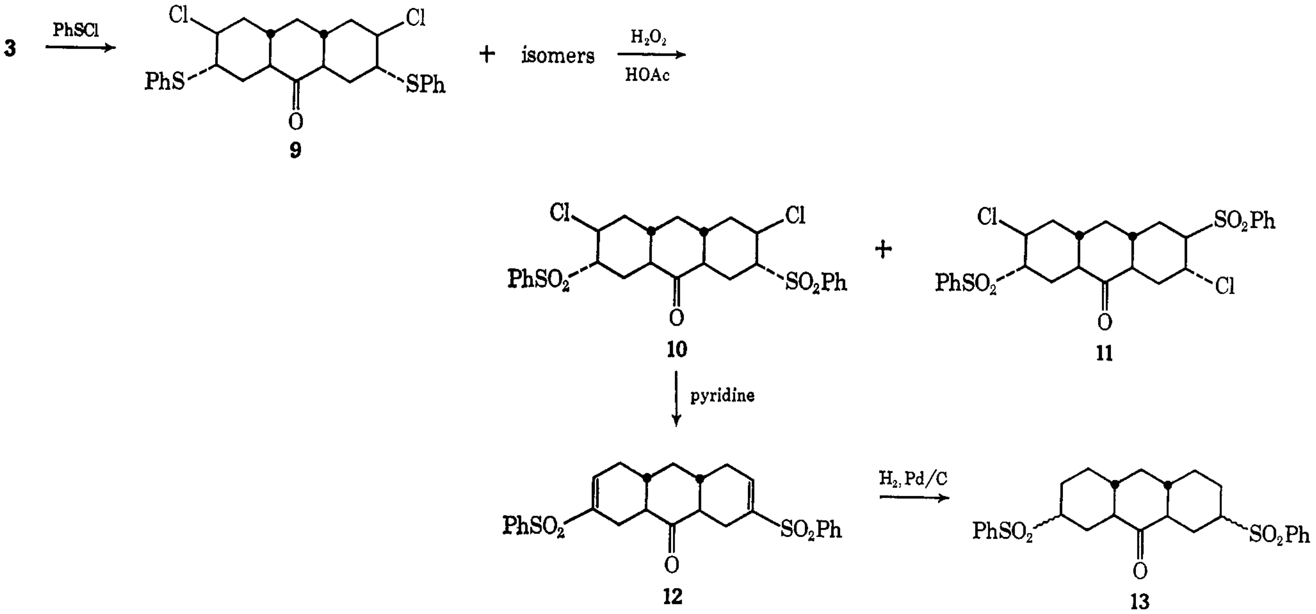
[7] N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *ibid.*, **88**, 2999 (1966).

[8] R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1620 (1962).

[9] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

[10] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953).

Scheme III



The selective placement of leaving groups at the carbon atoms γ to the carbonyl group depended on the long-range dipole interactions[11] of the carbonyl group, since the vinylic positions are nearly equivalent sterically. The choice of leaving groups was dictated by the means of introduction (electrophilic addition to the double bonds) and the capability of achieving the equatorial orientation necessary for γ elimination.[12] Sulfonyl groups[13] meet these requirements. They can be introduced by a reaction sequence involving the addition of sulfenyl halides[14,15] to the double bonds and would activate the adjacent protons, permitting equatorial orientation of the sulfonyl groups under conditions for a base-catalyzed elimination. The γ elimination of a sulfinate ion has been observed in an anomalous lithium aluminum hydride reaction[16] but formation of

$$R_2C(SO_2Et)_2 \xrightarrow{LiAlH_4} R_2C{=}CHCH_3$$

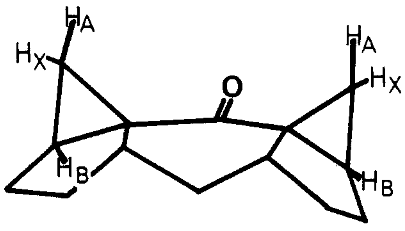
cyclopropanes by this route is unknown. Regarding the direction of addition of the sulfenyl halide, it was hoped that the carbonyl group would polarize the double bond such that the carbon atom γ to the carbonyl group would have a sufficiently increased electron density to cause attachment of the electrophile at that position.

Addition of 2 equiv of benzenesulfenyl chloride to **3** gave a mixture (assumed to be chiefly **9**) which was oxidized with hydrogen peroxide in acetic acid. Partial purification at this point gave impure **10** (70% from **3**) which melted at *ca.* 250–297°, and isomeric material, probably **11**, which melted at 133–136° but had a nearly identical infrared spectrum. Complete separation of the isomeric products for quantitative evaluation of the directive effect of the carbonyl group was impractical in this system, but the yields indicate that the effect was probably substantial. Dehydrohalogenation of **10** gave **12**, which was hydrogenated to give **13**. (See Scheme III.)

Several experiments were carried out to find the best conditions for elimination of benzenesulfinate from **13**. Prolonged refluxing of **13** in methanolic KOH gave no reaction, while brief treatment with NaH in dimethylformamide at 140° destroyed the starting material, giving little or no **5**. Encouraging results were obtained by heating **13** with potassium *t*-butoxide in dimethylformamide containing a little *t*-butyl alcohol at 80°. When the reaction was carried out on a preparative scale using these conditions and the products were separated by chromatography, a compound melting at 95–98.5° was obtained in 34% yield. The elemental analysis was in agreement with structure **5**.

The infrared spectrum (KBr) showed a carbonyl peak at 6.04 μ, and the near-infrared spectrum (in CCl_4) had a peak at 1.635 μ with an extinction coefficient of 0.603, confirming the presence of two cyclopropyl methylene groups.[17]

The nuclear magnetic resonance spectrum (in CCl_4) has a peak at 0.7 ppm, with two very small peaks (*not* spinning side bands) located at 9 Hz above and below it. Integration of this multiplet showed that it was caused by two protons. Examination of models of **5** shows that two of the cyclopropyl methylene protons (H_A) are probably in the strongly deshielding region near the carbonyl group.[18] The nuclear magnetic resonance



5

---

[11] H. B. Henbest, *Proc. Chem. Soc.*, 159 (1963).

[12] R. M. Dodson and B. Riegel, *J. Org. Chem.*, **13**, 424 (1948).

[13] The chemistry of sulfones is reviewed by J. Strating in "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, Chapter 15.

[14] Sulfenyl compounds are reviewed in ref 13 by I. B. Douglass, F. A. Drahowzal, and N. Kharasch in Chapters 30, 31, and 32.

[15] S. J. Cristol, R. P. Arganbright, G. D. Brindell, and R. M. Heitz, *J. Amer. Chem. Soc.*, **79**, 6035 (1957).

[16] M. W. Cronyn, *ibid.*, **74**, 1225 (1952).

[17] P. G. Gassman and F. V. Zalar, *J. Org. Chem.*, **31**, 166 (1966).

[18] L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1959, p 124.

spectrum of 3α,5-cyclo-5α-cholestan-6-one in benzene was taken for comparison. It showed a high field multiplet with an area that indicated four protons. The C-18 angular methyl group, which is found in this region, combined with the 4β proton, gives the expected integration.

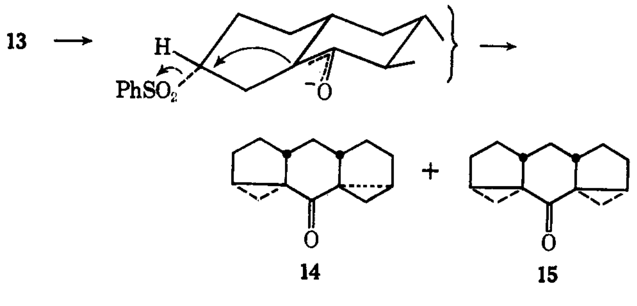
The high field absorption of **5** was considered to be the X part of an ABX system. The appearance of the spectrum in CCl_4 indicated that $J_{AX} = -J_{BX}$ and $\nu_A - \nu_B = 0$. Removal of the chemical shift degeneracy was accomplished by taking spectra in pyridine and in benzene. The H_X absorption in pyridine was a very poorly resolved triplet with two small peaks on either side, and in benzene a clean triplet was observed. Coupling constants (Table I) were estimated[19] from the spectra taken in CCl_4 and in pyridine. The values obtained are probably not very accurate because of uncertainty in measurements of the spectra, but they are in reasonable agreement with the range of values observed by other workers.

TABLE I

	Calcd, Hz	Usual range,[a] Hz
J_{AX}	−3.0	−4.2 to −6.0
J_{BX}	3.0	3.9 to 8.0
J_{AB}	8.5	7.3 to 11.2

[a] K. B. Wibert and B. J. Nist, *J. Amer. Chem. Soc.*, **85**, 2788 (1963); D. J. Patel, M. E. H. Howden, and J. D. Roberts, *ibid.*, **85**, 3218 (1963).

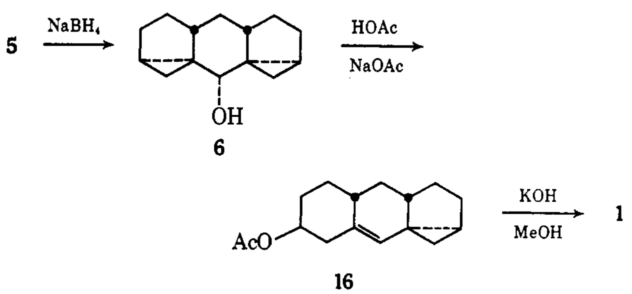
The formation of other isomers (**14** and **15**) of **5** from **13** would involve displacement of axially oriented sulfone groups (*via* the boat conformation). However,



β elimination of sulfones is a well-known reaction[13] and would probably predominate over γ elimination involving the boat conformation, in analogy to the observation that 3α-tosyloxycholestan-6-one undergoes β elimination to give cholest-2-en-6-one rather than γ elimination to give 3β,5-cyclo-5β-cholestan-6-one.[12] Structure **14** is inconsistent with the nmr spectrum of **5** unless the cyclopropyl protons of the epimeric rings happen to have the same chemical shifts in several solvents and the same coupling constants.

The pentacyclic ketone, **5**, was reduced with sodium borohydride, giving **6** with the hydroxyl group probably in the equatorial position.

In acetic acid, 2% in sodium acetate, **6** rearranges rapidly to give the acetate of **1** (**16**) which is saponified by treatment with potassium hydroxide in methanol. The last three reactions (**5** → **6** → **16** → **1**) were very



clean, and, when run successively without purification of intermediates, gave **1** (after purification) in 96.6% yield from **5**. The formation of **16** from the acetolysis of **6** supports the configuration assigned to the cyclopropyl rings of **5**. If **15** were the product of the base-catalyzed elimination, the sequence of reactions used to produce **1** would probably have given a hydroxymethylcyclopentyl derivative, in analogy to the formation of α-hydroxymethyl-A-norcholest-5-ene from 3β,5-cyclo-5β-cholestan-6β-ol upon treatment with acid.[20]

Experimental Section

Melting points, unless noted otherwise, were taken on a Kofler hot stage microscope and are uncorrected. Nmr spectra were taken on a Varian A-60 spectrometer, ultraviolet and near-infrared spectra on a Cary 14 spectrophotometer, and infrared spectra on a Perkin-Elmer Infracord spectrophotometer. Elemental analyses were done by Scandinavian Microanalytical Laboratories. Optical rotations were determined on a Perkin-Elmer Model 141 polarimeter. 1,4,4aβ,5,8,8aα,9aα,10aβ-Octahydroanthraquinone (**2**) was made as described by Alder and Stein.[2]

1,4,4aβ,5,8,8aα,9aα,10aβ-Octahydro-10-hydroxy-9-anthrones (7 and 8) by Lithium Aluminum Hydride Reduction.—To a solution of 0.177 g (0.818 mmol) of **2** in 20 ml of tetrahydrofuran, 0.60 ml (0.212 mmol) of a 0.353 *M* solution of lithium aluminum hydride in tetrahydrofuran was added under nitrogen with stirring over a period of 25 min. The solution was stirred for 15 min at room temperature and then was refluxed for 50 min. One ml of water was added and the resultant precipitate was filtered out. The solvent was removed and the residue was taken up in methylene chloride. The suspension was washed with water and dried ($MgSO_4$). Removal of solvent gave a solid from which a mixture of **7** and **8** was obtained by chromatography on alumina. (There was partial separation of **7** and **8** with the latter being eluted more quickly.) The mixture was recrystallized once from ethyl acetate to give somewhat impure **7** (13.8 mg), mp *ca.* 203°; ir (KBr) 5.89 μ.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.80; H, 8.43.

The residue from the filtrate was recrystallized several times from benzene, giving **8**, mp 151–165°; ir (KBr) 5.92 μ.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.96; H, 8.34.

Synthesis of 7 and 8 by Reduction of 2 with Lithium Tri-*t*-butoxyaluminohydride.—A solution of 29.4 g of Li(t-BuO)$_3$AlH (0.116 mol) in 300 ml of tetrahydrofuran was added dropwise under nitrogen over a period of 1 hr with stirring to a solution of **2** (25.0 g, 0.116 mol) in 1.75 l. of tetrahydrofuran. After 3.5 hr at room temperature, the solvent was removed *in vacuo*, and the residue was dissolved in a mixture of *ca.* 1.1 l. of methylene chloride and 200 ml of 10% sulfuric acid. The methylene chloride solution was dried (K_2CO_3) and the solvent was removed *in vacuo*. The residue was recrystallized from ethyl acetate (*ca.* 300 ml), giving 15.3 g (60.7%) of **7**, mp 211.5–213.0°. A sample recrystallized several times from ethyl acetate melted at 214–214.5°; nmr (CF_3CO_2H) δ 3.89 (t, J = 8.5 Hz) and 5.78 (s).

A second crop from the recrystallization of the crude reaction product gave 7.54 g (29.8%) of product, mp 151–178°. A

---

(19) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 132 ff.

(20) G. H. Whitham, *Proc. Chem. Soc.*, 330 (1962); W. G. Dauben and J. A. Ross, *J. Amer. Chem. Soc.*, **81**, 6521 (1959); G. H. Whitham and J. A. F. Wickramasinghe, *J. Chem. Soc.*, 1655 (1964); G. Bauslaugh, G. Just, and E. Lee-Ruff, *Can. J. Chem.*, **44**, 2837 (1966).

sample was recrystallized several times from benzene to give material melting at 153–159°, which was largely **8**, nmr (CF_3CO_2H) δ 4.17 (s, $W_{1/2}$ = 4.5 Hz) and 5.78 (s). The nmr spectra identify **7** as the 10β-alcohol and **8** as the 10α-alcohol, as discussed before.

1,4,4aβ,5,8,8aα,9aα,10aβ-Octahydroanthrone (3).—A solution of **7** (38.4 g) in 410 ml of pyridine (freshly purified) was cooled to 0°. A cold solution (0°) of 46 ml of methanesulfonyl chloride in 200 ml of pyridine was added and the mixture was kept at 0° for 24 hr. The mixture was then poured into 3.5 l. of ice-water and extracted with *ca.* 3 l. of benzene. The benzene solution was washed successively with water, cold 5% sulfuric acid, water, 2% sodium bicarbonate solution, and water, and was dried ($MgSO_4$) and boiled down until the product crystallized. The first crop gave 40.2 g of tan solid (77.2%), mp *ca.* 180–193°, and the second crop gave 6.2 g (11.9%), mp 181.5–186.5° with some material remaining up to 192°. The over-all yield of the crude methanesulfonate of **7** was 89.1%. Recrystallization from benzene gave an analytical sample, mp 188–192°; ir (KBr) 5.83, 6.03, 7.43, 8.49, 8.58 μ; nmr δ ($CHCl_3$) (rel area) 5.80 (s, 3.98), 4.79 (t, *J* = *ca.* 8.5 Hz, 1.16), 3.11 (very sharp s, 2.93), and 2.29 (broad envelope, 11.91).

Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80; S, 10.82. Found: C, 60.83; H, 6.72; S, 10.92.

The methanesulfonate was dissolved in 1.5 l. of purified tetrahydrofuran. Lithium aluminum hydride (38 g) was added, and the mixture was refluxed ($CaCl_2$ tube) for 24 hr. Ethyl acetate (184 g) was added dropwise with stirring (by hand when necessary). After 1 hr, 10 ml of water was added, and 500-ml portions of the reaction mixture were poured into 2-l. portions of cold 5% sulfuric acid. These mixtures were extracted with methylene chloride and the combined extracts were taken to dryness *in vacuo*. The residue was dissolved in methylene chloride–tetrahydrofuran and and the solution was dried (K_2CO_3). Removal of the solvent gave 35.1 g of crude 1,4,4aβ,5,8,8aα,9,9aα,10,10aβ-decahydroanthran-9-ol. (The theoretical yield is 32.1 g.) A sample from a previous run was purified by chromatography on alumina to give analytical material, mp 143–145.5°; ir (KBr) 2.95 and 6.04 μ.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.27; H, 9.54.

Chromium trioxide (12.0 g) was added to 120 ml of pyridine (with caution),[10] and a solution of 12.2 g of the decahydroanthranol in 120 ml of pyridine was added to the mixture. The flask was kept at 39° for 9 hr, and the contents were then poured into 1 l. of water. Carbon tetrachloride (300 ml) was added, and the mixture was filtered. The organic layer was separated and the aqueous layer was washed with more carbon tetrachloride. The carbon tetrachloride solution was dried ($MgSO_4$), and the solvent was removed *in vacuo*. The residue was chromatographed on 100 g of alumina, and eluted with benzene to give 8.64 g of crude **3** and with acetone to give 2.67 g of unchanged starting material. The crude **3** was recrystallized from ethanol to give 8.31 g (87.9% based on unrecovered starting material) of purified **3**, mp 125–129.0°. A sample of **3** recrystallized several times from methanol melted at 125.5–126°; ir (KBr) 5.87 and 6.04 μ; nmr (CCl_4) δ (rel area) 5.74 (3.8) and 2.19 (broad envelope, 14.2).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.94; H, 8.97.

4aβ,8aα,9aα,10aβ-Perhydro-2α,7α-diphenylthio-3β,6β-dichloro-9-anthrone (9).—Benzenesulfenyl chloride was made by the procedure of Lecher and Holschneider.[21] A solution of 13.3 g (0.0658 mol) of **3** in 150 ml of carbon tetrachloride was kept at 13–25° while a solution of 19.0 g (0.132 mol) of benzenesulfenyl chloride in 150 ml of carbon tetrachloride was added dropwise with stirring over a period of 1.25 hr. The solution became turbid near the end of the addition. The mixture was stirred at room temperature for 12 hr, after which the solvent was removed *in vacuo*, giving a white solid residue which occluded a large amount of solvent. A sample recrystallized twice from carbon tetrachloride and three times from benzene melted gradually to 202°; ir (KBr) 3.26, 5.84, 6.36, 6.82 μ.

Anal. Calcd for $C_{26}H_{28}Cl_2OS_2$: C, 63.53; H, 5.74; Cl, 14.43; S, 13.05. Found: C, 63.92; H, 5.80; Cl, 14.61; S, 13.31.

4aβ,8aα,9aα,10aβ-Perhydro-2α,7α-diphenylsulfonyl-3β,6β-dichloro-9-anthrone (10).—A solution of 57.0 ml of 28.3% H_2O_2 (0.526 mol) in 385 ml of acetic acid was added to the residue from the previous reaction. The mixture was heated to 80° on a steam bath to dissolve the solid. The temperature rose to *ca.* 84° and a water bath was used to cool the solution back to 80°. The solution was then stirred and allowed to cool (in air) to 65°. This took about 1 hr, during which time a precipitate formed. The mixture was stirred at 62–67° for 18 hr and then at 18–20° for 1 hr. The precipitate was filtered, washed with acetic acid, and dried *in vacuo*, giving 25.5 g of **10** (70% from **3**), mp *ca.* 250–297°. A sample was recrystallized three times from acetic acid and chromatographed on silica gel, eluting with 10% ether in methylene chloride, to give analytical material, mp *ca.* 270–297.5°; ir (KBr) 3.25, 5.86, 6.32, 6.77, 7.66, 8.70 μ; nmr of crude product (CF_3CO_2H) δ (rel area) 7.2–8.1 (9.5), 4.82 (1.68), 3.72 (1.83), 1.4–3.5 (15.0).

Anal. Calcd for $C_{26}H_{28}Cl_2O_5S_2$: C, 56.21; H, 5.08; Cl, 12.77; S, 11.54. Found: C, 55.85; H, 5.12; Cl, 13.03; S, 12.03.

Addition of water to the acetic acid filtrate gave a precipitate (**11**), mp 133–136°. The infrared spectrum of this material is nearly identical with that of the high-melting product.

1,4,4aβ,5,8,8aα,9aα,10aβ-Octahydro-2,7-diphenylsulfonyl-9-anthrone (12).—A solution of **10** (25.5 g) in 250 ml of pyridine was refluxed for 24 hr. The pyridine was mostly removed *in vacuo* and the residue was taken up in *ca.* 600 ml of methylene chloride, and washed with water, dilute hydrochloric acid (1:4), 10% sodium bicarbonate solution, and water. The solution was dried ($MgSO_4$), decolorized with charcoal, and taken to dryness. The residue was recrystallized from dimethylformamide, giving 16.3 g (73.5%) of **12**, mp 255–266.5°. In another run, the product in methylene chloride was filtered through silica gel (washing with ether), recrystallized three times from dioxane, chromatographed on silica gel and eluted with 5% ether in methylene chloride, and recrystallized twice from dimethylformamide to give an analytical sample, mp 255–267.5°; ir (KBr) 3.24, 5.84, 6.04, 6.33, 6.77, 7.70, 8.75 μ.

Anal. Calcd for $C_{26}H_{26}O_5S_2$: C, 64.70; H, 5.43; S, 13.29. Found: C, 64.72; H, 5.51; S, 13.10.

4aβ,8aα,9aα,10aβ-Perhydro-2,7-diphenylsulfonyl-9-anthrone (13).—One liter of 97% formic acid was added to 5.40 g of 10% Pd-C under nitrogen (formic acid ignites when added to the catalyst in air). The product of the previous reaction (16.3 g) was added, and the mixture was hydrogenated at 1 atm. The catalyst is poisoned slowly by **12**, but hydrogenation is complete under these conditions before the catalyst dies. The mixture was heated to 100° and filtered through Supercel on sintered glass, washing with 200 ml of boiling formic acid. Removal of the solvent *in vacuo* gave 13.7 g (83.6%) of white solid. Quantitative yields were obtained in runs done on a smaller scale where the catalyst was washed more completely. Trifluoroacetic acid is a good solvent for **13** and can be used for washing the catalyst (but *not* as a solvent for the hydrogenation). A sample recrystallized several times from formic acid had mp *ca.* 317–342° on a Kofler block and 336–344° dec (corrected) in an evacuated capillary; ir (KBr) 3.24, 5.90, 6.32, 6.77, 7.68, 8.71 μ; nmr (CF_3CO_2H) δ (rel area) 7.4–8.2 (9.65), 3.29 (2.36), and 0.8–2.9 (17.98).

Anal. Calcd for $C_{26}H_{30}O_5S_2$: C, 64.17; H, 6.21; S, 13.18. Found: C, 63.90; H, 6.14; S, 13.07.

2α,9aα-Cyclo-7α,8aα-cyclo-4aβ,10aβ-perhydro-9-anthrone (5).—A solution of **13** (13.7 g) and potassium *t*-butoxide (17.0 g, MSA Research Corporation) in 1.11 l. of dimethylformamide (Eastman Spectro Grade, dried over molecular sieves) and 59 ml of dry *t*-butyl alcohol was stirred at 80° under nitrogen for 6 hr and then cooled to 0°. The reaction mixture was mixed with 5 l. of water and extracted several times with ether. The ether solution was washed well with water and then with saturated sodium chloride solution, and was dried ($MgSO_4$) and stripped *in vacuo*, giving 4.77 g of material that mostly solidified on standing. Chromatography on 300 g of Florisil, eluting with benzene, followed by recrystallization of fractions containing **5** from ethyl acetate gave 1.96 g of **5**, mp 95–98.5°. The yield from **13** was 34.3%. A sample recrystallized several times from ethyl acetate gave analytical material, mp 96.5–97.0°; ir (KBr) 3.22–3.31 (3 weak peaks), and 6.04 μ; near-ir (in CCl_4, *c* 0.970 *M*, *l* = 1 cm) 1.635 μ (ε 0.603); nmr (CCl_4) δ (rel area) 2.65–2.03 (envelope, 1.87), 2.03–0.91 (13.99), 0.91–0.33 (triplet with very intense center peak at 0.72, 2.11); uv λ_{max} (ethanol) 275 mμ (ε 69); end absorption, ϵ^{220} 6500 (cyclohexane).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.38; H, 8.99.

2α,9aα-Cyclo-7α,8aα-cyclo-4aβ,10aβ-perhydroanthran-9α-ol (6).—A solution of 1.70 g of **5** and 1.70 g of sodium borohydride

---

[21] H. Lecher and F. Holschneider, *Ber.*, **57**, 755 (1924).

in 62 ml of 80% aqueous ethanol, 0.2 *N* in sodium hydroxide, was refluxed with stirring for 1.5 hr. The volume was reduced *in vacuo* and the residue was dissolved in ether and water. The ether solution was washed with water until neutral, washed with saturated sodium chloride solution, dried (K_2CO_3), and stripped in nitrogen stream, and the residue was dried *in vacuo*, giving 1.71 g (99.5%) of **6**. Material that had been recrystallized several times from ethyl acetate, 0.1% in triethylamine, melted at 148–150°; ir (CCl_4) 2.70, 3.26 (shoulder), and 3.33 μ; nmr ($CDCl_3$) δ (rel area) 4.36 (d, J = *ca.* 8.5 Hz, 0.73), 0.20–2.6 (19.27); mass spectrum m/e (rel intensity) 204 (100), 202 (89), 186 (296).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.46; H, 9.83.

1,2,3,4,4aβ,5,6,8,10,10aβ-Decahydro-7α,8aα-cyclo-2β-acetoxyanthracene (**16**).—The alcohol **6** (1.71 g) was dissolved in 34 ml of acetic acid, 2% in sodium acetate, with brief heating on a steam bath. After 3 hr at room temperature, the solution was poured into 150 ml of water and extracted with ether. The ether solution was washed with water, 5% sodium bicarbonate solution, water, and saturated sodium chloride solution, dried ($MgSO_4$), stripped to a small volume in a nitrogen stream, seeded, and taken to dryness in nitrogen. The residue was dried briefly *in vacuo*, giving 2.05 g (99.5%) of **16**. Material that had been recrystallized several times from methanol melted at 65.0–66.5°; ir (KBr) 3.24, 5.77, 6.05 (very weak), 8.00 μ; nmr (CCl_4) δ (rel area) 5.08 (0.94), *ca.* 4.5 (0.89), 1.97 (sharp s), *ca.* 0.5 (complex m, 2.05).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.06; H, 8.97.

1,2,3,4,4aβ,5,6,8,10,10aβ-Decahydro-7α,8aα-cycloanthran-2β-ol (**1**).—A solution of 2.05 g of **16** in 50 ml of 10% methanolic potassium hydroxide was stirred for 1.5 hr at room temperature. The volume of the solution was reduced *in vacuo* and the viscous liquid was poured into water and extracted with ether. The ether solution was washed with water until neutral and then with saturated sodium chloride solution, dried ($MgSO_4$), and stripped in nitrogen stream, and the residue was dried briefly *in vacuo*, tiving 1.69 g. The product was recrystallized from ethyl acetate to give 1.66 g (97.3%) of **1**, mp 117–119°. Analytical material was obtained by several recrystallizations from ethyl acetate and melted at 117–119°; ir (KBr) 3.02 μ; nmr (CCl_4) δ (rel area) 4.98 (0.95), *ca.* 3.4 (1.23), and 0.25–0.80 (complex m, 2.36); uv (cyclohexane) λ_{max} 218 mμ (ϵ 12,300).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.18; H, 9.88.

Registry No.—**1**, 20843-76-9; **3**, 20843-77-0; **5**, 20843-78-1; **6**, 20843-79-2; **7**, 20843-80-5; **7** (methanesulfonate), 20843-81-6; **8**, 20843-82-7; **9**, 20843-83-8; **10**, 20843-84-9; **11**, 20843-85-0; **12**, 20843-86-1; **13**, 20843-87-2; **16**, 20843-88-3; 1,4,4aβ,5,8,8aα,9,9-aα,10,10aβ-decahydroanthran-9-ol, 20843-89-4.

Acknowledgment.—Fellowship support from the National Science Foundation and the National Institutes of Health is gratefully acknowledged.

Arynes *via* Aprotic Diazotization of Anthranilic Acids[1]

LESTER FRIEDMAN AND FRANCIS M. LOGULLO[2]

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106

Received February 3, 1969

Aprotic diazotization of anthranilic acids generates the corresponding benzenediazonium-2-carboxylates which decompose *in situ* to give arynes, carbon dioxide, and nitrogen. Moderate to excellent yields of aryne-derived products are obtained when the reaction is conducted in the presence of suitable acceptors.

Arynes have been generated under a variety of conditions by fragmentation of suitable *ortho*-disubstituted benzenes.[3] Most of the methods suffer from either limited availability of benzyne precursor, involved experimental techniques, and/or low yields of benzyne-derived products. One of the more attractive benzyne precursors is benzenediazonium-2-carboxylate,[3f] in that benzyne formation can be effected in neutral aprotic media at moderate temperatures. However, this compound is extremely shock sensitive and hazardous to use. As a result, benzyne has not been utilized to the full extent that it could be.

In 1962, it was reported[4] that arylamines could be diazotized by amyl nitrite in excess benzene to give diazonium species which decompose *in situ* to give biaryls. If anthranilic acids[5] could be diazotized in a similar manner, the products would be benzenediazonium-2-carboxylates, which could, in principle, decompose as formed to arynes, nitrogen, and carbon dioxide.

Results and Discussion

It was found that anthranilic acids are readily diazotized by alkyl nitrites in aprotic media to give benzenediazonium-2-carboxylates, which undergo fragmentation to benzyne, nitrogen, and carbon dioxide. The intermediacy of benzyne[6] was demonstrated by trapping with anthracene (to give triptycene), furan (to give 1,4-dihydro-1,4-epoxynaphthalene), tetracyclone (to give 1,2,3,4-tetraphenylnaphthalene), iodine (to give diiodobenzene), and cyclopentadiene (to give benzonorbornadiene). This technique avoids the isolation and handling of the hazardous benzenediazonium-2-carboxylates and is a convenient preparative source of arynes.

---

(1) Part of this work was reported in a preliminary communication, L. Friedman and F. M. Logullo, *J. Amer. Chem. Soc.*, **85**, 1549 (1963).

(2) (a) Abstracted in part from the Ph.D. Thesis of F. M. Logullo, Case Institute of Technology, June 1965.

(3) (a) E. LeGoff, *J. Amer. Chem. Soc.*, **84**, 3786 (1962); (b) L. Horner and H. Bruggerman, *Ann.*, **635**, 22 (1960); (c) J. A. Kampmeier and E. Hoffmeister, *J. Amer. Chem. Soc.*, **84**, 3787 (1962); (d) M. Stiles and R. G. Miller, *ibid.*, **82**, 3802 (1960); (e) R. S. Berry, G. N. Spokes, and M. Stiles, *ibid.*, **82**, 5240 (1960); **84**, 3750 (1962); (f) M. Stiles, U. Burckhardt, and A. Haag, *J. Org. Chem.*, **27**, 4715 (1962); (g) G. Wittig and H. F. Ebel, *Angew. Chem.*, **72**, 564 (1960); *Ann.*, **650**, 20 (1961); (h) G. Wittig and R. W. Hoffmann, *Angew. Chem.*, **73**, 435 (1961); (i) E. McNelis, *J. Org. Chem.*, **28**, 3188 (1963), and references contained therein; (j) F. M. Beringer and S. J. Huang, *ibid.*, **29**, 445 (1964); (k) L. Verbit, J. S. Levy, H. Rabitz, and W. Kwalwasser, *Tetrahedron Lett.*, 1053 (1966); (l) C. D. Campbell and C. W. Rees, *Proc. Chem. Soc.*, 296 (1964); *Chem .Commun.*, 192 (1965); (m) E. K. Fields and S. Meyerson, *ibid.*, 474 (1965); 275 (1966); (n) M. P. Cava, M. J. Mitchell, D. C. DeJongh, and R. Y. Van Fossen, *Tetrahedron Lett.*, 2947 (1966); (o) R. F. C. Brown and R. K. Solly, *Chem. Ind.* (London), **181**, 1462 (1965); *Australian J. Chem.*, **19**, 1045 (1966).

(4) J. I. G. Cadogan, *J. Chem. Soc.*, 4257 (1962).

(5) A related example is diazotization of an alcoholic solution of sulfanilic acid with nitrous fumes to give the "internal" diazonium salt, benzenediazonium-4-sulfonate. R. Schmitt, *Ann.*, **112**, 118 (1859); **120**, 144 (1861).

(6) For an excellent recent review of benzyne chemistry, see G. Wittig, *Angew. Chem. Intern. Ed. Engl.*, **4**, 731 (1965); *Angew. Chem.*, **77**, 752 (1965).