Synthesis of Bridgehead Hydroxyl-Substituted Benzobicyclo[3.2.1]octenes and -octadienes via an Acyloin Rearrangement in the Benzobicyclo[2.2.2]octene Ring System

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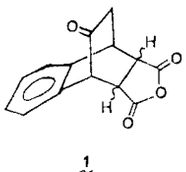
Received February 21, 1978

Maleic anhydride and 1,2-naphthalenediol, on heating to 180 °C, produced a mixture of the benzobicyclo[3.2.1]-octene derivative **2** and the benzobicyclo[2.2.2]octene derivative **3**. This was the result of Diels–Alder addition to form **3**, followed by extensive rearrangement of **3** to **2**. Purified compound **3** was converted to **2** in high yield via an acyloin rearrangement; this process occurred thermally or with acid or base catalysis. The utility of this rearrangement for the preparation of bridgehead hydroxyl-substituted benzobicyclo[3.2.1]octenes and -octadienes was demonstrated by the conversion of the anhydride **2** to the bisdecarboxylated hydroxy ketones **4** and **5** and the amino alcohol **6**. Presence of the bicyclo[3.2.1] ring system was confirmed crystallographically for the hydrochloride salt of **6**.

Benzobicyclo[2.2.2]- and -[3.2.1]octenes, -octadienes, and -octatrienes bearing bridgehead hydroxyl substituents are uncommon. Only one benzobicyclo[3.2.1]octadiene[1] and two benzobicyclo[2.2.2]octene[2] and -octatriene[3] examples are known. We report the synthesis of a bridgehead hydroxyl-substituted benzobicyclo[2.2.2]octene and its facile conversion to bridgehead hydroxyl-substituted benzobicyclo[3.2.1]octene and -octadiene derivatives via an acyloin rearrangement. Rearrangements in the benzobicyclo[2.2.2]octene, -octadiene, and -octatriene ring systems are well known and have been initiated by a cationic species (H^+, Br^+, Cl^+, NO^+)[4a-c] or by solvolysis of a sulfonate ester,[4d,e] producing a carbonium ion, or by irradiation;[4f,g,h] ours is the first example of an acyloin rearrangement in this ring system.

The Diels–Alder addition of maleic anhydride to 2-naphthol, producing **1**, has previously been reported as an entry



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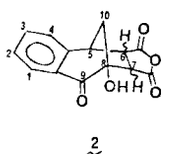

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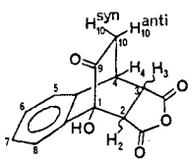

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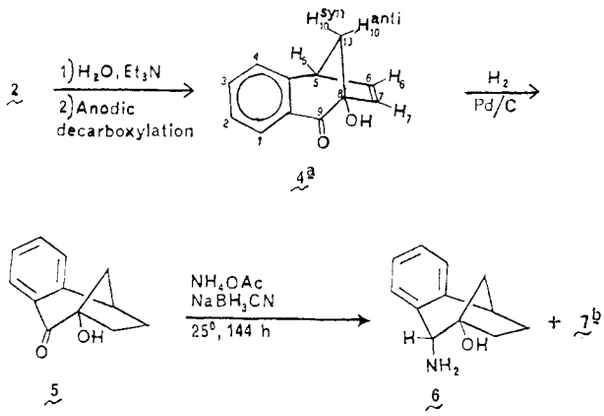
into the benzobicyclo[2.2.2]octene ring system.[5] When we attempted to extend this procedure by adding maleic anhydride to 1,2-naphthalenediol at 180 °C under inert atmosphere, we observed the formation of two isomeric products, **2** (major) and **3**, which were separable by column chromatography or by fractional recrystallization. Compound **2** was subsequently hydrolyzed and subjected to anodic decarboxylation to produce the olefin **4**. Catalytic hydrogenation of **4** to **5** followed by reductive amination gave the amine **6** (see Scheme I). All assigned structures were consistent with observed IR and NMR spectra, and the presence of the benzobicyclo[3.2.1]octene skeleton was confirmed by X-ray structure determination of the hydrochloride salt of **6**.

The minor product of the Diels–Alder reaction was the expected adduct **3**. The infrared spectrum of **3** was very similar to that of **1**; in particular, **3** had a ketone carbonyl absorption at 1735 cm^{-1} (cf. 1730 cm^{-1} observed for **1**). In addition, IR showed that the hydroxyl group is strongly intramolecularly hydrogen bonded, consistent with the presence of an α-hydroxy ketone. In the NMR spectrum of **3**, the methylene protons H_{10} appeared as a pair of doublets. $H_{10}{}^{anti}$ had a chemical shift of δ 2.68, while $H_{10}{}^{syn}$, which is shielded by the aromatic ring, appeared at δ 2.57. The aromatic protons of **3** appeared as a multiplet between 7.2 and 7.7 ppm. The mass spectral fragmentation patterns of **1** and **3** showed a number

Scheme I



2 → **4**[a] → **5** → **6** + **7**[b]

[a] The terms "syn" and "anti" are used relative to the aromatic ring. [b] Compound **7** constituted < 5% of the amine product and was not identified.

of similarities; significant among these was the appearance of a peak at M − 42, consistent with the retro-Diels–Alder loss of ketene. The UV spectrum provided further evidence for the assigned structure of **3**; it showed maxima at 255 and 292 nm, compared to literature values[6] of 265 and 295 nm for compound **1**.

In comparison, the major product **2** had a carbonyl absorption at 1690 cm^{-1} in the infrared and a strong UV maximum absorption at 251 nm (ϵ 12 600), indicative of a conjugated ketone. Intramolecular hydrogen bonding of the hydroxyl group was again observed by infrared spectroscopy, indicating the rearranged structure **2**. In contrast to the mass spectra of **1** and **3**, compound **2** showed no M − 42 fragment; this observation is also consistent with the presence of a rearranged carbon skeleton.

The yield and the product ratio in the Diels–Alder reaction were found to be dependent upon the purity of both the naphthalenediol and the maleic anhydride. Higher proportions of **3** relative to **2** and higher overall yields were observed when the naphthalenediol was dried over $MgSO_4$ and recrystallized from carbon disulfide and when commercial maleic anhydride (containing as much as 14% maleic acid) was sublimed prior to use. Table I lists yields and product ratios which were obtained under various conditions. Prolonged heating led to increased yields of **2** at the expense of **3**; this is consistent with initial formation of **3** and subsequent acyloin rearrangement to **2**.

Characteristic of acyloin rearrangements, the conversion of **3** to **2** occurs thermally and with acid and base catalysis. The

0022-3263/78/1943-3478$01.00/0

Table I. Product Ratios Obtained in the Diels–Alder Addition of Maleic Anhydride to 1,2-Naphthalenediol

conditions	ratio of 3 to 2[a]	% overall yield
commercial maleic anhydride,[b] 170 °C, 20 min	13:87	42.6
sublimed maleic anhydride, 180 °C, 20 min	25:75	61.3
sublimed maleic anhydride, 180–190 °C, 5 min	44:56	70.5

[a] Product ratios were determined by IR as described in the text. [b] This material was found to contain 14% maleic acid.

Table II. First-Order Rate Constants for the Rearrangement of 3 to 2 at 82 °C (Acetonitrile at Reflux)

conditions	k, h^{-1}
CH_3CN, Δ[a]	$2.46\ (\pm 0.22) \times 10^{-3}$
CH_3CN, p-TsOH, Δ[b]	$2.98\ (\pm 0.15) \times 10^{-3}$

[a] 202.8 mg of 3 in 75 mL of CH_3CN. [b] 204.2 mg of 3 + 3.2 mg of p-TsOH in 75 mL of CH_3CN.

crystalline hydroxy ketone 3 underwent rearrangement to 2 at its melting point. The reaction proceeded more slowly at 82 °C (acetonitrile at reflux) and was conveniently monitored by infrared spectroscopy. The changes in ketone carbonyl absorbance of 3 and 2 were linear with concentration over the range 0–37 mg/mL in acetonitrile solution. Table II lists first-order rate constants for the rearrangement in acetonitrile at reflux under neutral conditions and with added p-toluenesulfonic acid. The base-catalyzed rearrangement was complicated by competing condensation reactions, which interfered with the determination of rate constants; changes in the infrared spectra were, however, consistent with base catalysis. Rearrangement of 2 to 3 was not observed; this suggests that 2 is considerably more stable than 3 due to conjugation of the ketone carbonyl group. This is not always the case; Colard et al., for example, reported an instance (see Figure 1) in which a conjugated acyloin was less stable than its nonconjugated isomer.[8] Ring strain effects would probably favor the bicyclo[2.2.2] system over the bicyclo[3.2.1] system, according to results obtained with several equilibrating dibenzobicyclo[3.2.1]- and -[2.2.2]octadiene systems.[9]

Further evidence for the structure of 2 was afforded by conversion to the bicyclo[3.2.1]octadienone 4. Following hydrolysis, compound 2 readily underwent electrolytic decarboxylation[10] in pyridine to produce 4 in 49% yield from the anhydride. In the NMR spectrum of 4, the aromatic proton ortho to the carbonyl group (H_1) was deshielded relative to the other aromatic protons. The vinyl protons H_6 and H_7 appeared as a doublet of doublets and a doublet, respectively. The bridgehead proton H_5 appeared as a broad multiplet at δ 3.81. The methylene protons H_{10} produced a doublet of doublets centered at δ 2.90 and a doublet at δ 2.53. Irradiation of the bridgehead proton H_5 caused the methylene protons to appear as two doublets due to geminal coupling (J = 10 Hz). It was determined from a Dreiding model of 4 that H_5 should couple with H_{10}^{anti} (H–C–C–H dihedral angle ≈40°) but not with H_{10}^{syn} (H–C–C–H dihedral angle ≈80°), permitting the assignment of the peaks at δ 2.90 to H_{10}^{anti}, and the doublet at δ 2.53 to H_{10}^{syn}. The shielding effect on H_{10}^{syn} by the carbonyl and/or aromatic systems lends further support to these assignments.

Attempted anodic decarboxylation of 3 gave a low yield of a mixture of two ketones (Scheme II). The major product was compound 4; the presence of carbonyl absorption at 1740 cm^{-1}

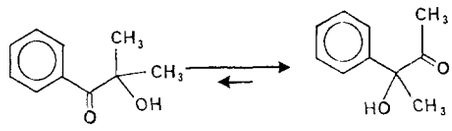
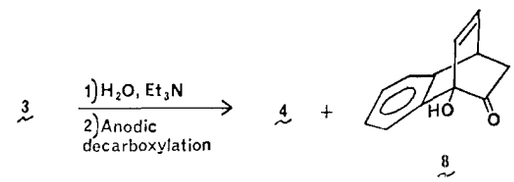


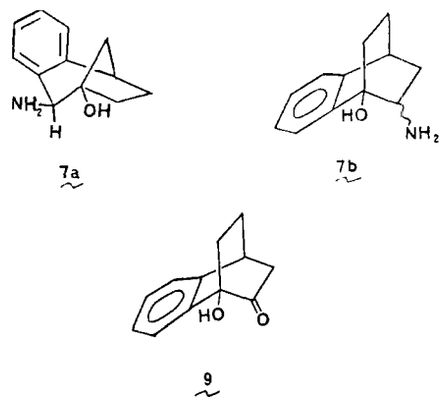
Figure 1.

Scheme II



in the ketone mixture suggested that the minor product was compound 8. The product ratio of 4 to 8 was estimated to be about 4:1 on the basis of the IR carbonyl absorptions. The susceptibility of 8 to rearrangement prevented thin layer or gas chromatographic isolation of a pure sample uncontaminated with 4.

The facile acyloin rearrangement of a benzobicyclo[2.2.2]-octene affords a convenient procedure for the synthesis of bridgehead hydroxyl-substituted benzobicyclo[3.2.1]octenes and -octadienes. For example, ketone 4 was readily hydrogenated to 5, which underwent reductive amination with ammonium acetate and sodium cyanoborohydride.[11] The reductive amination afforded a mixture of two amines, separable by LC. The major product, comprising 95% of the isolated



product, was shown to be the amine 6 by X-ray crystallographic analysis of the hydrochloride salt.[12] The minor product was not isolated in sufficient quantity to identify. It is likely that it was either 7a (the stereoisomer of 6) or 7b (arising from contamination of the ketone 5 with a small amount of the bicyclo[2.2.2]octenone 9).

Experimental Section

Infrared spectra were recorded on a Beckman IR-33 spectrophotomer. NMR spectra were obtained on a Varian T-60, EM360, or HA-100 spectrometer using tetramethylsilane as internal standard. UV spectra were recorded on a Cary 14 spectrophotometer. Melting points were determined on a Thomas-Hoover Uni-melt and are uncorrected. Mass spectra were obtained on a Varian CH5 spectrometer. Elemental analyses were performed on an F&M Model 185 by Mr. Tho Nguyen of The University of Kansas.

9-Keto-1,2,3,4-tetrahydro-1,4-ethanonaphthalene-2,3-dicarboxylic Anhydride (1). This material was prepared as described by Takeda et al.;[6] IR (KBr) 3075, 3025, 2980, 2950, 1865 and 1775 (anhydride C=O), 1730 (ketone C=O), 1470, 1450, 1395, 1345, 1285, 1255, 1235 (sh), 1215, 1195, 1170, 1140, 1095, 1060, 995, 970, 930, 900, 825, 805, 755, 735, 705, 680 cm^{-1}; NMR (Me_2SO-d_6) δ 7.35 (s, 4, aromatic), 3.43 (d, 1), 2.93 (m, 1), 2.44–2.68 (m, 2), 2.28–2.41 (m, 1), 2.03 (m, 1); mass spectrum m/e (rel intensity) 242 (19, M^+), 215 (7), 214 (48), 200 (2), 141 (6), 129 (11), 128 (100), 127 (5), 115 (6).

1,2-Naphthalenediol.[13] To a stirred solution of sodium dithionite (300 g, 1.72 mol) in distilled water (3.75 L) at 25 °C was added 1,2-

Table III

product (2) concn, M	time, h
Run 1: 202.8 mg of 3 Dissolved in 75 mL of CH_3CN at Reflux	
0.21×10^{-3}	16.50
0.31	37.92
1.45	76.50
2.27	116.00
Run 2: 204.2 mg of 3 + 3.2 mg of p-TsOH in 75 mL of CH_3CN at Reflux	
0.21×10^{-3}	16.67
0.72	38.08
1.96	76.67
2.79	116.17

naphthoquinone (50.0 g, 0.316 mol). The solution turned gray, then black, and then clarified as a small amount of tar formed. The mixture was stirred for 15 min and was filtered to remove the tar. The solution was saturated with NaCl and cooled to −5 °C for 30 min. The cream-colored precipitate was collected by filtration and immediately dissolved in 1.5 L of hot CS_2. The solution was dried with $MgSO_4$, filtered, and concentrated to 100 mL on a steam bath under a stream of argon. Upon cooling, 21.5 g (42.4%) of naphthalenediol was collected as purple-brown crystals, mp 103–105 °C (lit.[13] mp 104 °C). This material was of adequate purity for the Diels–Alder reaction; however, white crystals could be obtained by sublimation.

Reaction of Maleic Anhydride with 1,2-Naphthalenediol. Maleic anhydride was sublimed prior to use. 1,2-Naphthalenediol was freshly prepared as described above. Under argon atmosphere, a mixture of maleic anhydride (16.7 g, 0.170 mol) and 1,2-naphthalenediol (16.7 g, 0.104 mol) was heated at 180–190 °C for 5 min. The mixture was taken up in 150 mL of hot ethyl acetate and the solution was concentrated in vacuo to give a brown semisolid mass. This was shaken with 800 mL of ether and allowed to stand for 30 min. Filtration afforded 19.0 g (70.6%) of a mixture of the products **3** and **2** in a ratio of 44:56 as determined by IR analysis. A 2.9-g portion of the product mixture was separated by medium-pressure liquid chromatography on silica (Merck, 230–400 mesh), column size 25 × 1000 mm, eluting with hexane–ethyl acetate (3:2) at a pressure of 40 psi. The first 700 mL was discarded; the bicyclo[3.2.1] product **2** was contained in the next 150 mL. Another 350 mL was discarded, and the following 500 mL contained the bicyclo[2.2.2] product **3**, contaminated with traces of **2**; **3** was further purified by a recrystalization from toluene–ethyl acetate: mp 187–192 °C; UV λ_{max} (CH_3CN) 226 (ε 4350), 255 (347), 292 nm (377); IR (KBr) 3480 (OH), 2982, 1850 and 1775 (anhydride C=O), 1735 (ketone C=O, log ε 6.13), 1264, 1234, 1163, 1082, 1053 (sh), 1016, 934, 862, 763 (sh), 754 (sh), 740, and 732 cm^{-1}; NMR (CD_3CN) δ 7.2–7.7 (m, 4, aromatic), 4.63 (s, 1, **OH**), 3.92 (m, 2 of H_2, H_3, and H_4), 3.61 (m, 1 of H_2, H_3, and H_4), 2.68 (d, 1, H_{10}^{anti}), and 2.57 (d, 1, H_{10}^{syn}); mass spectrum *m/e* (rel intensity) 258 (M^+, 8), 231 (5), 230 (38), 216 (2), 160 (4), 157 (8), 156 (6), 144 (26), 133 (9), 132 (100), 131 (37), 129 (6), 128 (9), 116 (6), 115 (15), 103 (12), 77 (10), 51 (5). Anal. Calcd for $C_{14}H_{10}O_5$: C, 65.11; H, 3.90. Found: C, 65.36; H, 3.87.

Compound **2**: mp 204.5–205.5 °C; UV λ_{max} (C_2H_5OH) 251 (ε 12 600), 290 (1770), 297 nm sh (1740); IR (KBr) 3458 (OH), 1855 and 1775 (anhydride C=O), 1690 (ketone C=O, log ε 5.97), 1604, 1296, 1265 (sh), 1242 (sh), 1228, 1212 (sh), 1192, 1100, 1077, 929, 920 (sh), 771, 725, and 628 cm^{-1}; NMR (CD_3CN) δ 8.01–8.35 (m, 1, H_1), 7.35–7.95 (m, 3, H_2, H_3, H_4), 4.60 (s, 1, **OH**), 3.92 (t, 1, bridgehead), 3.57 (d, 1, methine), 3.26 (d, 1, methine), and 2.30 (m, 2, methylene); mass spectrum *m/e* (rel intensity) 258 (M^+, 20), 231 (15), 230 (88), 204 (7), 203 (7), 202 (30), 196 (7), 188 (11), 186 (30), 185 (15), 184 (27), 172 (5), 170 (8), 169 (6), 168 (27), 161 (6), 160 (48), 159 (5), 158 (21), 157 (27), 156 (27), 145 (14), 144 (100), 143 (8), 141 (5), 140 (7), 139 (6), 133 (13), 132 (91), 131 (100), 130 (13), 129 (27), 128 (30), 127 (15), 116 (16), 115 (36), 114 (5), 104 (7), 103 (36), 102 (15), 89 (9), 83 (8), 79 (8), 78 (30), 77 (45), 76 (12), 75 (8), 70 (10), 69 (6), 66 (7), 65 (9), 64 (21), 63 (16), 57 (12), 55 (15), 53 (7), 52 (9), 51 (30), 50 (10), 45 (7). Anal. Calcd for $C_{14}H_{10}O_5$: C, 65.11; H, 3.90. Found: C, 65.11; H, 3.82.

Rearrangement of 1-Hydroxy-9-keto-1,2,3,4-tetrahydro-1,4-ethanonaphthalene-2,3-dicarboxylic Anhydride (3) to 8-Hydroxy-9-keto-6,7,8,9-tetrahydro-5,8-methano-5*H*-benzocycloheptene-6,7-dicarboxylic Anhydride (2). Method A. Compound **3** (47 mg, 0.18 mmol) was heated under an argon atmosphere at 170–180 °C for 10 min. The product was cooled and crystallized from ethyl acetate–ether to yield **2** (41 mg, 87.2%), mp 205–206 °C, identical to an authentic sample by IR and mixed melting point.

Method B. The changes in ketone carbonyl absorbances of **3** and **2** were found to be linear with concentration over the concentration range 0–37 mg/mL in acetonitrile solution. Compound **3** was dissolved in acetonitrile at reflux with or without added *p*-toluenesulfonic acid. Periodically aliquots were withdrawn and the extent of rearrangement determined from the IR spectrum. First-order rate constants were determined by linear least-squares analysis of the concentration vs. time data. Experimental data for two runs are listed in Table III.

8-Hydroxy-8,9-dihydro-5,8-methano-5*H*-benzocyclohepten-9-one (4). A mixture of the anhydride **2** (1.25 g, 4.84 mmol), Et_3N (1.25 mL), and distilled water (10 mL) was heated at reflux for 30 min. This solution was added to pyridine (95 mL) in a water-jacketed electrolysis cell fitted with a rubber stopper through which a thermometer and a concentric pair of cylindrical platinum gauze electrodes of matched surface area (outer electrode 4-cm diameter × 5-cm long) had been inserted. The magnetically stirred solution was cooled to 18 °C, and an initial current of 0.8 A was applied to the solution, resulting in an observable evolution of gas within ~60 s. The solution was maintained at 17–23 °C, and within several hours became dark brown. The reaction was terminated after 24 h (final current 0.5 amp), although a slow evolution of gas was observable. The black solution was concentrated in vacuo to 5–10 mL, combined with concentrates from three other runs, and further concentrated in vacuo to give a viscous black oil. Dry column chromatography of this oil on a 5 cm × 50 cm column packed with silica (Woelm, activity III, 500 g) developed with $CHCl_3$ afforded 1.78 g (49.3%) of **4** as a pale yellow oil (isolated by extraction with ethyl acetate of a 28.8-cm long band beginning 8.8 cm from the base of the column and visualized by UV): IR ($CHCl_3$) 3630 and 3512 (OH), 2968, 2900, 1689 (ketone), 1600, 1450, 1381, 1359, 1324, 1286, 1226, 1135, 1116, 1090, 1055, 1029, 957, 932, 891, and 861 cm^{-1}; UV λ_{max} (C_2H_5OH) 246 (ε 8040), 295 (706) nm; NMR ($CDCl_3$) 7.83–8.23 (m, 1, aromatic), 7.00–7.83 (m, 3, aromatic), 6.66 (d of d, 1, H_6, J_{6-5} = 5 Hz, J_{6-7} = 6 Hz), 5.96 (d, 1, H_7, J_{7-6} = 6 Hz), 4.47 (s, 1, **OH**), 3.81 (m, 1, H_5), 2.70–3.10 (d of d, 1, H_{10}^{anti}, $J_{10^a-10^s}$ = 10 Hz, J_{10^a-5} = 5 Hz), and 2.53 (d, 1, H_{10}^{syn}, $J_{10^s-10^a}$ = 10 Hz). A high-resolution mass spectrum gave a parent ion of 186.06845 (calcd 186.06802).

Electrolytic Decarboxylation of 1-Hydroxy-9-keto-1,4-ethano-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic Anhydride (3). Anhydride **3** (357 mg, 1.38 mmol) was stirred in distilled water (4 mL) and Et_3N (1 mL) at room temperature for 10.5 h. The mixture was added to 100 mL of pyridine and the electrolysis reaction was carried out as described above. Medium-pressure liquid chromatography was carried out on silica (Merck, 230–400 mesh), column size 15 × 1000 mm, eluting with hexane–ethyl acetate (8:1) at a pressure of 40 psi. After a 550-mL forerun, 100 mL of eluate was collected and evaporated to leave 102 mg (39.7%) of a pale yellow oil. The IR spectrum was identical with that of **4** with an additional peak at 1740 cm^{-1}. The NMR was identical with that of **4** with additional absorption from δ 3.3 to 3.6. Using the ketone carbonyl absorbance vs. concentration correlations for anhydrides **3** and **2**, the ratio of **8** to **4** was estimated to be about 1:4. The following chromatographic procedures failed to achieve separation of the mixture: thin-layer chromatography using Merck silica plates (solvents, ratio, R_f of ketone mixture: benzene–$CHCl_3$, 1:1, 0.21; hexane–$CHCl_3$, 1:1, 0.06; hexane–EtOAc, 4:1, 0.37; hexane–benzene–EtOAc, 20:4:1, 0.08; hexane–EtOAc–$CHCl_3$, 21:2:2, 0.17; benzene, 0.11; $CHCl_3$, 0.33; hexane–EtOAc, 1:1, 0.77); gas chromatography on a 6 ft × 0.125 in. column of 5% FFAP on Chromasorb G at 140–200 °C; medium-pressure liquid chromatography on silica (Merck, 230–400 mesh) using hexane–EtOAc, 20:1, column size 15 × 1000 mm, at 40 psi.

8-Hydroxy-6,7,8,9-tetrahydro-5,8-methano-5*H*-benzocycloheptene-9-one (5). Ketone **4** (1.87 g, 10.0 mmol) in EtOH (15 mL) was hydrogenated over 5% Pd/C (320 mg) on a Parr Shaker at an initial pressure of 33 psi for 10 min, at which time 1 equiv of hydrogen had been consumed. The solution was filtered and the solvent removed in vacuo, leaving 1.86 g (98.9%) of a colorless oil: IR ($CHCl_3$) 3630 and 3510 (OH), 2964, 2886, 1682 (ketone), 1600, 1446 (br), 1376, 1320, 1291, 1263, 1130, 1114, 1084, 987, 947, and 894 cm^{-1}; NMR ($CDCl_3$) δ 7.84–8.14 (m, 1, aromatic), 7.07–7.84 (m, 3, aromatic), 4.15 (s, 1, **OH**), 3.29–3.53 (m, 1, bridgehead), and 0.80–3.20 (m, 6, aliphatic); UV (EtOH) λ_{max} 220 (ε 627), 246 (ε 8040), and 295 nm (ε 706). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.42. Found: C, 76.59; H, 6.36.

Reductive Amination of 5. The hydroxy ketone **5** (849 mg, 4.51 mmol) was stirred in 13.5 mL of absolute methanol with ammonium acetate (3.48 g, 45.1 mmol). Sodium cyanoborohydride (199 mg, 3.16 mmol) was added and the mixture was stirred at room temperature for 7 days. The mixture was cooled on an ice bath and concentrated HCl was added dropwise until the pH was <2. Methanol was removed in vacuo. Distilled water (6 mL) and 1 N HCl (4 mL) were added. The solution was extracted with 4 × 15 mL of ether. The ether layers were washed with 2 × 20 mL of 5% $NaHCO_3$ solution, dried with $MgSO_4$,

and evaporated to give 80 mg (9.4%) of the starting material **5**. The acidic aqueous portion was adjusted to pH 10 with solid NaOH and was extracted with 5 × 15 mL of ether. The ether layers were combined, dried with $MgSO_4$, and evaporated to give a brown semisolid mass. Trituration with ether (10 mL) provided 570 mg (66.8%) of an off-white solid. LC (Partisil 10/25, 25 cm × 4.6 mm column, methanol, flow rate = 5 mL/min) afforded separation into two components. A 147-mg sample was dissolved in 0.3 mL of CH_3OH and injected onto the column in 10-μL portions; collecting and evaporating the fractions yielded 141 mg of **6**: retention time 9.8 min; mp 101–102 °C; IR (KBr) 3355, 3290, 3075 (br), 3030 (sh), 2955, 2875, 2855 (sh), 1595, 1485, 1450, 1365, 1320, 1260, 1215, 1190, 1165, 1140, 1115, 1090, 1065, 1005, 980, 970 (sh), 935, 905, 755, and 725 cm^{-1}; NMR ($CDCl_3$) δ 6.90–7.50 (m, 4, aromatic), 4.03 (s, 1, methine), 2.97–3.15 (m, 1, bridgehead), and 0.80–2.38 (m, 6, aliphatic); mass spectrum *m/e* (rel intensity) 190 (M + 1, 7), 189 (M^+, 47), 188 (17), 173 (12), 172 (91), 171 (8), 157 (7), 145 (9), 144 (24), 143 (14), 133 (11), 132 (100), 131 (16), 130 (55), 129 (34), 128 (45), 127 (8), 118 (9), 117 (38), 116 (29), 115 (54), 103 (9), 92 (11), 91 (9), 90 (5), 89 (7), 77 (12), 65 (7), 51 (7). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.37; H, 8.04; N, 7.39.

Dry HCl gas was passed over the surface of a solution of **6** in ether. The solid product, **6**·HCl, was collected by filtration. Recrystallization from isopropyl alcohol gave crystals (mp 257 °C) suitable for X-ray analysis: IR (KBr) 3270, 3190, 3035, 2975 (sh), 2950, 2840, 2665 (sh), 2605 (sh), 1630, 1595, 1510, 1490 (sh), 1465 (sh), 1445, 1355, 1305, 1260, 1250, 1200, 1070, 765, and 725 cm^{-1}.

LC also provided 4.8 mg of an unidentified amine with a retention time of 16.9 min; its hydrochloride had mp 220 °C dec.

Acknowledgments. We acknowledge the support of NIH Training Grant GM-1341, NIH Research Grant GM-22938, the University of Kansas General Research Fund, and a Grant-in-Aid from the Kansas Heart Association.

Registry No.—**1**, 4428-22-2; **2**, 66792-54-9; **3**, 66792-55-0; **4**, 66792-51-6; **5**, 66792-52-7; **6**, 66808-36-4; **6** HCl, 66279-25-2; **8**, 66792-53-8; 1,2-naphthalenediol, 574-00-5; 1,2-naphthoquinone, 524-42-5; maleic anhydride, 108-31-6.

References and Notes

(1) H. Kappeler and E. Renk, *Helv. Chim. Acta*, **44**, 1541 (1961).
(2) V. R. Haddon and H. Chen, *Tetrahedron Lett.*, 4669 (1976).
(3) I. F. Mikhailova and V. A. Barkhash, *J. Org. Chem. (USSR)*, **6**, 2335 (1970).
(4) (a) T. P. Lobanova, E. I. Berus, and V. A. Barkhash, *J. Gen. Chem. USSR*, **39**, 2269 (1969); (b) H. Hart and G. M. Love, *Tetrahedron Lett.*, 2267 (1971); (c) H. Heaney and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 2711 (1974); (d) H. Tanida, K. Tori, and K. Kitahonoki, *J. Am. Chem. Soc.*, **89**, 3212 (1967); (e) A. Y. Spivak, V. S. Chertok, B. G. Derendyaev, and V. A. Barkhash, *Zh. Org. Khim.*, **9**, 2288 (1973); (f) R. S. Givens and W. F. Oettle, *J. Am. Chem. Soc.*, **93**, 3963 (1971); (g) J. Ipaktschi, *Tetrahedron Lett.*, 215 (1969); (h) H. E. Zimmerman, R. S. Givens, and R. M. Pagni, *J. Am. Chem. Soc.*, **90**, 4191 (1968).
(5) K. Kitahonoki and Y. Takano, *Tetrahedron Lett.*, 1567 (1963).
(6) K. Takeda, S. Nagakura and K. Kitahonoki, *Pharm. Bull.*, **1**, 135 (1953).
(7) For reviews of the acyloin rearrangement, see P. de Mayo, Ed., "Molecular Rearrangements", Wiley, New York, N.Y., 1964, Chapters 1 and 13–16.
(8) P. Colard, I. Elphimoff-Felkin, and M. Verrier, *Bull Soc. Chim. Fr.*, 516 (1961).
(9) S. J. Cristol, F. P. Parungo, D. E. Plorde, and K. Schwarzenbach, *J. Am. Chem. Soc.*, **87**, 2879 (1965).
(10) P. Radlick, R. Klem, S. Spurlock, J. J. Sims, E. E. van Tamelen, and T. Whitesides, *Tetrahedron Lett.*, 5117 (1968); H. H. Westberg and H. J. Dauben, Jr., *Ibid.*, 5123 (1968).
(11) R. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971).
(12) D. E. Walters, G. L. Grunewald, M. Staples, J. Rodgers, J. R. Ruble and B. Lee, *Acta Crystallogr., Sect. B*, **34**, 947 (1978).
(13) L. Fieser, *J. Am. Chem. Soc.*, **61**, 596 (1939).

Use of the Trimethylsilyl Group in Synthesis. Preparation of Sulfinate Esters and Unsymmetrical Disulfides[1a]

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Received December 30, 1977

Alkoxytrimethylsilanes and sulfinyl chlorides have been shown to couple efficiently to afford sulfinate esters; kinetic data indicate that a nonionic transition state is involved. The parallel reaction between aralkylthiotrimethylsilanes and sulfenyl chlorides gives unsymmetrical disulfides. An attempt to prepare sulfenate esters by the reaction of a sulfenyl chloride and an alkoxytrimethylsilane gave no reaction; in fact, sulfenate esters were shown to be cleaved by either chlorotrimethylsilane or trimethylsilyl cyanide to yield sulfenyl chlorides or thiocyanates, respectively. The reaction of *tert*-butyl hypochlorite with an alkylthiosilane gave disulfide.

A variety of silicon derivatives have seen widespread and growing use in the past few years[2] as protective groups and synthetic mediators. For instance, it is well known[2h,3] that acid chlorides react smoothly with alkoxysilanes to produce esters in good yield. Heteroatom analogues of this reaction could be of great utility; however, incomplete synthetic information and virtually no detailed mechanistic data are available for this reaction class[2h,4] (eq 1), which in principle encompasses

$$\mathrm{RC(=O)Cl + (CH_3)_3SiOR' \longrightarrow RC(=O)OR' + (CH_3)_3SiCl}$$

an impressive number of important functionalities. We wish to report on two facile syntheses using the trimethylsilyl group.

$$\mathrm{RXCl + (CH_3)_3SiYR' \rightarrow RXYR' + (CH_3)_3SiCl} \quad (1)$$

X = O, NR, S, S=O, PR, P(=O)R; Y = O, NR, S

When sulfinyl chlorides are treated with aralkoxytrimethylsilanes (eq 2), sulfinate esters (1) are cleanly produced in very good yield (Table I).[6]

$$\mathrm{RS(=O)Cl + R'OSi(CH_3)_3 \longrightarrow \underset{\mathbf{1}}{RS(=O)OR'} + (CH_3)_3SiCl} \quad (2)$$

R' = R = aralkyl

The precursor alcohols may be conveniently silylated[7] with hexamethyldisilazane using imidazole as catalyst. One equivalent of the alkoxytrimethylsilane is added to an equivalent of a sulfinyl chloride and the reaction is allowed to proceed at room temperature. The progress of the reactions may be conveniently followed by ^1H NMR spectroscopy, the singlet for chlorotrimethylsilane increasing at the expense of the peak for the trimethylsilyl group of the alkoxytrimethylsilane. Chlorotrimethylsilane may be easily removed by

0022-3263/78/1943-3481$01.00/0