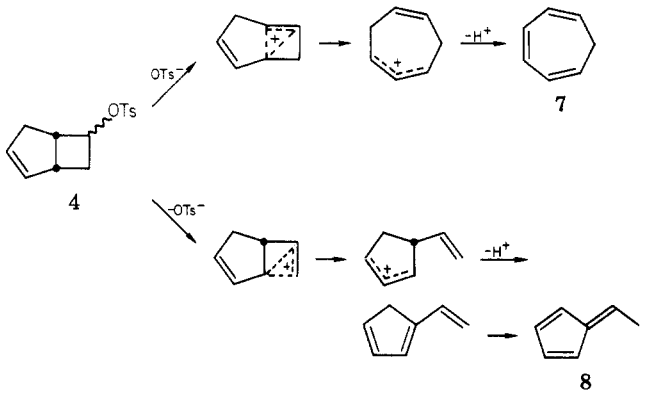
Scheme II



yellow C_7 triene is the fulvene 5-ethylidene-1,3-cyclopentadiene, 8, which can readily be envisioned as being formed from 4 by a mechanism similar to that postulated for formation of 7 (Scheme II).

Reduction of bicyclo[3.2.0]-2-hepten-6-one with lithium aluminum hydride at refluxing ether temperatures yielded a 70:30 mixture of *endo*- and *exo*-6, respectively. A corresponding mixture of the tosylates 4, heated with collidine, gave an intensely yellow product mixture which, before distillation, was found to be comprised of 70% 7, 15% 8, and 15% *exo*-4. The individual epimeric tosylates, *exo*-4 and *endo*-4, behave differently when heated with collidine. The *endo*-4 isomer undergoes clean elimination to yield only 7, while *exo*-4 did not react under the same conditions. However, when the ionizing power of the medium was increased by addition of 1.9 equivs of *p*-toluenesulfonic acid, then the exo isomer underwent elimination to produce a 1:4 mixture of 7 and 8, respectively. In the presence of *p*-toluenesulfonic acid epimerization can occur along with elimination[5] and *endo*-4, so formed from *exo*-4, could be the precursor of the 7 formed under these conditions. The substantially greater reactivity of *endo*-4 here compared to that of *exo*-4 is in full accord with the acetolysis rates.[8] Steric strain associated with having the bulky tosyl group in the endo position probably facilitates the ionization of *endo*-4.

The formation of both 7 and 8 accounts for the quantitative hydrogenation data when recalculated on the basis of a C_7 triene. Furthermore, the absorption maximum at 260 nm with a shoulder at 250 nm is reasonable, because 7, as mentioned, has a maximum at 261 nm (log ϵ 3.54)[9] and 5-ethylidene-1,3-cyclopentadiene has a maximum at 254 nm (log ϵ 4.16)[10] which tails off well into the visible region of the spectrum.

Experimental Section

The ^{1}H NMR spectra were taken on a Varian EM-390 spectrometer operating at 90 MHz.

The tosylate elimination reactions in collidine were carried out as previously described.[5]

Bicyclo[3.2.0]-2-hepten-6-one was prepared as previously described.[5]

***exo*- and *endo*-bicyclo[3.2.0]-2-hepten-6-ol, 6**, was prepared by lithium aluminum hydride reduction of bicyclo[3.2.0]-2-hepten-6-one in refluxing ether. From 14.4 g of bicyclo[3.2.0]-2-hepten-6-one was obtained 11.5 g of a 70:30 mixture of *endo*-6 and *exo*-6, respectively. The epimers were separated by preparative gas chromatography on a $^3/_8$ in × 16 ft Carbowax 20M column. *exo*-Bicyclo[3.2.0]-2-hepten-6-ol, *exo*-6: ^{1}H NMR (Me_2SO-d_6) δ 1.78–3.29 (m, 6 H), 3.50–3.82 (m, 1 H), 4.90 (d, 1 H, J = 6 Hz), 5.50–5.85 (m, 2 H). *endo*-Bicyclo[3.2.0]-2-hepten-6-ol, *endo*-6: ^{1}H NMR (Me_2SO-d_6) γ 1.30–3.28 (m, 6 H), 4.12–4.50 (m, 1 H), 4.68 (d, 1 H, J = 5 Hz), 5.73 (s, 2 H).

The *exo*- and *endo*-bicyclo[3.2.0]-2-hepten-6-yl tosylates, 4, were obtained individually or as a mixture from treatment of the corresponding alcohols for 1 h with 1.1 equiv of *p*-toluenesulfonyl chloride in the presence of excess pyridine at 0 °C. The reaction mixtures were stirred at room temperature for 15 h, diluted with ether, and then washed with 1 N hydrochloric acid, 5% sodium bicarbonate solution, and water. The ethereal layer was dried over potassium carbonate and the ether removed under reduced pressure. ***endo*-Bicyclo[3.2.0]-2-hepten-6-yl tosylate, *endo*-4**: ^{1}H NMR ($CDCl_3$) δ 1.62–3.30 (m, 6 H), 2.41 (s, 3 H), 4.90–5.18 (m, 1 H), 5.76 (br s, 2 H), 7.56 (d of d, 4 H). ***exo*-Bicyclo[3.2.0]-2-hepten-6-yl tosylate, *exo*-4**: ^{1}H NMR ($CDCl_3$) δ 1.95–3.28 (m, 6 H), 2.41 (s, 3 H), 4.37–4.60 (m, 1 H), 5.68 (br s, 2 H), 7.56 (d of d, 4 H).

Registry No. *exo*-4, 76036-47-0; *endo*-4, 76094-31-0; *exo*-6, 41524-25-8; *endo*-6, 13837-04-2; 7, 544-25-2; 8, 3839-50-7; bicyclo[3.2.0]-2-hepten-6-one, 13173-09-6.

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Synthetic Studies on Quassinoids: One-Step Transformation of α-Hydroxy Ketones into *O*-Methyl-Protected Diosphenols

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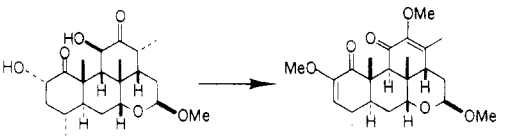
In conjunction with our efforts in the quassinoid area we required conditions for the direct one-step transformation of 1 into the fully protected bis(diosphenol) 2. Of



1 2

primary concern to us was the ability to simultaneously effect the inversion of configuration at C(9) (steroid numbering) so as to establish the trans,anti,trans arrangement of the ABC ring system common to the vast majority of quassinoids.

Examination of the literature reveals that numerous conditions have been developed over the years for the preparation of diosphenols from α-hydroxy ketones.[2-7] The majority of these procedures utilize either potassium carbonate or potassium hydroxide in aqueous methanol or ethanol in the presence of oxygen.[2] Many of these

(1) On leave from the University of Pavia, 1979–1980.
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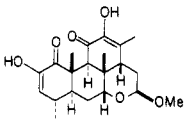
reports proved incompatible with our specific need (cf. 1 → 2).

One of the more classical reagents which has been employed for the oxidation of α-hydroxy ketones into diosphenols is bismuth(III) oxide.[3] The reaction is generally carried out by heating the substrate in the presence of Bi_2O_3 and acetic acid. Reported yields range from extremely low to near quantitative.[8] Attempts to oxidize 1 with Bi_2O_3 under a variety of conditions led to none of the expected bis(diosphenol) 3.

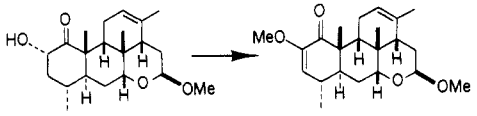
The inability of classical methods to effect the transformation 1 → 2 or provide access to the diosphenol 3



3

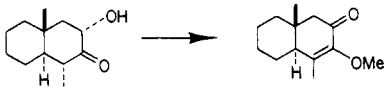
undoubtedly stems, in part, from the highly hindered nature of both the C(11) hydroxyl-bearing carbon and the C(9) proton. We detail conditions for the facile oxidation of α-hydroxy ketones which permit, within the same operation, subsequent protection of the resultant diosphenols. Furthermore, in connection with our specific need to effect an epimerization at C(9) (cf. 1 → 2), the conditions we have developed proved satisfactory.

After a series of preliminary experiments we found that α-hydroxy ketone 4,[9] upon treatment (35 min) with a large



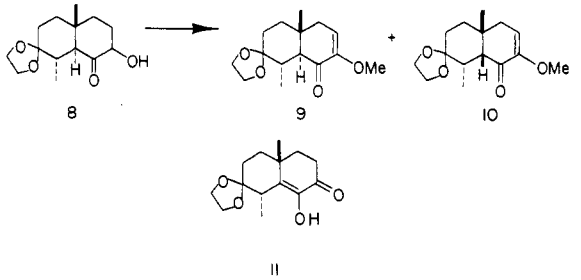
4 5

excess of sodium methoxide in Me_2SO–MeOH (10:1) at 55 °C followed by cooling to 10 °C and addition of methyl iodide, provided in 93% yield the crystalline *O*-methyldiosphenol 5, mp 151–152 °C. Similar treatment of compound 6 gave rise to an 80% yield of 7. Application of the



6 7

procedure to substrate 8 afforded (72%) a 5:1 ratio of protected diosphenols 9 and 10. The absence of any product derived from diosphenol 11 is not unexpected in view of the serious perilike interaction that exists between the C(4) methyl group and C(6) hydroxyl.



8 9 10 11

(8) Kupchan, S. M.; Britton, R. W.; Lacadie, J. A.; Ziegler, M. F.; Sigel, C. W. *J. Org. Chem.* **1975**, *40*, 648. Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742.

(9) The α-hydroxy ketones employed in this study were prepared by treatment at −10 °C of the corresponding lithium enolates with MoO_5·Py·HMPA [Vedejs, E.; Engler, D. A.; Telschow, J. E. *J. Org. Chem.* **1978**, *43*, 188].

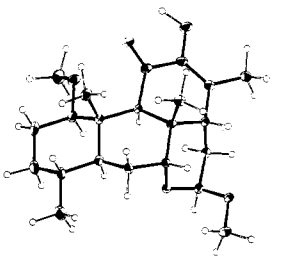
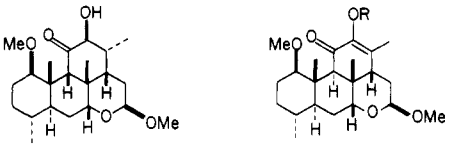


Figure 1. ORTEP view of diosphenol 13 (R = H).

We next focussed our attention on the conversion of 12 into 13 (R = Me) with simultaneous inversion of configuration at C(9). Oxidation of 12 was carried out as described



12 13

above [Me_2SO–MeOH (10:1), NaOMe, 55 °C, 30 min] followed by raising of the temperature to 95 °C (1 h) prior to cooling to 10 °C and addition of methyl iodide. There was obtained an 82% yield of 13 (R = Me) as a crystalline substance, mp 150–151 °C. Failure to add methyl iodide provided access to the corresponding diosphenol in high yield. For example, diosphenol 13 (R = H; mp 161–163 °C) could be isolated in 82% yield. The stereochemistry at C(9) was unambiguously established by single-crystal, X-ray analysis (Figure 1).[10]

By use of the above procedure with simultaneous methylation, bis(α-hydroxy ketone) 1[11] was transformed into β-*O*-methylneoquassin (2, mp 214–216 °C) in 57% overall yield. The identity of 2 was established by preparation (HCl, MeOH) of an authentic sample from natural neoquassin.[12]

All of the above reactions, with the exception of the conversion of 8 → 9 + 10 which was carried out in an open flask, were performed under an atmosphere of argon. It should be noted that oxygen was not rigorously excluded and that the solvents were not degassed. It appears that some oxygen is required since under conditions where oxygen was rigorously excluded, the reactions were extremely sluggish.[13] Use of an atmosphere of oxygen results in rapid build up of diosphenol, as evidenced by TLC analysis, which is further oxidized by oxygen, giving rise to none of the desired products.

Experimental Section

Melting points were determined on a Fisher-Johns hot-stage melting point apparatus. All melting points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 283 grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded at either 60 MHz (Varian A-60A

(10) Compound 13 (R = H) crystallizes in space group $P\bar{1}$ with cell dimensions (at −172 °C) of a = 7.607 (1) Å, b = 10.121 (2) Å, c = 15.522 (4) Å, α = 118.35 (1)°, β = 104.72 (1)°, and γ = 72.65 (1)°. The structure was solved by direct methods using 4585 unique intensities collected at −172 °C on a Picker goniostat equipped with a monochromated Mo source [for experimental methods and data reduction details see: Huffman, J. C.; Lewis, L. N.; Caulton, K. G. *Inorg. Chem.* **1980**, *19*, 2755]. All atoms, including hydrogens, were located and refined to final residuals of R(F) = 0.057 and R_w(F) = 0.062.

(11) Grieco, P. A.; Ferriño, S.; Vidari, G. *J. Am. Chem. Soc.* **1980**, *102*, 7586.

(12) Hanson, K. R.; Jaquiss, D. B.; Lamberton, J. A.; Robertson, A.; Savige, W. E. *J. Chem. Soc.* **1954**, 4238.

(13) Cf.: Russell, G. A.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 744; Talanty, E. R.; Russell, G. A. *Ibid.* **1965**, *87*, 4867.

or T-60 spectrometer) or at 220 MHz as indicated. Chemical shifts are reported in parts per million (δ) relative to Me_4Si (δ 0.0) as an internal standard. Microanalyses were performed by Galbraith Laboratories, Inc. "Dry" solvents were dried immediately before use. Dimethyl sulfoxide (Me_2SO) was distilled from calcium hydride.

(1β,16β)-1,12,16-Trimethoxypicras-12-en-11-one [13 (R = Me)]. A solution of 57 mg (0.16 mmol) of α-hydroxy ketone **12** in 2.0 mL of dry dimethyl sulfoxide containing 0.2 mL of methanol was added at room temperature to 172 mg (3.18 mmol) of freshly prepared sodium methoxide under argon. The reaction mixture was stirred at 55 °C for 30 min followed by raising of the temperature to 95 °C. After 1 h, the reaction was cooled to 10 °C and treated with 296 mg (4.67 mmol) of methyl iodide. The reaction was quenched after 15 min by the addition of 50 mL of ice–water. The product was isolated by extraction with ether (3 × 50 mL). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was chromatographed on 8.0 g of silica gel by using hexane–ether (2:1). There was obtained 48 mg (82%) of **13** (R = Me) as a white crystalline substance: IR ($CHCl_3$) 2991, 2930, 2900, 2830, 1688, 1645, 1461, 1440, 1390, 1375, 1362, 1340, 1296, 1265, 1254, 1243, 1225, 1194, 1185, 1164, 1132, 1120, 1112, 1100, 1080, 1051, 1036, 1004, 998, 973, 952, 928, 895, 887, 866, 848, 835, 820 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 4.86 (br d, 1 H, J = 2.5 Hz, C(16) proton), 3.58 (s, 4 H, C(7) proton, OCH_3), 3.36 (s, 3 H, OCH_3), 3.20 (s, 3 H, OCH_3), 2.77 (dd, 1 H, J = 4, 12 Hz, C(1) proton), 2.71 (s, 1 H, C(9) proton), 1.73 (s, 3 H, olefinic methyl), 1.34 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 0.82 (d, 3 H, J = 6.5 Hz, C(4) methyl). An analytical sample was prepared by recrystallization from ether; mp 150–151 °C. Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.38; H, 9.30.

(9β,16β)-2,16-Dimethoxypicras-2,12-dien-1-one (5). A solution of 61 mg (0.18 mmol) of α-hydroxy ketone **4** in 2.2 mL of dry dimethyl sulfoxide and 0.22 mL of methanol was added at room temperature to 192 mg (3.55 mmol) of sodium methoxide (freshly prepared) under argon. The reaction was stirred at 55 °C. After 35 min the reaction was cooled to 10 °C and 0.33 mL (5.29 mmol) of methyl iodide was added. The reaction was quenched after 15 min by the addition of 50 mL of ice–water. The product was isolated by extraction with ether (3 × 50 mL). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude product (61 mg) was purified on 8.0 g of silica gel. Elution with hexane–ether (1:1) gave 59 mg (93%) of pure diosphenol methyl ether **5** as a white crystalline compound: IR ($CHCl_3$) 2997, 2958, 2930, 2910, 1672, 1624, 1458, 1443, 1435, 1376, 1359, 1230, 1180, 1164, 1105, 1076, 1055, 1047, 990, 960, 840 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 5.50 (br s, 2 H, C(3) and C(12) olefinic protons), 4.5 (dd, 1 H, J = 5, 9 Hz, C(16) proton), 3.68 (br s, 1 H, C(7) proton), 3.58 (s, 3 H, OCH_3), 3.32 (s, 3 H, OCH_3), 1.62 (s, 3 H, C(13) olefinic methyl), 1.20 (s, 3 H, CH_3), 1.17 (d, 3 H, J = 6.5 Hz, C(4) methyl), 1.09 (s, 3 H, CH_3). An analytical sample was prepared by recrystallization from ether, mp 151–152 °C. Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.07; H, 8.92.

Neoquassin *O*-Methyl Ether (2). A solution of 60 mg (0.16 mmol) of bis(α-hydroxy ketone) **1** in 3.9 mL of dry dimethyl sulfoxide containing 0.39 mL of methanol was added at room temperature to 346 mg (6.37 mmol) of sodium methoxide (freshly prepared) under argon. The reaction was warmed to 55 °C, where stirring was continued for 30 min prior to raising of the temperature to 95 °C. After 2 h, the reaction was cooled to 10 °C, and 1.32 g (9.3 mmol) of methyl iodide was added. After 15 min, the reaction was quenched by the addition of 40 mL of ice–water. The product was isolated by extraction with ether (3 × 50 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude product (60 mg) was purified on 10 g of silica gel. Elution with ether–hexane (3:1) provided 36 mg (57%) of racemic neoquassin *O*-methyl ether as a crystalline substance: IR ($CHCl_3$) 2990, 2947, 2930, 2880, 2825, 1690, 1680, 1630, 1455, 1448, 1437, 1385, 1373, 1354, 1296, 1270, 1260, 1204, 1180, 1128, 1096, 1068, 1048, 1012, 1000, 977, 958, 936, 911, 889, 851, 835 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 5.27 (d, 1 H, J = 2.5 Hz, C(3) olefinic proton), 4.79 (br s, 1 H, C(16) proton), 3.61 (s, 4 H, OCH_3, C(7) proton), 3.57 (s, 3 H, OCH_3), 3.35 (s, 3 H, OCH_3), 3.19 (s, 1 H, C(9) proton), 2.41 (m, 1 H, C(4) proton), 2.29 (dd, 1 H, J = 5, 12 Hz), 1.80 (s, 3 H, C(13) olefinic methyl), 1.51 (s, 3 H, CH_3), 1.09 (d, 3 H, J = 6.5 Hz, C(4) methyl), 1.03 (s, 3 H, CH_3). An analytical sample was prepared by recrystallization from ether; mp 214–216 °C. Anal. Calcd for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 67.94; H, 8.20.

Oxidation–Methylation of α-Hydroxy Ketone 8. A solution of 120 mg (0.47 mmol) of α-hydroxy ketone **8** in 6.5 mL of dry Me_2SO and 0.65 mL of methanol was added to 510 mg (9.45 mmol) of sodium methoxide (freshly prepared). The reaction was stirred at 60 °C under an atmosphere of air. After 40 min, the temperature was lowered to 10 °C, and 2.01 g (14.2 mmol) of methyl iodide was added. After 15 min, the reaction was quenched by the addition of 50 mL of ice–water. The product was isolated by extraction with ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified on 15 g of silica gel. Elution with hexane–ether (1:1) provided 76 mg of **9**: R_f 0.34 (ether–hexane, 2:1); IR ($CHCl_3$) 3005, 2980, 2955, 2940, 2910, 2890, 1692, 1635, 1460, 1450, 1437, 1384, 1368, 1355, 1346, 1330, 1280, 1240, 1218, 1200, 1176, 1160, 1140, 1108, 1068, 1035, 1025, 1004, 980, 968, 948, 928, 914, 900, 882, 870 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 5.45 (dd, 1 H, J = 3.0, 6.0 Hz, olefinic proton), 3.95 (br s, 4 H, OCH_2CH_2O), 3.57 (s, 3 H, OCH_3), 2.52 (d, 1 H, J = 11.5 Hz, CHCO), 2.38 (dd, 1 H, J = 3.0, 18 Hz, HCHCH=C), 2.14 (m, 2 H, $CHCH_3$, HCHCH=C), 1.9–1.2 (m, 4 H), 1.02 (d, 3 H, J = 6.0 Hz, $CHCH_3$), 0.93 (s, 3 H, CH_3). An analytical sample was prepared by recrystallization from hexane–ether; mp 123.5–124.5 °C. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.54; H, 8.16. Continued elution afforded 14.5 mg of pure cis isomer **10**: mp 95–97 °C; R_f 0.22; IR ($CHCl_3$) 3002, 2955, 2885, 1668, 1628, 1458, 1450, 1441, 1400, 1380, 1368, 1235, 1196, 1171, 1148, 1076, 1055, 1025, 996, 960, 945, 925, 909, 889, 878, 828 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 5.75 (m, 1 H, olefinic proton), 3.93 (s, 4 H, OCH_2CH_2O), 3.64 (s, 3 H, OCH_3), 2.75 (d, 1 H, J = 18 Hz, HCHCH=C), 2.66 (d, 1 H, J = 5 Hz, CHCO), 2.2–1.3 (m, 6 H), 1.04 (s, 3 H), 0.94 (d, 3 H, J = 7 Hz). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.43; H, 8.29.

4a-*r*-5,6,7,8,8a-*trans*-Hexahydro-3-methoxy-4,8a-dimethyl-2(1*H*)-naphthalenone (7). A solution of 107 mg (0.55 mmol) of α-hydroxy ketone **6** in 7.5 mL of dry dimethyl sulfoxide and 0.75 mL of methanol was added to 600 mg (11.1 mmol) of freshly prepared sodium methoxide under argon. The mixture was stirred at 55 °C for 35 min followed by lowering of the temperature to 10 °C. Methyl iodide (1.03 mL) was added, and the reaction was quenched with ice–water (50 mL) after 15 min. The product was isolated by extraction with ether (3 × 50 mL). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude product was purified on 10 g of silica gel. Elution with hexane–ether (1:1) gave 91 mg (80%) of **7** as a colorless oil: IR ($CHCl_3$) 2990, 2980, 2930, 2860, 2855, 1662, 1610, 1438, 1405, 1371, 1321, 1302, 1190, 1160, 1152, 1145, 1121, 1090, 1075, 1060, 1021, 995, 988, 982, 920, 895, 840 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 3.60 (s, 3 H, OCH_3), 2.28 (s, 2 H, CH_2CO), 1.81 (s, 3 H, CH_3C=C), 0.90 (s, 3 H).

(1β,16β)-12-Hydroxy-1,16-dimethoxypicras-12-en-11-one [13 (R = H)]. A solution of 50 mg (0.13 mmol) of α-hydroxy ketone **12** in 1.0 mL of dry dimethyl sulfoxide was added to a suspension of 80 mg (1.48 mmol) of sodium methoxide (freshly prepared) in 1.0 mL of dimethyl sulfoxide under argon. The reaction mixture was stirred at 55 °C for 1 h followed by raising of the temperature to 95 °C. After 1 h the reaction was cooled to 10 °C and quenched by the addition of 10 mL of ice–water. The product was isolated by extraction with ethyl acetate (3 × 25 mL). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated in vacuo. The residue was chromatographed on 10 g of silica gel by using hexane–ether (2:1). There was obtained 41 mg (82%) of diosphenol **13** (R = H) as a white crystalline solid: mp 160–162 °C; IR ($CHCl_3$) 3400, 2970, 2930, 2910, 2830, 2808, 1691, 1665, 1460, 1440, 1390, 1385, 1378, 1363, 1348, 1332, 1320, 1310, 1289, 1261, 1241, 1193, 1160, 1125, 1046, 1030, 996, 971, 965, 950, 926, 898, 892, 862, 843, 827, 812 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 6.10 (s, 1 H, OH), 4.84 (br s, 1 H, C(16) proton), 3.57 (br t, 1 H, J = 3.5 Hz, C(7) proton), 3.34 (s, 3 H, OCH_3), 3.16 (s, 3 H, OCH_3), 2.78 (dd, 1 H, J = 4, 11 Hz, C(1) proton), 2.75 (s, 1 H, C(9) proton), 1.77 (s, 3 H, C(13) methyl),

1.23 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.80 (d, 3 H, J = 7 Hz, C(4) methyl). An analytical sample was prepared by recrystallization from ether; mp 161–163 °C. Anal. Calcd for $C_{22}H_{34}O_5$: C, 69.81; H, 9.05. Found: C, 69.78; H, 8.98.

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Registry No. 1, 75935-29-4; 2, 75924-48-0; 4, 76156-58-6; 5, 76156-59-7; 6, 76156-60-0; 7, 76156-61-1; 8, 76156-62-2; 9, 76156-63-3; 10, 76189-75-8; 12, 76156-64-4; 13 (R = H), 76156-65-5; 13 (R = Me), 76156-66-6.

Dichlorocarbene-Induced Deamination of Naphthalen-1,4-imines and Anthracen-9,10-imines

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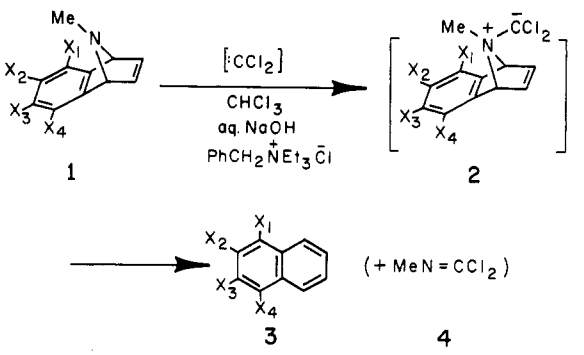
Arenimines are useful polycyclic aromatic hydrocarbon synthetic equivalents.[1-3] Previously, we[1] and others[2,3] have transformed *N*-alkyl-1,4-dihydroaren-1,4-imines into the corresponding aromatic hydrocarbons using mild oxidizing conditions (usually *m*-chloroperbenzoic acid), a reaction that may involve cheletropic extrusion[4] of a nitrosoalkane from the derived arenimine oxide.

We now report that dichlorocarbene, generated under phase-transfer conditions by using the Makosza method,[5] efficiently converts 9-methyl-1,4-dihydronaphthalen-1,4-imines (**1**) and 11-methyl-1,2,3,4-tetrachloro-9,10-dihydroanthracen-9,10-imine (**5**) to the corresponding naphthalenes (**3**, Scheme I) and 1,2,3,4-tetrachloroanthracene (**6**, Scheme II), respectively. Our results are summarized in Table I. By comparison, the peracid oxidation of naphthalenimines[1,3] proceeds in 66–94% yield, and the peracid or hydrogen peroxide oxidation of anthracenimines[1] proceeds in 26–92% yield.

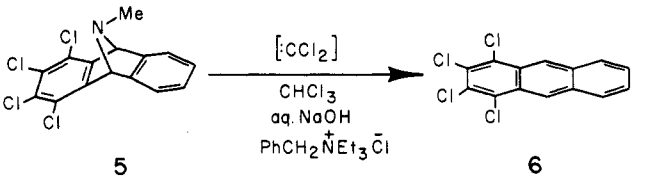
As suggested by the stereospecific fragmentation of aziridinium ylides (generated also from carbenes and aziridines),[6] the present reaction pathway may involve ammonium ylide **2** which suffers rapid cheletropic loss[4] of methyl isocyanide dichloride (**4**,[7] not isolated)[8] to furnish the arene.[9]

The requisite arenimines **1** and **5** were prepared by a Diels–Alder reaction between the appropriate benzyne and either *N*-methylpyrrole or *N*-methylisoindole, respectively.

Scheme I



Scheme II



The benzynes were generated by treating a polyhalobenzene with *n*-butyllithium and effecting either halogen–lithium exchange (e.g., chloropentafluorobenzene, hexachlorobenzene, and trichlorotrifluorobenzene) or lithiation (e.g., 1,2,4,5-tetrachlorobenzene). The syntheses of **1b–d** and **5** have not been previously described and are presented in the Experimental Section.

In summary, the dichlorocarbene-induced deamination of arenimines is a convenient alternative method to the oxidative deamination procedure[1-3] and avoids use of the moderately expensive *m*-chloroperbenzoic acid.

Experimental Section

Melting points were obtained with a Mel-Temp Laboratory Devices apparatus in open capillary tubes and are uncorrected. Microanalyses were determined by PCR, Inc., or by Atlantic Microlab, Inc. Infrared spectra were measured with a Perkin-Elmer 137 or 599 instrument, and NMR spectra were obtained with a Perkin-Elmer R-24 spectrometer. Woelm alumina was used for column chromatography and silica gel G (Merck) was used for TLC. Mass spectra were determined at 70 eV on a Finnigan 4023 GC/MS system by C. R. Hill and R. M. Soll.

9-Methyl-5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine (1a). To a magnetically stirred solution of chloropentafluorobenzene (15 g, 0.074 mol) in dry Et_2O (250 mL) under N_2 at −78 °C was added dropwise via syringe *n*-butyllithium (1.6 M in hexane; 50 mL, 0.080 mol). The solution was stirred for 30 min at −78 °C and then was treated with freshly distilled *N*-methylpyrrole (8 g, 0.1 mol) dropwise at −78 °C. The resulting golden yellow solution was allowed to warm slowly to room temperature overnight. The mixture was treated with H_2O (50 mL) and then extracted with 6 N HCl. The acidic extract was cooled in an ice bath, basified with 50% aqueous NaOH, and extracted with CH_2Cl_2. Rotary evaporation of the water-washed and dried (Na_2SO_4) extract gave 10.3 g of crude **1a** as a brown solid which was sublimed at 80 °C (0.5 torr) to give 7.7 g (46%) of **1a** as colorless crystals: mp 77–78 °C (lit.[11] mp 75–76 °C); ^1H NMR ($CDCl_3$) δ 2.2 (s, 3 H), 4.9 (m, 2 H), 6.9 (m, 2 H); IR ($CHCl_3$) 2950 (s), 1490 (s), 1480 (s) 1295 (m), 1270 (m), 1110 (m), 1080 (m), 1040 (s), 930 cm^{-1} (m); mass spectrum, *m/e* (relative intensity) 229 (26), 214 (10), 203 (100), 188 (46), 174 (14), 169 (19), 161 (33), 151 (29), 123 (16), 105 (12), 99 (18), 42 (96).

9-Methyl-5,6,7,8-tetrachloro-1,4-dihydronaphthalen-1,4-imine (1b). To a magnetically stirred slurry of hexachlorobenzene (38 g, 0.13 mol) (recrystallized from EtOH) in dry Et_2O (1500 mL)

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(8) We have made no attempt to ascertain the fate of **4**, but, presumably, it is hydrolyzed to methylamine and carbonate under the reaction conditions.
(9) We and others[10] have found that the methiodides of arenimines fragment to aromatic hydrocarbons upon treatment with base (KOH, MeMgI) or simply on standing for extended periods. These reactions may also involve ammonium ylide intermediates.
(10) P. S. Anderson (Merck Sharp and Dohme Research Laboratories), private communication.
(11) D. D. Callander, P. L. Coe, J. C. Tatlow, and A. J. Uff, *Tetrahedron*, 25, 25 (1969), prepared **1a** from pentafluorobenzene in a similar manner to that described herein.

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