97733-48-7; (±)-**16**, 97733-33-0; (±)-**17**, 97733-34-1; (±)-**18**, 97805-63-5; (±)-**19**, 97805-64-6; (±)-**20**, 97733-35-2; (±)-**21**, 95760-46-6; (±)-**22**, 97733-36-3; (±)-**23**, 97733-37-4; (±)-**24**, 97733-38-5; (±)-**25**, 97733-39-6; (±)-**26**, 97805-65-7; (±)-**27** (isomer 1), 97733-40-9; (±)-**27** (isomer 2), 97805-68-0; (±)-**27** (isomer 3), 97805-69-1; (±)-**27** (isomer 4), 97805-70-4; (±)-**28** (isomer 1), 97749-49-0; (±)-**28** (isomer 2), 97859-23-9; (±)-**28** (isomer 3), 97859-24-0; (±)-**28** (isomer 4), 97859-25-1; **29**, 97733-41-0; (±)-**31**, 97749-28-5; (±)-**32**, 97733-42-1; (±)-**34**, 97733-43-2; (±)-**35**, 97805-66-8; (±)-**36**, 97805-67-9; (±)-**36a**, 97733-49-8; (±)-**38**, 97749-29-6; (±)-**39**, 97733-44-3; (±)-**40**, 97749-50-3; CH_2=CHC-(CH_3)=CH_2, 78-79-5; CH_2BrCl, 74-97-5.

Supplementary Material Available: Details of the X-ray analysis of compound **38**, an ORTEP plot, and tables of final positional parameters, atomic thermal parameters, and bond distances and angles (6 pages). Ordering information is given on any current masthead page.

Conversion of Resin Acids into a Steroid Skeleton. Formation of the D Ring[1]

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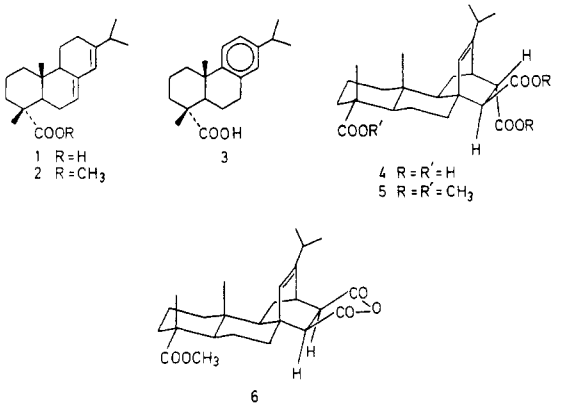
The conversion of abietic acid (**1**) to a 15-hydroxy-17-keto steroid is reported. This route uses the 13-isopropyl group of **1** as a building block for the D ring of the steroid skeleton. The diene system of the resin acid is protected by a Diels–Alder reaction with maleic or fumaric acid. No oxygen function is introduced in the B ring during the whole procedure.

The conversion of tricyclic diterpenoids into steroid compounds has attracted considerable effort and ingenuity. Several synthetic approaches to a steroid skeleton using resin acids as starting material have been reported in the literature.[2-11]

The most abundant resin acid, abietic acid (**1**), is unfortunately not a good starting material due to isomerization and autoxidation. Therefore the more stable dehydroabietic acid (**3**) has been used mostly for such synthetic conversions.



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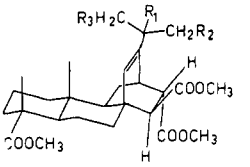
We have developed a synthetic route from **1** to a *C*-aryl 18-norsteroid skeleton using the isopropyl group as a building block for the D ring. The main synthetic problem in this approach was to attack the isopropyl group selectively, avoiding any reactions at the ring system. Selective bromination of this group could be achieved on compounds **4** and **6**, the Diels–Alder adducts of fumaric or maleic acid with **1**, using a similar procedure as described earlier.[12,15] The most important advantage of **4** is that it is stable and can be conveniently prepared directly from rosin without previous isolation of **1** or **2**.[13,14] Avoiding temperatures above 0 °C, bromination of the ester **5** (irradiating with a 1000-W light bulb) yielded **7** quantitatively.[15] Further



7 R_1=Br R_2=R_3=H
8 R_1=R_2=Br R_3=H
9 R_1=R_2=R_3=Br

bromination of **7** gave the di- and tribromo products **8** and **9**; no other products, obtained earlier from bromination reactions have been detected.[16-18] By addition of dry pyridine to the reaction mixture after the bromination, the olefin (**10**) could be obtained directly from **5** by a one-step procedure.[12]

Selective cleavage of the terminal double bond in **10** is possible by two procedures. With OsO_4/$NaIO_4$ **11** is obtained quantitatively. Reaction with ozone is better suited for large-scale preparations although the yield is lower (77%). Ozonolysis of **12** gave other products probably due

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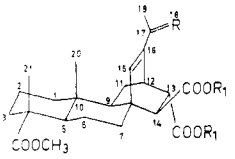
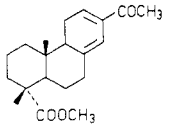


10 R = CH_2 R_1 = CH_3
11 R = O R_1 = CH_3
12 R = CH_2 R_1 = H

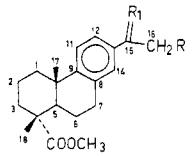
to neighbor group effects.[19,22] By thermal decomposition of **11** in the presence of a small amount of Se **14** was obtained.[20] From detailed investigations we conclude that the primary product (the keto acid **13**) is converted to **14**



13

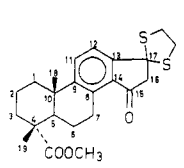
in a disproportionation reaction, thus limiting the yield to about 50%. Attempts to increase the yield by addition off an active hydrogen acceptor have not been successful.

14 could be converted to **15** in high yield with magnesium methyl carbonate.[21] Esterification with diazomethane in situ to **16** was necessary to avoid decarboxylation. To prevent deactivation of the aromatic nucleus



14 R = H R_1 = O
15 R = COOH R_1 = O
16 R = $COOCH_3$ R_1 = O
17 R = $COOCH_3$ R_1 = $-SCH_2CH_2S-$
18 R = COOH R_1 = $-SCH_2CH_2S-$

in the subsequent Friedel–Crafts reaction we protected the carbonyl group with ethanedithiol (**17**). Selective saponification of the terminal ester group gave compound **18**. Treatment of **18** with polyphosphoric acid resulted in D-ring formation, yielding a mixture of **19** and **20** in a ratio of 4:1 (GC analysis). Formation of the main product **19**



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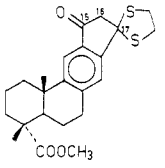
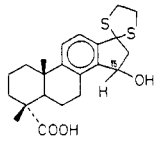


20

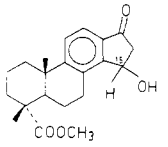
is in agreement with observations reported in the literature.[7] **19** and **20** have been separated by column chromatography on silica. **19** was converted to the diastereomeric alcohols **21** and **22** by reduction with sodium borohydride in methanol. NMR analysis revealed a ratio of 1:1, and separation was again achieved by column chromatography.

The configuration at C-15 of compound **21** has been established by NMR experiments. Saturation of the resonance of H-15 produced NOE effects at the signals of H-16 (syncoplanar to H-15) and equatorial H-7. Both



21 (15-R)
22 (15-S)

proton signals have also been identified by their characteristic couplings. Complexation of HO-15 with EuFOD deshielded the protons in positions 7 axial and 16b. These results establish R configuration at C-15 in compound **21**. *S* configuration at C-15 in **22** was confirmed by similar experiments as described above. Treatment of the diastereomeric alcohols **21** and **22** with NBS in aqueous acetone resulted in formation of **23** and **24**, respectively.



23 (15-R)
24 (15-S)

23 and **24** have a steroidal carbon skeleton and functional groups in favorable positions for further synthetic conversions to a steroid.

Experimental Section

Melting points were obtained on a Reichert Thermovar apparatus and are uncorrected. The ^1H NMR spectra were determined on a Bruker WM250 spectrometer in C_6D_6 if not otherwise stated (δ from internal Me_4Si). Mass spectra were obtained on a Varian CH 7 spectrometer with ionization energy of 70 eV and infrared absorption spectra on a Perkin-Elmer IR spectrometer 377 (solvent, CH_2Cl_2). Elemental analysis were performed by Dr. G. Zak at the Microanalytical Laboratory of the department of Physical Chemistry of the University of Vienna. A Carlo Erba HRGC5160 gas chromatograph was used for GC analysis (standard parameters: column, 20 m; SE 30, glass capillary column; injector temperature, 250 °C; oven program, 160–320 °C, 4 °C min^{-1}). The optical rotations were determined in EtOH with a Perkin-elmer polarimeter Model 241. UV spectra have been recorded on a Perkin-Elmer spectrophotometer 330 in EtOH. The starting material was a rosin acid fraction obtained by distillation of tall oil, available from Krems Chemie Ges.m.b.H. (Krems Austria), containing 40% abietic acid.

(4α,8α,12α,13*S*,14*S*)-16-(1-Bromo-1-methylethyl)-17,19-dinoratis-15-ene-4,13,14-tricarboxylic Acid Trimethyl Ester (7). **5** (230 g, 0.5 mol) was brominated as described earlier.[12,15] Yield: 270 g (100%), crude product.

(4α,8α,12α,13*S*,14*S*)-16-(1-Methylethenyl)-17,19-dinoratis-15-ene-4,13,14-tricarboxylic Acid Trimethyl Ester (10). **10** could be prepared in a one-step procedure from **5** using a similar procedure as described earlier for **7**.[12,15] After the reaction mixture [230 g (0.5 mol) of **5**] was heated for 24 h, 1.5 mol of dry pyridine was added and a temperature of 50 °C maintained for 1 h. The reaction mixture was washed with 1 N hydrochloric acid and with water to remove the pyridine. After drying with Na_2SO_4 and evaporation of CCl_4 in vacuo, **10** was further purified by column chromatography on silica (10:1 hexane–ethyl acetate). Yield: 206 g (90%).

(4α,8α,12α,13*S*,14*S*)-16-(1-Oxoethyl)-17,19-dinoratis-15-ene-4,13,14-tricarboxylic Acid Trimethyl Ester (11). (a) **10** (1 g, 2 mmol) was dissolved in 20 mL of a mixture of acetone and water (1:1) and at 0 °C 4 mmol of powdered Na_2IO_4 slowly added. The reaction mixture turned brown; however, this color disappeared at the end of the reaction. Ether was added, and the organic layers were washed several times with water. After the usual workup and evaporation of the ether, **11** was obtained in quantitative yield.

(b) **10** (206 g, 0.45 mol) dissolved in 4 L of methanol was cooled in a bath of acetone and liquid nitrogen to −96 °C and oxidized

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with ozone. After **10** had disappeared (TLC), air was bubbled through the reaction mixture for 1 h, and then it was poured in a beaker containing 1.5 L of water, 2 kg of ice, 700 mL of 5% aqueous NaOCl solution, and 100 mL of concentrated HCl. After the mixture was stirred for 1 h, the product had separated in form of a white solid and could be, isolated by filtration. Further purification was possible by distillation in high vacuum (10^{-4} torr). The oily product thus obtained was shown to be a single compound by TLC: yield, 163 g (77%); $[\alpha]^{20}_D$ 2.42° (*c* 1); ^{1}H NMR δ 0.22 (s, 3 H, CH_3-20), 0.51 (dt, 1 H), 0.83 (td, 1 H), 1.13 (s, 3 H, CH_3-21), 2.10 (s, 3 H, CH_3-19), 3.22 (s, 3 H, OCH_3), 3.32 (s, 3 H, OCH_3), 3.37 (s, 3 H, OCH_3), 3.98 (s, 1 H, H-12), 6.72 (s, 1 H, H-15); IR 2880, 1735, 1670, 1615 cm^{-1}; UV λ_{max} 242 nm (ϵ 4500); mass spectrum, *m/z* (relative intensity) 460 (17), 316 (44), 315 (92), 256 (22), 146 (51), 145 (24), 123 (3), 121 (46), 43 (100). Anal. Calcd for $C_{26}H_{36}O_7$: C, 67.80; H, 7.88. Found: C, 67.78; H, 7.71.

(4α,8α,12α,13*S*,14*S*)-16-(1-Methylethenyl)-17,19-dinoratis-15-ene-4,13,14-tricarboxylic Acid 4-Monomethyl Ester (12). **10** (15 g, 33 mmol) was dissolved in a mixture of 500 mL of EtOH and 250 mL of water containing 15 g of NaOH. After the mixture was heated for 4 h, it was treated with 200 mL of ether to remove remaining **10**. The aqueous layer was acidified with 2 N H_2SO_4 and extracted 3 times with ether. From the combined etheral solutions **12** was isolated and recyrstallized from toluene: yield, 10.5 g (74%); mp 242–250 °C; $[\alpha]^{20}_D$ 47.17° (*c* 1); ^{1}H NMR δ 0.45 (s, 3 H, CH_3-20), 0.65 (dt, 1 H, H-1_{ax}), 1.18 (s, 3 H, CH_3-21), 1.92 (s, 3 H, CH_3-19), 3.00 (d, 1 H, H-13), 3.23 (d, 1 H, H-14), 3.40 (s, 3 H, OCH_3), 3.67 (br s, 1 H, H-12), 4.90 (s, 1 H, H-15), 5.26 and 5.90 (2 s, 2 H, H-18); IR 2960, 1745, 1720, 1690 cm^{-1}; UV λ_{max} 242 nm (ϵ 15000); mass spectrum, *m/z* (relative intensity) 430 (7), 314 (45), 313 (23), 237 (40), 132 (58), 131 (73), 116 (57). Anal. Calcd for $C_{25}H_{34}O_6$: C, 69.74;, H, 7.96. Found: C, 69.76; H, 7.91.

1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(1-oxoethyl)-1-phenanthrenecarboxylic Acid Methyl Ester (14). **11** (13.3 g, 35.4 mmol) together with 100 mg of Se was heated under argon to 310–320 °C for 2 h. During this period, vigorous stirring was maintained. **14** was obtained from this mixture by vacuum distillation [310 °C (12 torr)] as yellow oil. After column chromatography on silica (10:1 hexane–ethylacetate) and recrystallization from *n*-hexane, **14** was isolated as white crystals: yield, 4.9 g (44%); mp 97–99 °C; $[\alpha]^{20}_D$ 59.77° (*c* 1); ^{1}H NMR δ 1.00 (s, 3 H, CH_3-17), 1.27 (s, 3 H, CH_3-18), 2.19 (s, 3 H, CH_3-16), 3.34 (s, 3 H, OCH_3), 7.06 (d, 1 H, H-14), 7.56 (dd, 1 H), 7.73 (dd, 1 H); IR 2940, 1728, 1690, 1610, 1570 cm^{-1}; UV λ_{max} 210 (ϵ 23000), 254 (15000); mass spectrum, *m/z* (relative intensity) 314 (8), 239 (30), 56 (11), 44 (100), 42 (21). Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.29; H, 8.33.

1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(2-carboxy-1-oxoethyl)-1-phenanthrenecarboxylic Acid Methyl Ester (16). **14** (4.9 g, 15.5 mmol) was dissolved in 75 mL of a 2 N solution of methyl magnesium carbonate (150 mmol) in DMF under Ar and heated to 115 °C for 1 h. After the mixture was cooled, 100 mL of ether, 100 g of ice, and 50 mL of concentrated HCl were added. The organic layer was separated and dried over Na_2SO_4. It was cooled to 0 °C and an ethereal solution of diazomethane added until a yellow color appeared, indicating an excess of reagent. After evaporation of the solvent and medium-pressure chromatography on silica (10:1 hexane–ethylacetate) 4.7 g of **16** were obtained. Recrystallization from hexane gave pure **16**. (^{1}H NMR in C_6D_6 showed relative concentrations of keto–enol form, 3:1): mp 47–90 °C (probably due to keto–enol tautomerism); IR 2940, 2880, 1745, 1725, 1685, 1650, 1625, 1610, 1560 cm^{-1}; mass spectrum, *m/z* (relative intensity) 372 (40), 357 (21), 299 (34), 298 (24), 297 (100), 283 (25), 265 (20) 231 (19). Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.95; H, 7.51. Found: C, 71.15; H, 7.78.

1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(2-carbomethoxy-1,1-(ethylenedithio)ethyl)-1-phenanthrenecarboxylic Acid Dimethyl Ester (17). To a solution of 5.2 g (14 mmol) of **15** in 150 mL of dry CH_2Cl_2 3 g (30 of mmol) 1,2-ethanedithiol and 1 mL of ethereal boron trifluoride etherate were added. This mixture was left for 12 h at room temperature and then hydrolized with 50 mL of 5% aqueous NaOH. The organic layer was separated, and after usual workup an oily residue was obtained. **16** was recrystallized from hexane: yield, 4.85 g (86%); mp 104–109 °C; $[\alpha^{20}_D$ 44.23° (*c* 1); ^{1}H NMR δ 1.02 (s, 3 H, CH_3-17), 1.26 (s, 3 H, CH_3-18), 3.13 (3, 3 H, OCH_3), 3.35 (s, 3 H, OCH_3), 3.58 (s, 2 H, H-16), 7.11 (d, 1 H, H-11), 7.66 (d, 1 H, H-14), 7.73 (dd, 1 H, H-12); IR 2930, 2880, 1745, 1725 cm^{-1}; UV λ_{max} 262 nm (ϵ 1200); mass spectrum, *m/z* (relative intensity) 448 (11), 377 (12), 376 (25), 375 (100), 237 (17). Anal. Calcd for $C_{24}H_{32}O_4S_2$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64,17; H, 7.25; S, 14.35.

1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(2-carboxy-1,1-(ethylenedithio)ethyl)-1-phenanthrenecarboxylic Acid Monomethyl Ester (18). **17** (4.85 g, 10.8 mmol) dispersed in a solution of 0.5 g (12.5 mmol) of NaOH in 100 mL of aqueous ethanol (water:ethanol = 1:1) was heated to 50 °C. After 2 h when all of the solid material was dissolved, the reaction mixture was cooled to room temperature and extracted with ether. The aqueous solution was acidified with 2 N H_2SO_4 and again extracted with ether 3 times. From the combined ethereal solutions pure **18** was obtained (TLC, NMR): yield, 4.1 g (87%); ^{1}H NMR δ 1.00 (s, 3 H, CH_3-17), 1.26 (s, 3 H, CH_3-18), 3.33 (s, 3 H, OCH_3), 3.46 (s, 2 H, H-16), 7.07 (d, 1 H, H-11), 7.51 (d, 1 H, H-14), 7.64 (dd, 1 H, H-12); IR 2960, 2870, 1760, 1725 cm^{-1}; mass spectrum, *m/z* (relative intensity) 343 (10), 376 (24), 375 (100), 255 (16), 233 (19). Anal. Calcd for $C_{23}H_{30}O_4S_2$: C, 63.56; H, 6.96; S, 14.76. Found: C, 63.74; H, 7.14; S, 14.38.

4-Carbomethoxy-3-desoxy-15-oxo-4-methyl-17,17-(ethylenedithio)-18-norandrosta-8,11,13-triene (19) and Isomer 20. Keto acid **18** (4.1 g, 9.4 mmol) was introduced in 50 g of polyphosphoric acid, and 5 g of P_2O_5 were added. this mixture was stirred and heated to 50 °C for 40 min. After cooling, it was poured into 500 mL of an ice-cold aqueous solution of $NaHCO_3$ and extracted several times with ether. After the usual workup of the combined ethereal solutions, we obtained 3.2 g of red oily product. The isomers **19** and **20** could be separated by column chromatography on silica (10:1 hexane–ethyl acetate).

19: yield, 1.4 g (36%); mp 215–225 °C; **1H** NMR δ 0.95 (s, 3 H, CH_3-18), 1.24 (s, 3 H, CH_3-19), 1.74 (dd, 1 H), 2.20 (dd, 1 H), 2.81 (m, 2 H), 2.96 (m, 2 H), 3.21 (m, 2 H), 3.34 (s, 2 H, H-16), 3.35 (s, 3 H, OCH_3), 3.59 (dd, 1 H, H-7_{eq}), 7.25 (d, 1 H), 7.77 (d, 1 H); IR 2940, 1725, 1715, 1705 cm^{-1}; mass spectrum, *m/z* (relative intensity) 416 (82), 388 (26), 85 (34), 61 (81), 59 (87), 55 (84), 43 (56), 41 (100). Anal. Calcd for $C_{23}H_{28}O_3S_2$: C, 66.33; H, 6.78; S, 15.37. Found: C, 66.53; H, 6.82; S, 14.96.

20: yield, 0.35 g (9%); ^{1}H NMR δ 0.86 (s, 3 H, CH_3-18), 1.19 (s, 3 H, CH_3-19), 1.83 (td, 1 H), 2.12 (dd, 1 H), 2.60 (m, 2 H), 2.78 (m, 2 H), 2.93 (m, 2 H), 3.33 (s, 3 H, OCH_3), 3.39 (s, 2 H, H-16), 7.53 (s, 1 H), 7.70 (s, 1 H); mass spectrum, *m/z* (relative intensity) 416 (17), 69 (23), 61 (22), 60 (36), 59 (46), 55 (56), 43 (66), 41 (100).

(4α,10β,15*R*)- and (4α,10β,15*S*)-4-Carbomethoxy-3-desoxy-15-hydroxy-4-methyl-17,17-(ethylenedithio)-18-norandrosta-8,11,13-triene 21 and 22. **19** (140 mg, 0.34 mmol) was dissolved in 100 mL of methanol and at 30 °C 100 mg (2.5 mmol) of $NaBH_4$ slowly added while the mixture was stirred and the pH of it maintained below 7. After complete addition, the mixture was stirred at 30 °C for 1 h. Then 100 mL of water was added and this solution acidified with 2 N H_2SO_4. Extraction with ether and evaporation of the organic solvent gave a mixture of **21** and **22** in a ratio of 1:1 (GC analysis).

Yield: 88 mg (62%) (**21** + **22**). Separation of **21** and **22** could be achieved by column chromatography on silica (5:1 hexane–ethyl acetate).

21: ^{1}H NMR δ 1.07 (s, 3 H, CH_3-18), 1.28 (s, 3 H, CH_3-19), 1.78 (d, 1 H), 2.00 (d, 1 H), 2.34 (dd, 1 H), 2.66 (dd, 1 H), 2.28 (dd, 1 H), 3.39 (s, 3 H, OCH_3), 4.87 (d, 1 H, H-15), 7.18 (d, 1 H), 7.65 (d, 1 H); IR 3600, 2940, 1724 cm^{-1}; mass spectrum, *m/z* (relative intensity) 316 (17), 241 (30), 91 (30), 84 (100), 55 (46), 43 (58), 41 (67). Anal. Calcd for $C_{23}H_{30}O_3S_2$: C, 65.99; H, 7.22; S, 15.32. Found: C, 66.52; H, 7.34; S, 14.97.

22: ^{1}H NMR δ 1.06 (s, 3 H, CH_3-18), 1.34 (s, 3 H, CH_3-19), 2.00 (d, 1 H), 2.88 (dd, 1 H), 2.65 (dd, 1 H), 2.71 (dd, 1 H), 2.88 (dd, 1 H), 3.05 (s, 3 H, OCH_3), 4.93 (d, 1 H, H-15), 7.18 (d, 1 H), 7.64 (d, 1 H); IR 3600, 2940, 1725 cm^{-1}; mass spectrum, *m/z* (relative intensity) 400 (1), 227 (38), 71 (40), 69 (47), 57 (95), 55 (78), 43 (100), 41 (80). Anal. Calcd for $C_{23}H_{30}O_3S_2$: C, 65.99; H, 7.22; S, 15.32. Found: C, 66.32; H, 7.24; S, 15.07

(4α,10β,15*R*)- and (4α,10β,15*S*)-4-Carbomethoxy-3-desoxy-4-methyl-15-hydroxy-17-oxo-18-norandrosta-8,11,13-triene 23 and 24. **21** (40 mg, 0.1 mmol) was dissolved in 2 mL,

of acetone (97% + 3% H_2O) and cooled with ice. This solution was added dropwise during stirring to an ice-cold solution of 120 mg of NBS in acetone. After complete addition, the mixture was cooled with ice for 10 min and after this period 1 mL of a saturated aqueous solution of Na_2SO_3 added. Extraction with 10 mL of hexane–CH_2Cl_2 (1:1) yielded an organic phase, which was washed with aqueous $NaHCO_3$ and dried (Na_2SO_4). After evaporation of the solvent and chromatography on silica (benzene) **23** was obtained: yield, 21 mg (63%); ^1H NMR δ 0.84 (s, 3 H, CH_3-18), 1,24 (s, 3 H, CH_3-19), 1.82 (d, 1 H), 2.08 (d, 1 H), 2.18 (dd, 1 H), 2.36 (dd, 1 H), 2.42 (m, 1 H), 2.80 (dd, 1 H), 3.08 (dd, 1 H), 3.39 (s, 3 H, OCH_3), 4.13 (d, 1 H), 4.90 (d, 1 H), 6.96 (d, 1 H), 7.59 (d, 1 H); IR 3600, 2960, 1725, 1597 cm^{-1}; mass spectrum, *m/z* (relative intensity) 341 (6), 324 (3), 227 (5), 84 (27), 71 (17), 69 (17), 57 (41), 55 (38), 43 (100). Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.40; H, 8.03.

24 was obtained by the same procedure as described for **23**. In the ^1H NMR spectrum an equilibrium of keto and enol forms could be observed: ^1H NMR (keto form) δ 1.01 (s, 3 H, CH_3-18), 1.30 (s, 3 H, CH_3-19), 2.22 (dd, 1 H), 2.63 (dd, 1 H), 2.80–3.14 (m, 1 H), 3.35 (s, 3 H, OCH_3), 4.62 (t, 1 H), 7.06 (d, 1 H), 7.69 (d, 1 H), (enol form) 0.92 (s, 3 H, CH_3-18), 1.27 (s, 3 H, CH_3-19), 2.89–3.35 (m, 3 H), 3.32 (s, 3 H, OCH_3), 4.16 (d, 1 H), 4.96 (d, 1 H), 6.96 (d, 1 H), 7.59 (d, 1 H); IR (3600, 2960, 1725, 1597 cm^{-1}; mass spectrum, *m/z* (relative intensity) 341 (6), 324 (3), 227 (5), 84 (27), 71 (17), 69 (15), 57 (41), 43 (100), 41 (54).

Registry No. **5**, 2115-43-7; **7**, 90164-49-1; **10**, 90164-55-9; **11**, 97644-60-5; **12**, 97644-61-6; **14**, 22465-61-8; **16**, 97644-62-7; **16** (enol), 97644-63-8; **17**, 97644-64-9; **18**, 97644-65-0; **19**, 97644-66-1; **20**, 97644-67-2; **21**, 97644-68-3; **22**, 97644-69-4; **23**, 97644-70-7; **24**, 97644-71-8; **24** (enol), 97644-72-9.

Directed Openings of 2,3-Epoxy Alcohols via Reactions with Isocyanates: Synthesis of (+)-*erythro*-Dihydrosphingosine

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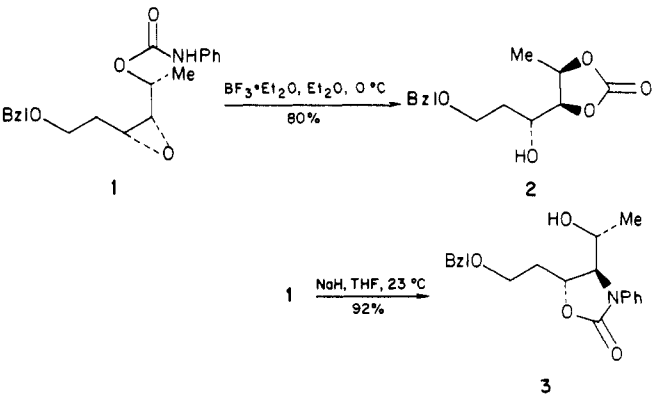
Two methods for the synthesis of 2-(*N*-alkylamino) 1,3-diols from 2,3-epoxy alcohols are described. In one procedure (method A) an epoxyurethane (**5**, **8**, **11**, **14**, **16**) prepared from the corresponding epoxy alcohol by standard procedures is cyclized to a 2-oxazolidinone derivative (**6**, **9**, **12**, **15**, **17**) in 81–90% yield by treatment with NaH in THF or NaOMe in MeOH. The second procedure (method B) involves treatment of the epoxy alcohol (**4**, **7**, **10**, **13**, **24**) with benzyl isocyanate, an NH_3 synthetic equivalent, and NaH in THF at reflux. Hydrolysis of the crude isoxazolidinones by exposure to LiOH in EtOH at reflux smoothly affords 2-(*N*-benzylamino) 1,3-diols (**22**, **23**, **30**, **31**) in 68–72% overall yield. These procedures are highly regioselective; products resulting from intramolecular addition of the urethane nitrogen atom to the epoxide β-position were not detected. This methodology was applied to a short, highly stereoselective synthesis of (+)-*erythro*-dihydrosphingosine (**26**) from palmitic aldehyde (47–54% overall yield).

Renewed interest in the use of 2,3-epoxy alcohols as intermediates in organic synthesis has greatly stimulated by the discovery of the Sharpless asymmetric epoxidation reaction.[2-4] Indeed, highly selective methods for converting the epoxy alcohol unit into a variety of useful functional groups via hydride reduction[5] or by nucleophilic substitution reactions (e.g., carbon,[6] oxygen,[7] and sulfur[7e,8] nucleophiles) have been developed in the past several years. During this period one of our interests has been the use of 2,3-epoxy alcohols in the synthesis of carbohydrates and related compounds.[9] We have observed, for example, that treatment of epoxyurethanes such as **1** with Lewis acids under aprotic conditions effected a



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