Synthesis of *trans*-2-Decalones with 9α Leaving Groups and 8β General Bases for 1β Proton Abstraction

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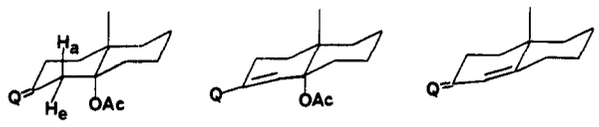
Substances **15**, **17**, **26**, and **27** have been synthesized as part of an effort to determine the rate acceleration which would be obtained in alpha deprotonation of carbonyl compounds if the base which accepted the proton were localized in the correct position rather than free in solution. These molecules possess both an intramolecular general base which can interact effectively with a proton alpha to a carbonyl and a beta leaving group, so that deprotonation is followed by formation of a chromophoric enone. The syntheses proceed from **6** via nucleophilic opening of epoxide **8** with allyl Grignard reagent to afford **12**, followed by permanganate–periodate oxidation to **16**. Jones oxidation of **16** yields **15**, and **17** is prepared by the sequence **16** → **18** → **19** → **17**. Conversion of **16** to **26** and **27** was accomplished by reduction to triol **28**, selective tosylation to form **30**, displacement by morpholine to yield **32**, and steps analogous to those used in the preparations of **15** and **17**.

In our studies of proton abstraction alpha[1] to carbonyl groups and derived iminium ions,[2] we have employed substrates in which deprotonation is always followed by essentially irreversible departure of a beta[1] leaving group to generate an easily monitored ultraviolet chromophore, as illustrated in **1a** → **2a** → **3a** and **1a** → **1b** → **2b** → **3b** → **3a**. Using this tactic, we have demonstrated that at



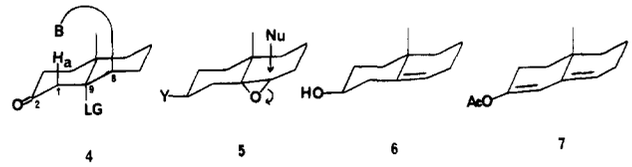
1a, Q = O **2a**, Q = O⁻ **3a**, Q = O

1b, Q = N̈HR **2b**, Q = NHR **3b**, Q = N̈HR

physiological pH an alpha proton can be removed by a given general base ca. 10^5 times more readily from an appropriate iminium ion (**1b**) than from the parent carbonyl compound (**1a**).[3] We have recently demonstrated further that alpha deprotonation of **1a** and **1b** occurs with stereoselective control: abstraction of the axial proton (H_a) is ca. 10^2 times faster than abstraction of the equatorial proton (H_e).[4]

In order to gain further insight into the details of this biochemically important[5] type of reaction, we wished to assess the rate acceleration which would be obtained if the basic atom which accepts alpha proton H_a were localized in the correct position rather than free in solution. Such correct "approximation"[6] is generally considered to be an important component of enzymic catalysis. Accordingly, we are extending our use of geometrically rigid *trans*-decalin derivatives to molecules incorporating, in addition to the features of substrate **1a**, an intramolecular general base. This paper describes the synthesis of several substances of this type, in which an 8β substituent on the decalin ring system, as shown in **4**, provides a potential proton-accepting functional group localized in what molecular models indicate to be an excellent position for interaction with the 1β proton (H_a). A subsequent publication will describe the kinetic studies comparing the intramolecular reactions of these substances with appropriate intermolecular analogues.

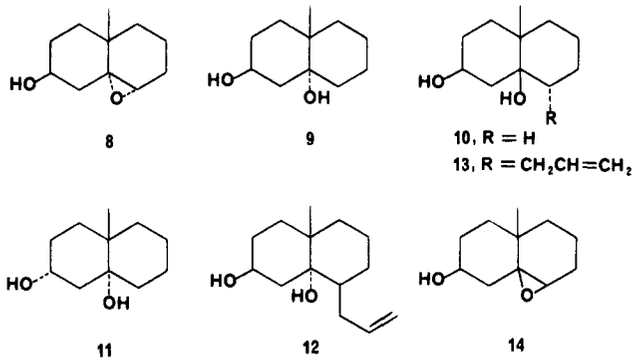
The strategy adopted for preparation of suitable examples of **4** was nucleophilic attack on an 8,9 α-oxide, as shown in **5**. A potentially useful starting material for



4 **5** **6** **7**

preparation of such an oxide appeared to be homoallylic alcohol **6**, which had been independently prepared by similar routes in two laboratories.[7,8] In our hands, the procedure of Julia,[7] involving preparation and reduction of dienol acetate **7**, proved more efficient.

Treatment of **6** with *m*-chloroperbenzoic acid afforded an oily mixture of epoxides. The major isomer (by TLC) could be crystallized in ca. 10% yield from this mixture and was shown to be the α-oxide **8** by lithium aluminum



8 **9** **10**, R = H; **13**, R = $CH_2CH{=}CH_2$

11 **12** **14**

hydride reduction to known diol **9**.[9] Analogous reduction of the crude epoxide mixture afforded about a 2:1 mixture of diols **9** and **10**,[9] as well as a small amount of a third known diol **11**,[9] indicating that the **6** used had been contaminated with some of the epimeric alcohol.[10]

(1) To avoid confusion, the words alpha and beta are used to denote the positions of carbons relative to the carbonyl or derived functional group, and the symbols α and β are used to denote substituents respectively underneath and above the decalin ring system.

(2) Review: T. A. Spencer, "Bioorganic Chemistry", Vol. 1, E. E. van Tamelen, Ed., Academic Press, New York, 1979, Chapter 13, p 313.

(3) D. J. Hupe, M. C. R. Kendall, and T. A. Spencer, *J. Am. Chem. Soc.*, **95**, 2271 (1973).

(4) H. E. Ferran, Jr., R. D. Roberts, J. N. Jacob, and T. A. Spencer, *J. Chem. Soc., Chem. Commun.*, 49 (1978)

(5) See, e.g.: ref 2; F. H. Westheimer, *Search*, 1, 34 (1970); W. A. Wood in "The Enzymes", Vol. V, P. D. Boyer, Ed., 3rd ed., Academic Press, New York, 1971, p 582.

(6) W. P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, 1969, Chapter 1.

(7) S. Julia, M. Julia, and L. Brasseur, *Bull. Soc. Chim. Fr.*, 374 (1962).

(8) C. H. Heathcock and T. R. Kelly, *Tetrahedron*, **24**, 1801 (1968).

(9) H. B. Henbest and J. McEntee, *J. Chem. Soc.*, 4478 (1961).

(10) The NMR spectrum of **6** prepared in our laboratory indicated that it did indeed contain some 2α alcohol (see Experimental Section). Julia et al.[7] give no NMR data. Heathcock and Kelly[8] report *only* a peak at δ 4.15 in CCl_4 for the "C2–H" of their **6**, in puzzling disagreement with our data. When the mixture of epoxides formed from our **6** was distilled, however, the material with a 2α-hydroxyl group was apparently separated, since the NMR signal for the equatorial 2β-H evident in our **6** had essentially disappeared in the distillate.

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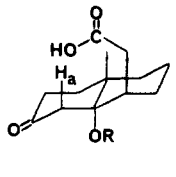
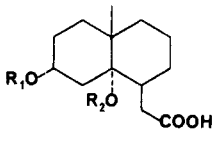
With crystalline α-oxide **8** in hand, its reaction with carbon nucleophiles was explored. We were unable to obtain any product resulting from nucleophilic attack of diethyl malonate anion on the epoxide function of **8**. Excess allyl Grignard reagent,[11] on the other hand, readily reacted with **8** to afford 91% of 8β-allyl-substituted diol **12**, mp 117–118 °C. All conversions described below follow from this convenient key step. In practice, diol **12** was prepared on a large scale by reaction of a distilled epoxide mixture[10] with allyl Grignard in 50% yield after separation by column chromatography. From this reaction there was also isolated 26% of the isomeric allyl-substituted diol **13**, mp 107–109 °C, derived from the β-epoxide **14** which had given rise to **10** in the hydride reduction of the epoxide mixture.

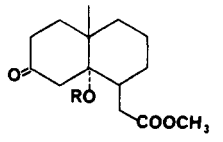
The first target compound of type **4** envisaged was hydroxy keto acid **15**. Molecular models indicate that the



15, R = H
17, R = Ac



16, $R_1 = R_2 = H$
18, $R_1 = R_2 = Ac$
19, $R_1 = H, R_2 = Ac$

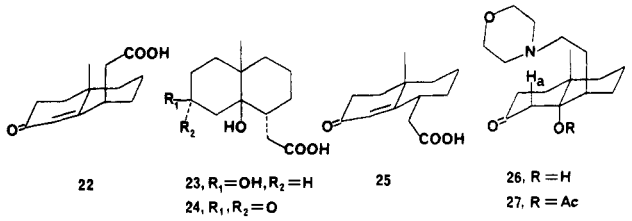


20, R = H
21, R = Ac

carboxylate anion of **15** can act effectively to accept the 1β proton (H_a). The oxidative cleavage of the terminal double bond of **12** which is required for its conversion to **15** was first attempted by ozonolysis, but initial results were not encouraging. Lemieux–von Rudloff periodate–permanganate oxidation[12] was then employed, and this afforded dihydroxy acid **16**, mp 215–216 °C, in up to 81% yield. Jones oxidation of **16** then yielded the desired **15**, mp 177–178 °C, in 65% yield.

Compound **17** with a 9α-acetoxyl substituent was also desired, in order to have a substrate with a sufficiently good leaving group to ensure that alpha-proton abstraction would be rate determining.[13] Preparation of **17** was accomplished by the same sequence found to be necessary in the synthesis of **1a**,[13] where direct acetylation of the corresponding beta ketol failed because it inevitably led to at least some elimination to enone **3**.[13] Accordingly, dihydroxy acid **16** was treated vigorously with isopropenyl acetate containing *p*-toluenesulfonic acid to afford diacetate **18**, mp 144–145 °C, which was selectively hydrolyzed to **19**, mp 158–159 °C, by treatment with dilute sodium hydroxide in methanol at room temperature for 20 min. Jones oxidation of **19** then afforded 79% of acetoxy keto acid **17**, mp 136–137 °C. Both **15** and **17** were converted by treatment with diazomethane to the corresponding methyl esters **20** and **21**, which were required as appropriate compounds lacking intramolecular general bases for comparisons of reactivity in alpha deprotonation with **15** and **17**.

Reaction of either **15** or **17** with dilute base (pH 11) afforded enone acid **22**, mp 95–97 °C, in excellent yield. Since **22** is susceptible to epimerization via removal of the 8α proton, it was considered important to confirm that the 8β stereochemistry assigned to the 95–97 °C melting point acid was correct. To this end, the 8α-allyl-substituted diol **13** was subjected to the same transformations as **12**. Thus,



22

23, $R_1 = OH, R_2 = H$
24, $R_1, R_2 = O$

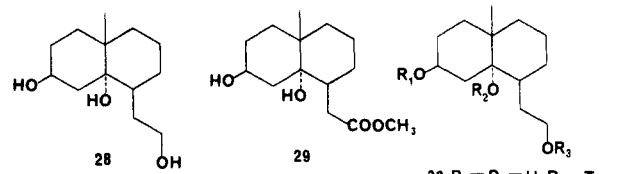
25

26, R = H
27, R = Ac

13 was converted via dihydroxy acid **23** to hydroxy keto acid **24**. Treatment of **24** with base afforded a different enone acid, mp 121–123 °C, which was assigned structure **25**. When **22** was treated with sodium methoxide in methanol, the anticipated epimerization of the 8β substituent was indeed realized, and **25** was obtained in 78% yield.

Compounds with a neutral general base rather than a potential carboxylate anion as the 8β substituent were also sought as substrates for kinetic studies. Particularly appealing candidates as such substrates were the morpholine derivatives **26** and **27**. Molecular models indicate that the nitrogen atom of **26** and **27** can readily adopt a position almost directly above[14] the C1 axial proton (H_a) in any reasonable transition state for deprotonation. Furthermore, the oxygen atom of the morpholine ring was expected to serve two useful purposes. First, it will lower the basicity of the nitrogen, making deprotonation slower and perhaps more easily measurable. Second, it should assist in orienting the nitrogen properly for abstraction of H_a because it should interact more favorably with a surrounding aqueous environment than would simple alkyl substituents on nitrogen, thus promoting adoption of the conformation shown in **26** and **27**.

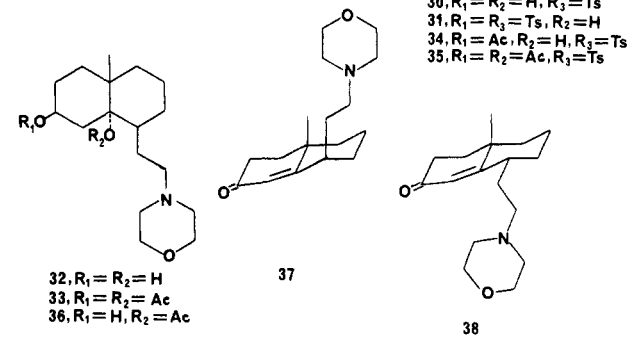
Synthesis of **26** and **27** was also accomplished starting from dihydroxy acid **16**. Vigorous treatment of **16** with lithium aluminum hydride afforded triol **28**, mp 174–176 °C. It was more efficient, however, to convert **16** to ester



28

29

30, $R_1 = R_2 = H, R_3 = Ts$
31, $R_1 = R_3 = Ts, R_2 = H$
34, $R_1 = Ac, R_2 = H, R_3 = Ts$
35, $R_1 = R_2 = Ac, R_3 = Ts$



32, $R_1 = R_2 = H$
33, $R_1 = R_2 = Ac$
36, $R_1 = H, R_2 = Ac$

37

38

29 with diazomethane and reduce **29**. This sequence afforded an 85% overall yield of pure **28** from **16**. Selective tosylation of the primary hydroxyl group[15] of triol **28** was then effected, but the yield of **30**, mp 93–94.5 °C, could not be raised above 48%, despite considerable effort to do

(11) Prepared by the method of O. Grummitt, E. P. Budewitz, and C. C. Chudd, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1963, p 749.
(12) R. V. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).
(13) D. J. Hupe, M. C. R. Kendall, and T. A. Spencer, *J. Am. Chem. Soc.*, **94**, 1254 (1972).
(14) J. Hine, M. S. Cholod, and R. A. King [*J. Am. Chem. Soc.*, **96**, 835 (1974)] have argued, on the basis of the preferred linearity of hydrogen bonds, that the proton-accepting basic atom, the alpha proton, and the alpha carbon should be collinear in the transition state for proton abstraction.
(15) W. S. Johnson, J. C. Collins, Jr., R. Pappo, M. B. Rubin, P. J. Kropp, W. F. Johns, J. E. Pike, and W. Bartmann, *J. Am. Chem. Soc.*, **85**, 1409 (1963).

so. The chief byproduct was ditosylate **31**. Reaction of **30** with morpholine in pyridine proceeded smoothly to afford 88% of **32**, mp 162–162.5 °C, and Jones oxidation of **32** yielded 79% of **26**, mp 138–138.5 °C.

For preparation of acetoxy ketone **27**, dihydroxy tosylate **30** was converted to morpholino diacetate **33** in about 60% overall yield by either of two routes. Acetylation of **30** with isopropenyl acetate under mild conditions yielded monoacetate **34**, mp 134–135 °C, but vigorous conditions afforded diacetate **35**, mp 88.5–89 °C. Treatment of **35** with morpholine then yielded oily **33**. Alternatively, acetylation of previously described morpholino diol **32** led to **33**.

Conversion of **33** to **27** followed the familiar pathway of selective hydrolysis to **36**, mp 119–120 °C, in 88% yield, followed by Jones oxidation to **27**, mp 120–121 °C, in 74% yield. For isolation of the reactive **27**, all operations had to be performed at −10 °C as rapidly as possible. In solution **27** readily undergoes elimination to form oily amino enone **37**. As had been done with carboxylic acid **22**, the β stereochemistry of the morpholinoethyl substituent of **37** was confirmed by observing isomerization to a different amino enone, presumably **38**, upon treatment of **37** with sodium methoxide.

Experimental Section

Melting points were determined in a Thomas-Hoover apparatus in unsealed capillaries and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer Model 137, 257, or 599 spectrophotometer. IR spectra were taken as KBr pellets for solids or as neat liquids on NaCl plates. Ultraviolet (UV) spectra were recorded on a Unicam SP800B spectrophotometer or on a Varian Cary 219 spectrophotometer in 1-cm quartz cuvettes. Proton nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ solution, unless otherwise indicated, on a Perkin-Elmer R-24 instrument or on a JEOL FX-60Q multinuclear Fourier transform spectrometer. Chemical shifts are reported in parts per million downfield from Me_4Si. Preparative thin-layer chromatography (TLC) was performed on 20 × 20 cm plates coated with 1.45 mm thick layers of silica gel 60 PF:254+366 (Brinkmann Instruments Inc.). UV light was used to visualize TLC plates. Qualitative TLC plates were coated with 0.25 mm thick layers of silica gel 60 PF:254+366 and were sprayed with a 5% isopropyl alcohol solution of phosphomolybdic acid (Eastman Kodak) and heated briefly at 110 °C. Mass spectra were determined at the MIT mass spectrometry facility, sponsored by USPHS Division of Research Resources Grant PR00317. Elemental analyses were performed by Spang Microanalytical Laboratory. Brine refers to saturated aqueous sodium chloride solution.

10β-Methyl-Δ^{8,9}-octal-2β-ol (6). Unsaturated alcohol **6** was prepared from 10-methyl-Δ^{1,9}-octal-2-one[16] by the method of Julia.[7] Conversion of 10-methyl-Δ^{1,9}-octal-2-one to dienol acetate **7**, bp 88–92 °C (0.3 mm), was effected in 82% yield. Treatment of **7** with $NaBH_4$ in CH_3OH–H_2O gave 82% of colorless oil: bp 82–84 °C (0.6 mm); NMR δ 1.08 (s), 2.75 (s), 3.5 (m), 4.05 (m), 5.40 (br s). The signal at 4.05 ppm integrates as about 15–20% of the signal at 3.5 ppm and is assigned to the 2β-H of isomeric 10β-methyl-Δ^{8,9}-octal-2α-ol contaminating **6**.[10]

Epoxidation of 6. To a solution of 2.06 g (12 mmol) of freshly distilled **6** in 20 mL of methylene chloride at 0 °C was added a solution of 2.54 g (15 mmol) of *m*-chloroperbenzoic acid (85% pure) in 80 mL of methylene chloride over 1 h. The mixture was cooled in ice and stirred for 21 h. The precipitate of *m*-chlorobenzoic acid was removed by filtration, and the filtrate was stirred with 30 g of calcium hydroxide for 1 h. The mixture was filtered, and the filtrate was evaporated to yield 2.12 g (97%) of a crude mixture of epoxides. In a large-scale epoxidation (41 g) the crude product was distilled to afford 80% of purified epoxide mixture: bp 100–110 °C (0.5 mm); IR 3440 cm^{-1}; NMR δ 1.07 (s), 1.10 (s), 2.95 (t), 3.20 (s), 3.75 (m).[10]

The 2.12 g of product was allowed to crystallize in ether to afford solid α-oxide **8**. Four crystallization from hexane–ethyl acetate afforded 0.210 g (10%) of pure **8**: mp 76–77 °C; IR 3400, 1440, 1025 cm^{-1}; NMR δ 1.1 (s, 3), 2.95 (t, 1), 3.8 (m, 1). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.37; H, 9.85.

Reduction of 8 to 10β-Methyl-*trans*-decalin-2β,9α-diol (9). A mixture of 31.7 mg (0.174 mmol) of **8**, mp 74–75 °C, and 25 mg of $LiAlH_4$ in 20 mL of anhydrous ether was stirred at reflux for 3 h. Excess hydride was destroyed by addition of ethyl acetate, followed by 5% sulfuric acid. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were extracted twice with brine, dried over $MgSO_4$, and evaporated to afford 28.0 mg (87%) of **9**, mp 154–156 °C. Recrystallization from ethyl acetate gave **9**, mp 157–159 °C, which was identical by IR and TLC (ethyl acetate) with authentic **9**.[17]

Reduction of Epoxide Mixture to Diols 9, 10, and 11. A mixture of 350 mg of crude, undistilled product from epoxidation of **6** and 170 mg of $LiAlH_4$ in 20 mL of ether was refluxed for 3 h and worked up as in the preceding experiment to afford 311 mg of oil. Fractional crystallization and preparative TLC (ethyl acetate) afforded 124 mg of **9**, mp 157–159 °C (lit.[9] mp 161.5–162.5 °C), 58 mg of **10**, mp 85–89 °C (lit.[9] mp 98.5–100 °C), and 22 mg of **11**, mp 119–121 °C (lit.[9] mp 130–131.5 °C). Diols **9**, **10**, and **11** were identified by TLC and IR comparison with authentic samples.[17]

8β-Allyl-10β-methyldecalin-2β,9α-diol (12). To a solution of 230 mg (1.26 mmol) of pure α-oxide **8** in 25 mL of dry THF under N_2 was added 40 mL of ether containing allylmagnesium bromide prepared[11] from 4.32 g (36 mmol) of allyl bromide and 2.2 g of magnesium. The initial cloudy suspension was dissolved by addition of 30 mL of THF, and the mixture was refluxed overnight. To the cooled mixture was then added saturated NH_4Cl solution followed by extraction four times with ethyl acetate. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to afford 550 mg of residue, which was crystallized from ethyl acetate to afford 258 mg (91%) of **12**: mp 117–118 °C; IR 3500–3300, 1640, 1380, 1025, 900 cm^{-1}; NMR δ 1.05 (s, 3), 4.2 (m, 1), 4.8–6.0 (m, 3). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.71; H, 10.93.

Conversion of the Mixture of Epoxides to 12 and 8α-Allyl-10β-methyldecalin-2β,9β-diol (13). As in the preceding experiment, 1.02 g (5.6 mmol) of the mixture of epoxides formed from **6** was treated with excess allylmagnesium bromide. The same workup afforded 1.80 g of crude product, which was chromatographed on neutral alumina. Elution with hexane and 1:1 hexane–benzene afforded 0.328 g (26%) of the α-allyl product **13**, mp 107–108 °C. Recrystallization from hexane afforded pure **13**: mp 107–109°; IR 3280, 3070, 1640 cm^{-1}; NMR δ 0.99 (s, 3), 4.2 (br s, 1), 4.8–6.0 (m, 3). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.11; H, 10.87.

Further elution with benzene and ether gave 0.620 g (50%) of **12**, mp 117–118 °C.

8β-(Carboxymethyl)-10β-methyldecalin-2β,9α-diol (16). According to a procedure based on that of Jacobson et al.,[18] a solution of 13.70 g (59.55 mmol) of KIO_4 and 0.24 g (1.52 mmol) of $KMnO_4$ in 1.5 L of distilled water was prepared and adjusted to pH 8–9 by addition of 11.76 g (85 mmol) of K_2CO_3. To this solution was added a solution of 2.00 g (8.93 mmol) of **12** in 200 mL of *tert*-butyl alcohol over 15 min. The mixture was stirred at room temperature for 22 h, acidified with 25 mL of concentrated HCl, decolorized with 23.0 g (121 mmol) of $Na_2S_2O_5$, diluted with 300 mL of 10% KOH solution, concentrated under reduced pressure to about half the volume, and extracted with ether. The aqueous layer was then filtered, acidified with concentrated HCl, saturated with NaCl, and extracted four times with 2-L, 1-L, and two 0.5-L portions of ethyl acetate. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to afford a residue which recrystallized to yield 1.75 g (81%) of **16**, mp 190–195 °C dec. Recrystallization from acetone afforded pure **16**: mp 215–216 °C; IR 3600–2400 (peaks at 3200, 2650), 1720, 1695 cm^{-1}; mass spectrum *m/e* 242.1538 (M$^+$) (calcd for $C_{13}H_{22}O_4$,

(16) Prepared by the method of N. C. Ross and R. Levine, *J. Org. Chem.*, **29**, 2341 (1964).

(17) Prepared in our laboratory by D. J. Hupe according to the method of Henbest and McEntee.[9]

(18) M. Jacobson, M. Beroza, and W. A. Jones, *J. Am. Chem. Soc.*, **83**, 4819 (1961).

242.1518). Anal. Calcd: C, 64.44; H, 9.15. Found: C, 64.25; H, 8.77.

8β-(Carboxymethyl)-10β-methyl-9α-hydroxydecal-2-one (15). To an ice-cooled solution of 169 mg (0.698 mmol) of **16** in 60 mL of acetone was added 1.4 mL of Jones reagent[19] dropwise with stirring. After 5 min the mixture was concentrated under reduced pressure, diluted with 20 mL of water, and extracted three times with methylene chloride. The aqueous layer was saturated with NaCl and extracted further with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and evaporated to afford 135 mg (80%) of crude **15**, mp 170–175 °C. Recrystallization from acetone gave 109 mg (65%) of pure **15**: mp 177–179 °C; IR 3400, 2800–2400, 1710 cm^{-1}; NMR (Me_2SO-d_6) δ 1.20 (s, 3), 2.88 (d, 1, J = 15 Hz). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.98; H, 8.32.

8β-(Carboxymethyl)-10β-methyl-2β,9α-diacetoxydecalin (18). A mixture of 0.300 g (1.24 mmol) of dihydroxy acid **16**, 25 mL of isopropenyl acetate (bp 96–97 °C), and a few crystals of *p*-toluenesulfonic acid was refluxed for 18 h. The excess isopropenyl acetate was evaporated under reduced pressure, and the residue was purified by preparative TLC using 1:1 ethyl acetate–hexane to afford 0.196 g (48%) of **18**, mp 132–134 °C. Recrystallization from ethyl acetate–hexane afforded 0.170 g (42%) of **18**: mp 144–145 °C; IR 3300–2600, 1740–1725, 1710 cm^{-1}; NMR δ 1.10 (s, 3), 2.00 (s, 3), 2.10 (s, 3), 4.75 (br m, 1), 9.5 (br s, 1). Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.67; H, 8.02.

8β-(Carboxymethyl)-9α-acetoxy-10β-methyldecal-2β-ol (19). A solution of 160 mg (0.49 mmol) of **18**, mp 140–143 °C, in a mixture of 0.2 mL of 50% aqueous NaOH and 3 mL of methanol was stirred at room temperature for 20 min, acidified with concentrated HCl, and extracted with ether (3 × 75 mL). The combined ether layers were washed twice with brine, dried over $MgSO_4$, and evaporated to afford 138 mg (99%) of crude **19**, which TLC analysis showed to contain traces of **16** and **18**. Recrystallization of this material was inefficient, so it was purified by preparative TLC using 13:2:10 chloroform–acetic acid–hexane to afford 98 mg (70%) of **19**, which, after recrystallization from ether, with difficulty, afforded pure **19**: mp 158–159 °C; IR 3500, 1730, 1715 cm^{-1}; NMR δ 1.08 (s, 3) 2.03 (s, 3). Anal. Calcd for $C_{15}H_{25}O_5$: C, 63.36; H, 8.51. Found: C, 63.37; H, 8.43.

8β-(Carboxymethyl)-9α-acetoxy-10β-methyldecal-2-one (17). To a solution of 50.0 mg (0.176 mmol) of **19**, mp 157–159 °C, in 10 mL of acetone at room temperature was added 0.080 mL of Jones reagent[19] with stirring. After 10 min the mixture was concentrated under reduced pressure with minimum heating. The residue was partitioned between 500 mL of ether and 100 mL of brine. The ether layer was washed with brine until the extracts were neutral, dried over $MgSO_4$, and evaporated to afford 47 mg of colorless oil which crystallized from 0.5 mL of ether to give 32 mg (64%) of **17**, mp 134–136 °C. From the mother liquors an additional 7.0 mg of **17**, mp 129–132 °C, was obtained for a total yield of 39 mg (79%). An analytical sample was prepared by recrystallization from ether–hexane: mp 136–137 °C; IR 3300, 1750, 1730, 1705 cm^{-1}; NMR δ 1.30 (s, 3), 1.98 (s, 3), 2.68 (d, 1, J = 15 Hz), 3.44 (d, 1, J = 15 Hz). Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.87; H, 7.90.

8β-[(Carbomethoxy)methyl]-10β-methyl-9α-hydroxydecal-2-one (20). To a cooled solution of excess distilled ethereal diazomethane prepared from EXR-101[20] was added a solution of 50.0 mg (0.208 mmol) of **15** in 10 mL of ether. This mixture was stirred for 1 h and evaporated, and the residue was crystallized from ether–hexane to give 40.0 mg (76%) of **20**: mp 123–124 °C; IR 3400, 1730, 1700 cm^{-1}; NMR δ 1.21 (s, 3), 2.84 (d, 1, J = 15 Hz), 3.65 (s, 3). Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.95; H, 8.75.

8β-[(Carbomethoxy)methyl]-10β-methyl-9α-acetoxydecal-2-one (21). Exactly as in the esterification of **15**, 50.0 mg (0.177 mmol) of **17** gave 55 mg of crude product which upon crystallization from ether–hexane afforded 24 mg (45%) of **21**: mp 75–76 °C; IR 1750, 1730, 1700 cm^{-1}; NMR δ 1.25 (s, 3), 1.95 (s, 3), 2.66 (d, 1, J = 13 Hz), 3.41 (d, 1, J = 13 Hz), 3.65 (s, 3). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.84; H, 8.15.

8β-(Carboxymethyl)-10β-methyl-Δ^{1,9}-octal-2-one (22). To a solution of 50 mg (0.21 mmol) of **15** in a mixture of 1 mL of methanol and 5 mL of water was added sufficient 0.01 M KOH solution to obtain pH 10.8. This mixture was stored at room temperature overnight, acidified with dilute HCl, saturated with NaCl, and extracted with chloroform and then ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, and evaporated to yield 43 mg of crude product which was purified by preparative TLC using 13:2:10 chloroform–acetic acid–cyclohexane to afford 24 mg (51%) of **22**: mp 95–97°; UV λ_{max} (99:1 H_2O–CH_3OH) 247.5 nm (ε 14 500);[21] IR 3300–2400, 1705, 1650, 1600 cm^{-1}; NMR δ 1.32 (s, 3), 5.89 (s, 1); mass spectrum m/e 222.1246 (M^+) (calcd for $C_{13}H_{18}O_3$, 222.1256). Anal. Calcd: C, 70.24; H, 8.16. Found: C, 69.91; H, 8.15.

8α-(Carboxymethyl)-10β-methyldecalin-2β,9β-diol (23). Exactly as in the oxidation of **12** to **16**, 83 mg (0.37 mmol) of **13** was treated with periodate–permanganate solution to afford 89 mg of crude product from which 37 mg (42%) of **23**, mp 158–159 °C, was obtained by crystallization from ether–hexane. An analytical sample was prepared by recrystallization from ethyl acetate: mp 161–163 °C; IR 3600–2400 (peaks at 3500, 3400), 1705 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.47; H, 9.12.

8α-(Carboxymethyl)-9β-hydroxy-10β-methyldecal-2-one (24). To a solution of 300 mg (1.24 mmol) of **23**, mp 161–163 °C, in 70 mL of acetone was added 0.60 mL of Jones reagent.[19] The mixture was stirred for 10 min and evaporated under reduced pressure with a minimum of heating. The residue was diluted with 50 mL of cold brine and extracted with cold ether (3 × 150 mL). The ether layers were combined, dried over $MgSO_4$, and evaporated to afford 250 mg of solid, which was recrystallized from ether to give 226 mg (76%) of **24**, mp 155–159 °C dec. Two further recrystallizations from ether–acetone gave pure **24**: mp 160–161 °C dec; IR 3600–2400 (peak at 3440), 1705 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.15; H, 8.44.

8α-(Carboxymethyl)-10β-methyl-Δ^{1,9}-octal-2-one (25). To a solution of 80 mg (0.333 mmol) of **24** in 10 mL of methanol was added 0.5 mL of 2 M KOH solution. The mixture was stirred at room temperature, and the disappearance of **24** was monitored by TLC using 13:2:10 chloroform–acetic acid–hexane. After 3 h the reaction was complete. Concentrated HCl was added to bring the pH to 2, and then the mixture was saturated with NaCl and extracted with ether (3 × 100 mL). The ether extracts were washed exhaustively with brine, dried over $MgSO_4$, and evaporated to yield 75 mg of yellow oil which was purified by preparative TLC to afford 65 mg (86%) of oily **25**, which was homogeneous by TLC. Crystallization from ether–hexane gave 36 mg (48%) of pure **25**: mp 121–123 °C; UV λ_{max} (99:1 H_2O–CH_3OH) 245.5 nm (ε 14 500);[21] IR 3300–2400, 1725, 1630, 1600 cm^{-1}; NMR δ 1.30 (s, 3), 5.74 (s, 1). Anal. Calcd for $C_{13}H_{22}O_3$: C, 70.24; H, 8.16. Found: C, 70.15; H, 8.36.

Conversion of 22 to 25. A solution of 40 mg (0.18 mmol) of **22**, mp 95–97 °C, in 10 mL of methanol was added dropwise to a solution of 58 mg (2.5 mmol) of Na metal in 15 mL of methanol, and the resulting mixture was stirred for 40 h at room temperature. The mixture was concentrated under reduced pressure to a volume of ca. 2 mL, diluted with 20 mL of brine, acidified with concentrated HCl, and extracted with ether. The ether extract was washed with brine, dried over $MgSO_4$, and evaporated to give 44 mg of yellow oil which TLC using 15:2:8 chloroform–acetic acid–hexane showed to be one major product with several minor impurities (both **22** and **25** have the same R_f value). This oil was purified by preparative TLC to afford 31 mg (76%) of **25**, mp 110–115 °C. Recrystallization from ether–hexane afforded 21 mg of **25**, mp 118–120 °C, which was identical by IR with previously prepared **25**. A mixture melting point was 117–120 °C.

8β-[(Carbomethoxy)methyl]-10β-methyldecalin-2β,9α-diol (29). To a solution of 2.0 g (8.3 mmol) of **16**, mp 195–197 °C dec, in a mixture of 200 mL of methanol and 300 mL of ether cooled

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(22) R. E. Schaub and M. J. Weiss, *J. Org. Chem.*, **26**, 1223 (1961).

to −10 °C was added the distilled ethereal diazomethane prepared from 6 g of EXR-101.[20] After the mixture was kept at room temperature for 2 h, excess diazomethane was destroyed by the addition of 0.5 mL of acetic acid, and the mixture was evaporated to afford a colorless oil which solidified on standing. Recrystallization from ether afforded 1.53 g (73%) of **29**, mp 106–108 °C. An analytical sample was prepared by recrystallization from ether: mp 106–107 °C; IR 3550, 3460, 1745, 1720 cm^{-1}; NMR δ 1.05 (s, 3), 3.65 (s, 3), 4.2 (m, 1). Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.50; H, 9.54.

8β-(2-Hydroxyethyl)-10β-methyldecalin-2β,9α-diol (28). Triol **28** was prepared both by direct reduction of **16** and more efficiently by reduction of **29**. As described above, 2.90 g (11.98 mmol) of **16** was esterified with ethereal diazomethane from 9 g of EXR-101.[20] The total crude product from this reaction was dissolved in 1.5 L of anhydrous ether and treated with 3.0 g of $LiAlH_4$. The mixture was stirred overnight at room temperature, and excess $LiAlH_4$ was destroyed by careful addition of ethyl acetate. Then, 150 mL of ethyl acetate, 150 mL of water, and 100 mL of 15% HCl were added. The organic layer was separated, washed with brine, dried over $MgSO_4$, and evaporated to give a residue which upon trituration with ether afforded 2.26 g (83%) of **28**, mp 173–175 °C. A further 0.065 g of pure **28** was obtained by the recrystallization from ethyl acetate of 0.395 g of impure second-crop material for a total yield of 2.32 g (85%). Recrystallization from ethanol afforded an analytical sample of **28**: mp 174–176 °C; IR 3480–3300 cm^{-1}; mass spectrum, m/e 228.1694 (M^+) (calcd for $C_{13}H_{24}O_3$, 228.1725). Anal. Calcd: C, 68.38; H, 10.59. Found: C, 67.94; H, 10.77.

8β-[2-(Tosyloxy)ethyl]-10β-methyldecalin-2β,9α-diol (30). To a solution of 1.140 g (5.00 mmol) of triol **28** in a mixture of 25 mL of pyridine and 20 mL of methylene chloride cooled in a dry ice–acetone bath was added an ice-cold solution of 1.24 g (6.50 mmol) of *p*-toluenesulfonyl chloride in 25 mL of methylene chloride dropwise with stirring over 10 min. The resulting mixture was stirred at −78 °C for 2 h, stored overnight at −10 °C, poured into 200 mL of H_2O, and extracted with a total of 750 mL of ethyl acetate. The organic layers were washed with 200 mL of H_2O, 5% HCl (3 × 150 mL), 5% K_2CO_3 (2 × 175 mL), and brine (3 × 150 mL), dried over $MgSO_4$, and concentrated under reduced pressure with only mild heating to afford 2.03 g of colorless oil, which TLC using ethyl acetate showed to contain a trace of **28**, one major component (**30**), and two less polar compounds. The product was chromatographed on a column of 100 g of grade I Florisil with ether–ethyl acetate as eluent. After elution of 0.696 g of oil with pure ether, crystalline fractions of **30** totaling 1.135 g were obtained as ethyl acetate was added to the eluent. Recrystallization from ether afforded 0.724 g of **30**, mp 90–94 °C. By further crystallization from mother liquors and by preparative TLC using ethyl acetate, a total of 0.924 g (48%) of pure **30**, mp 93–95 °C, was obtained. An analytical sample was prepared by recrystallization from ether: mp 93–94.5 °C; IR 3440, 3300, 1600, 1360, 1175 cm^{-1}; NMR δ 0.98 (s, 3), 2.43 (s, 3), 3.97 (t, 2), ~4.0 (m, 1), 7.59 (q, 4). Anal. Calcd for $C_{20}H_{30}O_5S$: C, 62.80; H, 7.91; S, 8.38. Found: C, 62.86; H, 7.98; S, 8.46.

The chief component of the earlier eluted oil is assumed to be **2β-(tosyloxy)-8β-[2-(tosyloxy)ethyl]-10β-methyldecal-9α-ol (31)** on the basis of its NMR spectrum: δ 0.95 (s, 3), 2.46 (s, 6), 3.96 (t, 2), 4.95 (m, 1), 7.57 (q, 8).

8β-[2-(*N*-Morpholino)ethyl]-10β-methyldecalin-2β,9α-diol (32). According to an adaptation of a procedure of Schaub and Weiss,[22] to a solution of 925 mg (2.42 mmol) of **30**, mp 92–95 °C, in 37 mL of pyridine was added 18.5 mL of distilled morpholine dropwise at room temperature with stirring. After 44 h at room temperature the reaction mixture was poured into 600 mL of ethyl acetate, washed with 75 mL of 5% $NaHCO_3$ and brine (2 × 75 mL), dried over $MgSO_4$, and evaporated to afford a residue which was crystallized from 120 mL of ether to yield 540 mg (76%) of **32**, mp 161–163 °C. A further 90 mg of impure solid **32** was obtained from the mother liquors for a total of 630 mg (88%). An analytical sample was prepared by recrystallization from ether: mp 162–162.5 °C; IR 3420, 3190 cm^{-1}; NMR δ 1.03 (s, 3), 2.3–2.5 (m, 6), 3.72 (~t, 4). Anal. Calcd for $C_{17}H_{31}NO_3$: C, 68.65; H, 10.51; N, 4.71. Found: C, 68.55; H, 10.40; N, 4.55.

8β-[2-(*N*-Morpholino)ethyl]-9α-hydroxy-10β-methyldecal-2-one (26). To a stirred solution at room temperature of 300 mg (1.01 mmol) of **32**, mp 161.5–163 °C, in 54 mL of acetone was added 0.40 mL of Jones reagent.[19] The mixture was stirred for 10 min, concentrated under reduced pressure to 10–15 mL, diluted with 100 mL of ice-cold 7.5% $NaHCO_3$, and extracted with ice-cold ether (3 × 175 mL). The combined ether layers were washed with ice-cold brine (3 × 75 mL), dried over $MgSO_4$, and evaporated to afford a residue which was crystallized from 8 mL of ether to yield 181 mg (61%) of **26**, mp 136–138 °C. From the mother liquors an additional 53 mg of solid **26** was obtained, for a total yield of 235 mg (79%). An analytical sample was prepared by recrystallization from ether: mp 138–138.5 °C; IR 3420, 1705 cm^{-1}; NMR δ 1.21 (s, 3), 2.3–2.5 (m, 6), 2.95 (d, 1, J = 15 Hz), 3.65 (~t, 4). Anal. Calcd for $C_{17}H_{29}NO_3$: C, 69.12; H, 9.89; N, 4.74. Found: C, 69.15; H, 9.82; N, 4.61.

8β-[2-(*N*-Morpholino)ethyl]-10β-methyl-2β,9α-diacetoxydecalin (33). A mixture of 230 mg (0.774 mmol) of **32**, 25 mL of isopropenyl acetate, bp 96–97 °C, and 175 mg (0.918 mmol) of *p*-toluenesulfonic acid was heated at 85 °C for 16 h and stored at room temperature for 4 h. The reaction mixture was diluted with an equal volume of benzene and concentrated under reduced pressure with minimum heating. The residue was dissolved in 300 mL of ether, washed with 5% $NaHCO_3$ (2 × 75 mL) and brine (2 × 25 mL), dried over $MgSO_4$, and evaporated to yield 290 mg (92%) of crude oily **33**, which TLC using 3:7 methanol–ethyl acetate showed to be one major component. Purification by preparative TLC gave 206 mg (68%) of pure colorless **33**. An analytical sample was prepared by distillation: bp 150 °C (0.05 mm); IR 1730 cm^{-1}; NMR δ 1.10 (s, 3), 2.02 (s, 3), 2.07 (s, 3), 2.3–2.8 (br m, 6), 3.7 (~t, 4), 4.8 (br m, 1). Anal. Calcd for $C_{21}H_{35}NO_5$: C, 66.11; H, 9.25; N, 3.67. Found: C, 66.06; H, 9.33; N, 3.76.

8β-[2-(Tosyloxy)ethyl]-10β-methyl-2β-acetoxydecal-9α-ol (34). A mixture of 244 mg (0.639 mmol) of **30**, mp 93–95 °C, 20 mL of isopropenyl acetate, bp 96–97 °C, and 20 mg of *p*-toluenesulfonic acid was stirred at room temperature for 3 h. The reaction mixture was diluted with an equal volume of benzene and concentrated under reduced pressure with minimum heating. The residue was purified by preparative TLC using 3:2 ethyl acetate–hexane to afford 262 mg of crude **34**. Crystallization from 1:1 ether–petroleum ether afforded, in several crops, a total of 220 mg (81%) of **34**, mp 128–132 °C. An analytical sample was prepared by recrystallization from ether: mp 134–135 °C; IR 3460, 1710 cm^{-1}; NMR δ 0.98 (s, 3), 2.00 (s, 3), 2.48 (s, 3), 3.97 (t, 2), 5.2 (m, 1), 760 (q, 4). Anal. Calcd for $C_{22}H_{32}O_6S$: C, 62.24; H, 7.60; S, 7.55. Found: C, 62.08; H, 7.53; S, 7.42.

8β-[2-(Tosyloxy)ethyl]-10β-methyl-2β,9α-diacetoxydecalin (35). A mixture of 729 mg (1.908 mmol) of **30**, mp 92–94 °C, 60 mL of isopropenyl acetate, and 100 mg of *p*-toluenesulfonic acid was stirred at 75–95 °C for 18 h. The reaction mixture was worked up as in the conversion of **32** to **33** to give a dark yellow oil which was purified by preparative TLC using 1:1 ethyl acetate–hexane to afford 906 mg of oil which was crystallized from ether–hexane to yield 711 mg (80%) of **35**, mp 81–88 °C. The mother liquors yielded 127 mg more of oily **35**. An analytical sample was prepared by recrystallization from ether–hexane: mp 88.5–89 °C; IR 1735, 1600 cm^{-1}; NMR δ 1.05 (s, 3), 1.97 (s, 3), 2.02 (s, 3), 2.45 (s, 3), 3.95 (t, 2), 4.85 (m, 1), 7.6 (q, 4). Anal. Calcd for $C_{24}H_{34}O_7S$: C, 61.78; H, 7.35; S, 6.87. Found: C, 61.93; H, 7.42; S, 6.92. It should be noted that even when quite pure, **35** decomposed upon prolonged storage. Diacetoxy tosylate **35** was also prepared from monoacetate **34** under comparable conditions.

Conversion of 35 to 33. As in the preparation of **32** from **30**, 600 mg (1.20 mmol) of **35**, mp 81–88 °C, in 20 mL of pyridine was treated with 10 mL of morpholine for 22 h. The same workup and purification by preparative TLC afforded 360 mg (73%) of **33**, identical in the IR region with **33** obtained from **32** by acetylation.

8β-[2-(*N*-Morpholino)ethyl]-9α-acetoxy-10β-methyldecal-2β-ol (36). To a solution of 360 mg (0.945 mmol) of **33** in 14.3 mL of methanol was added 1.34 mL of 5% NaOH, and the mixture was stirred at room temperature for 1 h. The mixture was diluted with 300 mL of ethyl acetate, washed with brine (3 × 80 mL), dried over $MgSO_4$, and concentrated to afford a solid residue, which TLC using 1:1 methanol–ethyl acetate showed to be principally one component, neither **35** nor **30**. Recrystallization from ether gave 283 mg (88%) of pure **36**, mp 118–120 °C. An analytical sample was obtained from ether: mp 119–120 °C; IR

3200, 1720 cm^{-1}; NMR δ 1.08 (s, 3), 2.00 (s, 3), 2.2–2.6 (br m, ~6), ~3.7 (m, 1), 3.75 (~t, 4). Anal. Calcd for $C_{19}H_{33}NO_4$: C, 67.22; H, 9.80; N, 4.13. Found: C, 67.07; H, 9.82; N, 3.97.

8β-[2-(*N*-Morpholino)ethyl]-9α-acetoxy-10β-methyldecal-2-one (27). To a solution of 75 mg (0.221 mmol) of **36**, mp 118–119.5 °C, in 12 mL of acetone was added 0.1 mL of Jones reagent[19] with stirring at room temperature. After 10.0 min, 40 mL of ice-cold 5% $NaHCO_3$ was added quickly, and the mixture was extracted quickly with 200 mL of ether which had been cooled to −10 °C. The organic layer was washed with brine (2 × 75 mL) at −10 °C, dried over $MgSO_4$, and concentrated under reduced pressure without heating to afford a solid residue which was quickly recrystallized from 4 mL of ether to afford 55.5 mg (74%) of **27**, mp 123–125 °C. An analytical sample was obtained from ether: mp 120–121 °C; IR 1725, 1710 cm^{-1}; NMR δ 1.28 (s, 3), 1.93 (s, 3), 2.25–2.5 (m, ~6), 2.75 (d, 1, J = 15 Hz), 3.37 (d, 1, J = 15 Hz), 3.7 (~t, 4). Anal. Calcd for $C_{19}H_{31}NO_4$: C, 67.63; H, 9.26; N, 4.15. Found: C, 67.69; H, 9.20; N, 4.11.

8β-[2-(*N*-Morpholino)ethyl]-10β-methyl-Δ^{1,9}-octal-2-one (37). A rapidly prepared solution of 24 mg (0.071 mmol) of **27**, mp 123–125 °C, in 250 μL of CD_3OD was monitored by NMR. Over a period of 55 min, a singlet developed at δ 5.77, and the initial singlet for the CH_3COO function of **27** at δ 1.92 was replaced by a singlet at δ 1.95, indicating conversion of **27** to **37** plus CH_3COOH. No further change in the NMR spectrum occurred over 24 h. The mixture was diluted with ether, washed twice with 5% $NaHCO_3$, and once with brine, dried over $MgSO_4$, and evaporated to give essentially pure **37**: NMR δ 1.30 (s, 3), 2.5 (~t, 6), 3.7 (~t, 4), 5.72 (s, 1). An analytical sample of **37** was prepared by two distillations of material formed by dehydration of **26** and had the following: bp 140–145 °C (0.05 mm); UV λ_{max} (99:1 H_2O–CH_3OH) 247 nm (ε 11 000);[21] IR 1740, 1610 cm^{-1}; NMR same as above. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.57; H, 9.72; N, 4.78.

8α-[2-(*N*-Morpholino)ethyl]-10β-methyl-Δ^{1,9}-octal-2-one (38). A sample of **37** was prepared from the reaction of 25 mg (0.085 mmol) of **26** in a mixture of 9 mL of CH_3OH and 1 mL of 5% K_2CO_3 solution at room temperature. The progress of the reaction was monitored by UV spectroscopy, and it was complete after 2 h. The mixture was concentrated under reduced pressure and partitioned between ether and water. The ether layer was dried over $MgSO_4$ and evaporated to afford 26 mg of oil which had an IR spectrum identical with that of **37** prepared above and had NMR (C_6D_6) peaks at δ 0.95 (s, 3), 2.15 (~t, 6), 3.6 (~t, 4), and 5.84 (s, 1), plus a trace of the peaks characteristic of **38** described below. To the C_6D_6 solution of this 26 mg of crude **37** was added 30 μL of a solution of 20 mg of sodium in 250 μL of CD_3OH, and the mixture was monitored by NMR. Over a period of about 40 h the peaks at δ 0.95 and 5.84 diminished and were replaced by peaks at δ 0.85 and 5.93, indicating conversion of **37** to **38**. After 4 days there still appeared to be a trace of **37**, but the mixture was partitioned between ether and water, and the ether layer was dried over $MgSO_4$ and evaporated to afford 22 mg of crude **38** which was distilled to give 12 mg of **38**, bp 150–160 °C (0.1 mm), still contaminated with a trace of **37**. This sample of **38** had an IR spectrum slightly different in the fingerprint region from that of **37** and had the following: UV λ_{max} (99:1 H_2O–CH_3OH) 247 nm (ε 11 000);[21] NMR (C_6D_6) δ 0.85 (s, 3), 2.15 (~t, 6), 3.6 (~t, 4), 5.93 (br s, 1); mass spectrum, m/e 277.2056 (M^+) (calcd for $C_{17}H_{27}NO_2$, 277.2042).

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Registry No. 3a, 4087-39-2; **6**, isomer 1, 18676-25-0; **6**, isomer 2, 72938-77-3; **7**, 72938-40-0; **8**, 72938-41-1; **9**, 72938-42-2; **10**, 72938-43-3; **11**, 72938-44-4; **12**, 72938-45-5; **13**, 72938-46-6; **14**, 72984-22-6; **15**, 72938-47-7; **16**, 72938-48-8; **17**, 72938-49-9; **18**, 72938-50-2; **19**, 72938-51-3; **20**, 72938-52-4; **21**, 72968-12-8; **22**, 72938-53-5; **23**, 72938-54-6; **24**, 72938-55-7; **25**, 72938-86-8; **26**, 72938-57-9; **27**, 72938-58-0; **28**, 72938-59-1; **29**, 72938-60-4; **30**, 72938-61-5; **31**, 72968-06-0; **32**, 72938-33-1; **33**, 72938-34-2; **34**, 72938-35-3; **35**, 72938-36-4; **36**, 72938-37-5; **37**, 72938-38-6; **38**, 72938-39-7.

Chemistry of Sulfenic Acids. 1. Synthesis of Trimethylsilyl Arenesulfenates (Arenesulfenic Acids)

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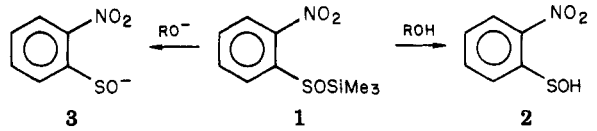
Trimethylsilyl arenesulfenates (**5**), masked sulfenic acids, are prepared in low yield by trapping the intermediate arenesulfenic acid generated by thermolysis of the corresponding *N*-benzylidenearenesulfinamide (**4**) with chlorotrimethylsilane–hexamethyldisilazane. Attempts to prepare **5** by oxidation of trialkyl(phenylthio)silanes (**8**) with 2-(benzenesulfonyl)-3-phenyloxaziridine (**11**), an aprotic oxidizing reagent, gave instead the previously unknown trialkylsilyl benzenesulfinates (**12**). These results are attributed to the enhanced nucleophilicity (α effect) of the intermediate trialkylsilyl arenesulfenate ester.

The importance of sulfenic acids (RSOH) as key intermediates in a wide variety of chemical transformations including biological ones is well recognized.[1] However, the difficulty in studying these species stems not only from their high reactivity but also from the lack of mild methods to generate them. Recently we reported that trimethylsilyl 2-nitrobenzenesulfenate (**1**) was a convenient, high-yield source of 2-nitrobenzenesulfenic acid (**2**) and 2-nitrobenzenesulfenate ion (**3**) when treated with alcohols and alkoxides, respectively.[2] The success of this approach in generating these species under comparatively mild,



3 **1** **2**

(1) For reviews of sulfenic acids see (a) F. A. Davis, A. J. Friedman, and U. K. Nadir, *J. Am. Chem. Soc.*, **100**, 2844 (1978); (b) D. R. Hogg in *Compr. Org. Chem.*, **4**, 261 (1979).

(2) F. A. Davis and A. J. Friedman, *J. Org. Chem.*, **41**, 897 (1976).

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