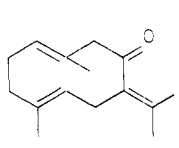
mophore may be overshadowed by contributions from the dissymmetric environment. In the present case the latter contributions seem to be weakly negative.

The absolute configurations shown in the formulas harmonize (model) with the positive Cotton effect in the 240-nm region if, as is generally assumed, the chirality of an α,β-unsaturated ketone chromophore is related to the sign of the π,π^* Cotton effect. However, since the sign and shape of the CD curves of 2–4 in the 240-nm region result from superposition of two Cotton effects—n,π^* of lactone and π,π^* of ketone—the observed agreement may be entirely fortuitous.



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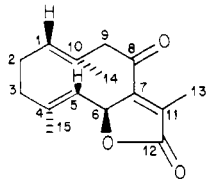

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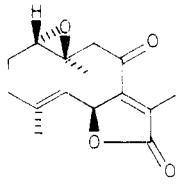

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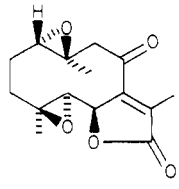

4

Experimental Section

Aerial parts (5.5 kg) (except for the wood) of *Wunderlichia mirabilis* Riedel, collected by Dr. Hermogenes de Freitas Leitão Filho in Serra da Canastra, Minas Gerais, Brasil, in December 1977, were extracted with $CHCl_3$ giving 140 g of crude extract which was worked up in the usual manner.[16] The resulting 15 g of crude gum was chromatographed over 420 g of silica gel, 450-mL fractions being eluted in the following order: 1–3 (hexane–EtOAc, 6.6:1), 4–13 (hexane–EtOAc, 4:1), 14–21 (hexane–EtOAc, 2.8:1), 22–31 (hexane–EtOAc, 2.2:1), 32–46 (EtOAc), 47–54 (EtOAc–MeOH, 2:1), 55 (MeOH). The solids of fractions 4 and 5 were combined and purified by recrystallization from hexane to give 220 mg of **2**: mp 116–118 °C; IR (KBr) 1767, 1678, 1660, 1635, 990, 980, 898, 850 cm^{-1}; UV λ_{max} 218, 314 nm (ϵ 13900, 740): CD curve (MeOH) $[\theta]_{308}$ 22900, $[\theta]_{257}$ −15300 (minimum), $[\theta]_{254}$ −15200 (inflecton), $[\theta]_{238}$ −19000 (minimum), $[\theta]_{214}$ 17000 (last reading).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37; mol wt 246.1255. Found: C, 73.24; H, 7.48; mol wt (mass spectrometry) 246.1278.

Other significant peaks in the high-resolution mass spectrum appeared at *m/e* (composition, %) 231 ($C_{14}H_{15}O_3$, $M^+ - CH_3$, 5.6), 228 ($C_{15}H_{16}O_2$, $M^+ - H_2O$, 4.6), 218 ($C_{14}H_{18}O_2$, $M^+ - CO$, 8.0), 217 ($C_{14}H_{17}O_2$, 11.4), 213 ($C_{14}H_{13}O_2$, 5.2), 204 ($C_{13}H_{16}O_2$, 5.2), 203 ($C_{13}H_{15}O_2$, 12.1), 200 ($C_{14}H_{16}O$, 5.5), 190 ($C_{11}H_{10}O_3$, 6.2), 185 ($C_{13}H_{13}O$, 5.6), 163 ($C_9H_7O_3$, 17.3), 149 ($C_9H_9O_2$, 19.0), 135 ($C_8H_7O_2$, 19.8), 124 ($C_6H_4O_3$, 100), 122 (C_9H_{14}, 14.3), 121 (C_9H_{13}, 58).

Epoxidation of 2. To an ice-cold solution of 50 mg of **2** in 3 mL of $CHCl_3$ was added 100 mg of *m*-chloroperbenzoic acid in 5 mL of $CHCl_3$. The solution was stirred for 1 h at 0 °C, washed with $NaHCO_3$ solution and water, and dried and evaporated. The residue was purified by TLC (silica gel, MeOH–$CHCl_3$, 2:1). The upper band containing the monoepoxide **3** was recrystallized from $CHCl_3$–hexane: yield 20 mg, mp 171–172 °C. The NMR spectrum is given in Table I.

Anal. Calcd for $C_{15}H_{18}O_4$: mol wt 262.1204. Found: mol wt (mass spectrometry) 262.1195 (3.3%).

Other significant peaks in the high-resolution mass spectrum appeared at *m/e* (composition, %) 247 ($M^+ - CH_3$, 1.0), 244 ($M^+ - H_2O$, 2.2), 234 ($M^+ - CO$, 0.6), 234 ($C_{14}H_{14}O_4$, 0.9), 219 ($C_{13}H_{15}O_3$, 3.4), 204 ($C_{12}H_{12}O_3$, 12.8), 202 ($C_{13}H_{14}O_2$, 2.4), 201 ($C_{13}H_{13}O_2$, 2.5), 194 ($C_{10}H_{10}O_4$, 1.8), 192 ($C_{11}H_{12}O_3$, 2.2), 191 ($C_{12}H_{15}O_2$, 1.6), 189 ($C_{11}H_9O_3$, 1.7), 187 ($C_{12}H_{11}O_2$, 1.4), 179 ($C_{10}H_{11}O_3$, 3.2), 178 ($C_{11}H_{14}O_2$, 5.4), 178 ($C_{10}H_{10}O_3$, 3.1), 177 ($C_{11}H_{13}O_2$, 7.6), 176 ($C_{11}H_{12}O_2$, 4.8), 175 ($C_{11}H_{11}O_2$, 3.9), 161 ($C_{10}H_9O_2$, 3.7), 150 ($C_9H_{10}O_2$, 6.5), 149 ($C_9H_9O_2$, 7.4), 140 ($C_7H_8O_3$, 88), 137 ($C_9H_{13}O$, 4.0), 135 ($C_9H_{11}O$, 4.1), 133 (C_9H_9O, 4.0), 131 (C_9H_{11}, 4.9), 124 ($C_6H_4O_3$, 55.9), 124 ($C_8H_{12}O$, 12.7), 81 (C_6H_9, 100).

The lower band from the TLC purification furnished the diepoxide **4** which was recrystallized from $CHCl_3$: yield 15 mg, mp 185–186 °C. The NMR spectrum is given in Table I.

Anal. Calcd for $C_{15}H_{18}O_5$: mol wt 278.1153. Found: mol wt (mass spectrometry) 278.1158 (1.0%).

Other significant peaks in the high-resolution mass spectrum appeared at *m/e* (composition, %) 260 ($C_{15}H_{16}O_4$, 2.9), 249 ($C_{14}H_{17}O_4$, 9.8), 235 ($C_{13}H_{15}O_4$, 19.1), 231 ($C_{14}H_{15}O_3$, 4.1), 222 ($C_{12}H_{14}O_4$, 2.8), 221 ($C_{13}H_{17}O_3$, 10.5), 220 ($C_{12}H_{12}O_4$, 9.1), 218 ($C_{13}H_{14}O_3$, 8.5), 217 ($C_{13}H_{13}O_3$, 18.3), 207 ($C_{12}H_{15}O_3$, 12.3), 193 ($C_{11}H_{13}O_3$, 23.0), 192 ($C_{11}H_{12}O_3$, 20.4), 191 ($C_{11}H_{11}O_3$, 17.6), 178 ($C_{10}H_{10}O_3$, 21.5), 176 ($C_{11}H_{12}O_2$, 30.3), 175 ($C_4H_{11}O_2$, 19.2), 161 ($C_{10}H_9O_2$, 14.0), 150 ($C_9H_{10}O_2$, 13.9), 149 ($C_9H_9O_2$, 15.3), 138 ($C_7H_6O_3$, 15.5), 131 ($C_{10}H_{11}$, 15.0), 125 ($C_6H_5O_3$, 40.3), 124 ($C_6H_4O_3$, 100).

Registry No. 1, 6902-91-6; 2, 70224-78-1; 3, 70224-79-2; 4, 70224-80-5.

(16) W. Herz and G. Högenauer, *J. Org. Chem.*, 27, 905 (1962).

Rotenoid Interconversion. Synthesis of Deguelin from Rotenone

Peter B. Anzeveno

Pharmaceutical Research and Development—Medicinal Chemistry Group, The Dow Chemical Company, Indianapolis, Indiana 46268

Received January 29, 1979

During an investigation of the inhibitory effects of various naturally occurring rotenoids on slow reacting substance of anaphylaxis (SRS-A), an important chemical mediator in the allergic response mechanism, we were met by the need to provide greater and more readily accessible amounts of deguelin (**1**) than we could obtain from natural sources. Consequently, we sought a convenient preparation of **1**.

The reported deguelin syntheses[1] are lengthy and low-yielding processes. Moreover, none afford optically pure product. Since we considered that a new deguelin total synthesis was unjustified, we thought a logistically better solution to our problem would be the development of a scheme for the conversion of the readily available (−)-rotenone (**2**) to **1**. An important benefit of this strategy was that it allowed the preparation of natural **1**. We have recently succeeded in achieving this conversion to natural (−)-**1** and, in this note, describe our results.

Unai and Yamamoto have reported the selective cleavage of the E ring of rotenone by reaction with boron tribromide (1 equiv) in dichloromethane at −10 °C.[2] The 1′,5′-seco bromide **3** so obtained possesses natural rotenoid stereochemistry at the B/C ring juncture. Our initial strategy (Scheme I) was to convert **3**, by syn elimination of phenylsulfinic or -seleninic acid from the sulfoxide (selenoxide) **4**, to diene **5** and thence to **1** by acid-catalyzed cyclization of **5**.

(1) (a) H. Fukami, J. Oda, S. Sakata, and M. Nakajima, *Agric. Biol. Chem.*, **25**, 252 (1961); (b) H. Omokawa and K. Yamashita, *ibid.*, **38**, 1731 (1974).

(2) T. Unai and I. Yamamoto, *Agric. Biol. Chem.*, **37**, 897 (1973).

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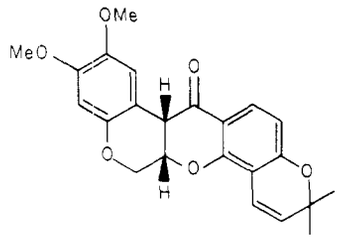
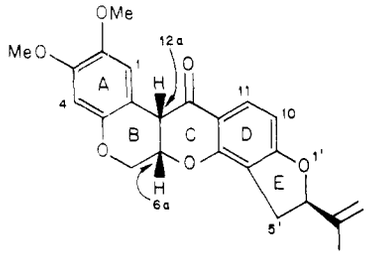
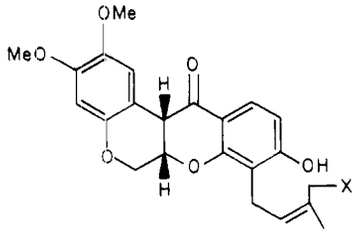


1

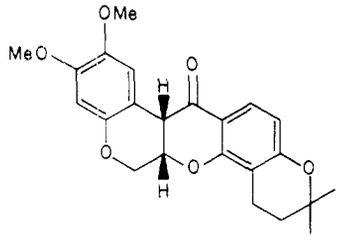


2

Treatment of **3** with sodium thiophenoxide, under a variety of reaction conditions, afforded sulfide **6** as the only



6, X = SPh
7, X = Br
8, X = H



9

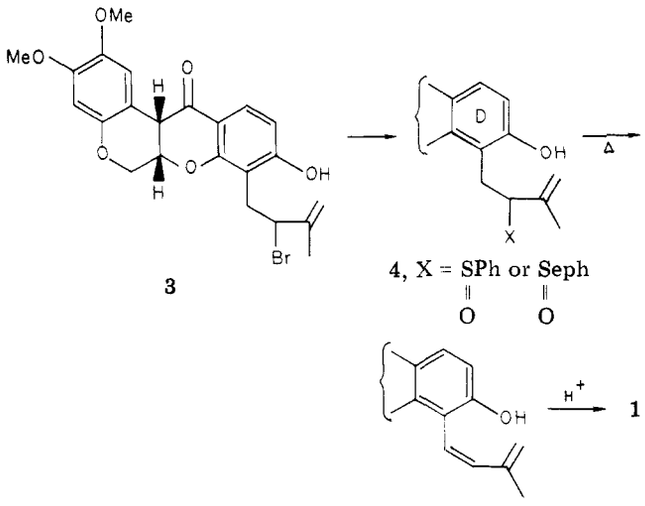
sulfur-containing product, formed, presumably, by reaction in an S_N2' sense. During these initial experiments, however, we happened upon a communication by Crombie et al., which argued, on the basis of ^1H and ^{13}C magnetic resonance data, that the structure of the boron tribromide cleavage product of rotenone was not **3** but **7**, generated by intramolecular S_N2' displacement of phenoxide by bromide in the intermediate benzofuran–boron tribromide complex.[3] This result served to corroborate our observed formation of **6**. We were forced, then, to seek alternate routes to **1**.

Crombie[3] had shown that reduction of **7** with sodium cyanoborohydride in hexamethylphosphoramide affords (−)-rot-2′-enonic acid (**8**). In our hands, reaction of **8** in refluxing benzene containing 10 mol % of *p*-toluenesulfonic acid gave a nearly quantitative yield of (−)-dihydrodegeulin (**9**), identical in all respects with that obtained by palladium-catalyzed hydrogenation of **1**[4] and with that material, called β-dihydrorotenone by Haller, generated by disso-

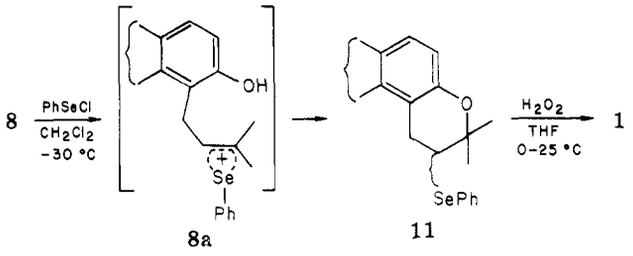
(3) (a) D. Carson, L. Crombie, and D. A. Whiting, *J. Chem. Soc., Chem. Commun.*, 851 (1975); (b) L. Crombie, P. W. Freeman, and D. A. Whiting, *ibid.*, 1277 (1973).

(4) H. L. Haller and F. B. La Forge, *J. Am. Chem. Soc.*, **56**, 2415 (1934).

Scheme I



Scheme II



lution of **8** in a hot acetic–sulfuric acid mixture.[5] We could find no method that would effect selective oxidation of the E ring of **9** in the presence of its more oxidatively labile B/C ring juncture.[6]

Nicolau and Lysenko have recently reported the preparation of cyclic β-phenylselenoethers by the low-temperature reaction of appropriately substituted olefinic alcohols with phenylselenyl chloride.[7] The reaction is believed to proceed by intramolecular opening of an initially formed phenylselenonium ion by the hydroxyl group. Mechanistic considerations led us to speculate that if **8** was subjected to these cyclization conditions, the major product would be that formed by cyclization in the desired deguelin sense; i.e., attack of the phenolic hydroxyl group at the more stable tertiary cationic center of the intermediate selenonium ion **8a** should be favored. This hypothesis had already been somewhat substantiated by the simple acid-catalyzed cyclization of **8**, a reaction which can be envisioned as proceeding through a like cationic species. Not surprisingly then, when **8** was treated at −30 °C in dichloromethane solution with 1 equiv of phenylselenyl chloride, the chromane selenoethers **11** (as an inseparable 1:1 mixture of epimers at carbon 5′) were the sole products isolated.[8] Peroxide oxidation of this mixture of selenoethers then gave an 82% yield of (−)-**1**, identical with the natural material in all respects (Scheme II).[4,9]

(5) H. L. Haller, *J. Am. Chem. Soc.*, **53**, 733 (1931).

(6) As an example, the crude product mixture, obtained upon workup after 1 h of a reaction of **9** and DDQ (1 equiv) in refluxing benzene, contained no deguelin and consisted predominantly of unreacted **9** and ~15% of 6a,12a-dehydrodihydrodeguelin. These conditions, reportedly effective for the conversion of chromanes to chromenes (G. Cardillo, R. Cricchio, and L. Merlini, *Tetrahedron*, **24**, 4825 (1968)), were the mildest we tried.

(7) K. C. Nicolau and Z. Lysenko, *Tetrahedron Lett.*, 1257 (1977).

(8) This selectivity to chromane cyclization products was established by the observation that no rotenoid (benzofuran) products could be detected upon subsequent peroxide oxidation of the mixture of phenylselenoethers **11**.

Experimental Section

All melting points were determined on a Thomas Hoover "Uni-Melt" capillary melting apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 727B grating spectrophotometer. Nuclear magnetic resonance spectra were recorded at 60 MHz on a Varian EM 360 A spectrometer, with tetramethylsilane used as an internal standard. Low resolution mass spectra were obtained on a Finnigan 4023 GC/MS/DS instrument operated in the electron impact mode (70 eV). Optical rotations were measured at ambient temperature on a Rudolph Model 62 polarimeter, using a 1-dm tube. Analytical TLC was performed on Brinkmann silica gel 60-F254 precoated (0.25 mm) glass plates and preparative layer chromatography on Brinkmann 20 × 20 cm glass plates coated with the same adsorbent (2 mm). Column chromatography was performed on columns packed with J. T. Baker ("Baker Analyzed") silica gel powder of 60–200-mesh particle size. Microanalyses were performed by either Galbraith Laboratories Inc. or Midwest Microlabs Inc.

4′-Bromo-rot-2′-enonic Acid (7). The method of Unai and Yamamoto was employed.[2] The white crystalline product was filtered, washed with a small amount of methanol, and dried in vacuo to give 6.1 g (51%) of **7**, mp 151–152 °C (lit.[2] mp 152–154 °C), based on 10.0 g (25.4 mmol) of rotenone and 6.4 g (25.5 mmol) of boron tribromide: NMR ($CDCl_3$) δ 7.73 (d, 1, J = 9 Hz), 6.78 (s, 1), 6.51 (d, 1, J = 9 Hz), 6.44 (s, 1), 5.60 (br t, 1, J = 7 Hz), 4.90 (m, 1), 4.60 (dd, 1, J = 12, 3.5 Hz), 4.14 (d, 1, J = 12 Hz, 3.89 (s, 2), 3.86 (d, 1, J = 3.5 Hz), 3.80 (s, 3), 3.74 (s, 3), 3.37 (d, 2, J = 7 Hz), 1.91 (s, 3).

4′-Phenylthio-rot-2′-enonic Acid (6). Thiophenol (0.3 g, 2.7 mmol) was added in one portion to a stirred suspension of 99% NaH (65 mg, 2.7 mmol) in 5 mL of anhydrous THF. The resulting mixture was stirred at room temperature under nitrogen until H_2 evolution ceased (1 h). A solution of **7** (1.2 g, 2.5 mmol) in 4 mL of THF was then added and the mixture stirred at room temperature for 12 h after which it was heated to reflux and refluxed for 30 min. After dilution with water (20 mL), the organic layer was separated and the aqueous layer further extracted with ether. The combined organic extracts were then washed with saturated brine, dried ($MgSO_4$), and evaporated. The residue (1.2 g) was purified by chromatography on silica gel (60 g) utilizing CH_2Cl_2–acetone mixtures (to 9:1) as eluent. Compound **6** was obtained as a yellow foam: 0.9 g (71%); $[\alpha]^{25}_D$ −7.3° (c 2.2, $CHCl_3$); NMR ($CDCl_3$) δ 7.80 (d, 1, J = 9 Hz), 6.95–7.40 (m, 6), 6.85 (s, 1), 6.58 (d, 1, J = 9 Hz), 6.50 (s, 1), 5.30 (br t, 1, J = 7 Hz), 4.68 (dd, 1, J = 12, 3.5 Hz), 4.78 (m, 1), 4.13 (d, 1, J = 12 Hz), 3.88 (d, 1, J = 3.5 Hz), 3.81 (s, 3), 3.75 (s, 3), 3.20–3.53 (m, 4), 1.93 (br s, 3); mass spectrum m/z (relative intensity) 504 (2), 394 (2), 203 (16), 192 (100). Anal. Calcd for $C_{29}H_{28}O_6S$: C, 69.04; H, 5.59. Found: C, 68.80; H, 5.32.

(−)-Rot-2′-enonic Acid (8). To a solution of **7** (1.9 g, 4.0 mmol) in 20 mL of HMPA was added 1.0 g (16 mmol) of sodium cyanoborohydride. The resulting solution was heated to 70 °C under nitrogen, maintained at that temperature for 2.5 h and then cooled to room temperature, and diluted with water (200 mL). The crude product which separated was extracted with ether–hexane (3:1). The combined extracts were then washed with saturated brine, dried ($MgSO_4$), and evaporated to dryness. Purification of the residue (1.4 g) by chromatography over 70 g of silica gel with CH_2Cl_2–acetone (9:1) afforded 1.1 g (70%) of pure **8**. An analytical sample was obtained by recrystallization from methanol: mp 207–208 °C (lit.[3] 206–208 °C); $[\alpha]^{27}_D$ +27.9° (c 2.0, $CHCl_3$); NMR ($CDCl_3$) δ 7.84 (d, 1, J = 9 Hz), 6.88 (s, 1), 6.75 (br s, 1), 6.60 (d, 1, J = 9 Hz), 6.54 (s, 1), 5.28 (br t, 1, J = 7 Hz), 4.99 (t, 1, J = 3.5 Hz), 4.70 (dd, 1, J = 12, 3.5 Hz), 4.20 (d, 1, J = 12 Hz), 3.88 (d, 1, J = 3.5 Hz), 3.83 (s, 3), 3.78 (s, 3), 3.40 (d, 2, J = 7 Hz), 1.80 (s, 3), 1.70 (s, 3). Anal. Calcd for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.80; H, 6.09.

(−)-Dihydrodeguelin (9). A solution of **8** (1.3 g, 3.2 mmol) and 0.2 g of tosic acid in benzene (60 mL) was refluxed with stirring under nitrogen for 1 h. The solution was then cooled to room temperature, diluted with more benzene (25 mL), washed successively with water, 5% $NaHCO_3$, and brine, and dried ($MgSO_4$). Concentration left 1.3 g of crude **9**. Recrystallization from methanol afforded analytically pure material: mp 155–156 °C (lit.[4] mp 155–156 °C); $[\alpha]^{27}_D$ −98.1° (c 4.1, benzene); NMR ($CDCl_3$) δ 7.80 (d, 1, J = 9 Hz), 6.90 (s, 1), 6.50 (d, 2, J = 9 Hz), 6.50 (s, 1), 4.95 (t, 1, J = 3.5 Hz), 4.70 (dd, 1, J = 12, 3.5 Hz), 4.20 (d, 1, J = 12 Hz), 3.87 (d, 1, J = 3.5 Hz), 3.84 (s, 3), 3.80 (s, 3), 2.69 (t, 2, J = 7 Hz), 1.77 (t, 2, J = 7 Hz), 1.34 (s, 3), 1.28 (s, 3). Anal. Calcd for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.75; H, 6.48.

(−)-Deguelin (1). To a stirred, nitrogen-blanketed solution of **8** (1.98 g, 5 mmol) in CH_2Cl_2 (60 mL), cooled to −30 °C in a dry ice–acetone bath, 1.05 g (5.5 mmol) of phenylselenyl chloride was added in one portion. The resulting solution was allowed to warm to room temperature during 2 h and stirred an additional 1 h. Evaporation of the solvent at reduced pressure left 2.9 g of a diastereomeric mixture (1:1) of phenylselenoethers **11**, contaminated with a small amount of PhSeCl: NMR ($CDCl_3$) δ 7.82 (d, 1, J = 9 Hz), 7.20–7.72 (m, 5), 6.87 (s, 1), 6.40–6.67 (m, 2), 4.94 (m, 1), 4.68 (dd, 1, J = 12, 3.5 Hz), 4.18 (d, 1, J = 12 Hz), 3.88 (d, 1, J = 3.5 Hz), 3.85 (s, 3), 3.80 (s, 3), 3.30–3.60 and 2.80–3.20 (m, total 3 H), 1.53, 1.47, 1.43, and 1.33 (s, total 6 H).

The above product mixture was dissolved in THF (60 mL), cooled to 0 °C and treated with 1.0 mL (~9 mmol) of 30% hydrogen peroxide solution. The resulting solution was stirred for 1 h at 0–5 °C and then at room temperature for 18 h, diluted with ether (60 mL), and washed successively with two 20-mL portions of 5% $NaHCO_3$ and saturated brine. After drying ($MgSO_4$), evaporation of the solvent left 2.1 g of oily residue which was chromatographed over 100 g of silica gel with CH_2Cl_2–acetone mixtures (to 95:5). Pure (−)-deguelin was obtained as a bright yellow oil: 1.6 g (81%); $[\alpha]^{27}_D$ −97.2° (c 0.2, benzene); NMR ($CDCl_3$) δ 7.83 (d, 1, J = 9 Hz), 6.87 (s, 1), 6.74 (d, 1, J = 10 Hz), 6.54 (s, 1), 6.54 (d, 1, J = 9 Hz), 5.61 (d, 1, J = 10 Hz), 4.97 (m, 1), 4.71 (dd, 1, J = 12, 3.5 Hz), 4.21 (d, 1, J = 12 Hz), 3.88 (d, 1, J = 3.5 Hz), 3.86 (s, 3), 3.82 (s, 3), 1.47 (s, 3), 1.40 (s, 3). Anal. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62. Found: C, 69.70; H, 5.32.

Acknowledgments. The author thanks his colleagues Dr. Robert J. Cregge and Dr. Norton P. Peet for helpful discussions and Mr. Robert J. Barbuch for the mass spectral and optical data.

Registry No. **1**, 522-17-8; **6**, 70145-43-6; **7**, 70191-70-7; **8**, 70191-71-8; **9**, 70145-44-7; **11** isomer 1, 70145-45-8; **11** isomer 2, 70191-72-9; thiophenol, 108-98-5; phenylselenyl chloride, 5707-04-0.

(9) D. G. Carlson, D. Weisleder, and W. H. Tallent, *Tetrahedron*, **29**, 2731 (1973).

Structural Studies of Organosulfur Compounds. 4. Stereochemistry and Conformational Properties of α- and β-2-Methoxy-*trans*-hexahydrobenzoxathiane 4,4-Dioxides

Dorothy Lee, John C. Keifer, Robert P. Rooney, Timothy B. Garner, and Slayton A. Evans, Jr.*

The William Rand Kenan, Jr., Laboratories of Chemistry, The University of North Carolina, Chapel Hill, North Carolina 27514

Received April 3, 1979

In previous report,[1] we described the stereochemistry and conformational properties of α- and β-2-methoxy-*trans*-hexahydrobenzoxathiane (**1α, 1β**) and our results indicated that the 2-methoxy group prefers the equatorial or α conformation by as much as 2.07 kJ/mol (0.49 kcal/mol) in cyclohexane solvent. We attributed this preference to repulsive steric and Coulombic interactions between the methoxy oxygen and the ring sulfur and the synaxial hydrogen at C9. The Coulombic interaction

(1) S. A. Evans, Jr., B. Goldsmith, R. L. Merrill, Jr., and R. E. Williams, *J. Org. Chem.*, **42**, 438 (1977).

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