C, 69.21; H, 7.74, neut equiv, 208.3. Found: C, 69.47; H, 7.94 neut equiv, 208.4.

Methyl 3-(4'-Methyl-3'-oxo-1'-cyclohexenyl)butanoate (11).[11]—The preceding acid (29.2 g, 0.14 mol) in purified tetrahydrofuran (600 ml) and dry *tert*-butyl alcohol (600 ml) was added gradually to distilled, stirred liquid ammonia (1500 ml). With continued stirring, lithium metal (16.7 g, 2.4 mol) was added in small pieces during 45 min. The deep blue solution was stirred for 5 hr, then quenched with methanol (150 ml) and stirred overnight during evaporation of the ammonia. Water was added and the organic solvents were removed *in vacuo*. The residue was diluted with water to 2 l., then cooled in ice, acidified with cold 4 *N* hydrochloric acid, and quickly extracted thrice with ether. The combined extracts were dried, cooled in ice, and mixed with an excess of ethereal diazomethane. The ether solution was washed with aqueous sodium bicarbonate and water, dried, and concentrated. The residue was stirred with 2.5 *N* hydrochloric acid (500 ml) for 3 hr, and organic material was isolated with ether. The extract was dried and concentrated, and the residual keto ester **11** distilled: bp 110° (0.25 mm) 22.4 g, 76%); λ_{max} (EtOH) 234 nm (ϵ 11,000); ir (film) 1735, 1720 (weak), 1665, 1635 cm^{-1}; nmr ($CDCl_3$) δ 0.90–1.30 (dd, 6), 3.60 (s, 3), 5.80 (s, 1). *Anal.* Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.44; H, 8.60.

Ethylene Dithioketal 12.—The above keto ester (22.8 g, 0.11 mol), 1,2-ethanedithiol (10.8 g, 0.115 mol), and methanol (200 ml) were stirred and cooled in ice during the dropwise addition of boron trifluoride etherate (17 ml). After 16 hr of stirring, excess ice–water was added and the product was isolated with ether. Evaporation of the dried extract gave the desired dithioketal **12**: bp 135° (0.1 mm) (24.7 g, 80%); ir (film) 1735 cm^{-1}; nmr ($CDCl_3$) δ 1.05 (d, 3, J = 7.0 Hz), 1.20 (d, 3, J = 6.5 Hz), 3.30 (m, 4), 3.80 (s, 3), 5.75 (s, broad, 1). *Anal.* Calcd for $C_{14}H_{22}O_2S_2$: C, 58.70; H, 7.75; S, 22.46. Found: C, 58.73; H, 7.77; S, 22.35.

4-(3',3'-Ethylenedithio-4'-methyl-1'-cyclohexenyl)-2-pentanone (14).—The dithioketal **12** (38.9 g, 0.136 mol) was refluxed with 2.5 *N* aqueous sodium hydroxide (500 ml) for 2 hr, then cooled, acidified with 6 *N* hydrochloric acid, and extracted with ether. The dried extract, containing the crude acid **13**, was stirred and cooled in ice during the gradual addition, under nitrogen, of ethereal methyllithium[6] (133 ml of 2 *N*), during 1 hr. After a further 2 hr of stirring the product was poured into ice–water and the organic phase was separated. The aqueous layer was extracted twice with ether and the combined extracts were washed with water, dried, and concentrated. The residual methyl ketone **14** distilled at 125° (0.01 mm) (30.7 g, 85%): ir (film) 1710, 1360 cm^{-1}; nmr ($CDCl_3$) δ 1.00 (d, 3, J = 6.0 Hz), 1.15 (d, 3, J = 6.0 Hz), 2.15 (s, 3), 3.30 (m, 4), 5.70 (s, broad, 1). *Anal.* Calcd for $C_{14}H_{22}OS_2$: C, 62.66; H, 8.20; S, 23.68. Found: C, 62.20; H, 8.23; S, 23.67.

1-Carbomethoxy-4-(3',3'-ethylenedithio-4'-methyl-1'-cyclohexenyl)-2-pentanone (15).[7]—Sodium hydride (11.0 g of a 50% dispersion in mineral oil, 0.23 mol) was washed thrice with petroleum ether (bp 30–60°) by decantation, then mixed with dry benzene (500 ml), dimethyl carbonate (20.5 g, 0.23 mol), and the foregoing methyl ketone (30.7 g, 0.23 mol). The whole was refluxed under nitrogen for 72 hr, then cooled, acidified cautiously with glacial acetic acid, and treated with ice–water. The organic layer was separated and the aqueous layer was extracted twice with ether. The combined extracts were shaken with aqueous sodium bicarbonate and water, dried, and concentrated. The remaining β-keto ester **15** distilled at 170–180° (bath, 0.01 mm) (35.4 g, 94%). It gave a wine-red color with ferric chloride, was soluble in cold, aqueous alkali, and formed a copper complex with cupric acetate: ir (film) 1730, 1706, 1639, 1621 cm^{-1}; nmr ($CDCl_3$) δ 1.00 (d, 3, J = 6.0 Hz), 1.17 (d, 3, J = 6.0 Hz), 3.30 (m, 4), 3.80 (s, 3), 5.60 (s, broad, 1). *Anal.* Calcd for $C_{16}H_{24}O_3S_2$: C, 58.52; H, 7.37; S, 19.53. Found: C, 58.63; H, 7.41; S, 19.32.

1-Carbomethoxy-4-(4'-methyl-3'-oxo-1'-cyclohexenyl)-2-pentanone (16).—The dithioketal above (10.5 g, 0.032 mol) was refluxed with methanol (300 ml), water (24 ml), mercuric oxide (5.4 g, 0.025 mol), and mercuric chloride (183 g, 0.0675 mol) for 4 hr.[8] Inorganic material was removed by filtration, the filtrate was diluted with water, and the product was isolated with ether. The ether extract was washed with aqueous ammonium chloride and water, dried, and concentrated. The residual β-keto ester **16** distilled at 160–165° (bath, 0.04 mm) (6.2 g, 77%). It showed the usual properties of an enolic compound, forming a bluish-gray copper complex with cupric acetate: ir (film) 1748, 1712, 1669, 1629 cm^{-1}; nmr ($CDCl_3$) δ 1.10 (two d, 4), 3.50 (s, 2), 3.70 (s, 3), 5.75 (s, broad, 1). *Anal.* Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.84; H, 8.25.

4,7-Dimethyl-1-methoxycarbonylspiro[4,5]decane-2,6-dione (17).—Sodium metal (0.455 g, 0.0198 mol) was dissolved in dry methanol (200 ml) and the preceding β-keto ester **16** (5.0 g, 0.0198 mol) was added, the solution being stirred under nitrogen at room temperature for 1 hr. After acidification with glacial acetic acid the solvent was removed *in vacuo*. Ice–water was added and the product was isolated with ether. The extract was concentrated to small bulk and shaken with an excess of aqueous cupric acetate for 2 hr. The light green copper complex was collected, washed with water, and dried; it crystallized from benzene in light green prisms, mp 213–214° dec. *Anal.* Calcd for $C_{28}H_{38}O_8Cu$: C, 59.42; H, 6.72. Found: C, 59.28; H, 6.81. The copper complex (5.0 g), suspended in ether, was shaken vigorously with cold 2 *N* sulfuric acid for 45 min. The clear layers were separated and the organic phase was washed with water, dried, and concentrated. The remaining spiro keto ester **17** distilled at 150–155° (bath, 0.05 mm) (2.75 g). It crystallized almost entirely on keeping and separated from methanol in prisms: mp 113°; ir (film) 1764, 1715 cm^{-1}, with broad OH and C=O bands characteristic of enolic form; nmr ($CDCl_3$) δ 1.05 (two d overlapping, 6), 3.75 (m, 3, keto–enol mixture). *Anal.* Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99; mol wt, 252.3. Found: C, 66.78; H, 8.02; mol wt, 252 (mass spectrum).

Registry No.—**7**, 34638-68-1; **8**, 34638-69-2; **11**, 34638-70-5; **12**, 34638-71-6; **14**, 34638-72-7; **15**, 34638-73-8; **16**, 34638-74-9; **16** copper complex, 34630-94-9; **17**, 34638-75-0.

(11) *Cf.* H. L. Dryden, G. M. Webber, R. R. Burtner, and J. A. Cella, *J. Org. Chem.*, **26**, 3237 (1961).

The Synthesis of Two Metabolites of (−)-Δ^8-Tetrahydrocannabinol

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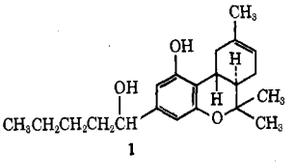
Recent studies from these laboratories have resulted in the isolation[1] of two *in vitro* dog liver metabolites of (−)-Δ^8-tetrahydrocannabinol. By inspection of their mass and nmr spectra and comparison of their nmr spectra with those of suitable monocyclic model compounds, structures **1** and **2** were established for these metabolites. The microgram quantities of these materials isolated from the metabolic mixtures were too small to allow determination of the configuration of the introduced hydroxyl groups. We now report the



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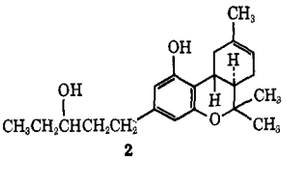

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unequivocal syntheses of these two metabolites as diasteromeric mixtures at the carbinol carbons.

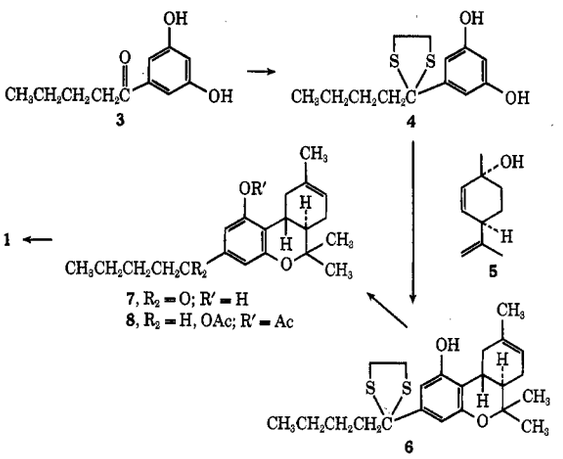
We envisioned the synthesis of **1** as proceeding *via* an acid-catalyzed condensation of the known[2] resorcinol

(1) D. E. Maynard, O. Gurny, R. G. Pitcher, and R. W. Kierstead, *Experientia*, **27**, 1154 (1971).

(2) R. Huls and A. Hubert, *Bull. Soc. Chim. Belg.*, **65**, 596 (1956).

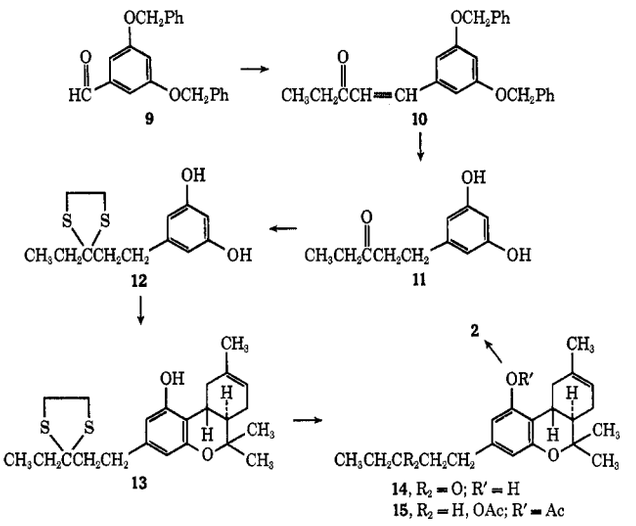
derivative **3** with a suitable terpene derivative, such as (−)-verbenol[3] or (+)-*trans*-*p*-mentha-2,8-dien-1-ol (**5**).[4] Since the latter compound was more readily available to us we attempted the condensation of **3** and **5**. However, **3** was recovered unchanged after the complete disappearance of **5** due to the reduced reactivity of the aromatic ring in **3**. The side chains of more reactive analogs of **3**, such as the corresponding alcohol, acetate, or benzoate, were too unstable under the condensation reaction conditions. The carbonyl group of **3** was therefore converted into the ethylene acetal. Upon attempted condensation with **5**, the ethylene acetal group was cleaved and **3** was recovered from the reaction mixture.

However, **3** was converted[5] readily to the dithioethylene acetal **4**, which on condensation with **5** gave a 50% yield of the desired **6**. Removal of the protecting



group of **6** was accomplished in three ways: shaking an aqueous suspension of **6** and mercuric acetate,[6] treating **6** with mercuric chloride[7] and cadmium carbonate in aqueous acetone, or, preferably, allowing **6** to react with mercuric oxide[8] and boron trifluoride etherate. Sodium borohydride reduction of **7** then gave **1**. Synthetic **1** (a 1:1 mixture of the two diasteromers at C-1′) was clearly identical by mass spectral criteria with **1** isolated[1] from the metabolic mixture. Acetylation of **1** gave the diacetate **8**, which was shown to be identical with the diacetate prepared[1] from the metabolically derived **1** by comparison of the nmr[9] and mass spectra and by identical mobility in several tlc and glpc systems.[1,10]

A similar approach was used for the synthesis of **2**. Condensation of the known[11] aldehyde **9** with methyl ethyl ketone in the presence of sodium hydroxide in methanol[12] gave a respectable yield of the linear product **10**. Attempted simultaneous hydrogenation and hydrogenolysis of **10** to give **11** by shaking under a hydrogen atmosphere either an ethyl acetate solution of **10** with platinum dioxide[13] or an ethanol solution of **10** with a 10% palladium on carbon catalyst was not promising. Heating a solution of **10** with cyclohexene and a palladium on carbon catalyst[14] gave, after 3 hr, predominantly the dibenzyl ether of **11**. After 8 hr



the monobenzyl ether of **11** predominated, and after 2.5 days of heating the major product was the desired **11**.[15] An attempted acid-catalyzed condensation of **11** with **5** failed and nonpolar products lacking a carbonyl group predominated. Analogs of **11** containing hydroxyl, ester, or ketal groups were also unsatisfactory. However, the dithioethyleneacetal **12** was readily prepared and converted into **13**.

Cleavage of the protecting group of **13** was not nearly as facile as with **6**. Treatment of **13** with an aqueous suspension of mercuric acetate[6] or oxidation of **13** with 1-chlorobenzotriazole followed by base cleavage[16] gave a number of products from which useful amounts of **14** could not be isolated. Cleavage of the dithioethylene acetal of **13** was accomplished with mercuric oxide[8] and boron trifluoride etherate, or better, with mercuric chloride[7] and cadmium carbonate. Reduction of **14** with sodium borohydride then gave **2** as a mixture of diastereomers at the carbinol carbon. Synthetic **2** was clearly identical with the sample of **2** isolated from the metabolic mixture by mass spectral criteria. Acetylation of **2** gave the diacetate **15**, identical with the diacetate of the metabolically derived **2** by nmr[9] and mass spectral, tlc, and glpc[10] criteria.

(3) R. Mechoulam, P. Braun, and Y. Gaoni, *J. Amer. Chem. Soc.*, **89**, 4552 (1967).
(4) T. Petrzilka and C. Sikemeier, *Helv. Chim. Acta*, **50**, 1416 (1967); T. Petrzilka, W. Haefliger, and C. Sikemeier, *ibid.*, **52**, 1102 (1969).
(5) L. F. Fieser, *J. Amer. Chem. Soc.*, **76**, 1945 (1954).
(6) G. P. Pollini, A. Barco, M. Anastasia, and G. Traverso, *Farmaco, Ed. Sci.*, **23**, 405 (1968).
(7) N. Pappas and H. R. Nace, *J. Amer. Chem. Soc.*, **81**, 4556 (1959).
(8) E. Vedejs and P. L. Fuchs, *J. Org. Chem.*, **36**, 366 (1971).
(9) We thank Mr. R. Pitcher for this comparison.
(10) We thank Mrs. O. Gurny for these comparisons.
(11) K. Wismayr, O. Schmid, and G. Zoelss, German Patent 1,233,410 (1967).
(12) M. G. J. Beets and H. van Essen, *Recl. Trav. Chim. Pays-Bas*, **77**, 1138 (1958).
(13) N. A. Burditt, M. C. Whiting, and L. M. Venanzi, *J. Chem. Soc. C*, 2273 (1967).
(14) We thank Mr. S. Teitel for suggesting these conditions.
(15) Earlier attempts to prepare **11** by cleavage of the *dimethyl* ether of **11** were unsuccessful. From a wide range of reaction conditions the major products were less polar than the starting material and lacked a carbonyl group. Cyclization to an indene had most probably taken place.
(16) P. R. Heaton, J. M. Midgley, and W. B. Whalley, *Chem. Commun.*, 750 (1971).

Experimental Section[17]

Butyl 3,5-Dihydroxyphenyl Ketone Dithioethylene Acetal (4).—To 3.60 g (17.1 mmol) of butyl 3,5-dihydroxyphenyl ketone (**3**) was added 4.00 ml of 1,2-ethanedithiol followed by 4.00 ml of boron trifluoride etherate. The reaction mixture was swirled until it became homogeneous, allowed to stand at ambient temperature for 10 min, and then washed onto a 100-g column of silica gel with dichloromethane. Dichloromethane and 2% ether in dichloromethane eluted odorous materials, and 5 and 10% ether in dichloromethane eluted 4.50 g (97%) of **4** as a colorless oil which soon crystallized, homogeneous by tlc in 10% methanol in chloroform and sufficiently pure for use in the next step.

(6a*R*:10a*R*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-valeryl-6*H*-dibenzo[*b*,*d*]pyran-1-ol Dithioethylene Acetal (6).—A mixture of 1.00 g (3.7 mmol) of **4**, 565 mg (4.15 mmol) of (1*S*:4*R*)-(+)-*trans*-*p*-mentha-2,8-dien-1-ol (**5**), and 110 mg of *p*-toluenesulfonic acid monohydrate in 40 ml of benzene was heated under reflux for 35 min, cooled, and washed onto a column of silica gel. Elution with benzene gave an oil which soon crystallized. Recrystallization from ether–hexane gave 742 mg (50%) of the analytical sample of **6** as colorless crystals: mp 130–132.5°; ir ($CHCl_3$) 3600, 1620, and 1570 cm^{-1}; no carbonyl absorptions; uv max (EtOH) 281 nm (ϵ 1620) and 287 (1640); nmr ($CDCl_3$) δ 6.70 and 6.56 (two d, J = 2 Hz, H-2 and H-4), 5.42 (m, H-8), 4.93 (s, OH), 3.26 (s, SCH_2CH_2S), 3.17 (m, H-10a), 1.70 (s, 9-CH_3), 1.37 and 1.10 (two s, 6,6-diCH_3), and 0.84 (t, H-5′); $[\alpha]^{25}D$ −225.6° (*c* 0.9259, $CHCl_3$).

Anal. Calcd for $C_{23}H_{32}O_2S_2$: C, 68.27; H, 7.97; S, 15.85. Found: C, 68.51; H, 8.17; S, 16.02.

(6a*R*:10a*R*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-valeryl-6*H*-dibenzo[*b*,*d*]pyran-1-ol (7).—To a vigorously stirred mixture of 8.1 g of red mercuric oxide, 100 ml of tetrahydrofuran, 26.3 ml of water, and 3.9 ml of boron trifluoride etherate was added dropwise a solution of 7.8 g (19.3 mmol) of **6** in 30 ml of tetrahydrofuran. The mixture was stirred for an additional 20 min, diluted with ether, and filtered. The filtrate was washed with water, sodium bicarbonate solution, and water, dried, and concentrated to a yellow oil. This was dissolved in benzene and adsorbed onto a column of silica gel. Elution with from 20% dichloromethane in benzene to 20% ether in dichloromethane gave 6.6 g (97%) of **7** as a colorless oil, homogeneous by tlc in 15% ethyl acetate in benzene and sufficiently pure for conversion into **1**. This oil soon crystallized and was recrystallized from dichloromethane–ether–hexane to give the analytical sample of **7** as colorless crystals: mp 96.5–98.5°; ir ($CHCl_3$) 3600, 3400 (broad), 1675, and 1575 cm^{-1}; uv max (EtOH) 277 nm (ϵ 10,400) and 325 (2230); nmr ($CDCl_3$) δ 7.27 and 6.98 (two sharp d, H-2 and H-4), 7.11 (s, OH), 5.42 (m, H-8), 3.30 (m, H-10a), 2.89 (t, H-2′), 1.68 (s, 9-CH_3), 1.38 and 1.08 (two s, 6,6-diCH_3), and 0.92 (t, H-5′); $[\alpha]^{25}D$ −322.6° (*c* 0.7019, $CHCl_3$).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.95; H, 8.55.

(6a*R*:10a*R*:1′*RS*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-(1-hydroxypentyl)-6*H*-dibenzo[*b*,*d*]pyran-1-ol (1).—To a solution of 2.40 g of crude **7** in 20 ml of ethanol was added 380 mg of sodium borohydride. The resulting green mixture was stirred at room temperature for 3 hr, another 160 mg of sodium borohydride was added, and after another 1 hr the reaction was diluted with water and extracted with dichloromethane. The solution was dried and concentrated to a colorless foam. This was dissolved in benzene and adsorbed onto a column of silica gel. Elution with from 15 to 50% ether in dichloromethane gave 1.19 g (51% overall from **6**) of **1** as a colorless foam, homogeneous by tlc in 15% ethyl acetate in benzene: ir ($CHCl_3$) 3600, 3360 (broad), 1625, and 1590 cm^{-1}; uv max (EtOH) 230 nm (infl) (ϵ 10,000), 277 (1520), and 284 (1620); nmr ($CDCl_3$) δ 7.32 and 7.01 (two sharp m, 1-OH), 6.42 and 6.25 (two sharp d, H-2 and H-4), 5.40 (m, H-8), 4.41 (m, H-1′), 3.38 (br d, H-10a), ~3.1 (m, 1′-OH, exch), 1.69 (s, 9-CH_3), 1.36 and 1.05 (two s, 6,6-diCH_3), and 0.87 (t, H-5′); low-resolution mass spectrum, molecular ion m/e 330 (100%), major fragments m/e (rel intensity) 274 (60) and 247 (65); high-resolution mass spectrum, molecular ion m/e 330.2069 ($C_{21}H_{30}O_3$).

(6a*R*:10a*R*:1′*RS*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-(1-acetoxypentyl-6*H*-dibenzo[*b*,*d*]pyran-1-ol Acetate (8).—The diol **1** obtained from 404 mg (1 mmol) of **6** *via* **7** was acetylated with acetic anhydride and pyridine overnight at room temperature. The solution was poured into water and extracted with dichloromethane. The organic layers were dried, passed over a short column of silica gel, and concentrated to give 227 mg (55% overall from **6**) of **8** as a colorless oil: ir ($CHCl_3$) 1765 and 1740 cm^{-1}; uv max (EtOH) 225 nm (infl) (ϵ 8155), 276 (1950), and 283 (2115); nmr ($CDCl_3$) δ 6.67 and 6.52 (two sharp m, H-2 and H-4), 5.64 (t, H-1′), 5.42 (m, H-8), 2.25 and 2.07 (two s, OAc's), 1.67 (s, 9-CH_3), 1.36 and 1.08 (two s, 6,6-diCH_3), and 0.85 (t, H-5′); compatible[9] with the time-averaged 211 scan spectrum obtained from the metabolically derived **8**; low-resolution mass spectrum, molecular ion m/e 414 (100%), major fragments m/e (rel intensity) 372 (95), 354 (50), 329 (35), 312 (35), 289 (50), and 269 (30); high-resolution mass spectrum, molecular ion m/e 414.2436 ($C_{25}H_{34}O_5$).

Heating a mixture of 100 mg of **8**, 100 mg of sodium bicarbonate, 9 ml of methanol, and 1 ml of water under reflux caused the formation of the 1′-acetate of **1** after 15 min and the regeneration of **1** within 2 hr.

1-(3,5-Dibenzyloxyphenyl)pent-1-en-3-one (10).—A solution of 1.125 g of sodium hydroxide in 125 ml of methanol was heated under reflux with an oil bath. A solution of 105.7 g (0.33 mol) of 3,5-dibenzyloxybenzaldehyde (**9**) in 202 ml of 2-butanone was heated to about 70° on the steam bath and added rapidly to the sodium hydroxide solution. The reaction mixture was heated under reflux for a further 10 min, cooled in an ice bath, acidified with acetic acid, diluted with water, and extracted with dichloromethane. The extracts were dried and concentrated to a mixture of oil and crystals. The oily portion was adsorbed onto a column of silica gel. Elution with from 50% benzene in hexane to 5% dichloromethane in benzene gave fractions rich in product. These were crystallized from ether–hexane and the combined solids were recrystallized to give 39.8 g (32%) of **10** as colorless crystals, mp 92–96°. Further recrystallization gave the analytical sample: mp 95.5–96.5°; ir ($CHCl_3$) 1690, 1665, 1615, and 1595 cm^{-1}; Raman (4880 Å, neat) 1655, 1620, and 1595 cm^{-1}; uv max (EtOH) 230 nm (ϵ 19,700) and 299 (18,600); nmr ($CDCl_3$) δ 7.35 (s, C_6H_5), 7.48 and 6.57 (two d, J = 16 Hz, H-1 and H-2), 5.02 (s, $OCH_2C_6H_5$), 2.58 (q, H-4), and 1.13 (t, H-5).

Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.71; H, 6.49.

1-(3,5-Dihydroxyphenyl)pentan-3-one (11).—A mixture of 33.4 g (0.09 mol) of **10**, 527 ml of cyclohexene, 5.06 g of a 10% palladium-on-charcoal catalyst, and 1 l. of tetrahydrofuran was heated under reflux for 2.5 days. The cooled catalyst-free solution was concentrated, dissolved in methanol, diluted with water, and extracted with dichloromethane and with ethyl acetate. The combined extracts were dried and concentrated. The residue was dissolved in dichloromethane, passed over a short column of silica gel, and concentrated. Crystallization from chloroform gave 9.3 g (53%) of **11** as colorless crystals, mp 89–93°. Further recrystallization gave the analytical sample: mp 92.5–93.5°; ir (KBr) 1710 and 1615 cm^{-1} plus strong OH absorption; uv max (EtOH) 225 nm (infl) (ϵ 7800), 276 (1710), and 282 (1680); nmr ($CDCl_3$ containing a little CD_3OD) δ 6.19 (s, aromatic), 2.72 (s, H-1 and H-2), 2.44 (q, H-4), and 1.02 (t, H-5).

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.03; H, 7.32.

1-(3,5-Dihydroxyphenyl)pentan-3-one Dithioethylene Acetal (12).—To 3.00 g (15.4 mmol) of **11** was added 3.3 ml of 1,2-ethanedithiol followed by 3.3 ml of boron trifluoride etherate. The mixture was swirled until it became homogeneous, allowed to stand at ambient temperature for 10 min, and washed onto a column of 180 g of silica gel with dichloromethane. After elution with less polar solvents, from 10 through 40% ether in dichloromethane eluted material which upon crystallization and recrystallization from methanol–water gave 3.04 g (73%) of **12** as colorless crystals: mp 83.5–85.5°; ir (KBr) 1675 (w), 1630, and 1605 cm^{-1}; uv max (EtOH) 225 nm (infl) (ϵ 15,000), 275

(17) Melting points were determined in a Thomas-Hoover melting point apparatus and are corrected. Infrared spectra were recorded on a Beckman instrument, Model IR-9. Ultraviolet spectra were recorded on a Cary instrument Model 15. Nuclear magnetic resonance spectra were recorded with a Varian A-60 or Varian HA-100 instrument using tetramethylsilane as internal standard. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter. Low-resolution mass spectra were recorded on a Jeolco JMS-01SG instrument at 70 eV. High-resolution mass spectra were recorded on a CEC 21-110 instrument at 70 eV. Gas-liquid partition chromatography was carried out on a Hewlett-Packard 402 instrument with a flame ionization detector.

(1450), and 282 (1415); nmr ($CDCl_3$ plus some DMSO-d_6) δ 6.15 (s, aromatic), 3.27 (s, SCH_2CH_2S), 2.60 and 2.14 (two m, H-1 and H-2), 1.95 (q, H-4), and 1.04 (t, H-5); low-resolution mass spectrum, molecular ion m/e 270 (55%), major fragments m/e (rel intensity) 241 (45), 177 (25), 137 (30), 133 (100), 123 (40), and 44 (30); high-resolution mass spectrum, molecular ion m/e 270.0765 ($C_{13}H_{18}O_2S_2$).

(6a*R*:10a*R*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b*,*d*]pyran-1-ol-3′-one Dithioethylene Acetal (13).—A mixture of 5.162 g (19.1 mmol) of **12**, 2.83 g (20.8 mmol) of **5**, and 575 mg of *p*-toluenesulfonic acid monohydrate in 200 ml of benzene was heated under reflux for 35 min, cooled, and washed onto a column of silica gel. Elution with benzene and dichloromethane gave 3.647 g (47%) of **13** as a colorless oil, suitable for use in subsequent steps: ir ($CHCl_3$) 3600, 1625, and 1580 cm^{-1}; uv max (EtOH) 235 nm (infl) (ϵ 12,200), 275 (1500), and 282 (1400); nmr ($CDCl_3$) δ 6.28 and 6.10 (two d, H-2 and H-4), 5.42 (m, H-8), 4.87 (s, OH), 3.24 (s, SCH_2CH_2S), 1.68 (s, 9-CH_3), 1.36 and 1.09 (two s, 6,6-diCH_3), and 1.07 (t, H-5′); low-resolution mass spectrum, molecular ion m/e 404 (35%), major fragments m/e (rel intensity) 311 (60), 271 (100), and 133 (80).

(6a*R*:10a*R*:3′*RS*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-(3-hydroxypentyl)-6*H*-dibenzo[*b*,*d*]pyran-1-ol (2).—A heterogeneous mixture of 3.02 g (7.5 mmol) of **13**, 3.00 g of mercuric chloride, and 3.00 g of cadmium carbonate in 300 ml of acetone and 15 ml of water was stirred at room temperature for 16 hr. Another 3.00 g of each inorganic salt was added, and 7 hr later a further 3.00 g of each salt was again added. The reaction was stirred for an additional 20 hr, the inorganic salts were removed by filtration through a filter aid, and the acetone was evaporated under vacuum. The residue was shaken with ether; the ether layer was washed with water, 10% potassium iodide solution, and water, dried, and concentrated. The green residue was dissolved in benzene and adsorbed onto a column of silica gel. Elution with 15–20% ether in dichloromethane gave 1.40 g of the ketone **14** as a light tan oil, almost homogeneous by tlc in 15% ethyl acetate in benzene. This oil was dissolved in 12 ml of ethanol, and 200 mg of sodium borohydride was added. The reaction was stirred for 2.5 hr, during which time an additional 125 mg of sodium borohydride was added. The reaction was diluted with water, acidified with hydrochloric acid, and extracted with dichloromethane. The extracts were washed with sodium bicarbonate solution, dried, and concentrated to 1.2 g of a yellow foam. This was chromatographed over silica gel. Twenty per cent ether in dichloromethane eluted 445 mg (17%) of **2** as a colorless foam: homogeneous by tlc in 15% ethyl acetate in benzene; ir ($CHCl_3$) 3605, 1625, and 1590 cm^{-1}; uv max (EtOH) 230 nm (infl) (ϵ 10,600), 276 (1330), and 283 (1380); nmr ($CDCl_3$) δ 6.35 (OH), 6.25 and 6.14 (two sharp m, H-2 and H-4), 5.42 (m, H-8), 3.55 (m, H-3′), 3.21 (br d, H-10a), 2.09 (OH), 1.65 (s, 9-CH_3), 1.35 and 1.07 (two s, 6,6-diCH_3), 0.90 (t, H-5′); low-resolution mass spectrum, molecular ion m/e 330 (25%), major fragment m/e (rel intensity) 258 (100); high-resolution mass spectrum, molecular ion m/e 330.2196 ($C_{21}H_{30}O_3$).

(6a*R*:10a*R*:3′*RS*)-6a,7,10,10a-Tetrahydro-6,6,9-trimethyl-3-(3-acetoxypentyl)-6*H*-dibenzo[*b*,*d*]pyran-1-ol Acetate (15).—A sample of **2** was acetylated with acetic anhydride in pyridine overnight at room temperature. The solution was then poured into water and extracted with dichloromethane. The solution was dried and concentrated. The residue was dissolved in benzene and adsorbed onto a column of silica gel. Elution with 5% ether in dichloromethane gave **15** as a colorless oil, homogeneous by tlc in benzene: nmr ($CDCl_3$) δ 6.54 and 6.39 (two sharp m, H-2 and H-4), 5.43 (m, H-8), 4.84 (t, H-3′), 2.25 and 2.01 (two s, OAc's), 1.68 (s, 9-CH_3), 1.37 and 1.08 (two s, 6,6-diCH_3), and 0.88 (t, H-5′); compatible[9] with the time-averaged 100 scan spectrum obtained from the metabolically derived **15**; low-resolution mass spectrum, molecular ion m/e 414 (100%), major fragments m/e (rel intensity) 372 (90), 312 (35), 298 (45), 289 (40), and 258 (70); high-resolution mass spectrum, molecular ion m/e 414.2385 ($C_{25}H_{34}O_5$).

Registry No.—**1** (1′-*R* isomer), 34589-81-6; **1** (1′-*S* isomer), 34589-82-7; **2** (3′-*R* isomer), 34589-83-8; **2** (3′-*S* isomer), 34589-84-9; **6**, 34589-85-0; **7**, 34589-86-1; **8** (1′-*R* isomer), 34589-87-2; **8** (1′-*S* isomer), 34589-88-3; **10**, 34589-89-4; **11**, 34589-90-7; **12**, 34589-91-8; **13**, 34635-37-5; **15** (3′-*R* isomer), 34589-92-9; **15** (3′-*S* isomer), 34589-93-0.

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1- and 3-Methoxy-3-phenyloxindoles. A Rearrangement of a Methoxy Group from Nitrogen to Carbon

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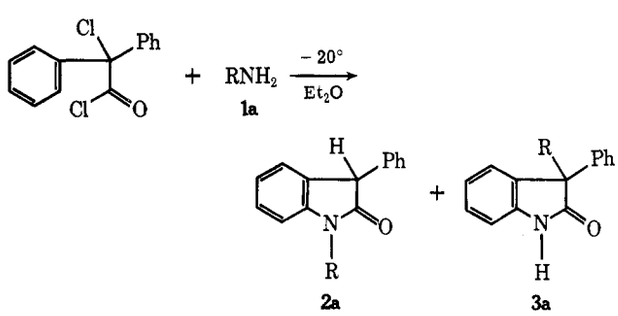
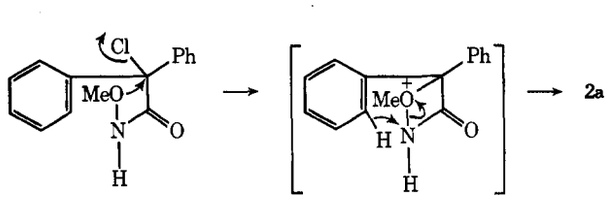
In connection with other work we desired 1-methoxy-3-phenyloxindole (**2a**). The preparation of **2a** should be analogous to that of 1-dimethylamino-3-phenyloxindole (**2b**). Compound **2b** is prepared[1] by the reaction at −20° between α,α-diphenylchloroacetyl chloride and *N*,*N*-dimethylhydrazine (**1b**). When this reaction was performed using methoxyamine (**1a**) the product isolated (by crystallization from aqueous methanol) had melting point, ir (N–H present), and nmr (Ar-CHC:O absent) properties strongly suggesting that it was 3-methoxy-3-phenyloxindole (**3a**). Comparison



a series, R = OCH_3
b series, R = $N(CH_3)_2$

with an authentic sample[2] confirmed this assignment.

When the crude oily reaction product, essentially solvent-free, was allowed to stand, the desired **2a** very slowly crystallized first and could be picked out. The residual oil afforded **3a**. The isolated ratio of **2a** to **3a** was approximately 1:4. Neither **2a** nor **3a** could be isomerized to the other by boiling in ether, by recrystallization, or by seeding the melt. This suggests that the isomerization occurs during the initial reaction steps, in



(1) R. F. Meyer, *J. Org. Chem.*, **30**, 3451 (1965).
(2) J. M. Bruce and F. K. Sutcliffe, *J. Chem. Soc.*, 4789 (1957). We thank Professor Bruce for kindly supplying a sample of **3a**.