Further elution gave 4-nitroaniline (97 mg, 0.7 mmol, 7%; mp 145 °C) identical with an authentic sample (mixture melting point, TLC, IR and mass spectra).

The aqueous solution F was extracted with ether to give a yellow solid (267 mg) which contained 4-aminodiphenyl sulfone and 4-nitroaniline (TLC, mass spectrum); this was not separated.

(c) 4-Nitrodiphenyl Sulfoxide. 4-Nitrodiphenyl sulfoxide (1.0 g, 4.04 mmol) in THF (25 mL) and potassamide (from 630 mg, 16.6 mmol, of potassium) in ammonia (200 mL) gave (3 h; 6 g of NH_4Cl) a black solid G and an aqueous solution H. Solid G was extracted with ether, and the ether solution was evaporated to give a gum which solidified on trituration with petroleum ether; this solid (80 mg) proved to be 4-nitroaniline (see later). Evaporation of the petroleum ether filtrate gave diphenyl disulfide: 125 mg, 0.58 mmol, 14%; mp and mmp 55–57 °C; the mass spectrum showed m/e 218 (M^+) and trace impurity at m/e 250.

The aqueous solution H was extracted with dichloromethane. Evaporation of the dichloromethane solution gave a gum which crystallized from ether/petroleum ether to give 4-nitroaniline (60 mg). Total recovery of 4-nitroaniline was 140 mg (1.0 mmol, 25%), mp 139–141 °C, identical with an authentic sample (mixture melting point, TLC, IR ^1H NMR, and mass spectra).

(d) 2-Nitrotoluene. 2-Nitrotoluene (2.75 g, 20.0 mmol) in THF (50 mL) and potassamide (from 11.7 g, 300 mmol, of potassium) in ammonia (650 mL) gave (12 h; 10 g of NH_4Cl) a yellow solid I and an aqueous solution. Solid I crystallized from chloroform to give 2,2′-dinitrobibenzyl (2.2 g, 8.0 mmol, 80%) as yellow prisms: mp 119–120 °C (lit.[12] mp 122 °C); ^1H NMR ($CDCl_3$) δ 8.07–7.85 (2 H, m), 7.55–7.3 (6 H, m), 3.25 (4 H, s); IR 2920 (CH), 1530 and 1345 (NO_2) cm^{-1}; mass spectrum, m/e (rel intensity) 272 (M^+, 1), 255 (M – OH, 7), 136 ($NO_2C_6H_4CH_2$, 100), 120 (66).

Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.78. Found: C, 61.76; H, 4.79.

(e) 4-Nitrotoluene. 4-Nitrotoluene (2.75 g, 20.0 mmol) in THF (50 mL) and potassamide (from 2.34 g, 60.0 mmol, of potassium) in ammonia (400 mL) gave (4 h; 6 g of NH_4Cl) a brown solid J and an aqueous solution. Solid J was extracted with hot acetic acid and filtered, leaving a yellow residue (400 mg, 1.46 mmol, 15%) of 4,4′-dinitrostilbene. The acidic solution was diluted with water, and the solid (2.2 g, 8.0 mmol, 80%) was filtered off, dried, and crystallized from benzene to give 4,4′-dinitrobibenzyl as yellow needles: 2.1 g, 7.7 mmol, 77%; mp 178.5–180 °C (lit.[8] mp 179.5–180.5 °C); ^1H NMR ($CDCl_3$) δ 8.16 (A) and 6.3 (B) (8 H, A_2B_2 q), 3.0 (4 H, s); IR 2920 (CH), 1500 and 1335 (NO_2) cm^{-1}; mass spectrum, m/e (rel intensity) 272 (M^+, 50), 256 (M – O, 7), 136 ($NO_2C_6H_4CH_2$, 100), 120 (17).

A sample of 4,4′-dinitrostilbene, recrystallized from ethanol, had mp 292–293 °C (lit.[13] mp 294–295 °C) and was identical with the sample prepared in f below (mixture melting point, TLC, mass spectrum).

(f) 4,4′-Dinitrobibenzyl. 4,4′-Dinitrobibenzyl (2.2 g, 8.1 mmol) in THF (50 mL) and potassamide (from 5.5 g, 141 mmol, of potassium) in ammonia (700 mL) gave (4 h; 5 g of NH_4Cl) a yellow solid K and an aqueous solution. Solid K crystallized from ethanol to give 4,4′-dinitrostilbene: 1.6 g, 5.9 mmol, 73%; mp 292–293 °C; mass spectrum, m/e (rel intensity) 270 (M^+, 32), 254 (M – O, 5), 240 (M – NO, 31), 210 (M – 2 – NO, 100).

Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.70; N, 10.37. Found: C, 61.93; H, 3.64; N, 10.20.

Concentration of the ethanolic mother liquor gave a further crop of 4,4′-dinitrostilbene (0.6 g, 2.2 mmol, 27%), slightly contaminated with 4,4′-dinitrobibenzyl.

Reactions with $NaNH_2$ in EDA: General Procedure. The nitro compound in dry, freshly distilled EDA was added to a mixture of sodamide and EDA which had been previously stirred for 30 min under nitrogen. The mixture was stirred under nitrogen at room temperature (reaction times in parentheses), poured into iced water, and extracted with ether. After drying and evaporation of the ether, the crude product was processed as noted.

(a) 4-Nitrobenzophenone. Treatment of 4-nitrobenzophenone (1.0 g, 4.4 mmol) in EDA (20 mL) with sodamide (600 mg, 15.4 mmol) in EDA (40 mL) gave (40 h) a gummy solid which solidified (250 mg, 0.64 mmol, 29%) on trituration with petroleum ether. Crystallization from acetone gave light brown plates, mp 205–208 °C, of 4,4′-dibenzoylazobenzene (m/e 390, M^+) contaminated with the azoxy compound (m/e 406, M^+). Repeated crystallization raised the melting point to 220–221 °C. This sample was identical with that prepared as described below.

Anal. Calcd for $C_{26}H_{18}N_2O_2$: N, 7.17; mol wt, 390.13670. Found N, 7.21; mol wt (mass spectrometry), 390.11786.

The petroleum ether filtrate apparently contained 4-nitrobenzophenone and 3-amino-4-nitrobenzophenone (TLC).

The azo compound was alternatively prepared in the following way. Zinc powder (2.3 g, 35 mmol) was added to a stirred mixture of 4-nitrobenzophenone (4.0 g, 17.6 mmol) in methanol (80 mL) and sodium hydroxide (2.8 g, 70 mmol) in water (7 mL). The mixture was refluxed for 8 h, during which time a yellow solid separated out. The mixture was filtered while hot and the filter cake was washed with hot methanol (50 mL), leaving a pale yellow solid (1.3 g, 3.3 mmol, 38%), mp 205–208 °C. Like the first crystallized product from the foregoing reaction, this showed only one spot on TLC and proved to be 4,4′-dibenzoylazobenzene (m/e 390, M^+) contaminated with the azoxy compound (m/e 406, M^+); the methanol washings showed two spots on TLC, one of which was identical with that for the azo compound. Recrystallization (ethanol) gave the same azo compound as above: ^1H NMR ($CDCl_3$) δ 8.0 (s), 7.9–7.4 (m); IR 1660 (C=O), 1580 (N=N) cm^{-1}; mass spectrum, m/e (rel intensity) 390 (M^+, 25), 209 (M – $C_{13}H_9O$, 4), 181 ($C_{13}H_9O$, 100), 105 (C_6H_5CO, 62).

(b) 4′-Nitrodiphenyl Sulfone. Treatment of 4-nitrodiphenyl sulfone (1.0 g, 3.8 mmol) in EDA (25 mL) with sodamide (700 mg, 18.0 mmol) in EDA (50 mL) gave (30 h) a gum (100 mg, 0.22 mmol, 8%) which crystallized from benzene to give light brown plates, mp 275–278 °C, of 4,4′-bis(benzenesulfonyl)azobenzene; IR 1590 (N=N), 1325, 1165 and 1150 (S=O) cm^{-1}; mass spectrum, m/e (rel intensity) 462 (M^+, 33), 245 (M – $C_{12}H_9SO_2$, 8), 217 ($C_{12}H_9SO_2$, 100), 141 ($C_6H_5SO_2$, 13), 125 (C_6H_5SO, 17).

Anal. Calcd for $C_{24}H_{18}N_2O_4S_2$: N, 6.08; mol wt, 462.07087. Found: N, 6.16; mol wt (mass spectrometry), 462.06464.

Acknowledgment. We wish to thank Professor K. Schofield (University of Exeter, England) for a sample of 2-amino-4-nitrobenzophenone and the National Research Council of Canada for financial support.

Registry No. 4,4′-Bis(phenylthio)azoxybenzene, 5333-73-3; 4-nitrodiphenyl sulfide, 1223-31-0; 4-nitrobenzophenone, 1144-74-7; 3-amino-4-nitrobenzophenone, 39070-69-4; benzoic acid, 65-85-0; 4-nitrodiphenyl sulfone, 1146-39-0; 4-ethoxydiphenyl sulfone, 14193-13-6; 4-ethoxynitrobenzene, 100-29-8; 4-aminodiphenyl sulfone, 7019-01-4; 4-nitroaniline, 100-01-6; 4-nitrodiphenyl sulfoxide, 955-45-3; diphenyl disulfide, 882-33-7; 2-nitrotoluene, 88-72-2; 2,2′-dinitrobibenzyl, 16968-19-7; 4-nitrotoluene, 99-99-0; 4,4′-dinitrostilbene, 2501-02-2; 4,4′-dinitrobibenzyl, 736-30-1; 4,4′-dibenzoylazobenzene, 19617-86-8; 4,4′-bis(benzenesulfonyl)azobenzene, 71819-33-5; potassamide, 17242-52-3; sodamide, 7782-92-5.

(12) M. Busch and B. Weiss, *Ber. Dtsch. Chem. Ges.*, **33**, 2709 (1900).
(13) P. L'Ecuyer, F. Turcotte, J. Giguere, C. A. Olivier, and P. Roberge, *Can. J. Res., Sect. B*, **26**, 70 (1948).

Reinvestigation of the Reaction of Ethyl Acetoacetate with Styrene Oxide

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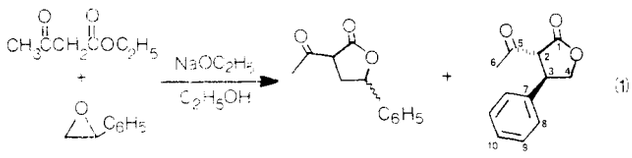
Adams and VanderWerf[2] have reported that the reaction of ethyl acetoacetate with styrene oxide gives α-acetyl-γ-phenyl-γ-butyrolactone (1) as the sole product. Subse-

(1) Present address: Monsanto Agricultural Products Co., St. Louis, Mo. 63166.
(2) R. M. Adams and C. A. VanderWerf, *J. Am. Chem. Soc.*, **72**, 4368 (1950).

0022-3263/79/1944-4707$01.00/0

quently, other investigators have utilized the reported regiospecificity of this reaction.[3] This note clearly establishes that the reaction is not regiospecific; in fact, *trans*-α-acetyl-β-phenyl-γ-butyrolactone (**2**) is the major isomer formed (eq 1).[4]



(1)

1, 45% 2, 55%

The reaction of ethyl acetoacetate with styrene oxide provides a mixture of γ-phenyl and β-phenyl positional isomers in 56% isolated yield. This mixture is not separable by distillation but can be conveniently separated by high-pressure LC into **1** (45%) and **2** (55%). The structure assignments for **1** and **2** were made by ^1H and ^{13}C NMR spectroscopy. The ^1H NMR spectra for **1** and **2** are consistent with the published spectra of γ-phenyl-γ-butyrolactone and β-phenyl-γ-butyrolactone, respectively.[5]

The 100-MHz ^1H NMR spectrum of the γ-phenyl isomer **1** shows two diastereomeric acetyl methyl group resonances of equal intensity at δ 2.42 and 2.45 and an enol methyl resonance at δ 1.92. The diastereomeric benzylic protons appear as two triplets characteristically downfield at δ 5.42 and 5.54.[5,7] For the β-phenyl isomer **2**, only one acetyl methyl group resonance is observed at δ 2.41 which suggests that only one diastereomer is formed. The corresponding enol methyl resonance is observed at δ 1.70. The relative amounts of **1** and **2** which are present in enol form were determined by integration to be 11% and 24%, respectively.

The ^{13}C NMR spectrum of the γ-phenyl isomer **1** shows two resonances of equal intensity for every carbon in the molecule except the lactone carbonyl carbon and the ortho carbons of the phenyl rings. The off-resonance ^1H-decoupled ^{13}C NMR spectrum shows a doublet for each diastereomeric benzylic carbon at δ 79.6 and 80.6. For the β-phenyl isomer **2**, only one resonance is observed for each carbon in the molecule and the off-resonance spectrum shows a doublet for the benzylic carbon at δ 42.6.

The fact that **2** is a crystalline solid which has only one ^1H NMR acetyl methyl group resonance and only one ^{13}C NMR resonance for each carbon substantiates the claim that **2** is a single diastereomer. The configuration of **2** is presumed to be trans from steric considerations. Dreiding models show that the α,β-steric interactions are much more severe for the cis diastereomer than for the trans diastereomer. Accordingly, one would predict that the trans diastereomer is more stable and should predominate in an equilibrium mixture. This argument is substantiated by the fact that *trans*-α-methyl-β-phenyl-γ-butyrolactone is known to be the predominant diastereomer at equilibrium.[8]

Experimental Section[9]

Materials. Commercially available ethyl acetoacetate and styrene oxide were distilled prior to use. Absolute ethanol was distilled directly into the reaction vessel after being dried by the addition of metallic sodium under an argon atmosphere.

Reaction of Ethyl Acetoacetate with Styrene Oxide. Following the procedure of Adams and VanderWerf,[2] 46.0 g (2.00 mol) of metallic sodium in 900 mL of dry ethanol was reacted with 280 g (2.15 mol) of ethyl acetoacetate and 258 g (2.15 mol) of styrene oxide. After workup, the crude product was vacuum distilled to give a 152-g forerun (unreacted ethyl acetoacetate and styrene oxide) and 227 g (56%) of a light yellow viscous oil which clearly showed two spots by TLC: bp 160–180 °C (2–3 mm). After several weeks of being stored in a refrigerator at 6 °C, a mass of crystals formed which was filtered and recrystallized from ethanol to give 42 g of colorless needles: mp 52–54 °C. This material was identical with pure **2** isolated via the high-pressure LC procedure outlined below.

High-Pressure LC Separation. A Waters Associates Prep LC/System 500 instrument was used. Base line separation of the positional isomers could be realized without the aid of recycling when 5-g samples were injected onto two 325-g Waters PrepPAK silica cartridges (average particle size 75 μm) which were connected in series. The solvent system used was 5% ethyl acetate in toluene. The solvent pressure was maintained at 4 atm and a flow rate of 200 mL/min was used. Five 5-g samples of the light yellow oil were injected onto the column. The major isomer had a retention time of 10.5 min and the minor isomer had a retention time of 14.5 min. The fractions were collected, concentrated in vacuo, and vacuum distilled. The total material recovered from this process was 23.5 g (94%).

α-Acetyl-γ-phenyl-γ-butyrolactone (1). The minor isomer fractions gave on distillation 10.6 g (45%) of colorless **1**: TLC R_f 0.45; bp 135–145 °C (2 mm); ^1H NMR ($CDCl_3$) δ 1.92 (s, 0.33, $CH_3C(OH)=C$), 2.05–3.40 (m, 4.68, CH_2 and CH_3CO), 3.60–4.70 (m, 1, CH_3COCH), 5.42 (t, 0.5, J = 7.0 Hz, $OCHC_6H_5$), 5.54 (t, 0.5, J = 7.0 Hz, $OCH'C_6H_5$), 7.30–7.45 (s, 5, ArH), 10.70–11.00 (s, 0.11, $CH_3C(OH)=C$); ^{13}C NMR ($CDCl_3$) δ 19.0 (C_6 enol), 29.0 (q, C_6), 29.6 (q, C_6'), 32.2 (t, C_3), 32.4 (t, C_3'), 54.0 (d, C_2), 54.3 (d, C_2'), 79.6 (d, C_4), 80.6 (d, C_4'), 95.3 (C_2 enol), 125.5 (d, C_9), 125.9 (d, C_9'), 126.8 (d, C_{10}), 127.5 (d, C_{10}'), 128.8 (d, C_8 and C_8'), 138.7 (s, C_7), 139.2 (s, C_7'), 140.6 (C_5 enol), 168.1 (C_1 enol), 172.2 (s, C_1 and C_1'), 200.2 (s, C_5), 200.6 (s, C_5'); IR (neat) 1780 (OC=O), 1725 (CH_3C=O), 1365, 1335, 1230, 1160, 1025, 945, 765, 705 cm^{-1}.

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.89; H, 6.09.

***trans*-α-Acetyl-β-phenyl-γ-butyrolactone (2).** The major isomer fractions gave on distillation 12.9 g (55%) of colorless **2**: TLC R_f 0.55; bp 130–145 °C (2 mm); mp 52–54 °C; ^1H NMR ($CDCl_3$) δ 1.70 (s, 0.72, $CH_3C(OH)=C$), 2.41 (s, 2.28, CH_3CO), 3.93 (dd, 0.76, $J_{\alpha,\beta}$ = 8.0 Hz, $J_{\alpha,\gamma}$ = 2.0 Hz, CH_3COCH), 4.05–4.45 (m, 2, CH_2), 4.50–4.80 (m, 1, CHC_6H_5), 7.20–7.50 (s, 5, ArH), 11.00–11.30 (s, 0.24, $CH_3C(OH)=C$); ^{13}C NMR ($CDCl_3$) δ 18.9 (C_6 enol), 29.8 (q, C_6), 42.6 (d, C_3), 60.0 (d, C_2), 72.2 (t, C_4), 99.8 (C_2 enol), 127.3 (d, C_9), 127.8 (d, C_{10}), 129.1 (d, C_8), 138.4 (s, C_7), 142.6 (C_5 enol), 171.0 (C_1 enol), 172.0 (s, C_1), 199.9 (s, C_5); IR (neat) 1780 (OC=O), 1725 (CH_3C=O), 1365, 1230, 1150, 1025, 765, 705 cm^{-1}.

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.66; H, 6.09.

Acknowledgment. I thank W. Warren Schmidt for helpful discussions; I am indebted to Steven A. Goldman

(3) M. Fedorchuk and F. T. Semeniuk, *J. Pharm. Sci.*, **52**, 733 (1963); G. B. Barlow and A. J. MacLeod, *J. Chem. Soc.*, 141 (1964).

(4) DePuy and co-workers[5] have corrected the work of Russell and VanderWerf[6] which claims that diethyl malonate reacts with styrene oxide regiospecifically to give only the γ-phenyl isomer.

(5) C. H. DePuy, F. W. Breitbeil, and K. L. Eilers, *J. Org. Chem.*, **29**, 2810 (1964).

(6) R. R. Russell and C. A. VanderWerf, *J. Am. Chem. Soc.*, **69**, 11 (1947).

(7) The 60-MHz ^1H NMR spectrum of **1** shows this area as a quartet.

(8) S. A. M. T. Hussain, W. D. Ollis, C. Smith, and J. F. Stoddart, *J. Chem. Soc., Perkin Trans. 1*, 1480 (1975).

(9) TLC R_f values were determined on 250-μm silica gel GF Fisherbrand Redi/Plates using 10% ethyl acetate in toluene as solvent. Boiling points were taken from distillations and are uncorrected. Melting points were determined on a Thomas-Hoover melting point apparatus and are likewise uncorrected. Nuclear magnetic resonance (NMR) spectra were taken on a Varian HA-100 or Varian CFT-20 spectrometer. Chemical shifts are reported in δ (ppm) relative to an internal tetramethylsilane (Me_4Si) standard. Infrared spectra were taken on a Perkin-Elmer 457 spectrophotometer. Elemental analyses were performed by Galbraith Laboratories.

for the HA-100 spectra, Barbara B. Morgan for the CFT-20 spectra, and Timothy E. Hof for technical assistance.

Registry No. *cis*-1, 71870-63-8; *trans*-1, 71870-64-9; **2**, 71870-65-0; ethyl acetoacetate, 141-97-9; styrene oxide, 96-09-3.

Uvarinol: A Novel Cytotoxic Tribenzylated Flavanone from *Uvaria chamae*

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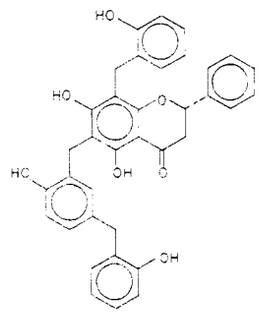
Recently we[1,2] and others[3] have isolated cytotoxic compounds from plants of the *Uvaria* genus. We now wish to report the structure of uvarinol (**1**), the most complex



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of the active compounds yet isolated. An ethanolic extract of the stem bark of *Uvaria chamae* (Annonaceae) showed activity in vivo against P-388 lymphocytic leukemia (PS) and in vitro against cells derived from human carcinoma of the nasopharynx (KB). Further fractionation of the ethanolic extract was guided by assay against KB.[4] The activity was concentrated in the ethyl acetate soluble portion of an ethyl acetate–water partition. Chromatography of the ethyl acetate fraction over silicic acid has resulted in the isolation of several cytotoxic C-benzylated flavanones and dihydrochalcones.[1-3] We now wish to report an additional novel cytotoxic flavanoid, for which the trivial name uvarinol (**1**) has been chosen. Uvarinol showed cytotoxicity[4] (ED_{50}) against KB cell cultures at 5.9 μg/mL and against PS cell cultures at 9.7 μg/mL as well as significant antimicrobial activity against *Staphylococcus aureus*, *Bacillus subtilis*, and *Mycobacterium smegmatis*.[5]

A molecular formula of $C_{36}H_{30}O_7$ was established by high-resolution mass spectroscopy and combustion analysis. The UV (λ_{max} (MeOH) 329 nm (ε 16 000)) and IR spectra (KBr, 3100 (broad, OH), 1628 cm^{-1} (CO)) were consistent with a dihydroxylated flavanone nucleus.[1,2] The

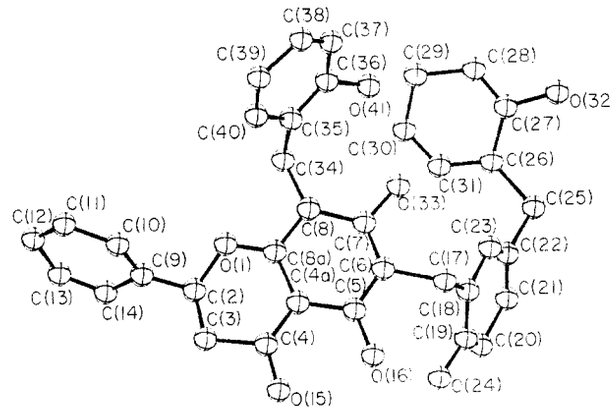

Figure 1. A perspective drawing of the X-ray model of uvarinol (**1**). Hydrogens are omitted for clarity, and the absolute configuration was deduced from CD data.

^1H NMR spectrum (60 MHz, acetone-d_6) clearly showed an ABX pattern characteristic of the protons at C-3 (δ 2.70–3.00, AB) and C-2 (δ 5.70, dd, X) of a flavanone. A 1 H singlet at δ 13.30 (OH at C-5, exchanges with D_2O), three 2 H singlets at δ 4.00, 3.97, and 3.87 (Ar**CH**$_2$Ar), sixteen aromatic protons between δ 6.60 and 7.90, and four additional exchangeable protons comprised the rest of the spectrum. The absence of an upfield aromatic proton suggested that both C-6 and C-8 were substituted.[1] The spectral data of uvarinol are similar to that for dichamenetin,[1,6] a C-dibenzylated flavanone, and suggest that **1** is a tribenzylated flavanone with two benzyl substituents at C-6 and C-8. There were no characteristic fragment ions in the mass spectrum to aid in locating the third benzyl substituent. Since the structural evidence for **1** was largely presumptive and incomplete, a single-crystal X-ray diffraction experiment was done.

Figure 1 is a perspective drawing of the X-ray model of one of the independent molecules of uvarinol. The X-ray experiment defined only the relative configuration, and the absolute configuration shown was chosen to agree with the CD data.[7] All bond distances and angles generally agree with accepted values, although the estimated standard deviations are high (0.05 Å and 3°). The conformations of the independent molecules are essentially the same. In one molecule O(1), C(4), C(4a), and C(8a) are coplanar within 0.05 Å, while C(2) and C(3) are 0.63 and 0.41 Å out of the plane. In the second molecule O(1′), C(4′), C(4a′), and C(8a′) are coplanar within 0.04 Å and C(2′) and C(3′) are 0.50 and 0.17 Å out of the plane. In both molecules there appear to be three intramolecular hydrogen bonds: O(16)H···O(15), O(24)H···O(16), and O(33)H···O(41). These latter two hydrogen bonds could play an important role in determining the molecular conformation. Molecules related by a *c*-axis translation are linked by two intermolecular hydrogen bonds: O(32)H···O(24) and O(41)H···O(15). Surprisingly only van der Waals interactions are found between symmetry-independent molecules.

Uvarinol (**1**) is thus a tribenzylated flavanone. The flavanones are of course widespread in the higher plants, but the addition of benzyl groups is quite rare and seems to be limited to *Uvaria*.[1-3] The benzyl groups presumably arise from a C_6–C_1 pathway, but the *o*-hydroxy functionality is unusual. Recently a biogenetic scheme that would generate *o*-hydroxybenzyl groups from isochorismate has been suggested.[8]

(1) C. D. Hufford and W. L. Lasswell, Jr., *J. Org. Chem.*, **41**, 1297 (1976).
(2) W. L. Lasswell, Jr., and C. D. Hufford, *J. Org. Chem.*, **42**, 1295 (1977).
(3) J. R. Cole, S. J. Torrance, R. M. Weidhopf, S. K. Arora, and R. B. Bates, *J. Org. Chem.*, **41**, 1852 (1976).
(4) Tumor-inhibitory activity and cytotoxicity were assayed under the auspices of the National Cancer Institute by procedures described in *Cancer Chemother. Rep., Part 3*, **3**, 1 (1972).
(5) C. D. Hufford and W. L. Lasswell, Jr., *Lloydia*, **41**, 156 (1978).
(6) C. D. Hufford and W. L. Lasswell, Jr., *Lloydia*, **41**, 151 (1978).
(7) W. Gaffield, *Tetrahedron*, **26**, 4093 (1978).

0022-3263/79/1944-4709$01.00/0