Two New Styryl Lactones, 9-Deoxygoniopypyrone and 7-epi-Goniofufurone, from Goniothalamus giganteus

Xin-Ping Fang, Jon E. Anderson, Ching-Jer Chang, Jerry L. McLaughlin, and Phillip E. Fanwick

J. Nat. Prod., **1991**, 54 (4), 1034-1043• DOI: 10.1021/np50076a017 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 54, No. 4, pp. 1034-1043, Jul-Aug 1991

TWO NEW STYRYL LACTONES, 9-DEOXYGONIOPYPYRONE AND 7-*EPI*-GONIOFUFURONE, FROM *GONIOTHALAMUS GIGANTEUS*

XIN-PING FANG, JON E. ANDERSON, CHING-JER CHANG, JERRY L. MCLAUGHLIN,*

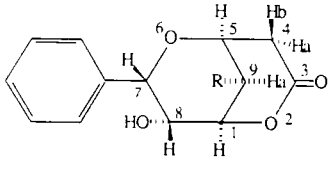
Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences

and PHILLIP E. FANWICK

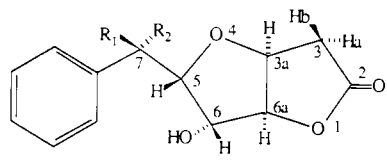
Department of Chemistry, School of Sciences, Purdue University, West Lafayette, Indiana 47907

ABSTRACT.—Two new styryl lactones, 9-deoxygoniopypyrone [**1**] and 7-*epi*-goniofufurone [**3**], and a known styryl lactone, goniodiol [**5**], were isolated from the stem bark of *Goniothalamus giganteus*. The structures were elucidated by ir, ms, ^{1}H-nmr, ^{13}C-nmr, and ^{1}H-^{1}H COSY spectra; the relative configurations were determined by X-ray crystallographic analysis. Unlike goniopypyrone [**2**] and goniofufurone [**4**], neither of the new styryl lactones **1** and **3** showed significant bioactivities to human tumor cells. However, goniodiol [**5**] showed significant and selective cytotoxicity against human lung tumor cells (A-549).

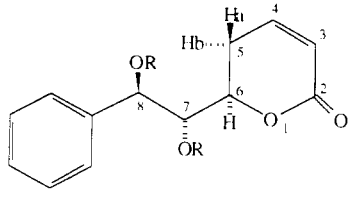
The EtOH extract of the stem bark of *Goniothalamus giganteus* Hook. f. & Thomas (Annonaceae) showed significant murine toxicity in the 3 PS lymphocytic leukemia system (1). Our previous bioactivity-directed studies of this plant have yielded the bioactive compounds altholactone (syn: goniothalenol, a furano-2-pyrone), goniothalamin (a styryl-2-pyrone), and pinocembrin (a flavanone) (2); goniotriol (a styryl-2-pyrone) (3); goniothalamicin, annonacin (4), and gigantecin (three acetogenins) (5); and goniofufurone (a furano-2-furanone), goniopypyrone (a pyrano-2-pyrone), and 8-acetylgoniotriol (6). Two new styryl lactones, 9-deoxygoniopypyrone [**1**] and 7-*epi*-goniofufurone [**3**], and a known styryl lactone, goniodiol [**5**] (7), have now been isolated from the same plant material in our continuing investigation. The structures were elucidated by ir, ms, ^{1}H-nmr, ^{13}C-nmr, and ^{1}H-^{1}H COSY spectra, and the relative configurations were determined by X-ray crystallographic analysis. Neither of the new



1 R=Hb
2 R=OH



3 R_1=OH, R_2=H
4 R_1=H, R_2=OH



5 R=H
6 R=Ac

[1]Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge CB2, 1EW, UK.

compounds **1** and **3** showed significant cytotoxic activity (ED_{50}<4 μg/ml) against A-549 (human lung carcinoma) (8), MCF-7 (human breast adenocarcinoma) (9), and HT-29 (human colon adenocarcinoma) cells (10), and they were not significantly toxic to brine shrimp (BS LC_{50}>400 μg/ml). However, goniodiol was significantly and selectively cytotoxic to the human lung tumor cells (A-549) (Table 1).

TABLE 1. Bioactivities of Compounds **1**, **3**, and **5**.

Compound	Cell line			
	BS LC_{50} (μg/ml)	A-549 ED_{50} (μg/ml)	MCF-7 ED_{50} (μg/ml)	HT-29 ED_{50} (μg/ml)
1	>500	27.20	25.35	7.38
3	475	85.49	49.11	>100
5	>500	1.22×10^{-1}	8.27	2.45
Adriamycin[a]	8×10^{-2}	6.84×10^{-3}	1.77×10^{-2}	4.16×10^{-3}

[a]Positive standard control. For the brine shrimp (BS) assay, adriamycin was dissolved in sea water directly and tested immediately.

RESULTS AND DISCUSSION

The mol wt of 9-deoxygoniopypyrone [**1**] was indicated by a prominent peak at *m/z* 235 $[MH]^+$ in the cims (isobutane) and a peak at *m/z* 234 $[M]^+$ in the eims. The measurement of hreims at *m/z* 234.0891 $[M]^+$ gave the molecular formula $C_{13}H_{14}O_4$ (calcd 234.0888). The presence of a hydroxyl moiety was indicated by peaks at *m/z* 217 $[MH - H_2O]^+$ in the cims, 216 $[M - H_2O]^+$ in the eims, and a broad absorption band at 3456 cm^{-1} in the ir spectrum. The existence of a saturated δ-lactone was supported by carbonyl bands at 1743 and 1720 cm^{-1} in the ir spectrum. The presence of a monosubstituted aromatic ring was indicated by ^1H-nmr and ^{13}C-nmr data (Tables 2 and 3).

The molecular structure of **1** was suggested as 8-hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one by comparing the ^1H-nmr, ^{13}C-nmr, and ms spectra with those of goniopypyrone [**2**] (Tables 2 and 3) (6). The ^1H-^1H COSY spectrum of **1** supported the above structure. The ^{13}C nmr of **1** was assigned by comparison with that of goniopypyrone [**2**], which had been assigned based on HETCOR (6). The eims of **1** had a similar mass fragmentation pattern to that of **2**. The relative configuration of **1** was then determined by X-ray crystallographic data (Figure 1).

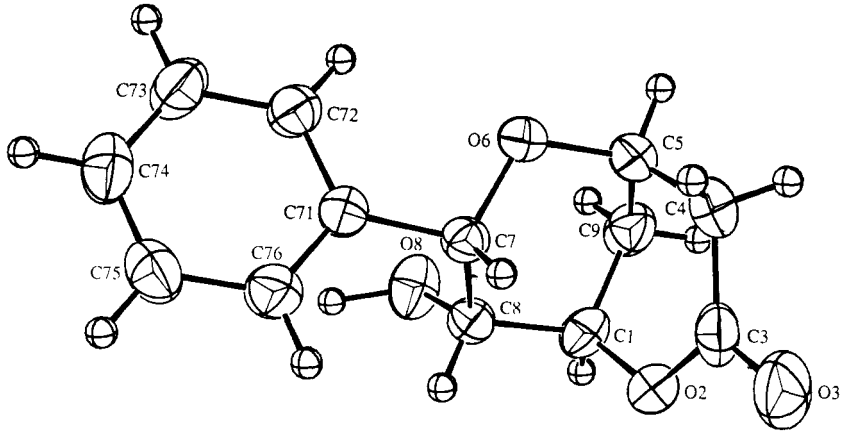


FIGURE 1. ORTEP plot of 9-deoxygoniopypyrone [**1**].

TABLE 2. ^{1}H-nmr Comparisons of Compounds **1–6**.[a]

Proton	Compound		Proton	Compound		Proton	Compound	
	1	**2**		**3**	**4**		**5**	**6**
H-1	4.89 m (4.2,4.0,2)	4.80 br dd (5.8,3.3)	Ha-3	2.77 dd (18.6,6.0)	2.74 dd (18.9,5.9)	H-3	5.98 dd (9.8,2.9)	6.02 ddd (9.8,2.6,1.3)
Ha-4	2.89 dd (19.4,5.2)	3.07 dd (19.5,5.1)	Hb-3	2.71 d (18.6)	2.66 br d (18.9,1.0)	H-4	6.91 ddd (9.8,6.4,2.3)	6.85 ddd (9.8,5.8,2.9)
Hb-4	2.99 dt (19.4,2,1.5)	2.99 dd (19.5,1.5)	H-3a	5.12 dd (6.0,4.0,<1)	5.10 m (5.9,4.2,1.0)	Ha-5	2.78 dddd (18.5,12.8, 2.9,2.3)	2.34 m (2H)
H-5	4.54 m (5.2,4.1,2,1.5)	4.46 m (5.1,1.7,1.5)	H-5	4.24 t (4.0,3.5)	4.08 dd (4.8,2.7)	Hb-5	2.16 ddd (18.5,6.4,3.7)	
H-7	4.97 br s (<1)	5.01 d (1.4)	H-6	4.43 br t (4.5,3.5,<1)	4.38 br t (2.7,<0.4)	H-6	4.77 ddd (12.8,3.7,2.2)	4.75 ddd (11,5.2,2.6)
H-8	3.97 q (4.2,3.3,<1)	4.11 br s	H-6a	4.90 dd (4.0,<1)	4.85 br d (4.2,<0.4)	H-7	3.71 t (8.0,7.0,2.2)	5.33 dd (8.6,2.6)
Ha-9	1.86 dd (14.2,4.0)	4.02 dq (10.6,3.3,1.7)	H-7	5.09 br t (5.0,4.0)	5.19 dd (4.8,2.8)	H-8	4.93 dd (7.0,5.0)	6.02 d (8.6)
Hb-9	2.61 dq (14.2,4.1,2,2)	—	6-OH	3.55 d (4.5)	4.15 d (2.7)	7-OH	2.34 d (8.0)	—
9-OH	—	4.09 d (10.6)	7-OH	2.72 d (5.0)	2.78 d (2.8)	8-OH	2.67 d (5.0)	—
8-OH	1.60 d (3.3)	2.13 d (3.2)	Ph	7.35–7.44 m	7.32–7.43 m	7-OAc	—	1.80 s (3H)
						8-OAc	—	2.07 s (3H)
Ph	7.35–7.43 m	7.34–7.45 m				Ph	7.29–7.41 m	7.27–7.37 m

[a]δ (J in Hz), 500 MHz, $CDCl_3$.

TABLE 3. ^{13}C-nmr Chemical Shift Comparisons of Compounds **1–5** (δ, 125 MHz).

Carbon	Compound		Carbon	Compound		Carbon	Compound
	1 ($CDCl_3$)	**2** [$(CD_3)_2CO$]		**3** [$(CD_3)_2CO$]	**4** [$(CD_3)_2CO$]		**5** ($CDCl_3$)
C-1	74.66	73.96	C-2	176.10	176.07	C-2	163.91
C-3	169.16	168.11	C-3	36.68	36.52	C-3	120.42
C-4	36.33	35.29	C-3a	78.09	78.07	C-4	146.30
C-5	66.08	71.49	C-5	85.81	85.03	C-5	26.04
C-7	70.50	71.09	C-6	75.35	74.80	C-6	76.76
C-8	68.24	70.39	C-6a	89.14	88.57	C-7	73.56
C-9	23.99	64.83	C-7	72.23	72.30	C-8	75.00
C-1′	136.63	139.11	C-1′	142.82	143.62	C-9	140.77
C-2′, -6′	126.08	127.33	C-2′, -6′	127.80	127.71	C-10, -14	126.54
C-3′, -5′	128.87	128.24	C-3′, -5′	128.79	128.81	C-11, -13	128.63
C-4′	128.30	127.69	C-4′	128.22	128.14	C-12	128.14

The mol wt of compound **3** was indicated by a prominent peak at *m/z* 251 $[MH]^+$ in the cims (isobutane). The measurement of hrcims at *m/z* 251.0914 $[MH]^+$ gave the molecular formula $C_{13}H_{15}O_5$ (calcd 251.0919). The presence of two hydroxyl moieties was indicated by peaks at *m/z* 233 $[MH-H_2O]^+$ and 215 $[MH-2H_2O]^+$ in the cims, peaks of two hydroxyl protons at δ 3.55 and 2.72 (exchangeable with D_2O) in the ^{1}H-nmr spectra (Table 2), and an absorption band at 3434 cm^{-1} in the ir spectrum. The existence of a saturated γ-lactone was indicated by a small peak at δ 176.10 in the ^{13}C-nmr spectrum and a carbonyl absorption band at 1737 cm^{-1} (reduced frequency due to formation of intermolecular H-bonds) in the ir spectrum. The presence of a monosubstituted aromatic ring was supported by ^{1}H- and ^{13}C-nmr data (Tables 2 and 3).

The ^{1}H- and ^{13}C-nmr spectral data of compound **3** were very similar to those of goniofufurone [**4**], and the cims was the same as that of **4** (6). The ^{1}H-nmr spectrum and ^{1}H-^{1}H COSY spectrum of **3** showed that the $J_{5/7}$ value (4.0 Hz) was similar to that of goniofufurone [**4**], but the chemical shifts of the H-5 and H-7 changed from δ 4.08 to 4.24 and from 5.19 to 5.09, respectively, thus causing overlap of the H-3a (δ 5.12) and H-7 signals, which were distinctly separated in the ^{1}H-nmr spectrum of **4**. The *J* values of the H-6 and H-7 with the 6-OH and 7-OH protons also changed from 2.7 to 4.5 Hz and from 2.8 to 5.0 Hz, respectively, from **3** to **4**. The melting point (190–192°) of compound **3** was higher than that (152–154°) of goniofufurone [**4**], and the two compounds showed different R_f values on tlc plates. The X-ray crystallographic analysis (Figure 2) then demonstrated that compound **3** was a stereoisomer at the chiral center C-7 of goniofufurone [**4**], and the structure of **3** was finally determined as (3a*S**, 5*S**, 6*R**, 6a*S**, 7*R**)-6-hydroxy-5-(α-hydroxybenzyl)-3a,5,6,6a-tetrahydrofuro[3,2-*b*]furan-2(3*H*)-one and named 7-*epi*-goniofufurone.

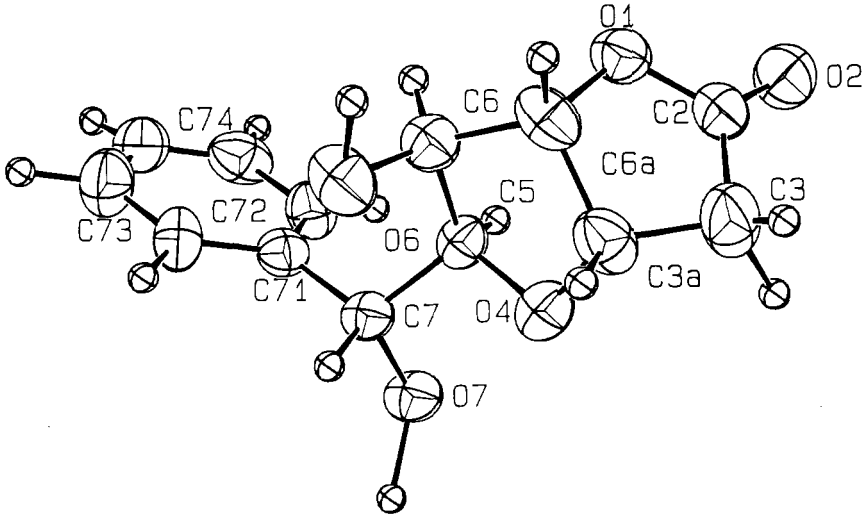


FIGURE 2. ORTEP plot of 7-*epi*-goniofufurone [**3**].

The higher melting point of compound **3** vs. **4** was possibly due to a lack of intramolecular H-bond formation, and both the 6-OH and 7-OH of **3** formed intermolecular H-bonds with carbonyls or hydroxyls from other molecules. The relatively lower melting point of **4** was possibly due to an intramolecular H-bond formed between the 6-OH and the 7-OH and less intermolecular H-bond formation, this information being indicated in the crystal packing data from the X-ray crystallography. 9-Deoxygoniopy-

pyrone [**1**] showed a higher melting point (203–204°) than that of goniopypyrone [**2**] (182–184°), and this was also possibly due to similar reasons.

The bioactive compound **5** was identified as goniodiol, which was previously isolated from other species of *Goniothalamus* (7). The structure was identified based on optical rotation, ir, cims, eims, ^{1}H-nmr, ^{13}C-nmr, and ^{1}H-^{1}H COSY data. However, the isolated **5** was a waxy oil, and goniodiol was previously reported as needlelike crystals (7). To confirm the structure of **5**, the diacetate derivative **6** was made, and fine crystals were obtained. The ^{1}H-nmr and X-ray crystallographic data of **6** proved that **5** was, indeed, goniodiol. The X-ray crystallographic data of goniodiol diacetate [**6**] (Figure 3) and the cytotoxicity of **5** (Table 1) have not been previously reported.

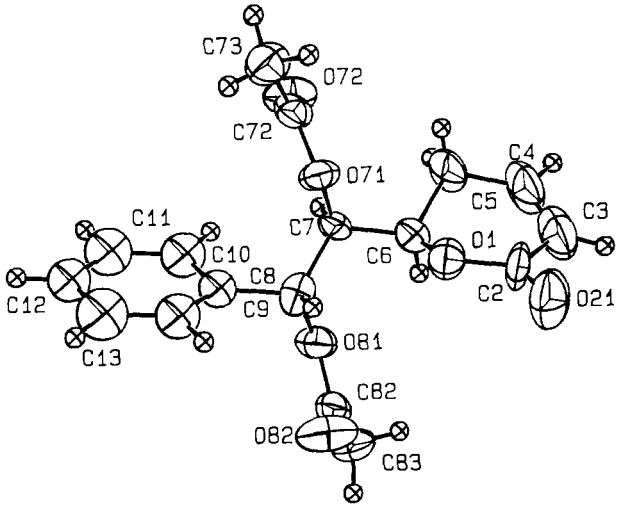


FIGURE 3. ORTEP plot of goniodiol diacetate [**6**].

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were determined on a Mettler FP5 hot-stage apparatus and are uncorrected. The optical rotations were determined on a Perkin-Elmer 241 polarimeter. Uv spectra were taken in EtOH on a Beckman DU-7 spectrophotometer. Ir spectra were obtained in KBr pellets on a Perkin-Elmer 1600 FTIR spectrophotometer. Low resolution ms were recorded on a Finnigan 400 mass spectometer. The exact masses were determined on a Kratos ms 50 spectrometer through peak matching. ^{1}H-nmr and ^{13}C-nmr spectra were recorded on a Varian XL-500S spectrometer.

PLANT MATERIAL.—The stem bark of *G. giganteus* was collected in Thailand in September 1978, under the auspices of Dr. Robert E. Perdue, Medicinal Plant Laboratory, USDA, Beltsville, Maryland, where voucher specimens are maintained.

BIOASSAYS.—Brine shrimp lethality (BS) (11) was tested in our laboratory. The cytotoxicity tests against A-549 (8), MCF-7 (9), and HT-29 (10) cells were performed in the Purdue Cell Culture Laboratory, Purdue Cancer Center, using standard protocols with adriamycin as a positive standard.

EXTRACTION AND ISOLATION.—The residue of the crude EtOH extract (F001) of 4 kg of the stem bark was partitioned between H_2O and $CHCl_3$ to give F003 ($CHCl_3$ layer), the residue of which was partitioned between hexane and 10% H_2O in MeOH to give F005 (MeOH layer, ca. 100 g dry residue). The residue of F005 was repeatedly chromatographed over Si gel columns, using gradients of C_6H_6/EtOAc/MeOH and hexane/EtOAc and gave crude crystals that were recrystallized from EtOAc/hexane to give colorless needles of **1** (7 mg) and **3** (8 mg) and a waxy oil of **5** (35 mg).

9-Deoxygoniopypyrone [**1**].—Mp 203–204°; $[\alpha]^{22}D$ +12 (c = 0.1, EtOH); uv (EtOH) λ max 212 nm (log ε 3.74); ir (KBr) ν max 3456 (OH), 1743 (δ-lactone), 1720 (H-bonding δ-lactone), 1637, 1187, 1058; cims (isobutane) m/z (%) $[MH]^+$ 235 (100), $[MH-H_2O]^+$ 217 (12); eims m/z (%) $[M]^+$ 234 (5.4), $[M-H_2O]^+$ 216 (1.4), 188 (1.5), 177 (3.7), 157 (2), 149 (6), 144 (4), 128 (13), 107 (65), 91 (50), 77

(54); hreims *m/z* 234.0891 for $C_{13}H_{14}O_4$ (calcd 234.0888); ^{1}H nmr (500 MHz, $CDCl_3$) see Table 2; ^{13}C nmr (125 MHz, $CDCl_3$) see Table 3; ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$).

7-epi-*Goniofufurone* [**3**].—Mp 190–192°, $[\alpha]^{22}D$ +108 (*c* = 0.2, EtOH); uv (MeOH) λ max 203 nm (log ε 3.17); ir (film) ν max 3434 (OH), 1737 (H-bonding γ-lactone), 1653, 1325, 1143, 1044, 1008 cm^{-1}; cims (isobutane) *m/z* (%) $[MH]^+$ 251 (62), $[MH-H_2O]^+$ 233 (100), $[MH-2H_2O]^+$ 215 (20); hrcims (isobutane) *m/z* 251.0914 for $C_{13}H_{15}O_5$ (calcd 251.0919); eims *m/z* (%) 232 (1), 173 (1), 149 (3), 143 (1), 126 (57), 107 (100), 105 (50), 97 (15), 91 (22), 82 (56), 77 (45); ^{1}H nmr (500 MHz, $CDCl_3$) see Table 2; ^{13}C nmr (125 MHz, CD_3COCD_3) see Table 3; ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$).

Goniodiol [**5**].—$[\alpha]^{22}D$ +74.4 (*c* = 0.3, $CDCl_3$) ir (film) ν max 3406 (OH), 1700 (δ-unsaturated lactone), 1389, 1255, 1030, 902, 816, 768, 701 cm^{-1}; cims (isobutane) *m/z* (%) $[MH]^+$ 235 (51), $[MH-H_2O]^+$ 217 (100), $[MH-2H_2O]^+$ 199 (1); eims *m/z* (%) $[M-OH]^+$ 217 (0.6), 128 (65), 120 (3), 110 (48), 107 (59), 105 (7), 99 (23), 97 (16), 91 (25), 82 (77), 79 (100), 77 (77); ^{1}H nmr (500 MHz, $CDCl_3$) see Table 2; ^{13}C nmr (125 MHz, $CDCl_3$) see Table 3; ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$).

Goniodiol diacetate [**6**].—Compound **5** (5 mg) was acetylated (Ac_2O/pyridine, 12 h, room temperature), and the mixture was partitioned between H_2O and $CHCl_3$. The $CHCl_3$ extract on concentration and chromatography afforded compound **6** (4 mg, needle crystals): mp 141–143°; ^{1}H nmr (500 MHz, $CDCl_3$) see Table 2.

X-RAY CRYSTALLOGRAPHIC ANALYSIS OF **1**[1].—*Data collection*.—A colorless rod of $C_{13}H_{14}O_4$ having approximate dimensions of 0.55 × 0.28 × 0.20 mm was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with MoKα radiation (λ = 0.7103 Å) on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer equipped with a graphite crystal, incident beam monochromator. Cell constants and an orientation matrix for data collection were obtained from least-squares refinement, using the setting angles of 25 reflections in the range $15<\theta<20°$, measured by the computer-controlled diagonal slit method of centering. The orthorhombic cell parameters and calculated volume are: *a* = 6.195 (1), *b* = 7.994 (1), *c* = 22.429 (2) Å, V = 1110.7 Å^3. For Z = 4 and formula wt = 234.235 the calculated density is 1.40 g·cm^{-3}. As a check on crystal quality, omega scans of 25 intense reflections were measured by 1/5000 sec; the width at half-height was 0.56° with a take-off angle of 3.2° indicating moderate crystal quality. From the systematic absences of *h*00 *h* = 2n + 1, 0*k*0 *k* = 2n + 1, 00*l* *l* = 2n + 1 and from subsequent least-squares refinement, the space group was determined to be $P2_12_12_1$ (no. 19). The data were collected at a temperature of 20 ± 1° using the ω–2θ scan technique. The scan rate varied from 1 to 20° min (in omega). Data were collected to a maximum 2θ of 55.0° by a ω/2θ mode with ω scan width = 0.56 + 0.350 tan θ. A total of 1536 reflections were collected (*h*, *k*, *l* limits: 0–8, 0–10, 0–29), of which 1536 were unique and not systematically absent. Lorentz and polarization corrections were applied to the data. The linear absorption coefficient is 1.0 cm^{-1} for Mo Kα radiation. No absorption correction was made (Tables 4 and 5, Figure 1).

Structure solution and refinement.—The structure was solved using the structure solution program SHELX-86 (G.M. Sheldrick, Institut für Anorganische Chemie der Universität Göttingen, Germany). The remaining atoms were located in succeeding difference Fourier syntheses. Hydrogen atoms were located and added to the structure factor calculations, but their positions were not refined. The structure was refined in full-matrix least-squares where the function minimized was $\Sigma w(|Fo|-|Fc|)^2$ and the weight w is defined by the Killean and Lawrence method (12) with terms of 0.020 and 1.0. Scattering factors were taken from Cromer and Weber (13). Anomalous dispersion effects were included in Fc (14); the values for δf′ and δf″ were those of Cromer and Weber (13). Only the 1087 reflections having intensities greater than 3.0 times their standard deviation were used in the refinements. The final cycle of refinement included 158 variable parameters and converged (largest parameter shift was 0.05 time ESD) with unweighted and weighted agreement factors of $R1 = \Sigma||Fo|-|Fc||/\Sigma|Fo| = 0.039$, $R2 = SQRT[\Sigma w(|Fo|-|Fc|)^2 / \Sigma w Fo^2] = 0.047$. The standard deviation of an observation of unit weight was 1.16. There were no correlation coefficients greater than 0.50. The highest peak in the final difference Fourier had a height of 0.18 e/Å^3 with an estimated error based on δF of 0.04. The refined values for the other enantiomorph are R = 0.039, Rw = 0.048, and the estimated standard deviation of an observation of unit weight = 1.182. Plots of $\Sigma w(|Fo|-|Fc|)^2$ versus |Fo|, reflection order in data collection, sin θ/λ, and various of indices showed no unusual trends. All calculations were performed on a VAX computer using SDP/VAX.

X-RAY CRYSTALLOGRAPHIC ANALYSIS OF **3** AND **6**[1].—Procedures were essentially the same as those followed for the X-ray crystallographic analysis of **1**, except the hydrogen positions and isotropic thermal parameters of **3** were refined, and the crystal data and data collection parameters were given in Table 5 (Figures 2, 3; Tables 4, 5).

TABLE 4. Atomic Fractional Co-ordinates (ESD) of Compounds **1**, **3**, and **6**.

Atom	1			Atom	3			Atom	6		
	x	*y*	*z*		*x*	*y*	*z*		*x*	*y*	*z*
O-2	1.5027(3)	0.4572(2)	0.1668(8)	O-1	−0.3944(3)	0.8764(2)	0.3032(2)	O-1	0.897(1)	0.3566(8)	0.1157(7)
O-3	1.4225(5)	0.2111(3)	0.1329(1)	O-2	−0.5209(4)	0.7257(3)	0.3670(2)	O-21	1.075(2)	0.345(1)	−0.0704(9)
O-6	1.0059(3)	0.6506(3)	0.1611(8)	O-4	−0.0233(4)	1.0418(2)	0.3639(2)	O-71	0.947(1)	0.4021(8)	0.4269(7)
O-8	1.3622(4)	0.8928(2)	0.1812(9)	O-6	−0.0130(4)	0.7272(2)	0.2501(3)	O-72	0.834(1)	0.5823(9)	0.5850(9)
C-1	1.4422(5)	0.6119(3)	0.1967(1)	O-7	0.2137(3)	0.8291(2)	0.2348(2)	O-81	0.31970	0.10590	0.13780
C-3	1.3592(6)	0.3365(3)	0.1563(1)	C-2	−0.4138(5)	0.7973(4)	0.3751(3)	O-82	0.412(2)	−0.1000(9)	0.002(1)
C-4	1.1273(6)	0.3595(4)	0.1749(1)	C-3	−0.2856(6)	0.8144(5)	0.4576(3)	C-2	0.956(2)	0.408(1)	0.005(1)
C-5	1.0703(5)	0.5262(4)	0.2038(1)	C-3a	−0.1570(5)	0.8909(4)	0.4123(3)	C-3	0.882(3)	0.545(1)	−0.018(1)
C-7	1.1708(4)	0.6919(3)	0.1187(1)	C-5	−0.0343(4)	0.8418(3)	0.2553(3)	C-4	0.822(3)	0.632(1)	0.090(1)
C-8	1.3803(5)	0.7405(3)	0.1497(1)	C-6	−0.1282(5)	0.9519(3)	0.2389(3)	C-5	0.781(3)	0.592(1)	0.229(1)
C-9	1.2603(6)	0.5851(4)	0.2397(1)	C-6a	−0.2533(5)	0.9497(3)	0.3272(3)	C-6	0.708(2)	0.407(1)	0.183(1)
C-71	1.0914(5)	0.8309(3)	0.0795(1)	C-7	0.1442(5)	0.8370(3)	0.2119(3)	C-7	0.678(2)	0.3473(9)	0.311(1)
C-72	0.9176(5)	0.9322(4)	0.0946(1)	C-71	0.1458(5)	0.8548(3)	0.0982(3)	C-8	0.579(2)	0.161(1)	0.258(1)
C-73	0.8537(6)	1.0626(4)	0.0578(1)	C-72	0.2183(6)	0.9495(3)	0.0569(3)	C-9	0.541(2)	0.092(1)	0.383(1)
C-74	0.9646(6)	1.0925(4)	0.0055(1)	C-73	0.2190(6)	0.9652(4)	−0.0478(4)	C-10	0.393(2)	0.152(1)	0.477(1)
C-75	1.1364(6)	0.9938(4)	0.0101(1)	C-74	0.1497(6)	0.8864(4)	−0.1107(3)	C-11	0.353(3)	0.083(2)	0.592(2)
C-76	1.1985(5)	0.8628(4)	0.0261(1)	C-75	0.0749(5)	0.7910(4)	−0.0701(3)	C-12	0.444(2)	−0.035(1)	0.607(1)
H(O-8)	1.345(8)	0.976(5)	0.157(2)	C-76	0.0732(5)	0.7742(3)	0.0336(3)	C-13	0.586(3)	−0.091(2)	0.514(2)
				H(O-6)	0.389(7)	0.403(5)	0.747(4)	C-14	0.626(2)	−0.022(1)	0.406(1)
				H(O-7)	0.640(8)	0.232(5)	0.214(4)	C-72	0.990(2)	0.518(1)	0.564(1)
								C-73	1.255(2)	0.545(1)	0.679(1)
								C-82	0.262(2)	−0.023(1)	0.008(1)
								C-83	0.000(2)	−0.054(1)	−0.103(1)

TABLE 5. Crystal Data and Data Collection Parameters of Compounds **1**, **3**, and **6**.

Data and Parameters	Compound		
	1	**3**	**6**
Formula	$O_4C_{13}H_{14}$	$O_5C_{13}H_{14}$	$O_6C_{17}H_{18}$
Formula weight	234.235	250.25	318.33
Space group	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)	$P1$ (No. 1)
a, Å	6.1946(7)	7.8365(6)	5.312(2)
b, Å	7.9942(7)	11.825(1)	9.135(3)
c, Å	22.429(2)	13.1699(8)	9.545(3)
V, Å^3	1110.7(3)	1220.5(3)	405.7(7)
Z	4	4	1
D_c, g·cm^{-3}	1.401	1.362	1.303
Crystal dimensions, mm	0.55 × 0.28 × 0.20	0.44 × 0.31 × 0.25	0.56 × 0.20 × 0.06
Temperature, deg C	20°	20°	20°
Radiation (wavelength)	MoKα (0.71073 Å)	MoKα (0.71073 Å)	MoKα (0.71073 Å)
Monochromator	graphite	graphite	graphite
Linear Absorption coefficient, cm^{-1}	0.97	0.98	0.93
Absorption correction applied	none	none	none
Diffractometer	Enraf-Nonius CAD4	Enraf-Nonius CAD4	Enraf-Nonius CAD4
Scan method	ω–2θ	ω–2θ	ω–2θ
h,k,l limits	*0 to 8, 0 to 10, 0 to 29*	*0 to 9, 0 to 14, 0 to 15*	*−6 to 6, −10 to 10, 0 to 11*
2θ range, deg	4.00–55.00	4.00–50.00	4.00–50.00
Scan width, deg	0.56 + 0.35 tan θ	0.49 + 0.35 tan θ	0.84 + 0.35 tan θ
Take-off angle, deg	3.15	2.95	2.95
Programs used	Enraf-Nonius SDP	Enraf-Nonius SDP	Enraf-Nonius SDP
F_{000}	496.0	528.0	168.0
p-factor used in weighting	0.040	0.040	0.040
Data collected	1536	1280	1422
Unique data	1536	1280	1422
Data with I>3.0 (I)	1087	1040	838
Number of variables	158	219	175
Largest shift/esd in final cycle	0.05	0.26	0.15
R	0.039	0.043	0.072
Rw	0.047	0.058	0.087
Goodness of fit	1.158	1.653	1.744

ACKNOWLEDGMENTS

This research was supported by R01 grant no. CA30909 from the National Cancer Institute, National Institutes of Health. Thanks are due to the Purdue Cell Culture Laboratory, Purdue Cancer Center, for cytotoxicity testing. We thank Dr. John M. Cassady for help in obtaining the plant material.

LITERATURE CITED

1. R.I. Geran, N.H. Greenberg, M.M. MacDonald, A.M. Schumacher, and B.J. Abbott, *Cancer Chemother. Rep.*, **3**, 1 (1972).
2. A.A. Ebrahim ElZayat, N.R. Ferrigni, T.G. McCloud, A.T. McKenzie, S.R. Byrn, J.M. Cassady, C.J. Chang, and J.L. McLaughlin, *Tetrahedron Lett.*, **26**, 955 (1985).
3. A. Alkofahi, W.W. Ma, A.T. McKenzie, S.R. Byrn, and J.L. McLaughlin, *J. Nat. Prod.*, **52**, 1371 (1989).
4. A. Alkofahi, J.K. Rupprecht, D.L. Smith, C.J. Chang, and J.L. McLaughlin, *Experientia*. **44**, 83 (1988).
5. A. Alkofahi, J.K. Rupprecht, Y.M. Liu, C.J. Chang, D.L. Smith, and J.L. McLaughlin, *Experientia*, **46**, 539 (1990).

6. X.P. Fang, J.E. Anderson, C.J. Chang, P.E. Fanwick, and J.L. McLaughlin, *J. Chem. Soc., Perkin Trans. 1*, 1655 (1990).
7. S.K. Talapatra, D. Basu, T. Deb, S. Goswami, and B. Talapatra, *Indian J. Chem.*, **24B**, 29 (1985).
8. D.J. Giard, S.A. Aronson, G.J. Todaro, P. Arnstein, J.H. Kersey, H. Dosik, and W.P. Parks, *J. Natl. Cancer Inst.*, **51**, 1417 (1973).
9. H.D. Soule, J. Vazquez, A. Long, S. Albert, and M. Brennan, *J. Natl. Cancer Inst.*, **51**, 1409 (1973).
10. J. Fogh and G. Trempe, in: "Human Tumor Cells in Vitro." Ed. by J. Fogh, Plenum Press, New York, 1975, p. 115.
11. B.M. Meyer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, and J.L. McLaughlin, *Planta Med.*, **45**, 31 (1982).
12. R.C.G. Killean and J.L. Lawrence, *Acta Crystallogr., Sect. B*, **25**, 1750 (1969).
13. D.T. Cromer and J.T. Weber, "International Tables for X-ray Crystallography," The Kynoch Press, Birmingham, England, Vol. 4, Table 2.2B (1974).
14. J.A. Ibers and W.C. Hamilton, *Acta Crystallogr.*, **17**, 781 (1964.

Received 4 December 1990