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CONFORMATION AND ABSOLUTE CONFIGURATION OF NATURALLY OCCURRING PARVIFOLINE AND SEVERAL SYNTHETIC DERIVATIVES

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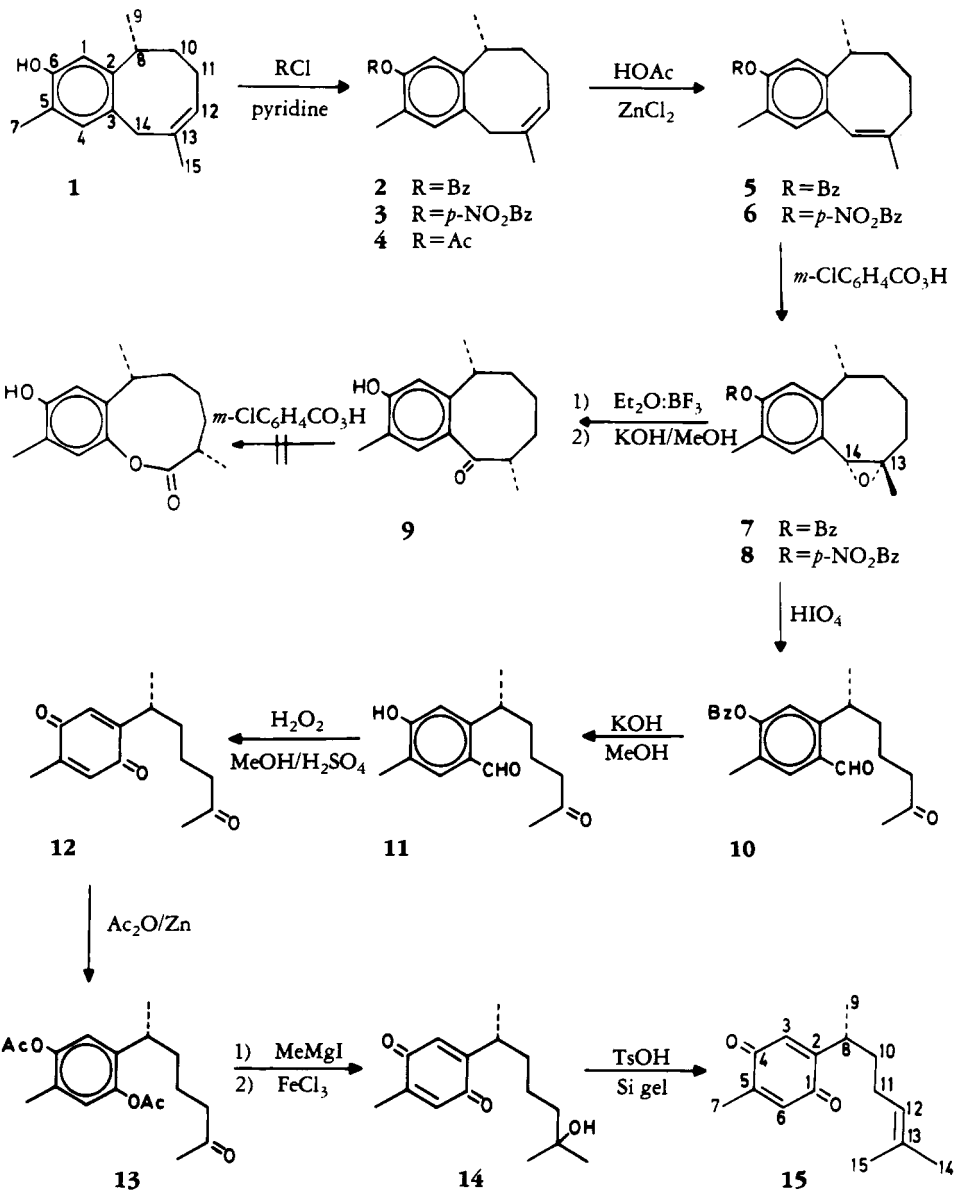
ABSTRACT.—Chemical transformation of parvifoline [**1**] to curcuquinone [**15**] established the absolute configuration of **1** as the *R* enantiomer. The solution conformation of four parvifoline derivatives containing eight-membered rings [**2**, **5**, **8**, and **9**] generated during this transformation is obtained from the vicinal coupling constants provided by their ^{1}H-nmr spectra. The eight-membered ring of **2** exists as a distorted twist-boat, that of **5** as a twist-boat, and that of **8** in a twist-boat-chair conformation. In **9** the ring exists in a conformation midway between boat and twist-boat. The conformation in the solid state of these compounds, obtained by X-ray diffraction analyses, is essentially the same as that found in solution. Furthermore, ^{13}C-nmr data of seven parvifoline and five curcuquinone derivatives are reported.

Parvifoline [**1**] (Scheme 1) is a bicyclic sesquiterpene found as a constituent of *Coreopsis parvifolia* (1), *Perezia carpholepis* (2), and *Perezia alamani* var. *oolepis* (3). Its structure was deduced from spectral data and chemical transformations, but no conclusive evidence about its absolute configuration was described (1). The present paper reports the chemical transformation of this benzocyclooctene **1** to curcuquinone [**15**] (4). Because the absolute configuration of **15** is known (4), this correlation establishes the absolute configuration of parvifoline and of its derivatives. In addition, the conformation of the eight-membered ring of four parvifoline derivatives (**2**, **5**, **8**, and **9**) generated in this transformation, in solution and in the solid state, is described.

RESULTS AND DISCUSSION

ABSOLUTE CONFIGURATION.—Chemical transformation of parvifoline [**1**] to curcuquinone [**15**] was carried out by means of the reaction sequence represented in Scheme 1. Treatment of the hexane extracts of the roots of *P. alamani* var. *oolepis* (3) with benzoyl chloride/pyridine gave parvifoline benzoate [**2**] in good yields. This procedure provided appropriate amounts of starting material **2** for the correlation. Comparison between **2** and **15** (Scheme 1) shows that cleavage of the C-3 to C-14 bond of **2** could lead to a sesquiterpene with a structure closely related to curcuquinone [**15**]. Thus, to correlate these two substances, the following reaction sequence involving such a cleavage was attempted. Isomerization of the double bond of **2** was achieved with HOAc/$ZnCl_2$ to yield isoparvifoline benzoate [**5**]. Epoxidation of **5** with *m*-chloroperbenzoic acid afforded **7**. Rearrangement of the epoxide **7** with Et_2O/BF_3 (5) yielded, after alkaline hydrolysis of the benzoate group, 14-oxodihydroparvifoline [**9**]. Treatment of the ketone **9** under Baeyer-Villiger conditions (6) would lead to a lactone with an oxygen atom attached to the aromatic ring. However, the last reaction was unsuccessful. An alternative procedure involving cleavage of the C-13 to C-14 bond was achieved starting with epoxide **7**. Periodic acid oxidation (7) of compound **7** gave the ketone-aldehyde **10**, which was converted to the *p*-benzoquinone **12** by alkaline hydrolysis with KOH/MeOH, followed by an oxidative decarbonylation with H_2O_2/MeOH/H_2SO_4 (8). Treatment of quinone **12** with Ac_2O/Zn protected the carbonyl groups as the hydroquinone diester. Introduction of a methyl group at C-13 by means of MeMgI with concomitant removal of the acetates, followed by oxidation of the reaction product with $FeCl_3$, afforded compound **14**. Finally, dehydration of the tertiary hydroxyl group



SCHEME 1. Reaction sequence for the transformation of parvifoline [**1**] to curcuquinone [**15**].

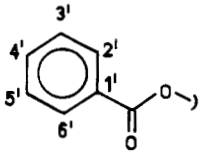
of **14** with silica gel/*p*-toluenesulfonic acid (9) yielded curcuquinone [**15**], identical to the natural product in all respects (4). Curcuquinone [**15**] obtained from parvifoline [**1**] showed $[\alpha]_D = -1.58°$, a value very similar to that reported for the natural product, $[\alpha]_D = -1.3°$ (4). Inasmuch as the absolute configuration of the natural curcuquinone is *R* (4), it follows that parvifoline has the same absolute configuration.

Structures for the compounds obtained during this transformation were established from their nmr spectra. ^{1}H-nmr data are reported in the Experimental section and ^{13}C-nmr data of parvifoline and curcuquinone derivatives are summarized in Tables 1 and 2, respectively. The ^{13}C-nmr assignments were achieved by comparison with previously reported data of related molecules (1,10) and from information provided by their ^{1}H-coupled ^{13}C-nmr spectra.

TABLE 1. ^{13}C-nmr Chemical Shifts of Parvifoline Derivatives.[a]

Carbon	Compound						
	2	**3**	**5**	**6**	**7**	**8**	**9**
1	117.8 (d)	117.5 (d)	117.8 (d)	117.5 (d)	117.5 (d)	117.5 (d)	113.2 (d)
2	144.2 (s)	144.6 (s)	143.0 (s)	143.3 (s)	144.4 (s)	145.0 (s)	143.8 (s)
3	136.3 (s)	137.0 (s)	140.5 (s)	141.0 (s)	132.7 (s)	133.5 (s)	131.5 (s)
4	131.9 (d)	132.1 (d)	130.6 (d)	130.8 (d)	131.0 (d)	131.4 (d)	131.0 (d)
5	126.8 (s)	126.5 (s)	126.3 (s)	126.0 (s)	127.6 (s)	127.5 (s)	121.8 (s)
6	148.9 (s)	148.5 (s)	148.4 (s)	148.0 (s)	149.4 (s)	149.3 (s)	157.3 (s)
7	15.7 (q)	15.7 (q)	15.6 (q)	15.6 (q)	15.7 (q)	15.7 (q)	15.3 (q)
8	33.3 (d)	33.4 (d)	33.4 (d)	33.5 (d)	34.3 (d)	34.4 (d)	36.1 (d)
9	19.3 (q)	19.4 (q)	21.2 (q)	21.2 (q)	22.0 (q)	22.0 (q)	22.9 (q)
10	40.0 (t)	40.0 (t)	39.2 (t)	39.2 (t)	40.7 (t)	40.8 (t)	35.7 (t)
11	23.9 (t)	23.9 (t)	22.3 (t)	22.2 (t)	24.0 (t)	24.0 (t)	23.5 (t)
12	123.7 (d)	123.7 (d)	35.4 (t)	35.4 (t)	33.0 (t)	33.1 (t)	32.4 (t)
13	137.3 (s)	137.3 (s)	135.6 (s)	136.1 (s)	61.9 (s)	62.0 (s)	46.4 (d)
14	41.9 (t)	41.9 (t)	122.3 (d)	122.0 (d)	63.0 (d)	63.0 (d)	210.4 (s)
15	26.3 (q)	26.3 (q)	26.2 (q)	26.2 (q)	22.1 (q)	22.1 (q)	17.0 (q)
CO	164.8 (s)	163.1 (s)	164.6 (s)	162.9 (s)	164.8 (s)	162.9 (s)	—
1′	129.9 (s)	135.1 (s)	129.6 (s)	134.9 (s)	129.3 (s)	134.9 (s)	—
2′,6′	130.1 (d)	131.2 (d)	129.9 (d)	131.0 (d)	129.9 (d)	131.2 (d)	—
3′,5′	128.5 (d)	123.7 (d)	128.4 (d)	123.5 (d)	128.4 (d)	123.7 (d)	—
4′	133.4 (d)	150.9 (s)	133.2 (d)	150.6 (s)	133.3 (d)	150.9 (s)	—

[a]In ppm from internal TMS. Benzoate group carbon numbering is according to the following figure:



. Multiplicities were observed in the coupled spectra.

CONFORMATION.—The conformations in solution were deduced from information extracted from the 300 MHz ^{1}H-nmr spectra of derivatives **2**, **5**, **8**, and **9**. Compound **8** was obtained in the same way as **7**, but using *p*-nitrobenzoyl chloride instead of benzoyl chloride when treating the *P. alamani* extracts. The signals of the protons of the eight-membered ring of the four compounds were assigned with the aid of homonuclear spin-spin decoupling experiments. Furthermore, because the ^{13}C-nmr spectra of these derivatives were fully assigned (Table 1), their two-dimensional ^{1}H/^{13}C heteronuclear chemical shift correlation diagrams (see Experimental) confirmed the hydrogen assignments. Vicinal proton coupling constants of the (C-8)-(C-10)-(C-11)-(C-12)-(C-13) fragment of **9** and of the (C-8)-(C-10)-(C-11)-(C-12) fragment of **2**, **5**, and **8** gave the conformational information. Estimations of the H-C-C-H dihedral angles were achieved (Table 3) by means of a generalized Karplus-type relationship (11). Although individual assignments of the methylene group signals of the four compounds were initially not known and application of the Karplus-type relationship (11) provided several dihedral angle values for each H-C-C-H fragment, observation of Dreiding models showed that only one was consistent with the eight-membered ring geometry and also with the dihedral angle values found for the other H-C-C-H fragments of the same molecule. This fact established the conformation and enabled individual ^{1}H-nmr assignments of the methylene protons. Vicinal coupling constants and their corresponding calculated dihedral angles are given in Table 3, while approximate projections of the Dreiding models of **2**, **5**, **8**, and **9** are drawn in Figures 1 to 4, respectively. According to published conformations for 1,3- and 1,4-cyclooctadiene (12,13) and for 1,3-

TABLE 2. ^{13}C-nmr Chemical Shifts of Curcuquinone Derivatives.[a]

Carbon	Compound				
	10	**11**	**12**	**13**	**14**
1	131.3 (s)	125.9 (s)	186.9 (s)	145.7 (s)	187.5 (s)
2	149.4 (s)	150.7 (s)	153.3 (s)	137.4 (s)	154.2 (s)
3	120.5 (d)	112.8 (d)	131.0 (d)	120.4 (d)	131.2 (d)
4	154.0 (s)	160.7 (s)	187.9 (s)	147.3 (s)	188.5 (s)
5	128.4 (s)	122.7 (s)	144.9 (s)	128.6 (s)	145.2 (s)
6	134.9 (d)	136.0 (d)	133.5 (d)	124.6 (d)	133.8 (d)
7	15.7 (q)	15.3 (q)	15.2 (q)	15.8 (q)	15.3 (q)
8	32.2 (d)	32.1 (d)	31.3 (d)	32.6 (d)	31.5 (d)
9	21.7 (q)	21.9 (q)	19.2 (q)	21.1 (q)	19.4 (q)
10	37.4 (t)	37.2 (t)	35.0 (t)	36.6 (t)	36.4 (t)
11	21.7 (t)	21.7 (t)	21.3 (t)	21.9 (t)	22.3 (t)
12	43.3 (t)	43.5 (t)	43.1 (t)	43.5 (t)	43.7 (t)
13	208.1 (s)	210.6 (s)	208.0 (s)	208.7 (s)	70.9 (s)
14	29.6 (q)	29.9 (q)	29.8 (q)	29.7 (q)	29.4 (q)
15	—	—	—	—	29.2 (q)
CHO	191.0 (d)	191.5 (d)	—	—	—
CO	163.9 (s)	—	—	—	—
1′	128.8 (s)	—	—	—	—
2′,6′	130.0 (d)	—	—	—	—
3′,5′	128.6 (d)	—	—	—	—
4′	133.7 (d)	—	—	—	—
MeCO(C-1)	—	—	—	169.5 (s)[b]	—
CH_3CO(C-1)	—	—	—	20.8 (q)[b]	—
MeCO(C-4)	—	—	—	168.9 (s)[b]	—
CH_3CO(C-4)	—	—	—	20.7 (q)[b]	—

[a]In ppm from internal Me_4Si. Carbon numbering is according to that of curcuquinone [**11**]. Multiplicities were observed in the coupled spectra.

[b]Acetate signals were distinguished taking into account the data of a series of curcumenes (P. Joseph-Nathan, R. Tovar-Miranda, E. Martínez, and R.L. Santillan, submitted for publication in *J. Nat. Prod.*).

cyclooctadiene mono-epoxide (12), the eight-membered ring of **2** appears as a distorted twist-boat, that of **5** as a twist-boat, and that of **8** as a twist-boat-chair. The eight-membered ring of compound **9** exists in a conformation midway between boat and twist-boat, in analogy with conformational nomenclature for *cis*-cyclooctene (14). Further evidence to support the conformation of **9** was obtained when an nOe between H-8 and H-13 (11%) was observed.

The X-ray diffraction analyses of compounds **2**, **5**, **8**, and **9** allowed comparison between the conformation in the solid state and in solution. The results show (Table 3) that in each case the conformation is essentially the same in both states. In addition, C-C-C-C torsion angles for **2** and **5** (Table 4) reasonably correspond with those reported (12,13) for the corresponding 1,4- and 1,3-cyclooctadiene conformations, respectively. Perspective views of the molecular structures of **2**, **5**, **8**, and **9** are drawn in Figures 1 to 4, respectively. The X-ray diffraction studies of **8** and **9** also provide the stereochemistry of the chiral centers located at C-13 and C-14 in **8** and at C-13 in **9**.

The eight-membered ring conformations of parvifoline [**1**] and of its acetate **4** were reported as boat-chair (1). However, a careful revision of the published ^{1}H-nmr spectral interpretation reveals several inconsistencies of the coupling constants owing to the signals at δ 1.07 (J = 3.5, 4.5, 12.5, and 12.5) [lit. (1): δ 1.10; J = 4, 10, 10, and 15 Hz] and at δ 1.54 (J = 3.5, 3.5, 8.0, and 13.0 Hz) [lit. (1): δ 1.54; J = 10, not assigned, 8, and 10 Hz] in the spectrum of **4**. The ^{1}H-nmr spectrum of **4** shows essen-

TABLE 3. Eight-membered Ring Vicinal ^{1}H-^{1}H Coupling Constants [J(Hz)], Calculated H_x-C-C-H_y Dihedral Angles for the Conformation in Solution[a] [ϕ_S (deg)], and X-ray H_x-C-C-H_y Dihedral Angles[b] [ϕ_{XR} (deg)] of Parvifoline Derivatives **2**, **5**, **8**, and **9**.

H_x-C-C-H_y		Compound											
		2			**5**			**8**			**9**		
x	y	J	ϕ_S	ϕ_{XR}	J	ϕ_S	ϕ_{XR}	J	ϕ_S	ϕ_{XR}	J	ϕ_S	ϕ_{XR}
8	10α	4.5	−52	−53.2 (0.1)	3.0	−61	−60.0 (0.1)	1.0	−85	−84.2 (0.2)	4.5	−52	−48.7 (0.1)
8	10β	12.0	−169	−171.9 (0.0)	11.0	−159	−178.5 (0.0)	10.0	153	157.9 (0.0)	11.0	−159	−166.2 (0.0)
10α	11α	3.5	−58	−58.1 (0.1)	(−)[c]	(−)[d]	−55.4 (0.1)	4.0	54	39.3 (0.3)	4.0	−55	−64.6 (0.1)
10α	11β	12.5	−162	−176.9 (0.0)	(−)[c]	(−)[d]	−173.9 (0.0)	4.0	−54	−75.7 (0.3)	10.0	148	177.0 (0.0)
10β	11α	3.5	57	60.7 (0.1)	(−)[c]	(−)[d]	63.4 (0.1)	11.0	152	157.3 (0.1)	4.0	54	53.0 (0.1)
10β	11β	3.5	−57	−58.1 (0.1)	(−)[c]	(−)[d]	−55.0 (0.1)	6.0	45	42.3 (0.3)	4.0	−55	−65.5 (0.1)
11α	12	8.0	30	15.0 (0.2)	—	—	—	—	—	—	—	—	—
11α	12α	—	—	—	0.0	87	77.9 (0.1)	2.5	−62	−67.9 (0.3)	2.0	67	56.8 (0.1)
11α	12β	—	—	—	8.5	−31	−39.0 (0.1)	11.5	156	175.5 (0.0)	(−)[c]	(−)[d]	−60.4 (0.1)
11β	12	8.0	147	133.9 (0.1)	—	—	—	—	—	—	—	—	—
11β	12α	—	—	—	11.0	−153	−163.3 (0.0)	6.0	45	47.2 (0.5)	11.0	152	175.3 (0.0)
11β	12β	—	—	—	0.0	87	79.9 (0.1)	2.0	−66	−69.4 (0.3)	(−)[c]	(−)[d]	58.1 (0.1)
12α	13	—	—	—	—	—	—	—	—	—	6.0	43	55.7 (0.1)
12β	13	—	—	—	—	—	—	—	—	—	9.5	149	172.9 (0.0)

[a]Estimated with the generalized Karplus-type relationship described in Haasnoot *et al.* (11) except 11α-12 and 11β-12 values of compound **2** which were estimated with the relationship $J = J_0\cos^2\phi$ where $J_0 = 10.6$ for $0° \leq \phi \leq 90°$ and $J_0 = 11.4$ for $90° \leq \phi \leq 180°$ (17).

[b]Estimated standard deviations are shown in parentheses.

[c]Not assigned.

[d]Not calculated.

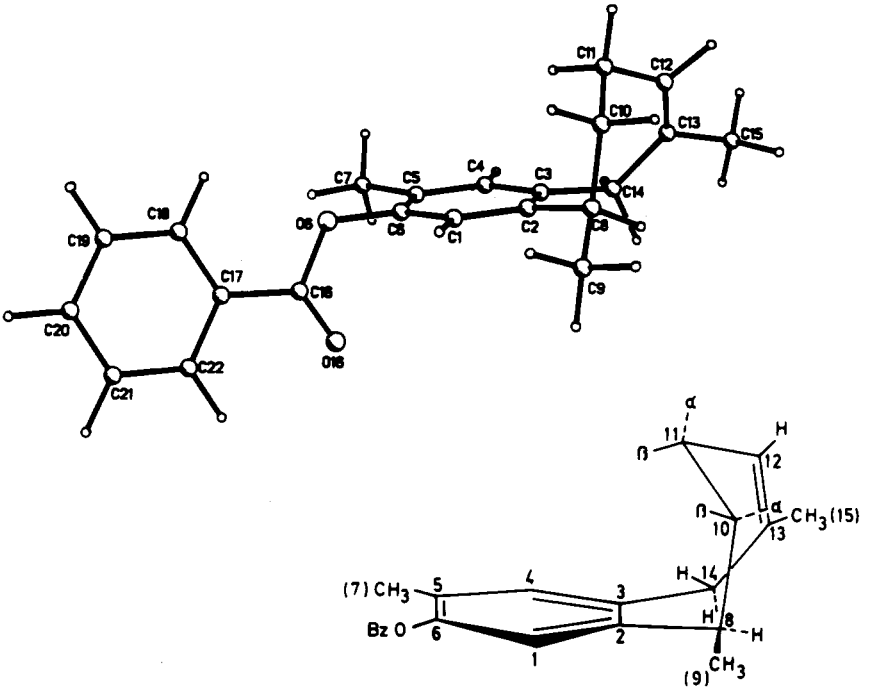


FIGURE 1. Molecular structure of parvifoline benzoate [2].

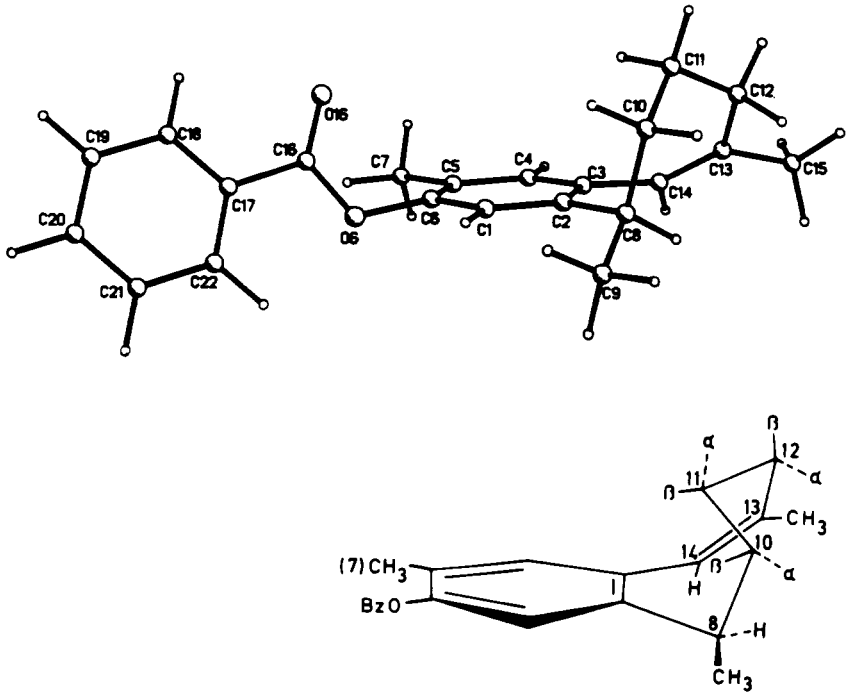


FIGURE 2. Molecular structure of isoparvifoline benzoate [5].

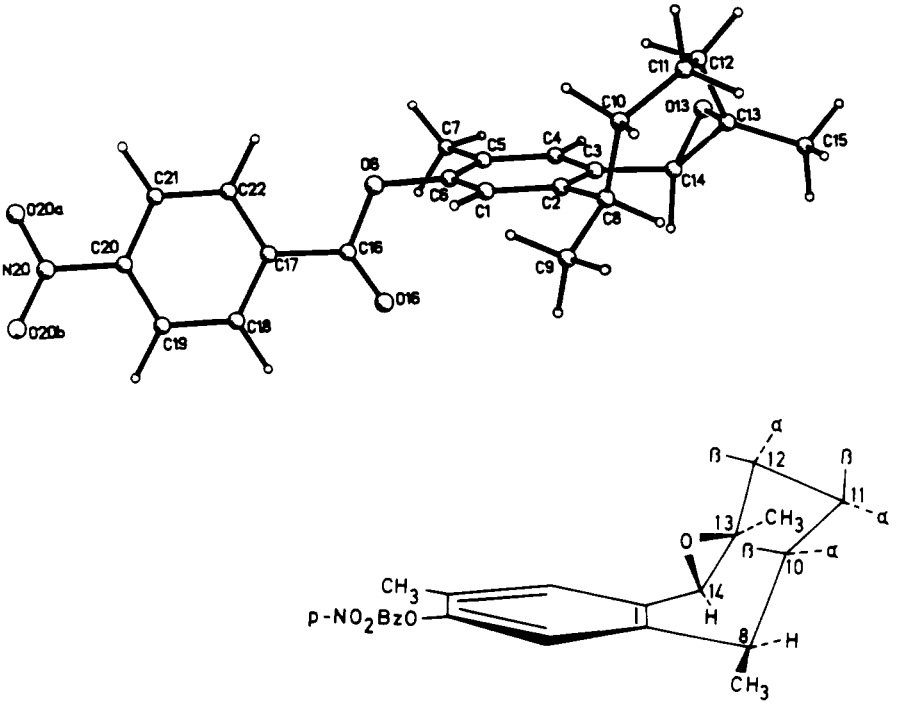


FIGURE 3. Molecular structure of 13,14-epoxyisoparvifoline *p*-nitrobenzoate [**8**].

tially the same chemical shifts and coupling constants as the spectrum of **2**. Thus, the eight-membered ring of **2** and **4** shows a distorted twist-boat conformation. The inconsistencies in the previously reported (1) coupling constants may be due to the use of oily, impure samples, instead of pure crystalline parvifoline [**1**] and its acetate **4** (2,3).

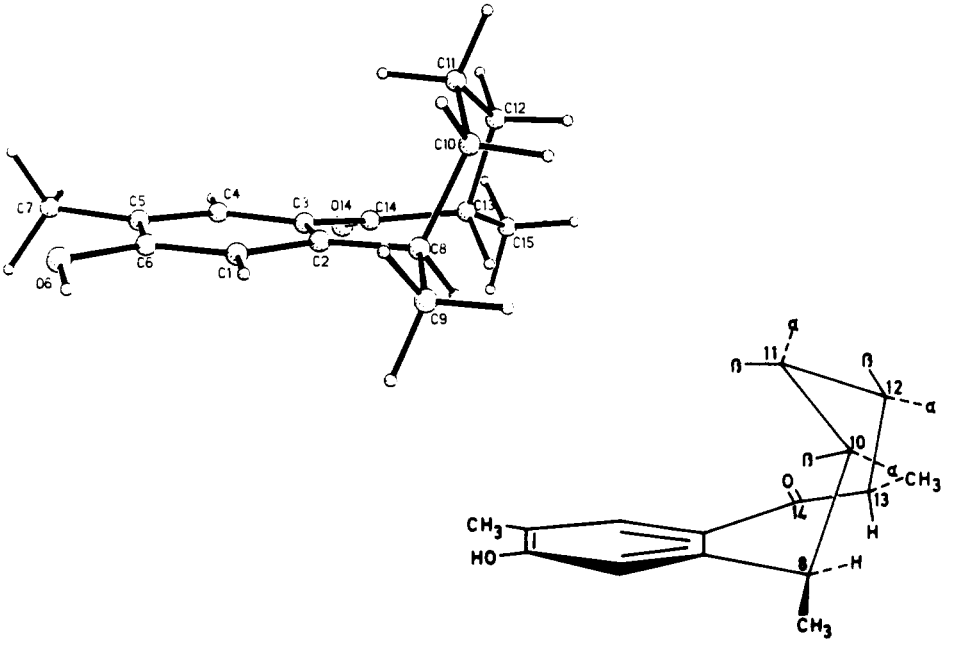


FIGURE 4. Molecular structure of 14-oxodihydroparvifoline [**9**].

TABLE 4. C-C-C-C Torsion Angles (degrees) of: Parvifoline Benzoate [**2**], Isoparvifoline Benzoate [**5**], 13,14-Epoxyisoparvifoline *p*-nitrobenzoate [**8**], and 14-Oxodihydroparvifoline [**9**].[a] For Comparative Purposes Torsion Angles of Distorted Twist-boat Conformation of *cis, cis*-1,4-cyclooctadiene[b] (DTB 1,4-) and Those of Twist-boat Conformation of *cis, cis*-1,3-cyclooctadiene[c] (TB 1,3-) Are Shown in Parentheses.

C-C-C-C	Compound					
	2	(DTB 1,4-)	**5**	(TB 1,3-)	**8**	**9**
2-3-14-13	−62.7 ± 0.5	(−38)	−45.7 ± 0.5	(−38)	−60.3 ± 0.7	−16.8 ± 0.4
3-14-13-12	3.3 ± 0.6	(−13)	−8.1 ± 0.6	(0)	−8.0 ± 1.0	−65.1 ± 0.4
14-13-12-11	2.8 ± 0.7	(−4)	0.2 ± 0.6	(−18)	88.0 ± 1.4	51.2 ± 0.4
13-12-11-10	74.7 ± 0.5	(88)	78.9 ± 0.4	(75)	−67.7 ± 1.9	57.5 ± 0.4
12-11-10-8	−58.5 ± 0.5	(−55)	−55.4 ± 0.4	(−78)	39.5 ± 1.6	−65.0 ± 0.4
11-10-8-2	−51.0 ± 0.4	(−52)	−56.5 ± 0.4	(−32)	−79.4 ± 0.8	−42.8 ± 0.4
10-8-2-3	88.3 ± 0.4	(90)	88.0 ± 0.3	(80)	88.1 ± 0.6	73.2 ± 0.3
8-2-3-14	11.7 ± 0.5	(3)	5.1 ± 0.4	(0)	5.9 ± 0.7	8.9 ± 0.4

[a]From their X-ray diffraction analyses.
[b]From Anet and Yavari (13). Angle signs have been inverted.
[c]From Anet and Yavari (12). Angle signs have been inverted.

Furthermore, the previous conformational arguments (1) attributed a shielding effect to the benzene ring instead of to the double bond of parvifoline [**1**], as already noticed (15). It is also worth mentioning that the specific rotations of parvifoline and isoparvifoline derivatives **2**, **3**, **5**, and **6** are high, probably due to the presence of inherently dissymmetric chromophores (16).

EXPERIMENTAL

Cc was done using Merck Si gel 60 (70–230 mesh ASTM). Melting points, determined on a Fisher-Johns apparatus, are uncorrected. Ir spectra in $CHCl_3$ were obtained on a Nicolet MX-1 spectrophotometer. Specific rotations in $CHCl_3$ were determined on a Perkin-Elmer 241 polarimeter. Uv spectra were obtained on a Unicam SP-800 spectrophotometer. The nmr spectra were measured with TMS as the internal reference on Varian Associates EM-390, XL-100A-FT-16K, and XL-300GS spectrometers. Microanalyses were performed by the Alfred Bernhard Laboratories (West Germany). X-ray data collections[1] were obtained on a Nicolet R3m four circle diffractometer equipped with CuKα radiation (λ = 1.54178 Å). The diffractometer was operated in the θ:2θ scanning mode. Crystal data for compounds **2**, **5**, **8**, and **9** are summarized in Table 5, and their fractional atomic coordinates are given in Tables 6–9. The data measured were corrected for background, Lorentz, and polarization effects, while crystal decay and absorption were negligible. The structures were solved by direct methods using the software provided by the manufacturer. For the structural refinements the non-hydrogen atoms were treated anisotropically; the hydroxyl hydrogen of **9** became evident from a Δ F synthesis, and the hydrogen atoms bonded to carbons, included in the structure factor calculation, were refined isotropically. A few reflections were excluded from the final refinement calculations to improve the fit.

(*R*)-(−)-PARVIFOLINE BENZOATE [**2**].—A solution of *P. alamani* var. *oolepis* extract (5 g) obtained as previously described (3) in pyridine (25 ml) was treated with benzoyl chloride (7.5 ml). The reaction mixture was heated on a steam bath for 3 h, poured over ice-H_2O, and extracted with EtOAc. The organic layer was washed with diluted HCl, H_2O, aqueous $NaHCO_3$, and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated. The oily residue was chromatographed on Si gel (110 g). Elution with hexane gave a solid compound. Recrystallization of this solid from $CHCl_3$/hexane yielded **2** (5.2 g) as white needles, mp 106–108°. Recrystallization from CH_2Cl_2/MeOH provided the pure compound: mp 110–111°; ir ν max 1731 (C=O) 1602 cm^{-1} (C=C aromatic); $[\alpha]D$ −110.20° (*c* = 1); uv λ max (cyclohexane) 274 (log ε 3.47), 227 nm (log ε 4.30); ^1H nmr (300 MHz, C_6D_6) δ 8.28 (2H, m, H-2′ and H-6′), 7.13 (3H, m, H-3′, H-4′, and H-5′), 7.08 (1H, s, H-1), 6.84 (1H, s, H-4), 5.40 (1H, t, $J_{11\alpha,12} = J_{11\beta,12} = 8.0$ Hz, H-12), 3.43 (1H, d, $J_{14,14'} = 18.0$ Hz, H-14), 3.17 (1H, ddq, $J_{8,9} = 7.0$, $J_{8,10\alpha} = 4.5$, $J_{8,10\beta} = 12$ Hz, H-8), 2.93 (1H, d, $J_{14,14'} = 18.0$ Hz, H-14′), 2.12 (3H, s, Me-7), 1.89 (1H, m, H-11β), 1.68 (1H, dddd, $J_{8,10\alpha} = 4.5$, $J_{10\alpha,10\beta} = 12.5$, $J_{10\alpha,11\alpha} = 3.5$, $J_{10\alpha,11\beta} = 12.5$ Hz, H-10α), 1.68 (3H, s, Me-15), 1.56

[1]Atomic coordinates for these structures 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.

TABLE 5. Crystal Data of Parvifoline Benzoate [**2**], Isoparvifoline Benzoate [**5**]; 13,14-Epoxyisoparvifoline *p*-nitrobenzoate [**8**], and 14-Oxodihydroparvifoline [**9**].

Parameters and Refinement	Compound			
	2	**5**	**8**	**9**
Crystal Parameters				
Chemical formula	$C_{22}H_{24}O_2$	$C_{22}H_{24}O_2$	$C_{22}H_{23}O_5N$	$C_{15}H_{20}O_2$
Molecular weight	320.4	320.4	381.4	232.3
Crystal system	orthorhombic	orthorhombic	monoclinic	monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P2_1$
Crystal size, mm	0.4×0.2×0.06	0.21×0.12×0.10	0.40×0.24×0.12	0.16×0.16×0.10
Crystal color	white	white	white	white
Cell constants				
a, Å	7.970(4)	7.348(4)	8.265(3)	5.092(2)
b, Å	12.467(5)	10.980(5)	20.478(6)	14.602(6)
c, Å	18.970(9)	22.924(10)	12.034(5)	9.005(3)
β, deg	90.00(0)	90.00(0)	90.989(29)	95.329(26)
Cell volume, Å^3	1884.8(1.5)	1849.6(2.0)	2036.5(1.2)	666.6(4)
ρ (calcd), g/cm	1.13	1.15	1.24	1.16
Z	4	4	4	2
F(000), e$^-$	688	688	808	252
Data Collection Parameters				
μ, cm^{-1}	5.6	5.7	7.3	6.0
Scan width, below $K_{\alpha 1}$, above $K_{\alpha 2}$, deg	0.9, 1.1	1.0, 1.4	1.0, 1.0	1.0, 1.1
2θ limits, deg	3–110	3–110	3–110	3–110
Scan speed, deg min^{-1}	variable, 4–29	variable, 4–29	variable, 4–29	variable, 4–29
Exposure time, h	28.6	26.0	55.5	19.4
Reflections collected	1418	1395	2891	1009
Observed reflections	1212	1346	2454	845
Structure Refinement				
Reflections for final refinement	1210	1327	2450	839
Parameters refined	233	233	533	169
R(F), %	4.38	6.38	6.61	3.34
R_w(F), %	4.99	7.46	8.12	3.87
Goodness of fit for the last cycle	1.186	1.117	1.101	1.093
Final G	0.00163	0.00822	0.00827	0.00152
Δ_e(e/Å^3)	+0.18, −0.13	+0.61, −0.22	+0.65, −0.22	+0.12, −0.09

(1H, m, H-11α), 1.20 (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9), and 1.08 ppm (1H, ddt, $J_{8,10}$ = 12.0, $J_{10\alpha,10\beta}$ = 12.5, $J_{10\beta,11\alpha}$ = $J_{10\beta,11\beta}$ = 3.5 Hz, H-10β). When H-12 was irradiated, H-11β was observed as a broad dd ($J_{10\alpha,11\beta}$ = 12.0, $J_{11\alpha,11\beta}$ = 13.0 Hz) and H-11α was observed as a dt ($J_{10\alpha,11}$ = $J_{10\beta,11}$ = 3.5, $J_{11\alpha,11\beta}$ = 13.0 Hz); ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 1; ^{13}C(^{1}H) heteronuclear chemical shift correlation [75.4 (300 MHz), C_6D_6] δ 42.2 (3.43 and 2.93), 40.3 (1.68 and 1.08), 33.5 (3.17), 26.5 (1.68), 24.1 (1.89 and 1.56), 19.3 (1.20), 15.9 (2.12). *Anal.* calcd for $C_{22}H_{24}O_2$: C 82.50, H 7.50, O 10.00; found C 82.38, H 7.44, O 10.01%. The X-ray analysis sample was obtained by recrystallization from $CHCl_3$/hexane.

(*R*)-(−)-PARVIFOLINE *p*-NITROBENZOATE [**3**].—A solution of *P. alamani* var. *oolepis* extract (1 g) obtained as previously described (3) in pyridine (5 ml) was treated with *p*-nitrobenzoyl chloride (2.6 g). The reaction mixture was refluxed during 30 min and worked up as for **2**. The residue was chromatographed on Si gel (25 g). Elution with petroleum ether-EtOAc (98:2) gave **3** (1 g) as a solid, mp 96–97°. The pure sample was obtained by recrystallization from CH_2Cl_2/MeOH as white prisms: mp 98–99°; ir 1739 (C=O), 1609 (C=C, aromatic), 1531 and 1350 cm^{-1} (NO_2); [α]D −111.00° (*c* = 1); uv λ max (cyclohexane) 256 (log ε 4.04), 213 nm (log ε 4.03); ^{1}H nmr (90 MHz, $CDCl_3$) δ 8.39 (4H, s, H-2′, H-3′, H-5′, and H-6′), 7.05 (1H, s, H-4), 6.88 (1H, s, H-1), 5.37 (1H, t, H-12), 3.60 (1H, d, $J_{14,14'}$ = 18.0 Hz, H-14), 3.20 (1H, m, H-8), 3.10 (1H, d, $J_{14,14'}$ = 18.0 Hz, H-14′), 2.15 (3H, s, Me-7), 1.78 (3H, s, Me-15), and 1.35 ppm (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9) [the remaining four protons (H-10α, H-10β, H-11α, and H-11β) overlap in the δ 1.9–0.8 region]; ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 1. *Anal.* calcd for $C_{22}H_{23}O_4N$: C 72.33, H 6.30, O 17.53, N 3.84; found C 72.38, H 6.25, O 17.44, N 3.89%.

(*R*)-(−)-PARVIFOLINE ACETATE [**4**].—Obtained as described by Joseph-Nathan *et al.* (2). ^{1}H nmr (300 MHz, C_6D_6) δ 6.98 (1H, s, H-1), 6.81 (1H, s, H-4), 5.36 (1H, t, $J_{11\alpha,12}$ = $J_{11\beta,12}$ = 8.0 Hz, H-

TABLE 7. Experimentally Refined Final Fractional Atomic Coordinates ($\times 10^4$) of Isoparvifoline Benzoate [**5**].[a]

Atom	x	y	z
C-1	7999(5)	2779(3)	8845(1)
C-2	8620(4)	3824(3)	9108(1)
C-3	10204(4)	3747(3)	9456(1)
C-4	11039(5)	2622(3)	9522(1)
C-5	10414(5)	1542(3)	9252(1)
C-6	8884(5)	1654(3)	8915(1)
C-7	11362(7)	337(3)	9348(2)
C-8	7635(5)	5024(3)	9021(2)
C-9	5565(5)	4900(4)	8922(2)
C-10	8475(5)	5687(3)	8496(2)
C-11	10558(5)	5914(4)	8543(1)
C-12	11098(5)	6596(3)	9089(2)
C-13	11233(4)	5948(3)	9667(1)
C-14	10942(5)	4775(3)	9797(1)
C-15	11932(6)	6795(4)	10149(2)
C-16	8613(5)	112(4)	8208(2)
C-17	7324(6)	−827(3)	7967(1)
C-18	8020(7)	−1577(4)	7519(2)
C-19	6850(9)	−2484(4)	7267(2)
C-20	5101(11)	−2571(4)	7491(2)
C-21	4501(7)	−1810(4)	7924(2)
C-22	5606(7)	−974(4)	8151(2)
O-6	7982(4)	626(2)	8681(1)
O-16	10093(6)	369(4)	8000(1)

[a]Estimated standard deviations in the least significant digits are shown in parentheses.

12), 3.42 (1H, d, $J_{14,14'}$ = 18.0 Hz, H-14), 3.15 (1H, ddq, $J_{8,9}$ = 7.0, $J_{8,10\alpha}$ = 4.0, $J_{8,10\beta}$ = 12.0 Hz, H-8), 2.93 (1H, d, $J_{14,14'}$ = 18.0 Hz, H-14′), 2.08 (3H, s, Me-7), 1.85 (1H, m, H-11β), 1.68 (1H, dddd, $J_{8,10\alpha}$ = 4.0, $J_{10\alpha,10\beta}$ = 12.0, $J_{10\alpha,11\alpha}$ = 3.0, $J_{10\alpha,11\beta}$ = 12.0 Hz, H-10α), 1.67 (3H, s, Me-15), 1.54 (1H, dddd, $J_{10\alpha,11\alpha}$ = $J_{10\beta,11\alpha}$ = 3.5, $J_{11\alpha,11\beta}$ = 13.0, $J_{11\alpha,12}$ = 8.0 Hz, H-11α), 1.22 (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9), and 1.07 ppm (1H, ddt, $J_{8,10\beta}$ = 12.0, $J_{10\alpha,10\beta}$ = 12.5, $J_{10\beta,11\alpha}$ = $J_{10\beta,11\beta}$ = 3.5 Hz, H-10β).

(*R*)-(+)-ISOPARVIFOLINE BENZOATE [**5**].—A solution of parvifoline benzoate [**2**] (5 g) in 25 ml of HOAc was treated with anhydrous $ZnCl_2$ (125 mg) and refluxed for 30 min. The reaction mixture was poured over ice-H_2O and extracted with EtOAc. The organic layer was washed with H_2O, aqueous $NaHCO_3$, and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The colorless oily residue was chromatographed on Si gel (100 g). Elution with hexane provided isoparvifoline benzoate [**5**] (4.69 g, 94%) as a solid compound, mp 82.5–84.5°. Recrystallization from $CHCl_3$/MeOH gave the pure compound as white prisms: mp 83–84°; ir ν max 1735 (C=O), 1605 cm^{-1} (C=C, aromatic); [α]D +321.00° (*c* = 1); uv λ max (cyclohexane) 238 (log ε 4.45), 230 (log ε 4.47), 223 nm (log ε 4.47); ^{1}H nmr (300 MHz, C_6D_6) δ 8.28 (2H, m, H-2′ and H-6′), 7.11 (3H, m, H-3′, H-4′, and H-5′), 6.95 (2H, 2s, H-1 and H-4), 6.22 (1H, br s, H-14), 3.10 (1H, ddq, $J_{8,9}$ = 7.0, $J_{8,10\alpha}$ = 3.0, $J_{8,10\beta}$ = 11 Hz, H-8), 2.12 (3H, s, Me-7), 2.00 (1H, ddd, $J_{11\alpha,12\beta}$ = 8.5, $J_{11\beta,12\beta}$ ~ 0.0, $J_{12\alpha,12\beta}$ = 17.0 Hz, H-12β), 1.82 (1H, ddd, $J_{11\alpha,12\alpha}$ ~ 0.0, $J_{11\beta,12\alpha}$ = 11.0, $J_{12\alpha,12\beta}$ = 17 Hz, H-12α), 1.74 (3H, d, $J_{14,15}$ = 1.0 Hz, Me-15), 1.57 (2H, 2m, H-10α and H-11β), 1.24 (2H, 2m, H-10β and H-11α), and 1.16 ppm (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9); ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 1; ^{13}C-^{1}H heteronuclear chemical shift correlation [75.4 (300 MHz), C_6D_6] δ 39.6 (1.57 and 1.24), 35.7 (2.00 and 1.82), 34.0 (3.10), 26.5 (1.74), 22.7 (1.57 and 1.24), 21.5 (1.16), 15.9 (2.12). *Anal.* calcd for $C_{22}H_{24}O_2$: C 82.50, H 7.50, O 10.00; found C 82.62, H 7.60, O 10.04%. The X-ray analysis sample was obtained by recrystallization from $CHCl_3$/MeOH.

(*R*)-(+)-ISOPARVIFOLINE *p*-NITROBENZOATE [**6**].—A solution of parvifoline *p*-nitrobenzoate [**3**] (1 g) in HOAc (5 ml) was treated with anhydrous $ZnCl_2$ (25 mg), refluxed for 30 min, and worked up as in the case of **5**. The oily green residue was chromatographed on Si gel (25 g). Elution with hexane-EtOAc

TABLE 6. Experimentally Refined Final Fractional Atomic Coordinates (× 10^4) of Parvifoline Benzoate [**2**].[a]

Atom	*x*	*y*	*z*
C-1	−2046(4)	8445(3)	6877(2)
C-2	−3587(4)	8650(3)	6545(2)
C-3	−4368(4)	9641(3)	6668(2)
C-4	−3557(5)	10400(3)	7092(2)
C-5	−2025(4)	10190(3)	7426(2)
C-6	−1325(4)	9204(3)	7312(2)
C-7	−1195(6)	11059(4)	7880(2)
C-8	−4327(5)	7863(3)	6014(2)
C-9	−4014(7)	6671(3)	6197(3)
C-10	−3578(6)	8135(4)	5284(2)
C-11	−3732(5)	9329(4)	5084(2)
C-12	−5523(5)	9726(3)	5073(2)
C-13	−6508(5)	9944(3)	5610(2)
C-14	−6120(4)	9907(3)	6399(2)
C-15	−8347(5)	10276(4)	5493(2)
C-16	229(4)	8439(3)	8253(2)
C-17	1931(4)	8232(3)	8530(2)
C-18	3360(4)	8694(3)	8238(2)
C-19	4913(4)	8461(4)	8512(2)
C-20	5058(4)	7768(3)	9083(2)
C-21	3650(5)	7314(3)	9383(2)
C-22	2075(4)	7539(3)	9110(2)
O-6	246(3)	8967(2)	7626(1)
O-16	−1053(3)	8195(3)	8535(2)

[a]Estimated standard deviations in the least significant digits are shown in parentheses.

(98:2) provided a solid compound that was recrystallized from petroleum ether yielding isoparvifoline *p*-nitrobenzoate [**6**] (900 mg, 90%) as yellow prisms: mp 84–86°; ir ν max 1740 (C=O), 1610 (C=C, aromatic), 1530 and 1350 cm^{-1} (NO_2); $[\alpha]_D$ +284.80° (*c* = 0.42); uv λ max (cyclohexane) 253 nm (log ε 4.20), 215 nm (log ε 4.16); ^1H nmr (90 MHz, $CDCl_3$) δ 8.42 (4H, 4s, H-2′, H-3′, H-5′, and H-6′), 7.03 (1H, s, H-4), 7.00 (1H, s, H-1), 6.23 (1H, br s, H-14), 3.20 (1H, m, H-8), 2.16 (3H, s, Me-7), 1.88 (3H, s, Me-15), 1.26 ppm (3H, d, $J_{8,9}$ = 7 Hz, Me-9) [the remaining six protons (H-10α, H-10β, H-11α, H-11β, H-12α, and H-12β) overlap in the 1.1–2.3 region]; ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 1.

(8*R*,13*S*,14*R*)-(+)-13,14-EPOXYISOPARVIFOLINE BENZOATE [**7**].—A solution of isoparvifoline benzoate [**5**] (4.5 g) and *m*-chloroperbenzoic acid (4.38 g) in CH_2Cl_2 (250 ml) was refluxed for 2 h, poured over ice-H_2O, and extracted with CH_2Cl_2. The organic layer was washed with aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The oily residue was chromatographed on Si gel (90 g). Elution with hexane-C_6H_6 (8:2) gave compound **7** (3.07 g, 65%) as a colorless oil: ir ν max 1731 (C=O), 900 cm^{-1} (epoxide); $[\alpha]_D$ +34.34° (*c* = 5.30); uv λ max (cyclohexane) 271 (log ε 3.34), 227 (log ε 4.19), 208 nm (log ε 3.92); ^1H nmr (90 MHz, $CDCl_3$) δ 8.30 (2H, 2m, H-2′ and H-6′), 7.60 (3H, 3m, H-3′, H-4′, and H-5′), 7.35 (1H, s, H-4), 7.04 (1H, s, H-1), 3.78 (1H, br s, H-14), 3.04 (1H, m, H-8), 2.20 (3H, s, Me-7), 1.53 (3H, s, Me-15), 1.30 (3H, d, $J_{8,9}$ = 7 Hz, Me-9) [the remaining six protons (H-10α, H-10β, H-11α, H-11β, H-12α, and H-12β) overlap in the δ 1.0–2.0 region]; ^{13}C nmr (25.1 MHz, $CDCl_3$) see Table 1.

(8*R*,13*S*,14*R*)-(+)-13,14-EPOXYISOPARVIFOLINE *p*-NITROBENZOATE [**8**].—A solution of isoparvifoline *p*-nitrobenzoate [**6**] (0.9 g) in $CHCl_3$ (30 ml) was refluxed with *m*-chloroperbenzoic acid (0.75 g) for 2 h, treated with aqueous $NaHCO_3$, and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was chromatographed on Si gel (20 g). Elution with hexane-EtOAc (9:1) gave compound **8** (0.65 g, 69%) as slightly green prisms, mp 123–125°. Recrystallization from Et_2O/MeOH provided the pure compound **8** as white prisms: mp 125°; ir ν max 1740 (C=O), 1530 and 1350 cm^{-1} (NO_2); $[\alpha]_D$ +29.72° (*c* = 0.74); uv λ max

TABLE 8. Experimentally Refined Final Fractional Atomic Coordinates ($\times 10^4$) of 13,14-Epoxyisoparvifoline *p*-nitrobenzoate [**8**].[a]

Atom	*x*	*y*	*z*
C-1	−90(7)	2600	4925(4)
C-2	−1486(6)	2914(2)	5252(4)
C-3	−2655(6)	2547(3)	5813(4)
C-4	−2376(6)	1895(2)	6082(4)
C-5	−961(6)	1564(2)	5755(4)
C-6	129(6)	1936(3)	5162(4)
C-7	−708(7)	850(3)	6019(5)
C-8	−1701(7)	3645(3)	5033(5)
C-9	−889(9)	3859(4)	3961(6)
C-10	−1041(9)	4049(3)	5999(6)
C-11	−2115(15)	4109(7)	7011(8)
C-12	−3041(2)	3648(8)	7477(8)
C-13	−4525(9)	3379(3)	6866(5)
C-14	−4254(6)	2829(3)	6138(4)
C-15	−6076(13)	3749(5)	6755(10)
C-16	1576(6)	1437(3)	3717(4)
C-17	3172(6)	1154(2)	3381(4)
C-18	3341(7)	998(3)	2281(5)
C-19	4819(8)	745(3)	1914(5)
C-20	6035(7)	657(3)	2667(5)
C-21	5904(7)	817(3)	3770(5)
C-22	4447(7)	1072(3)	4139(4)
N-20	7579(7)	376(3)	2282(5)
O-6	1573(4)	1630(2)	4781(3)
O-13	−4772(6)	2725(3)	7256(4)
O-16	419(5)	1485(3)	3127(4)
O-20a	8544(7)	183(4)	3011(6)
O-20b	7803(7)	345(4)	1303(5)
C-31	9078(8)	5649(3)	625(5)
C-32	8018(7)	5313(3)	1343(4)
C-33	7195(6)	5676(3)	2136(4)
C-34	7419(6)	6348(3)	2208(5)
C-35	8505(7)	6682(3)	1535(5)
C-36	9296(7)	6304(3)	761(5)
C-37	8766(8)	7411(3)	1700(7)
C-38	7733(8)	4580(3)	1190(4)
C-39	9304(10)	4211(4)	854(6)
C-40	6318(10)	4448(3)	363(5)
C-41	4626(11)	4430(5)	783(7)
C-42	4080(9)	5010(4)	1432(8)
C-43	4620(7)	5018(3)	2684(6)
C-44	6143(6)	5343(3)	2961(4)
C-45	4005(11)	4493(4)	3439(10)
C-46	11720(11)	6685(4)	418(5)
C-47	12929(11)	7046(3)	−446(5)
C-48	12460(8)	7157(3)	−1556(7)
C-49	13673(8)	7431(3)	−2291(5)
C-50	15164(7)	7548(3)	−1824(4)
C-51	15515(9)	7453(4)	−746(5)
C-52	14444(9)	7201(4)	−37(6)
N-50	16491(9)	7802(3)	−2578(6)
O-36	10372(6)	6640(3)	−37(4)
O-43	4616(4)	5663(2)	3182(3)
O-46	12247(7)	6519(4)	1248(4)
O-50a	17711(8)	7979(5)	−2187(7)
O-50b	16149(11)	7830(3)	−3552(5)

[a]Estimated standard deviations in the least significant digits are shown in parentheses.

TABLE 9. Experimentally Refined Final Fractional Atomic Coordinates ($\times 10^4$) of 14-Oxodihydroparvifoline [**9**].[a]

Atom	*x*	*y*	*z*
C-1	253(5)	7790(0)	5211(3)
C-2	−857(5)	7238(2)	6260(3)
C-3	−244(5)	6287(2)	6250(3)
C-4	1561(5)	5973(2)	5276(3)
C-5	2737(5)	6529(2)	4271(3)
C-6	1963(5)	7445(2)	4231(3)
C-7	4696(5)	6172(2)	3263(3)
C-8	−2614(5)	7691(2)	7337(3)
C-9	−3565(7)	8662(2)	6879(4)
C-10	−1193(6)	7763(3)	8941(3)
C-11	372(7)	6944(3)	9556(3)
C-12	−1260(7)	6097(3)	9784(3)
C-13	−2987(6)	5685(2)	8447(3)
C-14	−1434(5)	5534(2)	7113(3)
C-15	−4333(8)	4803(3)	8898(4)
O-6	2997(5)	7988(3)	3191(2)
O-14	−1125(5)	4746(3)	6695(3)
H-6	2190(69)	8585(32)	3127(37)

[a]Estimated standard deviations in the least significant digits are shown in parentheses.

(cyclohexane) 255 (log ε 3.77), 215 nm (log ε 3.71); ^{1}H nmr (300 MHz, $CDCl_3$) δ 8.40 (2H, 2m, J_{ortho} = 9.5 Hz, H-3′ and H-5′), 8.34 (2H, 2m, J_{ortho} = 9.5 Hz, H-2′ and H-6′), 7.32 (1H, br s, H-4), 7.05 (1H, s, H-1), 3.80 (1H, s, H-14), 3.05 (1H, ddq, $J_{8,9}$ = 7.0, $J_{8,10\alpha}$ = 1.0, $J_{8,10\beta}$ = 10 Hz, H-8), 2.20 (3H, s, Me-7), 1.88 (1H, ddd, $J_{11\alpha,12\alpha}$ = 2.0, $J_{11\beta,12\alpha}$ = 6.0, $J_{12\alpha,12\beta}$ = 14 Hz, H-12α), 1.80 (1H, ddt, $J_{8,10\alpha}$ = 1.0, $J_{10\alpha,10\beta}$ = 13, $J_{10\alpha,11\alpha}$ = $J_{10\alpha,11\beta}$ = 4 Hz, H-10α), 1.62 (2H, 2m, H-11α and H-11β), 1.56 (3H, s, Me-15), 1.36 (1H, dddd, $J_{8,10\beta}$ = 10, $J_{10\alpha,10\beta}$ = 13, $J_{10\beta,11\alpha}$ = 1, $J_{10\beta,11\beta}$ = 6 Hz, H-10β), 1.35 (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9), and 1.19 ppm (1H, ddd, $J_{11\alpha,12\beta}$ = 11.5, $J_{11\beta,12\beta}$ = 2.5, $J_{12\alpha,12\beta}$ = 13.5 Hz, H-12β); ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 1; ^{13}C-^{1}H heteronuclear chemical shift correlation [75.4 (300 MHz), $CDCl_3$] δ 63.0 (3.80), 40.8 (1.80 and 1.36), 34.4 (3.05), 33.1 (1.88 and 1.19), 24.0 (1.62), 22.1 (1.56), 22.0 (1.35), 15.7 (2.20). *Anal.* calcd for $C_{22}H_{23}O_5N$: C 69.30, H 6.04, O 20.99, N 3.67; found C 69.42, H 6.18, O 20.83, N 3.62%. The X-ray analysis sample was obtained by recrystallization from Et_2O/MeOH.

(8*R*,13*S*)-(+)-14-OXODIHYDROPARVIFOLINE [**9**].—A solution of epoxyisoparvifoline benzoate [**7**] (4.5 g) in anhydrous C_6H_6 (225 ml) was treated with Et_2O/BF_3 (4.5 ml), stirred at room temperature for 12 h, treated portionwise with H_2O, and extracted with EtOAc. The organic layer was washed with aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was chromatographed on Si gel (100 g). Elution with hexane-C_6H_6 (8:2) yielded a yellow oily substance (1.56 g, 35%) that was dissolved in MeOH (100 ml) and treated with a solution of KOH (0.5 g) in H_2O (5 ml). The reaction mixture was refluxed for 30 min, concentrated to a small volume, diluted with H_2O, and extracted with EtOAc. The organic layer was washed with diluted HCl and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was chromatographed on Si gel (60 g). Elution with hexane-EtOAc (9:1) gave compound **9** (660 mg, 61%) as white needles, mp 133–134°. Recrystallization from $CHCl_3$/hexane provided the pure sample: mp 136–137°; ir ν max 3599 and 3322 (OH), 1651 cm^{-1} (C=O); [α]D +37.03 (*c* = 0.54); uv λ max (dioxane) 273 (log ε 3.73), 235 nm (log ε 3.29); ^{1}H nmr (300 MHz, $CDCl_3$) δ 7.37 (1H, s, H-4), 6.72 (1H, s, H-1), 5.75 (1H, br s, which disappears upon addition of D_2O, OH), 3.32 (1H, ddq, $J_{8,9}$ = 7.0, $J_{8,10\alpha}$ = 4.5, $J_{8,10\beta}$ = 11 Hz, H-8), 3.13 (1H, ddq, $J_{12\alpha,13}$ = 6, $J_{12\beta,13}$ = 9.5, $J_{13,15}$ = 6.5 Hz, H-13), 2.22 (3H, s, Me-7), 1.80 (2H, 2m, H-12α and H-10α), 1.39 (ddt, $J_{8,10\beta}$ = 11, $J_{10\alpha,10\beta}$ = 18, $J_{10\beta,11\alpha}$ = $J_{10\beta,11\beta}$ = 4 Hz, H-10β), 1.27 (3H, d, $J_{8,9}$ = 7.0 Hz, Me-9), 1.20 ppm (3H, d, $J_{13,15}$ = 6.5 Hz, Me-15) [the remaining three protons (H-11α, H-11β, and H-12β) overlap in the δ 1.59–1.40 region]; addition of Eu(fod)$_3$ (5 mg) to a solution of **9** (10 mg) in $CDCl_3$ (0.6 ml) allowed observation of H-12α at δ 1.96 (1H, dddd, $J_{11\alpha,12\alpha}$ = 2.0, $J_{11\beta,12\alpha}$ = 11.0, $J_{12\alpha,12\beta}$ = 17.0, $J_{12\alpha,13}$ = 6.0 Hz) and H-10α at 1.87 ppm (dddd, $J_{8,10}$ = 4.5, $J_{10\alpha,10\beta}$ = 18.0, $J_{10\alpha,11\alpha}$ = 4.0, $J_{10\alpha,11\beta}$ = 10.0 Hz). NOe experiment: a solution of **9** (5 mg) in $CDCl_3$

(1.2 ml) placed in an nmr sample tube was bubbled with Ar during 1 h at room temperature. The tube was sealed. The irradiation of H-13 increased 11% H-8 integration. ^{13}C nmr (25.1 MHz, $CDCl_3$) see Table 1; ^{13}C-^1H heteronuclear chemical shift correlation [75.4 (300 MHz), $CDCl_3$] δ 46.4 (3.13), 36.1 (3.32), 35.7 (1.80 and 1.39), 32.4 (1.80 and 1.50), 23.5 (1.50), 22.9 (1.27), 17.0 (1.20), 15.3 (2.22). *Anal.* calcd for $C_{15}H_{20}O_2$: C 77.59, H 8.62, O 13.79; found C 77.51, H 8.67, O 13.62%. The X-ray analysis sample was obtained by recrystallization from $CHCl_3$/hexane.

(*R*)-(−)-6-(5-BENZOYLOXY-2-FORMYL-4-METHYLPHENYL)-HEPTAN-2-ONE [**10**].—A solution of **7** (4.5 g) in Et_2O-Me_2CO (1:1) was treated with a solution of HIO_4 (6.12 g) in H_2O (6 ml), stirred for 1 h at room temperature, poured over ice-H_2O, and extracted with Et_2O. The organic layer was washed with aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The oily residue was chromatographed on Si gel (100 g). Elution with hexane-EtOAc (8:2) yielded **6** (2.9 g, 62%) as a slightly green oil: ir ν max 2734 (C-H, aldehyde), 1737 (C=O, benzoate), 1705 cm^{-1} (C=O, aldehyde and ketone); [α]D −7.23° (*c* = 4.08); uv λ max (dioxane) 282 (log ε 3.85), 254 (log ε 4.37), 245 nm (log ε 4.28); ^1H nmr (90 MHz, $CDCl_3$) δ 10.26 (1H, s, CHO), 8.21 (2H, m, H-2′ and H-6′), 7.66 (1H, s, H-6), 7.51 (3H, m, H-3′, H-4′, and H-5′), 7.16 (1H, s, H-3), 3.68 (1H, m, H-8), 2.34 (2H, m, H-12 and H-12′), 2.26 (3H, s, Me-7), 2.03 (3H, s, Me-14), 1.70–1.45 (4H, m, H-10, H-10′, H-11, and H-11′), 1.20 ppm (3H, d, $J_{8,9}$ = 7 Hz, Me-9); ^{13}C nmr (25.1 MHz, $CDCl_3$) see Table 2.

(*R*)-(−)-6-(2-FORMYL-5-HYDROXY-4-METHYLPHENYL)-HEPTAN-2-ONE [**11**].—A solution of **10** (1.76 g) in MeOH (100 ml) was treated with a solution of KOH (200 mg) in H_2O (5 ml). The reaction mixture was refluxed for 20 min, neutralized with HCl, concentrated to a small volume, and extracted with EtOAc. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was chromatographed on Si gel (60 g). Elution with hexane-EtOAc (8:2) yielded **11** (1.1 g, 89%) as a yellow oil: ir ν max 3587 and 3275 (OH), 2729 (C-H, aldehyde), 1712 (C=O, ketone), 1690 cm^{-1} (C=O, aldehyde); [α]D −13.26° (*c* = 1.96); uv λ max (dioxane) 278 (log ε 4.02), 237 nm (log ε 3.45); ^1H nmr (90 MHz, $CDCl_3$) δ 10.18 (1H, s, CHO), 8.37 (1H, br s, which disappears upon addition of D_2O, OH), 7.65 (1H, s, H-6), 6.90 (1H, s, H-3), 3.87 (1H, m, H-8), 2.44 (2H, m, H-12 and H-12′), 2.28 (3H, s, Me-7), 2.15 (3H, s, Me-14), 1.70–1.45 (4H, m, H-10, H-10′, H-11, and H-11′), 1.22 ppm (3H, d, $J_{8,9}$ = 7 Hz, Me-9); ^{13}C nmr (25.1 MHz, $CDCl_3$) see Table 2.

(*R*)-(−)-6-(5-METHYL-1,4-BENZOQUINON-2-YL)-HEPTAN-2-ONE [**12**].—A solution of **11** (0.5 g) in MeOH (5 ml) was treated with H_2O_2 (30 wt % in H_2O) (0.35 ml) and H_2SO_4 (0.05 ml) at room temperature for 1 h, treated with aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The oily residue was dissolved in MeOH (10 ml) and treated with aqueous $FeCl_3$ (1 ml). The reaction mixture was stirred for 1 h, poured over ice-H_2O, and extracted with Et_2O. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by chromatography on Si gel (30 g). Elution with hexane-EtOAc (7:3) provided compound **12** (227 mg, 48%) as a yellow oil: ir ν max 1710 (C=O, ketone), 1645 cm^{-1} (C=O, quinone); [α]D −16.47° (*c* = 1.70); uv λ max (cyclohexane) 290 (log ε 2.70), 260 (log ε 4.29), 253 nm (log ε 4.32); ^1H nmr (90 MHz, $CDCl_3$) δ 6.53 (1H, q, $J_{6,7}$ = 2 Hz, H-6), 6.43 (1H, s, H-3), 2.86 (1H, m, H-8), 2.35 (2H, m, H-12 and H-12′), 2.06 (3H, s, Me-14), 2.00 (3H, d, $J_{6,7}$ = 2 Hz, Me-7), 1.47 (4H, m, H-10, H-10′, H-11, and H-11′), 1.12 ppm (3H, d, $J_{8,9}$ = 7 Hz, Me-9); ^{13}C nmr (25.1 MHz, $CDCl_3$) see Table 2.

(*R*)-(−)-6-(2,5-DIACETOXY-4-METHYLPHENYL)-HEPTAN-2-ONE [**13**].—A solution of quinone **12** (150 mg) in Ac_2O (1.5 ml) was treated with NaOAc (30 mg) and Zn (foil) (1.5 g), refluxed for 1 h, filtered, poured over ice-H_2O, and extracted with EtOAc. The organic layer was washed with aqueous $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by chromatography on Si gel (10 g). Elution with hexane-EtOAc (8:2) yielded diacetate **13** (160 mg, 78%) as a colorless oil: ir ν max 1757 (C=O, esters), 1712 cm^{-1} (C=O, ketone); [α]D −15.00° (*c* = 1.00); uv λ max (cyclohexane) 275 (log ε 2.92), 269 (log ε 2.90), 217 nm (log ε 3.80); ^1H nmr (90 MHz, $CDCl_3$) δ 6.83 (1H, s, H-3), 6.82 (1H, s, H-6), 2.73 (1H, m, H-8), 2.23 (6H, 2s, 2Ac), 2.08 (3H, s, Me-7), 1.95 (3H, s, Me-14), 1.47 (4H, m, H-10, H-10′, H-11, and H-11′), 1.14 (3H, d, $J_{8,9}$ = 7 Hz, Me-9) [the remaining two protons (H-12 and H-12′) overlap in the δ 2.10–2.40 region]; ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 2.

(*R*)-(−)-2-METHYL-6-(5-METHYL-1,4-BENZOQUINON-2-YL)-HEPTAN-2-OL [**14**].—A solution of diacetate **13** (360 mg) in Et_2O (10 ml) was added dropwise to an Et_2O solution of MeMgI [0.15 g of Mg (turnings) and 2 ml of MeI in 20 ml of Et_2O]. The reaction mixture was gently refluxed for 2 h, poured dropwise onto aqueous NH_4Cl, and diluted with Et_2O. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was dissolved in MeOH (20 ml) and treated with aqueous $FeCl_3$ (1 ml). The reaction mixture was stirred during 1 h and extracted with

Et_2O. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The oily residue was purified by chromatography on Si gel (20 g). Elution with petroleum ether-EtOAc (7:3) yielded compound **14** (190 mg, 68%) as a yellow oil: ir ν max 3603 and 3366 (OH), 1655 cm^{-1} (C=O, quinone); $[\alpha]_D$ −3.63° (c = 1.10); uv λ max (dioxane) 258 (log ϵ 3.79), 294 nm (log ϵ 3.16); ^1H nmr δ 6.56 (1H, q, $J_{6,7}$ = 2 Hz, H-6), 6.45 (1H, s, H-3), 2.90 (1H, m, H-8), 2.02 (3H, d, $J_{6,7}$ = 2 Hz, Me-7), 1.15 (6H, 2s, Me-14 and Me-15), 1.12 ppm (3H, d, $J_{8,9}$ = 7 Hz, Me-9) [the remaining seven protons (H-10, H-10′, H-11, H-11′, H-12, H-12′, and OH) overlap in the δ 1.65–0.65 region]; ^{13}C nmr (75.4 MHz, $CDCl_3$) see Table 2.

(*R*)-(−)-CURCUQUINONE [**15**].—A solution of quinone **14** (190 mg) in dry C_6H_6 (52 ml) was treated with Si gel (3.7 g) previously activated as described by D'Onofrio and Scettri (9). The reaction mixture was stirred at 35° for 45 min, diluted with petroleum ether (52 ml), cooled, and placed in a chromatographic column. Elution with petroleum ether-C_6H_6 (1:1) yielded curcuquinone **15** (70 mg, 40%) as a yellow oil $[\alpha]_D$ −1.58 (c = 6.63), [lit. (4) $[\alpha]_D$ −1.30 (c = 9.1)]; the ^1H-nmr data are in agreement with those reported by McEnroe and Fenical (4).

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