trans stereorelationship between the 4-methoxycarbonyl and 5-aryl groups has been confirmed as seen in the *ORTEP* drawing (Johnson, 1976), Fig. 1.

The lactone ring exists in an envelope conformation with atoms O(1), C(1), C(2) and C(4) planar to within 0·023 Å and C(3) out of this plane by 0·65 Å. The O(1)—C(1)—C(2) bond angle is 108·7 (8)°, deviating somewhat from an unconstrained trigonal carbon center. The bond angles C(2)—C(3)—C(4) and C(1)—C(2)—C(3) are 99·7 (7) and 101·1 (7)°, respectively, and in turn reflect angle compression due to ring size from that usually associated with aliphatic sp^3-hybridized carbon. Bond distances are unaffected by ring geometry in this compound. The bond distance between C(2) and C(3) is 1·55 (1) Å and that between C(3) and C(4) is 1·53 (1) Å. The torsion angles H(1)[C(3)]—C(3)—C(4)—H(1)[C(4)] and H(1)[C(2)]—C(2)—C(3)—H(1)[C(3)] of −154·4 and +151·0°, respectively, support an all-*trans* disposition of substituents at these centers, and are consistent with the relatively large ^{1}H NMR vicinal coupling constants (observed 8·72 and 10·62 Hz, respectively) associated with the major stereoisomer formed by our reaction procedure. The similarly large vicinal hydrogen coupling constant observed for H(1)[C(4)] of the non-crystalline minor isomer is hence consistent with our initial structural assignment that these compounds are simply epimeric at the 3-position (Peterson *et al.*, 1988). Finally, as anticipated, the aromatic ring atoms C(5)—C(10) define a plane to within 0·011 Å.

The authors are greatly indebted to the American Cancer Society, Illinois Division, Inc. (JRP, grant No. 87-53), the Milheim Foundation for Cancer Research (JRP, grant No. 87-32), the Elsa U. Pardee Foundation (JRP), the Donors of the Petroleum Research Fund (JRP and RDR), administered by the American Chemical Society, and to the Northern Illinois University Graduate School and Biomedical Research Support Group (JRP) for their generous support of this research. The US National Science Foundation's Chemical Instrumentation Program provided funding to purchase the diffractometer.

References

BYSTROM, S., HOGBERG, H. E. & NORIN, T. (1981). *Tetrahedron* **37**, 2249–2254.

FRISTAD, W. E. & PETERSON, J. R. (1985). *J. Org. Chem.* **50**, 10–18.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

PETERSON, J. R., DO, H. D. & SURJASASMITA, I. B. (1988). *Synth. Commun.* **18**(16). In the press.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination, locally modified. Univ. of Cambridge, England.

SURJASASMITA, I. B. (1987). *Toward the Synthesis of Podophyllotoxin*. MS Thesis, Northern Illinois Univ., DeKalb, Illinois, USA.

Acta Cryst. (1988). C**44**, 1786–1789

Anticancer-Agent Development: X-ray Structure of Dimethyl 2,3,4,5-Tetrahydro-3-(3,4-methylenedioxybenzoyl)-2-oxo-5β-(3,4,5-trimethoxyphenyl)-3α,4α-furandicarboxylate

BY JOHN R. PETERSON,* HOANG D. DO AND ROBIN D. ROGERS*

The Michael Faraday Laboratories, Department of Chemistry, Northern Illinois University, DeKalb, IL 60115, *USA*

(*Received* 28 *April* 1988; *accepted* 1 *June* 1988)

Abstract. $C_{25}H_{24}O_{12}$, $M_r = 516{\cdot}5$, triclinic, $P\bar{1}$, $a = 7{\cdot}383\ (5)$, $b = 11{\cdot}843\ (7)$, $c = 14{\cdot}775\ (9)$ Å, $\alpha = 104{\cdot}95\ (9)$, $\beta = 100{\cdot}30\ (8)$, $\gamma = 103{\cdot}09\ (7)°$, $V = 1176$ Å^3, $Z = 2$, $D_x = 1{\cdot}46$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0{\cdot}71073$ Å, $\mu = 0{\cdot}74$ cm^{-1}, $F(000) = 540$, $T = 293$ K, final $R = 0{\cdot}047$ for 2733 observed $[F_o \geq 5\sigma(F_o)]$ reflections. The observed structure reveals that the *trans* disposition of the substituents at positions 4 and 5 of the heterocycle is maintained in the reaction sequence, and that the major stereocomponent in the product mixture possesses a *cis*-3,4-bis(methoxycarbonyl) relationship. There is no crystallographically imposed symmetry.

---

* Authors to whom correspondence should be addressed.

0108-2701/88/101786-04$03.00

Introduction. The X-ray structure of the title compound was obtained in conjunction with our extensive investigations on novel synthetic approaches to the antineoplastic podophyllotoxins. The preparation of this compound afforded two chromatographically separable diastereomers. We felt, based upon a comparison of ^{1}H NMR chemical shifts and vicinal coupling constants, that the diastereomers were simply epimeric at the 3-position. Nevertheless, the assignment of substituent stereorelationships about a γ-lactone ring by ^{1}H NMR coupling-constant analysis has not always been reliable. Vicinal hydrogen coupling constants for *trans*-substituted γ-lactones have generally been larger than those of the *cis* isomer; however, several exceptions have been noted (Bystrom, Hogberg & Norin, 1981; Fristad & Peterson, 1985). One of our strategies to podophyllotoxin proceeds *via* a *cis*-fused dicinnamic acid dilactone (Surjasasmita, 1987; Peterson, Rogers & Do, 1988) and necessitates a *trans* stereochemical disposition of the 4-methoxycarbonyl and 5-aryl moieties in the title compound. In view of the possibility for epimerization at the 4-methoxycarbonyl center under the reaction conditions used to prepare this molecule, we felt compelled to establish firmly the structure for the major product by X-ray crystallography.

Experimental. The title compound was prepared by reaction of the potassium enolate of dimethyl 2,3,4,5-tetrahydro-2-oxo-5-(3,4,5-trimethoxyphenyl)-3,4-furandicarboxylate (Peterson, Do & Surjasasmita, 1988; Peterson, Rogers & Do, 1988) with 3,4-methylenedioxybenzoyl chloride in a manner described elsewhere (Surjasasmita, 1987). Flash chromatography of the crude product mixture on silica gel using 2% acetone–chloroform as eluent delivered pure α-aroyl-γ-lactone* in 60% yield. Crystals (m.p. 405–407 K) suitable for X-ray analysis were obtained by recrystallization from chloroform–pentane. D_m not determined. Crystal 0·13 × 0·25 × 0·35 mm. Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Mo $K\alpha$. Cell constants from setting angles of 19 reflections ($\theta > 20°$). Correction for Lorentz–polarization effect, no correction for absorption. $\theta_{max} = 50°$; h 0 to 8, k −14 to 14, l −17 to 17. Standard reflections observed every 3600 s of data collection time: 200, 060, 009. Variation = ± 2%. 4089 reflections measured, 2733 independent observed reflections [$F_o \geq 5\sigma(F_o)$]. Structure solved utilizing *MULTAN* (Germain, Main & Woolfson, 1971) direct-methods program. Geometrically constrained H atoms were placed 0·95 Å from the bonded C atom with a fixed isotropic thermal parameter $B = 5·5$ Å^2 and allowed to ride on that atom. The methyl H atoms were located from a difference Fourier map and included wih fixed contributions ($B = 5·5$ Å^2). Scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974); structure refined with *SHELX*76 (Sheldrick, 1976). $\sum w(|F_o| - |F_c|)^2$ minimized, weights = $[\sigma(F_o)^2 + 0·00005F_o^2]^{-1}$, 334 parameters varied. $R = 0·047$, $wR = 0·047$, $S = 1·38$. Δ/σ in final least-squares refinement cycle $< 0·01$, $\Delta\rho < 0·2$ e Å^{-3} in final difference map.

Table 1. *Final fractional coordinates and equivalent isotropic thermal parameters for* $C_{25}H_{24}O_{12}$

$B_{eq} = \frac{4}{3}(a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + ab\cos\gamma\beta_{12} + ac\cos\beta\beta_{13} + bc\cos\alpha\beta_{23})$.

	x	y	z	B_{eq}(Å^2)
O(1)	0·3847 (3)	0·0743 (2)	0·3094 (1)	3·04
O(2)	0·1939 (3)	0·0657 (2)	0·1719 (2)	3·58
O(3)	0·4564 (3)	0·3961 (2)	0·2790 (1)	3·60
O(4)	0·2368 (3)	0·5292 (2)	−0·0136 (2)	3·54
O(5)	0·1686 (3)	0·3631 (2)	−0·1480 (2)	3·84
O(6)	0·5929 (3)	0·0369 (2)	0·1269 (2)	3·88
O(7)	0·7429 (3)	0·2270 (2)	0·1336 (1)	3·07
O(8)	0·9666 (3)	0·2263 (2)	0·3473 (2)	4·80
O(9)	0·9115 (3)	0·4047 (2)	0·3524 (2)	4·11
O(10)	0·9149 (3)	0·1501 (2)	0·6879 (1)	3·30
O(11)	0·7044 (3)	0·2886 (2)	0·7665 (1)	3·08
O(12)	0·4052 (3)	0·3180 (2)	0·6595 (2)	3·61
C(1)	0·3452 (5)	0·1078 (3)	0·2298 (2)	2·82
C(2)	0·5193 (4)	0·2062 (2)	0·2273 (2)	2·33
C(3)	0·6445 (4)	0·2432 (2)	0·3314 (2)	2·46
C(4)	0·5834 (4)	0·1300 (2)	0·3628 (2)	2·69
C(5)	0·6018 (4)	0·1593 (2)	0·4694 (2)	2·63
C(6)	0·7440 (4)	0·1313 (3)	0·5261 (2)	2·75
C(7)	0·7763 (4)	0·1702 (3)	0·6256 (2)	2·60
C(8)	0·6631 (4)	0·2372 (2)	0·6681 (2)	2·58
C(9)	0·5135 (4)	0·2588 (2)	0·6101 (2)	2·74
C(10)	0·4825 (4)	0·2219 (3)	0·5109 (2)	2·84
C(11)	0·4498 (4)	0·3146 (2)	0·2082 (2)	2·51
C(12)	0·3738 (4)	0·3176 (3)	0·1109 (2)	2·51
C(13)	0·3462 (4)	0·4292 (3)	0·1035 (2)	2·58
C(14)	0·2733 (4)	0·4321 (3)	0·0135 (2)	2·75
C(15)	0·1461 (5)	0·4812 (3)	−0·1142 (2)	3·71
C(16)	0·2278 (4)	0·3321 (3)	−0·0678 (2)	2·90
C(17)	0·2481 (5)	0·2223 (3)	−0·0621 (2)	3·28
C(18)	0·3229 (4)	0·2165 (3)	0·0288 (2)	2·88
C(19)	0·6188 (4)	0·1444 (3)	0·1552 (2)	2·70
C(20)	0·8492 (5)	0·1768 (3)	0·0662 (3)	4·17
C(21)	0·8597 (4)	0·2875 (3)	0·3446 (2)	2·85
C(22)	1·1122 (6)	0·4611 (4)	0·3616 (4)	6·28
C(23)	1·0089 (5)	0·0632 (3)	0·6493 (2)	3·81
C(24)	0·6365 (7)	0·2120 (3)	0·8174 (3)	5·49
C(25)	0·2573 (5)	0·3499 (3)	0·6052 (3)	4·24

Discussion. Fractional coordinates and B_{eq} values are given in Table 1,* distances and angles in Table 2, and an *ORTEP* drawing (Johnson, 1976) in Fig. 1. The

---

* Physical data: IR (KBr) 3000, 2940, 2890, 2825, 1780, 1730, 1670, 1590, 1500, 1480, 1435, 1345, 1325, 1250, 1180, 1120, 1030, 1000, 750 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7·68 (*dd*, J = 8·38, 1·77 Hz, 1H), 7·50 (*d*, J = 1·77 Hz, 1H), 6·88 (*d*, J = 8·38 Hz, 1H), 6·59 (*s*, 2H), 6·07 (*s*, 2H), 5·78 (*d*, J = 10·46 Hz, 1H), 4·63 (*d*, J = 10·46 Hz, 1H), 3·86 (*s*, 9H), 3·80 (*s*, 3H), 3·68 (*s*, 3H); ^{13}C NMR (CDCl$_3$, 50 MHz) δ 185·07, 168·75, 166·78, 166·44, 153·71, 152·59, 148·05, 138·94, 130·94, 128·79, 127·39, 109·90, 107·96, 103·40, 102·13, 80·49, 70·87, 60·84, 56·28, 54·82, 54·05, 52·88. Analysis: calculated for $C_{25}H_{24}O_{12}$: C 58·14, H 4·68; found: C 57·94, H 4·82%.

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates least-squares-planes results and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51095 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

trans stereochemical disposition between the 4-methoxycarbonyl and 5-aryl groups is immediately obvious upon examination of the *ORTEP* diagram as is the *cis* relationship of the two methoxycarbonyl moieties.

Table 2. *Bond distances* (Å) *and angles* (°) *for* $C_{25}H_{24}O_{12}$

O(1)—C(1)	1·339 (3)	O(1)—C(4)	1·445 (3)
O(2)—C(1)	1·189 (3)	O(3)—C(11)	1·212 (3)
O(4)—C(14)	1·377 (3)	O(4)—C(15)	1·420 (4)
O(5)—C(15)	1·417 (4)	O(5)—C(16)	1·357 (3)
O(6)—C(19)	1·191 (3)	O(7)—C(19)	1·326 (3)
O(7)—C(20)	1·465 (3)	O(8)—C(21)	1·189 (3)
O(9)—C(21)	1·322 (3)	O(9)—C(22)	1·447 (4)
O(10)—C(7)	1·355 (3)	O(10)—C(23)	1·424 (4)
O(11)—C(8)	1·370 (3)	O(11)—C(24)	1·386 (4)
O(12)—C(9)	1·365 (3)	O(12)—C(25)	1·417 (4)
C(1)—C(2)	1·541 (4)	C(2)—C(3)	1·540 (4)
C(2)—C(11)	1·557 (4)	C(2)—C(19)	1·526 (4)
C(3)—C(4)	1·529 (4)	C(3)—C(21)	1·515 (4)
C(4)—C(5)	1·497 (4)	C(5)—C(6)	1·378 (4)
C(5)—C(10)	1·398 (4)	C(6)—C(7)	1·381 (4)
C(7)—C(8)	1·398 (4)	C(8)—C(9)	1·387 (4)
C(9)—C(10)	1·377 (4)	C(11)—C(12)	1·460 (4)
C(12)—C(13)	1·410 (4)	C(12)—C(18)	1·389 (4)
C(13)—C(14)	1·355 (4)	C(14)—C(16)	1·379 (4)
C(16)—C(17)	1·364 (4)	C(17)—C(18)	1·382 (4)

C(1)—O(1)—C(4)	111·6 (2)	C(14)—O(4)—C(15)	105·5 (2)
C(15)—O(5)—C(16)	106·1 (2)	C(19)—O(7)—C(20)	114·8 (2)
C(21)—O(9)—C(22)	117·3 (3)	C(7)—O(10)—C(23)	118·0 (2)
C(8)—O(11)—C(24)	116·0 (2)	C(9)—O(12)—C(25)	117·6 (3)
O(1)—C(1)—O(2)	122·6 (3)	O(1)—C(1)—C(2)	110·4 (3)
O(2)—C(1)—C(2)	127·0 (3)	C(1)—C(2)—C(3)	101·2 (2)
C(1)—C(2)—C(11)	108·7 (2)	C(3)—C(2)—C(11)	110·8 (2)
C(1)—C(2)—C(19)	107·7 (2)	C(3)—C(2)—C(19)	110·3 (2)
C(11)—C(2)—C(19)	116·9 (2)	C(2)—C(3)—C(4)	103·8 (2)
C(2)—C(3)—C(21)	116·2 (2)	C(4)—C(3)—C(21)	113·0 (2)
O(1)—C(4)—C(3)	103·9 (2)	O(1)—C(4)—C(5)	110·7 (2)
C(3)—C(4)—C(5)	113·2 (2)	C(4)—C(5)—C(6)	119·6 (3)
C(4)—C(5)—C(10)	119·4 (3)	C(6)—C(5)—C(10)	120·9 (3)
C(5)—C(6)—C(7)	120·1 (3)	O(10)—C(7)—C(6)	124·8 (3)
O(10)—C(7)—C(8)	115·7 (3)	C(6)—C(7)—C(8)	119·5 (3)
O(11)—C(8)—C(7)	121·1 (3)	O(11)—C(8)—C(9)	119·0 (3)
C(7)—C(8)—C(9)	119·9 (3)	O(12)—C(9)—C(8)	114·6 (3)
O(12)—C(9)—C(10)	124·6 (3)	C(8)—C(9)—C(10)	120·8 (3)
C(5)—C(10)—C(9)	118·7 (3)	O(3)—C(11)—C(2)	116·4 (3)
O(3)—C(11)—C(12)	120·9 (3)	C(2)—C(11)—C(12)	122·6 (2)
C(11)—C(12)—C(13)	116·4 (2)	C(11)—C(12)—C(18)	123·2 (3)
C(13)—C(12)—C(18)	120·3 (3)	C(12)—C(13)—C(14)	116·7 (3)
O(4)—C(14)—C(13)	128·2 (3)	O(4)—C(14)—C(16)	109·2 (3)
C(13)—C(14)—C(16)	122·5 (3)	O(4)—C(15)—O(5)	107·7 (2)
O(5)—C(16)—C(14)	109·7 (3)	O(5)—C(16)—C(17)	128·5 (3)
C(14)—C(16)—C(17)	121·8 (3)	C(16)—C(17)—C(18)	117·1 (3)
C(12)—C(18)—C(17)	121·6 (3)	O(6)—C(19)—O(7)	125·7 (3)
O(6)—C(19)—C(2)	123·6 (3)	O(7)—C(19)—C(2)	110·6 (2)
O(8)—C(21)—O(9)	124·8 (3)	O(8)—C(21)—C(3)	125·3 (3)
O(9)—C(21)—C(3)	109·9 (3)		

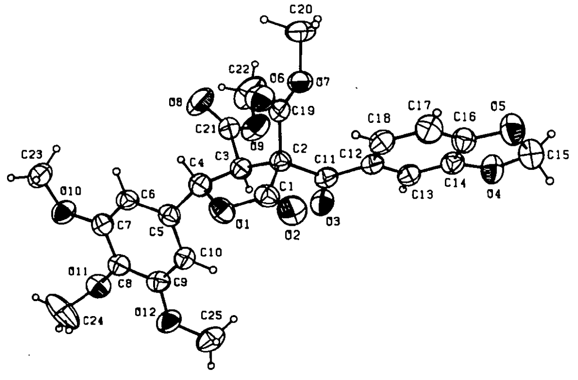

Fig. 1. Thermal-ellipsoid plot of the title compound showing the atom-numbering scheme.

The lactone ring exists in an envelope conformation with atoms O(1), C(1), C(2) and C(4) planar to within 0·034 Å and C(3) out of this plane by 0·46 Å. The bond angles C(1)—C(2)—C(3) and C(2)—C(3)—C(4) are 101·2 (2) and 103·8 (2)°, respectively, and reflect angle compression due to ring size from that usually associated with sp^3-hybridized carbon. This ring-angle compression manifests a broadening of the C(19)—C(2)—C(3) bond angle to 110·3 (2)°, and similarly the C(2)—C(3)—C(21) angle to 116·2 (2)°. Bond distances are unaffected by ring geometry in this compound. The bond distance between C(2) and C(3) is 1·540 (4) Å and that between C(3) and C(4) is 1·529 (4) Å. As expected, the aromatic rings define planes. The ring atoms C(5)—C(10) are planar to within 0·024 Å while the atoms C(12)—C(14) C(16)—C(18) are within 0·014 Å of planarity. The methylenedioxy ring atoms C(14), C(15), C(16), O(4) and O(5) also describe a plane to within 0·076 Å which intersects that defined by the attached aromatic ring at an angle of 2·5°. Finally, the torsion angle H(1)[C(3)]—C(3)—C(4)—H(1)[C(4)] of 147·8° supports a *trans* disposition of substituents at positions 4 and 5 of the heterocyclic ring, and is consistent with the observed large vicinal coupling constant (10·46 Hz) for these H atoms. The similarly large coupling constant associated with the minor stereocomponent of the reaction mixture is thus consonant with our initial structural assignment that the diastereomers are epimeric at the 3-position.

The authors are greatly indebted to the American Cancer Society, Illinois Division, Inc. (JRP, grant No. 87–53), the Milheim Foundation for Cancer Research (JRP, grant No. 87–32), the Elsa U. Pardee Foundation (JRP), the Donors of the Petroleum Research Fund (JRP and RDR), administered by the American Chemical Society, and to the Northern Illinois University Graduate School and Biomedical Research Support Group (JRP) for their generous support of this research. The US National Science Foundation's Chemical Instrumentation Program provided funding to purchase the diffractometer.

References

Bystrom, S., Hogberg, H. E. & Norin, T. (1981). *Tetrahedron*, **37**, 2249–2254.

Fristad, W. E. & Peterson, J. R. (1985). *J. Org. Chem.* **50**, 10–18.

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Peterson, J. R., Do, H. D. & Surjasasmita, I. B. (1988). *Synth. Commun.* **18**(16). In the press.

Peterson, J. R., Rogers, R. D. & Do, H. D. (1988). *Acta Cryst.* C**44**, 1784–1786.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination, locally modified. Univ. of Cambridge, England.

SURJASASMITA, I. B. (1987). *Toward the Synthesis of Podophyllotoxin*. MS Thesis, Northern Illinois Univ., DeKalb, Illinois, USA.

Acta Cryst. (1988). C**44**, 1789–1791

(−)-(1*R*,5*R*,9*R*)-2-Ethoxyethyl-2′-hydroxy-5,9-dimethyl-6,7-benzomorphan Hydrobromide*†

BY C. L. VERLINDE, N. M. BLATON, O. M. PEETERS AND C. J. DE RANTER‡

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

(*Received* 24 *December* 1987; *accepted* 10 *June* 1988)

Abstract. $C_{18}H_{28}NO_2^+.Br^-$, $M_r = 370·336$, orthorhombic, $P2_12_12_1$, $a = 8·0069\,(2)$, $b = 11·6213\,(3)$, $c = 19·7450\,(6)$ Å (refinement on θ only), $V = 1837·28\,(9)$ Å^3, $Z = 4$, $D_m = 1·33\,(2)$, $D_x = 1·335$ Mg m^{-3}, $\lambda(\mathrm{Cu}\,K\alpha) = 1·54178$ Å, $\mu(\mathrm{Cu}\,K\alpha) = 2·38$ mm^{-1}, $F(000) = 776$, 291 K, final $R = 0·034$ for 3055 observed reflections. The *N*-side-chain torsion angles starting from the asymmetric carbon towards the terminal methyl group are about at the global energy minimum in the four-dimensional torsional space: (−)-synclinal, (+)-synclinal, antiperiplanar and antiperiplanar respectively. An intramolecular (C—)H···O hydrogen bond is present.

Introduction. On the basis of *in vivo* pharmacological studies in mice the title compound was classified as a morphine-like agonist (Merz & Stockhaus, 1979). In spite of a large structural resemblance it lacks the kappa opioid properties of its (2″*S*)-*N*-tetrahydrofurfuryl analogue, of which it might be considered an opened ring counterpart. Only a moderate partial agonism has been observed in the rabbit vas deferens bioassay (Verlinde & De Ranter, 1988). The main purpose of this study is to gain further insight into the factors determining the conformation of the *N*-side chain, which is believed to be essential for opioid kappa activity (De Ranter, Verlinde, Blaton & Peeters, 1984).

Experimental. Crystals obtained at room temperature from an equimolar ethyl acetate–methanol solution. Density measured by flotation in *n*-heptane/CCl_4, ~0·5 × 0·2 × 0·2 mm, Hilger & Watts computer-controlled four-circle diffractometer, Ni-filtered Cu $K\alpha$ radiation, $\omega/2\theta$ scan technique ($2\theta_{\max} = 140°$, $0 \le h \le 8$, $0 \le k \le 14$, $-23 \le l \le 24$), cell dimensions by least-squares refinement of the θ values of 24 reflections with $44 < 2\theta < 50°$, space group $P2_12_12_1$ from systematic absences $h00$ for h odd, $0k0$ for k odd, $00l$ for l odd respectively. Four standard reflections (600, 060, 0010, $34\bar{3}$) monitored after each 50 reflections did not reveal a significant change in intensity. 3304 independent reflections measured (Friedel's law not obeyed), 3055 observed reflections [with $I > 3\sigma(I)$], Lorentz–polarization corrections, absorption corrections by the method of North, Phillips & Mathews (1968) with values between 0·997 and 0·818, scattering factors from Cromer & Mann (1968), and Stewart, Davidson & Simpson (1965) (for H), anomalous-dispersion correction for Br (*International Tables for X-ray Crystallography*, 1974).

The position of the Br was revealed through a Patterson synthesis at 0·25 0·225 0·215. Expansion of the model either by Fourier methods or by direct methods on the difference structure proved to be very hard. However, it was then realized that the Br atom is on a pseudo special position: it creates an inversion centre at 0 $\frac{1}{4}$ 0 yielding the space group *Pmcn*. Therefore the extra symmetry was destroyed and a Br at 0·22 0·225 0·215 served as input for *DIRDIF* (Beurskens *et al.*, 1981). The resulting *E* map now revealed the complete molecule. At this stage we again went through our earlier *DIRDIF* trials with the Br on the pseudo special position as an enantiomorph fixation procedure is present in the program to anticipate these troublesome cases. Indeed, in the maps a partial structure could now be recognized. Refinement with *XRAY76* (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) by block-diagonal least squares on *F*, first with isotropic temperature factors and then

---

[*] *Chemical Abstracts* name: (−)-(2*R*,6*R*,11*R*)-3-ethoxyethyl-1,2,3,4,5,6-hexahydro-6,11-dimethyl-2,6-methano-3-benzazocin-8-ol hydrobromide.

[†] Structural Studies of Substituted 6,7-Benzomorphan Compounds. IX. Part VIII: Verlinde, Blaton, De Ranter & Peeters (1984).

[‡] To whom correspondence should be addressed.

0108-2701/88/101789-03$03.00