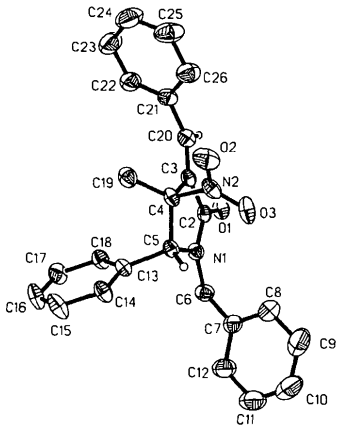

Fig. 1. *ORTEP*II plot (Johnson, 1976) of the molecule showing the atom-numbering scheme.

study of crystallographic data for 42 pyrrolidinone moieties, Georges, Norberg, Everard & Durant (1989) obtained the following values and statistical standard deviations (enclosed in parentheses) for the bond distances (Å) in the five-membered ring: N(1)—C(2) 1.354 (32), C(2)—C(3) 1.503 (27), C(3)—C(4) 1.510 (53), C(4)—C(5) 1.522 (34), C(5)—N(1) 1.419 (44) Å. Values obtained in the present case compare well with these values.

The *ORTEP*II plot (Johnson, 1976) of the molecule (Fig. 1) shows that the methyl C atom C(19) and the phenyl ring attached respectively to the two asymmetric centres C(4) and C(5), have the *cis* stereochemistry. Furthermore, the phenyl ring attached to the olefineic C atom C(20) is in *cis* orientation with respect to the methyl group attached to C(4).

The authors are grateful to Professor A. Chatterjee of the Department of Chemistry, Jadavpur University, for suggesting this investigation and for providing crystals of the compound suitable for X-ray study. Sincere thanks are also due to Dr Partha Basu, for collecting the intensity data at the National Facility for Single Crystal Diffractometry, Department of Inorganic Chemistry, Indian Association for the Cultivation of Science.

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Structure of 6-Benzyl-5-(3,4-dimethoxybenzyl)-3-methyl-5,6,7,8-tetrahydro-3*H*-oxazolo[5,4-*g*]isoquinolin-2-one

BY VINCENT WARIN,* JOCELYNE LAMIOT AND FRANÇOIS BAERT

Laboratoire de Dynamique et de Structure des Matériaux Moléculaires, ERA CNRS 801, *Université des Sciences et Techniques de Lille-Flandres-Artois*, 59655 *Villeneuve d'Ascq, France*

AND HAMID AIT MANSOUR, RAYMOND HOUSSIN AND DANIEL LESIEUR

Institut de Chimie Pharmaceutique, rue du Professeur Laguesse, 59006 *Lille, France*

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Abstract. $C_{27}H_{28}N_2O_4$, $M_r = 444.5$, monoclinic, $P2_1/n$, $a = 7.961$ (5), $b = 11.863$ (6), $c = 24.873$ (8) Å, $\beta = 92.29$ (1)°, $V = 2347.16$ Å^3, $Z = 4$, $D_x = 1.26$ g cm^{-3}, λ(Mo $K\alpha$) = 0.7107 Å, $\mu = 0.49$ cm^{-1}, $F(000) = 944.0$, $T = 293$ K, $R = 0.041$ for 2854 observed reflections with $I \geq 3\sigma(I)$. The title compound, obtained as a racemate, can be considered as a structural analogue of trimetoquinol, a therapeutic agent which displays various effects in relation to its configuration. It seems then important to specify the

* Author to whom correspondence should be addressed.

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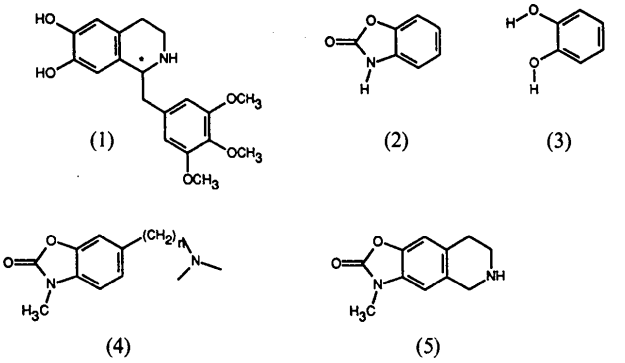
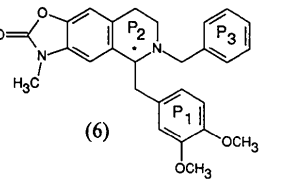
stereochemistry of each of the enantiomers in order to correlate their pharmacological properties with their structures. In a first approach, the structure of the racemate was ascertained by X-ray analysis.

Introduction. During recent years much evidence has been accumulated that many drugs act on specific target receptors in a stereoselective fashion to elicit pharmacological effects. The stereoselectivity is the extent to which a macromolecular structure (such as a receptor) exhibits affinity towards one molecule of a pair of stereoisomers in comparison, and in contrast, to the other isomer. The implication of the conformational aspects in the molecular recognition is clear if it is supposed that one single conformation of a flexible drug molecule is bound in the drug-receptor complex. If it is evident that the stereochemistry of the drug is closely related to the structure–activity relationships, the approach of binding site maps is possible and contributes to the elaboration of an efficient drug-design strategy. Trimetoquinol (1) is a potent β adrenoceptor agonist currently used in Japan in asthma therapy (Iwasawa & Kiyomoto, 1967). It is also a potent inhibitor of platelet aggregation by antagonizing the thromboxane A_2 receptor (Mayo, Navran, Miller & Feller, 1981). These two biological properties seem probably to be mediated by different mechanisms since the former is more pronounced with the S (−) isomer and the latter with the R (+) isomer. Moreover, the N-benzyl analogue of trimetoquinol has been shown to provide separation of these properties and to impart some selectivity for platelet antiaggregatory activity (Adejare, Miller, Fedyna, Ahn & Feller, 1986; Harrold, Grajzl, Shin, Romstedt, Feller & Miller, 1988; Kaiser, Oh, Garcia, Sulpizio, Hieble & Kruse, 1986), the response intensity depending on the electronic character and on the number of the benzyl substituents. Our continuing interest in the medicinal chemistry of 2-benzoxazolinone (2) led us to confirm its putative bioisosterism with pyrocatechol (3) (Vaccher, Lesieur, Lespagnol, Bonte, Lamar, Beaughard & Dureng, 1986; Bonte, Piancastelli, Lesieur, Lamar, Beaughard & Dureng, 1990). It seemed interesting to study the influence on the activity of the conformationally restricted analogues (5) of the aminoalkylbenzoxazolinones (4) structurally related to trimetoquinol, which exhibits cardiovascular and analgetic properties (Caignard, Couquelet, Lesieur, Lespagnol, Lamar, Beaughard & Leinot, 1985). Moreover, the corresponding N-benzyl derivatives would present a pharmacological profile closely related to the configuration around the asymmetric centre as mentioned for the prototype molecule. The synthetic route to the oxazolinotetrahydroisoquinoline (6) was chosen in order to afford the pair of enantiomers as the racemate. The racemate was crystallized from methanol and its structure established by a single-crystal X-ray determination. It was subsequently resolved in its constituents by high-performance liquid chromatography (HPLC) according to procedures which will be published elsewhere.



(1) Trimetoquinol
(2) Benzoxazolinone
(3) Pyrocatechol
(4) 6-Aminoalkylbenzoxazolinones
(5) Oxazolinotetrahydroisoquinoline
(6) Title compound



Experimental. White crystal, dimensions 0.30 × 0.40 × 0.40 mm. Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Mo $K\alpha$ radiation. ω–2θ scans. Cell dimensions from setting angles of 25 reflections with $10 \le \theta \le 20°$. 4953 independent reflections surveyed with $2\theta_{max} = 54°$; $-10 \le h \le 10$, $0 \le k \le 14$, $0 \le l \le 23$; 2854 reflections observed with $I \ge 3\sigma(I)$. Three reference reflections monitored every 2 h showed no significant variation in intensity (within 2% error). Absorption correction was not applied. Structure solved using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson,

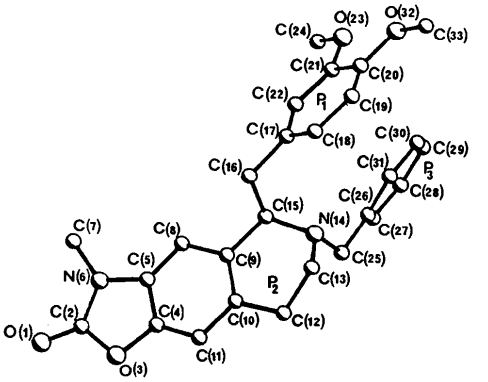


Fig. 1. *PLUTO* (Motherwell & Clegg, 1978) perspective view of the title compound.

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors* ($Å^2 \times 10^2$) *with e.s.d.'s in parentheses*

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j .$$

	x	y	z	U_{eq}
O(1)	6294 (3)	−7502 (2)	4593 (1)	78 (3)
C(2)	6716 (4)	−6590 (3)	4768 (1)	64 (4)
O(3)	7492 (2)	−5788 (2)	4465 (1)	65 (3)
C(4)	7781 (3)	−4858 (2)	4796 (1)	53 (3)
C(5)	7169 (3)	−5075 (2)	5295 (1)	49 (3)
N(6)	6523 (3)	−6170 (2)	5272 (1)	57 (3)
C(7)	5812 (4)	−6776 (2)	5705 (1)	79 (4)
C(8)	7264 (3)	−4280 (2)	5695 (1)	48 (2)
C(9)	8004 (3)	−3246 (2)	5577 (1)	44 (2)
C(10)	8662 (3)	−3047 (2)	5073 (1)	51 (3)
C(11)	8542 (3)	−3876 (2)	4672 (1)	61 (3)
C(12)	9486 (3)	−1937 (2)	4951 (1)	66 (3)
C(13)	9958 (3)	−1302 (2)	5463 (1)	57 (3)
N(14)	8561 (2)	−1229 (1)	5825 (1)	47 (2)
C(15)	8094 (3)	−2351 (2)	6016 (1)	45 (2)
C(16)	9305 (3)	−2724 (2)	6484 (1)	53 (3)
C(17)	9470 (3)	−1869 (2)	6927 (1)	49 (3)
C(18)	10894 (3)	−1224 (2)	7000 (1)	56 (3)
C(19)	11008 (3)	−388 (2)	7393 (1)	53 (3)
C(20)	9690 (3)	−196 (2)	7722 (1)	49 (3)
C(21)	8241 (3)	−853 (2)	7659 (1)	53 (3)
C(22)	8142 (3)	−1674 (2)	7266 (1)	48 (3)
O(23)	7001 (2)	−610 (2)	8008 (1)	69 (2)
C(24)	5466 (4)	−1189 (3)	7939 (1)	94 (5)
C(25)	7116 (3)	−608 (2)	5592 (1)	52 (3)
C(26)	6141 (3)	2 (2)	6011 (1)	50 (3)
C(27)	4417 (4)	116 (2)	5951 (1)	63 (3)
C(28)	3532 (4)	753 (3)	6310 (1)	96 (5)
C(29)	4366 (5)	1261 (3)	6739 (1)	101 (5)
C(30)	6074 (5)	1128 (2)	6811 (1)	76 (5)
C(31)	6960 (4)	503 (2)	6451 (1)	58 (3)
O(32)	9651 (2)	621 (2)	8112 (1)	60 (2)
C(33)	11097 (4)	1306 (3)	8189 (1)	67 (4)

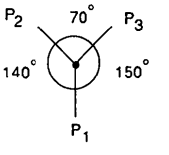
Table 2. *Selected bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

O(1)—C(2)	1.209 (4)	C(16)—C(17)	1.500 (3)
C(2)—O(3)	1.376 (4)	C(17)—C(18)	1.374 (3)
C(2)—N(6)	1.362 (4)	C(17)—C(22)	1.397 (3)
O(3)—C(4)	1.389 (3)	C(18)—C(19)	1.393 (3)
C(4)—C(5)	1.375 (3)	C(19)—C(20)	1.374 (3)
C(4)—C(11)	1.354 (3)	C(20)—C(21)	1.396 (3)
C(5)—N(6)	1.398 (3)	C(20)—O(32)	1.374 (3)
C(5)—C(8)	1.371 (3)	C(21)—C(22)	1.381 (3)
N(6)—C(7)	1.431 (4)	C(21)—O(23)	1.370 (3)
C(8)—C(9)	1.397 (3)	O(23)—C(24)	1.407 (4)
C(9)—C(10)	1.397 (3)	C(25)—C(26)	1.508 (3)
C(9)—C(15)	1.524 (3)	C(26)—C(27)	1.381 (4)
C(10)—C(11)	1.402 (3)	C(26)—C(31)	1.385 (4)
C(10)—C(12)	1.507 (3)	C(27)—C(28)	1.383 (4)
C(12)—C(13)	1.515 (3)	C(28)—C(29)	1.374 (4)
C(13)—N(14)	1.460 (3)	C(29)—C(30)	1.373 (6)
N(14)—C(15)	1.466 (3)	C(30)—C(31)	1.378 (4)
N(14)—C(25)	1.465 (3)	O(32)—C(33)	1.415 (4)
C(16)—C(15)	1.546 (3)		

O(1)—C(2)—O(3)	123.1 (3)	C(9)—C(15)—C(16)	110.5 (2)
O(1)—C(2)—N(6)	128.2 (3)	N(14)—C(15)—C(16)	110.2 (2)
O(3)—C(2)—N(6)	108.7 (3)	C(15)—C(16)—C(17)	113.1 (2)
C(2)—O(3)—C(4)	107.0 (2)	C(15)—C(16)—C(33)	120.2 (2)
O(3)—C(4)—C(5)	109.2 (2)	C(17)—C(16)—C(33)	98.0 (2)
O(3)—C(4)—C(11)	127.9 (2)	C(16)—C(17)—C(18)	121.4 (2)
C(5)—C(4)—C(11)	122.9 (2)	C(16)—C(17)—C(22)	120.6 (2)
C(4)—C(5)—N(6)	106.2 (2)	C(18)—C(17)—C(22)	118.0 (2)
C(4)—C(5)—C(8)	121.1 (2)	C(17)—C(18)—C(19)	121.2 (2)
N(6)—C(5)—C(8)	132.7 (2)	C(18)—C(19)—C(20)	120.4 (2)
C(2)—N(6)—C(5)	108.8 (2)	C(19)—C(20)—C(21)	119.3 (2)
C(2)—N(6)—C(7)	124.9 (2)	C(19)—C(20)—O(32)	125.2 (2)
C(5)—N(6)—C(7)	126.2 (2)	C(21)—C(20)—O(32)	115.5 (2)
C(5)—C(8)—C(9)	117.5 (2)	C(20)—C(21)—C(22)	119.7 (2)
C(8)—C(9)—C(10)	120.9 (2)	C(20)—C(21)—O(23)	115.2 (2)
C(8)—C(9)—C(15)	118.0 (2)	C(22)—C(21)—O(23)	125.1 (2)
C(10)—C(9)—C(15)	121.1 (2)	C(17)—C(22)—C(21)	121.4 (2)
C(9)—C(10)—C(11)	120.1 (2)	C(21)—O(23)—C(24)	117.7 (2)
C(9)—C(10)—C(12)	120.7 (2)	N(14)—C(25)—C(26)	112.7 (2)
C(11)—C(10)—C(12)	119.2 (2)	C(25)—C(26)—C(27)	120.6 (2)
C(4)—C(11)—C(10)	117.4 (2)	C(25)—C(26)—C(31)	120.8 (2)
C(10)—C(12)—C(13)	111.2 (2)	C(27)—C(26)—C(31)	118.5 (2)
C(12)—C(13)—N(14)	112.2 (2)	C(26)—C(27)—C(28)	120.9 (3)
C(13)—N(14)—C(15)	110.8 (2)	C(27)—C(28)—C(29)	119.9 (3)
C(13)—N(14)—C(25)	113.1 (2)	C(28)—C(29)—C(30)	119.6 (3)
C(15)—N(14)—C(25)	112.3 (2)	C(29)—C(30)—C(31)	120.6 (3)
C(9)—C(15)—N(14)	113.9 (2)	C(26)—C(31)—C(30)	120.4 (3)
		C(20)—O(32)—C(33)	117.3 (2)

1978). Full-matrix least-squares refinement on F using *SHELX*76 (Sheldrick, 1976), with non-H atoms having anisotropic temperature factors. The positions of all H atoms were found from a difference Fourier map. Their isotropic thermal parameters U were equal to the U_{eq} values of the atoms to which they are bonded. Final $R = 0.041$, $wR = 0.041$ ($w = 1$), $S = 3.48$, 382 parameters refined, $|\Delta\rho|_{min}$ in final map = 0.23, $|\Delta\rho|_{max} = 0.23$ e Å^{-3}; $(\Delta/\sigma) \leq 0.19$. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV), for H from Stewart, Davidson & Simpson (1965).

Discussion. Final atomic coordinates of non-H atoms and equivalent isotropic thermal parameters are listed in Table 1.* Bond lengths and angles are shown in Table 2. A *PLUTO* (Motherwell & Clegg, 1978) drawing of the molecule is shown in Fig. 1. The relative orientation of planes P_1, P_2 and P_3 is represented in the scheme below. This molecule is comprised of three fractions whose arrangement clearly minimizes the steric and electronic interactions. The tricyclic condensed moiety involving the aromatic isoquinolinyl part and the oxazolinyl ring constitutes a nearly planar structure P_2 from which only C(13) and N(14) deviate in opposite directions (0.397 and 0.338 Å respectively), conferring to the six-membered N-containing ring a slightly skewed conformation. In such an arrangement, the two other hydrophobic benzyl planar fractions P_1 and P_3 are oriented in such a way that the geometric constraints set by the methoxy substituents and the repulsive electronic interaction of the π electrons are reduced to a minimum. This spatial disposition around the C(25)—N(14)—C(15)—C(16) moiety is that of a propeller-like conformation. From the separation of isomers, activities in the platelet antiaggregatory area are specially under investigation.



* Lists of structure factors, anisotropic thermal parameters, least-squares-planes data and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54871 (21 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: PA0228]

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Structure of [1*R*-(*endo,anti*)]-3-Bromo-1,7-dimethyl-7-vinylbicyclo[2.2.1]heptan-2-one

BY JOHANN JAUCH AND HEINZ LADERER

Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle 18, *D*-7400 *Tübingen, Germany*

AND LEONHARD WALZ

Daimler-Benz AG, Forschungszentrum Ulm, FIW/FS, Wilhelm-Runge-Strasse 11, *D*-7900 *Ulm, Germany*

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Abstract. $C_{11}H_{15}BrO$ (1), $M_r = 243.14$, orthorhombic, $P2_12_12_1$, $a = 7.413$ (1), $b = 9.943$ (1), $c = 14.779$ (2) Å, $V = 1089.3$ (5) Å^3, $Z = 4$, $D_x = 1.483$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 36.38$ cm^{-1}, $F(000) = 496$, $T = 298$ K, final $R = 0.0459$ for 974 reflections [$F_o > 3\sigma(F_o)$]. This vinyl compound, synthesized from commercially available D(+)-3-bromocamphor-π-sulfonic acid, shows clearly that the π substituent is *anti* configured to the carbonyl group, which is in contrast to the description in several chemical supply catalogues and articles in the literature.

Introduction. A method for the determination of the enantiomeric purity of chiral compounds is complexation gas chromatography (Schurig, 1986) using chiral metal–β-diketonate complexes as stationary phases. Usually the β-diketone ligand is trifluoroacetyl- or heptafluorobutyryl-1*R*-camphor. To determine which factors influence the chiral recognition of these stationary phases, we decided to modify the camphor framework. In this regard, the D(+)-α-bromocamphor-π-sulfonic acid ammonium salt, listed in the *Aldrich Handbook of Fine Chemicals* 1990–1991, or the (+)-3-bromocamphor-8-sulfonic acid monohydrate, listed in the *Merck–Schuchardt Manual* 1989, seemed to be suitable starting materials, allowing us to modify the space required for potentially coordinated substrates during the separation of enantiomers. However, only the variation of the π substituent *syn* relative to the carbonyl group should influence this distinctly. ^{13}C NMR spectra of the vinyl derivative (1) revealed some doubt as to the orientation of the π substituent.

Experimental. Compound (1) was synthesized by chlorination of the sulfonic acid ammonium salt with PCl_5 and subsequent addition of diazomethane/triethylamine followed by elimination of N_2 and SO_2 (Laderer, 1990). Colourless needle-like crystals of (1) were obtained after vacuum distillation (5 Pa) and sublimation of the distillate. A single crystal of approximate dimensions 0.1 × 0.1 × 1.5 mm was used for the data collection. Lattice constants were determined from 88 reflections having $2\theta > 25°$ on a Stoe Stadi-4 diffractometer. 1581 reflections were measured with the scan mode ω–θ = 1:1 (hkl, $\bar{h}\bar{k}l$, $0 \le h \le 8$, $0 \le k \le 11$, $0 \le l \le 17$, $3 \le 2\theta \le 50°$). Three

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