uniquely determined, because the alternative position is not compatible with the position of P_5. Q_3 may have one of four positions indicated by Q_3^{i}, Q_3^{ii}, Q_3^{iii}, Q_3^{iv}. If Q_3 and P_5 are fixed, Q_4 is uniquely determined. Thus, only four stacking variants are in agreement with the observed lattice constants of form *B*.

The atomic coordinates of form *B* (Brückner, 1982, deposited data) show that the variants (ii) and (iii) do not exist in form *B*, whereas both the variants (i) and (iv) are present. This results because:

–it was impossible to decide between N and O atoms in the Fourier map;

–variants (i) and (iv) are almost identical and may be transformed into each other by interchanging O atoms and NH_2 groups.

More precise information on the occurrence of (i) and (iv) in form *B* could be obtained from a detailed investigation of the distribution of the intensities in reciprocal space. Possible results are, for instance:

–statistical occurrence of (i) and (iv) with approximately equal probabilities;

–alternating occurrence of (i) and (iv);

–the crystal consists of regions containing either only (i) or only (iv). The volume of the regions of type (i) and the volume of the regions of type (iv) are about the same.

In both variants (i) and (iv) the two possible kinds of triples of layers are present. In (i) as well as in (iv) their proportion is 3:1 in favour of the triple existing in form *A* (see Fig. 3*b*).

Concluding remark. The example discussed is also of interest in OD theory. No structure with a similar stacking of layers has been found so far. The combination of pairs of layers related by a centre of symmetry and pairs of layers related by a fourfold inversion axis is rather unusual.

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Structure–Potency Relationships for Three Isomers of (±)-1,2,3-Trimethyl-4-phenyl-4-piperidinol*

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Abstract

The three isomers of the title compound, $C_{14}H_{21}NO$, are known to have propionate esters with potency rankings $\gamma > \alpha > \beta$. The present X-ray analyses have shown their configurations to be: α-base, *t*-2-CH_3, *t*-3-CH_3, *r*-4-C_6H_5; β-base, *c*-2-CH_3, *t*-3-CH_3, *r*-4-C_6H_5; γ-HCl, *t*-2-CH_3, *c*-3-CH_3, *r*-4-C_6H_5, as deduced also from an independent NMR study. In the solid state, the three isomers have the piperidine ring in the chair conformation with the 1-methyl and 4-phenyl in equatorial positions. Intermolecular hydrogen bonding is present, as O–H···N′ in the α-base and β-base structures, and as O–H···Cl···H′–N′ in the γ-HCl. Comparison of the isomers of prodine, promedol alcohol, and the present compound shows that the potency is highest for the isomers with the configuration *c*-3-CH_3 (or *c*-5-CH_3), *r*-4-C_6H_5. Also, activity is most inhibited for the present β-2,3-dimethyl isomer, where 2-CH_3 is *cis* and 3-CH_3 is *trans* to 4-C_6H_5. Preliminary interpretation of the structure–potency relationships indicates that the degree of potency of these analgesics may be dependent on the preferred orientations of the 4-phenyl and/or 4-hydroxyl relative to the piperidine ring. [Crystal data: α-base: $M_r = 219{\cdot}33$, $Pna2_1$, $a = 10{\cdot}137\,(1)$, $b = 11{\cdot}446\,(1)$, $c = 10{\cdot}815\,(1)$ Å, $V = 1254{\cdot}8$ Å^3, $Z = 4$, $D_m = 1{\cdot}162$, $D_x = 1{\cdot}161$ g cm^{-3}, $F(000) = 480$, $T = 294$ K, λ(Cu $K\alpha_1$) = 1·54056 Å, $\mu = 5{\cdot}26$ cm^{-1}, $R = 0{\cdot}032$ for 1294 observed reflexions; β-base: $M_r = 219{\cdot}33$, $P2_1/a$, $a = 18{\cdot}434\,(1)$, $b = 9{\cdot}391\,(1)$, $c = 7{\cdot}445\,(2)$ Å, $\beta = 91{\cdot}27\,(1)°$, $V = 1288{\cdot}5$ Å^3, $Z = 4$, $D_m = 1{\cdot}130$, $D_x = 1{\cdot}130$ g cm^{-3}, $F(000) = 480$, $T = 294$ K, λ(Cu, $K\alpha_1$) = 1·54056 Å, $\mu = 5{\cdot}12$ cm^{-1}, $R = 0{\cdot}043$ for 1617 observed reflexions; γ-HCl: $M_r = 255{\cdot}80$, $P2_1/a$, $a =$

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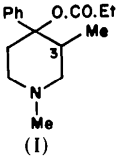
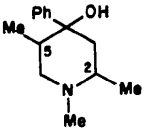
11·756 (1), $b = 16·299$ (2), $c = 7·483$ (1) Å, $\beta = 100·19$ (1)°, $V = 1411·2$ Å^3, $Z = 4$, $D_m = 1·206$, $D_x = 1·204$ g cm^{-3}, $F(000) = 552$, $T = 294$ K, Mo $K\alpha$ for intensities, Cu $K\alpha_1$ for cell parameters, $\lambda = 1·54056$ Å, $\mu = 2·54$ cm^{-1}, $R = 0·041$ for 1733 observed reflexions.]

Introduction

The potency of analgesics varies considerably among different compounds and among stereoisomers of the same compound. The factors contributing to these variations have been under investigation by pharmacological, spectroscopic and crystallographic techniques as described in a review article by Casy (1978). The structure–potency relations of the isomeric prodines (I) and the isomeric promedol alcohols (II) were summarized by Ahmed & De Camp (1972), and the present contribution extends the relations for the isomeric 1,2,3-trimethyl-4-phenyl-4-piperidinols (III). A brief account of these results has been reported by Cygler, Ahmed, Casy & Ogungbamila (1981).



(I)



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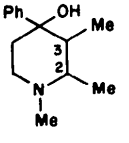


(III)

Compounds (III) were described first by Mistryukov & Shvetsov (1961) but without evidence of stereochemistry. Their solute molecular structures from ^{13}C NMR data have been reported by Casy, Ogungbamila & Rostron (1982) and the significance of their findings has been discussed by Casy (1982). The activity rankings of their propionate esters were established by Jacobson (1980) as $\gamma > \alpha > \beta$. The present X-ray analyses were carried out on the α-base, β-base and γ-HCl.

Experimental

Preparation of compounds (III) has been described by Casy *et al.* (1982) who also supplied us with the crystals. Densities by flotation in aqueous KI solution at 296 K. Nonius CAD-4 diffractometer, Ni-filtered Cu (Zr-filtered Mo for intensity data of the γ-HCl isomer only). Cell parameters by least squares on the angular settings of some high-order reflexions. Intensity measurements by ω–2θ scans. Three standard reflexions measured every 100 min of exposure time. Corrections for Lorentz and polarization effects but not for absorption. Atomic parameters refined by block-diagonal least-squares calculations on $|F_o|$. Anisotropic thermal parameters for non-hydrogen atoms (isotropic for H). Initial H positions from difference maps. Scattering-factor curves of Hanson, Herman, Lea & Skillman (1964) [Stewart, Davidson & Simpson (1965) for H]. Calculations with the *NRC* system of programs (Ahmed, Hall, Pippy & Huber, 1973), *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and *ORTEP* (Johnson, 1971). The crystal data are listed in the *Abstract*.

α-Base. Prismatic crystal 0·24 × 0·30 × 0·39 mm. Cell parameters from 20 reflexions with $\theta = 50$–60°. Scan range $\Delta\omega = 1·5$ (0·8 + 0·2 tan θ)°, *hkl* octant to $\theta = 76°$, intensity scale variation ±1·4%. 1380 independent reflexions, 1294 observed with $I > 1·0\sigma(I)$. Solution by direct methods; nine atoms determined from the E map and the remaining non-H atoms from a weighted Fourier map; least-squares weights $w^{-1} = 1 + [(F_o - 3·5)/8·7]^2$; final $R = 0·032$ for the observed reflexions, $R_w = 0·041$, $S = 0·3$; $(\Delta/\sigma)_{max} = 0·77$; residual electron density within −0·24 and 0·12 e Å^{-3}.

β-Base. Needle crystal 0·07 × 0·10 × 0·34 mm. Cell parameters from 20 reflexions with $\theta = 32$–45°. Scan range $\Delta\omega = 1·5$ (0·85 + 0·2 tan θ)°, *hkl* and $\bar{h}kl$ to $\theta = 75°$, intensity scale variation ±4·0%. 2634 independent reflexions, 1617 observed with $I > 1·5\sigma(I)$. Solution by direct methods; least-squares weights $w^{-1} = 1 + [(F_o - 5)/12·5]^2$; final $R = 0·043$ for observed reflexions, $R_w = 0·055$, $S = 0·42$; $(\Delta/\sigma)_{max} = 0·50$; residual electron density within −0·17 and 0·12 e Å^{-3}.

γ-HCl. Tabular crystal 0·30 × 0·24 × 0·11 mm. Cell parameters from 25 reflexions with θ(Cu) = 43–54°. Scan range $\Delta\omega$(Mo) = 1·5 (0·85 + 0·6 tan θ)°, *hkl* and $\bar{h}kl$ to $\theta = 25°$, intensity scale variation ±1·5%. 2470 independent reflexions, 1733 observed with $I > 1·5\sigma(I)$. Solution by heavy-atom method; least-squares weights $w^{-1} = 1 + [(F_o - 25)/16]^2$; final $R = 0·041$ for observed reflexions, $R_w = 0·038$, $S = 0·51$; $(\Delta/\sigma)_{max} = 0·61$; residual electron density within −0·15 and 0·18 e Å^{-3}.

The refined atomic parameters for the three isomers are listed in Table 1.*

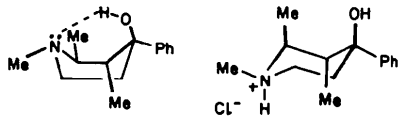
Discussion

Comparison of X-ray and NMR results

Fig. 1 presents the molecular structures of the three isomers of compound (III) as determined by this X-ray analysis. Their configurations, described in terms of the *cis*/*trans* relationships of the substituents, agree with the NMR results (Casy *et al.*, 1982). In the solid state, the three isomers have the piperidine ring in the chair conformation with the

* Lists of structure factors, anisotropic thermal parameters, H parameters, torsion and dihedral angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39184 (34 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

phenyl ring equatorial, and these findings also agree with the conclusions from the NMR studies (Casy *et al.*, 1982) for the α-base, β-base and γ-HCl. However, the NMR indications are that the γ-base in solution occurs predominantly in stereochemistry (1) where the piperidine ring is in the boat (or possibly twist-boat) conformation with the 3-methyl in pseudo-axial position, and that stereochemistry (2) is favoured in the γ-HCl where the strong O–H···N interaction is abolished by N protonation. The latter is the conformation obtained from this X-ray study.



(1) (2)

Bond lengths and angles

Table 2 lists the bond lengths and valence angles for the three isomers of (III). Corresponding bond lengths are comparable although some significant differences, $\leq 0{\cdot}027$ (4) Å, occur as a result of changes in the molecular configurations. Also, protonation of the N atom in the γ-HCl structure has the effect of

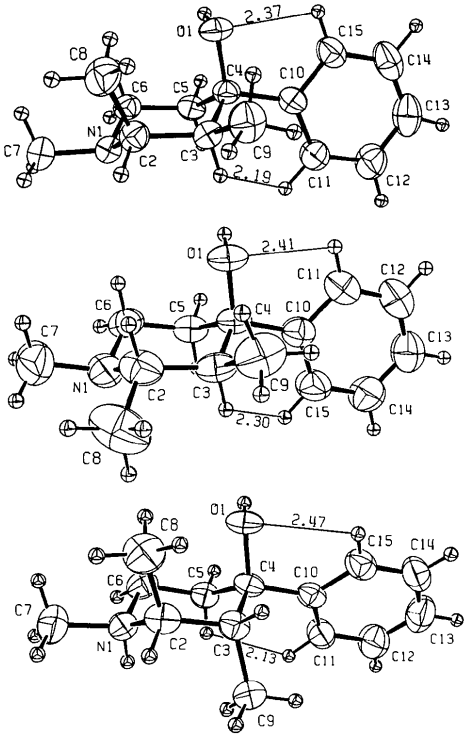


Fig. 1. Molecular structures in the solid state of (*a*) α-base, (*b*) β-base, and (*c*) γ-HCl for compound (III). The thermal ellipsoids are drawn at 50% probability. The intramolecular distances are in Å and their e.s.d.'s are 0·02–0·03 Å for H···O and 0·03–0·04 Å for H···H.

Table 1. *Fractional coordinates* ($\times 10^4$; Cl $\times 10^5$; H $\times 10^3$) *and equivalent isotropic temperature factors* (Å^2) ($B_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$)

	x	*y*	*z*	B_{eq}/B
(*a*) α-Base				
O	3818 (1)	1176 (1)	4058 (1)	3·5
N	901 (1)	2440 (1)	5301 (1)	3·2
C(2)	1050 (2)	1169 (2)	5105 (2)	3·3
C(3)	1495 (2)	957 (2)	3754 (2)	3·0
C(4)	2738 (2)	1648 (2)	3397 (1)	2·9
C(5)	2530 (2)	2938 (2)	3705 (2)	3·1
C(6)	2118 (2)	3090 (2)	5042 (2)	3·3
C(7)	448 (2)	2725 (2)	6555 (2)	4·2
C(8)	1865 (3)	533 (2)	6089 (2)	4·6
C(9)	1626 (2)	−341 (2)	3457 (3)	4·6
C(10)	2993 (2)	1531 (2)	1989 (2)	3·2
C(11)	2024 (2)	1826 (2)	1128 (2)	4·6
C(12)	2254 (3)	1726 (3)	−127 (2)	5·2
C(13)	3460 (3)	1337 (2)	−558 (2)	5·4
C(14)	4421 (2)	1041 (2)	269 (3)	5·0
C(15)	4190 (2)	1124 (2)	1537 (2)	3·9
H(O)	427 (3)	166 (3)	426 (3)	6·3 (7)
(*b*) β-Base				
O	3348 (1)	657 (1)	9320 (2)	4·5
N	1991 (1)	3221 (2)	8345 (2)	4·8
C(2)	2596 (1)	2926 (2)	7118 (3)	5·1
C(3)	3344 (1)	2979 (2)	8075 (3)	4·2
C(4)	3378 (1)	2124 (2)	9832 (2)	3·7
C(5)	2720 (1)	2488 (2)	10953 (3)	4·0
C(6)	2027 (1)	2288 (2)	9921 (3)	4·9
C(7)	1285 (2)	2982 (3)	7439 (5)	7·7
C(8)	2570 (2)	3979 (3)	5561 (3)	8·1
C(9)	3942 (1)	2493 (3)	6827 (3)	6·2
C(10)	4073 (1)	2448 (2)	10900 (3)	4·1
C(11)	4570 (1)	1405 (2)	11373 (4)	5·7
C(12)	5188 (1)	1712 (3)	12371 (4)	7·1
C(13)	5335 (1)	3070 (3)	12924 (3)	6·2
C(14)	4850 (1)	4124 (3)	12481 (3)	6·0
C(15)	4231 (1)	3812 (2)	11485 (3)	5·4
H(O)	322 (1)	17 (3)	1021 (3)	6·7 (6)
(*c*) γ-HCl				
Cl	42700 (6)	11062 (4)	12482 (11)	4·4
O	8476 (1)	2320 (1)	−903 (2)	3·7
N	6832 (2)	937 (1)	1037 (3)	3·5
C(2)	7363 (2)	733 (2)	−602 (3)	3·6
C(3)	7014 (2)	1383 (1)	−2091 (3)	3·2
C(4)	7242 (2)	2272 (1)	−1396 (3)	3·0
C(5)	6703 (2)	2410 (1)	282 (3)	3·2
C(6)	7109 (2)	1787 (2)	1742 (3)	3·7
C(7)	7066 (3)	309 (2)	2500 (4)	5·0
C(8)	8663 (2)	572 (2)	−58 (4)	5·1
C(9)	5768 (2)	1233 (2)	−3052 (3)	4·1
C(10)	6828 (2)	2896 (1)	−2899 (3)	3·3
C(11)	5742 (2)	3256 (2)	−3118 (4)	4·3
C(12)	5395 (3)	3803 (2)	−4525 (4)	5·5
C(13)	6105 (3)	3997 (2)	−5712 (4)	5·6
C(14)	7193 (3)	3655 (2)	−5505 (4)	5·3
C(15)	7543 (2)	3101 (2)	−4115 (4)	4·1
H(O)	863 (3)	271 (2)	−36 (4)	6·9 (8)
H(N)	609 (2)	93 (1)	78 (3)	3·4 (5)

increasing the N–C bond lengths by an average of 0·026 (3) Å. The largest differences, of magnitudes 4·2 (3)–5·7 (3)°, among corresponding valence angles occur in C(6)–N–C(7) and the three angles at C(2).

Hydrogen bonding is present in all three structures. In both the α- and β-bases, intermolecular O–H···N′ bonds link the molecules into chains along the **a** and **b** directions, respectively. In the γ-HCl, there are no direct links between the molecules, but each Cl accepts two hydrogen bonds to bridge the molecules into chains along **a**. The first is N–H···Cl and the second is O′–H′···Cl with an H···Cl···H′ angle of 105 (1)°. The pertinent information regarding these hydrogen bonds is given in Table 2.

Table 2. *Bond lengths* (Å) *and valence angles* (°)

	α-Base	β-Base	γ-HCl
O–C(4)	1·415 (2)	1·430 (2)	1·434 (3)
N–C(2)	1·478 (3)	1·483 (3)	1·508 (3)
N–C(6)	1·468 (2)	1·465 (3)	1·498 (4)
N–C(7)	1·469 (2)	1·470 (4)	1·488 (4)
C(2)–C(3)	1·548 (3)	1·539 (3)	1·540 (3)
C(2)–C(8)	1·531 (3)	1·524 (3)	1·533 (4)
C(3)–C(4)	1·537 (3)	1·535 (3)	1·547 (2)
C(3)–C(9)	1·526 (3)	1·527 (3)	1·533 (3)
C(4)–C(5)	1·528 (3)	1·526 (3)	1·520 (3)
C(4)–C(10)	1·550 (2)	1·523 (3)	1·531 (3)
C(5)–C(6)	1·515 (3)	1·488 (3)	1·506 (3)
C(10)–C(11)	1·395 (3)	1·381 (3)	1·388 (3)
C(10)–C(15)	1·389 (3)	1·382 (3)	1·384 (4)
C(11)–C(12)	1·382 (3)	1·377 (3)	1·385 (4)
C(12)–C(13)	1·382 (4)	1·365 (4)	1·359 (5)
C(13)–C(14)	1·365 (4)	1·369 (3)	1·379 (5)
C(14)–C(15)	1·394 (4)	1·378 (3)	1·384 (4)
C(2)–N–C(6)	112·7 (1)	111·1 (2)	113·3 (2)
C(2)–N–C(7)	112·5 (1)	111·0 (2)	113·4 (2)
C(6)–N–C(7)	109·1 (1)	107·5 (2)	112·1 (2)
N–C(2)–C(3)	108·6 (2)	112·8 (2)	109·9 (2)
N–C(2)–C(8)	115·1 (2)	109·6 (2)	111·0 (2)
C(3)–C(2)–C(8)	115·1 (2)	110·1 (2)	115·8 (2)
C(2)–C(3)–C(4)	113·3 (2)	113·4 (2)	113·2 (2)
C(2)–C(3)–C(9)	112·1 (2)	111·1 (2)	109·9 (2)
C(4)–C(3)–C(9)	112·1 (2)	110·2 (2)	113·7 (2)
O–C(4)–C(3)	108·1 (1)	106·0 (1)	104·2 (2)
O–C(4)–C(5)	111·4 (1)	109·6 (1)	109·3 (2)
O–C(4)–C(10)	109·5 (1)	111·0 (1)	109·2 (2)
C(3)–C(4)–C(5)	109·2 (2)	109·3 (2)	110·1 (2)
C(3)–C(4)–C(10)	109·8 (2)	111·0 (2)	111·2 (2)
C(5)–C(4)–C(10)	108·7 (2)	109·8 (2)	112·6 (2)
C(4)–C(5)–C(6)	110·9 (2)	111·9 (2)	112·0 (2)
N–C(6)–C(5)	110·8 (2)	111·2 (2)	110·3 (2)
C(4)–C(10)–C(11)	121·2 (2)	122·5 (2)	122·3 (2)
C(4)–C(10)–C(15)	121·4 (2)	121·2 (2)	119·5 (2)
C(11)–C(10)–C(15)	117·5 (2)	116·3 (2)	118·2 (2)
C(10)–C(11)–C(12)	121·1 (2)	121·7 (2)	120·2 (3)
C(11)–C(12)–C(13)	120·5 (3)	121·0 (2)	120·9 (3)
C(12)–C(13)–C(14)	119·4 (2)	118·6 (2)	119·8 (3)
C(13)–C(14)–C(15)	120·5 (2)	120·3 (2)	119·7 (3)
C(10)–C(15)–C(14)	121·1 (2)	122·2 (2)	121·1 (3)
Intermolecular hydrogen bonds (for α-base and β-base: D = O and A = N; for γ-HCl: $D \equiv$ O, N respectively, and $A \equiv$ Cl)			
D–H	0·75 (3)	0·84 (2)	0·76 (3), 0·86 (2)
H···*A*	2·25 (3)	2·16 (3)	2·33 (3), 2·25 (2)
D···*A*	2·962 (2)	2·949 (2)	3·084 (2), 3·056 (3)
D–H···*A*	159 (3)	155 (2)	175 (3), 157 (2)

Structure–potency relationships

The potency, configuration and solid-state conformation for the isomeric forms of compounds (I), (II) and (III) are summarized in Table 3, where the isomers of each compound are listed in ascending order of potency. It is clear from this table that the potency–configuration (*cis*/*trans*) relationships among the three isomers of (III) are consistent with those of (II) and are not altered by having a methyl substituent on C(3) instead of C(5). Furthermore, the most active isomer of each of the three compounds has a *cis* 3-methyl (or 5-methyl) relative to the 4-phenyl. In this configuration, the preferred orientation for the phenyl ring is ~30–45° from plane *X* through C(7), N, C(4), C(10) and O, as can be seen from the dihedral angles included in Table 3. This large twist round C(4)–C(10) seems to occur whether the phenyl ring is equatorial as in (I)-β and (III)-γ, or axial as in (II)-β. It is possible that this special orientation is more suited to the topography of the opiate receptor (Portoghese, 1978), and that the activity may depend on the ease or difficulty with which the phenyl ring is able to adopt this orientation in solution.

For the less active isomers, *i.e.* those with a 3-methyl (or 5-methyl) *trans* to the 4-phenyl, the activity is inhibited most for the isomers [of compounds (II) and (III)] which also have a 2-methyl *cis* to the 4-phenyl. However, in spite of the similarity in configurations and solid-state conformations of the γ-2,5-dimethyl and the β-2,3-dimethyl [the two least active isomers of compounds (II) and (III)], the corresponding ED_{50} values of 1·6 and 30·7 mg kg^{-1}, respectively, are widely different.

Table 3. *Structure–potency relations for* (I) *prodine,* (II) *promedol alcohol and* (III) *present compound, listed in ascending order of the potency rankings of their propionate esters* (Me = CH_3, Ph = C_6H_5, *e* = *equatorial*, *a* = *axial*)

	(I) (3-methyl)		(II) (2,5-dimethyl)			(III) (2,3-dimethyl)		
	α <	β	γ <	α <	β	β <	α <	γ
ED_{50} (mg kg^{-1})*	0·92	0·18	1·6	0·58	0·18	30·7	1·6	0·28
Configuration								
2-Me/4-Ph			*cis*	*trans*	*trans*	*cis*	*trans*	*trans*
3-Me†/4-Ph	*trans*	*cis*	*trans*	*trans*	*cis*	*trans*	*trans*	*cis*
Solid-state conformation								
2-Me			*e*	*a*	*e*	*e*	*a*	*a*
3-Me†	*e*	*a*	*e*	*e*	*e*	*e*	*e*	*a*
4-Ph	*e*	*e*	*e*	*e*	*a*	*e*	*e*	*e*
4-O	*a*	*a*	*a*	*a*	*e*	*a*	*a*	*a*
Dihedral angles (°)					$P2_1/n$ $R\bar{3}$			
Ph–piperidine	66·1	45·1	73·7	86·6	77·0 80·4	88·2 (2)	85·9 (2)	60·7 (3)
Ph–plane *X*‡	27·4	45·2	16·2	1·8	40·9 37·6	4·5 (2)	6·4 (2)	30·5 (3)
Intramolecular N···O (Å)	3·49	3·43	3·50	3·58	4·20 4·16	3·556 (2)	3·536 (2)	3·452 (2)
Reference§	(1)	(2)	(3)	(4)	(5) (6)	(7)	(7)	(7)

* For the esters in mouse hot-plate s.c.

† For (II), substitute 5-Me for 3-Me.

‡ Plane *X* contains C(7), N, C(4), C(10) and O.

§ (1) Kartha, Ahmed & Barnes (1960). (2) Ahmed & Barnes (1963). (3) De Camp & Ahmed (1972*a*). (4) Ahmed & De Camp (1972). (5) De Camp & Ahmed (1972*b*). (6) De Camp & Ahmed (1972*c*). (7) Present contribution.

Although the specific relevance of these structural differences is not understood fully at present, it seems logical to expect the substituents on C(2), C(3) and C(5) to influence the minimum-energy (preferred) orientations of the 4-phenyl and 4-OCOEt relative to the piperidine ring. As well as spatial requirements for the C(4) substituents, the vital factor for analgesic activity remains the accessibility of the lone pair on the N atom for interaction with the receptor as suggested by Belleau, Conway, Ahmed & Hardy (19˜4) and supported by comparison of the crystal structures of two isomers of the rigid 16,17-butanomorphinan-3-ol (Ahmed, 1981). The stereoelectronic nature of this interaction was discussed by Dimaio, Ahmed, Schiller & Belleau (1979).

The solid-state conformations of the isomers for (I), (II) and (III) are characterized by a piperidine ring in the chair form and an equatorial phenyl, except for the two crystalline forms of β-promedol alcohol, whose ester is the most active isomer of (II). There, the phenyl ring adopts an axial position while the piperidine ring remains in the chair form. The main features of an axial phenyl configuration are (1) the OH and the lone pair of the N atom are *cis*, (2) the phenyl ring has very little freedom of re-orientation through a twist about C(4)–C(10) (obvious from Fisher–Hirschfelder–Taylor atom model), and (3) the N···O separation is increased from 3·42–3·58 Å to 4·16–4·20 Å when the phenyl is equatorial. Further systematic comparisons with other analgesics are needed to ascertain which of the two conformations is the one actually adopted during interaction with the receptor.

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Book Reviews

Works intended for notice in this column should be sent direct to the Book-Review Editor (J. H. Robertson, School of Chemistry, University of Leeds, Leeds LS2 9JT, England). As far as practicable books will be reviewed in a country different from that of publication.

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Books Received

The following books have been received by the Editor. Brief and generally uncritical notices are given of works of marginal crystallographic interest; occasionally a book of fundamental interest is included under this heading because of difficulty in finding a suitable reviewer without great delay.

Vectors and tensors in crystallography. By DONALD E. SANDS. Pp. xvi+228. Reading, MA: Addison-Wesley Advanced Book Program/World Science Division, 1982. Price US $26.50. A review of this book, by J. Kopf, has been published in the May issue of *Acta Crystallographica*, Section A, p. 312.

The structure of non-crystalline materials, 1982. Edited by P. H. GASKELL, J. M. PARKER & E. A. DAVIS. Pp. xiii+609. London: Taylor & Francis, 1983. Price £28.00, US $62.00. A review of this book, by J. H. Robertson, has been published in the July issue of *Acta Crystallographica*, Section A, p. 488.

Fourier optics: an introduction. By E. G. STEWARD. Pp. 185. Chichester: Ellis Horwood Ltd (John Wiley & Sons), 1983. Price £15.00 (hard cover), £7.95, US $13.75 (paper). A review of this book, by A. D. Booth, has been published in the July issue of *Acta Crystallographica*, Section A, p. 487.