Acta Cryst. (1981). B37, 188–192

Structural Differences between 16α,17-Butanomorphinan-3-ol and 16β,17-Butanomorphinan-3-ol*

BY F. R. AHMED

Division of Biological Sciences, National Research Council of Canada, Ottawa, Canada K1A 0R6

(*Received* 14 *July* 1980; *accepted* 26 *August* 1980)

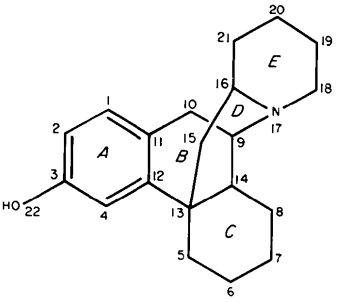
Abstract

The agonistic activity of butanomorphinanol is shown to be correlated to the relative spatial orientation of the N lone pair. 16α,17-Butanomorphinan-3-ol (I), which is inactive as agonist, has the N lone pair facing the same side of the molecule as the phenol. On the other hand, 16β,17-butanomorphinan-3-ol (II), which is active as agonist, has the N lone pair facing the opposite side and thus is not hindered by the phenol. Crystals of (I), $C_{20}H_{27}NO$, $M_r = 297{\cdot}44$, are monoclinic, $P2_1/a$, with $a = 23{\cdot}159\ (2)$, $b = 7{\cdot}440\ (2)$, $c = 10{\cdot}025\ (1)$ Å, $\beta = 111{\cdot}00\ (3)°$, $V = 1612{\cdot}6$ Å^3, $Z = 4$, $D_o = 1{\cdot}223$, $D_c = 1{\cdot}218$ Mg m^{-3}, $R = 0{\cdot}040$, $R_w = 0{\cdot}037$ for 2140 observed reflexions. The derivative $C_{20}H_{28}BrNO.0{\cdot}2(C_2H_5OH)$ of (II), $M_r = 387{\cdot}57$, is triclinic, $P\bar{1}$, with $a = 11{\cdot}822\ (3)$, $b = 14{\cdot}627\ (2)$, $c = 11{\cdot}404\ (2)$ Å, $\alpha = 88{\cdot}27\ (5)$, $\beta = 100{\cdot}86\ (5)$, $\gamma = 104{\cdot}65\ (5)°$, $V = 1873{\cdot}4$ Å^3, $Z = 4$, $D_o = 1{\cdot}365$, $D_c = 1{\cdot}373$ (1·341 if solvent is excluded) Mg m^{-3}, $R = 0{\cdot}054$, $R_w = 0{\cdot}063$ for 4717 observed reflexions.

Introduction

The rigidity of the morphinan molecules makes them a good basis for studies of structure–function relationships. The structure of *N*-methyl-D-normorphinan hydrobromide (Hardy & Ahmed, 1975) provided the first concrete evidence that the relative spatial orientations of the N lone pair in morphinans is of critical importance for their productive interaction with the opiate receptor (Belleau, Conway, Ahmed & Hardy, 1974). The present two structures of butanomorphinanol provide additional evidence confirming that conclusion (Dimaio, Ahmed, Schiller & Belleau, 1979). The results of these structures were presented as a poster at ECM-5 (Ahmed, 1979).

16α,17-Butanomorphinan-3-ol (I) is inactive as agonist and antagonist (like D-normorphinan, it produces ataxia), while 16β,17-butanomorphinan-3-ol (II) displays analgesic activity comparable to phentazocine ($ED_{50} = 3 \pm 0{\cdot}5$ mg kg^{-1}; mice) and is inactive as antagonist (oxomorphone Strobe tail assay). The X-ray analyses have been carried out on crystals of (I), and of a hydrobromide of (II). The latter crystals contain two molecules per asymmetric unit and a disordered solvent molecule near the centre of symmetry. The molecular formula and atom numbering of butanomorphinanol are shown below.



Experimental

Experimental details are presented in Table 1. X-ray measurements were carried out on a Picker diffractometer with Ni-filtered Cu $K\alpha$ radiation and a scintillation counter. The cell parameters were derived from the

Table 1. *Experimental details*

	I	II
μ (Cu $K\alpha$) (mm^{-1})	0·576	3·034
Crystal dimensions (mm)	0·13 × 0·20 × 0·33	0·07 × 0·13 × 0·20
Reflexions measured	2708	6399
Reflexions observed	2140	4717
R (for observed data)	0·040	0·054
R_w	0·037	0·063
Mean (Δ/σ)	0·08	0·10
Maximum (Δ/σ)	0·60	0·74
p_1*	30	25
p_2*	30	30

* Parameters in the weighting function
$w = \{1 + [(|F_o| - p_2)/p_1]^2\}^{-1}$.

* Issued as NRCC No. 18839.

0567-7408/81/010188-05$01.00

Table 2. *Fractional coordinates* ($\times 10^4$, *for* H $\times 10^3$) *and isotropic thermal parameters* (Å^2)

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

	x	y	z	B_{eq}/B
Compound (I)				
C(1)	2837 (1)	3232 (3)	8889 (2)	2·8
C(2)	3221 (1)	1802 (3)	9502 (2)	3·1
C(3)	3028 (1)	60 (3)	9077 (2)	3·0
C(4)	2460 (1)	−211 (3)	8008 (2)	2·8
C(5)	1396 (1)	−740 (3)	5287 (2)	3·1
C(6)	1734 (1)	−372 (3)	4262 (2)	4·0
C(7)	1475 (1)	1280 (3)	3365 (2)	3·9
C(8)	1505 (1)	2894 (3)	4325 (2)	3·2
C(9)	1189 (1)	4099 (2)	6349 (2)	2·4
C(10)	1861 (1)	4586 (2)	7198 (2)	2·6
C(11)	2258 (1)	2971 (2)	7826 (2)	2·4
C(12)	2069 (1)	1218 (2)	7367 (2)	2·3
C(13)	1417 (1)	845 (2)	6286 (2)	2·4
C(14)	1168 (1)	2516 (3)	5363 (2)	2·4
C(15)	985 (1)	455 (3)	7139 (2)	3·1
C(16)	532 (1)	1956 (3)	7090 (2)	2·7
N(17)	853 (1)	3709 (2)	7352 (1)	2·5
C(18)	412 (1)	5167 (3)	7273 (2)	3·3
C(19)	89 (1)	4926 (3)	8337 (2)	4·3
C(20)	−239 (1)	3130 (4)	8121 (2)	5·0
C(21)	220 (1)	1646 (3)	8173 (2)	4·0
O(22)	3378 (1)	−1424 (2)	9655 (1)	4·1
H(1)	295 (1)	450 (2)	922 (2)	2·6 (0·4)
H(2)	363 (1)	204 (3)	1024 (2)	3·3 (0·4)
H(4)	234 (1)	−147 (3)	773 (2)	3·5 (0·4)
H(5,1)	93 (1)	−96 (3)	472 (2)	3·0 (0·4)
H(5,2)	154 (1)	−187 (3)	585 (2)	3·6 (0·4)
H(6,1)	220 (1)	−21 (3)	482 (2)	3·4 (0·4)
H(6,2)	171 (1)	−139 (3)	364 (2)	3·8 (0·5)
H(7,1)	103 (1)	110 (3)	273 (2)	3·5 (0·4)
H(7,2)	171 (1)	158 (3)	271 (2)	4·7 (0·5)
H(8,1)	195 (1)	316 (3)	489 (2)	3·5 (0·4)
H(8,2)	133 (1)	400 (3)	374 (2)	3·4 (0·4)
H(9)	99 (1)	511 (2)	573 (2)	1·9 (0·4)
H(10,1)	203 (1)	527 (2)	658 (2)	2·8 (0·4)
H(10,2)	188 (1)	550 (2)	797 (2)	2·5 (0·4)
H(14)	73 (1)	228 (2)	479 (2)	1·8 (0·3)
H(15,1)	124 (1)	20 (3)	817 (2)	3·5 (0·4)
H(15,2)	74 (1)	−65 (3)	678 (2)	3·8 (0·5)
H(16)	20 (1)	198 (2)	609 (2)	2·2 (0·4)
H(18,1)	9 (1)	523 (3)	627 (2)	3·9 (0·5)
H(18,2)	66 (1)	633 (3)	743 (2)	4·1 (0·5)
H(19,1)	40 (1)	495 (3)	930 (2)	3·4 (0·4)
H(19,2)	−20 (1)	597 (3)	824 (2)	5·4 (0·6)
H(20,1)	−59 (1)	307 (3)	715 (2)	4·9 (0·5)
H(20,2)	−43 (1)	286 (3)	885 (2)	5·2 (0·6)
H(21,1)	55 (1)	156 (3)	916 (2)	3·8 (0·5)
H(21,2)	2 (1)	42 (3)	797 (2)	4·9 (0·5)
H(22)	360 (1)	−132 (3)	1054 (3)	6·5 (0·7)
Compound (II), molecule *A*				
Br	2933 (1)	9203·9 (4)	6615 (1)	4·9
C(1)	3264 (5)	2169 (4)	1013 (5)	3·2
C(2)	2469 (5)	2570 (4)	276 (5)	3·5
C(3)	1480 (5)	2677 (4)	691 (5)	3·1
C(4)	1335 (5)	2397 (4)	1838 (4)	3·0
C(5)	1333 (6)	2288 (4)	4435 (5)	3·9
C(6)	2122 (7)	3273 (5)	4716 (5)	5·1
C(7)	3276 (7)	3238 (5)	5547 (6)	5·4
C(8)	3914 (6)	2623 (4)	4988 (5)	4·0
C(9)	3720 (5)	1034 (4)	4064 (5)	3·0
C(10)	4051 (5)	1456 (4)	2910 (5)	3·3
C(11)	3124 (4)	1880 (3)	2176 (4)	2·6
C(12)	2135 (4)	2001 (3)	2590 (4)	2·5
C(13)	1921 (5)	1653 (4)	3833 (4)	2·9
C(14)	3094 (5)	1632 (4)	4648 (4)	3·0
C(15)	1146 (5)	637 (4)	3722 (5)	3·4
C(16)	1699 (5)	−63 (4)	3214 (5)	3·3
N(17)	2939 (4)	28 (3)	3887 (4)	3·2
C(18)	3523 (6)	−624 (4)	3362 (5)	4·1
C(19)	2829 (7)	−1644 (4)	3394 (6)	5·3
C(20)	1582 (7)	−1756 (4)	2747 (7)	5·5
C(21)	989 (6)	−1084 (4)	3244 (6)	4·8
O(22)	639 (4)	3059 (3)	34 (3)	4·7
H(1)	393 (4)	215 (3)	78 (4)	1·5 (0·9)
H(2)	255 (6)	271 (5)	−47 (6)	5·8 (1·7)
H(4)	73 (4)	241 (3)	206 (4)	1·6 (0·9)
H(5,1)	113 (4)	195 (3)	515 (4)	2·9 (1·1)
H(5,2)	53 (5)	224 (4)	398 (5)	3·3 (1·2)
H(6,1)	218 (5)	355 (4)	396 (5)	4·4 (1·3)
H(6,2)	175 (5)	357 (4)	513 (5)	4·8 (1·4)
H(7,1)	308 (5)	296 (4)	632 (5)	4·0 (1·3)
H(7,2)	376 (6)	386 (5)	571 (6)	7·2 (1·8)
H(8,1)	419 (5)	291 (4)	431 (5)	4·4 (1·5)
H(8,2)	461 (5)	256 (4)	556 (5)	3·9 (1·2)
H(9)	438 (5)	98 (4)	451 (5)	3·4 (1·2)
H(10,1)	420 (5)	99 (4)	244 (5)	4·6 (1·4)
H(10,2)	469 (4)	188 (4)	312 (5)	3·4 (1·1)
H(14)	293 (4)	138 (3)	530 (4)	2·5 (1·0)
H(15,1)	87 (4)	34 (3)	442 (4)	1·7 (0·9)
H(15,2)	31 (5)	55 (4)	318 (5)	4·1 (1·3)
H(16)	181 (4)	17 (3)	244 (4)	1·3 (0·8)
H(17)	287 (5)	−15 (4)	465 (5)	5·2 (1·5)
H(18,1)	354 (5)	−40 (4)	250 (5)	4·2 (1·4)
H(18,2)	434 (5)	−42 (4)	376 (5)	4·9 (1·4)
H(19,1)	286 (8)	−177 (6)	436 (8)	9·4 (2·4)
H(19,2)	319 (8)	−200 (7)	302 (8)	9·3 (2·6)
H(20,1)	153 (6)	−160 (5)	189 (6)	6·2 (1·7)
H(20,2)	118 (7)	−238 (5)	284 (7)	7·2 (2·0)
H(21,1)	89 (4)	−118 (3)	402 (4)	2·8 (1·1)
H(21,2)	21 (5)	−109 (4)	276 (5)	4·7 (1·4)
H(22)	74 (6)	314 (5)	−64 (6)	5·6 (1·6)
C(23)	−21	−2	7	10·0
C(24)	78	−20	−37	10·0
C(25)	182	12	14	10·0
Compound (II), molecule *B*				
Br	1113 (1)	3805·4 (4)	7476 (1)	4·5
C(1)	3760 (5)	8679 (3)	292 (5)	3·2
C(2)	4878 (5)	9038 (4)	1003 (5)	3·6
C(3)	5493 (5)	8389 (4)	1540 (4)	3·3
C(4)	5035 (5)	7429 (4)	1335 (4)	2·7
C(5)	3825 (5)	5393 (4)	1350 (5)	3·2
C(6)	3315 (6)	5498 (4)	2461 (5)	3·9
C(7)	1969 (5)	5246 (4)	2184 (5)	3·7
C(8)	1533 (5)	5844 (4)	1164 (5)	3·3
C(9)	1617 (5)	6340 (4)	−971 (4)	2·8
C(10)	2053 (5)	7400 (4)	−689 (5)	3·1
C(11)	3270 (4)	7713 (3)	91 (4)	2·5
C(12)	3912 (4)	7079 (3)	609 (4)	2·5
C(13)	3416 (4)	6019 (3)	328 (4)	2·4
C(14)	2046 (5)	5759 (3)	66 (4)	2·6
C(15)	3841 (5)	5809 (4)	−810 (4)	2·8
C(16)	3341 (5)	6273 (3)	−1937 (4)	2·7
N(17)	2000 (4)	6060 (3)	−2074 (3)	2·7

Table 2 (*cont.*)

	x	*y*	*z*	B_{eq}/B
C(18)	1423 (5)	6449 (4)	−3197 (5)	3·8
C(19)	1748 (6)	6088 (4)	−4288 (5)	4·2
C(20)	3083 (6)	6316 (5)	−4192 (5)	4·5
C(21)	3655 (5)	5934 (4)	−3049 (5)	3·5
O(22)	6596 (4)	8676 (3)	2243 (4)	4·7
H(1)	335 (5)	912 (4)	−5 (5)	4·9 (1·5)
H(4)	555 (4)	707 (3)	180 (4)	2·8 (1·0)
H(5,1)	354 (4)	475 (3)	101 (4)	2·2 (1·0)
H(5,2)	464 (5)	553 (4)	147 (5)	3·3 (1·2)
H(6,1)	371 (5)	621 (4)	283 (5)	3·7 (1·3)
H(6,2)	357 (4)	518 (4)	288 (4)	2·8 (1·1)
H(7,1)	169 (4)	459 (3)	196 (4)	2·3 (1·0)
H(7,2)	157 (5)	527 (4)	297 (5)	4·0 (1·3)
H(8,1)	171 (4)	637 (3)	138 (4)	1·4 (0·9)
H(8,2)	67 (4)	569 (4)	96 (4)	3·3 (1·1)
H(9)	81 (4)	614 (3)	−113 (4)	2·8 (1·1)
H(10,1)	154 (4)	754 (3)	−30 (4)	2·1 (1·0)
H(10,2)	209 (5)	778 (4)	−136 (5)	4·7 (1·4)
H(14)	182 (4)	514 (3)	−16 (4)	2·6 (1·0)
H(15,1)	359 (4)	518 (3)	−94 (4)	2·6 (1·0)
H(15,2)	472 (4)	599 (3)	−76 (4)	1·8 (1·0)
H(16)	360 (4)	686 (3)	−187 (4)	2·3 (1·0)
H(17)	181 (4)	543 (3)	−211 (4)	2·5 (1·0)
H(18,1)	172 (5)	705 (4)	−316 (5)	4·4 (1·3)
H(18,2)	58 (5)	629 (4)	−321 (5)	4·2 (1·3)
H(19,1)	145 (4)	537 (3)	−437 (4)	2·8 (1·1)
H(19,2)	134 (4)	633 (4)	−499 (4)	3·3 (1·1)
H(20,1)	344 (4)	702 (3)	−421 (4)	3·1 (1·1)
H(20,2)	325 (4)	606 (3)	−487 (4)	2·4 (1·0)
H(21,1)	338 (4)	524 (3)	−309 (4)	3·1 (1·1)
H(21,2)	448 (4)	606 (3)	−295 (4)	2·3 (1·0)
H(22)	670 (6)	922 (5)	246 (6)	5·5 (1·7)

angular settings of high-order axial reflexions [2θ = 70–130° for (I), and 48–90° for (II)] of $K\alpha_1$ and $K\alpha_2$ at 2θ and -2θ. Crystal densities were measured by flotation in a CCl_4 and C_6H_5Cl mixture. All non-equivalent lattice points with $2\theta < 130°$ were scanned by the θ–2θ procedure at a 2θ scan speed of 2° min^{-1} with the backgrounds measured for 20 s at each end of the scan. Two standard reflexions measured at short intervals during each data collection showed only small random fluctuations. The net intensities were corrected for Lorentz and polarization effects, and those of (II) were also corrected for absorption [$\exp(\mu R)$ = 1·19–1·57].

The structure of (I) was derived from an *E* map with 483 reflexions ($|E| \geq 1{\cdot}30$) whose phases had been estimated by the symbolic addition procedure (Karle & Karle, 1963). That of (II) was determined by the heavy-atom method. The H atoms were located from difference maps after partial refinement of the heavier atoms. In addition to the expected H peaks, the difference map of (II) contained a broad residual distribution of height 1·5 e Å^{-3} at the centre of symmetry and extending to about 2·5 Å from the centre. The residual density in that location did not change after refinement of the H parameters, and was interpreted as a disordered ethanol molecule (C_2H_5OH, M_r = 46·06). Since C and O of the solvent molecule were indistinguishable in the difference maps, a fairly good fit was obtained by trial and error assuming C(23), C(24) and C(25) (Table 2) with B = 10 Å^2 and occupancy = 0·5. The residual density in that area was reduced to within ±0·3 e Å^{-3}. No further refinement of these parameters was attempted.

The atomic parameters listed in Tables 2 and 3 were derived by block-diagonal least-squares refinement on $\sum w(|F_o| - |F_c|)^2$, with weights and refinement indicators as shown in Table 1.* The *f* curves were those of Hanson, Herman, Lea & Skillman (1964), except for H (Stewart, Davidson & Simpson, 1965). Calculations were performed with the NRC system of programs (Ahmed, Hall, Pippy & Huber, 1973).

Discussion

Molecular conformations

The two molecular structures, viewed from approximately the same direction, are presented in Figs. 1 and 2. The main difference is in the conformation of ring *D*,

* Lists of structure factors, anisotropic thermal parameters, and some mean planes for both compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35667 (30 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Bond lengths* (Å) *for* (I), (II*A*) *and* (II*B*)

E.s.d.'s are 0·003–0·004 Å for (I), and 0·007–0·008 Å for (II*A*,*B*) unless otherwise stated.

	(I)	(II*A*)	(II*B*)
C(1)–C(2)	1·382	1·373	1·397
C(1)–C(11)	1·395	1·407	1·393 (6)
C(2)–C(3)	1·387	1·386	1·397
C(3)–C(4)	1·382	1·387	1·381
C(3)–O(22)	1·369	1·355	1·367
C(4)–C(12)	1·395	1·381	1·406
C(5)–C(6)	1·523	1·511 (9)	1·529
C(5)–C(13)	1·537	1·537 (9)	1·542
C(6)–C(7)	1·514	1·519 (11)	1·513 (9)
C(7)–C(8)	1·525	1·531 (10)	1·525
C(8)–C(14)	1·534	1·540	1·512
C(9)–C(10)	1·526	1·513	1·529
C(9)–C(14)	1·527	1·518	1·520
C(9)–N(17)	1·504	1·523	1·515 (6)
C(10)–C(11)	1·507	1·501	1·510
C(11)–C(12)	1·400	1·392	1·392
C(12)–C(13)	1·536	1·536	1·533
C(13)–C(14)	1·534	1·524	1·539
C(13)–C(15)	1·559	1·531	1·542
C(15)–C(16)	1·521	1·526	1·525
C(16)–N(17)	1·477	1·496	1·515
C(16)–C(21)	1·522	1·520	1·517
N(17)–C(18)	1·472	1·506	1·501
C(18)–C(19)	1·517	1·513	1·516
C(19)–C(20)	1·514	1·490 (12)	1·512 (10)
C(20)–C(21)	1·521	1·520 (10)	1·511

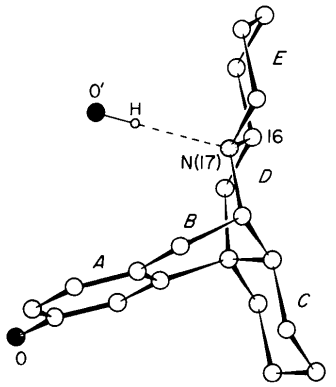


Fig. 1. Molecular conformation of the inactive 16α,17-butanomorphinan-3-ol.

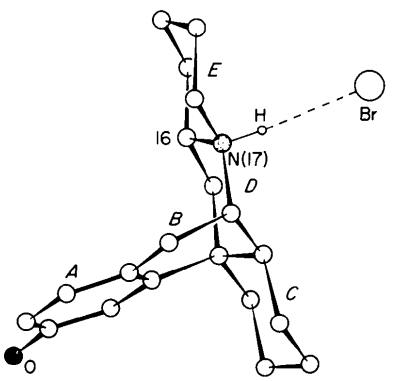


Fig. 2. Molecular conformation of the active 16β,17-butanomorphinan-3-ol.

which has a boat form in (I) and a chair form in (II), and the subsequent inversion of the direction of the N lone pair electrons as shown by the broken lines in the two figures. The agonistically inactive molecule (I) has the N lone pair facing the side of the molecule which is occupied by the phenol, while the agonistically active molecule (II) has the lone pair facing the opposite side which is unhindered by the phenol. This structural difference, and the lack of any other, points to the significant role of the N lone pair electrons in interaction of the morphinans with the opiate receptor. The stereoelectronic nature of this interaction has been discussed by Dimaio, Ahmed, Schiller & Belleau (1979).

Bond lengths and angles

Equivalent bond lengths and angles in molecules (I), (II*A*) and (II*B*) are essentially the same, Tables 3 and 4. However, as a result of the conformational change in ring *D*, some endocyclic torsion angles are considerably different in (I) and (II), Table 5. The orientation of the N lone pair in morphinan-like molecules may easily be seen from the exocyclic torsion angles C(10)–C(9)–N(17)–C(16) and C(12)–C(13)–C(15)–C(16) which have absolute values >100° if the lone pair is facing the same side as the phenol, and <70° if they are on the opposite side, as shown by the last four entries in Table 5.

Table 4. *Bond angles* (°) *for* (I), (II*A*) *and* (II*B*)

E.s.d.'s are 0·2° for (I) and 0·4–0·6° for (II*A*,*B*).

	(I)	(II*A*)	(II*B*)
C(2)–C(1)–C(11)	121·5	122·6	122·2
C(1)–C(2)–C(3)	119·8	118·5	117·6
C(2)–C(3)–C(4)	119·1	119·4	121·2
C(2)–C(3)–O(22)	123·1	123·2	121·6
C(4)–C(3)–O(22)	117·7	117·4	117·1
C(3)–C(4)–C(12)	121·8	122·5	120·5
C(6)–C(5)–C(13)	113·4	112·9	111·7
C(5)–C(6)–C(7)	110·9	110·6	111·2
C(6)–C(7)–C(8)	110·2	110·0	110·2
C(7)–C(8)–C(14)	111·4	111·2	112·1
C(10)–C(9)–C(14)	109·5	111·8	111·8
C(10)–C(9)–N(17)	110·0	112·3	112·8
C(14)–C(9)–N(17)	112·3	109·1	108·3
C(9)–C(10)–C(11)	113·0	113·8	115·3
C(1)–C(11)–C(10)	118·9	118·2	117·9
C(1)–C(11)–C(12)	118·8	118·5	119·3
C(10)–C(11)–C(12)	122·2	123·2	122·8
C(4)–C(12)–C(11)	118·9	118·5	119·2
C(4)–C(12)–C(13)	119·9	121·4	121·1
C(11)–C(12)–C(13)	120·9	120·1	119·7
C(5)–C(13)–C(12)	113·1	112·3	113·1
C(5)–C(13)–C(14)	108·2	107·9	108·0
C(5)–C(13)–C(15)	109·8	110·1	109·7
C(12)–C(13)–C(14)	110·0	110·4	110·6
C(12)–C(13)–C(15)	108·0	109·2	107·2
C(14)–C(13)–C(15)	107·8	106·9	108·1
C(8)–C(14)–C(9)	113·1	111·0	113·3
C(8)–C(14)–C(13)	112·7	113·3	112·4
C(9)–C(14)–C(13)	108·5	109·4	109·2
C(13)–C(15)–C(16)	114·6	114·0	115·0
C(15)–C(16)–N(17)	110·2	109·8	109·2
C(15)–C(16)–C(21)	111·4	113·4	112·3
N(17)–C(16)–C(21)	110·1	109·1	109·3
C(9)–N(17)–C(16)	113·5	115·3	112·3
C(9)–N(17)–C(18)	109·7	112·4	112·6
C(16)–N(17)–C(18)	110·2	110·7	112·9
N(17)–C(18)–C(19)	112·5	111·3	111·0
C(18)–C(19)–C(20)	110·6	109·9	111·0
C(19)–C(20)–C(21)	109·1	111·4	110·5
C(16)–C(21)–C(20)	111·7	111·5	113·5

Dihedral angles

Some angles between the mean planes of the five rings are presented in Table 6. The largest differences (>10°) between equivalent angles in molecules (I) and (II) are in the angles *B*–*E* and *C*–*D*.

Intermolecular H *bonds*

Intermolecular hydrogen bonds play an important role in both crystal structures. In (I), intermolecular

Table 5. *Some torsion angles* (°); $\sigma \leq 0{\cdot}4°$ *for* (I), *and* $<1{\cdot}0°$ *for* (II*A*,*B*)

	(I)	(II*A*)	(II*B*)*
C(9)–C(10)–C(11)–C(12)	15·6	9·0	−5·5
C(10)–C(11)–C(12)–C(13)	−5·6	−2·8	3·9
C(11)–C(12)–C(13)–C(14)	25·8	26·2	−30·1
C(12)–C(13)–C(14)–C(9)	−55·9	−55·3	57·8
C(13)–C(14)–C(9)–C(10)	67·8	63·4	−60·6
C(14)–C(9)–C(10)–C(11)	−46·1	−38·9	34·1
C(5)–C(6)–C(7)–C(8)	56·1	57·0	−55·8
C(6)–C(7)–C(8)–C(14)	−56·0	−54·6	55·1
C(7)–C(8)–C(14)–C(13)	56·4	55·0	−56·3
C(8)–C(14)–C(13)–C(5)	−53·9	−53·9	55·5
C(14)–C(13)–C(5)–C(6)	54·7	56·4	−56·4
C(13)–C(5)–C(6)–C(7)	−57·2	−59·5	58·3
C(13)–C(14)–C(9)–N(17)	−54·7	−61·3	64·3
C(14)–C(9)–N(17)–C(16)	−4·9	54·5	−62·3
C(9)–N(17)–C(16)–C(15)	55·2	−48·2	54·2
N(17)–C(16)–C(15)–C(13)	−46·1	51·0	−50·8
C(16)–C(15)–C(13)–C(14)	−11·7	−59·0	53·8
C(15)–C(13)–C(14)–C(9)	61·5	63·3	−59·3
C(16)–C(21)–C(20)–C(19)	−55·7	56·1	−55·2
C(21)–C(20)–C(19)–C(18)	54·0	−55·2	55·1
C(20)–C(19)–C(18)–N(17)	−56·7	57·1	−56·0
C(19)–C(18)–N(17)–C(16)	58·3	−59·3	56·2
C(18)–N(17)–C(16)–C(21)	−58·0	57·9	−53·9
N(17)–C(16)–C(21)–C(20)	58·1	−56·4	53·6
C(10)–C(9)–N(17)–C(16)	−127·1	−70·0	62·0
C(12)–C(13)–C(15)–C(16)	107·1	60·4	−65·4
C(12)–C(13)–C(14)–C(9)	−55·9	−55·3	57·8
C(10)–C(9)–C(14)–C(13)	67·8	63·5	−60·6

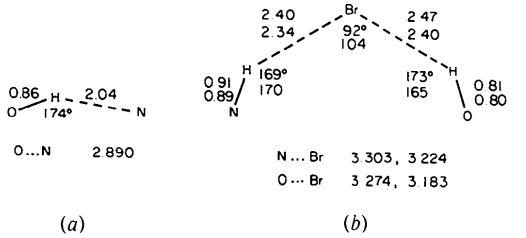
* Reverse signs for comparison with (I) and (II*A*).

Table 6. *Dihedral angles* (°)

E.s.d.'s are $<0{\cdot}6°$ for (I) and $<1{\cdot}0°$ for (II*A*,*B*).

Rings	(I)	(II*A*)	(II*B*)
A–*B*	3·6	5·0	5·8
B–*C*	75·4	76·7	73·7
B–*D*	83·7	82·8	81·8
B–*E*	71·1	89·7	89·0
C–*D*	21·2	7·4	8·4
D–*E*	12·9	7·2	8·2

N···HO bonds link the molecules into spirals parallel to **b**. In (II), each Br forms a hydrogen bond to a molecule of type *A* and another to a molecule of type *B*; these N–H···Br···H–O bonds combine to form a complex network of hydrogen bonding. There are no other direct links between the different molecules. The disordered solvent molecules fit in the cavities around the centres of symmetry but do not seem to be bonded to the other molecules. The nearest intermolecular distances to C(23), C(24) and C(25) are C(25)···H(16,*A*) = 2·63 (5) and C(25)···H(1′,*B*) = 2·64 (7) Å. The dimensions of the intermolecular hydrogen bonds are presented on the schematic drawings in Fig. 3.



(*a*) (*b*)

Fig. 3. Interatomic distances (Å) and angles (°) of the intermolecular hydrogen bonds in (*a*) structure (I), and (*b*) structure (II). E.s.d.'s in (I) are 0·002 Å for O···N, 0·03 Å for O–H and N···H, and 1° for O–H···N. Those in (II) are 0·004–0·005 Å for Br–N and Br–O, 0·04–0·07 Å for distances involving H, and 2–3° for the angles.

The author thanks Professor B. Belleau of McGill University for proposing this study and supplying the crystals, and Mrs M. Ξ. Pippy for assistance with the computations.

References

AHMED, F. R. (1979). Fifth European Crystallographic Meeting. Abstract 26-P1-1b, p. 57.

AHMED, F. R., HALL, S. R., PIPPY, M. E. & HUBER, C. P. (1973). NRC Crystallographic Programs for the IBM/360 System. Accession Nos. 133–147 in *J. Appl. Cryst.* **6**, 309–346.

BELLEAU, B., CONWAY, T., AHMED, F. R. & HARDY, A. D. (1974). *J. Med. Chem.* **17**, 907–908.

DIMAIO, J., AHMED, F. R., SCHILLER, P. & BELLEAU, B. (1979). *Recent Advances in Receptor Chemistry*, edited by F. GUALTIERI, M. GIANNELLA & C. MELCHIORRE. Amsterdam: Elsevier/North-Holland Biomedical Press.

HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040–1044.

HARDY, A. D. & AHMED, F. R. (1975). *Acta Cryst.* B**31**, 2919–2921.

KARLE, I. L. & KARLE, J. (1963). *Acta Cryst.* **16**, 969–975.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.