

Fig. 2. Projection of the structure along [100]. Dashed lines indicate intermolecular $\text{H}\cdots\text{N}$ interactions within the layer.

layers is illustrated in Fig. 2. According to the results obtained, the insolubility of (1a) and its remarkably high density have to be attributed to strong intermolecular hydrogen bonding in the crystal.

References

- B. A. FRENZ & ASSOCIATES INC. (1982). *Structure Determination Package*. 4th revised edition. College Station, Texas, and Enraf-Nonius, Delft.
- BERTINOTTI, F., GIACOMELLO, G. & LIQUORI, A. M. (1956). *Acta Cryst.* **9**, 510–514.
- GLEITER, R., SPANGET-LARSEN, J., FISCHER, H. & NEUGEBAUER, F. A. (1987). In preparation.
- HUFFMAN, J. C. (1981). *Cryst. Struct. Commun.* **10**, 227–229.
- International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- LIN, C.-H., LIEBER, E. & HOROWITZ, J. P. (1954). *J. Am. Chem. Soc.* **76**, 427–430.

Acta Cryst. (1987). C43, 1322–1325

Two Diastereomers of 1-Acetylperhydrocyclopenta[b]pyrrole-2-carbonitrile

BY E. F. PAULUS, R. HENNING AND H. URBACH

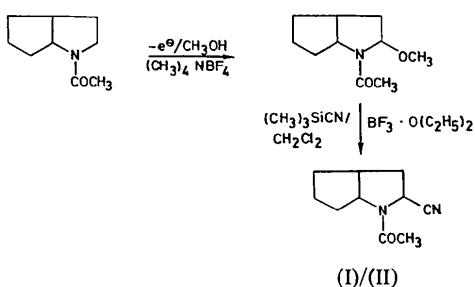
Hoechst AG, D-6230 Frankfurt am Main 80, Federal Republic of Germany

(Received 20 March 1986; accepted 28 January 1987)

Abstract. $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}$. The steric difference between the two diastereomers (*2SR,3aRS,6aRS*) (I) and (*2RS,3aRS,6aRS*) (II) is that the carbonitrile group in compound (I) is in an *exo* and in compound (II) an *endo* position. $M_r = 178.24$, both compounds are monoclinic, $P2_1/c$, $a = 12.137$ (2), $b = 10.329$ (1), $c = 7.783$ (1) Å, $\beta = 98.58$ (1)° [$a = 13.257$ (3), $b = 6.010$ (1), $c = 13.333$ (5) Å, $\beta = 115.46$ (5)°] [square brackets denote values for (II) differing from those for (I)], $U = 964.77$ [959.14] Å³, $Z = 4$, $F(000) = 384$, $D_m = 1.23$ [1.20] (flootation in CCl_4/n -heptane mixture), $D_x = 1.227$ [1.234] Mg m^{-3} , $\lambda(\text{Mo }K\alpha) = 0.7107$ Å, $\mu = 0.076$ mm⁻¹. The intensities of (I) were measured at 295 K, the intensities of (II) at 140 K and 295 K [at the latter temperature $a = 13.309$ (3), $b = 6.121$ (1), $c = 13.409$ (5) Å, $\beta = 115.13$ (5)°, $U = 988.74$ Å³, $D_x = 1.197$ Mg m^{-3}]. $wR = 0.034$ [0.055] for 1879 [2074] unique reflections [$F^2 > \sigma(F^2)$]. The respective values for compound (II) at room temperature are 0.056 and 1864 unique reflections. In both compounds the pyrrolidine ring has the envelope conformation; the five-membered rings are *cis*-fused. The tendency for the *endo* conformation of the methylene group at C6 is so large in (II) that at low

temperature the *endo* and *exo* conformations have almost equal weight, although the carbonitrile group is in the *endo* position and is causing steric hindrance.

Introduction. The anodic oxidation of racemic 2-acetyl-*cis*-2-azabicyclo[3.3.0]octane in methanol in the presence of $(\text{CH}_3)_4\text{NBF}_4$ and subsequent reaction with trimethylsilylcyanide at low temperature results in a product mixture containing (I) and (II), which can be separated by column chromatography (silica gel). X-ray analysis was needed to determine the structural and configurational differences; the conformations of the two different molecules also required investigation.



(I)/(II)

Earlier analyses (Paulus, Henning & Urbach, 1987; Paulus, Geiger, Henning, Teetz & Urbach, 1987) showed that the cyclopentane ring in the cyclopentapyrrole system can have an envelope or twist conformation depending on the substituents on the ring system. In the present case the relations should not be as complex as for the earlier compounds because here we do not have such bulky substituents.

Experimental. Suitable crystals for both compounds were obtained by recrystallization from diisopropyl ether. A crystal of dimensions $0.51 \times 0.48 \times 0.06$ [$0.85 \times 0.65 \times 0.05$] mm was sealed in a Lindemann-glass capillary, 25 reflections with $2\theta > 18^\circ$ were used for cell refinement, one standard reflection; 1879 [2074] of 2346 [2327] unique reflections had $I > \sigma(I)$ and were used for structure analysis; $h-15-15[-17-15]$, $k0-13[0-7]$, $l0-10[0-17]$; Nicolet R3 computer-controlled diffractometer, $2\theta/\theta$ scan, $2\theta_{\max} = 56^\circ$; 3° min^{-1} ; no correction for absorption or extinction. The phase problem was solved by direct methods quite easily; the signs of five structure factors were varied systematically, the set out of the 32 with the best figure of merit (Sheldrick, 1983) gave the solution. Compound (II) already showed in this state of refinement that there were two peaks for C6 from the low-temperature data and one smeared peak from the room-temperature data. The least-squares parameter refinement was performed by the cascade method (Sheldrick, 1983). A difference electron density synthesis revealed the positions of the H atoms in the case of compound (I), but not in the case of (II), where a model with idealized geometry (C—H: 0.96 Å) had to be used and temperature coefficients were fixed at 1.2 times the equivalent isotropic values for the C atoms to which they were attached; other atoms refined anisotropically; least-squares refinement on F with 1879 [2074] data, 174 [132] parameters, $w = 1/\sigma^2(F)$, $R = 0.0698$ [0.0736], $wR = 0.035$ [0.0548];* the ten largest peaks in a final difference electron density synthesis were between 0.16 [0.24] and 0.21 [0.45] e Å⁻³; max. $\Delta/\sigma < 0.1$; all calculations were performed with a Nova 3/12 computer and SHELXTL (Sheldrick, 1983); scattering factors from *International Tables for X-ray Crystallography* (1974). If not otherwise indicated the values given for (II) are those at low temperature.

Discussion. The molecular structures of the two diastereomers are shown in Figs. 1 and 2. Final

atomic coordinates and equivalent isotropic thermal parameters are given in Tables 1 and 2, and bond lengths and angles in Table 3. The values for compound (II) are low-temperature results only; the tables for room temperature are deposited (see deposition footnote).

It can be seen that the main difference between the two molecules is that the carbonitrile group is *exo* in compound (I) (Fig. 1) and *endo* in compound (II) (Fig. 2). The relative configurations are then (2SR,3aRS,6aRS) and (2RS,3aRS,6aRS) respectively. As can be seen from Table 2, the diastereomer (II) exists, at least at low temperature, in two distinct conformations, which are spread statistically over all the crystal: the methylene group C6 is positioned *endo* or *exo*, with probabilities 60 and 40% respectively. The *endo* carbonitrile group seems to prevent the favoured *endo* conformation of C6 which can be seen in the diastereomer (I) where the carbonitrile group is *exo* and no relevant steric hindrance results.

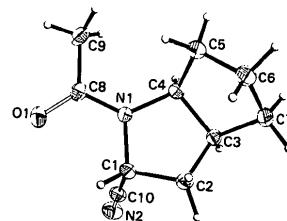


Fig. 1. Molecular structure of (I) at room temperature, showing 30% probability thermal ellipsoids for the non-hydrogen atoms and the atom-numbering scheme.

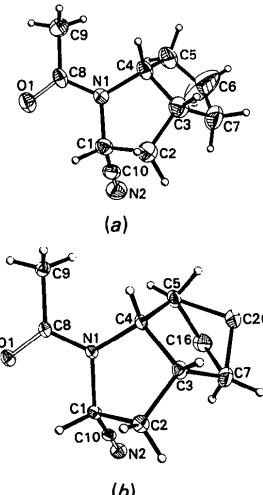


Fig. 2. (a) Molecular structure of (II) at room temperature, showing 30% probability thermal ellipsoids for the non-hydrogen atoms and the atom-numbering scheme. (b) Molecular structure of (II) at 140 K. C6 has the two distinct positions C16 and C26.

* Lists of structure factors, anisotropic temperature factors, hydrogen-atom coordinates and bond lengths and angles and tables of all the results and the structure factors of compound (II) at room temperature have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43760 (59 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The two five-membered rings are *cis*-fused in compounds (I) and (II). The same is true for two other derivatives of the same ring system investigated earlier by us (Paulus, Geiger, Henning, Teetz & Urbach, 1987; Paulus, Henning & Urbach, 1987): ethyl 2-(3-methyl-1,4-dioxoperhydrocyclopenta[4,5]pyrrolo[1,2-*alpha*]pyrazin-2-yl)-4-phenylbutyrate (III) and 2-[*N*-(1-carboxy-3-phenylpropyl)-L-alanyl]-2-azabicyclo[3.3.0]octane-3-carboxylic acid (IV) respectively. Table 4 shows the different conformations in these four compounds.

The first row of Table 4 gives the distances of N1 from the plane of its neighbouring atoms and the conformation relative to the ring system. As can be seen, N1 is always *endo* and the ligand thereon must always be *exo*. In all cases N1 is almost sp^2 hybridized as is usual in amides. The second row shows the details of the envelope conformations of the pyrrolidine ring. The distances of C2 from the plane of the other four atoms are always in the same range and the coplanarity of the latter four atoms is quite good, as can

Table 1. *Atomic coordinates and equivalent isotropic temperature factors for (I), exo, with e.s.d.'s in parentheses*

$$U_{\text{eq}} = (\text{trace } \tilde{\mathbf{U}})/3$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq} (Å ²)
O1	0.1531 (1)	0.0901 (1)	-0.1212 (1)	0.068
N1	0.2202 (1)	0.0457 (1)	0.1564 (2)	0.042
N2	0.4527 (1)	0.1736 (1)	0.0189 (2)	0.070
C1	0.3218 (1)	-0.0089 (1)	0.1079 (2)	0.043
C2	0.3753 (2)	-0.0764 (2)	0.2732 (2)	0.046
C3	0.3435 (1)	0.0084 (2)	0.4188 (2)	0.042
C4	0.2272 (1)	0.0602 (2)	0.3464 (2)	0.043
C5	0.1445 (1)	-0.0219 (2)	0.4308 (2)	0.064
C6	0.2119 (2)	-0.1242 (2)	0.5382 (2)	0.065
C7	0.3281 (2)	-0.0662 (2)	0.5827 (2)	0.056
C8	0.1428 (1)	0.0979 (2)	0.0332 (2)	0.050
C9	0.0459 (2)	0.1650 (2)	0.0929 (3)	0.064
C10	0.3946 (1)	0.0948 (2)	0.0551 (2)	0.049

Table 2. *Atomic coordinates and equivalent isotropic temperature factors for (II), endo, with e.s.d.'s in parentheses*

C16 and C26 represent the splitting of C6 into two components at low temperature

$$U_{\text{eq}} = (\text{trace } \tilde{\mathbf{U}})/3.$$

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{eq}}(\text{\AA}^2)$
O1	0.4628 (1)	0.6606 (3)	0.3609 (1)	0.037
N1	0.3328 (1)	0.3963 (3)	0.2805 (1)	0.027
N2	0.2105 (2)	0.5842 (4)	0.4452 (2)	0.043
C1	0.3374 (2)	0.3299 (4)	0.3879 (2)	0.029
C2	0.2995 (2)	0.0856 (4)	0.3704 (2)	0.037
C3	0.2233 (2)	0.0667 (4)	0.2457 (2)	0.037
C4	0.2620 (2)	0.2487 (4)	0.1888 (2)	0.030
C5	0.1537 (2)	0.3590 (5)	0.1051 (2)	0.043
C7	0.0987 (2)	0.1123 (5)	0.2126 (2)	0.057
C8	0.4023 (2)	0.5592 (4)	0.2767 (2)	0.062
C9	0.4011 (2)	0.6069 (4)	0.1657 (2)	0.055
C10	0.2650 (2)	0.4745 (4)	0.4193 (2)	0.028
C16	0.0757 (4)	0.3563 (9)	0.1565 (4)	0.036
C26	0.0561 (6)	0.1978 (14)	0.0942 (6)	0.032

be seen in the following line, which gives the largest deviation from the plane. The reason that C2 can be *endo* in (III), although the ligand on C1 is also *endo*, is surely that the carbonyl group is fixed in the diketopiperazine ring and the steric hindrance for C2 is therefore much smaller. The row $\Delta(\text{py})$ gives the Δ values (Romers, Altona, Buys & Hovinga, 1969) for the pyrrolidine ring in the four different compounds. It can be seen that these less obvious figures than in the lines before confirm the envelope conformation of the pyrrolidine ring in all four compounds.

Table 3. *Bond lengths (Å) and bonding angles (°) with the e.s.d.'s given in parentheses*

(I) <i>exo</i>	(II) <i>endo</i>	(I) <i>exo</i>	(II) <i>endo</i>		
O1—C8	1.229 (2)	1.225 (2)	O1—C8—N1	120.4 (1)	120.8 (2)
N1—C1	1.456 (2)	1.462 (3)	O1—C8—C9	122.2 (1)	122.2 (2)
N1—C4	1.476 (2)	1.475 (2)	N1—C1—C2	103.3 (1)	103.8 (2)
N1—C8	1.350 (2)	1.360 (3)	N1—C1—C10	110.8 (1)	110.9 (2)
N2—C10	1.139 (2)	1.136 (4)	N1—C4—C3	104.2 (1)	104.3 (2)
C1—C2	1.522 (2)	1.537 (3)	N1—C4—C5	115.4 (1)	113.9 (2)
C1—C10	1.486 (2)	1.482 (4)	N1—C8—C9	117.4 (1)	117.0 (2)
C2—C3	1.528 (2)	1.534 (3)	N2—C10—C1	178.0 (2)	178.8 (2)
C3—C4	1.535 (2)	1.539 (4)	C1—N1—C4	112.0 (1)	113.0 (2)
C3—C7	1.526 (2)	1.540 (4)	C1—N1—C8	119.8 (1)	119.3 (2)
C4—C5	1.535 (2)	1.539 (3)	C1—C2—C3	103.9 (1)	104.8 (2)
C5—C6	1.510 (3)		C2—C1—C10	111.6 (1)	113.2 (2)
C5—C16		1.467 (7)	C2—C3—C4	104.4 (1)	106.1 (2)
C5—C26		1.572 (9)	C2—C3—C7	114.0 (1)	115.0 (2)
C6—C7	1.524 (3)		C3—C4—C5	105.9 (1)	105.1 (2)
C7—C16		1.615 (6)	C3—C7—C6	103.5 (1)	
C7—C26		1.519 (8)	C3—C7—C16		105.1 (3)
C8—C9	1.497 (3)	1.501 (4)	C3—C7—C26		103.4 (4)
C16—C26		1.216 (10)	C4—N1—C8	126.9 (1)	127.0 (2)
			C4—C3—C7	105.2 (1)	106.0 (2)
			C4—C5—C6	106.8 (1)	
			C4—C5—C16		106.3 (3)
			C4—C5—C26		106.0 (3)
			C5—C6—C7	104.9 (2)	
			C5—C16—C7		101.3 (3)
			C5—C26—C7		100.9 (4)

Table 4. Comparison of the conformations for (I) and (II) with those for related compounds (see text for references and discussion; distances are in Å, angles

<i>in °)</i>				
	(I)	(II) (Low temperature)	(III)	(IV)
N1	0.093 <i>endo</i>	0.067 <i>endo</i>	0.066 <i>endo</i>	0.052 <i>endo</i>
C2	0.530 <i>endo</i>	0.433 <i>exo</i>	0.476 <i>endo</i>	0.374 <i>exo</i>
$\Delta(\text{py})$	<0.003	<0.017	<0.020	<0.008
	182, 29, 207, 328	168, 197, 113, 186	167, 198, 108, 188	173, 193, 118, 180
C6	0.481 <i>endo</i>	0.627 <i>exo</i> 0.576 <i>endo</i>	0.176 <i>endo</i>	0.641 <i>exo</i>
	<0.110	<0.073	<0.095	<0.080
C7	0.551 <i>exo</i>		0.297 <i>exo</i>	0.640 <i>endo</i>
	<0.024		<0.035	<0.090
$\Delta(\text{cp})$	317, 47, 24, 51	146, 73, 153, 357 (291, 75, 357, 77)	214, 1, 280, 12	286, 75, 357, 76
Angle (acetyl/pyrr.)	10.1	9.7	5.6	7.4

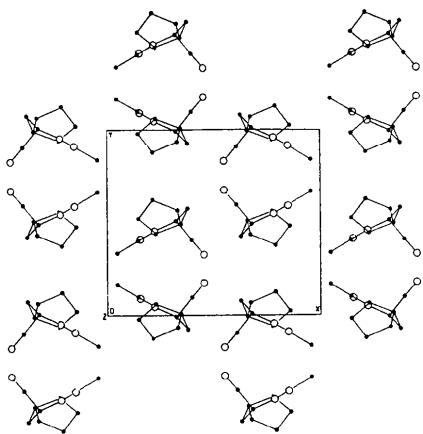


Fig. 3. Projection of the crystal structure of (I) at room temperature along the c axis.

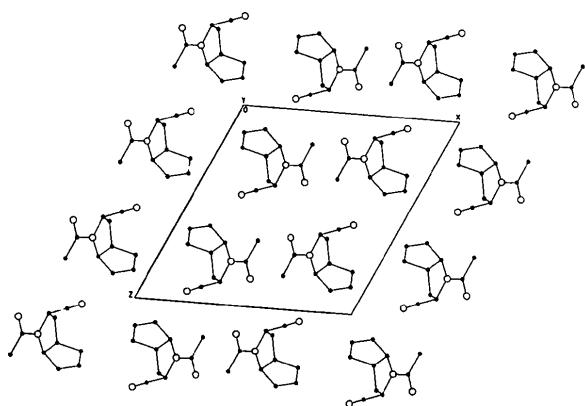


Fig. 4. Projection of the crystal structure of (II) at room temperature along the b axis.

The rows C6 and C7 of Table 4 give details of the conformation of the cyclopentane ring. The differences are much larger than in the pyrrolidine ring: (I) has an envelope conformation with C7 0.551 Å out of the plane of the other four atoms, (II) and (III) are disordered in this ring and (IV) has a twist conformation. This again indicates that the conformation of the cyclopentane ring is quite sensitive to the substituents of the ring system. In the line $\Delta(\text{cp})$ the Δ values for the four compounds are shown. These emphasize that the cyclopentane ring has an envelope conformation in (I) and a twist conformation in (IV). The formal results for the disordered compound (II) at low temperature are twist in both forms and also twist for the disordered compound (III). Because always only one atom in the ring is disordered, one can conclude that in both disordered compounds there is in reality an envelope conformation. In the last row the angles of the plane of the acetyl group with the plane of the pyrrolidine ring can be found; these are rather small.

Plots of the crystal structures of (I) and (II) are given in Figs. 3 and 4. The various symmetry elements can be recognized quite easily. The structure of compound (II) shown in Fig. 4 is that at room temperature.

References

- International Tables for X-ray Crystallography (1974). Vol. IV, pp. 99, 149. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)
- PAULUS, E. F., GEIGER, R., HENNING, R., TEETZ, V. & URBACH, H. (1987). *Acta Cryst. C*43, 938–941.
- PAULUS, E. F., HENNING, R. & URBACH, H. (1987). *Acta Cryst. C*43, 941–945.
- ROMERS, C., ALTONA, C., BUYS, H. R. & HAVINGA, E. (1969). *Top. Stereochem.* 4, 39.
- SHELDICK, G. M. (1983). *SHELXTL. An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data*. Univ. of Göttingen.

Acta Cryst. (1987). **C43**, 1325–1328

Structures of Two Active Inotropic Cardiac Agents: Milrinone [5-Cyano-2-methyl-(3,4'-bipyridin)-6(1H)-one] (I) and Amrinone [5-amino-(3,4'-bipyridin)-6(1H)-one] (II)

BY VIVIAN CODY

Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, New York 14203, USA

(Received 10 August 1986; accepted 24 March 1987)

Abstract. Milrinone (I), $C_{12}H_9N_3O$, $M_r = 211.22$, $P2_1/c$, $a = 7.067$ (1), $b = 10.089$ (1), $c = 15.477$ (2) Å, $\beta = 100.74$ (1)°, $V = 1082.2$ (3) Å³, $Z = 4$, $D_x = 1.29$ g cm⁻³, Cu $K\alpha$, $\lambda = 1.54018$ Å, $\mu = 6.67$ cm⁻¹, $F(000) = 440$, $T = 257$ K, $R = 0.060$ for 1969 unique

reflections. Amrinone (II), $C_{10}H_9N_3O$, $M_r = 187.2$, $P2_1/c$, $a = 9.257$ (5), $b = 17.064$ (6), $c = 22.845$ (6) Å, $\beta = 99.71$ (1)°, $V = 3557.2$ (4) Å³, $Z = 16$, $D_x = 1.39$ g cm⁻³, Mo $K\alpha$, $\lambda = 0.71069$ Å, $\mu = 0.89$ cm⁻¹, $F(000) = 1568$, $T = 257$ K, $R = 0.091$ for 3255 unique