the nucleotide units related by a 2_1 screw axis parallel to **b** form an infinite hydrogen-bonded chain in which the —O(5')—[PO$_3$H]$^-$ phosphate group is a hydrogen donor to O(3') of another molecule.

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Conformational Comparison of 1,2-Dimethyl-6-oxo-1,6-dihydro-3,4'-bipyridine-5-carbonitrile Free Base and its Hydrobromide Monohydrate Salt

BY VIVIAN CODY, KINGA SUWIŃSKA* AND ANDRZEJ WOJTCZAK†

Medical Foundation of Buffalo, Inc., 73 High St, Buffalo, NY 14203, USA

Abstract. C$_{13}$H$_{11}$N$_3$O (I), $M_r = 225.25$, monoclinic, $P2_1/c$, $a = 11.713$ (4), $b = 7.891$ (3), $c = 12.154$ (4) Å, $\beta = 92.27$ (4)°, $V = 1123$ (1) Å^3, $Z = 4$, $D_x = 1.333$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.082$ mm^{-1}, $F(000) = 472$, $T = 293$ K, $R = 0.063$ for 2579 reflections. 5-Cyano-1,2-dimethyl-6-oxo-1,6-dihydro-3,4'-bipyridinium bromide monohydrate, C$_{13}$H$_{12}$N$_3$O$^+$.Br$^-$.H$_2$O (II), $M_r = 324.18$, orthorhombic, *Pbca*, $a = 7.2893$ (8), $b = 18.955$ (3), $c = 19.814$ (3) Å, $V = 2738$ (1) Å^3, $Z = 8$, $D_x = 1.573$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 2.972$ mm^{-1}, $F(000) = 1312$, $T = 293$ K, $R = 0.086$ for 2292 reflections. The twist angle around the bipyridine C(1)—C(1)' bond is 66.6 (2) and 44.1 (8)° for the free base (I) and its salt (II), respectively. The larger C(3)'—N(4)'—C(5)' pyridine ring angle [121.8 (5)°] in the salt structure compared with the corresponding value for the free base [116.1 (1)°] suggests that N(4)' is a protonation site. The water molecule in the salt structure (II) is disordered with occupancy refined to 0.6 and 0.4.

Introduction. A new class of bipyridine derivatives which act as positive cardiac inotropic agents have been developed for the treatment of congestive heart failure (Endoh, Yamashita & Taira, 1982). Biological tests reveal that one of the series, milrinone (6-oxo-

* Permanent address: Institute of Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland.

† Permanent address: Institute of Chemistry, N. Copernicus University, Gagarina 7, 87-100 Toruń, Poland.

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\text{Å}^2 \times 10^2$) *with e.s.d.'s for* (I)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
C(1)	2837 (1)	1243 (2)	4284 (1)	271 (3)
C(2)	2569 (1)	293 (2)	5185 (1)	268 (3)
N(3)	3297 (1)	254 (2)	6097 (1)	277 (3)
C(4)	4320 (1)	1174 (2)	6195 (1)	272 (3)
C(5)	4591 (1)	2104 (2)	5223 (1)	268 (3)
C(6)	3881 (1)	2123 (2)	4304 (1)	284 (4)
C(1')	2066 (1)	1390 (2)	3284 (1)	288 (4)
C(2')	1015 (1)	2201 (3)	3313 (2)	368 (4)
C(3')	358 (2)	2364 (3)	2351 (2)	421 (5)
N(4')	659 (1)	1776 (2)	1374 (1)	428 (4)
C(5')	1665 (2)	992 (3)	1357 (2)	382 (5)
C(6')	2392 (1)	775 (2)	2273 (1)	328 (4)
C(21)	1513 (2)	−765 (3)	5210 (2)	368 (5)
O(4)	4918 (1)	1137 (2)	7048 (1)	380 (3)
C(51)	5649 (1)	3023 (2)	5244 (1)	314 (4)
N(52)	6485 (1)	3757 (2)	5237 (1)	430 (4)
C(31)	3042 (2)	−787 (3)	7060 (2)	410 (5)

Table 2. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\text{Å}^2 \times 10$) *with e.s.d.'s for* (II)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
Br	4927 (1)	3792 (1)	1434 (1)	32 (1)
C(1)	3715 (8)	2963 (3)	4899 (3)	18 (1)
C(2)	4241 (8)	3228 (3)	4268 (3)	19 (1)
C(4)	3961 (9)	2046 (3)	3771 (3)	26 (2)
C(5)	3476 (8)	1796 (3)	4438 (3)	22 (1)
C(6)	3395 (8)	2245 (3)	4974 (3)	22 (1)
C(21)	4776 (9)	3964 (3)	4139 (3)	29 (2)
C(31)	4849 (12)	3029 (4)	3052 (3)	41 (2)
C(51)	3070 (9)	1063 (3)	4491 (3)	28 (2)
C(1')	3470 (8)	3425 (3)	5496 (3)	19 (1)
C(2')	2558 (8)	4065 (3)	5456 (3)	23 (1)
C(3')	2377 (10)	4485 (3)	6025 (4)	32 (2)
C(5')	3908 (10)	3641 (3)	6675 (3)	31 (2)
C(6')	4105 (10)	3195 (3)	6132 (3)	26 (2)
N(3)	4363 (7)	2758 (3)	3734 (2)	22 (1)
N(52)	2720 (10)	479 (3)	4533 (3)	43 (2)
N(4')	3063 (9)	4261 (3)	6617 (3)	32 (1)
O(4)	4054 (8)	1658 (2)	3277 (2)	41 (1)
O(W1)	2919 (14)	190 (5)	2879 (5)	53 (2)
O(W2)	2360 (19)	−226 (6)	2576 (7)	44 (3)

2-methyl-1,6-dihydro-3,4'-bipyridine-5-carbonitrile), stimulates the Ca^{2+}–ATPase activity in rabbit myocardial membrane in a manner similar to that of thyroid hormones whereas amrinone, its 2-desmethyl-5-amino derivative, does not (Mylotte, Cody, Davis, Davis, Blas & Schoenl, 1985). It was also shown that milrinone, but not amrinone, shows structural homology with thyroxine (Cody, 1987). Here we report the structure of the N(3)-methyl derivative (I) of milrinone, as well as the structure of its hydrobromide monohydrate (II), as a part of a research program to delineate those features required for biological activity.

Experimental. Samples were obtained from Sterling–Winthrop. Crystals of (I) from EtOH/MeOH/water solution, for (II) from MeOH/HBr/water; cell parameters from 25 reflections $20.19 < 2\theta < 29.16°$ (I), 25 reflections $22.99 < 2\theta < 29.69°$ (II); Syntex P3 diffractometer, Mo $K\alpha$ radiation, Nb filter, $\lambda = 0.71073$ Å, θ–2θ scan; 4361 reflections $4 < 2\theta < 60°$ ($-17 < h < 17$, $0 < k < 12$, $0 < l < 18$) measured for a $0.12 \times 0.44 \times 0.80$ mm crystal of (I), 4037 reflections $4 < 2\theta < 55°$ ($0 < h < 10$, $0 < k < 25$, $0 < l < 26$) measured for a $0.12 \times 0.30 \times 0.64$ mm crystal of (II); six standards measured every 138 reflections for (I) and three standards measured every 140 reflections for (II) show no significant intensity variation, no absorption or extinction corrections; 3286 unique reflections for (I) and 2581 observed [$I > 3\sigma(I)$], 3167 unique reflections for (II) and 2295 observed [$I > 3\sigma(I)$]; direct methods used *MULTAN78* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and *NQEST* (De Titta, Edmonds, Langs & Hauptman, 1975), $\Sigma w(|F_o| - |F_c|)^2$ minimized with full-matrix least squares. H-atom positions for (I) from difference map, anisotropic refinement for

non-H and isotropic for H atoms. For (II), H-atom positions calculated from geometry and not refined, water molecule disordered, occupancy refined to 0.6 and 0.4 and fixed in last refinement cycles, water oxygen refined isotropically, other non-H atoms refined anisotropically, water and pyridinium N(4)' H atoms not found on final difference map. Weights $w = 1/\sigma^2(F)$ for (I) and (II) based on counting statistics. Final $|\Delta/\sigma| < 0.08$, $\Delta\rho_{max} = 0.33$ and $\Delta\rho_{min} = -0.24$ e Å^{-3} for (I); $|\Delta/\sigma| < 0.02$ and $\Delta\rho_{max} = 1.48$ and $\Delta\rho_{min} = -1.82$ e Å^{-3} for (II). Final $R = 0.063$, $wR = 0.069$ and $S = 2.457$ for (I), $R = 0.086$, $wR = 0.083$ and $S = 2.675$ for (II). Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV). Other programs used: data-processing programs described by Blessing (1989) and those from the Enraf–Nonius crystallographic package, VAX8600 computer.

Discussion. Fractional coordinates are listed in Tables 1 and 2,* bond distances and angles in Table 3, and hydrogen-bond details for (II) in Table 4. The molecular conformation and packing diagrams are shown in Figs. 1, 2 and 3.

The torsion angles [C(2)—C(1)—C(1)'—C(2)'] between the two rings are 66.6 (2) and 44.1 (8)° for (I) and (II), respectively. By contrast, in the structures of milrinone and its HCl salt, the 52.2° angle in the salt form is larger than the 42.4° angle in the free

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* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and best planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53176 (37 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. Bond lengths (Å) and angles (°) with e.s.d.'s for (I) and (II)

	(I)	(II)
C(1)—C(2)	1·374 (2)	1·401 (8)
C(1)—C(6)	1·405 (2)	1·390 (8)
C(1)—C(1)'	1·490 (2)	1·481 (8)
C(2)—C(21)	1·494 (2)	1·472 (8)
C(2)—N(3)	1·372 (2)	1·385 (7)
N(3)—C(31)	1·470 (3)	1·489 (8)
N(3)—C(4)	1·403 (2)	1·383 (8)
C(4)—O(4)	1·229 (2)	1·227 (8)
C(4)—C(5)	1·437 (2)	1·448 (9)
C(5)—C(51)	1·435 (2)	1·425 (8)
C(51)—N(52)	1·139 (2)	1·138 (9)
C(5)—C(6)	1·365 (2)	1·362 (8)
C(1)'—C(2)'	1·389 (2)	1·386 (8)
C(2)'—C(3)'	1·379 (3)	1·386 (9)
C(3)'—N(4)'	1·336 (3)	1·344 (9)
N(4)'—C(5)'	1·332 (3)	1·332 (9)
C(5)'—C(6)'	1·386 (3)	1·376 (9)
C(6)'—C(1)'	1·389 (2)	1·413 (8)
C(2)—C(1)—C(6)	118·8 (1)	119·4 (4)
C(21)—C(2)—C(1)	122·5 (2)	124·6 (4)
N(3)—C(2)—C(1)	120·1 (2)	118·0 (4)
N(3)—C(2)—C(21)	117·4 (2)	117·3 (4)
C(31)—N(3)—C(2)	121·1 (2)	119·2 (4)
C(4)—N(3)—C(2)	123·9 (2)	124·9 (4)
C(4)—N(3)—C(31)	114·9 (2)	115·8 (4)
O(4)—C(4)—N(3)	121·1 (2)	122·1 (4)
C(5)—C(4)—N(3)	114·3 (2)	114·8 (4)
C(5)—C(4)—O(4)	124·7 (2)	123·1 (5)
C(6)—C(5)—C(4)	122·0 (2)	121·1 (4)
C(51)—C(5)—C(4)	117·5 (2)	115·9 (4)
N(52)—C(51)—C(5)	178·6 (2)	179·0 (5)
C(6)—C(5)—C(51)	120·5 (2)	122·9 (4)
C(1)—C(6)—C(5)	120·7 (2)	121·5 (4)
C(2)—C(1)—C(1)'	122·8 (1)	122·3 (4)
C(6)—C(1)—C(1)'	118·4 (1)	118·3 (4)
C(1)—C(1)'—C(2)'	121·7 (1)	122·0 (4)
C(1)—C(1)'—C(6)'	121·0 (1)	119·4 (4)
C(2)'—C(1)'—C(6)'	117·3 (1)	118·6 (4)
C(1)'—C(2)'—C(3)'	119·2 (2)	120·1 (5)
C(2)'—C(3)'—N(4)'	124·2 (2)	119·6 (5)
C(3)'—N(4)'—C(5)'	116·1 (1)	121·8 (5)
N(4)'—C(5)'—C(6)'	124·1 (1)	121·5 (5)
C(5)'—C(6)'—C(1)'	119·1 (1)	118·3 (5)

Table 4. Hydrogen bonds for (II)

D—H···A	Acceptor symmetry operator	D···A (Å)
N(4)'···O(W1)	x, 0·5 − y, 0·5 + z	2·711 (11)
N(4)'···O(W2)	x, 0·5 − y, 0·5 + z	2·686 (14)
O(W1)···Br	1 − x, −0·5 + y, 0·5 − z	3·372 (13)
O(W1)···N(52)	x, y, z	3·326 (12)
O(W1)···O(4)	x, y, z	3·009 (10)
O(W2)···Br	0·5—x, −0·5 + y, z	3·372 (13)
O(W2)···Br	1 − x, −0·5 + y, 0·5 − z	3·350 (13)
van der Waals distance		
N(4)'···O(4)	−0·5 + x, 0·5 − y, 1 − z	3·409 (8)

base (Cody, 1987; Robertson, Beedle, Swart-zendruber, Jones, Elzey, Kauffman, Wilson & Hayes, 1986).

The geometry of the pyridone ring reflects its non-aromaticity compared to that of the pyridine ring. This is indicated by the mean deviations from the best pyridone ring plane of 0·015 (3) and 0·016 (8) Å for (I) and (II), respectively. The effect of
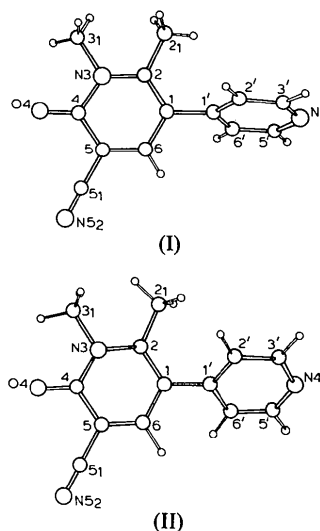

Fig. 1. Atomic numbering scheme for 1,2-dimethyl-6-oxo-1,6-dihydro-3,4'-bipyridine-5-carbonitrile (I) and 5-cyano-1,2-dimethyl-6-oxo-1,6-dihydro-3,4'-bipyridinium bromide monohydrate (II).
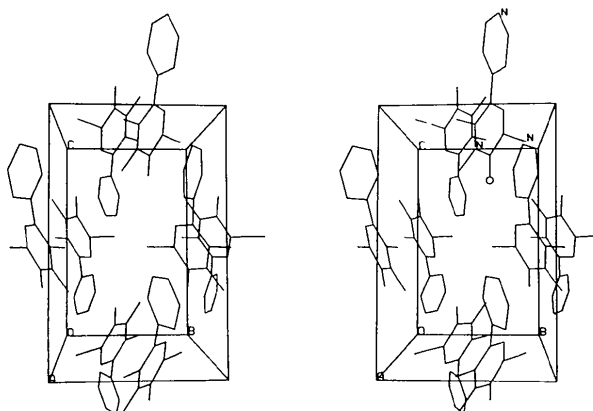

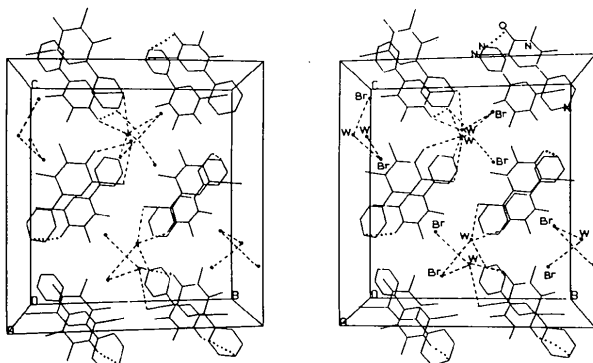Fig. 2. Stereoview of the packing diagram for (I).

Fig. 3. Stereoview of the packing diagram for (II). Hydrogen bonds are indicated as broken lines, averaged water molecule positions indicated as W, and the N(4)'···O(4) contact indicated as a dotted line.

methylation at N(3) is to lengthen the bonds about N(3) (Table 3) compared to those observed in milrinone [1·359 (2) and 1·371 (2) Å for C(2)—N(3) and N(3)—C(4), respectively] (Cody, 1987). There is also a shortening of the 2-methyl bond length in (II), not observed in (I) or milrinone.

In both reported structures the pyridine ring C—N bond lengths are shortened (average 1·33 Å) compared to the C—N values in the pyridone ring (average 1·38 Å). This shortening is also observed in the structures of milrinone and amrinone (Cody, 1987). In (II) the C(3)'—N(4)'—C(5)' angle is significantly larger than in (I) or milrinone free base (Cody, 1987), suggesting that it is a site of protonation of this salt. The pyridinium ring angles of (II) at C(1)', C(3)' and C(5)' are also significantly different than those of (I) (Table 3). These differences are indicative of the positive charge of the pyridinium ring of the salt (II).

There are no hydrogen-bonding functions in (I), and as illustrated in Fig. 2, there is stacking of the pyridone rings (C···C 3·4 Å). There is a network of hydrogen bonds in the hydrobromide hydrate structure (II) (Fig. 3). The water molecules are involved in a series of hydrogen bonds with the bromide ion and the cyano nitrogen (Table 4). The pyridinium nitrogen forms a hydrogen bond with one of the disordered water molecules, and is also involved in a close van der Waals contact (3·41 Å) with the keto oxygen of a neighboring molecule (Fig. 3).

That the free base of (I) has a larger torsion angle between rings than the HBr salt (II), in contrast to that observed for milrinone (Cody, 1987) and its HCl salt (Robertson *et al.*, 1986), appears to be an effect of hydrogen bonds involving the pyridone ring N—H group in both milrinone structures which are not observed for the methylated analogues reported here.

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Structure of Benzil Benzoylphenylhydrazone

BY D. D. BRAY

Chemistry Department, Fordham University, Bronx, New York 10458, USA

AND C. S. RUSSELL

Chemistry Department, The City College of New York, New York, New York 10031, USA

Abstract. 2'-(α-Benzoylbenzylidene)-1'-phenylbenzohydrazide, $C_{27}H_{20}N_2O_2$, $M_r = 404·47$, orthorhombic, $P2_12_12_1$, $a = 5·742$ (2), $b = 17·383$ (4), $c = 21·487$ (4) Å, $V = 2145$ (5) Å^3, $Z = 4$, $D_x = 1·252$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 5·97$ cm^{-1}, $F(000) = 848$, $T = 293$ K, final $wR = 0·043$ for 1465 reflections with $|F_o| > 3\sigma$. This compound is the product of the thermal rearrangement of α-benzoyloxy-β-phenylazostilbene. The structure is the one predicted by a cyclic intermediate or transition state with the C_6H_5C=O group rotated away from the migration terminus.

Introduction. α-Benzoyloxy-β-phenylazostilbene (I*a*) rearranges on heating, in solution, in the melt or in the solid state, to form benzil benzoylphenylhydrazone (III*a*) as the sole product (Russell & Weisleder, 1967). Kinetic studies in decalin solution showed that