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2,9β-Dimethyl-6,7-benzomorphan Hydrochloride

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Abstract. $C_{14}H_{20}NCl$, M.W. 237·77, orthorhombic, space group $Pna2_1$, $a=15·198$ (3), $b=11·563$ (3), $c=7·351$ (2) Å, $Z=4$, $D_c=1·22$, $D_x=1·23$ g cm^{-3} (flotation). Crystals obtained from 2-propanol/ether. The structure determination has confirmed the benzomorphan ring structure and the β configuration of the C(9) methyl group. The molecular structure is similar to the reported structures of two 9α-6,7-benzomorphans.

Introduction. Intensity data were collected from a $0·12\times0·17\times0·20$ mm crystal on a Nonius CAD-4 diffractometer in a θ–2θ scan mode using graphite-monochromated Cu $K\alpha$ radiation. Cell dimensions were determined by a least-squares refinement of 39 2θ values. Systematic absences (from Weissenberg photographs) were observed for $0kl$ with $k+l$ odd, $h0l$ and $h00$ with h odd, $0k0$ with k odd, and $00l$ with l odd. The intensities of 1437 independent reflections were measured, of which 1352 were considered to be observed (intensity $>2\sigma$). The data were corrected for Lorentz and polarization factors, but no corrections were made for absorption. The structure was solved by Patterson and Fourier methods and was refined by full-matrix least-squares procedures. The 20 hydrogen atoms were located in a difference Fourier map and

Table 1. *Fractional coordinates and thermal parameters for 2,9β-dimethyl-6,7-benzomorphan hydrochloride*

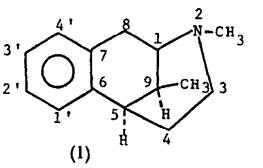
Coordinates are $\times10^4$ for the non-hydrogen atoms and $\times10^3$ for the hydrogen atoms. The anisotropic temperature factor is of the form $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)\times10^{-4}]$. The isotropic thermal parameters of the hydrogen atoms are those of the atoms to which they are bonded and were not refined. The standard deviations from the least-squares refinement are given in parentheses.

	X/a	Y/b	Z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	2021 (1)	240 (1)	7500	53 (1)	61 (1)	147 (1)	2 (1)	6 (1)	−12 (1)
C(1)	1837 (1)	1507 (2)	2667 (4)	33 (1)	57 (1)	150 (4)	1 (1)	−4 (2)	4 (2)
N	1886 (1)	1883 (2)	690 (3)	40 (1)	55 (1)	160 (4)	−8 (1)	13 (1)	−10 (2)
C(3)	1121 (2)	2618 (2)	156 (4)	65 (1)	74 (2)	138 (5)	12 (1)	5 (2)	20 (2)
C(4)	272 (2)	1989 (3)	551 (5)	45 (1)	117 (3)	172 (5)	12 (1)	−24 (2)	−19 (3)
C(5)	212 (1)	1550 (2)	2521 (4)	32 (1)	91 (2)	179 (4)	−13 (1)	4 (2)	−24 (3)
C(6)	185 (1)	2549 (2)	3856 (4)	35 (1)	73 (2)	145 (4)	0 (1)	8 (2)	6 (2)
C(7)	967 (1)	3044 (2)	4463 (3)	42 (1)	56 (1)	121 (4)	0 (1)	1 (2)	5 (2)
C(8)	1858 (1)	2534 (2)	3980 (4)	33 (1)	65 (2)	146 (4)	−4 (1)	−4 (2)	−12 (2)
C(9)	1007 (2)	781 (2)	2946 (3)	49 (1)	55 (1)	142 (5)	−11 (1)	6 (2)	2 (2)
C(10)	1016 (3)	−363 (2)	1902 (5)	84 (2)	58 (2)	187 (6)	−20 (1)	28 (3)	−3 (3)
C(11)	2743 (2)	2433 (3)	213 (5)	59 (1)	104 (3)	246 (7)	−37 (2)	46 (3)	−46 (4)
C(1′)	−612 (2)	2989 (3)	4475 (5)	39 (1)	104 (2)	206 (6)	6 (1)	18 (2)	16 (3)
C(2′)	−648 (2)	3912 (3)	5671 (5)	58 (1)	103 (2)	223 (6)	25 (1)	38 (3)	20 (3)
C(3′)	125 (2)	4424 (2)	6233 (4)	81 (2)	74 (2)	172 (5)	21 (2)	16 (3)	−12 (3)
C(4′)	927 (2)	3994 (2)	5633 (4)	59 (1)	65 (2)	162 (5)	3 (1)	−3 (2)	−7 (2)

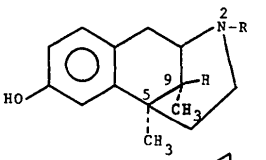
	X/a	Y/b	Z/c	B_{iso}		X/a	Y/b	Z/c	B_{iso}
H(1)	238 (2)	98 (2)	281 (4)	3·1	H(10,1)	108 (2)	−24 (3)	74 (6)	4·8
H(N)	186 (1)	128 (2)	−13 (4)	3·2	H(10,2)	54 (2)	−89 (2)	229 (6)	4·8
H(3,1)	117(2)	340 (2)	87 (5)	4·2	H(10,3)	145 (2)	−89 (3)	246 (5)	4·8
H(3,2)	117 (2)	278 (2)	−113 (5)	4·2	H(11,1)	265 (2)	325 (3)	89 (5)	4·9
H(4,1)	26 (2)	139 (3)	−39 (5)	4·4	H(11,2)	286 (2)	255 (3)	−115 (6)	4·9
H(4,2)	−18 (2)	262 (3)	13 (5)	4·4	H(11,3)	319 (2)	178 (3)	68 (5)	4·9
H(5)	−30 (2)	104 (2)	267 (4)	3·7	H(1′)	−120 (2)	263 (2)	392 (5)	4·5
H(8,1)	225 (2)	233 (2)	529 (4)	3·1	H(2′)	−122 (2)	429 (3)	613 (5)	4·9
H(8,2)	223 (2)	309 (2)	343 (4)	3·1	H(3′)	19 (2)	511 (3)	704 (6)	4·9
H(9)	99 (2)	59 (2)	423 (5)	3·5	H(4′)	149 (2)	430 (2)	589 (4)	4·1

the entire structure was refined (non-hydrogen atoms anisotropically) to an agreement residual of 0·035 for the 1437 reflections, using weights based on counting statistics.* A final difference Fourier showed no electron density greater than 0·5 e $Å^{-3}$. The scattering factors for carbon, nitrogen and chlorine were those of Cromer & Waber (1965), while that for hydrogen was from Stewart, Davidson & Simpson (1965). The computer programs used were those of Shiono (1968). The final atomic coordinates and thermal motion parameters are given in Table 1. The interatomic distances and angles for the non-hydrogen atoms are given in Fig. 1. The average C–H bond distance is 1·01 (6) Å.

Discussion. 2,9β-dimethyl-6,7-benzomorphan (I) was synthesized by Oh-ishi, Jacobsen, Wilson, Yeh & May (1974) in the course of their investigations on the analgesic activity of benzomorphans.



(I)



(IIa) R = CH_2–cyclopropyl

(IIb) R = CH_2–CH=CH_2

This compound showed appreciable analgesic activity, appearing to be as active as codeine in preliminary animal testing. The usual synthetic route to 6,7-benzomorphans was not successful for this molecule, hence a new synthetic scheme was developed. Although chemical and spectral evidence strongly supported the assigned structure, it was of importance to confirm the presence of the benzomorphan ring structure* and the β configuration which had been assigned to the C(9) methyl group (*i.e.* where the hydrogen atoms on C(5)

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30772 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

* The *Chemical Abstracts* name for the benzomorphan ring system is 1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocine.

Table 2. *Torsion angles for three* 6,7-*benzomorphans*

	(I)*	(II*a*)	(II*b*)
C(1)–N——C(3)–C(4)	55·6	57·2	55·7
C(1)–C(8)–C(7)–C(6)	−4·7	3·2	−11·6
C(1)–C(8)–C(7)–C(4′)	179·1	177·5	174·2
C(1)–C(9)–C(5)–C(4)	−59·2	−60·6	−65·0
C(1)–C(9)–C(5)–C(6)	62·9	59·7	54·5
N——C(1)–C(8)–C(7)	−89·5	−94·2	−81·3
N——C(1)–C(9)–C(5)	62·1	64·5	63·5
N——C(1)–C(9)–C(10)	−65·2	−171·3†	−171·9†
N——C(3)–C(4)–C(5)	−53·8	−56·3	−55·9
C(3)–N——C(1)–C(8)	62·0	62·7	65·2
C(3)–N——C(1)–C(9)	−61·5	−63·5	−60·4
C(3)–C(4)–C(5)–C(6)	−65·3	−60·4	−57·0
C(3)–C(4)–C(5)–C(9)	55·8	58·5	61·2
C(4)–C(3)–N——C(11)	−176·2	−175·8	−176·6
C(4)–C(5)–C(6)–C(7)	85·5	88·2	89·3
C(4)–C(5)–C(6)–C(1′)	−93·9	−95·3	−81·5
C(4)–C(5)–C(9)–C(10)	67·8	176·9†	169·8†
C(5)–C(6)–C(7)–C(8)	6·4	−3·1	5·6
C(5)–C(6)–C(7)–C(4′)	−177·4	177·6	179·5
C(5)–C(6)–C(1′)–C(2′)	179·0	−176·0	177·1
C(5)–C(9)–C(1)–C(8)	−62·2	−61·5	−64·1
C(6)–C(5)–C(9)–C(10)	170·1	−62·9†	−70·7†
C(6)–C(7)–C(4′)–C(3′)	−1·9	−2·5	7·6
C(6)–C(1′)–C(2′)–C(3′)	−1·3	−0·9	−0·2
C(7)–C(6)–C(5)–C(9)	−35·7	−28·7	−27·4
C(7)–C(6)–C(1′)–C(2′)	−0·5	0·7	5·6
C(7)–C(8)–C(1)–C(9)	32·9	30·1	41·2
C(7)–C(4′)–C(3′)–C(2′)	0·1	2·3	−1·6
C(8)–C(1)–N——C(11)	−65·8	−63·7	−58·0
C(8)–C(1)–C(9)–C(10)	170·6	62·6†	60·5†
C(8)–C(7)–C(6)–C(1′)	−174·1	−179·7	176·8
C(8)–C(7)–C(4′)–C(3′)	174·4	178·2	−178·3
C(9)–C(1)–N——C(11)	170·7	170·1	176·4
C(9)–C(5)–C(6)–C(1′)	144·9	147·9	161·9
C(1′)–C(6)–C(7)–C(4′)	2·1	0·9	−9·3
C(1′)–C(2′)–C(3′)–C(4′)	1·5	−0·6	−2·0

* Enantiomer of the molecule with coordinates in Table 1.
† α configuration.

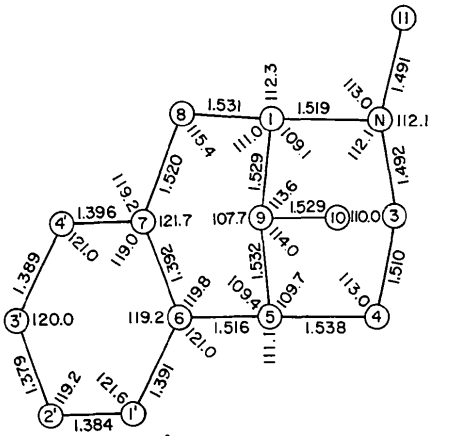


Fig. 1. Bond distances (Å) and angles (°) for 2,9β-dimethyl-6,7-benzomorphan hydrochloride. The e.s.d.'s are 0·003–0·004 Å and 0·2–0·3°.

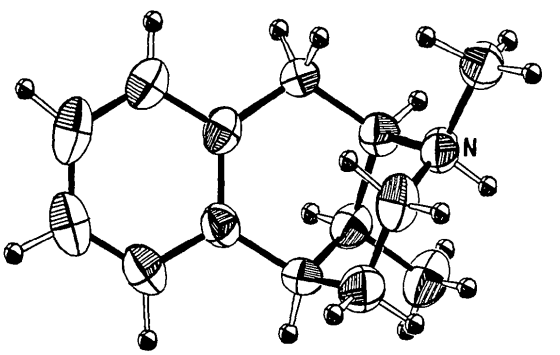


Fig. 2. Perspective drawing of the 2,9β-dimethyl-6,7-benzomorphan cation (enantiomer of the molecule with coordinates in Table 1). The thermal vibrational ellipsoids of the non-hydrogen atoms are scaled to 50% probability. The hydrogen atoms are shown as spheres of an arbitrary size.

and C(9) are *cis* with respect to the hydroaromatic ring). It is readily apparent from Fig. 2 that the assigned structure is correct.

The molecular structure of (I) is very similar to the structures reported for two other 6,7-benzomorphans. Karle, Gilardi, Fratini & Karle (1969) reported the crystal structure of cyclazocine hydrobromide (2-cyclopropylmethyl-2′-hydroxy-5,9-dimethyl-6,7-benzomorphan) (II*a*) and Fedeli, Giacomello, Cerrini & Vaciago (1970) reported the crystal structure of 2-allyl-2′-hydroxy-5,9-dimethyl-6,7-benzomorphan hydrobromide (II*b*). Both of these compounds have a C(5) methyl substituent and an α configuration for the C(9) methyl group. As is apparent from the torsion angles in Table 2, the structural differences between (I) and (II*a*) and (II*b*) do not lead to any consistent significant differences in the conformation of the benzomorphan ring system. Larger differences exist between (II*a*) and (II*b*) than between (I) and (II*a*) or (II*b*).

The chloride ion at $X, Y, Z-1$ acts as a hydrogen-bond acceptor for the amino hydrogen; N···Cl 3·025 Å, N–H(N) 0·92 Å, H(N)···Cl 2·13 Å, N–H(N)···Cl 162·6°.

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Génisteine

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Abstract. $C_{14}O_5H_{10}$, orthorhombic, *Pbca*, $a=23{\cdot}643$ (9), $b=6{\cdot}956$ (4), $c=14{\cdot}545$ (6) Å, $Z=8$. The crystals were grown from methanol solution. 1540 independent reflexions, 0·039. There is an intramolecular chelation between two oxygens (2·614 Å).

Introduction. La génisteine est un dérivé trihydroxylé de l'isoflavonne possédant une faible activité oestrogène. On la rencontre dans de nombreuses espèces végétales. Son affinité pour le récepteur de l'utérus est beaucoup plus faible (200 fois) que celle de l'oestradiol

Tableau 1. *Paramètres atomiques*

Coordonnées atomiques ont été multipliées par 10^4.

	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	1859 (1)	4779 (4)	4334 (2)	13 (0)	142 (6)	38 (1)	3 (3)	9 (1)	−14 (5)
C(2)	2424 (1)	4895 (4)	4577 (2)	14 (1)	164 (6)	33 (1)	−3 (3)	0 (1)	−14 (5)
C(3)	2823 (1)	4547 (4)	3907 (2)	11 (0)	134 (6)	37 (1)	−1 (3)	−1 (1)	1 (5)
O(4)	3376 (1)	4700 (3)	4174 (1)	11 (0)	218 (5)	33 (1)	1 (2)	−2 (1)	−26 (4)
C(5)	3785 (1)	4402 (4)	3539 (2)	10 (0)	197 (7)	40 (1)	4 (3)	0 (1)	−18 (5)
C(6)	3698 (1)	3984 (4)	2649 (2)	12 (0)	148 (6)	35 (1)	0 (3)	3 (1)	−8 (5)
C(7)	3121 (1)	3807 (4)	2324 (2)	13 (0)	136 (5)	34 (1)	3 (3)	0 (1)	1 (4)
C(8)	2683 (1)	4075 (4)	3000 (2)	12 (0)	130 (5)	28 (1)	0 (3)	1 (1)	3 (4)
C(9)	2099 (1)	3915 (4)	2787 (2)	13 (0)	134 (6)	31 (1)	−7 (3)	−4 (1)	3 (4)
C(10)	1695 (1)	4266 (4)	3445 (2)	12 (0)	164 (6)	38 (1)	−1 (3)	1 (1)	−1 (5)
O(11)	1437 (1)	5170 (3)	4937 (1)	12 (0)	275 (6)	40 (1)	−7 (2)	9 (1)	−45 (4)
C(12)	4182 (1)	3672 (4)	2016 (2)	11 (0)	181 (6)	36 (1)	5 (3)	−1 (1)	−13 (5)
C(13)	4606 (1)	5023 (4)	1909 (2)	14 (0)	179 (6)	42 (1)	−6 (3)	−2 (1)	−19 (5)
C(14)	5060 (1)	4691 (4)	1320 (2)	12 (0)	175 (7)	47 (2)	−12 (3)	3 (1)	2 (5)
C(15)	5090 (1)	2993 (4)	839 (2)	11 (0)	200 (7)	34 (1)	9 (3)	−1 (1)	9 (5)
C(16)	4667 (1)	1630 (4)	937 (2)	14 (1)	182 (7)	43 (1)	−2 (3)	3 (1)	−33 (6)
C(18)	4217 (1)	1971 (4)	1518 (2)	12 (0)	181 (7)	41 (1)	−10 (3)	4 (1)	−11 (5)
O(19)	1934 (1)	3401 (3)	1930 (1)	14 (0)	249 (5)	32 (1)	−3 (2)	−7 (1)	−16 (4)
O(17)	3006 (1)	3459 (3)	1493 (1)	14 (0)	248 (5)	28 (1)	1 (2)	−2 (1)	−16 (4)
O(25)	5526 (1)	2552 (3)	254 (1)	13 (0)	228 (5)	47 (1)	5 (2)	13 (1)	−6 (4)