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2-[(3-Furoyl)aminomethyl]-1,7-dimethyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-4-ium Chloride

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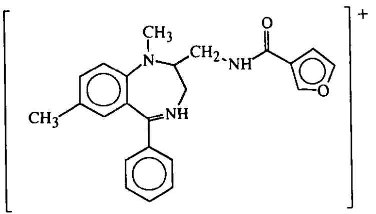
Abstract

The seven-membered ring of $C_{23}H_{24}N_3O_2^+.Cl^-$ has a conformation halfway between a distorted boat and a distorted sofa. The 3-furoylaminomethyl moiety is in an extended conformation. This conformation is stabilized by two hydrogen bonds with the Cl^- anion, one from the protonated basic N atom of the heptadiene ring and another from the amidic N atom.

Comment

The title compound, (I), belongs to a series of 2-acylaminomethylbenzodiazepine derivatives with opioid activity. This single-crystal structure analysis is part of a structure–activity study on κ-opioid agonists related to tifluadom. Fig. 1 shows the molecule. Apart from the differences between corresponding internal angles of the benzo moiety caused by the position of the methyl substituent, the structure is very similar to that of the 1,8-dimethyl analogue (Blaton, Peeters & De Ranter, 1995). Compared with an unsubstituted benzo part (Meurisse, Blaton, Peeters & De Ranter, 1992), the deformations of the internal angles agree quite well with the values given by Domenicano & Murray-Rust (1979). Bond lengths and remaining angles show little deviation from values found in other compounds of the series (Peeters, Blaton, Meurisse & De Ranter, 1994*a*,*b*, and references therein). The puckering parameters [q_2 = 0.696 (2), q_3 = 0.277 (3) Å, φ_2 = −37.0 (2), φ_3 = −129.3 (4)°] and asymmetry parameters [$\Delta C_s(C_3)$ = 0.066 (1)] of the seven-membered ring indicate a conformation halfway between a distorted boat and a distorted sofa. The 3-furoylaminomethyl side chain has an extended conformation and substitutes the diazepine ring axially at position 2. This side chain is stabilized by two N—H···Cl hydrogen bonds [N4···Cl = 3.051 (2), H4···Cl = 2.25 Å, N4—H4···Cl = 155°; N12···Cl = 3.328 (2), H12···Cl = 2.51 Å, N12—H12···Cl = 160°].



(I)

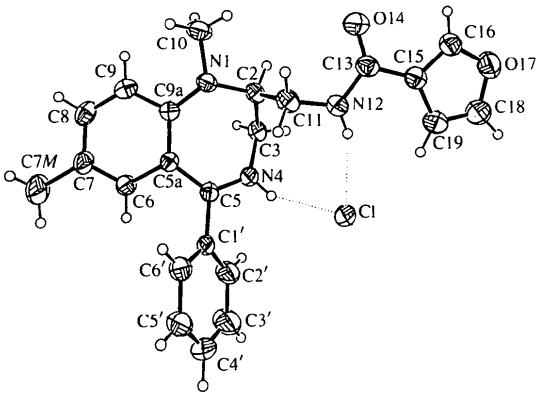


Fig. 1. Perspective view of the title compound with the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level.

Experimental

Crystal data

$C_{23}H_{24}N_3O_2^+.Cl^-$
M_r = 409.90
Orthorhombic
$P2_12_12_1$
a = 6.178 (1) Å
b = 13.787 (2) Å
c = 24.819 (6) Å
V = 2114.1 (7) Å^3
Z = 4
D_x = 1.288 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 24 reflections
θ = 7.5–10.1°
μ = 0.20 mm^{-1}
T = 293 K
Block
0.60 × 0.40 × 0.40 mm
Dark orange

Data collection

Stoe Stadi-4 four-circle diffractometer
ω scans
Absorption correction: ψ scans (*EMPIR*; Stoe & Cie, 1992*b*)
T_{min} = 0.937, T_{max} = 0.999
4938 measured reflections
3936 independent reflections

2946 observed reflections [$F^2 > 2\sigma(F^2)$]
R_{int} = 0.0181
θ_{max} = 27.63°
$h = -2 \rightarrow 8$
$k = -2 \rightarrow 17$
$l = -2 \rightarrow 32$
3 standard reflections
frequency: 60 min
intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0407
$wR(F^2)$ = 0.1109

$(\Delta/\sigma)_{max}$ = 0.037
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}

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$S = 1.030$
3936 reflections
264 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.0538P)^2 + 0.3112P]$
where $P = (F_o^2 + 2F_c^2)/3$
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2B and 2.3.1)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)*

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
Cl	0.3639 (1)	0.95024 (5)	0.74141 (3)	0.0553 (2)
N1	1.0115 (4)	0.6702 (2)	0.74788 (8)	0.0439 (6)
C2	0.8094 (4)	0.7067 (2)	0.7708 (1)	0.0422 (7)
C3	0.6373 (4)	0.7186 (2)	0.72783 (9)	0.0436 (7)
N4	0.6770 (4)	0.8023 (2)	0.69361 (8)	0.0424 (7)
C5	0.8328 (4)	0.8088 (2)	0.65849 (8)	0.0379 (7)
C5a	0.9968 (4)	0.7349 (2)	0.65298 (9)	0.0365 (7)
C6	1.0983 (5)	0.7304 (2)	0.6019 (1)	0.0462 (8)
C7	1.2562 (5)	0.6647 (2)	0.5882 (1)	0.052 (1)
C7*M*	1.3688 (8)	0.6668 (3)	0.5339 (1)	0.094 (2)
C8	1.3054 (5)	0.5956 (2)	0.6272 (1)	0.0544 (9)
C9	1.2150 (5)	0.5956 (2)	0.6773 (1)	0.0486 (9)
C9a	1.0640 (4)	0.6677 (2)	0.69408 (9)	0.0366 (7)
C10	1.1261 (5)	0.6067 (2)	0.7860 (1)	0.061 (1)
C11	0.8455 (5)	0.7994 (2)	0.8042 (1)	0.0497 (9)
N12	0.6528 (4)	0.8296 (2)	0.83257 (8)	0.0507 (7)
C13	0.6114 (6)	0.8008 (2)	0.8839 (1)	0.0483 (9)
O14	0.7286 (4)	0.7463 (2)	0.90908 (8)	0.0703 (8)
C15	0.4118 (5)	0.8423 (2)	0.9083 (1)	0.0464 (9)
C16	0.3439 (6)	0.8221 (2)	0.9589 (1)	0.056 (1)
O17	0.1616 (4)	0.8716 (2)	0.97096 (8)	0.0704 (8)
C18	0.1153 (6)	0.9239 (3)	0.9257 (1)	0.065 (1)
C19	0.2588 (5)	0.9090 (2)	0.8867 (1)	0.054 (1)
C1′	0.8274 (5)	0.8956 (2)	0.62316 (9)	0.0424 (8)
C2′	0.6309 (6)	0.9232 (3)	0.6009 (1)	0.072 (1)
C3′	0.6186 (8)	1.0058 (4)	0.5692 (2)	0.106 (2)
C4′	0.7983 (9)	1.0595 (3)	0.5596 (2)	0.095 (2)
C5′	0.9921 (7)	1.0341 (2)	0.5816 (1)	0.068 (1)
C6′	1.0098 (5)	0.9513 (2)	0.61337 (9)	0.0492 (9)

Table 2. *Selected geometric parameters (Å, °)*

N1—C2	1.461 (3)	C11—N12	1.444 (4)
N1—C9a	1.375 (3)	N12—C13	1.359 (3)
N1—C10	1.472 (4)	C13—O14	1.216 (4)
C2—C3	1.514 (4)	C13—C15	1.488 (4)
C2—C11	1.540 (4)	C15—C16	1.354 (4)
C3—N4	1.454 (3)	C15—C19	1.423 (4)
N4—C5	1.301 (3)	C16—O17	1.349 (4)
C5—C5a	1.444 (4)	O17—C18	1.365 (4)
C5—C1′	1.484 (3)	C18—C19	1.329 (5)
C5a—C6	1.416 (4)	C1′—C2′	1.387 (5)
C5a—C9a	1.439 (3)	C1′—C6′	1.385 (4)
C6—C7	1.374 (4)	C2′—C3′	1.386 (6)
C7—C7*M*	1.516 (4)	C3′—C4′	1.355 (7)
C7—C8	1.394 (4)	C4′—C5′	1.362 (7)
C8—C9	1.362 (4)	C5′—C6′	1.392 (4)
C9—C9a	1.426 (4)		
C9a—N1—C10	119.7 (2)	N1—C9a—C5a	127.1 (2)
C2—N1—C10	111.5 (2)	C2—C11—N12	112.5 (2)
C2—N1—C9a	126.1 (2)	C11—N12—C13	121.9 (3)
N1—C2—C11	111.8 (2)	N12—C13—C15	115.2 (2)
N1—C2—C3	111.3 (2)	N12—C13—O14	123.3 (3)
C3—C2—C11	113.0 (2)	O14—C13—C15	121.5 (2)
C2—C3—N4	112.3 (2)	C13—C15—C19	130.2 (3)
C3—N4—C5	124.8 (2)	C13—C15—C16	123.8 (3)
N4—C5—C1′	115.8 (2)	C16—C15—C19	106.1 (3)
N4—C5—C5a	122.3 (2)	C15—C16—O17	111.1 (3)
C5a—C5—C1′	121.9 (2)	C16—O17—C18	105.1 (3)
C5—C5a—C9a	126.2 (2)	O17—C18—C19	112.2 (3)
C5—C5a—C6	115.3 (2)	C15—C19—C18	105.6 (3)
C6—C5a—C9a	118.6 (2)	C5—C1′—C6′	122.2 (2)
C5a—C6—C7	124.4 (2)	C5—C1′—C2′	118.4 (3)
C6—C7—C8	115.7 (3)	C2′—C1′—C6′	119.3 (3)
C6—C7—C7*M*	122.3 (3)	C1′—C2′—C3′	120.0 (3)
C7*M*—C7—C8	122.1 (3)	C2′—C3′—C4′	120.2 (4)
C7—C8—C9	123.0 (3)	C3′—C4′—C5′	120.6 (4)
C8—C9—C9a	122.4 (3)	C4′—C5′—C6′	120.5 (4)
C5a—C9a—C9	115.5 (2)	C1′—C6′—C5′	119.3 (3)
N1—C9a—C9	117.2 (2)		
C2—N1—C9a—C5a	31.9 (4)	C3—N4—C5—C5a	−5.4 (4)
C10—N1—C9a—C9	5.9 (3)	N4—C5—C1′—C2′	−44.1 (4)
C9a—N1—C2—C11	−112.9 (3)	N4—C5—C5a—C9a	−24.6 (4)
C9a—N1—C2—C3	14.5 (3)	C5—C5a—C9a—N1	−10.9 (4)
N1—C2—C11—N12	−172.8 (2)	C2—C11—N12—C13	92.5 (3)
N1—C2—C3—N4	−74.1 (3)	C11—N12—C13—C15	177.0 (2)
C2—C3—N4—C5	70.3 (3)		

The structure was solved by direct methods and refined on F^2 by full-matrix least-squares methods. H atoms were included at calculated positions and refined using a riding model. According to the procedure of Flack (1983), the absolute configuration could not be determined reliably [Flack parameter = 0.51 (8)].

Data collection: *DIF*4 (Stoe & Cie, 1992*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1992*c*). Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEX*2.1 (McArdle, 1994). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, torsion angles and complete geometry have been deposited with the IUCr (Reference: NA1198). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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