organic papers

(+)-N,N'-Bis[(7,7-dimethyl-2-oxobicyclo[2.2.1]-heptan-1-yl)methylsulfonyl]piperazine

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In the title compound, $C_{24}H_{38}N_2O_6S_2$, which was synthesized from (+)-10-camphorsulfonic acid chloride and piperazine, the central piperazine ring adopts a chair conformation. The two camphorlsulfonyl groups are bound to the piperazine N atoms in equatorial positions. The molecule has approximate non-crystallographic twofold symmetry.

Comment

Various N,N'-dicamphorsulfonylpiperazines, including the title compound, (I), have been described earlier (Garcia & Bermejol, 1978), but their molecular structures were never reported. According to the cited patent, this class of compounds exhibits strong central analgesic, cardiac stimulating and spasmolytic action. In addition to these physiological properties, a local anesthetic effect and remarkable anticholinergic activity were also noted. Simultaneously, they showed a very low acute toxicity. Recently, chiral sulfonamides and bis(sulfonamides) derived from camphor have received considerable attention since they can act as chiral controllers in asymmetric synthesis, both as auxiliaries and as catalysts, especially in the alkylation of aldehydes and in the arylation of prochiral ketones (Hwang & Uang, 1998; Seydan-Penne, 1995; Royo et al., 2000; Ramon & Yus, 1997; Yus et al., 2002, 2003; Bauer & Gajewiak, 2003; Martinez et al., 2004).

(I)
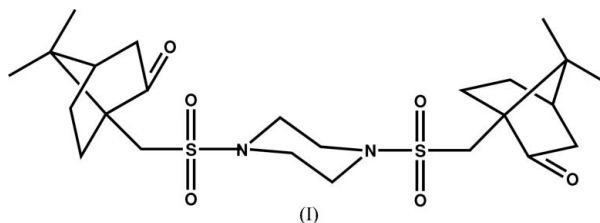
The molecule has a non-crystallographic twofold axis running approximately through the mid-points of the piperazine C11—C12 and C13—C14 bonds. Both the bornylsulfonyl groups are bound to the piperazine bridge N atoms in equatorial positions. The overall orientation of the camphor units relative to the piperazine bridge is similar, differing by only 12.6 (2)°, as calculated by the dihedral angle between the C1—C7—C5 and C1a—C7a—C5a bridges. In the crystal structure, methyl groups of the bornyl unit are positioned in the space formed by the piperazine rings of adjacent molecules.

The geometry of the bornyl unit is typical, with C—C bond distances ranging from 1.506 (3) to 1.568 (3) Å. The piperazine bridge has a normal chair conformation, the ring torsion angles having alternating positive and negative values ranging from 56.1 (2) to 59.5 (2)°. However, the angles C13—N1—C11 and C14—N1a—C14 are significantly larger then those
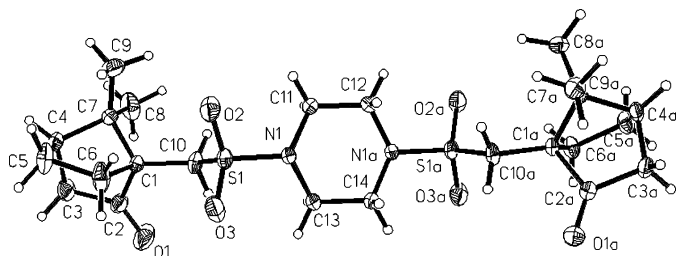
Figure 1
A view of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

reported by Wang *et al.* (2004) which were close to 108°. The difference seems to result from the steric effects of the sulfonic group adjacent to the piperazine N atoms.

Experimental

Piperazine (2.56 g, 29.8 mmol) in triethylamine (7.60 g, 75.1 mmol) was added to CH_2Cl_2 (15 ml). A solution of (+)-10-camphorsulfonic acid chloride (15.00 g, 59.8 mmol) in CH_2Cl_2 (75 ml) was then added dropwise over a period of approximately 20 min at 273 K. The reaction mixture was stirred at the same temperature for 2 h and at 253 K for 1 h. It was then quenched by pouring it into 1 *M* aqueous HCl (50 ml). The resulting layers were separated and extracted with CH_2Cl_2. The combined organic solutions were washed successively with saturated aq. $NaHCO_3$ solution and water (2 × 50 ml). After drying over anhydrous Na_2SO_4 and filtering, the solvent was evaporated under vacuum. The oily residue was dissolved in CH_2Cl_2, precipitating a solid product using a mixture of EtOAc and hexane. The filtered precipitate was crystallized from CH_3CN to give 14.59 g (28.38 mmol, 95.3% reaction yield) diffraction quality crystals of (I). The melting point was measured on a Boetius apparatus and was uncorrected; m.p. 567.5–568.0 [literature m.p. 553 K (nitrobenzene); Garcia & Bermejol, 1978]. $[\alpha]_D^{20}$ 38.7 (*c* = 3.60, $CHCl_3$).

Crystal data

$C_{24}H_{38}N_2O_6S_2$	$Z = 4$
$M_r = 514.68$	$D_x = 1.335$ Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 8.4677$ (3) Å	$\mu = 0.25$ mm^{-1}
$b = 11.1826$ (4) Å	$T = 20$ (2) K
$c = 27.0427$ (10) Å	Block, colorless
$V = 2560.70$ (16) Å^3	0.34 × 0.33 × 0.25 mm

Data collection

Oxford Sapphire CCD diffractometer	25421 measured reflections
$\theta/2\theta$ scans	7818 independent reflections
Absorption correction: numerical (*CrysAlis RED*; Oxford Diffraction, 2000)	6202 reflections with $I > 2\sigma(I)$
$T_{min} = 0.920$, $T_{max} = 0.940$	$R_{int} = 0.042$
	$\theta_{max} = 31.3°$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0664P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.048$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.124$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.08$	$\Delta\rho_{max} = 0.31$ e Å^{-3}
7818 reflections	$\Delta\rho_{min} = -0.28$ e Å^{-3}
311 parameters	Absolute structure: Flack (1983), 3125 Friedel pairs
H-atom parameters constrained	Flack parameter: −0.01 (6)

Table 1
Selected geometric parameters (Å, °).

C1—C10	1.526 (2)	C12—N1a	1.476 (2)
C2—O1	1.206 (3)	N1a—C14	1.462 (2)
C10—S1	1.773 (2)	N1a—S1a	1.637 (1)
S1—O2	1.416 (2)	S1a—O3a	1.427 (2)
S1—O3	1.428 (2)	S1a—O2a	1.432 (2)
S1—N1	1.638 (2)	S1a—C10a	1.777 (2)
N1—C13	1.464 (2)	C10a—C1a	1.528 (2)
N1—C11	1.474 (2)	C2a—O1a	1.202 (2)
C11—C12	1.523 (3)		
O1—C2—C3	126.8 (2)	C14—N1a—S1a	118.9 (1)
O1—C2—C1	126.0 (2)	C12—N1a—S1a	118.5 (1)
C3—C2—C1	107.2 (2)	N1—C13—C14	108.8 (2)
C1—C7—C4	94.6 (2)	N1a—C14—C13	108.8 (2)
O2—S1—O3	119.6 (1)	O3A—S1a—O2a	119.1 (1)
N1—S1—C10	106.09 (9)	N1a—S1a—C10a	106.06 (8)
C13—N1—C11	113.3 (2)	C1a—C10a—S1a	117.2 (1)
C13—N1—S1	117.9 (1)	C4a—C7a—C1a	93.9 (1)
C11—N1—S1	118.9 (1)	O1a—C2a—C3a	126.8 (2)
N1—C11—C12	108.7 (2)	O1a—C2a—C1a	126.6 (2)
N1a—C12—C11	108.2 (2)	C3a—C2a—C1a	106.6 (2)
C14—N1a—C12	113.1 (2)		

H atoms were placed in calculated positions and treated as riding (C—H = 0.98 Å, aromatic C—H = 0.93 Å, and U_{iso}(H) values fixed at 0.08 Å^2.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2000); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2000); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *CIFTAB* (Sheldrick, 1997).

References

Bauer, T. & Gajewiak, J. (2003). *Tetrahedron*, **59**, 10009–100012.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Garcia, A. A. & Bermejol, J. R. C. (1978). US Patent No. 4 087 425.
Hwang, C.-D. & Uang, B.-J. (1998). *Tetrahedron Asymmetry*, **9**, 3979–3984.
Martinez, A. G., Vilar, E. T., Jimenez, F. M. & Garcia, A. M. A. (2004). *Tetrahedron Asymmetry*, **15**, 293–298.
Oxford Diffraction (2000). *CrysAlis RED* and *CrysAlis CCD*. Oxford Diffraction, Abingdon, Oxfordshire, England.
Ramon, D. J. & Yus, M. (1997). *Tetrahedron Asymmetry*, **8**, 2479–2496.
Royo, E., Betancort, J. M., Davis, T. J., Caroll, P. & Walsh, P. J. (2000). *Organometallics*, **19**, 4840–4851.
Seydan-Penne, J. (1995). *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*. New York: John-Wiley & Sons.
Sheldrick, G. M. (1997). *SHELXS97, SHELXL97* and *CIFTAB*. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Wang, H.-B., Chen, J.-H., Pu, Y.-Q. & Wang, J.-T. (2004). *Acta Cryst.* E**60**, o2041–o2042.
Yus, M., Ramon, D. J. & Prieto, O. (2002). *Tetrahedron Asymmetry*, **13**, 1573–1579.
Yus, M., Ramon, D. J. & Prieto, O. (2003). *Tetrahedron Asymmetry*, **14**, 1103–1114.