C11	0.4473 (3)	0.6496 (2)	0.95378 (11)	0.0526 (5)
N3	0.5372 (3)	0.6799 (2)	1.00374 (12)	0.0703 (6)
C12	0.2915 (3)	0.7386 (2)	0.84392 (11)	0.0528 (5)
N4	0.2583 (3)	0.8366 (3)	0.80851 (13)	0.0762 (7)
O1	0.0429 (3)	0.2866 (2)	0.89409 (10)	0.0640 (5)
C13	0.0279 (6)	0.1443 (3)	0.8664 (2)	0.0957 (12)

Table 4. *Selected geometric parameters* (Å, °) *for* (2)

C1—O1	1.414 (3)	C5—C6	1.597 (2)
C1—C2	1.516 (3)	C6—C10	1.468 (3)
C1—C8	1.531 (3)	C6—C9	1.479 (2)
C1—C6	1.582 (3)	C7—C8	1.497 (4)
C2—C3	1.356 (3)	C9—N1	1.134 (2)
C3—C4	1.509 (3)	C10—N2	1.148 (3)
C4—C7	1.518 (3)	C11—N3	1.133 (3)
C4—C5	1.585 (3)	C12—N4	1.133 (3)
C5—C12	1.475 (3)	O1—C13	1.425 (3)
C5—C11	1.481 (3)		
O1—C1—C2	114.5 (2)	C11—C5—C6	112.22 (14)
O1—C1—C8	114.5 (2)	C4—C5—C6	108.09 (15)
C2—C1—C8	109.5 (2)	C10—C6—C9	107.42 (15)
O1—C1—C6	103.79 (14)	C10—C6—C1	107.89 (15)
C2—C1—C6	105.7 (2)	C9—C6—C1	109.16 (15)
C8—C1—C6	108.2 (2)	C10—C6—C5	111.53 (15)
C3—C2—C1	113.9 (2)	C9—C6—C5	112.52 (14)
C2—C3—C4	114.0 (2)	C1—C6—C5	108.20 (14)
C3—C4—C7	109.0 (2)	C8—C7—C4	111.2 (2)
C3—C4—C5	107.0 (2)	C7—C8—C1	110.6 (2)
C7—C4—C5	107.7 (2)	N1—C9—C6	178.5 (2)
C12—C5—C11	107.6 (2)	N2—C10—C6	177.9 (2)
C12—C5—C4	108.8 (2)	N3—C11—C5	175.6 (3)
C11—C5—C4	108.3 (2)	N4—C12—C5	175.7 (2)
C12—C5—C6	111.77 (15)	C1—O1—C13	115.6 (2)
C1—C2—C3—C4	1.0 (2)	C4—C5—C6—C1	3.3 (2)
C4—C7—C8—C1	2.5 (2)	C2—C1—C6—C5	−59.5 (2)

For both compounds, data collection: Enraf–Nonius CAD-4 software; cell refinement: *CELSIUS* (local software); data reduction: *CORINC* (local software); program(s) used to solve structures: *SHELXS*86 (Sheldrick, 1990); program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *SCHAKAL*92 (Keller, 1992); software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: SE1061). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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N^2-Cyano-N^1-isopropyl-N^3-[4-(3-methylphenylamino)-3-pyridylsulfonyl]guanidine

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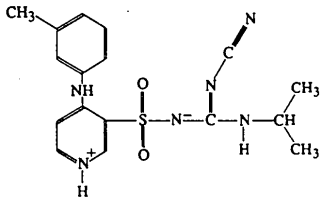
Abstract

The title compound, $C_{17}H_{20}N_6O_2S$, is a bioisoster of torasemide, a loop diuretic whose structure has been described previously. The sulfonylurea chain of torasemide is replaced by a sulfonylcyanoguanidine function. Whereas the torasemide molecule and some sulfonylurea derivatives exhibit one of the three α, β or γ conformations, the conformation being assigned according to the torsion angles in the side chain, the title compound displays a new δ conformation. This conformation is stabilized by two intramolecular N—H···O hydrogen bonds. A prototropic form of the title compound corresponding to a zwitterion [—S—N$^-$—C—, N$^+$—H (pyridinium)] is observed {*i.e* N^2-cyano-N^1-isopropyl-N^3-[4-(3-methylphenylamino)-3-pyridiniosulfonyl]guanidin-3-ide}. The crystal cohesion is the result of both van der Waals interactions and one intermolecular N$^+$—H···N$^-$ hydrogen bond involving the N atoms of the zwitterion.

Comment

N^2-Cyano-N^1-isopropyl-N^3-[4-(3-methylphenylamino)-3-pyridylsulfonyl]guanidine, (I), is a bioisoster of torasemide, a loop diuretic (Friedel & Buckley, 1991) whose structure has been described previously (Dupont, Campsteyn, Lamotte & Vermeire, 1978; Dupont, Lamotte, Campsteyn & Vermeire, 1978). The structure differs from that of torasemide in that the sulfonylurea side

chain is replaced by a sulfonylcyanoguanidine function. The present crystal structure determination contributes to the study of this never-before-described function. Its synthesis and biological activity are to be published elsewhere.



(I)

In the title crystal, the torasemide molecule exhibits three different conformations, denoted α, β and γ, as defined by Dupont, Dideberg & Delarge (1981). All sulfonylurea derivatives of torasemide studied previously by cystallography belong to one of these three categories. According to the values of the torsion angles C1—C5—S1—N3, C5—S1—N3—C6, S1—N3—C6—N4 and N3—C6—N4—C7 found in the present work, compound (I) displays a new conformation, denoted δ, defined by the typical values +90, +90 (arbitrarily positive), 0 and 180°, respectively, for the above torsion angles. Therefore, two intramolecular hydrogen bonds are possible N1—H1*A*···O1 [N1···O1 2.792 (3), H1*A*···O1 2.047 (3) Å, N1—H1*A*···O1 144.4 (9)°] and N4—H4*A*···O2 [N4···O2 2.816 (3), H4*A*···O2 2.123 (3) Å, N4—H4*A*···O2 137.3 (9)°].

The distances and angles within the pyridine ring and the sulfonyl–NCN–isopropyl chain, in particular S1—N3 [1.576 (2) Å] and C3—N2—C4 [120.5 (2)°], suggest a prototropic zwitterionic formula where atom N3 is deprotonated and possesses a negative charge and atom N2 is protonated producing a pyridinium ring (Dupont, Dideberg, Delarge, Dive & Thunus, 1982). A significantly better *R* factor in the refinement reinforces this hypothesis.

The angle between the phenylamino and the aminopyridinium least-squares planes is 23.61 (7)°. The crystal cohesion is the result of van der Waals interactions and an N2$^+$—H2*A*···N3$^-$($\frac{1}{2}+x$, $\frac{3}{2}-y$, $\frac{1}{2}+z$) hydrogen bond [N2···N3 2.869 (3), H2*A*···N3 2.016 (3) Å, N2—H2*A*···N3 170.85 (8)°].

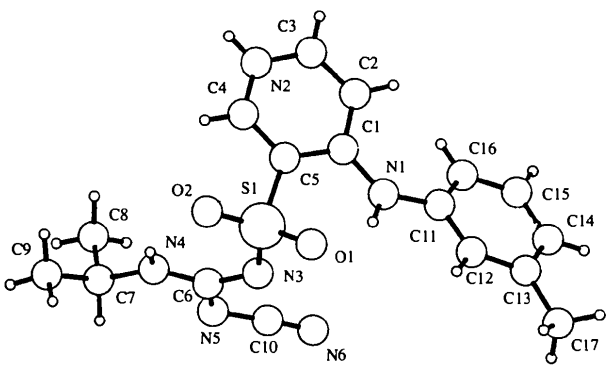


Fig. 1. Molecular structure of the title compound with the atom-labelling scheme.

Experimental

Crystal data

$C_{17}H_{20}N_6O_2S$
M_r = 372.45
Monoclinic
$P2_1/n$
a = 11.7356 (10) Å
b = 13.5707 (14) Å
c = 12.4426 (11) Å
β = 110.975 (8)°
V = 1850.3 (3) Å^3
Z = 4
D_x = 1.337 Mg m^{-3}

Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 40 reflections
θ = 25.20–41.19°
μ = 1.763 mm^{-1}
T = 293 (2) K
Prism
0.61 × 0.34 × 0.15 mm
Colourless
Crystal source: Laboratory of Medicinal Chemistry, Univ. of Liège

Data collection

Stoe Siemens AED four-circle diffractometer
ω scans
Absorption correction: semi-empirical
T_{min} = 0.479, T_{max} = 0.681
2667 measured reflections
2537 independent reflections
1854 observed reflections [$I > 2\sigma(I)$]

R_{int} = 0.0293
θ_{max} = 57.50°
$h = -11 \rightarrow 12$
$k = 0 \rightarrow 14$
$l = -13 \rightarrow 0$
2 standard reflections monitored every 100 reflections
intensity decay: 4.9%

Refinement

Refinement on F^2
$R(F)$ = 0.0387
$wR(F^2)$ = 0.1129
S = 0.983
2537 reflections
241 parameters
H atoms were included as riding atoms at calculated positions
$w = 1/[\sigma^2(F_o^2) + (0.0854P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.221 e Å^{-3}
$\Delta\rho_{min}$ = −0.227 e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0077 (6)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

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

	x	y	z	U_{eq}
C1	0.6442 (2)	0.8330 (2)	0.0283 (2)	0.0441 (6)
C2	0.7236 (2)	0.9073 (2)	0.0899 (2)	0.0518 (7)
C3	0.7873 (2)	0.8964 (2)	0.2044 (2)	0.0550 (7)
C4	0.7088 (2)	0.7386 (2)	0.2038 (2)	0.0455 (6)
C5	0.6415 (2)	0.7450 (2)	0.0895 (2)	0.0409 (6)
C6	0.3548 (2)	0.6683 (2)	0.0825 (2)	0.0472 (6)
C7	0.3309 (3)	0.5897 (2)	0.2534 (2)	0.0656 (8)
C8	0.3616 (4)	0.6730 (3)	0.3394 (3)	0.0919 (11)
C9	0.3719 (4)	0.4908 (3)	0.3105 (3)	0.0989 (12)

C10	0.2294 (2)	0.7950 (2)	−0.0056 (2)	0.0546 (7)
C11	0.5384 (2)	0.9175 (2)	−0.1636 (2)	0.0478 (6)
C12	0.4801 (2)	0.8905 (2)	−0.2785 (2)	0.0539 (7)
C13	0.4322 (2)	0.9605 (2)	−0.3644 (2)	0.0576 (7)
C14	0.4479 (3)	1.0590 (2)	−0.3339 (3)	0.0652 (8)
C15	0.5078 (3)	1.0852 (2)	−0.2211 (3)	0.0640 (8)
C16	0.5509 (2)	1.0166 (2)	−0.1350 (2)	0.0566 (7)
C17	0.3652 (3)	0.9282 (3)	−0.4874 (2)	0.0837 (11)
N1	0.5736 (2)	0.83871 (15)	−0.0851 (2)	0.0528 (6)
N2	0.7791 (2)	0.8142 (2)	0.2604 (2)	0.0512 (6)
N3	0.4117 (2)	0.67763 (14)	0.0037 (2)	0.0440 (5)
N4	0.3896 (2)	0.6036 (2)	0.1676 (2)	0.0591 (6)
N5	0.2573 (2)	0.7234 (2)	0.0720 (2)	0.0553 (6)
N6	0.1978 (2)	0.8602 (2)	−0.0699 (2)	0.0663 (7)
O1	0.55310 (14)	0.63347 (11)	−0.08854 (13)	0.0460 (5)
O2	0.59174 (15)	0.56223 (12)	0.10331 (13)	0.0489 (4)
S1	0.54599 (5)	0.64297 (4)	0.02414 (5)	0.0403 (2)

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

C1—N1	1.359 (3)	C10—N6	1.161 (4)
C1—C2	1.400 (3)	C10—N5	1.326 (4)
C1—C5	1.423 (3)	C11—C16	1.386 (3)
C2—C3	1.359 (3)	C11—C12	1.395 (3)
C3—N2	1.337 (3)	C11—N1	1.407 (3)
C4—N2	1.346 (3)	C12—C13	1.391 (4)
C4—C5	1.360 (3)	C13—C14	1.384 (4)
C5—S1	1.783 (2)	C13—C17	1.513 (4)
C6—N4	1.322 (3)	C14—C15	1.373 (4)
C6—N5	1.334 (3)	C15—C16	1.372 (4)
C6—N3	1.375 (3)	N3—S1	1.576 (2)
C7—N4	1.476 (3)	O1—S1	1.440 (2)
C7—C9	1.513 (4)	O2—S1	1.442 (2)
C7—C8	1.509 (4)		
N1—C1—C2	124.5 (2)	C13—C12—C11	121.6 (3)
N1—C1—C5	118.8 (2)	C14—C13—C12	118.1 (3)
C2—C1—C5	116.7 (2)	C14—C13—C17	121.8 (3)
C3—C2—C1	120.3 (2)	C12—C13—C17	120.0 (3)
N2—C3—C2	121.4 (2)	C15—C14—C13	120.0 (3)
N2—C4—C5	121.1 (2)	C16—C15—C14	122.2 (3)
C4—C5—C1	119.8 (2)	C15—C16—C11	118.9 (3)
C4—C5—S1	117.6 (2)	C1—N1—C11	133.1 (2)
C1—C5—S1	122.6 (2)	C4—N2—C3	120.5 (2)
N4—C6—N5	117.3 (2)	C6—N3—S1	124.8 (2)
N4—C6—N3	122.8 (2)	C6—N4—C7	125.0 (2)
N5—C6—N3	119.8 (2)	C10—N5—C6	117.5 (2)
N4—C7—C9	107.5 (2)	O1—S1—O2	117.37 (10)
N4—C7—C8	111.2 (3)	O1—S1—N3	105.85 (10)
C9—C7—C8	112.1 (3)	O2—S1—N3	116.30 (10)
N6—C10—N5	174.4 (3)	O1—S1—C5	105.51 (10)
C16—C11—C12	119.1 (2)	O2—S1—C5	105.00 (10)
C16—C11—N1	125.6 (2)	N3—S1—C5	105.71 (10)
C12—C11—N1	115.2 (2)		
N1—C1—C2—C3	177.5 (2)	C8—C7—N4—C6	−74.0 (4)
N1—C1—C5—S1	−1.6 (3)	N6—C10—N5—C6	−171.9 (29)
N1—C11—C12—C13	175.1 (2)	N4—C6—N5—C10	173.3 (2)
C2—C1—N1—C11	−15.2 (4)	N3—C6—N5—C10	−9.1 (4)
C12—C11—N1—C1	170.1 (3)	C6—N3—S1—O1	159.9 (2)
N4—C6—N3—S1	−21.8 (3)	C6—N3—S1—O2	27.6 (2)
N5—C6—N3—S1	160.8 (2)	C6—N3—S1—C5	−88.4 (2)
N5—C6—N4—C7	−1.7 (4)	C1—C5—S1—O1	41.3 (2)
N3—C6—N4—C7	−179.2 (2)	C1—C5—S1—O2	165.9 (2)
C9—C7—N4—C6	162.9 (3)	C1—C5—S1—N3	−70.6 (2)

Data collection: *DIF*4 (Stoe & Cie, 1988*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1988*b*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *PLUTO* (Motherwell, 1976). Software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry, including bond distances and angles involving H atoms, and torsion angles have been deposited with the IUCr (Reference: PA1139). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Nimesulide

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Abstract

4-Nitro-2-phenoxymethanesulfonanilide, $C_{13}H_{12}N_2O_5S$, is an anti-inflammatory drug. The molecular conformation is stabilized by an intramolecular N—H···O hydrogen bond. The angle between the two phenyl rings

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