Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} < 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.055$	$\Delta\rho_{max} = 0.240$ e Å^{-3}
$wR(F^2) = 0.087$	$\Delta\rho_{min} = -0.310$ e Å^{-3}
$S = 0.973$	Extinction correction: none
4609 reflections	Scattering factors from *International Tables for Crystallography* (Vol. C)
301 parameters	
H atoms: see below	
$w = 1/[\sigma^2(F) + 0.0005F^2]$	

Table 1. *Selected geometric parameters (Å, °)*

S1—C6	1.760 (6)	O2—C10	1.381 (7)
S1—C7	1.846 (5)	C7—C8	1.519 (9)
Cl1—C16	1.750 (13)	C8—C9	1.540 (9)
N1—C5	1.428 (6)	C10—C11	1.330 (8)
N1—C9	1.473 (6)	C10—C25	1.485 (6)
N1—C12	1.370 (8)	C11—C12	1.460 (6)
O1—C12	1.233 (7)	C11—C26	1.499 (7)
O2—C9	1.438 (5)		
C6—S1—C7	101.4 (3)	N1—C9—O2	108.9 (4)
C5—N1—C9	122.2 (5)	N1—C9—C8	112.5 (4)
C5—N1—C12	119.6 (4)	N1—C9—C19	112.3 (5)
C9—N1—C12	118.2 (4)	O2—C10—C11	121.4 (4)
C9—O2—C10	114.3 (4)	O2—C10—C25	110.2 (5)
S1—C7—C8	113.8 (4)	C10—C11—C12	119.2 (5)
S1—C7—C13	110.2 (4)	N1—C12—C11	116.1 (5)
C7—C8—C9	117.9 (4)		

The structure of the title compound was solved by direct methods. H atoms were included riding on their host atoms with an overall isotropic displacement parameter of 0.08 Å^2. The two phenyl groups (C19–C24 and C26–C31) were restrained as regular hexagons with C—C distances of 1.39 Å. Their H atoms were fixed geometrically with C—H = 0.95 Å, and allowed to ride on those atoms to which they are attached, with isotropic displacement parameters of 0.05 Å^2.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1993). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *XP* in *SHELXS*86.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1209). Services for accessing these data are described at the back of the journal.

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New Gastroprokinetic Agent TKS159: 4-Amino-5-chloro-*N*-[(2*S*,4*S*)-1-ethyl-2-hydroxymethyl-4-pyrrolidinyl]-2-methoxybenzamide

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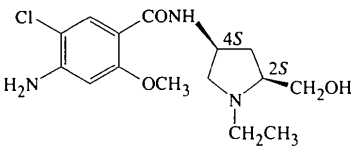
Abstract

The absolute configuration of the title compound (TKS159, $C_{15}H_{22}ClN_3O_3$) has been determined. The bent conformation of the molecule, in which the aromatic and pyrrolidine rings are at nearly 60° to each other, is maintained by intra- and intermolecular hydrogen bonds. A three-dimensional network of hydrogen bonds is formed among the amino, hydroxy and carbonyl groups of neighbouring molecules.

Comment

TKS159 is a novel gastroprokinetic benzamide derivative (Sakiyama *et al.*, 1993). Metoclopramide, a widely reputed benzamide derivative, has been known to show some unfavourable side effects, such as extrapyramidal symptoms, arising from its antagonistic action on the dopamine D_2 receptor. In contrast, TKS159 is believed

to act on the 5-HT_4 receptor (Matsuyama *et al.*, 1996), which is the most probable reason why TKS159 shows only minor side effects. In order to determine structural requirements for the minimization of side effects, the crystal structure analysis of TKS159 was carried out to establish the absolute configuration around the pyrrolidine ring.



TKS159

The pyrrolidine ring has an envelope conformation with the N3 atom located on the flap (Fig. 1). The absolute configuration of the chiral centres on the pyrrolidine ring is revealed to be 2*S*,4*S*, as expected from the synthetic route. The dihedral angle between the least-squares plane of the aromatic ring (C1–C6) and that of the pyrrolidine ring (C9–C12) is 59.6 (4)°. An intramolecular hydrogen bond [N2···O1 2.628 (2) Å] forms a pseudo-six-membered ring fused to the aromatic ring, and thus adds conformational rigidity to this part of the molecule. A three-dimensional network of hydrogen bonds is formed among the amino, hydroxy and carbonyl groups of neighbouring molecules [N1···O2 2.951 (2), N1···O3 2.944 (3) and O3···O2 2.847 (3) Å] (Fig. 2). The intra- and intermolecular hydrogen bonds enhance the tight molecular packing in the crystal. It is interesting to point out that among benzamide derivatives of the metoclopramide family which display simple hydrogen-bonding structures (Cesario *et al.*, 1981), only TKS159, possessing free NH_2 and OH groups, forms such an integrated hydrogen-bond network in the crystal. The relationship between these structural differences and the pharmacological profile will be elucidated more explicitly by measuring the NMR spectra in solution; this is currently under investigation.

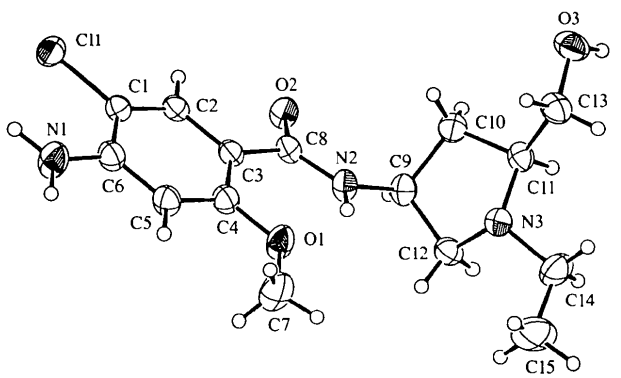


Fig. 1. Displacement ellipsoid plot (30% probability level) of TKS159 with the atomic numbering. H atoms are represented as spheres equivalent to B = 1.0 Å^2.

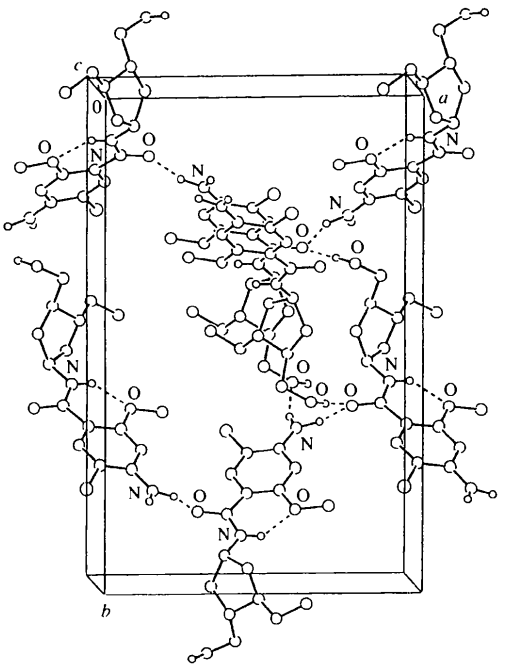


Fig. 2. Perspective view of the molecular packing. Hydrogen bonds are shown by broken lines.

Experimental

Crystals of the title compound were obtained by recrystallization from ethyl acetate.

Crystal data

$C_{15}H_{22}ClN_3O_3$
M_r = 327.81
Orthorhombic
$P2_12_12_1$
a = 13.3780 (6) Å
b = 20.6464 (6) Å
c = 6.2510 (4) Å
V = 1726.6 (1) Å^3
Z = 4
D_x = 1.261 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 24 reflections
θ = 31.6–32.5°
μ = 2.094 mm^{-1}
T = 296 K
Prismatic
0.40 × 0.40 × 0.30 mm
Colourless

Data collection

Rigaku AFC-5*R* diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North *et al.*, 1968)
T_{min} = 0.440, T_{max} = 0.534
3039 measured reflections
1514 independent reflections (plus 1041 Freidel reflections)
2439 reflections with $I > 2\sigma(I)$
R_{int} = 0.041
θ_{max} = 60.1°
h = −15 → 15
k = −23 → 23
l = −7 → 7
3 standard reflections every 150 reflections
intensity decay: none

Refinement

Refinement on F
$R = 0.046$
$wR = 0.065$
$S = 1.895$
2555 reflections
203 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o) + 0.00002|F_o|^2]$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.31$ e Å^{-3}
Extinction correction: $I_{corr} = I_o(1 + gI_c)$
Extinction coefficient: $g = 1.11 \times 10^{-5}$
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute configuration: Flack (1983)
Flack parameter = 0.02 (2)

Table 1. *Selected geometric parameters (Å, °)*

Cl1—C1	1.745 (3)	N3—C12	1.458 (4)
O1—C4	1.364 (4)	N3—C14	1.457 (4)
O1—C7	1.415 (4)	C3—C8	1.494 (4)
O2—C8	1.243 (3)	C9—C10	1.525 (4)
O3—C13	1.416 (4)	C9—C12	1.512 (4)
N1—C6	1.351 (4)	C10—C11	1.526 (4)
N2—C8	1.326 (4)	C11—C13	1.509 (4)
N2—C9	1.456 (4)	C14—C15	1.497 (6)
N3—C11	1.465 (4)		
C4—O1—C7	119.6 (3)	N2—C9—C10	113.2 (3)
C8—N2—C9	124.2 (2)	N2—C9—C12	109.7 (3)
C11—N3—C12	103.5 (2)	C10—C9—C12	103.4 (2)
C11—N3—C14	113.2 (3)	C9—C10—C11	105.8 (3)
C12—N3—C14	112.3 (3)	N3—C11—C10	103.4 (2)
O1—C4—C3	116.9 (3)	N3—C11—C13	113.1 (2)
O1—C4—C5	122.5 (3)	C10—C11—C13	113.7 (3)
C3—C4—C5	120.7 (3)	N3—C12—C9	103.9 (2)
O2—C8—N2	121.2 (3)	O3—C13—C11	111.3 (3)
O2—C8—C3	120.1 (3)	N3—C14—C15	113.6 (4)
N2—C8—C3	118.7 (3)		
O2—C8—N2—C9	−4.5 (4)	N3—C12—C9—C10	30.9 (3)
O2—C8—C3—C4	170.4 (3)	C8—N2—C9—C10	82.6 (3)
N2—C8—C3—C4	−9.9 (4)	C8—N2—C9—C12	−162.5 (3)
N3—C11—C10—C9	−20.6 (3)	C11—C10—C9—C12	−6.1 (3)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2N···O1	0.946	1.892	2.628 (2)	132.8
O3—H3O···O2^{i}	1.07 (5)	1.78 (5)	2.847 (3)	173 (4)
N1—H1N*A*···O2^{ii}	0.949	2.184	2.951 (2)	137.1
N1—H1N*B*···O3^{iii}	0.950	2.135	2.944 (3)	142.3

Symmetry codes: (i) $-\frac{1}{2} - x, -1 - y, \frac{1}{2} + z$; (ii) $\frac{1}{2} + x, -\frac{1}{2} - y, 1 - z$; (iii) $-x, \frac{1}{2} + y, \frac{1}{2} - z$.

Refinement was carried out using full-matrix least-squares methods. Anomalous-dispersion effects were included in F_c (Ibers & Hamilton, 1964); the values for $\Delta f'$ and $\Delta f''$ were those of Creagh & McAuley (1992). The values for the mass attenuation coefficients are those of Creagh & Hubbel (1992). All non-H atoms were refined anisotropically, and all H atoms, except for H3O, were placed in calculated positions and were not refined. Atom H3O was located in a difference Fourier map and refined isotropically.

Data collection: *Rigaku AFC Software* (Rigaku Corporation, 1990). Cell refinement: *Rigaku AFC Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1993). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985) and *DIRDIF*94 (Beurskens *et al.*, 1994). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *TEXSAN*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1037). Services for accessing these data are described at the back of the journal.

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Two Oxazolidinone Derivatives

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Abstract

The structures of two substituted oxazolidinones, namely, 4-hydroxymethyl-4-methyloxazolidin-2-one [$C_5H_9NO_3$, (1)] and 4-ethyl-4-hydroxymethyloxazolidin-2-one [$C_6H_{11}NO_3$, (2)], are reported. Bond distances in the two structures are almost identical. The oxazolidinone rings both adopt envelope conformations; the fold in (1) is significantly larger than that in (2). There is no