O1—C1—O2	124.00 (18)	N1—C3—C4	106.75 (16)
O1—C1—C2	112.05 (16)	C3—C4—C5	129.84 (18)
O2—C1—C2	123.95 (18)	C8—C9—C10	129.88 (18)
N1—C2—C1	109.24 (15)	N1—C10—C9	102.20 (14)
N1—C2—C21	112.79 (15)		

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

*Cg*1 is the ring centroid of the isoindolinone phenyl ring and *Cg*2 is the ring centroid of the 3-phenyl ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O3^{i}	0.87	1.78	2.625 (2)	163
C5—H5···O2^{ii}	0.93	2.36	3.281 (3)	171
C6—H6···*Cg*2^{iii}	0.93	2.69	3.623 (2)	176
C16—H16···*Cg*1^{iv}	0.93	2.97	3.739 (2)	141

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

H atoms were allowed for as riding atoms with C—H distances in the range 0.93–0.98 Å; the coordinates of the carboxylic acid H atom were located in a difference Fourier map in the latter stages of refinement and included in the structure-factor calculations with O—H 0.87 Å and C—O—H 110°.

Data collection: *CAD-4-PC Software* (Enraf–Nonius, 1992). Cell refinement: *SET*4 and *CELDIM* in *CAD-4-PC Software*. Data reduction: *DATRD*2 in *NRCVAX*96 (Gabe *et al.*, 1989). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*a*). Program(s) used to refine structure: *NRCVAX*96 and *SHELXL*97 (Sheldrick, 1997*b*). Molecular graphics: *NRCVAX*96, *ORTEP*II (Johnson, 1976) and *PLUTON* (Spek, 1997*b*). Software used to prepare material for publication: *NRCVAX*96, *SHELXL*97 and *WordPerfect* macro *PRPCIF*97 (Ferguson, 1997).

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6-(4-Chlorophenyl)-3-methyl-2,4a-diphenyl-5,6-dihydro-1*H*,4a*H*-1,3-oxazino[2,3-*d*][1,5]-benzothiazepin-1-one

JIAXI XU,[a] SHENG JIN,[a] ZEYING ZHANG[b] AND THOMAS C. W. MAK[b]

[a]*College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, People's Republic of China, and* [b]*Department of Chemistry, The Chinese University of Hong Kong, Shatin, NT, Hong Kong. E-mail: jxxu@chemms.chem.pku.edu.cn*

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Abstract

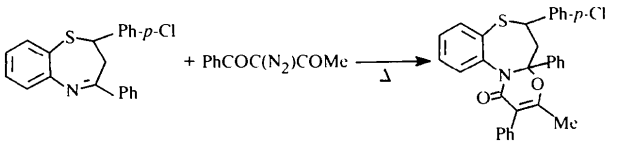
The title compound, $C_{31}H_{24}ClNO_2S$, has a *cis*-ring-fusion tricyclic structure, which is formed from a benzene ring, a seven-membered heterocyclic thiazepine ring and a 1,3-oxazinone ring. The 1,5-thiazepine ring has a slightly distorted boat-like conformation, whereas the 1,3-oxazinone ring adopts a half-chair conformation.

Comment

Benzothiazepines, especially those with a fused heterocyclic ring, are potential pharmaceutical agents (Corral *et al.*, 1985; Bock *et al.*, 1989; Xu & Jin, 1994). 5,6-Dihydro-1*H*,4a*H*-1,3-oxazino[2,3-*d*][1,5]benzothiazepin-1-one derivatives with potential anxiolytic and hypnotic activities (Sternbach, 1979; Xu & Jin, 1992) were synthesized by the Diels–Alder reaction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepine derivatives and α-diazo-β-diketone (Capuano & Gartner, 1981; Capuano & Wamprecht, 1986). When an asymmetric α-diazo-β-diketone, such as 2-diazo-1-phenyl-1,3-butanedione, is

used as the potential diene, two possible α-carbonyl ketenes may be generated by Wolff rearrangement, *viz.* acetyl phenyl ketene and benzoyl methyl ketene by phenyl- or methyl-group migration, respectively. It is well known that 2-diazo-1-phenyl-1,3-butanedione undergoes thermal Wolff rearrangement in methanol, with migratory ability in the order Ph > Me (Tomioka *et al.*, 1983; Sawaki *et al.*, 1983).

In order to elucidate the cycloaddition mechanism of the thermal Wolff rearrangement of asymmetric 2-diazo-1-phenyl-1,3-butanedione in the Diels–Alder reaction in non-polar xylene, and to study the conformation of its cycloadduct with 2,3-dihydro-1,5-benzothiazepine, the title compound, 6-(4-chlorophenyl)-3-methyl-2,4a-diphenyl-5,6-dihydro-1*H*,4a*H*-1,3-oxazino[2,3-*d*][1,5]-benzothiazepin-1-one, (I), was synthesized and studied by X-ray diffraction analysis.



(I)

The molecular backbone is a tricyclic system, formed from a benzene ring, a seven-membered heterocyclic thiazepine ring and a 1,3-oxazinone ring. The central seven-membered heterocycle is in a slightly distorted boat-like conformation, and is *cis*-fused to the 1,3-oxazinone ring at the N1 and C9 atoms, while the latter moiety is in a half-chair conformation. The *p*-chlorophenyl group on C7 and the phenyl group on C9 are equatorial in the central ring (Fig. 1), hence the cycloaddition reaction is a *cis*-addition reaction. The methyl group on C10 suggests that the cycloadduct might be obtained from acetyl phenyl ketene and benzothiazepine; hence, we may conclude that the thermal Wolff rearrangement of 2-diazo-1-phenyl-1,3-butanedione gives mainly acetyl phenyl ketene in non-polar xylene under heating conditions, and that the migratory ability of the phenyl group is greater than that of the methyl group under these conditions.

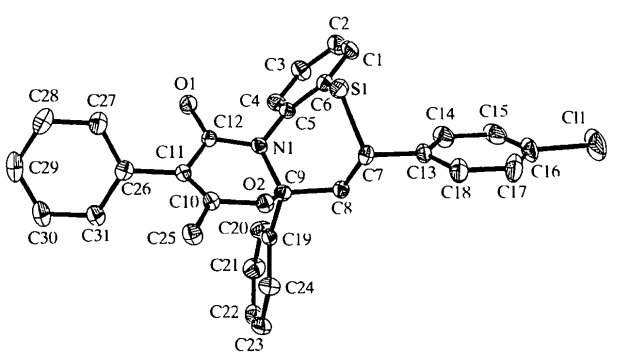


Fig. 1. Perspective view of the title compound with the atom labelling. Displacement ellipsoids are shown at the 30% probability level.

The slightly twisted boat-like conformation of the central ring may not be favourable, but is probably stabilized by the presence of the heteroatoms (S and N) in the ring, as well as by the bulky exocyclic phenyl substituents attached to atoms C7 and C9. The molecule contains two chiral C atoms, C7 and C9, with a *rel*-(*R*,*S*) configuration.

The conformation of the central seven-membered ring was determined using the least-squares plane passing through atoms S1, N1 and C9. Atoms C5, C6, C7 and C8 lie 1.024 (2), 1.139 (3), 0.432 (2) and 0.892 (2) Å, respectively, above this plane. The dihedral angle of 13.8 (2)° between the S1, N1, C7 and S1, N1, C9 planes in the seven-membered thiazepine ring also shows it to be in a twist-boat conformation. Atomic deviations from the plane defined by atoms C11, C10 and O2 are −0.234 (3), −0.087 (2) and 0.554 (3) Å for atoms C12, N1 and C9, respectively. The bond lengths S1—C6(Ar) [1.760 (6) Å] and S1—C7 [1.846 (5) Å] are unequal, as the former is affected by the conjugation of the π-electron system in an aromatic ring. No significant intermolecular or interatomic contacts could be found.

Experimental

2-(4-Chlorophenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (4 mmol) and 2-diazo-1-phenyl-1,3-butanedione (4.4 mmol; Meier *et al.*, 1986) were dissolved in xylene (10 ml). The mixture was then stirred for 10–15 min at 373 K. Xylene was evaporated at reduced pressure to give a brown oil. This material was recrystallized from benzene to yield white crystalline (I). Colourless single crystals were obtained by evaporation from a saturated ethyl acetate solution.

Crystal data

$C_{31}H_{24}ClNO_2S$
M_r = 510.05
Monoclinic
$P2_1/c$
a = 12.672 (3) Å
b = 15.430 (3) Å
c = 14.731 (3) Å
β = 114.77 (3)°
V = 2615.4 (13) Å^3
Z = 4
D_x = 1.295 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 2.0–25.0°
μ = 0.255 mm^{-1}
T = 294 (2) K
Plate
0.30 × 0.18 × 0.10 mm
Colourless

Data collection

Rigaku AFC-7*R* diffractometer
ω scans
Absorption correction: none
4829 measured reflections
4609 independent reflections
1983 reflections with $I > 6\sigma(I)$

R_{int} = 0.027
θ_{max} = 25°
h = 0 → 15
k = 0 → 18
l = −17 → 15
3 standard reflections
every 150 reflections
intensity decay: none

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

TSUTOMU ADACHI,[a] JUN-ICHI MIZOGUCHI,[a] YASUO HAYASHI,[a] YUKO YAMASHOJI,[b] NOBUKO KANEHISA,[c] YASUSHI KAI[c] AND YOSHIHISA INOUE[b]

[a]*Research and Development Department, Teikoku Chemical Industries Co. Ltd, 5-41 Senzo, Itami, Hyogo 664, Japan,* [b]*Department of Molecular Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan, and* [c]*Department of Material Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan. E-mail: yamashoj@chem.eng.osaka-u.ac.jp*

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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