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4-(3,4-Dichlorophenyl)-9-(4-methylphenylsulfonyl)-4,9-diazatetracyclo-[5.3.1.0^{2,6}.0^{8,10}]undecane-3,5-dione and 4-(4-chlorophenyl)-9-(4-methylphenylsulfonyl)-4,9-diazatetracyclo-[5.3.1.0^{2,6}.0^{8,10}]undecane-3,5-dione

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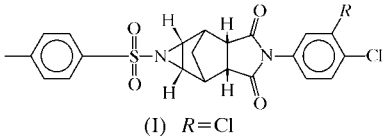
The title compounds, $C_{22}H_{18}Cl_2N_2O_4S$, (I), and $C_{22}H_{19}ClN_2O_4S$, (II), respectively, are structural cyclic imide analogues of pharmaceutical interest. The configurations *exo–endo* for (I) and *endo–endo* for (II) were established.

Comment

Maleimides and aziridines are well known for the diversity of their applications in medicinal chemistry. A great number of compounds with an aziridine ring have been synthesized, many of which have shown significant cytotoxicity against some tumour cells, such as mitomycin C, which is a bioreductive alkylating agent used in anticancer therapy (Kim *et al.*, 1996; Kumar *et al.*, 1996). Maleimides have also shown activity against some types of tumour, together with other pharmacological properties such as sedative, hypnotic, antihypertensive and diuretic properties, and in chemotherapy for tuberculosis. An example of a useful maleimide is mitonafide, which is already used as a drug and which has also been used as a model in the development of new drugs with improved effectiveness and reduced adverse effects (Asbury *et al.*, 1994; Cechinel Filho *et al.*, 2003).



(I) R=Cl
(II) R=H

In order to obtain additional proof that the products we synthesized here the *exo–endo*, in (I), and *endo–endo*, in (II), configurations, we have determined the molecular and crystal structures by X-ray diffraction and the results are presented here. According to a recent search of the Cambridge Structural Database (CSD, Version 5.25; Allen, 2002), the title compounds are the first examples of disubstituted norbornane with *p*-toluenesulfonamide and maleimide groups to be characterized by X-ray diffraction.

Compounds (I) (Fig. 1) and (II) (Fig. 2) show the *endo* configuration with respect to the maleimide ring (C4/C5/N6/C7/C8), which is essentially planar in both structures. The dihedral angles between the planes of the C4/C5/N6/C7/C8 and N1/C2/C10 rings [54.9 (1)° in (I) and 2.6 (2)° in (II)] clearly indicate the different configurations, *exo* and *endo*, respectively, with respect to the aziridine ring (N1/C2/C10). In addition, the torsion angles N1—C2—C3—C11 and C11—C3—C4—C5 (Tables 1 and 2) also confirm the configurations as *exo–endo* for (I) and *endo–endo* for (II).

The three-membered aziridine ring is an almost-perfect isosceles triangle in both stereoisomers, with the N1—C2 and N1—C10 bond lengths being equal within experimental error and the sums of the internal angles being very close to 180° (Tables 1 and 2). The C—N bonds in the aziridine rings are about 0.1 Å longer than those in the maleimide rings. This results from a combination of factors, such as a high level of tension in the three-membered ring, the substitution of the phenylsulfonyl moiety at N1 [due to the electron-withdrawing effect from this group, as described by Govindasamy *et al.* (1998)] and the hybridization character at atoms N1 and N6. The sums of the angles around N1 [290.0° in (I) and 288.6° in (II)] and N6 [360.1° in (I) and 359.4° in (II)] indicate essen-

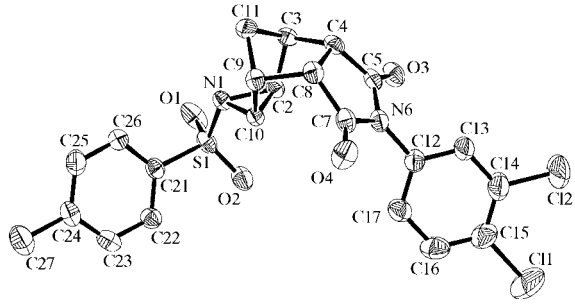


Figure 1
The molecular structure of (I), with the atom-labelling scheme. Displacement ellipsoids are shown at the 40% probability level and H atoms have been omitted for clarity.

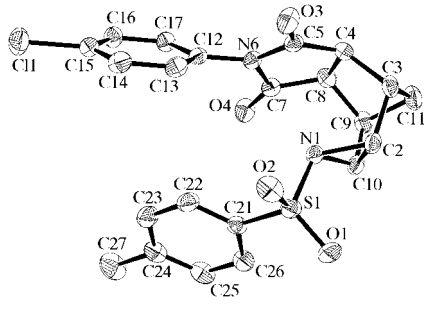


Figure 2
The molecular structure of (II), with the atom-labelling scheme. Displacement ellipsoids are shown at the 40% probability level and H atoms have been omitted for clarity.

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tially sp^3 and sp^2 hybridization, respectively. This is as expected and is in agreement with related structures (Kajfez *et al.*, 2003; Matthews *et al.*, 2001; Yoshihara *et al.*, 1999; Massa *et al.*, 1983). In the norbornane skeletons of both (I) and (II), the C2—C10 bond is a little shorter than the neighbouring C—C bonds (Tables 1 and 2). This should be induced by the restriction imposed by the formation of the aziridine ring and was also observed in the related structures reported by Matthews *et al.* (2001), and references therein.

The environment around the S atoms in both compounds is best described as a distorted tetrahedron, with angles ranging from 101.02 (14) to 118.64 (10)°, as observed in similar structures (Massa *et al.*, 1983; Seshadri *et al.*, 2002). Other geometric parameters show normal values and are within the expected ranges.

The three-dimensional packing of the title compounds is strongly influenced by van der Waals interactions. There is no evidence of π–π stacking involving the phenyl rings. All O atoms in (I) and three O atoms (two from the maleimide ring and one from the sulfonyl moiety) in (II) participate in C—H···O interactions. The geometric parameters of these interactions are available in the archived CIF.

Experimental

For the preparation of the *exo–endo* compound, (I), *p*-tolylsulfonyl azide (2.00 g, 10.1 mmol) was added to a mixture of 4-(3,4-dichlorophenyl)-4-azatricyclo[5.2.1.0^{2,6}-*endo*]dec-8-ene-3,5-dione (2.50 g, 8.11 mmol) in acetonitrile (25 ml), prepared as described by Salakhov *et al.* (1979) and Chenier *et al.* (1992). The reaction was refluxed for 18 h and the solvent was evaporated *in vacuo*. The solid residue was triturated with methanol–chloroform (3:7) and filtered off with suction to give the crude product. The formation of the *endo–endo* isomer was also observed together with (I), but unfortunately the former isomer could not afford crystals for X-ray studies. The two isomers were isolated by column chromatography (silica gel, dichloromethane–hexane, 1:4). For the preparation of the *endo–endo* compound, (II), *p*-tolylsulfonyl azide (2.92 g, 14.8 mmol) was added to 4-(4-chlorophenyl)-4-azatricyclo[5.2.1.0^{2,6}-*endo*]dec-8-ene-3,5-dione (2.00 g, 7.31 mmol) in acetonitrile (20 ml), prepared as described by Salakhov *et al.* (1979) and Chenier *et al.* (1992). The reaction was refluxed for 18 h and the solvent was evaporated *in vacuo*. The solid residue was triturated with methanol–chloroform (3:7) and filtered off with suction to give the crude product. The *endo–endo* and *exo–endo* products were purified by column chromatography (silica gel, ethyl acetate–acetone–hexane, 6:3:11). The latter isomer could not afford crystals for X-ray analysis. Compounds (I) and (II) were crystallized from solutions in methanol–chloroform (1:2) by slow evaporation of the solvent mixture.

Compound (I)

Crystal data

$C_{22}H_{18}Cl_2N_2O_4S$
M_r = 477.34
Monoclinic, $P2_1/c$
a = 12.856 (1) Å
b = 15.689 (1) Å
c = 10.727 (1) Å
β = 100.27 (1)°
V = 2128.9 (3) Å^3
Z = 4
D_x = 1.489 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 6.6–12.2°
μ = 0.44 mm^{-1}
T = 293 (2) K
Irregular plate, colourless
0.50 × 0.40 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.844, T_{max} = 0.934
3962 measured reflections
3785 independent reflections
2300 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 25.1°
$h = -15 \rightarrow 0$
$k = 0 \rightarrow 18$
$l = -12 \rightarrow 12$
3 standard reflections
every 200 reflections
intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.137
S = 1.03
3785 reflections
291 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0571P)^2 + 1.0126P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.52 e Å^{-3}
$\Delta\rho_{min}$ = −0.46 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0073 (9)

Table 1
Selected geometric parameters (Å, °) for (I).

S1—O1	1.429 (3)	N1—C2	1.495 (4)
S1—O2	1.431 (3)	C2—C10	1.481 (4)
S1—N1	1.658 (3)	C2—C3	1.526 (4)
S1—C21	1.761 (3)	C4—C8	1.548 (4)
N1—C10	1.493 (4)		
O1—S1—O2	117.21 (18)	C10—N1—S1	116.8 (2)
O1—S1—N1	105.57 (15)	C2—N1—S1	113.8 (2)
O2—S1—N1	112.42 (14)	C10—C2—N1	60.22 (19)
O1—S1—C21	110.71 (16)	C5—N6—C7	113.1 (3)
O2—S1—C21	108.70 (16)	C5—N6—C12	124.5 (3)
N1—S1—C21	101.02 (14)	C7—N6—C12	122.5 (3)
C10—N1—C2	59.42 (18)	C2—C10—N1	60.37 (18)
N1—C2—C3—C11	30.5 (3)	C2—C3—C4—C8	−72.3 (3)
N1—C2—C3—C4	134.4 (3)	C4—C8—C9—C10	68.0 (3)
C2—C3—C4—C5	42.3 (3)	C7—C8—C9—C11	−153.4 (3)
C11—C3—C4—C5	148.3 (3)	C8—C9—C10—N1	−135.4 (2)

Compound (II)

Crystal data

$C_{22}H_{19}ClN_2O_4S$
M_r = 442.90
Triclinic, $P\overline{1}$
a = 8.975 (2) Å
b = 10.167 (5) Å
c = 12.876 (1) Å
α = 105.06 (2)°
β = 109.89 (2)°
γ = 100.97 (3)°
V = 1015.4 (6) Å^3
Z = 2
D_x = 1.449 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 8.6–17.6°
μ = 0.32 mm^{-1}
T = 293 (2) K
Irregular block, colourless
0.43 × 0.40 × 0.36 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
3941 measured reflections
3764 independent reflections
3118 reflections with $I > 2\sigma(I)$
R_{int} = 0.013
θ_{max} = 25.5°
$h = -10 \rightarrow 10$
$k = -11 \rightarrow 12$
$l = -15 \rightarrow 0$
3 standard reflections
every 200 reflections
intensity decay: 1%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0472P)^2 + 0.3187P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.036$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.097$	$\Delta\rho_{max} = 0.24$ e Å^{-3}
$S = 1.04$	$\Delta\rho_{min} = -0.26$ e Å^{-3}
3764 reflections	Extinction correction: *SHELXL*97
273 parameters	Extinction coefficient: 0.027 (2)
H-atom parameters constrained	

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

S1—O2	1.4318 (15)	N1—C2	1.500 (2)
S1—O1	1.4334 (15)	C2—C10	1.483 (3)
S1—N1	1.6688 (15)	C2—C3	1.526 (3)
S1—C21	1.759 (2)	C4—C8	1.539 (3)
N1—C10	1.498 (2)		
O2—S1—O1	118.64 (10)	C10—N1—S1	116.28 (11)
O2—S1—N1	105.22 (8)	C2—N1—S1	113.05 (11)
O1—S1—N1	111.40 (9)	C10—C2—N1	60.32 (11)
O2—S1—C21	108.83 (9)	C5—N6—C7	111.87 (14)
O1—S1—C21	109.13 (10)	C5—N6—C12	124.13 (14)
N1—S1—C21	102.35 (8)	C7—N6—C12	123.41 (14)
C10—N1—C2	59.29 (11)	C2—C10—N1	60.39 (11)
N1—C2—C3—C4	3.7 (2)	C7—C8—C9—C10	−48.3 (2)
N1—C2—C3—C11	−99.41 (17)	C7—C8—C9—C11	−151.95 (16)
C2—C3—C4—C5	53.6 (2)	C8—C9—C10—N1	−3.8 (2)
C11—C3—C4—C5	156.92 (16)	C11—C9—C10—N1	99.95 (16)

H atoms were placed in idealized positions and refined using a riding model, with C—H distances of 0.98, 0.97, 0.96 and 0.93 Å, and with U_{iso}(H) values fixed at 1.2, 1.2, 1.5 and 1.2U_{eq}(C) for CH, CH_2, CH_3 and aromatic CH H atoms, respectively. In (I), a C_2 rotation on the N6—C12 bond causes structural disorder at atom Cl2, which is partially bonded to atoms C14 and C16, with occupancy factors of 0.862 (3) and 0.138 (3), respectively. The complementary occupancy factors at atoms C14 and C16 are occupied by H atoms fixed geometrically. The H atoms on C27 were placed in the atom list using an idealized disordered model for a methyl group.

For both compounds, data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *SET*4 in *CAD*-4 *EXPRESS*; data reduction: *HELENA* (Spek, 1996); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1757). Services for accessing these data are described at the back of the journal.

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