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Two (*E*)-2-arylidene-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline compounds: supramolecular frameworks built with C—H···O and C—H···π(arene) hydrogen bonds and π–π stacking interactions

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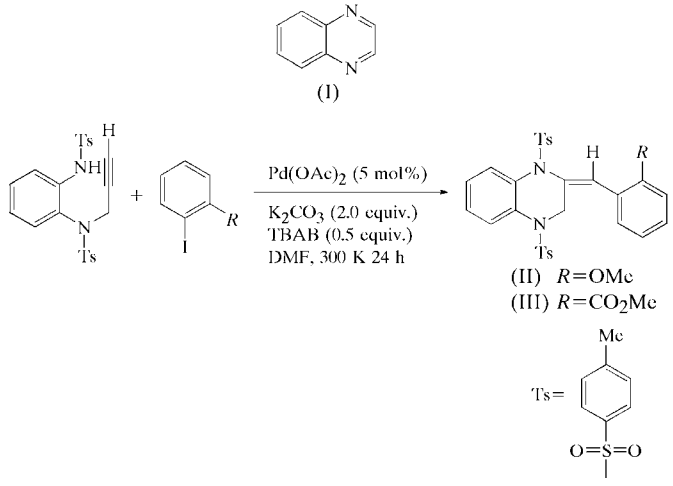
The pyrazine ring in two N-substituted quinoxaline derivatives, namely (*E*)-2-(2-methoxybenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, $C_{30}H_{28}N_2S_2O_5$, (II), and (*E*)-methyl 2-[(1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxalin-2-ylidene)methyl]benzoate, $C_{31}H_{28}N_2S_2O_6$, (III), assumes a half-chair conformation and is shielded by the terminal tosyl groups. In the molecular packing of the compounds, intermolecular C—H···O hydrogen bonds between centrosymmetrically related molecules generate dimeric rings, *viz.* $R_2^2(22)$ in (II) and $R_2^2(26)$ in (III), which are further connected through C—H···π(arene) hydrogen bonds and π–π stacking interactions into novel supramolecular frameworks.

Comment

The quinoxaline heterocycle, (I), has been an integral part in many natural products (Dell *et al.*, 1975). Several quinoxaline derivatives have been successfully used in the pharmaceutical industry as synthetic precursors of antihypertensives, analgesics and neurotransmitter antagonists (Fuente *et al.*, 2000; Kher *et al.*, 1995). Furthermore, the *in vitro* anticancer activity of quinoxaline compounds has recently emerged as a promising modality against cancer and allied diseases (Lorgia *et al.*, 1995; Bonnett, 1995). The DNA photocleaving property of quinoxaline-based compounds with substitutions at the C-positions of the pyrazine ring has been attributed to the conjugated C=N bonds in these systems (Toshima *et al.*, 2002). Although the syntheses and crystal structure analyses of different C-substituted quinoxalines have been reported (Dobrzańska & Lloyd, 2005; Zhao & Du, 2003; Sessler *et al.*, 2002; Chowdhury *et al.*, 2001), the corresponding reports of N-substituted quinoxalines have been rather sparse (Banerjee *et al.*, 2001). As part of an ongoing programme on the synthesis and structural characterization of novel N-substituted quinoxalines, we synthesized two 2-alkylidene-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxalines *via* palladium-catalyzed hetero-annulation of N-substituted phenylamines. In order to establish the regio- and stereospecificities of the reaction and to build up a hierarchy for such systems, X-ray analyses of (*E*)-2-(2-methoxybenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, (II), and (*E*)-methyl 2-[(1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxalin-2-ylidene)methyl]benzoate, (III), were undertaken.



The title compounds (Figs. 1 and 2) consist of a quinoxaline ring system with two *p*-tosyl and one substituted benzylidene group at the 1-, 4- and 2-positions, respectively. The *E* configuration of the molecules of (II) and (III), as established from the $^3J_{C-H}$ coupling constant (Moreau *et al.*, 1991; Cabiddu *et al.*, 1986) value of 7.76 Hz for both compounds, is confirmed by the N1—C22—C23—C24 torsion angle of

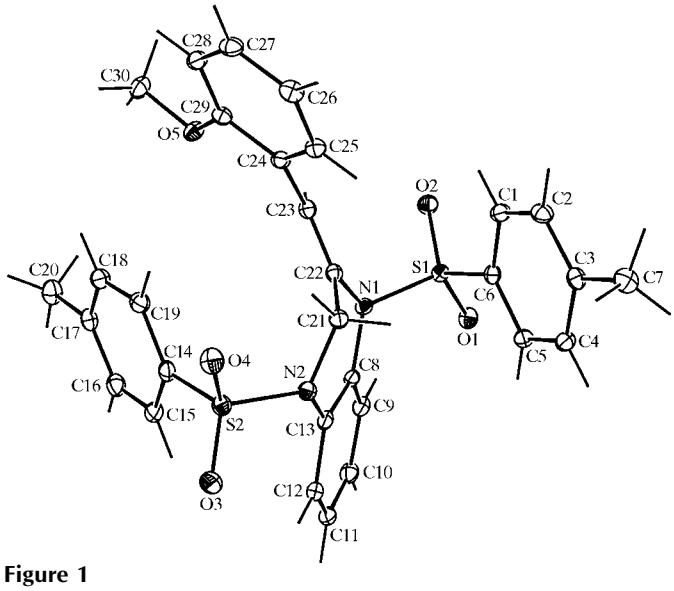


Figure 1
A view of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

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−172.0 (1)° for (II) and 171.7 (2)° for (III). The pyrazine ring (*B*; N1/C8/C13/N2/C21/C22) fused to the benzene ring (*A*; C8–C13) in both compounds assumes a half-chair conformation, with ring-puckering parameters (Cremer & Pople, 1975) Q, θ and φ of 0.413 (1) Å, 49.7 (2)° and 264.5 (2)°, respectively, for (II), and 0.413 (2) Å, 132.0 (3)° and 77.8 (3)°, respectively, for (III). The deviations of atom C21 from the corresponding least-squares planes through the remaining endocyclic atoms of the C_4N_2 ring are 0.543 (2) and −0.557 (2) Å, respectively, for (II) and (III).

The molecular geometries of (II) and (III) (Tables 1 and 3) agree well with the corresponding values reported for similar N-substituted quinoxaline compounds (Banerjee *et al.*, 2001). The sums of the valence angles at the two N atoms (N1 and N2) of the pyrazine ring are 349.1 (1) and 348.5 (1)°, respectively, for (II), and 348.2 (1) and 347.8 (1)°, respectively, for (III), deviating significantly from 360°, showing that these atoms display pyramidal distortion. The conformation of the molecules can be described by the torsion angles C6—S1—N1—C8 and C14—S2—N2—C21, which are −91.8 (1) and 84.8 (1)°, respectively, in (II), and 84.8 (2) and −77.3 (1)°, respectively, in (III). These values indicate that the tosyl groups in the compounds adopt folded conformations, with the benzene rings *C* (C1–C6) and *D* (C14–C19) shielding the central quinoxaline moiety. The dihedral angle between the essentially planar benzene rings *C* and *D* is 7.3 (1)° in (II) and 4.7 (1)° in (III). The S═O bond distances in the compounds are in the range 1.427 (1)–1.434 (1) Å (Tables 1 and 3) and are consistent with those found in structures containing sulfonyl groups (Ghosh *et al.*, 2006; Wardell *et al.*, 2005). However, the angular disposition of the bonds about atoms S1 and S2 in the two compounds deviates considerably from that of a regular tetrahedron; the largest and the smallest angles are O1—S1—O2 of 119.5 (1)° and N1—S1—C6 of 104.1 (1)°, respectively, in (II). Similar distortion in sulfonyl geometry has been reported in the literature (Chumakov *et al.*, 2005; Sonar *et al.*, 2004) and can be attributed to the repulsive interaction between the short S═O bonds. Although both compounds (II) and (III) contain four essentially planar benzene rings (*A*, *C*, *D* and *E*), the lack of π-bonding in the branches between the benzene rings precludes any possible π conjugation across the whole molecules. The aromatic nature of the rings is therefore localized within the rings and on their direct substituents.

The similarity of the lattice parameters and space groups between (II) and other N-substituted quinoxaline compounds reported earlier by Banerjee *et al.* (2001), namely 2-(4-

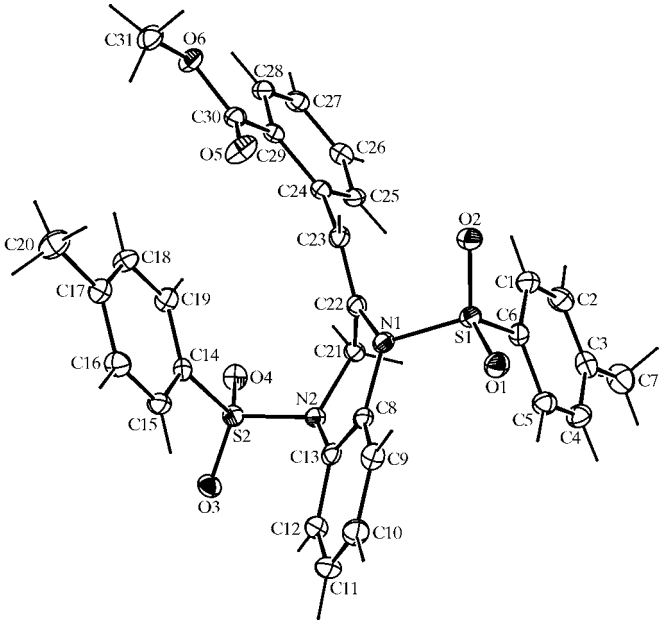

Figure 2
A view of (III), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbritary radii.

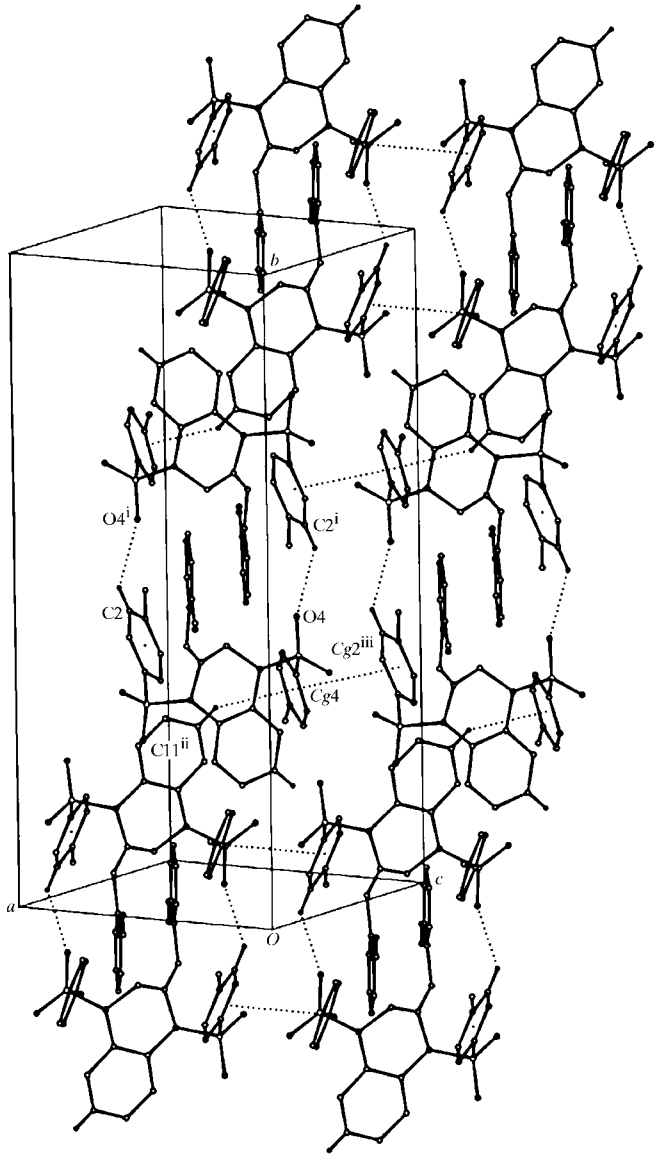

Figure 3
The three-dimensional supramolecular framework in (II) formed by C—H···O and C—H···π(arene) hydrogen bonds and π–π stacking interactions. [Symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $x, \frac{1}{2}-y, -\frac{1}{2}+z$; (iii) $-1+x, y, z$.]

methylbenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, 2-(4-methoxybenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline and 2-(3-chlorobenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, hereinafter denoted (IV), (V) and (VI), respectively, suggests some degree of isostructurality among the compounds. The results (Table 5) of the calculation of the unit-cell similarity descriptor π (Kálmán *et al.*, 1993), the isostructurality index I_i (Kálmán *et al.*, 1993) and the volumetric isostructurality index I_v (Fábián & Kálmán, 1999) reveal a high degree of isostructurality between compounds (II) and (VI). The volumetric index of isostructurality between compounds (II) and (VI) amounts to 77% for the whole unit cell, with four molecules indicating significant packing similarity between the two structures. The large values of the isostructurality index $I_i(61)$ between (II) and (IV) and between (II) and (V) (Table 5) indicate that compound (II) is not isostructural with compounds (IV) or (V). This is probably a consequence of the exchange of cell-axis lengths in compound (II) compared with those in (IV) and (V), which results in different packing arrangements in these compounds.

Despite the close similarity between compounds (II) and (III) in terms of their overall constitutions and detailed molecular geometries, there are some significant differences in the nature of their supramolecular aggregation. The molecules of (II) are linked into a three-dimensional framework by a combination of C—H···O and C—H···π(arene) hydrogen bonds (Table 2), and by π–π stacking interactions. It is convenient to consider the substructures generated by each type of hydrogen bond acting individually, and then the combination of substructures to build up the resulting assembly. The molecules in (II) related by inversion, with benzene atom C2 in the molecule at (x, y, z) acting as a donor to sulfonamide atom O4 in the molecule at $(1-x, 1-y, 1-z)$, generate a centrosymmetric $R_2^2(22)$ (Bernstein *et al.*, 1995) dimeric ring centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$. Propagation of these dimers through C—H···π(arene) hydrogen bonds (Table 3) produces two chains, the first running parallel to the [010] direction and generated by the 2_1 screw axis along $(0, y, \frac{1}{4})$ and the second running parallel to the [001] direction and generated by the *c*-glide plane at $y = \frac{1}{4}$. The combination of [010] and [001] chains in (II) produces a complex sheet parallel to (100). Finally, the interconnection of molecular sheets through a π–π stacking interaction (Table 3) between the C1–C6 and C14–C19 aryl rings of the molecules at (x, y, z) and $(1+x, y, z)$, respectively, forms a three-dimensional supramolecular assembly (Fig. 3) in (II).

In (III), a pair of intermolecular C—H···O hydrogen bonds between centrosymmetrically related molecules involving the tosyl atom C16 at (x, y, z) and methoxycarbonyl atom O5 at $(1-x, -y, -z)$ generates an $R_2^2(26)$ dimeric ring centred at $(\frac{1}{2}, 0, 0)$. Propagation of these $R_2^2(26)$ rings along the [100] direction forms a $C(11)$ chain *via* another type of intermolecular C—H···O hydrogen bond between benzene atom C18 and sulfonamide atom O1 (Table 4). The molecular packing in (III) is such that the π–π stacking interactions between the aryl rings in the methoxycarbonylphenyl groups of adjacent polymeric chains are optimized. Benzene rings C24–C29 of the molecules at (x, y, z) and $(1-x, 1-y, -z)$ are strictly parallel, with an interplanar spacing of 3.417 Å, and a ring centroid separation of 3.938 (1) Å, corresponding to a ring offset of 1.96 Å. The combination of C—H···O hydrogen bonds and π–π interactions results in a two-dimensional supramolecular framework in (III) (Fig. 4).

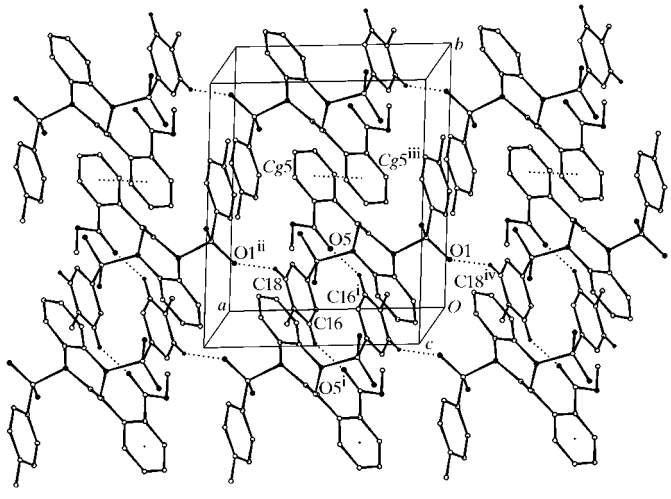

Figure 4
The two-dimensional supramolecular architecture in (III). H atoms not involved in hydrogen bonding have been omitted. [Symmetry codes: (i) $1-x, -y, -z$; (ii) $1+x, y, z$; (iii) $1-x, 1-y, -z$; (iv) $x-1, y, z$.]

Experimental

A mixture of aryl iodide [2-methoxyiodobenzene (0.268 g, 1.14 mmol) for (II) and 2-(methoxycarbonyl)iodobenzene (0.30 g, 1.14 mmol) for (III)], palladium(II) acetate, $[Pd(OAc)_2]$ (0.009 g, 5 mmol%), anhydrous potassium carbonate (0.304 g, 2.2 mmol) and tetrabutylammonium bromide (TBAB) (0.142 g, 0.44 mmol) was stirred in dimethylformamide (DMF, 10 ml) under a nitrogen atomosphere at room temperature (300 K) for 1 h. The acetylenic compound *N*-(prop-2-ynyl)-*N*,*N*′-1,2-phenylenedi-*p*-tosylamide (0.4 g, 0.88 mmol) was added to the mixture, followed by stirring for a further 24 h at room temperature. After the usual work-up, the crude product was purified by column chromatography through silica gel (60–120 mesh) using chloroform as eluant, affording the title compounds, (II) (yield 47%) and (III) (yield 50%). Single crystals of (II) and (III) suitable for X-ray analyses were obtained from solutions in a chloroform–light petroleum (333–353 K) mixture (1:1 *v*/*v*). Compound (II): m.p. 442 (2) K; analysis found: C 64.32, H 4.96, N 5.02%; calculated for $C_{30}H_{28}N_2O_5S_2$: C 64.28, H 5.00, N 5.00%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (*s*, 3H, Ar—CH_3), 2.42 (*s*, 3H, Ar—CH_3), 3.84 (*s*, 3H, –OCH_3), 4.05 (*s*, 2H, –CH_2), 6.92 (*s*, 1H, ═CH), 6.94–7.83 (*m*, 16H, Ar—H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5 (Ar—CH_3), 21.53 (Ar—CH_3), 21.6 (Ar—OCH_3), 43.5 (—CH_2–), 55.25 (═CH–). Compound (III): m.p. 441 (2) K; analysis found: C 62.88, H 4.80, N 4.67%; calculated for $C_{31}H_{28}N_2O_6S_2$: C 63.26, H 4.76, N 4.76%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.35 (*s*, 3H, Ar—CH_3), 2.46 (*s*, 3H, Ar—CH_3), 3.87 (*s*, 3H, –$COOCH_3$), 4.15 (*s*, 2H, –CH_2), 7.10 (*s*, 1H, ═CH), 7.12–8.09 (*m*, 16H, Ar—H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5 (Ar—CH_3), 21.6 (–$COOCH_3$), 44.5 (–CH_2–), 52.1 (═CH–).

Compound (II)

Crystal data

$C_{30}H_{28}N_2O_5S_2$
M_r = 560.66
Monoclinic, $P2_1/c$
a = 10.4081 (5) Å
b = 24.0202 (11) Å
c = 10.2842 (5) Å
β = 93.314 (10)°
V = 2566.8 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.25 mm^{-1}
T = 100 (2) K
0.50 × 0.50 × 0.40 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.887, T_{max} = 0.908
14680 measured reflections
5223 independent reflections
4688 reflections with $I > 2\sigma(I)$
R_{int} = 0.030

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.032
$wR(F^2)$ = 0.090
S = 1.07
5223 reflections
352 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.44 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

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

S1—O2	1.4291 (10)	S2—O3	1.4269 (11)
S1—O1	1.4318 (10)	S2—O4	1.4340 (11)
S1—N1	1.6930 (11)	O5—C29	1.3686 (17)
S1—C6	1.7545 (14)	O5—C30	1.4250 (17)
O2—S1—O1	119.54 (6)	N1—S1—C6	104.13 (6)
O1—S1—N1	107.74 (6)	C23—C22—N1	118.92 (12)
O1—S1—C6	109.09 (6)	C23—C22—C21	127.79 (12)
N1—C22—C23—C24	−172.0 (1)	S1—N1—C22—C23	73.8 (1)
N2—C21—C22—C23	127.2 (1)	C14—S2—N2—C21	84.8 (1)
C6—S1—N1—C8	−91.8 (1)		

Table 2
Hydrogen-bond geometry (Å, °) for (II).

*Cg*2 and *Cg*4 are the centroids of the C1–C6 and C14–C19 rings, respectively.

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2···O4^{i}	0.93	2.56	3.318 (2)	139
C11—H11···*Cg*4^{ii}	0.93	2.88	3.697 (2)	147
*Cg*2···*Cg*4^{iii}			3.948 (1)	

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

Compound (III)

Crystal data

$C_{31}H_{28}N_2O_6S_2$
M_r = 588.67
Triclinic, $P\overline{1}$
a = 10.1431 (7) Å
b = 11.7721 (4) Å
c = 11.8879 (9) Å
α = 101.0930 (10)°
β = 103.928 (2)°
γ = 91.248 (3)°
V = 1348.55 (15) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.25 mm^{-1}
T = 100 (2) K
0.45 × 0.45 × 0.40 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.897, T_{max} = 0.907
9605 measured reflections
4625 independent reflections
4153 reflections with $I > 2\sigma(I)$
R_{int} = 0.027

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.094
S = 1.04
4625 reflections
370 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (III).

S1—O1	1.4267 (13)	S2—O4	1.4309 (13)
S1—O2	1.4279 (13)	S2—O3	1.4314 (13)
S1—N1	1.6967 (15)	O5—C30	1.198 (2)
S1—C6	1.7547 (18)		
O1—S1—O2	119.25 (8)	O4—S2—O3	119.36 (8)
O2—S1—N1	107.06 (7)	C23—C22—N1	117.92 (16)
N1—S1—C6	104.95 (8)	C23—C22—C21	128.83 (16)
N1—C22—C23—C24	171.7 (2)	S1—N1—C22—C23	−72.5 (2)
N2—C21—C22—C23	−128.1 (2)	C14—S2—N2—C21	−77.3 (1)
C6—S1—N1—C8	84.8 (2)		

Table 4
Hydrogen-bond geometry (Å, °) for (III).

*Cg*5 is the centroid of the C24–C29 ring.

D—H···A	D—H	H···A	D···A	D—H···A
C16–H16···O5^{i}	0.93	2.54	3.238 (2)	132
C18—H18···O1^{ii}	0.93	2.54	3.396 (3)	154
*Cg*5···*Cg*5^{iii}			3.938 (1)	

Symmetry codes: (i) $1-x, -y, -z$; (ii) $1+x, y, z$; (iii) $1-x, 1-y, -z$.

Table 5
Isostructurality indices calculated for compounds (II), (IV), (V) and (VI).

Structures	π	$I_i(61)$	I_v %	I_v^{max} %
(II)–(IV)	0.0107	−1133.9	11.2	98.9
(II)–(V)	0.0079	−1090.4	12.7	99.9
(II)–(VI)	0.0097	7.3	76.8	98.5

H atoms were positioned geometrically and treated as riding, with C—H = 0.93–0.97 Å and U_{iso}(H) = 1.5–1.8U_{eq}(C).

For both compounds, data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SMART*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Version 1.06; Farrugia, 1997) and *CAMERON* (Watkin *et al.*, 1993); software used to prepare material for publication: *SHELXL97* and *PARST* 95 (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3138). Services for accessing these data are described at the back of the journal.

References

Banerjee, S., Mukherjee, A. K., Mukhopadhyay, R., Kundu, N. G. & Welch, A. J. (2001). *Acta Cryst.* C**57**, 861–864.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Bonnett, R. (1995). *Chem. Soc. Rev.* **24**, 19–33.

Bruker (1998). *SMART*. Version 5.054. Bruker AXS Inc., Madison, Wisconsin, USA.

Cabiddu, S., Floris, C., Melis, S., Sotgiu, F. & Cerioni, G. (1986). *J. Heterocycl. Chem.* **23**, 1815–1820.

Chowdhury, K., Mukhopadhyay, R., Mukherjee, M., Broder, C. K. & Kundu, N. G. (2001). *Acta Cryst.* E**57**, o794–o795.

Chumakov, Y. M., Tsapkov, V. I., Bocelli, G. & Antosyak, B. Y. (2005). *Acta Cryst.* C**61**, o460–o463.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Dell, A., Williams, D. H., Morris, H. R., Smith, G. A., Feeny, J. & Roberts, G. C. K. (1975). *J. Am. Chem. Soc.* **97**, 2497–2502.

Dobrzańska, L. & Lloyd, G. O. (2005). *Acta Cryst.* E**61**, o2114–o2116.

Fábián, L. & Kálmán, A. (1999). *Acta Cryst.* B**55**, 1099–1108.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Fuente, J. R. D., Canete, A., Zanacco, A. L., Saitz, C. & Jullian, C. (2000). *J. Org. Chem.* **65**, 7949–7958.

Ghosh, S., Mukhopadhyay, R., Helliwell, M. & Mukherjee, A. K. (2006). *Z. Kristallogr.* **221**, 739–745.

Kálmán, A., Párkányi, L. & Argay, G. (1993). *Acta Cryst.* B**49**, 1039–1049.

Kher, S. M., Cai, S. X., Weber, E. & Keana, J. F. W. (1995). *J. Org. Chem.* **60**, 5838–5842.

Lorgia, M., Fiore, M., Sannaand, P. & Paglietti, G. (1995). *Il Farmaco*, **50**, 289–301.

Moreau, P., Neirabeyeh, M. A., Guillaumet, G. & Condert, G. (1991). *Tetrahedron Lett.* **32**, 5525–5528.

Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.

Sessler, J. L., Maeda, H., Mizuno, T., Lynch, V. M. & Furuta, H. (2002). *Chem. Commun.* pp. 862–863.

Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Sonar, V. N., Parkin, S. & Crooks, P. A. (2004). *Acta Cryst.* C**60**, o659–o661.

Toshima, K., Takano, R., Ozawa, T. & Matsumura, S. (2002). *Chem. Commun.* pp. 212–213.

Wardell, J. L., Skakle, J. M. S., Low, J. N. & Glidewell, C. (2005). *Acta Cryst.* C**61**, o634–o638.

Watkin, D. M., Pearce, L. & Prout, C. K. (1993). *CAMERON*. Chemical Crystallography Laboratory, University of Oxford, England.

Zhao, X.-J. & Du, M. (2003). *Acta Cryst.* C**59**, o496–o498.