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A series of three (*E*)-2-alkylidene-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline compounds

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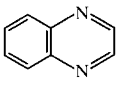
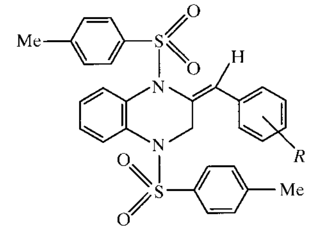
The three title quinoxaline derivatives, (*E*)-2-(4-methylbenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, $C_{30}H_{28}N_2O_4S_2$, (II), (*E*)-2-(4-methoxybenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, $C_{30}H_{28}N_2O_5S_2$, (III), and (*E*)-2-(3-chlorobenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, $C_{29}H_{25}ClN_2O_4S_2$, (IV), were synthesized by palladium-catalyzed hetero-annulation. The *E* configuration of the exocyclic double bond in the three compounds has been established by the present X-ray study. The saturated part of the quinoxaline moiety in all three compounds assumes a distorted chair conformation. The numerical descriptors indicate a high degree of isostructurality between compounds (II) and (III), but no isostructurality with compound (IV).

Comment

The quinoxaline system, (I), and its derivatives have been successfully used in medicinal chemistry, particularly as synthetic precursors of antihypertensives, analgesics and neurotransmitter antagonists (Fuente *et al.*, 2000; Kher *et al.*, 1995; Manca *et al.*, 1992). Many of these compounds also exhibit *in vitro* anticancer activity (Loriga *et al.*, 1995). Although some preliminary information concerning the substituent-directing effects of quinoxaline derivatives is available (Porter, 1984), to our knowledge, no X-ray crystal structure of *N*-substituted quinoxaline has been reported previously. As part of an ongoing program on the synthesis and characterization of quinoxaline-containing heterocyclic systems, we synthesized three 2-alkylidene-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxalines *via* palladium-catalyzed reaction between *N*-(prop-2-ynyl)-*N*,*N*′-1,2-phenylene-di-*p*-tosylamide and aryl iodides. To establish the regio- and stereospecificities of the reaction and to build up a hierarchy for such systems, X-ray analyses of 2-(4-methylbenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, (II), 2-(4-methoxybenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, (III), and 2-(3-chlorobenzylidene)-1,4-di-*p*-tosyl-1,2,3,4-tetrahydroquinoxaline, (IV), were undertaken.


(I)



(II) *R* = 4-Me
(III) *R* = 4-OMe
(IV) *R* = 3-Cl

The title compounds (Figs. 1–3) consist of a quinoxaline system with two *p*-tosyl and one substituted phenylmethylidene group at the 1, 4 and 2 positions, respectively. The *E* configurations of the molecules of (II), (III) and (IV) are established by the torsion angle N1—C8—C9—C10 of 174.7 (2)° for (II), 176.8 (2)° for (III) and 178.4 (3)° for (IV). As expected, the pyrazine ring *B* (N1/C1/C6/N2/C7/C8) fused to the phenyl ring *A* (C1–C6) in the compounds deviates significantly from planarity, with ring-puckering parameters (Cremer & Pople, 1975) Q = 0.410 (2), 0.411 (2) and 0.404 (3) Å, θ = 133.2 (3), 134.8 (3) and 47.1 (4)°, and φ = 82.9 (4), 88.0 (4) and −90.8 (5)° for (II), (III) and (IV), respectively. The heterocyclic ring (C_4N_2) in all three compounds assumes a distorted chair conformation, with the C1 and C7 atoms deviating by −0.117 (2) and 0.566 (2) Å in (II), −0.147 (2) and 0.560 (2) Å in (III), and −0.127 (3) and 0.541 (3) Å in (IV), respectively, from the least-squares plane through the remaining endocyclic atoms.

A comparison of the molecular geometries of (II), (III) and (IV) reveals the similarity of all bond lengths among the three compounds (Tables 1, 3 and 5). The two N atoms of the pyrazine ring (N1 and N2), with the sum of bond angles deviating significantly from 360° [346.8 (2) and 350.0 (2)° in (II), 345.4 (2) and 347.3 (2)° in (III), and 349.7 (2) and

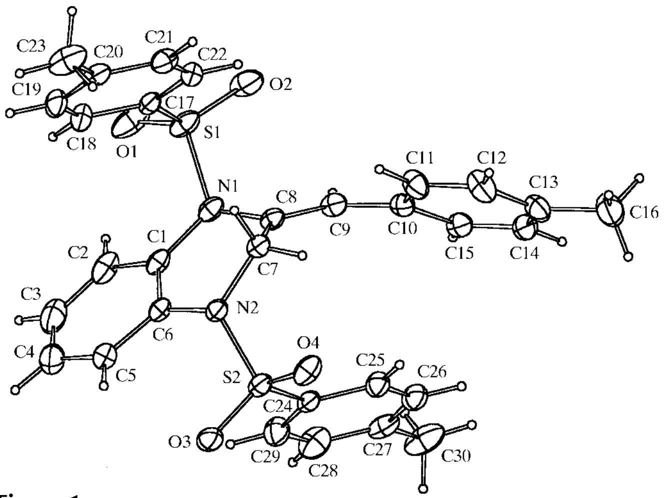


Figure 1
The molecular structure of (II) showing 50% probability displacement ellipsoids.

348.4 (2)° in (IV)] indicating pyramidal distortions, occupy axial orientations with respect to their substituents (Tables 1, 3 and 5). The geometry at the S atoms deviates significantly from that of a regular tetrahedron, with the largest deviation in the O—S—O angle (Tables 1, 3 and 5). The widening of the O—S—O angle [119.7 (1)–120.3 (2)°] from the ideal tetrahedral value is presumably the result of the repulsive interaction between the short S═O bonds. The tosyl groups in (II), (III) and (IV) adopt folded conformations, in which the phenyl rings *C* [C17–C22 in (II) and (III); C16–C21 in (IV)] and *D* [C24–C29 in (II) and (III); C23–C28 in (IV)] shield the quinoxaline moiety (*AB*). The dihedral angles between *A*/*C* and *A*/*D* are similar in all three structures [53.5 (1) and 55.8 (1)° in (II), 52.2 (1) and 53.2 (1)° in (III), and 50.5 (1) and 57.1 (1)° in (IV)].

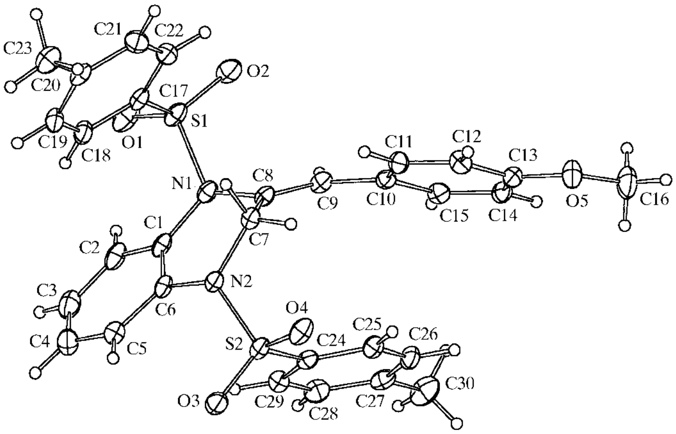


Figure 2
The molecular structure of (III) showing 50% probability displacement ellipsoids.

In compounds (II) and (IV), the phenyl rings *C* and *D* are almost parallel to one another [the dihedral angle *C*/*D* is 2.3 (1)° in (II) and 7.7 (1)° in (IV)], whereas in compound (III), the *C* and *D* rings are inclined by 27.2 (1)°. This is probably to minimize the steric hindrance introduced by the methoxyphenyl group in (III). The S—O [1.417 (2)–1.439 (3) Å], S—C [1.749 (2)–1.762 (2) Å] and S—N [1.673 (2)–1.707 (2) Å] bond distances (Tables 1, 3 and 5) are consistent with the corresponding values reported in *International Tables for Crystallography* (Allen *et al.*, 1992). The lack of π-bonding in the branches among the phenyl rings precludes any possible π conjugation across the whole molecule in (II), (III) and (IV). The aromatic nature of the rings is therefore localized within the rings and on their direct substituents.

The identical space groups and the similarity of lattice parameters of (II), (III) and (IV) suggest some degree of isostructurality among the compounds. The results of calculation (Table 7) of the unit-cell similarity descriptor Π (Kálmán *et al.*, 1993), the asphericity index A (Rutherford, 1997), 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 (III).

The volumetric index of isostructurality between compounds (II) and (III) amounts to 82% for the whole unit cell, with four molecules indicating significant packing similarity of the related structures. The large values of the asphericity index (A) and the isostructurality index, $I_i(37)$, between (II)/(IV) and (III)/(IV) (Table 7) indicate that compound (IV) is not isostructural with compound (II) or (III). This is probably a consequence of the exchange of cell-axis lengths in compound (IV) compared with those in (II) and (III), and the different positions of substituents in the benzylidene moiety [4-methyl in (II), 4-methoxy in (III) and 3-chloro in (IV)] of the structures.

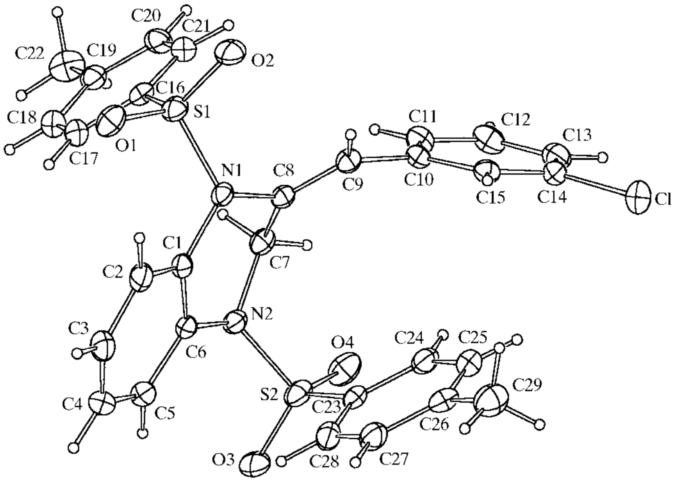


Figure 3
The molecular structure of (IV) showing 50% probability displacement ellipsoids.

In all three compounds, the crystal packing is stabilized by weak C—H$\cdots$O intermolecular interactions (Tables 2, 4 and 6) involving the sulfonyl and methoxy O atoms.

Experimental

A mixture of aryl iodide [4-methyliodobenzene for (II), 4-methoxyiodobenzene for (III) and 3-chloroiodobenzene for (IV)] (1.15 mmol), palladium(II) acetate (5 mol%), anhydrous potassium carbonate (4.40 mmol) and tetrabutylammonium bromide (4.40 mmol) was stirred in 10 ml of dimethylformamide for 30 min. The acetylenic compound *N*-(prop-2-ynyl)-*N*,*N*′-1,2-phenylenedi-*p*-tosylamide (0.88 mmol) was added and the mixture was stirred for a further 24 h at room temperature. After usual work-up, the crude product was purified by column chromatography through silica gel using chloroform as eluant yielded the title compounds (II), (III) and (IV). Single crystals of (II), (III) and (IV) suitable for X-ray analysis were obtained from a chloroform/light petroleum (333–353 K) mixture (1:1). Compound (II): m.p. 428 (1) K; analysis found: C 66.43, H 5.23, N 4.87%; calculated for $C_{30}H_{28}N_2O_4S_2$: C 66.17, H 5.14, N 5.14%. Compound (III): m.p. 425 (1) K; analysis found: C 64.04, H 5.06, N 4.88%; calculated for $C_{30}H_{28}N_2O_5S_2$: C 64.28, H 5.14, N 5.10%. Compound (IV): m.p. 418 (1) K; analysis found C 61.94, N 4.36, N 4.78%; calculated for $C_{29}H_{25}ClN_2O_4S_2$: C 61.65, H 4.42, N 4.46%.

Compound (II)

Crystal data

$C_{30}H_{28}N_2O_4S_2$
$M_r = 544.66$
Monoclinic, $P2_1/c$
$a = 10.559$ (4) Å
$b = 11.658$ (4) Å
$c = 23.169$ (7) Å
$\beta = 100.54$ (3)°
$V = 2803.9$ (17) Å^3
$Z = 4$
$D_x = 1.290$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 37 reflections
$\theta = 1.9$–16.3°
$\mu = 0.23$ mm^{-1}
$T = 293$ (2) K
Block, colourless
0.64 × 0.52 × 0.48 mm

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: empirical (North *et al.*, 1968)
$T_{\min} = 0.866$, $T_{\max} = 0.896$
6386 measured reflections
4923 independent reflections
3664 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.027$
$\theta_{\max} = 25.0°$
$h = -1 \rightarrow 12$
$k = -1 \rightarrow 13$
$l = -27 \rightarrow 27$
3 standard reflections every 97 reflections intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.130$
$S = 1.03$
4923 reflections
346 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0604P)^2 + 0.6663P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.003$
$\Delta\rho_{\max} = 0.21$ e Å^{-3}
$\Delta\rho_{\min} = -0.31$ e Å^{-3}

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

S1—O2	1.419 (2)	S2—O4	1.4293 (18)
S1—O1	1.431 (2)	S2—N2	1.6729 (18)
S1—N1	1.707 (2)	S2—C24	1.757 (2)
S1—C17	1.749 (2)	N2—C7	1.471 (3)
N1—C8	1.439 (3)	C7—C8	1.505 (3)
S2—O3	1.4250 (18)	C8—C9	1.335 (3)
O2—S1—O1	120.14 (15)	O3—S2—O4	120.01 (12)
O2—S1—N1	106.87 (13)	O3—S2—N2	106.84 (10)
O1—S1—N1	105.77 (11)	O4—S2—N2	105.28 (10)
N1—S1—C17	106.30 (9)	N2—S2—C24	107.47 (9)
C8—N1—C1	115.81 (18)	C6—N2—C7	115.32 (17)
C8—N1—S1	113.60 (16)	C6—N2—S2	119.20 (14)
C1—N1—S1	117.41 (14)	C7—N2—S2	115.54 (14)
N1—C8—C9—C10	174.7 (2)	N1—S1—C17—C18	−86.3 (2)
N2—C7—C8—N1	53.9 (2)	N2—S2—C24—C25	99.5 (2)

Table 2
Hydrogen-bonding and short-contact geometry (Å, °) for (II).

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C30—H30*C*⋯O1$^{\rm i}$	0.96	2.78	3.282 (4)	113
C23—H23*B*⋯O3$^{\rm ii}$	0.96	2.96	3.296 (4)	102
C14—H14⋯O1$^{\rm iii}$	0.93	2.49	3.340 (3)	153
C21—H21⋯O4$^{\rm iv}$	0.93	2.86	3.397 (3)	118
C19—H19⋯O2$^{\rm v}$	0.93	2.52	3.402 (4)	159
C11—H11⋯O4$^{\rm iv}$	0.93	2.58	3.438 (4)	153

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

Compound (III)

Crystal data

$C_{30}H_{28}N_2O_5S_2$
$M_r = 560.66$
Monoclinic, $P2_1/c$
$a = 10.5460$ (10) Å
$b = 11.8440$ (10) Å
$c = 21.985$ (3) Å
$\beta = 101.250$ (10)°
$V = 2693.3$ (5) Å^3
$Z = 4$
$D_x = 1.383$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 57 reflections
$\theta = 6.7$–38.5°
$\mu = 0.24$ mm^{-1}
$T = 160$ (2) K
Block, colourless
0.36 × 0.32 × 0.16 mm

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: empirical (North *et al.*, 1968)
$T_{\min} = 0.932$, $T_{\max} = 0.962$
6072 measured reflections
4693 independent reflections
3531 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.038$
$\theta_{\max} = 25.0°$
$h = -1 \rightarrow 12$
$k = -1 \rightarrow 14$
$l = -25 \rightarrow 25$
3 standard reflections every 97 reflections intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.110$
$S = 1.02$
4693 reflections
355 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0447P)^2 + 1.4501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.52$ e Å^{-3}
$\Delta\rho_{\min} = -0.36$ e Å^{-3}

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

S2—O3	1.4286 (19)	S1—N1	1.705 (2)
S2—O4	1.4349 (18)	S1—C17	1.760 (2)
S2—N2	1.6776 (19)	N1—C8	1.451 (3)
S2—C24	1.762 (2)	N2—C7	1.484 (3)
S1—O2	1.428 (2)	C7—C8	1.506 (3)
S1—O1	1.428 (2)	C8—C9	1.330 (3)
O3—S2—O4	119.79 (11)	N1—S1—C17	106.25 (11)
O3—S2—N2	106.89 (10)	C1—N1—C8	115.44 (19)
O4—S2—N2	105.62 (10)	C1—N1—S1	116.01 (15)
N2—S2—C24	106.85 (10)	C8—N1—S1	113.98 (16)
O2—S1—O1	119.72 (12)	C6—N2—C7	115.16 (19)
O2—S1—N1	106.71 (11)	C6—N2—S2	117.73 (16)
O1—S1—N1	105.94 (11)	C7—N2—S2	114.41 (15)
N1—C8—C9—C10	176.8 (2)	N1—S1—C17—C18	109.2 (2)
N2—C7—C8—N1	54.1 (3)	N2—S2—C24—C25	−71.2 (2)

Table 4
Hydrogen-bonding and short-contact geometry (Å, °) for (III).

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C21—H21⋯O2$^{\rm i}$	0.93	2.66	3.311 (3)	128
C25—H25⋯O5$^{\rm ii}$	0.93	2.58	3.324 (3)	137
C16—H16*B*⋯O2$^{\rm iii}$	0.96	2.81	3.409 (4)	122
C12—H12⋯O1$^{\rm iii}$	0.93	2.56	3.434 (3)	157
C15—H15⋯O4$^{\rm iv}$	0.93	2.57	3.454 (3)	158

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

Compound (IV)

Crystal data

$C_{29}H_{25}ClN_2O_4S_2$
$M_r = 565.08$
Monoclinic, $P2_1/c$
$a = 10.5361$ (10) Å
$b = 24.040$ (3) Å
$c = 10.6146$ (10) Å
$\beta = 93.863$ (10)°
$V = 2682.4$ (5) Å^3
$Z = 4$
$D_x = 1.399$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 34 reflections
$\theta = 3.4$–12.5°
$\mu = 0.34$ mm^{-1}
$T = 293$ (2) K
Needle, colourless
0.56 × 0.32 × 0.28 mm

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: empirical (North *et al.*, 1968)
$T_{\min} = 0.866$, $T_{\max} = 0.910$
5563 measured reflections
4509 independent reflections
2437 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.050$
$\theta_{\max} = 25.0°$
$h = -1 \rightarrow 12$
$k = -28 \rightarrow 1$
$l = -12 \rightarrow 12$
3 standard reflections every 97 reflections intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.108$
$S = 0.96$
4509 reflections
345 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0318P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.007$
$\Delta\rho_{\max} = 0.23$ e Å^{-3}
$\Delta\rho_{\min} = -0.20$ e Å^{-3}

Table 5
Selected geometric parameters (Å, °) for (IV).

S1—O2	1.417 (2)	S2—C23	1.758 (3)
S1—O1	1.428 (3)	Cl—C14	1.741 (3)
S1—N1	1.695 (3)	N1—C8	1.447 (4)
S1—C16	1.750 (3)	N2—C7	1.491 (4)
S2—O4	1.421 (3)	C7—C8	1.494 (4)
S2—O3	1.439 (3)	C8—C9	1.328 (4)
S2—N2	1.675 (3)	C9—C10	1.476 (4)
O2—S1—O1	120.27 (17)	N2—S2—C23	106.65 (14)
O2—S1—N1	105.71 (14)	C1—N1—C8	115.3 (2)
O1—S1—N1	107.04 (15)	C1—N1—S1	119.7 (2)
N1—S1—C16	104.51 (14)	C8—N1—S1	114.7 (2)
O4—S2—O3	119.72 (17)	C6—N2—C7	114.9 (2)
O4—S2—N2	105.69 (15)	C6—N2—S2	117.5 (2)
O3—S2—N2	106.46 (15)	C7—N2—S2	116.0 (2)
N1—C8—C9—C10	178.4 (3)	N1—S1—C16—C17	80.0 (3)
N2—C7—C8—N1	−53.5 (3)	N2—S2—C23—C24	81.5 (3)

For all compounds, data collection: *XSCANS* (Siemens, 1995); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *MULTAN*88 (Debaerdemaeker *et al.*, 1988); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1995); software used to prepare material for publication: *SHELXL*97 and *PARST*95 (Nardelli, 1995).

Table 6
Hydrogen-bonding and short-contact geometry (Å, °) for (IV).

D—H···A	D—H	H···A	D···A	D—H···A
C29—H29*C*···O2$^{\rm i}$	0.96	2.85	3.321 (5)	112
C20—H20···O4$^{\rm ii}$	0.93	2.82	3.364 (4)	119
C18—H18···O1$^{\rm iii}$	0.93	2.72	3.388 (4)	129
C17—H17···O1$^{\rm iii}$	0.93	2.94	3.488 (4)	119

Symmetry codes: (i) $1 + x, y, z$; (ii) $2 - x, 2 - y, 1 - z$; (iii) $x, \frac{3}{2} - y, z - \frac{1}{2}$.

Table 7
Isostructurality indices (see *Comment* for definition) calculated for compounds (II), (III) and (IV).

Structures	Π	A	$I_i(37)$%	I_v%	$I_v^{\max}$%
(II)–(III)	0.023	1.13	60.9	82.4	98.8
(II)–(IV)	0.002	20.16	−732.2	13.4	99.9
(III)–(IV)	0.021	208.68	−741.6	13.1	98.7

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1466). Services for accessing these data are described at the back of the journal.

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