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Synthesis and cytotoxicity of novel γ-piperidone-containing dibenzo-1,7-diaza-14-crown-4 ethers

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All new compounds gave satisfactory spectroscopic and analytical results. Their IR, MS, ^{1}H NMR and ^{13}C NMR spectra were consistent with the structures show in the Scheme 1.

N,N-Bis(2-tosyloxyethyl)-*N*-tosylamine **1** was synthesized by general methods [S1, S2, S3]

Synthesis of podands 3a,b

A mixture of salicylic aldehyde **2a** (1.61g, 13.22 mmol) or 2-hydroxy-1-naphthaldehyde **2b** (2.27 g, 13.22 mmol), K_2CO_3 (2.19 g, 15.87 mmol) and KI (2.63g, 15.84 mmol) in DMF (50 ml) was stirred at 80°C for 30 minutes. Tritosyl derivative **1** (3.0g, 5.29 mmol) was then added dropwise, and the mixture was stirred at 100°C for 12 hours. The reaction mixture was cooled to room temperature and then poured into ice water, the yellow precipitate thus formed was filtered off, washed with water and recrystallized form ethanol/dichloromethane to give products **3a,b**.

1,5-Bi-(2-formylphenoxy)-3-tosyl-3-azapentane **3a**. Yield 48%, mp 136-138°C. R_f = 0.66 (EtOAc:hexane = 1:3). ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 10.28 (s, 2H, C<u>H</u>O), 7.75 (d.d, 2H, H-3, H-19, ^{3}J 7.5, ^{5}J 1.5 Hz), 7.70 (d, 2H, H-26, H-30, ^{3}J 8.0 Hz), 7.51 (d.t, 2H, H-5, H-17, ^{3}J 8.5, ^{5}J 1.5 Hz), 7.21 (d, 2H, H-27, H-29, ^{3}J 8.0 Hz), 7.03 (t, 2H, H-4, H-18, ^{3}J 7.5 Hz), 6.09 (d, 2H, H-6, H-16, ^{3}J 8.5 Hz), 3.78 (t, 4H, -C<u>H</u>$_2$-N(Ts)-C<u>H</u>$_2$-, ^{3}J 5.5 Hz), 4.30 (t, 4H, 2xO-C<u>H</u>$_2$-, ^{3}J 6.0 Hz), 2.36 (s, 3H, CH_3). MS, *m/z*: 466 $[M-H]^-$.

1,5-Bis(1-formylnaphthalen-2-yloxy)-3-tosyl-3-azapentane **3b**. Yield 48%, mp 154 - 156°C. R_f = 0.60 (EtOAc:hexane = 1:2). ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 10.77 (s, 2H, C<u>H</u>O), 9.10 (d, 2H, H-4, H-4', ^{3}J 8.5 Hz), 7.93 (d, 2H, H-9, H-9', ^{3}J 9.5 Hz), 7.72 (d, 2H, H-7,H-7', ^{3}J 8.5 Hz), 7.67 (d, 2H, H-26, H-30, ^{3}J 8.0 Hz), 7.55 (t.d, 2H, H-5, H-5', ^{3}J 7.0, ^{5}J 1.5 Hz), 7.37 (t.d, 2H, H-6, H-6', ^{3}J 8.0, ^{5}J 1.0 Hz), 7.21 (d, 2H, H-27, H-29, ^{3}J 8.0 Hz), 7.17 (d, 2H, H-10, H-10', ^{3}J 9.0 Hz), 3.79 (t, 4H, -C<u>H</u>$_2$-N(Ts)-C<u>H</u>$_2$-, ^{3}J 5.5 Hz), 4.46 (t, 4H, 2xO-C<u>H</u>$_2$, ^{3}J 6.0 Hz), 2.26 (s, 3H, CH_3). MS, *m/z*: 568 $[M+H]^+$.

Synthesis of crown compounds 5,6

Ethyl 23-oxo-11-tosyl-8,14-dioxa-11,25-diazatetracyclo[19.3.1.0^{2,7}.0^{15,20}]pentacosa-2,4,6,15(20),16,18-hexaen-22-carboxylate **5b**.

Yield 22%, mp. 194 - 196°C. R_f = 0.62 (hexane:EtOAc = 1:1). IR (KBr, *ν/cm^{-1}*): 3315.63; 2920.23; 2852.72; 1730.15; 1710.86 .^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 7.74 (d, 2H, H-26, H-30, ^{3}J 8.0 Hz), 7.29 (d, 2H, H-27, H-29, ^{3}J 8.0 Hz), 7.05 -7.22 (br.m, 4H, H-3, H-4, H-18, H-19), 6.93 (br.s, 2H, H-5, H-17), 6.83 (br.d, 2H, H-6, H-16, ^{3}J 7.5 Hz), 4.20 – 4.42 (br.m, 6H, H-1, H-21, H-22, NH-25, <u>CH</u>$_2$-CH_3), 3.45 - 3.78 (br.m, 5H, H-24^{ax}, 2xH-9, 2xH-13), 3.05 – 3.45 (br.s, 4H, 2xH-10, 2xH-12), 2.58 (d.d, 1H, H-24^{eq}, ^{3}J 13.0, ^{5}J 2.0 Hz), 2.40 (s, 3H, <u>CH</u>$_3$), 0.88 (br. t, 3H, CH_2C<u>H</u>$_3$, ^{3}J 7.0Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C ppm: 210.84, 156.69, 144.10, 129.95, 129.67, 128.93, 128.83, 127.47, 126.27, 121.74, 112.62, 70.20, 67.25, 63.28, 52.05, 48.77, 34.17, 31.93, 31.52, 30.34, 30.16, 29.69, 29.36, 29.25, 29.14, 24.93, 22.69, 21.49, 14.11. HRMS, *m/z:* 579.2161 $[M+H]^+$ and 611.2421 $[M+CH_3OH+H]^+$.Calc. for $C_{31}H_{35}N_2O_7S^+$: 579.2159 and $C_{32}H_{39}N_2O_8S^+$: 611.2422.

22-Methyl-11-tosyl-8,14-dioxa-11,25-diazatetracyclo[19.3.1.0^{2,7}.0^{15,20}]pentacosa-2,4,6,15(20),16,18-hexaen-23-one **5c**.

Yield 52 %, mp 172 – 174°C. R_f = 0.55 (hexane:EtOAc = 1:1). IR (KBr, *ν/cm^{-1}*): 3265.49; 2920.23; 2850.79; 1710.86. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 7.73 (d, 2H, H-26, H-30, ^3J 8.5 Hz), 7.29 (d, 2H, H-27, H-29, ^3J 8.0 Hz), 7.18 – 7.26 (br.m, 4H, H-3, H-4, H-18, H-19), 6.93 (br.t, 1H, H-5, ^3J 7.5 Hz), 6.90 (br.t, 1H, H-17, ^3J 7.5 Hz), 6.85 (d, 1H, H-6, ^3J 8.0 Hz), 6.81 (d, 1H, H-16, ^3J 8.5 Hz), 4.15 - 4.45 (br.m, 6H, H-1, H-21, 2xH-13, 2xH-9), 4.02 - 4.12 (br.m, 2H, H-22, NH-25), 3.45 - 3.90 (br.m, 4H, 2xH-10, 2xH-12), 3.15 (br.t, 1H, H-24^{ax}, ^3J 12.0 Hz), 2.61 (d.d, 1H, H-24^{eq}, ^3J 13.5, ^5J 3.0 Hz), 2.39 (s, 3H, $\underline{CH_3}$), 1.08 (t, 3H, $C\underline{H_3}$ ^3J 7.0 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C ppm: 158.07, 157.90, 144.85, 130.92, 130.71, 129.78, 129.61, 128.79, 121.98, 121.61, 113.53, 62.87, 60.50, 52.89, 52.33, 37.74, 33.44, 32.61, 27.70, 23.30, 21.38, 14.40, 14.31. HRMS, *m/z:* $[M+H]^+$ 521.2686. Calc. for $C_{29}H_{33}N_2O_5S^+$: 521.2105.

22-Phenyl-11-tosyl-8,14-dioxa-11,25-diazatetracyclo[19.3.1.0^{2,7}.0^{15,20}]pentacosa-2,4,6,15(20),16,18-hexaen-23-one **5d**.

Yield 75%, mp 230 - 232°C. R_f = 0.7 (hexane:EtOAc = 1:1). IR (KBr, *ν/cm^{-1}*): 3311.78; 2916.37; 2848.86; 1699.29. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 7.76 (d, 2H, H-26, H-30, *J* 8.0 Hz), 7.32 (d, 2H, H-27, H-29, *J* 8.0 Hz), 7.24 (br.t, 2H, H-4, H-18, ^3J 7.0 Hz); 7.14 (br.t, 2H, H-5, H-17, ^3J 7.5 Hz), 7.08 (br.d, 1H, H_{Ph}, ^3J 7.0 Hz), 6.94 – 7.04 (m, 4H, H-3, H-6, H-16, H-19), 6.89 (br.d, 2H, H_{Ph}, ^3J 8.0 Hz), 6.76 (br.d, 1H, H_{Ph}, ^3J 8.5 Hz), 6.64 (br.s, 1H, H_{Ph}), 4.10 – 4.50 (br. m, 7H, H-1, H-21, 2xH-13, 2xH-9, NH-25), 3.30 – 3.90 (br.m, 6H, H-22, H-24^{ax}, 2xH-10, 2xH-12), 2.72 (d.d, 1H, H-24^{eq}, ^3J 13.5, ^3J 3.0 Hz), 2.41 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C ppm: 156.72, 156.25, 144.15, 129.97, 129.56, 129.38, 129.01, 128.49, 127.97, 127.54, 126.60, 121.78, 112.79, 51.76, 31.57, 21.49, 14.08. HRMS, *m/z:* $[M+H]^+$ 583.2268 and $[M+CH_3OH+H]^+$ 615.2531. Calc. for $C_{34}H_{35}N_2O_5S^+$: 583.2261 and for $C_{35}H_{39}N_2O_6S^+$: 615.2523.

30,32-Diphenyl-15-tosyl-12,18-dioxa-15,33-diazahexacyclo[27.3.1.0^{2,11}.0^{3,8}.0^{19,28}.0^{22,27}]-tritriaconta-2,4,6,8,10,19(20),21,23,25,27-decaen-31-one **6a**.

Yield 36%, mp 293 – 295°C. R_f = 0.4 (hexane:EtOAc = 1:1). IR (KBr, *ν/cm^{-1}*): 3342.64; 3028.24; 2920.23; 1701.22. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 8.37 (d, 2H, H-4, H-26, ^3J 9.0 Hz), 7.93 (d, 2H, H-7, H-23, ^3J 8.0 Hz), 7.70 (d, 2H, 2xH$^{\alpha}$, ^3J 9.0 Hz), 7.65 (d, 2H, H-9, H-21, ^3J 7.5 Hz), 7.56 (d, 2H, H-10, H-20, *J* 8.0 Hz), 7.46 (d, 2H, 2xH$^{\beta}$, ^3J 9.0 Hz), 7.39 (t, 2H, H-6, H-24, ^3J 8.0 Hz), 7.29 (d, 4H, 2xH^{orthor}, 2xH$^{orthor'}$, ^3J 7.0 Hz), 7.21 (t, 2H, H-5, H-25, ^3J 7.0 Hz), 6.95 (t, 4H, 2xH^{meta}, 2xH$^{meta'}$, ^3J 7.5 Hz), 6.83 (t, 2H, H^{para}, H$^{para'}$, ^3J 7.5 Hz), 5.79 (t, 2H, H-1, H-29, ^3J 11.5 Hz), 5.31 (d, 2H, H-30, H-32, ^3J 11.0 Hz), 4.75 (t, 1H, NH-33, ^3J 12.0 Hz), 4.64 – 4.67 (m, 2H, 2xH-19), 4.56 – 4.59 (m, 2H, 2xH-13), 3.99 – 4.03 (m, 2H, 2xH-14), 3.39 - 3.43 (m, 2H, 2xH-16), 2.48 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C ppm: 154.07, 144.71, 132.40, 130.11, 129.59, 129.51, 128.18, 127.87, 127.47, 126.43, 126.28, 123.57, 123.07, 114.05, 67.67, 62.31, 61.81, 51.99, 21.54, 13.82. HRMS, *m/z:* 759.2892 $[M+H]^+$ and 791.2799 $[M+CH_3OH+H]^+$. Calc. for $C_{48}H_{43}N_2O_5S^+$: 759.2887 and for $C_{49}H_{47}N_2O_6S^+$: 791.3149.

Ethyl 31-oxo-15-tosyl-12,18-dioxa-15,33-diazahexacyclo[27.3.1.0^{2,11}.0^{3,8}.0^{19,28}.0^{22,27}]-tritriaconta-2,4,6,8,10,19(20),21,23,25,27-decaen-30-carboxylate **6b**.

Yield 26.2%, mp 178 - 180°C. R_f = 0.45 (hexane:EtOAc = 1:1). IR (KBr, *ν/cm^{-1}*): 3350.35; 2981.95; 2927.94; 1732.08; 1707.00; 1622.13. ^{1}H-NMR (500 MHz, $CDCl_3$, TMS) δ_H ppm: 8.27 (d, 1H, H-23, ^3J 8.5 Hz), 8.10 (d, 1H, H-26, ^3J 8.5 Hz), 7.75 - 7.79 (m, 3H, H-9, H-10, H-21), 7.77 (d, 2H, H$^{\alpha}$, ^3J 8.0 Hz), 7.70 (d, 1H, H-20, ^3J 8.0 Hz), 7.50 – 7.56 (m, 2H, H-6, H-24), 7.37 (t, 2H, H-5, H-25, ^3J 7.5 Hz), 7.32 (d, 2H, H$^{\beta}$, ^3J 8.0 Hz), 7.22 (d, 1H, H-4, ^3J 9.0 Hz), 7.18 (d, 1H, H-7, ^3J 9.0 Hz), 5.45 (t, 1H, H-29, ^3J 12.0Hz), 5.20 (t, 1H, H-1, ^3J 12.0 Hz), 5.00 (t, 1H, NH-33, ^3J 12.5Hz), 4.64 – 4.67 [m, 2H, -O-$\underline{CH_2}$-CH_3], 4.58 (d, 1H, H-30, ^3J 11.0Hz), 4.35 – 4.43 (m, 2H, 2xH-13), 3.75 – 3.91 (m, 5H, 2xH-14, 2xH-16, H-19), 3.55 (m, 1H, H-19), 3.35 (t, 1H, H-32^{ax}, ^3J 13.5 Hz), 2.76 (d.d, 1H, H-32^{eq}, ^3J 14.0, ^5J 3.0Hz), 2.39 (s, 3H, CH_3), 0.81 (t, 3H, $CH_2\underline{CH_3}$, ^3J 7.0 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C ppm: 168.97, 154.62, 154.31, 132.20, 131.56, 130.22, 130.04, 129.77, 129.65, 129.58, 128.70, 128.26, 127.62, 127.18, 126.87, 123.95, 123.69, 122.27, 121.10, 114.31, 113.61, 68.99, 67.63, 62.55, 60.69, 57.64, 55.62, 52.29, 51.47, 46.59, 21.51, 13.71. HRMS, *m/z:* 679.2474 $[M+H]^+$ and 711.2738 $[M+CH_3OH+H]^+$. Calc. for $C_{39}H_{39}N_2O_7S^+$: 679.2472 and for $C_{40}H_{43}N_2O_8S^+$: 711.2735.

Cytotoxicity assay

Vero cell line and five human cancer cell lines were obtained from the American Type Culture Collection (Manassas, VA) ATCC as RD (human rhabdomyosarcoma), HepG2 (human hepatocellular carcinoma), MCF7 (human breast adenocarcinoma), Lu1 (human lung adenocarcinoma), HeLa (HeLa cervical cancer cells).

The MTT is based on the protocol described by Skehan & etc (1990) [S4] and Likhiwitayawuid & etc (1993) [S5]. This method has worldwide application and is recommended by National Cancer Institute (NCI) and College of Medicine, University of Illinois at Chicago for routine drug screening.

X-ray diffraction experimental data

Compound **5a**	
Chemical formula	$C_{40}H_{38}N_2O_5S$
M_r	658.78
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	100
a, *b*, *c* (Å)	11.606 (2), 13.856 (3), 14.920 (3)
α, β, γ (°)	83.37 (3), 67.38 (3), 71.40 (3)
V (Å^3)	2099.0 (9)
Z	2
Radiation type	Synchrotron, λ = 0.96330 Å
μ (mm^{-1})	0.25
Crystal size (mm)	0.15 × 0.12 × 0.10
Data collection	
Diffractometer	Rayonix SX165 CCD
Absorption correction	Multi-scan *SCALA* (Evans, 2006)
T_{min}, T_{max}	0.951, 0.966
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	21088, 8513, 4201
R_{int}	0.118
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.645
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.118, 0.289, 0.95
No. of reflections	8513
No. of parameters	435
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (eÅ^{-3})	0.79, -0.45

Table S1. Hydrogen bonds for **5a** [Å and °].

D*—H···A*	d(D—H)	d(H···A)	d(D···A)	∠DHA
C10—H10A···O23[a]	0.99	2.35	3.312(5)	164
C12—H12B···O23[a]	0.99	2.36	3.321(4)	164
N25—H25···O8	0.90	2.23	2.851(4)	126
N25—H25···O14	0.90	2.28	2.879(3)	124

* D – proton donor; A – proton acceptor;
Symmetry transformations used to generate equivalent atoms: [a] $-x+1$, $-y+1$, $-z+1$

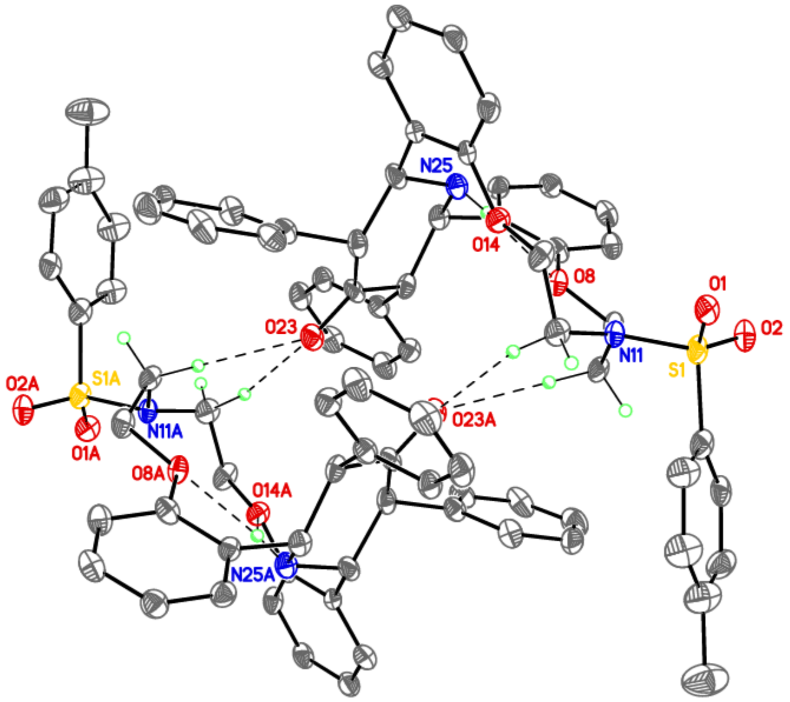

Figure S1. The H-bonded centro symmetrical dimers of **5a**. The intramolecular N—H···O and intermolecular C—H···O hydrogen bonds are depicted by dashed lines.

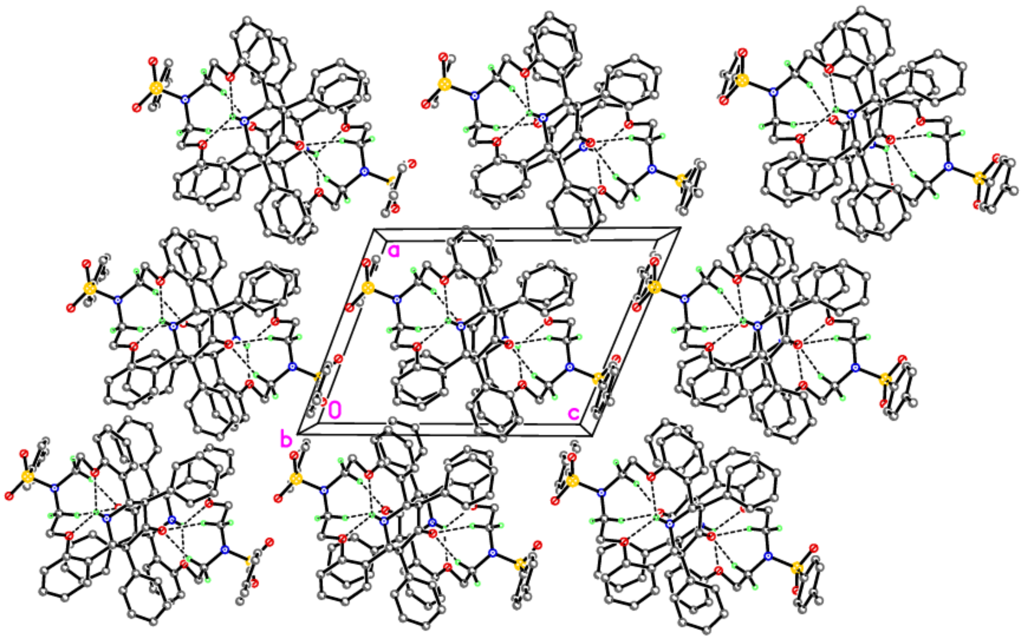

Figure S2. Crystal packing of the H-bonded dimers of **5a**. The intramolecular N─H···O and intermolecular C─H···O hydrogen bonds are depicted by dashed lines.

Full crystallographic data (5a)

Crystal data

$C_{40}H_{38}N_2O_5S$	$Z = 2$
$M_r = 658.78$	$F(000) = 696$
Triclinic, $P\bar{1}$	$D_x = 1.042$ Mg m^{-3}
$a = 11.606$ (2) Å	Synchrotron radiation, $\lambda = 0.96330$ Å
$b = 13.856$ (3) Å	Cell parameters from 500 reflections
$c = 14.920$ (3) Å	$\theta = 2.0–30.0°$
$\alpha = 83.37$ (3)°	$\mu = 0.25$ mm^{-1}
$\beta = 67.38$ (3)°	$T = 100$ K
$\gamma = 71.40$ (3)°	Prism, colourless
$V = 2099.0$ (9) Å^3	0.15 × 0.12 × 0.10 mm

Data collection

Rayonix SX165 CCD diffractometer	4201 reflections with $I > 2\sigma(I)$
φ scan	$R_{int} = 0.118$
Absorption correction: multi-scan *SCALA* (Evans, 2006)	$\theta_{max} = 38.4°$, $\theta_{min} = 2.0°$
$T_{min} = 0.951$, $T_{max} = 0.966$	$h = -12÷14$
21088 measured reflections	$k = -14÷17$
8513 independent reflections	$l = -19÷19$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)] = 0.118$	H-atom parameters constrained
$wR(F^2) = 0.289$	$w = 1/[\sigma^2(F_o^2)]$
$S = 0.95$	$(\Delta/\sigma)_{max} < 0.001$
8513 reflections	$\Delta\rho_{max} = 0.79$ eÅ^{-3}
435 parameters	$\Delta\rho_{min} = -0.45$ eÅ^{-3}
0 restraints	Extinction correction: *SHELXL*, $F_c^* = kF_c[1+0.001 \times F_c^2\lambda^3/\sin(2\theta)]^{-1/4}$
Primary atom site location: difference Fourier map	Extinction coefficient: 0.033 (3)

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2) for (**5a**)*

	x	y	z	U_{iso}*/U_{eq}
S1	0.26548 (10)	0.45557 (7)	0.97257 (5)	0.0371 (3)
O1	0.3675 (3)	0.39958 (18)	1.00850 (15)	0.0426 (7)
O2	0.1400 (3)	0.4351 (2)	1.01140 (16)	0.0461 (7)
C1	0.3837 (4)	0.2581 (3)	0.5307 (2)	0.0333 (9)
H1	0.4194	0.2116	0.4735	0.040*
C2	0.2425 (4)	0.2548 (3)	0.5894 (2)	0.0311 (9)
C3	0.1834 (4)	0.2017 (3)	0.5555 (3)	0.0383 (10)
H3	0.2296	0.1699	0.4933	0.046*
C4	0.0582 (4)	0.1940 (3)	0.6100 (3)	0.0424 (10)
H4	0.0200	0.1574	0.5853	0.051*
C5	-0.0100 (4)	0.2406 (3)	0.7013 (3)	0.0430 (10)
H5	-0.0945	0.2348	0.7394	0.052*
C6	0.0451 (4)	0.2957 (3)	0.7367 (2)	0.0399 (10)
H6	-0.0020	0.3270	0.7991	0.048*
C7	0.1692 (4)	0.3055 (3)	0.6813 (2)	0.0355 (9)
O8	0.2317 (2)	0.35814 (18)	0.71144 (14)	0.0333 (6)
C9	0.1532 (4)	0.4238 (3)	0.7945 (2)	0.0417 (10)
H9A	0.1287	0.3828	0.8538	0.050*
H9B	0.0721	0.4683	0.7864	0.050*
C10	0.2329 (4)	0.4884 (3)	0.8037 (2)	0.0355 (9)
H10A	0.2831	0.5085	0.7379	0.043*
H10B	0.1720	0.5514	0.8403	0.043*
N11	0.3265 (3)	0.4353 (2)	0.85368 (18)	0.0309 (7)
C12	0.4646 (4)	0.4332 (3)	0.8045 (2)	0.0402 (10)
H12A	0.4838	0.4775	0.8410	0.048*
H12B	0.4773	0.4620	0.7387	0.048*
C13	0.5618 (4)	0.3273 (3)	0.7954 (2)	0.0429 (11)
H13A	0.6496	0.3325	0.7835	0.052*
H13B	0.5342	0.2891	0.8562	0.052*
O14	0.5662 (2)	0.27458 (18)	0.71465 (15)	0.0379 (6)
C15	0.6654 (4)	0.1810 (3)	0.6834 (2)	0.0322 (9)
C16	0.7358 (4)	0.1249 (3)	0.7388 (2)	0.0401 (10)
H16	0.7179	0.1491	0.8012	0.048*
C17	0.8325 (4)	0.0333 (3)	0.7035 (2)	0.0411 (10)
H17	0.8809	-0.0047	0.7416	0.049*

C18	0.8579 (4)	-0.0023 (3)	0.6122 (3)	0.0426 (10)
H18	0.9240	-0.0645	0.5875	0.051*
C19	0.7862 (4)	0.0538 (3)	0.5572 (3)	0.0384 (10)
H19	0.8051	0.0296	0.4945	0.046*
C20	0.6848 (4)	0.1467 (3)	0.5930 (2)	0.0318 (9)
C21	0.6024 (4)	0.2051 (3)	0.5331 (2)	0.0372 (10)
H21	0.6292	0.1616	0.4752	0.045*
C22	0.6311 (4)	0.3069 (3)	0.4939 (2)	0.0365 (10)
H22	0.6228	0.3439	0.5508	0.044*
C23	0.5298 (4)	0.3754 (3)	0.4537 (2)	0.0326 (9)
O23	0.5552 (3)	0.44639 (18)	0.39722 (15)	0.0406 (7)
C24	0.3910 (4)	0.3657 (3)	0.4898 (2)	0.0343 (9)
H24	0.3365	0.4148	0.5453	0.041*
N25	0.4634 (3)	0.2155 (2)	0.58930 (19)	0.0349 (8)
H25	0.4351	0.2561	0.6411	0.042*
C25	0.2347 (4)	0.5884 (3)	0.9889 (2)	0.0412 (10)
C26	0.3361 (4)	0.6226 (3)	0.9934 (3)	0.0497 (12)
H26	0.4172	0.5757	0.9914	0.060*
C27	0.3117 (5)	0.7277 (4)	1.0007 (3)	0.0558 (12)
H27	0.3789	0.7517	1.0022	0.067*
C28	0.1914 (6)	0.7993 (4)	1.0058 (3)	0.0675 (15)
C29	0.0932 (5)	0.7622 (3)	1.0029 (3)	0.0553 (12)
H29	0.0113	0.8094	1.0069	0.066*
C30	0.1120 (4)	0.6589 (3)	0.9945 (2)	0.0415 (10)
H30	0.0443	0.6358	0.9925	0.050*
C31	0.1659 (6)	0.9111 (4)	1.0170 (4)	0.0912 (19)
H31A	0.1362	0.9481	0.9660	0.137*
H31B	0.2466	0.9239	1.0116	0.137*
H31C	0.0982	0.9343	1.0808	0.137*
C32	0.7710 (4)	0.2913 (3)	0.4208 (2)	0.0348 (9)
C33	0.8078 (4)	0.2603 (3)	0.3265 (3)	0.0427 (10)
H33	0.7451	0.2480	0.3066	0.051*
C34	0.9374 (5)	0.2464 (3)	0.2588 (3)	0.0526 (12)
H34	0.9619	0.2249	0.1941	0.063*
C35	1.0308 (5)	0.2653 (3)	0.2899 (3)	0.0577 (12)
H35	1.1173	0.2590	0.2451	0.069*
C36	0.9952 (5)	0.2922 (3)	0.3832 (3)	0.0595 (12)
H36	1.0577	0.3026	0.4046	0.071*
C37	0.8675 (4)	0.3046 (3)	0.4482 (3)	0.0438 (10)
H37	0.8449	0.3229	0.5136	0.053*
C38	0.3289 (4)	0.3977 (3)	0.4129 (2)	0.0347 (9)
C39	0.2035 (4)	0.4675 (3)	0.4335 (3)	0.0391 (10)
H39	0.1554	0.4967	0.4967	0.047*
C40	0.1485 (4)	0.4947 (3)	0.3621 (3)	0.0485 (11)
H40	0.0642	0.5429	0.3771	0.058*
C41	0.2154 (4)	0.4524 (3)	0.2702 (3)	0.0479 (11)
H41	0.1779	0.4715	0.2220	0.057*
C42	0.3389 (4)	0.3810 (3)	0.2490 (2)	0.0459 (11)
H42	0.3852	0.3506	0.1862	0.055*
C43	0.3939 (4)	0.3545 (3)	0.3195 (2)	0.0380 (10)
H43	0.4779	0.3058	0.3040	0.046*

Atomic displacement parameters (Å^2) for ***(5a)***

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0442 (7)	0.0486 (7)	0.0173 (4)	-0.0098 (5)	-0.0135 (4)	0.0005 (4)
O1	0.057 (2)	0.0486 (17)	0.0206 (11)	-0.0043 (14)	-0.0240 (12)	0.0059 (10)
O2	0.0427 (19)	0.0619 (18)	0.0274 (13)	-0.0175 (14)	-0.0054 (12)	0.0023 (11)

C1	0.041 (3)	0.043 (2)	0.0221 (17)	-0.0139 (19)	-0.0168 (17)	-0.0006 (15)
C2	0.031 (2)	0.034 (2)	0.0275 (17)	-0.0079 (18)	-0.0117 (17)	0.0006 (15)
C3	0.041 (3)	0.039 (2)	0.0336 (19)	-0.009 (2)	-0.0137 (19)	-0.0017 (16)
C4	0.047 (3)	0.045 (2)	0.039 (2)	-0.016 (2)	-0.018 (2)	0.0039 (18)
C5	0.039 (3)	0.054 (3)	0.041 (2)	-0.023 (2)	-0.018 (2)	0.0148 (19)
C6	0.043 (3)	0.053 (3)	0.0263 (18)	-0.017 (2)	-0.0159 (19)	0.0054 (17)
C7	0.045 (3)	0.045 (2)	0.0262 (18)	-0.019 (2)	-0.0213 (18)	0.0110 (16)
O8	0.0273 (15)	0.0483 (15)	0.0243 (12)	-0.0119 (12)	-0.0083 (11)	-0.0026 (11)
C9	0.049 (3)	0.055 (3)	0.0204 (17)	-0.014 (2)	-0.0127 (18)	-0.0017 (17)
C10	0.043 (3)	0.042 (2)	0.0190 (16)	-0.0034 (19)	-0.0148 (17)	-0.0049 (15)
N11	0.029 (2)	0.0414 (18)	0.0218 (14)	-0.0099 (15)	-0.0084 (13)	-0.0007 (12)
C12	0.050 (3)	0.046 (3)	0.0286 (18)	-0.010 (2)	-0.0217 (19)	-0.0022 (16)
C13	0.047 (3)	0.055 (3)	0.0243 (18)	0.000 (2)	-0.0210 (18)	-0.0058 (17)
O14	0.0468 (18)	0.0379 (16)	0.0244 (12)	-0.0030 (13)	-0.0167 (12)	0.0017 (11)
C15	0.032 (2)	0.033 (2)	0.0230 (17)	-0.0115 (19)	-0.0014 (16)	0.0046 (15)
C16	0.035 (3)	0.054 (3)	0.0240 (18)	-0.005 (2)	-0.0130 (18)	0.0078 (18)
C17	0.040 (3)	0.046 (3)	0.033 (2)	-0.010 (2)	-0.0152 (19)	0.0160 (18)
C18	0.039 (3)	0.041 (2)	0.040 (2)	-0.012 (2)	-0.0099 (19)	0.0108 (18)
C19	0.041 (3)	0.044 (3)	0.037 (2)	-0.021 (2)	-0.0171 (19)	0.0083 (18)
C20	0.034 (2)	0.030 (2)	0.0238 (17)	-0.0094 (19)	-0.0034 (16)	0.0029 (15)
C21	0.057 (3)	0.040 (2)	0.0206 (16)	-0.025 (2)	-0.0138 (18)	0.0048 (15)
C22	0.042 (3)	0.052 (3)	0.0210 (16)	-0.024 (2)	-0.0085 (18)	-0.0007 (16)
C23	0.056 (3)	0.036 (2)	0.0148 (15)	-0.023 (2)	-0.0173 (17)	0.0074 (15)
O23	0.0536 (19)	0.0468 (16)	0.0251 (12)	-0.0193 (14)	-0.0156 (12)	0.0025 (12)
C24	0.032 (3)	0.045 (2)	0.0209 (16)	-0.0062 (19)	-0.0078 (16)	-0.0037 (16)
N25	0.038 (2)	0.043 (2)	0.0278 (15)	-0.0145 (16)	-0.0140 (15)	0.0027 (13)
C25	0.051 (3)	0.053 (3)	0.0223 (18)	-0.012 (2)	-0.0181 (19)	-0.0029 (17)
C26	0.063 (3)	0.049 (3)	0.047 (2)	-0.009 (2)	-0.038 (2)	-0.0010 (19)
C27	0.059 (3)	0.062 (3)	0.065 (3)	-0.010 (3)	-0.048 (2)	0.000 (2)
C28	0.106 (5)	0.056 (3)	0.054 (3)	-0.008 (3)	-0.056 (3)	-0.003 (2)
C29	0.070 (4)	0.051 (3)	0.042 (2)	-0.004 (3)	-0.026 (2)	-0.0098 (19)
C30	0.048 (3)	0.056 (3)	0.0191 (17)	-0.013 (2)	-0.0151 (18)	0.0064 (17)
C31	0.140 (6)	0.056 (4)	0.096 (4)	-0.008 (3)	-0.079 (4)	0.000 (3)
C32	0.042 (3)	0.041 (2)	0.0284 (18)	-0.0166 (19)	-0.0180 (18)	0.0073 (16)
C33	0.037 (3)	0.055 (3)	0.041 (2)	-0.019 (2)	-0.018 (2)	0.0078 (18)
C34	0.060 (3)	0.048 (3)	0.032 (2)	-0.005 (2)	-0.008 (2)	0.0033 (18)
C35	0.041 (3)	0.060 (3)	0.066 (3)	-0.022 (2)	-0.012 (2)	0.013 (2)
C36	0.061 (4)	0.067 (3)	0.058 (3)	-0.036 (3)	-0.024 (3)	0.025 (2)
C37	0.050 (3)	0.046 (3)	0.045 (2)	-0.021 (2)	-0.026 (2)	0.0119 (18)
C38	0.041 (3)	0.038 (2)	0.0280 (18)	-0.012 (2)	-0.0169 (18)	0.0078 (16)
C39	0.041 (3)	0.045 (3)	0.0331 (19)	-0.010 (2)	-0.0177 (19)	0.0017 (17)
C40	0.050 (3)	0.059 (3)	0.042 (2)	-0.018 (2)	-0.026 (2)	0.0167 (19)
C41	0.050 (3)	0.058 (3)	0.046 (2)	-0.017 (3)	-0.033 (2)	0.015 (2)
C42	0.057 (3)	0.062 (3)	0.0275 (19)	-0.026 (3)	-0.019 (2)	0.0028 (18)
C43	0.043 (3)	0.046 (2)	0.0276 (18)	-0.017 (2)	-0.0142 (18)	0.0019 (17)

*Geometric parameters (Å, º) for (**5a**)*

S1—O1	1.448 (3)	C21—C22	1.549 (5)
S1—O2	1.454 (3)	C21—H21	1.0000
S1—N11	1.658 (3)	C22—C32	1.530 (5)
S1—C25	1.786 (4)	C22—C23	1.531 (5)
C1—N25	1.457 (4)	C22—H22	1.0000
C1—C2	1.546 (5)	C23—O23	1.251 (4)
C1—C24	1.559 (5)	C23—C24	1.535 (5)
C1—H1	1.0000	C24—C38	1.532 (5)
C2—C3	1.394 (5)	C24—H24	1.0000
C2—C7	1.429 (5)	N25—H25	0.9000

C3—C4	1.399 (5)	C25—C30	1.424 (5)
C3—H3	0.9500	C25—C26	1.427 (6)
C4—C5	1.395 (5)	C26—C27	1.401 (6)
C4—H4	0.9500	C26—H26	0.9500
C5—C6	1.391 (5)	C27—C28	1.411 (7)
C5—H5	0.9500	C27—H27	0.9500
C6—C7	1.399 (5)	C28—C29	1.408 (7)
C6—H6	0.9500	C28—C31	1.498 (6)
C7—O8	1.388 (4)	C29—C30	1.391 (5)
O8—C9	1.434 (4)	C29—H29	0.9500
C9—C10	1.526 (5)	C30—H30	0.9500
C9—H9A	0.9900	C31—H31A	0.9800
C9—H9B	0.9900	C31—H31B	0.9800
C10—N11	1.505 (4)	C31—H31C	0.9800
C10—H10A	0.9900	C32—C33	1.381 (5)
C10—H10B	0.9900	C32—C37	1.399 (5)
N11—C12	1.476 (5)	C33—C34	1.418 (6)
C12—C13	1.521 (5)	C33—H33	0.9500
C12—H12A	0.9900	C34—C35	1.434 (6)
C12—H12B	0.9900	C34—H34	0.9500
C13—O14	1.456 (4)	C35—C36	1.352 (6)
C13—H13A	0.9900	C35—H35	0.9500
C13—H13B	0.9900	C36—C37	1.392 (6)
O14—C15	1.414 (4)	C36—H36	0.9500
C15—C16	1.385 (5)	C37—H37	0.9500
C15—C20	1.394 (4)	C38—C43	1.402 (5)
C16—C17	1.392 (5)	C38—C39	1.405 (5)
C16—H16	0.9500	C39—C40	1.401 (5)
C17—C18	1.393 (5)	C39—H39	0.9500
C17—H17	0.9500	C40—C41	1.379 (5)
C18—C19	1.391 (5)	C40—H40	0.9500
C18—H18	0.9500	C41—C42	1.396 (6)
C19—C20	1.427 (5)	C41—H41	0.9500
C19—H19	0.9500	C42—C43	1.388 (5)
C20—C21	1.538 (5)	C42—H42	0.9500
C21—N25	1.472 (4)	C43—H43	0.9500
O1—S1—O2	119.81 (16)	C20—C21—H21	106.8
O1—S1—N11	106.84 (15)	C22—C21—H21	106.8
O2—S1—N11	107.44 (15)	C32—C22—C23	111.9 (3)
O1—S1—C25	108.19 (17)	C32—C22—C21	112.6 (3)
O2—S1—C25	107.54 (18)	C23—C22—C21	112.2 (3)
N11—S1—C25	106.28 (15)	C32—C22—H22	106.5
N25—C1—C2	108.9 (3)	C23—C22—H22	106.5
N25—C1—C24	113.6 (3)	C21—C22—H22	106.5
C2—C1—C24	113.3 (3)	O23—C23—C22	120.3 (3)
N25—C1—H1	106.8	O23—C23—C24	118.7 (3)
C2—C1—H1	106.8	C22—C23—C24	120.8 (3)
C24—C1—H1	106.8	C38—C24—C23	112.3 (3)
C3—C2—C7	118.0 (3)	C38—C24—C1	111.5 (3)
C3—C2—C1	121.5 (3)	C23—C24—C1	113.0 (3)
C7—C2—C1	120.5 (3)	C38—C24—H24	106.5
C2—C3—C4	122.0 (3)	C23—C24—H24	106.5
C2—C3—H3	119.0	C1—C24—H24	106.5
C4—C3—H3	119.0	C1—N25—C21	111.4 (3)
C5—C4—C3	119.2 (3)	C1—N25—H25	109.5
C5—C4—H4	120.4	C21—N25—H25	109.2
C3—C4—H4	120.4	C30—C25—C26	120.8 (4)
C6—C5—C4	120.3 (4)	C30—C25—S1	120.2 (3)

C6—C5—H5	119.8	C26—C25—S1	118.9 (3)
C4—C5—H5	119.8	C27—C26—C25	117.6 (4)
C5—C6—C7	120.6 (3)	C27—C26—H26	121.2
C5—C6—H6	119.7	C25—C26—H26	121.2
C7—C6—H6	119.7	C26—C27—C28	122.7 (4)
O8—C7—C6	124.3 (3)	C26—C27—H27	118.6
O8—C7—C2	115.8 (3)	C28—C27—H27	118.6
C6—C7—C2	119.8 (3)	C29—C28—C27	117.8 (4)
C7—O8—C9	116.8 (3)	C29—C28—C31	120.3 (5)
O8—C9—C10	108.3 (3)	C27—C28—C31	121.8 (5)
O8—C9—H9A	110.0	C30—C29—C28	122.1 (4)
C10—C9—H9A	110.0	C30—C29—H29	118.9
O8—C9—H9B	110.0	C28—C29—H29	118.9
C10—C9—H9B	110.0	C29—C30—C25	118.8 (4)
H9A—C9—H9B	108.4	C29—C30—H30	120.6
N11—C10—C9	113.9 (3)	C25—C30—H30	120.6
N11—C10—H10A	108.8	C28—C31—H31A	109.5
C9—C10—H10A	108.8	C28—C31—H31B	109.5
N11—C10—H10B	108.8	H31A—C31—H31B	109.5
C9—C10—H10B	108.8	C28—C31—H31C	109.5
H10A—C10—H10B	107.7	H31A—C31—H31C	109.5
C12—N11—C10	118.0 (3)	H31B—C31—H31C	109.5
C12—N11—S1	114.9 (2)	C33—C32—C37	117.6 (4)
C10—N11—S1	114.2 (2)	C33—C32—C22	121.3 (3)
N11—C12—C13	114.0 (3)	C37—C32—C22	121.0 (3)
N11—C12—H12A	108.8	C32—C33—C34	121.2 (4)
C13—C12—H12A	108.8	C32—C33—H33	119.4
N11—C12—H12B	108.8	C34—C33—H33	119.4
C13—C12—H12B	108.8	C33—C34—C35	118.8 (4)
H12A—C12—H12B	107.6	C33—C34—H34	120.6
O14—C13—C12	108.3 (3)	C35—C34—H34	120.6
O14—C13—H13A	110.0	C36—C35—C34	119.6 (4)
C12—C13—H13A	110.0	C36—C35—H35	120.2
O14—C13—H13B	110.0	C34—C35—H35	120.2
C12—C13—H13B	110.0	C35—C36—C37	120.3 (4)
H13A—C13—H13B	108.4	C35—C36—H36	119.9
C15—O14—C13	117.7 (2)	C37—C36—H36	119.9
C16—C15—C20	121.8 (3)	C36—C37—C32	122.4 (4)
C16—C15—O14	123.4 (3)	C36—C37—H37	118.8
C20—C15—O14	114.8 (3)	C32—C37—H37	118.8
C15—C16—C17	120.4 (3)	C43—C38—C39	117.2 (3)
C15—C16—H16	119.8	C43—C38—C24	120.7 (4)
C17—C16—H16	119.8	C39—C38—C24	122.0 (3)
C16—C17—C18	119.7 (3)	C40—C39—C38	120.9 (3)
C16—C17—H17	120.2	C40—C39—H39	119.6
C18—C17—H17	120.2	C38—C39—H39	119.6
C19—C18—C17	119.7 (4)	C41—C40—C39	120.7 (4)
C19—C18—H18	120.1	C41—C40—H40	119.6
C17—C18—H18	120.1	C39—C40—H40	119.6
C18—C19—C20	121.4 (3)	C40—C41—C42	119.3 (4)
C18—C19—H19	119.3	C40—C41—H41	120.3
C20—C19—H19	119.3	C42—C41—H41	120.3
C15—C20—C19	116.8 (3)	C43—C42—C41	120.0 (3)
C15—C20—C21	122.5 (3)	C43—C42—H42	120.0
C19—C20—C21	120.7 (3)	C41—C42—H42	120.0
N25—C21—C20	109.6 (3)	C42—C43—C38	121.8 (4)
N25—C21—C22	114.3 (3)	C42—C43—H43	119.1
C20—C21—C22	112.2 (3)	C38—C43—H43	119.1

N25—C21—H21	106.8		
N25—C1—C2—C3	-120.7 (3)	C32—C22—C23—C24	153.0 (3)
C24—C1—C2—C3	111.8 (4)	C21—C22—C23—C24	25.3 (4)
N25—C1—C2—C7	58.5 (4)	O23—C23—C24—C38	34.3 (4)
C24—C1—C2—C7	-69.0 (4)	C22—C23—C24—C38	-152.0 (3)
C7—C2—C3—C4	-2.5 (5)	O23—C23—C24—C1	161.5 (3)
C1—C2—C3—C4	176.8 (3)	C22—C23—C24—C1	-24.9 (4)
C2—C3—C4—C5	0.0 (5)	N25—C1—C24—C38	168.5 (3)
C3—C4—C5—C6	1.2 (5)	C2—C1—C24—C38	-66.5 (3)
C4—C5—C6—C7	0.2 (6)	N25—C1—C24—C23	40.9 (4)
C5—C6—C7—O8	-179.4 (3)	C2—C1—C24—C23	166.0 (2)
C5—C6—C7—C2	-2.8 (5)	C2—C1—N25—C21	173.1 (3)
C3—C2—C7—O8	-179.3 (3)	C24—C1—N25—C21	-59.5 (4)
C1—C2—C7—O8	1.4 (5)	C20—C21—N25—C1	-172.3 (3)
C3—C2—C7—C6	3.8 (5)	C22—C21—N25—C1	60.7 (3)
C1—C2—C7—C6	-175.5 (3)	O1—S1—C25—C30	-156.8 (2)
C6—C7—O8—C9	-13.8 (5)	O2—S1—C25—C30	-26.1 (3)
C2—C7—O8—C9	169.5 (3)	N11—S1—C25—C30	88.7 (3)
C7—O8—C9—C10	-169.6 (3)	O1—S1—C25—C26	25.1 (3)
O8—C9—C10—N11	-82.3 (3)	O2—S1—C25—C26	155.8 (3)
C9—C10—N11—C12	128.2 (3)	N11—S1—C25—C26	-89.4 (3)
C9—C10—N11—S1	-92.2 (3)	C30—C25—C26—C27	-1.7 (5)
O1—S1—N11—C12	-39.1 (3)	S1—C25—C26—C27	176.4 (3)
O2—S1—N11—C12	-168.8 (2)	C25—C26—C27—C28	1.4 (6)
C25—S1—N11—C12	76.3 (3)	C26—C27—C28—C29	-0.3 (6)
O1—S1—N11—C10	-179.9 (2)	C26—C27—C28—C31	177.9 (4)
O2—S1—N11—C10	50.3 (3)	C27—C28—C29—C30	-0.5 (6)
C25—S1—N11—C10	-64.6 (3)	C31—C28—C29—C30	-178.7 (4)
C10—N11—C12—C13	-128.3 (3)	C28—C29—C30—C25	0.2 (5)
S1—N11—C12—C13	92.4 (3)	C26—C25—C30—C29	0.9 (5)
N11—C12—C13—O14	79.1 (3)	S1—C25—C30—C29	-177.2 (3)
C12—C13—O14—C15	170.2 (3)	C23—C22—C32—C33	-51.3 (4)
C13—O14—C15—C16	16.9 (5)	C21—C22—C32—C33	76.3 (4)
C13—O14—C15—C20	-165.2 (3)	C23—C22—C32—C37	131.0 (3)
C20—C15—C16—C17	2.4 (6)	C21—C22—C32—C37	-101.5 (4)
O14—C15—C16—C17	-179.8 (3)	C37—C32—C33—C34	-2.5 (5)
C15—C16—C17—C18	-0.4 (6)	C22—C32—C33—C34	179.7 (3)
C16—C17—C18—C19	-0.3 (5)	C32—C33—C34—C35	-0.1 (6)
C17—C18—C19—C20	-1.1 (6)	C33—C34—C35—C36	2.4 (6)
C16—C15—C20—C19	-3.6 (5)	C34—C35—C36—C37	-2.0 (6)
O14—C15—C20—C19	178.5 (3)	C35—C36—C37—C32	-0.6 (6)
C16—C15—C20—C21	176.6 (4)	C33—C32—C37—C36	2.9 (5)
O14—C15—C20—C21	-1.3 (5)	C22—C32—C37—C36	-179.2 (4)
C18—C19—C20—C15	2.9 (5)	C23—C24—C38—C43	53.4 (4)
C18—C19—C20—C21	-177.3 (3)	C1—C24—C38—C43	-74.6 (4)
C15—C20—C21—N25	-59.2 (4)	C23—C24—C38—C39	-129.4 (4)
C19—C20—C21—N25	121.0 (3)	C1—C24—C38—C39	102.6 (4)
C15—C20—C21—C22	68.9 (4)	C43—C38—C39—C40	-2.0 (5)
C19—C20—C21—C22	-110.8 (3)	C24—C38—C39—C40	-179.3 (4)
N25—C21—C22—C32	-169.4 (3)	C38—C39—C40—C41	1.0 (6)
C20—C21—C22—C32	65.1 (3)	C39—C40—C41—C42	0.5 (6)
N25—C21—C22—C23	-42.0 (3)	C40—C41—C42—C43	-0.9 (6)
C20—C21—C22—C23	-167.6 (3)	C41—C42—C43—C38	-0.1 (5)
C32—C22—C23—O23	-33.4 (4)	C39—C38—C43—C42	1.6 (5)
C21—C22—C23—O23	-161.1 (3)	C24—C38—C43—C42	178.9 (3)

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