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Synthesis and cytotoxic activity of new annulated furazan derivatives

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Table of contents

General information S1

Synthesis procedure and analytical data for dioxadecaazadicyclopenta[*e*,*l*]pyrenes **2a-e** S2

NMR and MS spectra of compounds **2a-e** S5

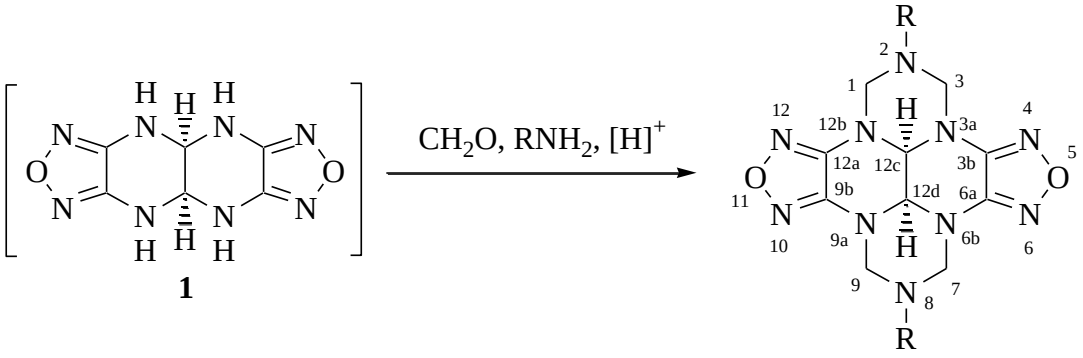
X-ray data of compound **2c** and **2e** S15

Biological assay S20

General information

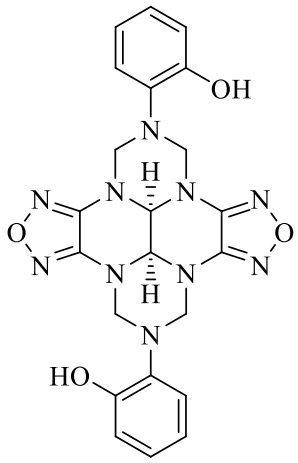
The NMR spectra including two-dimensional homo- (COSY) and heteronuclear (HSQC, HMBC) ones were recorded on a Bruker Avance 500 spectrometer at 500.17 MHz for ^{1}H and 125.78 MHz for ^{13}C according to standard Bruker procedures. DMSO-d_6 or $CDCl_3$ were used as the solvents, and tetramethylsilane as the internal standard. The MALDI TOF/TOF mass spectra (positive ion detection, sinapic acid matrix) were obtained on a Bruker AutoflexTM III Smartbeam mass spectrometer. Samples were prepared by the dried drop technique. Solutions of a matrix and analyte were mixed at a ratio of 50:1 to 100:1, and a drop of the resulting mixture was applied to a target and dried in a stream of warm air. The sample was transferred from the target to the gas phase by laser pulses (200 pulses at a frequency of 100 Hz) using a solid state UV laser (λ 355 nm). The elemental analyses were obtained on a Carlo Erba 1106 analyzer. The melting points were determined on a PHMK 80/2617 melting point apparatus. Column chromatography was performed on KSK silica gel (100–200 μm), visualization with iodine vapor. The X-ray diffraction measurements for compounds **2c,e** were performed on an Agilent XCalibur (Eos, Gemini) automated four-circle diffractometer (graphite monochromator, MoKα radiation, λ = 0.71073 Å, ω-scan mode, $2\theta_{max}$ = 62°) at ambient temperature (293–298 K). 4a,5,9a,10-Tetrahydro-4*H*,9*H*-[1,2,5]oxadiazolo[3,4-*b*][1,2,5]oxadiazolo[3',4':5,6]pyrazino[2,3-*e*]-pyrazine (1,4,5,8-tetraazadifurazano[3,4-*c*][3,4-*h*]decalin) (**1**) was obtained as described previously [R. L. Willer and D. W. Moore, *J. Org. Chem.*, 1985, **50**, 5123]. The reagents used in the work were acquired by Sigma-Aldrich and Acros Organics.

Cyclocondensation of 1,4,5,8-tetraazadifurazano[3,4-*c*][3,4-*h*]decalin (1) with formaldehyde and (het)arylamines (general procedure). A round-bottom flask equipped with a magnetic stirring bar was charged with the appropriate (het)arylamine (2.00 mmol) in MeOH (10 mL), 37 wt% aq formaldehyde (0.45 mL, 4.00 mmol) and 1,4,5,8-tetraazadifurazano[3,4-*c*][3,4-*h*]decalin **1** (0.23 g, 1.00 mmol) in DMSO (1 mL). Then concentrated hydrochloric acid (0.002 g, 0.05 mmol) was added, and the resultant mixture was stirred at 20 °C for 3 h. The mixture was then concentrated. The residue was collected by filtration and washed twice with MeOH (2x10 mL) or was purified by column chromatography (silica gel, MeOH). Compounds **2a–e** were obtained as powders or crystals (recrystallized from DMSO, DMF or $CHCl_3$).



1 **2a-e**

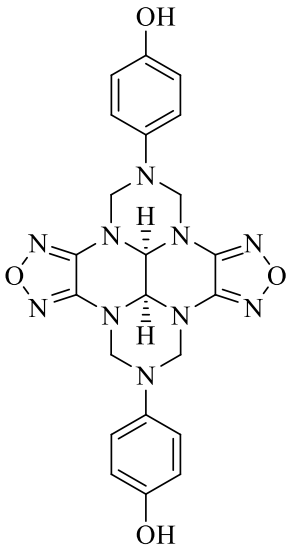
Analytical data for dioxa decaazadicyclopenta[*e,l*]pyrenes 2a-e



2a

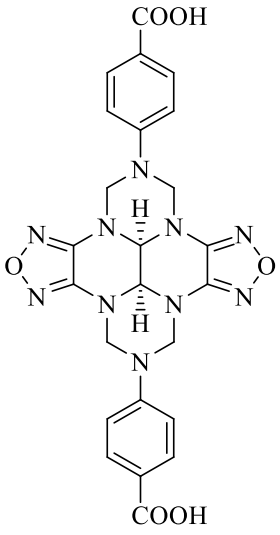
2,8-Bis(2-hydroxyphenyl)-2,3,8,9,12c,12d-hexahydro-1*H*,7*H*-5,11-dioxa-2,3a,4,6,6b,8,9a,10,12,12b-decaazadicyclopenta[*e,l*]pyrene (2a). Pale yellow powdered crystals, 0.29 g (59 % yield), mp 212–214 ºC, R_f 0.53 (MeOH). ^{1}H NMR (500.17 MHz, DMSO-d_6): δ = 4.82 d (4H, CH_2, $^2J_{ab}$ = 12.8 Hz, H_a-1, 3, 7, 9), 5.32 d (4H, CH_2, $^2J_{ba}$ = 12.4 Hz, H_b-1, 3, 7, 9), 5.44 br. s (2H, CH, H-12c, 12d), 6.64 t (2H, CH, H-4′, 4″, ^3J = 6.8 Hz), 6.79–6.86 m (4H, CH, H-3′, 3″, 5′, 5″), 6.91 d (2H, CH, H-6′, 6″, ^3J = 8 Hz), 9.59 br. s (2H, OH). ^{13}C NMR (125.78 MHz, DMSO-d_6): δ = 65.8 (C-1, C-3, C-7, C-9), 66.8 (C-12c, C-12d), 116.3 (C-5′, C-5″), 119.5 (C-6′, C-6″), 119.7 (C-4′, C-4″), 124.5 (C-3′, C-3″), 136.0 (C-2′, C-2″), 147.9 (C-3b, C-6a, C-9b, C-12a), 150.0 (C-1′, C-1″). MALDI TOF/TOF, *m/z* (%): 487 $[M–H]^+$ (10). Anal. Calcd for $C_{22}H_{20}N_{10}O_4$: C, 54.10; H, 4.12; N, 28.68; O, 13.10. Found: C, 53.94; H, 4.09; N, 28.63.

2,8-Bis(4-hydroxyphenyl)-2,3,8,9,12c,12d-hexahydro-1*H*,7*H*-5,11-dioxa-2,3a,4,6,6b,8,9a,10,12,12b-decaazadicyclopenta[*e,l*]pyrene (2b). Pale yellow powdered crystals, 0.31 g (63 % yield), mp 210–212 ºC, R_f 0.52 (MeOH). ^{1}H



2b

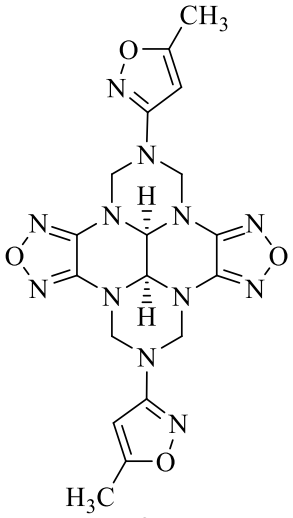
NMR (500.17 MHz, DMSO-d_6): δ = 4.77 d (4H, CH_2, $^2J_{ab}$ = 12.4 Hz, H_a-1, 3, 7, 9), 5.17 d (4H, CH_2, $^2J_{ba}$ = 12.4 Hz, H_b-1, 3, 7, 9), 5.41 br. s (2H, CH, H-12c, 12d), 6.63 d (4H, CH, H-2′, 2″, 6′, 6″, ^3J = 8.8 Hz), 6.90 d (4H, CH, H-3′, 3″, 5′, 5″, ^3J = 8.8 Hz), 9.09 br. s (2H, OH). ^{13}C NMR (125.78 MHz, DMSO-d_6): δ = 66.7 (C-12c, C-12d), 67.0 (C-1, C-3, C-7, C-9), 116.1 (C-2′, C-2″, C-6′, C-6″), 120.7 (C-3′, C-3″, C-5′, C-5″), 140.4 (C-4′, C-4″), 148.0 (C-3b, C-6a, C-9b, C-12a), 153.1 (C-1′, C-1″). MALDI TOF/TOF, *m/z* (%): 487 $[M–H]^+$ (100). Anal. Calcd for $C_{22}H_{20}N_{10}O_4$: C, 54.10; H, 4.12; N, 28.68; O, 13.10. Found: C, 53.95; H, 4.08; N, 28.62.



2c

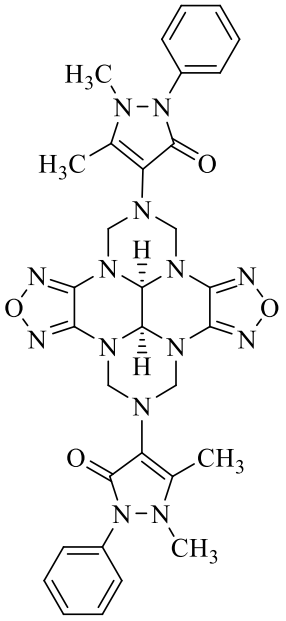
2,8-Bis(4-carboxyphenyl)-2,3,8,9,12c,12d-hexahydro-1*H*,7*H*-5,11-dioxa-2,3a,4,6,6b,8,9a,10,12,12b-decaazadicyclopenta[*e*,*l*]pyrene (2c). Colourless crystals, 0.30 g (55 % yield), mp 214–216 °C, R_f 0.53 (MeOH). ^1H NMR (500.17 MHz, DMSO-d_6): δ = 4.91 d (4H, CH_2, $^2J_{ab}$ = 12.8 Hz, H_a-1, 3, 7, 9), 5.52 br. s (2H, CH, H-12c, 12d), 5.60 d (4H, CH_2, $^2J_{ba}$ = 12.8 Hz, H_b-1, 3, 7, 9), 7.13 d (4H, CH, H-3′, 3″, 5′, 5″ ^3J = 8.8 Hz), 7.80 d (4H, CH, H-2′, 2″, 6′, 6″ ^3J = 8.8 Hz). ^{13}C NMR (125.78 MHz, DMSO-d_6): δ = 64.8 (C-1, C-3, C-7, C-9), 67.1 (C-12c, C-12d), 116.7 (C-3′, C-3″, C-5′, C-5″), 123.2 (C-1′, C-1″), 131.2 (C-2′, C-2″, C-6′, C-6″), 147.9 (C-3b, C-6a, C-9b, C-12a), 151.3 (C-4′, C-4″), 167.4 (COOH). Anal. Calcd for $C_{24}H_{20}N_{10}O_6$: C, 52.94; H, 3.70; N, 25.73; O, 17.63. Found: C, 52.86; H, 3.68; N, 25.67. Crystal data: $C_{30}H_{34}N_{12}O_8$ (*M* = 690.69), monoclinic, space group *C*2/*c*: *a* = 11.8738(15), *b* = 8.6947(9) and *c* = 32.191(4) Å, *β* = 92.819(13)°, *V* = 3319.3(7) Å^3, *Z* = 4, d_{calc} = 1.382 g cm^{-3}, *μ*(MoK*α*) = 0.104 mm^{-1}, *F*(000) = 1448.0. Total of 6698 were collected (3779 independent reflections, R_{int} = 0.0504) and used in the refinement, which converged to $wR_2$0.1742, GOOF 1.074 for all independent reflections [R_1 = 0.0730 was calculated for 3779 reflections with $I > 2\sigma(I)$].

2,8-Bis(5-methylisoxazol-3-yl)-2,3,8,9,12c,12d-hexahydro-1*H*,7*H*-5,11-dioxa-2,3a,4,6,6b,8,9a,10,12,12b-decaazadicyclopenta[*e*,*l*]pyrene (2d). White powdered crystals, 0.19 g (41 % yield), mp 218–220 °C, R_f 0.58



2d

(MeOH). ^{1}H NMR (500.17 MHz, DMSO-d$_6$): δ = 2.50 br. s (6H, CH$_3$, H-6′, 6″), 4.81 d (4H, CH$_2$, $^{2}J_{ab}$ = 12.5 Hz, H$_a$-1, 3, 7, 9), 5.47 d (4H, CH$_2$, $^{2}J_{ba}$ = 12.5 Hz, H$_b$-1, 3, 7, 9), 5.48 br. s (2H, CH, H-12c, 12d), 6.27 br. s (2H, CH, H-4′, 4″). ^{13}C NMR (125.78 MHz, DMSO-d$_6$): δ = 12.6 (C-6′, C-6″), 62.9 (C-1, C-3, C-7, C-9), 66.8 (C-12c, C-12d), 94.6 (C-4′, C-4″), 147.8 (C-3b, C-6a, C-9b, C-12a), 164.7 (C-3′, C-3″), 169.9 (C-5′, C-5″). MALDI TOF/TOF, *m/z* (%): 505 [M+K]$^+$ (50), 489 [M+Na]$^+$ (100), 467 [M+H]$^+$ (20). Anal. Calcd for $C_{18}H_{18}N_{12}O_4$: C, 46.35; H, 3.89; N, 36.04; O, 13.72. Found: C, 46.27; H, 3.82; N, 35.97.

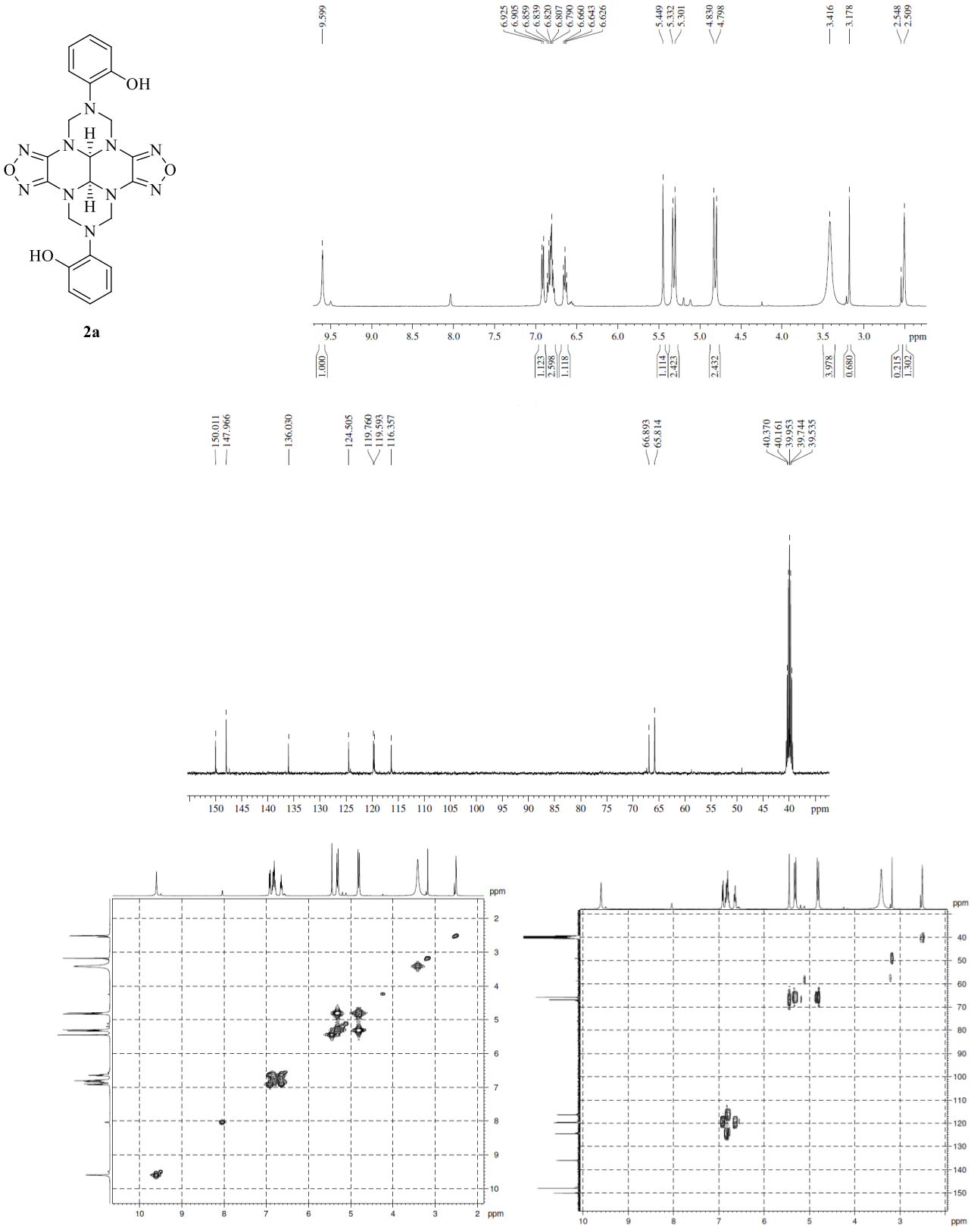


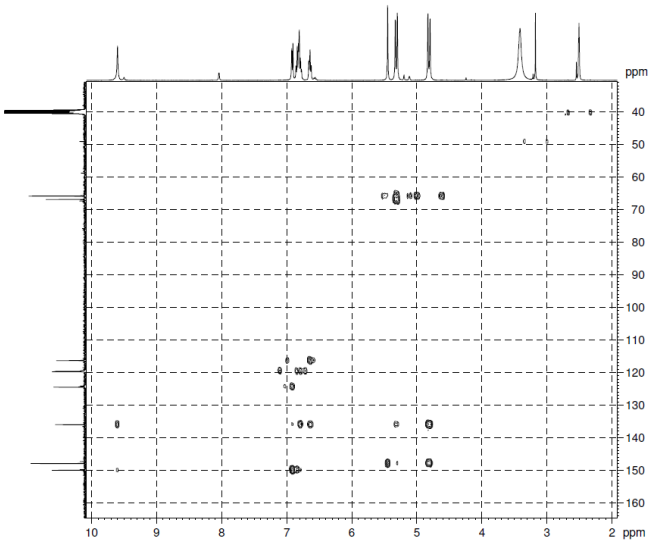
2e

2,8-Bis(1,5-dimethyl-3-oxo-2-phehyl-1,2-dihydro-3*H*-pyrazol-4-yl)-2,3,8,9,12c,12d-hexahydro-1*H*,7*H*-5,11-dioxa-2,3a,4,6,6b,8,9a,10,12,12b-decaazadicyclopenta[*e*,*l*]pyrene (2e). Orange crystals, 0.31 g (46 % yield), mp 220–222 °C, R_f 0.55 (MeOH). ^{1}H NMR (500.17 MHz, CDCl$_3$): δ = 2.19 br. s (6H, CH$_3$, H-14′, 14″), 3.07 br. s (6H, CH$_3$, H-13′, 13″), 4.85 d (4H, CH$_2$, $^{2}J_{ab}$ = 11.2 Hz, H$_a$-1, 3, 7, 9), 4.98 br. s (2H, CH, H-12c, 12d), 5.01 d (4H, CH$_2$, $^{2}J_{ba}$ = 11.2 Hz, H$_b$-1, 3, 7, 9), 7.28 br. s (2H, CH, H-10′, 10″), 7.33–7.38 m (4H, CH, H-8′, 8″, 12′, 12″), 7.46–7.49 m (4H, CH, H-9′, 9″, 11′, 11″). ^{13}C NMR (125.78 MHz, CDCl$_3$): δ = 10.0 (C-14′, C-14″), 35.8 (C-13′, C-13″), 66.8 (C-1, C-3, C-7, C-9), 66.9 (C-12c, C-12d), 116.0 (C-4′, C-4″), 124.1 (C-8′, C-8″, C-12′, C-12″), 127.0 (C-10′, C-10″), 129.2 (C-9′, C-9″, C-11′, C-11″), 134.4 (C-7′, C-7″), 147.5 (C-3b, C-6a, C-9b, C-12a), 152.3 (C-5′, C-5″), 163.2 (C-3′, C-3″). MALDI TOF/TOF, *m/z* (%): 676 [M]$^+$ (10%). Anal. Calcd for $C_{32}H_{32}N_{14}O_4$: C, 56.80; H, 4.76; N, 28.98; O, 9.46. Found: C, 56.73; H, 4.70; N, 28.91. Crystal data for (**6**): $C_{32}H_{32}N_{14}O_4$(*M* = 676.71), monoclinic, space group $P2_1/c$: *a* = 16.6130(11), *b* = 11.0964(5) and *c* = 18.7678(12) Å, *β* = 109.229(7)°, *V* = 3266.7(4) Å^3, *Z* = 4, d_{calc} = 1.376 g cm^{-3}, *μ*(MoK*α*) = 0.097 mm^{-1}, *F*(000) = 1416.0. Total of 16188 were collected (7479 independent reflections, R_{int} = 0.0385) and used in the refinement, which converged to $wR_2$0.0996, GOOF 0.841 for all independent reflections [R_1 = 0.0524 was calculated for 7479 reflections with $I > 2\sigma(I)$].

NMR and MS spectra of compounds 2a-e

Figure S1. NMR and MS spectra of compound **2a**

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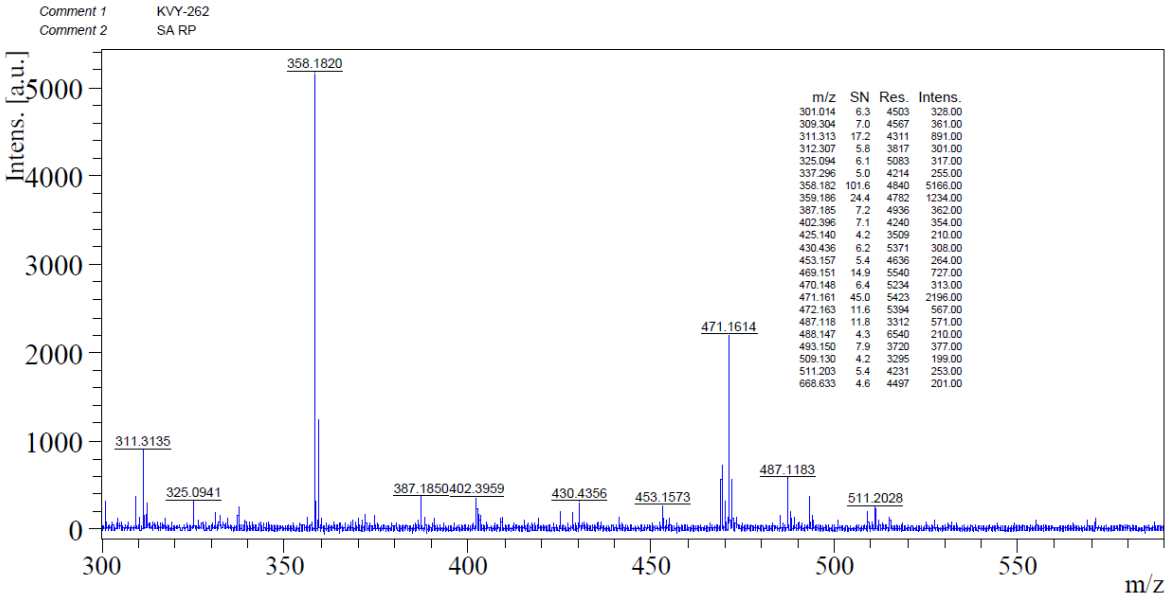
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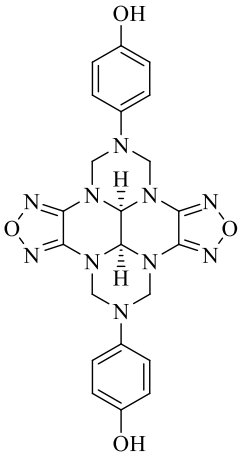
Figure S2. NMR and MS spectra of compound **2b**



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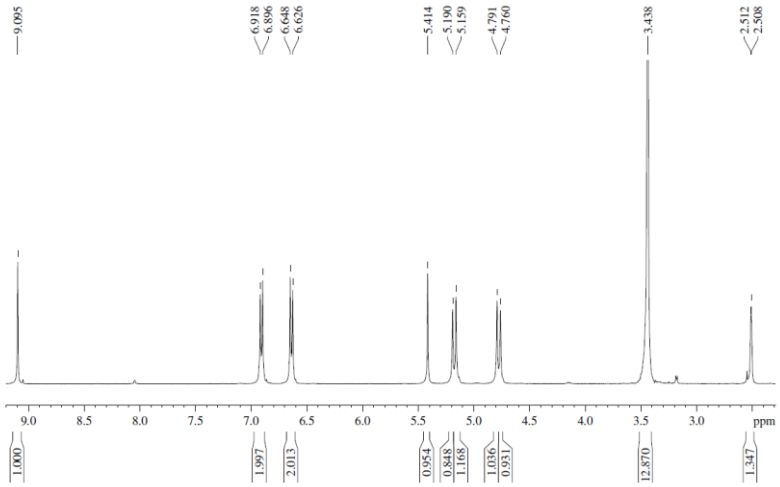

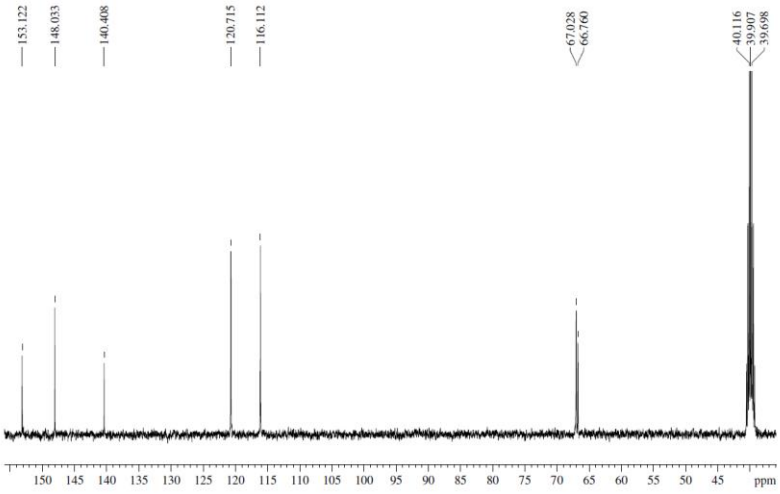

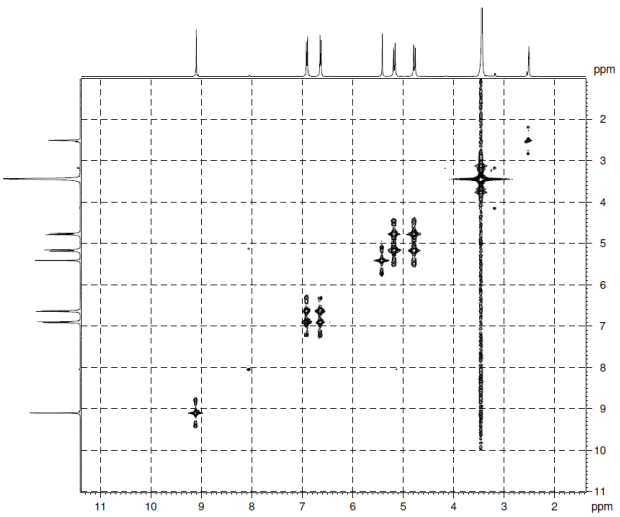

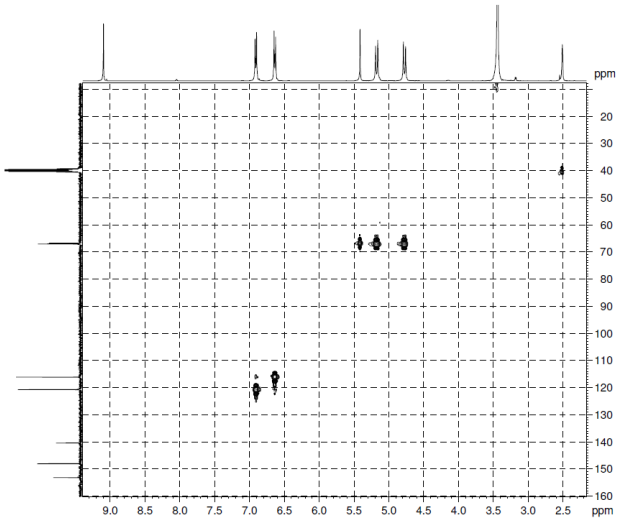

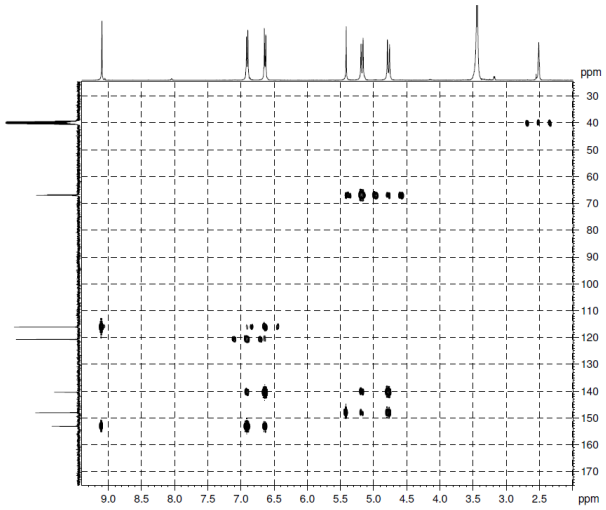
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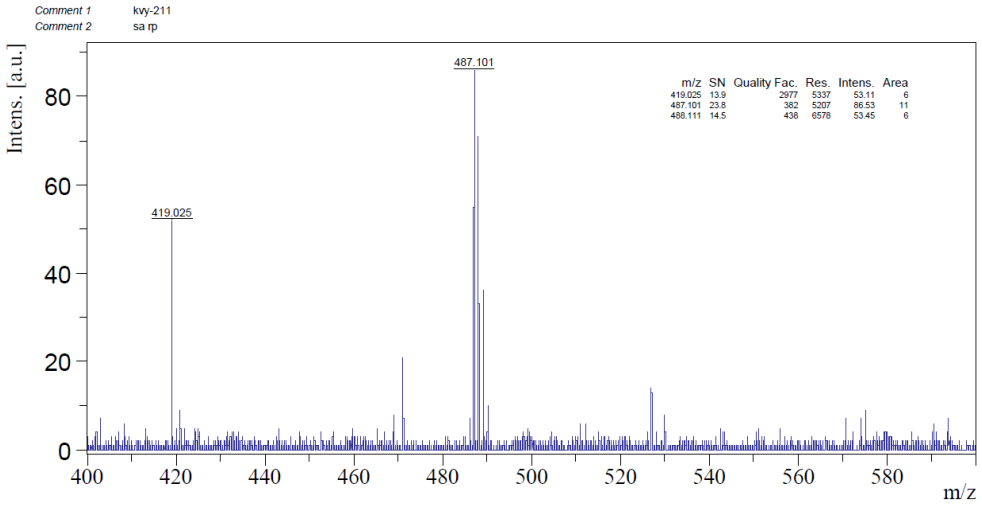
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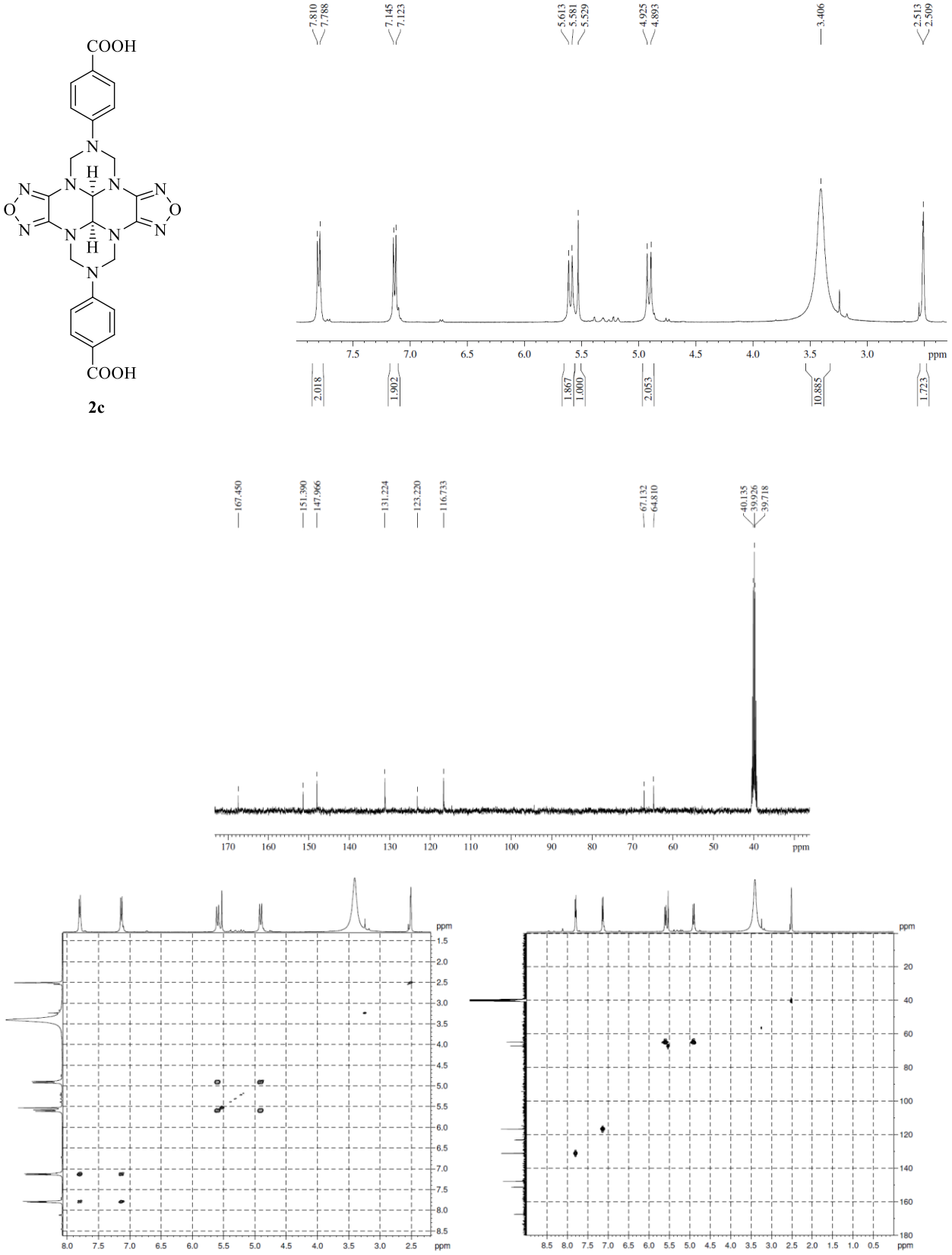
Figure S3. NMR and MS spectra of compound **2c**



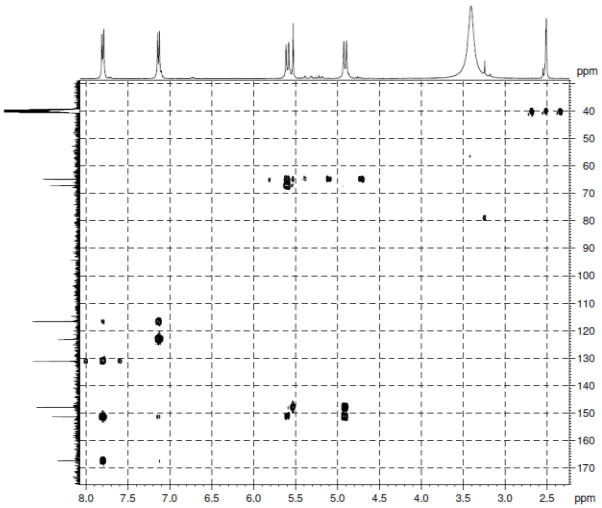

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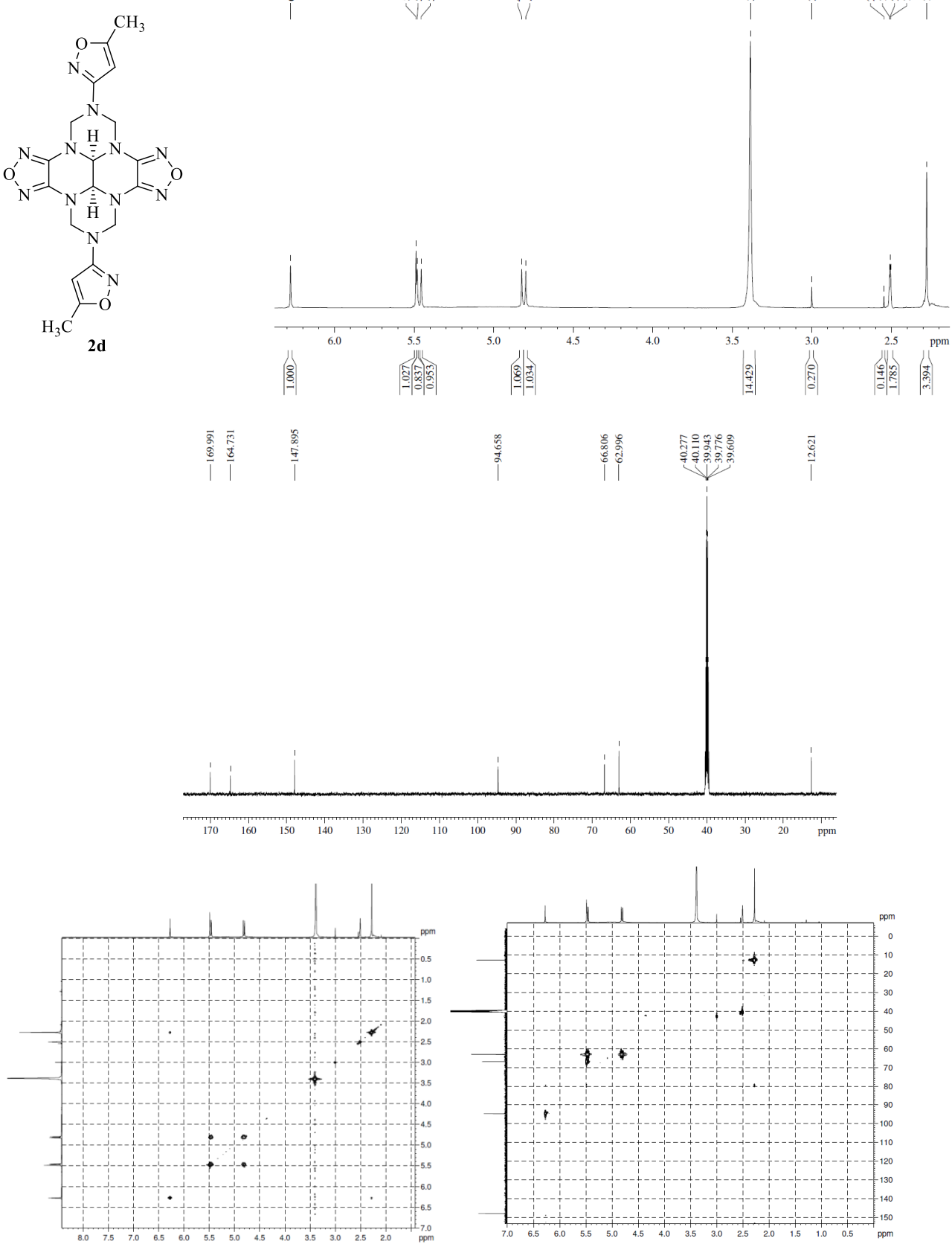
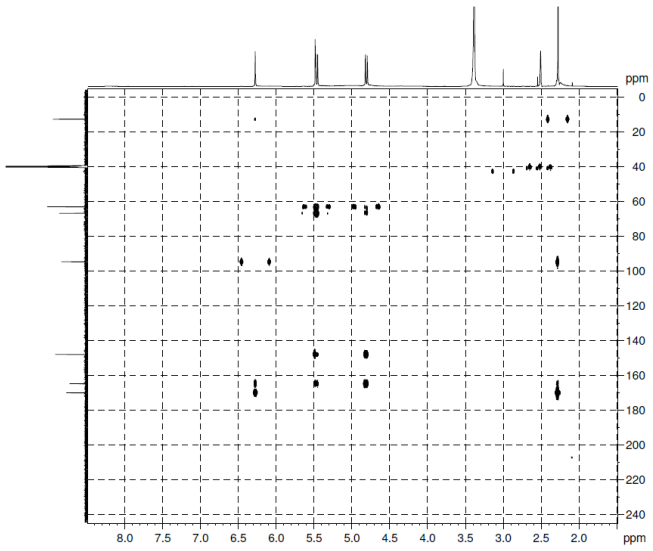
Figure S4. NMR and MS spectra of compound **2d**

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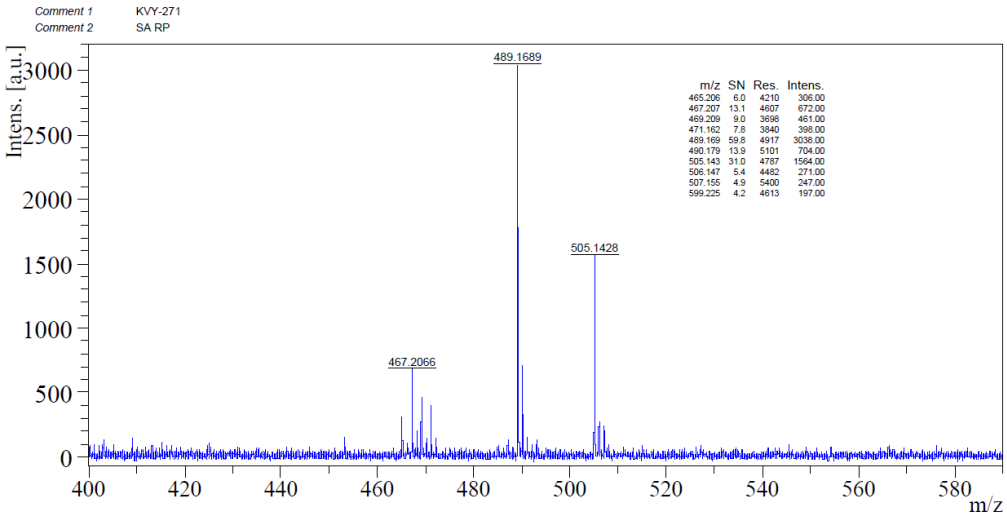
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Intens. [a.u.]
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2500
2000
1500
1000
500
0
489.1689
505.1428
467.2066
m/z SN Res. Intens.
465.206 6.0 4210 306.00
467.207 13.1 4607 672.00
469.209 9.0 3698 461.00
471.162 7.8 3840 398.00
489.169 59.8 4917 3036.00
490.179 13.9 5101 704.00
505.143 31.0 4787 1564.00
506.147 5.4 4482 271.00
507.155 4.9 5400 247.00
599.225 4.2 4613 197.00
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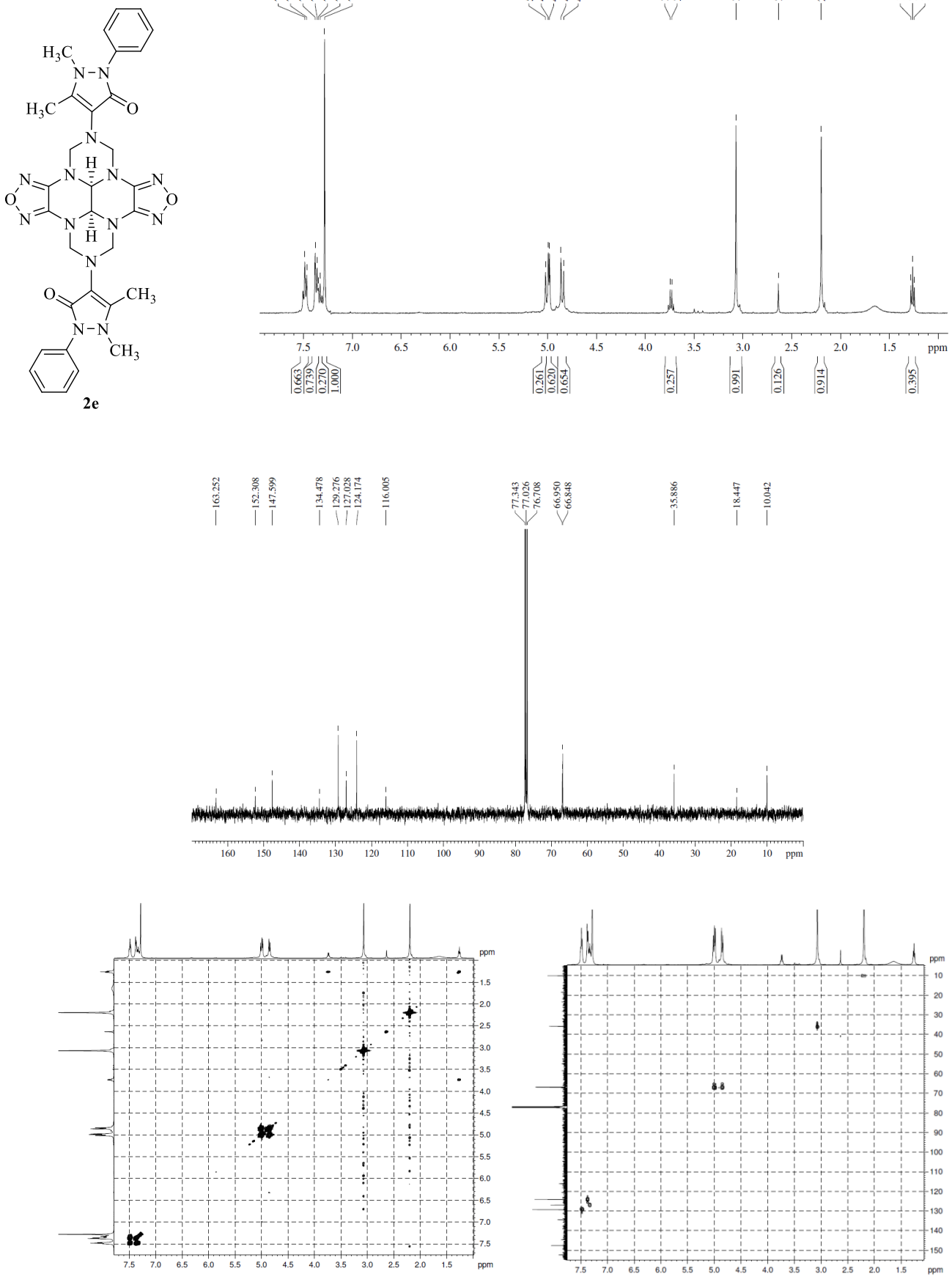
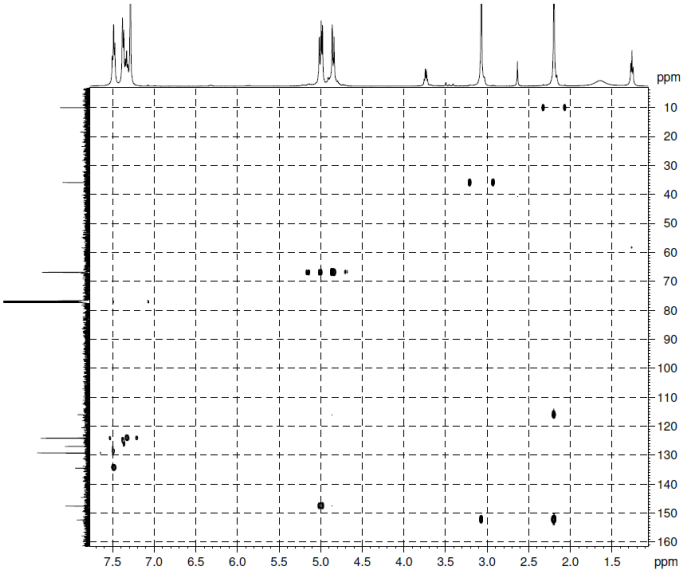
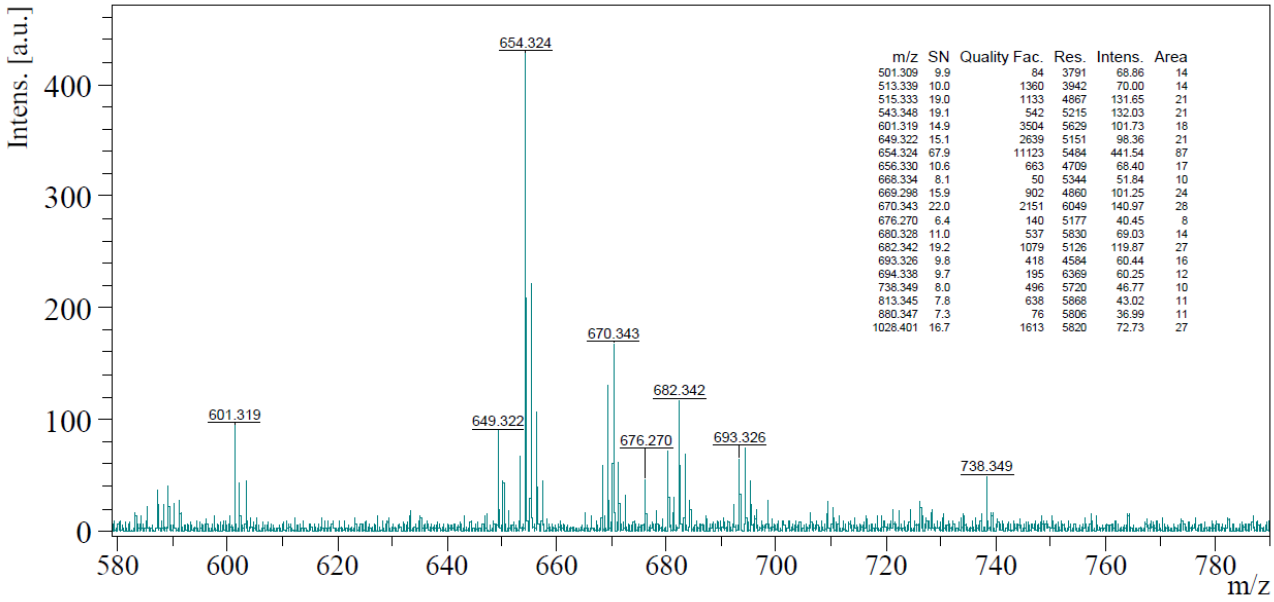
420
440
460
480
500
520
540
560
580
m/z

Figure S5. NMR and MS spectra of compound **2e**





Comment 1 KVY-244
Comment 2 SA RP



m/z	SN	Quality Fac.	Res.	Intens.	Area
501.309	9.9	84	3791	68.86	14
513.339	10.0	1360	3942	70.00	14
515.333	19.0	1133	4867	131.65	21
543.348	19.1	542	5215	132.03	21
601.319	14.9	3504	5629	101.73	18
649.322	15.1	2639	5151	98.36	21
654.324	67.9	11123	5484	441.54	87
656.330	10.6	663	4709	68.40	17
668.334	8.1	50	5344	51.84	10
669.298	15.9	902	4860	101.25	24
670.343	22.0	2151	6049	140.97	28
676.270	6.4	140	5177	40.45	8
680.328	11.0	537	5830	69.03	14
682.342	19.2	1079	5126	119.87	27
693.326	9.8	418	4584	60.44	16
694.338	9.7	195	6369	60.25	12
738.349	8.0	496	5720	46.77	10
813.345	7.8	638	5868	43.02	11
880.347	7.3	76	5806	36.99	11
1028.401	16.7	1613	5820	72.73	27

X-ray data of compound 2c

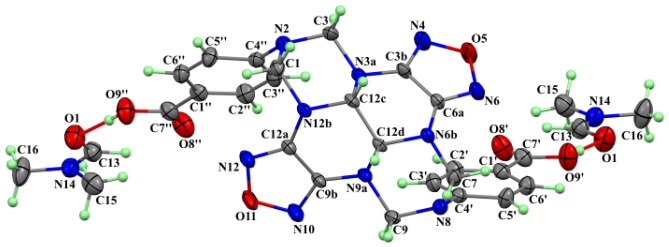


Figure S6. Molecular structure of compound **2c** with atomic numbering according to X-ray data.

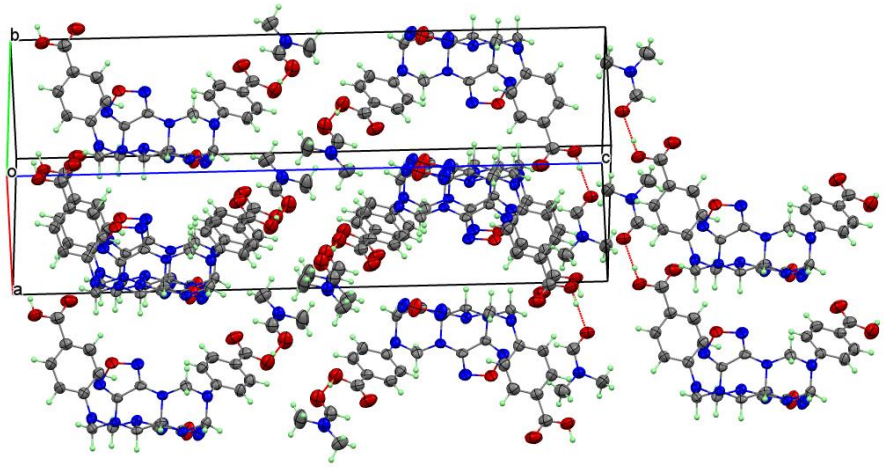


Figure S7. Packing of molecules in **2c**.

Table S1. Crystal data and structure refinement for compound **2c.**

CCDC	2042588
Empirical formula	$C_{30}H_{34}N_{12}O_8$
Formula weight	690.69
Temperature/K	293(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	11.8738(15)
b/Å	8.6947(9)
c/Å	32.191(4)
α/°	90
β/°	92.819(13)
γ/°	90
Volume/Å^3	3319.3(7)
Z	4
ρ_{calc}g/cm^3	1.382
μ/mm^{-1}	0.104
F(000)	1448.0
Radiation	MoKα (λ = 0.71073 Å)
2Θ range for data collection/°	5.068 to 57.93
Index ranges	$-9 \le h \le 14$, $-11 \le k \le 11$, $-43 \le l \le 36$
Reflections collected	6698
Independent reflections	3779 (R_{int} = 0.0504)
Goodness-of-fit on F^2	1.074
Final R indexes [I>=2σ (I)]	R_1 = 0.0730, wR_2 = 0.1742
Final R indexes [all data]	R_1 = 0.1083, wR_2 = 0.1981
Largest diff. peak/hole / e Å^{-3}	

Table S2. Bond Lengths for compound **2c**, Å

Bond		Bond	
N3A–C12C	1.479(3)	C1'–C6'	1.394(4)
N3A–C3B	1.376(3)	N6–C8	1.292(3)
N3A–C3	1.496(3)	N6–O5[1]	1.404(3)
N12B–C12C	1.454(3)	C4'–C5'	1.403(4)
N12B–C8	1.389(3)	C4'–C3'	1.390(4)
N12B–C1	1.484(3)	N14–C16	1.465(5)
C12C–C12C[1]	1.537(5)	N14–C13	1.318(4)
N2–C4'	1.425(4)	N14-C15	1.451(5)
N2–C3	1.446(3)	O5–N4	1.418(3)
N2–C1	1.463(4)	C2'–C3'	1.390(4)
C3B–C8[1]	1.434(4)	C5'–C6'	1.377(4)
C3B–N4	1.302(3)	C7'–O8'	1.209(4)
C1'–C2'	1.395(4)	C7'–O9'	1.330(4)
C1'–C7'	1.482(4)	O1–C13	1.236(4)

Table S3. Bond Angles for compound **2c**, °

Angle		Angle	
C12C–N3A–C3	113.6(2)	N6–C8–N12B	127.0(2)
C3B–N3A–C12C	111.3(2)	N6–C8–C3B[1]	110.6(2)
C3B–N3A–C3	116.9(2)	C5'–C4'–N2	117.0(3)
C12C–N12B–C1	111.21(19)	C3'–C4'–N2	124.2(3)
C8–N12B–C12C	114.05(19)	C3'–C4'–C5'	118.8(3)
C8–N12B–C1	118.1(2)	N2–C3–N3A	111.1(2)
N3A–C12C–C12C[1]	110.81(16)	N2–C1–N12B	111.8(2)
N12B–C12C–N3A	109.57(19)	C13–N14–C16	119.8(3)
N12B–C12C–C12C[1]	111.2(2)	C13–N14–C15	123.0(3)
C4'–N2–C3	119.5(3)	C15–N14–C16	117.2(3)
C4'–N2–C1	115.3(2)	N6[1]–O5–N4	111.39(18)
C3–N2–C1	110.7(2)	C3B–N4–O5	103.8(2)
N3A–C3B–C8[1]	122.8(2)	C3'–C2'–C1'	121.0(3)
N4–C3B–N3A	127.2(2)	C6'–C5'–C4'	120.5(3)
N4–C3B–C8[1]	109.9(2)	O8'–C7'–C1'	123.7(3)
C2'–C1'–C7'	119.3(3)	O8'–C7'–O9'	123.2(3)
C6'–C1'–C2'	118.4(3)	O9'–C7'–C1'	113.1(3)
C6'–C1'–C7'	122.3(3)	C4'–C3'–C2'	120.2(3)
C8–N6–O5[1]	104.3(2)	C5'–C6'–C1'	121.0(3)
N12B–C8–C3B[1]	122.3(2)	O1–C13–N14	124.7(3)

X-ray data of compound 2e

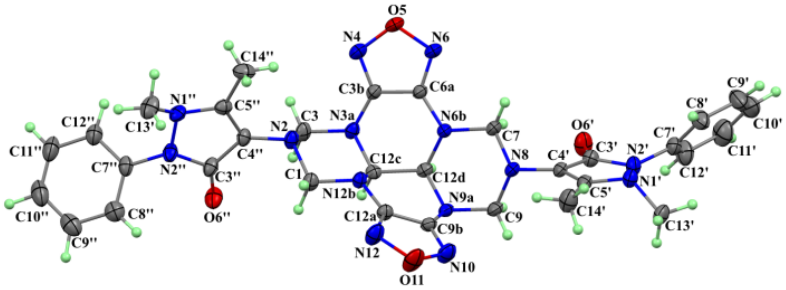


Figure S8. Molecular structure of compound **2e** with atomic numbering according to X-ray data.

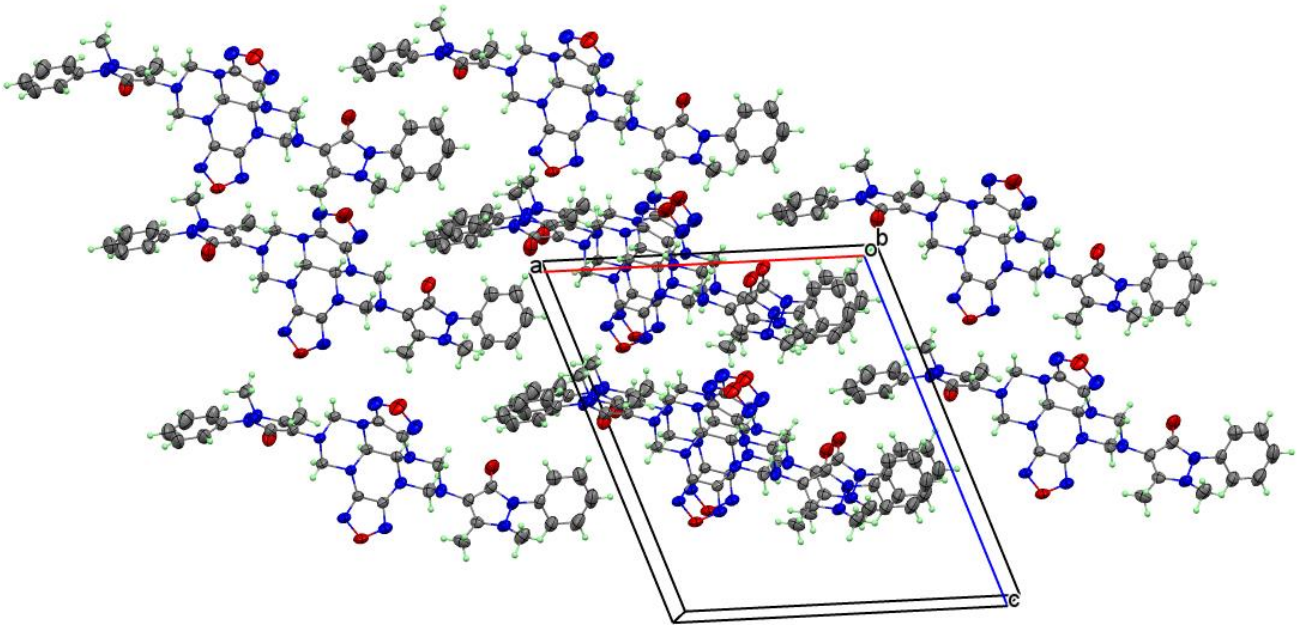


Figure S9. Packing of molecules in **2e**,view along *b* axis.

Table S4. Crystal data and structure refinement for compound **2e**.

CCDC	2042590
Empirical formula	$C_{32}H_{32}N_{14}O_4$
Formula weight	676.71
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	16.6130(11)
b/Å	11.0964(5)
c/Å	18.7678(12)
α/°	90
β/°	109.229(7)
γ/°	90
Volume/Å^3	3266.7(4)
Z	4
ρ_{calc}g/cm^3	1.376
μ/mm^{-1}	0.097

F(000)	1416.0
Radiation	MoKα (λ = 0.71073 Å)
2Θ range for data collection/°	4.33 to 58.24
Index ranges	$-17 \leq h \leq 22$, $-14 \leq k \leq 14$, $-25 \leq l \leq 25$
Reflections collected	16188
Independent reflections	7479(R_{int} = 0.0385)
Goodness-of-fit on F^2	0.841
Final R indexes [I>=2σ (I)]	R_1 = 0.0524, wR_2 = 0.0996
Final R indexes [all data]	R_1 = 0.1307, wR_2 = 0.1204
Largest diff. peak/hole / e $Å^{-3}$	0.15/-0.20

Table S5. Bond Lengths for compound **2e**, Å

Bond		Bond	
O6"–C3"	1.238(2)	N2'–C3'	1.390(2)
N12B–C12C	1.471(2)	N2'–C7'	1.419(2)
N12B–C12A	1.371(2)	O11–N12	1.406(2)
N12B–C1	1.464(2)	O11–N10	1.401(2)
N6B–C6A	1.371(2)	N4–C3B	1.290(2)
N6B–C12D	1.472(2)	N6–C6A	1.295(2)
N6B–C7	1.469(2)	C6A–C3B	1.425(3)
N9A–C12D	1.450(2)	N12–C12A	1.297(2)
N9A–C9B	1.369(2)	C12C–C12D	1.527(3)
N9A–C9	1.460(2)	C12A–C9B	1.421(3)
O6'–C3'	1.231(2)	N10–C9B	1.294(2)
N3A–C12C	1.452(2)	C4'–C5'	1.343(3)
N3A–C3B	1.379(2)	C4'–C3'	1.436(3)
N3A–C3	1.460(2)	C5"–C4"	1.344(3)
O5–N4	1.402(2)	C5"–C14"	1.487(3)
O5–N6	1.406(2)	C5'–C14'	1.484(3)
N1"–N2"	1.400(2)	C4"–C3"	1.432(3)
N1"–C5"	1.371(2)	C7"–C12"	1.376(3)
N1"–C13"	1.462(3)	C7"–C8"	1.385(3)
N8–C4'	1.430(2)	C7'–C8'	1.369(3)
N8–C9	1.472(3)	C7'–C12'	1.375(3)
N8–C7	1.460(3)	C12"–C11"	1.383(3)
N1'–N2'	1.409(2)	C8"–C9"	1.387(4)
N1'–C5'	1.387(2)	C8'–C9'	1.389(4)
N1'–C13'	1.470(3)	C10"–C9"	1.362(4)
N2"–C3"	1.392(2)	C10"–C11"	1.359(4)
N2"–C7"	1.422(2)	C12'–C11'	1.382(4)
N2–C4"	1.428(2)	C10'–C9'	1.357(4)
N2–C3	1.465(2)	C10'–C11'	1.359(4)
N2–C1	1.460(3)		

Table S6. Bond Angles for compound **2e**, °

Angle		Angle	
C12A–N12B–C12C	113.32(15)	N12–C12A–C9B	110.21(19)
C12A–N12B–C1	117.37(16)	N3A–C3B–C6A	122.45(19)
C1–N12B–C12C	113.52(15)	N4–C3B–N3A	127.30(18)
C6A–N6B–C12D	113.99(15)	N4–C3B–C6A	110.05(19)
C6A–N6B–C7	118.36(16)	C9B–N10–O11	104.45(16)
C7–N6B–C12D	113.28(16)	N8–C4'–C3'	125.73(18)
C12D–N9A–C9	112.39(16)	C5'–C4'–N8	125.22(18)
C9B–N9A–C12D	114.35(16)	C5'–C4'–C3'	108.97(17)
C9B–N9A–C9	117.41(17)	N1"–C5"–C14"	121.2(2)
C12C–N3A–C3	112.52(17)	C4"–C5"–N1"	109.95(18)
C3B–N3A–C12C	113.83(15)	C4"–C5"–C14"	128.8(2)
C3B–N3A–C3	117.11(18)	N9A–C9B–C12A	122.59(18)
N4–O5–N6	111.05(15)	N10–C9B–N9A	127.05(19)
N2"–N1"–C13"	116.7(2)	N10–C9B–C12A	110.10(18)
C5"–N1"–N2"	106.39(16)	N1'–C5'–C14'	120.7(2)
C5"–N1"–C13"	121.49(19)	C4'–C5'–N1'	110.33(17)
C4'–N8–C9	111.79(16)	C4'–C5'–C14'	128.9(2)
C4'–N8–C7	113.62(16)	N2–C4"–C3"	125.74(19)
C7–N8–C9	109.78(18)	C5"–C4"–N2	125.16(19)
N2'–N1'–C13'	113.85(18)	C5"–C4"–C3"	109.10(18)
C5'–N1'–N2'	105.55(15)	O6"–C3"–N2"	124.18(19)
C5'–N1'–C13'	119.59(19)	O6"–C3"–C4"	131.42(19)
N1"–N2"–C7"	120.83(16)	N2"–C3"–C4"	104.35(19)
C3"–N2"–N1"	109.66(16)	O6'–C3'–N2'	124.29(19)
C3"–N2"–C7"	127.61(18)	O6'–C3'–C4'	130.97(19)
C4"–N2–C3	113.08(15)	N2'–C3'–C4'	104.71(18)
C4"–N2–C1	111.89(16)	N3A–C3–N2	109.42(16)
C1–N2–C3	111.23(18)	C12"–C7"–N2"	120.7(2)
N1'–N2'–C7'	119.95(16)	C12"–C7"–C8"	120.5(2)
C3'–N2'–N1'	110.09(15)	C8"–C7"–N2"	118.7(2)
C3'–N2'–C7'	124.85(18)	N2–C1–N12B	108.57(17)
N10–O11–N12	111.10(15)	C8'–C7'–N2'	121.3(2)
C3B–N4–O5	104.55(16)	C8'–C7'–C12'	120.2(2)
C6A–N6–O5	104.12(16)	C12'–C7'–N2'	118.4(2)
N6B–C6A–C3B	122.31(19)	N9A–C9–N8	108.68(17)
N6–C6A–N6B	127.43(18)	N8–C7–N6B	107.56(16)
N6–C6A–C3B	110.21(19)	C7"–C12"–C11"	119.1(3)
C12A–N12–O11	104.11(16)	C7"–C8"–C9"	119.1(3)
N12B–C12C–C12D	112.20(15)	C7'–C8'–C9'	119.5(3)
N3A–C12C–N12B	108.05(15)	C11"–C10"–C9"	120.9(3)
N3A–C12C–C12D	111.70(16)	C7'–C12'–C11'	119.4(3)
N6B–C12D–C12C	112.20(16)	C10"–C9"–C8"	119.9(3)
N9A–C12D–N6B	108.03(15)	C10"–C11"–C12"	120.4(3)
N9A–C12D–C12C	111.57(16)	C9'–C10'–C11'	120.4(3)
N12B–C12A–C9B	122.24(18)	C10'–C9'–C8'	120.1(3)
N12–C12A–N12B	127.49(18)	C10'–C11'–C12'	120.4(3

Biological assay data

Cell culturing. Cells (Jurkat, K562, U937, Fibroblats) were purchased from European Collection of Authenticated Cell Cultures (ECACC) and cultured according to standard mammalian tissue culture protocols and sterile technique. Human cancer cell line HeLa was obtained from the HPA Culture Collections (UK). All cell lines used in the study were tested and shown to be free of mycoplasma and other viral contamination. HeLa cell line was cultured as monolayers and maintained in Dulbecco's modified Eagle's medium (DMEM, Gibco BRL) supplemented with 10% foetal bovine serum and 1% penicillin-streptomycin solution at 37 °C in a humidified incubator under a 5%CO_2 atmosphere. Suspension cell cultures were maintained in RPMI 1640 (Jurkat, K562, U937) (Gibco) and adgesion cell cultures (Fibroblats) were maintained in DMEM (Gibco) supplemented with 4 mM glutamine, 10% FBS (Sigma) and 100 units per ml penicillin–streptomycin (Sigma). All types of cells were grown in an atmosphere of 5% CO_2 at 37 ^oC. The cells were sub cultured at 2–3 days intervals. Adherent cells (HeLa) were suspended using trypsin/EDTA and counted after they have reached 80% confluency. Cells were then seeded in 24 well plates at 5×10^4 cells per well and incubated overnight. Jurkat, K562, U937, fibroblats cells were sub cultured at 2 days intervals with a seeding density of 1 x 10^5 cells per 24 well plates in DMEM or in RPMI with 10% FBS.

Cytotoxicity assay. Viability (live/dead) assessment was performed by staining cells with 7-AAD (7-Aminoactinomycin D) (Biolegend). After treatment cells were harvested, washed 1-2 times with phosphate-buffered saline (PBS) and centrifuged at 400 g for 5 min. Cell pellets were resuspended in 200 mL of flow cytometry staining buffer (PBS without Ca^{2+} and Mg^{2+}, 2,5% FBS) and stained with 5 μL of 7-AAD staining solution for 15 min at room temperature in the dark. Samples were acquired on NovoCyteTM 2000 FlowCytometry System (ACEA) equipped with 488 nm argon laser. Detection of 7-AAD emission was collected through a 675/30 nm filter in FL4 channel.