Discovery of a new class of 16-membered (2Z,11Z)-3,11-di(aryl/naphthyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-dienes as novel anti-tumor agents

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Physical and Spectral Characterization:

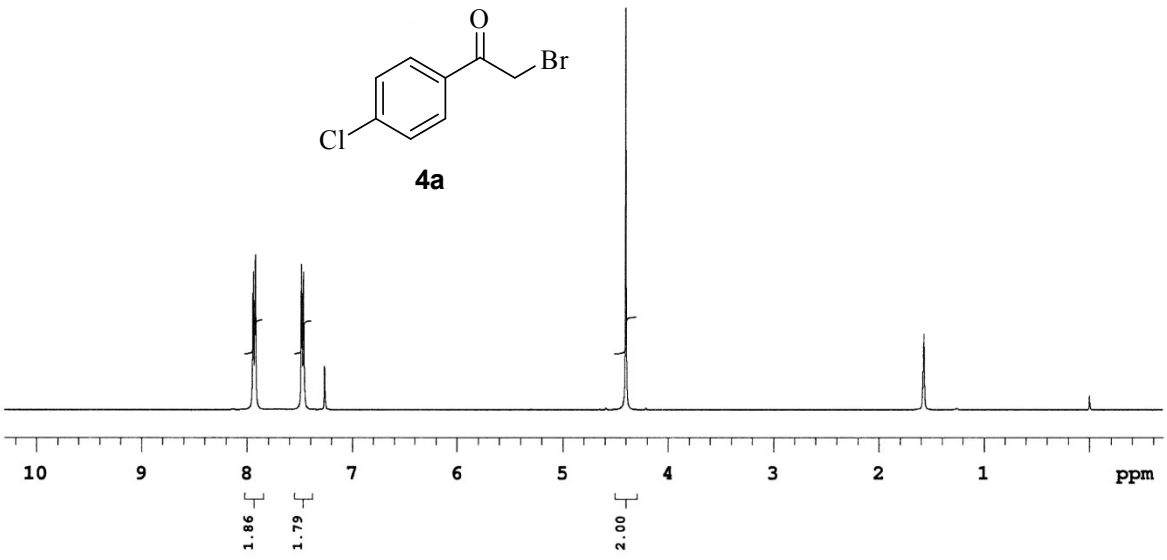
2-bromo-1-(4-chlorophenyl)ethanone (**4a**):

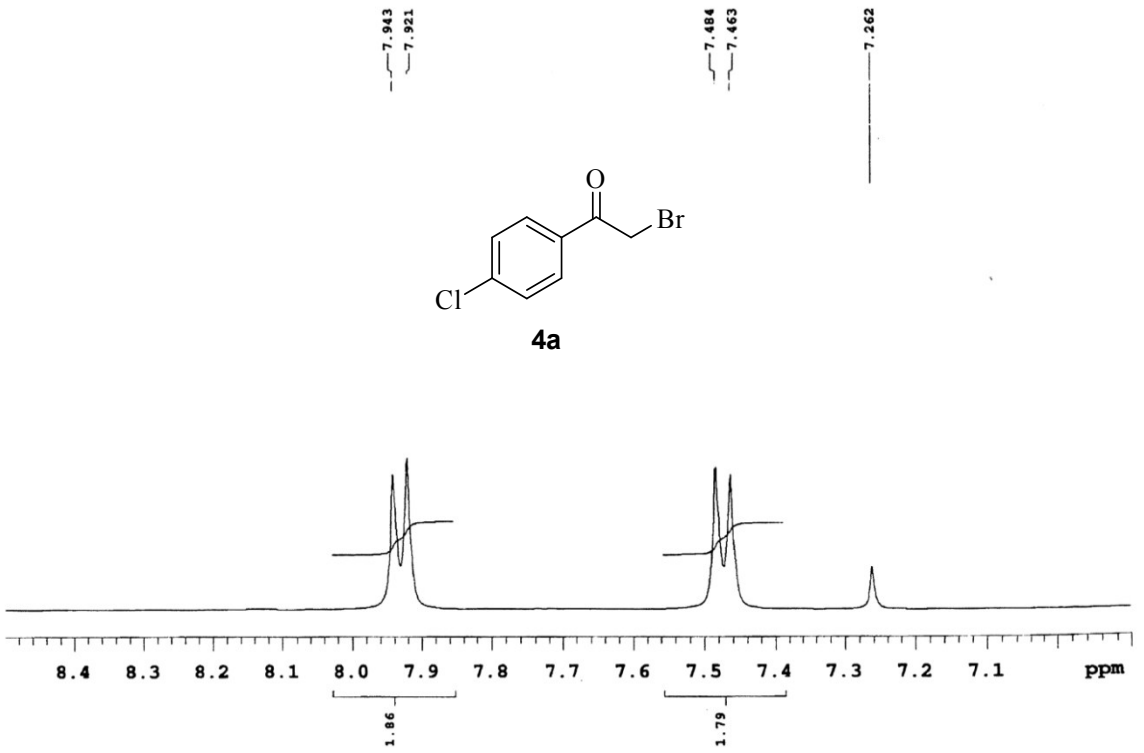
Off-white solid. Yield: 91%.; mp. 94-96°C.

^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.93 (d, J = 8.8 Hz, 2H, arom H), 7.47 (d, J = 8.4 Hz, 2H, arom H), 4.40 (s, 2H, -CH_2).

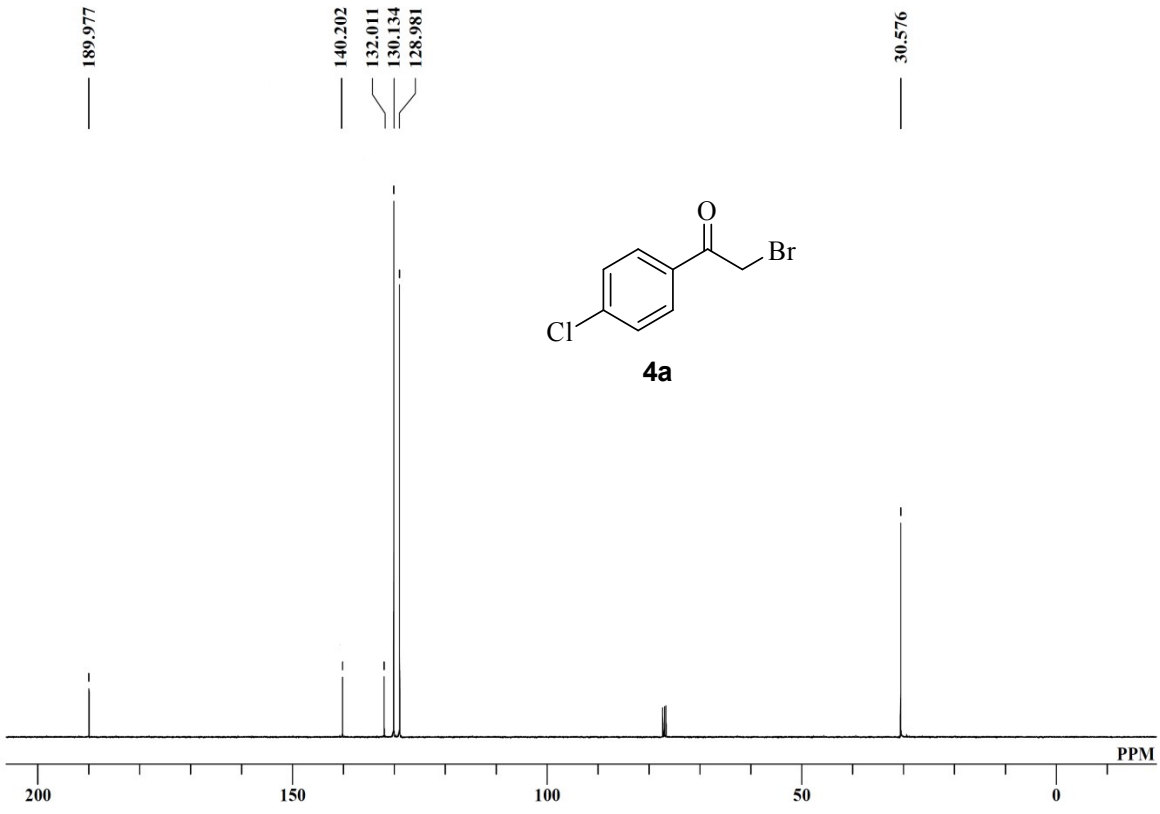
^{13}C NMR (100 MHz, $CDCl_3$, δ/ppm): 189.98 (C), 140.20 (C), 132.01 (C), 130.13 (2C), 128.98 (2C), 30.58 (C).

MS (ESI): *m/z* $[M+H]^+$ 233.00, $[M+H+2]^+$ 234.90.

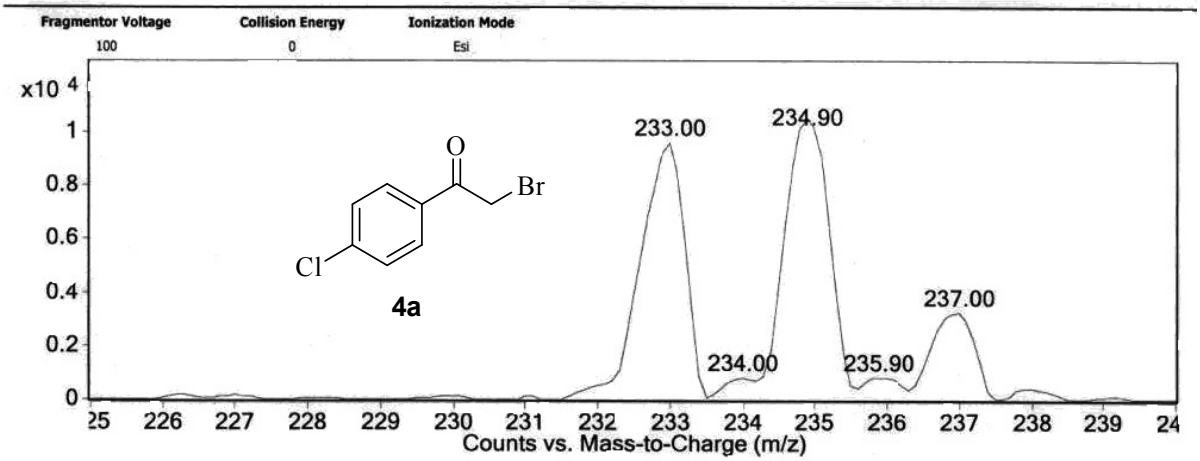



7.943
7.921
7.484
7.463
7.262
O
Br
Cl
8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
1.86
1.79

4a


189.977
140.202
132.011
130.134
128.981
30.576
O
Br
Cl
PPM
200 150 100 50 0

4a



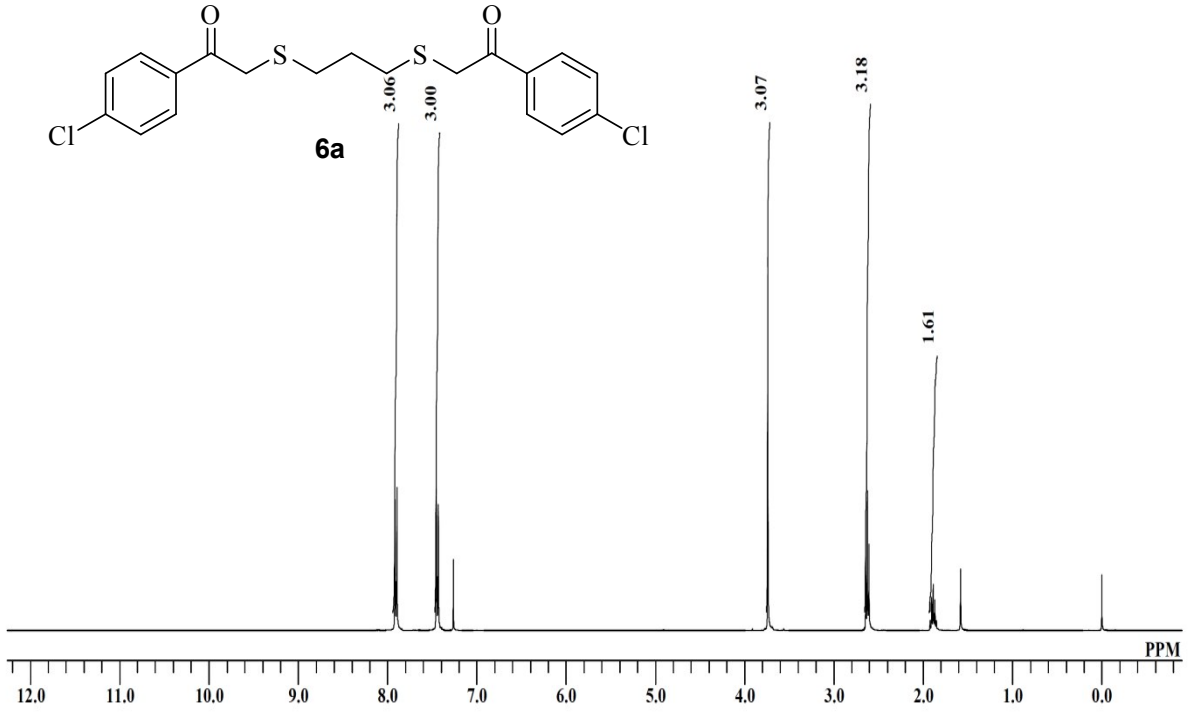
Spectral data for 2,2'-(propane-1,3-diylbis(sulfanediyl))bis(1-(4-chlorophenyl)ethanone) (6a):

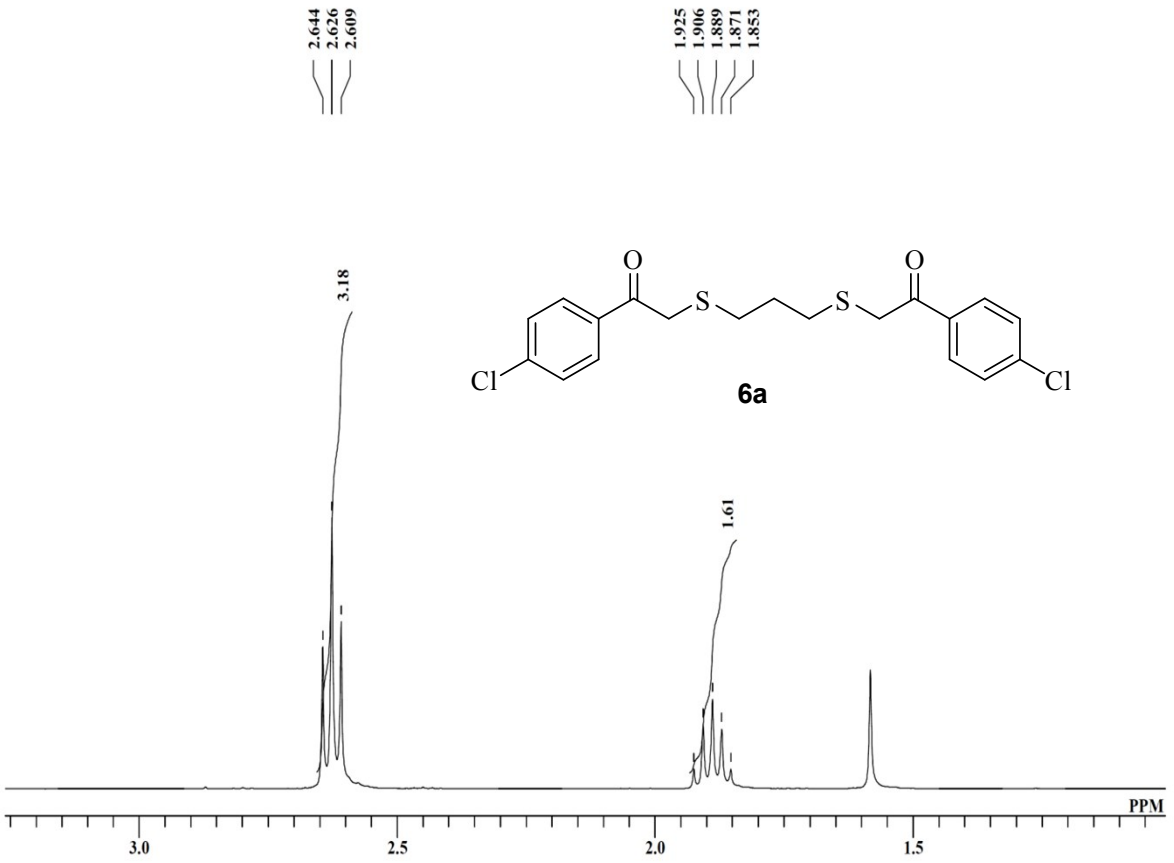
Pale yellow solid. Yield: 95%.; mp. 58-60°C.

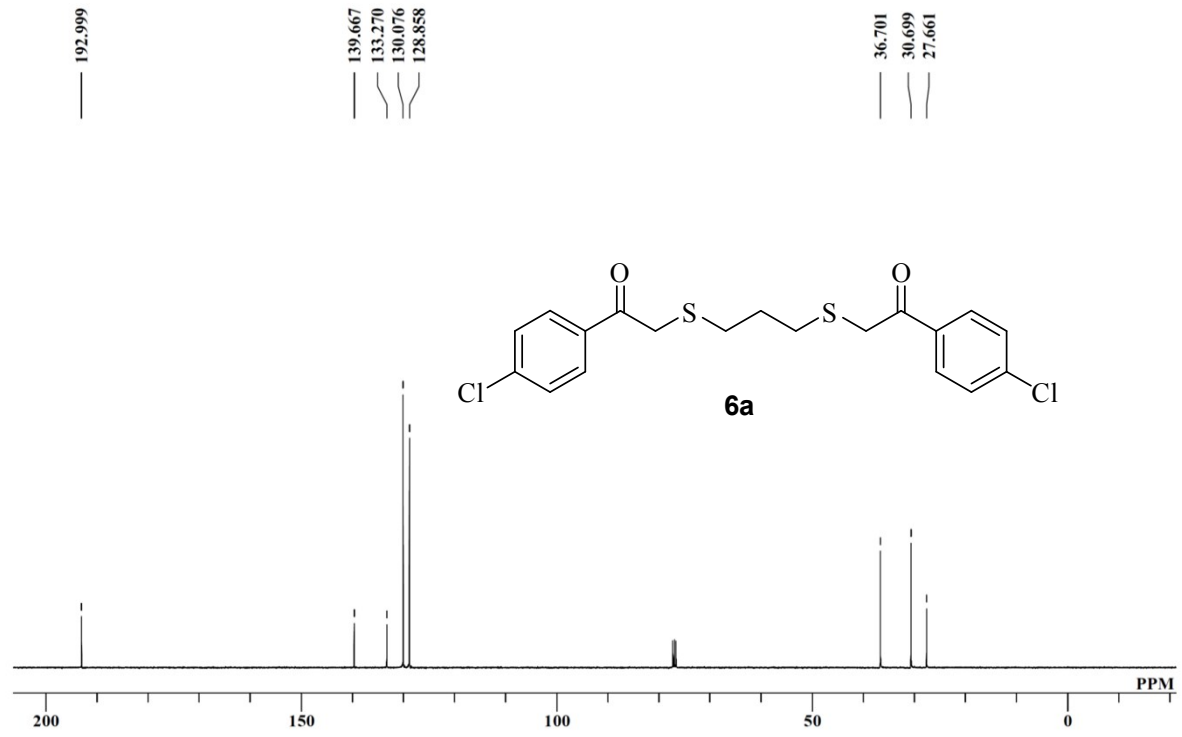
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.91 (d, J = 8.4 Hz, 4H, arom H), 7.44 (d, J = 8.4 Hz, 4H, arom H), 3.74 (s, 4H, 2- CH_2), 2.63 (t, J = 7.2 Hz, 4H, 2-SCH_2), 1.89 (quint, J = 7.6 Hz, 2H, -CH_2).

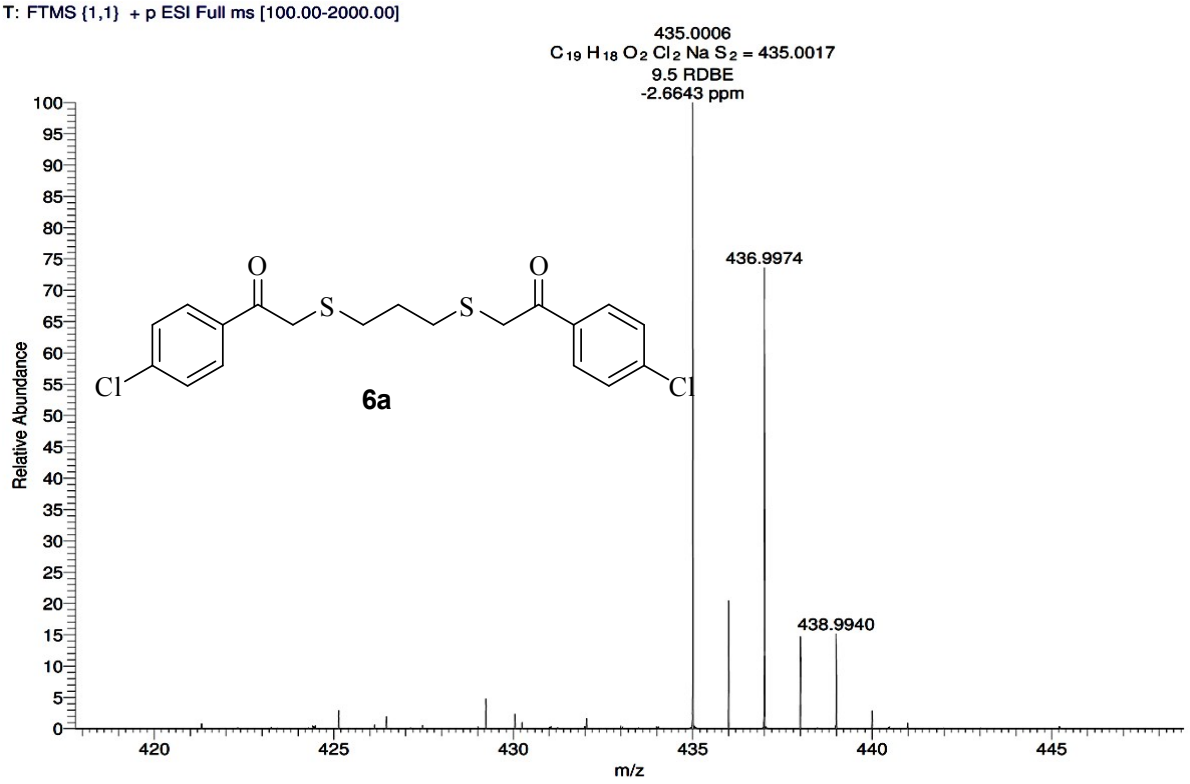
^{13}C NMR (100 MHz, $CDCl_3$, δ/ppm): 193.0 (2C), 139.67 (2C), 133.27 (2C), 130.08 (4C), 128.86(4C), 36.70 (2C), 30.70(2C), 27.66 (C).

HRMS (ESI) : $[M+Na]^+$ Calcd for $C_{19}H_{18}O_2Cl_2N_2Na$ 435.0017, found 435.0006.




2.644
2.626
2.609
1.925
1.906
1.889
1.871
1.853
3.18
1.61
O
S
S
O
Cl
Cl
6a
PPM
3.0
2.5
2.0
1.5


192.999
139.667
133.270
130.076
128.858
36.701
30.699
27.661
O
S
S
O
Cl
Cl
6a
PPM
200
150
100
50
0



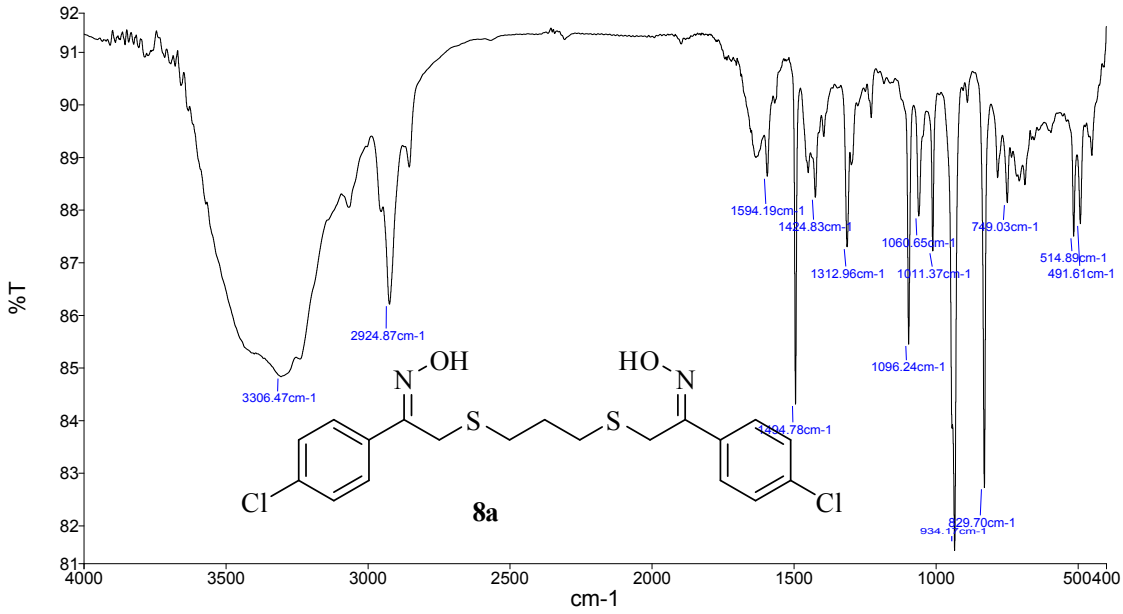
Spectral data for (1Z,1'Z)-1-(4-chlorophenyl)-2-(3-((Z)-2-(4-chlorophenyl)-2-(hydroxyimino)ethylthio)propylthio)ethanone oxime (8a):

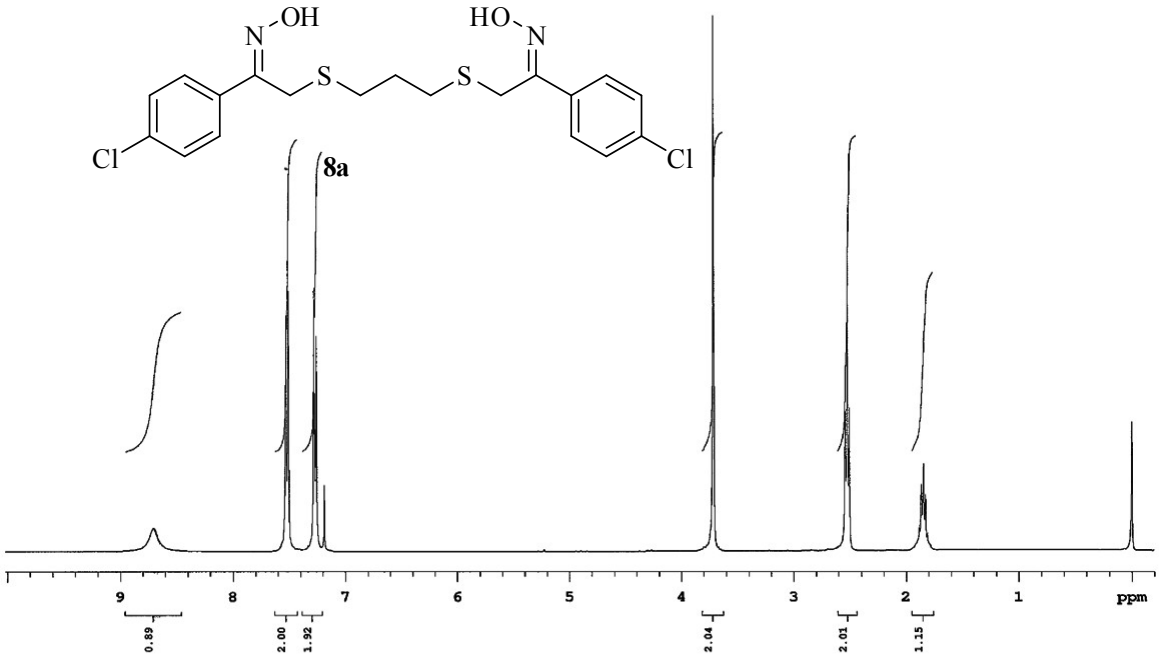
Off-white solid. Yield: 98%.; mp. 105-107°C

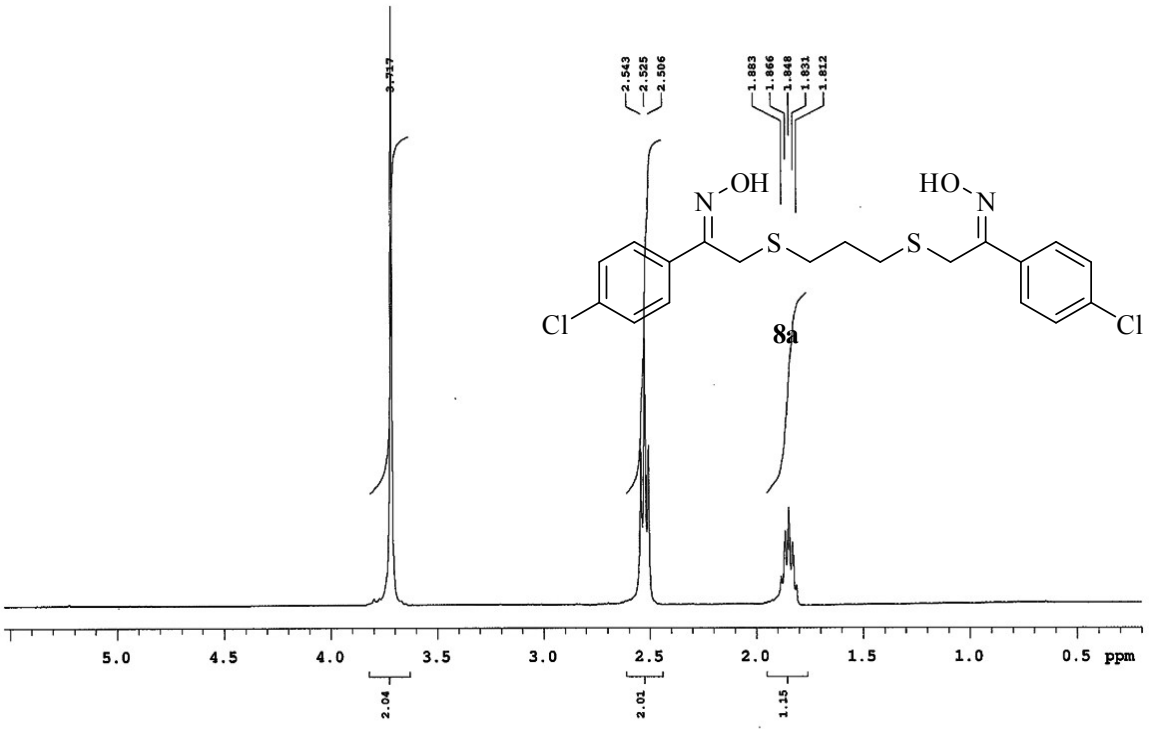
FT-IR (KBr, cm^{-1}): 3306.4, 2924.8, 1640.0, 1594.2, 1494.8, 1096.2, 934.1, 829.7, 749.0, 686.0

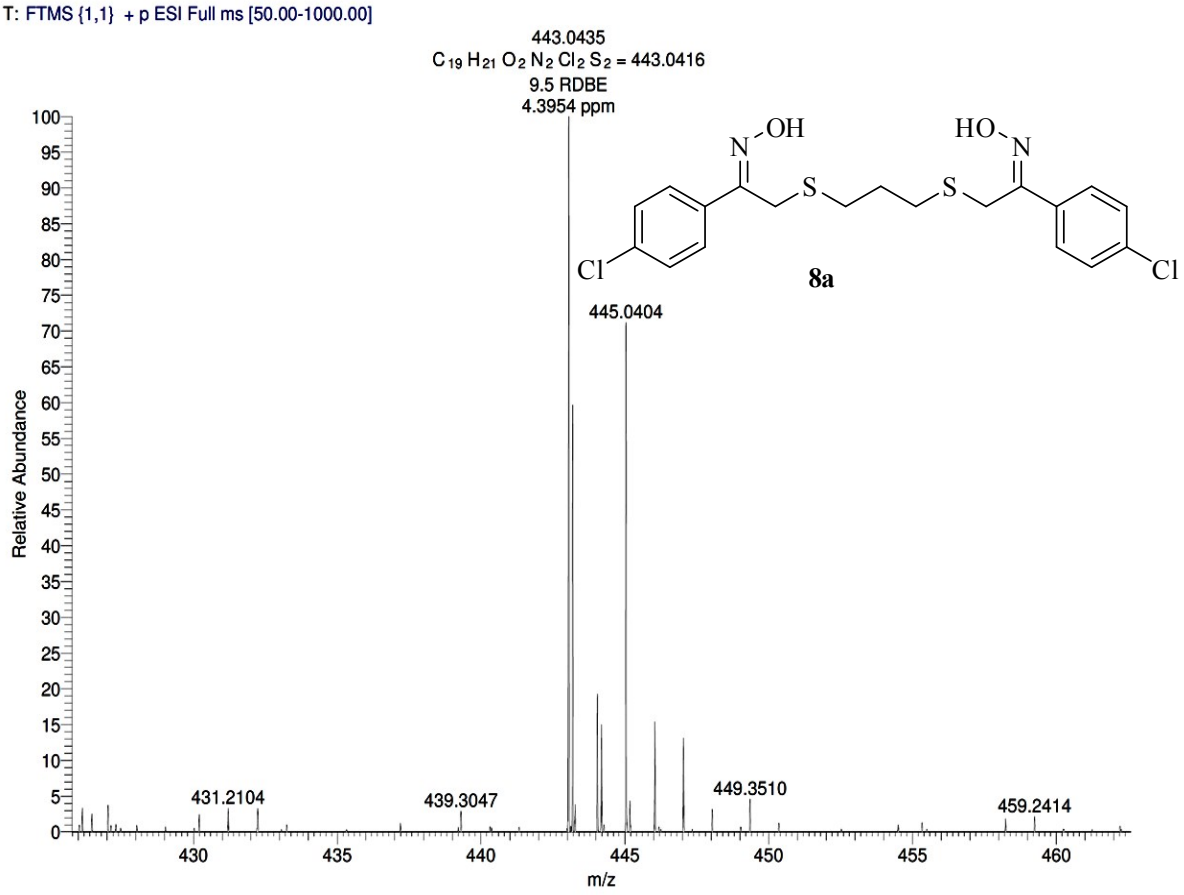
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 8.71 (br s, 2H, 2-OH), 7.52 (d, *J* = 8.4 Hz, 4H, arom H), 7.27 (d, *J* = 8.8 Hz, 4H, arom H), 3.72 (s, 4H, 2-CH_2), 2.52 (t, *J* = 7.6 Hz, 4H, 2-SCH_2), 1.85 (quint, *J* = 7.6 Hz, 2H, -CH_2)

HRMS (ESI) : $[M+H]^+$ Calcd for $C_{19}H_{21}O_2N_2Cl_2S_2$ 443.0416, found 443.0435.


%T
cm-1
3306.47cm-1
2924.87cm-1
1594.19cm-1
1424.83cm-1
1312.96cm-1
1096.24cm-1
1060.65cm-1
1011.37cm-1
749.03cm-1
514.89cm-1
491.61cm-1
829.70cm-1
8a


8a
ppm
0.89
2.00
1.92
2.04
2.01
1.15


3.737
2.543
2.525
2.506
1.883
1.866
1.848
1.831
1.812
N
OH
HO
N
S
S
Cl
Cl
8a
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5 ppm
2.04
2.01
1.15


T: FTMS {1,1} + p ESI Full ms [50.00-1000.00]
443.0435
C19 H21 O2 N2 Cl2 S2 = 443.0416
9.5 RDBE
4.3954 ppm
N
OH
HO
N
S
S
Cl
Cl
8a
445.0404
Relative Abundance
431.2104
439.3047
449.3510
459.2414
m/z

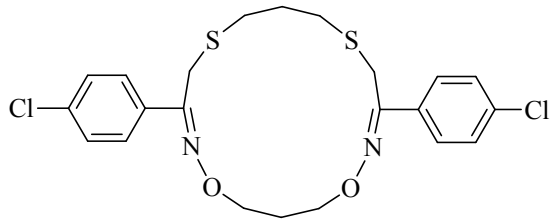
Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-bis(4-chlorophenyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1a):

Off-white solid; Yield: 73.7%; mp 146-148°C.

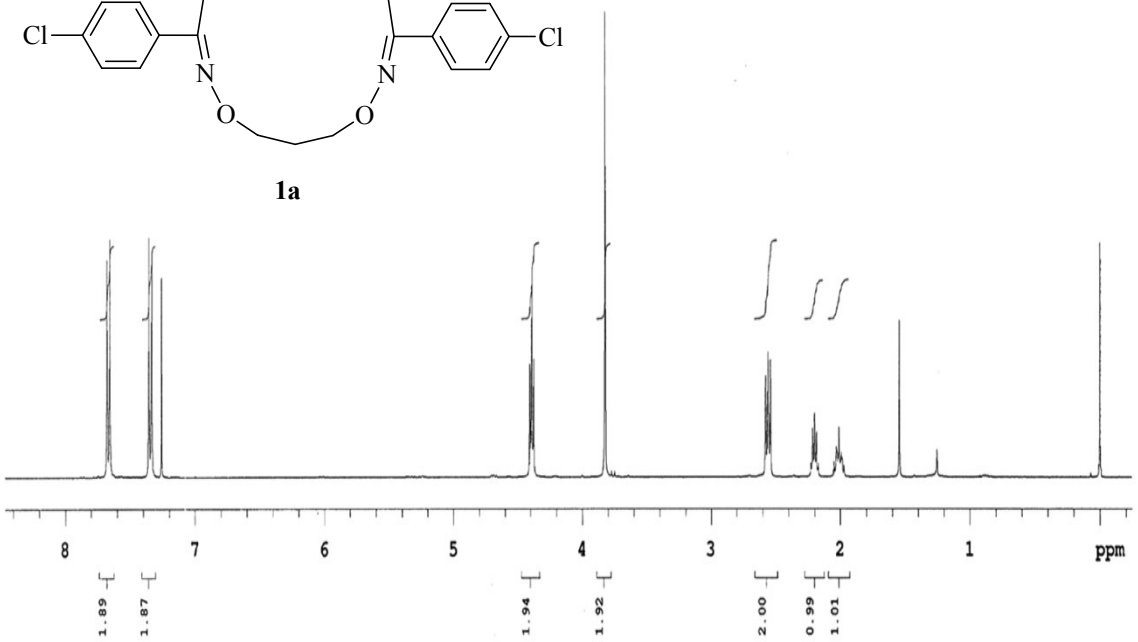
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.67 (d, *J* = 8.8 Hz, 4H, arom H), 7.35 (d, *J* = 8.8 Hz, 4H, arom H), 4.39 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.82 (s, 4H, 2-CH_2), 2.56 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.20 (quint, *J* = 6.0 Hz, 2H, -CH_2), 2.02 (quint, *J* = 7.6 Hz, 2H, -CH_2).

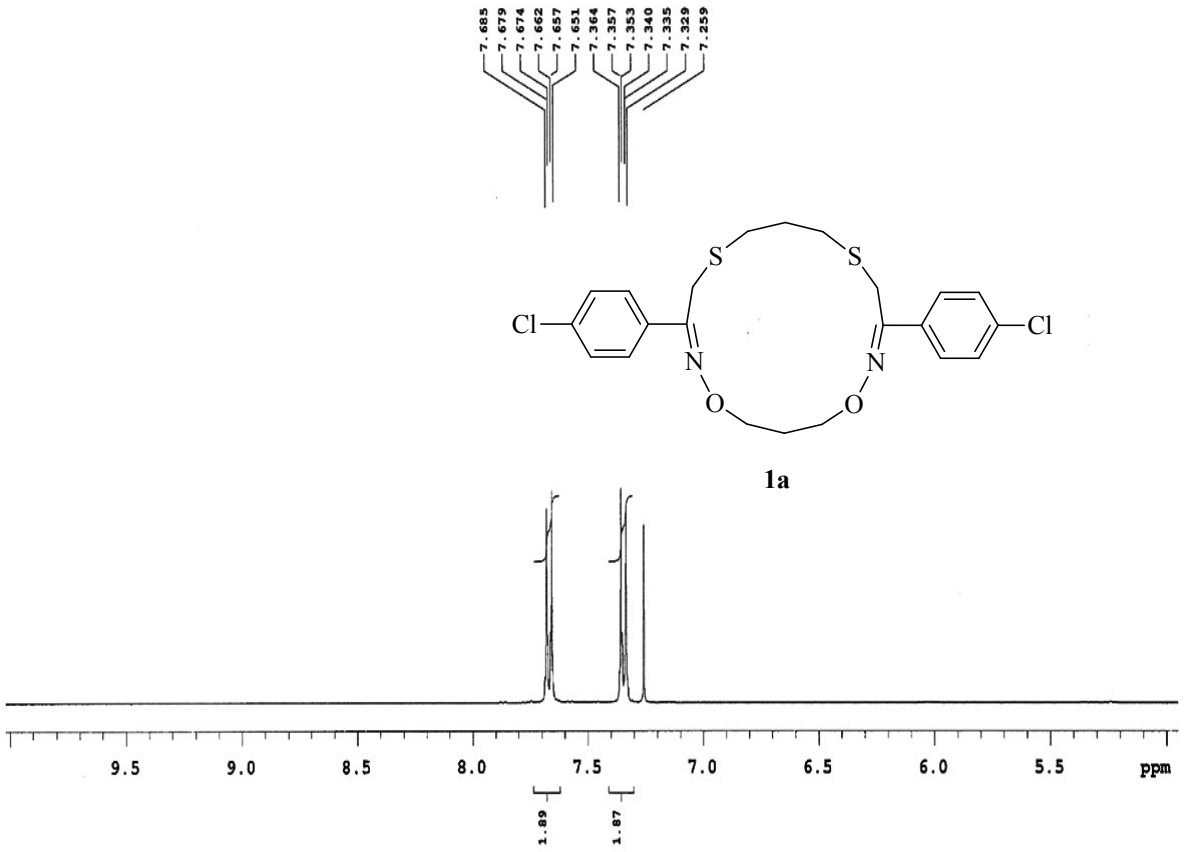
^{13}C NMR (100 MHz, $CDCl_3$, δ/ppm): 153.65 (2C), 135.40 (2C), 132.78 (2C), 128.68 (4C), 127.63(4C), 70.46 (2C), 31.03 (C), 30.78(2C), 28.21 (2C), 24.37 (C).

HRMS (ESI) : $[M+H]^+$ Calcd for $C_{22}H_{25}O_2N_2Cl_2S_2$ 483.0729, found 483.0749.

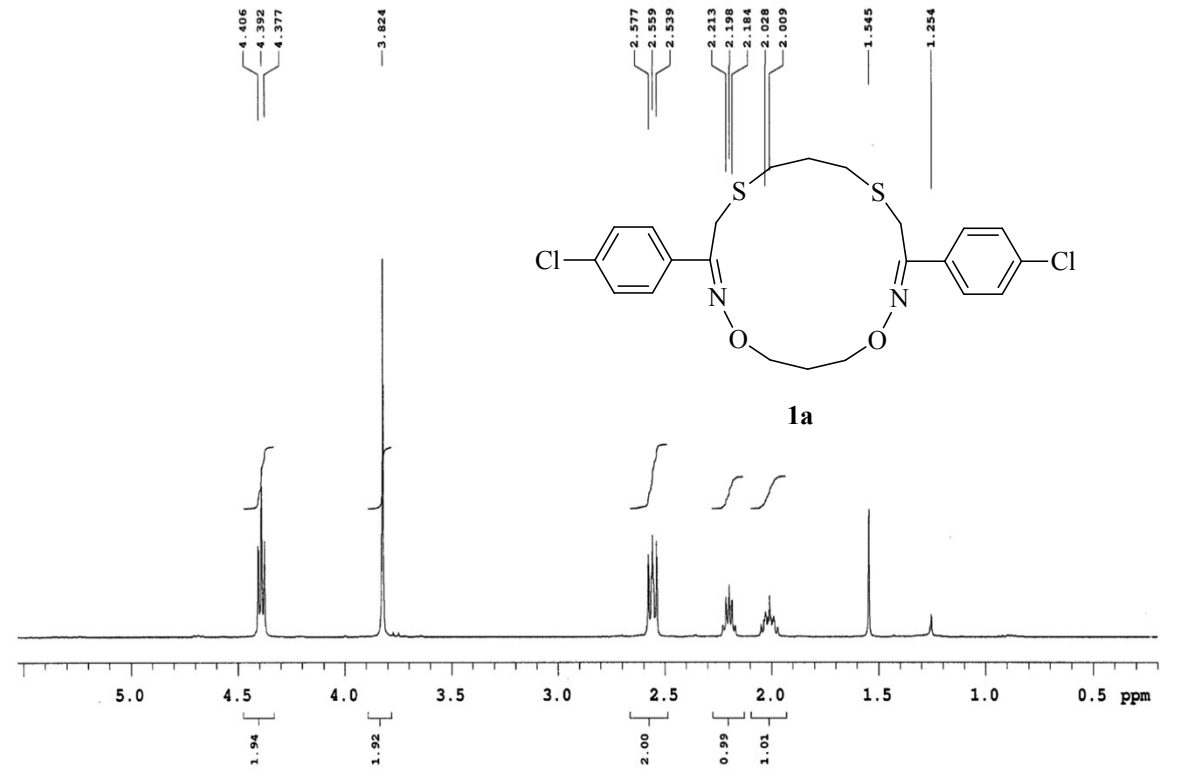


1a

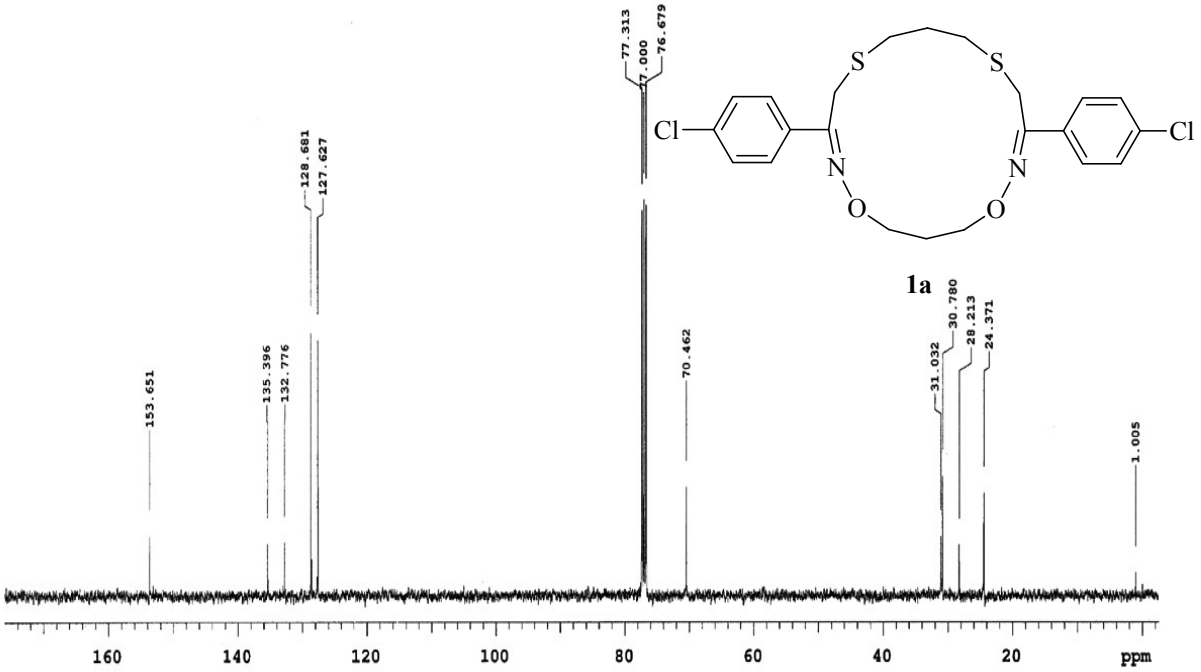



7.685
7.679
7.674
7.662
7.657
7.651
7.364
7.357
7.353
7.340
7.335
7.329
7.259
S
S
Cl
Cl
N
N
O
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm
1.89
1.87

1a

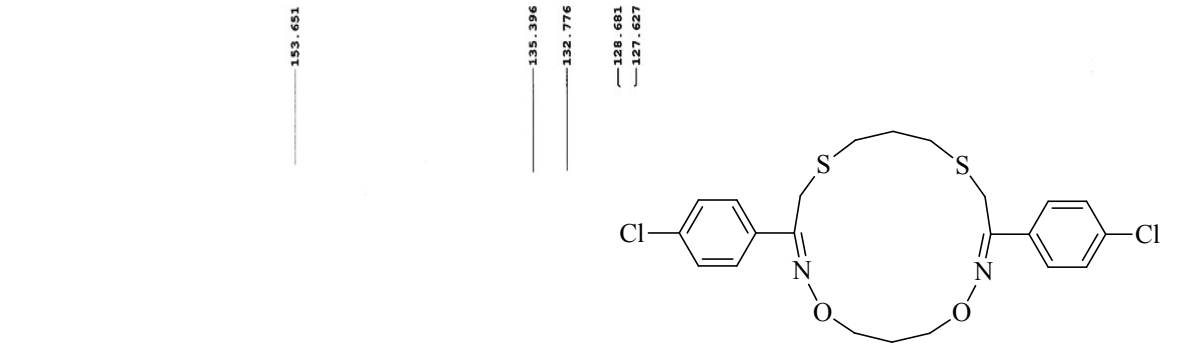

4.406
4.392
4.377
3.824
2.577
2.559
2.539
2.213
2.198
2.184
2.028
2.009
1.545
1.254
S
S
Cl
Cl
N
N
O
O
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.94
1.92
2.00
0.99
1.01

1a


77.313
77.000
76.679
128.681
127.627
153.651
135.396
132.776
70.462
31.032
30.780
28.213
24.371
1.005
160
140
120
100
80
60
40
20
ppm

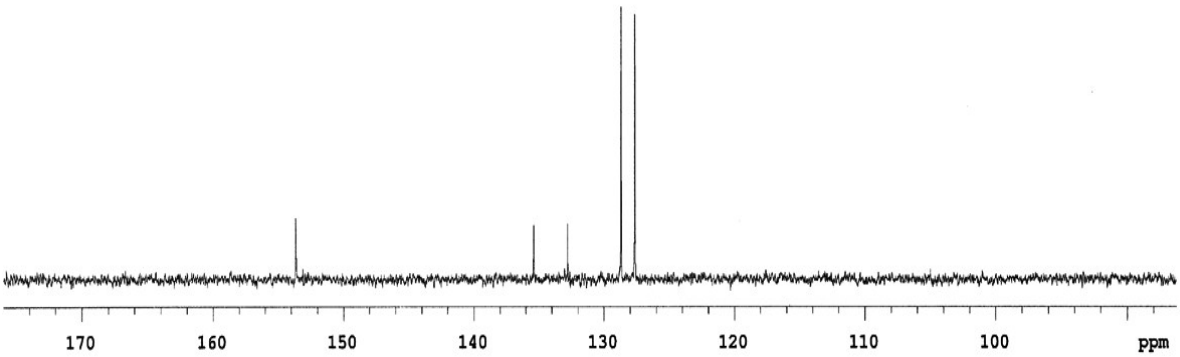
S
S
Cl
Cl
N
N
O
O

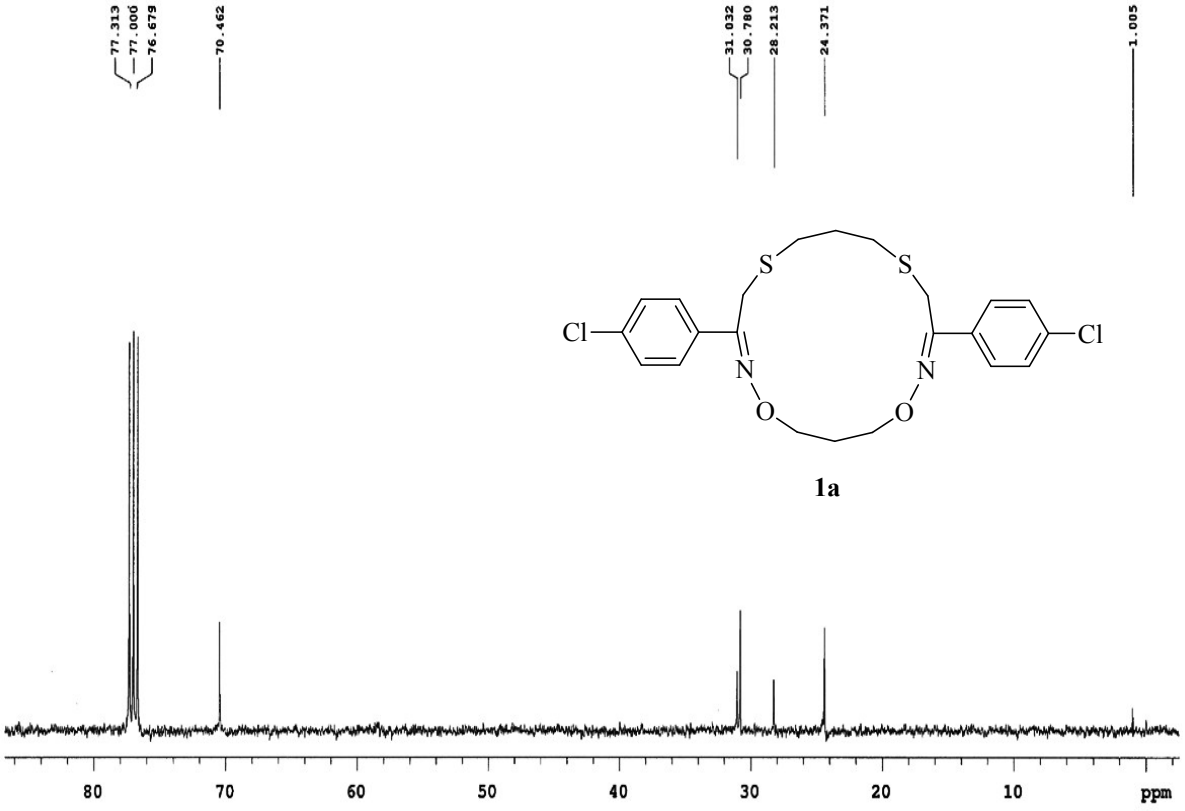
1a


153.651
135.396
132.776
128.681
127.627

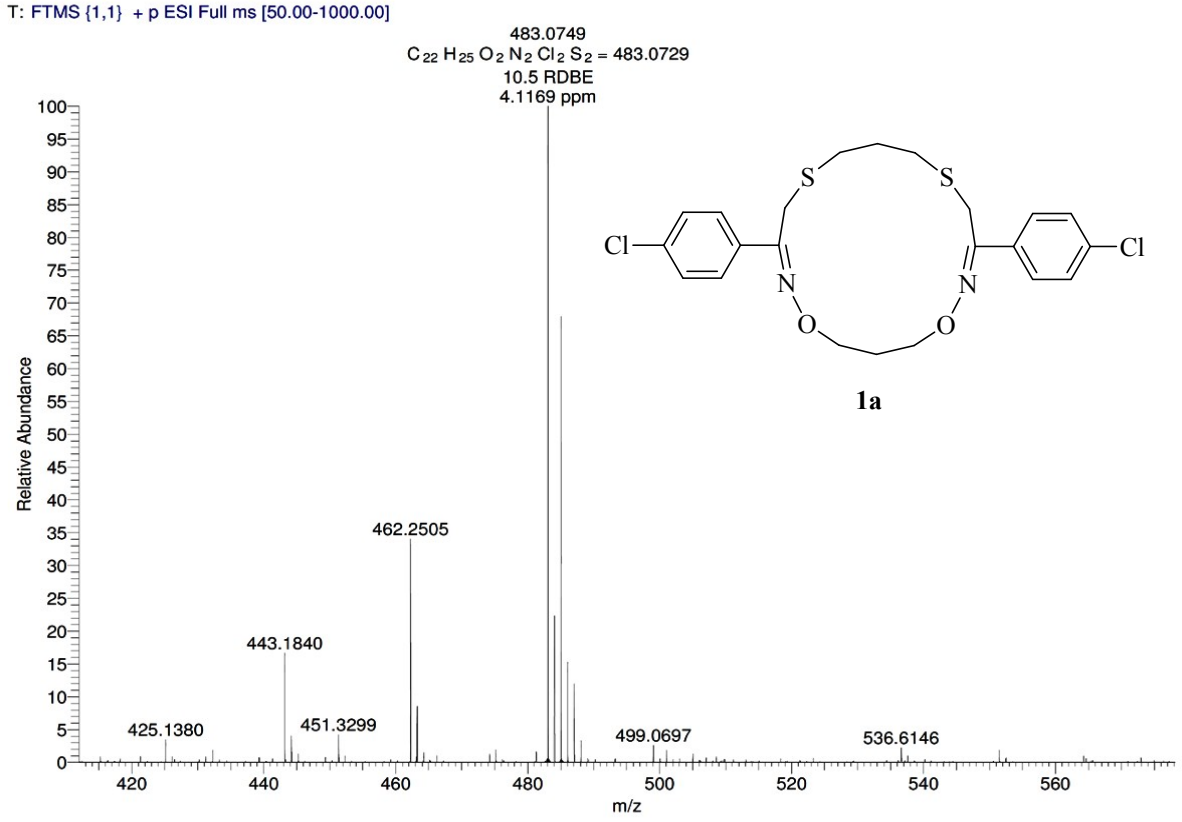
S
S
Cl
Cl
N
N
O
O

1a


170
160
150
140
130
120
110
100
ppm


77.313
77.000
76.679
70.462
31.032
30.780
28.213
24.371
1.005
S
S
Cl
Cl
N
N
O
O
80
70
60
50
40
30
20
10
ppm

1a


T: FTMS {1,1} + p ESI Full ms [50.00-1000.00]
483.0749
C22 H25 O2 N2 Cl2 S2 = 483.0729
10.5 RDBE
4.1169 ppm
Relative Abundance
462.2505
443.1840
425.1380
451.3299
499.0697
536.6146
m/z

1a

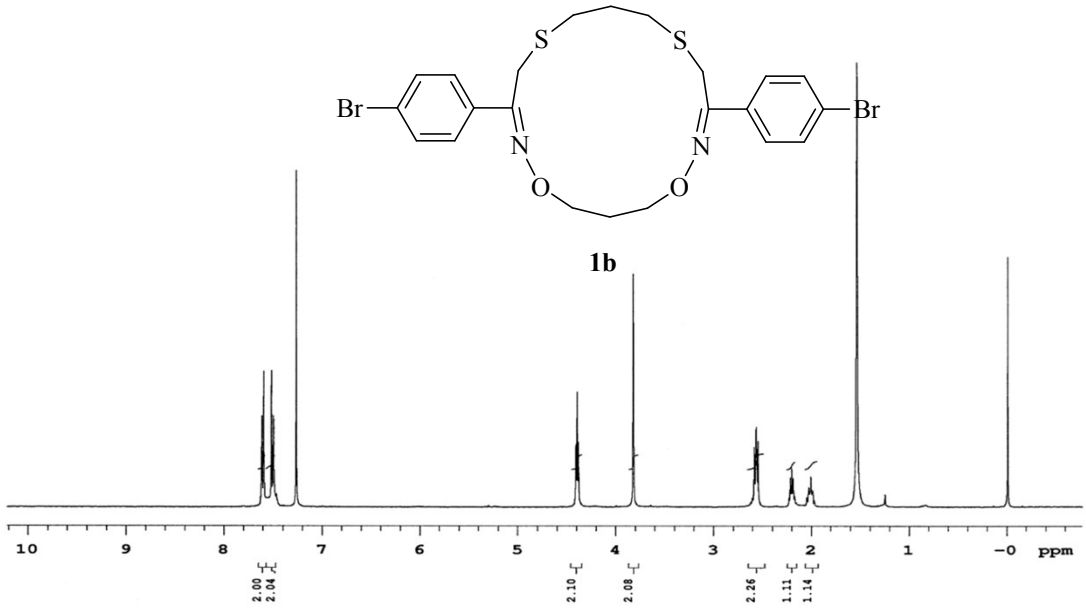
Physical and Spectral data for 16-membered macrocycle, (2Z, 11Z)-3,11-bis(4-bromophenyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1b):

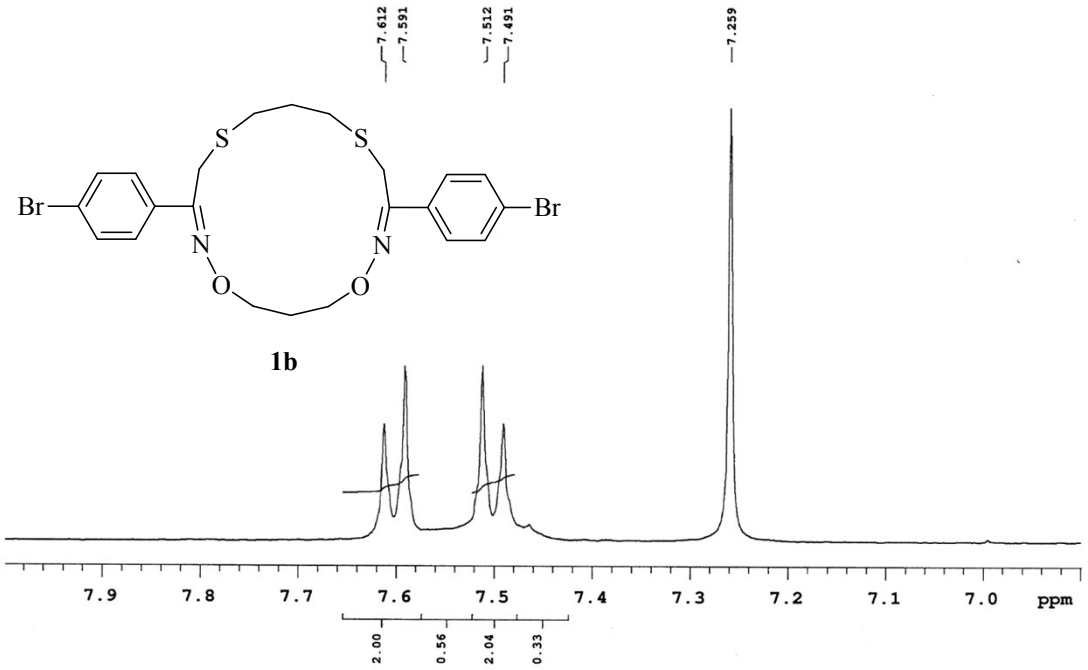
Pale yellow solid;Yield: 68.2%; mp 129-131°C.

^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.60 (d, *J* = 8.8 Hz, 4H, arom H), 7.50 (d, *J* = 8.8 Hz, 4H, arom H), 4.39 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.82 (s, 4H, 2-CH_2), 2.55 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.20 (quint, *J* = 5.6 Hz, 2H, -CH_2), 2.01 (quint, *J* = 7.6 Hz, 2H,-CH_2).

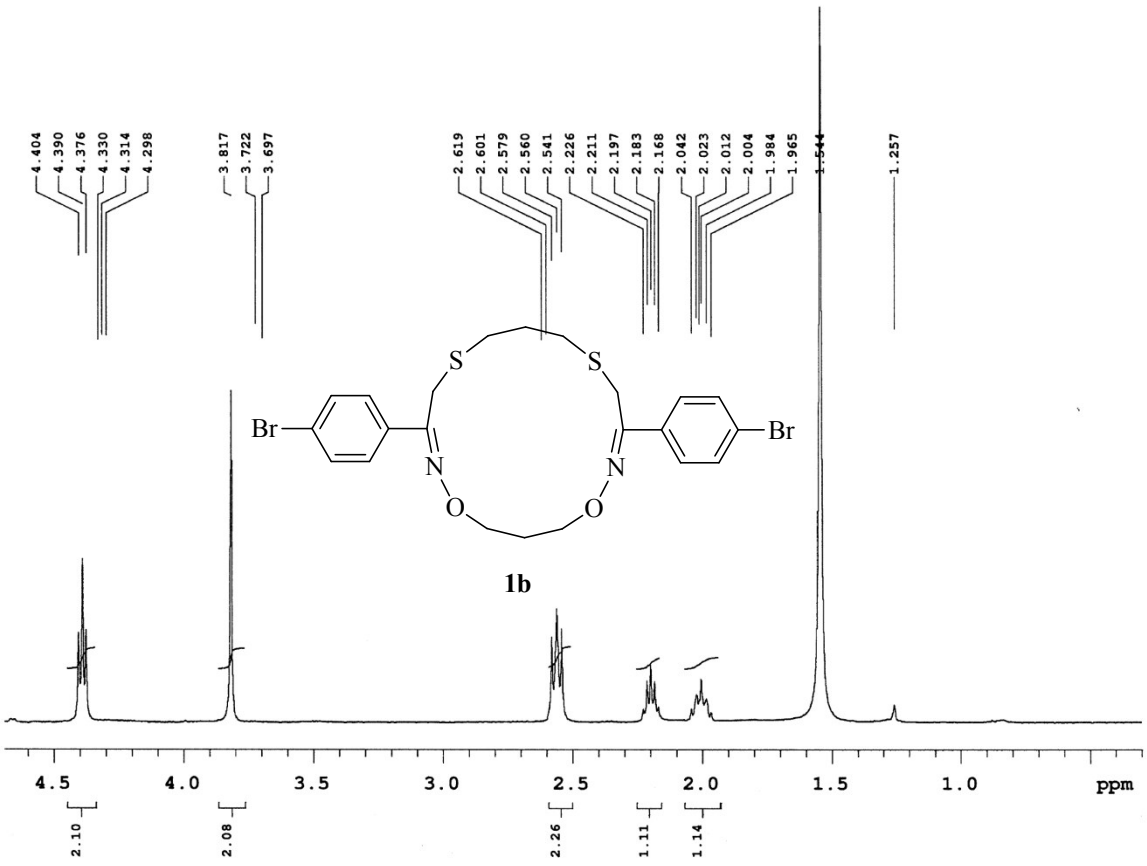
^{13}C NMR: δ 153.80 (2C), 133.35 (2C), 131.69 (4C), 127.95 (4C), 123.77 (2C), 70.59 (2C), 31.07(C), 30.88(2C), 28.30(2C), 24.43(C).

HRMS (ESI): $[M+H]^+$ Calcd for $C_{22}H_{25}O_2N_2Br_2S_2$ 570.9719, found 570.9738.

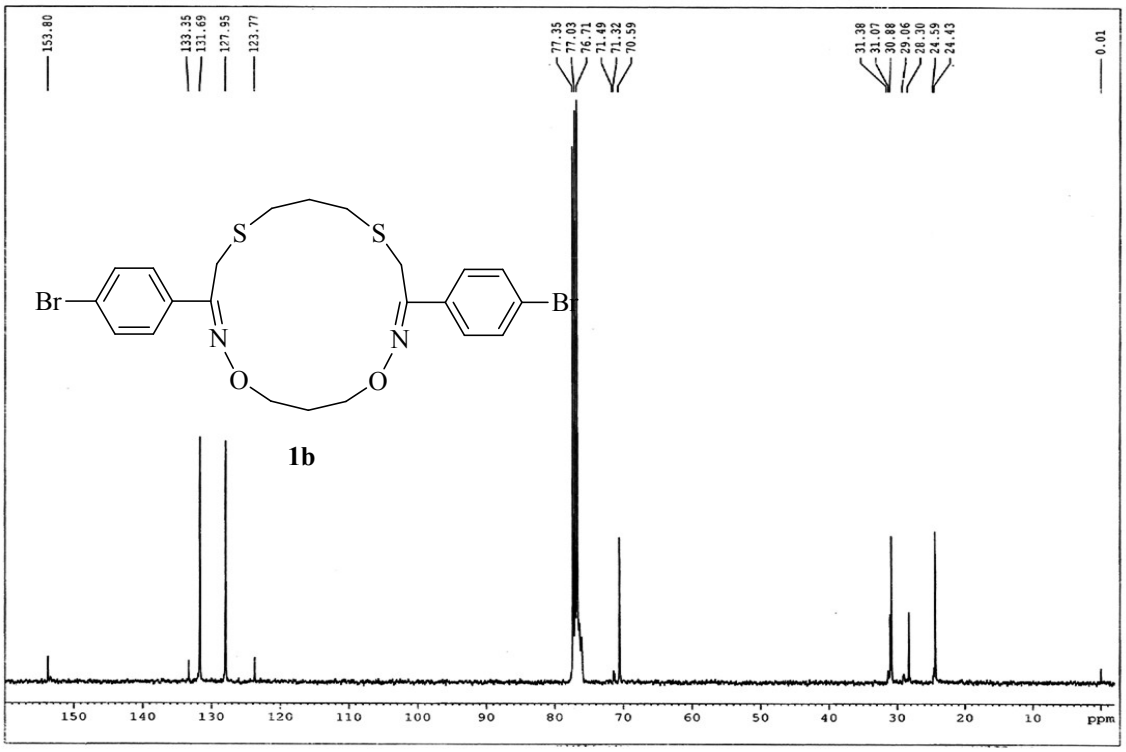



7.612
7.591
7.512
7.491
7.259
S
S
Br
Br
N
N
O
O
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
ppm
2.00
0.56
2.04
0.33

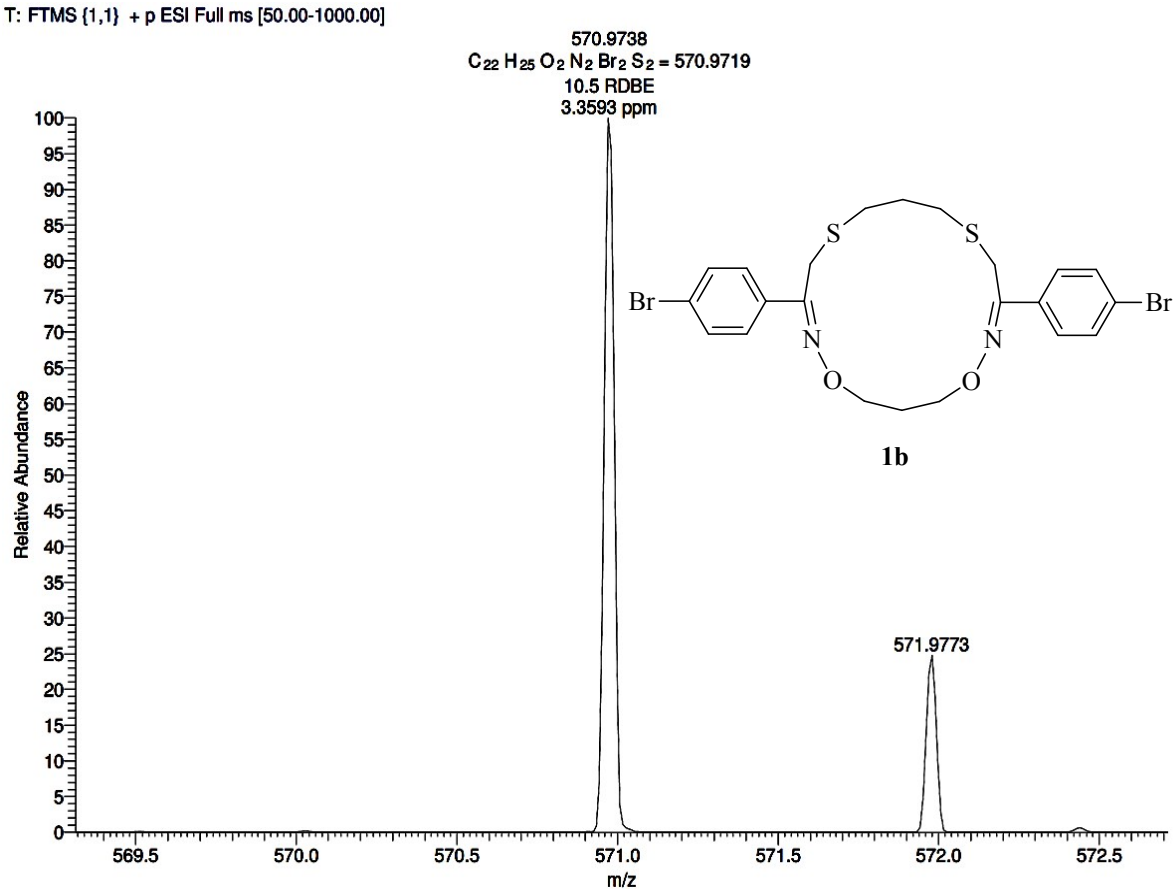
1b


4.404
4.390
4.376
4.330
4.314
4.298
3.817
3.722
3.697
2.619
2.601
2.579
2.560
2.541
2.226
2.211
2.197
2.183
2.168
2.042
2.023
2.012
2.004
1.984
1.965
1.544
1.257
S
S
Br
Br
N
N
O
O
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.10
2.08
2.26
1.11
1.14

1b


153.80
133.35
131.69
127.95
123.77
77.35
77.03
76.71
71.49
71.32
70.59
31.38
31.07
30.88
29.06
28.30
24.59
24.43
0.01
S
S
Br
Br
N
N
O
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

1b


T: FTMS {1,1} + p ESI Full ms [50.00-1000.00]
570.9738
C22 H25 O2 N2 Br2 S2 = 570.9719
10.5 RDBE
3.3593 ppm
571.9773
Relative Abundance
m/z
569.5
570.0
570.5
571.0
571.5
572.0
572.5
S
S
Br
Br
N
N
O
O

1b

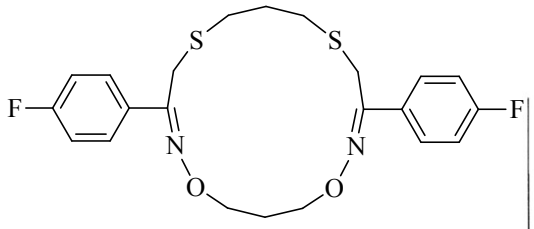
Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-bis(4-fluorophenyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1e):

Off-white solid; Yield: 73.4%; mp 120-122°C.

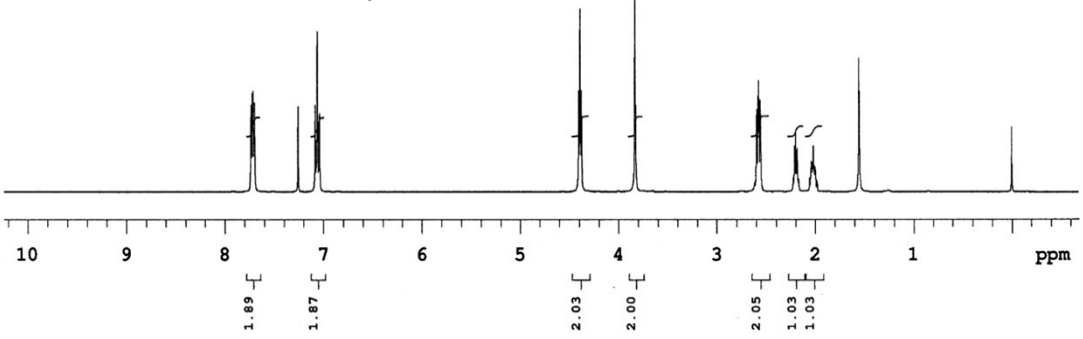
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7. 71 (dd, *J* = 9.2, 5.6 Hz, 4H, arom H), 7.06 (t, 4H, *J* = 9.2 Hz, arom H), 4.39 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.83 (s, 4H, 2-CH_2), 2.57 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.20 (quint, *J* = 6.0 Hz, 2H, -CH_2), 2.02 (quint, *J* = 8.0 Hz, 2H, -CH_2).

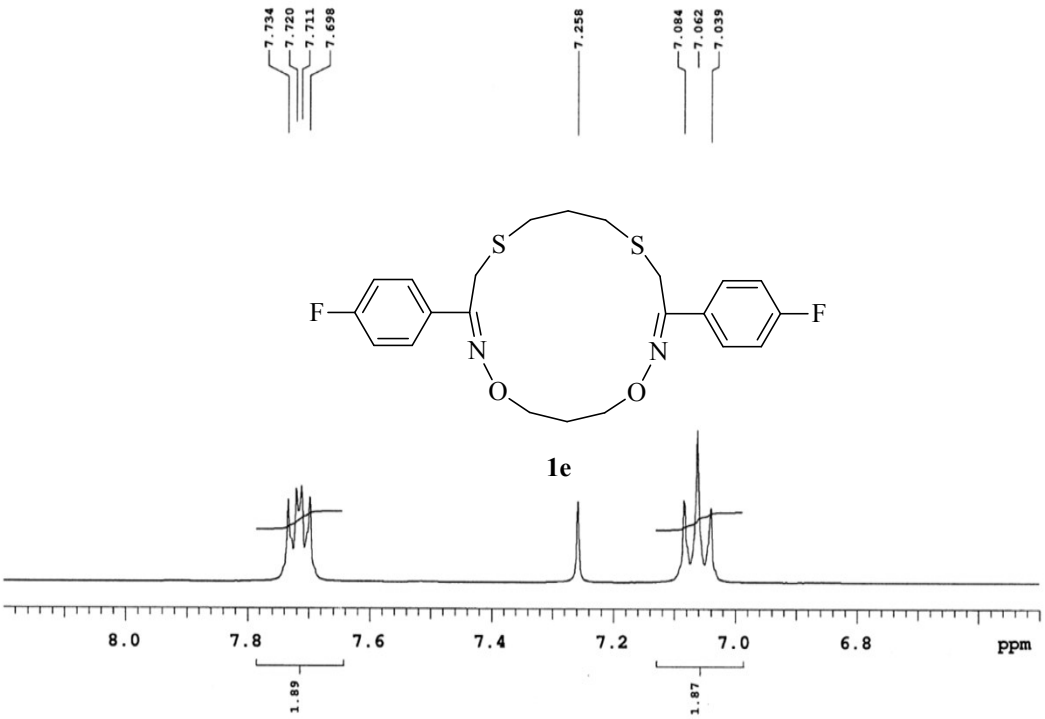
^{13}C NMR (100 MHz, $CDCl_3$, δ/ppm): 163.55 (d, $^{1}J_{C\text{-}F}$ = 248 Hz, 2C), 153.79 (2C), 130.57 (2C), 128.29 (d, $^{3}J_{C\text{-}F}$ = 9.0 Hz, 4C), 115.50 (d, $^{2}J_{C\text{-}F}$ = 22.0 Hz, 4C), 70.47 (2C), 31.11 (1C), 30.88 (2C), 28.31 (2C), 24.64 (1C).

HRMS (ESI): $[M+nNa]^+$ Calcd for $C_{22}H_{24}S_2O_2N_2F_2$ 473.1130, found 473.1139

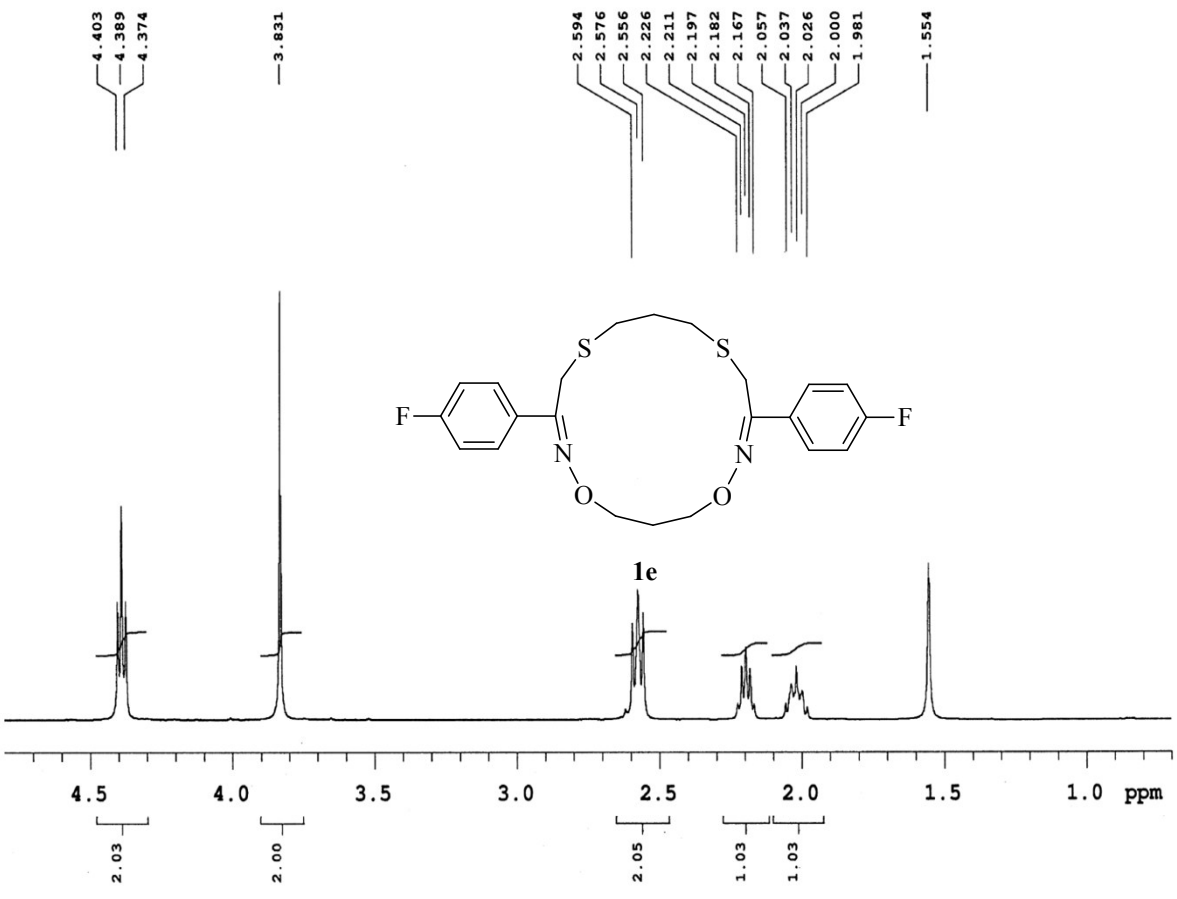


1e

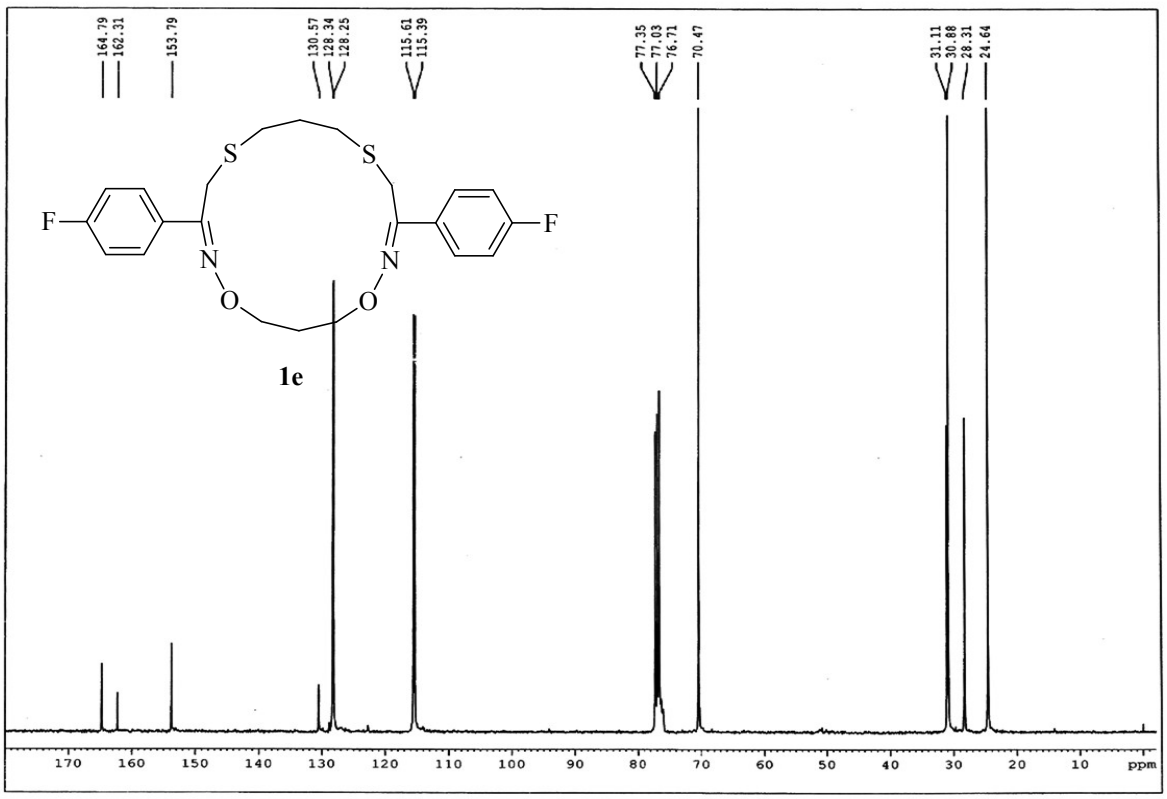


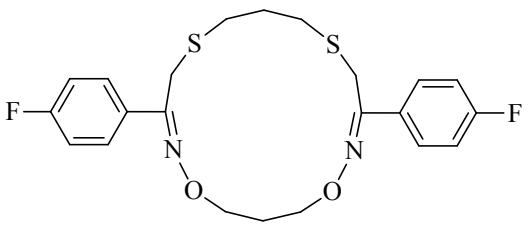

7.734
7.720
7.711
7.698
7.258
7.084
7.062
7.039
S
S
F
F
N
N
O
O
8.0
7.8
7.6
7.4
7.2
7.0
6.8
ppm
1.89
1.87

1e

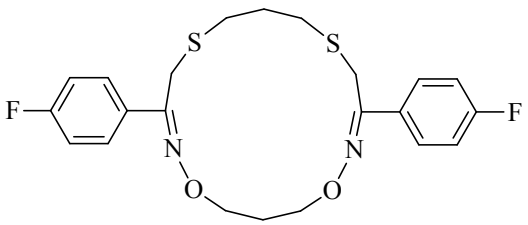

4.403
4.389
4.374
3.831
2.594
2.576
2.556
2.226
2.211
2.197
2.182
2.167
2.057
2.037
2.026
2.000
1.981
1.554
S
S
F
F
N
N
O
O
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.03
2.00
2.05
1.03
1.03

1e


164.79
162.31
153.79
130.57
128.34
128.25
115.61
115.39
77.35
77.03
76.71
70.47
31.11
30.88
28.31
24.64
S
S
F
F
N
N
O
O
1e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


S
S
F
F
N
N
O
O

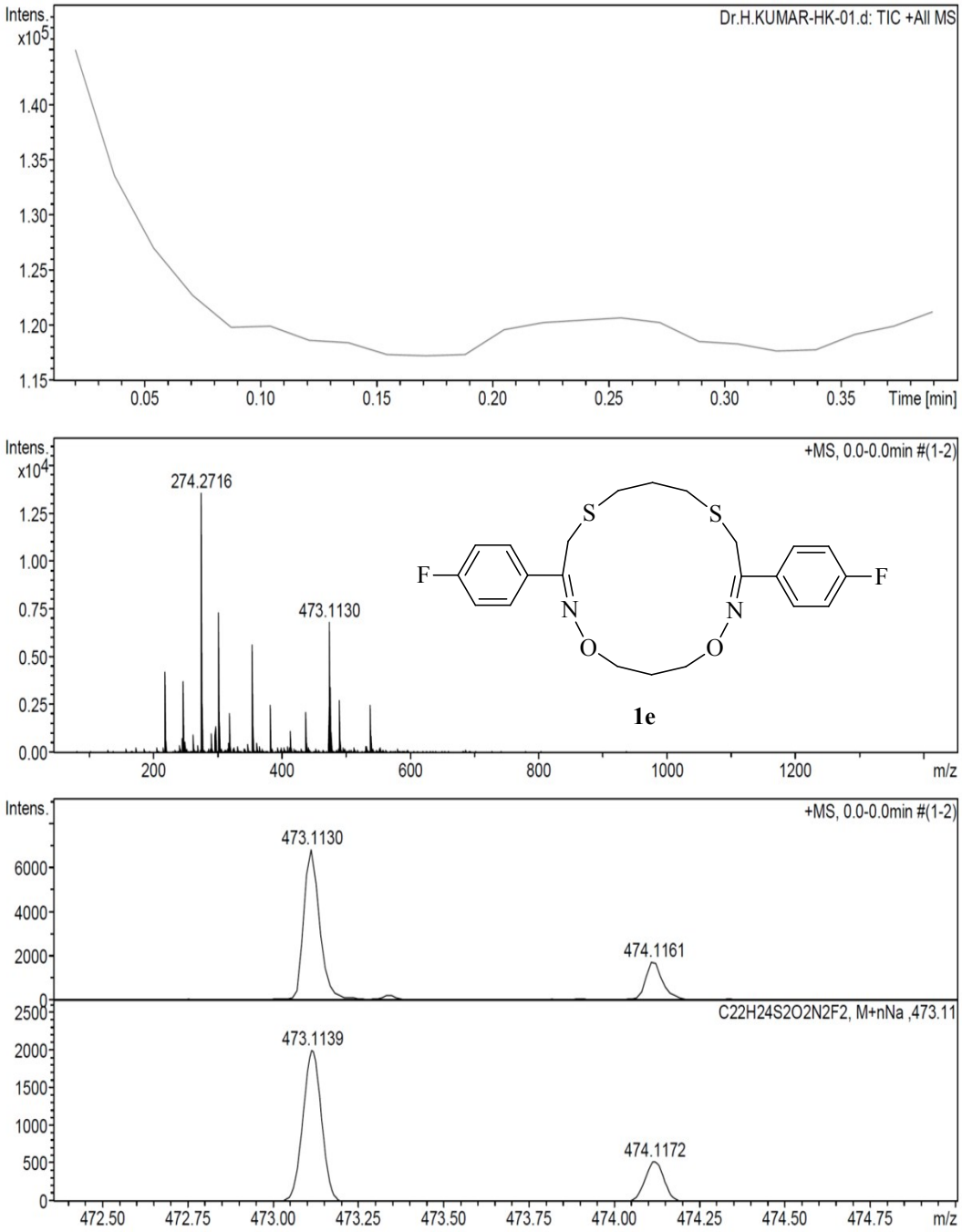
1e


S
S
F
F
N
N
O
O

1e

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4600 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	80.0 Vpp	Set Divert Valve	Waste



Development of Single Crystal:

The fine single crystals of compound **1e** were grown by slow evaporation of its petroleum ether and ethyl acetate (10:50 ratio) solution at room temperature.

Single crystals of macrocyclic compound (**1e**).

X-ray Diffraction Studies of Single Crystal:

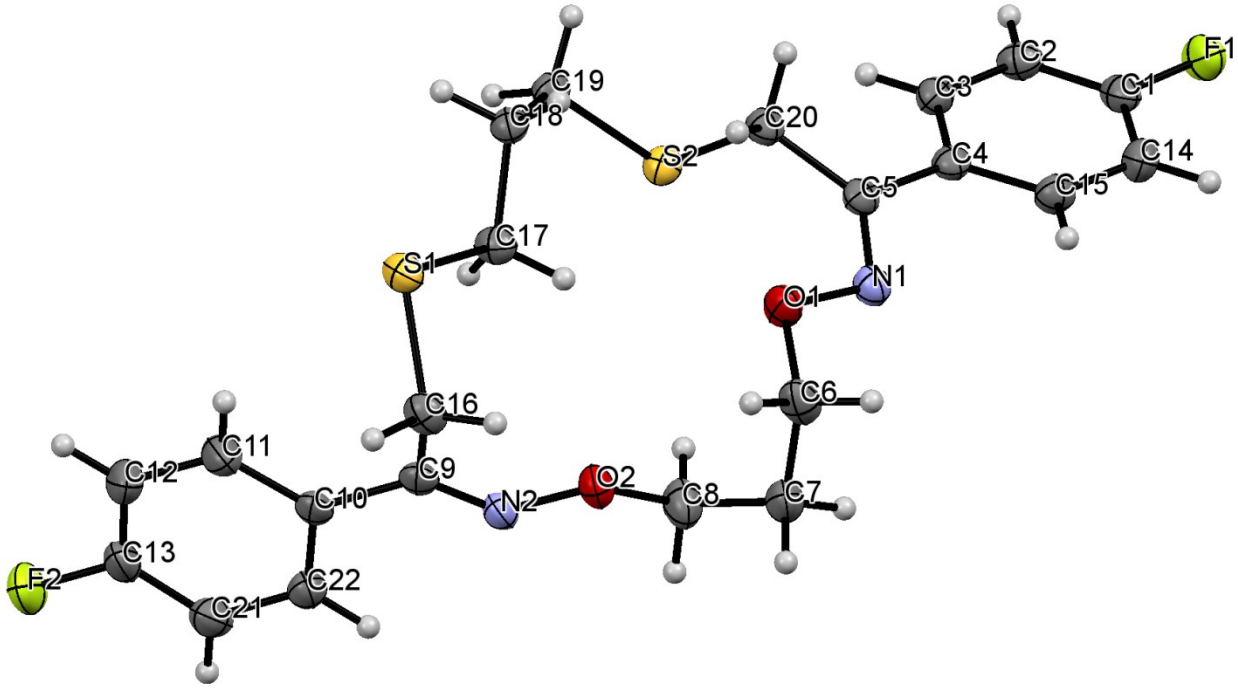
A specimen of $C_{22}H_{24}F_2N_2O_2S_2$, approximate dimensions 0.20 x 0.16 0 x 12 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The X-ray diffraction data were collected on a Bruker Apex ii diffractometer with CCD detector MoKα radiation (λ = 0.71069 Å) operating ω-2θ scanning mode at room temperature. A total of scans were 3781. There were no significant variations in intensity for standard reflections with average change -0.66%. Decay correction was not applied. The linear absorption coefficient, μ, for Mo-Kα radiation was 1.92 cm^{-1}.

Table 2. Crystal and experimental data.

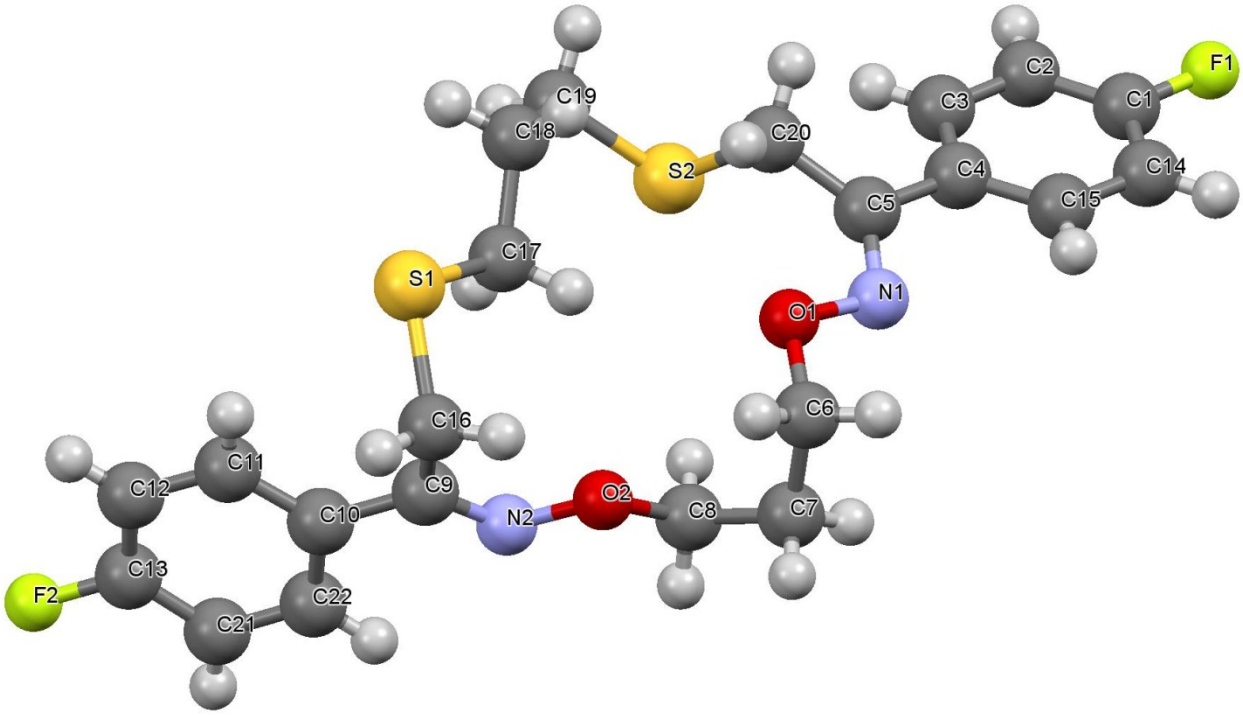
S. No	Parameters	Properties of crystal
1	Crystal morphology	Colorless, Plate
2	Crystal dimensions	0.20 x 0.16 x 0.12 mm
3	Chemical formula	$C_{22}H_{24}F_2N_2O_2S_2$
4	Molecular weight	Triclinic
5	Crystal system	P-1
6	Space group	a 5.2062(2)
7	Lattice parameters	b11.8917(4)
		c17.4814 (6)A
		α 88.3900(10)°
		β 83.6170(10)°
		γ 85.2230(10)°
8	Number of formula units Z	2
9	Cell Volume	1071.64 (7) A3

10	R-factor(%)	2.61
11	Absorption coefficient (μ)	0.287 cm-1
12	Radiation	MoKα
13	Wavelength (λ)	0.71069 A
		F(000) 924
14	Scan type	ω−2θ
15	2_θ max	29.36(theta max)
16	No. of reflections measured	3781
17	No. of reflections used	3546
18	R(F^2)	0.0645
19	Rw(F^2)	0.0630
20	Weighting scheme	w=1/[\s^2^(Fo^2^)+(0.0241P)^2^+0.5251P]
		where P=(Fo^2^+2Fc^2^)/3'
21	Goodness-of-fit on F^2	1.040
22	No. of parameters refined	271

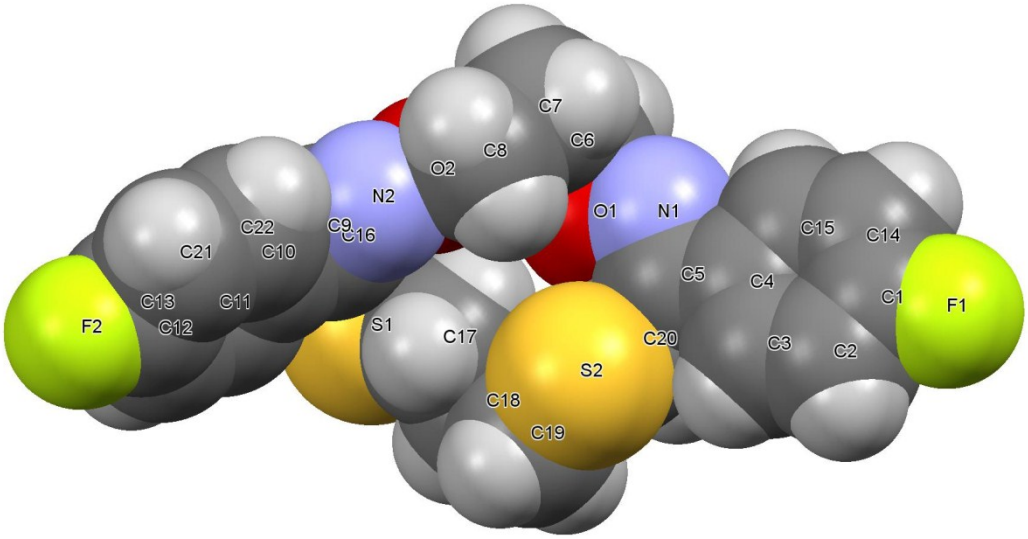
The ORTEP view of 16-membered macrocycle, (2Z,11Z)-3,11-bis(4-fluorophenyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (**1e**) as shown in below figure.

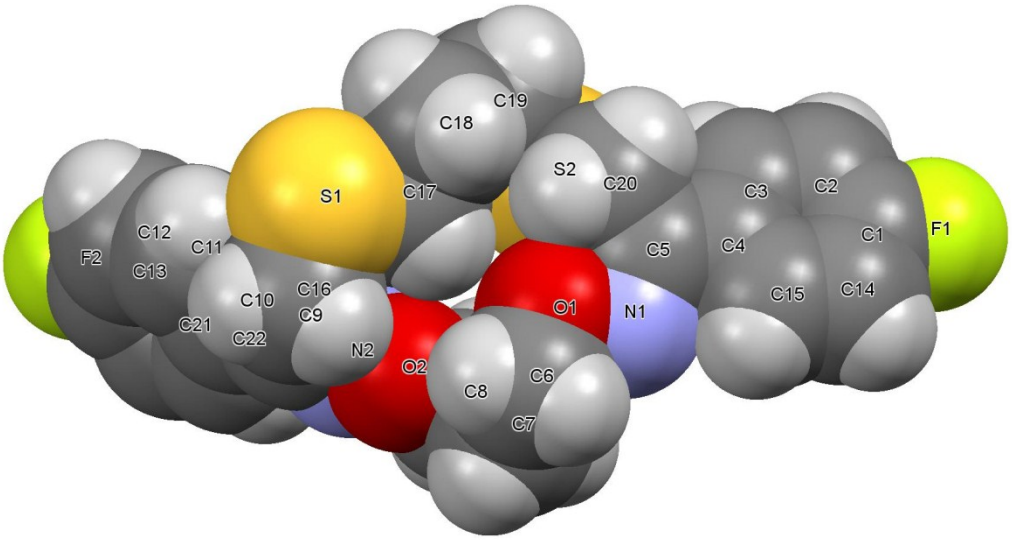


ORTEP view of macrocycle (**1e**)

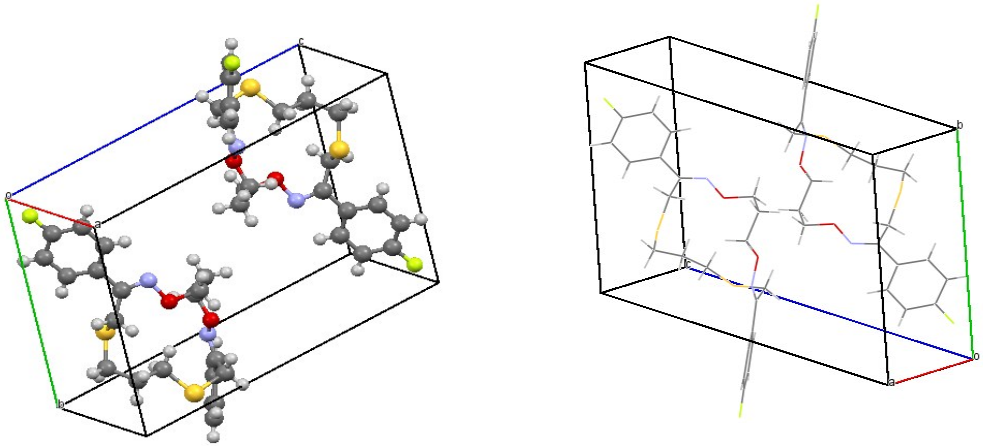


Ball and stick view of macrocycle (**1e**)





Space fill of macrocycle (**1e**)



Crystal packing of macrocycle (**1e**)

Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-bis(4-methoxyphenyl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1f):

Off-white solid; Yield: 65.7%; mp 122-124°C.

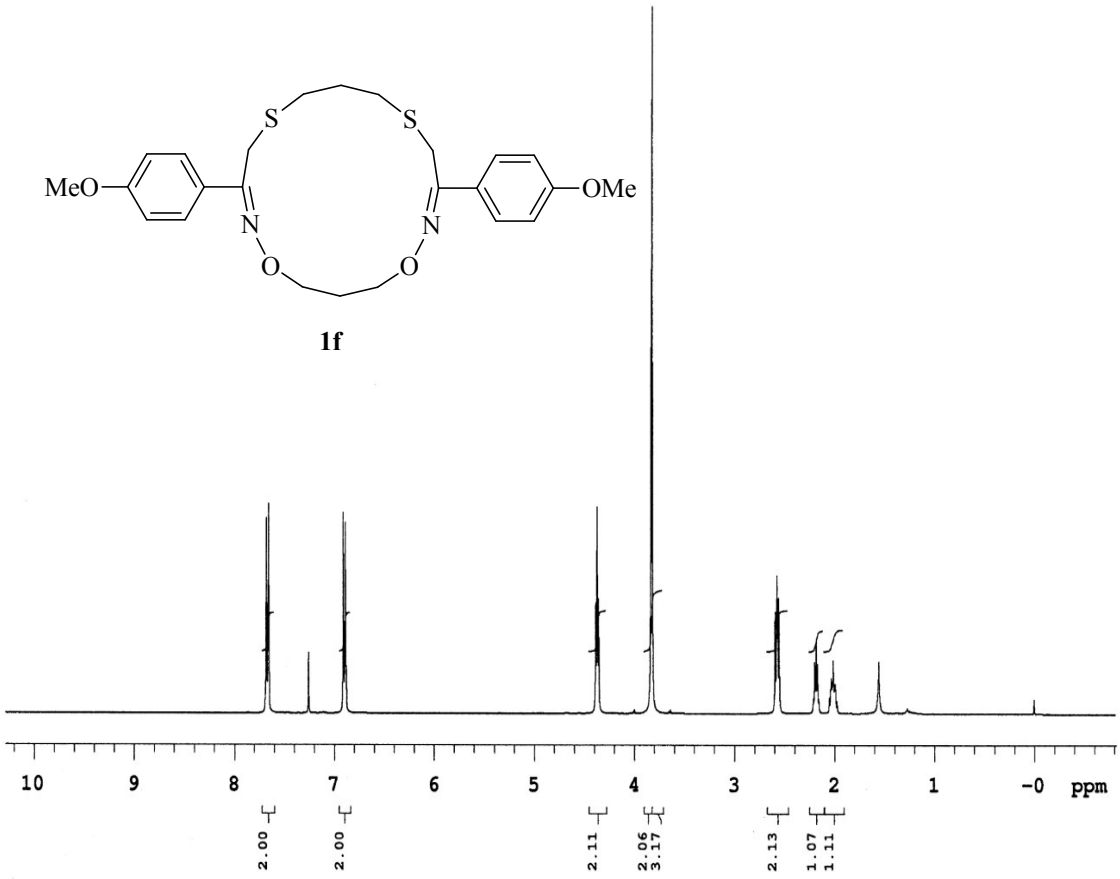
^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.66 (d, *J* = 8.8 Hz, 4H, arom H), 6.90 (d, *J* = 8.8 Hz, 4H, arom H), 4.37 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.83 (s, 4H, 2-CH_2), 3.82 (s, 6H, 2-OCH_3), 2.57 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.18 (quint, *J* = 6.0 Hz, 2H,-CH_2), 2.01 (quint, *J* = 8.0 Hz, 2H,-CH_2).

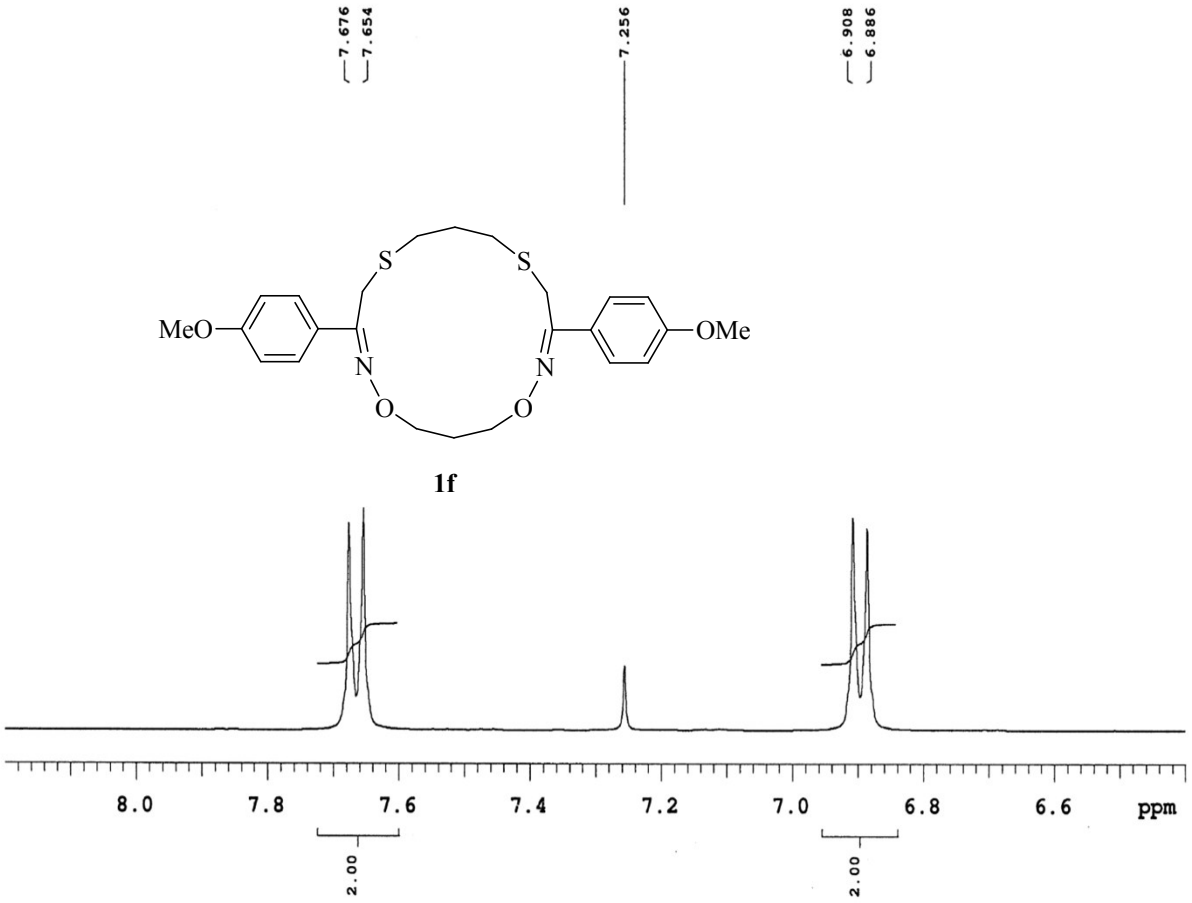
^{13}C NMR (400 MHz, $CDCl_3$, δ/ppm): 160.63(2C), 154.34(2C), 127.77 (4C), 126.97(2C), 113.93(4C), 70.24 (2C), 55.33(2C), 31.24(C), 30.89 (2C), 28.38(2C), 24.55(C).

HRMS (ESI): $[M+H]^+$ Calcd for $C_{24}H_{31}O_4N_2S_2$ 475.1720, found 475.1739.

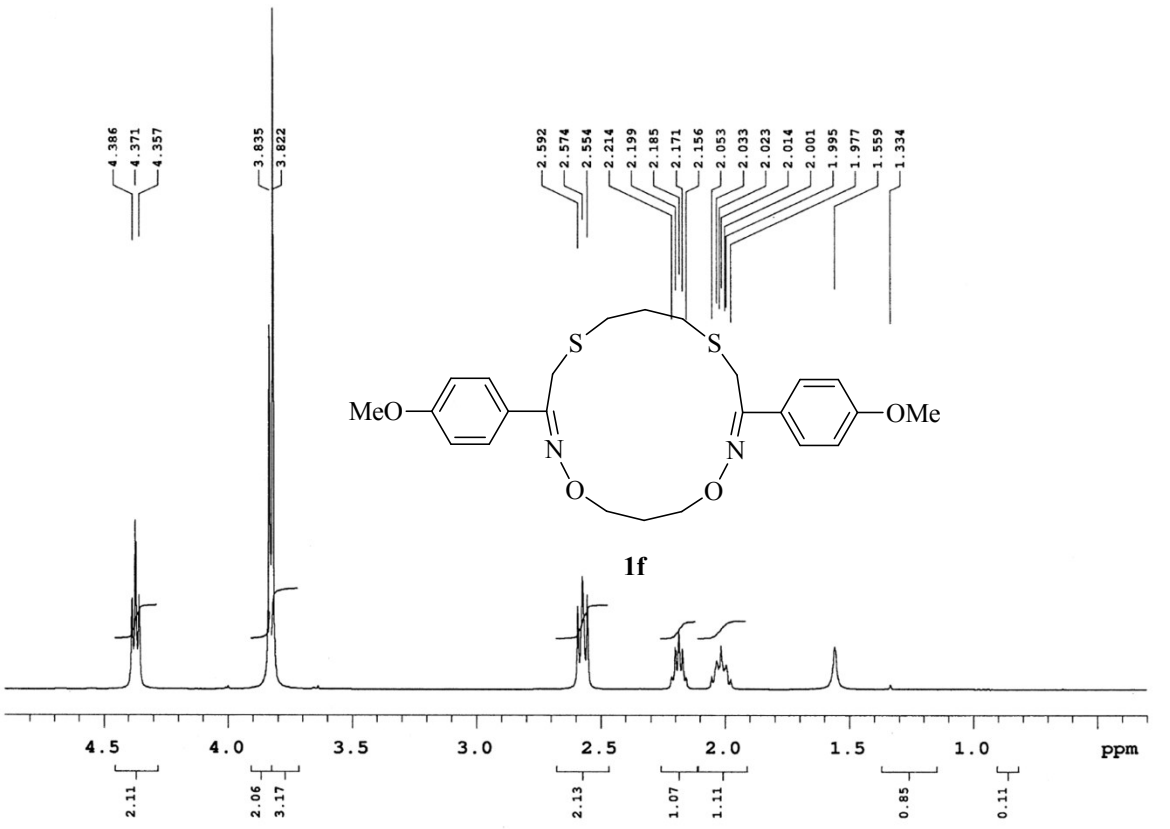
MeO
OMe
S
S
N
N
O
O

1f

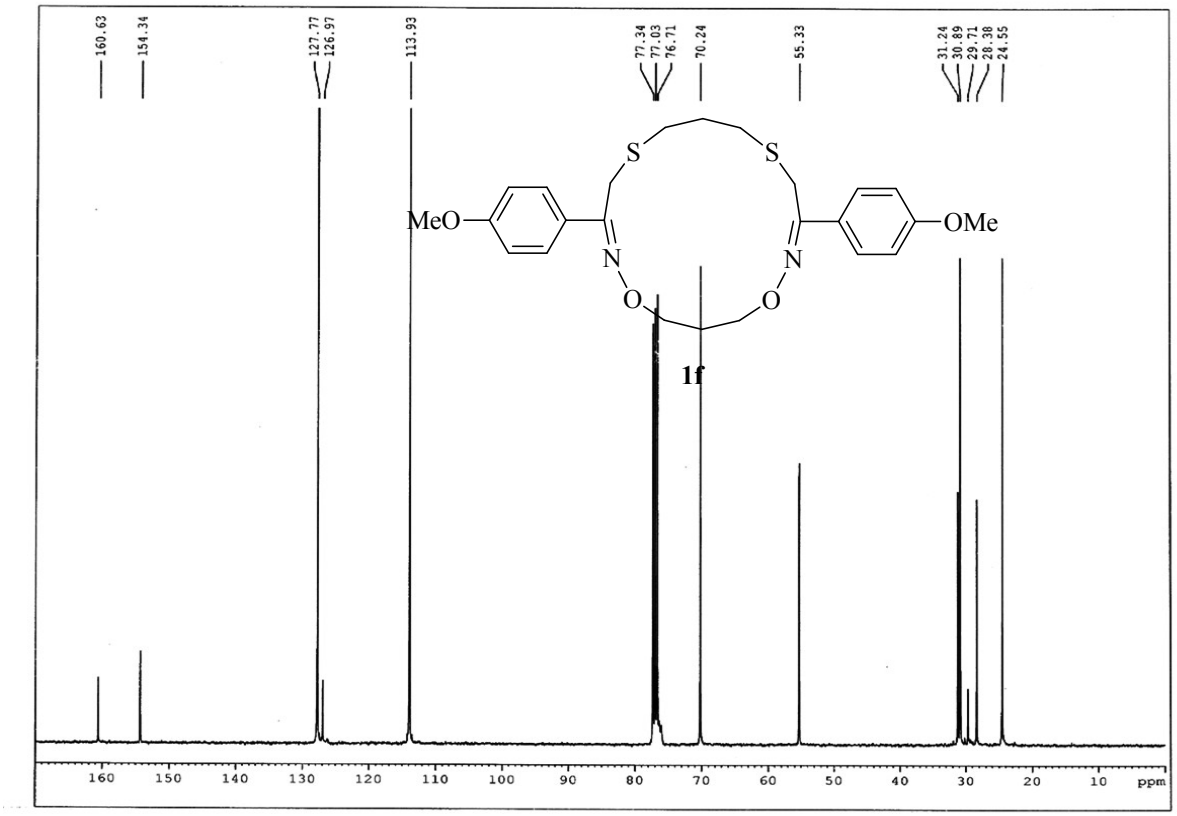

10
9
8
7
6
5
4
3
2
1
-0
ppm
2.00
2.00
2.11
2.06
3.17
2.13
1.07
1.11


7.676
7.654
7.256
6.908
6.886
MeO
OMe
S
S
N
N
O
O
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
ppm
2.00
2.00

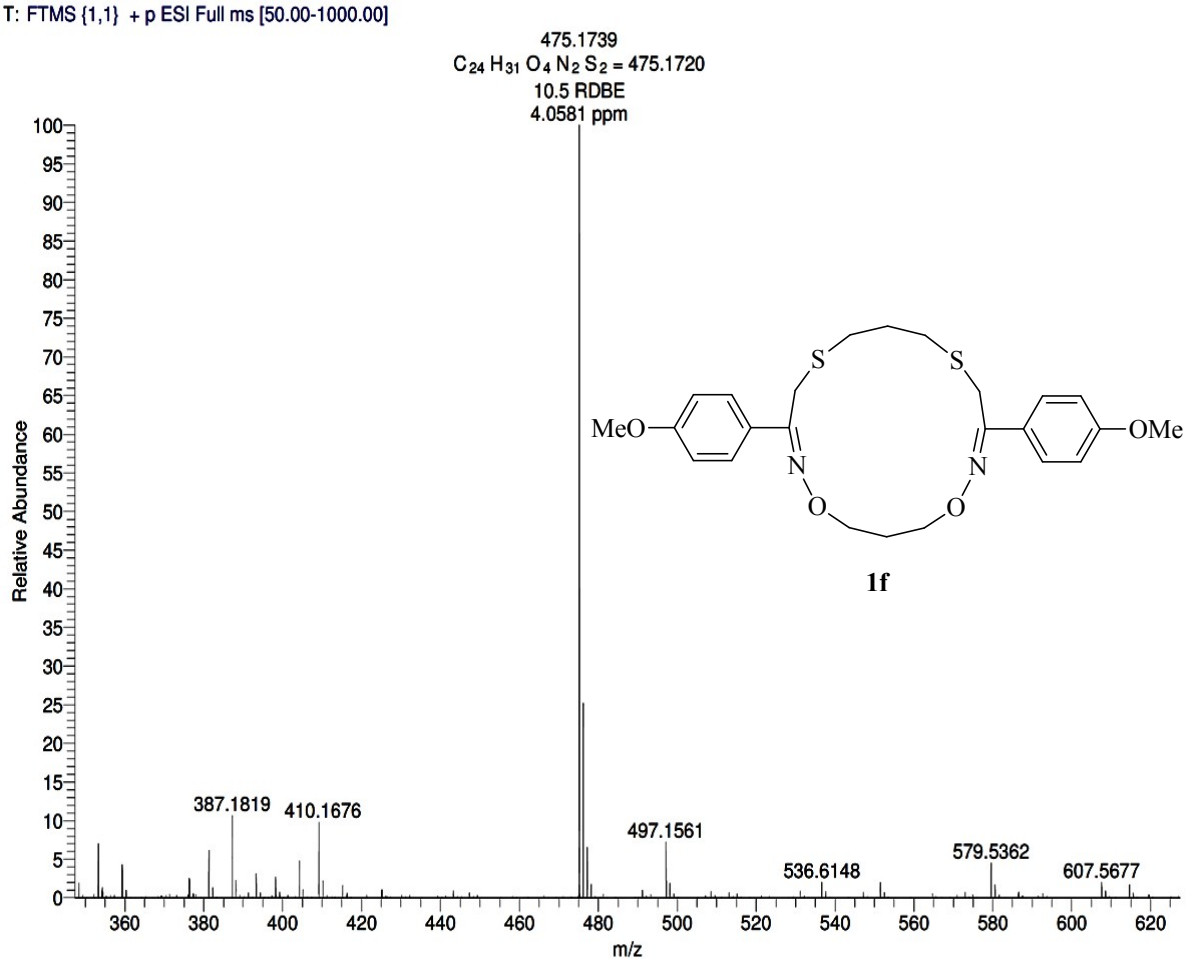
1f


4.386
4.371
4.357
3.835
3.822
2.592
2.574
2.554
2.214
2.199
2.185
2.171
2.156
2.053
2.033
2.023
2.014
2.001
1.995
1.977
1.559
1.334
MeO
OMe
S
S
N
N
O
O
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.11
2.06
3.17
2.13
1.07
1.11
0.85
0.11

1f


160.63
154.34
127.77
126.97
113.93
77.34
77.03
76.71
70.24
55.33
31.24
30.89
29.71
28.38
24.55
MeO
OMe
S
S
N
N
O
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

1f


T: FTMS {1,1} + p ESI Full ms [50.00-1000.00]
475.1739
C24 H31 O4 N2 S2 = 475.1720
10.5 RDBE
4.0581 ppm
Relative Abundance
m/z
387.1819
410.1676
497.1561
536.6148
579.5362
607.5677
MeO
OMe
S
S
N
N
O
O

1f

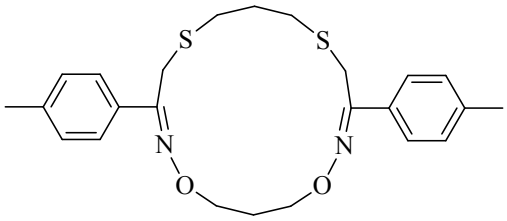
Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-dip-tolyl-1,13-dioxa-5, 9-dithia-2,12-diazacyclohexadeca-2,11-diene (1g):

Off-white solid;Yield: 63.5%; mp 111-113°C

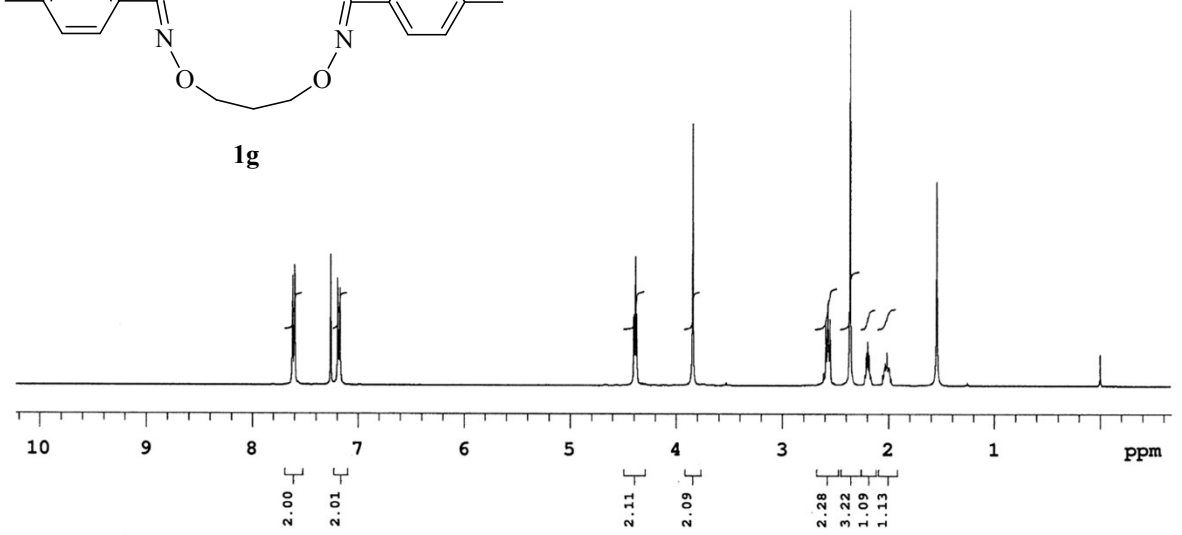
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.60 (d, *J* = 7.6 Hz, 4H, arom H), 7.18 (d, *J* = 8.0 Hz, 4H, arom H), 4.38 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.84 (s, 4H, 2-CH_2), 2.57 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.36 (s, 6H, 2-CH_3), 2.19 (quint, *J* = 6.4 Hz, 2H, -CH_2), 2.01 (quint, *J* = 5.6 Hz, 2H, -CH_2).

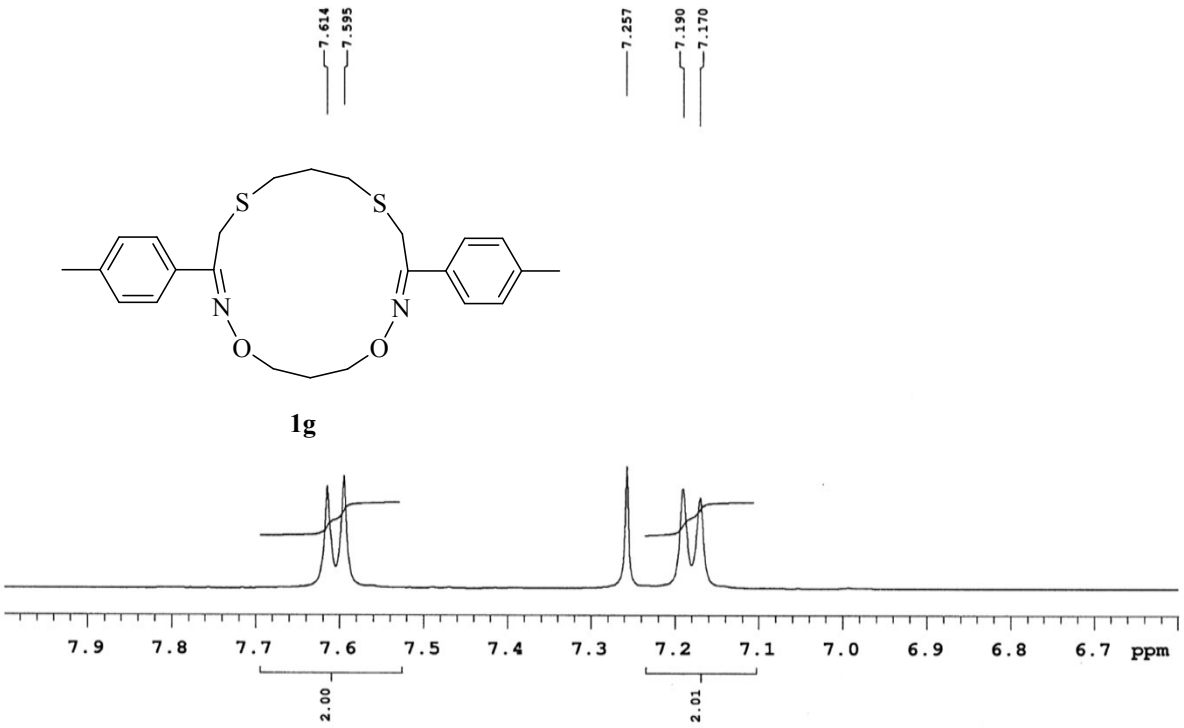
^{13}C-NMR (100 MHz, $CDCl_3$, δ/ppm): 154.73 (2C), 139.42 (2C), 131.66 (2C), 129.19 (4C), 126.29(4C), 70.30 (2C), 31.19 (C), 30.92 (2C), 28.37(2C), 24.61(C), 21.28(2C).

HRMS (ESI): $[M+H]^+$ Calcd for $C_{24}H_{31}O_2N_2S_2$ 443.1821, found 443.1840.

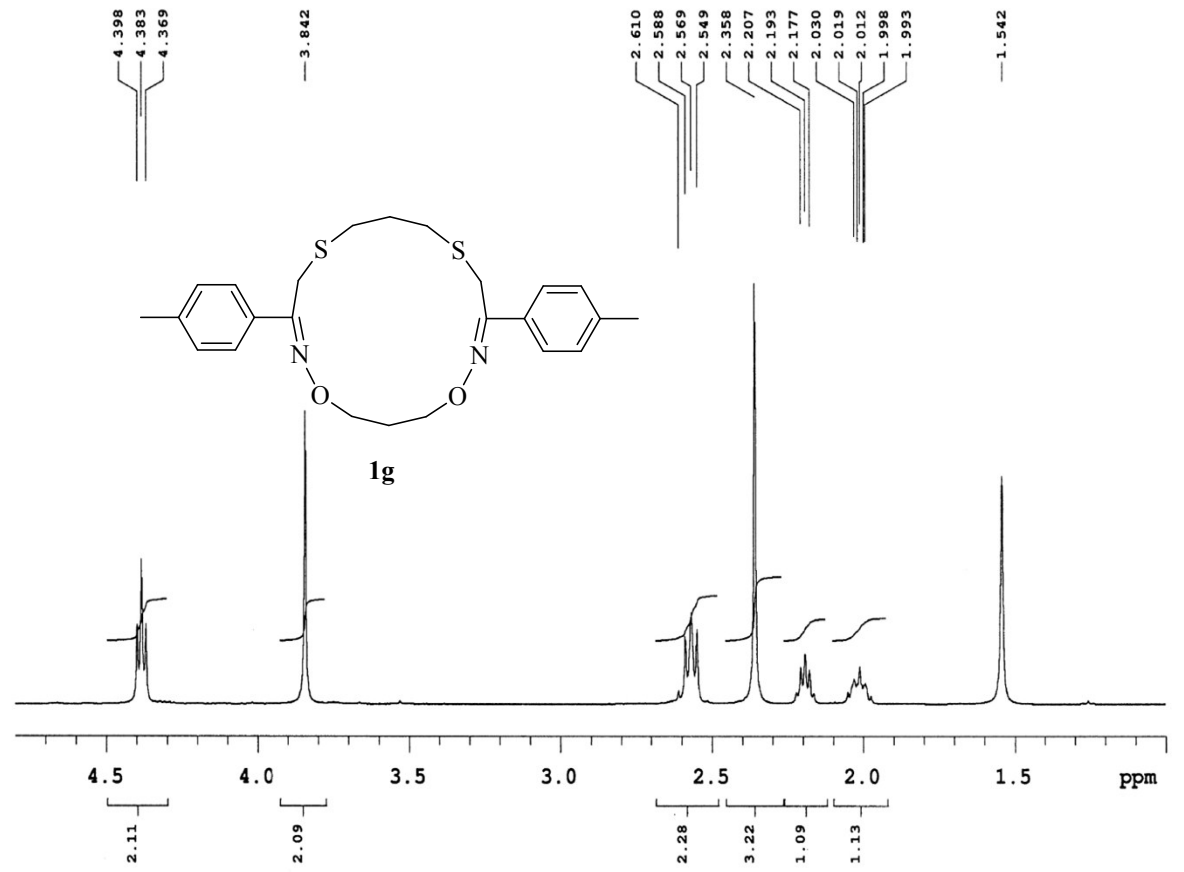


1g

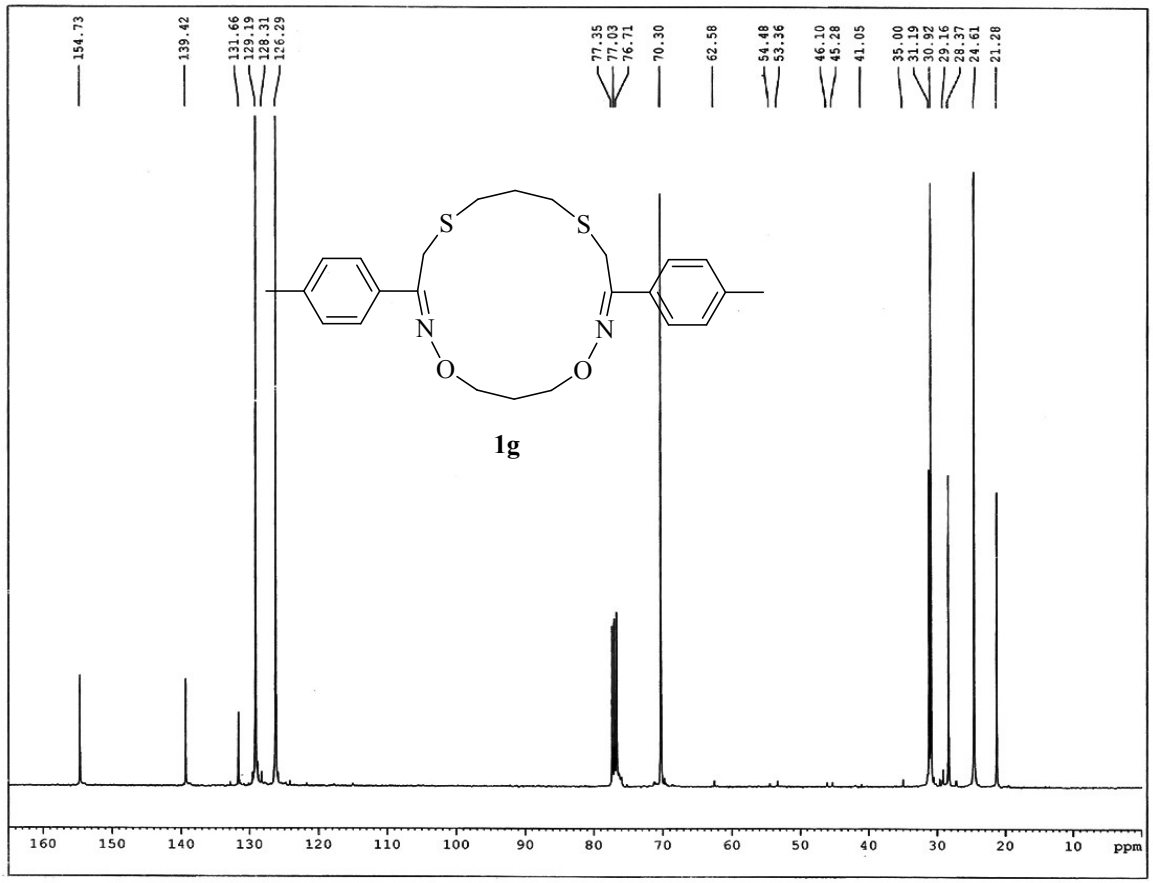



7.614
7.595
7.257
7.190
7.170
S
S
N
N
O
O
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
ppm
2.00
2.01

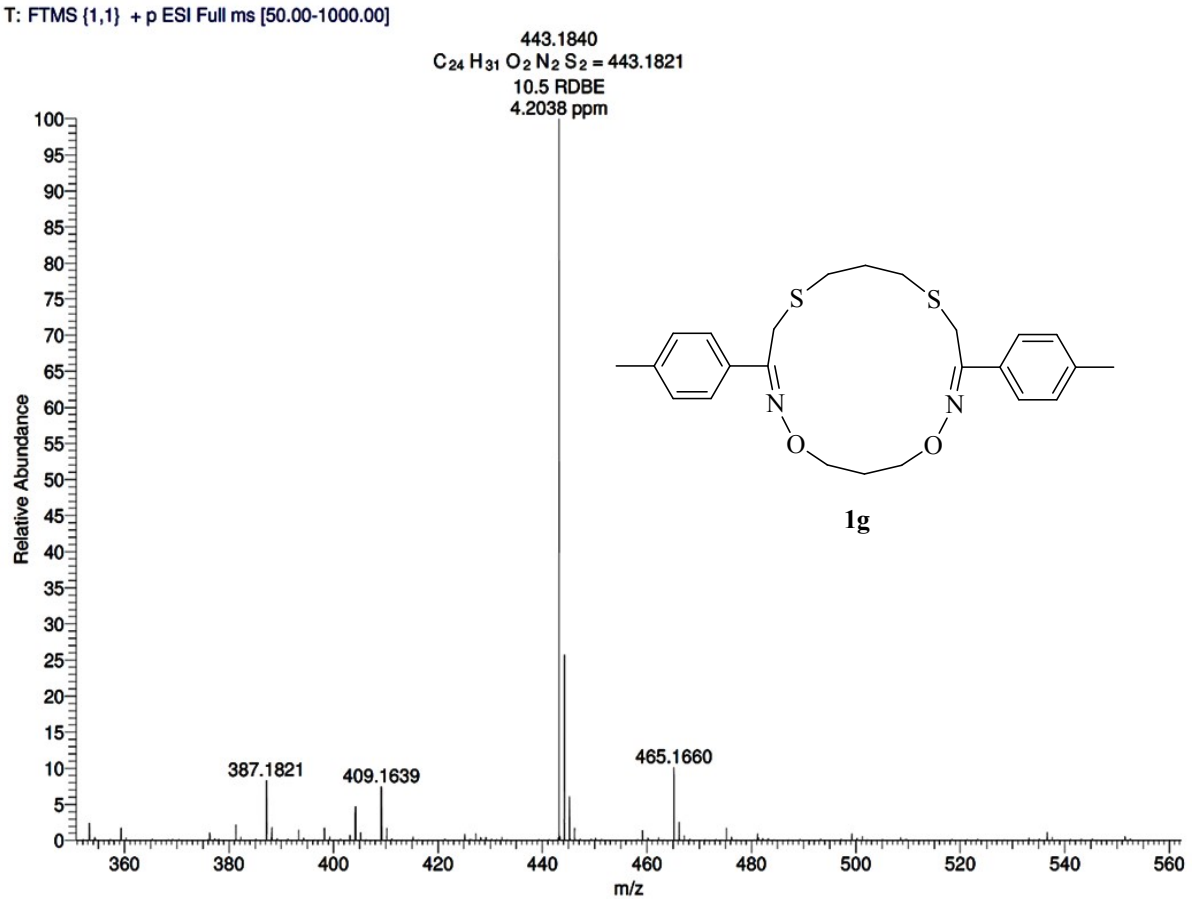
1g


4.398
4.383
4.369
3.842
2.610
2.588
2.569
2.549
2.358
2.207
2.193
2.177
2.030
2.019
2.012
1.998
1.993
1.542
S
S
N
N
O
O
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
2.11
2.09
2.28
3.22
1.09
1.13

1g


154.73
139.42
131.66
129.19
128.31
126.29
77.35
77.03
76.71
70.30
62.58
54.48
53.36
46.10
45.28
41.05
35.00
31.19
30.92
29.16
28.37
24.61
21.28
S
S
N
N
O
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

1g


T: FTMS {1,1} + p ESI Full ms [50.00-1000.00]
443.1840
C24 H31 O2 N2 S2 = 443.1821
10.5 RDBE
4.2038 ppm
Relative Abundance
387.1821
409.1639
465.1660
m/z

1g

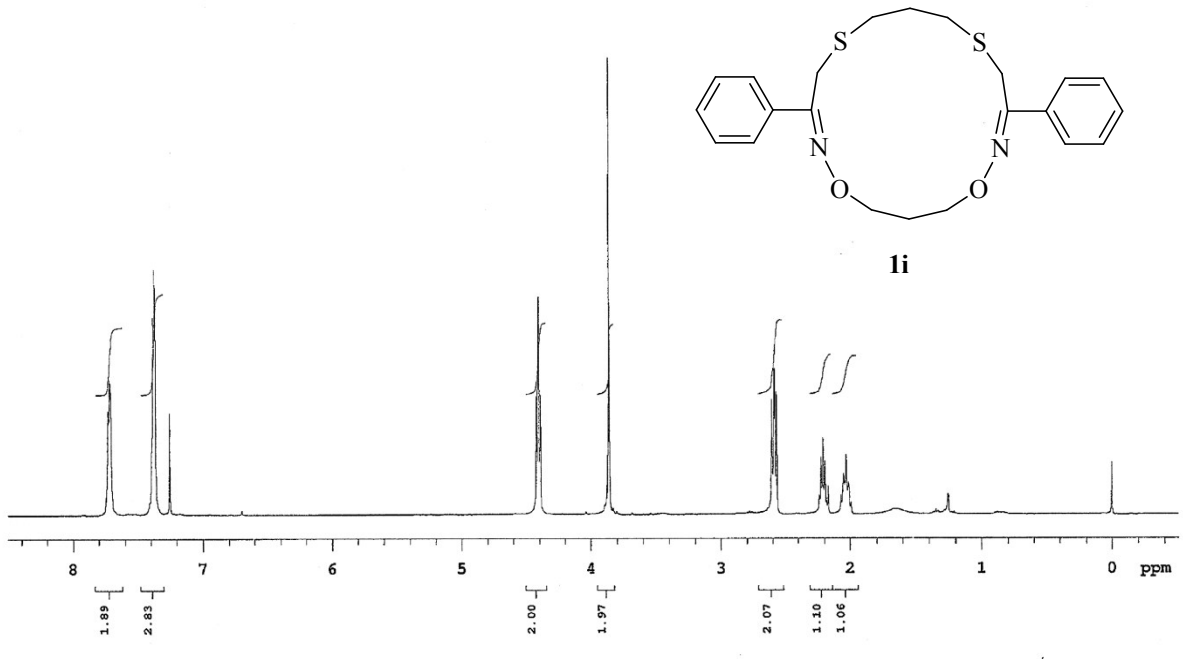
Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-diphenyl-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1i):

Off-white solid; Yield: 71.2%; mp. 91-93°C.

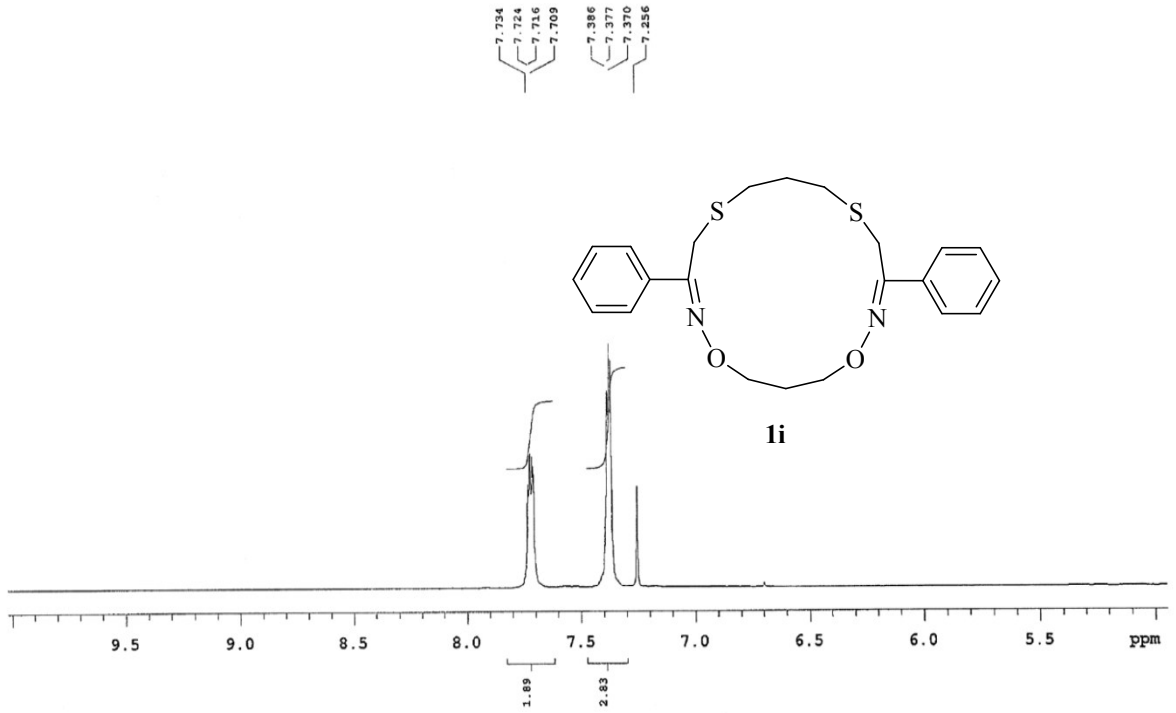
^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 7.72 (dd, *J* = 7.2, 4.0 Hz, 4H, arom H), 7.38 – 7.37 (m, 6H, arom H), 4.40 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.86 (s, 4H, 2-CH_2), 2.59 (t, *J* = 7.6Hz, 4H,2-SCH_2), 2.21 (quint, *J* = 5.6Hz, 2H,-CH_2), 2.03 (quint, 2H, *J* = 8.0Hz, -CH_2).

^{13}C NMR (100 MHz, $CDCl_3$, δ/ppm): 154.68 (2C), 134.37 (2C), 129.34 (2C), 128.43 (4C), 126.3 (4C), 70.25 (2C), 31.05 (C), 30.82 (2C), 28.24 (2C), 24.5 (C).

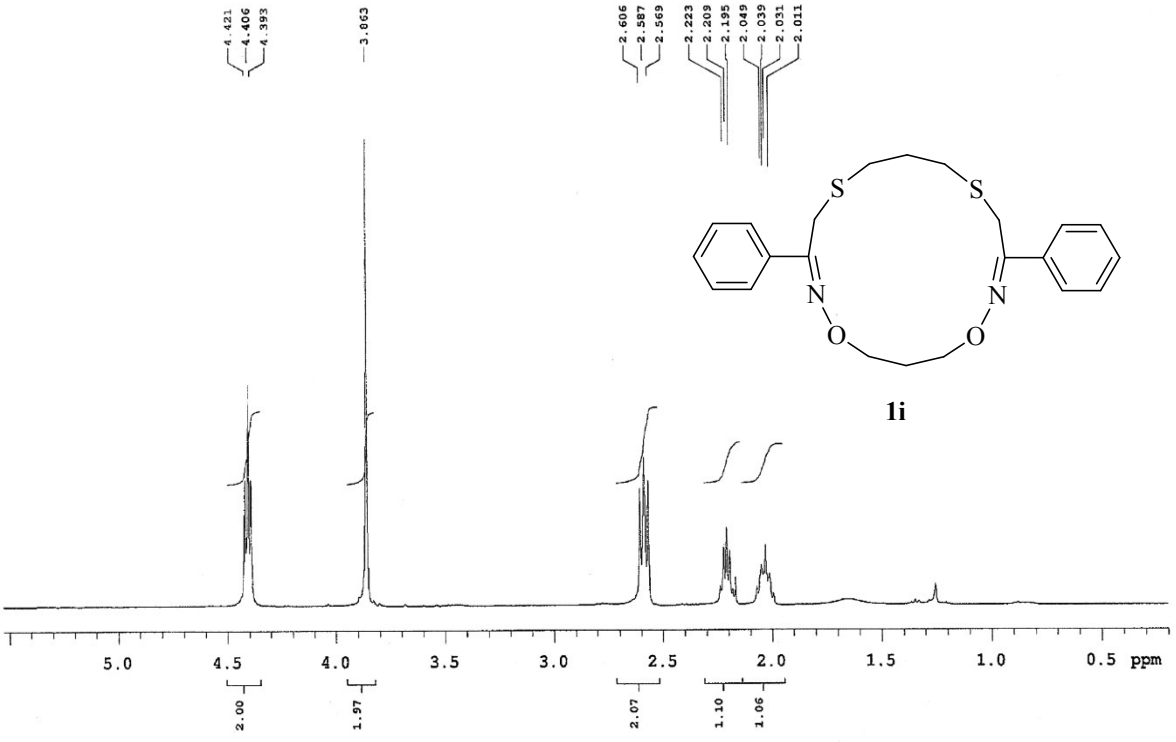
HRMS (ESI): $[M+H]^+$ Calcd for $C_{22}H_{27}N_2O_2S_2$ 415.1514 found 415.1494.



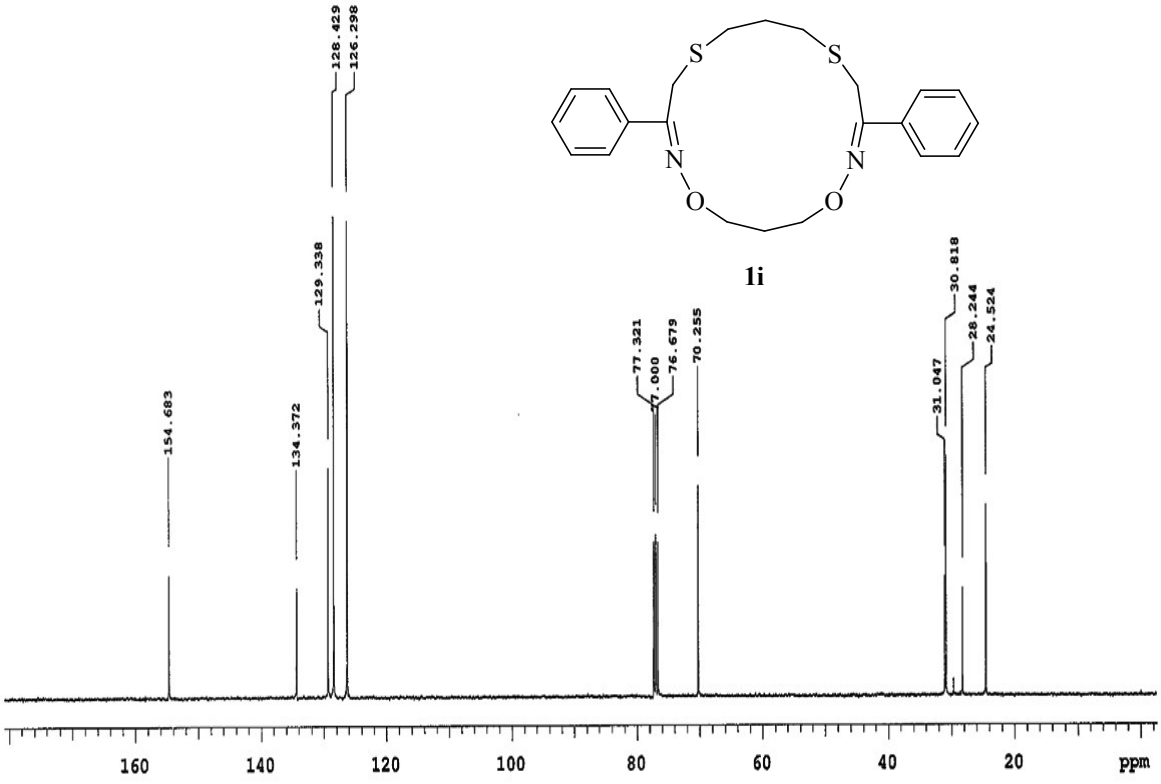
1i


7.734
7.724
7.716
7.709
7.386
7.377
7.370
7.256
S
S
N
N
O
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm
1.89
2.83

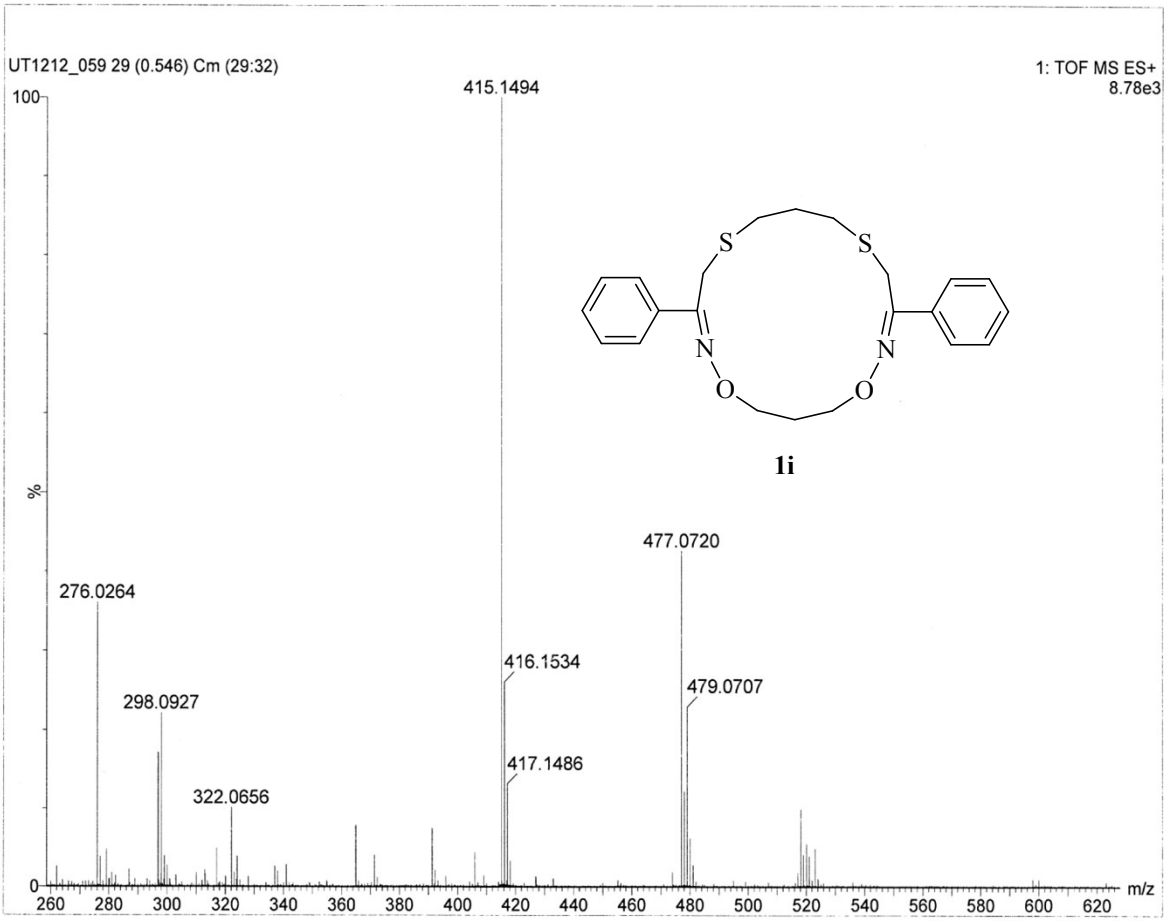
1i


4.421
4.406
4.393
3.063
2.606
2.587
2.569
2.223
2.209
2.195
2.049
2.039
2.031
2.011
S
S
N
N
O
O
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.97
2.07
1.10
1.06

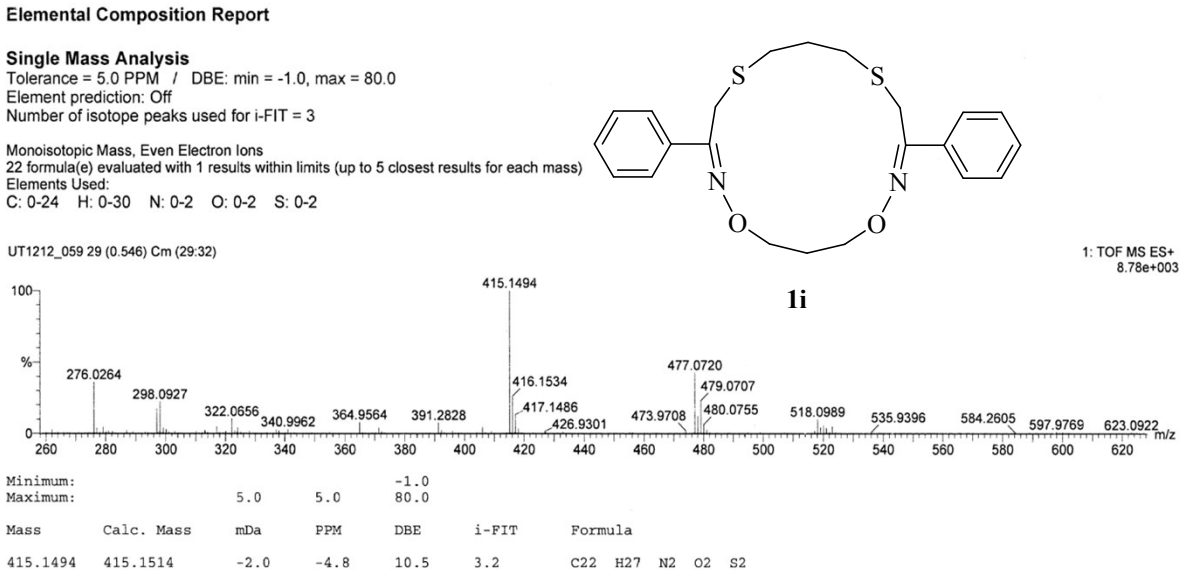
1i


126.429
126.298
129.338
154.683
134.372
77.321
77.000
76.679
70.255
30.818
28.244
24.524
31.047
160
140
120
100
80
60
40
20
ppm

1i


UT1212_059 29 (0.546) Cm (29:32)
1: TOF MS ES+
8.78e3
100
%
0
415.1494
477.0720
276.0264
416.1534
479.0707
298.0927
417.1486
322.0656
260
280
300
320
340
360
380
400
420
440
460
480
500
520
540
560
580
600
620
m/z

1i



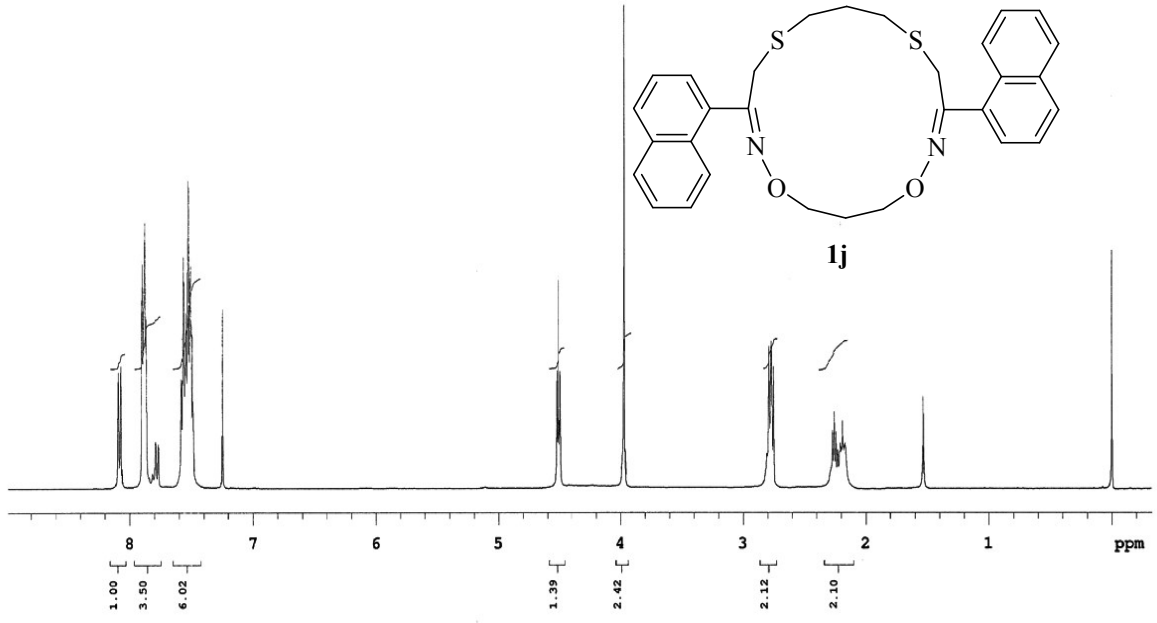
1i

Physical and Spectral data for 16-membered macrocycle, (2Z, 11Z)-3,11-di(naphthalen-1-yl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1j):

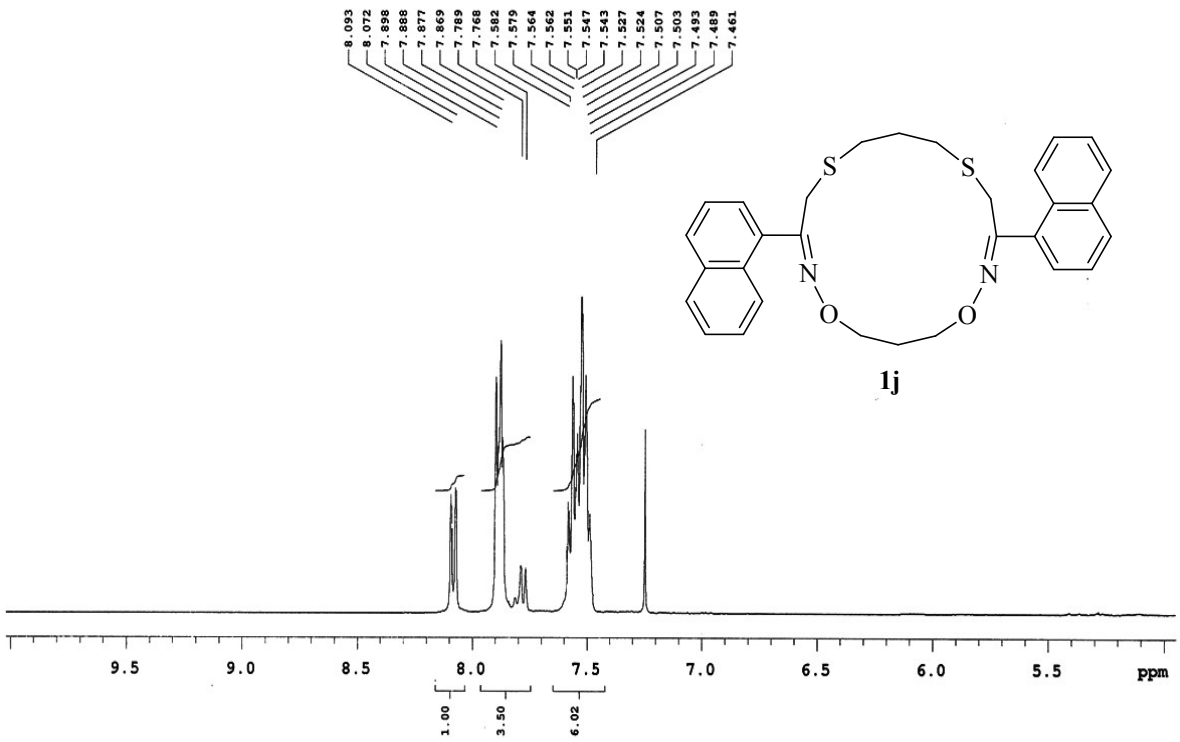
Off-white solid; Yield: 56.2%; mp 124-125°C

^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 8.08 (d, *J* = 8.4Hz, 2H, arom H), 7.90-7.7.79 (m, 6H, arom H),7.58-7.46 (m, 6H, arom H), 4.51 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 3.97 (s, 4H, $2CH_2$), 2.77 (t, 4H, *J* = 7.6 Hz, 2-SCH_2), 2.23 (quint, *J* = 6.0 Hz, 2H,-CH_2), 2.21-2.15 (m, 2H,-CH_2)

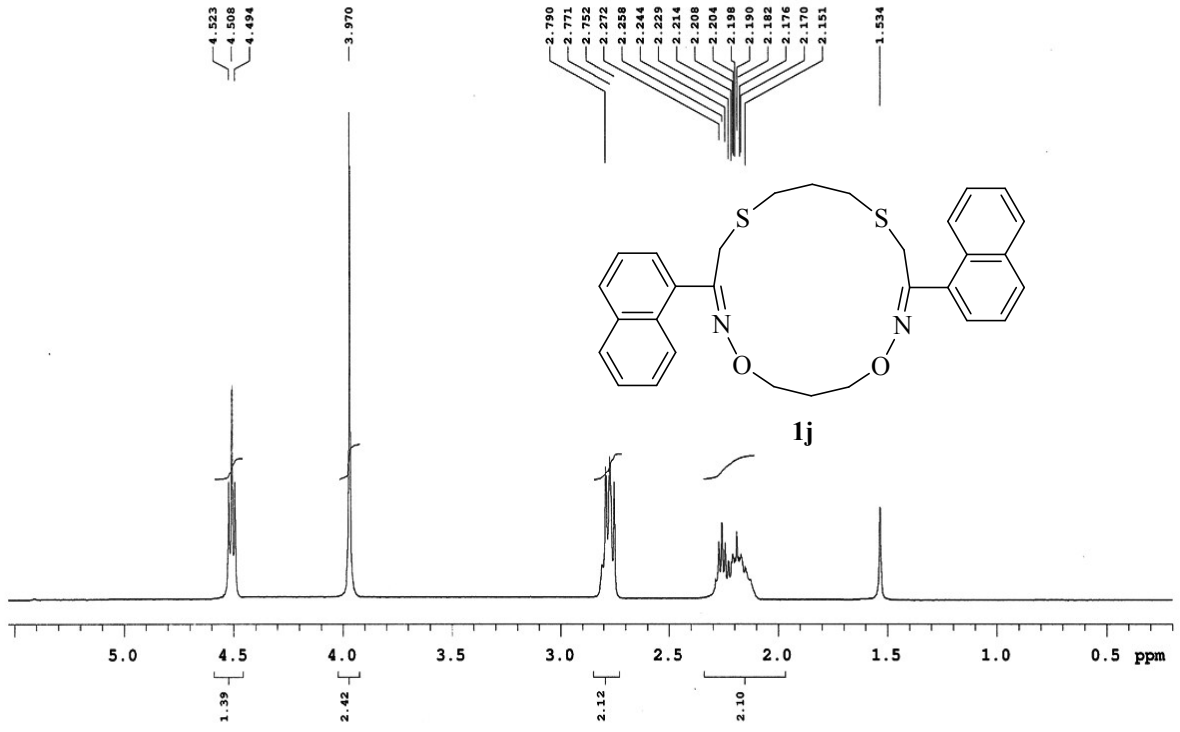
HRMS (ESI) : $[M+H]^+$ Calcd for $C_{30}H_{31}N_2O_2S_2$ 515.1827, found 515.1820



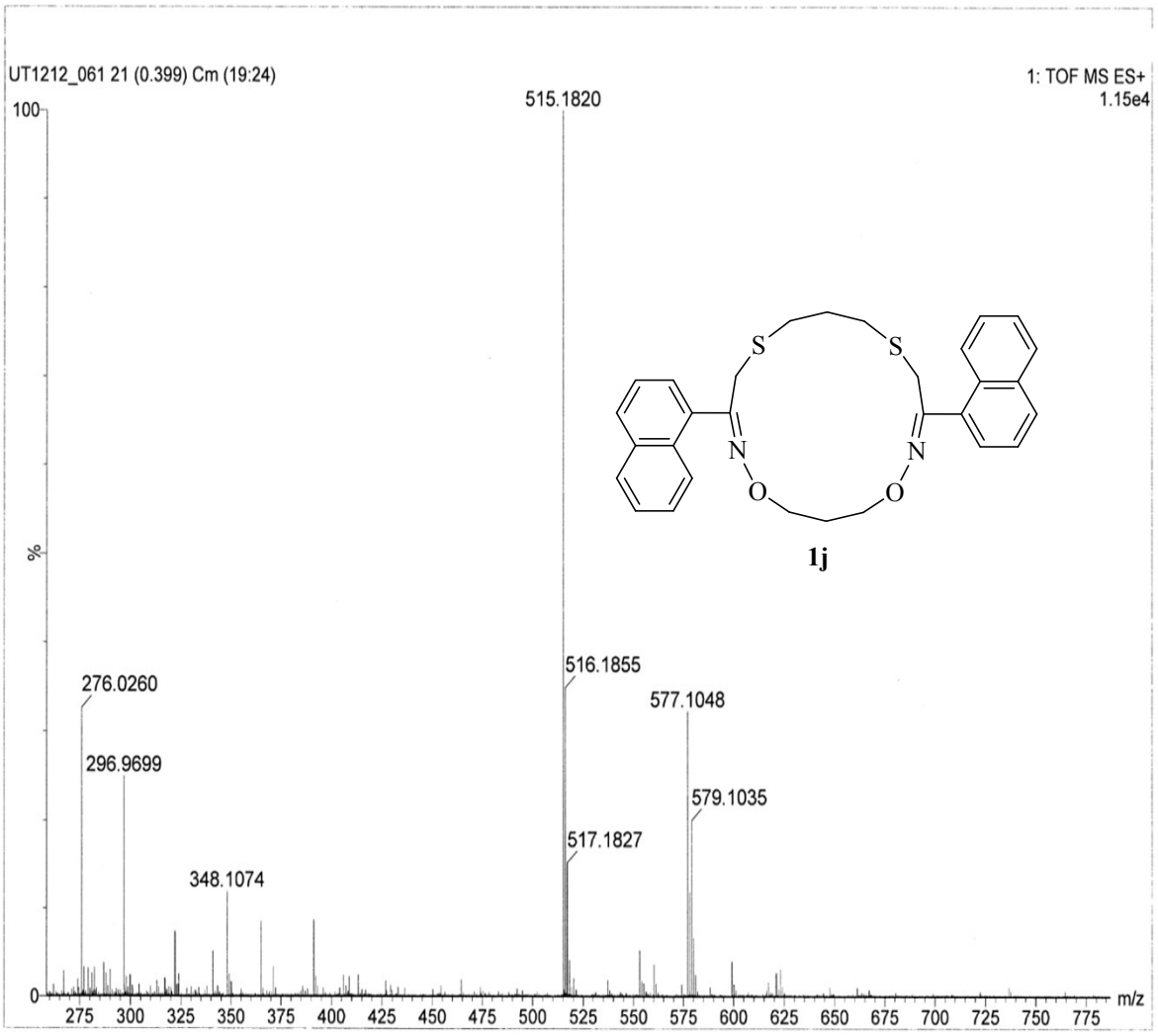
1j


8.093
8.072
7.898
7.888
7.877
7.869
7.789
7.768
7.582
7.579
7.564
7.562
7.551
7.547
7.543
7.527
7.524
7.507
7.503
7.493
7.489
7.461
S
S
N
N
O
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm
1.00
3.50
6.02

1j


4.523
4.508
4.494
3.970
2.790
2.771
2.752
2.272
2.258
2.244
2.229
2.214
2.208
2.204
2.198
2.190
2.182
2.176
2.170
2.151
1.534
S
S
N
N
O
O
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.39
2.42
2.12
2.10

1j

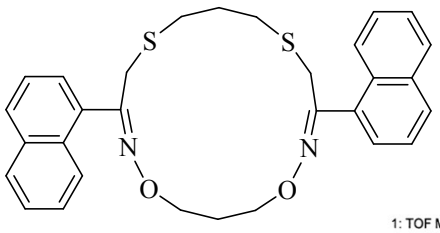


1j

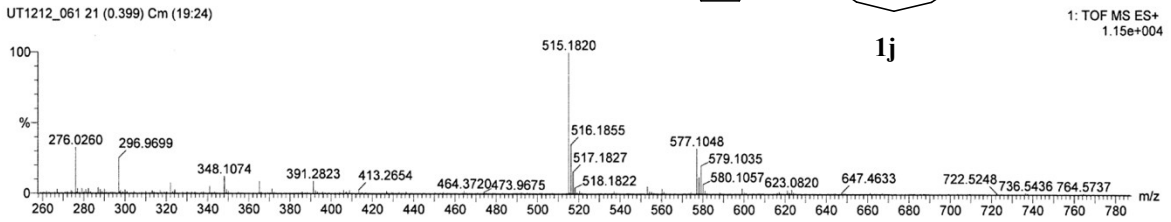
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
37 formula(e) evaluated with 1 results within limits (up to 5 closest results for each mass)
Elements Used:
C: 0-35 H: 0-35 N: 0-2 O: 0-2 S: 0-2



1j



Minimum:				-1.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
515.1820	515.1827	-0.7	-1.4	16.5	2.4	C30 H31 N2 O2 S2

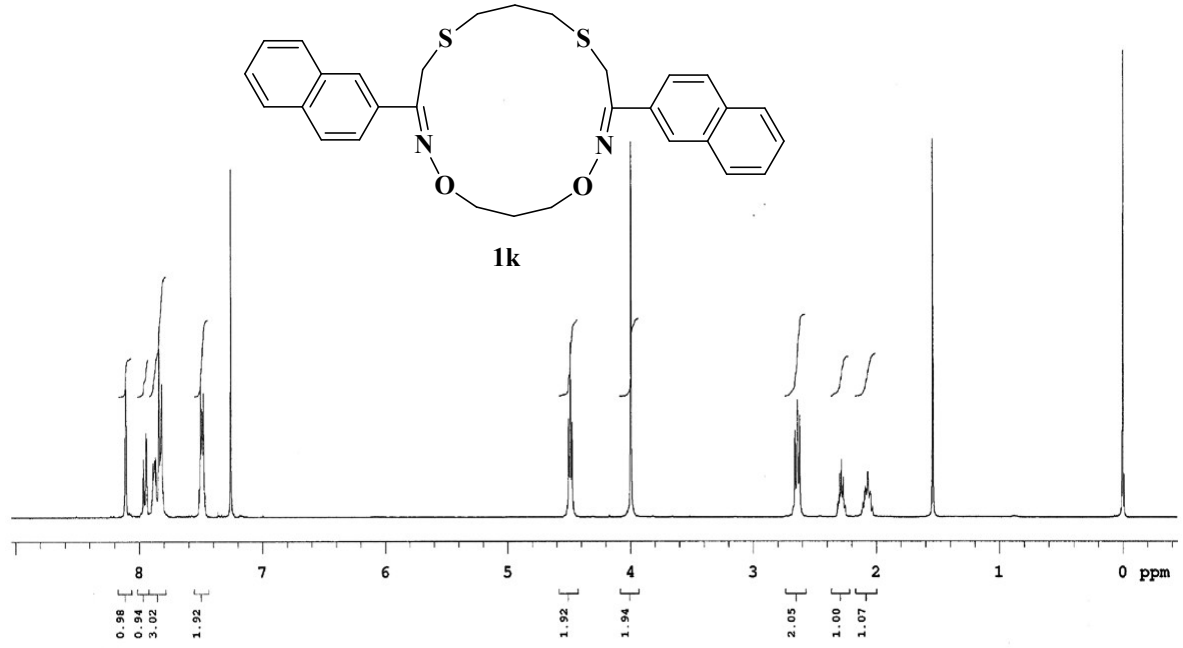
Physical and Spectral data for 16-membered macrocycle, (2Z,11Z)-3,11-di(naphthalen-2-yl)-1,13-dioxa-5,9-dithia-2,12-diazacyclohexadeca-2,11-diene (1k):

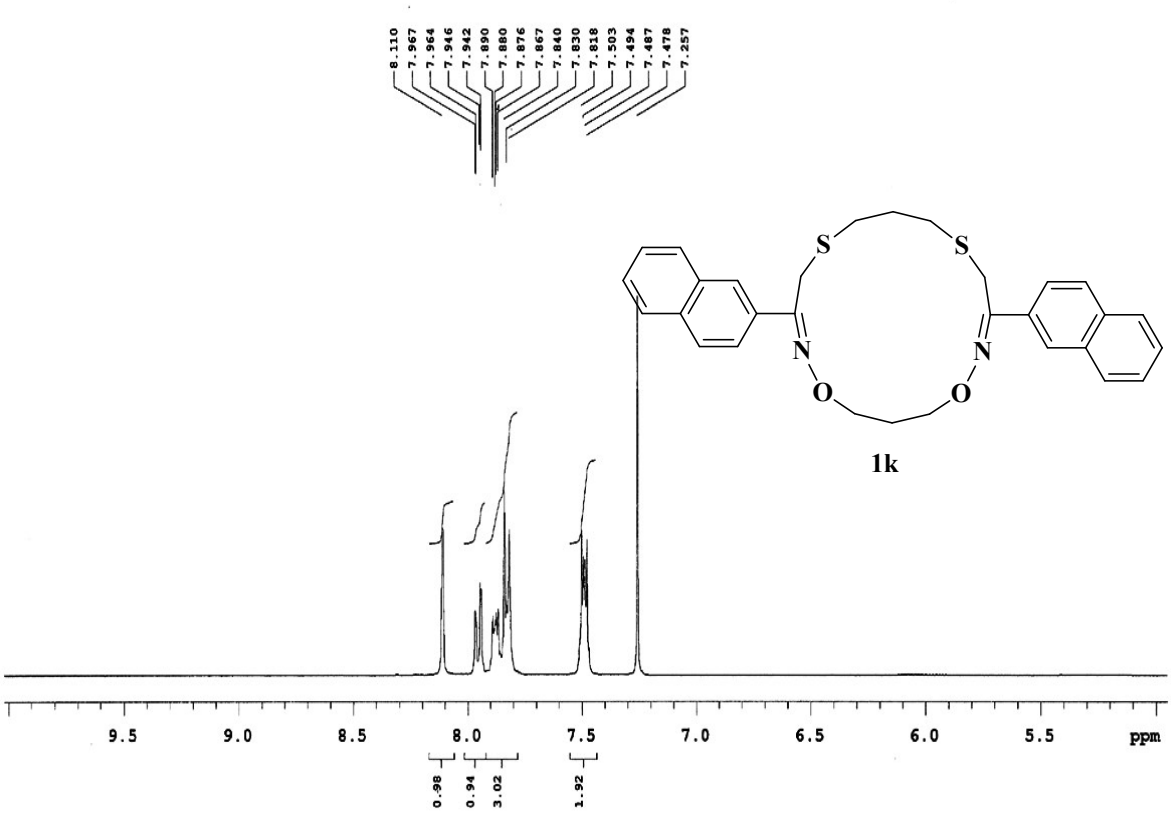
Pale yellow solid;Yield: 61%; mp 106-108°C

^{1}H NMR (400 MHz, $CDCl_3$, δ/ppm): 8.11 (s, 2H, arom H), 7.95 (dd, *J* = 8.4, 1.6 Hz, 2H, arom H), 7.88 (dd, *J* = 5.6, 3.6 Hz, 2H, arom H), 7.83 (t, *J* = 4.8 Hz, 4H, arom H), 7.49 (dd, *J* = 6.4, 3.6 Hz, 4H, arom H), 4.49 (t, *J* = 6.0 Hz, 4H, 2-OCH_2), 4.0 (s, 4H, 2-CH_2), 2.64 (t, *J* = 8.0 Hz, 4H, 2-SCH_2), 2.28 (quint, *J* = 6.0 Hz, 2H, -CH_2), 2.08 (quint, *J* = 4.4 Hz, 2H, -CH_2)

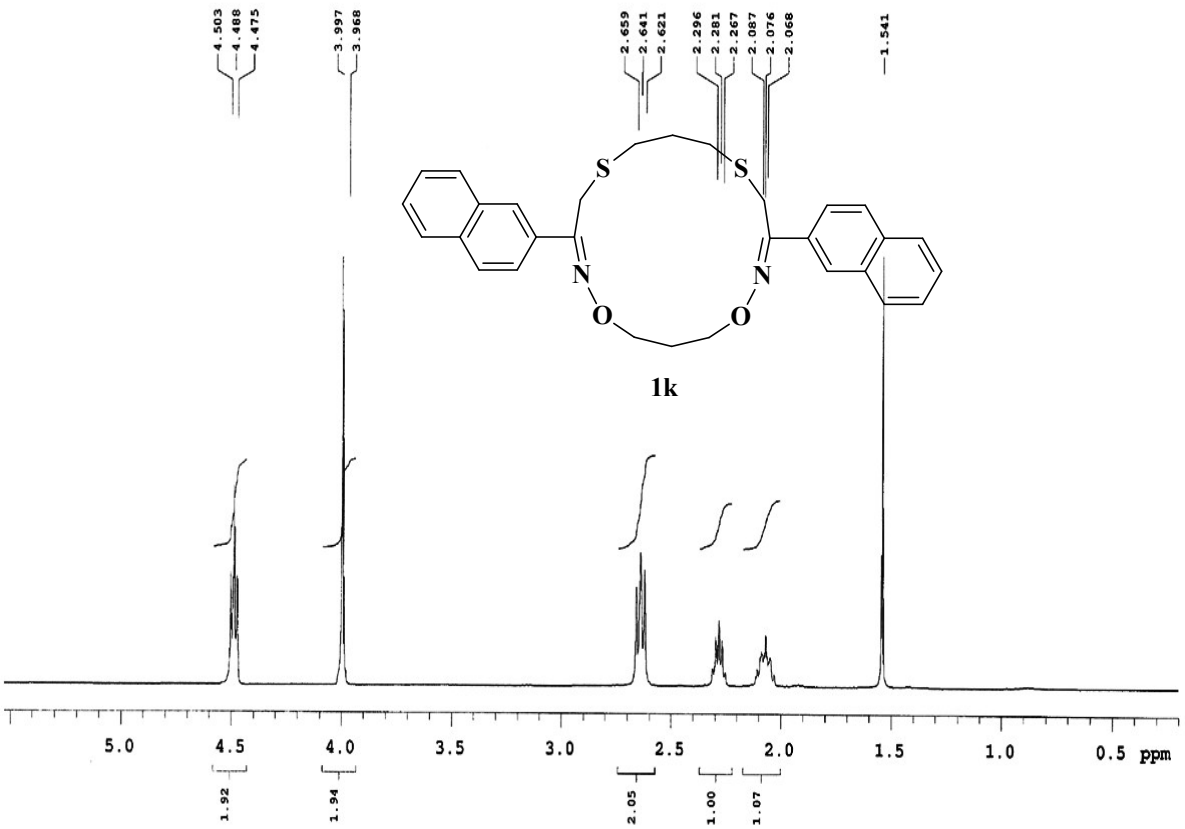
^{13}C NMR (400 MHz, $CDCl_3$, δ/ppm): 154.58 (2C), 133.75 (2C), 133.06 (2C), 131.69 (2C), 128.57 (2C), 128.11 (2C), 127.59 (2C), 126.66 (2C), 126.29 (2C), 126.15 (2C), 123.56 (2C), 70.45 (2C), 31.05 (C), 30.92 (2C), 28.36 (2C), 24.4 (C).

HRMS (ESI): $[M+H]^+$ Calcd for $C_{30}H_{31}N_2O_2S_2$ 515.1827, found 515.1833

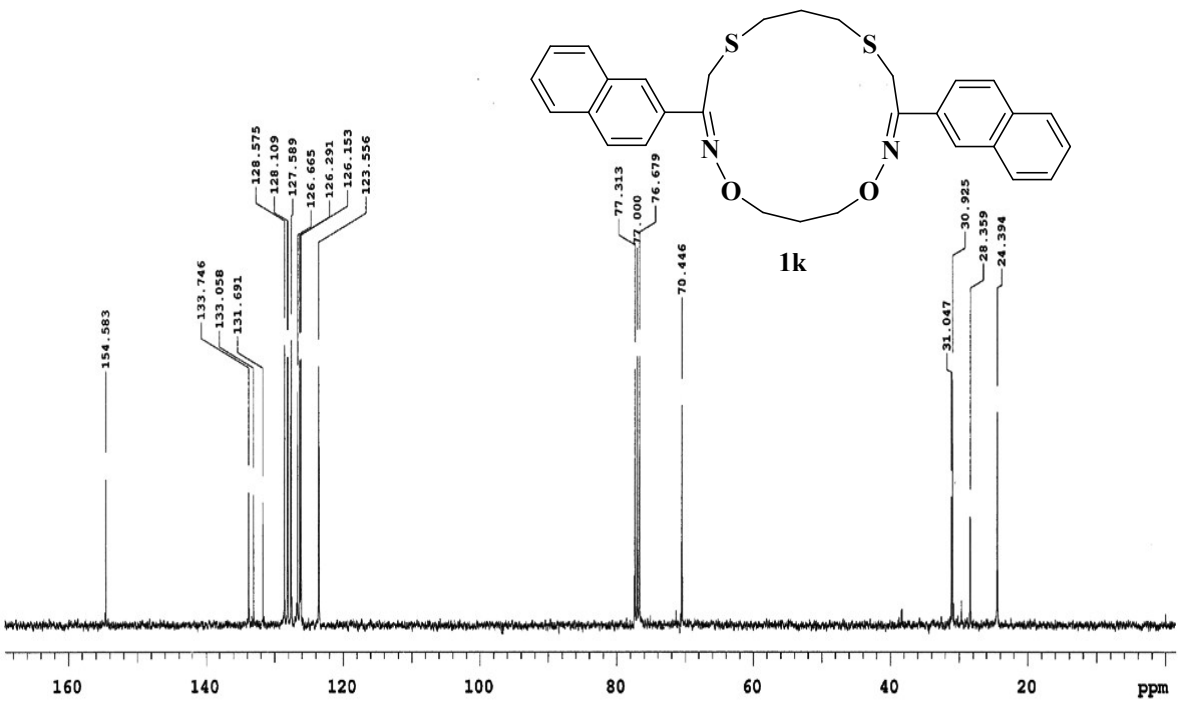


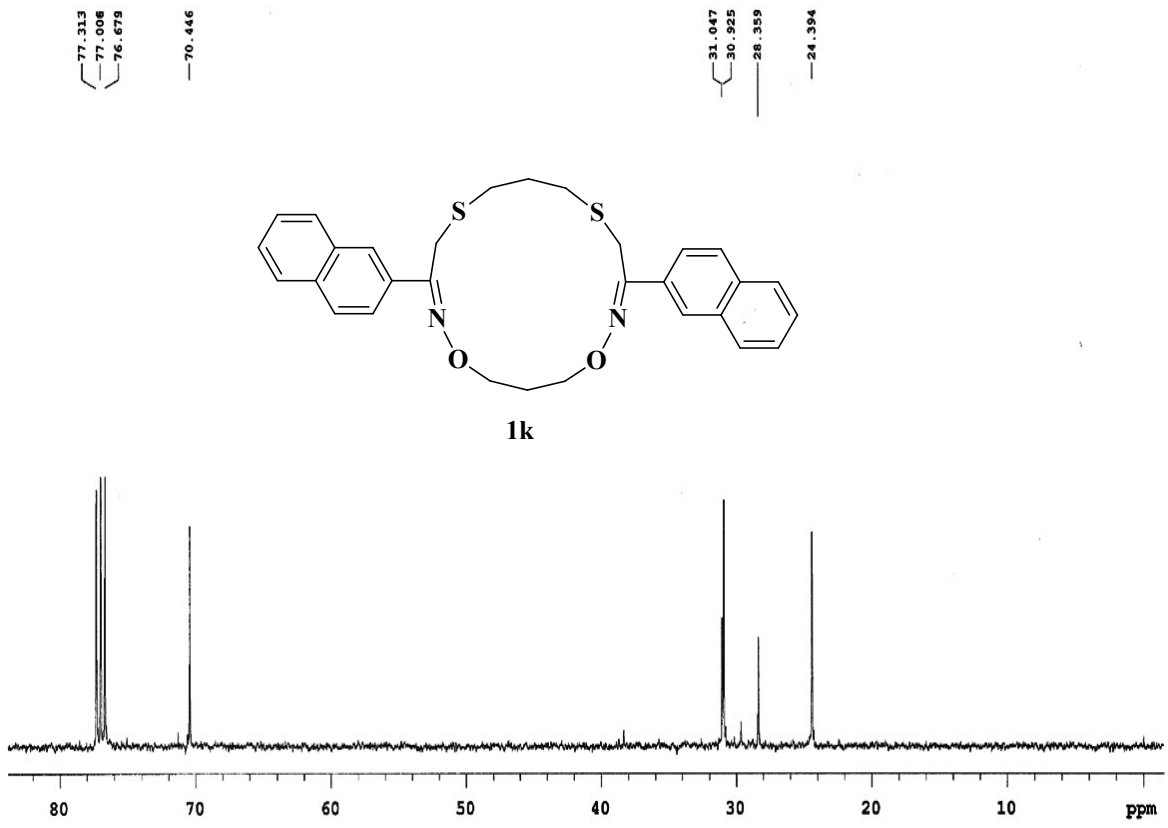

8.110
7.967
7.964
7.946
7.942
7.890
7.880
7.876
7.867
7.840
7.830
7.818
7.503
7.494
7.487
7.478
7.257
S
S
N
N
O
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm
0.98
0.94
3.02
1.92

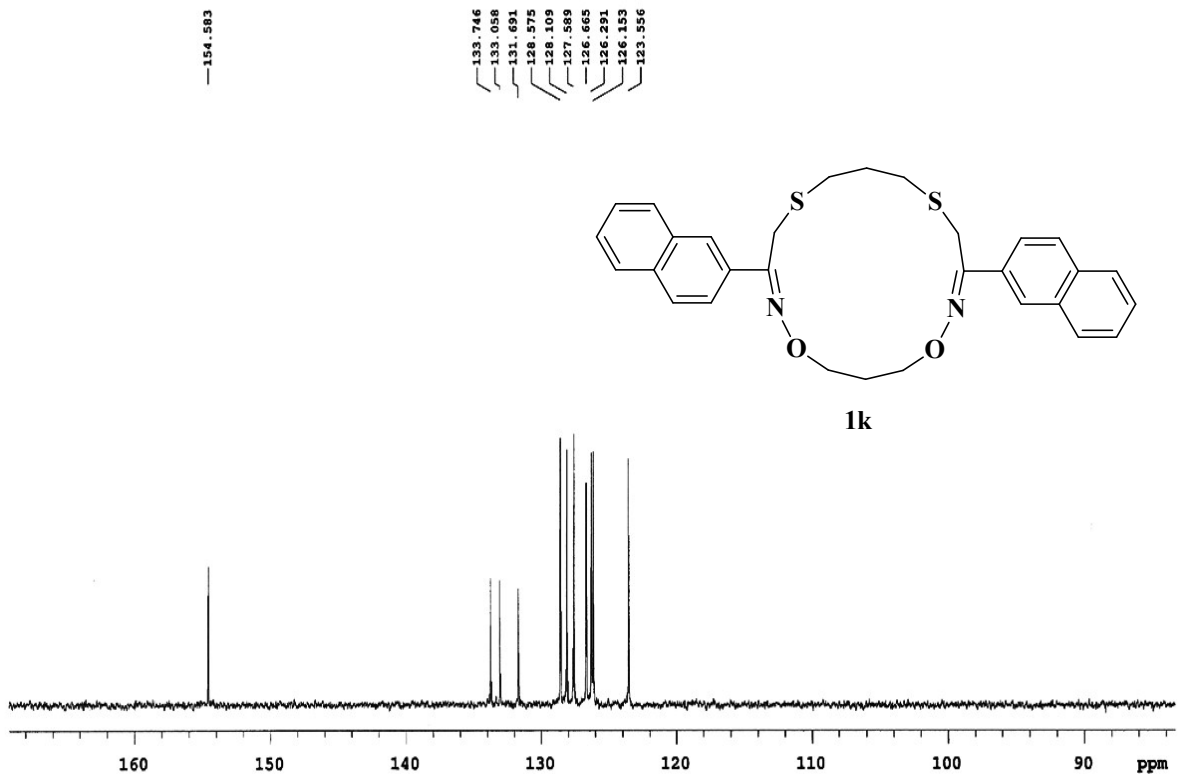
1k


4.503
4.488
4.475
3.997
3.968
2.659
2.641
2.621
2.296
2.281
2.267
2.087
2.076
2.068
1.541
S
S
N
N
O
O
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5 ppm
1.92
1.94
2.05
1.00
1.07

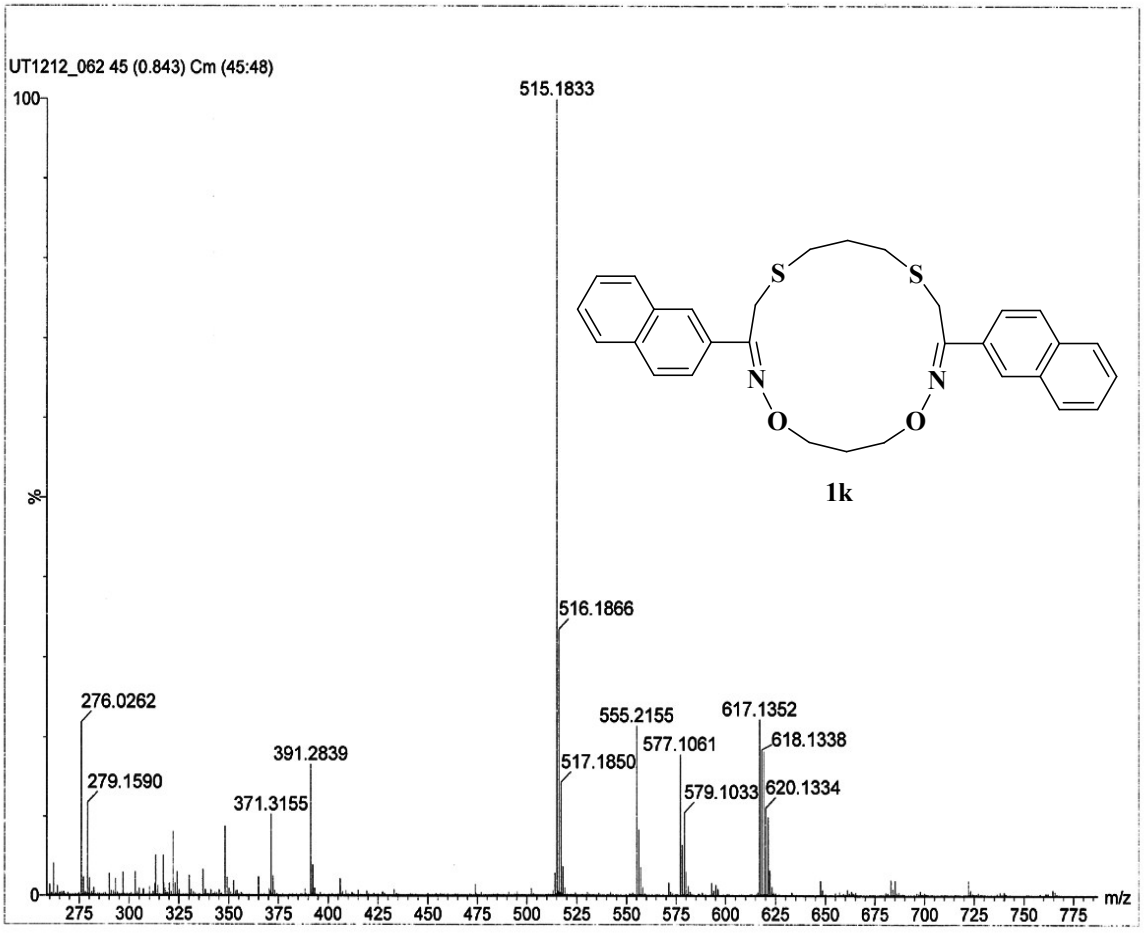
1k


S
S
N
N
O
O
1k
154.583
133.746
133.058
131.691
128.575
128.109
127.589
126.665
126.291
126.153
123.556
77.313
77.000
76.679
70.446
31.047
30.925
28.359
24.394
160
140
120
100
80
60
40
20
ppm


77.313
77.006
76.679
70.446
31.047
30.925
28.359
24.394
S
S
N
N
O
O
1k
80
70
60
50
40
30
20
10
ppm


154.583
133.746
133.058
131.691
128.575
128.109
127.589
126.665
126.291
126.153
123.556
S
S
N
N
O
O
160
150
140
130
120
110
100
90
ppm

1k

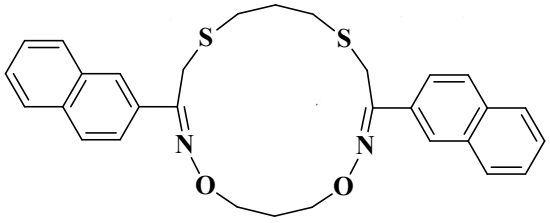

UT1212_062 45 (0.843) Cm (45:48)
100
%
0
515.1833
516.1866
276.0262
279.1590
371.3155
391.2839
517.1850
555.2155
577.1061
579.1033
617.1352
618.1338
620.1334
275 300 325 350 375 400 425 450 475 500 525 550 575 600 625 650 675 700 725 750 775
m/z
S
S
N
N
O
O

1k

Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

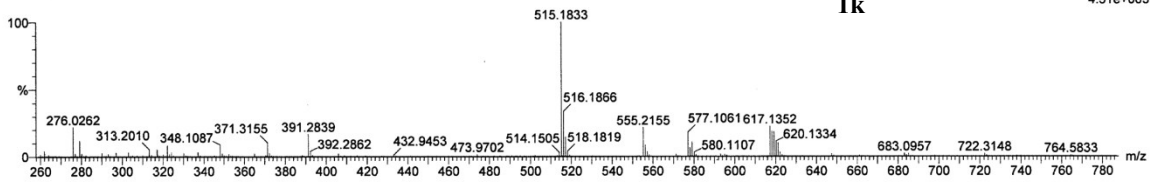
Monoisotopic Mass, Even Electron Ions
37 formula(e) evaluated with 1 results within limits (up to 5 closest results for each mass)
Elements Used:
C: 0-35 H: 0-35 N: 0-2 O: 0-2 S: 0-2



1k

UT1212_062 45 (0.843) Cm (45:48)

1: TOF MS ES+
4.51e+003



Minimum:				-1.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
515.1833	515.1827	0.6	1.2	16.5	4.9	C30 H31 N2 O2 S2