Supporting Information

for

Examination of structure-activity relationship of new *N*-acylhydrazones

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1. Organic Synthesis

Experimental procedure for synthesis of aldehyde 1a. 5-metil-2-hydroxyisophthalaldehyde. 2,6-(dihydroxymethyl)-*p*-cresol was suspended in chloroform and activated MnO_2 (in the oven at 140°C overnight) was added (20 equivalents). The reaction was left at reflux until full conversion of the alcohol. When necessary, manganese dioxide was further added to ensure complete oxidation. The mixture was filtered on celite and the collected fractions were evaporated, yielding pure product.[1] yield 90%.*m.p.* 124-126°C. R_f=0.55 (silica, ethyl acetate: petroleum ether=1:4). ^{1}H NMR (500.13 MHz, $CDCl_3$): δ= 11.45 (s, 1H, -OH), 10.21 (s, 2H, H-5, -CHO), 7.77 (s, 2H, H-3), 2.38 (s, 3H, $-CH_3$) ppm. ^{13}C NMR (125.77 MHz, $CDCl_3$): δ= 192.2 (C-5, -CHO), 161.8 (C-1), 138.0 (C-3), 129.5 (C-4), 122.9 (C-2) ppm.

[1] W. Huang , S. Gou, D. Hu, Q. Meng, Synth. Commun. **2000**, *30*, 1555-1561.

General experimental procedure for synthesis of aldehydes1b-d. The corresponding phenol is treated with urotropine (4 equivalents) and trifluoroacetic acid (14 equivalents) and the mixture is heated to reflux until complete conversion, as monitored by TLC. Water is then added and the resulted precipitate is stirred at heating for 1-2 hours, filtered and washed thoroughly with water. Purification is performed by recrystallization.

Aldehyde 1b.5-bromo-2-hydroxyisophthalaldehyde. Purifications performed by recrystallization from ethanol-water,[2]yield 58%. *m.p.*138-140°C. R_f=0.67 (silica, ethyl acetate: petroleum ether=1:3). ^{1}H NMR (500.13 MHz, $CDCl_3$): δ= 11.54 (s, 1H, -OH), 10.19 (s, 2H, H-5, -CHO), 8.06 (s, 2H, H-3)ppm. ^{13}C NMR (125.77 MHz, $CDCl_3$): δ= 191.0 (C-5, -CHO), 162.3 (C-1), 139.8 (C-3), 124.6 (C-2), 112.2 (C-4) ppm.

Aldehyde 1d. 5-nitro-2-hydroxyisophthalaldehyde. Purification is performed by recrystallization from ethanol-water,[3] yield 58% (3.9 g). *m.p.*124-126°C. R_f=0.50 (silica, ethyl acetate: petroleum ether=1:2).- ^{1}H NMR (500.13 MHz, DMSO-*d6*): δ= 10.29 (s, 2H, H-5, -CHO), 8.67 (s, 2H, H-3) ppm. ^{13}C NMR (125.77 MHz, DMSO-*d6*): δ= 190.6 (C-5, -CHO), 168.1 (C-1), 138.1 (C-4), 130.6 (C-3), 124.9 (C-2) ppm.

2. Single crystal X-Ray Diffraction

Table S1 Selected bond lengths for compound **3b** (Å)

C1-N1 = 1.460(13)	C15-C17 = 1.462(12)
C2-N1 = 1.463(13)	C16-O2 = 1.338(11)
C3-C4 = 1.364(13)	C17-N4 = 1.288(10)
C3-C8 = 1.423(13)	C18-O3 = 1.217(10)
C4-C5 = 1.389(13)	C18-N5 = 1.365(11)
C5-N1 = 1.332(12)	C18-C19 = 1.460(12)
C5-C6 = 1.408(12)	C19-C24 = 1.381(10)
C6-C7 = 1.380(11)	C19-C20 = 1.383(12)
C7-C8 = 1.380(12)	C20-C21 = 1.390(12)
C8-C9 = 1.474(12)	C21-C22 = 1.398(12)
C9-O1 = 1.217(11)	C22-N6 = 1.379(12)
C9-N2 = 1.383(10)	C22-C23 =1.412(12)
C10-N3 = 1.278(10)	C23-C24 =1.378(11)
C10-C11 = 1.418(13)	C25-N6 =1.430(11)
C11-C16 = 1.388(12)	C26-N6 =1.446(11)
C11-C12 = 1.401(12)	C27-S1 =1.723(12)
C12-C13 = 1.357(12)	C28-S1 =1.461(14)
C13-C14 = 1.383(12)	N2-N3 =1.365(9)

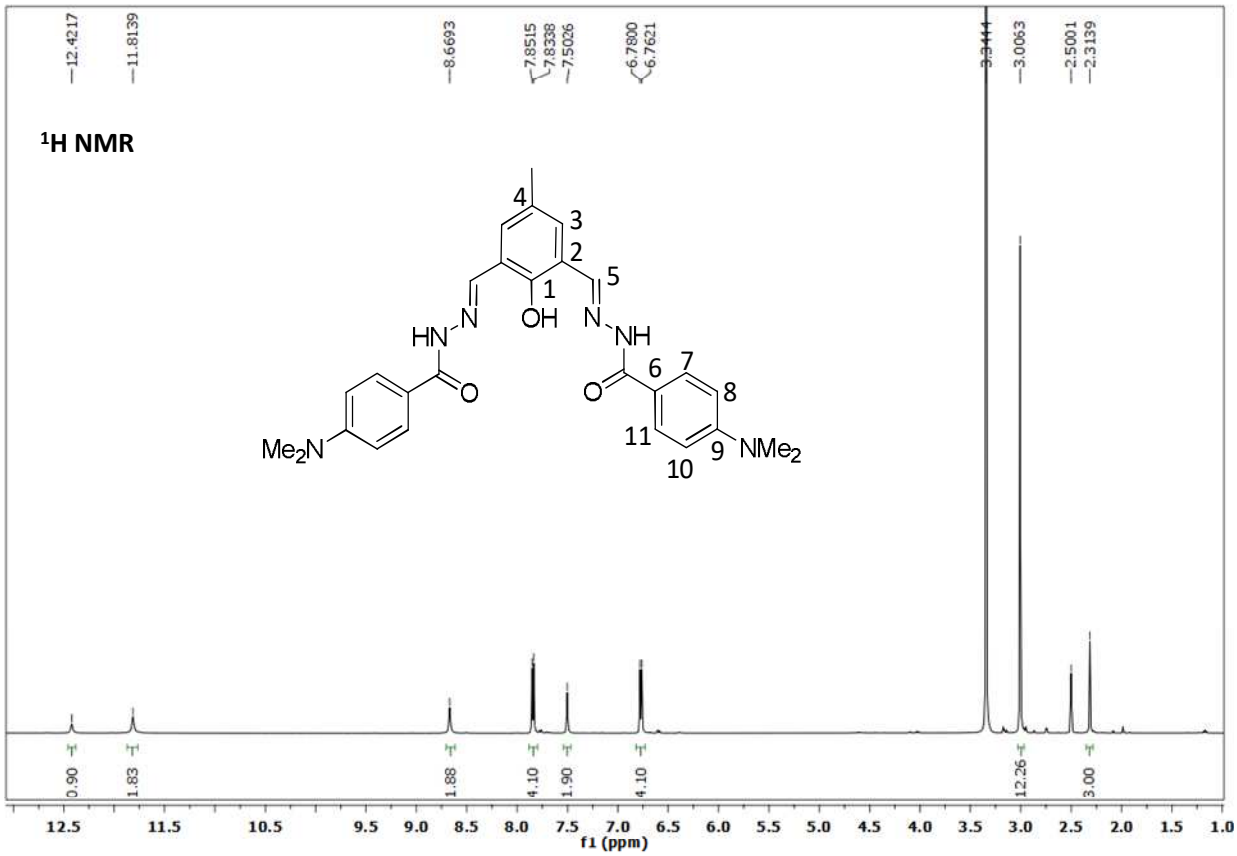
[2]Y-P. Chan, L. Fana, Q. You, W.-H. Chan, A.W.M. Lee, S. Shuang, *Tetrahedron***2013**, *69*, 5874-5879.
[3] A. Hryniewicka, A. Koz1owska, S. Witkowski, *J. Organomet. Chem.***2012**, *701*, 87-92.

C13-Br1 = 1.894(9)	N4 N5 =1.398(10)
C14-C15 = 1.415(11)	O4 S1 = 1.291(8)
C15-C16 = 1.394(12)	

Table S2 Crystallographic data, details of data collection and structure refinement parameters for **3b**

Compound	**3b**
Chemical formula	$C_{28}H_{33}BrN_6O_4S$
M (g mol^{-1})	629.57
Temperature, (K)	293(2)
Wavelength, (Å)	0.71073
Crystal system	*Monoclinic*
Space group	$P2_1/c$
a(Å)	10.0560(17)
b(Å)	13.243(2)
c(Å)	22.886(4)
α(°)	90
β(°)	99.773(14)
γ(°)	90
V(Å^3)	3003.6(9)
Z	4
D_c (g cm^{-3})	1.392
μ (mm^{-1})	1.481
Goodness-of-fit on F^2	0.704
Final $R1, wR_2$ [$I>2\sigma(I)$]	0.0538, 0.0656
$R1$, wR_2(all data)	0.3008, 0.1203
Largest diff. peak and hole (eÅ^{-3})	0.390, -0.281

3. NMR spectra and numberring scheme for NMR interpretation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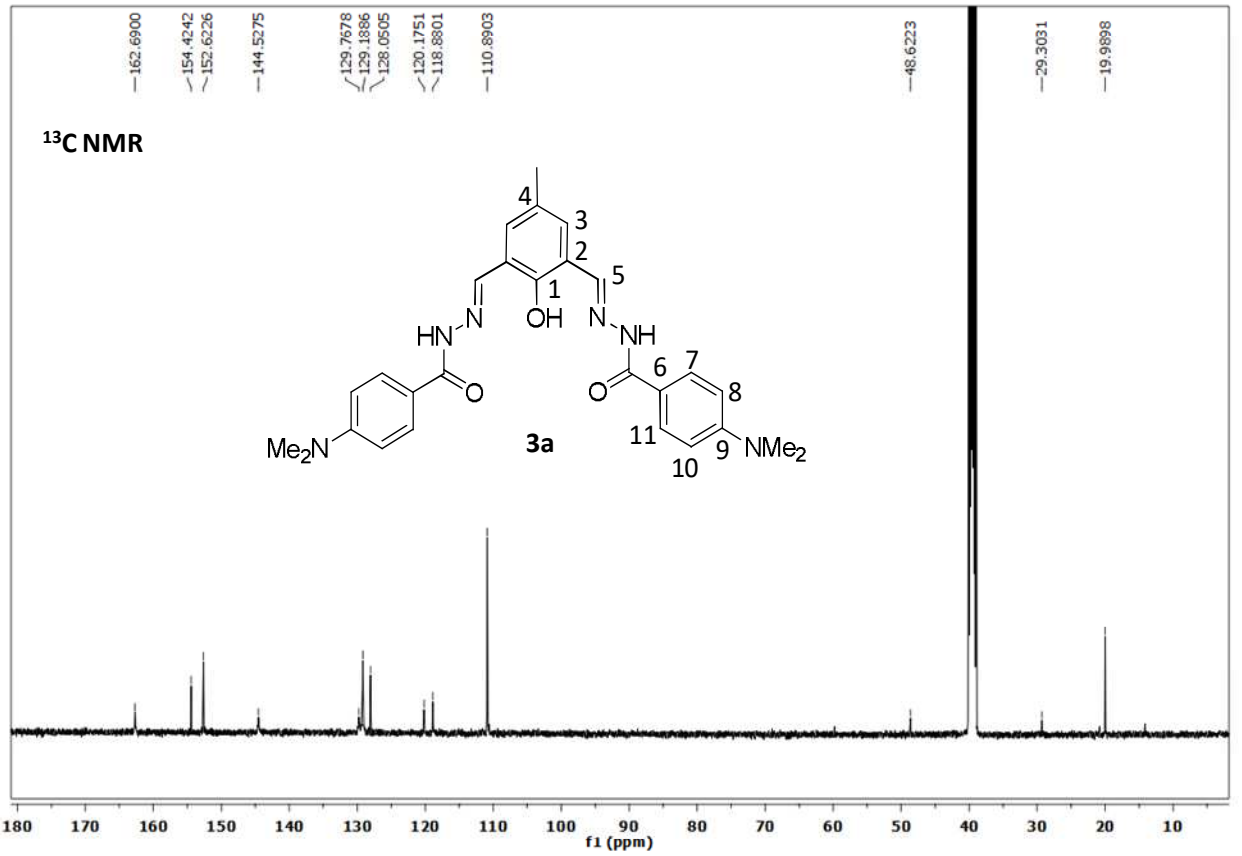
4.10
1.90
4.10
12.26
3.00
f1 (ppm)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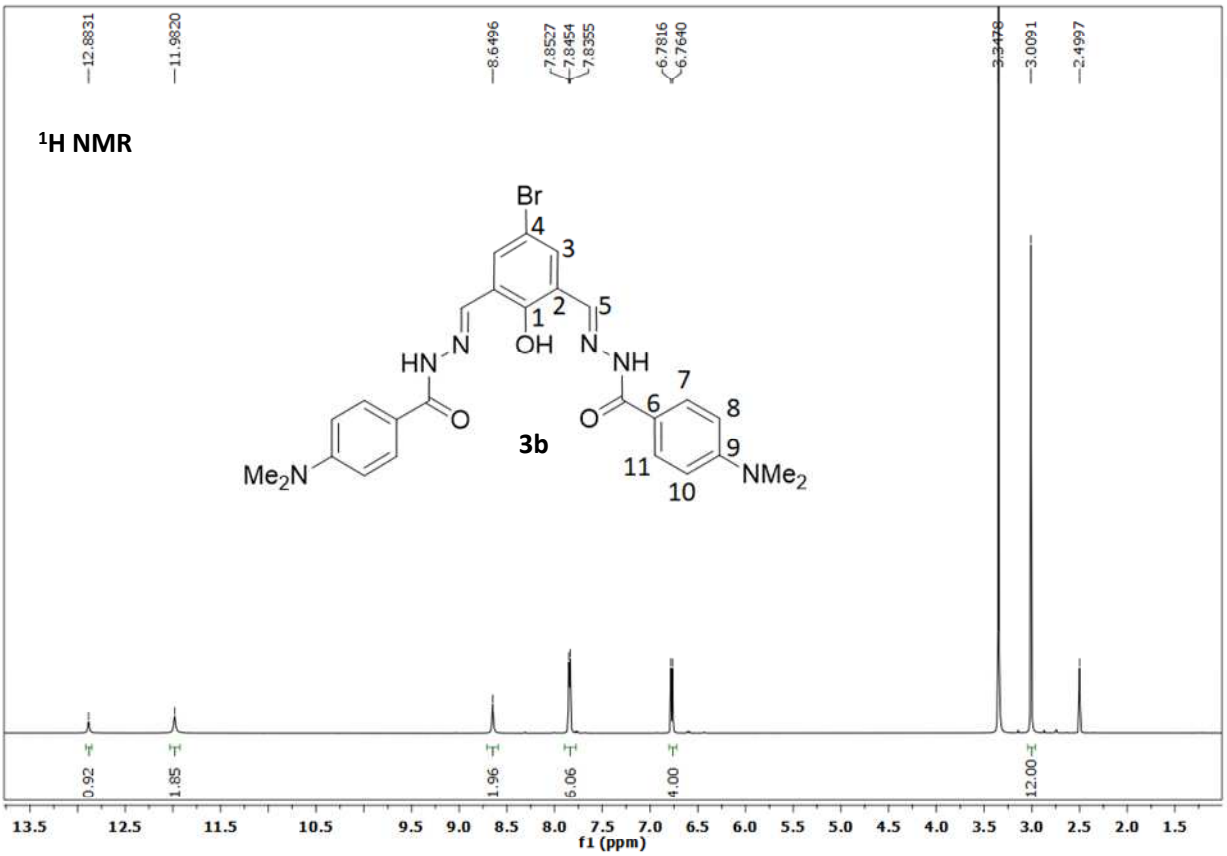
13C NMR
3a
f1 (ppm)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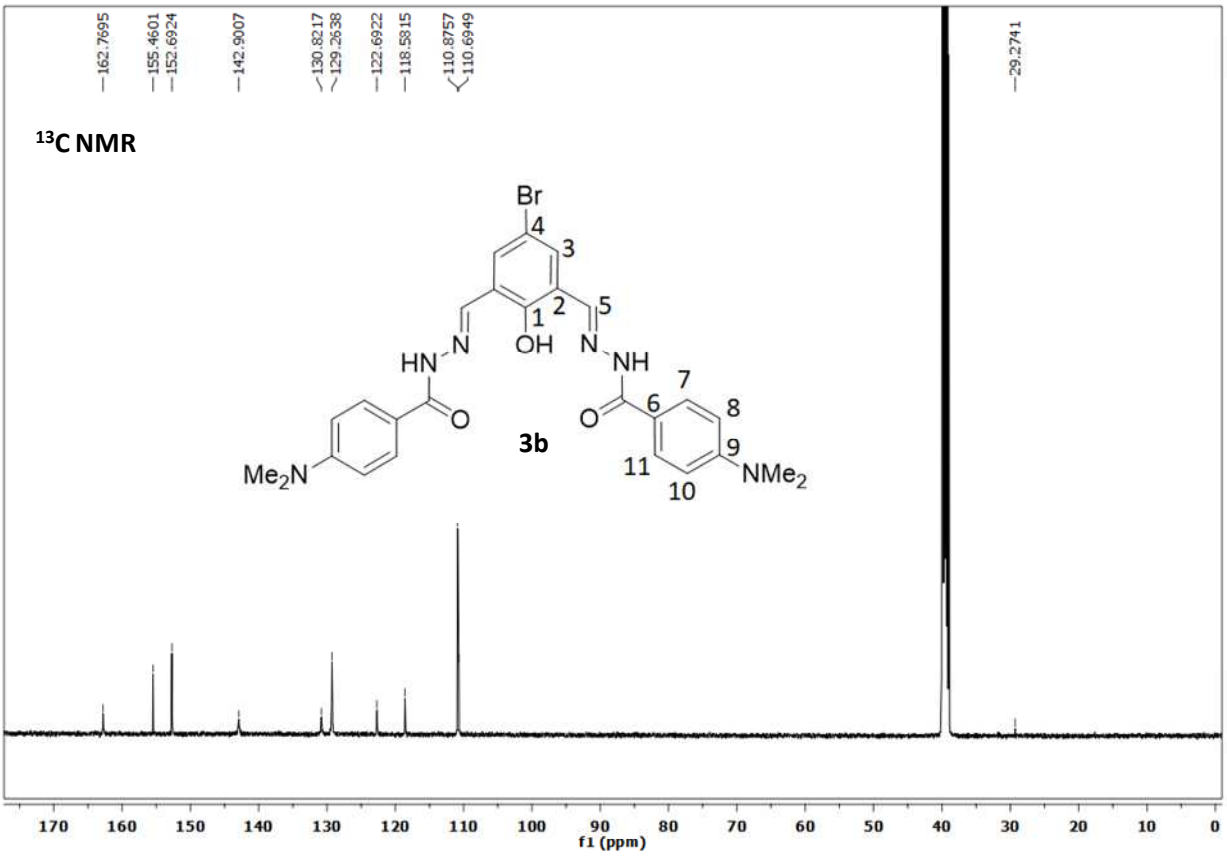
2.4997
1H NMR
Br
4
3
2
1
5
OH
N
HN
NH
O
6
7
8
9
11
10
Me2N
NMe2
3b
0.92
1.85
1.96
6.06
4.00
12.00
f1 (ppm)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29.2741
13C NMR
Br
4
3
2
1
5
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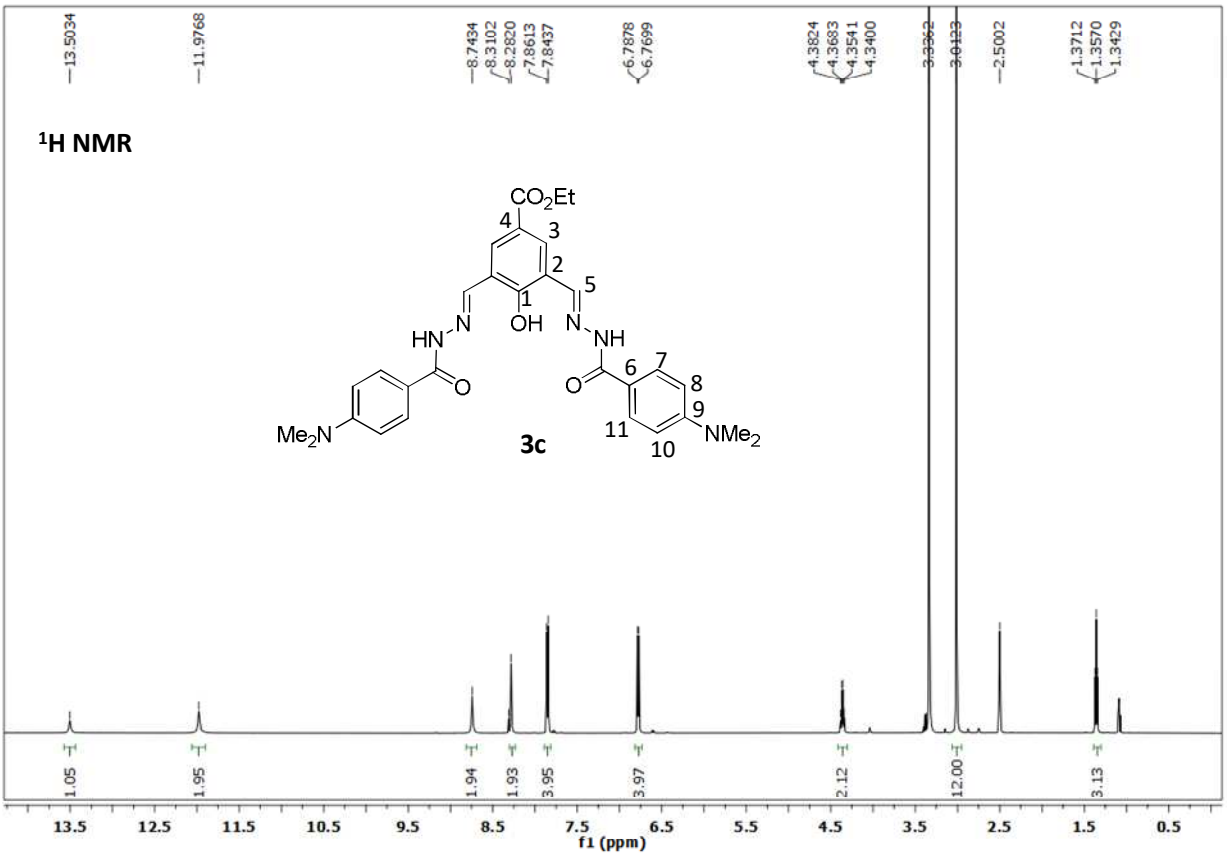
N
HN
NH
O
6
7
8
9
11
10
Me2N
NMe2
3b
f1 (ppm)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3.3362
3.0123
2.5002
1.3712
1.3570
1.3429
1H NMR
CO2Et
OH
HN
NH
Me2N
NMe2
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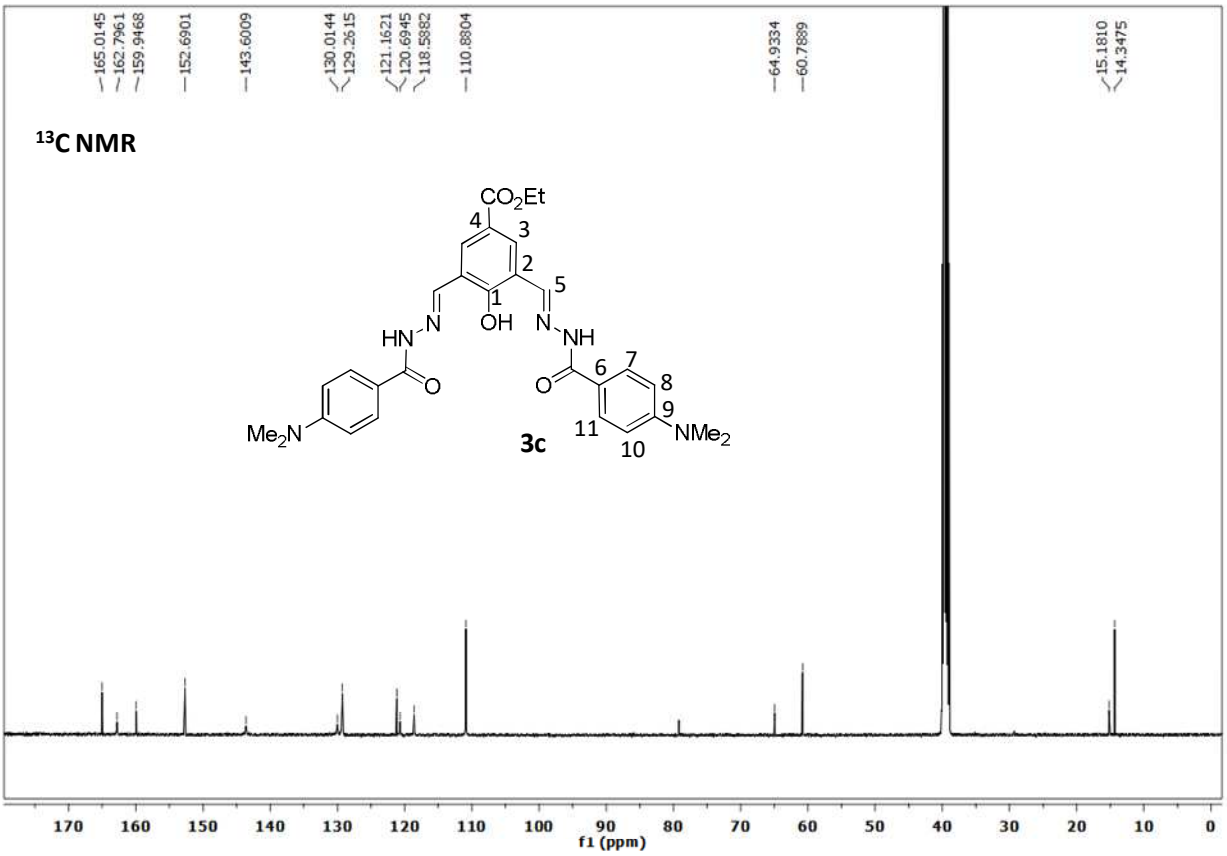
1.93
3.95
3.97
2.12
12.00
3.13
f1 (ppm)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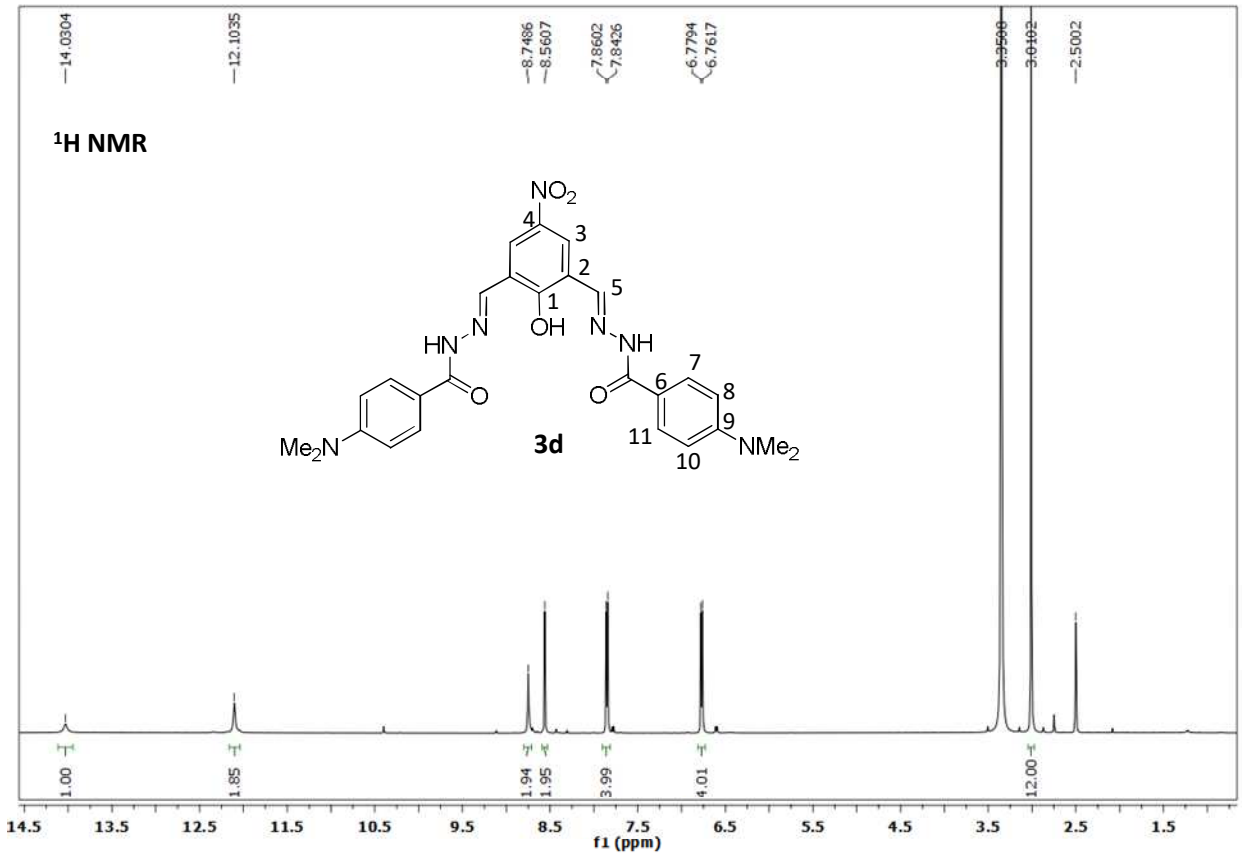
OH
HN
NH
Me2N
NMe2
3c
f1 (ppm)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2.5002
1H NMR
NO2
4
3
2
1
5
OH
HN
N
N
NH
O
O
6
7
8
9
11
10
Me2N
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1.85
1.94
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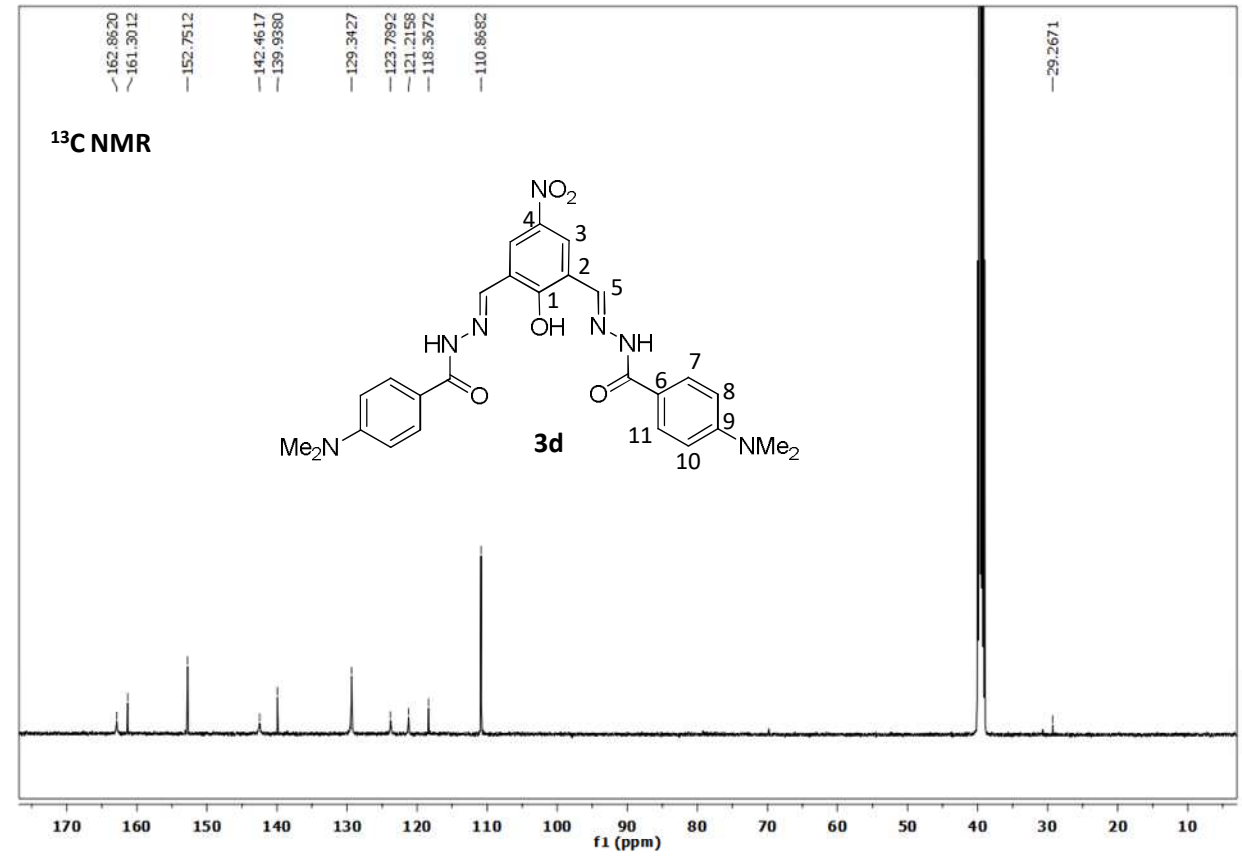
3.99
4.01
12.00
f1 (ppm)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13C NMR
NO2
4
3
2
1
5
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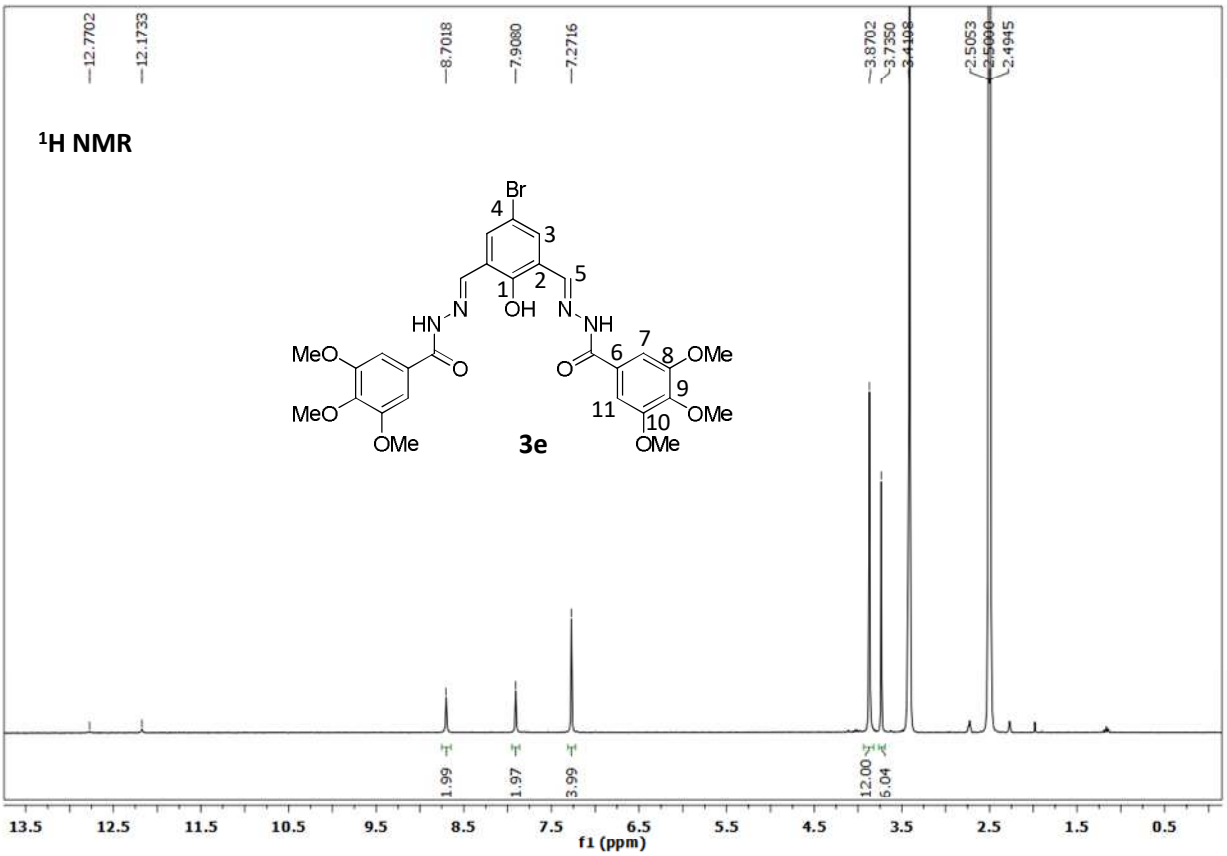
HN
N
N
NH
O
O
6
7
8
9
11
10
Me2N
NMe2
3d
f1 (ppm)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1H NMR
Br
4
3
2
1
5
OH
N
HN
NH
O
MeO
MeO
OMe
6
7
8
OMe
9
11
10
OMe
OMe
3e
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1.97
3.99
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13.5
12.5
11.5
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1.5
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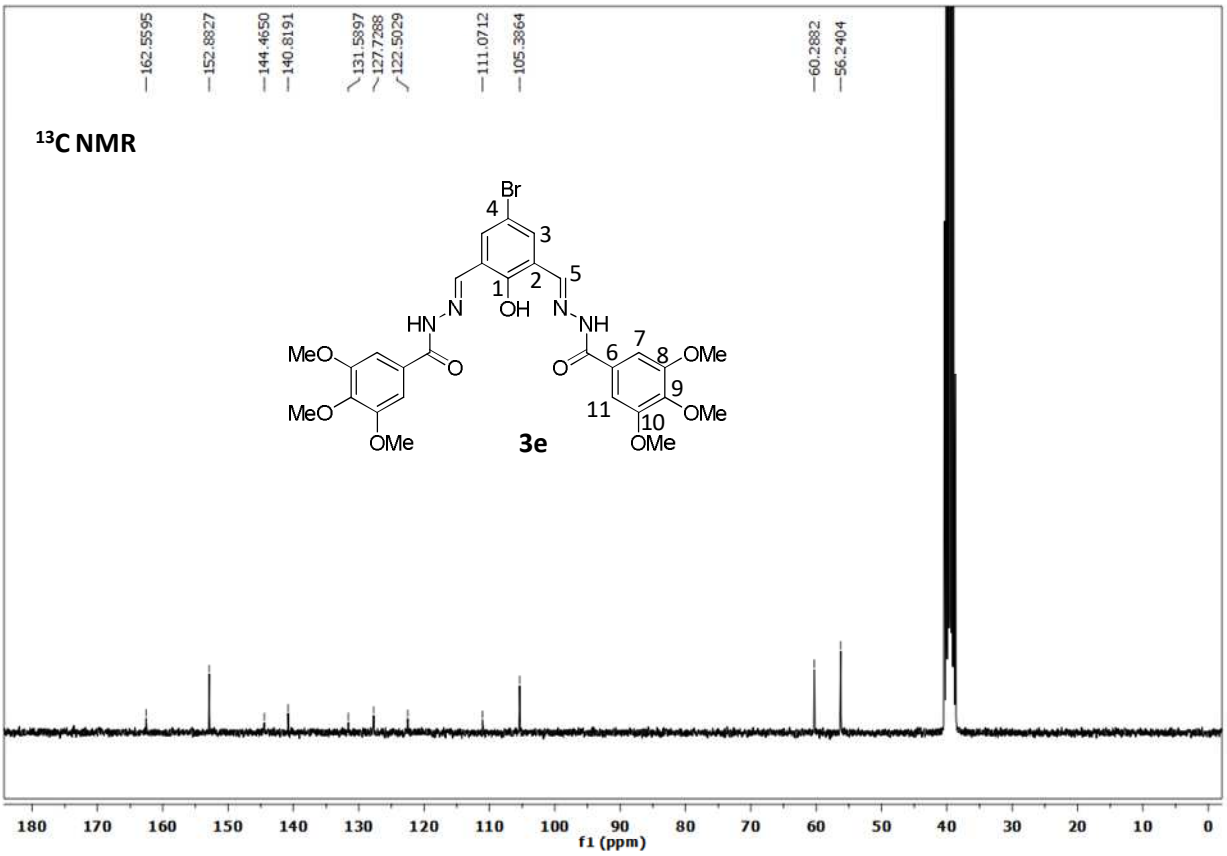
f1 (ppm)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13C NMR
Br
4
3
2
1
5
OH
N
HN
NH
O
MeO
MeO
OMe
6
7
8
OMe
9
11
10
OMe
OMe
3e
180
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160
150
140
130
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110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)