Supporting Information

1,8-Naphthyridinetetraones from One-pot Reactions of 2-Methylimidazoline and 2-Methyl-1,4,5,6-Tetrahydropyrimidine with 1,3-Diacid Chlorides.

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General Information

The FT-IR spectra were recorded as films on KBr plates. The ^{1}H and ^{13}C-NMR spectra were recorded using a 300 MHz spectrometer operating at 300 MHz for proton and 75 MHz for carbon, or using a 600 MHz spectrometer operating at 600 MHz for proton and 150 MHz for carbon. Chemical shifts were reported in ppm downfield from Me_4Si which was used as the internal standard for all NMR spectra ($CDCl_3$ and DMSO-d_6 were used as solvents). Splitting patterns are designed as "s, d, t, q and m"; these symbols indicate "singlet, doublet, triplet, quartet and multiplet," respectively. All reactions were carried out under nitrogen. Acetonitrile and triethylamine were distilled from calcium hydride under nitrogen. Dichloromethane was pre-dried with $CaCl_2$ and then distilled from calcium hydride under nitrogen. Tetrahydrofuran (THF) was distilled from Na metal/benzophenone. The starting substrates,

2-methylimidazoline (**1)** and 2-methyl-1,4,5,6-tetrahydropyrimidine **(2)**, were prepared according to literature procedures (*J. Org. Chem.* **1987**, *52*, 1017-1021). All other commercially obtained reagents were used as received. The silica gel used for the column chromatography was purchased from Aldrich Company (70-230 mesh, 60Å).

Experimental Data

General procedure for cyclization reactions (Table 1):

5,5,8,8-tetramethyl-1,2-dihydroimidazo[1,2,3-*ij*][1,8]naphthyridine-4,6,7,9(5*H*,8*H*)-tetraone (3a).

To a stirred solution of dimethylmalonyl chloride (0.42g, 2.5mmol) in 15mL of MeCN, triethylamine (0.8g, 8mmol) was added dropwise under nitrogen at room temperature. 2-Methylimidazoline (**1**) (0.084g, 1mmol) was dissolved in 10 mL of MeCN and then added dropwise into the above solution at room temperature. The reaction system was then refluxed for 3 hrs and the solvent was removed by rotary evaporation. Acetone (15mL) was added to the residue to give a solid/liquid mixture. The mixture was filtered and thoroughly washed with acetone (3×15mL). The filtrate was concentrated in *vacuo* and the residue was purified by flash column chromatography (silica gel, 1:3 hexane/ethyl acetate) to give **3a** (199mg, 72%). R_f = 0.37 (ethyl acetate); white solid; mp = 258-260 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.24 (s, 4H), 1.48 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.1, 173.6, 158.8, 92.9, 53.3, 42.2, 24.3 ; IR (KBr, cm^{-1}): 1715, 1679, 1602, 1510, 1466, 1383, 1351, 1272, 1210, 1063, 1042; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{14}H_{16}N_2NaO_4$, 299.1008; found, 299.0982.

5,5,8,8-tetraethyl-1,2-dihydroimidazo[1,2,3-*ij*][1,8]naphthyridine-4,6,7,9(5*H*,8*H*)-tetraone (3b).

The title compound **3b** was prepared using 2-methylimidazoline (**1**) (0.084g, 1mmol) and diethylmalonyl chloride (0.49g, 2.5mmol) by the general procedure (163mg, 49%). Flash column chromatography (silica gel, 2:1 to 1:1 hexane/ethyl acetate); R_f = 0.22 (1:1 hexane/ethyl acetate); white solid; mp = 260-262 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.29 (s, 4H), 2.01 (m, 8H), 0.79 (t, J = 7.3 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.5, 172.9, 159.6, 98.3, 63.9, 41.8, 32.6, 9.6; IR (KBr, cm^{-1}): 1708, 1698, 1603, 1559, 1498, 1477, 1455, 1382, 1370, 1324, 1245, 1177, 1094, 1036; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{18}H_{24}N_2NaO_4$, 355.1634; found, 355.1596.

5,5,8,8-tetrapropyl-1,2-dihydroimidazo[1,2,3-*ij*][1,8]naphthyridine-4,6,7,9(5*H*,8*H*)-tetraone (3c).

The title compound **3c** was prepared using 2-methylimidazoline (**1**) (0.084g, 1mmol) and dipropylmalonyl chloride (0.57g, 2.5mmol) by the general procedure (237mg, 61%). Flash column chromatography (silica gel, 4:1 to 3:1 hexane/ethyl acetate); R_f = 0.32 (2:1 hexane/ethyl acetate); white solid; mp = 105-107 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.23 (s, 4H), 2.05 (td, J = 12.6, 4.7 Hz, 4H), 1.85 (td, J = 12.6, 4.7 Hz, 4H), 1.13 (m, 8H), 0.82 (t, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.7, 173.1, 159.4, 97.8, 62.6, 42.2, 41.8, 18.5, 14.0; IR (KBr, cm^{-1}): 1711, 1678, 1603, 1499, 1456, 1377, 1349, 1235, 1182, 1075. HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{22}H_{32}N_2NaO_4$, 411.2260; found, 411.2224.

1',2'-dihydro-6'*H*,7'*H*-dispiro[cyclobutane-1,5'-imidazo[1,2,3-*ij*][1,8]naphthyridine-8',1''-cyclobutane]-4',6',7',9'-tetraone (3d)

The title compound **3d** was prepared using 2-methylimidazoline (**1**) (0.084g, 1mmol) and

cyclobutane-1,1-dicarbonyl dichloride (0.45g, 2.5mmol) by the general procedure (246mg, 82%). After refluxing for 3 hrs and removal of MeCN, dichloromethane (15mL) was added to the residue to give a solid/liquid mixture. The mixture was filtered and washed thoroughly with dichloromethane (5×15mL). The insoluble white solid was identified as **3d**. No flash column chromatography was needed; R_f = 0.31 (1:1 hexane/acetone); white solid; mp = 285-287 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 4.06 (s, 4H), 2.45 (m, 8H), 2.05 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 188.1, 172.2, 162.4, 93.4, 55.7, 43.0, 29.1, 15.5; IR (KBr, cm^{-1}): 1706, 1669, 1600, 1507, 1462, 1384, 1365, 1291, 1217, 1171, 1018; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{16}H_{16}N_2NaO_4$, 323.1008; found, 323.1005.

1',2'-dihydro-6'*H*,7'*H*-dispiro[cyclohexane-1,5'-imidazo[1,2,3-*ij*][1,8]naphthyridine-8',1''-cyclohexane]-4',6',7',9'-tetraone (3e)

The title compound **3e** was prepared using 2-methylimidazoline (**1**) (0.084g, 1mmol) and cyclohexane-1,1-dicarbonyl dichloride (0.52g, 2.5mmol) by the general procedure (225mg, 63%). Flash column chromatography (silica gel, 2:1 to 1:1 hexane/ethyl acetate); R_f = 0.27 (1:1 hexane/ethyl acetate); white solid; mp = 274-276 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.20 (s, 4H), 1.96 (m, 4H), 1.82 (m, 4H), 1.73 (m, 8H), 1.57 (m, 2H), 1.42 (tt, J = 6.7, 12.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 190.2, 172.9, 158.1, 92.9, 57.1, 42.1, 31.7, 24.6, 21.5; IR (KBr, cm^{-1}): 1716, 1683, 1612, 1500, 1455, 1363, 1223, 998; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{20}H_{24}N_2NaO_4$, 379.1634; found, 379.1586.

2,2,10,10-tetramethyl-6,7-dihydro-1*H*-pyrimido[1,2,3-*ij*][1,8]naphthyridine-1,3,9,11(2*H*,5*H*,10*H*)-tetraone (8a)

The title compound **8a** was prepared using 2-methyl-1,4,5,6-tetrahydropyrimidine (**7**) (0.098g, 1mmol) and dimethylmalonyl chloride (0.42g, 2.5mmol) by the general procedure (212mg, 73%). Flash column chromatography (silica gel, 1:2 hexane/ethyl acetate to pure ethyl acetate); R_f = 0.40 (ethyl acetate); white solid; mp = 235-237 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.01 (t, J = 6.0 Hz, 4H), 2.21 (quintet, J = 6.0 Hz, 2H), 1.46 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.1, 175.6, 157.4, 95.8, 52.9, 41.6, 23.9,19.6; IR (KBr, cm^{-1}): 1714, 1674, 1604, 1530, 1492, 1443, 1386, 1349, 1223, 1141, 1078. HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{15}H_{18}N_2NaO_4$, 313.1164; found, 313.1152.

2,2,10,10-tetraethyl-6,7-dihydro-1*H*-pyrimido[1,2,3-*ij*][1,8]naphthyridine-1,3,9,11(2*H*,5*H*,10*H*)-tetraone (8b)

The title compound **8b** was prepared using 2-methyl-1,4,5,6-tetrahydropyrimidine (**7**) (0.098g, 1mmol) and diethylmalonyl chloride (0.49g, 2.5mmol) by the general procedure (180mg, 52%). Flash column chromatography (silica gel, 3:1 to 1:1 hexane/ethyl acetate); R_f = 0.25 (1:1 hexane/ethyl acetate); white solid; mp = 155-157 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.05 (t, J = 5.6 Hz, 4H), 2.19 (br m, 2H), 1.99 (m, 8H), 0.80 (t, J = 7.3 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.2, 175.0, 158.3, 100.6, 62.6, 41.5, 32.3,19.8, 9.4; IR (KBr, cm^{-1}): 1706, 1673, 1614, 1531, 1491, 1455, 1243, 1142, 1095. HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{19}H_{26}N_2NaO_4$, 369.1790; found, 369.1766.

2,2,10,10-tetrapropyl-6,7-dihydro-1*H*-pyrimido[1,2,3-*ij*][1,8]naphthyridine-1,3,9,11(2*H*,5*H*,10*H*)-tetraone (8c)

The title compound **8c** was prepared using 2-methyl-1,4,5,6-tetrahydropyrimidine (**7**) (0.098g, 1mmol)

and dipropylmalonyl chloride (0.57g, 2.5mmol) by the general procedure (262mg, 65%). Flash column chromatography (silica gel, 4:1 to 3:1 hexane/ethyl acetate); R_f = 0.34 (2:1 hexane/ethyl acetate); colorless liquid; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.03 (t, J = 5.6 Hz, 4H), 2.19 (br m, 2H), 2.03 (dt, J = 4.4, 12.6 Hz, 4H), 1.81 (dt, J = 4.4, 12.6 Hz, 4H), 1.22 (m, 4H), 1.08 (m, 4H), 0.82 (t, J = 7.2 Hz, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 189.5, 175.3, 158.3, 100.3, 61.4, 42.0, 41,6, 19.8, 18.3, 14.1; IR (KBr, cm^{-1}): 1708, 1699, 1538, 1488, 1436, 1381, 1199, 1137; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{23}H_{34}N_2NaO_4$, 425.2416; found, 425.2393.

6',7'-dihydro-1'*H*,5'*H*,11'*H*-dispiro[cyclobutane-1,2'-pyrimido[1,2,3-*ij*][1,8]naphthyridine-10',1''-cyclobutane]-1',3',9',11'-tetraone (8d)

The title compound **8d** was prepared using 2-methyl-1,4,5,6-tetrahydropyrimidine (**7**) (0.098g, 1mmol) and cyclobutane-1,1-dicarbonyl dichloride (0.45g, 2.5mmol) by the general procedure (132mg, 42%). Flash column chromatography (silica gel, 1:1 hexane/ethyl acetate to pure ethyl acetate); R_f = 0.25 (ethyl acetate); white solid; mp = 252-254 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.02 (t, J = 6.1 Hz, 4H), 2.65 (m, 4H), 2.49 (m, 4H), 2.19 (td, J = 6.1, 12.2 Hz, 2H), 2.11 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 187.6, 173.7, 157.9, 95.9, 55.8, 41.6, 28.9, 19.7, 15.0; IR (KBr, cm^{-1}): 1703, 1661, 1606, 1524, 1493, 1443, 1385, 1362, 1327, 1247, 1196, 1181, 1168, 1075, 1028; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{17}H_{18}N_2NaO_4$, 337.1164; found, 337.1139.

6',7'-dihydro-1'*H*,5'*H*,11'*H*-dispiro[cyclohexane-1,2'-pyrimido[1,2,3-*ij*][1,8]naphthyridine-10',1''-cyclohexane]-1',3',9',11'-tetraone (8e)

The title compound **8e** was prepared using 2-methyl-1,4,5,6-tetrahydropyrimidine (**7**) (0.098g, 1mmol) and cyclohexane-1,1-dicarbonyl dichloride (0.52g, 2.5mmol) by the general procedure (241mg, 65%). Flash column chromatography (silica gel, 2:1 to 1:1 hexane/ethyl acetate); R_f = 0.29 (1:1 hexane/ethyl acetate); white solid; mp = 240-242 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.94 (t, J = 6.0 Hz, 4H), 2.16 (td, J = 6.0, 12.2 Hz, 2H), 1.99 (ddd, J = 4.2, 7.6, 13.2 Hz, 4H), 1.86 (ddd, J = 4.2, 7.6, 13.2 Hz, 4H), 1.73 (m, 4H), 1.67 (m, 4H), 1.45 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 190.7, 174.9, 156.1, 96.3, 57.1, 41.1, 32.0, 24.9, 21.7, 19.8; IR (KBr, cm^{-1}): 1707, 1683, 1544, 1486, 1469, 1432, 13689, 1355, 1287, 1172, 1134, 1068; HRMS (ESI-TOF, $[M+Na]^+$): calcd for $C_{21}H_{26}N_2NaO_4$, 393.1790; found, 393.1766.

Thermal Ellipsoid Drawings of 3c's THF Solvate

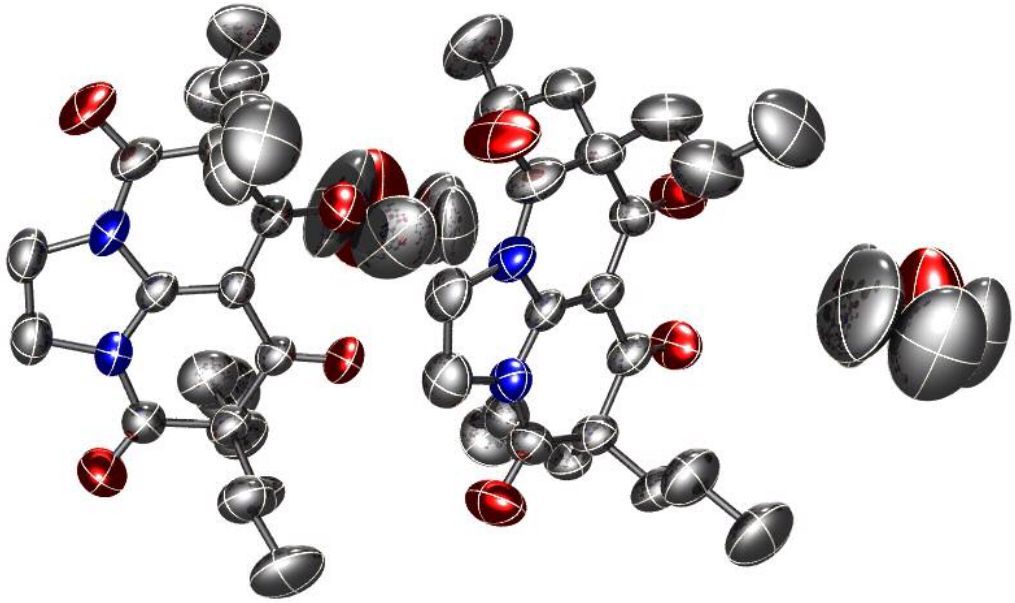


Figure 1. Thermal ellipsoid drawing of **3c**'s THF solvate which contains two crystallographically independent molecules of **3c** and two independent molecules of THFs. The thermal ellipsoids are drawn with 50% probability (gray: C; red: O; blue: N). Hydrogen atoms are omitted for clarity.

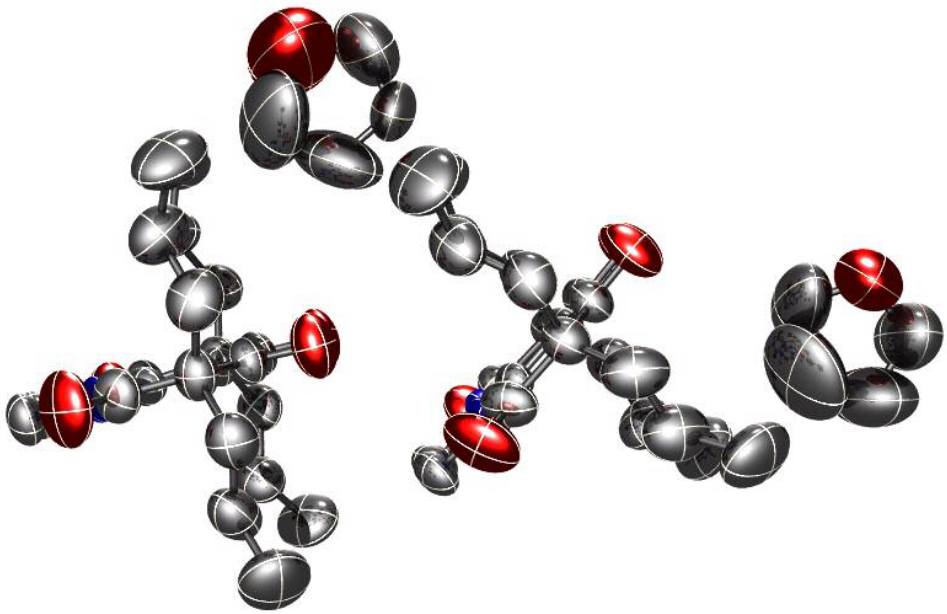
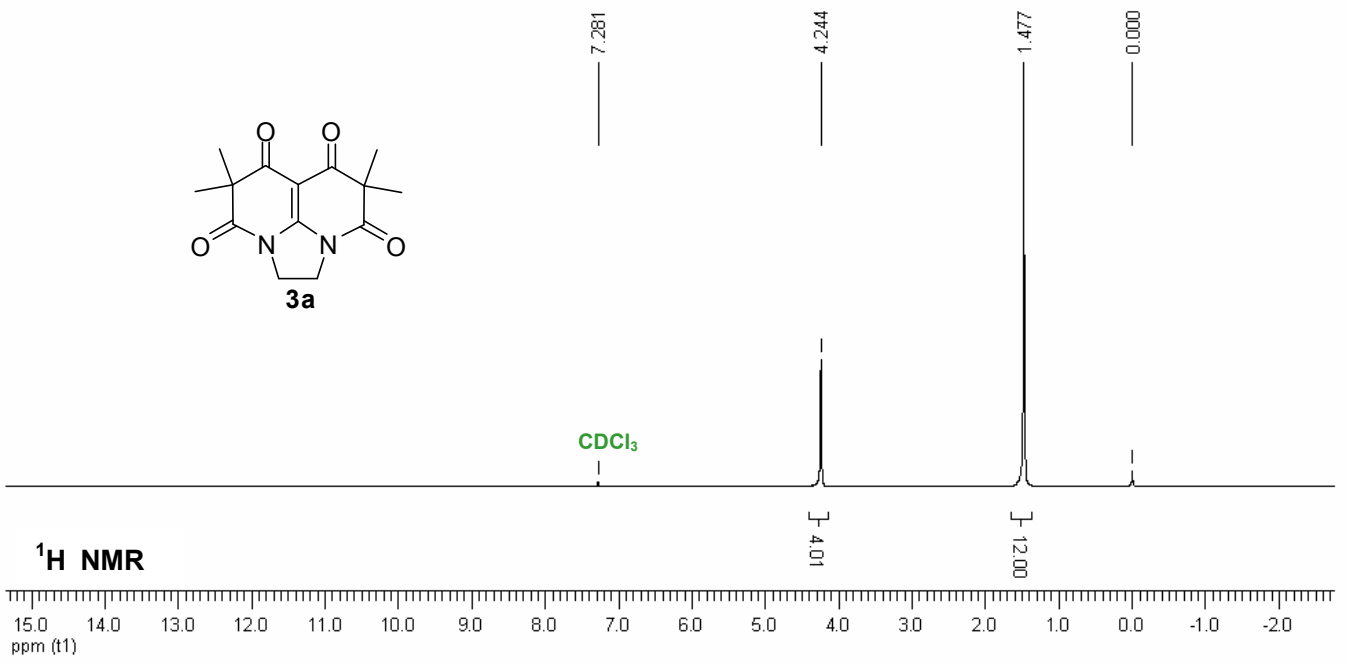
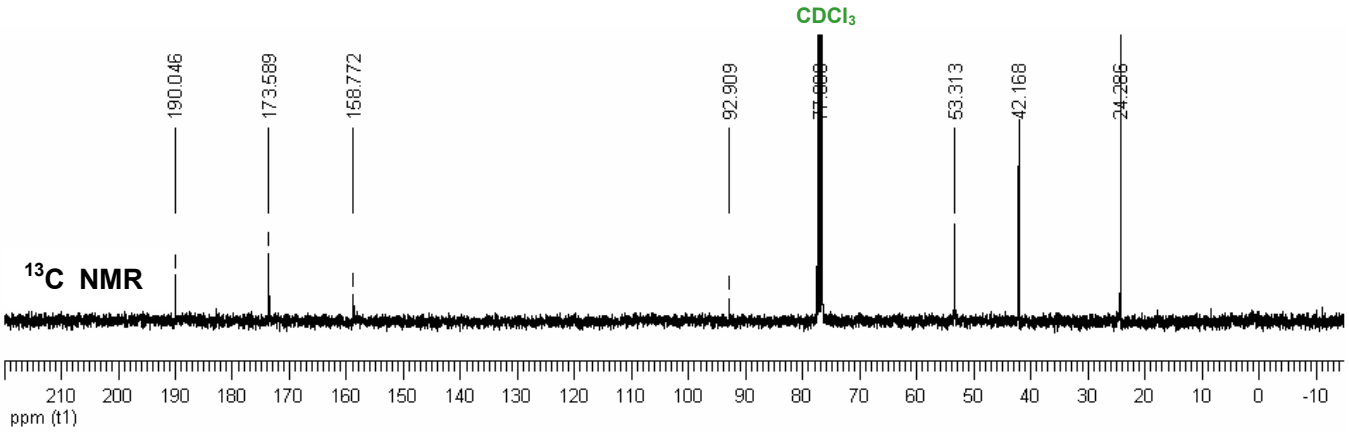
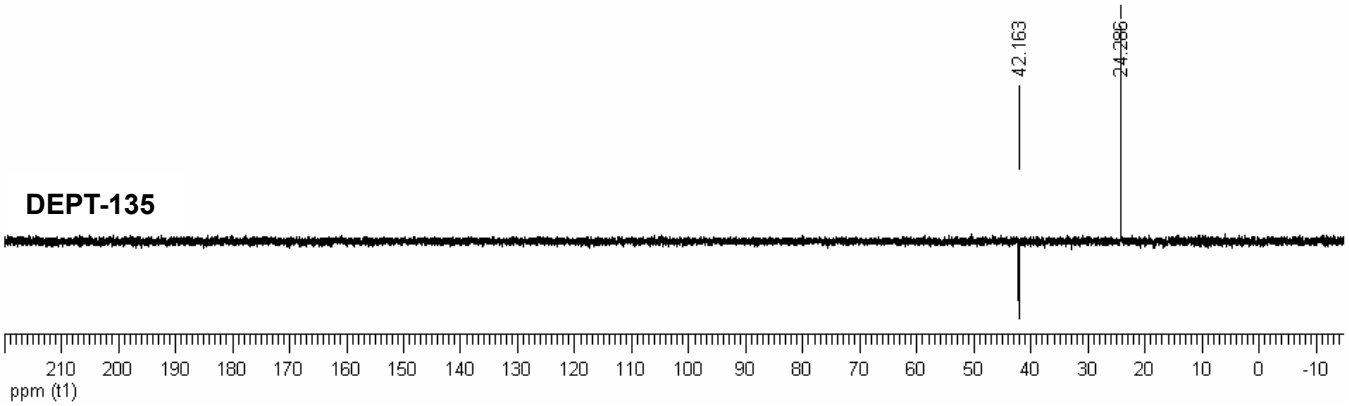


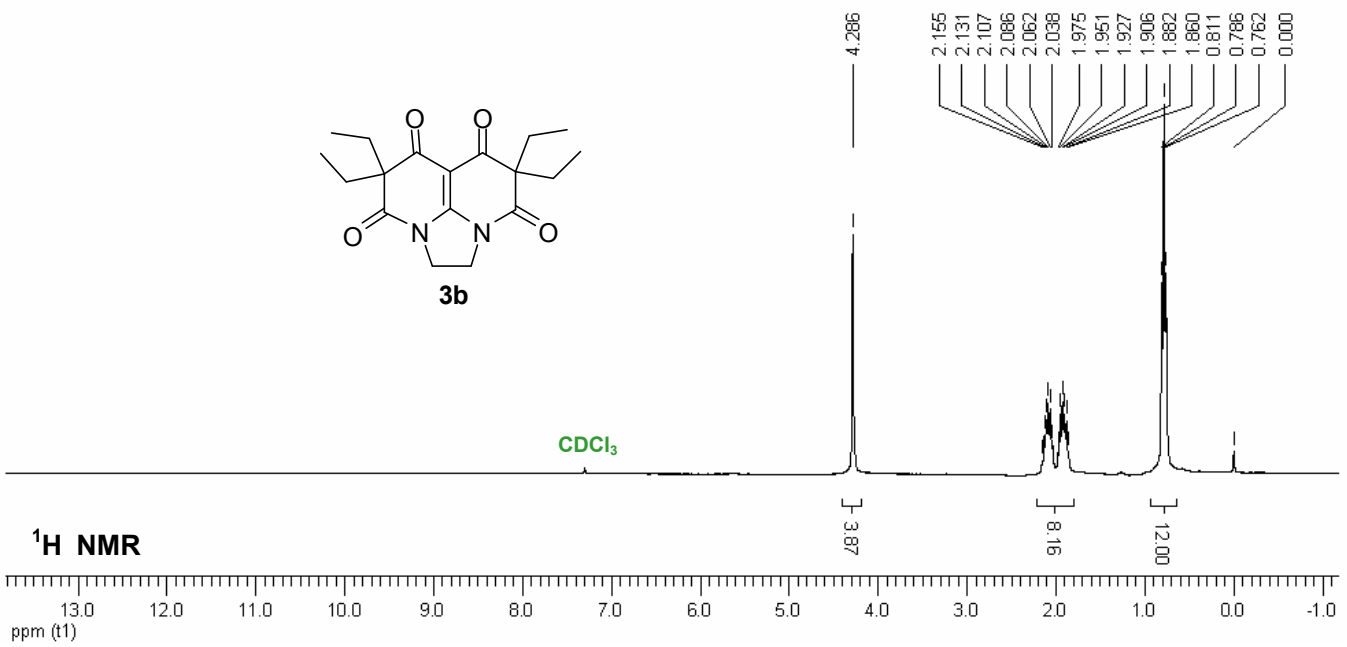
Figure 2. Thermal ellipsoid drawing of **3c**'s THF solvate from another perspective view. The interactions between propyl groups and THFs are suggested.

^{1}H and ^{13}CNMR Spectra





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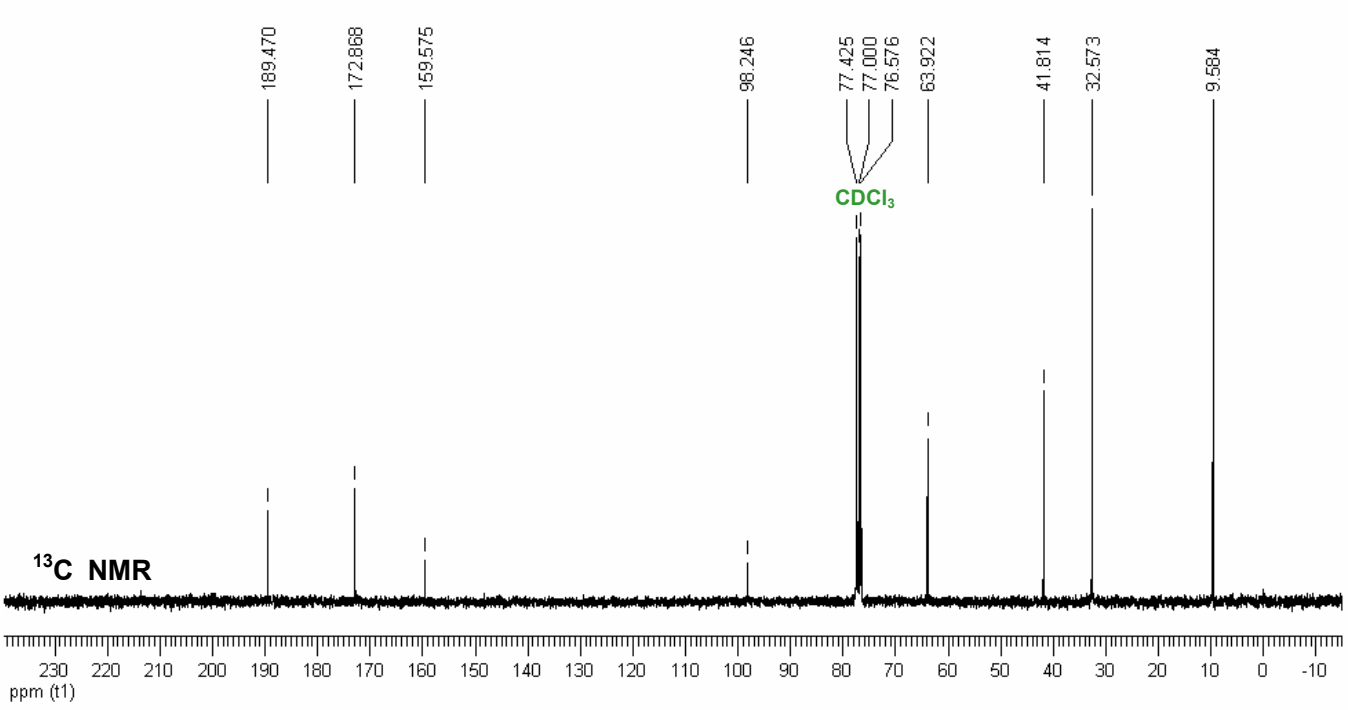
2.155
2.131
2.107
2.086
2.062
2.038
1.975
1.951
1.927
1.906
1.882
1.860
0.811
0.786
0.762
0.000
CDCl3
3.87
8.16
12.00
1H NMR
13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0
ppm (t1)

3b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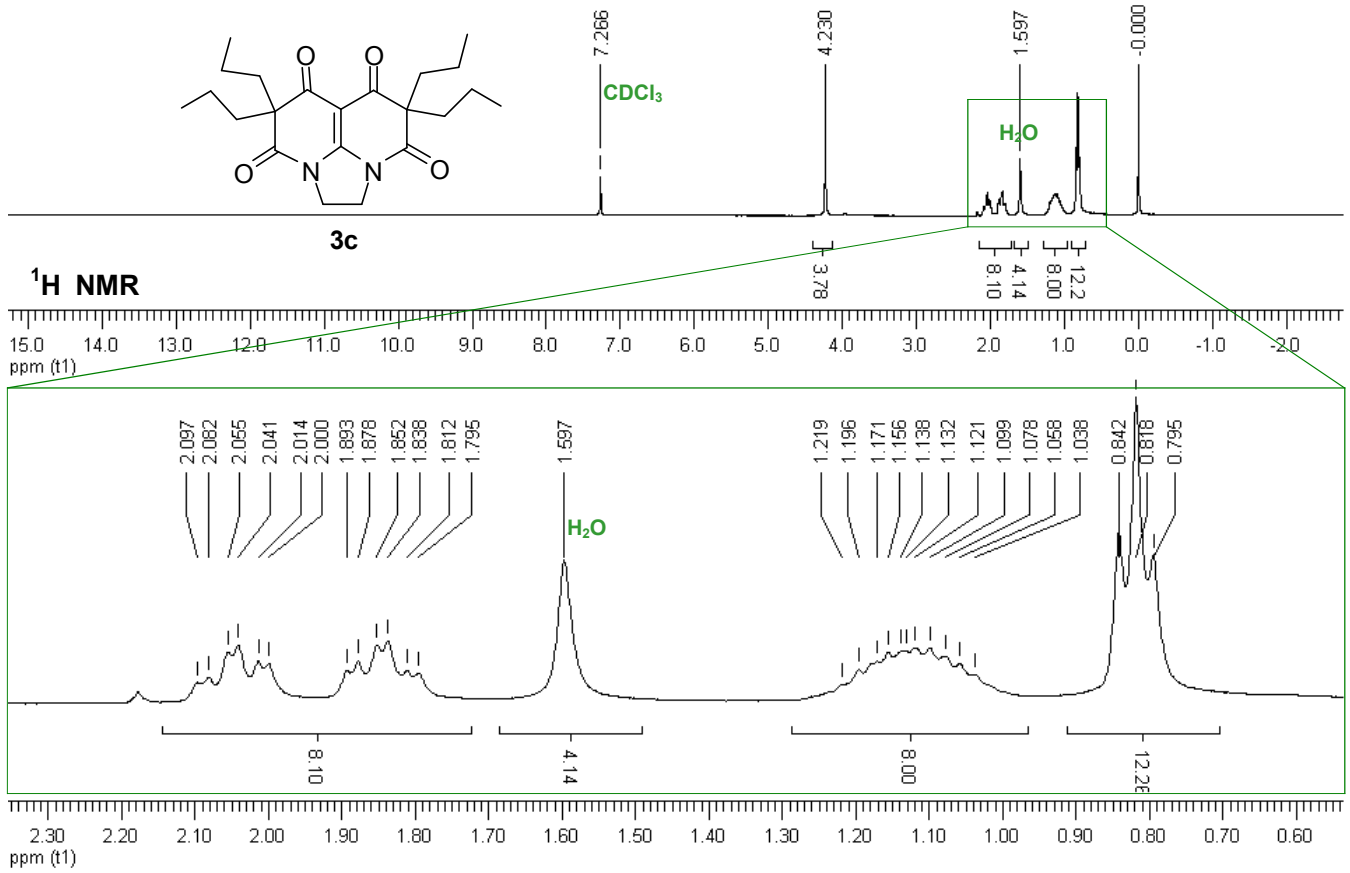
172.868
159.575
98.246
77.425
77.000
76.576
63.922
41.814
32.573
9.584
CDCl3
13C NMR
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)


3c
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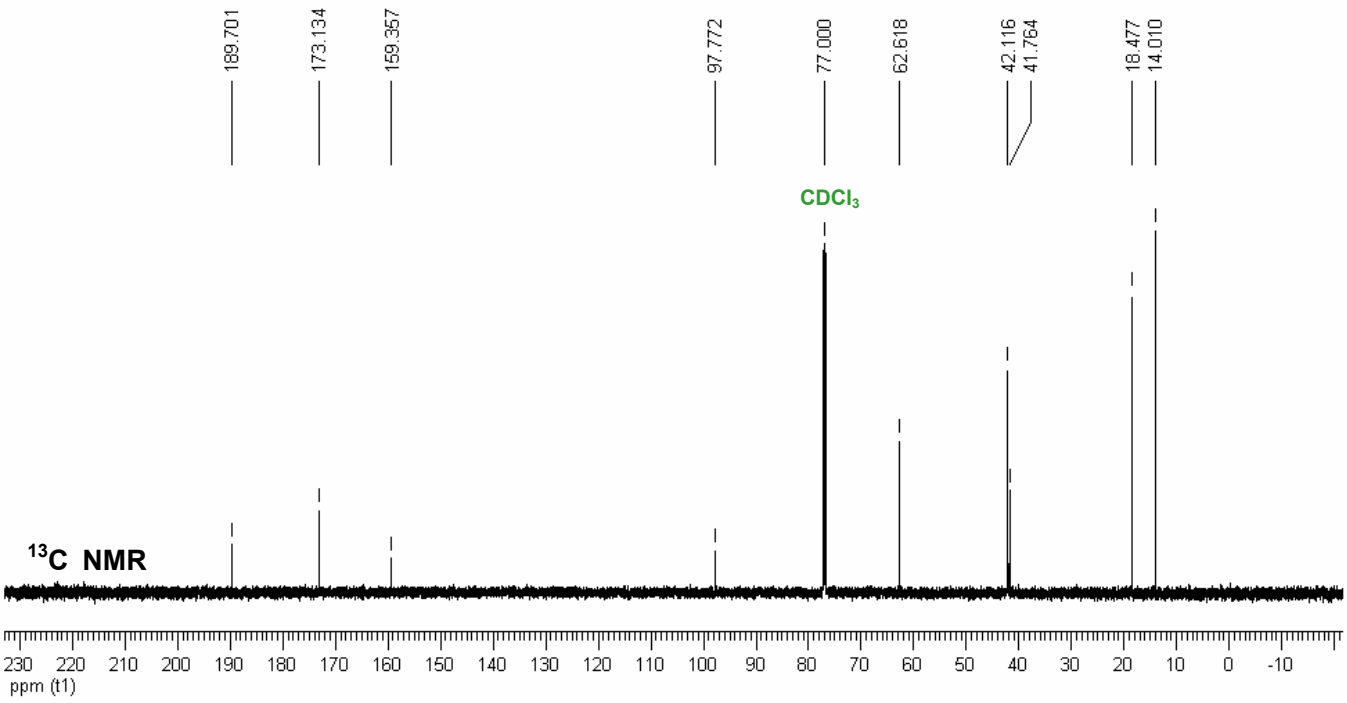
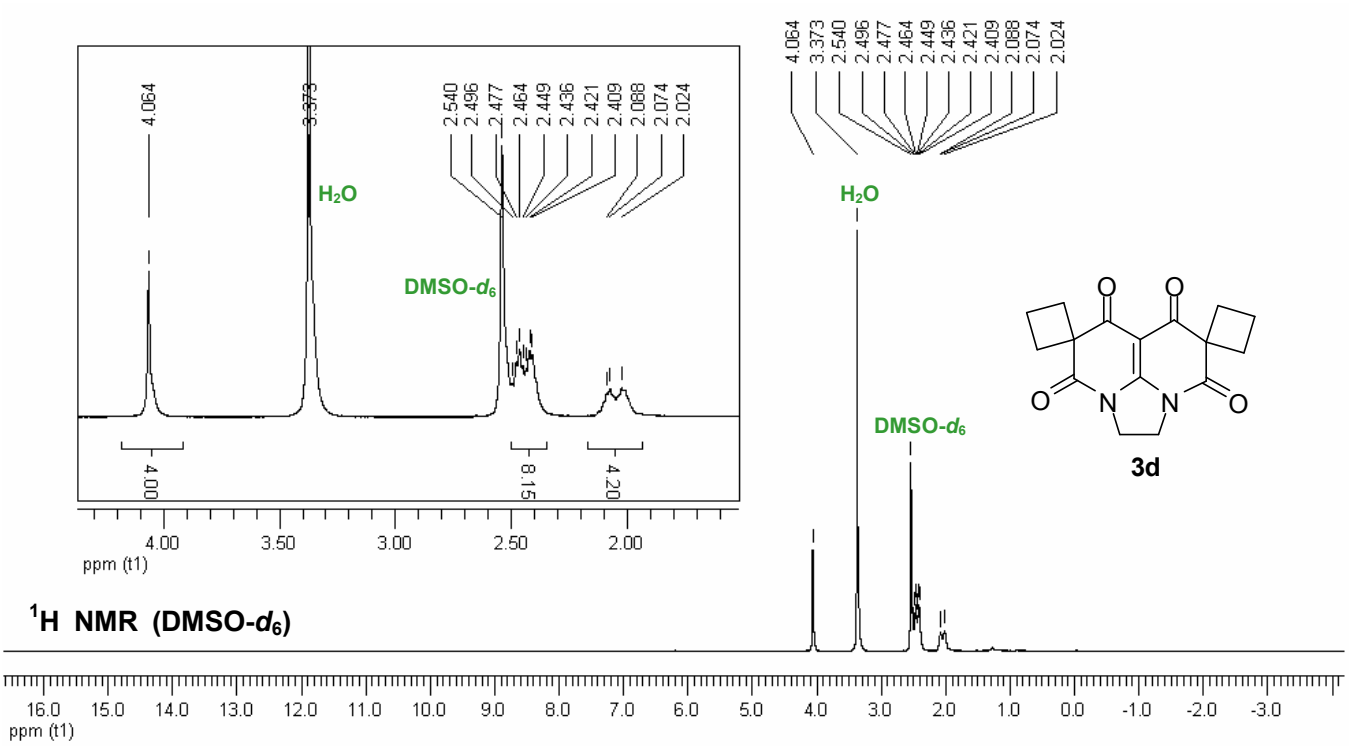
7.266
CDCl$_3$
4.230
1.597
H$_2$O
-0.000
3.78
8.10
4.14
8.00
12.2
15.0 14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2.0
ppm (t1)
2.097 2.082 2.055 2.041 2.014 2.000 1.893 1.878 1.852 1.838 1.812 1.795
1.597
H$_2$O
1.219 1.196 1.171 1.156 1.138 1.132 1.121 1.099 1.078 1.058 1.038
0.842 0.818 0.795
8.10
4.14
8.00
12.26
2.30 2.20 2.10 2.00 1.90 1.80 1.70 1.60 1.50 1.40 1.30 1.20 1.10 1.00 0.90 0.80 0.70 0.60
ppm (t1)


189.701
173.134
159.357
97.772
77.000
62.618
42.116
41.764
18.477
14.010
CDCl$_3$
^{13}C NMR
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)


4.064
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2.540
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2.477
2.464
2.449
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2.409
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2.074
2.024
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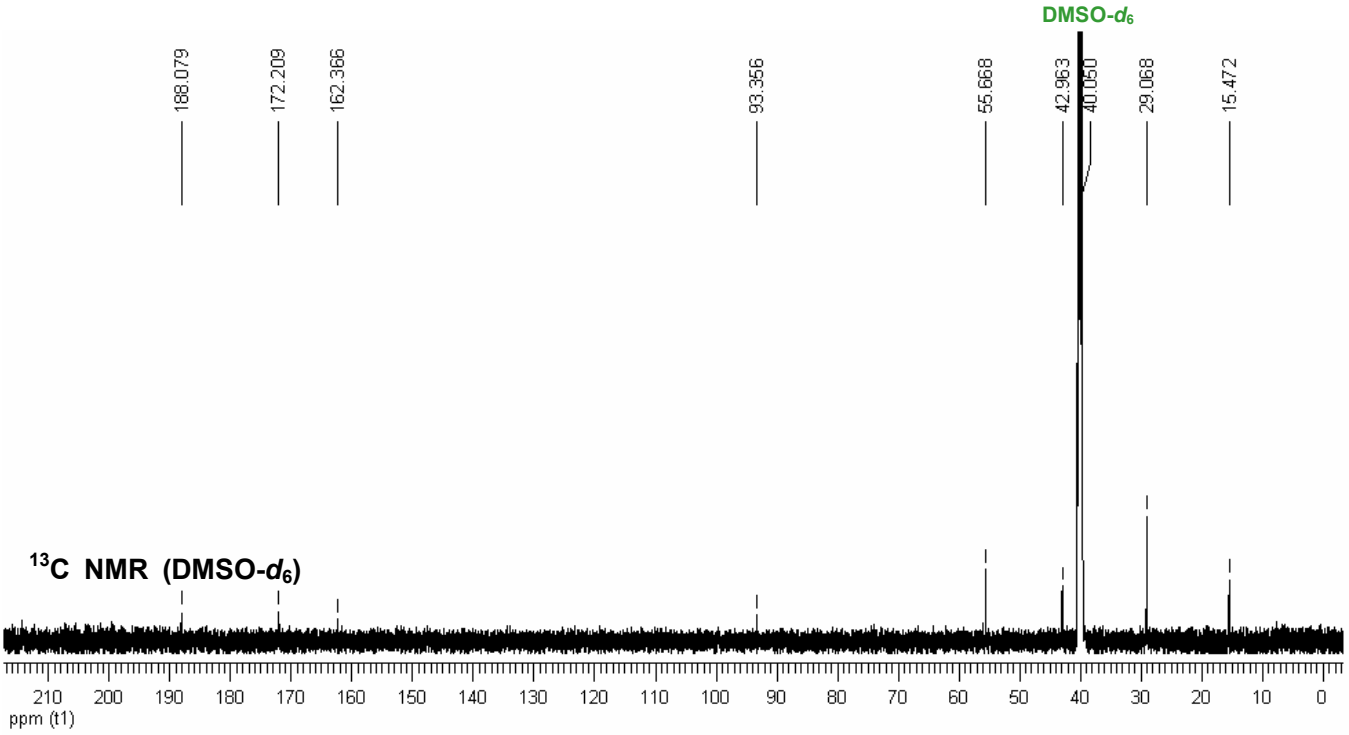
4.00
8.15
4.20
ppm (t1)
3d
1H NMR (DMSO-d6)
ppm (t1)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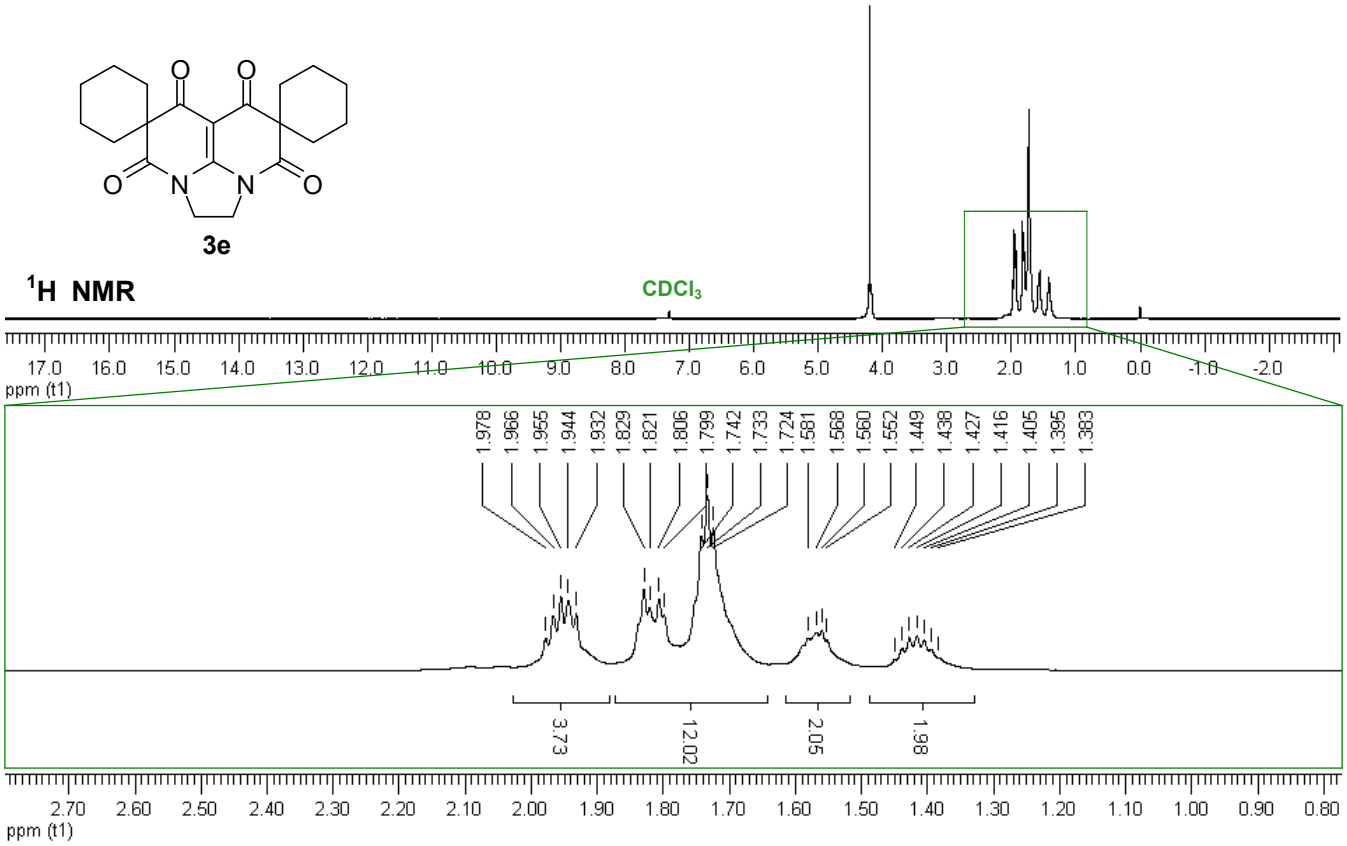
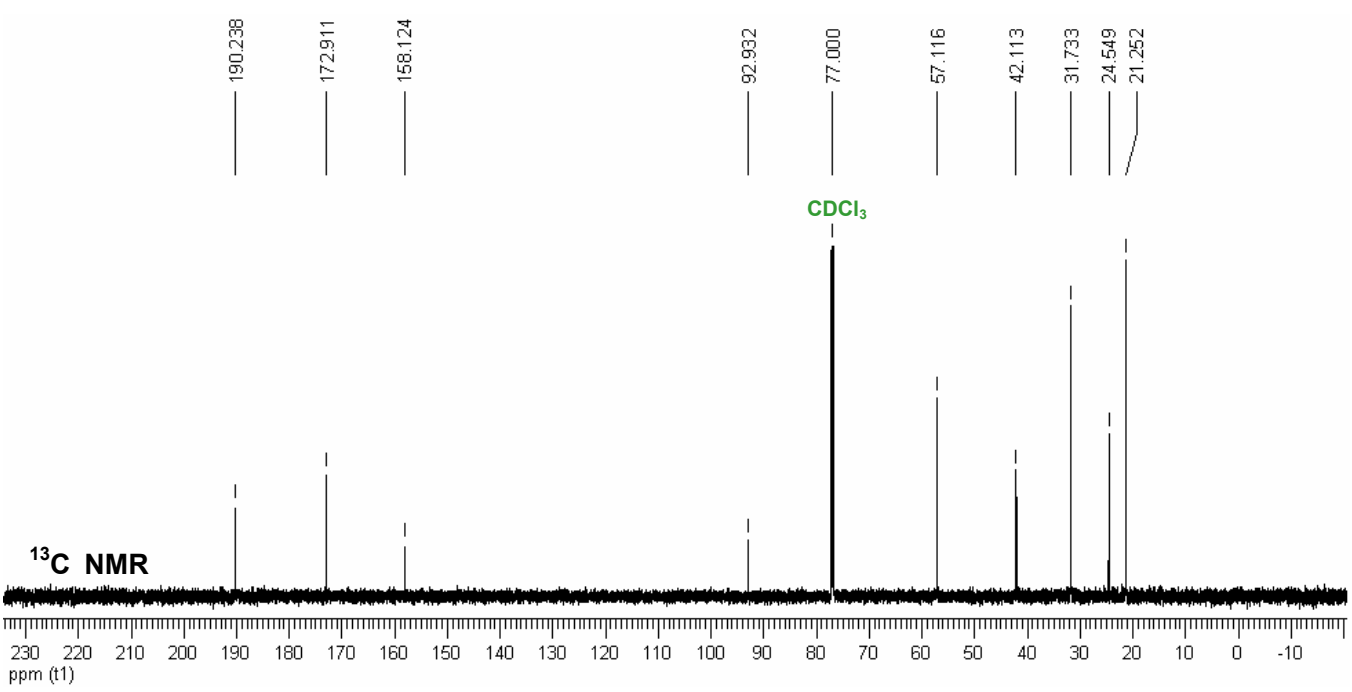
93.356
55.668
42.963
40.050
29.068
15.472
13C NMR (DMSO-d6)
ppm (t1)


3e
^{1}H NMR
CDCl$_3$
17.0 16.0 15.0 14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2.0
ppm (t1)
1.978 1.966 1.955 1.944 1.932 1.829 1.821 1.806 1.799 1.742 1.733 1.724 1.581 1.568 1.560 1.552 1.449 1.438 1.427 1.416 1.405 1.395 1.383
3.73 12.02 2.05 1.98
2.70 2.60 2.50 2.40 2.30 2.20 2.10 2.00 1.90 1.80 1.70 1.60 1.50 1.40 1.30 1.20 1.10 1.00 0.90 0.80
ppm (t1)


190.238 172.911 158.124 92.932 77.000 57.116 42.113 31.733 24.549 21.252
CDCl$_3$
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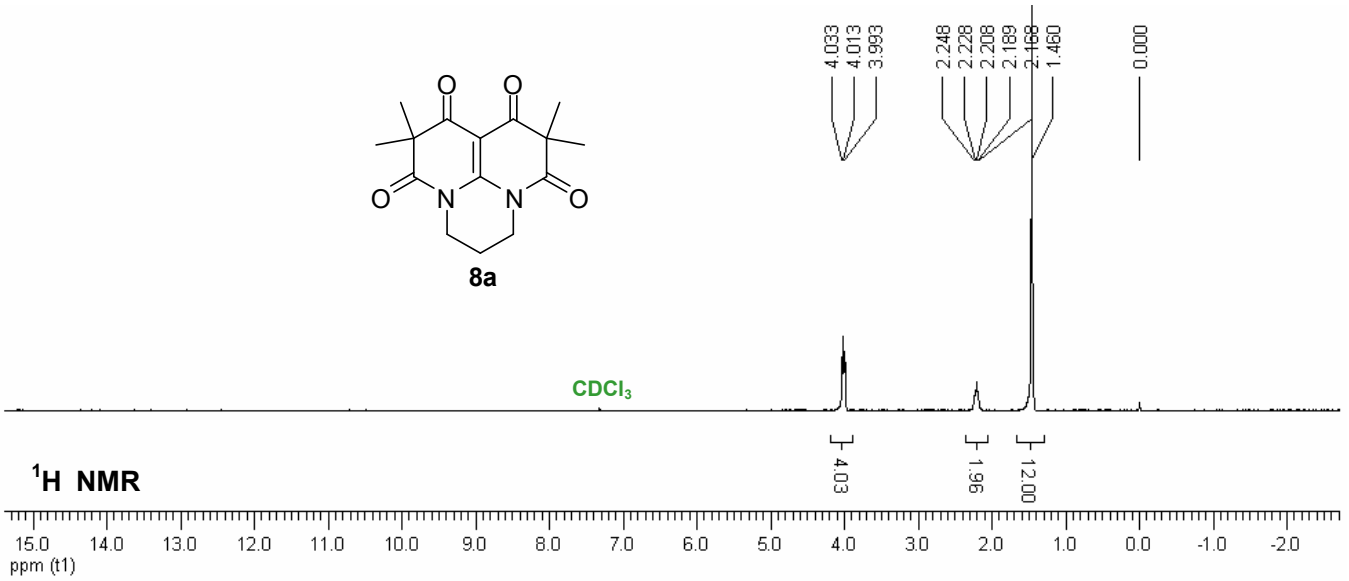
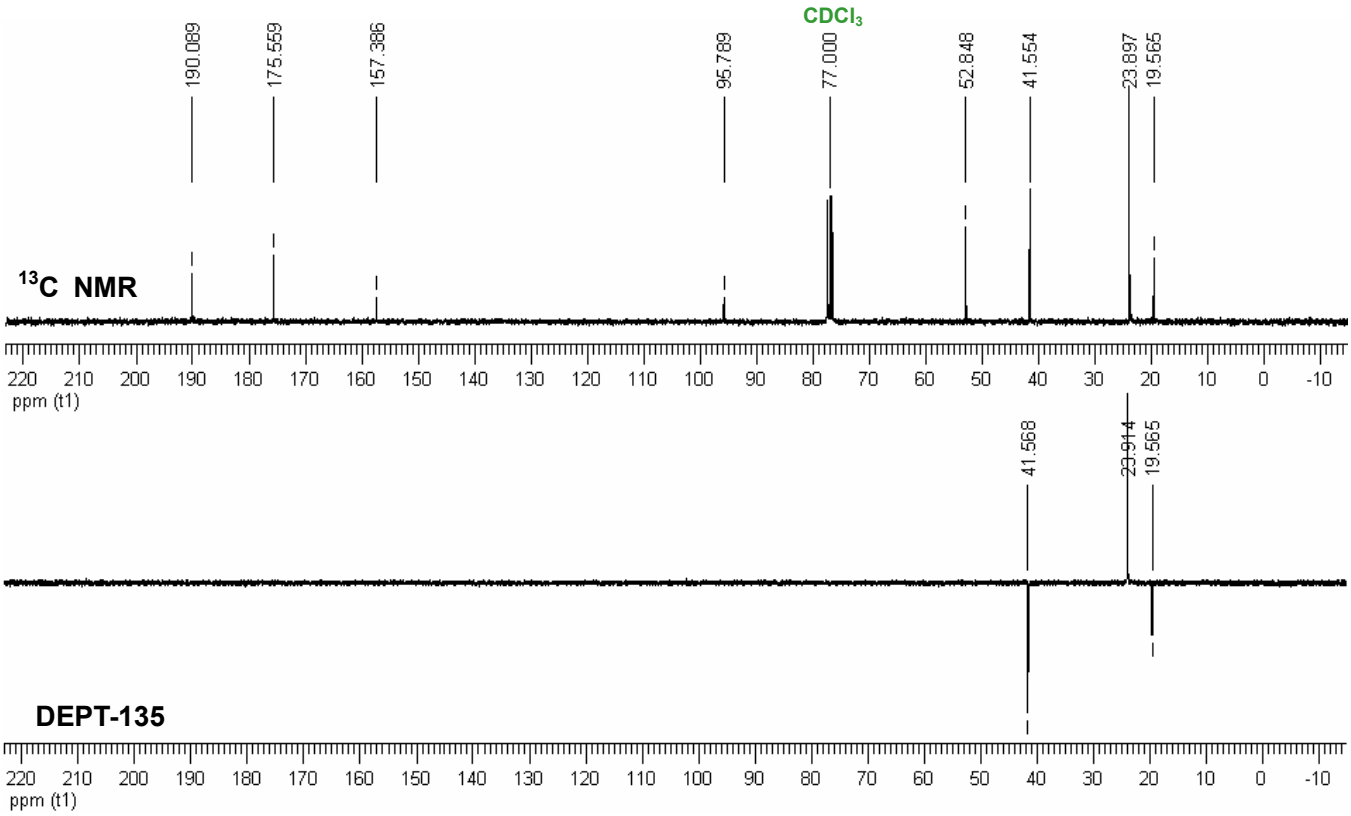
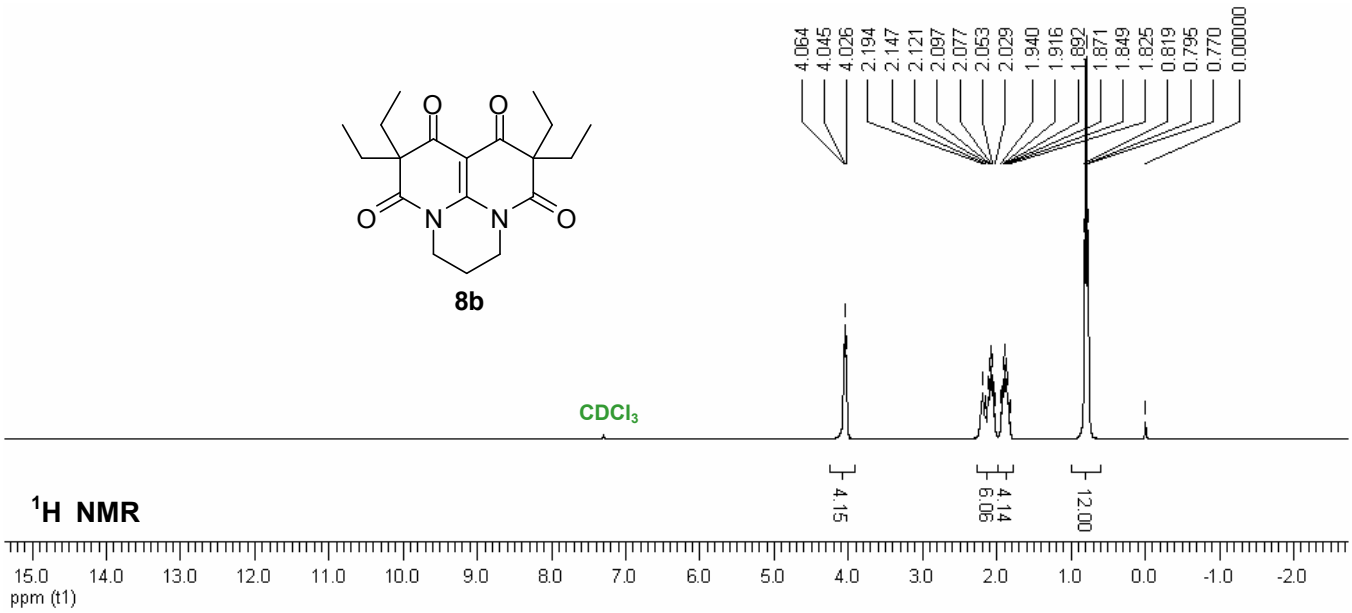
ppm (t1)

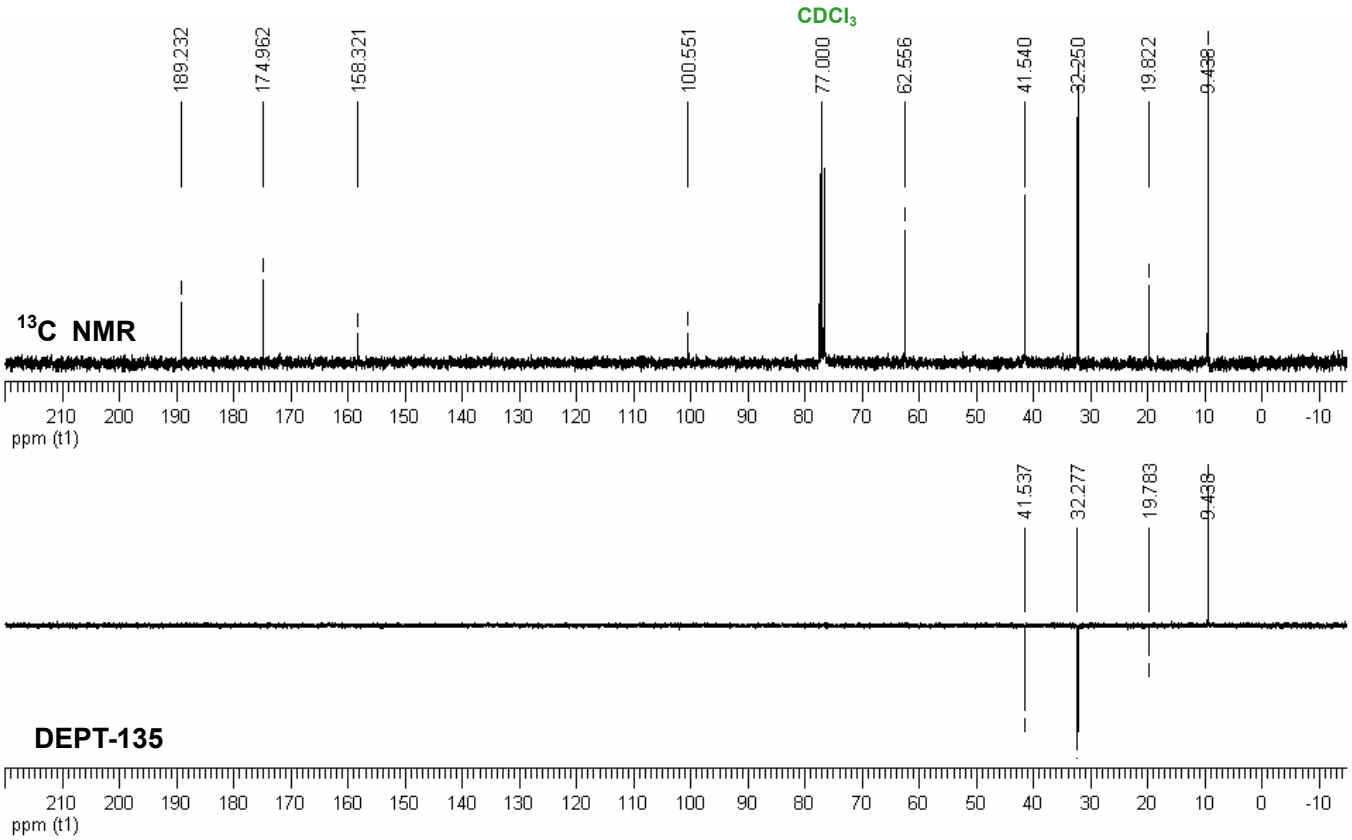

4.033
4.013
3.993
2.248
2.228
2.208
2.189
2.168
1.460
0.000
CDCl3
4.03
1.96
12.00
1H NMR
15.0 14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2.0
ppm (t1)

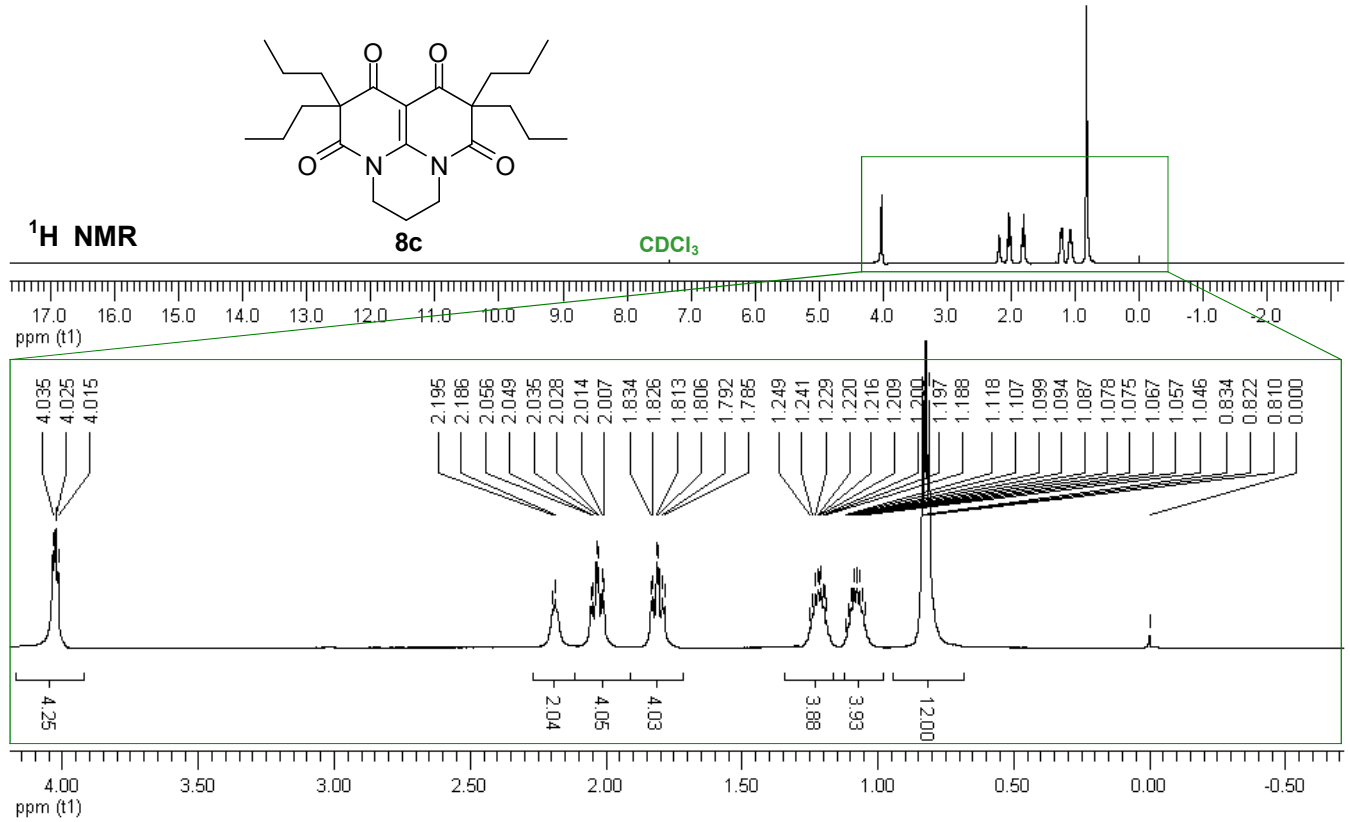
8a

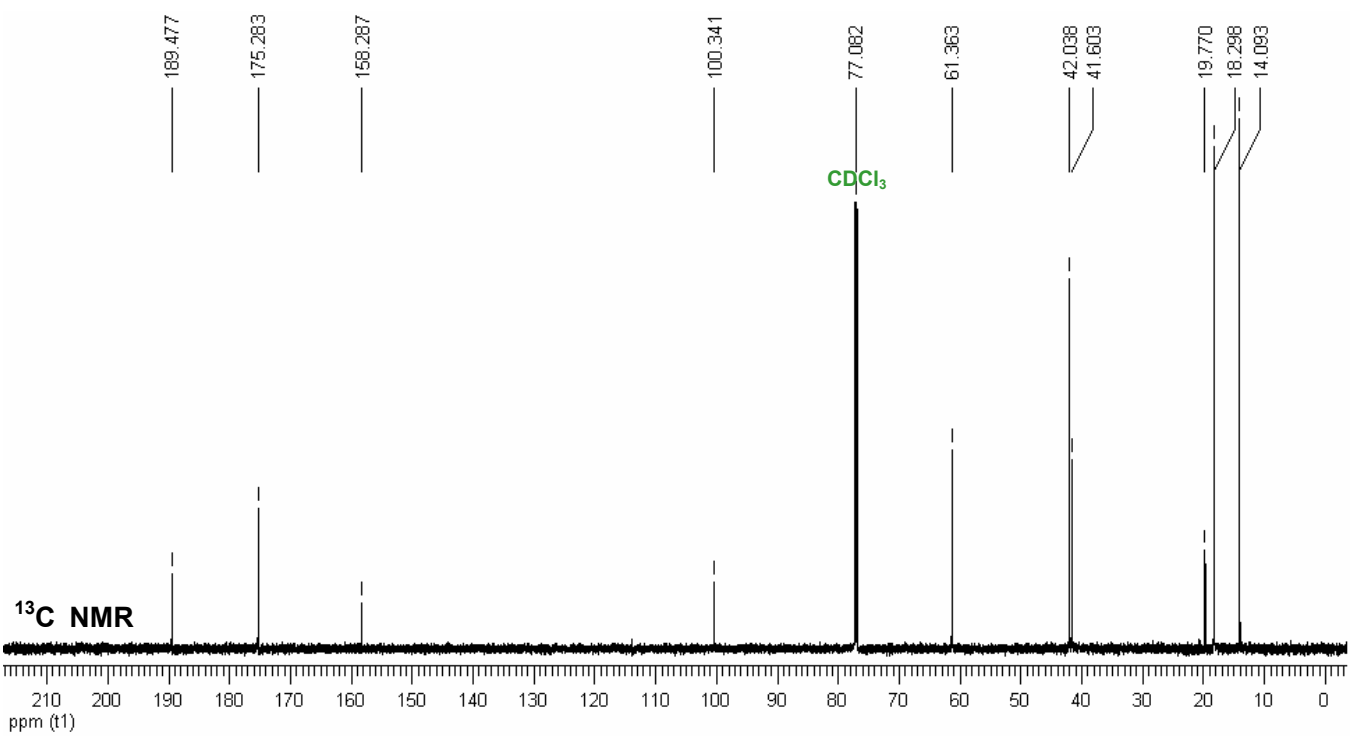

CDCl3
190.089
175.559
157.386
95.789
77.000
52.848
41.554
23.897
19.565
13C NMR
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)
41.568
23.914
19.565
DEPT-135
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)

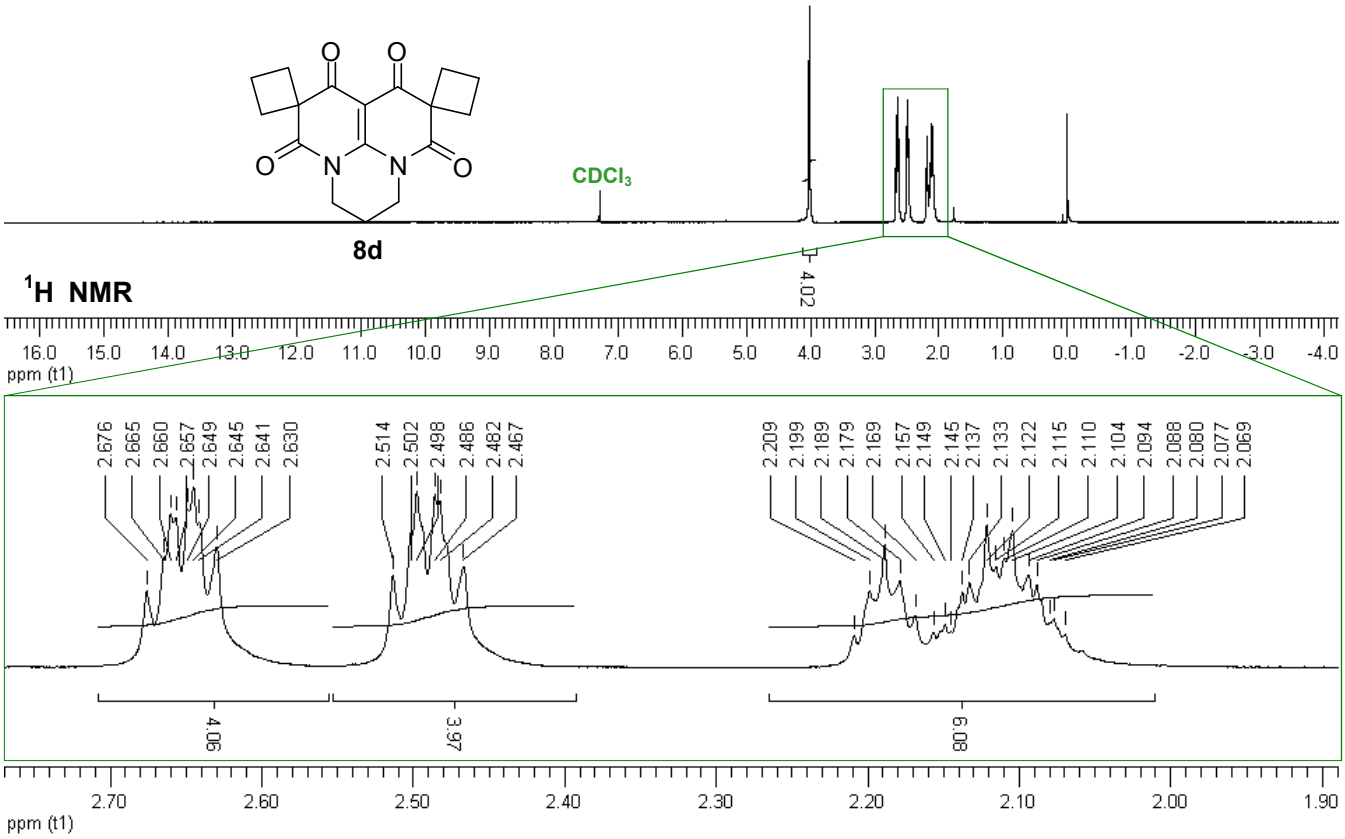

4.064
4.045
4.026
2.194
2.147
2.121
2.097
2.077
2.053
2.029
1.940
1.916
1.892
1.871
1.849
1.825
0.819
0.795
0.770
0.00000
CDCl3
4.15
6.06
4.14
12.00
1H NMR
15.0 14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2.0
ppm (t1)

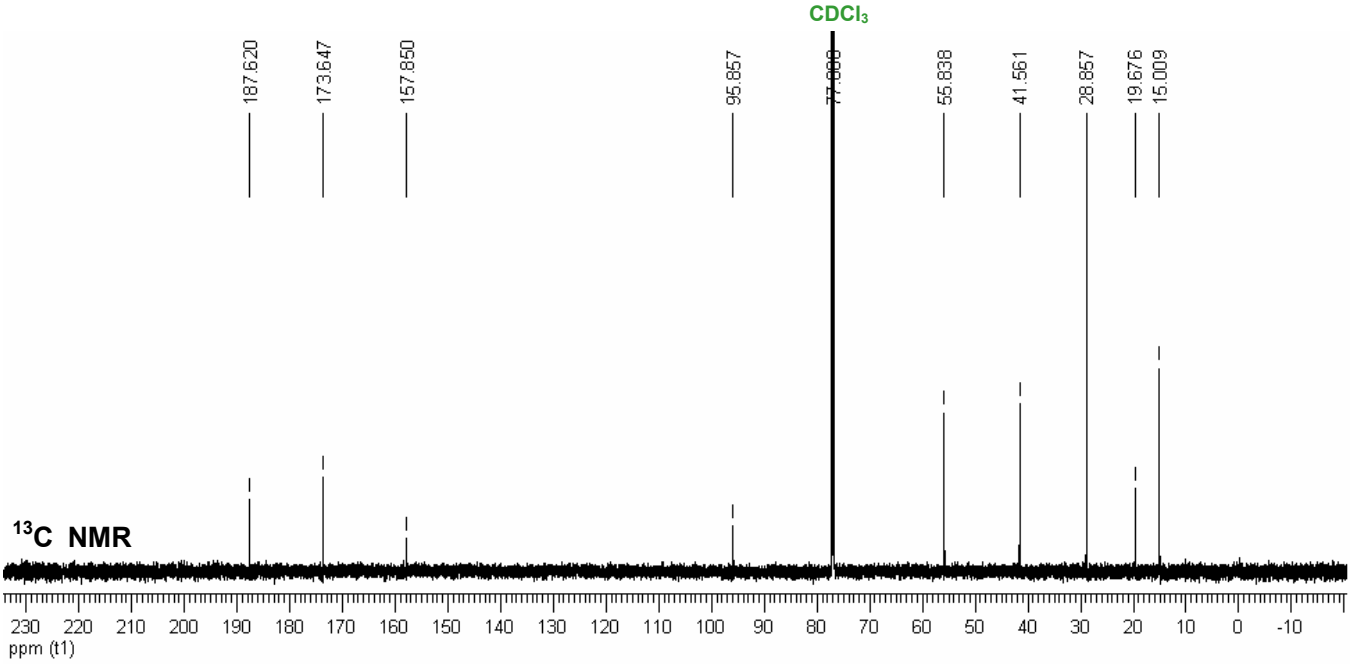
8b

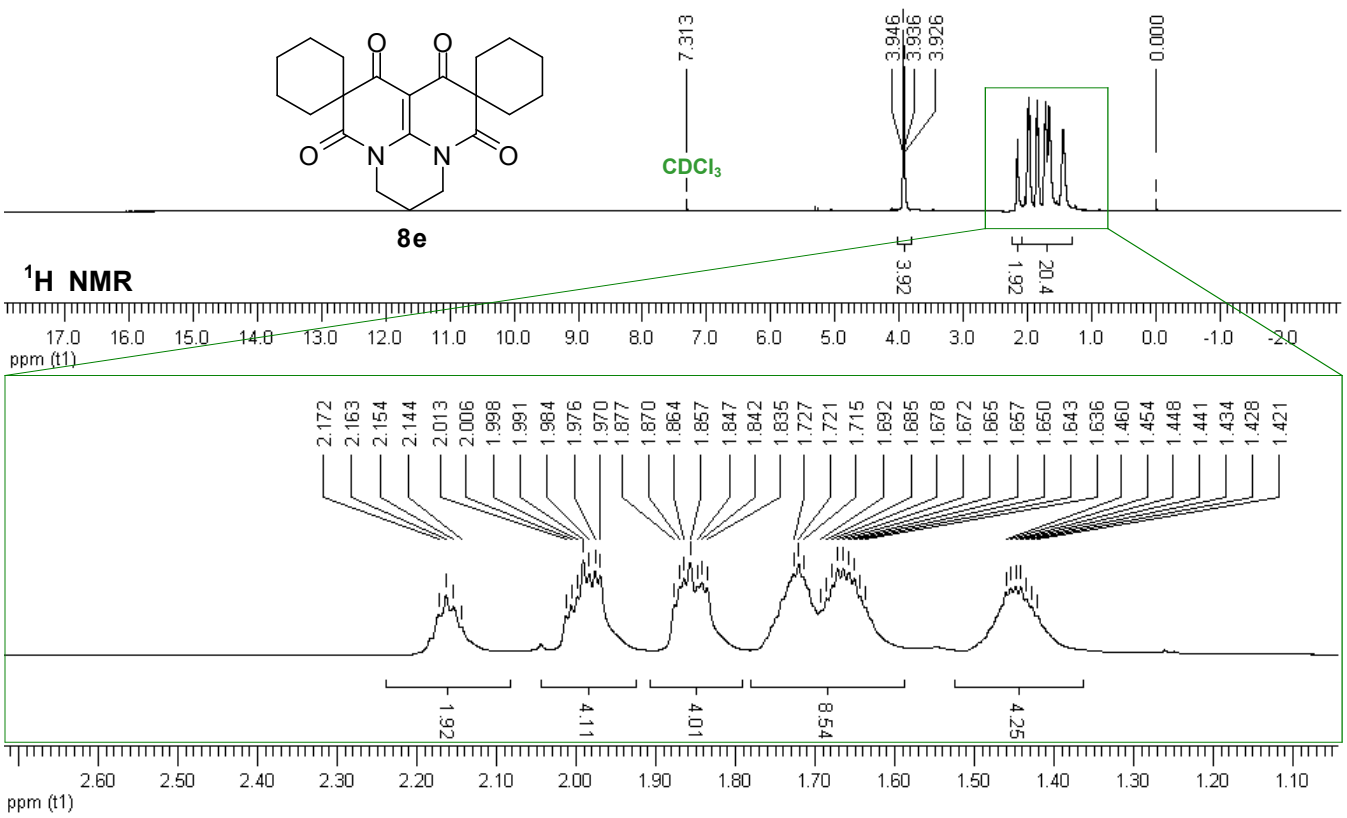

CDCl3
189.232
174.962
158.321
100.551
77.000
62.556
41.540
32.250
19.822
9.438
13C NMR
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)
41.537
32.277
19.783
9.438
DEPT-135
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm (t1)

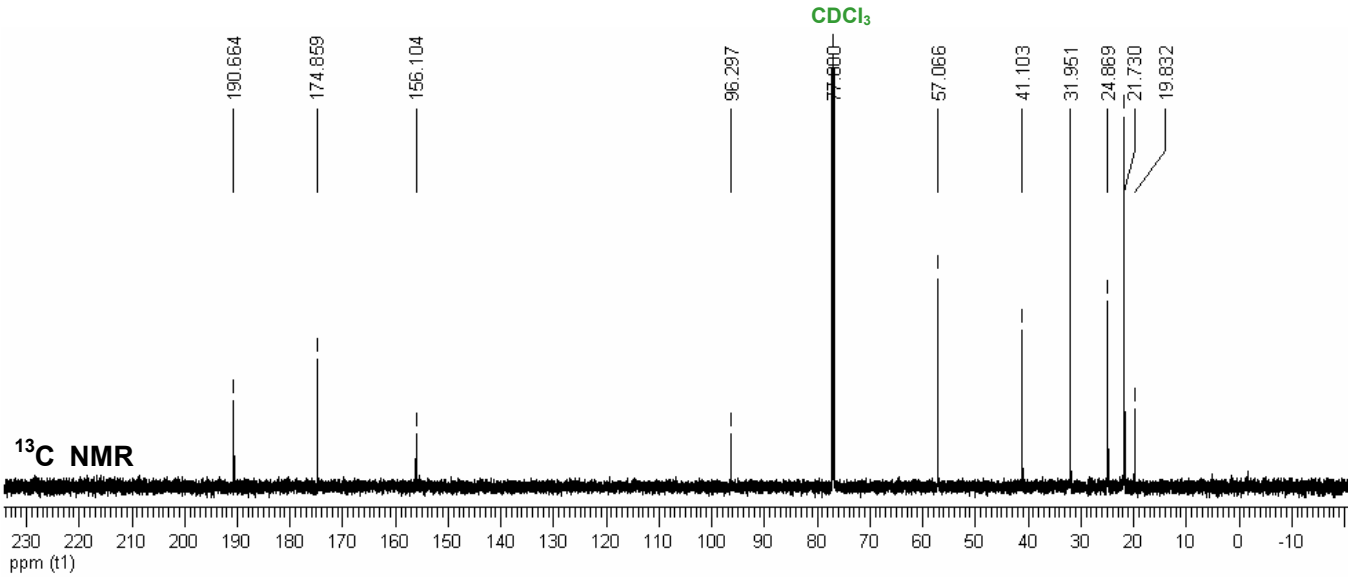

8c
^{1}H NMR
CDCl$_3$
ppm (t1)
4.035
4.025
4.015
2.195
2.186
2.056
2.049
2.035
2.028
2.014
2.007
1.834
1.826
1.813
1.806
1.792
1.785
1.249
1.241
1.229
1.220
1.216
1.209
1.200
1.197
1.188
1.118
1.107
1.099
1.094
1.087
1.078
1.075
1.067
1.057
1.046
0.834
0.822
0.810
0.000
4.25
2.04
4.05
4.03
3.88
3.93
12.00


189.477
175.283
158.287
100.341
77.082
CDCl$_3$
61.363
42.038
41.603
19.770
18.298
14.093
^{13}C NMR
ppm (t1)


CDCl3
8d
1H NMR
4.02
ppm (t1)
2.676
2.665
2.660
2.657
2.649
2.645
2.641
2.630
2.514
2.502
2.498
2.486
2.482
2.467
2.209
2.199
2.189
2.179
2.169
2.157
2.149
2.145
2.137
2.133
2.122
2.115
2.110
2.104
2.094
2.088
2.080
2.077
2.069
4.06
3.97
6.08


CDCl3
187.620
173.647
157.850
95.857
77.000
55.838
41.561
28.857
19.676
15.009
13C NMR
ppm (t1)


8e
^{1}H NMR
CDCl$_3$
7.313
3.946
3.936
3.926
0.000
3.92
1.92
20.4
ppm (t1)
2.172
2.163
2.154
2.144
2.013
2.006
1.998
1.991
1.984
1.976
1.970
1.877
1.870
1.864
1.857
1.847
1.842
1.835
1.727
1.721
1.715
1.692
1.685
1.678
1.672
1.665
1.657
1.650
1.643
1.636
1.460
1.454
1.448
1.441
1.434
1.428
1.421
1.92
4.11
4.01
8.54
4.25


^{13}C NMR
CDCl$_3$
190.664
174.859
156.104
96.297
77.000
57.066
41.103
31.951
24.869
21.730
19.832
ppm (t1)