Chemical Communications

A Switchable Macrocycle–Clip Complex That Functions as a NOR Logic Gate

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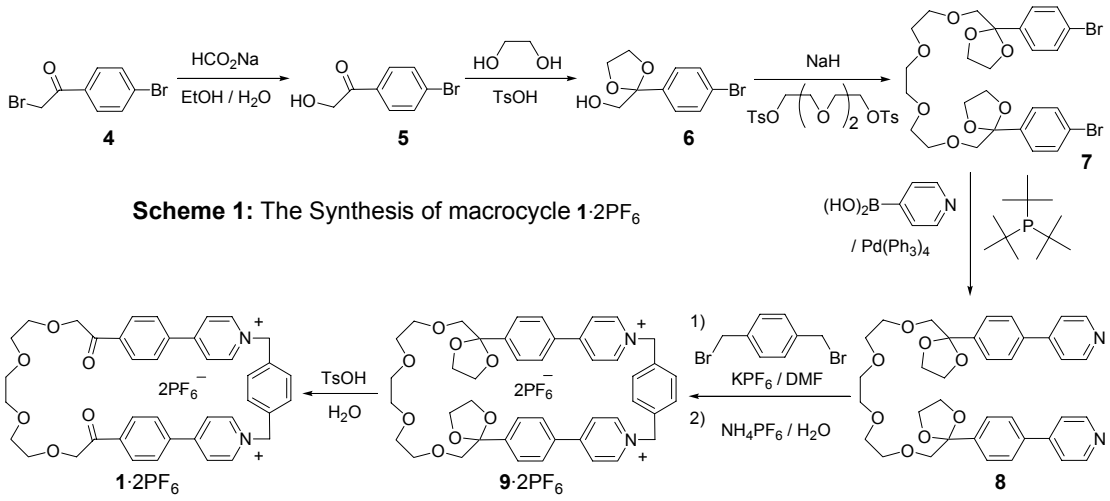
SUPPORTING INFORMATION



Scheme 1: The Synthesis of macrocycle **1**·2PF_6

Alcohol 5: 2,4′-Dibromoacetophenone (**4**; 2.23 g, 8.0 mmol) and sodium formate (3.49 g, 50 mmol) were dissolved in $EtOH_{(aq)}$ (85%, 21 mL) and heated under reflux for 12 h. The organic solvent was evaporated under reduced pressure and H_2O (30 mL) was added to precipitate the product. After filtration and recrystalization (95% EtOH), alcohol **5** was obtained as a white solid (1.04 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.82 (s, 2H), 7.62 (d, *J* = 7 Hz, 2H), 7.76 (d, *J* = 7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.5, 128.7, 129.1, 131.6, 131.9, 196.6; HRMS (FAB): *m/z* calcd for $[M + H]^+$ $C_8H_8BrO_2$, 214.9708, found 214.9706.

Alcohol 6: Alcohol **5** (6.45g, 30 mmol), ethylene glycol (9.3 g, 0.15 mol) and TsOH (200 mg, 11.6 mmol) were dissolved in benzene (300 mL) and the reaction mixture was heated under reflux for 3 h in an apparatus equipped with a Dean–Stark apparatus. The reaction mixture was then cooled to room temperature and the organic solvent was evaporated. The residue was partitioned between H_2O (300 mL) and CH_2Cl_2 (300 mL) and the organic layer was dried ($MgSO_4$) and concentrated. The crude product was then purified by column chromatography (SiO_2: hexane/CH_2Cl_2, 4:7) to give alcohol **6** as a white solid (5.65, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 2H), 3.83–3.86 (m, 2H), 4.08–4.12 (m, 2H), 7.34 (d, *J* = 6 Hz, 2H), 7.47 (d, *J* = 6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.8, 67.2, 109.2, 122.9, 128.0, 131.5, 138.7 (one carbon is missing possibly because of signal overlap); HRMS (FAB): *m/z* calcd for $[M + H]^+$ $C_{10}H_{12}BrO_3$ 258.9970, found 259.0000.

***p*-Substituted bromobenzene 7**: Alcohol **6** (2.26 g, 8.9 mmol) and NaH (370 mg; 60%, 15 mmol) were added to DMF (70 mL). The mixture was stirred at room temperature for 1 h before tri(ethylene glycol) ditosylate (1.36 g, 3 mmol) was added

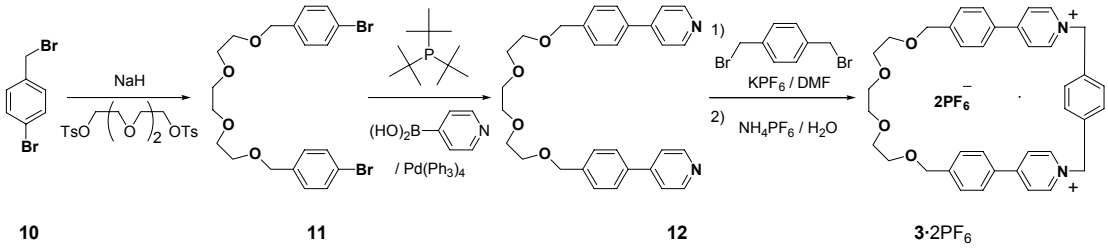
slowly. The resulting mixture was stirred for 4 h and then the reaction was quenched by the addition of MeOH (5 mL). The organic solvent was evaporated under reduced pressure and the residue was partitioned between H_2O (100 mL) and CH_2Cl_2 (100 mL). The organic layer was collected, dried ($MgSO_4$), and concentrated to afford a crude product. The crude product was then purified by column chromatography (SiO_2: MeCN/CH_2Cl_2, 3:97) to give compound **7** as a yellow oil (1.02 g, 54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =3.49 (s, 4H), 3.53–3.55 (m, 4H), 3.63–3.67 (m, 8H), 3.79–3.83 (m, 4H), 4.06–4.09 (m, 4H), 7.35 (d, *J* = 6 Hz, 4H), 7.43 (d, *J* = 6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.2, 70.5, 70.5, 71.6, 75.2, 108.4, 122.0, 127.6, 130.7, 138.8; HRMS (FAB): *m/z* calcd for $[M + H]^+$ $C_{26}H_{33}Br_2O_8$ 631.0542, found 631.0500.

***p*-Substituted pyridine 8**: 4-Pyridineboronic acid (0.22 g, 1.8 mmol), MeOH (6 mL), and saturated aqueous Na_2CO_3 (3 mL) were added in turn to a mixture of **7** (0.4 g, 0.6 mmol), $Pd(PPh_3)_4$ (42 mg, 0.04 mmol) and tri-*tert*-butylphosphine (1.44 mL; 0.025 M, 0.04 mmol) in toluene (9 mL). This mixture was then heated under reflux for 24 h. After cooling to room temperature, the mixture was partitioned between aqueous NH_4OH (0.1 M, 20 mL) and CH_2Cl_2 (20 mL). The organic phase was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 4:96) to give compound **8** as a light-yellow oil (289 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.51 (s, 4H), 3.54–3.66 (m, 4H), 3.67–3.69 (m, 4H), 3.70 (s, 4H), 3.84–3.87 (m, 4H), 4.10–4.13 (m, 4H), 7.49 (d, *J* = 6 Hz, 4H), 7.60 (s, 8H), 8.63 (b, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.2, 71.5, 75.2, 108.6, 121.4, 126.5, 126.8, 137.7, 141.1, 147.8, 149.8 (two carbon are missing possibly because of signal overlap); HRMS (FAB): *m/z* calcd for $[M + H]^+$ $C_{36}H_{41}N_2O_8$ 629.2863, found 629.2900.

Macrocycle 9·2PF_6: A DMF solution (230 mL) of **8** (1.0 g, 1.6 mmol), α,α´-dibromo-*p*-xylene (0.4 g, 1.6 mmol), and KPF_6 (0.33 g, 1.6 mmol) was stirred at room temperature for 7 d. The organic solvent was evaporated under reduced pressure and the residue was dissolved in MeCN (20 mL) followed by adding saturated aqueous NH_4PF_6 (30 mL). The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to afford a white solid, which was purified by column chromatography (SiO_2: MeOH/CH_2Cl_2, 5/95) to afford macrocycle **9**·2PF_6 as a yellow solid (1.40 g, 86%). ^{1}H NMR (400 MHz, CD_3CN): δ = 3.33–3.36 (m, 8H), 3.47–3.49 (m, 4H), 3.66 (s, 4H), 3.83–3.85 (m, 4H), 4.03–4.05 (m, 4H), 5.70 (s, 4H), 7.60 (s, 4H), 7.66 (d, *J* = 9 Hz, 4H), 7.82 (d, *J* = 9 Hz, 4H), 8.19 (d, *J* = 7 Hz, 4H), 8.69 (d, *J* = 7 Hz, 4H); ^{13}C NMR (100 MHz, CD_3CN): δ

= 26.2, 64.2, 65.9, 68.2, 70.6, 70.7, 71.8, 75.6, 108.8, 126.1, 128.5, 131.1, 133.9, 136.1, 145.0, 146.0, 157.0; MS (FAB) 877.4 $[\mathbf{9}\cdot PF_6]^+$.

Macrocycle 1$\cdot 2PF_6$**:** Macrocycle **9**$\cdot 2PF_6$ (0.4 g, 0.5 mmol) and TsOH (8.5 mg, 0.04 mmol) were dissolved in a mixture of H_2O (1 mL) and acetone (2 mL) and heated under reflux for 3 d. The organic solvent was evaporated under reduced pressure and the residue was dissolved in MeCN (20 mL) followed by adding saturated aqueous NH_4PF_6 (30 mL). The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to give a crude product, which was then purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 5:95) to afford the macrocycle **1**$\cdot 2PF_6$ as a light-yellow solid (127 mg, 43%). ^{1}H NMR (400 MHz, CD_3CN): δ = 3.46 (s, 4H), 3.51–3.54 (m, 4H), 3.63–3.65 (m, 4H), 4.67 (s, 4H), 5.71 (s, 4H), 7.62 (s, 4H), 7.89 (d, *J* = 8 Hz, 4H), 8.08 (d, *J* = 8 Hz, 4H), 8.19 (d, *J* = 8 Hz, 4H), 8.74 (d, *J* = 8 Hz, 4H); ^{13}C NMR (100 MHz, CD_3CN): δ = 65.1, 71.3, 71.6, 71.9, 76.2, 127.3, 129.8, 130.9, 131.8, 136.9, 138.9, 139.1, 145.6, 156.9, 198.2; MS (FAB) *m/z* 789.3 $[M - PF_6]^+$.

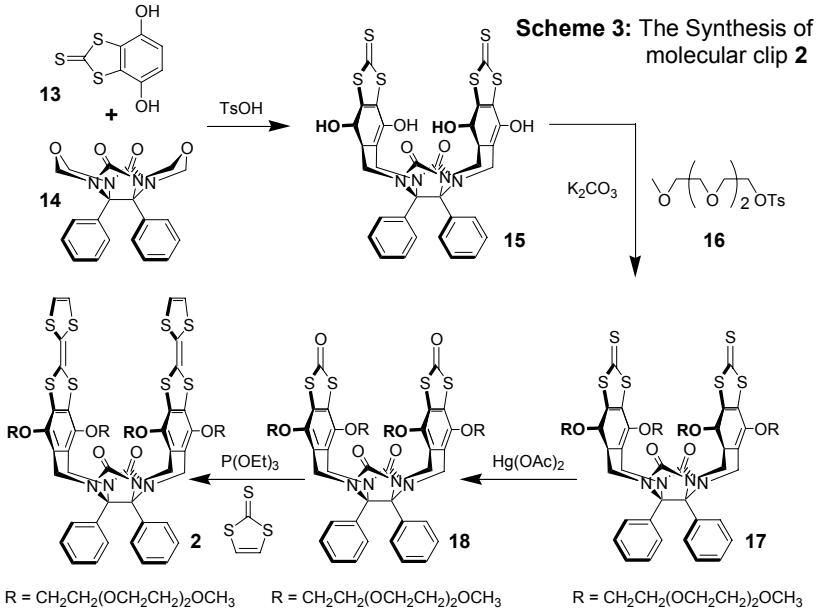


Scheme 2: The Synthesis of macrocycle **3**$\cdot 2PF_6$

***p*-Substituted bromobenzene 11**: NaH (60%; 1.0 g, 24 mmol) was added in small portions to a solution of triethylene glycol (1.2 g, 8 mmol) in DMF (80 mL) and then the resulting mixture was stirred at room temperature for 1 h. 4-Bromobenzyl bromide **10** (6.0 g, 24 mmol) was added and the mixture was stirred at ambient temperature for 18 h. MeOH (5 mL) was added to quench the reaction and then the organic solvent was evaporated under reduced pressure. The residue was partitioned between H_2O (50 mL) and CH_2Cl_2 (50 mL) and the organic layer was dried ($MgSO_4$) and concentrated to give a crude product, which was purified by column chromatography (SiO_2; EtOAc/hexane, 3:7) to give compound **11** as a yellow oil (3.49 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.59–3.61 (m, 4H), 3.65–3.67 (m, 8H), 4.83 (s, 4H), 7.19 (d, *J* = 8 Hz, 4H), 7.43 (d, *J* = 8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.6, 70.6, 70.6, 72.4, 121.3, 129.1, 131.3, 137.1; MS (FAB): *m/z* 489.1 $[M + H]^+$.

***p*-Substituted pyridine 12:** 4-Pyridineboronic acid (0.7 g, 5.5 mmol), MeOH (18 mL), and saturated aqueous Na_2CO_3 (9 mL) were added in turn to a mixture of **11** (1.1 g, 2.0 mmol), $Pd(PPh_3)_4$ (130 mg, 0.11 mmol), and tri-*tert*-butylphosphine (0.025 M, 4.5 mL, 0.11 mmol) in toluene (28 mL). The mixture was then heated under reflux for 24 h. After cooled to room temperature, the mixture was partitioned between aqueous NH_4OH (0.1 M, 80 mL) and CH_2Cl_2 (80 mL). The organic phase was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was purified by column chromatography (SiO_2; $MeOH/CH_2Cl_2$, 2.5:97.5) to give compound **12** as a light-yellow oil (680 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.64–3.70 (m, 12H), 4.60 (s, 4H), 7.42–7.48 (m, 8H), 7.58 (d, *J* = 8 Hz, 4H), 8.61 (d, *J* = 6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.7, 70.7, 70.7, 72.9, 121.4, 126.9, 128.2, 137.0, 139.4, 148.1, 149.7; MS (FAB): *m/z* 485.3 $[M + H]^+$.

Macrocycle 3·$2PF_6$: A mixture of **12** (700 mg, 1.4 mmol), α,α´-dibromo-*p*-xylene (380 mg, 1.4 mmol), and KPF_6 (270 mg, 1.4 mmol) was stirred in DMF (200 mL) at room temperature for 7 d. The organic solvent was evaporated under reduced pressure and the residue was dissolved in MeCN (20 mL) followed by adding saturated aqueous NH_4PF_6 (30 mL). The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to afford a white solid, which was purified by column chromatography (SiO_2; $MeOH/CH_2Cl_2$, 3:97) to afford macrocycle **3**·$2PF_6$ as a yellow solid (550 mg, 43%). ^{1}H NMR (400 MHz, CD_3CN): δ = 3.53 (s, 4H), 3.56 (s, 8H), 4.56 (s, 4H), 7.50 (d, *J* = 8 Hz, 4H), 7.62 (s, 4H), 7.77 (d, *J* = 8 Hz, 4H), 8.13 (d, *J* = 7 Hz, 4H), 8.68 (d, *J* = 7 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 64.4, 70.7, 71.1, 71.4, 72.7, 125.9, 128.9, 129.5, 131.1, 133.1, 136.6, 144.5, 144.6, 157.1; MS (FAB): 733.4 $[\mathbf{3}\cdot PF_6]^+$.



Scheme 3: The Synthesis of molecular clip **2**

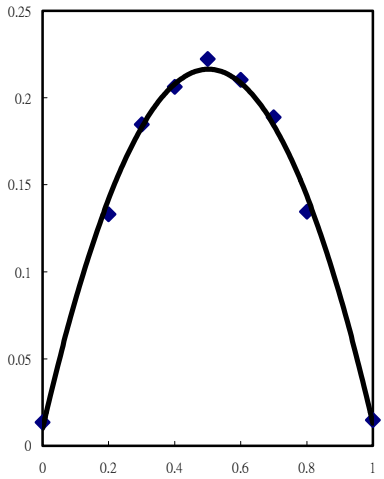
Molecular Clip 15: TsOH (3.9 g, 10 mmol) and 1,2-dichloroethane (100 mL) were and heated under reflux in a two-neck flask equipped with a Dean–Stark apparatus. Molecular clip **14** (4 g, 10 mmol), and 1,3-benzodithiole-2-thione **13** (8.9 g, 41 mmol) was added and the mixture was heated under reflux for 24 h. The mixture was poured into MeOH (150 mL). The precipitate was filtered off, suspended in DMSO (150 mL), heated to 90 °C for 30 min, and then poured into MeOH (150 mL). The resulting precipitate was filtered off, washed with MeOH (50 mL), and dried to give molecular clip **15** as a light-yellow solid (6.75 g, 84%). ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 3.79 (d, *J* = 16 Hz, 4H), 5.35 (d, *J* = 16 Hz, 4H), 7.04–7.23 (m, 10H), 9.66 (s, 4H); ^{13}C NMR (100 MHz, CD_3SOCD_3): δ = 37.0, 84.5, 126.6, 127.6, 128.5, 128.6, 129.9, 133.0, 140.6, 156.6, 212.3; MS (FAB): 775.0 $[M + H]^+$.
Molecular clip **14** and 1,3-benzodithiole-2-thione **13** and was obtained according to literature procedure, see : (a) *J. Org. Chem*. **1989**, *54*, 3710-3717 and (b) *Angew. Chem. Int. Ed.* **1998**, *37*, 2107 – 2110.

Molecular Clip 17: K_2CO_3 (2 g, 14.5 mmol) was added to a solution of molecular clip **15** (1.0 g, 1.3 mmol) in DMF (25 mL). After stirring at room temperature for 30 min, a solution of tri(ethylene glycol) monomethyl ether tosylate **16** (3 g, 9.4 mmol) in DMF (5 mL) was added and the mixture was stirred for another 12 h at ambient temperature. The solvent was evaporated under reduced pressure and the residue was partitioned between H_2O (150 mL) and CH_2Cl_2 (150 mL). The organic layer was washed with H_2O (2 × 100 mL), dried ($MgSO_4$), and concentrated to give a crude product, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 2:98) to provide molecular clip **17** as a yellow solid (0.258 g, 15%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.35 (s, 12H), 3.55 (q, *J* = 8 Hz, 8H), 3.66–3.78 (m, 28 H), 3.82 (d, *J* = 16 Hz, 4H), 3.91–3.96 (m, 4H), 4.04–4.09 (m, 4H), 4.46–4.50 (m, 4H), 5.45 (d, *J* = 16 Hz, 4H) 7.05–7.15 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.9, 59.0, 70.2, 70.6, 70.8, 71.9, 73.4, 85.1, 127.9, 128.8, 129.0, 130.9, 132.7, 135.2, 145.6, 157.0, 211.5 (one carbon is missing possibly because of signal overlap); MS (MALDI-TOF): 1359.0 $[M + H]^+$.

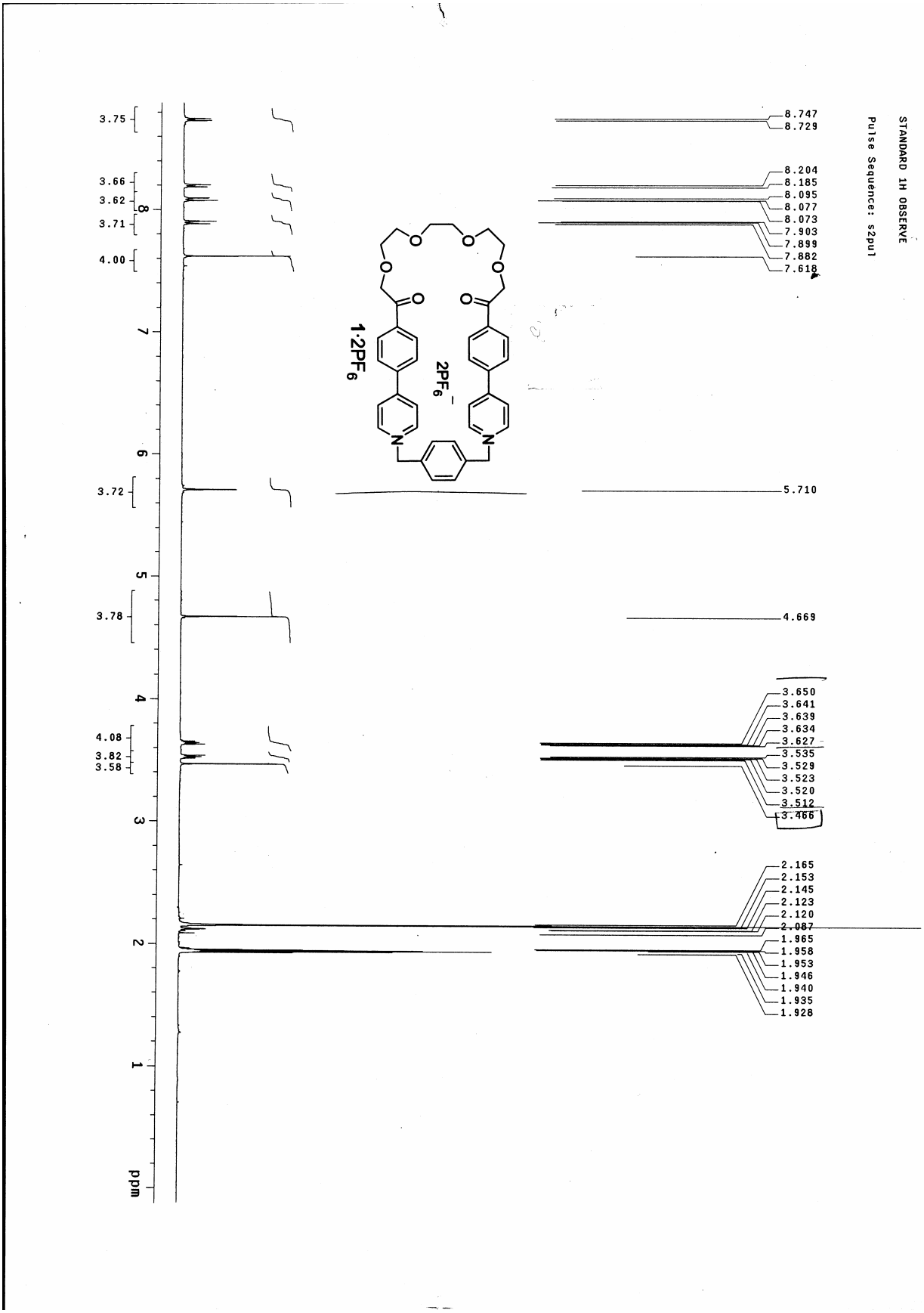
Molecular Clip 18: A mixture of molecular clip **17** (205 mg, 0.15 mmol) and $Hg(OAc)_2$ (250 mg, 0.78 mmol) in glacial acetic acid (1.1 mL) and CH_2Cl_2 (1.5 mL) was stirred at ambient temperature for 15 min. The suspension was filtered through celite and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 75 mL) and water (75 mL). The organic layer was dried ($MgSO_4$) and concentrated to give molecular clip **18** as a white solid (160 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ

= 3.35 (s, 12H), 3.55 (q, *J* = 8 Hz, 8H), 3.66–3.78 (m, 28H), 3.82 (d, *J* = 16 Hz, 4H), 3.89–3.94 (m, 4H), 4.02–4.06 (m, 4H), 4.43–4.48 (m, 4H), 5.44 (d, *J* = 16 Hz, 4H), 7.05–7.15 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.8, 58.9, 70.1, 70.5, 70.5, 70.7, 71.8, 72.9, 85.0, 127.0, 127.8, 128.6, 128.9, 130.0, 132.7, 147.0, 156.9, 189.1; MS (FAB): 1327.3 $[M + H]^+$.

Molecular Clip 2: Triethyl phosphite (3.1 mL) was added to a mixture of molecular clip **18** (160 mg, 0.12 mmol) and 1,3-dithio-2-thione (200 mg, 1.5 mmol). The mixture was stirred at 130 °C for 3.5 h, cooled to room temperature, and filtered. The filtrate was washed with hexane (10 mL) to afford molecular clip **2** as a light-yellow solid (37 mg, 21%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 3.33 (s, 12H), 3.54 (q, *J* = 8 Hz, 8H), 3.63–3.80 (m, 28H), 3.79 (d, *J* = 16 Hz, 4H), 3.89–3.94 (m, 4H), 4.03–4.08 (m, 4H), 4.39–4.43 (m, 4H), 5.38 (d, 4H), 6.35 (s, 4H), 7.10–7.17 (m, 10H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 38.4, 59.2, 71.0, 71.1, 71.2, 72.4, 72.8, 85.5, 106.5, 115.4, 119.0, 128.4, 128.7, 128.8, 130.2, 131.6, 133.6, 146.5, 157.1; MS (FAB): 1500.4 $[M + H]^+$.



Job plot (based on the charge-transfer absorption at 533 nm) for complexation of clip **2** with macrocycle **1**·2PF_6 at 25 °C in CH_3CN.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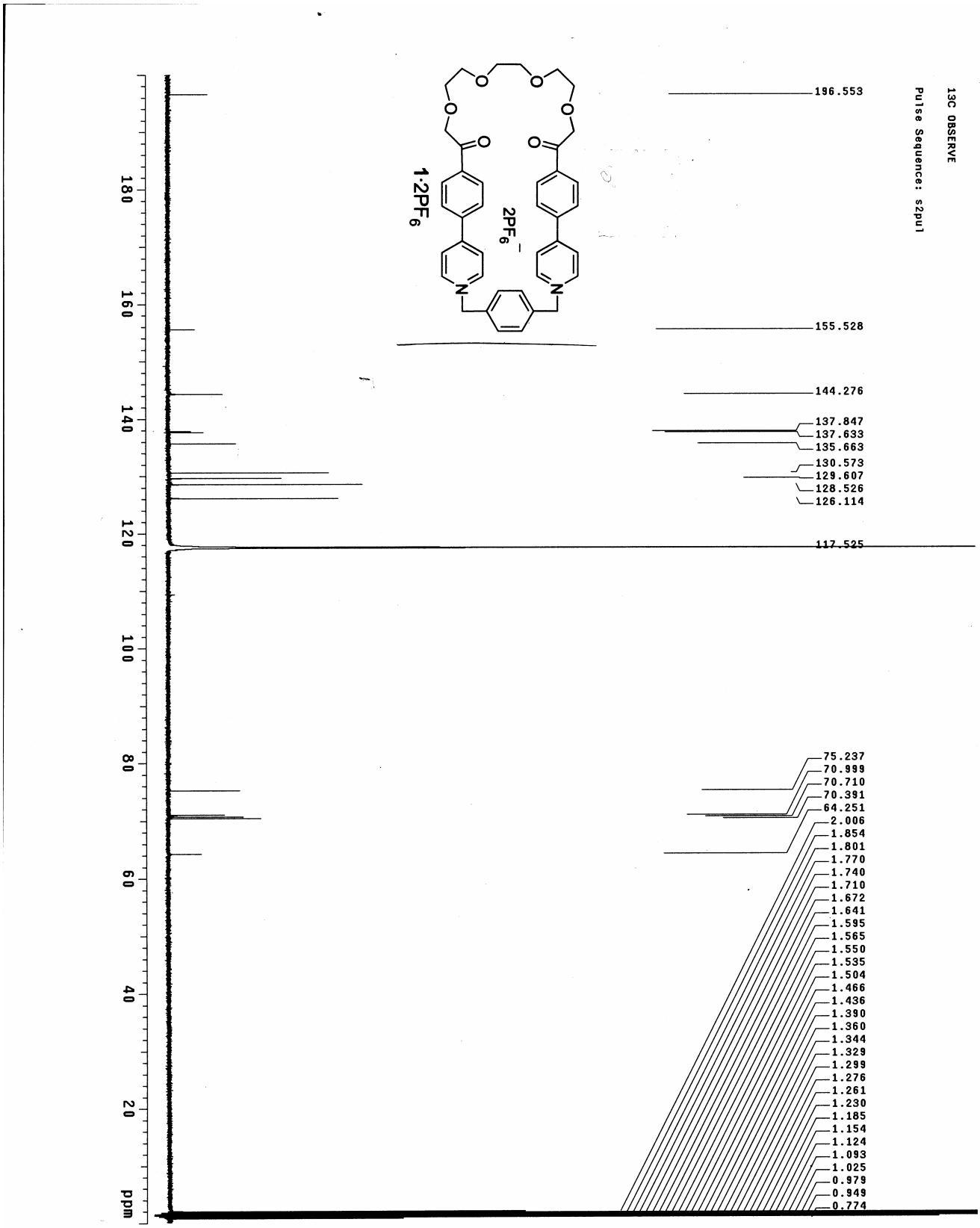
ppm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ppm
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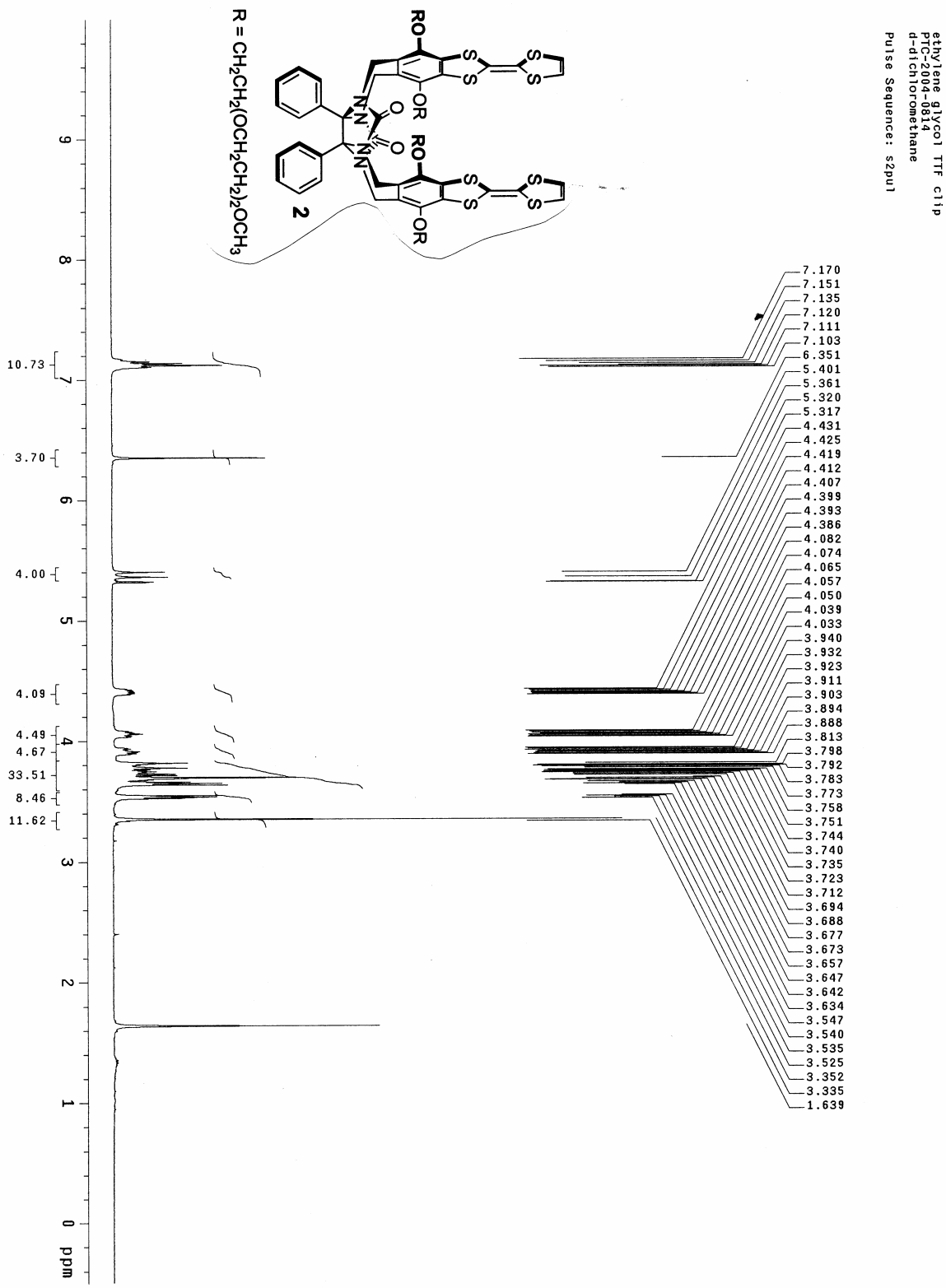
2PF6−


ethylene glycol TTF clip
PTC-2004-0814
d-dichloromethane
Pulse Sequence: s2pul
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2
RO
OR
O
N
S
10.73
3.70
4.00
4.09
4.49
4.67
33.51
8.46
11.62
ppm
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13C ethylene glycol TTF clip
2004-09-02
d-Dichloromethane

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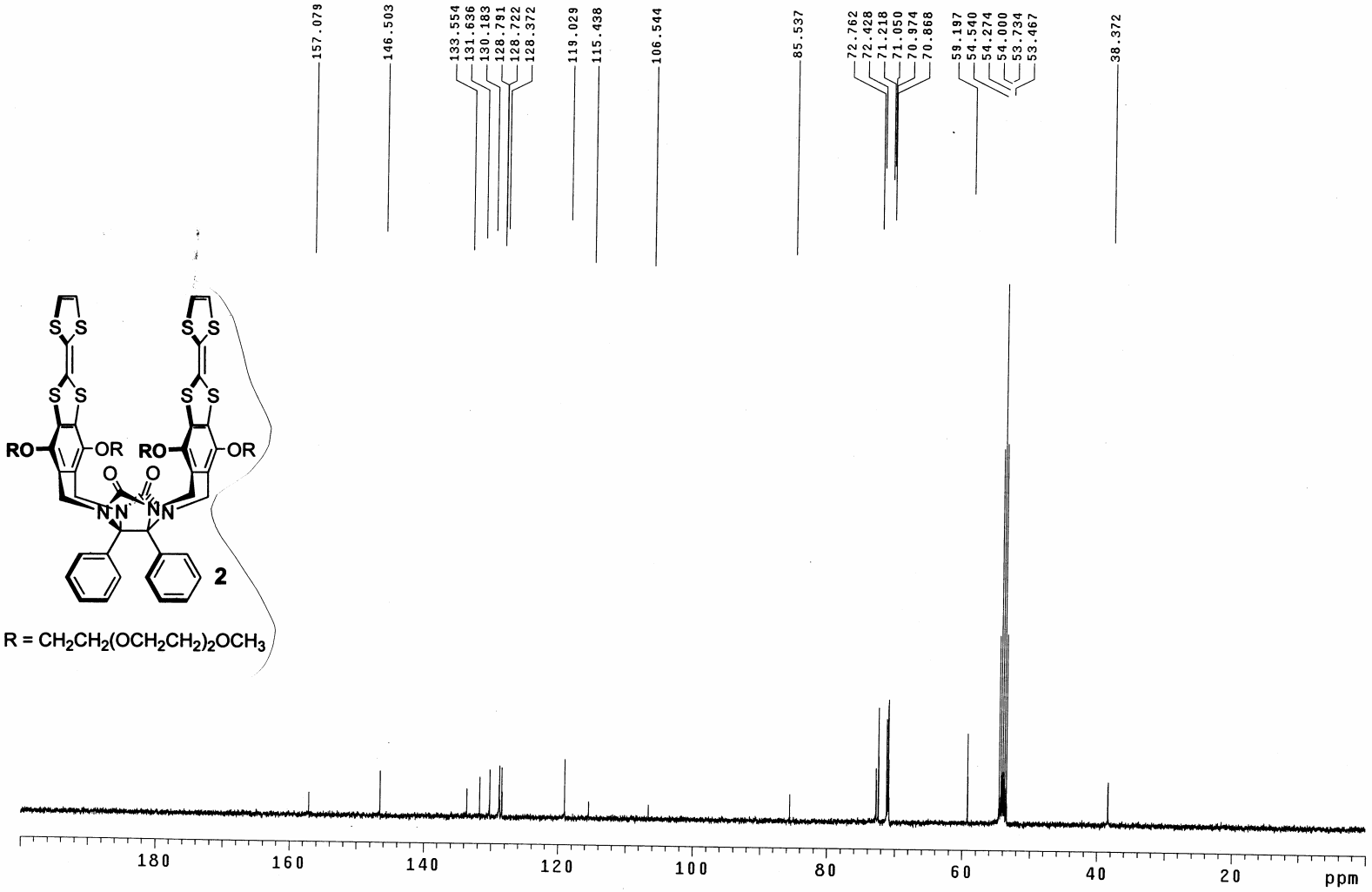

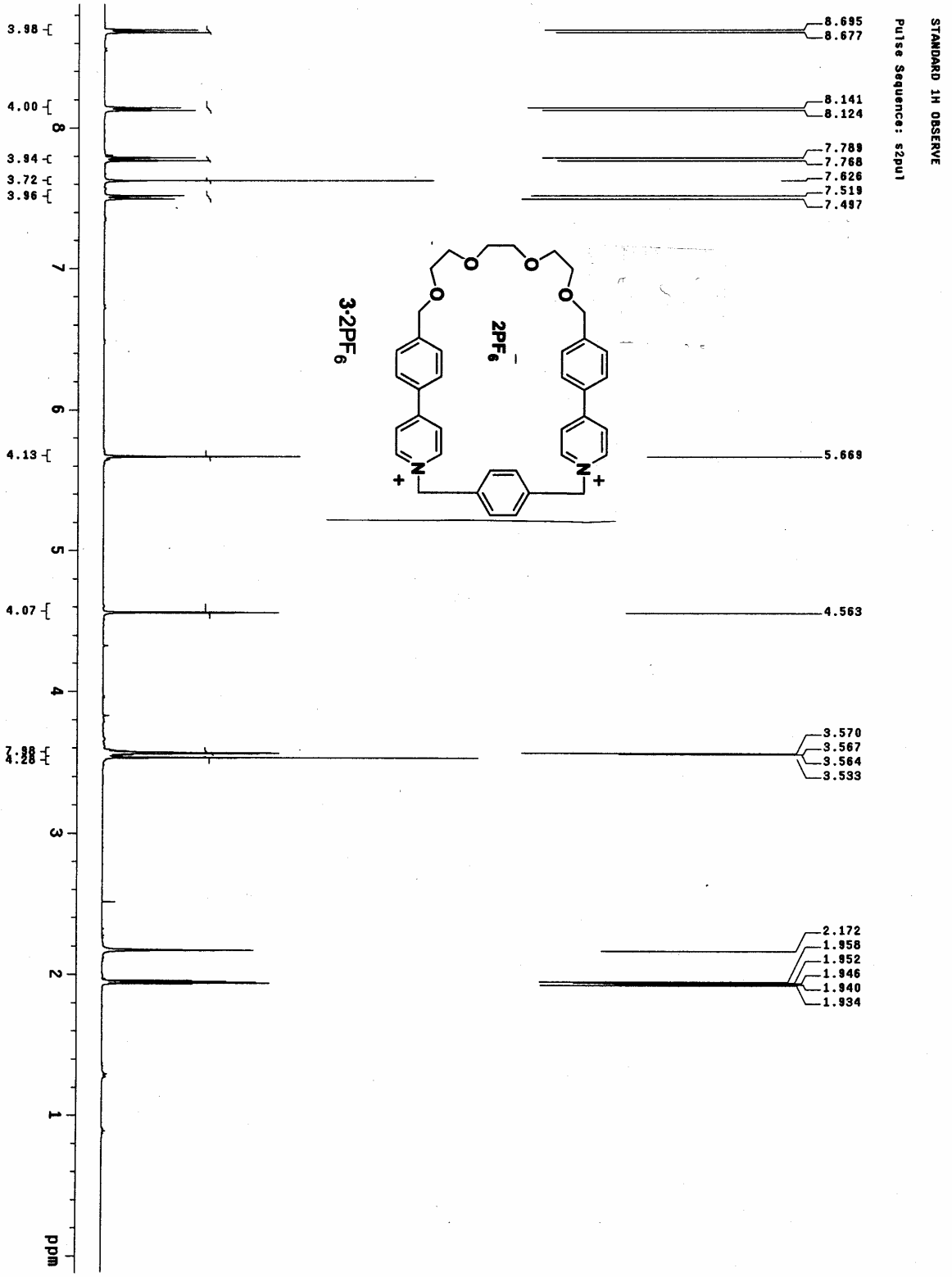
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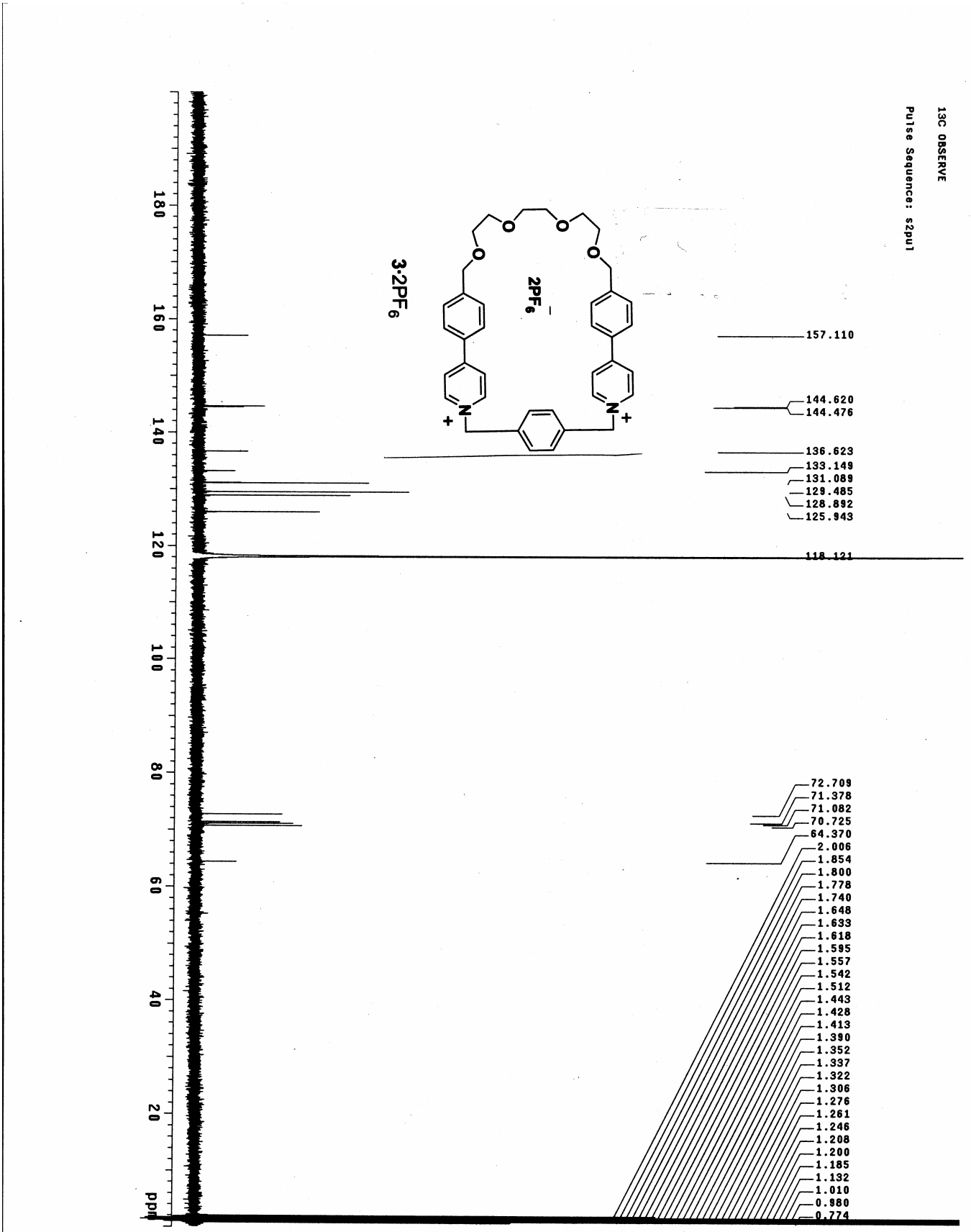
3·2PF6
2PF6−
ppm


13C OBSERVE
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1.633
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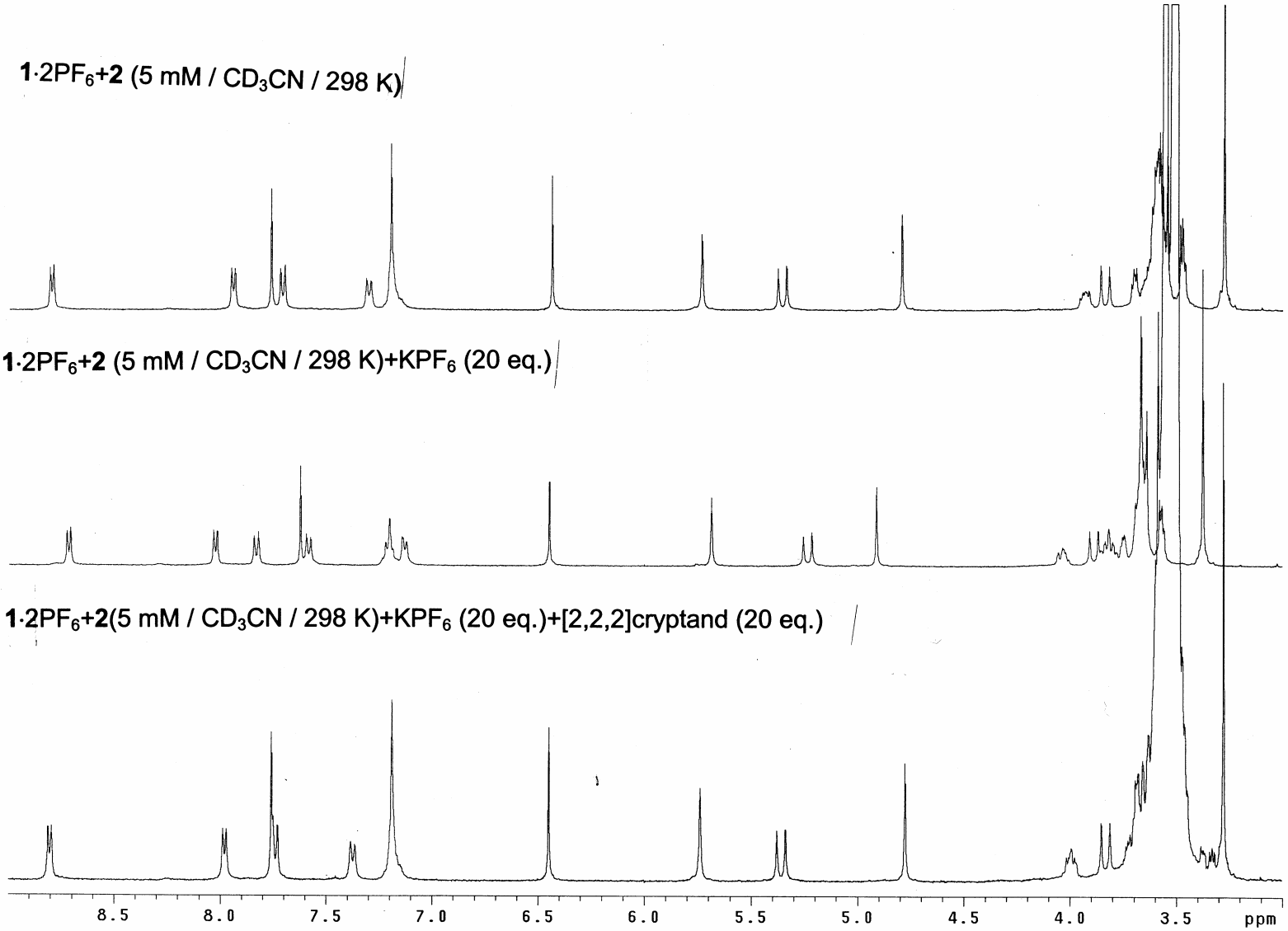
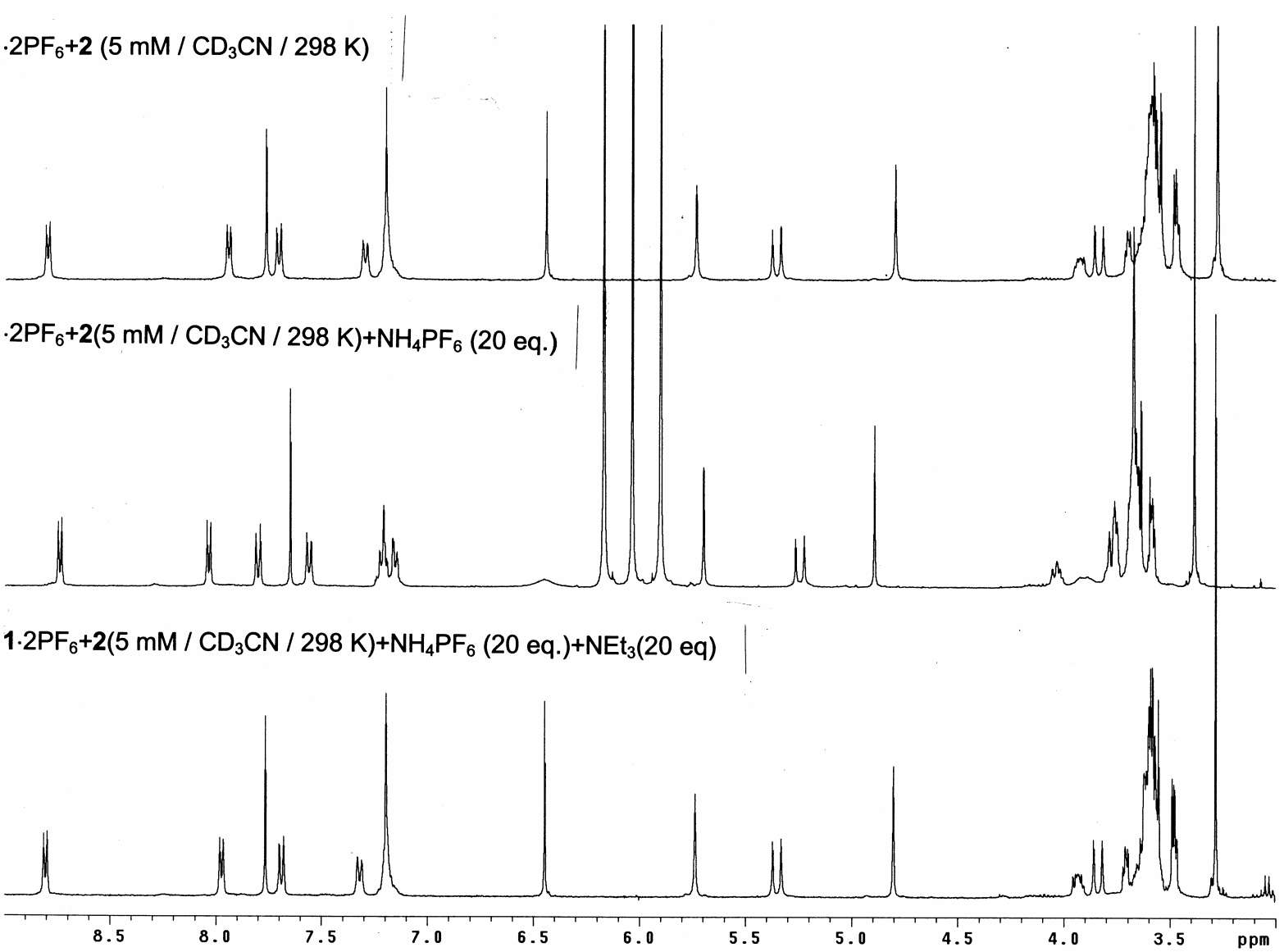
1.557
1.542
1.512
1.443
1.428
1.413
1.390
1.352
1.337
1.322
1.306
1.276
1.261
1.246
1.208
1.200
1.185
1.132
1.010
0.980
0.774
180
160
140
120
100
80
60
40
20
ppm


1·2PF6+2 (5 mM / CD3CN / 298 K)
1·2PF6+2 (5 mM / CD3CN / 298 K)+KPF6 (20 eq.)
1·2PF6+2(5 mM / CD3CN / 298 K)+KPF6 (20 eq.)+[2,2,2]cryptand (20 eq.)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm


1·2PF6+2 (5 mM / CD3CN / 298 K)
1·2PF6+2(5 mM / CD3CN / 298 K)+NH4PF6 (20 eq.)
1·2PF6+2(5 mM / CD3CN / 298 K)+NH4PF6 (20 eq.)+NEt3(20 eq)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm