# Quantitative Active Transport in [2]Rotaxane Using a One-Shot Acylation Reaction Toward the Linear Molecular Motor

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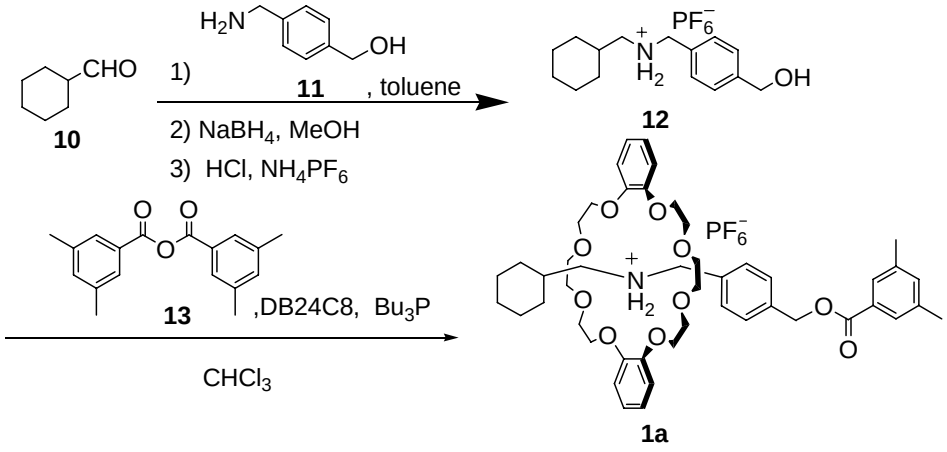
**Methods and Materials.**

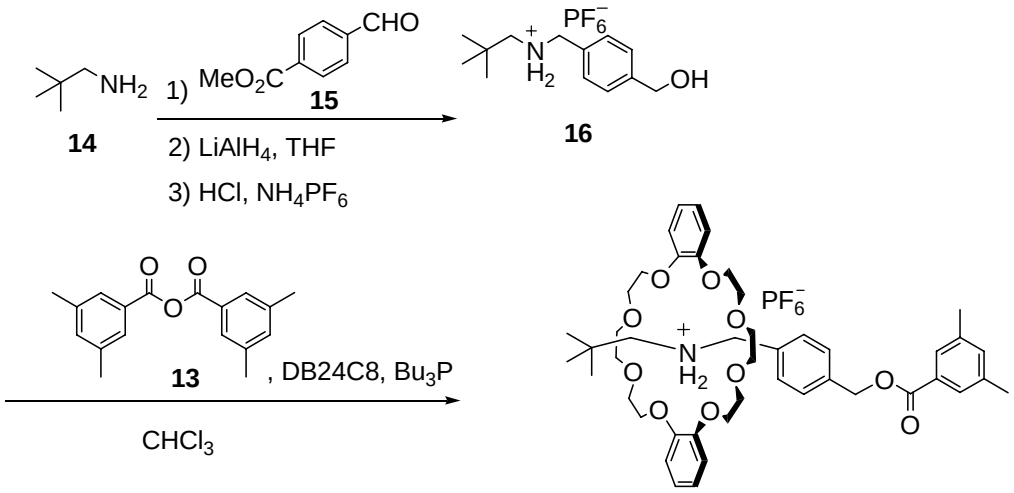
$^{1}$H-NMR and $^{13}$C-NMR spectra were recorded on a 400 and 500 MHz spectrometer with the appropriate deuterated solvents. Amino alcohol **11**,[1] ammonium salt **24**,[2] and 3,5-dimethylbenzoic anhydride **13**[2] were prepared according to the literatures. Acetonitrile, *N*,*N*-dimethylformamide, and triethylamine were used after distillation over calcium hydride. Dichloromethane and chloroform were dried with phosphorous pentoxide before distillation over calcium hydride. Other chemicals were reagent grade and used without further purification.

**Scheme S1.**




**Rotaxane (1a).** A solution of **10** (1.64 g, 14.6 mmol) and **11** (2.00 g, 14.6 mmol) in toluene (50 mL) was refluxed for 2 h with azeotropic distillation. After toluene was evapolated *in vacuo*, the residue was dissolved in methanol (50 mL). To the methanol solution sodium tetrahydroborate (1.65 g, 43.6 mmol) was added, and the mixture was stirred at room temperature for 20 h. After methanol was evapolated *in vacuo*, the residue was dissolved in ethyl acetate. The solution was washed with water, dried over anhydrous magnesium sulfate, and evaporated. The crude product was dissolved in a mixture of methanol and 3 M hydrochloric acid (1.0 mL), and was poured into saturated ammonium hexafluorophosphate solution. The mixture was extracted with ethyl acetate, and the organic layer was washed with water, dried over anhydrous magnesium sulfate, and evaporated in vacuo to give 2.84 g of the crude **12** as white solid. To a solution of **12** (500 mg, 1.32 mmol) and DB24C8 (710 mg, 1.58 mmol) in dichloromethane (8 mL) were added 3,5-dimethylbenzoic anhydride **13** (744 mg, 2.64 mmol) and tributylphosphane (32 μL, 0.13 mmol). The reaction mixture was allowed to stand at room temperature over night, and was directly purified by preparative GPC (chloroform) to obtain 809 mg (72%, from **12**) of rotaxane **1a** as a white powder.

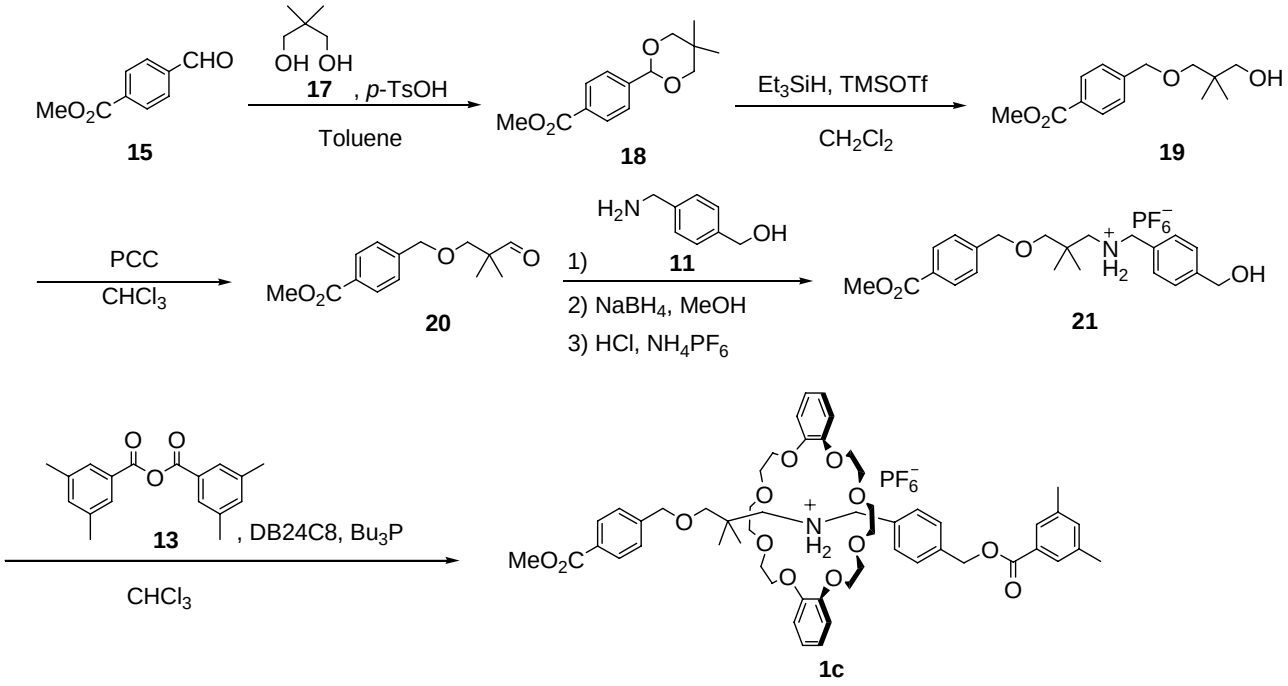
**Scheme S2**




**Ammonium salt (16).** A solution of **14** (1.56 g, 17.9 mmol) and **15** (2.94 g, 17.9 mmol) in toluene (50 mL) was refluxed for 2 h with azeotropic distillation. After toluene was evapolated *in vacuo*, the residue was dissolved in THF (100 mL). The solution was added dropwise to a suspension of lithium aluminum hydride (1.80 g, 48.0 mmol) in THF at 0 ºC, and the reaction mixture was refluxed for 3h. After addition of saturated sodium sulfate solution, the precipitate was filtered off and washed with ether. The combined filtrate was washed with water and brine, dried with anhydrous magnesium sulfate, and evaporated. The crude product was dissolved in 12 M hydrochloric acid, and was poured into saturated ammonium hexafluorophosphate solution. The precipitate was collected by filtration, washed with water, and dried *in vacuo* to give 4.05 g (63 % from **14**) of **16** as a white solid. $^{1}$H NMR (500 MHz, DMSO) δ 8.47 (brs, 2H), 7.48 (d, 2H, *J* = 8.3 Hz), 7.39 (d, 1H, *J* = 8.7 Hz) 4.53 (s, 2H), 4.15 (s, 2H), 2.67 (s, 2H), 0.94 (s, 9H) ppm. $^{13}$C NMR (125 MHz, DMSO) δ 143.63, 130.12, 129.50, 126.60, 62.48, 57.37, 51.10, 30.21, 27.06 ppm. mp 164-165 °C. HRMS (ESI-TOF) Calcd. for $C_{13}H_{22}N_1O_1$: 208.1696 ($[M\text{-}PF_6]^+$), Found: 208.1660 $[M\text{-}PF_6]^+$. Anal, calcd for $C_{46}H_{62}F_6NO_{10}P$: C 58.87, H 6.71, N 1.49; found: C 58.89, H 6.76, N 1.50.

**Rotaxane (1b).** To a solution of **16** (100 mg, 0.28 mmol) and DB24C8 (178 mg, 0.40 mmol) in dichloromethane (1.0 mL) were added 3,5-dimethylbenzoic anhydride **13** (211 mg, 0.40 mmol) and tributylphosphane (17 μL, 0.28 mmol). The reaction mixture was allowed to stand at room temperature over night, and was directly purified by preparative GPC (chloroform). The product was further recrystallized from ethanol/dicholoromethane to give 219 mg (85%) of rotaxane **1b** as a colorless prism.

**Scheme S3**




**Acetal (18).** A solution of **15** (25.0 g, 152 mmol), **17** (15.9 g, 152 mmol), and *p*-toluenesulfonic acid monohydrate (2.6 g, 15 mmol) in toluene (200 mL) was refluxed for 24 h with azeotropic distillation. The resulting solution was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulfate, and evaporated in vacuo. The residue was recrystallized from hexane/ethyl acetate to give 25.1 g (66%) of **18** as a plate crystal. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, 2H, *J* = 8.7 Hz), 7.57 (d, 2H, *J* = 8.7 Hz), 5.39 (s, 1H), 3.88 (s, 3H) 3.75 (d, 2H, *J* = 11.0 Hz), 3.62 (d, 2H, *J* = 11.0 Hz), 1.27 (s, 3H), 0.77 (s, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.70, 143.10, 130.40, 129.51, 126.22, 100.82, 77.56, 51.99, 30.17, 22.97, 21.76 ppm. mp 107-108 °C. ESI-MS m/z 273.1 $[M+Na]^+$.

**Alcohol (19).** A solution of trimethylsilyl triflate (44 mg, 0.2 mmol) in dichloromethane at 0 ºC under nitrogen atomosphere was added triethylsilane (3.26 g, 28 mmol) and **18** (5.00 g, 20 mmol), and the reaction mixture was stirred at room temperature for 24 h. After dillution by ethyl acetate, the solution was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulfate, and evaporated in vacuo. The residue was chromatographed silica gel (eluent: ethyl acetate/hexane = 1/4 (v/v)) to give 1.63 g (33%) of **19** as a colorless oil. $^{1}$H NMR (400 MHz,$CDCl_3$, rt) δ 8.02 (d, 2H, *J* = 8.0 Hz), 7.39 (d, 2H, *J* = 8.0 Hz), 4.57 ( s, 2H), 3.92 (s, 3H) 3.47 (brs, 2H), 3.31 (s, 2H), 1.29 (s, 3H), 0.94 (s, 6H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.03, 143.63, 129.86, 129.54, 127.13, 79.42, 73.00, 71.40, 52.20, 36.50, 21.93 ppm. HRMS (ESI-TOF) Calcd. for $C_{14}H_{20}NaO_4$: 275.1259 ($[M+Na]^+$), Found: 275.1265 $[M+Na]^+$.

**Aldehyde (20).** To a solution of **19** (1.51 g, 6.0 mmol) in dichloromethane (6 mL) was added pyridinium chlorochromate (1.35 g, 6.3 mmol) at room temperature for 6h. The precipitate was

filtered off through Celite®, and the filtrate was evaporated in vacuo. The residue was purified by silica gel column chromatography (eluent: ethyl acetate/hexane = 1/4 (v/v)) to give 1.17 g (78%) of **20** as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$, rt) δ 9.58 (s, 1H), 8.01 (s, 2H, *J* = 8.0 Hz), 7.36 (s, 2H, *J* = 8.0 Hz), 4.56 (s, 2H), 3.91 (s, 3H), 3.47 (s, 2H), 1.11 (s, 6H) ppm. ESI-MS (internal standard; reserpine) m/z 273.1 $[M+Na]^+$.

**Ammonium salt (21).** A solution of **20** (1.00 g, 4.0 mmol) and **11** (548 mg, 4.0 mmol) in toluene (100 mL) was refluxed for 4 h with azeotropic distillation. After toluene was evapolated *in vacuo*, the residue was dissolved in methanol (50 mL). To this solution sodium tetrahydroborate (453 mg, 12.0 mmol) was added, and the reaction mixture was stirred at room temperature for 20 h. After methanol was evapolated *in vacuo*, the residue was dissolved in ethyl acetate. The solution was washed with water, dried over anhydrous magnesium sulfate, and evaporated in vacuo. The crude product was dissolved in methanol and 3 M hydrochloric acid (1.0 mL), and was poured into saturated ammonium hexafluorophosphate solution. The organic layer was extracted with ethyl acetate, washed with water, dried over anhydrous magnesium sulfate, and evaporated in vacuo to give 1.76 g (85%) of **21** as an white solid. $^1$H NMR (500 MHz, $CD_3CN$) δ 7.95 (d, 2H, *J* = 8.3 Hz ), 7.38 (d, 2H, *J* = 8.3 Hz ), 7.33 (d, 2H, *J* = 8.3 Hz ), 7.27 (d, 2H, *J* = 8.3 Hz ), 4.59 (s, 2H), 4.55 (s, 2H), 4.12-4.10 (m, 2H), 3.89 (s, 3H), 3.40 (s, 2H), 3.01-2.98 (m, 2H), 1.01 (s, 6H) ppm. $^{13}$C NMR (125 MHz, $CD_3CN$) δ 167.68, 144.71, 143.80, 130.90, 130.53, 128.90, 128.23, 80.53, 73.67, 62.20, 58.02, 52.86, 52.79, 34.90, 22.98, 12, 137.44, 121.77, 121.69, 114.33, 112.81, 107.47, 77.41, 77.16, 76.90, 71.39, 71.17, 70.09, 69.96, 69.60, 69.33, 24.60 ppm. mp 88-90 °C. HRMS (ESI-TOF) Calcd. for $C_{22}H_{30}NO_4$: 372.2169 ($[M-PF_6]^+$), Found: 372.2135 $[M-PF_6]^+$.

**Rotaxane (1c).** To a solution of **21** (100 mg, 0.19 mmol) and DB24C8 (87 mg, 0.19 mmol) in dichloromethane (0.5 mL) were added 3,5-dimethylbenzoic anhydride **13** (160 mg, 0.57 mmol) and tributylphosphane (5.0 μL, 0.02 mmol). The reaction mixture was allowed to stand at room temperature over night, and was directly purified by preparative GPC (chloroform) to give 156 mg (75%) of rotaxane **1c** as a colorless prism.

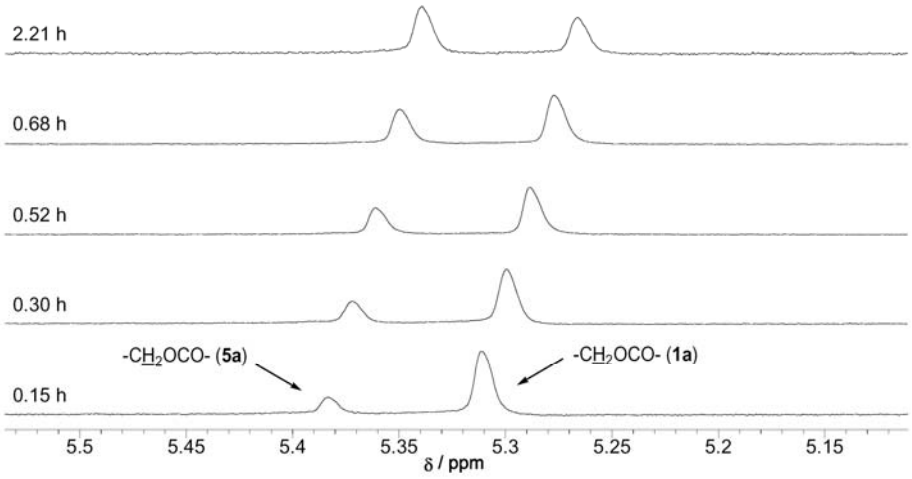



**Figure S-1.** Partial $^{1}$H NMR (500 MHz) spectra change for the progress of the decomposition of **1a** to form its components ( **5a** and DB24C8) in $CD_3CN$ at 333 K.

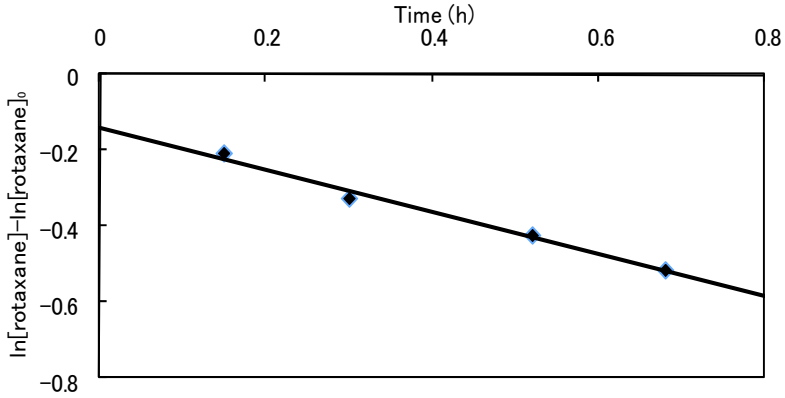



**Figure S-2.** First order kinetic plots of the decomposition of **1a** (●) at 333 K in $CD_3CN$.

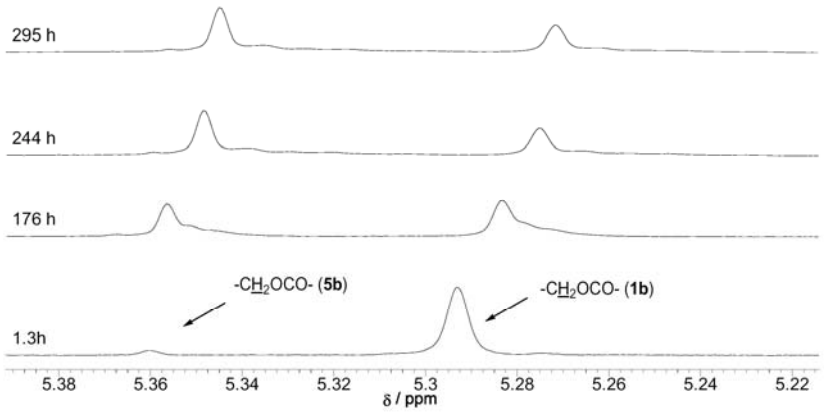



**Figure S-3.** Partial $^{1}$H NMR (500 MHz) spectra change for the progress of the decomposition of **1b** to form its components ( **5b** and DB24C8) in $CD_3CN$ at 333 K.

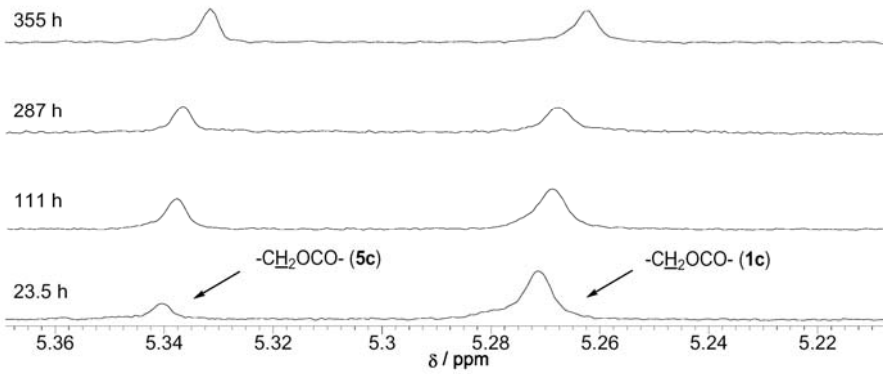



**Figure S-4.** Partial $^{1}$H NMR (500 MHz) spectra change for the progress of the decomposition of **1c** to form its components ( **5c** and DB24C8) in $CD_3CN$ at 333 K.

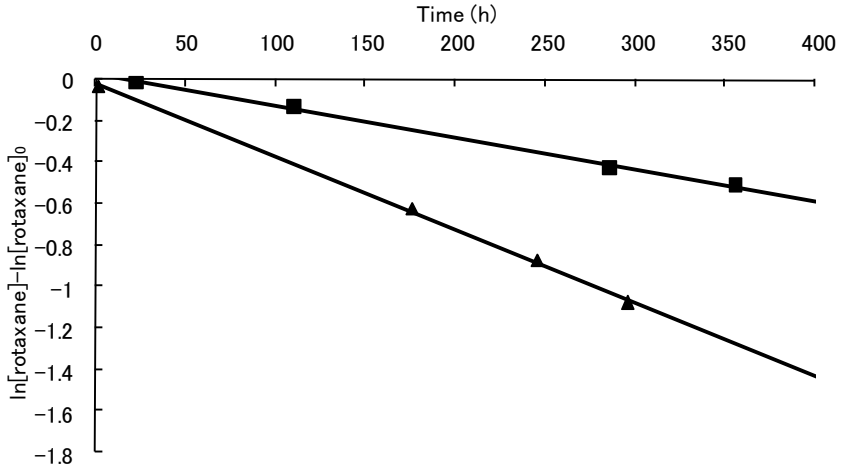
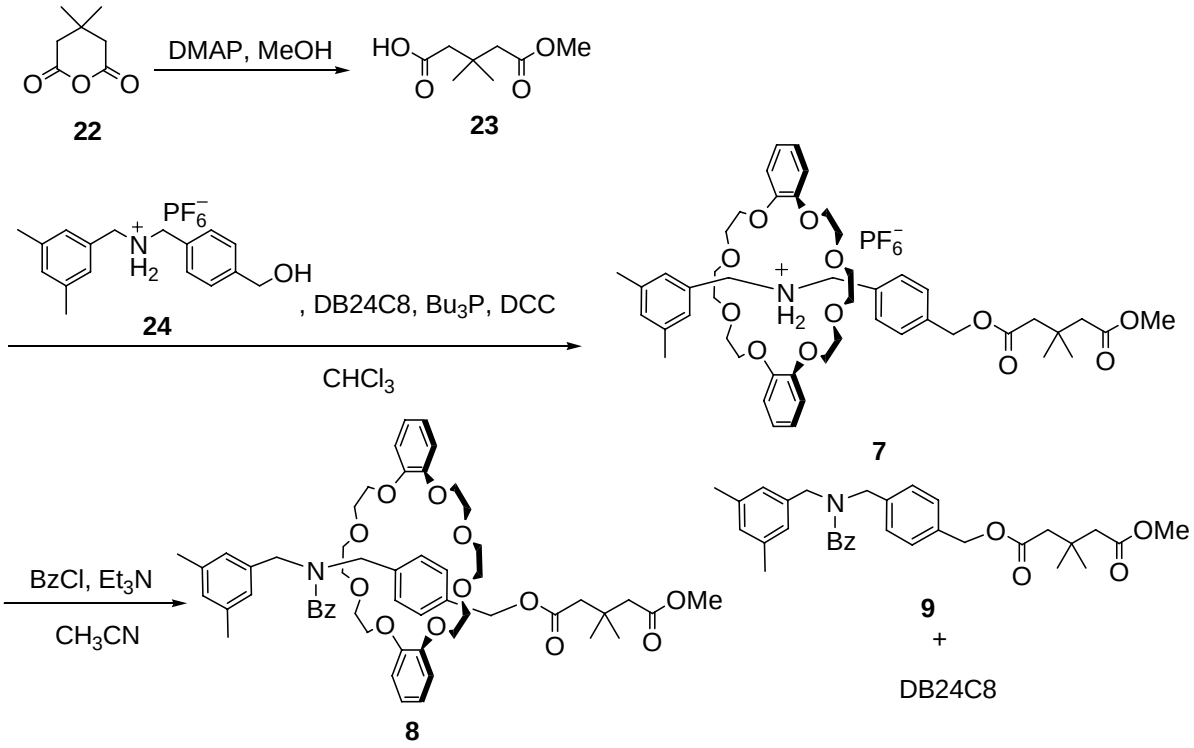



**Figure S-5.** First order kinetic plots of the decomposition of **1b** (■), and **1c** (▲) at 333 K in $CD_3CN$.

**Scheme S5**




**Carboxylic acid (23).** A solution of **22** (1.00 g, 7.0 mmol), DMAP (86 mg, 0.70 mmol), and triethylamine (1.0 mL, 7.0 mmol) in methanol (10 mL) at room temperature over night. . The residue was dissolved in ether and the solution was washed with 3M hydrochloric acid, dried over anhydrous magnesium sulfate, and evaporated in vacuo to give a 1.16 g of **23** (95%) as a colorless oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.88 (brs, 1H), 3.57-3.55 (m, 3H), 2.36-2.35 (m, 4H) 1.04-1.03 (m, 6H), ppm. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 177.41, 172.57, 51.28, 44.87, 44.78, 32.36, 27.56 ppm.

**Rotaxane 7**[3]**.** A solution of 100 mg (0.50 mmol) of DCC in chloroform (0.2 mL) was added to a solution of 50 mg (0.13 mmol) of **24**, 56 mg (0.53 mmol) of DB24C8, 44 mg (0.25 mmol) of **23**, and 38 μL (0.013 mmol) of tributylphosphane in chloroform (0.5 mL). After stirring at 0 ºC for 3h, the reaction mixture was directly purified by preparative GPC (eluent: chloroform) to isolate 98 mg (75%) of **7** as a colorless solid.

***N*-Acylated rotaxane (8)**[4]**.**

A solution of **7** (51 mg, 0.050 mmol), benzoyl chloride (14 mg, 0.10 mmol), and triethylamine (35 μL, 0.25 mmol) in DMF (1.0 mL) was allowed to stand at 0 ºC for 0.5 h. The reaction mixture was diluted with ethyl acetate. The solution was washed with 1M hydrochloric acid, 5% aqueous sodium carbonate, then brine, dried over magnesium sulfate, and evaporated in vacuo. The crude product was purified by preparative GPC (eluent: chloroform).

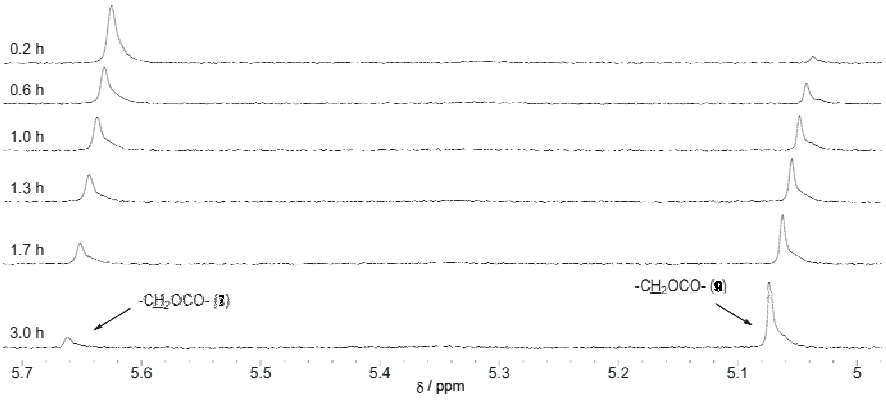



**Figure S-6.** Partial $^1$H NMR (500 MHz) spectra change for the progress of the decomposition of **8** to form its components ( **9** and DB24C8) in $CD_3CN$ at 333 K.

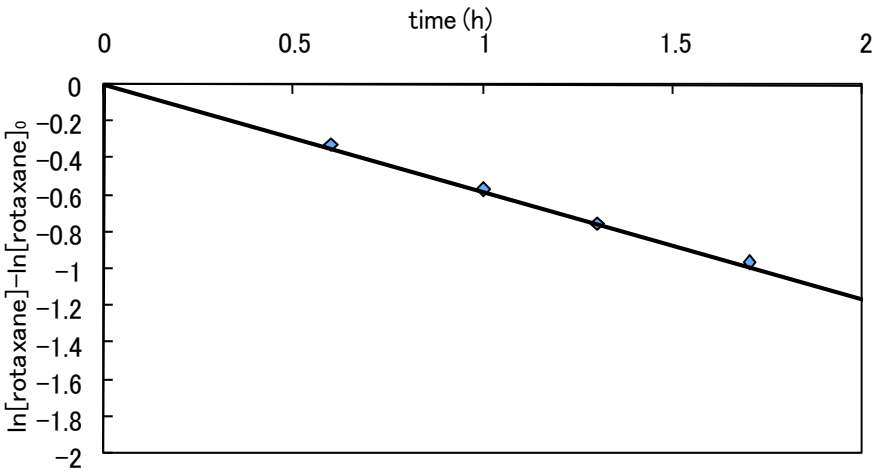



**Figure S-7.** First order kinetic plots of the decomposition of **8** (○) at 333 K in $CD_3CN$.

**References**

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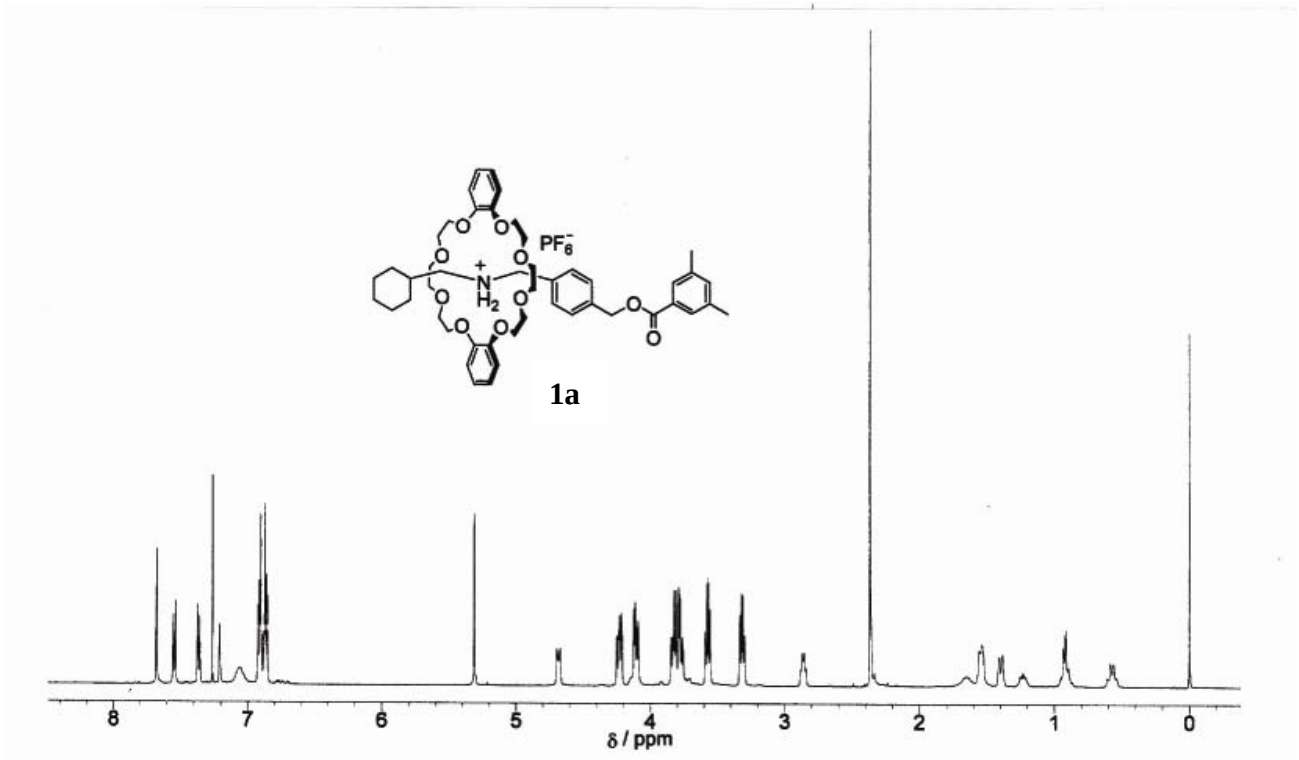
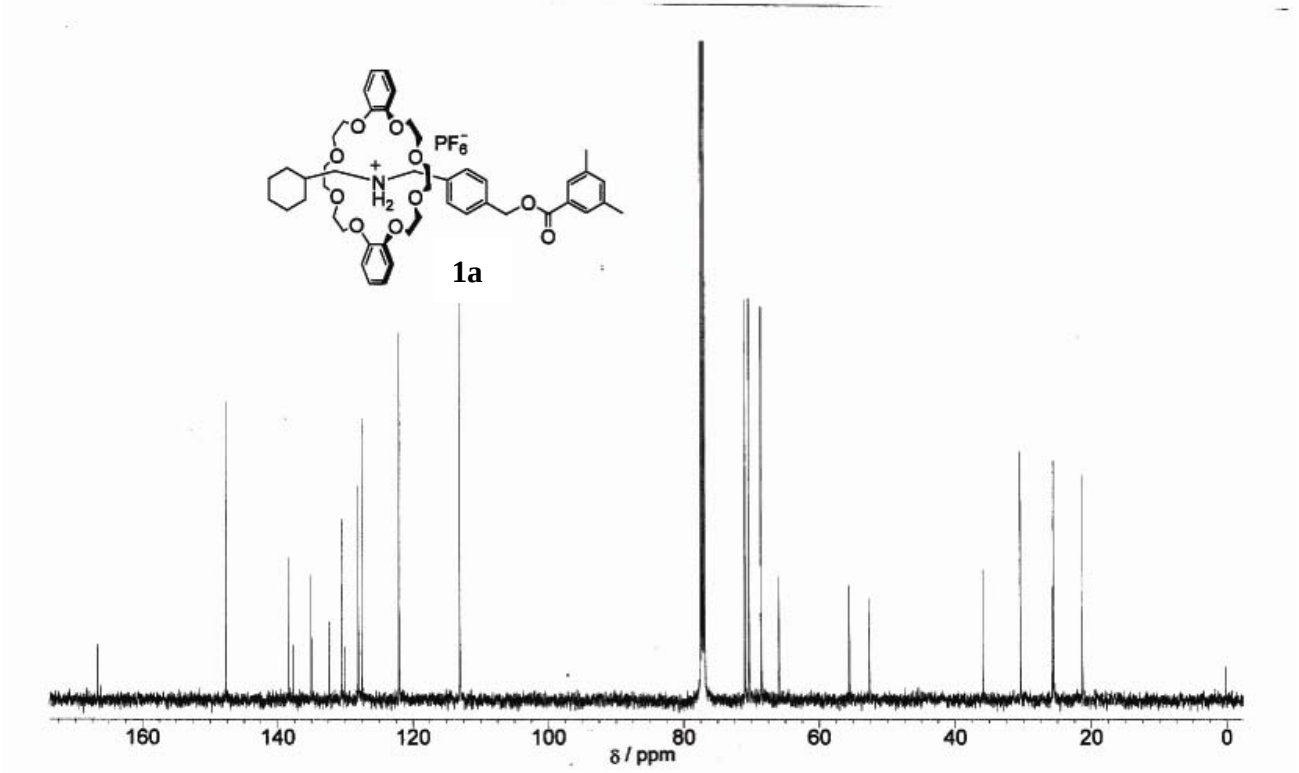
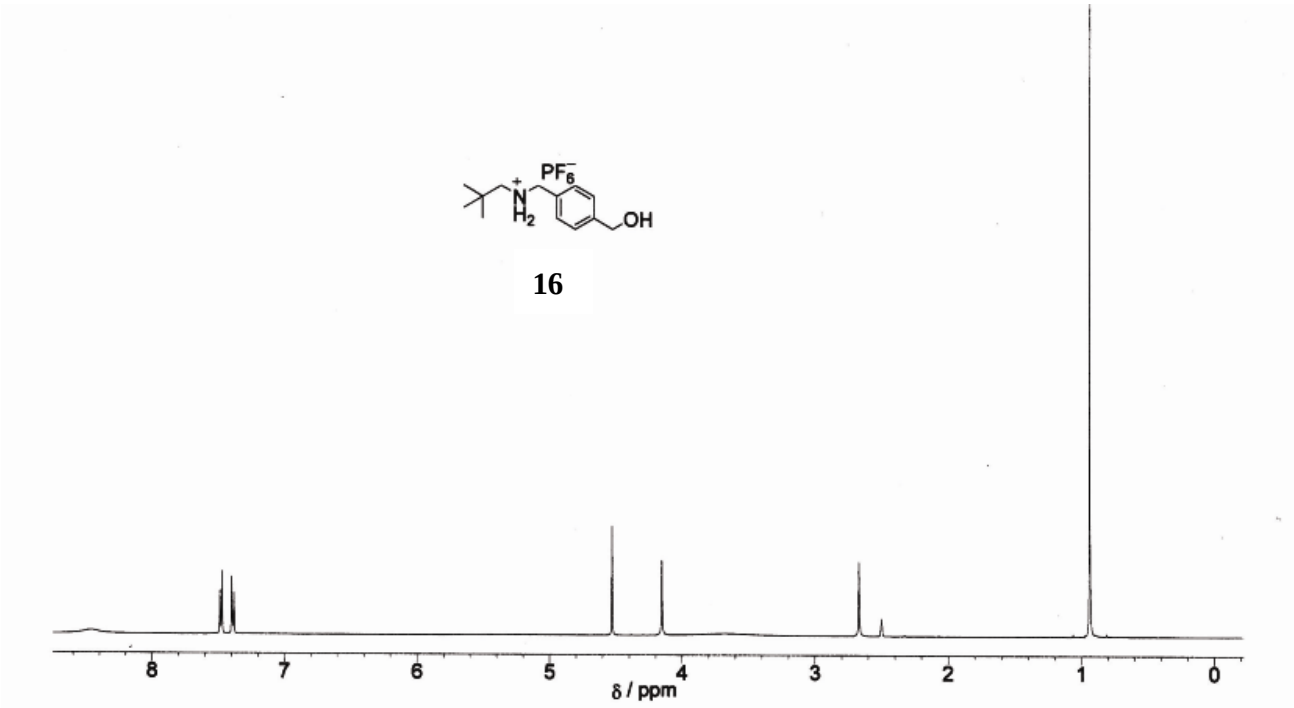
2) Y. Tachibana, H. Kawasaki, N. Kihara, T. Takata, *J. Org. Chem.* **2006**, *71*, 5093-5104.
3) Y. Makita, N. Kihara, T. Takata, *Chem. Lett*. **2007**, 102-103.
4) Y. Tachibana, N. Kihara, Y. Furusho, T. Takata, *Org. Lett.* **2004**, *6,* 4507-4509.




$^{1}$H NMR spectrum of rotaxane **1a**.

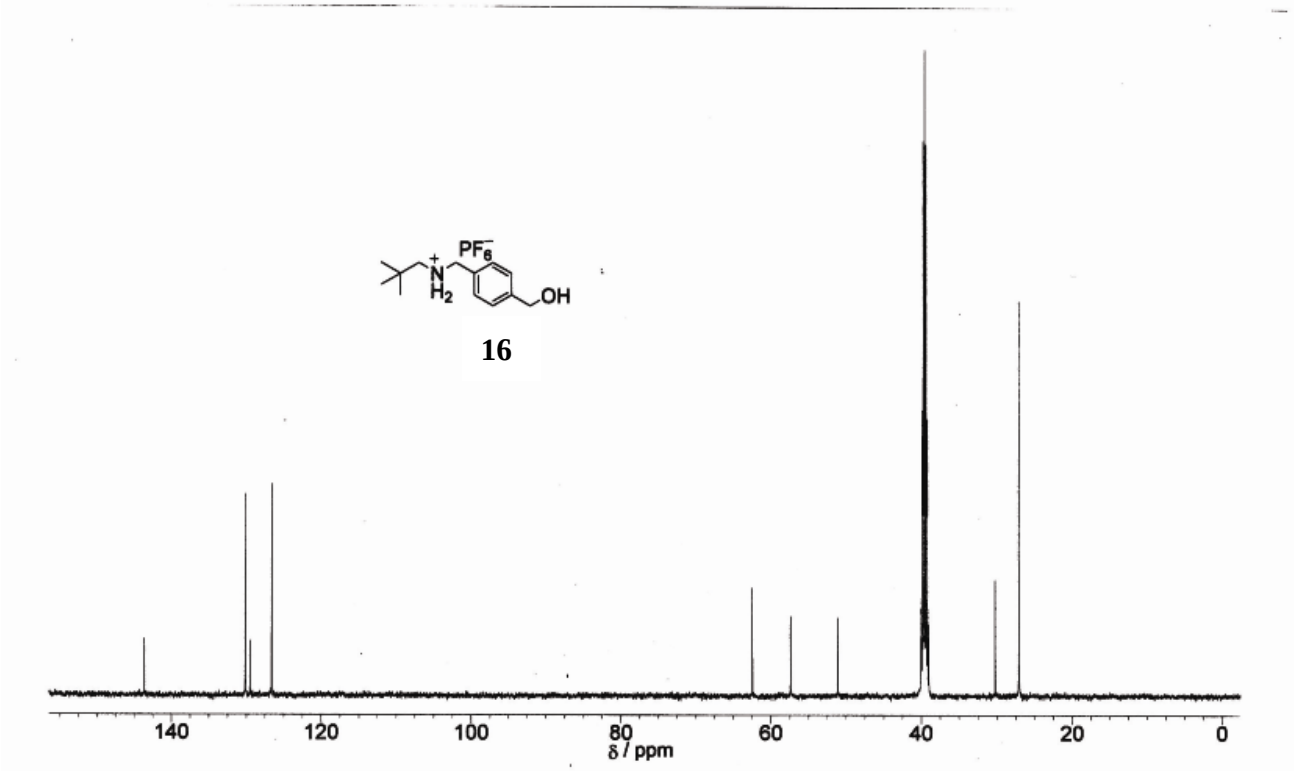



$^{13}$C NMR spectrum of rotaxane **1a**.



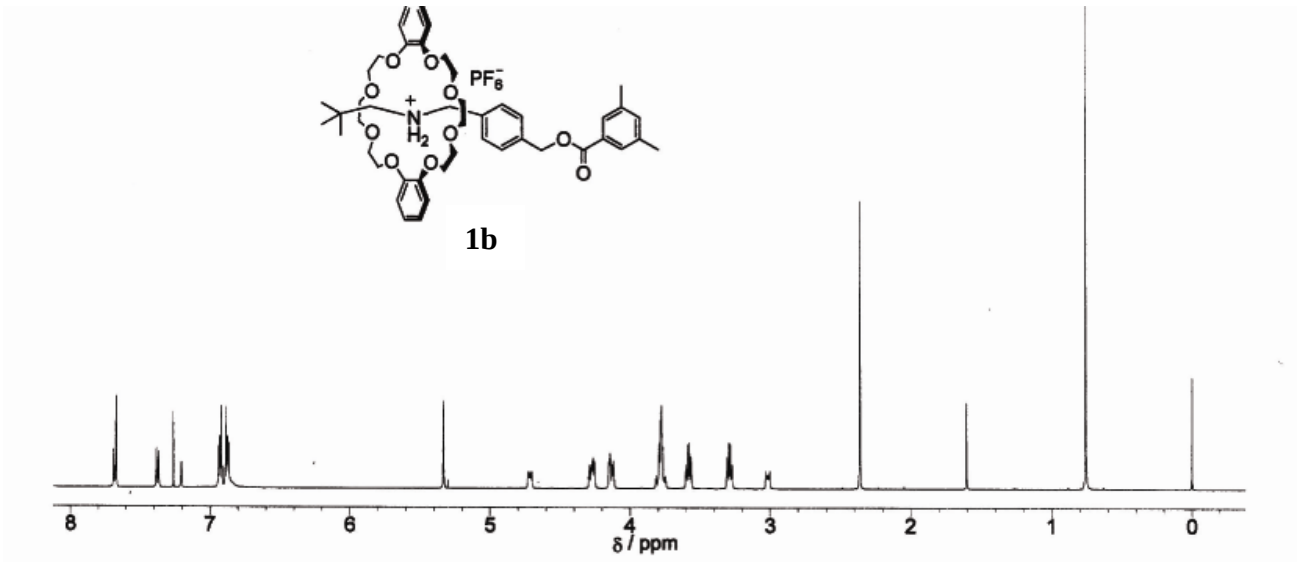

**16**

$^{1}$H NMR spectrum of ammonium salt **16**.

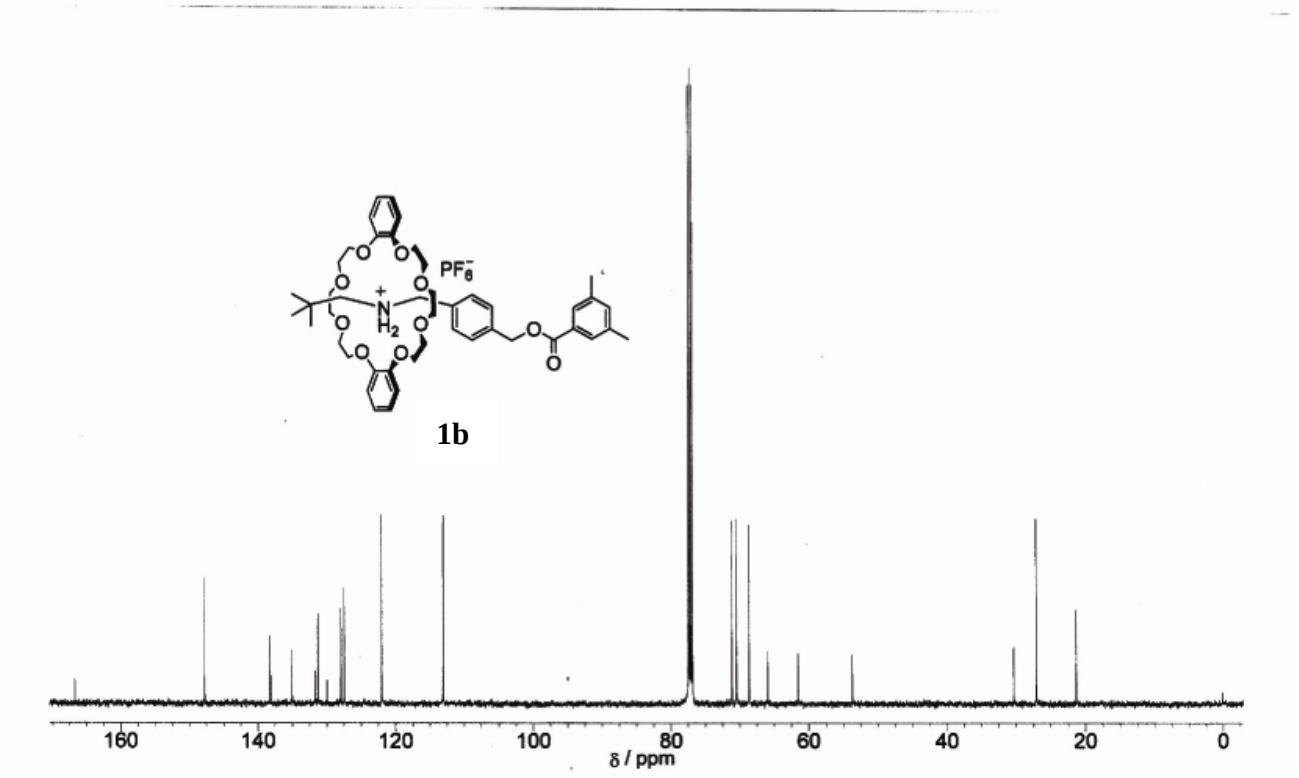



**16**

$^{13}$C NMR spectrum of ammonium salt **16**.




$^{1}$H NMR spectrum of rotaxane **1b**.

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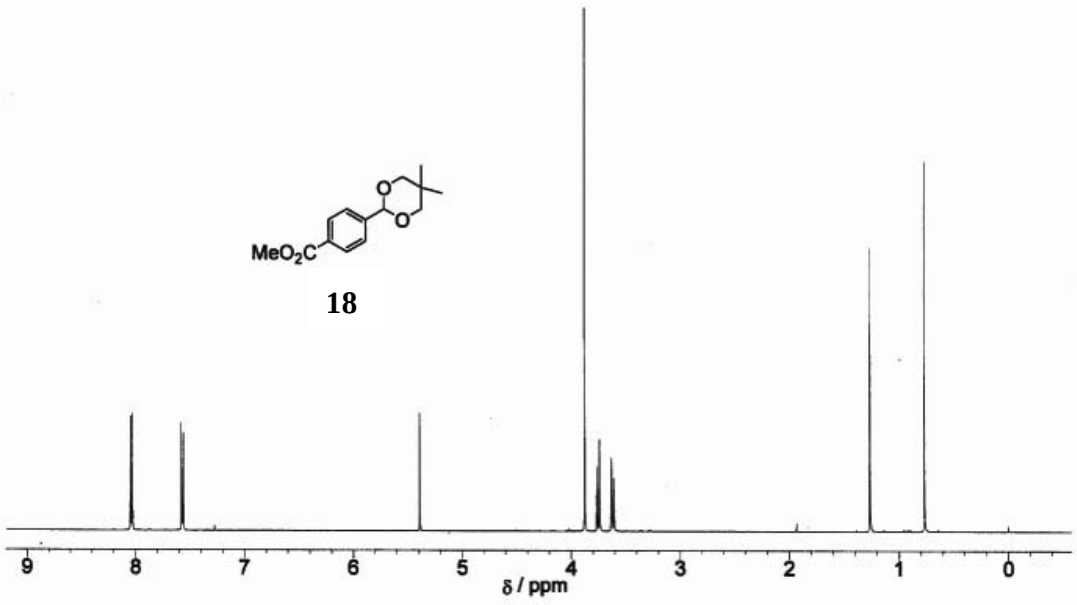
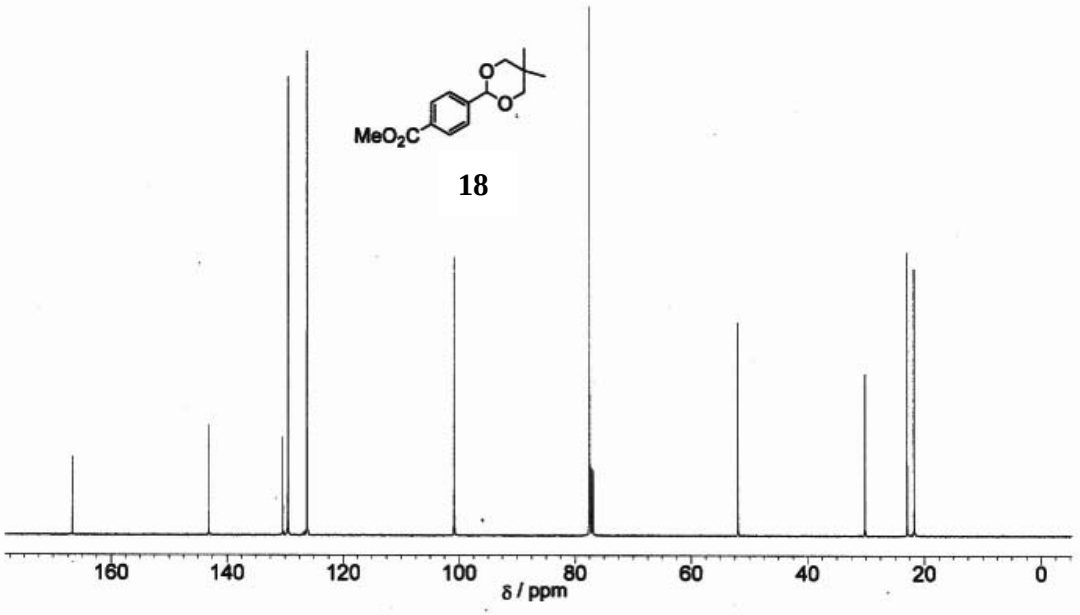
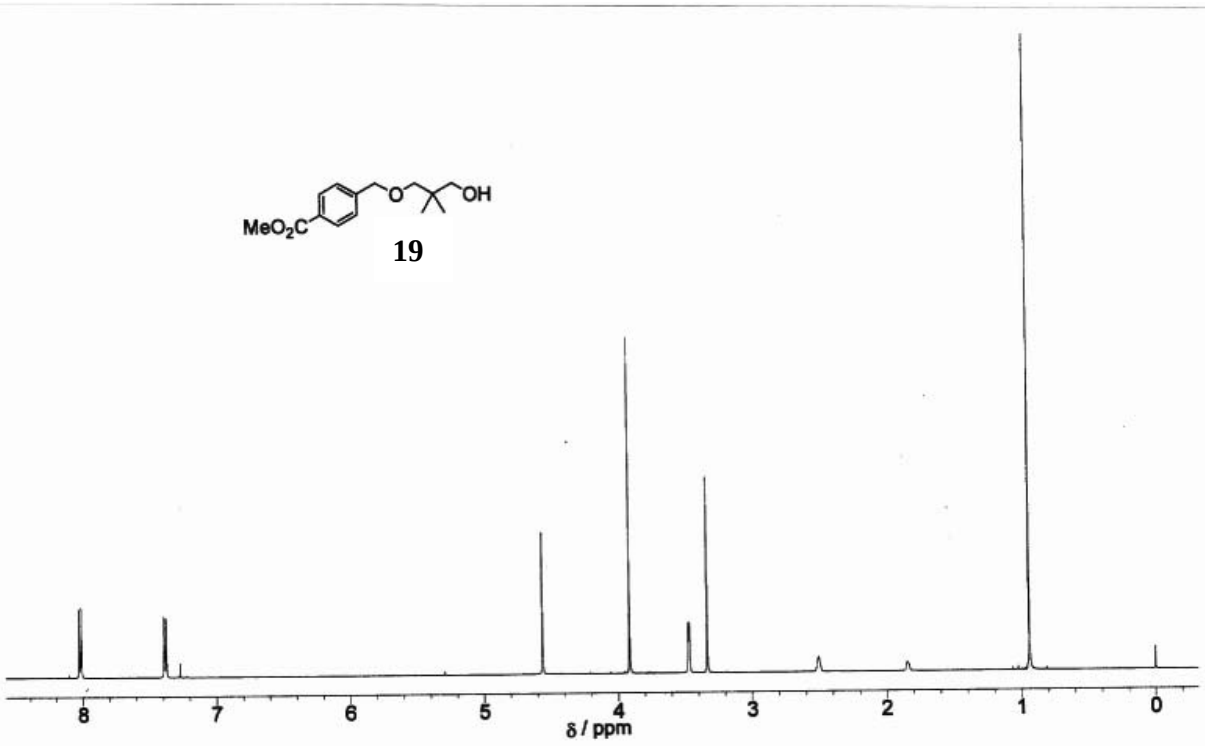


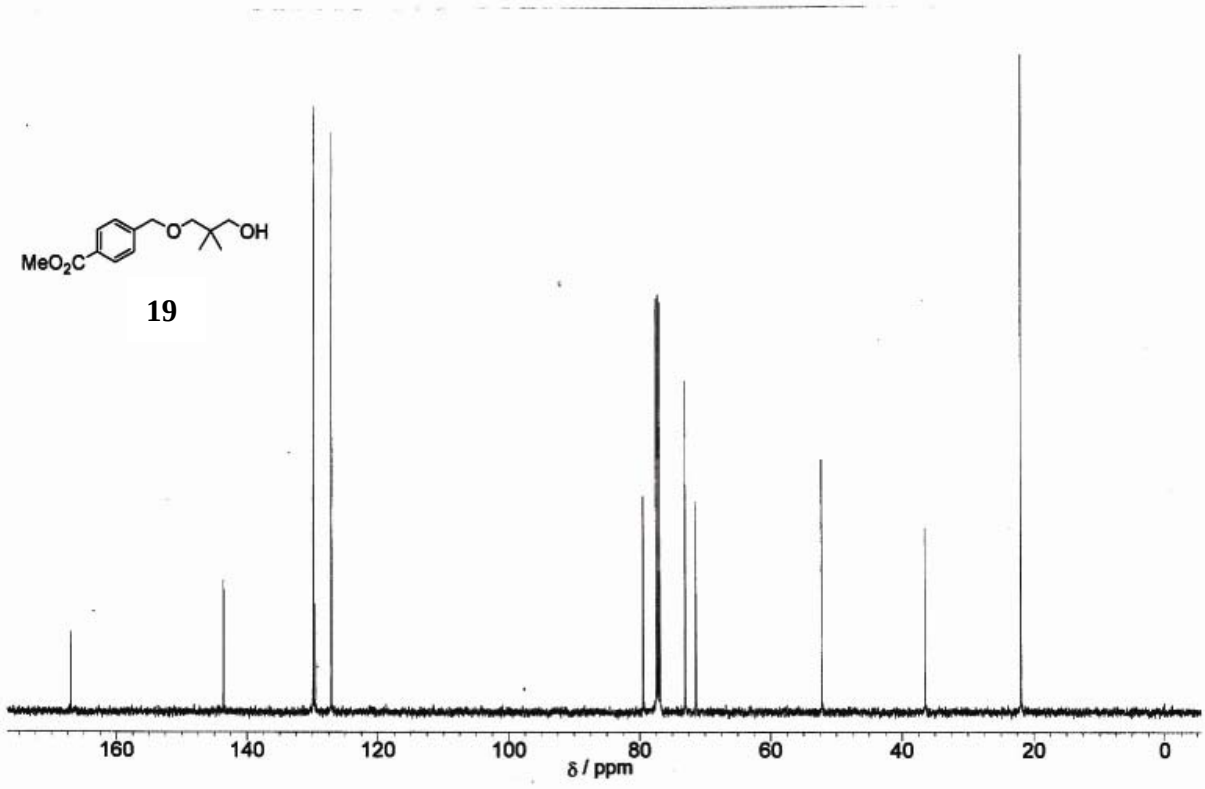

$^{1}$H NMR spectrum of acetal **18**.



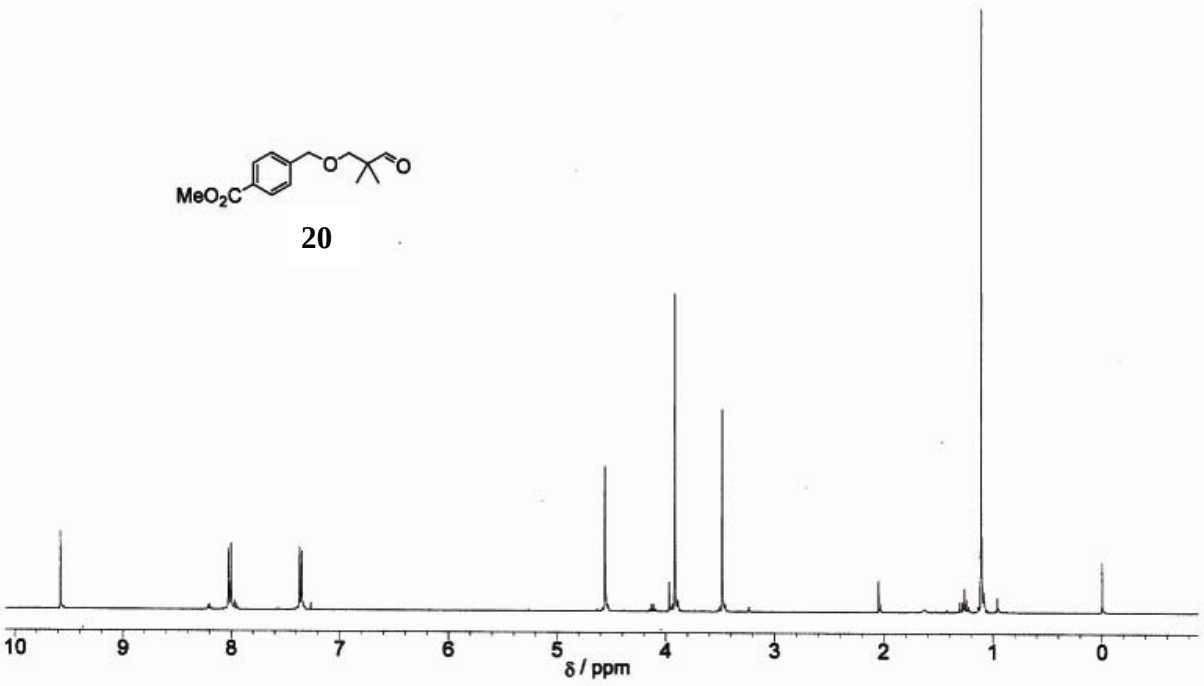

$^{13}$C NMR spectrum of acetal **18**.




$^{1}$H NMR spectrum of alcohol **19**.

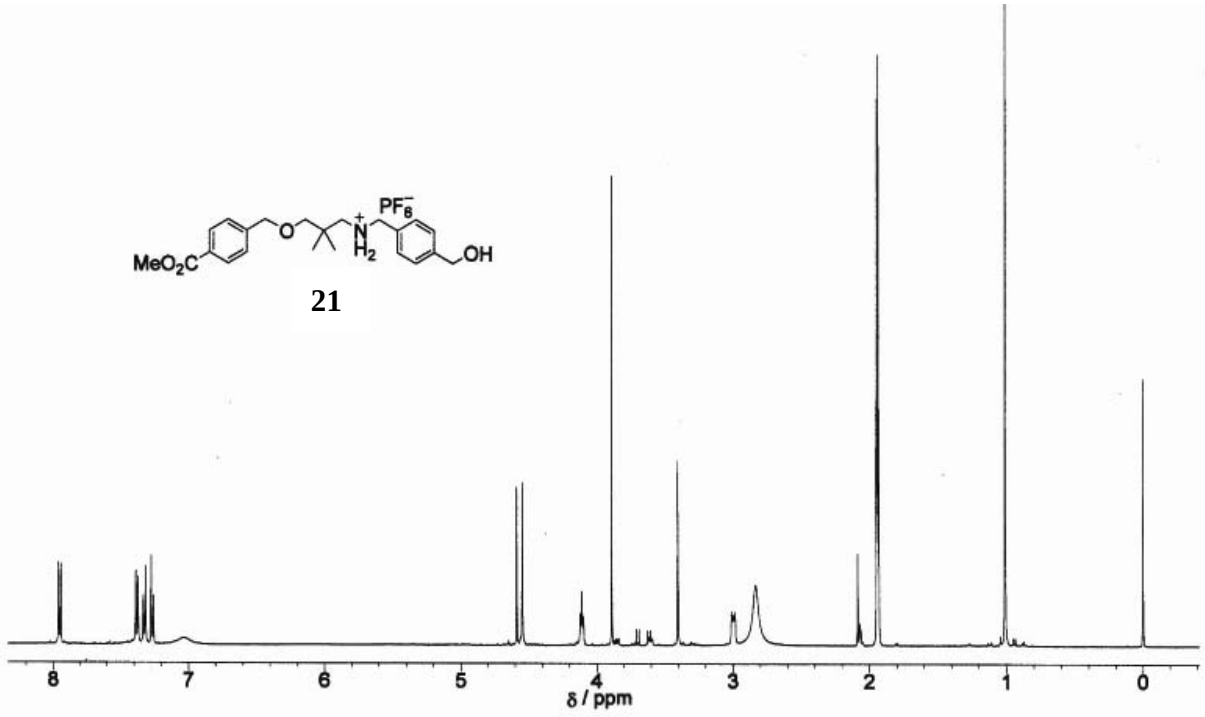



$^{13}$C NMR spectrum of alcohol **19**.

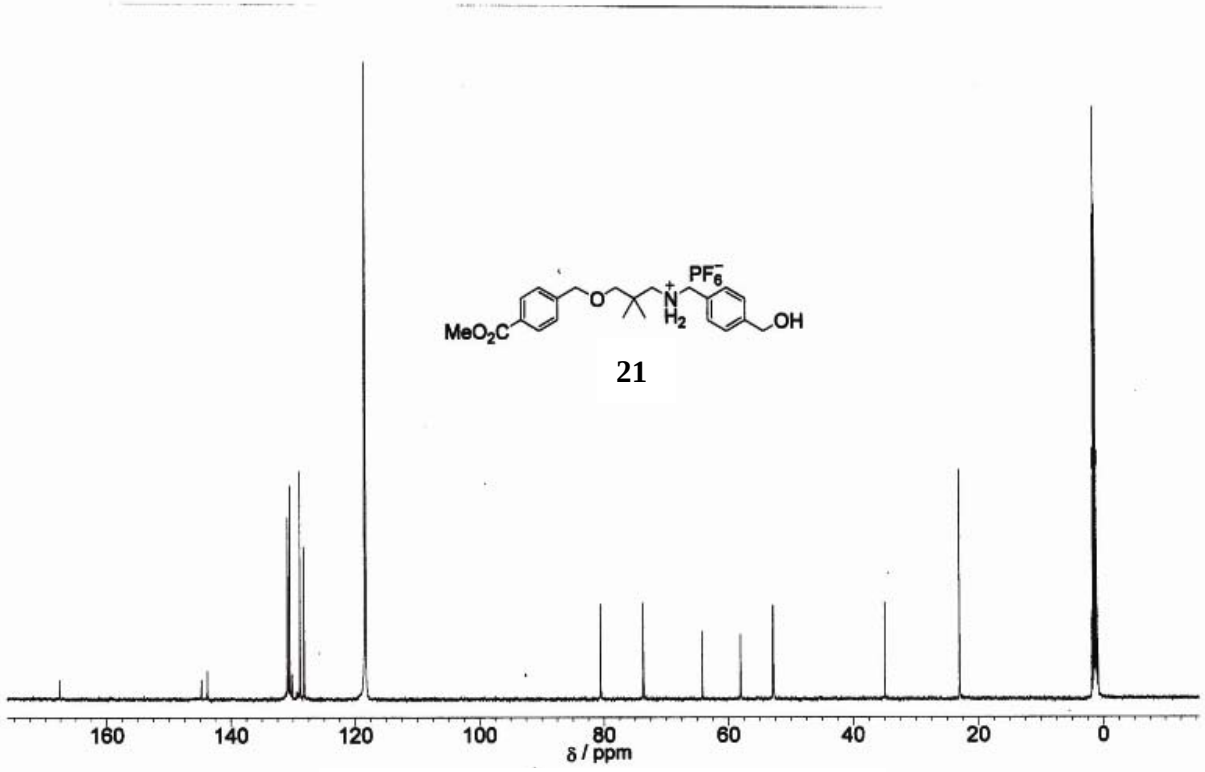



**20**

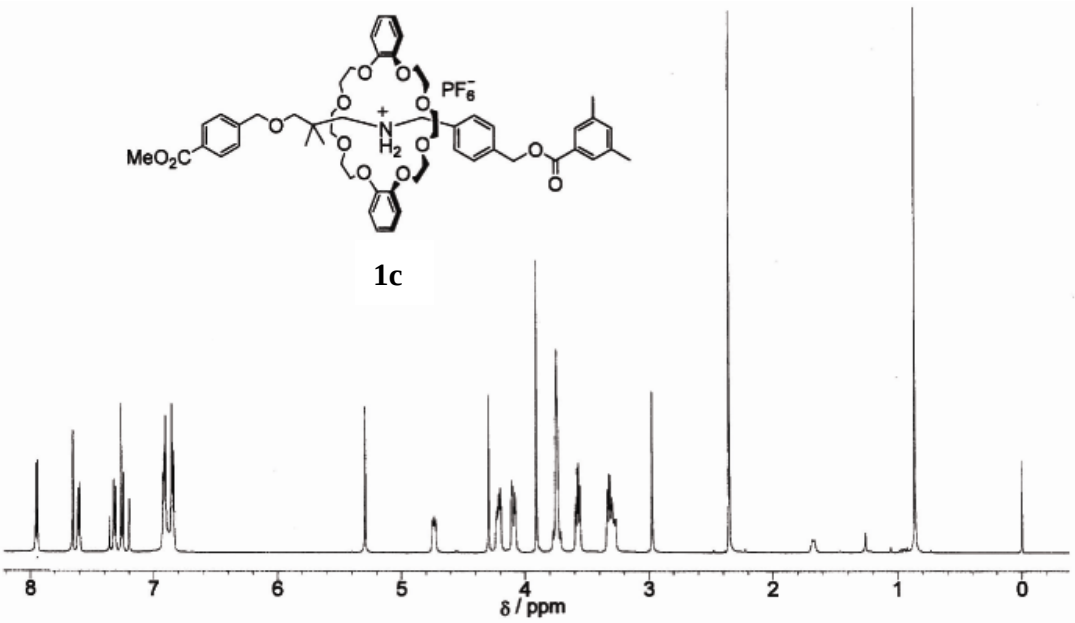
$^{1}$HNMR spectrum of aldehyde **20**.



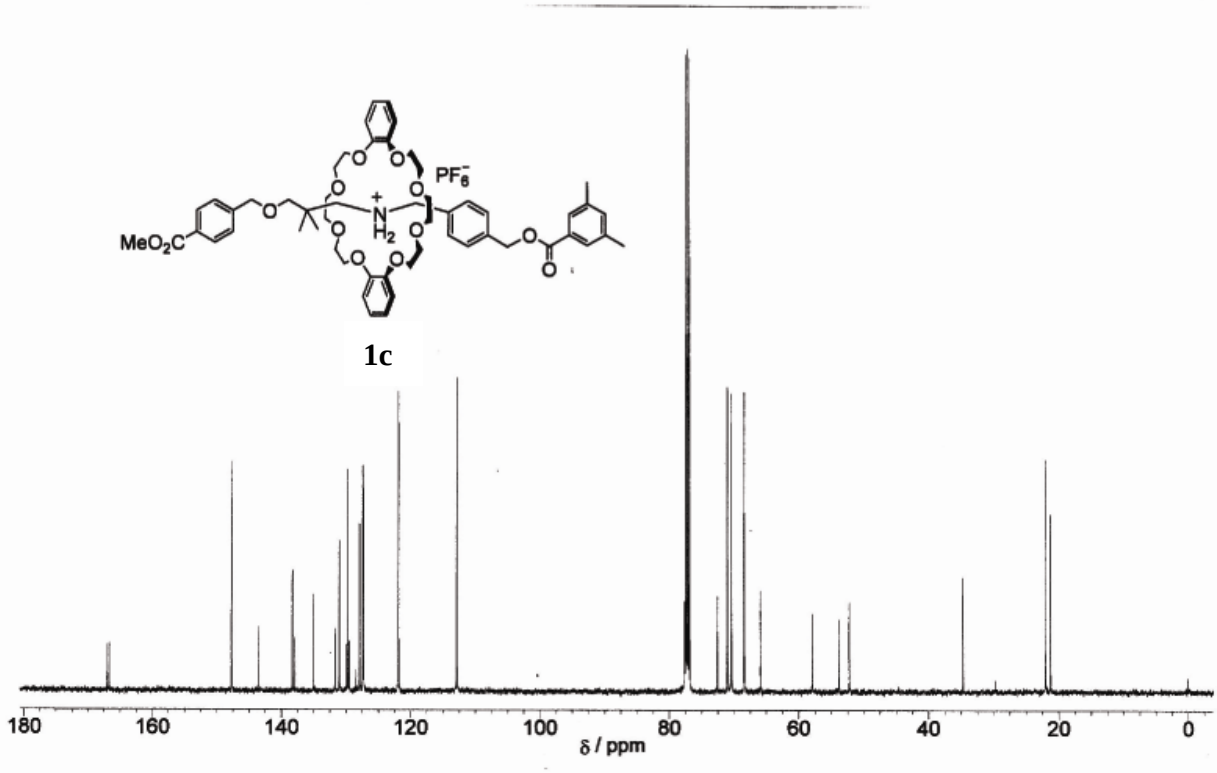

$^{1}$H NMR spectrum of ammonium salt **21**.



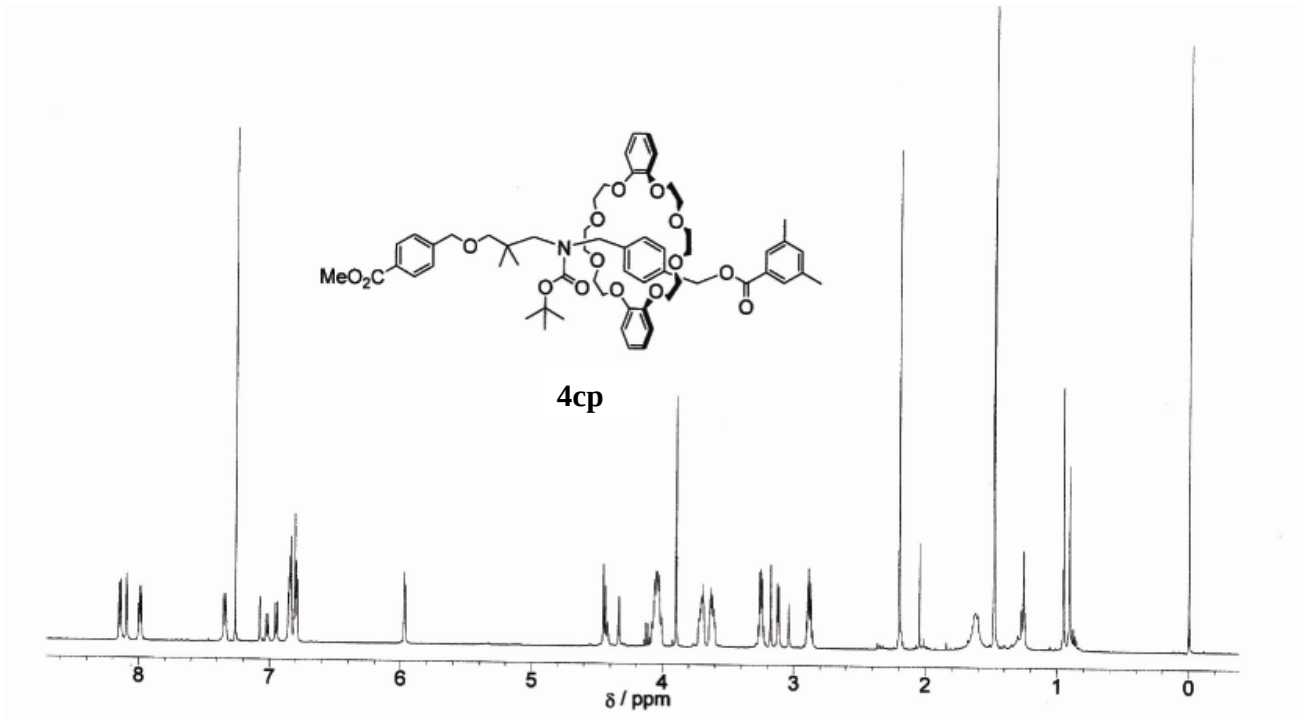

$^{13}$C NMR spectrum of ammonium salt **21**.



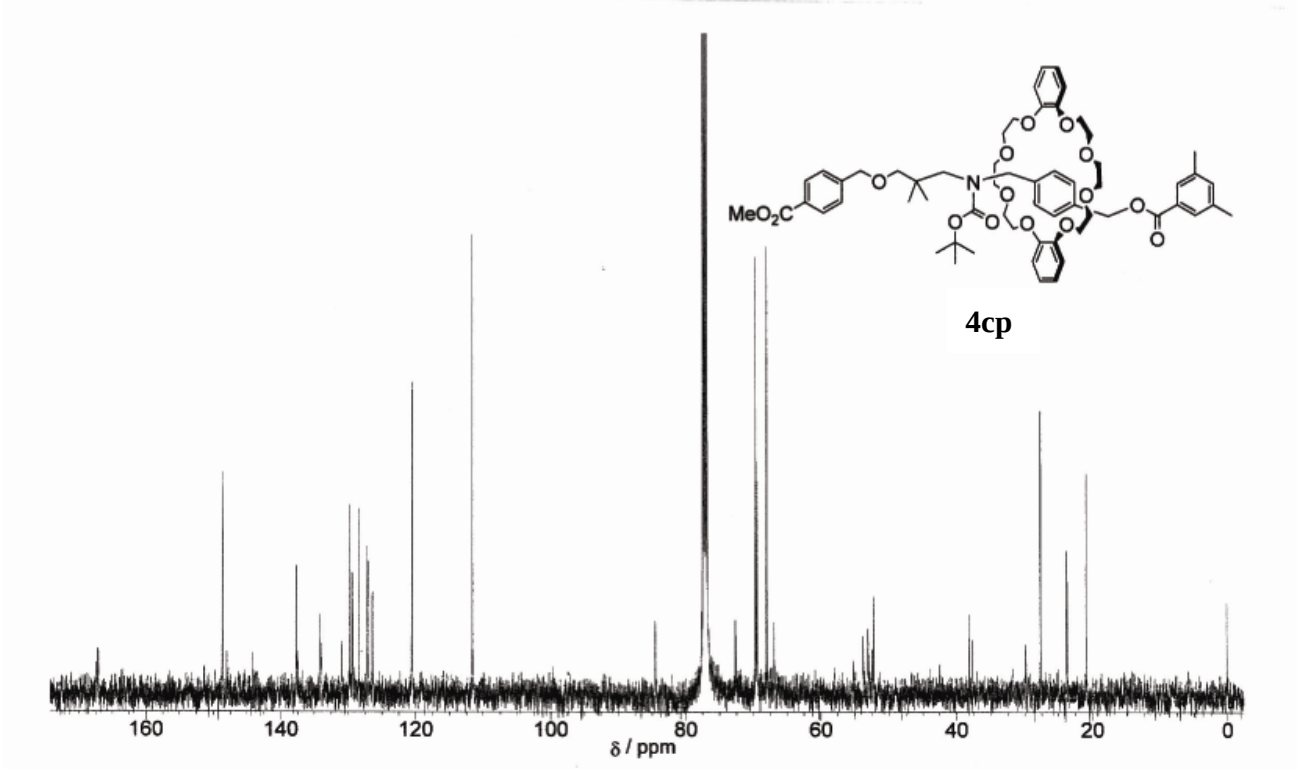

$^{1}$H NMR spectrum of rotaxane **1c**.



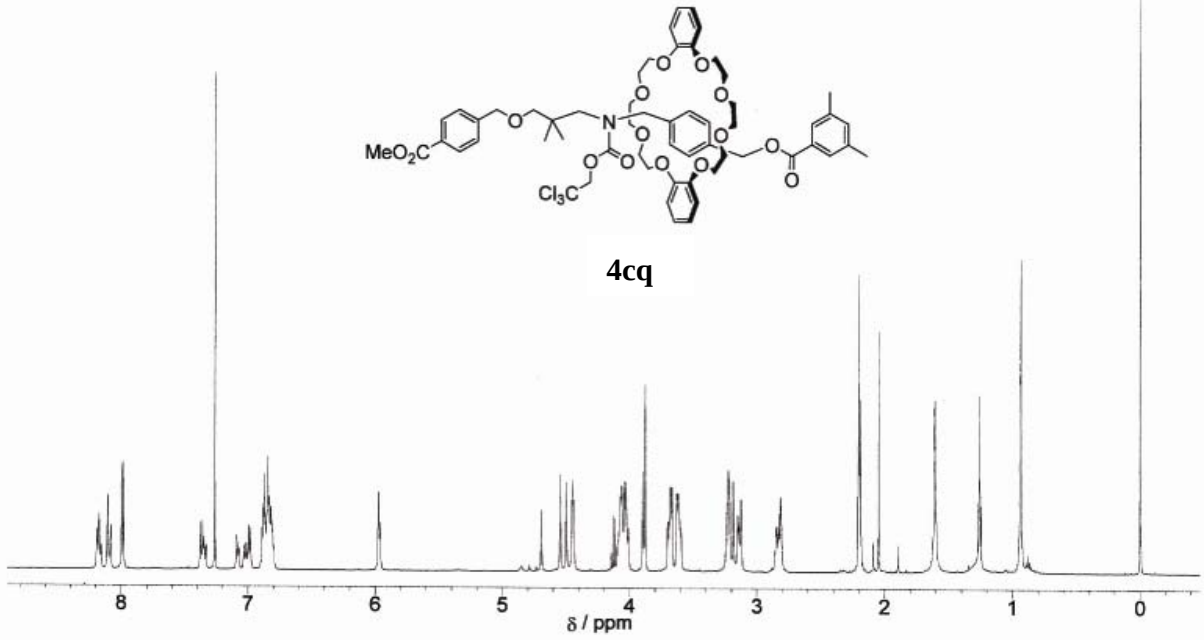

$^{13}$C NMR spectrum of rotaxane **1c**.



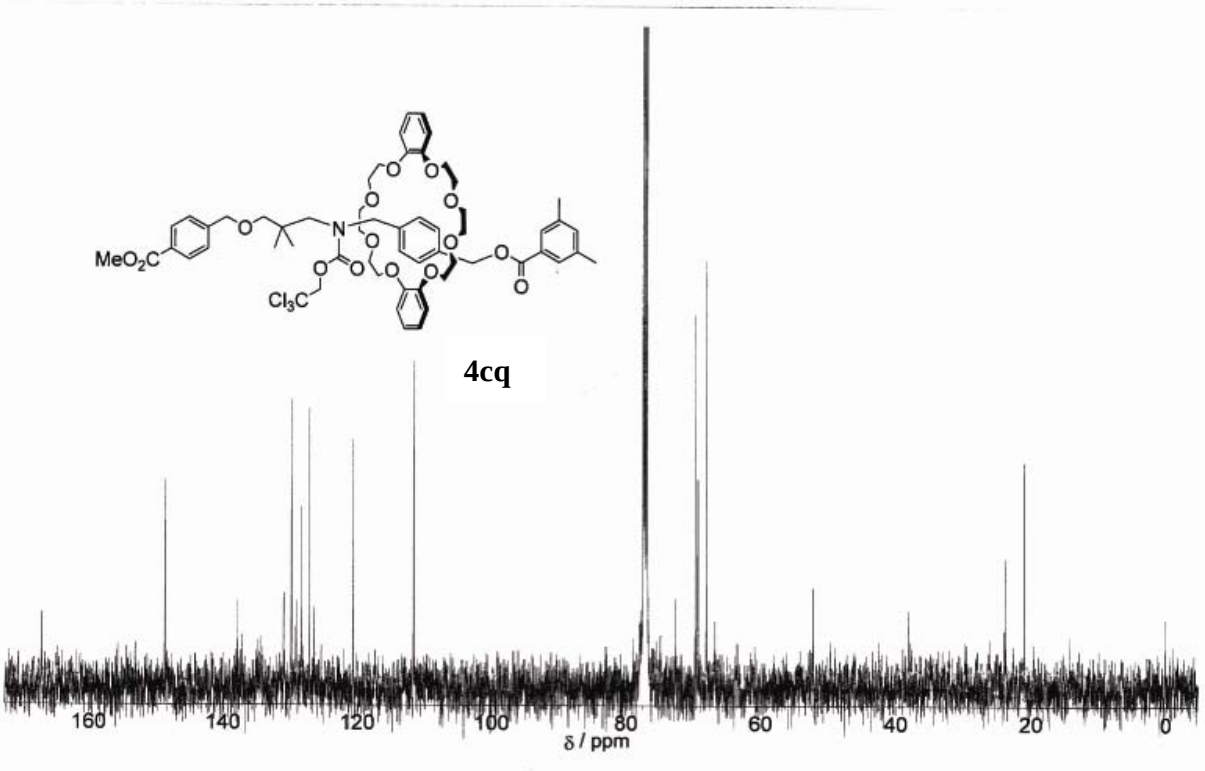

$^{1}$H NMR spectrum of *N*-aclylated rotaxane **4cp**.



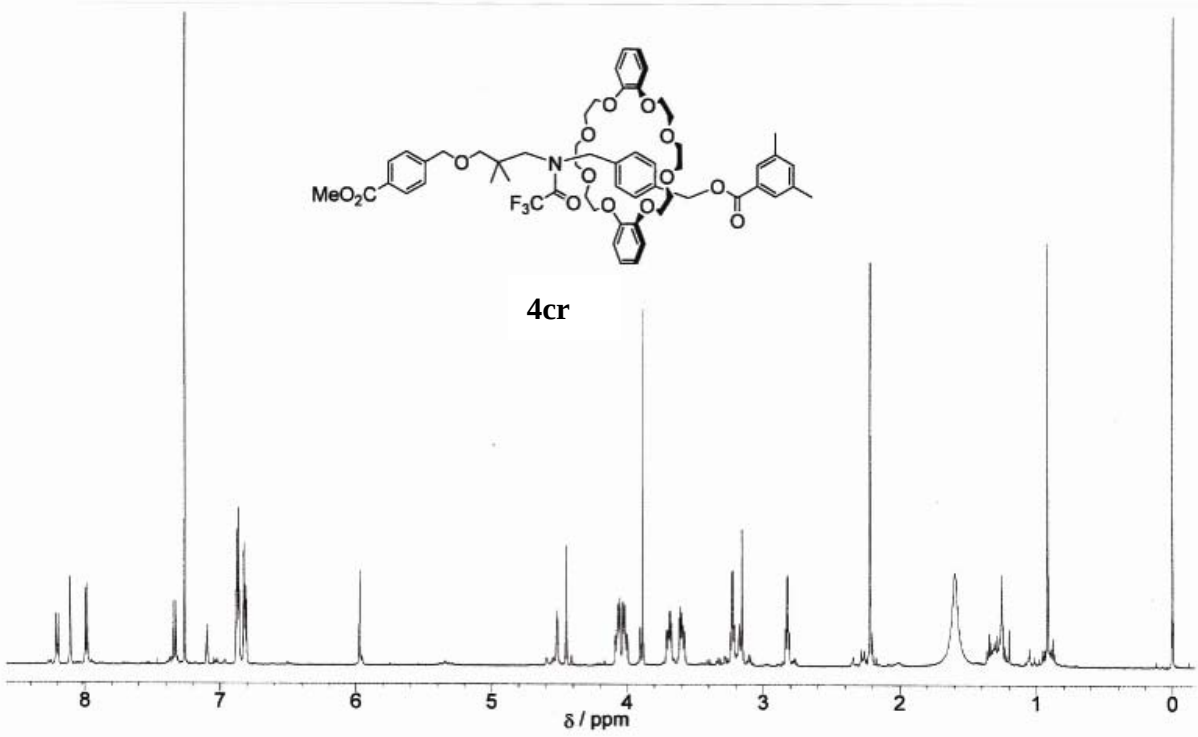

$^{13}$C NMR spectrum of *N*-aclylated rotaxane **4cp**.




$^{1}$H NMR spectrum of *N*-aclylated rotaxane **4cq**

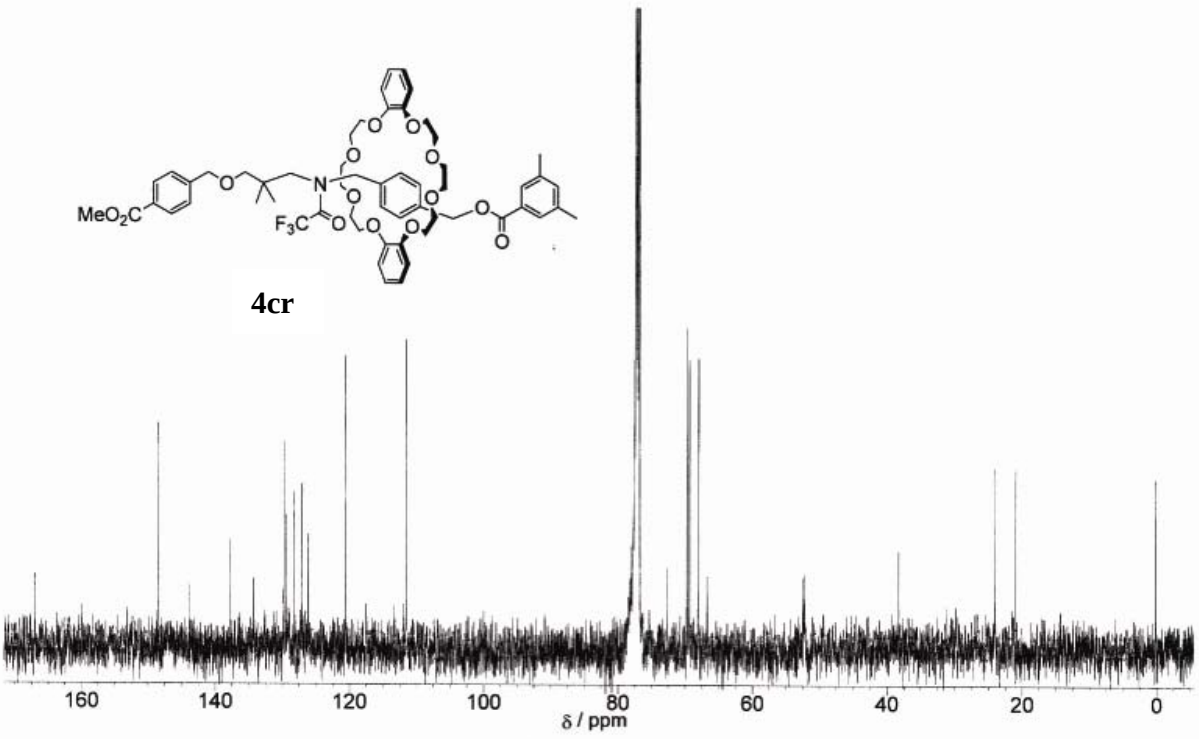



$^{13}$C NMR spectrum of *N*-aclylated rotaxane **4cq**



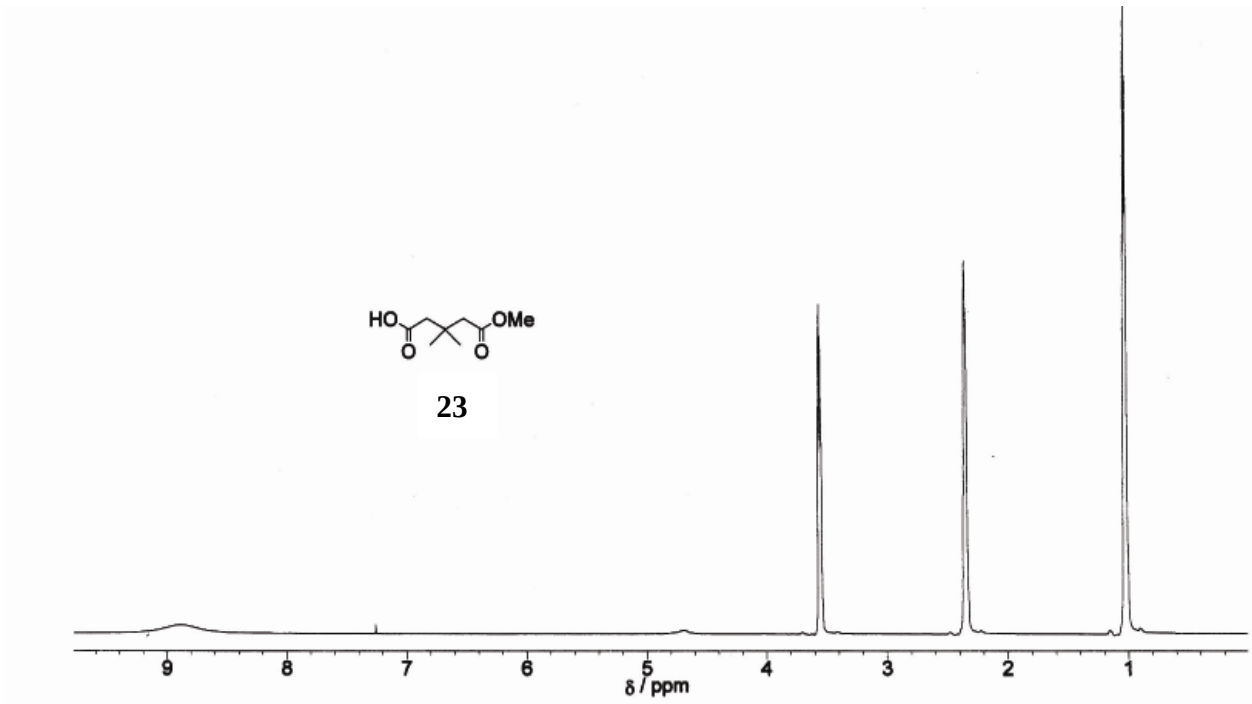

**4cr**

$^{1}$H NMR spectrum of *N*-aclylated rotaxane **4cr**.



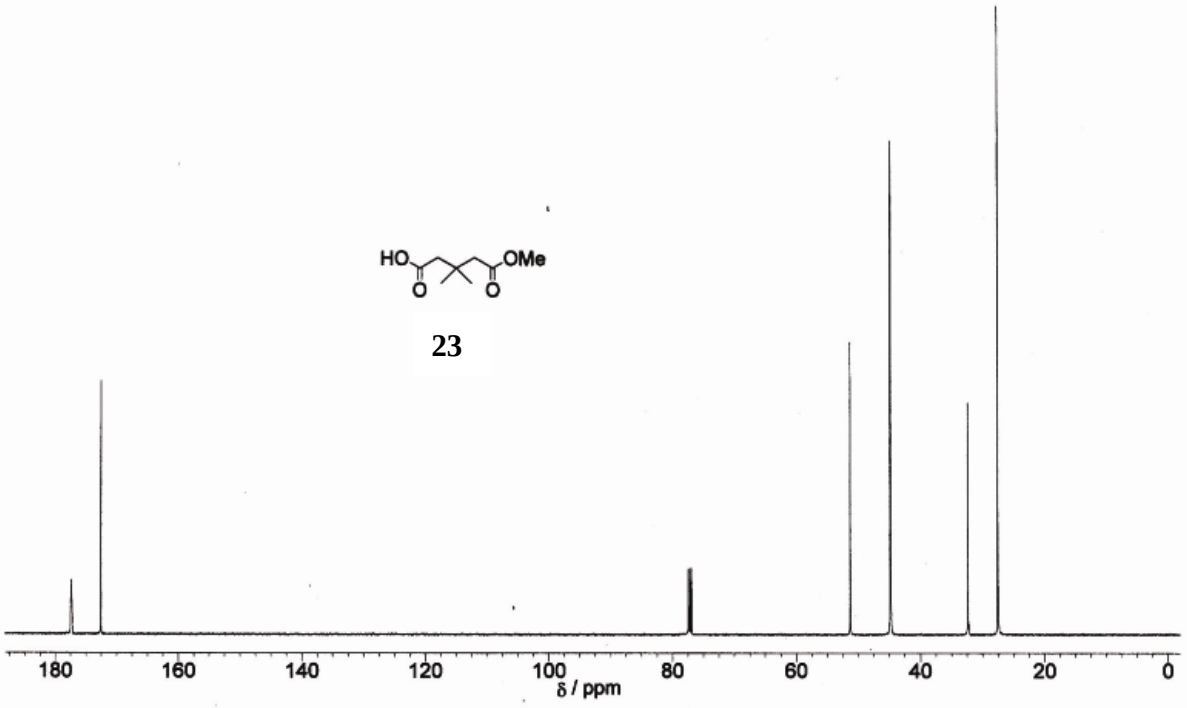

**4cr**

$^{13}$C NMR spectrum of *N*-aclylated rotaxane **4cr**.



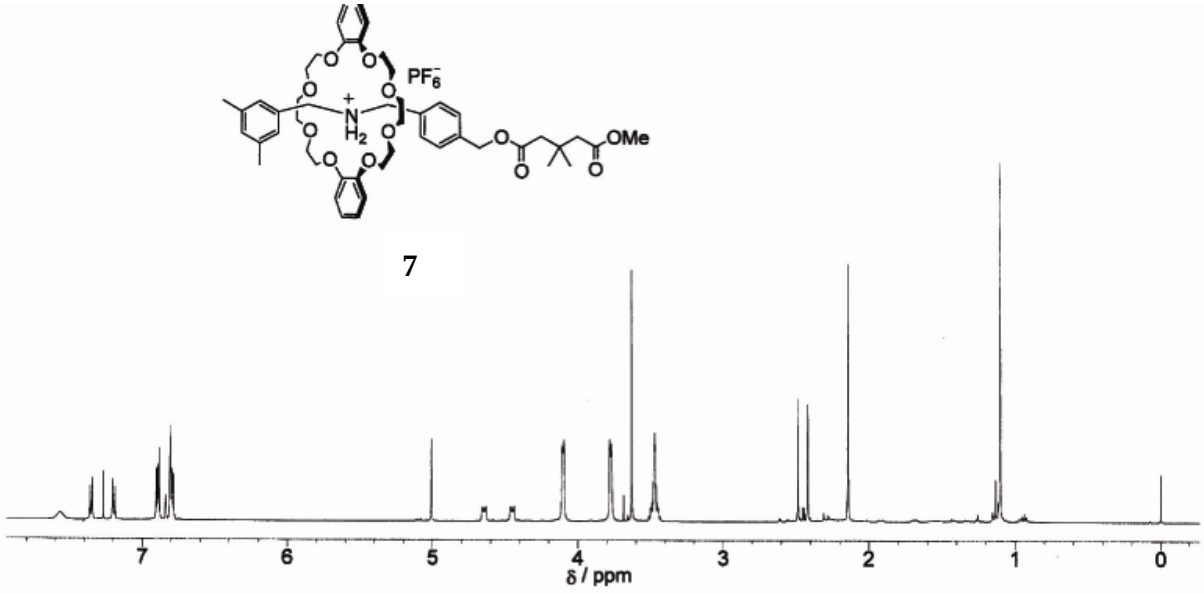

**23**

$^{1}$H NMR spectrum of carboxylic acid **23**.

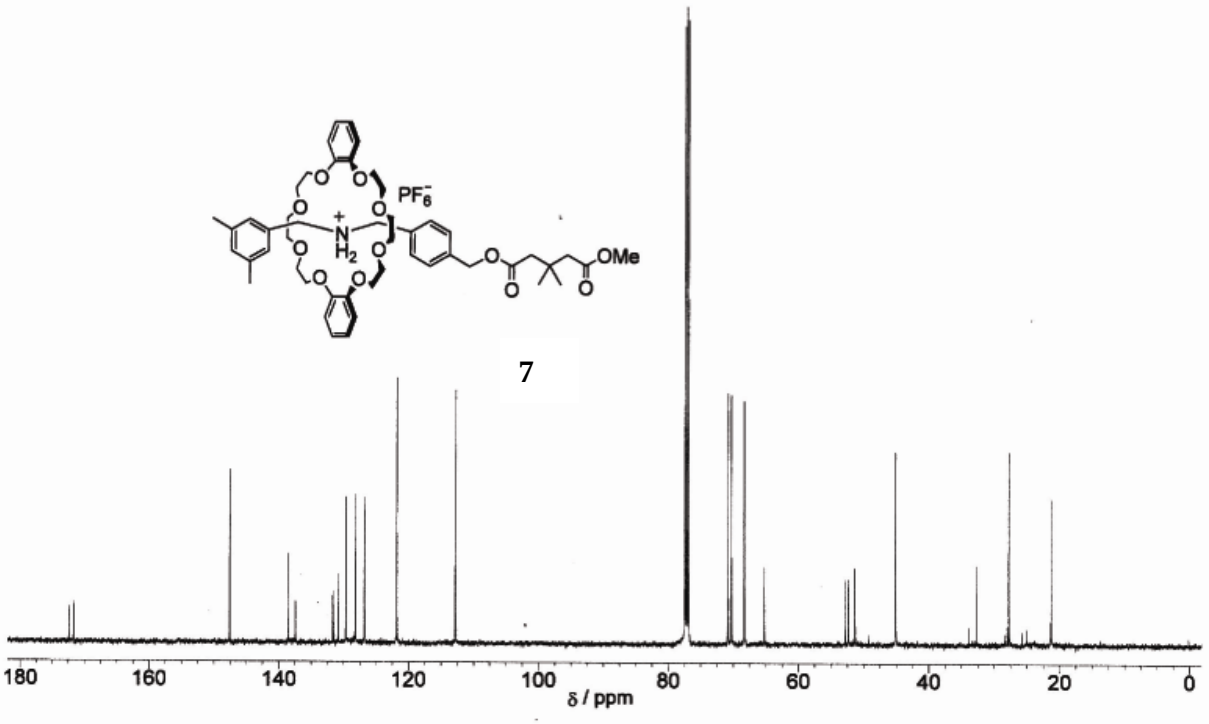



**23**

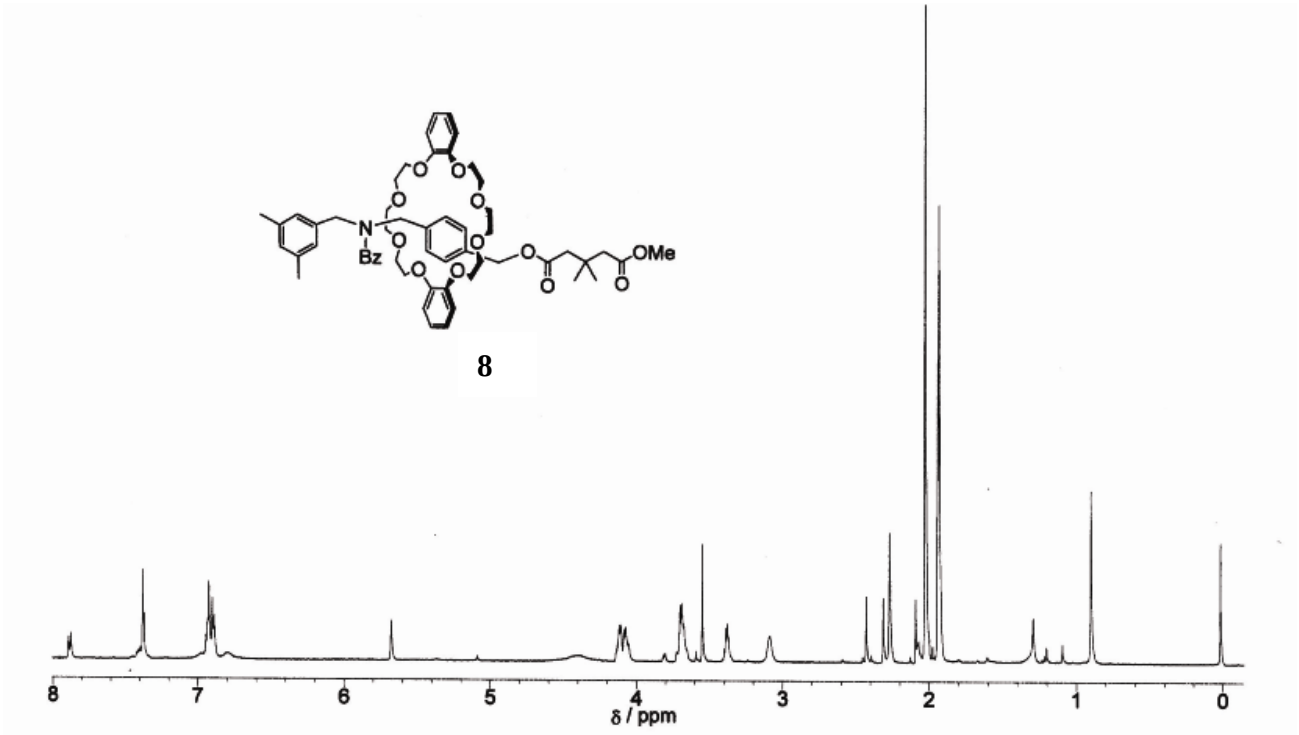
$^{13}$C NMR spectrum of carboxylic acid **23**.



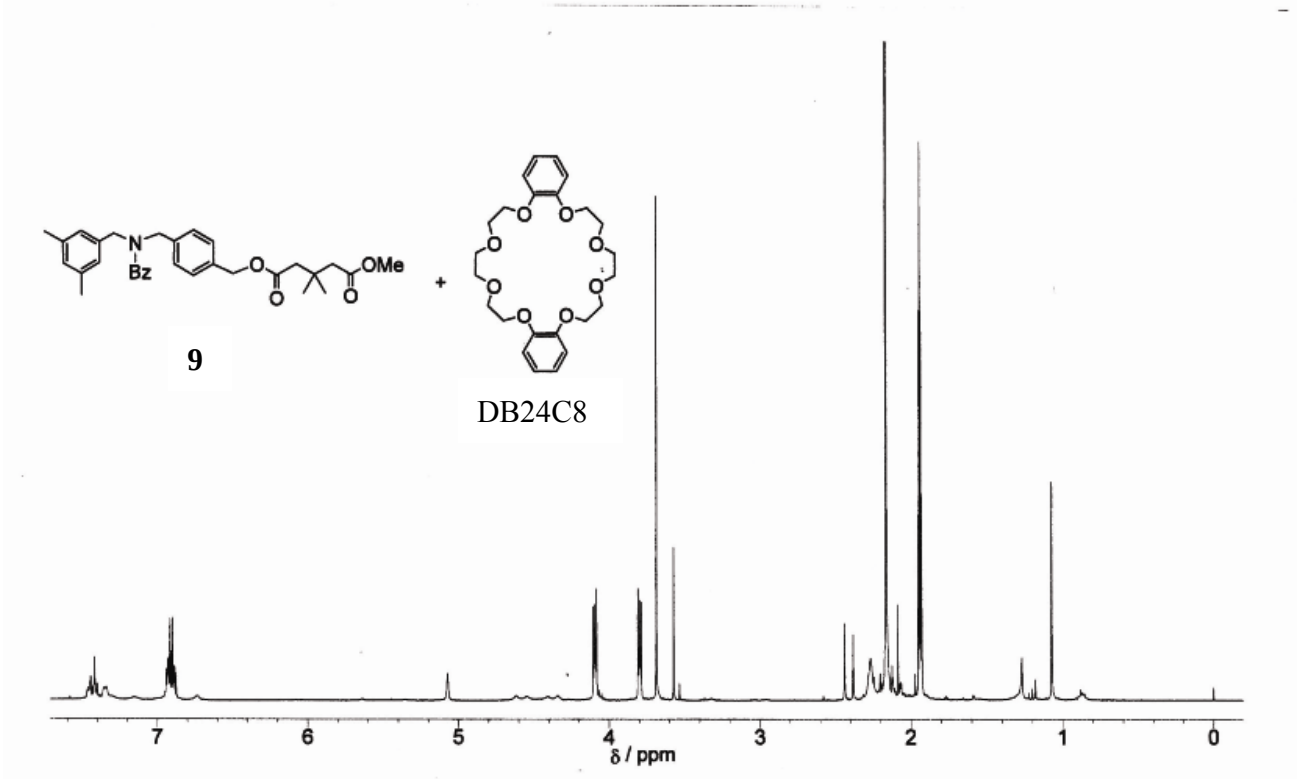

$^{1}$H NMR spectrum of rotaxane **7**.




$^{13}$C NMR spectrum of rotaxane **7**.




$^{1}$H NMR spectrum of *N*-aclylated rotaxane **8**.




$^{1}$H NMR spectrum of axle **9** and DB24C8.