Physical Sciences – Chemistry

Efficient Production of [*n*]Rotaxanes using Template-Directed Clipping Reactions

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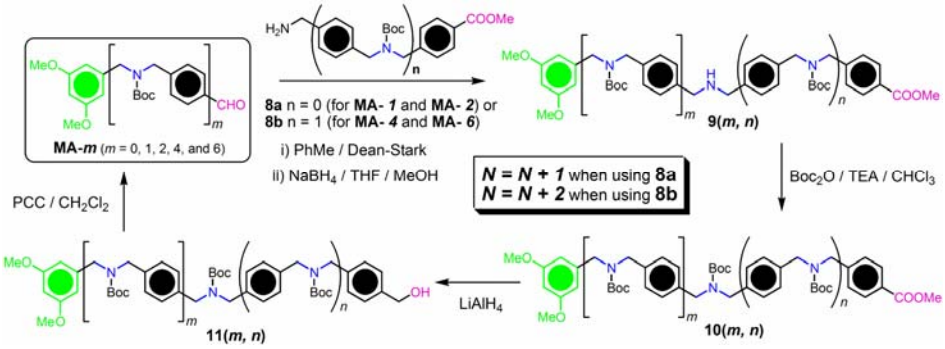
Supporting Information

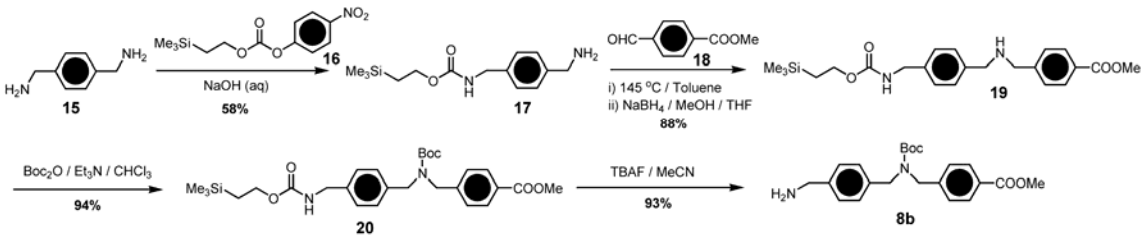
I. Synthesis of the Intermediates MA-*m* and DA-*m*.

Although a detailed description on the synthesis of **MA-*m*** and **DA-*m*** is presented in the main text, it is also shown here in Scheme 1 and Scheme 2, respectively. The compound **8b** was prepared according to the procedure shown in Scheme 3. The reaction of *p*-xylene diamine (**15**) with 4-nitrophenyl 2-(trimethylsilyl)ethyl carbonate (**16**) under basic conditions in *tert*-butanol gave the 2-(trimethylsilyl)ethyl carbamate (Teoc) mono-protected xylene diamine **17** in 58% yield. Condensation of amine **17** with aldehyde **18**, with subsequent reduction by $NaBH_4$, afforded compound **19** in 88% yield. The free amine group in compound **19** was protected by a Boc group by reaction with Boc_2O and triethylamine (TEA) in chloroform to give compound **20** in 94% yield. The Teoc group in compound **20** was then removed by treating with tetrabutylammonium fluoride (TBAF) in MeCN to afford compound **8b** in 93% yield.



*Scheme 1. Synthetic route to the monoaldehyde oligomers **MA-m**.*

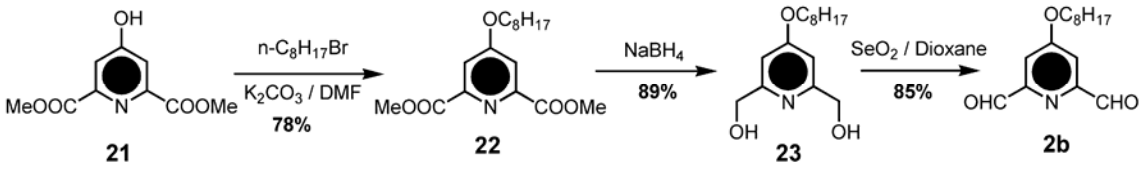
*Scheme 2. Synthetic route to the dialdehyde oligomers **DA-m**.*



*Scheme 3. Synthetic route to compound **8b**.*

II. Synthesis of Compound 2b.

Compound **2b** was synthesized according to the procedure shown in Scheme 4. Reaction of compound **21** with 1-bromooctane in the presence of K_2CO_3 in DMF gave compound **22** in 78% yield. The ester functions in compound **22** were then reduced to hydroxymethyl groups by $NaBH_4$ to afford the diol **23** in 89% yield. Dialdehyde **2b** was then prepared by an oxidation of the diol **23** with SeO_2 in dioxane in 85% yield.



*Scheme 4. Synthetic route to compound **2b**.*

Spectroscopic Characterizations of the Dumbbells DB-H_n·nPF_6 and the [*n*]Rotaxanes

(1) The HR-ESI mass spectra of the neutralized dumbbell compounds (Fig. 9).

(2) The HR ESI mass spectra of the dynamic [*n*]rotaxanes (n = 3, 4, 5 and 7) obtained after mixing the **DB-H_n**·nPF_6, **2a** and **3** in CD_3NO_2 (Fig. 10).

(3) The ^{1}H NMR spectra (400 MHz) of the dynamic [*n*]rotaxanes (n = 3, 4 and 5) after mixing the corresponding dumbbells **DB-H_n**·nPF_6, **2b** and **3** in CD_3NO_2 (Fig. 11).

(4) The HR ESI mass spectra of the dynamic [*n*]rotaxanes (n = 3, 4, 5, 7 and 11) after

mixing the corresponding dumbbells **DB-H**$_n$·nPF$_6$, **2b** and **3** in CD_3NO_2 (Fig. 12).

(5) HR-ESI Mass spectra of the 'fixed' [*n*]rotaxanes (*n* = 3, 4 and 5) (Fig.13)

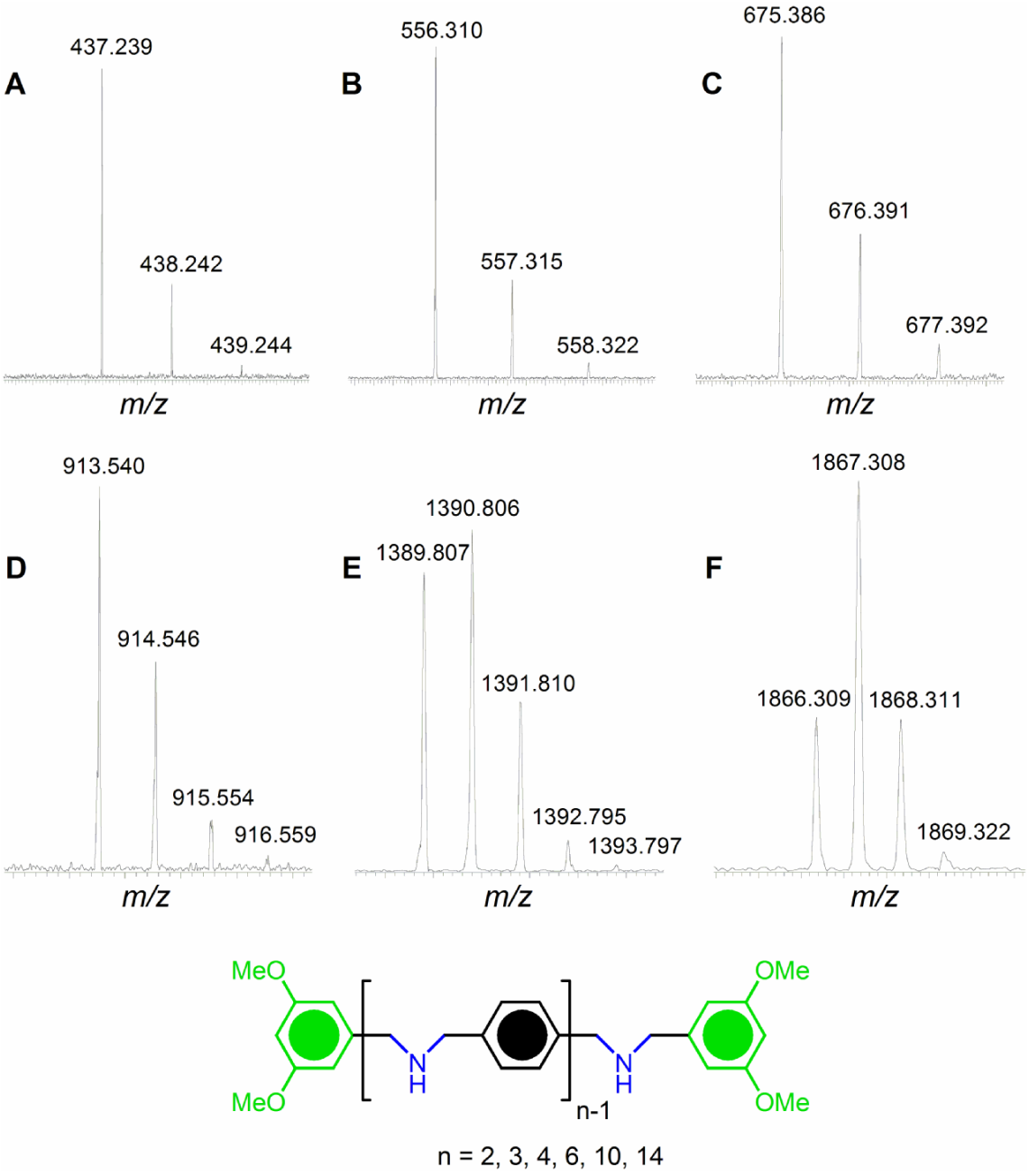


*Fig. 9. The HR ESI mass spectra of the neutralized dumbbell molecules: (**A**) – (**F**) correspond to n= 2, 3, 4, 6, 10 and 14, respectively.*

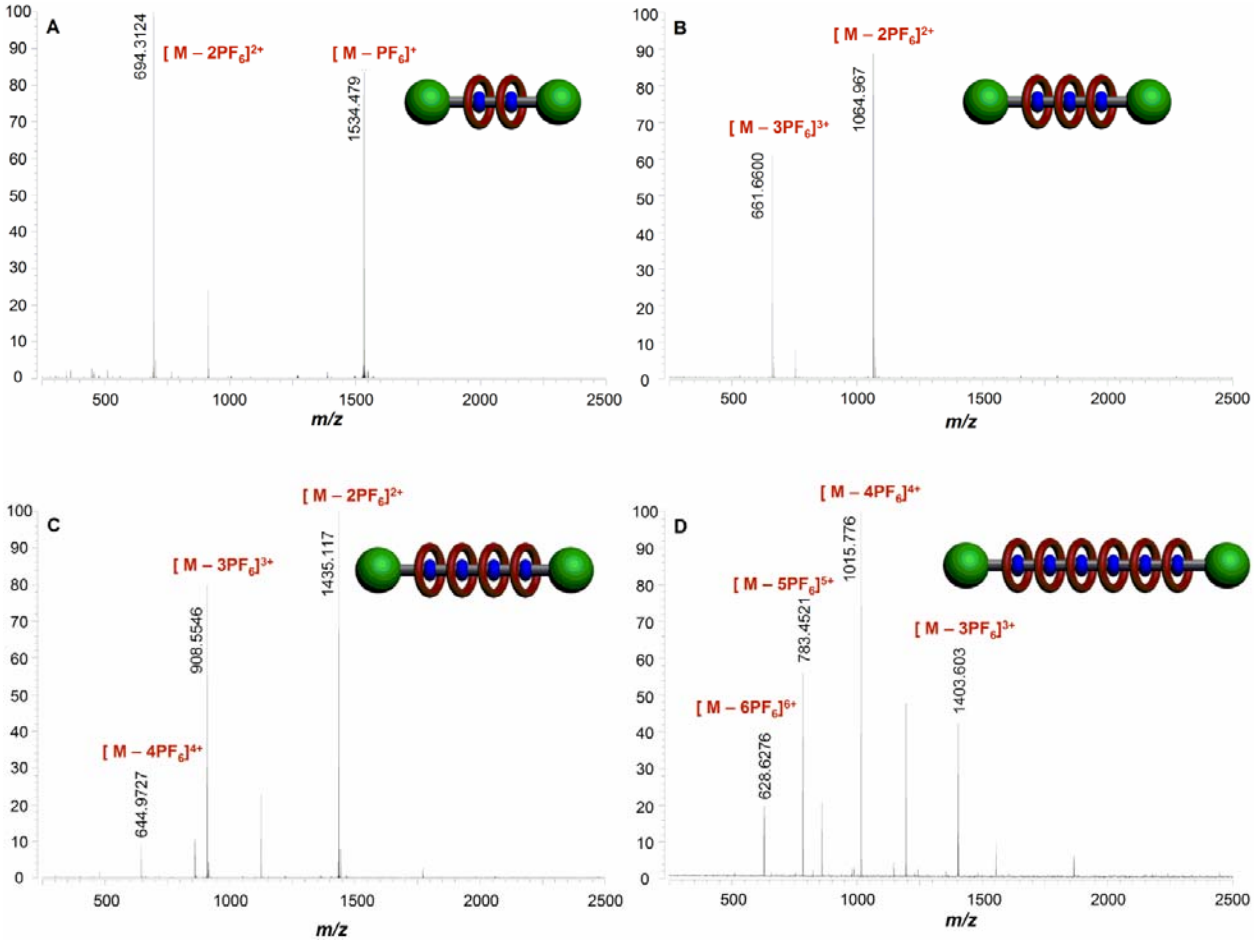


Fig. 10. The HR ESI mass spectra of the dynamic [n]rotaxanes after mixing the ***DB-H***$_n$·*n*PF_6, ***2a*** *and* ***3*** *in* CD_3NO_2. ***A***-***D*** *correspond to the [3]-, [4]-, [5]-, and [7]rotaxane, respectively.*

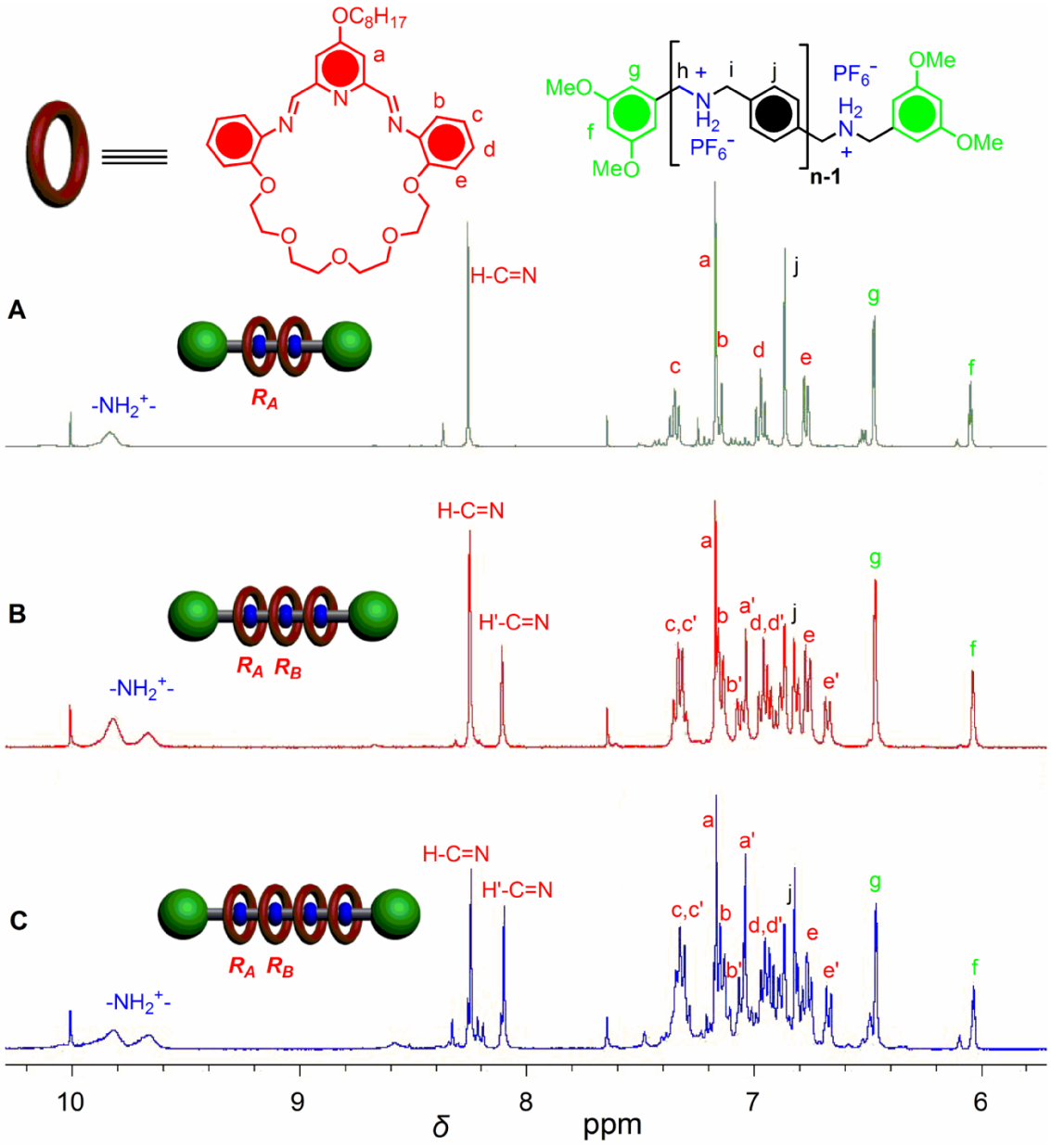


Fig. 11. The [1]H NMR spectra (400 MHz) of the dynamic [n]rotaxanes (n = 3, 4 and 5) after mixing the corresponding dumbbells ***DB-H***$_n$*·nPF*$_6$*,* ***2b*** *and* ***3*** *in* CD_3NO_2*.* ***A-C*** *correspond to [3]-, [4]-, and [5]rotaxane, respectively.*

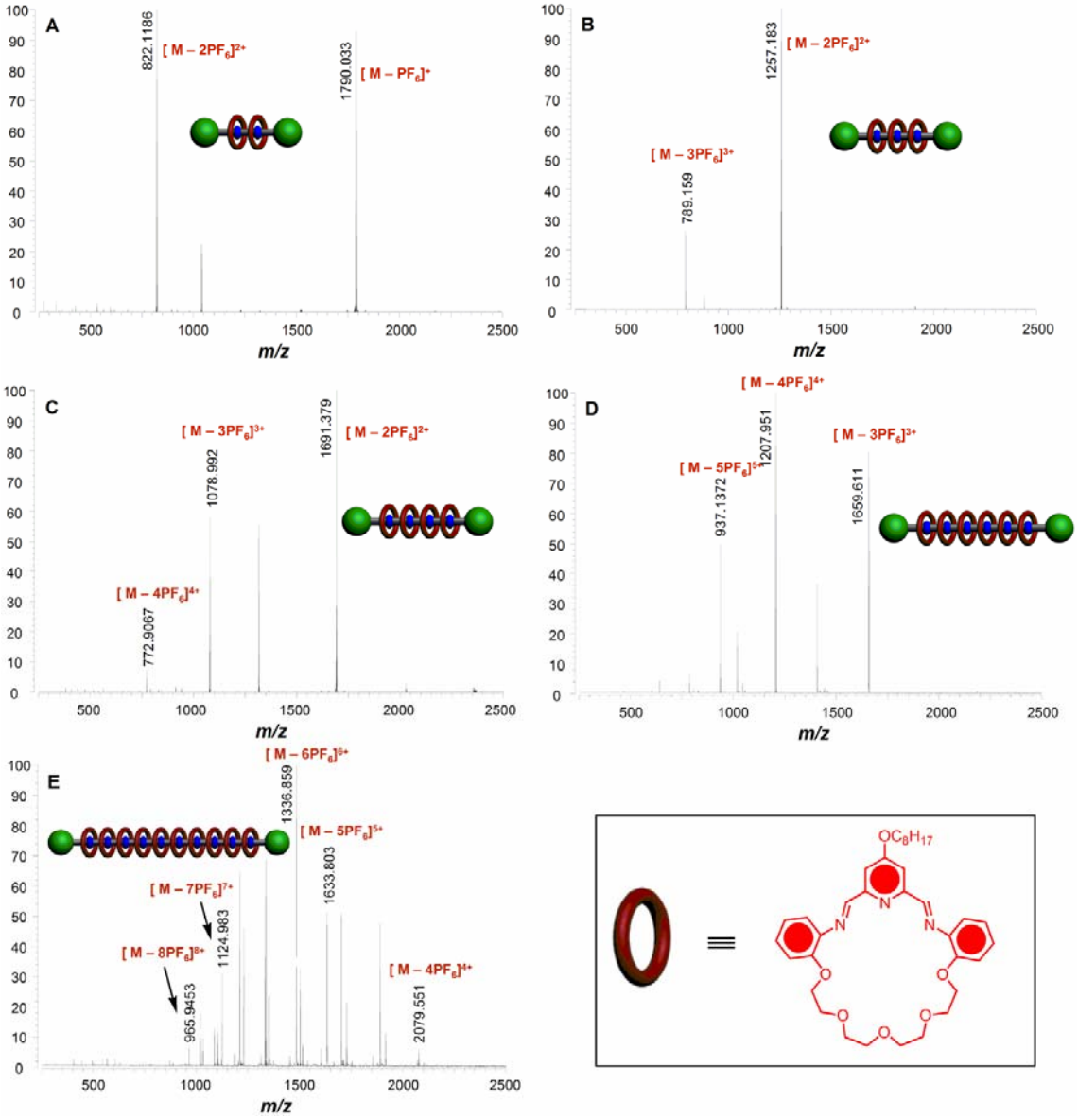


Fig. 12. The HR ESI mass spectra of the dynamic [n]rotaxanes (n = 3, 4, 5, 7 and 11) after mixing the corresponding dumbbells ***DB-H***$_n$·*nPF*$_6$, ***2b*** *and* ***3*** *in* CD_3NO_2. ***A-E*** *correspond to [3]-, [4]-, [5]-, [7]- and [11]rotaxane, respectively.*

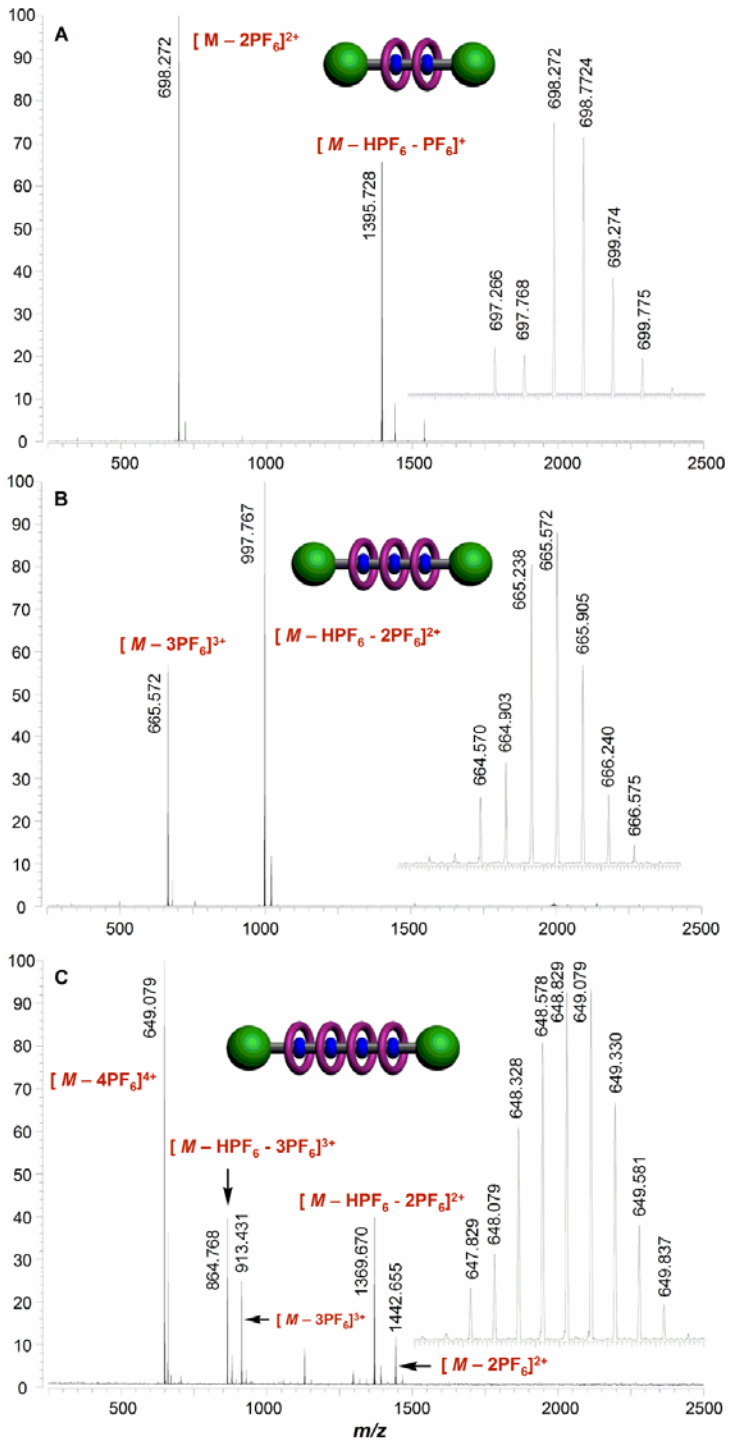


Fig. 13. HR-ESI Mass spectra of the 'fixed' [n]rotaxanes (n = 3, 4 and 5). ***A****: for [3]rotaxane, m/z = 698.272 ($[M\text{-}2PF_6]^{2+}$), 1395.728 ($[M\text{-}HPF_6\text{-}PF_6]^{+}$);* ***B****: for [4]rotaxane, m/z = 665.572 ($[M\text{-}3PF_6]^{3+}$), 997.767 ($[M\text{-}HPF_6\text{-}2PF_6]^{2+}$); and* ***C****: for [5]rotaxane, m/z = 649.079 ($[M\text{-}4PF_6]^{4+}$), 864.768 ($[M\text{-}HPF_6\text{-}3PF_6]^{3+}$), 913.431 ($[M\text{-}3PF_6]^{3+}$), 1369.670 ($[M\text{-}HPF_6\text{-}2PF_6]^{2+}$), 1442.655 ($[M\text{-}2PF_6]^{2+}$).*

Detailed Synthetic Procedures and Characterization Data for all Intermediate Compounds and Dumbbells

General procedure A *for reductive aminations*

A mixture of aldehyde (**MA-*m*** or **DA-*m***) and amines (**4**, **6**, **8a** or **8b**, -CHO/-NH_2 = 1:1) in dry toluene (PhMe, 0.05-0.2 M) was heated to 140 ^oC for 16–24 h using a Dean-Stark apparatus under argon atmosphere. In this manner, water molecules generated from the condensation were removed from the system. After removal of the solvent, the resulting imines were shown to have been formed in quantitative yields by ^1H NMR spectroscopy. The imines were then dissolved in dry tetrahydrofuran (THF) and methanol (MeOH) (1:1, v/v, 0.1 M) and sodium borohydride (5 equiv per imine bond) was added in portions. The mixture was stirred at room temperature for 16–24 h and the excess of solvents were removed under vacuum. Water was added and the mixture was then extracted with dichloromethane (CH_2Cl_2). The organic layer was washed with water for 3–4 times until the solution became clear, and dried (Na_2SO_4). After removal of the excess of solvent, the dialkylamines (**5(*m*)**, **7(*m*)**, **9(*m*,*n*)**, or **12(*m*,*n*)**) were obtained in good yields, and no further purification was needed.

General procedure B *for Boc-protection of dialkylamines*

The dialkylamine (**5(*m*)**, **7(*m*)**, **9(*m*,*n*)**, or **12(*m*,*n*)**) was dissolved in dry chloroform (0.1 M) and then Boc_2O (2 equiv per amine) and triethylamine (TEA, 2.2 equiv per amine) were added. The mixture was stirred at room temperature for 24 h and the excess of solvents were removed under vacuum. The residue was purified by column chromatography (silica gel, mixture solvents of CH_2Cl_2 and ethyl acetate (EtOAc) as eluent) to give the Boc-protected dialkylamine (**10(*m*,*n*)**, or **13(*m*,*n*)**).

General procedure C *for reduction of ester groups*

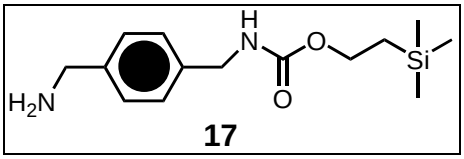
The Boc-protected dialkylamine (**10(*m*,*n*)**, or **13(*m*,*n*)**) was dissolved in dry THF (0.1 M), and the solution was cooled down to 0 ^oC. Lithium aluminum hydride ($LiAlH_4$, 2 equiv per ester) was added in portion and the resulting mixture was allowed to warm to room temperature and was stirred for 16–24 h. The reaction was quenched by adding slowly the ground powder of $Na_2SO_4 \cdot 10H_2O$ and Celite (1:1, w/w). After stirring for 30 min, the mixture was filtered and the excess of solvent in the filtrate was removed under vacuum to give the alcohol (**11(*m*,*n*)** or **14(*m*,*n*)**). The product was used for next step without further purification.

General procedure D *for oxidation of alcohols to aldehydes*

The alcohol (**11(*m*,*n*)** or **14(*m*,*n*)**) was dissolved in dry CH_2Cl_2 (0.2 M) and the solution was added dropwise to a suspension of the pyridinium chlorochromate (PCC, 2 equiv per –CH_2OH) in CH_2Cl_2 (0.1 M) at 0 ^oC. The mixture was allowed to warm to room temperature before being stirred for 6 h under argon atmosphere. The reaction was quenched by adding 1 M NaOH (aq) and the organic phase was washed with water. The excess of solvents were removed and the residue was purified by column chromatography (silica gel, mixture solvents of CH_2Cl_2 and EtOAc as eluent) to give the aldehyde (**MA-*m*** and **DA-*m***).

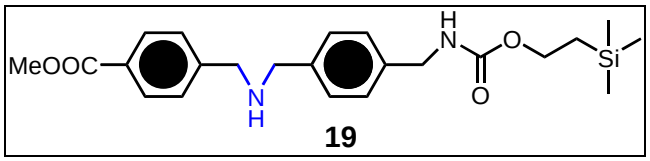
General procedure E *for cationic dumbbells (**DB-H**$_n$·nPF$_6$) formation after Boc-deprotection, protonation and counterion exchange*

Compound **5(*m*)** or **7(*m*)** was dissolved in dry CH_2Cl_2 (0.01 ~ 0.05M) and trifluoroacetic acid (TFA, 10 equiv per Boc) was added. The mixture was stirred at room temperature for 24 h and then the excess of solvent was removed under vacuum. The residue was dissolved in minimum amount of MeOH and the saturated aqueous NH_4PF_6 solution was added to yield a white precipitate. The mixture was then concentrated during which most of the MeOH was removed, and the precipitate (**DB-H**$_n$·nPF$_6$) was collected, washed with water and dried under vacuum in the presence of phosphorus pentaoxide.



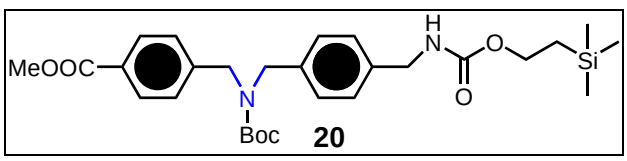
17

A solution of 4-nitrophenyl 2-(trimethylsilyl)ethyl carbonate (**16**, 5.0 g) in *tert*-butanol (40 mL) was added dropwise into a mixture of *p*-xylene diamine (**15**, 7.21 g) and 2M NaOH (8.82 mL) in *tert*-butanol (150 mL). The mixture was stirred at room temperature for 2 h and the yellow precipitate was filtered and washed by CH_2Cl_2. The excess of solvents of the filtrate were removed under vacuum and the residue was purified by column chromatography (silica gel, EtOAc/MeOH = 4:1) to give pure compound **17** (3.22 g, 58%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.27 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 5.21 (s, 1H, -NH-C(O)), 4.29 (d, *J* = 6.1 Hz, 2H), 4.15 (t, *J* = 8.4 Hz, 2H), 3.81 (s, 2H), 1.69 (s, 2H), 0.99 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H, TMS). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 156.88, 142.68, 137.51, 127.38, 127.24, 62.94, 45.94, 44.47, 17.64, –1.84. ESI MS: *m/z* = 561.33 ([2*M*–H]$^+$), calcd. exact mass: 280.16.



19

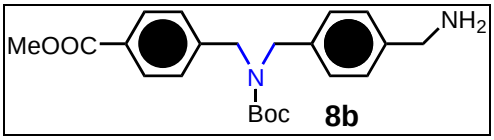
Following the ***General Procedure A***, condensation of compound **17** (5.85 g) with methyl 4-formylbenzoate (**18**, 3.42g) and subsequent reduction by $NaBH_4$ (3.7 g) gave compound **19** in 88% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.93 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 5.22 (s, 1H, -NH-C(O)), 4.26 (d, *J* = 6.1 Hz, 2H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 3.79 (s, 2H), 3.72 (s, 2H), 0.94 (t, *J* = 8.4 Hz, 2H), 0.00 (s, 9H, TMS). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.82, 156.90, 146.07, 139.47, 137.86, 129.51, 129.48, 128.83, 128.29, 127.94, 127.32, 62.95, 51.86, 44.49, 17.67, –1.81. ESI MS: *m/z* = 428.71 ([*M*–H]$^+$), 857.43 ([2*M*–H]$^+$); calcd. exact mass: 428.21.



20

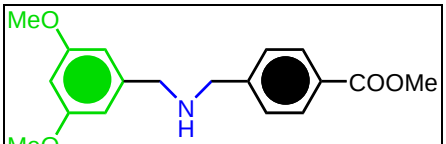
Following the ***General Procedure B***, the reaction of **19** (8.56 g) with Boc_2O (8.73 g) and TEA

(5.58 mL) in $CHCl_3$ (200 mL) gave compound **20** in 94% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.28 (br, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.18(br, 2H), 5.16 (s, 1H, -NH-C(O)), 4.39 (br, 4H), 4.31 (d, *J* = 6.1 Hz, 2H), 4.16 (t, *J* = 8.4 Hz, 2H), 3.88 (s, 3H), 1.46 (br, 9H, Boc), 0.98 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H, TMS). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.67, 155.69, 138.28, 137.02, 129.61, 129.13, 127.45, 80.08, 62.97, 51.91, 28.07, 17.65, -1.83. MALDI-TOF MS: *m/z* = 550.59 ([*M* + Na^+]); calcd. exact mass: 528.26.



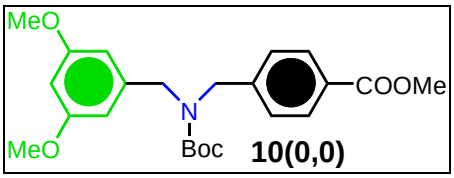
8b

Compound **20** (3.0 g) was dissolved in acetonitrile (MeCN, 80 mL) and tetrabutylammonium fluoride trihydrate (3.6 g) was added. The mixture was stirred at 40 °C for 24 h and the excess of solvent was removed under vacuum. The residue was then extracted by CH_2Cl_2 and the organic layer was washed by water for four times. The organic layer was dried over anhydrous Na_2SO_4 and the excess of solvent was removed under vacuum to give compound **8b** in 93% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 4H), 7.18 (br, 2H), 4.40 (br, 4H), 3.88 (s, 3H), 3.82 (s, 2H), 1.47 (br, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.66, 155.70, 142.98, 136.21, 129.61, 129.11, 127.89, 127.60, 127.21, 80.00, 58.80, 51.90, 46.05, 28.09, 23.93, 19.71, 13.41. ESI MS: *m/z* = 385.23 ([*M*–H]$^+$); calcd. exact mass: 384.48.



9(0,0)

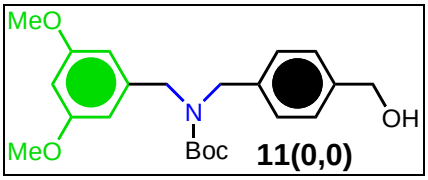
Following the ***General Procedure A***, condensation of aldehyde **MA-0** (8.31 g) with methyl 4-(aminomethyl)benzoate (**8a**, 8.25 g) and subsequent reduction by $NaBH_4$ (9.0 g) gave compound **9(0,0)** in 84% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.50 (d, ^4J = 2.3 Hz, 2H), 6.35 (t, ^4J = 2.3 Hz, 1H), 3.89 (s, 3H), 3.84(s, 2H), 3.78 (s, 6H), 3.74(s, 2H). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.80, 160.91, 146.10, 142.93, 129.45, 129.10, 128.85, 127.93, 105.80, 98.74, 55.21, 51.82. ESI MS: *m/z* = 316.08. ([*M*–H]$^+$); calcd. exact mass: 315.15.



10(0,0)

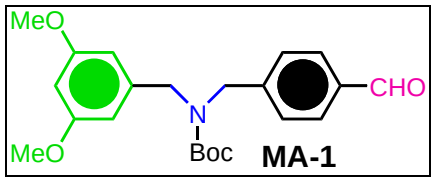
Following the ***General Procedure B***, the reaction of **9(0,0)** (8.2 g) with Boc_2O (11.35 g) and TEA (7.25 mL) in $CHCl_3$ (200 mL) gave compound **10(0,0)** in 78% yield, after purification by column chromatography (silica gel, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J*

= 8.2 Hz, 2H), 7.28 (br, 2H), 6.35 (br, 3H), 4.44-4.30 (br, 4H), 3.88 (s, 3H), 3.74 (s, 6H), 1.47 (br, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.66, 161.04, 155.69, 140.43, 129.59, 129.10, 99.03, 80.06, 55.20, 51.87, 28.06. MALDI-TOF MS: *m/z* = 437.16 ([*M* + Na^+]); calcd. exact mass: 415.20.



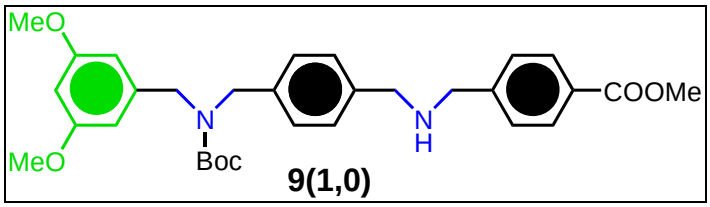
11(0,0)

Following the ***General Procedure C***, compound **10(0,0)** (8.2 g) was reduced by $LiAlH_4$ (1.5 g) in dry THF (250 mL) to give compound **10(0,0)** in 82% yield, after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.32 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.36 (br, 3H), 4.63 (s, 2H), 4.38–4.30(br, 4H), 3.77 (s, 6H), 1.49 (br, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 161.01, 155.83, 140.41, 137.34, 127.03, 105.45, 105.29, 98.99, 79.92, 64.60, 55.20, 28.14, 13.98. MALDI-TOF MS: *m/z* = 387.51; calcd. exact mass: 387.20.



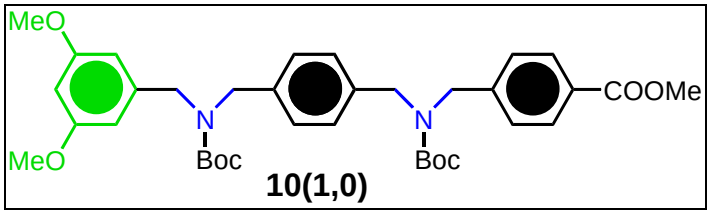
MA-1

Following the ***General Procedure D***, compound **10(0,0)** (6.0 g) was oxidized with PCC (6.68 g) in dry CH_2Cl_2 (450 mL) to give **MA-1** in 70% yield, after purification by column chromatography (silica gel, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.98 (s, 1H, CHO), 7.83 (d, *J* = 8.2 Hz, 2H), 7.39 (br, 2H), 6.36 (br, 3H), 4.48-4.32 (br, 4H), 3.77 (s, 6H), 1.46 (br, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.66, 161.07, 155.66, 140.35, 135.60, 129.75, 105.50, 99.05, 80.15, 55.20, 28.07. MALDI-TOF MS: *m/z* = 385.62; calcd. exact mass: 385.19.



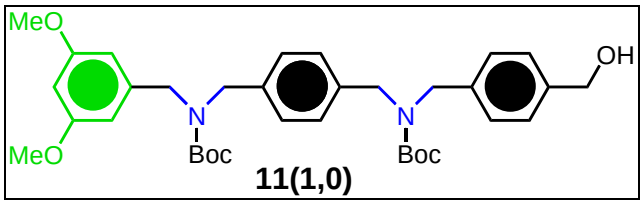
9(1,0)

Following the ***General Procedure A***, condensation of aldehyde **MA-1** (2.0 g) with methyl 4-(aminomethyl)benzoate (**8a**, 857 mg) and subsequent reduction by $NaBH_4$ (981 mg) gave compound **9(1,0)** in 90% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.98 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.34 (br, 3H), 4.38–4.28 (br, 4H), 3.88 (s, 3H), 3.85 (s, 2H), 3.78 (s, 2H), 3.74 (s, 6H), 1.48 (br, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.80, 160.98, 155.73, 146.13, 140.78, 139.40, 136.92, 129.45, 129.11, 128.83, 128.20, 127.94, 105.21, 99.89, 79.76, 55.19, 51.84, 30.58, 29.68, 28.12. ESI MS: *m/z* = 535.28 ([*M*–H]$^+$); calcd. exact mass: 534.27.



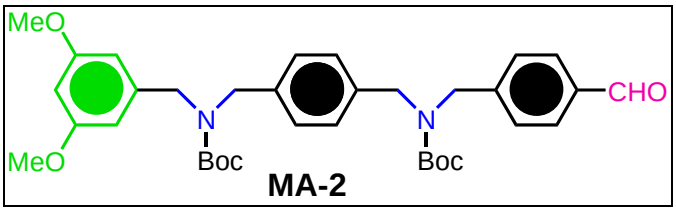
10(1,0)

Following the ***General Procedure B***, the reaction of **9(1,0)** (2.72 g) with Boc_2O (2.23 g) and TEA (1.42 mL) in $CHCl_3$ (50 mL) gave compound **10(1,0)** in 88% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.28 (br, 2H), 7.18 (br, 4H), 6.35 (br, 3H), 4.42–4.28 (br, 8H), 3.88 (s, 3H), 3.75 (s, 6H), 1.49 (br, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.65, 160.99, 155.72, 140.72, 137.37, 136.92, 129.61, 129.13, 127.95, 127.17, 105.23, 98.91, 80.06, 79.80, 55.19, 51.89, 28.13, 28.08. MALDI-TOF MS: *m/z* = 656.30 ([*M* + Na^+]); calcd. exact mass: 634.32.



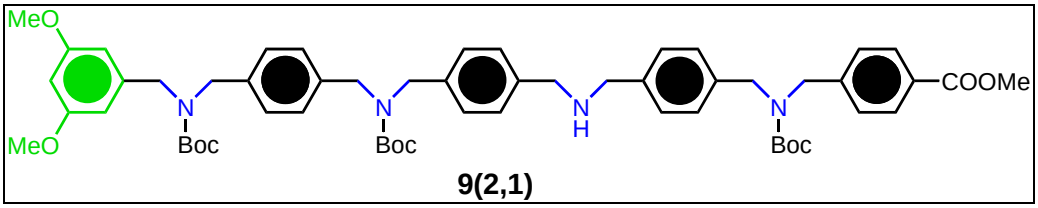
11(1,0)

Following the ***General Procedure C***, compound **10(1,0)** (2.7 g) was reduced by $LiAlH_4$ (323 mg) in dry THF (80 mL) to give compound **11(1,0)** in 92% yield after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.31 (d, *J* = 8.2 Hz, 2H), 7.17 (br, 6H), 6.35 (br, 3H), 4.64 (s, 2H), 4.37–4.30 (br, 8H), 3.75 (s, 6H), 1.48 (s, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.98, 155.75, 140.28, 137.32, 127.83, 126.99, 105.21, 98.95, 79.83, 67.73, 64.70, 55.20, 28.12. MALDI-TOF MS: *m/z* = 628.55 ([*M* + Na^+]); calcd. exact mass: 606.33.



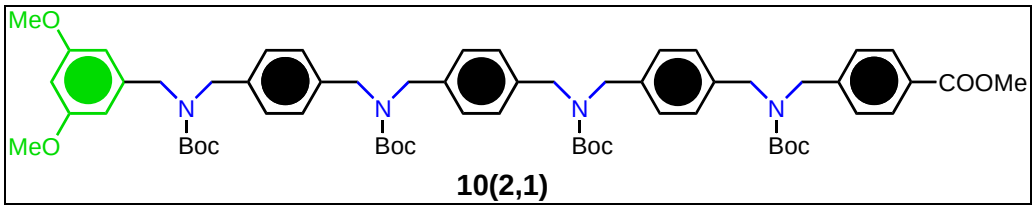
MA-2

Following the ***General Procedure D***, compound **11(1,0)** (2.43 g) was oxidized with PCC (1.72 g) in dry CH_2Cl_2 (250 mL) to give **MA-2** in 50% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 20:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.98 (s, 1H, CHO), 7.83 (d, *J* = 8.2 Hz, 2H), 7.39 (br, 2H), 7.18 (br, 4H), 6.35 (br, 3H), 4.42–4.27 (br, 8H), 3.75 (s, 6H), 1.48 (br, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.70, 160.98, 155.71, 140.70, 137.42, 136.81, 135.58, 129.77, 127.73, 105.211, 98.89, 80.16, 79.82, 55.20, 28.12, 28.06. MALDI-TOF MS: *m/z* = 626.80 ([*M* + Na^+]); calcd. exact mass: 604.31.



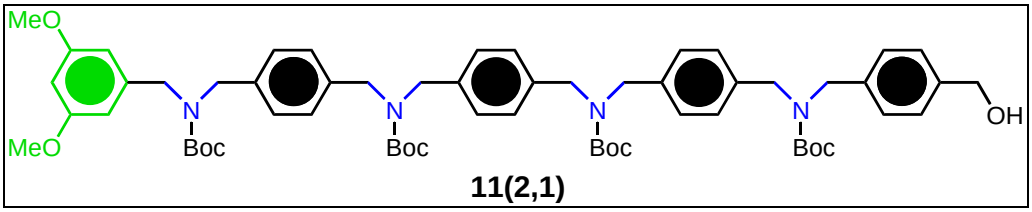
9(2,1)

Following the ***General Procedure A***, condensation of aldehyde **MA-2** (1.24 g) with **8b** (780 mg) and subsequent reduction by $NaBH_4$ (378 mg) gave compound **9(2,1)** in 88% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.33-7.28 (br, 6H), 7.18 (br, 8H), 6.35 (br, 3H), 4.38–4.29 (br, 12H), 3.87 (s, 3H), 3.78 (s, 4H), 3.75 (s, 6H), 1.48 (br, 27H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.66, 160.98, 155.72, 139.81, 139.66, 137.21 136.51, 129.59, 129.11, 128.24, 128.20, 127.69, 105.20, 99.86, 80.01, 79.79, 79.76, 55.20, 51.88, 28.13. ESI MS: *m/z* = 973.51 ($[M–H]^+$); calcd. exact mass: 972.52.



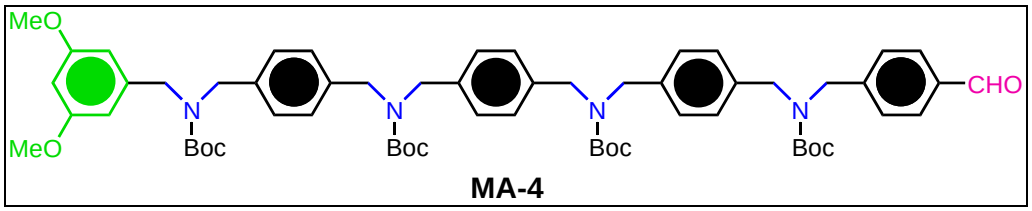
10(2,1)

Following the ***General Procedure B***, the reaction of **9(2,1)** (1.9 g) with Boc_2O (436 g) and TEA (0.30 mL) in $CHCl_3$ (15 mL) gave compound **10(2,1)** in 92% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 9:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.28 (br, 2H), 7.19 (br, 12H), 6.35 (br, 3H), 4.35 (br, 16H), 3.87 (s, 3H), 3.75 (s, 6H), 1.48 (br, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 167.05, 161.38, 156.14, 137.56, 137.34, 129.99, 129.53, 128.20, 106.00, 99.31, 80.46, 80.21, 55.59, 52.29, 49.54, 28.52. MALDI-TOF MS: *m/z* = 1094.34 ($[M + Na^+]$); calcd. exact mass: 1072.58.



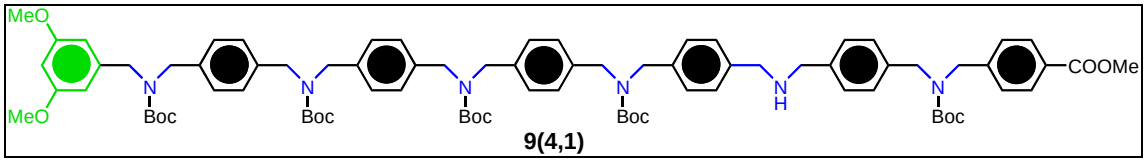
11(2,1)

Following the ***General Procedure C***, compound **10(2,1)** (2.14 g) was reduced by LAH (152 mg) in dry THF (80 mL) to give compound **11(2,1)** in 90% yield, after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 (d, *J* = 8.2 Hz, 2H), 7.18–7.17 (br, 14H), 6.35 (br, 3H), 4.64 (s, 2H), 4.37–4.32 (br, 16H), 3.75 (s, 6H), 1.48 (s, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.98, 155.78, 140.28, 137.15, 127.76, 127.00, 107.93, 79.87, 67.74, 67.56, 64.70, 62.59, 55.20, 28.11. MALDI-TOF MS: *m/z* = 1066.75 ($[M + Na^+]$); calcd. exact mass: 1044.58.



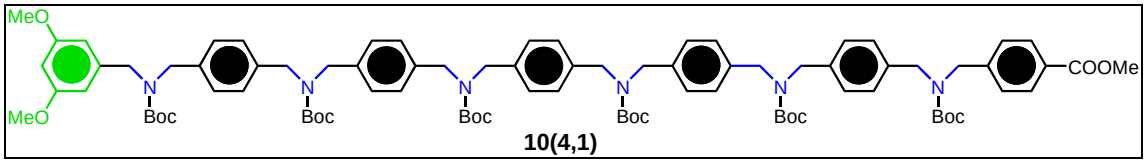
MA-4

Following the ***General Procedure D***, compound **11(2,1)** (2.09 g) was oxidized with PCC (862 mg) in dry CH_2Cl_2 (150 mL) to give **MA-4** in 36% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 95:5). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.98 (s, 1H, CHO), 7.83 (d, *J* = 8.2 Hz, 2H), 7.37 (br, 2H), 7.19 (br, 12H), 6.35 (br, 3H), 4.43–4.34 (br, 16H), 3.75 (s, 6H), 1.48 (br, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.67, 160.98, 155.73, 137.15, 136.85, 135.58, 129.77, 127.74, 105.44, 99.91, 80.17, 79.71, 79.81, 55.19, 28.12. MALDI-TOF MS: *m/z* = 1063.95 ([*M* + Na^+]); calcd. exact mass: 1042.57.



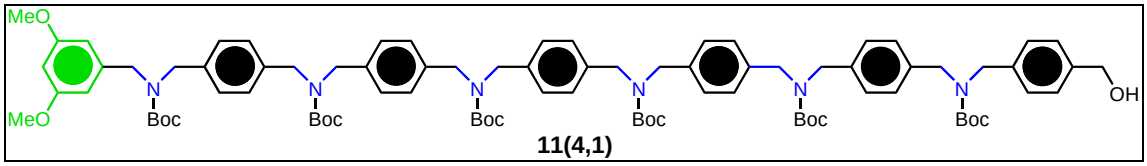
9(4,1)

Following the ***General Procedure A***, condensation of aldehyde **MA-4** (500 mg) with **8b** (204 mg) and subsequent reduction by $NaBH_4$ (90 mg) gave compound **9(4,1)** in 91% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.96 (d, *J* = 8.2 Hz, 2H), 7.32-7.26 (br, 6H), 7.19 (br, 16H), 6.34 (br, 3H), 4.37–4.34 (br, 20H), 3.87 (s, 3H), 3.78 (s, 4H), 3.74 (s, 6H), 1.47 (br, 45H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.65, 160.99, 155.71, 139.80, 139.68, 137.22 136.50, 129.57, 129.12, 128.22, 128.24, 127.66, 105.21, 99.84, 80.02, 79.80, 79.76, 55.19, 51.89, 28.12. ESI MS: *m/z* = 1412.72 ([*M*–H]$^+$), 1433.71 ([M + Na^+]); calcd. exact mass: 1410.78.



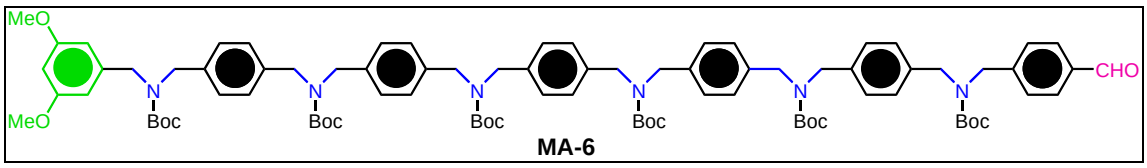
10(4,1)

Following the ***General Procedure B***, the reaction of **9(4,1)** (635 mg) with Boc_2O (196 mg) and TEA (0.15 mL) in $CHCl_3$ (15 mL) gave compound **10(4,1)** in 81% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 9:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 2H), 7.28 (br, 2H), 7.20 (br, 20H), 6.35 (br, 3H), 4.38–4.35 (br, 24H), 3.87 (s, 3H), 3.75 (s, 6H), 1.48 (br, 54H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 167.02, 160.98, 155.74, 137.20, 129.60, 129.52, 127.82, 105.92, 99.24, 79.81, 55.20, 51.89, 28.13. MALDI-TOF MS: *m/z* = 1532.63 ([*M* + Na^+]); calcd. exact mass: 1510.83.



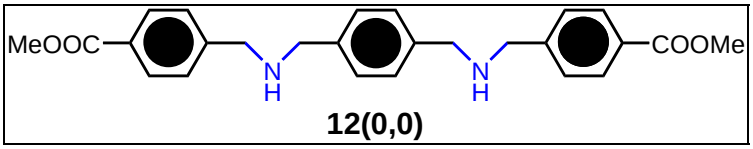
11(4,1)

Following the ***General Procedure C***, compound **10(4,1)** (604 mg) was reduced by $LiAlH_4$ (38 mg) in dry THF (20 mL) to give compound **11(4,1)** in 86% yield, after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.31 (d, *J* = 8.2 Hz, 2H), 7.20 (br, 22H), 6.36 (br, 3H), 4.64 (s, 2H), 4.39–4.35 (br, 24H), 3.75 (s, 6H), 1.48 (s, 54H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.96, 155.76, 140.26, 137.12, 127.75, 127.02, 107.92, 80.07, 67.50, 67.43, 64.71, 62.50, 55.19, 28.13. MALDI-TOF MS: *m/z* = 1504.83 ([*M* + Na^+]); calcd. exact mass: 1482.83.



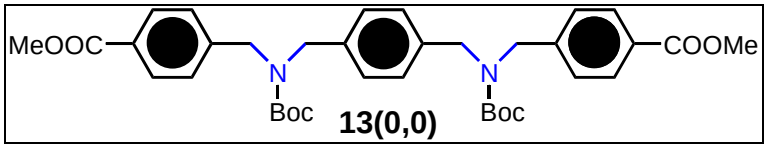
MA-6

Following the ***General Procedure D***, compound **11(4,1)** (590 mg) was oxidized with PCC (215 mg) in dry CH_2Cl_2 (25 mL) to give **MA-6** in 59% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 9:1). ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 10.02 (s, 1H, CHO), 7.87 (d, *J* = 8.0 Hz, 2H), 7.40 (br, 2H), 7.24 (br, 20H), 6.39 (br, 3H), 4.42–4.38 (br, 24H), 3.79 (s, 6H), 1.52 (br, 54H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.69, 160.99, 155.74, 137.16, 136.88, 135.56, 129.77, 127.78, 103.84, 99.93, 80.17, 79.73, 55.19, 28.12. MALDI-TOF MS: *m/z* = 1503.26 ([*M* + Na^+]); calcd. exact mass: 1480.82.



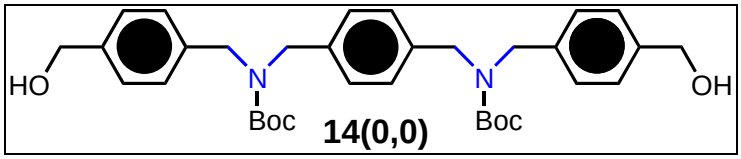
12(0,0)

Following the ***General Procedure A***, condensation of terephthalaldehyde (**DA-0**, 1.51 g) with 4-(aminomethyl)benzoate (**8a**, 3.72 g) and subsequent reduction by $NaBH_4$ (4.16g) gave compound **12(0,0)** in 90% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 4H), 7.44 (d, *J* = 8.2 Hz, 4H), 7.30 (s, 4H), 3.87 (s, 6H), 3.85 (s, 4H), 3.78 (s, 4H). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.80, 146.16, 139.13, 129.44, 128.81, 128.10, 127.93, 51.85. ESI MS: *m/z* = 865.41([M_2–H]$^+$); calcd. exact mass: 432.20.



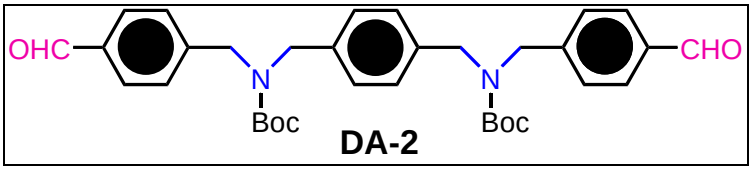
13(0,0)

Following the ***General Procedure B***, the reaction of **12(0,0)** (4.75 g) with Boc_2O (9.6 g) and TEA (6.13 mL) in $CHCl_3$ (200 mL) gave compound **13(0,0)** in 72% yield, after purification by column chromatography (silica gel, DCM/EtOAc = 9:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.98 (d, *J* = 8.2 Hz, 4H), 7.28 (br, 4H), 7.18 (br, 4H), 4.43–4.36 (br, 8H), 3.88 (s, 6H), 1.48 (br, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.6, 155.68, 137.08, 129.61, 129.13, 127.98, 127.20, 80.07, 49.62, 28.08. MALDI-TOF MS: *m/z* = 654.52 ([*M* + Na^+]); calcd. exact mass: 632.31.



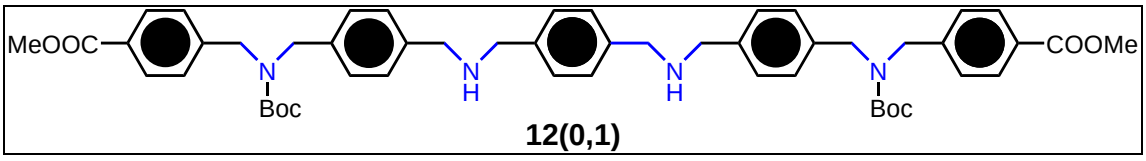
14(0,0)

Following the ***General Procedure C***, compound **13(0,0)** (5 g) was reduced by $LiAlH_4$ (1.2 g) in dry THF (100 mL) to give compound **14(0,0)** in 82% yield after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.25 (d, *J* = 8.2 Hz, 4H), 7.16 (br, 8H), 4.45 (d, *J* = 5.6 Hz, 4H), 4.30-4.24 (br, 8H), 1.37 (s, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 155.52, 141.90, 137.10, 128.08, 127.75, 127.06, 107.43, 79.67, 67.05, 63.12, 28.46. MALDI-TOF MS: *m/z* = 598.39 ([*M* + Na^+]); calcd. exact mass: 576.32.



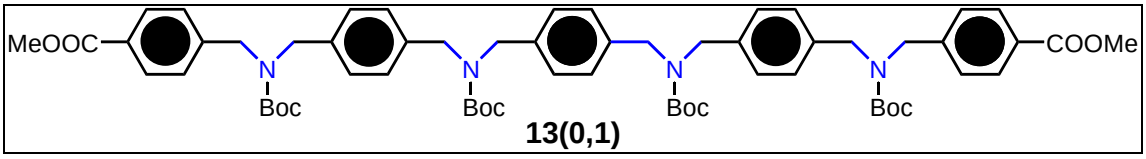
DA-2

Following the ***General Procedure D***, compound **14(0,0)** (3.5 g) was oxidized with PCC (5.23 g) in dry CH_2Cl_2 (400 mL) to give **DA-2** in 67% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.98 (s, 2H, CHO), 7.83 (d, *J* = 8.0 Hz, 4H), 7.37 (br, 4H), 7.18 (br, 4H), 4.44 (br, 8H), 1.47 (s, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.70, 155.67, 137.04, 135.59, 129.78, 127.76, 80.21, 28.06. MALDI-TOF MS: *m/z* = 594.52 ([*M* + Na^+]); calcd. exact mass: 572.29.



12(0,1)

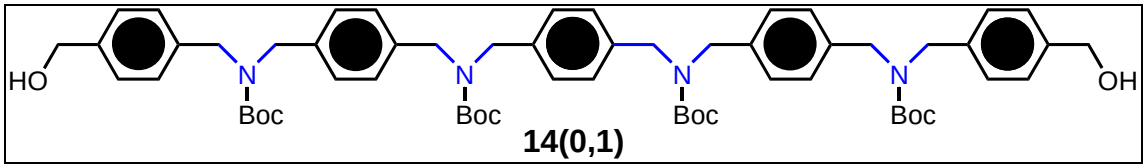
Following the ***General Procedure A***, condensation of terephthalaldehyde (**DA-0**, 488 mg) with **8b** (2.8 g) and subsequent reduction by $NaBH_4$ (1.38 g) gave compound **12(0,1)** in 87% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 4H), 7.30–7.14 (br, 16H), 4.42–4.39 (br, 8H), 3.87 (s, 6H), 3.78 (s, 8H), 1.46 (s, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.57, 155.71, 139.80, 139.23, 136.50, 129.57, 129.10, 128.26, 128.06, 127.53, 127.18, 127.01, 80.02, 49.47, 28.13. ESI MS: *m/z* = 871.44 ([*M*–H]$^+$); calcd. exact mass: 870.46.



13(0,1)

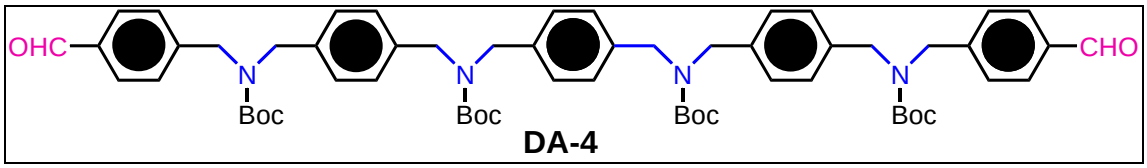
Following the ***General Procedure B***, the reaction of **12(0,1)** (3.13 g) with Boc_2O (3.14 g) and TEA (2.1 mL) in $CHCl_3$ (100 mL) gave compound **13(0,1)** in 69% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.97 (d, *J* = 8.2 Hz, 4H), 7.28 (br, 4H), 7.19 (br, 12H), 4.37 (br, 16H), 3.87 (s, 6H), 1.48 (s, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.64, 155.73, 155.69, 137.32, 137.18,

136.95, 129.60, 129.13, 127.72, 80.06, 79.82, 49.46, 28.12. MALDI-TOF MS: *m/z* =1092.12 ([*M* + Na^+]); calcd. exact mass: 1070.56.



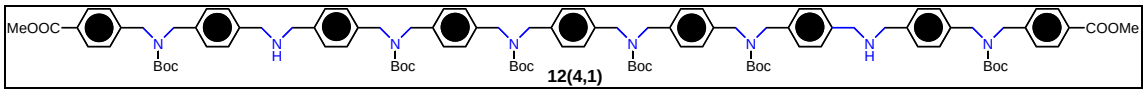
14(0,1)

Following the ***General Procedure C***, compound **13(0,1)** (2.5 g) was reduced by $LiAlH_4$ (354 mg) in dry THF (100 mL) to give compound **14(0,1)** in 86% yield, after work-up. ^1H NMR (400 MHz, CD_2Cl_2): δ = 7.35 (d, *J* = 8.2 Hz, 4H), 7.18 (br, 16H), 4.64 (s, 4H), 4.38–4.32 (br, 16H), 1.48 (s, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 155.87, 140.34, 137.82, 137.14, 127.82, 127.01, 107.91, 80.00, 79.97, 67.77, 67.54, 64.59, 62.51, 28.13. MALDI-TOF MS: *m/z* = 1036.35 ([*M* + Na^+]); calcd. exact mass: 1014.57.



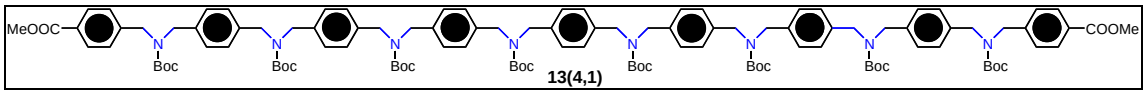
DA-4

Following the ***General Procedure D***, compound **14(0,1)** (2.33 g) was oxidized with PCC (1.98 g) in dry CH_2Cl_2 (200 mL) to give **DA-4** in 66% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1). ^1H NMR (400 MHz, CD_2Cl_2): δ = 9.98 (s, 2H, CHO), 7.83 (d, *J* = 8.0 Hz, 4H), 7.38 (br, 4H), 7.19 (br, 12H), 4.44–4.38 (br, 16H), 1.48 (s, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.67, 155.73, 137.38, 137.18, 136.86, 135.59, 129.77, 127.75, 80.17, 79.83, 28.07. MALDI-TOF MS: *m/z* = 1033.67 ([*M* + Na^+]); calcd. exact mass: 1010.54.



12(4,1)

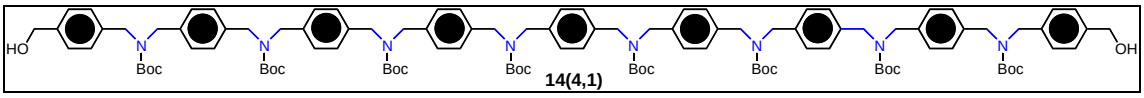
Following the ***General Procedure A***, condensation of aldehyde **DA-4** (400 mg) with **8b** (360 mg) and subsequent reduction by $NaBH_4$ (150 mg) gave compound **12(4,1)** in 82% yield. ^1H NMR (400 MHz, CD_2Cl_2): δ = 7.96 (d, *J* = 8.2 Hz, 4H), 7.32–7.19 (br, 32H), 4.37–4.34 (br, 24H), 3.87 (s, 6H), 3.78 (s, 8H), 1.47 (s, 54H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.55, 155.74, 139.81, 139.25, 136.52, 129.53, 129.12, 128.21, 128.08, 127.58, 127.12, 127.03, 80.05, 49.42, 28.12. ESI MS: *m/z* = 1747.92 ([*M*–H]$^+$); calcd. exact mass: 1746.96.



13(4,1)

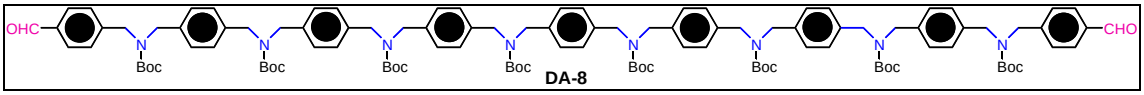
Following the ***General Procedure B***, the reaction of **12(4,1)** (680 mg) with Boc_2O (340 mg) and TEA (0.22 mL) in $CHCl_3$ (15 mL) gave compound **13(4,1)** in 82% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 9:1). ^1H NMR (400 MHz, CD_2Cl_2): δ

= 7.97 (d, J = 8.2 Hz, 4H), 7.28 (br, 4H), 7.20 (br, 28H), 4.38–4.36 (br, 32H), 3.87 (s, 6H), 1.48 (s, 72H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 166.65, 155.75, 137.20, 136.95, 129.60, 129.13, 127.82, 80.07, 79.82, 51.89, 28.13. MALDI-TOF MS: m/z = 1968.58 ([M + Na^+]); calcd. exact mass: 1947.06.



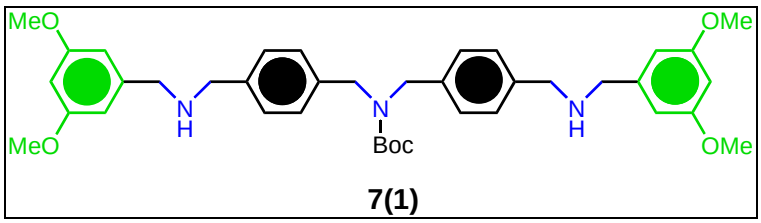
14(4,1)

Following the ***General Procedure C***, compound **13(4,1)** (570 mg) was reduced by $LiAlH_4$ (45 mg) in dry THF (15 mL) to give compound **14(4,1)** in 82% yield, after work-up. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 (d, J = 8.2 Hz, 4H), 7.19–7.17 (br, 32H), 4.64 (s, 4H), 4.37–4.32 (br, 32H), 1.44 (s, 72H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 155.80, 140.31, 137.80, 137.15, 127.87, 127.00, 107.94, 80.02, 79.89, 67.74, 67.56, 64.56, 62.50, 28.12. MALDI-TOF MS: m/z = 1913.02 ([M + Na^+]); calcd. exact mass: 1891.08.



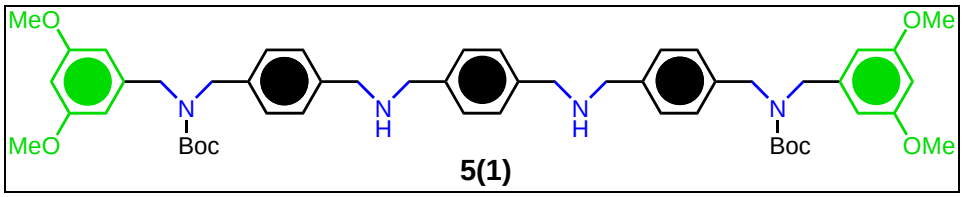
DA-8

Following the ***General Procedure D***, compound **14(4,1)** (540 mg) was oxidized with PCC (250 mg) in dry CH_2Cl_2 (25 mL) to give **DA-8** in 39% yield, after purification by column chromatography (silica gel, CH_2Cl_2/EtOAc = 8:1). ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 10.02 (s, 2H, CHO), 7.87 (d, J = 8.0 Hz, 4H), 7.41 (br, 4H), 7.25 (br, 28H), 4.43–4.39 (br, 32H), 1.53 (s, 72H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.52, 170.62, 155.60, 137.07, 136.72, 135.46, 129.63, 127.69, 80.03, 79.68, 27.99. MALDI-TOF MS: m/z = 1909.10 ([M + Na^+]); calcd. exact mass: 1887.04.



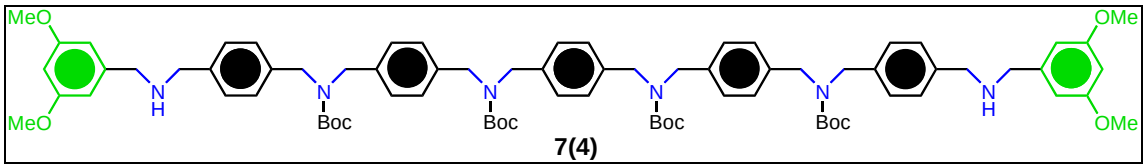
7(1)

Following the ***General Procedure A***, condensation of **6** (111 mg) with aldehyde **DA-1** (117 mg) and subsequent reduction by $NaBH_4$ (125 mg) gave compound **7(1)** in 83% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 (d, J = 7.4 Hz, 4H), 7.17 (d, J = 7.4 Hz, 4H), 6.50 (s, 4H), 6.33 (s, 2H), 3.75 (s, 12H), 3.71 (s, 8H), 1.42 (s, 9H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.87, 129.11, 128.19, 105.77, 80.03, 55.21, 28.12. ESI MS: m/z = 656.35 ([M–H]$^+$), 678.33 ([M + Na^+]); calcd. exact mass: 655.36.



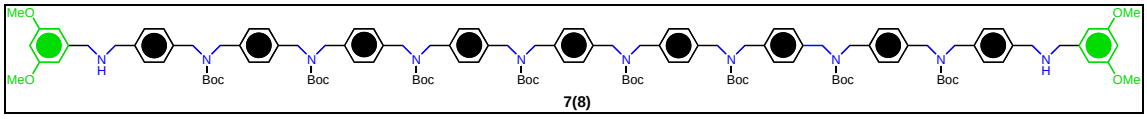
5(1)

Following the ***General Procedure A***, condensation of **4** (88 mg) with aldehyde **MA-1** (500 mg) and subsequent reduction by $NaBH_4$ (245 mg) gave compound **5(1)** in 92% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.29 (s, 4H), 7.27 (d, *J* = 7.6 Hz, 4H), 7.17 (d, *J* = 7.6 Hz, 4H), 6.34 (s, 6H), 4.37–4.28 (br, 8H), 3.78 (s, 8H), 3.73 (s, 12H), 1.49 (s, 18H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.98, 155.62, 139.66, 139.24, 128.18, 128.05, 117.20, 105.02, 98.92, 79.76, 55.19, 28.12. ESI MS: *m/z* = 875.48, ([*M*–H]$^+$); calcd. exact mass: 874.49.



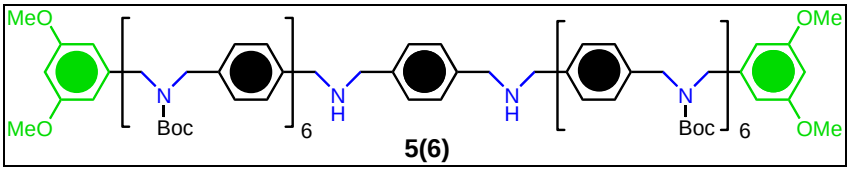
7(4)

Following the ***General Procedure A***, condensation of **6** (46.5 mg) with aldehyde **DA-4** (140 mg) and subsequent reduction by $NaBH_4$ (37 mg) gave compound **7(4)** in 81% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 (d, *J* = 8.0 Hz, 4H), 7.18 (br, 16H), 6.50 (s, 4H), 6.33 (s, 2H), 4.37–4.33 (br, 16H), 3.76 (s, 12H), 3.73 (br, 8H), 1.47 (s, 36H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.88, 129.15, 128.13, 105.72, 80.01, 55.21, 28.11. ESI MS: *m/z* = 1313.58 ([*M*–H]$^+$); calcd. exact mass:1312.74.



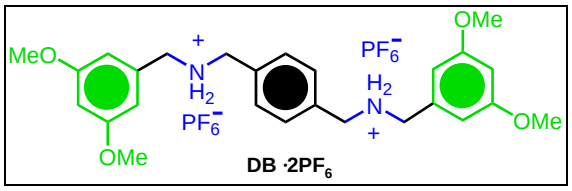
7(8)

Following the ***General Procedure A***, condensation of **6** (13.5 mg) with aldehyde **DA-8** (75 mg) and subsequent reduction by $NaBH_4$ (37 mg) gave compound **7(8)** in 80% yield. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.31 (d, *J* = 7.9 Hz, 4H), 7.20 (br, 32H), 6.51 (s, 4H), 6.34 (s, 2H), 4.38–4.34 (br, 32H), 3.78 (s, 4H), 3.76 (s, 12H), 3.74 (s, 4H), 1.48 (s, 72H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.88, 129.15, 128.13, 105.72, 80.01, 55.21, 28.11. ESI MS: *m/z* = 2190.16 ([*M*–H] $^+$); calcd. exact mass: 2189.24.

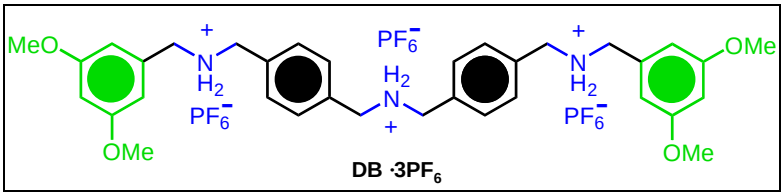


5(6)

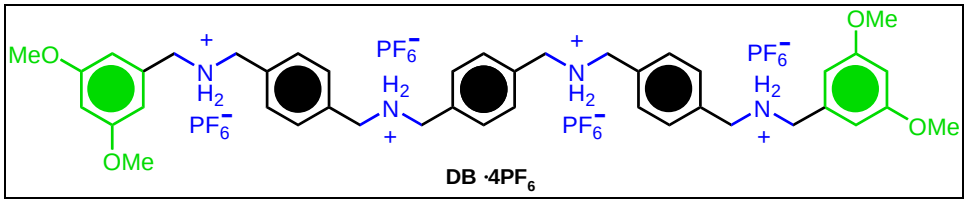
Following the ***General Procedure A***, condensation of **4** (5.0 mg) with aldehyde **MA-6** (100 mg) and subsequent reduction by $NaBH_4$ (76 mg) gave compound **5(6)** in 79% yield. ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.36 (br, 8H), 7.25 (br, 48H), 6.40 (s, 6H), 4.43–4.39 (br, 48H), 3.83 (s, 8H), 3.80 (s, 12H), 1.53 (s, 108H, Boc). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.86, 155.62, 137.07, 128.10, 127.94, 127.55, 105.72, 98.80, 79.68, 55.06, 28.00. ESI MS: *m/z* = 1534.78 ([*M*–2H]$^{2+}$), 1545.77 ([*M* + H$^+$ + Na$^+$]); calcd. exact mass: 3065.75.



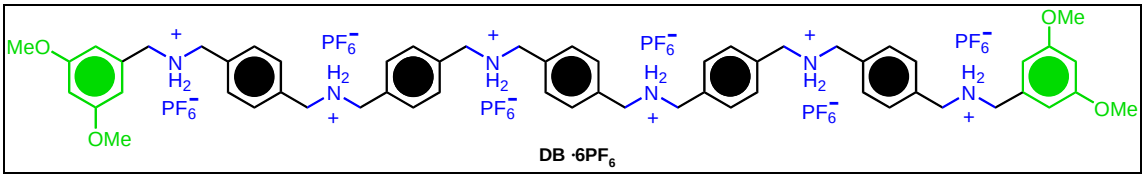
Following the ***General Procedure A***, condensation of **6** (1.67 g) with aldehyde **DA-0** (670 mg) and subsequent reduction by $NaBH_4$ (1.89 g) gave compound **7(0)** in 90% yield. Following the ***General Procedure E***, the **DB-H$_2$**·2PF_6 was obtained in 89% yield. ^{1}H NMR (400 MHz, CD_3NO_2): δ = 7.61(s, 4H), 6.64(d, ^4J = 2.0 Hz, 4H), 6.59 (t, ^4J = 2.0 Hz, 2H), 4.56 (s, 4H), 4.43 (s, 4H), 3.81 (s, 12H). ESI MS obtained after neutralization of the **DB-H$_2$**·2PF_6 with NaOH (aq), found: *m/z* = 437.24 ([*M*–H]$^+$), 459.22 ([*M* + Na$^+$]); calcd. exact mass: 436.24.



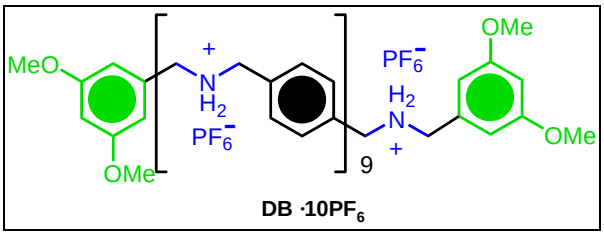
Following the ***General Procedure E***, the **DB-H$_3$**·3PF_6 was obtained from **7(1)** in 84% yield. ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 9.61 (s, 6H, -NH_2^+-), 7.51(s, 8H), 6.61(d, ^4J = 2.0 Hz, 4H), 6.53(t, ^4J = 2.0 Hz, 2H), 4.16 (s, 8H), 4.06 (s, 4H), 3.73 (s, 12H). ESI MS obtained after neutralization of the **DB-H$_3$**·3PF_6 with NaOH (aq), found: *m/z* = 556.31 ([*M*–H]$^+$), 578.30 ([*M* + Na$^+$]); calcd. exact mass: 555.31.



Following the ***General Procedure E***, the **DB-H$_4$**·4PF_6 was obtained from **5(1)** in 88% yield. ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 9.18 (s, 8H, -NH_2^+-), 7.51(s, 12H), 6.62 (d, ^4J = 2.4 Hz, 4H), 6.54 (t, ^4J = 2.4 Hz, 2H), 4.17 (s, 12H), 4.07 (s, 4H), 3.73 (s, 12H). ESI MS obtained after neutralization of the **DB-H$_4$**·4PF_6 with NaOH (aq), found: *m/z* = 675.39 ([*M*–H]$^+$), 697.37 ([*M* + Na$^+$]); calcd. exact mass: 674.38.

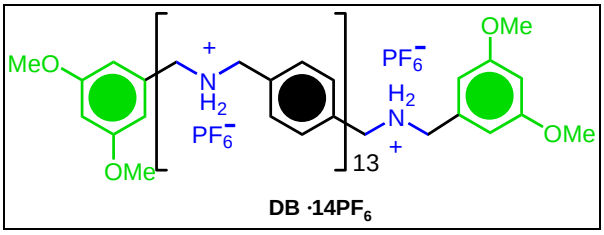


Following the ***General Procedure E***, the **DB-H$_6$**·6PF_6 was obtained from **7(4)** in 82% yield. ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 9.22 (s, 8H, -NH_2^+-), 9.18 (s, 4H, -NH_2^+-), 7.51(s, 20H), 6.61 (d, ^4J = 2.0 Hz, 4H), 6.54 (t, ^4J = 2.0 Hz, 2H), 4.18 (s, 20H), 4.06 (s, 4H), 3.73 (s, 12H). ESI MS obtained after neutralization of the **DB-H$_6$**·6PF_6 with NaOH (aq), found: *m/z* = 913.54 ([*M*–H]$^+$), 935.53 ([*M* + Na$^+$]); calcd. exact mass: 912.53.



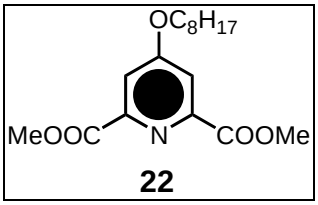
DB ·10PF$_6$

Following the ***General Procedure E***, the **DB-H**$_{10}$·10PF$_6$ was obtained from **7(8)** in 80% yield. ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 9.22 (br, 20H, -NH_2^+-), 7.52 (s, 36H), 6.62 (d, ^4J = 2.0 Hz, 4H), 6.54 (br, 2H), 4.19 (s, 36H), 4.06 (s, 4H), 3.73 (s, 12H). ESI MS obtained after neutralization of the **DB-H**$_{10}$·10PF$_6$ with NaOH (aq), found: *m/z* = 1390.83 ([*M*–H]$^+$), 1412.78 ([*M* + Na$^+$]); calcd. exact mass: 1388.82.



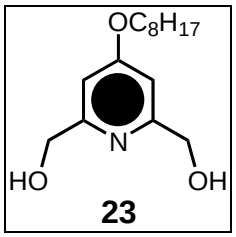
DB ·14PF$_6$

Following the ***General Procedure E***, the **DB-H**$_{14}$·14PF$_6$ was obtained from **5(6)** in 76% yield. ^{1}H NMR (400 MHz, CD_3SOCD_3): δ = 9.24 (br, 28H, -NH_2^+-), 7.54 (s, 52H), 6.64 (s, 4H), 6.54 (s, 2H), 4.17 (s, 52H), 4.08 (s, 4H), 3.76 (s, 12H). ESI MS obtained after neutralization of the **DB-H**$_{14}$·14PF$_6$ with NaOH (aq), found: *m/z* = 1867.31 ([*M*–H]$^+$); calcd. exact mass: 1865.12.



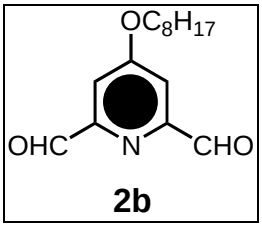
22

A mixture of compound **21** (1.5 g), 1-bromooctane (4.11 g), K_2CO_3 (3.92 g) in dry DMF (60 mL) was heated to 60 °C under argon atmosphere for 18 h. The solvent was removed under vacuum, and the residue was extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and the excess of solvent was then removed under vacuum. The residue was purified by column chromatography (silica gel, CH_2Cl_2/EtOAc = 10:1) to give compound **22** in 78% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (s, 2H), 4.16 (t, *J* = 6.4 Hz, 2H), 4.04 (s, 6H), 1.86 (pent, *J* = 6.7 Hz, 2H), 1.49 (br, 2H), 1.32 (br, 8H), 0.92 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.01, 165.094, 149.57, 114.41, 68.99, 53.08, 31.61, 29.05, 29.01, 28.57, 25.68, 22.49, 13.94. MALDI-TOF MS: *m/z* = 323.62; calcd. exact mass: 323.17.



23

Compound **22** (1.4 g) was dissolved in a mixture of solvents of MeOH (25 mL) and THF (50 mL), powder of $NaBH_4$ (655 mg) was then added in portions. The mixture was stirred at room temperature for 18 h and the excess of solvent was removed under vacuum. The residue was extracted with EtOAc and the organic layer was washed with water. The excess of solvent was removed to give compound **23** in 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26 (s, 2H), 4.67 (s, 4H), 4.33 (s, 2H), 4.00 (t, *J* = 6.5 Hz, 2H), 1.77 (pent, *J* = 6.5 Hz, 2H), 1.42 (br, 2H), 1.27 (br, 8H), 0.69 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.85, 160.16, 105.79, 68.29, 64.05, 31.66, 29.14, 29.07, 28.73, 25.77, 22.53, 13.98. MALDI-TOF MS: *m/z* = 267.53; calcd. exact mass: 267.18.

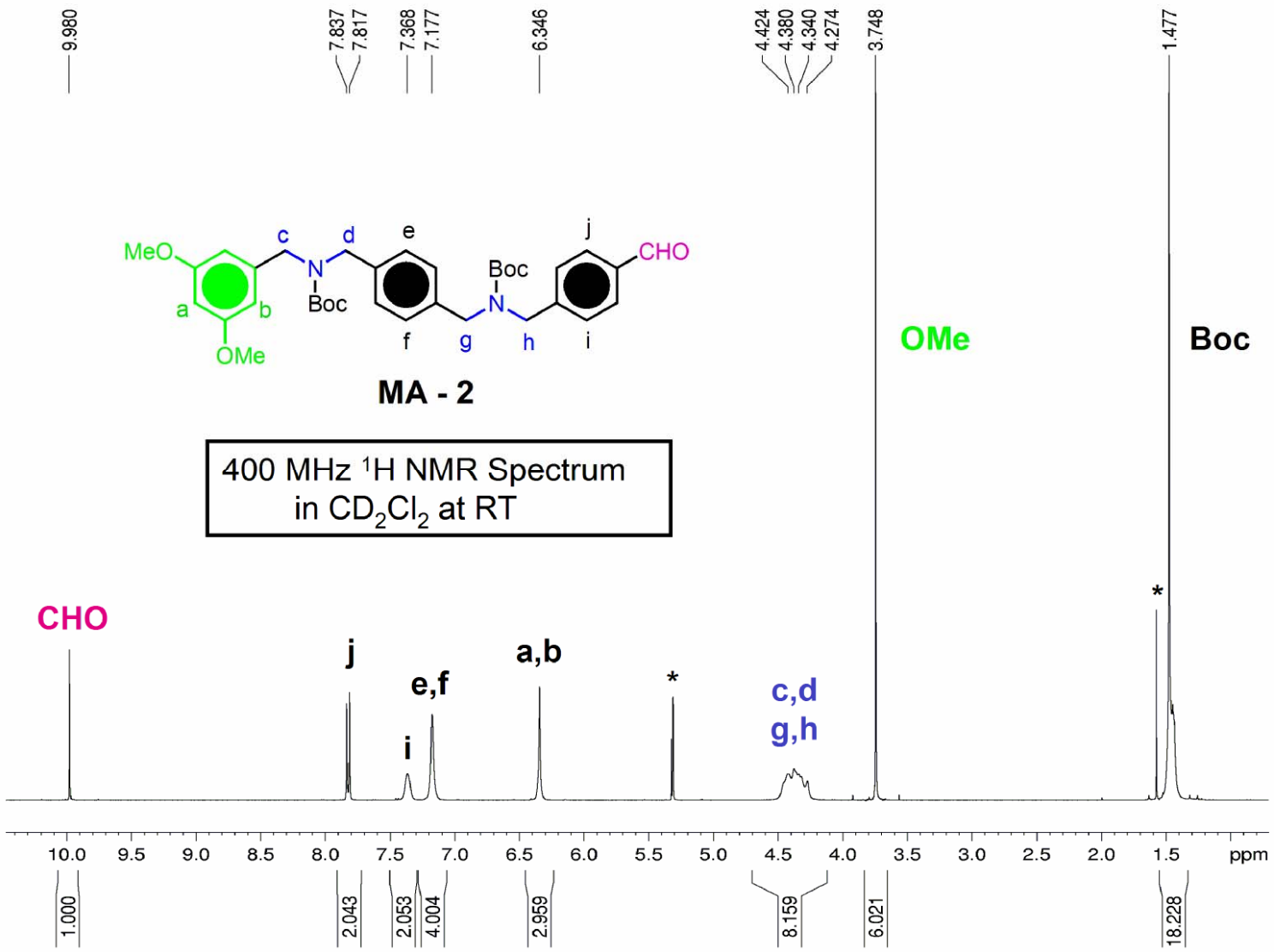


2b

A mixture of **23** (600 mg) and SeO_2 (500 mg) in dioxane (10 mL) was heated to 90 ^{o}C under argon atmosphere for 16 h. After cooling, the mixture was filtered through a celite pad and washed with more dioxane. The excess of solvent in the filtrate was removed under vacuum and the residue was purified by column chromatography (silica gel, CH_2Cl_2) to give compound **2b** in 85% yield. ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 10.06 (s, 2H, CHO), 7.60 (s, 2H), 4.14 (t, *J* = 6.6 Hz, 2H), 1.83 (pent, *J* = 6.5 Hz, 2H), 1.45 (m, 2H), 1.28 (br, 8H), 0.87 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 191.63, 167.06, 154.67, 111.13, 69.30, 31.62, 29.04, 29.02, 28.52, 25.61, 22.49, 13.70. MALDI-TOF MS: *m/z* = 264.56; calcd. exact mass: 263.15.

Appendix

Additional ^{1}H NMR Spectra for Some Key Compounds.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7.817
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6.346
4.424
4.380
4.340
4.274
3.748
1.477
MeO
OMe
CHO
Boc
a
b
c
d
e
f
g
h
i
j
MA - 2
400 MHz ¹H NMR Spectrum
in CD2Cl2 at RT
CHO
j
e,f
i
a,b
*
c,d
g,h
OMe
Boc
*
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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2.959
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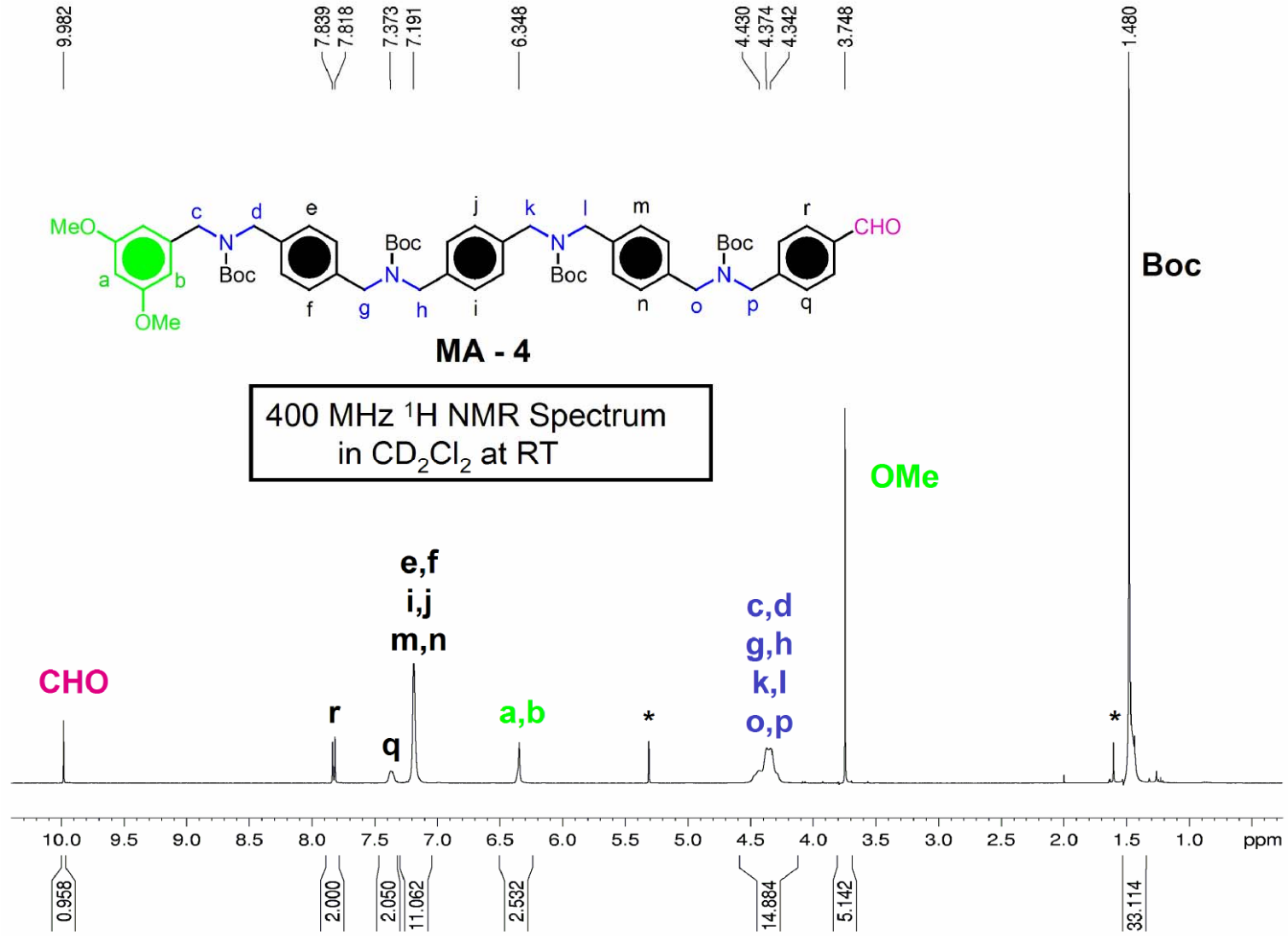
6.021
18.228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7.373
7.191
6.348
4.430
4.374
4.342
3.748
1.480
MeO
OMe
Boc
CHO
a
b
c
d
e
f
g
h
i
j
k
l
m
n
o
p
q
MA - 4
400 MHz 1H NMR Spectrum
in CD2Cl2 at RT
CHO
r
q
e,f
i,j
m,n
a,b
*
c,d
g,h
k,l
o,p
OMe
*
Boc
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
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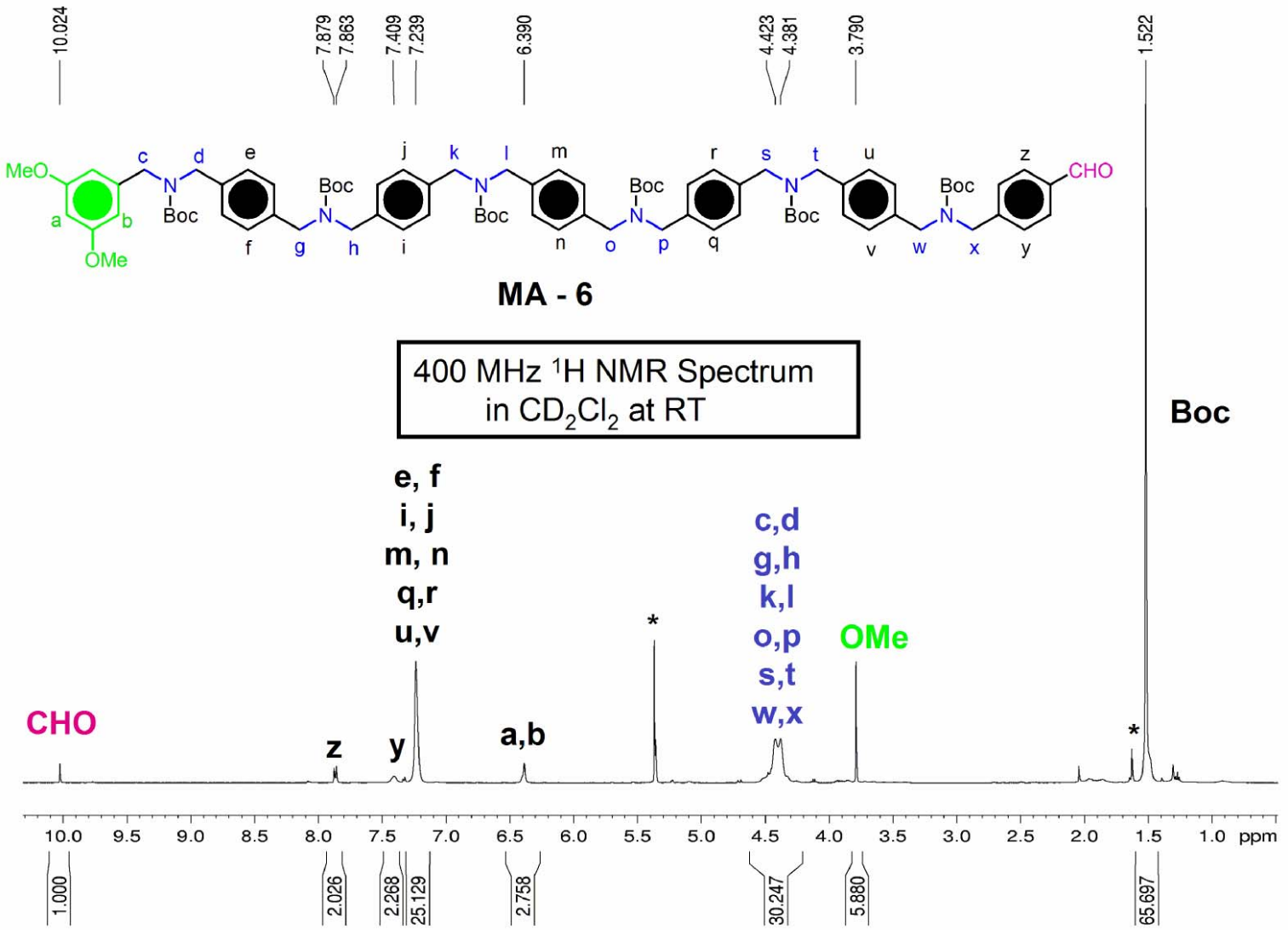
33.114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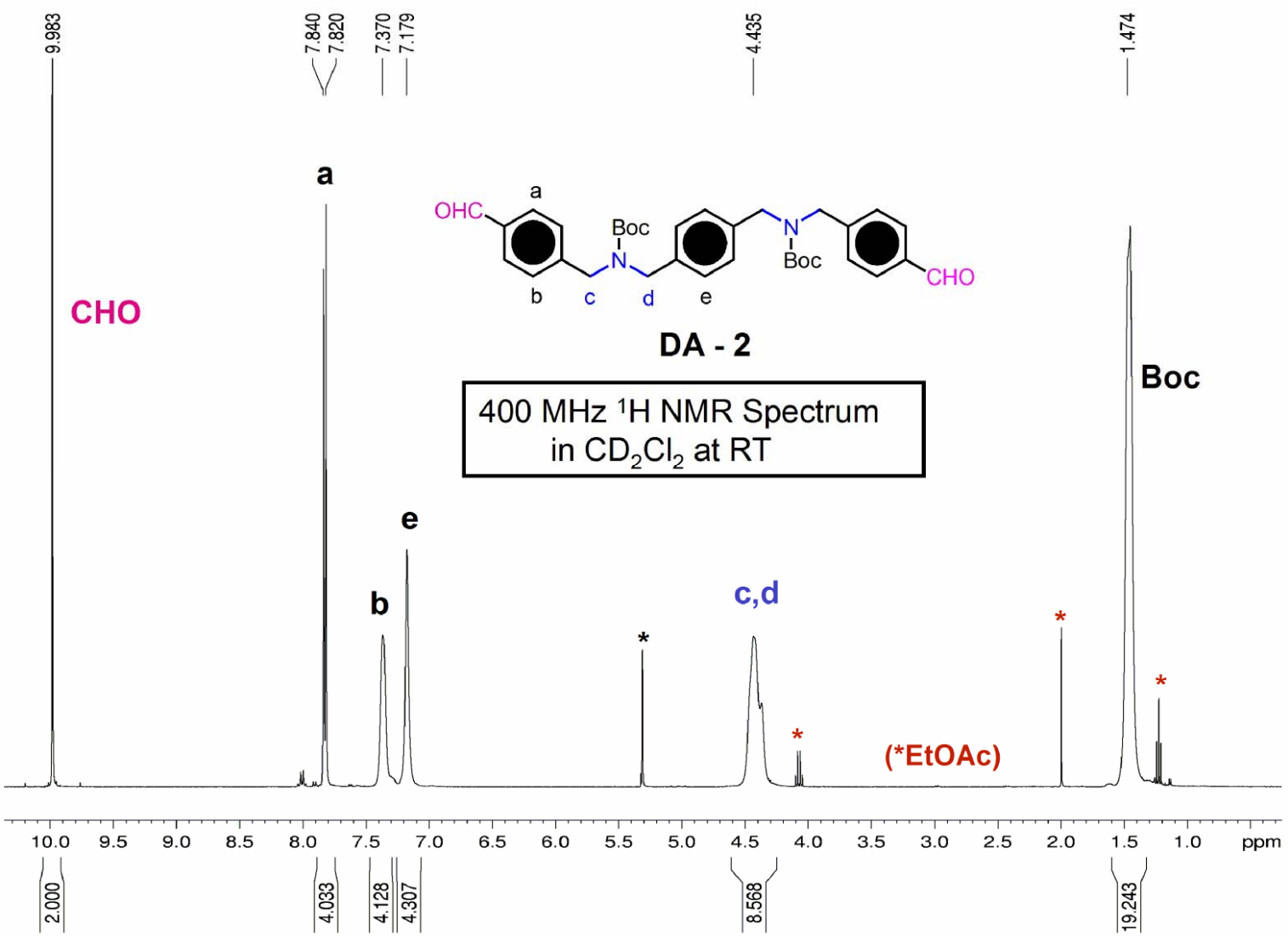
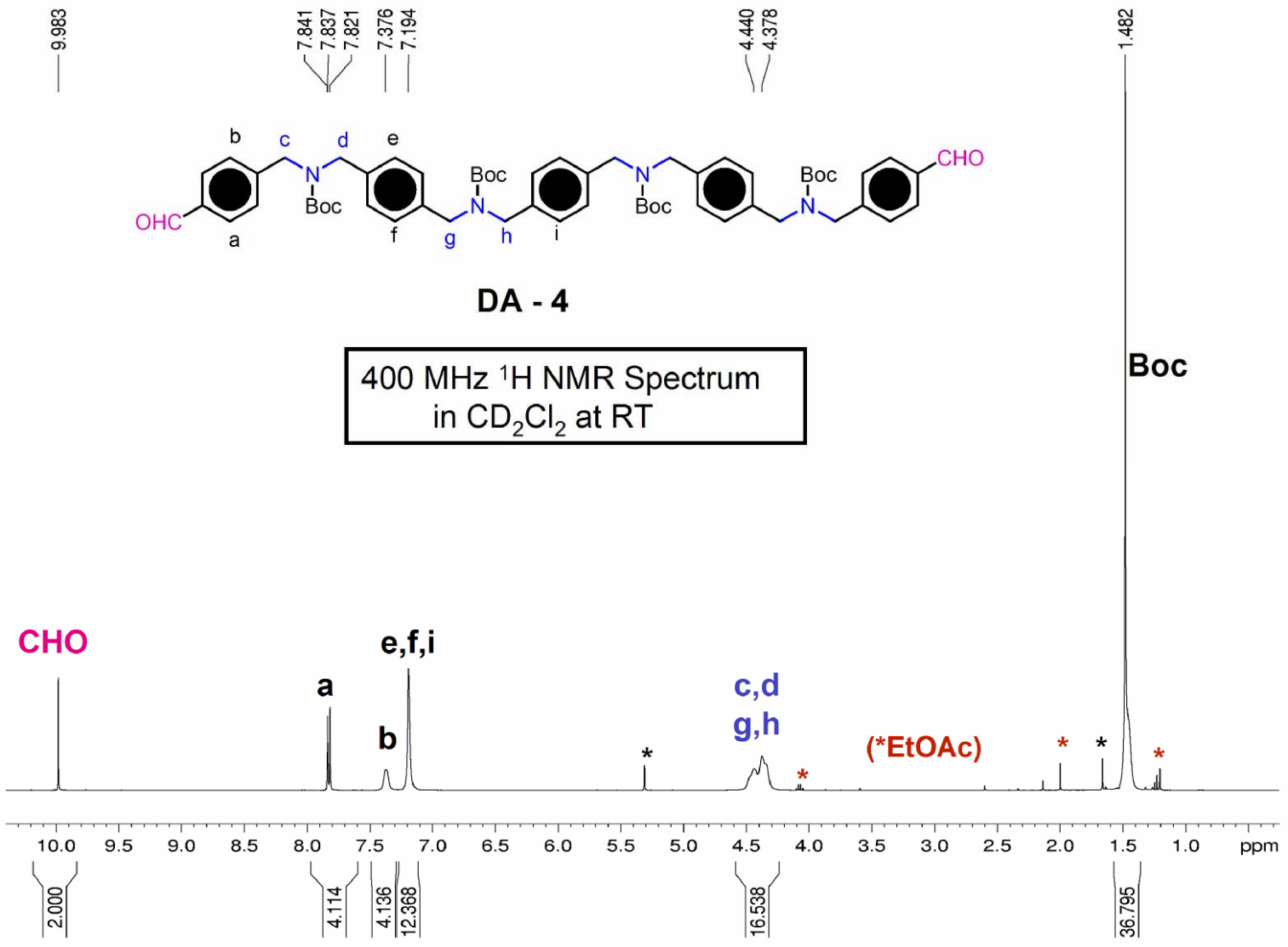
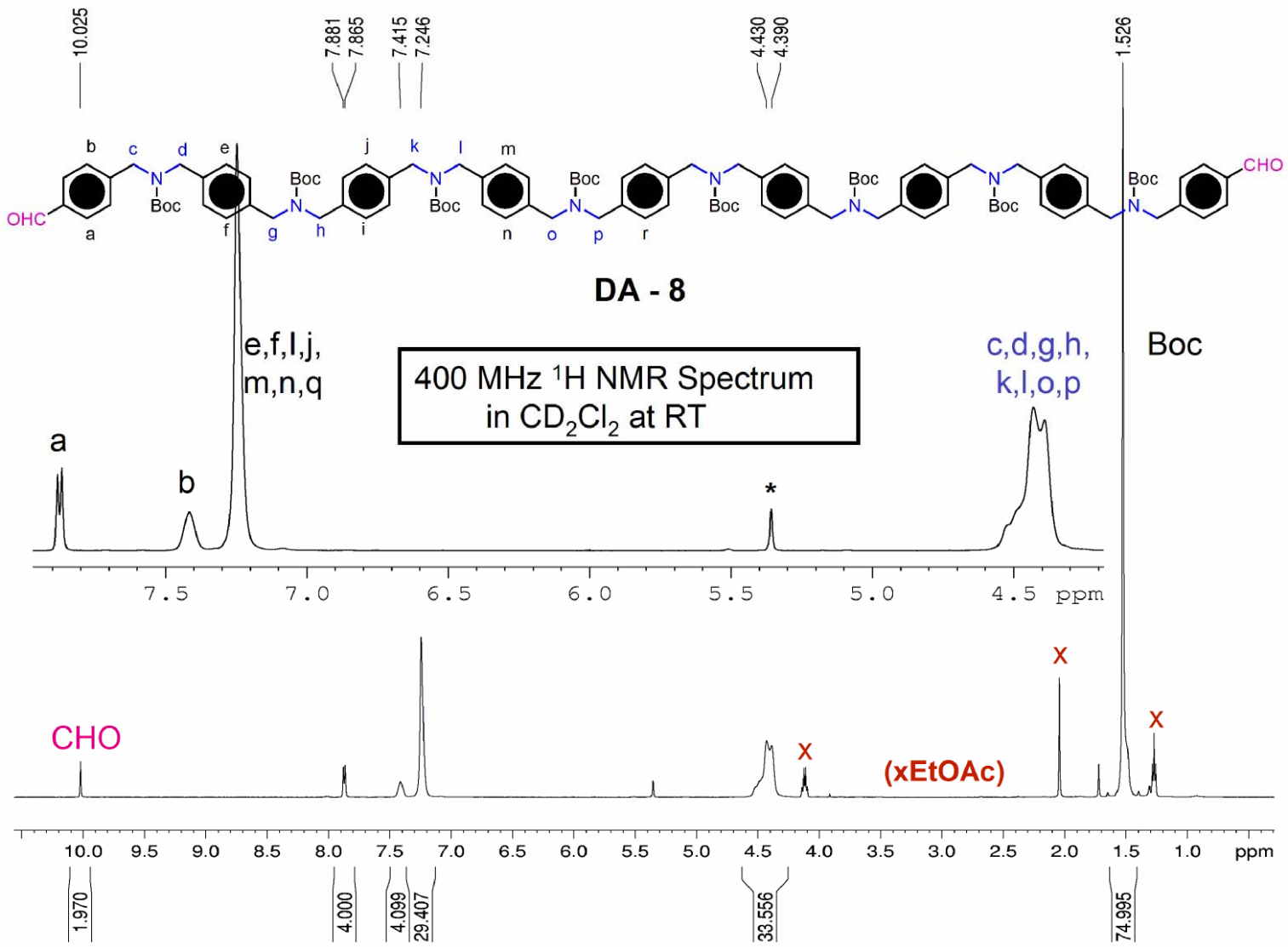
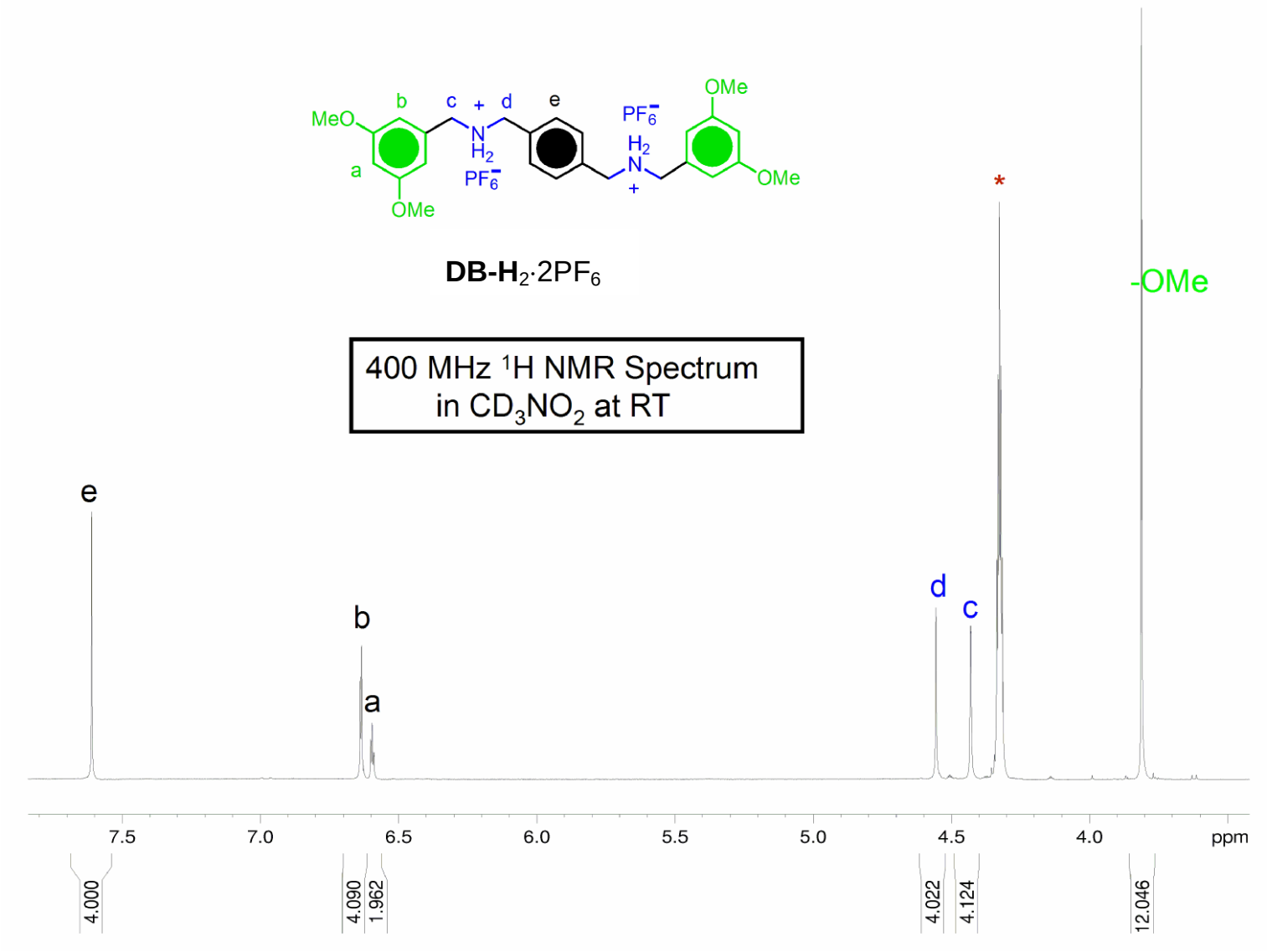
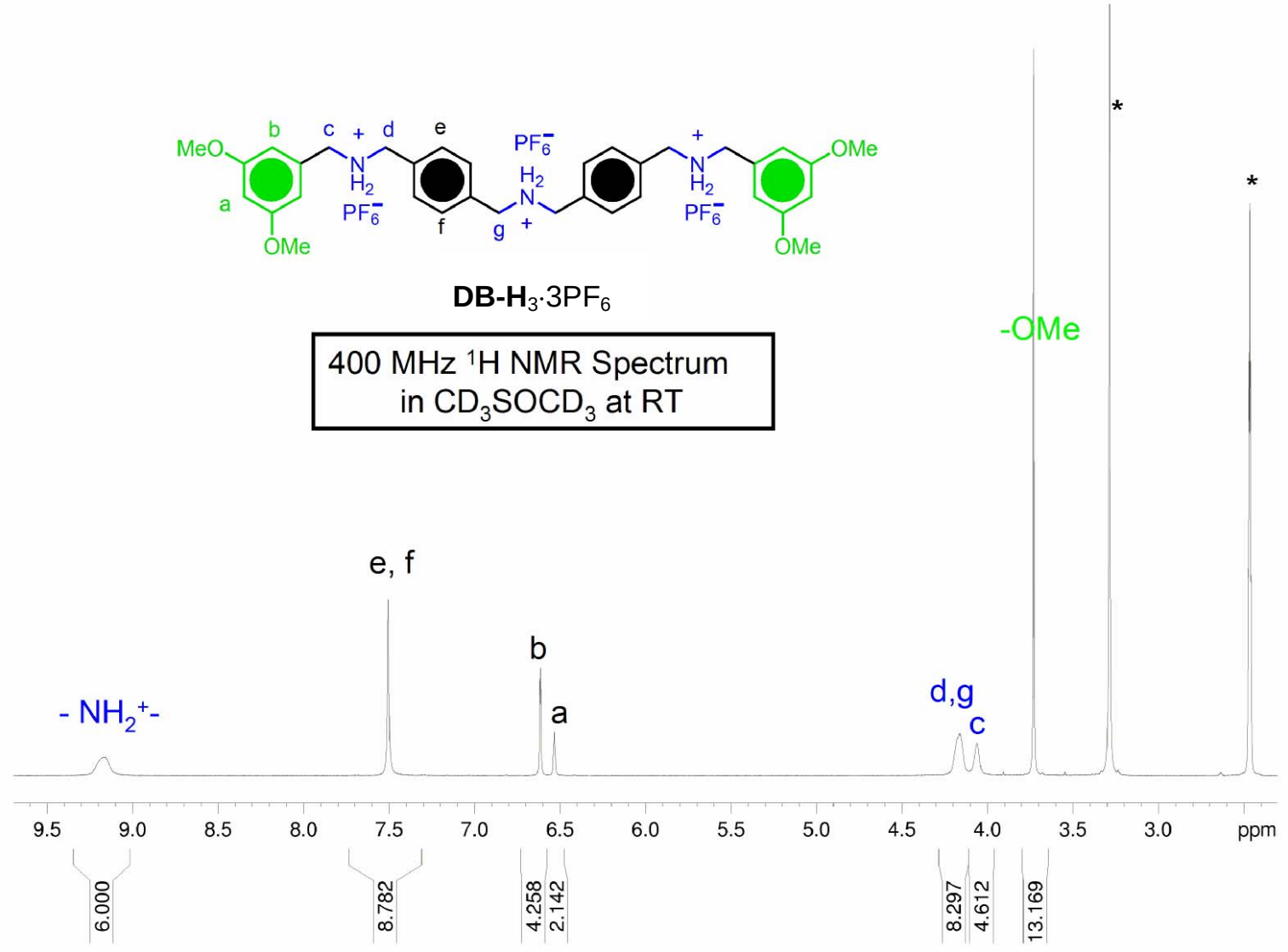
6.390
4.423
4.381
3.790
1.522
MeO
OMe
Boc
CHO
MA - 6
400 MHz ¹H NMR Spectrum
in CD2Cl2 at RT
e, f
i, j
m, n
q,r
u,v
c,d
g,h
k,l
o,p
s,t
w,x
OMe
Boc
CHO
z
y
a,b
*
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.000
2.026
2.268
25.129
2.758
30.247
5.880
65.697

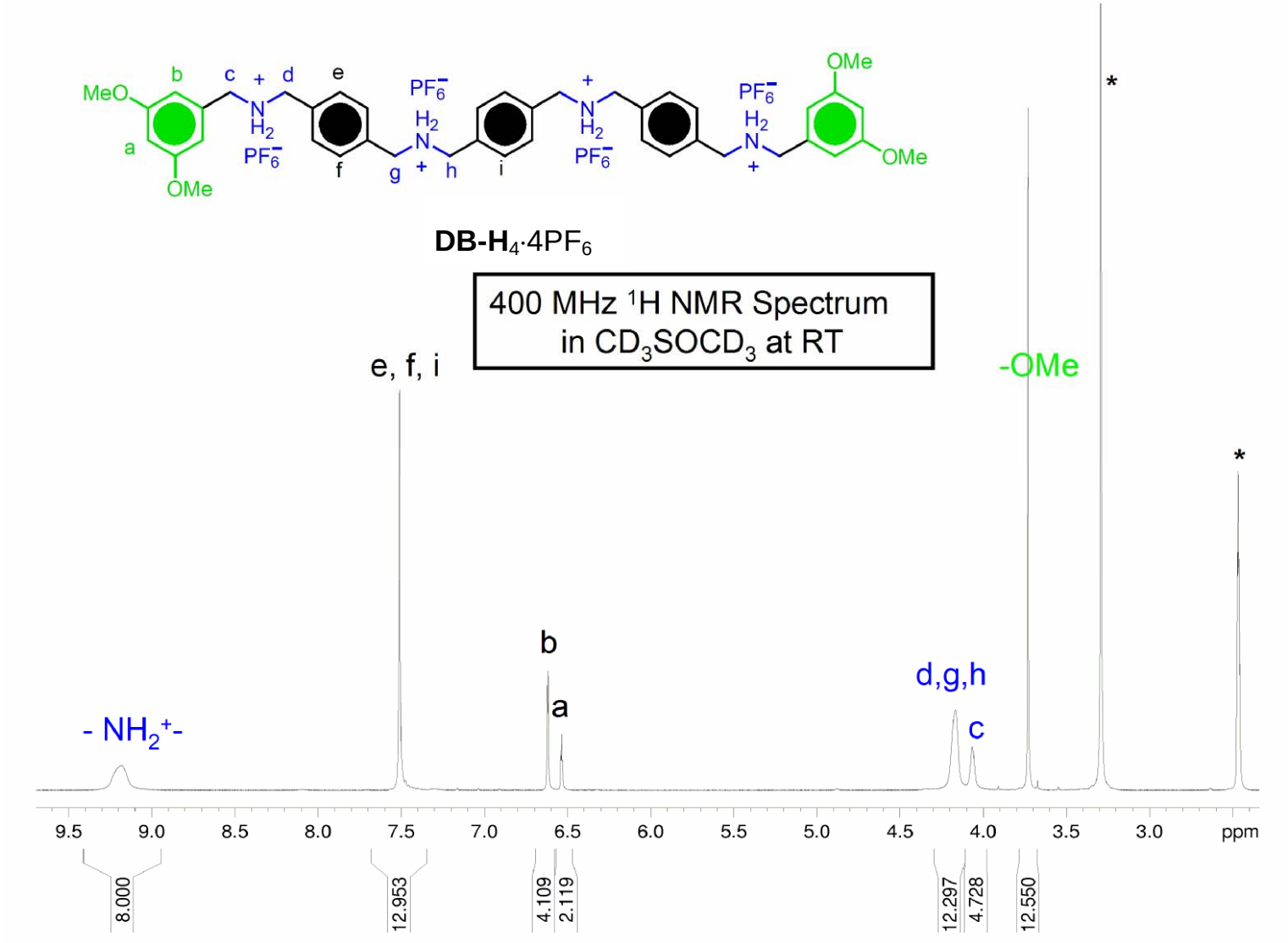

9.983
7.840
7.820
7.370
7.179
4.435
1.474
a
CHO
OHC
a
Boc
N
Boc
N
CHO
b
c
d
e
DA - 2
400 MHz ¹H NMR Spectrum
in CD2Cl2 at RT
Boc
e
b
c,d
*
*
*
*
(*EtOAc)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.000
4.033
4.128
4.307
8.568
19.243

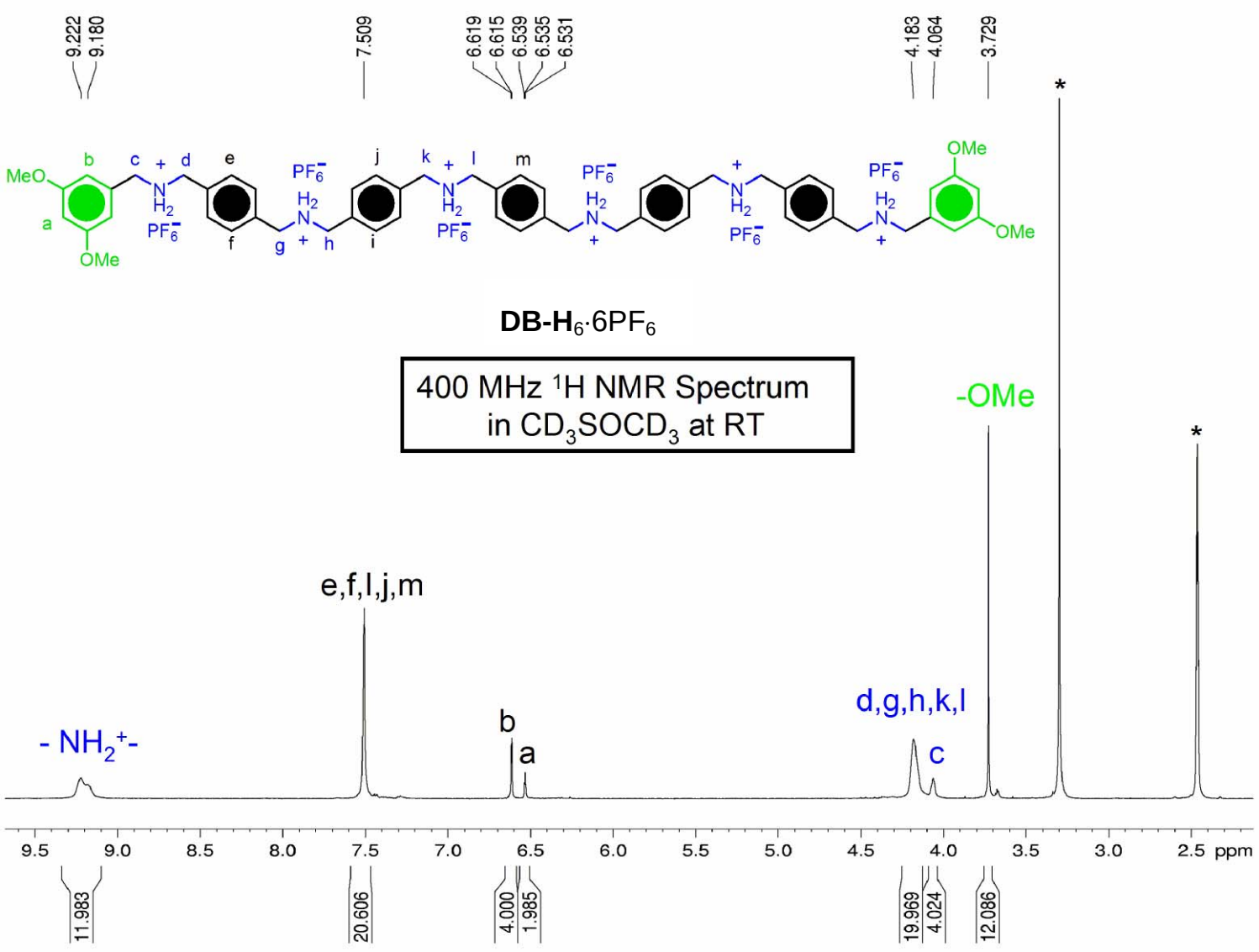

9.983
7.841
7.837
7.821
7.376
7.194
4.440
4.378
1.482
b
c
d
e
N
Boc
Boc
N
N
Boc
Boc
N
CHO
OHC
a
f
g
h
i
DA - 4
400 MHz 1H NMR Spectrum
in CD2Cl2 at RT
Boc
CHO
e,f,i
a
b
c,d
g,h
(*EtOAc)
*
*
*
*
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.000
4.114
4.136
12.368
16.538
36.795

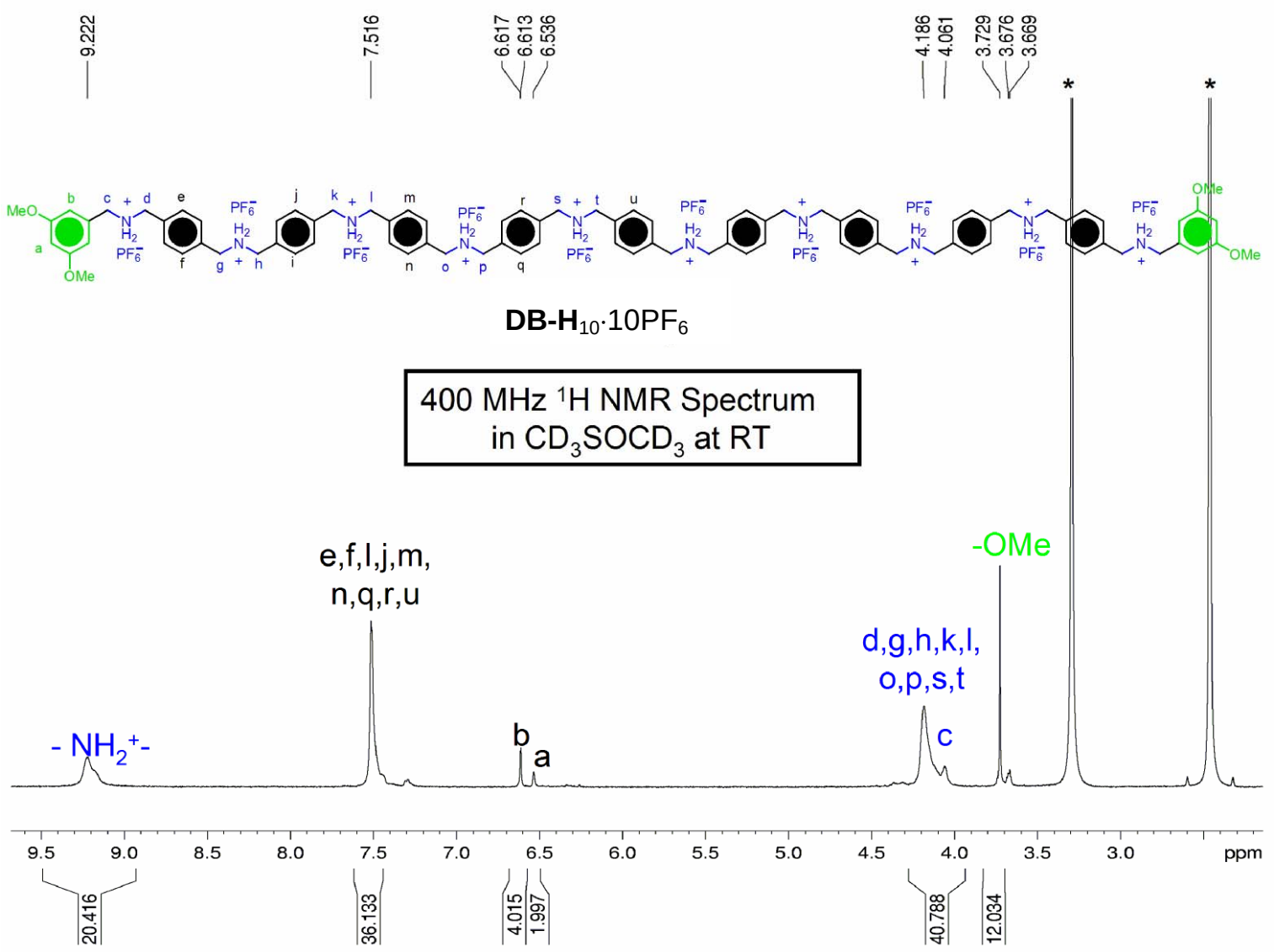

10.025
7.881
7.865
7.415
7.246
4.430
4.390
1.526
OHC
CHO
Boc
DA - 8
400 MHz ^{1}H NMR Spectrum
in CD_2Cl_2 at RT
a
b
e,f,l,j,
m,n,q
c,d,g,h,
k,l,o,p
Boc
*
7.5
7.0
6.5
6.0
5.5
5.0
4.5 ppm
CHO
X
(xEtOAc)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.970
4.000
4.099
29.407
33.556
74.995

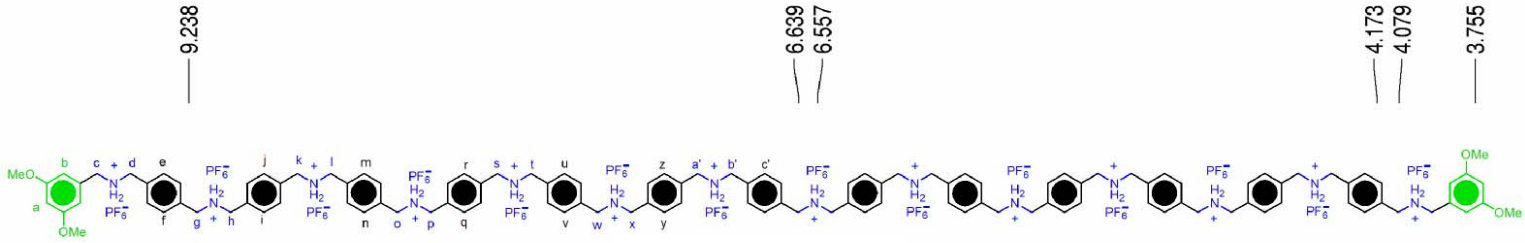

MeO
b
c
+
d
e
PF6
OMe
a
N
H2
PF6
H2
N
+
OMe
OMe
DB-H2·2PF6
400 MHz 1H NMR Spectrum
in CD3NO2 at RT
*
-OMe
e
b
a
d
c
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm
4.000
4.090
1.962
4.022
4.124
12.046


MeO
OMe
OMe
OMe
a
b
c
d
e
f
g
PF6
PF6
PF6
H2
N
+
DB-H3·3PF6
400 MHz 1H NMR Spectrum
in CD3SOCD3 at RT
-OMe
*
*
e, f
b
a
d,g
c
- NH2+-
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
6.000
8.782
4.258
2.142
8.297
4.612
13.169


MeO
OMe
OMe
OMe
PF6
PF6
PF6
PF6
DB-H4·4PF6
400 MHz 1H NMR Spectrum
in CD3SOCD3 at RT
e, f, i
-OMe
*
*
b
a
d,g,h
c
- NH2+-
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
8.000
12.953
4.109
2.119
12.297
4.728
12.550


9.222
9.180
7.509
6.619
6.615
6.539
6.535
6.531
4.183
4.064
3.729
MeO
OMe
OMe
OMe
DB-H6·6PF6
400 MHz 1H NMR Spectrum
in CD3SOCD3 at RT
-OMe
e,f,l,j,m
b
a
d,g,h,k,l
c
- NH2+-
*
*
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5 ppm
11.983
20.606
4.000
1.985
19.969
4.024
12.086


9.222
7.516
6.617
6.613
6.536
4.186
4.061
3.729
3.676
3.669
*
*
DB-H10·10PF6
400 MHz 1H NMR Spectrum
in CD3SOCD3 at RT
e,f,l,j,m,
n,q,r,u
-OMe
d,g,h,k,l,
o,p,s,t
- NH2+-
b
a
c
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
20.416
36.133
4.015
1.997
40.788
12.034



DB-H$_{14}$·14PF$_6$

400 MHz ^{1}H NMR Spectrum
in CD_3SOCD_3 at RT