Supplementary information

The synthesis and conformation of oxygenated trianglimine macrocycles [#]

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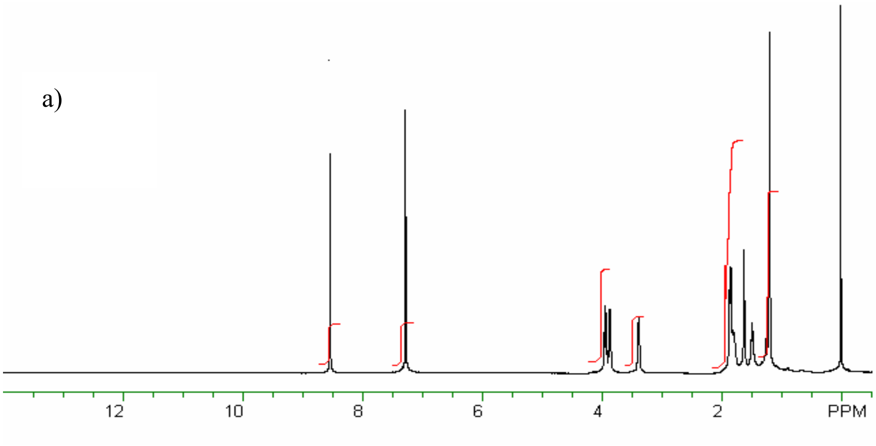
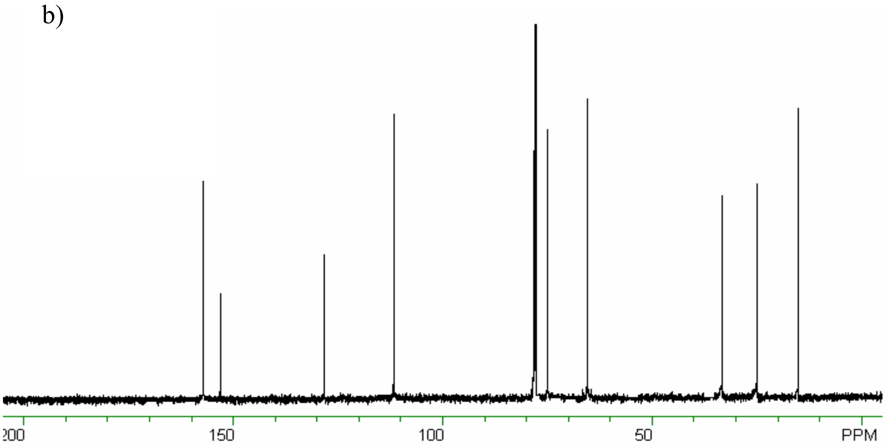
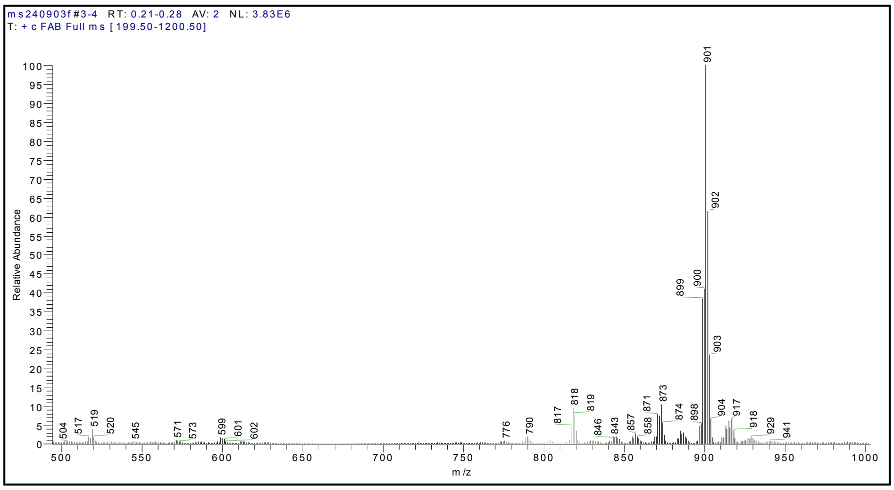
Additional Figure: a) ^{1}H-NMR (500 MHz) in $CDCl_3$ and b) ^{13}C-NMR (67.5 MHz) spectra of compound **15a** in $CDCl_3$

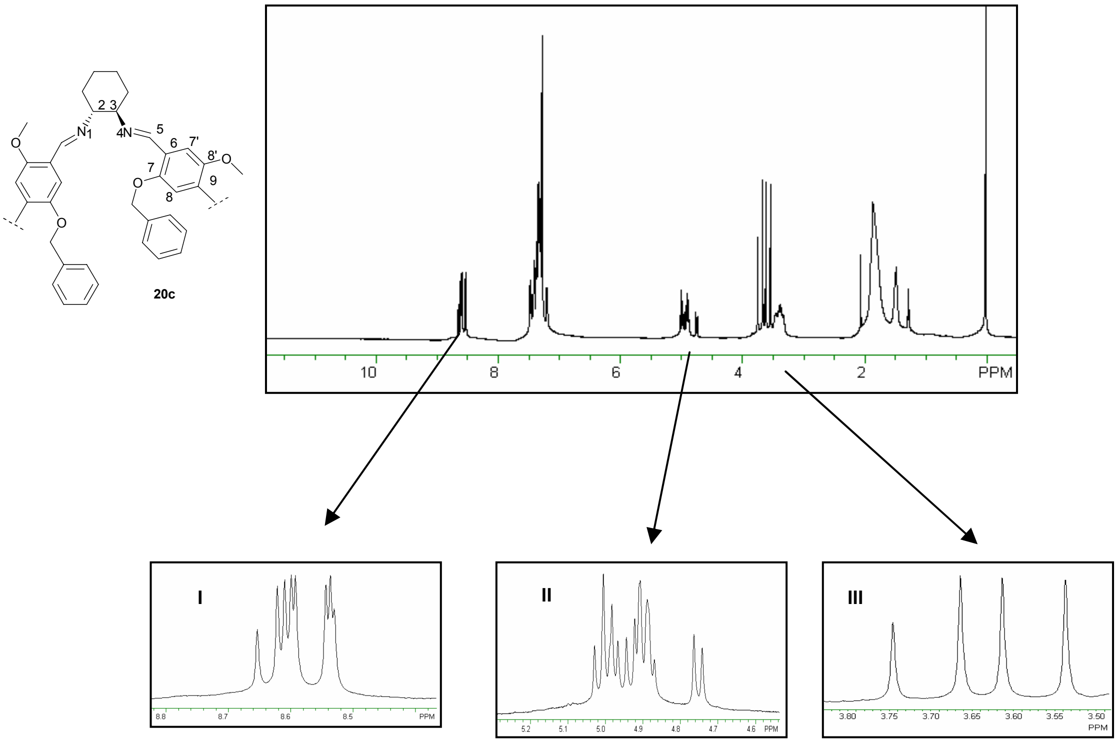




Additional Figure: FAB mass spectrum of **15a**



Additional Figure: Expanded ^{1}H NMR spectrum of **20c** in $CDCl_3$ (500 MHz) with enlarged imine and OR regions (enlargements **I-III** are shown below)



Supplementary experimental section:

1,4-Dibromo-2,5-dipropoxybenzene 13b [44]

A solution of bromine (530 μl, 1.65 g, 10.31 mmol) in glacial acetic acid (2 ml) was added to a solution of 1,4-dipropoxybenzene **12c** (1 g, 5.15 mmol) and anhydrous potassium acetate (96 mg, 1.17 mmol) in glacial acetic acid (12 ml) at 17 ºC. The solution was stirred for three hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from CH_2Cl_2 to give the title compound **13b** (317 mg, 17.5%), as light yellow powder; R_f 0.89 [Ethyl acetate-hexane (1:1)]; mp. 68 ºC (lit.[44] 74 ºC); IR ν_{max} (nujol)/ cm^{-1} 1462 (C=C), 1375, 1269 (C-O), 1021, 809, 455 (C-Br); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 7.08 (2H, s, -H_3 and -H_6), 3.89 (4H, t, J 7.6, -$OCH_2CH_2CH_3$), 1.81 (4H, sextet, J 7.6, -$OCH_2CH_2CH_3$), 1.4 (6H, t, J 7.6, -$OCH_2CH_2CH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 150.74 (C_2-O), 119.13 (C_3), 111.77 (C_1-Br), 66.47 (-$OCH_2CH_2CH_3$), 23.01 (-$OCH_2CH_2CH_3$), 10.95 (-$OCH_2CH_2CH_3$); *m/z* (EI) 353.9/ 351.9/ 349.9 (20%, M^+ ^{81}Br, ^{79}Br), 311.9/ 309.9/ 307.9 (10%, M + H^+ ^{81}Br, ^{79}Br -$CH_2CH_2CH_3$), 269.9/ 267.9/ 265.9 (100%, M + H_2^+ ^{81}Br, ^{79}Br-2 $CH_2CH_2CH_3$); CHN requires for $C_{12}H_{16}Br_2O_2$: C 40.94%, H 4.58%; found: C 41.21%, H 4.64%.

1,4-Dibromo-2,5-dibutoxybenzene 13c

A solution of bromine (462 μl, 1.4 g, 9 mmol) in glacial acetic acid (2 ml) was added to a solution of 1,4-dibutoxybenzene **12c** (1 g, 4.5 mmol) and anhydrous potassium acetate (84 mg, 1.02 mmol) in glacial acetic acid (12 ml) at 17 ºC. The solution was stirred for three hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from CH_2Cl_2 to give the *title compound* **13c** (1.38 g, 80.6%) as a light orange powder; R_f 0.85 [Ethyl acetate-hexane (1:1)]; mp. 72 ºC; IR ν_{max} (nujol)/ cm^{-1} 1499 (C=C), 1465, 1376, 1275 (C-O), 1037, 846 (C-Br); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 7.08 (2H, s, -H_3 and -H_6), 3.95 (4H, t, J 6.1, -$OCH_2CH_2CH_2CH_3$), 1.76 (4H, quintet, J 6.1, -$OCH_2CH_2CH_2CH_3$), 1.56 (4H, sextet, J 6.1, -$OCH_2CH_2CH_2CH_3$), 0.97 (6H, t, J 6.1, -$OCH_2CH_2CH_2CH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 150.77 (C_2-O), 119.08 (C_3), 111.76 (C_1-Br), 70.55 (-$OCH_2CH_2CH_2CH_3$), 31.67 (-$OCH_2CH_2CH_2CH_3$), 19.66 (-$OCH_2CH_2CH_2CH_3$), 14.29 (-$OCH_2CH_2CH_2CH_3$); found (EI) 380.9910 [M + H^+], $C_{14}H_{21}{}^{81}Br^{79}BrO_2$ requires 380.9882; *m/z* (EI) 382.1/ 380.1/ 378.1 (25%, M^+ ^{81}Br, ^{79}Br), 326/ 324/ 322 (10%, M + H^+ ^{81}Br, ^{79}Br -C_4H_9), 270/ 268/ 266 (100%, M + H_2^{2+} ^{81}Br, ^{79}Br-2 C_4H_9); CHN requires for $C_{14}H_{20}Br_2O_2$: C 44.24%, H 5.30%; found: C 45.18%, H 5.59%.

1,4-Dibromo-2,5-di(benzyloxy)benzene 13d [52]

A solution of bromine (277 µl, 0.863 g, 5.40 mmol) in glacial acetic acid (5 ml) was added to a solution of 1,4-di(benzyloxy)benzene **12d** (0.8 g, 2.70 mmol) and anhydrous potassium acetate (51.4 mg, 0.630 mmol) in glacial acetic acid (60 ml) at 17 ºC. The solution was stirred for three hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from CH_2Cl_2 to give the title compound **13d** as light yellow powder (851 mg, 70.4%); R_f 0.88 [Ethyl acetate-hexane (1:1)]; mp. 165-166 ºC (lit.[52] 167 ºC); ν_{max} (nujol)/ cm^{-1} 1454 (C=C), 1379, 1274 (C-O), 1071, 841, 694 (C-Br); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 7.45 (4H, d, J 8.3, $H_{2'}$), 7.39 (4H, t, J 8.3, $H_{3'}$), 7.34 (2H, d, J 8.3, $H_{4'}$), 7.20 (2H, s, -H_3 and -H_6), 5.08 (4H, s, -OCH_2Ph); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 154.24 (C_2-O), 137.34 ($C_{1'}$), 129.29 ($C_{3'}$), 129.22 ($C_{4'}$) 128.59 ($C_{2'}$), 120.71 (C_1-Br), 115.29 (C_3), 72.37 (-OCH_2Ph); found (EI) 448.9536, $C_{20}H_{16}Br_2O_2$ requires 448.9569; *m/z* (CI) 450/ 448/ 446 (10%, M^+ ^{81}Br, ^{79}Br), 369/ 367 (15%, M^+ ^{81}Br, ^{79}Br –^{79}Br), 279/ 277 (98%, M + H^+ ^{81}Br- [^{81}Br + C_7H_7]); (EI) 450/ 448/ 446 (100%, M^+ ^{81}Br, ^{79}Br); CHN requires for $C_{20}H_{16}Br_2O_2$: C 53.60%, H 3.60%; found: C 53.44%, H 3.94%.

1,4-Dibromo-2,5-di[(4'-fluorobenzyl)oxy]benzene 13e

A solution of bromine (314 µl, 0.979 g, 6.13 mmol) in glacial acetic acid (5 ml) was added to a solution of di-(4'-fluorobenzyloxy)benzene **12e** (1 g, 3.06 mmol) and anhydrous potassium acetate (57.05 mg, 0.69 mmol) in glacial acetic acid (20 ml) at 17 ºC. The solution was stirred for three hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from CH_2Cl_2-ethyl acetate (3:1) to give the *title compound* **13e** (0.734 g, 49.6%) as a light yellow powder; R_f 0.87 [Ethyl acetate-hexane (1:1)]; mp. 174-175 ºC; IR ν_{max} (nujol)/ cm^{-1} 1463 (C=C), 1377, 1206 (C-O), 1062, 843, 721 (C-Br); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 7.44 (4H, dd, J_1 8.6, J_2 5.3, $H_{2'}$), 7.17 (2H, s, H_3), 7.08 (4H, dd, J_1 8.6, J_2 6.3, $H_{3'}$), 5.03 (4H, s, -OCH_2-(*p*-F)C_4H_6); ^{13}C-NMR (67.5 MHz, $CDCl_3$*) δ_C: 129.42 ($C_{2'}$, $^3J_{CF}$ 8.6), 119.53 (C_3), 115.29 ($C_{3'}$, $^2J_{CF}$ 21.1), 114.91 (C_1-Br), 71.59 (-OCH_2Ph); *m/z* (EI) 486/ 484/ 482 (10%, M^+ ^{81}Br, ^{79}Br); CHN requires for $C_{20}H_{14}Br_2F_2O_2$: C 49.62%, H 2.91%; found: C 50.21%, H 2.73%.

* Not all C_q are detectable due to the poor solubility of **13e** in $CDCl_3$.

2,5-Dipropoxyterephthalaldehyde 14b

n-BuLi (3.55 ml, 1.6 M in hexane, 5.68 mmol) was added to a solution of 1,4-dibromo-2,5-dipropoxybenzene **13b** (400 mg, 1.14 mmol) in anhydrous THF (3 ml) at - 78 ºC under nitrogen atmosphere. The solution was stirred for two hours at the same temperature. Anhydrous DMF (441.6 µl, 5.68 mmol) was added to the reaction mixture. The solution was stirred for 30 minutes and then allowed to warm to room temperature. Distilled water (4 ml) and a 2 M solution of HCl (1.5 ml) were added. The solution was extracted with diethyl ether (3 x 15 ml). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with hexane-ethyl acetate (10:1) to give the title compound **14b** (114 mg, 40.0%) as a yellow powder; R_f 0.32 [Hexane-ethyl acetate (10:1)]; mp. 73 ºC; IR ν_{max} (nujol)/cm^{-1} 1692 (CO), 1499, 1379, 1163; ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 10.52 (2H, s, -C*H*O), 7.42 (2H, s, -H_3 and -H_6), 4.05 (4H, t, J 7.5, -O$CH_2$$CH_2$$CH_3$), 1.82 (4H, sextet, J 7.5, -$OCH_2$$CH_2$$CH_3$), 1.06 (6H, t, J 7.5, -$OCH_2CH_2CH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 190.23 (-*C*HO), 155.96 (C_2 and C_5), 124.80 (C_1 and C_4), 112.27 (C_3 and C_6), 71.24 (-O$CH_2CH_2CH_3$), 22.89 (-$OCH_2CH_2CH_3$) 10.96 (-$OCH_2CH_2CH_3$); *m/z* (EI) 251.2 (25%, M + H$^+$), 222.2 (95%, M + H$^+$- CHO); CHN requires for $C_{14}H_{18}O_4$: C 67.18%, H 7.25%; found C 66.97%, H 7.62%.

2,5-Dibutoxyterephthalaldehyde 14c

tert-BuLi (3.5 ml, 1.5 M in pentane, 5.26 mmol) was added to a solution of 1,4-dibromo-2,5-dibutoxybenzene **13c** (400 mg, 1.05 mmol) in anhydrous THF (4 ml) at - 78 ºC under nitrogen atmosphere. The solution was stirred for three hours at the same temperature. Anhydrous DMF (361 µl, 5.26 mmol) was added to the reaction mixture. The solution was stirred for one hours and then allowed to warm to room temperature.

Distilled water (4 ml) and a 2 M solution of HCl (1.5 ml) were added. The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from petroleum ether (40 – 60 ºC) to give the *title compound* **14c** (103 mg, 35.3%) as a yellow powder; R_f 0.81 [Hexane-ethyl acetate (10:1)]; mp. 55 ºC; IR ν_{max} (nujol)/cm^{-1} 1682 (CO), 1618, 1494, 1379, 1071; ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 10.51 (2H, s, -*C*HO), 7.43 (2H, s, -H_3 and -H_6), 4.09 (4H, t, J 7.1, -$OCH_2CH_2CH_2CH_3$), 1.80 (4H, quintet, J 7.1, -$OCH_2CH_2CH_2CH_3$), 1.52 (4H, sextet, J 7.1, -$OCH_2CH_2CH_2CH_3$), 0.98 (6H, t, J 7.1, -$OCH_2CH_2CH_2CH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$*) δ_C: 190.18 (-*C*HO), 112.18 (C_3 and C_6), 69.40 (-$OCH_2CH_2CH_2CH_3$), 31.50 (-$OCH_2CH_2CH_2CH_3$), 19.62 (-$OCH_2CH_2CH_2CH_3$), 14.16 (-$OCH_2CH_2CH_2CH_3$); found (EI) 279.156 [M + H$^+$], $C_{16}H_{23}O_4$ requires 279.1591; m/z (EI) 279 (15%, M$^+$), 250 (10%, M + H$^+$-CHO), 164 (100%, M$^+$-2 C_4H_9), 135 (40%, M$^+$-[CHO+2 C_4H_9]); CHN requires for $C_{16}H_{22}O_4$: C 69.04%, H 7.97%; found: C 67.52%, H 8.46%.

* C_q are not detectable because of the poor solubility of **14c** in $CDCl_3$.

2,5-Di(benzyloxy)terephthalaldehyde 14d

n-BuLi (2.78 ml, 1.6 M in hexane, 4.46 mmol) was added to a solution of 1,4-dibromo-2,5-di (benzyloxy)benzene **13d** (400 mg, 0.89 mmol) in anhydrous THF (10 ml) at - 78 ºC under nitrogen atmosphere. The solution was stirred for two hours at the same temperature. Anhydrous DMF (346.8 µl, 4.46 mmol) was added to the reaction mixture. The solution was stirred for 30 minutes and then allowed to warm to room temperature. Distilled water (4 ml) and HCl 2 M (1.5 ml) were added. The solution was extracted with diethyl ether (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was recrystallised from petroleum ether (40 - 60 ºC) to give the *title* *compound* **14d** (293 mg, 95.1%) as a yellow powder; R$_f$ 0.86 [Hexane-Ethyl acetate (10:1)]; mp. 119-120 ºC; IR ν_{max} (nujol)/cm^{-1} 1677 (-CHO), 1463, 1378, 1136; ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 10.54 (2H, s, -C*H*O), 7.56 (2H, s, -*H_3* and -*H_6*), 7.42 (4H, d, J 5.3 -*$H_{2'}$*), 7.40 (4H, dd, J$_1$ 6.4, J$_2$ 5.3, -*$H_{3'}$*), 7.35 (2H, d, J 6.4, -*$H_{4'}$*), 5.19 (4H, s, -OC*H_2*Ph); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 189.90 (-*C*HO), 155.74 (*C_2*-O and *C_5*-O), 136.35 (*$C_{1'}$*), 129.46 (*$C_{2'}$* or *$C_{3'}$* or *$C_{4'}$*), 129.13 (*$C_{2'}$* or *$C_{3'}$* or *$C_{4'}$*), 128.26 (*$C_{2'}$* or *$C_{3'}$* or *$C_{4'}$*), 119.04 (*C_1*-CHO and *C_4*-CHO), 113.02 (*C_3* and *C_6*), 71.73 (-O*C*H_2Ph); *m/z* (EI) 347 (45%, M^+), 288 (70%, M^+-2 CHO), 255 (20%, M^+- C_7H_7); CHN requires for $C_{22}H_{18}O_4$: C 76.29%, H 5.24%; found C 76.14%, H 5.35%.

2,5-Di[(4’-fluorobenzyl)oxy]terephthalaldehyde 14e

n-BuLi (2.00 ml, 1.6 M in hexane, 3.09 mmol) was added to a suspension of 1,4-dibromo-2,5-di[(4’-fluorobenzyl)oxy]benzene **13e** (300 mg, 0.62 mmol) in anhydrous THF (12 ml) at - 78 ºC under nitrogen atmosphere. The solution was stirred for two hours at the same temperature. Anhydrous DMF (241 µl, 3.09 mmol) was added to the reaction mixture. The solution was stirred for 30 minutes and then allowed to warm to room temperature. Distilled water (4 ml) and a 2 M solution of HCl (1.5 ml) were added. The solution was extracted with diethyl ether (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was recrystallised from petroleum ether (40 – 60 ºC)-ethyl acetate (3:2) to give the *title compound* **14e (**133 mg, 56.3%) as a yellow powder; R$_f$ 0.85 [Hexane-Ethyl acetate (10:1)]; mp. 130-131 ºC; IR ν_{max} (nujol)/cm^{-1} 1678 (CO), 1460, 1378, 1224; ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 10.52 (2H, s, -C*H*O), 7.54 (2H, s, -*H_3* and -*H_6*), 7.42 (4H, dd, J$_1$ 6.5, J$_2$ 2.4, *$H_{2'}$*), 7.09 (4H, dd, J$_1$ 6.5, J$_2$ 6.4, *$H_{3'}$*), 5.16 (4H, s, -OC*H_2*-(*p*-F)C_6H_4); ^{13}C-NMR (67.5 MHz, $CDCl_3^*$) δ_C: 189.11 (-

*C*HO), 129.81 ($C_{2'}$, $^3J_{CF}$ 8.1), 115.84 ($C_{3'}$, $^2J_{CF}$ 21.8), 112.61 (C_3 and C_6) 70.74 (-O*C*H_2-(*p*-F)C_6H_4); found (EI) 382.1038 [M^+], $C_{22}H_{16}F_2O_4$ requires 382.1011; *m/z* (EI) 382 (10%, M^+), 273 (10%, M^+-C_7H_6F), 106 (100%, M^+-[2 (C_7H_6F)+ 2 (CHO)]; CHN requires for $C_{22}H_{16}F_2O_4$: C 69.11%, H 4.22%; found: C 65.14%, H 4.04%.

[*] C_q are not detectable because of the poor solubility of **14e** in $CDCl_3$.

1-(2’-methoxyethoxy)-4-methoxybenzene 17d

To dimethyl sulphoxide (30 ml), potassium hydroxide powder (4.5 g, 80.55 mmol) was added. After stirring for 5 minutes, 4-methoxyphenol **16** (2.5 g, 20.14 mmol) was added, followed immediately by the 2-chloroethyl methyl ether (3.7 ml, 3.83 g, 40.28 mmol) and sodium iodide (30 mg). Stirring was continued for four hours, after which the mixture was poured into distilled water (100 ml) and extracted three times with dichloromethane (3 x 50 ml). The combined organic extracts were washed with distilled water (5 x 200 ml), dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash cromatography on silica gel eluting with ethyl acetate-hexane (1:1) to give the *title compound* **17d** (1.5 g, 41.6%) as an oil; R_f 0.85 [Ethyl acetate-hexane (1:1)]; IR ν_{max} (liquid)/ cm^{-1} 1508 (C=C Ar), 1456, 1234 (O-CH_2-); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 6.87 (2H, d, J 6.2, -H_2 or -H_3), 6.81 (2H, d, J 6.2, -H_2 or -H_3), 4.02 (2H, AA’ part of AA’XX’ system, N 9.2, -O$CH_2$$CH_2$-O$CH_3$), 3.71 (3H, s, -$CH_2OCH_3$ or Ph-OCH_3), 3.68 (2H, XX’ part of AA’XX’ system, N 14.0, -O$CH_2$$CH_2$-O$CH_3$), 3.04 (3H, s, -$CH_2OCH_3$ or Ph-OCH_3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 154.25 (C_4-OCH_3), 153.24 (C_1-O$CH_2$$CH_2OCH_3$), 115.75 ($C_2$-H), 114.76 ($C_3$-H), 71.25 (-O$CH_2$*C*$H_2OCH_3$), 67.98 (-O*C*$H_2$$CH_2OCH_3$) 59.09 (-O$CH_2$$CH_2$O*C*$H_3$), 55.56 (-O*C*$H_3$); found (EI) 183.1019, $C_{10}H_{15}O_3$ requires 183.1016; *m/z* (EI) 183 (100%, M + H^+), 123 (95%, M^+-C_3H_7O); CHN requires for $C_{10}H_{14}O_3$: C 65.91%, H 7.74%; found: C 64.05%, H 7.78%.

1,4-Dibromo-2-propoxy-5-methoxybenzene 18b

A solution of bromine (618 μl, 1.9 g, 12.04 mmol) in glacial acetic acid (3 ml) was added to a solution of 1-propoxy-4-methoxybenzene **17b** (1 g, 6.02 mmol) and anhydrous potassium acetate (112.4 mg, 1.4 mmol) in glacial acetic acid (10 ml) at 17 ºC. The solution was stirred for two hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from petroleum ether to give the *title compound* **18b** (1.71 g, 87.7%), as light yellow powder; R_f 0.74 [Ethyl acetate-hexane (1:1)]; mp. 69 ºC; IR ν_{max} (nujol)/ cm^{-1} 1495 (C=C), 1460, 1364, 1270 ($O-CH_2-$), 1067, 785 (C-Br); ^1H-NMR (270 MHz, $CDCl_3$) δ_H: 7.09 (2H, s, $-H_3$ and $-H_6$), 3.91 (2H, t, J 7.6, $-OCH_2CH_2CH_3$), 3.84 (3H, s, $-OCH_3$), 1.84 (2H, sextet, J 7.6, $-OCH_2CH_2CH_3$), 1.05 (3H, t, J 7.6, $-OCH_2CH_2CH_3$); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 151.62 (C_2 or C_5), 150.92 (C_2 or C_5), 119.45 (C_3 or C_6), 117.68 (C_3 or C_6), 112.03 (C_1 or C_4), 110.96 (C_1 or C_4), 72.43 ($-OCH_2CH_2CH_3$), 57.58 ($-OCH_3$), 22.93 ($-OCH_2CH_2CH_3$), 10.91 ($-OCH_2CH_2CH_3$); *m/z* (CI) 327/ 325/ 323 (100%, $M + H^{+}$ ^{81}Br, ^{79}Br), 285/ 283/ 281 (45%, $M + H_2^{2+}$ ^{81}Br- C_3H_7), 246/ 244 (20%, $M + H^{+81}Br-^{81}Br$); (EI) 326/ 324/ 322 (30%, M^{+} ^{81}Br, ^{79}Br), 284/ 282/ 280 (100%, $M + H^{+}$ ^{81}Br- C_3H_7), 269/ 267/ 265 (40%, $M + H^{+}$ ^{81}Br, ^{79}Br - C_4H_{10}); CHN requires for $C_{10}H_{12}Br_2O_2$: C 37.07%, H 3.73%; found: C 37.08%, H 3.74%.

1,4-Dibromo-2-(benzyloxy)-5-methoxybenzene 18c

A solution of bromine (479 μl, 1.49 g, 9.33 mmol) in glacial acetic acid (3 ml) was added to a solution of 1-(benzyloxy)-4-methoxybenzene **17c** (1g, 4.67 mmol) and anhydrous potassium acetate (87.1 mg, 1.06 mmol) in glacial acetic acid (12 ml) at 17 ºC. The solution was stirred for 4 hours at the same temperature. The mixture was poured into distilled water (100 ml). The precipitate was filtered and dried under reduced pressure. The residue was recrystallised from petroleum ether to give the *title compound* **18c** (1.37 g, 79.1%) as a light yellow powder; R_f 0.83 [Ethyl acetate-hexane (1:1)]; mp. 116 ºC; IR ν_{max} (nujol)/ cm^{-1} 1508 (C=C), 1457, 1379, 1292 (O-CH_2-), 1113, 763 (C-Br); ^{1}H-NMR (270 MHz, $CDCl_3$) δ_H: 7.46 (2H, d, J 6.3, -$H_{2'}$), 7.41 (2H, dd, J_1 6.3, J_2 13.3, -$H_{3'}$), 7.38 (H, d, J 13.3, -$H_{4'}$), 7.17 (1H, s, -H_3 or -H_6), 7.12 (1H, s, -H_3 or -H_6), 5.05 (2H, s, -OCH_2Ph), 3.83 (3H, s, -OCH_3); ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ_C: 151.13 (C_2 or C_5), 149.84 (C_2 or C_5), 136.38 ($C_{1'}$), 128.83 ($C_{3'}$), 128.35 ($C_{4'}$), 127.47 ($C_{2'}$), 119.68 (C_3 or C_6), 117.16 (C_3 or C_6), 111.93 (C_1 or C_4), 110.56 (C_1 or C_4), 72.27 (-O*C*H_2Ph), 57.17 (-O*C*H_3); *m/z* (CI) 374/ 372/ 370 (100%, M^+ ^{81}Br, ^{79}Br), 294/ 293/ 291 (80%, M^+ ^{81}Br-^{81}Br); CHN requires for $C_{14}H_{12}Br_2O_2$: C 45.20%, H 3.25%; found: C 46.14%, H 3.21%.

1,4-Dibromo-2-(2'-methoxyethoxy)-5-methoxybenzene 18d

A solution of bromine (570 µl, 1.77 g, 11.09 mmol) in glacial acetic acid (3 ml) was added to a solution of 1-(2-methoxyethoxy)-4-methoxy benzene **17d** (1 g, 5.55 mmol) and anhydrous potassium acetate (103 mg, 1.26 mmol) in glacial acetic acid (12 ml) at 17 ºC. The solution was stirred for three hours at the same temperature. The mixture was poured into distilled water (100 ml) and extracted with CH_2Cl_2 (3 x 30 ml). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was recrystallised from petroleum ether to give the *title compound* **18d** (1.53 g, 81.4%) as a light yellow powder; R_f 0.86 [Ethyl acetate-hexane (1:1)]; mp. 42 ºC; IR ν_{max} (nujol)/ cm^{-1} 1508 (C=C Ar), 1456, 1234

(O-CH_2-); ^{1}H-NMR (270 MHz, CDCl_3) δ_H: 7.15 (1H, s, -H_3 or -H_6), 7.07 (1H, s, -H_3 or -H_6), 4.10 (2H, AA'XX' part of AA'XX' system, N 9.4, $\text{-OC}H_2\text{CH}_2\text{-OCH}_3$ or $\text{-OCH}_2\text{C}H_2\text{-OCH}_3$), 3.83 (3H, s, $\text{Ph-OC}H_3$), 3.75 (2H, XX' part of AA'XX' system, N 9.4, $\text{-OC}H_2\text{CH}_2\text{-OCH}_3$ or $\text{-OCH}_2\text{C}H_2\text{-OCH}_3$), 3.45 (3H, s, $\text{-OCH}_2\text{CH}_2\text{-OC}H_3$); ^{13}C-NMR (67.5 MHz, CDCl_3) δ_C: 151.39 (C_2 or C_5), 150.40 (C_2 or C_5), 119.84 (C_3 or C_6), 117.25 (C_3 or C_6), 112.00 (C_1 or C_4), 110.76 (C_1 or C_4), 71.23 ($\text{-OCH}_2C\text{H}_2\text{OCH}_3$), 70.46 ($\text{-O}C\text{H}_2\text{CH}_2\text{OCH}_3$), 59.72 ($\text{-OCH}_2\text{CH}_2\text{O}C\text{H}_3$), 57.26 ($\text{-O}C\text{H}_3$); *m/z* (EI) 342/ 340/ 338 (50%, M^+ ^{81}Br, ^{79}Br), 284/ 282/ 280 (100%, M + H^+ ^{81}Br, $^{79}\text{Br-C}_3\text{H}_7\text{O}$); CHN requires for $\text{C}_{10}\text{H}_{12}\text{Br}_2\text{O}_3$: C 35.32%, H 3.56%; found: C 35.22%, H 3.54%.