Supplementary Material (ESI) for Green Chemistry

Supporting Information

Task-specific ionic liquids as reaction media for the cobalt-catalysed cyclotrimerisation reaction of arylethynes

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General Methods

^{1}H and ^{13}C NMR were recorded on a Varian Inova 300 and on a Varian Gemini 200; chemical shifts (δ) are reported in ppm relative to TMS. Gas chromatographic analyses were performed with a HP5890 II instrument at 70 eV coupled to a HP5971 quadrupole mass detector and using a HP-5MS cross-linked 5% phenyl-methyl silicone glass capillary column, 0.25-μm film thickness.

LC-electron spray ionization (ESI+) mass spectra were obtained either with an AGILENT Technologies MSD 1100 single-quadrupole mass spectrometer or with a Waters Micromass® ZQ™ 4000 (ESI+) mass spectrometer.

Analytical gas chromatography (GC) was performed on a Hewlett-Packard HP 6890 gas chromatograph with a flame ionization detector and split mode capillary injection system, using a HP-5MS cross-linked 5% phenyl-methyl silicone glass capillary column, 0.25-μm film thickness column (25 m, flow rate 15mL/min).

Preparative HPLC separations were performed using an AGILENT 1100 SERIES instrument (Zorbax eclipse XB-C18 column, 21,2X150 mm, CH_3CN as mobile phase) coupled to UV-VIS detector AGILENT 1100 SERIES. Chromatographic separations were performed on columns of SiO_2 (Merck, 230-400 mesh) at medium pressure.

Synthesis and characterization of ionic liquids

*Synthesis of 1-cyanomethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide [(mCN)mim][NTf$_2$] (**2a**).*

Chloroacetonitrile (104 g, 1.34 mol) and 1-methylimidazole (103 g, 1.25 mol) were combined with 200 mL acetonitrile and stirred under reflux at 80 °C for 3 hours. The solution was cooled to room temperature and the resulting chloride salt was recovered by the addition of ethyl acetate, isolated

by filtration, rinsed with further washings of ethyl acetate and dried under vacuum (Yield: 144 g, 73%). The isolated chloride salt (85.7 g, 0.54 mol) was dissolved in 200 mL of deionised water, to which was added an aqueous solution of $H[N(SO_2CF_3)_2]$ (326 g, 70 wt %, 0.81 mol). After stirring the resulting two-phase mixture for 1 h, 50 mL of dichloromethane was added and the organic and aqueous phases were separated. The organic phase was washed with deionised water and then dried under vacuum to remove both the dichloromethane and residual water. After heating under vacuum at 75 °C for 8 h, a light yellow liquid remained. Yield: 183 g, 84 %. ESI-MS: positive ion, 122 $[C_6H_8N_3]^+$; negative ion, 280 $[N(SO_2CF_3)_2]^-$. ^{1}H NMR (d_6-DMSO): δ = 9.25 (s, 1H), 7.89 (s, 1H), 7.77 (s, 1H), 5.59 (s, 2H), 3.91 (s, 3H). Chloride content (Metrohm IC): < 5 ppm. Water content (Metrohm KF): 133 ppm.

*Synthesis of N-cyanomethyl-N,N-dimethylethylammonium bis(trifluoromethylsulfonyl)imide [(mCN)dmea][NTf$_2$] (**4**).*

Chloroacetonitrile (115 g, 1.52 mol) and *N*,*N*-dimethylethylamine (101 g, 1.39 mol) were combined with 200 mL acetonitrile and stirred under reflux at 80 °C for 1 hour. The solution was cooled to room temperature and the resulting chloride salt was recovered by addition of ethyl acetate, isolated by filtration, rinsed with further washings of ethyl acetate and dried under vacuum (Yield: 147 g, 91%). The isolated chloride salt (114 g, 0.77 mol) was dissolved in 200 mL of deionised water, to which was added an aqueous solution of $H[N(SO_2CF_3)_2]$ (460 g, 70 wt %, 1.14 mol). After stirring the resulting two phase mixture for 1 h, 50 mL of dichloromethane was added and the organic and aqueous phases were separated. The organic phase was washed with deionised water and then dried under vacuum to remove both the dichloromethane and residual water. After heating under vacuum at 75 °C for 8 h, a light yellow liquid remained. Yield: 246 g, 81 %. ESI-MS: positive ion, 113 $[C_6H_{13}N_2]^+$; negative ion, 280 $[N(SO_2CF_3)_2]^-$. ^{1}H NMR (d_6-DMSO): δ = 4.82 (s, 2H), 3.52 (q, *J*= 7.3 Hz, 2H), 3.18 (s, 6H), 1.31 (t, *J* = 7.3 Hz, 3H). Chloride content (Metrohm IC): 10 ppm. Water content (Metrohm KF): 255 ppm.

Cobalt-catalysed cylotrimerisation of phenylethyne using $NaBH_4$ as the reducing agent: general procedure

The reaction was carried out under argon in a 20 mL screw-capped vial equipped with a Teflon-faced rubber septum under efficient magnetic stirring. Commercial $CoBr_2 \cdot 2H_2O$ (0.026 g, 0.1 mmol) was flamed under a positive argon pressure until the color turned from purple to bright green, then $ZnI_2 \cdot 2H_2O$ (0.071 g, 0.2 mmol) was added and again the two salts were flamed together under a positive argon pressure. The ionic liquid **2a** (1.5 mL), dried for 12 h at 80 °C under vacuum,

was added and the mixture was stirred at 130 °C degrees for 10 min, until salts were completely dissolved, giving a greenish grey solution. While cooling to 40 °C, solution turned pink. Then phenylethyne (0.226 mL, 2 mmol) was added, followed by the addition of $NaBH_4$ (14 mg, 0.37 mmol) under vigorous stirring. A few seconds after the addition of the reducing agent, the solution turned dark brown. The reaction was stirred for 2 h at the same temperature, then the crude reaction mixture was directly poured on the top of a silica-gel column. Cycloadducts **5a** and **6a** were co-eluted (0**.** 194 mg, 95%) using cyclohexane as solvent. Alternatively, cycloadducts could be extracted with n-hexane, however at least 10 extractions with 2 mL of solvent were required to ensure a recovery comparable to the previous procedure.

Cobalt-catalysed cylotrimerisation of phenylethyne using Et_2Zn as the reducing agent: general procedure

To the solution of $CoBr_2$ (0.1 mmol) and ZnI_2 (0.2 mmol) in IL **2a** prepared according the previously reported procedure, phenylethyne (0.226 mL, 2 mmol) and Et_2Zn (0.150 mL of a solution 1M in *n*-Hexane) were added under vigorous stirring at 40 °C. Upon addition of Et_2Zn the reaction color immediately turned dark brown. After stirring for 2 h at 40 °C, the crude reaction mixture was subjected to flash chromatography purification (silica gel/cyclohexane) affording a mixture of **5a** + **6a** (0. 173 mg, 85%).

1,2,4-Triphenylbenzene (5a) and **1,3,5-triphenylbenzene (6a)** were identified by GC-Ms and by comparison of ^{1}H NMR and ^{13}C NMR spectra with literature data[1,2,3].The isomeric ratio was determined using GC (140 °C isotherm 2 min, then ramping to 250 °C at 10 °C/minute) using peaks with t_R (1,2,4-triphenylbenzene) = 26.66 min, and t_R (1,3,5-triphenylbenzene) = 37.59 min.

1,2,4-Triphenylbenzene (5a): GC-MS (70 eV): m/z(%): 306 $[M]^+$ (100), 289 (15)

1,3,5-Triphenylbenzene (6a): GC-MS(70 eV): m/z(%): 306 (100), 289 (10)

Tris-(2-naphthyl)benzene

1,3,5-Tris-(2-naphthyl)benzene (6b) was identified spectroscopically by comparison of ^{1}H NMR and ^{13}C NMR spectra with the literature data[4].

The regioisomers were separated and purified by preparative HPLC (solvent: acetonitrile). The regioisomer ratio was determined by integration of ^{1}H NMR signals at δ = 8.19 (d) (1,2,4-tris-(2-naphthyl)benzene), and at δ = 8.23 (s) and 8.08(s) (1,3,5-tris-(2-naphthyl)benzene)

1,2,4-tris-(2-naphthyl)benzene (5b): ^{1}H NMR (300 Mz, 300 K, $CDCl_3$): δ = 8.19 (d, *J* = 1.5 Hz, 1H), 7.99-7.86 (m, 8H), 7.81-7.71 (m, 5H), 7.57 (dd, *J* = 3 Hz, *J* = 9 Hz, 2H), 7.51 (dt, *J* = 2 Hz, *J* = 10 Hz, 2H), 7.45 (m, 4H), 7.26 (dd, *J* = 1.5 Hz, *J* = 7 Hz, 1H), 7.22 (dd, *J* = 1.2 Hz, *J* = 7 Hz, 1H)

^{13}C NMR (50 MHz, $CDCl_3$) δ = 141.06, 140.47, 139.6, 139.23, 138.80, 137.85, 133.73, 133.42, 132.76, 132.13, 131.71, 130.144, 128.56, 128.39, 128.34 128.24, 128.03, 127.29, 127.06, 127.31, 127.26, 126.60, 126.38, 126.05, 126, 125.97, 125.86, 125.47

1,3,5-Tris-(2-naphthyl)benzene (6b): ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.23 (s, 3H), 8.08 (s, 3H), 7.90-8.02 (m, 12H), 7.54 (m, 6H)

^{13}C NMR (50Mz, $CDCl_3$): δ = 142.5, 138.5, 133.7, 132.8, 128.6, 128.3, 127.7, 126.4, 126.1, 125.7

MS (ESI+): m/z: 479 $[M+Na]^+$, 457 $[M+H]^+$

Tris-(4-methoxylphenyl)benzene

1,2,4-Tris-(4-methoxylphenyl)benzene (5c) and **1,3,5-tris-(4-methoxylphenyl)benzene (6c)** were identified spetroscopically by comparison of ^{1}H NMR and ^{13}C NMR spectra with the literature[1,5,6] The isomeric ratio was determined using GC (isotherm 300 °C) using peaks at t_R (1,2,4-tris-(4-methoxylphenyl)benzene) = 21.62 min, and t_R (1,3,5- tris-(4-methoxylphenyl)benzene) = 39.41 min

1**,2,4-Tris-(4-methoxylphenyl)benzene (5c)**: GC-MS (70 eV): m/z(%) 396 $[M]^+$ (100), 381(9). MS (ESI+): m/z:435 $[M+K]^+$, 419 $[M+Na]^+$.

1,3,5-Tris-(4-methoxylphenyl)benzene (6c): GC-MS (70eV): m/z(%) 396 $[M]^+$ (100), 381 (18).

Tris-(4-methylphenyl)benzene

1,2,4-Tris-(4-methylphenyl)benzene (5d) and **1,3,5-tris-(4-methylphenyl)benzene (6d)** were identified spetroscopically by comparison of ^{1}H NMR and ^{13}C NMR spectra with literature data[1,6,7] The isomeric ratio was determined using GC (250 °C, isotherm) using peaks at t_R (1,2,4-tris-(4-methylphenyl)benzene) = 15.02 min, and t_R (1,3,5- tris-(4-methylphenyl)benzene) = 27.41 min.

1,2,4-Tris-(4-methylphenyl)benzene (5d): GC-MS (70 eV): m/z(%) 348 $[M]^+$(100), 333(15), 318(18). MS (ESI+): m/z (%) 387 $[M+K]^+$, 371 $[M+Na]^+$.

1,3,5-Tris-(4-methylphenyl)benzene (6d): GC-MS (70 eV): m/z(%) 348 $[M]^+$(100).

Tris-(4-fluorolphenyl)benzene

1,2,4-Tris-(4-fluorolphenyl)benzene (5e) and **1,3,5-tris-(4-fluorophenyl)benzene (6e)**[6,8] could not be separated by preparative HPLC. Regioisomers in ^{1}H NMR and ^{13}C NMR spectra are not separately assigned:

^{1}H NMR (300 Mz, 300K, $CDCl_3$): δ: 7.67-7.57 (m), 7.47 (s), 7.45 (s), 7.22-7.08 (m), 6.99-6.92 (m)

^{13}C NMR (75 Mz, 300K, $CDCl_3$): δ: 164.25, 163.46, 141.24, 140.01, 139.06, 139.25, 138.49, 137.13, 136.96, 136.73, 136.47, 131.39, 131.35, 131.29, 131.25, 131.06, 129.15, 128.92, 128.82, 128.7, 128.5, 128.4, 127.27, 126.14, 124.83, 115.89, 115.6, 115.17, 114.89, 114.05.

The isomeric ratio was determined using GC (140 °C, isotherm 2 minute, then ramping to 250 °C at 10 °C/min), using peaks at t_R (1,2,4-tris-(4-fluorophenyl)benzene) = 25.2 min, and t_R (1,3,5- tris-(4-fluorophenyl)benzene) = 34.72 min.

1,2,4-Tris-(4-fluorolphenyl)benzene (5e): GC-MS (70 eV): m/z(%) 361 (25), 360 $[M]^+$ (100), 338 (13).

1,3,5-Tris-(4-fluorophenyl)benzene (6e): GC-MS (70 eV): m/z(%) 361 $[M]^+$ (30), 360 $[M]^+$ (100), 338 (9).

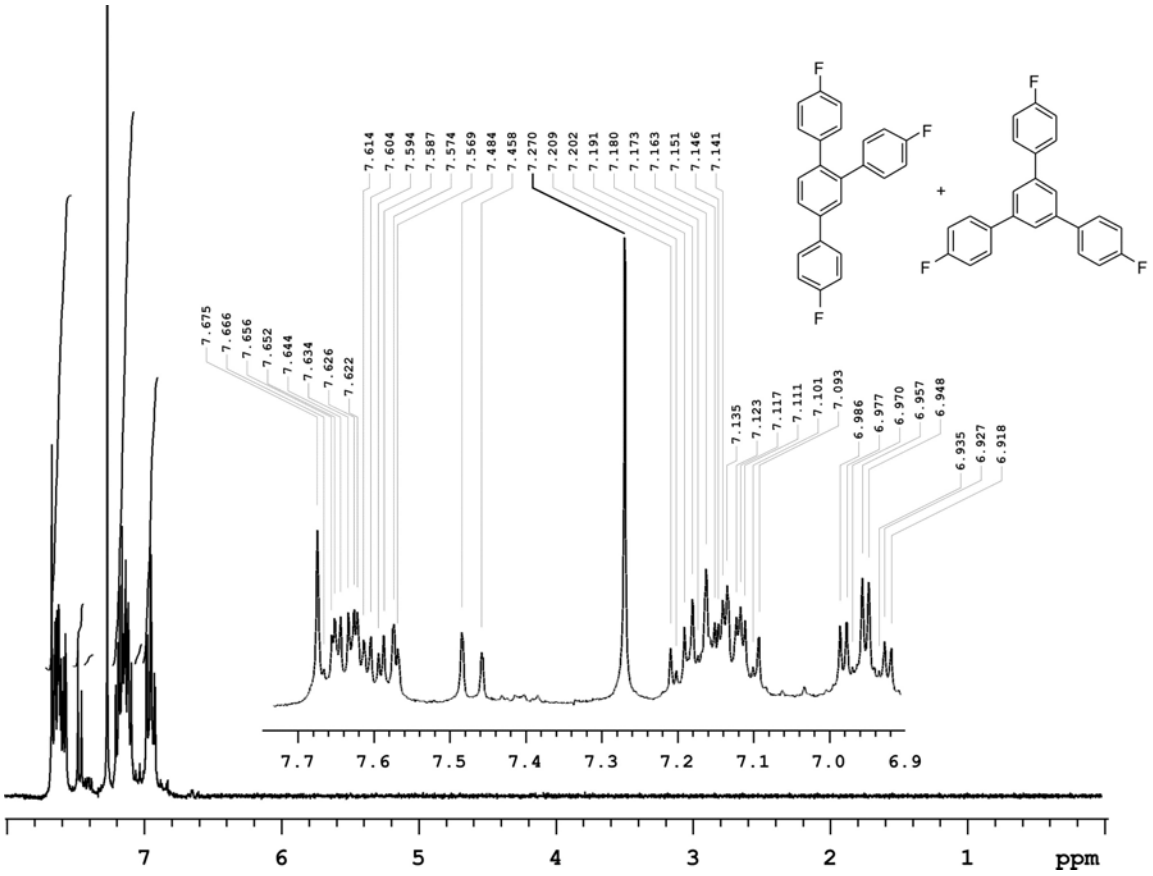
Benzene-tricarboxylic acid triethyl ester

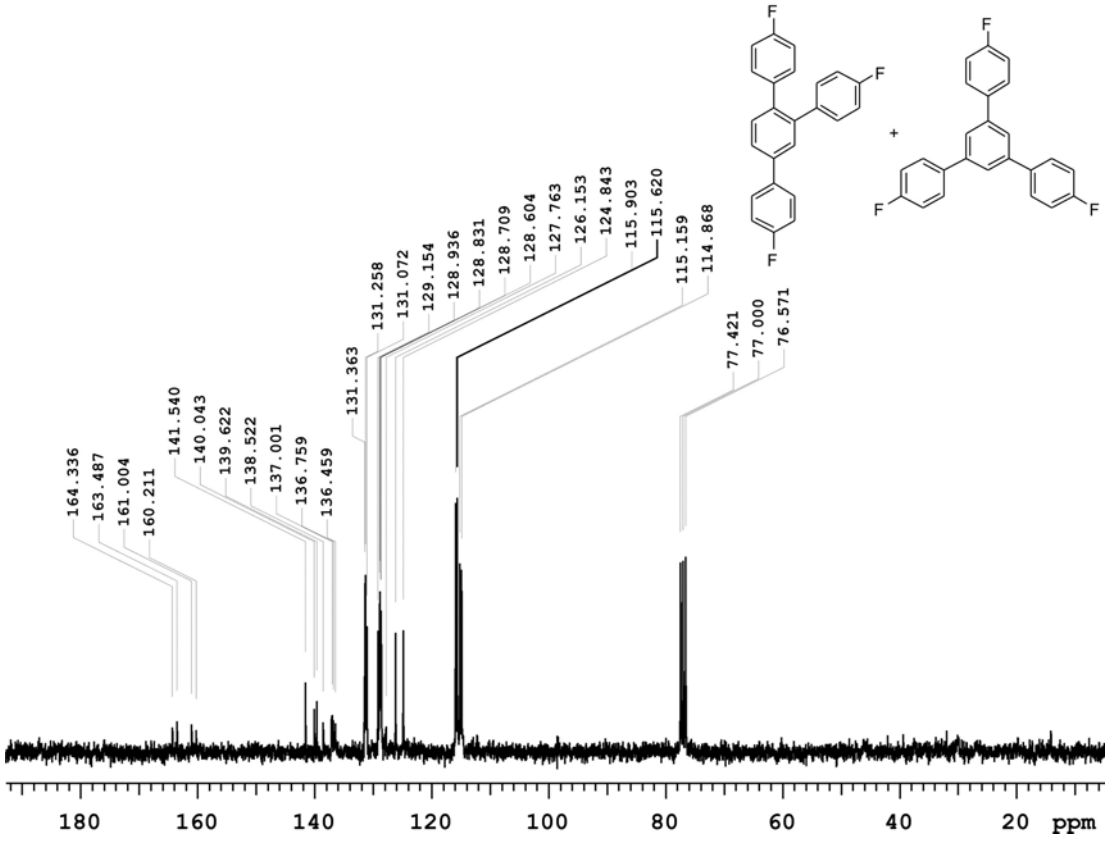
Benzene-1,2,4-tricarboxylic acid triethyl ester (5f) and **benzene-1,3,5 tricarboxylic acid triethyl ester (6f)** were identified spetroscopically by comparison of ^{1}H NMR and ^{13}C NMR spectra with literature data[9]

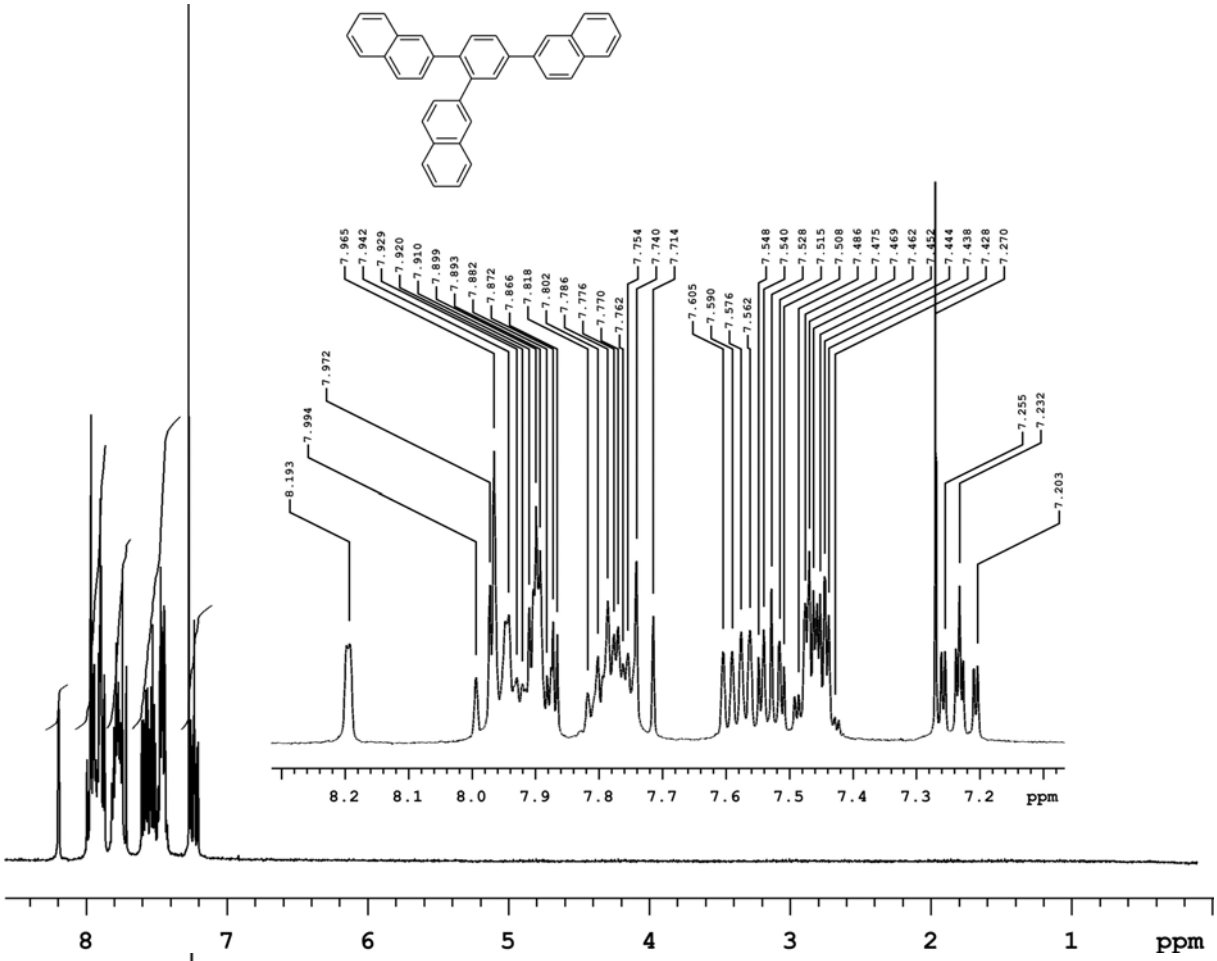
The isomeric ratio was determined by GC (140 °C isotherm, ramping to 250 °C at 10 °C/minute) using peaks at t_R (benzene-1,2,4-tricarboxylic acid triethyl ester) = 12.7 min, and at t_R (benzene-1,3,5 tricarboxylic acid triethyl ester) = 13.32 min.

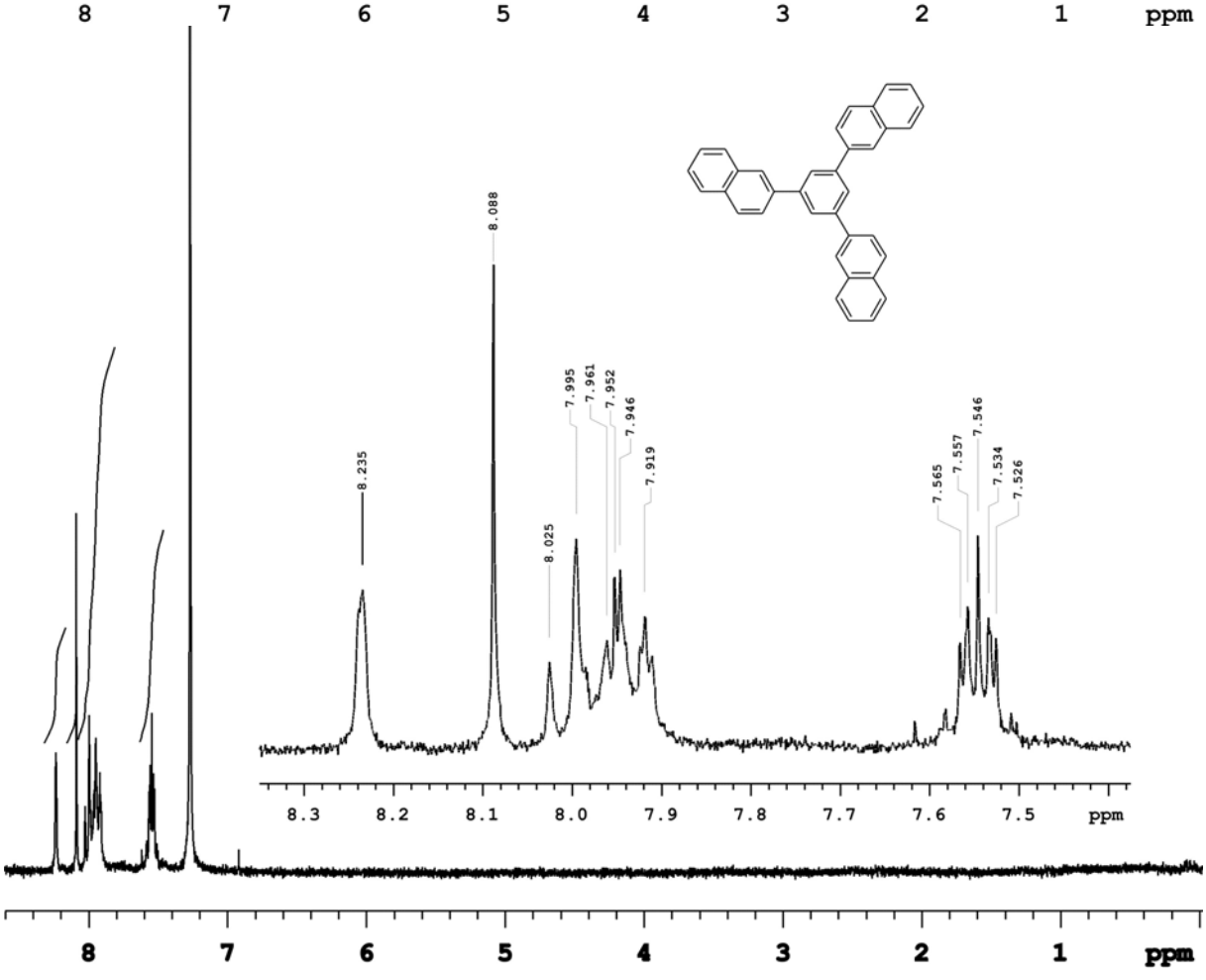
Benzene-1,2,4-tricarboxylic acid triethyl ester (5f): GC-MS (70 eV): m/z (%): 294 $[M]^+$ (5), 249 (38), 221 (100).

Benzene-1,3,5 tricarboxylic acid triethyl ester (6f): GC-MS (70 eV): m/z (%): 294 $[M]^+$ (14), 249 (100), 221 (62).









1 Tagliatesta, P.; Floris, B.; Galloni, P.; Leoni, A.; D'Arcangelo, G. *Inorg. Chem.* **2003**, *42* 7701.

2 Hill, J. E.; Balaich, G.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1993** ,*12*, 2911.

3 Breschi, C.; Piparo, L.; Pesticci, P.; Caporosso A. M.; Virtulli, G. *J. Organomet. Chem.* **2000**, *607*, 57.

4 Li, Z.; Sun, W. -S.; Jin X.; Shao, C. *Synlett* **2001**, 1947.

5 Rodriguez, J. G.; Lafuente A.; Martin-Villamil R. *J. Polym. Sci. Part A: Polymer Chemistry* **2005**, *43*, 5987.

6 Griesbaum, K.; Ramana Rao V. V.; Leifker, G. *J. Org. Chem*., **1982**, *47*, 4975.

7 Li, J.; Jiang H.; Chen, M. *J. Org. Chem*. **2001**, *66*, 3627.

8 Berthiol, F.; Kondolff, I.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2004**, *689*, 2786.

9 Tanaka, K.; Toyoda, K.; Wada, A.; Shirasaka K.; Hirano, M. *Chem. Eur. J*. **2005**, *11*, 1145.