SUPPORTING INFORMATION

Palladium-Catalyzed C(sp^3)–H Arylation of Diarylmethanes at Room Temperature: Synthesis of Triarylmethanes via Deprotonative-Cross-Coupling Processes (DCCP)

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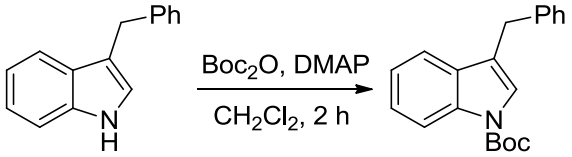
General Methods. All reactions were performed under nitrogen using oven-dried glassware and standard Schlenk or vacuum line techniques. Air- and moisture-sensitive solutions were handled under nitrogen and transferred via syringe. Anhydrous CPME, dioxane, and 2-MeTHF were purchased from Sigma-Aldrich and used as solvent without further purification. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were obtained from Sigma-Aldrich, Acros, TCI America or Matrix Scientific, and solvents were purchased from Fisher Scientific. The progress of the reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 μm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with ceric ammonium molybdate (CAM) stain or iodine. Silica gel (230–400 mesh, Silicycle) was used for flash chromatography. The ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were obtained using a Brüker AM-500 Fourier-transform NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts are reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants are reported in hertz. The infrared spectra were obtained with KBr plates using a Perkin-Elmer Spectrum 100 Series FTIR spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Melting points were determined on a Unimelt Thomas-Hoover melting point apparatus and are uncorrected.

Preparation of Diarylmethanes.

Compounds **1q**[1] and **1r**[2] were prepared according to literature procedures.

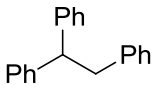
Compound **1l** (***N*-*tert*-butyl 3-benzylindole carboxylate**):



To a solution of 3-benzyl-1*H*-indole (829 mg, 4.0 mmol) and DMAP (48.9 mg, 0.4 mmol) in CH_2Cl_2 (8 mL) was added $(Boc)_2O$ (1.31 g, 6.0 mmol) at 24 ℃, and the solution was stirred for 2 h at this temperature. The resulting mixture was concentrated *in vacuo*. Silica gel chromatography using 10% to 20% EtOAc/hexanes afforded 1.21 g (98% yield) of the desired compound as a white solid. R_f = 0.25 (EtOAc:hexanes = 1:9). The NMR spectral data match the previously published data.[3]

Procedure and Characterization for the Deprotonation/Benzylation of Diphenylmethane.

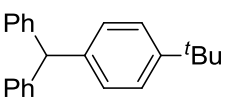
General Procedure A: An oven-dried 10 mL reaction vial equipped with a stir bar was charged with $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol, 4 equiv) under a nitrogen atmosphere followed by 1 mL of dry dioxane, and the reaction mixture was stirred for 5 min at 24 ℃. Diphenylmethane (66.9 μL, 0.40 mmol, 4 equiv) was added to the reaction mixture followed by benzyl chloride (11.5 μL, 0.1 mmol, 1 equiv). The reaction mixture was stirred for 12 h at 24 ℃ (or 110 ℃). The reaction mixture was quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude material was loaded onto a silica gel column and purified by flash chromatography.



1,1,2-Triphenylethane: The reaction was performed following General Procedure A with diphenylmethane (**1a**) (66.9 μL, 0.40 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and benzyl chloride (11.5 μL, 0.1 mmol) in 1 mL of dioxane at 110 ℃. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95) to give the product (23.8 mg, 92% yield) as a colorless oil. R_f = 0.25 (hexanes). The NMR spectral data match the previously published data.[4]

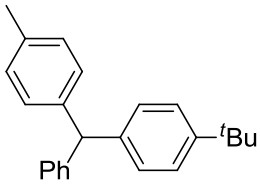
Procedure and Characterization for the Pd-Catalyzed DCCP of Diarylmethanes.

General Procedure B: An oven-dried 10 mL reaction vial equipped with a stir bar was charged with $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol, 3 equiv) under a nitrogen atmosphere. A solution (from a stock solution) of $Pd(OAc)_2$ (1.12 mg, 0.0050 mmol) and NiXantphos (4.14 mg, 0.0075 mmol) in 1 mL of dry CPME was taken up by syringe and added to the reaction vial. After stirring for 5 min at 24 ℃, diphenylmethane (20.1 μL, 0.12 mmol, 1.2 equiv) was added to the reaction mixture followed by 1-bromo-4-*tert*-butylbenzene (17.3 μL, 0.1 mmol, 1 equiv). Note that the diarylmethane or aryl bromide in a solid form was added to the reaction vial prior to $KN(SiMe_3)_2$. The reaction mixture was stirred for 12 h at 24 ℃, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude material was loaded onto a silica gel column and purified by flash chromatography.

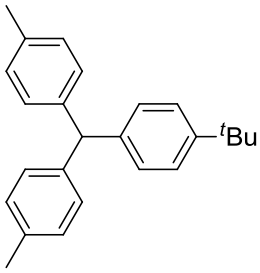


3aa – (4-*tert*-Butylphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and

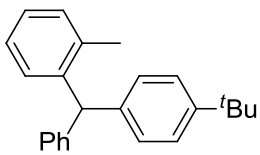
2a (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (28.5 mg, 95% yield) as a white solid. R_f = 0.33 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.23 (m, 6H), 7.21 – 7.16 (m, 2H), 7.12 (d, *J* = 7.0 Hz, 4H), 7.03 (d, *J* = 8.5 Hz, 2H), 5.50 (s, 1H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.2, 144.4, 140.9, 129.7, 129.2, 128.5, 126.4, 125.4, 56.6, 34.6, 31.6 ppm; IR (thin film): 3060, 3026, 2963, 2903, 2868, 1599, 1515, 1494, 1450, 1270, 1031, 736, 701, 608 cm^{-1}; HRMS calc'd for $C_{23}H_{24}^+$ 300.1878, observed 300.1867 [M]$^+$.



3ba – (4-*tert*-Butylphenyl)(4-methylphenyl)phenylmethane: The reaction was performed following General Procedure B with **1b** (22.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (25.5 mg, 81% yield) as a colorless oil. R_f = 0.33 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.16 (m, 5H), 7.12 (d, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.02 (t, *J* = 8.0 Hz, 4H), 5.47 (s, 1H), 2.31 (s, 3H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.1, 144.6, 141.4, 141.2, 135.9, 129.6, 129.5, 129.18, 129.16, 128.4, 126.3, 125.3, 56.3, 34.6, 31.6, 21.2 ppm; IR (thin film): 3025, 2963, 2903, 2868, 1511, 1493, 1451, 1020, 701 cm^{-1}; HRMS calc'd for $C_{24}H_{26}^+$ 314.2035, observed 314.2037 [M]$^+$.

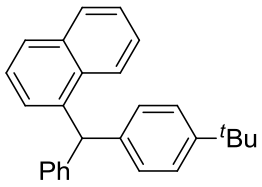


3ca – (4-*tert*-Butylphenyl)bis(4-methylphenyl)methane: The reaction was performed following General Procedure B with **1c** (60.1 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (32.1 mg, 98% yield) as a white solid. R_f = 0.25 (hexanes); m.p. = 94–96 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 4H), 7.05 – 6.98 (m, 6H), 5.42 (s, 1H), 2.30 (s, 6H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.0, 141.6, 141.4, 135.8, 129.5, 129.14, 129.11, 125.3, 55.9, 34.6, 31.6, 21.2 ppm; IR (thin film): 2962, 2923, 2867, 1510, 1462, 1363, 1269, 1109, 1021, 808, 765 cm^{-1}.

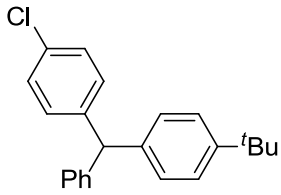


3da – (4-*tert*-Butylphenyl)(2-methylphenyl)phenylmethane: The reaction was performed following General Procedure B with **1d** (54.7 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by

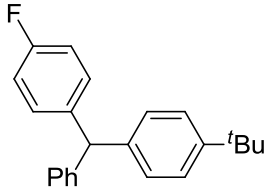
flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (27.6 mg, 88% yield) as a colorless oil. R_f = 0.35 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.04 (m, 10H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 7.5 Hz, 1H), 5.63 (s, 1H), 2.22 (s, 3H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.1, 143.8, 142.9, 140.4, 136.8, 130.5, 129.8, 129.6, 129.4, 128.4, 126.5, 126.3, 125.9, 125.3, 53.2, 34.6, 31.6, 20.2 ppm; IR (thin film): 3060, 3025, 2963, 2904, 2868, 1493, 1461, 1363, 1269, 756, 734, 701 cm^{-1}; HRMS calc'd for $C_{24}H_{26}^+$ 314.2035, observed 314.2022 [M]$^+$.



3ea – (4-*tert*-Butylphenyl)(1-naphthyl)phenylmethane: The reaction was performed following General Procedure B with **1e** (26.2 mg, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 1:99) to give the product (35.0 mg, 99% yield) as a colorless oil. R_f = 0.15 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.46 – 7.33 (m, 3H), 7.30 – 7.17 (m, 5H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 7.0 Hz, 1H), 6.24 (s, 1H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.3, 144.2, 140.7, 140.4, 134.1, 132.2, 129.8, 129.5, 128.9, 128.6, 127.8, 127.4, 126.5, 126.2, 125.6, 125.5, 124.6, 52.9, 34.6, 31.6 ppm; IR (thin film): 2962, 2867, 1509, 1493, 1394, 1268, 1019, 789, 781, 726, 702 cm^{-1}.

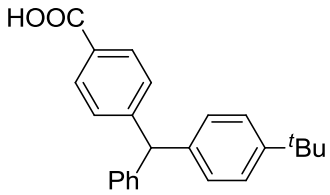


3fa – (4-*tert*-Butylphenyl)(4-chlorophenyl)phenylmethane: The reaction was performed following General Procedure B with **1f** (22.0 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (29.8 mg, 89% yield) as a colorless oil. R_f = 0.35 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 – 7.18 (m, 7H), 7.10 (d, *J* = 7.5 Hz, 2H), 7.05 (d, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 5.47 (s, 1H), 1.30 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.5, 143.9, 143.0, 140.5, 132.3, 131.0, 129.6, 129.1, 128.6, 126.6, 125.5, 56.0, 34.6, 31.6 ppm; IR (thin film): 3026, 2963, 2903, 2868, 1489, 1364, 1269, 1090, 1015, 818, 702 cm^{-1}; HRMS calc'd for $C_{23}H_{23}Cl^+$ 334.1488, observed 334.1436 [M]$^+$.

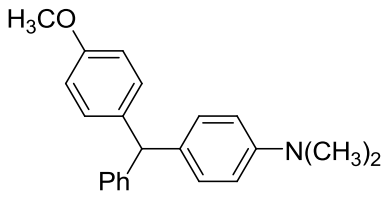


3ga – (4-*tert*-Butylphenyl)(4-fluorophenyl)phenylmethane: The reaction was performed following General Procedure B with **1g** (20.5 μL, 0.12 mmol), $KN(SiMe_3)_2$

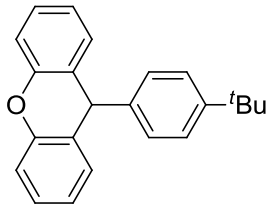
(59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (30.6 mg, 96% yield) as a colorless oil. R_f = 0.33 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.18 (m, 5H), 7.13 – 6.89 (m, 8H), 5.48 (s, 1H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.6 (d, J = 243 Hz), 149.4, 144.2, 140.8, 140.1 (d, J = 3 Hz), 131.1 (d, J = 8 Hz), 129.6, 129.1, 128.6, 126.6, 125.5, 115.2 (d, J = 21 Hz), 55.9, 34.6, 31.6 ppm; IR (thin film): 3027, 2963, 2904, 2869, 1602, 1507, 1494, 1224, 1158, 824, 701 cm^{-1}; HRMS calc'd for $C_{23}H_{23}F^+$ 318.1784, observed 318.1774 $[M]^+$.



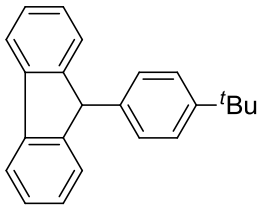
3ha – 4-((4-*tert*-Butylphenyl)(phenyl)methyl)benzoic acid: The reaction was performed following General Procedure B with **1h** (25.5 mg, 0.12 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and **2a** (17.3 μL, 0.1 mmol) at 110 ℃. The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O. The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 3:7 to 4:6) to give the product (32.0 mg, 93% yield) as a white solid. R_f = 0.50 (EtOAc:hexanes = 4:6); m.p. = 75–78 ℃; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, J = 8.0 Hz, 2H), 7.33 – 7.26 (m, 4H), 7.26 – 7.20 (m, 3H), 7.11 (d, J = 7.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 5.57 (s, 1H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 172.4, 150.8, 149.7, 143.4, 140.0, 130.5, 129.8, 129.6, 129.2, 128.7, 127.6, 126.8, 125.6, 56.7, 34.6, 31.6 ppm; IR (thin film): 2964, 2672, 2550, 1694, 1608, 1423, 1288, 1180, 1019, 737, 702 cm^{-1}; HRMS calc'd for $C_{24}H_{23}O_2^-$ 343.1698, observed 343.1697 $[M-H]^-$.



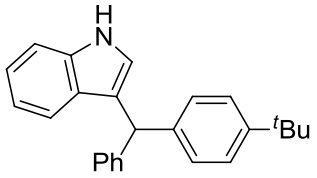
3ij – (4-*N*,*N*-Dimethylphenyl)(4-methoxyphenyl)phenylmethane: The reaction was performed following General Procedure B with **1i** (57.4 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2j** (19.8 mg, 0.099 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95) to give the product (30.5 mg, 97% yield) as a colorless oil. R_f = 0.25 (EtOAc:hexanes = 5:95); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.15 (m, 3H), 7.11 (d, J = 7.0 Hz, 2H), 7.03 (d, J = 9.0 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 5.41 (s, 1H), 3.76 (s, 3H), 2.90 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 158.0, 149.2, 145.2, 137.1, 132.5, 130.5, 130.1, 129.5, 128.4, 126.2, 113.7, 112.7, 55.4, 55.3, 40.9 ppm; IR (thin film): 2951, 2834, 1611, 1509, 1450, 1348, 1247, 1176, 1034, 812, 700 cm^{-1}; HRMS calc'd for $C_{22}H_{24}NO^+$ 318.1858, observed 318.1848 $[MH]^+$.



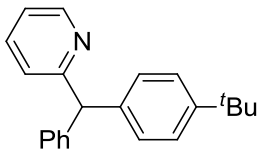
3ja – 9-(4-*tert*-Butylphenyl)xanthene: The reaction was performed following General Procedure B with **1j** (27.3 mg, 0.15 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (31.3 mg, 99% yield) as a white solid. R_f = 0.17 (hexanes); m.p. = 136–140 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.22 (m, 2H), 7.22 – 7.16 (m, 2H), 7.14 – 7.05 (m, 6H), 7.00 – 6.94 (m, 2H), 5.21 (s, 1H), 1.26 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 151.4, 149.5, 143.6, 129.9, 128.00, 127.98, 125.8, 125.0, 123.4, 116.7, 44.2, 34.6, 31.5 ppm; IR (thin film): 2960, 2925, 2866, 1577, 1481, 1452, 1261, 745 cm^{-1}; HRMS calc'd for $C_{22}H_{23}O^+$ 315.1749, observed 315.1745 $[MH]^+$.



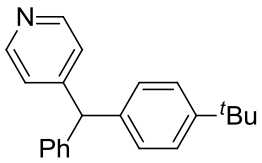
3ka – 9-(4-*tert*-Butylphenyl)fluorene: The reaction was performed following General Procedure B with **1k** (33.2 mg, 0.20 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol) at 85 °C in THF. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (26.0 mg, 87% yield) as a white solid. R_f = 0.30 (hexanes). The NMR spectral data match the previously published data.[5]



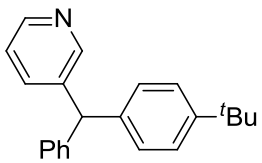
3la – 3-((4-*tert*-Butylphenyl)(phenyl)methyl)-1*H*-indole: The reaction was performed following General Procedure B with **1l** (36.9 mg, 0.12 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and **2a** (17.3 μL, 0.1 mmol). The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O to ensure complete removal of the Boc group. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 1:9) to give the product (30.2 mg, 89% yield) as a pale yellow oil. R_f = 0.50 (EtOAc:hexanes = 1:9); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (s, br, 1H), 7.33 (d, J = 7.5 Hz, 1H), 7.30 – 7.12 (m, 11H), 6.98 (m, 1H), 6.58 (m, 1H), 5.63 (s, 1H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.1, 144.4, 141.0, 136.9, 129.2, 128.7, 128.4, 127.3, 126.3, 125.3, 124.2, 122.2, 120.4, 120.2, 119.5, 111.2, 48.5, 34.6, 31.6 ppm; IR (thin film): 3420, 3057, 2963, 2902, 2867, 1513, 1493, 1456, 1267, 1094, 742, 703 cm^{-1}; HRMS calc'd for $C_{25}H_{24}N^+$ 338.1909, observed 338.1896 $[M-H]^+$.



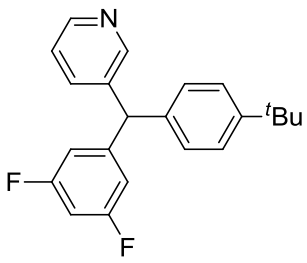
3ma – (4-*tert*-Butylphenyl)(2-pyridyl)phenylmethane: The reaction was performed following General Procedure B with **1m** (19.3 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95 to 1:9) to give the product (28.8 mg, 96% yield) as a colorless oil. R_f = 0.30 (EtOAc:hexanes = 1:9); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (m, 1H), 7.61 – 7.55 (td, *J* = 7.5 Hz, 1.5 Hz, 1H), 7.32 – 7.25 (m, 4H), 7.23 – 7.16 (m, 3H), 7.13 – 7.05 (m, 4H), 5.66 (s, 1H), 1.29 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.7, 149.7, 149.4, 143.1, 139.8, 136.6, 129.6, 129.1, 128.6, 126.6, 125.5, 123.9, 121.5, 59.2, 34.6, 31.6 ppm; IR (thin film): 2962, 2903, 1587, 1495, 1468, 1432, 748, 701 cm^{-1}; HRMS calc'd for $C_{22}H_{24}N^+$ 302.1909, observed 302.1898 $[MH]^+$.



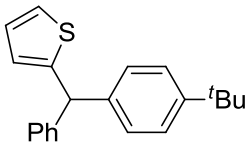
3na – (4-*tert*-Butylphenyl)(4-pyridyl)phenylmethane: The reaction was performed following General Procedure B with **1n** (19.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol) at 110 ℃. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:8 to 3:7) to give the product (29.8 mg, 99% yield) as a colorless oil. R_f = 0.33 (EtOAc:hexanes = 3:7); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (d, *J* = 6.0 Hz, 2H), 7.34 – 7.21 (m, 5H), 7.10 (d, *J* = 7.5 Hz, 2H), 7.07 – 6.98 (m, 4H), 5.46 (s, 1H), 1.30 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 153.2, 150.0, 149.9, 142.6, 139.1, 129.5, 129.1, 128.7, 127.0, 125.7, 124.8, 56.0, 34.6, 31.5 ppm; IR (thin film): 3027, 2963, 2904, 2868, 1594, 1514, 1494, 1412, 818, 702 cm^{-1}; HRMS calc'd for $C_{22}H_{24}N^+$ 302.1909, observed 302.1911 $[MH]^+$.



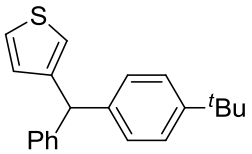
3oa – (4-*tert*-Butylphenyl)(3-pyridyl)phenylmethane: The reaction was performed following General Procedure B with **1o** (19.3 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:8 to 3:7) to give the product (29.6 mg, 98% yield) as a colorless oil. R_f = 0.50 (EtOAc:hexanes = 3:7); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 – 8.41 (m, 2H), 7.44 – 7.38 (m, 1H), 7.35 – 7.27 (m, 4H), 7.27 – 7.17 (m, 2H), 7.11 (d, *J* = 7.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 5.51 (s, 1H), 1.30 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 151.1, 149.7, 147.9, 143.1, 139.8, 139.7, 136.9, 129.5, 129.1, 128.7, 126.8, 125.6, 123.4, 54.2, 34.6, 31.6 ppm; IR (thin film): 3027, 2963, 2903, 2868, 1574, 1515, 1495, 1476, 1421, 1026, 716, 702 cm^{-1}; HRMS calc'd for $C_{22}H_{24}N^+$ 302.1909, observed 302.1911 $[MH]^+$.



3pa – (4-*tert*-Butylphenyl)(3-pyridyl)(3,5-difluorophenyl)methane: The reaction was performed following General Procedure B with **1p** (41.0 mg, 0.20 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol) at 85 ℃ in THF. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 1:9 to 2:8) to give the product (31.4 mg, 93% yield) as a colorless oil. R_f = 0.20 (EtOAc:hexanes = 2:8); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (dd, *J* = 5.0 Hz, 1.0 Hz, 1H), 8.41 (d, *J* = 2.0 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.26 – 7.22 (m, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.72 – 6.60 (m, 3H), 5.47 (s, 1H), 1.31 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.3 (d, *J* = 247 Hz), 163.2 (d, *J* = 247 Hz), 150.9, 150.4, 148.4, 147.2 (t, *J* = 8 Hz), 138.5, 138.4, 136.7, 128.9, 125.9, 123.6, 112.5 (d, *J* = 19 Hz), 112.4 (d, *J* = 19 Hz), 102.5 (t, *J* = 25 Hz), 53.8, 34.7, 31.5 ppm; IR (thin film): 3030, 2964, 2905, 2869, 1623, 1597, 1459, 1317, 1118, 1026, 992, 847, 716 cm^{-1}; HRMS calc'd for $C_{22}H_{22}NF_2^+$ 338.1720, observed 338.1715 $[MH]^+$.

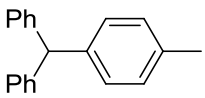


3qa – (4-*tert*-Butylphenyl)(2-thienyl)phenylmethane: The reaction was performed following General Procedure B with **1q** (20.9 mg, 0.12 mmol), $KN(SiMe_3)_2$ (29.9 mg, 0.15 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes) to give the product (30.5 mg, 99% yield) as a colorless oil. R_f = 0.22 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.27 (m, 4H), 7.24 – 7.17 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.94 – 6.90 (m, 1H), 6.71 – 6.68 (m, 1H), 5.64 (s, 1H), 1.30 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.7, 148.4, 144.3, 140.9, 129.0, 128.59, 128.56, 126.8, 126.7, 126.5, 125.5, 124.6, 51.9, 34.6, 31.6 ppm; IR (thin film): 3061, 3027, 2962, 2903, 2868, 1514, 1494, 1452, 1364, 1269, 700 cm^{-1}; HRMS calc'd for $C_{21}H_{22}S^+$ 306.1442, observed 306.1427 $[M]^+$.

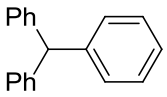


3ra – (4-*tert*-Butylphenyl)(3-thienyl)phenylmethane: The reaction was performed following General Procedure B with **1r** (26.1 mg, 0.15 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2a** (17.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes) to give the product (23.6 mg, 77% yield) as a colorless oil. R_f = 0.35 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 – 7.24 (m, 5H), 7.23 – 7.19 (m, 1H), 7.18 – 7.15 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.88 (dd, *J* = 5.0 Hz, 1.0 Hz, 1H), 6.76 – 6.72 (m, 1H), 5.47 (s, 1H), 1.30 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.4, 145.4, 144.3, 140.9, 129.2, 129.0, 128.7, 128.5, 126.6, 125.6, 125.4, 122.9, 52.4,

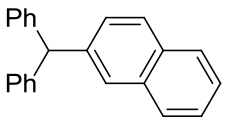
34.6, 31.6 ppm; IR (thin film): 3026, 2962, 2902, 2867, 1514, 1494, 1451, 1269, 835, 782, 701 cm^{-1}; HRMS calc'd for $C_{21}H_{23}S^+$ 307.1520, observed 307.1514 $[MH]^+$.



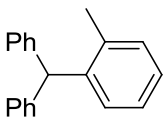
3ab – (4-Methylphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2b** (12.3 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (25.1 mg, 97% yield) as a colorless oil. R_f = 0.38 (hexanes). The NMR spectral data match the previously published data.[6]



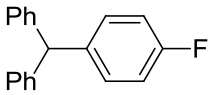
3ac – Triphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2c** (10.7 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (22.5 mg, 92% yield) as a white solid. R_f = 0.40 (hexanes). The NMR spectral data match the previously published data.[7]



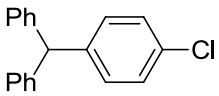
3ad – (2-Naphthyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2d** (20.7 mg, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 1:99) to give the product (29.5 mg, 99% yield) as a white solid. R_f = 0.30 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 – 7.67 (m, 3H), 7.49 – 7.40 (m, 3H), 7.32 – 7.26 (m, 5H), 7.26 – 7.20 (m, 2H), 7.18 – 7.13 (m, 4H), 5.70 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 143.9, 141.7, 133.6, 132.4, 129.8, 128.6, 128.3, 128.1, 128.0, 127.8, 126.6, 126.2, 125.8, 57.2 ppm; IR (thin film): 3083, 3058, 3025, 2923, 1600, 1493, 1450, 1030, 814, 747, 722, 699 cm^{-1}; HRMS calc'd for $C_{23}H_{19}^+$ 295.1487, observed 295.1486 $[MH]^+$.



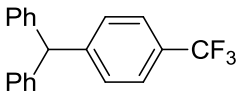
3ae – (2-Methylphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2e** (12.0 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (24.2 mg, 94% yield) as a white solid. R_f = 0.40 (hexanes). The NMR spectral data match the previously published data.[6]



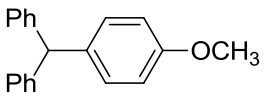
3af – (4-Fluorophenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2f** (11.0 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (21.3 mg, 82% yield) as a white solid. R_f = 0.33 (hexanes). The NMR spectral data match the previously published data.[8]



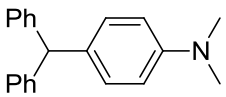
3ag – (4-Chlorophenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2g** (19.1 mg, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (19.7 mg, 71% yield) as a colorless oil. R_f = 0.30 (hexanes). The NMR spectral data match the previously published data.[6]



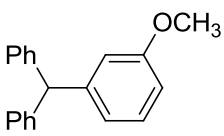
3ah – (4-Trifluoromethylphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (39.9 mg, 0.20 mmol) and **2h** (14.0 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 2:98) to give the product (20.5 mg, 66% yield) as a colorless oil. R_f = 0.33 (hexanes). The NMR spectral data match the previously published data.[6]



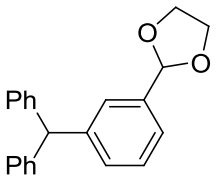
3ai – (4-Methoxyphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2i** (12.5 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95) to give the product (27.4 mg, 99% yield) as a colorless oil. R_f = 0.25 (hexanes). The NMR spectral data match the previously published data.[6]



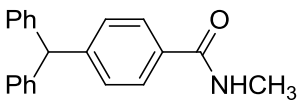
3aj – (*N*,*N*-Dimethylaminophenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2j** (20.2 mg, 0.101 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95) to give the product (29.4 mg, 99% yield) as a white solid. R_f = 0.30 (EtOAc:hexanes = 5:95). The NMR spectral data match the previously published data.[9]



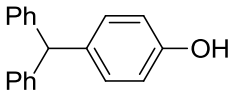
3ak – (3-Methoxyphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2k** (12.7 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95) to give the product (25.2 mg, 92% yield) as a colorless oil. R_f = 0.25 (hexanes). The NMR spectral data match the previously published data.[10]



3al – 2-(3-Benzhydrylphenyl)-1,3-dioxolane: The reaction was performed following General Procedure B with **1a** (20.1 μL, 0.12 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2l** (15.1 μL, 0.1 mmol). The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95 to 1:9) to give the product (30.4 mg, 96% yield) as a white solid. R_f = 0.30 (EtOAc:hexanes = 1:9); m.p. = 72–74 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.15 (m, 9H), 7.13 – 7.06 (m, 5H), 5.72 (s, 1H), 5.56 (s, 1H), 4.12 – 3.91 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.2, 143.9, 138.0, 130.5, 129.7, 128.6, 128.5, 128.0, 126.5, 124.6, 104.0, 65.5, 57.0 ppm; IR (thin film): 3060, 3025, 2885, 1599, 1494, 1450, 1387, 1223, 1151, 1079, 1030, 966, 737, 700 cm^{-1}; HRMS calc'd for $C_{22}H_{21}O_2^+$ 317.1542, observed 317.1542 $[MH]^+$.

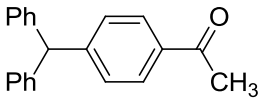


3am – 4-(Diphenylmethyl)-*N*-methylbenzamide: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and **2m** (21.4 mg, 0.1 mmol) at 110 °C. The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 4:6 to 6:4) to give the product (24.8 mg, 82% yield) as a colorless oil. R_f = 0.5 (EtOAc:hexanes = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 8.5 Hz, 2H), 7.32 – 7.26 (m, 4H), 7.24 – 7.20 (m, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 7.5 Hz, 4H), 6.23 (m, br, 1H), 5.57 (s, 1H), 2.97 (d, J = 5.0 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.3, 147.7, 143.4, 132.9, 129.8, 129.6, 128.6, 127.1, 126.8, 56.8, 27.0 ppm; IR (thin film): 3322, 3060, 3026, 1636, 1552, 1503, 1495, 1311, 756, 735, 700 cm^{-1}; HRMS calc'd for $C_{21}H_{20}NO^+$ 302.1545, observed 302.1548 $[MH]^+$.

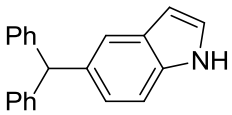


3an – (4-Hydroxyphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and

2m (21.4 mg, 0.1 mmol) at 110 ℃. The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 1:9 to 2:8) to give the product (25.0 mg, 95% yield) as a white solid. R_f = 0.33 (EtOAc:hexanes = 2:8). The NMR spectral data match the previously published data.[11]



3ao – (4-Acetylphenyl)diphenylmethane: The reaction was performed following General Procedure B with **1a** (50.2 μL, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol) and **2o** (20.2 mg, 0.101 mmol). The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O. The crude material was purified by flash chromatography on silica gel (eluted with EtOAc:hexanes = 5:95 to 1:9) to give the product (24.5 mg, 86% yield) as a white solid. R_f = 0.33 (EtOAc:hexanes = 1:9). The NMR spectral data match the previously published data.[12]



3ap – 5-(Diphenylmethyl)-1*H*-indole: The reaction was performed following General Procedure B with **1a** (33.4 μL, 0.20 mmol), $KN(SiMe_3)_2$ (79.8 mg, 0.40 mmol) and **2p** (19.6 mg, 0.1 mmol) at 110 ℃. The reaction was quenched with 50 μL of 37% hydrochloric acid instead of with two drops of H_2O. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to EtOAc:hexanes = 5:95 to 2:8) to give the product (22.1 mg, 78% yield) as a colorless oil. R_f = 0.25 (EtOAc:hexanes = 1:9); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (s, br, 1H), 7.34 – 7.23 (m, 6H), 7.23 – 7.11 (m, 7H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.45 (m, 1H), 5.67 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 145.0, 135.8, 134.6, 129.8, 128.4, 128.1, 126.3, 124.6, 124.4, 121.5, 111.0, 102.9, 57.1 ppm; IR (thin film): 3425, 3058, 3024, 2924, 1599, 1493, 1473, 1451, 1343, 1090, 1030, 751, 728, 700 cm^{-1}; HRMS calc'd for $C_{21}H_{16}N^+$ 282.1283, observed 282.1283 $[M-H]^+$.

Representative Microscale High-throughput Experimentation for Base & Catalyst Identification.

General Experimental:

The experimental procedures in this work were similar to those reported.[13] Parallel synthesis was accomplished in an MBraun glovebox operating with a constant N_2-purge (oxygen typically <5 ppm). The experimental design was accomplished using Accelrys Library Studio. Screening reactions were carried out in 1 mL vials (30 mm height × 8 mm diameter) in a 96-well plate aluminum reactor block. Liquid chemicals were dosed using multi-channel or single-channel pipettors. Solid chemicals were dosed manually as solutions or slurries in appropriate solvents. Undesired additional solvent was removed using a GeneVac system located inside the glovebox. The reactions were

heated and stirred on a heating block with a tumble-stirrer (V&P Scientific) using 1.98 mm diameter × 4.80 mm length parylene stir bars. The tumble stirring mechanism helped to insure uniform stirring throughout the 96-well plate. The reactions were sealed in the 96-well plate during reaction. Below each reactor vial in the aluminum 96-well plate was a 0.062 mm thick silicon-rubber gasket. Directly above the glass vial reactor tops was a Teflon perfluoroalkoxy copolymer resin sealing gasket and above that, two more 0.062 mm thick silicon-rubber gaskets. The entire assembly was compressed between an aluminum top and the reactor base with 9 evenly-placed screws.

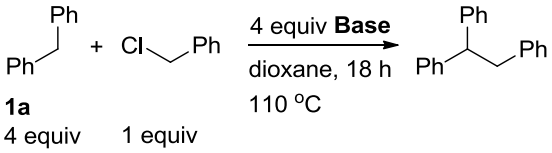
Set up:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 96-well aluminum block containing 1 mL glass vials was predosed manually with $Pd(OAc)_2$ (0.5 μmol) and NiXantphos (1 μmol) in THF. The solvent was evacuated to dryness using a GeneVac vacuum centrifuge, and $KN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac, and a parylene stir bar was then added to each reaction vial. 1-Bromo-4-*tert*-butylbenzene (10 μmol/reaction), diphenylmethane (12 μmol/reaction) and biphenyl (1 μmol/reaction) (used as an internal standard to measure HPLC yields) were then dosed together into each reaction vial as a solution in CPME (100 μL, 0.1 M). The 96-well plate was then sealed and stirred for 18 h at 110 ℃.

Work up:

Upon opening the plate to air, 500 μL of acetonitrile was syringed into each vial. The plate was then covered again and the vials stirred for 20 min to extract the product and to ensure good homogenization. Into a separate 96-well LC block was added 700 μL of acetonitrile, followed by 40 μL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat, and mounted on HPLC instrument modified with an autosampler for analysis.

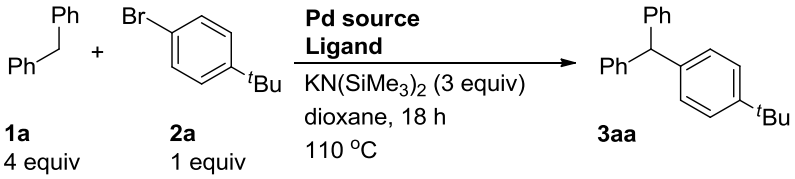
(1) Base Screening:



12 Bases: $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, LiO^tBu, KO^tBu, NaO^tBu, LDA, LiH, KH, LiOH, KOH, and K_2CO_3.

The lead hit from the screening was **$KN(SiMe_3)_2$**, giving 90% assay yield of the desired benzylation product. A scale-up reaction on a 0.1 mmol scale using General Procedure A for the deprotonation/benzylation of diphenylmethane proved successful with isolation of the benzylation product in 92% yield.

(2) Ligand Screening:



Ligand was used in a 4:1 ratio relative to Pd for monodentate ligands and 2:1 ratio for bidentate ligands.

2a. $PdCl_2(PPh_3)_2$ (5 mol %) was used to test 96 sterically and electronically diverse, mono- and bidentate phosphine ligands (ligands 1-96 from the Table below).

2b. 4 Pd sources [$PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, $PdCl_2(CH_3CN)_2$, and $Pd_2(dba)_3$] and 2 catalyst loadings (5 and 10 mol %) were screened with 16 sterically and electronically diverse, mono- and bidentate phosphine (ligands 97-112 from the Table below).

The lead hit from the screening was the combination of **$PdCl_2(PPh_3)_2$** (5 mol %) and **NiXantphos** (10 mol %), giving 93% assay yield of the desired DCCP product **3aa**. A scale-up reaction on a 0.1 mmol scale using the same procedure as HTE proved successful with isolation of **3aa** in 94% yield.

	Ligand libraries (1 – 96)	**3aa AY (%)**
1	2-Di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl (*t*Bu-XPhos)	18.5
2	2-(Dicyclohexylphosphino)-2'-methylbiphenyl (MePhos)	31.0
3	2-(Di-*t*-butylphosphino)-2'-methylbiphenyl (*t*Bu-MePhos)	30.1
4	2-(Dicyclohexylphosphino)biphenyl (Cy-JohnPhos)	29.4
5	2-Di-t-butylphoshino-2'-(*N*,*N*-dimethylamino)biphenyl (*t*Bu-DavePhos)	41.9
6	Racemic-2-(di-*t*-butylphosphino)-1,1'-binaphthyl	24.1
7	1-[2-[Bis(*t*-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (TrippyPhos)	50.4
8	5-(Di-*t*-butylphosphino)-1', 3', 5'-triphenyl-1'H-[1,4']bipyrazole (BippyPhos)	22.1
9	Dicyclohexyl-[2-(*o*-tolyl)indol-1-yl]phosphane	40.4
10	Di-*t*-butyl(2,2-diphenyl-1-methyl-1-cyclopropyl)phosphine (cBRIDP [MoPhos])	23.8
11	Dicyclohexyl-(1-methyl-2,2-diphenyl-cyclopropyl)phosphane (Cy-cBRIDP)	24.1
12	Dicyclohexyl-(1-methyl-2,2-diphenyl-vinyl)phosphane (Cy-vBRIDP)	23.7
13	*N*-phenyl-2-(dicyclohexylphosphino)pyrrole (cataCXium PCy)	24.8

14	*N*-phenyl-2-(di-*t*-butylphosphino)pyrrole (cataCXium PtB)	43.2
15	Dicyclohexyl-(1-phenylindol-2-yl)phosphane (cataCXium PInCy)	27.5
16	Di-*t*-butyl-(1-phenylindol-2-yl)phosphane (cataCXium PIntB)	35.2
17	1-(2-Methoxylphenyl)-2-(dicyclohexylphosphino)pyrrole (cataCXium POMeCy)	32.3
18	Di-*t*-butyl-[1-(2-methoxyphenyl)pyrrol-2-yl]phosphane (cataCXium POMetB)	80.9
19	1-(2,4,6-Trimethylphenyl)-2-(dicyclohexylphosphino)imidazole (cataCXium PICy)	34.1
20	Di-(2-pyridyl)(dicyclohexylphosphino)amine (cataCXium KCy)	37.9
21	Di-(2-pyridyl)(diphenylphosphino)amine (cataCXium KPh)	45.2
22	(9-Butylfluoren-9-yl)-dicyclohexyl-phosphonium tetrafluoroborate (cataCXium FBu)	16.2
23	Dicyclohexyl-(9-phenethylfluoren-9-yl)phosphonium tetrafluoroborate (cataCXium FPrPh)	19.1
24	(9-Benzylfluoren-9-yl)-dicyclohexyl-phosphane; trifluoroborane; hydrofluoride (cataCXium FBn)	14.7
25	Trimethylphosphonium tetrafluoroborate	27.8
26	Trithylphosphonium tetrafluoroborate	17.7
27	Triisopropylphosphonium tetrafluoroborate	49.8
28	Tricyclohexylphosphonium tetrafluoroborate	45.1
29	Tribenzylphosphine	2.2
30	Di-*t*-butylmethylphosphonium tetrafluoroborate	40.4
31	*t*-Butyldicyclohexylphosphine	64.4
32	Di-*t*-butylcyclohexylphosphine	34.1
33	Benzyldi-1-adamantylphosphine (cataCXium ABn)	31.0
34	Di-*t*-butylneopentylphosphonium tetrafluoroborate	36.2
35	(Z)-1-*t*-butyl-2,3,6,7-tetrahydro-1H-phosphepinium tetrafluoroborate (Ellman ligand)	9.1
36	1,3,5-Triaza-7-phosphaadamantane	39.7
37	Di-*t*-butylphenylphosphonium tetrafluoroborate	24.9
38	Dicyclohexylphenylphosphine	14.3
39	(*o*-Tolyl)dicyclohexylphosphine	41.7
40	Dicyclohexyl-(2,4,6-trimethylphenyl)phosphine	41.5

41	Dicyclohexyl-(2,6-diisopropylphenyl)phosphine	59.1
42	1-Dicyclohexylphosphino-4-dimethylaminobenzene	40.7
43	1,3,5,7-Tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.13,7]decane	50.7
44	2-(Dicyclohexylphosphino)benzophenone	48.5
45	2'-(Dicyclohexylphosphino)acetophenone ethylene ketal	51.0
46	1-Di-*i*-propylphosphino-2-(*N*,*N*-dimethylamino)-1H-indene	50.1
47	11-Dicyclohexylphosphino-12-phenyl-9,10-ethenoanthracene (KitPhos)	38.1
48	11-Dicyclohexylphosphino-12-(2-methoxyphenyl)-9,10-ethenoanthracene (*o*-Meo-Kitphos)	33.2
49	Triphenylphosphine	37.9
50	Tri-*o*-tolylphosphine	46.0
51	Trimesitylphosphine	46.5
52	Tri(2-furyl)phosphine	65.9
53	Tris(2-methoxyphenyl)phosphine	53.3
54	Tris(4-methoxyphenyl)phosphine	50.2
55	Tris(2,4,6-trimethoxyphenyl)phosphine	34.7
56	Tris(4-fluorophenyl)phosphine	33.0
57	Tris(pentafluorophenyl)phosphine	0
58	Tris[3,5-bis(trifluoromethyl)phenyl]phosphine	22.1
59	Tri(1-naphthyl)phosphine	51.3
60	1,2-Bis(diphenylphosphino)ethane monooxide	5.6
61	Cyclohexyldiphenylphosphine	50.2
62	*t*-Butyldiphenylphosphine	54.5
63	Benzyldiphenylphosphine	2.6
64	4-(Dimethylamino)phenyldiphenylphosphine	49.1
65	Diphenyl-2-pyridylphosphine	29.7
66	2-(1,1-Dimethylpropyl)-6-(diphenylphosphino)pyridine (AlpyPhos)	40.1
67	2-(Diphenylphosphino)-6-(2,4,6-triphenylphenyl)pyridine (ArpyPhos)	26.1
68	1-Diphenylphosphino-2-(*N*,*N*-dimethylamino)-1H-indene	42.7
69	2-(Diphenylphosphino)-2'-(*N*,*N*-dimethylamino)biphenyl (Ph-DavePhos)	45.6

70	Tris(2,4-di-tert-butylphenyl)phosphite	65.0
71	(1,1'-Ferrocenediyl)phenylphosphine (1,1'-(PhP)-ferrocene)	7.4
72	1,4-Bis(diphenylphosphino)butane monooxide	2.3
73	Bis(diphenylphosphino)methane	1.8
74	1,2-Bis(diphenylphosphino)ethane (dppe [diphos])	4.5
75	1,3-Bis(diphenylphosphino)propane (dppp)	0
76	1,4-Bis(diphenylphosphino)butane (dppb)	10.2
77	1,5-Bis(diphenylphosphino)pentane (dpppe)	16.3
78	1,8-Bis(diphenylphosphino)octane (dppo)	22.6
79	1,2-Bis(dipentafluorophenylphosphino)ethane	6.5
80	1,2-Bis(di-2-pyridylphosphino)ethane	7.8
81	1,2-Bis(diphenylphosphinomethyl)benzene	3.6
82	1,2-Bis(diphenylphosphino)benzene (dppbz)	2.7
83	1,8-Bis(diphenylphosphanyl)naphthalene	47.4
84	1,2,3,4-(Diphenylphosphinomethyl)cyclopentane (Tedicyp)	3.3
85	Bis(2-diphenylphosphinophenyl)ether (DPEPhos)	21.4
86	2,2'-Bis(diphenylphosphino)benzophenone (dpbp)	18.3
87	9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (Xantphos)	37.2
88	4,6-Bis(diphenylphosphino)phenoxazine (NiXantphos)	93.2
89	(*S*)-(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl ((*S*)-BINAP)	2.3
90	(R)-(+)-2,2'-bis(di-p-tolylphosphino)-1,1'-binaphthyl ((R)-Tol-BINAP)	3.5
91	2,2'-Bis(diphenylphosphino)-1,1'-biphenyl (Biphep)	1.7
92	3,3'-Bis(diphenylphosphino)-5,5',6,6',7,7',8,8'-octahydro[2,2']binaphthalene hemichloroform adduct (Cy-Nu-Biphep)	1.1
93	6,6'-Bis(diphenylphosphino)-1,1',3,3'-tetrahydro[5,5']biisobenzofuran (Thf-Nu-Biphep)	1.6
94	Tetramethyl 6,6'-bis(diphenylphosphino)-1,1',3,3'-tetrahydro[5,5']biindenyl-2,2',2,2'-tetracarboxylate	11.5
95	2-(Diphenylphosphino)ethylamine	7.6
96	2-[2-(Diphenylphosphino)ethyl]pyridine	27.5

1 – 24: Monodentate dialkyl biaryl phosphine ligands; **25 – 48**: Monodentate trialkyl and dialkylaryl phosphine ligands; **49 – 72**: Monodentate triaryl and diarylalkylphosphine ligands; **73 – 96**: Bidentate electron-poor phosphine ligands.

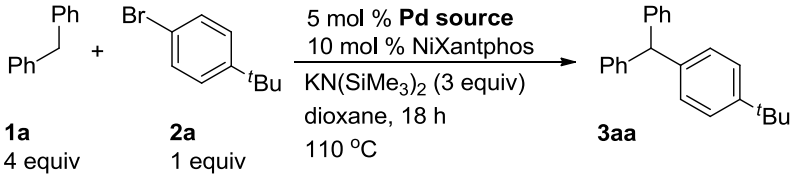
	Ligand libraries (97 – 112)	$PdCl_2(PPh_3)_2$	
		5 mol %	**10 mol %**
97	2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (XPhos)	41.0	52.1
98	2-Dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (SPhos)	49.5	52.9
99	2-(Di-*t*-butylphosphino)biphenyl (JohnPhos)	38.5	24.9
100	2-Dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl (DavePhos)	35.9	44.5
101	2-Dicyclohexylphosphino-2',6'-di-i-propoxy-1,1'-biphenyl (RuPhos)	46.7	55.7
102	2-Di-*t*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me-4-*t*Bu-XPhos)	62.6	80.6
103	Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)	21.9	27.7
104	Butyldi-1-adamantylphosphine (cataCXium A)	18.9	28.6
105	1,2,3,4,5-Pentaphenyl-1'-(di-*t*-butylphosphino)ferrocene (QPhos)	30.3	37.4
106	Tri-*t*-butylphosphonium tetrafluoroborate	25.8	36.2
107	(4-(*N*,*N*-dimethylamino)phenyl)di-*t*-butyl phosphine (AmPhos)	30.6	39.9
108	1,1'-Bis(di-*t*-butylphosphino)ferrocene (dtbpf)	17.4	20.7
109	1,1'-Bis(diphenylphosphino)ferrocene (dppf)	4.0	3.8
110	1,1'-Bis(diisopropylphosphino)ferrocene (dippf)	11.7	11.5
111	(*R*)-(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl ((R)-BINAP)	2.4	2.0
112	(R)-(-)-1-[(S)-2-(Dicyclohexylphosphino)ferrocenyl]ethyldi-*t*-butylphosphine (JosiPhos SL-J009-1)	47.6	49.0

97 – 108: Monodentate phosphine ligands; **109 – 112**: Bidentate and monodentate phosphine ligands.

	$Pd(OAc)_2$		$PdCl_2(CH_3CN)_2$		$Pd_2(dba)_3$	
Ligand	**5 mol %**	**10 mol %**	**5 mol %**	**10 mol %**	**2.5 mol %**	**5 mol %**
1	0	3.6	3.6	5.0	0	0
14	6.1	7.0	6.9	7.4	3.3	5.7

28	37.5	61.7	41.4	84.7	31.9	39.3
50	12.9	17.6	14.5	14.5	0	14.1
75	0	0.6	0	20.2	0	0
76	5.2	5.8	8.4	2.9	3.0	0
85	43.4	41.3	47.3	55.5	35.8	27.8
87	67.5	69.6	65.9	69.9	24.5	64.1
97	41.0	52.1	41.1	49.7	28.3	37.2
98	49.5	52.9	36.8	40.9	27.0	24.2
99	38.5	24.9	12.2	13.9	6.3	8.1
100	35.9	44.5	22.0	11.1	15.4	15.1
101	46.7	55.7	21.1	21.2	12.3	14.0
102	62.6	80.6	0	4.5	0	0
103	21.9	27.7	7.6	8.6	4.1	13.5
104	18.9	28.6	8.9	12.4	7.2	9.8
105	30.3	37.4	13.6	11.7	12.1	7.8
106	25.8	36.2	6.7	11.1	10.0	3.3
107	30.6	39.9	16.7	22.6	13.2	15.6
108	17.4	20.7	52.3	52.9	36.2	37.8
109	4.0	3.8	13.8	25.3	29.4	0
110	11.7	11.5	19.3	31.4	18.0	0
111	2.4	2.0	2.4	33.8	1.8	9.5
112	47.6	49.0	49.2	42.6	45.6	52.2

(3) Pd Source Screening:



6 Pd sources: $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, $PdCl_2(CH_3CN)_2$, $[Pd(allyl)Cl]_2$, $Pd(COD)Cl_2$, and $Pd_2(dba)_3$.

Entry	Catalyst	Ligand	AY (%)
1	$PdCl_2(PPh_3)_2$	no ligand added	46
2	$PdCl_2(PPh_3)_2$	NiXantphos	93
3	$Pd(OAc)_2$	no ligand added	no reaction
4	$Pd(OAc)_2$	NiXantphos	100
5	$PdCl_2(CH_3CN)_2$	no ligand added	no reaction
6	$PdCl_2(CH_3CN)_2$	NiXantphos	90
7	$Pd_2(dba)_3$	no ligand added	no reaction
8	$Pd_2(dba)_3$	NiXantphos	88
9	$Pd(COD)Cl_2$	no ligand added	no reaction
10	$Pd(COD)Cl_2$	NiXantphos	96

11	$[Pd(allyl)Cl]_2$	no ligand added	no reaction
12	$[Pd(allyl)Cl]_2$	NiXantphos	91

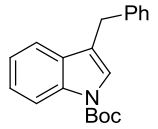
The lead hit from the screening was the combination of **$Pd(OAc)_2$** (5 mol %) and **NiXantphos** (10 mol %), giving 100% assay yield of the desired DCCP product **3aa**. A scale-up reaction on a 0.1 mmol scale using General Procedure B for the Pd-Catalyzed DCCP of **1a** proved successful with > 95% yield of **3aa** determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

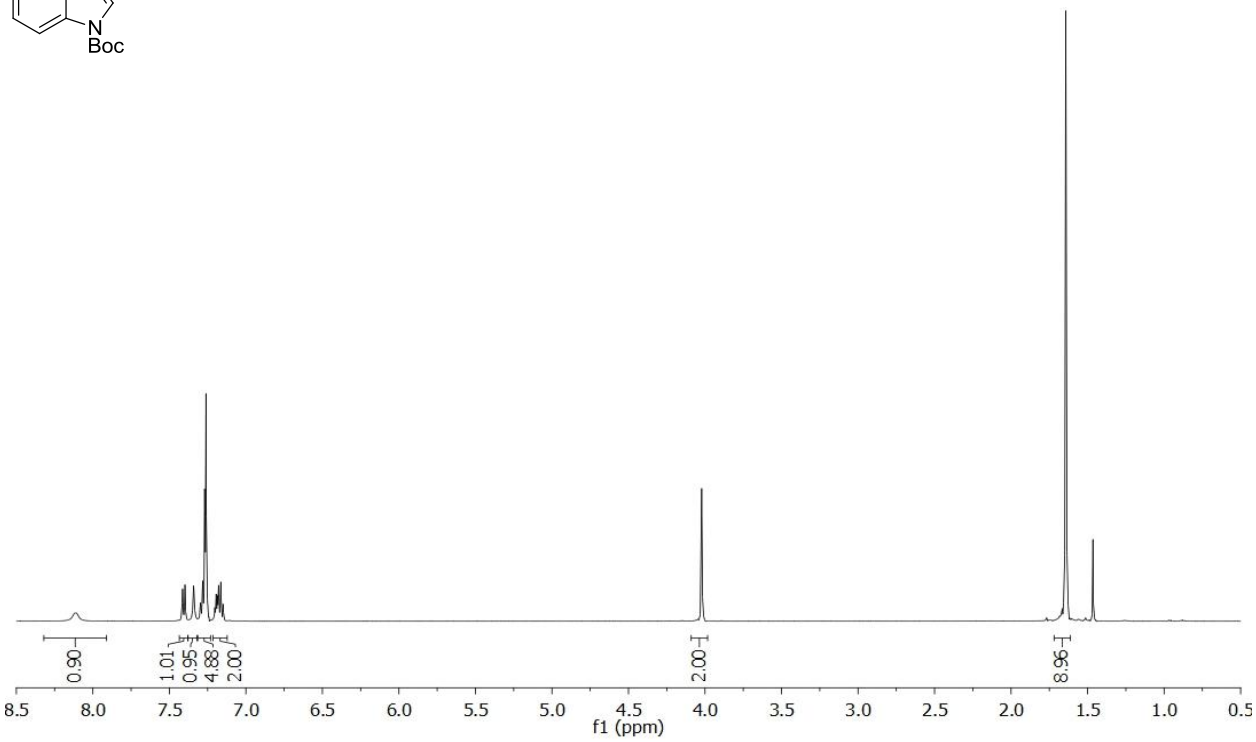
References.

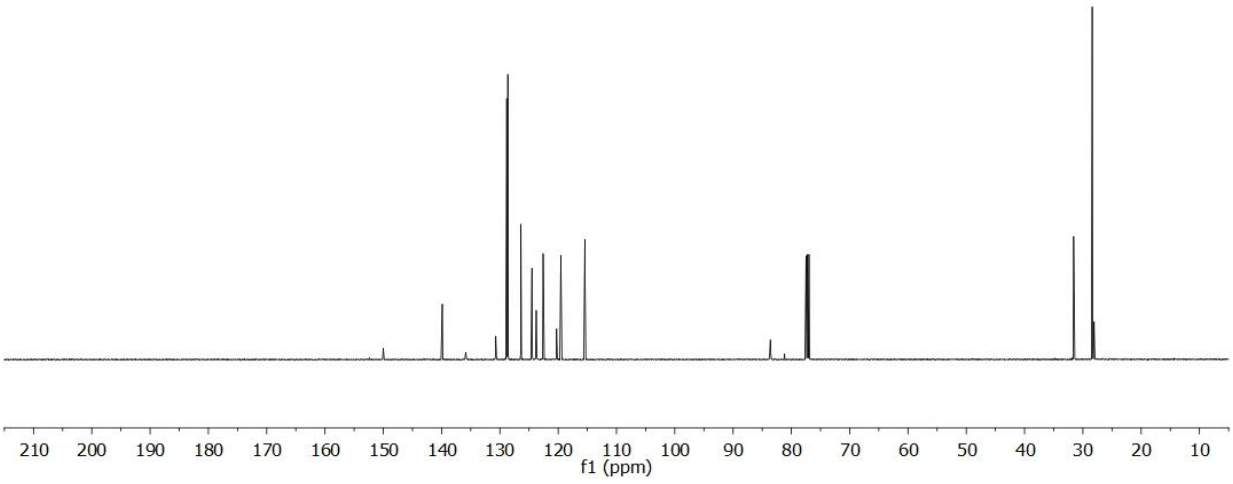
1. Engel, J. F. Insecticidal Perhaloalkylvinylcyclopropanecarboxylates US Patent US4332815 (A1), 1982.
2. Henry, N.; Enguehard-Gueiffier, C.; Thery, I.; Gueiffier, A. *Eur. J. Org. Chem.* **2008**, 4824.
3. Fuwa, H.; Sasaki, M. *Org. Biomol. Chem.* **2007**, *5*, 2214.
4. Fessard, T. C.; Motoyoshi, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2078.
5. Robinson, P. D.; McLean, A. W.; Meyers, C. Y. *Acta Cryst.* **2003**, *C59*, o539.
6. Yu, J-Y; Kuwano, R. *Org. Lett.* **2008**, *10*, 973.
7. Aoyama, T.; Kubota, S.; Takido, T.; Kodomari, M. *Chem. Lett.* **2011**, *40*, 484.
8. Prakash, G. K. S.; Panja, C.; Shakhmin, A.; Shah, E.; Mathew, T.; Olah, G. A. *J. Org. Chem.* **2009**, *74*, 8659.
9. Cho, B. P.; Blankenship, L. R.; Moody, J. D.; Doerge, D. R.; Beland, F. A.; Culp, S. J. *Tetrahedron* **2000**, *56*, 7379.
10. Bandaranayake, W. M.; Riggs, N. V. *Aust. J. Chem.* **1981**, *34*, 115.
11. Li, H.; Li, W.; Liu, W.; He, Z.; Li, Z. *Angew. Chem., Int. Ed.* **2011**, *50*, 2975.
12. Alexander, C.; Feast, W. J. *Synthesis* **1992**, 735.
13. Dreher, S. D.; Dormer, P. G.; Sandrock, D. L.; Molander, G. A. *J. Am. Chem. Soc.* **2008**, *130*, 9257.

NMR Spectra.

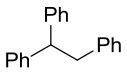
1l – *N-tert*-butyl 3-benzylindole carboxylate

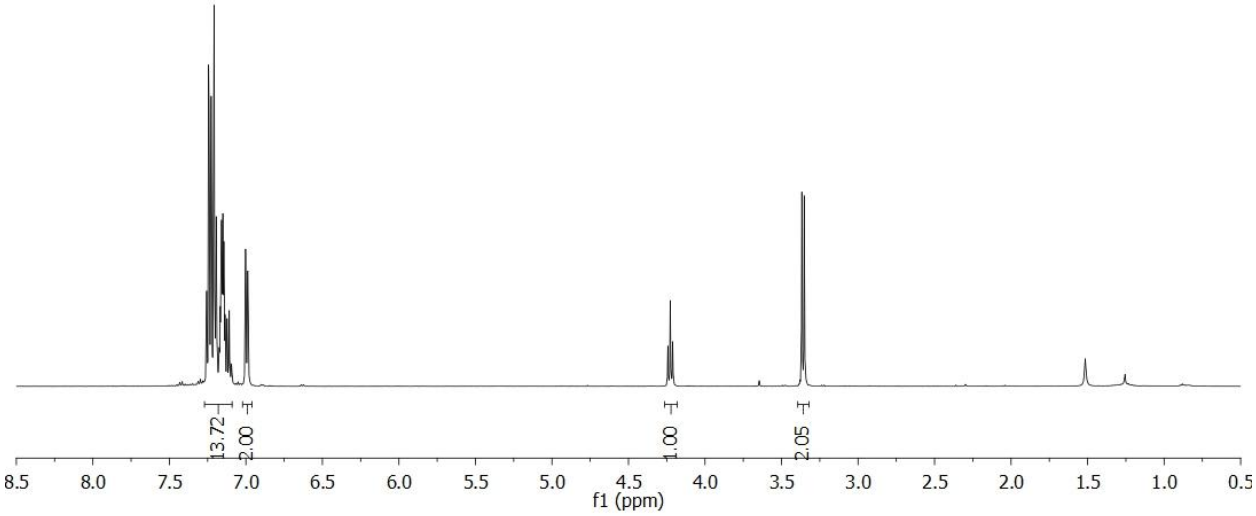


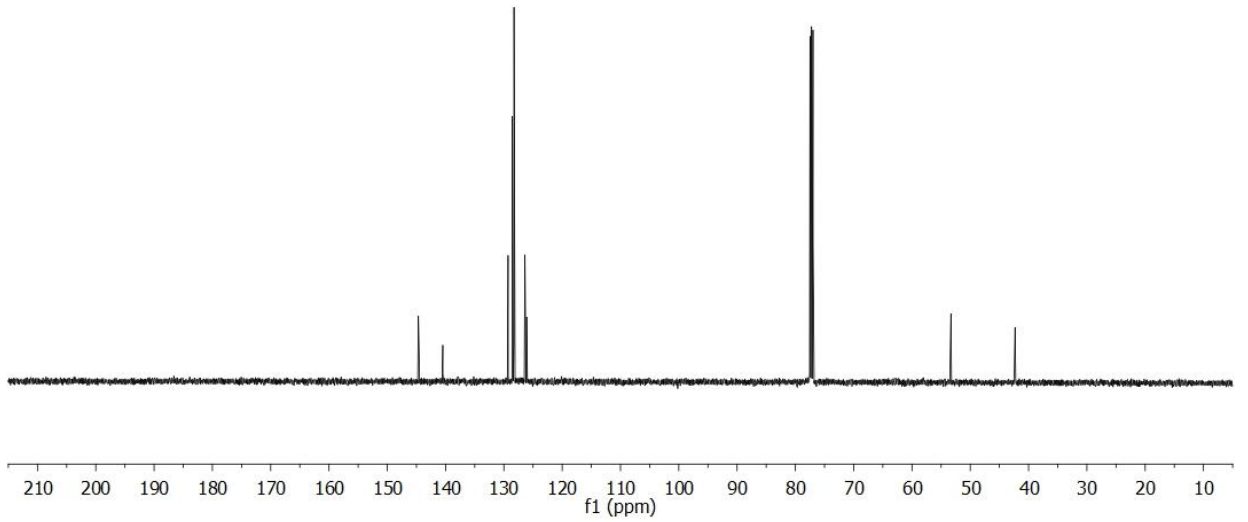




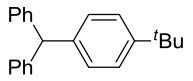
1,1,2-triphenylethane

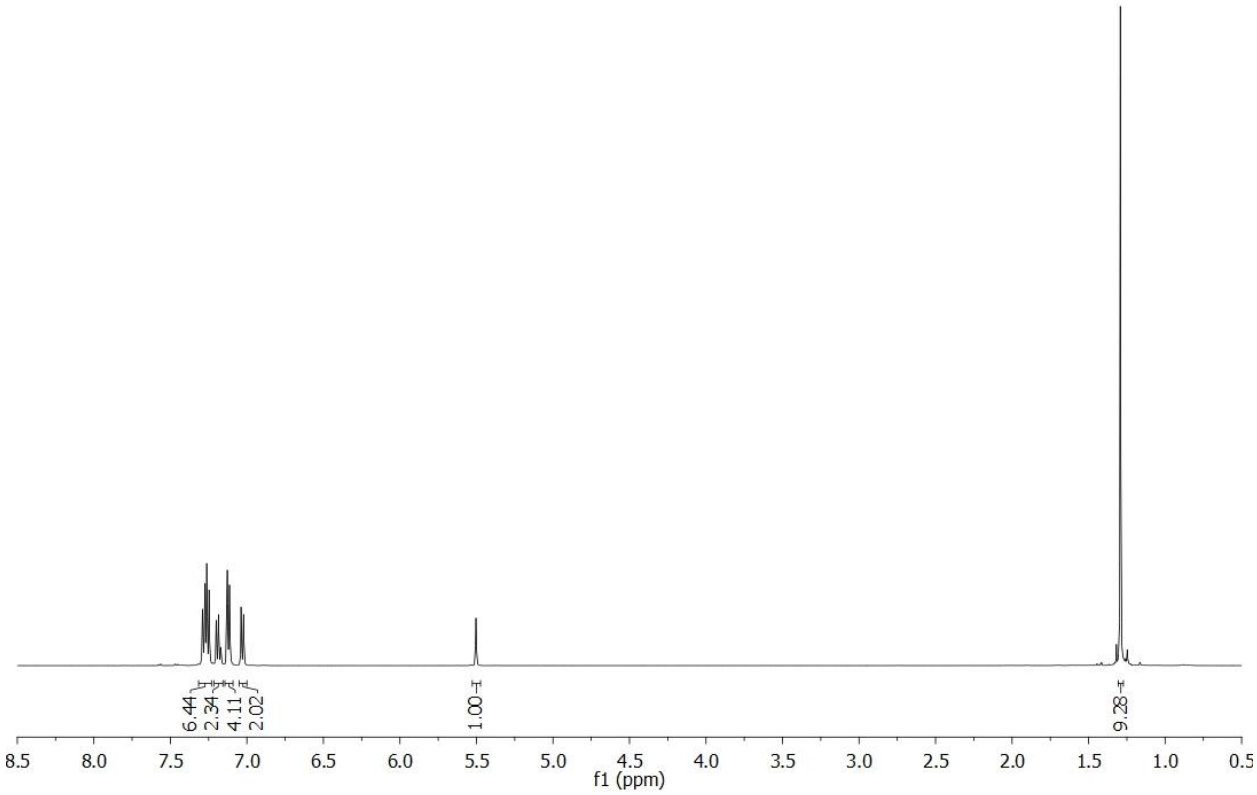


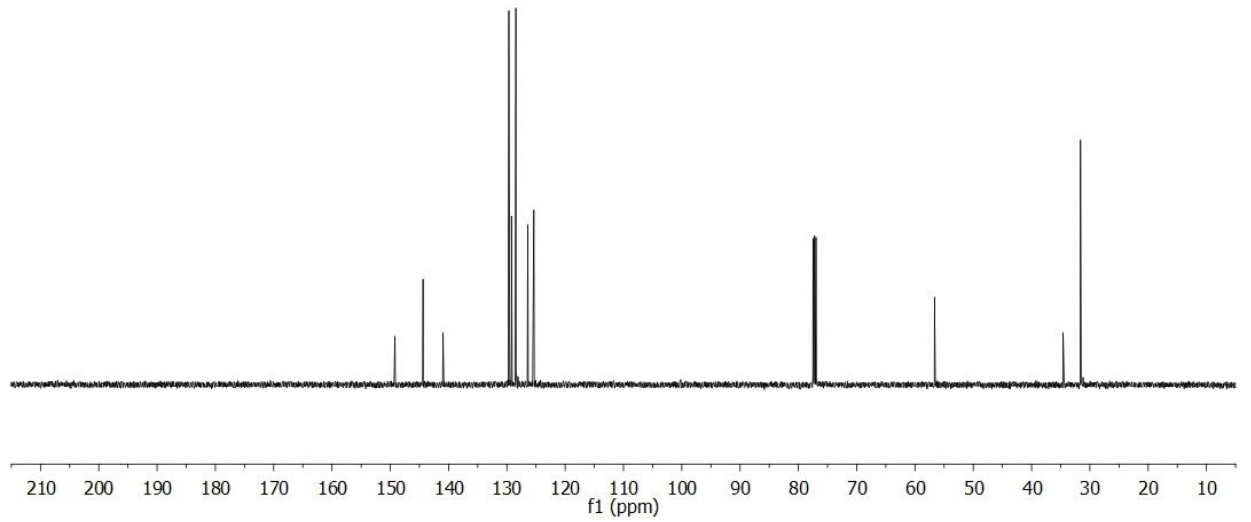




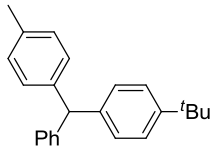
3aa – (4-*tert*-butylphenyl)diphenylmethane

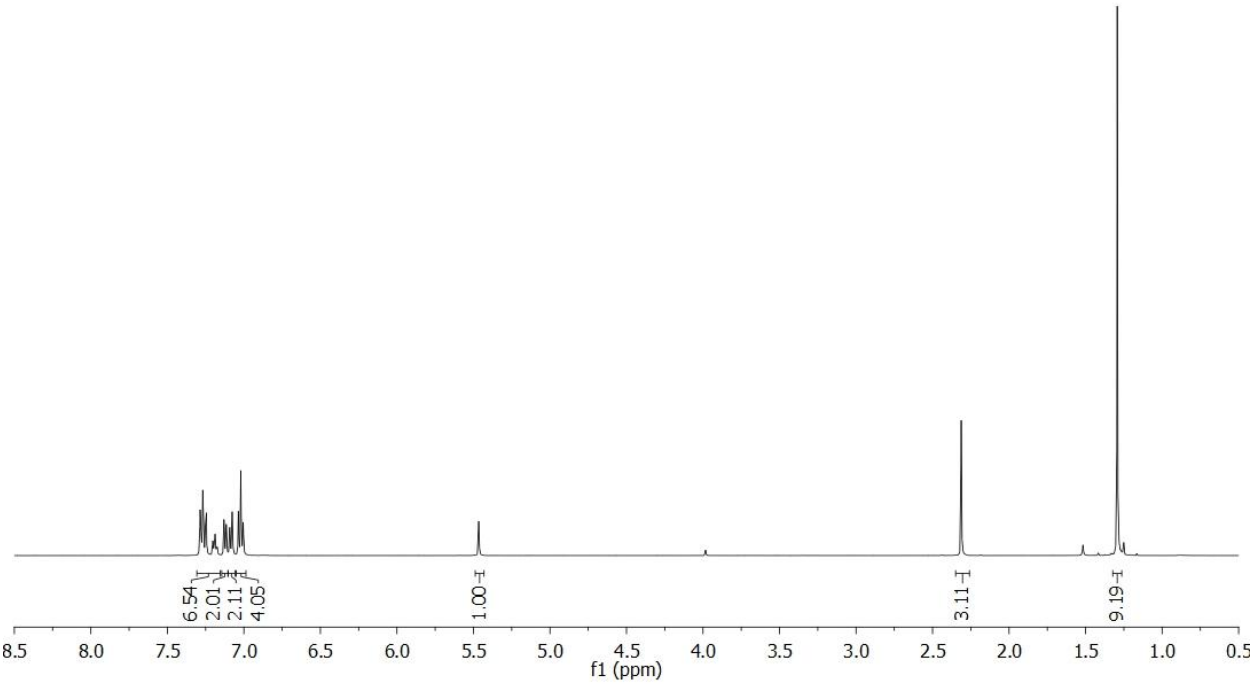


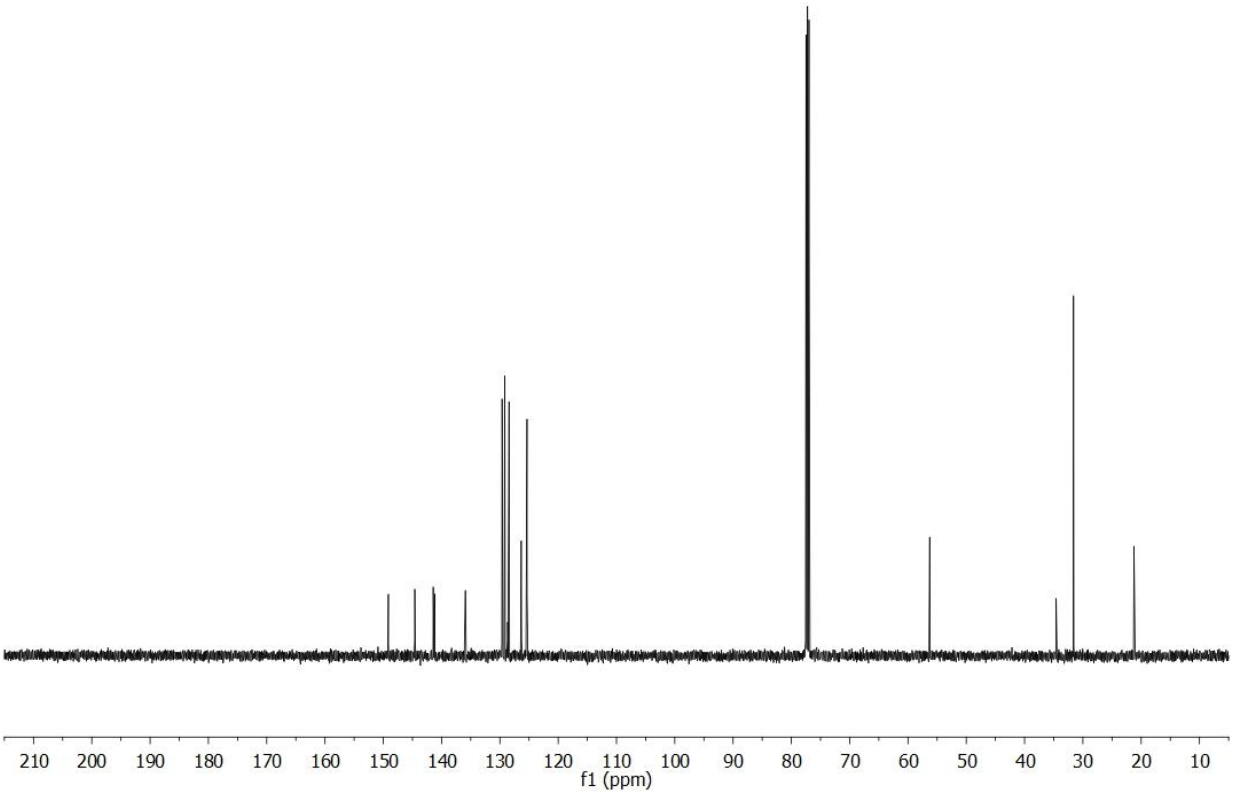




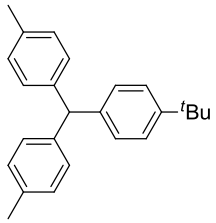
3ba – (4-*tert*-butylphenyl)(4-methylphenyl)phenylmethane

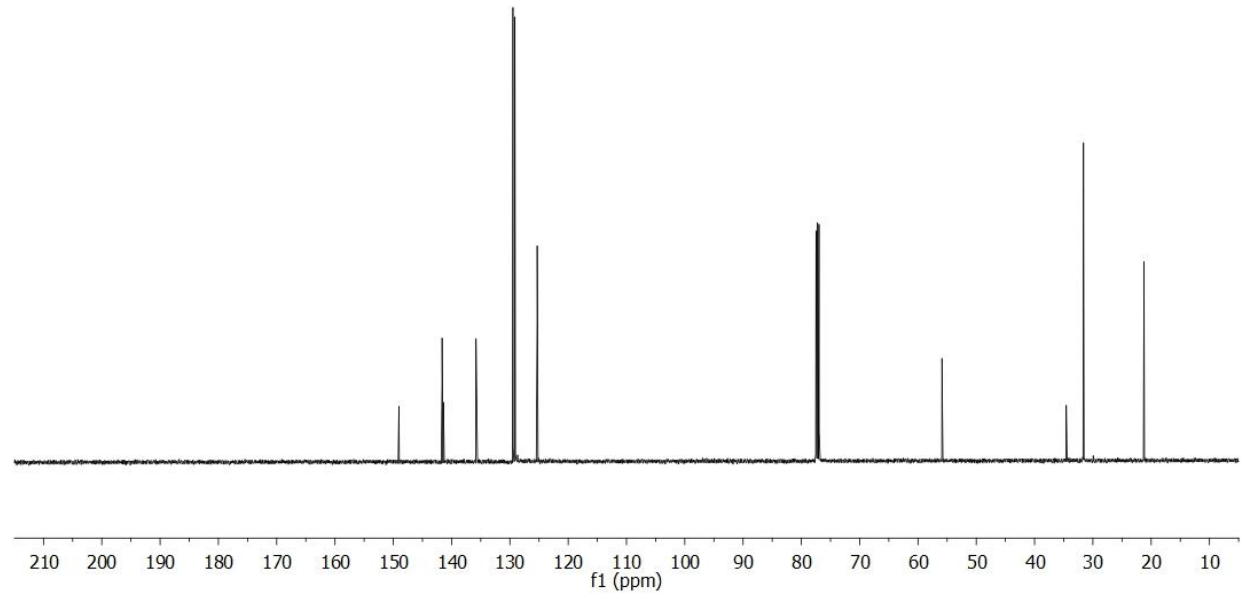




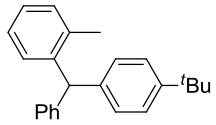


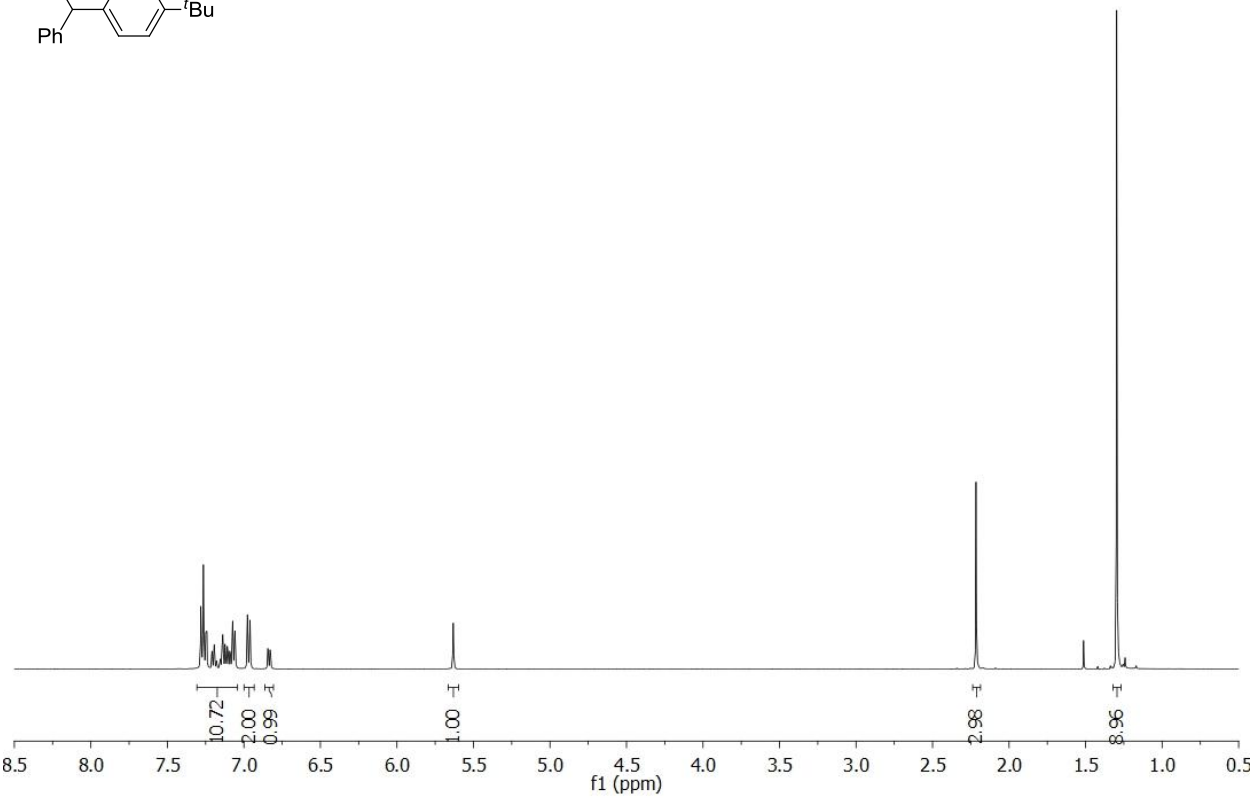
3ca – (4-*tert*-butylphenyl)bis(4-methylphenyl)methane

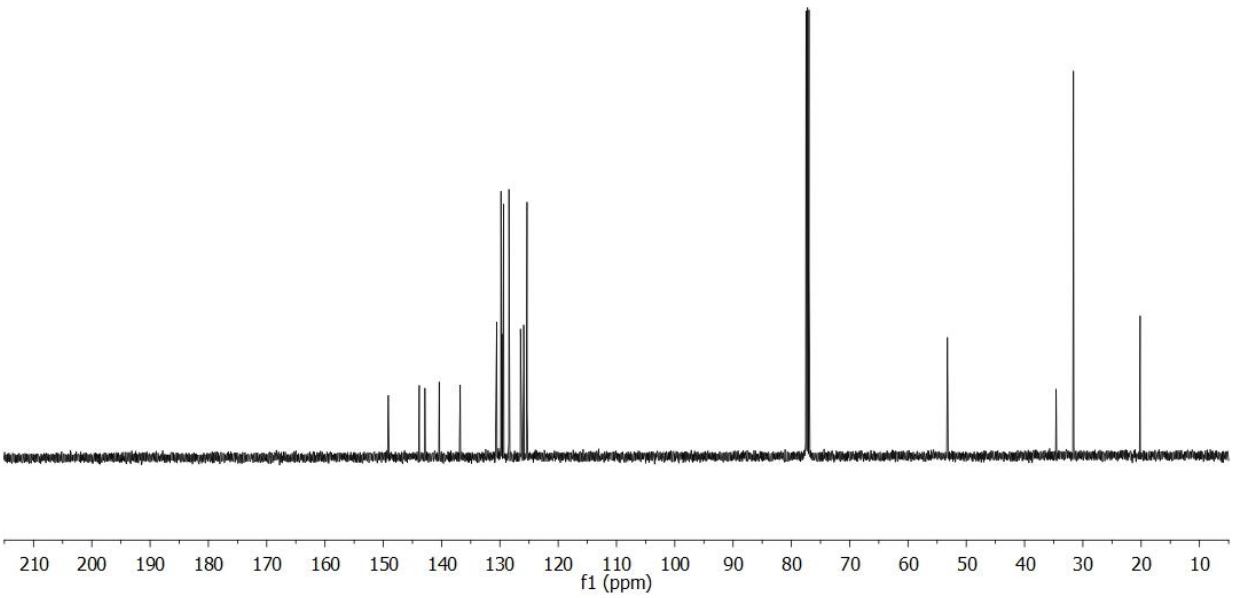




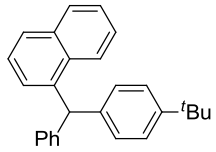
3da – (4-*tert*-butylphenyl)(2-methylphenyl)phenylmethane

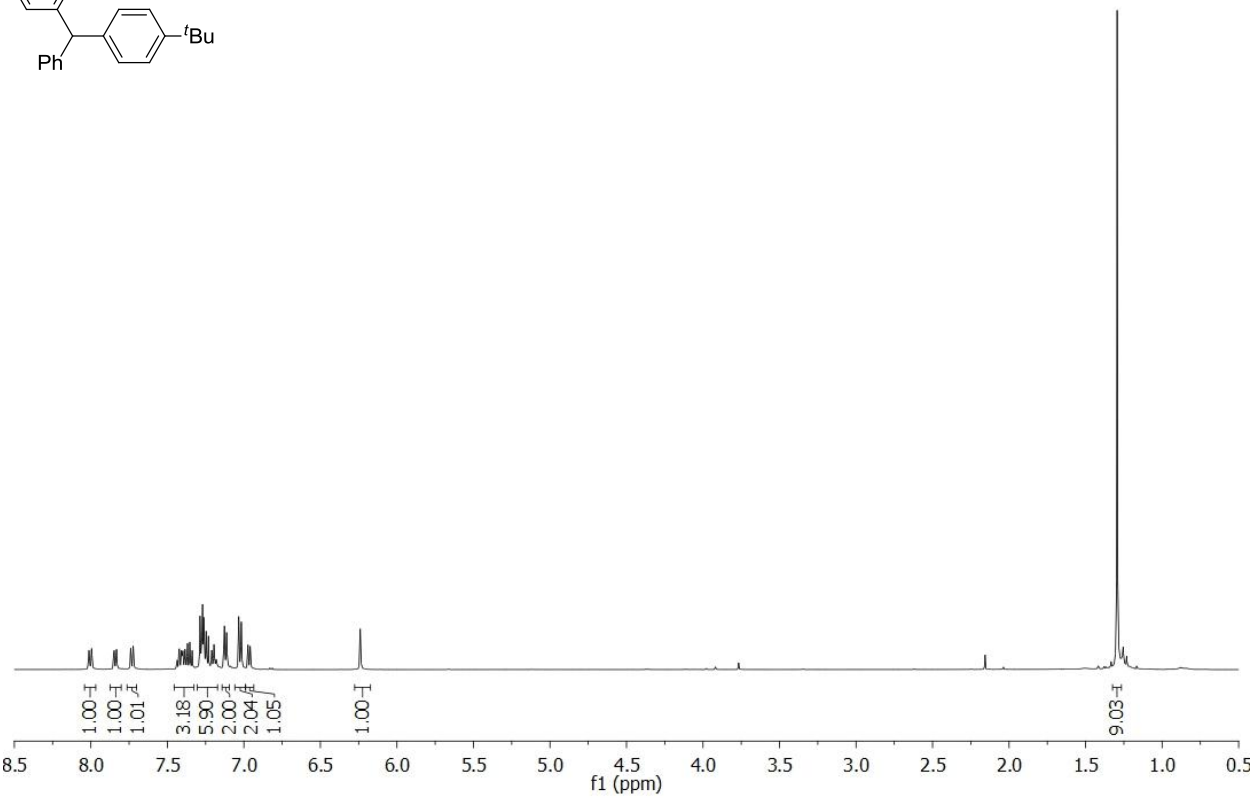


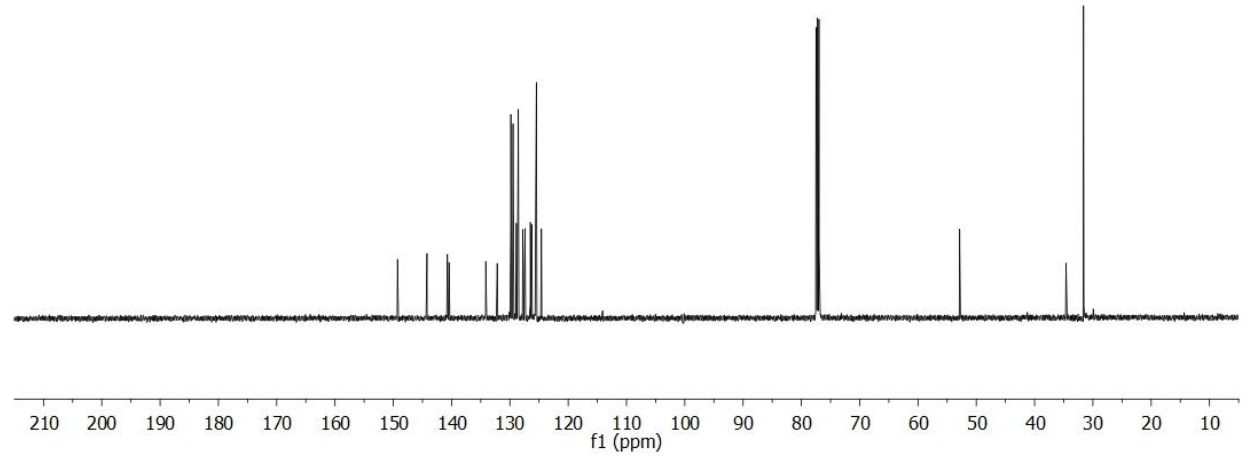




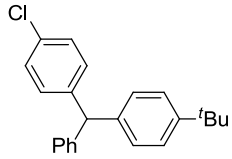
3ea – (4-*tert*-butylphenyl)(1-naphthyl)phenylmethane

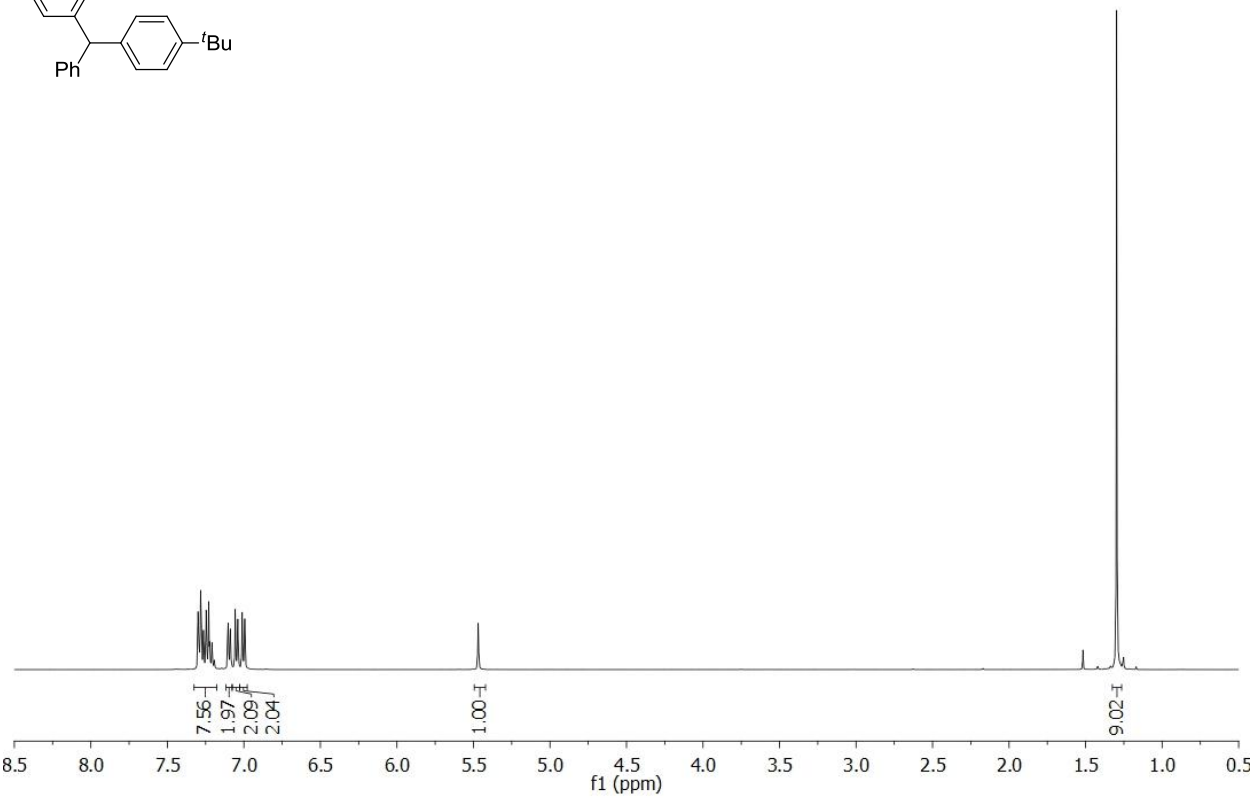


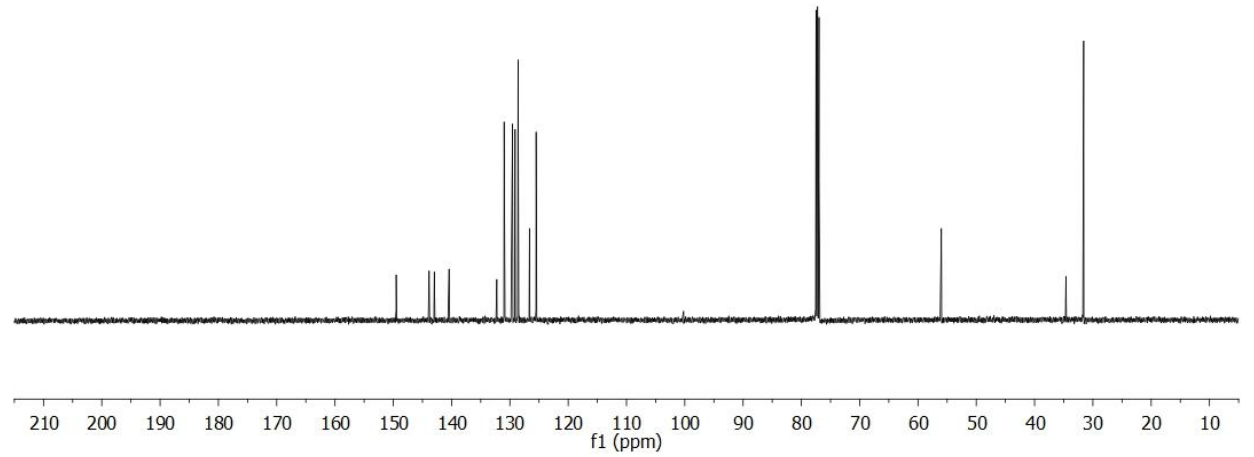




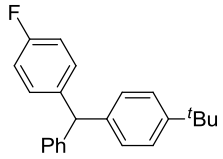
3fa – (4-*tert*-butylphenyl)(4-chlorophenyl)phenylmethane

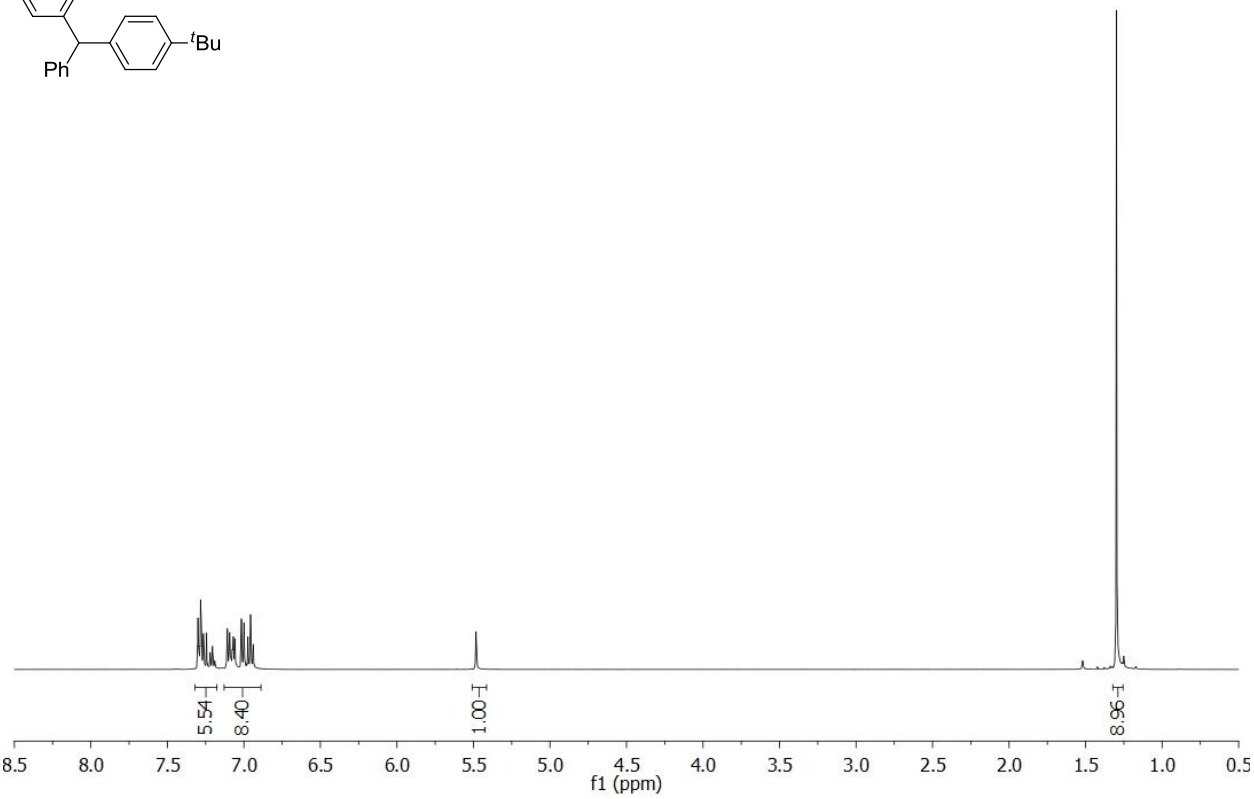


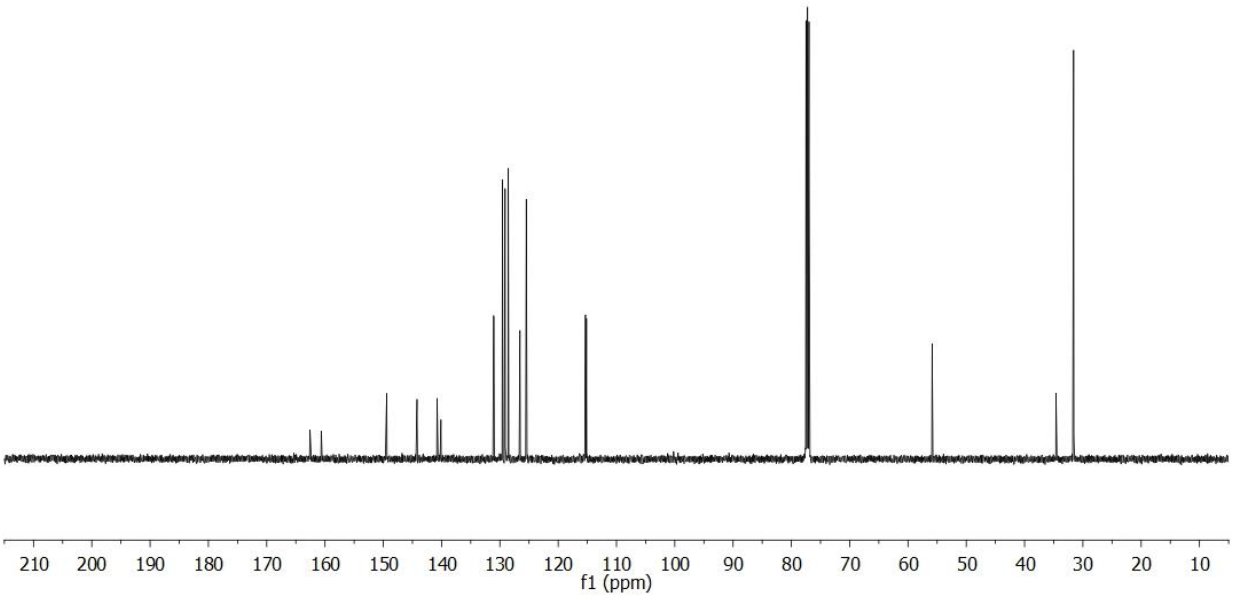




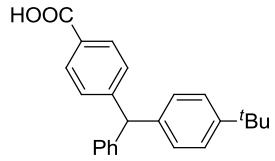
3ga – (4-*tert*-butylphenyl)(4-fluorophenyl)phenylmethane

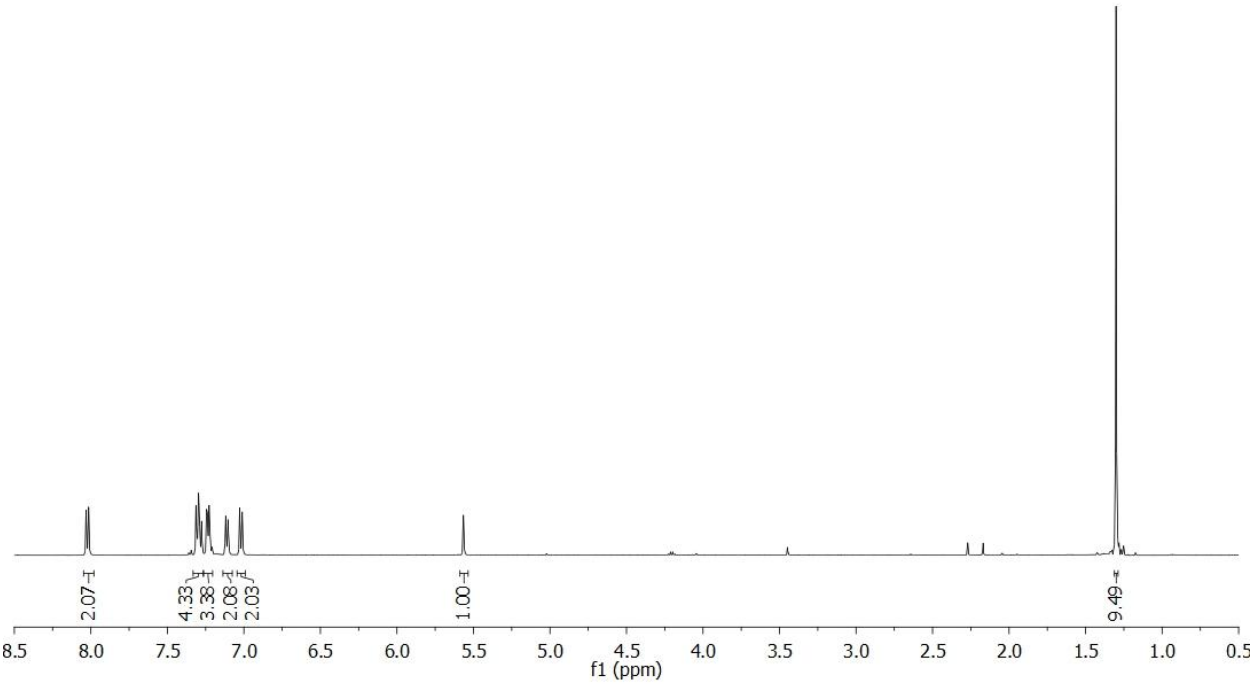


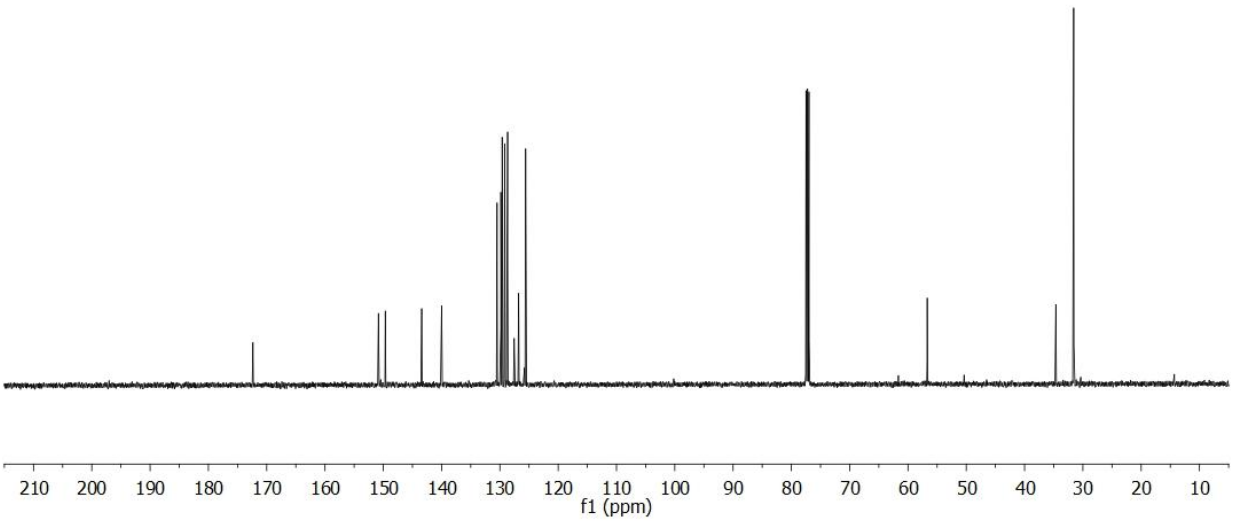




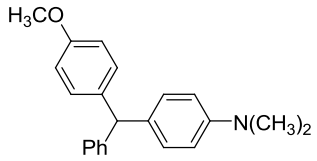
3ha – 4-((4-*tert*-butylphenyl)(phenyl)methyl)benzoic acid

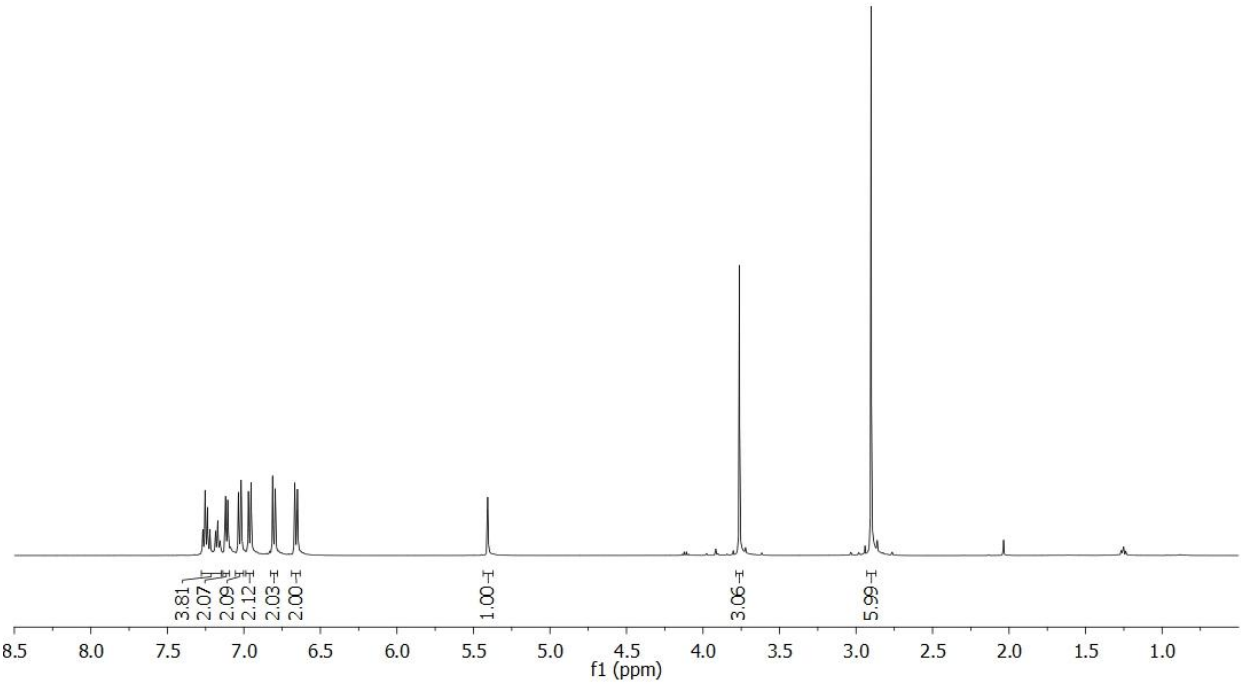


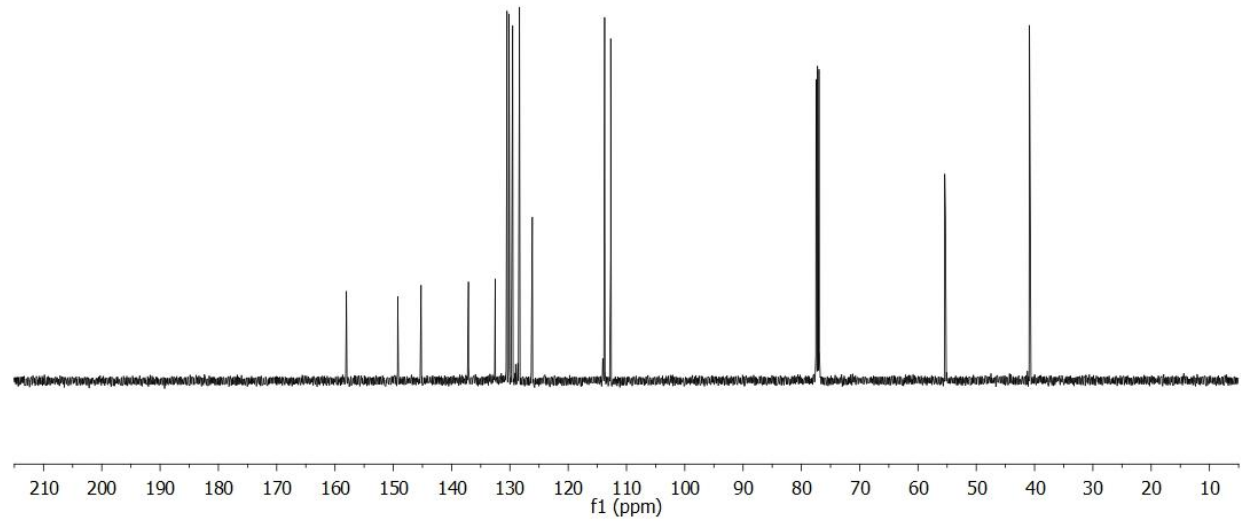




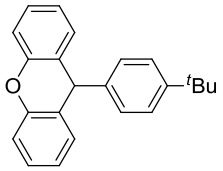
3ij – (4-*N*,*N*-dimethylphenyl)(4-methoxyphenyl)phenylmethane

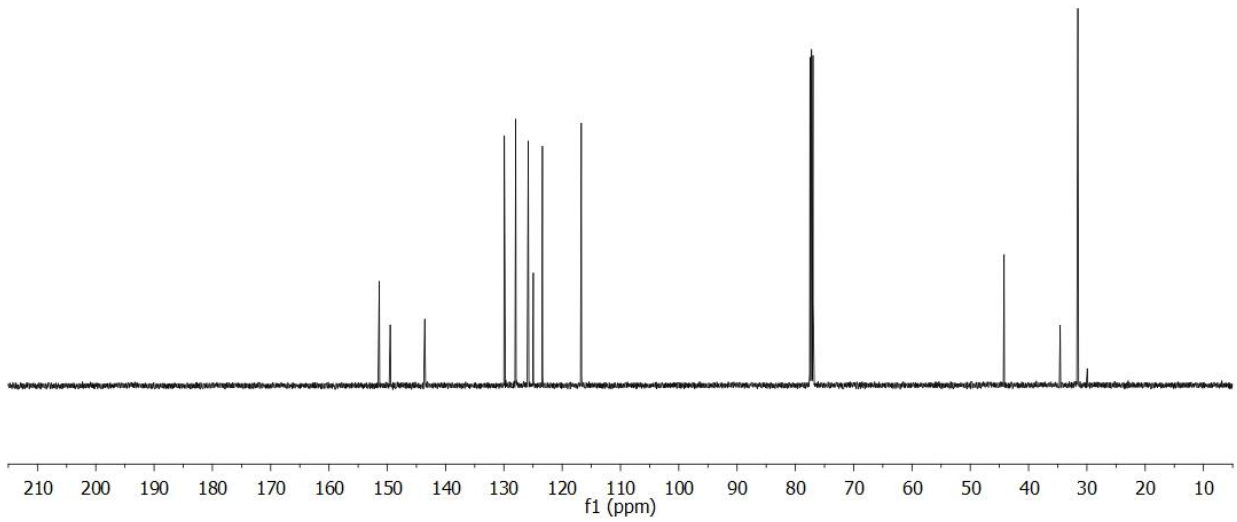




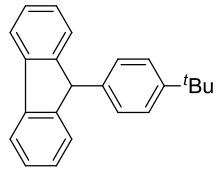


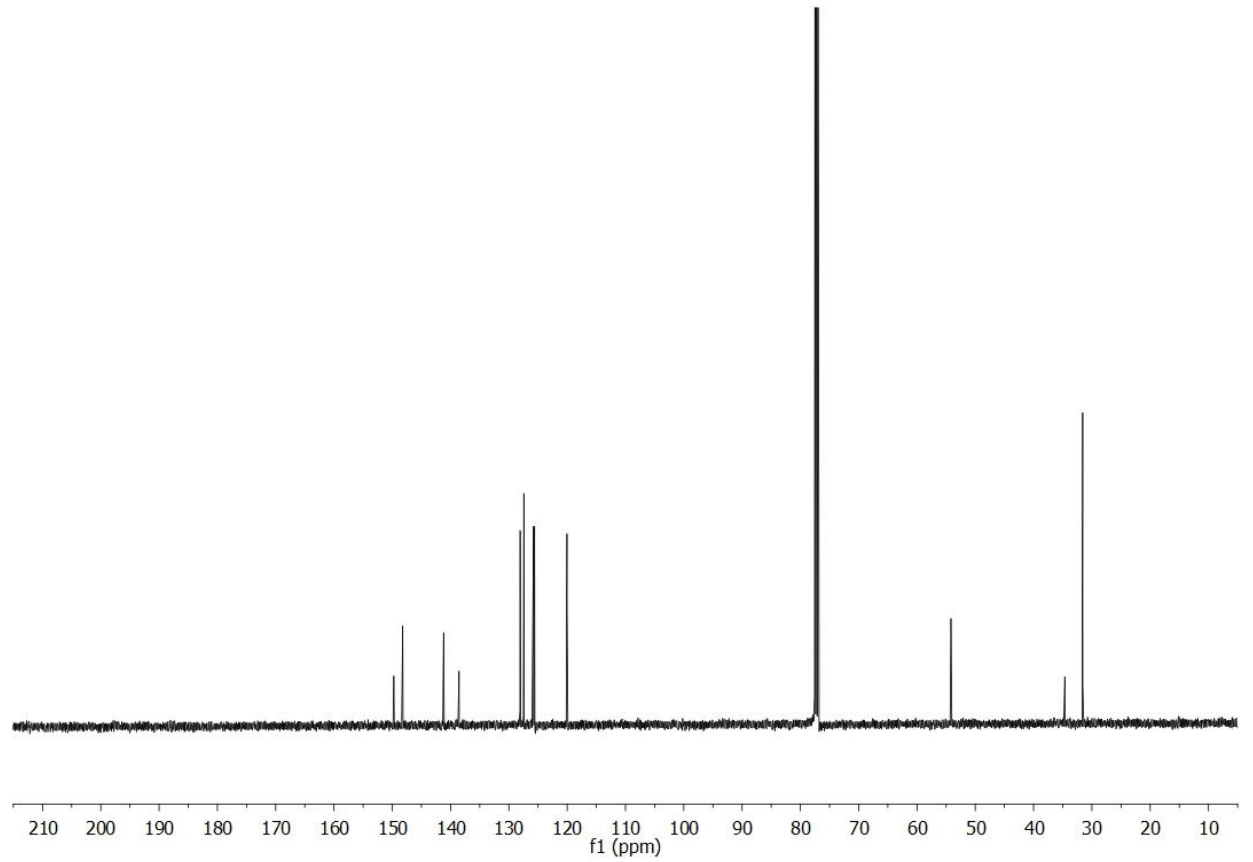
3ja – 9-(4-*tert*-butylphenyl)xanthene



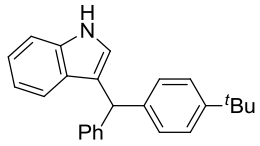


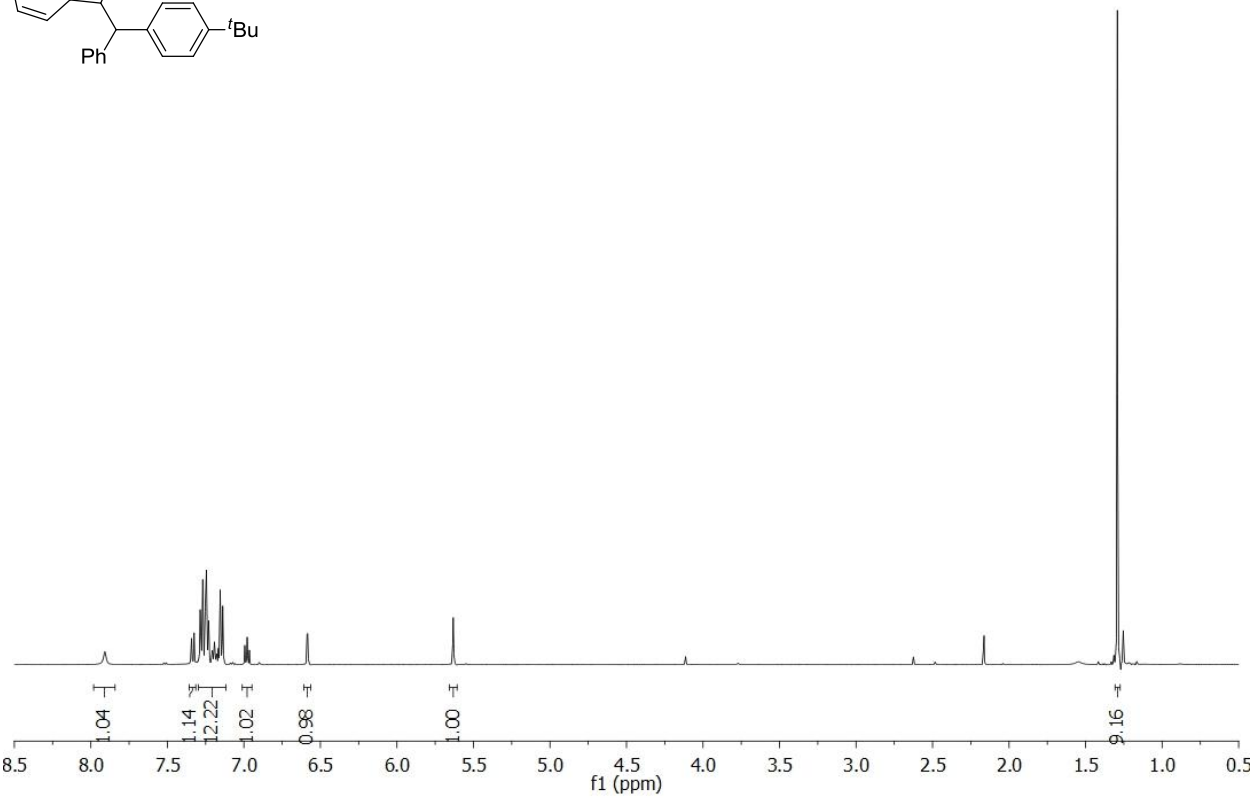
3ka – 9-(4-*tert*-butylphenyl)fluorene

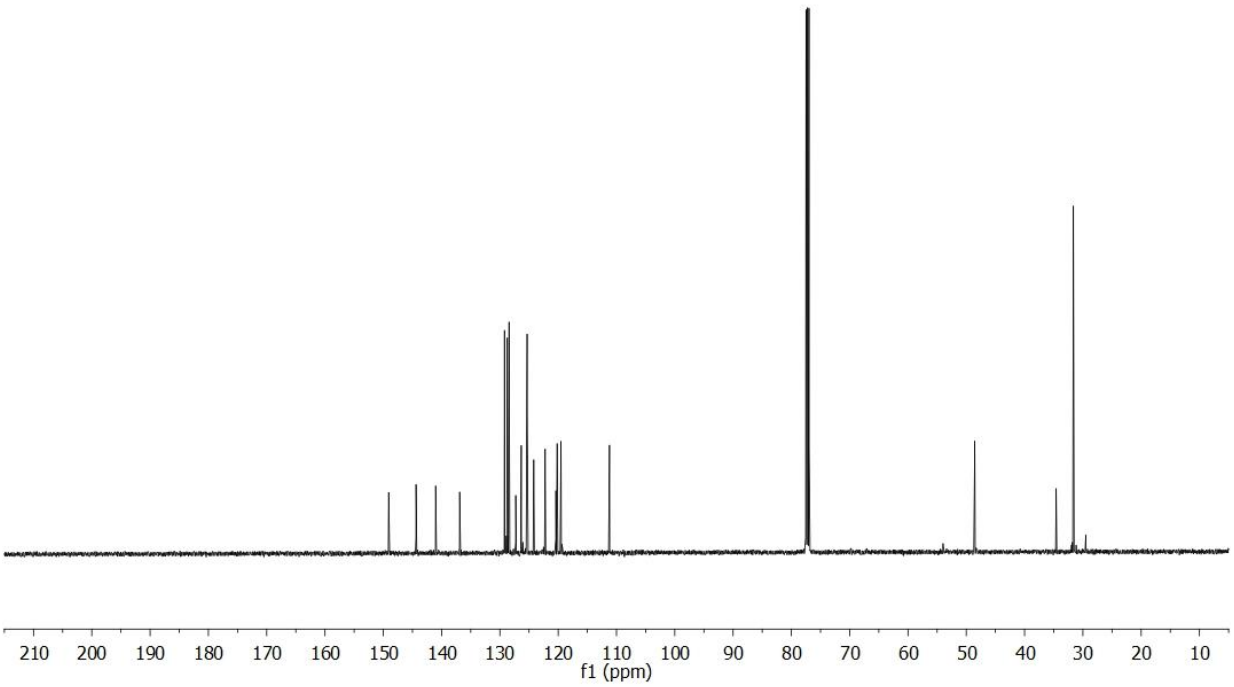




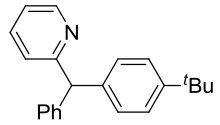
3la – 3-((4-*tert*-butylphenyl)(phenyl)methyl)-1*H*-indole

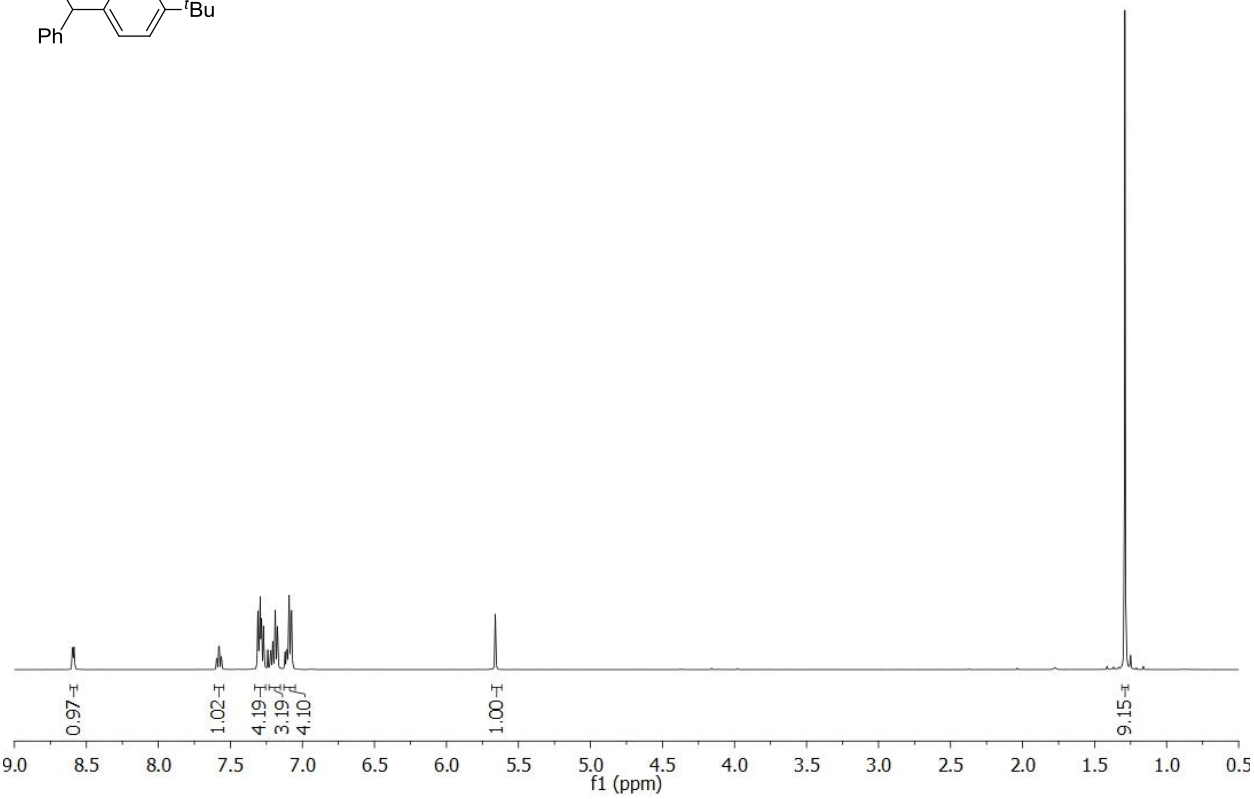


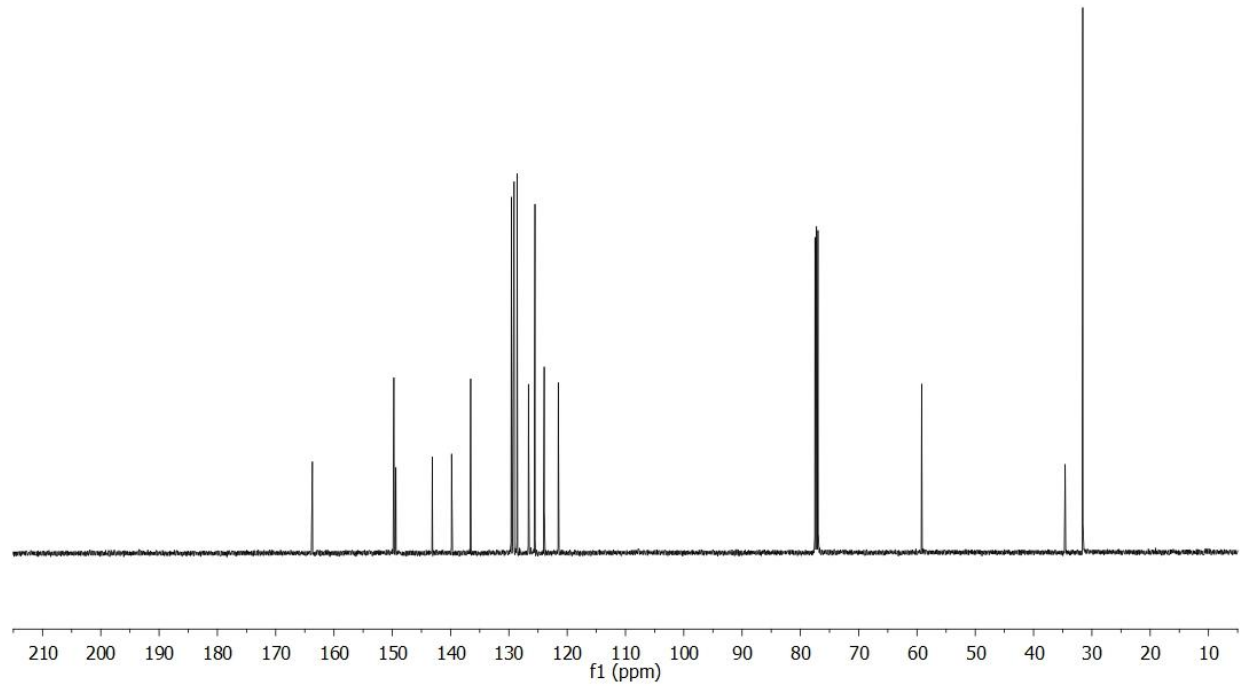




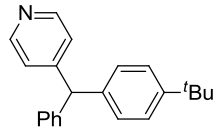
3ma – (4-*tert*-butylphenyl)(2-pyridyl)phenylmethane

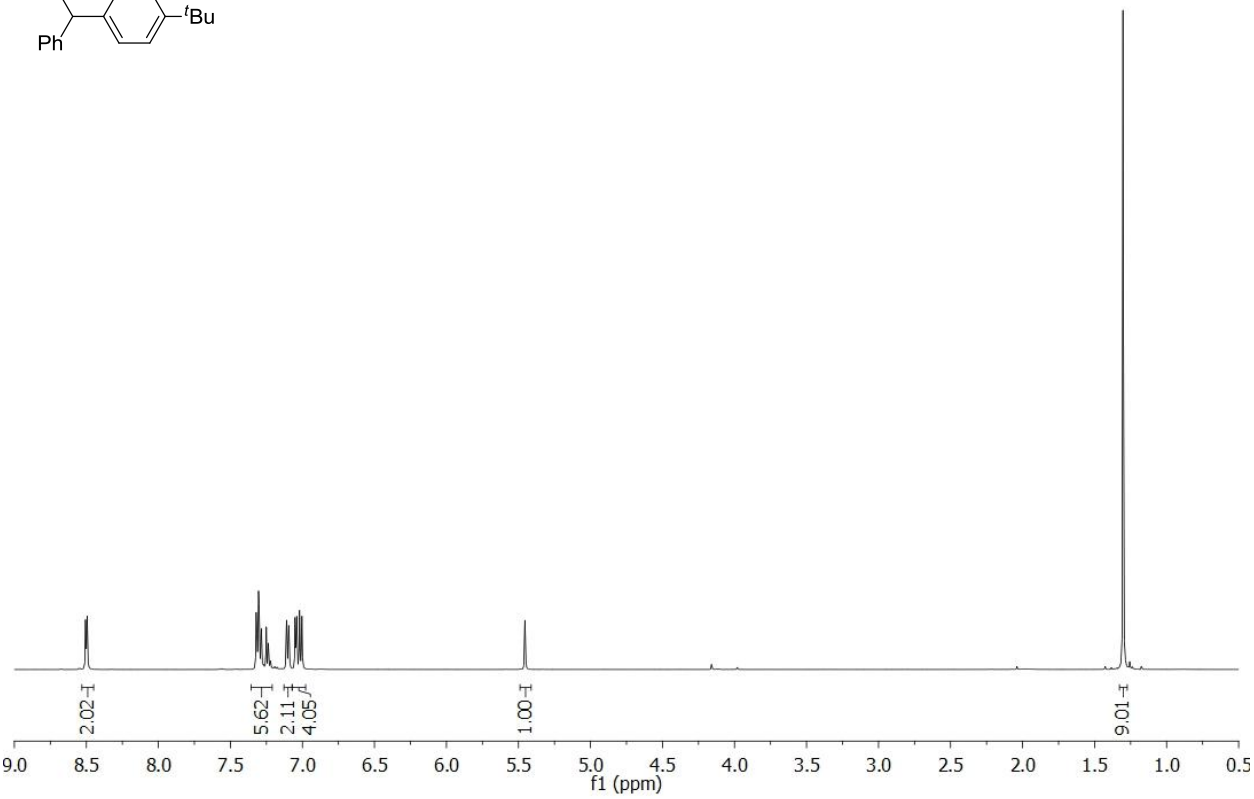


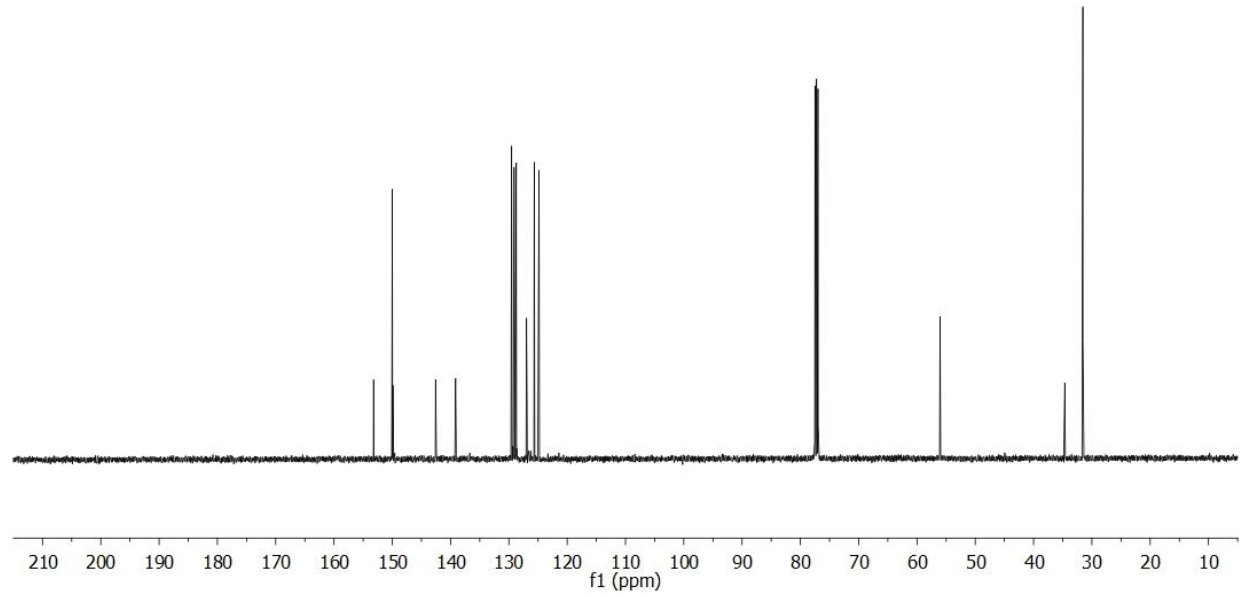




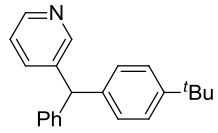
3na – (4-*tert*-butylphenyl)(4-pyridyl)phenylmethane

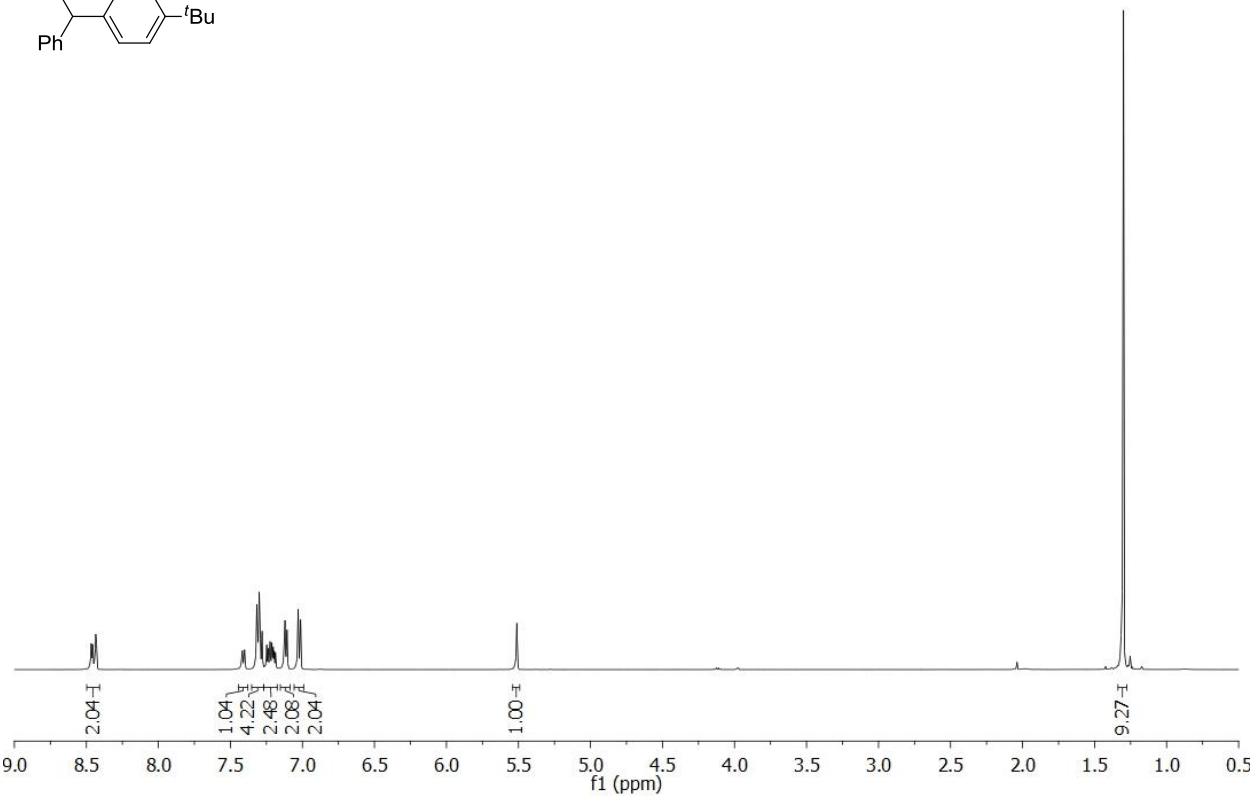


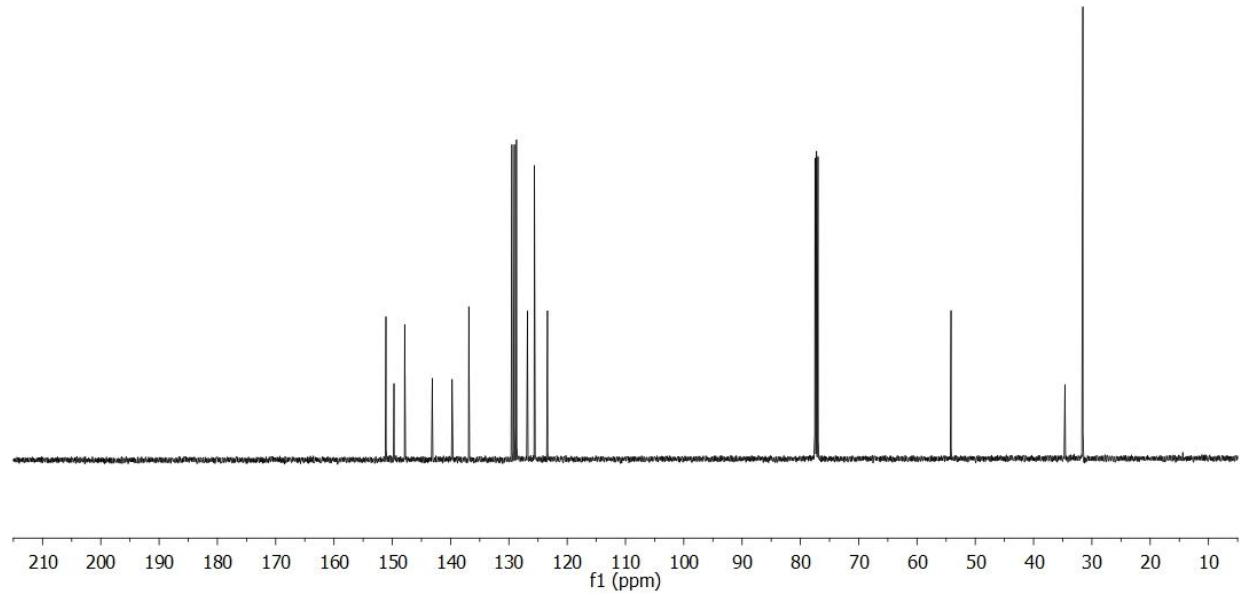




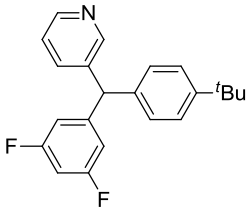
3oa – (4-*tert*-butylphenyl)(3-pyridyl)phenylmethane

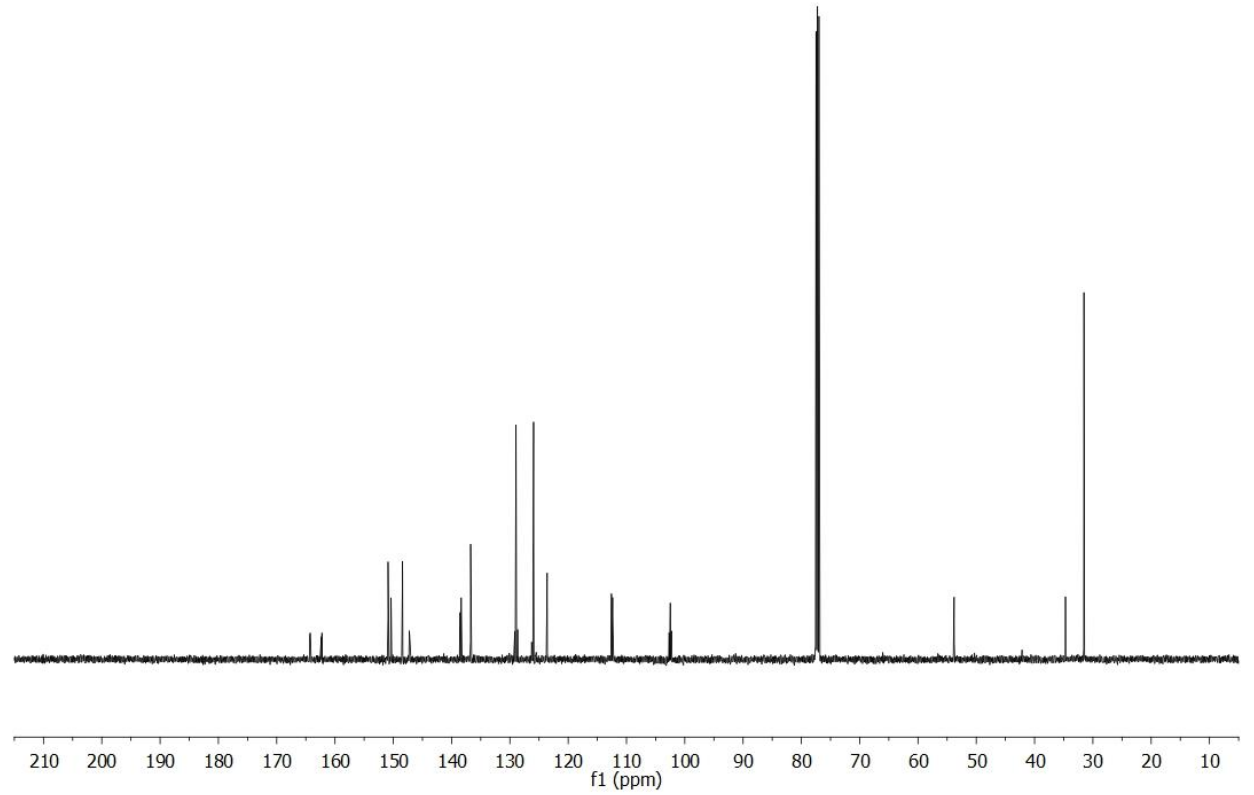




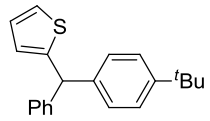


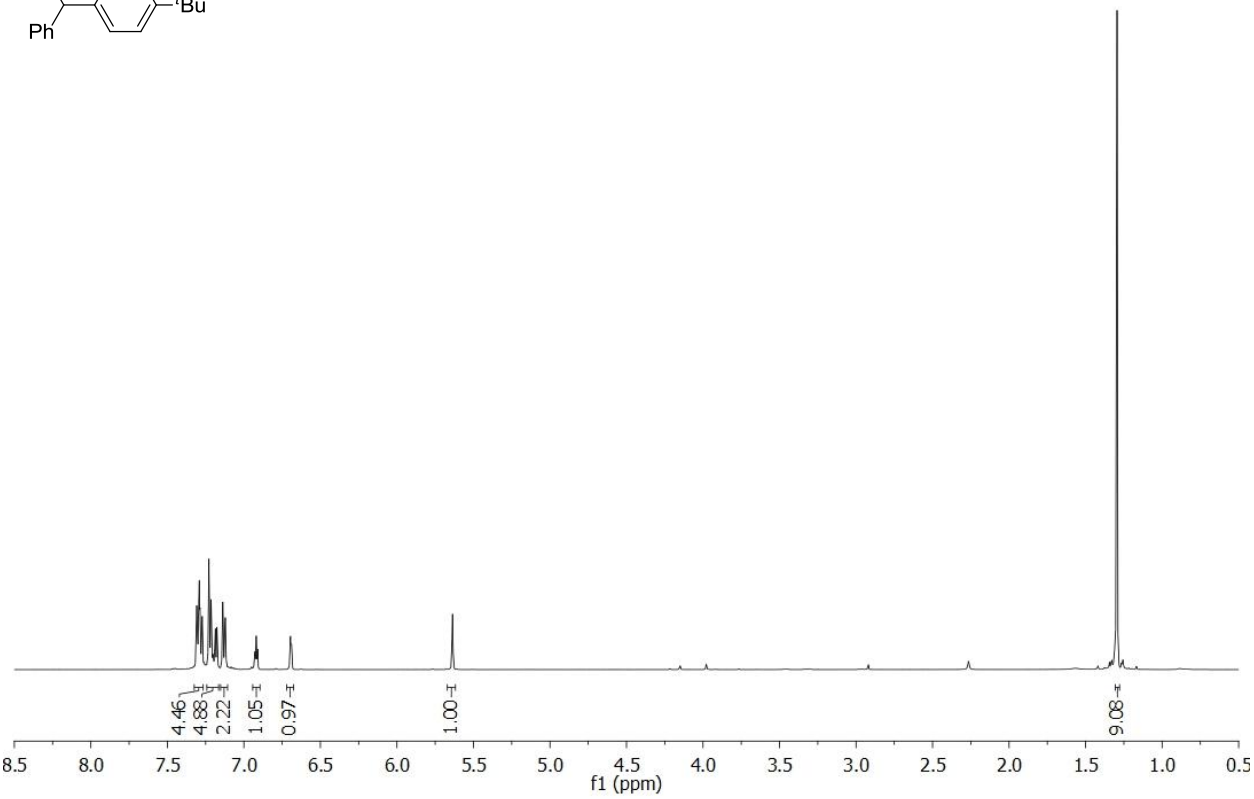
3pa – (4-*tert*-butylphenyl)(3-pyridyl)(3,5-difluorophenyl)methane

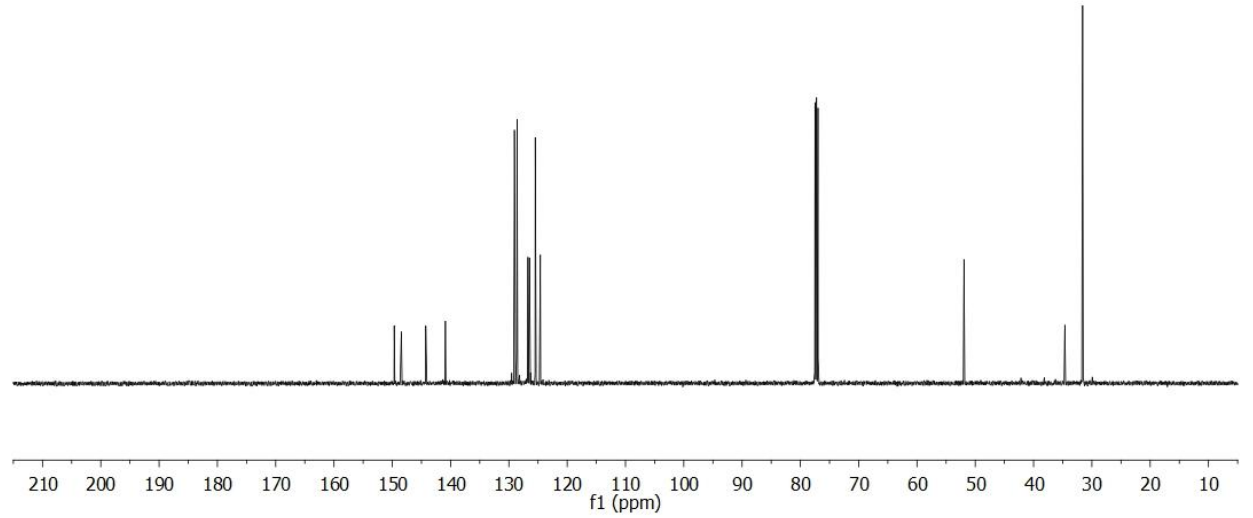




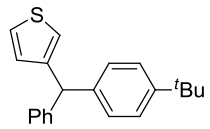
3qa – (4-*tert*-butylphenyl)(2-furyl)phenylmethane

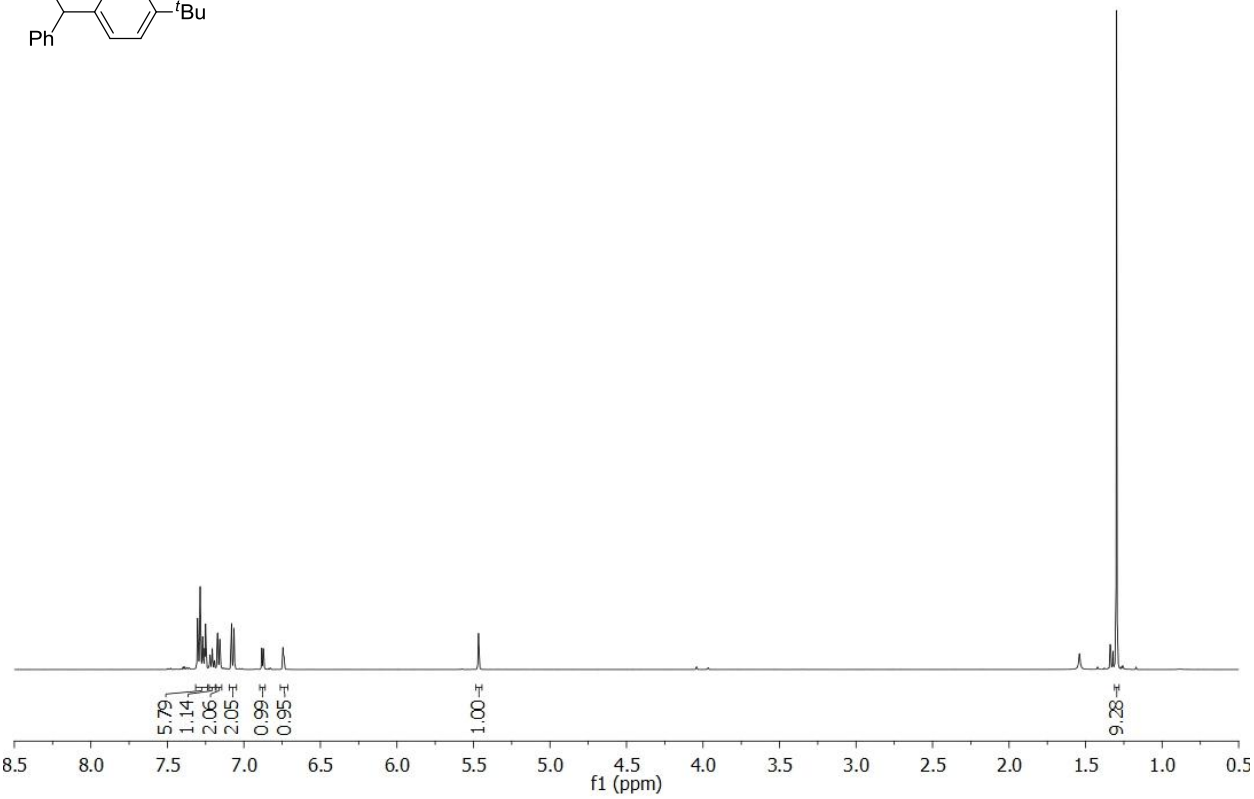


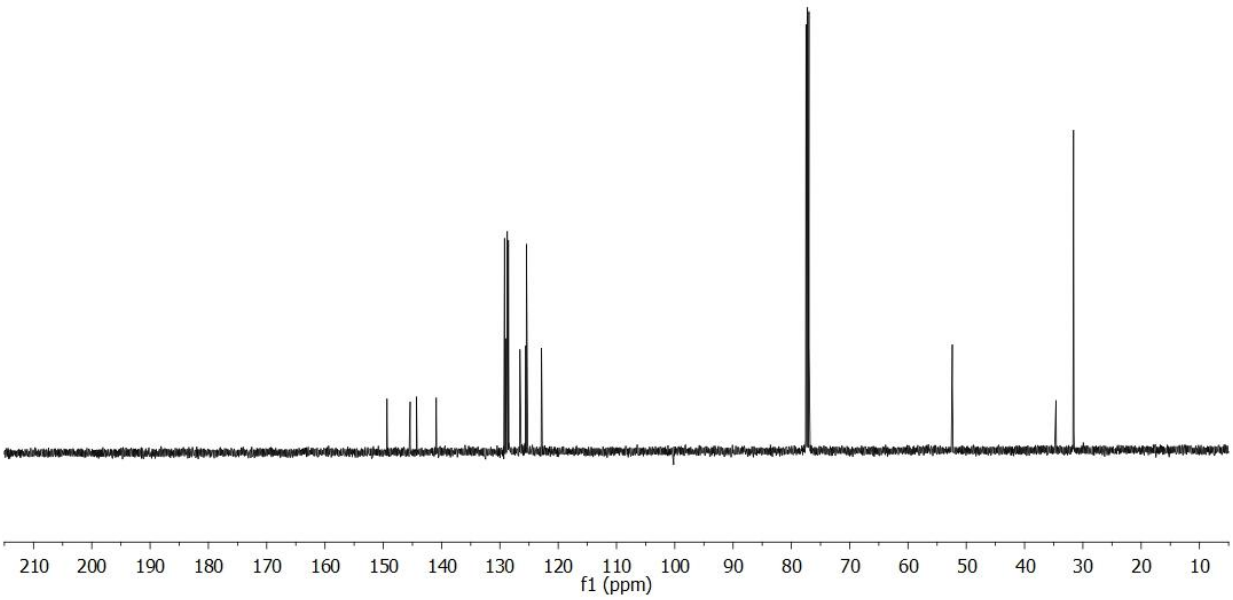




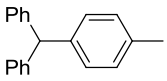
3ra – (4-*tert*-butylphenyl)(3-furyl)phenylmethane

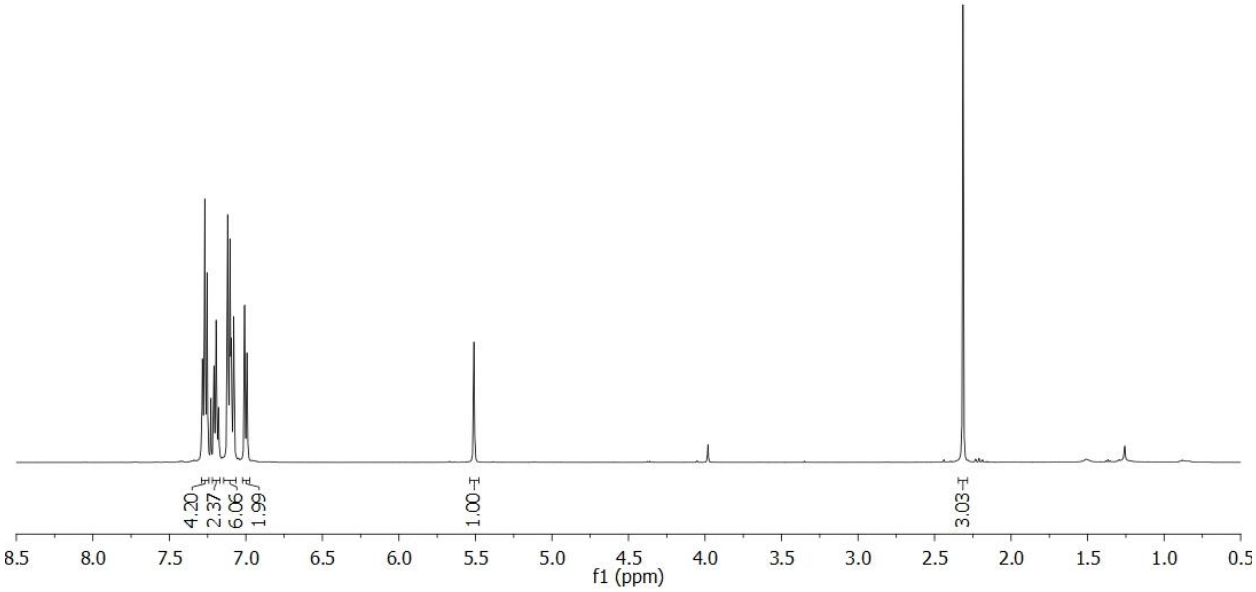


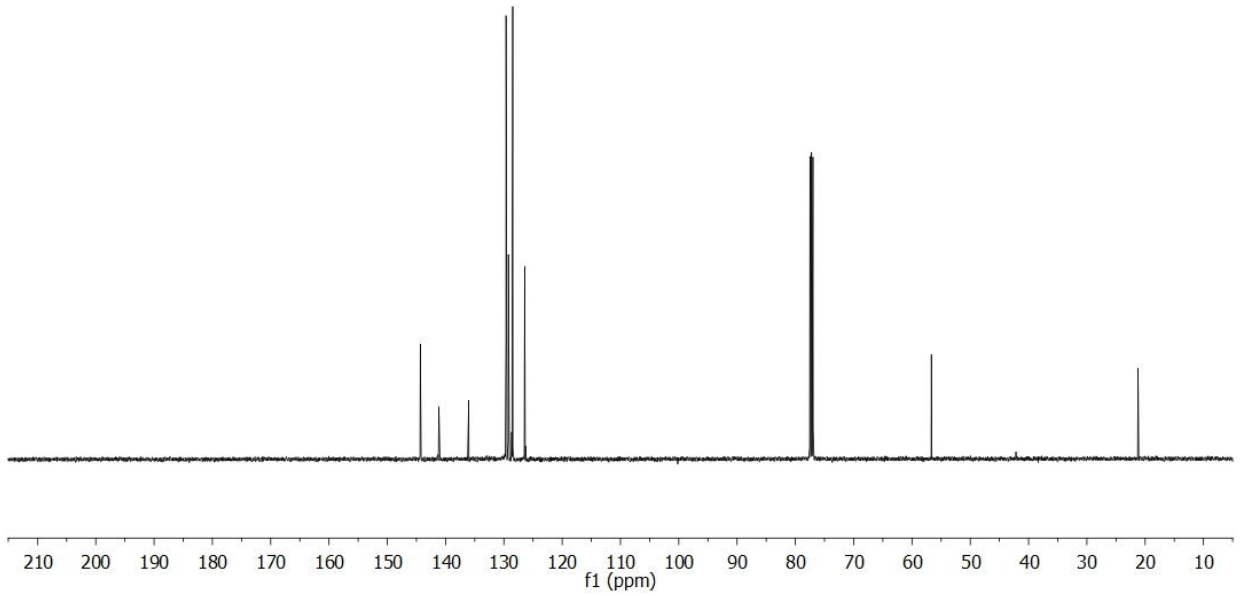




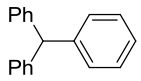
3ab – (4-methylphenyl)diphenylmethane

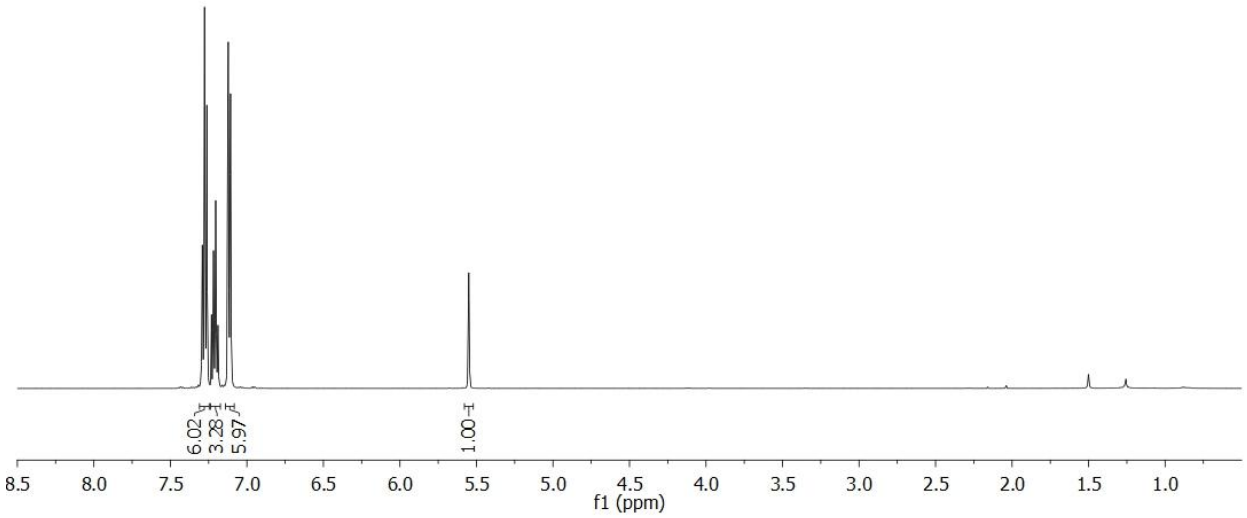


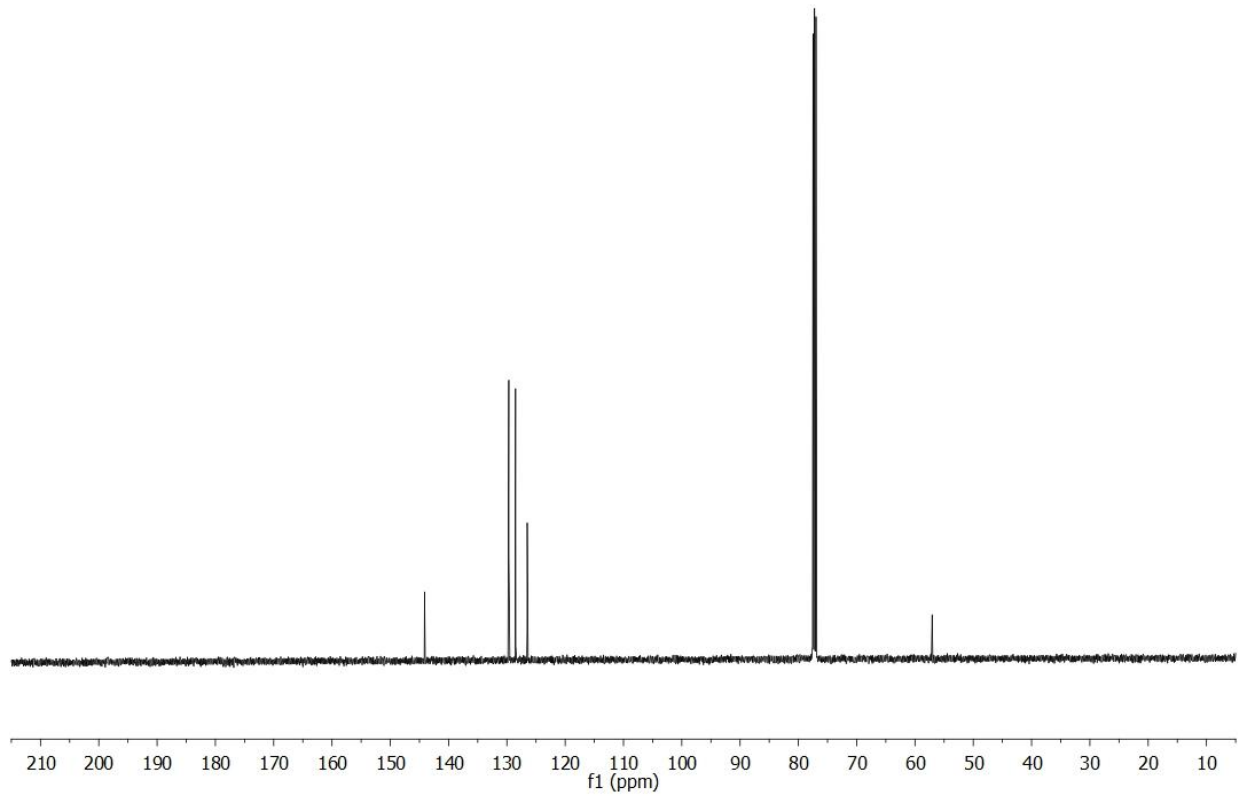




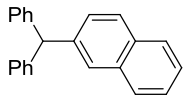
3ac – triphenylmethane

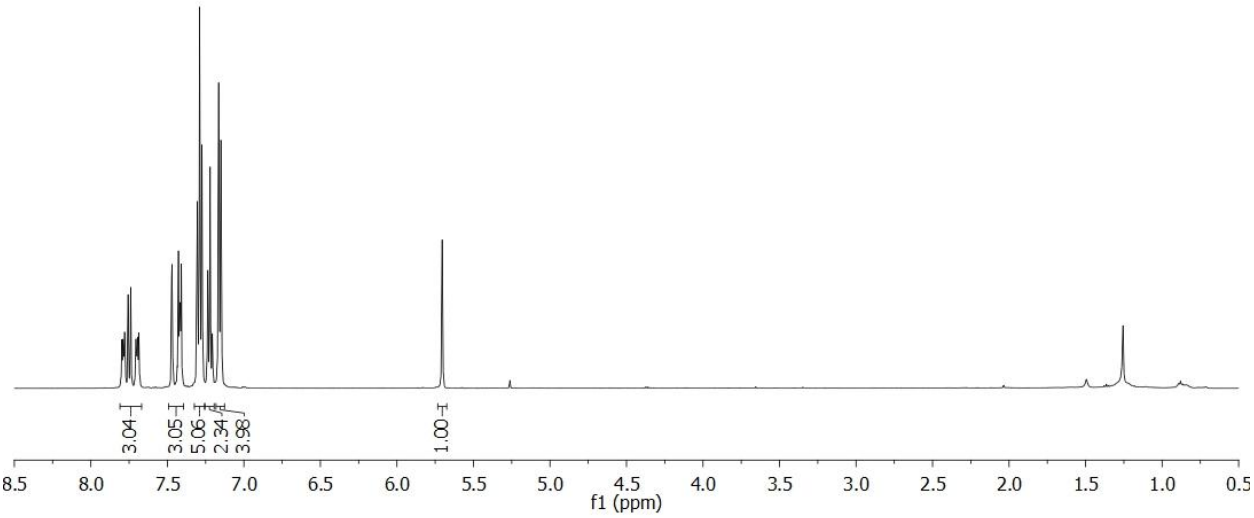


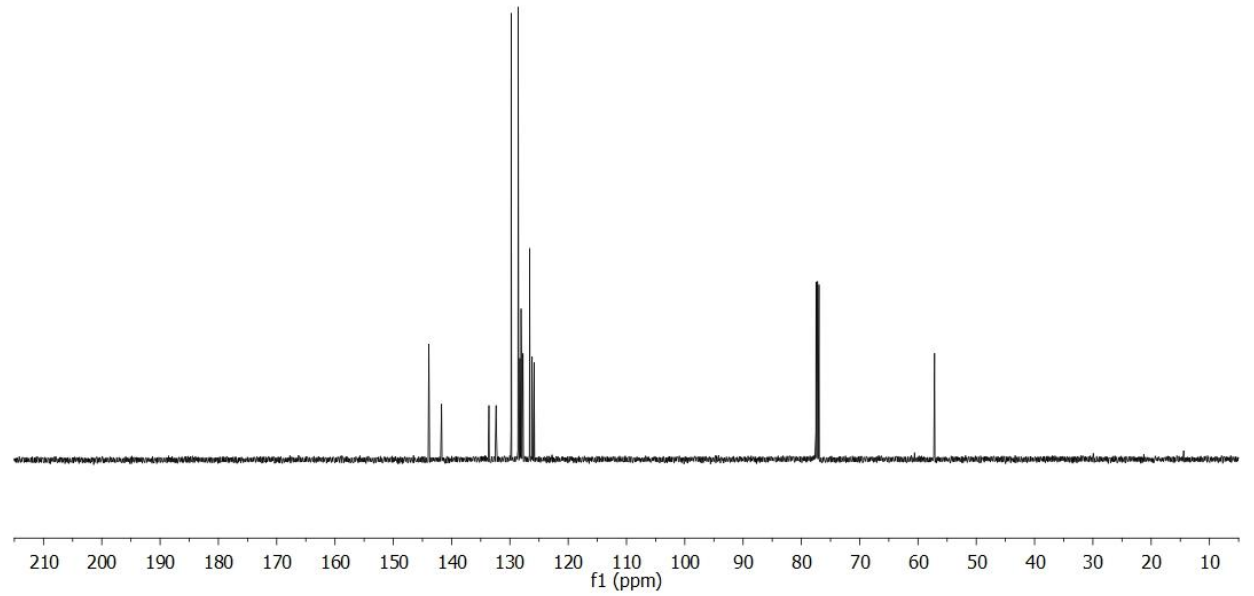




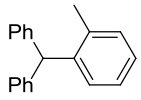
3ad – (2-naphthyl)diphenylmethane

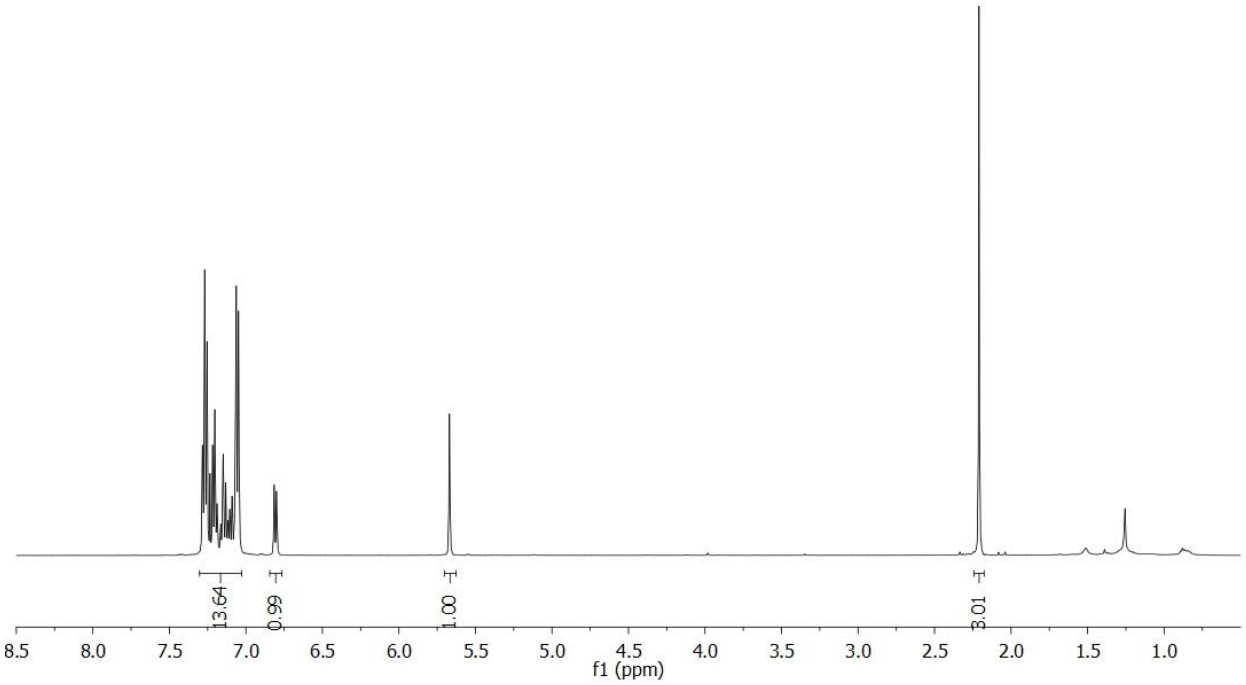


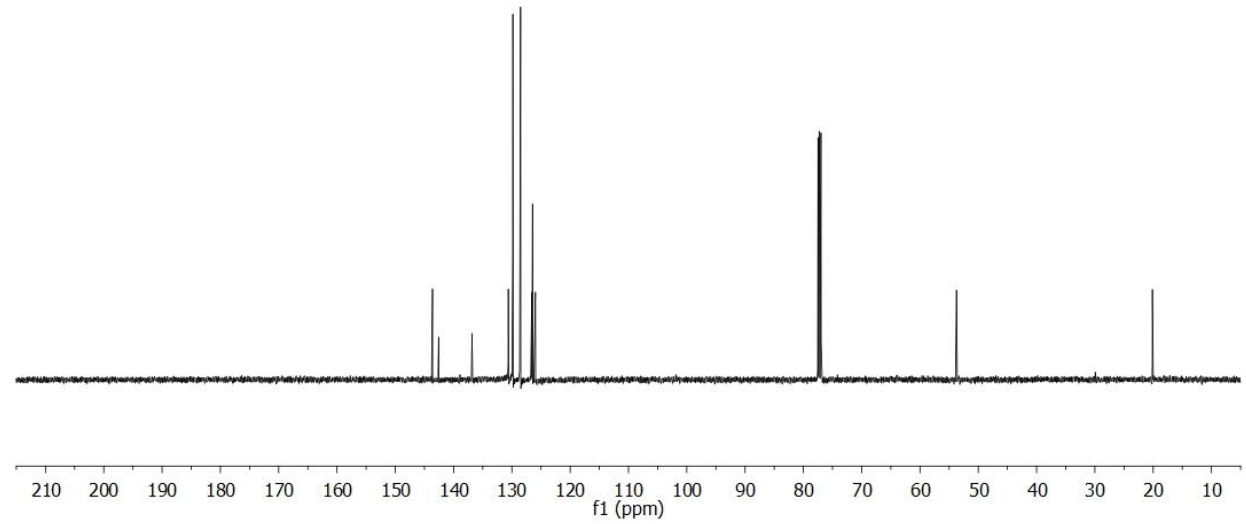




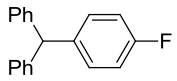
3ae – (2-methylphenyl)diphenylmethane

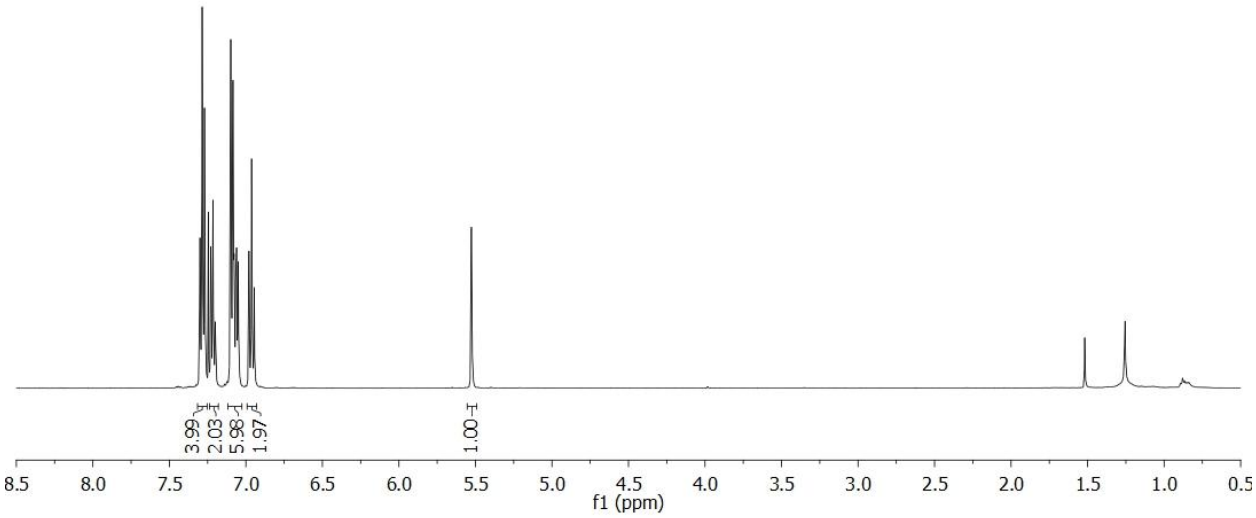


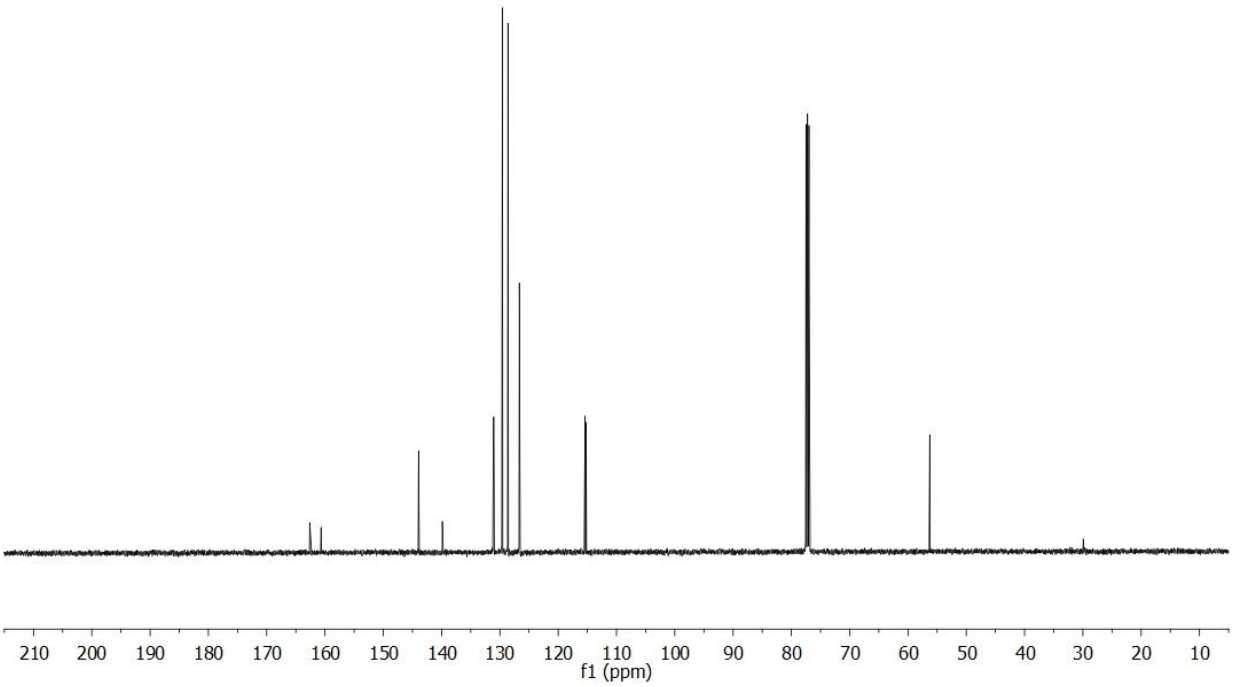




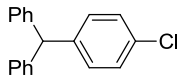
3af – (4-fluorophenyl)diphenylmethane

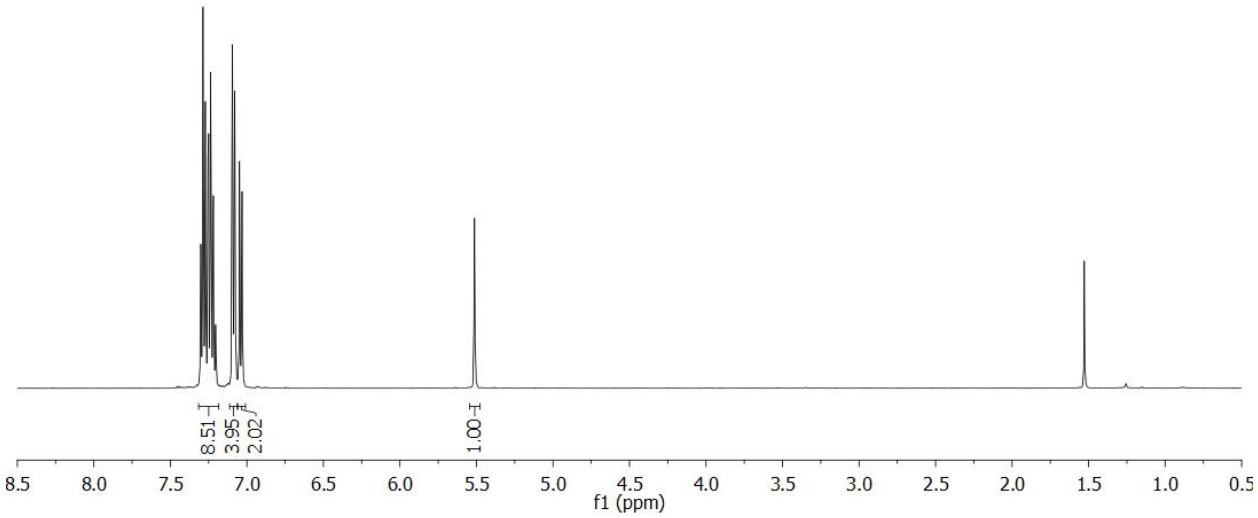


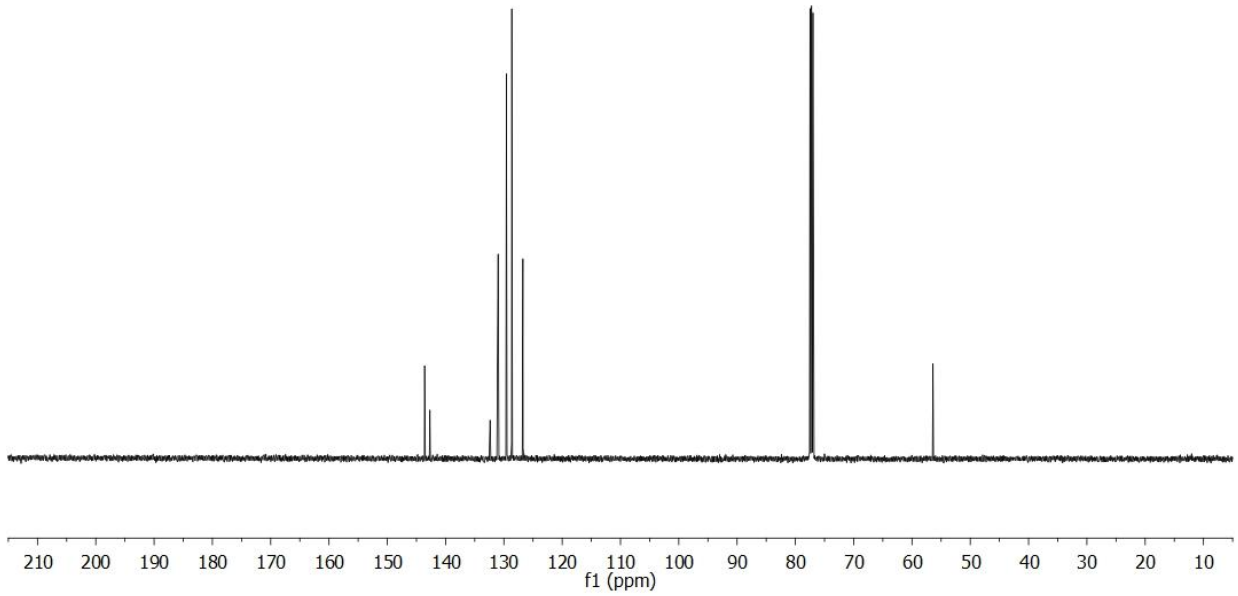




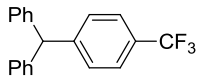
3ag – (4-chlorophenyl)diphenylmethane

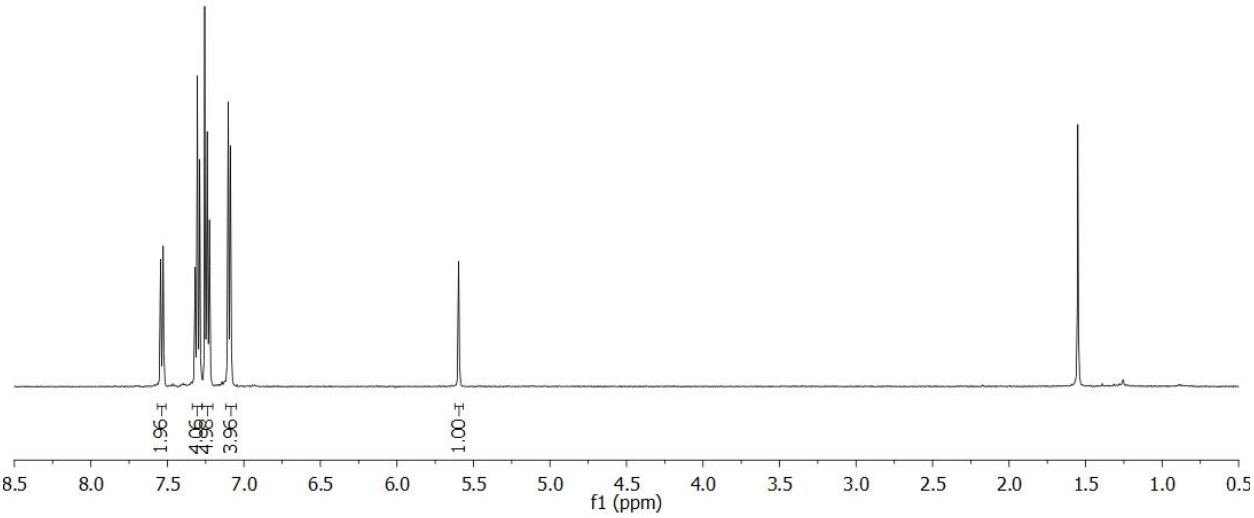


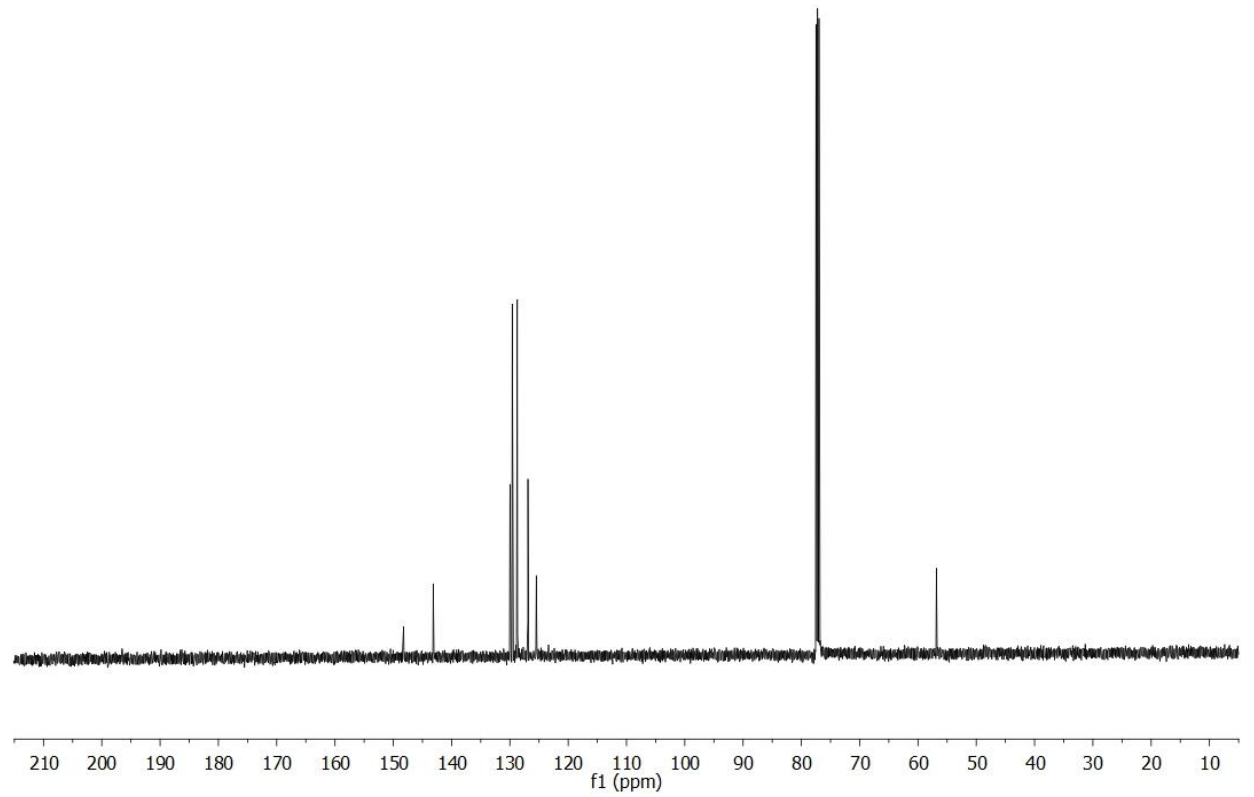




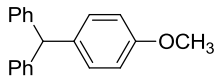
3ah – (4-trifluoromethylphenyl)diphenylmethane

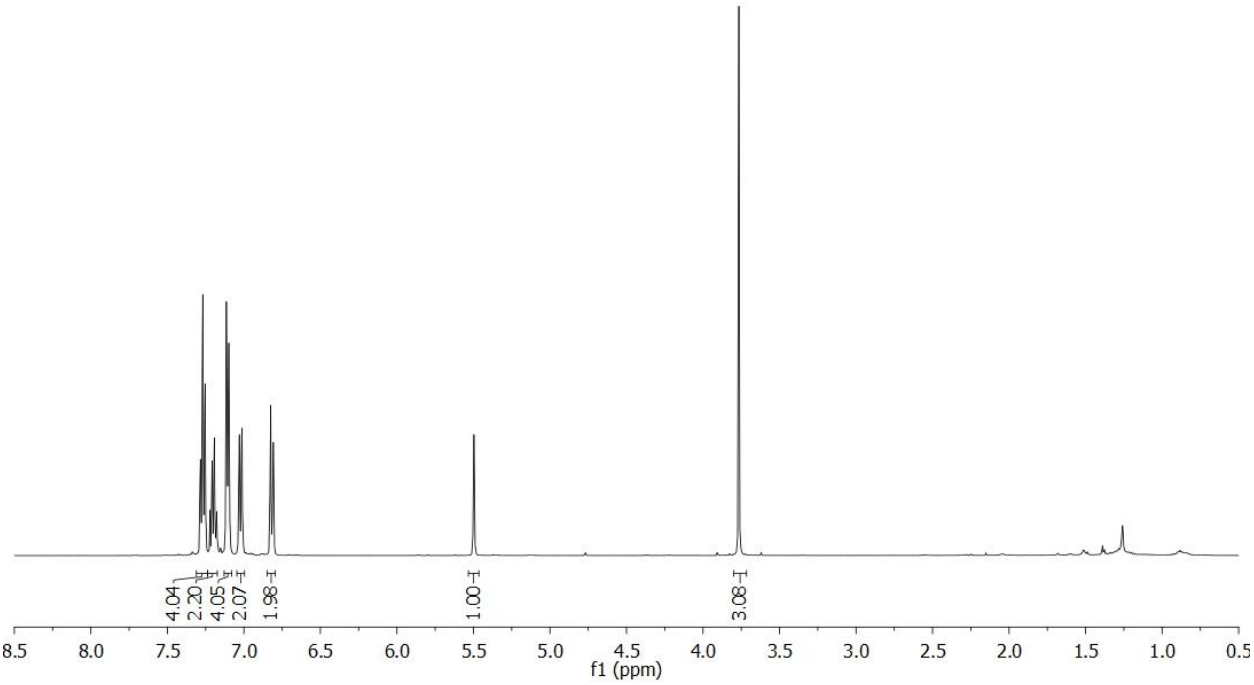


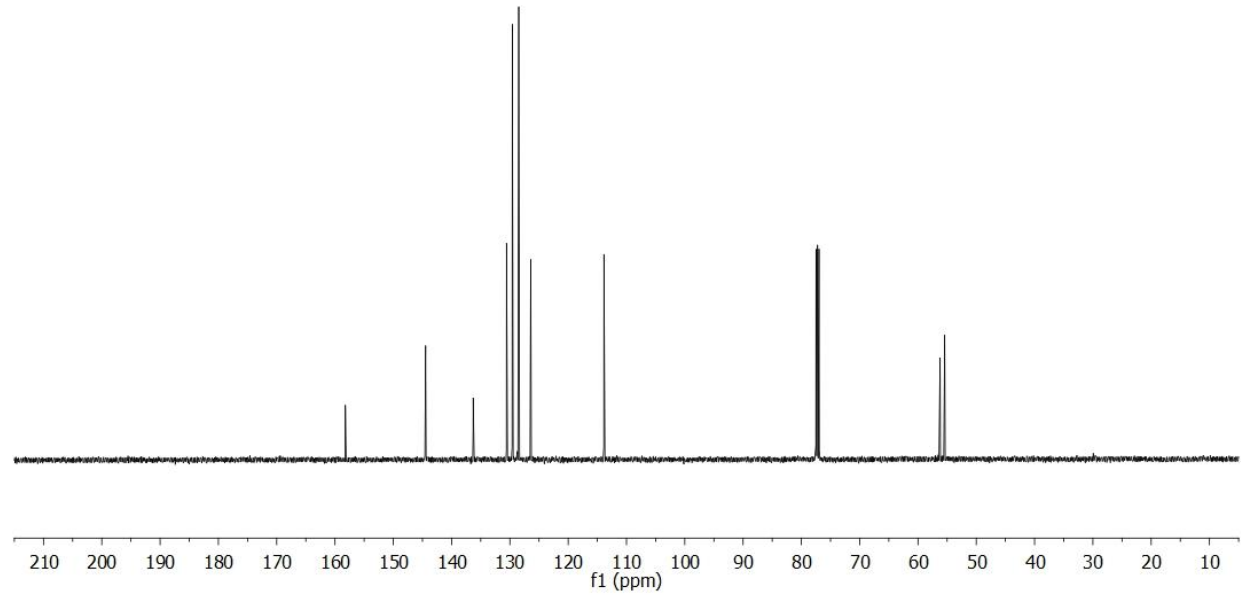




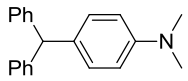
3ai – (4-methoxyphenyl)diphenylmethane

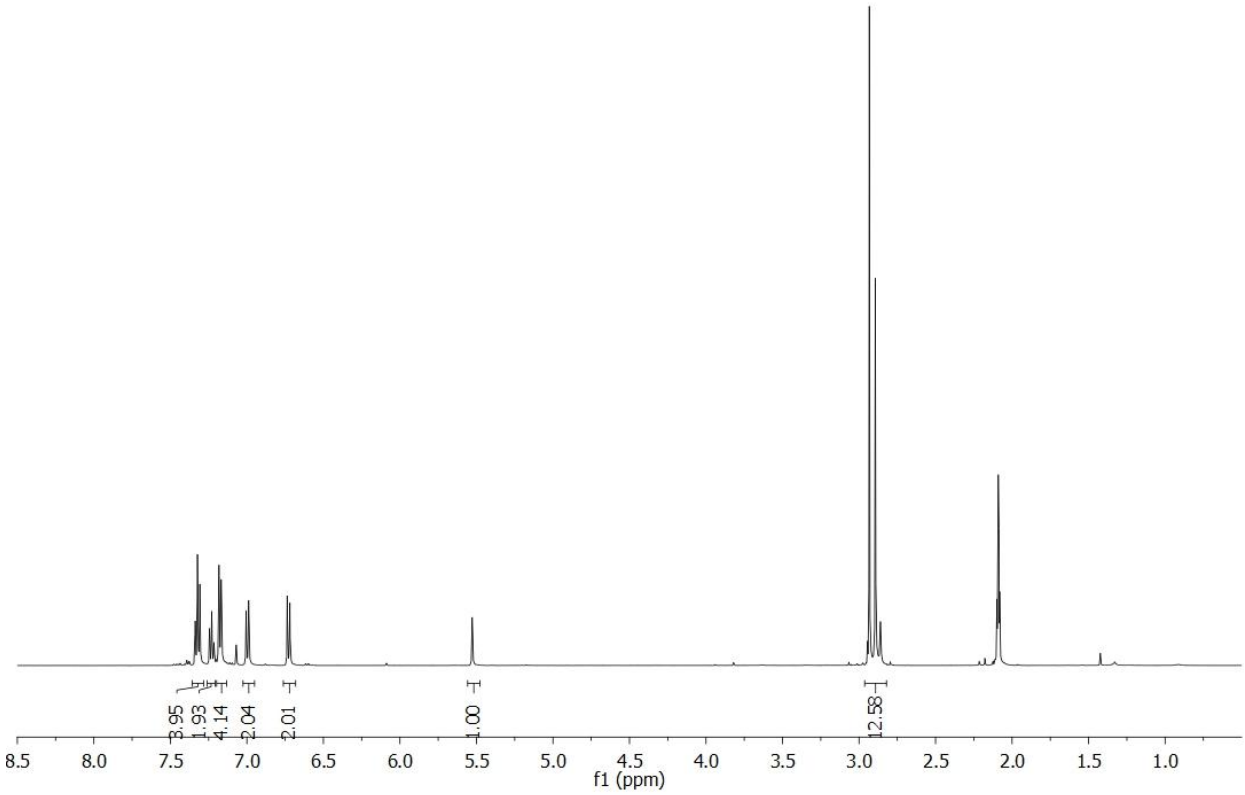


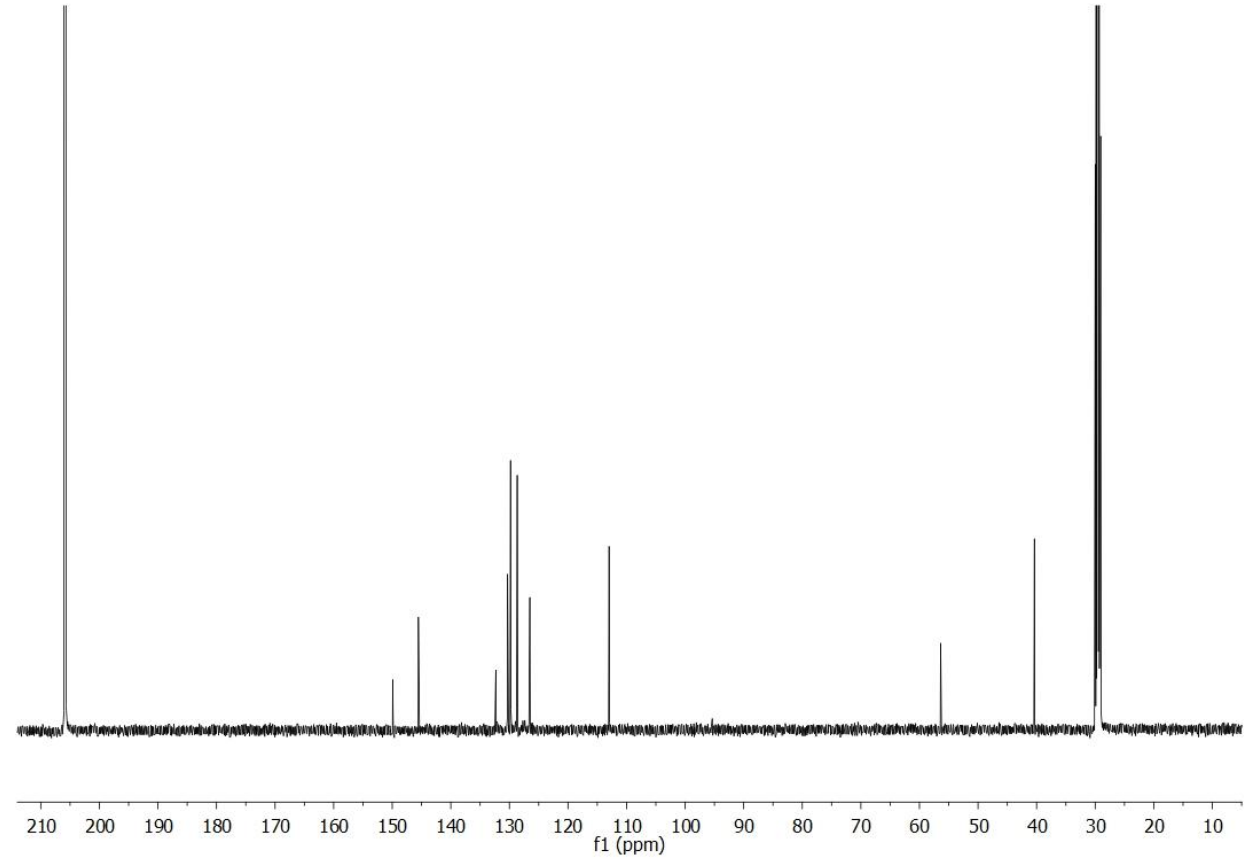




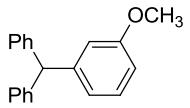
3aj – (*N*,*N*-dimethylaminophenyl)diphenylmethane

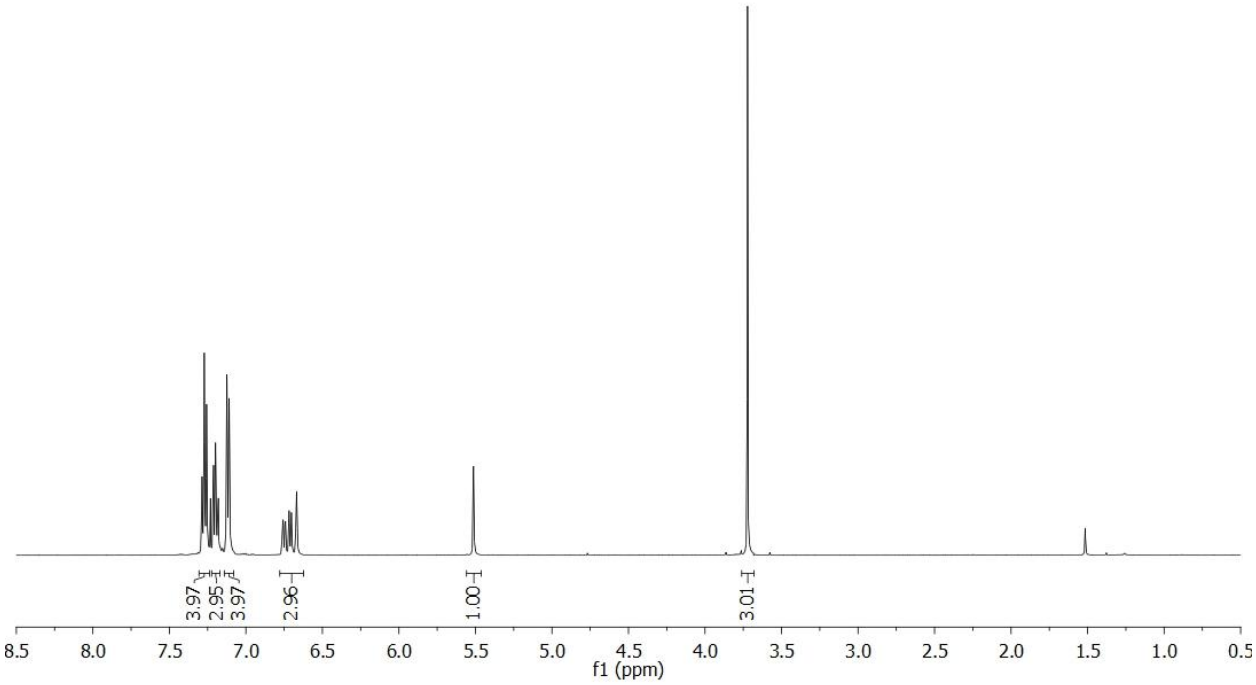


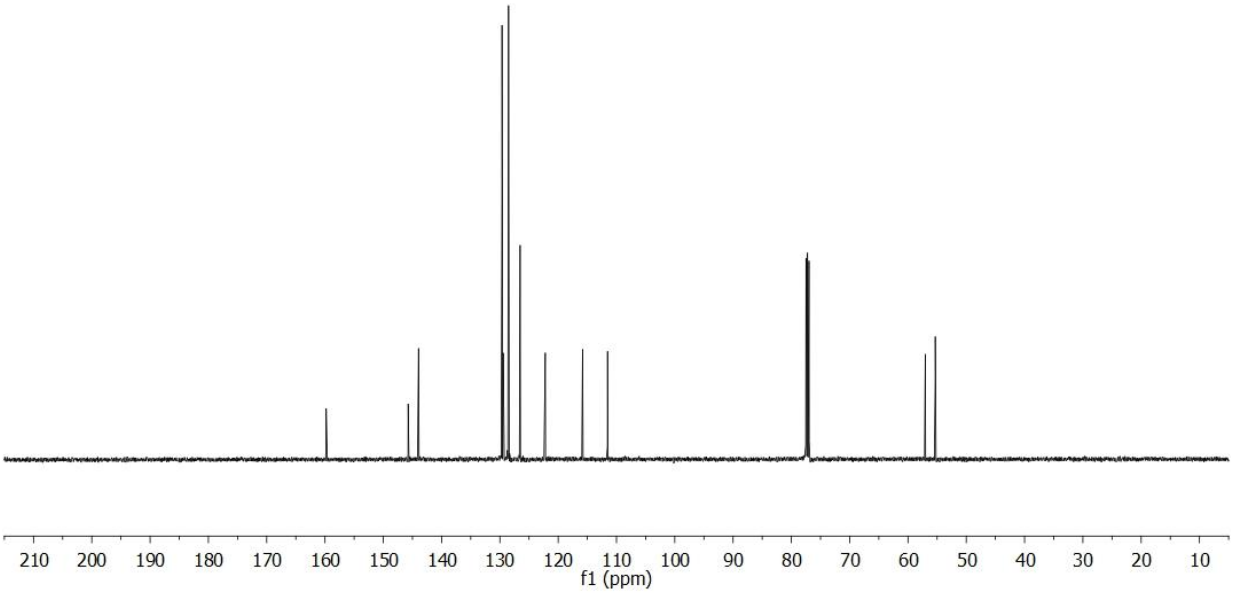




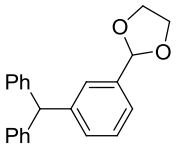
3ak – (3-methoxyphenyl)diphenylmethane

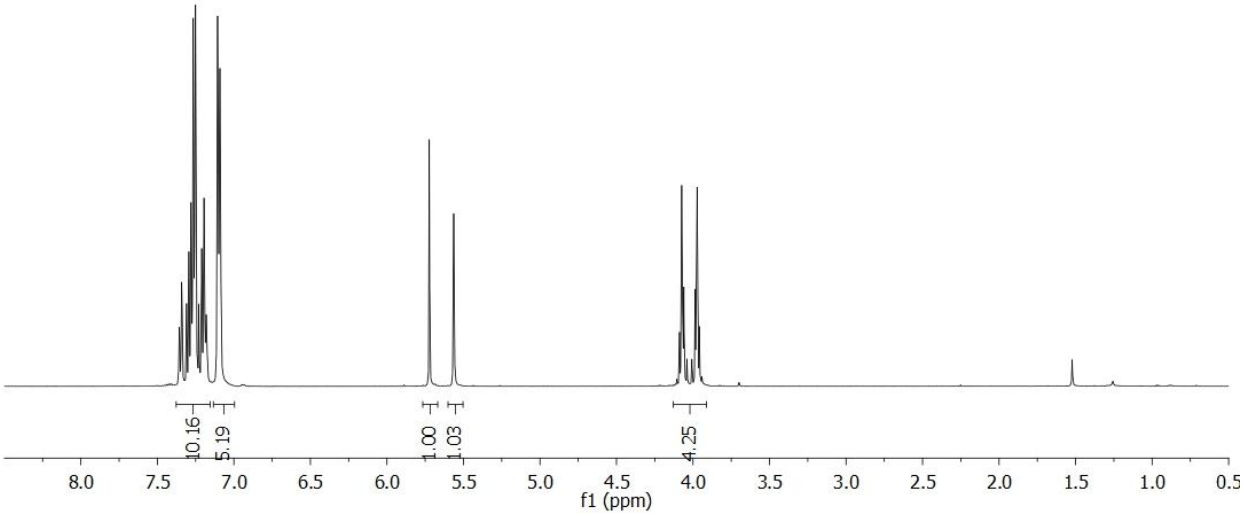


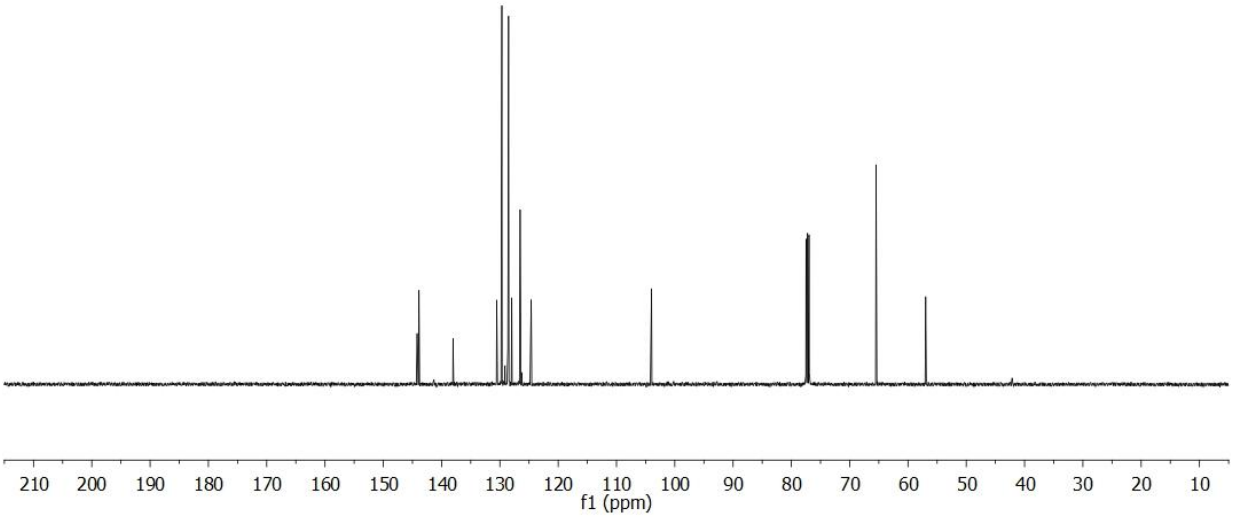




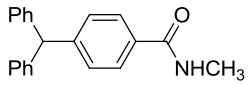
3al – 2-(3-benzhydrylphenyl)-1,3-dioxolane

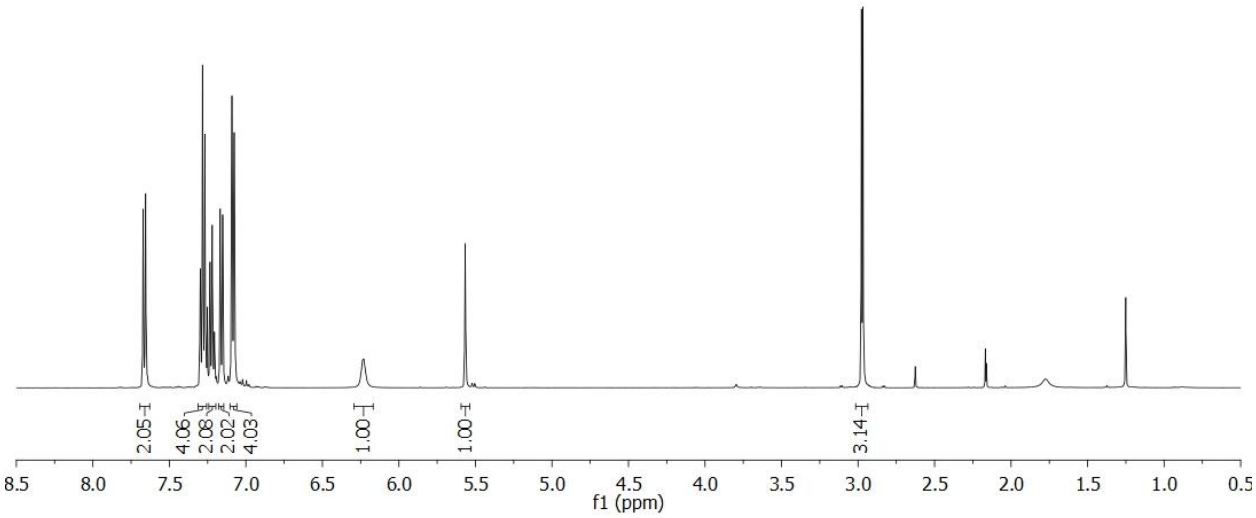


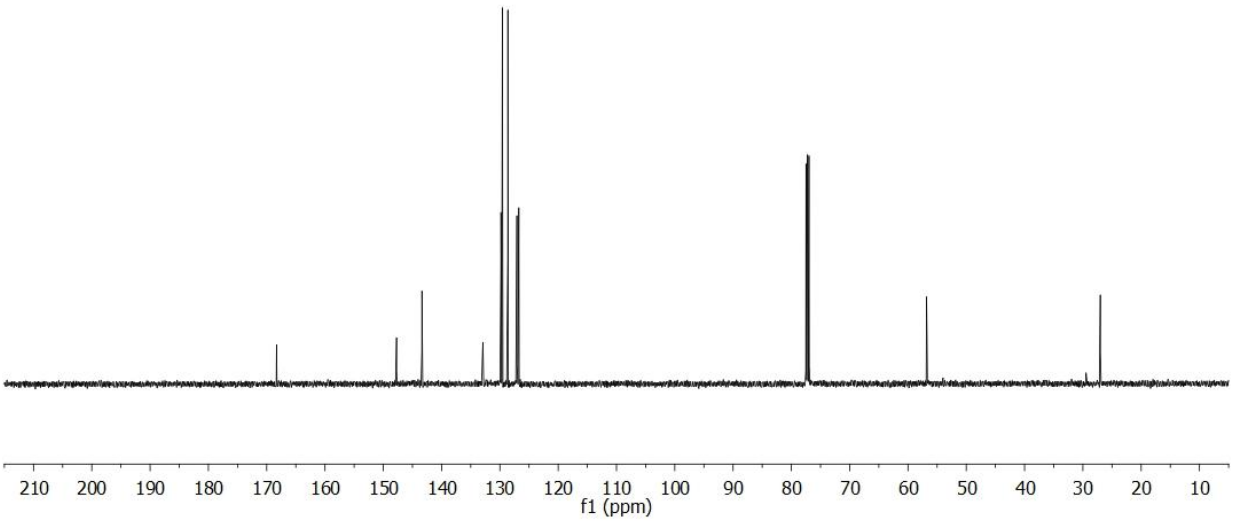




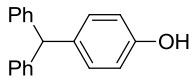
3am – 4-(diphenylmethyl)-*N*-methylbenzamide

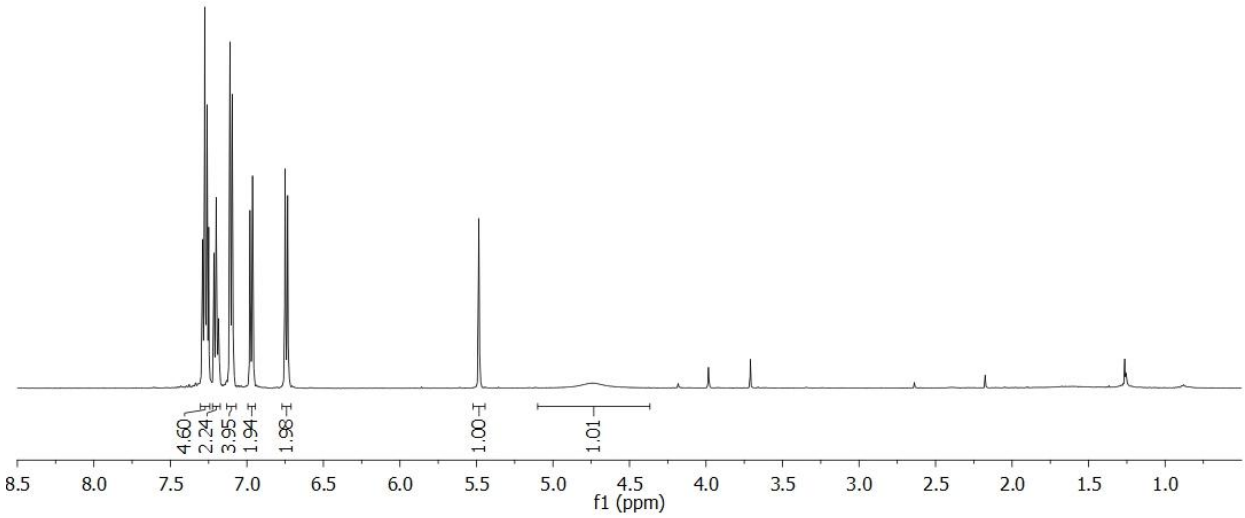


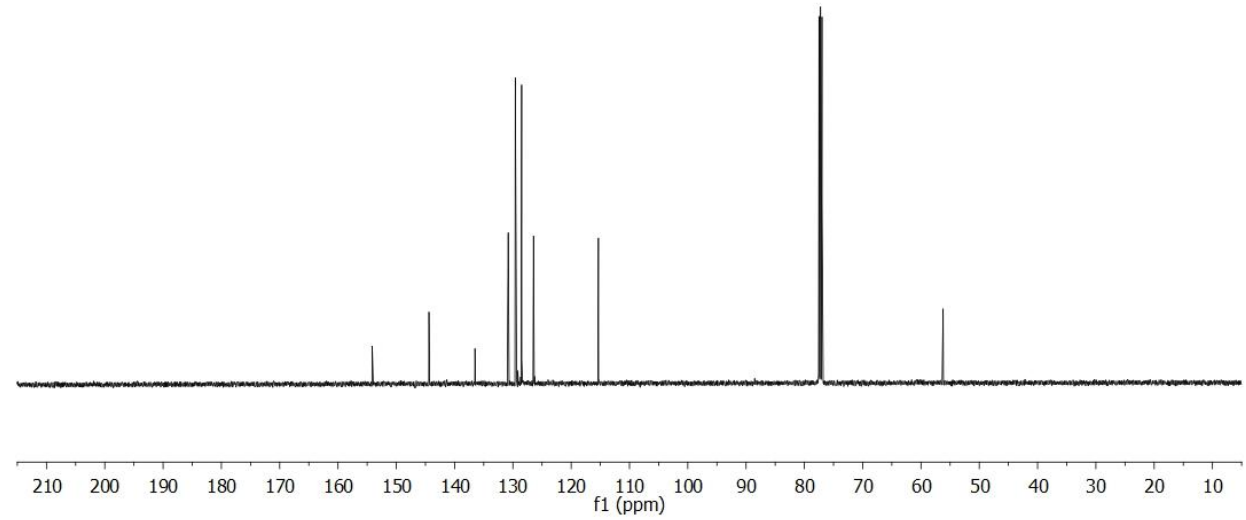




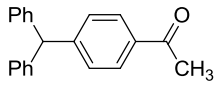
3an – (4-hydroxyphenyl)diphenylmethane

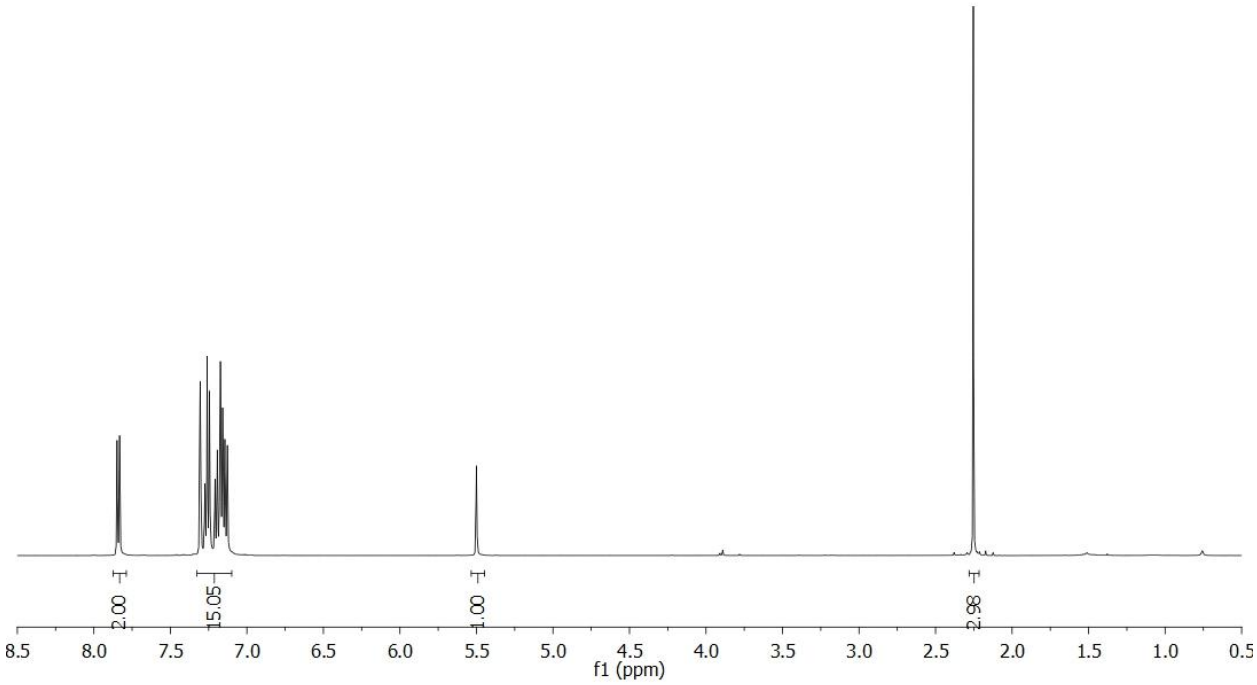


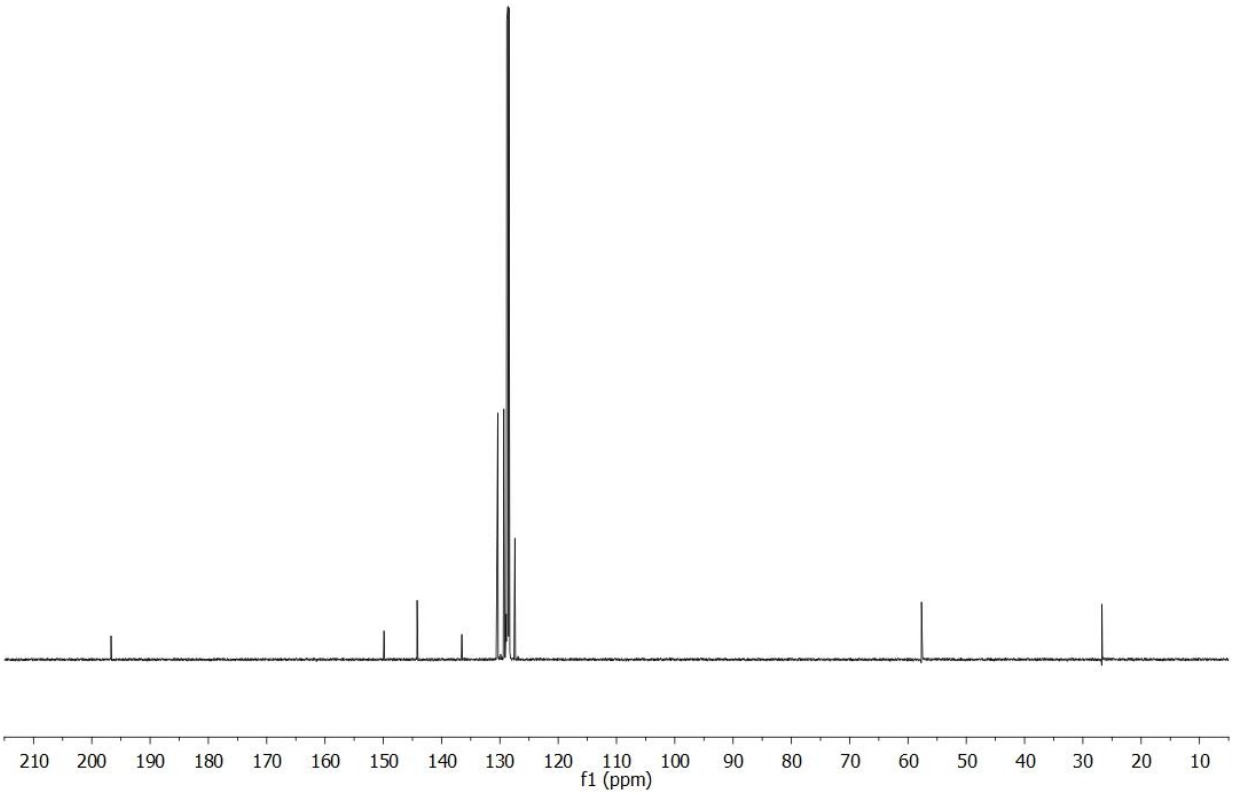




3ao – (4-acetylphenyl)diphenylmethane







3ap – 5-(diphenylmethyl)-1*H*-indole