Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Smaller, faster, better: Modular synthesis of unsymmetrical am-monium salt-tagged NHC-gold(I) complexes and their application as recyclable catalysts in water

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Supporting Information

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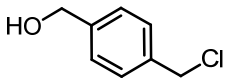
General Methods. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Dry CH_2Cl_2 and MeCN were taken from the Solvent Purification System MB SPS 800 from MBraun. Dry MeOH was purchased from Acros Organics. 1M Triethylammonium acetate buffer solution was acquired from Merck Millipore. All other solvents were used at technical grade. NHC-AuCl complexes were synthesized using $Au(SMe_2)Cl$ from Sigma Aldrich. IR spectra were recorded on a FT-IR spectrometer. As internal standard for ^1H and ^{13}C NMR the signal of the corresponding non-deuterated solvent was used. Melting points were obtained without correction. Column chromatography was performed with silica 60 (40-63 μm) from Macherey-Nagel.

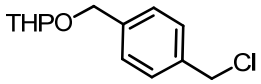
1. Synthesis of Ammonium Salt-tagged NHC-Gold Complexes

(4-(Chloromethyl)phenyl)methanol (6)



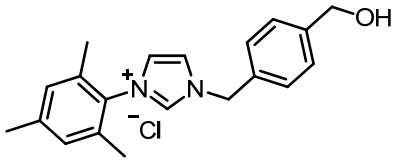
Methyl 4-(chloromethyl)benzoate **5** (5 g, 27.08 mmol) was dissolved in CH_2Cl_2 (160 mL) under an Ar atmosphere and cooled down to -78 °C. Then, DIBAL-H (89.37 mL, 1 M in hexane) was added dropwise and the solution was warmed up to 0 °C. The reaction mixture was carefully quenched, and the white precipitate was dissolved by adding conc. HCl. The phases were separated, and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic phases were washed with brine, dried with $MgSO_4$ and filtered. The solvent was evaporated to give **6** as white solid (4.08 g, 26.05 mmol, 96%). MP: 59.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (m, 4H), 4.67 (s, 2H), 4.60 (s, 2H), 2.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 136.9, 128.9, 127.4, 64.9, 46.1. Known compound.[1]

2-((4-(Chloromethyl)benzyl)oxy)tetrahydro-2*H*-pyran (3):



Compound **6** (4.08 g, 26.05 mmol) was dissolved in dry CH_2Cl_2 (130 mL) under an Ar atmosphere. Then PPTS (327 mg, 1.30 mmol) and DHP (3.53 mL, 39.08 mmol) were added. The mixture was stirred overnight at room temp., then aqueous $NaHCO_3$ was added, and the phases were separated. The aqueous phase was extracted several times with CH_2Cl_2. The combined organic phases were washed with brine, and dried with $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by column chromatography (SiO_2;EtOAc/cyclohexane, 1:6) to give **3** (3.93 g, 16.33 mmol, 63%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (s, 4H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.72 (t, *J* = 3.5 Hz, 1H), 4.60 (s, 2H), 4.52 (d, *J* = 12.4 Hz, 1H), 3.93 (ddd, *J* = 11.2, 8.1, 3.5 Hz, 1H), 3.53-3.60 (m, 1H), 1.52-1.96 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 136.8, 128.7, 128.2, 97.9, 68.4, 62.2, 46.2, 30.6, 25.5, 19.4. Known compound.[2]

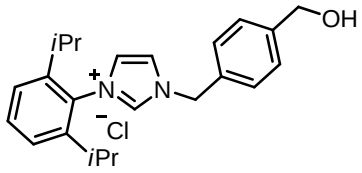
3-(4-(Hydroxymethyl)benzyl)-1-mesityl-1*H*-imidazol-3-ium chloride (7a):



Compound **3** (2 g, 8.31 mmol) was dissolved in MeCN (30 mL) and mesityl imidazole **2a** (1.55 g, 8.31 mmol) was added. The solution was stirred under reflux overnight. Then HCl (10 mL, 12.5 mmol, 1.25 M solution in EtOH) was added and the solution was stirred for 15 min. After the reaction mixture cooled down to room temperature, the solvent was evaporated and the residue was dissolved in CH_2Cl_2 (5 mL). Et_2O was added; the precipitate was filtrated and washed with Et_2O. The solid was dried under high vacuo to give **7a** (2.22 g, 6.47 mmol, 78%) as light grey powder. MP = 134.5 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.85 (s, 1H, CH), 8.12 (t, *J* = 1.8 Hz, 1H), 7.96 (t, *J* = 1.6 Hz, 1H), 7.42 (m, 4H), 7.15 (s, 2H), 5.55 (s, 2H), 5.36 (t, *J* = 5.7 Hz, 1H), 4.51 (d, *J* = 5.5 Hz, 2H), 2.33 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 143.4, 140.2, 137.6, 134.2, 133.1, 131.1, 129.3, 128.0, 127.0, 124.2, 123.1, 62.4, 52.1, 20.6, 16.9; IR (neat) υ = 3245, 2987, 1560, 1545, 1492, 1465, 1448, 1371, 1199, 1157 cm^{-1}; HRMS calcd for $C_{20}H_{23}ON_2$ $[M]^+$: 307.1805, found: 307.1808.

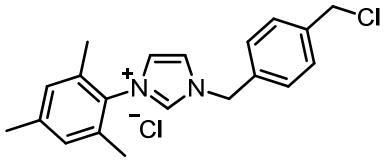
[1] Redwan, I. N.; Grøtli, M. *J. Org. Chem.* **2012**, *77*, 7071–7075.
[2] Drescher, S.; Sonnenberger, S.; Meister, A.; Blume, A.; Dobner, B. *Monatshefte für Chemie* **2012** , *143*, 1533–1543.

1-(2,6-Diisopropylphenyl)-3-(4-(hydroxymethyl)benzyl)-1*H*-imidazol-3-ium chloride (7b):



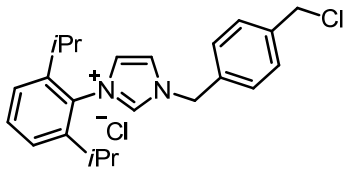
Compound **7b** was synthesized according to the procedure of **7a**. **3** (1 g, 4.15 mmol) was dissolved in MeCN (15 mL) and 2,6-diisopropylphenyl imidazole **2b** (948 mg, 4.15 mmol) was added to give **7b** (1.21 g, 3.14 mmol, 76%) as light brown powder; MP: 127.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.05 (s, 1H), 8.21 (t, J = 1.6 Hz, 1H), 8.12 (t, J = 1.6 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.35-7.49 (m, 6H), 5.59 (s, 2H), 4.51 (s, 2H), 2.20 (spt, J =6.6 Hz, 2H), 1.12 (d, J = 6.6 Hz, 12H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 145.0, 143.4, 138.0, 133.1, 131.4, 130.5, 127.8, 126.9, 125.3, 124.4, 123.4, 62.3, 52.1, 28.1, 23.8, 23.5; IR (neat) υ = 3268, 2961, 2925, 2868, 1560, 1543, 1455, 1366 cm^{-1}; HRMS calcd for $C_{23}H_{29}ON_2$ [M]$^+$: 349.2274, found: 349.2279.

3-(4-(Chloromethyl)benzyl)-1-mesityl-1*H*-imidazol-3-ium chloride (8a):



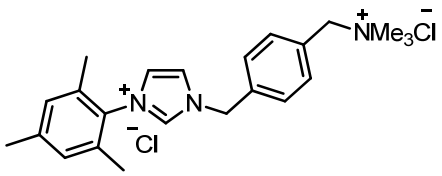
Compound **7a** (2.11 g, 6.15 mmol) was dissolved in $CHCl_3$ (60 mL) and pyridine (25 µL, 0.31 mmol) thionyl chloride (1.11 mL, 15.3 mmol) were added. The solution was stirred at rt for 30 min. Aqueous $NaHCO_3$ was added and the phases were separated. The aqueous phase was extracted with $CHCl_3$ and the combined organic phases were washed with aqueous NaCl, dried with $MgSO_4$ and filtrated. The solvent was evaporated in vacuo. Then CH_2Cl_2 (10 mL) was added, followed by Et_2O. The resulting precipitate was filtrated, washed with Et_2O and dried in vacuo to give **8a** (2.14 g, 5.92 mmol, 96%) as a yellow solid. MP: 93.7 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.83 (s, 1H), 7.84 (s, 1H), 7.64 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.11 (s, 1H), 6.95 (s, 2H), 5.95 (s, 2H), 4.54 (s, 2H), 2.30 (s, 3H), 2.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.3, 138.7, 138.6, 134.2, 134.1, 130.8, 129.9, 129.7, 129.6, 123.3, 122.9, 52.9, 45.6, 21.2, 17.7; IR (neat) υ = 3375, 2949, 1608, 1560, 1545, 1516, 1485, 1444, 1370 cm^{-1}; HRMS calcd for $C_{20}H_{22}N_2Cl$ [M]$^+$: 325.1466, found: 325.1468.

3-(4-(Chloromethyl)benzyl)-1-(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium chloride (8b):



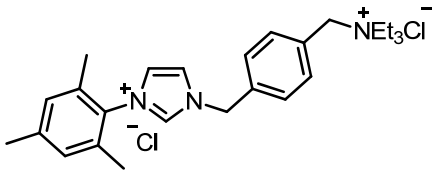
Compound **8b** synthesized according to the procedure of **8a**. **7b** (1.14 g, 2.97 mmol) was dissolved in $CHCl_3$ (30 mL), then pyridine (12 µL, 0.15 mmol) and thionyl chloride (538 µL, 7.42 mmol) were added to give **8b** (1.08 g, 2.68 mmol, 90%) as yellow powder. MP: 89.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.80 (s, 1H), 8.07 (s, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 7.9 Hz, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 7.9 Hz, 2H), 7.11 (s, 1H), 6.00 (s, 2H), 4.53 (s, 2H), 2.19 (spt, J = 6.8 Hz, 2H), 1.15 (d, J = 6.9 Hz, 6H), 1.08 (d, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4, 138.8, 138.6, 134.4, 131.9, 130.4, 129.7, 129.5, 124.7, 124.2, 123.3, 52.8, 45.7, 28.8, 24.5, 24.0; IR (neat) υ = 2962, 2927, 2870, 1544, 1455, 1367 cm^{-1}; HRMS calculated $C_{23}H_{28}N_2Cl$ [M]$^+$: 367.1936, found: 367.1932.

3-(4-((Trimethylammonium)methyl)benzyl)-1-mesityl-1*H*-imidazol-3-ium chloride (9aa):



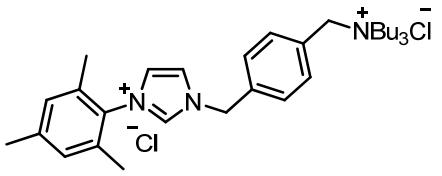
8a (200 mg, 0.554 mmol) was dissolved in dry MeOH (5 mL) und Ar atmosphere and Me_3N (2.51 mL, 10.517 mmol, 33 w% in EtOH) was added. After stirring under reflux overnight, the excess of Me_3N was removed in vacuo. The residue was dissolved in MeOH (3 mL) and Et_2O was added to precipitate the product. The solid was filtrated, washed with Et_2O and dried in vacuo to give **9aa** (80 mg, 0.190 mmol, 69%) as white powder. ^{1}H NMR (300MHz, CD_3OD) δ 9.42 (s, 1H), 7.97 (d, J = 1.8 Hz, 1H), 7.80 (d, J = 1.8 Hz, 1H), 7.69 (dd, J = 8.4, 19.4 Hz, 4H), 7.14 (s, 2H), 5.69 (s, 2H), 4.62 (s, 2H), 3.15 (s, 9H), 2.37 (s, 3H), 2.08 (s, 6H); ^{13}C NMR (75MHz, CD_3OD) δ 179.8, 142.8, 138.2, 135.9, 135.3, 132.6, 130.9, 130.6, 130.5, 126.1, 124.9, 69.8, 54.0, 53.4, 21.3, 17.5. HRMS calcd for $C_{23}H_{31}N_3$ $[M]^{2+}$: 174.6254; found: 174.6257.

3-(4-((Triethylammonium)methyl)benzyl)-1-mesityl-1*H*-imidazol-3-ium chloride (9ab):



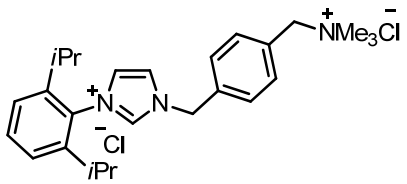
Compound **9ab** was synthesized according to the procedure of **9aa**. **8a** (400 mg, 1.107 mmol) was dissolved in MeOH (15 mL) and Et_3N (2.92 mL, 21.035 mmol) was added to give **9ab** (390 mg, 0.8432 mmol, 76%) as brownish powder. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.27 (s, 1H), 8.03 (s, 1H), 7.66 (dd, J = 17.2, 8.1 Hz, 4H), 7.15 (s, 2H), 5.74 (s, 2H), 4.59 (s, 2H), 3.21 (q, J = 7.0 Hz, 6H), 2.32 (s, 3H), 2.02 (s, 6H), 1.30 (t, J = 7.0 Hz, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 140.2, 138.1, 136.9, 134.2, 133.2, 131.1, 129.3, 128.8, 128.5, 124.2, 123.2, 59.1, 52.1, 51.4, 20.6, 17.0, 7.6; HRMS calcd for $C_{26}H_{37}N_3$ $[M]^+$: 391.2982; found: 391.2981.

3-(4-((Tributylammonium)methyl)benzyl)-1-mesityl-1*H*-imidazol-3-ium chloride (9ac):



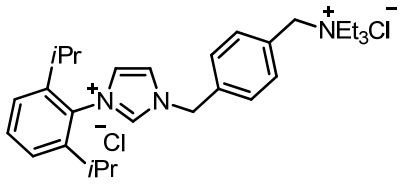
Compound **9ac** was synthesized according to the procedure of **9aa**. **8a** (400 mg, 1.107 mmol) was dissolved in MeOH (15 mL) and Bu_3N (5 mL, 21.035 mmol) was added to give **9ac** (400 mg, 0.7317 mmol, 66%) as brownish powder. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.29 (s, 1H), 8.03 (s, 1H), 7.67 (m, 4H), 7.15 (s, 2H), 5.75 (s, 2H), 4.65 (s, 2H), 3.12-3.17 (m, 6H), 2.32 (s, 4H), 2.02 (s, 6H), 1.71 (br. s., 6H), 1.29 (sxt, J = 7.0 Hz, 6H), 0.93 (t, J = 7.3 Hz, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 140.2, 138.1, 137.1, 134.1, 133.2, 131.1, 129.3, 128.9, 128.6, 124.1, 123.3, 60.9, 57.6, 51.4, 23.3, 20.6, 19.2, 16.9, 13.5; HRMS calcd for $C_{32}H_{49}N_3$ $[M]^+$: 475.3921; found: 475.3931.

3-(4-((Trimethylammonium)methyl)benzyl)-1-(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium chloride (9ba):



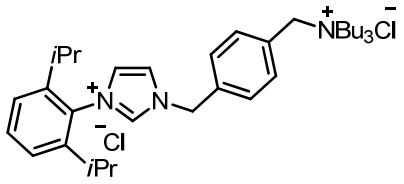
Compound **9ba** was synthesized according to the procedure of **9aa**. **8b** (200 mg, 0.496 mmol) was dissolved in MeOH (5 mL) and Me_3N (1.69 mL, 9.42 mmol, 33wt% in EtOH) was added to give **9ba** (198 mg, 0.428 mmol, 86%) as brownish powder. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.30 (s, 1H), 8.16 (s, 1H), 7.73-7.60 (m, 5H), 7.46 (d, J = 7.6 Hz, 2H), 5.74 (s, 2H), 4.71 (s, 2H), 3.09 (s, 9H), 2.23 (spt, J = 6.6 Hz, 2H), 1.13 (t, J = 7.6 Hz, 12H); ^{13}C NMR (125MHz, DMSO-d_6) δ 144.9, 138.3, 136.9, 133.5, 131.4, 130.5, 129.1, 128.6, 125.2, 124.4, 123.6, 66.8, 51.7, 51.6, 28.1, 23.8, 23.5; HRMS calcd for $C_{26}H_{37}N_3$ $[M]^+$: 195.6488; found: 195.6494.

3-(4-((Triethylammonium)methyl)benzyl)-1-(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium chloride (9bb):



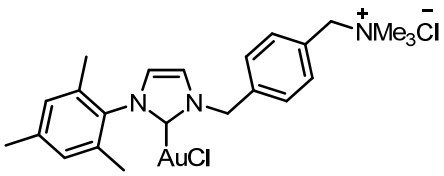
9bb was synthesized according to the procedure of **9aa**. **8b** (400 mg, 0.992 mmol) was dissolved in MeOH (15 mL) and Et_3N (2.61 mL, 18.840 mmol) was added to give **9bb** (350 mg, 0.6936 mmol, 70%) as brownish powder. ^{1}H NMR (500 MHz, DMSO- d_6) δ 10.34 (s, 1H), 8.37 (t, J = 1.5 Hz, 1H), 8.15 (t, J = 1.5 Hz, 1H), 7.66 (dd, J = 19.9, 8.0 Hz, 4H), 7.63 (dd, J = 15.3, 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 2H), 5.77 (s, 2H), 4.59 (s, 2H), 3.21 (q, J = 7.1 Hz, 6H), 2.20 (spt, J = 6.8 Hz, 2H), 1.30 (t, J = 7.1 Hz, 9H), 1.12 (t, J = 7.3 Hz, 12H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 144.9, 138.3, 137.0, 133.2, 131.4, 130.5, 128.8, 128.5, 125.2, 124.4, 123.5, 59.2, 52.1, 51.5, 28.1, 23.8, 23.5, 7.6; HRMS calcd for $C_{29}H_{43}N_3$ $[M]^+$: 433.3452; found: 433.3470.

3-(4-((Tributylammonium)methyl)benzyl)-1-(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium chloride (9bc):



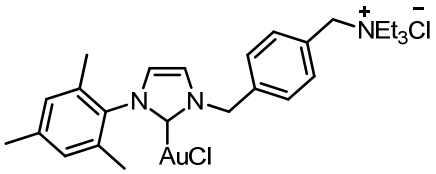
9bc was synthesized according to the procedure of **9aa**. **8b** (400 mg, 0.992 mmol) was dissolved in MeOH (15 mL) and Bu_3N (4.48 mL, 18.840 mmol) was added to give **9bc** (220 mg, 0.3737 mmol, 38%) as brownish powder. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.34 (t, J = 1.5 Hz, 1H), 8.15 (t, J = 1.7 Hz, 1H), 7.64 (m, 5H), 7.46 (d, J = 8.0 Hz, 2H), 5.75 (s, 2H), 4.63 (s, 2H), 3.13 (m, 6H), 2.21 (spt, J = 6.7 Hz, 2H), 1.72 (dt, J = 15.3, 7.3 Hz, 6H), 1.30 (sxt, J = 7.3 Hz, 6H), 1.12 (t, J = 6.9 Hz, 12H), 0.94 (t, J = 7.5 Hz, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 144.9, 138.3, 137.1, 133.2, 131.4, 130.5, 128.7, 128.5, 125.2, 124.4, 123.6, 60.9, 57.6, 51.6, 28.1, 23.8, 23.5, 23.3, 19.2, 13.4; HRMS calcd for $C_{35}H_{55}N_3$ $[M]^{2+}$: 258.7193; found: 258.7199.

(1-(4-((Trimethylammonio)methyl)benzyl)-3-mesityl-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1aa):



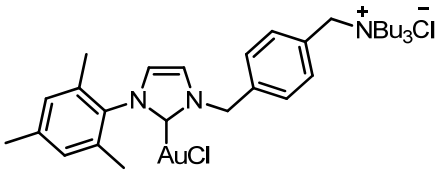
9aa (71 mg, 0.170 mmol) was dissolved in dry MeOH (5 mL) under Ar atmosphere with exclusion from light and KO*t*Bu (19 mg, 0.169 mmol) and Au(SMe_2)Cl (50 mg, 0.169 mmol) were added. The mixture was heated to reflux overnight. After cooling to rt the solution was concentrated and the product was precipitated by dropwise addition of Et_2O. **1aa** (63 mg, 0.102 mmol, 60%) was obtained as an off-white powder. ^{1}H NMR (500MHz, DMSO-d_6) δ 7.88 (d, *J* = 1.1 Hz, 1H), 7.64-7.57 (m, 3H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.08 (s, 2H), 5.57 (s, 2H), 4.63 (s, 2H), 3.07 (s, 9H), 2.31 (s, 3H), 1.98 (s, 6H); ^{13}C NMR (125MHz, DMSO-d_6) δ 170.3, 138.9, 138.9, 134.9, 134.4, 133.2, 129.0, 128.2, 127.4, 123.4, 122.7, 67.0, 53.1, 51.7, 20.6, 17.3; HRMS calcd for $C_{23}H_{30}N_3AuCl$ $[M]^+$: 580.1788; found: 580.1790.

(1-(4-((Triethylammonio)methyl)benzyl)-3-mesityl-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1ab):



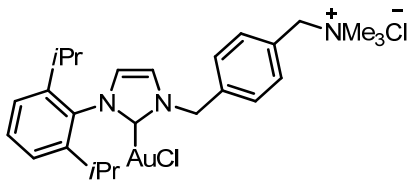
According to the synthesis of **1aa**, **9ab** (79 mg, 0.170 mmol) was dissolved in MeOH (5 mL) and KO*t*Bu (19 mg, 0.169 mmol) and Au(SMe_2)Cl (50 mg, 0.169 mmol) were added. **1ab** (81 mg, 0.123 mmol, 72%) was obtained as an off-white powder. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 3H), 7.54 (d, *J* = 1.9 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 6.92 (s, 2H), 5.55 (s, 2H), 4.84 (s, 2H), 3.39 (q, *J* = 7.1 Hz, 6H), 2.30 (s, 3H), 2.00 (s, 6H), 1.42 (t, *J* = 7.3 Hz, 12H); ^{13}C NMR (125MHz, $CDCl_3$) δ 172.0, 139.7, 138.7, 134.8, 134.7, 133.5, 129.5, 128.4, 127.7, 122.8, 122.2, 61.0, 54.1, 53.2, 21.2, 18.0, 8.6; HRMS calcd for $C_{26}H_{36}N_3AuCl$ $[M]^+$: 622.2258; found: 622.2261.

(1-(4-((Tributylammonio)methyl)benzyl)-3-mesityl-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1ac):



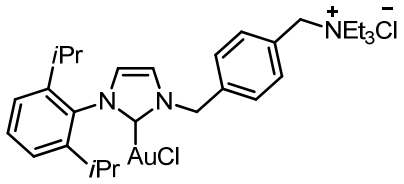
According to the synthesis of **1aa**, **9ac** (93 mg, 0.170 mmol) was dissolved in MeOH (5 mL) and KO*t*Bu (19 mg, 0.169 mmol) and Au(SMe_2)Cl (50 mg, 0.169 mmol) were added. **1ac** (90 mg, 0.121 mmol, 71%) was obtained as an off-white powder. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.66-7.55 (m, 4H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.92 (s, 2H), 5.53 (s, 2H), 4.92 (s, 2H), 3.31-3.22 (m, 6H), 2.29 (s, 3H), 1.98 (s, 6H), 1.80-1.72 (m, 6H), 1.38 (dd, *J* = 7.3, 14.5 Hz, 6H), 0.95 (t, *J* = 7.6 Hz, 12H); ^{13}C NMR (125MHz, $CDCl_3$) δ 172.2, 139.7, 138.9, 134.8, 134.7, 133.4, 129.5, 128.6, 127.9, 122.7, 122.2, 62.8, 58.8, 54.2, 24.6, 21.2, 19.9, 17.9, 13.8; HRMS calcd for $C_{32}H_{48}N_3AuCl$ $[M]^+$: 706.3197; found: 706.3208.

(1-(2,6-Diisopropylphenyl)-3-(4-((trimethylammonio)methyl)benzyl)-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1ba):



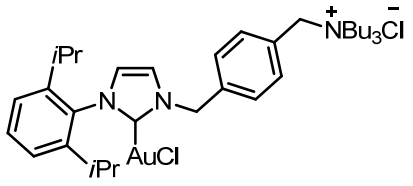
According to the synthesis of **1aa**, **9ba** (112 mg, 0.242 mmol) was dissolved in MeOH (5 mL) and KO*t*Bu (27 mg, 0.241 mmol) and Au(SMe$_2$)Cl (71 mg, 0.241 mmol) were added. **1ba** (120 mg, 0.182 mmol, 75%) was obtained as an off-white powder. ^{1}H NMR (500MHz, DMSO-d$_6$) δ 7.89 (d, *J* = 1.5 Hz, 1H), 7.74 (d, *J* = 1.5 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.56-7.51 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 2H), 5.57 (s, 2H), 4.60 (s, 2H), 3.05 (s, 9H), 2.33 (spt, *J* = 6.8 Hz, 2H), 1.21 (d, *J* = 6.9 Hz, 6H), 1.12 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125MHz, DMSO-d$_6$) δ 171.4, 145.3, 139.0, 134.3, 133.2, 130.3, 128.2, 127.4, 124.6, 123.9, 122.6, 67.2, 53.1, 51.7, 28.0, 23.9, 23.7; HRMS calcd for $C_{26}H_{36}N_3AuCl$ [M+H]$^+$: 622.2258; found: 622.2259.

(1-(2,6-Diisopropylphenyl)-3-(4-((triethylammonio)methyl)benzyl)-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1bb):



According to the synthesis of **1aa**, **9bb** (85 mg, 0.170 mmol) was dissolved in MeOH (5 mL) and KO*t*Bu (19 mg, 0.169 mmol) and Au(SMe$_2$)Cl (50 mg, 0.169 mmol) were added. **1bb** (115 mg, 0.164 mmol, 96%) was obtained as an off-white powder. ^{1}H NMR (500MHz, CDCl$_3$) δ 7.66 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 1.9 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 1.9 Hz, 1H), 5.56 (s, 2H), 4.95 (s, 2H), 3.42 (q, *J* = 7.1 Hz, 6H), 2.38 (spt, *J* = 6.8 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 9H), 1.26 (d, *J* = 6.9 Hz, 6H), 1.13 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (125MHz, CDCl$_3$) δ 173.1, 145.7, 138.8, 134.2, 133.5, 130.7, 128.6, 127.7, 124.3, 123.9, 122.1, 61.1, 54.3, 53.2, 28.5, 24.5, 24.3, 8.6; HRMS calcd for $C_{29}H_{42}N_3AuCl$ [M]$^+$: 664.2727; found: 664.2741.

(1-(2,6-Diisopropylphenyl)-3-(4-((tributylammonio)methyl)benzyl)-2,3-dihydro-1*H*-imidazol-2-yl)gold(I) chloride (1bc):



According to the synthesis of **1aa**, **9bc** (100 mg, 0.170 mmol) was dissolved in MeOH (5 mL) and KO*t*Bu (19 mg, 0.169 mmol) and Au(SMe$_2$)Cl (50 mg, 0.169 mmol) were added. **1bc** (107 mg, 0.136 mmol, 80%) was obtained as an off-white powder. ^{1}H NMR (500MHz, DMSO-d$_6$) δ 7.63-7.56 (m, 3H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 1.5 Hz, 1H), 5.56 (s, 2H), 4.98 (s, 2H), 3.30-3.24 (m, 6H), 2.37 (spt, *J* = 6.8 Hz, 2H), 1.78 (td, *J* = 7.9, 15.2 Hz, 6H), 1.39 (sxt, *J* = 7.3 Hz, 6H), 1.25 (d, *J* = 6.9 Hz, 6H), 1.11 (d, *J* = 6.9 Hz, 6H), 0.97 (t, *J* = 7.5 Hz, 9H); ^{13}C NMR (125MHz, DMSO-d$_6$) δ 171.4, 145.2, 139.2, 134.3, 132.9, 130.3, 127.7, 127.6, 124.5, 123.9, 122.7, 60.9, 57.5, 53.0, 28.0, 23.8, 23.7, 23.2, 19.2, 13.4; HRMS calcd for $C_{35}H_{54}N_3AuCl$ [M]$^+$: 748.3666; found: 748.3684.

2. Gold-catalyzed Cyclization of Carboxylic Acids

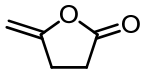
Alkynoic acids

10a was purchased from AlfaAesar. **10b** was synthesized similar to the procedure of **10d**, instead of l-trimethylsilyl-3-bromopropyne, propargyl bromide (80 w% in THF) was used and the residue was distilled to give **10b** at 110 °C, 20 mbar. **10c** and **10d** were obtained following known procedures[3,4]. The methyl ester of **10e** was synthesized according to reference[5] and the ester was cleaved with NaOH according to reference[3].

General procedure for the cycloisomerization of alkynoic acids

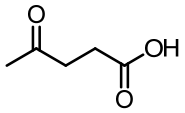
Alkynoic acid **10** (40 mg) was dissolved in 1M $Et_3N{\cdot}HOAc$ buffer solution (2mL) under air. Carboxylic acids which are not soluble in water were dissolved in THF first to give a 0.5 M solution. Then catalyst **1a**/**1b** (2.5 mol%) was added. The reaction was monitored by TLC. After full conversion, the solution was extracted with Et_2O (5x2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography gave γ-alkylidene lactone **11**. The recycling was performed by addition of fresh alkynoic acid to the aqueous phase and repetition of the procedure.

5-Methylenedihydrofuran-2-one (11a):



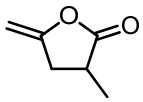
Colorless oil. ^{1}H NMR (500MHz, $CDCl_3$) δ 4.75 (dd, *J* = 2.3, 4.2 Hz, 1H), 4.32 (dd, *J* = 1.9, 4.2 Hz, 1H), 2.93-2.84 (m, 2H), 2.72-2.63 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 175.0, 155.8, 88.9, 28.1, 25.2. Known compound.[6]

4-Oxopentanoic acid (12a):



12a was synthesized according to the general procedure for the cycloisomerization of alkynoic acids. As starting material **11a** was used. Colorless oil. ^{1}H NMR (500MHz, $CDCl_3$) δ 8.89 (br.s, 1H), 2.77-2.73 (m, 2H), 2.63 (t, *J* = 6.5 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 206.7, 178.4, 37.8, 29.9, 27.9. Known compound.[7]

3-Methyl-5-methylenedihydrofuran-2-one (11b):



Colorless oil. ^{1}H NMR (300MHz, $CDCl_3$) δ 4.74 (dd, *J* = 2.6, 4.0 Hz, 1H), 4.34-4.30 (m, 1H), 3.06 (tdd, *J* = 1.5, 9.5, 15.7 Hz, 1H), 2.91-2.76 (m, 1H), 2.52 (tdd, *J* = 2.2, 8.4, 15.8 Hz, 1H), 1.33 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 177.9, 154.3, 89.0, 35.0, 33.8, 16.0. Known compound.[8]

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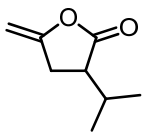
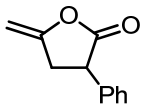
[3] Spencer, R. W.; Tam, T. F.; Thomas, E.; Robison, V. J.; Krantz, A. *J. Am. Chem. Soc*. **1986**, *108*, 5589–5597.
[4] Krafft, G. A.; Katzenellenbogen, J. A., *J. Am. Chem. Soc*. **1981**, *103*, 5459-5466.
[5] Nakamura, I.; Ching, S. C.; Araki, T.; Terada, M.; Yamamoto, Y. *Org. Lett*., **2008**, *10*, 309–312.
[6] Nagendiran, A.; Verho, O.; Haller, C.; Johnston, E. V.; Bäckvall, J.-E. *J. Org. Chem.* **2014**, *79*, 1399–1405.
[7] Alemán, J.; del Solar, V.; Cubo, L.; Quiroga, A. G.; Navarro Ranninger, C. *Dalton Trans.* **2010**, *39*, 10601–10607.
[8] Günther, H. J.; Guntrum, E.; Jäger, V., *Liebigs Ann. Chem.* **1984**, 15–30.

3-Isopropyl-5-methylenedihydrofuran-2-one (11c):



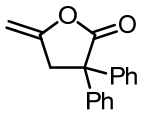
Yellowish oil. ^{1}H NMR (300MHz, $CDCl_3$) δ 4.72-4.66 (m, 1H), 4.31-4.26 (m, 1H), 2.92-2.78 (m, 1H), 2.76-2.60 (m, 2H), 2.19 (dtd, *J* = 4.8, 6.9, 13.7 Hz, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 176.6, 154.9, 88.4, 46.0, 29.1, 27.8, 20.1, 18.2. IR (neat) υ = 2961, 2928, 2874, 1754, 1653, 1366 cm^{-1}; Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63; Found: C, 68.3; H, 8.7.

5-Methylene-3-phenyldihydrofuran-2-one (11d):



Colorless oil. ^{1}H NMR (300MHz, $CDCl_3$) δ 7.44-7.18 (m, 5H), 4.84 (dd, *J* = 2.2, 4.4 Hz, 1H), 4.42 (dd, *J* = 1.8, 4.4 Hz, 1H), 3.98 (dd, *J* = 7.7, 9.9 Hz, 1H), 3.33 (tdd, *J* = 1.8, 10.1, 16.3 Hz, 1H), 3.00 (tdd, *J* = 2.0, 7.7, 16.4 Hz, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 175.1, 154.1, 136.7, 129.1, 128.0, 127.6, 89.2, 46.0, 34.5. Known compound.[3]

5-Methylene-3,3-diphenyldihydrofuran-2-one (11e):



Colorless oil. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.36 (d, *J* = 4.2 Hz, 7H), 7.35-7.29 (m, 3H), 4.82 (dd, *J* = 1.9, 4.6 Hz, 1H), 4.45 (dd, *J* = 1.5, 4.2 Hz, 1H), 3.59 (t, *J* = 1.7 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 175.2, 152.8, 141.0, 128.8, 127.8, 127.5, 89.5, 57.3, 41.8. Known compound.[9]

Table 1. Detailed information for the cyclization reactions of carboxylic acids 10.

Product	R^1	R^2	Catalyst	Time in h[a]	Yield in %[b]
11a	H	H	**1aa**	0.5	69
			1ab	1	89
			1ac	1	85
			1ba	1	77
			1bb	1	78
			1bc	1	77
11b	Me	H	**1aa**	2.5	77
			1ab	2	85
			1ac	2.5	83
			1ba	2.5	67
			1bb	2	71
			1bc	4	65

[9] Rudler, H.; Harris, P.; Parlier, A.; Cantagrel, F.; Denise, B.; Bellassoued, M.; Vaissermann, J. *J. Organomet. Chem.* **2001**, *624*, 186–202.

Product	R^1	R^2	Catalyst	Time in h[a]	Yield in %[b]
11c[c]	iPr	H	**1aa**	0.5	86
			1ab	0.5	94
			1ac	2.5	91
			1ba	1.5	72
			1bb	1	78
			1bc	6	71
11d[c]	Ph	H	**1aa**	4	72
			1ab	4.5	84
			1a[d]	2.5	77
			1ba	4	77
			1bb	4.5	86
			1bc[d]	3	74
11e[c,d]	Ph	Ph	**1aa**	1	81
			1ab	0.5	84
			1ac	1.5	72
			1ba	1	71
			1bb	2	76
			1bc	4	69

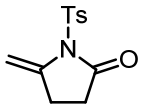
[a] Required time until full conversion was achieved; [b] Isolated yields; [c] 0.5 M carboxylic acid in THF was added; [d] 50°C.

3. Gold-catalyzed Cyclization of Amides

General procedure for the cycloisomerization of alkynoic amides

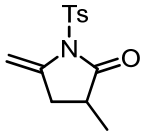
A solution of 0.3 M amide **13** (40 mg) in THF was added to 1M $Et_3N{\cdot}HOAc$ buffer solution (2mL) under air. Then catalyst **1a**/**1b** (2.5 mol%) was added. The reaction was monitored by TLC. After full conversion, the solution was extracted with Et_2O (5x2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography gave γ-alkylidene lactam **14**. The recycling was performed by addition of fresh amide to the aqueous phase and repetition of the procedure.

5-Methylene-1-tosylpyrrolidin-2-one (14a):



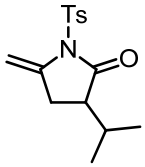
Colorless solid. MP: 87°C; ^{1}H NMR (300MHz, C_6D_6) □ = 8.10 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.1 Hz, 2H), 5.73 (q, *J* = 1.8 Hz, 1H), 4.22 (q, *J* = 1.7 Hz, 1H), 1.79 (s, 3H), 1.70-1.61 (m, 2H), 1.49-1.39 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 173.8, 145.6, 141.1, 135.5, 129.8, 129.8, 128.2, 128.0, 126.5, 94.4, 30.0, 26.0, 21.8. IR (neat) υ = 3357, 3259, 1762, 1658, 1595, 1356, 1298 cm^{-1}; HRMS calcd for $C_{12}H_{14}O_3NS$ $[M+H]^+$: 252.0689; found: 252.0688.

3-Methyl-5-methylene-1-tosylpyrrolidin-2-one (14b):



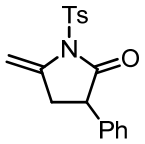
Yellow oil. ^{1}H NMR (500MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.52-5.50 (m, 1H), 4.59 (dd, *J* = 1.9, 3.1 Hz,1 H), 2.86 (dd, *J* = 9.2, 15.3 Hz, 1H), 2.63-2.53 (m, 1H), 2.46 (s, 3H), 2.32 (tdd, *J* = 2.2, 8.5, 15.1 Hz, 1H), 1.18 (d, *J* = 7.3 Hz, 3H) ^{13}C NMR (75MHz, $CDCl_3$) δ 176.5, 145.6, 139.8, 135.5, 129.8, 128.1, 94.5, 36.3, 35.1, 21.9, 15.6; IR (neat) υ = 2975, 2931, 2876, 1759, 1654, 1597, 1363 cm^{-1}; HRMS calcd for $C_{13}H_{16}O_3NS$ $[M+H]^+$: 266.0845; found: 266.0848.

3-Isopropyl-5-methylene-1-tosylpyrrolidin-2-one (14c):



Yellowish oil. ^{1}H NMR (500MHz, C_6D_6) δ 8.08 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 5.79 (dd, *J* = 1.5, 3.4 Hz, 1H), 4.33 (dd, *J* = 1.9, 3.1 Hz, 1H), 1.94-1.82 (m, 2H), 1.79 (s, 3H), 1.78-1.67 (m, 2H), 0.55 (d, *J* = 6.5 Hz, 3H), 0.47 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 175.5, 145.5, 140.4, 135.7, 129.7, 128.2, 94.0, 46.8, 29.1, 28.8, 21.8, 20.1, 17.8; IR (neat) υ = 2961, 2929, 2874, 1752, 1652, 1597, 1364 cm^{-1}; HRMS calcd for $C_{15}H_{19}O_3NNaS$ $[M+Na]^+$: 316.0978; found: 316.0981.

5-Methylene-3-phenyl-1-tosylpyrrolidin-2-one (14d):



Yellow oil. ^{1}H NMR (500MHz ,$CDCl_3$) δ = 7.96 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.31-7.24 (m, 3H), 7.10 (dd, *J* = 1.5, 7.6 Hz, 2H), 5.60 (d, *J* = 1.5 Hz, 1H), 4.68 (d, *J* = 1.5 Hz, 1H), 3.72 (dd, *J* = 7.5, 9.8 Hz, 1H), 3.12 (tdd, *J* = 1.5, 9.6, 15.7 Hz, 1H), 2.84 (tdd, *J* = 1.8, 7.3, 15.6 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 173.8, 145.7, 139.8, 137.1, 135.4, 129.8, 129.0, 128.3, 127.9, 127.6, 94.8, 47.2, 35.4, 27.1, 21.9; IR (neat) υ =3063, 3030, 2924, 1755, 1719, 1655, 1597, 1361 cm^{-1}; HRMS calcd for $C_{18}H_{18}O_3NS$ $[M+H]^+$: 328.1002; found: 328.1008.

Table 2. Detailed information for the cyclization reactions of amides 13.

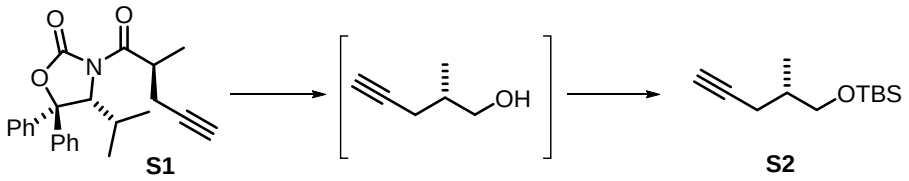
Product[a]	R	Catalyst	Time in h[b]	Yield in %[c]
14a	H	**1aa**	1	95
		1ab	2	92
		1ac	2	89
		1ba	1	86
		1bb	2	90
		1bc	2	92

14b	Me	**1aa**	1	84
		1ab	1	78
		1ac	2	80
		1ba	1	87
		1bb	1	79
		1bc	3	72
14c	iPr	**1aa**	1	85
		1ab	1	80
		1ac	3	82
		1ba	2	78
		1bb	1.5	84
		1bc	3	75
14d	Ph	**1aa**	1	77
		1ab	1.5	90
		1ac	2.5	89
		1ba	2	81
		1bb	2	92
		1bc	4	91

[a] 0.3 M amide in THF was added; [b] Required time until full conversion was achieved; [c] Isolated yields.

4. Synthesis of 2-*epi*-Clausemarine A (16)

(*S*)-*tert*-Butyldimethyl((2-methylpent-4-in-1-yl)oxy)silane (S2)

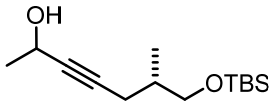


S1 **S2**

S1[10,11,12] (13.4 g, 35.8 mmol) was dissolved in THF (90 mL) and a solution of $NaBH_4$ (6.77 g, 179.0 mmol) in water (50 mL) was added dropwise. The mixture was stirred overnight at rt and then hydrolyzed with aqueous NH_4Cl and water. The solvent was removed in vacuo and the precipitate was filtrated and washed with a small amount of MeOH to give the Evans auxiliary as a brownish solid which can be purified by recrystallization with MeOH. The filtrate was extracted with Et_2O several times and the combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed under reduced pressure (max. down to 200 mbar) to give the (*S*)-2-methylpent-4-in-1-ol which was converted without further purification.
The alcohol was dissolved in dry DMF (30 mL) under an Ar atmosphere and imidazole (4.60 g, 67.6 mmol) and *tert*-Butyldimethylsilyl chloride (4.27 g, 28.3 mmol) were added at 0 °C. After 2 h at rt water was added and the phases were separated. The aqueous phase was extracted with Et_2O several times, dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 5:1) **S2** (4.82 g, 22.7 mmol, 63% over 2 steps) was given as colorless oil. ^{1}H NMR (500MHz, $CDCl_3$) δ = 3.52 (dd, *J* = 5.7, 9.9 Hz, 1H), 3.48 (dd, *J* = 6.5, 9.6 Hz, 1H), 2.30 (ddd, *J* = 2.7, 6.1, 16.8 Hz, 1H), 2.13 (ddd, *J* = 2.7, 6.9, 16.8 Hz, 1H), 1.94 (t, *J* = 2.7 Hz, 1H), 1.85 (qd, *J* = 6.3, 12.8 Hz, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125MHz, $CDCl_3$) δ = 83.3, 69.2, 66.9, 35.3, 27.1, 26.1, 22.2, 18.5, 16.1, -5.2, -5.3. Known compound.[13]

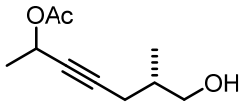
[10] Brenner, M.; La Vecchia, L.; Leutert, T.; Seebach, D., *Org. Synth., Coll.Vol. 11,* **2009**, 896–902.
[11] Hintermann, T.; Seebach, D., *Helv. Chim. Acta* **1998**, *81*, 2093–2126.
[12] Sawant, P.; Maier, M. E., *Synlett* **2011**, *20*, 3002–3004.
[13] Ireland, R. E.; Liu, L.; Roper, T. D. *Tetrahedron* **1997**, *53*, 13221–13256.

(*6S*)-7-((*tert*-Butyldimethylsilyl)oxy)-6-methylhept-3-yn-2-ol (S3):



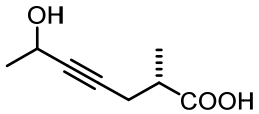
Under an Ar atmosphere, alkyne **S2** (1.80 g, 8.47 mmol) was dissolved in dry THF (10 mL). At -78°C *n*BuLi (4.40 mL, 10.2 mmol, 2.5M in hexane) was added and the solution was stirred for 30 min. Then acetaldehyde (0.72 mL, 12.7 mmol) was added and the solution was warmed up to 0 °C during 1 h. Then aqueous NH_4Cl and Et_2O were added and the phases were separated. The aqueous phase was extracted with Et_2O several times and the combined organic phases were dried with $MgSO_4$, filtrated and the solvent was evaporated in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 2:1) **S3** (1.69 g, 6.60 mmol, 78%) was isolated as colorless oil. ^{1}H NMR (200MHz, $CDCl_3$) δ = 4.60-4.43 (m, 1H), 3.48 (dd, *J* = 2.2, 6.1 Hz, 2H), 2.31 (ddd, *J* = 2.2, 5.9, 16.9 Hz, 1H), 2.12 (ddd, *J* = 2.2, 6.8, 16.6 Hz, 1H), 1.93-1.69 (m, 2H), 1.44 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (50MHz, $CDCl_3$) δ = 83.3, 83.3, 66.9, 58.8, 51.7, 35.4, 26.1, 24.9, 22.4, 18.5, 16.2, -5.2; IR (neat): ν = 3347, 2955, 2930, 2857, 1471, 1253 cm^{-1};HRMS: calcd for $C_{14}H_{29}O_2Si$ $[M+H]^+$: 257.1931.; found: 257.1939.

(*6S*)-7-Hydroxy-6-methylhept-3-yn-2-ylacetate (S4):



S3 (1.13 g, 4.41 mmol) was dissolved in DCM (110 mL) under an Ar atmosphere and Ac_2O (0.87 mL, 9.25 mmol), Et_3N (1.28 mL, 9.25 mmol) and DMAP (108 mg, 0.88 mmol) were added at rt. After 3 h the reaction was hydrolyzed with diluted HCl. The organic phase was washed with aqueous $NaHCO_3$ and the aqueous phase was extracted with DCM several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. The product was identified as colorless oil, which was converted without further purification.
Under Ar atmosphere the silyl ether was dissolved in dry THF (15 mL) and TBAF (4.86 mL, 4.86 mmol, 1M in THF) was added at 0 °C. After 3 h at rt THF was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 10:1, 7:1) **S4** (716 mg, 3.88 mmol, 88% over 2 steps) was given as colorless oil. ^{1}H NMR (200MHz, C_6D_6) δ = 5.52 (tq, *J* = 1.6, 6.6 Hz, 1H), 3.34 (d, *J* = 6.1 Hz, 2 H), 2.36 (br. s., 1H), 2.20 (ddd, *J* = 1.8, 6.0, 16.9 Hz, 1H), 2.05 (ddd, *J* = 2.0, 6.6, 16.6 Hz, 1H), 1.81-1.66 (m, *J* = 7.6 Hz, 1H), 1.64 (s, 3H), 1.31 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (50MHz, C_6D_6) δ = 169.9, 84.3, 81.0, 66.9, 61.3, 35.8, 23.0, 22.1, 21.0, 16.6; IR (neat): ν = 3462, 2985, 2962, 2936, 2876, 1733, 1450, 1372, 1234 cm^{-1}; HRMS: calcd for $C_{10}H_{20}O_3N$ $[M+NH_4]^+$: 202.1434.; found: 202.1439.

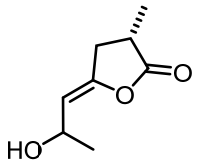
(*2S*)-6-Hydroxy-2-methylhept-4-ynoic acid (17):



S4 (745 mg, 4.04 mmol) was dissolved in dry DMSO (15 mL) under an Ar atmosphere and IBX (3.40 g, 12.13 mmol) was added. After 3 h at rt the solution was added to an ice/water bath and the precipitate was removed by filtration. The filtrate was extracted with Et_2O several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. The product was given as colorless oil and was converted without further purification.
The aldehyde was dissolved in 2-methyl-2-butene (3.66 mL, 34.4 mmol) and *t*BuOH (90 mL) and then a solution of $NaClO_2$ (3.51 g, 38.8 mmol) and NaH_2PO_4 (3.53 g, 29.4 mmol) in water (25 mL) was added. After 1 h at rt a pH value of 8 was adjusted by addition of diluted NaOH and *t*BuOH was removed in vacuo. Then water and brine were added and the solution was extracted with cyclohexane once. Then the pH value was adjusted at 3 by addition of diluted HCl and the aqueous phase was extracted with EtOAc several times. The combined EtOAc phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 5:1, 1:1) **17** (380 mg, 2.43 mmol, 60% over

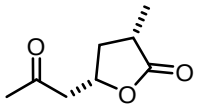
2 steps) was given as colorless oil. ^{1}H NMR (200MHz, C_6D_6) δ = 6.60 (br. s., 1H), 4.32 (tq, *J* = 1.7, 6.6 Hz, 1H), 2.48-2.14 (m, 3H), 1.30 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (50MHz, C_6D_6) δ = 181.3, 85.3, 81.3, 58.8, 39.4, 25.0, 25.0, 23.3, 16.4; IR (neat): ν = 2980, 2937, 1705, 1461 cm^{-1}; HRMS: calcd for $C_8H_{11}O_2$ $[(M+H)-H_2O]^+$: 139.0754.; found: 139.0754.

(*3S,Z*)-5-(2-Hydroxypropyliden)-3-methyldihydrofuran-2-one (18):



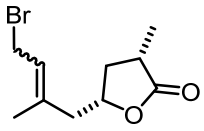
17 (100 mg, 0.640 mmol) was dissolved in 1M triethylammonium acetate in water (2 mL) and THF (0.5 mL). Then catalyst **1ab** (4.2 mg, 0.064 mmol) was added and the solution was stirred for 2 h. EtOAc was added and the phases were separated. The aqueous phase was extracted with EtOAc several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 2:1) **18** (77 mg, 0.493 mmol, 77%) was given as colorless oil. ^{1}H NMR (300MHz, C_6D_6, major diastereomer*, *dr* = 60:40) δ = 4.81 (td, *J* = 6.6, 12.8 Hz, 1H), 4.50-4.41 (m, 1H), 2.19-1.86 (m, 3H), 1.68 (ddd, *J* = 2.2, 8.1, 15.4 Hz, 1H), 1.61* (ddd, *J* = 1.5, 7.7, 15.0 Hz, 1H), 1.75-1.55 (m, 1H), 1.24 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.80* (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75MHz, C_6D_6) δ = 177.10*, 177.06, 147.2, 147.1*, 109.9, 63.08*, 63.05, 34.34, 34.29*, 33.5*, 33.4, 24.3, 15.9*, 15.8; IR (neat): ν = 3376, 2973, 1794, 1704, 1457, 1196 cm^{-1};HRMS: calcd for $C_8H_{12}O_3Na$ $[M+Na]^+$: 179.0679.; found: 179.0680.

(*3S,5S*)-3-Methyl-5-(2-oxopropyl)dihydrofuran-2-one (19):



18 (440 mg, 2.81 mmol) was dissolved in dry MeOH (10 mL) under H_2 atmosphere and Pd/C (300 mg) was added. The solution was stirred overnight at rt and the catalyst was removed by filtration over celite. The solvent was evaporated in vacuo and the product was converted without further purification.
The alcohol was dissolved in dry DMSO (10 mL) under an Ar atmosphere and IBX (2.36 g, 8.43 mmol) was added. The solution was stirred overnight and then poured into iced water. The precipitate was removed by filtration and the filtrate was extracted with Et_2O several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 1:1), **19** (180 mg, 1.15 mmol, 41% over 2 steps) was given as yellowish oil. ^{1}H NMR (500MHz, C_6D_6) δ = 4.19 (ddd, *J* = 5.4, 10.7, 11.9 Hz, 1H), 2.21 (dd, *J* = 6.5, 16.8 Hz, 1H), 1.96-1.86 (m, 1H), 1.83-1.78 (m, 1H), 1.75 (dd, *J* = 6.1, 17.2 Hz, 1H), 1.57 (s, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.75 (dt, *J* = 10.5, 12.1 Hz, 1H); ^{13}C NMR (125MHz, C_6D_6) δ = 203.6, 178.0, 73.5, 48.6, 37.5, 35.7, 30.3, 15.4; IR (neat): ν = 2975, 2936, 2879, 1760, 1714, 1455, 1378, 1356 cm^{-1}; HRMS: calcd for $C_8H_{12}O_3Na$ $[M+Na]^+$: 179.0679.; found: 179.0681.

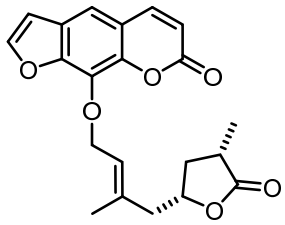
(*3S,5S*)-5-(4-Bromo-2-methylbut-2-en-1-yl)-3-methyldihydrofuran-2-one (20):



19 (120 mg, 0.768 mmol) was dissolved in dry THF (1 mL) under an Ar atmosphere and vinylmagnesium bromide (1.65 mL, 1.15 mmol, 0.7M in THF) was added. The turbid solution was hydrolyzed after 30 min by addition of aqueous NH_4Cl, the phases were separated and the aqueous phase was extracted with EtOAc several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. The product was converted without further purification.
The tertiary alcohol was dissolved in dry Et_2O (3 mL) and PBr_3 (130 µL, 1.38 mmol) was added at 0 °C. After 30 min Et_2O was added and the solution was hydrolyzed by addition of aqueous $NaHCO_3$. The phases were separated and the organic phase was washed with brine, dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 3:1), **20** (58 mg,

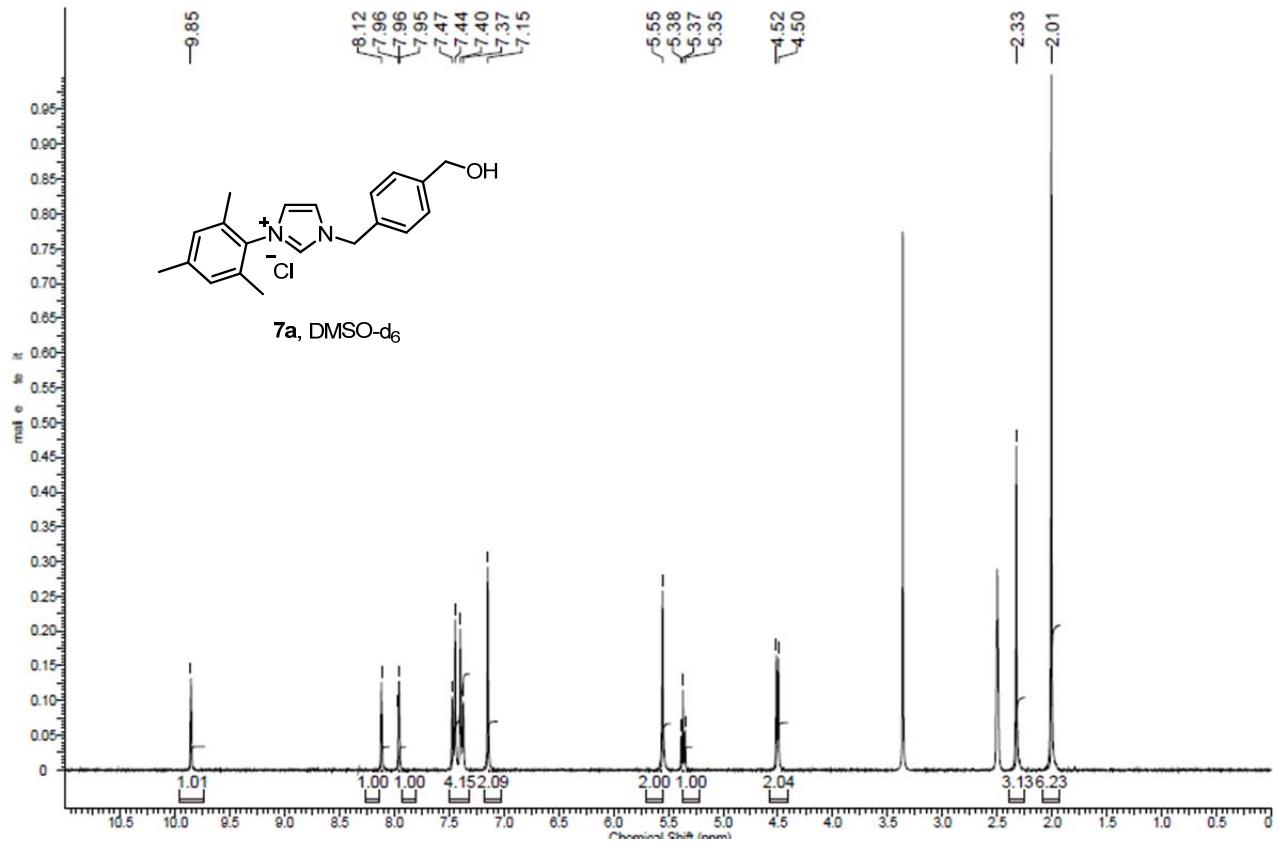
0.235 mmol, 31% over 2 steps, *E*/*Z* = 60:40) was given as yellowish oil ^{1}H NMR (500MHz, C_6D_6, major diastereomer*, *dr* = 60:40) δ = 5.34* (t, *J* = 8.6 Hz, 1H), 5.24 (t, *J* = 8.4 Hz, 1H), 3.72-3.46 (m, 3H), 2.04* (dd, *J* = 7.6, 14.1 Hz, 1H), 1.95 (dd, *J* = 7.5, 14.3 Hz, 1H), 1.92-1.85 (m, *J* = 7.3 Hz, 1H), 1.81* (dd, *J* = 5.2, 14.3 Hz, 1H), 1.65 (dd, *J* = 5.5, 14.3 Hz, 1H), 1.56* (s, 3H), 1.50-1.45 (m, *J* = 6.9 Hz, 1H), 1.43 (s, 3H), 0.98* (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.3 Hz, 3H), 0.86-0.74 (m, 1H); ^{13}C NMR (125MHz, C_6D_6) δ = 177.8, 177.7*, 138.3, 138.0*, 124.7*, 124.2, 75.9, 75.8*, 45.0, 37.3*, 37.1, 35.9*, 35.7, 28.5*, 28.3, 24.2, 15.2, 15.1*; IR (neat): ν = 2972, 2932, 2877, 1769, 1453 cm^{-1}; HRMS: calcd for $C_{10}H_{15}O_2$ $[M\text{-}Br]^+$: 167.0167.; found: 167.1070

2-*epi*-Clausemarine A (16)

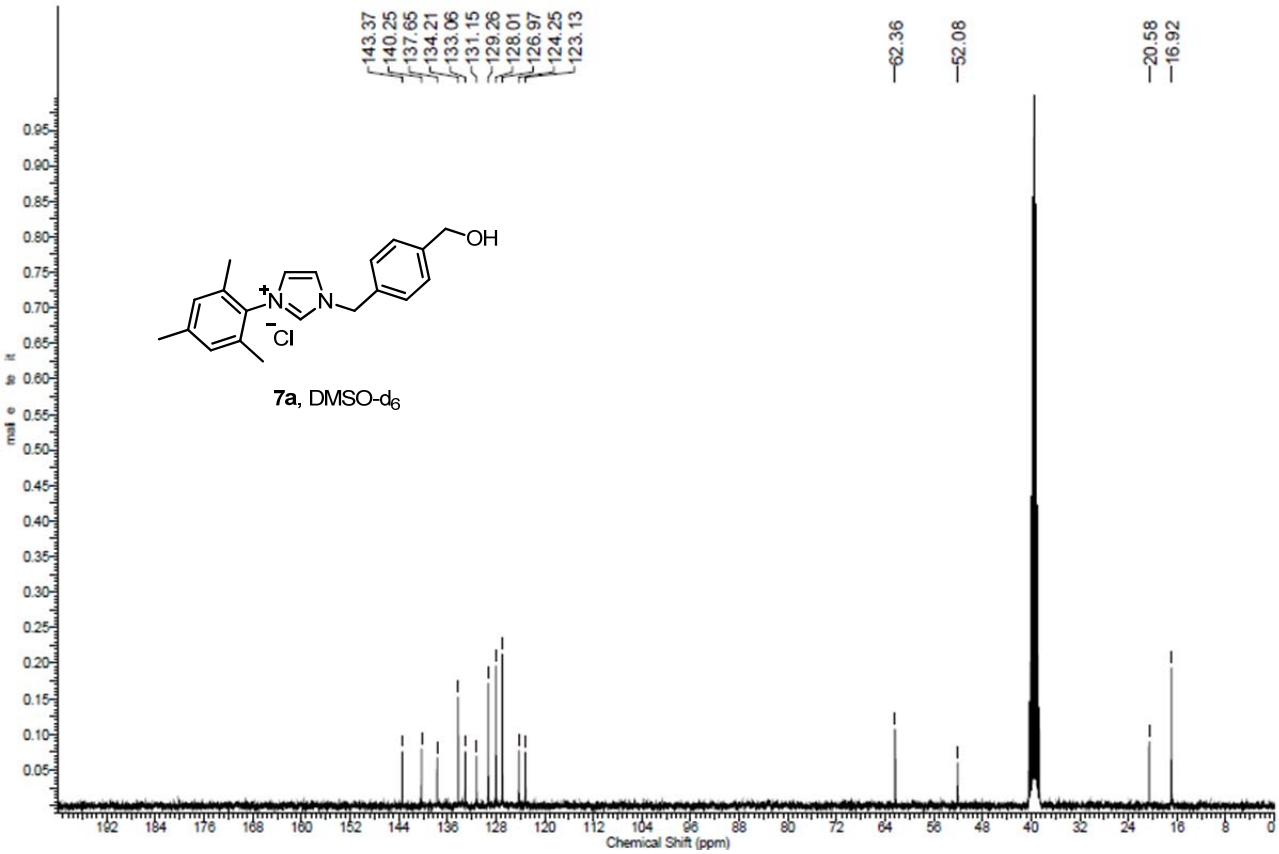


16 (40 mg, 0.162 mmol) was dissolved in dry acetone (2 mL) under an Ar atmosphere and xanthotoxol (33 mg, 0.162 mmol) and dry K_2CO_3 (22 mg, 0.162 mmol) were added. The solution was heated to reflux overnight. After cooling to rt the solution was neutralized with 10% citric acid and the solvent was removed in vacuo. The residue was dissolved in DCM and water was added. The phases were separated and the aqueous phase was extracted with DCM several times. The combined organic phases were dried with $MgSO_4$, filtrated and the solvent was removed in vacuo. After purification by column chromatography (SiO_2, cyclohexane/EtOAc, 2:1), 2-*epi*-Clausemarine A **16** (27 mg, 0.073 mmol, 45%, *E*/*Z* = 80:20) was given as yellowish oil. $[\alpha]_D^{20} = +16$, c = 0.75, MeOH; ^{1}H NMR (500MHz, $CDCl_3$, major diastereomer, *dr* = 80:20) δ = 7.77 (d, *J* = 9.9 Hz, 1H), 7.70 (d, *J* = 2.3 Hz, 1H), 7.38 (s, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 6.36 (d, *J* = 9.6 Hz, 1H), 5.70 (t, *J* = 7.1 Hz, 1H), 5.08-4.98 (m, 2H), 4.40 (ddd, *J* = 5.7, 11.1, 12.1 Hz, 1H), 2.64-2.59 (m, 2H), 2.48 (dd, *J* = 7.3, 14.1 Hz, 1H), 2.37-2.31 (m, 1H), 2.28 (dd, *J* = 5.0, 13.4 Hz, 1H), 1.74 (s, 3H), 1.47-1.35 (m, 1H), 1.22 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ = 179.3, 160.6, 148.8, 146.8, 144.5, 137.8, 131.5, 126.0, 123.4, 116.6, 114.8, 113.6, 106.9, 77.0, 69.7, 45.2, 37.2, 35.8, 17.2, 15.1; IR (neat): ν = 2974, 2933, 2872, 1765, 1723, 1622, 1585, 1439, 1401 cm^{-1}; HRMS: calcd for $C_{21}H_{21}O_6$ $[M+H]^+$: 369.1333.; found: 369.1350. Signals, which could be assigned to the minor diastereomer: ^{1}H NMR (500MHz, $CDCl_3$) δ = 5.82 (t, *J* = 7.1 Hz, 1H), 4.98-4.90 (m, 2H), 4.52 (tdd, *J* = 5.4, 7.6, 10.6 Hz, 1H), 1.28-1.25 (m, 3H).

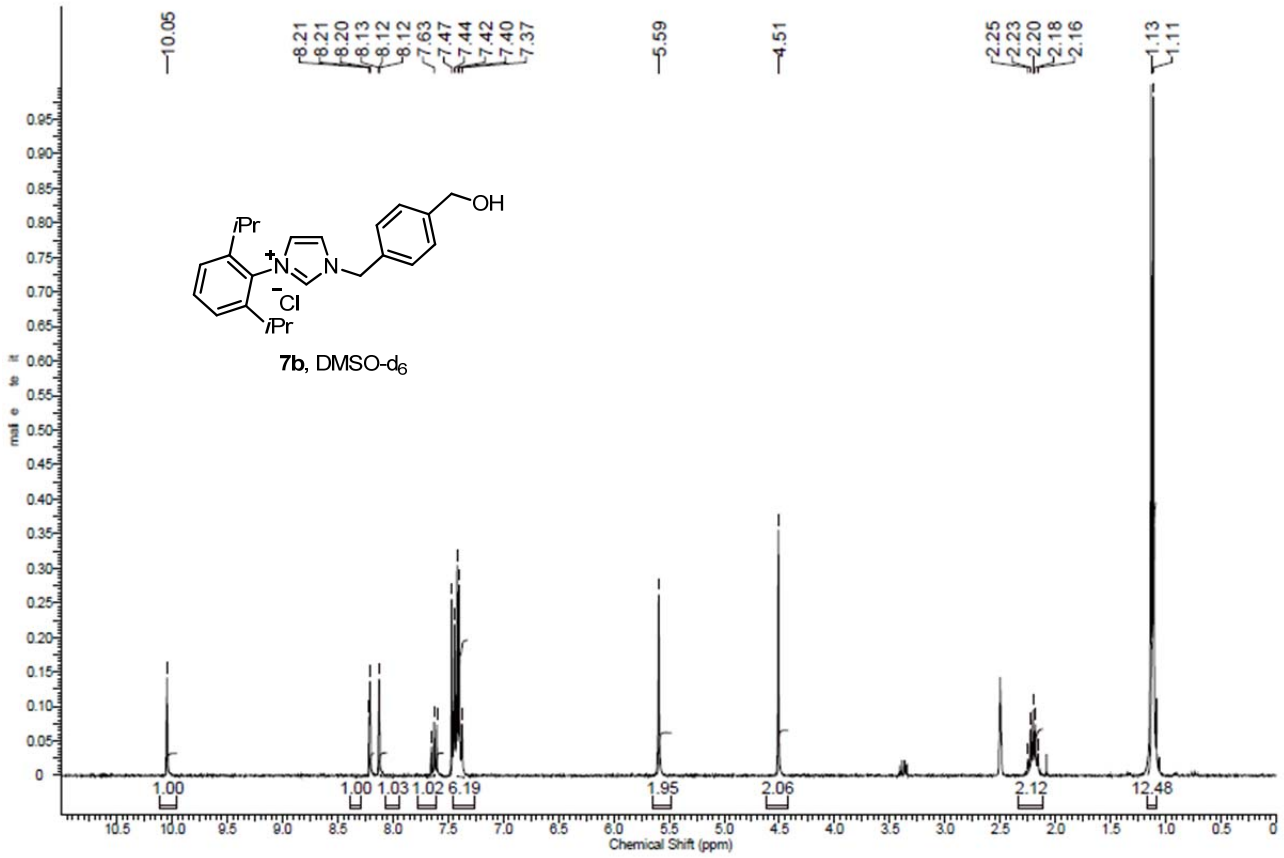
5. NMR-spectra



7a, DMSO-d_6



7a, DMSO-d_6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8.21
8.21
8.20
8.13
8.12
8.12
7.63
7.47
7.44
7.42
7.40
7.37
5.59
4.51
2.25
2.23
2.20
2.18
2.16
1.13
1.11
OH
iPr
iPr
Cl
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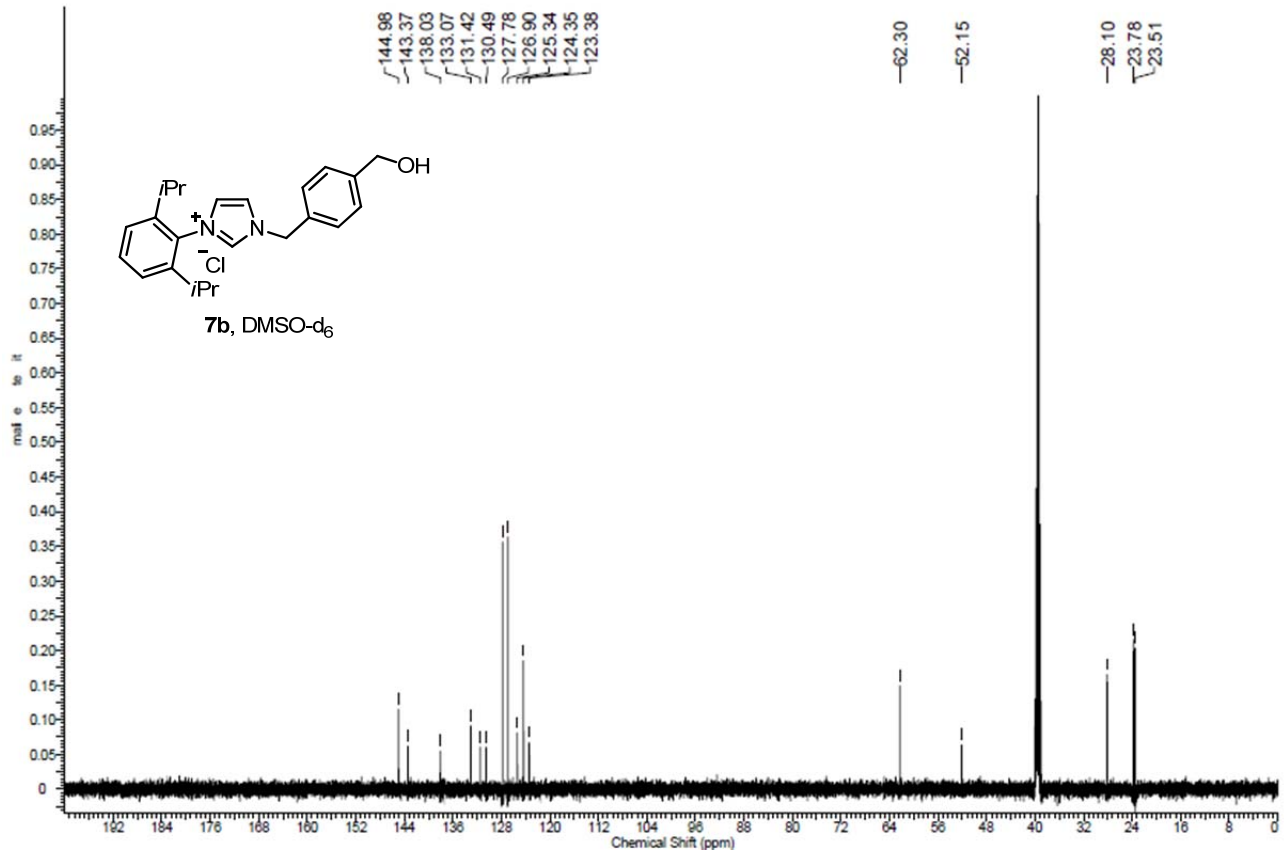
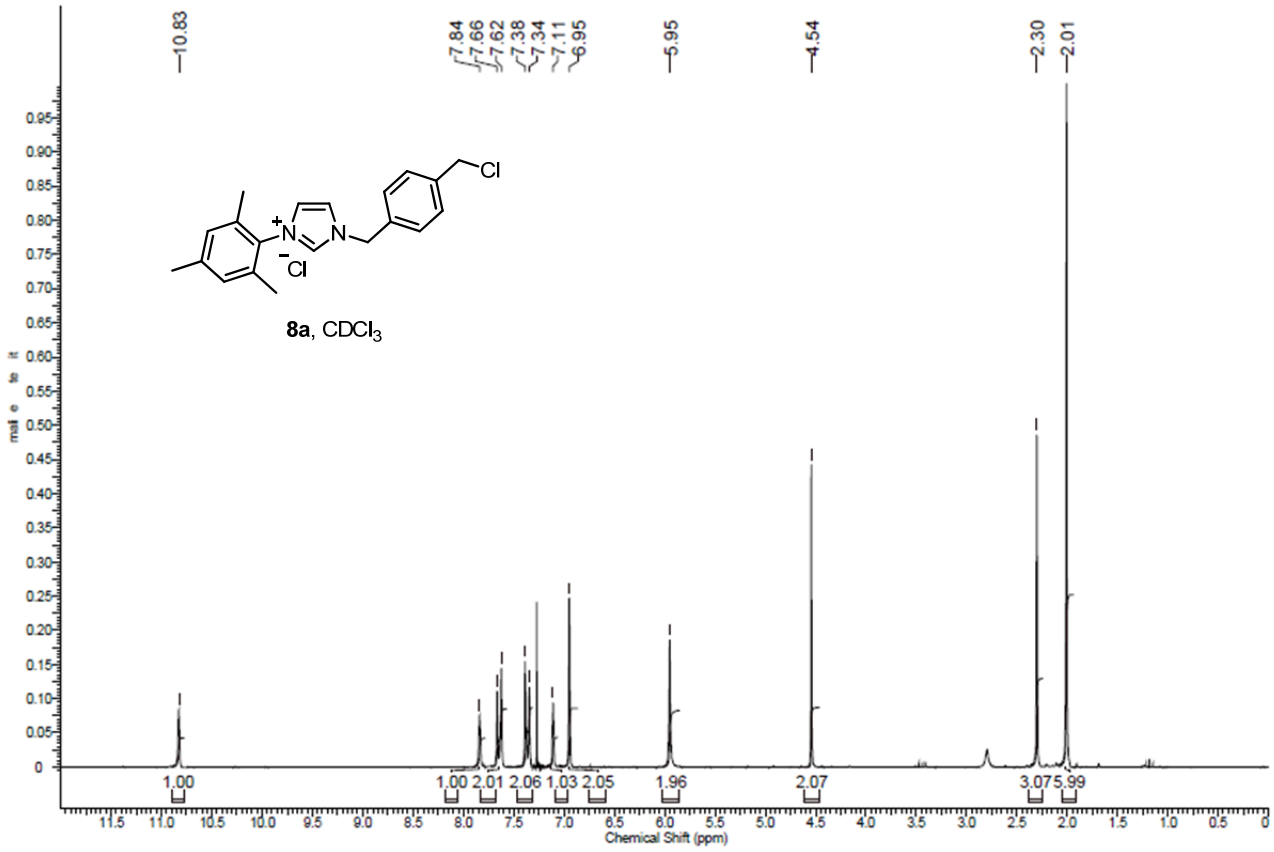
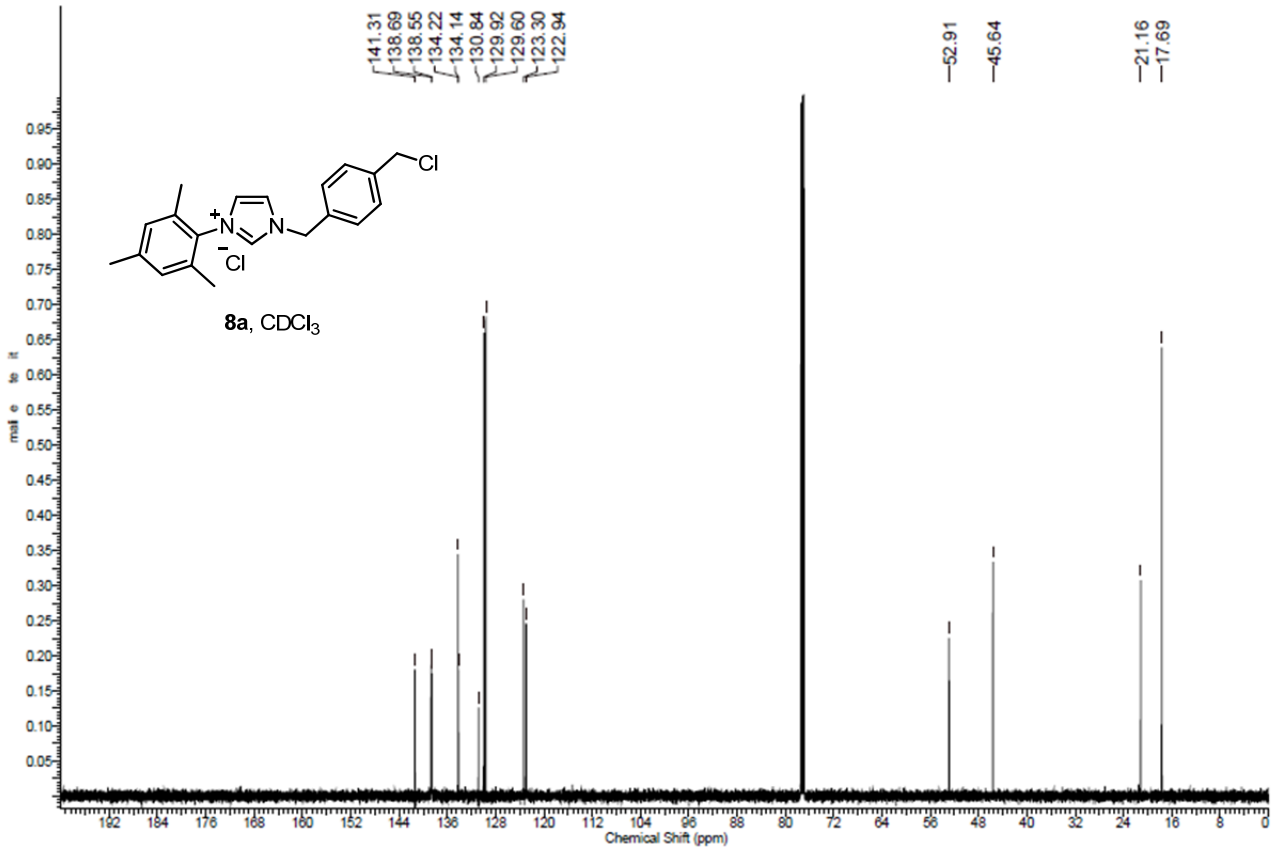
1.95
2.06
2.12
12.48
Chemical Shift (ppm)

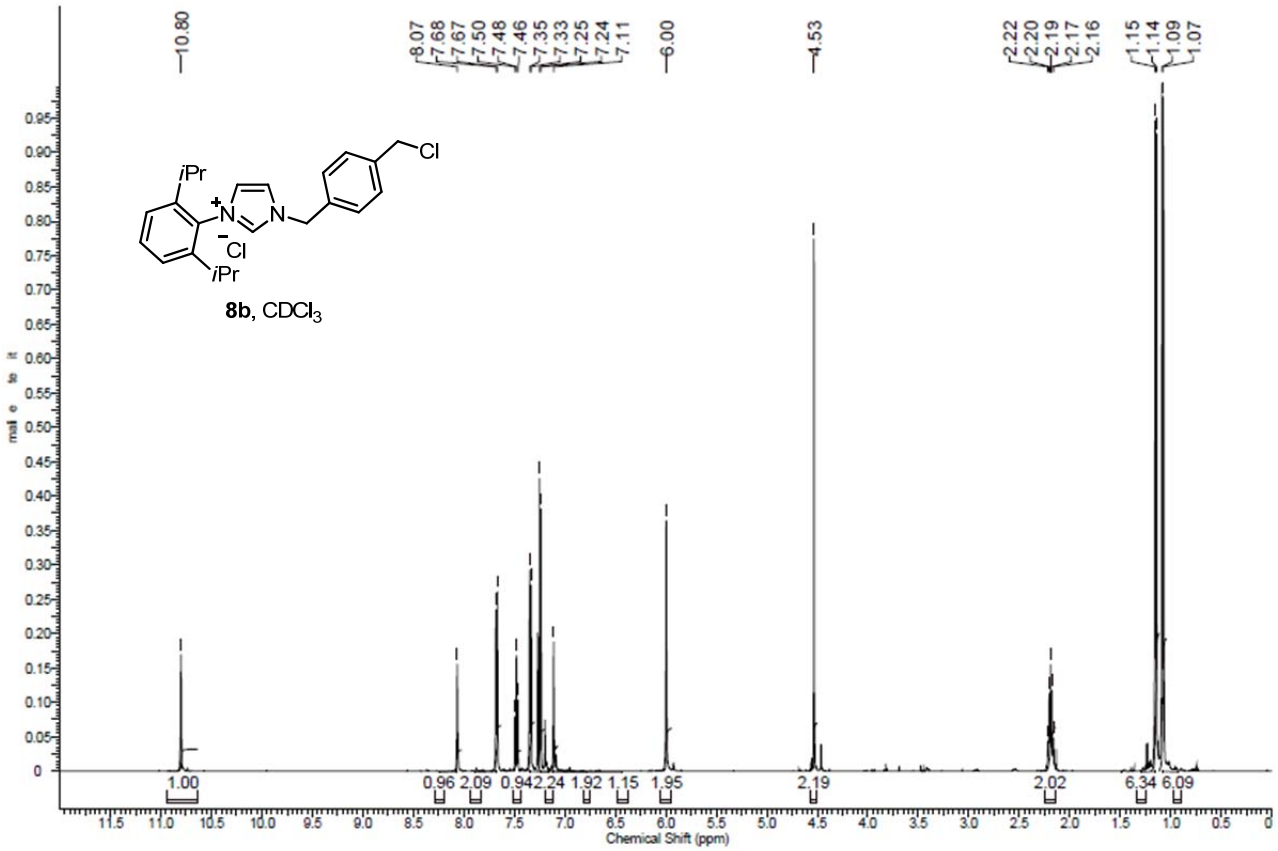

144.98
143.37
138.03
133.07
131.42
130.49
127.78
126.90
125.34
124.35
123.38
62.30
52.15
28.10
23.78
23.51
OH
iPr
iPr
Cl
7b, DMSO-d6
Chemical Shift (ppm)

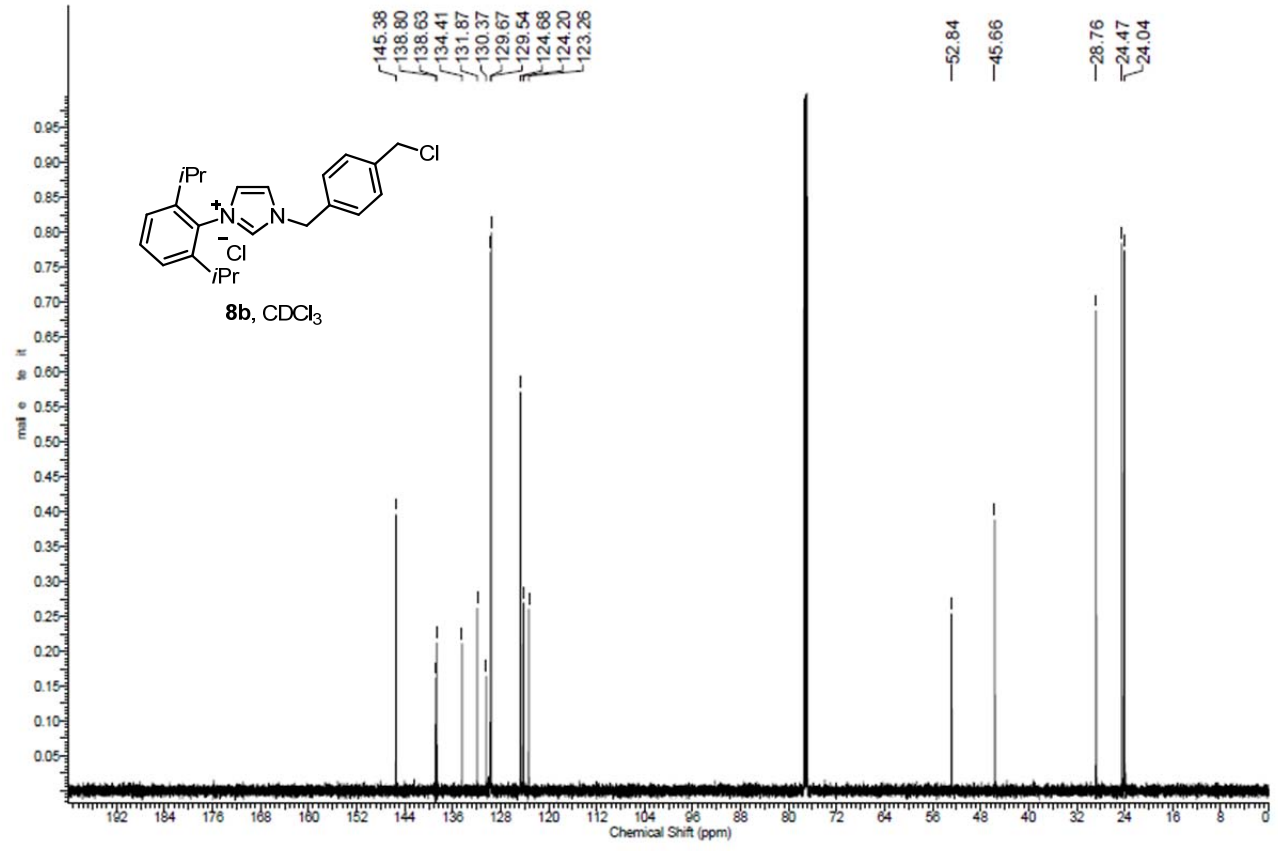


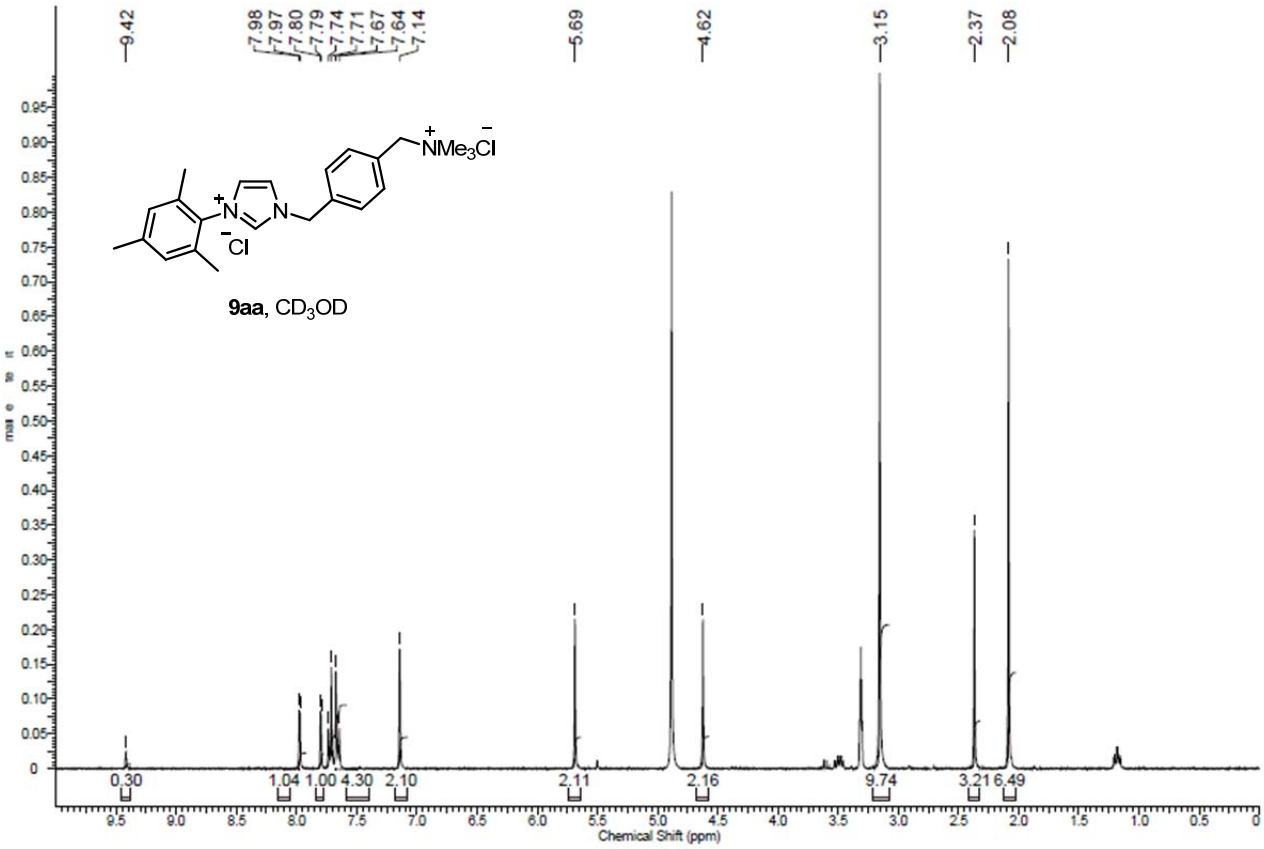
8a, $CDCl_3$



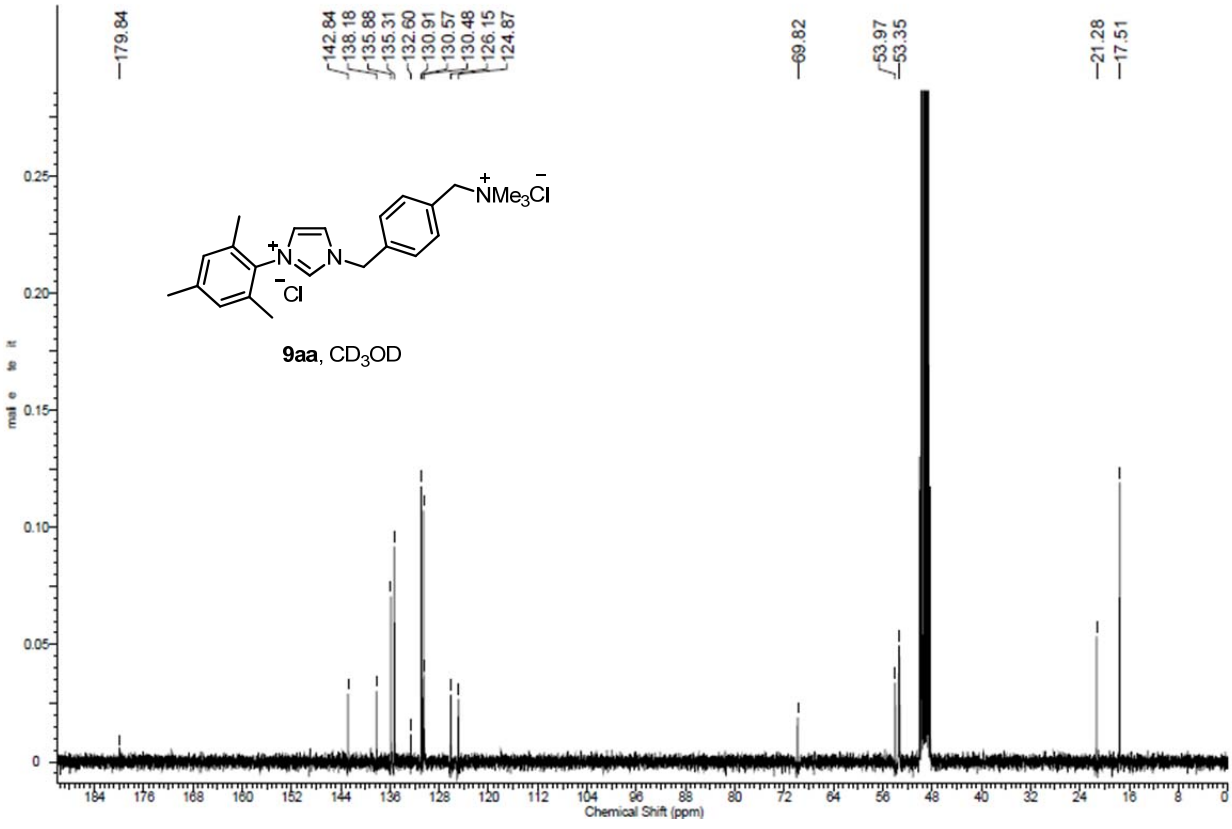
8a, $CDCl_3$


10.80
8.07
7.68
7.67
7.50
7.48
7.46
7.35
7.33
7.25
7.24
7.11
6.00
4.53
2.22
2.20
2.19
2.17
2.16
1.15
1.14
1.09
1.07
iPr
Cl
Cl
iPr
8b, CDCl3
1.00
0.96
2.09
0.94
2.24
1.92
1.15
1.95
2.19
2.02
6.34
6.09
Chemical Shift (ppm)

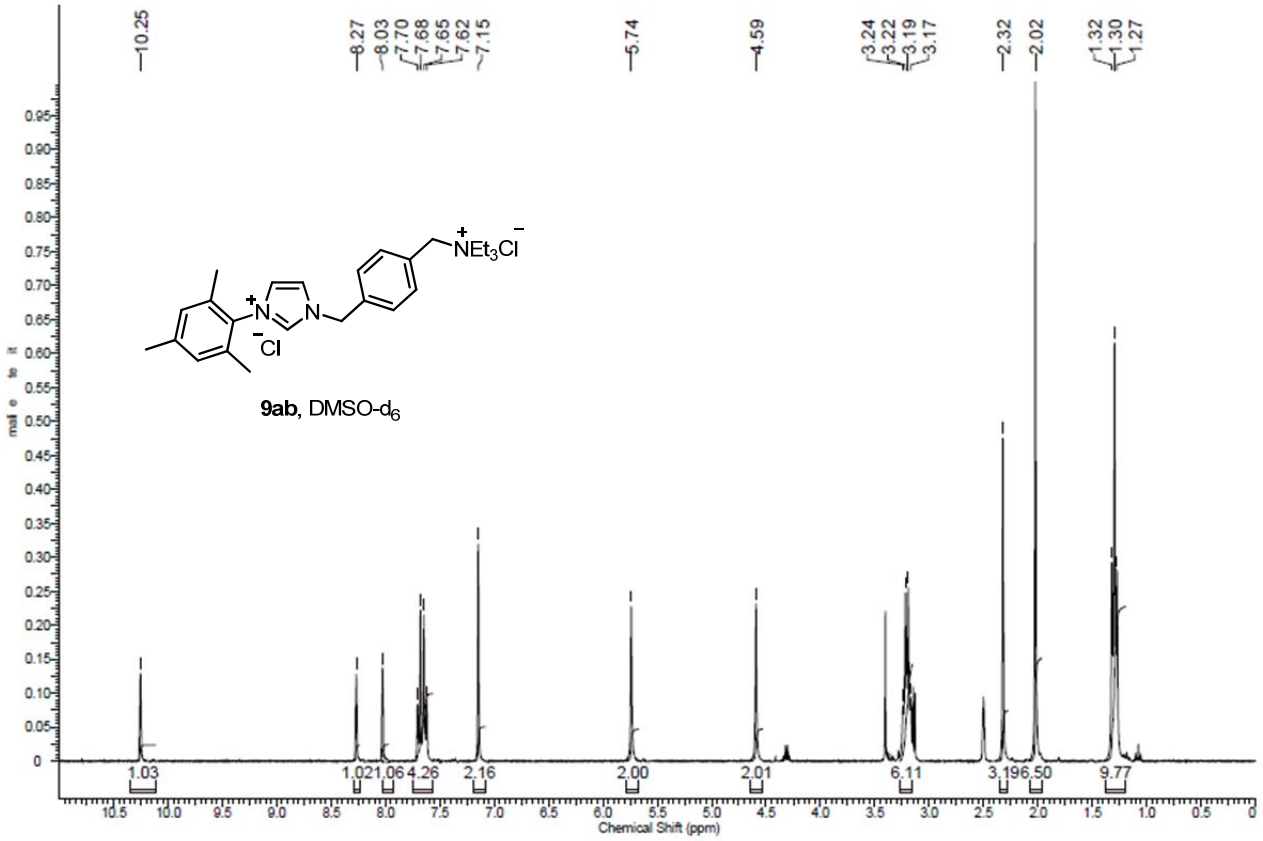

145.38
138.80
138.63
134.41
131.87
130.37
129.67
129.54
124.68
124.20
123.26
52.84
45.66
28.76
24.47
24.04
iPr
Cl
Cl
iPr
8b, CDCl3
Chemical Shift (ppm)



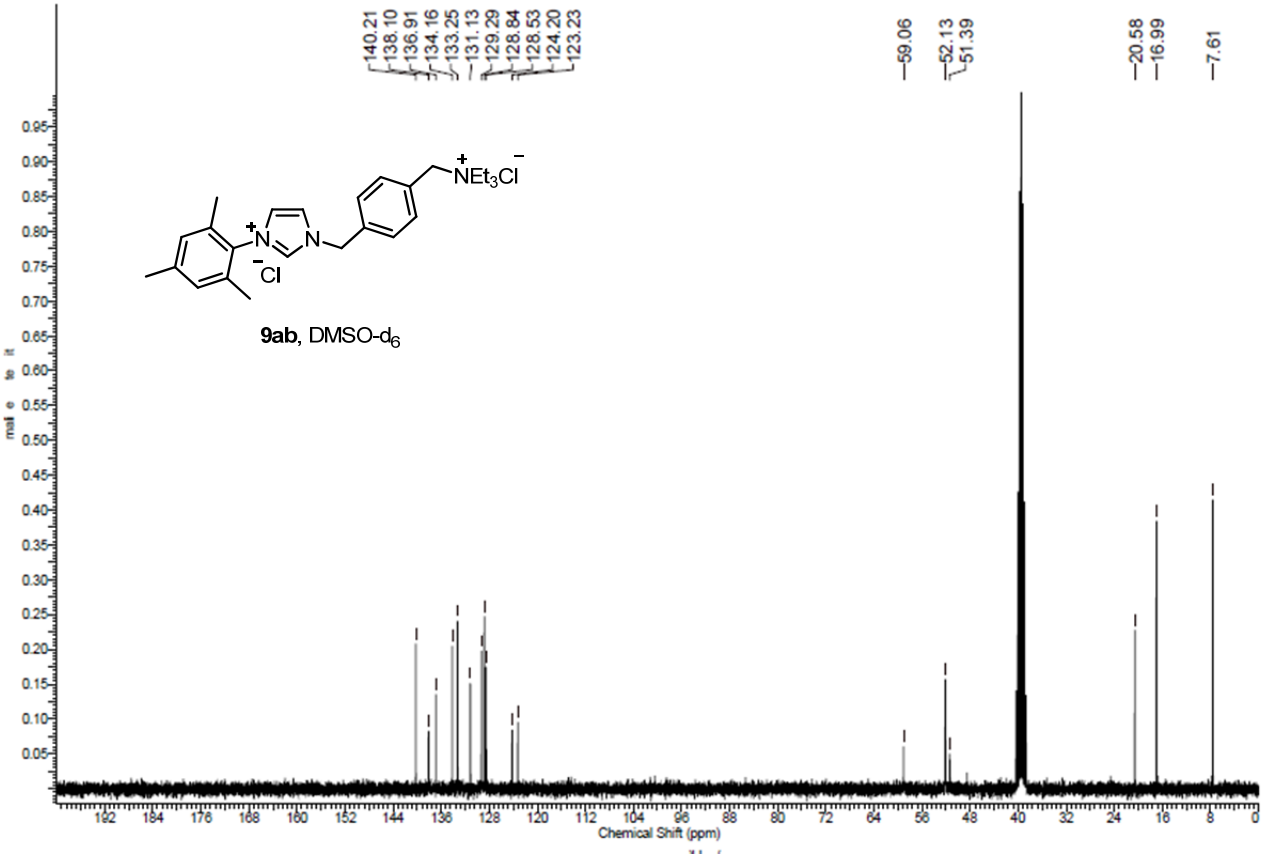
9aa, CD_3OD



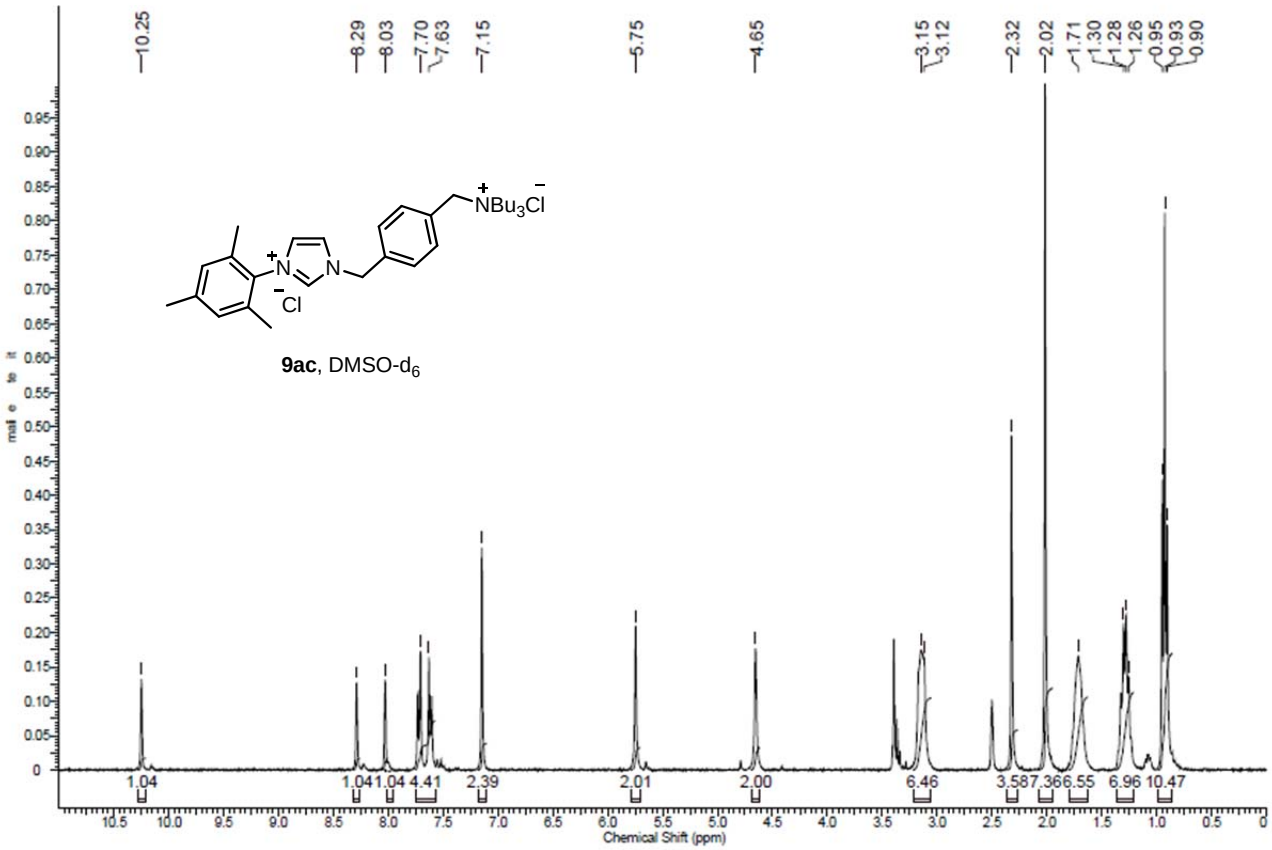
9aa, CD_3OD



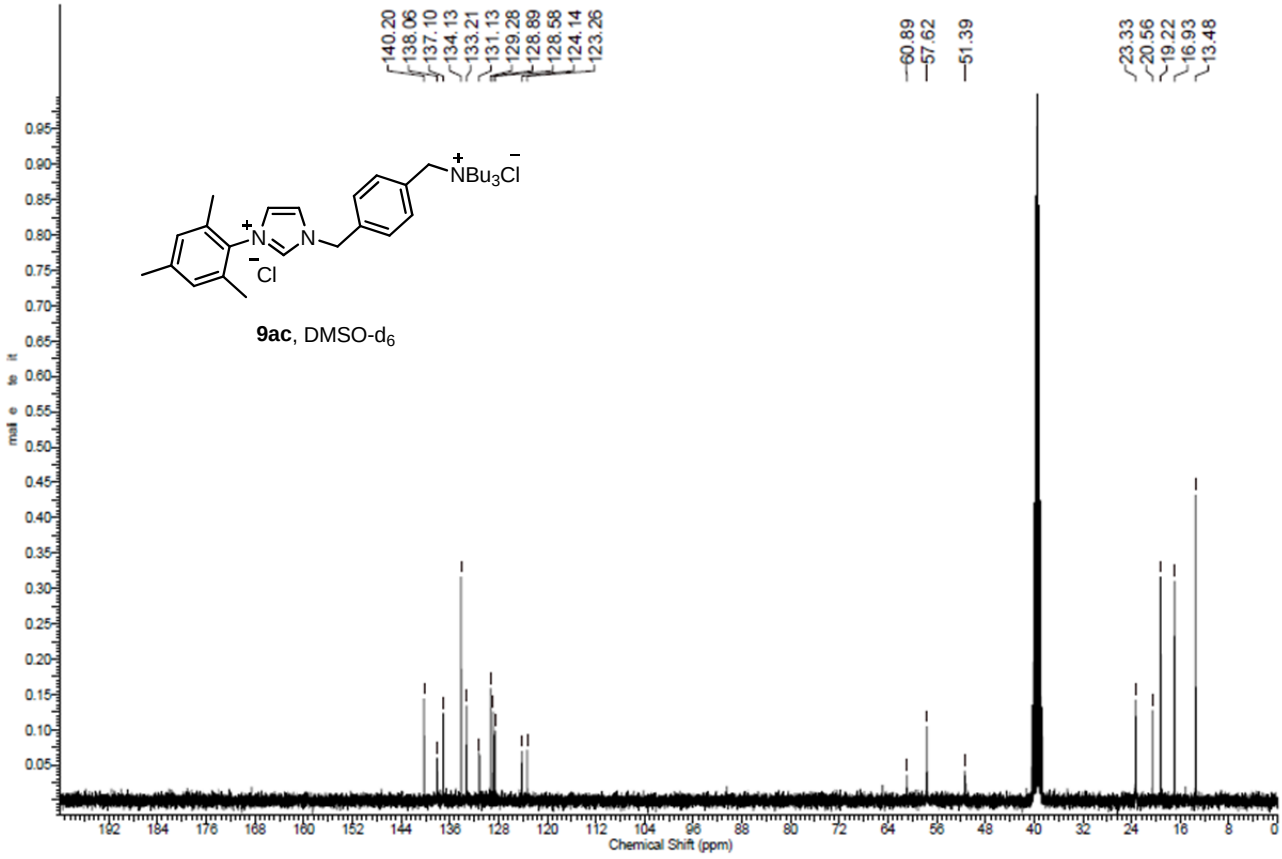
9ab, DMSO-d_6



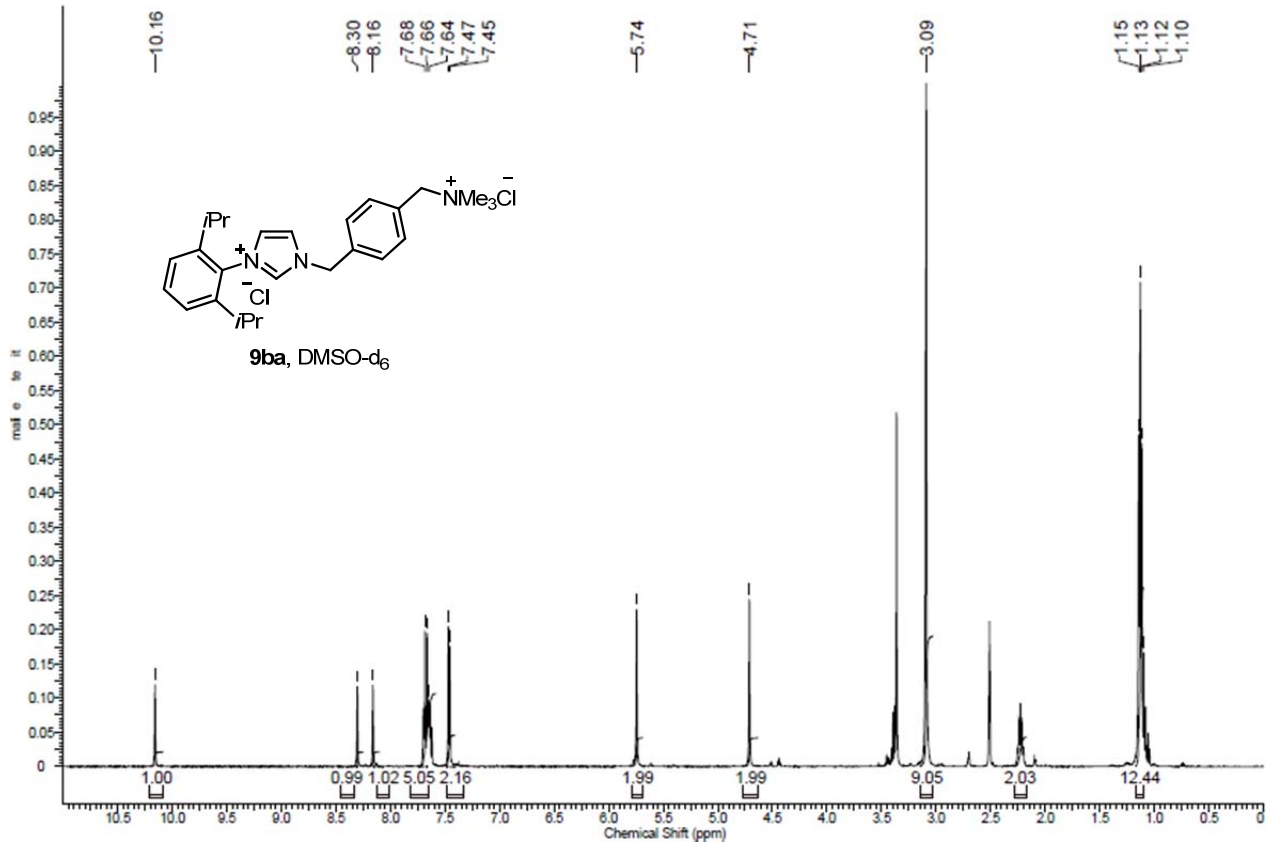
9ab, DMSO-d_6



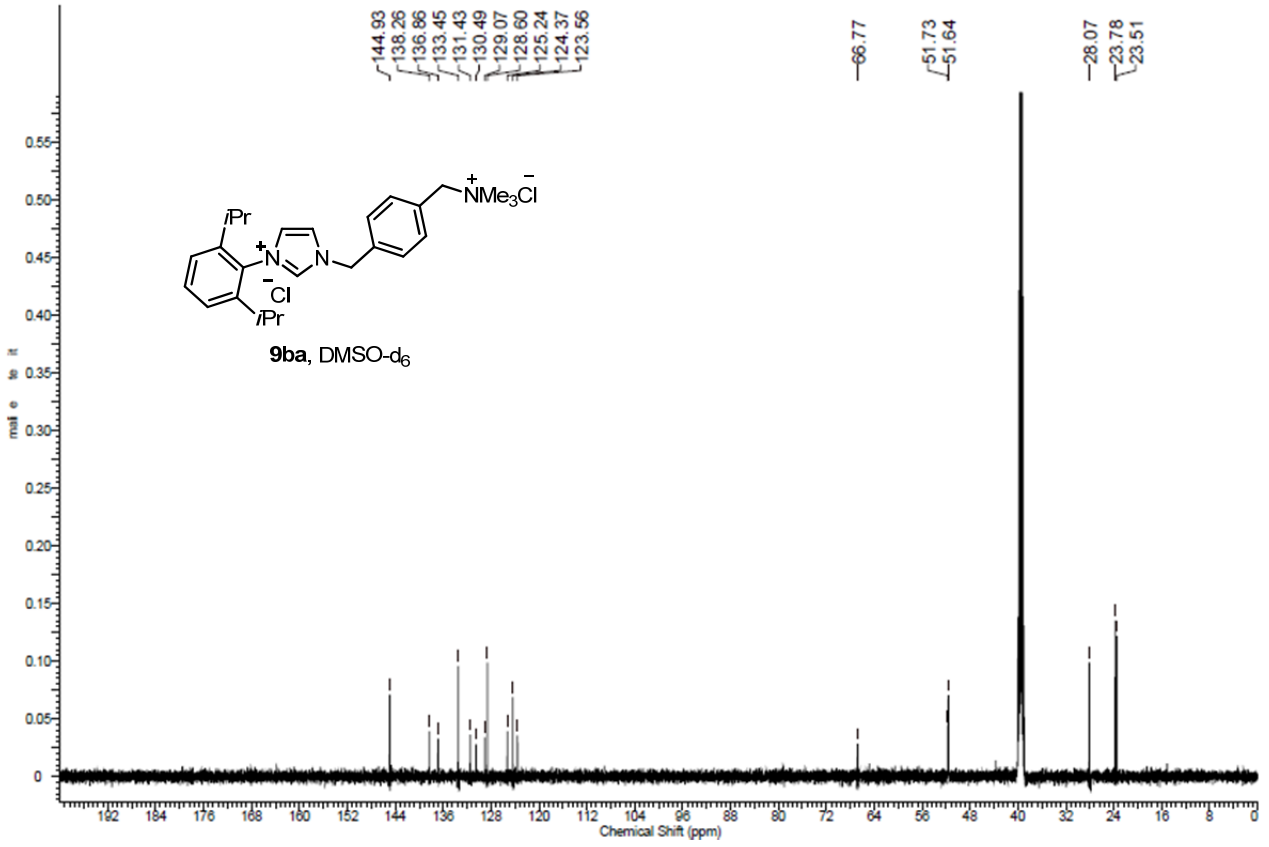
9ac, DMSO-d_6



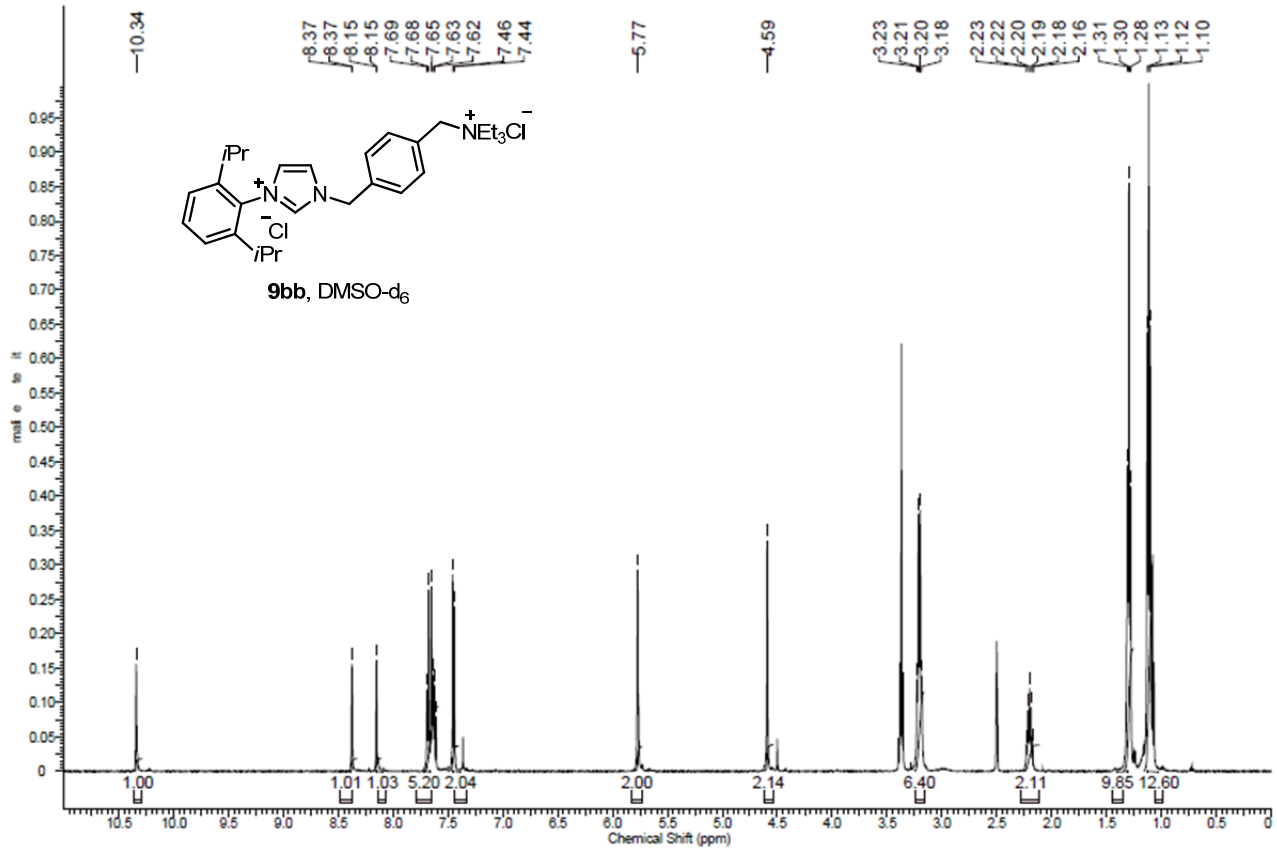
9ac, DMSO-d_6

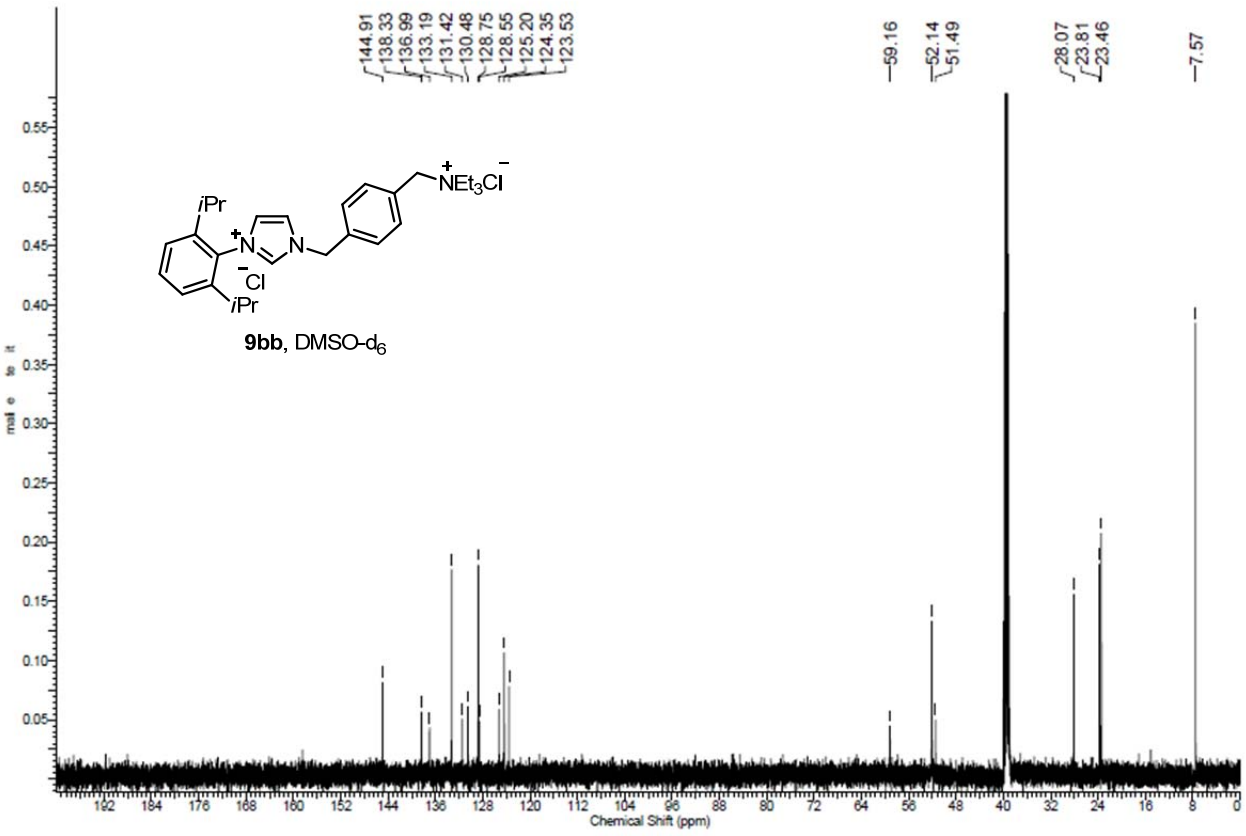


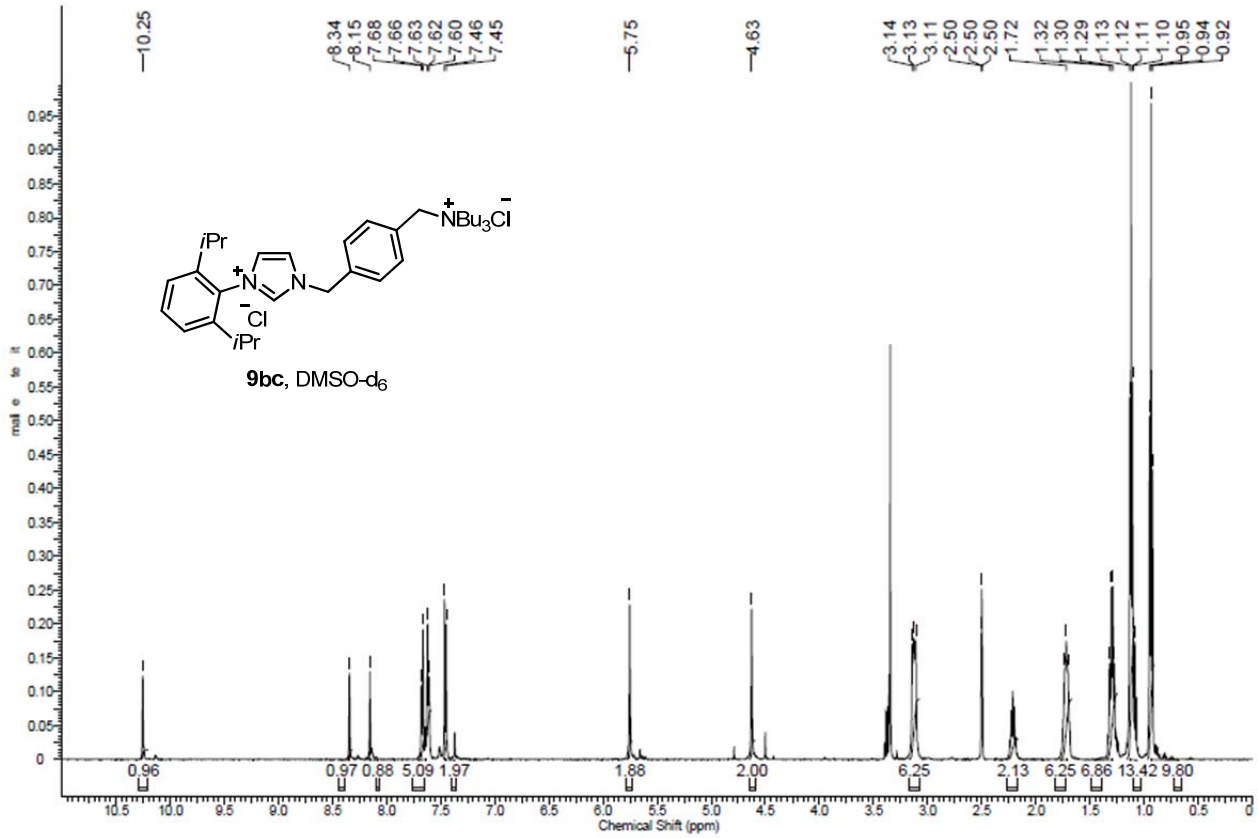
9ba, DMSO-d_6



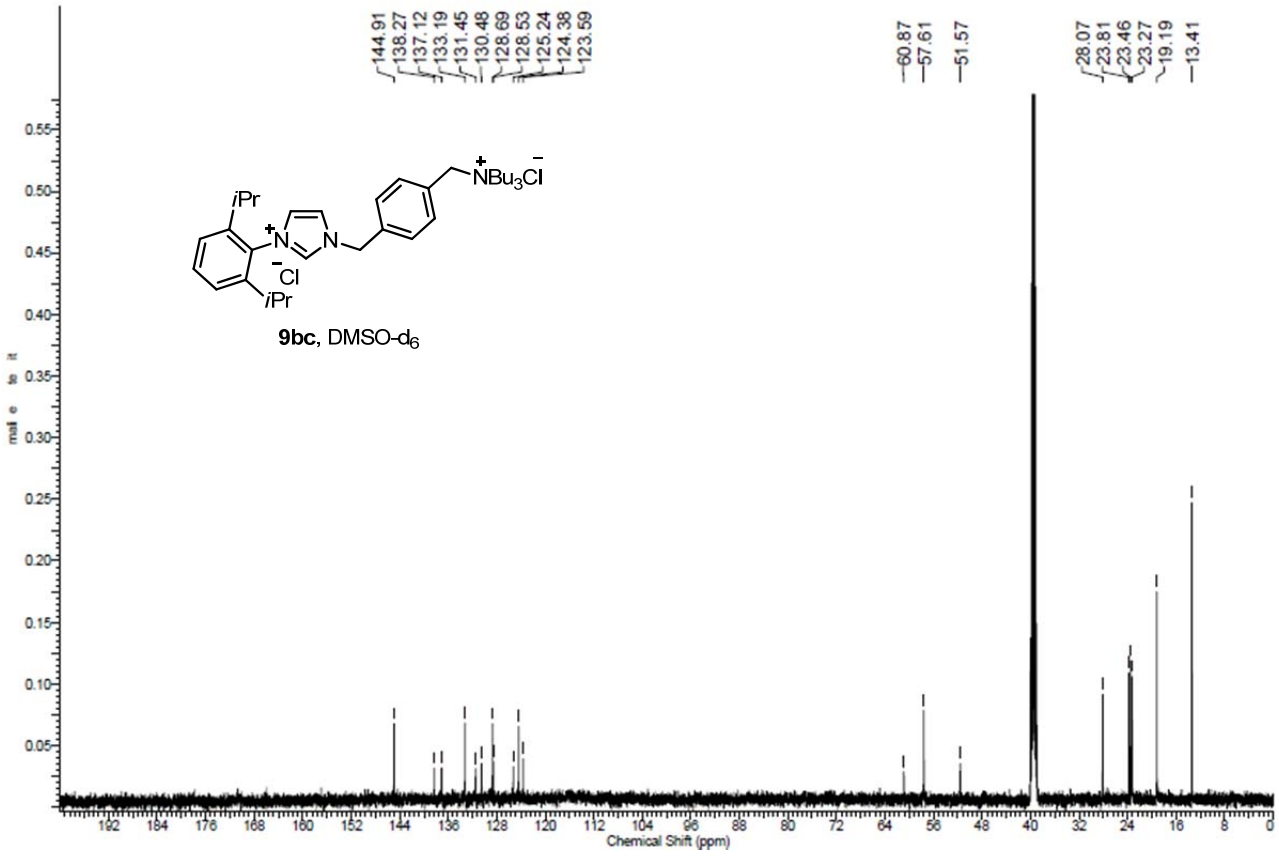
9ba, DMSO-d_6


10.34
8.37
8.37
8.15
8.15
7.69
7.68
7.65
7.63
7.62
7.46
7.44
5.77
4.59
3.23
3.21
3.20
3.18
2.23
2.22
2.20
2.19
2.18
2.16
1.31
1.30
1.28
1.13
1.12
1.10
iPr
NEt3Cl
Cl
iPr
9bb, DMSO-d6
1.00
1.01
1.03
5.20
2.04
2.00
2.14
6.40
2.11
9.85
12.60
Chemical Shift (ppm)

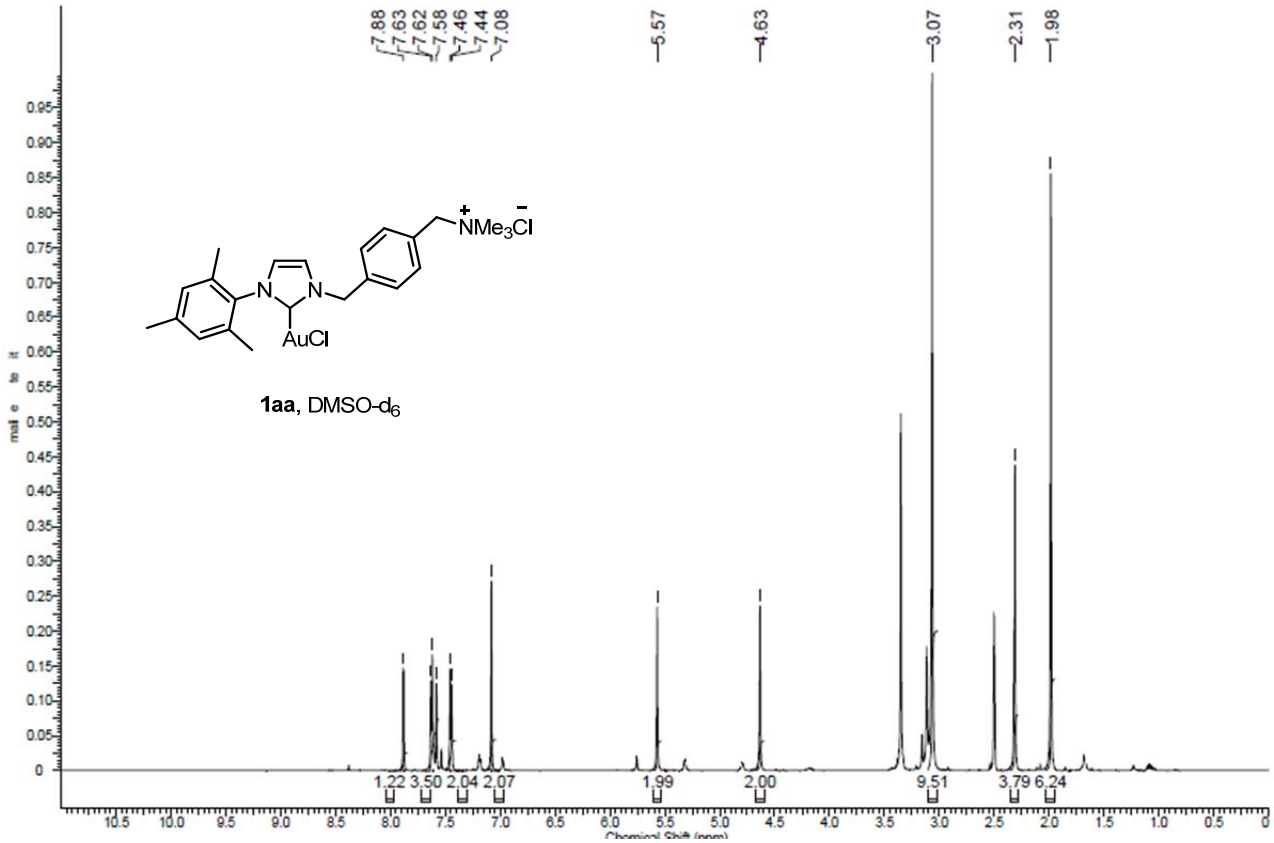

144.91
138.33
136.99
133.19
131.42
130.48
128.75
128.55
125.20
124.35
123.53
59.16
52.14
51.49
28.07
23.81
23.46
7.57
iPr
NEt3Cl
Cl
iPr
9bb, DMSO-d6
Chemical Shift (ppm)



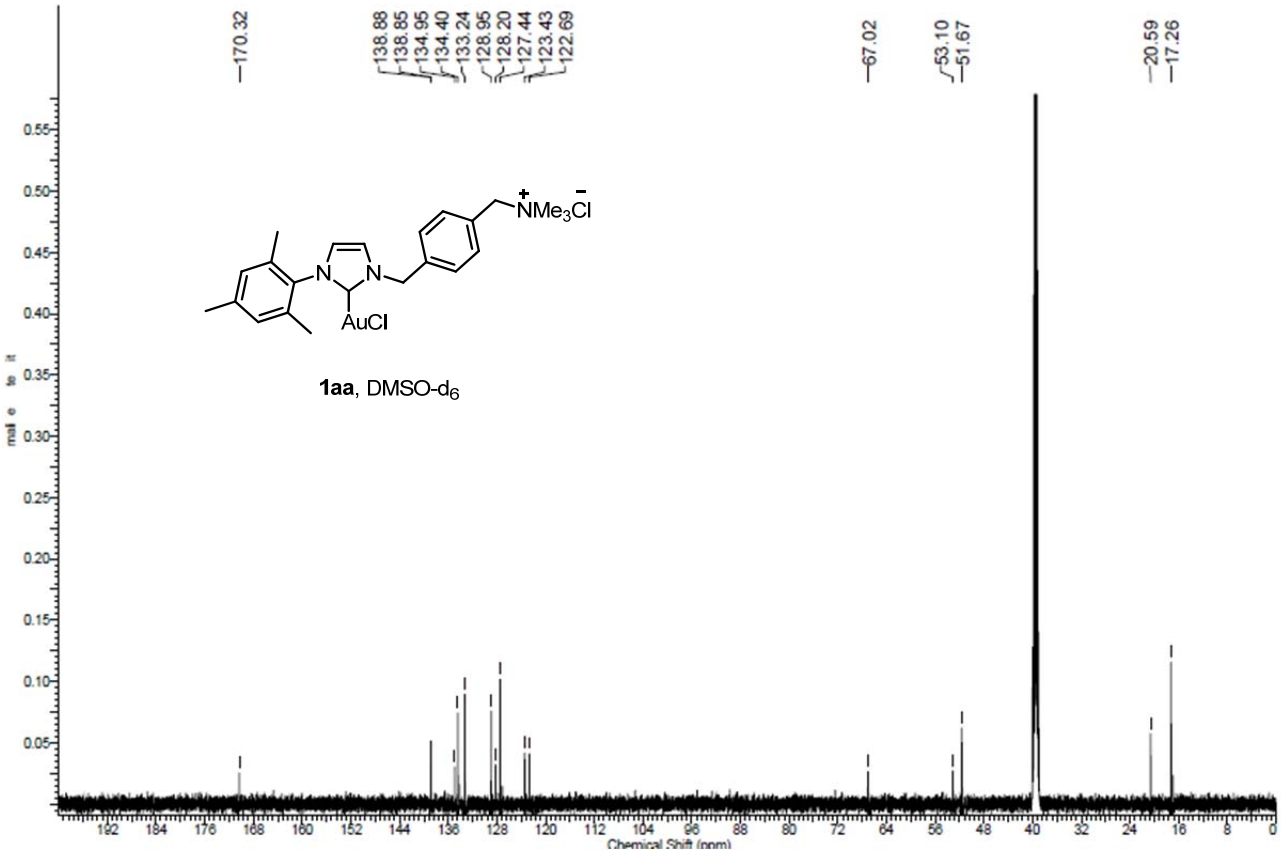
9bc, DMSO-d_6



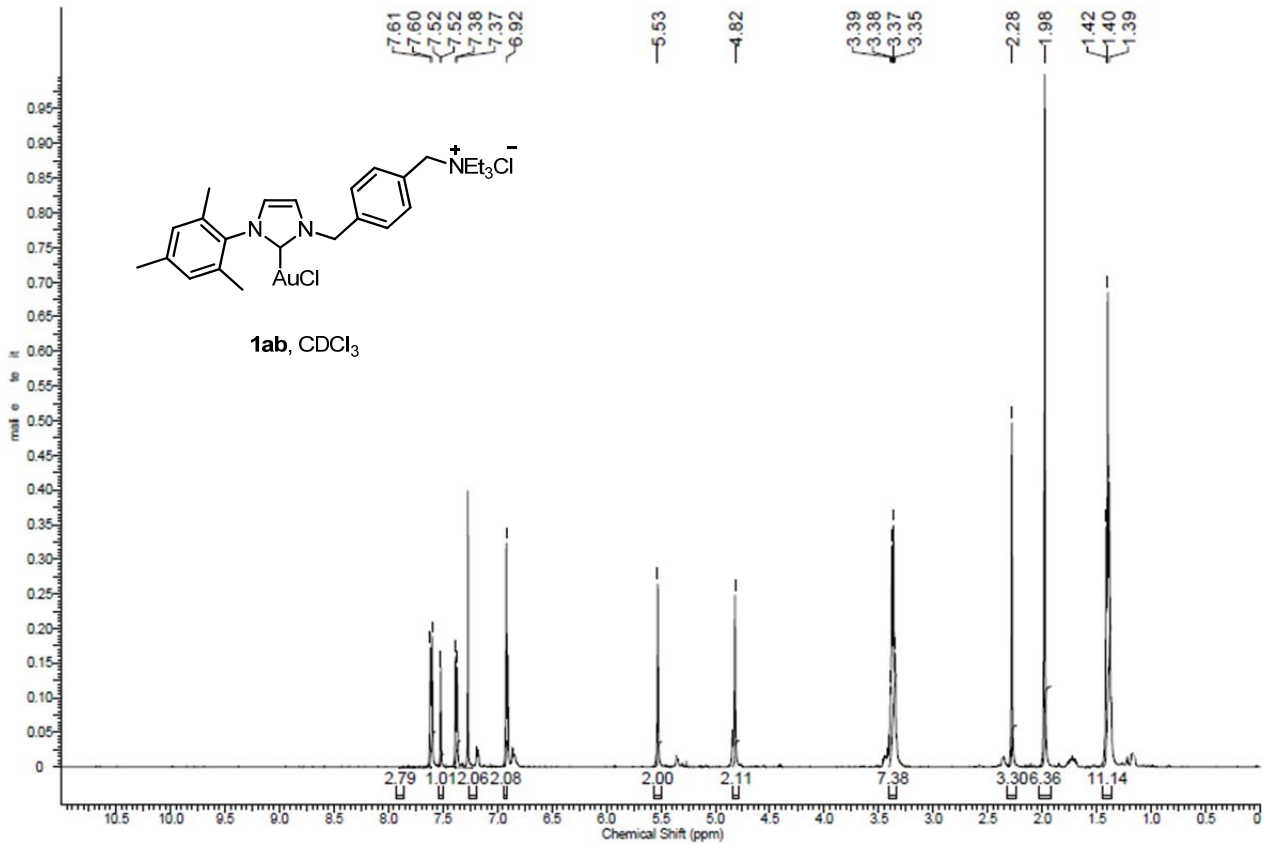
9bc, DMSO-d_6



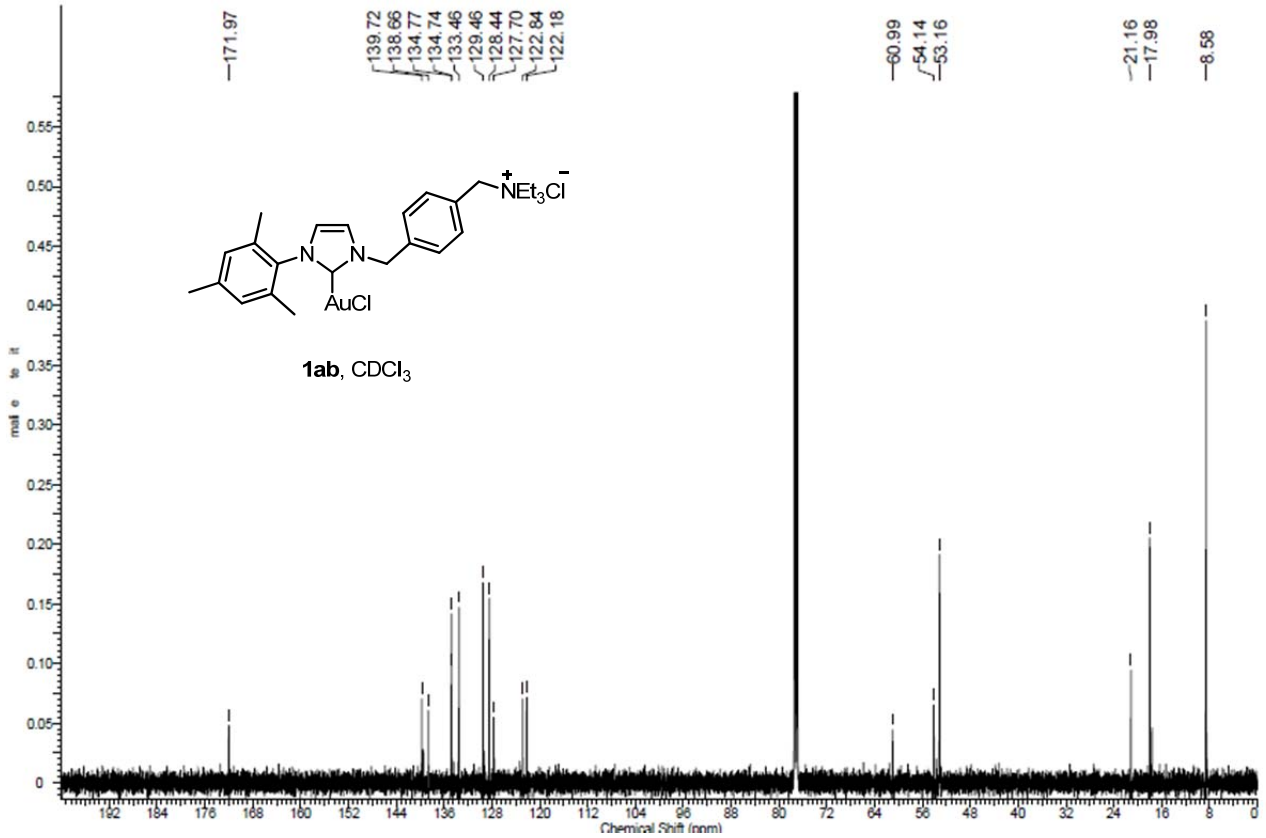
1aa, DMSO-d_6



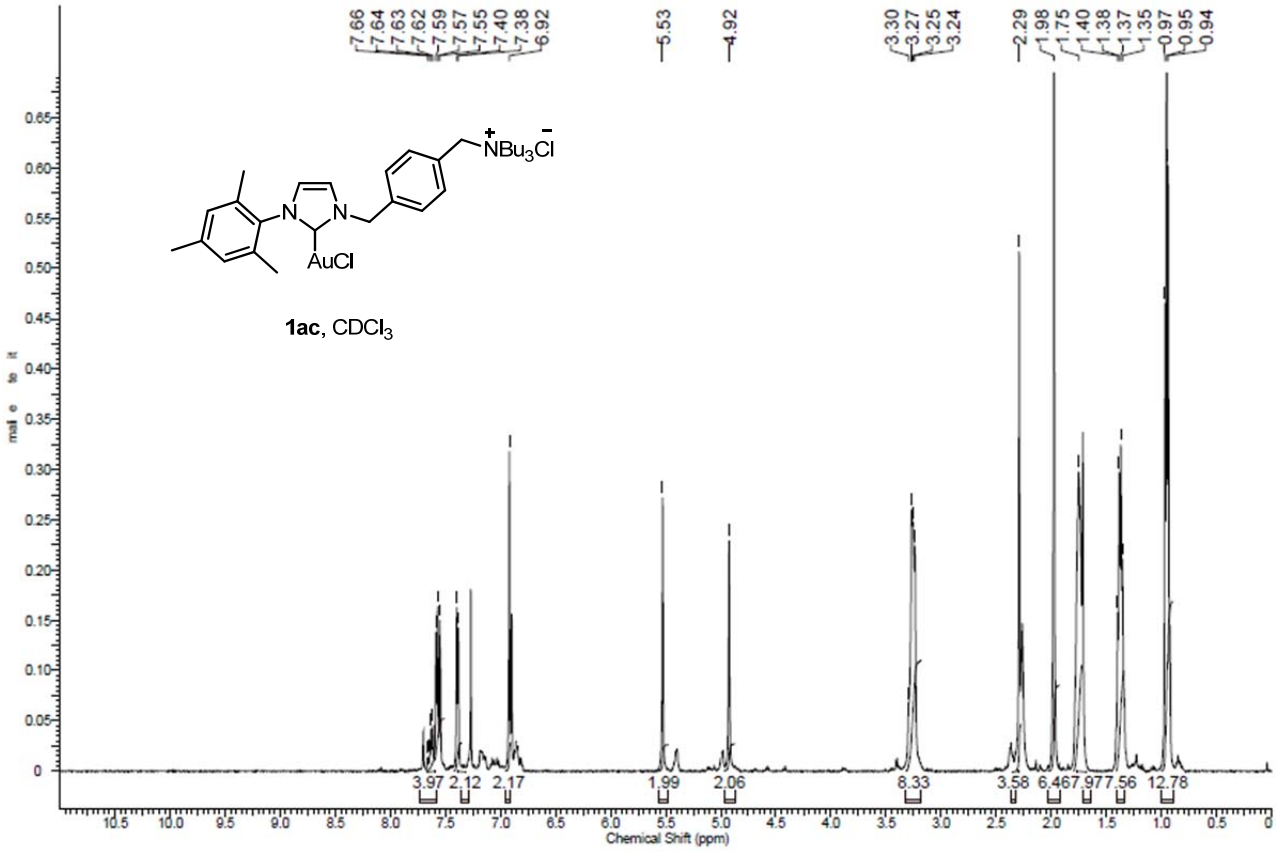
1aa, DMSO-d_6



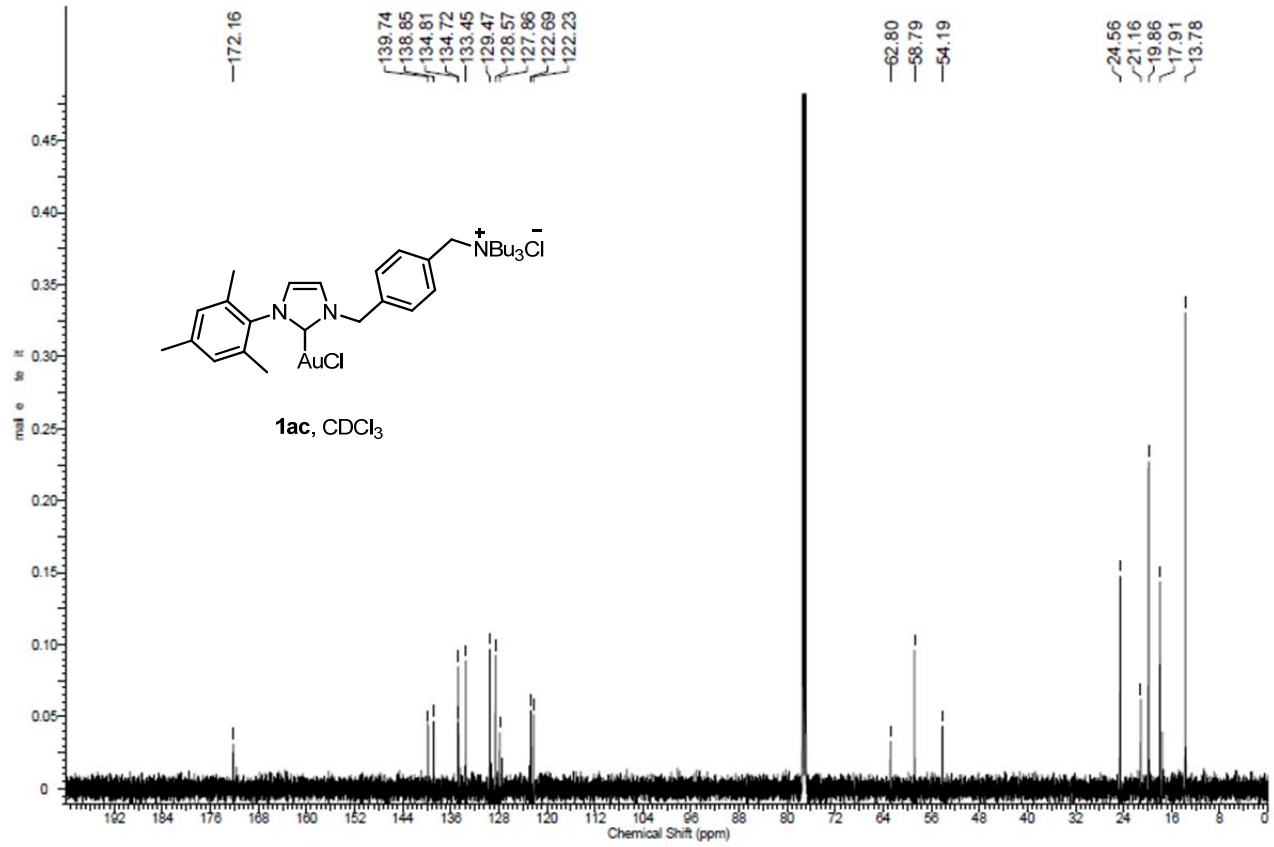
1ab, $CDCl_3$



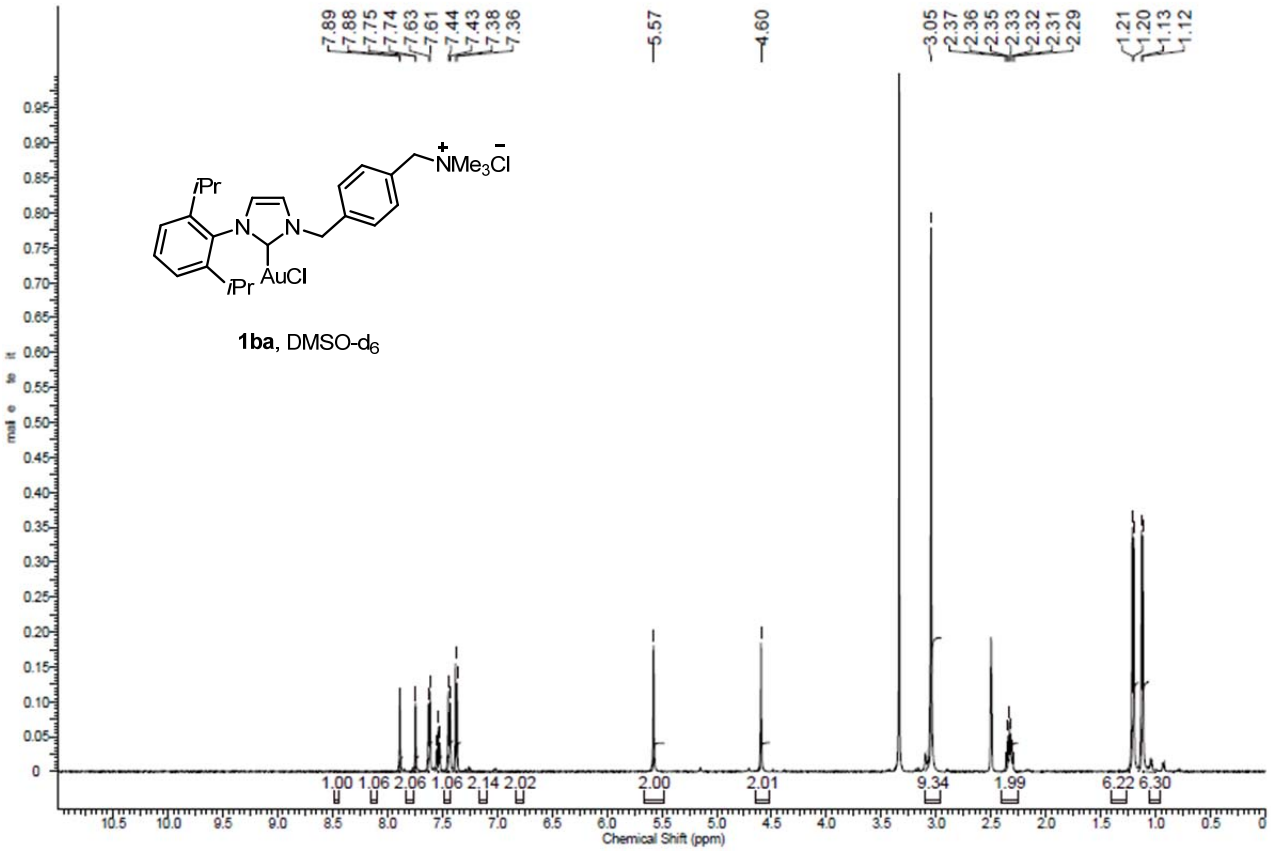
1ab, $CDCl_3$



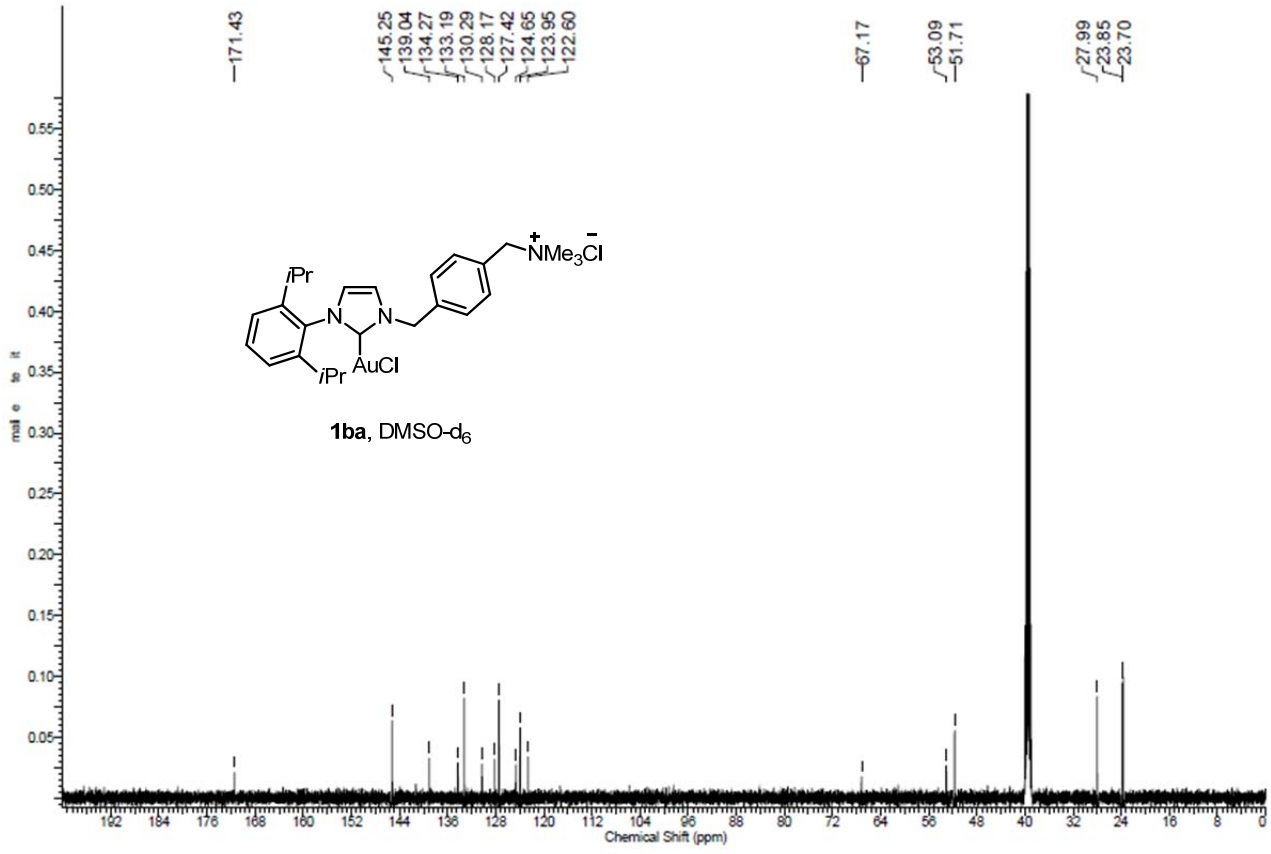
1ac, $CDCl_3$



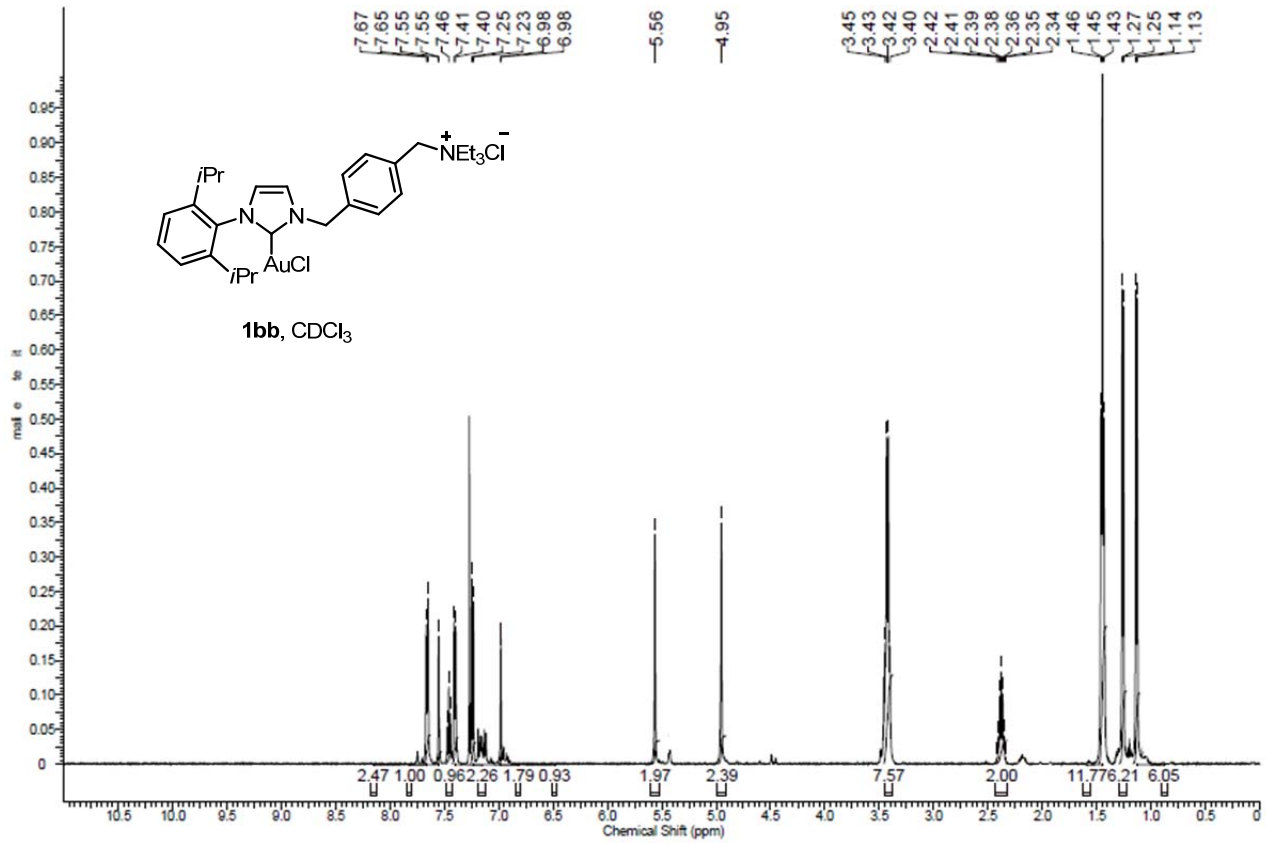
1ac, $CDCl_3$



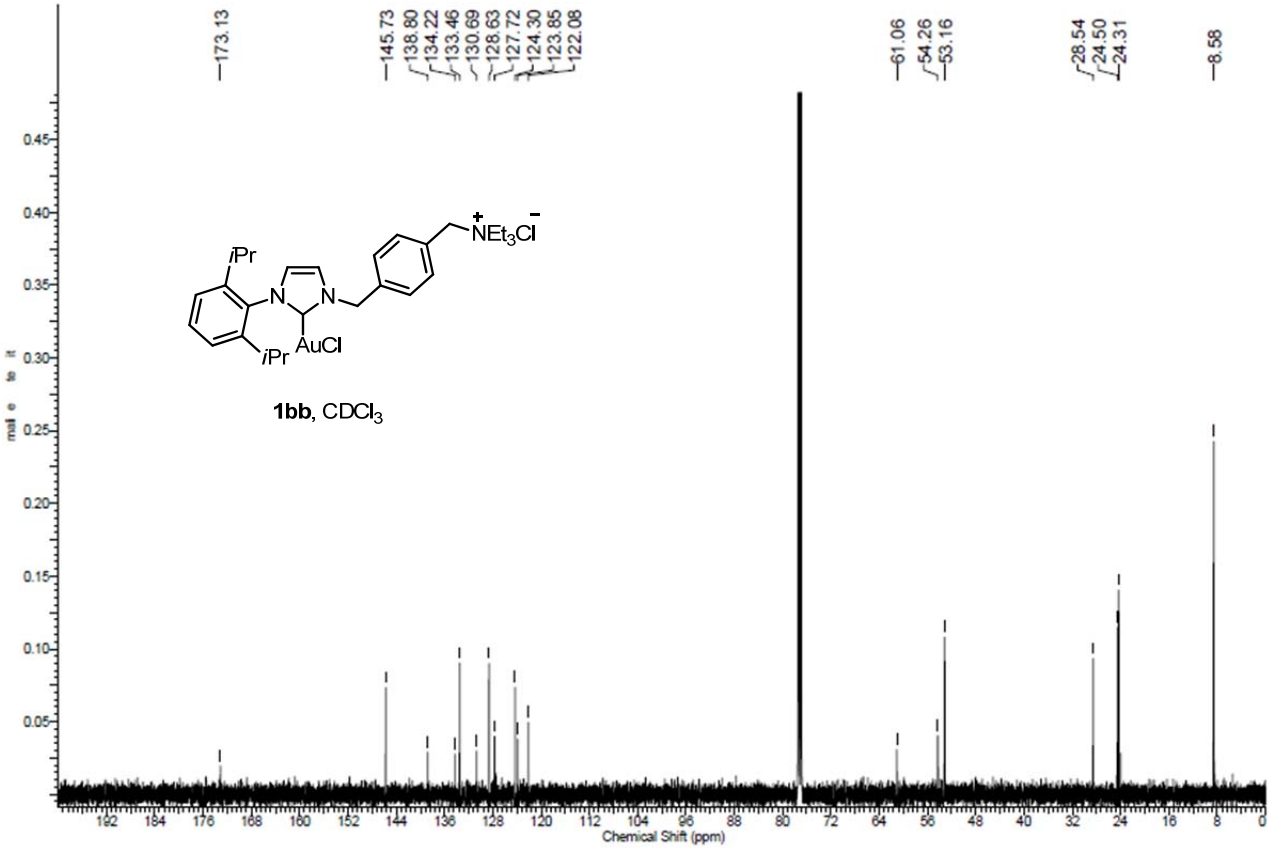
1ba, DMSO-d_6



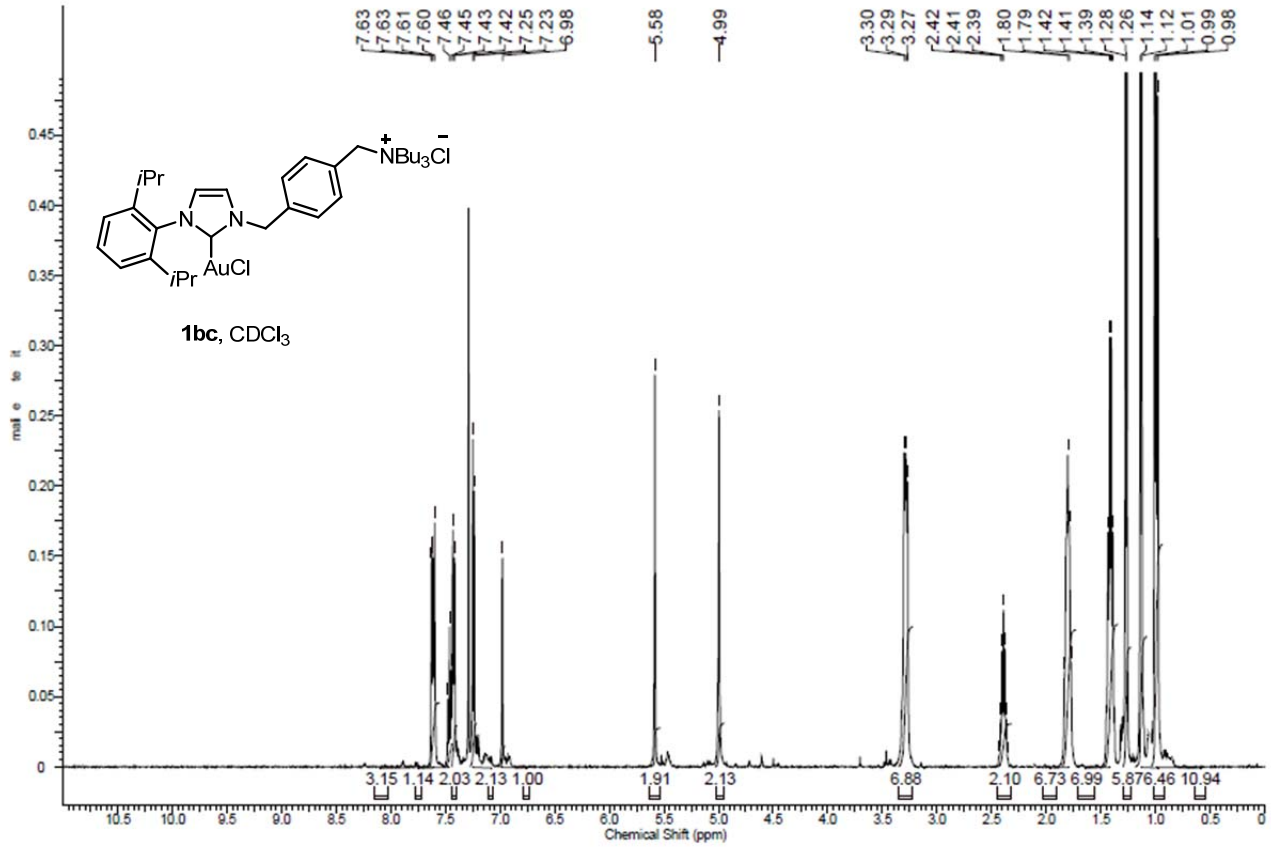
1ba, DMSO-d_6

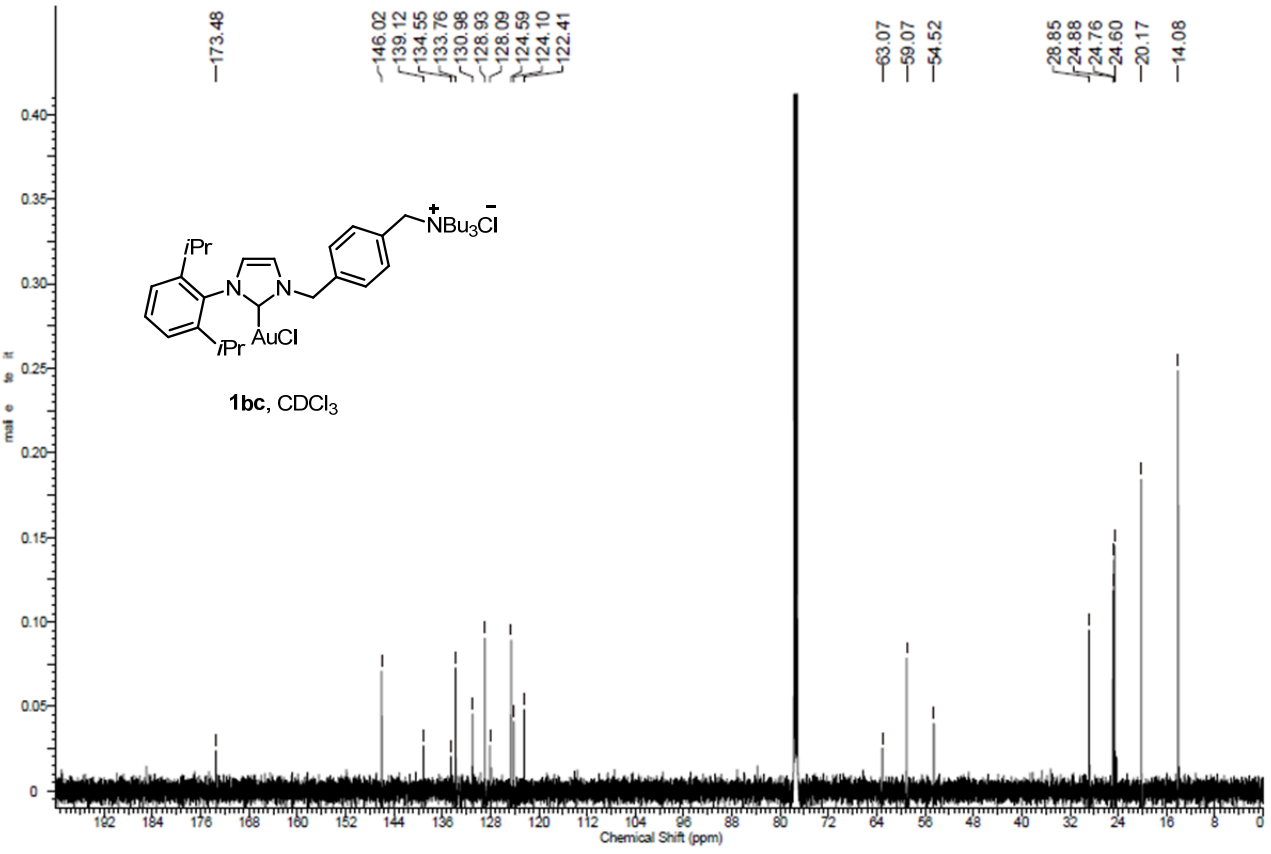


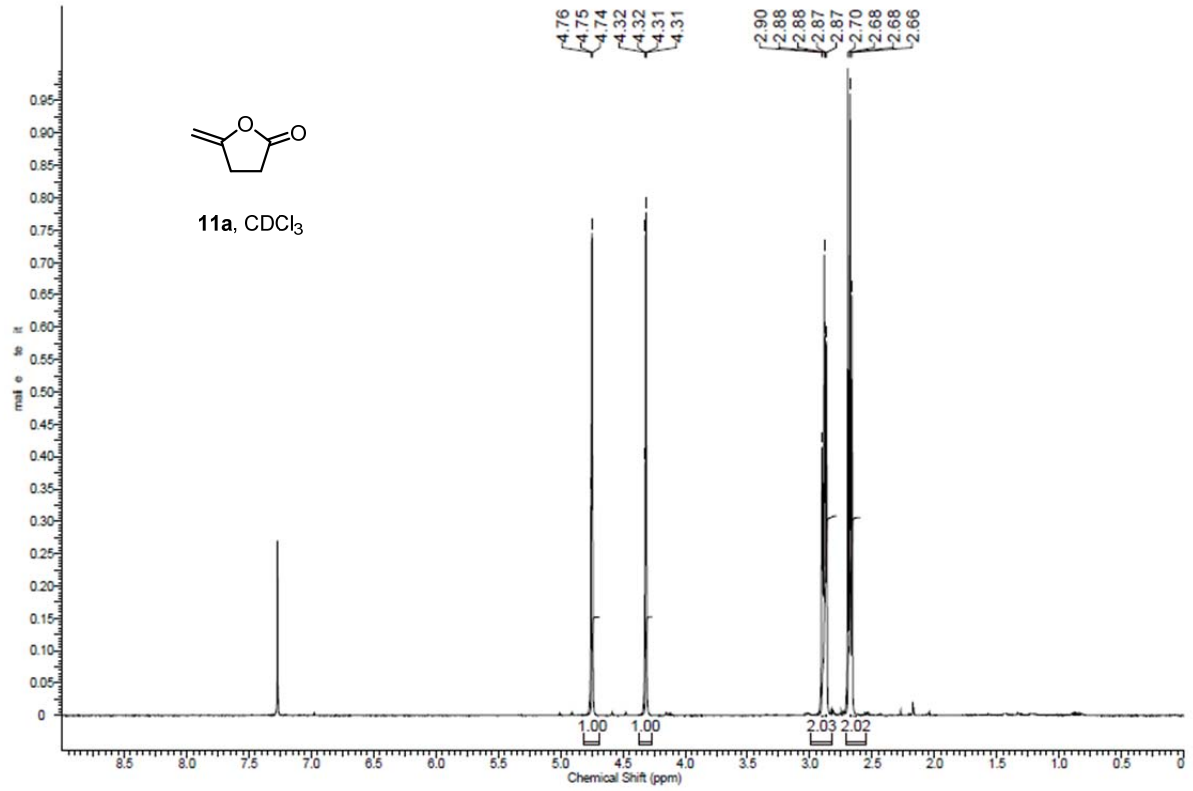
1bb, $CDCl_3$



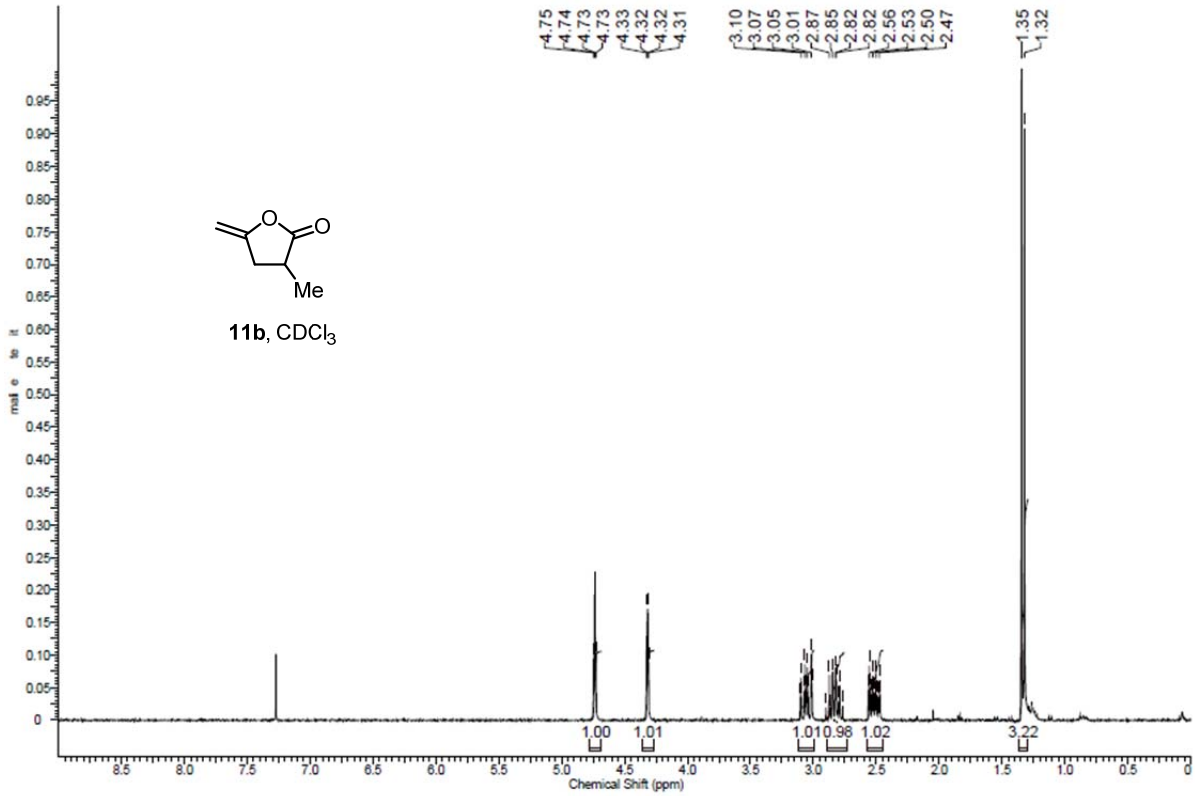
1bb, $CDCl_3$


7.63
7.63
7.61
7.60
7.46
7.45
7.43
7.42
7.25
7.23
6.98
5.58
4.99
3.30
3.29
3.27
2.42
2.41
2.39
1.80
1.79
1.42
1.41
1.39
1.28
1.26
1.14
1.12
1.01
0.99
0.98
iPr
iPr
AuCl
NBu3Cl
1bc, CDCl3
3.15 1.14 2.03 2.13 1.00
1.91
2.13
6.88
2.10
6.73 6.99 5.87 6.46 10.94
Chemical Shift (ppm)

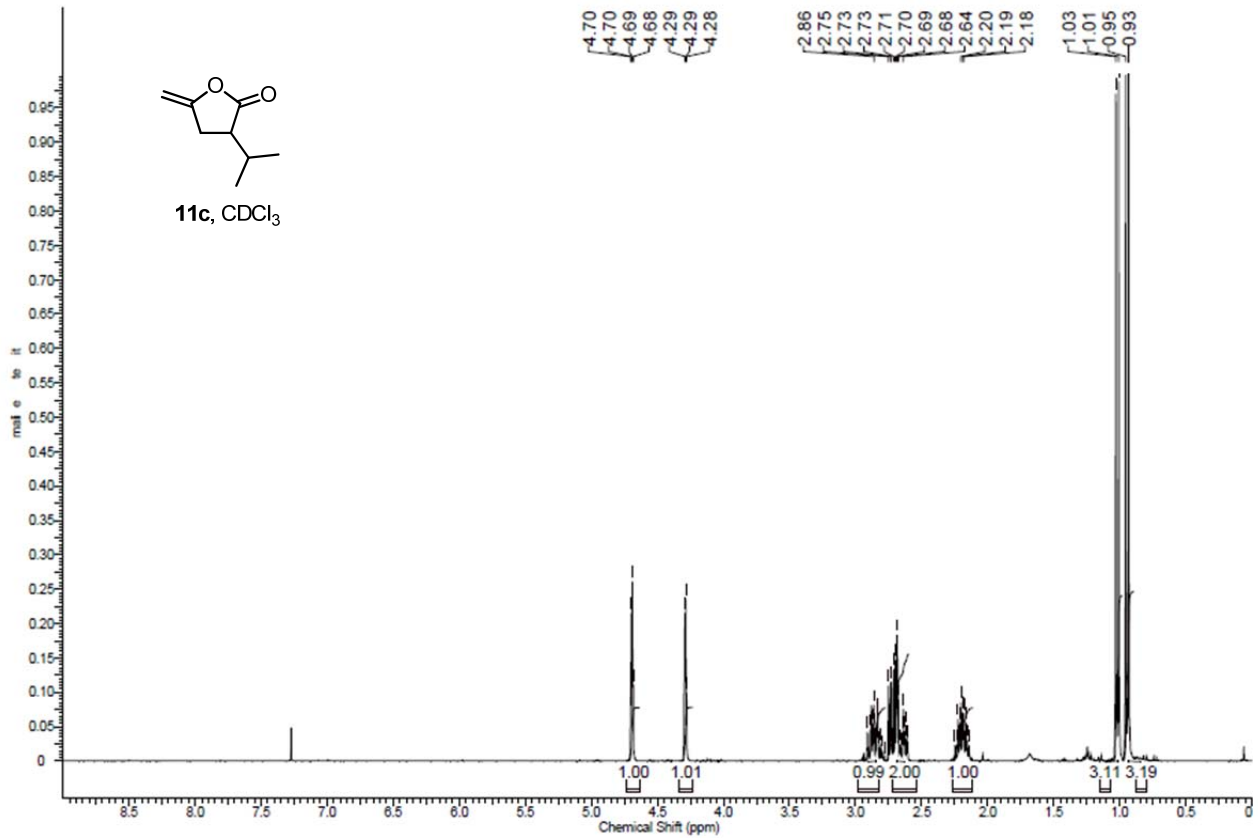

173.48
146.02
139.12
134.55
133.76
130.98
128.93
128.09
124.59
124.10
122.41
63.07
59.07
54.52
28.85
24.88
24.76
24.60
20.17
14.08
iPr
iPr
AuCl
NBu3Cl
1bc, CDCl3
Chemical Shift (ppm)



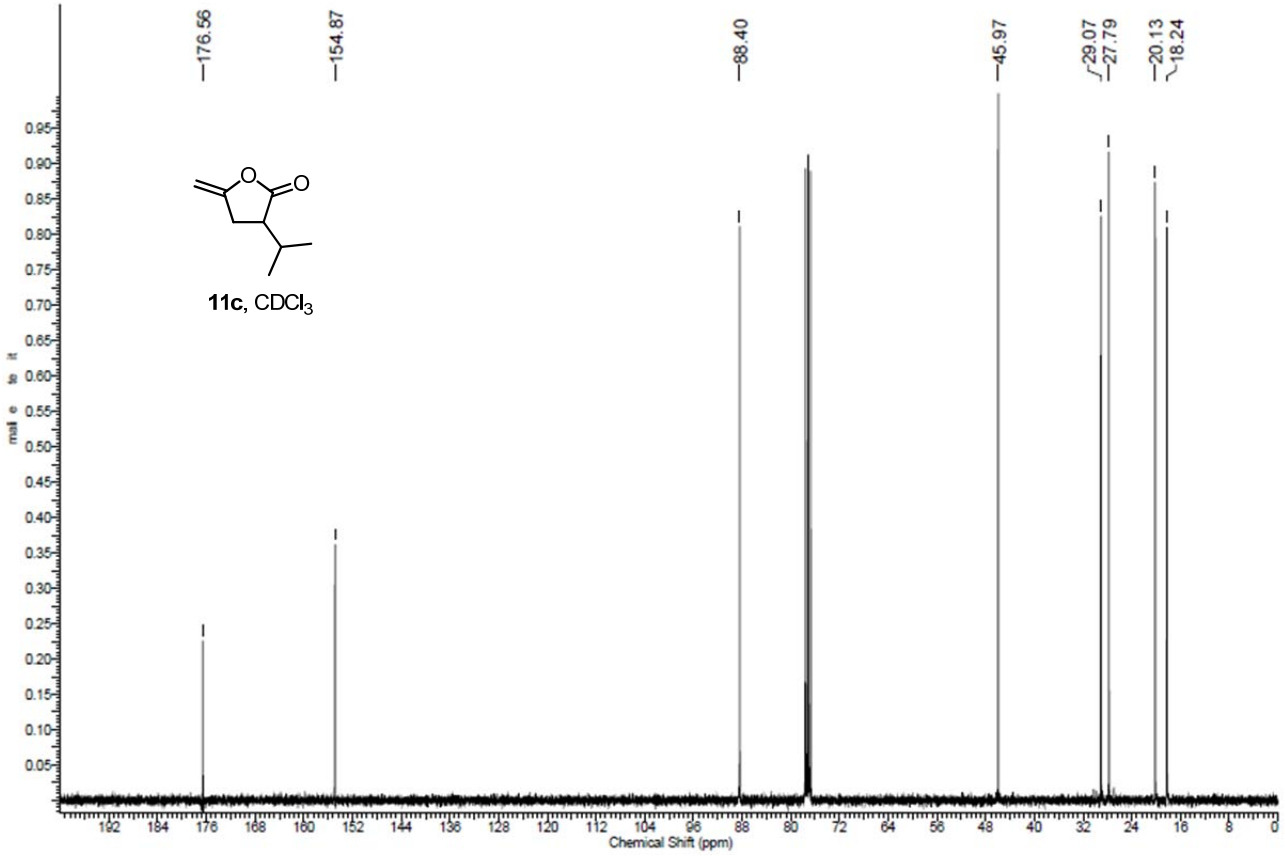
11a, $CDCl_3$



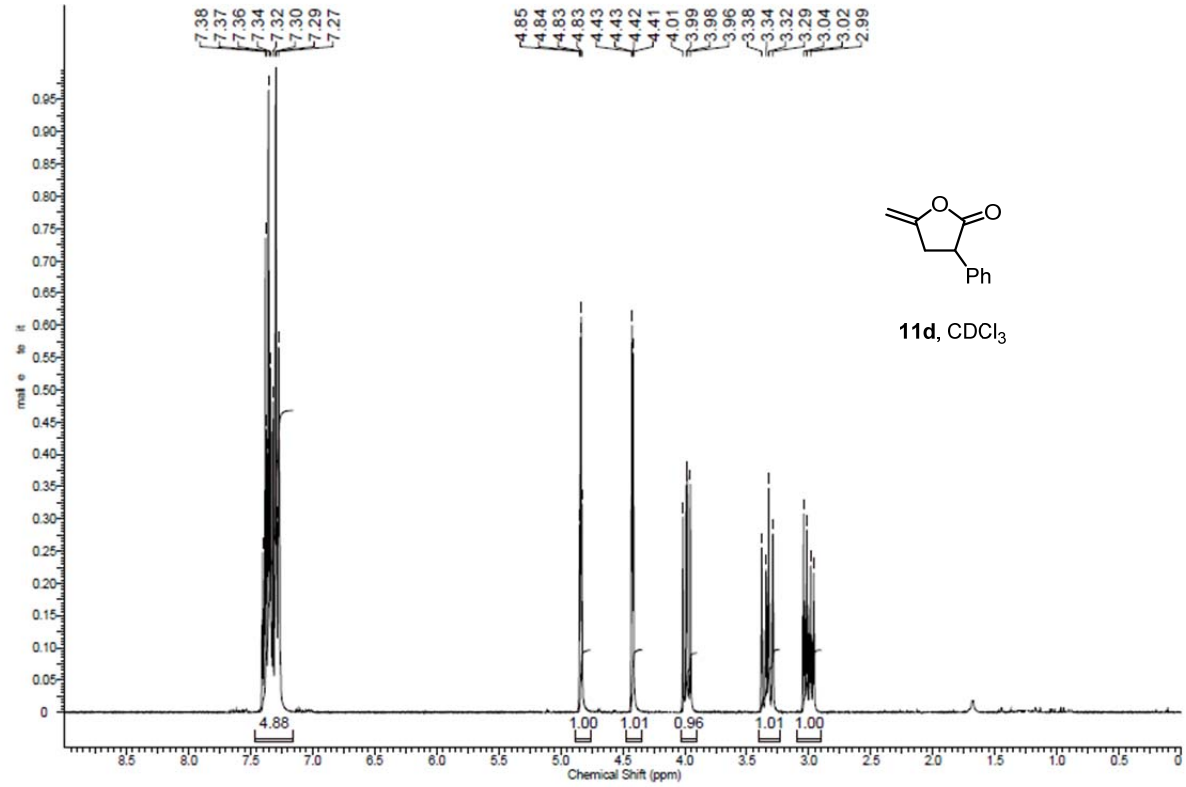
11b, $CDCl_3$



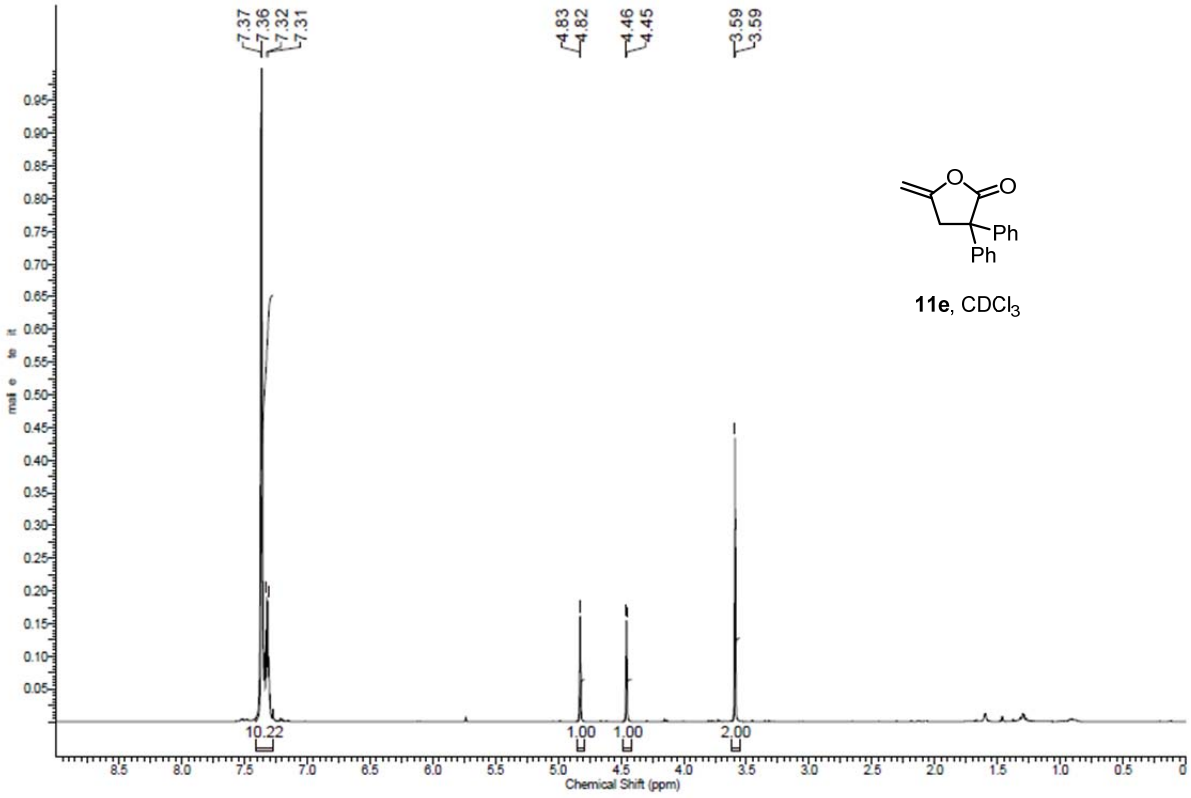
11c, $CDCl_3$



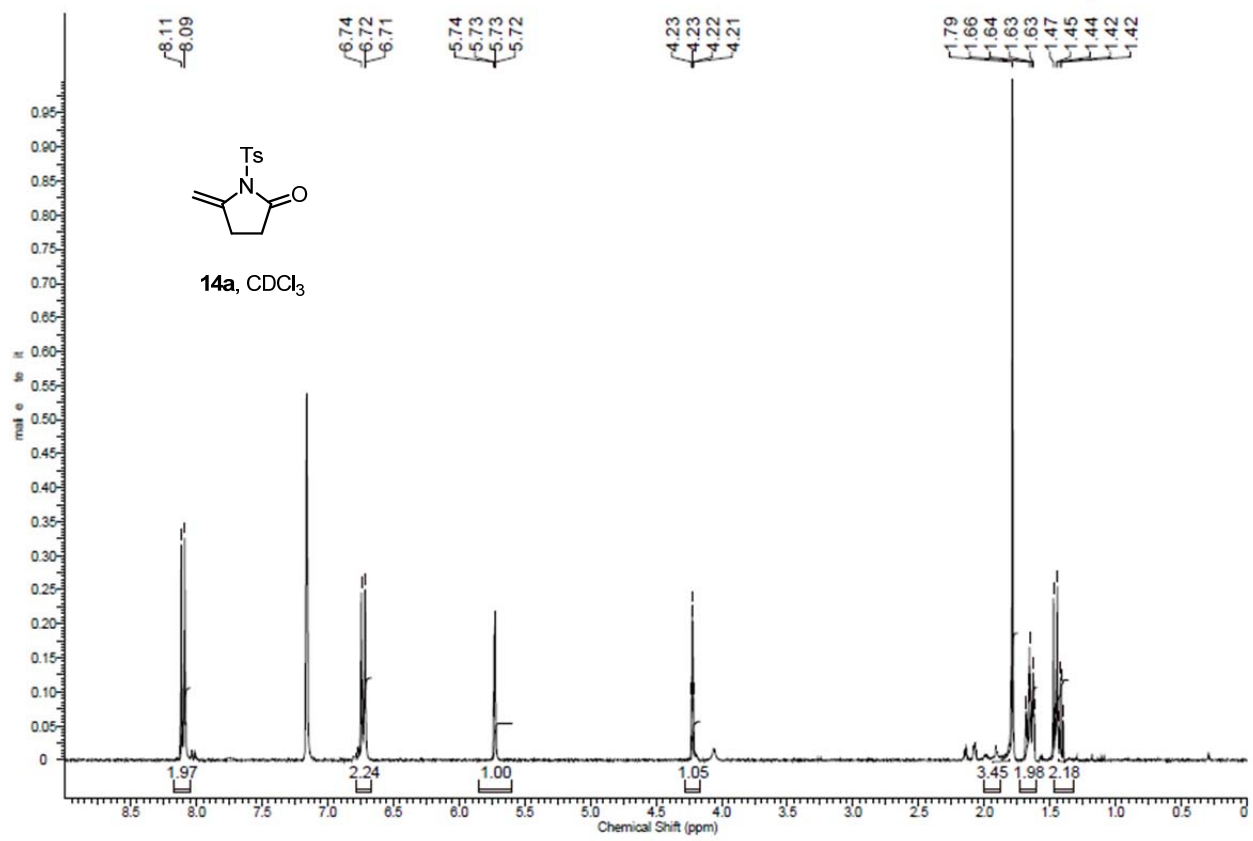
11c, $CDCl_3$

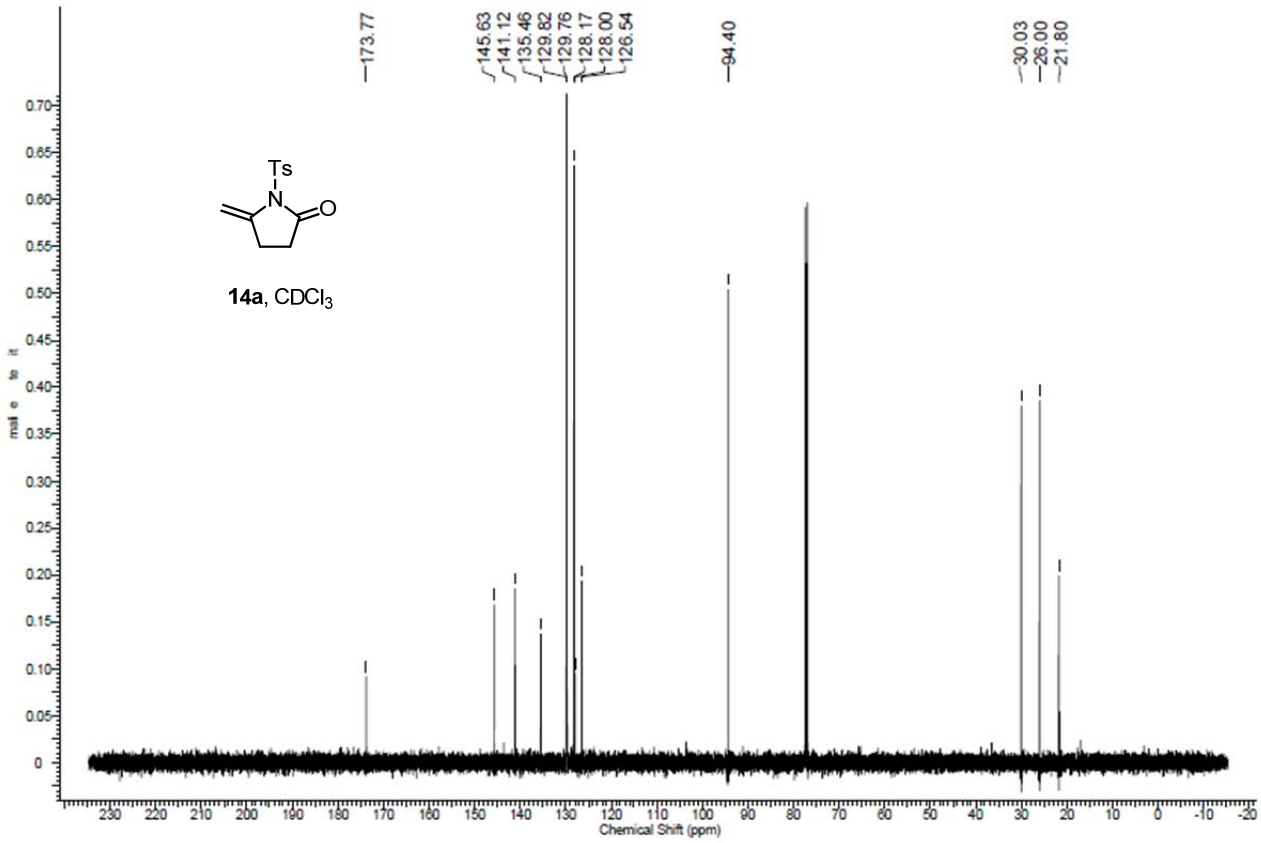


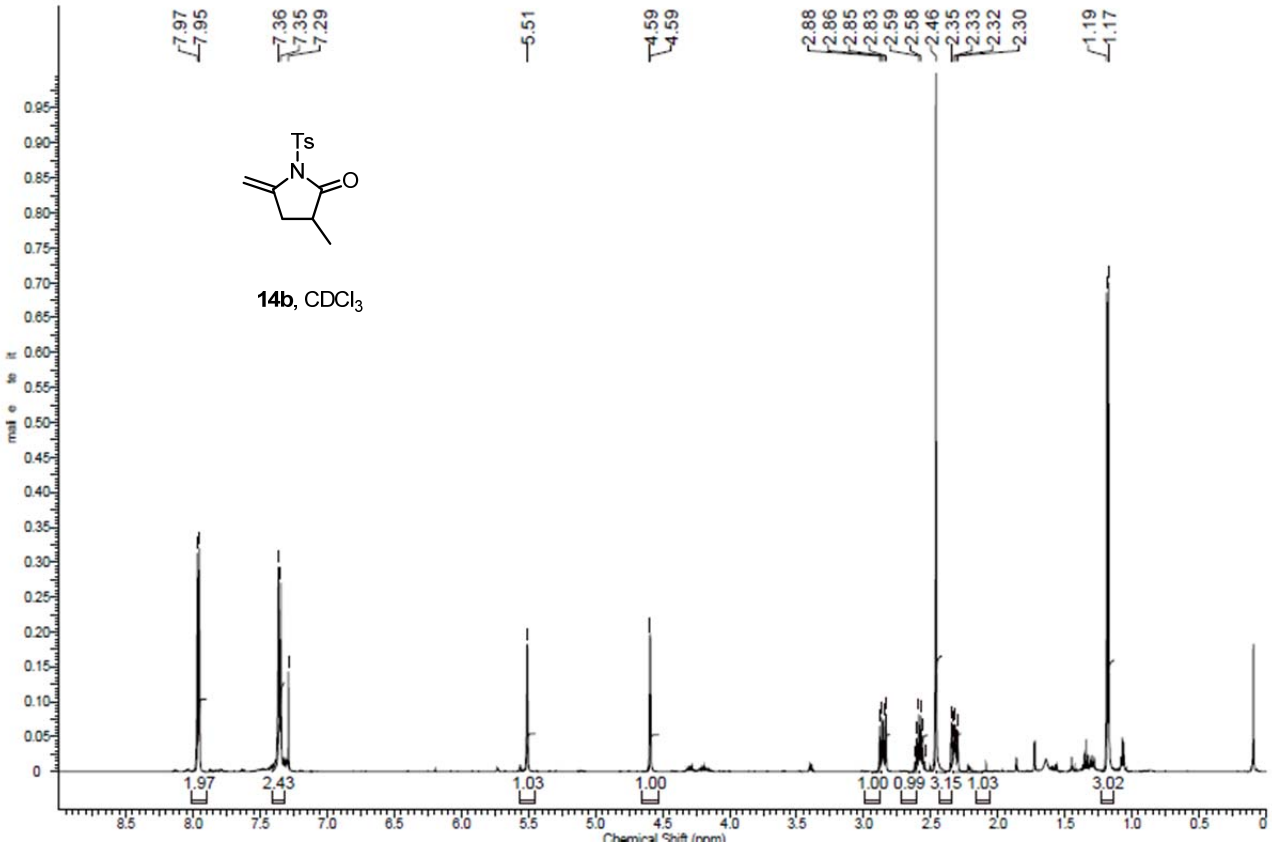
11d, $CDCl_3$



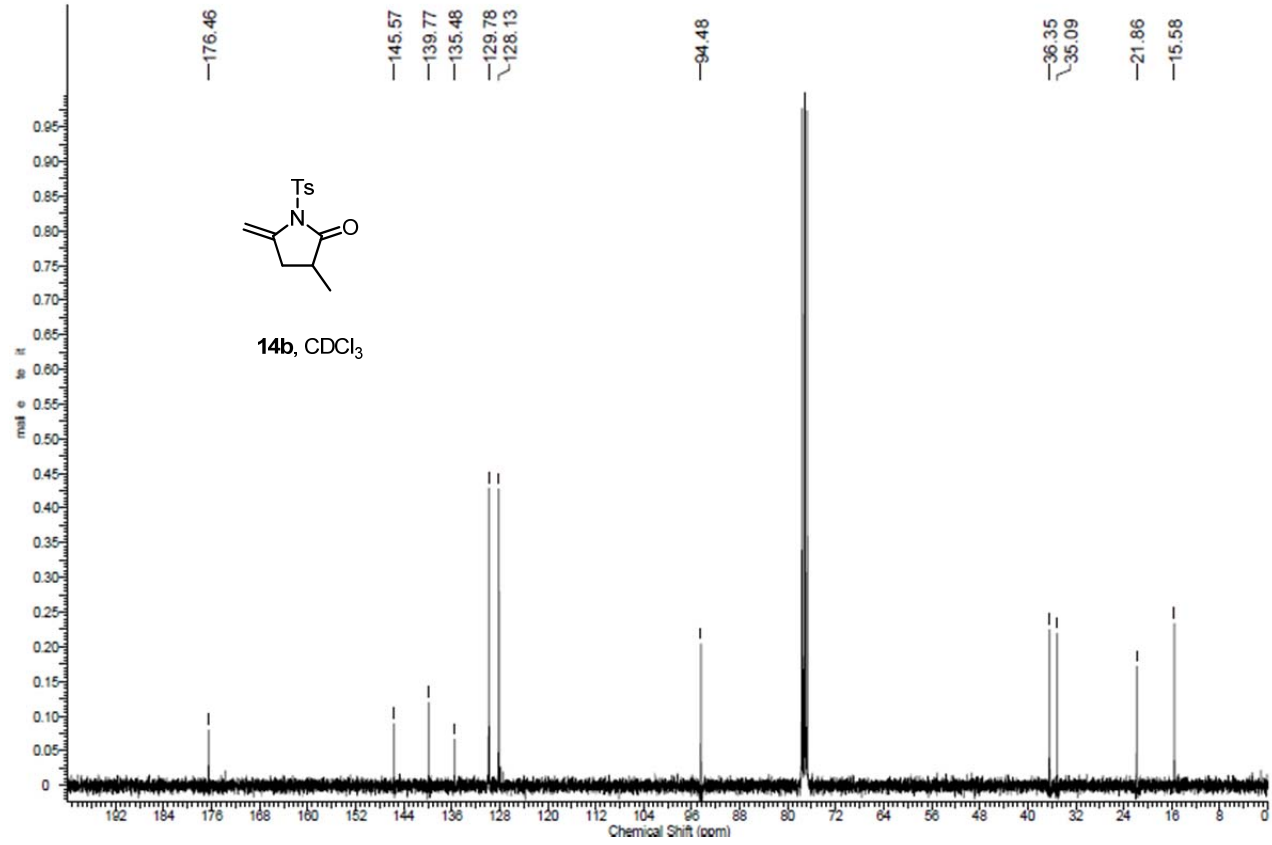
11e, $CDCl_3$


8.11
8.09
6.74
6.72
6.71
5.74
5.73
5.73
5.72
4.23
4.23
4.22
4.21
1.79
1.66
1.64
1.63
1.63
1.47
1.45
1.44
1.42
1.42
Ts
N
O
14a, CDCl3
1.97
2.24
1.00
1.05
3.45
1.98
2.18
Chemical Shift (ppm)

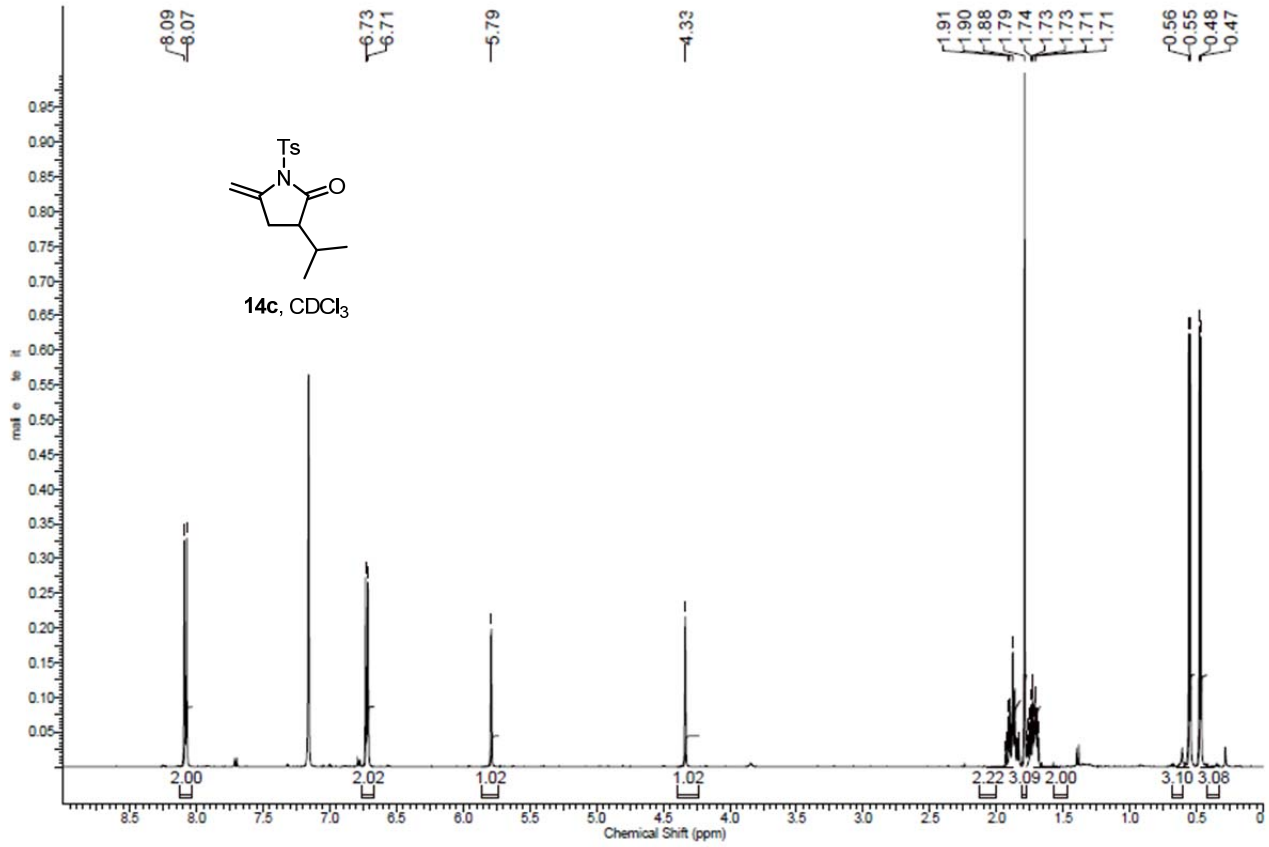

173.77
145.63
141.12
135.46
129.82
129.76
128.17
128.00
126.54
94.40
30.03
26.00
21.80
Ts
N
O
14a, CDCl3
Chemical Shift (ppm)

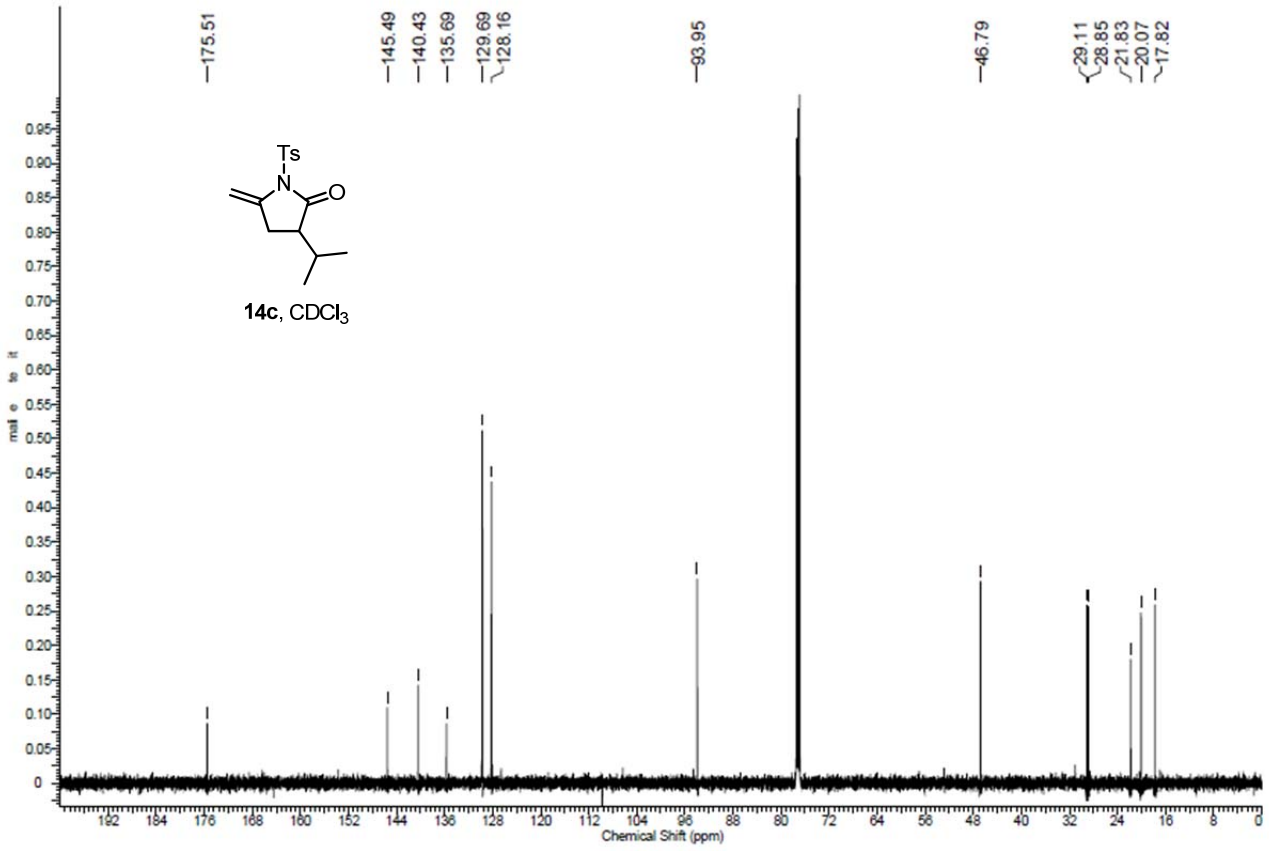


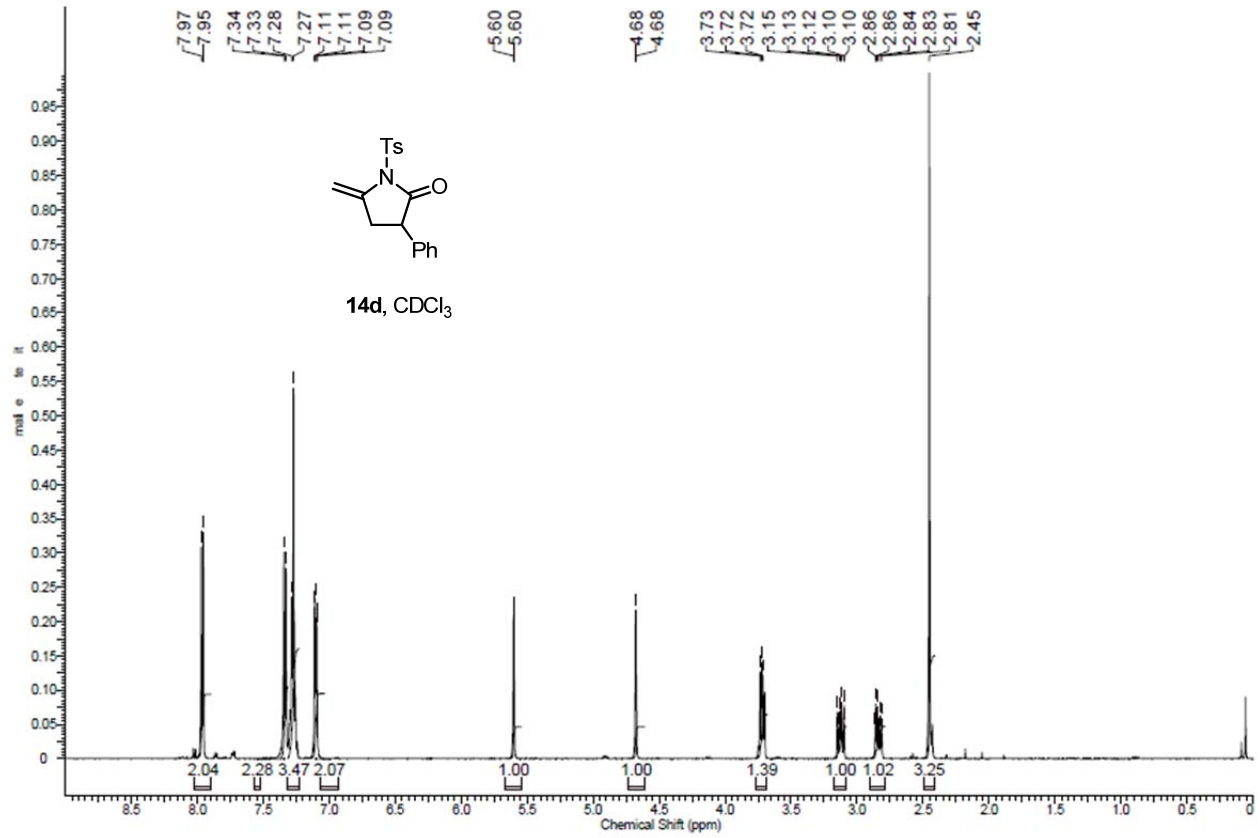
14b, $CDCl_3$



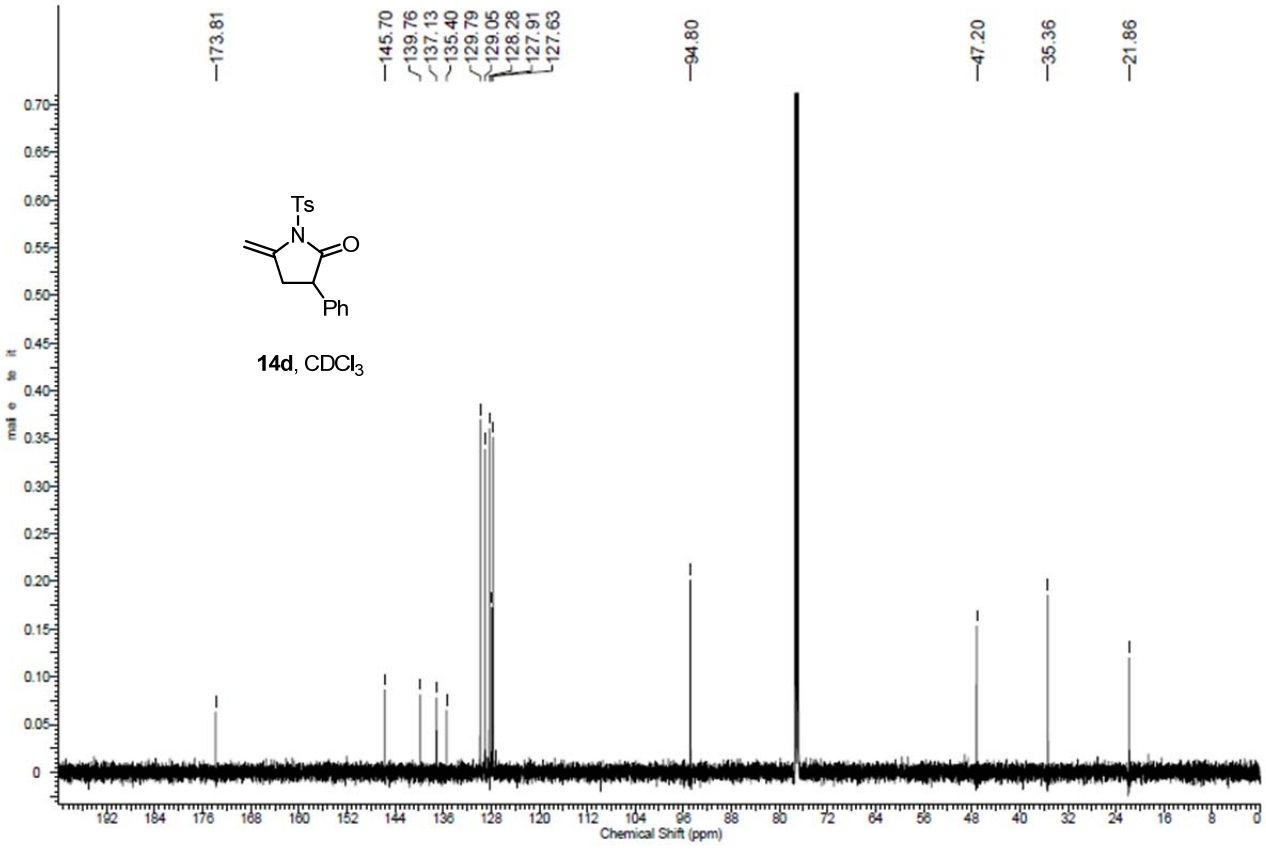
14b, $CDCl_3$


8.09
8.07
6.73
6.71
5.79
4.33
1.91
1.90
1.88
1.79
1.74
1.73
1.73
1.71
1.71
0.56
0.55
0.48
0.47
Ts
N
O
14c, CDCl3
2.00
2.02
1.02
1.02
2.22
3.09
2.00
3.10
3.08
Chemical Shift (ppm)

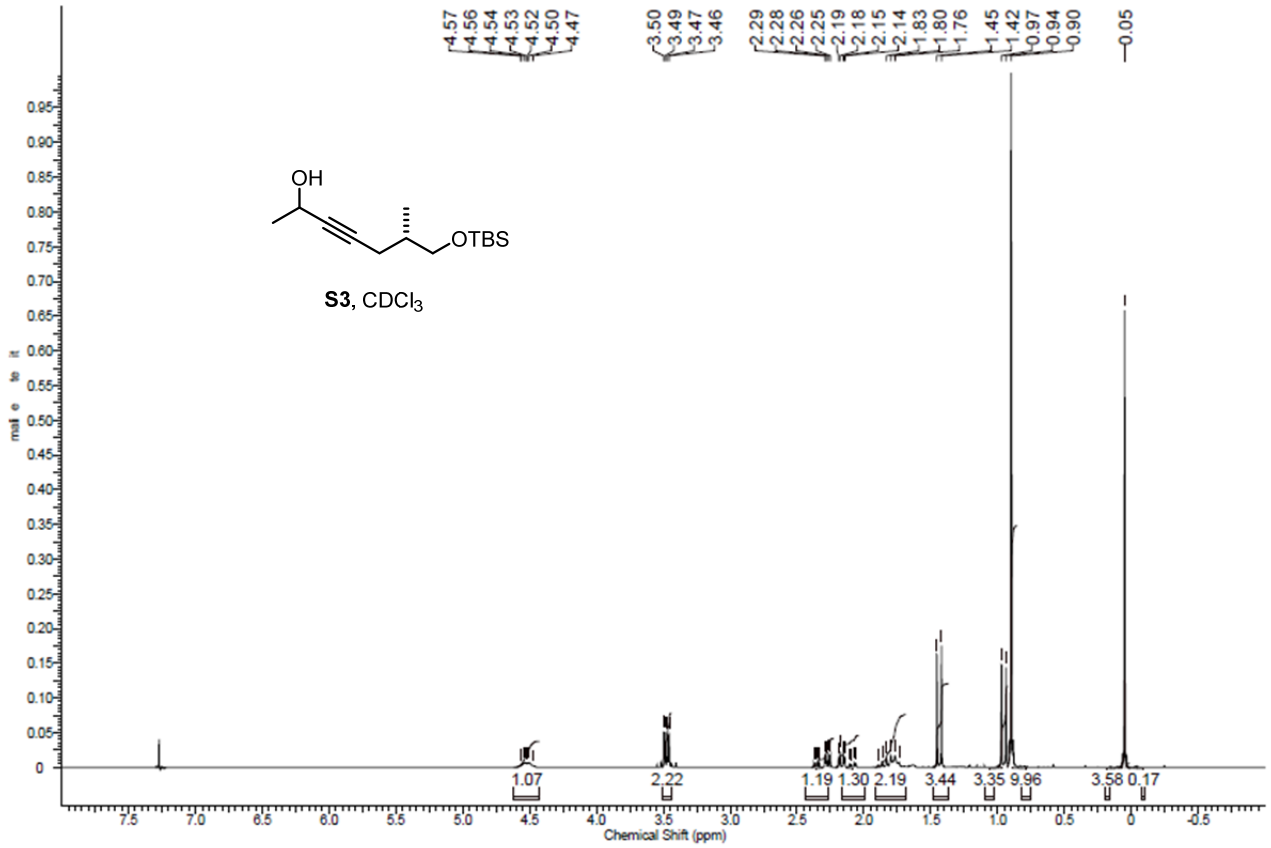

175.51
145.49
140.43
135.69
129.69
128.16
93.95
46.79
29.11
28.85
21.83
20.07
17.82
Ts
N
O
14c, CDCl3
Chemical Shift (ppm)

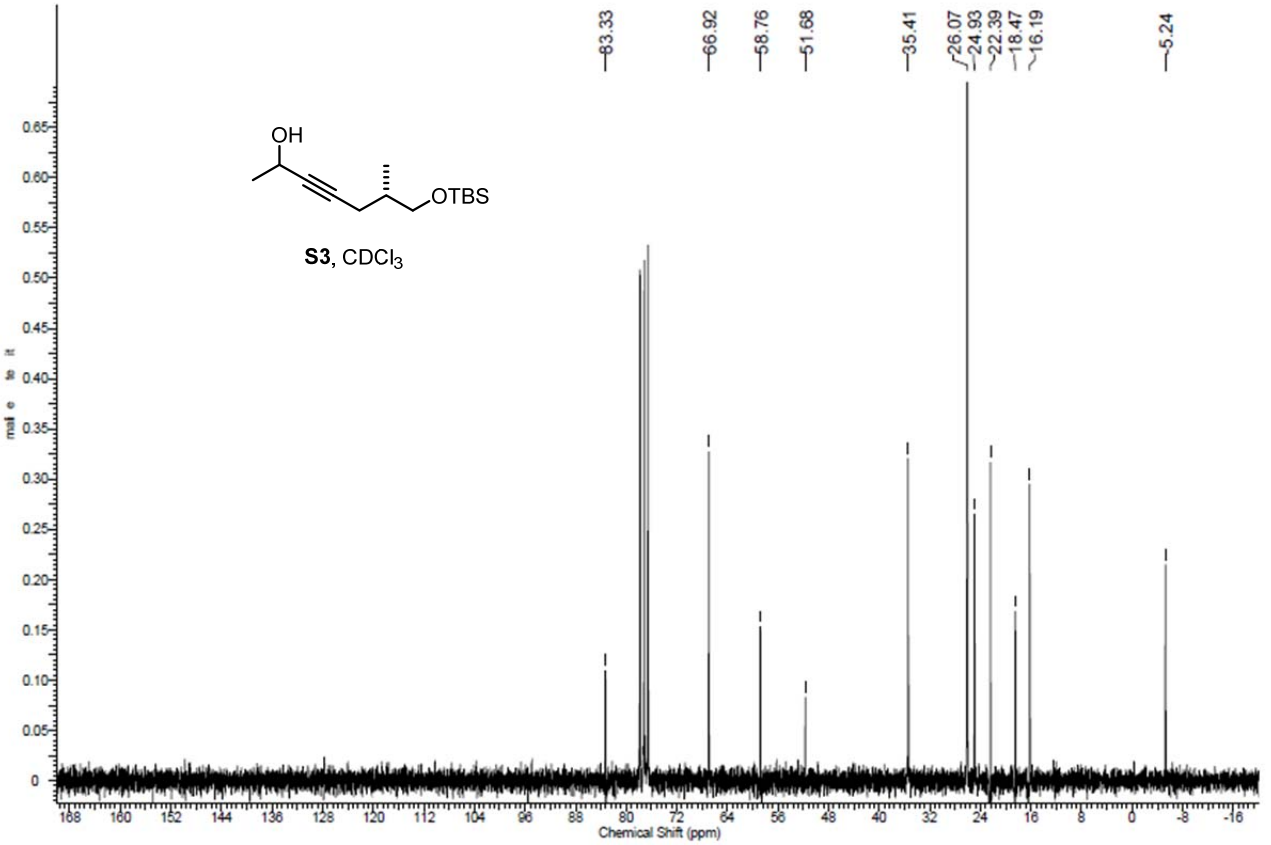


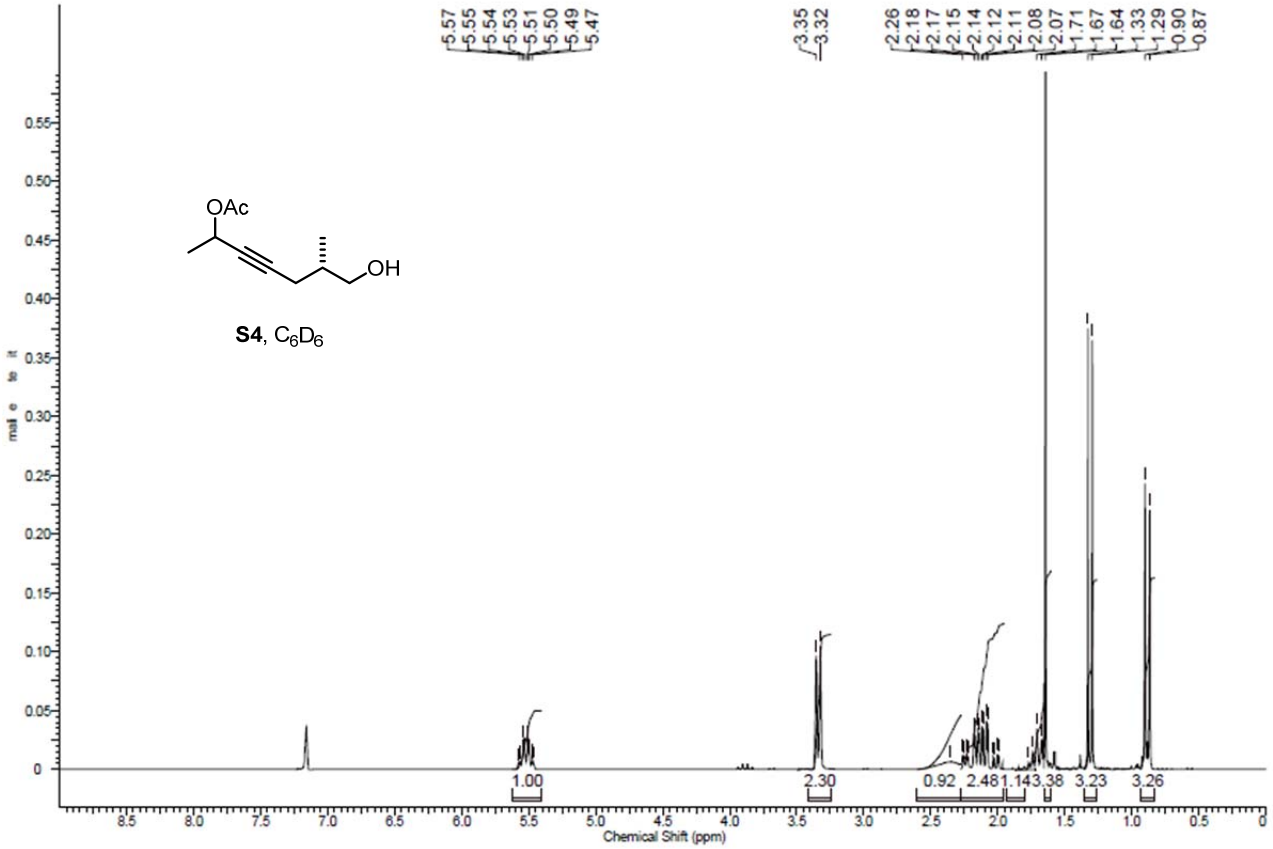
14d, $CDCl_3$

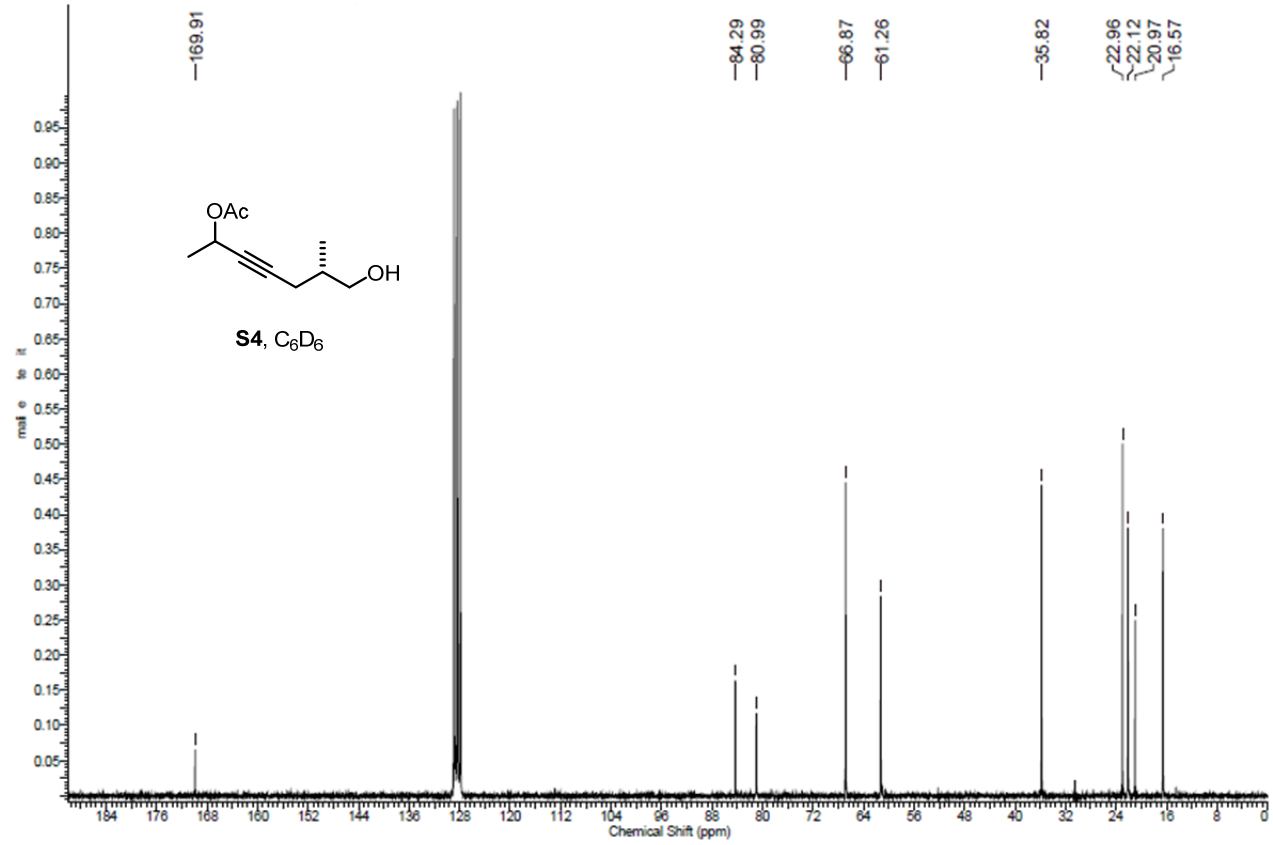


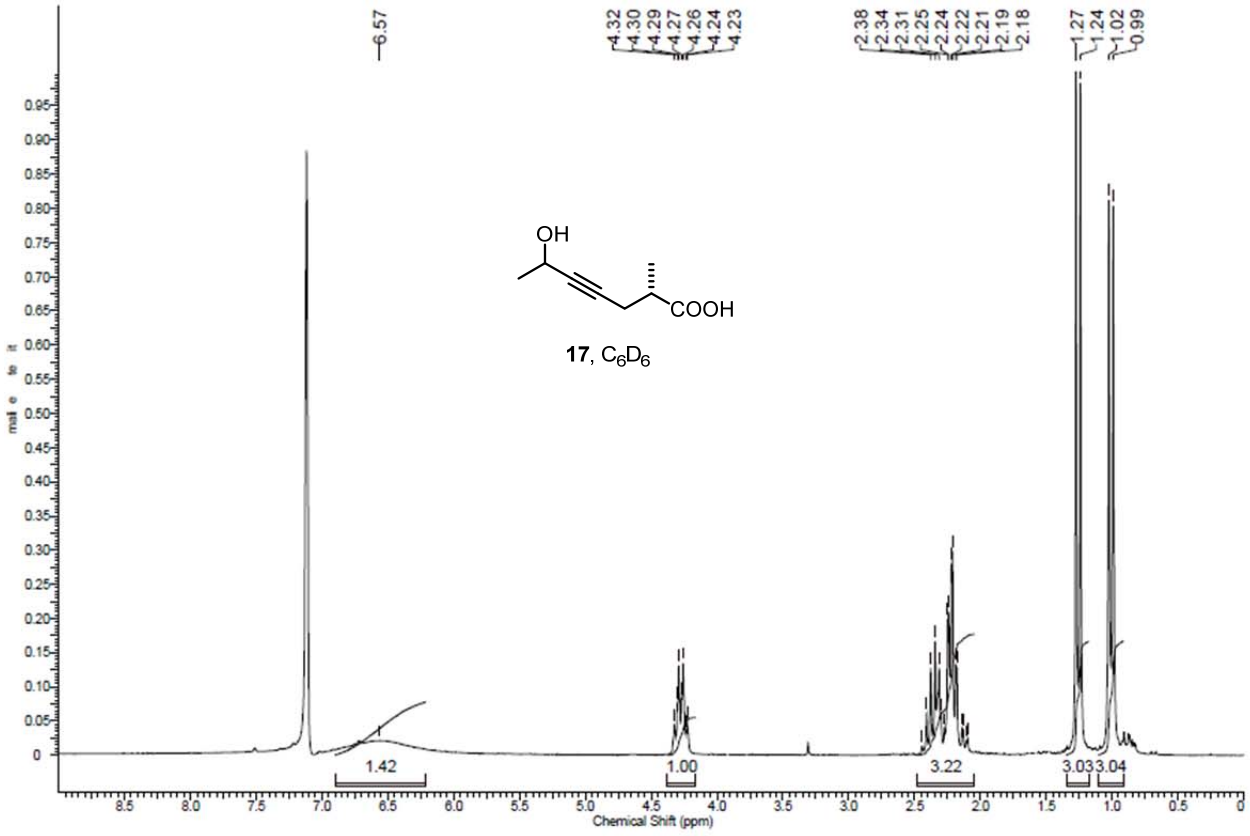
14d, $CDCl_3$

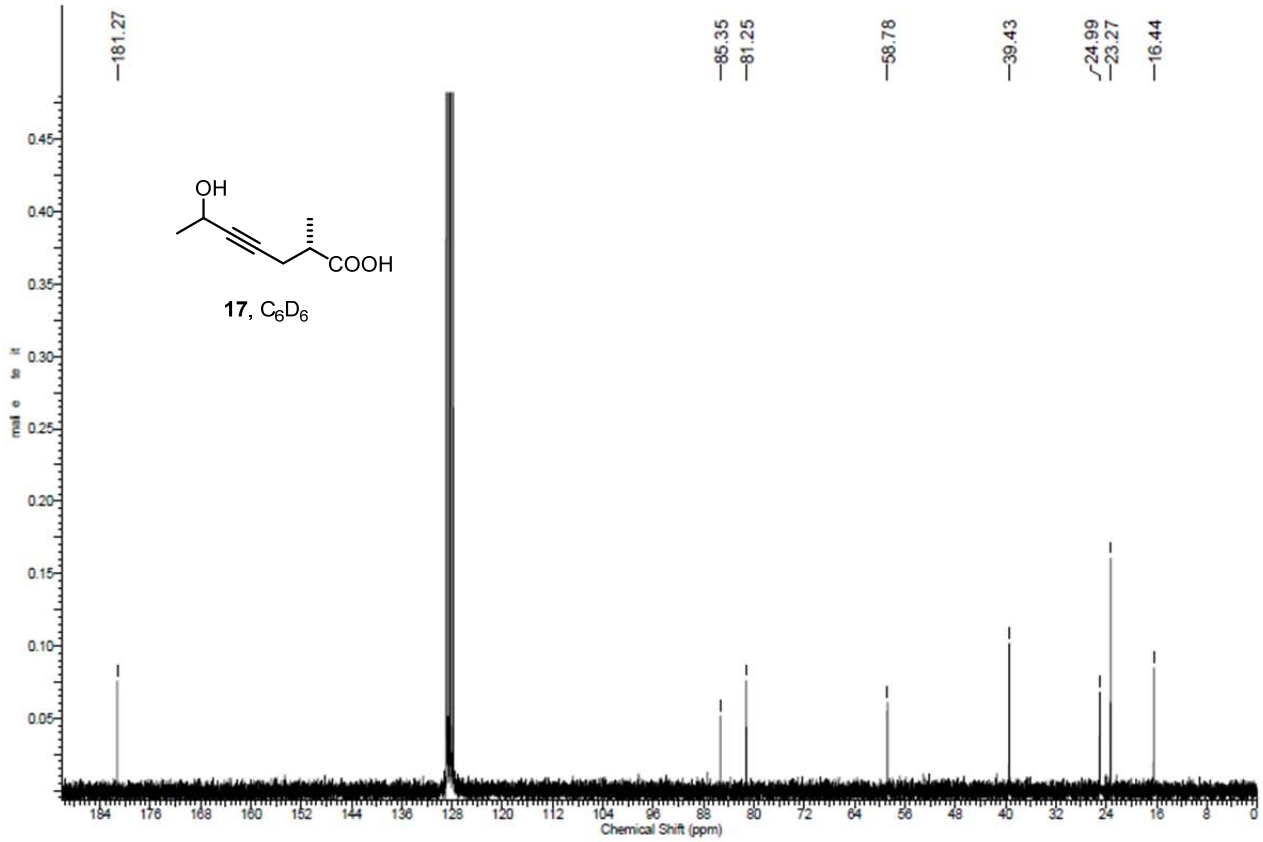

4.57
4.56
4.54
4.53
4.52
4.50
4.47
3.50
3.49
3.47
3.46
2.29
2.28
2.26
2.25
2.19
2.18
2.15
2.14
1.83
1.80
1.76
1.45
1.42
0.97
0.94
0.90
0.05
OH
OTBS
S3, CDCl3
1.07
2.22
1.19
1.30
2.19
3.44
3.35
9.96
3.58
0.17
Chemical Shift (ppm)

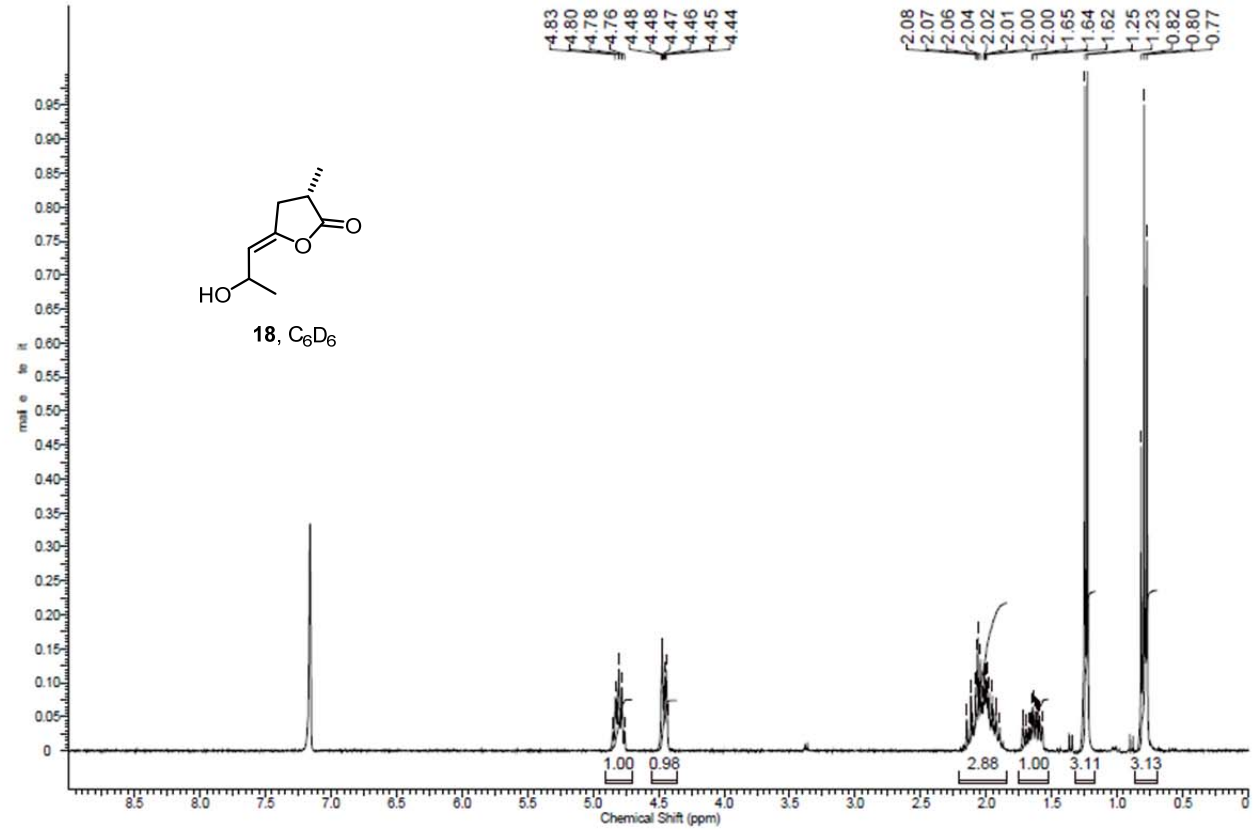

83.33
66.92
58.76
51.68
35.41
26.07
24.93
22.39
18.47
16.19
5.24
OH
OTBS
S3, CDCl3
Chemical Shift (ppm)


5.57
5.55
5.54
5.53
5.51
5.50
5.49
5.47
3.35
3.32
2.26
2.18
2.17
2.15
2.14
2.12
2.11
2.08
2.07
1.71
1.67
1.64
1.33
1.29
0.90
0.87
OAc
OH
S4, C6D6
1.00
2.30
0.92
2.48
1.14
3.38
3.23
3.26
Chemical Shift (ppm)

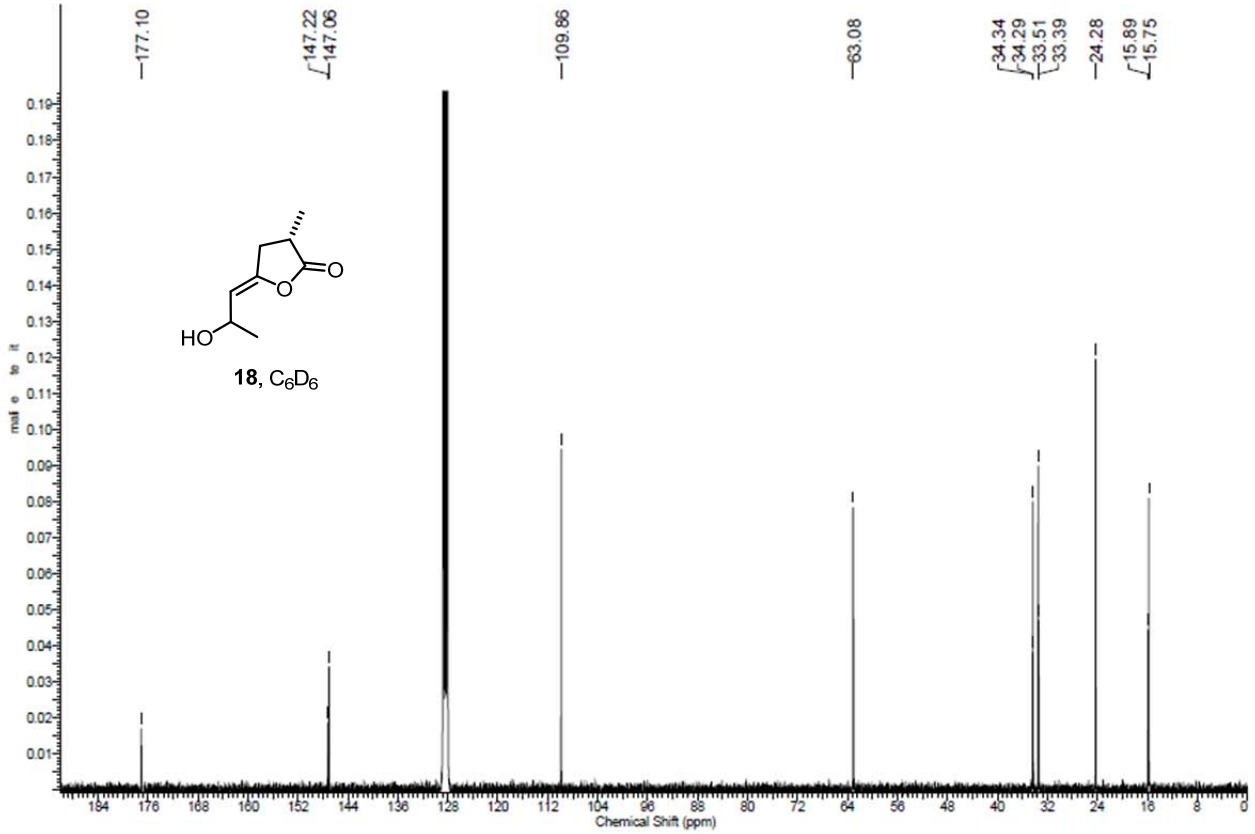

169.91
84.29
80.99
66.87
61.26
35.82
22.96
22.12
20.97
16.57
OAc
OH
S4, C6D6
Chemical Shift (ppm)


6.57
4.32
4.30
4.29
4.27
4.26
4.24
4.23
2.38
2.34
2.31
2.25
2.24
2.22
2.21
2.19
2.18
1.27
1.24
1.02
0.99
OH
COOH
17, C6D6
1.42
1.00
3.22
3.03
3.04
Chemical Shift (ppm)

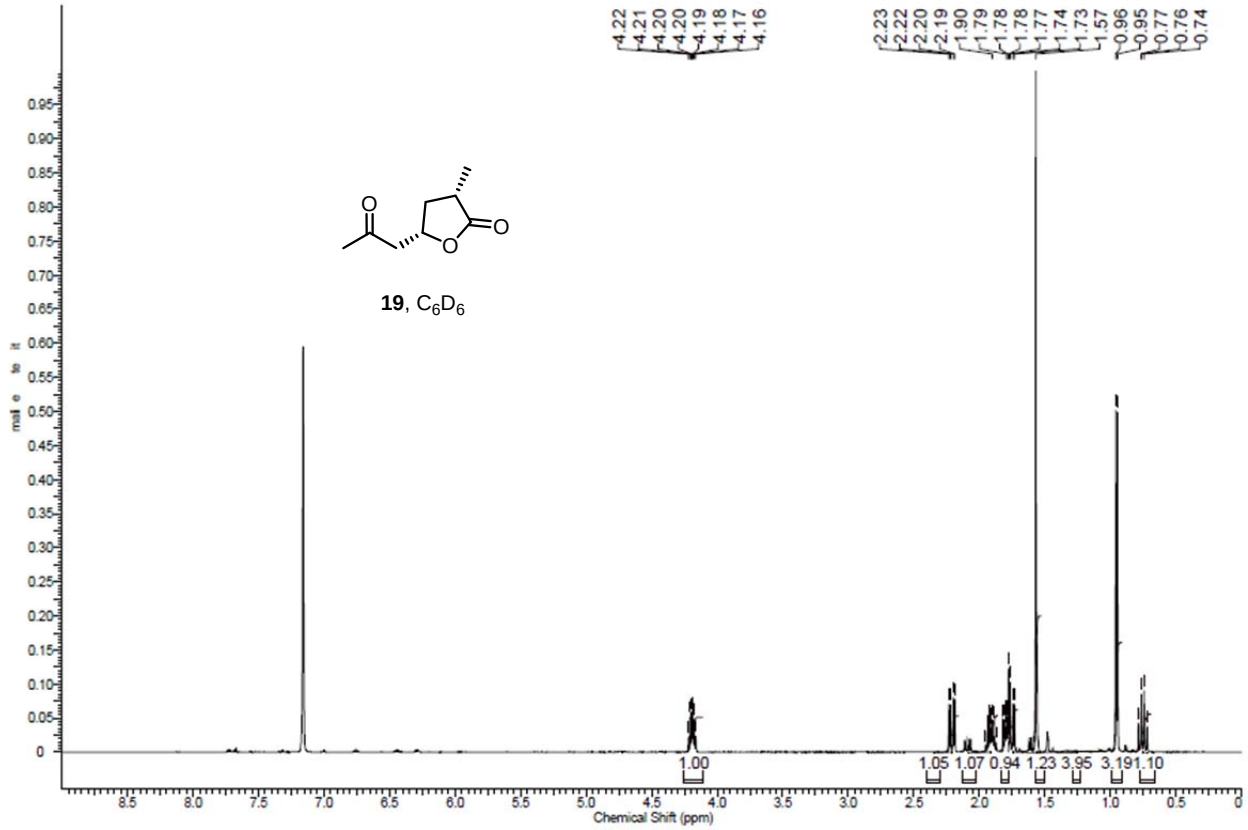

181.27
85.35
81.25
58.78
39.43
24.99
23.27
16.44
OH
COOH
17, C6D6
Chemical Shift (ppm)



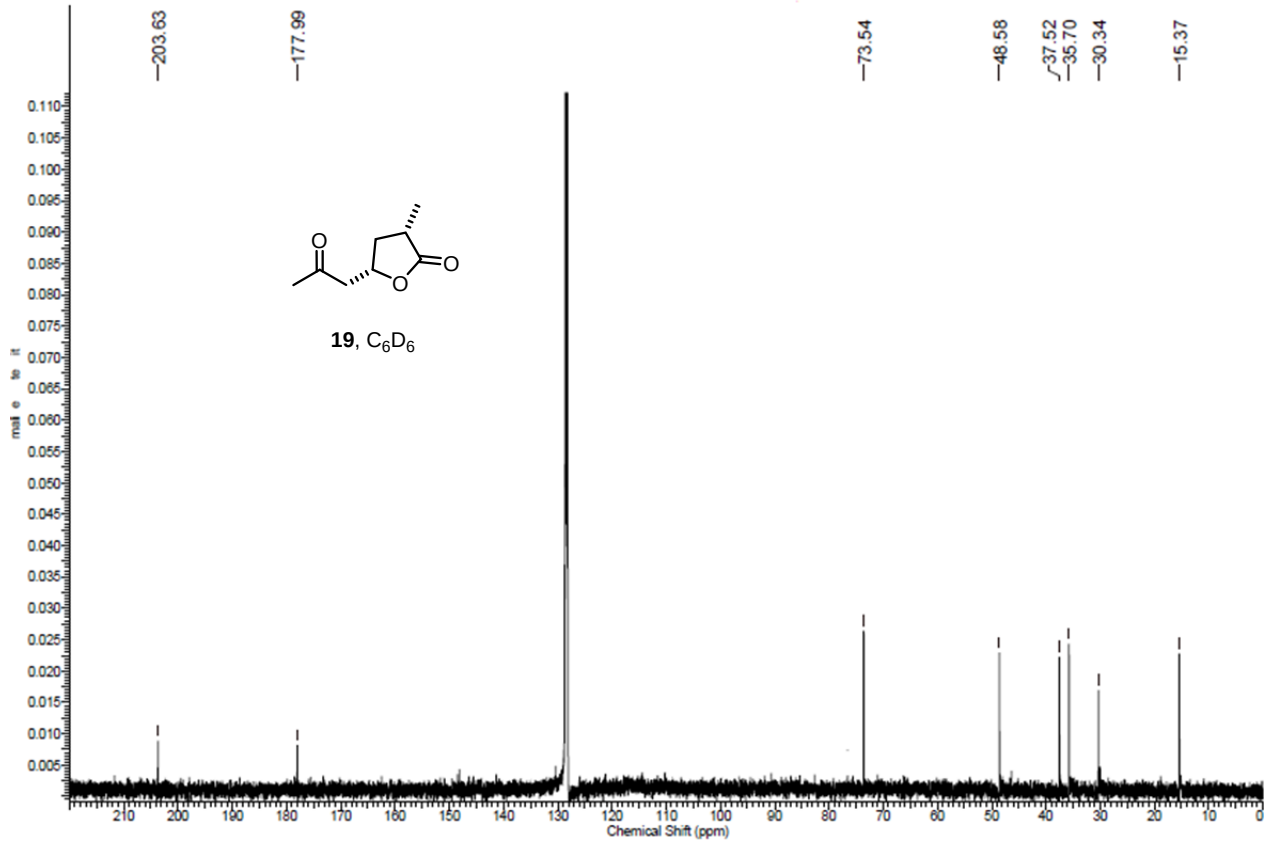
18, C_6D_6



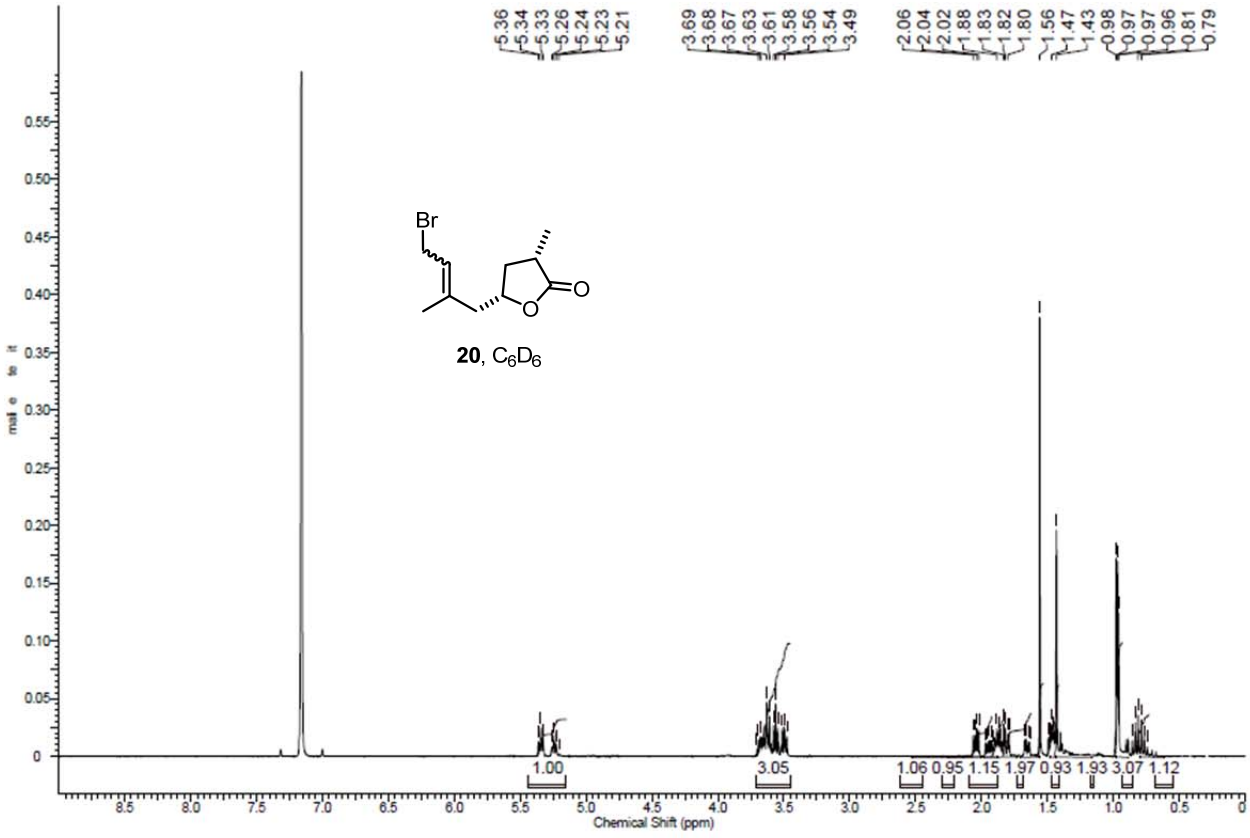
18, C_6D_6

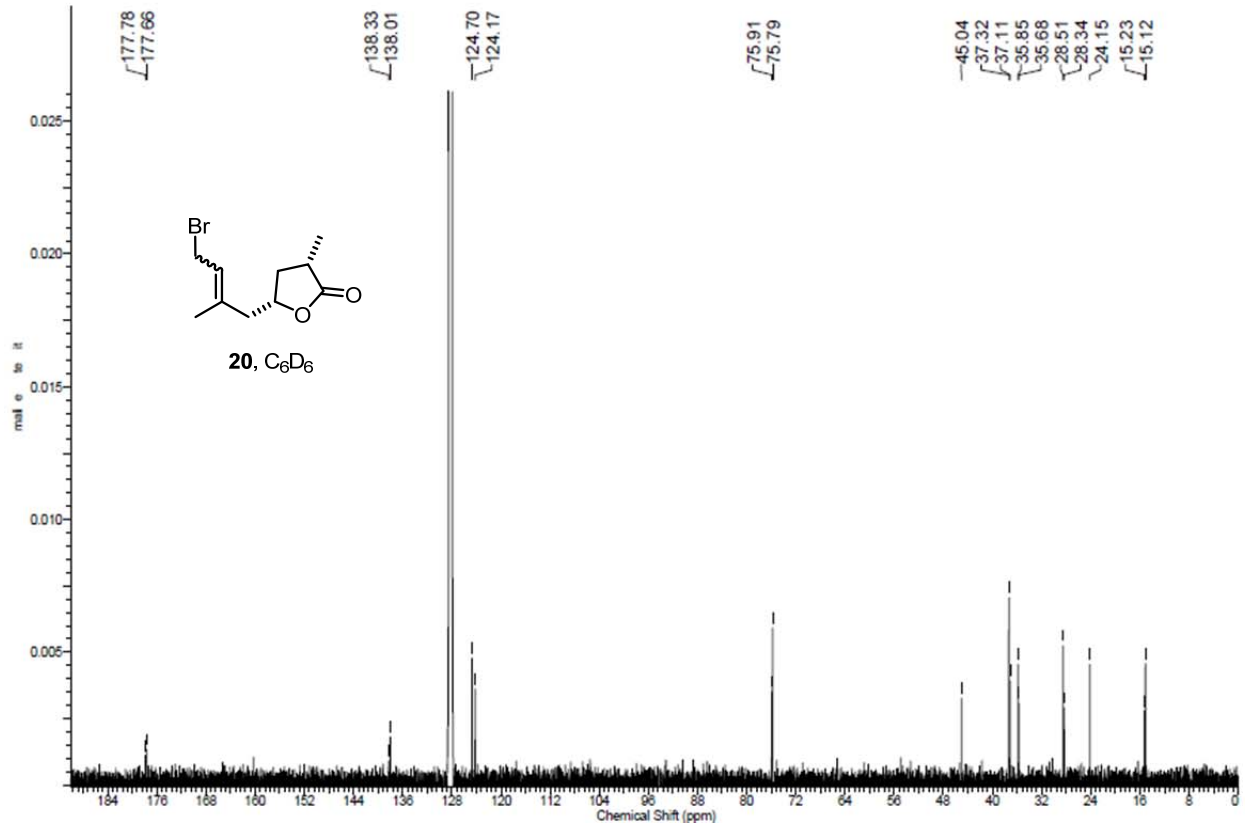


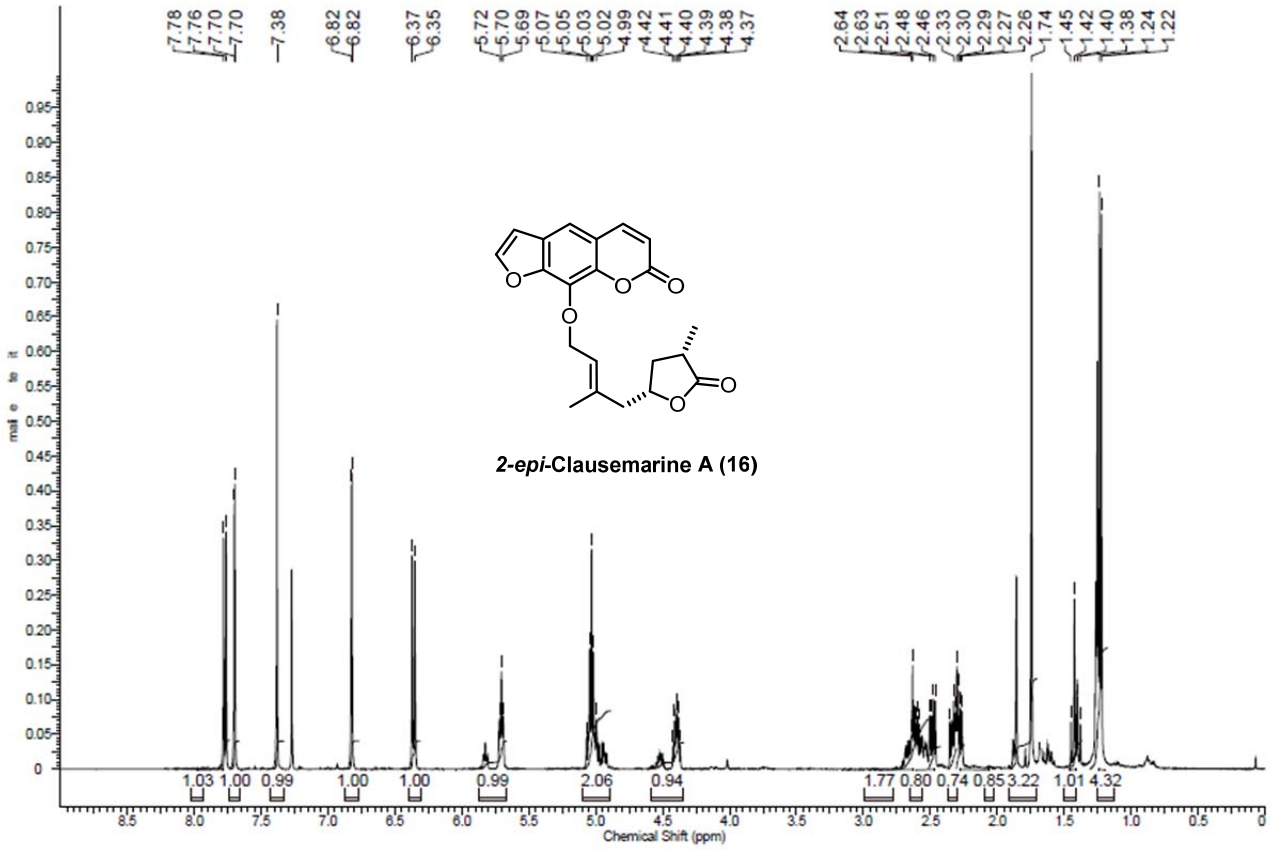
19, C_6D_6



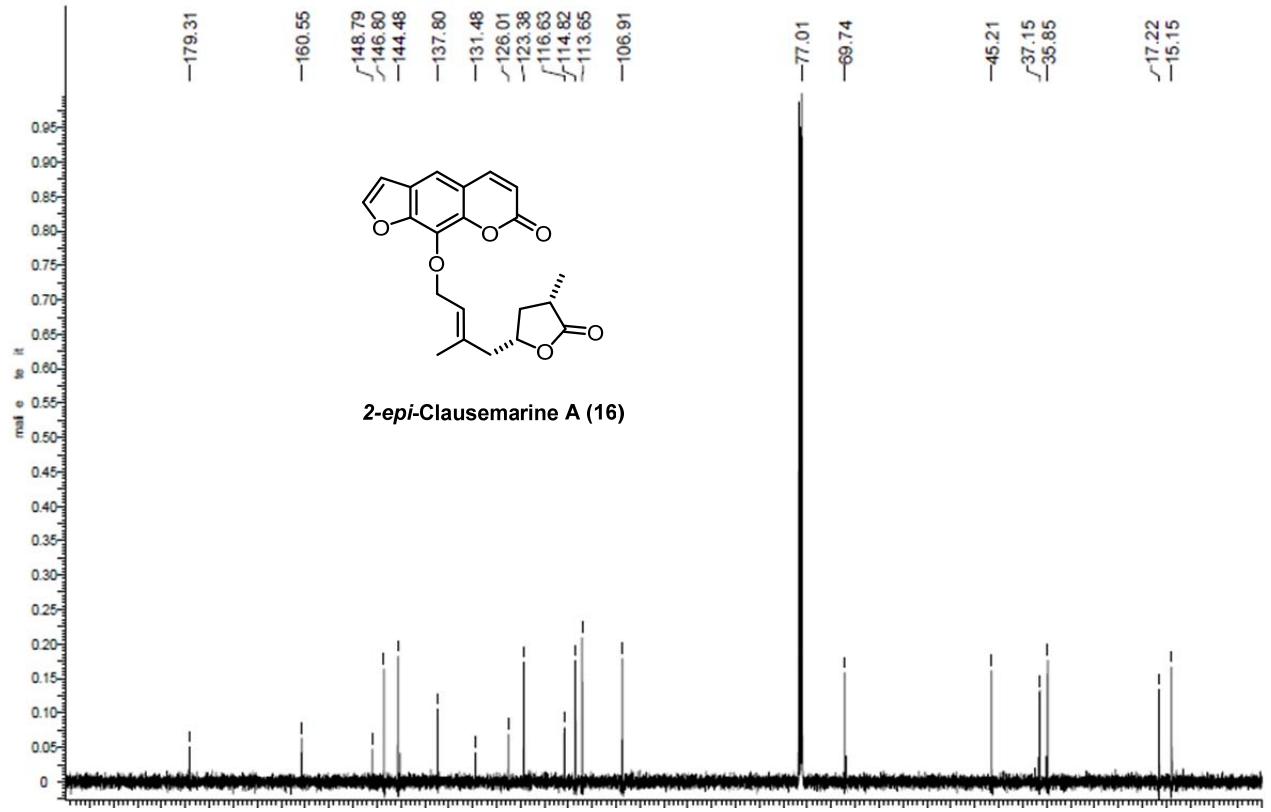
19, C_6D_6


5.36
5.34
5.33
5.26
5.24
5.23
5.21
3.69
3.68
3.67
3.63
3.61
3.58
3.56
3.54
3.49
2.06
2.04
2.02
1.88
1.83
1.82
1.80
1.56
1.47
1.43
0.98
0.97
0.97
0.96
0.81
0.79
Br
O
O
20, C6D6
1.00
3.05
1.06 0.95 1.15 1.97 0.93 1.93 3.07 1.12
Chemical Shift (ppm)


177.78
177.66
138.33
138.01
124.70
124.17
75.91
75.79
45.04
37.32
37.11
35.85
35.68
28.51
28.34
24.15
15.23
15.12
Br
O
O
20, C6D6
Chemical Shift (ppm)



2-epi-Clausemarine A (16)



2-epi-Clausemarine A (16)