Supporting Informations

Palladium-Catalyzed Sequential Alkylation-Alkenylation Reactions: New Three-Component Coupling Leading to Oxacycles.

Sandrine Pache and Mark Lautens*

Davenport Research Laboratories, Chemistry Department, University of Toronto, Toronto, Ontario, Canada M5S 3H6

mlautens@chem.utoronto.ca

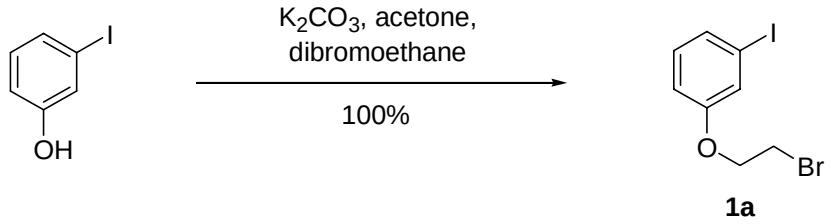
Experimental Section

General. The following includes general experimental procedures, specific details for representative reactions, and isolation and spectroscopic information for new compounds. All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform using residual chloroform as internal standard on a 400 MHz spectrometer, δ are given in ppm, J are given in Hz. IR spectra were recorded in CH_2Cl_2 using a NaCl cell, ν are given in cm^{-1}, relative intensities are given in parenthesis (w = weak, m = medium, s = strong). Mass spectra were obtained by electron impact at 70 eV; relative intensities are given in parenthesis (%). High-resolution mass spectra were obtained at 70 eV. Dry DME was freshly distilled from sodium/benzophenone. PPh_3 was recrystallized from hexane. Other reagents were purchased from Aldrich or Strem and were used without purification. *Tert*-butyl-(3-iodo-propoxy)-dimethyl-silane[1] and 2-iodomethyl-oxirane[2] were prepared using litterature procedures. All reactions were performed under nitrogen.

[1] Nicolaou, K. C.; Papahatjis, D. P.; Claremon, D. A.; Magolda, R. L.; Dolle, R. E. *J. Org. Chem.* **1985**, *50*, 1440.
[2] Evans, R. D.; Magee, J. W.; Schauble, J. H. *Synthesis* **1988**, 862.

Synthesis of substrates

*1-(2-Bromo-ethoxy)-3-iodo-benzene (**1a**)*



1a

3-Iodophenol (2.299 g, 10.4 ml) was dissolved in acetone (3ml). 1,2-Dibromoethane (3 ml, 34.7 mmol, 3.3 eq.) and K_2CO_3 were added and the mixture refluxed for 2 days. The reacting mixture was cooled to RT, diluted with CH_2Cl_2 and washed with water. After drying over $MgSO_4$ and evaporation of volatiles, the crude product was purified by FC (SiO_2, hexane/AcOEt 20:1), giving 3.406 g (10.4 mmol, quantitative yield) of a viscous oil that solidified on standing.

^{1}H-NMR: δ 7.31 (dm, 1H, J=10.5); 7.26 (m, 1H); 7.00 (t, 1H, J=10.5); 6.88 (dd, 1H, J=10.5 and 3.5), 4.26 (t, 2H, J=8.2), 3.63 (t, 2H, J=8.2).

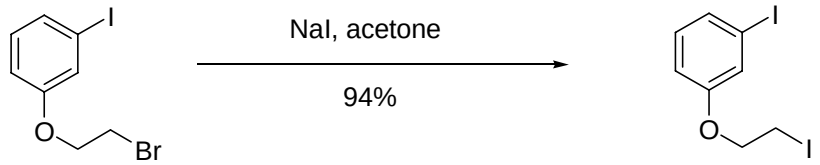
^{13}C-NMR: δ 158.8, 131.1, 130.8, 124.2, 114.6, 94.6, 68.2, 29.0.

IR: 3943 (w), 3756 (w), 3691 (w), 3059 (s), 2986 (s), 2684 (w), 2520 (w), 2409 (w), 2305 (m), 1584 (w), 1550 (w), 1422 (s), 1280 (s), 1252 (s), 1156 (w), 1017 (w), 990 (w), 896 (s).

MS: 328 (98, M^+), 326 (100, M^+), 220, (54), 203 (11), 191 (7), 120 (12), 109 (76), 93 (20), 92 (19), 91 (7), 76 (12), 65 (12), 64 (23), 63 (24), 62 (5).

HR-MS: 325.880007 (C_8H_8BrIO, calc. 325.880328).

*1-Iodo-3-(2-iodo-ethoxy)-benzene (**1b**)*



1a **1b**

1-(2-Bromo-ethoxy)-3-iodo-benzene (7.67 g, 23.5 mmol) was dissolved in acetone (250 ml) and NaI (7.04 g, 47 mmol, 2 eq.) was added. The mixture was stirred at RT for 2 days, the acetone was evaporated, the residue dissolved in diethyl ether, washed with water and dried over $MgSO_4$. Purification by FC (SiO_2, hexane/AcOEt 10:1) afforded the product (8.32 g, 22.2 mmol, 94%) as a colorless oil that solidified on standing.

^{1}H-NMR: δ 7.37 (dm, 1H, J=8.0); 7.31 (m, 1H); 7.06 (t, 1H, J=8.0); 6.92 (dm, 1H, J=8.0), 4.27 (t, 2H, J=6.6), 3.45 (t, 2H, J=6.6).

^{13}C-NMR: δ 158.5, 130.9, 130.6, 124.1, 114.4, 94.4, 68.8, 0.7.

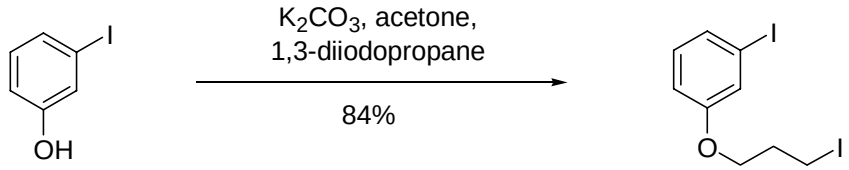
IR: 3943 (w), 3756 (w), 3690 (w), 3060 (s), 2986 (s), 2684 (w), 2520 (w), 2409 (w), 2305 (m), 2125 (w), 2054 (w), 1584 (w), 1550 (w), 1422 (s), 1280 (s), 1249 (s), 1156 (w), 1017 (w), 989 (w), 894 (s).

MS: (83, M^+), 346 (46), 220 (7), 219 (35), 203 (7), 191 (15), 155 (100), 127 (8), 93 (8), 92 (29), 91 (5), 76 (13), 65 (9), 64 (25), 63 (26), 62 (8).

HR-MS: 373.868134 ($C_8H_8I_2O$, calc. 373.866469).

Elemental analysis: found C 25.92%, H 2.14% (calc. C 25.69%, H 2.16%).

*1-Iodo-3-(3-iodo-propoxy)-benzene (**2b**)*



2b

3-iodophenol (1.11 g, 5.0 mmol) was dissolved in acetone (4.5 ml). 1,3-Diiodopropane (1.15 ml, 10 mmol, 2 eq.) and K_2CO_3 (1.38 g, 10 mmol, 2 eq.) were added and the mixture was stirred at 50°C for 2 days. The mixture was diluted with diethyl ether, washed with water and dried over $MgSO_4$. Purification by FC (silica, hexane/AcOEt 20:1 to 10:1) afforded the desired product (1.63 g, 4.2 mmol, 84%) as a colorless liquid.

^{1}H-NMR: 7.33 (dm, 1H, J=8.0); 7.32 (m, 1H); 7.04 (t, 1H, J=8.0); 6.91 (dm, 1H, J=8.0), 4.40 (t, 2H, J=6.2), 3.39 (t, 2H, J=6.2), 2.30 (q, 2H, J=6.2).

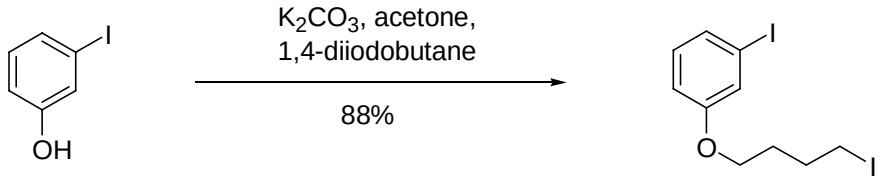
^{13}C-NMR: 159.3, 130.9, 130.2, 123.8, 114.3, 94.5, 67.5, 32.8, 2.4.

IR: 2943 (m), 3757 (w), 3691 (w), 3060 (s), 2987 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (m), 2305 (s), 2125 (w), 2054 (w), 1550 (w), 1421 (s), 1249 (s), 1156 (m), 1018 (w), 988 (w), 896 (s).

MS: 388 (100, M^+), 302 (15), 261 (13), 260 (5), 233 (17), 220 (21), 203 (23), 191 (8), 169 (55), 141 (6), 135 (17), 134 (93), 133 (9), 128 (6), 127 (20), 119 (13), 106 (9), 105 (5), 93 (16), 92 (20), 91 (7), 78 (8), 77 (7), 76 (29), 75 (8), 74 (7), 65 (18), 64 (24), 63 (39), 62 (11), 51 (5).

HR-MS: 387.881291 ($C_9H_{10}I_2O$, calc. 387.882119).

*1-Iodo-3-(4-iodo-butoxy)-benzene (**3b**)*



3b

3-iodophenol (1.11 g, 5.0 mmol) was dissolved in acetone (4.5 ml). 1,4-Diiodobutane (1.32 ml, 10 mmol, 2 eq.) and K_2CO_3 (1.38 g, 10 mmol, 2 eq.) were added and the mixture was stirred at 50°C for 2 days. The mixture was diluted with diethyl ether, washed with water and dried over $MgSO_4$. Purification by FC (silica, hexane/AcOEt 20:1 to 10:1) afforded the desired product (1.76 g, 4.4 mmol, 88%) as a colorless liquid.

^{1}H-NMR: 7.32 (dm, 1H, J=8.4); 7.28 (m, 1H); 7.03 (t, 1H, J=8.4); 6.89 (dm, 1H, J=8.4), 3.98 (t, 2H, J=6.0), 3.29 (t, 2H, J=6.8), 2.02-2.08 (m, 2H), 1.88-1.96 (m, 2H).

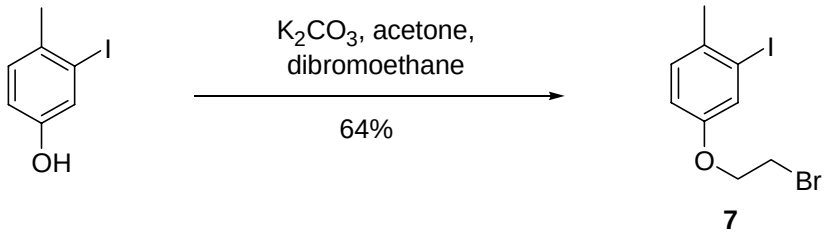
^{13}C-NMR: δ 159.5, 130.9, 129.9, 123.7, 114.2, 94.5, 66.9, 30.1, 30.0, 6.4.

IR: 3943 (m), 3756 (w), 3691 (w), 3059 (s), 2986 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2155 (w), 2125 (w), 2054 (w), 1584 (m), 1567 (w), 1550 (w), 1422 (s), 1248 (s), 1157 (m), 1023 (w), 989 (w), 895 (s).

MS: 402 (23, M^+), 275 (11), 233 (12), 220 (21), 203 (16), 191 (6), 183 (100), 155 (12), 137 (10), 135 (10), 127 (12), 106 (5), 93 (16), 92 (15), 91 (13), 76 (21), 65 (19), 64 (20), 63 (32), 56 (10), 55 (86).

HR-MS: 401.898526 ($C_{10}H_{12}I_2O$, calc. 401.897769).

4-(2-Bromo-ethoxy)-2-iodo-1-methyl-benzene (7)



7

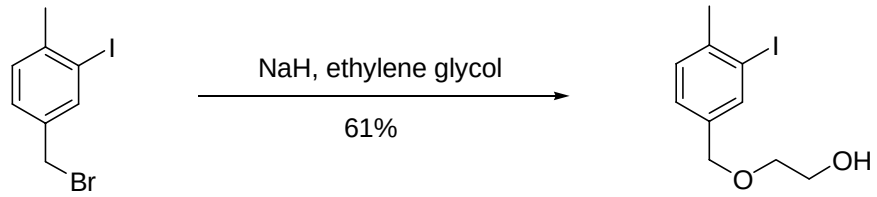
4-methyl-3-iodophenol[3] (237 mg, 1.01 mmol), K_2CO_3 (280 mg, 2.03 mmol, 2 eq.), 1 ml of 1,2-dibromoethane and 1 ml of acetone were mixed and stirred under nitrogen for 24h. at 55°C. The reacting mixture was cooled down to RT, diluted with diethyl ether and washed with water. After drying over $MgSO_4$ and evaporation of volatiles, the crude product was purified by FC (SiO_2, hexane/AcOEt 20:1), giving 220 mg (0.65 mmol, 64%) of a red liquid that decomposed slowly (even at -20°C) and was therefore used immediately for the next reaction.

^{1}H-NMR: δ 7.42 (d, 1H, J=2.8); 7.6 (d, 1H, J=8.4); 6.86 (dd, 1H, J=8.4 and 2.8); 4.28 (t, 1H, J=6.3); 3.65 (t, 2H, J=6.3); 2.40 (s, 3H).

^{13}C-NMR: δ 156.3, 134.3, 129.9, 125.1, 115.0, 100.8, 68.2, 28.9, 26.9.

[3] Synthesis: see Pummerer, R.; Puttfarcken, H.; Schopflocher, P. *Chem. Ber.* **1925**, *58*, 1818.

2-(3-Iodo-4-methyl-benzyloxy)-ethanol



NaH (60% in mineral oil, 144 mg, 3.6 mmol, 1 eq.) was suspended in dry THF (50 ml) and the mixture cooled to 0°C. Ethylene glycol (0.605 ml, 10.8 mmol, 3 eq.) was added and the mixture stirred at RT for 1 h. 3-Iodo-4-methyl benzyl bromide (1.12 g, 3.6 mmol, 1 eq.) and a catalytic amount of nBu$_4$NI dissolved in THF (10 ml) were added and the mixture refluxed overnight. After cooling to RT, the reaction was quenched with water, extracted with diethyl ether and dried over magnesium sulfate. Purification by FC (silica, hexane/AcOEt 4:1 to 2:1 afforded the desired product (633 mg, 2.2 mmol, 61%) as a slightly yellow oil.

^{1}H-NMR: δ 7.79 (s, 1H); 7.20 (s, 2H); 4.47 (s, 2H); 3.76 (t, 2H, J=4.5); 3.58 (t, 2H, J=4.5), 2.41 (s, 3H).

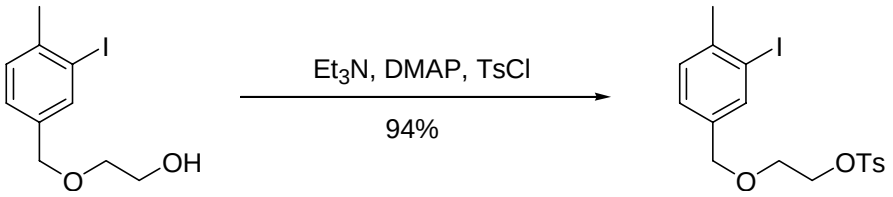
^{13}C-NMR: δ 140.8, 138.2, 137.5, 129.7, 127.7, 101.2, 72.0, 71.7, 61.7, 27.8.

IR: 3943 (m), 3757 (w), 3691 (w), 3599 (w), 3059 (s), 2986 (s), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2155 (w), 2125 (w), 2054 (w), 1551 (w), 1422 (s), 1249 (s), 1156 (m), 1111 (w), 1056 (w), 1034 (w), 987 (w), 894 (s).

MS: 292 (64, M^+), 277 (11), 247 (31), 232 (23), 231 (100), 165 (8), 121 (23), 105 (15), 104 (33), 103 (23), 93 (6), 92 (11), 91 (10), 78 (14), 77 (16), 51 (6).

HR-MS: 291.995103 ($C_{10}H_{13}IO_2$, calc. 291.996032).

Toluene-4-sulfonic acid 2-(3-iodo-4-methyl-benzyloxy)-ethyl ester



2-(3-Iodo-4-methyl-benzyloxy)-ethanol (1.055 g, 3.6 mmol), tosyl chloride (1.032 g, 5.4 mmol, 1.5 eq.), Et_3N (1.0 ml, 7.2 mmol, 2 eq.) and DMAP (44 mg, 0.36 mmol, 0.1 eq.) were dissolved in CH_2Cl_2 (20 ml) and the mixture stirred at RT overnight. The mixture was extracted (dichloromethane/water), dried over magnesium sulfate and volatiles were evaporated. Purification by FC (silica, hexane/AcOEt 10:1) afforded 1.504 g (3.4 mmol, 94%) of the desired product as a colorless liquid.

^{1}H-NMR: δ 7.83 (d, 2H, J=8.4); 7.73 (d, 1H, J=1.2); 7.35 (d, 2H, J=8.4); 7.22 (d, 1H, J=7.6); 7.16 (dd, 1H, J=7.6 and 1.2); 4.42 (s, 2H); 4.22 (t, 2H, J=4.7); 3.67 (t, 2H, J=4.7); 2.47 (s, 3H); 2.44 (s, 3H).

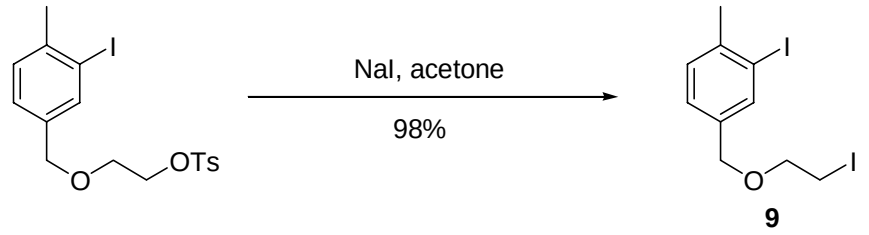
^{13}C-NMR: δ 144.9, 140.9, 138.0, 137.8, 133.0, 129.0, 129.6, 128.0, 127.6, 101.1, 72.0, 69.3, 67.6, 27.8, 21.7.

IR: 3943 (m), 3757 (w), 3691 (w), 3058 (s), 2986 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2154 (w), 2125 (w), 2054 (w), 1598 (w), 1550 (w), 1421 (s), 1249 (s), 1189 (w), 1177 (m), 1156 (m), 1019 (w), 986 (w), 895 (s).

MS: 446 (44, M^+), 291 (20), 247 (37), 246 (100), 245 (27), 232 (8), 231 (69), 230 (7), 199 (26), 172 (18), 155 (20), 147 (5), 120 (10), 119 (11), 118 (7), 105 (14), 104 (36), 103 (26), 92 (19), 91 (71), 90 (7), 89 (8), 78 (18), 77 (19), 65 (23), 63 (8), 51 (7).

HR-MS: 446.004891 ($C_{17}H_{19}IO_4S$, calc. 446.004883).

*2-Iodo-4-(2-iodo-ethoxymethyl)-1-methyl-benzene (**9**)*



9

Toluene-4-sulfonic acid 2-(3-iodo-4-methyl-benzyloxy)-ethyl ester (1.30 g, 2.9 mmol) was dissolved in acetone (25 ml) and NaI (0.874 g, 5.8 mmol, 2 eq.) was added. The mixture was stirred at RT for 2 days, the acetone was evaporated, the residue dissolved in diethyl ether, washed with water and dried over $MgSO_4$. Purification by FC (SiO_2, hexane/AcOEt 10:1) afforded the product (1.152 g, 2.8 mmol, 98%) as a colorless oil.

^{1}H-NMR: δ 7.84 (s, 1H); 7.23-7.28 (m, 2H); 4.53 (s, 2H); 3.76 (t, 2H, J=6.7); 3.31 /t, 2H, J=6.7); 2.46 (s, 3H).

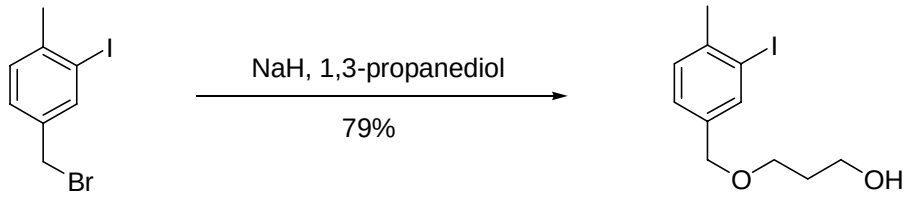
^{13}C-NMR: 140.9, 138.2, 137.2, 129.7, 127.7, 101.2, 71.6, 70.8, 27.9, 3.0.

IR: 3943 (m), 3757 (w), 3691 (w), 3059 (s), 2985 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2155 (w), 2125 (w), 2054 (w), 1550 (w), 1422 (s), 1251 (s), 1156 (m), 1018 (w), 986 (w), 896 (s).

MS: 402 (50, M^+), 356 (11), 354 (11), 245 (7), 233 (5), 232 (60), 231 (100), 155 (32), 119 (10), 109 (9), 107 (9), 105 (26), 104 (31), 103 (28), 92 (24), 91 (14), 90 (7), 89 (6), 78 (12), 77 (16), 65 (6), 63 (6), 57 (8), 51 (7).

HR-MS: 401.897251 ($C_{10}H_{12}I_2O$, calc. 401.897769).

3-(3-Iodo-4-methyl-benzyloxy)-propan-1-ol



NaH (60% in mineral oil, 4 g, 100 mmol, 20 eq.) was suspended in dry THF (30 ml) and the mixture cooled to 0°C. 1,3-Propane-diol (7.23 ml, 100 mmol, 20 eq.) was added and the mixture stirred at RT for 1 h. 3-Iodo-4-methyl benzyl bromide (1.555 g, 5 mmol) and a catalytic amount of nBu$_4$NI dissolved in THF (10 ml) were added and the mixture refluxed overnight. After cooling to RT, the reaction was quenched with water, extracted with diethyl ether and dried over magnesium sulfate. Purification by FC (silica, hexane/AcOEt 5:1 afforded the desired product (1.186 g, 3.9 mmol, 79%) as a slightly yellow oil.

^{1}H-NMR: δ 7.80 (s, 1H); 7.22 (s, 2H); 4.45 (s, 2H); 3.79 (t, 2H, J=5.8); 3.65 (t, 2H, J=5.8); 2.44 (s, 3H); 1.89 (quintet, 2H, J=5.8).

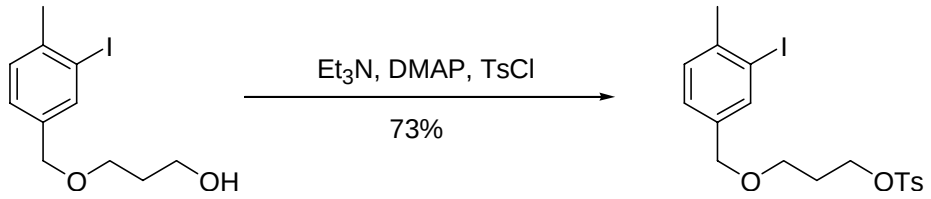
^{13}C-NMR: δ 140.8, 138.1, 137.6, 129.7, 127.6, 101.1, 72.0, 69.1, 61.4, 32.2, 27.8.

IR: 3943 (m), 3757 (w), 3691 (w), 3060 (s), 2986 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2155 (w), 2125 (w), 2054 (w), 1550 (w), 1421 (s), 1249 (s), 1156 (m), 1018 (w), 986 (w), 897 (s).

MS: 306 (29, M^+), 248 (11), 247 (100), 232 (10), 231 (59), 121 (11), 105 (13), 104 (22), 103 (19), 93 (7), 92 (23), 91 (12), 78 (10), 77 (14), 51 (5).

HR-MS: 306.011474 ($C_{11}H_{15}IO_2$, calc. 306.011682).

Toluene-4-sulfonic acid 3-(3-iodo-4-methyl-benzyloxy)-propyl ester



3-(3-Iodo-4-methyl-benzyloxy)-propan-1-ol (2.46 g, 8.0 mmol), tosyl chloride (2.30 g, 12 mmol, 3 eq.), Et_3N (2.2 ml, 16 mmol, 2 eq.) and DMAP (98 mg, 0.8 mmol, 0.1 eq.) were dissolved in CH_2Cl_2 (40ml) and the mixture stirred at RT overnight. The mixture was extracted (dichloromethane/water), dried over magnesium sulfate and volatiles were evaporated. Purification by FC (silica, hexane/AcOEt 5:1) afforded 2.682 g (5.8 mmol, 73%) of the desired product as a colorless liquid.

^{1}H-NMR: δ 7.82 (d, 2H, J=8.0); 7.72 (s, 1H); 7.36 (d, 2H, J=8.0); 7.22 (d, 1H, J=7.6); 7.16 (d, 1H, J=7.6); 4.34 (s, 2H); 4.19 (t, 2H, J=6.0); 3.51 (t, 2H; J=6.0); 2.46 (s, 3H); 2.45 (s, 3H); 1.97 (quintet, 2H, J=6.0).

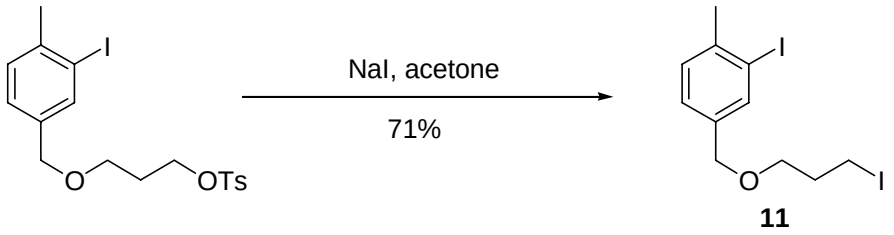
^{13}C-NMR: δ 144.8, 140.7, 137.9, 137.6, 133.0, 129.9, 129.6, 127.9, 127.5, 101.1, 71.8, 67.6, 65.7, 29.3, 27.8, 21.7.

IR: 3973 (m), 3756 (w), 3691 (w), 3053 (s), 2986 (s), 2684 (m), 2520 (w), 2409 (w), 2305 (s), 2125 (w), 2053 (w), 1598 (w), 1550 (w), 1421 (s), 1279 (s), 1249 (s), 1189 (m), 1177 (m), 1097 (w), 1034 (w), 1019 (w), 977 (w), 949 (w), 894 (s).

MS: 460 (28, M^+), 305 (12), 188 (14), 287 (26), 273 (26), 260 (5), 248 (6), 247 (51), 246 (32), 245 (30), 244 (8), 232 (18), 231 (95), 230 (12), 214 (10), 213 (23), 173 (25), 172 (36), 162 (19), 161 (100), 155 (38), 132 (8), 120 (13), 119 (51), 107 (6), 105 (24), 104 (43), 103 (31), 102 (5), 92 (35), 91 (88), 90 (14), 89 (13), 79 (7), 78 (22), 77 (25), 65 (31), 63 (11), 51 (10).

HR-MS: 460.021106 ($C_{18}H_{21}IO_4S$, calc. 460.020533).

*2-Iodo-4-(3-iodo-propoxymethyl)-1-methyl-benzene (**10**)*



11

Toluene-4-sulfonic acid 3-(3-iodo-4-methyl-benzyloxy)-propyl ester (2.578 g, 5.6 mmol) was dissolved in acetone (40 ml) and NaI (1.68 g, 11.2 mmol, 2 eq.) was added. The mixture was stirred at RT overnight, the acetone was evaporated, the residue dissolved in diethyl ether, washed with water and dried over $MgSO_4$. Purification by FC (SiO_2, hexane/AcOEt 10:1) afforded the product (1.653 g, 4.0 mmol, 71%) as a colorless oil.

^{1}H-NMR: δ 7.82 (s, 1H); 7.25 (m, 2H); 4.47 (s, 2H); 3.56 (t, 2H, J=5.8); 3.34 (t, 2H, J=5.8); 2.46 (s, 3H); 2.12 (2H, quintet, J=5.8).

^{13}C-NMR: δ 140.8, 138.1, 137.7, 129.6, 127.6, 101.1, 71.9, 69.7, 33.4, 27.8, 3.4.

IR: 3943 (m), 3756 (w), 3690 (w), 3057 (s), 2985 (s), 2828 (w), 2648 (m), 2520 (w), 2410 (w), 2305 (s), 2124 (w), 2054 (w), 1602 (w), 1550 (w), 1421 (s), 1281 (s), 1249 (s), 1156 (m), 1103 (w), 897 (s).

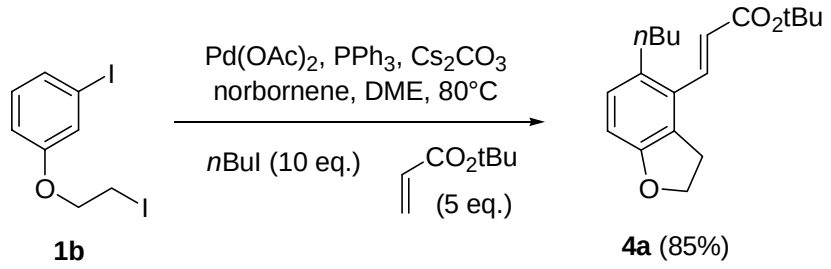
MS: 416 (34, M^+), 289 (6), 233 (7), 232 (53), 231 (100), 169 (23), 105 (30), 104 (31), 103 (29), 92 (7), 91 (10), 89 (6), 78 (16), 77 (18).

HR-MS: 415.912876 ($C_{11}H_{14}I_2O$, calc. 415.913419).

Cyclization reactions, three-component couplings

General procedure. Substrate (0.2 mmol), alkyl iodide (2 mmol, 10 eq.), Heck acceptor (1 mmol, 5 eq.), norbornene (1 mmol, 5 eq.), Cs_2CO_3 (1 mmol, 5 eq.), $Pd(OAc)_2$ (10 mol%) and PPh_3 (20 mol%) were dissolved in 2 ml of degassed dry DME. The mixture was flushed with N_2 and heated at 80°C for 16 h. After cooling at RT, the mixture was diluted with diethyl ether, washed with water, dried over magnesium sulfate and purified by FC.

*3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4a**)*



1b **4a** (85%)

Purification by FC (silica, hexane/AcOEt 10:1) afforded 52 mg (0.17 mmol, 85%) of the product as a colorless oil.

^{1}H-NMR: δ 7.89 (d, 1H, J=16.4); 7.01 (d, 1H, J=8.4); 6.76 (d, 1H, J=8.4); 6.13 (d, 1H, J=16.4); 4.60 (t, 2H, J=8.6); 3.36 (t, 2H, J=8.6); 2.70 (t, 2H, J=7.8); 1.51-1.62 (m, 2H); 1.58 (s, 9H); 1.37-1.44 (m, 2H); 0.966 (t, 3H, J=7.4).

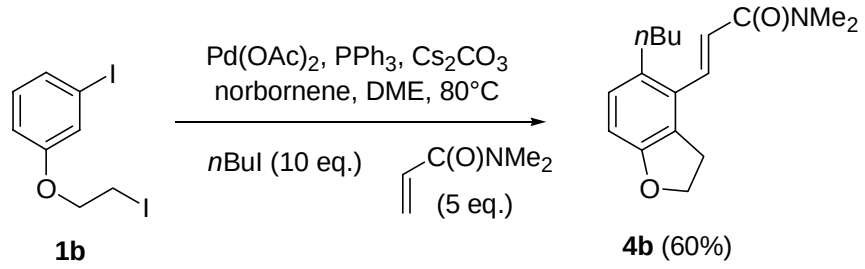
^{13}C-NMR: δ 166.4, 158.7, 140.7, 134.9, 130.1, 129.6, 125.8, 123.5, 110.3, 80.6, 71.2, 34.1, 32.8, 31.2, 28.2, 22.4, 14.0.

IR: 3943 (m), 3757 (w), 3691 (w), 3055 (s), 2985 (s), 2830 (w), 2685 (m), 2521 (w), 2410 (w), 2305 (s), 2125 (w), 2054 (w), 1703 (m). 1634 (w), 1550 (w), 1422 (s), 1251 (s), 1154 (m), 1018 (w), 986 (w), 897 (s).

MS: 302 (75, M^{+}), 247 (18), 246 (50), 233 (6), 232 (25), 230 (5), 229 (24), 227 (7), 204 (25), 203 (100), 201 (10), 189 (7), 186 (8), 185 (10), 175 (14), 173 (18), 172 (8), 171 (16), 169 (8), 168 (5), 165 (8), 160 (10), 159 (53), 158 (29), 157 (34), 151 (10), 145 (6), 144 (11), 141 (12), 134 (9), 133 (8), 131 (15), 130 (6), 129 (21), 128 (24), 127 (13), 116 (10), 115 (24), 109 (7), 107 (8), 105 (7), 103 (6), 91 (13), 86 (8), 84 (21), 78 (7), 77 (11), 70 (8), 65 (7), 63 (5), 58 (8), 57 (85), 55 (8), 51 (10).

HR-MS: 302.187253 ($C_{19}H_{26}O_3$, calc. 302.188195).

*3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-N,N-dimethyl-acrylamide (**4b**)*



1b **4b** (60%)

Purification by FC (silica, hexane/AcOEt 1:1) afforded 33 mg (0.12 mmol, 60%) of the product as a white solid.

^{1}H-NMR: δ 7.90 (d, 2H, J=16.0); 7.00 (d, 1H, J=8.0); 6.75 (d, 1H, J=8.0); 6.64 (d, 1H, J=16.0); 4.59 (t, 2H, J=8.6); 3.33 (t, 2H, J=8.6); 3.17 (s, 3H); 3.11 (s, 3H); 2.70 (t, 2H, J=7.8); 1.50-1.60 (m, 2H), 1.35-1.45 (m, 2H); 0.95 (t, 3H, J=7.2).

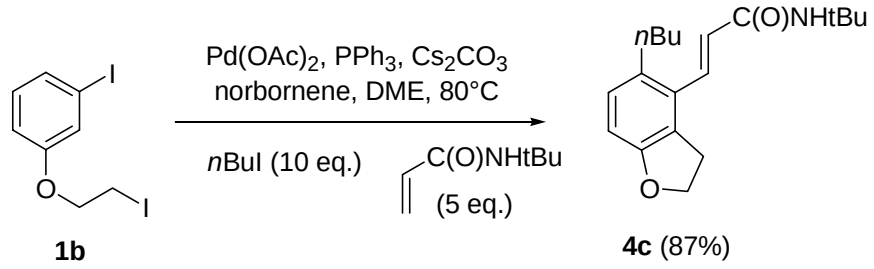
^{13}C-NMR: δ 166.7, 158.5, 139.6, 134.6, 131.3, 129.5, 125.3, 121.4, 109.8, 71.1, 37.4, 35.9, 34.0, 32.8, 31.1, 22.5, 14.0.

IR: 3944 (m), 3689 (w), 3599 (w), 3060 (s), 2986 (s), 2932 (w), 2873 (w), 2684 (w), 2520 (w), 2410 (w), 2305 (s), 1651 (m), 1607 (m), 1479 (w), 1459 (w), 1422 (s), 1280 (s), 1251 (s), 1142 (m), 1027 (w), 986 (w), 952 (w), 896 (s).

MS: 273 (34, M^{+}), 230 (6), 229 (8), 216 (14), 206 (17), 201 (8), 200 (9), 187 (8), 186 (15), 185 (9), 173 (16), 172 (5), 171 (11), 163 (5), 159 (7), 158 (5), 157 (9), 129 (6), 128 (10), 127 (5), 119 (11), 115 (10), 91 (9), 87 (6), 84 (7), 73 (7), 72 (100), 57 (21).

HR-MS: 273.173117 ($C_{17}H_{23}NO_2$, calc. 273.172879).

*N-tert-Butyl-3-(5-butyl-2,3-dihydro-benzofuran-4-yl)-acrylamide (**4c**)*



1b **4c** (87%)

Purification by FC (silica, hexane/AcOEt 1:1) afforded 52 mg (0.17 mmol, 87%) of the product as a colorless oil.

^{1}H-NMR: δ 7.84 (d, 1H, J=15.8); 6.99 (d, 1H, J=8.2); 6.74 (d, 1H, J=8.2); 6.08 (d, 1H, J=15.8); 5.50 (broad s, 1H); 4.58 (t, 2H, J=8.6); 3.31 (t, 2H, J=8.4); 2.69 (t, 2H, J=7.8); 1.50-1.60 (m, 2H); 1.47 (s, 9H); 1.32-1.43 (m, 2H); 0.94 (t, 3H, J=7.4).

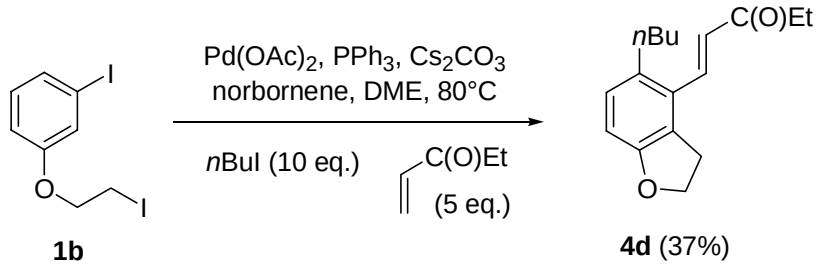
^{13}C-NMR: δ 165.1, 158.5, 137.6, 134.7, 130.7, 129.4, 125.5, 125.4, 109.8, 71.1, 51.6, 33.9, 32.7, 31.1, 29.0, 22.5, 14.0.

IR: 3944 (w), 3690 (w), 3431 (w), 3060 (s), 2987 (s), 2684 (w), 2520 (w), 2410 (w), 2305 (s), 1673 (w), 1625 (w), 1510 (w), 1422 (s), 1281 (s), 1249 (s), 1156 (w), 988 (w), 896 (s).

MS: 301 (56, M^{+}), 245 (5), 244 (8), 229 (15), 202 (13), 201 (19), 200 (16), 199 (5), 188 (17), 187 (6), 186 (22), 185 (14), 173 (22), 172 (7), 171 (17), 160 (16), 159 (100), 158 (8), 157 (16), 149 (5), 145 (6), 144 (5), 141 (6), 131 (8), 129 (11), 128 (13), 127 (7), 121 (5), 116 (5), 115 (18), 112 (7), 91 (8), 87 (5), 77 (5), 58 (25), 57 (95).

HR-MS: 301.204721 ($C_{19}H_{27}NO_2$, calc. 301.204179).

*1-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-pent-1-en-3-one (**4d**)*



1b **4d** (37%)

Purification FC (silica, hexane/AcOEt 20:1 to 5:1) afforded 19 mg (0.07 mmol, 37%) of the product as a colorless oil.

^{1}H-NMR: δ 7.85 (d, 1H, J=16.4); 7.02 (d, 1H, J=8.0); 6.78 (d, 1H, J=8.0); 6.51 (d, 1H, J=16.4); 4.61 (t, 2H, J=8.6); 3.35 (t, 2H, J=8.6); 2.68-2.76 (m, 4H); 1.51-1.60 (m, 2H); 1.36-1.45 (m, 2H); 1.22 (t, 3H, J=7.4); 0.97 (t, 3H, J=7.4).

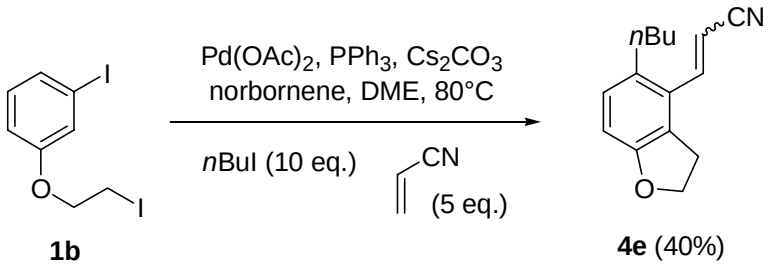
^{13}C-NMR: δ 201.0, 158.8, 139.5, 135.1, 130.2, 129.7, 129.6, 125.9, 110.6, 71.2, 34.1, 34.0, 32.9, 31.2, 22.5, 14.0, 8.2.

IR: 2960 (s), 2933 (s), 2873 (m), 2304 (w), 1692 (m), 1666 (s), 1586 (m), 1479 (w), 1461 (s), 1378 (w), 1355 (w), 1322 (w), 1189 (m), 1122 (m), 1048 (w), 1023 (w), 981 (m).

MS: 258 (23, M^{+}), 229 (11), 202 (6), 201 (42), 173 (5), 159 (14), 157 (5), 149 (8), 129 (5), 128 (8), 115 (9), 111 (5), 57 (100), 55 (7).

HR-MS: 258.162050 ($C_{17}H_{22}O_2$, calc. 258.161980).

*3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-acrylonitrile (**4e**)*



1b **4e** (40%)

Purification by FC (silica, hexane/AcOEt 10:1) afforded 18 mg (0.08 mmol, 40%, 7:1 mixture of trans/cis isomer) of the product as a colorless oil.

^{1}H-NMR: δ *(trans-isomer)* 7.68 (d, 1H, J=16.8); 7.03 (d, 1H, J=8.0); 6.82 (d, 1H, 8.0); 5.68 (d, 1H, J=16.4); 4.63 (t, 2H, J=8.6); 3.31 (t, 2H, J=8.6); 2.63-2.68 (m, 2H); 1.48-1.60 (m, 2H); 1.35-1.46 (m, 2H); 0.96 (t, 3H, J=3.8).

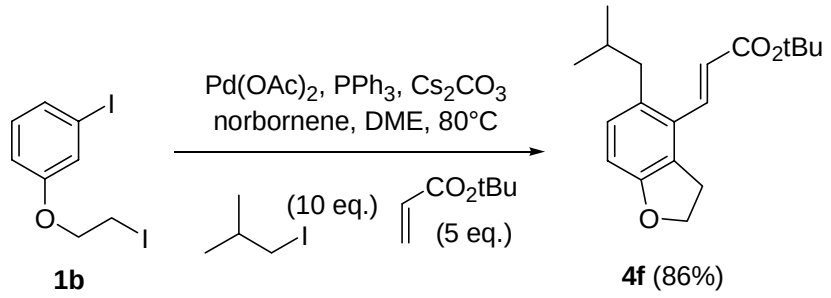
^{13}C-NMR: δ *(trans-isomer)* 159.0, 148.2, 134.6, 130.1, 129.1, 125.6, 118.3, 111.6, 99.9, 71.2, 34.2, 32.8, 30.9, 22.5, 13.9.

IR: 2961 (s), 2932 (s), 2873 (m), 2220 (s), 1877 (w), 1732 (m), 1616 (s), 1586 (s), 1460 (s), 1379 (w), 1364 (w), 1242 (s), 1192 (w), 1141 (w), 1104 (w), 1032 (w), 991 (m), 968 (m), 822 (m).

MS: 227 (40, M^{+}), 185 (23), 184 (100), 166 (5), 157 (15), 156 (8), 140 (6), 129 (9), 128 (10), 127 (6), 115 (9).

HR-MS: 227.130828 ($C_{15}H_{17}NO$, calc. 227.131014).

*3-(5-Isobutyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4f**)*



Purification by FC (silica, hexane/AcOEt 10:1), affording 52 mg (0.17 mmol, 86%) of the product as a colorless oil.

^{1}H-NMR: δ 7.88 (d, 1H, J=16.0); 6.96 (d, 1H, J=8.0); 6.77 (d, 1H, J=8.0); 6.12 (d, 1H, J=16.0); 4.61 (t, 2H, J=8.6); 3.37 (t, 2H, J=8.6); 2.58 (d, 2H, J=6.8); 1.75-1.87 (m, 1H); 1.58 (s, 9H); 0.94 (d, 6H, J=6.8).

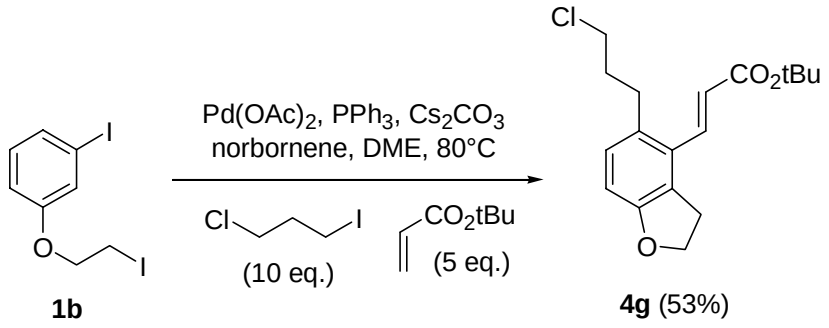
^{13}C-NMR: δ 140.9, 133.8, 130.6, 123.3, 110.0, 80.5, 71.2, 42.4, 31.3, 30.5, 28.3, 22.4.

IR: 3686 (w), 3050 (m), 2957 (s), 2932 (s), 2869 (s), 2305 (m), 1703 (s), 1632 (m), 1587 (m), 1461 (s), 1423 (m), 1392 (m), 1368 (s), 1317 (s), 1243 (m), 1218 (m), 1153 (s), 1088 (w), 1030)m), 987 (m), 948 (w), 895 (m).

MS: 302 (42, M^{+}), 259 (5), 247 (14), 146 (14), 229 (13), 204 (12), 203 (54), 201 (6), 186 (6), 185 (9), 175 (8), 173 (10), 171 (9), 160 (8), 159 (42), 158 (20), 157 (23), 144 (7), 141 (8), 131 (9), 129 (15), 128 (15), 127 (8), 116 (7), 115 (29), 91 (9), 77 (7), 58 (12), 57 (100), 55 (8).

HR-MS: 302.188701 ($C_{19}H_{26}O_3$, calc. 302.188195).

*3-[5-(3-Chloro-propyl)-2,3-dihydro-benzofuran-4-yl]-acrylic acid tert-butyl ester (**4g**)*



Purification by FC (silica, hexane/AcOEt 10:1) afforded 34 mg (0.11 mmol, 53%) of the product as a yellow oil.

^{1}H-NMR: δ 7.86 (d, 1H, J=16.4); 7.04 (d, 1H, J=8.0); 6.78 (d, 1H, J=8.0); 6.14 (d, 1H, J=16.4); 4.61 (t, 2H, J=8.6); 3.56 (t, 2H, J=6.4); 3.36 (t, 2H, J=8.6); 2.88 (t, 2H, J=7.4); 2.00-2.07 (m, 2H); 1.58 (s, 9H).

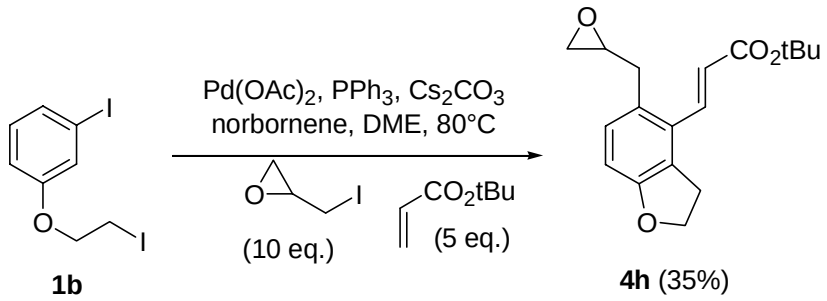
^{13}C-NMR: δ 166.2, 159.1, 140.2, 132.5, 130.3, 129.9, 126.2, 124.1, 110.4, 80.8, 71.2, 44.2, 34.2, 31.2, 30.0, 28.2.

IR: 3944 (w), 3757 (w), 3691 (w), 3060 (s), 2986 (s), 2684 (w), 2410 (w), 2305 (m), 1704 (m), 1633 (w), 1587 (w), 1421 (s), 1368 (w), 1317 (w), 1281 (s), 1250 (s), 1154 (m), 1030 (w), 986 (w), 950 (w), 896 (s).

MS: 324 (24), 323 (14), 322 (60, M^{+}), 268 (23), 267 (11), 266 (56), 251 (7), 249 (22), 221 (7), 204 (19), 203 (100), 189(9), 185 (12), 175 (10), 173 (7), 172 (8), 171 (16), 160 (7), 159 (49), 158 (29), 157 (35), 155 (6), 144 (8), 141 (10), 131 (11), 129 (20), 128 (24), 127 (12), 116 (7), 115 (23), 103 (5), 91 (11), 77 (10), 69 (6), 57 (70), 56 (6), 55 (9), 51 (6).

HR-MS: 322.133455 ($C_{18}H_{23}ClO_3$, calc. 322.133573).

*3-(5-Oxiranylmethyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4h**)*



Purification by FC (silica, hexane/AcOEt 5:1) afforded 21 mg (0.07 mmol, 35%) of the product as a colorless oil.

^{1}H-NMR: δ 7.86 (d, 1H, J=16.0); 7.09 (d, 1H, J=8.0); 6.79 (d, 1H, J=8.0); 6.14 (d, 1H, J=16.0); 4.62 (t, 2H, J=8.6); 3.36 (t, 2H, 8.6); 3.10-3.15 (m, 1H); 2.92-3.06 (m, 2H); 2.78-2.82 (m, 1H); 2.56 (dd, 1H, J=5.0 and 2.6); 1.57 (s, 9H).

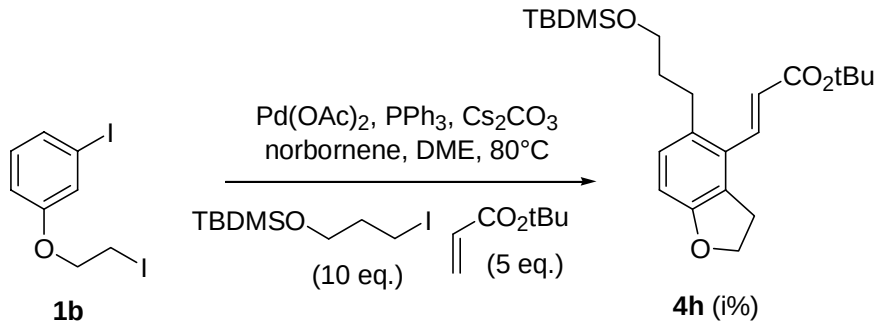
^{13}C-NMR: δ 166.2, 159.5, 140.5, 131.1, 130.4, 128.6, 126.2, 124.4, 110.4, 80.8, 71.3, 52.2, 47.0, 35.5, 31.0, 28.2.

IR: 3004 (m), 2966 (m), 1703 (s), 1634 (s), 1601 (m), 1587 (m), 1479 (m), 1463 (s), 1393 (m), 1368 (s), 1318 (s), 1151 (s), 1030 (m), 986 (m), 909 (m), 850 (m), 828 (m).

MS: 303 (21), 302 (100, M^{+}), 246 (23), 203 (35), 183 (43), 173 (15), 172 (13), 171 (67), 170 (11), 169 (22), 159 (43), 158 (21), 157 (41), 155 (13), 141 (17), 131 (16), 129 (18), 128 (26), 127 (11), 115 (32), 91 (11), 57 (80).

HR-MS: 302.152598 ($C_{18}H_{22}O_4$, calc. 302.151809).

*3-{5-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-2,3-dihydro-benzofuran-4-yl}-acrylic acid tert-butyl ester (**4i**)*



1b **4h** (i%)

Purification by FC (silica, hexane/AcOEt 20:1) afforded 50 mg (0.12 mmol, 60%) of the product as a colorless oil.

^{1}H-NMR: δ 7.87 (d, 1H, J=16.0); 7.02 (d, 1H, J=8.0); 6.76 (d, 1H, J=8.0); 6.13 (d, 1H, J=16.0); 4.60 (t, 2H, J=8.6); 3.66 (t, 2H, J=6.2); 3.35 (t, 2H, J=8.6); 2.76 (t, 2H, J=7.8); 1.75-1.84 (m, 2H); 1.57 (s, 9H); 0.94 (s, 9H); 0.09 (s, 6H).

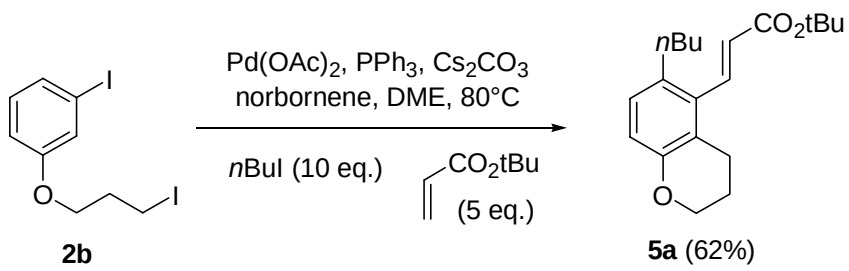
^{13}C-NMR: δ 166.3, 158.8, 140.6, 134.1, 130.3, 129.7, 126.0, 123.8, 110.2, 80.6, 71.2, 62.3, 34.6, 31.1, 29.3, 28.2, 26.0, 18.3, -5.3.

IR: 2955 (s), 2895 (s), 2856 (s), 2253 (w), 1704 (s), 1632 (m), 1587 (m), 1479 (m), 1462 (s), 1436 (w), 1419 (m), 1392 (m), 1368 (s), 1317 (s), 1209 (m), 1153 (s), 1098 (s), 1029 (w), 987 (m), 909 (m), 837 (s).

MS: 419 (1, M^+), 345 (5, M^+-OtBu), 306 (27), 305 (100), 287 (15), 243 (18), 215 (10), 213 (32), 187 (11), 185 (57), 171 (14), 159 (37), 157 (11), 115 (12), 75 (58), 73 (18), 57 (59).

HR-MS: 345.188975 ($C_{20}H_{29}O_3Si$, M^+ - C_4H_9O, calc. 345.188598).

*3-(6-Butyl-chroman-5-yl)-acrylic acid tert-butyl ester (**5a**)*



2b **5a** (62%)

Purification by FC (silica, hexane/AcOEt 10:1) afforded 40 mg (0.13 mmol, 62%) of the product as a colorless oil.

^{1}H-NMR: δ 7.71 (d, 1H, J=16.4); 7.01 (d, 1H, J=8.4); 6.77 (d, 1H, J=6.4), 5.98 (d, 1H, J=16.4); 4.17 (t, 2H, J=5.2); 2.76 (t, 2H, J=6.4); 2.57-2.62 (m, 2H); 1.98-2.03 (m, 2H); 1.58 (s, 9H); 1.48-1.58 (m, 2H); 1.35- 1.42 (m, 2H); 0.95 (t, 3H, J=7.2).

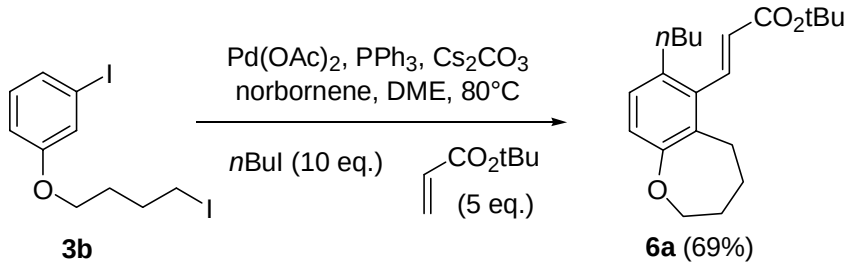
^{13}C-NMR: δ 165.9, 153.0, 141.8, 134.5, 133.2, 128.2, 126.1, 120.3, 116.9, 80.6, 65.8, 33.5, 32.7, 28.2, 24.4, 22.5, 22.4, 13.9.

IR: 3944 (m), 3756 (w), 3690 (w), 3060 (s), 2986 (s), 2957 (m), 2872 (m), 2684 (m), 2520 (w), 2410 (w), 2305 (s), 1704 (s), 1640 (w), 1592 (w), 1478 (m), 1466 (m), 1421 (s), 1280 (s), 1249 (s), 1154 (m), 1099 (w), 1072 (w), 1040 (w), 984 (w), 896 (s).

MS: 316 (58, M^{+}), 261 (12), 260 (49), 243 (19), 218 (21), 217 (100), 215 (10), 203 (9), 199 (6), 189 (12), 187 (23), 185 (7), 174 (7), 173 (43), 172 (17), 171 (22), 159 (8), 157 (7), 145 (19), 144 (9), 131 (8), 129 (9), 128 (13), 127 (6), 117 (6), 116 (9), 115 (19), 91 (7), 86 (7), 83 (10), 57 (80).

HR-MS: 316.203047 ($C_{20}H_{28}O_3$, calc. 316.203845).s

*3-(7-Butyl-2,3,4,5-tetrahydro-benzo[b]oxepin-6-yl)-acrylic acid tert-butyl ester (**6a**)*



3b **6a** (69%)

Purification by FC (silica, hexane/AcOEt 10:1), affording 46 mg (0.14 mmol, 69%) of the product as a colorless oil.

^{1}H-NMR: δ 7.77 (d, 1H, J=16.4); 6.99 (d, 1H, J=8.0); 6.93 (d, 1H, J=8.0); 6.00 (d, 1H, J=16.4); 4.03 (t, 2H, J=5.2); 2.85-2.90 (m, 2H); 2.54-2.60 (m, 2H); 1.97-2.01 (m, 2H); 1.68-1.75 (m, 2H); 1.58 (s, 9H); 1.49-1.55 (m, 2H); 1.35-1.42 (m, 2H); 0.95 (t, 3H, J=7.2).

^{13}C-NMR: δ 165.8, 159.1, 142.8, 136.4, 135.0, 133.9, 127.6, 126.6, 120.8, 80.6, 73.7, 33.2, 33.1, 32.1, 29.6, 28.2, 25.7, 22.5, 13.9.

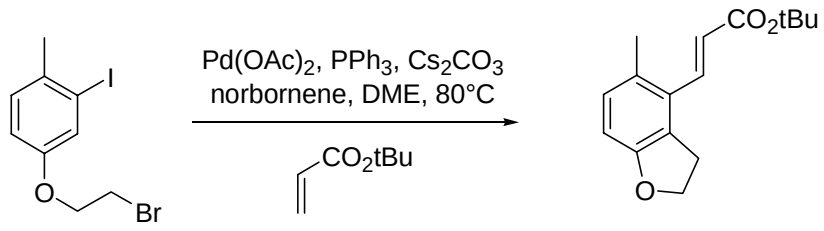
IR: 3944 (m), 3690 (w), 3062 (s), 2986 (s), 2960 (s), 2933 (s), 2872 (m), 2684 (m), 2410 (w), 2305 (s), 1704 (s), 1639 (w), 1584 (w), 1471 (m), 1422 (s), 1393 (w), 1368 (m), 1282 (s), 1249 (s), 1208 (w), 1153 (s), 1100 (w), 1034 (m), 984 (w), 895 (s).

MS: 330 (51, M^{+}), 275 (12), 274 (54), 157 (17), 232 (20), 231 (100), 229 (12), 217 (13), 203 (6), 201 (22), 189 (6), 187 (21), 186 (7), 185 (14), 182 (21), 173 (7), 171 (8), 161 (5), 159 (8), 157 (8), 145 (26), 144 (5), 131 (6), 129 (7), 128 (8), 117 (6), 115 (13), 91 (6), 86 (11), 84 (18), 57 (65), 55 (30), 51 (7).

HR-MS: 330.219875 ($C_{21}H_{30}O_3$, calc. 330.219495).

Cyclization reactions, ortho substituted substrates

*3-(5-Methyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**8**)*



7 69% **8**

4-(2-Bromo-ethoxy)-2-iodo-1-methyl-benzene (68 mg, 0.2 mmol), *tert*-butyl acrylate (0.146 ml, 1 mmol, 5 eq.), norbornene (96 mg, 1 mmol, 5 eq.), Cs_2CO_3 (195 mg, 0.6 mmol, 3 eq.), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and PPh_3 (10.5 mg, 20 mol%) were dissolved in 2 ml of degassed dry dimethoxyethane. The mixture was flushed with N_2 and heated at 80°C for 16 h. After cooling at RT, the mixture was diluted with diethyl ether, washed with water, dried over magnesium sulfate and purified by FC (silica, hexane/AcOEt 15:1), affording 36 mg (0.14 mmol, 69%) of the product as a yellow oil.

^{1}H-NMR: δ 7.84 (d, 1H, J=16.0); 7.00 (d, 1H, J=8.0); 6.73 (d, 1H, J=8.0); 6.14 (d, 1H, J=16.0); 4.60 (t, 2H, J=8.6); 3.34 (t, 2H, J=8.6); 2.39 (s, 3H); 1.58 (s, 9H).

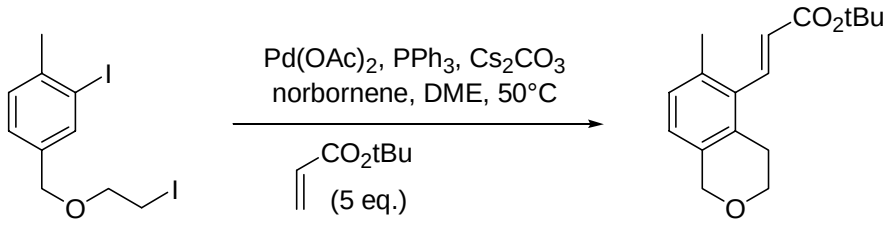
^{13}C-NMR: δ 166.5, 158.7, 140.7, 130.5, 130.1, 129.6, 126.1, 123.5, 110.2, 80.6, 71.1, 31.0, 28.2, 19.8.

IR: 2979 (m), 2932 (m), 1702 (s), 1633 (s), 1588 (m), 1392 (m), 1318 (s), 1160 (s), 1039 (w), 986 (m), 950 (w).

MS: 261 (29), 260 (100, M^+), 233 (25), 205 (27), 204 (93), 189 (25), 187 (50), 186 (20), 185 (18), 172 (13), 171 (31), 159 (47), 158 (37), 157 (23), 155 (25), 147 (11), 145 (49), 144 (18), 141 (10), 133 (10), 132 (10), 131 (32), 130 (11), 129 (23), 128 (18), 116 (15), 115 (30), 106 (11), 105 (14), 91 (19), 78 (19), 77 (21), 57 (38), 52 (10), 51 (16).

HR-MS: 260.141562 ($C_{16}H_{20}O_3$, calc. 260.141245).

*3-(6-Methyl-isochroman-5-yl)-acrylic acid tert-butyl ester (**11**)*



9 **11** (62%)

2-Iodo-4-(2-iodo-ethoxymethyl)-1-methyl-benzene (80.4 mg, 0.2 mmol), *tert*-butyl acrylate (0.146 ml, 1 mmol, 5 eq.), norbornene (96 mg, 1 mmol, 5 eq.), Cs_2CO_3 (196 mg, 0.6 mmol, 3 eq.), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and PPh_3 (10.5 mg, 20 mol%) were dissolved in 2 ml of degassed dry dimethoxyethane. The mixture was flushed with N_2 and heated at 50°C for 48 h. After cooling at RT, the mixture was diluted with diethyl ether, washed with water, dried over magnesium sulfate and purified by FC (silica, hexane/AcOEt 10:1 to 10:1), affording 34 mg (0.12 mmol, 62%) of the product as a colorless oil.

^{1}H-NMR: δ 7.72 (d, 1H, J=16.4); 7.09 (d, 1H, J=8.0); 7.01 (d, 1H, J=8.0); 6.00 (d, 1H, J=16.4); 4.80 (s, 2H); 3.98 (t, 2H, J=5.8); 2.85 (t, 2H, J=5.8); 2.37 (s, 3H); 1.58 (s, 9H).

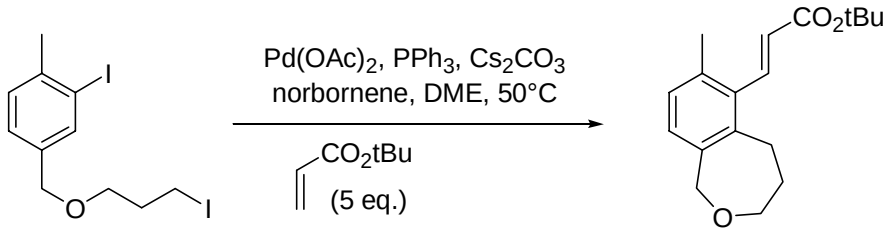
^{13}C-NMR: δ 166.0, 141.2, 134.7, 134.0, 132.7, 131.9, 128.2, 126.2, 124.5, 80.7, 68.0, 28.2, 27.6, 20.8.

IR: 3943 (m), 3756 (w), 3690 (w), 3058 (s), 2985 (s), 2830 (w), 2684 (m), 2520 (w), 2410 (w), 2305 (s), 2124 (w), 2054 (w), 1704 (m). 1639 (w), 1550 (w), 1421 (s), 1281 (s), 1250 (s), 1153 (m), 1111 (m), 1073 (w), 983 (w), 896 (s).

MS: (18, M^+), 219 (5), 218 (30), 217 (23), 206 (15), 204 (5), 203 (34), 202 (7), 201 (48), 200 (100), 189 (6), 188 (8), 185 (12), 182 (8), 175 (6), 174 (7), 173 (16), 172 (16), 171 (38), 170 (6), 159 (7), 158 (22), 157 (19), 156 (30), 155 (93), 147 (9), 145 (26), 144 (20), 143 (71), 142 (10), 141 (17), 131 (7), 130 (10), 129 (28), 128 (38), 127 (9), 119 (11), 117 (7), 116 (6), 115 (20), 105 (6), 91 (13).

HR-MS: 274.156613 ($C_{17}H_{22}O_3$, calc. 274.156895).

3-(7-Methyl-1,3,4,5-tetrahydro-benzo[c]oxepin-6-yl)-acrylic acid tert-butyl ester ***(12)***



10 **12** (61%)

2-Iodo-4-(3-iodo-propoxymethyl)-1-methyl-benzene (83.2 mg, 0.2 mmol), tert-butyl acrylate (0.146 ml, 1 mmol, 5 eq.), norbornene (96 mg, 1 mmol, 5 eq.), Cs_2CO_3 (196 mg, 0.6 mmol, 3 eq.), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and PPh_3 (10.5 mg, 20 mol%) were dissolved in 2 ml of degassed dry dimethoxyethane. The mixture was flushed with N_2 and heated at 50°C for 48 h. After cooling at RT, the mixture was diluted with diethyl ether, washed with water, dried over magnesium sulfate and purified by FC (silica, hexane/AcOEt 10:1 to 10:1), affording 35 mg (0.12 mmol, 61%) of the product as a colorless oil.

^{1}H-NMR: δ 7.70 (d, 1H, J=16.0); 7.08 (d, 1H, J=7.2); 7.03 (d, 1H, J=7.2); 5.87 (d, 1H, J=16.0); 4.68 (s, 2H); 4.05-4.08 (m, 2H); 3.08-3.11 (m, 2H), 2.31 (s, 3H); 181-1.83 (m, 2H); 1.59 (s, 9H).

^{13}C-NMR: δ 165.8, 143.1, 140.6, 138.3, 135.9, 134.6, 128.5, 127.6, 126.7, 80.7, 75.2, 74.6, 30.6, 30.0, 28.3, 21.1.

IR: 3944 (m), 3690 (w), 3049 (s), 2987 (s), 2851 (w), 2684 (m), 2520 (w), 2410 (w), 2305 (s), 1705 (m). 1642 (w), 1604 (w), 1421 (s), 1280 (s), 1249 (s), 1153 (m), 1106 (m), 1036 (w), 984 (w), 895 (s).

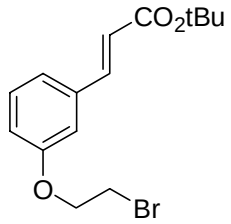
MS: 288 (25, M^+), 233 (14), 232 (78), 231 (8), 217 (13), 216 (7), 215 (52), 214 (59), 202 (22), 201 (8), 199 (16), 197 (6), 196 (22), 195 (5), 189 (15), 188 (28), 187 (19), 186 (32), 185 (45), 184 (6), 183 (21), 181 (17), 175 (30), 174 (5), 173 (22), 172 /56), 171 (18), 170 (41), 169 (86), 168 (13), 167 (8), 161 (7), 160 (5), 159 (20), 158 (32), 157 (100), 156 (20), 155 (42), 154 (7), 153 (12), 145 (26),

144 (38), 143 (63), 142 (72), 141 (40), 131 (11), 130 (13), 129 (36), 128 (34), 127 (12), 119 (8), 117 (7), 116 (10), 115 (31), 105 (6), 91 (13), 77 (8), 57 (75), 55 (6).

HR-MS: 288.172276 ($C_{18}H_{24}O_3$, calc. 288.172545).

By-products of the three-component coupling

*3-[3-(2-Bromo-ethoxy)-phenyl]-acrylic acid tert-butyl ester (**C**)*



C

^{1}H-NMR: δ 7.57 (d, 1H, J=16.0); 7.33 (t, 1H, J=8.0); 7.17 (d, 1H, J=8.0); 7.08 (br s, 1H), 6.96 (dd, 1H, J=8.0 and 2.5); 6.39 (d, 1H, J=16.0); 4.35 (t, 2H, J=6.3); 3.68 (t, 2H, J=6.3); 1.57 (s, 9H).

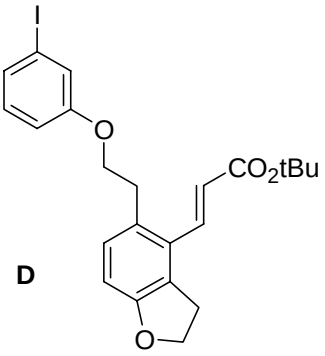
^{13}C-NMR: δ 166.2, 158.4, 143.2, 136.2, 130.0, 121.4, 120.8, 116.5, 113.8, 80.6, 68.0, 29.0, 28.2.

IR: 3060 (s), 2986 (s), 2684 (w), 2520 (w), 2409 (w), 2305 (m), 2124 (w), 2054 (w), 1702 (m), 1638 (m), 1550 (w), 1421 (s), 1368 (w), 1278 (s), 1248 (s), 1154 (m), 1076 (w), 1021 (w), 983 (w), 897 (s).

MS: 329 (10), 328 (44, M^+, ^{81}Br), 327 (10), 326 (44, M^+, ^{79}Br), 273 (22), 272 (97), 271 (23), 270 (97), 256 (43), 253 (42), 164 (45), 163 (22), 147 (27), 146 (15), 136 (11), 119 (13), 118 (35), 115 (14), 109 (79), 107 (81), 91 (29), 90 (23), 89 (25), 87 (12), 65 (14), 64 (11), 63 (17), 57 (100), 56 (12).

HR-MS: 326.051630 ($C_{15}H_{19}BrO_3$, calc. 326.051756).

*3-{5-[2-(3-Iodo-phenoxy)-ethyl]-2,3-dihydro-benzofuran-4-yl}-acrylic acid tert-butyl ester (**D**)*



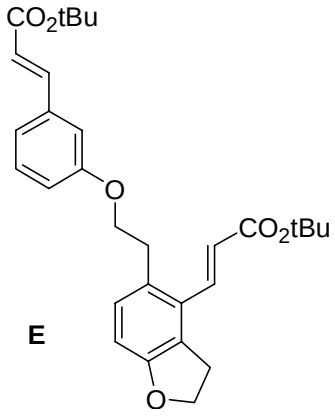
D

^{1}H-NMR: δ 7.60 (d, 1H, 16.0); 7.28-7.38 (m, 2H); 7.18 (d, 1H, J=8.4); 6.92-6.95 (m, 1H); 6.89 (d, 1H, 8.4); 6.84 (t, 1H, J=2.0); 6.12 (d, 1H, J=16.0); 4.69 (t, 2H, J=8.6); 4.30 (t, 2H, J=7.0); 3.41-3.50 (m 4H); 1.58 (s, 9H).

MS: 492 (10, M^+), 437 (16), 436 (75), 419 (11), 391 (33), 237 (45), 236 (100), 208 (13), 207 (17), 155 (13), 87 (11), 84 (10), 57 (32).

HR-MS: 492.081115 ($C_{23}H_{25}IO_4$, calc. 492.079762).

*3-(3-{2-[4-(2-tert-Butoxycarbonyl-vinyl)-2,3-dihydro-benzofuran-5-yl]-ethoxy}-phenyl)-acrylic acid tert-butyl ester (**E**)*



E

^{1}H-NMR: δ 7.96 (d, 1H, J=16.6); 7.55 (d, 1H, 16.0); 7.26-7.31 (m, 1H); 7.12 (d, 1H, J=8.0); 7.10 (d, 1H, J=7.2); 7.01-7.02 (m, 1H); 6.91 (dd, 1H, J=8.2 and 2.6); 6.81 (d, 1H, J=8.0); 6.36 (d, 1H, J=16.0); 6.18 (d, 1H, J=16.6); 4.62 (t, 2H, J=8.6); 4.14 (t, 2H, J=6.9); 3.37 (t, 2H, J=8.6); 3.21 (t, 2H, J=6.9); 1.57 (s, 9H); 1.56 (s, 9H).

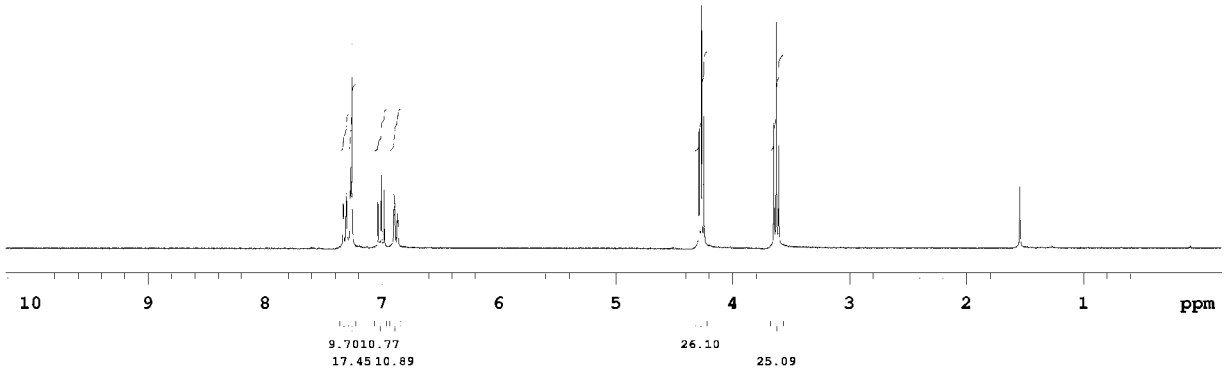
^{13}C-NMR: δ 166.3, 166.2, 159.4, 159.1, 143.5, 140.4, 136.0, 131.0, 130.5, 129.8, 129.7, 126.2, 124.4, 120.8, 120.5, 116.4, 113.4, 110.5, 80.8, 80.5, 71.3, 68.6, 32.8, 31.1, 28.2, 28.2.

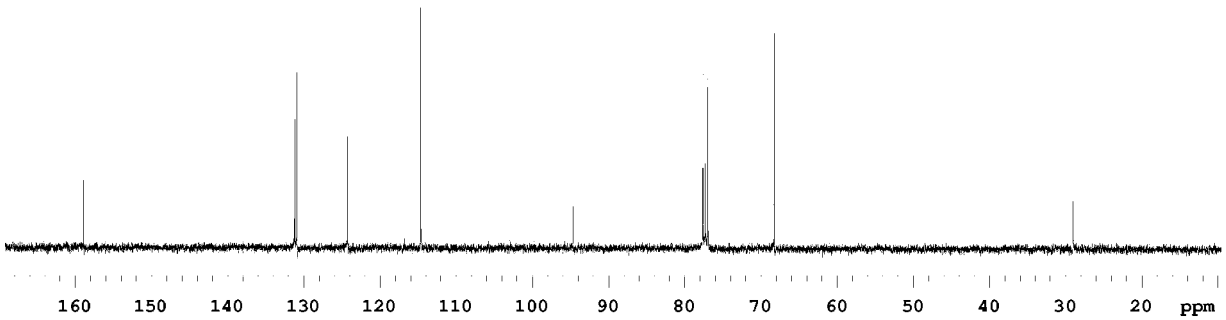
IR: 2960 (m), 2948 (m), 2872 (m), 1703 (s), 1637 (m), 1586 (m), 1462 (m), 1392 (w), 1368 (m), 1318 (s), 1153 (s), 1040 (w), 983 (m), 850 (w).

MS: 492 (4, M^{+}), 436 (10), 381 (14), 380 (28), 364 (12), 363 (40), 362 (44), 343 (10), 273 (30), 236 (13), 218 (13), 217 (63), 216 (18), 203 (17), 199 (13), 198 (10), 185 (15), 173 (19), 172 (21), 171 (50), 159 (18), 158 (15), 157 (21), 147 (11), 129 (12), 128 (15), 115 (13), 91 (10), 87 (12), 57 (100).

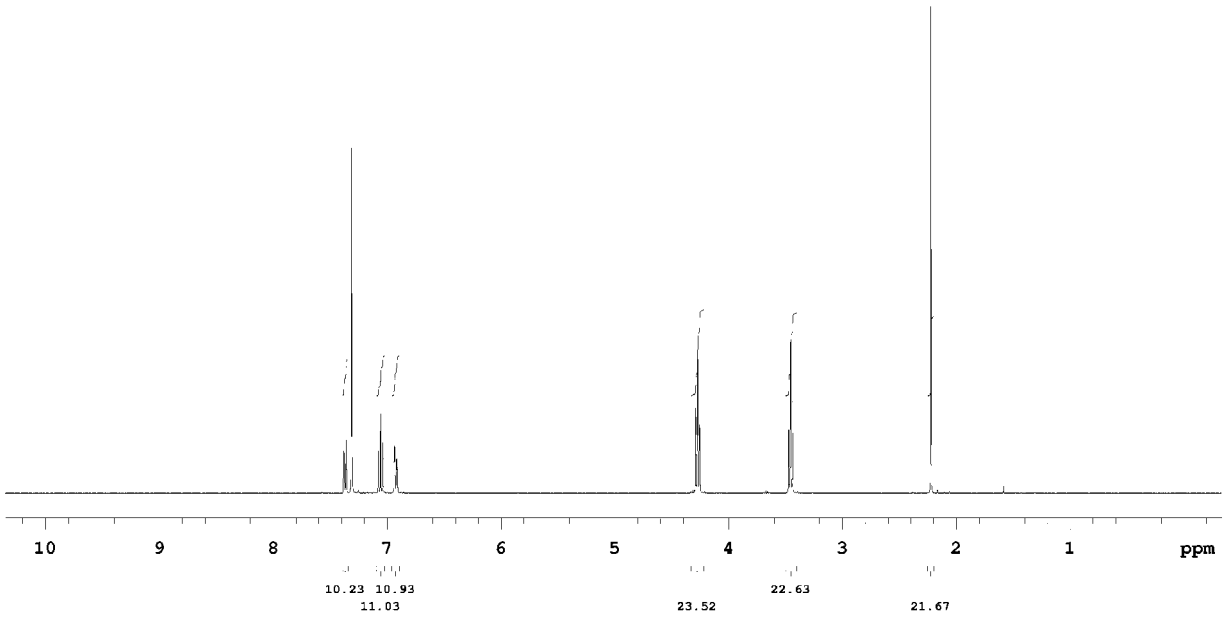
HR-MS: 492.252506 ($C_{30}H_{36}O_6$, calc. 492.251189).

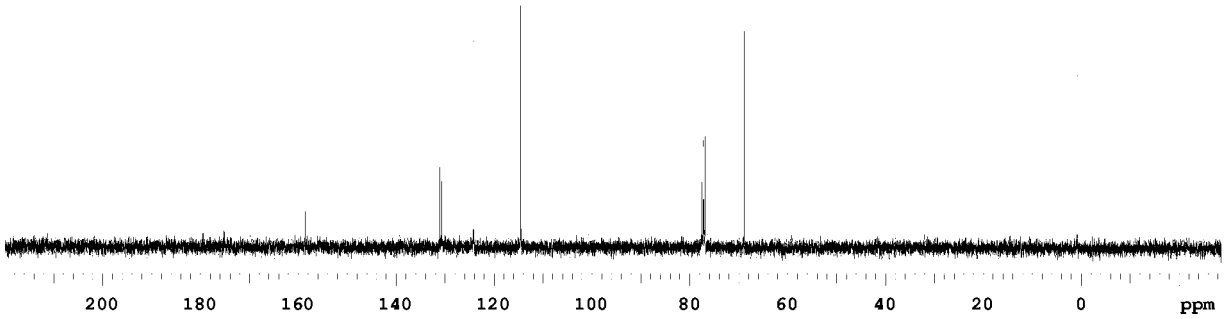
1-(2-Bromo-ethoxy)-3-iodo-benzene (**1a**): ^{1}H and ^{13}C-NMR in $CDCl_3$



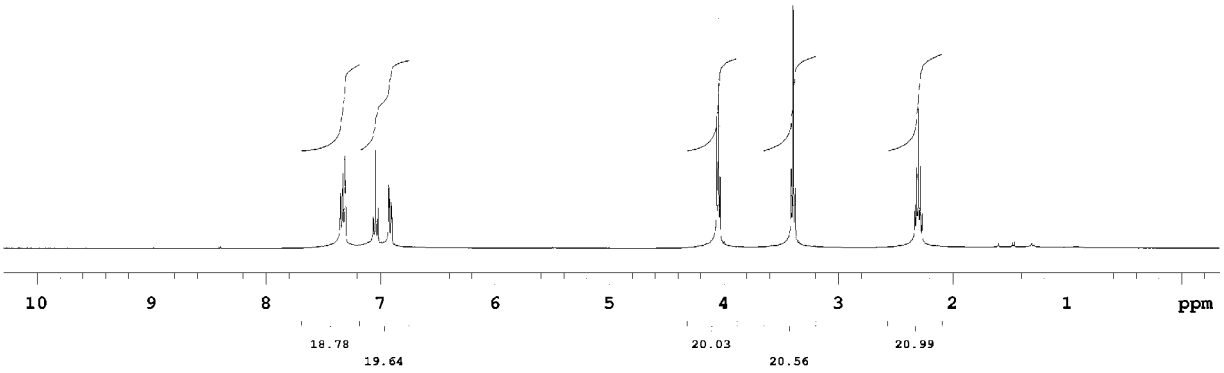


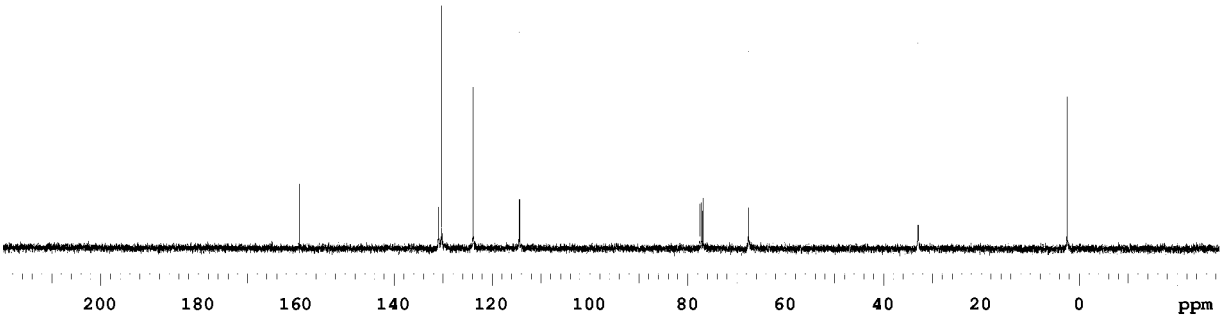
1-Iodo-3-(2-iodo-ethoxy)-benzene (**1b**): ^{1}H and ^{13}C-NMR in $CDCl_3$



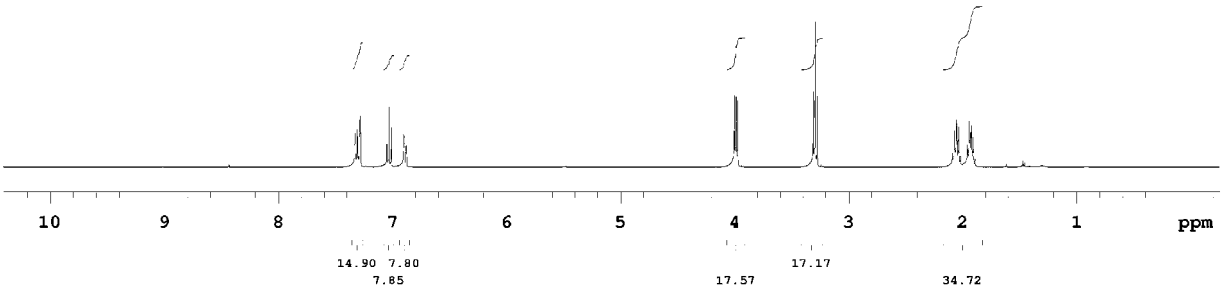


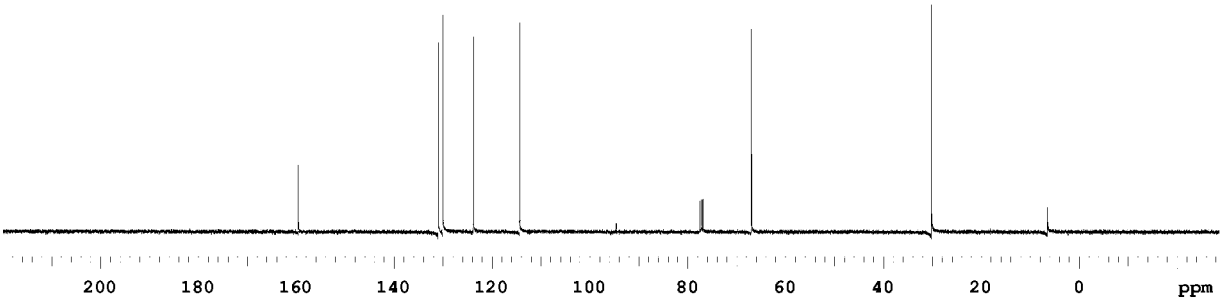
1-Iodo-3-(3-iodo-propoxy)-benzene (**2b**): ^{1}H and ^{13}C-NMR in $CDCl_3$



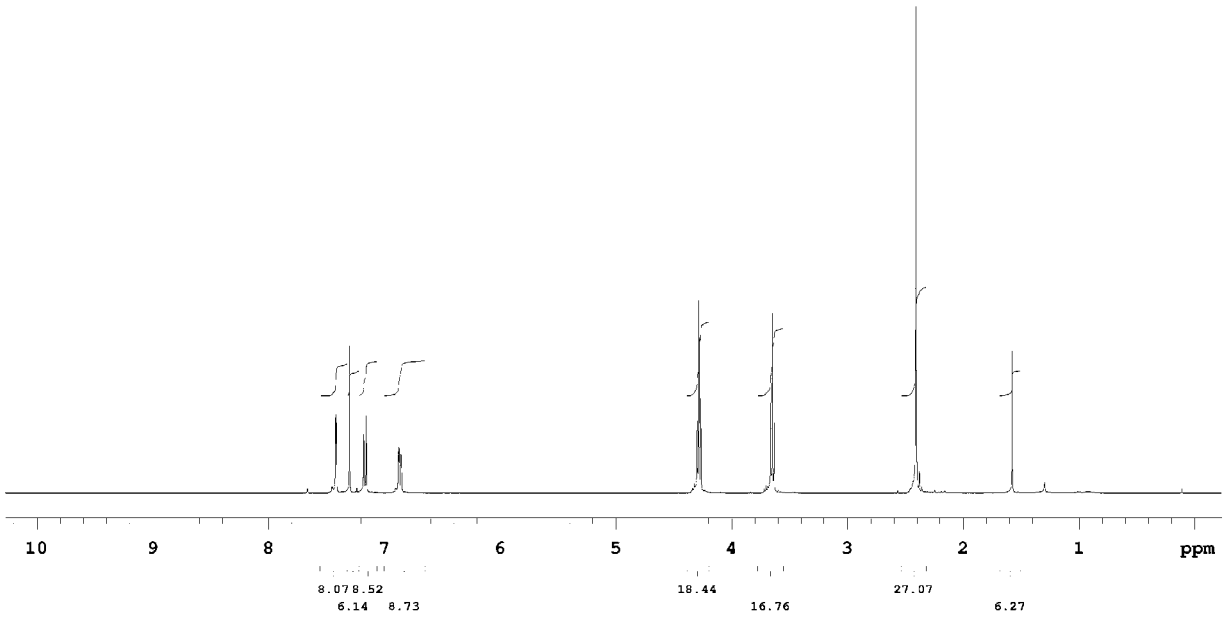


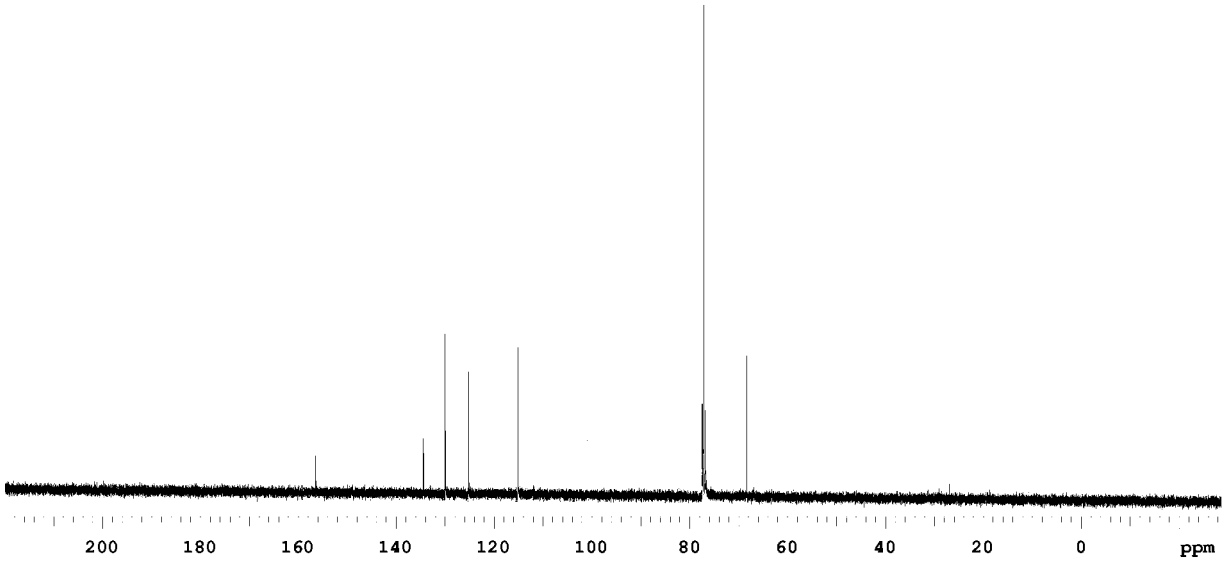
1-Iodo-3-(4-iodo-butoxy)-benzene (**3b**): ^{1}H and ^{13}C-NMR in $CDCl_3$



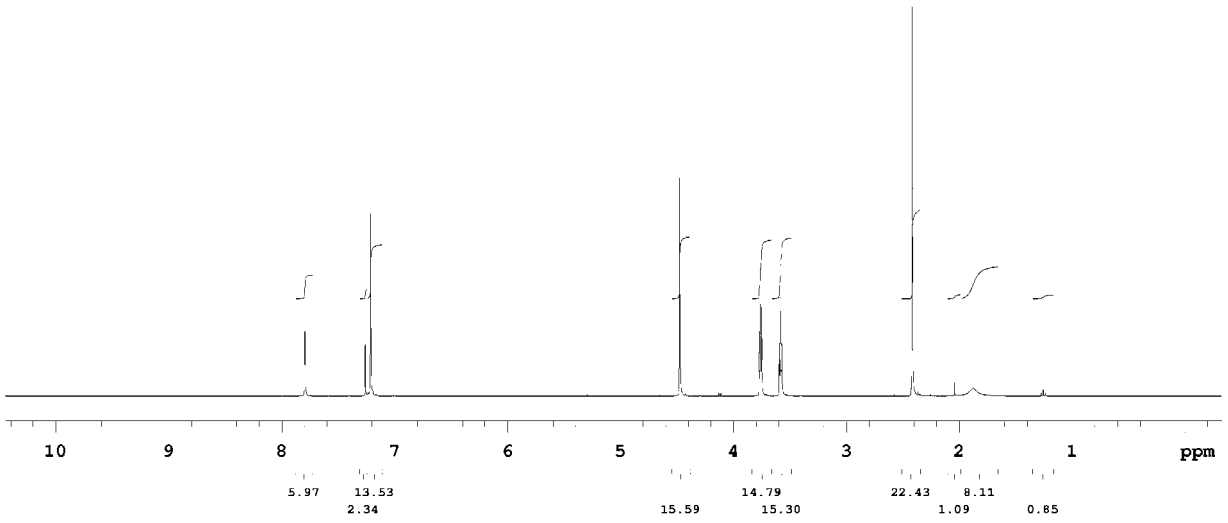


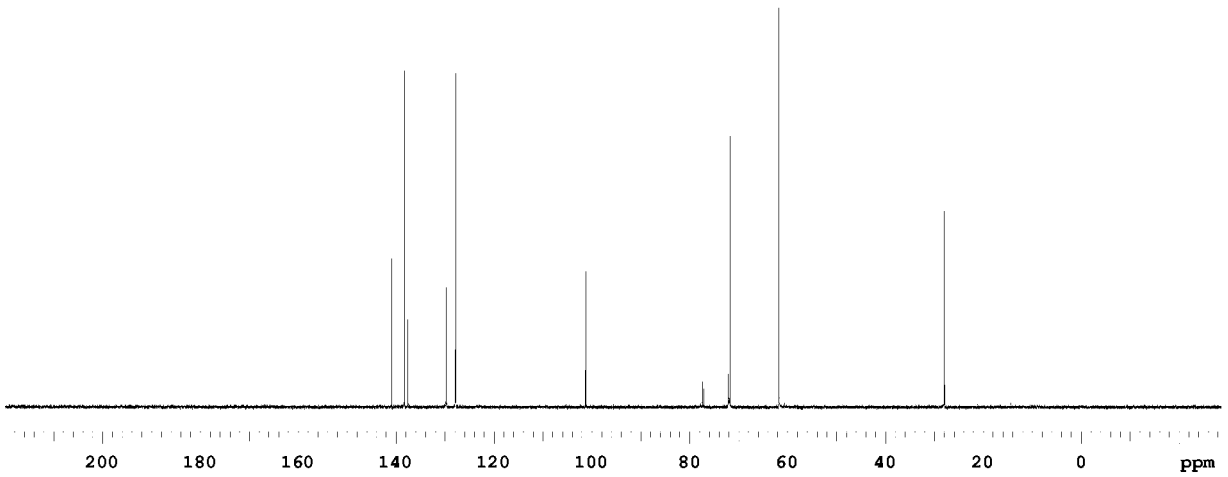
4-(2-Bromo-ethoxy)-2-iodo-1-methyl-benzene (**7**):



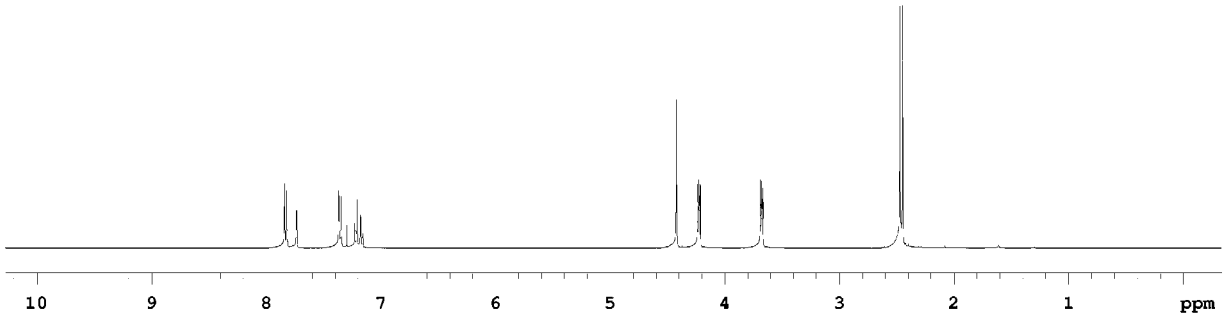


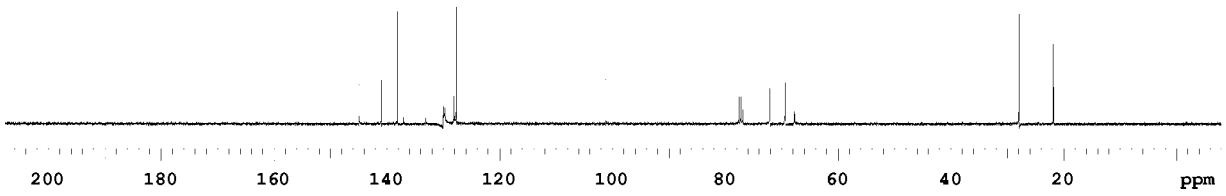
2-(3-Iodo-4-methyl-benzyloxy)-ethanol: ^{1}H and ^{13}C-NMR in $CDCl_3$



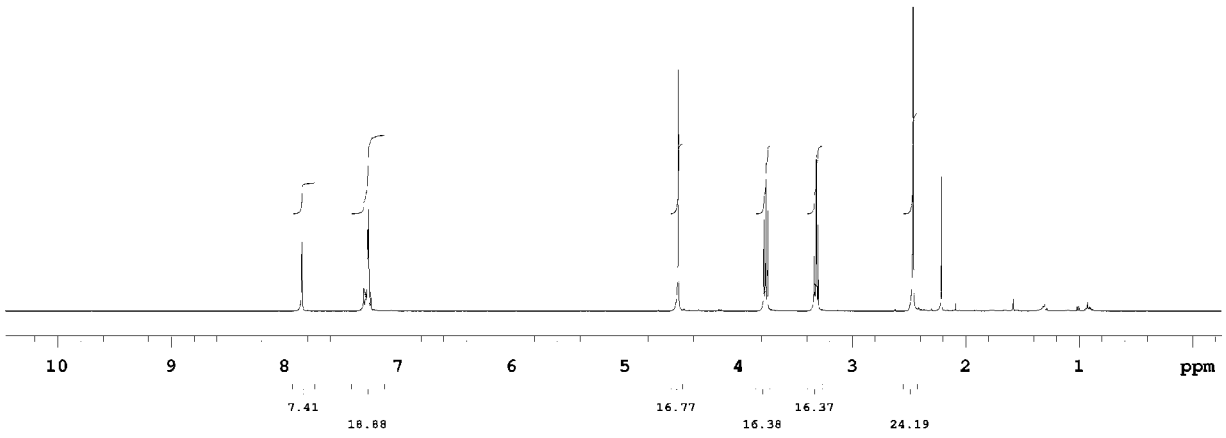


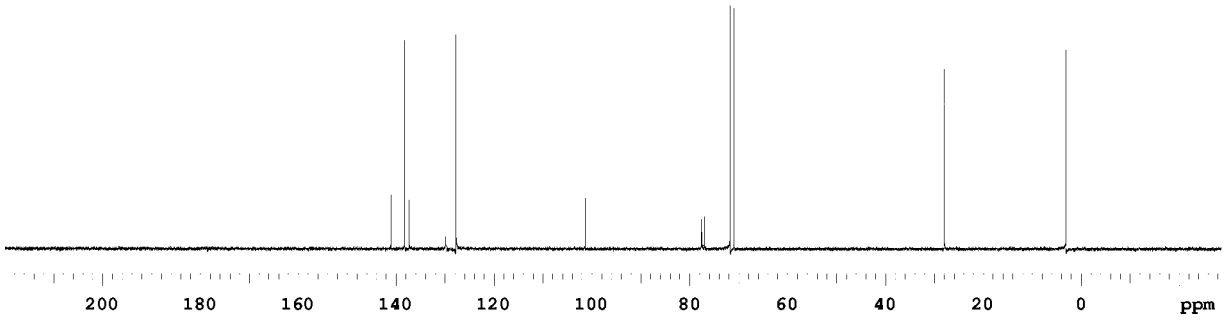
Toluene-4-sulfonic acid 2-(3-iodo-4-methyl-benzyloxy)-ethyl ester: ^{1}H and ^{13}C-NMR in $CDCl_3$



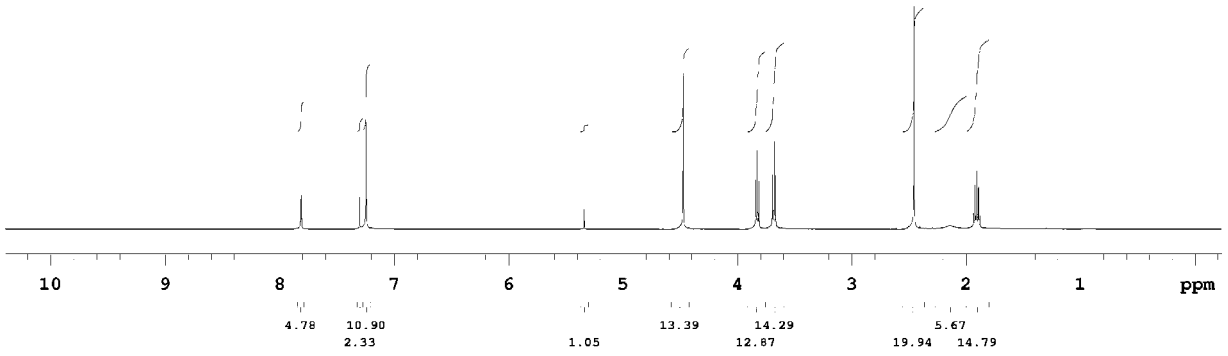


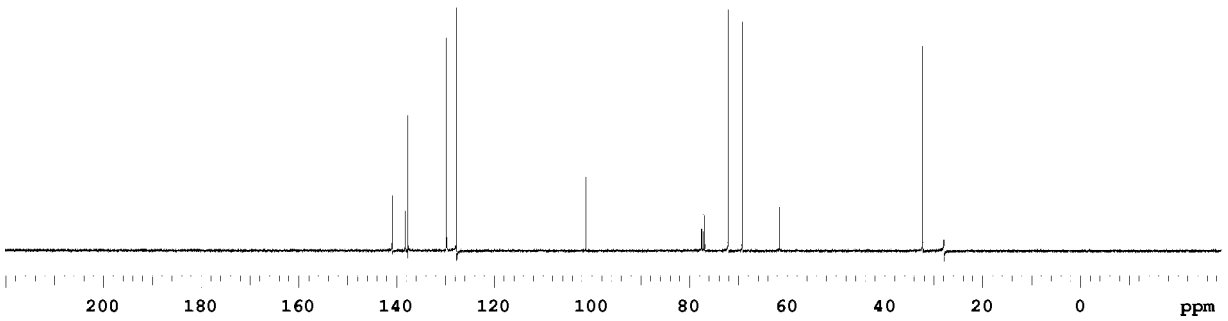
2-Iodo-4-(2-iodo-ethoxymethyl)-1-methyl-benzene (**9**): ^{1}H and ^{13}C-NMR in $CDCl_3$



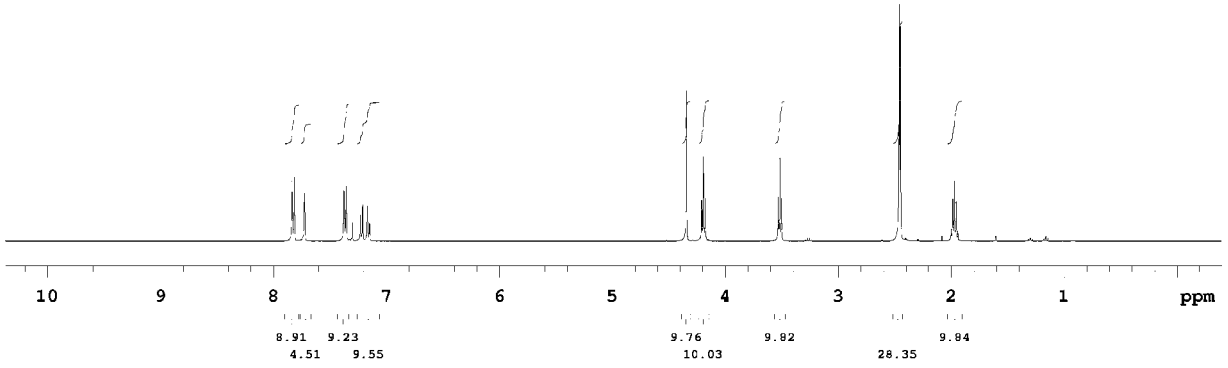


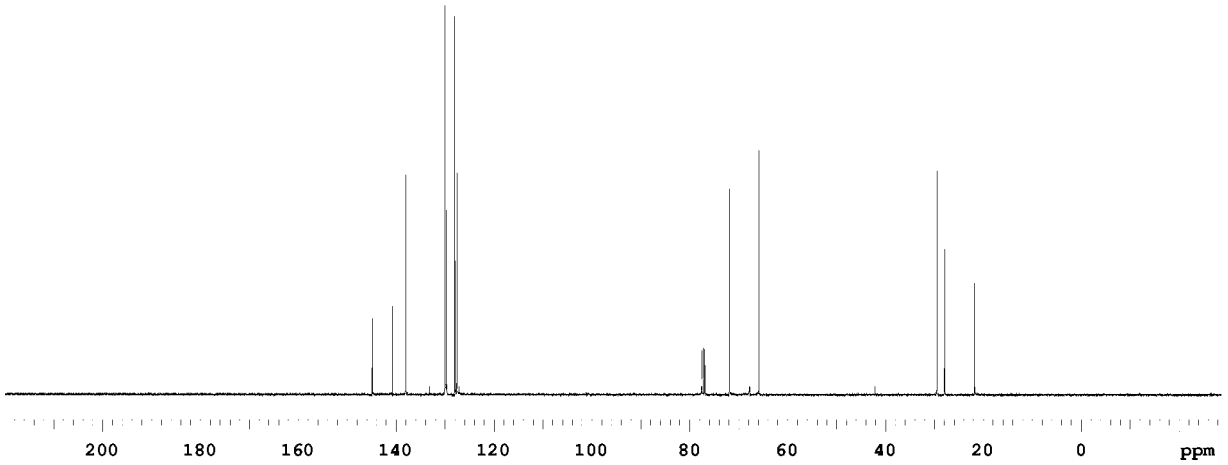
3-(3-Iodo-4-methyl-benzyloxy)-propan-1-ol: ^{1}H and ^{13}C-NMR in $CDCl_3$



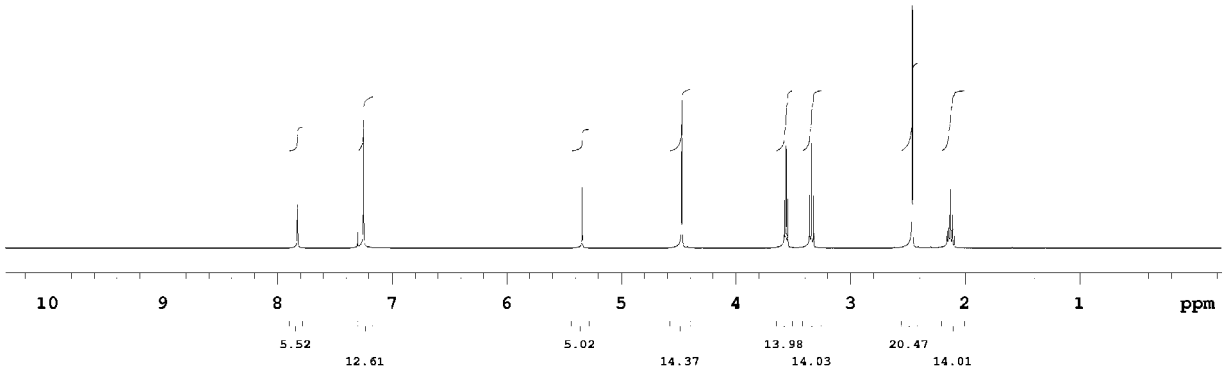


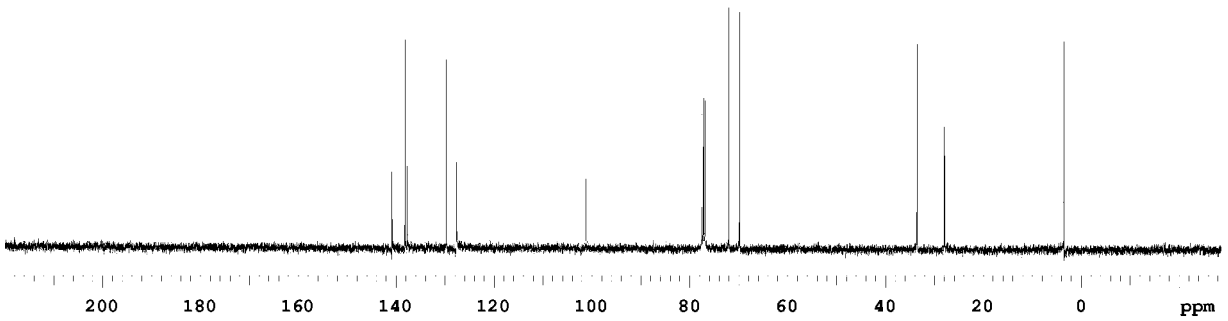
Toluene-4-sulfonic acid 3-(3-iodo-4-methyl-benzyloxy)-propyl ester: ^{1}H and ^{13}C-NMR in $CDCl_3$



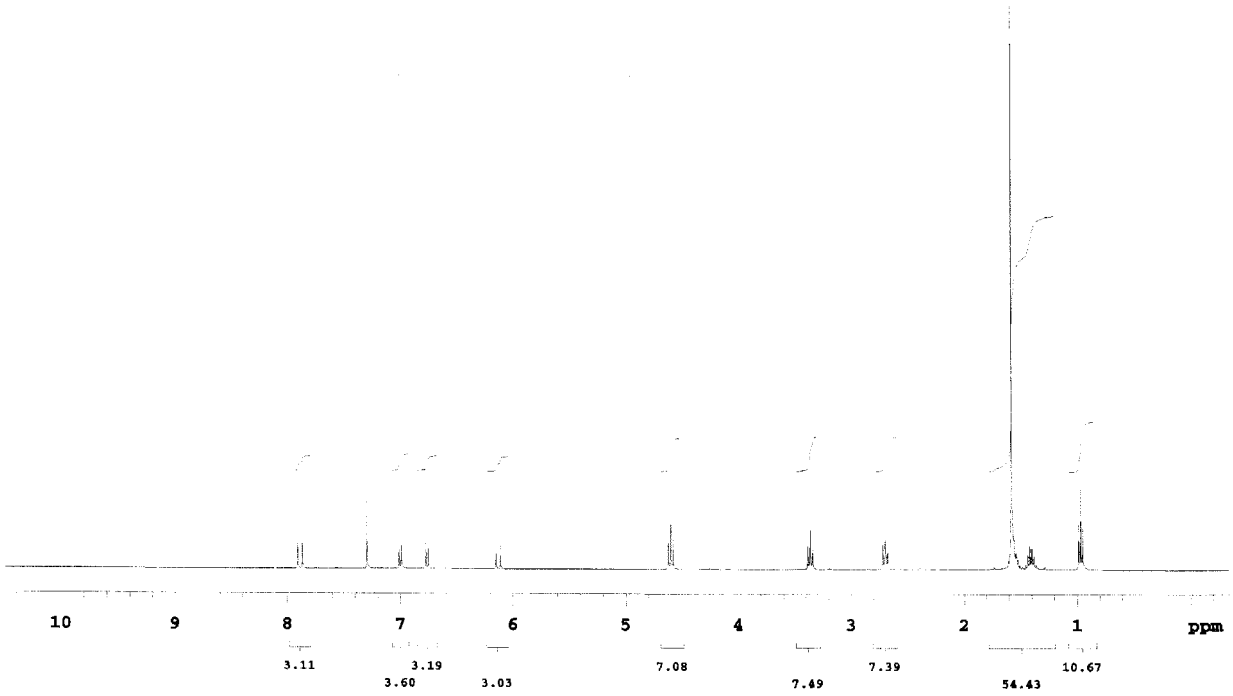


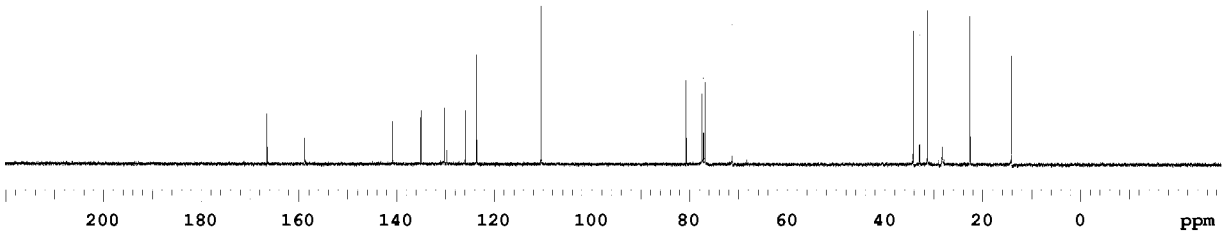
2-Iodo-4-(3-iodo-propoxymethyl)-1-methyl-benzene (**10**): ^{1}H and ^{13}C-NMR in $CDCl_3$



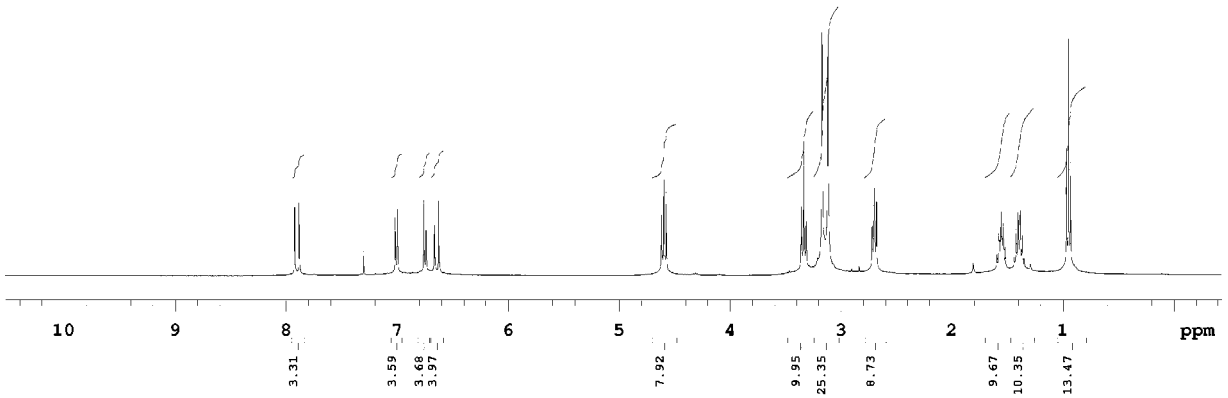


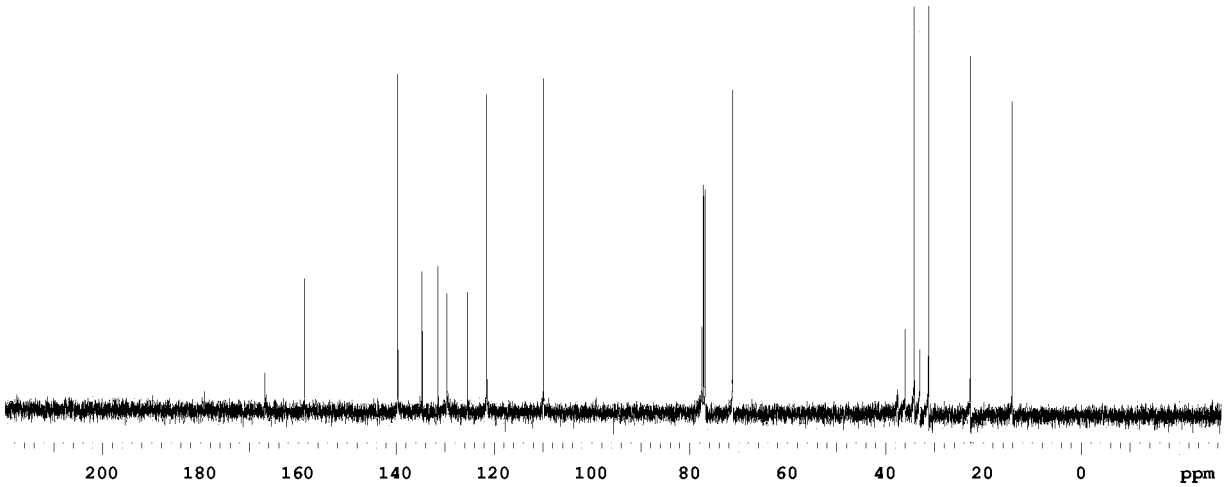
3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4a**): ^{1}H and ^{13}C-NMR in $CDCl_3$



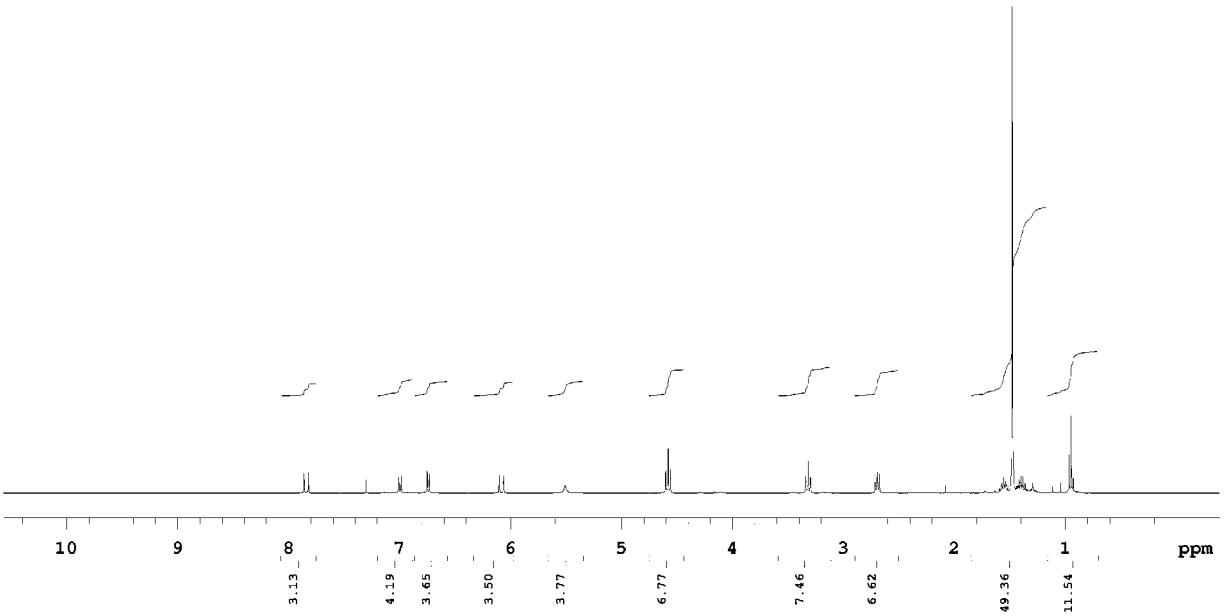


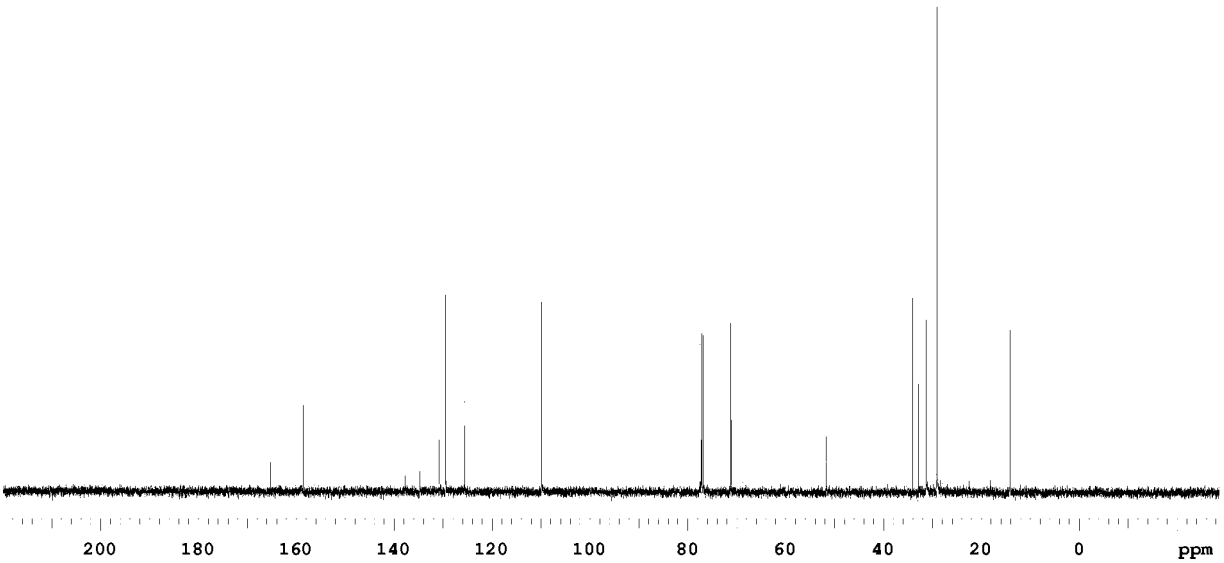
3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-N,N-dimethyl-acrylamide (**4b**): ^{1}H and ^{13}C-NMR in $CDCl_3$



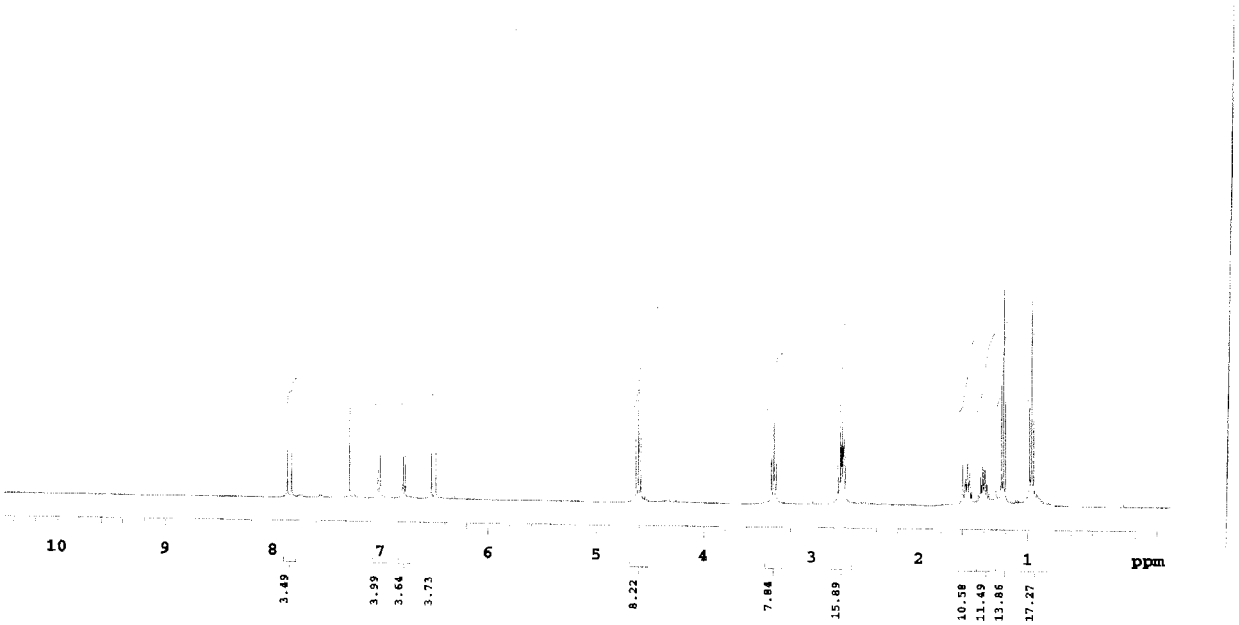


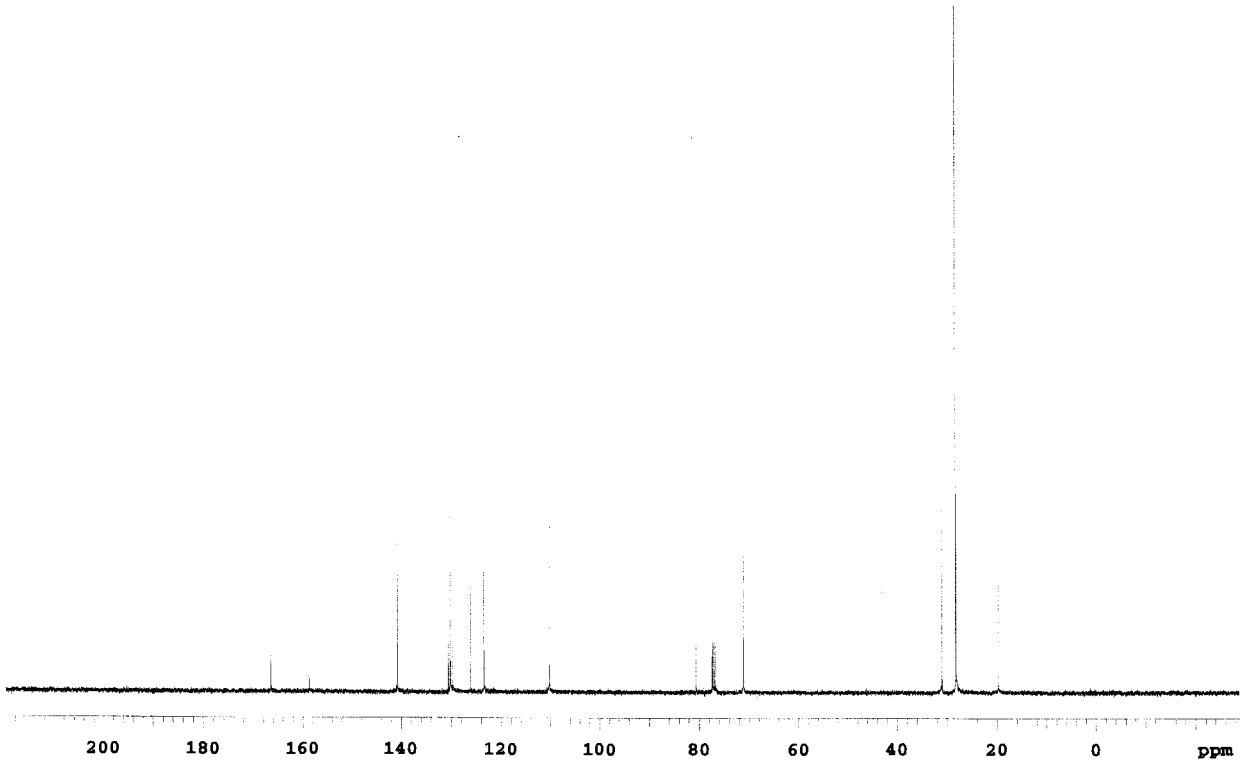
N-tert-Butyl-3-(5-butyl-2,3-dihydro-benzofuran-4-yl)-acrylamide (**4c**): ^{1}H and ^{13}C-NMR in $CDCl_3$



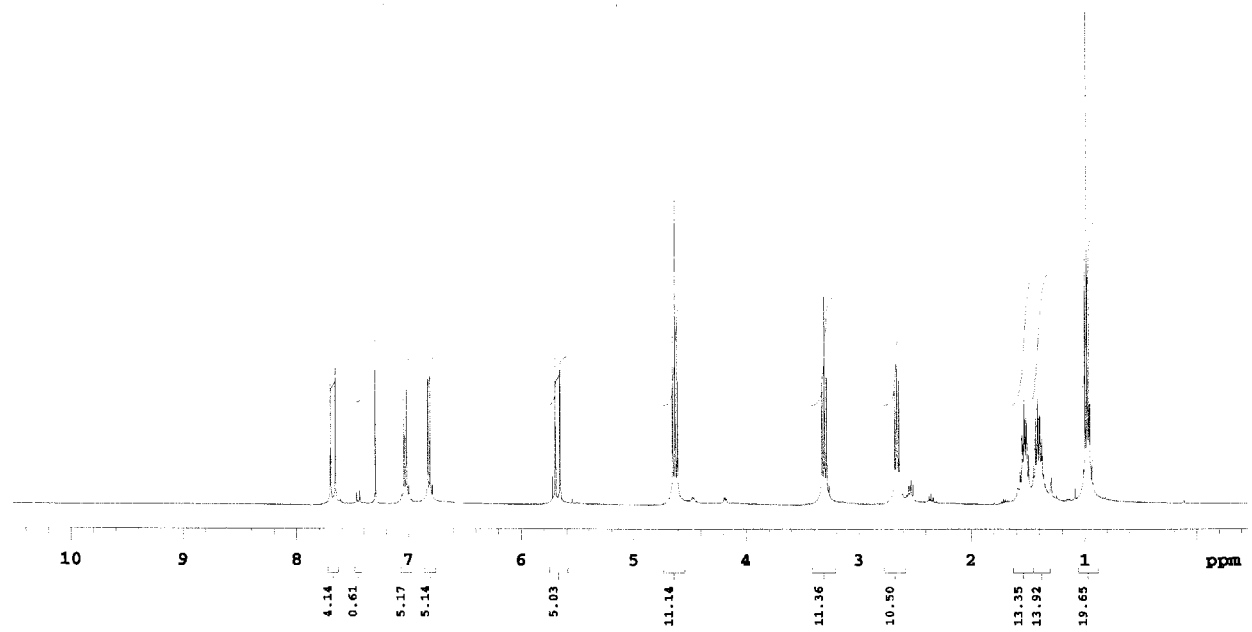


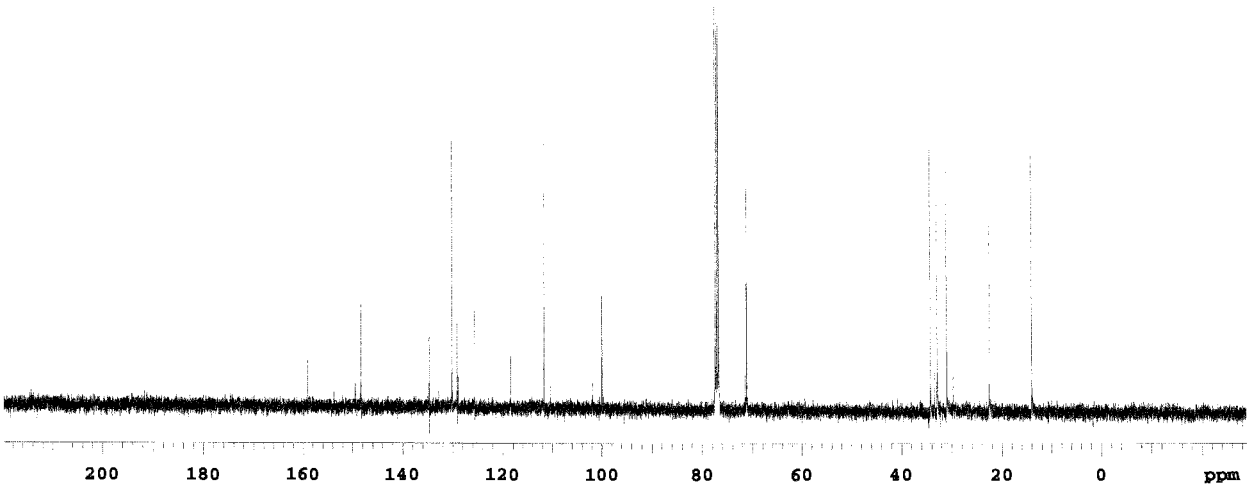
1-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-pent-1-en-3-one (**4d**): ^{1}H and ^{13}C-NMR in $CDCl_3$



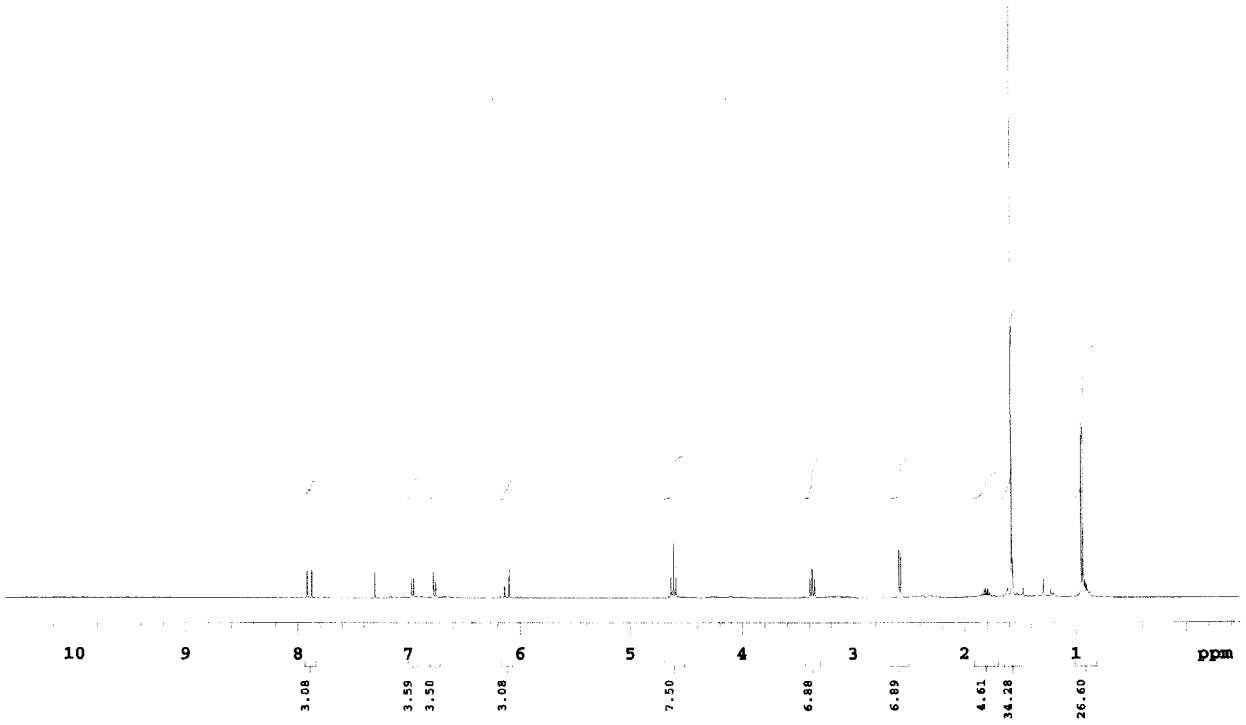


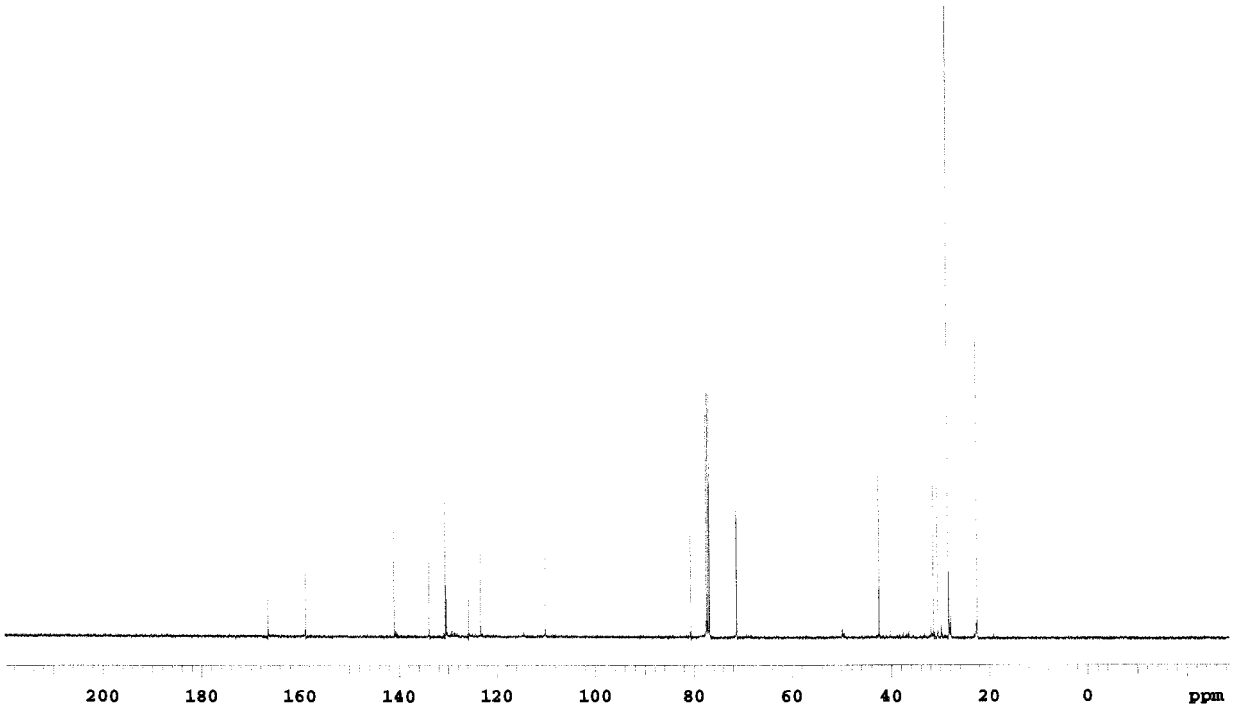
3-(5-Butyl-2,3-dihydro-benzofuran-4-yl)-acrylonitrile (**4e**): ^{1}H and ^{13}C-NMR in $CDCl_3$



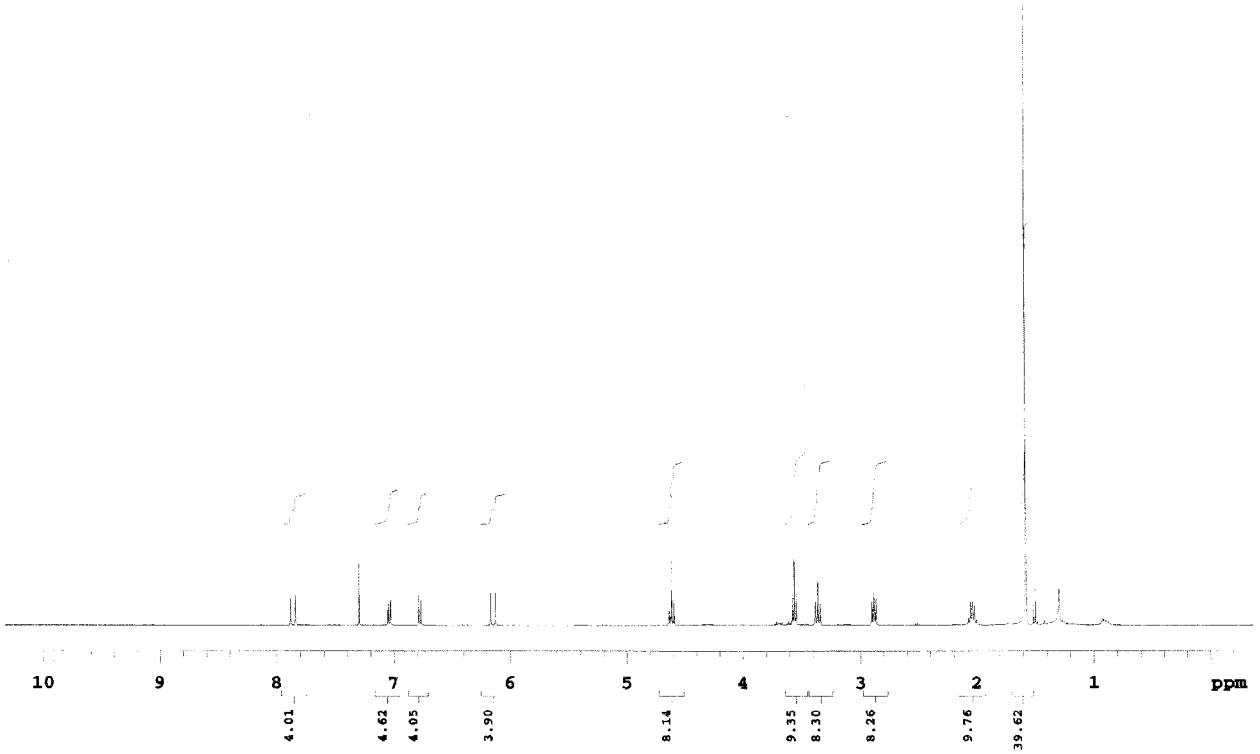


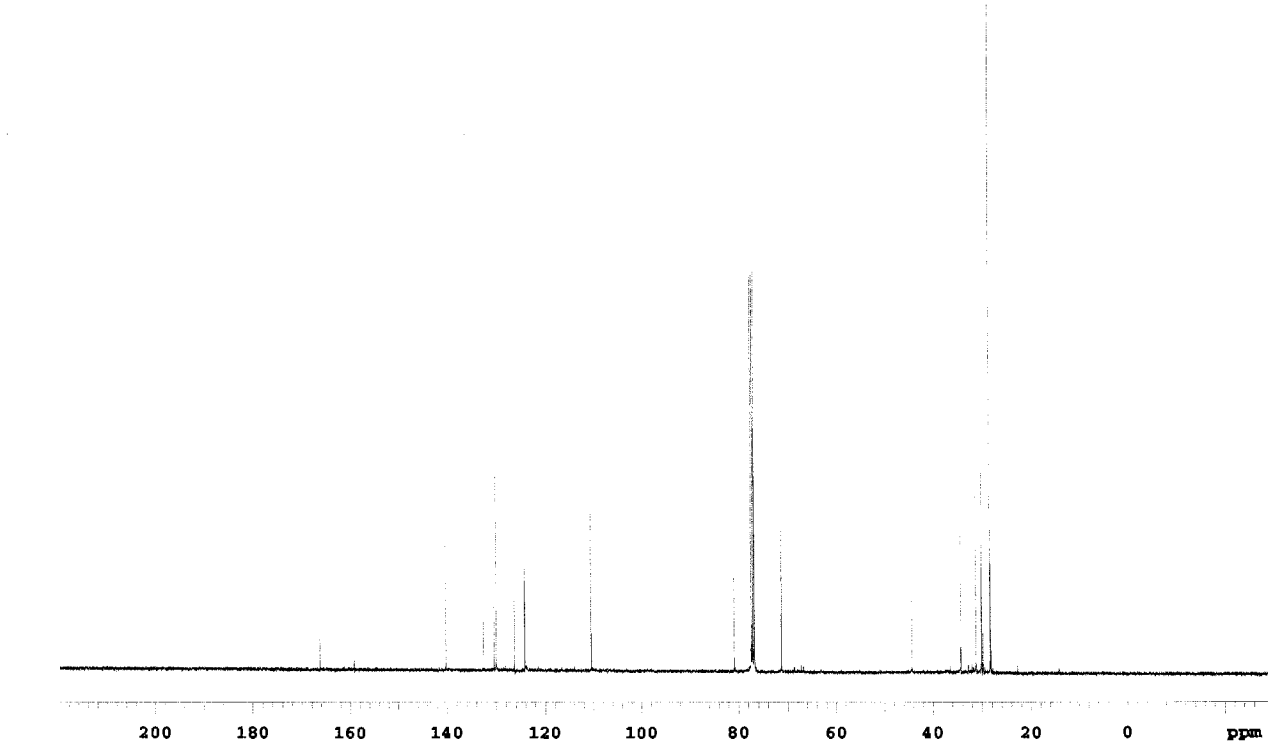
3-(5-Isobutyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4f**): ^{1}H and ^{13}C-NMR in $CDCl_3$



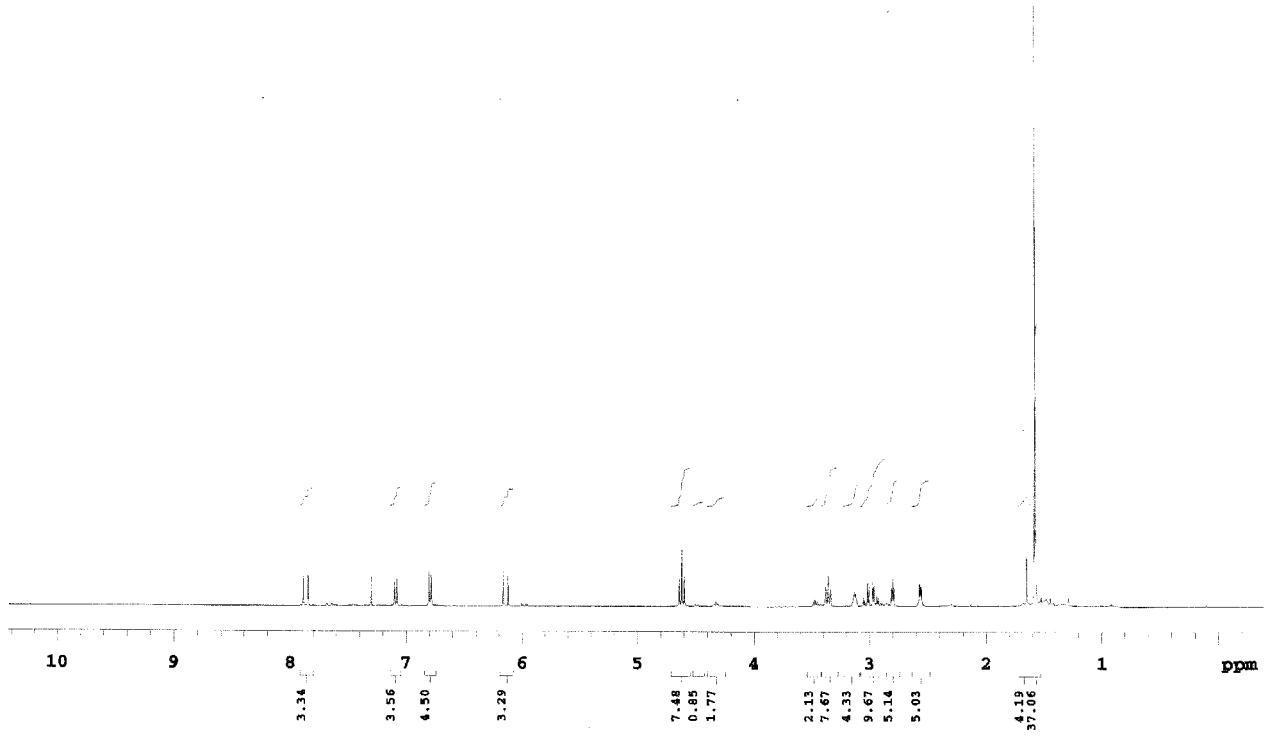


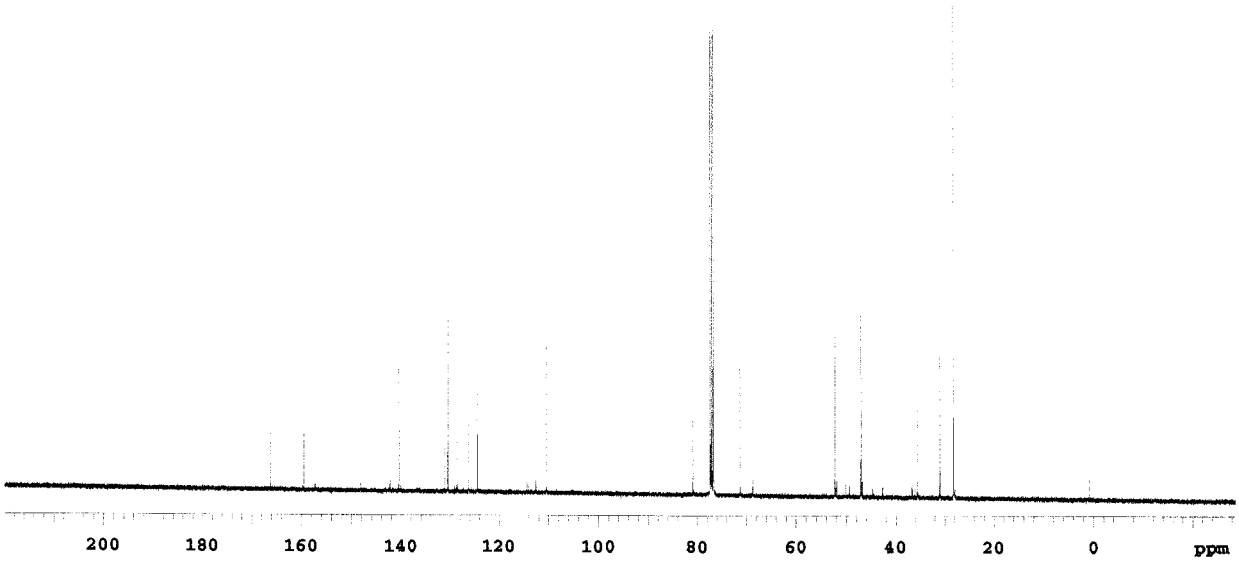
3-[5-(3-Chloro-propyl)-2,3-dihydro-benzofuran-4-yl]-acrylic acid tert-butyl ester (**4g**): ^{1}H and ^{13}C-NMR in $CDCl_3$



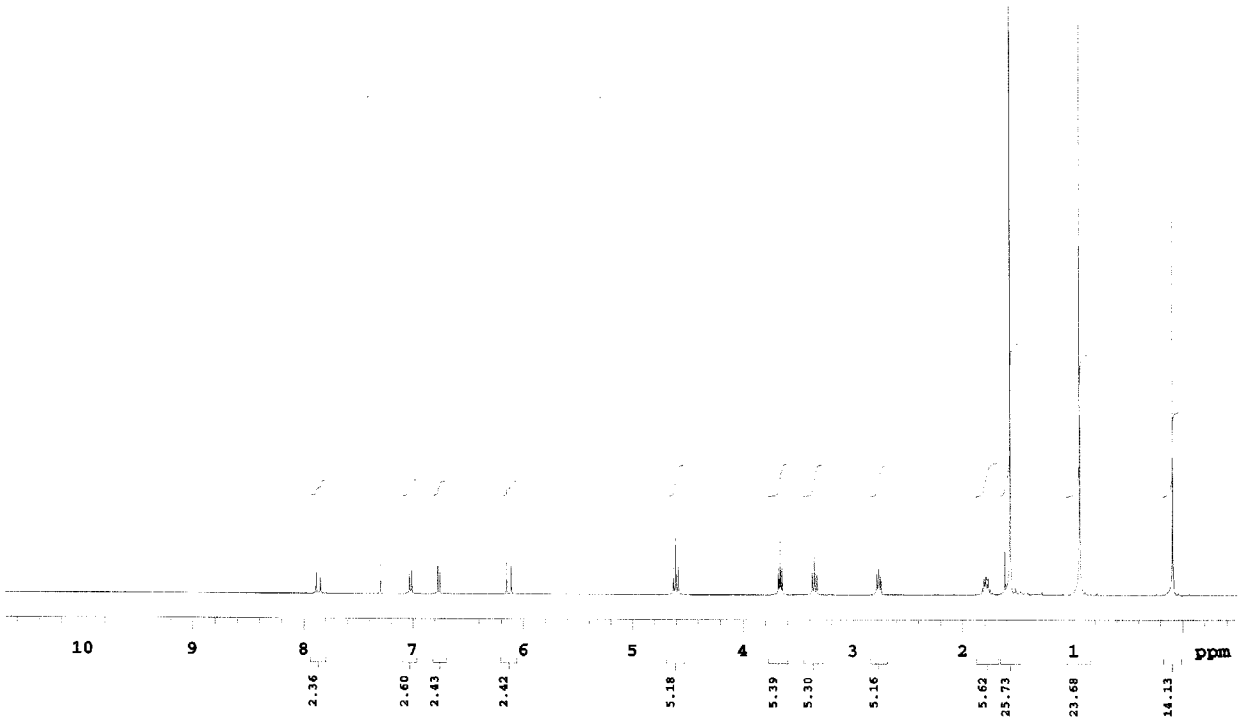


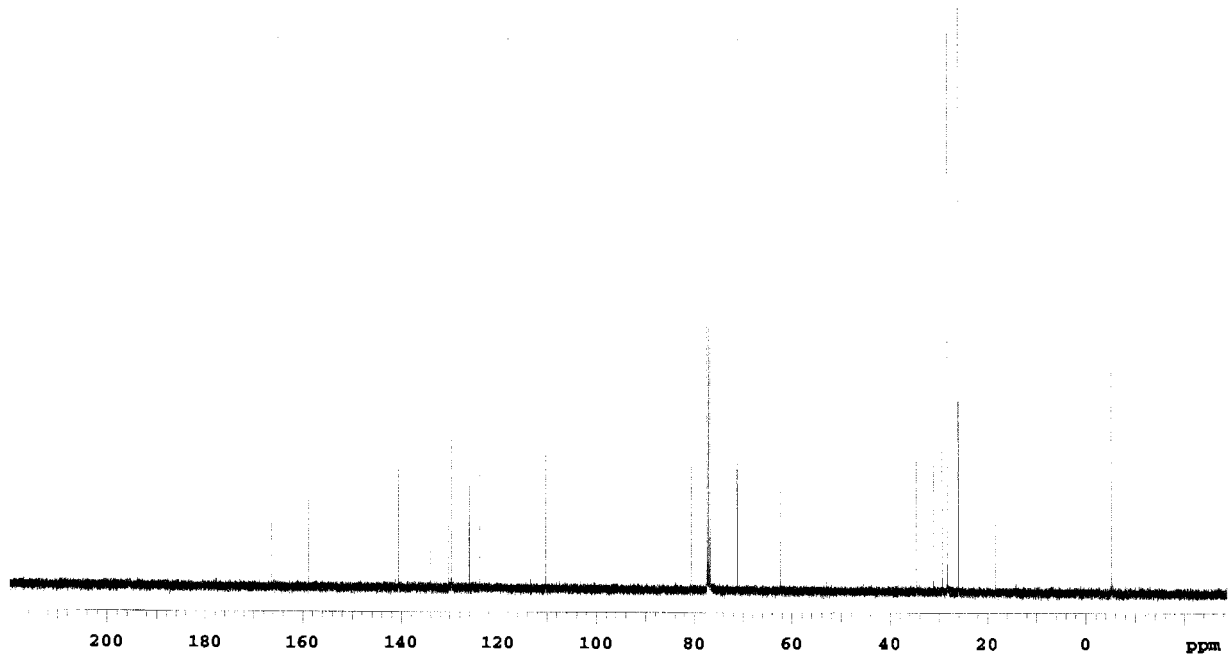
3-(5-Oxiranylmethyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**4h**): ^{1}H and ^{13}C-NMR in $CDCl_3$



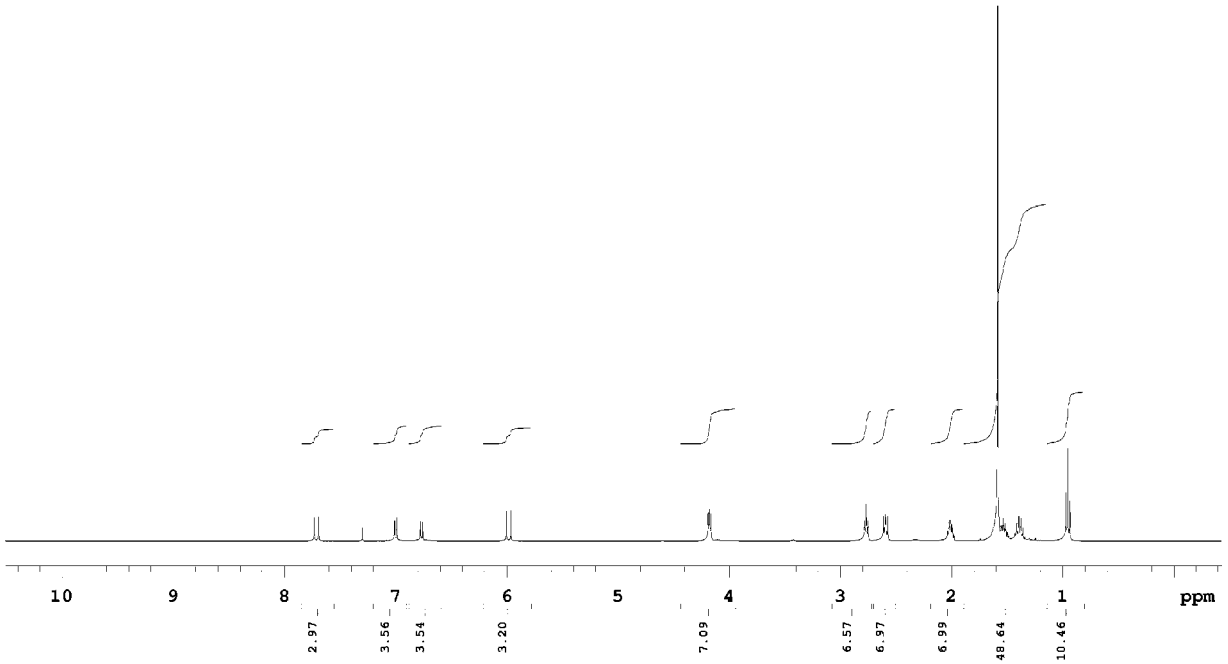


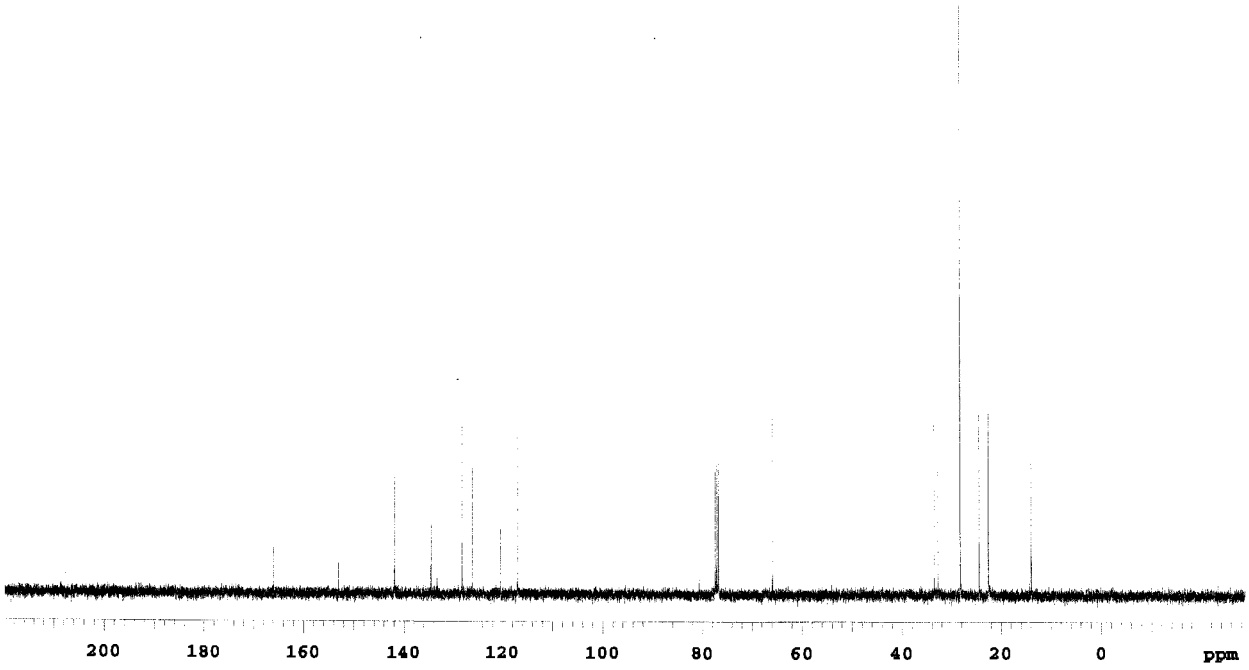
3-{5-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-2,3-dihydro-benzofuran-4-yl}-acrylic acid tert-butyl ester (**4i**): ^{1}H and ^{13}C-NMR in $CDCl_3$



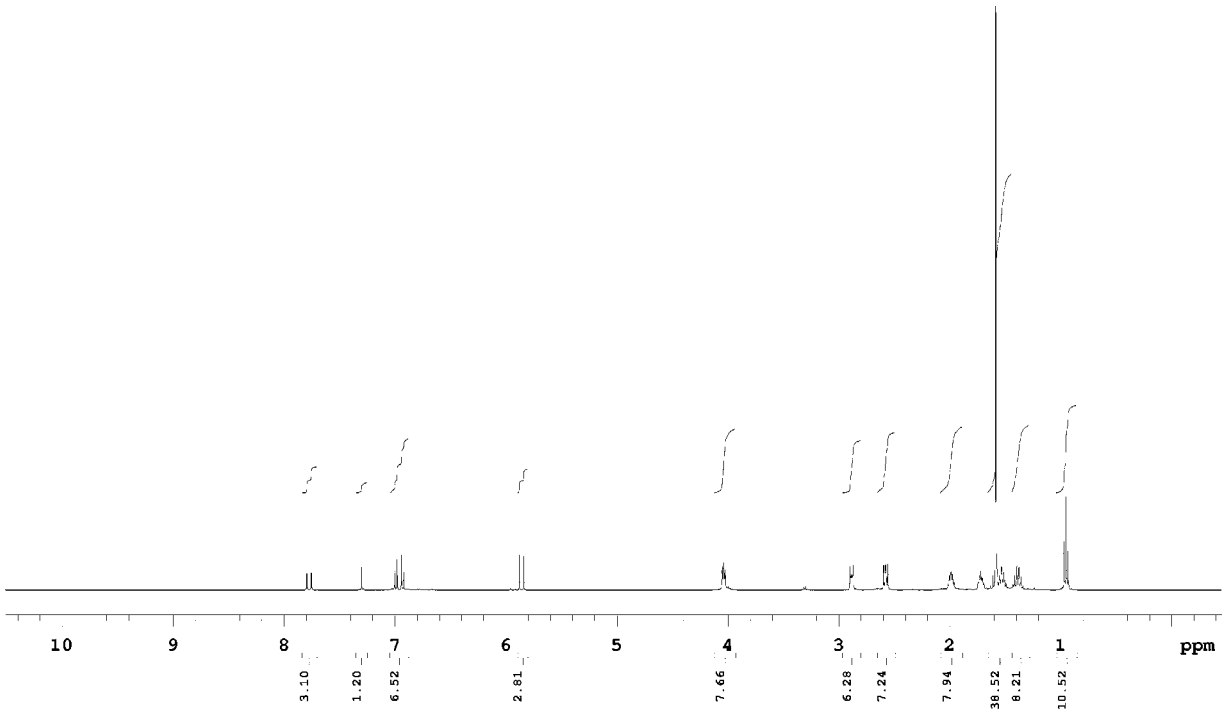


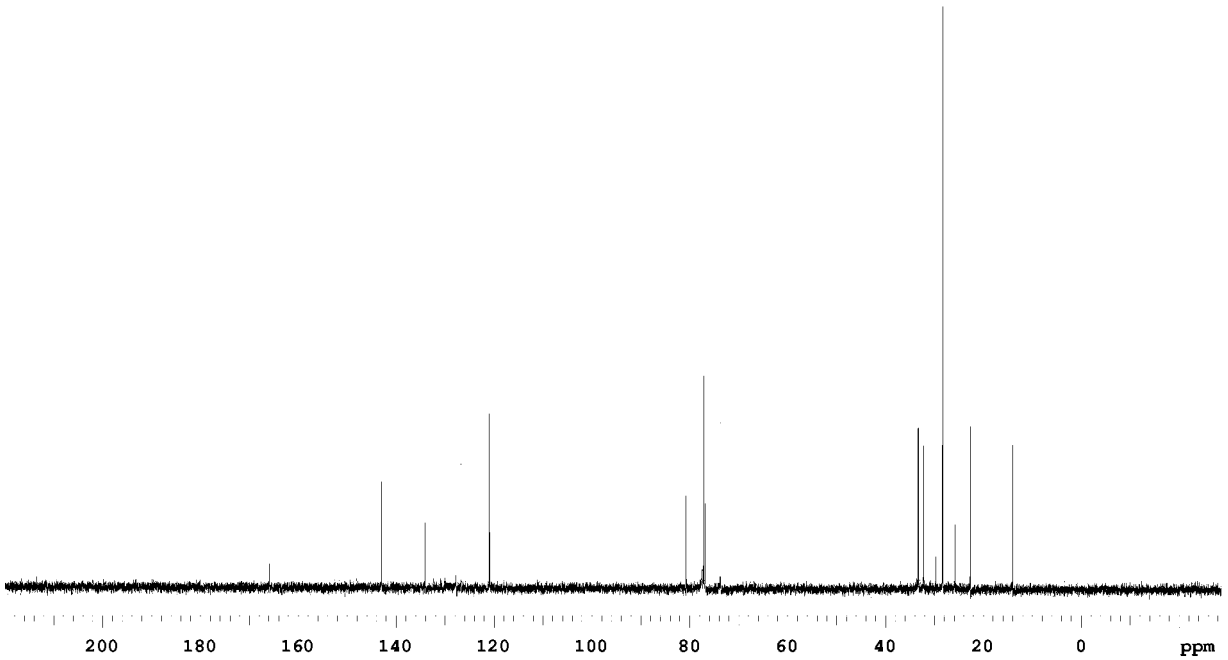
3-(6-Butyl-chroman-5-yl)-acrylic acid tert-butyl ester (**5a**):



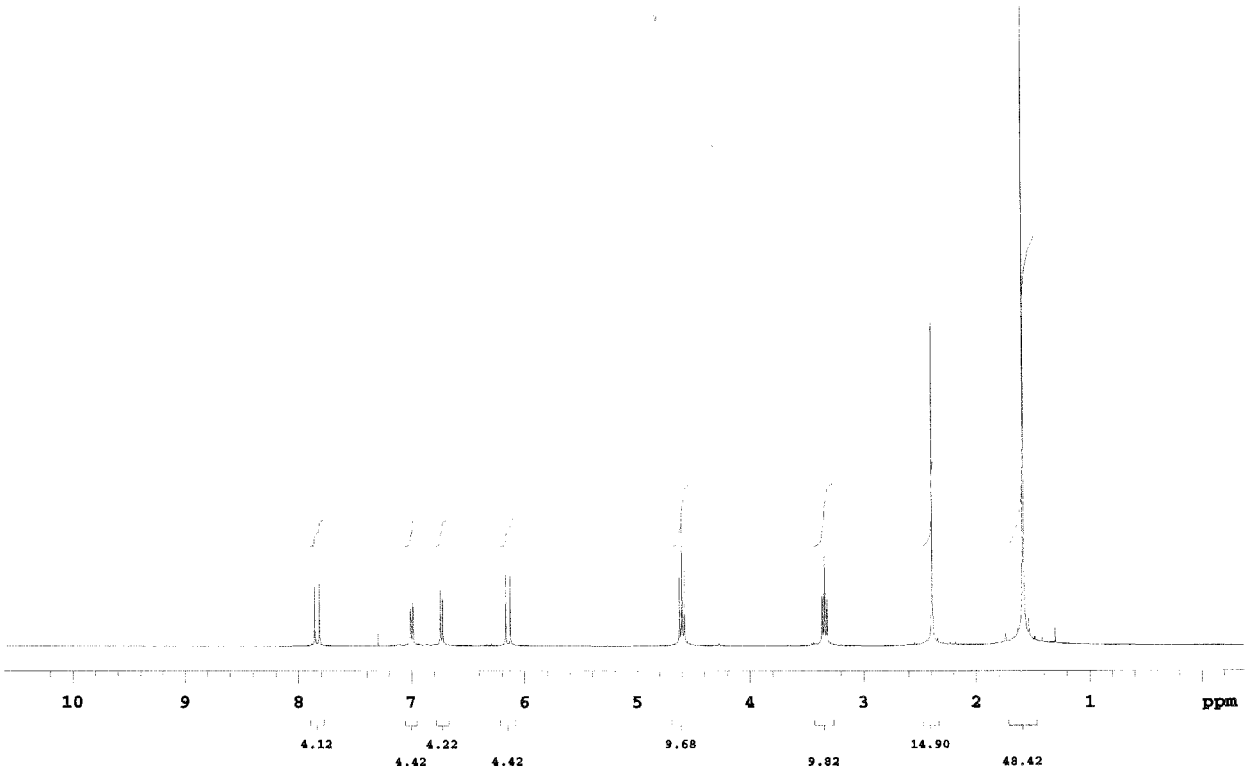


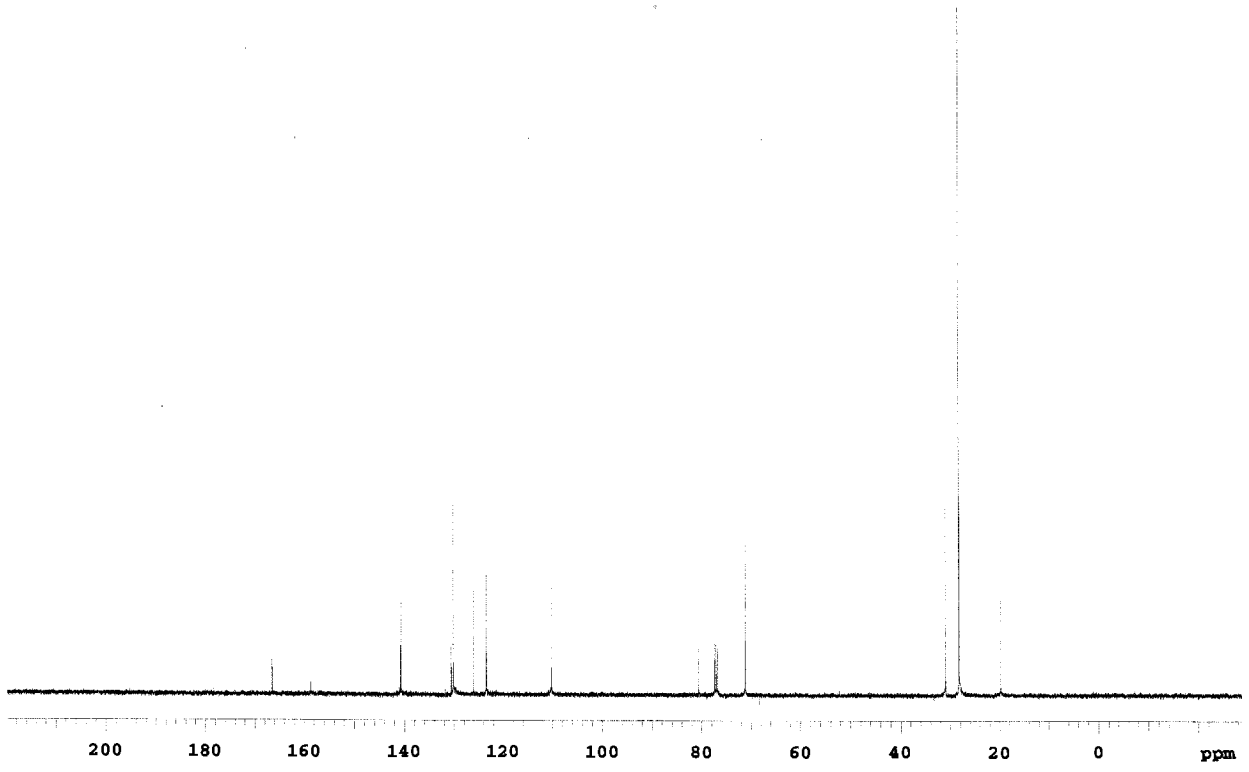
3-(7-Butyl-2,3,4,5-tetrahydro-benzo[b]oxepin-6-yl)-acrylic acid tert-butyl ester (**6a**): ^{1}H and ^{13}C-NMR in $CDCl_3$



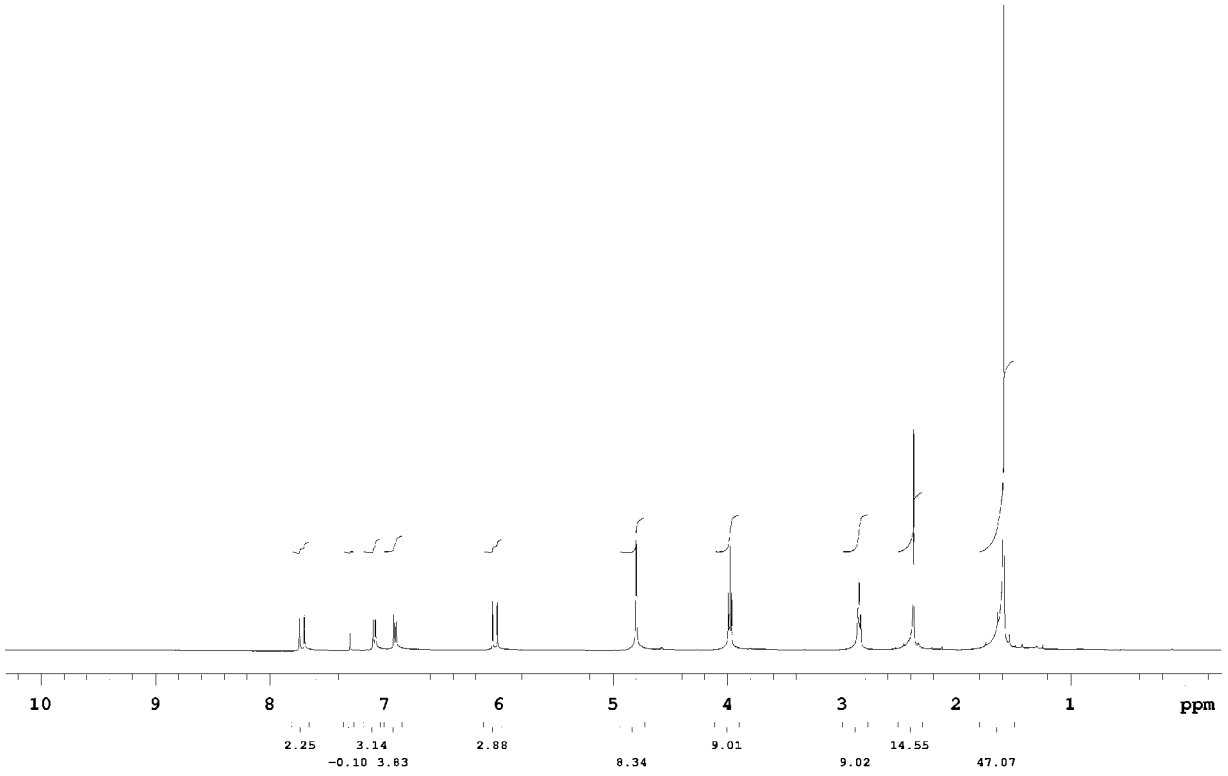


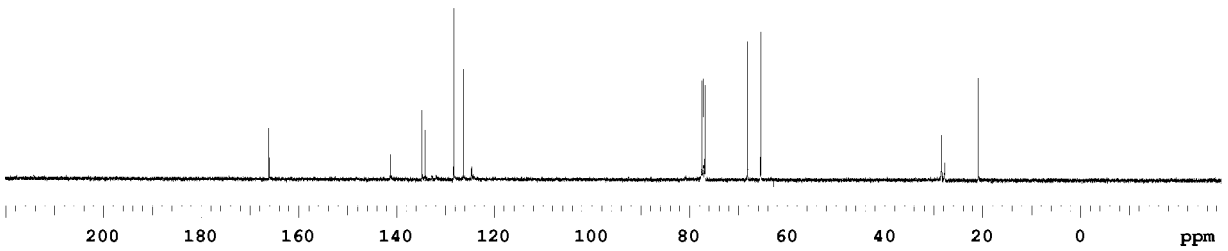
3-(5-Methyl-2,3-dihydro-benzofuran-4-yl)-acrylic acid tert-butyl ester (**8**): ^{1}H and ^{13}C-NMR in $CDCl_3$



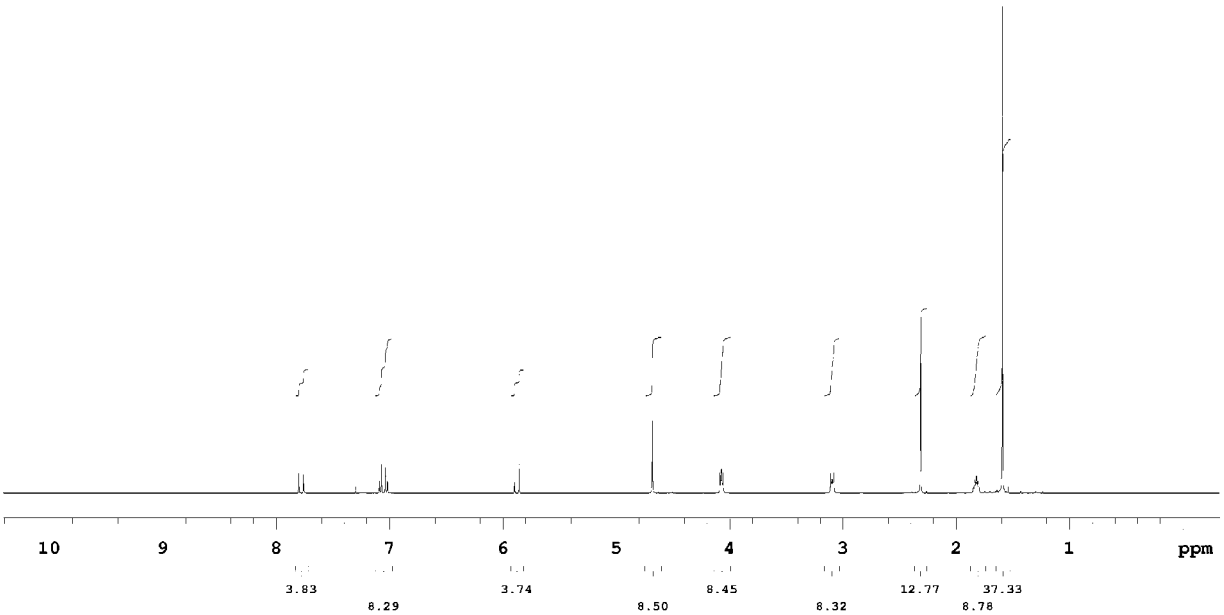


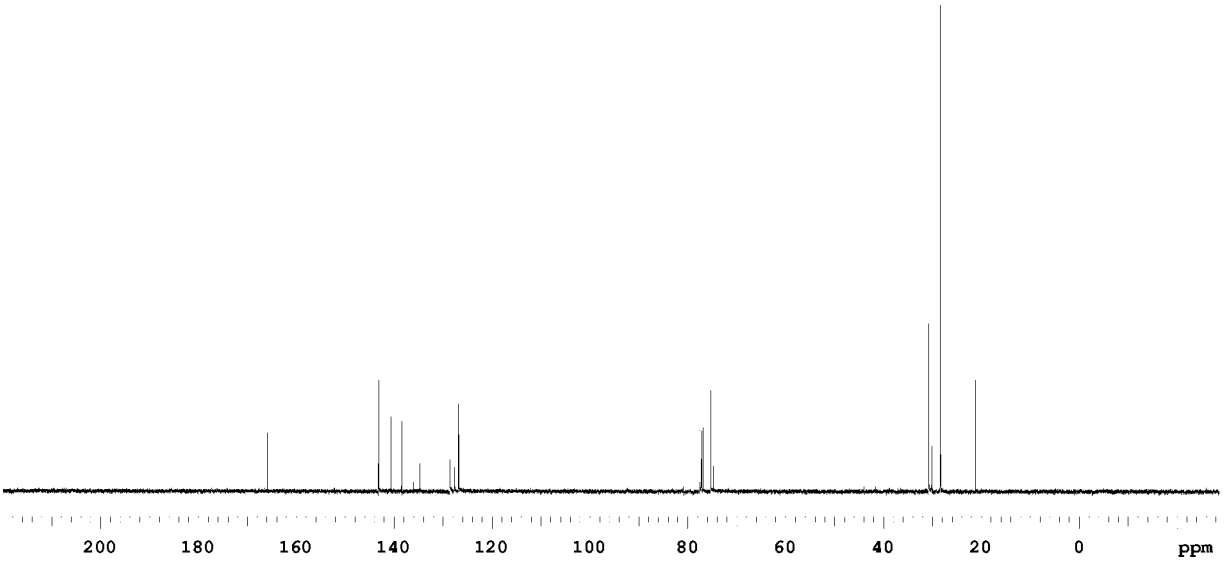
3-(6-Methyl-isochroman-5-yl)-acrylic acid tert-butyl ester (**11**): ^{1}H and ^{13}C-NMR in $CDCl_3$



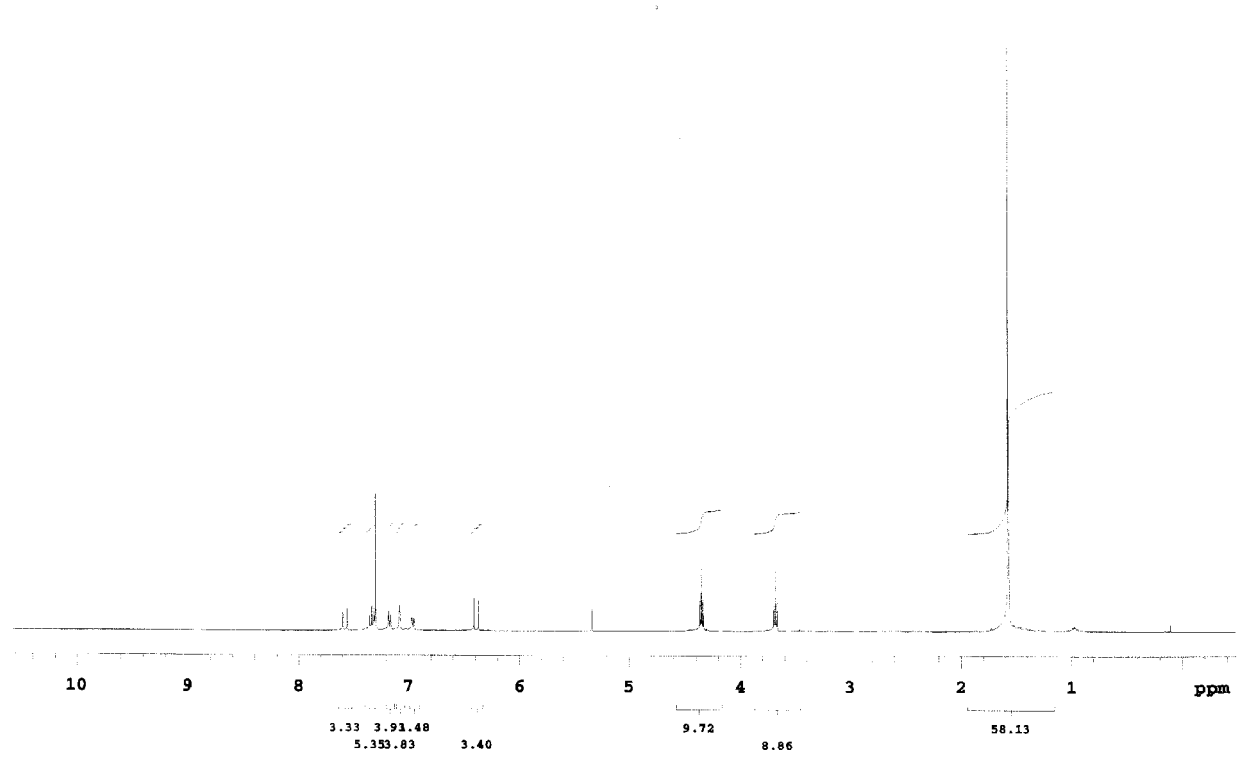


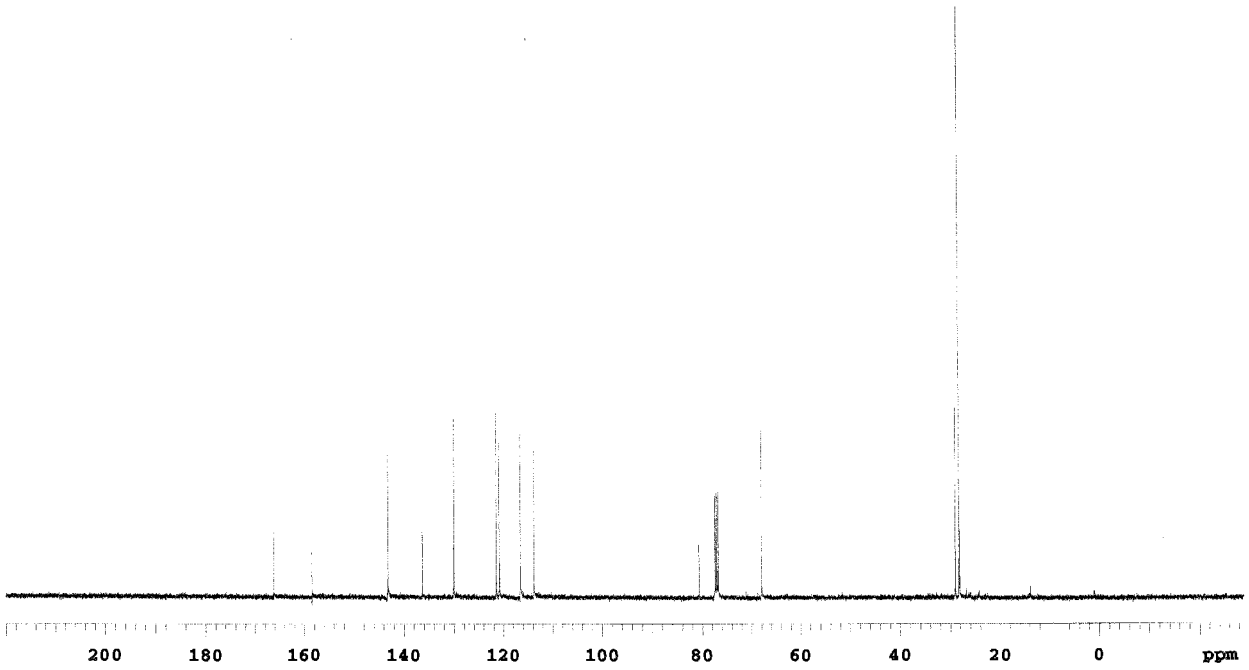
3-(7-Methyl-1,3,4,5-tetrahydro-benzo[c]oxepin-6-yl)-acrylic acid tert-butyl ester (**12**): ^{1}H and ^{13}C-NMR in $CDCl_3$



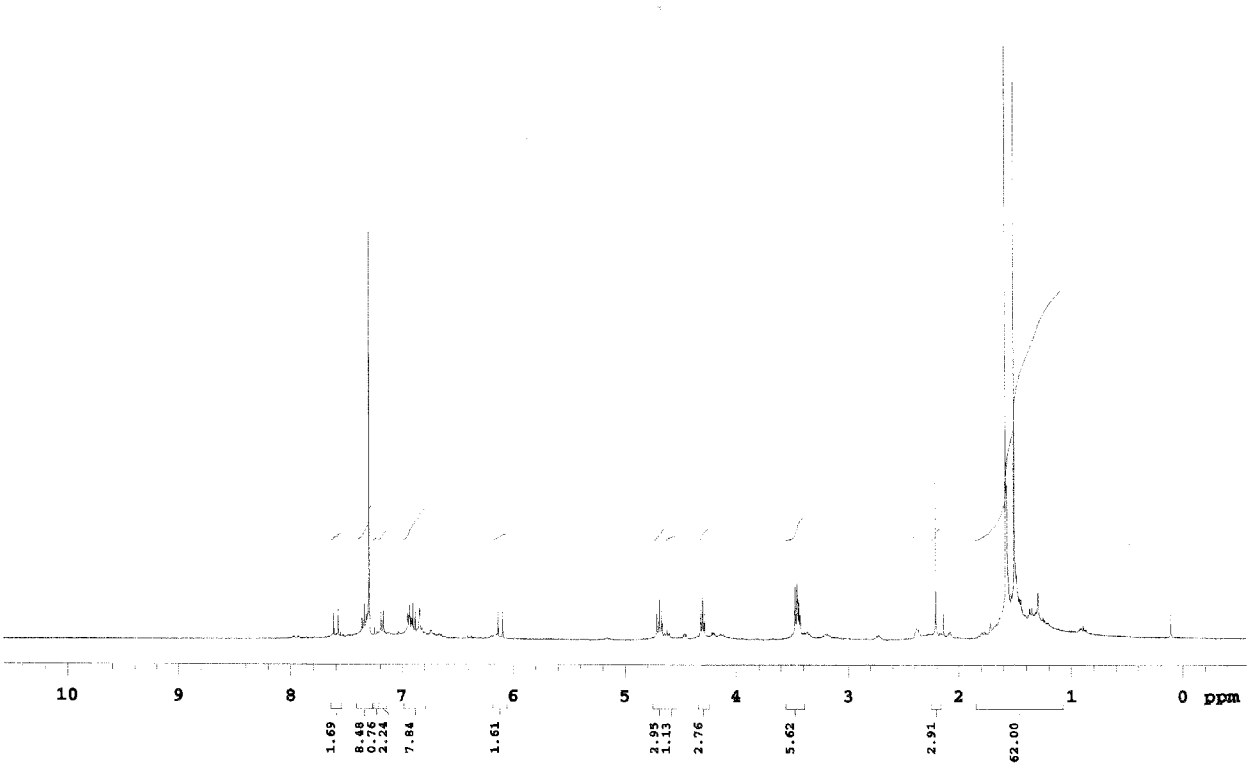


3-[3-(2-Bromo-ethoxy)-phenyl]-acrylic acid tert-butyl ester (**C**): ^{1}H and ^{13}C-NMR in $CDCl_3$





3-{5-[2-(3-Iodo-phenoxy)-ethyl]-2,3-dihydro-benzofuran-4-yl}-acrylic acid tert-butyl ester (**D**): ^{1}H-NMR in $CDCl_3$



3-(3-{2-[4-(2-tert-Butoxycarbonyl-vinyl)-2,3-dihydro-benzofuran-5-yl]-ethoxy}-phenyl)-acrylic acid tert-butyl ester (**E**): ^{1}H and ^{13}C-NMR in $CDCl_3$