Supporting Information

N-Heterocyclic Carbene (NHC) Catalyzed Chemoselective Acylation of Alcohols in the Presence of Amines with Various Acylating Reagents

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Experimental section

General: All reactions involving air or moisture sensitive reagents or intermediates were carried out in dried glassware under an argon atmosphere. THF was distilled from potassium under argon. Diethyl ether was distilled from sodium or potassium under argon. All other solvents and reagents were purified according to standard procedures or were used directly from *Sigma Aldrich*, *Acros Organics*, *ABCR*, *Alfa Aesar* or *Fluka* as received. NMR spectroscopy: *Bruker DPX 300* (at 300 K), *Bruker* AV400, *Varian Unity plus* 600, *Varian Inova* 500. Chemical shifts, δ (in ppm), are reported relative to TMS (δ(^{1}H) 0.0 ppm, δ(^{13}C) 0.0 ppm) which was used as the inner reference. TLC: *Merck* silica gel 60 F 254 plates; detection with UV light or by dipping into a solution of $KMnO_4$ (1.5 g in 400 mL H_2O, 5 g $NaHCO_3$) or a solution of $Ce(SO_4)_2$ x H_2O (10 g), phosphormolybdic acid hydrate (25 g), and conc. H_2SO_4 (60 mL) in H_2O (940 mL), followed by heating. Flash column chromatography (FC): *Merck* or *Fluka* silica gel 60 (40-63 µm) at approximately 0.4 bar. Infrared spectra were recorded on a *Varian Associates* FT-IR 3100 Excalibur and *Shimadzu* FTIR 8400S and reported as wavenumber (cm^{-1}). Mass spectra were recorded on a *Finnigan MAT 4200S*, a *Bruker Daltonics MicroTof*, a *Waters Micromass Quatro LCZ* (ESI), spectrometer; and peaks are given in *m/z* (% of basis peak).

X-ray analysis

X-ray data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Z. Otwinowski, W. Minor, *Methods in Enzymology*, **1997**, *276*, 307-326), absorption correction Denzo (Z.Otwinowski, D. Borek, W. Majewski & W. Minor, *Acta Cryst.* **2003**, *A59*, 228-234), structure solution SHELXS-97 (G.M. Sheldrick, *Acta Cryst.* **1990**, *A46*, 467-473), structure refinement SHELXL-97 (G.M. Sheldrick, *Acta Cryst.* **2008**, *A64*, 112-122), graphics SCHAKAL (E. Keller, Universität Freiburg, 1997). *R*-values are given for the observed reflections, wR^2-values for all reflections. Graphics show the thermal displacement parameters with 50% probability.

X-ray crystal structure analysis for **5a**: formula $C_{13}H_{13}F_3N_2O_4S$, M = 350.31, colorless crystal 0.37 x 0.17 x 0.12 mm, a = 6.2339(1), b = 8.9683(2), c = 14.0067(3) Å, α = 81.624(2), β = 89.228(2), γ = 75.671(1)°, V = 750.42(3) Å^3, ρ_{calc} = 1.550 g cm^{-3}, μ = 2.453 mm^{-1}, empirical absorption correction (0.464 ≤ T ≤ 0.757), Z = 2, triclinic, space group P1bar (No. 2), λ= 1.54178 Å, T = 223 K, ω and φ scans, 7153 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60

$Å^{-1}$, 2534 independent (R_{int} = 0.036) and 2360 observed reflections [$I \geq 2\ \sigma(I)$], 210 refined parameters, R = 0.046, wR^2 = 0.120, max. residual electron density 0.26 (-0.35) e $Å^{-3}$, hydrogen atoms calculated and refined as riding atoms.

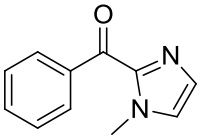
X-ray crystal structure analysis for **5b**: formula $C_{15}H_{17}F_3N_2O_4S$, M = 378.37, colorless crystal 0.33 x 0.10 x 0.07 mm, a = 9.6013(1), b = 7.0186(1), c = 25.4572(4) Å, β = 92.806(1)°, V = 1713.44(4) $Å^3$, ρ_{calc} = 1.467 g cm^{-3}, μ = 2.191 mm^{-1}, empirical absorption correction ($0.532 \leq T \leq 0.862$), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ= 1.54178 Å, T = 223 K, ω and φ scans, 11633 reflections collected ($\pm h, \pm k, \pm l$), [$(\sin\theta)/\lambda$] = 0.60 $Å^{-1}$, 2930 independent (R_{int} = 0.042) and 2588 observed reflections [$I \geq 2\ \sigma(I)$], 228 refined parameters, R = 0.050, wR^2 = 0.140, max. residual electron density 0.39 (-0.33) e $Å^{-3}$, hydrogen atoms calculated and refined as riding atoms.

These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk].

General procedure I for the synthesis of various acyl imidazole ketones (4):

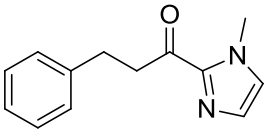
*n*BuLi (1.6 molar n-hexane solution, 18.8 mL, 30.1 mmol) was added slowly to a stirred solution of TMEDA (4.80 mL, 31.8 mmol) in THF (10 mL) at -78^{o} C under argon atmosphere in a heatgun dried Schlenk flask. A solution of 1-methylimidazole (2.00 mL, 25.1 mmol) in THF (10 mL) was added slowly to the reaction mixture at -78^{o} C and stirring was continued for 1 hour at the same temperature. A solution of the ester (26.0 mmol, 1.04 equiv) in THF (10 mL) was added dropwise over a period of 1 hour at -78^{o} C and was stirred for another 1 hour at this temperature. Then the reaction mixture was allowed to warm to room temperature and stirring was continued overnight. Aqueous $NaHCO_3$ solution (30 mL) and EtOAc (30 mL) were added. The organic layer was separated and the aqueous layer was washed with EtOAc (30 mL). The organic layers were combined and dried over $MgSO_4$. After evaporation of the solvent the crude product was purified by silica gel flash column chromatography to give **4a, 4b, 4c** with 54-70% yield. The physical data are in agreement with those reported in the literature.[S1]

(1-Methyl-1H-imidazol-2-yl)(phenyl)methanone (4a):



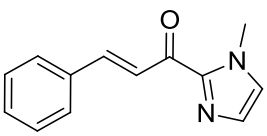
4a was synthesized according to the general procedure I with TMEDA (4.80 mL, 31.8 mmol), *n*BuLi (1.6 molar n-hexane solution, 18.8 mL, 30.1 mmol), 1-methylimidazole (2.00 mL, 25.1 mmol) and ethyl benzoate (3.70 mL, 26.0 mmol) in THF (30 mL) for 18h and silica gel column chromatography (pentane:MTBE, 2:1) to afford the title compound as a colourless oil (3.25 g, 70%).

1-(1-Methyl-1H-imidazol-2-yl)-3-phenylpropan-1-one (4b):



4b was synthesized according to the general procedure I with TMEDA (4.80 mL, 31.8 mmol), *n*BuLi (1.6 molar n-hexane solution, 18.8 mL, 30.1 mmol), 1-methylimidazole (2.00 mL, 25.1 mmol) and ethyl 3-phenylpropanoate (4.70 mL, 26.0 mmol) in THF (30 mL) for 16h and silica gel column chromatography (pentane:MTBE, 2:1) to give the title compound as a colourless oil (3.90 g, 73%).

(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)-3-phenylprop-2-en-1-one (4c)



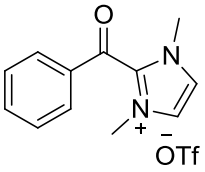
4c was synthesized according to the general procedure I with TMEDA (4.80 mL, 31.8 mmol), *n*BuLi (1.6 molar n-hexane solution, 18.8 mL,

30.1 mmol), 1-methylimidazole (2.00 mL, 25.1 mmol) and *trans*-methyl cinnamate (4.21 g, 26.0 mmol) in THF (30 mL) for 18h and silica gel column chromatography (pentane:MTBE, 1:1) to afford title compound as a white solid (2.85 g, 54%).

General procedure II **for methylation of the acyl 1-methylimidazole ketones (5):**

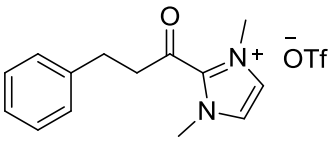
Acyl-1-methylimidazole ketone (0.50 mmol, 1 equiv) was dissolved in a heatgun dried Schlenk flask in dry Et_2O (10 mL) under argon atmosphere. Methyl triflate (114 µL, 1.01 mmol) was added and stirring was continued for 24 h at room temperature. The solvent was evaporated and the crude product was purified by crystallization using CH_2Cl_2/hexane as a solvent system to give the corresponding acyl azolium salts in 82-99% yield.

2-Benzoyl-1,3-dimethyl-1H-imidazol-3-ium trifluoromethanesulfonate (5a):



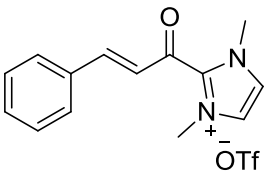
5a was synthesized according to the general procedure II with **4a** (93 mg, 0.50 mmol) and methyl triflate (114 µL, 1.01 mmol) in dry Et_2O (10 mL) for 24h. Crystallization (DCM/hexane) afforded the title compound as a white crystalline solid (149 mg, 85%). FTIR: $\tilde{\nu}$ = 3118, 1668, 1521, 1416, 1257, 1149, 1028, 922, 817 cm^{-1}. ^1H NMR (300 MHz, THF-d_8) δ = 8.08 (d, *J* = 7.3 Hz, 2H), 7.92 (s, 2H), 7.80 (t, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 2H), 3.88 (s, 6H). ^{13}C NMR (101 MHz, THF-d_8) δ = 181.8, 140.3, 136.9, 136.3, 131.5, 130.7, 126.9, 37.8. HRMS (ESI) exact mass calculated for $C_{12}H_{13}N_2O^+$ $[M]^+$: 201.1022, found: 201.1030.

1,3-Dimethyl-2-(3-phenylpropanoyl)-1H-imidazol-3-ium trifluoromethanesulfonate (5b):



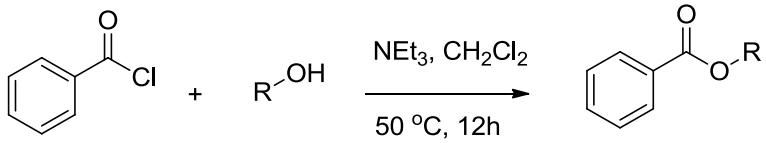
5b was synthesized according to the general procedure II with **4b** (107 mg, 500 µmol) and methyl triflate (114 µL, 1.01 mmol) in dry Et_2O (10 mL) for 24h. Crystallization (DCM/hexane) afforded the title compound as a white crystalline solid (187 mg, 99%). FTIR: $\tilde{\nu}$ = 3127, 1702, 1515, 1415, 1224, 1164, 1025, 981 cm^{-1}. ^1H NMR (300 MHz, THF-d_8) δ = 7.69 (s, 2H), 7.30 (d, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 4.07 (s, 6H), 3.48 (t, *J* = 7.4 Hz, 2H), 3.05 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (75 MHz, THF-d_8) δ = 187.9, 141.6, 140.1, 129.7, 129.3, 127.0, 126.6, 45.5, 39.3, 30.1. HRMS (ESI) exact mass calculated for $C_{14}H_{17}N_2O^+$ $[M]^+$: 229.1335, found: 229.1333; $C_{15}H_{21}N_2O_2^+$ $[M+CH_3OH]^+$: 261.1598, found: 261.1599.

2-Cinnamoyl-1,3-dimethyl-1H-imidazol-3-ium trifluoromethanesulfonate (5c):



5c was synthesized according to the general procedure II with **4c** (106 mg, 500 µmol) and methyl triflate (114 µL, 1.01 mmol) in dry Et_2O (10 mL) for 24h. Crystallization (DCM/hexane) afforded the title compound as a white crystalline solid (154 mg, 82%). All the analytical data are in agreement with previous reports from the literature.[S2]

Experimental procedure for preparation of active esters 6a and 6b:



R = CH_2CF_3, **6a**, 98%
= $CH(CF_3)_2$, **6b**, 85%

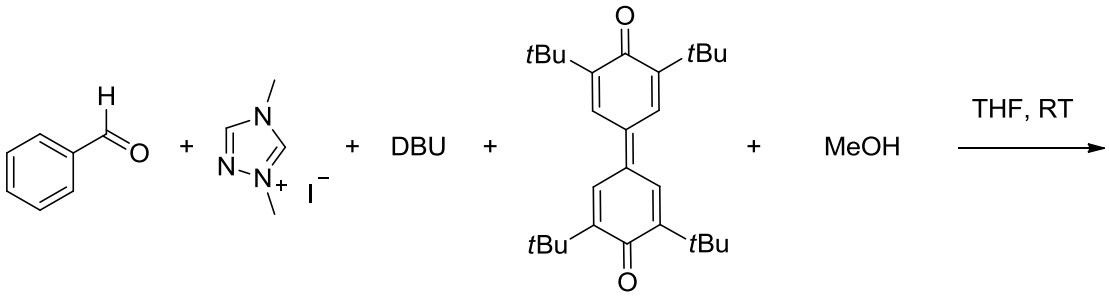
2,2,2-Trifluoroethyl benzoate (6a): Benzoyl chloride (1.7 mL, 15 mmol) was added to a mixture of 2,2,2-trifluoroethanol (0.72 mL, 10 mmol) and triethylamine (1.7 mL, 12 mmol) in dichloromethane (15 mL). The reaction mixture was refluxed for 12h. After completion of the reaction the mixture was concentrated under reduced pressure and EtOAc (50 mL) was added. Then it was washed with $NaHCO_3$ (2x 25 mL) and brine (25 mL) respectively. The organic phase was dried over anhydrous $MgSO_4$ and concentrated, the crude product was purified by silica gel flash column chromatography (pentane:Et_2O, 20:1) to give the ester **6a** as a colourless oil (1.87 g, 98%). All the analytical data are in agreement with those reported in literature. [S3]

1,1,1,3,3,3-Hexafluoropropan-2-yl benzoate (6b): Benzoyl chloride (1.2 mL, 10 mmol) was added to a mixture of 1,1,1,3,3,3-hexafluoropropan-2-ol (1.6 mL, 15 mmol) and triethylamine (1.7 mL, 12 mmol) in dichloromethane (20 mL). The reaction mixture was refluxed for 12 h. After completion, the reaction mixture was concentrated under reduced pressure and EtOAc (50 mL) was added. Then it was washed with $NaHCO_3$ (2x 25 mL) and brine (25 mL) respectively. The organic phase was dried over anhydrous $MgSO_4$ and concentrated, the crude product was purified by silica gel flash column chromatography (pentane:MTBE, 35:1) to afford **6b** as a white crystalline solid (1.87 g, 98%). FTIR: $\tilde{\nu}$ = 3021, 2717, 1755, 1386, 1354, 1262, 1215, 1110, 755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ = 8.13 (d, *J* = 8.5 Hz, 2H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 6.04 (hept, *J* = 6.1 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -73.22. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4, 134.9, 130.6, 129.0, 127.1, 126.4-

115.2 (q, 282.0 Hz, 3F), 68.5-65.8 (hept, 34.7 Hz, 6F). EI mass, $C_{10}H_6F_6O_2$ $[M]^+$: 272.0; fragments 105.0 and 77.0.

S-Ethyl benzothioate (8): To a stirred suspension of ethanethiol (0.37 mL, 5.0 mmol), *N*-methylimidazole (0.60 mL, 7.5 mmol), TMEDA (1.1mL, 7.5 mmol) and K_2CO_3 (1.1 g, 7.9 mmol) in CH_3CN (5 mL) at 0 ^oC was added benzoyl chloride (0.90 mL, 7.5 mmol) under argon atmosphere. The reaction mixture was stirred at that temperature for 1 h and was then allowed to warm to room temperature and stirring was continued for another 2 h. Water (25 mL) was added and the resulting mixture was extracted with EtOAc (3x25 mL). The organic layers were combined and washed with water (40 mL) and brine (40 mL), dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel flash column chromatography (pentane:Et_2O, 20:1) to give **8** as a colorless liquid (0.82 g, 99%). All the analytical data are in agreement to those reported in the literature. [S4]

Variation of rate constants with different concentration of catalyst in oxidative esterification:



In a heatgun dried Schlenk tube 1,4-dimethyl-4H-1,2,4-triazol-1-ium iodide (1.1 mg, 4.8 µmol, 67 µmol solution in CH_3CN), DBU (7.5 µL, 50 µmol), 3,3',5,5'-tetra-tert-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (204 mg, 500 µmol) and dry methanol (0.5 mL) were taken with dry THF (2.0 mL). Stirring was continued for 5 minutes at room temperature prior to the addition of benzaldehyde (51 µL 0.50 mmol). The conversion was determined by gas chromatography at certain time intervals using dodecane as internal standard. Observed rate constant was determined by plotting -ln[**PhCHO**]/[**PhCHO**]$_0$ against time (Sec). The same experiment was performed at another four different catalyst concentrations (7.0, 9.6, 12 and 14 µmol). The observed rate constants depend linearly with varying catalyst concentrations (Figure 1).

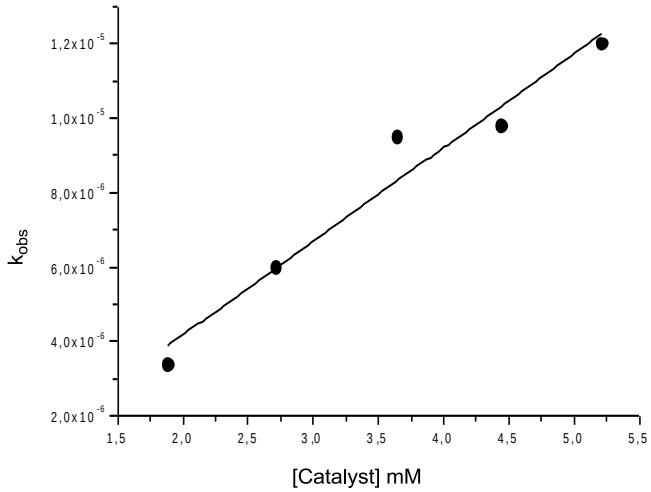
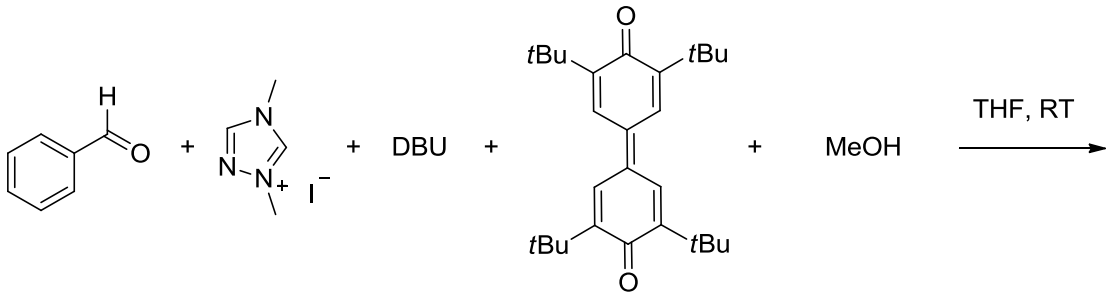


Figure 1. Plot of observed rate constant vs catalyst concentration

Oxidative esterification is found to be zero order with respect to alcohol:



In a heatgun dried Schlenk tube 1,4-dimethyl-4H-1,2,4-triazol-1-ium iodide (2.0 mg, 8.8 µmol, 44 µmol solution in CH_3CN), DBU (7.5 µL, 50 µmol), 3,3',5,5'-tetra-tert-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (164 mg, 401 µmol) and dry methanol (0.6 mL, 37 equiv) were taken with dry THF (1.7 mL). Stirring was continued for 5 minutes at room temperature prior to the addition of benzaldehyde (41 µL 0.40 mmol). The conversion was determined by gas chromatography at certain time intervals using dodecane as internal standard. The same experiment was repeated with 1.0 mL (62 equiv) of methanol. The -ln[**PhCHO**]/[**PhCHO**]$_0$ was plotted against time (sec), indicates that the reaction is zero order in alcohol concentration (Figure 2).

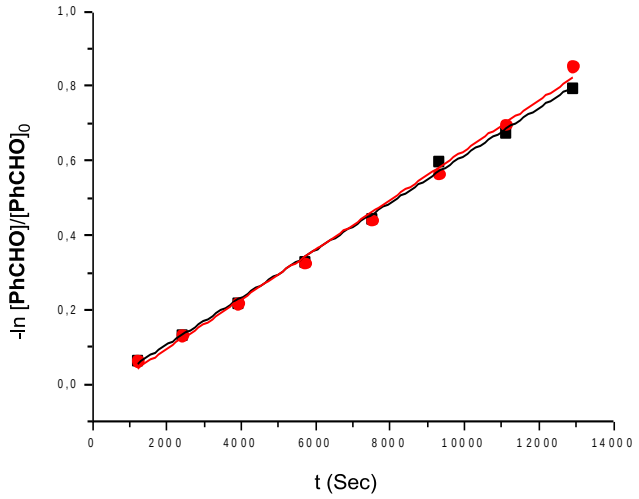
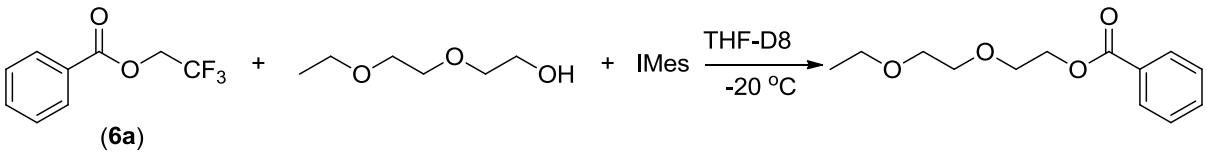


Figure 2. Plot of –ln [**PhCHO**]/ [**PhCHO**]$_0$ vs t (sec) at different alcohol concentrations (red dots with 62 equiv MeOH; black squares with 37 equiv MeOH).

Kinetics of the reaction of trifluoroethyl ester 6a with HO(CH$_2$)$_2$O(CH$_2$)$_2$OEt in the presence of IMes:



(**6a**)

In an oven dried NMR tube IMes (4.5 mg, 15 µmol) and HO(CH$_2$)$_2$O(CH$_2$)$_2$OEt (0.14 mL, 1.0 mmol) were dissolved in THF-D8 (0.5 mL). The reaction mixture was cooled to -78 ^{o}C and compound **6a** (21 mg, 0.10 mmol) was added. The tube was placed into the NMR instrument which was precooled to -20 ^{o}C and ^{1}H spectra were recorded in two minutes intervals. The decay of **6a** was plotted with respect to time to obtain k_{obs} at a fixed carbene concentration. The same experiment was repeated at three different carbene concentrations (18, 23 and 29 µmol). From the experiments -ln[**6a**]/[**6a**]$_0$ were plotted as a function of time (t) at four different carbene concentrations (Figure 3). Observed rate constants showed linear dependence on the IMes concentration. From the plot of K_{obs} vs IMes concentration the second order rate constant was obtained k = 1.8x10^{-2} M^{-1}s^{-1}.

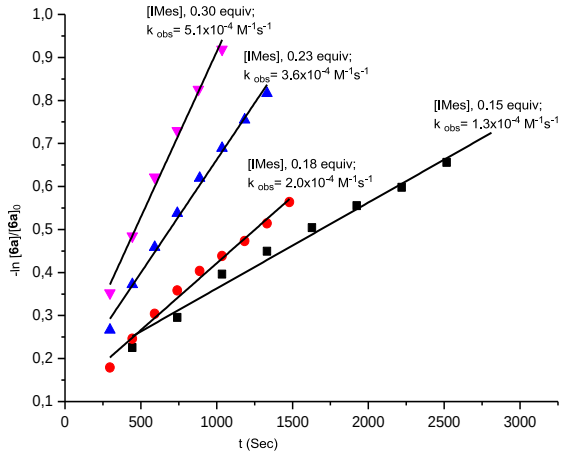
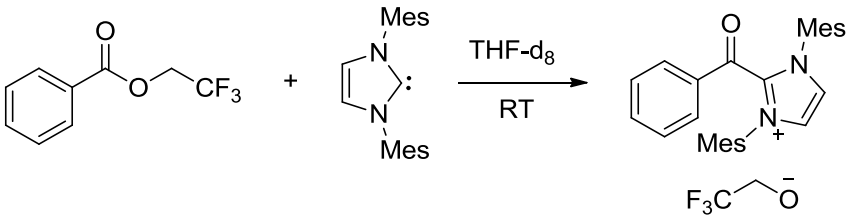


Figure 3. Plot of -ln[**6a**]/[**6a**]$_0$ versus time (t); [**6a**]$_0$ is the initial concentration of **6a** and [**6a**] is concentration after a certain time from the starting of the reaction.

Kinetics of the reaction between 6a and IMes:



In an oven dried NMR tube IMes (46 mg, 0.15 mmol) was dissolved in dry THF-D8 (1.0 mL). ^{1}H NMR was recorded at room temperature. The **6a** (8.0 mg, 40 µmol) was added and ^{1}H NMR of the reaction mixture was recorded at certain time intervals. The decay of **6a** was plotted as a function of time to give the rate constant k = 4.3x10^{-5} M^{-1}s^{-1} (Figure 4). This is far slower than the rate of IMes catalyzed transesterification from 6a and hence the reaction does not proceed via acyl azolium ion formation.

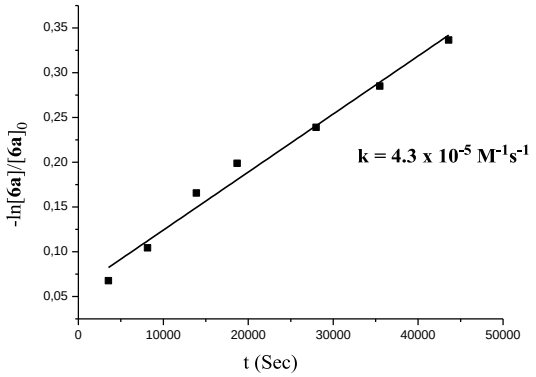
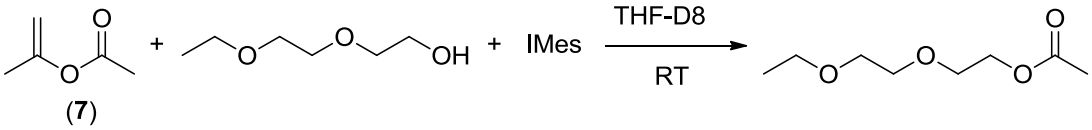


Figure 4. Plot of -ln[**6a**]/[**6a**]$_0$ versus time (t); [**6a**]$_0$ is the initial concentration of **6a** and [**6a**] is concentration after a certain time from the starting of the reaction.

Kinetics of the reaction of 7 with $HO(CH_2)_2O(CH_2)_2OEt$ in presence of IMes:



In an oven dried NMR tube IMes (2.4 mg, 7.9 μmol) and $HO(CH_2)_2O(CH_2)_2OEt$ (0.14 mL, 1.0 mmol) were dissolved in THF-D8 (0.5 mL). Compound **7** (11 μL, 0.10 mmol) was added and the tube was placed into the NMR instrument and ^1H spectra were recorded in two minutes intervals. The decay of **7** was plotted as a function of time to give k_{obs} at a fixed carbene concentration. The same experiment was repeated at three different carbene concentrations (9.8, 11.8 and 14.7 μmol). The obtained rate constants showed linear dependence on the IMes concentration (Figure 5).

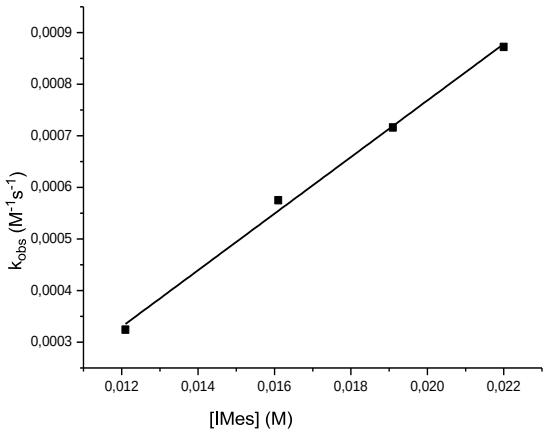
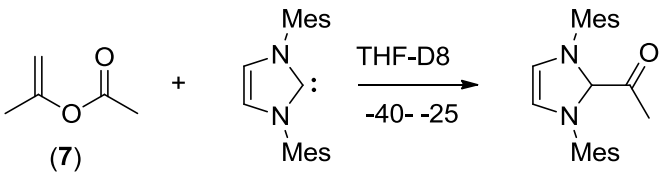


Figure 5. Linear dependence of k_{obs} on the IMes concentration

Eyring plot for the reaction between 7 and IMes:



In an oven dried NMR tube IMes (18 mg, 59 μmol) was dissolved in dry THF-D8 (0.5 mL) and the mixture was cooled to -78 ^{o}C prior to placing it into the NMR probe which was precooled to the requisite temperature. ^{1}H NMR was recorded, the sample was again cooled to -78 ^{o}C and prop-1-en-2-yl acetate (32 μL, 0.29 mmol) was added. ^{1}H NMR of the reaction mixture was recorded at two minutes intervals. The experiment was performed at four different temperatures (-25, -30, -35, -40 ^{o}C). The Eyring plot (Figure 6) fits a straight line and from this plot the room temperature rate constant (k_{rt}) for acyltransfer was calculated, k_{rt} = 5.7 x 10^{-2} $M^{-1}s^{-1}$.

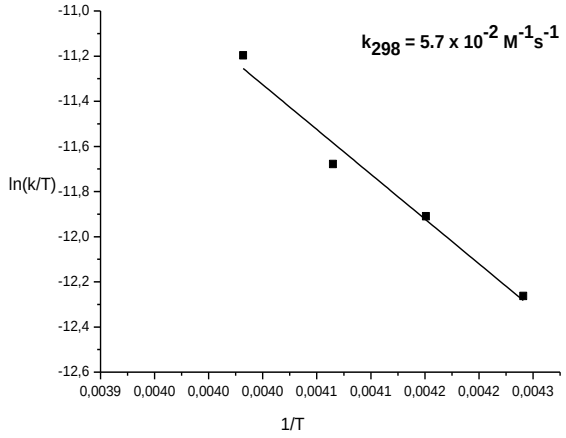
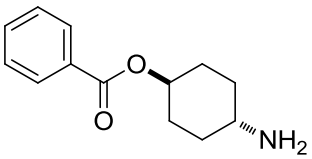


Figure 6. Eyring plot for the acyl transfer reaction between prop-1-en-2-yl acetate and IMes.

NHC catalyzed chemoselective acylation of amino alcohols using trifluoroethanol ester as acyl donor (Method A):

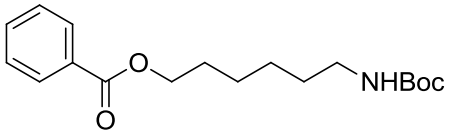
In a heatgun dried Schlenk tube an amino alcohol (1.5-1.0 equiv) and IMes (0.10-0.20 equiv) were dissolved in dry THF (2.0 mL). 2,2,2-Trifluoroethyl benzoate (1.0-1.2 equiv) was added to the reaction mixture and stirring was continued at room temperature. Completion of the reaction was checked by silica gel thin layer chromatography. Products were purified by silica gel flash column chromatography and analyzed by standard spectroscopic analysis techniques.

***trans*-4-Aminocyclohexyl benzoate(2b):**



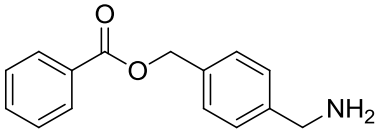
2b was prepared according to method A. *trans*-4-Aminocyclohexanol (35 mg, 0.30 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (41 mg, 0.20 mmol) in the presence of IMes (12 mg, 39 μmol) in dry THF (2 mL) at room temperature for 24h. Pure product was obtained by silica gel flash column chromatography (MTBE:MeOH, 3:1) as a white solid (37 mg, 85%). All the analytical data are in agreement with the literature values.[S5]

6-((*tert*-Butoxycarbonyl)amino)hexyl benzoate (9):



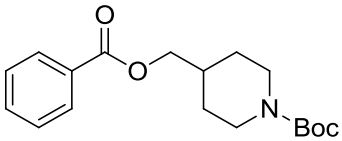
9 was prepared according to method A. 6-Aminohexan-1-ol (35 mg, 0.30 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (41 mg, 0.20 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Then Boc_2O (88 mg, 0.40 mmol) and Et_3N (56 µL, 0.40 mmol) were added to the reaction mixture and stirring was continued overnight. Pure product was obtained by silica gel flash column chromatography (pentane:MTBE, 6:1) as a colourless highly viscous oil (58 mg, 91%). All the analytical data are in agreement with literature values.[S5]

4-(Aminomethyl)benzyl benzoate (10):



10 was prepared according to method A. (4-(Aminomethyl)phenyl)methanol (28 mg, 0.20 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (49 mg, 0.24 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Pure product was obtained by silica gel flash column chromatography (MTBE:MeOH, 3:1) as a white solid (48 mg, 99%). FTIR: $\tilde{\nu}$ = 3018, 1715, 1657, 1519, 1272, 1215, 1112, 744, 667 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 7.4 Hz, 2H), 7.56-7.52 (m, 1H), 7.44-7.40 (m, 4H), 7.36-7.31 (m, 2H), 5.34 (s, 2H), 3.87 (s, 2H), 2.06 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.5, 143.0, 134.7, 133.0, 130.2, 129.7, 128.5, 128.4, 127.4, 66.5, 46.1. HRMS (ESI) exact mass calculated for $C_{15}H_{16}NO_2^+$ $[M+H]^+$: 242,1176, found: 242,1179, $C_{15}H_{15}NNaO_2^+$ $[M+Na]^+$: 264,0995, found: 264,0994, $C_{30}H_{31}N_2O_4^+$ $[2M+H]^+$: 483,2278, found: 483,2278.

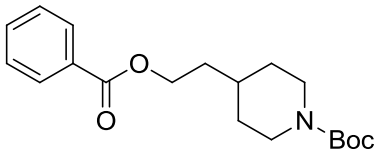
***tert*-Butyl 4-((benzoyloxy)methyl)piperidine-1-carboxylate (11):**



11 was prepared according to method A. Piperidin-4-ylmethanol (23 mg, 0.20 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (49 mg, 0.24 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Then Boc_2O (88 mg, 0.40 mmol) and Et_3N (56 µL, 0.40 mmol) were added to the reaction mixture and stirring was continued overnight. Pure product was obtained by silica gel flash column chromatography

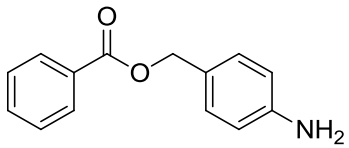
(pentane:MTBE, 5:1) as a colourless highly viscous oil (60 mg, 94%). All the analytical data are in agreement with literature values.[S5]

***tert*-Butyl 4-(2-(benzoyloxy)ethyl)piperidine-1-carboxylate (12):**



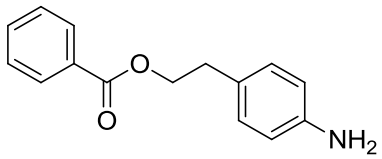
12 was prepared according to method A. 2-(Piperidin-4-yl)ethanol (26 mg, 0.20 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (49 mg, 0.24 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Then Boc_2O (88 mg, 0.40 mmol) and Et_3N (56 µL, 0.40 mmol) were added to the reaction mixture and stirring was continued overnight. Pure product was obtained by silica gel flash column chromatography (pentane:MTBE, 4:1) as a colourless highly viscous oil (61 mg, 92%). All the analytical data are in agreement with literature values.[S5]

4-Aminobenzyl benzoate (13):



13 was prepared according to method A. (4-Aminophenyl)methanol (25 mg, 0.20 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (49 mg, 0.24 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Pure product was obtained by silica gel flash column chromatography (pentane:EtOAc, 2:1) as a colourless oil (39 mg, 86%). FTIR: $\tilde{\nu}$ = 3021, 1711, 1620, 1520, 1272, 1215, 1113, 743, 668 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.42 (t, *J* = 7.1 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 6.69 (d, *J* = 8.3 Hz, 2H), 5.25 (s, 2H), 3.63 (bs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.6, 146.7, 132.8, 130.5, 130.2, 129.7, 128.3, 125.9, 115.0, 66.9. HRMS (ESI) exact mass calculated for $C_{14}H_{14}NO_2^+$ $[M+H]^+$: 228,1019, found: 228,1015, $C_{14}H_{13}NNaO_2^+$ $[M+Na]^+$: 250,0838, found: 250,0834, $C_{28}H_{26}N_2NaO_4^+$ $[2M+Na]^+$: 477,1785, found: 477,1780.

4-Aminophenethyl benzoate (14):



14 was prepared according to method A. 2-(4-Aminophenyl)ethanol (41 mg, 0.30 mmol) was reacted with 2,2,2-trifluoroethyl benzoate (41 mg, 0.20 mmol) in the presence of IMes (6.1 mg, 20 µmol) in dry THF (2 mL) at room temperature for 24h. Pure product was obtained by silica gel flash column chromatography (pentane:EtOAc, 2.5:1) as a yellow oil which solidified upon standing overnight (47 mg, 98%). FTIR: $\tilde{\nu}$ = 3019, 1712,

1623, 1517, 1274, 1215, 1116, 746, 667 cm^{-1}. 1H NMR (300 MHz, $CDCl_3$) δ = 8.04 (d, *J* = 8.5 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 4.48 (t, *J* = 7.1 Hz, 2H), 3.60 (bs, 1H), 2.98 (d, *J* = 7.08 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.6, 145.1, 132.9, 130.5, 129.9, 129.7, 128.4, 127.8, 115.4, 66.0, 34.5. HRMS (ESI) exact mass calculated for $C_{15}H_{16}NO_2^+$ $[M+H]^+$: 242,1176, found: 242,1176; $C_{15}H_{15}NNaO_2^+$ $[M+Na]^+$: 264,0995, found: 264,0994; $C_{30}H_{31}N_2O_4^+$ $[2M+H]^+$: 483,2278, found: 483,2272; $C_{30}H_{30}N_2NaO_4^+$ $[2M+Na]^+$: 505,2098, found: 505,2093.

NHC catalyzed chemoselective acylation of amino alcohols using oxidative carbene catalysis:

Method B: In an heatgun dried Schlenk tube an amino alcohol (1.5 equiv), IMes (0.030 equiv) and 3,3',5,5'-tetra-*tert*-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (1.0 equiv) were dissolved in dry THF (0.1 M). The mixture was stirred at room temperature for 1 minute and then benzaldehyde (1.0 equiv) was added. Stirring was continued for 16-48 hours (reaction was monitored by thin layer chromatography). Crude products were purified by silica gel flash column chromatography to obtain the esters with moderate to good yields and complete chemoselectivity [in some cases products were purified after treatment with Boc_2O (2.0 equiv) and Et_3N (2 equiv)].

Method C: In an heatgun dried Schlenk tube an amino alcohol (1.5 equiv), 1,4-dimethyl-4H-1,2,4-triazol-1-ium iodide (0.020 equiv), DBU (1.1 equiv) and 3,3',5,5'-tetra-*tert*-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (1.0 equiv) were dissolved in dry THF (0.10 M). The mixture was stirred at room temperature for five minutes and then benzaldehyde (1.0 equiv) was added. Stirring was continued for 24 hours (reaction was monitored by thin layer chromatography). Crude products were purified by silica gel flash column chromatography to obtain the esters with good yields and complete chemoselectivity [in some cases products were purified after treatment with Boc_2O (2.0 equiv) and Et_3N (2 equiv)].

Theoretical Methods and Technical Details of the Computations:

The quantum chemical calculations have been performed with the TURBOMOLE suite of programs.[S6] As Gaussian AO basis for the structure optimizations, large triple-zeta (denoted as TZVPP) sets of Ahlrichs et al.[S7] have been employed. In standard notation these are

[5s3p2d1f] for C, N, O, and [3s2p1d] for H. All geometries have been fully optimized at the DFT level using the B97-D semi-local GGA density functional[S8] that also includes an empirical correction for London dispersion (also called van der Waals) interactions.[S8,S9] For a detailed description of this dispersion correction, that is of great importance in studies of large molecules, including many illustrative examples see Ref.[S9,S10,S11] In all DFT treatments, the RI-approximation has been used[S12] for the Coulomb integrals which speeds the computations up significantly without any significant loss of accuracy. These structures were used in subsequent single-point computations of the interaction energy using MP2 which provides a rather accurate description of hydrogen bonds. In all the perturbation treatments and also for the HF part (dubbed RI-K and RI-MP2, respectively), the RI-approximation using corresponding optimized auxiliary basis sets[S13] have been used. These calculations employ the Dunning[S14] basis sets cc-pVTZ and cc-pVQZ extrapolated to the AO basis set limt (CBS)[S15] in both, the MP2 as well as the HF part. In all calculations the basis sets used are so large that the remaining incompleteness effects for the energies (called basis set super-position error, BSSE) are so small (typically <5% of the interaction energy) so that approximate counter-poise corrections are unnecessary (and furthermore inconsistent at the CBS level). For a detailed discussion of this point see refs.[S8,S16]

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S13. a) F. Weigend, A. Köhn and C. Hättig, J. Chem. Phys. 2002, 116, 3175. b) F. Weigend, *Phys.Chem.Chem.Phys.* **2002**, *4*, 4285.

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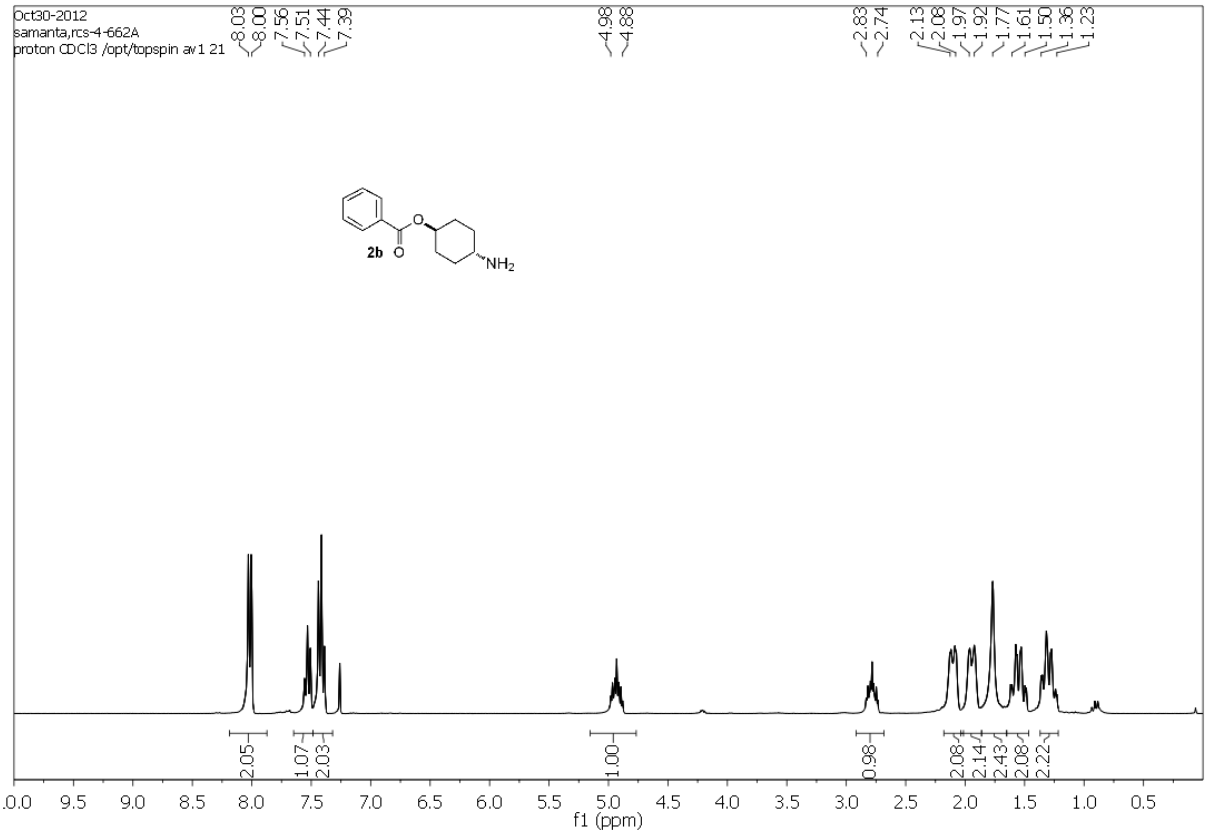
NMR data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7.51
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2.74
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1.77
1.61
1.50
1.36
1.23
2b
O
O
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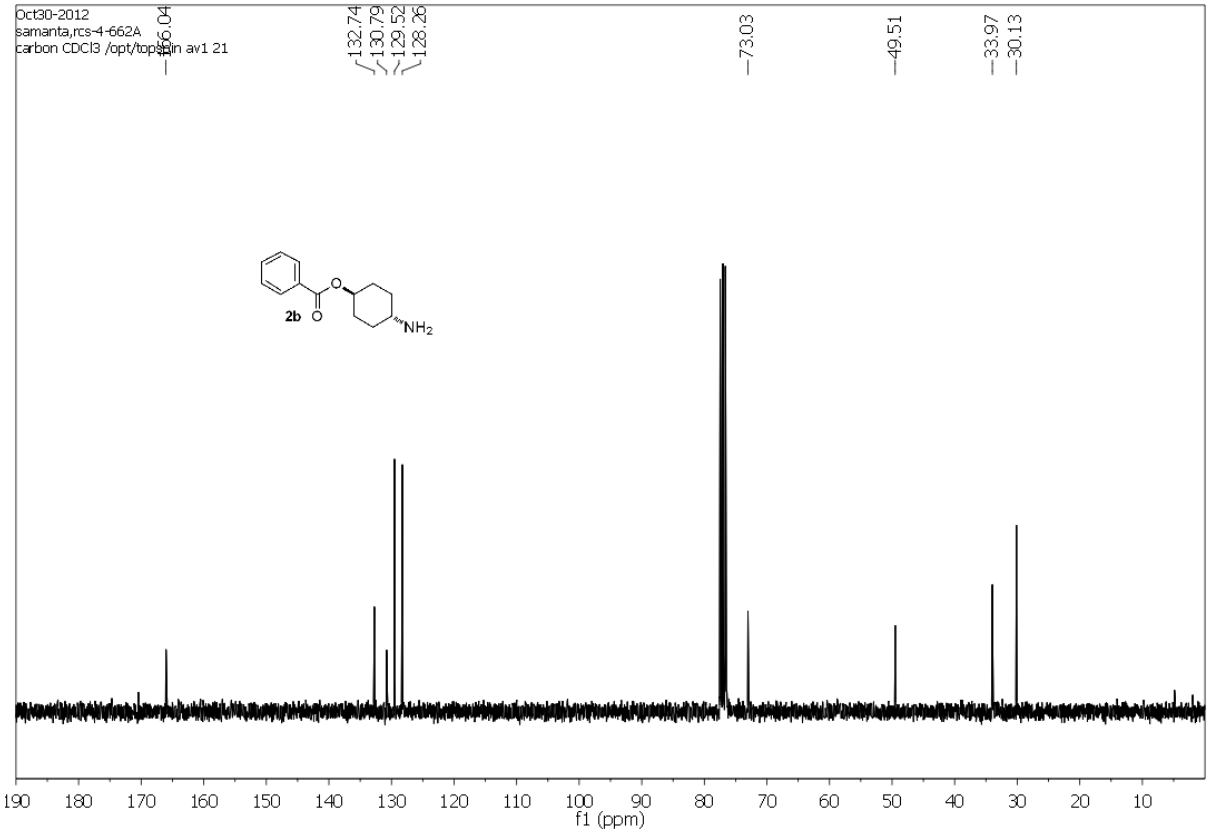
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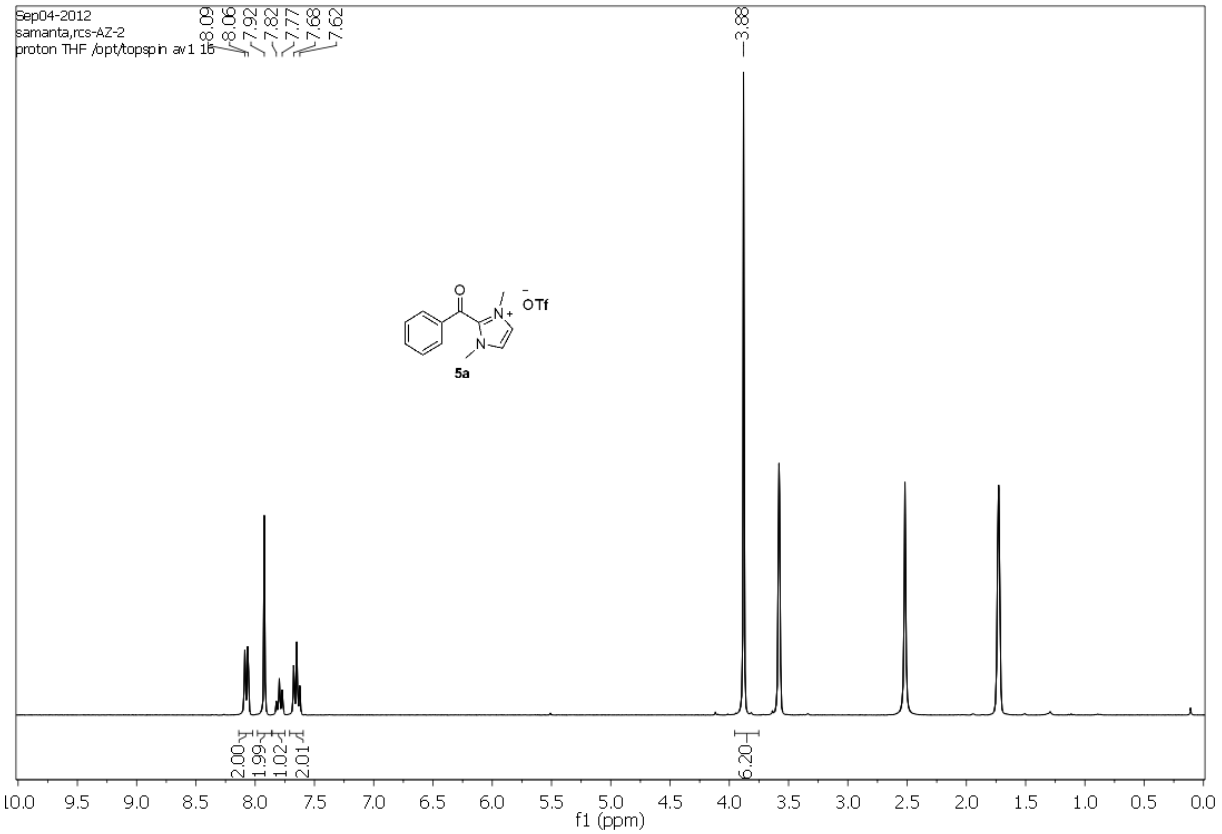
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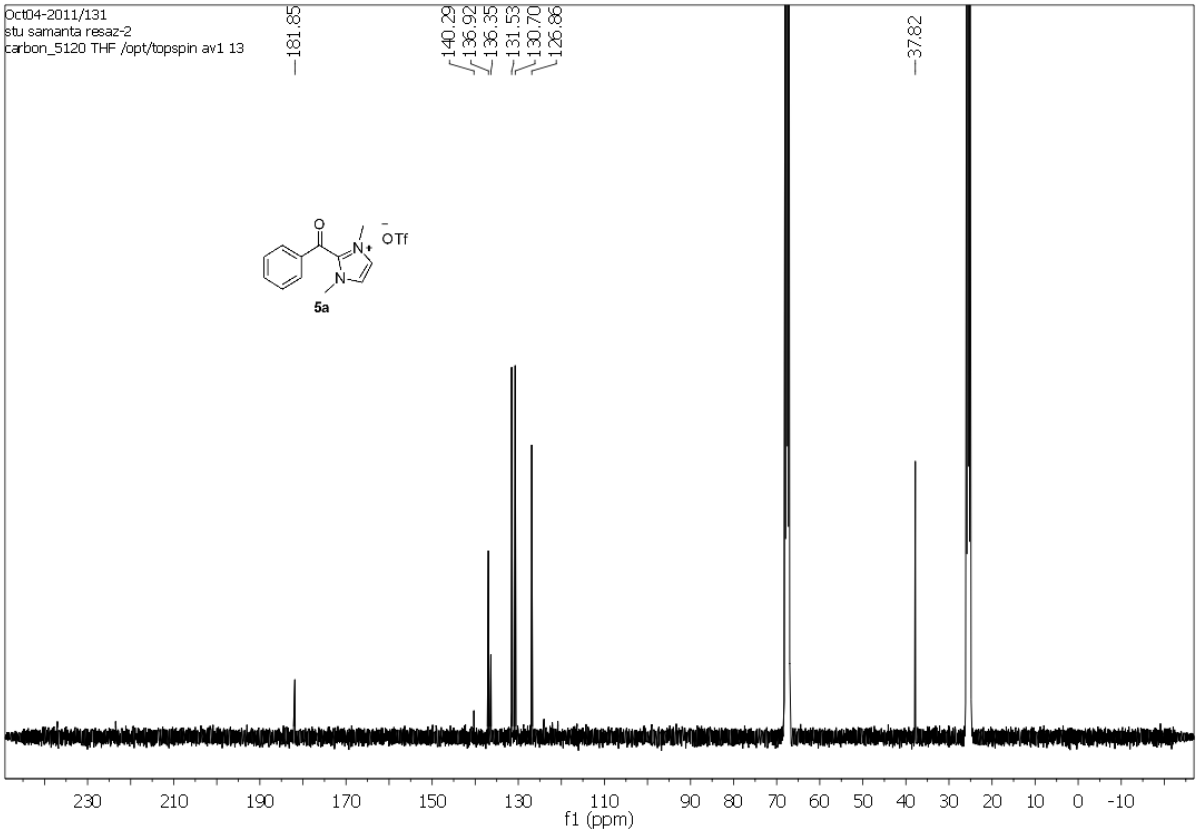

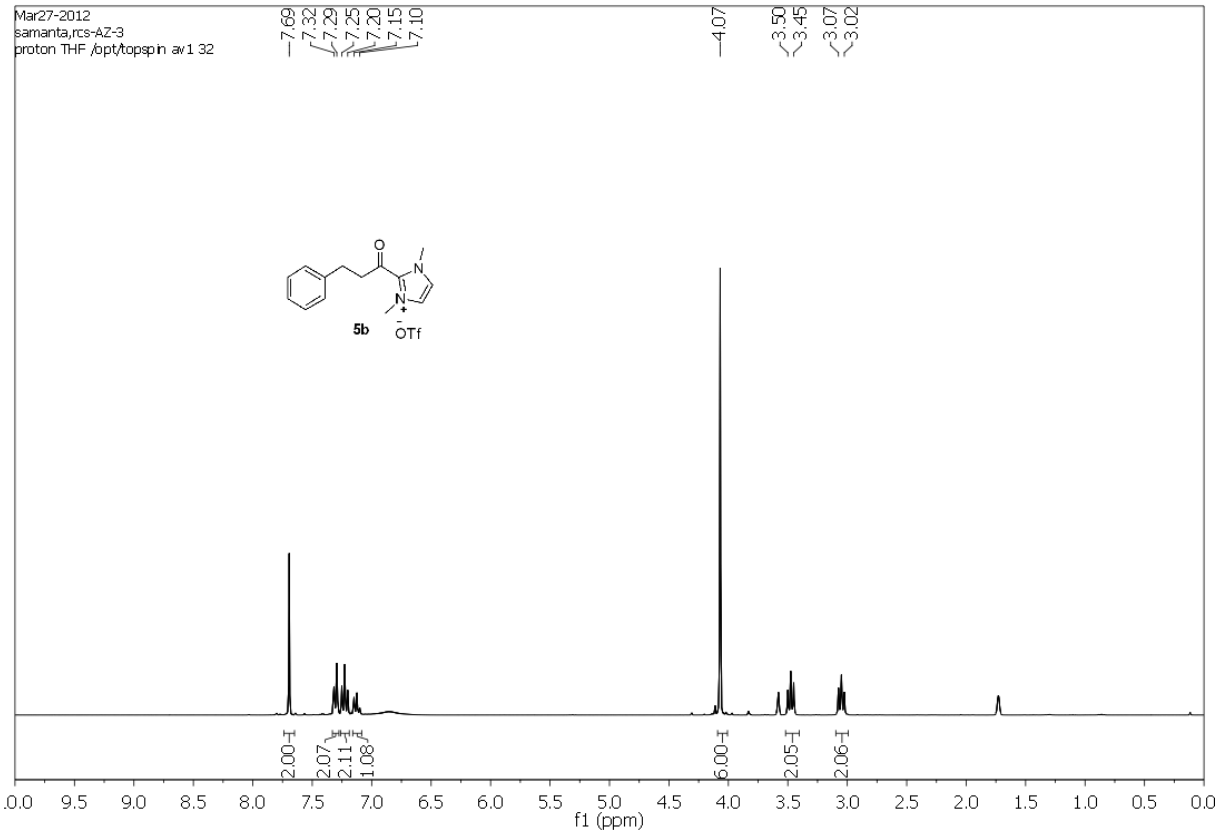

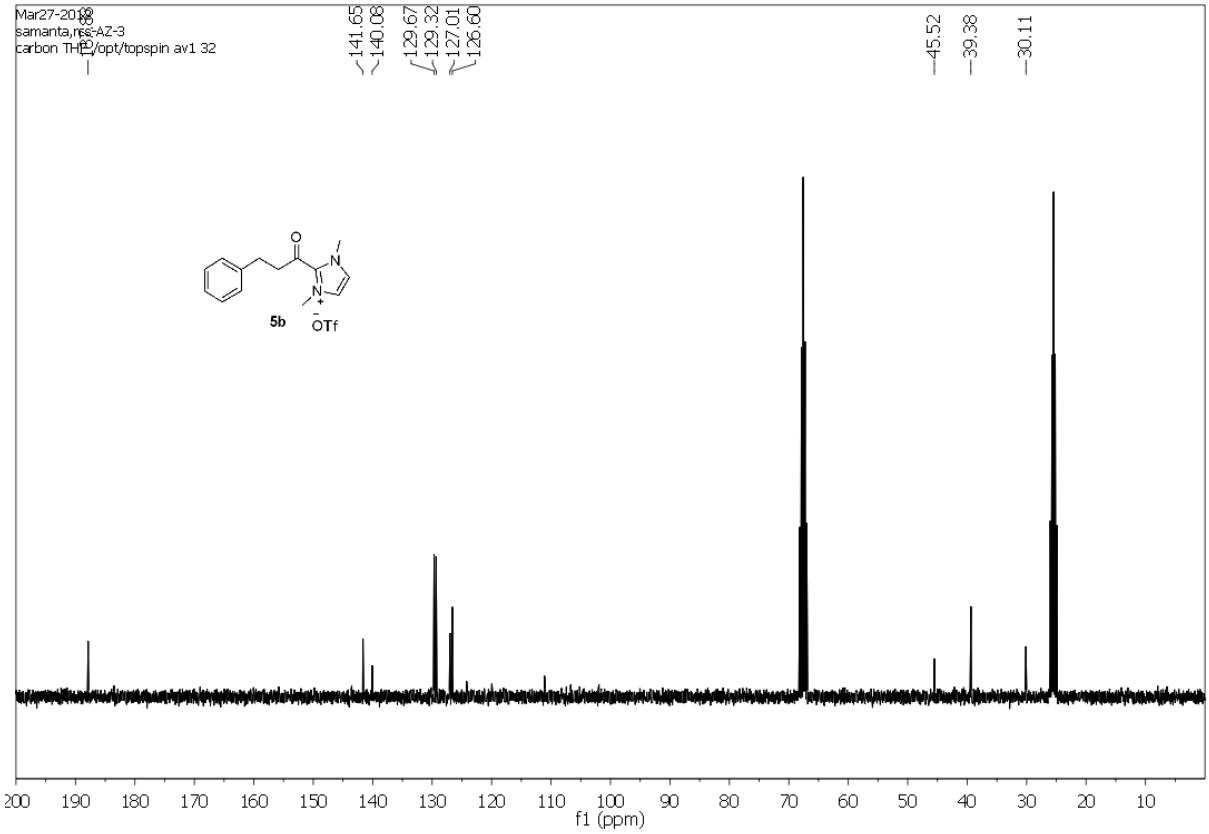
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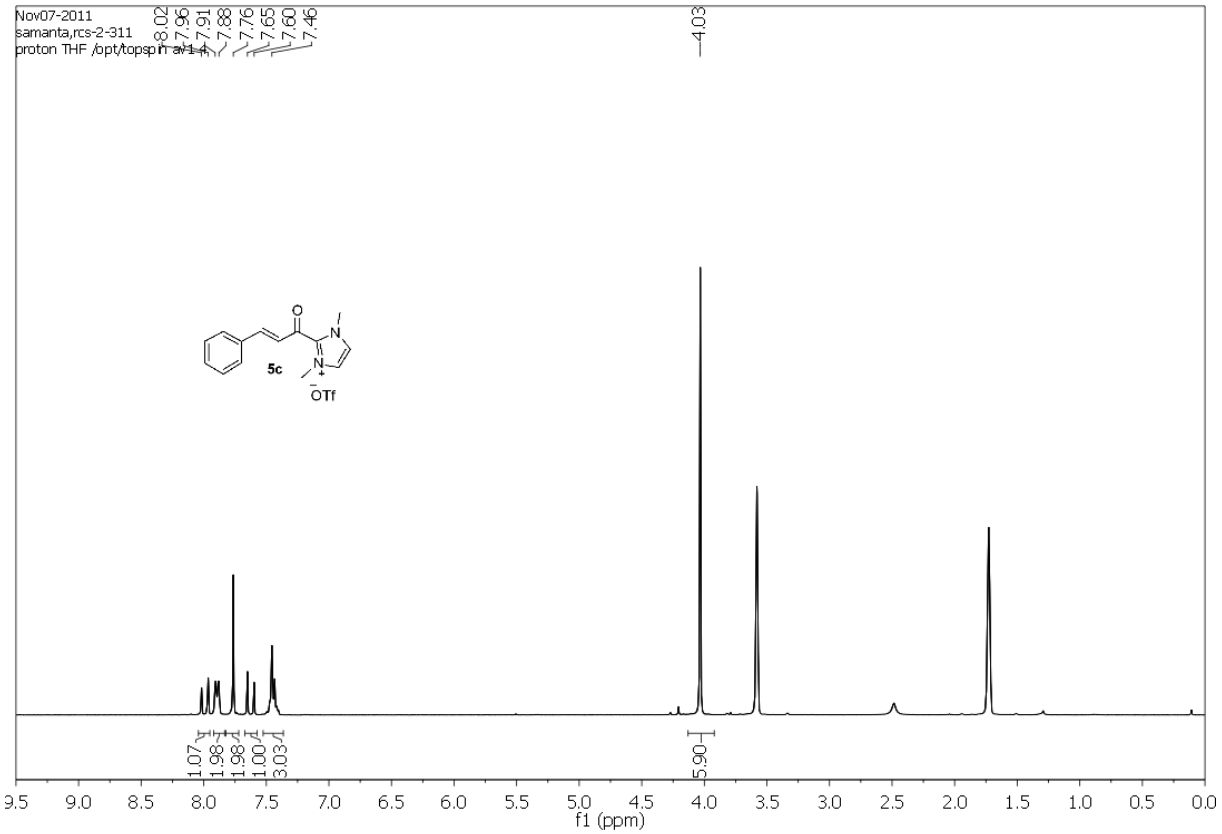
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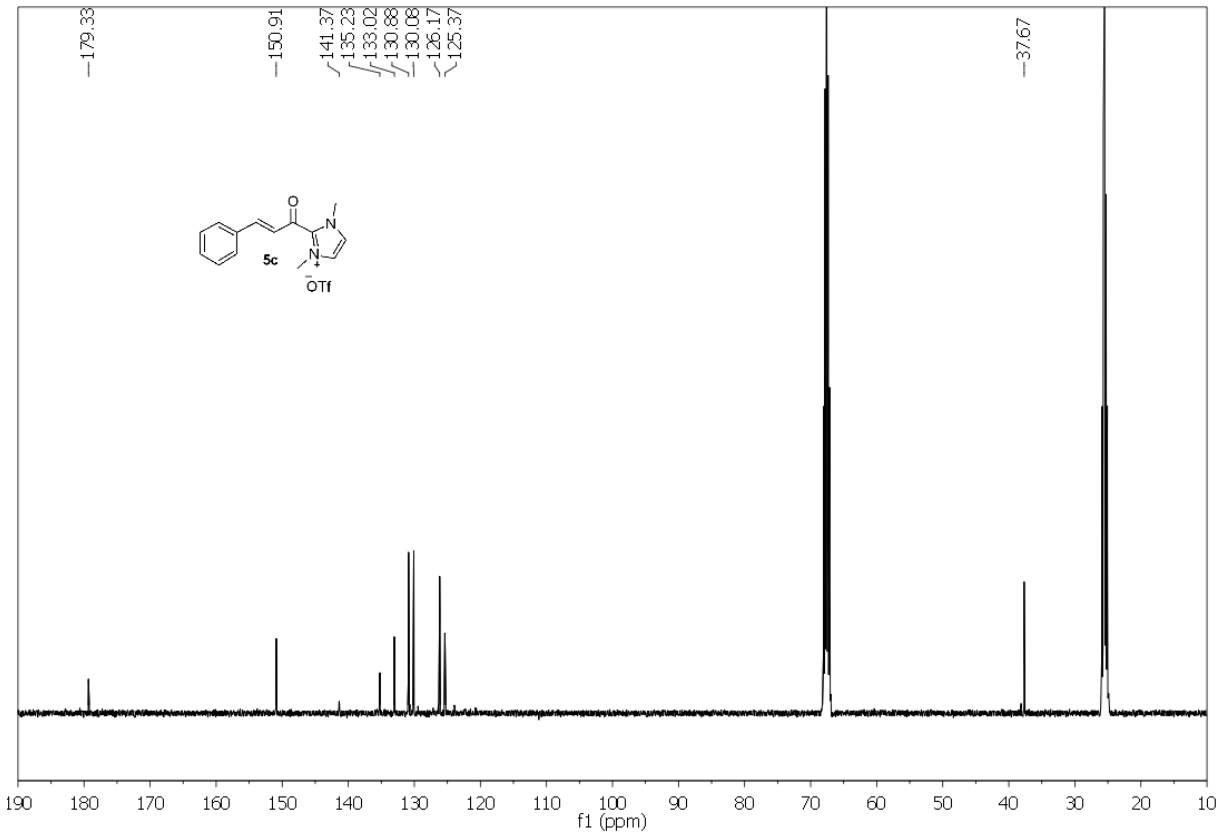
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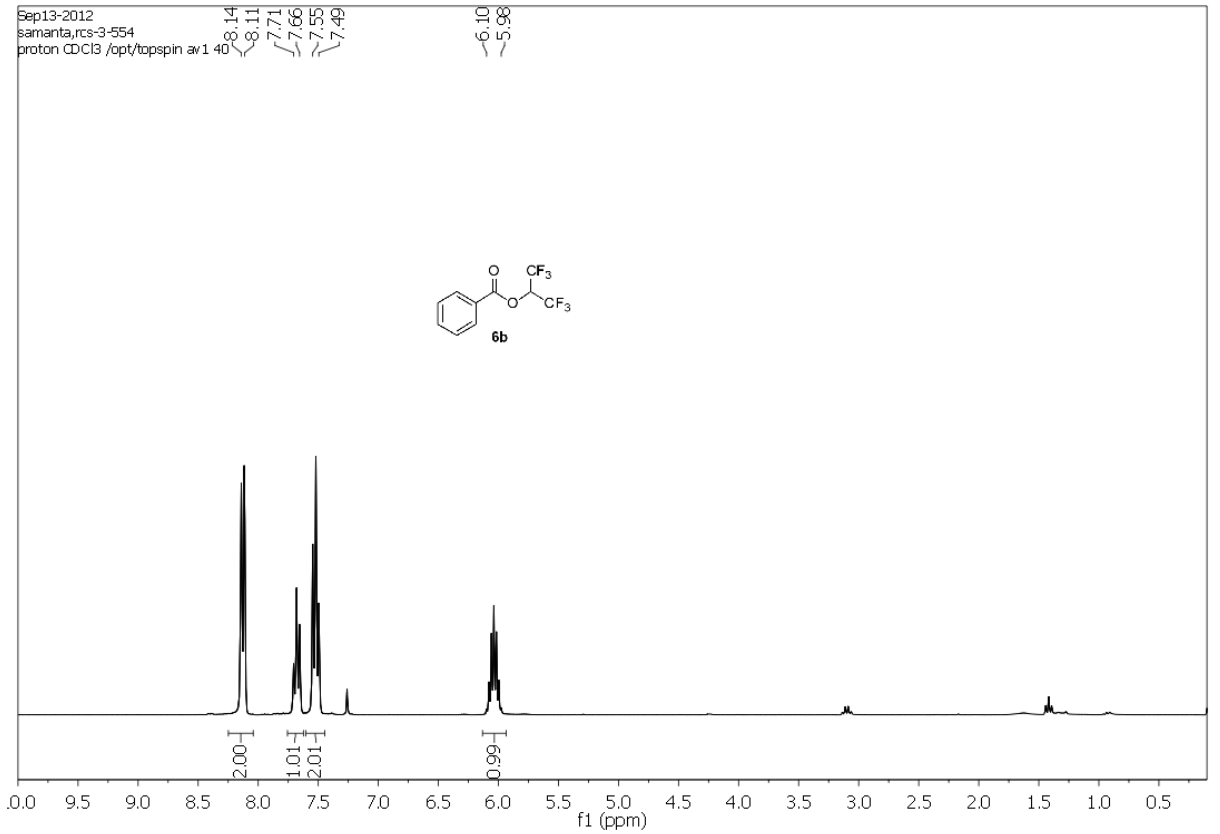
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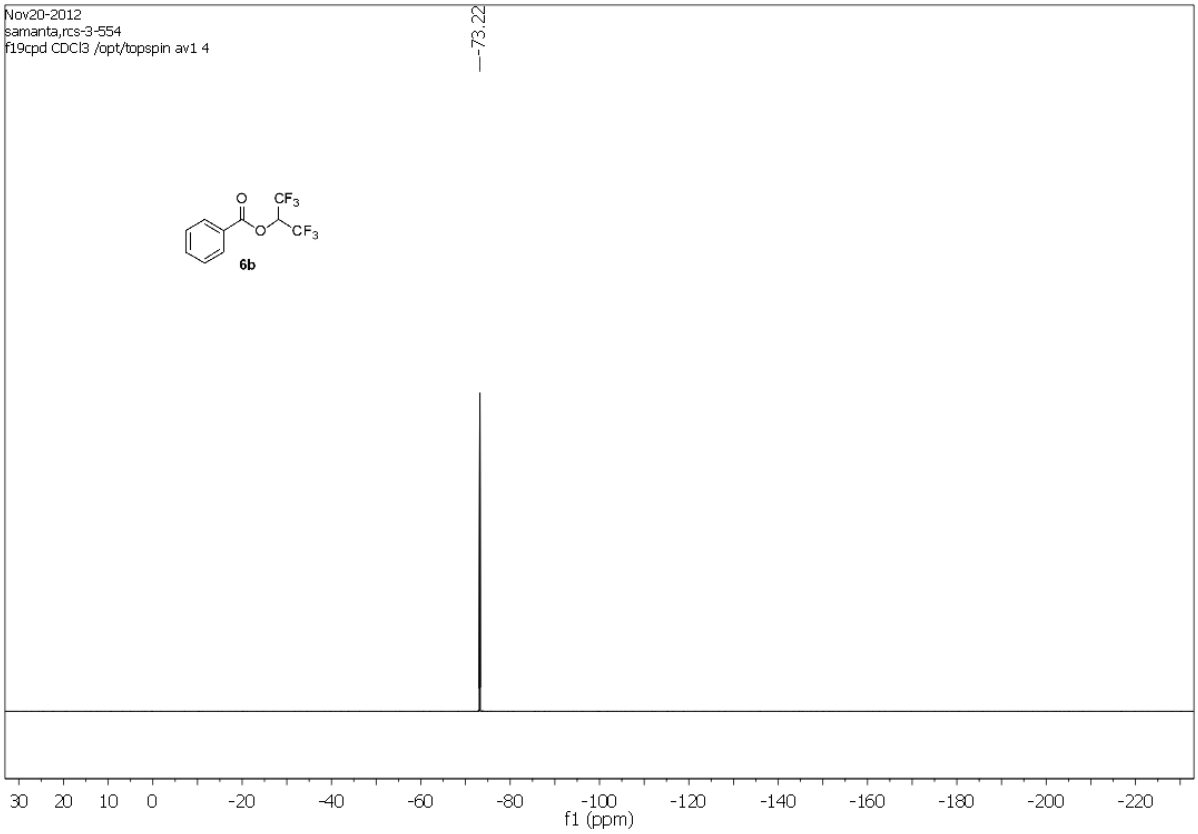
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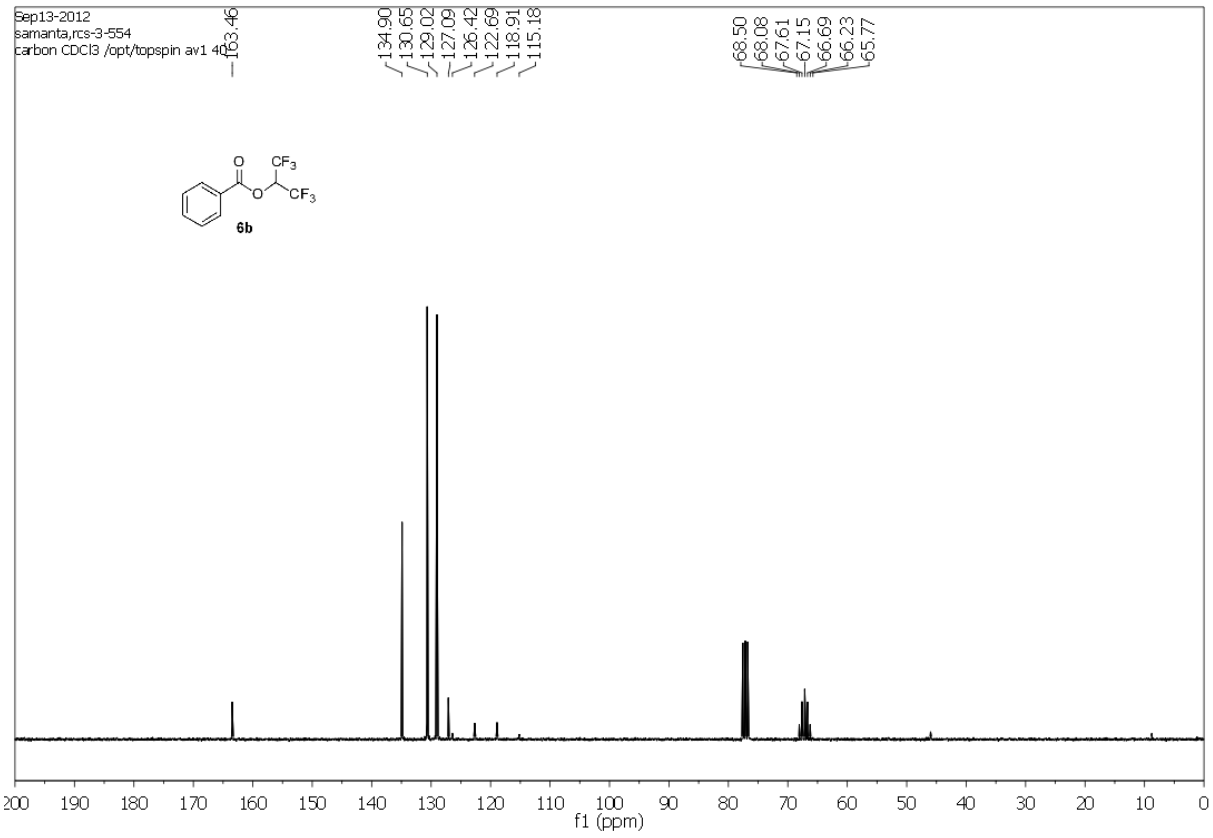
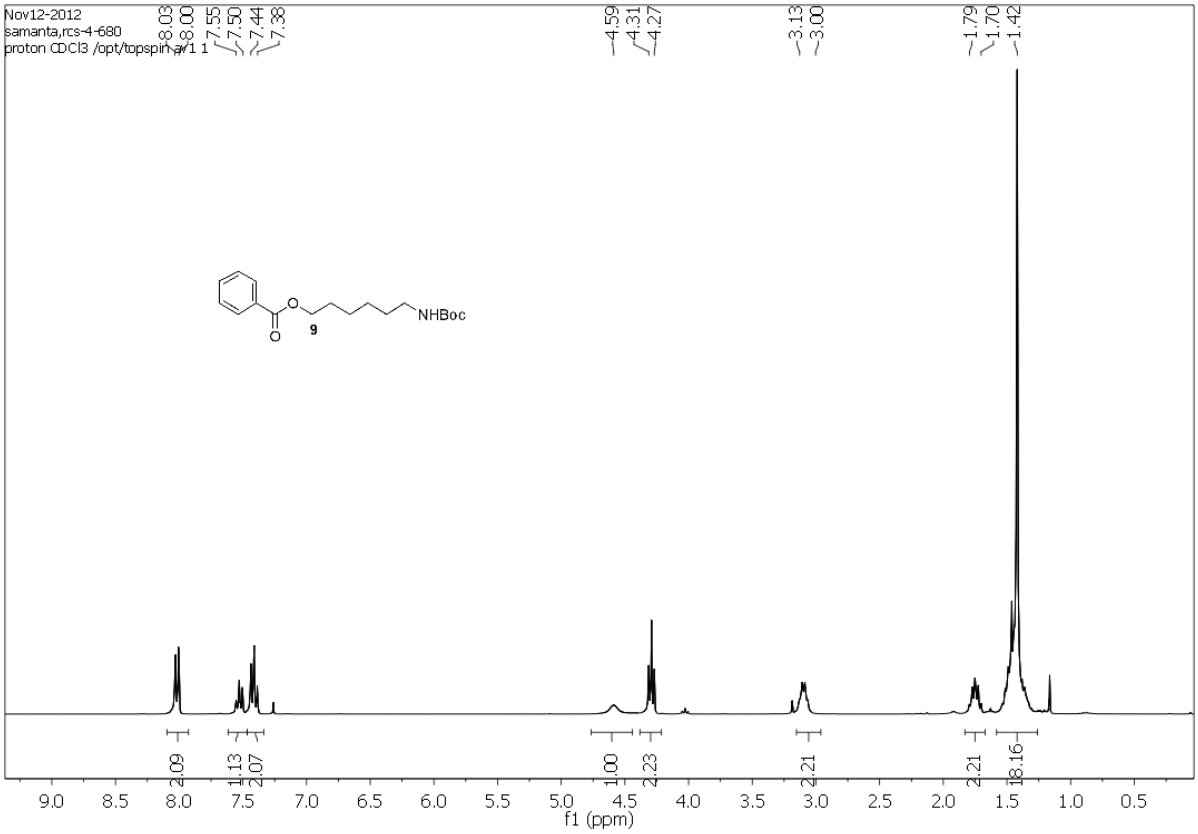
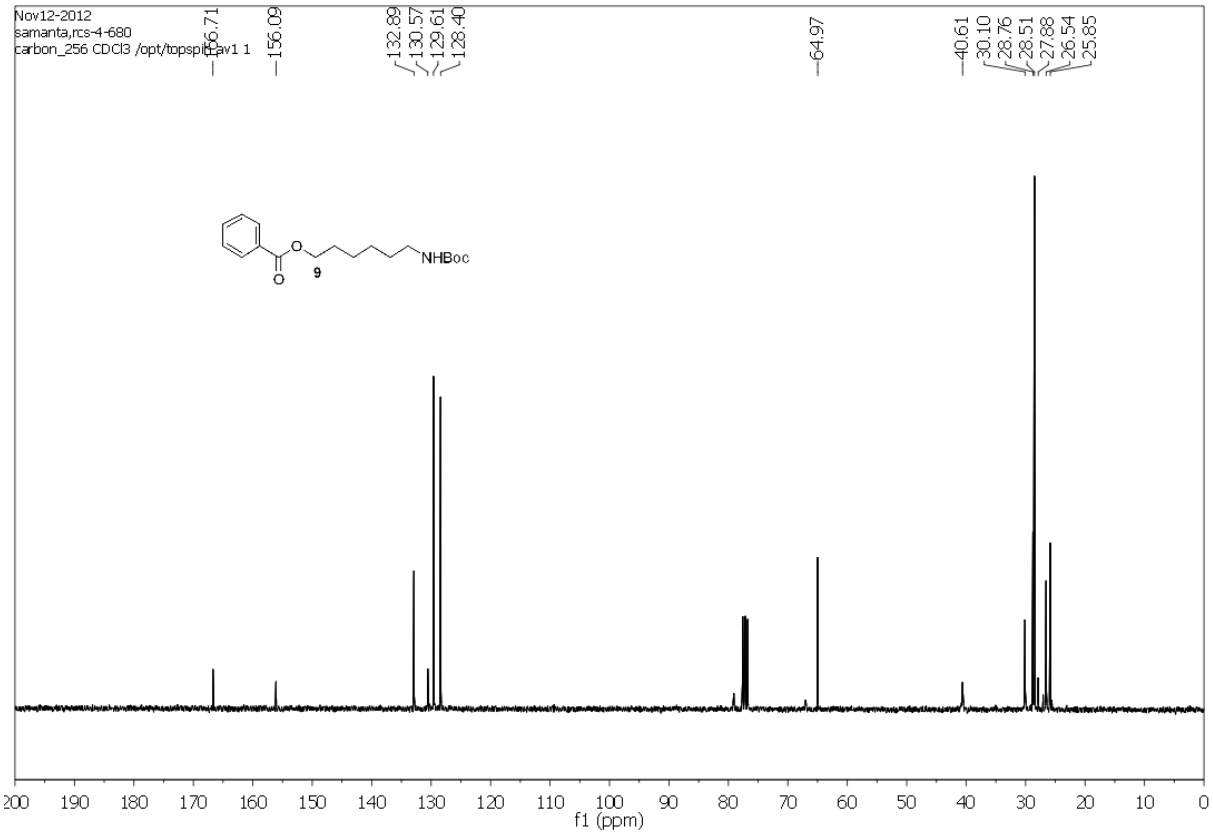
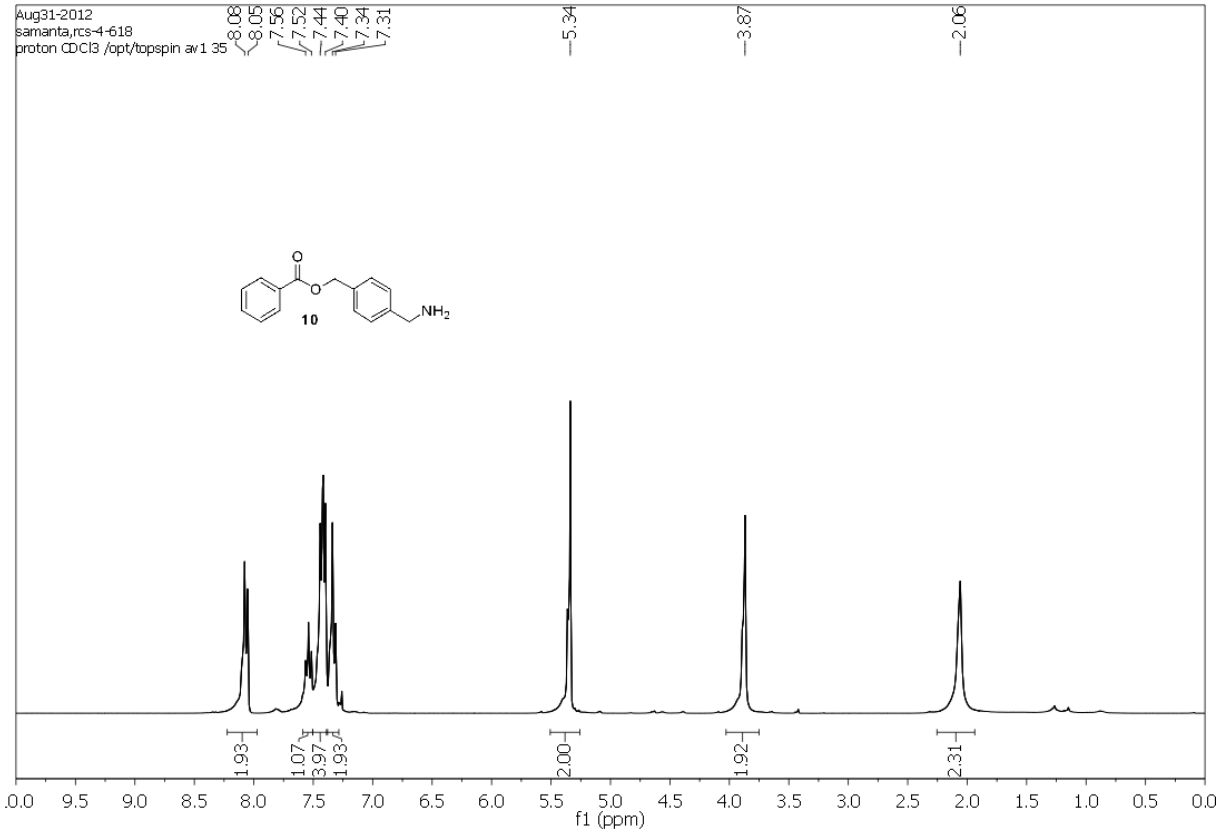
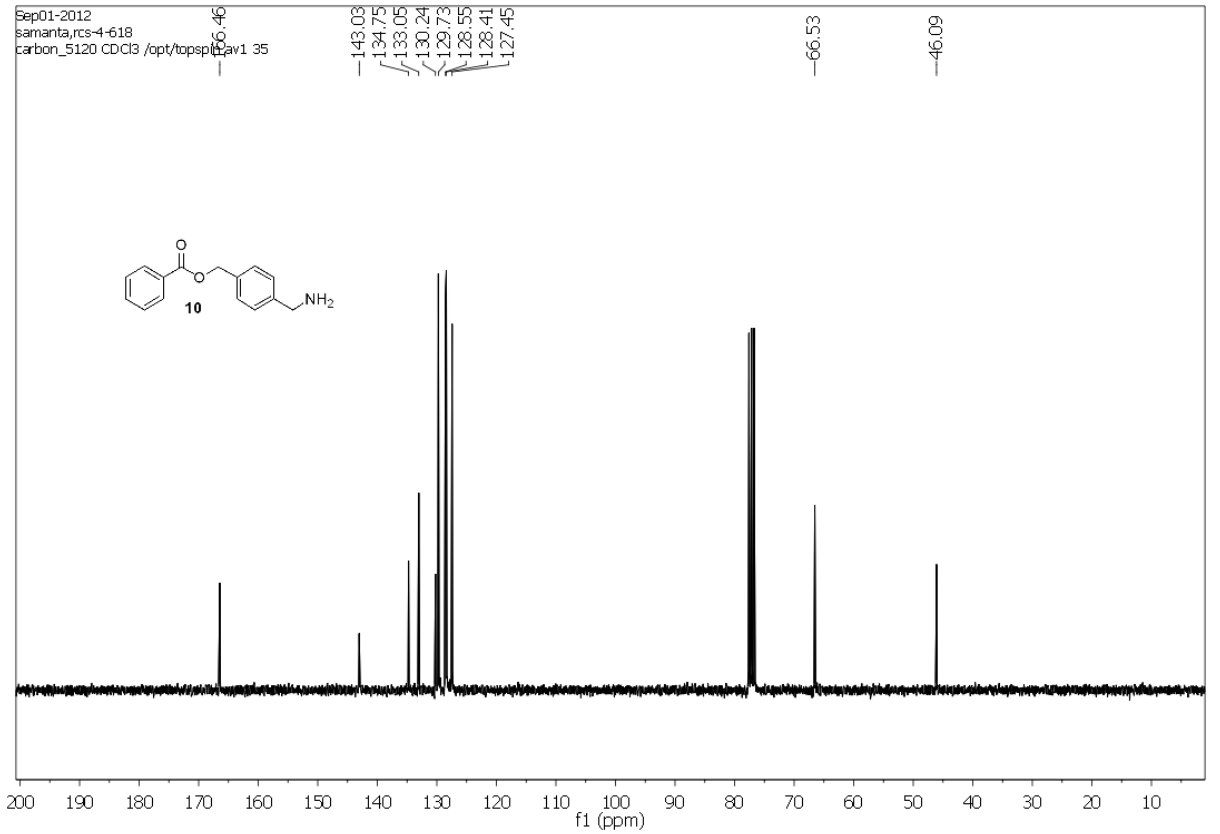
30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

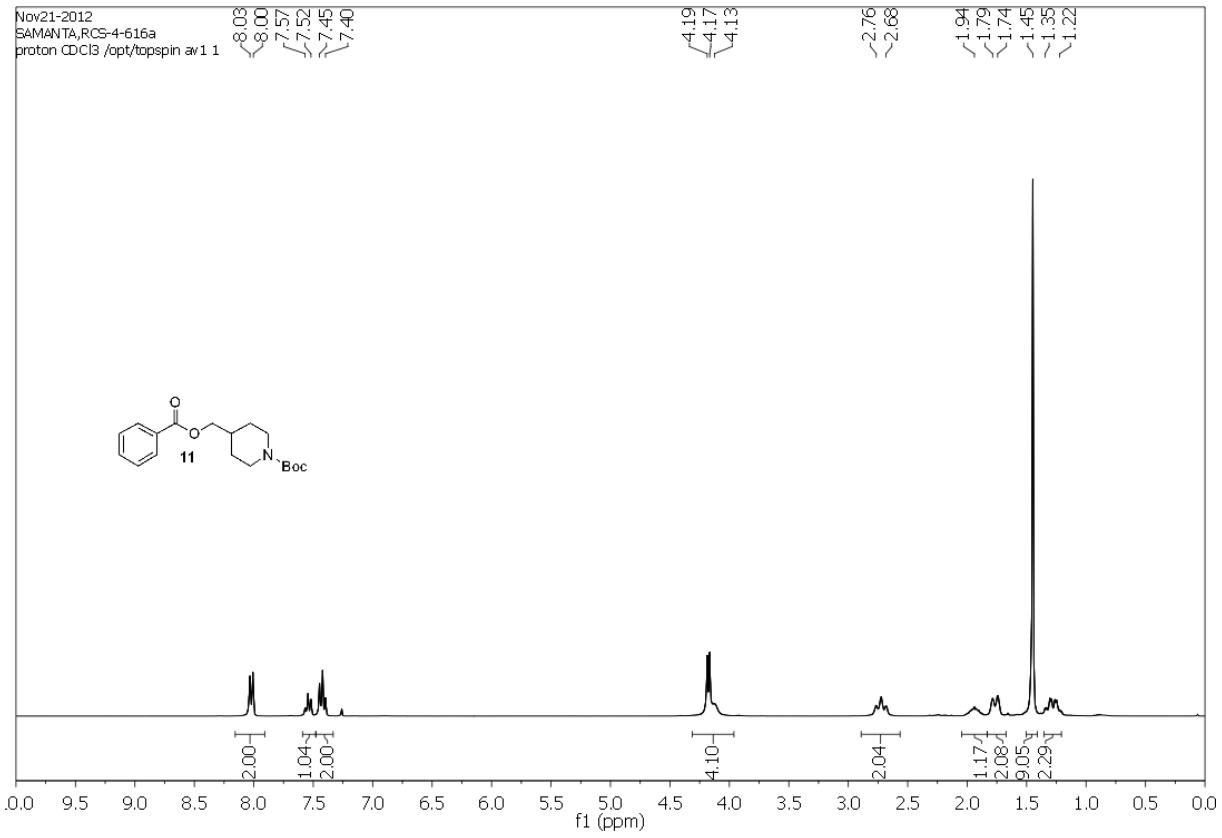

Sep13-2012
samanta,rcs-3-554
carbon CDCl3 /opt/topspin av1 4
163.46
134.90
130.65
129.02
127.09
126.42
122.69
118.91
115.18
68.50
68.08
67.61
67.15
66.69
66.23
65.77
6b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

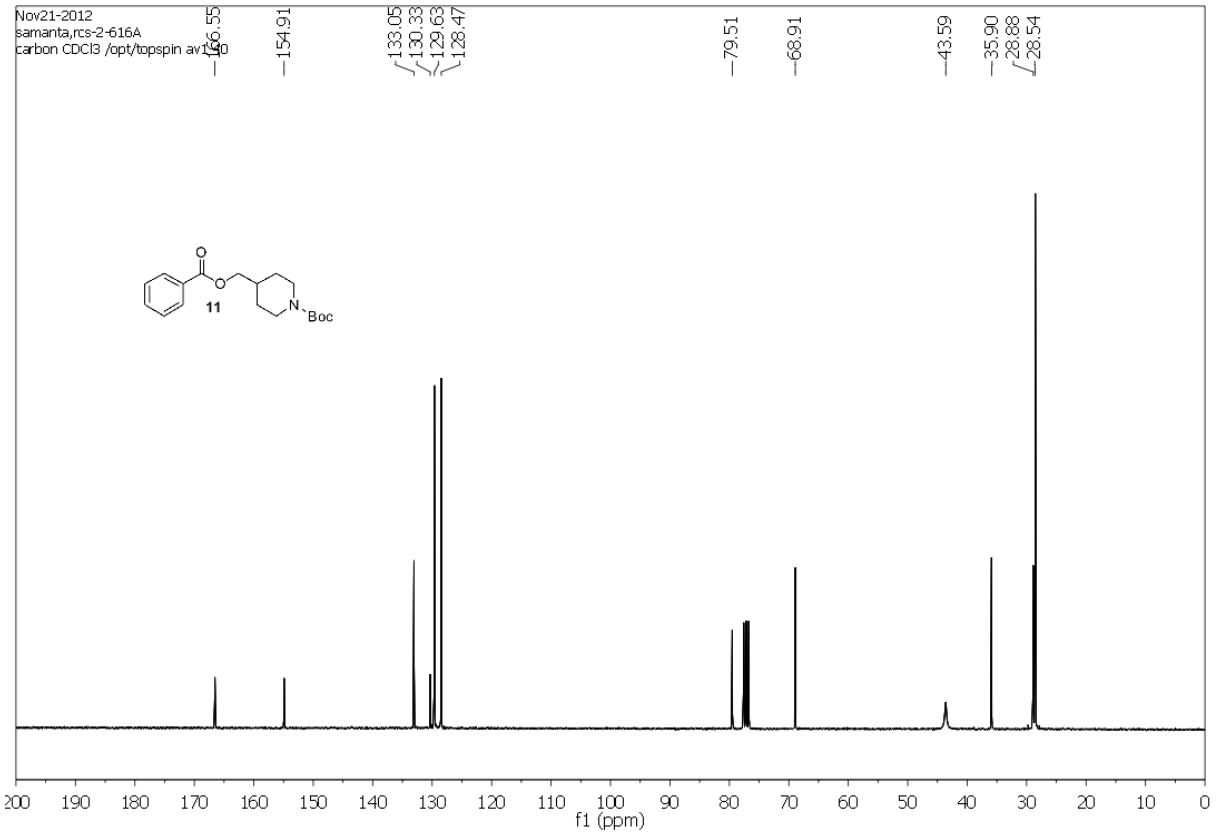

Nov12-2012
samanta,rcs-4-680
proton CDCl3 /opt/topspin-av1 1
8.03
8.00
7.55
7.50
7.44
7.38
4.59
4.31
4.27
3.13
3.00
1.79
1.70
1.42
NHBoc
9
2.09
1.13
2.07
1.00
2.23
2.21
2.21
18.16
f1 (ppm)

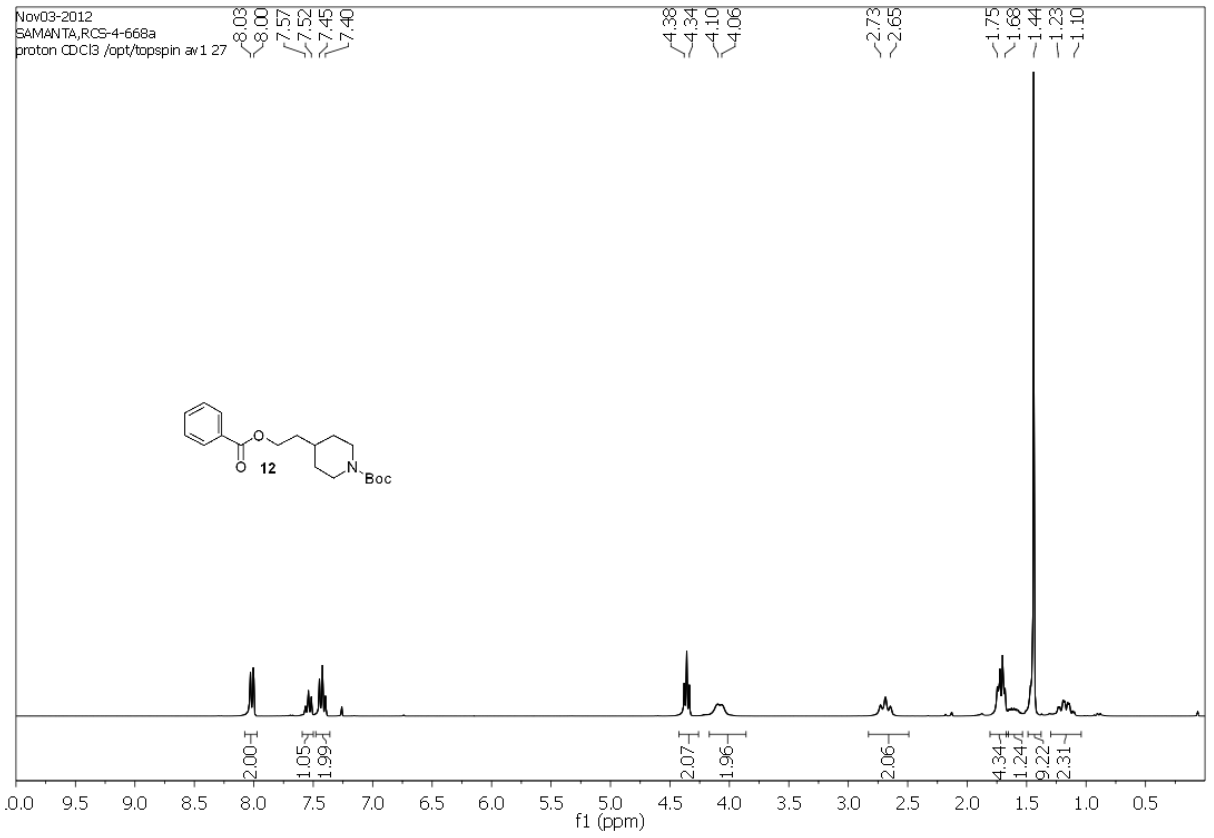

Nov12-2012
samanta,rcs-4-680
carbon_256 CDCl3 /opt/topspin-av1 1
166.71
156.09
132.89
130.57
129.61
128.40
64.97
40.61
30.10
28.76
28.51
27.88
26.54
25.85
NHBoc
9
f1 (ppm)

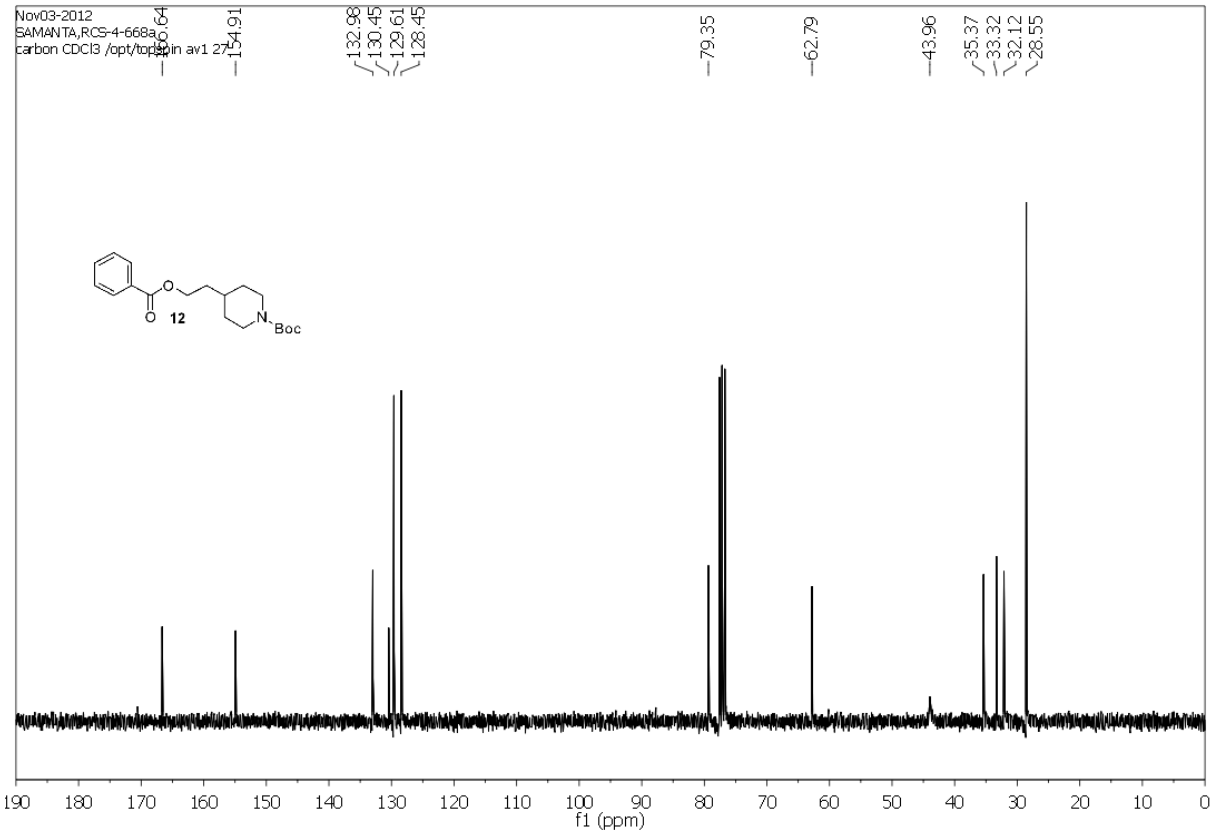

Aug31-2012
samanta,rcs-4-618
proton CDCl3 /opt/topspin av1 35
8.08
8.05
7.56
7.52
7.44
7.40
7.34
7.31
5.34
3.87
2.06
O
O
NH2
10
1.93
1.07
3.97
1.93
2.00
1.92
2.31
f1 (ppm)

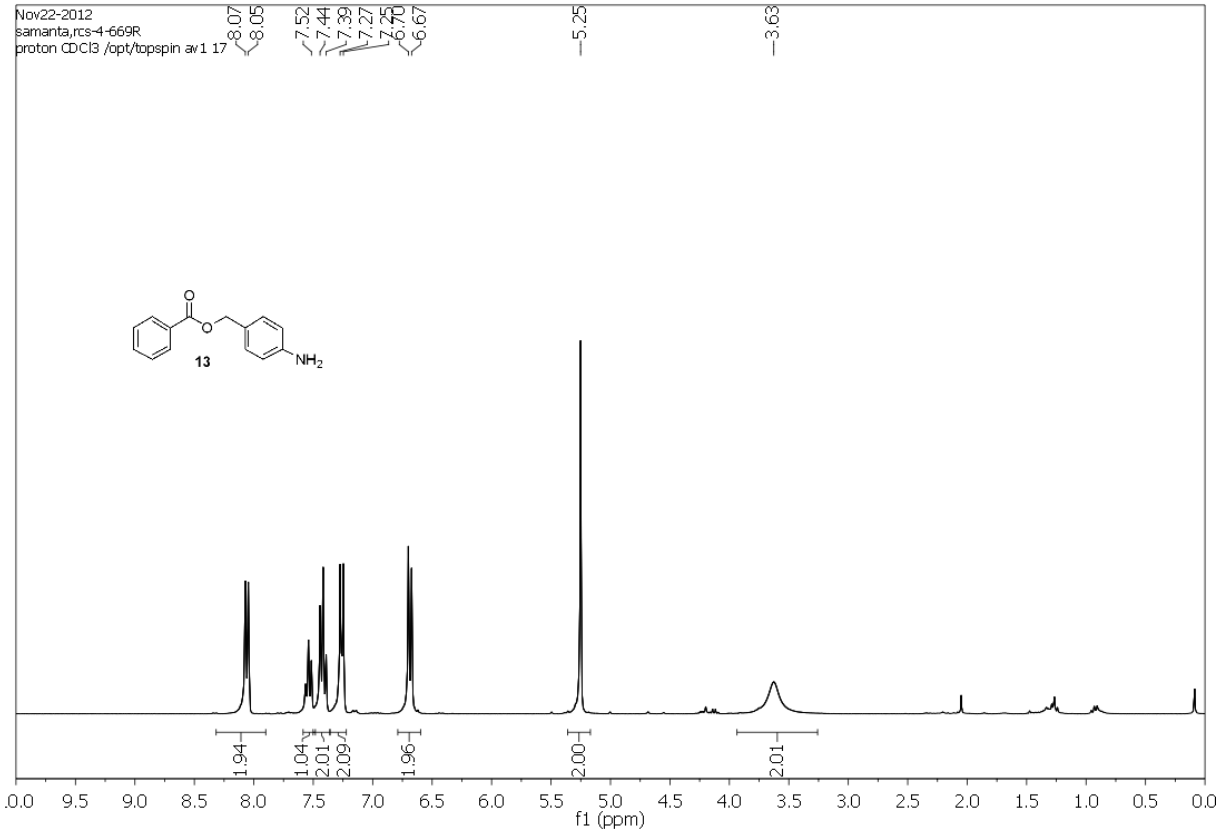

Sep01-2012
samanta,rcs-4-618
carbon_5120 CDCl3 /opt/topspin av1 35
166.46
143.03
134.75
133.05
130.24
129.73
128.55
128.41
127.45
66.53
46.09
O
O
NH2
10
f1 (ppm)

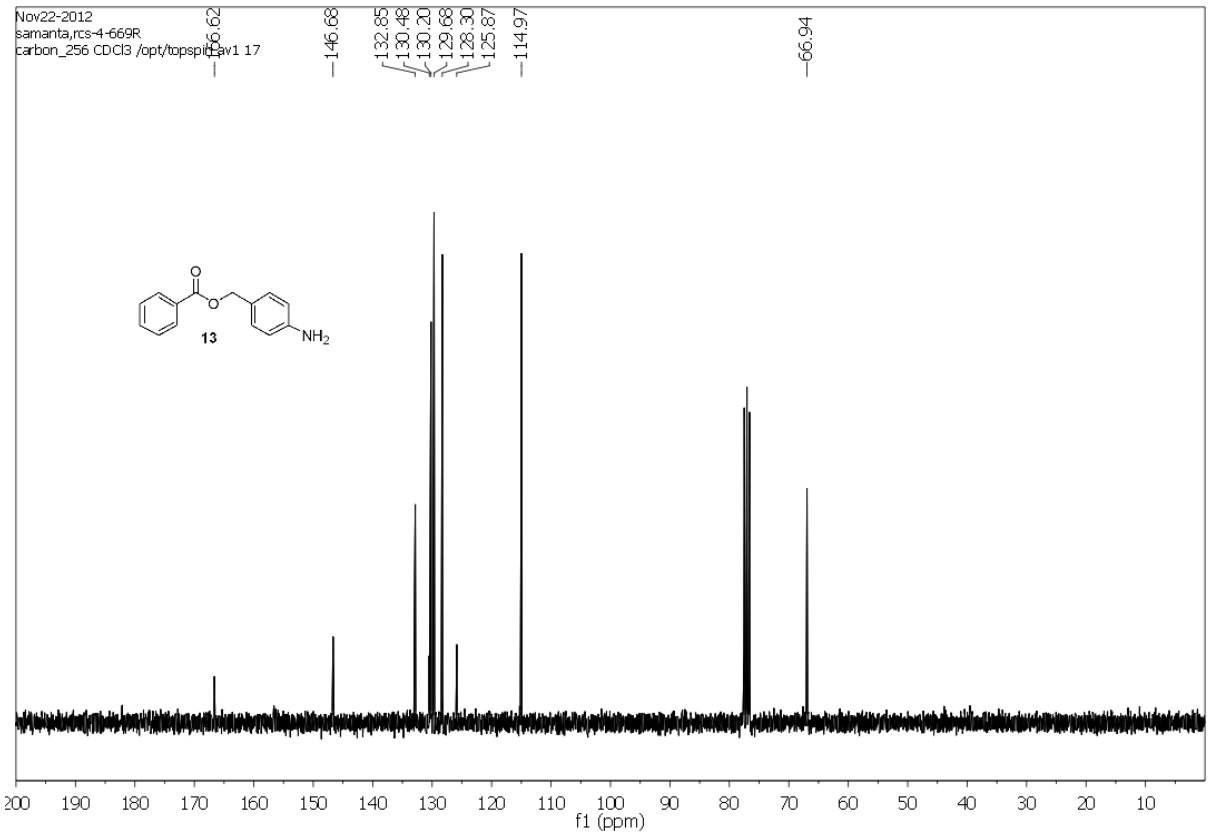

Nov21-2012
SAMANTA,RCS-4-616a
proton CDCl3 /opt/topspin av1 1
8.03
8.00
7.57
7.52
7.45
7.40
4.19
4.17
4.13
2.76
2.68
1.94
1.79
1.74
1.45
1.35
1.22
11
Boc
2.00
1.04
2.00
4.10
2.04
1.17
2.08
9.05
2.29
f1 (ppm)

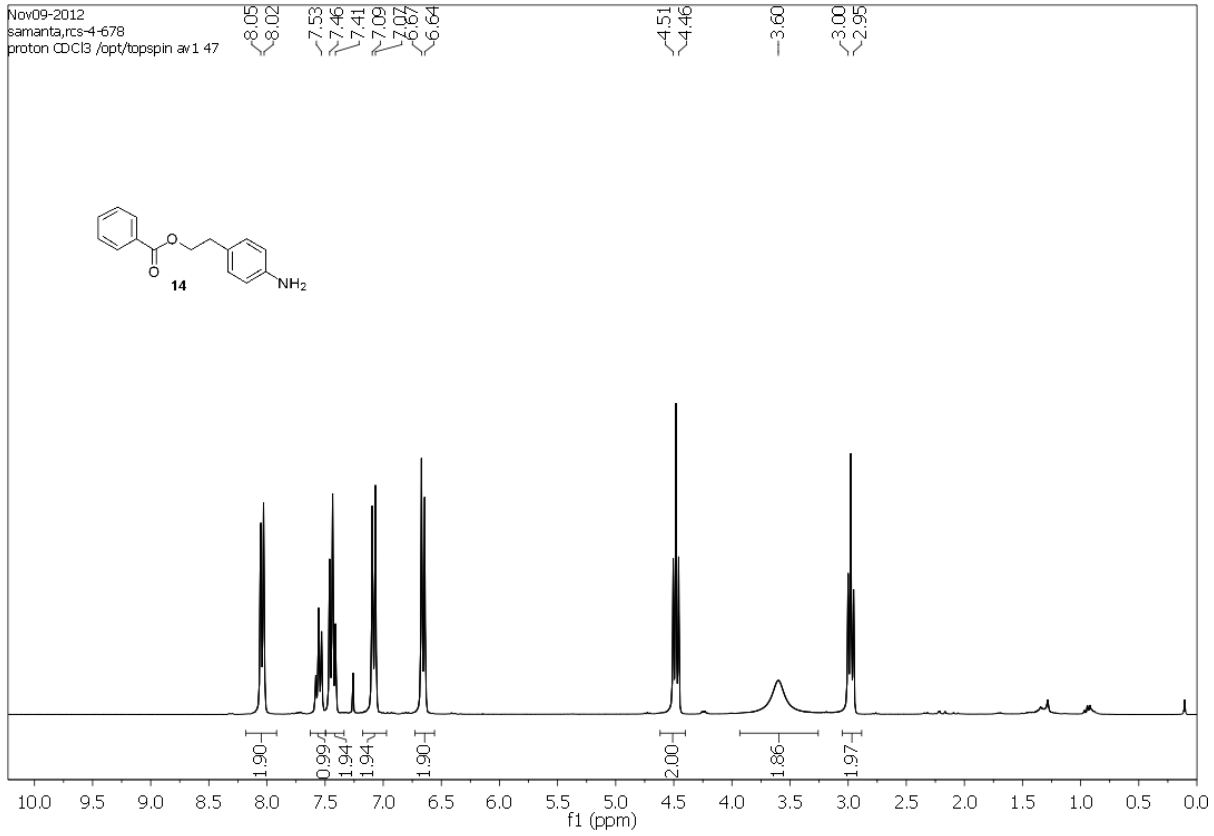

Nov21-2012
samanta,rcs-2-616A
carbon CDCl3 /opt/topspin av1
166.55
154.91
133.05
130.33
129.63
128.47
79.51
68.91
43.59
35.90
28.88
28.54
11
Boc
f1 (ppm)

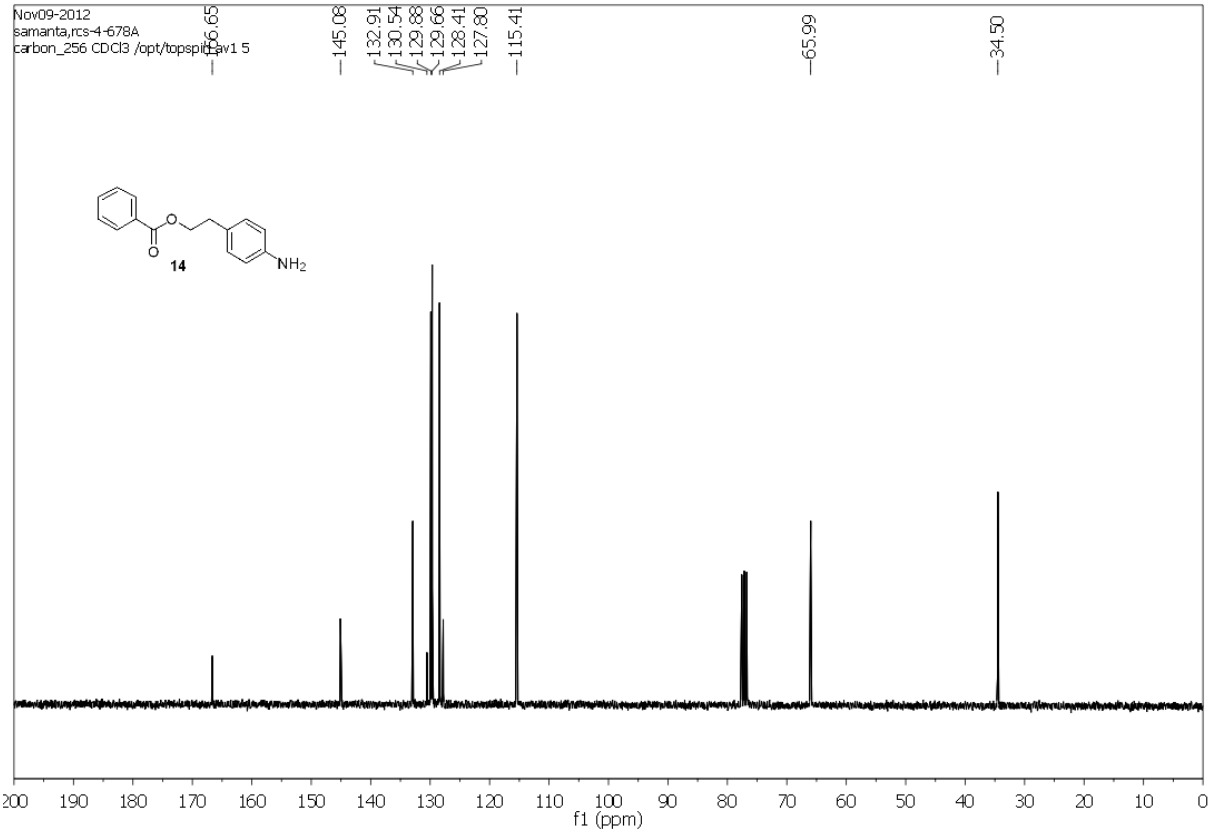

Nov03-2012
SAMANTA,RCS-4-668a
proton CDCl3 /opt/topspin av1 27
8.03
8.00
7.57
7.52
7.45
7.40
4.38
4.34
4.10
4.06
2.73
2.65
1.75
1.68
1.44
1.23
1.10
12
Boc
2.00
1.05
1.99
2.07
1.96
2.06
4.34
1.24
9.22
2.31
f1 (ppm)


Nov03-2012
SAMANTA,RCS-4-668a
carbon CDCl3 /opt/topspin av1 27
166.64
154.91
132.98
130.45
129.61
128.45
79.35
62.79
43.96
35.37
33.32
32.12
28.55
12
Boc
f1 (ppm)


Nov22-2012
samanta,rcs-4-669R
proton CDCl3 /opt/topspin av1 17
8.07
8.05
7.52
7.44
7.39
7.27
7.25
6.70
6.67
5.25
3.63
13
NH2
1.94
1.04
2.01
2.09
1.96
2.00
2.01
f1 (ppm)


Nov22-2012
samanta,rcs-4-669R
carbon_256 CDCl3 /opt/topspin av1 17
166.62
146.68
132.85
130.48
130.20
129.68
128.30
125.87
114.97
66.94
13
NH2
f1 (ppm)


Nov09-2012
samanta,rcs-4-678
proton CDCl3 /opt/topspin av1 47
8.05
8.02
7.53
7.46
7.41
7.09
7.07
6.67
6.64
4.51
4.46
3.60
3.00
2.95
14
NH2
1.90
0.99
1.94
1.94
1.90
2.00
1.86
1.97
f1 (ppm)


Nov09-2012
samanta,rcs-4-678A
carbon_256 CDCl3 /opt/topspin av1 5
166.65
145.08
132.91
130.54
129.88
129.66
128.41
127.80
115.41
65.99
34.50
14
NH2
f1 (ppm)