Supporting Information

Anaerobic Nitroxide-Catalyzed Oxidation of Alcohols Using the NO^+/NO• Redox Pair

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General: All reactions were conducted in oven-dried glassware under a nitrogen atmosphere. Diethyl ether was dried over Na/benzophenone and dichloromethane over CaH_2, respectively, under an argon atmosphere. Methanol and hexane were distilled from Mg/I_2 and P_2O_5 respectively prior to use. BF_3•OEt_2 and a $LiBF_4$ solution (1M in CH_3CN) were used as received. Silica gel on TLC-PET foils with fluorescent indicator 254 nm (Sigma-Aldrich) or an Agilent 6850 Series GC System with FID were used for monitoring reactions. Flash column chromatographic separations were performed on silica gel 60 (Fluka, 230-400 mesh). HPLC analysis was performed with a Smartline 1000 isocratic pump (Knauer) and a Smartline 2500 UV detector (Knauer) on a Chiralcel OJ-H (250 × 4.6 mm, 5 μm particle size, Daicel) column. IR spectra were taken on a Bruker ALPHA FT-IR spectrometer as neat samples using an ATR device. ^1H, ^{19}F and ^{13}C NMR spectra were recorded, unless otherwise noted, in $CDCl_3$ on a Bruker Avance 400 spectrometer at 400.1 MHz for ^1H NMR, 376.3 MHz for ^{19}F NMR and 100.6 MHz for ^{13}C NMR, respectively. Connectivity was determined by ^1H-^1H COSY experiments. ^{13}C NMR assignments were obtained from APT and HSQC experiments. ESI-mass spectra were obtained on a Thermo Fisher Scientific LCQ Fleet spectrometer, sample concentration approx. 1 μg/mL, spray voltage pos. mode: 3.3 kV. CI and ESI HRMS spectra were measured on a Waters Q-Tof micro spectrometer, resolution: 100000. Combustion analyses were performed at the Microanalytical Laboratories of IOCB AS CR Prague. Melting points are uncorrected.

Starting materials: 6-(Triethylsilyloxy)hexan-1-ol **5l**,[S1] c*is*-4-(*tert*-butyl)cyclohexanol *cis*-**5m**,[S2] *trans*-4-(*tert*-butyl)cyclohexanol *trans*-**5m**,[S2] (*S*)-4-(*tert*-butyldiphenylsilyloxy)-2-methylbutanol **5p**,[S3] and (*S*)-*N*-(*tert*-butyloxycarbonyl)prolinol **5q**[S4] were prepared according to literature procedures.

2,2,6,6-tetramethyl-*N*-oxopiperidinium tetrafluoroborate 4:

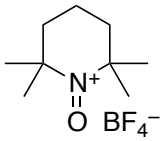


Table 1, entries 1 and 2: *t*-BuONO (120 µL, 1 mmol) was added to a solution of BF_3•OEt_2 (for amounts see Table 1) in dry Et_2O (4 mL) at room temperature under a nitrogen atmosphere. A solution of TEMPO **1** (156 mg, 1 mmol) in Et_2O (0.5 mL) was added and the inhomogeneous reaction mixture was stirred for 1 h. The yellow precipitate was filtered off, washed with cold Et_2O and dried in vacuum.

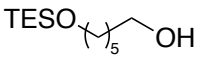
Table 1, entry 3: *t*-BuONO (180 µL, 1.5 mmol) was added to a solution of BF_3•OEt_2 (166 µL, 1.35 mmol) in dry CH_2Cl_2 (4 mL) at 0 °C under a nitrogen atmosphere, upon which precipitation of colorless crystals occurred. The reaction mixture was warmed to room temperature and a solution of TEMPO **1** (156 mg, 1 mmol) in CH_2Cl_2 (0.5 mL) was added. The inhomogeneous reaction mixture was stirred for 3 h. The yellow precipitate that formed upon addition of Et_2O (10 mL) was filtered off, washed with cold Et_2O and dried in vacuum.

Table 1, entry 4: HBF_4 (130 µL, 48 wt. % in H_2O) was added to a solution of TEMPO **1** (156 mg, 1 mmol) in dry Et_2O (4 mL). *t*-BuONO (120 µL, 1 mmol) was added to the inhomogeneous reaction mixture at room temperature under a nitrogen atmosphere. The inhomogeneous reaction mixture was stirred for 1 h. The yellow precipitate was filtered off, washed with cold Et_2O and dried in vacuum.

Table 1, entry 5: *t*-BuONO (180 µL, 1.5 mmol) was added to a solution of $LiBF_4$ (1 mL, 1M in CH_3CN) in dry Et_2O (4 mL) at room temperature under a nitrogen atmosphere. A solution of TEMPO **1** (156 mg, 1 mmol) in Et_2O (0.5 mL) was added and the inhomogeneous mixture was stirred overnight. The reaction mixture was cooled to –20 °C, the yellow precipitate was filtered off and washed with cold Et_2O. The yellow precipitate was dissolved in CH_3CN (4 mL) and filtered through a paper filter. The solvent was evaporated, Et_2O (4 mL) was added and yellow precipitate was filtered off, washed with cold Et_2O and dried in vacuum.

For yields see Table 1. Yellow solid. m. p. 155 °C with decomposition. - $C_9H_{18}BF_4NO$: calc. C 44.47 H 7.46 N 5.76; found C 44.48 H 7.62 N 5.55.

6-(Triethylsilyloxy)hexan-1-ol 5l:

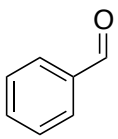


The analytical data were not previously given in the literature.[S1] Column chromatography (hexane/EtOAc 5:1) gave 827 mg (71%) of a colorless liquid. - R_f = 0.6, hexane/EtOAc 1:1. - IR: $\tilde{\nu}$ = 3600-3000, 2944, 2922, 2885, 1464, 1419, 1390, 1242, 1096, 1059, 1008, 799, 726, 672 cm^{-1}. - MS (+ESI) *m/z* (%): 255 ([M+Na^+], 100), 233 ([M+H^+], 3). - $C_{12}H_{28}O_2Si$: calc. C 62.01 H 12.14; found C 61.88 H 12.26. - ^{1}H NMR (400 MHz): δ = 0.53 (q, *J* = 7.9 Hz, 6H, $Si(CH_2CH_3)_3$), 0.89 (t, *J* = 7.9 Hz, 9H, $Si(CH_2CH_3)_3$), 1.20 (br s, 1H, CH_2OH), 1.26-1.35 (m, 4H, $SiOCH_2CH_2CH_2CH_2CH_2CH_2OH$), 1.45-1.55 (m, 4H, $SiOCH_2CH_2CH_2CH_2CH_2CH_2OH$), 3.54 (t, *J* = 6.7 Hz, 2H, $SiOCH_2CH_2$), 3.58 (br t, *J* = 6.0 Hz, 2H, CH_2CH_2OH). - ^{13}C NMR (100 MHz): δ = 4.6 (t, $Si(CH_2CH_3)_3$), 6.9 (q, $Si(CH_2CH_3)_3$), 25.7, 25.8 (t, $SiOCH_2CH_2CH_2CH_2CH_2CH_2OH$), 32.95, 33.00 (t, $SiOCH_2CH_2CH_2CH_2CH_2CH_2OH$), 63.0, 63.2 (t, $SiOCH_2CH_2CH_2CH_2CH_2CH_2OH$).

Oxidation of benzyl alcohol in the presence of TEMPO (Optimization procedure): BF_3•OEt_2 (for amounts see Table 2) and *t*-BuONO (476 µL, 4 mmol) were added subsequently to a solution of **5a** (2 mmol) in dry CH_2Cl_2 (10 mL) at room temperature under a nitrogen atmosphere. After heating to reflux a solution of **1** (for amounts see Table 2) in CH_2Cl_2 (0.2 mL) was added. After stirring for the appropriate time (see Table 2) at reflux the pale yellow reaction mixture was diluted with diethyl ether (10 mL). The yellow precipitate of **4** that formed, was removed by filtration through a plug of silica gel. The solvent was evaporated and the resulting pale orange mixture was purified by column chromatography to give benzaldehyde **6a** (for yields see Table 2).

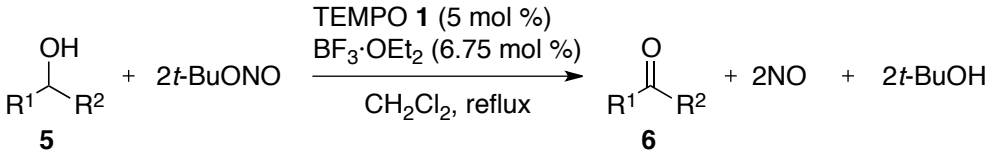
Note: The formation of NO was proven upon exposure to air, because red vapors of NO_2 formed.

Benzaldehyde 6a:



Purification by column chromatography (pentane/Et_2O 20:1) as a colorless liquid. For yields see Table 2. The NMR data corresponded to those reported in the literature.[S5]

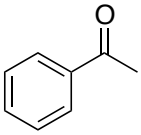
Oxidation of benzyl alcohol in the absence of TEMPO: BF_3•OEt_2 (17 µL, 0.135 mmol) and *t*-BuONO (476 µL, 4 mmol) were added subsequently to a solution of **5a** (2 mmol) in dry CH_2Cl_2 (10 mL) at room temperature under a nitrogen atmosphere. After heating to reflux for 5.5 h the solvent was evaporated and the resulting yellow mixture was purified by column chromatography (pentane/Et_2O 20:1) to give 156 mg (73%) of benzaldehyde **6a**. The mechanism of this oxidation is different from the TEMPO-catalyzed oxidation, since the nitrosonium ion acts as direct oxidant as reported in the literature[S6] and no formation of NO_2 was observed upon exposure to air.



Oxidation of aromatic and allylic alcohols (General procedure): BF_3•OEt_2 (17 µL, 0.135 mmol) and *t*-BuONO (715 µL, 6 mmol) were added subsequently to a solution of **5** (2 mmol) in dry CH_2Cl_2 (10 mL) at room temperature under a nitrogen atmosphere. After heating to reflux a solution of **1** (16 mg, 0.1 mmol) in CH_2Cl_2 (0.2 mL) was added. After stirring for the appropriate time (see Scheme 1) at reflux the pale yellow reaction mixture was diluted with diethyl ether (10 mL). The yellow precipitate of **4** that formed was removed by filtration through a plug of silica gel. The solvent was evaporated and the resulting pale orange mixture was purified by column chromatography.

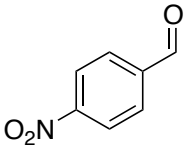
Note: Deviations from the standard procedure are described at the individual compounds.

Acetophenone 6b:



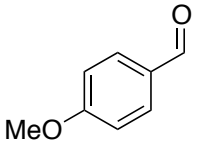
Column chromatography (pentane/Et_2O 20:1) gave 193 mg (80%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S7]

***p*-Nitrobenzaldehyde 6c:**



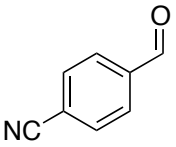
Column chromatography (pentane/Et_2O 5:1) gave 264 mg (87%) of colorless crystals. m. p. 106-107 °C; (lit.: 106-107 °C).[S8] The NMR data corresponded to those reported in the literature.[S9]

***p*-Methoxybenzaldehyde 6d:**



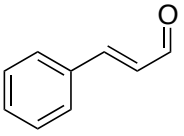
Column chromatography (pentane/Et_2O 5:1) gave 275 mg (99%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S10]

***p*-Cyanobenzaldehyde 6e:**



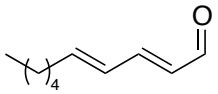
Column chromatography (pentane/Et_2O 2:1) gave 222 mg (87%) of colorless crystals. m. p. 100-101 °C; (lit.: 99-100 °C).[S11] The NMR data corresponded to those reported in the literature.[S12]

***trans*-Cinnamaldehyde 6f:**



Prepared from cinnamyl alcohol **5f** (402 mg, 3 mmol). Column chromatography (pentane/Et_2O 5:1) gave 350 mg (88%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S13]

***trans,trans*-Deca-2,4-dienal 6g:**



$LiBF_4$ was used instead of BF_3•OEt_2 and the order of addition of the reaction components was changed as follows. *t*-BuONO (360 µL, 3 mmol) and a solution of **1** (8 mg, 0.05 mmol) in CH_2Cl_2 (0.2 mL) were added subsequently to a solution of $LiBF_4$ (50 µL, 5 mol %, 1M in CH_3CN) in dry CH_2Cl_2 (5 mL) at room temperature under a nitrogen atmosphere. After heating to reflux, **5g** (154 mg, 1 mmol) was added as the last component to the reaction mixture. After stirring at reflux for 3 h the reaction mixture was diluted with diethyl ether (5 mL) and the precipitate of **4** was removed by filtration through a plug of silica gel. The solvent was evaporated and the resulting mixture was purified by column chromatography (pentane/Et_2O 10:1) to give 92 mg (60%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S14]

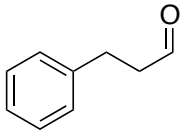
Oxidation of aliphatic alcohols (General procedure): BF_3•OEt_2 (12 µL, 0.1 mmol) and *t*-BuONO (715 µL, 6 mmol) were added subsequently to a solution of **5** (2 mmol) in dry CH_2Cl_2 (10 mL) at room temperature under a nitrogen atmosphere. After heating to reflux a solution of **1** (16 mg, 0.1 mmol) in CH_2Cl_2 (0.2 mL) was added. After 1 h another portion of **1** (16 mg, 0.1 mmol) in CH_2Cl_2 (0.2 mL) was added. After stirring for the appropriate time (see Scheme 3) at reflux the pale yellow reaction mixture was diluted with diethyl ether (10 mL). The yellow precipitate of **4** that formed, was removed by filtration through a plug of silica gel. The solvent was evaporated and the resulting pale orange mixture was purified by column chromatography.

Note: Deviations from the standard procedure are described at the individual compounds.

Dodecanal 6h:

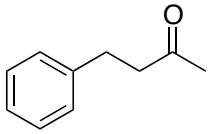
Prepared from dodecanol **5h** (186 mg, 1 mmol). Column chromatography (pentane/Et_2O 40:1 gradient to 20:1) gave 154 mg (83%) of a colorless wax. The NMR data corresponded to those reported in the literature.[S15]

3-Phenylpropanal 6i:



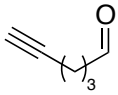
Column chromatography (pentane/Et_2O 20:1 gradient to 10:1) gave 234 mg (87%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S16]

4-Phenylbutan-2-one 6j:



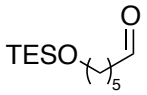
Column chromatography (pentane/Et_2O 20:1 gradient to 10:1) gave 263 mg (88%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S17]

Hex-5-ynal 6k:



Column chromatography (pentane/Et_2O 10:1) gave 133 mg (69%) of a pale orange liquid. The NMR data corresponded to those reported in the literature.[S18]

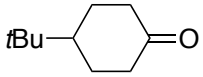
6-(Triethylsilyloxy)hexanal 6l:



$LiBF_4$ was used instead of BF_3•OEt_2 and the order of addition of the reaction components was changed as follows. *t*-BuONO (360 µL, 3 mmol) and a solution of **1** (8 mg, 0.05 mmol) in dry CH_2Cl_2 (0.2 mL) were added subsequently to a solution of $LiBF_4$ (50 µL, 5 mol %, 1M in CH_3CN) in CH_2Cl_2 (5 mL) at room temperature under a nitrogen atmosphere. After heating to reflux, **5l** (232 mg, 1 mmol) was added as the last component to the reaction mixture. After 1 h another portion of **1** (8 mg, 0.05 mmol) in CH_2Cl_2 (0.2 mL) was added. After stirring for 8 h at reflux the reaction mixture was diluted with diethyl ether (5 mL) and the formed precipitate of **4** was removed by filtration through a plug of silica gel. The solvent was evaporated and the resulting mixture was purified by column chromatography (pentane/Et_2O 10:1) to give 168 mg (73%) of a pale orange liquid. - R_f = 0.55, hexane/EtOAc

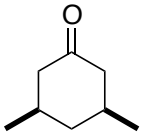
5:1. - IR: $\tilde{\nu}$ = 2946, 2921, 2885, 2823, 2724, 1732, 1463, 1418, 1393, 1243, 1095, 1008, 727, 672 cm^{-1}. - MS (+ESI) *m/z* (%): 483 ([2M+Na^+], 10), 269 ([M+K^+], 11), 253 ([M+Na^+], 100), 231 ([M+H^+], 9). - $C_{12}H_{26}O_2Si$ (230.42): calc. C 62.55 H 11.37; found C 62.57 H 11.18. - HRMS (+ESI) *m/z* [$C_{12}H_{26}O_2SiNa^+$]: calc. 253.1594; found 253.1595. - ^{1}H NMR (400 MHz): δ = 0.53 (q, *J* = 7.9 Hz, 6H, Si(C*H*$_2$CH$_3$)$_3$), 0.89 (t, *J* = 7.9 Hz, 9H, Si(CH$_2$C*H*$_3$)$_3$), 1.32 (m, 2H, OCH$_2$CH$_2$C*H*$_2$), 1.48 (m, 2H, OCH$_2$C*H*$_2$CH$_2$), 1.59 (quint, *J* = 7.4 Hz, 2H, C*H*$_2$CH$_2$CHO), 2.37 (dt, *J* = 7.4, 1.8 Hz, 2H, CH$_2$C*H*$_2$CHO), 3.54 (t, *J* = 6.5 Hz, OC*H*$_2$CH$_2$CH$_2$), 9.71 (t, *J* = 1.8 Hz, CH$_2$CH$_2$C*H*O). - ^{13}C NMR (100 MHz): δ = 4.4 (t, Si(*C*H$_2$CH$_3$)$_3$), 6.8 (q, Si(CH$_2$*C*H$_3$)$_3$), 22.0 (t, OCH$_2$*C*H$_2$CH$_2$), 25.5 (t, OCH$_2$CH$_2$*C*H$_2$), 32.6 (t, *C*H$_2$CH$_2$CHO), 43.9 (t, CH$_2$*C*H$_2$CHO), 62.6 (t, O*C*H$_2$CH$_2$CH$_2$), 202.7 (d, CH$_2$CH$_2$*C*HO).

4-(*tert*-Butyl)cyclohexanone 6m:



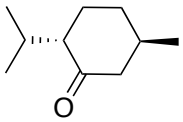
Evaporation of the crude reaction mixture gave 311 mg (99%) of a colorless solid material. m. p. 47-48 °C; (lit.: 47-49 °C).[S19] The NMR data corresponded to those reported in the literature.[S20]

3,5-Dimethylcyclohexanone 6n:



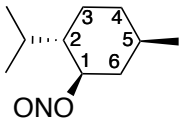
Column chromatography (pentane/Et_2O 10:1) gave 190 mg (75%) of a pale orange liquid. The NMR data corresponded to those reported in the literature.[S21]

L-Menthone 6o:



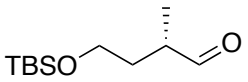
Prepared from menthol **5o** (156 mg, 1 mmol) and AZADO **2** (8 + 8 mg, 5 + 5 mol %, 0.1 mmol) instead of TEMPO **1**. Column chromatography (pentane/Et_2O 10:1) gave 147 mg (95%) of a colorless liquid. The NMR data corresponded to those reported in the literature.[S22]

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl nitrite 7o:



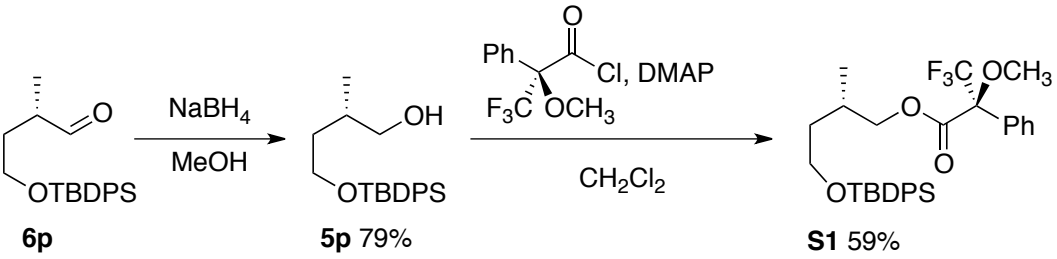
Column chromatography (pentane) gave 302 mg (81%) of a colorless liquid. - R_f = 0.85, hexane/EtOAc 5:1. - IR: $\tilde{\nu}$ = 2966, 2936, 2881, 1642, 1461, 1376, 1024, 932, 883, 798, 762, 675 cm^{-1}. - MS (+CI) *m/z* (%): 155 ($[M–NO]^+$, 18), 139 ($[M–HONO+H^+]$, 100). - $C_{10}H_{19}NO_2$ (185.26): calc. C 64.83 H 10.34 N 7.56; found C 65.06 H 10.34 N 7.34. - $[\alpha]_D^{20}$ = –37.7 (*c* = 0.411, CH_3OH). - ^1H NMR (400 MHz): δ = 0.77 (d, *J* = 7.0 Hz, 3H, $CH(CH_3)_2$), 0.90 (d, *J* = 7.0 Hz, 3H, $CH(CH_3)_2$), 0.92 (m, 1H, eq.-H4), 0.96 (d, *J* = 6.5 Hz, 3H, $CHCH_3$), 1.19 (m, 1H, eq.-H3), 1.23 (m, 1H, eq.-H6), 1.48 (m, 1H, ax.-H2), 1.61 (m, 1H, ax.-H5), 1.75 (m, 1H, ax.-H4), 1.79 (m, 1H, ax.-H3), 1.81 (m, 1H, $CH(CH_3)_2$), 2.03 (m, 1H, ax.-H6), 5.26 (dt, *J* = 11.2, 4.5 Hz, ax.-H1). - ^{13}C NMR (100 MHz): δ = 15.9 (q, $CH(CH_3)_2$), 20.8 (q, $CH(CH_3)_2$), 22.2 (q, $CHCH_3$), 23.7 (t, C3), 26.0 (d, $CH(CH_3)_2$), 31.9 (d, C5), 34.3 (t, C4), 42.2 (t, C6), 46.8 (d, C2), 80.1 (d, C1).

(*S*)-4-(*tert*-Butyldiphenylsilyloxy)-2-methylbutanal 6p:



Prepared from (*S*)-4-(*tert*-butyldiphenylsilyloxy)-2-methylbutanol **5p** (82 mg, 0.24 mmol). Evaporation of the crude reaction mixture gave 80 mg (98%) of a colorless oil. The NMR data corresponded to those reported in the literature.[S23] - $[\alpha]_D^{20}$ = +10.1 (*c* = 1.000, $CHCl_3$); (lit.: $[\alpha]_D^{28}$ = +8.9 (*c* = 1.000, $CHCl_3$)[S23]).

Apart from comparison of the optical rotation values, the integrity of the stereogenic center was confirmed by subsequent reduction[S24] and transformation to Mosher ester **S1** (Scheme S1).

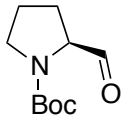


Scheme S1. Transformation of **6p** to Mosher ester **S1**.

Reduction of 6p: $NaBH_4$ (10 mg, 0.277 mmol) was added to a stirred solution of **6p** (59 mg, 0.173 mmol) in methanol (1.5 mL). The reaction mixture was stirred at room temperature for 15 min, diluted with ethyl acetate (10 mL) and washed with water (3 × 10 mL). The aqueous layer was washed with ethyl acetate (2 × 10 mL) and the combined organic fractions were dried over anhydrous $MgSO_4$. The solvent was evaporated, the inhomogeneous residue was preadsorbed on silica gel and purified by column chromatography (hexane/EtOAc 5:1) to give 47 mg (79%) of **5p** as a colorless oil. The NMR data corresponded to those reported in the literature.[S24] Reduced **5p**: $[\alpha]_D^{20} = -6.4$ (c = 1.000, $CHCl_3$); starting **5p**: $[\alpha]_D^{20} = -6.5$ (c = 1.013, $CHCl_3$); (lit.: $[\alpha]_D^{20} = -7.1$ (c = 1.000, $CHCl_3$)[S24]).

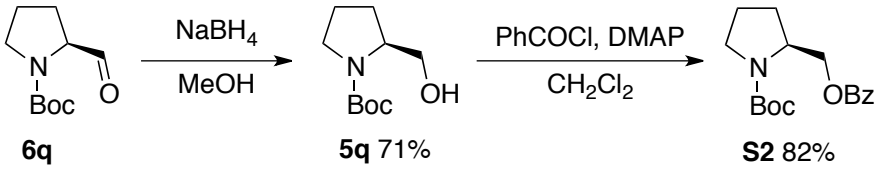
Mosher ester S1: DMF (8 µL) and oxalyl chloride (100 µL, 1 mmol) were added subsequently to a stirred solution of Mosher's acid (*S*)-(–)-MTPA (24 mg, 0.1 mmol) in hexane (5 mL). The reaction mixture was stirred at room temperature for 2 h, during which a white precipitate formed. The reaction mixture was filtered through glass wool and the solvent was removed under high vacuum. The crude acid chloride was dissolved in CH_2Cl_2 (1 mL), DMAP (24 mg, 0.2 mmol) was added, followed by **5p** (19 mg, 0.055 mmol) in CH_2Cl_2 (1 mL) obtained above. The reaction mixture was stirred at room temperature overnight, quenched with saturated NH_4Cl solution (5 mL), diluted with diethyl ether (40 mL), washed with saturated $NaHCO_3$ solution (5 × 5 mL) and brine (5 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to give 25 mg of a mixture of **S1** (59%) and recovered **5p** (37%). The comparison of NMR data of **S1** with those reported in the literature revealed a negligible amount of epimerization.[S25]

(*S*)-*N*-(*tert*-Butyloxycarbonyl)prolinal 6q:



Prepared from (*S*)-*N*-(*tert*-butyloxycarbonyl)prolinol **5q** (101 mg, 0.5 mmol). Column chromatography (hexane/EtOAc 5:1) gave 40 mg (40%) of a colorless oil. The use of $LiBF_4$ instead of $BF_3 \bullet OEt_2$ did not lead to an improvement, **6q** was isolated in 42% yield. The NMR data corresponded to those reported in the literature.[S26] - $[\alpha]_D^{20} = -84.7$ (c = 0.660, $CHCl_3$); (lit.: $[\alpha]_D^{25} = -99.5$ (c = 0.660, $CHCl_3$)[S27]).

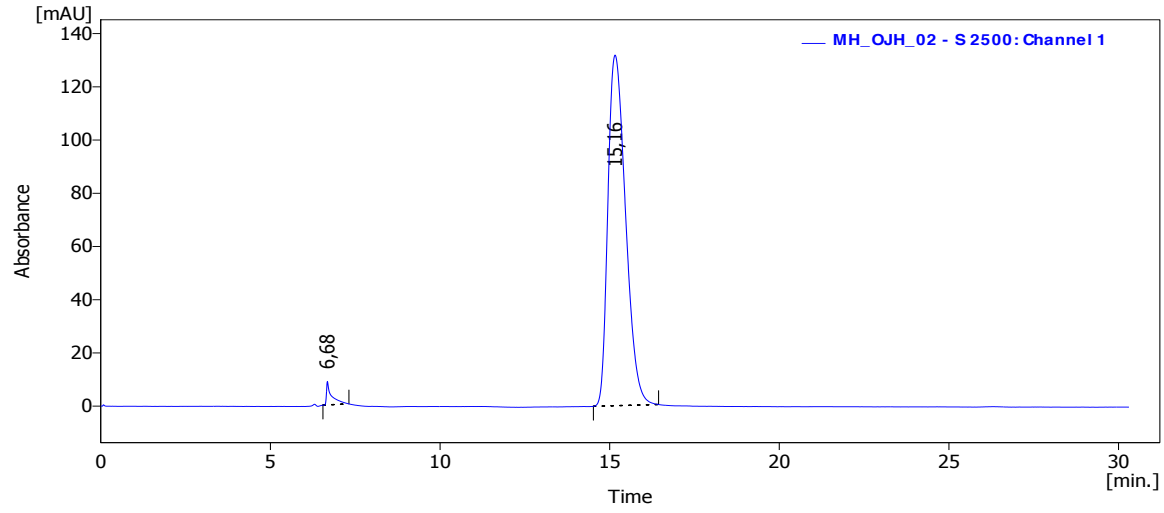
Apart from comparison of the optical rotation values, the integrity of the stereogenic center was confirmed by subsequent reduction and transformation to benzoate **S2** (Scheme S2).



Scheme S2. Transformation of **6q** to benzoate **S2**.

Reduction of 6q: The procedure for reduction of **6q** was identical to that used for reduction of **6p**. Column chromatography (hexane/EtOAc 2:1) gave 30 mg (71%) of **5q** as a colorless oil. The NMR data corresponded to those reported in the literature.[S28] Reduced **5q**: $[\alpha]_D^{20} = -45.9$ (c = 1.019, CH_3OH); starting **5q**: $[\alpha]_D^{20} = -53.4$ (c = 1.000, CH_3OH); (lit.: $[\alpha]_D^{25} = -45.7$ (c = 1.000 g/100 ml, CH_3OH)[S28b]).

Benzoate S2: DMAP (24 mg, 0.2 mmol) and a solution of **5q** (8 mg, 0.04 mmol) in CH_2Cl_2 (1 mL) obtained above were added subsequently to a stirred solution of benzoyl chloride (12 µL, 0.1 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred at room temperature overnight, quenched with saturated NH_4Cl solution (5 mL), diluted with diethyl ether (40 mL), washed with saturated $NaHCO_3$ solution (5 × 5 mL) and brine (5 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated, the inhomogeneous residue was preadsorbed on silica gel and purified by column chromatography (pentane/Et_2O 5:1) to give 10 mg (82%) of **S2** as a colorless oil. The NMR data corresponded to those reported in the literature.[S29] The HPLC trace (Chiralcel OJ-H, heptane/*i*PrOH 39:1, 0.5 mL/min, 254 nm) showed only one peak at 15.2 min corresponding to (*S*)-*tert*-butyl 2-(benzoyloxymethyl)pyrrolidine-1-carboxylate **S2**. Previously reported conditions (Chiralcel OJ, hexane/*i*PrOH 39:1, 0.5 mL/min) gave retention times of 15.4 min for the (*S*)-enantiomer of **S2** and 17.0 min for the (*R*)-enantiomer of **S2**.[S29]

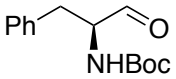


Result Table (Uncal - MH_OJH_02 - S 2500: Channel 1)

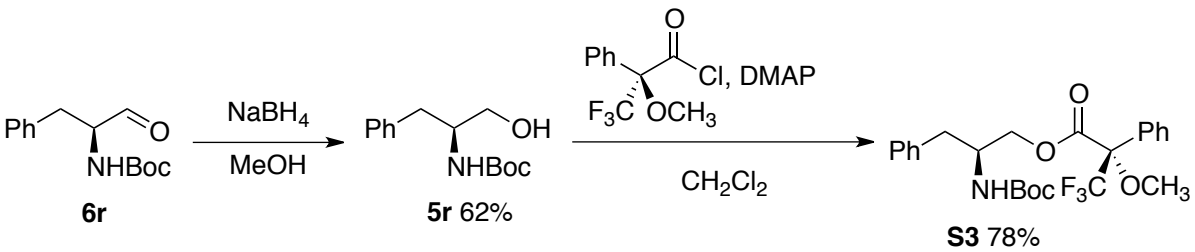
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]
1	6,680	94,65	8,771	1,9	6,2	0,11
2	15,160	4766,12	131,772	98,1	93,8	0,57
	Total	4860,77	140,543	100,0	100,0	

Figure S1. HPLC trace of (*S*)-*tert*-butyl 2-(benzoyloxymethyl)pyrrolidine-1-carboxylate **S2**.

(*S*)-*N*-(*tert*-Butyloxycarbonyl)phenylalaninal 6r:



Column chromatography (hexane/EtOAc 2:1 gradient to 1:1) gave 137 mg (27%) of **6r** as a colorless oil accompanied by 79 mg (14%) of (*S*)-*N*-(*tert*-butyloxycarbonyl)-*N*-nitrosophenylalaninal **7r** as a yellow oil. The NMR data corresponded to those reported in the literature.[S30] The integrity of the stereogenic center was confirmed by subsequent reduction and transformation to Mosher ester **S3** (Scheme S3). CAUTION: *N*-Nitrosamines such as **7r** are potentially carcinogenic and proper care must be taken, when working with them.



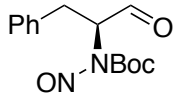
Scheme S3. Transformation of **6r** to Mosher ester **S3**.

Reduction of 6r: The procedure for reduction of **6r** was identical to that used for reduction of **6p**. Column chromatography (hexane/EtOAc 2:1) gave 78 mg (62%) of **5r** as a colorless

solid. m. p. 90-92 °C; (lit.: 91-92 °C).[S31] The NMR data corresponded to those reported in the literature.[S32] Reduced **5r**: $[\alpha]_D^{20} = -18.1$ (c = 1.000, $CHCl_3$); starting **5r**: $[\alpha]_D^{20} = -33.4$ (c = 0.996, $CHCl_3$); (lit.: $[\alpha]_D^{20} = -22.0$ (c = 1.000, $CHCl_3$)[S32]).

Mosher ester S3: DMF (8 µL) and oxalyl chloride (100 µL, 1 mmol) were added subsequently to a stirred solution of Mosher's acid (*S*)-(–)-MTPA (24 mg, 0.1 mmol) in hexane (5 mL). The reaction mixture was stirred at room temperature for 2 h, during which a white precipitate formed. The reaction mixture was filtered through glass wool and the solvent was removed under high vacuum. The crude acid chloride was dissolved in CH_2Cl_2 (1 mL), DMAP (24 mg, 0.2 mmol) was added, followed by **5r** (23 mg, 0.09 mmol) in CH_2Cl_2 (1 mL) obtained above. The reaction mixture was stirred at room temperature overnight, quenched with saturated NH_4Cl solution (5 mL), diluted with diethyl ether (40 mL), washed with saturated $NaHCO_3$ solution (5 × 5 mL) and brine (5 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to give 38 mg of a mixture of **S3** (78%) and recovered **5r** (21%). The comparison of NMR data of **S3** with those reported in the literature revealed a negligible amount of epimerization.[S33]

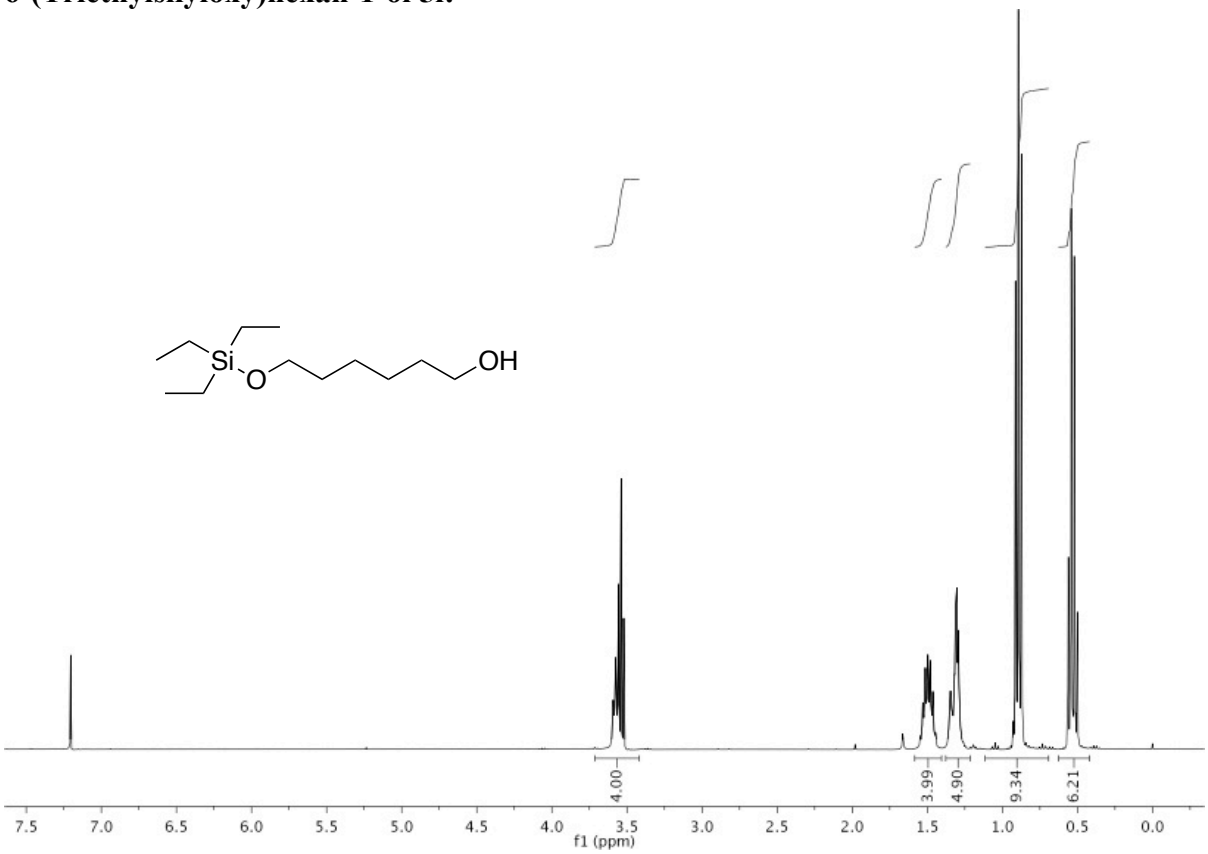
(*S*)-*N*-(*tert*-Butyloxycarbonyl)-*N*-nitrosophenylalaninal 7r:

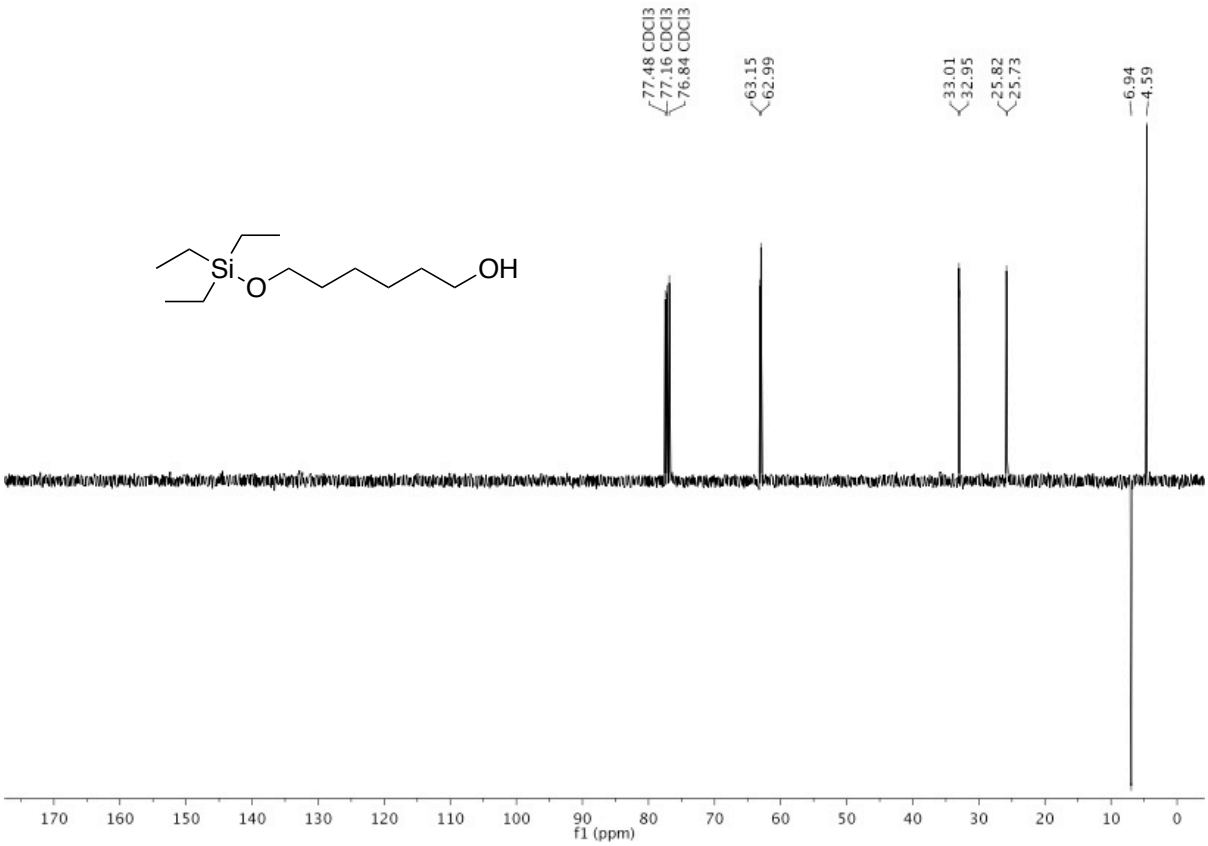


Prepared from **5r** (125 mg, 0.5 mmol) and *t*-BuONO (600 µL, 5 mmol) under reflux for 24 h. Column chromatography (hexane/EtOAc 10:1 gradient to 5:1) gave 66 mg (47%) of **7r** as a yellow oil accompanied by 18 mg (14%) of **6r** as a colorless oil. CAUTION: *N*-Nitrosamines are potentially carcinogenic and proper care must be taken, when working with them. - R_f = 0.65, hexane/EtOAc 2:1. - IR: $\tilde{\nu}$ = 2991, 2944, 2832, 2725, 1746, 1604, 1528, 1502, 1461, 1373, 1297, 1258, 1144, 1090, 1051, 967, 843, 767, 734, 702 cm^{-1}. - $C_{14}H_{18}N_2O_4$ (278.30): calc. C 60.42 H 6.52 N 10.07; found C 60.40 H 6.59 N 9.92. - $[\alpha]_D^{20} = -44.3$ (c = 0.467, CH_3OH). - ^{1}H NMR (400 MHz): δ = 1.48 (s, 9H, C(C*H*$_3$)$_3$), 2.36 (dd, J = 14.2, 5.5 Hz, 1H, C*H*$_2$Ph), 2.87 (dd, J = 14.2, 9.7 Hz, 1H, C*H*$_2$Ph), 5.10 (dd, J = 9.7, 5.5 Hz, 1H, C*H*CHO), 7.00 (m, 2H, *o*-Ph), 7.20 (m, 3H, Ph), 9.27 (s, 1H, C*H*O). - ^{13}C NMR (100 MHz): δ = 28.0 (q, C(*C*H$_3$)$_3$), 32.5 (t, *C*H$_2$Ph), 61.3 (d, *C*HCHO), 86.7 (s, *C*(CH$_3$)$_3$), 127.2 (d, *p*-Ph), 128.8 (d, Ph), 129.2 (d, Ph), 135.8 (s, *ipso*-Ph), 151.3 (s, *C*ON), 193.8 (d, *C*HO). Mass spectra could not be obtained under any conditions.

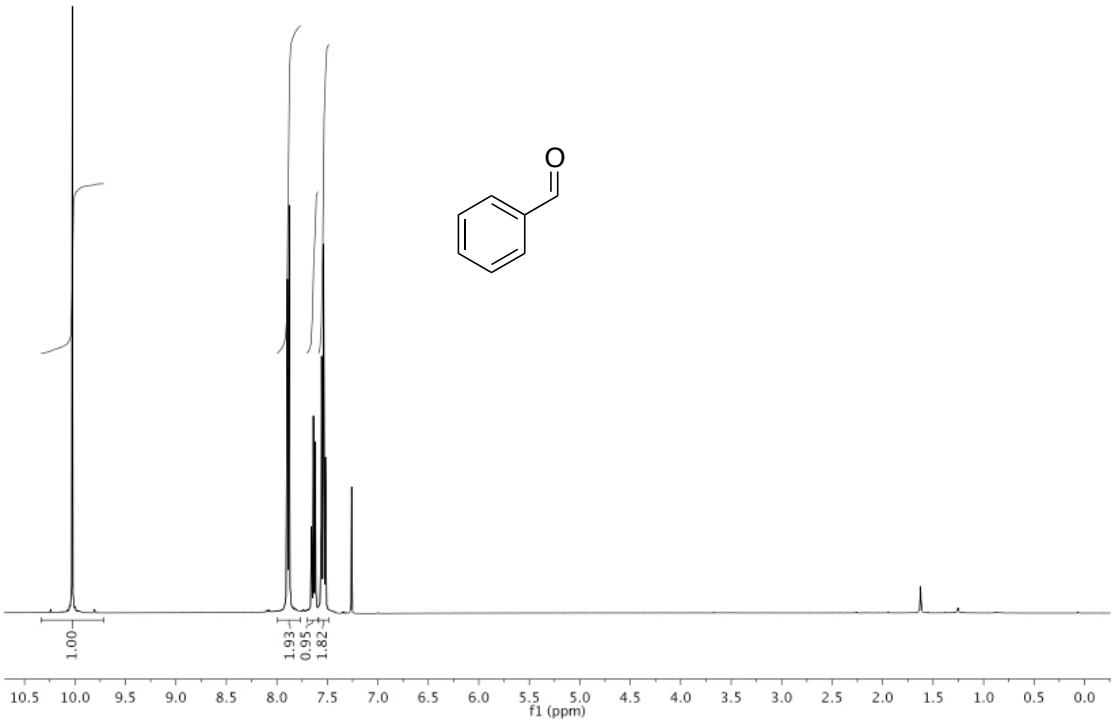
Copies of ^{1}H, ^{19}F and ^{13}C NMR spectra

6-(Triethylsilyloxy)hexan-1-ol 5l:

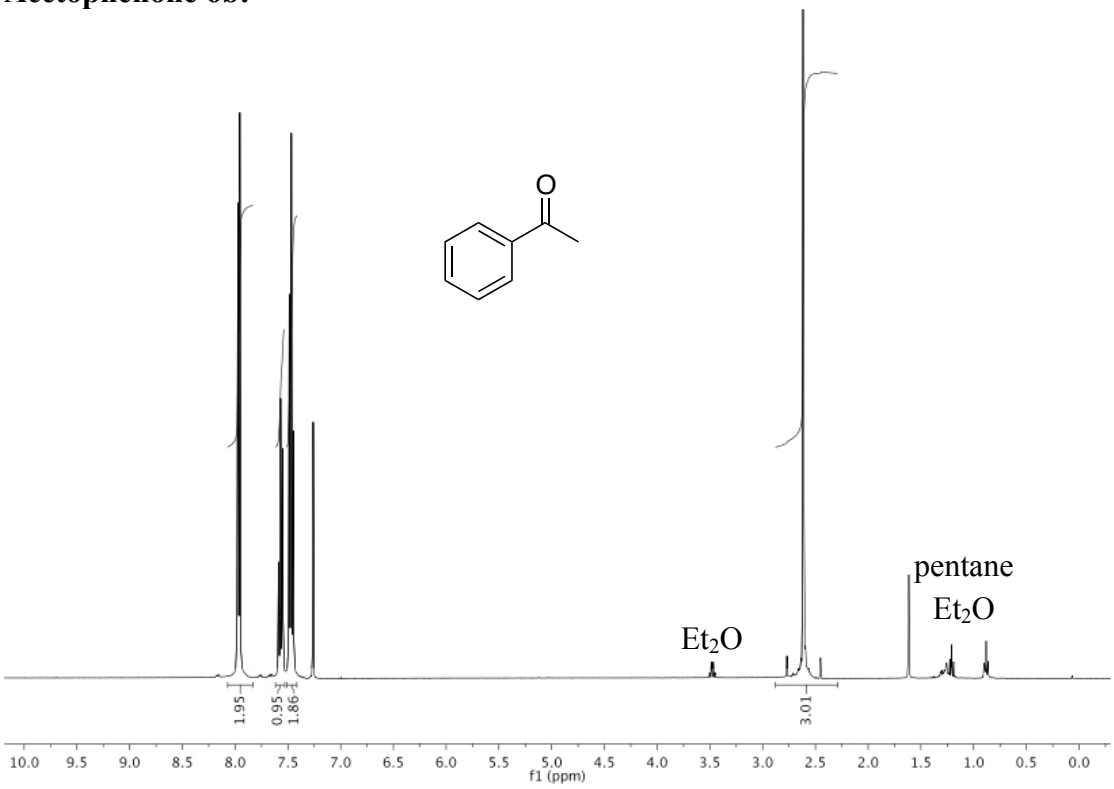




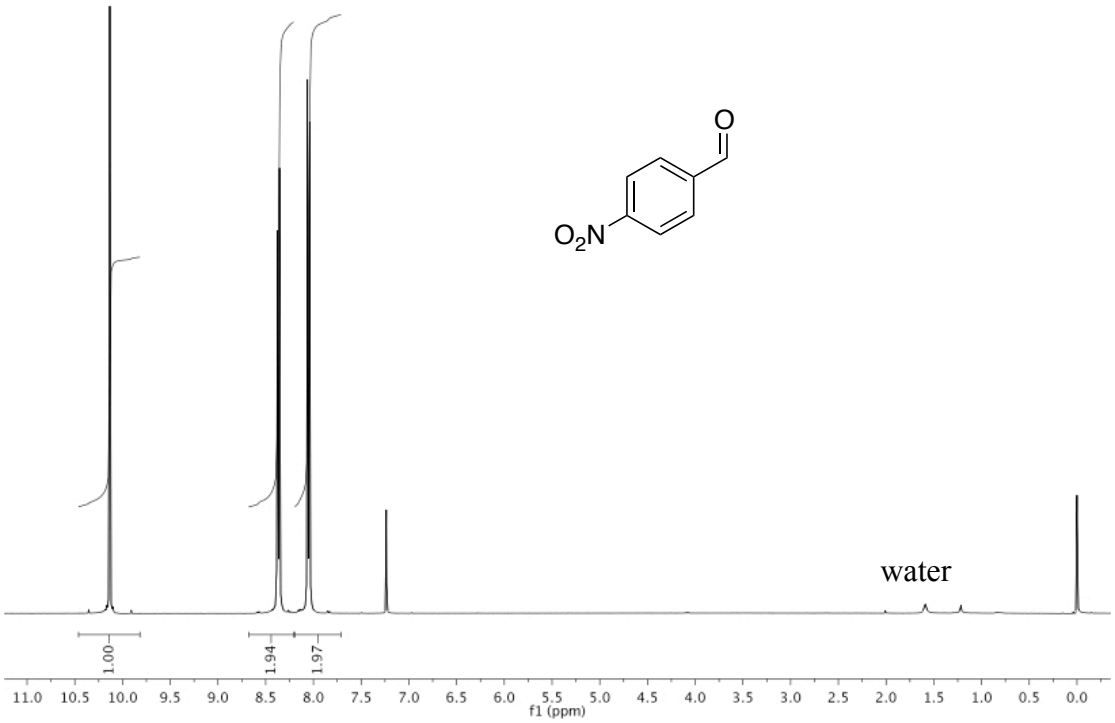
Benzaldehyde 6a:

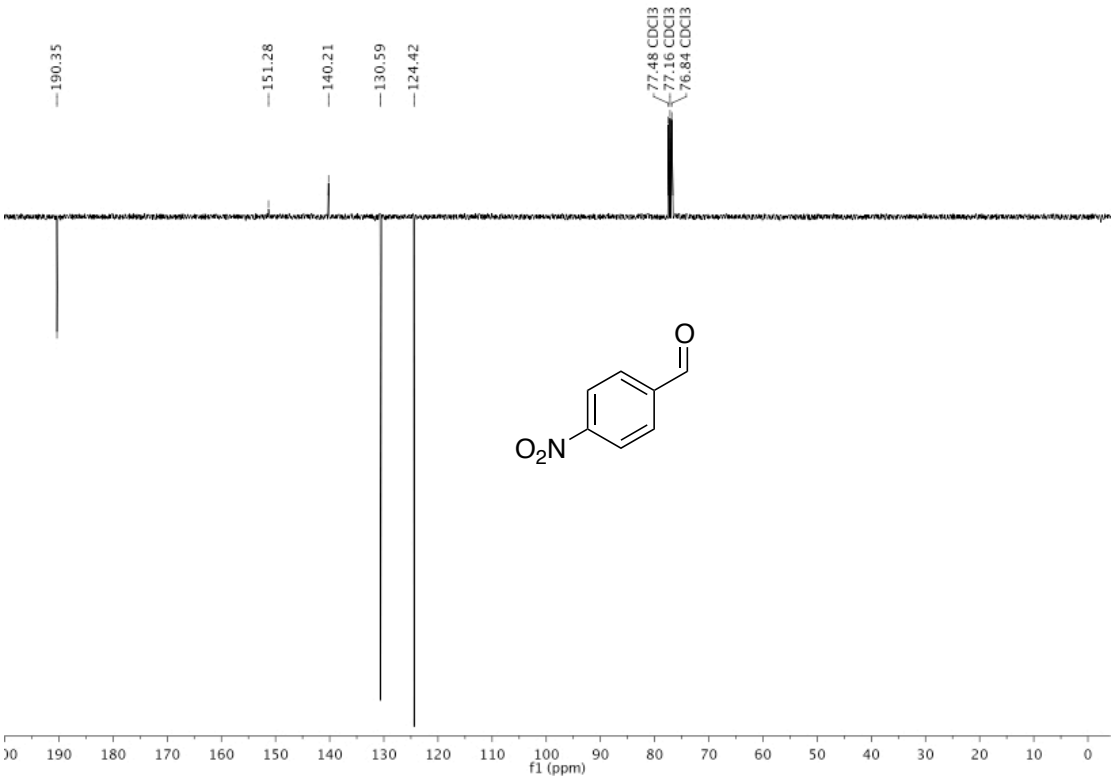


Acetophenone 6b:



***p*-Nitrobenzaldehyde 6c:**





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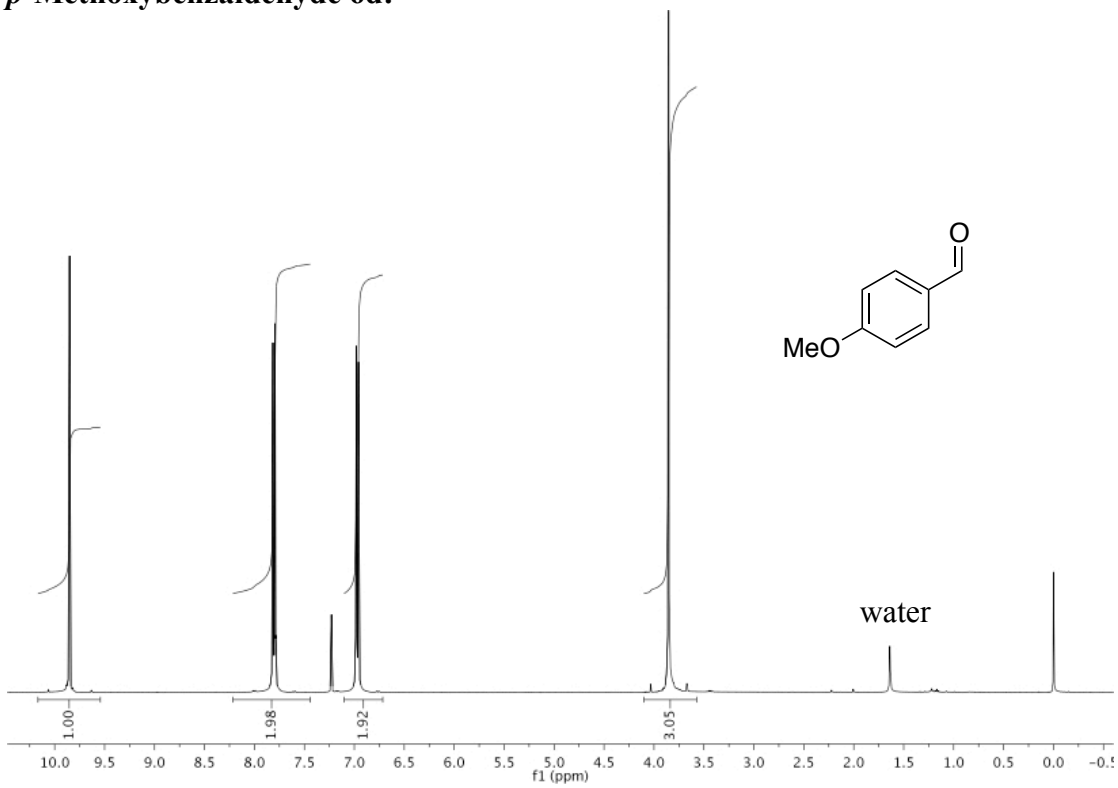

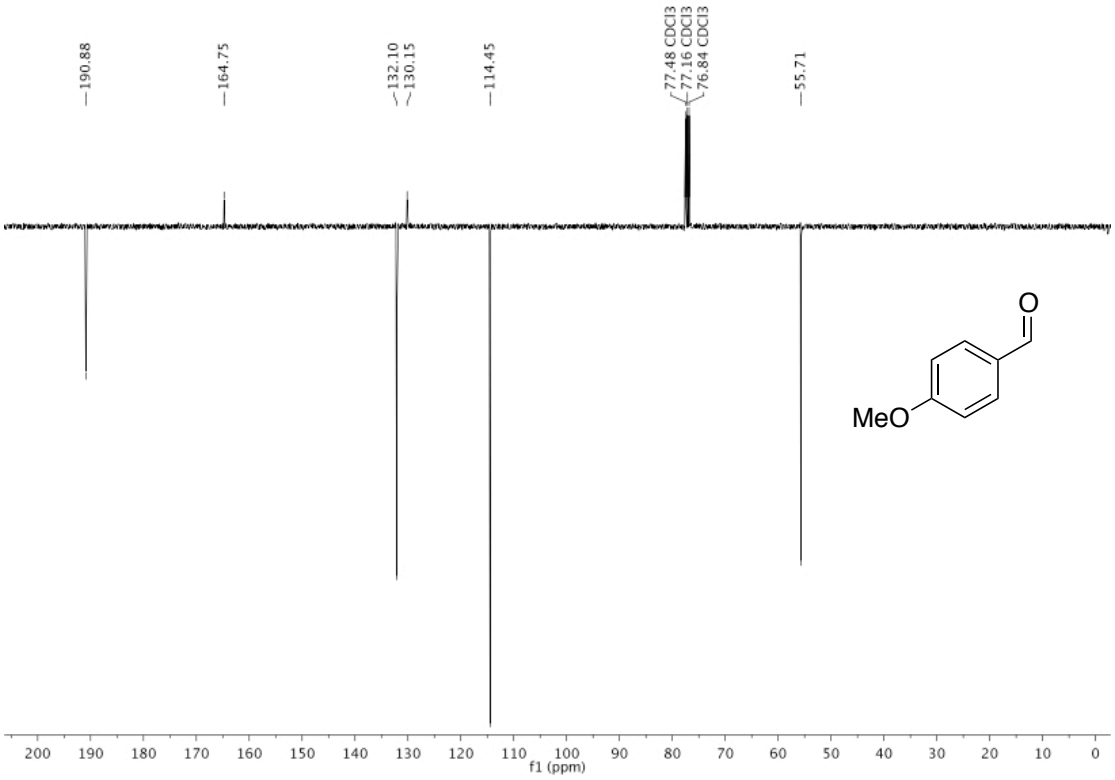

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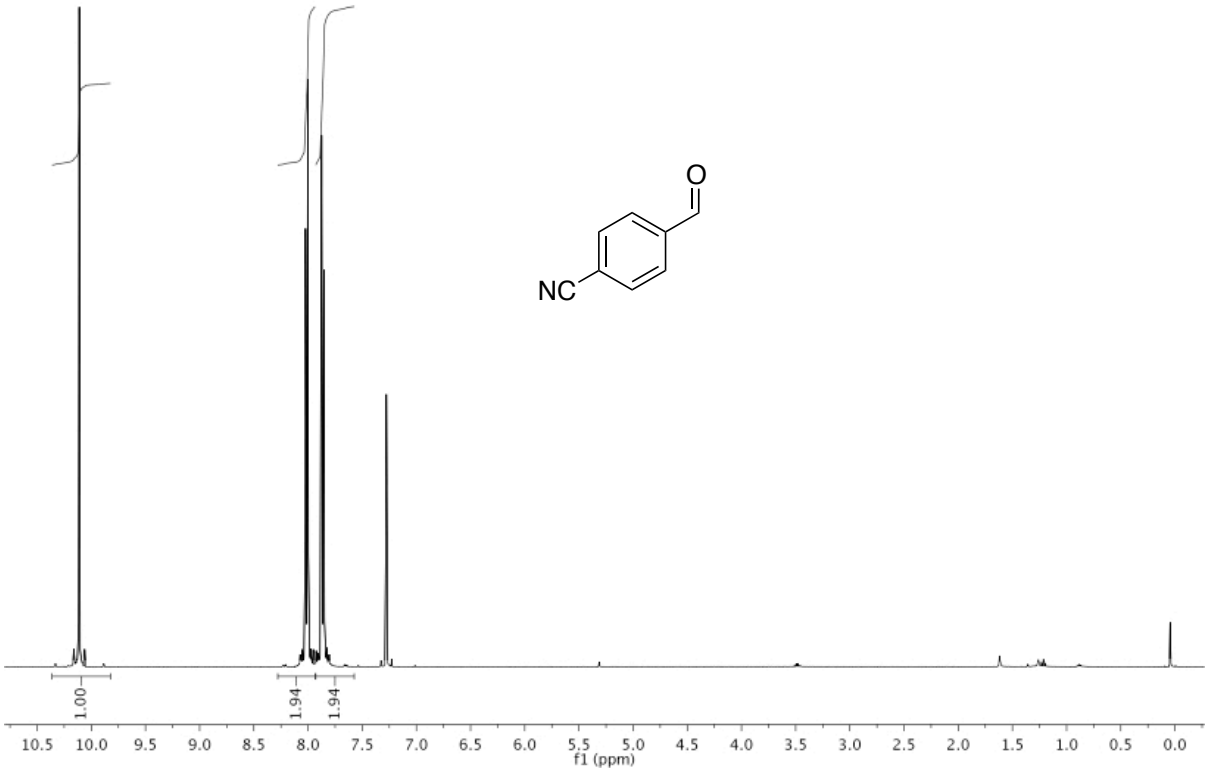
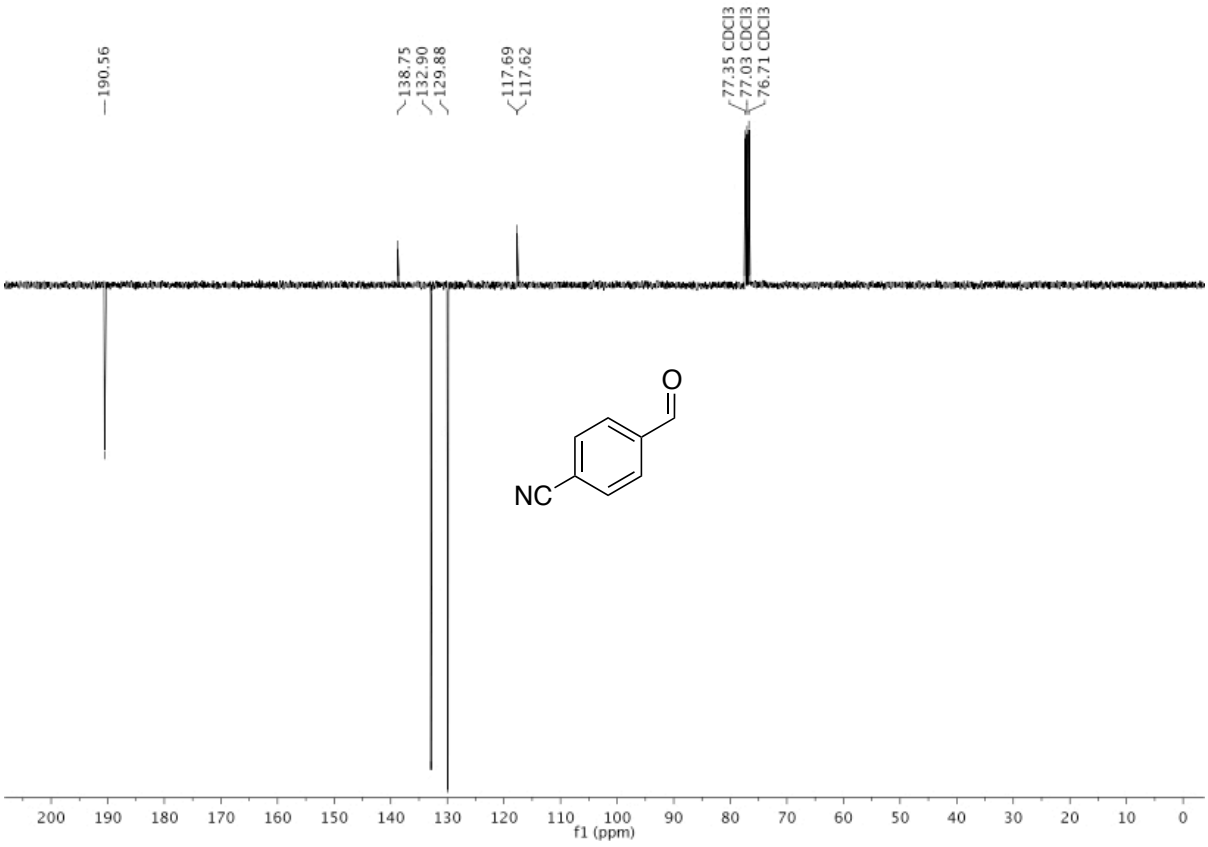
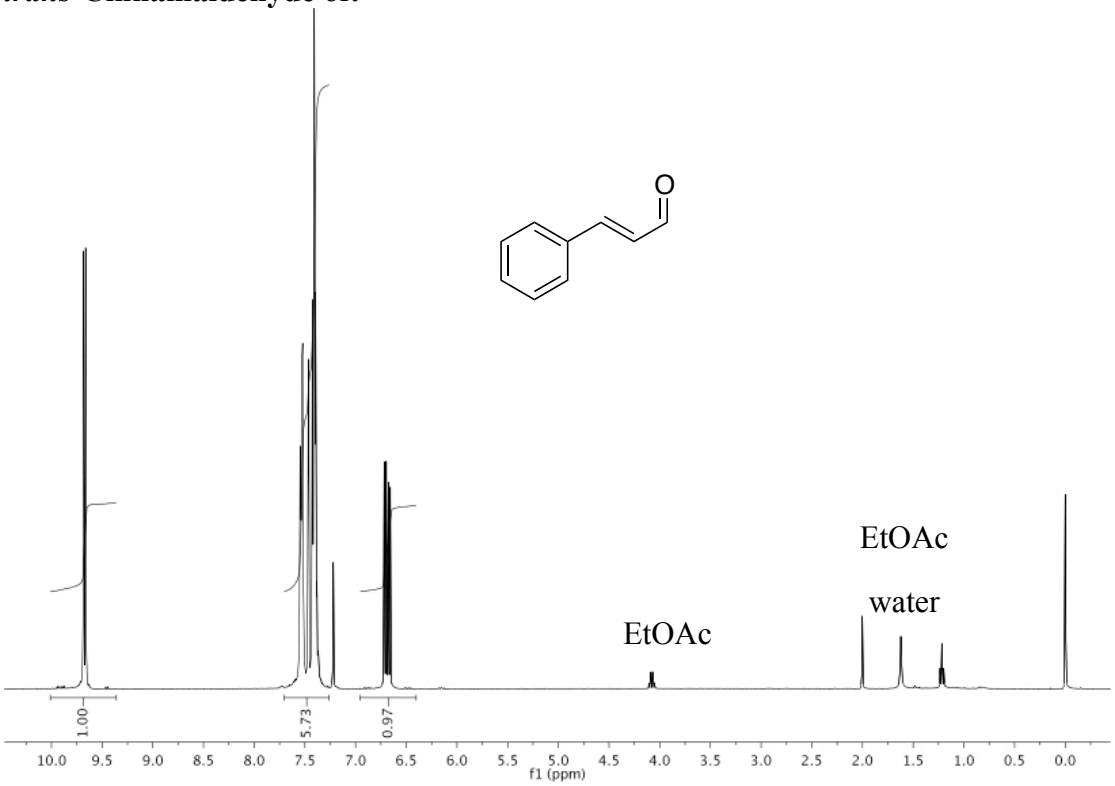
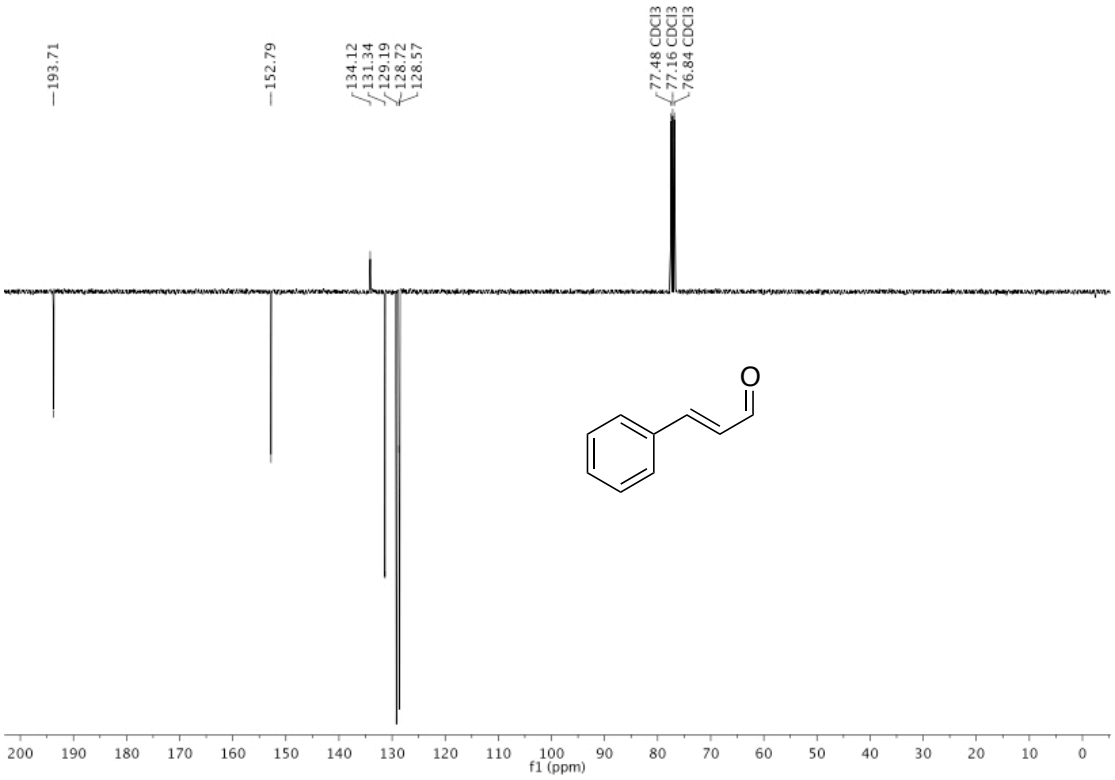


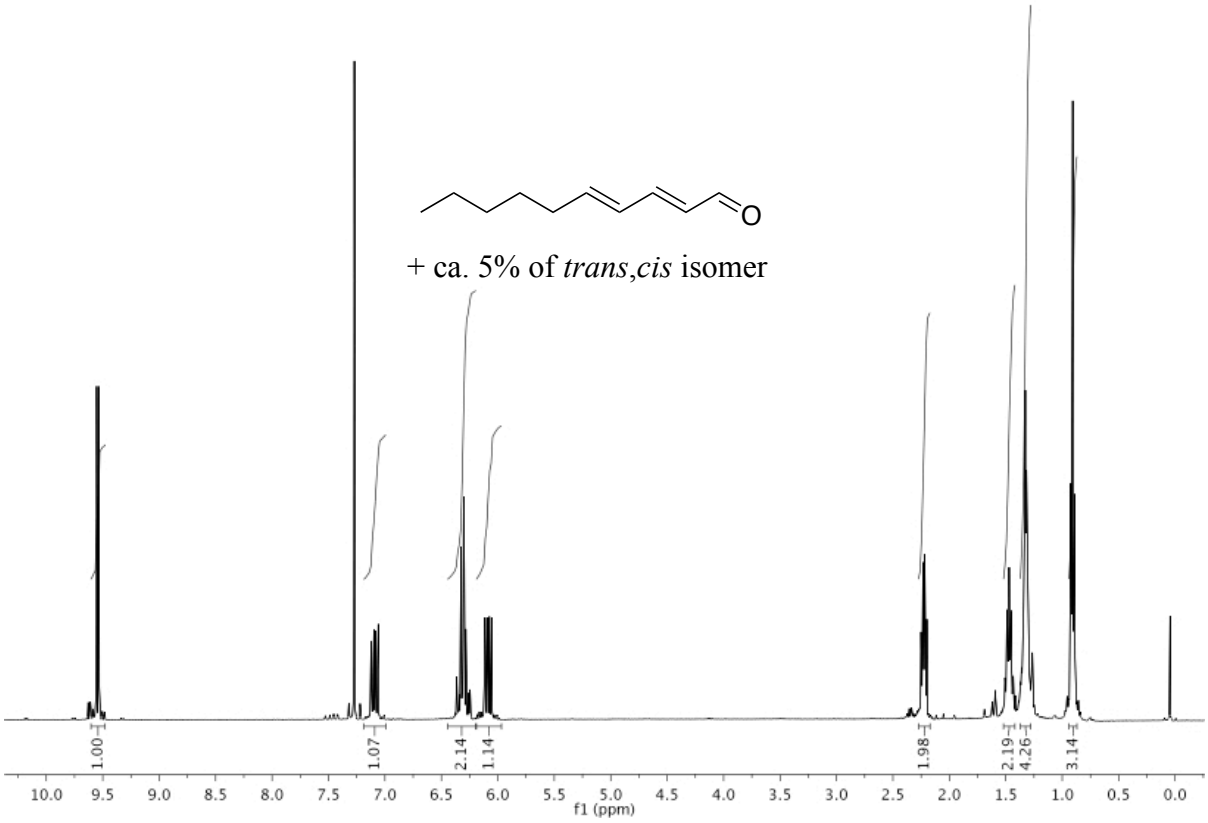


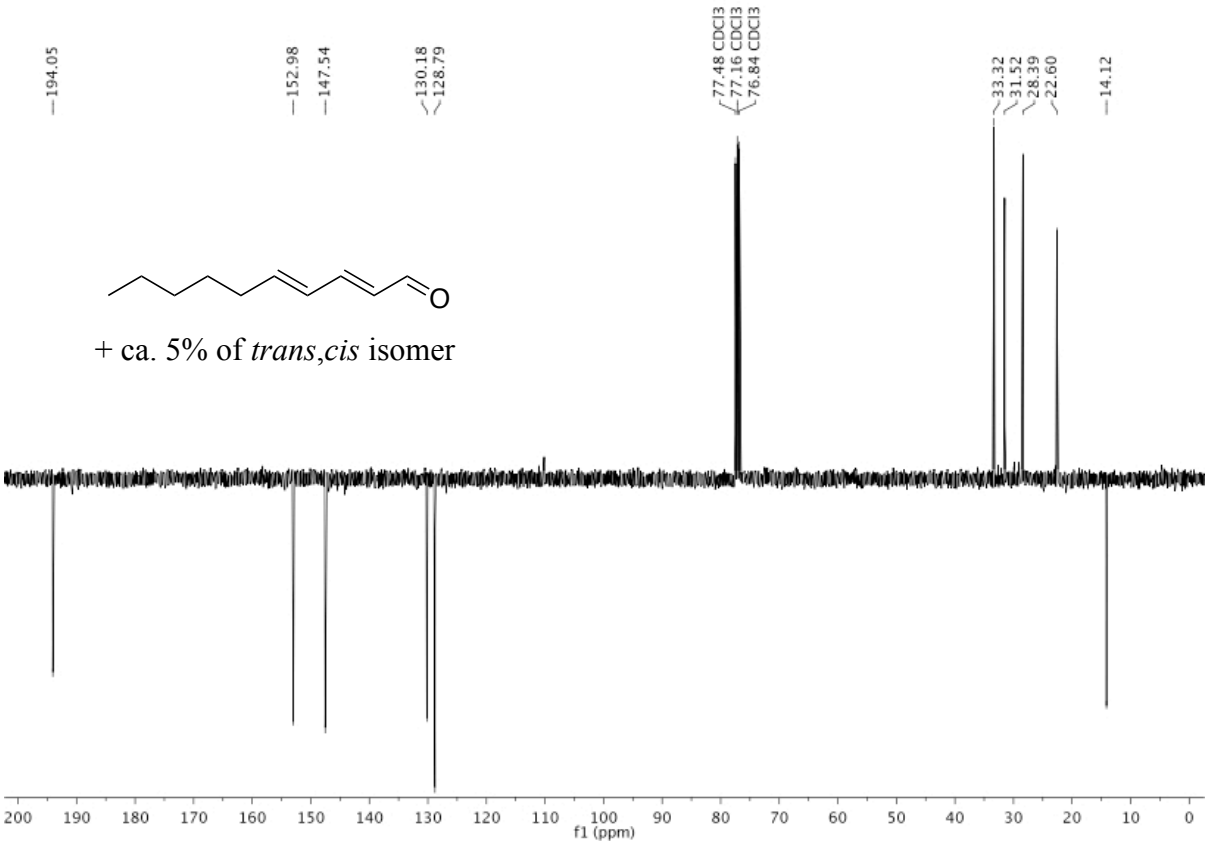
***trans*-Cinnamaldehyde 6f:**



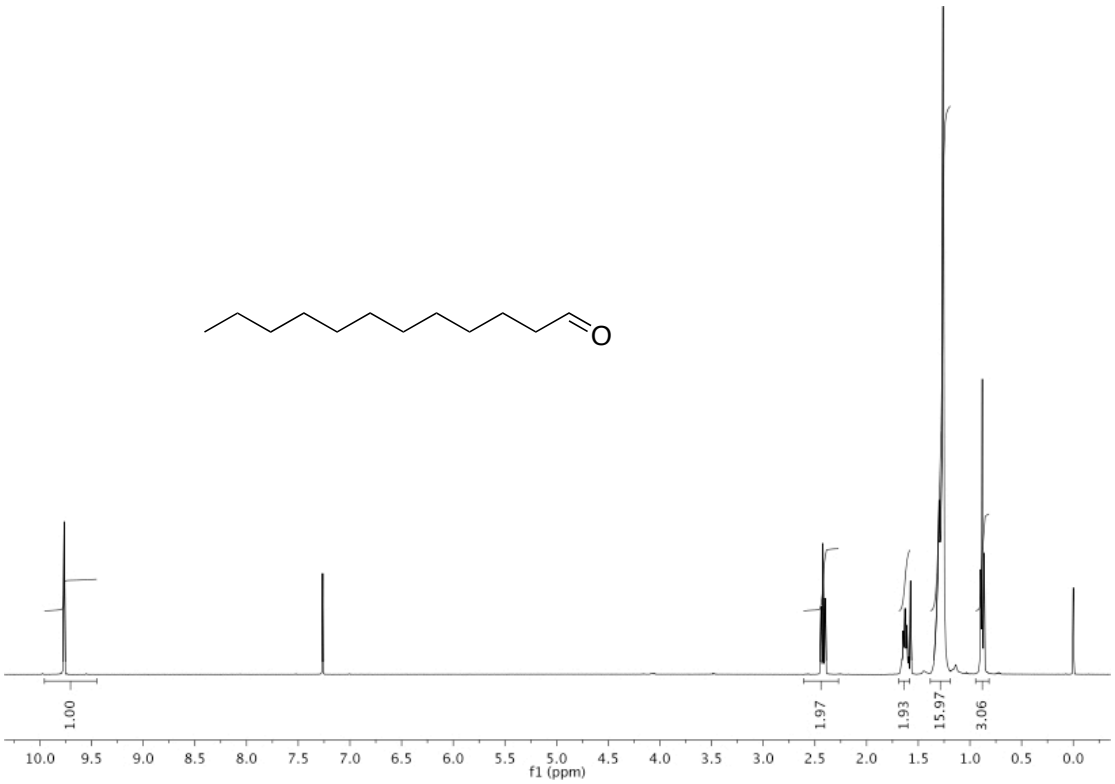


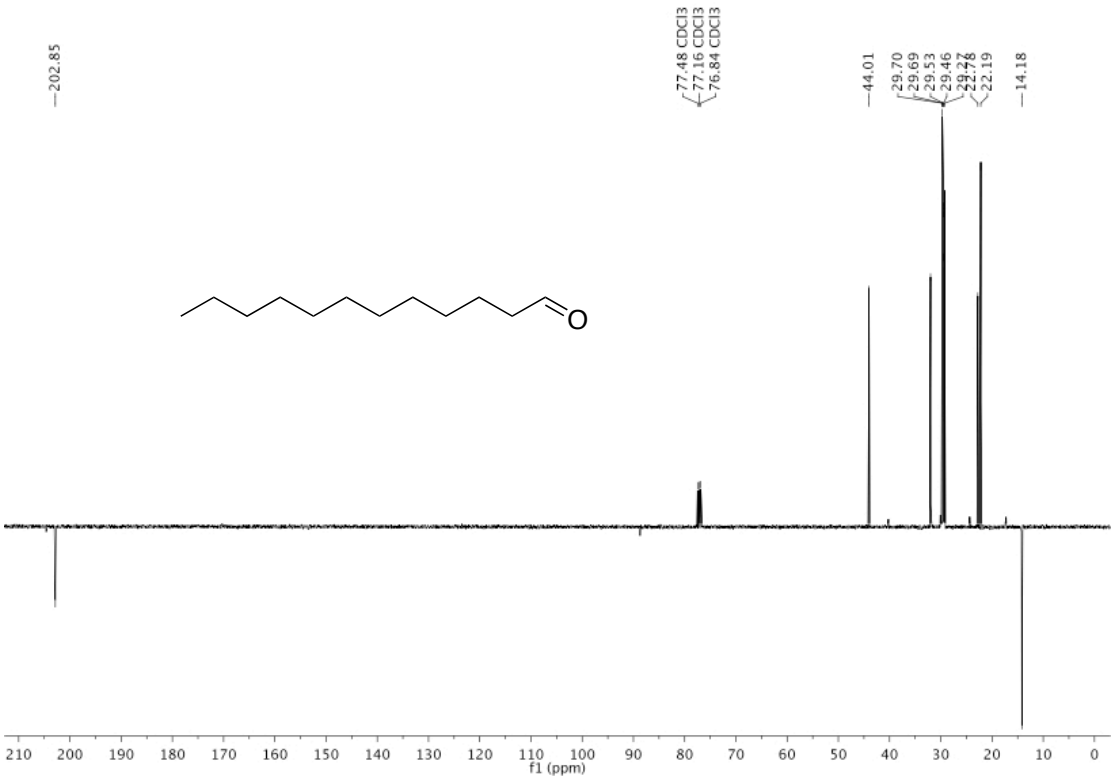
***trans,trans*-Deca-2,4-dienal 6g:**



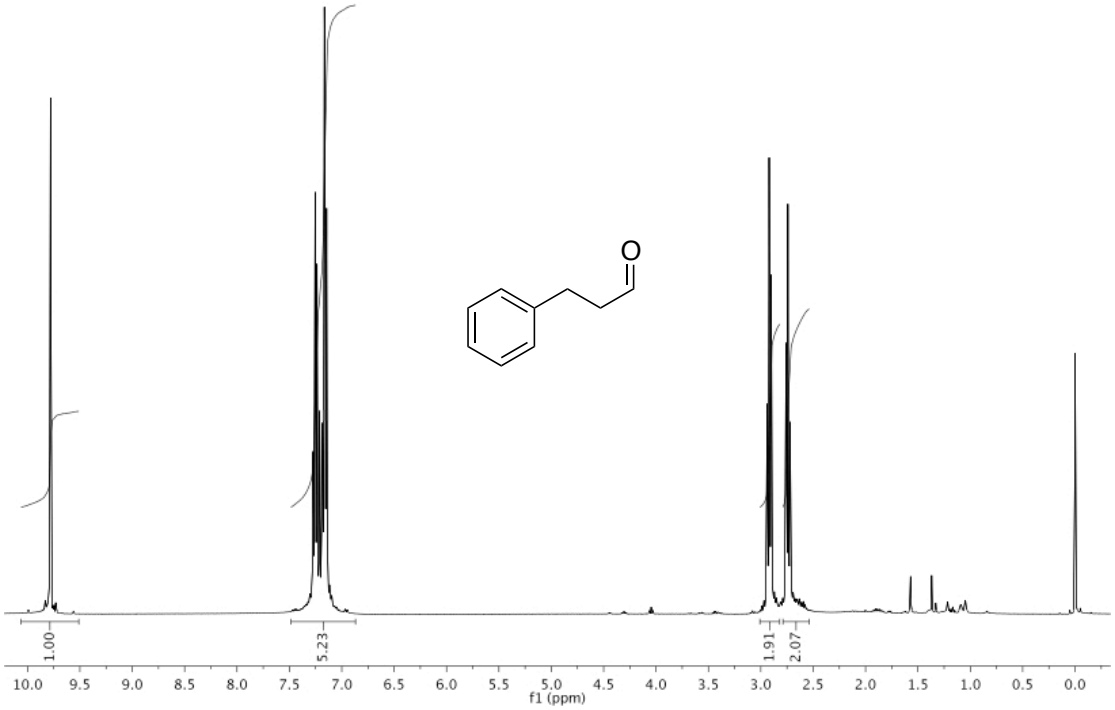


Dodecanal 6h:

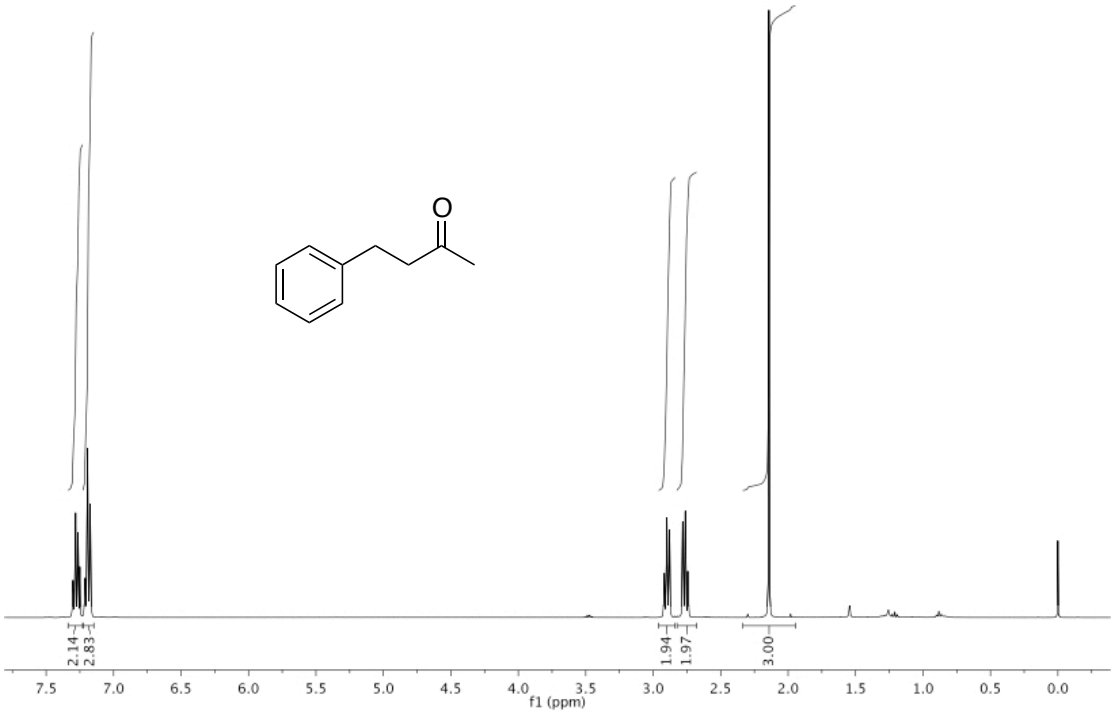




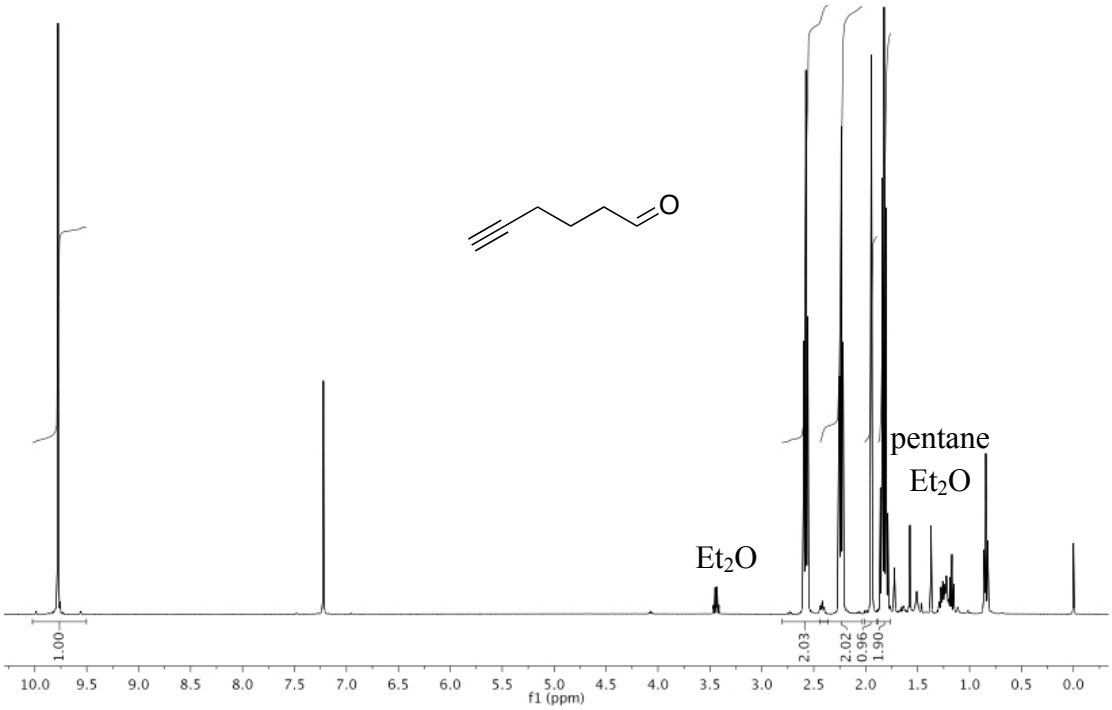
3-Phenylpropanal 6i:

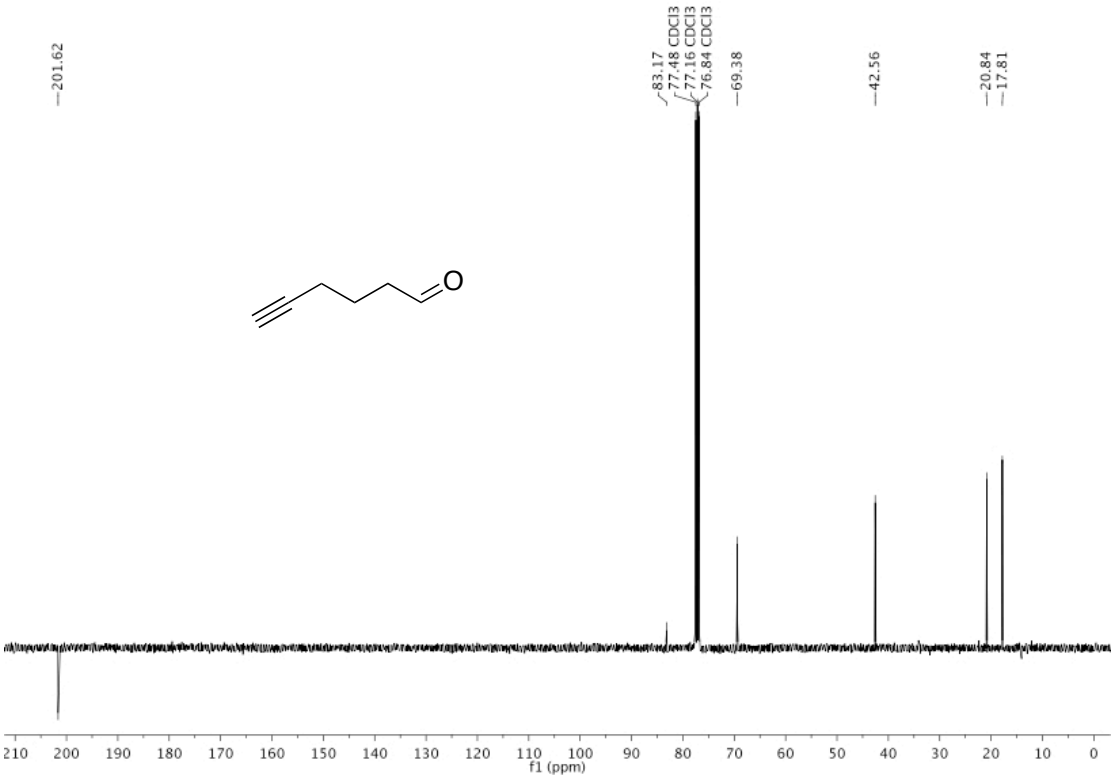


4-Phenylbutan-2-one 6j:

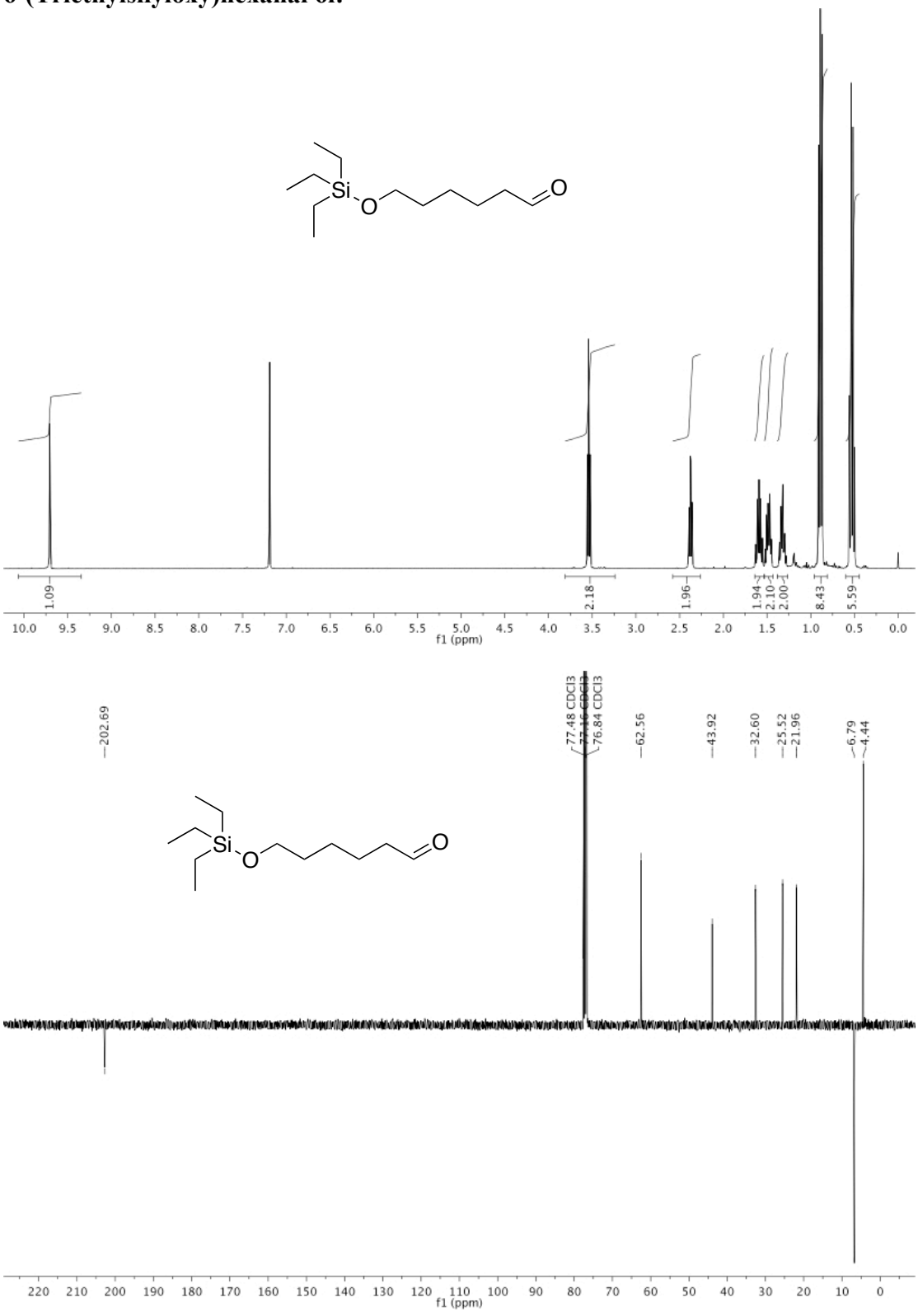


Hex-5-ynal 6k:

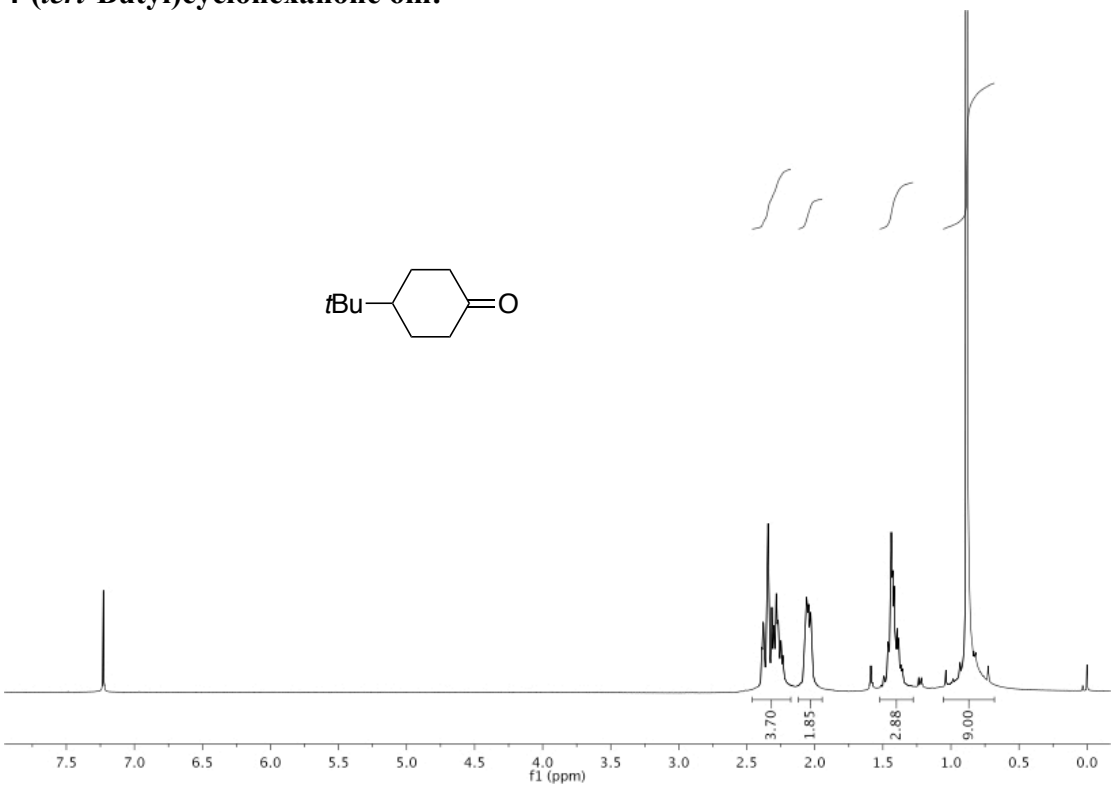

O
pentane
Et_2O
Et_2O
1.00
2.03
2.02
0.96
1.90
f1 (ppm)

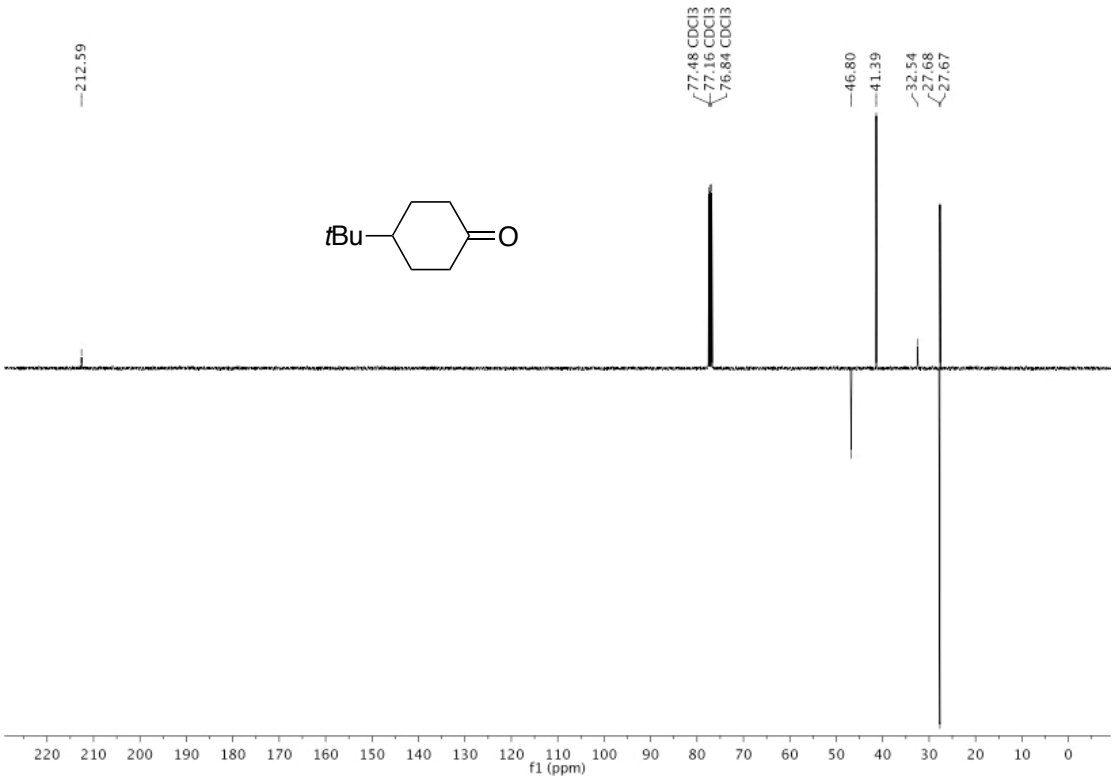

201.62
83.17
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.38
42.56
20.84
17.81
O
f1 (ppm)

6-(Triethylsilyloxy)hexanal 6l:

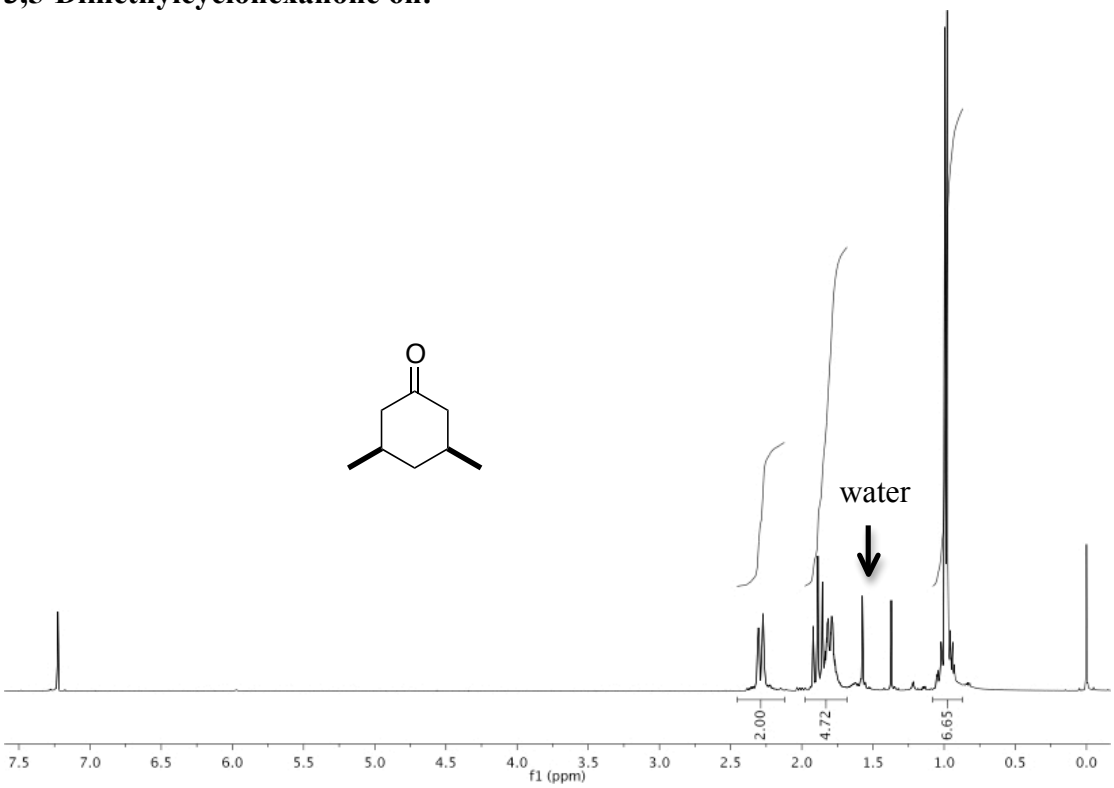


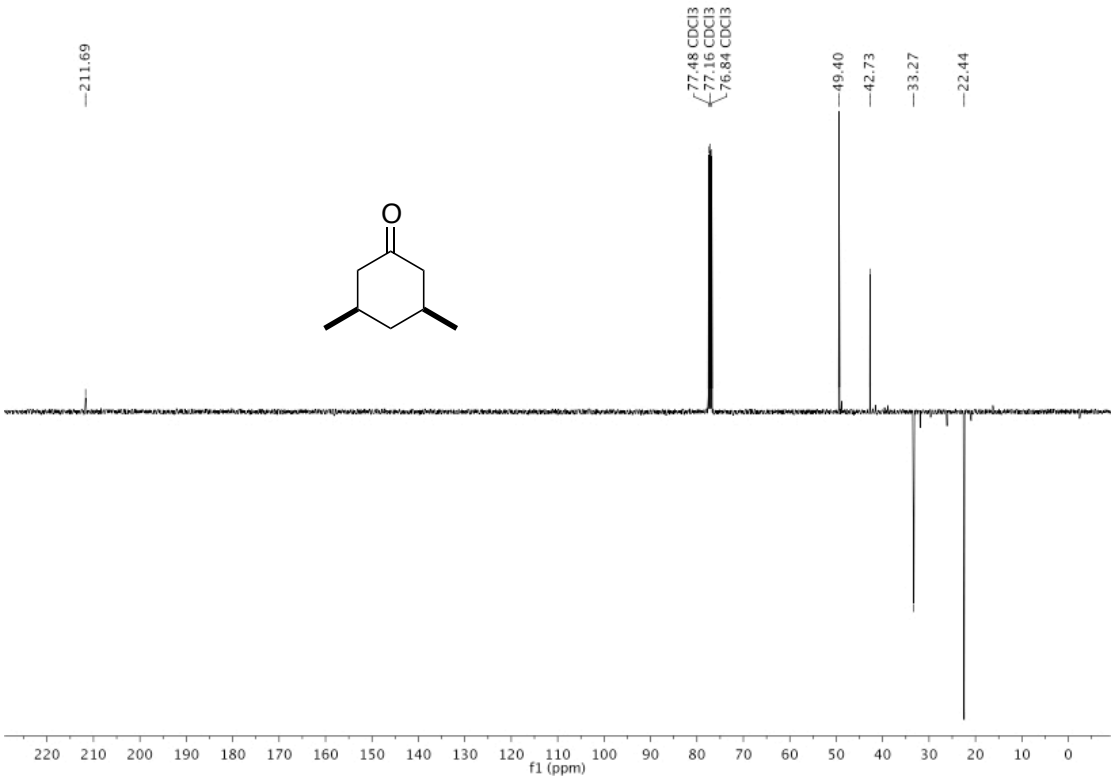
4-(*tert*-Butyl)cyclohexanone 6m:



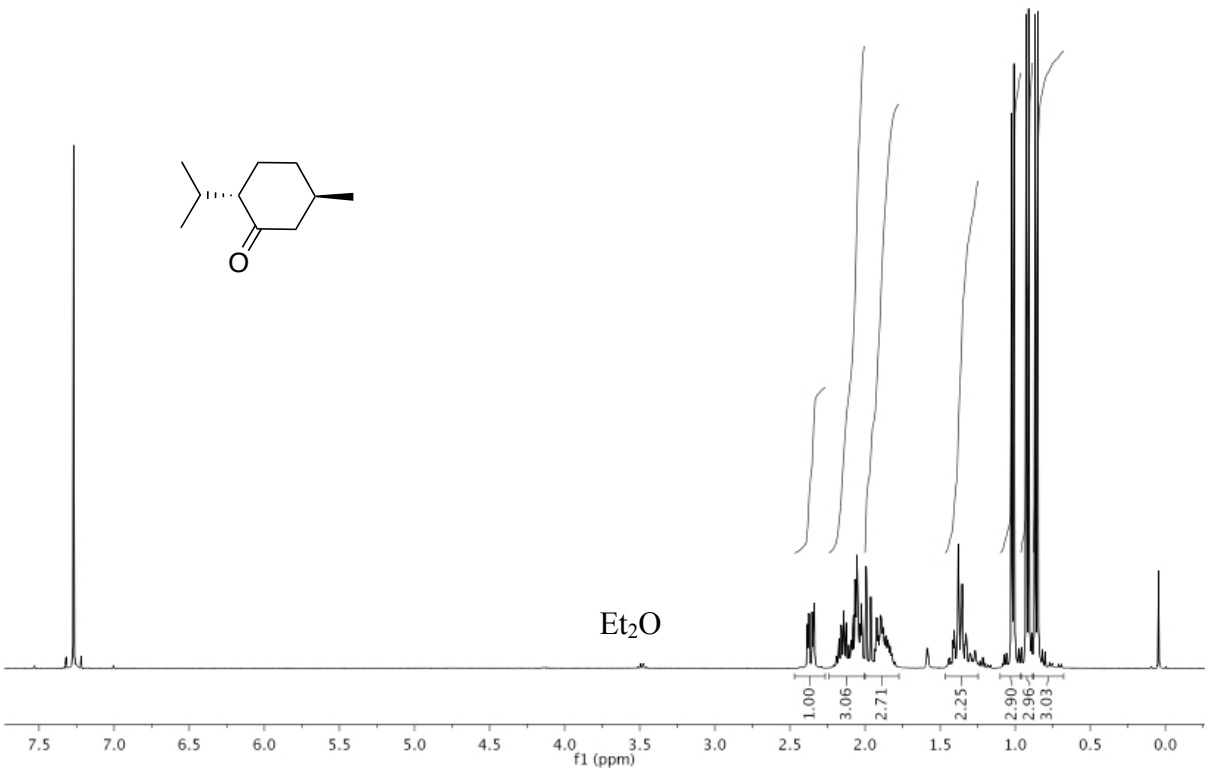


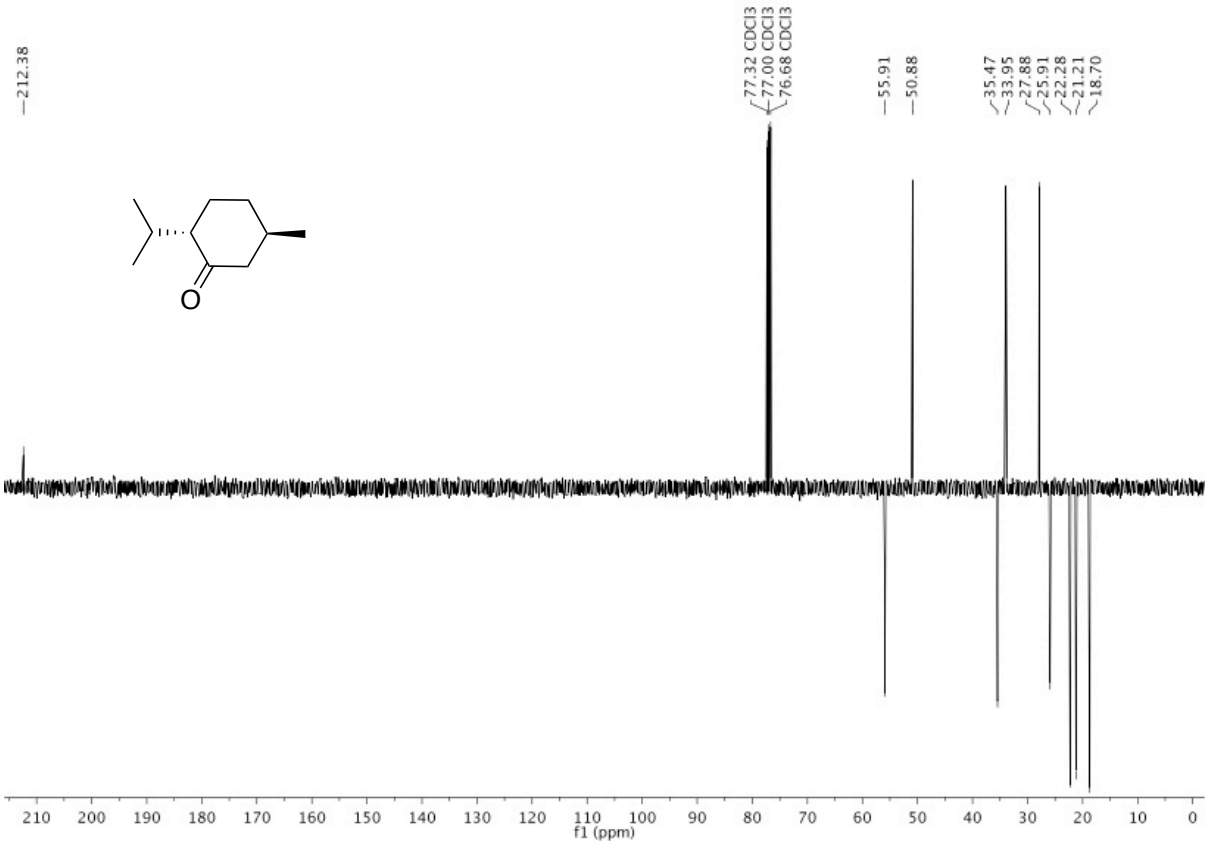
3,5-Dimethylcyclohexanone 6n:



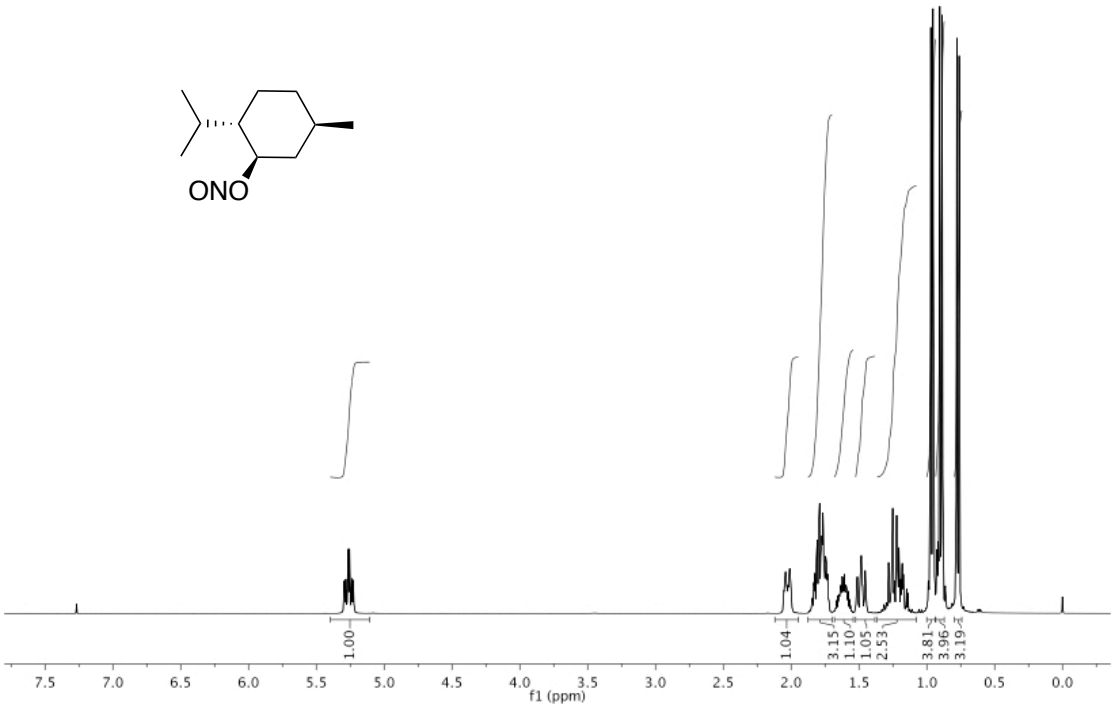


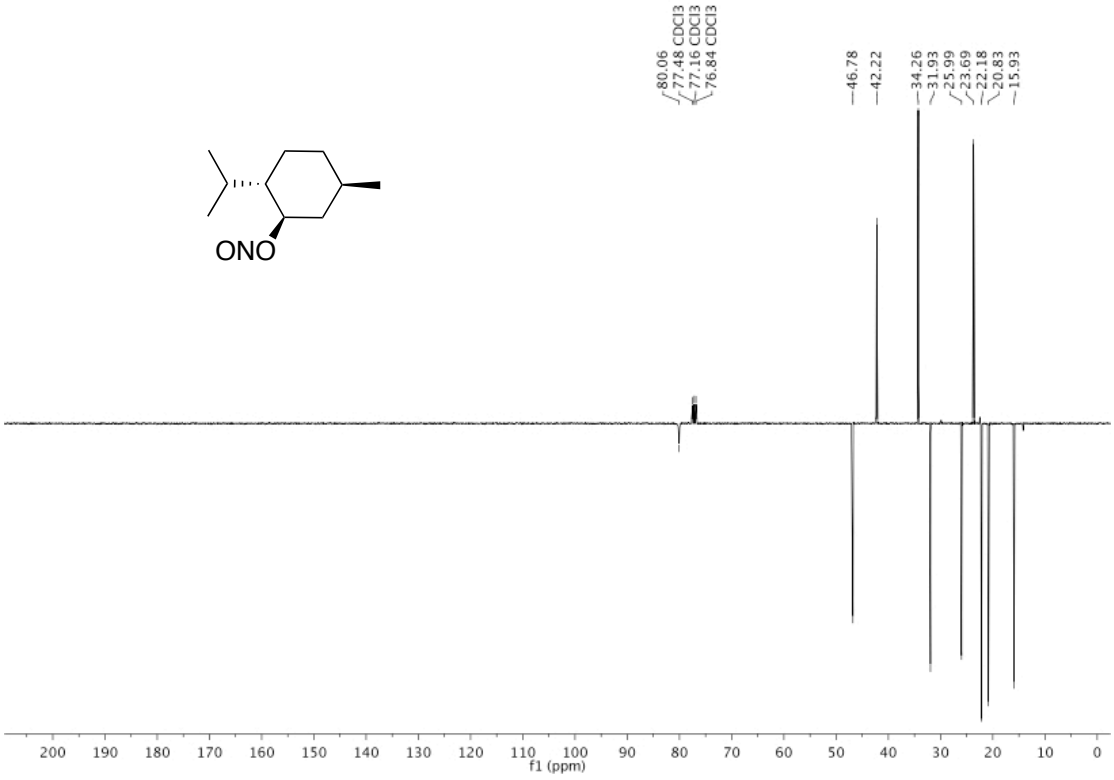
L-Menthone 6o:



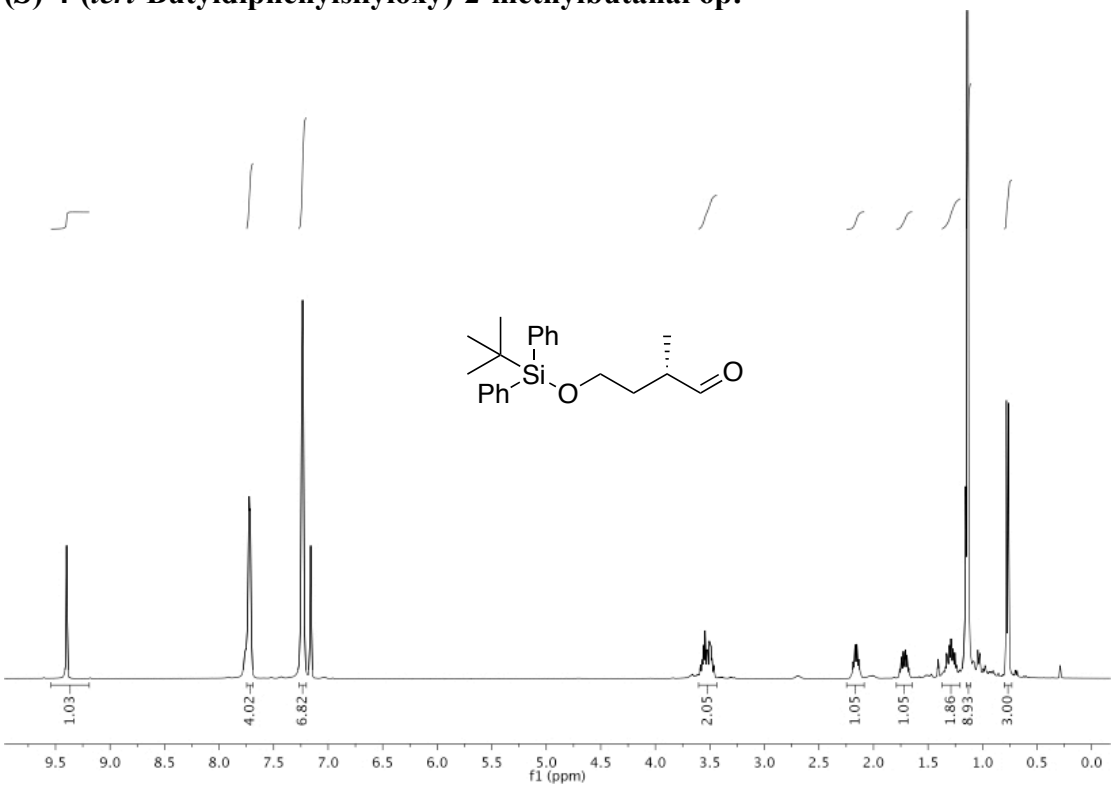


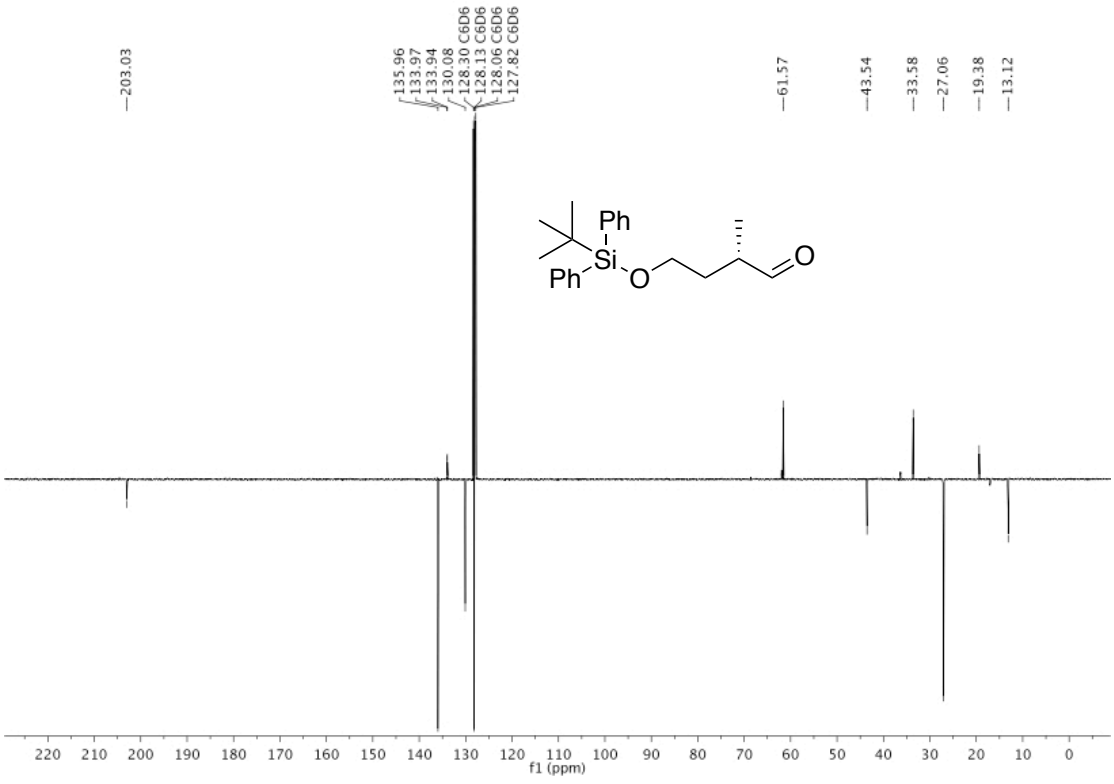
(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl nitrite 7o:





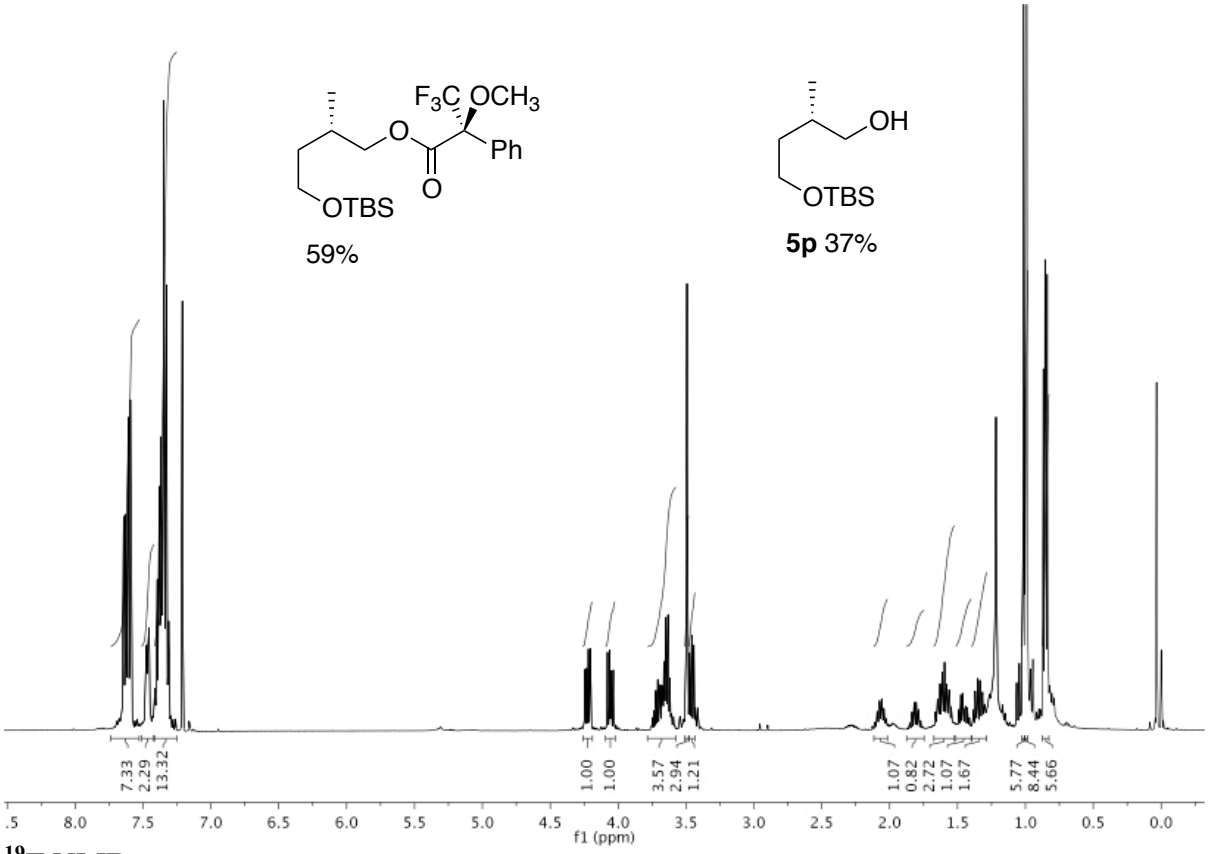
(*S*)-4-(*tert*-Butyldiphenylsilyloxy)-2-methylbutanal 6p:



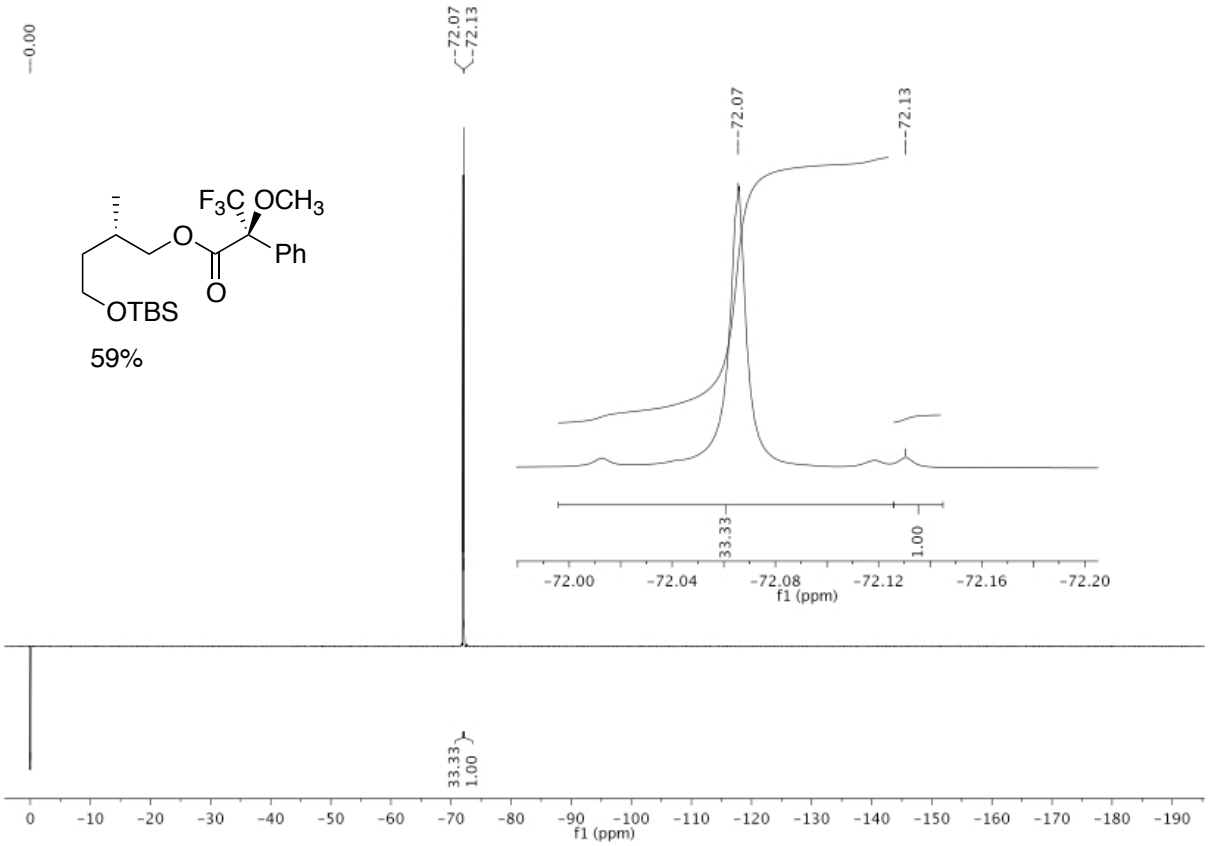


Crude spectra of Mosher ester S1:

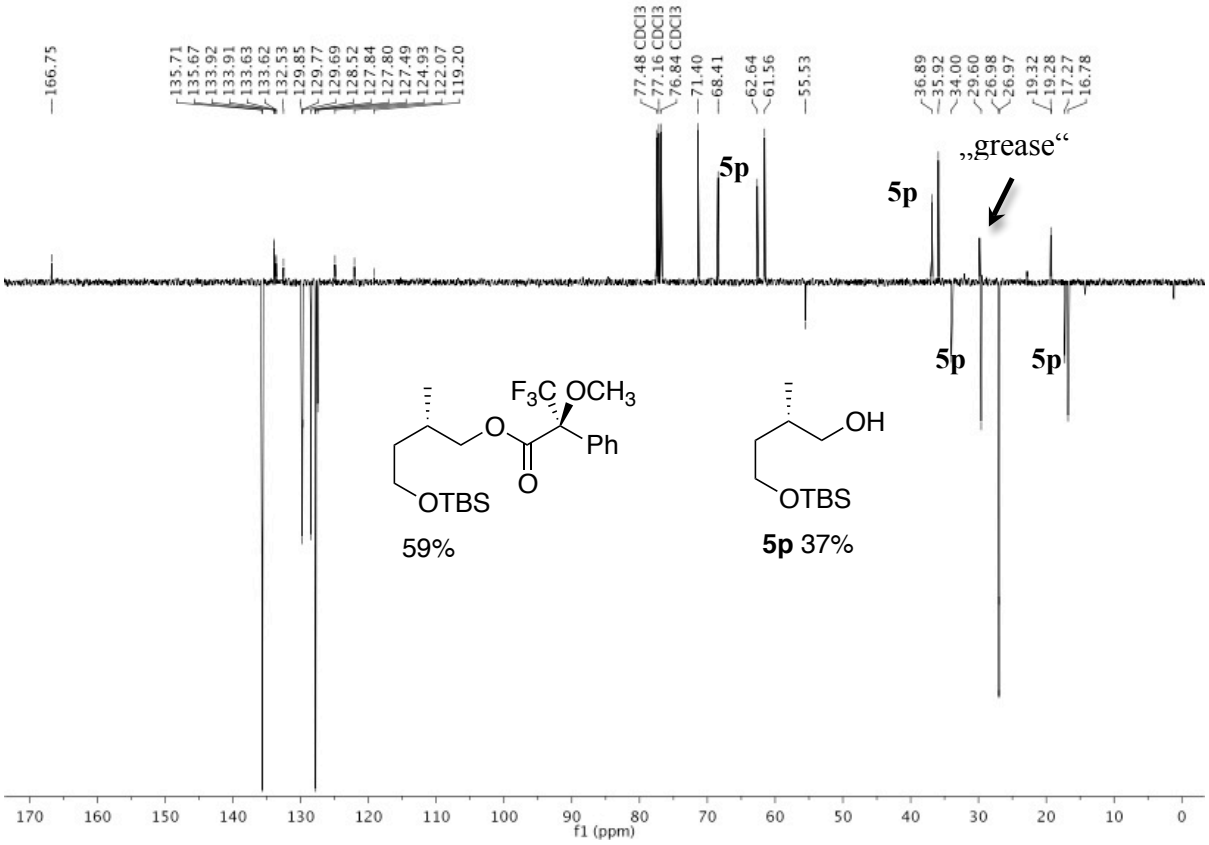
^{1}H NMR



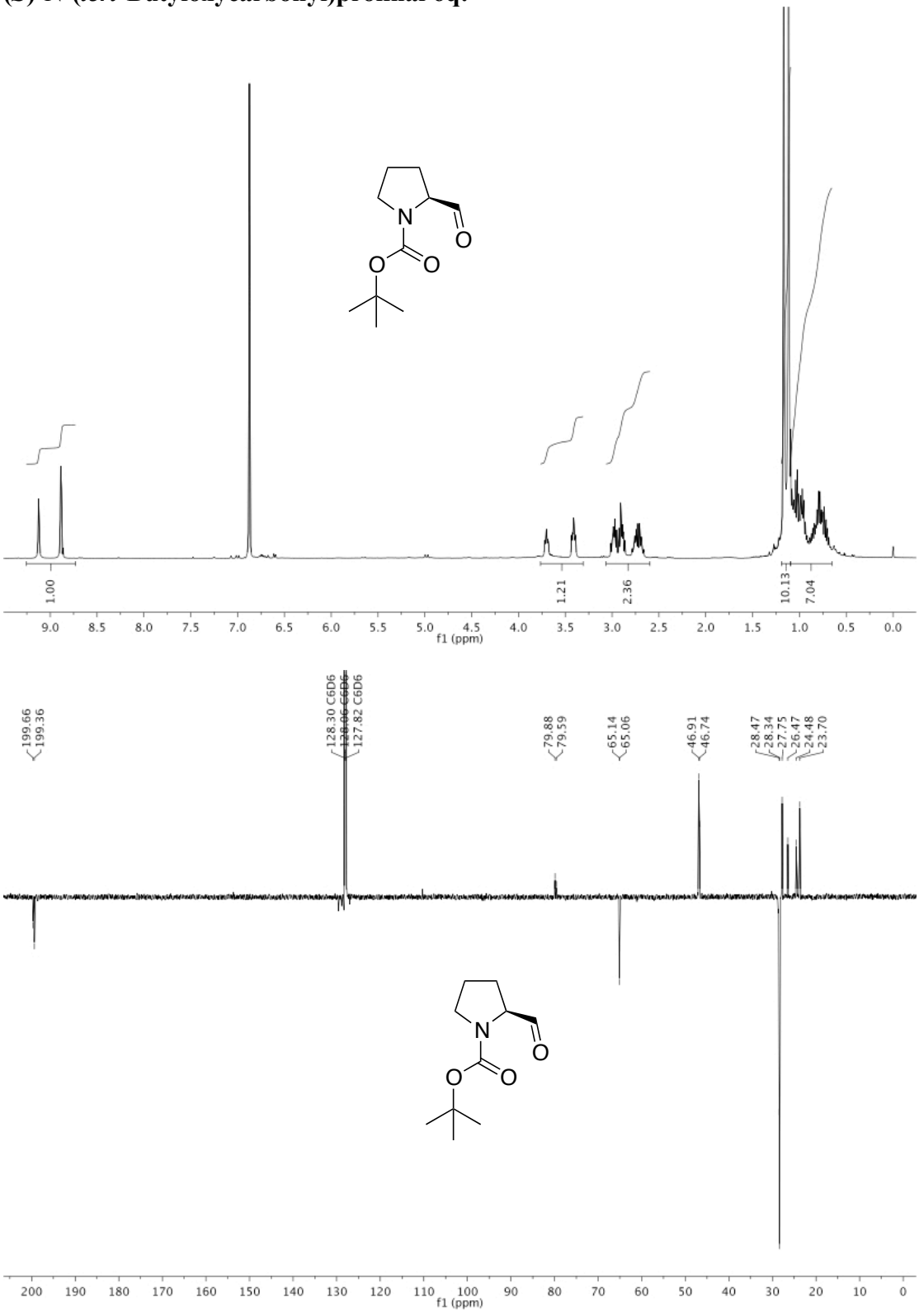
^{19}F NMR



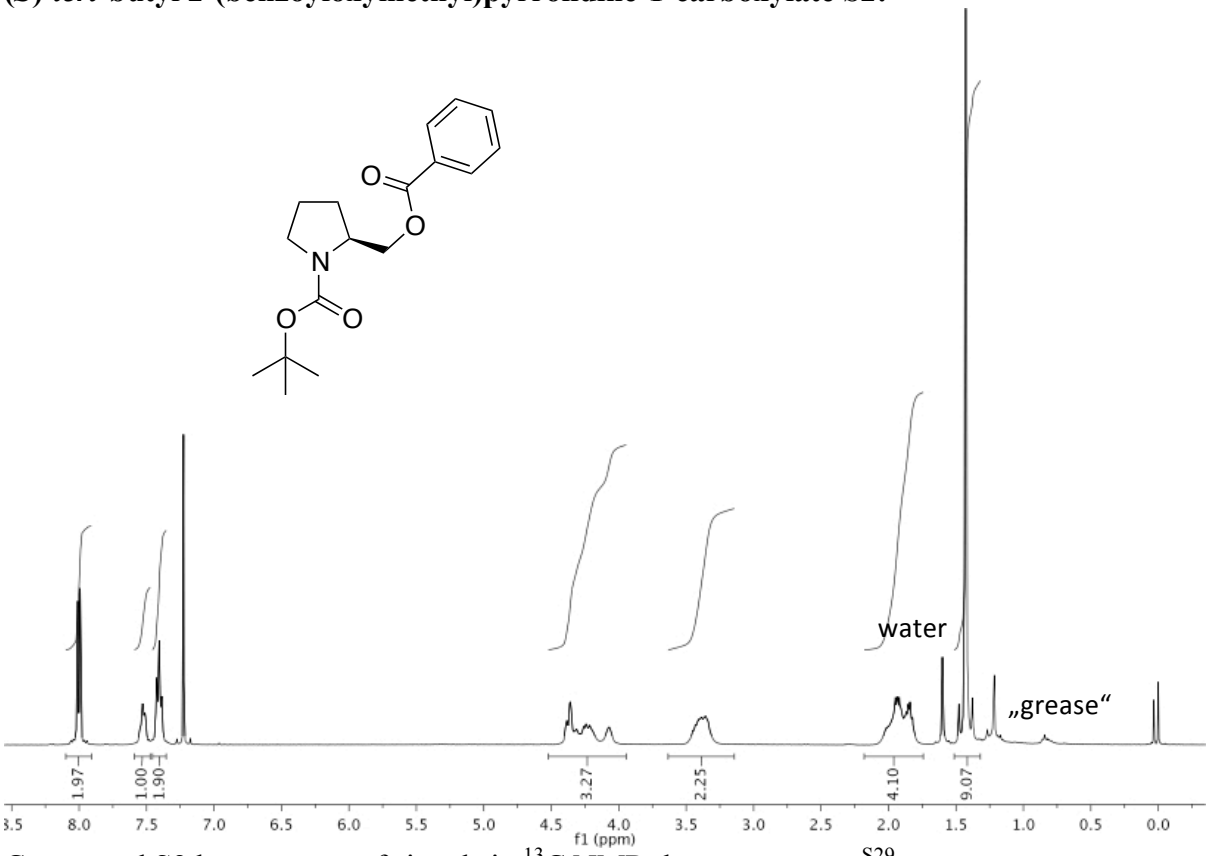
^{13}C NMR


166.75
135.71
135.67
133.92
133.91
133.63
133.62
132.53
129.85
129.77
129.69
128.52
127.84
127.80
127.49
124.93
122.07
119.20
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
71.40
68.41
62.64
61.56
55.53
36.89
35.92
34.00
29.60
26.98
26.97
19.32
19.28
17.27
16.78
„grease“
5p
5p
5p
5p
F3C OCH3
O
Ph
O
OTBS
59%
OH
OTBS
5p 37%
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

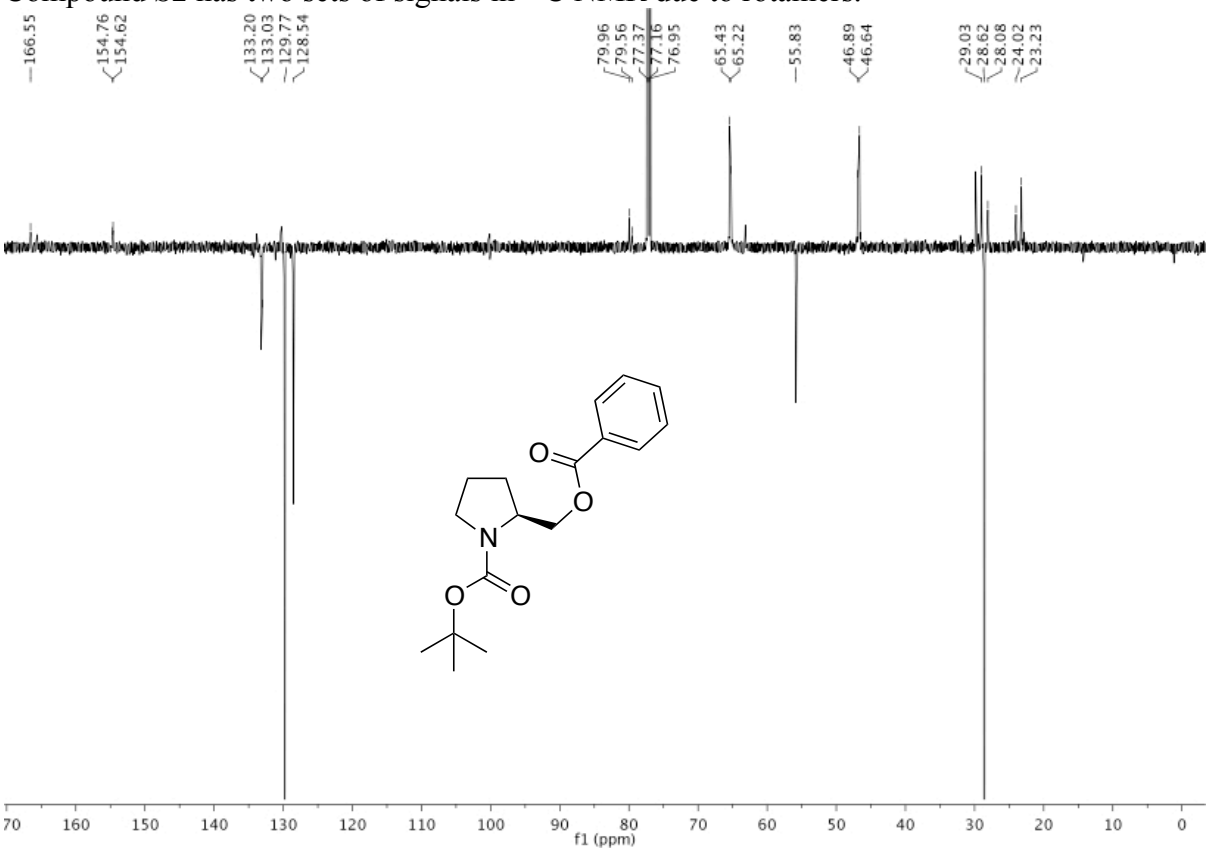
(*S*)-N-(*tert*-Butyloxycarbonyl)prolinal 6q:



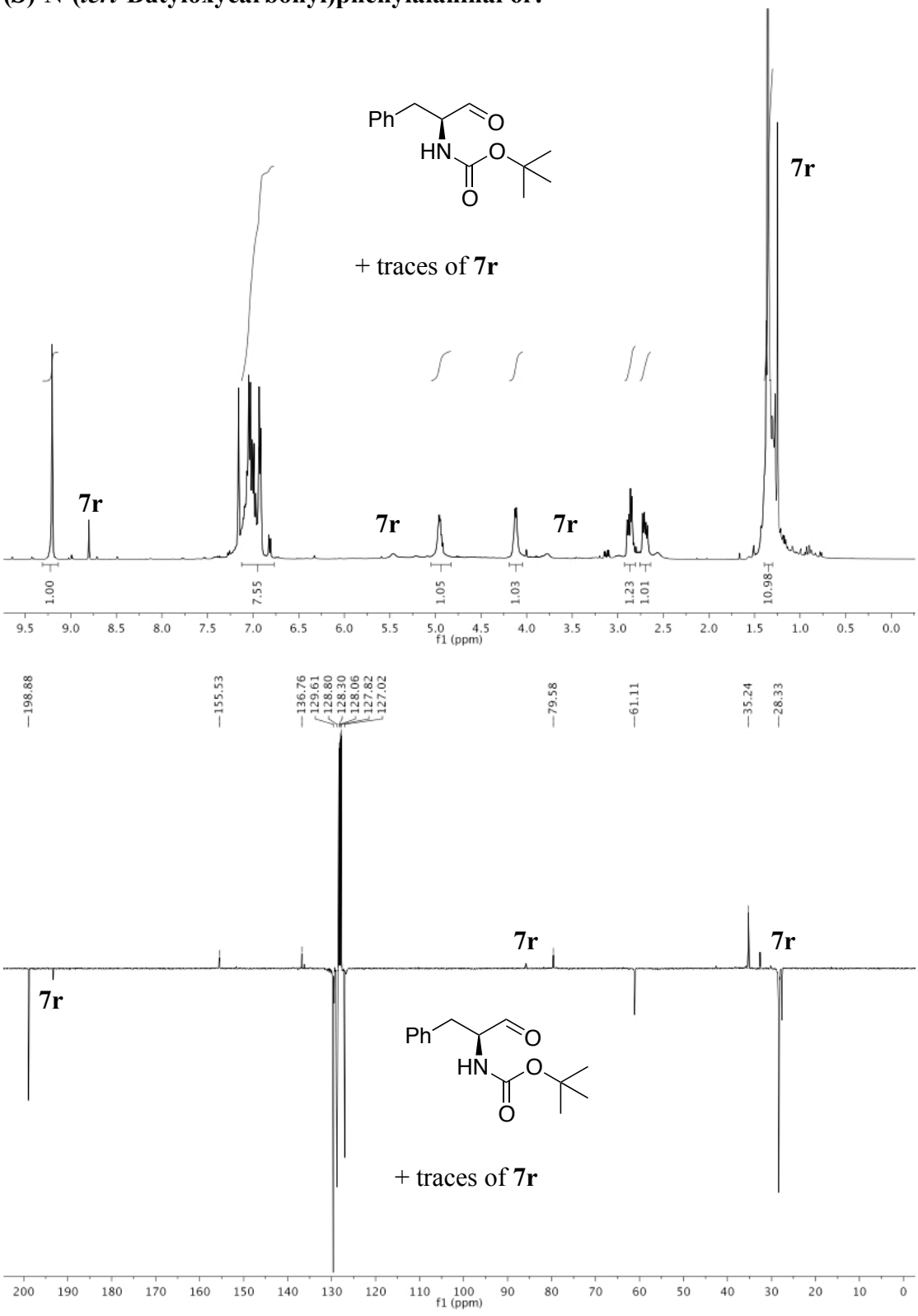
(*S*)-*tert*-butyl 2-(benzoyloxymethyl)pyrrolidine-1-carboxylate S2:



Compound **S2** has two sets of signals in ^{13}C NMR due to rotamers.[S29]

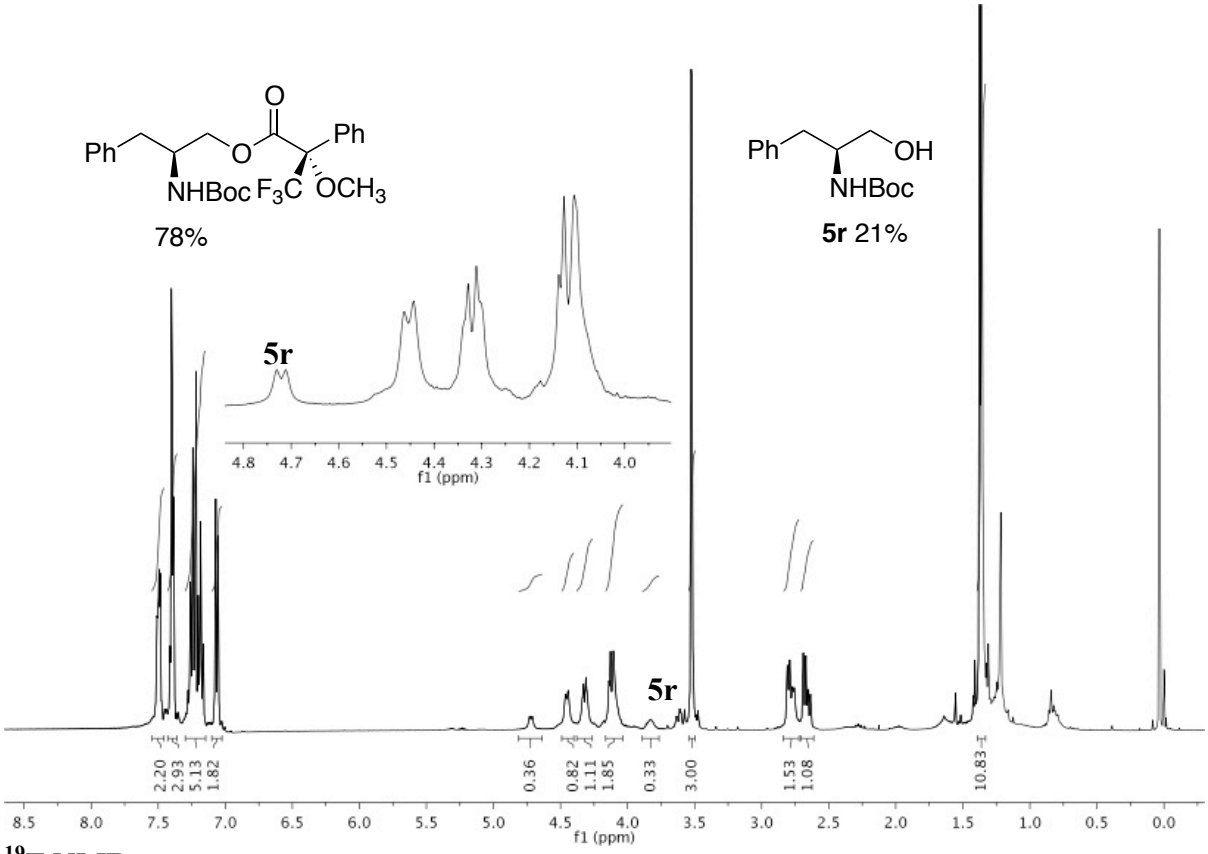


(*S*)-N-(*tert*-Butyloxycarbonyl)phenylalaninal 6r:

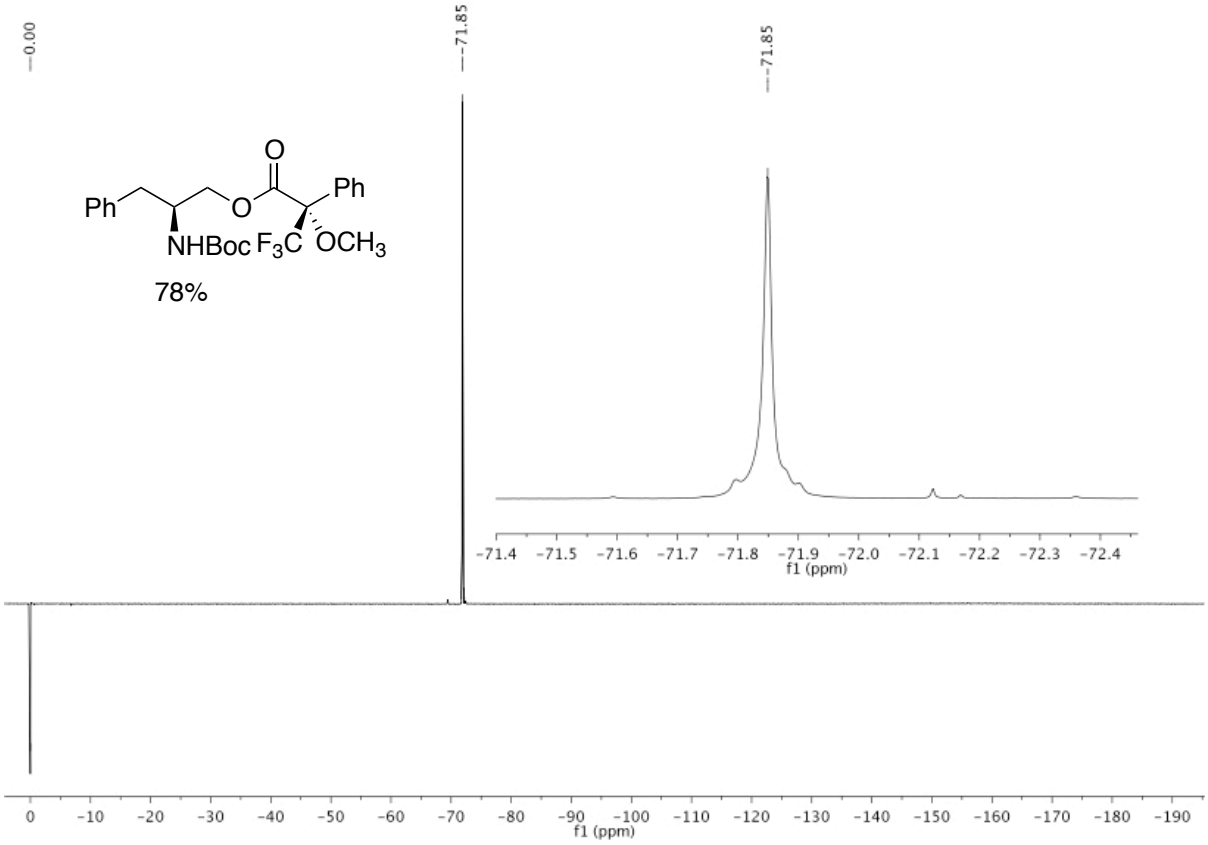


Crude spectra of Mosher ester S3:

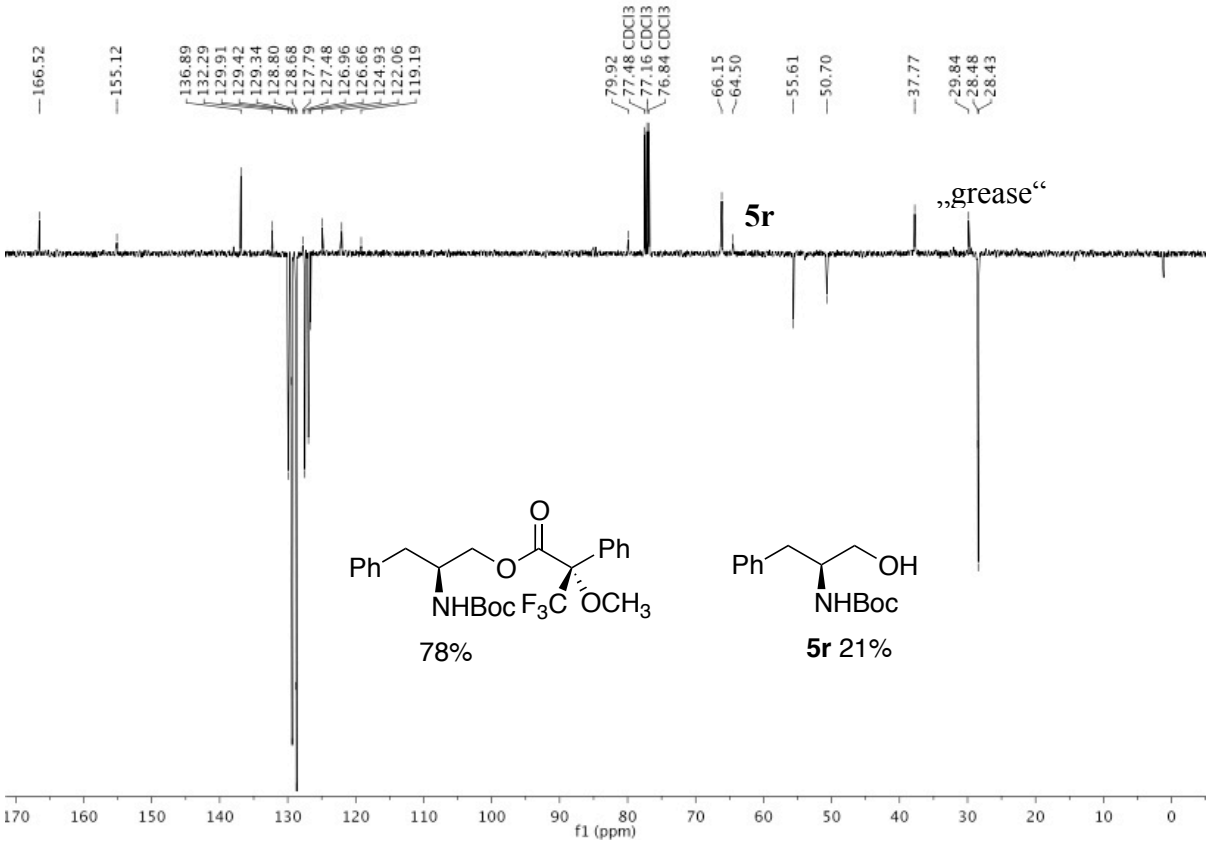
^{1}H NMR



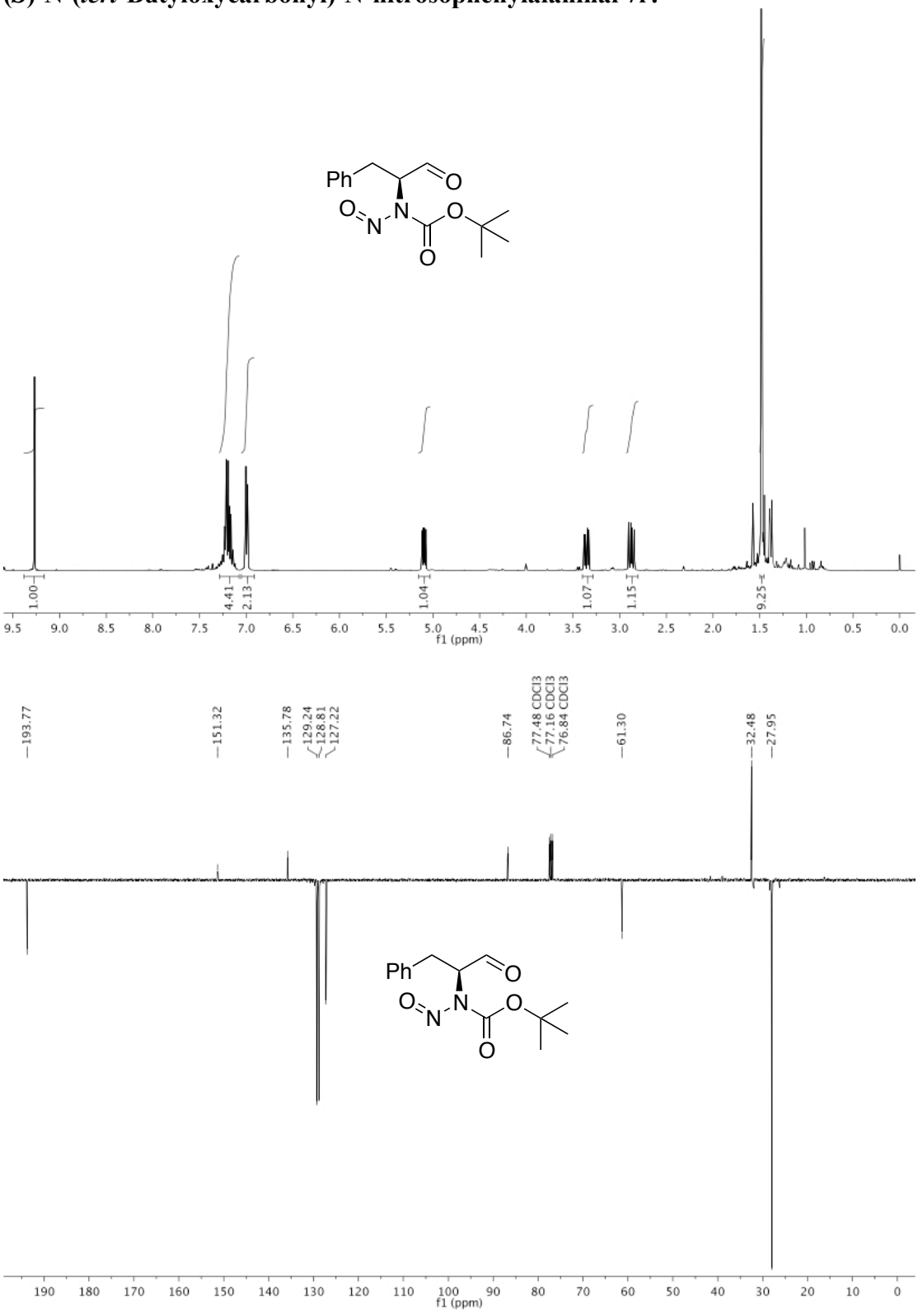
^{19}F NMR



^{13}C NMR


166.52
155.12
136.89
132.29
129.91
129.42
129.34
128.80
128.68
127.79
127.48
126.96
126.66
124.93
122.06
119.19
79.92
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
66.15
64.50
55.61
50.70
37.77
29.84
28.48
28.43
5r
„grease“
Ph
O
O
Ph
NHBoc
F3C
OCH3
78%
Ph
OH
NHBoc
5r 21%
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(*S*)-N-(*tert*-Butyloxycarbonyl)-N-nitrosophenylalaninal 7r:



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