Novel Defluorinative Alkylation of Trifluoroacetaldehyde *N*,*O*-Acetal Derivatives and Its Application to Multi-component Reaction

Hikaru Yanai and Takeo Taguchi*

School of Pharmacy, Tokyo University of Pharmacy and Life Sciences,1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

taguchi@ps.toyaku.ac.jp

Electronic Supplementary Information

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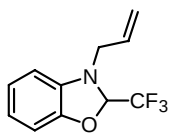
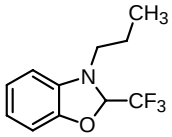
1. General and materials

All reactions were carried out under argon atmosphere. ^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX400 spectrometer, and chemical shifts were reported in parts per million (ppm) using $CHCl_3$ (7.26 ppm) in $CDCl_3$ for ^{1}H NMR, and $CDCl_3$ (77.01 ppm) for ^{13}C NMR as an internal standard, respectively. ^{19}F NMR spectra were taken on a Varian Mercury 300 spectrometer, and chemical shifts were reported in parts per million using benzotrifluoride (0 ppm) as a standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-620 or RT/IR-420 infrared spectrophotometers. Mass spectra (MS) were obtained on a Micromass LCT (ESI-TOF) or a Micromass AutoSpec (EI). Medium pressure liquid chromatography (MPLC) was performed using pre-packed column (KUSANO pre-packed column Si-10, 40 x 300 mm I. D., silica gel, 50 μm) with UV detector. Trifluoroacetaldehyde ethyl hemiacetal (TFAE) was provided by TOSOH F-Tech, Inc.

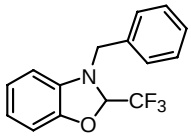
2. Preparation of trifluoroacetaldehyde *N,O*-acetals (1)



1a



1b



1c

3-Allyl-2-(trifluoromethyl)-2,3-dihydro-1,3-benzoxazole (1a)

To a round-bottom flask equipped with Dean-Stark apparatus, 2-(allylamino)phenol[1] (2.99 g, 20 mmol), TFAE (5.76 g, 40 mmol), *p*-toluenesulfonic acid monohydrate (200 mg, 1.1 mmol) and benzene (150 mL) was added. After being refluxed for 4 h, reaction mixture was quenched with saturated $NaHCO_3$ aqueous solution, extracted with Et_2O (30 mL x 3) and evaporated. The resulting residue was purified by column chromatography on silica gel to give **1a** (4.03g, 17.6 mmol, 88% yield) as a pale yellow oil. IR (neat) 3064, 2983, 1487, 1291, 1156, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.77 (1H, dd, J = 15.8, 6.9 Hz), 3.91 (1H, dd, J = 15.8, 5.2 Hz), 5.28 (1H, dd, J = 8.7, 1.4 Hz), 5.32 (1H, dd, J = 15.6, 1.4 Hz), 5.66 (1H, q, $J_{H\text{-}F}$ = 4.0 Hz), 5.78-5.89 (1H, m), 6.73 (1H, d, J = 7.7 Hz), 6.78-6.83 (2H, m), 6.84-6.91 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.2, 92.8 (q, $J_{C\text{-}F}$ = 35.8 Hz), 108.3, 110.4, 119.3, 121.3, 121.8 (q, $J_{C\text{-}F}$ = 284.5 Hz), 122.2, 136.1, 138.0, 150.2; ^{19}F NMR (282 Hz, $CDCl_3$) δ -21.3 (3F, d, $J_{H\text{-}F}$ = 4.0 Hz); MS (ESI-TOF) m/z 230 $[M+H]^+$; HRMS calcd for $C_{11}H_{11}F_3NO$ $[M+H]^+$, 230.0793; found, 230.0804.

3-Propyl-2-(trifluoromethyl)-2,3-dihydro-1,3-benzoxazole (1b)

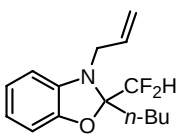
Under H_2 atmosphere (1 atm), a mixture of 3-allyl-2-(trifluoromethyl)-2,3-dihydro-1,3-benzoxazole **1a** (462.2 mg, 2.0 mmol) and 10% palladium on carbon (50% wet., 212 mg, 0.1 mmol) in EtOAc (5.0 mL) was stirred for 6 h at room temperature. A resulting mixture was filtrated through celite pad and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give **1b** (450.8 mg, 1.95 mmol, 97% yield) as colorless oil. IR (neat) 3063, 2968, 2879, 1489, 1292, 1245, 1154, 1058, 854, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (3H, t, J = 7.4 Hz), 1.58-1.74 (2H, m), 3.13-3.26 (2H, m), 5.64 (1H, q, $J_{H\text{-}F}$ = 4.2 Hz), 6.69 (1H, d, J = 7.2 Hz), 6.65-6.83 (2H, m), 6.86-6.91 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.2, 21.2, 54.2, 94.0 (q, $J_{C\text{-}F}$ = 35.4 Hz), 108.1, 110.0, 120.9, 121.7 (q, $J_{C\text{-}F}$ = 284.0 Hz), 122.2, 138.7, 150.0; ^{19}F NMR (282 Hz, $CDCl_3$) δ -21.4 (3F, d, $J_{H\text{-}F}$ = 4.2 Hz); MS (ESI-TOF) m/z 232 $[M+H]^+$; HRMS calcd for $C_{11}H_{13}F_3NO$ $[M+H]^+$, 232.0949; found, 232.0950.

3-Benzyl-2-(trifluoromethyl)-2,3-dihydro-1,3-benzoxazole (1c)

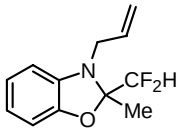
According to the preparation of **1a**, this compound was obtained in 87% yield (3.63 g, 13.0 mmol) from 2-(benzylamino)phenol[2] (2.99 g, 15 mmol) and TFAE (4.33 g, 30 mmol). Pale yellow oil; IR (neat) 3065, 2888, 1601, 1488, 1292, 1254, 1153, 739, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.35 (1H, d, J = 15.4 Hz), 4.54 (1H, d, J = 15.4 Hz), 5.68 (1H, q, $J_{H\text{-}F}$ = 4.0 Hz), 6.67 (1H, brd, J = 6.9 Hz), 6.78-6.88 (3H, m), 7.28-7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 93.0 (q, $J_{C\text{-}F}$ = 35.8 Hz), 108.3, 110.0, 121.1, 121.8 (q, $J_{C\text{-}F}$ = 284.3 Hz), 122.2, 127.8, 128.0, 128.8, 136.2, 138.4,

149.9; ^{19}F NMR (282 Hz, $CDCl_3$) δ -20.9 (3F, d, $J_{H\text{-}F}$ = 4.0 Hz); MS (ESI-TOF) *m*/*z* 280 $[M+H]^+$; HRMS calcd for $C_{15}H_{13}F_3NO$ $[M+H]^+$, 280.0949; found, 280.0968.

3. Defluorinative alkylation reaction



2aa



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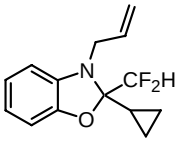

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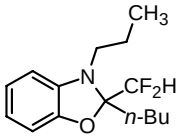
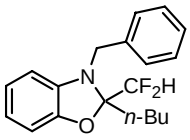


2ba



2ca

3-Allyl-2-butyl-2-(difluoromethyl)-2,3-dihydro-1,3-benzoxazole (2aa)

To a solution of **1a** (114.5 mg, 0.5 mmol) in Et_2O (2.0 mL), *n*-BuLi (1.55 M in hexane, 0.77 mL, 1.2 mmol) was added at -78 °C over 15 min. After being stirred for 4 h at the same temperature, the mixture was poured into ice water and Et_2O, which was extracted with Et_2O (20 mL x 3). The organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The obtained residue was purified by short column chromatography on silica gel to give the product **2aa** (110.8 mg, 0.42 mmol, 83%) as colorless oil. IR (neat) 3064, 2959, 2873, 1599, 1456, 1398, 1311, 1235, 1201, 1116, 1073, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, *J* = 7.2 Hz), 1.25-1.59 (4H, m), 1.97 (2H, t, *J* = 7.9 Hz), 3.76-3.95 (2H, m), 5.21 (1H, dd, *J* = 10.3, 1.5 Hz), 5.33 (1H, dd, *J* = 17.2, 1.5 Hz), 5.68 (1H, t, $J_{H\text{-}F}$ = 55.4 Hz), 5.83-5.94 (1H, m), 6.39 (1H, dd, *J* = 7.5, 1.0 Hz), 6.54-6.62 (1H, m), 6.65 (1H, dd, *J* = 7.6, 1.0 Hz), 6.70-6.77 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.4, 28.8, 46.9, 100.9 (t, $J_{C\text{-}F}$ = 23.6 Hz), 105.2, 106.8, 114.0 (dd, $J_{C\text{-}F}$ = 254.8, 251.0 Hz), 116.8, 117.9, 121.6, 133.9, 139.0, 148.9; ^{19}F NMR (282 Hz, $CDCl_3$) δ -71.3 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.4 Hz), -66.7 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.4 Hz); MS (ESI-TOF) *m*/*z* 268 $[M+H]^+$; HRMS calcd for $C_{15}H_{20}F_2NO$ $[M+H]^+$, 268.1513; found, 268.1500.

3-Allyl-2-(difluoromethyl)-2-methyl-2,3-dihydro-1,3-benzoxazole (2ab)

This compound was obtained in 81% yield (91.1 mg, 0.40 mmol) by the reaction of **1a** (114.3 mg, 0.5 mmol) and methyllithium (1.09 M in Et_2O, 1.10 mL, 1.2 mmol) in Et_2O-THF (3 : 1, 4 mL) for 4 h at -24 °C. Brown oil; IR (neat) 3064, 2986, 1599, 1494, 1394, 1302, 1227, 1096, 1074, 735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (3H, brs), 3.79 (1H, dd, *J* = 16.8, 5.6 Hz), 3.90-3.98 (1H, m), 5.21 (1H, dd, *J* = 10.3, 1.5 Hz), 5.31 (1H, dd, *J* = 17.1, 1.5 Hz), 5.67 (1H, t, $J_{H\text{-}F}$ = 55.3 Hz), 5.83-8.94 (1H, m), 6.46 (1H, d, *J* = 7.5 Hz), 6.61-6.70 (2H, m), 6.74-6.81 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 47.5, 99.4 (t, $J_{C\text{-}F}$ = 25.0 Hz), 106.8, 107.5, 113.7 (dd, *J* = 254.9, 249.6 Hz), 116.9, 118.7, 121.7, 134.2, 138.4, 148.4; ^{19}F NMR (282 Hz, $CDCl_3$) δ -70.9 (1F, dd, $J_{F\text{-}F}$ = 287.3 Hz, $J_{H\text{-}F}$ = 55.3 Hz), -66.8 (1F, dd, $J_{F\text{-}F}$ = 287.3 Hz, $J_{H\text{-}F}$ = 55.3 Hz); MS (EI) *m*/*z* 225 (M^+, 100); Anal. Calcd for $C_{12}H_{13}F_2NO$: C, 63.99; H, 5.82; N, 6.22. Found: C, 63.82; H, 5.91; N, 6.40.

3-Allyl-2-cyclopropyl-2-(difluoromethyl)-2,3-dihydro-1,3-benzoxazole (2ac)

This compound was obtained in 74% yield (92.9 mg, 0.37 mmol) by the reaction of **1a** (114.6 mg, 0.5

mmol) and cyclopropyllithium (1.2 M in hexane, 1.0 mL, 1.2 mmol) in Et_2O (2 mL) for 4 h at -78 °C. Pale yellow oil; IR (neat) 3064, 3015, 2980, 1599, 1494, 1230, 1074, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.48-0.55 (2H, m), 0.65-0.72 (1H, m), 0.86-0.92 (1H, m), 1.38-1.46 (1H, m), 3.91 (1H, dd, J = 16.7, 5.4 Hz), 4.14 (1H, dd, J = 16.7, 5.2 Hz), 5.23 (1H, d, J = 10.3 Hz), 5.36 (1H, J = 17.2 Hz), 5.72 (1H, t, $J_{H\text{-}F}$ = 55.5 Hz), 5.91-6.03 (1H, m), 6.47 (1H, d, J = 7.6 Hz), 6.58-6.66 (1H, m), 6.76 (1H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.6, 1.8, 9.9, 48.0, 99.2 (t, $J_{C\text{-}F}$ = 23.7 Hz), 106.26 107.0, 114.1 (dd, $J_{C\text{-}F}$ = 252.9, 250.9 Hz), 116.6, 118.3, 121.6, 134.6, 139.3, 148.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -71.8 (1F, dd, $J_{F\text{-}F}$ = 285.2 Hz, $J_{H\text{-}F}$ = 55.5 Hz), -67.4 (1F, dd, $J_{F\text{-}F}$ = 285.2 Hz, $J_{H\text{-}F}$ = 55.5 Hz); MS (ESI-TOF) m/z 252 $[M+H]^+$; HRMS calcd for $C_{14}H_{16}F_2NO$ $[M+H]^+$, 252.1200; found, 252.1179.

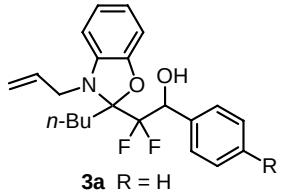
2-Butyl-2-(difluoromethyl)-3-propyl-2,3-dihydro-1,3-benzoxazole (2ba)

This compound was obtained in 58% yield (78.1 mg, 0.29 mmol) by the reaction of **1a** (115.4 mg, 0.5 mmol) and *n*-BuLi (1.55 M in hexane, 0.77 mL, 1.2 mmol) in Et_2O (2 mL) for 5 h at -78 °C. Colorless oil; IR (neat) 3062, 2962, 2874, 1599, 1496, 1235, 1116, 1072, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 7.3 Hz), 0.97 (3H, t, J = 7.4 Hz), 1.21-1.53 (4H, m), 1.62-1.80 (2H, m), 1.93-2.00 (2H, m), 3.16 (2H, t, J = 7.8 Hz), 5.67 (1H, t, $J_{H\text{-}F}$ = 55.5 Hz), 6.37 (1H, dd, J = 7.5, 1.0 Hz), 6.54-6.60 (1H, m), 6.64 (1H, dd, J = 7.6, 1.0 Hz), 6.71-6.79 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 13.9, 22.2, 22.7, 23.9, 46.3, 101.0 (t, $J_{C\text{-}F}$ = 23.7 Hz), 104.2, 106.7, 114.1 (dd, $J_{C\text{-}F}$ = 254.8, 251.0 Hz), 117.4, 121.6, 139.6, 148.9; ^{19}F NMR (282 Hz, $CDCl_3$) δ -71.3 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.5 Hz), -66.6 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.5 Hz); MS (ESI-TOF) m/z 270 $[M+H]^+$; HRMS calcd for $C_{15}H_{22}F_2NO$ $[M+H]^+$, 270.1669; found, 270.1668.

3-Benzyl-2-butyl-2-(difluoromethyl)-2,3-dihydro-1,3-benzoxazole (2ca)

This compound was obtained in 73% yield (115.8 mg, 0.37 mmol) by the reaction of **1a** (139.8 mg, 0.5 mmol) and *n*-BuLi (1.55 M in hexane, 0.77 mL, 1.2 mmol) in Et_2O (2 mL) for 5 h at -78 °C. Pale yellow crystals; Mp. 62.5-63.0 °C; IR (neat) 3063, 2959, 2872, 1645, 1600, 1494, 1235, 1074, 732, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (3H, t, J = 7.1 Hz), 1.29-1.44 (3H, m), 1.52-1.61 (1H, m), 2.01-2.07 (2H, m), 4.43 (1H, d, J = 16.1 Hz), 4.54 (1H, d, J = 16.1 Hz), 5.78 (1H, t, $J_{H\text{-}F}$ = 55.3 Hz), 6.12 (1H, d, J = 7.3 Hz), 6.59-6.73 (3H, m), 7.27-7.43 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.7, 23.6, 295, 48.7, 101.2 (t, $J_{C\text{-}F}$ = 23.3 Hz), 106.0, 106.9, 114.3 (dd, $J_{C\text{-}F}$ = 254.5, 251.5 Hz), 118.4, 121.6, 126.8, 127.3, 128.7, 137.7, 139.4, 149.0; ^{19}F NMR (282 Hz, $CDCl_3$) δ -71.0 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.3 Hz), -66.4 (1F, dd, $J_{F\text{-}F}$ = 285.4 Hz, $J_{H\text{-}F}$ = 55.3 Hz); MS (EI) m/z 317 (M^+, 39), 266 (M^+-CHF_2, 100); Anal. Calcd for $C_{19}H_{21}F_2NO$: C, 71.90; H, 6.67; N, 4.41. Found: C, 72.03; H, 6.80; N, 4.41.

4. Multi-component reaction of 1a, *n*-BuLi and aldehydes



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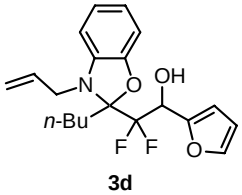
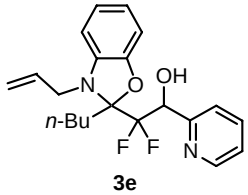
3b R = OMe
3c R = CF_3



3d



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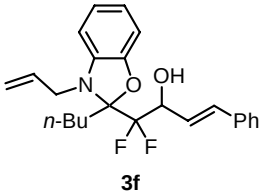

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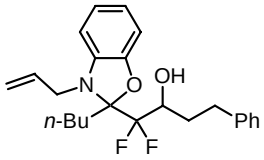
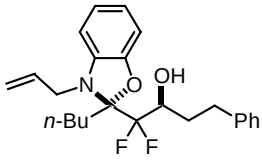


3g



3h (*anti* isomer)

2-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-2,2-difluoro-1-phenylethan-1-ol (3a)

To a solution of **1a** (114.6 mg, 0.5 mmol) in Et_2O (2 mL), *n*-BuLi (1.55 M in hexane, 0.81 mL, 1.25 mmol) was added at -78 °C over 15 min. After being stirred for 4 h at the same temperature, the mixture was treated by a solution of freshly-distilled benzaldehyde (106.9 mg, 1.0 mmol) in Et_2O (1 mL) for 30 min at -78 °C. The resulting mixture was poured into ice water and Et_2O, which was extracted with Et_2O (20 mL x 3). The organic phase was washed with brine, dried over $MgSO_4$ and evaporated. Purification of the residue by silica gel column chromatography (hexane/EtOAc = 20 : 1) and additional MPLC (hexane/EtOAc = 10 : 1) gave **3a-*less*** (66.3 mg, 0.18 mmol, 36%) and **3a-*more*** (92.4 mg, 0.25 mmol, 49%).

3a-*less* Colorless oil; IR (neat) 3543, 3064, 2959, 2872, 1599, 1495, 1401, 1317, 1239, 1031, 731, 731, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.3 Hz), 1.12-1.26 (1H, m), 1.26-1.52 (3H, m), 2.00-2.13 (1H, m), 2.22-2.35 (1H, m), 2.77 (1H, br, OH), 3.70-3.82 (2H, m), 5.19-5.26 (2H, m), 5.33 (1H, d, J = 17.2 Hz), 5.77-5.90 (1H, m), 6.40 (1H, d, 7.6 Hz), 6.62 (1H, t, J = 7.6 Hz), 6.70 (1H, d, J = 7.6 Hz), 6.79 (1H, t, J = 7.6 Hz), 7.29-7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.5, 30.5, 47.7 (d, $J_{C\text{-}F}$ = 2.7 Hz), 72.3 (dd, $J_{C\text{-}F}$ = 30.5, 22.4 Hz), 104.3 (t, $J_{C\text{-}F}$ = 29.3 Hz), 105.5, 106.8, 117.1, 118.1, 119.1 (dd, $J_{C\text{-}F}$ = 265.5, 254.0 Hz), 122.0, 128.05, 128.09, 128.6, 133.9, 136.5, 139.3, 148.6; ^{19}F NMR (282 Hz, $CDCl_3$) δ -60.4 (1F, dd, $J_{F\text{-}F}$ = 269.6 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -52.0 (1F, dd, $J_{F\text{-}F}$ = 269.6 Hz, $J_{H\text{-}F}$ = 4.0 Hz); MS (ESI-TOF) m/z 396 $[M+Na]^+$; HRMS calcd for $C_{22}H_{25}F_2NNaO_2$ $[M+Na]^+$, 396.1751; found, 396.1777. Anal. Calcd for $C_{22}H_{25}F_2NO_2$: C, 70.76; H, 6.75; N, 3.75. Found: C, 70.58; H, 6.98; N, 3.58.

3a-*more* Colorless oil; IR (neat) 3540, 3064, 2959, 2872, 1599, 1465, 1316, 1239, 1086, 1062, 929, 732, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.2 Hz), 1.16-1.52 (4H, m), 2.00-2.18 (2H, m), 3.85 (1H, dd, J = 16.2, 6.5 Hz), 3.96-4.04 (1H, m), 5.13-5.22 (1H, m), 5.29 (1H, dd, J = 10.2, 1.3 Hz), 5.40 (1H, dd, J = 17.2, 1.3 Hz), 5.94-6.07 (1H, m), 6.51 (1H, d, J = 7.5 Hz), 6.60-6.67 (2H, m), 6.74-6.83 (1H, m), 7.30-7.38 (3H, m), 7.39-7.45 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.6, 30.4, 48.1, 72.7 (dd, $J_{C\text{-}F}$ = 28.7, 23.8 Hz), 103.7 (t, $J_{C\text{-}F}$ = 29.6 Hz), 105.9, 106.9, 117.6, 118.5, 118.7 (dd, $J_{C\text{-}F}$ = 260.9, 257.8 Hz), 121.8, 128.0, 128.2, 128.5, 133.9, 136.2, 139.1, 148.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -63.6 (1F, dd, $J_{F\text{-}F}$ = 269.3 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -51.0 (1F, d, $J_{F\text{-}F}$ = 269.3 Hz); MS (ESI-TOF) m/z 396 $[M+H]^+$; HRMS calcd for $C_{22}H_{25}F_2NNaO_2$ $[M+Na]^+$,

396.1751; found, 396.1726. Anal. Calcd for $C_{22}H_{25}F_2NO_2$: C, 70.76; H, 6.75; N, 3.75. Found: C, 70.75; H, 6.77; N, 3.66.

2-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-ol (3b)

This compound was obtained in 79% yield (***less*** 63.8 mg, 0.16 mmol; ***more*** 95.6 mg, 0.24 mmol) by the reaction of **1a** (115.2 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and *p*-anisaldehyde (136.4 mg, 1.0 mmol) in Et_2O (3 mL) for 30 min at -78 °C.

3b-*less* Colorless oil; IR (neat) 3469, 3064, 2958, 2871, 1613, 1599, 1514, 1496, 1249, 1069, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, d, J = 7.3 Hz), 1.12-1.26 (1H, m), 1.26-1.51 (3H, m), 2.00-2.11 (1H, m), 2.22-2.34 (1H, m), 2.69 (1H, br, OH), 3.74 (1H, dd, J = 16.4, 6.1 Hz), 3.76-3.84 (1H, m), 3.80 (3H, s), 5.19 (1H, dd, $J_{H\text{-}F}$ = 17.8, 4.2 Hz), 5.24 (1H, d, J = 10.3 Hz), 5.33 (1H, d, J = 17.2 Hz), 5.78-5.90 (1H, m), 6.39 (1H, m), 6.58-6.64 (1H, m), 6.69 (1H, d, J = 7.6 Hz), 6.75-6.80 (1H, m), 6.86 (2H, d, J = 8.6 Hz), 7.28 (2H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.5, 30.5, 47.6 (d, $J_{C\text{-}F}$ = 2.5 Hz), 55.2, 71.9 (dd, $J_{C\text{-}F}$ = 30.6, 22.7 Hz), 104.2 (t, $J_{C\text{-}F}$ = 29.5 Hz), 105.4, 106.8, 113.5, 117.1, 118.0, 119.2 (dd, $J_{C\text{-}F}$ = 265.6, 253.5 Hz), 122.0, 128.7, 129.3, 133.9, 139.3, 148.6, 159.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -60.7 (1F, dd, $J_{F\text{-}F}$ = 269.3 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -51.3 (1F, dd, $J_{F\text{-}F}$ = 269.5 Hz, $J_{H\text{-}F}$ = 4.2 Hz); MS (ESI-TOF) m/z 426 $[M+Na]^+$; HRMS calcd for $C_{23}H_{27}F_2NNaO_3$ $[M+Na]^+$, 426.1857; found, 426.1863.

3b-*more* Colorless oil; IR (neat) 3485, 3064, 2959, 2872, 1613, 1599, 1514, 1496, 1248, 1176, 1070, 1034, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (3H, d, J = 7.2 Hz), 1.14-1.50 (4H, m), 1.99-2.16 (2H, m), 3.21 (1H, br, OH), 3.80 (3H, s), 3.83 (1H, dd, J = 16.3, 6.2 Hz), 3.96-4.03 (1H, m), 5.09-5.16 (1H, m), 5.27 (1H, dd, J = 10.2, 1.4 Hz), 5.39 (1H, dd, J = 17.2, 1.4 Hz), 5.92-6.05 (1H, m), 6.47 (1H, d, J = 7.5 Hz), 6.59-6.64 (2H, m), 6.73-6.80 (1H, m), 6.86 (2H, d, J = 8.6 Hz), 7.32 (2H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.6, 30.4, 48.1, 55.2, 72.3 (dd, $J_{C\text{-}F}$ = 29.3, 23.2 Hz), 103.7 (t, $J_{C\text{-}F}$ = 28.6 Hz), 105.9, 106.9, 113.5, 117.6, 118.5, 118.8 (dd, $J_{C\text{-}F}$ = 260.6, 257.5 Hz), 121.8, 128.3 (d, $J_{C\text{-}F}$ = 1.2 Hz), 129.4, 133.9, 139.1, 148.8, 159.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -63.7 (1F, dd, $J_{F\text{-}F}$ = 267.3 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -51.3 (1F, d, $J_{F\text{-}F}$ = 267.3 Hz); MS (ESI-TOF) m/z 426 $[M+Na]^+$; HRMS calcd for $C_{23}H_{27}F_2NNaO_3$ $[M+Na]^+$, 426.1857; found, 426.1836.

2-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-2,2-difluoro-1-[4-(trifluoromethyl)phenyl]ethan-1-ol (3c)

This compound was obtained in 85% yield (***less*** 69.5 mg 0.16 mmol; ***more*** 118.2 mg, 0.27 mmol) by the reaction of **1a** (115.2 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and 4-trifluoromethylbenzaldehyde (174.1 mg, 1.0 mmol) in Et_2O (3 mL) for 30 min at -78 °C.

3c-*less* Colorless oil; IR (neat) 3485, 3067, 2961, 2874, 1599, 1496, 1326, 1239, 1167, 1127, 1068, 1018, 930, 782, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.2 Hz), 1.12-1.25 (1H, m), 1.26-1.50 (3H, m), 2.01-2.14 (1H, m), 2.19-2.31 (1H, m), 2.95 (1H, br, OH), 3.70-3.86 (2H, m), 5.21-5.34 (2H, m), 5.34 (1H, d, J = 16.3 Hz), 5.74-5.90 (1H, m), 6.42 (1H, d, J = 7.5 Hz),

6.60-6.69 (1H, m), 6.42 (1H, d, J = 7.5 Hz), 6.60-6.69 (1H, m), 6.70 (1H, d, J = 7.5 Hz), 6.77-6.84 (1H, m), 7.47 (2H, d, J = 8.2 Hz), 7.59 (2H, d, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.4, 30.4, 47.9 (d, $J_{C\text{-}F}$ = 3.0 Hz), 71.9 (dd, $J_{C\text{-}F}$ = 29.5, 23.3 Hz), 104.4 (t, $J_{C\text{-}F}$ = 29.4 Hz), 105.8, 107.0, 117.3, 118.5, 118.8 (dd, $J_{C\text{-}F}$ = 266.2, 254.3 Hz), 122.3, 124.1 (q, $J_{C\text{-}F}$ = 272.0 Hz), 124.9 (q, $J_{C\text{-}F}$ = 3.7 Hz), 128.5, 130.7 (q, $J_{C\text{-}F}$ = 32.5 Hz), 133.7, 139.2, 140.2, 148.4; ^{19}F NMR (282 Hz, $CDCl_3$) δ -59.7 (1F, dd, $J_{F\text{-}F}$ = 269.6, $J_{H\text{-}F}$ = 18.0 Hz), -52.3 (1F, d, $J_{F\text{-}F}$ = 269.6 Hz), 0.05 (3F, s); MS (ESI-TOF) m/z 464 $[M+Na]^+$; HRMS calcd for $C_{23}H_{24}F_5NNaO_2$ $[M+Na]^+$, 464.1625; found, 464.1628.

3c-*more* Colorless oil; IR (neat) 3500, 3067, 2961, 2874, 1599, 1494, 1326, 1239, 1166, 1127, 1067, 1019, 735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 7.2 Hz), 1.21-1.52 (4H, m), 2.04-2.20 (2H, m), 3.54 (1H, br, OH), 3.84 (1H, dd, J = 16.1, 6.6 Hz), 3.96-4.04 (1H, m), 5.19-5.28 (1H, m), 5.30 (1H, dd, J = 10.2, 1.4 Hz), 5.42 (1H, dd, J = 17.2, 1.4 Hz), 5.94-6.07 (1H, m), 6.53 (1H, d, J = 7.6 Hz), 6.57-6.68 (2H, m), 6.76-6.84 (1H, m), 7.52 (2H, d, J = 8.3 Hz), 7.58 (2H, d, J = 8.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.6, 23.5, 30.3, 48.4, 72.3 (dd, $J_{C\text{-}F}$ = 28.9, 23.7 Hz), 103.7 (t, $J_{C\text{-}F}$ = 28.7 Hz), 106.3, 107.1, 117.9, 118.3 (t, $J_{C\text{-}F}$ = 260.3 Hz), 119.0, 122.0, 124.1 (q, $J_{C\text{-}F}$ = 272.2 Hz), 124.8, (q, $J_{C\text{-}F}$ = 3.6 Hz), 128.6, 130.5 (q, $J_{C\text{-}F}$ = 32.4 Hz), 133.7, 139.0, 140.0, 148.6; ^{19}F NMR (282 Hz, $CDCl_3$) δ -63.4 (1F, dd, $J_{F\text{-}F}$ = 269.7, 17.9 Hz), -50.8 (1F, d, $J_{F\text{-}F}$ = 269.7 Hz), 0.05 (3F, s); MS (ESI-TOF) m/z 442 $[M+H]^+$; HRMS calcd for $C_{23}H_{25}F_5NO_2$ $[M+H]^+$, 442.1805; found, 442.1800.

2-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-2,2-difluoro-1-(2-furyl)ethan-1-ol (3d)

This compound was obtained in 87% yield (***less*** 71.9 mg, 0.198 mmol; ***more*** 86.3 mg, 0.237 mmol) by the reaction of **1a** (115.3 mg, 0.50 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and furfural (96.1 mg, 1.0 mmol) in Et_2O (3 mL) for 1 h at -78 °C.

3d-*less* Colorless oil; IR (neat) 3442, 3065, 2959, 2872, 1599, 1496, 1239, 1110, 1080, 924, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, d, J = 7.2 Hz), 1.14-1.52 (4H, m), 2.00-2.12 (1H, m), 2.20-2.31 (1H, m), 2.68 (1H, br, OH), 3.78 (1H, dd, J = 16.3, 6.3 Hz), 3.81-3.89 (1H, m), 5.19-5.30 (2H, m), 5.33 (1H, d, J = 17.2 Hz), 5.79-5.83 (1H, m), 6.28-6.36 (2H, m), 6.38 (1H, d, J = 7.6 Hz), 6.75 (1H, td, J = 7.6, 1.0 Hz), 6.65 (1H, d, J = 7.6, 1.0 Hz), 6.71-6.79 (1H, m), 7.39-7.42 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.5, 30.4, 47.6, 66.9 (dd, $J_{C\text{-}F}$ = 30.6, 24.4 Hz), 103.6 (t, $J_{C\text{-}F}$ = 28.4 Hz), 105.3, 106.7, 109.3, 110.4, 117.1, 118.0, 119.0 (dd, $J_{C\text{-}F}$ = 264.6, 256.0 Hz), 121.8, 134.0, 139.2, 142.7, 147.7, 149.7; ^{19}F NMR (282 Hz, $CDCl_3$) δ -59.2 (1F, dd, $J_{F\text{-}F}$ = 267.3 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -51.3 (1F, dd, $J_{F\text{-}F}$ = 267.3 Hz, $J_{H\text{-}F}$ = 5.9 Hz); MS (ESI-TOF) m/z 386 $[M+Na]^+$; HRMS calcd for $C_{20}H_{23}F_2NNaO_3$ $[M+Na]^+$, 386.1544; found, 386.1543.

3d-*more* Colorless oil; IR (neat) 3521, 3064, 2959, 2872, 1599, 1496, 1240, 1110, 1083, 1060, 1013, 923, 791, 734 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (3H, t, J = 7.2 Hz), 1.13-1.25 (1H, m), 1.25-1.49 (3H, m), 1.93-2.03 (1H, m), 2.04-2.15 (1H, m), 2.98 (1H, br, OH), 3.83 (1H, dd, J = 16.3, 6.3 Hz), 3.95-4.05 (1H, m), 5.17-5.30 (1H, m), 5.26 (1H, dd, J = 10.3, 1.5 Hz), 5.38 (1H, dd, J = 17.2, 1.5 Hz), 5.91-6.04 (1H, m), 6.32 (2H, d, J = 1.3 Hz), 6.46 (1H, d, J = 7.2 Hz), 6.55-6.63 (2H, m),

6.71-6.79 (1H, m), 7.40 (1H, t, J = 1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.5, 23.5, 30.1, 48.0, 66.9 (dd, $J_{C\text{-}F}$ = 29.0, 24.9 Hz), 103.3 (t, $J_{C\text{-}F}$ = 28.0 Hz), 105.8, 106.9, 109.6, 110.4, 117.5, 118.4, 118.7 (t, $J_{C\text{-}F}$ = 260.0 Hz), 121.7, 133.9, 139.1, 142.7, 148.8, 149.4 (d, $J_{C\text{-}F}$ = 3.0 Hz); ^{19}F NMR (282 Hz, $CDCl_3$) δ -60.7 (1F, dd, $J_{F\text{-}F}$ = 267.6 Hz, $J_{H\text{-}F}$ = 15.8 Hz), -51.3 (1F, dd, $J_{F\text{-}F}$ = 267.6 Hz, $J_{H\text{-}F}$ = 7.9 Hz); MS (ESI-TOF) m/z 386 $[M+Na]^+$; HRMS calcd for $C_{20}H_{23}F_2NNaO_3$ $[M+Na]^+$, 386.1544; found, 386.1542.

2-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-2,2-difluoro-1-pyridin-2-ylethan-1-ol (3e)

This compound was obtained in 87% yield (***less*** 125.8 mg, 0.34 mmol; ***more*** 37.0 mg, 0.099 mmol) by the reaction of **1a** (115.6 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and 2-pyridinecarbaldehyde (106.9 mg, 1.0 mmol) in Et_2O (3 mL) for 15 min at -78 °C.

3e-*less* Colorless oil; IR (neat) 3365, 3063, 2958, 2871, 1597, 1496, 1402, 1315, 1239, 1206, 1110, 1085, 935, 754, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7.2 Hz), 1.20-1.60 (4H, m), 2.06-2.18 (1H, m), 2.53-2.66 (1H, m), 3.86 (1H, dd, J = 16.5, 6.0 Hz), 3.94 (1H, dd, J = 16.5, 5.6 Hz), 5.06-5.60 (1H, br, OH), 5.20 (1H, dd, J = 10.4, 1.2 Hz), 5.25 (1H, $J_{H\text{-}F}$ = 21.7 Hz), 5.34 (1H, dd, J = 17.2, 1.2 Hz), 5.84-5.97 (1H, m), 6.49 (1H, d, J = 7.5 Hz), 6.57 (1H, t, J = 7.5 Hz), 6.65 (1H, d, J = 7.5 Hz), 6.75 (1H, t, J = 7.5 Hz), 7.24-7.28 (1H, m), 7.34 (1H, dd, J = 7.8, 2.7 Hz), 7.61-7.69 (1H, m), 8.54 (1H, d, J = 4.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 23.8, 31.2, 47.2, 70.7 (dd, $J_{C\text{-}F}$ = 32.4, 24.3 Hz), 103.7 (dd, $J_{C\text{-}F}$ = 29.3, 24.5 Hz), 104.5, 106.4, 116.8, 117.2, 120.1 (dd, $J_{C\text{-}F}$ = 264.8, 255.4 Hz), 121.4, 123.47, 123.50 (t, $J_{C\text{-}F}$ = 5.4 Hz), 134.1, 136.4, 139.4, 147.7, 149.2, 153.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -61.8 (1F, dd, $J_{F\text{-}F}$ = 263.4 Hz, $J_{H\text{-}F}$ = 21.7 Hz), -51.0 (1F, d, $J_{F\text{-}F}$ = 263.4 Hz); MS (ESI-TOF) m/z 397 $[M+Na]^+$; HRMS calcd for $C_{21}H_{24}F_2N_2NaO_2$ $[M+Na]^+$, 397.1704; found, 397.1714. Anal. Calcd for $C_{21}H_{24}F_2N_2O_2$: C, 67.36; H, 6.46; N, 7.48. Found: C, 67.35; H, 6.53; N, 7.42.

3e-*more* Colorless oil; IR (neat) 3361, 2958, 2871, 1597, 1495, 1401, 1313, 1241, 1207, 1109, 1085, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.1 Hz), 1.15-1.51 (4H, m), 2.13-2.31 (2H, m), 3.87 (1H, dd, J = 16.7, 5.7 Hz), 4.03-4.12 (1H, m), 5.10 (1H, dd, $J_{H\text{-}F}$ = 17.8, 4.6 Hz), 5.24 (1H, dd, J = 10.3, 1.5 Hz), 5.39 (1H, dd, J = 17.2, 1.5 Hz), 5.91-6.02 (1H, m), 6.41 (1H, d, J = 7.5 Hz), 6.47 (1H, d, J = 7.6 Hz), 6.51-6.57 (1H, m), 6.70-6.77 (1H, m), 7.26-7.31 (1H, m), 7.34 (1H, d, J = 8.0 Hz), 7.63-7.70 (1H, m), 8.58 (1H, d, J = 4.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 23.7, 31.0, 47.6, 70.9 (dd, $J_{C\text{-}F}$ = 29.8, 26.2 Hz), 103.6 (t, $J_{C\text{-}F}$ = 26.5 Hz), 105.3, 106.3, 116.8, 117.7, 119.5 (dd, $J_{C\text{-}F}$ = 263.0, 257.9 Hz), 121.4, 123.3 (br), 123.5, 134.2, 136.6, 139.6, 147.7, 149.1, 153.9; ^{19}F NMR (282 Hz, $CDCl_3$) δ -60.6 (1F, dd, $J_{F\text{-}F}$ = 265.6 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -51.6 (1F, dd, $J_{F\text{-}F}$ = 265.6 Hz, $J_{H\text{-}F}$ = 4.6 Hz); MS (ESI-TOF) m/z 397 $[M+Na]^+$; HRMS calcd for $C_{21}H_{24}F_2N_2NaO_2$ $[M+Na]^+$, 397.1704; found, 397.1678. Anal. Calcd for $C_{21}H_{24}F_2N_2O_2$: C, 67.36; H, 6.46; N, 7.48. Found: C, 67.41; H, 6.66; N, 7.43.

(*E*)-1-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-1,1-difluoro-4-phenylbut-3-en-2-ol (3f)

This compound was obtained in 87% yield (***less*** 86.5 mg, 0.236 mmol; ***more*** 72.1 mg, 0.199 mmol)

by the reaction of **1a** (115.5 mg, 0.50 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and cinnamaldehyde (132.2 mg, 1.0 mmol) in Et_2O (3 mL) for 1 h at -78 °C.

3f-*less* Colorless oil; IR (neat) 3417, 3061, 2959, 2871, 1599, 1496, 1238, 1070, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7.2 Hz), 1.17-1.55 (4H, m), 2.05-2.17 (1H, m), 2.22-2.34 (1H, m), 2.52 (1H, br, OH), 3.82 (1H, dd, J = 16.3, 6.3 Hz), 3.94 (1H, dd, J = 16.3, 5.1 Hz), 4.80 (1H, ddd, $J_{H\text{-}F}$ = 13.8, 9.9 Hz, $J_{H\text{-}H}$ = 6.9 Hz), 5.22 (1H, d, J = 10.2 Hz), 5.34 (1H, d, J = 17.2 Hz), 5.86-5.99 (1H, m), 6.28 (1H, dd, J = 15.9, 6.9 Hz), 6.37 (1H, d, J = 7.5 Hz), 6.52 (1H, d, J = 15.9 Hz), 6.60 (1H, t, J = 7.5 Hz), 6.68 (1H, d, J = 7.5 Hz), 6.74 (1H, t, J = 7.5 Hz), 7.22-7.37 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.5, 23.4, 30.4, 47.8, 71.6 (t, $J_{C\text{-}F}$ = 26.4 Hz), 103.5 (t, $J_{C\text{-}F}$ = 29.0 Hz), 105.4, 106.7, 117.2, 118.0, 119.8 (dd, $J_{C\text{-}F}$ = 261.8, 257.1 Hz), 122.4, 123.5 (t, $J_{C\text{-}F}$ = 3.2 Hz), 126.7, 127.9, 128.4, 133.7, 133.9, 136.1, 139.2, 148.7; ^{19}F NMR (282 Hz, $CDCl_3$) δ -57.6 (1F, dd, $J_{F\text{-}F}$ = 267.6 Hz, $J_{H\text{-}F}$ = 13.8 Hz), -56.4 (1F, dd, $J_{F\text{-}F}$ = 267.6 Hz, $J_{H\text{-}F}$ = 9.9 Hz); MS (ESI-TOF) m/z 422 $[M+Na]^+$; HRMS calcd for $C_{24}H_{27}F_2NNaO_2$ $[M+Na]^+$, 422.1908; found, 422.1899. Anal. Calcd for $C_{24}H_{27}F_2NO_2$: C, 72.16; H, 6.81; N, 3.51. Found: C, 71.91; H, 6.83; N, 3.49.

3f-*more* Colorless oil; IR (neat) 3426, 3061, 2959, 2872, 1599, 1495, 1239, 1069, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (3H, t, J = 7.2 Hz), 1.12-1.51 (4H, m), 2.05-2.21 (2H, m), 2.69 (1H, br, OH), 3.82 (1H, dd, J = 16.2, 6.4 Hz), 3.98 (1H, dd, J = 16.2, 4.9 Hz), 4.75 (1H, ddd, $J_{H\text{-}F}$ = 23.8, 9.2 Hz, $J_{H\text{-}H}$ = 7.0 Hz), 5.25 (1H, d, J = 10.2 Hz), 5.36 (1H, d, J = 17.1 Hz), 5.90-6.03 (1H, m), 6.26 (1H, dd, J = 16.0, 7.0 Hz), 6.45 (1H, d, J = 7.6 Hz), 6.50-6.58 (3H, m), 6.69-6.78 (1H, m), 7.20-7.33 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.4, 30.2, 48.1, 71.8 (dd, $J_{C\text{-}F}$ = 27.9, 24.5 Hz), 103.4 (t, $J_{C\text{-}F}$ = 28.6 Hz), 105.6, 107.3, 117.5, 118.4, 119.4 (t, $J_{C\text{-}F}$ = 259.1 Hz), 121.7, 123.4 (t, $J_{C\text{-}F}$ = 3.3 Hz), 126.7, 127.9, 128.4, 133.9, 134.1, 136.2, 139.1, 148.7; ^{19}F NMR (282 Hz, $CDCl_3$) δ -60.8 (1F, dd, $J_{F\text{-}F}$ = 266.4 Hz, $J_{H\text{-}F}$ = 12.8 Hz), -54.9 (1F, dd, $J_{F\text{-}F}$ = 266.4 Hz, $J_{H\text{-}F}$ = 9.2 Hz); MS (ESI-TOF) m/z 422 $[M+Na]^+$; HRMS calcd for $C_{24}H_{27}F_2NNaO_2$ $[M+Na]^+$, 422.1908; found, 422.1883. Anal. Calcd for $C_{24}H_{27}F_2NO_2$: C, 72.16; H, 6.81; N, 3.51. Found: C, 71.91; H, 6.91; N, 3.32.

1-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-1,1-difluoro-4-phenylbutan-2-ol (3g)

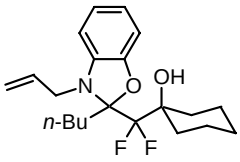
This compound was obtained in 76% yield (152.6 mg, 0.38 mmol) as an inseparatable mixture of diastereomers in a ratio of 1 : 10.7 (*less*/*more*) by the reaction of **1a** (114.9 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and 3-phenylpropionaldehyde (137.1 mg, 1.0 mmol) in Et_2O (3 mL) for 3 h at -24 °C. Spectra date only for the major isomer (less polar isomer) are only shown. Colorless oil; IR (neat) 3547, 3063, 3027, 2959, 2871, 1599, 1495, 1240, 1085, 734, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7.2 Hz), 1.19-1.33 (1H, m), 1.34-1.59 (3H, m), 1.93-2.06 (1H, m), 2.06-2.20 (3H, m), 2.67-2.78 (2H, m), 2.89-3.00 (1H, m), 3.85 (1H, dd, J = 16.3, 6.3 Hz), 3.96-4.04 (1H, m), 4.08-4.21 (1H, m), 5.28 (1H, d, J = 10.2 Hz), 5.37 (1H, d, J = 17.2 Hz), 5.89-6.01 (1H, m), 6.51 (1H, d, J = 7.5 Hz), 6.67-6.76 (2H, m), 6.81-6.87 (1H, m), 7.18-7.28 (3H, m), 7.29-7.36 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.6, 30.3, 31.4, 48.1, 69.4 (dd, $J_{C\text{-}F}$ = 29.0, 23.7 Hz), 103.6 (t, $J_{C\text{-}F}$ = 28.9 Hz), 105.9, 106.8, 117.4, 118.5, 119.5 (t, $J_{C\text{-}F}$ = 258.6 Hz), 121.8, 125.8,

128.3, 128.4, 133.8, 139.0, 141.4, 148.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -64.0 (1F, dd, $J_{F\text{-}F}$ = 267.3 Hz, $J_{H\text{-}F}$ = 17.8 Hz), -54.6 (1F, d, $J_{F\text{-}F}$ = 267.3 Hz); MS (ESI-TOF) *m*/*z* 424 $[M+Na]^+$; HRMS calcd for $C_{24}H_{29}F_2NNaO_2$ $[M+Na]^+$, 424.2064; found, 424.2044.

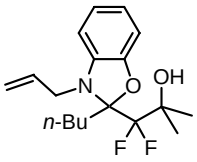
(1*S)-2-[(2*S**)-3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-1-cyclohexyl-2,2-difluoroethan-1-ol (*anti*-3h).**

This compound was obtained in 81% yield (153.7 mg, 0.40 mmol) as an inseparatable mixture of diastereomers in a ratio of 1 : 10.5 by the reaction of **1a** (115.4 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and cyclohexanecarbaldehyde (112.3 mg, 1.0 mmol) in Et_2O (3 mL) for 8 h at 0 °C. Spectra date only for major ***anti*-3h** are shown. Colorless crystals; Mp. 49.0-50.0 °C; IR (neat) 3564, 2929, 2854, 1599, 1496, 1240, 1089, 924, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, *J* = 7.2), 1.08-1.52 (9H, m), 1.53-1.61 (1H, m), 1.62-1.70 (1H, m), 1.70-1.94 (4H, m), 2.11 (2H, t, *J* = 7.4 Hz), 2.51 (1H, br, OH), 3.81 (1H, dd, *J* = 16.3, 6.3 Hz), 3.86-4.06 (2H, m), 5.27 (1H, dd, *J* = 10.3, 1.4 Hz), 5.38 (1H, dd, *J* = 17.1, 1.4 Hz), 5.91-6.04 (1H, m), 6.47 (1H, d, *J* = 7.5 Hz), 6.59-6.70 (2H, m), 6.73-6.80 (1H, td, *J* = 7.5, 1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ for major isomer 13.9, 22.6, 23.7, 26.1, 26.2 (2C), 26.7, 30.2, 30.4, 38.4 (d, $J_{C\text{-}F}$ = 2.5 Hz), 48.2, 73.1 (dd, $J_{C\text{-}F}$ = 28.2, 22.2 Hz), 103.8 (t, $J_{C\text{-}F}$ = 28.9 Hz), 105.8, 106.7, 117.4, 118.4, 120.2 (t, $J_{C\text{-}F}$ = 260.4 Hz), 121.7, 134.0, 139.3, 149.0; ^{19}F NMR (282 Hz, $CDCl_3$) δ for major isomer -60.6 (1F, dd, $J_{F\text{-}F}$ = 269.6 Hz, $J_{H\text{-}F}$ = 21.7 Hz), -52.6 (1F, d, $J_{F\text{-}F}$ = 269.6 Hz), for minor isomer -58.3 (1F, dd, $J_{F\text{-}F}$ = 265.6 Hz, $J_{H\text{-}F}$ = 21.7 Hz), -55.5 (1F, d, $J_{F\text{-}F}$ = 265.6 Hz); MS (ESI-TOF) *m*/*z* 402 $[M+Na]^+$; HRMS calcd for $C_{22}H_{31}F_2NNaO_2$ $[M+Na]^+$, 402.2221; found, 402.2206. Anal. Calcd for $C_{22}H_{31}F_2NO_2$: C, 69.63; H, 8.23; N, 3.69. Found: C, 69.82; H, 8.11; N, 3.73.

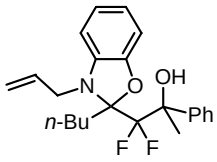
5. Multi-component reaction of 1a, *n*-BuLi and ketones



4a



4b



4c

1-[(3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl)(difluoro)methyl]cyclohexanol (4a)

This compound was obtained in 84% yield (153.5 mg, 0.42 mmol) by the reaction of **1a** (115.7 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and cyclohexanone (97.2 mg, 1.0 mmol) in Et_2O (3 mL) for 5 h at 0 °C.

4a Colorless oil; IR (neat) 3548, 3064, 2936, 2864, 1599, 1496, 1239, 1086, 989, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (3H, t, *J* = 7.3 Hz), 1.08-1.22 (2H, m), 1.24-1.48 (3H, m), 1.51-1.79 (8H, m), 1.91-2.00 (1H, m), 2.02-2.13 (1H, m), 2.23-2.34 (1H, m), 2.26 (1H, brs, OH), 3.81 (1H, dd, *J* = 16.2, 6.5 Hz), 3.94-4.03 (1H, m), 5.25 (1H, dd, *J* = 10.2, 1.4 Hz), 5.37 (1H, dd, *J* = 17.2, 1.4 Hz), 5.91-6.03 (1H, m), 6.45 (1H, d, *J* = 7.5 Hz), 6.57-6.67 (2H, m), 6.75 (1H, td, *J* = 7.5, 1.4 Hz); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 14.0, 20.8, 20.9, 22.6, 23.8, 25.3, 30.6 (m), 31.5 (t, $J_{C\text{-}F}$ = 3.3 Hz), 32.2, 48.3, 75.4 (t, $J_{C\text{-}F}$ = 25.2 Hz), 105.2 (t, $J_{C\text{-}F}$ = 28.8 Hz), 105.6, 106.6, 117.3, 118.1, 120.7 (t, $J_{C\text{-}F}$ = 260.9 Hz), 121.6, 134.1, 139.3, 148.9; ^{19}F NMR (282 Hz, $CDCl_3$) δ -57.4 (1F, d, $J_{F\text{-}F}$ = 271.6 Hz), -55.8 (1F, d, $J_{F\text{-}F}$ = 271.6 Hz); MS (ESI-TOF) *m*/*z* 388 $[M+Na]^+$; HRMS calcd for $C_{21}H_{29}F_2NNaO_2$ $[M+Na]^+$, 388.2064; found, 388.2071. Anal. Calcd for $C_{21}H_{29}F_2NO_2$: C, 69.02; H, 8.00; N, 3.83. Found: C, 68.98; H, 7.91; N, 3.73.

1-(3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl)-1,1-difluoro-2-methylpropan-2-ol (4b):

This compound was obtained in 89% yield (144.8 mg, 0.45 mmol) by the reaction of **1a** (115.7 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and acetone (58.2 mg, 1.0 mmol) in Et_2O (3 mL) for 9 h at room temperature.

4b Colorless oil; IR (neat) 3464, 3064, 2959, 2873, 1599, 1496, 1239, 1071, 732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, *J* = 7.3 Hz), 1.11-1.25 (1H, m), 1.26-1.50 (3H, m), 1.36 (3H, s), 1.40 (3H, s), 2.03-2.16 (1H, m), 2.22-2.36 (1H, m), 2.59 (1H, brs, OH), 3.82 (1H, dd, *J* = 16.1, 6.5 Hz), 3.99 (1H, dd, *J* = 16.1, 4.9 Hz), 5.26 (1H, d, *J* = 10.3 Hz), 5.38 (1H, d, *J* = 17.2 Hz), 5.91-6.06 (1H, m), 6.47 (1H, d, *J* = 7.4 Hz), 6.58-6.67 (2H, m), 6.73-6.80 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.6, 23.7, 14.7 (t, $J_{C\text{-}F}$ = 3.2 Hz), 25.6 (t, J = 3.3 Hz), 31.9, 48.4, 74.2 (t, $J_{C\text{-}F}$ = 26.4 Hz), 104.8 (dd, $J_{C\text{-}F}$ = 30.4, 29.6 Hz), 105.7, 106.7, 117.4, 118.3, 120.7 (t, $J_{C\text{-}F}$ = 260.9 Hz), 121.7, 134.0, 139.1, 148.8; ^{19}F NMR (282 Hz, $CDCl_3$) δ -55.9 (1F, d, *J* = 271.4 Hz), -53.6 (1F, d, *J* = 271.4 Hz); MS (ESI-TOF) *m*/*z* 326 $[M+H]^+$; HRMS calcd for $C_{18}H_{26}F_2NO_2$ $[M+H]^+$, 326.1964; found, 326.1964.

1-[3-Allyl-2-butyl-2,3-dihydro-1,3-benzoxazol-2-yl]-1,1-difluoro-2-phenylpropan-2-ol (4c)

This compound were obtained in 79% yield (***less*** 98.4 mg, 0.254 mmol; ***more*** 54.6 mg, 0.141 mmol) by the reaction of **1a** (115.6 mg, 0.5 mmol), *n*-BuLi (1.42 M in hexane, 0.88 mL, 1.25 mmol) and acetophenone (120.3 mg, 1.0 mmol) in Et_2O (3 mL) for 9 h at room temperature.

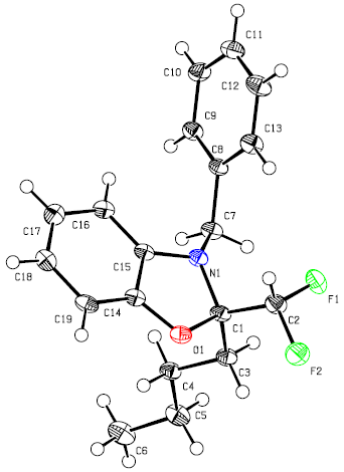
4c-*less* Colorless oil; IR (neat) 3542, 3062, 2959, 2872, 1599, 1496, 1239, 1093, 1067, 925, 732, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (3H, t, *J* = 7.2 Hz), 1.04-1.17 (1H, m), 1.18-1.38 (3H, m), 1.76 (3H, s), 1.79-1.89 (1H, m), 1.89-2.00 (1H, m), 3.82 (1H, dd, *J* = 16.0, 6.8 Hz), 3.92-4.01 (1H, m), 4.06 (1H, br, OH), 5.34 (1H, dd, *J* = 10.2, 1.4 Hz), 5.44 (1H, dd, *J* = 17.2, 1.4 Hz), 5.99-6.01 (1H, m), 6.33 (1H, dd, *J* = 7.7, 0.9 Hz), 6.52 (1H, dd, *J* = 7.5, 1.1 Hz), 6.55-6.60 (1H, m), 6.75-6.81 (1H, m), 7.24-7.33 (3H, m), 7.46-7.52 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 22.4, 23.4, 25.5 (t, $J_{C\text{-}F}$ = 3.7 Hz), 31.5, 48.5, 76.7-77.3 (m), 105.0 (t, $J_{C\text{-}F}$ = 29.9 Hz), 106.0, 106.9, 117.8, 118.7, 119.9 (t, $J_{C\text{-}F}$ = 264.0 Hz), 121.6, 125.4 (d, $J_{C\text{-}F}$ = 2.4 Hz), 127.2, 127.6, 133.9, 138.8, 142.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 148.3; ^{19}F NMR (282 Hz, $CDCl_3$) δ -53.8 (1F, d, $J_{F\text{-}F}$ = 271.3 Hz), -48.9 (1F, d, $J_{F\text{-}F}$ = 271.3 Hz); MS (ESI-TOF) *m*/*z* 410 $[M+Na]^+$; HRMS calcd for $C_{23}H_{27}F_2NNaO_2$ $[M+Na]^+$, 410.1908; found, 410.1872. Anal. Calcd for $C_{23}H_{27}F_2NO_2$: C, 71.30; H, 7.02; N, 3.61. Found: C, 71.32; H, 7.04; N, 3.48.

4c-*more* Colorless oil; IR (neat) 3548, 3062, 2959, 2872, 1599, 1496, 1239, 1090, 1074, 921, 732,

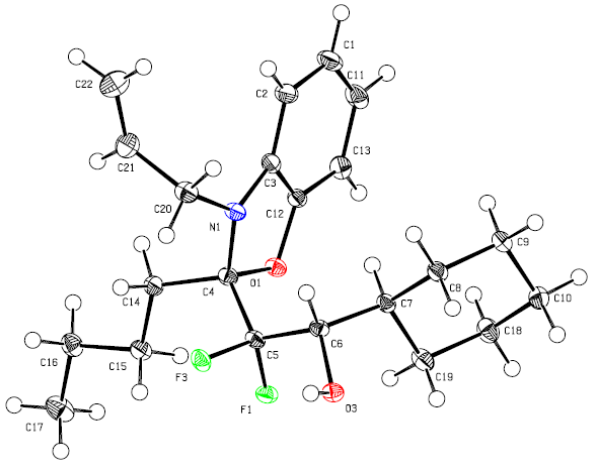
701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (3H, t, J = 7.2 Hz), 1.08-1.20 (1H, m), 1.22-1.41 (3H, m), 1.74 (3H, s), 1.93-2.04 (1H, m), 2.15-2.25 (1H, m), 3.23 (1H, br, OH), 3.62 (1H, dd, J = 16.2, 5.4 Hz), 3.69 (1H, dd, J = 16.2, 6.6 Hz), 5.21 (1H, dd, J = 10.2, 1.4 Hz), 5.30 (1H, dd, J = 17.2, 1.4 Hz), 5.81-5.94 (1H, m), 6.26 (1H, dd, J = 7.5, 1.0 Hz), 6.47 (1H, dd, J = 7.6, 1.0 Hz), 6.54-6.61 (1H, m), 6.68-6.74 (1H, m), 7.23-7.34 (3H, m), 7.42-7.49 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.5, 23.5, 26.4 (t, J_{C-F} = 3.5 Hz), 31.7, 47.7, 76.5-77.1 (m), 104.8 (t, J_{C-F} = 29.8 Hz), 105.7, 106.7, 117.4, 118.0, 120.2 (t, J_{C-F} = 263.8 Hz), 121.5, 126.1, 127.2, 127.5, 133.9, 138.6, 141.4 (d, J_{C-F} = 2.8 Hz), 148.6; ^{19}F NMR (282 Hz, $CDCl_3$) δ -52.4 (1F, d, J_{F-F} = 271.3 Hz), -50.2 (1F, d, J_{F-F} = 271.3 Hz); MS (ESI-TOF) m/z 410 $[M+Na]^+$; HRMS calcd for $C_{23}H_{27}F_2NNaO_2$ $[M+Na]^+$, 410.1908; found, 410.1889.

6. X-ray crystallographic data of 2ca and *anti*-3h

Crystallographic data for the X-ray crystal structure analysis of **2ca** and ***anti*-3h** have been deposited with Cambridge Crystallographic Data Center (CCDC) as supplementary publication Nos. CCDC 702162 (**2ca**) and 702163 (***anti*-3h**). These data can be obtained free of charge from the CCDC *via* www.ccdc.cam.ac.uk/data_request/cif.



X-ray structure of **2ca**



X-ray structure of ***anti*-3h**

Table 1. Crystal data and structure refinement for compound **2ca**.

Empirical formula	C19 H21 F2 N O	
Formula weight	317.37	
Temperature	90 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.979(6) Å	α= 97.534(11)°.
	b = 9.368(6) Å	β= 97.342(11)°.
	c = 10.983(13) Å	γ = 113.009(8)°.

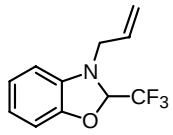
Volume	826.5(12) $Å^3$
Z	2
Density (calculated)	1.275 Mg/m^3
Absorption coefficient	0.094 mm^{-1}
F(000)	336
Crystal size	0.29 x 0.17 x 0.14 mm^3
Theta range for data collection	1.91 to 27.42°.
Index ranges	-8<=h<=11, -11<=k<=12, -13<=l<=9
Reflections collected	3930
Independent reflections	3073 [R(int) = 0.0253]
Completeness to theta = 27.42°	81.3 %
Absorption correction	Empirical
Max. and min. transmission	0.9870 and 0.9734
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3073 / 0 / 209
Goodness-of-fit on F^2	1.088
Final R indices [I>2sigma(I)]	R1 = 0.0577, wR2 = 0.1747
R indices (all data)	R1 = 0.0710, wR2 = 0.1877
Largest diff. peak and hole	0.366 and -0.306 $e.Å^{-3}$

Table 2. Crystal data and structure refinement for compound ***anti*-3h**.

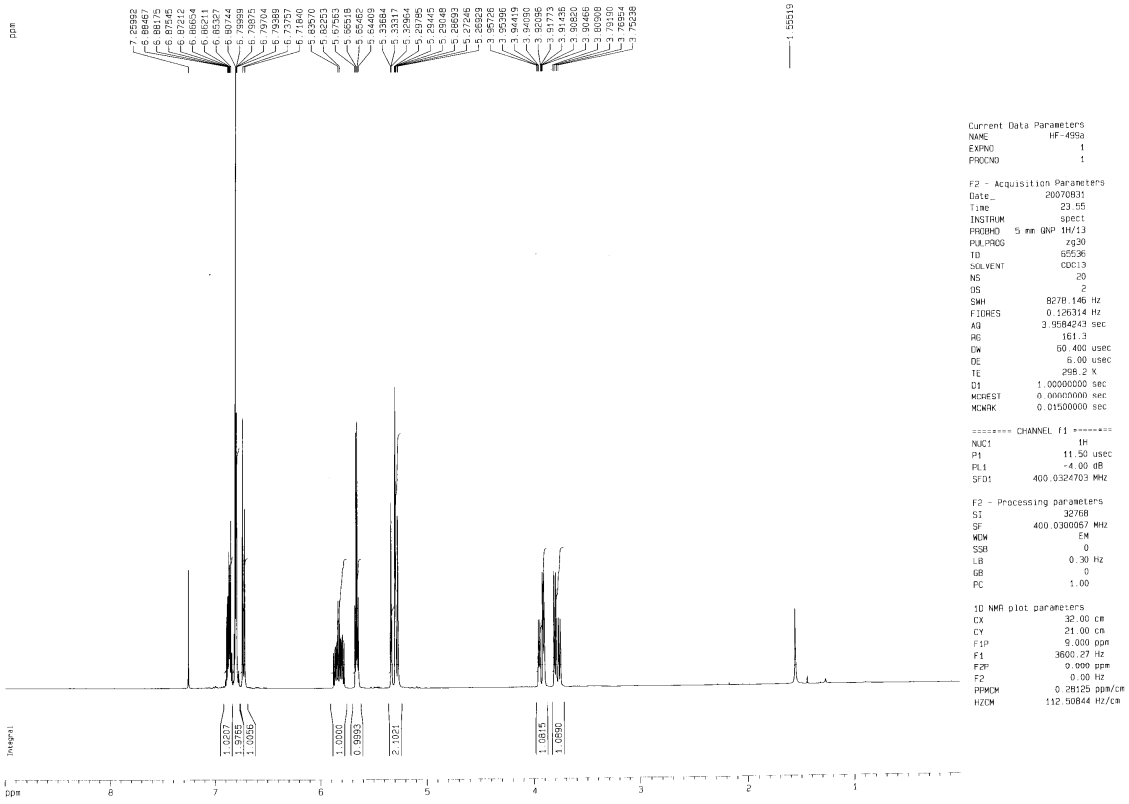
Empirical formula	C22 H31 F2 N O2
Formula weight	379.48
Temperature	90 K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 12.9702(11) Å α= 76.3530(10)°.
	b = 13.2002(11) Å β= 68.1340(10)°.
	c = 13.8440(12) Å γ = 67.3330(10)°.
Volume	2017.9(3) $Å^3$
Z	4
Density (calculated)	1.249 Mg/m^3
Absorption coefficient	0.091 mm^{-1}
F(000)	816
Crystal size	0.27 x 0.25 x 0.24 mm^3
Theta range for data collection	1.59 to 27.62°.
Index ranges	-16<=h<=16, -17<=k<=17, -17<=l<=18
Reflections collected	23356

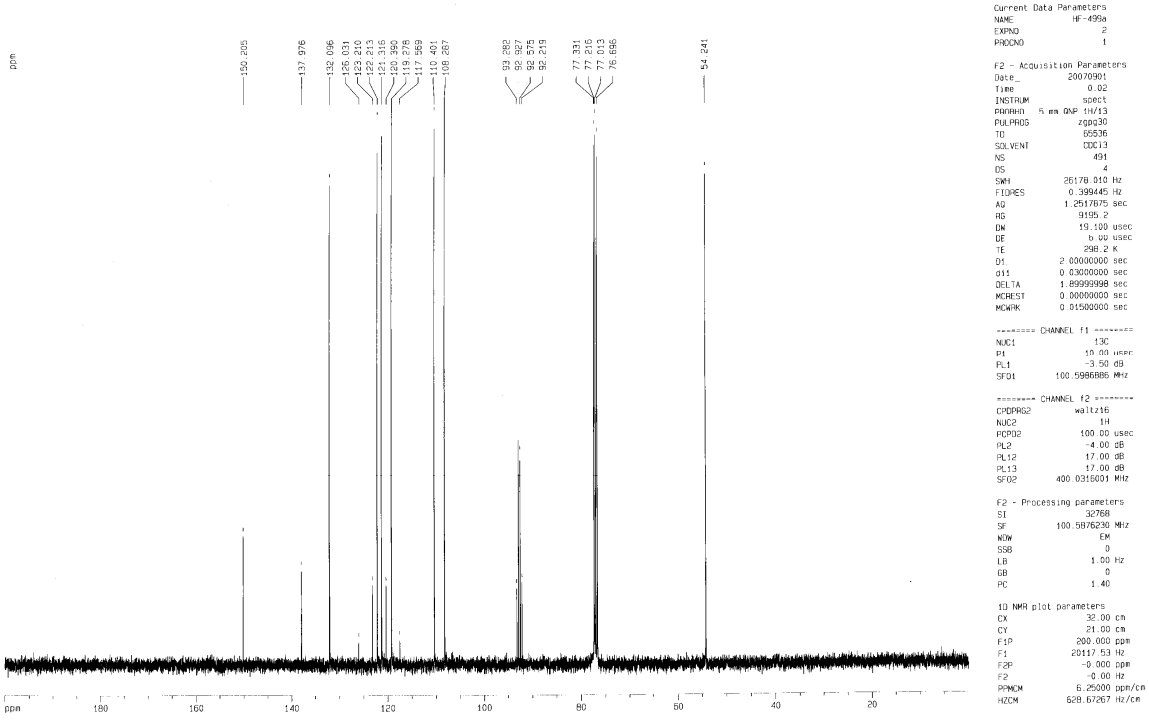
Independent reflections	9165 [R(int) = 0.0201]
Completeness to theta = 27.62°	97.7 %
Absorption correction	Empirical
Max. and min. transmission	0.9784 and 0.9758
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9165 / 0 / 491
Goodness-of-fit on F^2	0.992
Final R indices [I>2sigma(I)]	R1 = 0.0370, wR2 = 0.0989
R indices (all data)	R1 = 0.0414, wR2 = 0.1027
Largest diff. peak and hole	0.430 and -0.238 e.$Å^{-3}$

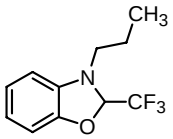
7. ^{1}H and ^{13}C NMR spectra of trifluoroacetaldehyde *N,O*-acetal 1



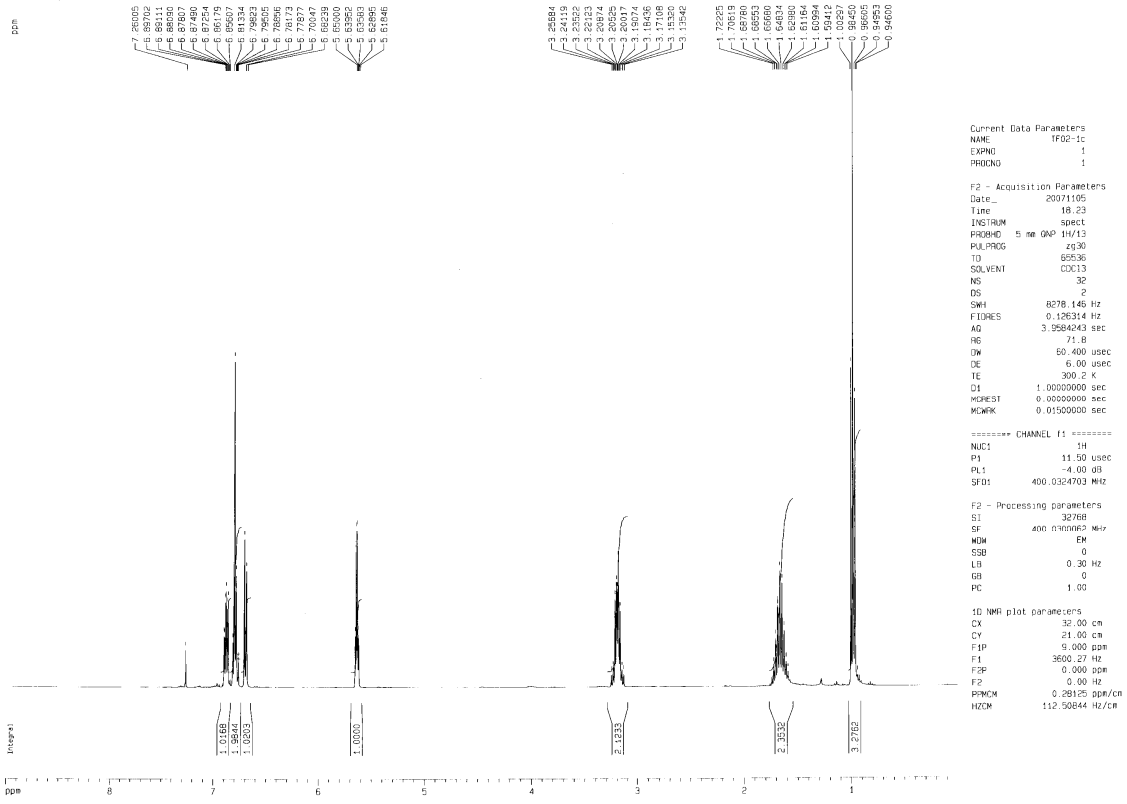
1a

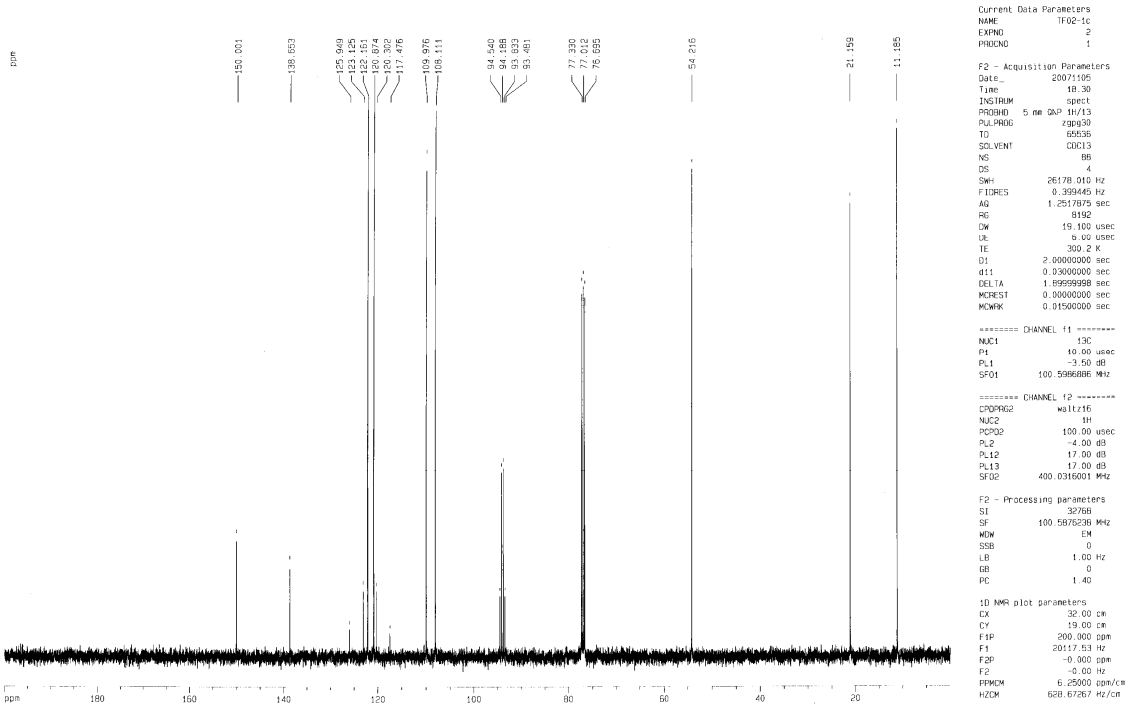


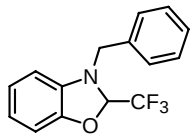



CH3
N
CF3
O

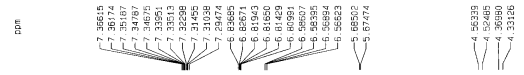
1b

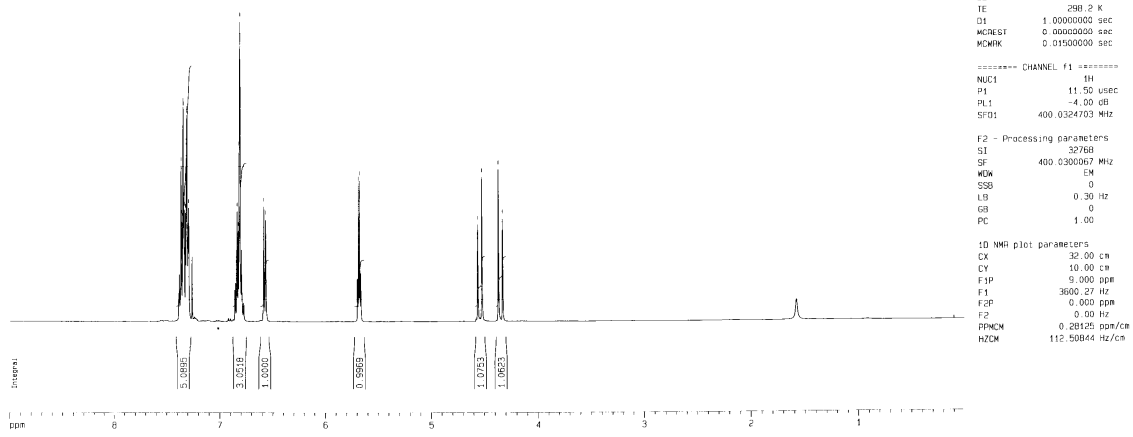

Current Data Parameters
NAME 1F02-1c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 18.23
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8278.145 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 71.8
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324709 MHz
F2 - Processing parameters
SI 32768
SF 400.0300062 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 32.00 cm
CY 21.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm


Current Data Parameters
NAME 1F02-1c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 18.30
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 86
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 8192
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986886 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz
F2 - Processing parameters
SI 32768
SF 100.5876236 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm



1c





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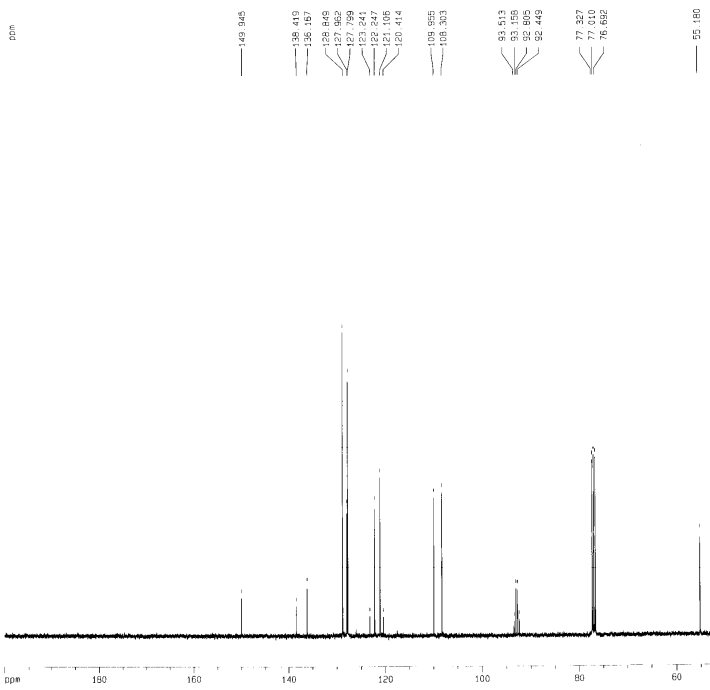
Current Data Parameters
NAME                  CF2H-1a
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070907
Time                  18.00
INSTRUM               spect
PROBHD   5 mm QNP 1H/13
PULPROG               zg30
TD                   65536
SOLVENT               CDCl3
NS                          8
DS                          2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                        128
DW                   60.400 usec
DE                    6.00 usec
TE                   298.2 K
D1                 1.00000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     11.50 usec
PL1                    -4.00 dB
SFO1           400.0324703 MHz

F2 - Processing parameters
SI                        32768
SF                 400.0300067 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00

1D NMR plot parameters
CX                        32.00 cm
CY                        10.00 cm
F1P                     9.000 ppm
F1                   3600.27 Hz
F2P                     0.000 ppm
F2                      0.00 Hz
PPMCM                0.28125 ppm/cm
HZCM               112.50844 Hz/cm
```



```
Current Data Parameters
NAME                  CF2H-1a
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070907
Time                  18.09
INSTRUM               spect
PROBHD   5 mm QNP 1H/13
PULPROG             zgpg30
TD                   65536
SOLVENT               CDCl3
NS                        220
DS                          4
SWH               26178.010 Hz
FIDRES            0.399445 Hz
AQ                1.2517875 sec
RG                     5160.6
DW                   19.100 usec
DE                    6.00 usec
TE                   298.2 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.00 usec
PL1                    -3.50 dB
SFO1           100.5986886 MHz

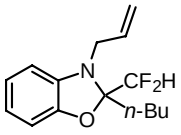
======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                    -4.00 dB
PL12                   17.00 dB
PL13                   17.00 dB
SFO2           400.0316001 MHz

F2 - Processing parameters
SI                        32768
SF                 100.5876262 MHz
WDW                          EM
SSB                           0
LB                         1.00 Hz
GB                            0
PC                         1.40

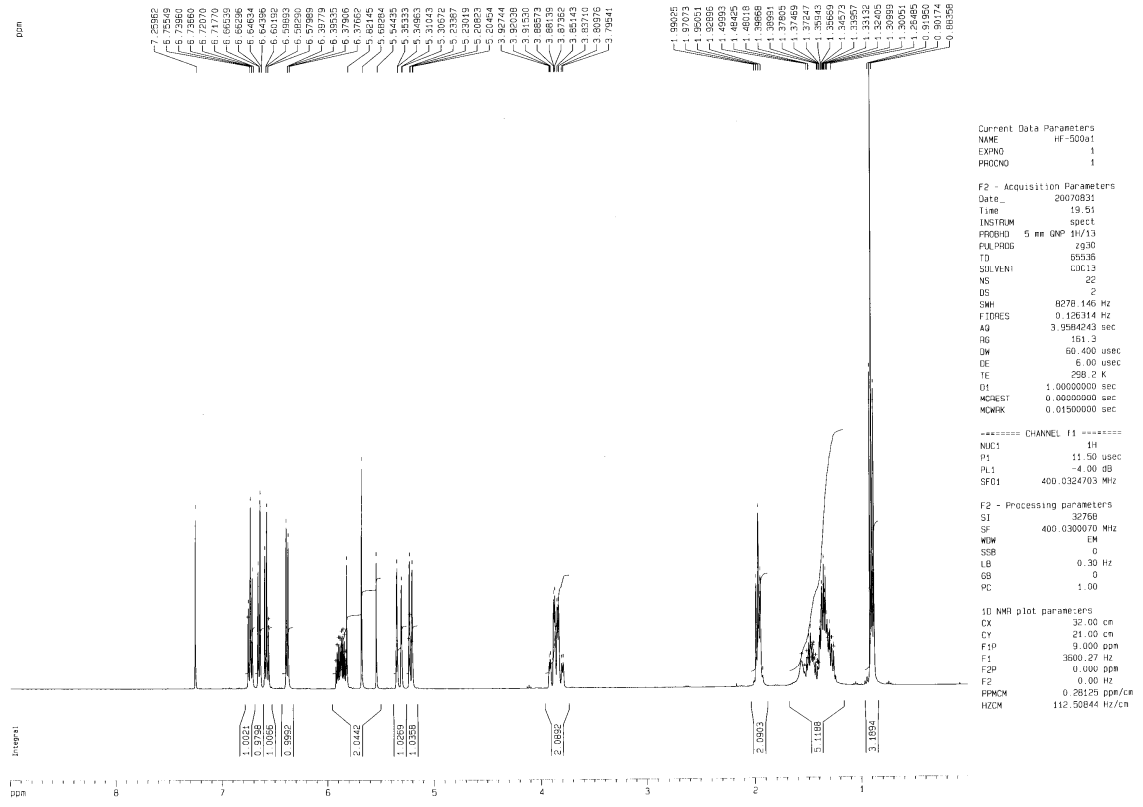
1D NMR plot parameters
CX                        32.00 cm
CY                        10.00 cm
F1P                     200.000 ppm
F1                   20117.53 Hz
F2P                    -0.000 ppm
F2                     -0.00 Hz
PPMCM                6.25000 ppm/cm
HZCM               628.67267 Hz/cm
```

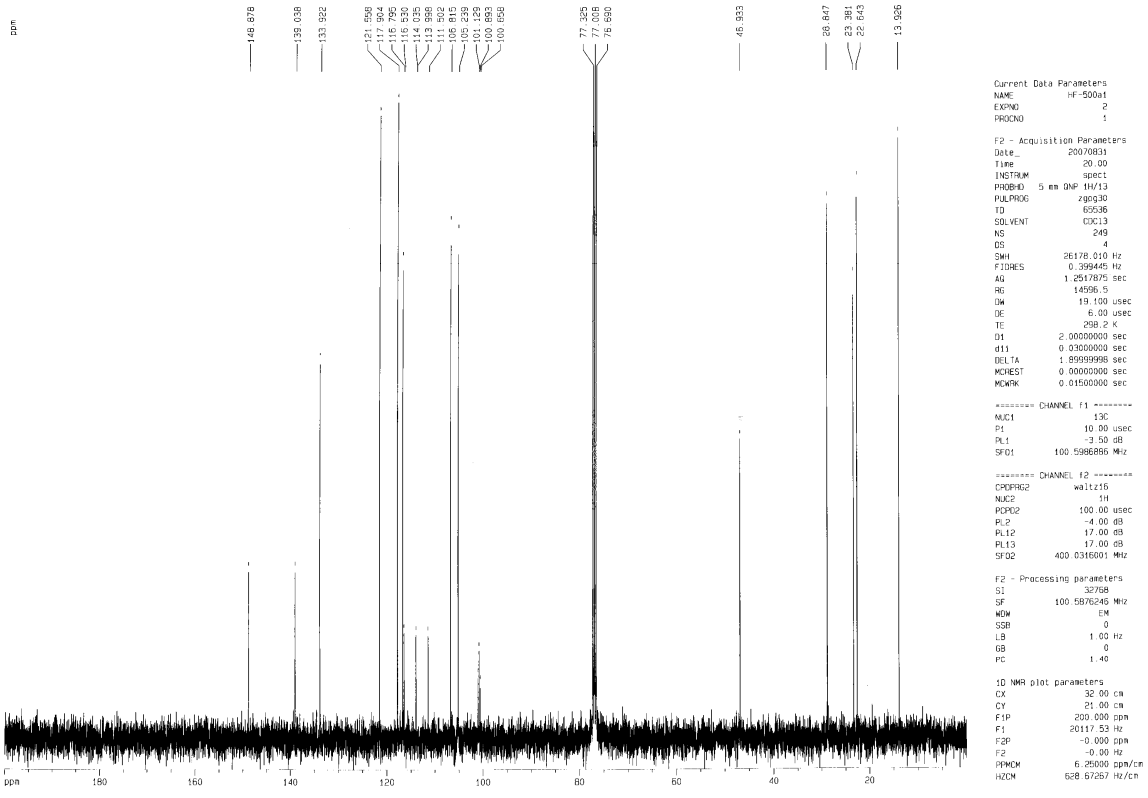
8. ^{1}H and ^{13}C NMR spectra of products 2, 3 and 4

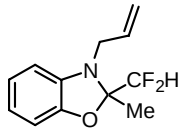
8.1. ^{1}H and ^{13}C NMR spectra of compound 2



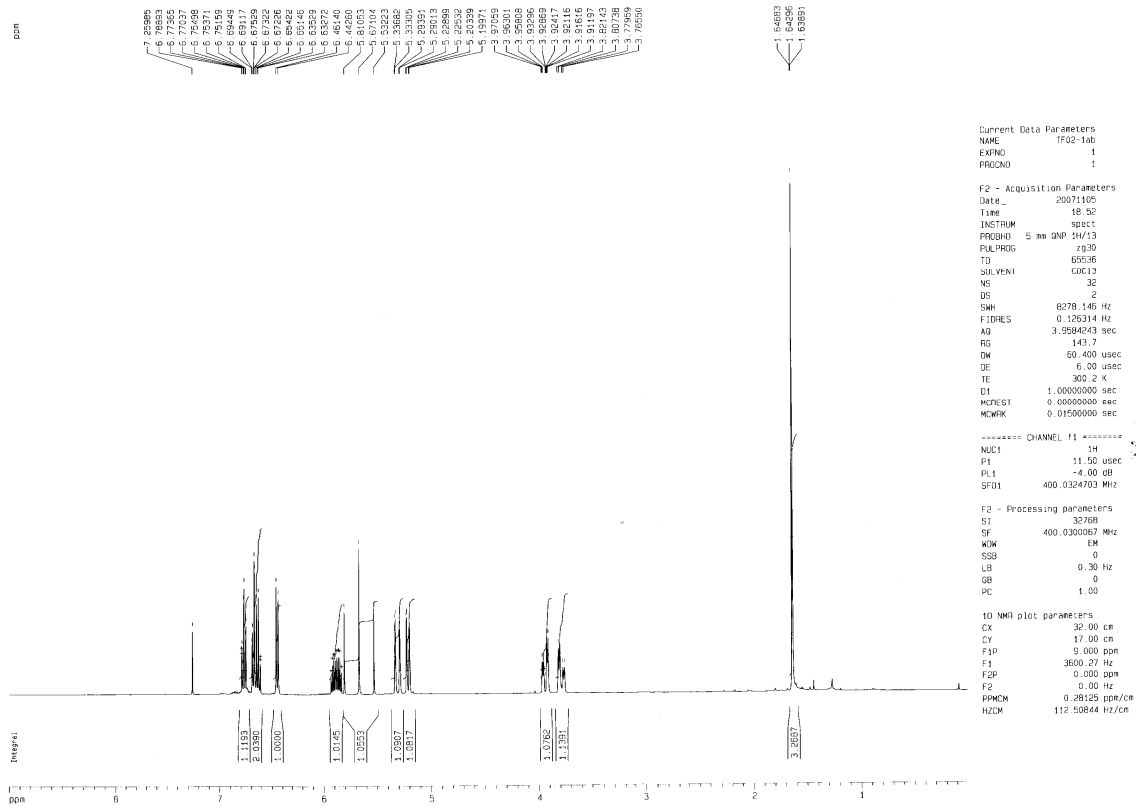
2aa

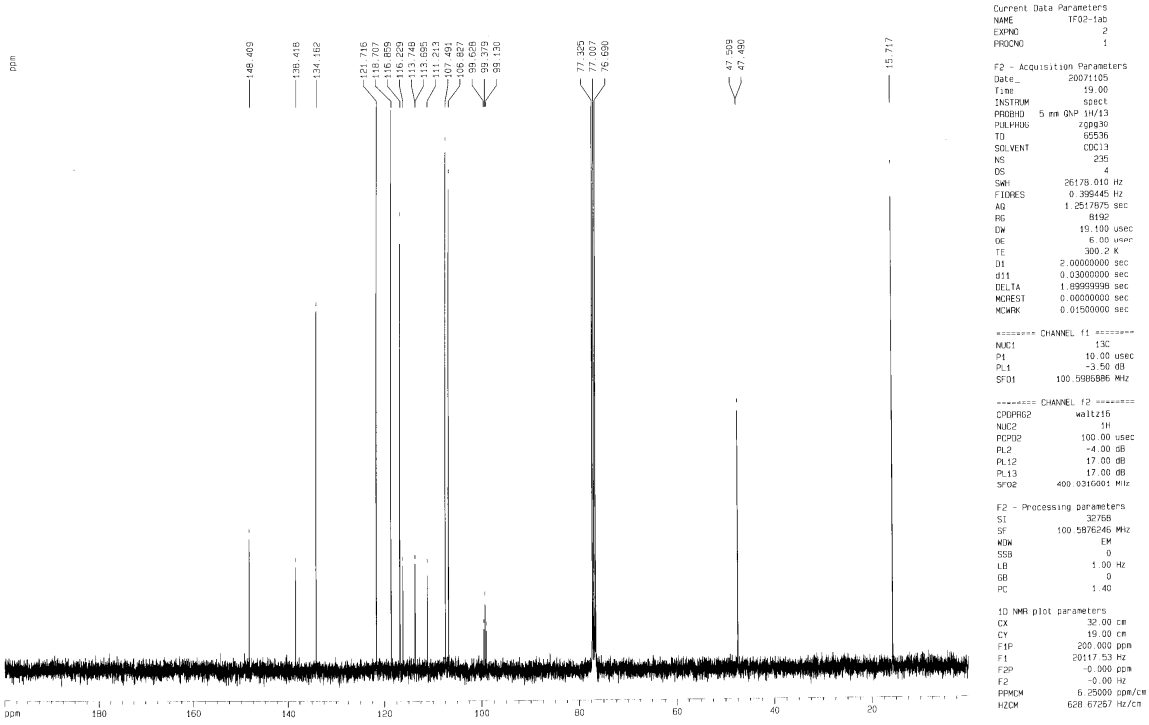





N
CF2H
Me
O

2ab


ppm
7.26986
6.78893
6.77365
6.77037
6.75498
6.75171
6.75155
6.69449
6.69117
6.67922
6.67726
6.67562
6.65146
6.63529
6.63272
6.46140
6.44680
5.81653
5.81004
5.53223
5.33682
5.33305
5.28391
5.28013
5.22899
5.22532
5.20139
5.19971
3.97059
3.96301
3.95808
3.93296
3.92819
3.92677
3.92116
3.91616
3.91197
3.82143
3.80798
3.77459
3.76898
1.64683
1.64296
1.63893
Integral
1.1193
2.0380
1.0000
1.0145
1.0553
1.0907
1.0817
1.0762
1.1381
3.2657
ppm
Current Data Parameters
NAME TF02-1ab
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 18.52
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 143.7
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz
F2 - Processing parameters
SI 32768
SF 400.0300067 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 32.00 cm
CY 17.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm


ppm
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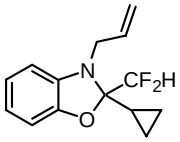
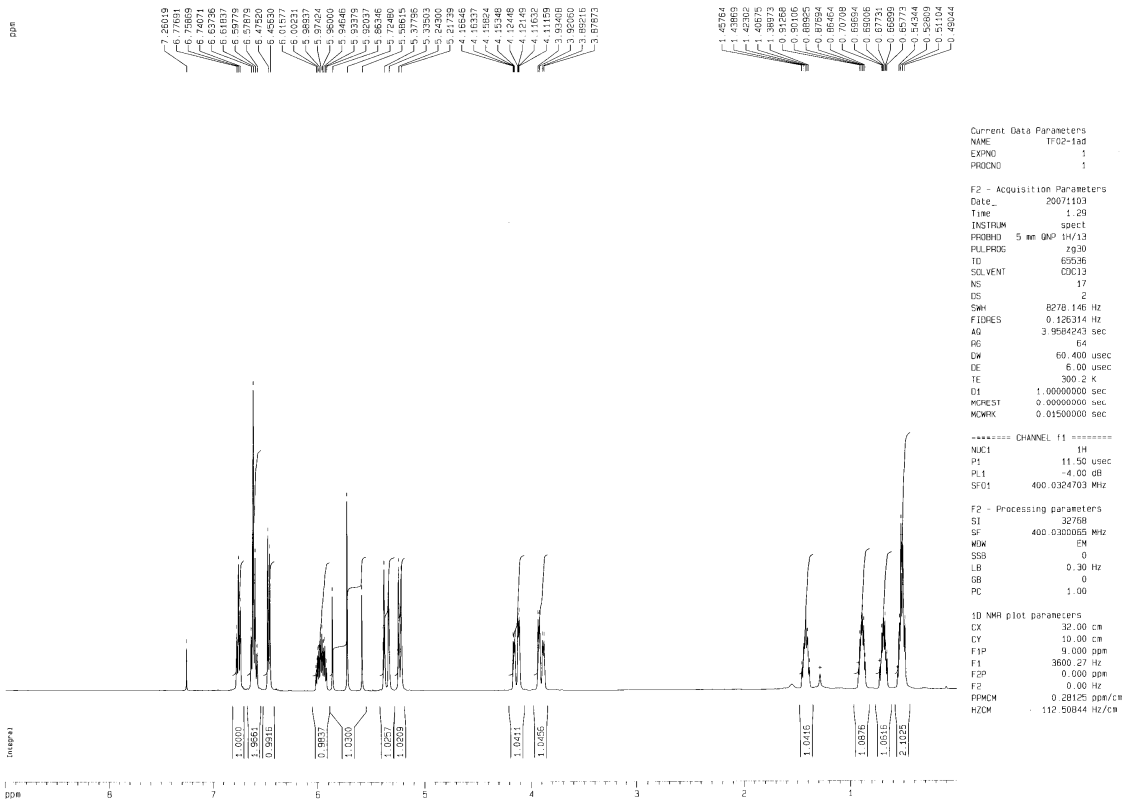
138.416
134.162
121.716
118.707
116.859
116.229
113.748
113.395
111.243
107.491
106.827
99.628
99.379
99.130
77.325
77.007
76.690
47.509
47.490
15.717
ppm
Current Data Parameters
NAME TF02-1ab
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 19.00
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 235
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517675 sec
RG 8192
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986886 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz
F2 - Processing parameters
SI 32768
SF 100.5876246 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm


N
CF2H
O

2ac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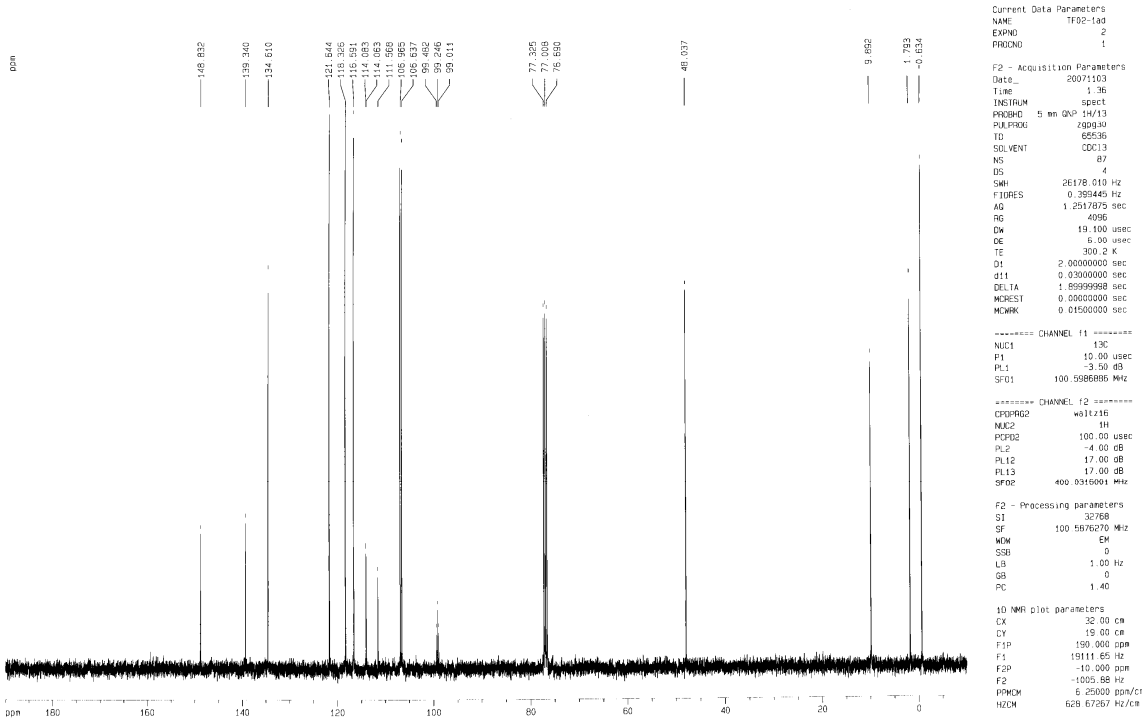
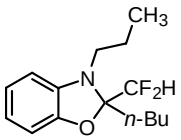
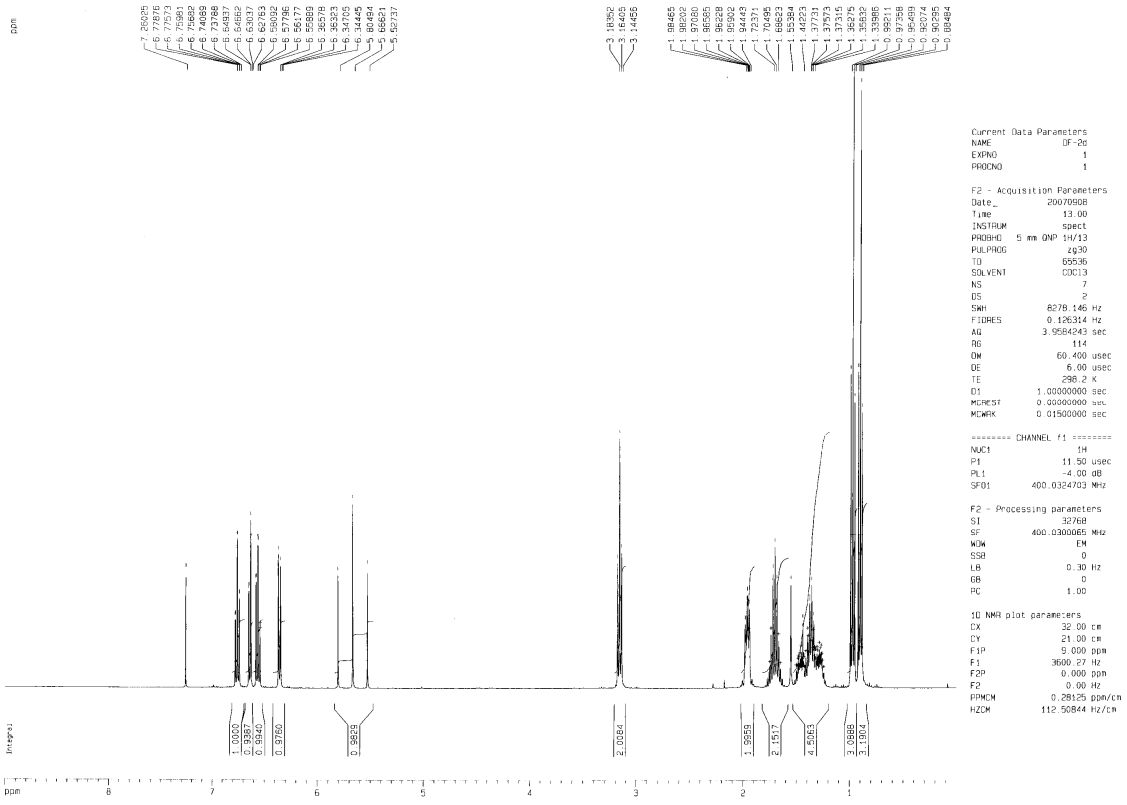
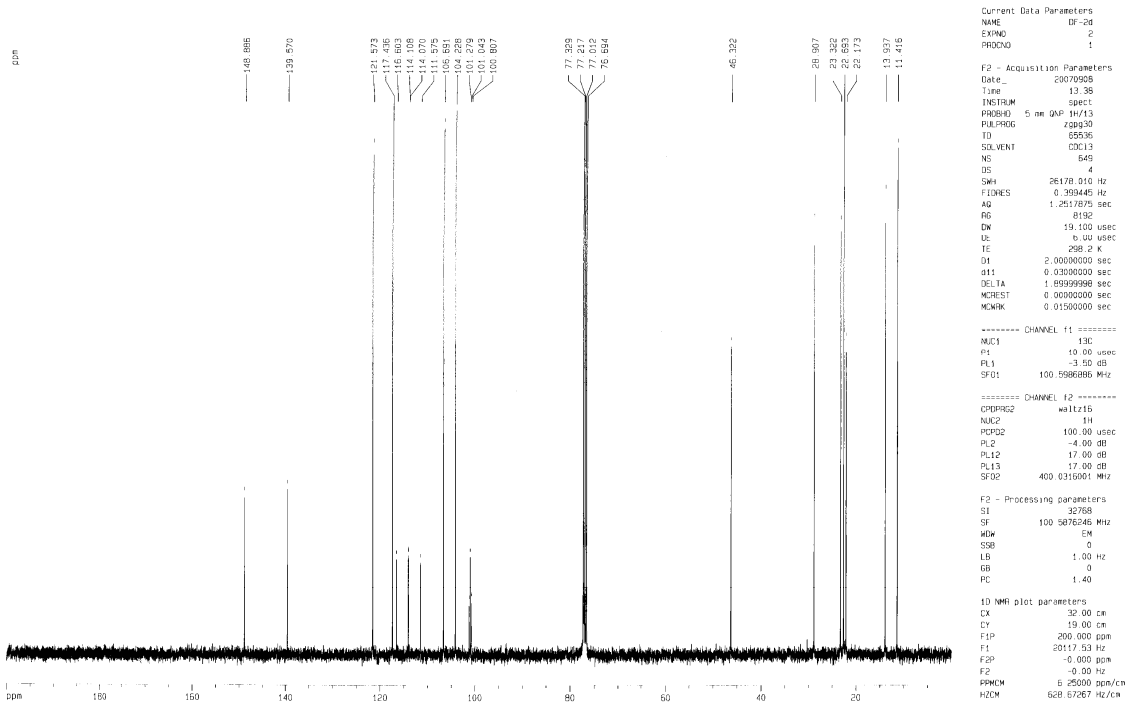
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071103
Time 1.29
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 17
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 64
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz
F2 - Processing parameters
SI 32768
SF 400.0300065 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 32.00 cm
CY 10.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm
ppm
Integral
1.0000
1.9561
0.9916
0.9837
1.0300
1.0257
1.0269
1.0411
1.0456
1.0415
1.0876
1.0515
2.1025

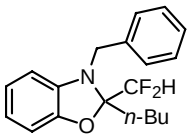

Current Data Parameters
NAME TF02-1ad
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071103
Time 1.36
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 87
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 4096
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999968 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986886 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz
F2 - Processing parameters
SI 32768
SF 100.5676270 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 190.000 ppm
F1 19111.65 Hz
F2P -10.000 ppm
F2 -1005.88 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm
ppm
148.832
139.340
134.610
121.644
118.386
116.591
114.883
114.063
111.568
105.965
105.637
99.482
99.246
99.011
77.325
77.008
76.690
48.037
9.852
1.793
0.634



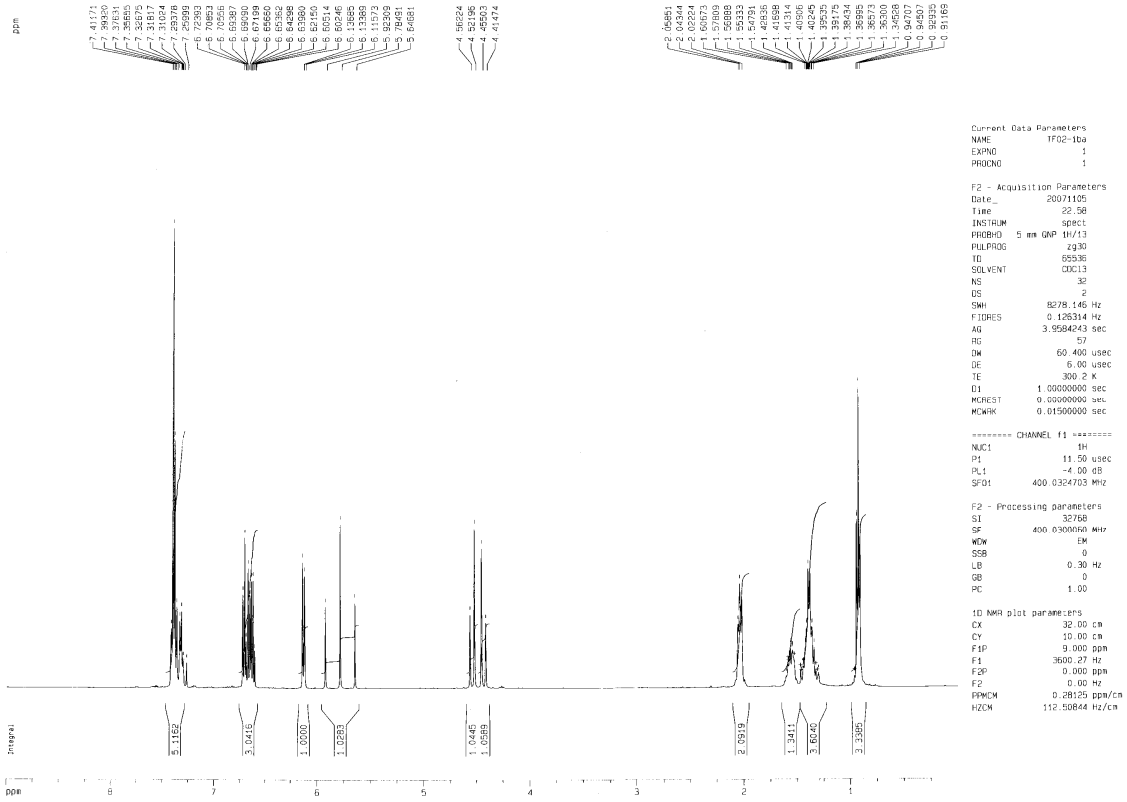
2ba

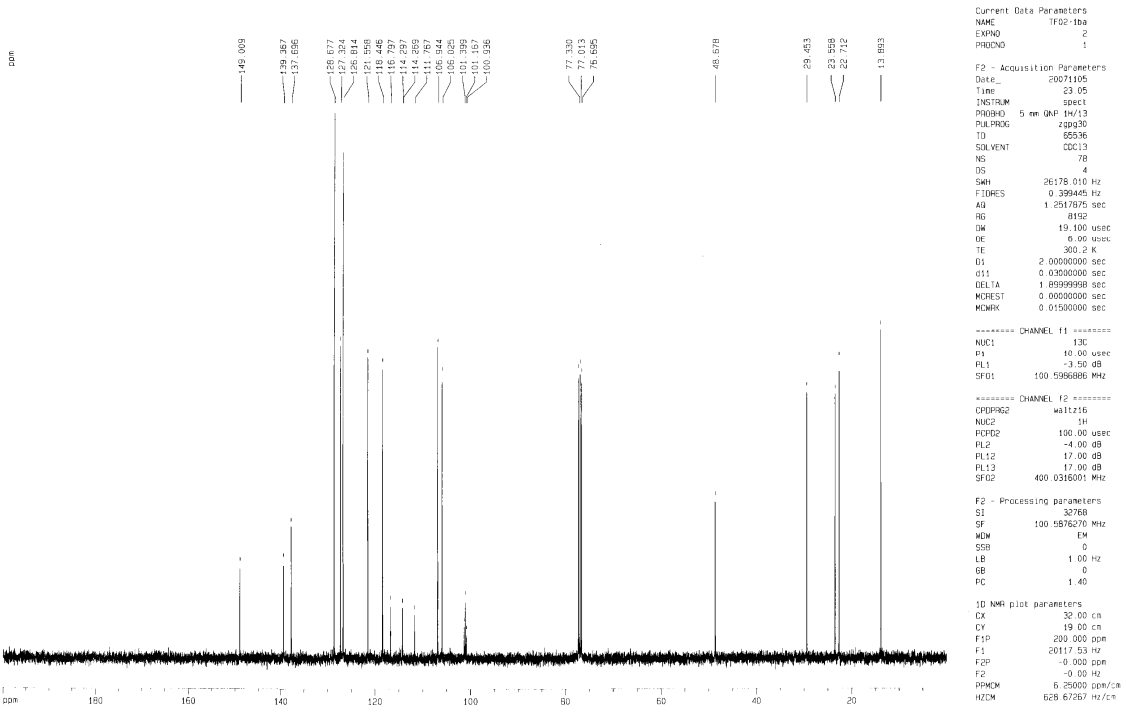




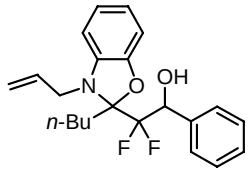

N
CF2H
n-Bu
O

2ca


Current Data Parameters
NAME TF02-1ba
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 22.58
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 57
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz
F2 - Processing parameters
SI 32768
SF 400.0300060 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 32.00 cm
CY 10.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm

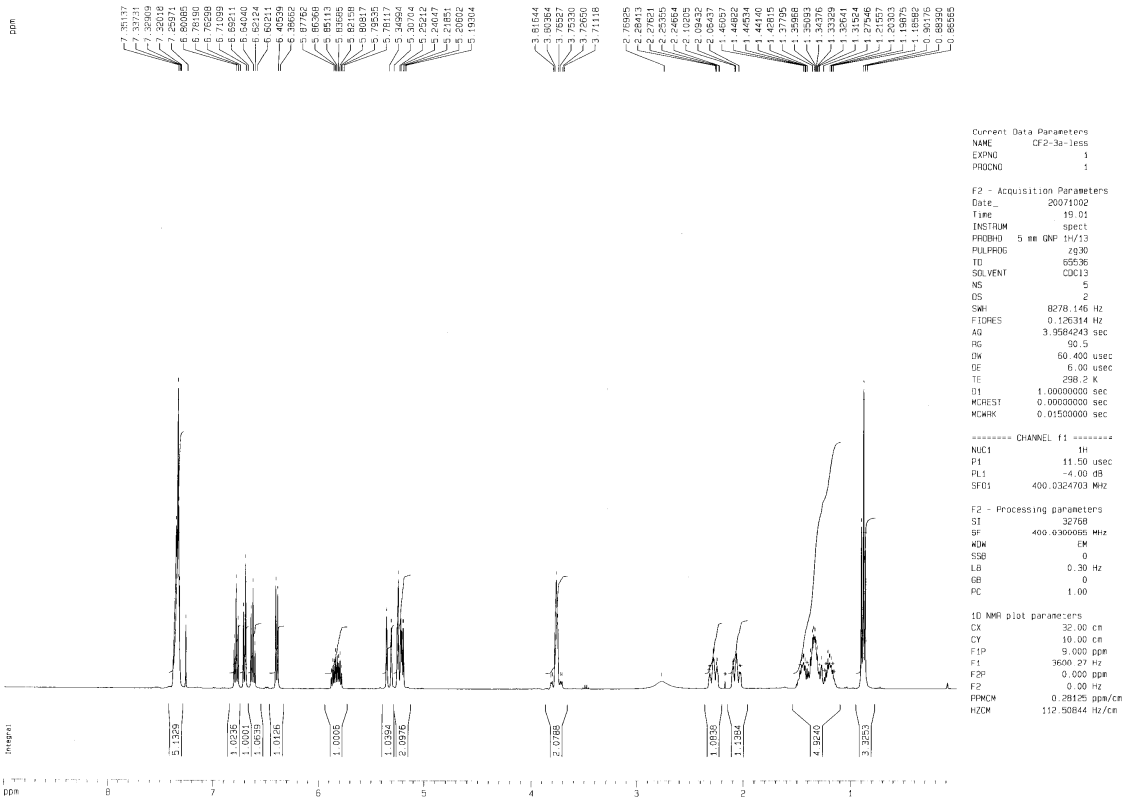

Current Data Parameters
NAME TF02-1ba
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071105
Time 23.05
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 78
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 8192
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5966886 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz
F2 - Processing parameters
SI 32768
SF 100.5876270 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm

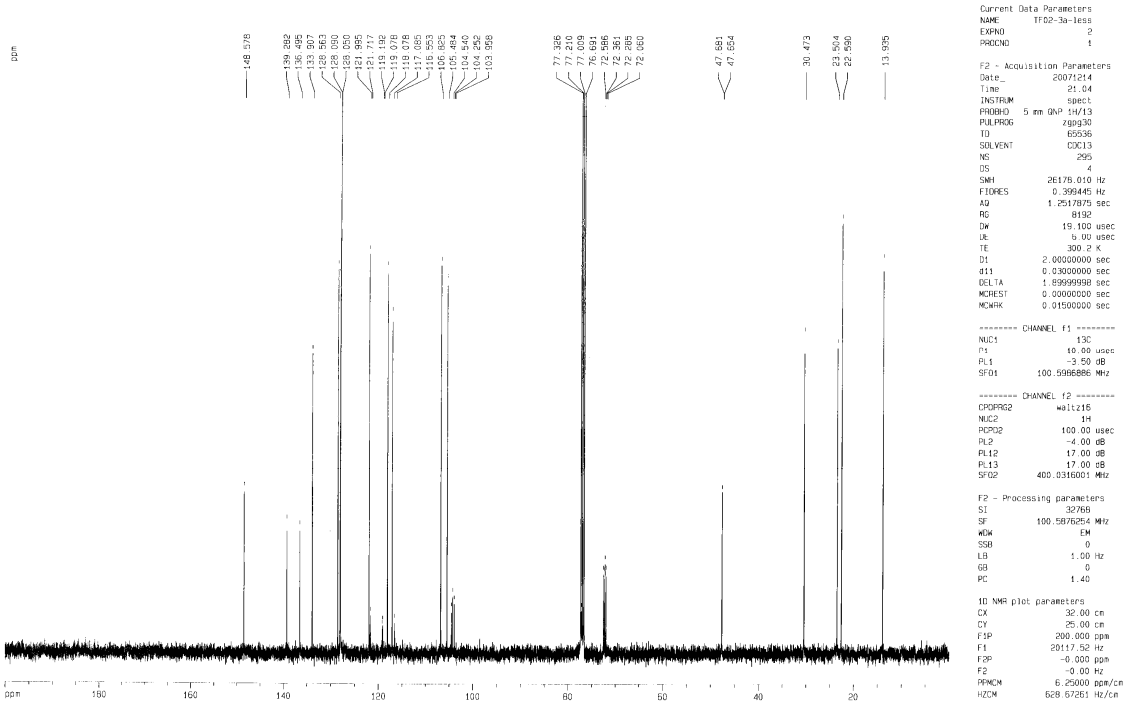
8.2. ^{1}H and ^{13}C NMR spectra of compound 3



3a

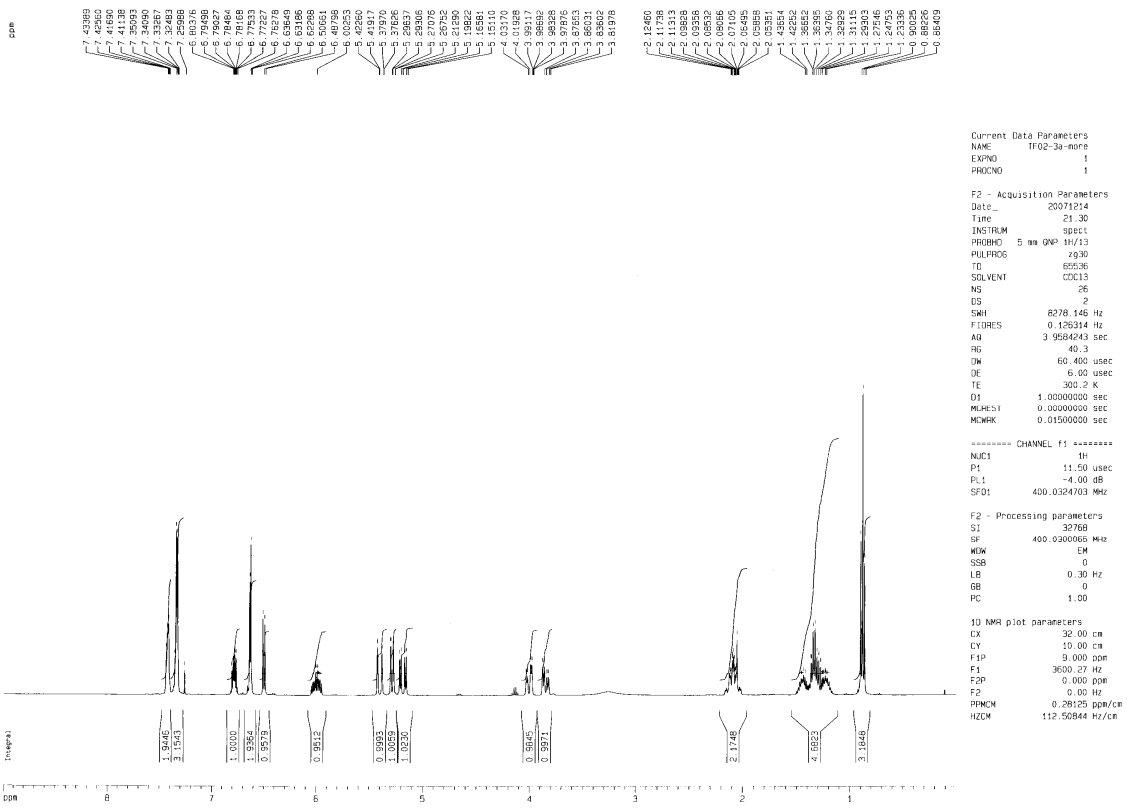
For **3a-*less***

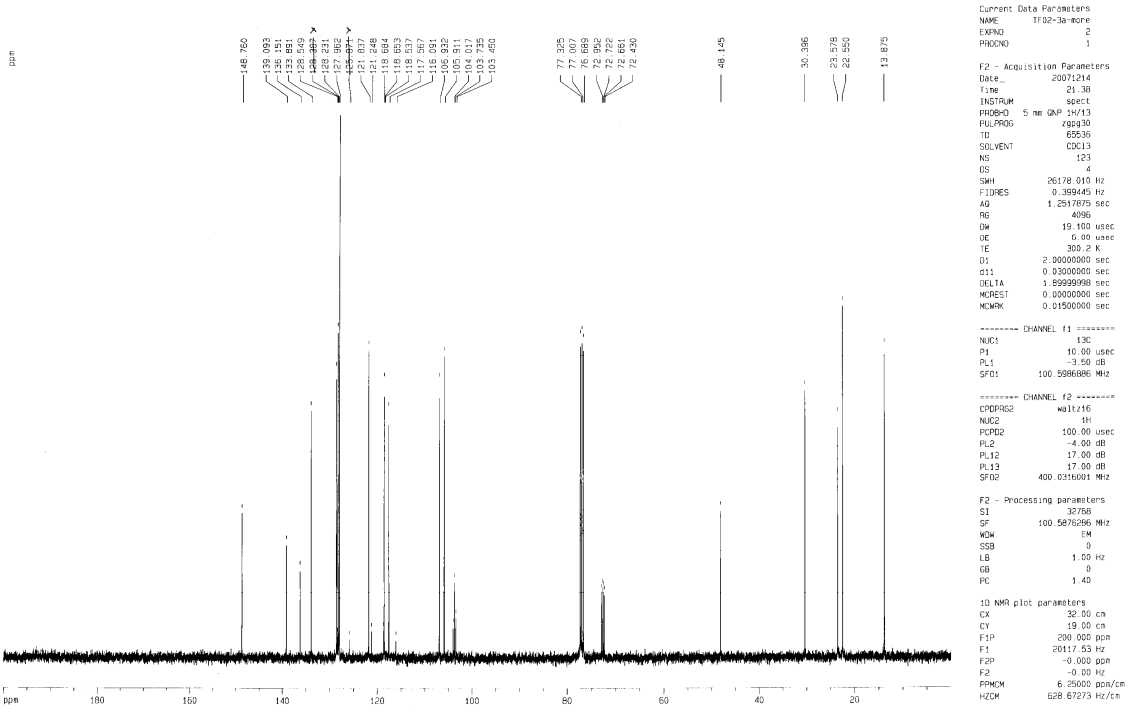




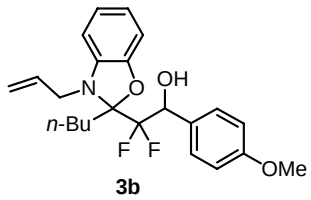
- S23 -

For **3a-*more***



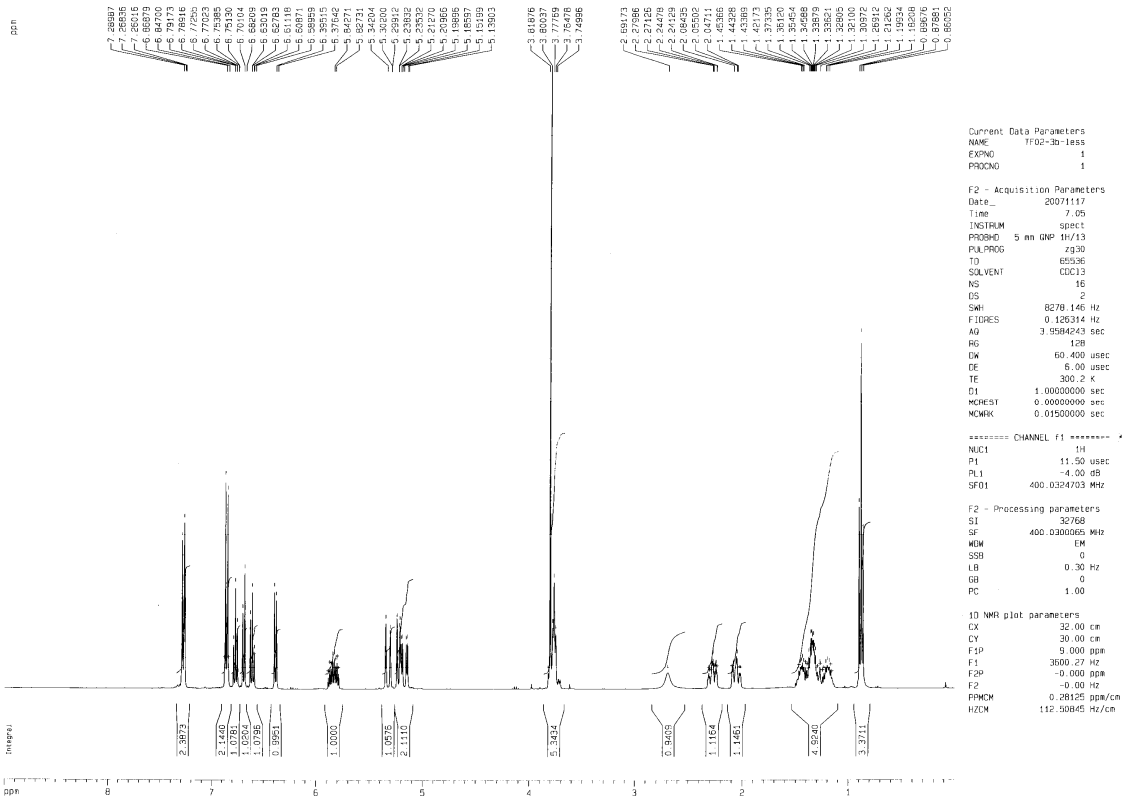


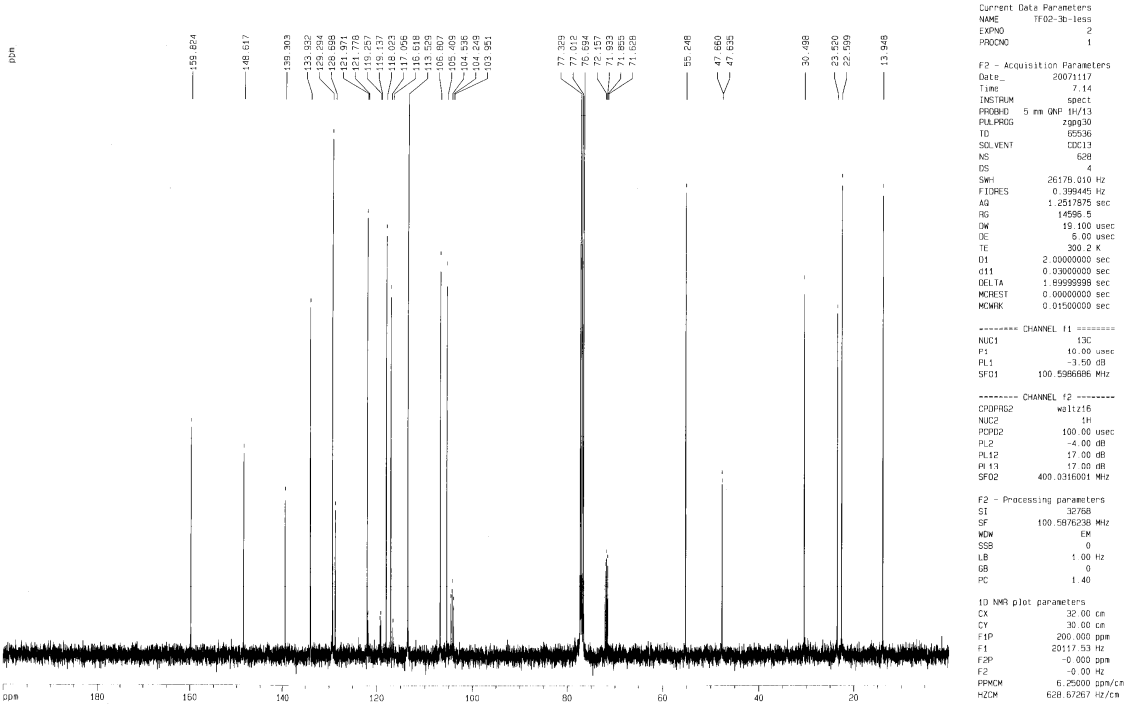
- S24 -



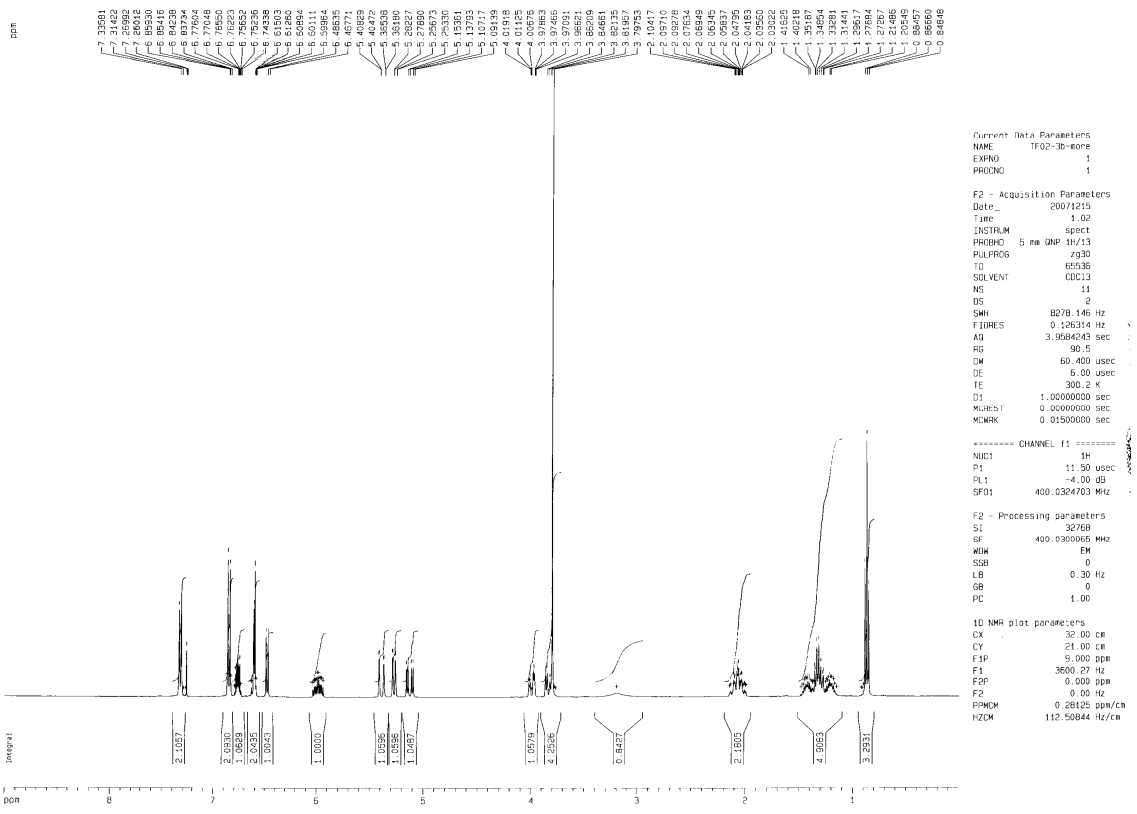
3b

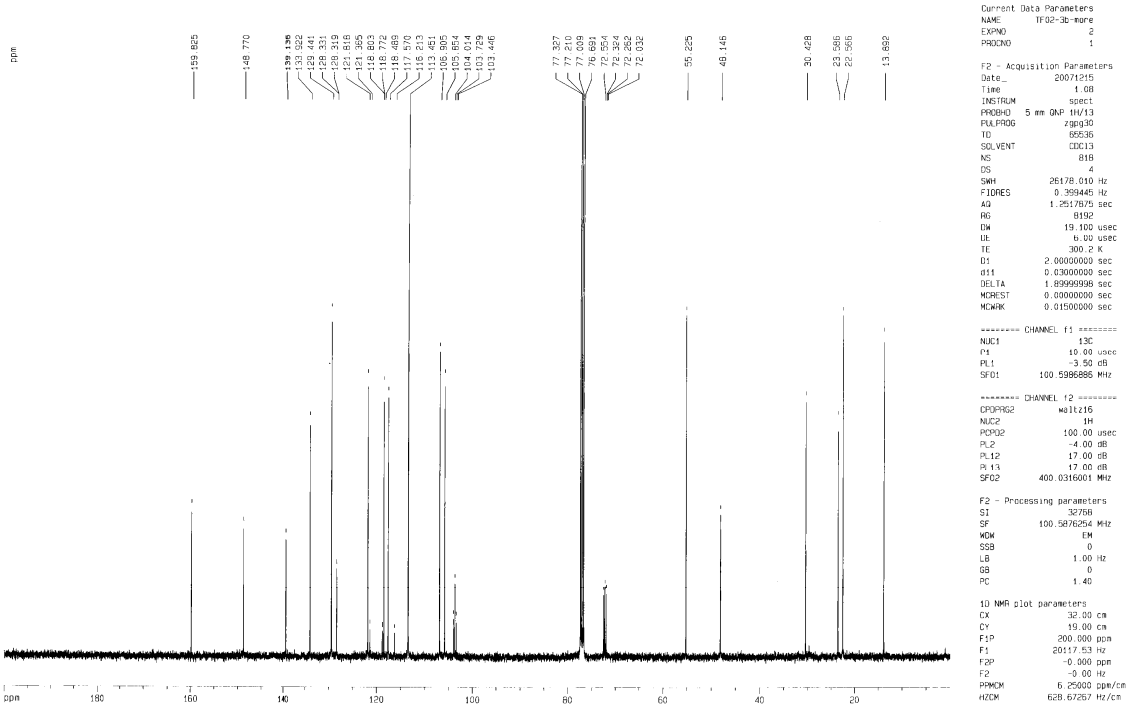
For **3b-*less***

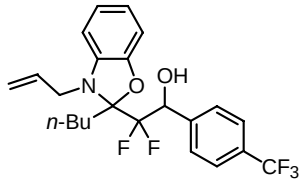




For **3b-*more***

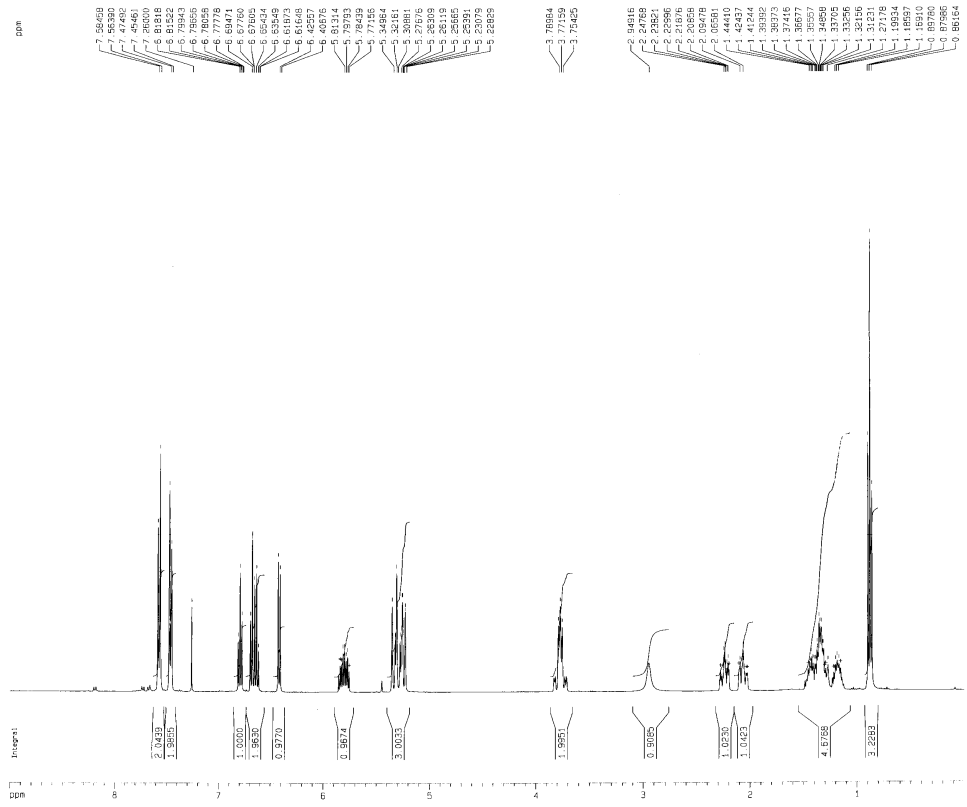


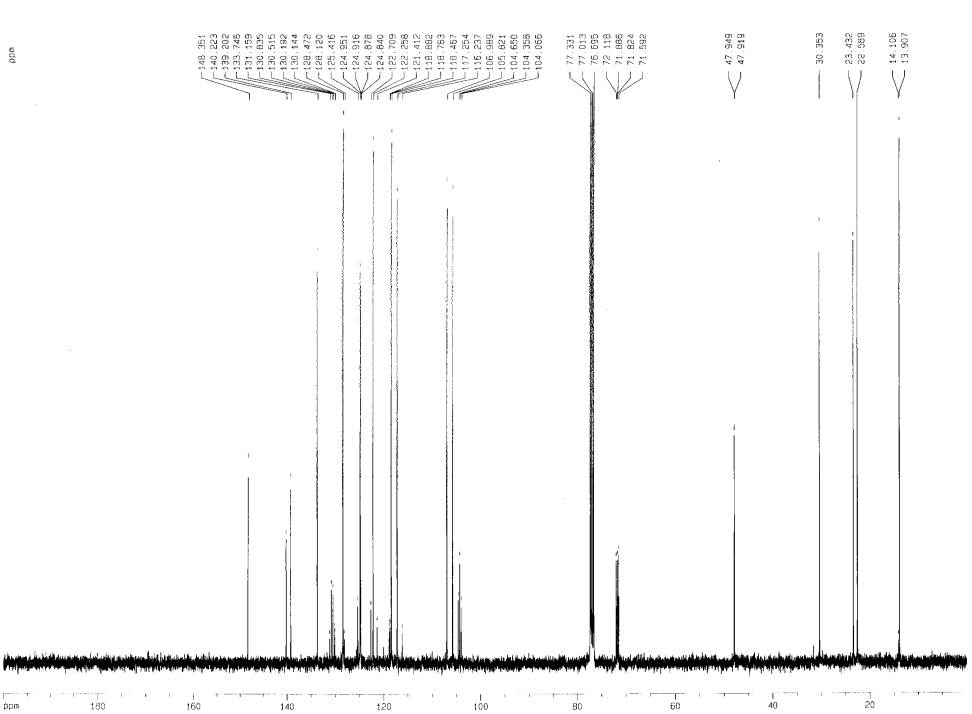




3c

For **3c-*less***





Current Data Parameters
NAME TF02-3c-less
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071117
Time 3.54
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 7
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 101.6
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz

F2 - Processing parameters
SI 32768
SF 400.0300065 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 32.00 cm
CY 15.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50845 Hz/cm

Current Data Parameters
NAME TF02-3c-less
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071117
Time 4.03
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 1000
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 13004
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

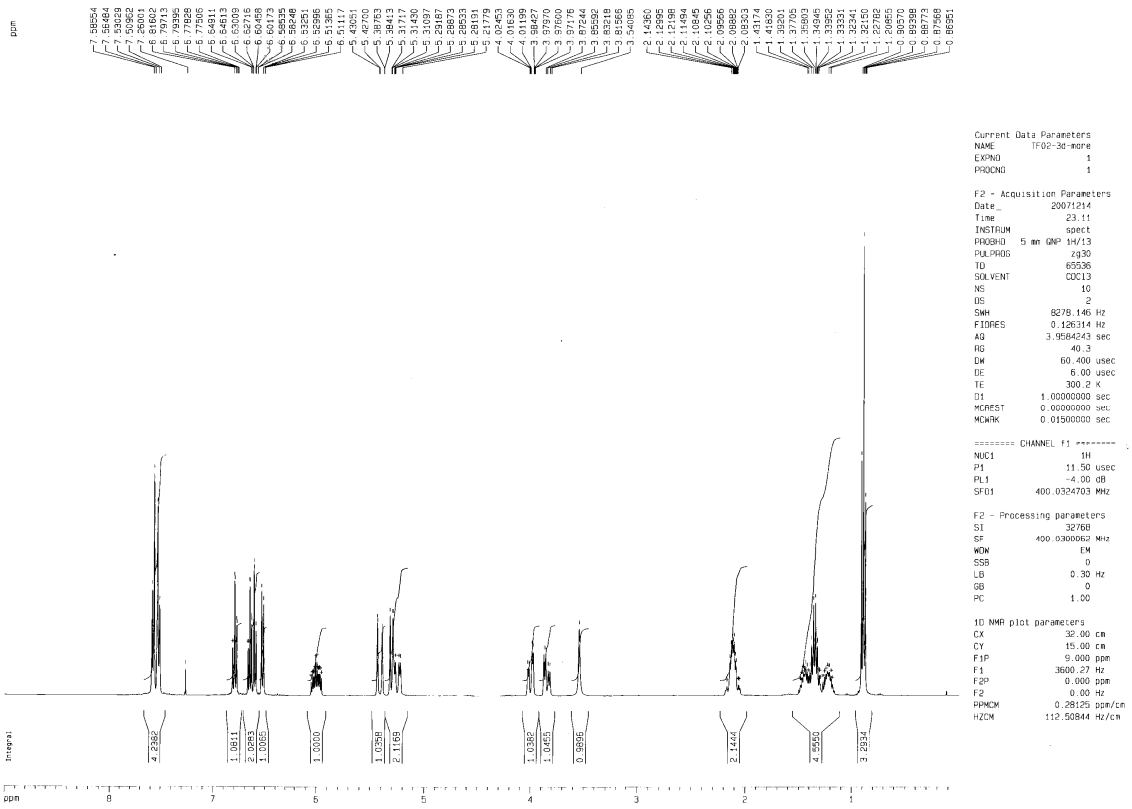
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986886 MHz

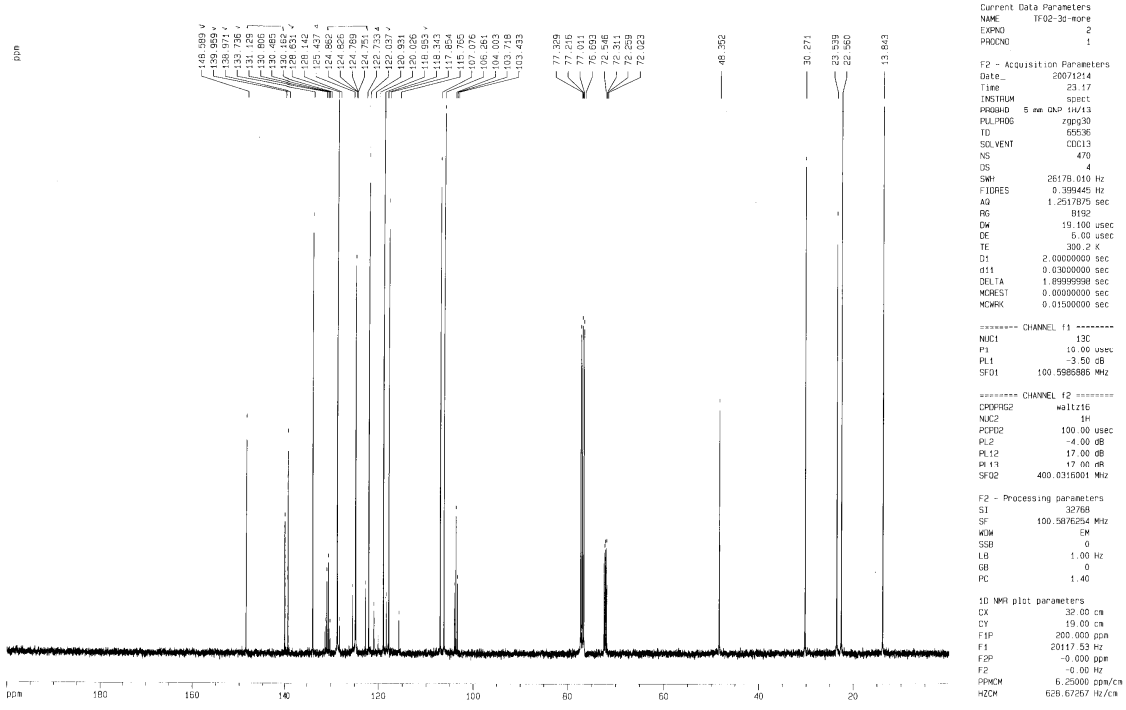
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz

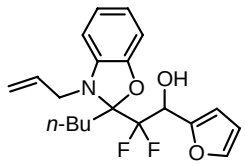
F2 - Processing parameters
SI 32768
SF 100.5876236 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm

For **3c-*more***

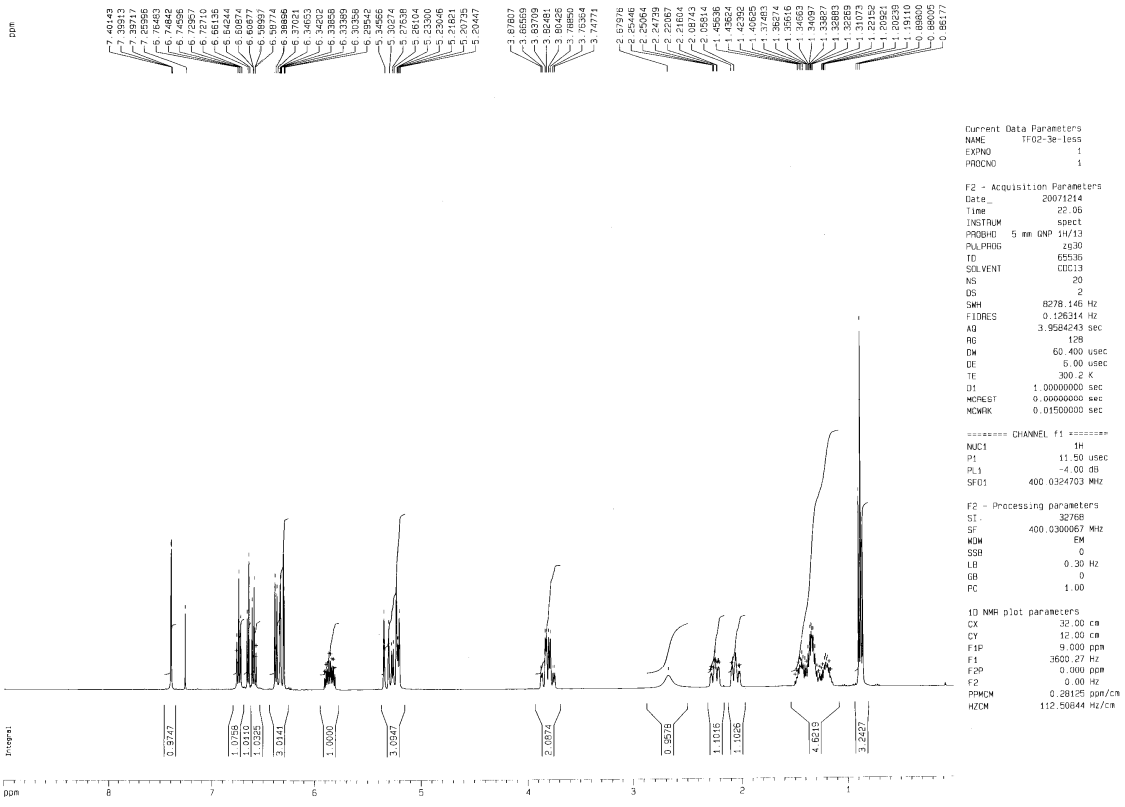


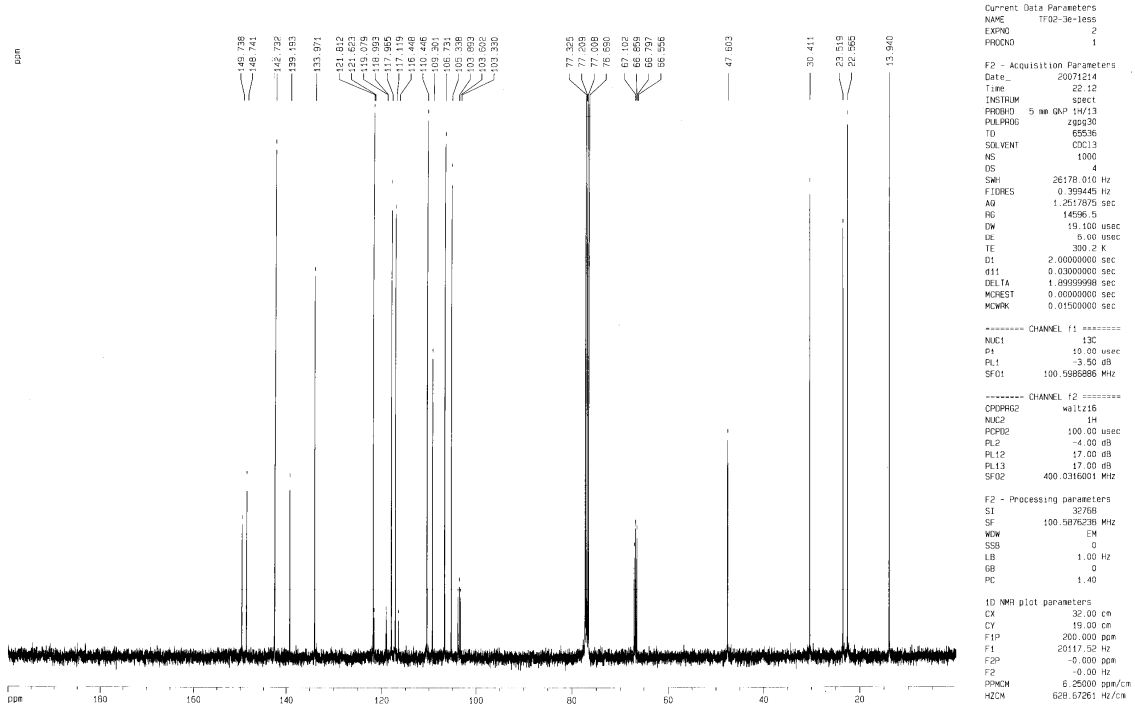




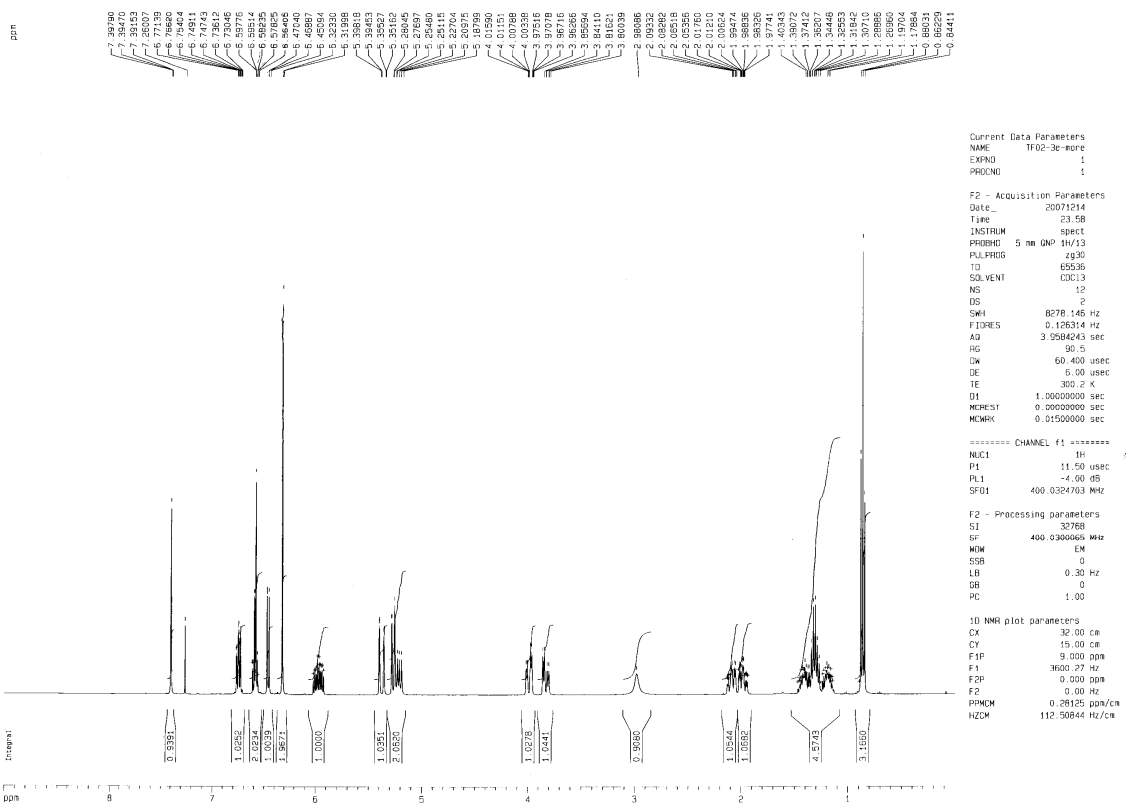
3d

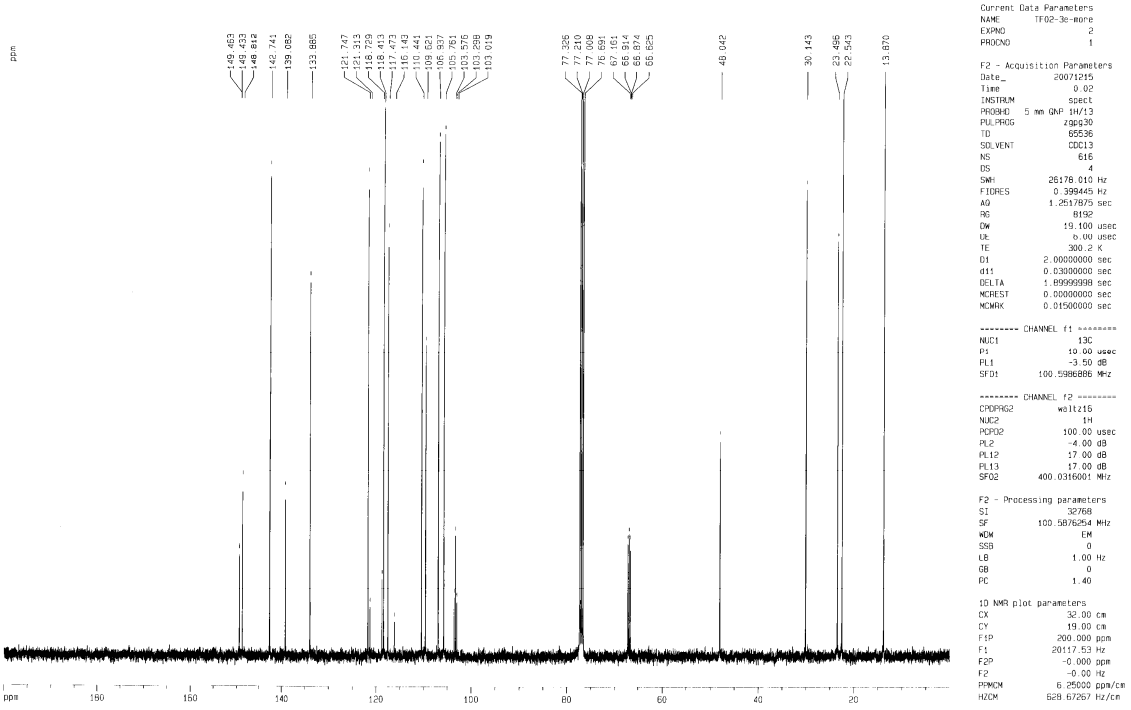
For **3d-*less***

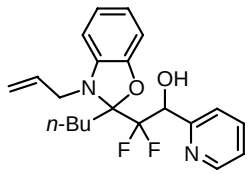




For **3d-*more***

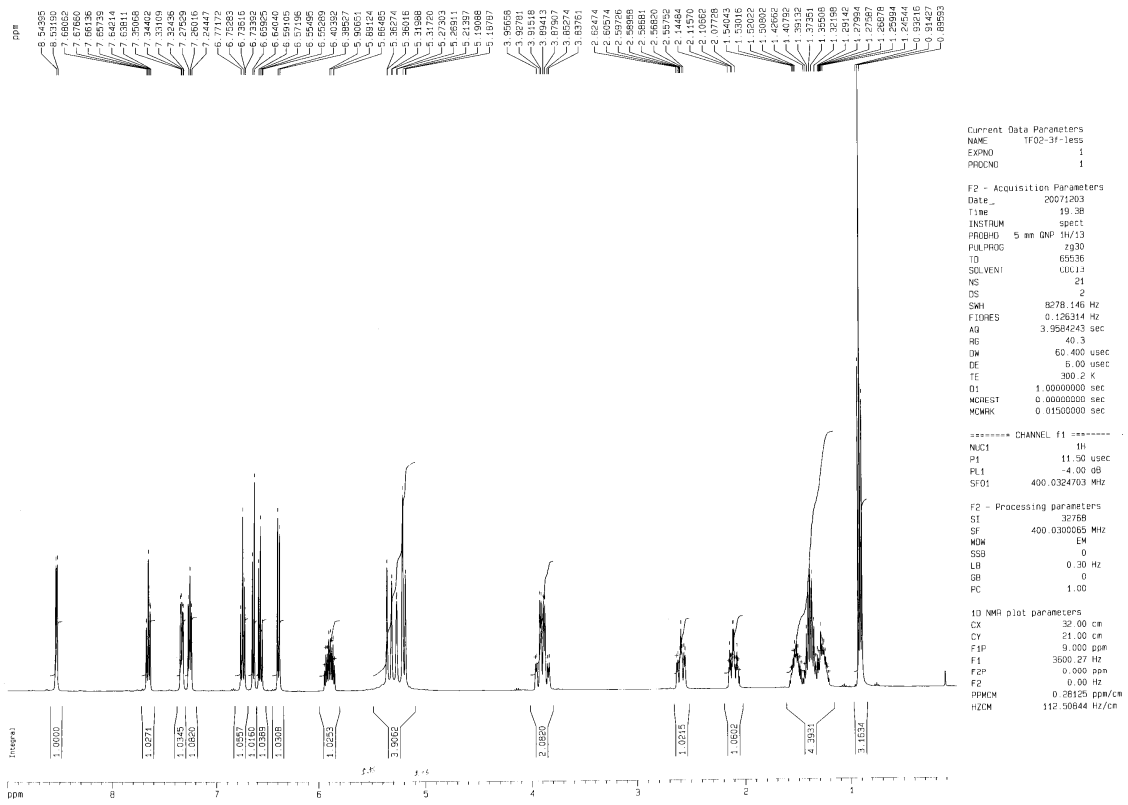


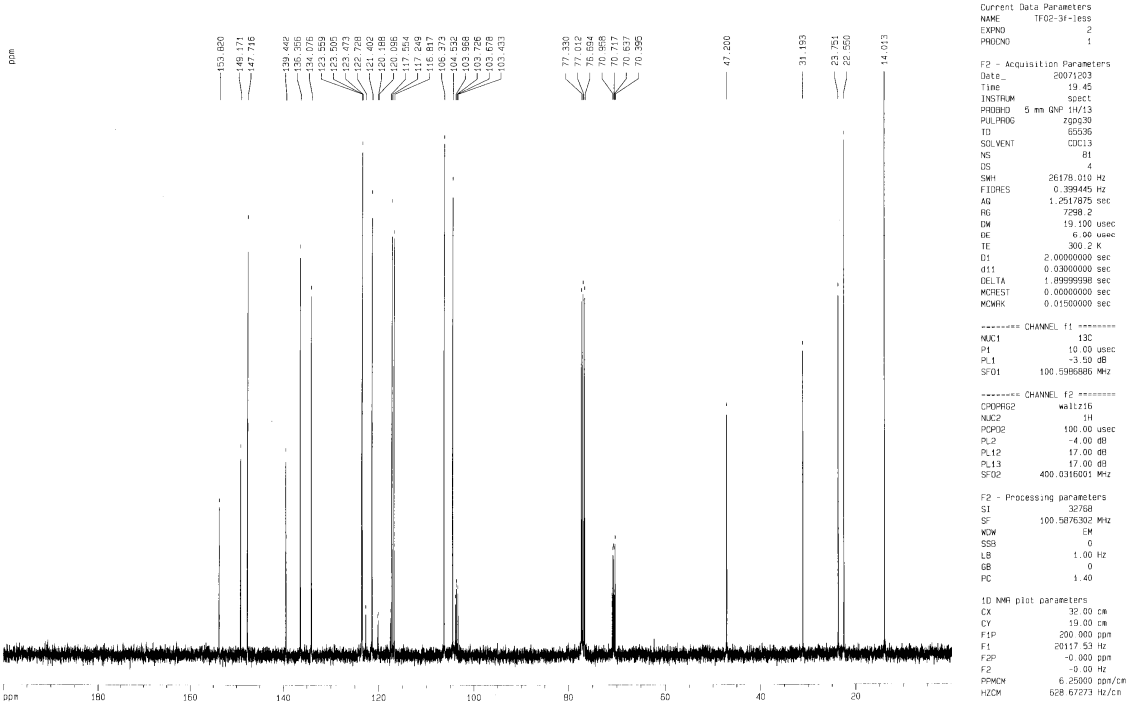




3e

For **3e-*less***





Current Data Parameters
NAME TF02-3f-less
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071203
Time 19.38
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 21
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 40.3
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz

F2 - Processing parameters
SI 32768
SF 400.0300065 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 32.00 cm
CY 21.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm

Current Data Parameters
NAME TF02-3f-less
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071203
Time 19.45
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 81
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 7298.2
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

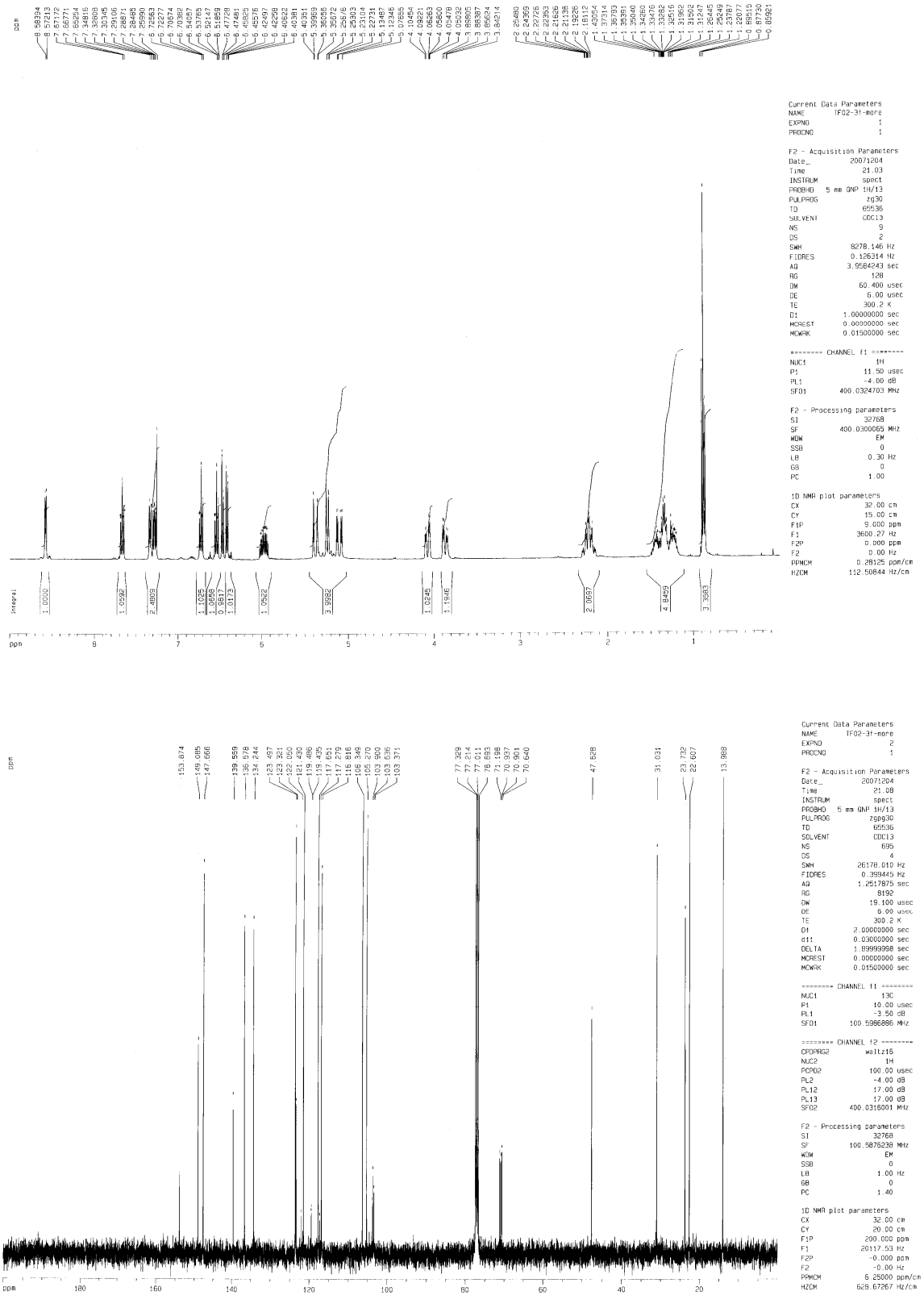
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986686 MHz

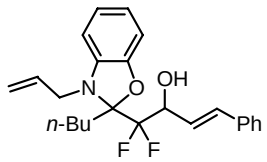
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz

F2 - Processing parameters
SI 32768
SF 100.5876302 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 32.00 cm
CY 19.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67273 Hz/cm

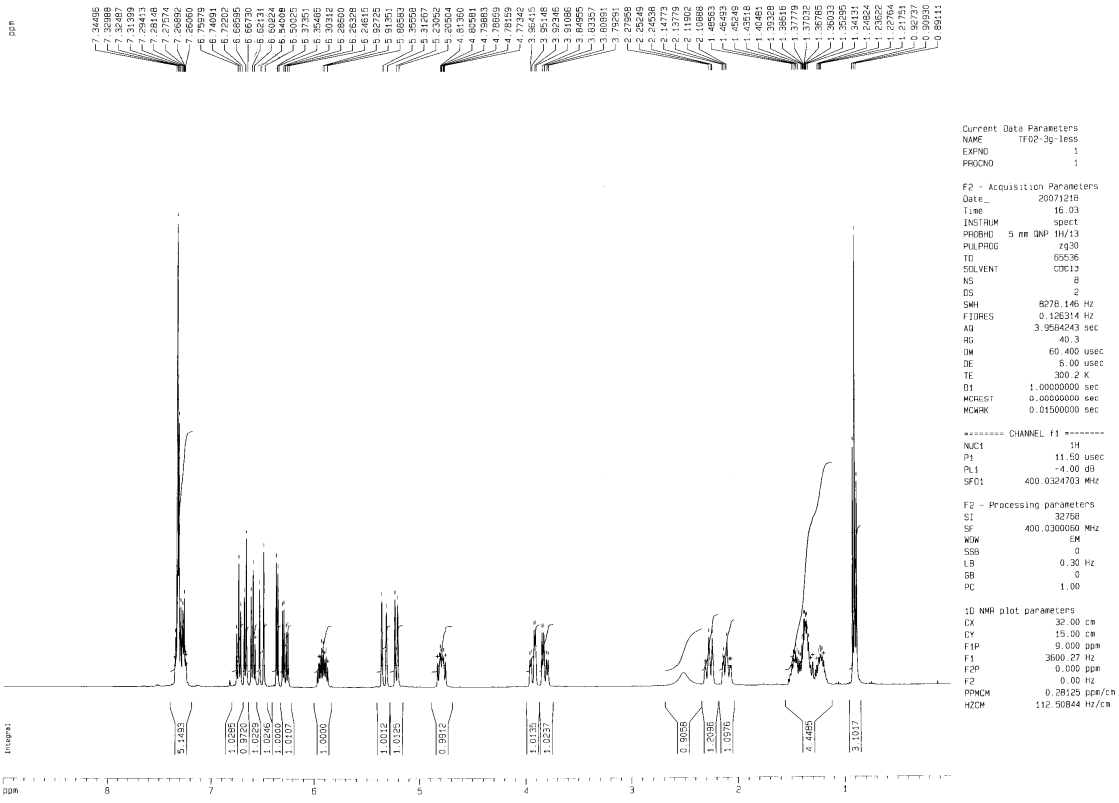
For **3e-*more***

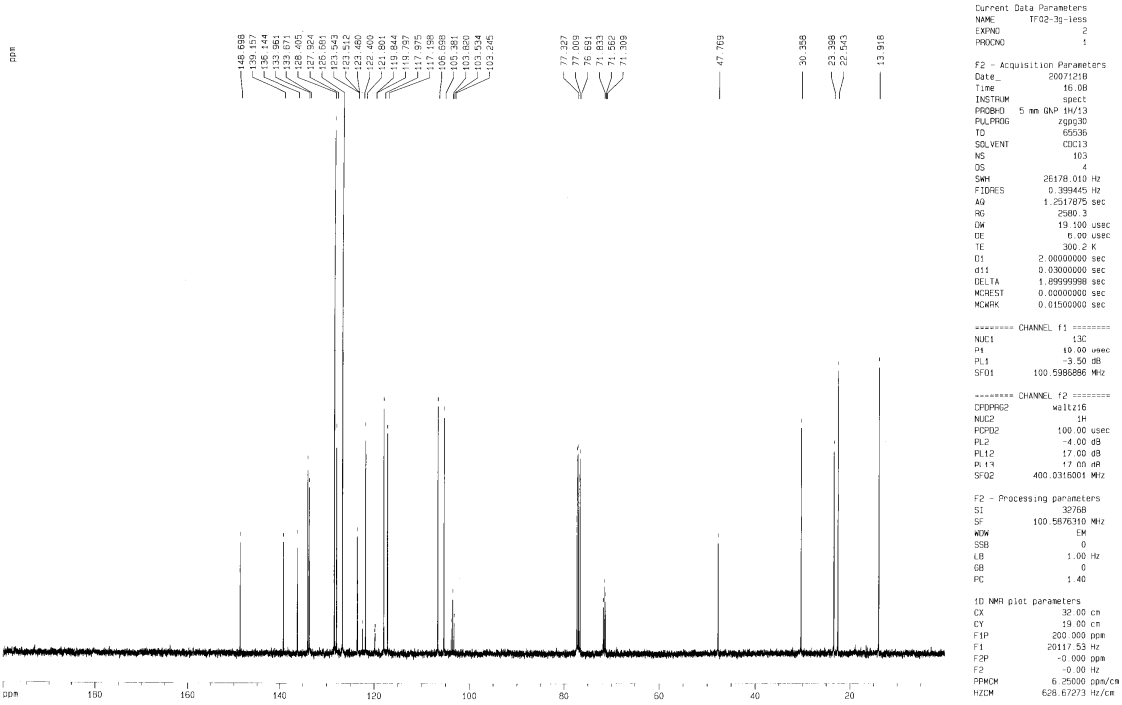




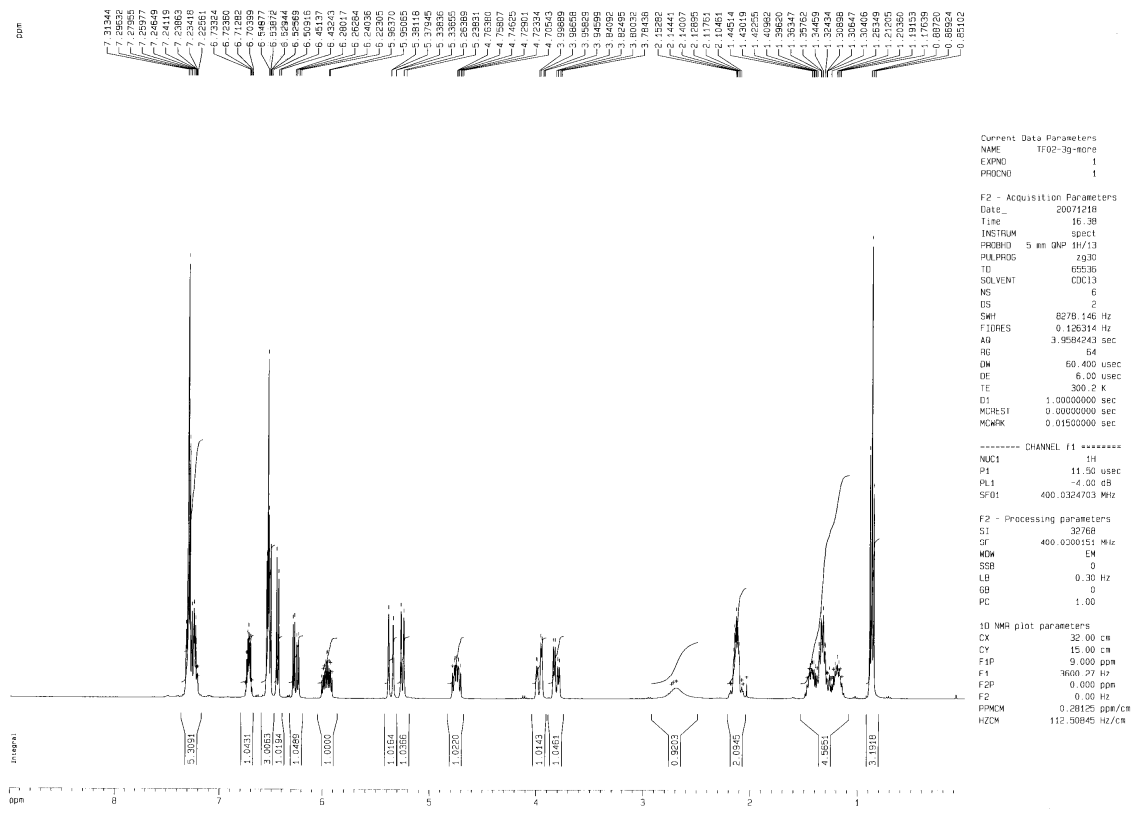
3f

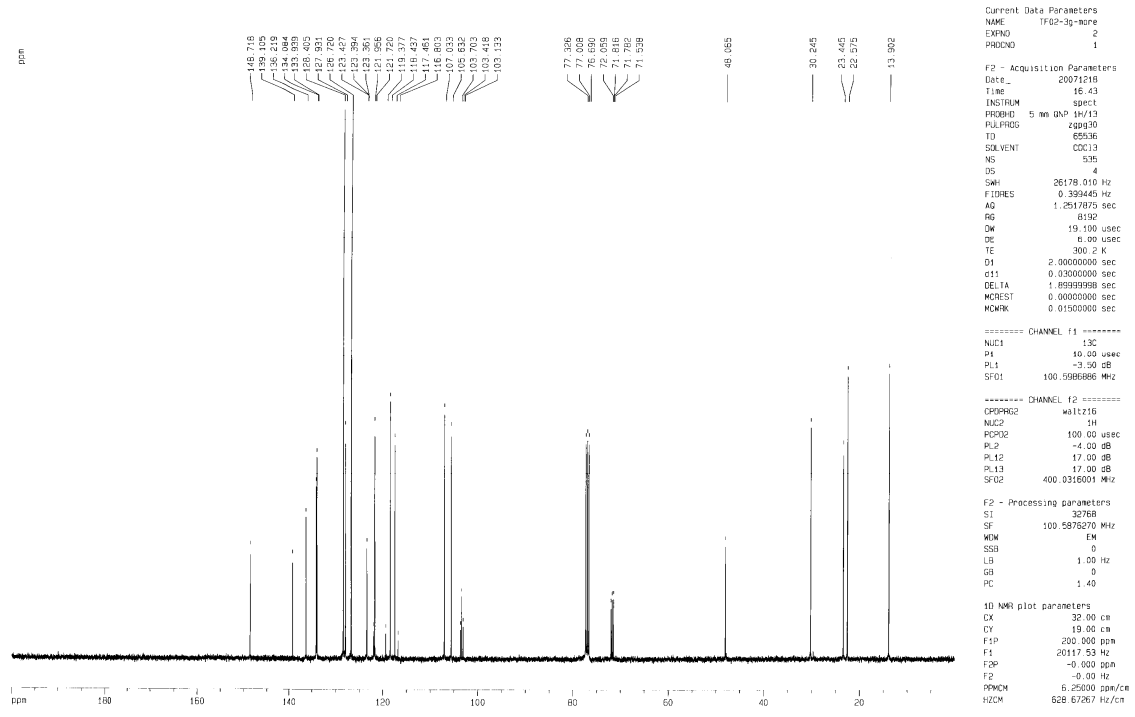
For **3f-*less***



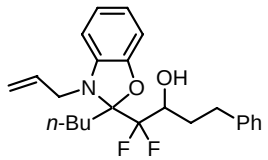


For **3f-*more***



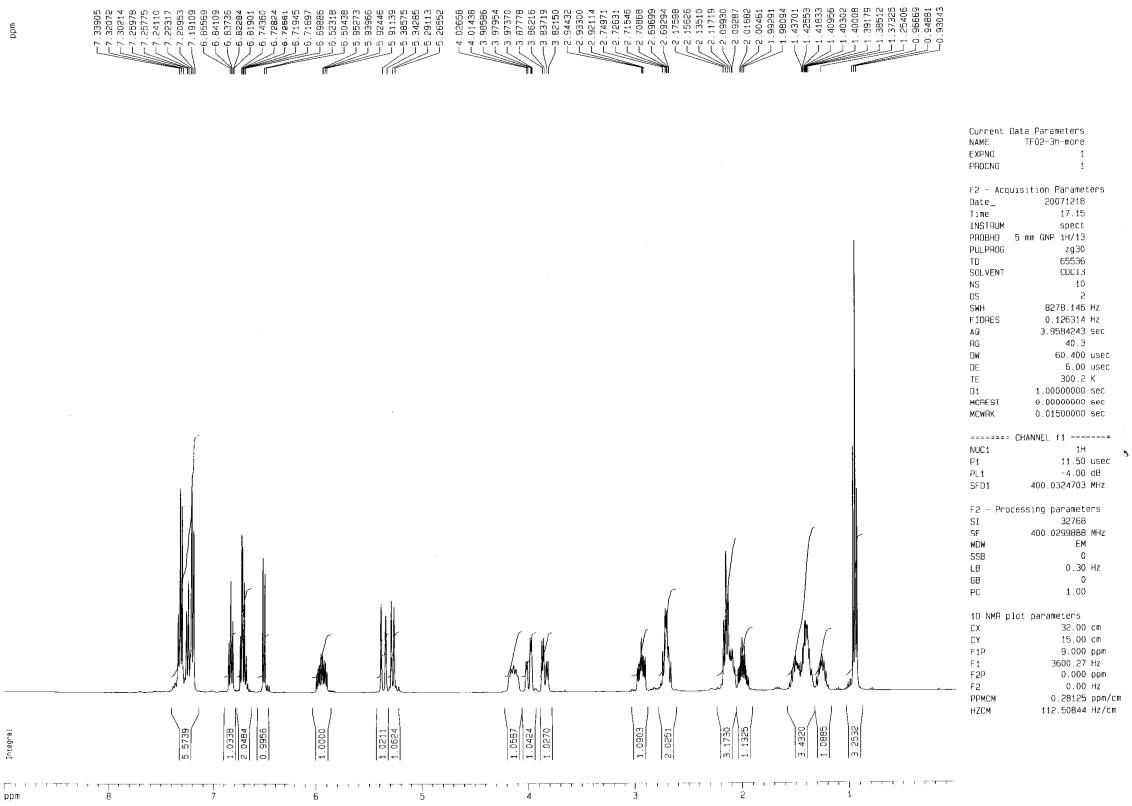


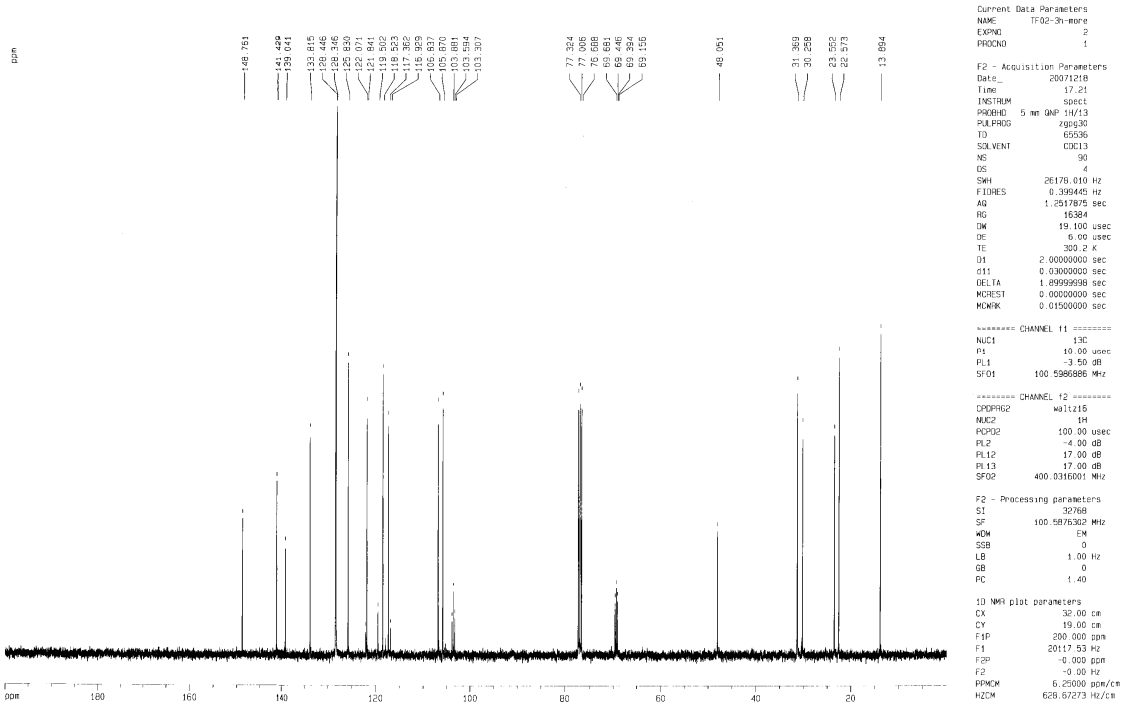
- S34 -

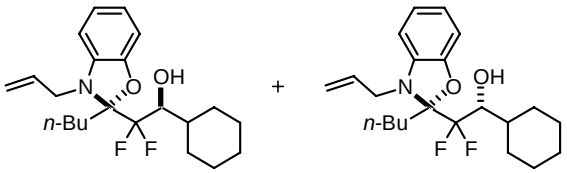


3g

As a mixture of diastereomer in a ratio of 11 : 1

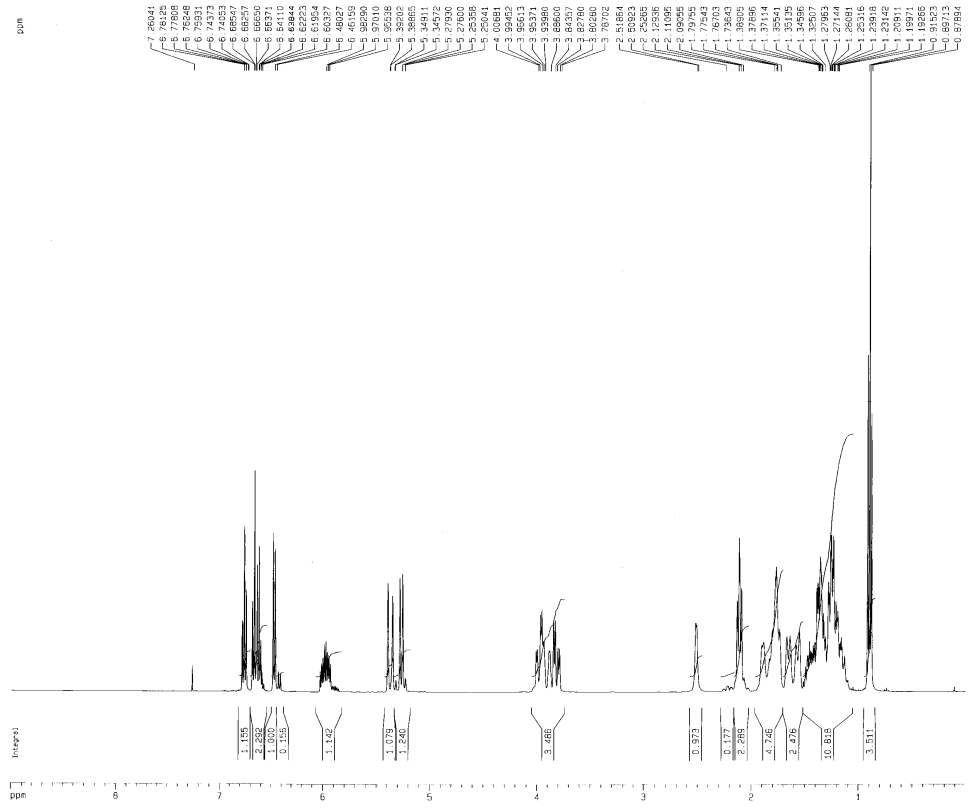


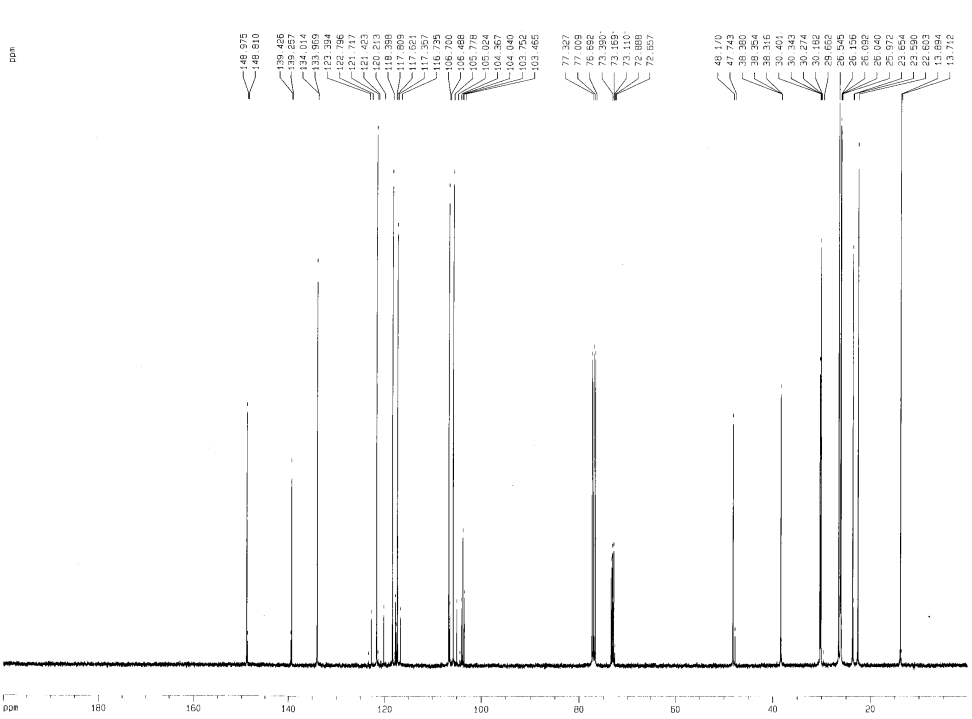




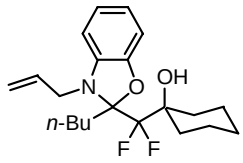
***anti*-3h** **syn-3h**

As a mixture of diastereomer in a ratio of 11 : 1 (*anti*/*syn*)

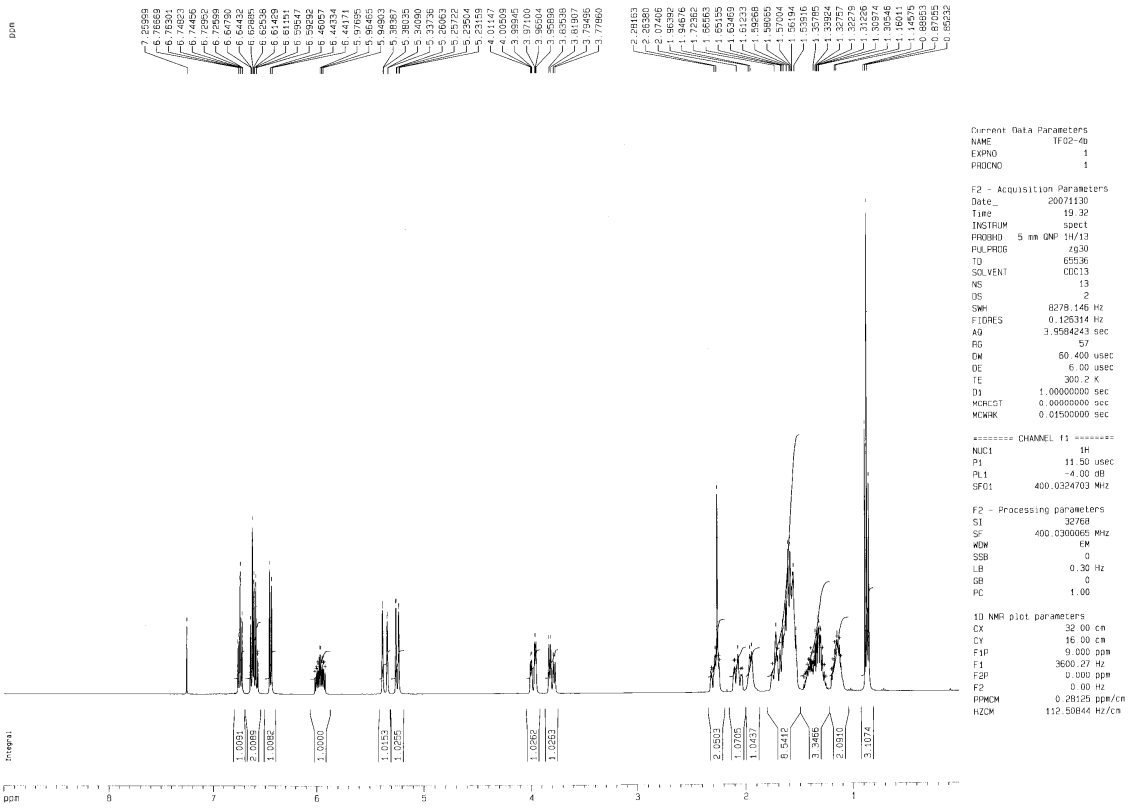


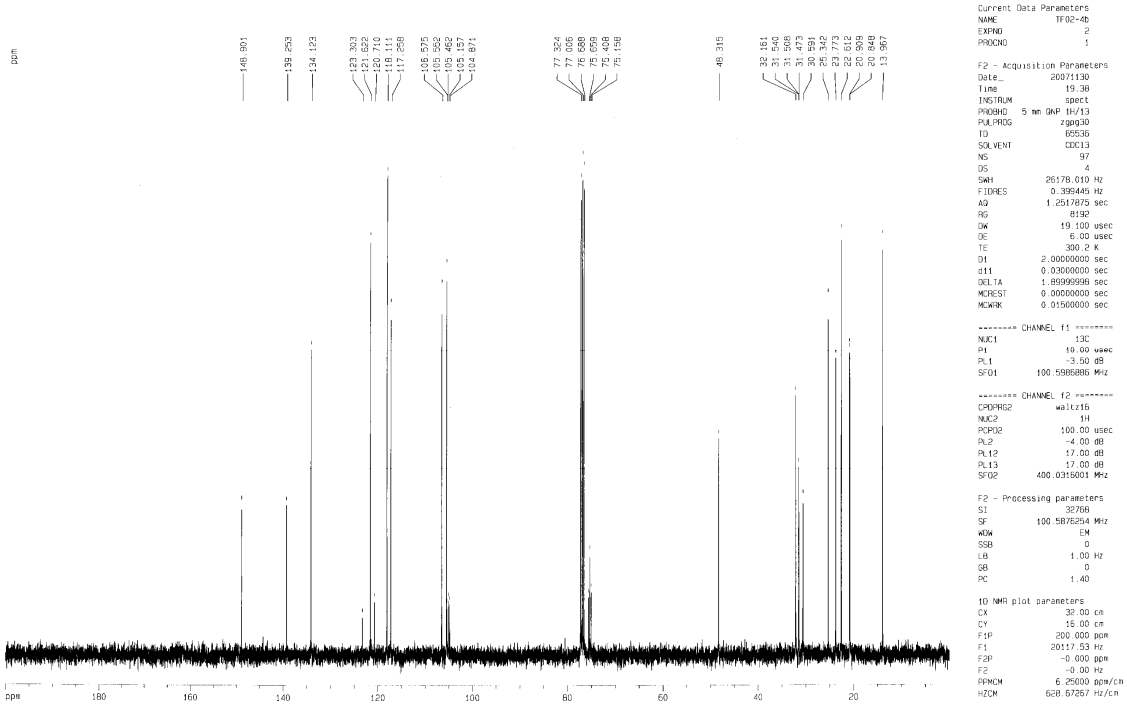


8.3. ^{1}H and ^{13}C NMR spectra of compound 4

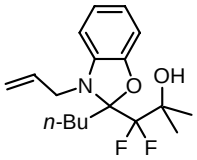


4a

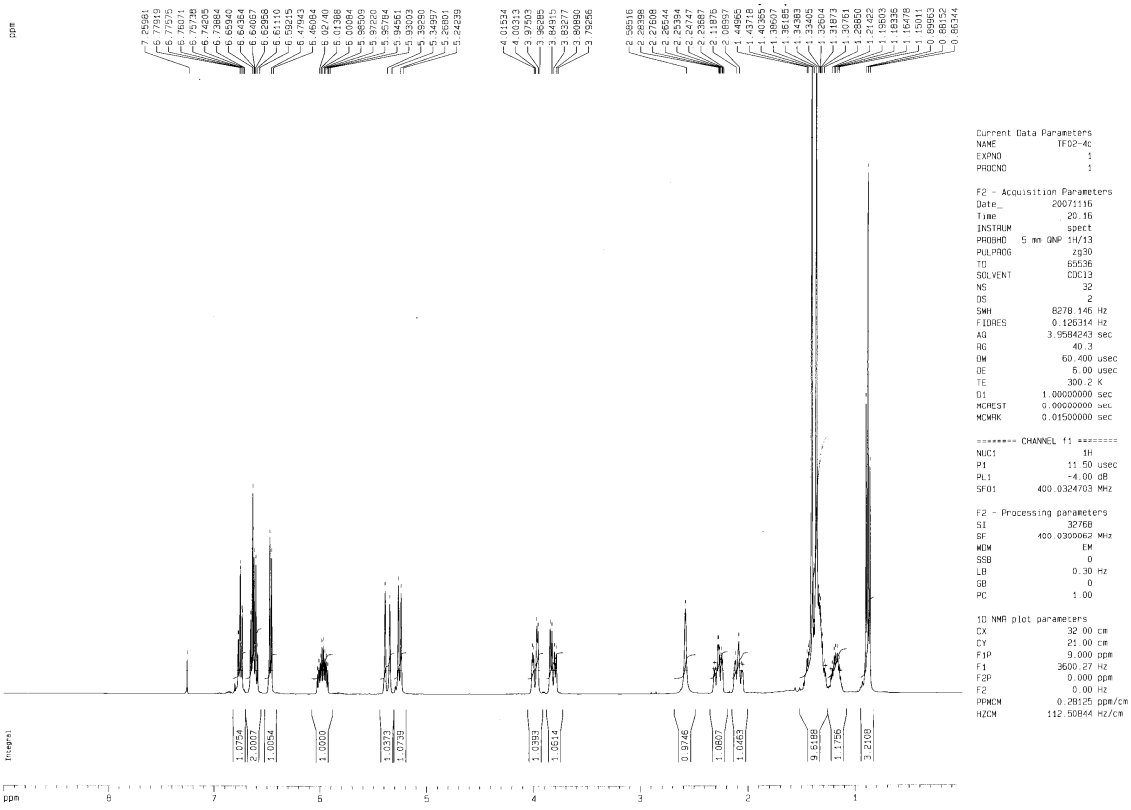


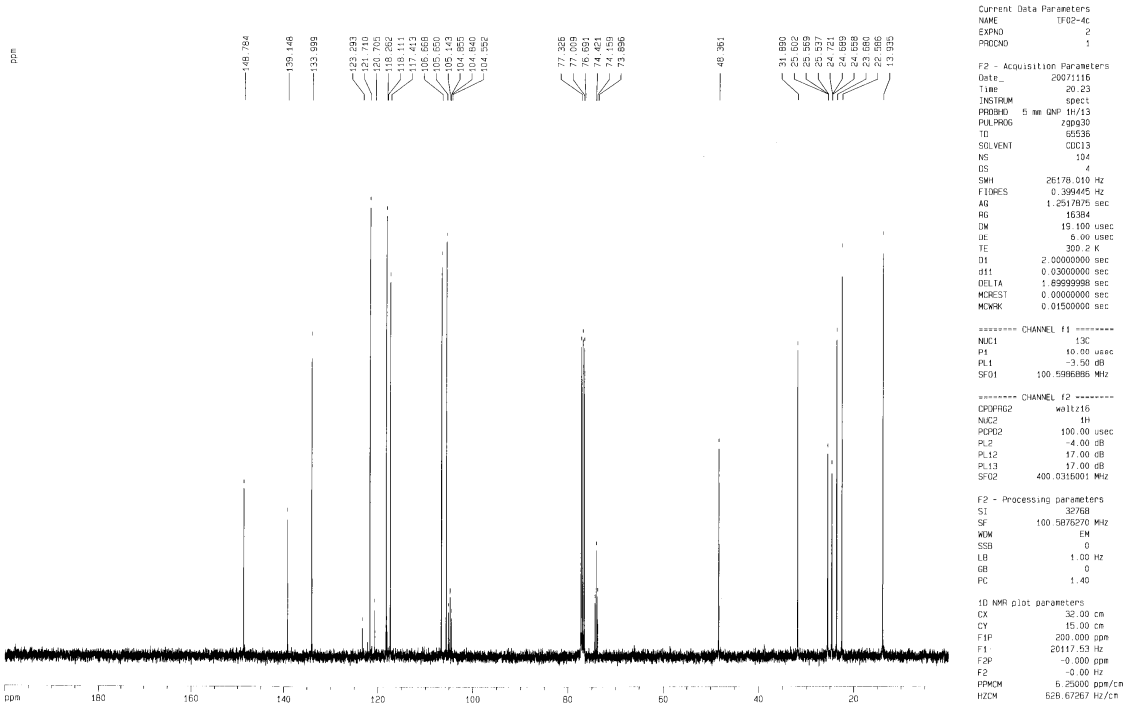


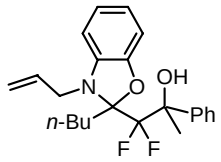
- S37 -


OH
N
O
n-Bu
F F

4b

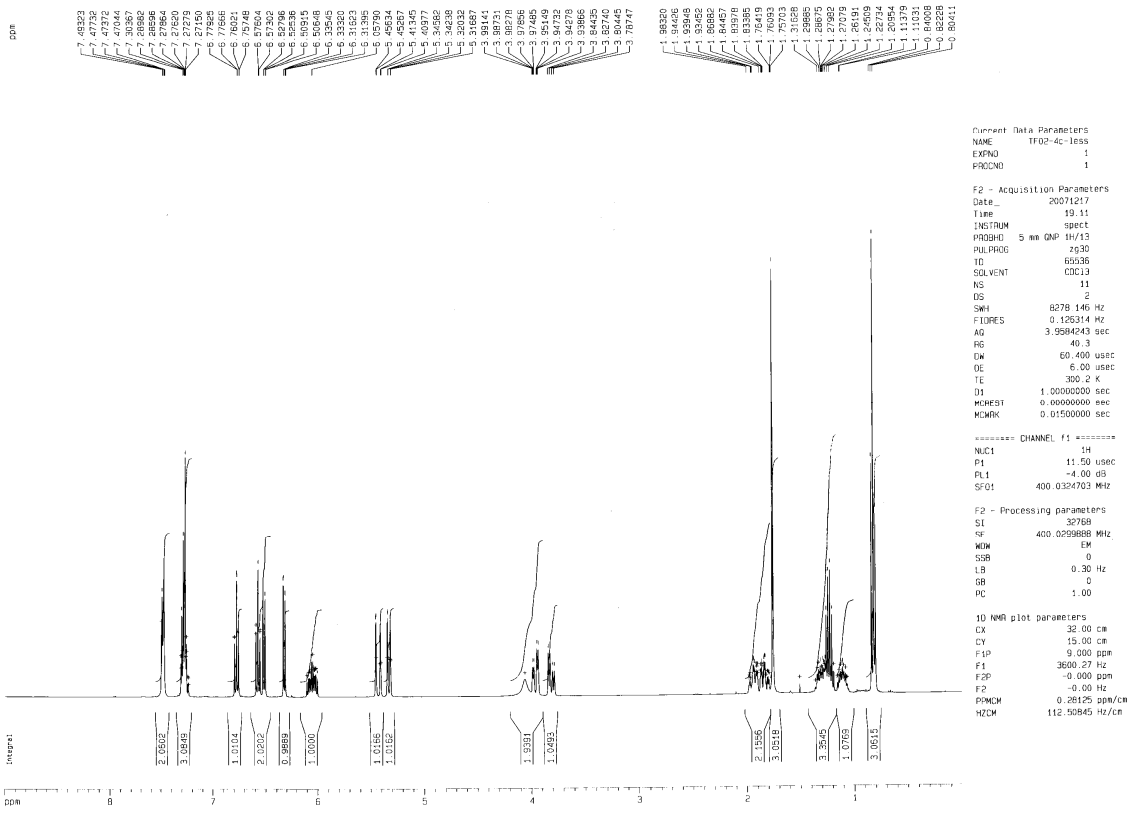

Current Data Parameters
NAME TF02-4c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071116
Time 20.16
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 40.3
DW 60.400 usec
DE 6.00 usec
TE 300.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 -4.00 dB
SFO1 400.0324703 MHz
F2 - Processing parameters
SI 32768
SF 400.0300062 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 32.00 cm
CY 21.00 cm
F1P 9.000 ppm
F1 3600.27 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.28125 ppm/cm
HZCM 112.50844 Hz/cm

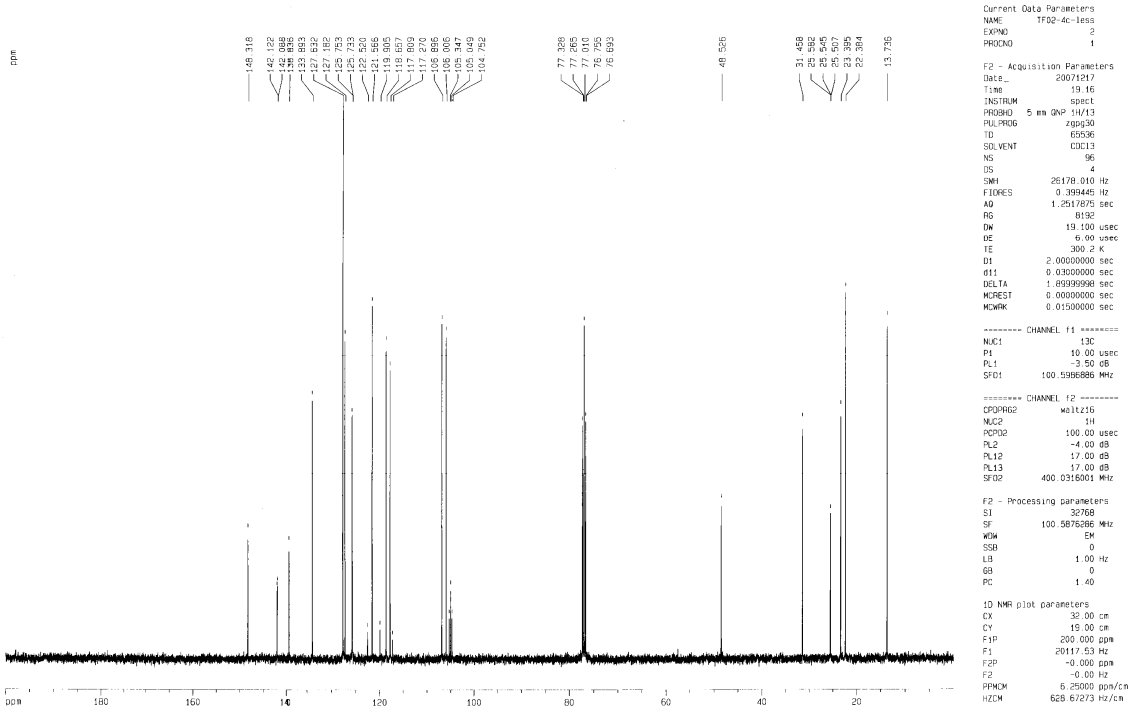

Current Data Parameters
NAME TF02-4c
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071116
Time 20.23
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 104
DS 4
SWH 26178.010 Hz
FIDRES 0.399445 Hz
AQ 1.2517875 sec
RG 16384
DW 19.100 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -3.50 dB
SFO1 100.5986886 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -4.00 dB
PL12 17.00 dB
PL13 17.00 dB
SFO2 400.0316001 MHz
F2 - Processing parameters
SI 32768
SF 100.5876270 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 32.00 cm
CY 15.00 cm
F1P 200.000 ppm
F1 20117.53 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 6.25000 ppm/cm
HZCM 628.67267 Hz/cm



4c

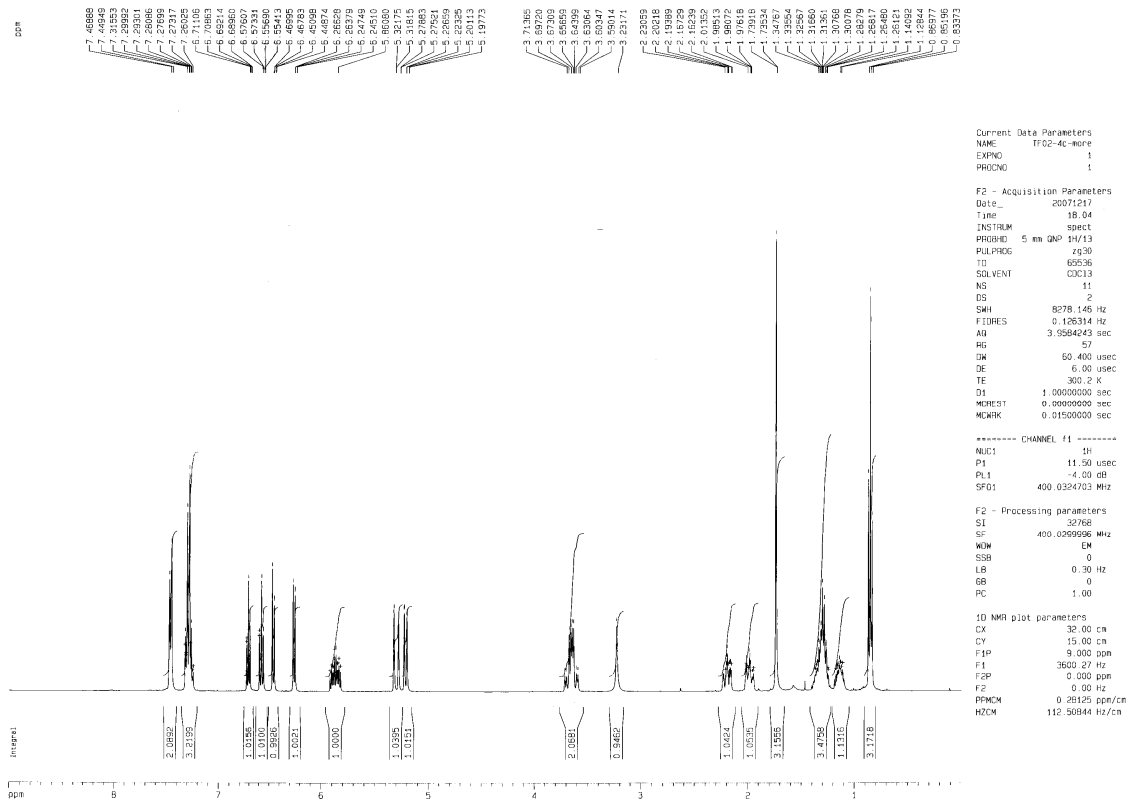
For **4c-*less***

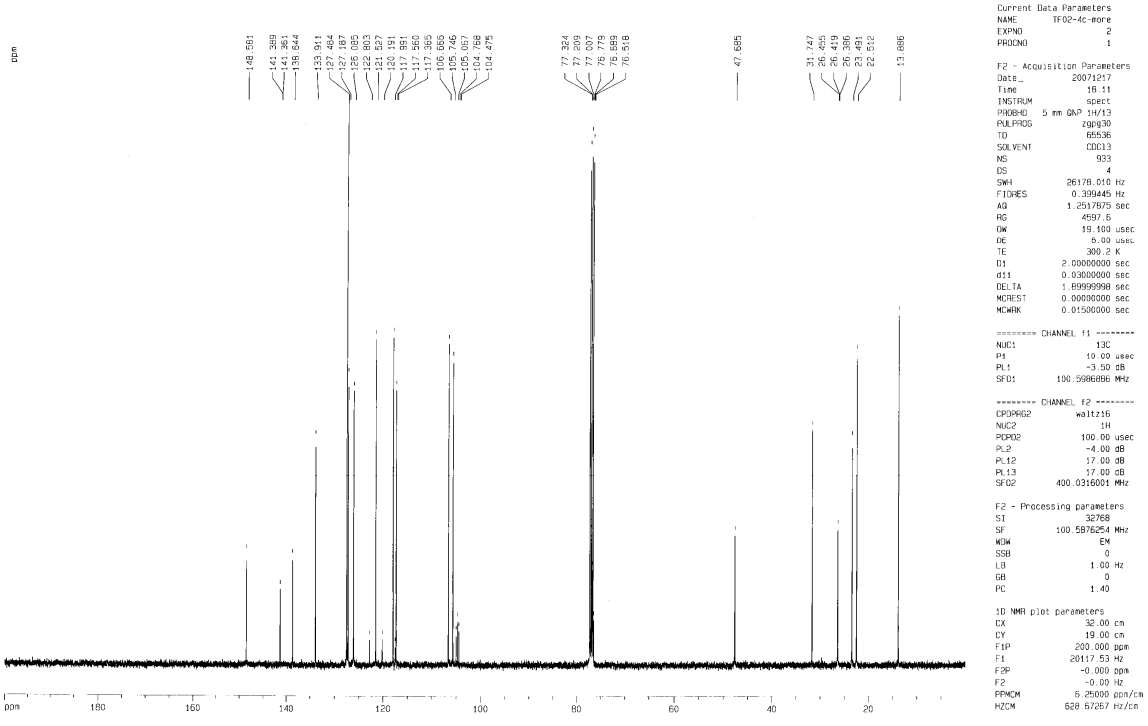




- S39 -

For **4c-*more***





9. References

1. Yang, S.-C.; Lai, H.-C.; Tsai, Y.-C. *Tetrahedron Lett.* **2004**, *45*, 2693-2697.
2. Masuoka, Y.; Asako, T.; Goto, G.; Noguchi, S. *Chem. Pharm. Bull.* **1986**, *34*, 130-139.