# Construction of fully substituted carbon centers containing a heteroatom and a $CF_3$ group *via p*-quinone methides generated *in situ*

Kyu Terashima,[a] Tomoko Kawasaki-Takasuka,[a] and Takashi Yamazaki*[a]

*a Division of Applied Chemistry, Institute of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Nakamachi, Koganei 184-8588, Japan. E-mail: tyamazak@cc.tuat.ac.jp*

Index

**General information**

Most of reactions where an organic solvent was employed were performed under argon with magnetic stirring using a flame-dried glassware. Unless otherwise noted, materials were obtained from commercial suppliers including anhydrous THF, $Et_2O$, and $CH_2Cl_2$, and were used without further purification. DMSO was freshly dried over 4Å MS which was activated by irradiating with a microwave for 1 min and heating under vacuum for 1 h. The substrates **2aa-ea** and **2ab** were prepared following to our previous report[1].

Analytical thin-layer chromatography (TLC) was routinely used for monitoring reactions by generally using a mixture of hexane and ethyl acetate. Spherical neutral silica gel (63–210 μm) was employed for usual column chromatography.

$^1H$ (300.40 MHz), $^{13}C$ (75.45 Hz), and $^{19}F$ (282.65 Hz) NMR spectra were recorded in $CDCl_3$ unless otherwise noted, and chemical shifts were reported in parts per million (ppm), downfield from internal tetramethylsilane ($Me_4Si$: δ 0.00, for $^1H$ and $^{13}C$) or hexafluorobenzene ($C_6F_6$: δ –163.00 for $^{19}F$). Data were tabulated in the following order: number of protons or fluorines, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sept, septet; m, multiplet; b, broad peak), coupling constants in Hertz. In the case of $^{13}C$ NMR, because it is difficult to observe perfluoroalkyl carbon atoms even after long time data acquisition due to multiple coupling, these data are not shown. Infrared (IR) spectra were reported in wave numbers ($cm^{-1}$). High resolution mass spectrometry was performed by the positive ionization mode. Melting points were measured by Differential Scanning Calorimetry.

**General procedure for the reaction of 2 with amines, followed by deprotection (GP1)**

To a test tube under an argon atmosphere were introduced **2aa** (0.1682 g, 0.4000 mmol), an amine (0.48 mmol) and 4.0 mL of DMSO. In some case, $Li_2CO_3$ (0.0014 g, 0.020 mmol, 5 mol%) was also added. This reaction mixture was stirred for appropriate time at 50 °C (see Table 2). After cooling to 30 °C, KF (0.0350 g, 0.602 mmol, 1.5 eq.) was added to the reaction mixture which was further stirred for 30 min at the same temperature. After addition of $H_2O$, the reaction mixture was extracted three times with $Et_2O$ or AcOEt and the combined organic phase was dried over anhydrous $Na_2SO_4$. After filtration, evaporation of the volatiles afforded a crude material which was purified by silica gel column chromatography to furnish the desired product.

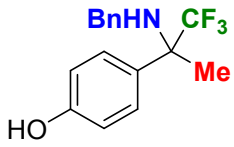
**General procedure for the reaction of 2 with amines, followed by TBS protection (GP2)**

Following to **GP1**, after cooling to 30 °C and quenched with $H_2O$, the mixture was extracted three times with AcOEt and the combined organic phase was washed with sat. NaCl aq. After drying over anhydrous $Na_2SO_4$, evaporation of the volatiles afforded a crude material which was introduced to a 30 mL round-bottomed flask containing a mixture of imidazole (0.0544 g, 0.799 mmol, 2.0 eq.) and $CH_2Cl_2$ (0.8 mL). To this solution was added TBSCl (0.0906 g, 0.601 mmol, 1.5 eq.) at 30 °C, and the mixture was stirred for 1 h at that temperature. After the reaction mixture was quenched with sat. $NH_4Cl$ aq., usual workup afforded a crude product which was purified by column chromatography to give the desired product.

**General procedure for the reaction of 2 with amines in the presence of acid as the additive (GP3)**

To a test tube were introduced *p*-TsOH·$H_2O$ (0.0038 g, 0.020 mmol, 5 mol%) or AcOH (0.0144 g, 0.240 mmol, 60 mol%), an amine (0.48 mmol) and 2.0 mL of DMSO. This reaction mixture was stirred for 5 min at 30 °C where, **2aa** (0.1682 g, 0.4000 mmol) in DMSO 2.0 mL was added, and the resultant mixture was stirred for appropriate time at 50 °C. After cooling to 30 °C, depending on the desired product, two types of procedures, deprotection or protection following to **GP1** or **GP2**, respectively, were selected. In both cases, after the whole mixture was quenched with $H_2O$, the resultant solution was extracted three times with AcOEt and the combined organic phase was successively washed with sat. $NaHCO_3$ and sat. NaCl aq. The usual workup and chromatographic separation afforded the desired products.

4-(2-Benzylamino-1,1,1-trifluoroprop-2-yl)phenol (**3aa**)




Following to **GP1**, benzylamine (0.0515 g, 0.0481 mmol) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3aa** as a pale-yellow oil (0.0942 g, 0. 3189 mmol, 80%).

Rf = 0.33 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 1.72 (s, 3H), 1.85 (brs, 1H), 3.56 (d, *J* = 12.6 Hz, 1H), 3.65 (d, *J* = 12.9 Hz, 1H), 4.84 (brs, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 7.21-7.41 (m, 5H), 7.52 (d, *J* = 8.4 Hz, 2H).

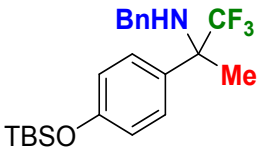
$^{13}$C NMR: δ 21.1, 46.7, 62.8 (q, *J* = 25.5 Hz), 115.3, 126.7 (q, *J* = 286.3 Hz), 127.2, 128.1, 128.5, 129.1, 129.3, 139.7, 155.4.

$^{19}$F NMR: δ –77.78 (s).

IR ($CHCl_3$) ν 3340, 3066, 3033, 3010, 1614, 1515, 1455, 1381, 1278, 1156 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{16}H_{16}F_3NO_2$, 296.1262; Found, 296.1233.

2-Benzylamino-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4aa).**




Following to **GP2**, benzylamine (0.0515 g, 0.0481 mmol) was used, and the crude product was purified by column chromatography (hexane:$CH_2Cl_2$ = 4:1) to give the desired product **4aa** as a colorless oil (0.1460 g, 0.3564 mmol, 89%).

Rf = 0.37 (hexane:$CH_2Cl_2$ = 4:1).

$^{1}$H NMR: δ 0.21 (s, 6H), 0.99 (s, 9H), 1.71 (s, 3H), 1.84 (s, 1H), 3.56 (d, *J* = 12.9 Hz, 1H), 3.64 (d, *J* = 12.9 Hz, 1H), 6.82-6.40 (m, 2H), 7.23-7.38 (m, 5H), 7.49 (d, *J* = 8.7 Hz, 2H).

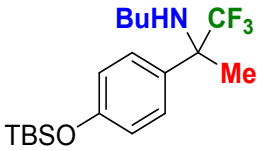
$^{13}$C NMR: δ –4.4, 18.2, 21.7 (q, *J* = 1.8 Hz), 25.6, 46.7, 62.8 (q, *J* = 25.4 Hz), 119.7, 127.07, 127.09 (q, *J* = 286.3 Hz), 128.0, 128.4, 128.8 (q, *J* = 1.3 Hz), 130.2, 140.3, 155.5.

$^{19}$F NMR: δ –77.46 (s).

IR ($CHCl_3$) ν 2957, 2931, 2886, 2858, 1607, 1510, 1472, 1270, 1150, 916 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{23}H_{30}F_3NOSi$, 409.2049; Found, 409.2021.

2-Butylamino-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4ab).**




Following to **GP2**, butylamine (0.0357 g, 0.488 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 20:1 as an eluent to give the desired product **4ab** as a colorless oil (0.1310 g, 0.3488 mmol, 87%).

Rf = 0.37 (hexane:AcOEt = 20:1).

$^{1}$H NMR: δ 0.21 (s, 6H), 0.88 (t, *J* = 7.2 Hz, 1H), 0.98 (s, 9H), 1.26-1.49 (m, 4H), 1.63 (s, 3H), 2.33 (dt, *J* = 11.1, 7.2 Hz, 1H), 2.46 (dt, *J* = 11.1, 7.2 Hz, 1H), 6.79-6.84 (m, 2H), 7.38 (d, *J* = 8.7 Hz, 2H).

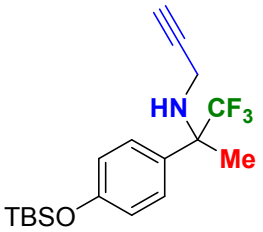
$^{13}$C NMR: δ –4.4, 13.9, 18.1, 20.3, 21.1, 25.6, 31.9, 41.9, 62.5 (q, *J* = 25.5 Hz), 119.6, 127.1 (q, *J* = 286.4 Hz), 128.7, 130.5, 155.3.

$^{19}$F NMR: δ –78.14 (s).

IR ($CHCl_3$) ν 2959, 2931, 2859, 1608, 1511, 1463, 1268, 1157, 917, 840 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{19}H_{32}F_3NOSi$, 375.2205; Found, 375.2218.

4-(1,1,1-Trifluoro-2-propalgylminoprop-2-yl)phenol (**4ac**)




Following to **GP2**, propalgylamine (0.0260 g, 0.472 mmol, 1.2 eq.) was used was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 4:1 as an eluent to give the desired product **4ac** as a slightly yellow oil (0.1230 g, 0.3874 mmol, 97%).

Following to **GP3**, cyclohexylamine (0.0260 g, 0.472 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the same purification process to the crude product similarly afforded **4ac** (0.1160 g, 0.3676 mmol, 92%).

Rf = 0.22 (hexane:$CH_2Cl_2$ = 4:1).

$^{1}$H NMR: δ 0.21 (s, 6H), 0.98 (m, 6H) 1.62 (brs, 1H), 1.67 (s, 3H), 2.21 (t, *J* = 2.7 Hz, 1H), 3.25 (s, 2H), 6.81-6.86 (m, 2H), 7.40 (d, *J* = 8.4 Hz, 2H).

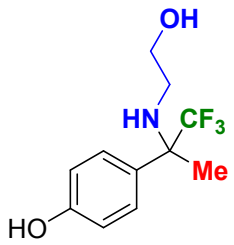
$^{13}$C NMR: δ –4.4, 18.1, 21.2, 25.6, 32.2 62.8 (q, *J* = 26.0 Hz), 71.2, 82.1, 119.8, 126.7 (q, *J* = 285.7 Hz), 128.8, 129.1, 155.7.

$^{19}$F NMR: δ –77.96 (s).

IR ($CHCl_3$) ν 3308, 3018, 2958, 2931, 2858, 1608, 1512, 1270, 1157, 917 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{18}H_{27}F_3NOSi$, 358.1814; Found, 358.1820.

4-[1,1,1-Trifluoro-{2-(hydroxyethyl)amino}prop-2-yl)]phenol **(3ad).**




Following to **GP1**, ethanolamine (0.0293 g, 0.480 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 to 1:2 as an eluent to give the desired product **3ad** as a pale-yellow solid (0.0801 g, 0.321 mmol, 80%).

Following to **GP3**, ethanolamine (0.0291 g, 0.480 mmol, 1.2 eq.) and *p*-TsOH (0.0038 g, 0.0020 mmol, 5 mol%) were used, and the same purification process to the crude product similarly afforded **3ad** (0.0856 g, 0.343 mmol, 86%).

Rf = 0.47 (hexane:AcOEt = 1:2).

m.p.: 122.9 °C.

$^1$H NMR (acetone-$d_6$): δ 1.16 (s, 1H), 1.52 (s, 3H), 2.33 (dt, $J$ = 10.8, 5.1 Hz, 1H), 2.46 (dt, $J$ = 10.8, 5.1 Hz, 1H), 3.49 (q, $J$ = 5.1 Hz, 2H), 3.59 (t, $J$ = 5.1 Hz, 1H), 6.69-6.74 (m, 2H), 7.30 (d, $J$ = 8.1 Hz, 2H), 8.33 (s, 1H).

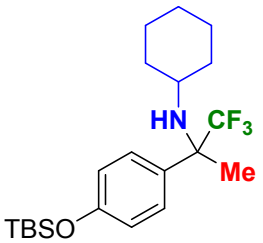
$^{13}$C NMR (acetone-$d_6$): δ 20.7, 45.1, 62.3, 62.9 (q, $J$ = 24.9 Hz), 115.8, 128.2 (q, $J$ = 284.9 Hz), 129.2, 130.0, 158.0.

$^{19}$F NMR (acetone-$d_6$): δ –76.46 (s).

IR (KBr) ν 3414, 3252, 2926, 2849, 1615, 1522, 1462, 1278, 1160, 1077 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{11}H_{15}F_3NO_2$, 250.1055; Found, 250.1050.

2-(Cyclohexylamino)-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4ae).**




Following to **GP2**, cyclohexylamine (0.0476 g, 0.480 mmol, 1.2 eq.) was used was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 4:1 as an eluent to give the desired product

**4ae** as a colorless oil (0.0985 g, 0.248 mmol, 62%).

Following to **GP3**, cyclohexylamine (0.0476 g, 0.480 mmol, 1.2 eq.) and *p*-TsOH·$H_2O$ (0.0038 g, 0.020 mmol, 5 mol%) were used, and the same purification process to the crude product similarly afforded **4ae** (0.1410 g, 0.3511 mmol, 88%).

Rf = 0.33 (hexane:$CH_2Cl_2$ = 3:1).

$^1$H NMR: δ 0.21 (s, 6H), 0.92-1.19 (m, 6H) 0.99 (s, 9H), 1.59-1.71 (m, 4H), 1.67 (s, 3H), 1.76-1.81 (m, 1H), 2.34-2.42 (m, 1H), 6.78-6.83 (m, 2H), 7.42 (d, *J* = 8.4 Hz, 2H).

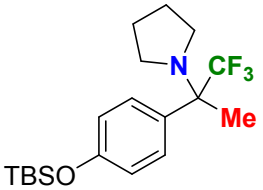
$^{13}$C NMR: δ –4.4, 18.2, 21.5, 25.4, 25.5, 25.6, 25.7, 36.1, 36.6, 51.4, 62.6 (q, *J* = 25.5 Hz), 119.4, 127.1 (q, *J* = 288.0 Hz), 128.9, 132.0, 155.0.

$^{19}$F NMR: δ –78.65 (s).

IR ($CHCl_3$) ν 2931, 2857, 1608, 1511, 1471, 1270, 1156, 1076, 916, 840 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{21}H_{34}F_3NOSi$, 401.2362; Found, 401.2376.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-(*N*-pyrrolidino)propane (**4ag**)**.**




Following to **GP2**, pyrrolidine (0.0342 g, 0.481 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 20:1 as an eluent to give the desired product **4ag** as a colorless oil (0.1261 g, 0.3376 mmol, 84%).

Rf = 0.71 (hexane:AcOEt = 10:1).

$^1$H NMR: δ 0.20 (s, 6H), 0.98 (s, 9H), 1.55 (s, 3H), 1.67-1.74 (m, 4H), 2.60-2.64 (m, 4H), 6.76-6.81 (m, 2H), 7.45 (d, *J* = 8.7 Hz, 2H).

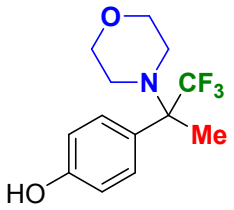
$^{13}$C NMR: δ –4.4, 13.6, 18.2, 23.8, 25.6, 46.7 (q, *J* = 1.3 Hz), 64.5 (q, *J* = 24.9 Hz), 119.3, 127.3 (q, *J* = 288.8 Hz), 128.8, 132.6, 155.2.

$^{19}$F NMR: δ –72.80 (s).

IR ($CHCl_3$) ν 2958, 2632, 2858, 1607, 1509, 1472, 1267, 1150, 916, 840 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{19}H_{30}F_3NOSi$, 373.2049; Found, 373.2074.

4-{1,1,1-Trifluoro-(*N*-morpholino)prop-2-yl}phenol (**3ah**).




Following to **GP1**, morpholine (0.0420 g, 0.482 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 to 2:1 as an eluent to give the desired product **3ah** as a pale-yellow oil (0.0915 g, 0.3324 mmol, 83%).

Following to **GP3**, cyclohexylamine (0.0476 g, 0.480 mmol, 1.2 eq.) and *p*-TsOH·$H_2O$ (0.0038 g, 0.020 mmol, 5 mol%) were used, and the same purification process to the crude product similarly afforded **3ah** (0.1021 g, 0.3709 mmol, 93%).

Rf = 0.13 (hexane:AcOEt = 1:4).

$^1$H NMR: δ 1.54 (s, 3H), 2.64-2.67 (m, 4H), 3.67-3.70 (m, 4H), 5.14 (brs, 1H), 6.78-6.84 (m, 2H), 7.50 (d, *J* = 8.7 Hz, 2H).

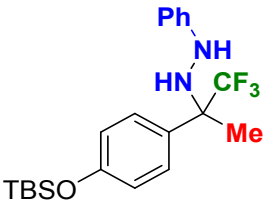
$^{13}$C NMR: δ 17.3, 47.4, 66.9 (q, *J* = 23.9 Hz), 67.8 115.1, 127.3 (q, *J* = 287.4 Hz), 128.8, 131.2, 155.7.

$^{19}$F NMR: δ –69.25 (s).

IR ($CHCl_3$) ν 3304, 3003, 2915, 2857, 1615, 1514, 1377, 1264, 1145, 1109 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{13}H_{16}F_3NO_2$, 275.1133; Found, 275.1105.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenylhydrazinopropane **(4ai)**




Following to **GP2**, phenylhydrazine (0.0860 g, 0.795 mmol, 2.0 eq.) and $Li_2CO_3$ (0.0014 g, 0.019 mmol, 5 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane as an eluent to give the desired product **4ai** as a yellow oil (0.1123 g, 0.2735 mmol, 68% (without $Li_2CO_3$, 0.0854 g, and usage of 1.2 eq. of phenylhydrazine 0.208 mmol, 52%)).

Following to **GP3**, phenylhydrazine (0.0520 g, 0.481 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the same purification process to the crude product similarly afforded **4ai** (0.1101 g, 0.2682 mmol, 67%).

Rf = 0.27 (hexane:AcOEt = 3:1).

m.p.: 134.1 °C.

$^{1}$H NMR: δ 0.21 (s, 6H), 0.98 (s, 9H), 1.26 (brs, 1H), 1.79 (s, 3H), 6.81 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.48-7.51 (m, 3H), 7.76-7.81 (m, 2H).

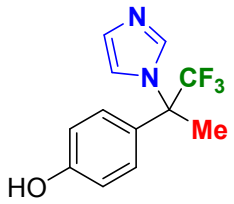
$^{13}$C NMR: δ –4.4, 17.3 (q, *J* = 1.9 Hz), 18.2, 25.6, 76.7 (q, *J* = 26.1 Hz), 119.7, 122.7, 126.2 (q, *J* = 283.9 Hz), 129.1, 129.2 (q, *J* = 1.3 Hz), 130.1, 131.5, 151.7, 155.7.

$^{19}$F NMR: δ –76.38 (s).

IR ($CHCl_3$) ν 3007, 2957, 2931, 2857, 1608, 1510, 1472, 1270, 1178, 916 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{21}H_{29}F_3N_2OSi$, 410.2001; Found, 410.2002.

4-{1,1,1-Trifluoro-(1*H*-imidazolyl)prop-2-yl}phenol **(3aj).**




Following to **GP1**, imidazole (0.0544 g, 0.799 mmol, 2.0 eq.) and $Li_2CO_3$ (0.0014 g, 0.019 mmol, 5 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 2:1 to 0:1 as an eluent to give the desired product **3aj** as a white solid (0.0863 g, 0.337 mmol, 84% (without $Li_2CO_3$ and usage of 1.2 eq. of imidazole: 0.0880 g, 0.0 343 mmol, 86%) ).

Following to **GP3**, imidazole (0.0328 g, 0.482 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the same purification process to the crude product similarly afforded **3aj** (0.0905 g, 0.353 mmol, 88%).

Rf = 0.33 (hexane:AcOEt = 1:2).

m.p.: 155.6 °C.

$^{1}$H NMR (acetone-$d_6$): δ 2.17 (s, 3H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.00 (s, 1H), 7.08 (s, 1H), 7.13 (d, *J* = 8.7 Hz, 2H), 7.68 (s, 1H), 8.88 (brs, 1H)

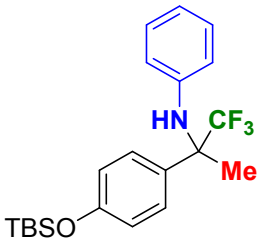
$^{13}$C NMR (acetone-$d_6$): δ 24.2, 66.7 (q, *J* = 27.9 Hz), 116.5, 120.3, 126.4 (q, *J* = 285.1 Hz), 128.3, 128.6 (q, *J* = 1.9 Hz), 129.2, 137.9, 159.3.

$^{19}$F NMR: δ –74.83 (s).

IR (KBr) ν 3401, 3141, 3140, 2925, 2819, 1615, 1522, 1517, 1385, 1148, 818 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{12}H_{12}F_3N_2O$, 257.0902; Found, 257.0882.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenylaminopropane **(4ak).**




Following to **GP2**, aniline (0.1117 g, 1.118 mmol, 3.0 eq.) and $Li_2CO_3$ (0.0014 g, 0.019 mmol, 5 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 30:1 as an eluent to give the desired product **4ak** as a colorless oil (0.0987 g, 0.2495 mmol, 62% (without $Li_2CO_3$ and usage of 1.2 eq. of aniline: 0.1411 g, 0.3567 mmol, 89%)).

Following to **GP3**, aniline (0.0447 g, 0.480 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the same purification process to the crude product the similarly afforded **4ak** (0.1376 g, 0.3479 mmol, 87%).

Rf = 0.27 (hexane:$CH_2Cl_2$ = 4:1).

$^1$H NMR: δ 0.21 (s, 6H), 0.98 (s, 9H), 1.85 (s, 3H), 4.22 (s, 1H), 6.35-6.38 (m, 2H), 6.68-6.74 (m, 1H), 6.82-6.86 (m, 2H), 7.02 (t, *J* = 8.7 Hz, 2H), 7.46 (d, *J* = 8.7 Hz, 2H).

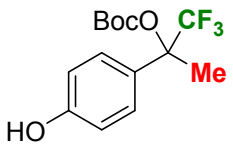
$^{13}$C NMR: δ –4.4, 18.2, 20.2, 25.6, 62.6 (q, *J* = 26.1 Hz), 116.5, 118.9, 120.0, 126.4 (q, *J* = 287.1 Hz), 128.7, 129.2, 129.5, 144.0, 155.8.

$^{19}$F NMR: δ –79.89 (s).

IR ($CHCl_3$) ν 3416, 3006, 2956, 2931, 2886, 2858, 1606, ,1509, 1270, 1158 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{21}H_{29}F_3NOSi$, 396.1971; Found, 396.1995.

4-[{2-(*tert*-Butoxycarbonyl)oxy}-1,1,1-trifluoroprop-2-yl}phenol **(6aa).**




Following to **GP3**, aniline (0.0442 g, 0.475 mmol, 1.2 eq.) and *p*-TsOH·$H_2O$ (0.0038 g, 0.020 mmol, 5 mol%) were used, and the reaction mixture was quenched with 1 *M* HCl aq. After usual work up, the crude mixture was purified by column chromatography using hexane:AcOEt = 3:1 as an eluent to give **6a** as a pale-yellow solid (0.0425 g, 0.139 mmol, 35%). (58% of **2aa** was recovered (0.0969 g, 0.2304 mmol).)

Rf = 0.33 (hexane:AcOEt = 3:1).

m.p.: 117.5 °C.

$^1$H NMR: δ 1.42 (s, 9H), 2.09 (q, *J* = 1.2 Hz, 3H), 5,12 (brs, 1H), 6.78-6.83 (m, 2H), 7.81 (d, *J* = 8.4

Hz, 2H).

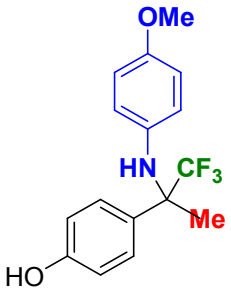
$^{13}$C NMR: δ 18.3, 27.8, 82.1 (q, $J$ = 26.0 Hz), 83.6, 115.3, 123.9 (q, $J$ = 283.8 Hz), 127.2, 127.9, 150.5, 156.4.

$^{19}$F NMR: δ –82.19 (s).

IR (KBr) ν 3432, 3074, 2997, 2937, 1726, 1616, 1517, 1464, 1175, 917 cm$^{-1}$.

HRMS (FAB+, *m/z*): [M]$^{+}$ Calcd for $C_{14}H_{17}F_3O_4$, 306.1079; Found, 306.1100.

4-[1,1,1-Trifluoro-2-{(4-methoxyphenyl)amino}prop-2-yl}phenol **(3al).**




Following to **GP1**, *p*-anisidine (0.0591 g, 0.480 mmol, 1.2 eq.) and $Li_2CO_3$ (0.0014 g, 0.019 mmol, 5 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3al** as a colorless oil (0.0955 g, 0.307 mmol, 72% (without $Li_2CO_3$, 0.1159 g, 0.3723 mmol, 93%)).

Following to **GP3**, *p*-anisidine (0.0592 g, 0.481 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the same purification process to the crude product the similarly afforded **3al** (0.1222 g, 0.3925 mmol, 98%).

Rf = 0.23 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 1.78 (s, 3H), 3.69 (s, 3H), 3.93 (brs, 1H), 4.91 (brs, 1H), 6.37-6.40 (m, 2H), 6.60-6.66 (m, 2H), 6.83-6.87 (m, 2H), 7.51 (d, $J$ = 8.4 Hz, 2H).

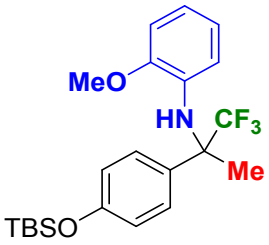
$^{13}$C NMR: δ 20.1, 55.6, 62.7 (q, $J$ = 26.1 Hz), 114.3, 115.3, 118.9, 126.4 (q, $J$ = 285.1 Hz), 129.3, 129.4, 137.7, 153.1, 155.7.

$^{19}$F NMR: δ –79.71 (s).

IR ($CHCl_3$) ν 3382, 3001, 2953, 2836, 1614, 1511, 1462, 1270, 1154, 825 cm$^{-1}$.

HRMS (FAB+, *m/z*): [M]$^{+}$ Calcd for $C_{16}H_{16}F_3NO_2$, 311.1133; Found, 311.1152.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-(2-methoxyphenyl)amino-propane **(4am).**




Following to **GP2**, *o*-anisidine (0.0592 g, 0.481 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 4:1 as an eluent to give the desired product **4am** as a colorless oil (0.0908 g, 0.213 mmol, 53%).

Following to **GP3**, *o*-anisidine (0.0592 g, 0.481 mmol, 1.2 eq.) and AcOH (0.0144 g, 0.240 mmol, 60 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 4:1 as an eluent to give the desired product **4am** as a colorless oil (0.1357 g, 0.3196 mmol, 80%).

Rf = 0.33 (hexane:$CH_2Cl_2$ = 4:1).

$^1$H NMR: δ 0.21 (s, 6H), 0.98 (s, 9H), 1.84 (s, 3H), 3.89 (s, 3H), 5.04 (s, 1H), 5.98 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.52 (td, *J* = 7.8, 1.5 Hz, 1H) 6.65 (td, *J* = 7.8, 1.5 Hz, 1H), 6.77-6.86 (m, 3H), 7.46 (d, *J* = 8.4 Hz, 2H).

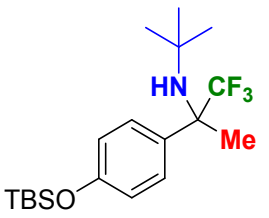
$^{13}$C NMR: δ –4.4, 18.2, 20.1, 25.6, 55.6, 62.3 (q, *J* = 26.7 Hz), 109.7, 114.5, 117.9, 120.0, 120.4, 126.5 (q, *J* = 285.2 Hz), 129.3, 129.7, 133.8, 147.8, 155.7.

$^{19}$F NMR: δ –79.89 (s).

IR ($CHCl_3$) ν 3382, 3001, 2953, 2836, 1614, 1511, 1462, 1270, 1154, 825 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{22}H_{31}F_3NO_2Si$, 426.2076; Found, 426.2095.

2-*tert*-Butyl-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4af).**




Following to **GP3**, *t*-butylamine (0.0352 g, 0.481 mmol, 1.2 eq.) and *p*-TsOH•$H_2O$ (0.0038 g, 0.020 mmol, 5 mol%) were used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 4:1 as an eluent to give the desired product **4af** as a colorless oil (0.0284 g, 0.0756 mmol, 19%) in addition to other products of 0.0683 g of **7** (0.225 mmol, 56%) and 0.0111 g of **8** (0.0226 mmol, 6%))

Rf = 0.33 (hexane:$CH_2Cl_2$ = 4:1).

$^1$H NMR: δ 0.20 (s, 6H), 0.98 (s, 9H), 1.00 (s, 9H), 1.79 (q, *J* = 0.9 Hz, 3H), 6.77-6.82 (m, 2H), 7.41 (d, *J* = 8.4 Hz, 2H).

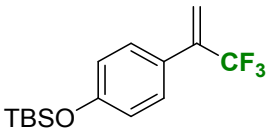
$^{13}$C NMR: δ –4.4, 18.2, 21.3, 25.6, 32.4, 51.7, 62.4 (q, *J* = 24.9 Hz), 119.2, 126.8 (q, *J* = 284.6 Hz), 128.9, 133.6, 155.3.

$^{19}$F NMR: δ –80.55 (s).

IR ($CHCl_3$) ν 3019, 2959, 2931, 2859, 1607, 1510, 1471, 1270, 1153, 916 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{19}H_{32}F_3NOSi$, 375.2205; Found, 375.2224.

1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene **(7)**




Rf = 0. 33 (hexane).

$^1$H NMR: δ 0.21 (s, 6H), 0.98 (s, 9H), 5.69 (q, *J* = 1.8 Hz, 1H), 5.86 (q, *J* = 1.2 Hz, 1H), 6.81-6.89 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 2H).

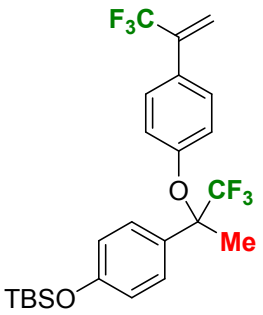
$^{13}$C NMR: δ –4.4, 18.2, 25.7, 118.8 (q, *J* = 6.2 Hz), 120.1, 123.4 (q, *J* = 274.0 Hz), 126.6, 128.6, 138.4 (q, *J* = 29.8 Hz), 156.5.

$^{19}$F NMR: δ –66.06 (s).

IR ($CHCl_3$) ν 3019, 2958, 2931, 2859, 1607, 1513, 1267, 1217, 1129, 915, $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{15}H_{22}F_3OSi$, 303.1392; Found, 303.1384.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-{4-(3,3,3-trifluoroprop-1-en-2-yl)phenoxy}propane. **(8)**




$^1$H NMR: δ 0.23 (s, 6H), 0.99 (s, 9H), 1.85 (s, 3H), 5.66 (q, *J* = 1.5 Hz, 1H), 5.86 (q, *J* = 1.2 Hz, 1H) 6.68-6.73 (m, 2H), 6.84-6.89 (m, 2H), 7.25 (d, *J* = 9.3 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H).

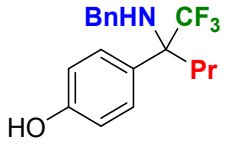
$^{13}$C NMR: δ –4.4, 17.9, 18.2, 25.6, 81.5 (q, *J* = 29.2 Hz), 119.4 (q, *J* = 5.6 Hz), 120.0, 123.3 (q, *J* = 274.1 Hz), 124.7 (q, *J* = 284.4 Hz), 127.8, 128.2, 128.8, 129.0, 138.1 (q, *J* = 29.8 Hz), 154.7, 156.5.

$^{19}$F NMR: δ –82.56 (s, 3F), –66.13 (s, 3F)

IR ($CHCl_3$) ν 3363, 3004, 2952, 1615, 1516, 1459, 1281, 1171, 1121, 970 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{24}H_{29}F_6O_2Si$, 491.1841; Found, 491.1824.

4-{2-(Benzylamino)-1,1,1-trifluoropent-2-yl}phenol. (**3ba**)




Following to **GP1**, benzylamine (0.0514 g, 0.480 mmol, 1.2 eq.) and **2ba** (0.1794 g, 0.3995 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3ba** as a pale-yellow oil (0.1193 g, 0.3689 mmol, 92%).

Rf = 0.33 (hexane:AcOEt = 4:1).

$^1H$ NMR: δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.33-1.46 (m, 2H), 1.62 (s, 1H), 2.04-2.24 (m, 2H), 3.54 (d, *J* = 11.1 Hz, 1H), 3.75 (d, *J* = 11.1 Hz, 1H), 5.00 (brs, 1H), 6.81-6.86 (m, 2H), 7.21-7.31 (m, 5H), 7.50 (d, *J* = 8.1 Hz, 2H).

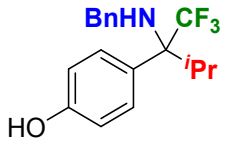
$^{13}C$ NMR: δ 14.3, 16.3, 38.1, 46.9, 65.6 (q, *J* = 25.0 Hz), 115.2, 127.1, 127.6 (q, *J* = 290.7 Hz), 127.8, 128.5, 128.8, 129.4, 140.5, 155.0.

$^{19}F$ NMR: δ –71.73 (s).

IR ($CHCl_3$) ν 3351, 2965, 2934, 2875, 1608, 1513, 1269, 1165, 916, 761 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{23}H_{30}F_3O_3Si$, 324.1575; Found, 324.1574

4-{2-(Benzylamino)-1,1,1-trifluoro-3-methylbut-2-yl}phenol. (**3ca**)




Following to **GP1**, benzylamine (0.0514 g, 0.480 mmol, 1.2 eq.) and **2ca** (0.1794 g, 0.3995 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3ca** as a pale-yellow oil (0.0906 g, 0.2802 mmol, 70%).

Rf = 0.33 (hexane:AcOEt = 4:1).

$^1H$ NMR: δ 0.81 (d, *J* = 6.9 Hz, 3H), 1.06 (dq, *J* = 6.9, 1.5 Hz, 3H), 1.77 (brs, 1H), 2.19 (sept, *J* = 6.9 Hz, 1H) , 3.78 (s, 2H), 4.84 (brs, 1H), 6.81-6.84 (m, 2H), 7.28-7.53 (m, 7H).

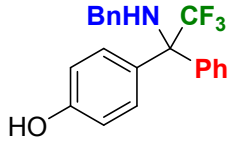
$^{13}C$ NMR: δ 17.6, 17.8, 36.7, 47.0, 69.1 (q, *J* = 22.3 Hz), 114.9, 127.0, 127.5, 128.0 (q, *J* = 294.4 Hz), 128.4, 128.8, 129.5, 140.9, 154.7.

$^{19}F$ NMR: δ –64.37 (s).

IR ($CHCl_3$) ν 3370, 2970, 2938, 2879, 1615, 1514, 1240, 1145, 907, 834 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{18}H_{21}F_3NO$, 324.1575; Found, 324.1578.

4-{1-(Benzylamino)-2,2,2-trifluoro-1-phenyleth-2-yl}phenol **(3da)**




Following to **GP1**, benzylamine (0.0514 g, 0.480 mmol, 1.2 eq.) and **2da** (0.1930 g, 0.3999 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3da** as a pale-yellow oil (0.1366 g, 0.3822 mmol, 96%).

Rf = 0.37 (hexane:AcOEt = 4:1).

$^1$H NMR: δ 1.26 (s, 1H), 2.31 (brs, 1H), 3.66 (s, 2H), 6.77-6.81 (m, 2H), 7.28-7.47 (m, 12H).

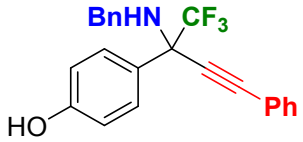
$^{13}$C NMR: δ 48.2, 70.0 (q, *J* = 24.9 Hz), 115.0, 126.9 (q, *J* = 290.2 Hz), 127.1, 127.97, 128.01, 128.1, 128.4, 128.5 (q, *J* = 1.8 Hz), 130.0 (q, *J* = 1.1 Hz), 131.4, 139.3, 140.4, 155.2.

$^{19}$F NMR: δ –68.59 (s).

IR ($CHCl_3$) ν 3352, 3064, 2920, 2866, 1614, 1514, 1448, 1259, 1150, 832 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{21}H_{19}F_3NO$, 358.1419; Found, 358.1401.

4-{2-(Benzylamino)-1,1,1-trifluoro-4-phenylbut-3-yn-2-yl}phenol **(3ea)**




Following to **GP1**, benzylamine (0.0514 g, 0.480 mmol, 1.2 eq.) and **2ea** (0.2031 g, 0.4009 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **3ea** as a brown oil (0.1358 g, 0.3561 mmol, 89%).

Rf = 0.37 (hexane:AcOEt = 4:1).

$^1$H NMR: δ 3.62 (d, *J* = 12.0 Hz, 1H), 3.94 (d, *J* = 12.0 Hz, 1H), 6.86-6.91 (m, 2H), 7.27-7.41 (m, 8H) 7.57-7.60 (m, 2H), 7.82 (d, *J* = 8.7 Hz, 2H).

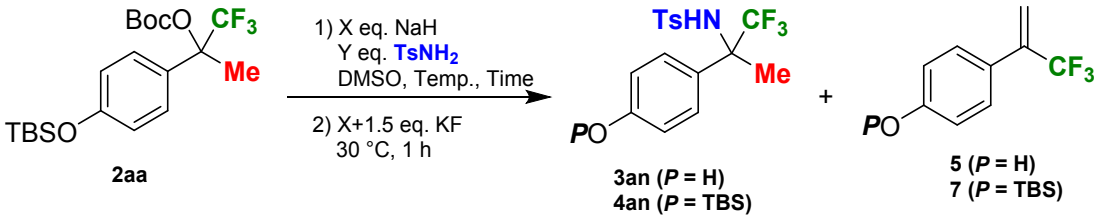
$^{13}$C NMR: δ 48.0, 70.0 (q, *J* = 29.2 Hz), 84.3, 88.5, 115.3, 121.7, 124.3 (q, *J* = 284.5 Hz), 125.8, 127.3, 128.3, 128.4, 128.5, 129.0, 130.3, 131.9, 139.3, 156.5.

$^{19}$F NMR: δ –78.68 (s).

IR ($CHCl_3$) ν 3592, 3333, 3066, 3017, 1613, 1597, 1511, 1267, 1193, 1163, 916 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{19}H_{33}F_3NOSi$, 376.2284; Found, 376.2257.

**Table S1 Investigation of the reaction condition with 2aa and $TsNH_2$**



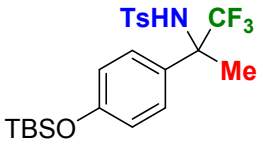

| Entry | X | Y | Temp. (°C) | Time (h) | $^{19}$F NMR yield (%) | |
|---|---|---|---|---|---|---|
| | | | | | 3an+4an | 5+7 |
| 1[a)] | 0.05 | 1.2 | 50 | 24 | 14 | 75 |
| 2[a)] | 0.05 | 2.0 | 50 | 24 | 13 | 62 |
| 3 | 1.1 | 1.2 | 50 | 1 | 43 | 37 |
| 4 | 0.5 | 1.2 | 50 | 1 | 25 | 52 |
| **5** | **2.0** | **2.2** | **50** | **1** | **54 [49][b)]** | **40 [38][c)]** |
| 6 | 3.0 | 3.3 | 50 | 1 | 51 | 42 |
| 7[d)] | 2.0 | 2.2 | 50 | 1 | 0 | trace |
| 8 | 2.0 | 2.2 | 70 | 0.5 | 53 | 45 |
| 9 | 2.0 | 2.2 | 30 | 4 | 54 | 38 |

a) Usage of $Li_2CO_3$ instead of NaH. b) Isolated yield of **4an** after TBS protection of the crude mixture. c) Isolated yield of **7** after TBS protection of the crude mixture. d) Usage of THF instead of DMSO.

**General procedure of reaction of amide or imide (GP4)**

To a test tube containing 55% suspension of NaH in mineral oil (0.0349 g, 0.800 mmol) in DMSO (2.0 mL) was introduced an amide or imide (0.88 mmol, 2.2 eq.), and this reaction mixture was stirred for 15-30 min at 30 °C. Then, **2aa** (0.1682 g, 0.4000 mmol) in DMSO 2.0 mL was added to the reaction mixture, and the whole solution was further stirred for 1 h at 50 °C. After cooling to 30 °C and quenched with sat. $NH_4Cl$ aq., TBS protection was conducted by **GP2**. Then, after usual work up, evaporation of the volatiles afforded a white solid which was washed by hexane to remove the excess imide or amide. Evaporation of hexane from the filtrate afforded crude oils which were purified by silica gel column chromatography to furnish the desired product.

*N*-[1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoroprop-2-yl]-4-methylbenzenesulfonamide **(4an)**




Following to **GP4**, *p*-toluenesulfonamide (0.1510 g, 0.8820 mmol, 2.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 1:2 as an eluent to give the desired product **4an** as a colorless oil (0.0928 g, 0.196 mmol, 49%).

Rf = 0.25 (hexane:$CH_2Cl_2$ = 1:2).

$^1$H NMR: δ 0.20 (s, 6H), 0.98 (s, 9H), 1.87 (s, 3H), 2.41 (s, 3H), 5.31 (s, 1H), 6.68-6.73 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H).

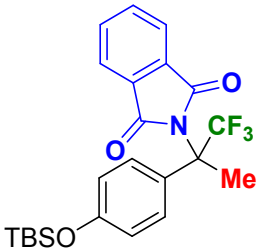
$^{13}$C NMR: δ –4.4, 18.1, 19.2, 21.4, 25.6, 63.3 (q, *J* = 28.0 Hz), 119.5, 125.3 (q, *J* = 283.6 Hz), 127.1, 128.3, 128.4, 129.4, 138.8, 143.4, 156.0.

$^{19}$F NMR: δ –79.89 (s).

IR ($CHCl_3$) ν 3376, 3027, 2957, 2859, 1608, 1513, 1269, 1165, 916, 761 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{22}H_{30}F_3NO_3SSi$, 473.1668; Found, 473.1667.

*N*-[1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoroprop-2-yl]phtalimide **(4ao)**




Following to **GP4**, phthalimide (0.1294 g, 0.8795 mmol, 2.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 2:1 as an eluent to give the desired product **4ao** as a colorless oil (0.0560 g, 0.1246 mmol, 31%).

Rf = 0.33 (hexane:$CH_2Cl_2$ = 2:1).

$^1$H NMR: δ 0.21 (s, 6H), 0.98 (s, 9H), 2.23 (s, 3H), 6.79-6.82 (m, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.71-7.76 (m, 2H), 7.78-7.82 (m, 2H).

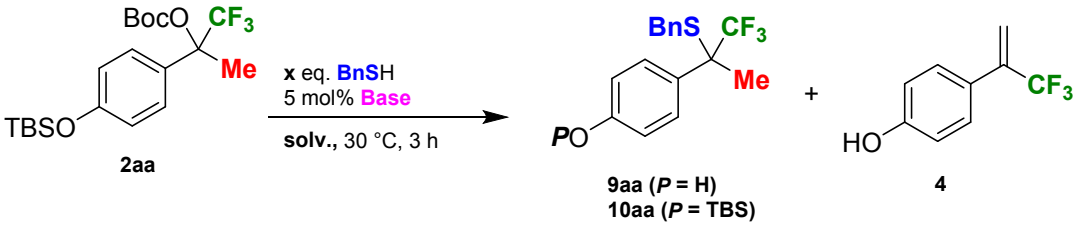
$^{13}$C NMR: δ –4.4, 18.1, 24.6, 25.6, 63.9 (q, *J* = 29.1 Hz), 119.8, 123.3, 125.8 (q, *J* = 286.9 Hz), 126.3, 131.3, 131.4, 134.3, 155.0, 167.5.

$^{19}$F NMR: δ –72.68 (s).

IR ($CHCl_3$) ν 3019, 2954, 2931, 2861, 1728, 1514, 1273, 1216, 918, 761 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{23}H_{26}F_3NO_3Si$, 449.1634; Found, 449.1637.

**Table S2 Optimisation of the reaction condition with thiol and 2aa**

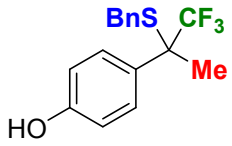



| Entry | x | Base | solv. | $^{19}$F NMR Yield (%) | | |
|---|---|---|---|---|---|---|
| | | | | 9aa+10aa | 5 | Other products |
| 1 | 1.5 | TBAF | DMSO | 73 | 2 | 4 |
| 2 | 1.5 | TBAF | DMF | 94 | 4 | 2 |
| 3 | 1.5 | TBAF | THF | 99 | 1 | trace |
| 4 | 1.5 | TBAF | Toluene | 5 | 0 | 0 |
| 5 | 1.5 | TBAF | $CH_2Cl_2$ | 5 | 0 | 0 |
| 6 | 1.5 | TBAF | MeCN | >99 | 0 | 0 |
| 7 | 1.5 | $K_2CO_3$ | MeCN | 0 | 0 | 0 |
| 8 | 1.5 | DBU | MeCN | 88 | 0 | 0 |
| **9** | **1.2** | **TBAF** | **MeCN** | **>99** | **0** | **0** |
| 10 | 1.1 | TBAF | MeCN | 87 | trace | 13 |

**General procedure for the reaction with thiols (GP5)**

To a test tube under an argon atmosphere were introduced **2aa** (0.1682 g, 0.4000 mmol), a thiol (0.48 mmol, 1.2 eq.) and 4.0 mL of MeCN, where tetrabutylammonium fluoride (a 1.0 *M* THF solution, 0.02 mL, 0.02 mmol, 5 mol%) was added. This reaction mixture was stirred for appropriate time at 30 °C or 50 °C (see Table 11). Then, $H_2O$ (2.0 mL) and KF (0.0350 g, 0.602 mmol, 1.5 eq.) was added to the mixture which was further stirred for 2 h at the same temperature. After addition of sat. $NH_4Cl$ aq., the reaction mixture was extracted three times with AcOEt and the combined organic phase was dried over anhydrous $Na_2SO_4$. After filtration, evaporation of the volatiles afforded a crude material which was purified by silica gel column chromatography to furnish the desired product**.**

4-[1,1,1-Trifluoro-2-{(phenylmethane)sulfenyl}prop-2-yl]phenol **(9aa).**




Following to **GP5,** benzyl mercaptan (0.0597 g, 0.481 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using AcOEt:hexane=3:1 to 1:1 as an eluent to give the desired product **9aa** as a white solid (0.1157 g, 0.3702 mmol, 93%).

Rf = 0.37 (hexane:AcOEt = 4:1).

m.p.: 63.6 °C.

$^{1}$H NMR: δ 1.88 (s, 3H), 3.53 (d, *J* = 11.4 Hz, 1H), 3.73 (d, *J* = 11.7 Hz, 1H), 4.92 (brs, 1H), 6.82-6.87 (m, 2H), 7.17-7.29 (m, 5H), 7.55 (d, *J* = 8.7 Hz, 2H)

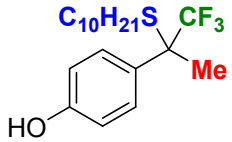
$^{13}$C NMR: δ 22.4 (q, *J* = 1.9 Hz), 35.3, 55.3 (q, *J* = 26.3 Hz), 115.2, 127.3, 127.4 (q, *J* = 281.6 Hz), 128.5, 129.06, 129.10, 129.4 (q, *J* = 1.3 Hz), 155.1.

$^{19}$F NMR: δ –72.07 (s).

IR (KBr) ν 3245, 3028, 2932, 2740, 1614, 1515, 1455, 1245, 1155, 1074 cm$^{-1}$.

HRMS (FAB+, *m/z*): [M]$^{+}$ Calcd for $C_{16}H_{15}F_3OS$, 312.0796; Found, 312.0802.

4-{1,1,1-Trifluoro-2-(decanesulfenyl)prop-2-yl}phenol **(9ab).**




Following to **GP5,** 1-decanthiol (0.0841 g, 0.4812 mmol, 1.2 eq.) was used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 6:1 as an eluent to give the desired product **9ab** as a white solid (0.1198 g, 0.3308 mmol, 83%).

Rf = 0.40 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 0.88 (t, *J* = 6.6 Hz, 3H), 1.22 (brs, 14H), 1.45 (quint., *J* = 7.2 Hz, 2H), 1.85 (s, 3H), 2.36 (dt, *J* = 11.1, 7.2 Hz, 1H), 2.46 (dt, *J* = 11.1, 7.2 Hz, 1H), 4.87 (brs, 1H), 6.79-6.84 (m, 2H), 7.55 (d, *J* = 8.4 Hz, 2H).

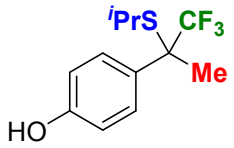
$^{13}$C NMR: δ 14.0, 22.4 (q, *J* = 1.8 Hz), 22.6, 28.6, 28.9, 29.1, 29.3, 29.4, 29.5, 30.2, 31.9, 54.3 (q, *J* = 26.3 Hz), 115.1, 127.5 (q, *J* = 278.9 Hz), 129.3, 129.5, 155.0.

$^{19}$F NMR: δ –72.52 (s).

IR ($CHCl_3$) ν 3370, 2927, 2855, 1614, 1514, 1465, 1378, 1262, 1164, 1076 cm$^{-1}$.

HRMS (FAB+, *m/z*): [M]$^{+}$ Calcd for $C_{19}H_{29}F_3OS$, 362.1891; Found, 362.1909.

4-[1,1,1-Trifluoro-2-{(1-methylethane)sulfenyl}prop-2-yl]phenol **(9ac)**




Following to **GP1**, 2-propanethiol (0.0365 g, 0.479 mmol, 1.2 eq.) was used, the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **9ac** as a colorless oil(0.0807 g, 0.305 mmol, 76%).

Rf = 0.33 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 1.13 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H) 1.88 (s, 3H), 2.82 (sept., *J* = 6.9 Hz, 1H), 4.84 (brs, 1H), 6.82 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H).

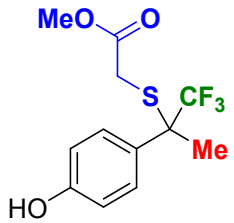
$^{13}$C NMR: δ 22.9 (q, *J* = 1.8 Hz), 24.9, 25.0, 35.3, 55.1 (q, *J* = 26.4 Hz), 115.0, 127.3 (q, *J* = 278.3 Hz), 129.5, 129.8, 155.0.

$^{19}$F NMR: δ –72.67 (s).

IR ($CHCl_3$) ν 3370, 2966, 2928, 2868, 1613, 1514, 1462, 1259, 1165, 1075 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{12}H_{15}F_3OS$, 264.0796; Found, 264.0767.

Methyl 2-{1,1,1-trifluoro-2-(4-hydroxyphenyl)prop-2-yl}thioacetate (**9ad**)




Following to **GP5**, methyl thioglycolate (0.0509 g, 0.480 mmol, 1.2 eq.) was used, the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 2:1 as an eluent to give the desired product **9ad** as a colorless oil (0.1017 g, 0.3456 mmol, 86%).

Rf = 0.33 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 1.87 (s, 3H), 3.15 (d, *J* = 15.3 Hz, 1H), 3.30 (d, *J* = 15.6 Hz, 1H), 3.65 (s, 3H), 5.04 (brs, 1H), 6.81-6.86 (m, 2H), 7.49 (d, *J* = 8.7 Hz, 2H).

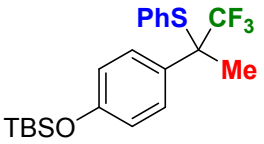
$^{13}$C NMR: δ 22.3 (q, *J* = 1.9 Hz), 32.9, 52.8, 55.0 (q, *J* = 26.3 Hz), 115.4, 127.2 (q, *J* = 278.9 Hz), 127.6, 129.3, 155.8, 170.8.

$^{19}$F NMR: δ –72.27 (s).

IR ($CHCl_3$) ν 3415, 3028, 3009, 2955, 1731, 1614, 1516, 1438, 1263, 1164 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{12}H_{13}F_3O_3S$, 294.0538; Found, 294.0549.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]]-1,1,1-trifluoro-2-phenylthiopropane **(10ae)**




Following to **GP5,** thiophenol (0.0597 g, 0.481 mmol) was used, and after quenching with $H_2O$, following to **GP2**, TBS protection was conducted. The crude mixture was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 15:1 as an eluent to give the desired product **10ae** as a white solid (0.1012 g, 0.2453 mmol, 61%).

Rf = 0.23 (hexane:AcOEt = 4:1).

m.p.: 63.6 °C.

$^1$H NMR: δ 0.21 (s, 6H), 0.99 (s, 9H), 1.75 (s, 3H), 6.80 (d, *J* = 8.7 Hz, 2H), 7.21-7.39 (m, 5H), 7.45 (d, *J* = 8.7 Hz, 2H).

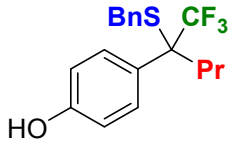
$^{13}$C NMR: δ –4.4, 18.2, 21.5, 25.7, 56.9 (q, *J* = 24.9 Hz), 119.6, 127.1 (q, *J* = 282.0 Hz), 128.5, 129.3, 129.6, 129.8, 130.1, 137.5, 157.6.

$^{19}$F NMR: δ –71.88 (s).

IR (KBr) ν 3348, 2965, 2933, 2875, 1614, 1514, 1243, 1160, 1101, 826 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{21}H_{28}F_3OSSi$, 413.1582; Found, 413.1563.

4-[1,1,1-Trifluoro-2-{(phenylmethane)sulfenyl}pent-2-yl]phenol **(9ba)**




Following to **GP5**, benzyl mercaptan (0.0596 g, 0.480 mmol, 1.2 eq.) and **2ba** (0.1794 g, 0.3995 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **9ba** as a pale-yellow oil (0.1192 g, 0.3502 mmol, 88%).

Rf = 0.30 (hexane:AcOEt = 4:1).

$^1$H NMR: δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.36-1.41 (m, 2H), 2.08-2.22 (m, 2H), 3.54 (d, *J* = 11.1 Hz, 1H), 3.75 (d, *J* = 11.1 Hz, 1H), 4.99 (brs, 1H), 6.82-6.87 (m, 2H), 7.19-7.31 (m, 5H) 7.50 (d, *J* = 8.1 Hz, 2H).

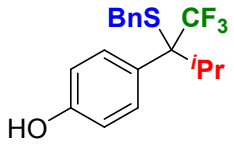
$^{13}$C NMR: δ 14.2, 17.5, 35.1 (q, *J* = 1.9 Hz), 36.7, 59.9 (q, *J* = 26.1 Hz), 115.3, 127.3, 127.5, 127.8 (q, *J* = 285.0 Hz), 128.5, 129.2, 129.6, 136.3, 155.0.

$^{19}$F NMR: δ –69.0 (s).

IR ($CHCl_3$) ν 3348, 2965, 2933, 2875, 1614, 1514, 1243, 1160, 1101, 826 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{18}H_{19}F_3OS$, 340.1109; Found, 340.1116.

4-[1,1,1-Trifluoro-3-methyl-2-{(phenylmethane)sulfenyl}but-2-yl]phenol **(9ca).**




Following to **GP5**, benzyl mercaptan (0.0596 g, 0.480 mmol, 1.2 eq.) and **2ca** (0.1794 g, 0.3995 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **9ca** as a pale-yellow oil (0.1260 g, 0.3702 mmol, 93%).

Rf = 0.37 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 1.00 (d, *J* = 7.2 Hz, 6H), 2.42 (sept., *J* = 7.2 Hz, 1H), 3.31 (d, *J* = 11.1 Hz, 1H), 3.70 (d, *J* = 11.1 Hz, 1H), 4.95 (brs, 1H), 6.86-6.89 (m, 2H), 7.22-7.31 (m, 5H) 7.63 (d, *J* = 8.7 Hz, 2H).

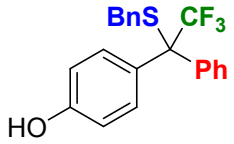
$^{13}$C NMR: δ 18.6 (d, *J* = 1.8 Hz), 19.1 (d, *J* = 1.9 Hz), 35.3 (q, *J* = 1.9 Hz), 38.5, 65.6 (q, *J* = 24.3 Hz), 115.2, 127.3, 128.2 (q, *J* = 286.3 Hz) 128.6, 129.1, 129.1, 129.9 (q, *J* = 1.9 Hz), 136,7, 154.6.

$^{19}$F NMR: δ –60.31 (s).

IR ($CHCl_3$) ν 3385, 2972, 2942, 2884, 1614, 1514, 1455, 1247, 1153, 818 $cm^{-1}$.

HRMS (FAB-, *m/z*): $[M-H]^-$ Calcd for $C_{18}H_{19}F_3O_3S$, 339.1030; Found, 339.1010.

4-[1,1,1-Trifluoro-1-phenyl-2-{(phenylmethane)sulfenyl}ethyl]phenol **(9da)**




Following to **GP5**, benzyl mercaptan (0.0596 g, 0.480 mmol, 1.2 eq.) and **2da** (0.1930 g, 0.3999 mmol) instead of **2aa** were used, and the crude product was purified by silica gel column chromatography using hexane:AcOEt = 4:1 as an eluent to give the desired product **9da** as a pale-yellow oil (0.1260 g, 0.3702 mmol, 93%).

Rf = 0.40 (hexane:AcOEt = 4:1).

$^{1}$H NMR: δ 3.42 (d, *J* = 11.4 Hz, 1H), 3.50 (d, *J* = 11.4 Hz, 1H), 4.96 (brs, 1H), 6.76-6.81 (m, 2H), 7.10-7.13 (m, 2H) 7.19-7.27 (m, 3H), 7.31-7.38 (m, 5H), 7.48-7.51 (m, 2H).

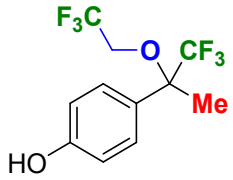
$^{13}$C NMR: δ 36.1 (q, *J* = 1.9 Hz), 64.2 (q, *J* = 26.1 Hz), 114.9, 127.1 (q, *J* = 283.1 Hz), 127.3, 128.0, 128.1, 128.5, 129.2, 129.6 (q, *J* = 1.3 Hz), 131.1, (q, *J* = 1.3 Hz), 136,0, 138.4, 155.1.

$^{19}$F NMR: δ –66.76 (s).

IR ($CHCl_3$) ν 3363, 3064, 2939, 1614, 1512, 1454, 1371, 1253, 1160, 1036 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{21}H_{17}F_3OS$, 374.0952; Found, 374.0976.

4-{1,1,1-Trifluoro-2-(2,2,2-trifluoroethoxy)prop-2-yl}phenol (**11aa**)




To a test tube were introduced 55% suspension of NaH in mineral oil (0.0347 g, 0.795 mmol, 2.0 eq.), 2,2,2-trifluoroethanol (0.0880 g, 0.88 mmol, 2.0 eq.) and 2.0 mL of DMSO were added. This reaction mixture was stirred for 15-30 min at 30 °C. Then, **2aa** (0.1682 g, 0.4000 mmol) and DMSO 2.0 mL was added to the reaction mixture, and this reaction mixture was stirred for 1 h at 50 °C. After cooling to 30 °C and quenched with sat. $NH_4Cl$, following to **GP1**, deprotection of TBS group was conducted. Then, after usual work up, evaporation of the volatiles of the residue afforded a crude material which was purified by silica gel column chromatography using hexane:AcOEt = 5:1 as an eluent to give the desired product **11aa** as a colorless oil (0.0580 g, 0.2013 mmol, 50%).

Rf = 0.17 (hexane:AcOEt = 5:1).

$^1$H NMR: δ 1.79 (s, 3H), 3.65 (dq, *J* = 11.1, 8.1 Hz, 1H), 3.71 (dq, *J* = 11.1, 8.1 Hz, 1H), 6.85-6.90 (m, 2H), 7.39 (d, *J* = 9.0 Hz, 2H).

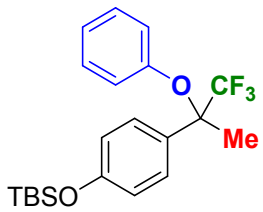
$^{13}$C NMR: δ 18.3, 61.5 (q, *J* = 35.4 Hz), 80.2 (q, *J* = 29.2 Hz), 115.5, 123.5 (q, *J* = 277.7 Hz), 124.6 (q, *J* = 284.6 Hz), 126.6, 129.3, 156.5.

$^{19}$F NMR: δ –80.72 (s, 3F), –75.35 (t, *J* = 9.0 Hz, 3F).

IR ($CHCl_3$) ν 3363, 3004, 2952, 1615, 1516, 1459, 1281, 1171, 1121, 970 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{11}H_{10}F_6O_2$, 288.0585; Found, 288.0566.

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenoxypropane (**12ab**)




Follwing to **GP2**, phenol (0.0752 g, 0.799 mmol, 2.0 eq.), TBSCl (0.1809 g, 1.200 mmol, 3.0 eq.) and imidazole (0.1633 g, 2.399 mmol, 6.0 eq.) were used, and the crude product was purified by silica gel column chromatography using hexane:$CH_2Cl_2$ = 10:1 as an eluent to give the desired product **12ab** as a colorless oil (0.0696 g, 0.1755 mmol, 43%)

Rf = 0.30 (hexane).

$^1$H NMR: δ 0.22 (s, 6H), 0.99 (s, 9H), 1.80 (q, *J* = 0.9 Hz, 3H), 6.71-6.75 (m, 2H), 6.84-6.89 (m, 2H), 6.97 (tt, *J* = 7.5, 1.2 Hz, 1H), 7.11-7.18 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H).

$^{13}$C NMR: δ –4.4, 18.0, 18.2, 25.6, 81.3 (q, *J* = 24.9 Hz), 116.1, 117.2, 118.9, 127.6 (q, *J* = 284.7 Hz),

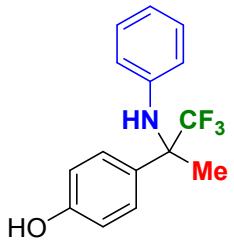
128.9, 129.2, 130.0, 145.7, 158.2

$^{19}$F NMR: δ –71.88 (s).

IR ($CHCl_3$) ν 2954, 2931, 2878, 2853, 1608, 1509, 1491, 1271, 1174, 770 $cm^{-1}$. HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{21}H_{28}F_3O_2Si$, 397.1811; Found, 397.1829.

**Deprotection of the TBS group in 4ak**

4-{1,1,1-Trifluoro-2-(phenylaminoprop)-2-yl}phenol (**3ak**)




**3ak** was synthesized by deprotection of **4ak** (0.1586 g, 0.4010 mmol) by TBAF (a 1.0 *M* THF solution, 0.44 mL, 0.44 mmol, 1.1 eq.) in THF (1.0 mL) at 0 ° C to 30 ° C for 30 min. After addition of sat. $NH_4Cl$ aq., the reaction mixture was extracted three times with AcOEt and the combined organic phase was dried over anhydrous $Na_2SO_4$. After filtration, evaporation of the volatiles afforded a crude material which was purified by silica gel column chromatography using hexane:AcOEt = 10:1 to 5:1 as an eluent to give the desired product **3ak** as a white solid (0.0978 g, 0.3477 mmol, 87%).

Rf = 0.17 (hexane:AcOEt = 5:1).

m.p.: 128.1 °C.

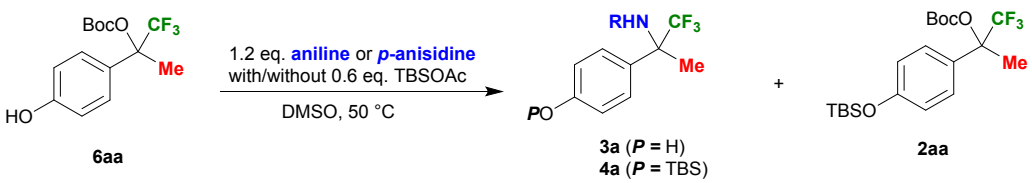
$^1$H NMR: δ 1.86 (s, 3H), 4.23 (s, 1H), 4.83 (brs, 1H), 6.38 (d, *J* = 7.5 Hz, 2H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.82-6.86 (m, 2H), 7.04 (t, *J* = 7.5 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H).

$^{13}$C NMR (acetone-$d_6$): δ 21.1 (q, *J* = 1.9 Hz), 63.1 (q, *J* = 26.1 Hz), 116.5, 118.9, 120.0, 126.4 (q, *J* = 287.1 Hz), 128.7, 129.2, 129.5, 144.0, 155.8.

$^{19}$F NMR: δ –80.18 (s).

IR ($CHCl_3$) ν 3499, 3380, 3042, 2999, 2953, 1608, 1508, 1279, 1262, 1182 $cm^{-1}$. HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{15}H_{15}F_3NO$, 282.1106; Found, 282.1122.

**Reactions of 6aa with aniline or *p*-anisidine in the absence or presence of TBSOAc**



To a test tube were introduced **6aa** (0.1225 g, 0.4000 mmol), *p*-anisidine (0.0591 g, 0.480 mmol) or aniline (0.0447 g, 0.480 mmol), with or without TBSOAc (0.0417g, 0.0241 mmol, 0.6 eq.) and 4.0 mL of DMSO, and this solution was stirred at 50 °C. Yields of **3ak** as well as the remained **6aa** were determined at a specific time by using $^{19}$F NMR whose results are summarized in Table S3 (without TBSOAc) and Table S4 (with TBSOAc). In Table S5 (without TBSOAc) and Table S6 (with TBSOAc) were tabulated the data when *p*-anisidine was employed as an amine. In a different batch, the desired compound **3al** was isolated in 85% yield as a slightly yellow oil (0.1061 g, 0.3408 mmol).

**Table S3 $^{19}$F NMR yields of 3ak and the remained 6aa by using aniline without TBSOAc**

| | $^{19}$F NMR yield (%) | |
|---|---|---|
| Time (min) | **6aa** | **3ak** |
| 5 | 27 | 30 |
| 15 | 16 | 41 |
| 30 | 6 | 55 |
| 60 | 2 | 55 |
| 120 | 0 | 55 |

**Table S4 $^{19}$F NMR yields of 3ak, 4ak, the remained 6aa, and 2aa by using aniline with TBSOAc**

| | $^{19}$F NMR yield (%) | | | |
|---|---|---|---|---|
| Time (min) | **6aa** | **2aa** | **3ak** | **4ak** |
| 5 | 68 | 16 | 16 | 0 |
| 15 | 46 | 22 | 30 | 2 |
| 30 | 28 | 25 | 43 | 3 |
| 45 | 19 | 26 | 49 | 4 |
| 60 | 16 | 24 | 53 | 3 |
| 120 | 11 | 20 | 57 | 7 |
| 240 | 7 | 11 | 64 | 12 |
| 480 | 0 | 1 | 75 | 16 |
| 720 | 1 | 0 | 78 | 13 |

**Table S5 $^{19}$F NMR yields of 3al and the remained 6aa by using *p*-anisidine without TBSOAc**

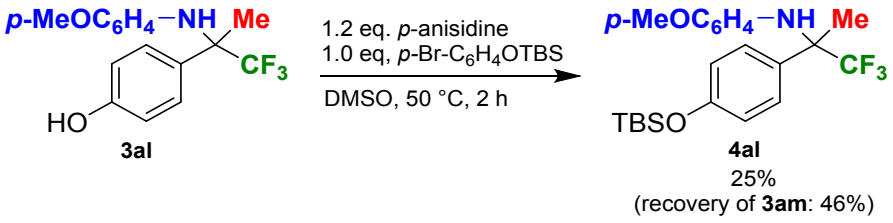
| | $^{19}$F NMR yield (%) | |
|---|---|---|
| Time (min) | **6aa** | **3al** |
| 5 | 11 | 74 |
| 15 | 1 | 86 |
| 30 | 0 | 86 |
| 60 | 0 | 85 |
| 120 | 0 | 86 |

**Table S6 $^{19}$F NMR yields of 3al, 4al, the remained 6aa, and 2aa by using *p*-anisidine with TBSOAc**

| | $^{19}$F NMR yield (%) | | | |
|---|---|---|---|---|
| Time (min) | **6aa** | **2aa** | **3al** | **4al** |
| 5 | 62 | 20 | 19 | 0 |
| 15 | 53 | 22 | 25 | 0 |
| 30 | 29 | 26 | 43 | 2 |
| 45 | 18 | 29 | 49 | 3 |
| 60 | 20 | 25 | 51 | 4 |
| 120 | 15 | 23 | 55 | 7 |
| 240 | 9 | 16 | 66 | 9 |
| 480 | 5 | 8 | 72 | 15 |
| 720 | 2 | 3 | 79 | 16 |

**Control experiments**

**(a)**




To a test tube were introduced **3al** (0.0311 g, 0.0999 mmol), *p*-anisidine (0.0147 g, 0.119 mmol), 1-bromo-4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]benzene[2] (0.0287 g, 0.0999 mmol), and 1.0 mL of DMSO, and this solution was stirred for 2 h at 50 °C. After cooling to 30 °C and quenched with $H_2O$,

the resultant solution was extracted three times with AcOEt and the combined organic phase was washed with sat. NaCl aq. After drying over anhydrous $Na_2SO_4$, evaporation of the volatiles afforded a crude material which was purified by column chromatography using hexane:AcOEt = 8:1 to 4:1 as an eluent to give **4al** as a brown oil (0.0105 g, 0.0247 mmol, 25%) in addition to recovery of 0.0143 g of **3al** (0.0459 mmol, 46%).

2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-{(4-methoxyphenyl)amino}-propane **(4al).**

$^1$H NMR: δ 0.22 (s, 6H), 0.99 (s, 9H), 1.77 (s, 3H), 3.69 (s, 3H), 3.93 (brs, 1H), 6.35-6.40 (m, 2H), 6.59-6.64 (m, 2H), 6.82-6.87 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 2H).

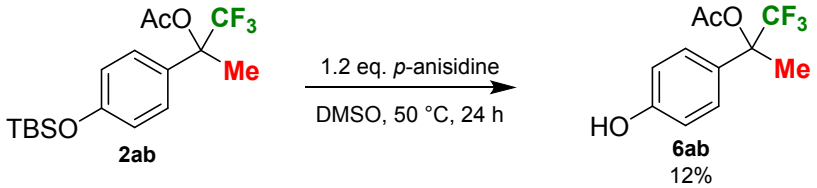
$^{13}$C NMR: δ –4.4, 18.2, 20.4, 25.6, 55.4, 62.8 (q, *J* = 26.1 Hz), 114.2, 119.1, 119.9, 126.5 (q, *J* = 285.8 Hz), 129.2 (q, *J* = 1.3 Hz), 130.1, 137.6, 153.5, 155.7.

$^{19}$F NMR: δ –79.71 (s).

IR ($CHCl_3$) ν 3019, 2957, 2932, 2858, 1510, 1266, 1219, 1157, 916, 769 cm$^{-1}$.

HRMS (FAB+, *m/z*): $[M]^+$ Calcd for $C_{22}H_{30}F_3NO_2Si$, 425.1998 Found, 420.2010.

**(b)**




Following to **GP1**, *p*-anisidine (0.0591 g, 0.480 mmol, 1.2 eq.) and **2ab** (0.1449 g, 0.4000 mmol) instead of **2aa** were used, and the reaction mixture was quenched with 1 *M* HCl aq. After usual work up, the crude mixture was purified by column chromatography using hexane:AcOEt = 2:1 as an eluent and the obtained compound was washed with hexane to give **6ab** as a white solid (0.0115 g, 0.0463 mmol, 12%) in addition to recovery of 0.0975 g of **2ab** (0.269 mmol, 67%).

1,1,1-Trifluoro-2-(4-hydroxyphenyl)prop-2-yl acetate (**6ab**)

Rf = 0.40 (hexane:AcOEt = 2:1).

m.p.: 129.9 °C.

$^1$H NMR: δ 2.08 (q, *J* = 1.2 Hz, 3H), 2.14 (s, 3H), 5.13 (brs, 1H), 6.76-6.81 (m, 2H), 7.26 (d, *J* = 8.1 Hz, 2H).

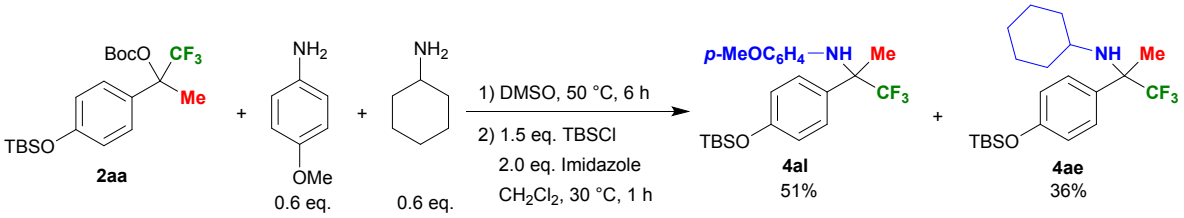
$^{13}$C NMR: δ 18.4, 21.9, 81.7 (q, *J* = 29.1 Hz), 115.3, 124.1 (q, *J* = 286.5 Hz), 127.0, 127.9, 156.3, 168.9.

$^{19}$F NMR: δ –82.62 (s).

IR (KBr) ν 3441, 3041, 2939, 1737, 1517, 1262, 1176, 1114, 959, 821 $cm^{-1}$.

HRMS (FAB+, *m/z*): $[M+H]^+$ Calcd for $C_{11}H_{11}F_3O_3$, 248.0660; Found, 248.0657.

**(c)**




Following to **GP2**,a mixture of *p*-anisidine (0.0295 g, 0.240 mmol, 0.6 eq.) and cyclohexylamine (0.0238 g, 0.240 mmol, 0.6 eq.) were used, and the crude mixture was purified by column chromatography using hexane:$CH_2Cl_2$ = 1:0 to 2:1 as an eluent to give **4al** (0.0936 g, 0.206 mmol, 51%) and **4ae** (0.0573 g, 0.143 mmol, 36%).

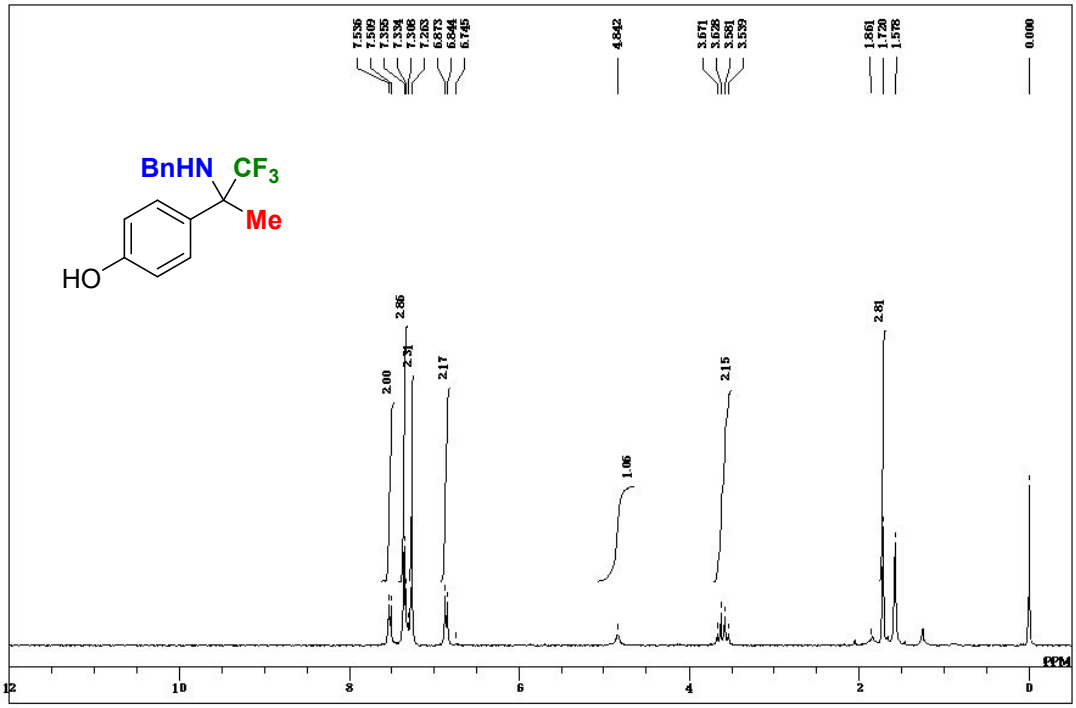
1 K. Terashima, T. Kawasaki-Takasuka, T. Agou, T. Kubota and T. Yamazaki, *Chem. Commun.*, 2020, **56**, 3031.

2 U. E. Hille, Q. Hu, C. Vock, M. Negri, M. Bartels, U. Müller-Vieira, T. Lauterbach and R. W. Hartmann, *Eur. J. Med. Chem.*, 2009, **44**, 2765.

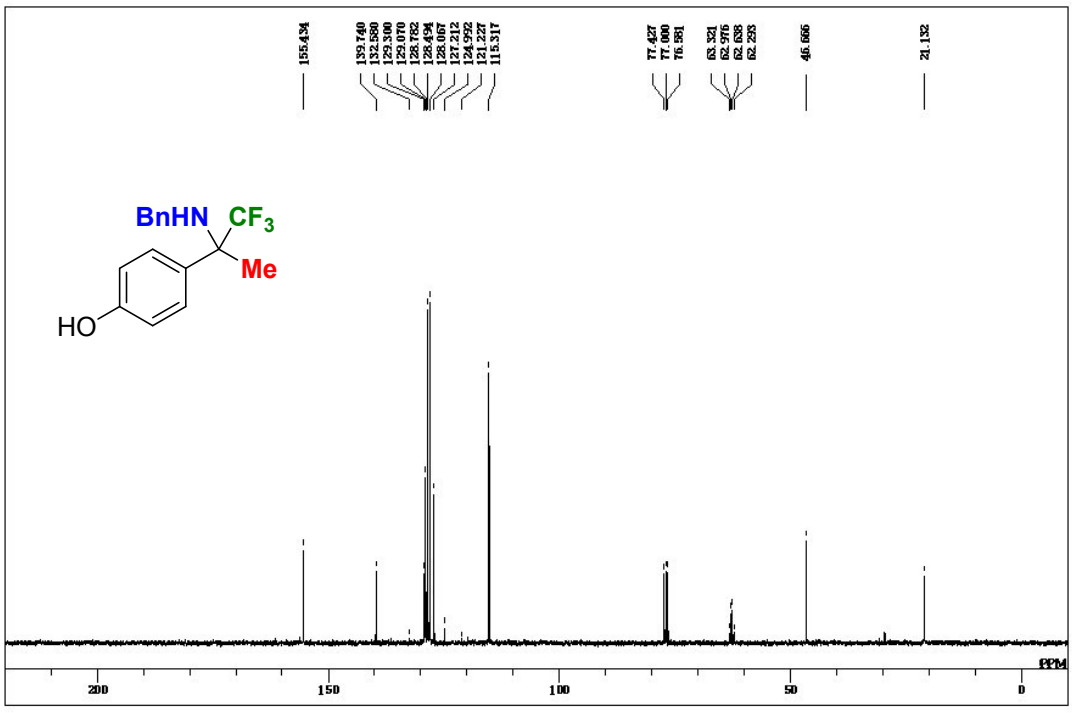
**$^{1}$H and $^{13}$C NMR spectra**

4-(2-Benzylamino-1,1,1-trifluoroprop-2-yl)phenol (**3aa**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

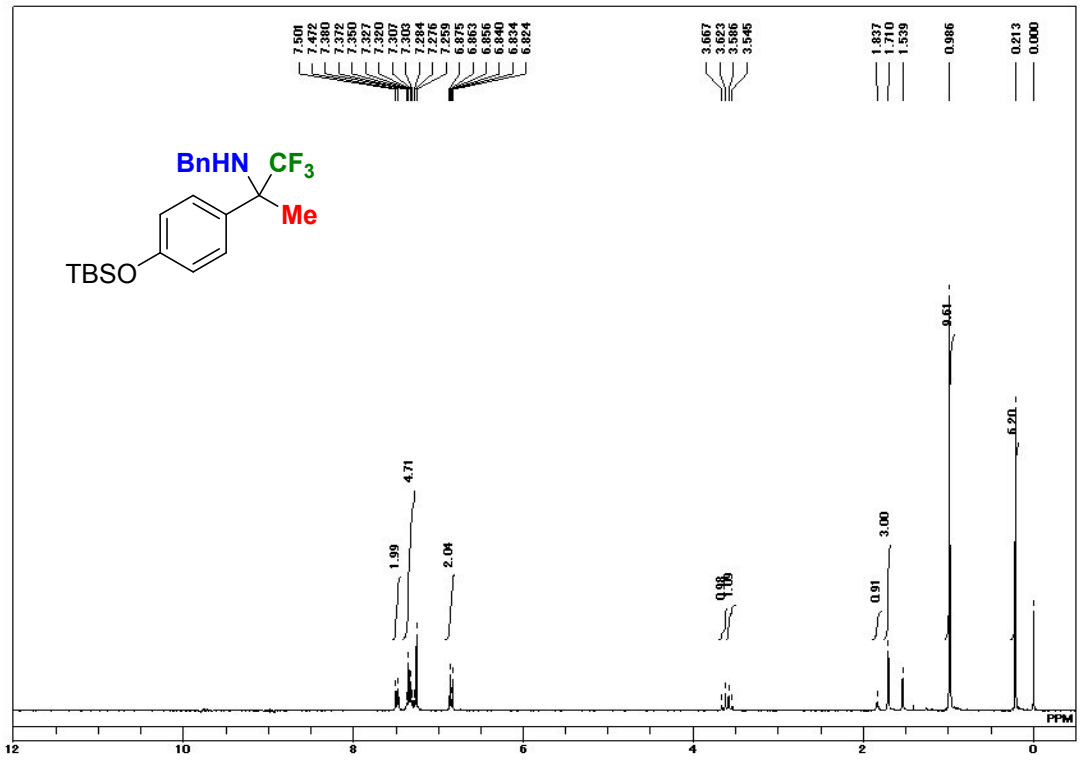



$^{13}$C NMR (300 MHz, $CDCl_3$)

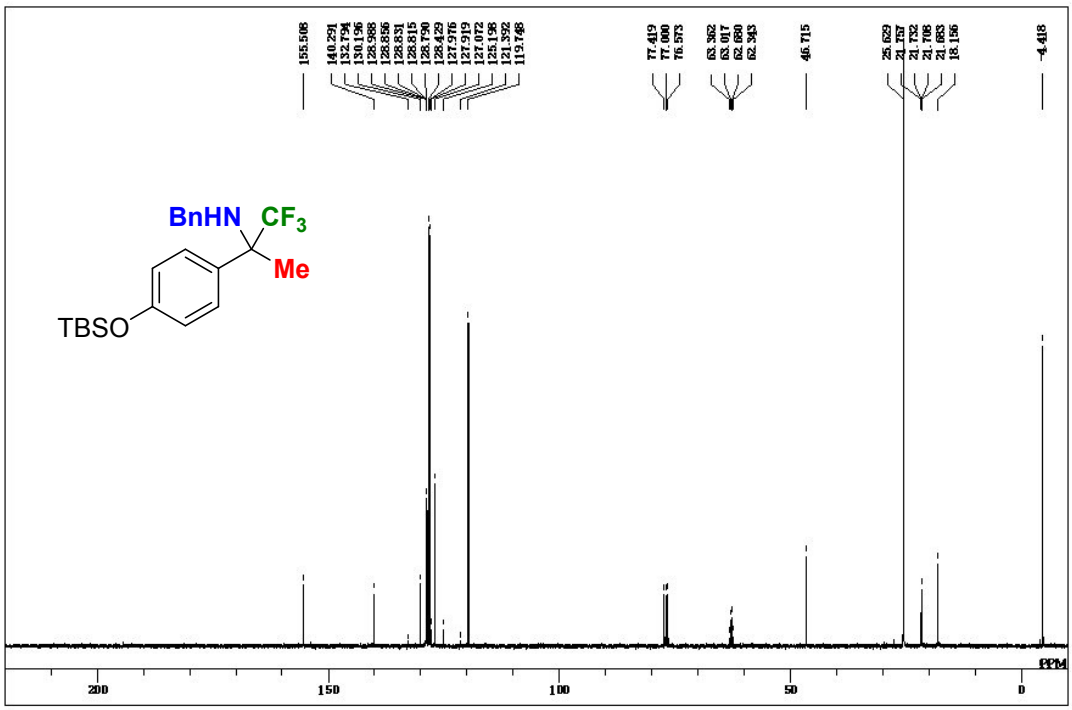


2-Benzylamino-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4aa).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

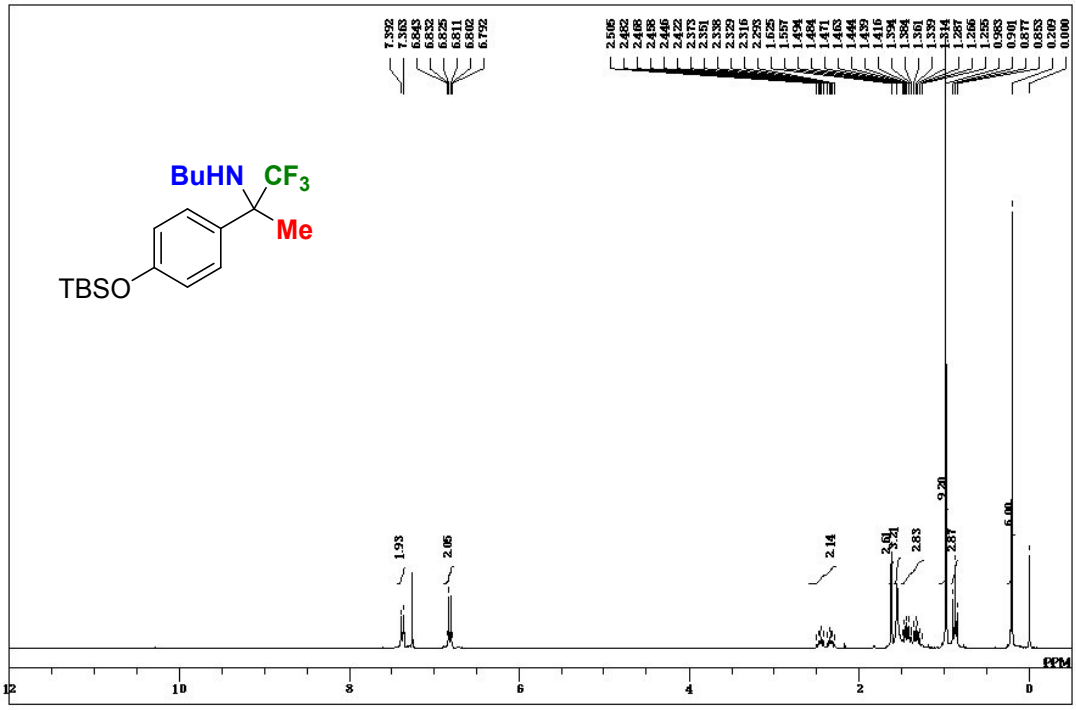



$^{13}$C NMR (300 MHz, $CDCl_3$)

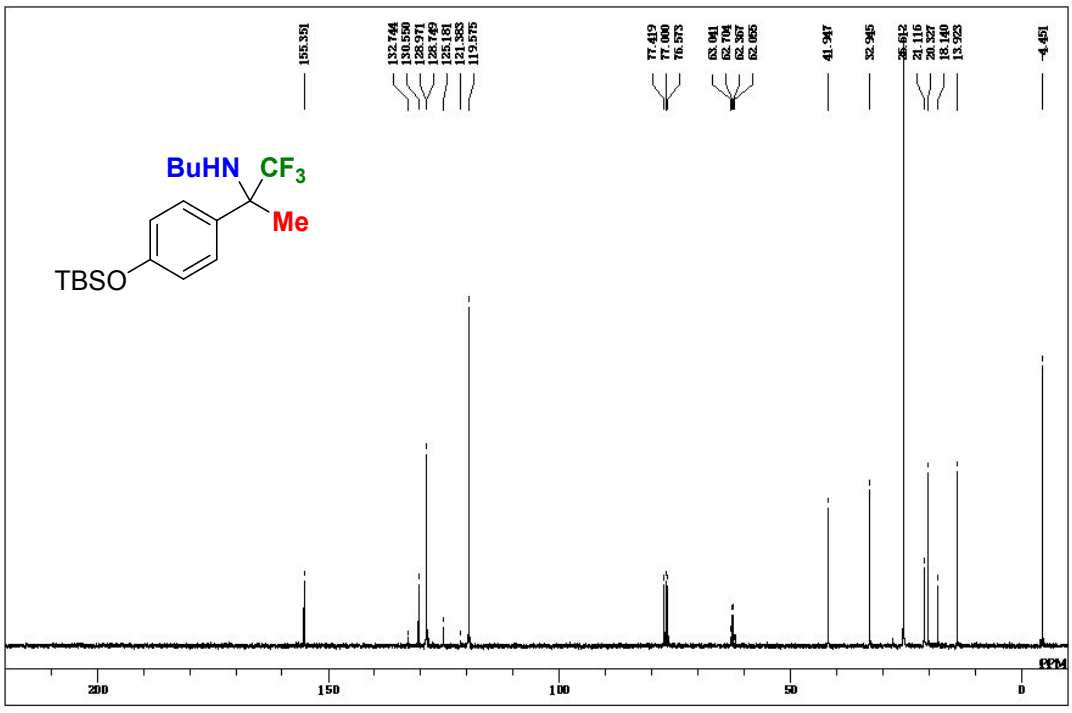


2-Butylamino-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4ab).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

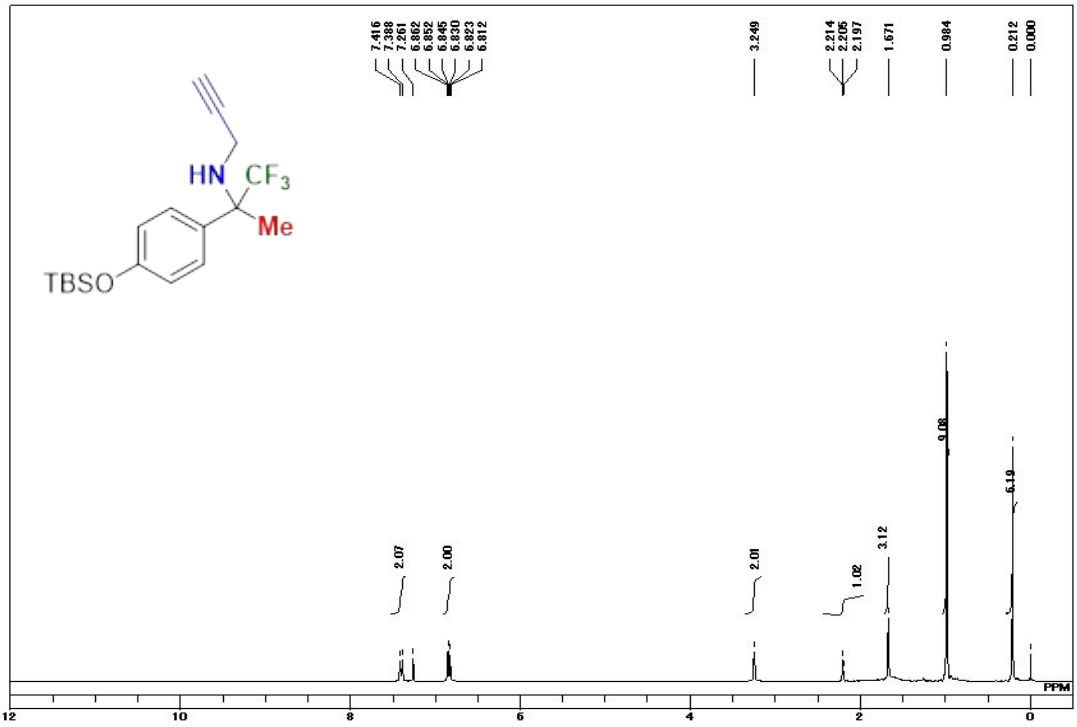



$^{13}$C NMR (300 MHz, $CDCl_3$)

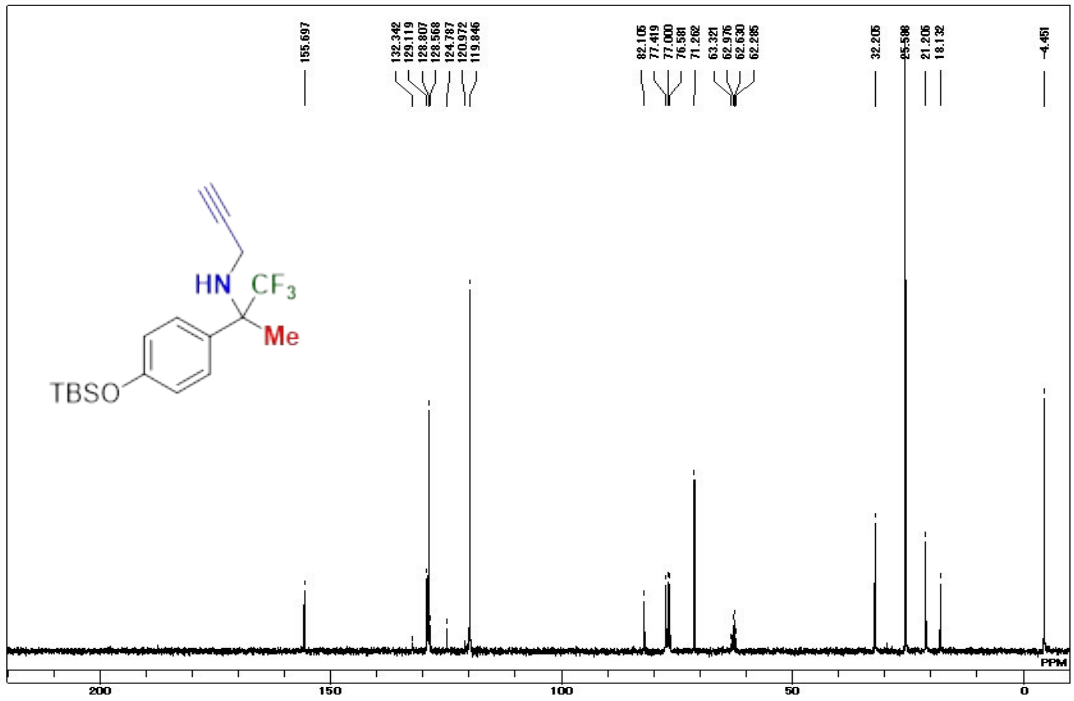


4-(1,1,1-Trifluoro-2-propalgylminoprop-2-yl)phenol (**4ac**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

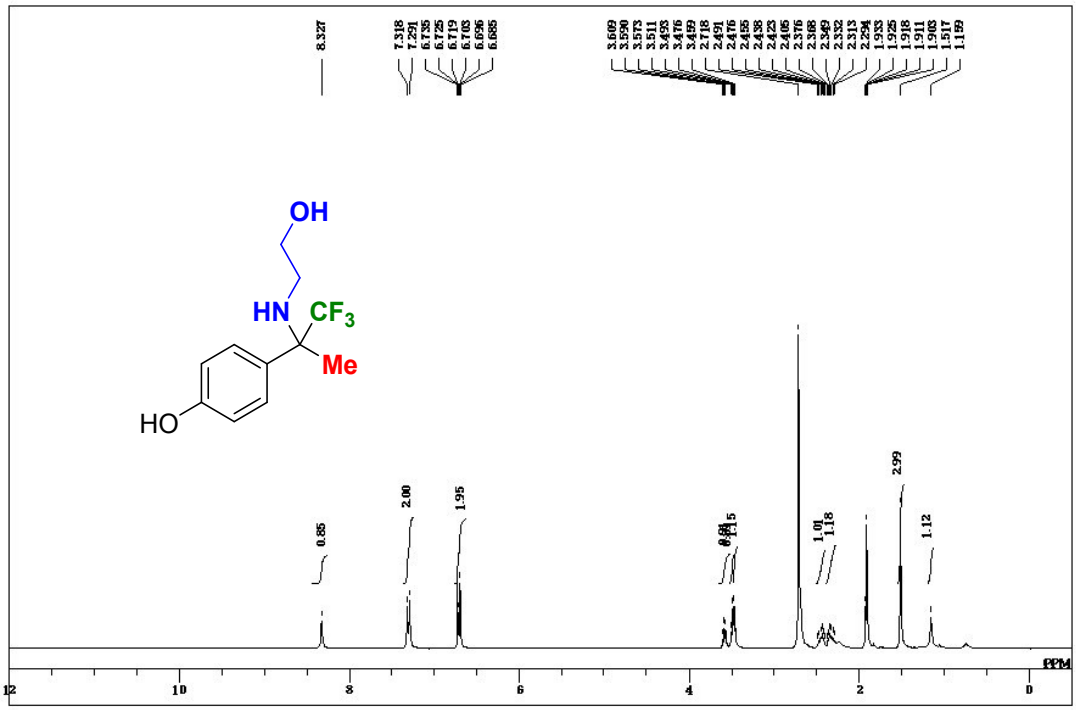



$^{13}$C NMR (300 MHz, $CDCl_3$)

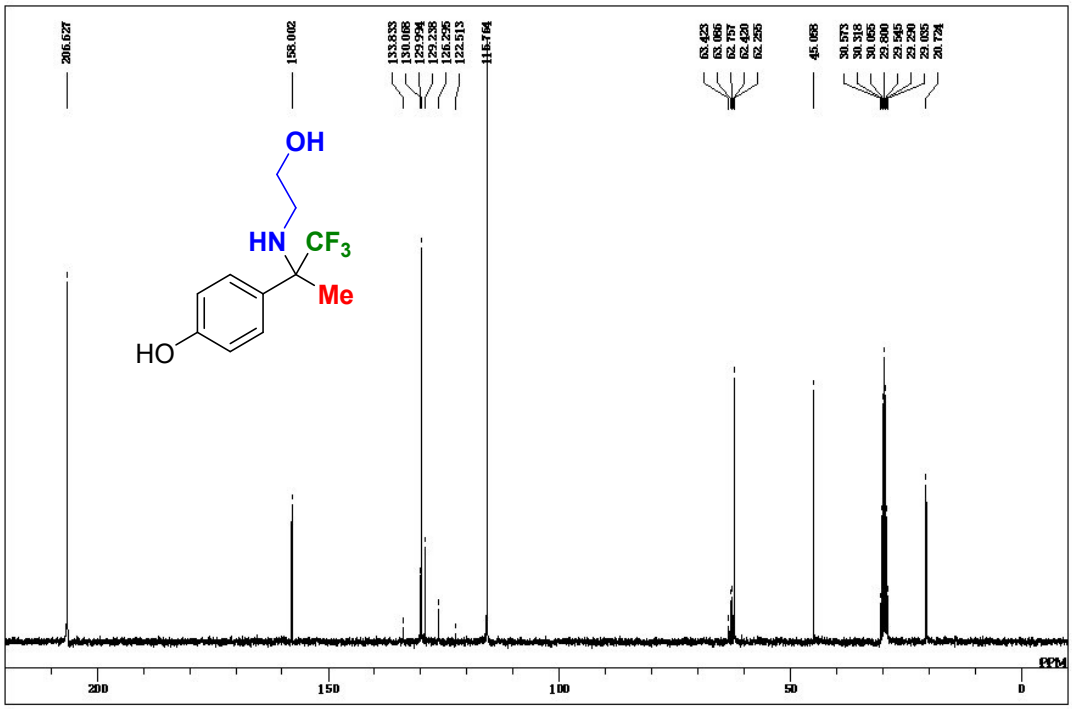


4-[1,1,1-Trifluoro-{2-(hydroxyethyl)amino}prop-2-yl)]phenol **(3ad).**

$^{1}$H NMR (300 MHz, acetone-*d*6)

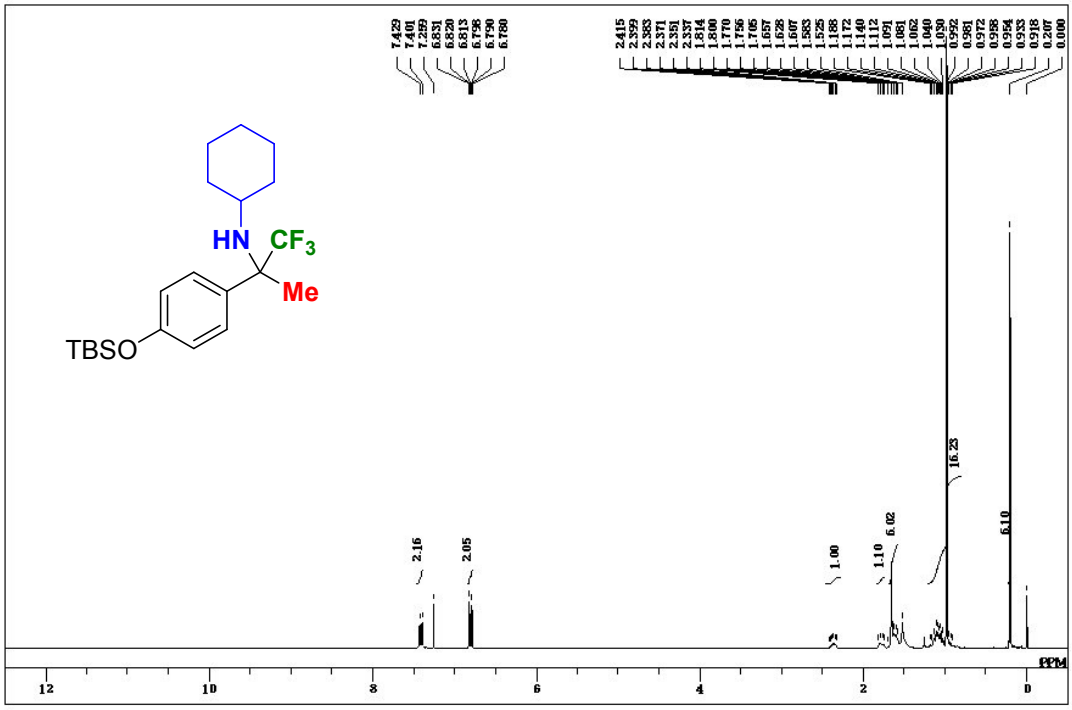



$^{13}$C NMR (300 MHz, acetone-*d*6)

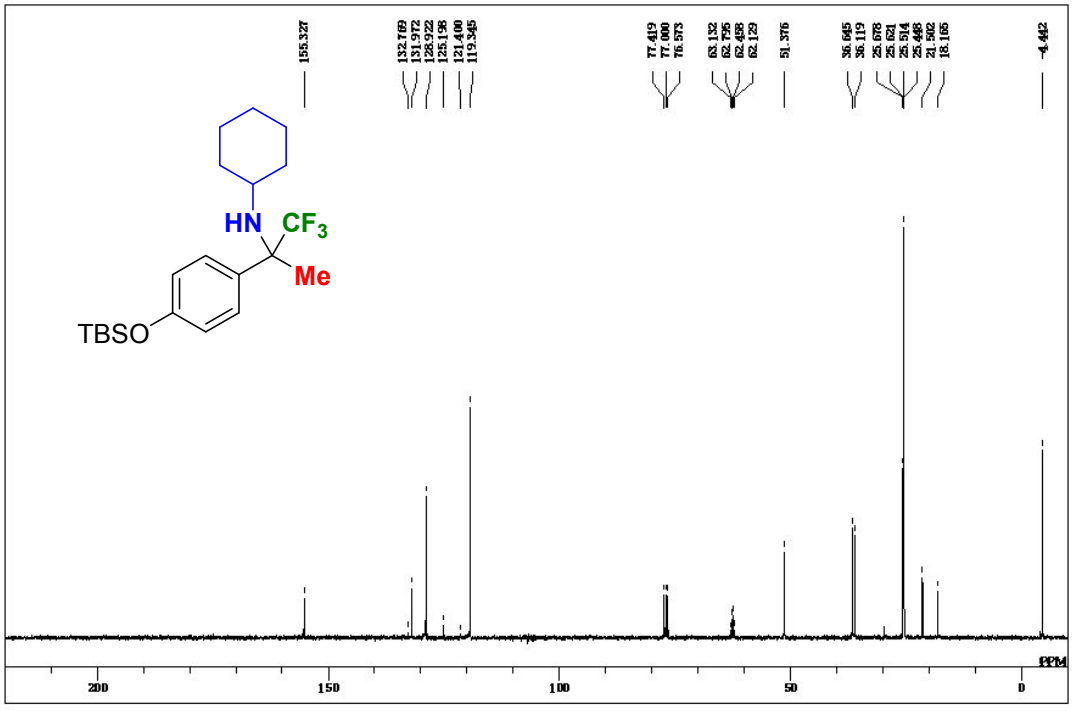


2-(Cyclohexylamino)-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4ae).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

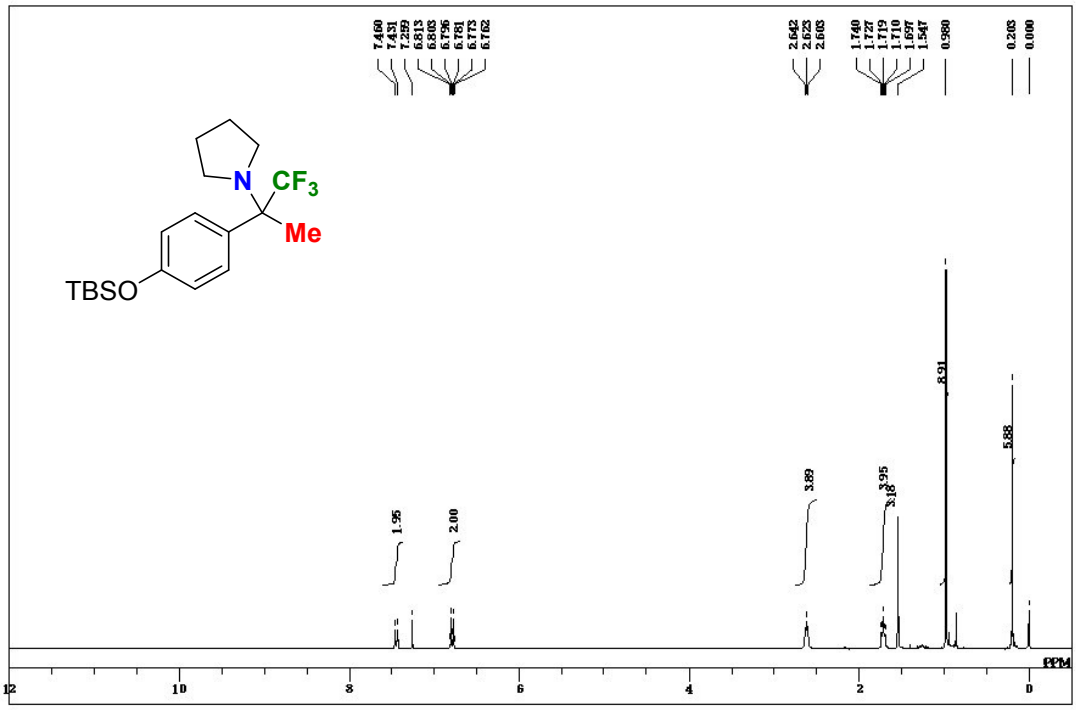



$^{13}$C NMR (300 MHz, $CDCl_3$)

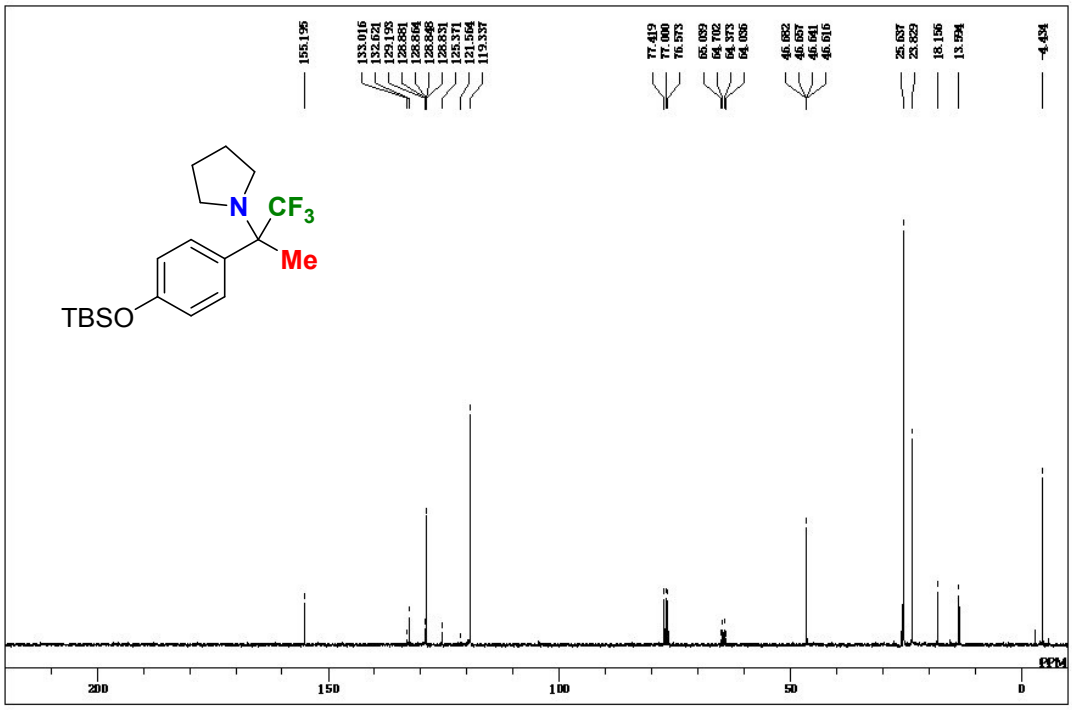


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-(*N*-pyrrolidino)propane **(3ag).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

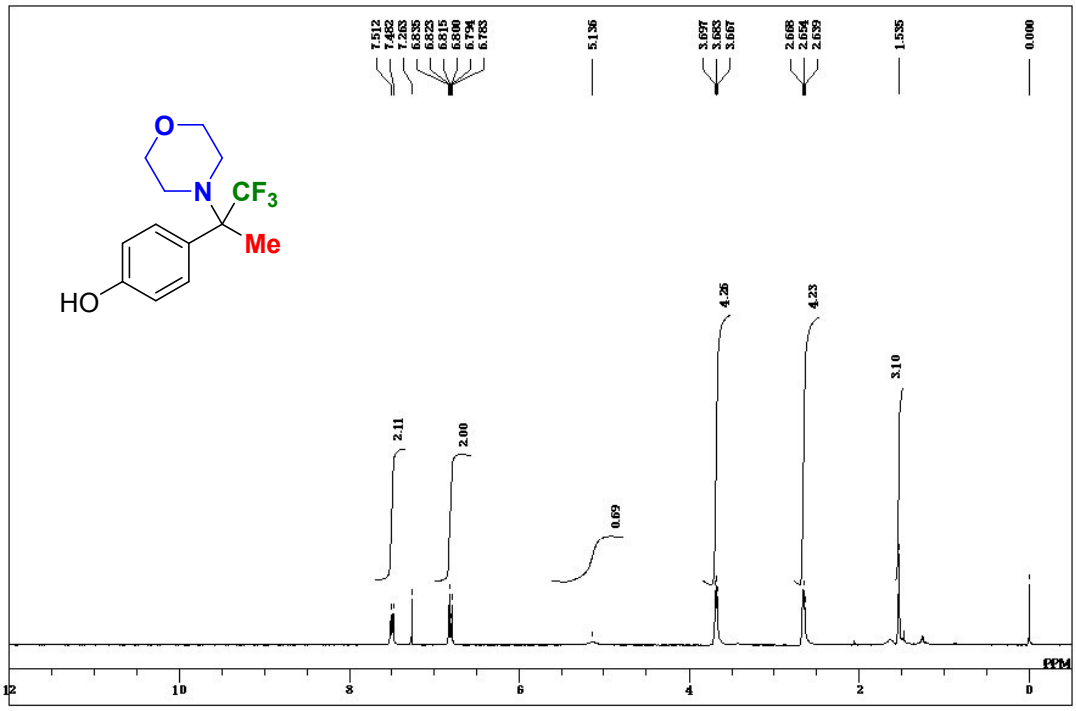



$^{13}$C NMR (300 MHz, $CDCl_3$)

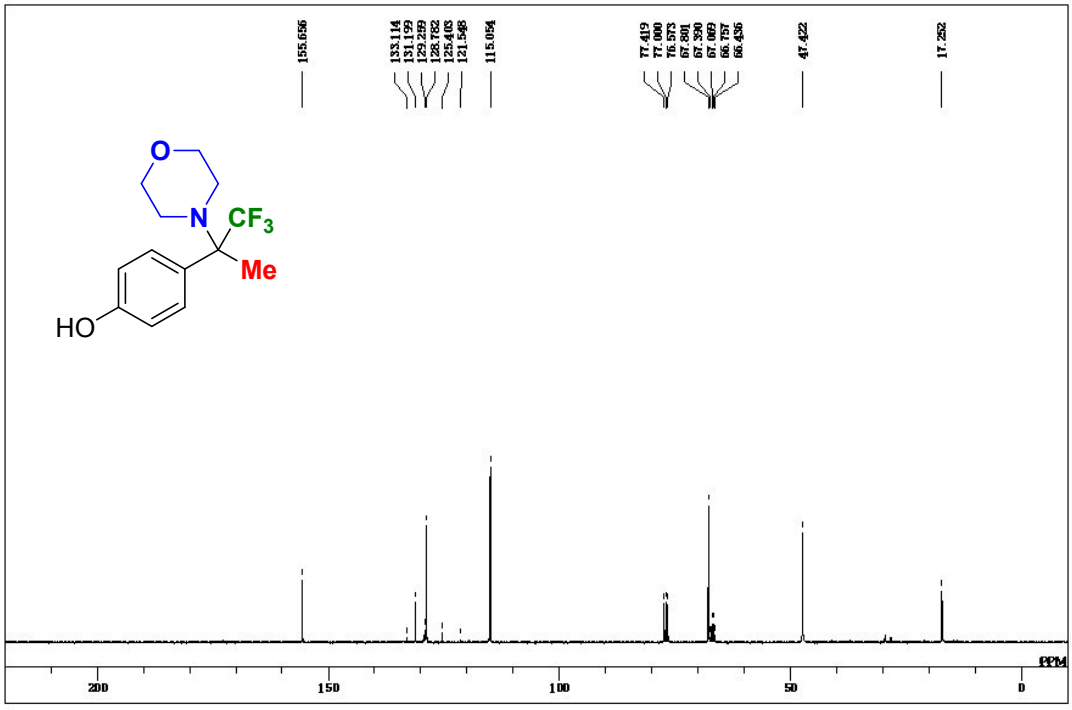



4-{1,1,1-Trifluoro-(*N*-morpholino)prop-2-yl}phenol (**3ah**).

$^{1}$H NMR (300 MHz, $CDCl_3$)

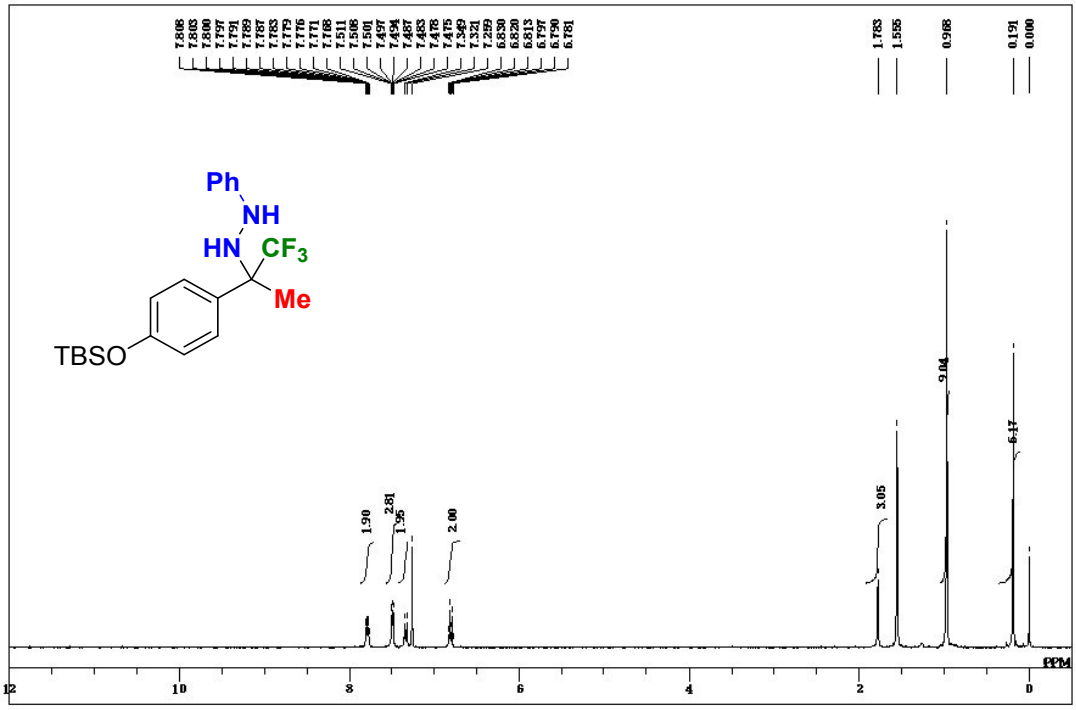



$^{13}$C NMR (300 MHz, $CDCl_3$)

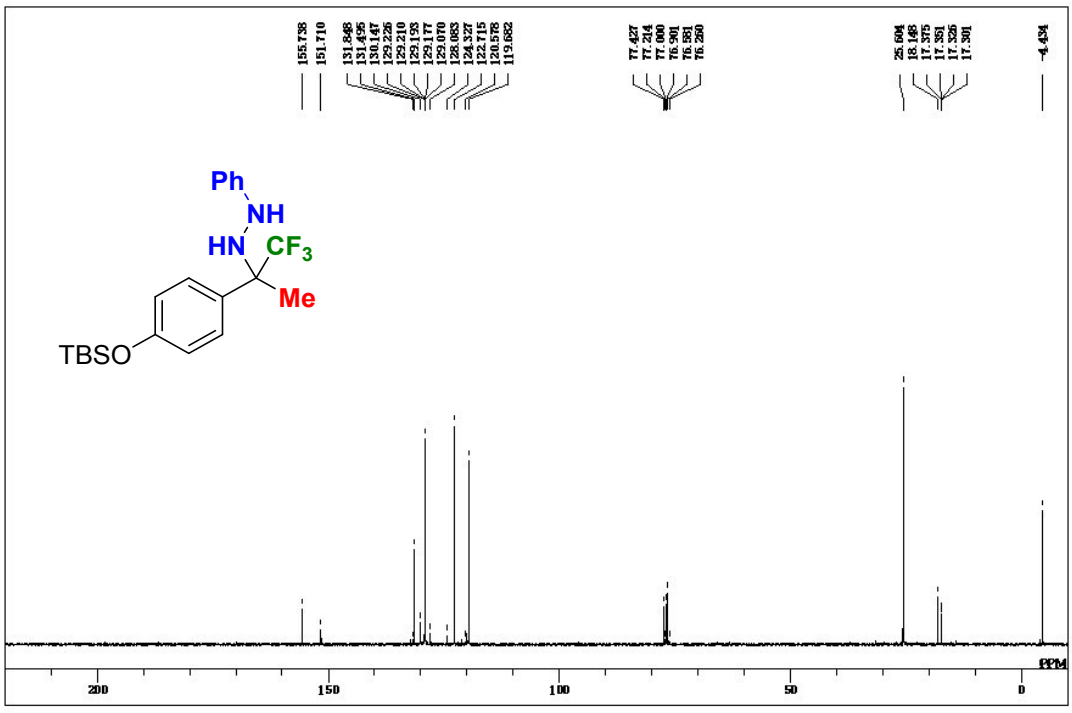


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenylhydrazinopropane **(4ai)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

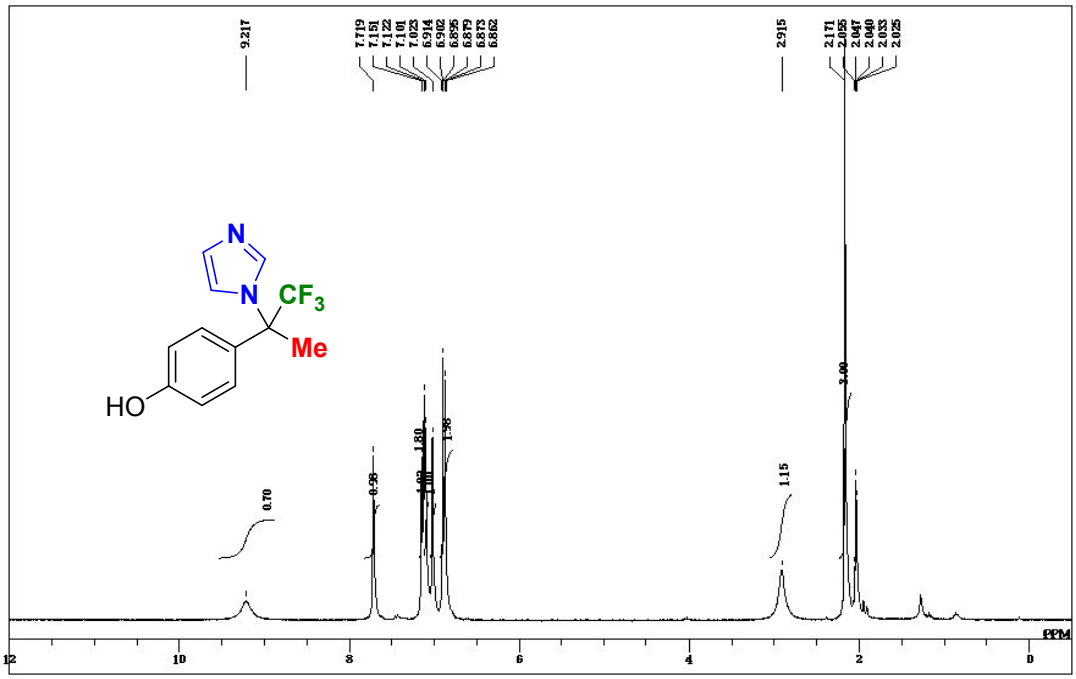



$^{13}$C NMR (300 MHz, $CDCl_3$)

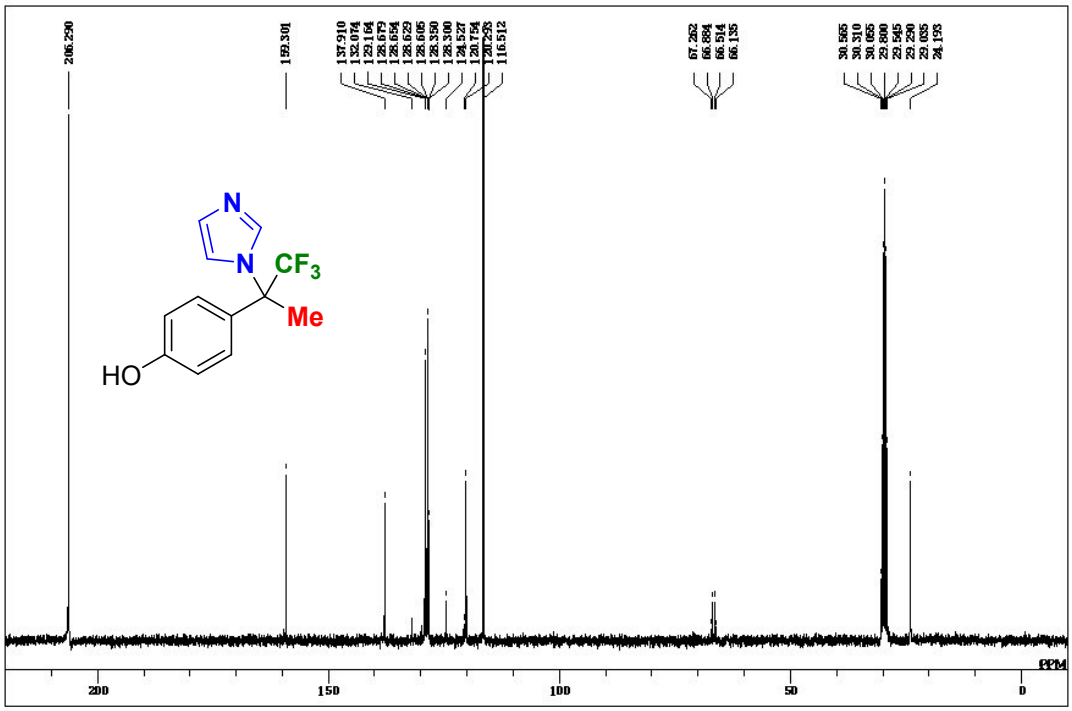


4-{1,1,1-Trifluoro-(1*H*-imidazolyl)prop-2-yl}phenol **(3aj).**

$^{1}$H NMR (300 MHz, acetone-*d*6)

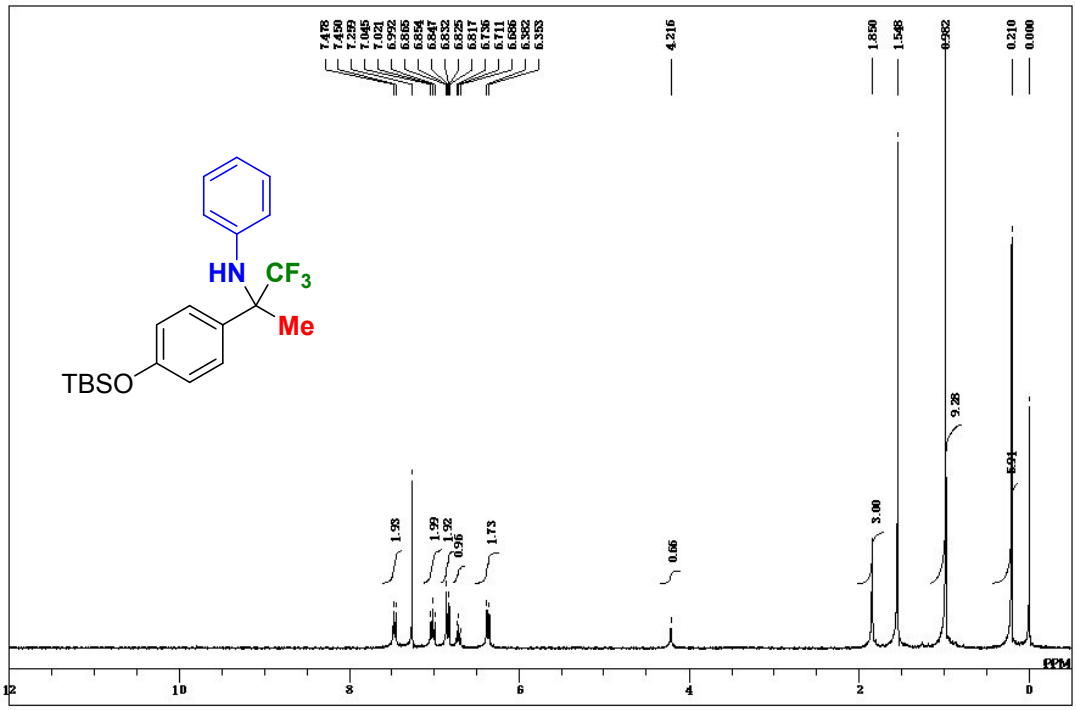



$^{13}$C NMR (300 MHz, acetone-*d*6)

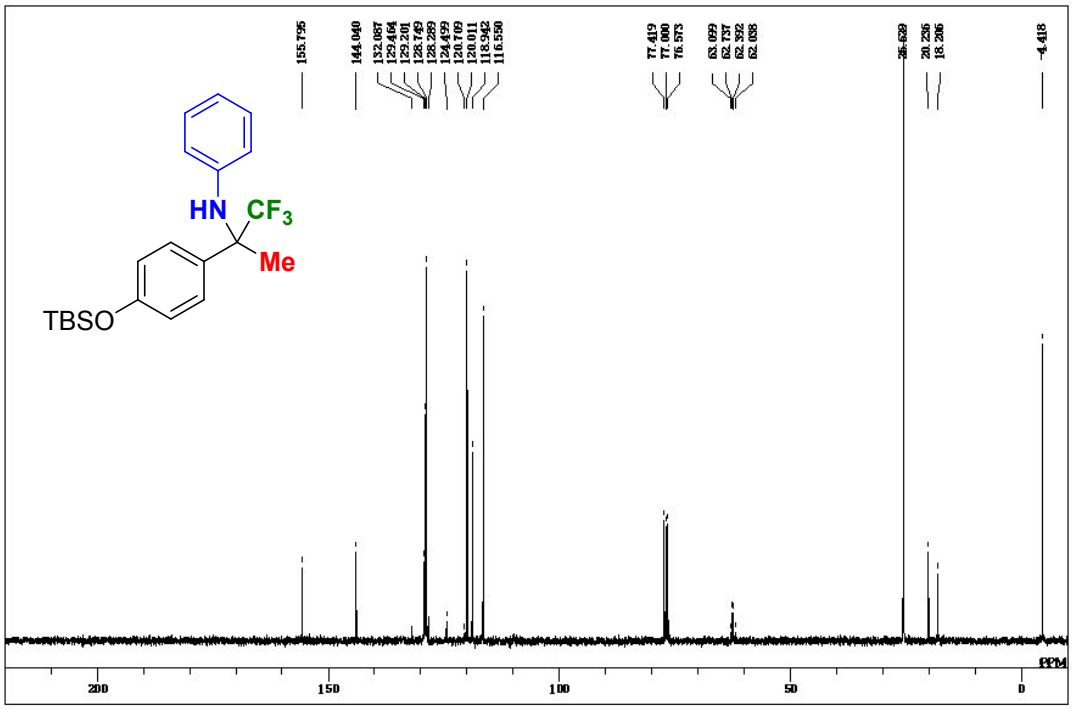


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenylaminopropane **(4ak).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

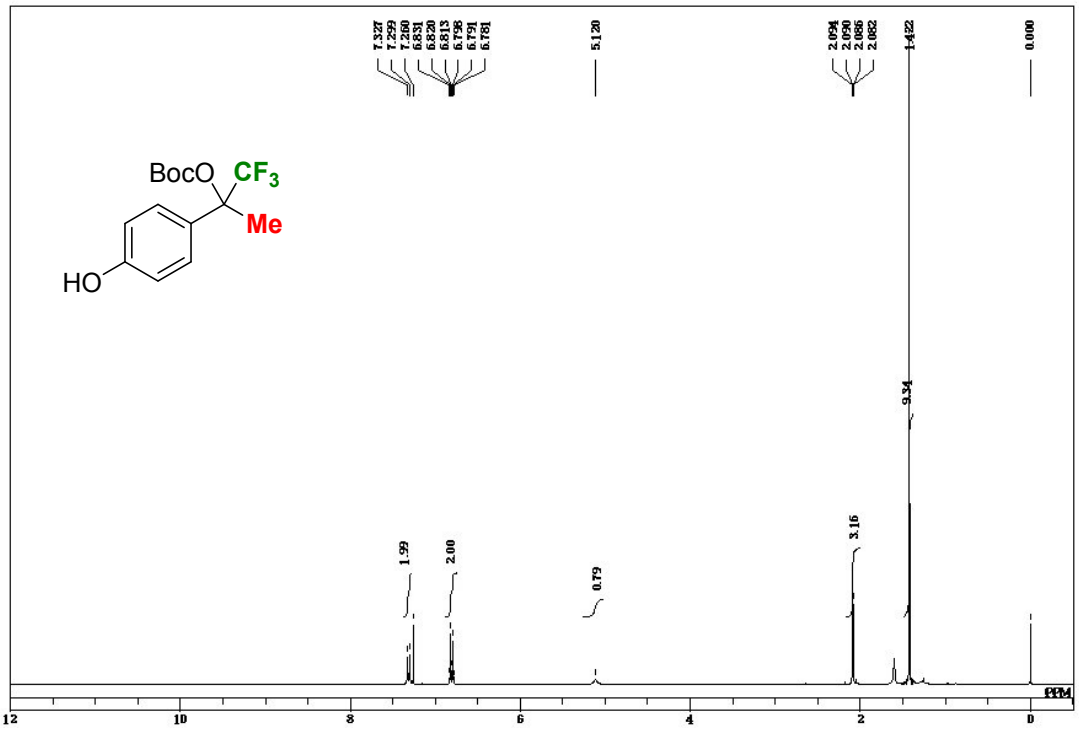



$^{13}$C NMR (300 MHz, $CDCl_3$)

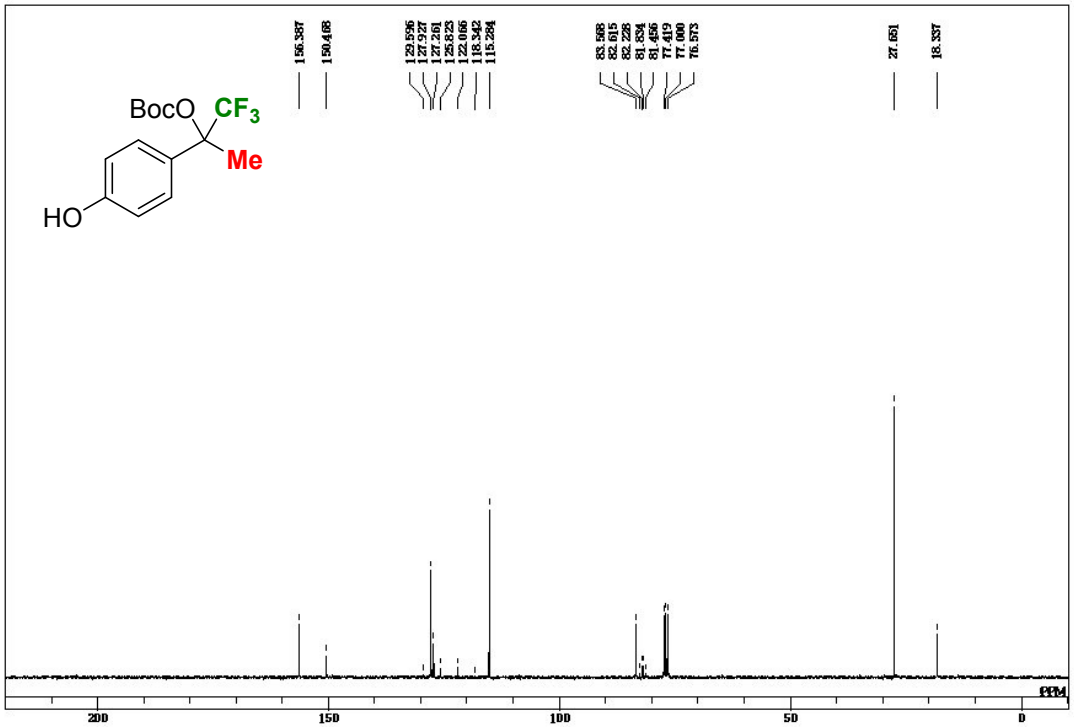


4-[{2-(*tert*-Butoxycarbonyl)oxy}-1,1,1-trifluoroprop-2-yl}phenol **(6a).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

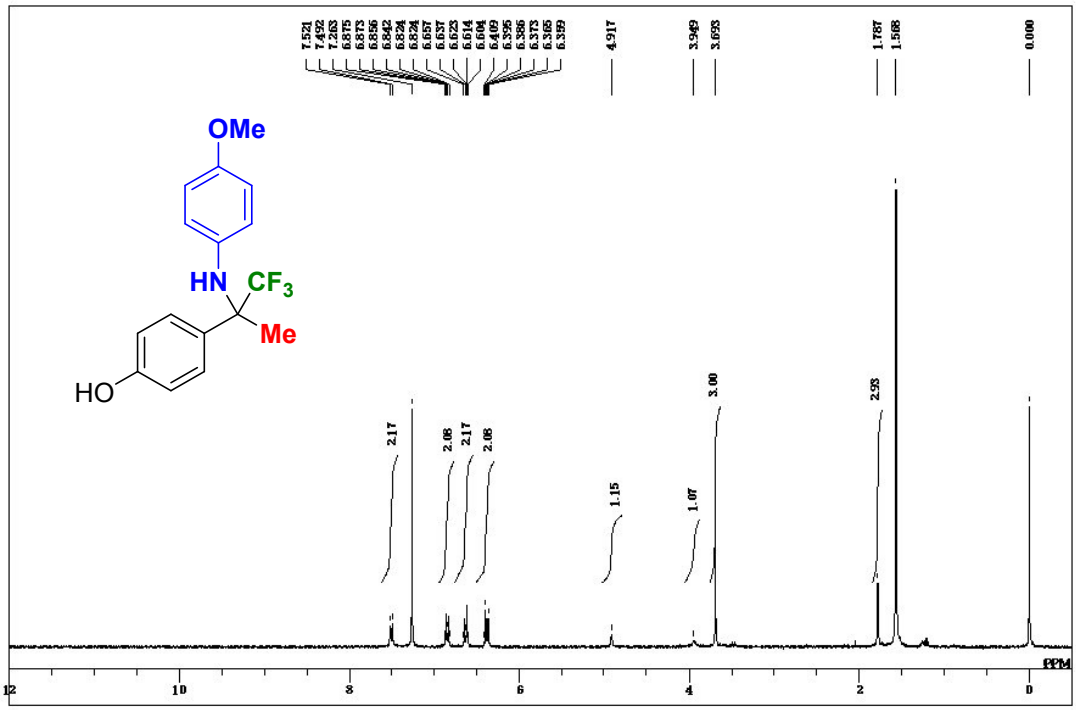



$^{13}$C NMR (300 MHz, $CDCl_3$)

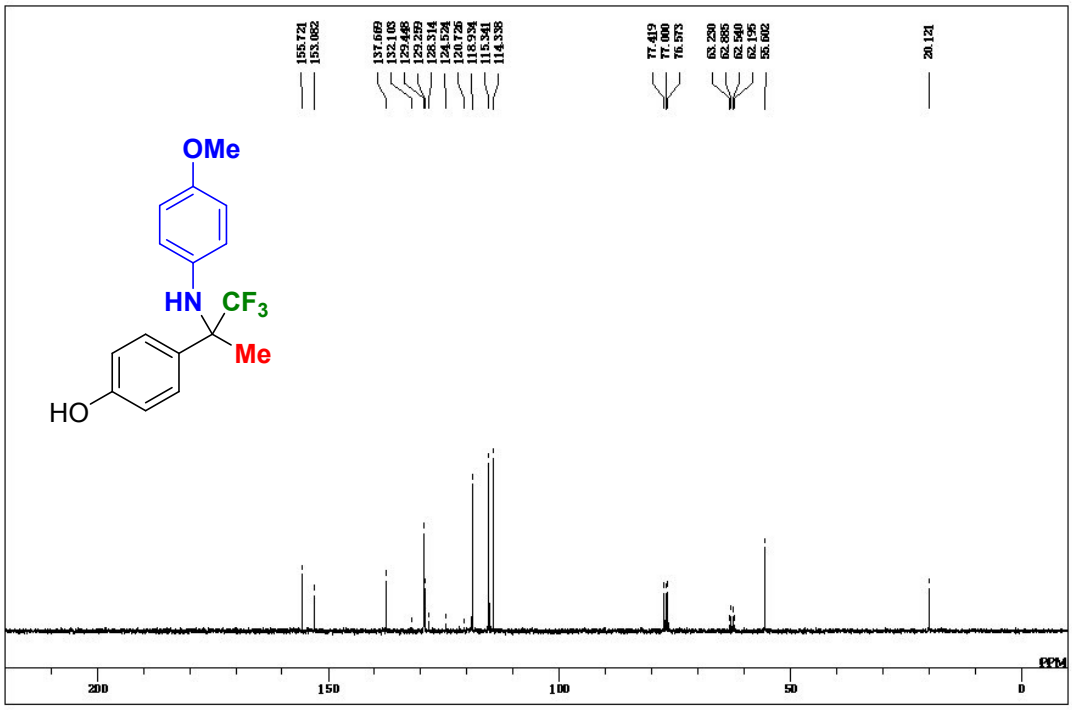


4-[1,1,1-Trifluoro-2-{(4-methoxyphenyl)amino}prop-2-yl}phenol **(3al).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

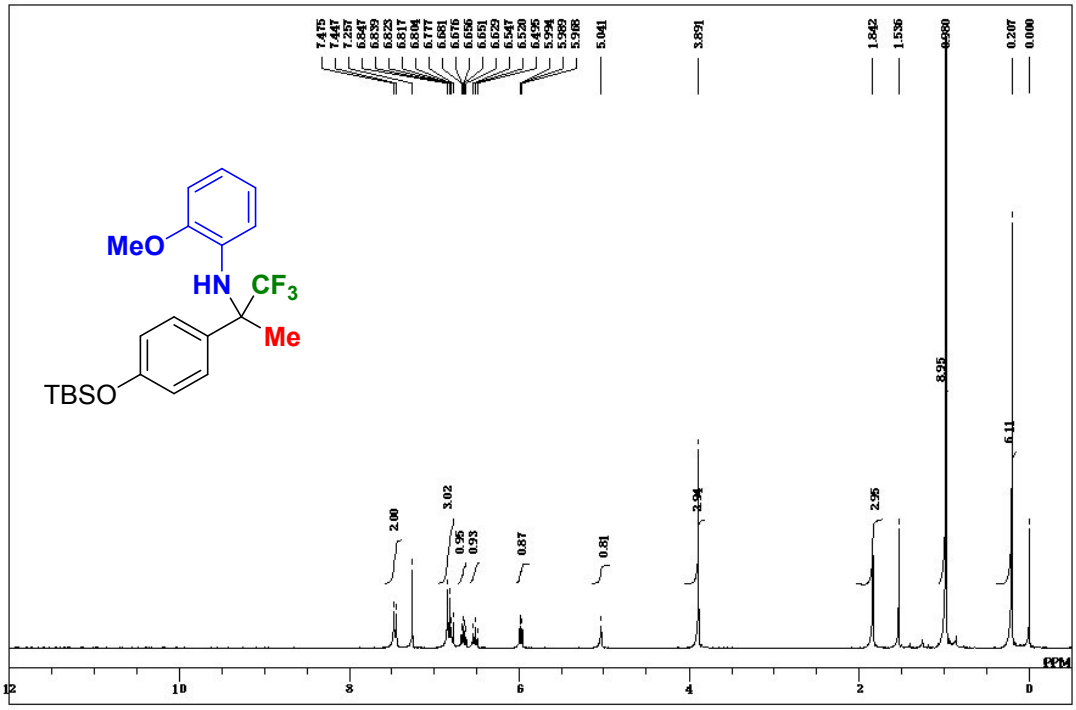



$^{13}$C NMR (300 MHz, $CDCl_3$)

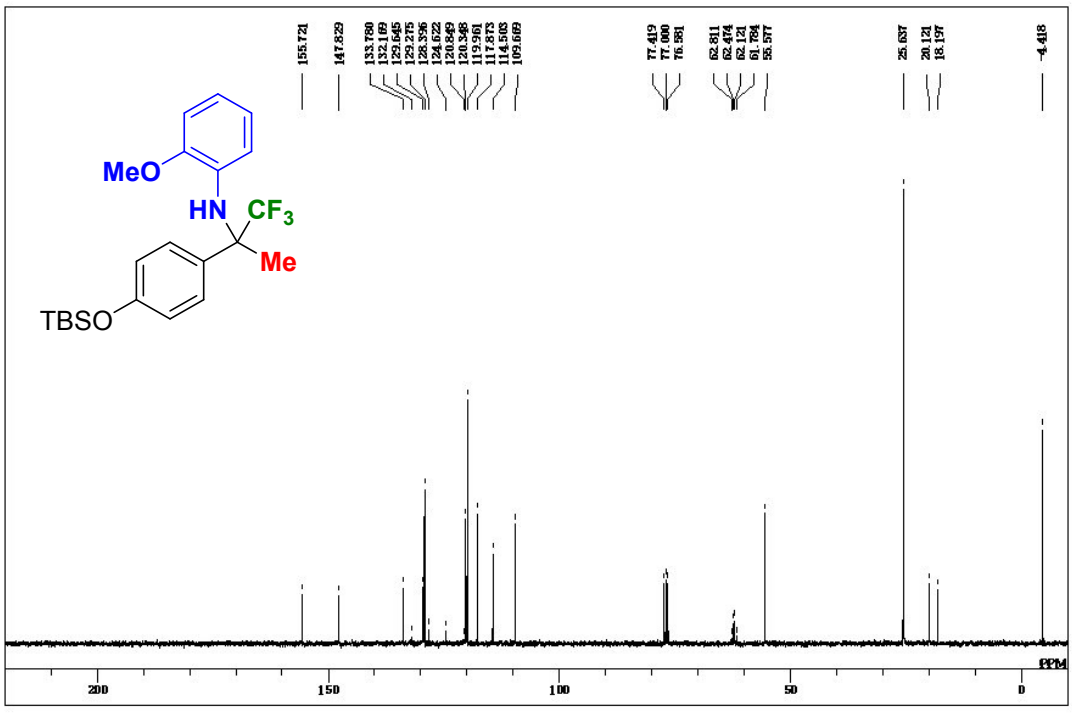


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-(2-methoxyphenyl)aminopropane **(4am).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

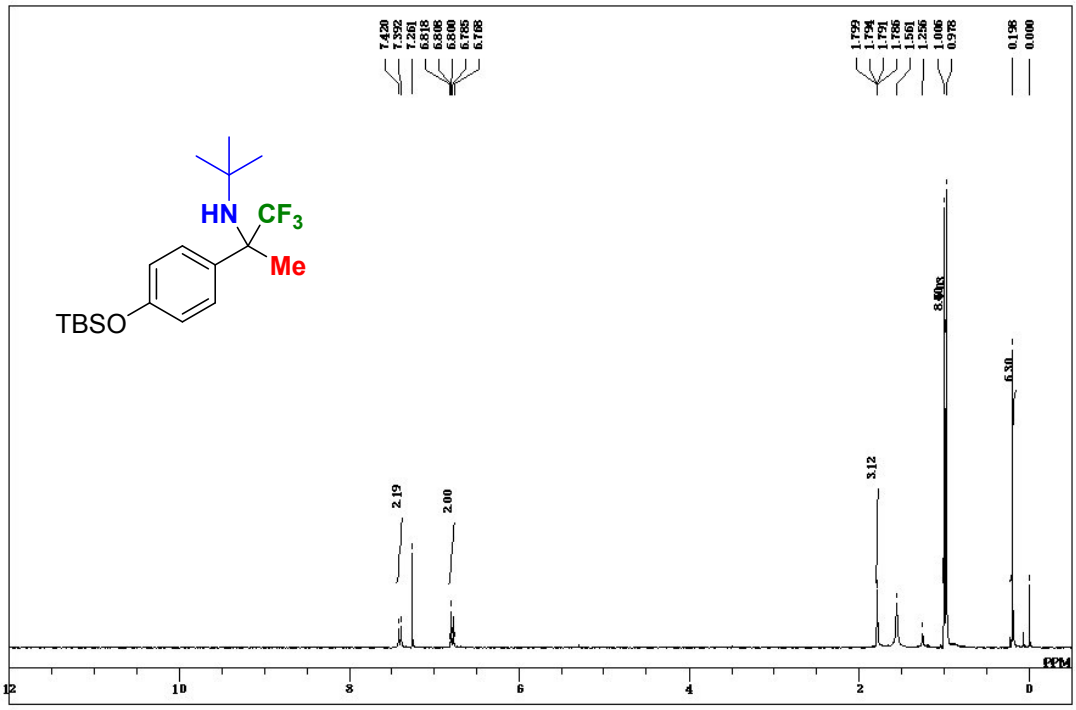



$^{13}$C NMR (300 MHz, $CDCl_3$)

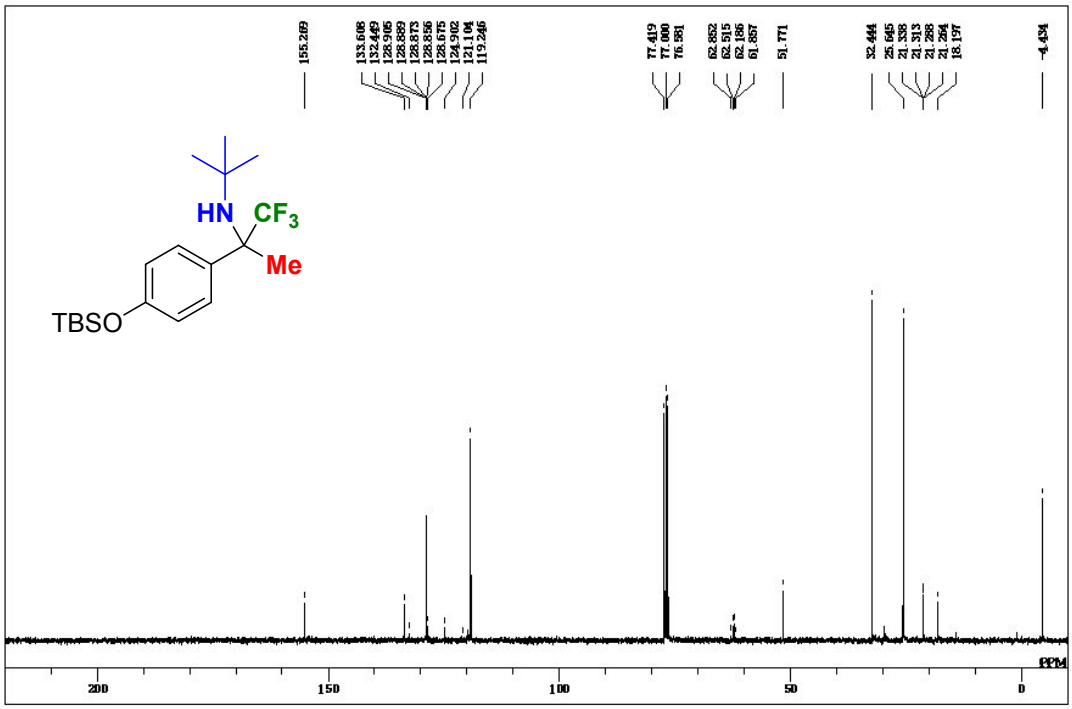


2-*tert*-Butyl-2-[4-[{(1,1-dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoropropane **(4af).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

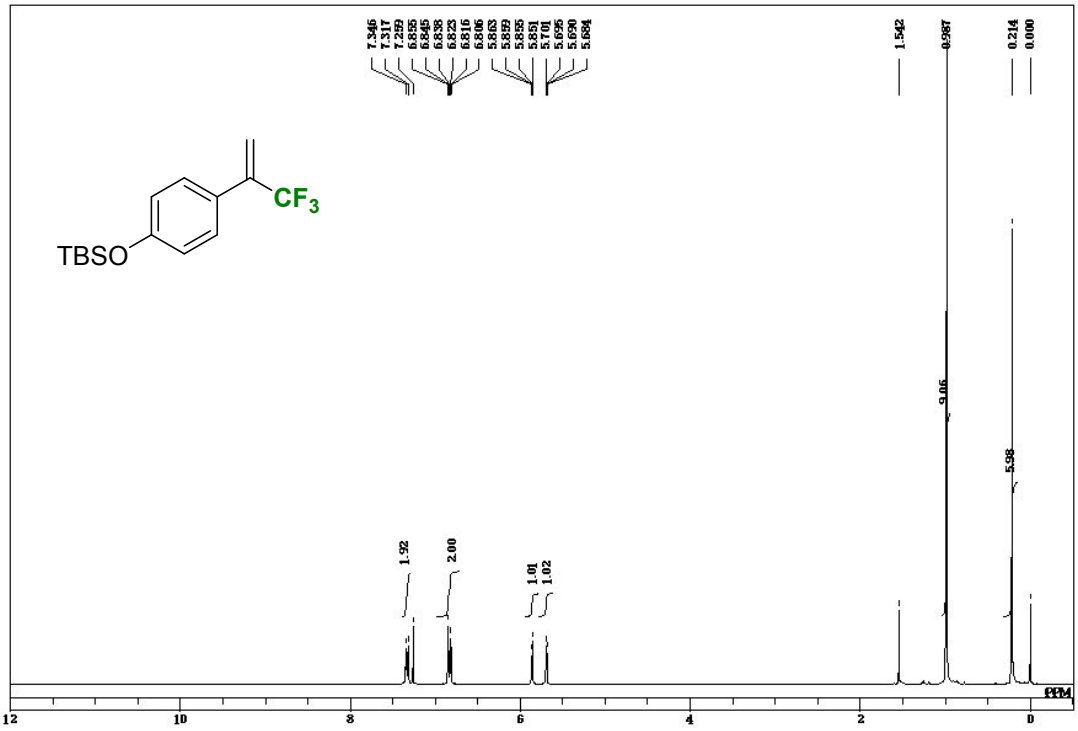



$^{13}$C NMR (300 MHz, $CDCl_3$)

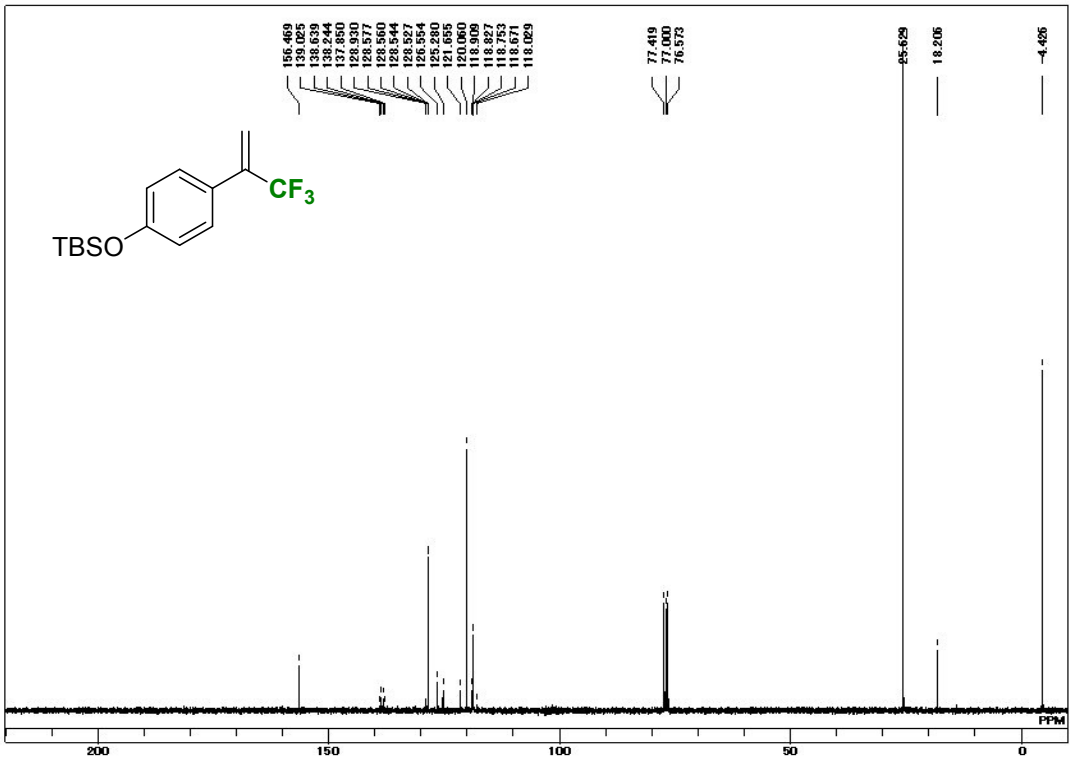


1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene **(7)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

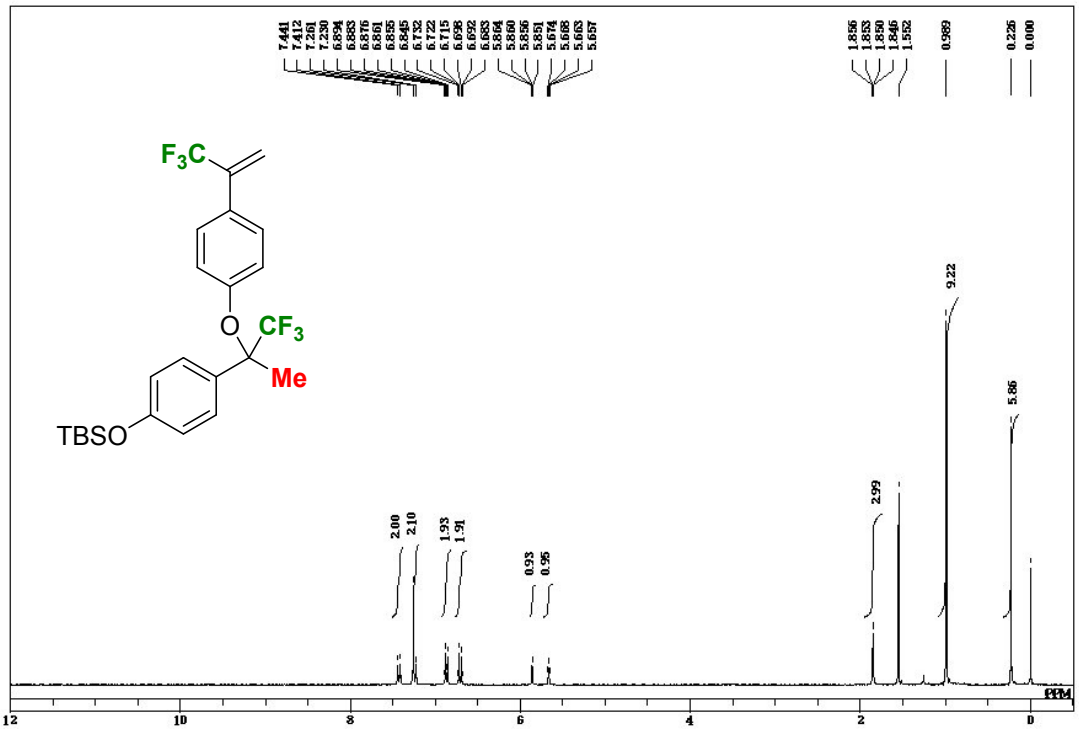



$^{13}$C NMR (300 MHz, $CDCl_3$)

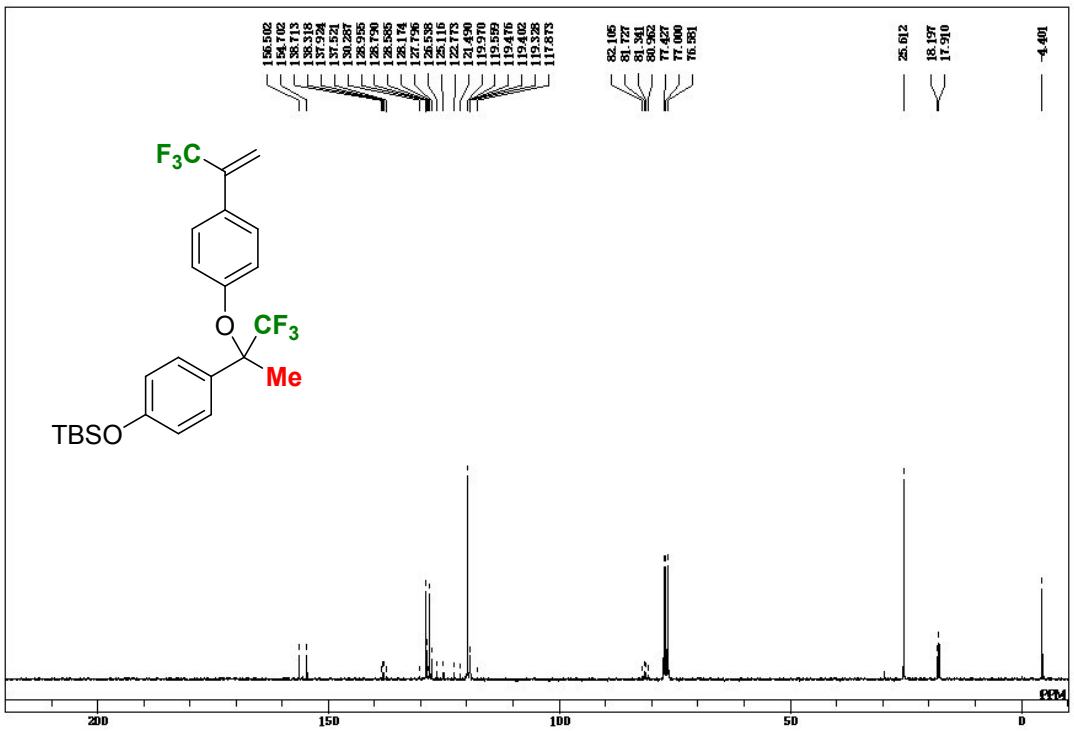


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-{4-(3,3,3-trifluoroprop-1-en-2-yl)phenoxy}propane. **(8)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

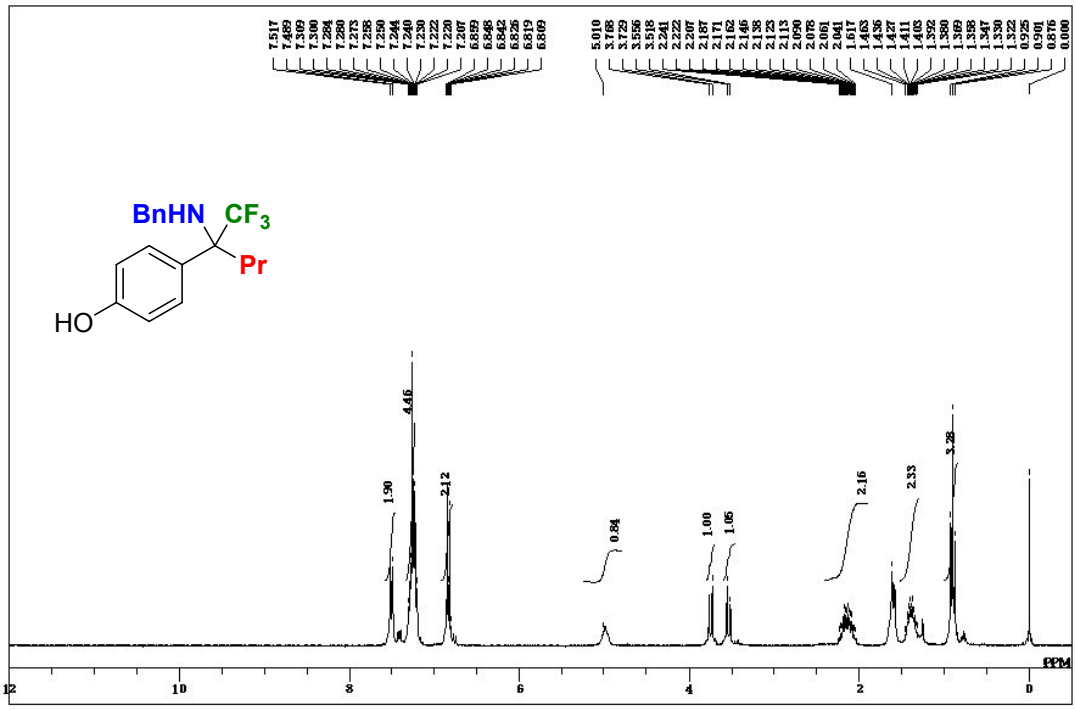



$^{13}$C NMR (300 MHz, $CDCl_3$)

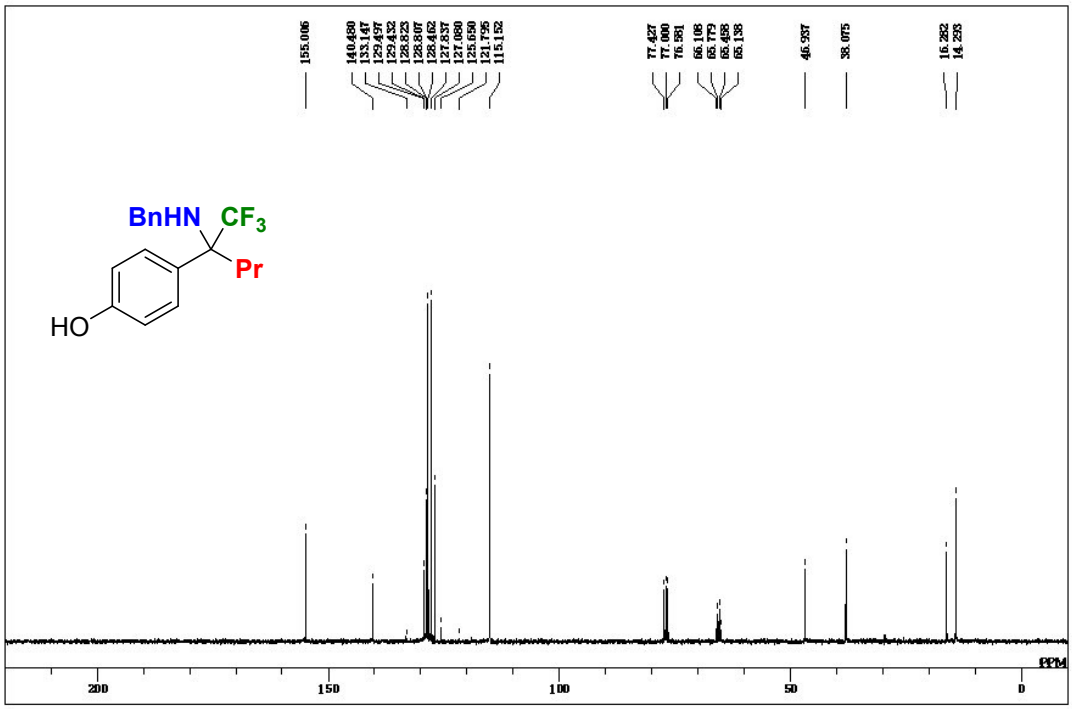


4-{2-(Benzylamino)-1,1,1-trifluoropent-2-yl}phenol. (**3ba**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

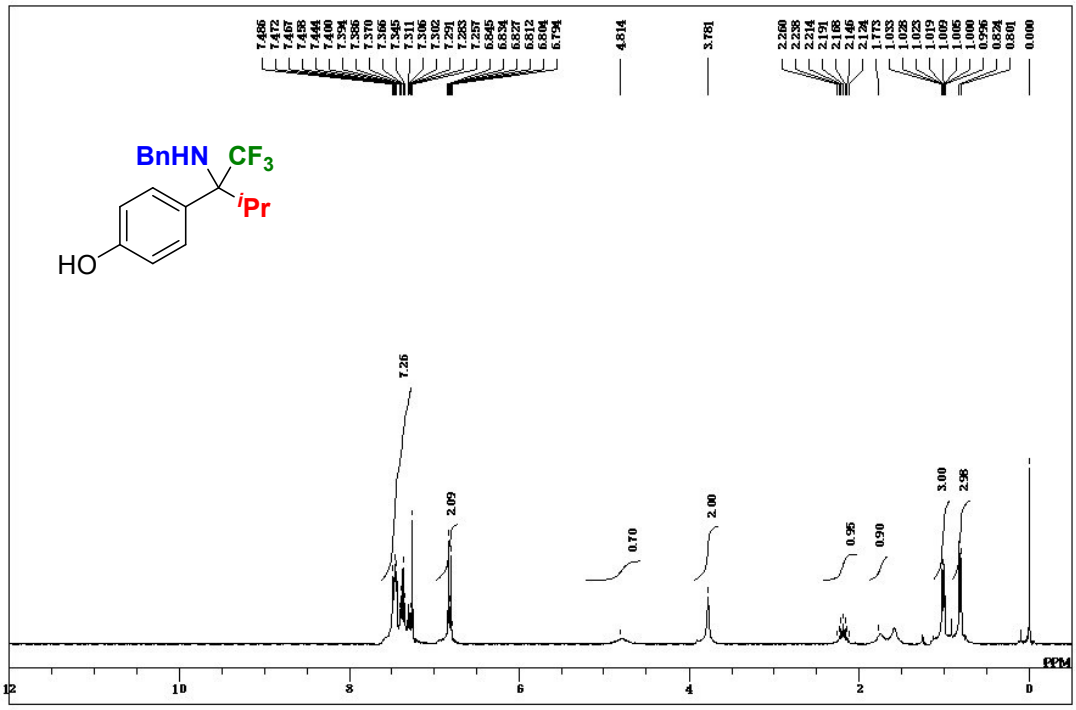



$^{13}$C NMR (300 MHz, $CDCl_3$)

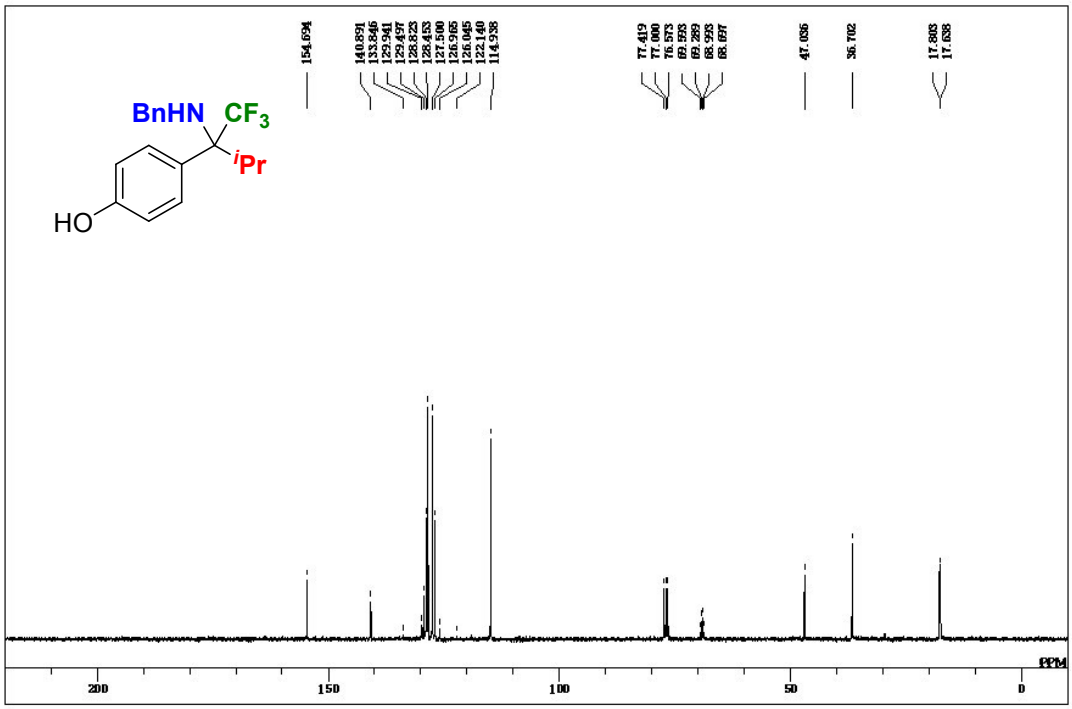


4-{2-(Benzylamino)-1,1,1-trifluoro-3-methylbut-2-yl}phenol. (**3ca**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

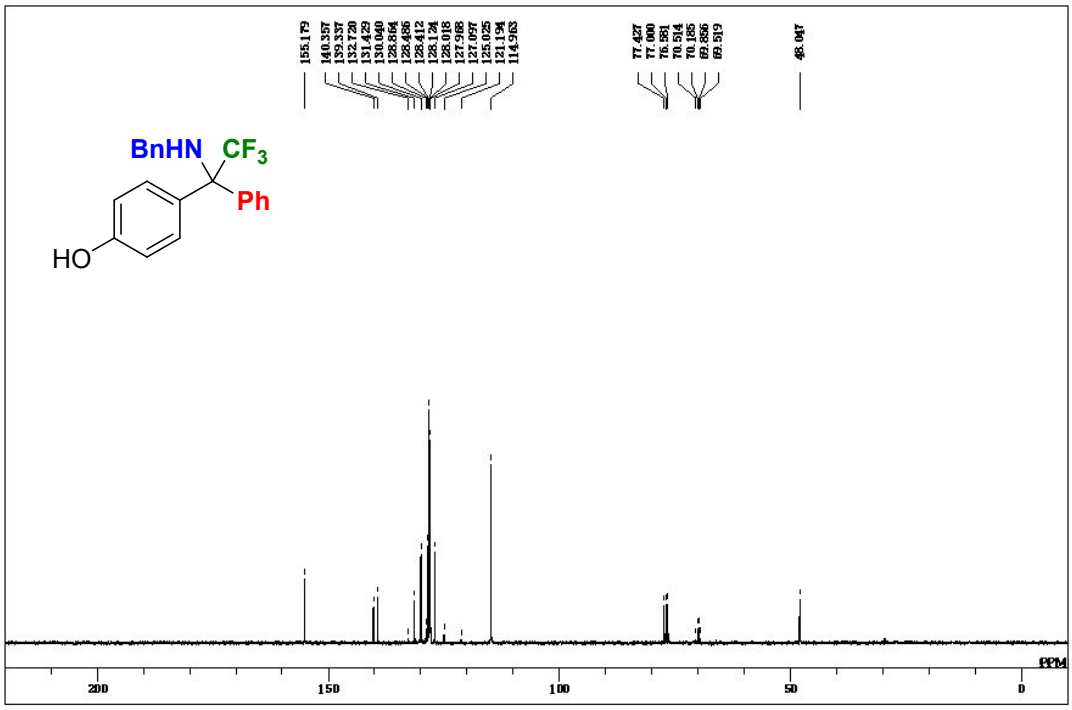



$^{13}$C NMR (300 MHz, $CDCl_3$)

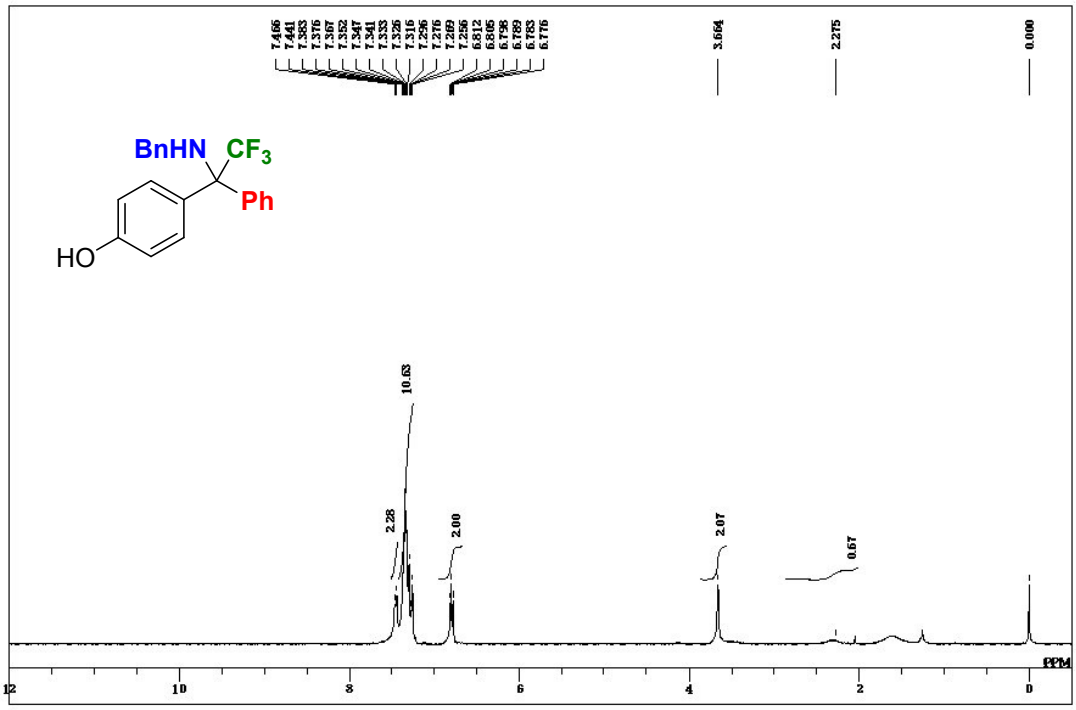


4-{1-(Benzylamino)-2,2,2-trifluoro-1-phenyleth-2-yl}phenol **(3da)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

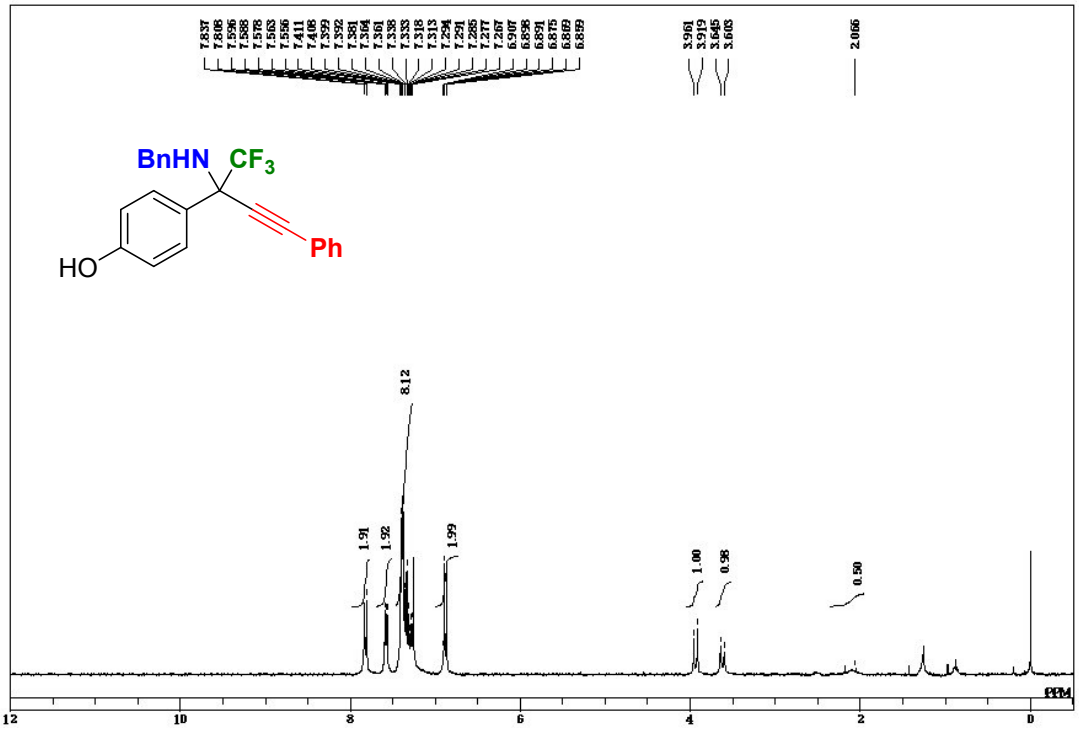



$^{13}$C NMR (300 MHz, $CDCl_3$)

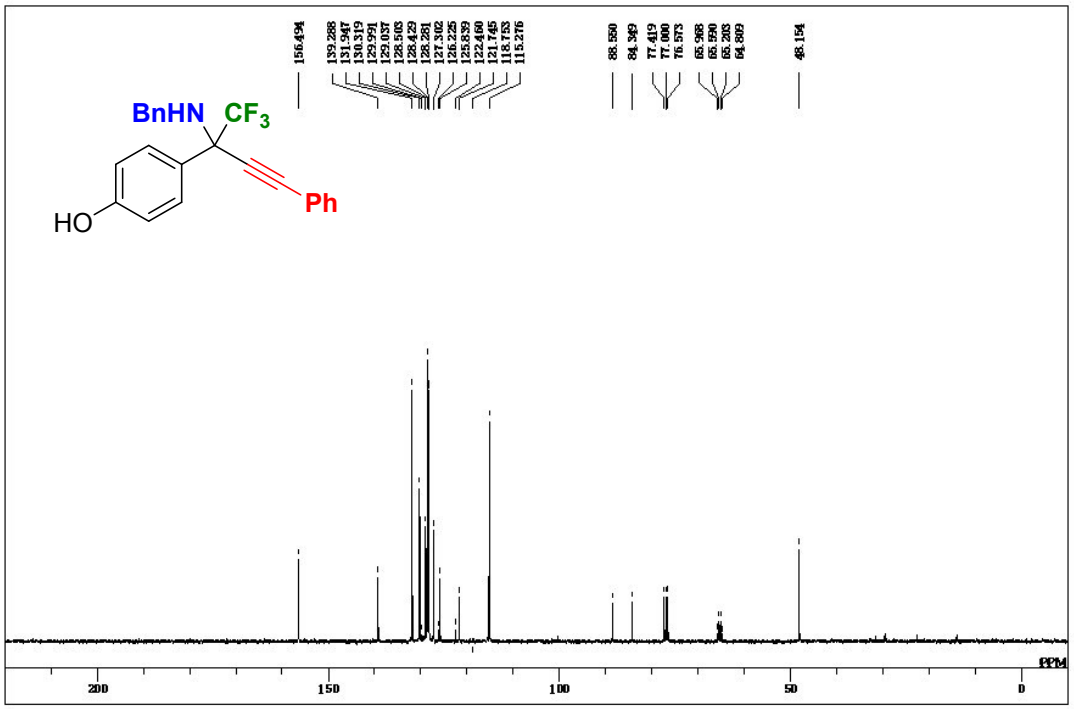


4-{2-(Benzylamino)-1,1,1-trifluoro-4-phenylbut-3-yn-2-yl}phenol **(3ea)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

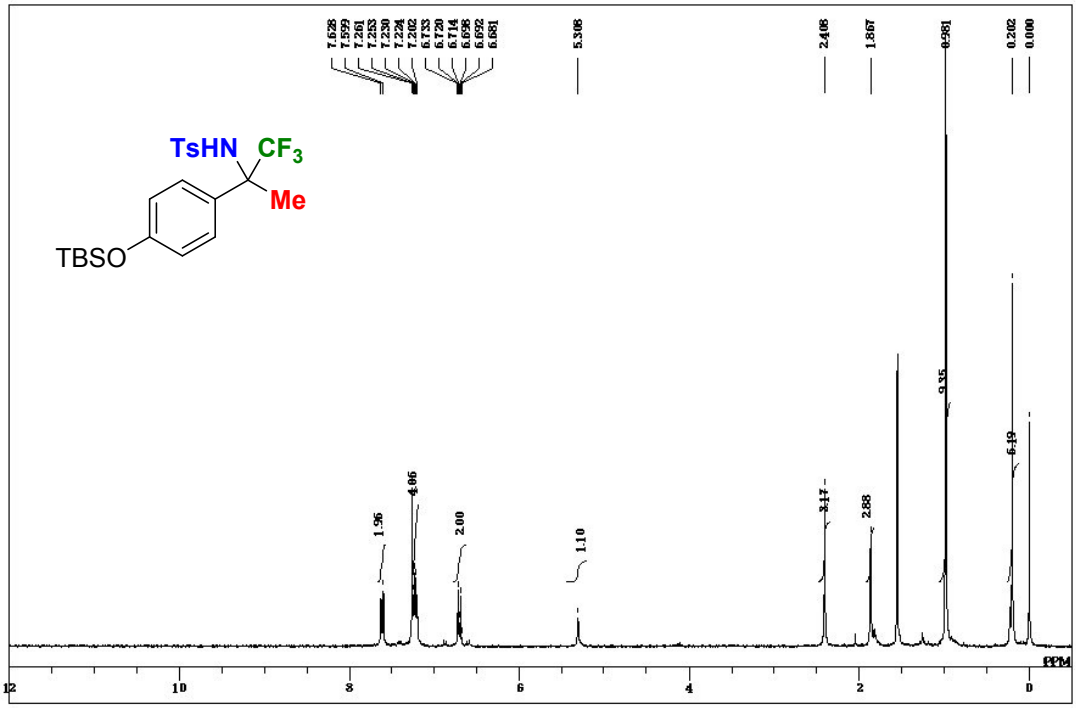



$^{13}$C NMR (300 MHz, $CDCl_3$)

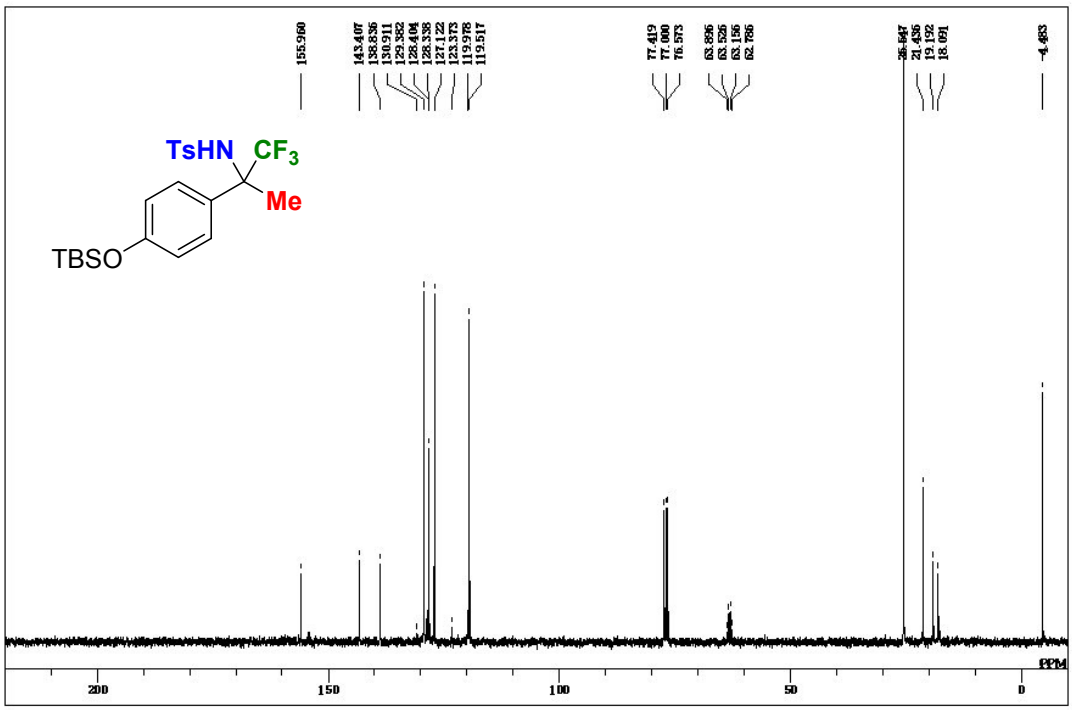


*N*-[1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoroprop-2-yl]-4-methylbenzenesulfonamide **(4an)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

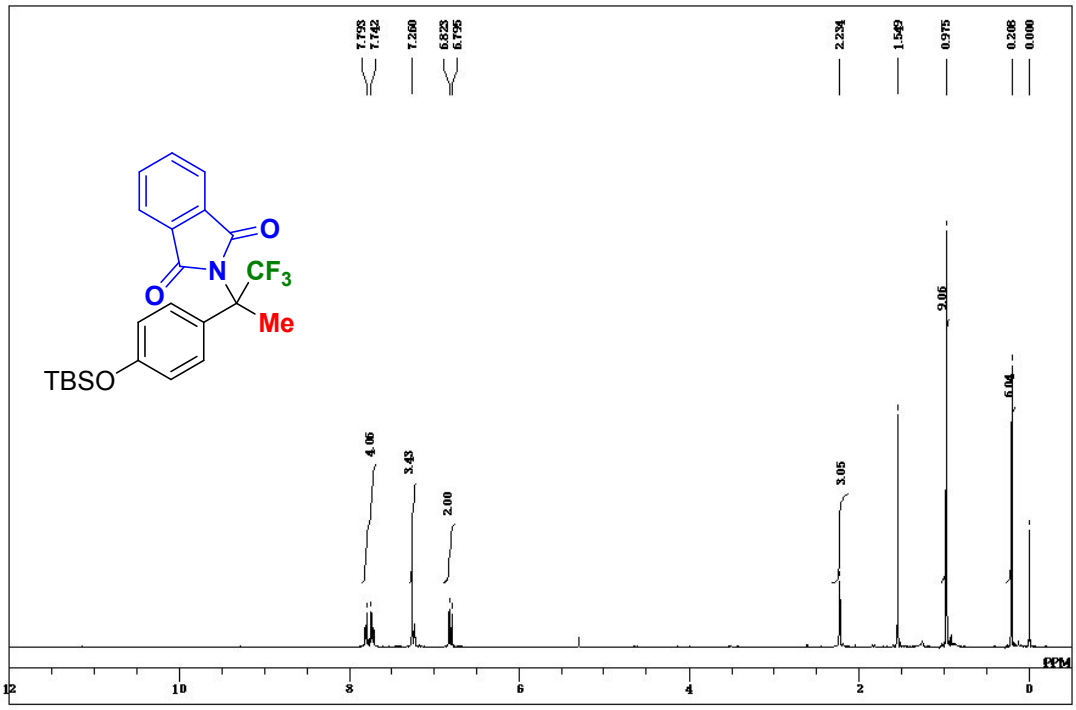



$^{13}$C NMR (300 MHz, $CDCl_3$)

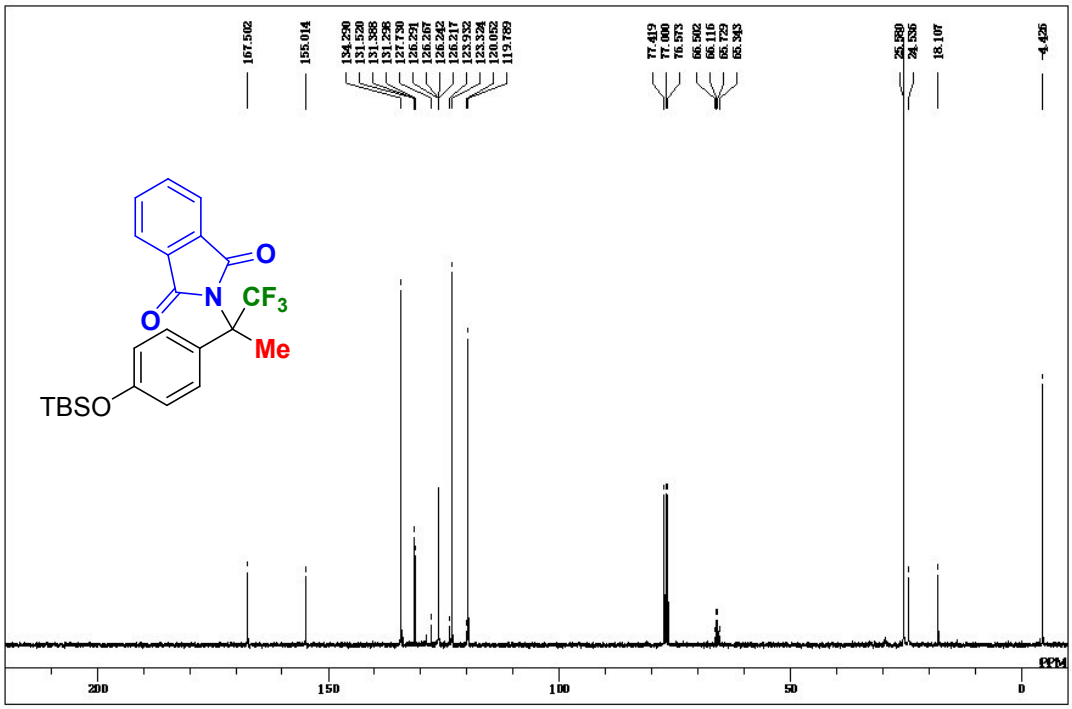


*N*-[1-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoroprop-2-yl]phtalimide (**4ao**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

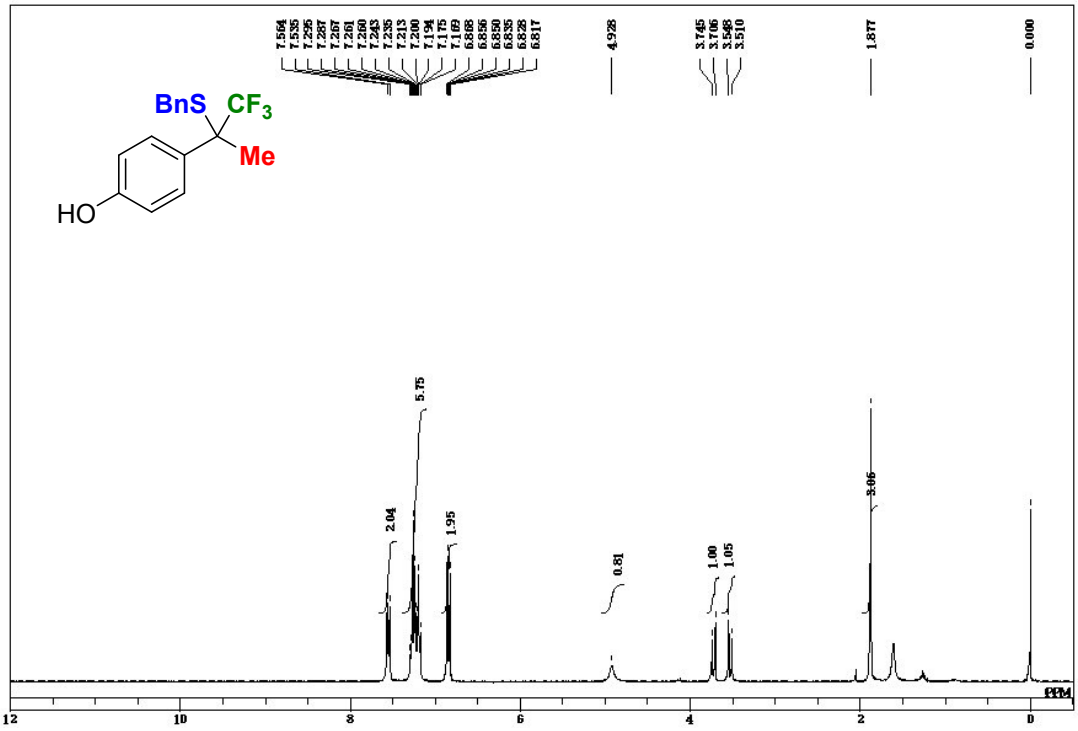



$^{13}$C NMR (300 MHz, $CDCl_3$)

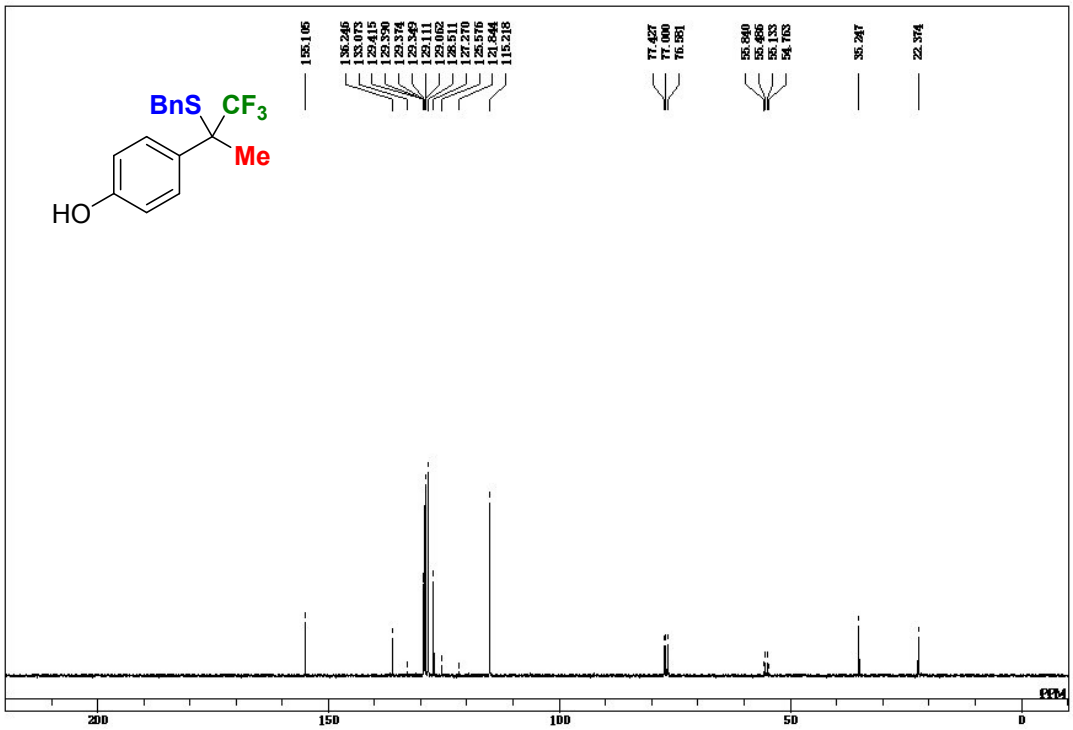


4-[1,1,1-Trifluoro-2-{(phenylmethane)sulfenyl}prop-2-yl]phenol **(9aa).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

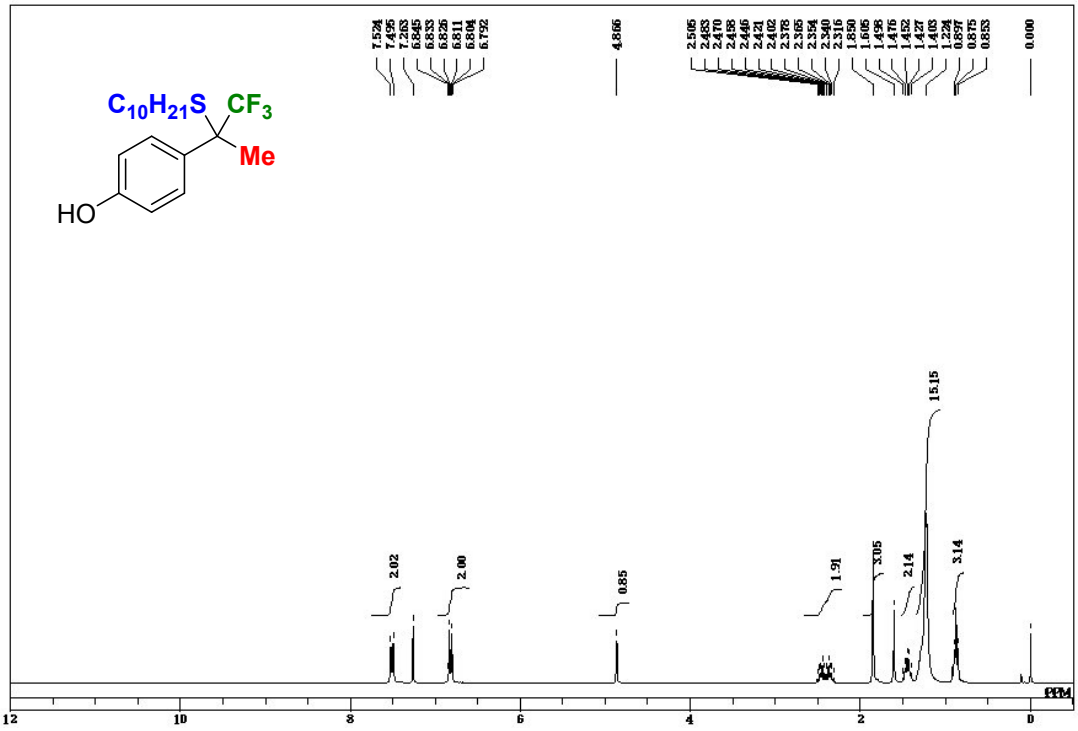



$^{13}$C NMR (300 MHz, $CDCl_3$)

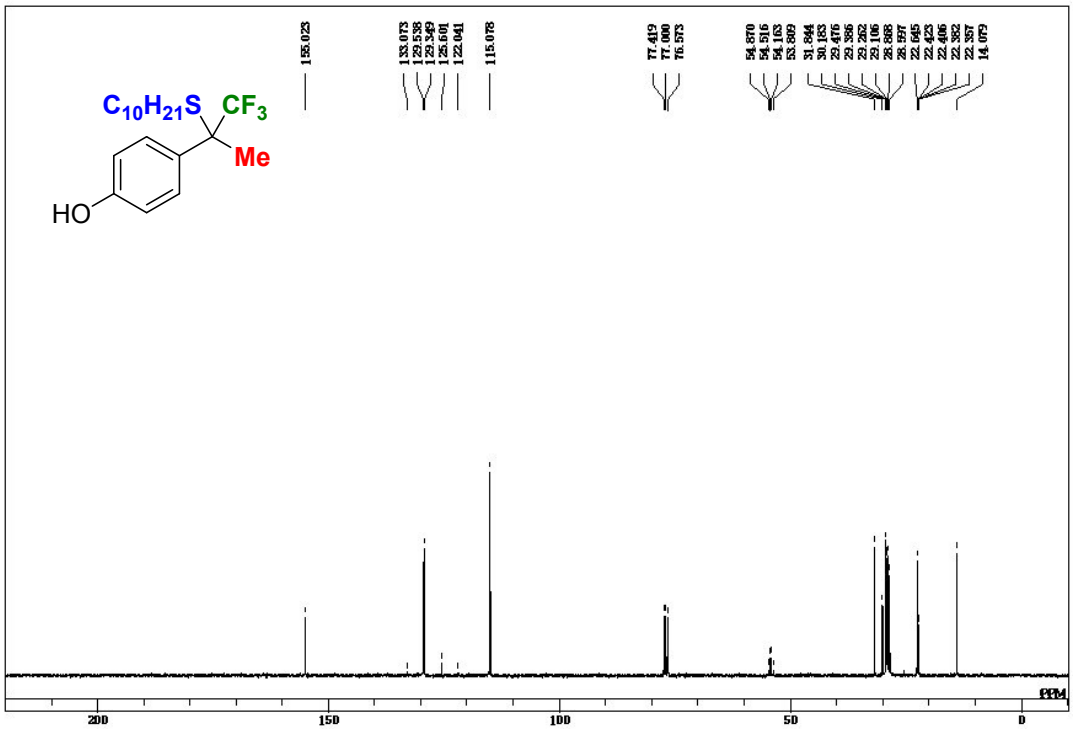


4-{1,1,1-Trifluoro-2-(decanesulfenyl)prop-2-yl}phenol **(9ab).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

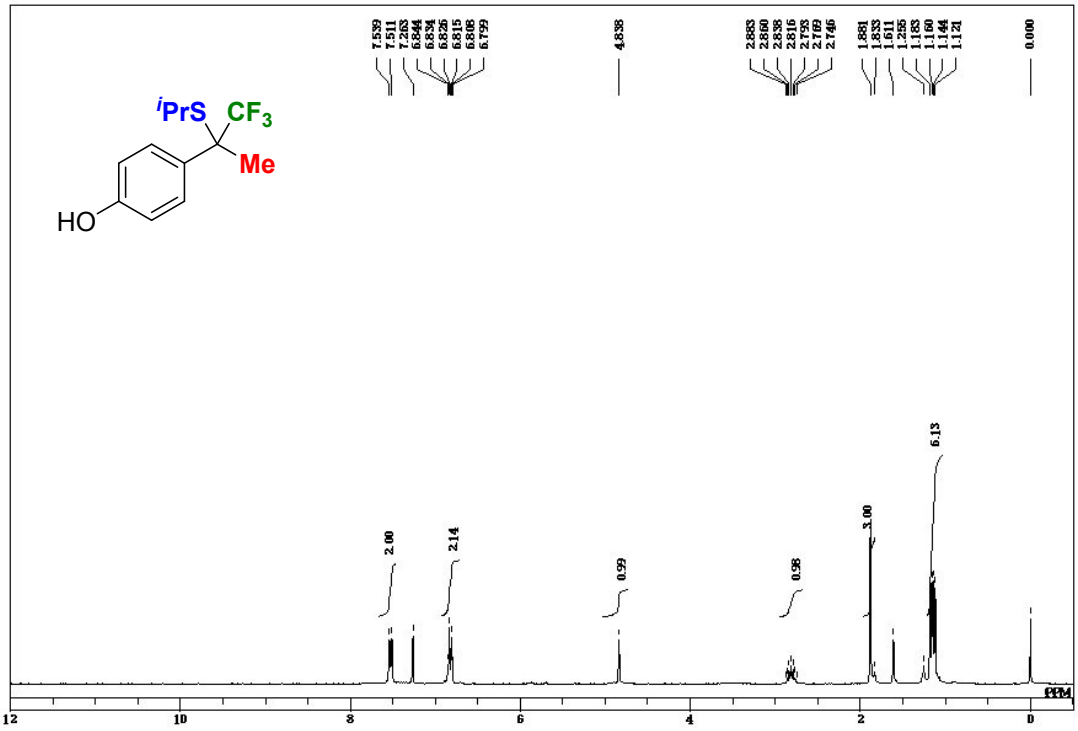



$^{13}$C NMR (300 MHz, $CDCl_3$)

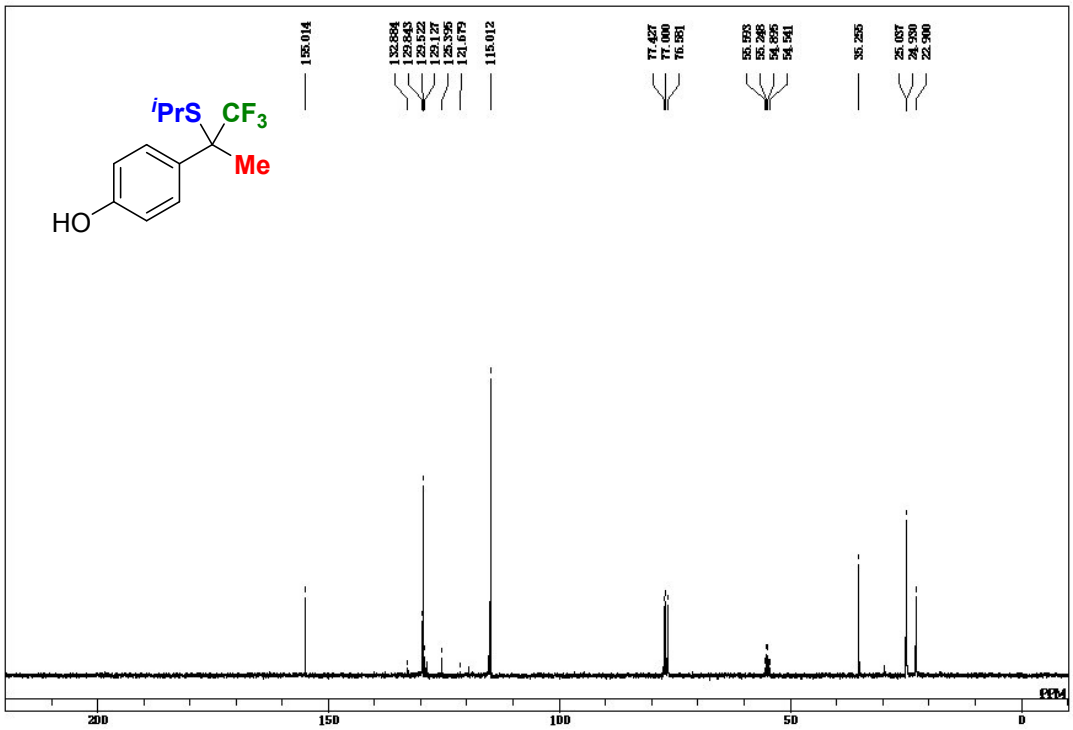


4-[1,1,1-Trifluoro-2-{(1-methylethane)sulfenyl}prop-2-yl]phenol **(9ac)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

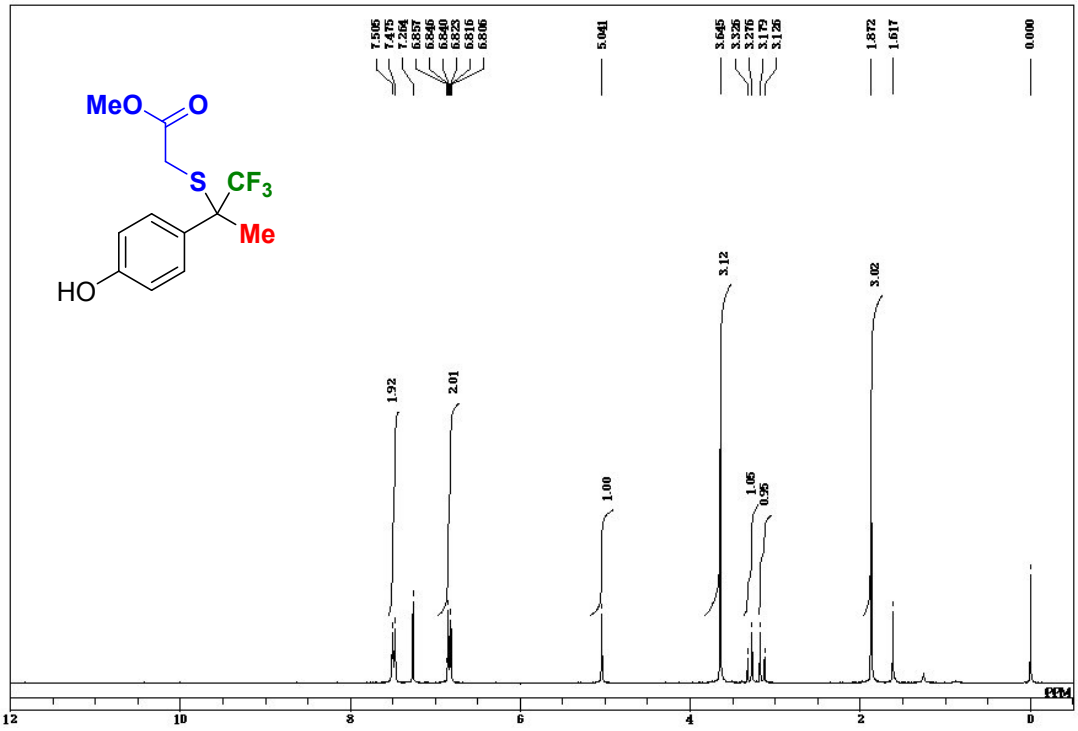



$^{13}$C NMR (300 MHz, $CDCl_3$)

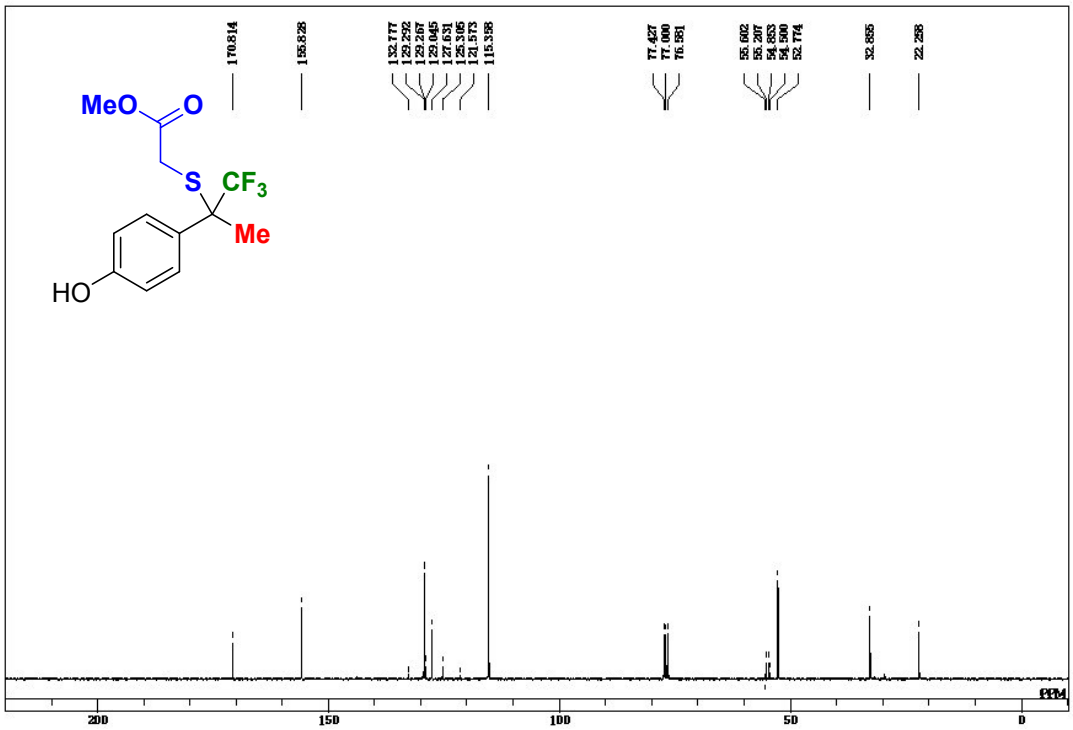


Methyl 2-{1,1,1-trifluoro-2-(4-hydroxyphenyl)prop-2-yl}thioacetate (**9ad**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

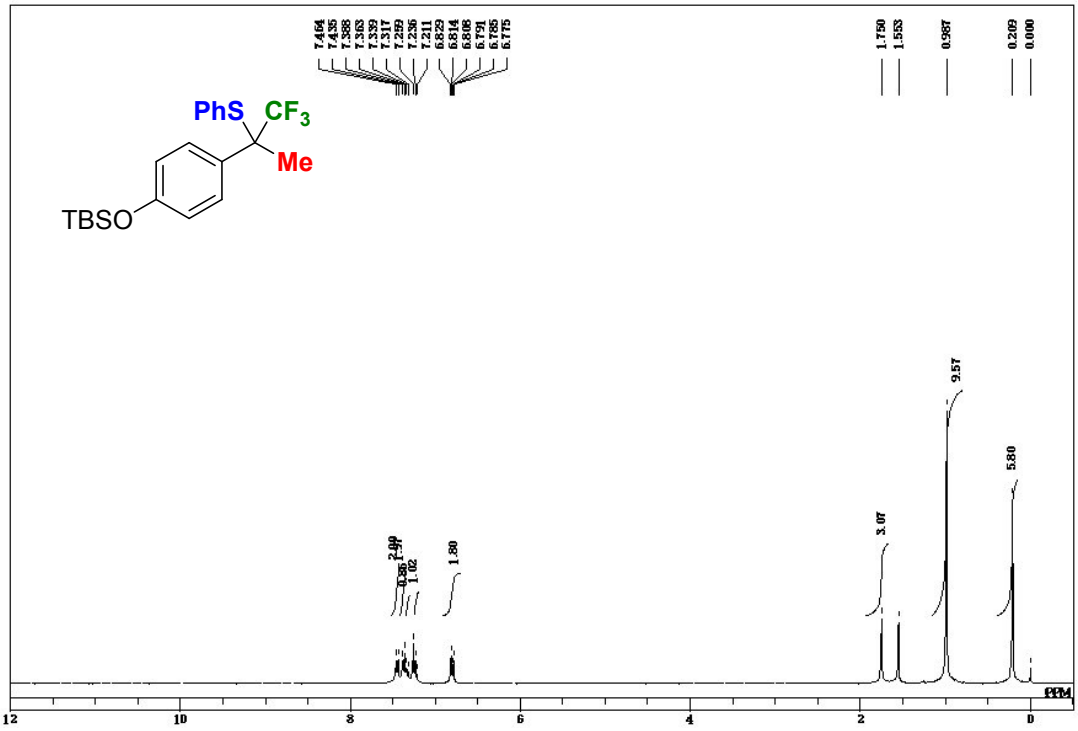



$^{13}$C NMR (300 MHz, $CDCl_3$)

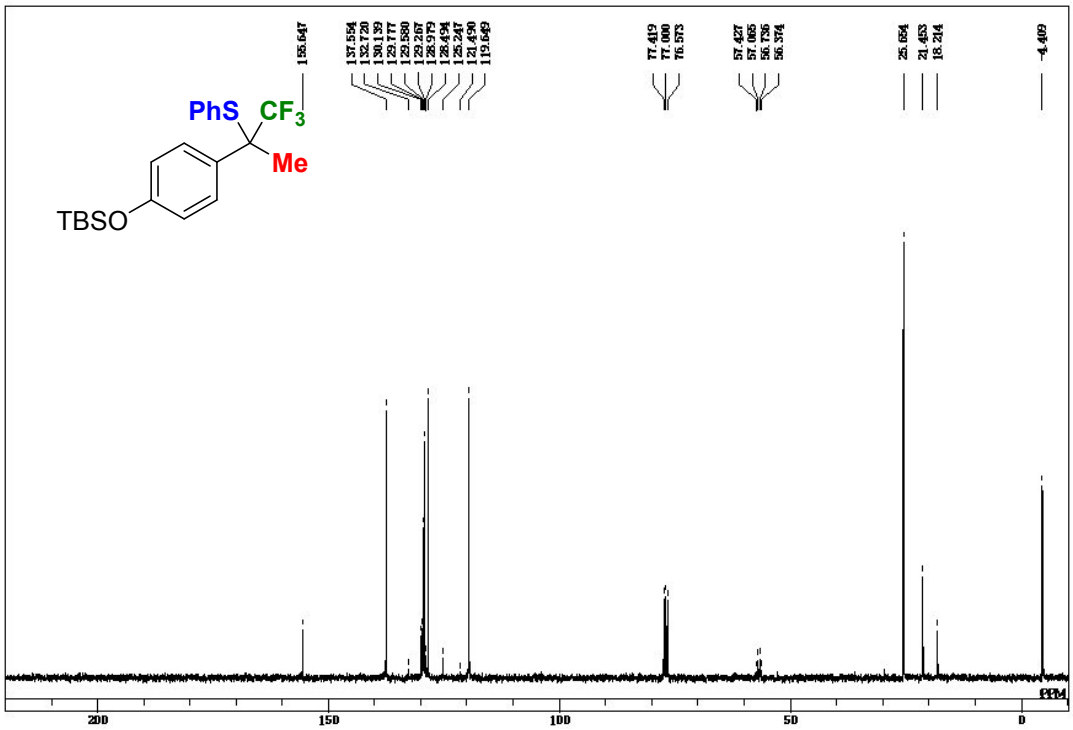


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]]-1,1,1-trifluoro-2-phenylthiopropane **(10ae)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

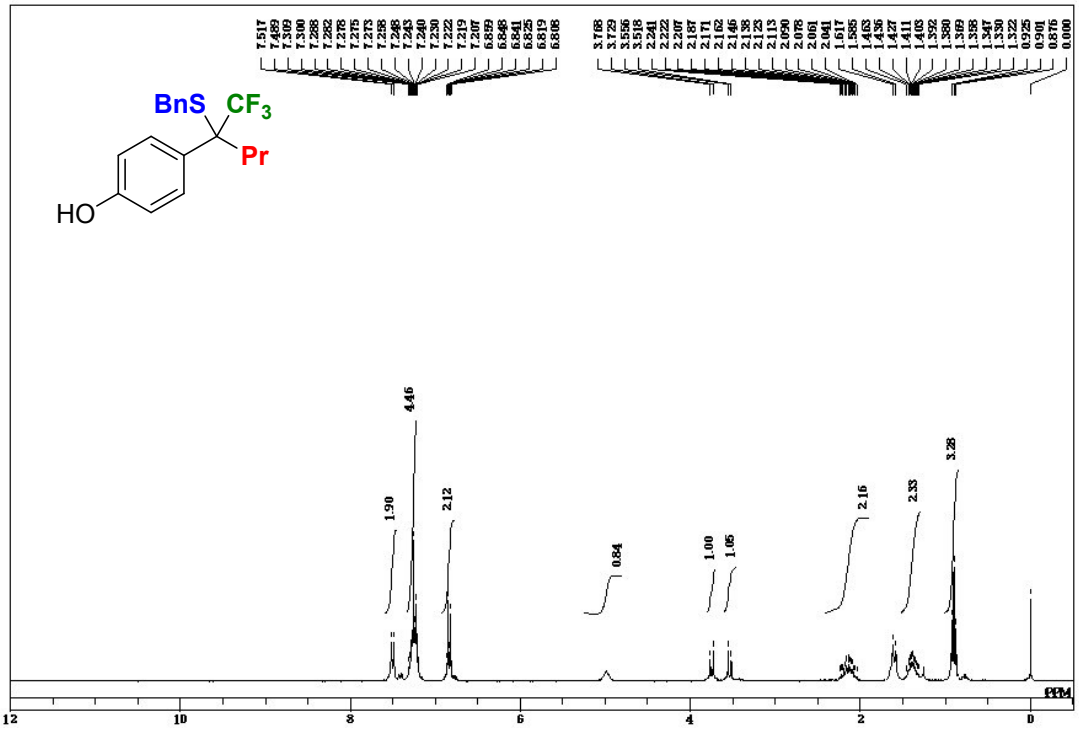



$^{13}$C NMR (300 MHz, $CDCl_3$)

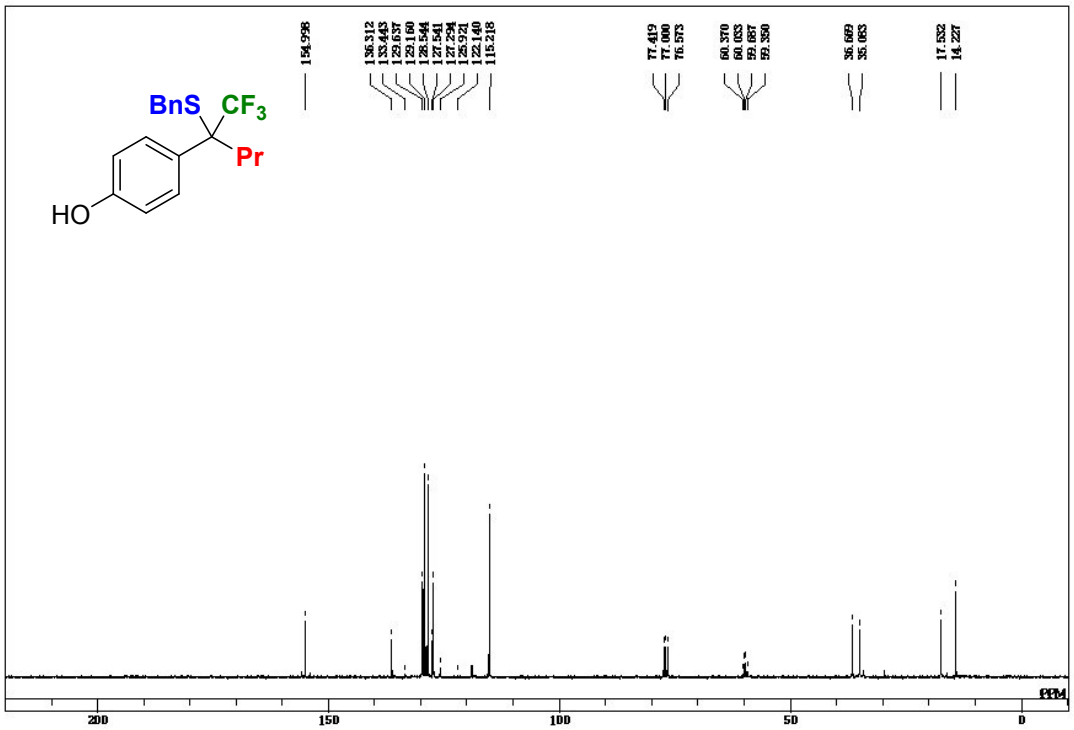


4-[1,1,1-Trifluoro-2-{(phenylmethane)sulfenyl}pent-2-yl]phenol **(9ba)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

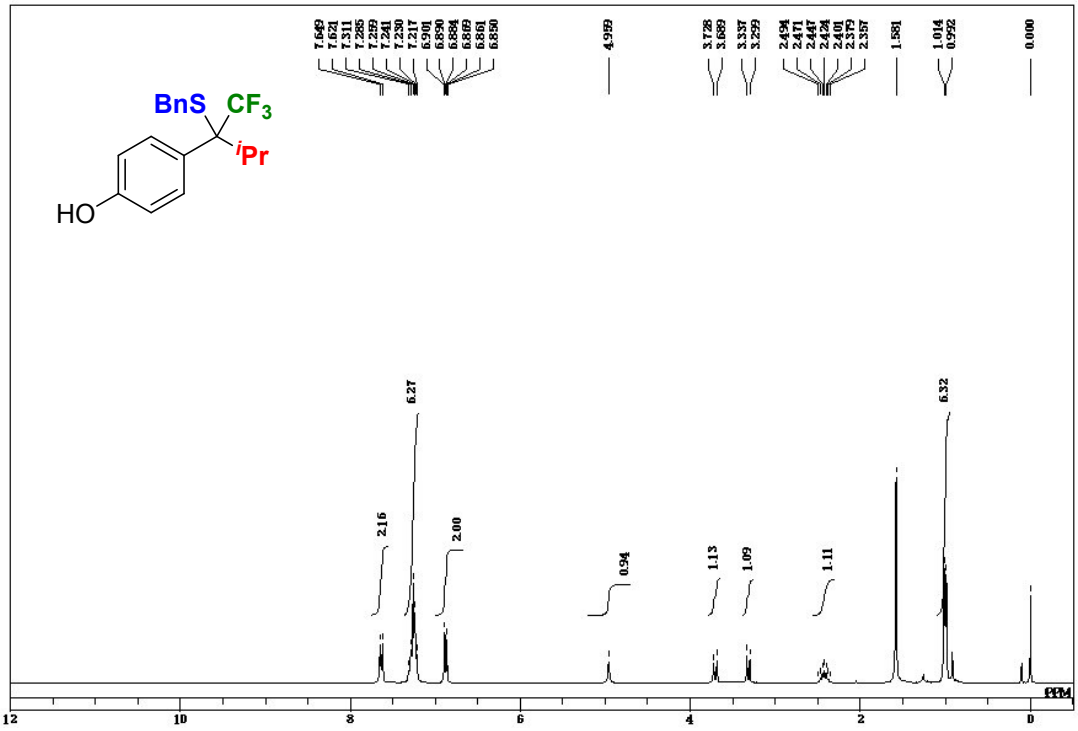



$^{13}$C NMR (300 MHz, $CDCl_3$)

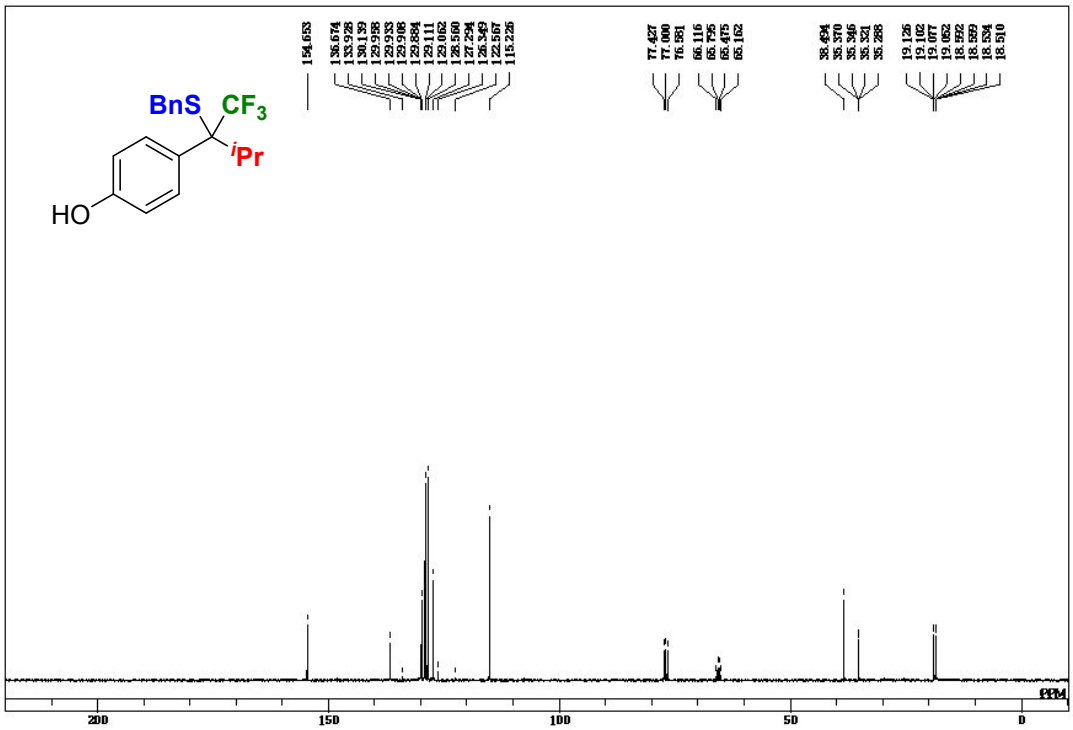


4-[1,1,1-Trifluoro-3-methyl-2-{(phenylmethane)sulfenyl}but-2-yl]phenol **(9ca).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

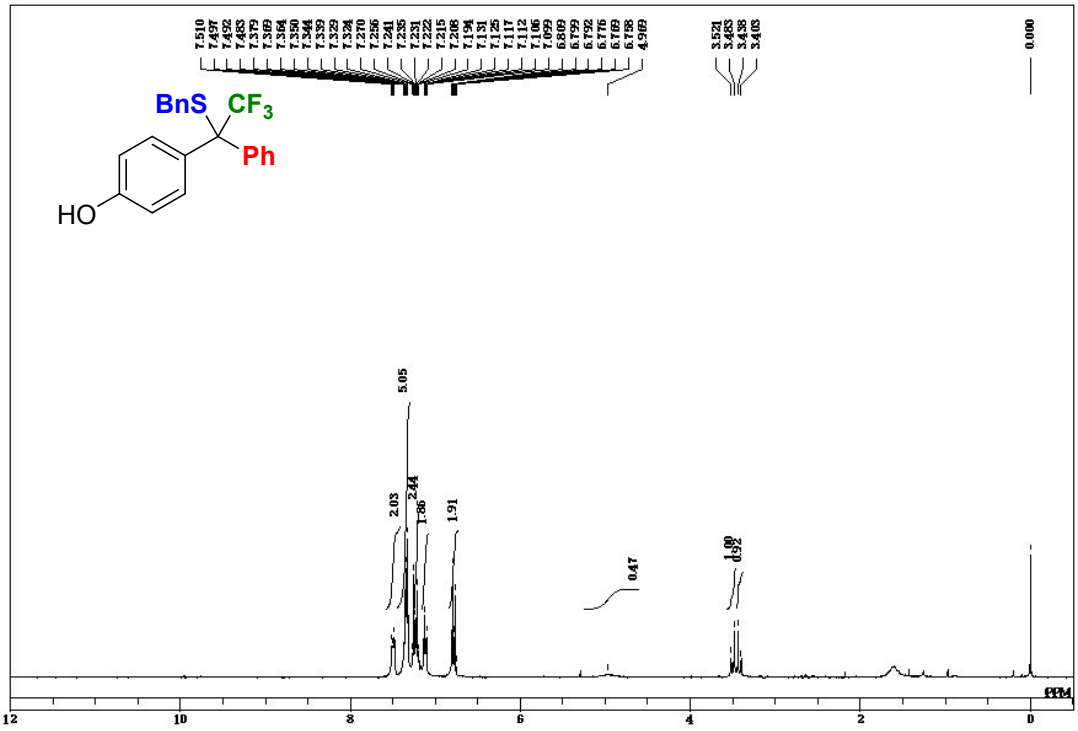



$^{13}$C NMR (300 MHz, $CDCl_3$)

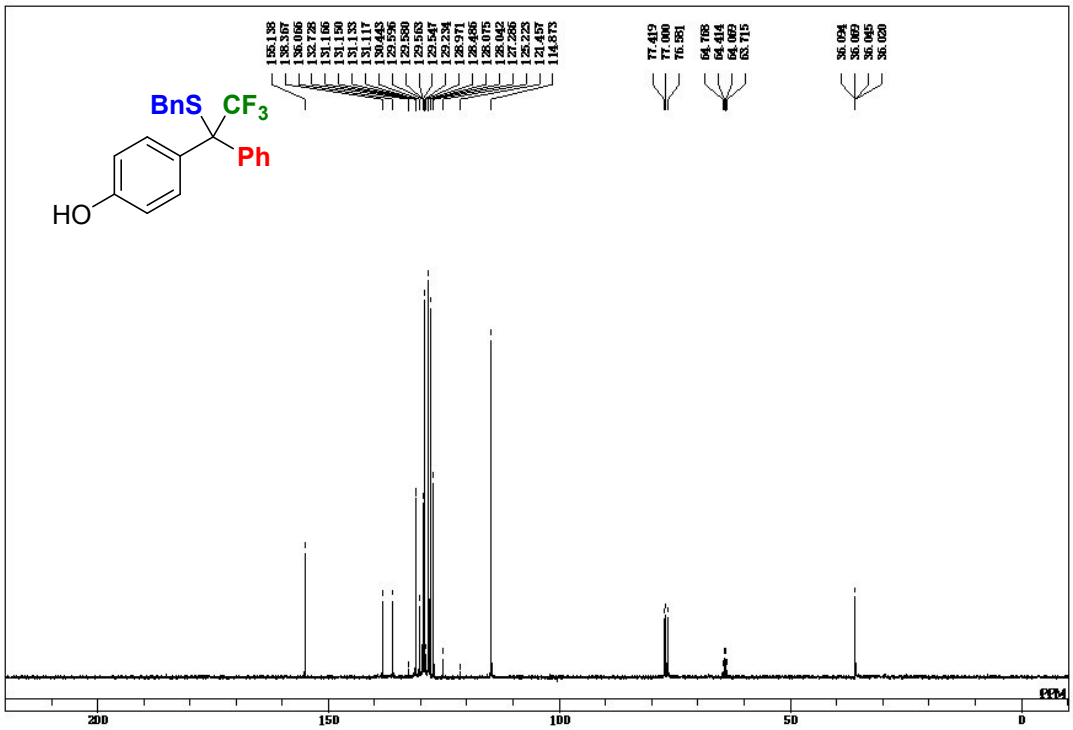


4-[1,1,1-Trifluoro-1-phenyl-2-{(phenylmethane)sulfenyl}ethyl]phenol **(9da)**

$^{1}$H NMR (300 MHz, $CDCl_3$)

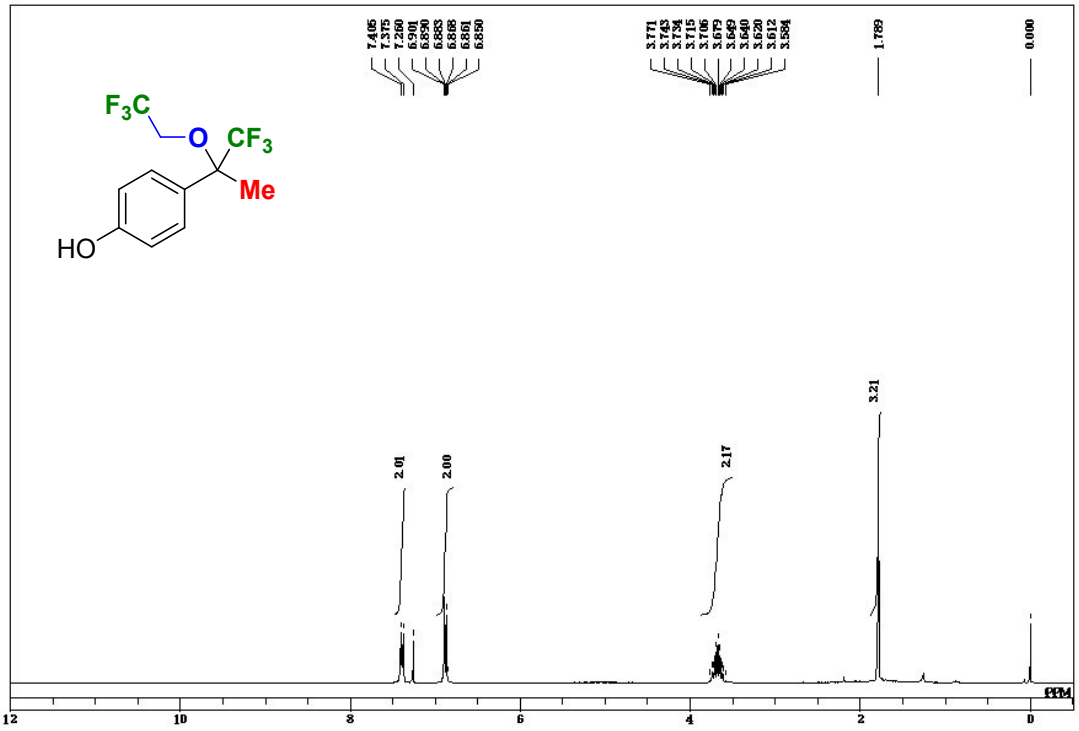



$^{13}$C NMR (300 MHz, $CDCl_3$)

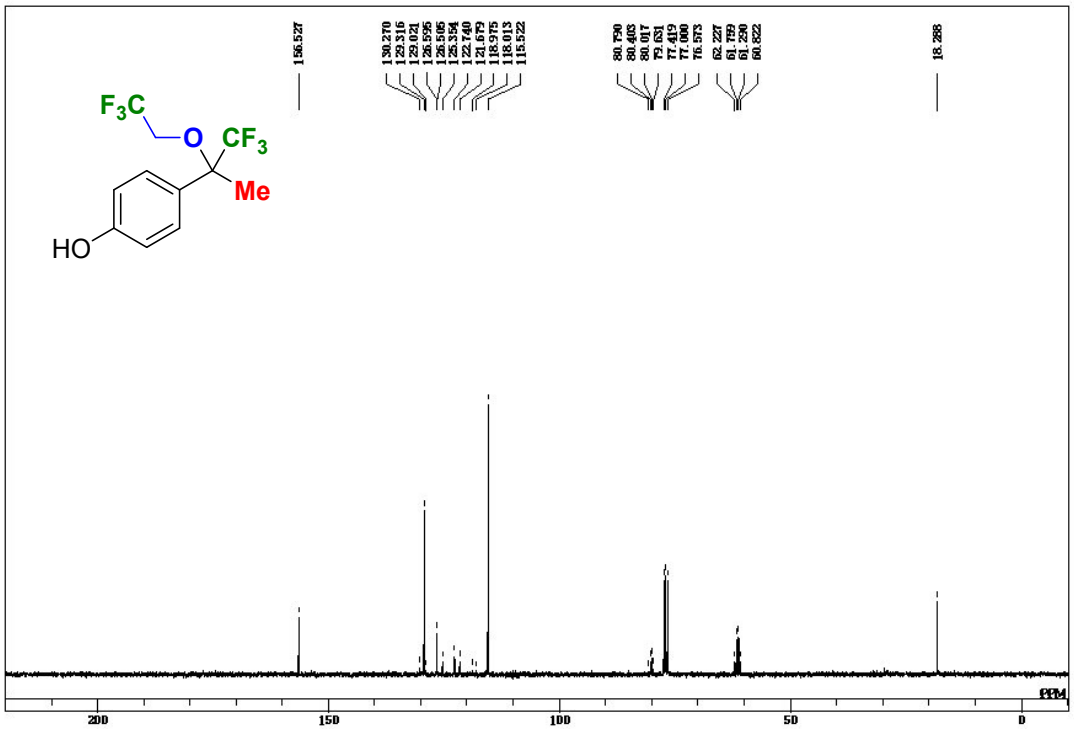


4-{1,1,1-Trifluoro-2-(2,2,2-trifluoroethoxy)prop-2-yl}phenol (**11aa**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

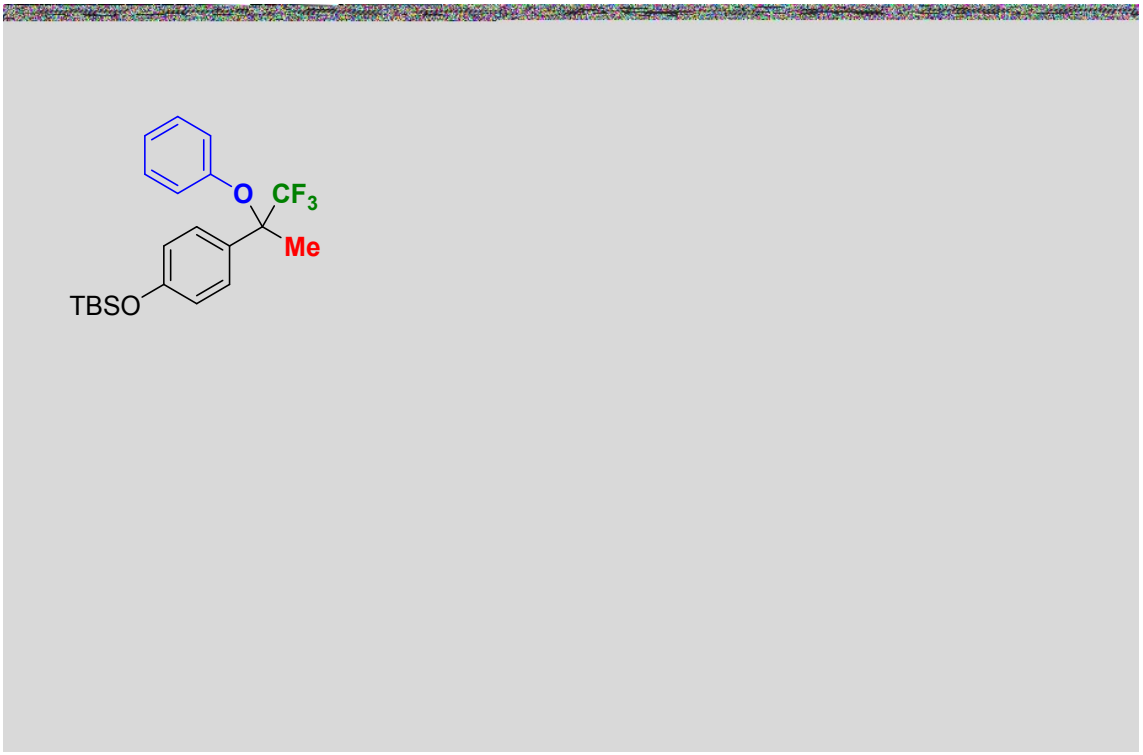



$^{13}$C NMR (300 MHz, $CDCl_3$)

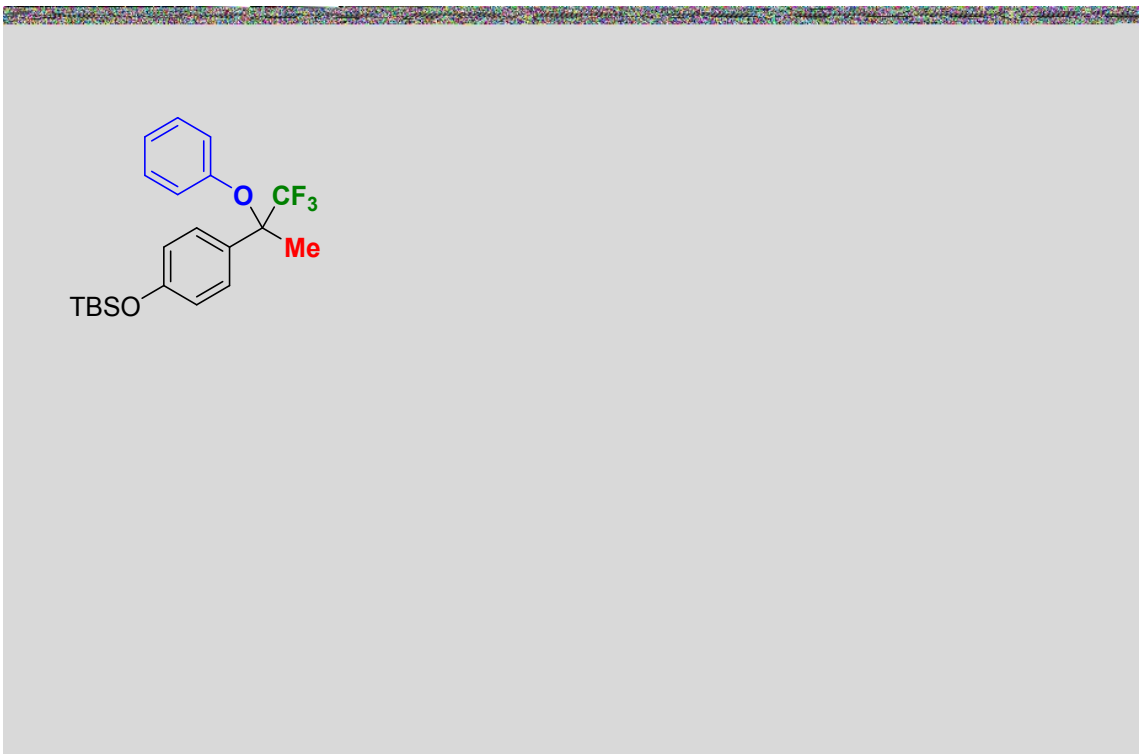


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-phenoxypropane (**12ab**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

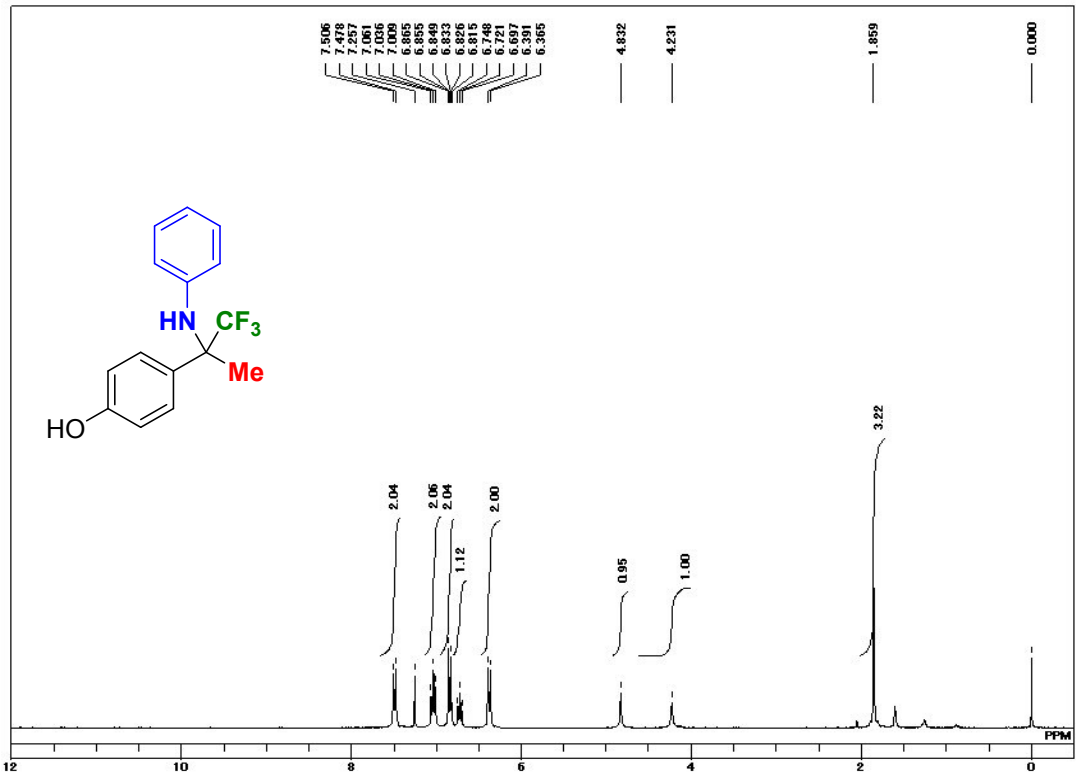



$^{13}$C NMR (300 MHz, $CDCl_3$)

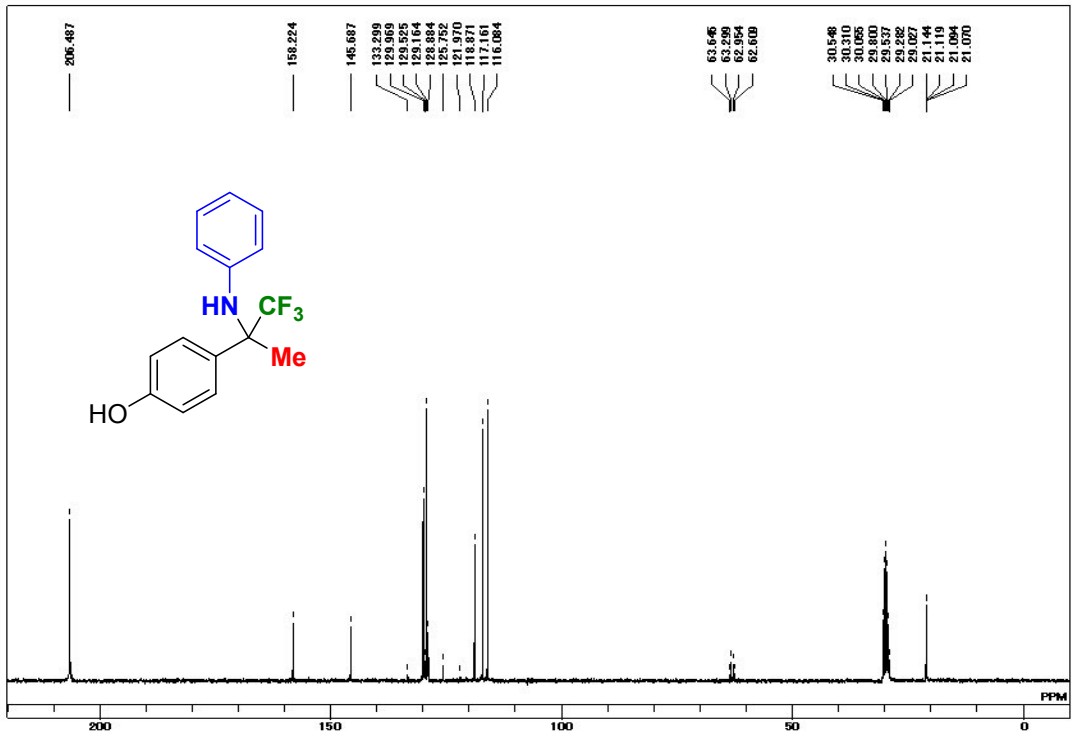


4-{1,1,1-Trifluoro-2-(phenylaminoprop)-2-yl}phenol (**3ak**)

$^{1}$H NMR (300 MHz, $CDCl_3$)

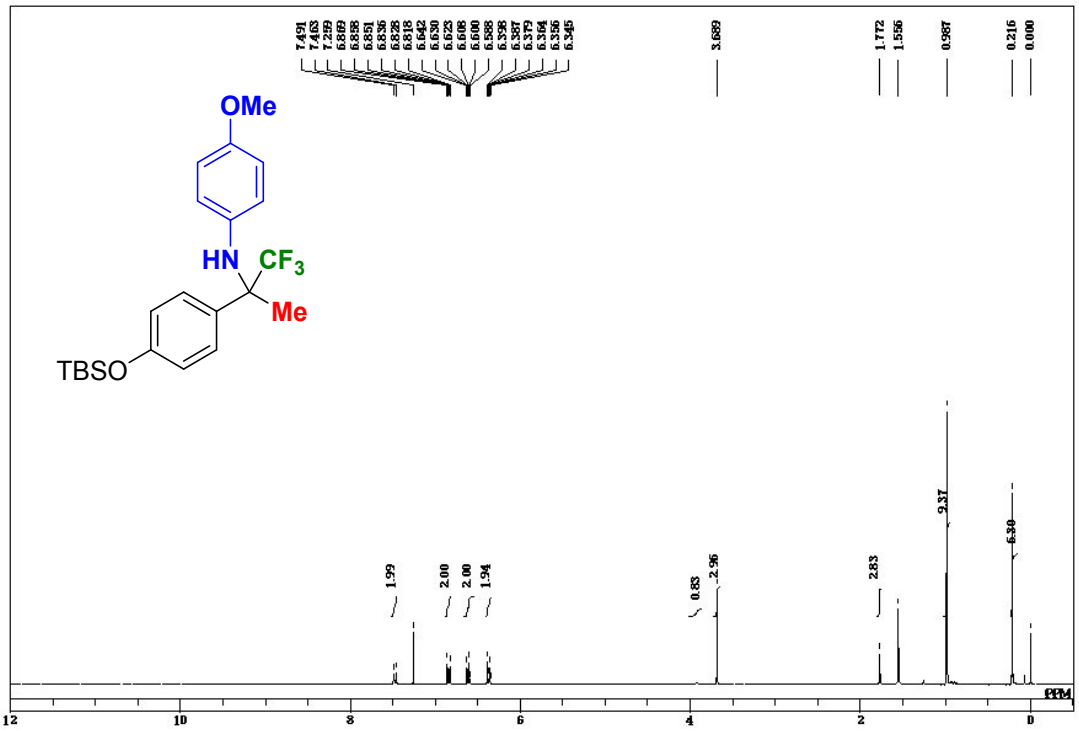



$^{13}$C NMR (300 MHz, acetone-*d*6)

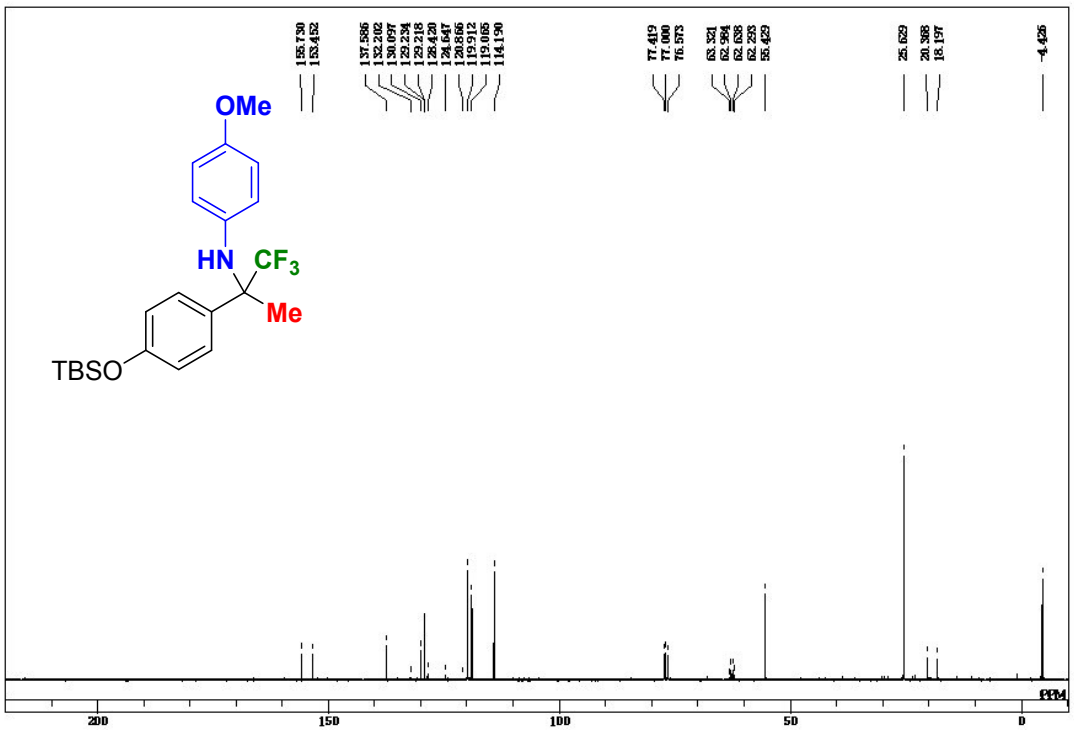


2-[4-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]phenyl]-1,1,1-trifluoro-2-{(4-methoxyphenyl)amino}propane **(4al).**

$^{1}$H NMR (300 MHz, $CDCl_3$)

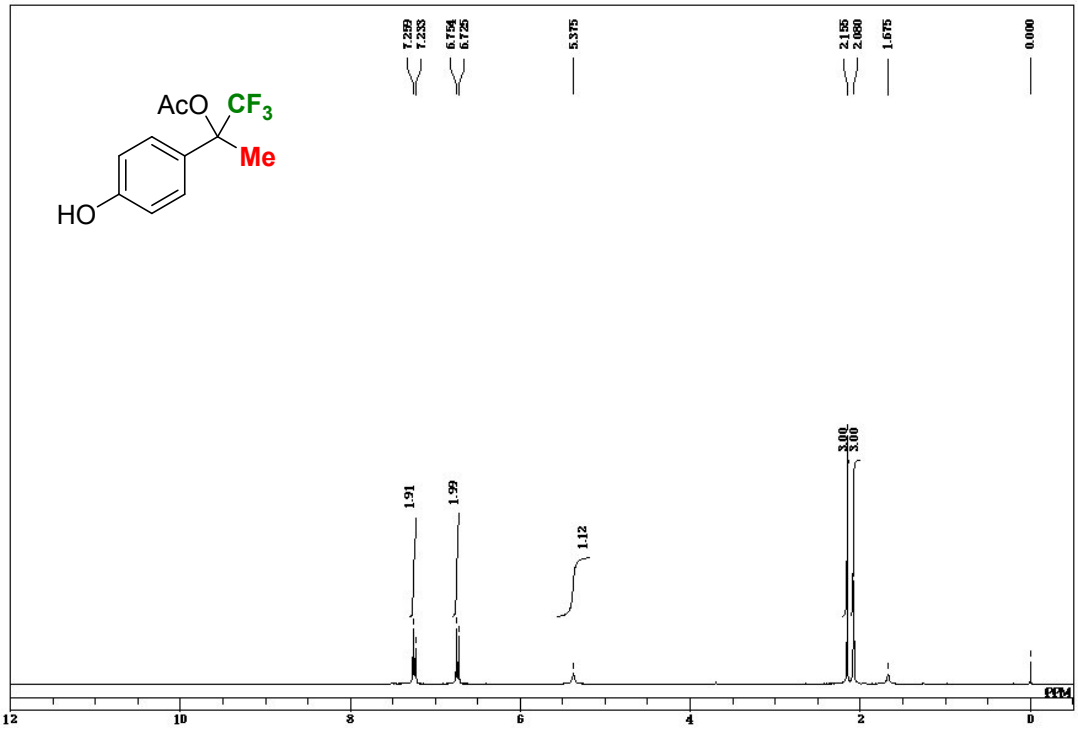



$^{13}$C NMR (300 MHz, $CDCl_3$)



1,1,1-Trifluoro-2-(4-hydroxyphenyl)prop-2-yl acetate

$^{1}H$ NMR (300 MHz, $CDCl_3$)




$^{13}C$ NMR (300 MHz, $CDCl_3$)