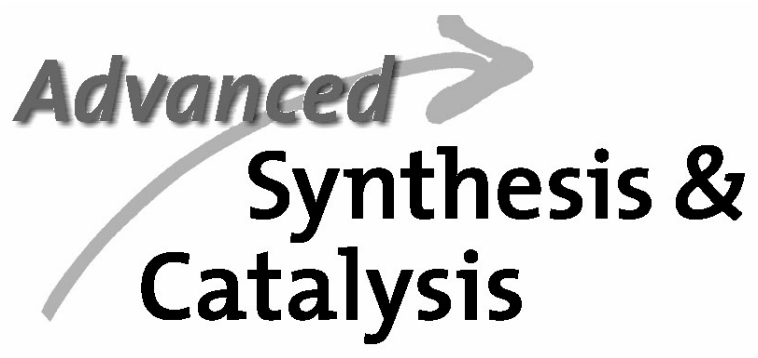

Supporting Information

SUPPORTING INFORMATION

Fast and Enantioselective Production of 1-Aryl-1-propanols Through a Single Pass, Continuous Flow Process

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General Experimental Details.

All anhydrous solvents were dispensed under nitrogen from a Solvent Purification System (SPS). Liquid aldehydes (**5a-e**) were purchased and distilled before using. Solid aldehyde (**5f**) was dissolved in CH_2Cl_2 and washed with an aqueous saturated solution of $NaHCO_3$. Diethylzinc (1.1 M solution in toluene) was purchased from Aldrich and used as received. Merrifield resin (2% DVB, *f*=0.91 mmol Cl/g) was obtained from Novabiochem. Solution ^1H NMR, ^{13}C NMR experiments were performed with a Bruker Avance 400 Ultrashield spectrometer in $CDCl_3$ at room temperature. TMS served as internal standard (δ = 0 ppm) for ^1H NMR and $CDCl_3$ (δ = 77 ppm) for ^{13}C NMR spectra. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. Elemental analysis were carried out in a Carlos Erba microanalyser EA 1108 by the "Servei de Recursos cientifics i Tècnics" of the Universidad Rovira i Virgili of Tarragona. Conversion, selectivity and enantioselectivity were determined by GC analysis with a 6890N Agilent chromatograph using a Supelco ß-Dex 120^{TM} chiral column (30 m x 0.25 mm x 0.25 µm film thickness), He was used as the carrier gas. The synthesis and anchoring of (*R*)-1,1,2-triphenyl-2-(piperazin-1-yl)ethanol onto the Merrifield resin was performed as described in reference 6e.

Characterization of 6a-6f

(*S*)-1-phenylpropanol (6a).

GC conditions and retention times: 115ºC

t_R (*R*-isomer): 22.5 min

t_R (*S*-isomer): 23.4 min

^{1}H-NMR (400 MHz, $CDCl_3$) d 0.92 (t, *J*=7.6 Hz, 3H), 1.76 (m, 2H), 3.30 (br, 1H), 4.52 (m, 1H), 7.33 (m, 4H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 10.0 (CH_3), 22.1 (CH_2), 76.0 (CH), 126.1 (CH), 127.5 (CH), 128.7 (CH), 145.0 (C) ppm.

(*S*)-1-(2-fluorophenyl)propanol (6b).

GC conditions and retention times: 115ºC

t_R (*R*-isomer): 22.6 min

t_R (*S*-isomer): 24.0 min

^{1}H-NMR (400 MHz, $CDCl_3$) d 0.92 (t, *J*=7.5 Hz, 3H), 1.78 (m, 2H), 2.25 (br, 1H), 4.90 (t, *J*=6.5 Hz, 1H), 6.99 (m, 1H), 7.12 (m, 1H), 7.22 (m, 1H), 7.42 (m, 1H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 9.9 (CH_3), 30.9 (CH_2), 69.6 (CH), 115.2 (d, *J*=22 Hz, CH), 124.2 (d, *J*=3 Hz, CH), 127.3 (d, *J*=4 Hz, CH), 128.7 (d, *J*=8 Hz, CH), 131.5 (d, *J*=13 Hz, C), 159.9 (d, *J*=244 Hz, C) ppm.

(*S*)-1-(4-fluorophenyl)propanol (6c).

GC conditions and retention times: 115ºC

t_R (*R*-isomer): 25.5 min

t_R (*S*-isomer): 27.7 min

^{1}H-NMR (400 MHz, $CDCl_3$) d 0.87 (t, *J*=7.4 Hz, 3H), 1.71 (m, 2H), 2.20 (br, 1H), 4.53 (t, *J*=6.6 Hz, 1H), 7.00 (dd, *J*=8.6 Hz, *J*=8.7 Hz, 2H), 7.27 (dd, *J*=5.6 Hz, *J*=8.6 Hz, 2H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 10.0 (CH_3), 32.0 (CH_2), 75.3 (CH), 115.1 (d, *J*=21 Hz, CH), 127.6 (d, *J*=8 Hz, CH), 140.3 (d, *J*=3 Hz, C), 162.1 (d, *J*=244 Hz, C) ppm.

(*S*)-1-(2-(trifluoromethyl)phenyl)propanol (6d).

GC conditions and retention times: 115ºC

t_R (*R*-isomer): 17.5 min

t_R (*S*-isomer): 18.7 min

^{1}H-NMR (400 MHz, $CDCl_3$) d 0.99 (t, *J*=7.4 Hz, 3H), 1.76 (m, 2H), 2.03 (br, 1H), 5.03 (t, *J*=6.4 Hz, 1H), 7.36 (dd, *J*=7.6 Hz, *J*=7.8 Hz, 1H), 7.57 (dd, *J*=7.6 Hz, *J*=7.8 Hz, 1H), 7.61 (d, *J*=7.8 Hz, 1H), 7.75 (d, *J*=7.8 Hz, 1H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 10.5 (CH_3), 32.1 (CH_2), 70.9 (CH), 124.2 (c, *J*=272 Hz, C), 125.4 (c, *J*=6 Hz, CH), 127.1 (c, *J*=30 Hz, C), 127.4 (s, CH), 127.5 (s, CH), 132.2 (c, *J*=1 Hz, CH), 143.9 (c, *J*=2 Hz, C) ppm.

(*S*)-1-(4-(trifluoromethyl)phenyl)propanol (6e).

GC conditions and retention times: 115ºC

t_R (R-isomer): 28.7 min

t_R (S-isomer): 32.1 min

^{1}H-NMR (400 MHz, $CDCl_3$) d 0.92 (t, *J*=7.3 Hz, 3H), 1.77 (m, 2H), 2.04 (br, 1H), 4.66 (t, *J*=6.4 Hz, 1H), 7.44 (d, *J*=8.0 Hz, 2H), 7.59 (d, *J*=8.0 Hz, 2H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 9.9 (CH_3), 32.0 (CH_2), 75.3 (CH), 124.2 (c, *J*=270 Hz, C), 125.3 (c, *J*=4 Hz, CH), 126.2 (s, CH), 129.6 (c, *J*=32 Hz, C), 148.5 (s, C) ppm.

(*S*)-1-(4-cyanophenyl)propanol (6f).

GC conditions and retention times: 180ºC

t_R (R-isomer): 11.7 min

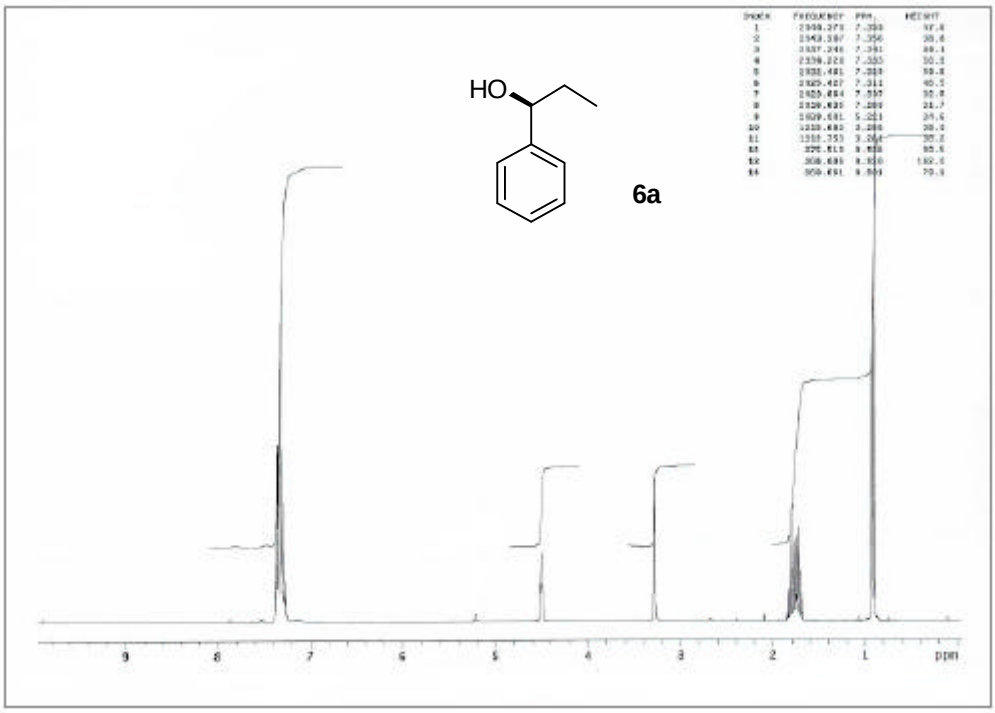
t_R (S-isomer): 12.1 min

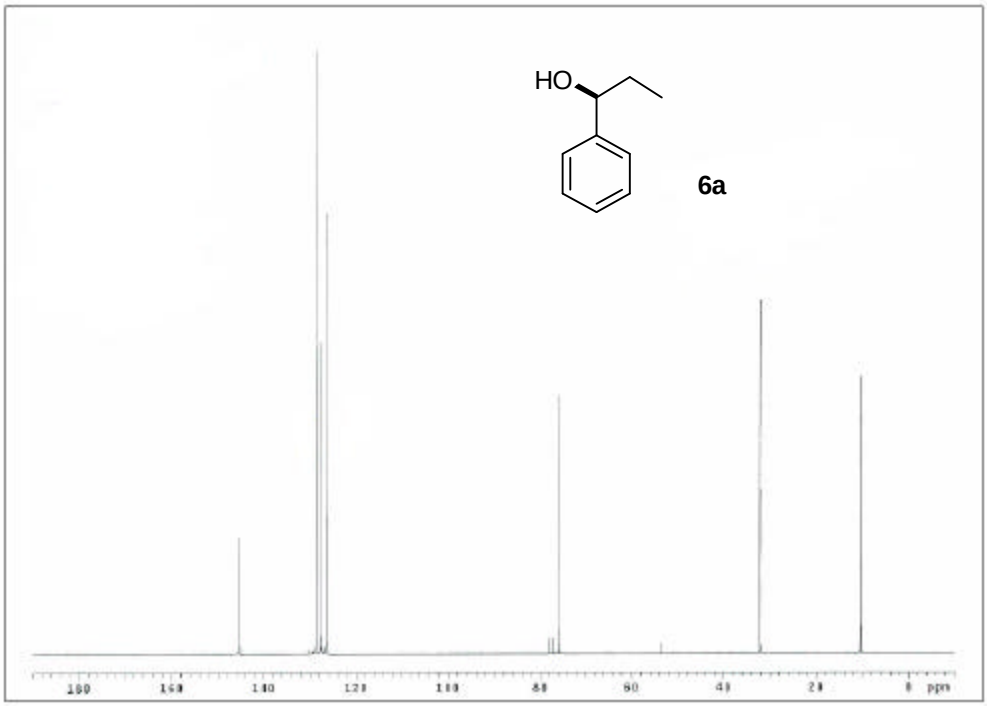
^{1}H-NMR (400 MHz, $CDCl_3$) d 0.85 (t, *J*=7.2 Hz, 3H), 1.69 (m, 2H), 3.01 (br, 1H), 4.61 (m, 1H), 7.38 (d, *J*= 8.0 Hz, 2H), 7.52 (d, *J*=8.0 Hz, 2H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) d 9.9 (CH_3), 32.1 (CH_2), 74.4 (CH), 110.2 (C), 128.9 (C), 126.7 (CH), 132.5 (CH), 150.9 (C) ppm.

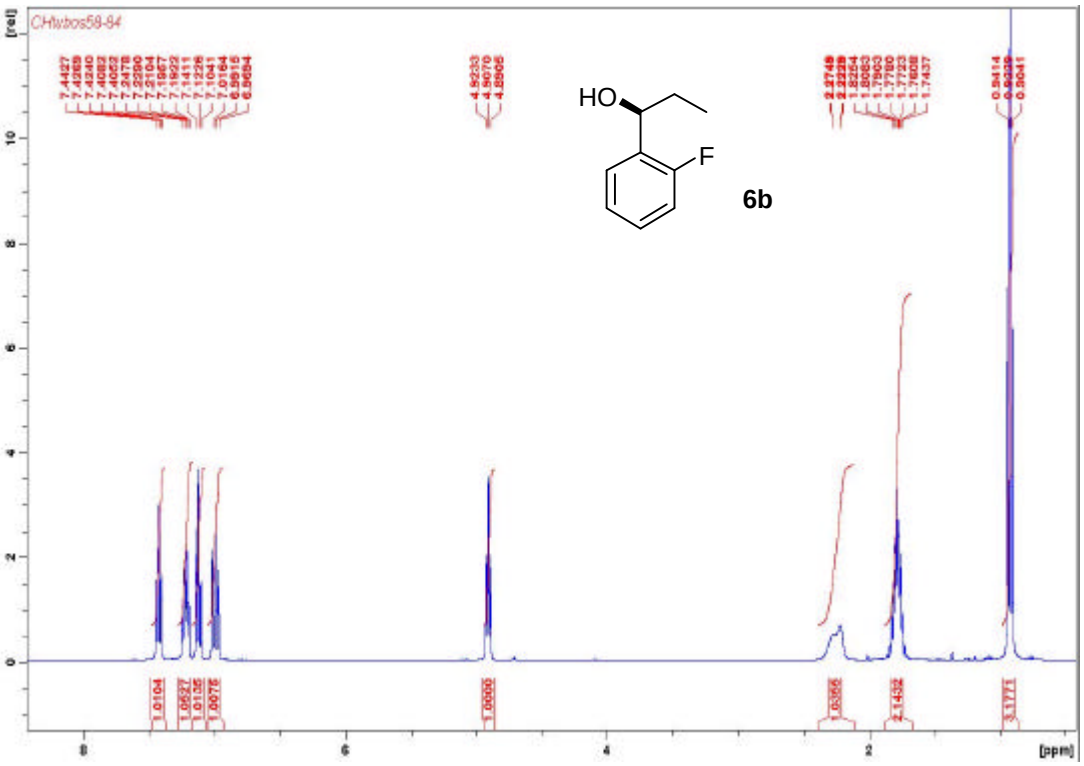
1H and 13C NMR spectra

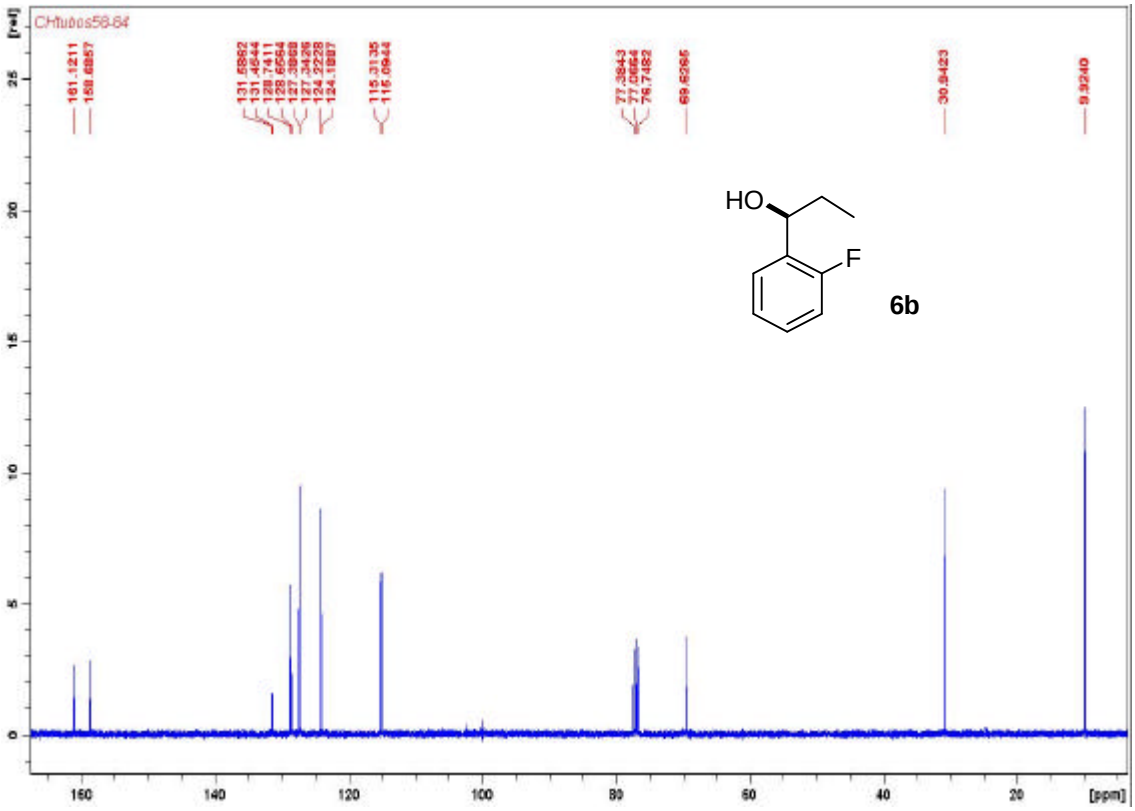
(*S*)-1-phenylpropanol (6a)



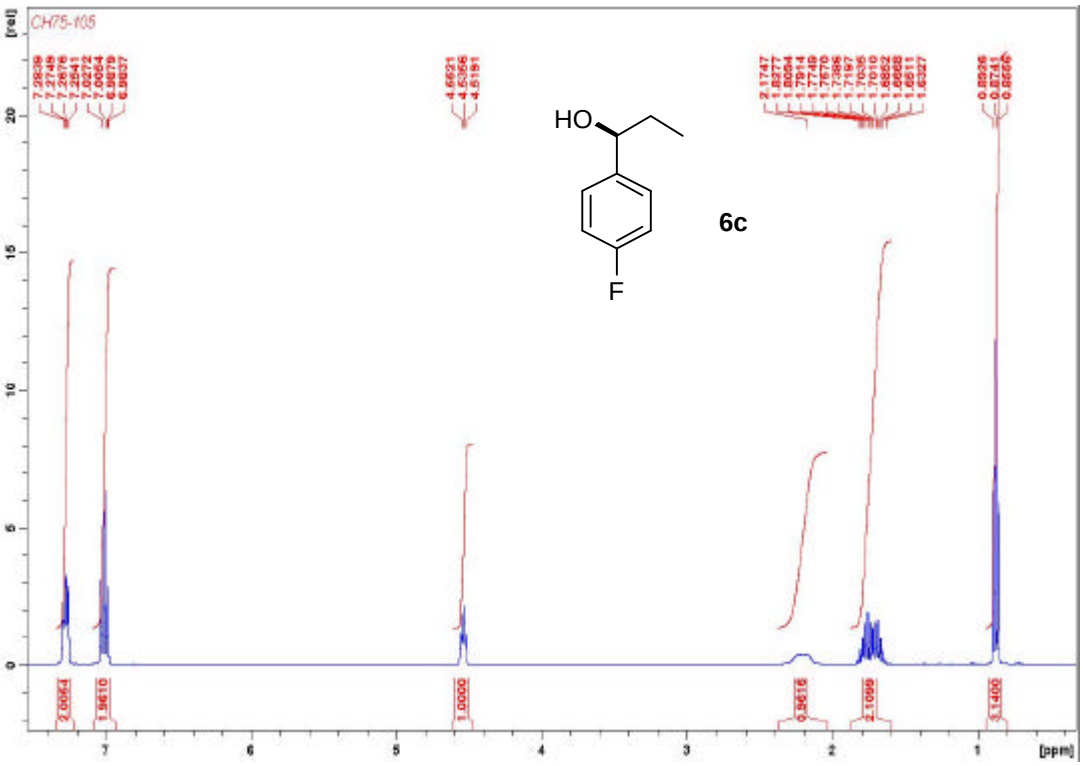


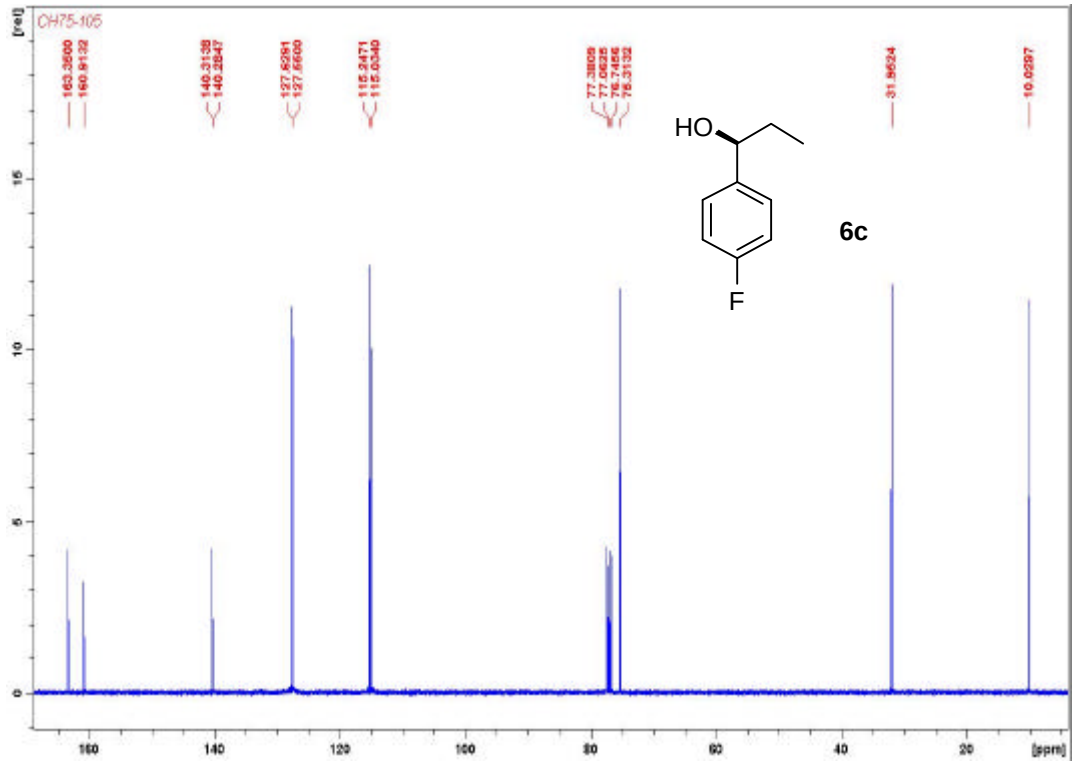
(*S*)-1-(2-fluorophenyl)propanol (6b).



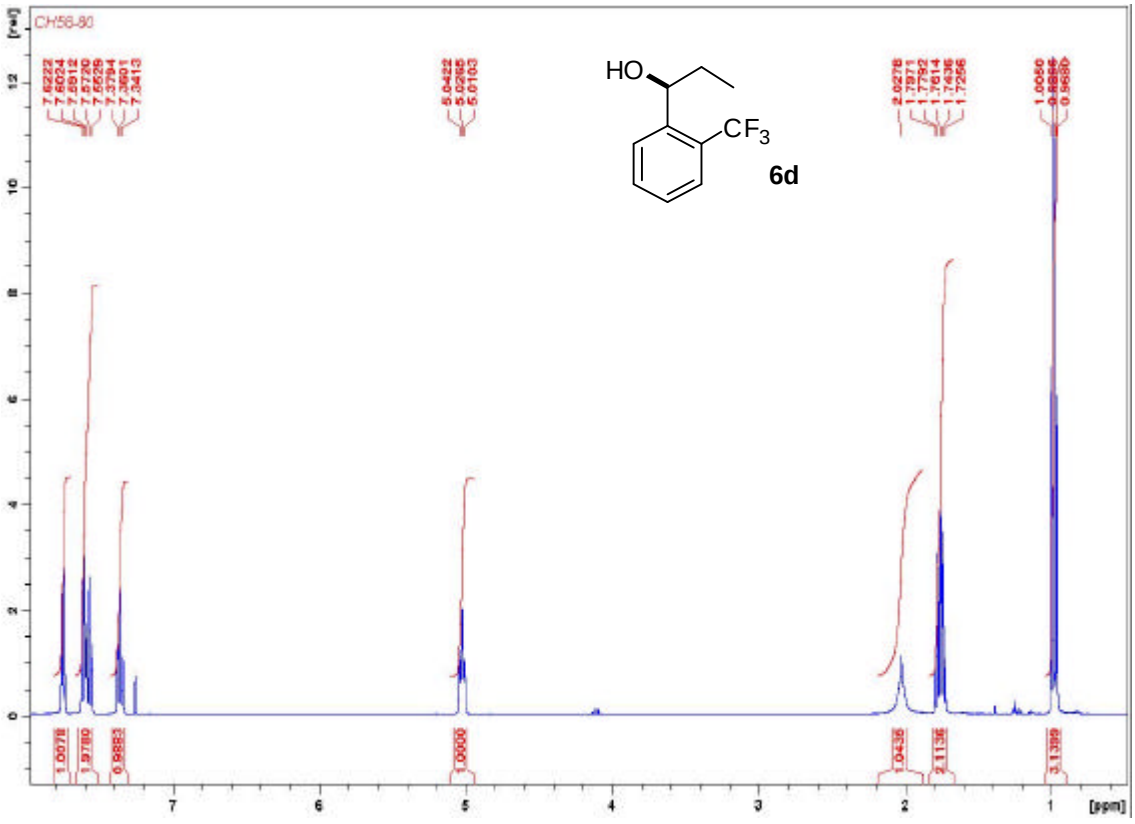


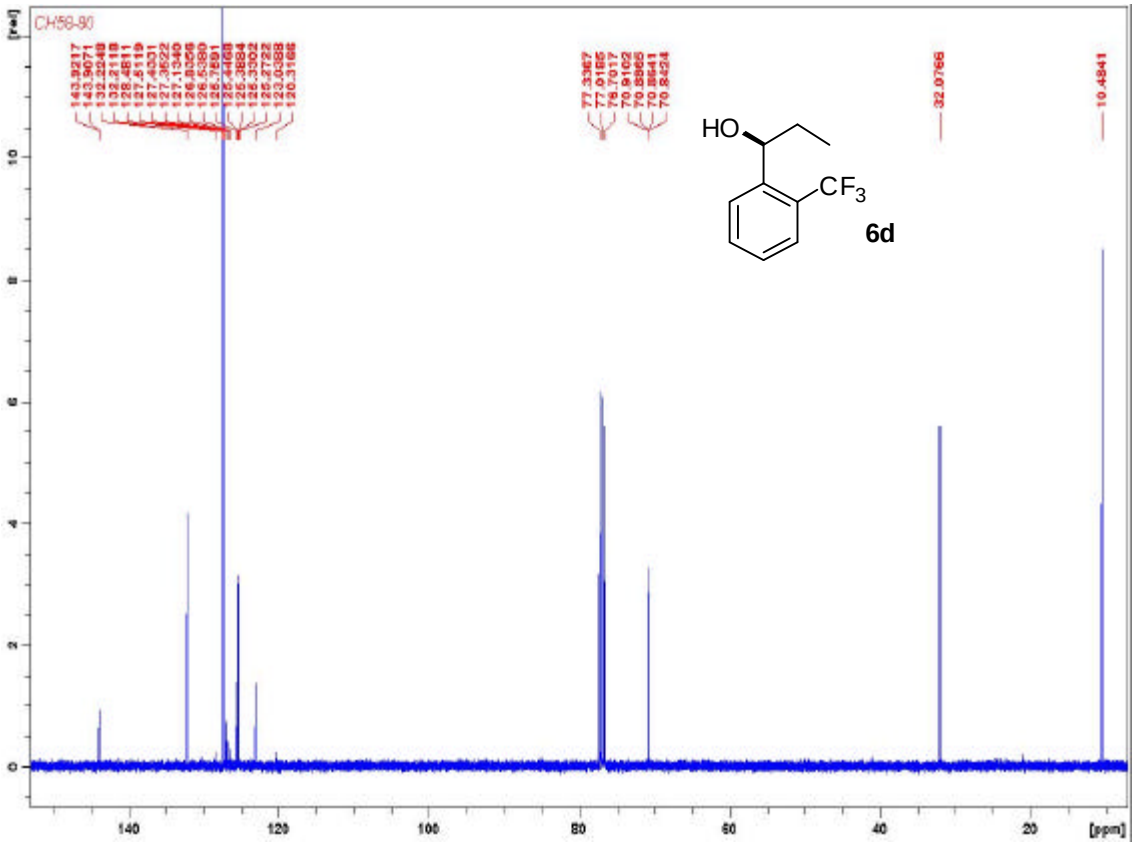
(*S*)-1-(4-fluorophenyl)propanol (6c).



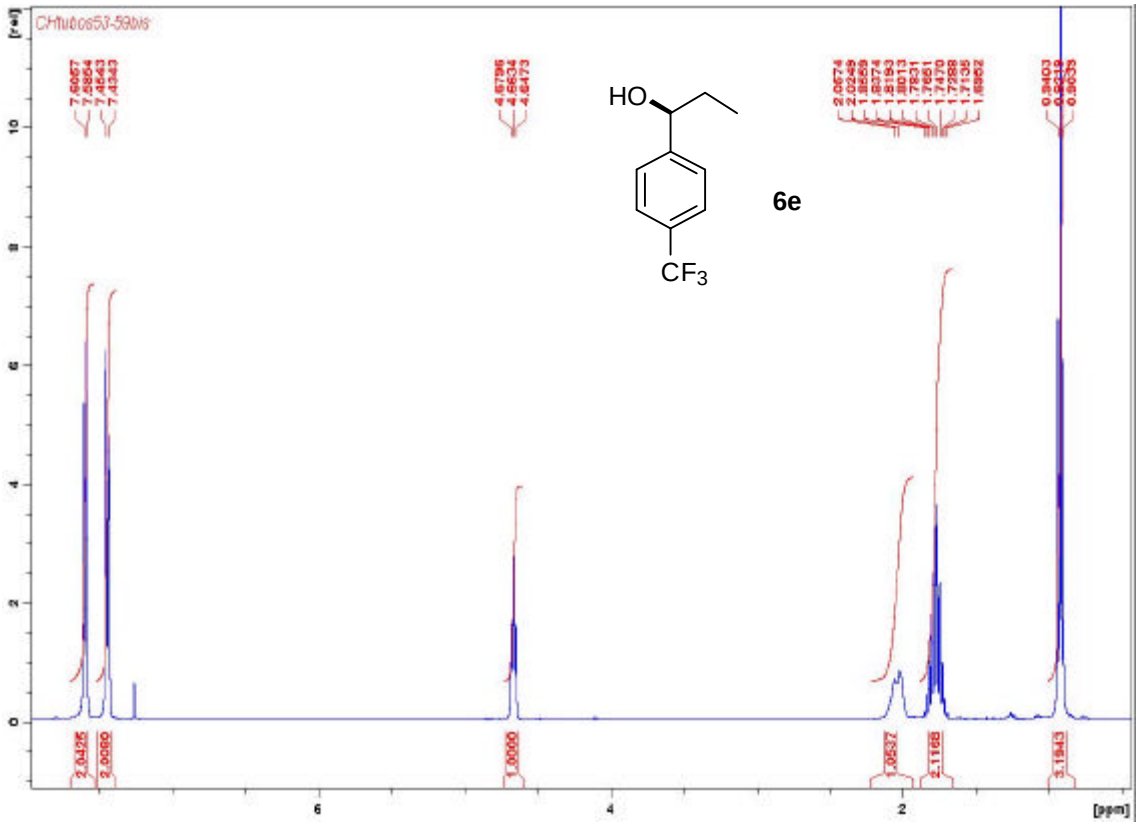


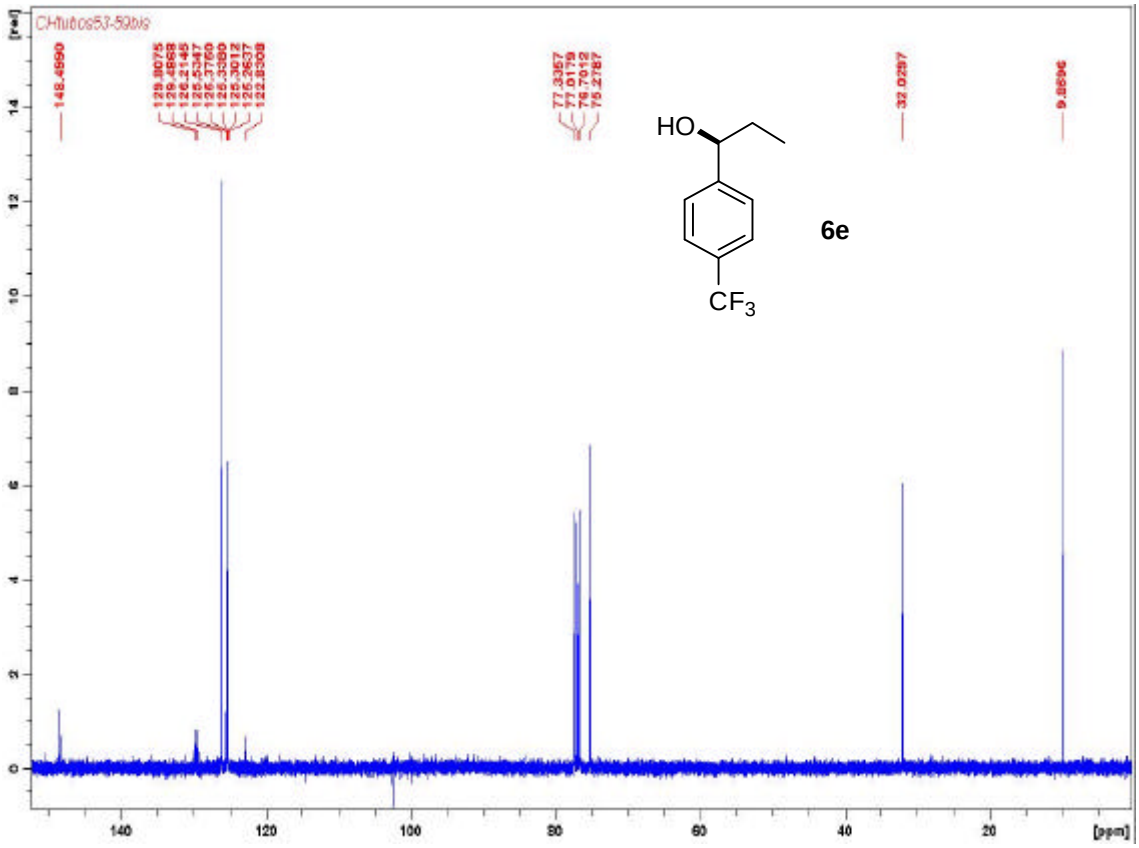
(*S*)-1-(2-(trifluoromethyl)phenyl)propanol (6d).





(*S*)-1-(4-(trifluoromethyl)phenyl)propanol (6e).





(*S*)-1-(4-cyanophenyl)propanol (6f).