RSC Advances

Supporting Information

Synthesis of Enantiopure *m*-Substituted 1-Phenylethanols in High Space-Time Yield using *Bacillus subtilis* Esterase**

Gao-Wei Zheng,[a] Xu-Yun Liu,[a] Zhi-Jun Zhang,[a] Ping Tian,[b,*] Guo-Qiang Lin,[b] and Jian-He Xu[a,*]

[a]Laboratory of Biocatalysis and Synthetic Biotechnology, State Key Laboratory of Bioreactor Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China. Fax: (+86)-21-6425-0840; E-mail: jianhexu@ecust.edu.cn

[b]Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 345 Lingling Road, Shanghai 200032, China

TABLE OF CONTENTS:

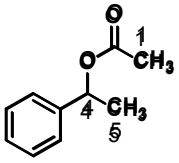
1. General Information

The racemic alcohols were purchased from Sigma (Shanghai, China), J&K Chemical Ltd (Shanghai, China) and Alfa Aesar (Tianjin, China). The ^{1}H NMR spectra were recorded on a Bruker spectrometer (400 MHz) and the ^{13}C NMR spectra were recorded on a Bruker spectrometer (100 MHz). Optical rotations were measured on a Polarimat (Rudolph Research Autopol I). Mass spectra were recorded on a QP2010 SE GC-MS device (electron impact, 70 eV, Shimadzu, Japan). Column chromatography was performed using silica gel (300−400 mesh).

2. General Protocol for Synthesis of Substrates 1−18

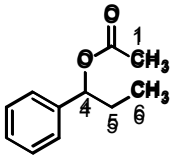
A 30 mmol solution of the alcohol (1.0 equiv.) in dry toluene (20 mL) and sodium acetate (0.05 equiv.) were sequentially added to a solution of acetic anhydride (1.2 equiv.) in toluene (30 mL), and sodium acetate (0.05 equiv.), and the resultant mixture was refluxed until the alcohol was completely consumed (as monitored by thin layer chromatography). The product was extracted into ethyl acetate (3 × 50 mL) and washed with an aqueous solution of saturated sodium bicarbonate (3 × 20 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure.

(*R/S*)-1-Phenylethyl acetate (1):[1]



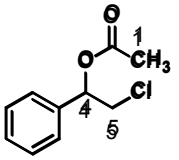
Yield: 95% (4.68 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36-7.25 (m, 5H, Ar-H), 5.88 (q, 1H, J = 6.4 Hz, H4), 2.07 (s, 3H, H1), 1.53 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 164 (M^+), 122, 104, 77, 43.

(*R/S*)-1-Phenylpropyl acetate (2):[2]



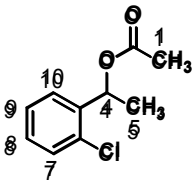
Yield: 92% (4.92 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36-7.25 (m, 5H, Ar-H), 5.66 (t, 1H, J = 7.2 Hz, H4), 2.07 (s, 3H, H1), 1.96-1.70 (m, 2H, H5), 0.88 (t, 3H, J = 7.2 Hz, H6); MS (EI): m/z = 178 (M^+), 136, 118, 43.

(*R/S*)-2-Chloro-1-phenylethyl acetate (3):[3]



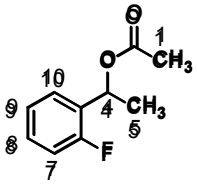
Yield: 95% (5.30 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40-7.32 (m, 5H, Ar-H), 5.96 (dd, J = 8.4 Hz, 1H, J = 4.8 Hz, H4), 3.82-3.70 (m, 2H, H5), 2.14 (s, 3H, H1).

(*R/S*)-1-(2-Chlorophenyl)ethyl acetate (4):[4]



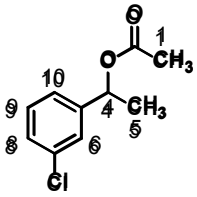
Yield: 94% (5.60 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45 (dd, 1H, J = 7.6 Hz, J = 1.2 Hz, H7), 7.35 (d, 1H, J = 8 Hz, H10), 7.30-7.19 (m, 2H, H7+H8), 6.22 (q, 1H, J = 6.4 Hz, H4), 2.10 (s, 3H, H1), 1.52 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 198 (M^+), 163, 121, 103, 43.

(*R/S*)-1-(2-Fluorophenyl)ethyl acetate (5):



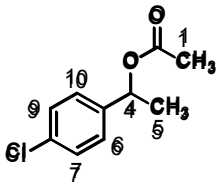
Yield: 85% (4.65 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39 (m, 1H, Ar-H), 7.30-7.23 (m, 1H, Ar-H), 7.13 (m, 1H, Ar-H), 7.03 (m, 1H, Ar-H), 6.14 (q, 1H, J = 6.8 Hz, H4), 2.08 (s, 3H, H1), 1.55 (d, 3H, J = 6.8 Hz, H5); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.11, 159.76 (d, J_{CF} = 245.9 Hz), 129.37 (d, J_{CF} = 8.3 Hz), 128.99 (d, J_{CF} = 13.7 Hz), 127.17 (d, J_{CF} = 4.5 Hz), 124.27 (d, J_{CF} = 3.8 Hz), 115.61 (d, J_{CF} = 21.3 Hz), 66.71 (t, J_{CF} = 2.3 Hz), 25.95, 21.27 (t, J_{CF} = 1.5 Hz); MS (EI): m/z = 182 (M^+), 140, 122, 43.

(*R/S*)-1-(3-Chlorophenyl)ethyl acetate (6):[5]



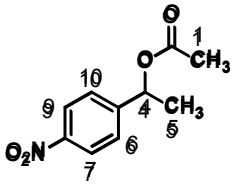
Yield: 93% (5.54 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 (s, 1H, H6), 7.28-7.20 (m, 3H, H8-10), 5.83 (q, 1H, J = 6.8 Hz, H4), 2.00 (s, 3H, H1), 1.52 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 198 (M^+), 156, 138, 43.

(*R/S*)-1-(4-Chlorophenyl)ethyl acetate (7):[6]



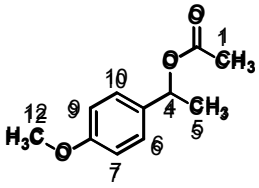
Yield: 90% (5.36 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33-7.20 (m, 4H, Ar-H), 5.84 (q, 1H, J = 6.8 Hz, H4), 2.07 (s, 3H, H1), 1.51 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 198 (M^+), 156, 138, 43.

(*R/S*)-1-(4-Nitrophenyl)ethyl acetate (8):[6]



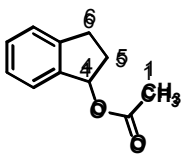
Yield: 85% (5.33 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.22 (d, 2H, J = 8.8 Hz, H7+H9), ,7.51 (d, 2H, J = 8.8 Hz, H6+H10), 5.92 (q, 1H, J = 6.8 Hz, H4), 2.11 (s, 3H, H1), 1.56 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 209 (M^+), 167, 43.

(*R/S*)-1-(4-Methoxyphenyl)ethyl acetate (9):[6]



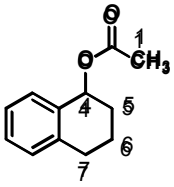
Yield: 96% (5.59 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29 (d, 2H, J = 8.8 Hz, H6+H10), 6.88 (d, 2H, J = 8.4 Hz, H7+H9), 5.92 (q, 1H, J = 6.8 Hz, H4), 3.80 (s, 3H, H12), 2.05 (s, 3H, H1), 1.52 (d, 3H, J = 7.2 Hz, H5); MS (EI): m/z = 194 (M^+), 152, 134, 43.

(*R/S*)-2,3-Dihydro-1*H*-inden-1-yl acetate (10):[6]



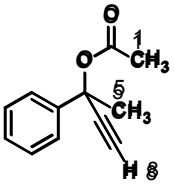
Yield: 91% (4.81 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 (d, 1H, J = 7.6 Hz, Ar-H), 7.32-7.20 (m, 3H, Ar-H), 6.20 (dd, 1H, J = 7.2, 4.0 Hz , H4), 3.16-3.07 (m, 1H, H6), 2.92-2.84 (m, 1H, H6), 2.55-2.45 (m, 1H, H5), 2.14-2.07 (m, 1H, H5), 2.06 (s, 3H, H1); MS (EI): m/z = 176 (M^+), 133, 116, 43.

(*R/S*)-1,2,3,4-Tetrahydronaphthalen-yl acetate (11):[6]



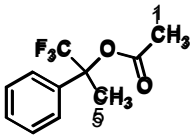
Yield: 82% (4.68 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28-7.11 (m, 4H, Ar-H), 6.00 (t, 1H, J = 4.0 Hz, H4), 2.90-2.84 (m, 1H, H7), 2.79-2.70 (m, 1H, H7), 2.08 (s, 3H, H1), 2.02-1.78 (m, 4H, H5+H6); MS (EI): m/z= 190(M^+), 148, 130, 43.

(*R/S*)-2-Phenylbut-3-yn-2-yl acetate (12):[7]



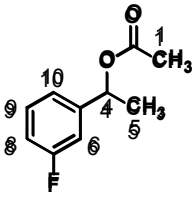
Yield: 78% (4.68 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57 (d, 2H, J = 7.6 Hz, Ar-H), 7.38-7.28 (m, 3H, Ar-H), 2.81 (s, 1H, H8), 2.08 (s, 3H, H1), 1.89 (s, 3H, H5); MS (EI): m/z= 188(M^+), 145, 43.

(*R/S*)-1,1,1-Trifluoro-2-phenylpropan-2-yl acetate (13):



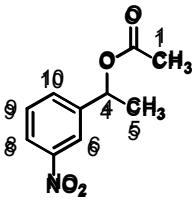
Yield: 75% (5.22 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41-7.36 (m, 5H, Ar-H), 2.16 (s, 3H, H5), 2.12 (s, 3H, H1); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.20, 135.41, 128.99, 128.45, 126.49, 125.60, 122.78, 81.68 (d, J_{CF} = 28.8 Hz), 21.89, 18.58 (q, J_{CF} = 1.6 Hz); MS (EI): m/z= 232 (M^+), 190, 121, 109, 77.

(*R/S*)-1-(3-Fluorophenyl)ethyl acetate (14):



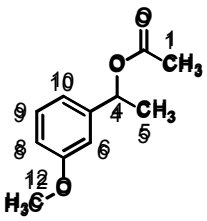
Yield: 95% (5.19 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33-7.27 (m, 1H, Ar-H), 7.12-7.04 (m, 2H, Ar-H), 6.97 (dt, 1H, J = 8.0, 2.0 Hz , Ar-H), 5.86 (q, 1H, J = 6.4 Hz, H4), 2.00 (s, 3H, H1), 1.52 (d, 3H, J = 6.8 Hz, H5); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.27, 162.95 (d, J_{CF} = 245.2 Hz), 144.39 (d, J_{CF} = 6.8 Hz), 130.13 (d, J_{CF} = 8.3 Hz), 121.24 (d, J_{CF} = 3.0 Hz), 114.77 (d, J_{CF} = 21.3 Hz), 113.30 (d, J_{CF} = 22.0 Hz), 71.63 (d, J_{CF} = 1.5 Hz), 22.30, 21.34; MS (EI): m/z = 182(M^+), 140, 122, 43.

(*R/S*)-1-(3-Nitrophenyl)ethyl acetate (15):[8]



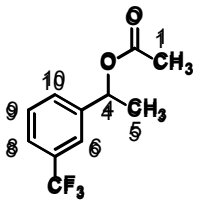
Yield: 86% (5.40 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.23 (s, 1H, H6), 8.16 (d, 1H, J = 8 Hz, H8), 7.67 (d, 1H, J = 7.6 Hz, H10), 7.531 (t, 1H, J = 8.0 Hz, H9), 5.94 (q, 1H, J = 6.8 Hz, H4), 2.11 (s, 3H, H1), 1.58 (d, 3H, J = 6.4 Hz, H5); MS (EI): m/z = 209 (M^+), 167, 43.

(*R/S*)-1-(3-Methoxyphenyl)ethyl acetate (16):[9]



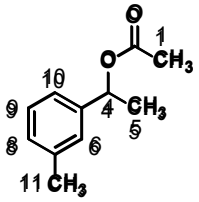
Yield: 92% (5.36 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26 (t, 1H, J = 8.0 Hz, H9), 6.93 (d, 1H, J = 8.0 Hz, H10), 6.90 (d, 1H, J = 2.0 Hz, H6), 6.83 (dd, 1H, J = 8.0, 2.4 Hz, H8), 5.85 (q, 1H, J = 6.4 Hz, H4), 3.81 (s, 3H, H12), 2.07 (s, 3H, H1), 1.52 (d, 3H, J = 6.4 Hz, H5); MS (EI): m/z = 194 (M^+), 152, 134, 43.

(*R/S*)-1-(3-(Trifluoromethyl)phenyl)ethyl acetate (17):[10]



Yield: 87% (6.06 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61-7.45 (m, 4H, Ar-H), 5.91 (q, 1H, J = 6.8 Hz, H4), 2.09 (s, 3H, H1), 1.55 (d, 3H, J = 6.8 Hz, H4); MS (EI): m/z = 232 (M^+), 190, 172, 43.

(*R/S*)-1-(3-Methylphenyl)ethyl acetate (18):[11]



Yield: 91% (4.86 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24-7.09 (m, 4H, Ae-H), 5.85 (q, 1H, J = 6.4 Hz, H4), 2.36 (s, 3H, H11), 2.07 (s, 3H, H1), 1.52 (d, 3H, J = 6.8 Hz, H5); MS (EI): m/z = 178 (M^+), 136, 118, 43.

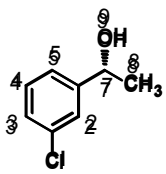
3. General Protocol for BsE-catalyzed Hydrolysis Reactions on an Analytic Scale

To a stirred solution of substrate (50 mM) in phosphate buffer (100 mM, pH 8.0) with 10% (v/v) of EtOH as a cosolvent in a total volume of 10 mL, was added 120 U the crude esterase. The reaction mixture was then stirred magnetically at 30°C. The samples were extracted with ethyl acetate and dried over anhydrous sodium sulfate. Enantioselectivity and conversion were calculated according to the method reported by Chen et al.[12]

4. General Protocol for BsE-catalyzed Hydrolysis Reactions on Preparative Scale

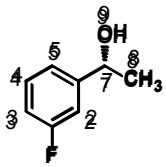
To a stirred solution of substrate (10 mmol) in phosphate buffer (100 mM, pH 8.0) with 10% (v/v) of EtOH as a co-solvent in a total volume of 10 mL was added the esterase BsE (200 mg crude enzyme powder, 470 kU), and the resulting reaction mixture was stirred magnetically at 30°C. The pH of the mixture was then automatically adjusted to 8.0 by titrating 2 M NaOH. Following the removal of the enzyme from the reaction mixture by filtration, the filtrate was extracted three times with ethyl acetate. The organic layers were combined and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. Purification was performed by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

(*R*)-1-(3-Chlorophenyl)ethanol (6a):[13]



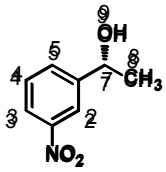
Yield: 42% (0.328 g). $[\alpha]_D^{30}$: +43.9 (*c* 1.00, $CHCl_3$), 98% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36 (s, 1H, H2), 7.29-7.21 (m, 3H, H3-5), 4.88-4.82 (m, 1H, H7), 2.10 (d, 1H, J = 3.2 Hz, H9), 1.47 (d, J = 6.0 Hz, 3H, H8).

(*R*)-1-(3-Fluorophenyl)ethanol (14a): [14]



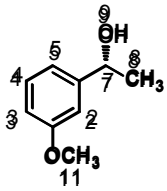
Yield: 45% (0.63 g); $[\alpha]_D^{30}$: +38.0 (*c* 1.03, $CHCl_3$), 98% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.25-7.18 (m, 1H), 7.06-7.00 (m, 2H), 6.87 (dt, *J* = 8.4 Hz, 2.4 Hz , 1H), 4.81(q, *J* = 6.4 Hz, 1H), 2.69 (s,1H), 1.40 (d, *J* = 6.4 Hz, 3H).

(*R*)-1-(3-Nitrophenyl)ethanol (15a): [15]



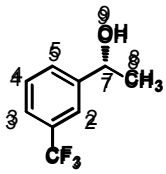
Yield: 40% (0.67 g); $[\alpha]_D^{30}$: +30.5 (*c* 1.00, $CHCl_3$), 99% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.25 (s, 1H, H2), 8.23 (dd, 1H, *J* = 8.4, 0.6 Hz, H3), 7.72 (d, 1H, *J* = 7.2 Hz, H5), 7.52 (t, 1H, *J* = 8.0 Hz, H4), 5.04-5.01(m, 1H, H7), 2.13 (d, 1H, *J* = 3.2 Hz, H9), 1.54 (d, 3H, *J* = 6.4 Hz, H8).

(*R*)-1-(3-Methoxyphenyl)ethanol (16a): [16]



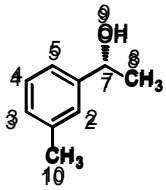
Yield: 38% (0.58 g); $[\alpha]_D^{30}$: +42.6 (*c* 1.03, $CHCl_3$), 99% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26 (t, 1H, *J* = 8.0 Hz, H4), 6.95-6.93 (m, 2H, H3+H5), 6.83-6.79 (m, 1H, H2),4.88-4.85(m, 1H, H7), 3.83 (s, 3H, H11), 1.82 (s, 1H, H9), 1.54 (d, 3H, *J* = 6.4 Hz, H8).

(*R*)-1-(3-(Trifluoromethyl)phenyl)ethanol (17a): [17]



Yield: 36% (0.68 g); $[\alpha]_D^{30}$: +25.6 (*c* 1.02, $CHCl_3$), 96% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.65 (s, 1H, H2), 7.57-7.44 (m, 3H, H3-5), 4.96 (q, 1H, *J* = 6.4 Hz, H7), 1.99 (s, 1H, H9), 1.51 (d, 3H, *J* = 6.4 Hz, H8).

(*R*)-1-(3-Methylphenyl)ethanol (18a): [13]



Yield: 41% (0.**56** g); $[\alpha]_D^{30}$: +62.0 (*c* 1.00, $CHCl_3$), 94% *ee*; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.25-7.15(m, 3H, Ar-H), 7.09 (d, 1H, *J* = 7.2Hz, Ar-H), 4.86(q, 1H, *J*=6.4 Hz, H7), 2.36 (s, 3H, H10), 1.82 (s, 1H, H9), 1.48 (d, 3H, *J* = 6.8 Hz, H8).

5. Enzyme Activity Assays

The enzymatic activity of BsE was assayed as described previously in the literature. [18]

6. Chiral GC or HPLC Analyses

The *ee* of substrates **1**−**2** and **4**−**18,** and products **1a**−**2a** and **4a**−**18a** were determined using a GC-14 gas chromatography (Shimadzu, Kyoto, Japan) equipped with different chiral columns (Alpha: Alpha DEX^{TM}120 chiral column (Supelco, 30 m × 0.25 mm × 0.25 μm); Beta: Beta DEX-^{TM}120 chiral column (Supelco, 30 m × 0.25 mm × 0.25 μm); CP: CP-Chirasil-DEX CB (Varian, 30 m × 0.25 mm × 0.25 μm). Details have been given in **Table 1**.

For compounds **3** and **3a**, the ee values were determined by HPLC (Agilent 6890, USA) using a chiral column (Chiralcel OD, 25 cm × ⌀ 0.46 cm, Daicel Co., Japan), with hexane/2-propanol (94:6, v/v, 1.0 ml min^{-1}) as the mobile phase and monitored with a UV detector at 254 nm.

Table 1. Details of chiral GC analyses

Compound	T_{column} [°C]	Column	Retention time [min]	
1	120	Beta	11.0 (*S*)	11.5 (*R*)
1a	120	Beta	16.8 (*R*)	17.5 (*S*)
2	120	Beta	15.2 (*S*)	15.5 (*R*)
2a	120	Beta	16.9 (*R*)	17.6 (*S*)
4	P1[a]	CP	36. 0 (*S*)	36.6 (*R*)
4a	P1[a]	CP	41.3 (*R*)	41.8 (*S*)
5	120	CP	5.3 (*S*)	5.5 (*R*)
5a	120	CP	9.2 (*R*)	10.2 (*S*)
6	140	CP	6.0 (*S*)	6.6 (*R*)
6a	140	CP	10.5 (*R*)	11.7 (*S*)
7	130	Beta	20.5 (*S*)	21.4 (*R*)
7a	130	Beta	23.3 (*R*)	25.1 (*S*)
8	160	Beta	27.4 (*S*)	27.9 (*R*)
8a	160	Beta	38.6 (*R*)	41.4 (*S*)
9	130	CP	28.4 (*S*)	29.1 (*R*)
9a	130	CP	36.4 (*R*)	36.9 (*S*)
10	120	Alpha	24.7 (*S*)	26.1 (*R*)
10a	120	Alpha	32.3 (*R*)	32.9 (*S*)
11	130	CP	18.4 (*R*)	19.3 (*S*)
11a	130	CP	24.8 (*S*)	25.8 (*R*)
12	110	CP	16.9 (*S*)	18.0 (*R*)
12a	110	CP	26.3 (*R*)	27.2 (*S*)
13	110	CP	5.7 (*S*)	6.6 (*R*)
13a	110	CP	14.1 (*R*)	14.7 (*S*)
14	140	CP	3.2 (*S*)	3.5 (*R*)
14a	140	CP	4.7 (*R*)	5.1 (*S*)
15	P2[b]	CP	8.9 (*S*)	9.4 (*R*)
15a	P2[b]	CP	18.6 (*R*)	19.0 (*S*)
16	140	CP	7.8 (*S*)	8.3 (*R*)
16a	140	CP	11.1 (*R*)	11.8 (*S*)
17	140	CP	3.0 (*S*)	3.2 (*R*)
17a	140	CP	4.6 (*R*)	4.9 (*S*)
18	140	CP	4.3 (*S*)	4.5 (*R*)
18a	140	CP	5.7 (*R*)	5.9 (*S*)

[a]P1: temperature program: 80 °C for 20 min, 3 °C min^{-1} to 130 °C for 2 min, and then 20 °C min^{-1} to 180 °C for 5 min;

[b]P2: temperature program: 160 °C for 18 min, 20 °C min^{-1} to 200 °C for 2 min.

7. References

[1] M. T. Reetz, A. Eipper, P. Tielmann, R. Mynott, *Adv. Synth. Catal.* **2002**, *344*, 1008–1016.

[2] H. Matsuda, S. Ando, T. Morikawa, S. Kataoka, M. Yoshikawa, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1949–1953.

[3] A. Träff, K. Bogár, M. Warner, J. E. Bäckvall, *Org. Lett.* **2008**, *10*, 4807–4810.

[4] Y. M. Cheng, G. Xu, J. P. Wu, C. S. Zhang, L. R. Yang, *Tetrahedron Lett.* **2010**, *51*, 2366–2369.

[5] C. Rodríguez, G. de Gonzalo, D. E. T. Pazmiño, M. W. Fraaije, V. Gotor, *Tetrahedron: Asymmetry* **2009**, *20*, 1168–1173.

[6] M. Päiviö, D. Mavrynsky, R. Leino, L.T. Kanerva, *Eur. J. Org. Chem.* **2011**, 1452–1457.

[7] E. Henke, J. Pleiss, U. T. Bornscheuer, *Angew. Chem. Int. Ed.* **2002**, *41*, 3211–3213.

[8] N. S. Hatzakis, I. Smonou, *Bioorg. Chem.* **2005**, *33*, 325–337.

[9] J. Mangas-Sánchez, M. Rodríguez-Mata, E. Busto, V. Gotor-Fernández, V. Gotor, *J. Org. Chem.* **2009**, *74*, 5304–5310.

[10] C. Rodríguez, G. de Gonzalo, D. E. T. Pazmiño, M. W. Fraaije, V. Gotor, *Tetrahedron: Asymmetry* **2008**, *19*, 197–203.

[11] M. J. Kim, H. M. Kim, D. Kim, Y. Ahn, J. Park, *Green Chem.* **2004**, *6*, 471–474.

[12] C. S. Chen, Y. Fujimoto, G. Girdaukas, C. J. Sih, *J. Am. Chem. Soc.* **1982**, *104*, 7294–7299.

[13] M. N. Cheemala, M. Gayral, J. M. Brown, K. Rossen, P. Knochel, *Synthesis* **2007**, *24*, 3877–3885.

[14] P. N. Liu, J. G. Deng, Y. Q. Tu, S. H. Wang, *Chem. Commun.* **2004**, 2070–2071.

[15] H. Lin, Y. Z. Chen, X. Y. Xu, S. W. Xia, L. X. Wang, *J. Mol. Catal. B: Enzymatic* **2009**, *57*, 1–5.

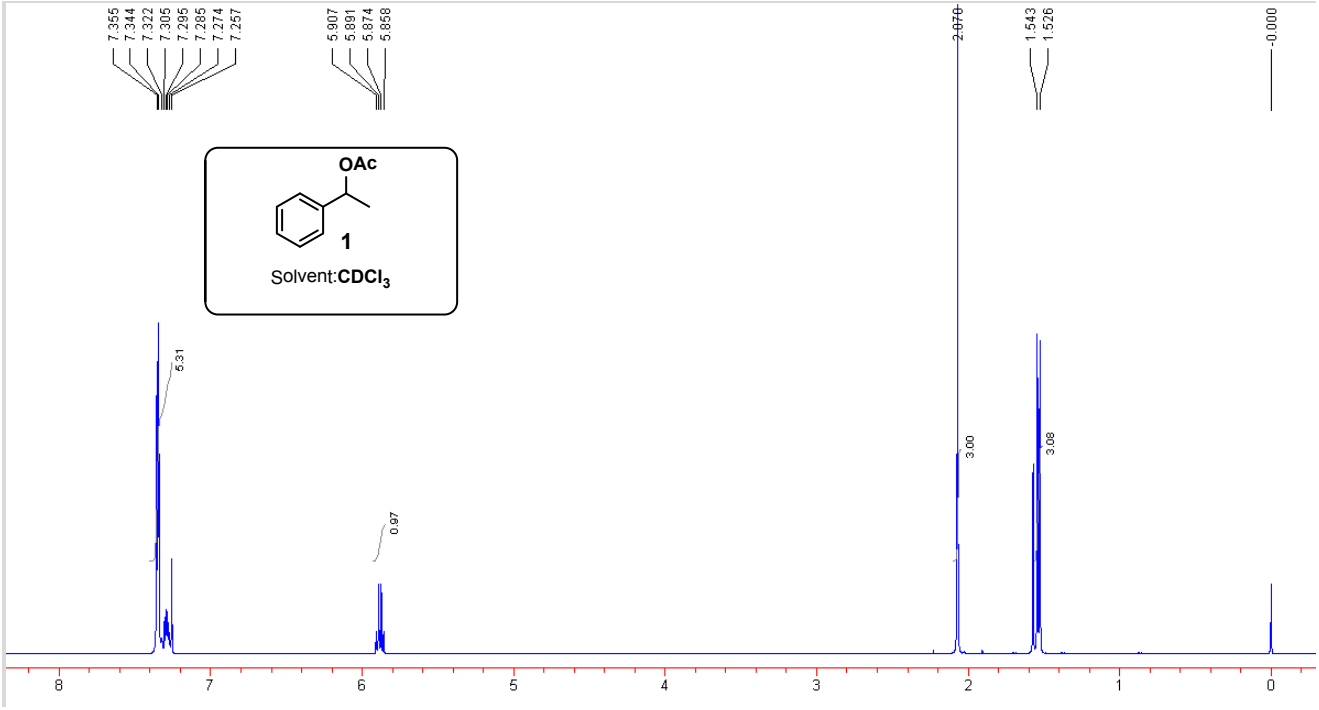
[16] T. Inagaki, A. Ito, J. Ito, H. Nishiyama, *Angew. Chem. Int. Ed.* **2010**, *49*, 9384–9387.

[17] J. Xiao, Z. Z. Wong, Y. P. Lu, T. P. Loh, *Adv. Synth. Catal.* **2010**, *352*, 1107–1112.

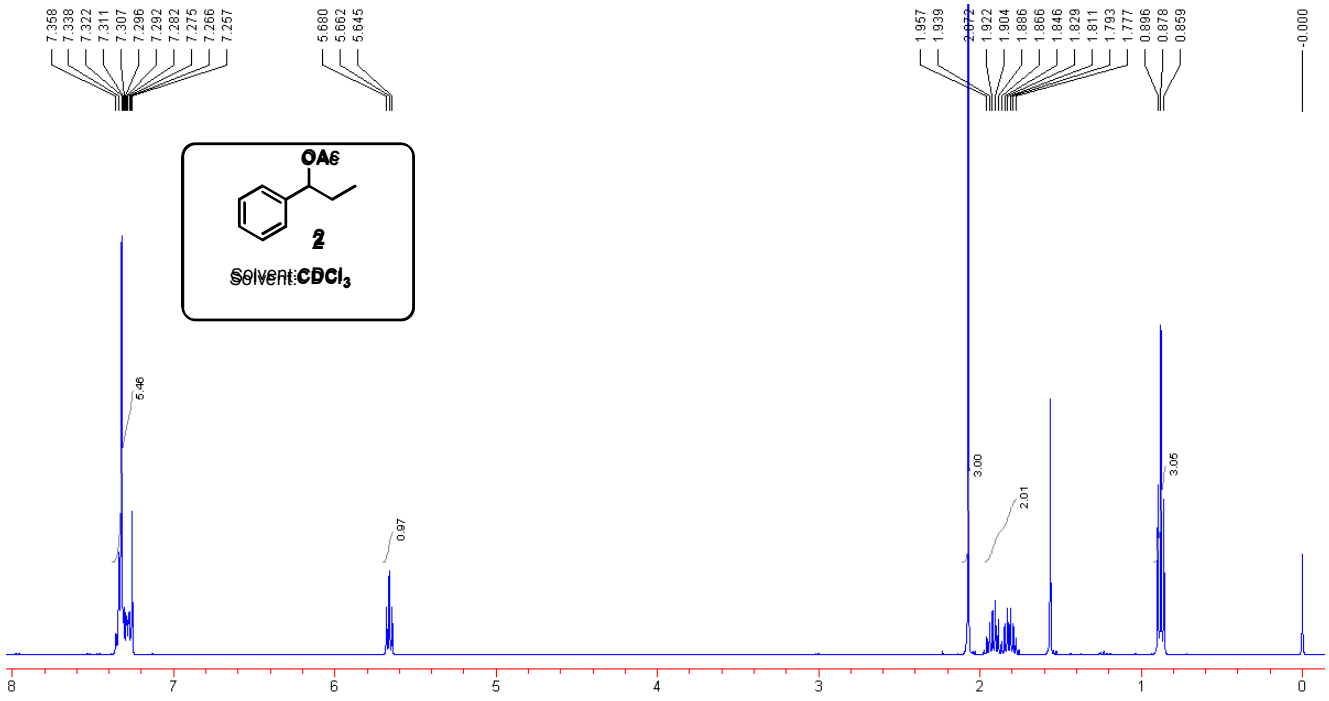
[18] G. W. Zheng, J. Pan, H. L. Yu, M. T. Ngo-Thi, C. X. Li, J. H. Xu, J. Biotechnol. 2010, 150, 108–114.

8. ^{1}H NMR Copies of Compounds 1 to 18.

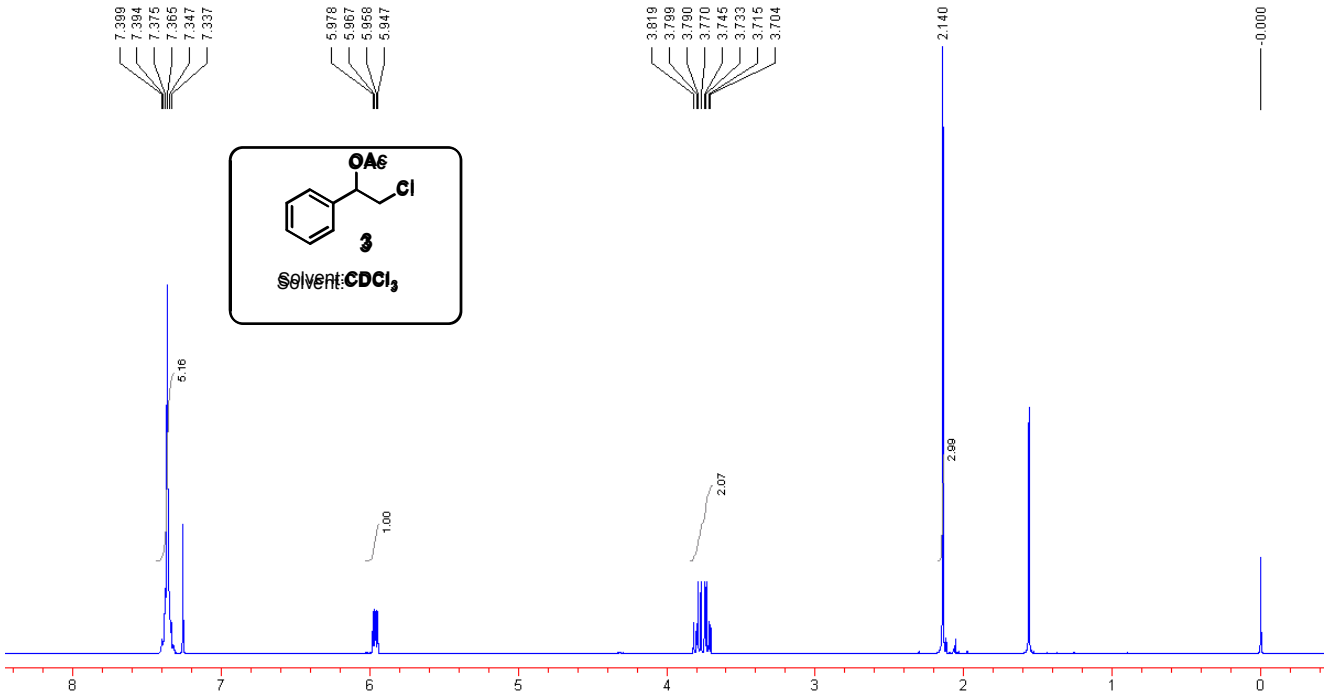
^{1}H NMR spectra of compound 1



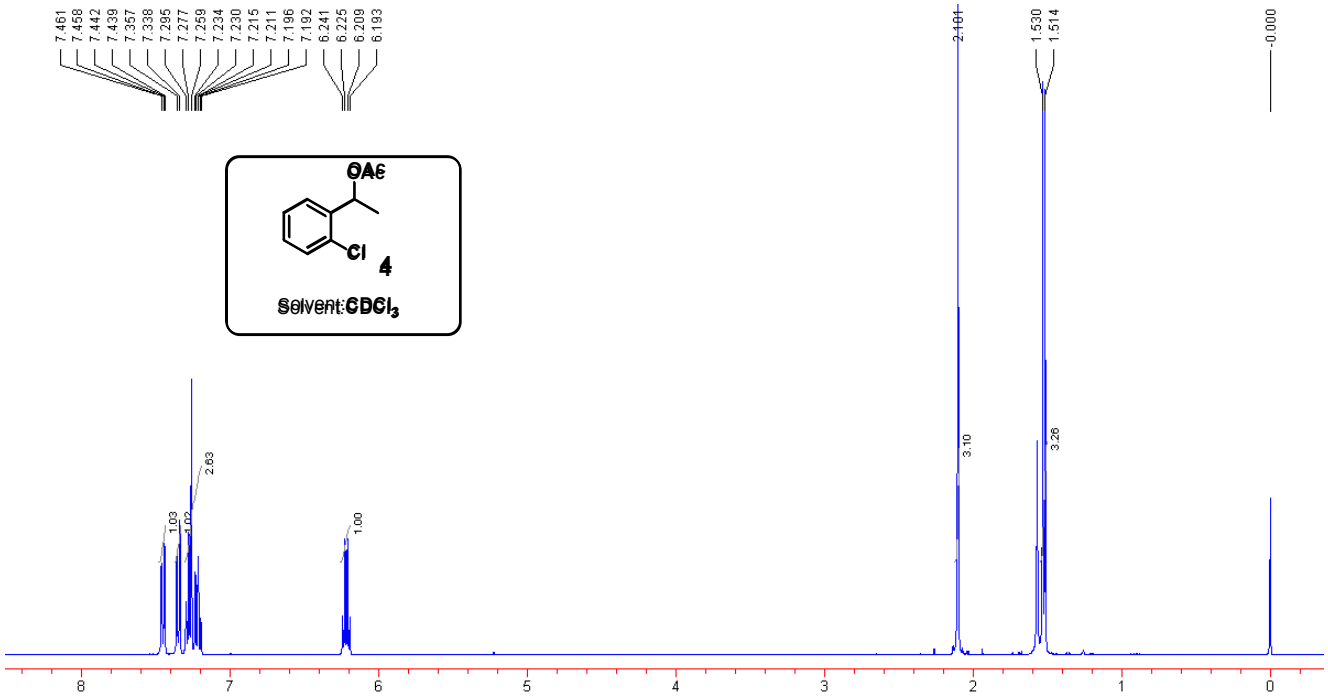
^{1}H NMR spectra of compound 2



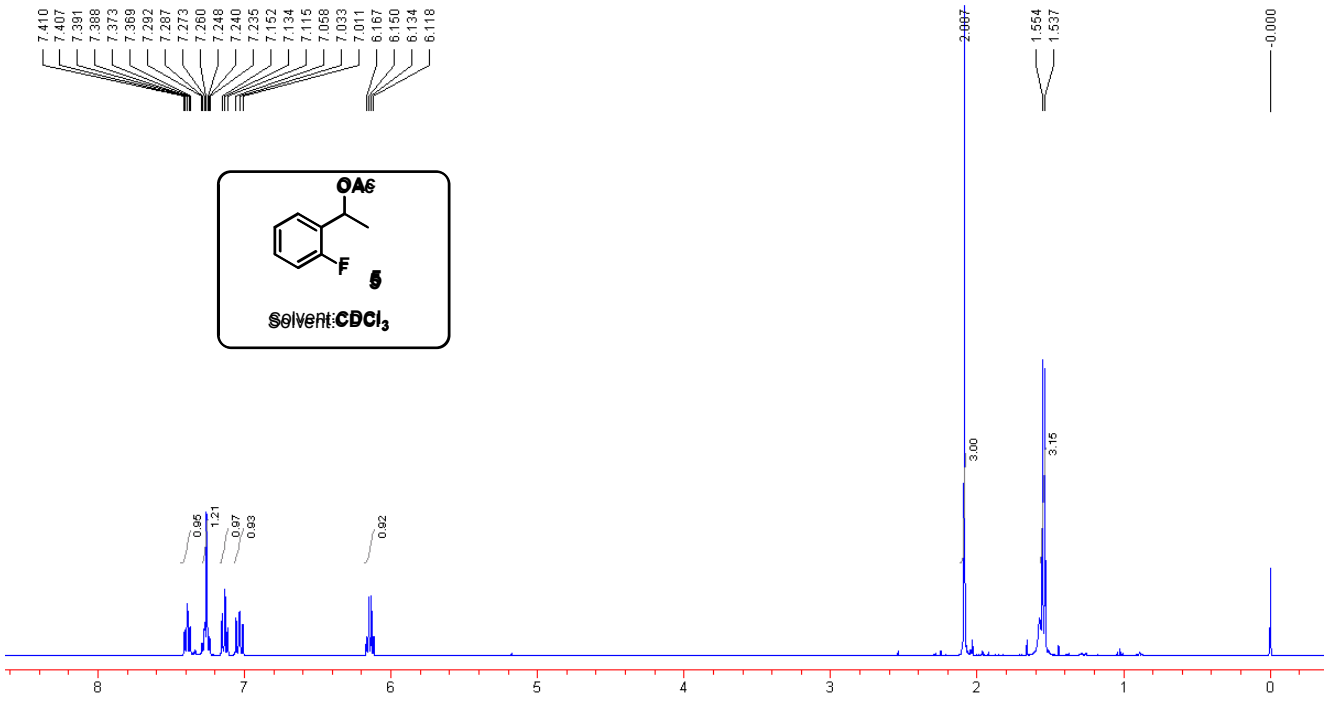
^{1}H NMR spectra of compound 3



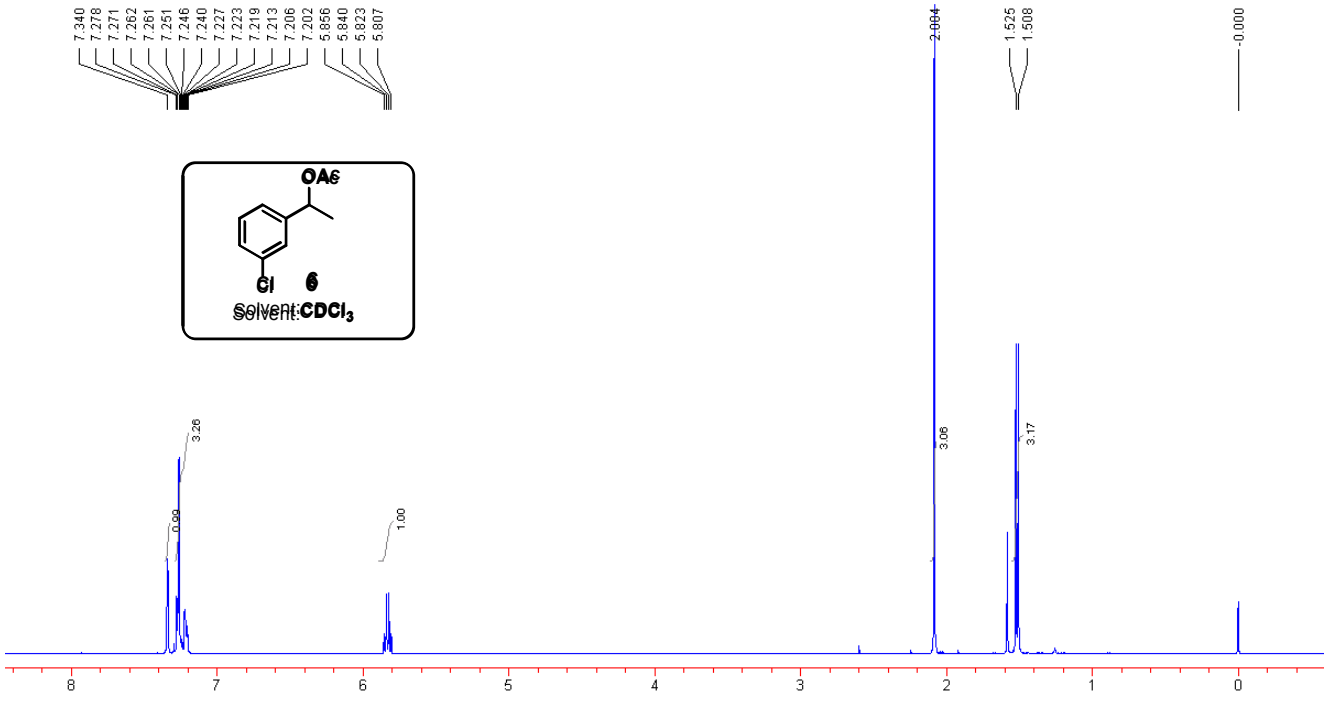
^{1}H NMR spectra of compound 4



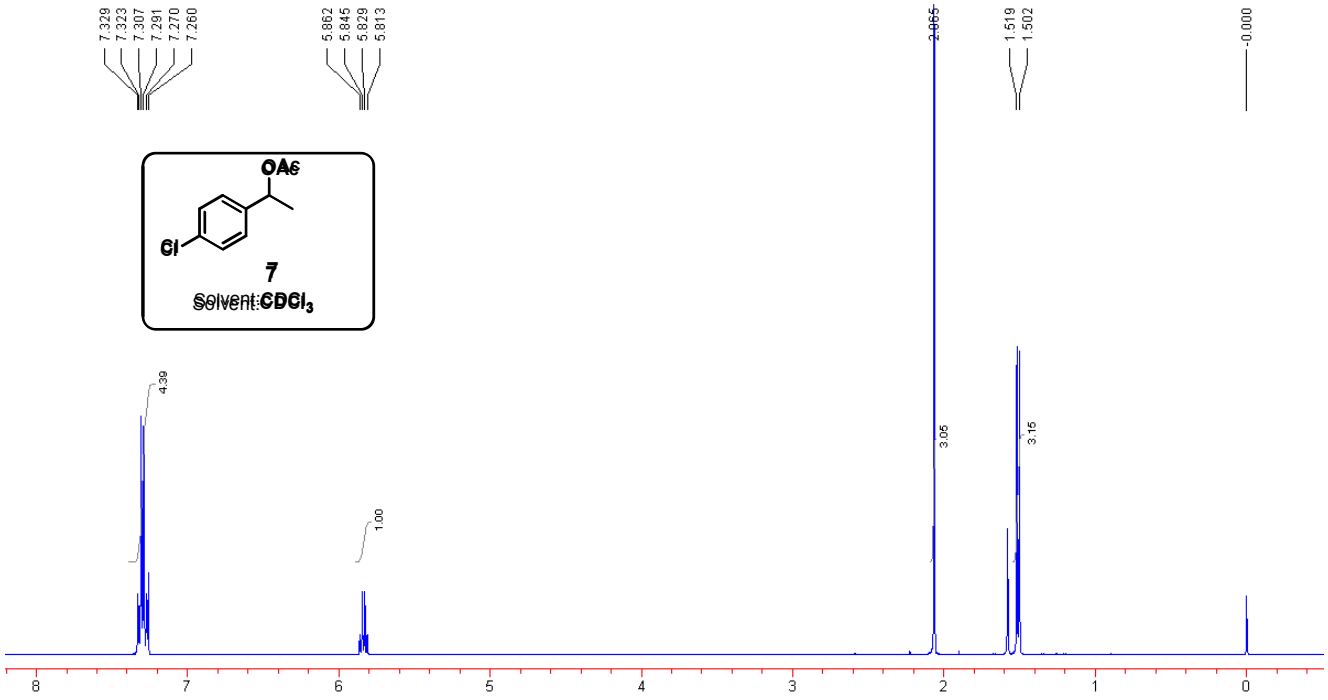
^{1}H NMR spectra of compound 5



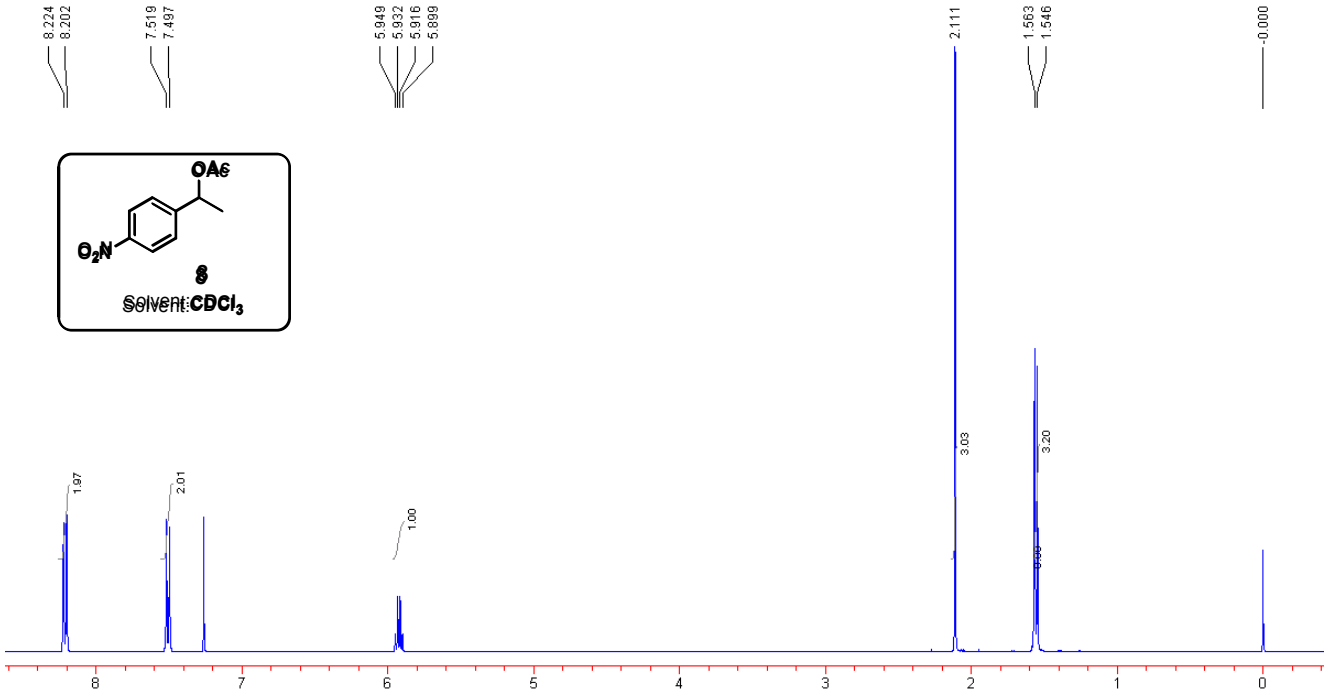
^{1}H NMR spectra of compound 6



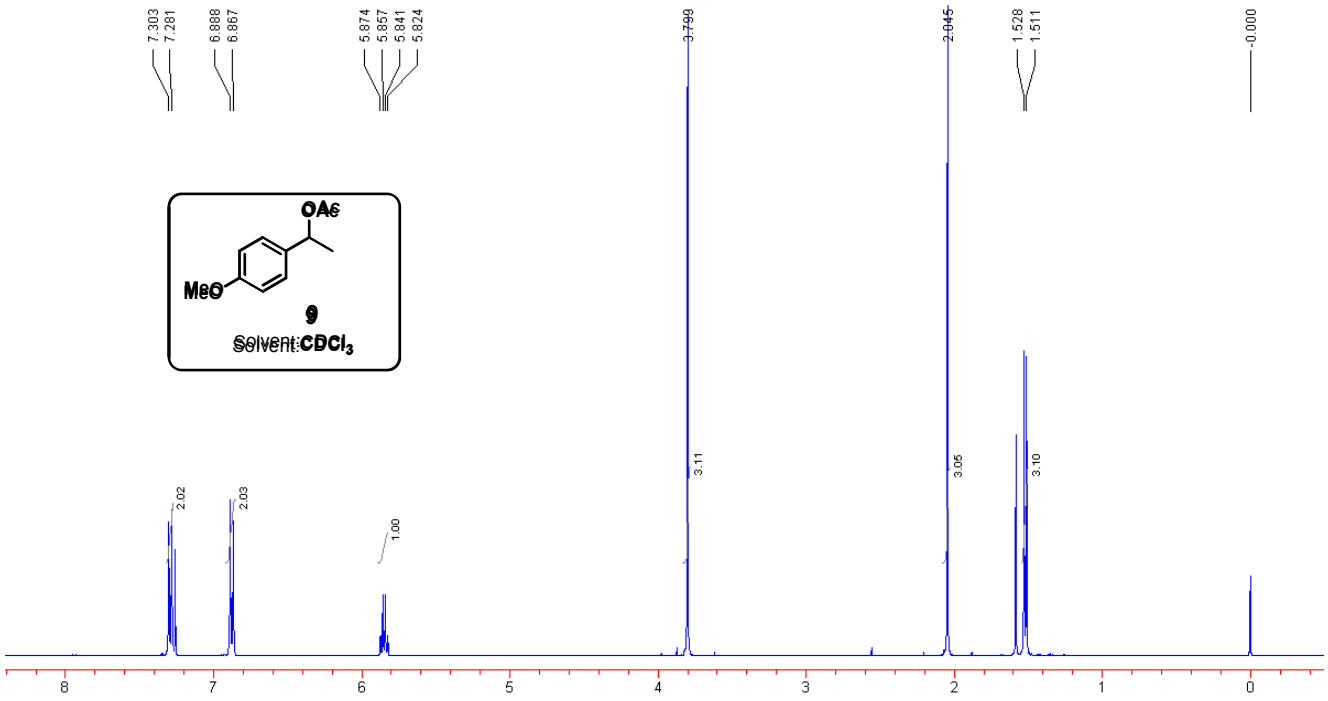
^{1}H NMR spectra of compound 7



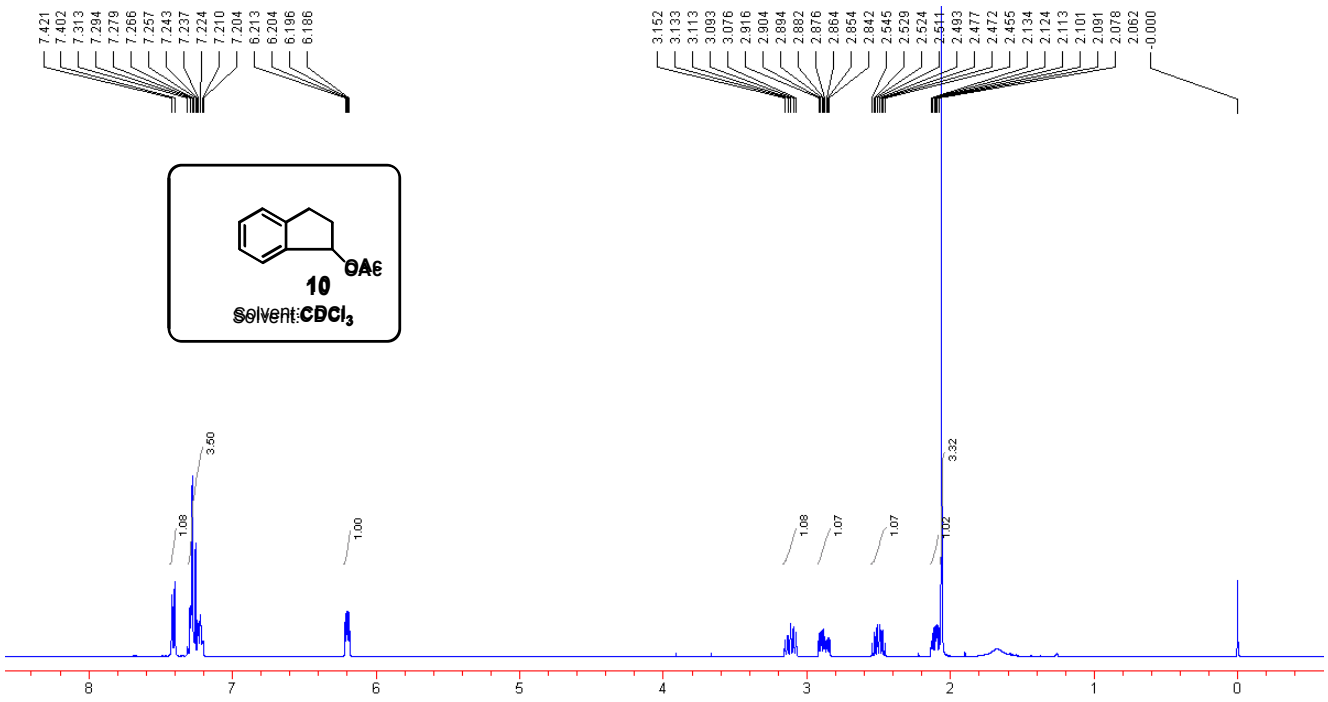
^{1}H NMR spectra of compound 8



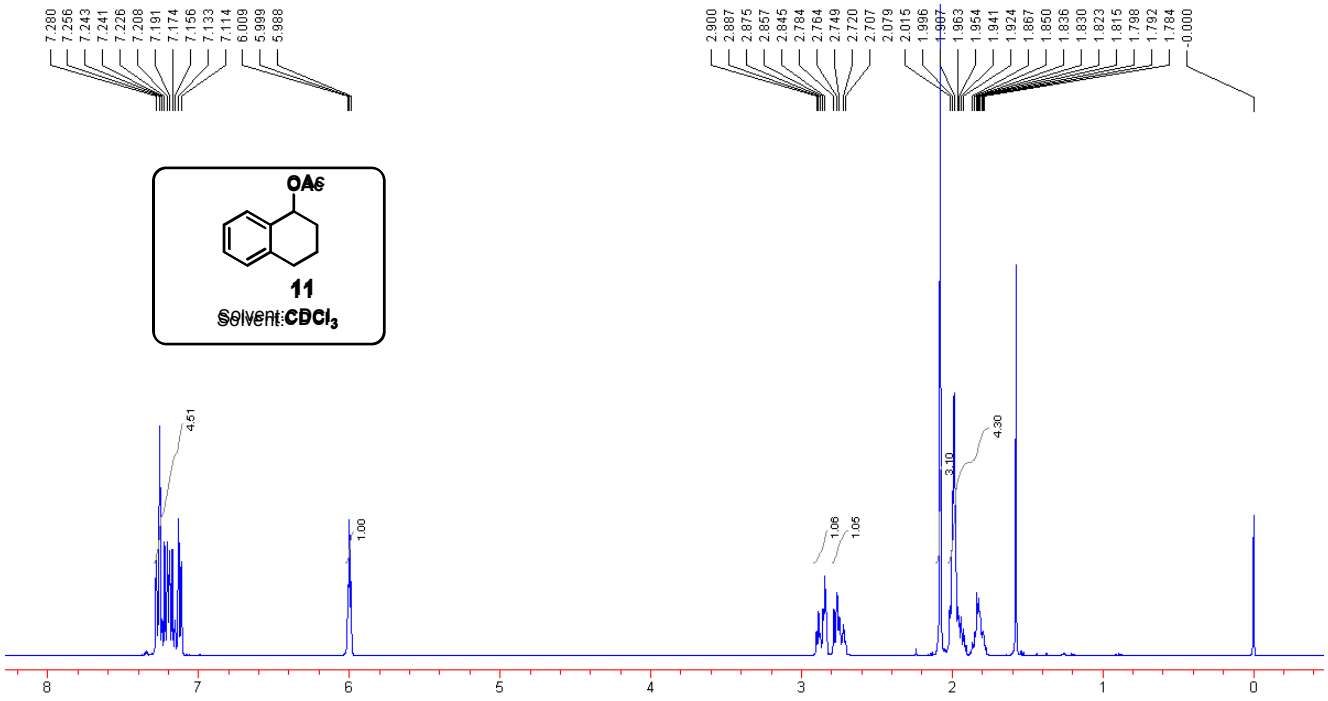
^{1}H NMR spectra of compound 9



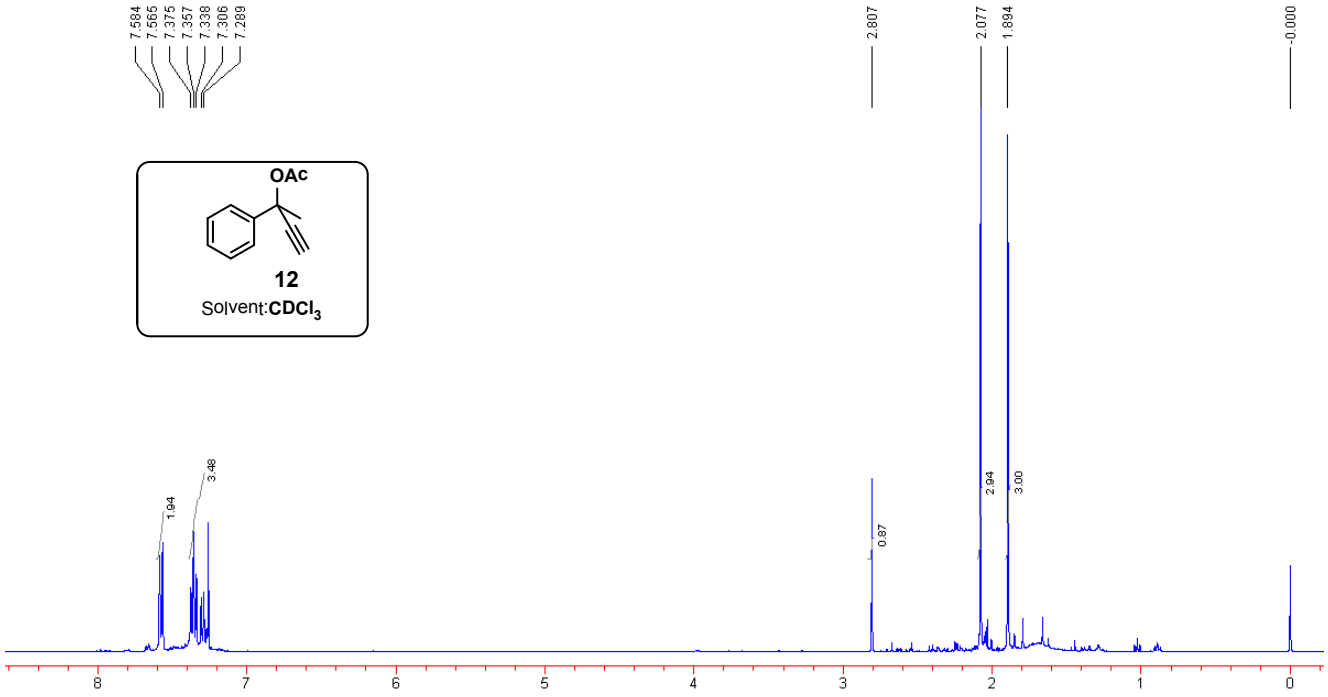
^{1}H NMR spectra of compound 10



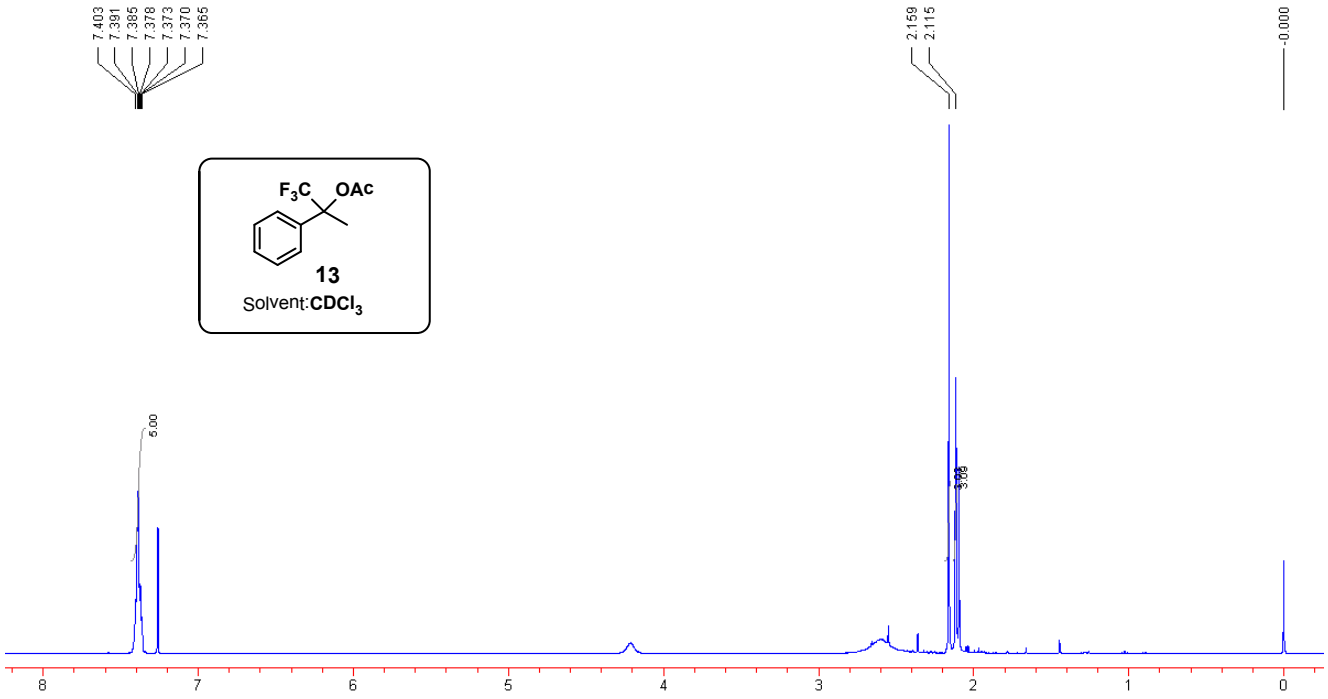
^{1}H NMR spectra of compound 11



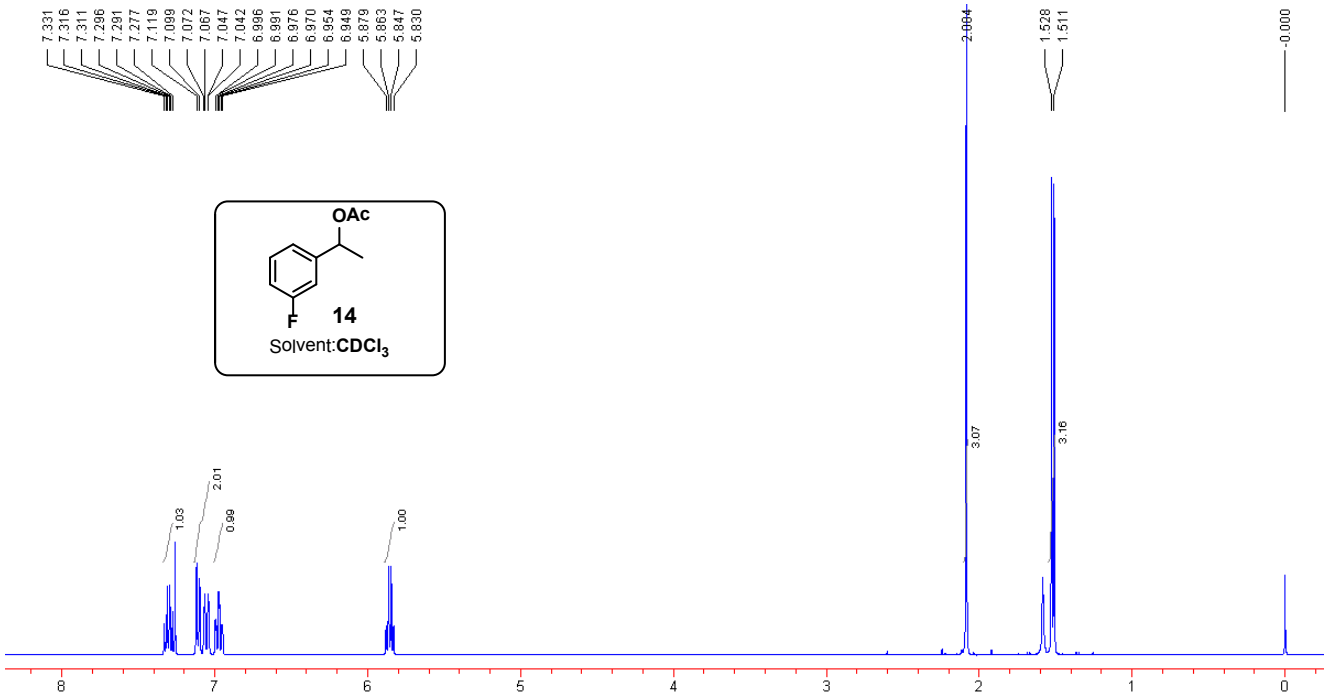
^{1}H NMR spectra of compound 12



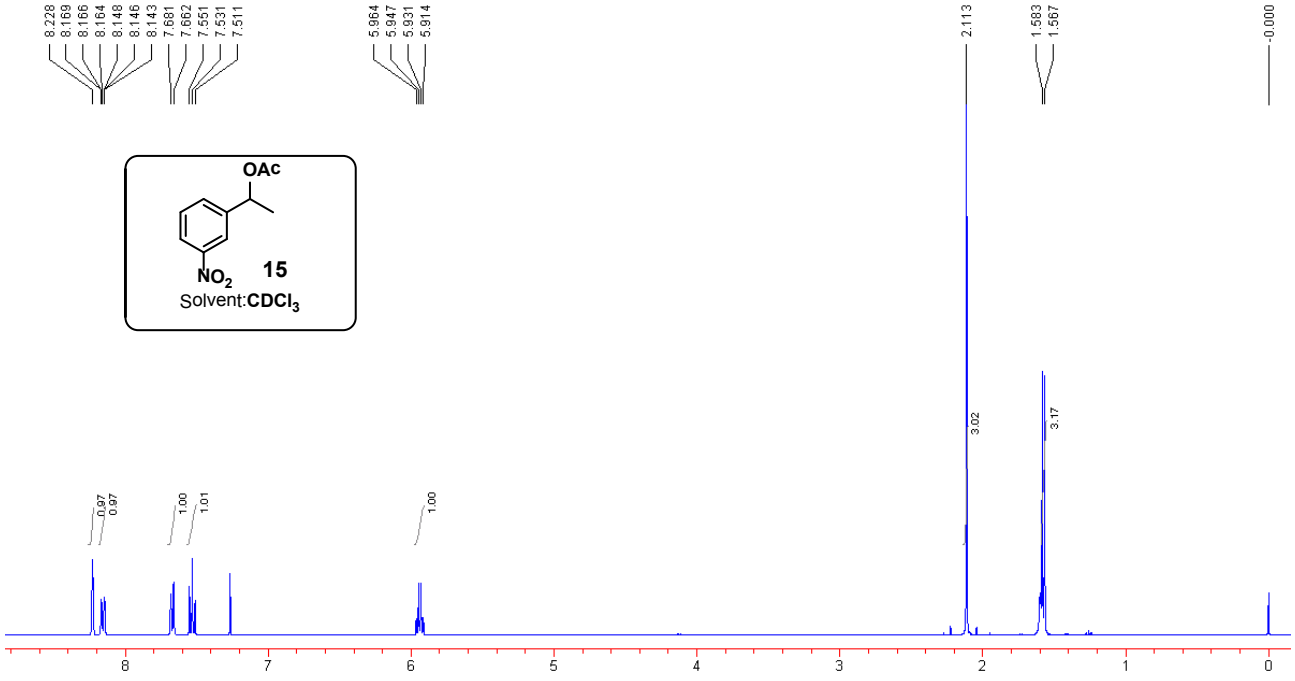
^{1}H NMR spectra of compound 13



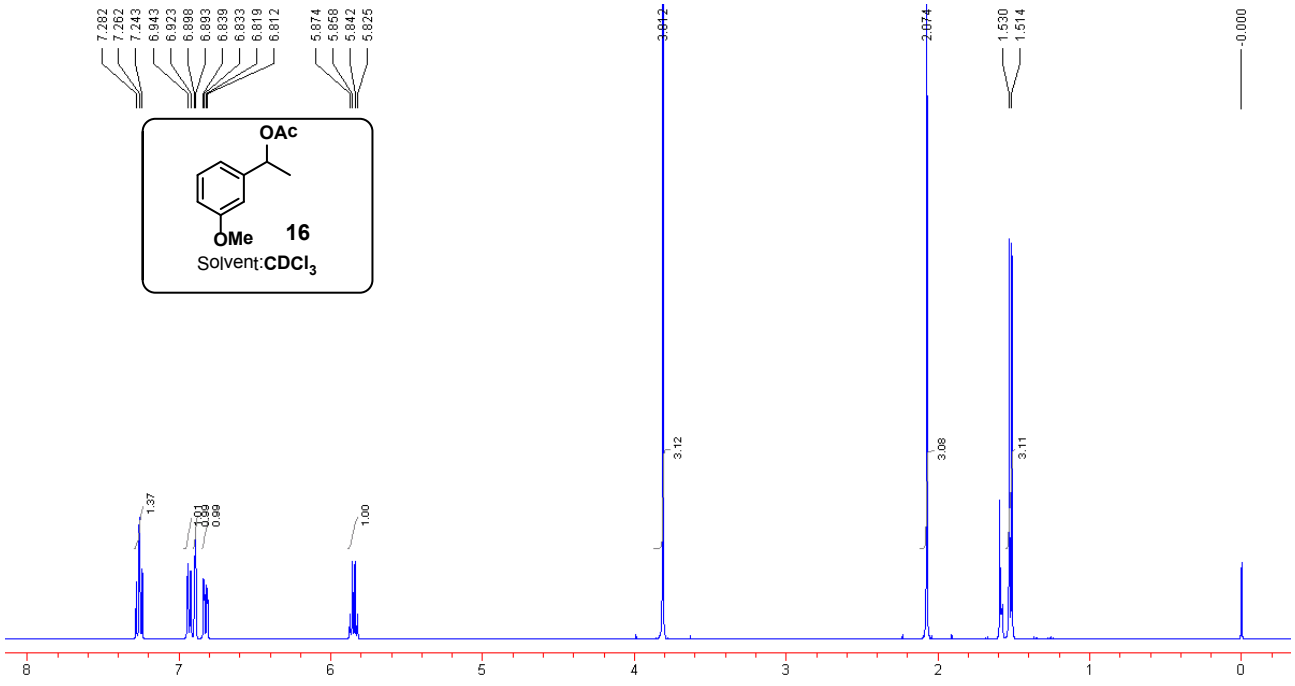
^{1}H NMR spectra of compound 14



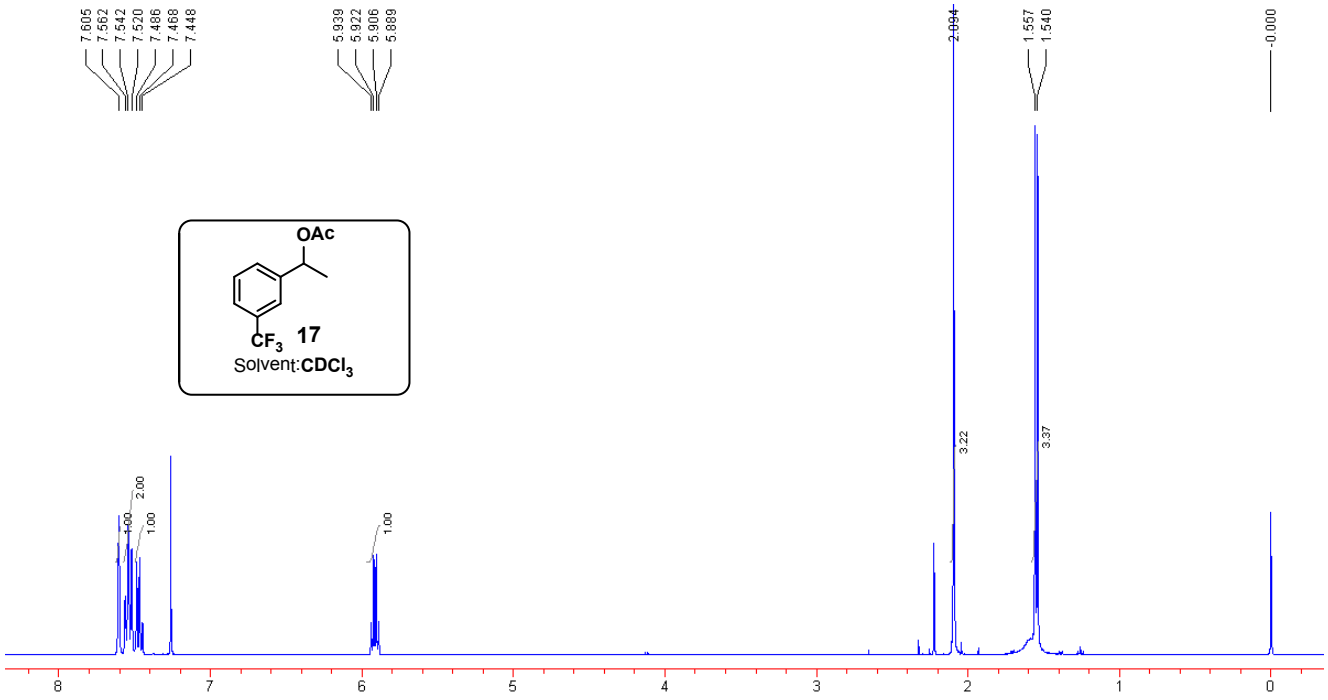
^{1}H NMR spectra of compound 15



^{1}H NMR spectra of compound 16



^{1}H NMR spectra of compound 17



^{1}H NMR spectra of compound 18