Supplementary Information

Preparation, Characterization and Catalytic Activity of Palladium Catalyst Supported on $MgCO_3$ for Dynamic Kinetic Resolution of Amines

Marina M. M. Ferreira,[a] Camila R. Cabreira,[a] Pedro H. K. Chaves,[a] Gabriela M. Labussiére,[a] Renata C. Zimpeck,[a] Sania M. de Lima*[b] and Fernanda A. de Siqueira*[a]

[a]Laboratório de Síntese Orgânica e Catálise, Instituto de Ciências Ambientais, Químicas e Farmacêuticas, Departamento de Química, Universidade Federal de São Paulo (UNIFESP), Campus Diadema, Rua Prof. Arthur Riedel, 275, Bairro Jardim Eldorado, 09972-270 Diadema-SP, Brazil

[b]Laboratório de Processos Ambientais, Bioquímicos e Químicos (LABQ), Instituto de Ciências Ambientais, Químicas e Farmacêuticas, Departamento de Engenharia Química, Universidade Federal de São Paulo (UNIFESP), Campus Diadema, Rua São Nicolau, 210, Centro, 09913-030 Diadema-SP, Brazil

Experimental

General methods

The X-ray powder diffraction (XRD) pattern of the catalysts were obtained with nickel-filtered CuKα radiation (λ = 1.5418 Å) using a Siemens D5005 diffractometer. The XRD data were collected between 2θ = 5 and 80° (in steps of 2° min^{-1}). Transmission electron microscopy (TEM) images were obtained using a Tecnai FEI G20 operated at 200 kV. Samples were prepared by drop casting an alcoholic suspension of nanomaterial in carbon coated copper grid. ^1H nuclear magnetic resonance (NMR) spectra were recorded at 300 MHz instrument with chemical shifts reported relative to tetramethylsilane (TMS), with $CDCl_3$ as solvent. Enantiomeric excesses (ee) were determined by gas chromatography (GC) analysis using a TRACETM 1310 Thermo Scientific™ chromatograph with a beta cyclodextrin capillary column. The low-resolution mass spectra (LRMS) were recorded on a Shimadzu GCMS-QP2010 Plus mass-spectrometer. Optical rotations were performed on A.Krüss Optronic automatic polarimeter P3000 (λ 589 nm) using a cell with a path length of 50 mm.

All racemic amide products were prepared by reaction with Ac_2O in the presence of Et_3N, using CH_2Cl_2 as the solvent, following the procedure described in "General procedure for racemization of (*S*)-1-phenylethylamine" section.

*e-mail: smlima@unifesp.br; fasiqueira@unifesp.br

Preparation of the catalyst

$Pd/MgCO_3$ containing 4.7% Pd

Basic magnesium carbonate (0.100 g, 12.0 mmol) was dispersed in a solution of palladium acetate (0.010 g, 0.040 mmol) in H_2O (2.0 mL), and it was stirred at 80 °C for 1 h. The mixture was cooled to room temperature. A previously prepared reduction solution of formaldehyde (0.5 mL, 37%) and sodium hydroxide (0.5 mL, 30%) was added. The heating was continued for 30 min at 80 °C. The catalyst was filtered, washed with distilled water and dried under vacuum at 60 °C for 8 h.

General procedure for racemization of (*S*)-1-phenylethylamine

To a solution of (*S*)-(–)-1-phenylethylamine (0.061 g, 0.50 mmol) in toluene, dimethyl sulfoxide (DMSO) or acetonitrile (5.0 mL), it was added $Pd/MgCO_3$ loading 4.7% Pd (0.061 g) and Na_2CO_3 (0.053 g). The reaction was sealed with a rubber septum and parafilm, followed by hydrogen introduction at 1 atm pressure. The mixture was stirred and warmed (80 or 60 °C) for 24 h. After that, the solution was filtered and the residue was washed with ethyl acetate. The organic phase was washed with distilled water, with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. The crude was purified by flash column chromatography, using an isocratic elution of MeOH:CH_2Cl_2 (1:1). 1-Phenylethylamine was isolated as pale yellow oil and was dissolved in dichloromethane (4.0 mL). To this solution it was added triethylamine (0.6 mL) and acetic anhydride (0.25 mL), under ice bath. The reaction was stirred at room temperature for 24 h. The organic phase was washed with distilled water, with brine and then dried over anhydrous $MgSO_4$. The percentage of ee was determined by GC analysis (β-cyclodextrin column, (*S*)-enantiomer = 16.08 min, (*R*)-enantiomer = 17.18 min).

Table S1. Data for the racemization reactions of (*S*)-1-phenylethylamine

entry	Solvent	Additive	Temperature / °C	Product / mg	Yield / %	ee / %
1	toluene	–	80	46.4	76	1
2	toluene	Na_2CO_3	80	31.1	51	16
3	toluene	–	60	26.2	43	60
4	toluene	Na_2CO_3	60	28.1	46	46
5	DMSO	–	80	17.7	29	99
6	DMSO	Na_2CO_3	80	18.3	30	99
7	DMSO	–	60	25.0	41	98
8	CH_3CN	Na_2CO_3	80	11.0	18	5
9	CH_3CN	–	60	20.7	34	3
10	CH_3CN	Na_2CO_3	60	18.3	30	8

Procedures for dynamic kinetic resolution

Reaction with alpha-methylbenzylamine[1,2]

In a glass tube, it was added alpha-methylbenzylamine (0.0610 g, 0.504 mmol), 4.7% Pd/$MgCO_3$ catalyst (0.0730 g), toluene (3.5 mL), Na_2CO_3 (0.0530 g), CaLB (0.060 g) and acyl donor (isopropyl acetate, ethyl acetate, isoamyl acetate) (0.3 mL). The tube was sealed with a rubber septum and parafilm, followed by hydrogen introduction at 1 atm pressure. The reactions were heated (60 or 80 °C) and stirred for 24 h. The mixture was filtered, washed with ethyl acetate and then with methanol. The solvent was removed under reduced pressure. The crude was purified by flash column chromatography (isocratic elution with ethyl ether). The product was isolated as a yellowish white solid. $[\alpha]_D^{20}$ +118.4 (*c* 1.51, EtOH); mp 98-102 °C; LRMS (*m/z*, %): 163 ($M^{\bullet+}$, 40), 106 (M-57, 100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H, Ph–H), 5.95 (br s, 1H, NH), 5.11 (quint, 1H, *J* 6.9 Hz, CH), 1.96 (s, 3H, CH_3), 1.47 (d, 3H, *J* 6.9 Hz, CH_3); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.1, 143.1, 128.6, 127.3, 126.1, 48.7, 23.4, 21.7. GC analysis: β-cyclodextrin column, (*S*)-enantiomer = 16.08 min, (*R*)-enantiomer = 17.18 min.

Table S2. Data for the DKR reactions of alpha-methylbenzylamine

entry	Temperature / °C	Acyl donor	time / h	Product / mg	Yield / %	ee / %
1	80	isopropyl acetate	24	51.8	63	90
2	60	isopropyl acetate	24	80.6	98	> 99
3	60	isoamyl acetate	24	67.3	82	98
4	60	ethyl acetate	24	61.7	75	> 99

Reactions with 4-fluoro-alpha-methylbenzylamine[2,3]

The reactions were performed as described in "Reaction with alpha-methylbenzylamine" section, but using 4-fluoro-alpha-methylbenzylamine (0.072 g, 0.52 mmol), CALB (0.069 g), Pd/$MgCO_3$ (0.069 g), acyl donor (ethyl acetate, isopropyl acetate) (0.25 mL), Na_2CO_3 (0.062 g) in toluene (4.2 mL). The reactions were heated (60 °C) and stirred for 24 or 36 h. The crude was purified by flash column chromatography (gradient elution 0-70% EtOAc in hexane). The corresponding acetamide was isolated as a white solid. $[\alpha]_D^{20}$ +121.8 (*c* 1.61, EtOH); mp 116-118 °C; LRMS (*m/z*, %): 181 ($[M]^+$, 35), 124 ($[M - 57]^+$, 100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.25 (m, 2H, Ph–H), 7.03-6.97 (m, 2H, Ph–H), 5.97 (br s, 1H, NH), 5.13-5.03 (m, 1H, CH), 1.96 (s, 3H, CH_3), 1.45 (d, 3H, *J* 6.9 Hz, CH_3); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.2, 161.9 (d, *J* 243.9 Hz), 139.0 (d, *J* 3.0 Hz), 127.7 (d, *J* 8.0 Hz), 115.3 (d, *J* 21.2 Hz), 48.1, 23.3, 21.7. GC analysis: β-cyclodextrin column, (*S*)-enantiomer = 18.33 min, (*R*)-enantiomer = 19.32 min.

Table S3. Data for the DKR reactions of 4-fluoro-alpha-methylbenzylamine

entry	Temperature / °C	Acyl donor	time / h	Product / mg	Yield / %	ee / %
1	60	isopropyl acetate	24	40.5	43	99
2	60	isopropyl acetate	36	89.6	95	99
3	60	ethyl acetate	36	84.8	90	98

Reactions with 1-(4-methylphenyl)ethylamine[2,3]

The reactions were performed as described in "Reaction with alpha-methylbenzylamine" section, but using 1-(4-methylphenyl)ethylamine (0.068 g, 0.504 mmol), CaLB (0.069 g), Pd/$MgCO_3$ (0.069 g), acyl donor (ethyl acetate, isopropyl acetate, isoamyl acetate) (0.25 mL), Na_2CO_3 (0.062 g) in toluene (4.2 mL). The reactions were heated (60, 80 or 100 °C) and stirred for 24 or 48 h. The crude was purified by flash column chromatography (gradient elution 0-70% EtOAc in hexane). The corresponding acetamide was isolated as a white solid. $[\alpha]_D^{20}$ +130.5 (*c* 0.71, EtOH); mp 80-82 °C; LRMS (*m/z*, %): 177 ($[M]^+$, 27), 120 ($[M - 57]^+$, 100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19-7.06 (m, 4H, Ph–H), 5.80 (br s, 1H, NH), 5.00 (m, 1H, CH), 2.25 (s, 3H, CH_3), 1.88 (s, 3H, CH_3), 139 (d, 3H, *J* 9 Hz, CH_3); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.0, 140.1, 137.0, 129.3, 126.1, 48.5, 23.5, 21.6, 21.0. GC analysis: β-cyclodextrin column, (*S*)-enantiomer = 27.94 min, (*R*)-enantiomer = 29.68 min.

Table S4. Data for the DKR reactions of 1-(4-methylphenyl)ethylamine

entry	Temperature / °C	Acyl donor	time / h	Product / mg	Yield / %	ee / %
1	60	isopropyl acetate	24	26.1	29	95
2	60	ethyl acetate	48	42.2	47	95
3	60	isoamyl acetate	24	41.8	47	99
4	80	isoamyl acetate	24	52.7	59	99
5	100	isoamyl acetate	24	59.2	66	99

Reactions with 1,2,3,4-tetrahydro-1-naphthylamine[4]

The reactions were performed as described in "Reaction with alpha-methylbenzylamine" section, but using 1,2,3,4-tetrahydro-1-naphthylamine (0.0735 g, 0.50 mmol), CaLB (0.0730 g), $Pd/MgCO_3$ (0.0730 g), acyl donor (ethyl acetate, isopropyl acetate) (0.25 mL), Na_2CO_3 (0.064 g) in toluene (4.3 mL). The reactions were heated (60 or 80 °C) and stirred for 36 h. The crude was purified by flash column chromatography (gradient elution 0-70% EtOAc in hexane). The corresponding acetamide was isolated as a white solid. $[\alpha]_D^{20}$ +97.7 (*c* 1.0, $CHCl_3$); mp 144-146 °C; LRMS (*m/z*, %): 189 ($[M]^+$, 4), 130 ($[M - 59]^+$, 100); ^{1}H NMR (300 MHz, $CHCl_3$) δ 7.20-7.00 (m, 4H, Ph–H), 5.72 (br s, 1H, NH), 5.13-5.06 (m, 1H, CH), 2.74-2.68 (m, 2H, CH_3), 1.93 (s, 4H, CH_2, CH_3), 1.79-1.70 (m, 3H, CH_2); ^{13}C NMR (75 MHz, $CHCl_3$) δ 169.3, 137.6, 136.7, 129.2, 128.8, 127.3, 126.3, 47.5, 30.1, 29.2, 23.5, 19.9. GC analysis: β-cyclodextrin column, (*S*)-enantiomer = 12.64 min, (*R*)-enantiomer = 13.57 min.

Table S5. Data for the DKR reactions of 1,2,3,4-tetrahydro-1-naphthylamine

entry	Temperature / °C	Acyl donor	time / h	Product / mg	Yield / %	ee / %
1	60	isopropyl acetate	36	43.1	45	90
2	80	ethyl acetate	36	85.3	90	> 99

References

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2. Li, G.; Antilla, J. C.; *Org. Lett.* **2009**, *11*, 1075.
3. Hu, X.-P.; Zheng, Z.; *Org. Lett.* **2004**, *6*, 3585.
4. Zhang, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Zhang, X.; *J. Org. Chem.* **1999**, *64*, 1774; Kim, M.-J.; Kim, W.-H.; Han, K.; Choi, Y. K.; Park, J.; *Org. Lett.* **2007**, *9*, 1157.

NMR spectra section

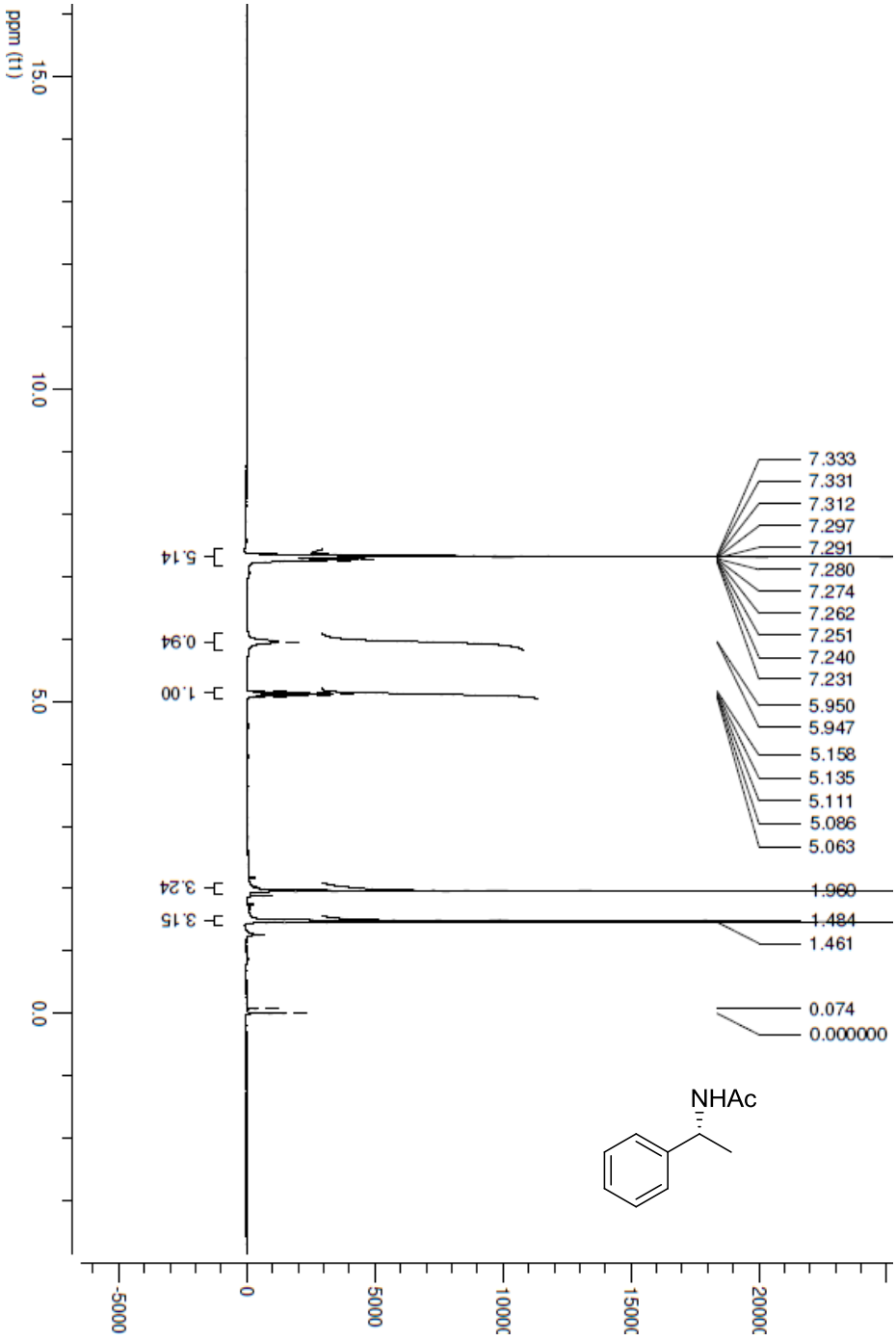

Figure S1. ^{1}H NMR spectra (300 MHz, $CDCl_3$) of acetamide **11**.

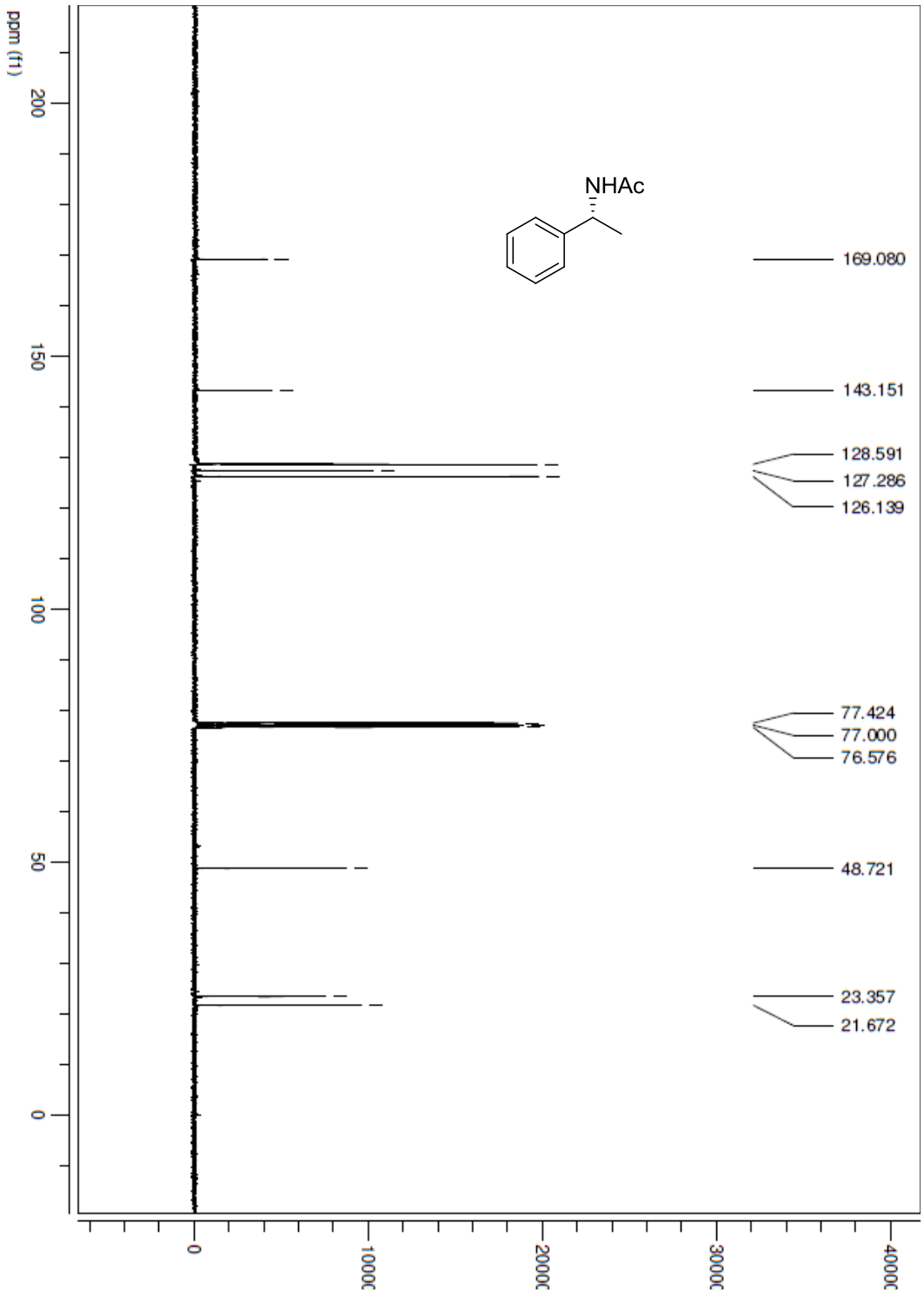

Figure S2. ^{13}C NMR spectra (75 MHz, $CDCl_3$) of acetamide **11**.

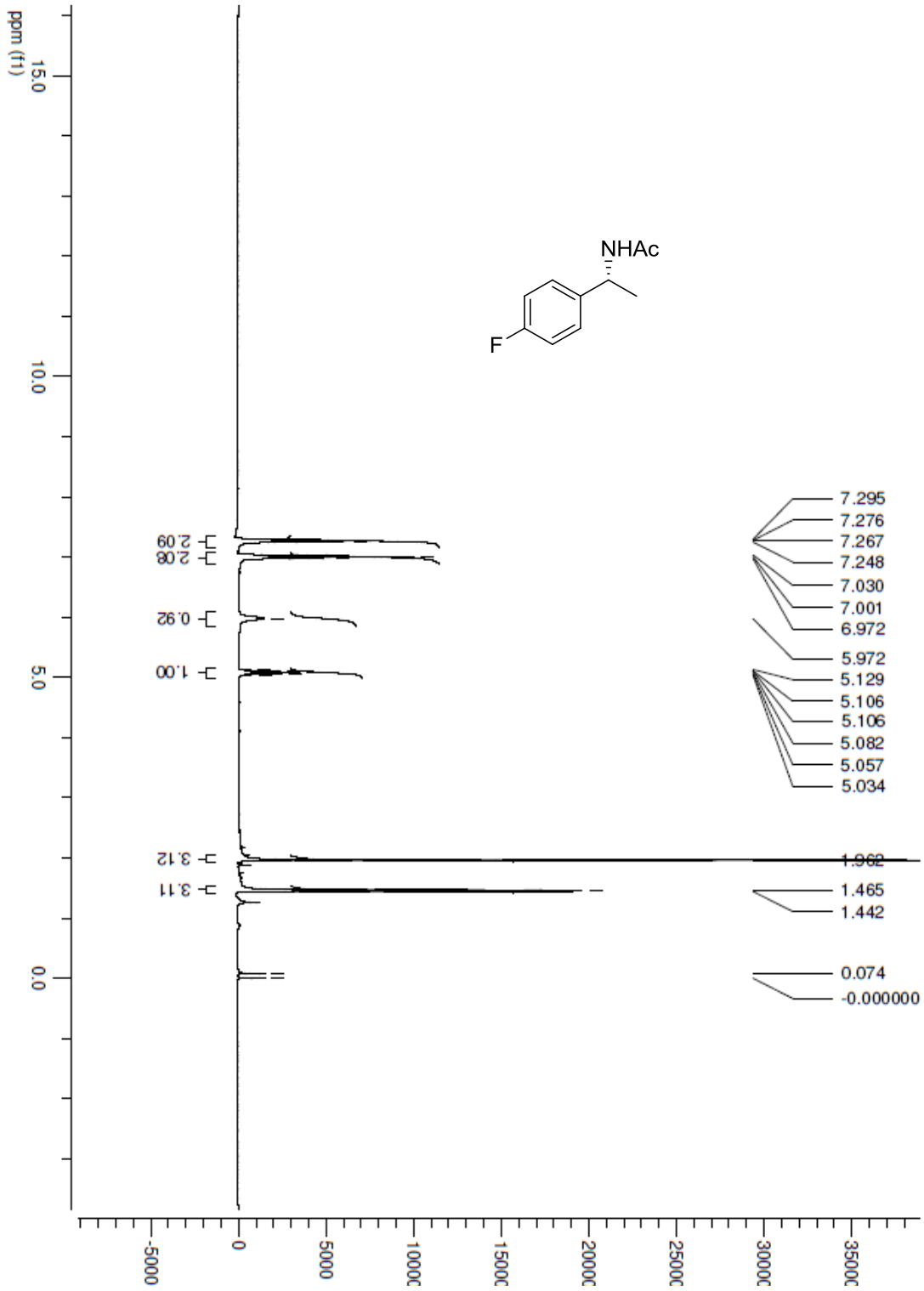

Figure S3. ^{1}H NMR spectra (300 MHz, $CDCl_3$) of acetamide **12**.

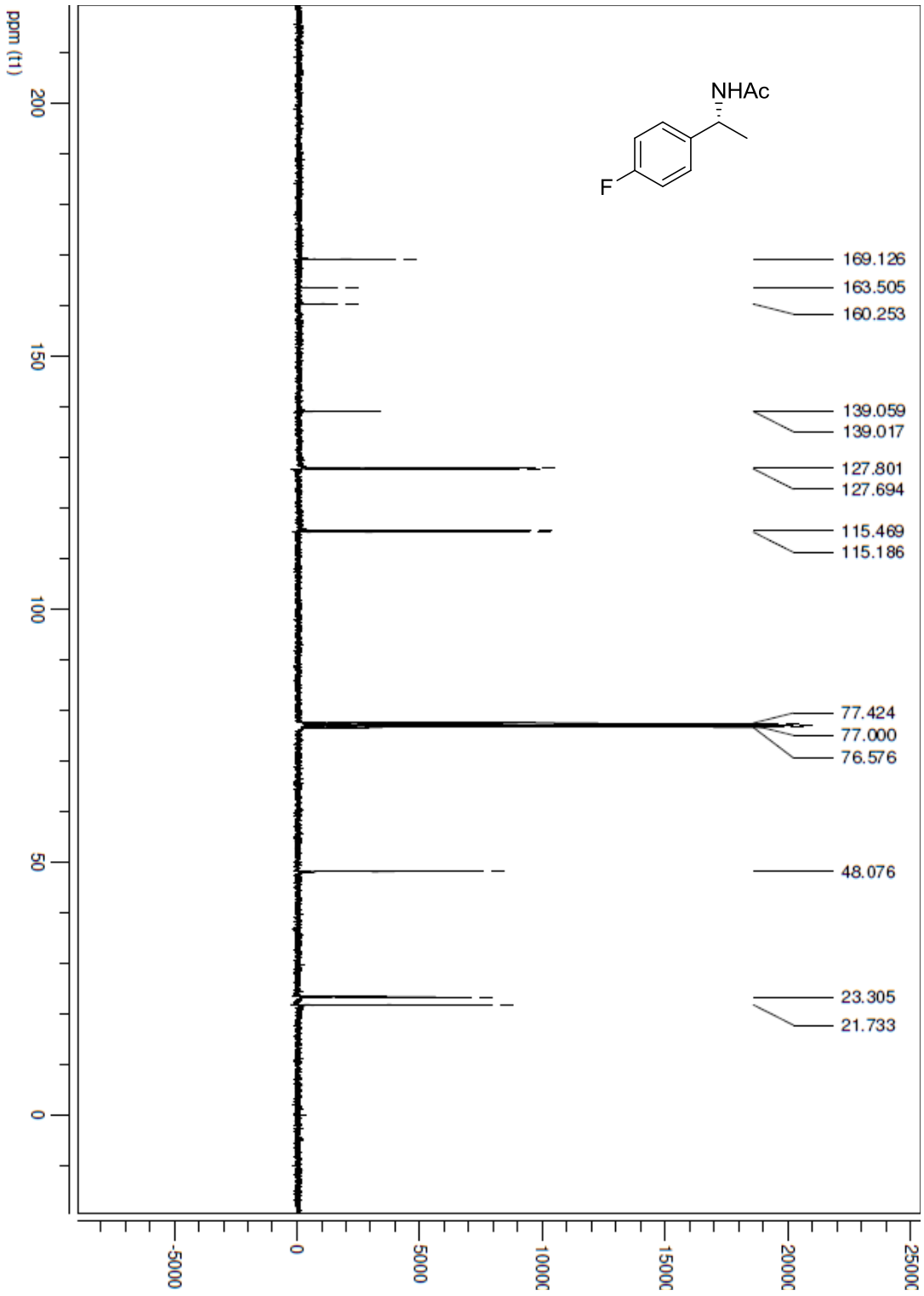

Figure S4. ^{13}C NMR spectra (75 MHz, $CDCl_3$) of acetamide **12**.

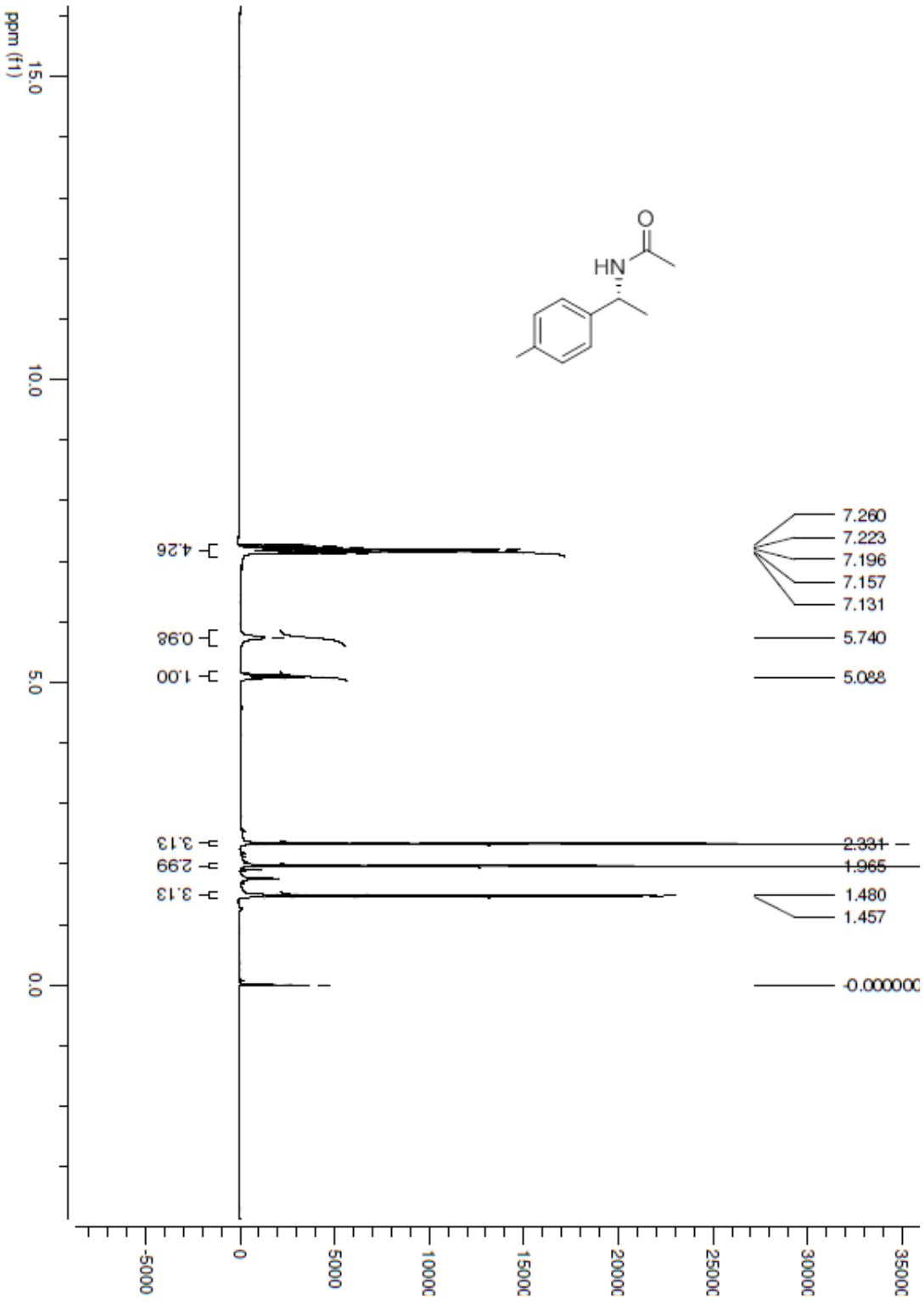

Figure S5. ^{1}H NMR spectra (300 MHz, $CDCl_3$) of acetamide **13**.

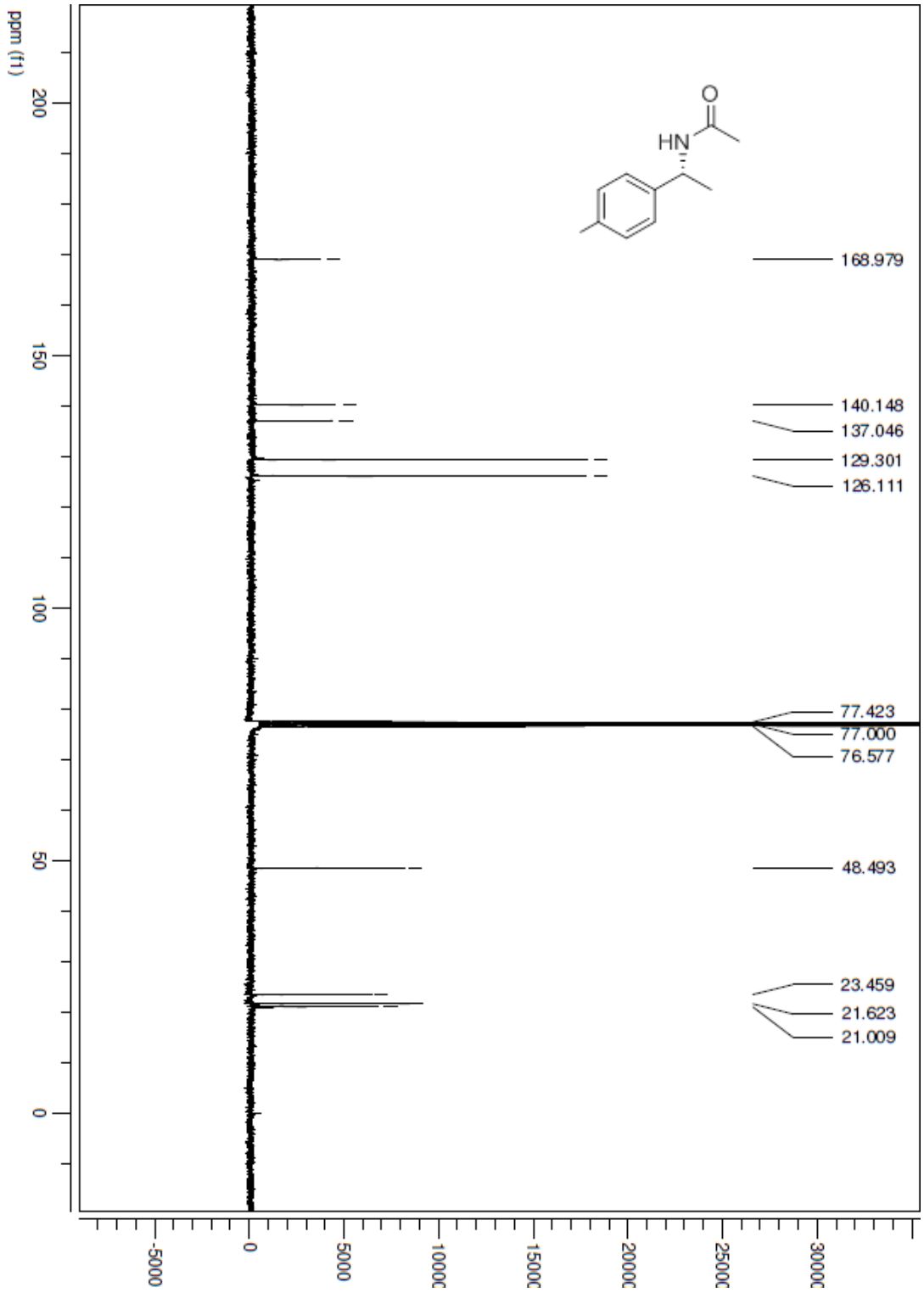

Figure S6. ^{13}C NMR spectra (75 MHz, $CDCl_3$) of acetamide **13**.

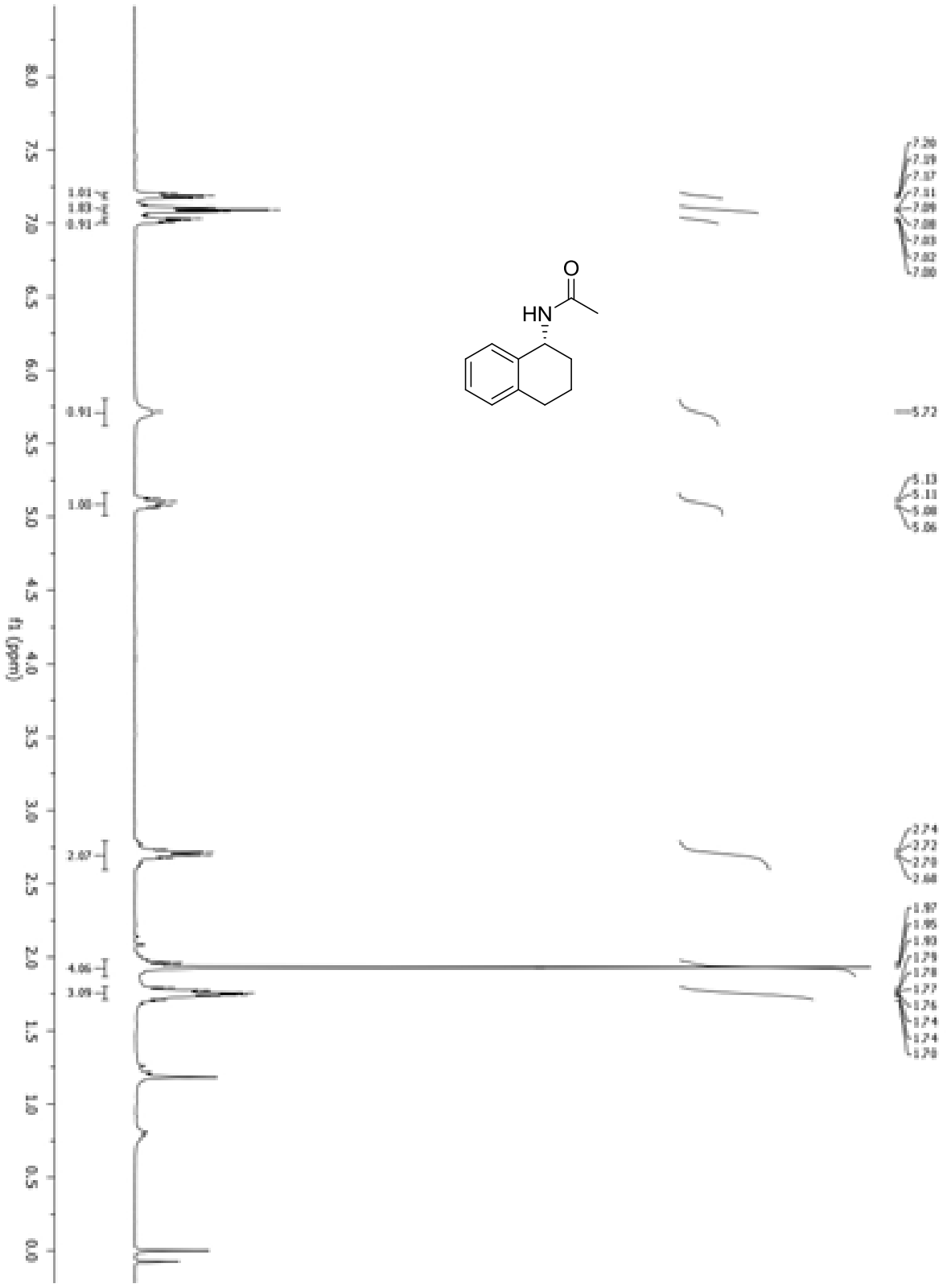

Figure S7. ^{1}H NMR spectra (300 MHz, $CDCl_3$) of acetamide **14**.

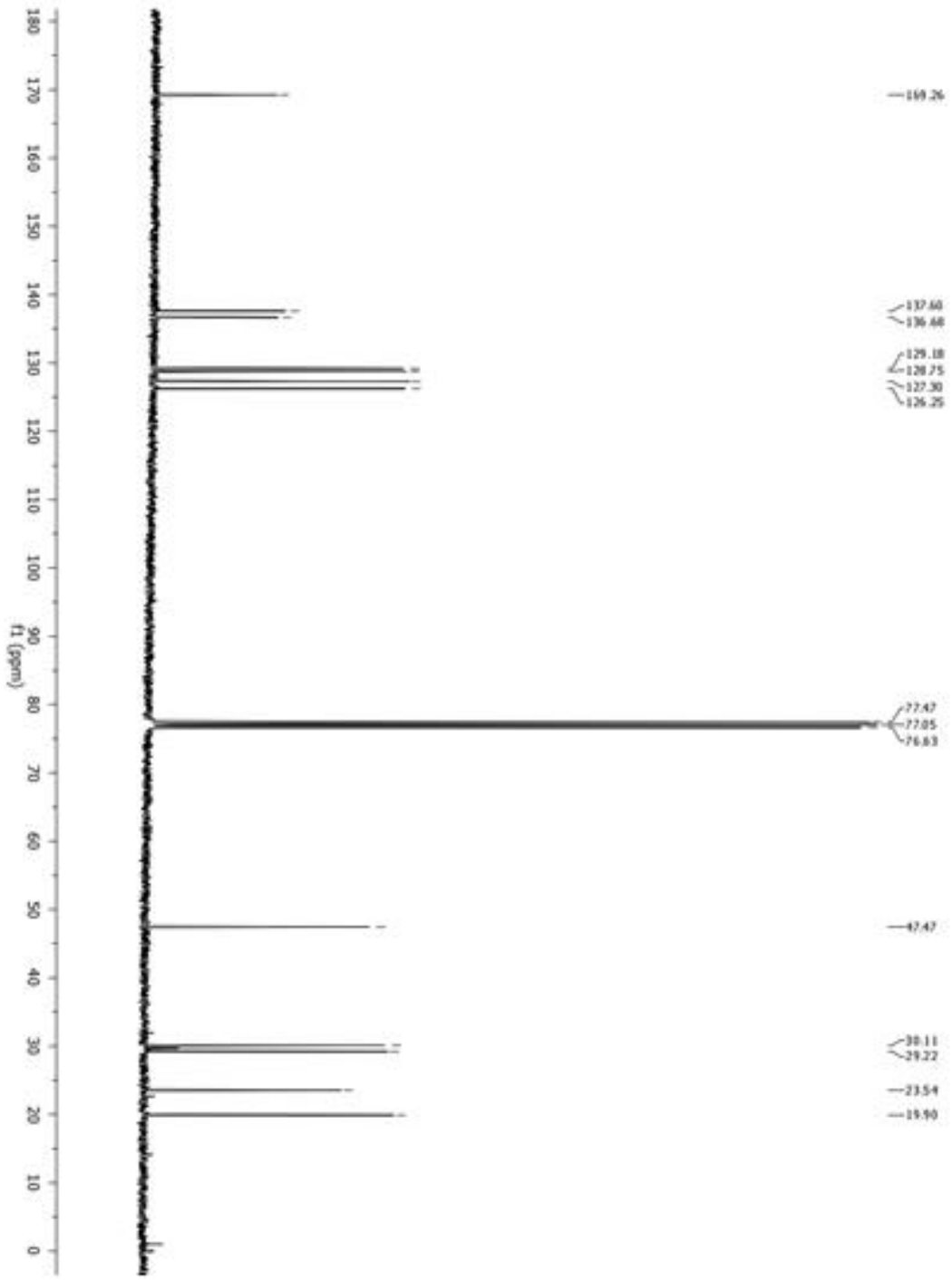

Figure S8. ^{13}C NMR spectra (75 MHz, $CDCl_3$) of acetamide **14**.

Chromatogram

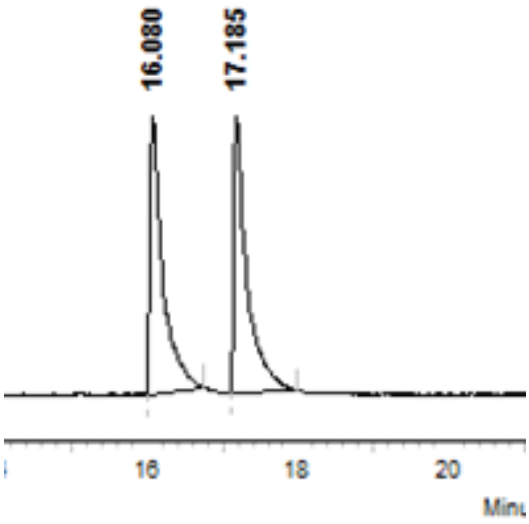

Figure S9. Chromatogram of racemic mixture **2**.

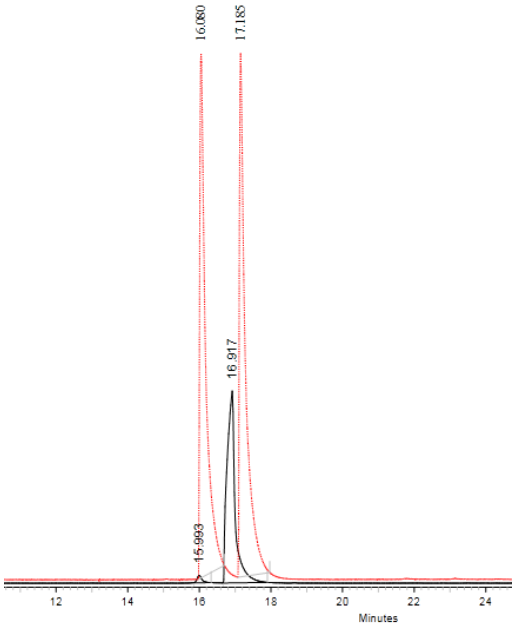

Figure S10. Chromatogram of racemic mixture **2**, superposed to the chromatogram of **11**.

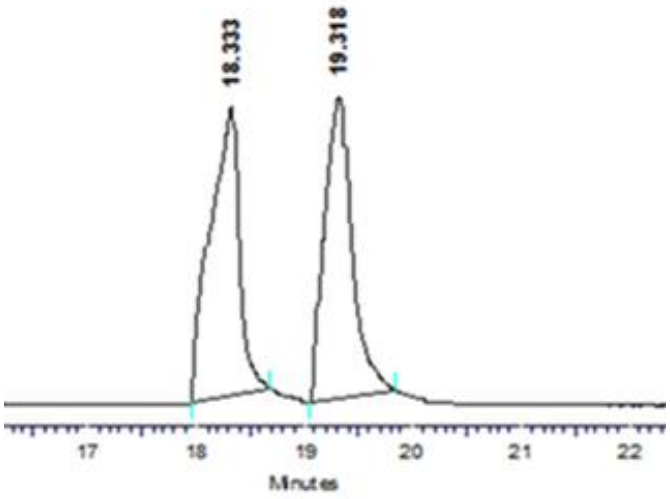

Figure S11. Chromatogram of racemic mixture **8**.

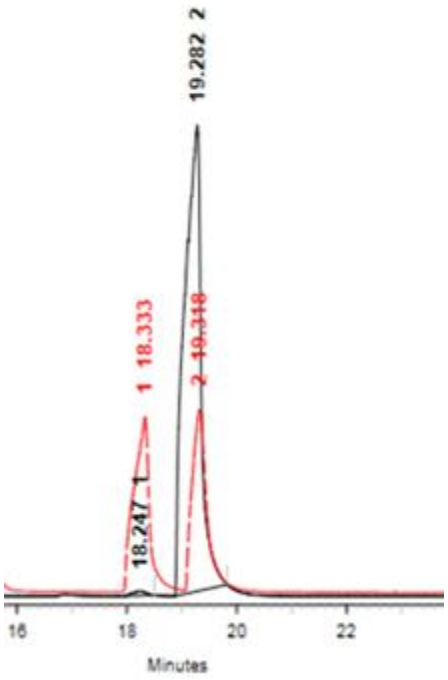

Figure S12. Chromatogram of racemic mixture **8**, superposed to the chromatogram of **12**.

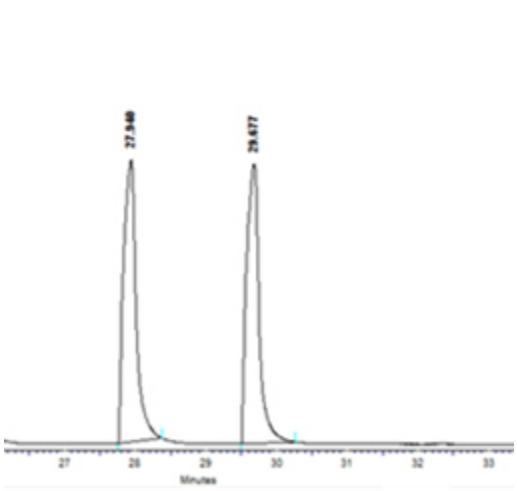

Figure S13. Chromatogram of racemic mixture **9**.

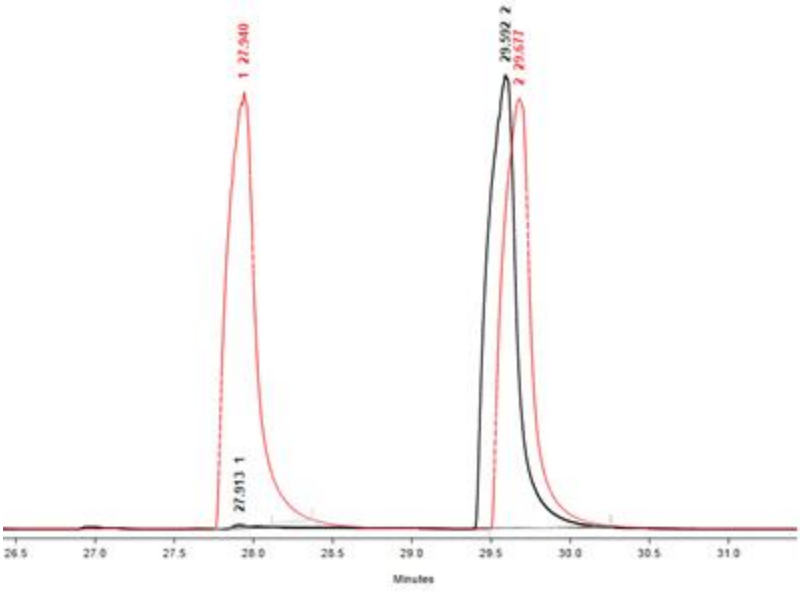

Figure S14. Chromatogram of racemic mixture **9**, superposed to the chromatogram of **13**.

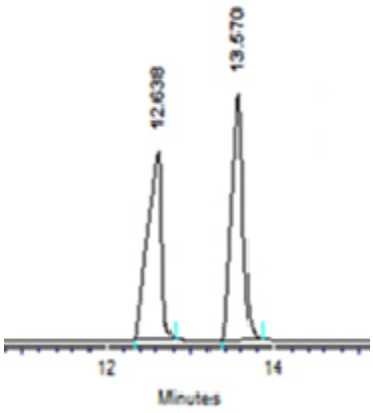

Figure S15. Chromatogram of racemic mixture **10**.

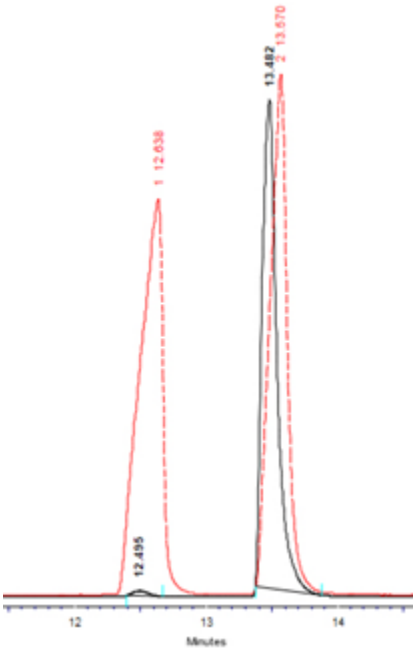

Figure S16. Chromatogram of racemic mixture **10**, superposed to the chromatogram of **14**.