A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

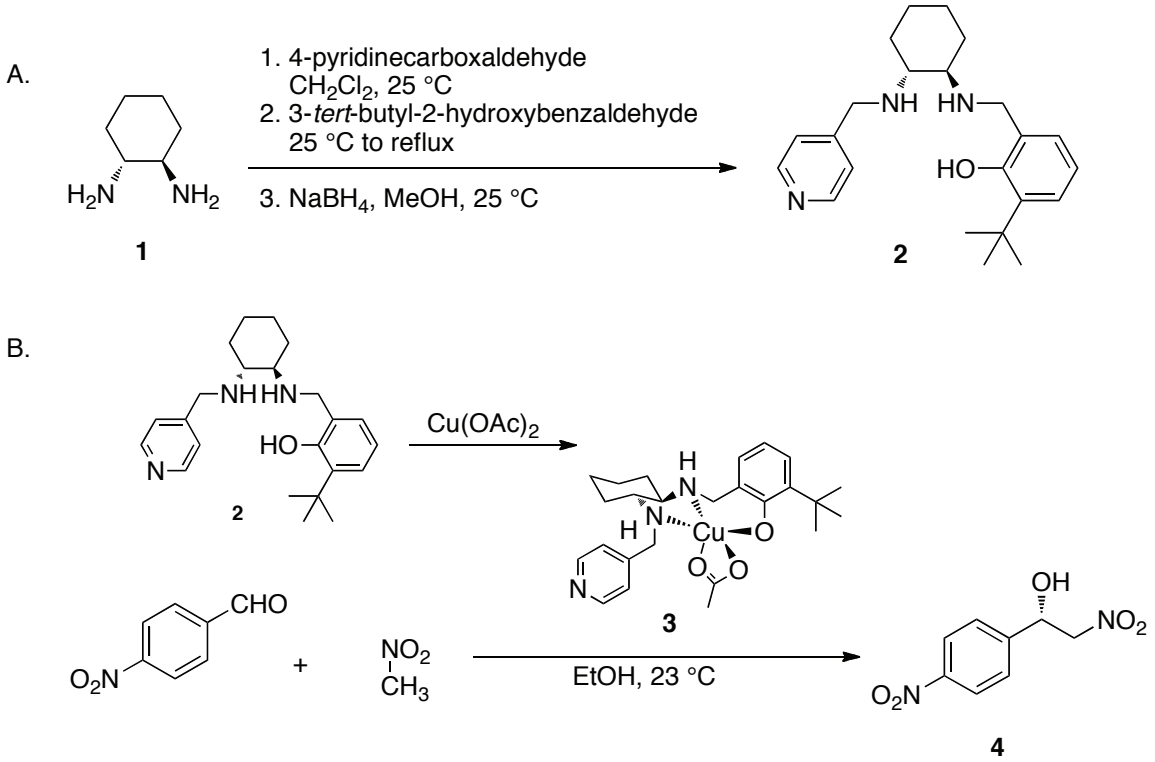
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.090.0052

Enantioselective Nitroaldol (Henry) Reaction of *p*-Nitrobenzaldehyde and Nitromethane Using a Copper (II) Complex Derived from (*R*,*R*)-1,2-Diaminocyclohexane: (1*S*)-1-(4-Nitrophenyl)-2-nitroethane-1-ol



Submitted by Antoinette Chougnet and Wolf-D. Woggon.[1]
Checked by Larissa Pauli and Andreas Pfaltz.

1. Procedure

*A. 2-(1,1-Dimethylethyl)-6-[[[(1R,2R)-2-[(4-pyridinylmethyl)amino]-cyclohexyl]amino]methyl]-phenol (**2**).* An oven dried, 250-mL, two-necked flask equipped with a magnetic stir bar (cylindrical, 2 × 1 cm), a reflux condenser (central neck) with a two-tap Schlenk adapter connected to a bubbler and an argon/vacuum manifold (Note 1) is assembled hot and cooled under a stream of argon. The flask is charged with (1*R*,2*R*)-1,2-diaminocyclohexane (**1**, 350 mg, 3.00 mmol, 1.00 equiv) in dry dichloromethane (30 mL) (Note 2) and the remaining neck is equipped with a rubber septum. A solution of 4-pyridinecarboxaldehyde (328 mg, 3.00 mmol, 1.00 equiv) in dichloromethane (30 mL) (Note 2) is added to the

Org. Synth. **2013**, *90*, 52-61
Published on the Web 8/27/2012

stirred solution *via* syringe pump over 2 h at 25 °C (Note 3). After complete addition the light yellow reaction mixture is stirred for another hour at ambient temperature. Subsequently a solution of 3-*t*-butyl-2-hydroxybenzaldehyde (558 mg, 3.00 mmol, 1.00 equiv) in dichloromethane (15 mL) (Note 2) is added in one portion and the reaction mixture is refluxed for 19 h (Note 4). The dark yellow solution is concentrated in the reaction flask by rotary evaporation (45 °C water bath, 150 mmHg) and the residue, containing the imines (Note 5), is dissolved in methanol (45 mL) (Note 2). A magnetic stir bar (cylindrical, 2 × 1 cm) and an excess of sodium borohydride (768 mg, 19.9 mmol, 6.6 equiv) (Note 2) is added in small portions over 5 min. Because of the slightly exothermic reaction the reflux condenser is attached, and the solution is stirred for 2 h at ambient temperature (Notes 6 and 7). The reaction is quenched with 1N HCl (3 mL) and after stirring for 5 min 4N NaOH (9 mL) is added and the mixture is transferred to a 500-mL separatory funnel containing 90 mL of saturated aqueous $NaHCO_3$ solution. After the first portion of ethyl acetate (75 mL) is added to the dichloromethane solution, the phases are separated and the aqueous phase is extracted with ethyl acetate (2 × 75 mL). The combined organic phase is washed with distilled water (100 mL), dried over anhydrous magnesium sulfate (4 g), filtered, and concentrated by rotary evaporation (45 °C water bath, 38 mmHg) to afford a pale yellow oil (Note 7), which is chromatographed on silica gel (Note 8). Fractions containing the product were collected, concentrated by rotary evaporation (45 °C water bath, 75 mmHg) and dried under high vacuum (25 °C, 0.2 mmHg) to obtain ligand **2** (579–582 mg, 1.58 mmol, 52–53% yield, > 99% ee) as a white solid (Notes 9, 10 and 11).

*B. (1S)-1-(4-Nitrophenyl)-2-nitroethane-1-ol (**4**).* A 100-mL, round-bottomed flask equipped with a magnetic stir bar (cylindrical, 2 × 1 cm) is charged with 2-(1,1-dimethylethyl)-6-[[[(1*R*,2*R*)-2-[(4-pyridinylmethyl)-amino]cyclohexyl]amino]methyl]-phenol (**2**, 606 mg, 1.65 mmol, 5.7 mol%) (Note 12), copper acetate (273 mg, 1.47 mmol, 5.1 mol%) and 30 mL of ethanol (Note 12). Within minutes the reaction mixture becomes deep green. After stirring for 45 min at 23 °C to complete the formation of the Cu(II) complex **3**,[2] solid *p*-nitrobenzaldehyde (4.48 g, 29.1 mmol, 1.00 equiv) and nitromethane (16.2 mL, 18.3 g, 295 mmol, 10 equiv) (Note 13) are added. Stirring is continued for an additional 3 h (Note 14). The deep green solution is concentrated by rotary evaporation (21 °C water bath, 24 mmHg) to give 8.01 g of a dark green solid (92% *ee*) (Note 15). The residue is dissolved in

4.4 mL of methanol (Note 13) and immediately purified by column chromatography (Note 16). Fractions containing the product are combined in a 50-mL round-bottomed flask, concentrated by rotary evaporation (21 °C water bath, 24 mmHg) and dissolved in a minimal amount of methanol (4.4 mL, dissolution aided by use of ultrasound). To facilitate the crystallization the flask is placed in a refrigerator (3 °C, 5 h) and freezer (−20 °C, 12 h). The mother liquor is removed with a pasteur pipette and the yellowish crystals are washed with cold dichloromethane (taken from the freezer; 3 × 0.5 mL), which is removed each time with a Pasteur pipette, and dried (23 °C, 0.2 mmHg) to provide product **4** (4.24 g, 69% yield, 95% *ee*). The mother liquor is concentrated by rotary evaporation (21 °C water bath, 8 mmHg), layered with dichloromethane (ca. 0.5 mL) and cooled (3 °C, 2 h then −20 °C, 24 h). The mother liquor is removed with a pasteur pipette and the yellowish crystals are washed with cold dichloromethane (taken from the freezer; 3 × 0.5 mL), which is again removed each time with a Pasteur pipette, and dried (23 °C, 0.2 mmHg) to give a second crop of yellow crystals (0.77 g, 12% yield, 94% *ee*). The two crops were combined to provide *(1S)-1-(4-nitrophenyl)-2-nitroethane-1-ol (4)* (5.01 g, 81% yield, 95% *ee*) (Notes 15, 17, 18 and 19).

2. Notes

1. A two-tap Schlenk adapter connected to a bubbler and an argon/vacuum manifold is illustrated in Yu, J.; Truc, V.; Riebel, P.; Hierl, E.; Mudryk, B. *Org. Synth.* **2008**, *85*, 64–71.

2. Reagents and solvents were purchased from companies named in parentheses and used without further purification: (1*R*,2*R*)-1,2-diaminocyclohexane (98%, 99% *ee*, Aldrich), 4-pyridinecarboxaldehyde (98%, Acros), 3-*t*-butyl-2-hydroxybenzaldehyde (96%, Aldrich), sodium borohydride (98+%, Acros), anhydrous dichloromethane (puriss., over molecular sieves, ≥99.5%, Sigma-Aldrich), checkers purchased methanol (puriss., over molecular sieves, ≥99.5%) from Sigma-Aldrich and submitters from J. T. Baker (HPLC Gradient Grade). The number of mmol of reagents given in the procedure are calculated based on the purities listed above.

3. In order to achieve the yield given for ligand **2** it is important to add first 4-pyridinecarboxaldehyde followed by 3-*t*-butyl-2-hydroxybenzaldehyde. In case of reversed addition the C_2 symmetric *bis* phenol diaminocyclohexane ligand is the main product.

4. Reaction progress can be monitored by ^{1}H NMR (disappearance of the aldehyde signals at 11.8 and 10.1 ppm). The dark yellow color of the reaction is characteristic of imine formation. The submitters report that the reaction mixture is heated under reflux for 1 h and subsequently stirred for 16 h at ambient temperature, which completed the formation of the imines.

5. A mixture of mono- and diimines is formed; it is not advisable to purify the desired diimine by chromatography since the compound is not stable under the chromatography conditions used (dichloromethane/methanol).

6. The dark yellow solution becomes colorless after reduction of the diimines.

7. The TLC (checkers used Polygram® SIL/UV_{254}-TLC-plates from Macherey-Nagel and submitters from E. Merck) of the reaction mixture (dichloromethane/methanol, 10%) shows the C_1-symmetric ligand **2** as the main spot R_f = 0.35, with two minor impurities at R_f = 0.62 and R_f = 0.77 (UV 254 nm, $KMnO_4$ stain).

8. Column chromatography: 4 cm diameter × 40 cm height of silica gel (145 g) (checkers used "Silica Gel 60" (0.040-0.063 mm) from E. Merck, and submitters used "Silica Gel 60" from Aldrich), eluting with 1.5 L of 3 vol% methanol in dichloromethane and collecting 10 mL fractions. Fraction purity can be assayed by TLC (Note 7). Fractions 42–66 were combined.

9. *2-(1,1-Dimethylethyl)-6-[[[(1R,2R)-2-[(4-pyridinylmethyl)-amino]-cyclohexyl]amino]methyl]-phenol (**2**)* exhibits the following physical and spectroscopic properties: mp 109–110 °C; $[\alpha]_D^{20}$ −109.8 (*c* 1.01, dichloromethane); >99% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.97–1.09 (m, 1 H), 1.11–1.30 (m, 3 H), 1.42 (s, 9 H), 1.68–1.81 (m, 2 H), 2.17–2.36 (m, 4 H), 3.72 (d, *J* = 14.4 Hz, 1 H), 3.83 (d, *J* = 13.5 Hz, 1 H), 3.95 (d, *J* = 14.3 Hz, 1 H), 4.04 (d, *J* = 13.4 Hz, 1 H), 6.72 (t, *J* = 7.6 Hz, 1 H), 6.87 (br. dd, *J* = ca. 7.5, 1.6 Hz, 1 H), 7.19 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.29 (overlaps with $CHCl_3$ residual signal, dd , *J* = 4.4, 1.6 Hz, 2 H), 8.52 (dd, *J* = 4.4, 1.6 Hz, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 24.7, 25.2, 29.7, 31.1, 31.9, 34.8, 49.7, 50.7, 60.5, 62.2, 118.3, 123.1, 124.1, 125.9, 126.3, 137.1, 149.7, 150.0, 157.4; IR (ATR) 3287, 2920, 2363, 1600, 1562, 1435, 1429, 1415, 1385, 1355, 1250, 1114, 1085, 991, 967, 848, 797, 752, 668 cm^{-1}; MS (EI, 70 eV): *m/z* (%) 367 ([M^+], 11), 276 (19), 275 (100), 178 (11), 163 (31), 162 (20), 147 (47), 121 (11), 119 (27), 113 (52), 107 (15), 96 (48), 93 (85), 92 (22),

91 (11), $C_{23}H_{33}N_3O$ (367.53); Anal. calcd: C, 75.16; H, 9.05; N, 11.43. Found: C, 75.03; H, 8.83; N, 11.37.

10. The submitters report that on a reaction scale of 1 mmol (1*R*,2*R*)-1,2-diaminocyclohexane (**1)** and conditions stated in Note 4 the ligand **2** can be isolated in 59% yield exhibiting the following physical properties: mp 111–113 °C; $[\alpha]_D^{20}$ –84.3 (*c* 0.528, ethanol).

11. Because of the strong peak tailing, the enantiomeric excess of the ligand, 2-(1,1-dimethylethyl)-6-[[[(1*R*,2*R*)-2-[(4-pyridinylmethyl) amino]cyclohexyl]amino]methyl]-phenol, could not be determined with high accuracy. However, a more precise measurement was possible for the (1*S*,2*S*) enantiomer prepared from (1*S*,2*S*)-1,2-diaminocyclohexane by the same procedure ($[\alpha]_D^{20}$ +109.5 (*c* 1.01, dichloromethane)). The analysis was performed using HPLC with a Chiralcel® OD-H column (0.46 cm × 25 cm) obtained from Daicel Chemical Industries, Ltd. and a diode array detector. The assay conditions were 95:5 *n*-heptane:*i*-propanol, 20 °C, 0.5 mL/min flow rate, with detection at 220 nm and 263 nm, retention times: (1*R,*2*R*) enantiomer = 31.9 min, (1*S,* 2*S*) enantiomer = 35.2 min. The signal of the minor (1*R,*2*R*) enantiomer was not visible, implying an enantiomeric excess of >99%.

12. In order to accomplish short reaction times and high enantiomeric excess, it is important to use a small excess of ligand over copper acetate.

13. Reagents and solvents were purchased from companies named in parentheses and used without further purification: *p*-nitrobenzaldehyde (99%, Acros), nitromethane (puriss., over molecular sieves, ≥98.5%, Sigma-Aldrich), copper acetate (purum, anhydrous, >98%, Fluka), ethanol (puriss., over molecular sieves, ≥99.8% (v/v), Fluka), dichloromethane (HPLC Gradient Grade, J. T. Baker) and hexane (HPLC Gradient Grade, J. T. Baker), submitters purchased methanol (puriss., over molecular sieves, ≥99.5%) from Sigma-Aldrich.

14. Reaction progress can be monitored by TLC (silica gel, dichloromethane) (checkers used Polygram®SIL/UV254-TLC-plates from Macherey-Nagel) R_f *p*-nitrobenzaldehyde = 0.44, R_f (1*S*)-1-(4-nitrophenyl)-2-nitroethane-1-ol = 0.12 (UV 254 nm, $KMnO_4$ stain).

15. Enantiomeric excess was determined by HPLC with Chiralcel® OD-H column (0.46 cm × 25 cm) obtained from Daicel Chemical Industries, Ltd. and a diode array detector. The assay conditions were 85:15 *n*-heptane:*i*-propanol, 20 °C, 0.8 mL/min flow rate, with detection at 220 nm and

254 nm, retention times: (*R*) enantiomer = 20.0 min, (*S*) enantiomer = 24.8 min.

16. Column chromatography: 3 cm diameter × 20 cm height of silica gel (66 g) ("Silica Gel 60" from Aldrich), eluting with 350 mL of 4:1 dichloromethane/hexanes, then 300 mL of 95:5 hexanes/ethyl acetate, collecting 20 mL fractions. The fraction size collected was changed to 10 mL beginning with fraction 19. Fraction purity was assayed by TLC (Note 13). Fractions containing product (13–48) were combined.

17. Two runs at the 3 g scale afforded yields of 77–81%.

18. *(1S)-1-(4-Nitrophenyl)-2-nitroethane-1-ol* (**4**) exhibits the following physical and spectroscopic properties: mp 83–85 °C; $[\alpha]_D^{20}$ + 25.9 (*c* 0.69, ethanol); 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.13 (s, 1 H), 4.58 (dd, *J* = 16, 14 Hz, 1 H), 4.60 (dd, *J* = 20, 14 Hz, 1 H), 5.61 (m, 1 H), 7.63/8.27 (AA'BB' system, 4 H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 70.1, 80.7, 124.4, 127.1, 145.0, 148.3; IR (ATR) 3479, 1609, 1545, 1506, 1418, 1377, 1346, 1315, 1290, 1215, 1186, 1105, 1076, 1040, 895, 860, 837, 756, 733, 698, 648 cm^{-1}; MS (EI, 70 eV): *m/z* (%) 165 (66), 152 (25), 151 (99), 152 (100), 105 (23), 104 (16), 92 (11), 91 (26), 77 (51), 76 (15), 65 (11), 61 (18), 51 (34), 50 (17), $C_8H_8N_2O_5$ (212.16); Anal. calcd: C, 45.29; H, 3.80; N, 13.20. Found: C, 45.06; H, 3.78; N, 13.21.

19. The submitters report that on a reaction scale of 10 mmol *p*-nitrobenzaldehyde the product *(1S)-1-(4-nitrophenyl)-2-nitroethane-1-ol* (**4**) is obtained in 86% yield exhibiting the following physical properties: mp 91–93 °C; $[\alpha]_D^{20}$ + 26.6 (*c* 0.519, ethanol); ee 98%.

Handling and Disposal of Hazardous Chemicals

The procedures in this article are intended for use only by persons with prior training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011 www.nap.edu). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

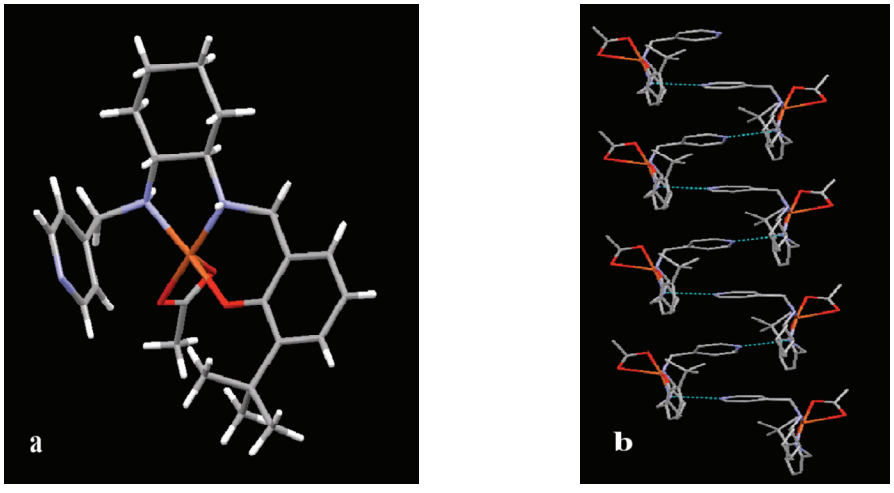
These procedures must be conducted at one's own risk. *Organic Syntheses, Inc*., its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby

disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

3. Discussion

Commercially available chiral 1,2-diaminocyclohexanes have been extensively used to synthesize salen ligands in order to prepare their metal complexes for various catalytic reactions.[2] In recent years the corresponding and less explored diamine ligands were investigated.[3] Except for a few cases[4] most of the diamine ligands were C2 symmetric due to their facile synthesis. In the course of our investigation it was discovered[5] that if aldehydes are employed displaying considerable difference in reactivity C1 symmetric ligands can be easily prepared if the less reactive aldehyde is reacted first to form the monoimine. The two-step, high yielding procedure reported here is not an exception as we have prepared more than 50 C1 symmetric ligands in the same manner since our first paper in this area was published.[5] Hence, this method appears to be of general interest and application.

The Henry (nitro aldol) reaction is an important carbon-carbon bond forming process yielding α-hydroxy nitro compounds that are versatile intermediates in organic synthesis.[6] Asymmetric, catalytic versions of this reaction are of particular interest and significant progress has been achieved using chiral complexes of Zn(II),[7] Cr(III),[8] La(III)[9] and Co(II).[10] However, most investigations were pursued with chiral Cu(II) complexes containing a C2 symmetric four-dentate ligand sphere.[11]



Solid state structure of Cu(II) complex **3**.

The nitro aldol (Henry) reaction described herein is catalyzed by the C1 symmetric Cu(II) complex **3** generated *in situ* from $Cu(OAc)_2$ and ligand **2** derived from commercially available (*R*,*R*)-1,2-diaminocyclohexane. According to X-ray crystallography of complex **3** a helical, supramolecular structure is formed, see **3a** and **3b**, that most likely is maintained in solution.[5] The complex has a high catalytic activity and the nitroaldol reaction can be performed without additives such as organic bases. The procedure provides a valuable method to prepare enantiomerically enriched β-nitro alcohols from nitromethane and various aromatic and aliphatic aldehydes (Table 1).

Table 1. Asymmetric Henry Reactions of Aromatic and Aliphatic Aldehydes with Nitromethane in the presence of catalyst **3**.[5]

entry[a]	aldehyde (R)	time (h)	yield (%)[d]	*ee* (%)[e]
1[b]	2-$NO_2C_6H_4$	3	94	98
2[b]	3-$NO_2C_6H_4$	3	95	96
3[b]	3-pyridyl	3	94	96
4[b]	4-pyridyl	3	96	95
5[b]	Ph	48	75	90
6[b]	4-ClC_6H_4	24	65	90
7[b]	4-FC_6H_4	24	72	87
8[c]	2-thiophenyl	60	58	93
9[c]	2-MeC_6H_4	60	63	88
10[c]	4-MeC_6H_4	60	54	93
11[c]	1-naphthyl	60	75	93
12[c]	4-$MeOC_6H_4$	60	51	85
13[c]	*n*-butyl	60	88	98
14[c]	*t*-butyl	60	91	99
15[c]	cyclohexyl	60	92	98

[a] All reactions were performed at 0.5M concentration of aldehyde in EtOH using 5.4 mol% of ligand **2**, 5 mol% $Cu(OAc)_2$ and 10 equiv. of nitromethane. [b] Reactions were run at r.t. [c] Reactions were run at 0 ^oC. [d] Isolated yield. [e] Enantiomeric excess was determined by chiral HPLC using a Chiralcel® OD-H column. The absolute configuration of products was determined as *S* by comparison of their optical rotations with literature values.

1. Department of Chemistry, University of Basel, St. Johann-Ring 19, CH-4056 Basel, Switzerland.
2. (a) Kleij, A. W., *Eur. J. Inorg. Chem.* **2009**, 193–205; (b) Katsuki, T., *Synlett* **2003**, 281–297.
3. (a) Bandini, M.; Cabbidu, S.; Cadoni, E.; Olivelli, P.; Sinisi, R.; Umani-Ronchi, A.; Usai. M., *Chirality* **2009**, *21*, 239–244; (b) Kowalczyk, R.; Sidorowicz, L.; Skarzewski, J., *Tetrahedron Asymmetry* **2008**, *19*, 2310–2315; (c) Xiong, Y.; Wang, F.; Huang, X.; Wen, Y.; Feng, X., *Chem. Eur. J.* **2007**, *13*, 829–833; (d) Matsumoto, K.; Saito, B.; Katsuki, T., *Chem. Commun.* **2007**, 3619–3627.
4. (a) Steurer, M.; Bolm, C., *J. Org. Chem.* **2010**, *75*, 3301–3310; (b) Arai, T.; Watanabe, M.; Fujiwara, A.; Yokoyama, N.; Yanagisawa, A., *Angew. Chem. Int. Ed.* **2006**, *45*, 5978–5981.
5. Zhang, G.; Yashima, E.; Woggon, W.-D., *Adv. Synth. Catal.* **2009**, *351*, 1255–1262.
6. Palomo, C.; Oiarbide M.; Laso A. *Eur. J. Org. Chem.*, **2007**, 2561–2574.
7. Bulut, A.; Aslan A.; Dogan, O. *J. Org. Chem.*, **2008**, *73*, 7373–7375.
8. Zulauf, A.; Mellah, M.; Schulz E., *J.Org. Chem.*, **2009**, *74,* 2242–2245.
9. Sasai, H.; Suzuki, T.; Arai, S.; Shibazaki, M., *J. Am. Chem. Soc.*, **1992**, *114*, 4418–4420.
10. Kogami, Y.; Nakajima,T.; Ikeno,T.; Yamada, T., *Synthesis,* **2004,** 1947–1950.
11. Evans, D. A.; Rueping, M.; Lam, H.W.; Shaw, J. T.; Downey, C. W., *J. Am. Chem. Soc.*, **2003**, *125*, 12692–12693.

Appendix
Chemical Abstracts Nomenclature; (Registry Number)

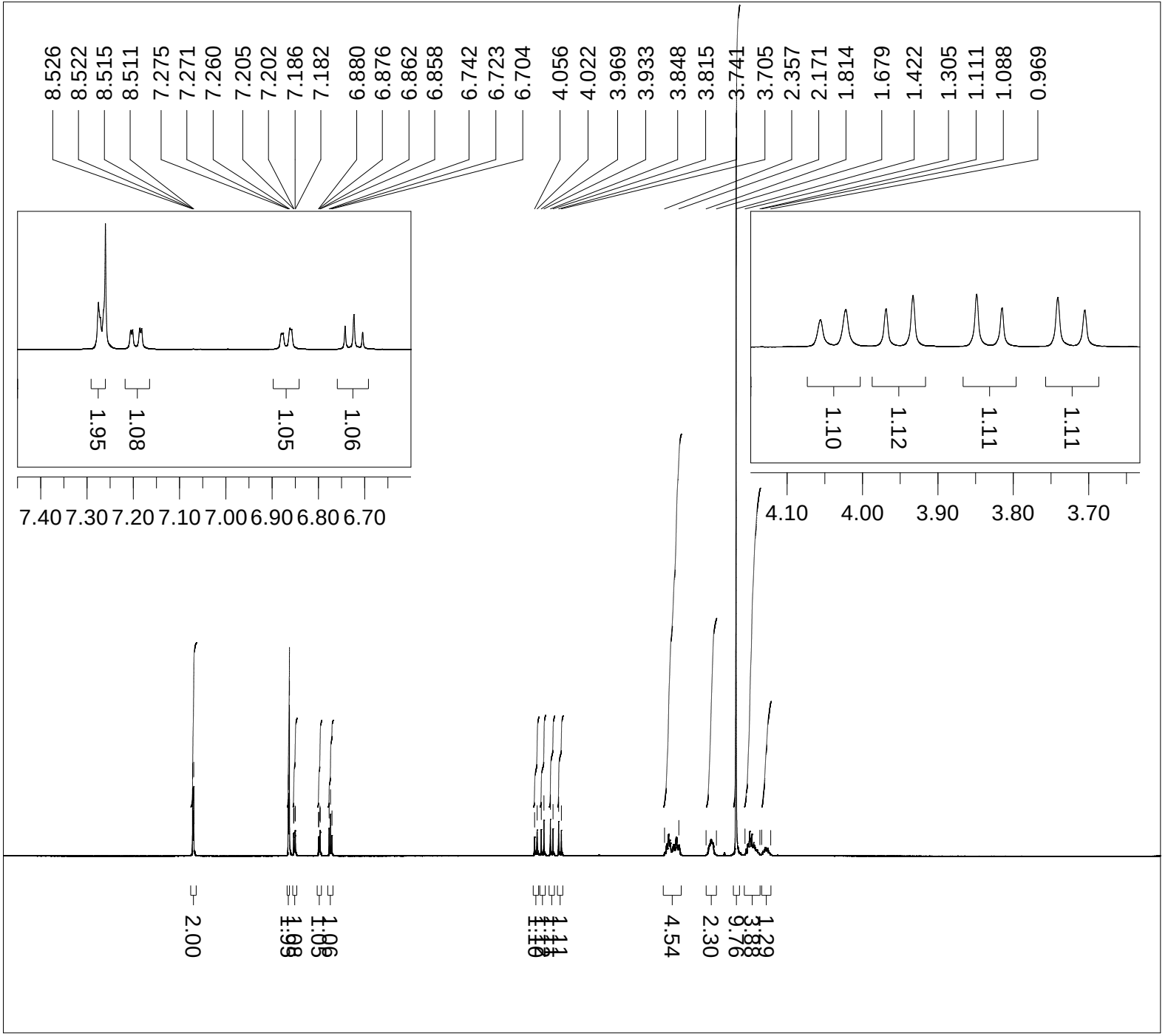
(1*R*,2*R*)-1,2-Diaminocyclohexane; (20439-47-8)
4-Pyridinecarboxaldehyde; (872-85-5)
3-*t*-Butyl-2-hydroxybenzaldehyde: Benzaldehyde, 3-(1,1-dimethylethyl)-2-hydroxy-; (24623-65-2)
Sodium borohydride: Borate(1-), tetrahydro-, sodium (1:1); (16940-66-2)
Copper acetate: Acetic acid, copper(2+) salt (2:1); (142-71-2)
p-Nitrobenzaldehyde: Benzaldehyde, 4-nitro-; (555-16-8)
Nitromethane: Methane, nitro-; (75-52-5)

2-(1,1-Dimethylethyl)-6-[[[(1*R*,2*R*)-2-[(4-pyridinylmethyl)amino]-cyclohexyl]amino]methyl]-phenol; (1200403-97-9)
(1*S*)-1-(4-Nitrophenyl)-2-nitroethane-1-ol; (454217-09-5

Wolf-D. Woggon was born in 1942 in Berlin, Germany. He completed his undergraduate education in Geology and Chemistry at the Freie Universität Berlin and his PhD in Organic Chemistry at the University of Zurich with the late Hans Schmid. After a postdoctoral stay with Alan Battersby in Cambridge (UK) he started his independent research at the University of Zurich and completed his habilitation in 1985. In 1995 he became professor at the University of Basel where he stayed ever since. His research interests include the synthesis of enzyme models, enzymatic reaction mechanisms, the isolation of new enzymes, the synthesis of vitamins, and the development of new ligand-scaffolds for metallo-organic catalysis.

Antoinette Chougnet (born 1949 in France) has completed her undergraduate studies and her PhD+habilitation in 1980 with Andrée Marquet at the University of Paris. She spent one year at Collège de France as a post-doctoral researcher in the group of J. Glowinski. She became professor at the University of Paris in 1988. From 1990 to 2000, she worked at Hoffmann-La Roche (Basel) as head of the group Drug metabolism. In 2000 she joined the University of Basel where her research interests include the study of several cytochromes P450 isoenzymes and the total synthesis of tocopherol together with the biosynthesis of that natural compound.

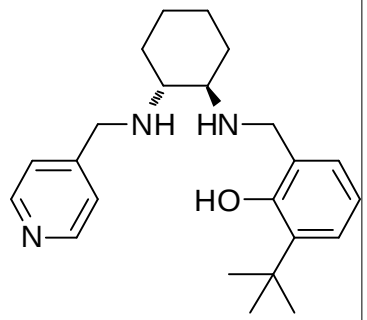
Larissa Pauli was born in Karkaralinsk (Kasachstan) in 1981. She studied chemistry at the University of Basel (Switzerland) where she obtained her B.Sc. in Chemistry in 2008 and her M.Sc. in 2010. She started her Ph.D. studies in 2010 under the supervision of Prof. Andreas Pfaltz at the University of Basel and is currently working in the field of Ir-catalyzed enantioselective hydrogenation.

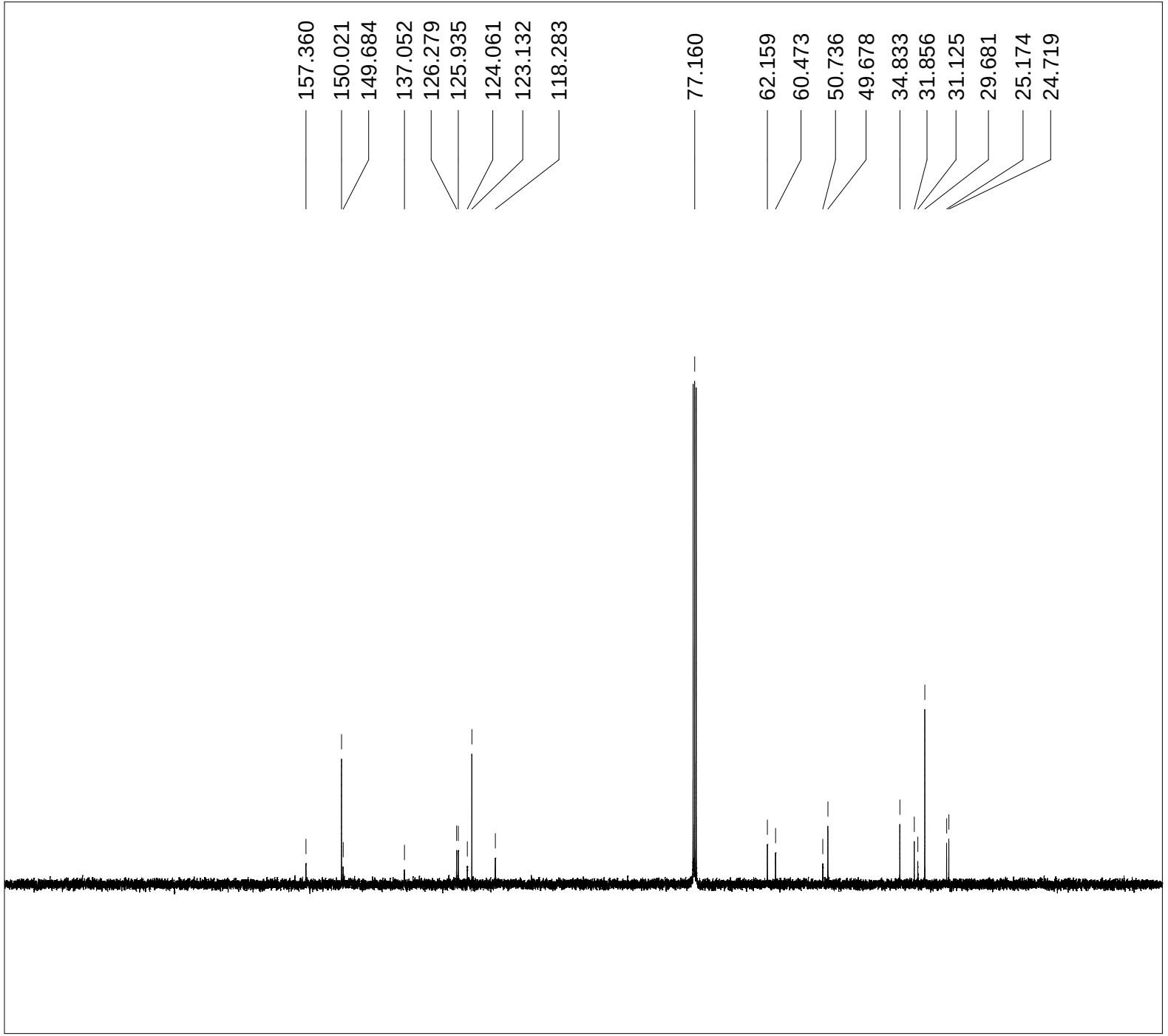


Date:
24 May 2012
Document's Title:
LP057_F42-66_1H

Spectrum Title:
LP057_F42-66
_Proton_16 CDCl3 /opt/topspin pauli 52

Frequency (MHz):
(f1) 400.132
Original Points Count:
(f1) 16446
Actual Points Count:
(f1) 262144
Acquisition Time (sec):
(f1) 1.9998
Spectral Width (ppm):
(f1) 20.552
Pulse Program:
ZG30
Temperature:
300
Number of Scans:
16
Acq. Date:
Tue May 22 05:50:30 PM

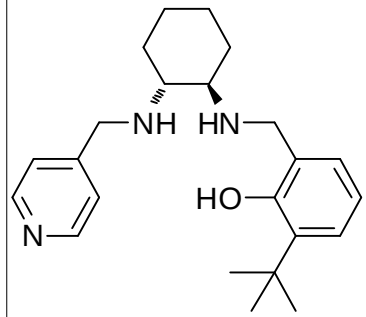


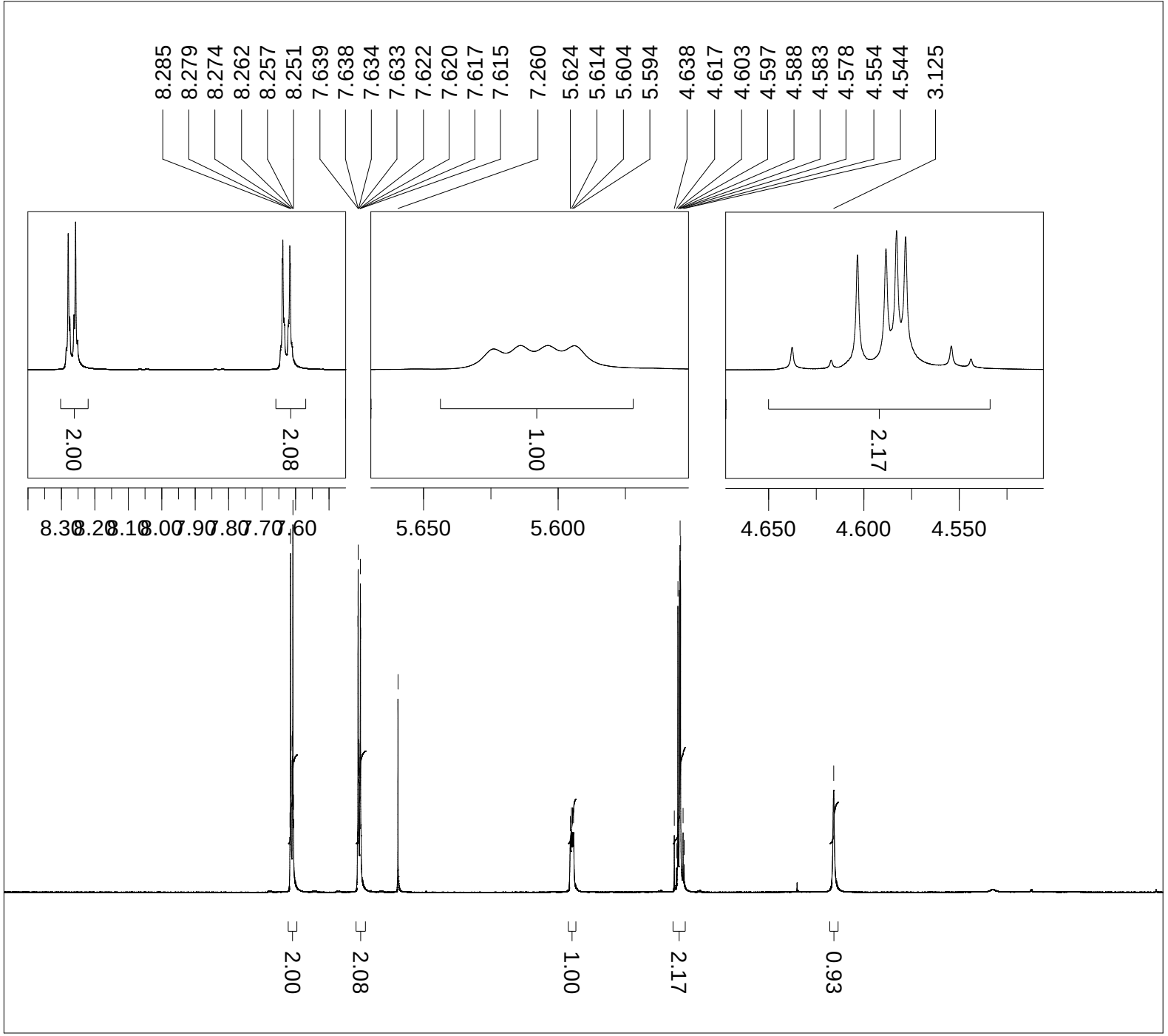


Date:
24 May 2012
Document's Title:
LP057_F42-66_13C

Spectrum Title:
LP057_F42-66
_13Ccpd_ns256 CDCl3 /opt/topspin pauli 52

Frequency (MHz):
(f1) 100.623
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 262144
Acquisition Time (sec):
(f1) 1.3631
Spectral Width (ppm):
(f1) 238.897
Pulse Program:
ZGPG30
Temperature:
300
Number of Scans:
256
Acq. Date:
Tue May 22 09:58:14 PM

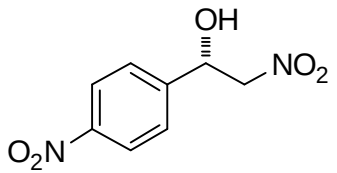


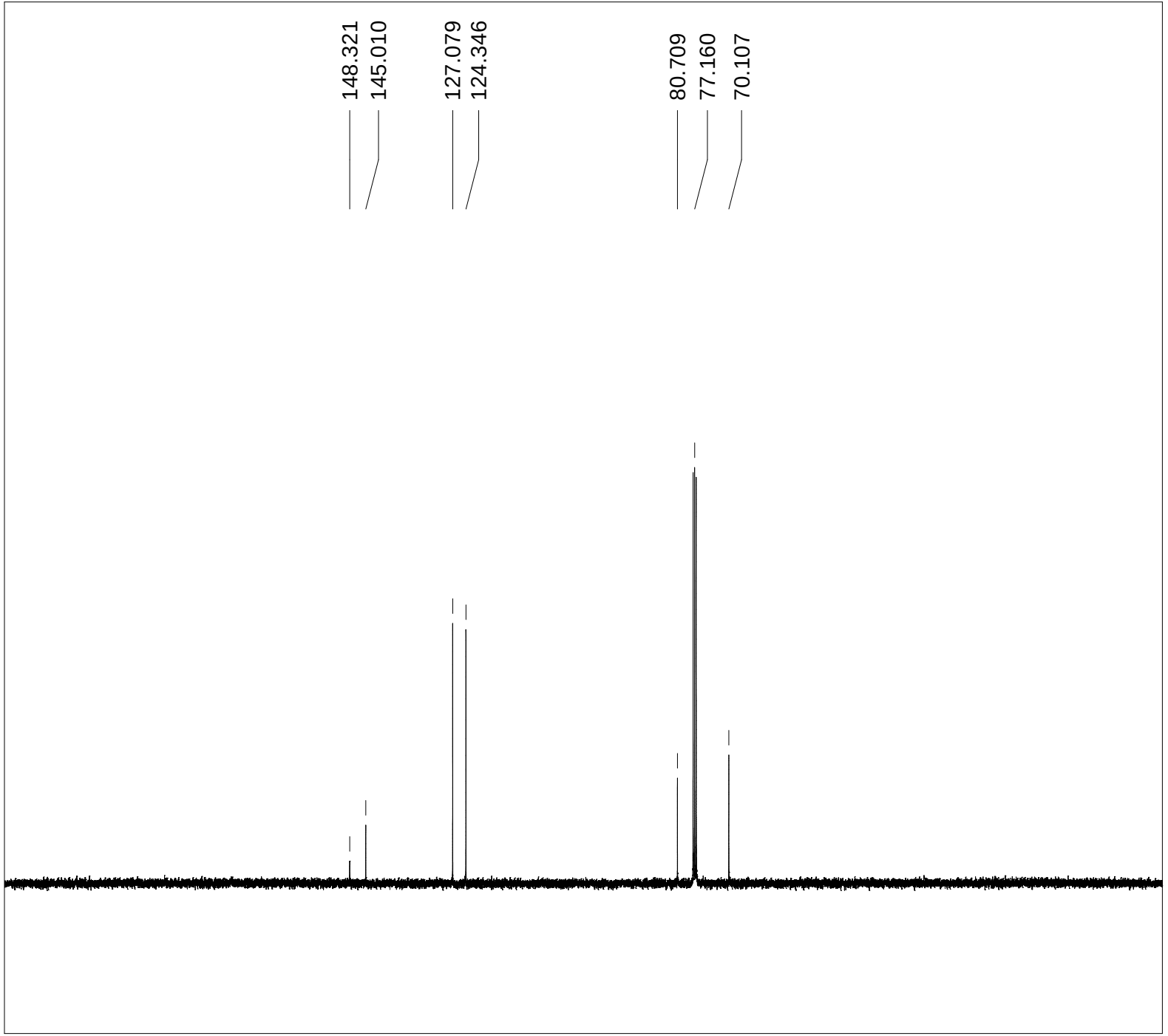


Date:
24 May 2012
Document's Title:
LP101_F14-48_K1_1H

Spectrum Title:
LP101_F14-48_K1
_Proton_16 CDCl3 /opt/topspin pauli 53

Frequency (MHz):
(f1) 400.132
Original Points Count:
(f1) 16446
Actual Points Count:
(f1) 262144
Acquisition Time (sec):
(f1) 1.9998
Spectral Width (ppm):
(f1) 20.552
Pulse Program:
ZG30
Temperature:
300
Number of Scans:
16
Acq. Date:
Tue May 22 05:54:53 PM





Date:
24 May 2012
Document's Title:
LP101_F14-48_K1_13C

Spectrum Title:
LP101_F14-48_K1
_13Ccpd_ns256 CDCl3 /opt/topspin pauli 53

Frequency (MHz):
(f1) 100.623
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 262144
Acquisition Time (sec):
(f1) 1.3631
Spectral Width (ppm):
(f1) 238.897
Pulse Program:
ZGPG30
Temperature:
300
Number of Scans:
256
Acq. Date:
Tue May 22 10:16:59 PM