#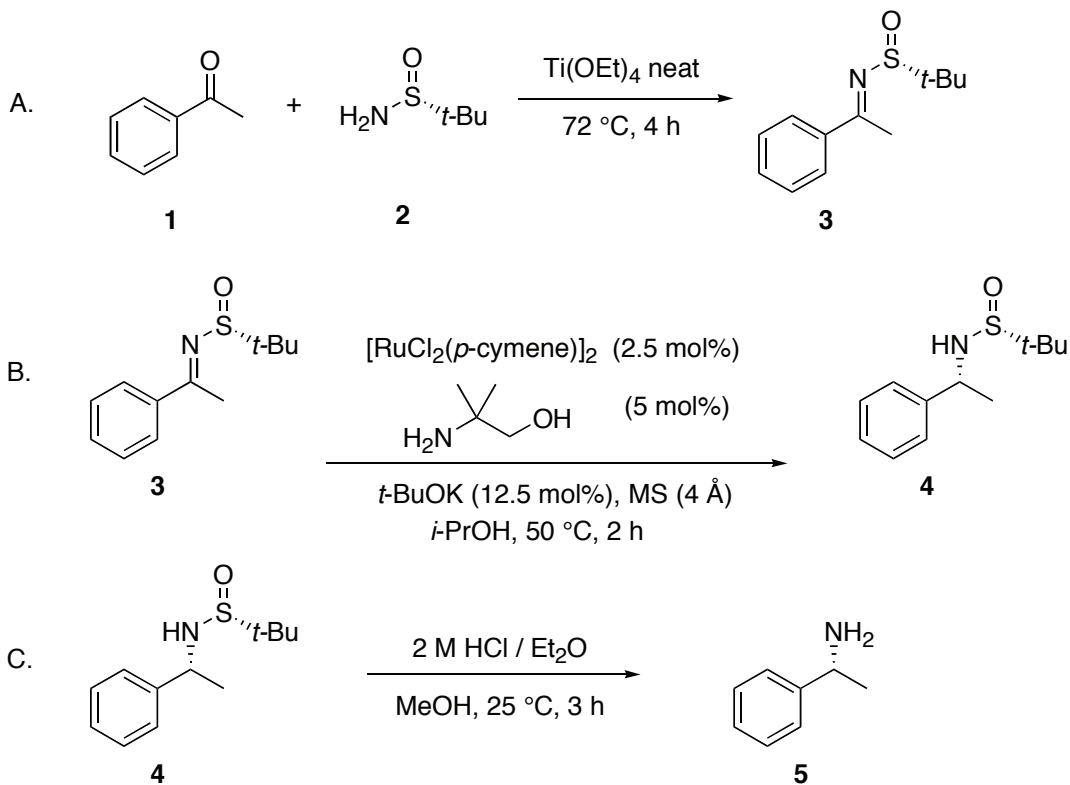 Synthesis of Highly Enantiomerically Enriched Amines by Asymmetric Transfer Hydrogenation of *N-(tert-Butylsulfinyl)*Imines

Submitted by David Guijarro, Óscar Pablo and Miguel Yus.[1]
Checked by Chintan S. Sumaria and Viresh H. Rawal.

1. Procedure

A.   (R$_S$)-N-[1-Phenylethylidene]-2-methylpropane-2-sulfinamide (**3**). An oven-dried 100-mL two-necked round-bottomed flask containing an octagonal Teflon-coated magnetic stirring bar (3.2 × 0.8 cm), fitted with a vacuum adapter and a rubber septum, is charged with acetophenone (**1**) (6.01 g, 50.0 mmol, 1.0 equiv) and (R$_S$)-2-methylpropane-2-sulfinamide (**2**) (6.06 g, 50.0 mmol, 1.0 equiv) (Note 1). After applying vacuum followed by flushing with argon, the stirred mixture is treated with Ti(OEt)$_4$ (21.3 mL, 22.8 g, 100 mmol, 2.0 equiv) (Note 2), added by syringe. At this point, the reaction shows an intense yellow color. The rubber septum is replaced with a glass stopper, and the stirred (700 rpm) mixture is heated so as to maintain the temperature of the oil bath at 72 ºC for 4 h (Note 3), during which period

its color changes to orange. The reaction mixture is cooled to room temperature using a water bath, diluted with ethyl acetate (40 mL), and then transferred to a 250-mL Erlenmeyer flask containing a mixture of ethyl acetate:brine (25 mL:25 mL). The resulting pale yellow suspension is filtered through a short plug of Celite (Note 4), which is washed with ethyl acetate (about 1000 mL total) until no more product elutes (as checked by TLC). The organic layer is concentrated by rotary evaporation (40–80 mmHg, 28 ºC bath temperature) to afford crude imine **3** as a yellow oil (Note 5). The crude material is purified by flash column chromatography (24 × 4.5 cm column containing 160 g of silica gel) (Note 6). A mixture of hexanes:ethyl acetate is used as the eluent, with a gradient of polarity as follows: hexanes:ethyl acetate 100:0 (about 500 mL), 20:1 (about 300 mL), 15:1 (about 300 mL), 9:1 (about 600 mL), 3:2 (about 300 mL), and finally 1:1 until no more product elutes (about 300 mL) (Notes 7 and 8). Fractions containing pure product are concentrated by rotary evaporation (40-80 mmHg, 28 ºC bath temperature) and the resultant product is then subjected to high vacuum (5 mmHg, 40 °C bath temperature) to afford imine **3** (9.54–9.78 g, 85–88% yield) as a yellow solid (Notes 9 and 10).

B.   *(R,R$_S$)-N-(1-Phenylethyl)-2-methylpropane-2-sulfinamide* (**4**).   An oven-dried 500-mL two-necked round-bottomed flask is equipped with an octagonal Teflon-coated magnetic stirring bar (3.8 × 0.9 cm), a condenser topped with a vacuum adapter with an argon inlet, and a rubber septum. After applying vacuum and flushing with argon, the flask is charged with [RuCl$_2$(*p*-cymene)]$_2$ (490 mg, 0.8 mmol, 0.025 equiv), 2-amino-2-methylpropan-1-ol (143 mg, 1.6 mmol, 0.05 equiv), and 4 Å MS (3 g) while maintaining a positive pressure of argon (Notes 11 and 12). The system is again evacuated and filled with argon [5 cycles vacuum (6 seconds), then argon], and a positive pressure of argon is maintained throughout the remainder of the experiment. Dry isopropyl alcohol (25 mL) is added using a syringe (Note 13) and the rubber septum is replaced by a glass stopper. The stirred (450 rpm) reaction mixture is then placed in a preheated oil bath (bath temperature 86 ºC) for 25 min, resulting in a color change to cherry-red (Note 14). The oil-bath is replaced with a water-bath (preheated to 50 ºC) and heating is adjusted to maintain the temperature at about 50 °C (Note 15). After replacing the glass stopper with a rubber septum, a previously prepared solution of imine **3** (7.147 g, 32.0 mmol, 1.0 equiv) in dry isopropyl alcohol (160 mL) under argon is added to the reaction mixture using a cannula (over about 10 min), and the stirring speed is increased to

600 rpm. The temperature of the system is allowed to stabilize at 50 ℃ over approximately 5 minutes, then a previously prepared solution of potassium *tert*-butoxide (449 mg, 4.0 mmol, 0.125 equiv) in dry isopropyl alcohol (40 mL) is added to the reaction mixture using a syringe (Note 16). The resulting brownish mixture is stirred at 50 ℃ (external temperature) for 2 h (Note 17). The reaction mixture is cooled to room temperature using a water bath for 15 min, then filtered through a short plug of silica gel (Note 18), which is washed with ethyl acetate (about 600 mL total) until no more product elutes (as checked by TLC). In order to ensure the removal of the ruthenium complex, solvents are removed by rotary evaporation (40–80 mmHg, 28 ℃ bath temperature) and the residue is dissolved in 40 mL of ethyl acetate and passed through a short plug of silica gel (Note 19), which is washed with ethyl acetate (about 500 mL total) until no more product elutes (as checked by TLC). The filtrate is concentrated by rotary evaporation (40–80 mmHg, 28 ℃ bath temperature) and then subjected to high vacuum (5 mmHg, 40 °C bath temperature) to afford pure sulfinamide **4** (7.20–7.22 g, >99% yield) as a brown oil (Notes 20, 21, and 22).

C. (R)-1-Phenylethanamine (**5**). A 250-mL one-necked round-bottomed flask is equipped with an octagonal Teflon-coated magnetic stirring bar (3.2 × 0.8 cm) and sealed with a septum fitted with needle connected to a vacuum/nitrogen line. The flask is purged using a vacuum followed by nitrogen introduction (3 times) and maintained under a positive pressure of nitrogen. It is then charged with **4** (6.76 g, 30.0 mmol, 1.0 equiv) and dry methanol (60 mL) (Note 23) using a syringe. The solution is cooled to 0−5 ℃ using an ice-water bath. While stirring, a 2M solution of HCl in diethyl ether (75 mL, 150 mmol, 5.0 equiv) is added by syringe (Note 24). After 5 min, the cooling bath is removed and the reaction mixture is stirred (600 rpm) at room temperature for 3 h. The solvent is removed by rotary evaporation (10–80 mmHg, 28 ℃ bath temperature). The residue is dissolved in aqueous 2M HCl solution (100 mL) then extracted with ethyl acetate (2 × 80 mL). While the combined organic layers are discarded, the acidic aqueous layer is cooled to 0−5 ℃ using an ice-water bath and treated with aqueous 6M NaOH solution (100 mL), which is added in portions over 5 min while stirring, resulting in a pH > 12. The resulting mixture is extracted with ethyl acetate (3 × 50 mL) and the combined organic layers are washed with H_2O (25 mL) and brine (25 mL). The organic layer is dried over anhydrous magnesium sulfate (4 g), filtered, then concentrated by rotary evaporation (40–80 mmHg, 28 ℃ bath temperature) (Note 25) to

afford pure amine **5** (3.09–3.22 g, 85–88% yield, 95% *ee* of the (*R*)-enantiomer) as a pale yellow oil (Notes 26 and 27).

2. Notes

1. Acetophenone **1** (98%) was purchased from Acros Organics (Ref. No. 102412500). (*R*$_S$)-2-Methylpropane-2-sulfinamide **2** (99%) was purchased from AK Scientific, Inc. (Ref. No. 70308). Both compounds were used as received.

2. Titanium tetraethoxide (33-35% TiO$_2$) was purchased from Alfa Aesar (Ref. 77142) and used as received.

3. The reaction progress can be monitored by TLC analysis on Merck Silica Gel 60 F$_{254}$ glass plates (Ref. 1057150001) and visualization with a UV lamp. Using hexanes:ethyl acetate (7:3) as eluent, acetophenone **1** has an R$_f$ = 0.64, sulfinamide **2** has an R$_f$ = 0 and *N*-(*tert*-butylsulfinyl)imine **3** has an R$_f$ = 0.30.

4. The dimensions of the plug of Celite: 8 cm diameter × 2 cm height.

5. ^{1}H NMR analysis of the reaction crude showed that the conversion to imine **3** was around 90%.

6. Silica gel 60, 230-400 mesh (pore size 60 Å, particle size 40-63 μm) purchased from Sorbent Technologies was used.

7. Imine **3** has an intense yellow color while the other reagents are colorless, allowing visual monitoring of product elution. When the yellow band reaches the bottom of the column (after about 500 mL of 9:1 hexanes:ethyl acetate) fractions of 20 mL are collected using 30 mL test-tubes until no more product is eluted.

8. The column fractions were checked by TLC analysis as described in Note 3.

9. The submitters note that if **3** does not solidify after removing the solvent under reduced pressure, the resulting oil solidifies to a yellow solid when kept in a freezer (under argon atmosphere, ca. −25 ºC) overnight.

10. The physical and spectroscopic properties of imine **3** are as follows:[2] mp 36 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ: 1.33 (s, 9 H), 2.77 (s, 3 H), 7.38–7.52 (m, 3 H), 7.89 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ: 19.7, 22.4 (3 C), 57.3, 127.1 (2 C), 128.3 (2 C), 131.6, 138.6, 176.3; IR (neat, cm^{-1}) 2979, 1606, 1594, 1572, 1276, 1089, 1067; HRMS (ES+) m/z calcd for C$_{12}$H$_{17}$NOSNa (M$^+$ + Na): 246.0929 Found: 246.0927. [α]$^{20}_D$ −14.4 (c 1.09, CH$_2$Cl$_2$), {Submitters: [α]$^{20}_D$ −13.0 (c 2.22, CH$_2$Cl$_2$)}.

Anal. calcd. for $C_{12}H_{17}NOS$: C, 64.53; H, 7.67; N, 6.27. Found: C, 64.76; H, 7.57; N, 6.30.

11. [RuCl$_2$(*p*-cymene)]$_2$ (98%) was purchased from Strem Chemicals (Ref. 44-0190). 2-Amino-2-methylpropan-1-ol (≥95%) was purchased from Sigma-Aldrich Chemical Co. (Ref. A9199). Both were used as received.

12. Molecular sieves (4 Å; 8-12 mesh beads), purchased from Fischer Scientific (Ref. M514-500), were activated before use by heating at 190 ºC for 3 h in a Kugelrohr apparatus under reduced pressure (5 mmHg).

13. Isopropyl alcohol (puriss, absolute over MS, ≥99.5%) (H$_2$O ≤ 0.005%) was purchased from Sigma-Aldrich Chemical Co. (Ref. 59309) and used as received.

14. The submitters report that ruthenium complex formation was incomplete if the oil-bath temperature was lower than 82 ºC.

15. The change from an oil-bath to a water-bath speeds up cooling of the reaction mixture to 50 ºC.

16. Potassium *tert*-butoxide (≥98%) was purchased from Sigma-Aldrich Chemical Co. (Ref. 156671). It was activated before use by heating for 4 h at 175 ºC in a Kugelrohr apparatus under reduced pressure (5 mmHg).

17. The reaction progress can be monitored by TLC analysis on Merck Silica Gel 60 F$_{254}$ glass plates (Ref. 1057150001) and visualized with phosphomolibdic acid (5% in EtOH). Using hexanes:ethyl acetate (7:3) as eluent, imine **3** has an R$_f$ = 0.30 and the reduction product **4** has an R$_f$ = 0.15.

18. Silica gel 60 plug (230-400 mesh, pore size 60 Å, particle size 40-63 µm): 6 cm diameter × 7 cm height.

19. Silica gel 60 plug (230-400 mesh, pore size 60 Å, particle size 40-63 µm): 5 cm diameter × 5 cm height.

20. ^{1}H NMR and ^{13}C NMR analysis of the isolated crude material indicated that imine **3** had cleanly and completely converted to sulfinamide **4**, making further purification unnecessary.

21 The physical and spectroscopic properties of compound **4** are as follows:[3] ^{1}H NMR (500 MHz, CDCl$_3$) δ: 1.24 (s, 9 H), 1.51 (d, J = 6.5 Hz, 3 H), 3.42 (br s, 1 H), 4.55 (qd, J = 6.5, 3.0 Hz, 1 H), 7.27–7.38 (m, 5 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ: 22.6 (3 C), 22.7, 53.9, 55.4, 126.5 (2 C), 127.8, 128.7 (2 C), 144.0; IR (neat, cm^{-1}) 3214, 2974, 2927, 1455, 1363, 1055, 938, 762, 700; HRMS (ES+) *m/z* calcd for $C_{12}H_{19}NOSNa$ (M$^+$ + Na): 248.1085 Found: 248.1087. Checkers: [α]$^{20}_D$ −40.6 (c 1.2, EtOAc); Submitters: [α]$^{20}_D$

−42.5 (c 1.9, EtOAc). Anal. Calcd. For $C_{12}H_{19}NOS$: C, 63.96; H, 8.50; N, 6.22. Found: C, 63.67; H, 8.34; N, 6.29.

22. A 300 mg sample was purified by column chromatography (6 × 1.5 cm column containing 6 g of silica gel). A mixture of hexanes:ethyl acetate was used as eluent, with a gradient of polarity as follows: 7:3 (10 mL), 3:2 (20 mL), 1:1 (20 mL), and 2:3 until no more product elutes (about 50 mL). Compound **4** was isolated by rotary evaporation (276 mg, 92 % recovery). ^{1}H and ^{13}C NMR spectra, as well as $[\alpha]_D^{20}$, were identical to the crude product (Note 21). Anal. Calcd. For $C_{12}H_{19}NOS$: C, 63.96; H, 8.50; N, 6.22. Found: C, 64.03; H, 8.49; N, 6.30.

23. Anhydrous methanol (99.8%) was purchased from Sigma-Aldrich Chemical Co. (Ref. 322415) and used as received.

24. The 2M solution of HCl in diethyl ether was purchased from Alfa Aesar (Ref. H26914) and used as received.

25. **Important:** The final product <u>should not</u> be concentrated to dryness. The concentration should be halted with about 5 mL of liquid remaining. Final solvent removal was carried out by gently blowing a stream of nitrogen or argon over the top of the liquid at atmospheric pressure for 5-10 min, until NMR showed the clean product.

26. The physical and spectroscopic properties of amine **5** are as follows:[4] ^{1}H NMR (300 MHz, CDCl$_3$) δ: 1.39 (d, J = 6.5 Hz, 3 H), 1.56 (br s, 2 H), 4.11 (q, J = 6.5 Hz, 1 H), 7.20–7.27 (m, 1 H), 7.30–7.39 (m, 4 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ: 25.6, 51.3, 125.6 (2 C), 126.7, 128.4 (2 C), 147.8; IR (neat, cm^{-1}) 3364, 3029, 2969, 1617, 1559, 1474, 1450, 1376, 1027, 764, 696; HRMS (ES+) *m/z* calcd for $C_8H_{11}NNa$ (M$^+$ + Na): 144.0789 Found: 144.0780. Submitters: $[\alpha]^{20}_D$ +31.5 (c 2.7, CHCl$_3$); Aldrich {Ref. 77879, for (*R*)-**5** (99% *ee*)}: $[\alpha]^{20}_D$ +33.8 (c 1.2, CHCl$_3$).

27. The enantiomeric excess of amine **5** was evaluated as follows. A solution of **5** (24 mg, 0.2 mmol) in dichloromethane (5 mL) was cooled to 0−5 ºC using an ice-water bath. An aqueous 2M NaOH solution (5 mL) was added followed by benzoyl chloride (46 μL, 0.4 mmol), and the resulting mixture was stirred for 4 h at room temperature. The organic layer was separated and washed with aqueous 2M NaOH solution (2 × 5 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness under reduced pressure (40–80 mmHg), to afford the corresponding benzamide **6** (40 mg, 89% yield) as a white solid. Compound **6** was analyzed by HPLC on an Agilent 1100-series instrument equipped with a Chiracel OD-H column (25 × 0.46 cm), using 10% isopropyl alcohol

in *n*-hexane as eluent, a flow rate of 0.5 mL/min and UV detection at 240 nm. The retention times of the two enantiomers were 27.2 min (*R*, 97.4%) and 39.9 min (*S*, 2.6%). The racemic amine *rac*-**5** was prepared by reductive alkylation of ammonia by acetophenone following a literature procedure[5] and was benzoylated as described above.

6
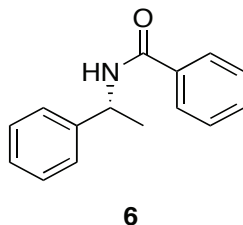
Handling and Disposal of Hazardous Chemicals

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.
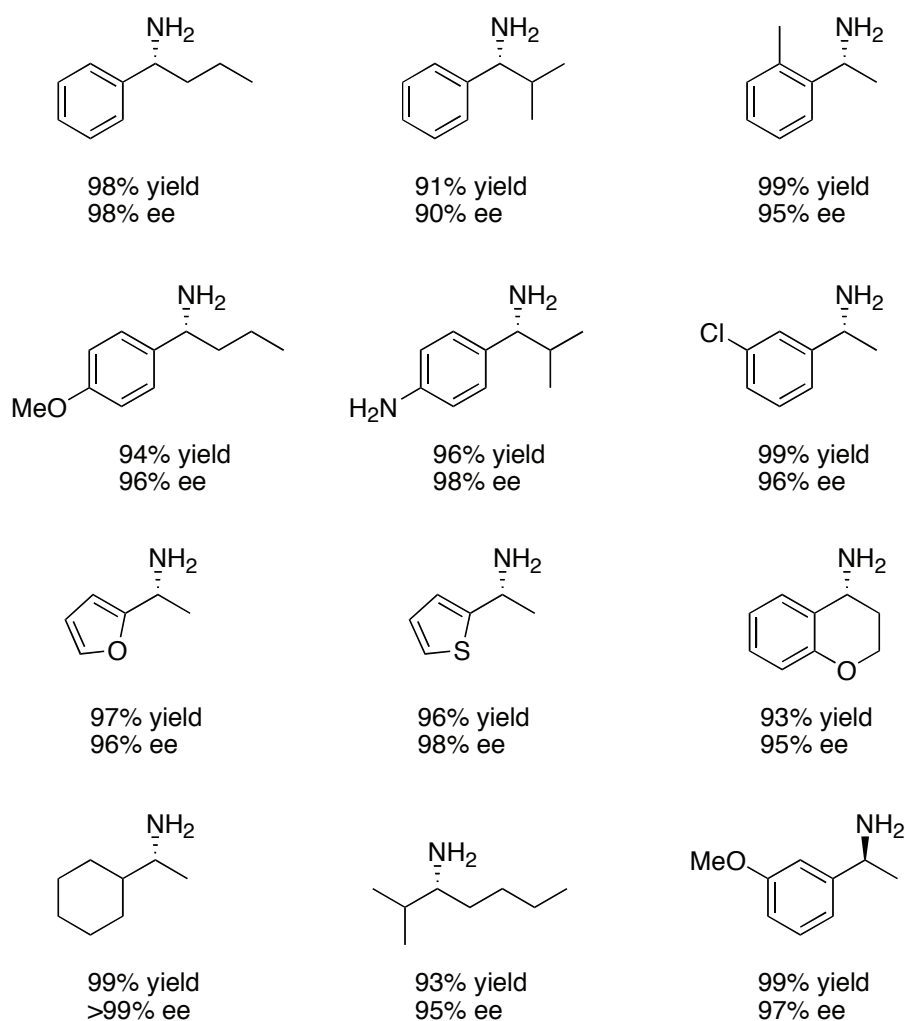
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3. Discussion

The diastereoselective reduction of *N*-(*tert*-butylsulfinyl)ketimines is among the most useful methods for the preparation of enantiomerically enriched amines. The asymmetric reduction of this type of imine has been performed using boranes,[6a,6b,7] sodium or lithium borohydrides,[6,7,8] aluminium hydrides,[6b,7,8] and diethylzinc in the presence of Ni(acac)$_2$.[9] The present procedure utilizes a methodology based on asymmetric transfer hydrogenation, which is a very convenient reduction protocol because it avoids the handling of molecular hydrogen or metallic hydrides, among other reasons. Thus, highly enantiomerically enriched α-branched primary

344

amines are obtained in excellent yields by the diastereoselective reduction of a variety of sulfinylimines followed by desulfinylation of the nitrogen atom.[10] The *N*-(*tert*-butylsulfinyl)imines are prepared by reaction of stoichiometric amounts of the corresponding ketones and 2-methylpropane-2-sulfinamide in the presence of two equivalents of Ti(OEt)$_4$ under solvent-free conditions.[11] The obtained imines **3** are reduced by asymmetric transfer hydrogenation using isopropyl alcohol as hydrogen source and, as a catalyst, a ruthenium complex bearing a commercially available simple achiral β-aminoalcohol: 2-amino-2-methylpropan-1-ol. This catalyst has been shown to be very versatile, giving good results for the reduction of a variety of aromatic, heteroaromatic and aliphatic sulfinylketimines, including several examples of sterically congested imines. The reduction products **4** are treated with a solution of HCl in a mixture of Et$_2$O and MeOH to afford the

Table 1. Other primary amines prepared by this procedure

98% yield 98% ee	91% yield 90% ee	99% yield 95% ee
94% yield 96% ee	96% yield 98% ee	99% yield 96% ee
97% yield 96% ee	96% yield 98% ee	93% yield 95% ee
99% yield >99% ee	93% yield 95% ee	99% yield 97% ee

corresponding free primary amines **5** in excellent yields and enantiomeric excesses (Table 1).

It is worth noting that very good results are obtained for the reduction of the less reactive aliphatic imines. Our procedure represents a general method for the synthesis of highly enantiomerically enriched aromatic and aliphatic primary amines. The enantiomeric (*S*)-amines are also readily accessible with the same optical purity using the same ruthenium catalyst by changing the absolute configuration of the sulphur atom in the starting sulfinamide (see the last example in Table 1).

The synthetic utility of some of the obtained α-branched primary amines has already been shown. For instance, (*S*)-1-(3-methoxyphenyl)ethanamine has been used as a key intermediate in a short total synthesis of (*S*)-Rivastigmine, a cholinesterase inhibitor used for the treatment of moderate dementia in patients with Alzheimer or Parkinson diseases.[12]
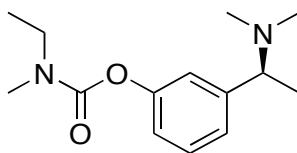
(*S*)-Rivastigmine

1. Departamento de Química Orgánica, Facultad de Ciencias and Instituto de Síntesis Orgánica (ISO), Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain. E-mail: dguijarro@ua.es; oscar.pablo@ua.es; yus@ua.es. We thank the Spanish Ministerio de Ciencia e Innovación (MICINN; grant no. CONSOLIDER INGENIO 2010-CSD2007-00006, CTQ2007-65218 and CTQ11-24151), the Generalitat Valenciana (Grant No. PROMETEO/2009/039 and FEDER), and the University of Alicante for generous and continuous financial support, as well as MEDALCHEMY S.L. for a gift of chemicals. O. P. thanks the Spanish Ministerio de Educación for a predoctoral fellowship (Grant no. AP-2008-00989).

2. Imine **3** is a known compound. See, for instance: Colyer, J. T.; Andersen, N. G.; Tedrow, J. S.; Soukup, T. S.; Faul, M. M. *J. Org. Chem.* **2006**, *71*, 6859.

3. Sulfinamide **4** is a known compound. See, for instance: Cano, R.; Ramón, D. J.; Yus, M. *J. Org. Chem.* **2011**, *76*, 5547.

4. The physical and spectroscopic properties of the obtained amine **5** matched those of a commercially available sample (99% *ee*) purchased from Aldrich (Ref. 77879).

5. Miriyala, B.; Bhattacharyya, S.; Williamson, J. S. *Tetrahedron* **2004**, *60*, 1463.

6. See, for instance: (a) Ellman, J. A. *Pure & Appl. Chem.* **2003**, *75*, 39. (b) Zhou, P.; Chen, B.-C.; Davis, F. A. *Tetrahedron* **2004**, *60*, 8003. (c) Ferreira, F.; Botuha, C.; Chemla, F.; Pérez-Luna, A. *Chem. Soc. Rev.* **2009**, *38*, 1162.

7. See, for instance: (a) Dutheuil, G.; Couve-Bonnaire, S.; Pannecoucke, X. *Angew. Chem. Int. Ed.* **2007**, *46*, 1290. (b) Liu, Z.-J.; Liu, J.-T. *Chem. Commun.* **2008**, 5233. (c) Martjuga, M.; Shabashov, D.; Belyakov, S.; Liepinsh, E.; Suna, E. *J. Org. Chem.* **2010**, *75*, 2357.

8. See, for instance: (a) Peltier, H. M.; Ellman, J. A. *J. Org. Chem.* **2005**, *70*, 7342. (b) Tanuwidjaja, J.; Peltier, H. M.; Ellman, J. A. *J. Org. Chem.* **2007**, *72*, 626. (c) Denolf, B.; Leemans, E.; De Kimpe, N. *J. Org. Chem.* **2007**, *72*, 3211.

9. Xiao, X.; Wang, H.; Huang, Z.; Yang, J.; Bian, X.; Qin, Y. *Org. Lett.* **2006**, *8*, 139.

10. Pablo, O.; Guijarro, D.; Kovács, G.; Lledós, A.; Ujaque, G.; Yus, M. *Chem. Eur. J.* **2012**, *18*, 1969.

11. Collados, J. F.; Toledano, E.; Guijarro, D.; Yus, M. *J. Org. Chem.* **2012**, *77*, 5744.

12. Mangas-Sánchez, J.; Rodríguez-Mata, M.; Busto, E.; Gotor-Fernández, V.; Gotor, V. *J. Org. Chem.* **2009**, *74*, 5304.

Appendix
Chemical Abstracts Nomenclature; (Registry Number)

Acetophenone: 1-phenyl-ethanone; (98-86-2)

(R_S)-2-Methylpropane-2-sulfinamide: [*S*(*R*)]-2-methyl-2-propanesulfinamide; (196929-78-9)

Titanium(IV) ethoxide: tetraethyl titanate; (3087-36-3)

[RuCl$_2$(*p*-cymene)]$_2$: Di-μ-chlorodichlorobis[(1,2,3,4,5,6-μ)-1-methyl-4-(1-methylethyl)benzene]di-Ruthenium; (52462-29-0)

2-Amino-2-methylpropan-1-ol: 2-amino-2-methyl-1-propanol; (124-68-5)

(*R*)-1-Phenylethanamine: (*R*)-α-methyl-benzenemethanamine; (3886-69-9)

Miguel Yus was born in Zaragoza (Spain) in 1947, and received his BSc (1969), MSc (1971) and PhD (1973) degrees from the University of Zaragoza. After spending two years as a postdoctoral fellow at the Max Planck Institut für Kohlenforschung in Mülheim, Ruhr he returned to the University of Oviedo where he became associate professor in 1977, being promoted to full professor in 1987. In 1988 he moved to the University of Alicante where he is currently the head of the Organic Synthesis Institute (ISO). His current research interest is focused on the preparation of reactive functionalized organometallic compounds and their use in synthetic organic chemistry and asymmetric catalysis.

David Guijarro was born in Alicante in 1967. He received his BSc (1990), MSc (1991) and PhD (1994) degrees in Chemistry from the University of Alicante. He did a postdoctoral stay at the University of Uppsala (Sweden) (1995-1997), after which he went back to the University of Alicante, where he has occupied the following academic positions: University College Professor (2000-2003), Associate Professor (2003-2011) and Full Professor (currently). He has been visiting scientist at the University of Warwick (Coventry, UK) (2009). His current research interests are focused on asymmetric synthesis, especially in stereoselective additions of organozinc reagents to carbonyl compounds and imines and in reduction processes of the same type of compounds by hydrogen transfer reactions.

Óscar Pablo Rodríguez was born in 1985 in Alicante (Spain). He obtained his BSc in Chemistry in 2008 from the University of Alicante with an honorary mention for his academic achievements. In 2008 he started his PhD studies at the same university under the supervision of Professors Miguel Yus and David Guijarro. His current research activities are focused on the asymmetric transfer hydrogenation of activated imines. He is interested in asymmetric synthesis and the development of new synthetic methodologies. He is co-author of 5 publications in international journals.

Chintan S. Sumaria was born in 1987 in Mumbai, India. He obtained his undergraduate education at the Indian Institute of Technology – Bombay (IIT Bombay), Mumbai, where he carried out undergraduate research in the areas of chemical biology and synthetic methodology. In 2011, he joined the University of Chicago Chemistry Graduate Program and has been working on expanding the scope the Inverse-Electron Demand Diels Alder reactions of azadienes in the research group of Professor Viresh H. Rawal. He has been the recipient of the KVPY scholarship funded by the Department of Science and Technology of the Government of India and the Burjor-Godrej scholarship offered by the Department of Chemistry, IIT Bombay.
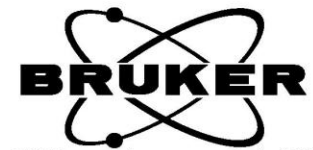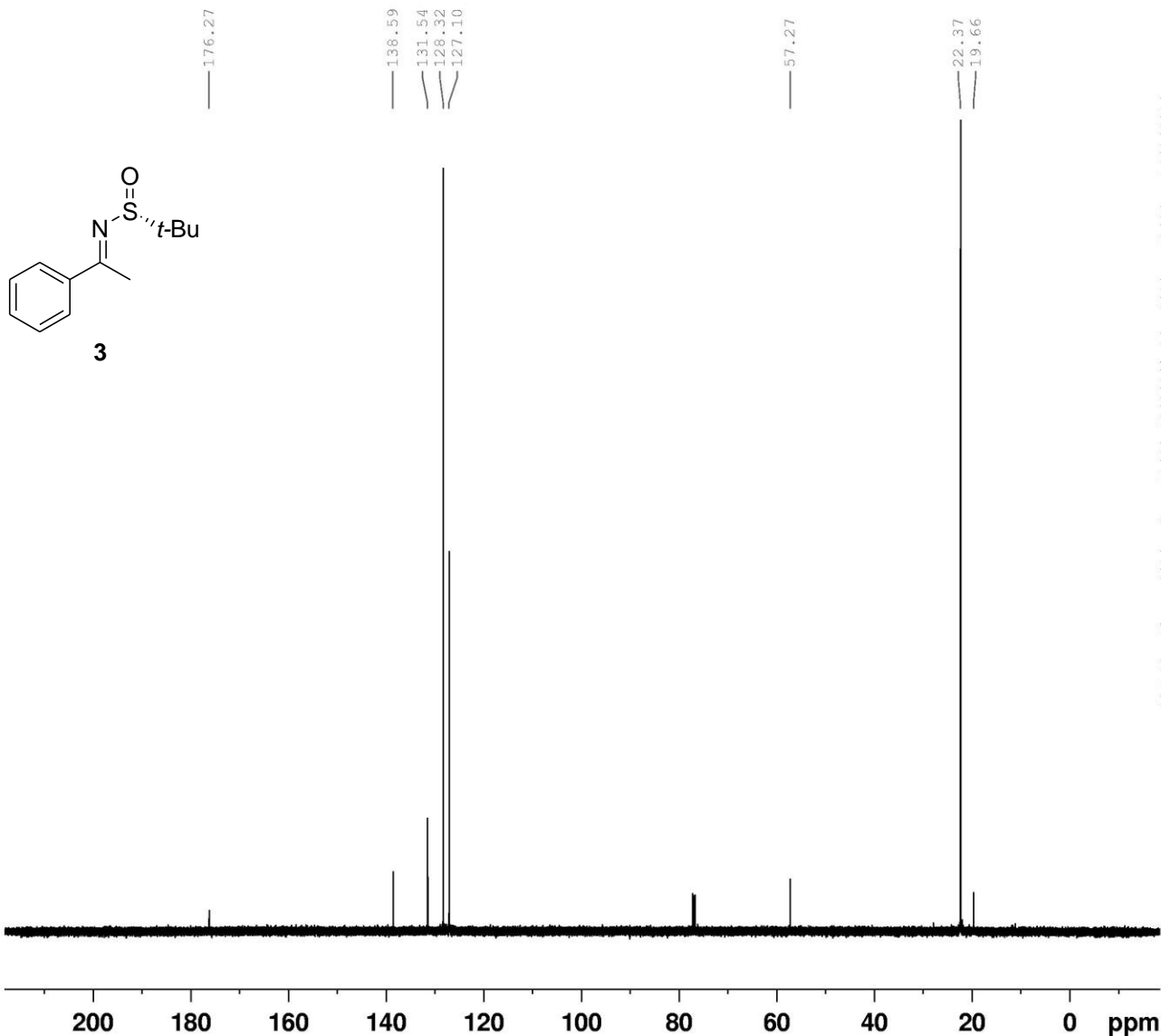
(*R*_s)-N-[1-1Phenylethylidene]-2-methylpropane-2-sulfinamide (**3**)

(R_s)-N-[1-1Phenylethylidene]-2-methylpropane-2-sulfinamide (**3**)

7.898
7.883
7.501
7.486
7.482
7.474
7.472
7.438
7.424
7.422
7.407

2.768

1.327

3
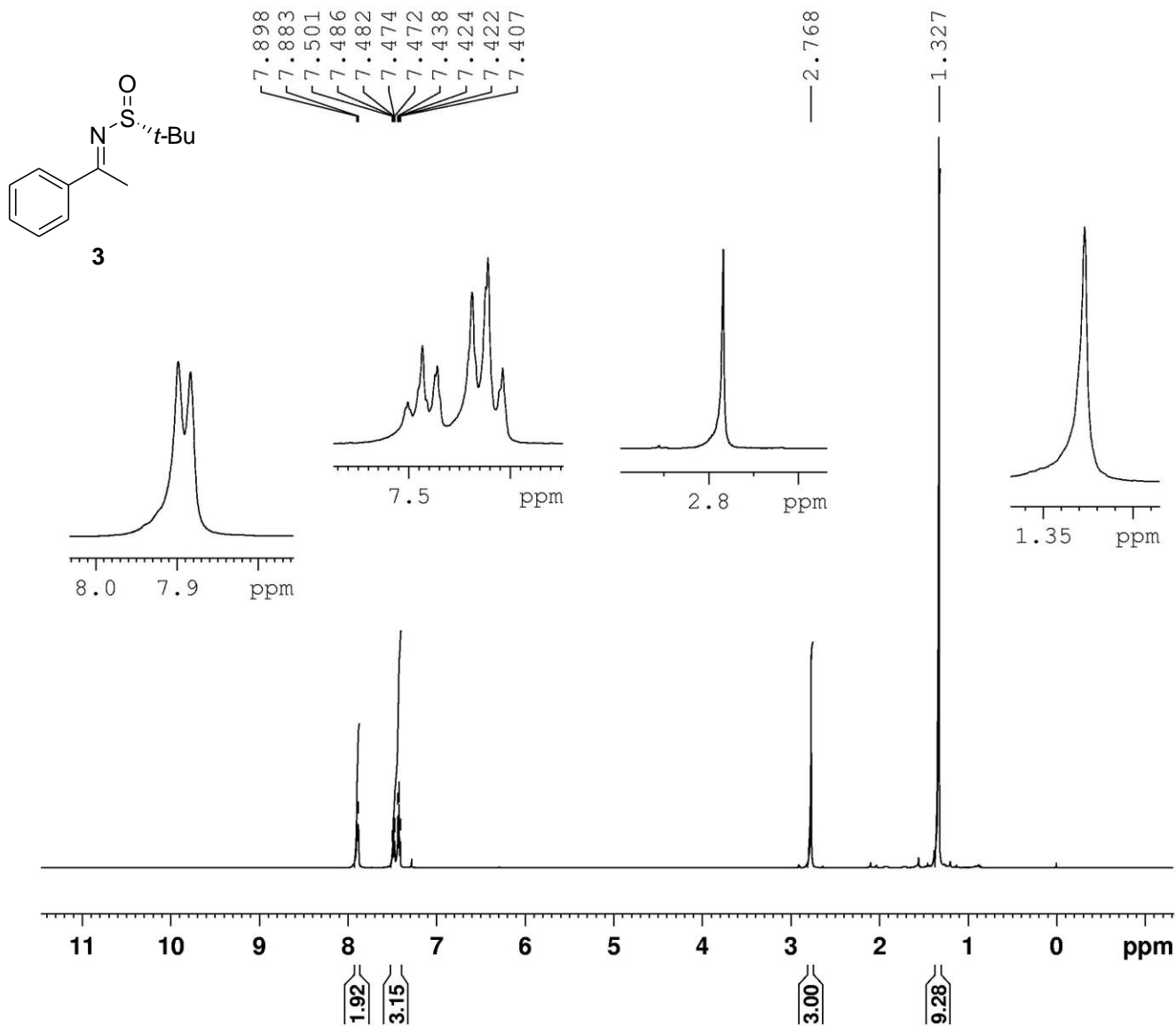
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FIDRES   0.166672 Hz
AQ   2.9999499 sec
RG   97.37
DW   50.000 usec
DE   10.00 usec
TE   295.6 K
D1   5.00000000 sec
TD0   1

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SFO1   500.1330885 MHz
NUC1   1H
P1   8.00 usec
SI   65536
SF   500.1300018 MHz
WDW   no
SSB   0
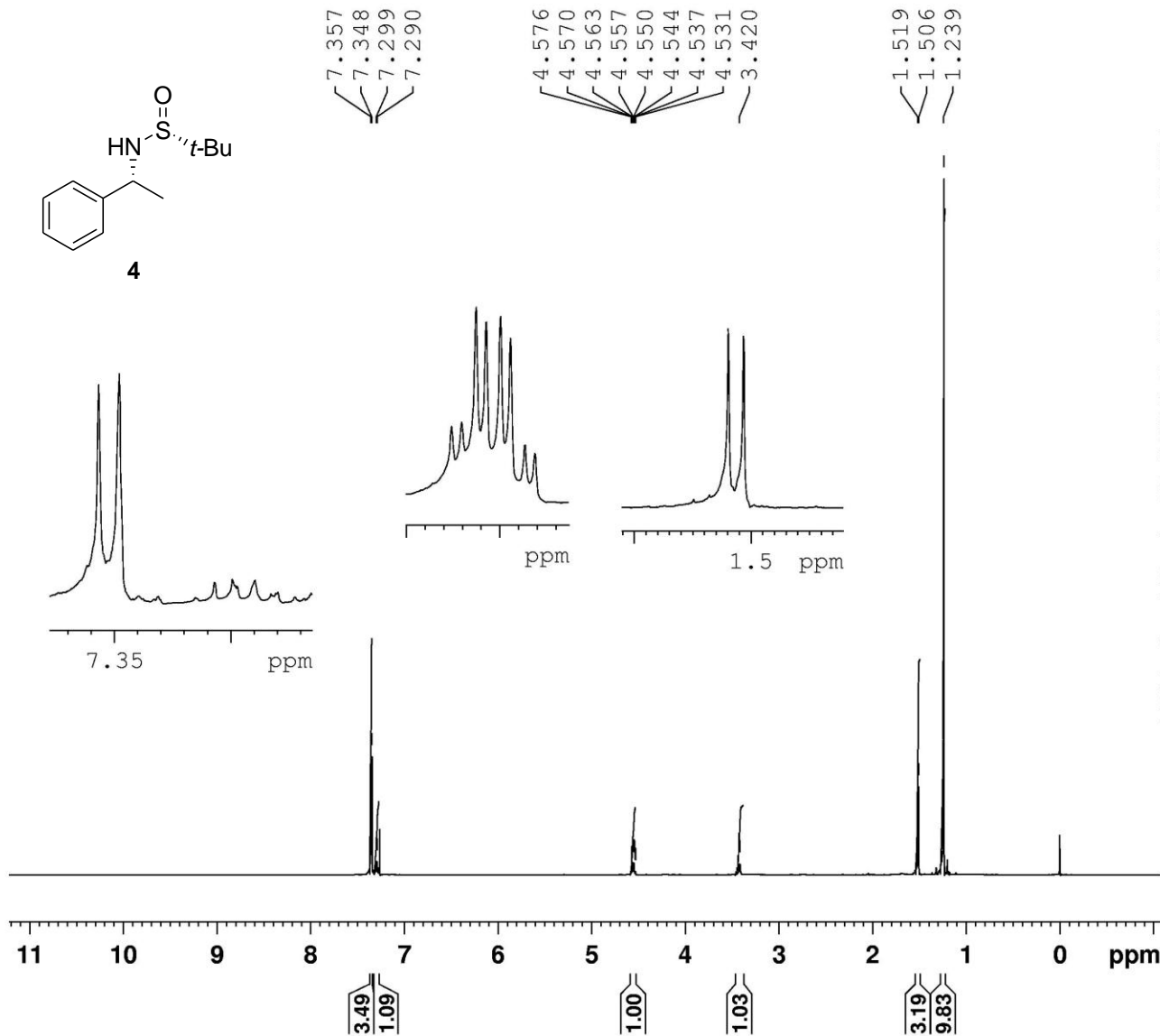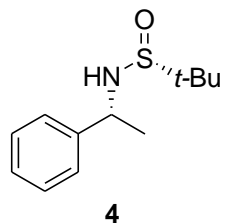LB   0.00 Hz
GB   0
PC   1.00

8.0   7.9   ppm

7.5   ppm

2.8   ppm

1.35   ppm

11 10 9 8 7 6 5 4 3 2 1 0 ppm

1.92
3.15

3.00

9.28

(R$_s$)-N-[1-1Phenylethylidene]-2-methylpropane-2-sulfinamide (**3**)

176.27

138.59
131.54
128.32
127.10

57.27

22.37
19.66

NAME   1.css.os.1.1.13C
EXPNO   1
PROCNO   1
Date_   20130423
Time   16.46
INSTRUM   spect
PROBHD   5 mm PATXI 1H/
PULPROG   zgdc
TD   178568
SOLVENT   CDCl3
NS   200
DS   0
SWH   29761.904 Hz
FIDRES   0.166670 Hz
AQ   2.9999924 sec
RG   196.79
DW   16.800 usec
DE   10.00 usec
TE   295.4 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
SFO1   125.7703643 MHz
NUC1   13C
P1   14.00 usec
SI   131072
SF   125.7578087 MHz
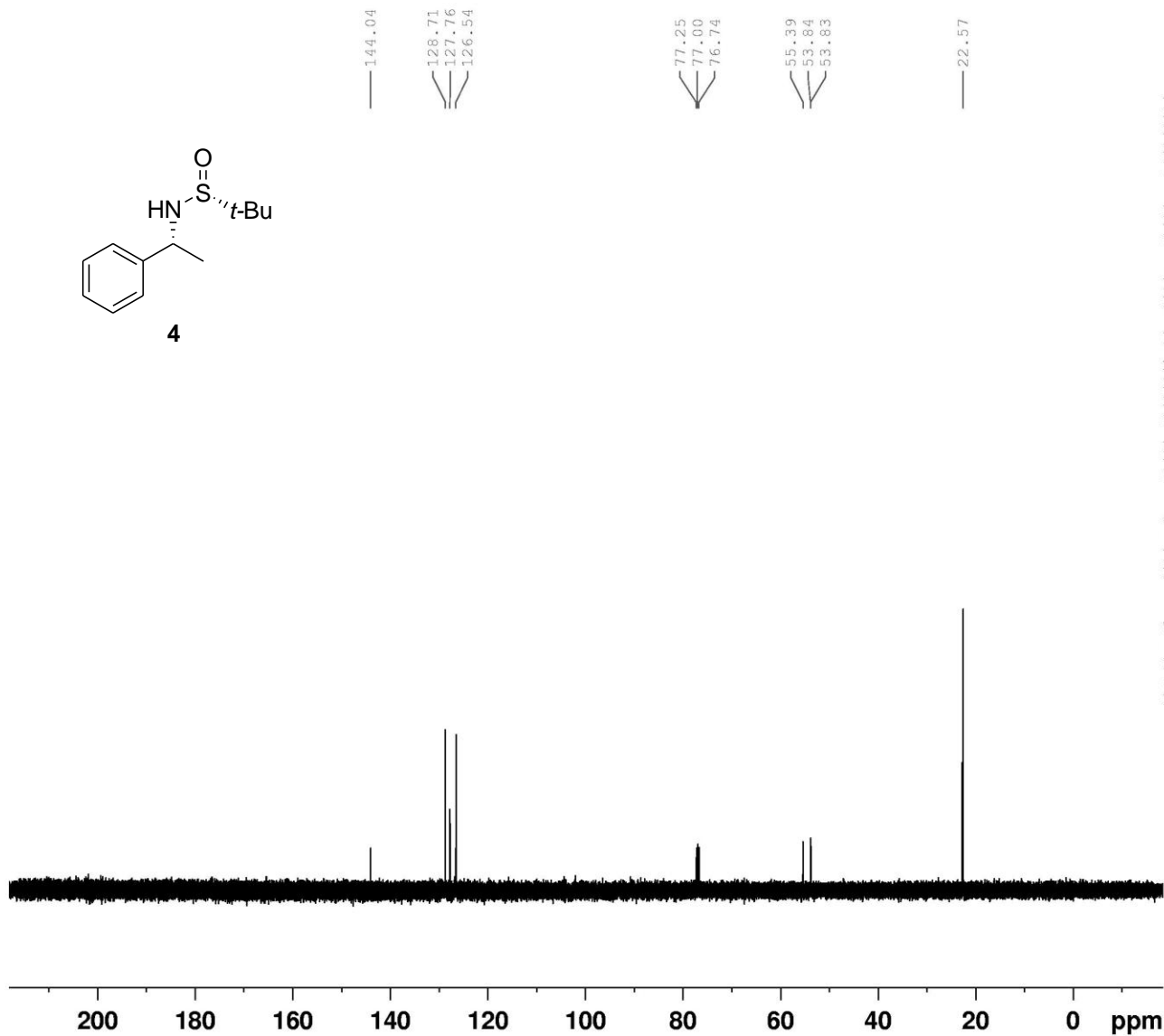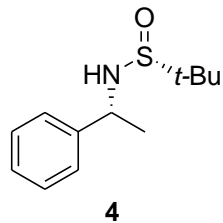WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.40

3

200 180 160 140 120 100 80 60 40 20 0 ppm

(R,Rₛ)-N-[1-1Phenylethy]-2-methylpropane-2-sulfinamide (**4**)

Structure **4**: HN–S(=O)–*t*-Bu with phenyl and methyl substituents

Peak labels:
7.357, 7.348, 7.299, 7.290

4.576, 4.570, 4.563, 4.557, 4.550, 4.544, 4.537, 4.531, 3.420

1.519, 1.506, 1.239

7.35 ppm expansion

ppm expansion (~4.5)

1.5 ppm expansion

Integrations: 3.49, 1.09 (~7.3); 1.00 (~4.5); 1.03 (~3.4); 3.19, 9.83 (~1.2–1.5)

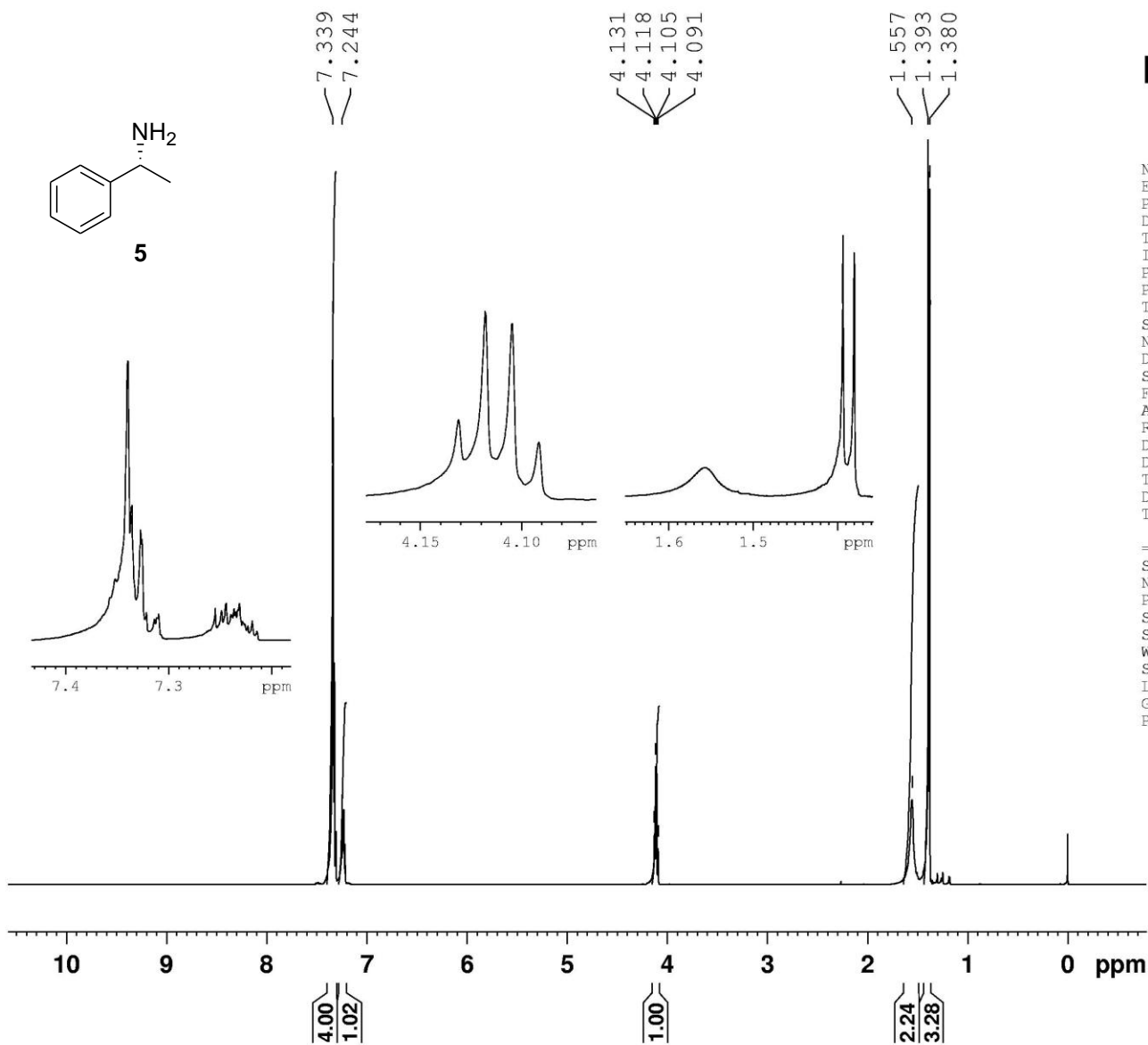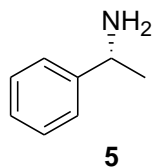# *(R,R$_s$)*-N-[1-1Phenylethy]-2-methylpropane-2-sulfinamide (**4**)

NAME   1.css.os.2.a2.13C
EXPNO   1
PROCNO   1
Date_   20130412
Time   12.00
INSTRUM   spect
PROBHD   5 mm PATXI 1H/
PULPROG   zgdc
TD   178568
SOLVENT   CDCl3
NS   150
DS   0
SWH   29761.904 Hz
FIDRES   0.166670 Hz
AQ   2.9999924 sec
RG   196.79
DW   16.800 usec
DE   10.00 usec
TE   297.0 K
D1   2.00000000 sec
D11   0.03000000 sec
TDO   1

======== CHANNEL f1 ========
SFO1   125.7703643 MHz
NUC1   13C
P1   14.00 usec
SI   131072
SF   125.7577969 MHz
WDW   no
SSB   0
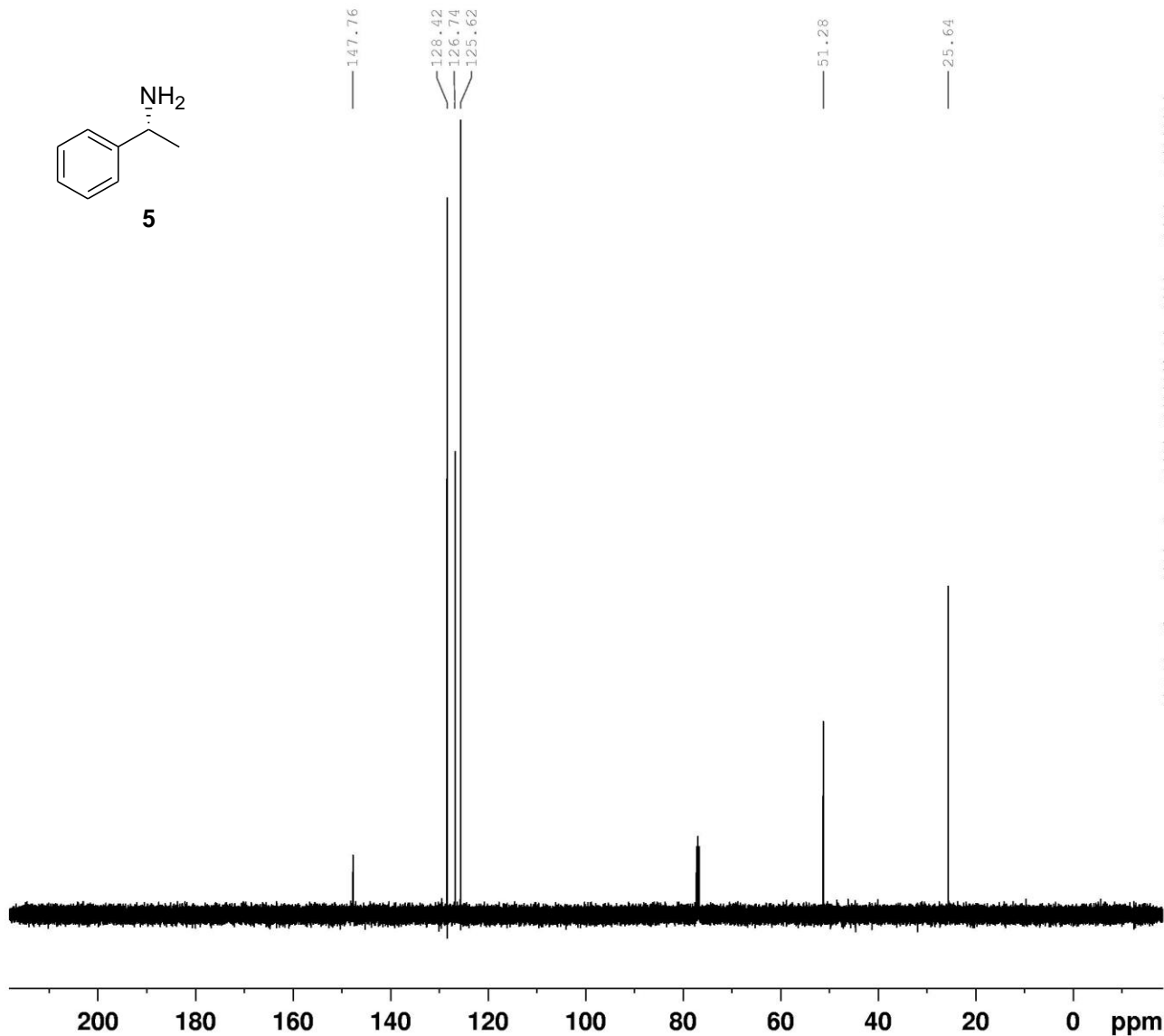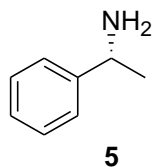LB   0.00 Hz
GB   0
PC   1.40

(R)-1-Phenylethanamine (**5**)

NH$_2$

5

7.339
7.244

4.131
4.118
4.105
4.091

1.557
1.393
1.380

4.15   4.10   ppm

1.6   1.5   ppm

7.4   7.3   ppm

NAME   1.css.os.3.a5
EXPNO   1
PROCNO   1
Date_   20130502
Time   17.41
INSTRUM   spect
PROBHD   5 mm PATXI 1H/
PULPROG   zg
TD   59998
SOLVENT   CDCl3
NS   12
DS   0
SWH   10000.000 Hz
FIDRES   0.166672 Hz
AQ   2.9999499 sec
RG   55.8
DW   50.000 usec
DE   10.00 usec
TE   295.8 K
D1   5.00000000 sec
TD0   1

======== CHANNEL f1 ========
SFO1   500.1330885 MHz
NUC1   1H
P1   8.00 usec
SI   65536
SF   500.1300155 MHz
WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.00

10   9   8   7   6   5   4   3   2   1   0 ppm

4.00
1.02

1.00

2.24
3.28

(R)-1-Phenylethanamine (**5**)

NH$_2$

5

147.76

128.42
126.74
125.62

51.28

25.64

NAME   1.css.os.3.a5.13C
EXPNO   1
PROCNO   1
Date_   20130502
Time   18.18
INSTRUM   spect
PROBHD   5 mm PATXI 1H/
PULPROG   zgdc
TD   178568
SOLVENT   CDCl3
NS   225
DS   0
SWH   29761.904 Hz
FIDRES   0.166670 Hz
AQ   2.9999924 sec
RG   196.79
DW   16.800 usec
DE   10.00 usec
TE   296.5 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
SFO1   125.7703643 MHz
NUC1   13C
P1   14.00 usec
SI   131072
SF   125.7577984 MHz
WDW   no
SSB   0
LB   0.00 Hz
GB   0
PC   1.40

200   180   160   140   120   100   80   60   40   20   0   ppm