Copper-Catalyzed Borylative Coupling of Vinylazaarenes and *N*-Boc Imines

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Supporting Information

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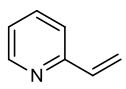
1. General Information

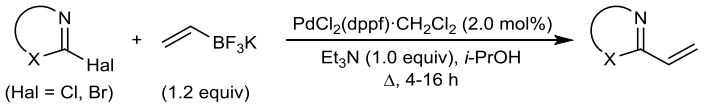
All commercially available reagents were used as received. THF was dried and purified by passage through activated alumina columns using a solvent purification system. "Petroleum ether" refers to Sigma-Aldrich product 24587 (petroleum ether boiling point 40–60 °C). Thin layer chromatography (TLC) was performed on Merck DF-Alufoilien $60F_{254}$ 0.2 mm precoated plates. Product spots were visualized by UV light at 254 nm, and subsequently developed using potassium permanganate or vanillin solution as appropriate. Flash column chromatography was carried out using silica gel (Fisher Scientific 60Å particle size 35–70 micron) or using an Interchim Puriflash 430 Series automated purification system with IR-50SI 50µm pre-packed columns. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Infra-red spectra were recorded on a Nicolet Avatar 360 FT instrument on the neat compound using an attenuated total reflection (ATR) accessory with a diamond crystal and a germanium sample plate, or on a Bruker Tensor 27 FT instrument as a $CHCl_3$ solution or using an attenuated total reflection (ATR) accessory with a diamond crystal and a germanium sample plate. ^{1}H and ^{13}C NMR spectra were acquired on Bruker AV(III)500, Bruker AV400, Bruker AV(III)400, or Bruker DPX400 spectrometers. Spectra were referenced to external tetramethylsilane via the residual protonated solvent (^{1}H) or the solvent itself (^{13}C). All chemical shifts are reported in parts per million (ppm). For CD_3OD the shifts are referenced to 3.31 ppm and ^{1}H NMR spectroscopy and 49.00 ppm for ^{13}C NMR spectroscopy. For $(CD_3)_2SO$ the shifts are referenced to 2.50 ppm for ^{1}H NMR spectroscopy and 39.52 ppm for ^{13}C NMR spectroscopy. Abbreviations used in the description of resonances in ^{1}H NMR spectra are: s (singlet), d (doublet), t (triplet), q (quartet), app (apparent), br (broad), and m (multiplet). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. Assignments in ^{13}C NMR spectra were made with the assistance of HMQC spectra. Proton-decoupled ^{19}F NMR spectra were recorded on Bruker AV(III)400 (376 MHz), Bruker AV400 (376 MHz), or Bruker DPX400 (376 MHz) spectrometers. Chemical shifts are quoted in parts per million (ppm) downfield of $CFCl_3$ (δ = 0 ppm), using trifluoroacetic acid contained within a sealed glass tube as an internal standard (CF_3COOH at –76.55 ppm). High resolution mass spectra were recorded using electrospray ionization (ESI). X-ray diffraction data were collected at 120 K on an Agilent SuperNova diffractometer using CuKα radiation.

2. Preparation Vinylazaarenes

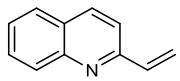


2-Vinylpyridine (1a). Commercially available.

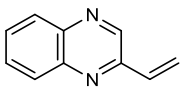
General Procedure A



In a slight modification of procedure reported previously,[1] a solution of the corresponding chloro- or bromo-heterocycle (1.0 equiv), potassium vinyltrifluoroborate (1.2 equiv), $PdCl_2(dppf)\cdot CH_2Cl_2$ (2 mol%), and Et_3N 1.0 equiv) in *i*-PrOH (10 mL/mmol) was heated to reflux for 16 h. The reaction was cooled to room temperature, concentrated *in vacuo*, before the addition of water (50 mL) and extraction with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography gave the vinylazaarene.

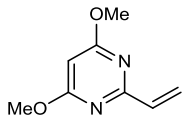


2-Vinylquinoline (1b). The title compound was prepared according to General Procedure A from 2-chloroquinoline (1.64 g, 10.0 mmol), potassium vinyltrifluoroborate (1.61 g, 12.0 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (163 mg, 0.200 mmol), and Et_3N (1.40 mL, 10.0 mmol), and purified by flash column chromatography (0 to 10% EtOAc/petroleum ether) to give a pale yellow oil (1.18 g, 76%) that displayed spectroscopic data consistent with those reported previously.[2]

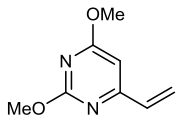


2-Vinylquinoxaline (1c). The title compound was prepared according to General Procedure A from 2-chloroquinoxaline (1.35 g, 8.00 mmol), potassium vinyltrifluoroborate (1.29 g, 9.60 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (130 mg, 0.159 mmol), and Et_3N (1.12 mL, 8.00 mmol), and purified by flash column chromatography (5% EtOAc/*n*-hexane) to give a pale yellow oil which solidified on standing (1.04 g, 83%). Spectroscopic data were consistent with those reported previously.[3]

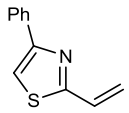
1. Molander, G. A.; Rivero, M. R. *Org. Lett.* **2001,** *4*, 107–109.
2. Fakhfakh, M. A.; Franck, X.; Fournet, A.; Hocquemiller, R.; Figadère, B. *Tetrahedron Lett.* **2001**, *42*, 847–3850.
3. Saxena, A.; Choi, B.; Lam, H. W. *J. Am. Chem. Soc.* **2012**, *134*, 8428–8431.



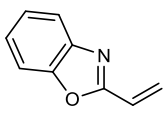
4,6-Dimethoxy-2-vinylpyrimidine (1d). The title compound was prepared according to General Procedure A from 2-chloro-4,6-dimethoxypyrimidine (1.40 g, 8.00 mmol), potassium vinyltrifluoroborate (1.29 g, 9.60 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (130 mg, 0.159 mmol), and Et_3N (1.12 mL, 8.00 mmol), and purified by flash column chromatography (0 to 10% EtOAc/petroleum ether) to give a pale yellow oil (0.448 g, 34%) that displayed spectroscopic data consistent with those reported previously.[3]



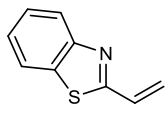
2,4-Dimethoxy-6-vinylpyrimidine (1e). The title compound was prepared according to General Procedure A from 6-chloro-2,4-dimethoxypyrimidine (1.19 g, 6.79 mmol), potassium vinyltrifluoroborate (1.07 g, 8.01 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (114 mg, 0.140 mmol), and Et_3N (0.95 mL, 6.8 mmol), and purified by flash column chromatography (0 to 10% EtOAc/*n*-hexane) to give a pale yellow oil (0.75 g, 70%) that displayed spectroscopic data consistent with those reported previously.[3]



4-Phenyl-2-vinylthiazole (1f). The title compound was prepared according to General Procedure A from 1-bromo-4-phenyl-thiazole (2.97 g, 12.4 mmol), potassium vinyltrifluoroborate (1.99 g, 14.9 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (202 mg, 0.247 mmol), and Et_3N (1.74 mL, 12.4 mmol), and purified by flash column chromatography (0 to 40% toluene/*n*-hexane) to give a pale yellow solid (1.39 g, 60%) that displayed spectroscopic data consistent with those reported previously.[3]



2-Vinylbenzoxazole (1g). The title compound was prepared according to General Procedure A from 2-chlorobenzoxazole (1.64 g, 10.5 mmol), potassium vinyltrifluoroborate (1.69 g, 12.6 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (171 mg, 0.209 mmol), and Et_3N (1.47 mL, 10.5 mmol), and purified by flash column chromatography (0 to 5% acetone/*n*-hexane) to give a pale yellow oil (1.11 g, 73%) that displayed spectroscopic data consistent with those reported previously.[4]



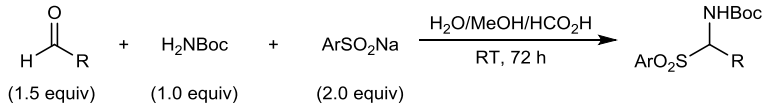
2-Vinylbenzathiazole (1h). The title compound was prepared according to General Procedure A from 2-chlorobenzothiazole (0.65 mL, 5.00 mmol), potassium vinyltrifluoroborate (804 mg, 6.00 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (82 mg, 0.10 mmol),

4. Minami, T.; Isonaka, T.; Okada, Y.; Ichikawa, J. *J. Org. Chem.* **1993,** *58*, 7009–7015.

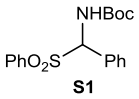
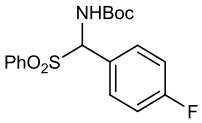
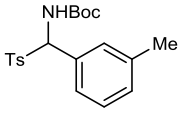
and Et_3N (0.70 mL, 5.00 mmol), and by flash column chromatography (3% EtOAc/*n*-hexane) to give a pale yellow oil which solidified on standing (0.70 g, 87%) that displayed spectroscopic data consistent with those reported previously.[5]

3. Preparation of *N*-Boc Imines

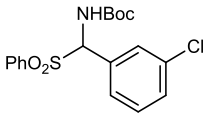
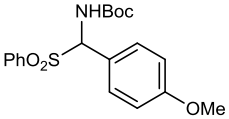
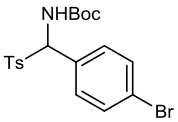
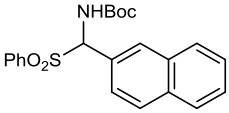
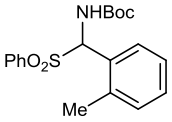
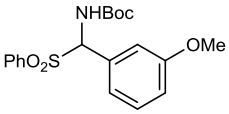
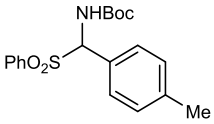
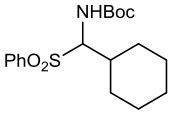
tert-Butyl *N*-[(benzenesulfonyl)(phenyl)methyl]carbamates and *tert*-butyl *N*-{[(4-methylbenzene)sulfonyl](phenyl)methyl}carbamates



Following a slightly modified literature procedure,[6] the appropriate aldehyde (1.50 equiv) was suspended in 2:1:0.7 H_2O/MeOH/HCO_2H (4 mL/mmol) and stirred until the mixture became homogeneous. Additional MeOH and/or gentle heating was sometimes required to achieve complete dissolution. Sodium benzenesulfinate (2.0 equiv) or sodium 4-methylbenzenesulfinate (2.0 equiv) and *tert*-butyl carbamate[7] (1.0 equiv) were then added sequentially. The reaction mixture was stirred for 72 h, the solids collected by filtration and triturated with H_2O, and then the organic solvent/mixture specified to leave the sulfonylcarbamate.

Sulfonylcarbamate	Scale (mmol)	Additional MeOH/heat	Trituration solvents	Yield (%)	Known?
 **S1**	45	–	*n*-hexane	99	Yes[6]
 **S2**	10	–	*n*-hexane	83	Yes[8]
 **S3**	10	–	*iso*-hexane:toluene (5:3)	20	Yes[9]

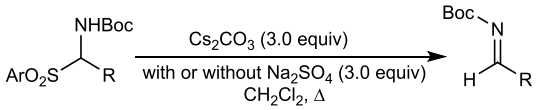
5. Choi, B.; Saxena, A.; Lam, H. W. *Synlett* **2015**, *26*, 350–354.
6. Jones, C. R.; Dan Pantoş, G.; Morrison, A. J.; Smith, M. D. *Angew. Chem., Int. Ed.* **2009**, *48*, 7391–7394.
7. Best, D.; Kujawa, S.; Lam, H. W. *J. Am. Chem. Soc.* **2012**, *134*, 18193-18196.
8. Huang, L.; Wulff, W. D. *J. Am. Chem. Soc.* **2011**, *133*, 8892–8895.
9. Gomez-Bengoa, E.; Linden, A.; López, R.; Múgica-Mendiola, I.; Oiarbide, M.; Palomo, C. *J. Am. Chem. Soc.* **2008**, *130*, 7955–7966.

Sulfonylcarbamate	Scale (mmol)	Additional MeOH/heat	Trituration solvents	Yield (%)	Known?
 **S4**	10	10 mL	*iso*-hexane:CH_2Cl_2 (10:1)	88	Yes[10]
 **S5**	10	–	*iso*-hexane:Et_2O (4:1)	87	Yes[11]
 **S6**	10	20 mL; heat	*iso*-hexane:Et_2O (1:1); toluene	49	Yes[7]
 **S7**	10	25 mL; heat	*iso*-hexane:Et_2O (1:1)	56	Yes[11]
 **S8**	10	15 mL	*iso*-hexane:Et_2O (4:1)	37	Yes[11]
 **S9**	10	5 mL; heat	*iso*-hexane:toluene (5:3)	87	Yes[7]
 **S10**	10	10 mL	Et_2O	61	Yes[11]
 **S11**	10	15 mL; heat	*iso*-hexane	69	Yes[8]

10. Reingruber, R.; Braese, S.; Baumann, T.; Dahmen, S. *Adv. Synth. Catal.* **2009**, *351*, 1019–1024.
11. Guy Goodman, C.; Do, D. T.; Johnson, J. S. *Org. Lett.* **2013**, *15*, 2446–2449.

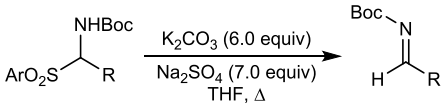
Elimination of Sulfonylcarbamates

General Procedure B

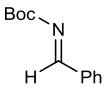


The appropriate sulfonylcarbamate (1.0 equiv) was added to a flask containing flame-dried Cs_2CO_3 (3.0 equiv) with or without Na_2SO_4 (3.0 equiv) as specified. Alcohol-free CH_2Cl_2 (20 mL per mmol of sulfonylcarbamate) was added and the mixture heated at reflux. Small aliquots were removed periodically, filtered, and analyzed by ^{1}H NMR spectroscopy (using $CDCl_3$ treated with K_2CO_3 to remove trace HCl which promotes hydrolysis of the *N*-Boc imine) to confirm completion of the reaction. The reaction mixture was cooled to room temperature, diluted with *iso*-hexane (20 mL per mmol of sulfonylcarbamate), filtered, and concentrated *in vacuo* at <20 °C to leave the *N*-Boc imine.

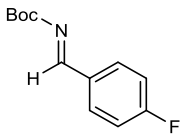
General Procedure C



The appropriate sulfonylcarbamate (1.0 equiv) was added to a flask containing K_2CO_3 (6.0 equiv) and Na_2SO_4 (7.0 equiv), both of which had been dried under vacuum at 150 ºC for 1 h. The flask was purged with N_2 (10 min) before the addition of anhydrous THF (10 mL per mmol of sulfonylcarbomate). The mixture was heated at reflux for 16 h and cooled to room temperature. The reaction was diluted with *iso*-hexane (10 mL per mmol of sulfonylcarbamate), filtered, and concentrated *in vacuo* at <20 °C to leave the *N*-Boc imine.

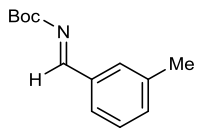


Benzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2a). The title compound was prepared according to General Procedure B from sulfonylcarbamate **S1** (1.25 g, 3.61 mmol), flame-dried Cs_2CO_3 (3.52 g, 10.8 mmol), and Na_2SO_4 (1.53 g, 10.8 mmol) for a reaction time of 2 h to give a colorless oil (0.75 g, 84%) that displayed spectroscopic data consistent with those reported previously.[6]

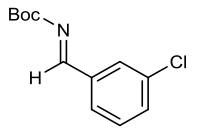


4-Fluorobenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2b). The title compound was prepared according to General Procedure C from sulfonylcarbonate **S2** (1.35 g, 3.69 mmol), K_2CO_3 (3.07 g, 22.2 mmol), and Na_2SO_4 (3.68 g, 25.9 mmol) to

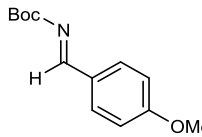
give a white solid (0.52 g, 64%) that displayed spectroscopic data consistent with those reported previously.[12]



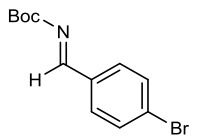
3-Methylbenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2c). The title compound was prepared according to General Procedure B from sulfonylcarbamate **S3** (700 mg, 1.86 mmol), Cs_2CO_3 (1.82 g, 5.59 mmol), and Na_2SO_4 (794 mg, 5.59 mmol) for a reaction time of 16 h to give a colorless oil (0.20 g, 49%) that displayed spectroscopic data consistent with those reported previously.[13]



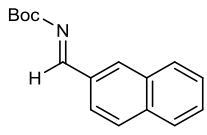
3-Chlorobenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2d). The title compound was prepared according to General Procedure C from sulfonylcarbonate **S4** (2.00 g, 5.20 mmol), K_2CO_3 (4.31 g, 31.2 mmol), and Na_2SO_4 (5.17 g, 36.4 mmol) to give a pale yellow oil (1.24 g, 99%) that displayed spectroscopic data consistent with those reported previously.[14]



4-Cyanobenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2e). The title compound was prepared according to General Procedure C from sulfonylcarbonate **S5** (1.89 g, 5.00 mmol), K_2CO_3 (4.15 g, 30.0 mmol), and Na_2SO_4 (4.97 g, 35.0 mmol) to give a white solid (1.15 g, 98%) that displayed spectroscopic data consistent with those reported previously.[13]

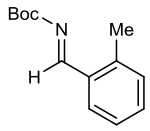


4-Bromobenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2f). The title compound was prepared according to General Procedure B from sulfonylcarbamate **S6** (2.12 g, 4.87 mmol), Cs_2CO_3 (4.76 g, 14.6 mmol), and Na_2SO_4 (2.07 g, 14.6 mmol) for a reaction time of 2.5 h to give a white solid (1.30 g, 94%) that displayed spectroscopic data consistent with those reported previously.[13]

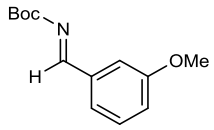


2-Naphthaldehyde *N*-(*tert*-butoxycarbonyl)imine (2g). The title compound was prepared according to General Procedure C from sulfonylcarbonate **S7** (650 mg, 1.64 mmol), K_2CO_3 (1.36 g, 9.84 mmol), and Na_2SO_4 (1.63 g, 11.5 mmol) to give a white solid (0.33 g, 78%) that displayed spectroscopic data consistent with those reported previously.[12]

12. Wenzel, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 12964–12965.
13. Karimi, B.; Jafari, E.; Enders, D. *Chem. Eur. J.* **2013**, *19*, 10142–10145.
14. Rampalakos, C.; Wulff, W. D. *Adv. Synth. Catal.* **2008,** *350*, 1785–1790.

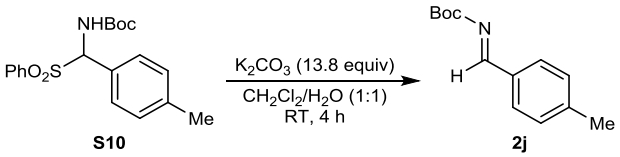


2-Methylbenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2h). The title compound was prepared according to General Procedure B from sulfonylcarbamate **S8** (1.09 g, 3.00 mmol), Cs_2CO_3 (2.93 g, 9.00 mmol), and Na_2SO_4 (1.28 g, 9.00 mmol) for a reaction time of 16 h to give a a colorless oil (0.64 g, 97%) that displayed spectroscopic data consistent with those reported previously.[13]

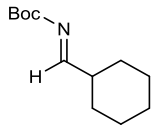


3-Methoxybenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2i). The title compound was prepared according to General Procedure C from sulfonylcarbonate **S9** (1.89 g, 5.00 mmol), K_2CO_3 (4.15 g, 30.0 mmol), and Na_2SO_4 (4.97 g, 35.0 mmol) to give a white crystalline solid (1.18 g, >98%) that displayed spectroscopic data consistent with those reported previously.[15]

4-Methylbenzaldehyde *N*-(*tert*-butoxycarbonyl)imine (2j)



A solution of sulfonylcarbamate **S10** (2.20 g, 6.09 mmol) in a 1:1 biphasic mixture of CH_2Cl_2 (60 mL) and aqueous K_2CO_3 solution (1.4 M, 60 mL, 84 mmol) was stirred at room temperature for 4 h. The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* at <20 °C to leave *N*-Boc imine **2j** as a white solid (1.22 g, 91%) that displayed spectroscopic data consistent with those reported previously.[7]

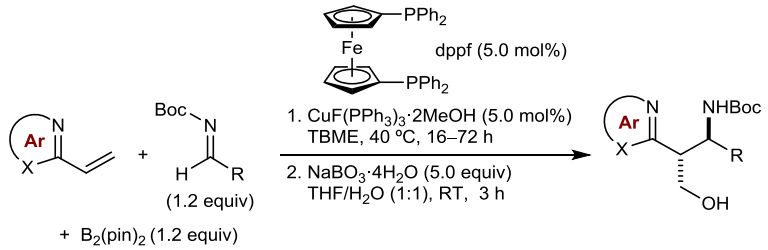


Cyclohexanecarbaldehyde *N*-(*tert*-butoxycarbonyl)imine (2k). The title compound was prepared according to General Procedure B from sulfonylcarbamate **S11** (1.06 g, 3.00 mmol), Cs_2CO_3 (2.93 g, 9.00 mmol), and Na_2SO_4 (1.28 g, 9.00 mmol) for a reaction time of 2.5 h to give a colorless oil (0.51 g, 80%) that displayed spectroscopic data consistent with those reported previously.[13]

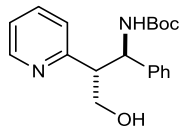
15. Trost, B. M.; Silverman, S. M. *J. Am. Chem. Soc.* **2012**, *134*, 4941–4954.

4. Copper-Catalyzed Borylative Coupling of Vinylazaarenes with Imines

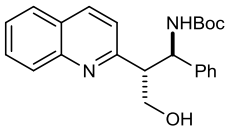
General Procedure D



A mixture of $CuF(PPh_3)_3$·2MeOH (23.3 mg, 0.0250 mmol), dppf (13.9 mg, 0.0250 mmol), and $B_2(Pin)_2$ (152 mg, 0.600 mmol) in TBME (1.25 mL) was stirred at room temperature for 20 min. The resulting suspension was added *via* cannula to a microwave vial containing the appropriate vinylazaarene (0.50 mmol) and *N*-Boc imine (0.60 mmol), and the mixture was stirred at 40 °C for the indicated time. The reaction was cooled to room temperature and concentrated *in vacuo*. A 1:1 mixture of THF:H_2O (5 mL). $NaBO_3$·$4H_2O$ (384 mg, 2.50 mmol) was added in one portion and the mixture was stirred vigorously for 3 h, before diluting with H_2O (20 mL). The aqueous layer was separated and extracted with EtOAc (3 × 15 mL). The combined organic fractions were washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography gave the azaaryl-containing amino alcohol.

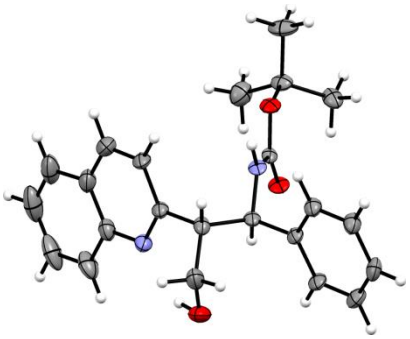


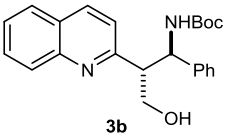
(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-3-hydroxy-1-phenyl-2-(pyridin-2-yl)propyl]carbamate (3a). The title compound was prepared according to General Procedure D from 2-vinylpyridine (**1a**) (53 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 20 h, and purified by flash column chromatography (0 to 60% EtOAc/petroleum ether) to give a white solid (77 mg, 47%). m.p. 147–149 °C (Et_2O); IR (ATR) 3378 (NH and OH), 1678 (C=O), 1524, 1253, 1170, 1071 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.54 (1H, d, *J* = 4.0 Hz, Ar**H**), 7.61 (1H, td, *J* = 7.7, 1.8 Hz, Ar**H**), 7.32–7.12 (7H, m, Ar**H** and N**H**), 7.10–7.06 (1H, m, Ar**H**), 5.01 (1H, t, *J* = 7.9 Hz, NHC**H**), 4.41 (1H, t, *J* = 5.1 Hz, O**H**), 3.71–3.51 (2H, m, C$\mathbf{H}_2$), 3.35–3.19 (1H, m, CH_2C**H**), 1.26 (9H, s, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 160.3 (C), 154.3 (C), 148.2 (CH), 142.5 (C), 135.5 (CH), 127.5 (2 × CH), 126.3 (2 × CH), 126.2 (CH), 124.7 (CH), 121.3 (CH), 77.4 (C), 62.2 (CH_2), 55.0 (CH), 53.9 (CH), 27.8 (3 × CH_3); HRMS (ESI) Exact mass calculated for $C_{19}H_{24}N_2NaO_3$ $[M+Na]^+$: 351.1679, found: 351.1655.



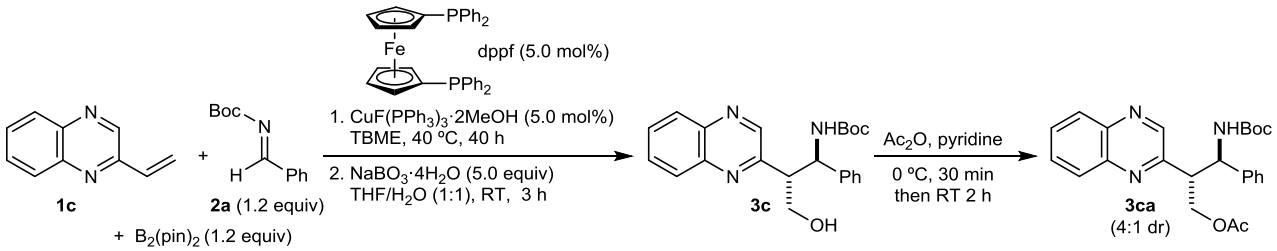
(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-3-hydroxy-1-phenyl-2-(quinolin-2-yl)propyl]carbamate (3b). The title compound was prepared according to General Procedure D from 2-vinylquinoline (**1b**) (78 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 16 h, and purified by column chromatography (0 to 8% EtOAc/CH_2Cl_2) to give a white solid (132 mg, 70%). m.p. 209–211 °C ($CHCl_3$/petroleum ether); IR (ATR) 3375 (NH and OH), 2920, 2855, 1674 (C=O), 1522, 1169 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.18 (1H, d, *J* = 8.4 Hz, Ar**H**), 8.00 (1H, d, *J* = 8.4 Hz, Ar**H**), 7.91 (1H, d, *J* = 8.1 Hz, Ar**H**), 7.74 (1H, ddd, *J* = 8.4, 6.9, 1.4 Hz, Ar**H**), 7.55 (1H, ddd, *J* = 8.0, 6.9, 1.1 Hz, Ar**H**), 7.40–7.23 (6H, m, Ar**H** and N**H**), 7.19 (1H, ddd, *J* = 8.5, 4.5, 1.4 Hz, Ar**H**), 5.13 (1H, t, *J* = 8.4 Hz, NHC**H**), 4.49 (1H, t, *J* = 5.1 Hz, O**H**), 3.76–3.66 (1H, m, C**H**$_2$), 3.66–3.58 (1H, m, C**H**$_2$), 3.53–3.42 (1H, m, CH_2C**H**), 1.19 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 161.7 (C), 154.3 (C), 146.7 (C), 142.5 (C), 135.0 (CH), 128.9 (CH), 128.1 (CH), 127.6 (2 × CH), 127.3 (CH), 126.5 (2 × CH and C), 126.3 (CH), 125.5 (CH), 122.9 (CH), 77.4 (C), 62.3 (CH_2), 55.0 (CH), 54.6 (CH), 27.7 (3 × CH_3); HRMS (ESI) Exact mass calculated for $C_{23}H_{26}N_2O_3$ $[M+H]^+$: 379.2016, found: 379.2023.

Slow diffusion of petroleum ether into a solution of **3b** in $CHCl_3$ provided crystals that were suitable for X-ray crystallography:





3-{[(*tert*-Butoxy)carbonyl]amino}-3-phenyl-2-(quinoxalin-2-yl)propyl acetate (3ca)

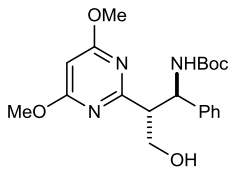


General Procedure D was followed using 2-vinylquinoxoline (**1c**) (78 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 40 h to give the crude amino alcohol **3c**. This

material was transferred to a 5 mL flask which was then flushed with N_2 (5 min). The flask was cooled to 0 °C and a 1:1 mixture by volume of pyridine and Ac_2O (total 1 mL) was added. The mixture was stirred at 0 °C for 30 min and then at room temperature for 2 h. The reaction was concentrated *in vacuo*, and the residue was purified by flash column chromatography (0 to 25% EtOAc/petroleum ether) to give the *acetate ester* **3ca** as a 4:1 mixture of diastereomers as a pale yellow solid (121 mg, 57%). IR (ATR) 3388 (NH and OH), 2975, 1734 (C=O), 1708, 1682 (C=O), 1515, 1244, 1168 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{24}H_{26}N_3O_4$ $[M-H]^+$: 420.1929, found: 420.1937.

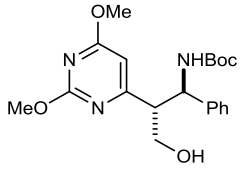
Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.87 (1H, s, Ar**H**), 8.12–8.05 (2H, m, Ar**H**), 7.89–7.79 (2H, m, Ar**H**), 7.51–7.45 (2H, m, Ar**H**), 7.41–7.34 (2H, m, Ar**H**), 7.33–7.18 (2H, m, Ar**H** and N**H**), 5.12 (1H, t, *J* = 9.7 Hz, NHC**H**), 4.28 (1H, dd, *J* = 11.1, 8.3 Hz, C**H**$_2$), 4.13 (1H, dd, *J* = 11.1, 4.8 Hz, C**H**$_2$), 3.88 (1H, ddd, *J* = 10.1, 8.3, 4.8 Hz, CH_2C**H**), 1.77 (3H, s, C**H**$_3$C=O), 1.09 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.4 (C), 155.1 (C), 154.0 (C), 146.4 (CH), 141.1 (C), 141.0 (C), 140.8 (C), 129.67 (CH), 129.2 (CH), 128.5 (CH), 128.5 (CH), 128.1 (2 × CH), 127.1 (CH), 126.8 (2 × CH), 77.6 (C), 64.0 (CH_2), 55.6 (CH), 49.2 (CH), 27.5 (3 × CH_3), 19.9 (CH_3).

Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.61 (1H, s, Ar**H**), 8.04–7.94 (2H, m, Ar**H**), 7.81–7.72 (2H, m, Ar**H**), 7.26–7.20 (2H, m, Ar**H**), 7.14–7.08 (2H, m, Ar**H**), 7.08–7.01 (1H, m, Ar**H**), 5.20 (1H, t, *J* = 9.6 Hz, NHC**H**), 4.68 (1H, dd, *J* = 10.9, 8.7 Hz, C**H**$_2$), 4.56 (1H, dd, *J* = 10.9, 4.3 Hz, C**H**$_2$), 3.96 (1H, ddd, *J* = 9.8, 8.7, 4.3 Hz, CH_2C**H**), 1.83 (3H, s, C**H**$_3$C=O), 1.33 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.6 (C), 154.8 (C), 154.6 (C), 146.1 (CH), 140.8 (C), 140.4 (C), 129.70 (CH), 128.4 (CH), 128.4 (CH), 127.6 (2 × CH), 126.9 (2 × CH), 126.6 (CH), 77.9 (C), 64.0 (CH_2), 55.6 (CH), 49.4 (CH), 27.8 (3 × CH_3), 20.0 (CH_3).

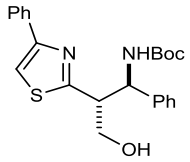


(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(4,6-dimethoxypyrimidin-2-yl)-3-hydroxy-1-phenylpropyl]carbamate (3d). The title compound was prepared according to General Procedure D from 2-vinyl-4,6-dimethoxypyrimidine (**1d**) (83 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 24 h, and purified by flash column chromatography (0 to 14% Et_2O/CH_2Cl_2) to give a viscous pale yellow oil (116 mg, 59%). IR (ATR) 3347 (NH and OH), 2969, 1684 (C=O) 1586, 1523, 1374, 1185, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.32–7.13 (5H, m, Ar**H**), 7.09 (1H, br s, N**H**), 6.02 (1H, s, Ar**H**), 5.07 (1H, t, *J* = 8.0 Hz, NHC**H**), 4.40 (1H, t, *J* = 5.4 Hz, O**H**), 3.87 (6H, s, 2 × OC**H**$_3$), 3.70 (1H, ddd, *J* = 10.5, 7.3, 5.6 Hz, C**H**$_2$), 3.61–3.51 (1H, m, C**H**$_2$), 3.29 (1H, m,

CH_2CH), 1.29 (9H, s, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 170.5 (C), 168.5 (C), 154.3 (C), 142.0 (C), 127.6 (2 × CH), 126.4 (2 × CH), 126.3 (CH), 86.7 (CH), 77.4 (C), 61.8 (CH_2), 55.4 (CH), 54.3 (CH), 53.4 (2 × CH_3), 27.8 (3 × CH_3); HRMS (ESI) Exact mass calculated for $C_{20}H_{27}N_3NaO_5$ $[M+Na]^+$: 412.1843, found: 412.1806.



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxy-1-phenylpropyl]carbamate (3e). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 20 h, and purified by flash column chromatography (0 to 6% acetone/CH_2Cl_2) to give a white solid (118 mg, 62%). m.p. 132–134 °C (Et_2O); IR (ATR) 3383 (NH and OH), 2968, 2926, 1678 (C=O) 1564, 1520, 1171, 1105 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.30 (4H, app d, *J* = 4.3 Hz, Ar**H**), 7.26–7.19 (1H, m, Ar**H**), 7.11 (1H, br s, N**H**), 6.31 (1H, s, Ar**H**), 4.94 (1H, t, *J* = 8.5 Hz, NHC**H**), 4.34 (1H, t, *J* = 5.3 Hz, O**H**), 3.94 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.56 (1H, ddd, *J* = 10.5, 7.8, 5.8 Hz, CH_2), 3.46–3.35 (1H, m, CH_2), 3.20–3.08 (1H, m, CH_2CH), 1.26 (9H, s, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.3 (C), 170.7 (C), 164.3 (C), 154.3 (C), 141.9 (C), 127.7 (2 × CH), 126.51 (2 × CH), 126.47 (CH), 101.7 (CH), 77.5 (C), 61.5 (CH_2), 54.4 (CH), 53.81 (CH_3), 53.77 (CH), 53.1 (CH_3), 27.7 (3 × CH_3); HRMS (ESI) Exact mass calculated for $C_{20}H_{27}N_3NaO_5$ $[M+Na]^+$: 412.1843, found: 412.1846.

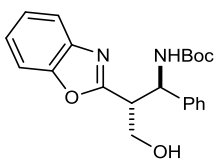


(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-3-hydroxy-1-phenyl-2-(4-phenyl-1,3-thiazol-2-yl)propyl]carbamate (3f). The title compound was prepared according to General Procedure D from 4-phenyl-2-vinylthiazole (**1f**) (94 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 48 h, and purified by flash column chromatography (15% Et_2O/CH_2Cl_2) to give a 3.5:1 mixture of diastereomers as a pale yellow solid (137 mg, 67%). IR (ATR) 3339 (NH and OH), 2978, 2926, 1682 (C=O), 1165, 735 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{23}H_{26}N_2NaO_3S$ $[M+Na]^+$: 433.1556, found: 433.1560.

Major diastereomer: ^1H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.02–7.93 (2H, m, Ar**H**), 7.87 (1H, s, Ar**H**), 7.51–7.42 (2H, m, Ar**H**), 7.38–7.27 (4H, m, Ar**H**), 7.27–7.19 (2H, m, Ar**H**), 5.08 (1H, t, *J* = 8.2 Hz, NHC**H**), 4.69 (1H, t, *J* = 4.9 Hz, O**H**), 3.67–3.51 (3H, m, CH_2 and CH_2CH), 1.28 (9H, s, $C(CH_3)_3$), N**H** signal appears as a very broad singlet over the range ~7.4–7.2 ppm; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.5 (C), 154.3 (C), 153.1 (C), 141.6 (C), 134.2 (C), 128.3 (2 × CH),

127.7 (2 × CH), 127.5 (CH), 126.6 (3 × CH), 125.7 (2 × CH), 113.3 (CH), 77.6 (C), 61.9 (CH_2), 55.2 (CH), 51.0 (CH), 27.8 (3 × CH_3).

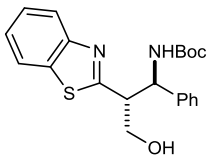
Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.90–7.84 (2H, m, Ar**H**), 7.76 (1H, s, Ar**H**), 7.51–7.42 (2H, m, Ar**H**), 7.38–7.27 (3H, m, Ar**H**), 7.27–7.19 (2H, m, Ar**H**), 7.16–7.07 (1H, m, Ar**H**), 5.08 (, *J* = 8.2 Hz, NHC**H**), 4.78 (1H, t, *J* = 5.0 Hz, O**H**), 3.96–3.83 (2H, m, C**H**$_2$), 3.71–3.64 (1H, m, CH_2C**H**), 1.36 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.3 (C), 154.6 (C), 153.0 (C), 141.2 (C), 134.2 (C), 128.2 (2 × CH), 127.5 (2 × CH), 127.3 (CH), 126.8 (2 × CH), 126.4 (CH), 125.7 (2 × CH), 113.2 (CH), 77.8 (C), 61.5 (CH_2), 56.0 (CH), 51.0 (CH), 27.9 (3 × CH_3).



(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-2-(1,3-benzoxazol-2-yl)-3-hydroxy-1-phenylpropyl]carbamate (3g). The title compound was prepared according to General Procedure D from 2-vinylbenzoxazole (**1g**) (73 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 40 h, and purified by flash column chromatography (0 to 10% Et_2O/CH_2Cl_2) to give a 4:1 mixture of diastereomers as a white solid (118 mg, 64%). IR (ATR) 3386 (NH and OH), 2980, 1702, 1692 (C=O), 1498, 1455, 1244, 1167 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{21}H_{25}N_2O_4$ $[M+H]^+$: 369.1809, found: 369.1794.

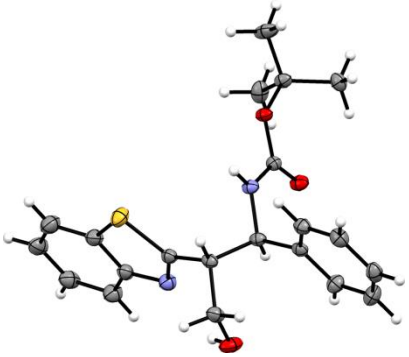
Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.72–7.66 (1H, m, Ar**H**), 7.66–7.60 (1H, m, Ar**H**), 7.42–7.36 (2H, m, Ar**H**), 7.36–7.29 (4H, m, Ar**H**), 7.29–7.23 (1H, m, Ar**H**), 5.07 (1H, t, *J* = 9.1 Hz, NHC**H**), 4.69 (1H, t, *J* = 5.3 Hz, O**H**), 3.74–3.58 (2H, m, C**H**$_2$ and CH_2C**H**), 3.53–3.45 (1H, m, C**H**$_2$), 1.19 (9H, s, C(C**H**$_3$)$_3$), N**H** signal appears as a very broad singlet at ~7.2 ppm; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 166.1 (C), 154.2 (C), 149.9 (C), 141.0 (C), 140.7 (C), 127.9 (2 × CH), 126.9 (CH), 126.62 (2 × CH), 124.2 (CH), 123.7 (CH), 118.9 (CH), 110.1 (CH), 77.7 (C), 61.0 (CH_2), 54.4 (CH), 48.3 (CH), 27.7 (3 × CH_3).

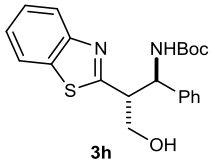
Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.60–7.55 (1H, m, Ar**H**), 7.55–7.51 (1H, m, Ar**H**), 7.41–7.23 (4H, m, Ar**H**), 7.18–7.13 (2H, m, Ar**H**), 7.12–7.07 (1H, m, Ar**H**), 5.14–4.99 (1H, m, NHC**H**), 4.73 (1H, t, *J* = 5.3 Hz, O**H**), 4.00–3.88 (2H, m, C**H**$_2$), 3.74–3.58 (1H, m, CH_2C**H**), 1,35 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 165.6 (C), 149.7 (C), 140.5 (C), 127.6 (2 × CH), 126.9 (CH), 126.6 (2 × CH), 124.1 (CH), 123.6 (CH), 118.9 (CH), 110.0 (CH), 77.9 (C), 60.8 (CH_2), 48.1 (CH), 27.9 (3 × CH_3).



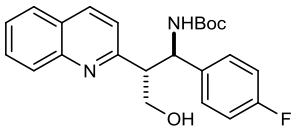
(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-2-(1,3-benzothiazol-2-yl)-3-hydroxy-1-phenylpropyl]carbamate (3h). The title compound was prepared according to General Procedure D from 2-vinylbenzathoazole (**1h**) (81 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol) for a reaction time of 48 h, and purified by flash column chromatography (0 to 40% EtOAc/petroleum ether) to give a white solid (128 mg, 67%). m.p. 154–156 °C (*i*-PrOH); IR (ATR) 3372 (NH and OH), 2978, 2926, 1682 (C=O), 1167 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.01 (1H, d, *J* = 7.9 Hz, Ar**H**), 7.98 (1H, d, *J* = 7.8 Hz, Ar**H**) 7.49 (1H, ddd, *J* = 8.2, 7.3, 1.3 Hz, Ar**H**), 7.44–7.37 (3H, m, Ar**H**), 7.37–7.29 (2H, m, Ar**H**), 7.25 (1H, ddd, *J* = 7.2, 3.7, 1.2 Hz, Ar**H**), 7.17 (1H, br s, N**H**), 5.09 (1H, t, *J* = 8.9 Hz, NHC**H**), 4.70 (1H, t, *J* = 5.0 Hz, O**H**), 3.79–3.68 (1H, m, CH_2CH), 3.60 (2H, t, *J* = 5.5 Hz, $OHCH_2$), 1.21 (9H, s, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.3 (C), 154.3 (C), 152.1 (C), 141.4 (C), 134.5 (C), 127.8 (2 × CH), 126.7 (3 × CH), 125.4 (CH), 124.3 (CH), 121.9 (CH), 121.4 (CH), 77.6 (C), 61.8 (CH_2), 55.6 (CH), 51.8 (CH), 27.7 (3 × CH_3); HRMS (ESI) Exact mass calculated for $C_{21}H_{24}N_2NaO_3S$ $[M+Na]^+$: 407.1400, found: 407.1398.

Slow evaporation of a solution of **3h** in *i*-PrOH provided crystals that were suitable for X-ray crystallography:



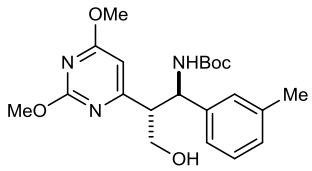


3h
CCDC 1431895



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-1-(4-fluorophenyl)-3-hydroxy-2-(quinolin-2-yl)propyl]carbamate (4a). The title compound was prepared according to General Procedure D from 2-vinylquinoline (**1b**) (78 mg, 0.50 mmol) and *N*-Boc imine **2b** (134 mg, 0.600 mmol) for a reaction time of 48 h, and purified by flash column chromatography (0 to 20% Et_2O/CH_2Cl_2) to give a pale yellow solid (144 mg, 73%). m.p. 165–167 °C (Et_2O); IR (ATR) 3365 (NH and OH), 2962, 1675 (C=O), 1601, 1527, 1511, 1289, 1252, 1227, 1163, 1074 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.20 (1H, d, *J* = 8.4 Hz, Ar**H**), 7.99 (1H, d, *J* = 8.4 Hz, Ar**H**), 7.91 (1H, d, *J* = 7.7 Hz, Ar**H**), 7.79–7.69 (1H, m, Ar**H**), 7.60–7.50 (1H, m, Ar**H**), 7.42–7.24 (4H, m, Ar**H** and N**H**), 7.14–7.01 (2H, m, Ar**H**), 5.15 (1H, t, *J* = 8.5 Hz, NHC**H**), 4.51 (1H, t, *J* = 5.1 Hz, O**H**), 3.80–3.57 (2H, m, CH_2), 3.55–3.40 (1H, m, CH_2CH), 1.19 (9H, s, $C(CH_3)_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 161.6 (C), 160.8 (d, *J* = 242.5 Hz, C),

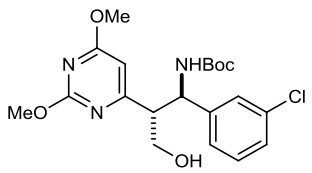
154.3 (C), 146.7 (C), 138.6 (C), 135.1 (CH), 128.9 (CH), 128.4 (d, J = 8.0 Hz, 2 × CH), 128.1 (CH), 127.3 (CH), 126.5 (C), 125.5 (CH), 122.8 (CH), 114.3 (d, J = 21.2 Hz, 2 × CH), 77.4 (C), 62.2 (CH_2), 54.6 (CH), 54.4 (CH), 27.7 (3 × CH_3); ^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ –116.5; HRMS (ESI) Exact mass calculated for $C_{23}H_{26}FN_2O_3$ $[M+H]^+$: 419.1741, found: 419.1733.



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxy-1-(3-methylphenyl)propyl]carbamate (4b). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2c** (132 mg, 0.600 mmol), and purified by column chromatography (0 to 20% Et_2O/CH_2Cl_2) to give a 7.5:1 mixture of diastereomers as a white solid (168 mg, 83%). IR (ATR) 3369 (NH and OH), 2971, 1684 (C=O), 1596, 1565, 1483, 1362, 1252, 1165 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{21}H_{29}O_5N_3Na$ $[M+Na]^+$: 426.1999, found: 426.1957.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.27–6.91 (5H, m, Ar**H** and N**H**), 6.32 (1H, s, Ar**H**), 5.03–4.74 (1H, m, NHC**H**), 4.34 (1H, s, O**H**), 3.94 (3H, s, OC**H**$_3$), 3.87 (3H, s, OC**H**$_3$), 3.57–3.50 (1H, m, C**H**$_2$), 3.45–3.31 (1H, m, C**H**$_2$), 3.11 (1H, s, CH_2C**H**), 2.29 (3H, s, CC**H**$_3$), 1.26 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.4 (C), 170.7 (C), 164.3 (C), 154.2 (C), 141.9 (C), 136.8 (C), 127.6 (CH), 127.2 (CH), 127.1 (CH), 123.6 (CH), 101.8 (CH), 77.4 (C), 61.5 (CH_2), 54.4 (CH), 53.9 (CH), 53.8 (CH_3), 53.1 (CH_3), 27.7 (3 × CH_3), 20.7 (CH_3);

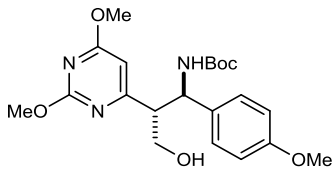
Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.27–6.91 (5H, m, Ar**H** and N**H**), 6.11 (1H, s, Ar**H**), 5.03–4.74 (1H, m, NHC**H**), 3.80 (3H, s, OC**H**$_3$), 2.21 (1H, s, CC**H**$_3$), 1.36 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.3 (C), 136.3 (C), 127.5 (CH), 126.8 (CH), 123.9 (CH), 101.1 (CH), 77.6 (C), 61.0 (CH_2), 53.7 (CH_3), 53.0 (CH_3), 27.9 (3 × CH_3), 20.6 (CH_3).



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-1-(3-chlorophenyl)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxypropyl]carbamate (4c). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2d** (144 mg, 0.600 mmol), and purified by column chromatography (80% Et_2O/toluene) to give a 5:1 mixture of diastereomers as a white solid (129 mg, 60%). IR (ATR) 3351 (NH and OH), 2974, 1693 (C=O), 1596, 1567, 1482, 1364, 1250, 1165, 1106 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{20}H_{27}ClN_3O_5$ $[M+H]^+$: 424.1634, found: 424.1628.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.40 (1H, t, *J* = 1.8 Hz, Ar**H**), 7.36–7.31 (1H, m, Ar**H**), 7.30–7.25 (2H, m, Ar**H**), 6.34 (1H, s, Ar**H**), 4.95 (1H, t, *J* = 8.5 Hz, NHC**H**), 4.39 (1H, dd, *J* = 5.7, 5.0 Hz, O**H**), 3.94 (3H, s, OC**H**$_3$), 3.88 (3H, s, OC**H**$_3$), 3.59–3.50 (1H, m, C**H**$_2$) 3.46–3.36 (1H, m, C**H**$_2$), 3.20–3.10 (1H, m, CH_2C**H**), 1.26 (9H, s, C(C**H**$_3$)$_3$), N**H** signal appears as a very broad singlet over the range ~7.2–7.1 ppm ; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 170.9 (C), 170.8 (C), 164.3 (C), 154.2 (C), 144.5 (C), 132.7 (C), 129.6 (CH), 126.53 (CH), 126.48 (CH), 125.4 (CH), 101.7 (CH), 77.7 (C), 61.4 (CH_2), 54.0 (CH), 53.8 (CH_3), 53.5 (CH), 53.1 (CH_3), 27.7 (3 × CH_3).

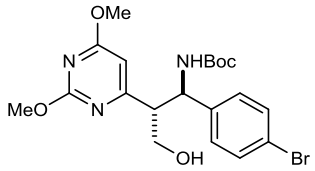
Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.30–7.25 (1H, m, Ar**H**) 7.22–7.09 (3H, m, Ar**H**), 6.16 (1H, s, Ar**H**), 4.95 (1H, t, *J* = 8.5 Hz, NHC**H**), 4.45 (1H, t, *J* = 5.2 Hz, O**H**), 3.87 (3H, s, OC**H**$_3$), 3.84–3.77 (5H, m, OC**H**$_3$ and C**H**$_2$), 3.22–3.15 (1H, m, CH_2C**H**), 1.33 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 164.2 (C), 154.6 (C), 144.2 (C), 132.3 (C), 129.2 (CH), 126.8 (CH), 126.2 (CH), 125.6 (CH), 101.2 (CH), 77.9 (C), 61.1 (CH_2), 53.7 (CH_3), 53.5 (CH), 53.0 (CH_3), 27.8 (3 × CH_3).



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxy-1-(4-methoxyphenyl)propyl]carbamate (4d). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2e** (141 mg, 0.600 mmol), and purified by column chromatography (0 to 100% Et_2O/toluene) to give an 18:1 mixture of diastereomers as a white solid (121 mg, 58%). IR 3375 (NH and OH), 2958, 1677 (C=O), 1596, 1567, 1513, 1463, 1357, 1250, 1163 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{21}H_{30}N_3O_6$ $[M+H]^+$: 420.2129, found: 420.2124.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.27–7.18 (2H, m, Ar**H**), 7.04 (1H, br s, N**H**) 6.89–6.83 (2H, m, Ar**H**), 6.32 (1H, s, Ar**H**), 4.87 (1H, t, *J* = 8.7 Hz, NHC**H**), 4.30 (1H, t, *J* = 5.3 Hz, O**H**), 3.94 (3H, s, OC**H**$_3$), 3.88 (3H, s, OC**H**$_3$), 3.74 (3H, s, OC**H**$_3$), 3.59–3.50 (1H, m, C**H**$_2$), 3.43–3.33 (1H, C**H**$_2$), 3.15–3.05 (1H, m, CH_2C**H**), 1.26 (9H, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.5 (C), 170.7 (C), 164.3 (C), 158.0 (C), 154.2 (C), 134.0 (C), 127.6 (2 × CH), 113.3 (2 × CH), 101.7 (CH), 77.3 (C), 61.5 (CH_2), 54.8 (CH_3), 54.0 (2 × CH), 53.8 (CH_3), 53.1 (CH_3), 27.7 (3 × CH_3).

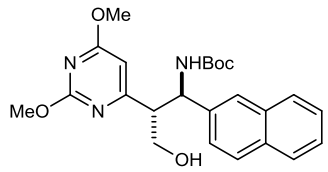
Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) 7.12–7.08 (2H, m, Ar**H**), 6.76–6.72 (2H, m, Ar**H**), 6.10 (1H, s, Ar**H**), 4.95–4.80 (1H, m, NHC**H**), 4.36 (1H, t, *J* = 5.2 Hz, O**H**), 3.79 (3H, s, OC**H**$_3$), 3.68 (3H, s, OC**H**$_3$), 1.35 (9H, s, C(C**H**$_3$)$_3$).



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-1-(4-bromophenyl)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxypropyl]carbamate (4e). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2f** (170 mg, 0.600 mmol), and purified by column chromatography (35 to 75% Et_2O/toluene) to give a 5:1 mixture of diastereomers as a white solid (144 mg, 60%). IR (ATR) 3366 (NH and OH), 2980, 1688 (C=O), 1596, 1566, 1485, 1363, 1250, 1165, 1105 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{20}H_{27}BrN_3O_5$ $[M+H]^+$: 468.1129, found: 468.1127.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.53–7.44 (2H, m, Ar**H**), 7.30–7.22 (2H, m, Ar**H**), 6.31 (1H, s, Ar**H**), 4.93 (1H, t, *J* = 8.7 Hz, NHC**H**), 4.39 (1H, dd, *J* = 5.6, 5.0 Hz, O**H**), 3.93 (3H, s, OC$\mathbf{H}_3$), 3.88 (3H, s, OC$\mathbf{H}_3$), 3.54 (1H, ddd, *J* = 10.6, 7.6, 5.7 Hz, C$\mathbf{H}_2$), 3.45–3.36 (1H, m, C$\mathbf{H}_2$), 3.15–3.08 (1H, m, CH_2C**H**), 1.27 (9H, s, C(C$\mathbf{H}_3)_3$), N**H** signal appears as a very broad singlet over the range ~7.2–7.1 ppm; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 171.0 (C), 170.8 (C), 164.3 (C), 154.2 (C), 141.4 (C), 130.7 (2 × CH), 128.8 (2 × CH), 119.6 (C), 101.7 (CH), 77.6 (C), 61.4 (CH_2), 53.8 (CH and CH_3), 53.5 (CH), 53.1 (CH_3), 27.7 (3 × CH_3).

Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.39–7.34 (2H, m, Ar**H**), 7.16–7.12 (2H, m, Ar**H**), 6.13 (1H, s, Ar**H**), 4.93 (1H, t, *J* = 8.7 Hz, NHC**H**), 4.43 (1H, t, *J* = 5.2 Hz, O**H**), 3.87 (3H, s, OC$\mathbf{H}_3$), 3.83–3.78 (5H, m, C$\mathbf{H}_2$ and OC$\mathbf{H}_3$), 3.15–3.08 (1H, m, CH_2C**H**), 1.34 (9H, s, C(C$\mathbf{H}_3)_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 170.9 (C), 170.7 (C), 164.2 (C), 154.3 (C), 141.1 (C), 130.3 (2 × CH), 129.1 (2 × CH), 119.3 (C), 101.2 (CH), 77.8 (C), 61.2 (CH_2), 53.7 (CH_3), 53.5 (CH), 53.0 (CH_3), 27.9 (3 × CH_3).

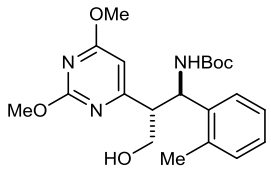


(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxy-1-(naphthalen-2-yl)propyl]carbamate (4f). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2g** (153 mg, 0.600 mmol), and purified by column chromatography (30% acetone and 1% Et_3N/petroleum ether) to give an 11:1 mixture of diastereomers as a white solid (122 mg, 56%). IR ($CHCl_3$) 3441 (NH and OH), 3014, 1692 (C=O), 1599, 1567, 1503, 1463, 1393, 1367, 1251, 1163, 1107, 1054 cm^{-1}; Exact mass calculated for $C_{20}H_{34}O_5N_3$ $[M+H]^+$: 440.2180, found: 440.2183.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.89 (2H, m, Ar**H**), 7.79 (1H, s, Ar**H**), 7.60–7.40 (4H, m, Ar**H** and N**H**), 6.39 (1H, s, Ar**H**), 5.08 (1H, t, *J* = 9.3 Hz, NHC**H**), 4.51 (1H, t, *J* = 5.1 Hz, O**H**), 3.94 (3H, s, OC$\mathbf{H}_3$), 3.86 (3H, s, OC$\mathbf{H}_3$), 3.57–3.48 (1H, m, CH_2C**H**), 3.31–3.16

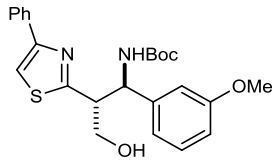
(2H, m, C**H**$_2$), 1.23 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, (CD$_3$)$_2$SO) δ 171.7 (C), 170.9 (C), 164.6 (C), 154.6 (C), 139.6 (C), 132.7 (C), 132.2 (C), 127.9 (CH), 127.7 (CH), 127.5 (CH), 126.2 (CH), 125.7 (CH), 125.7 (CH), 125.1 (CH), 102.2 (CH), 77.7 (C), 61.8 (CH$_2$), 54.5 (CH), 54.2 (CH$_3$), 54.0 (CH), 53.5 (CH$_3$), 28.0 (3 × CH$_3$).

Characteristic signals for minor diastereomer: ^{1}H NMR (400 MHz, (CD$_3$)$_2$SO) δ 6.12 (1H, s, Ar**H**), 4.98–4.89 (1H, m, NHC**H**), 4.60 (1H, t, *J* = 5.1 Hz, O**H**), 3.69 (3H, s, OC**H**$_3$), 1.34 (9H, s, C(C**H**$_3$)$_3$).



(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxy-1-(2-methylphenyl)propyl]carbamate (4g). The title compound was prepared according to General Procedure D from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2h** (132 mg, 0.600 mmol), and purified twice by column chromatography (5% acetone/CH$_2$Cl$_2$) to give a white solid (83 mg, 41%). A second fraction consisting of a 2:1 mixture of diastereomers was also obtained as a white solid (34 mg, 17%). m.p. decomposed >80 °C (petroleum ether); IR (CHCl$_3$) 3391 (NH and OH), 2982, 1707 (C=O), 1598, 1567, 1506, 1484, 1462, 1393, 1366, 1164, 1108 cm^{-1}; ^{1}H NMR (400 MHz, (CD$_3$)$_2$SO, 393 K) δ 7.27–7.21 (1H, m, Ar**H**), 7.16–7.06 (3H, m, Ar**H**), 6.84 (1H, d, *J* = 8.3 Hz, N**H**), 6.27 (1H, s, Ar**H**), 5.28 (1H, t, *J* = 8.5 Hz, NHC**H**), 4.16 (1H, t, *J* = 5.3 Hz, O**H**), 3.97 (3H, s, OC**H**$_3$), 3.89 (3H, s, OC**H**$_3$), 3.62 (1H, ddd, *J* = 10.4, 7.5, 5.8 Hz, C**H**$_2$), 3.47 (1H, dt, *J* = 10.4, 4.9 Hz, C**H**$_2$), 3.13 (1H, td, *J* = 7.8, 5.0 Hz, CH$_2$C**H**), 2.42 (3H, s, CC**H**$_3$), 1.28 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, (CD$_3$)$_2$SO, 393 K) δ 171.0 (C), 170.6 (C), 164.1 (C), 154.0 (C), 140.1 (C), 134.4 (C), 129.3 (CH), 125.8 (CH), 125.7 (CH), 125.1 (CH), 101.5 (CH), 77.3 (C), 61.1 (CH$_2$), 53.4 (CH$_3$ and CH) 52.7 (CH$_3$), 50.4 (CH), 27.5 (3 × CH$_3$), 18.1 (CH$_3$); Exact mass calculated for $C_{21}H_{30}O_5N_3$ [M+H]$^+$: 404.2180, found: 404.2174.

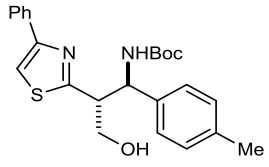
Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, (CD$_3$)$_2$SO, 393 K) δ 7.38 (1H, d, *J* = 7.5 Hz, Ar**H**), 7.15–7.05 (1H, m, Ar**H**), 7.05–6.96 (2H, m, Ar**H**), 6.83 (1H, t, *J* = 9.9 Hz, N**H**), 6.14 (1H, s, Ar**H**), 5.28 (1H, t, *J* = 8.4 Hz, NHC**H**), 4.22 (1H, t, *J* = 5.2 Hz, O**H**), 3.94–3.86 (5H, m, OC**H**$_3$ & C**H**$_2$), 3.81 (3H, s, OC**H**$_3$), 3.21 (1H, ddd, *J* = 8.8, 7.2, 4.3 Hz, CH$_2$C**H**), 2.29 (3H, s, C**H**$_3$), 1.35 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, (CD$_3$)$_2$SO, 393 K) δ 171.2 (C), 170.5 (C), 154.4 (C), 139.8 (C), 129.1 (CH), 126.4 (CH), 125.8 (CH), 124.8 (CH), 100.5 (CH), 77.5 (C), 60.9 (CH$_2$), 53.3 (CH$_3$), 53.0 (CH), 52.6 (CH$_3$), 51.1 (CH), 27.6 (3 × CH$_3$), 18.0 (CH$_3$).



(±)-*tert*-butyl *N*-[(1*R*,2*R*)-3-hydroxy-1-(3-methoxyphenyl)-2-(4-phenyl-1,3-thiazol-2-yl)propyl]carbamate (4h). The title compound was prepared according to General Procedure D from 4-phenyl-2-vinylthiazole (**1f**) (94 mg, 0.50 mmol) and *N*-Boc imine **2i** (141 mg, 0.600 mmol), and purified by column chromatography (20% EtOAc/CH_2Cl_2 then 20% acetone/petroleum ether) to give a 5:1 mixture of diastereomers as a white solid (129 mg, 58%); IR (ATR) 3408, 3371 (NH and OH), 2976, 1677 (C=O), 1601, 1522, 1490, 1254, 1162, 1040 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{24}H_{29}O_4N_2S$ $[M+H]^+$: 441.1843, found: 441.1846.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.99–7.93 (2H, m, Ar**H**), 7.87 (1H, s, Ar**H**), 7.49–7.42 (2H, m, Ar**H**), 7.37–7.32 (1H, m, Ar**H**), 7.30–7.14 (1H, m, Ar**H** and N**H**), 6.95–6.89 (2H, m, Ar**H**), 6.83–6.77 (1H, m, Ar**H**), 5.04 (1H, t, *J* = 8.0 Hz, NHC**H**), 4.67 (1H, t, *J* = 4.9 Hz, O**H**), 3.73 (3H, s, OC$\mathbf{H}_3$), 3.69–3.52 (3H, m, C$\mathbf{H}_2$C**H**), 1.28 (9H, s, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.5 (C), 159.0 (C), 154.3 (C), 153.1 (C), 143.2 (C), 134.2 (C), 128.8 (CH), 128.3 (2 × CH), 127.4 (CH), 125.7 (2 × CH), 119.0 (CH), 113.3 (CH), 112.4 (CH), 112.3 (CH), 77.6 (C), 61.9 (CH_2), 55.3 (CH), 54.7 (CH_3), 51.0 (CH), 27.8 (3 × CH_3);

Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.91–7.86 (2H, m, Ar**H**), 7.77 (1H, s, Ar**H**), 7.45–7.39 (2H, m, Ar**H**), 7.37–7.30 (1H, m, Ar**H**), 7.14–7.08 (1H, m, Ar**H**), 6.83–6.78 (2H, m, Ar**H**), 6.72–6.68 (1H, m, Ar**H**), 5.04 (1H, t, *J* = 8.0 Hz, NHC**H**), 4.77 (1H, t, *J* = 4.8 Hz, O**H**), 3.93–3.84 (2H, m, C$\mathbf{H}_2$), 3.65 (3H, s, OC$\mathbf{H}_3$), 3.69–3.52 (1H, m, CH_2C**H**), 1.37 (9H, s, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.3 (C), 158.7 (C), 154.6 (C), 153.0 (C), 128.5 (CH), 128.2 (2 × CH), 127.4 (CH), 125.7 (2 × CH), 119.2 (CH), 113.2 (CH), 112.7 (CH), 112.2 (CH), 77.8 (C), 61.5 (CH_2), 54.6 (CH_3), 50.7 (CH), 27.9 (3 × CH_3).

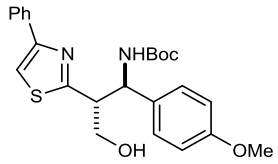


(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-3-hydroxy-1-(4-methylphenyl)-2-(4-phenyl-1,3-thiazol-2-yl)propyl]carbamate (4i). The title compound was prepared according to General Procedure D from 4-phenyl-2-vinylthiazole (**1f**) (94 mg, 0.50 mmol) and *N*-Boc imine **2j** (132 mg, 0.600 mmol), and purified by column chromatography (0 to 5% Et_2O/CH_2Cl_2) to give a 4:1 mixture of diastereomers as a white solid (147 mg, 69%). IR (ATR) 3372 (NH and OH), 2977, 2924, 1679 (C=O), 1520, 1167 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{24}H_{28}O_3N_2SNa$ $[M+Na]^+$: 447.1713, found: 447.1661.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.01–7.93 (2H, m, Ar**H**), 7.87 (1H, s, Ar**H**), 7.48–7.41 (2H, m, Ar**H**), 7.37–7.32 (1H, m, Ar**H**), 7.29–7.15 (3H, m, Ar**H** and N**H**), 7.15–7.09 (2H, m, Ar**H**), 5.04 (1H, t, *J* = 8.1 Hz, NC**H**), 4.69–4.62 (1H, m, O**H**), 3.71–3.49 (3H, m, C$\mathbf{H}_2$C**H**), 2.28 (3H, s, ArC$\mathbf{H}_3$), 1.28 (9H, s, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (101 MHz, $CD_3)_2SO$, 343 K) δ

169.6 (C), 154.3 (C), 153.1 (C), 138.6 (C), 135.7 (C), 134.16 (C), 128.33 (2 × CH), 128.28 (2 × CH), 127.44 (CH), 126.5 (2 × CH), 125.7 (2 × CH), 113.3 (CH), 77.5 (C), 62.0 (CH_2), 55.0 (CH), 51.1 (CH), 27.8 (3 × CH_3), 20.22 (CH_3);

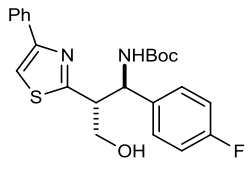
Minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.92–7.84 (2H, m, Ar**H**), 7.76 (1H, s, Ar**H**), 7.48–7.38 (2H, m, Ar**H**), 7.37–7.32 (1H, m, Ar**H**), 7.15–7.09 (2H, m, Ar**H**), 7.01 (2H, d, *J* = 7.9 Hz, Ar**H**), 5.04 (1H, t, *J* = 8.1 Hz, NHC**H**), 4.76 (1H, t, *J* = 4.9 Hz, O**H**), 3.92–3.82 (2H, m, C**H**$_2$), 3.71–3.49 (1H, m, CH_2C**H**), 2.21 (3H, s, ArC**H**$_3$), 1.36 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.4 (C), 154.6 (C), 153.0 (C), 138.2 (C), 135.4 (C), 134.18 (C), 128.2 (2 × CH), 128.1 (2 × CH), 127.35 (CH), 126.7 (2 × CH), 125.7 (2 × CH), 113.2 (CH), 77.7 (C), 61.5 (CH_2), 50.7 (CH), 27.9 (3 × CH_3), 20.16 (CH_3).



(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-3-hydroxy-1-(4-methoxyphenyl)-2-(4-phenyl-1,3-thiazol-2-yl)propyl]carbamate (4j). The title compound was prepared according to General Procedure D from 4-phenyl-2-vinylthiazole (**1f**) (94 mg, 0.50 mmol) and *N*-Boc imine **2e** (141 mg, 0.600 mmol), and purified by column chromatography (30% Et_2O/CH_2Cl_2) to give a 4:1 mixture of diastereomers as a white solid (131 mg, 60%); IR (ATR) 3366 (NH and OH), 2978, 2932, 1676 (C=O), 1515, 1293, 1240, 1164 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{24}H_{29}N_2O_4S$ $[M+H]^+$: 441.1843, found: 441.1840.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.01–7.93 (2H, m, Ar**H**), 7.87 (1H, s, Ar**H**), 7.50–7.41 (2H, m, Ar**H**), 7.38–7.30 (1H, m, Ar**H**), 7.31–7.24 (2H, m, Ar**H**), 6.91–6.83 (2H, m, Ar**H**), 5.02 (1H, t, *J* = 8.0 Hz, NHC**H**), 4.65 (1H, t, *J* = 4.8 Hz, O**H**), 3.74 (3H, s, OC**H**$_3$), 3.67–3.50 (3H, m, C**H**$_2$C**H**), 1.27 (9H, s, C(C**H**$_3$)$_3$), N**H** signal appears as a very broad singlet over the range ~7.2–7.1 ppm; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.7 (C), 158.0 (C), 154.3 (C), 153.1 (C), 134.2 (C), 133.7 (C), 128.3 (2 × CH), 127.7 (2 × CH), 127.4 (CH), 125.7 (2 × CH), 113.33 (2 × CH), 113.29 (CH), 77.5 (C), 62.0 (CH_2), 54.8 (CH_3 and CH), 51.2 (CH), 27.8 (3 × CH_3).

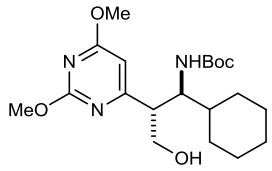
Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.92–7.86 (2H, m, Ar**H**), 7.76 (1H, s, Ar**H**), 7.44–7.38 (2H, m, Ar**H**), 7.36–7.30 (1H, m, Ar**H**), 7.18–7.13 (2H, m, Ar**H**), 6.79–6.73 (2H, m, Ar**H**), 5.02 (1H, t, *J* = 8.0 Hz, NHC**H**), 4.75 (1H, t, *J* = 4.8 Hz, O**H**), 3.88 (1H, m, C**H**$_2$), 3.67 (3H, s, OC**H**$_3$), 3.66–3.52 (1H, m, CH_2C**H**), 1.37 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.5 (C), 157.8 (C), 154.6 (C), 153.0 (C), 133.3 (C), 128.2 (2 × CH), 128.0 (2 × CH), 127.3 (CH), 125.7 (2 × CH), 113.2 (CH), 113.1 (2 × CH), 77.7 (C), 61.6 (CH_2), 54.7 (CH_3), 50.9 (CH), 27.9 (3 × CH_3).



(±)-*tert*-Butyl *N*-[(1*R*,2*R*)-1-(4-fluorophenyl)-3-hydroxy-2-(4-phenyl-1,3-thiazol-2-yl)propyl]carbamate (4k). The title compound was prepared according to General Procedure D from 4-phenyl-2-vinylthiazole (**1f**) (94 mg, 0.50 mmol) and *N*-Boc imine **2b** (134 mg, 0.600 mmol), and purified by column chromatography (0 to 9% acetone/CH_2Cl_2) to give a 3.5:1 mixture of diastereomers as a white solid (137 mg, 64%). IR (ATR) 3375 (NH and OH), 2979, 1679 (C=O), 1510, 1226, 1167, 725 cm^{-1}; HRMS (ESI) Exact mass calculated for $C_{24}H_{26}FO_5N_2S$ $[M+HCO_2]^-$: 473.1552, found: 473.1556.

Major diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 8.00–7.94 (2H, m, Ar**H**), 7.88 (1H, s, Ar**H**), 7.48–7.42 (2H, m, Ar**H**), 7.42–7.31 (3H, m, Ar**H**), 7.15–7.08 (2H, m, Ar**H**), 5.08 (1H, t, *J* = 8.4 Hz, NHC**H**), 4.70 (1H, t, *J* = 4.9 Hz, O**H**), 3.70–3.50 (3H, m, C**H**$_2$C**H**), 1.27 (9H, s, C(C**H**$_3$)$_3$), N**H** signal appears as a very broad singlet over the range ~7.3–7.1 ppm; ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.4 (C), 160.9 (d, *J* = 242.9 Hz, C), 154.3 (C), 153.14 (C), 137.8 (C), 134.1 (C), 128.5 (d, *J* = 8.0 Hz, 2 × CH), 128.3 (2 × CH), 127.5 (CH), 125.7 (2 × CH), 114.5 (d, *J* = 21.2 Hz, 2 × CH), 113.39 (CH), 77.7 (C), 61.8 (CH_2), 54.6 (CH), 51.0 (CH), 27.8 (3 × CH_3); ^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ –116.1.

Characteristic signals for the minor diastereomer: ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 7.91–7.84 (2H, m, Ar**H**), 7.76 (1H, s, Ar**H**), 7.42–7.22 (5H, m, Ar**H**), 7.03–6.97 (2H, m, Ar**H**), 5.14–5.00 (1H, m, NHC**H**), 4.80 (1H, t, *J* = 4.8 Hz, O**H**), 3.95–3.83 (1H, m, C**H**$_2$), 3.71–3.65 (1H, m, CH$_2$C**H**), 1.37 (9H, s, C(C**H**$_3$)$_3$); ^{13}C NMR (101 MHz, $(CD_3)_2SO$, 343 K) δ 169.1 (C), 160.7 (d, *J* = 243.4 Hz, CF), 154.6 (C), 153.08 (C), 128.8 (d, *J* = 7.9 Hz, 2 × CH), 128.2 (2 × CH), 127.4 (CH), 125.7 (2 × CH), 114.1 (d, *J* = 21.2 Hz, 2 × CH), 113.2 (CH), 77.9 (C), 61.5 (CH_2), 50.8 (CH), 27.9 (3 × CH_3); ^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ –116.5.

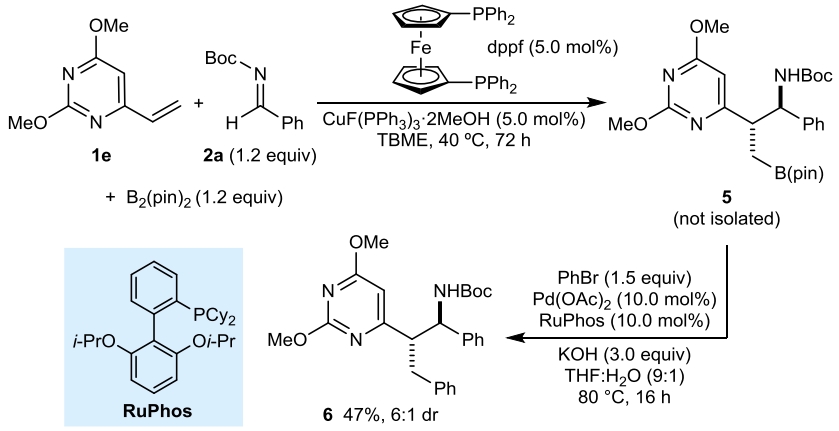


(±)-*tert*-Butyl *N*-[(1*S*,2*S*)-1-cyclohexyl-2-(2,6-dimethoxypyrimidin-4-yl)-3-hydroxypropyl]carbamate (4l). The title compound was prepared according to General Procedure F from 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2k** (127 mg, 0.600 mmol), and purified by column chromatography (30% acetone in 1% Et_3N/petroleum ether) to give a white solid (74 mg, 37%). m.p. 109–111 °C (cyclohexane); IR ($CHCl_3$) 3423 (NH and OH), 2933, 2856, 1680 (C=O), 1596, 1566, 1507, 1383, 1165, 1107 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$, 343 K) δ 6.38 (1H, s, Ar**H**), 6.15 (1H, br s, N**H**), 4.10 (1H, br s, O**H**), 3.92 (3H, s, OC**H**$_3$), 3.91 (3H, s, OC**H**$_3$), 3.78–3.70 (1H, m, NHC**H**), 3.68 (2H, d, *J* = 6.5 Hz, C**H**$_2$OH), 2.99–3.05 (1H, m, CH$_2$C**H**), 1.77–1.63 (4H, m, 2 × C**H**$_2$), 1.62–1.54 (1H, m, C**H**$_2$), 1.42–1.26 (1H, m, C**H**), 1.36 (9H, s,

C(C**H**$_3$)$_3$), 1.21–1.08 (3H, m, C**H**$_2$), 1.08–0.95 (2H, m, C**H**$_2$); ^{13}C NMR (101 MHz, (CD$_3$)$_2$SO, 343 K) δ 171.5 (C), 170.7 (C), 164.0 (C), 155.0 (C), 101.0 (CH), 76.9 (C), 62.0 (CH$_2$), 54.6 (CH), 53.4 (CH$_3$), 52.7 (CH$_3$), 49.4 (CH), 39.6 (CH), 29.5 (CH$_2$), 27.6 (3 × CH$_3$ and CH$_2$), 25.4 (CH$_2$), 25.0 (CH$_2$), 24.9 (CH$_2$); Exact mass calculated for $C_{20}H_{34}O_5N_3$ $[M+H]^+$: 396.2493, found: 396.2486.

Sequential Borylative Coupling and Suzuki Reaction

(±)-*tert*-Butyl *N*-[(1*R*,2*S*)-2-(2,6-dimethoxypyrimidin-4-yl)-1,3-diphenylpropyl]carbamate (6)

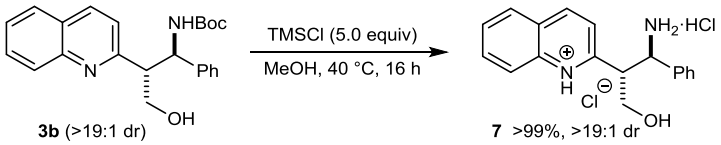


A mixture of CuF(PPh$_3$)$_3$·2MeOH (23.3 mg, 0.0250 mmol), dppf (13.9 mg, 0.0250 mmol), and B$_2$(Pin)$_2$ (152 mg, 0.600 mmol) in TBME (1.25 mL) was stirred at room temperature for 20 min. The resulting suspension was added *via* cannula to a microwave vial containing 6-vinyl-2,4-dimethoxypyrimidine (**1e**) (83 mg, 0.50 mmol) and *N*-Boc imine **2a** (123 mg, 0.600 mmol), and the mixture was stirred at 40 °C for 72 h. The reaction was cooled to room temperature, filtered through a short silica plug using Et$_2$O/petroleum ether (3:1) as the eluent, and concentrated *in vacuo*. To the residue was added Pd(OAc)$_2$ (11.2 mg, 0.050 mmol), RuPhos (23.3 mg, 0.050 mmol), KOH (84.2 mg, 1.50 mmol) and THF/H$_2$O (9:1) (5 mL). The mixture was heated at 50 °C for 48 h, cooled to room temperature, diluted with H$_2$O (15 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed (brine), dried (Na$_2$SO$_4$), and concentrated *in vacuo*. Purification of the residue by column chromatography (0 to 18% EtOAc/petroleum ether) gave the title compound **6** as a white solid (107 mg, 47%). m.p. 99–101 °C (Et$_2$O); IR (CHCl$_3$) 3369 (NH), 3012, 1709 (C=O), 1599, 1568, 1482, 1392, 1367, 1169, 1106 cm^{-1}; ^{1}H NMR (400 MHz, (CD$_3$)$_2$SO) δ 7.37–7.28 (4H, m, Ar**H**), 7.27–7.20 (1H, m, Ar**H**), 7.17–7.11 (2H, m, Ar**H**), 7.11–7.04 (1H, m, Ar**H**), 6.97–6.88 (2H, m, Ar**H**), 6.04 (1H, s, Ar**H**), 4.86 (1H, t, *J* = 8.6 Hz, NHC**H**), 3.95 (3H, s, OC**H**$_3$), 3.79 (3H, s, OC**H**$_3$), 3.35 (1H, ddd, *J* = 10.1, 8.3, 4.8 Hz, CH$_2$C**H**), 2.96 (1H, dd, *J* = 13.5, 10.2 Hz, C**H**$_2$CH), 2.65 (1H, dd, *J* = 13.5, 4.6 Hz, C**H**$_2$CH), 1.29 (9H, s, C(C**H**$_3$)$_3$), N**H** signal appears as a very broad singlet over the range ~7.2–7.0 ppm; ^{13}C NMR (101 MHz, (CD$_3$)$_2$SO) δ

171.3 (C), 170.6 (C), 164.3 (C), 154.2 (C), 141.8 (C), 139.0 (C), 128.2 (2 × CH), 127.9 (2 × CH), 127.7 (2 × CH), 126.6 (3 × CH), 125.5 (CH), 101.7 (CH), 77.5 (C), 57.2 (CH), 53.8 (CH_3), 53.0 (CH_3), 52.8 (CH), 37.0 (CH_2), 27.7 (3 × CH_3); Exact mass calculated for $C_{26}H_{32}O_4N_3$ $[M+H]^+$: 450.2387, found: 450.2405.

Removal of Boc Group from Product 3b

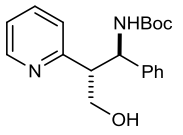
(±)-2-[(1*R*,2*S*)-1-Azaniumyl-3-hydroxy-1-phenylpropan-2-yl]quinolin-1-ium dichloride (7)



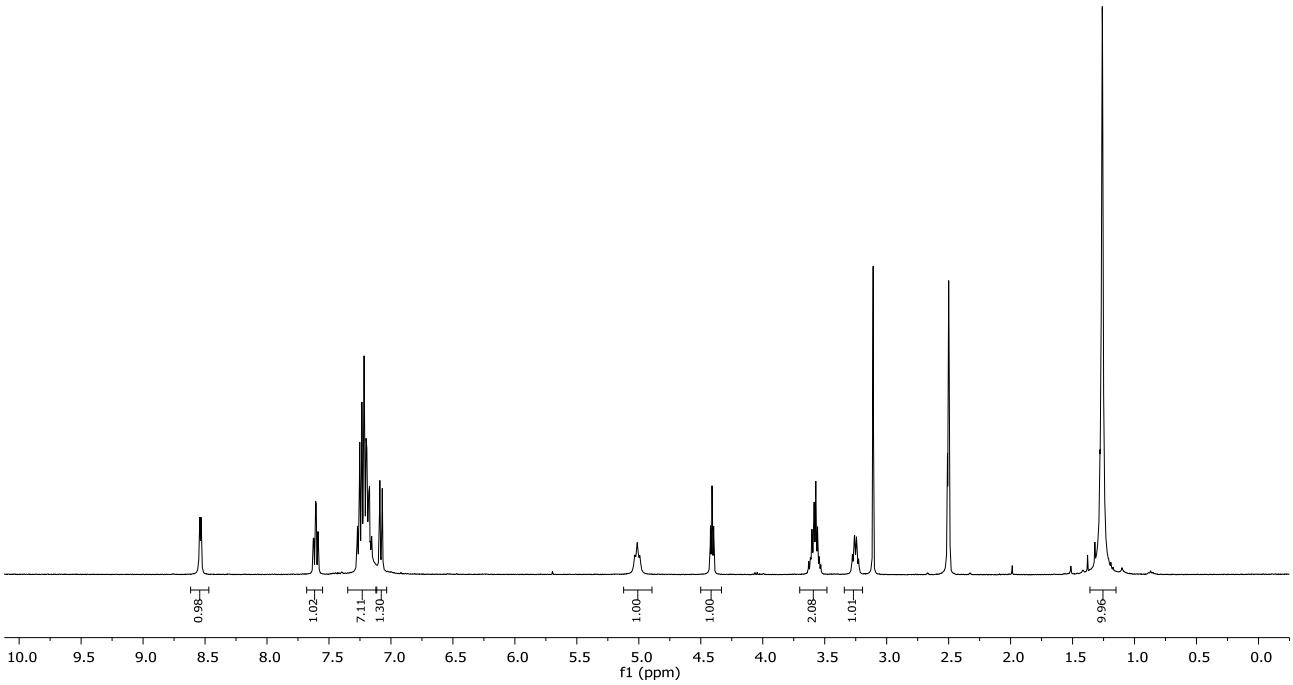
3b (>19:1 dr) **7** >99%, >19:1 dr

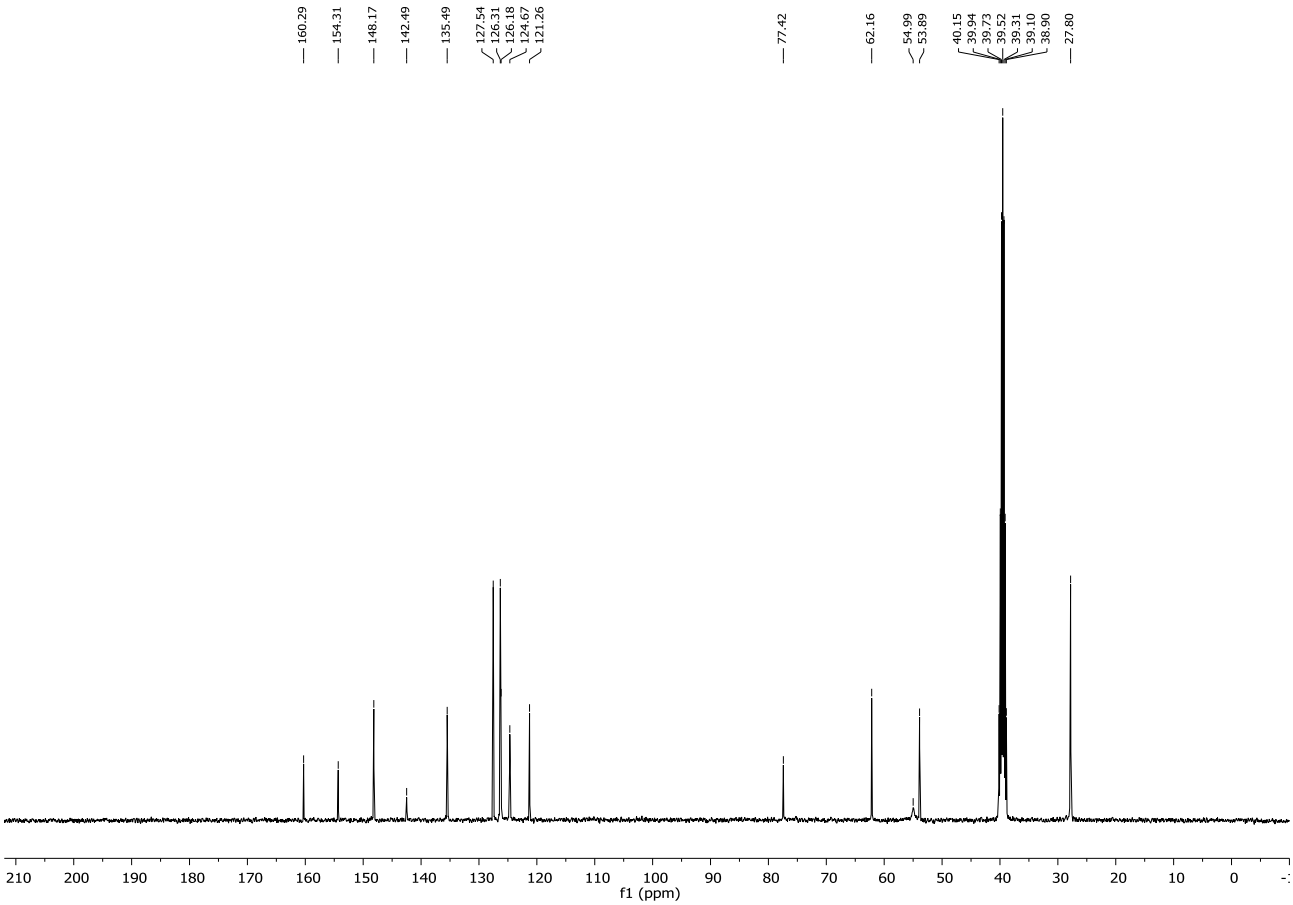
MeOH (3 mL) was added to TMSCl (190 µL, 1.50 mmol) and the resulting solution was stirred for 10 min before the addition of the carbamate **3b** (113 mg, 0.300 mmol, single diastereomer). The mixture was heated at 40 °C for 16 h, cooled to room temperature, and concentrated *in vacuo* to leave the *bishydrochloride salt* **7** as pale yellow solid (105 mg, >99%). m.p. decomposed >135 °C (MeOH); IR (ATR) 3412 (NH and OH), 2913, 2725, 2619, 2595, 1647, 1614, 1602, 1521, 1390, 1079 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 9.25 (1H, d, *J* = 8.6 Hz, Ar**H**), 8.54 (1H, dd, *J* = 8.6, 0.6 Hz, Ar**H**), 8.40 (1H, d, *J* = 8.1 Hz, Ar**H**), 8.37 (1H, d, *J* = 8.6 Hz, Ar**H**), 8.24 (1H, ddd, *J* = 8.5, 7.0, 1.3 Hz, Ar**H**), 8.03 (1H, ddd, *J* = 8.2, 7.1, 1.0 Hz, Ar**H**), 7.79–7.73 (2H, m, Ar**H)**, 7.64–7.52 (3H, m, Ar**H**), 5.33 (1H, *J* = 10.9 Hz, C**H**NH), 4.35 (1H, ddd, *J* = 10.9, 6.9, 4.1 Hz, CH_2C**H**), 3.80 (1H, dd, *J* = 11.1, 6.9 Hz, C$\mathbf{H}_2$), 3.63 (1H, dd, *J* = 11.1, 4.1 Hz, C$\mathbf{H}_2$); ^{13}C NMR (101 MHz, CD_3OD) δ 158.3 (C), 148.9 (CH), 140.3 (C), 136.6 (CH), 135.7 (C), 131.4 (CH), 130.9 (3 × CH), 130.5 (CH), 130.2 (C), 129.0 (2 × CH), 123.8 (CH), 121.8 (CH), 62.7 (CH_2), 56.8 (CH), 52.3 (CH); Exact mass calculated for $C_{18}H_{18}ON_2Na$ $[M+Na–2HCl]^+$: 301.1311, found: 301.1379.

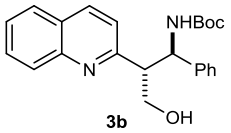
NMR Spectra



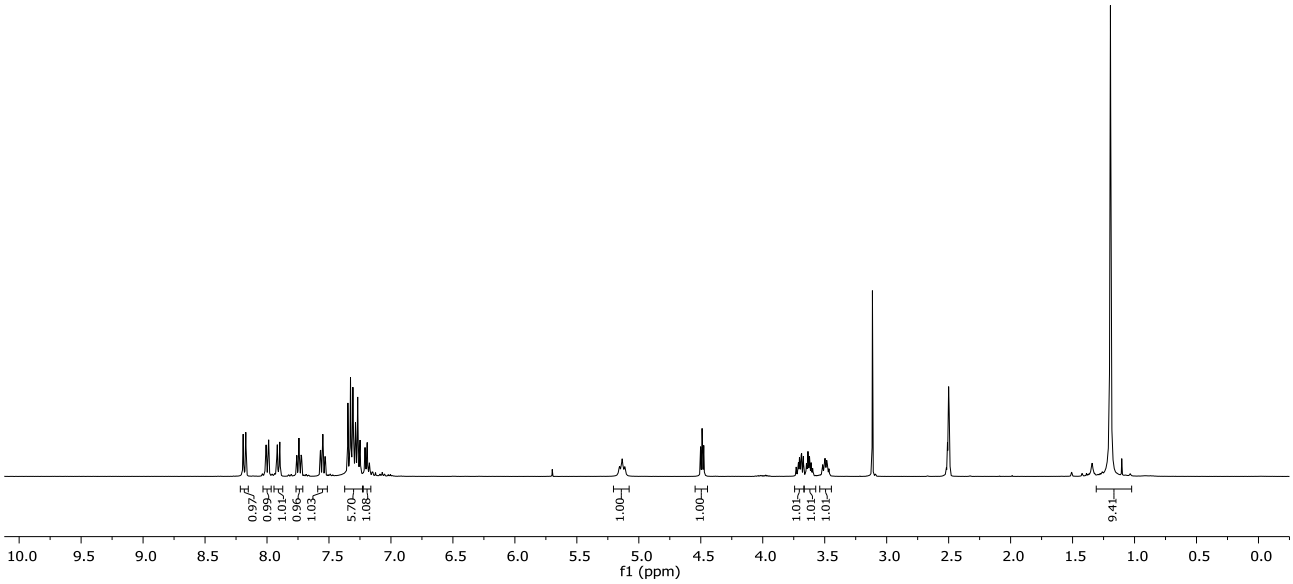
3a

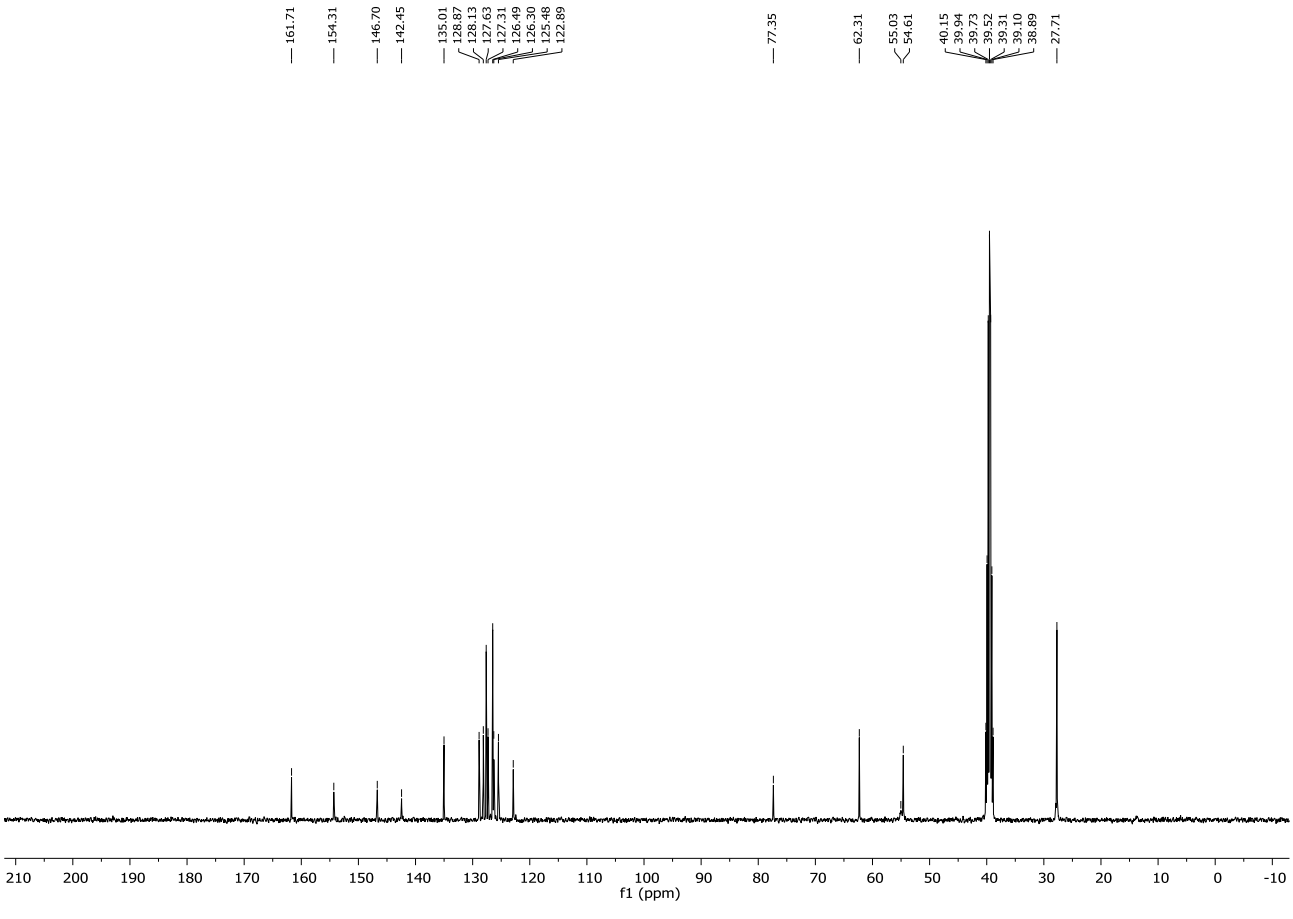


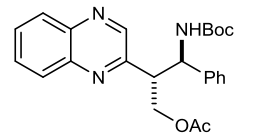



NHBoc
Ph
N
OH

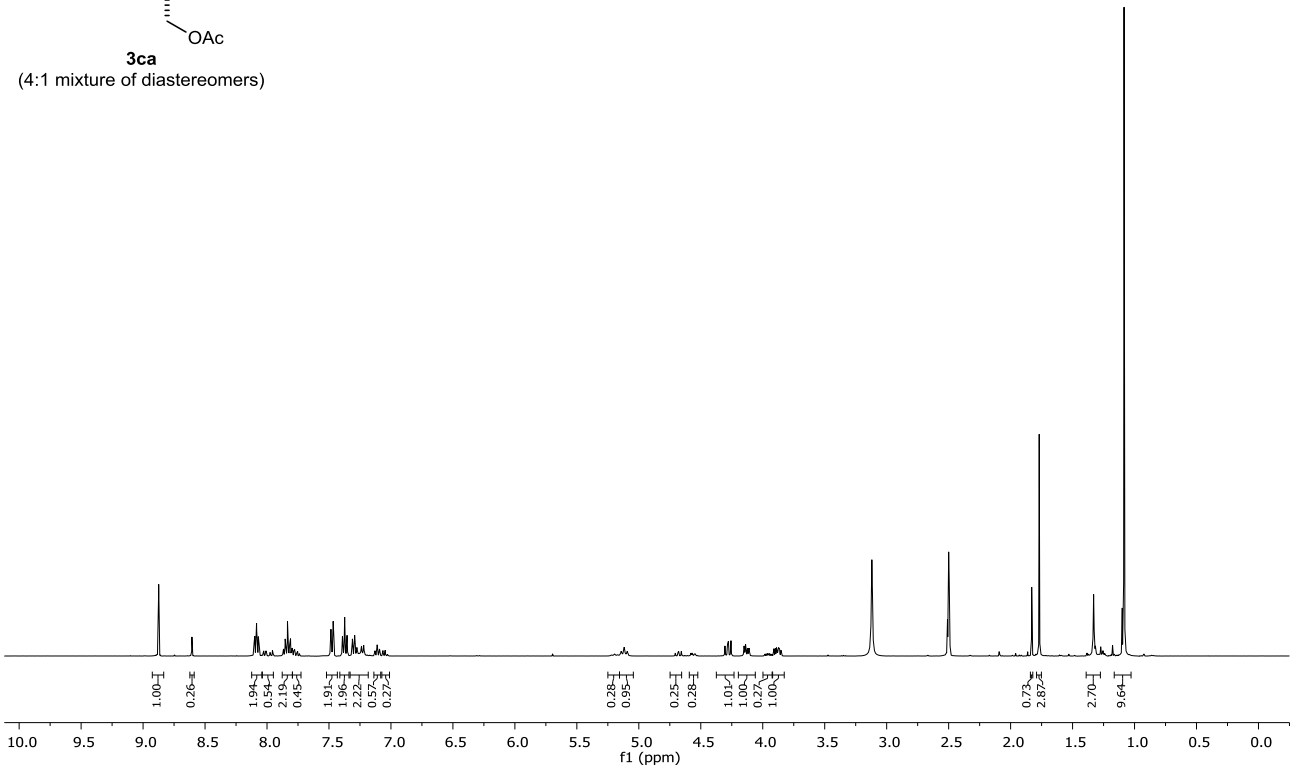
3b

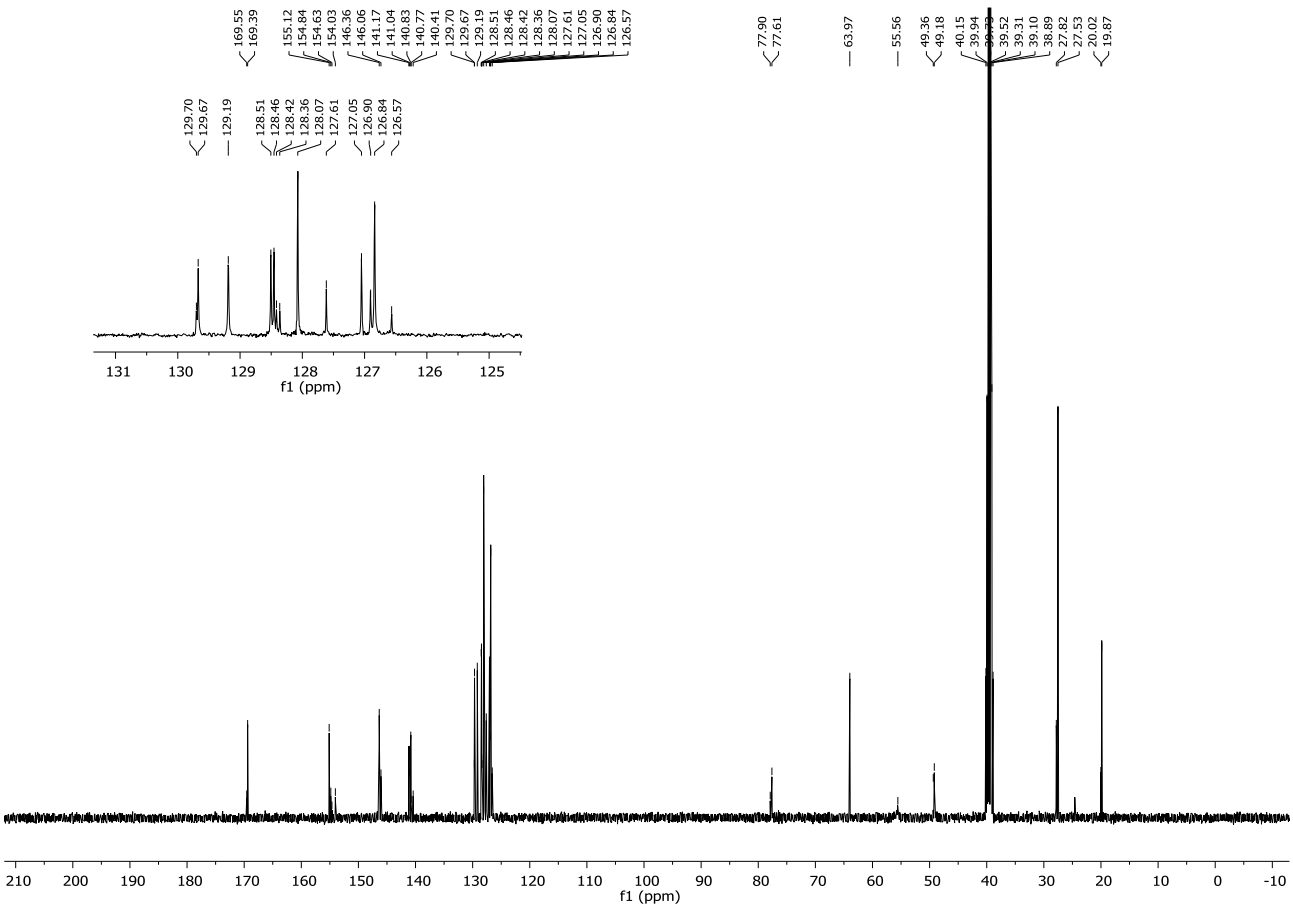

0.97
0.99
1.01
0.96
1.03
5.70
1.08
1.00
1.00
1.01
1.01
1.01
9.41
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

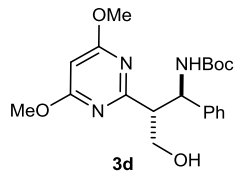

161.71
154.31
146.70
142.45
135.01
128.87
128.13
127.63
127.31
126.49
126.30
125.48
122.89
77.35
62.31
55.03
54.61
40.15
39.94
39.73
39.52
39.31
39.10
38.89
27.71
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



3ca
(4:1 mixture of diastereomers)

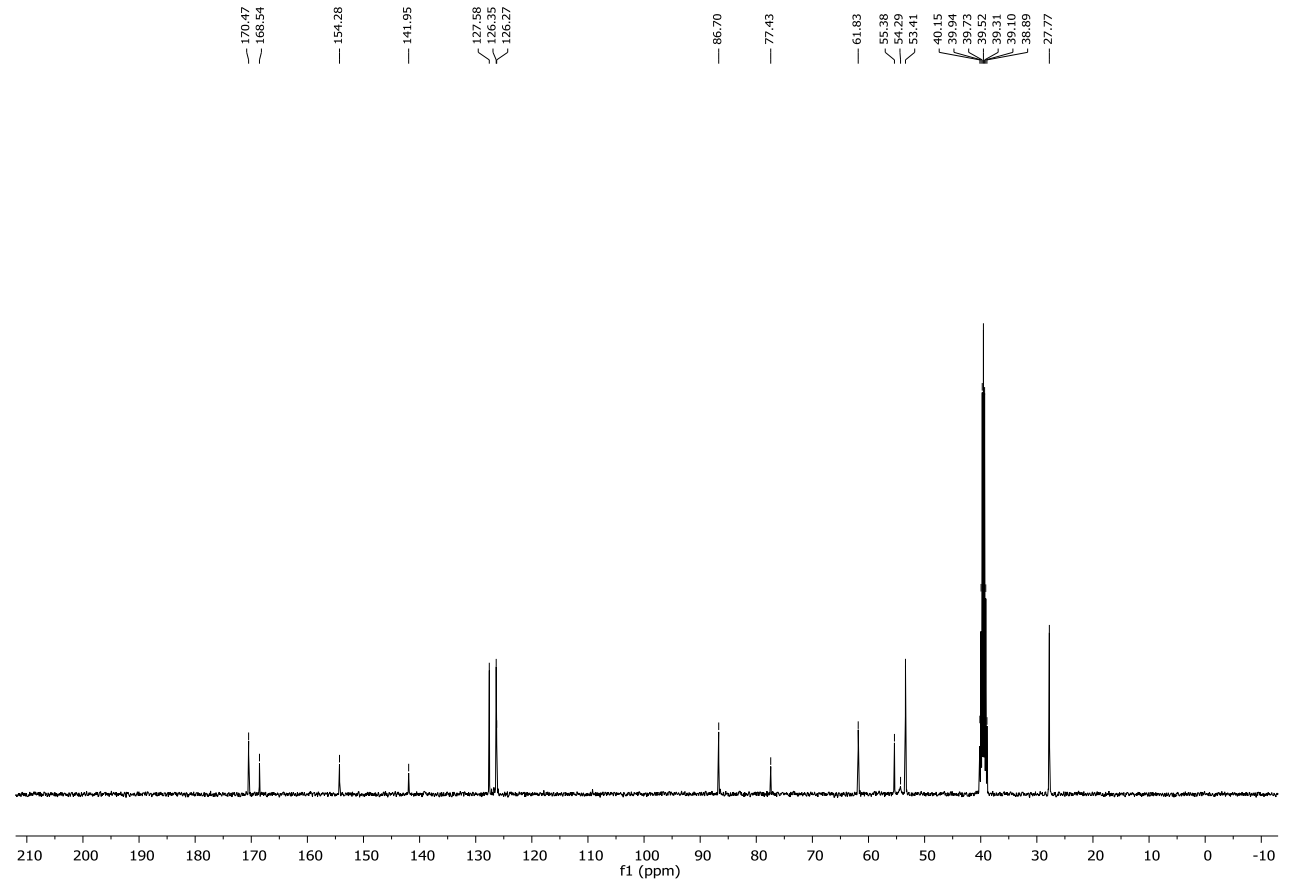





OMe
N
NHBoc
MeO
N
Ph
OH

3d

5.39
0.84
0.94
1.00
0.98
6.09
1.07
1.01
1.06
9.73
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.47
168.54
154.28
141.95
127.58
126.35
126.27
86.70
77.43
61.83
55.38
54.29
53.41
40.15
39.94
39.73
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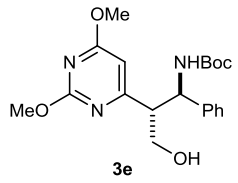
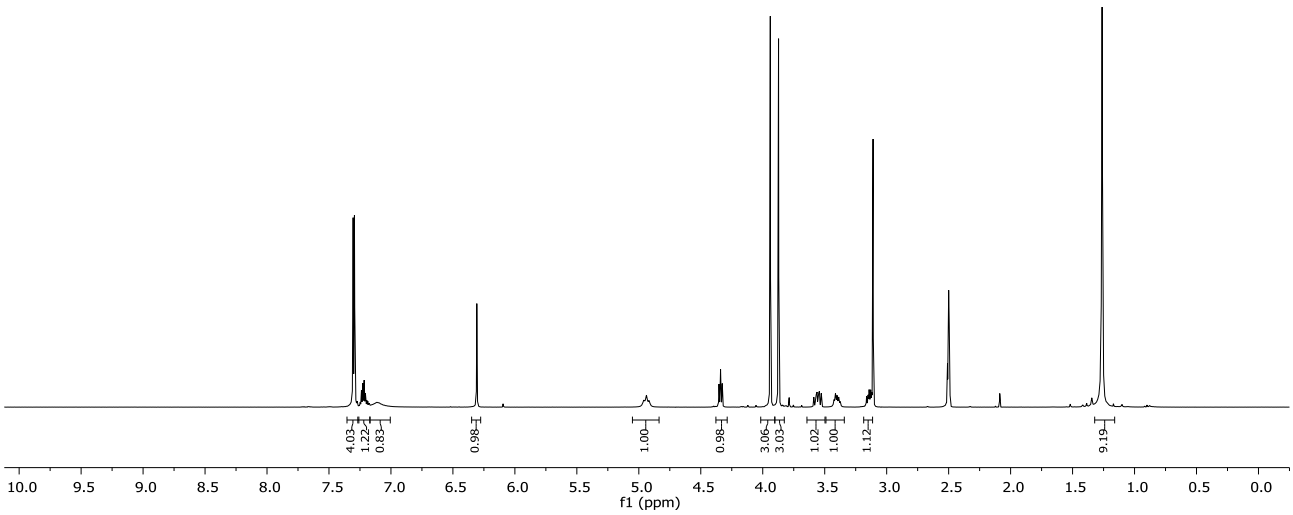
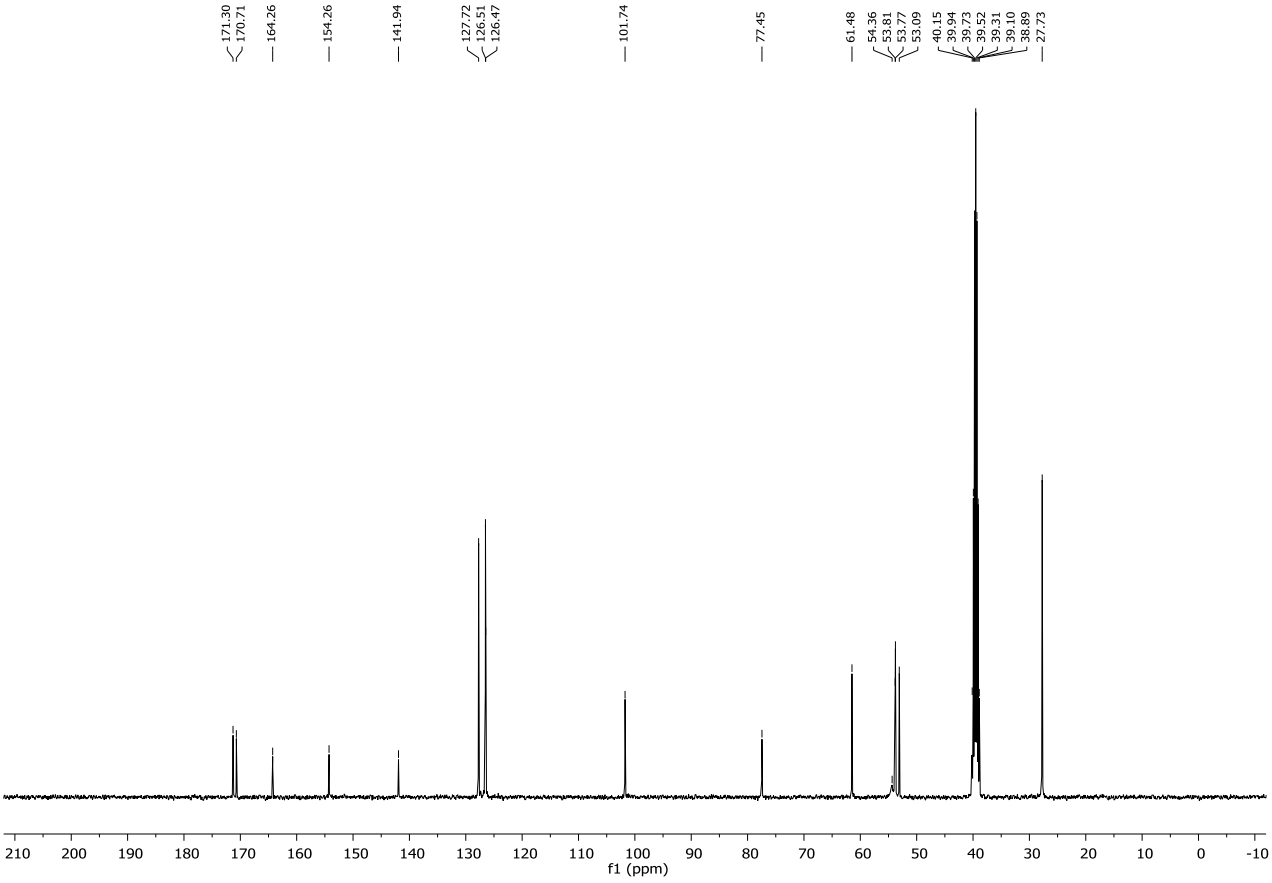
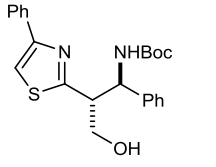
f1 (ppm)


OMe
N
NHBoc
MeO
N
Ph
OH

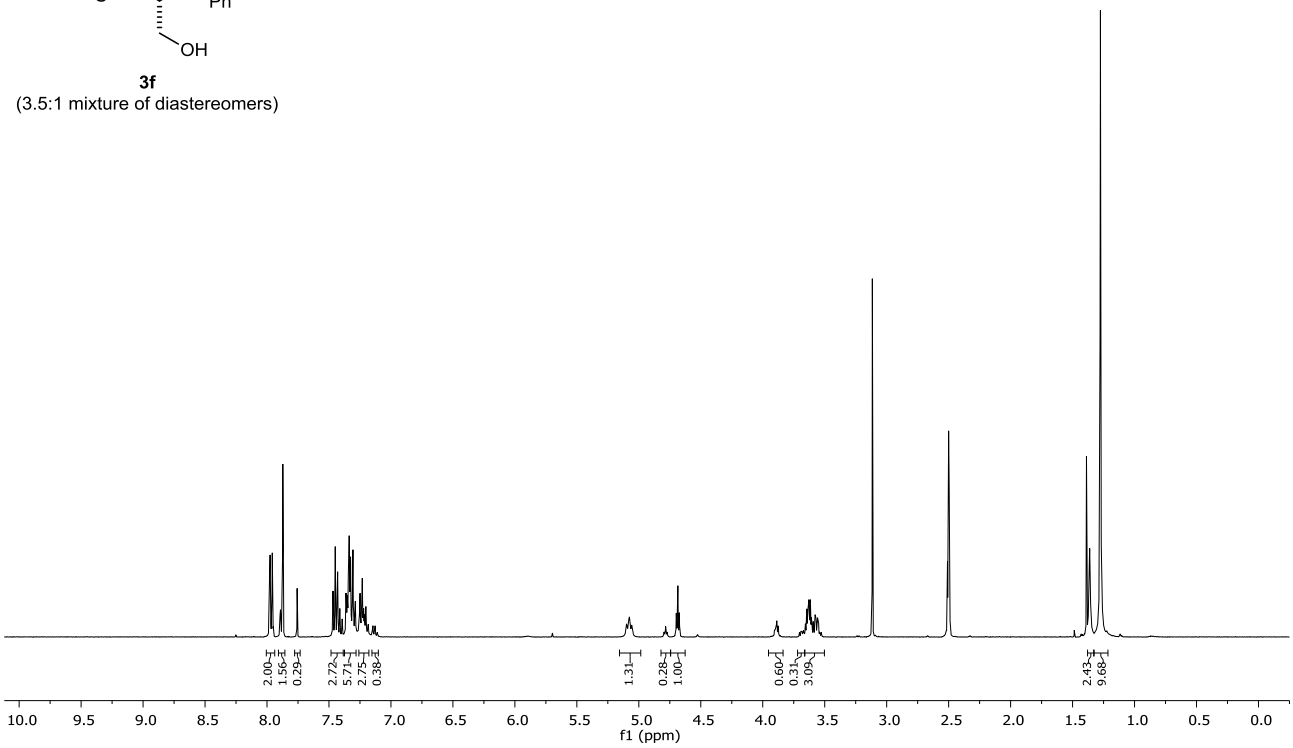
3e

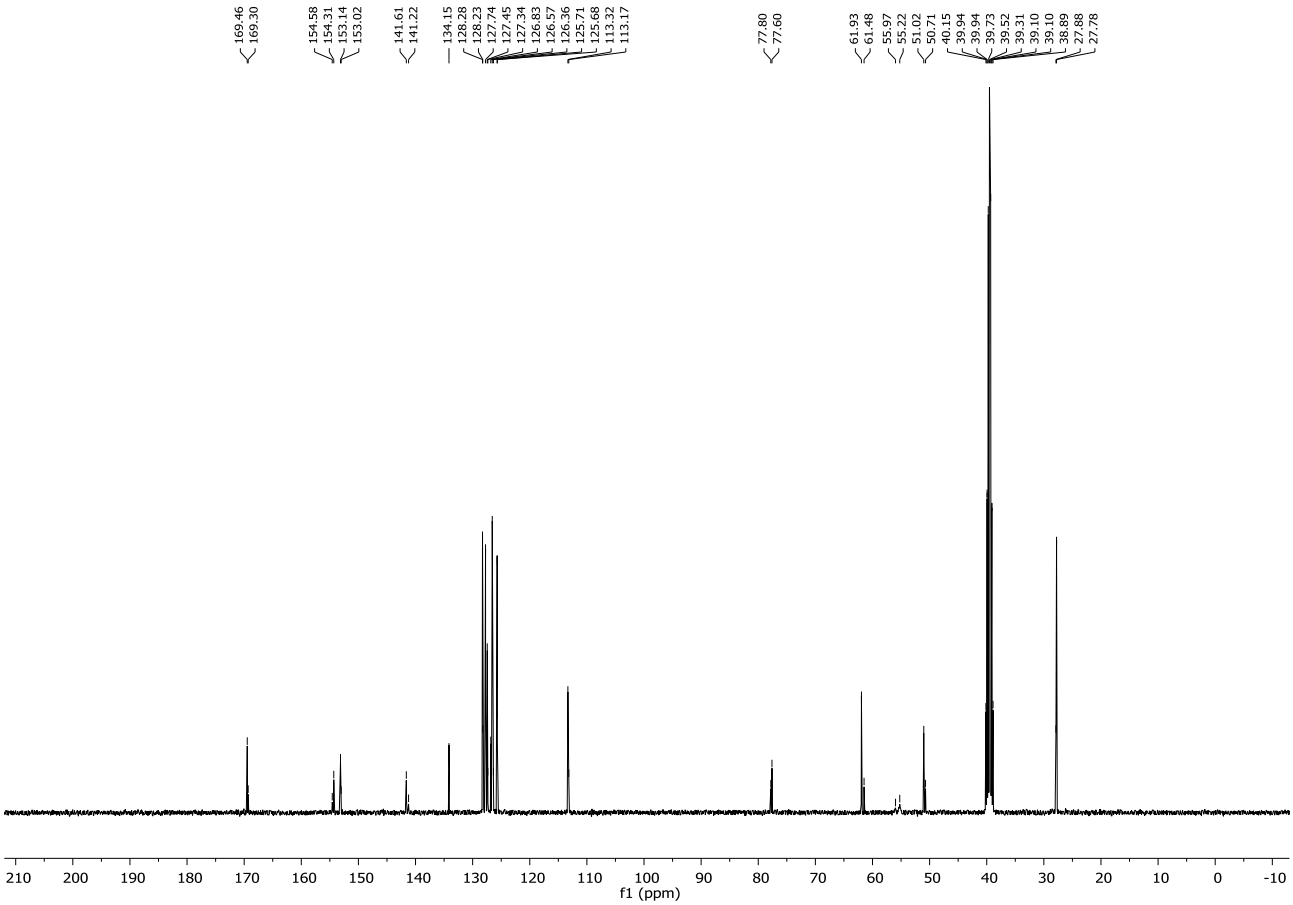

4.03
1.22
0.83
0.98
1.00
0.98
3.06
3.03
1.02
1.00
1.12
9.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

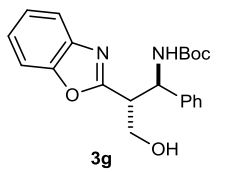

171.30
170.71
164.26
154.26
141.94
127.72
126.51
126.47
101.74
77.45
61.48
54.36
53.81
53.77
53.09
40.15
39.94
39.73
39.52
39.31
39.10
38.89
27.73
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



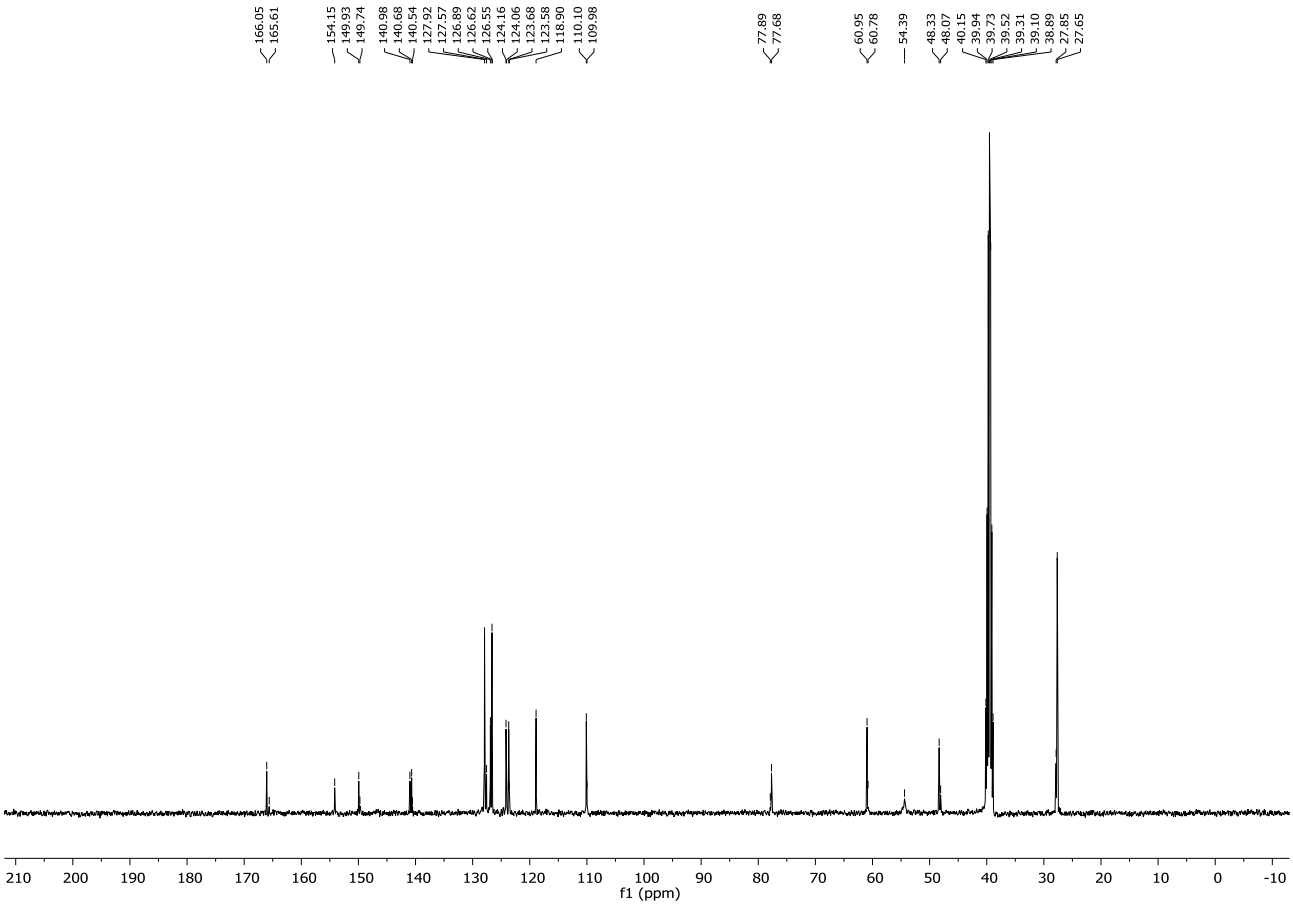
3f
(3.5:1 mixture of diastereomers)

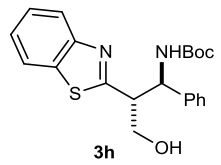






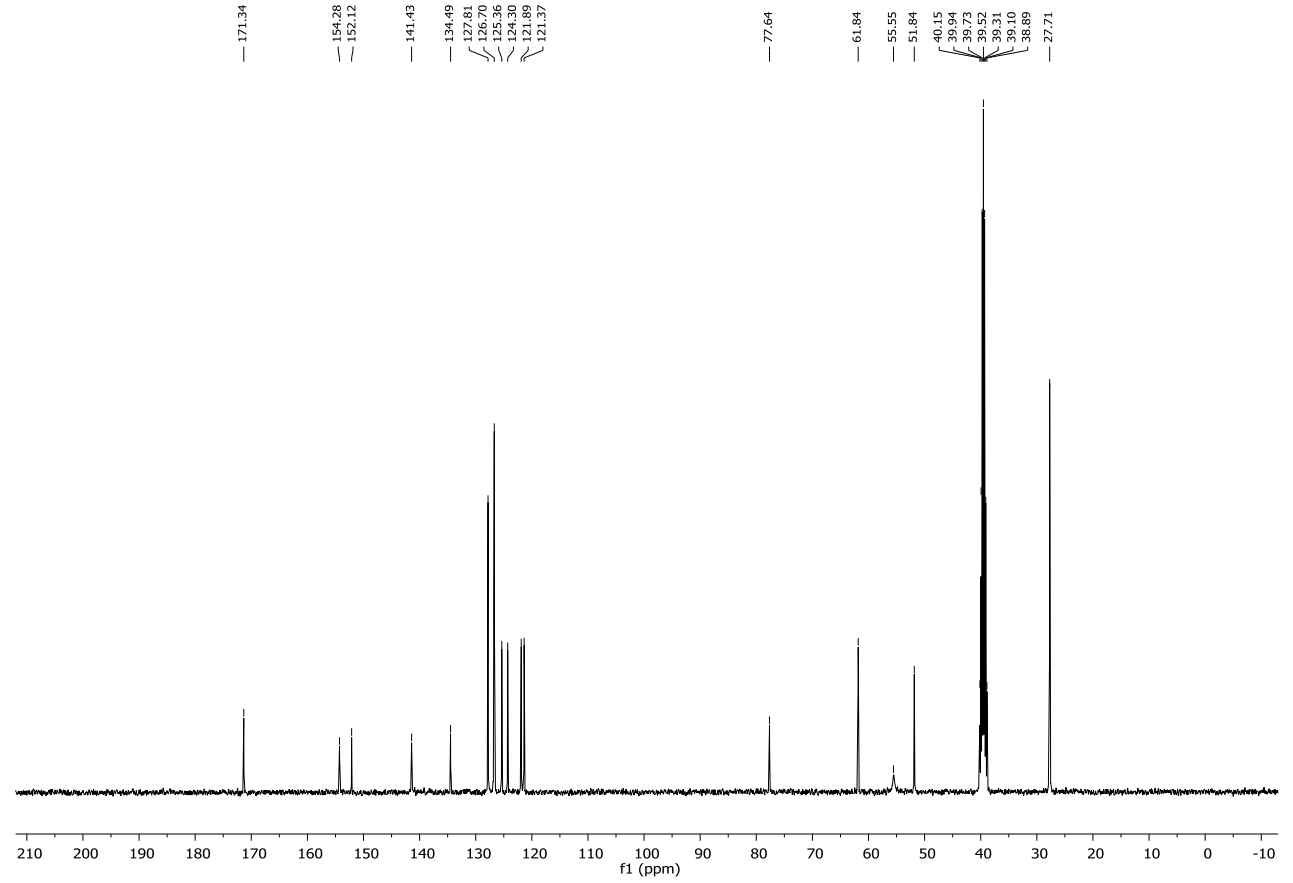
3g
(4:1 mixture of diastereomers)




N
S
NHBoc
Ph
OH

3h

1.93
1.06
3.06
2.10
1.11
0.83
1.00
1.00
1.06
2.04
9.52
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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154.28
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126.70
125.36
124.30
121.89
121.37
77.64
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55.55
51.84
40.15
39.94
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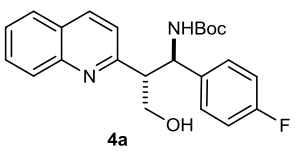
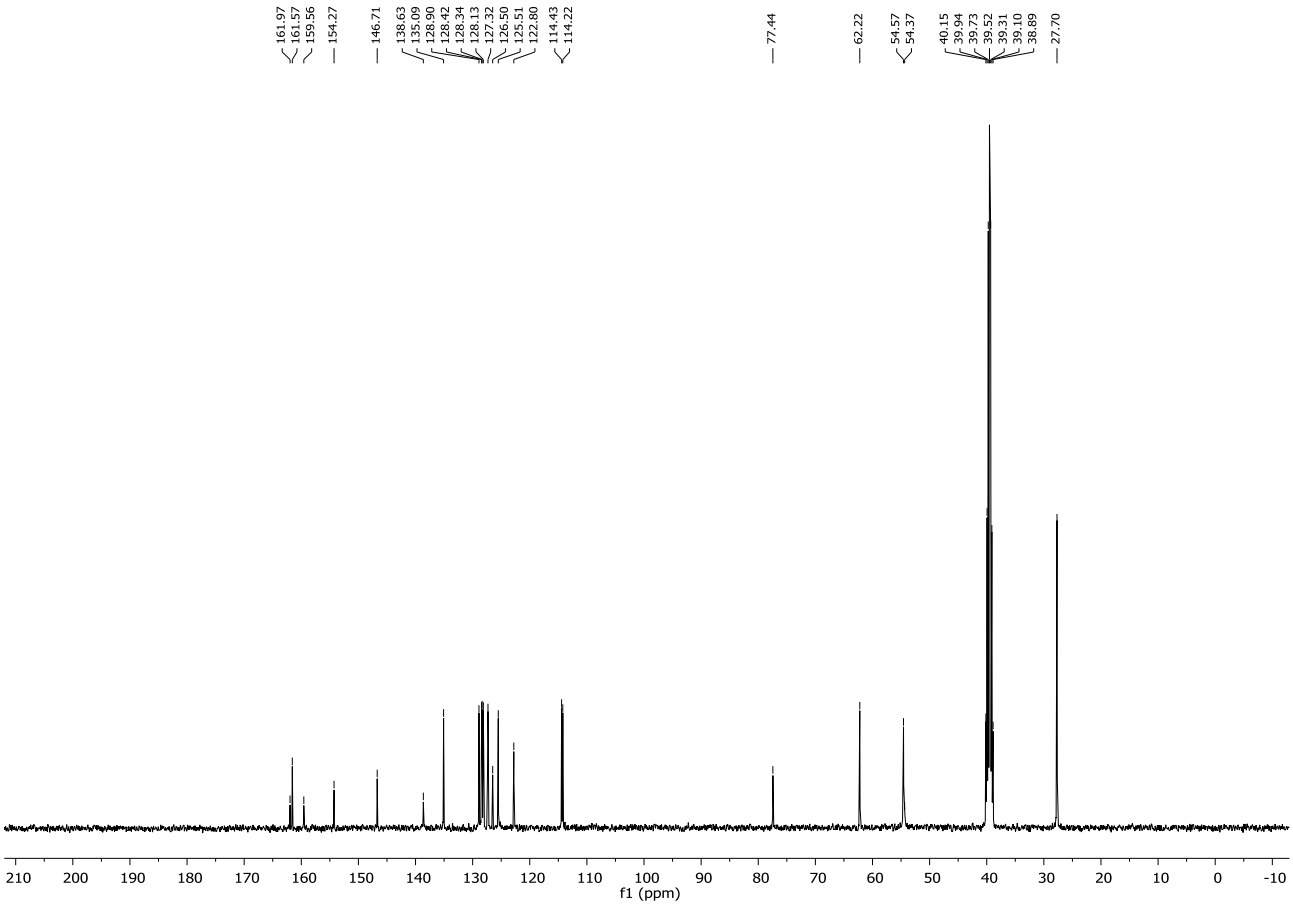
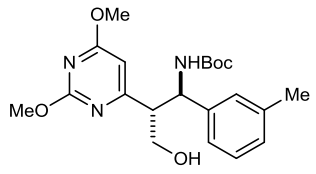
f1 (ppm)


NHBoc
N
OH
F

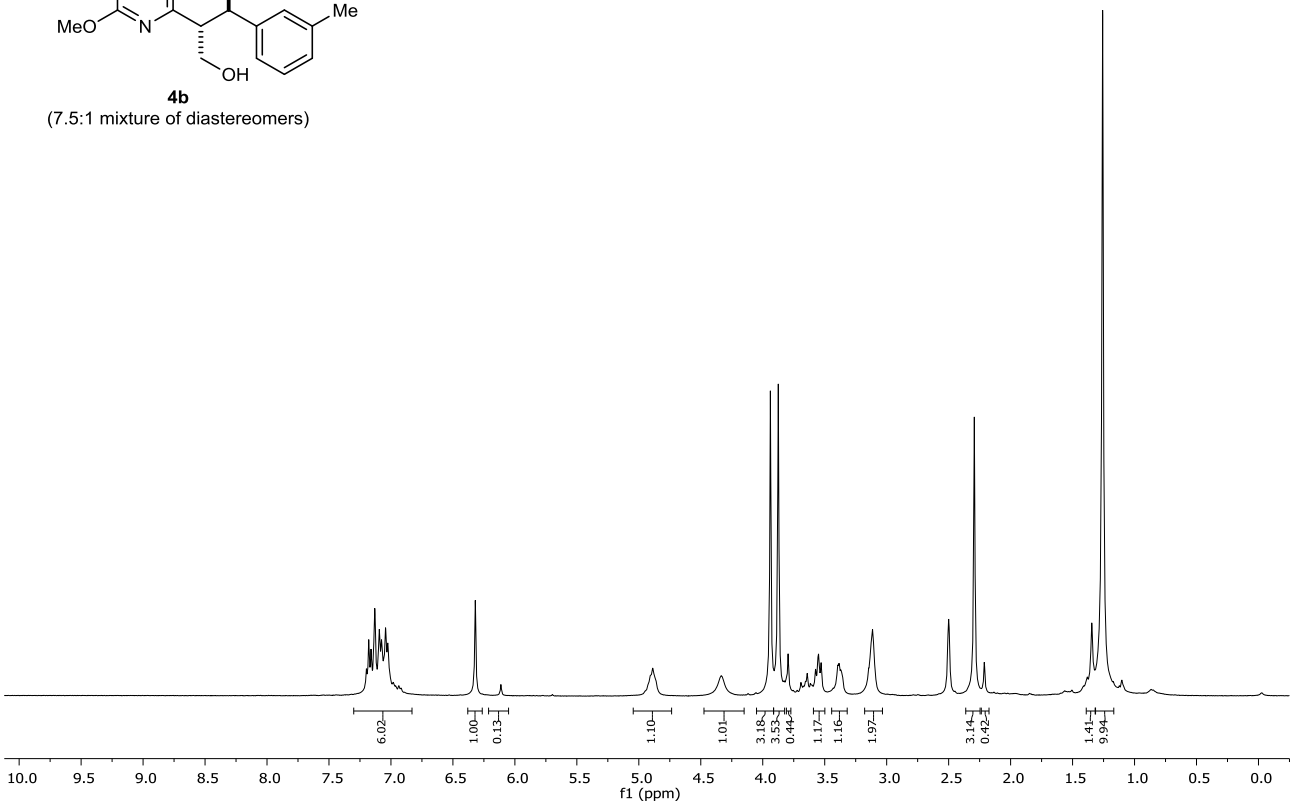
4a

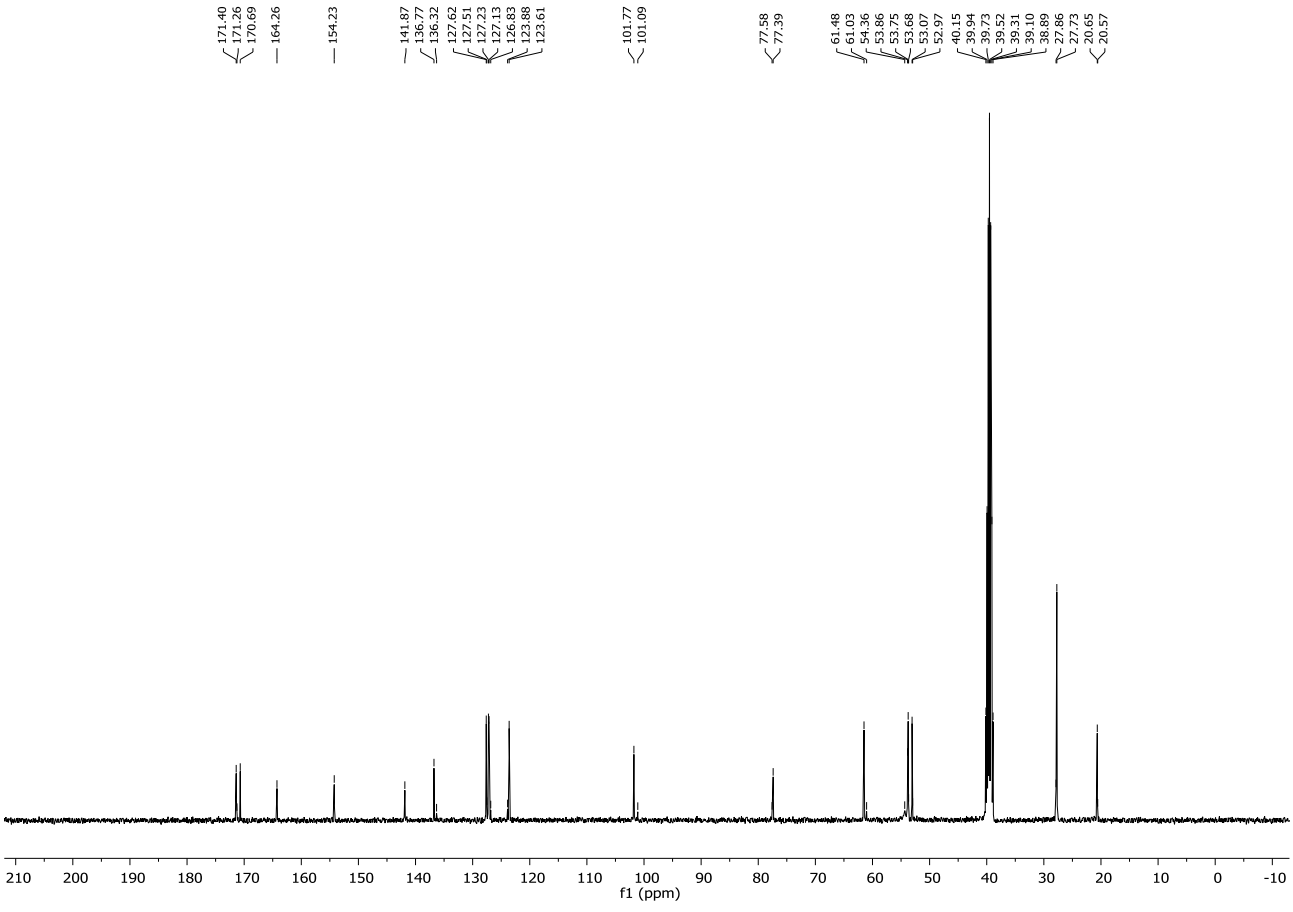
1.00
1.00
0.98
1.00
1.02
1.02
3.78
2.00
0.98
0.97
1.97
1.03
9.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

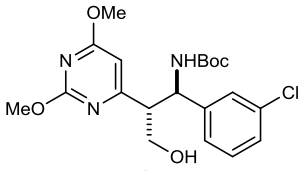

161.97
161.57
159.56
154.27
146.71
138.63
135.09
128.90
128.42
128.34
128.13
127.32
126.50
125.51
122.80
114.43
114.22
77.44
62.22
54.57
54.37
40.15
39.94
39.73
39.52
39.31
39.10
38.89
27.70
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



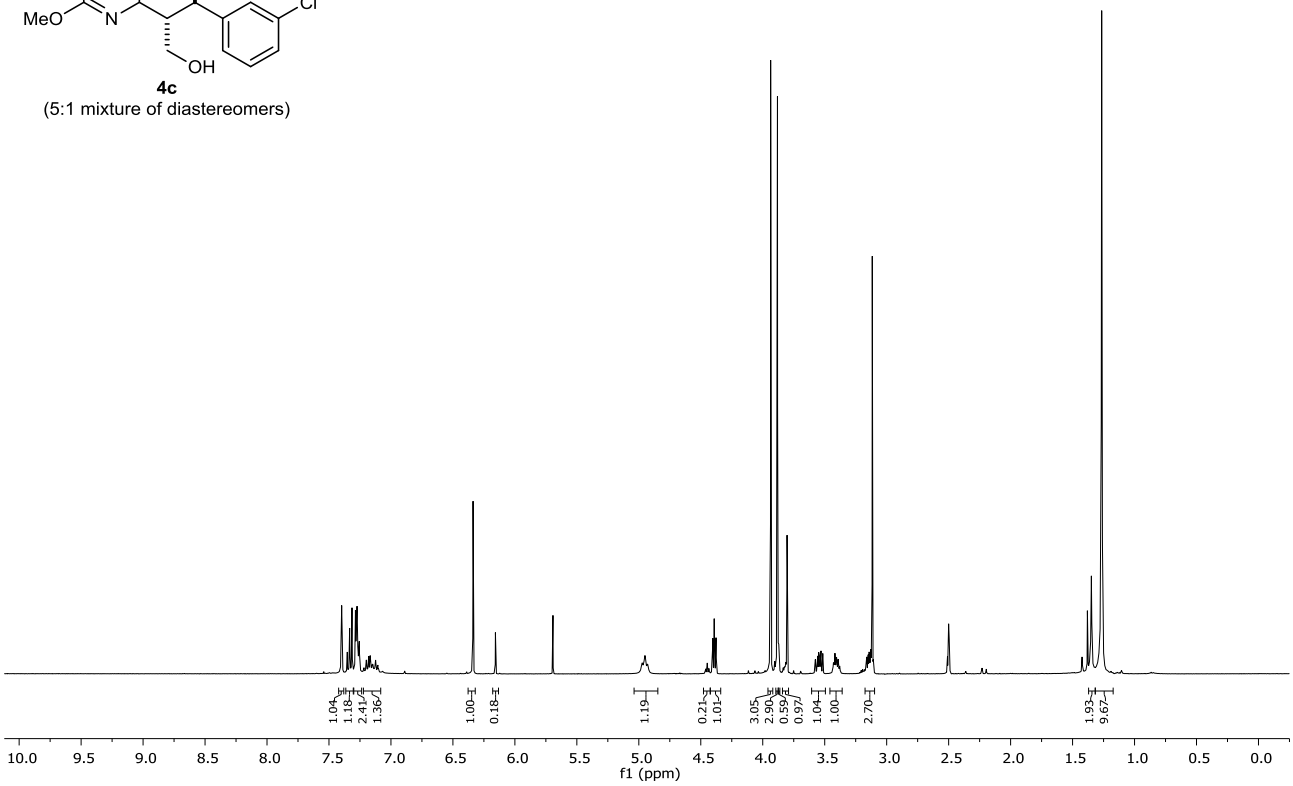
4b
(7.5:1 mixture of diastereomers)

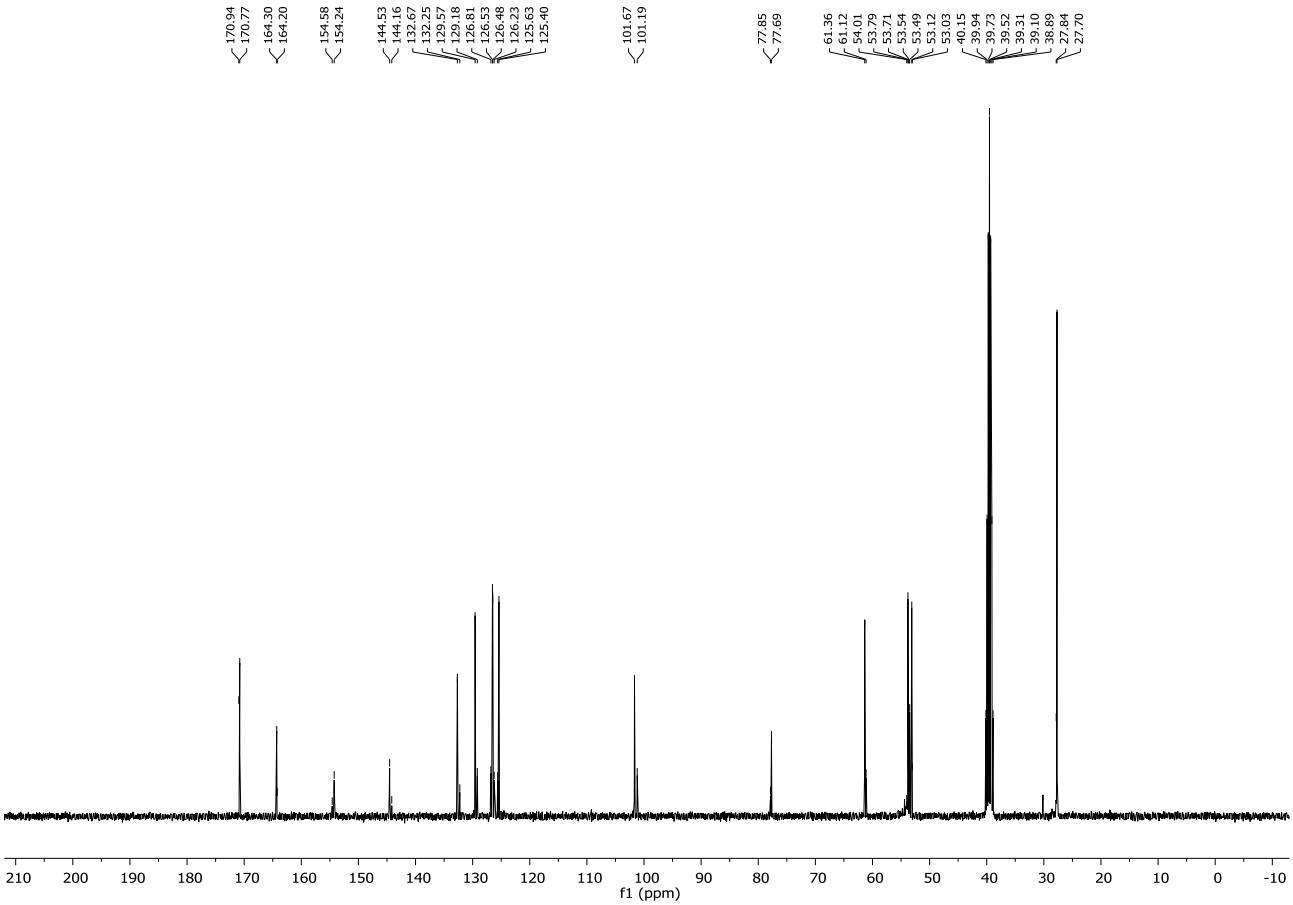


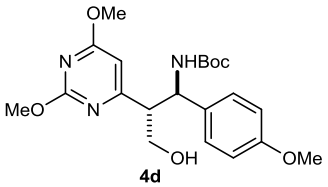




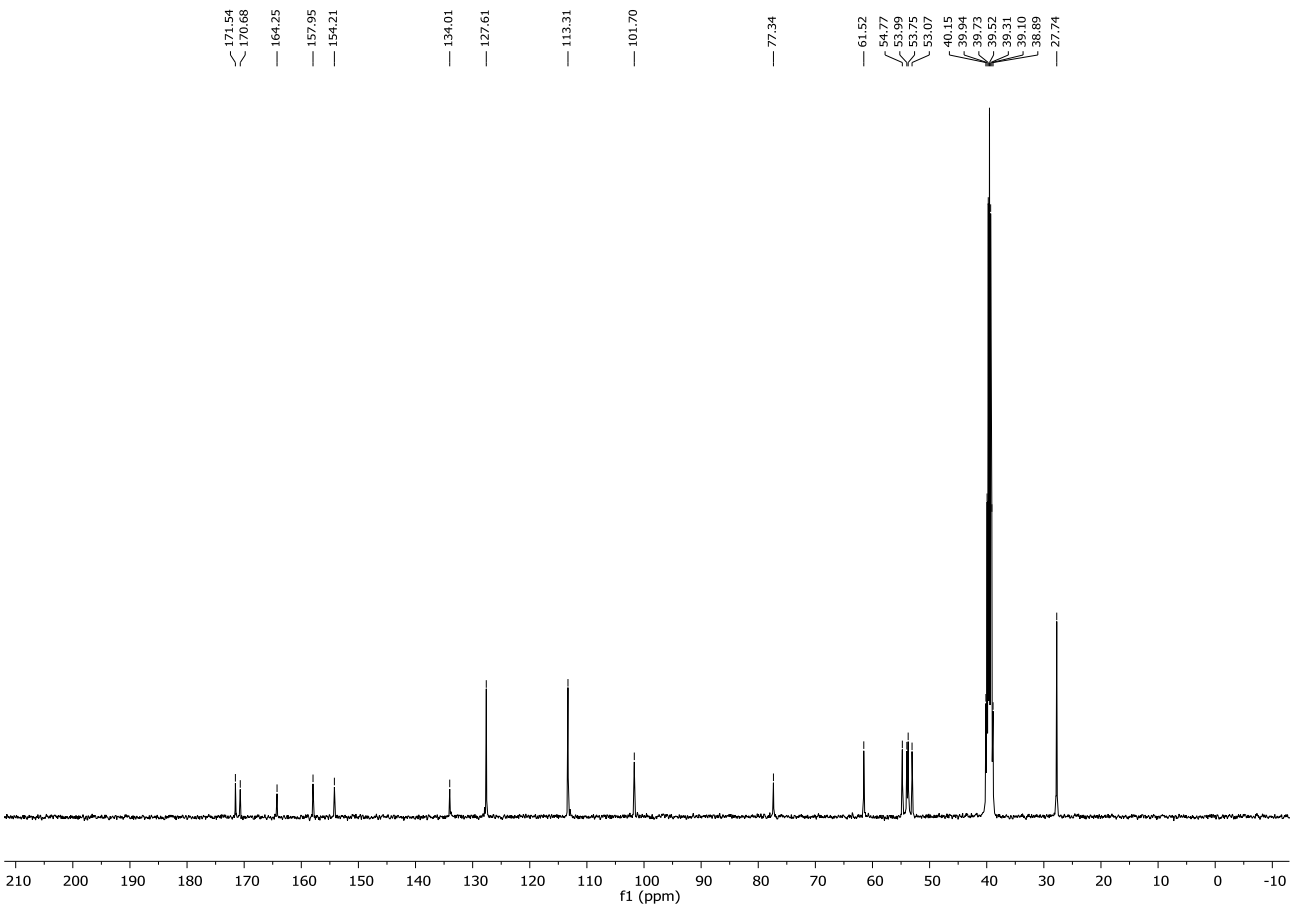
4c
(5:1 mixture of diastereomers)

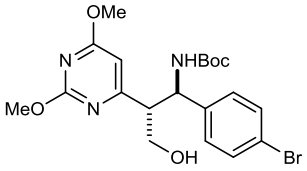




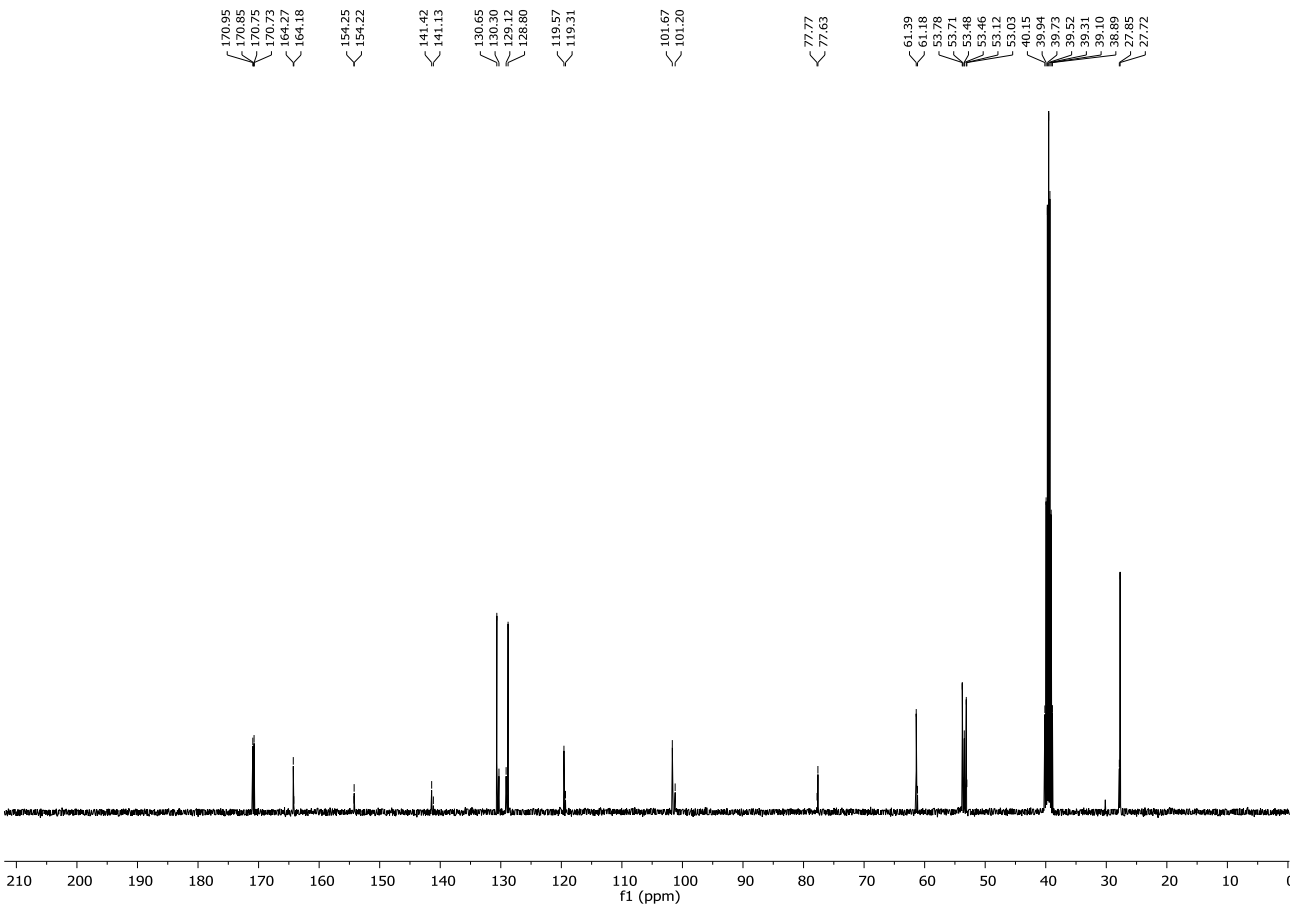


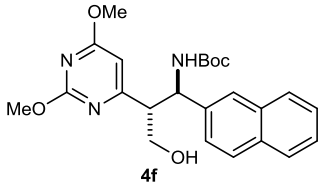
4d
(18:1 mixture of diastereomers)



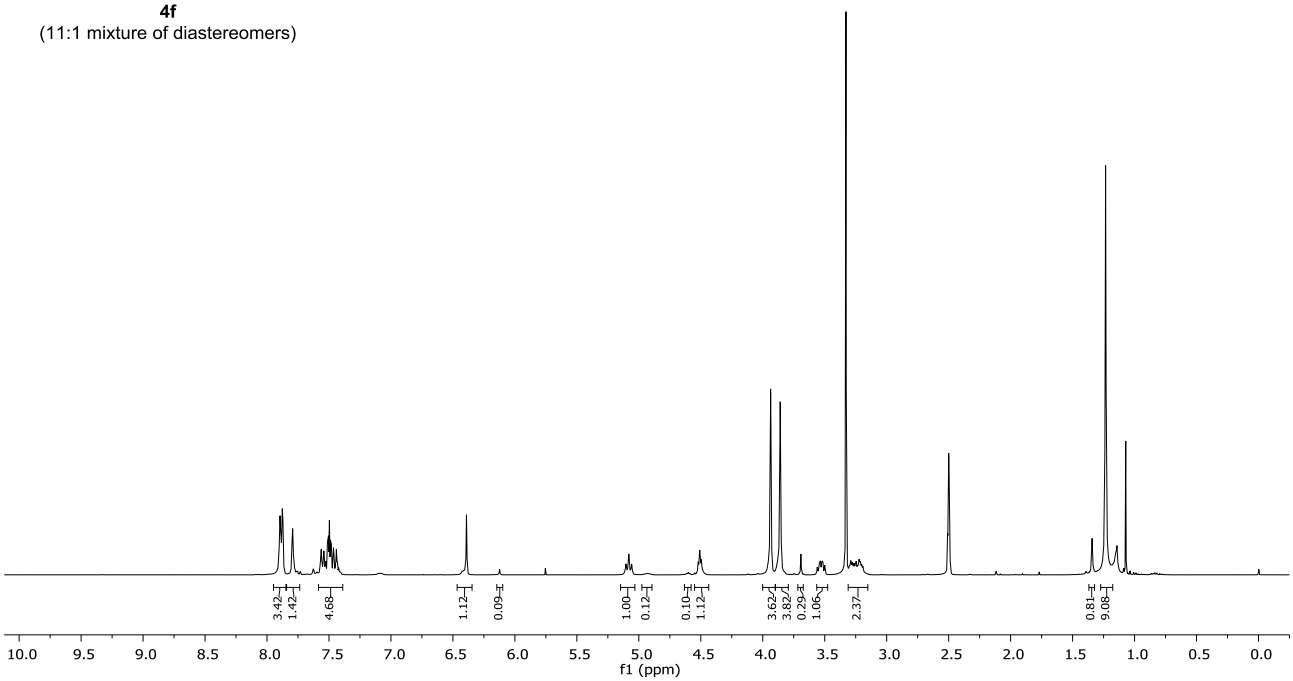


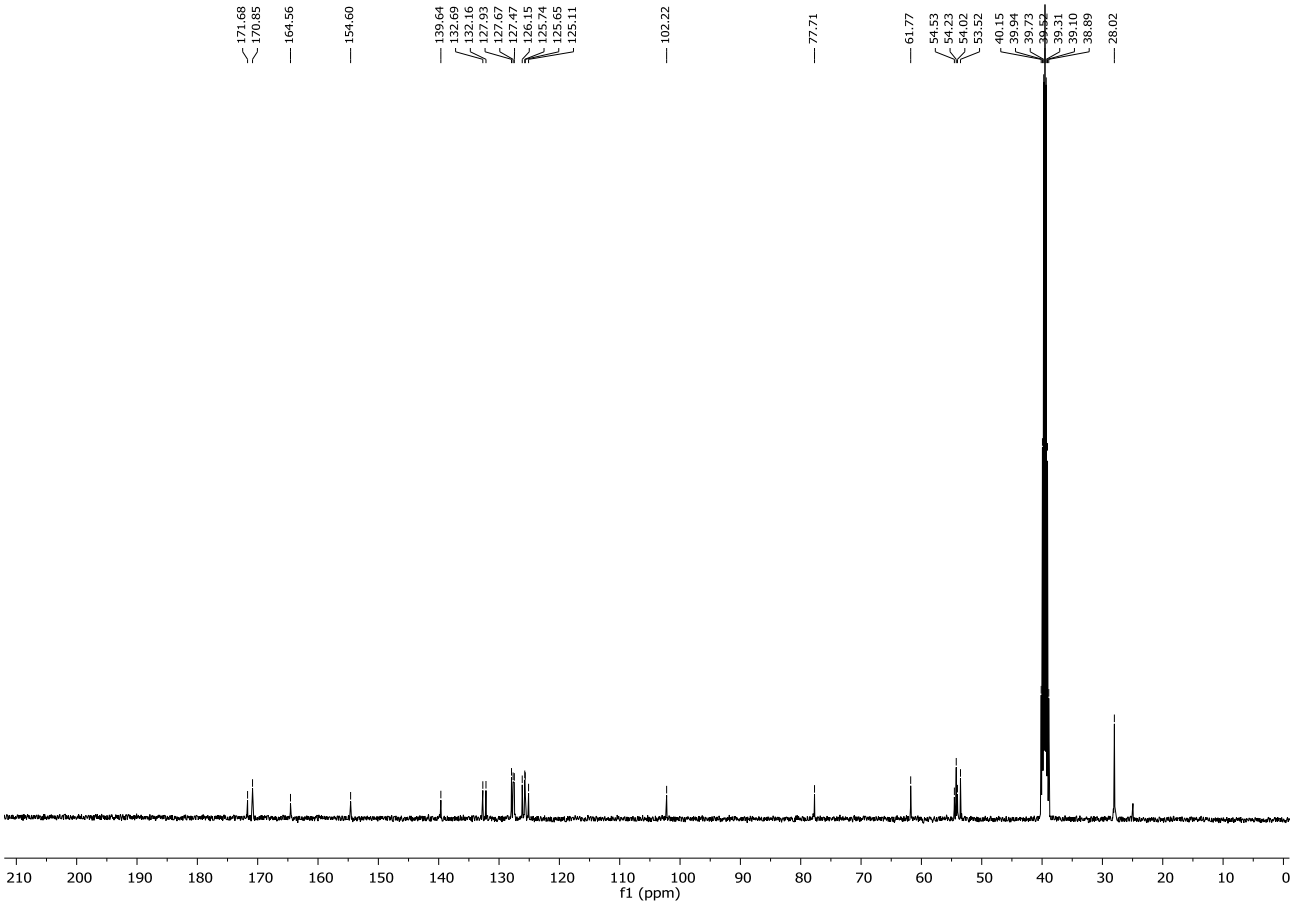
4e
(5:1 mixture of diastereomers)

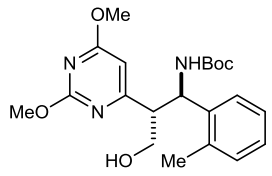




4f
(11:1 mixture of diastereomers)

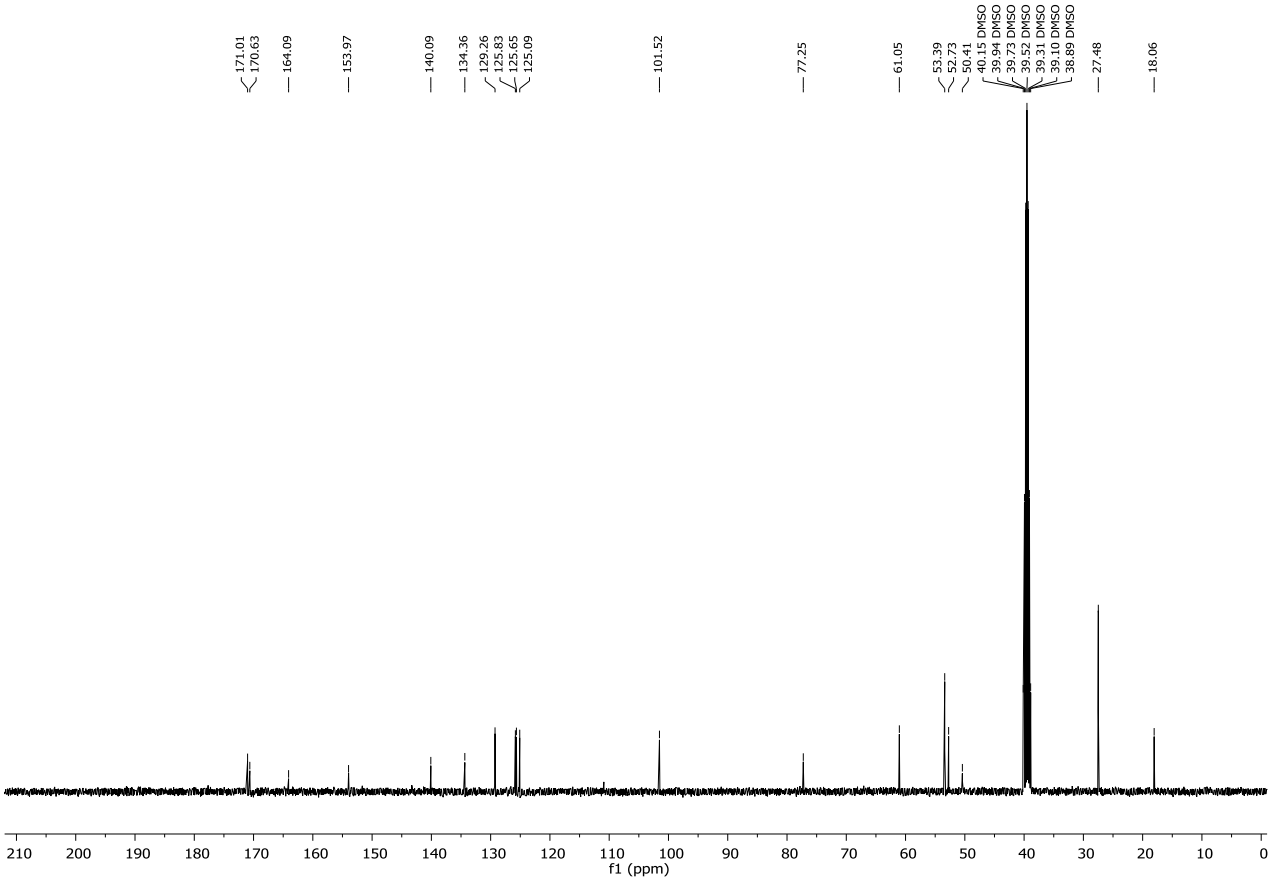


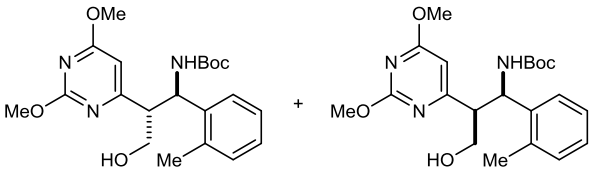



OMe
N
NHBoc
MeO
N
HO
Me

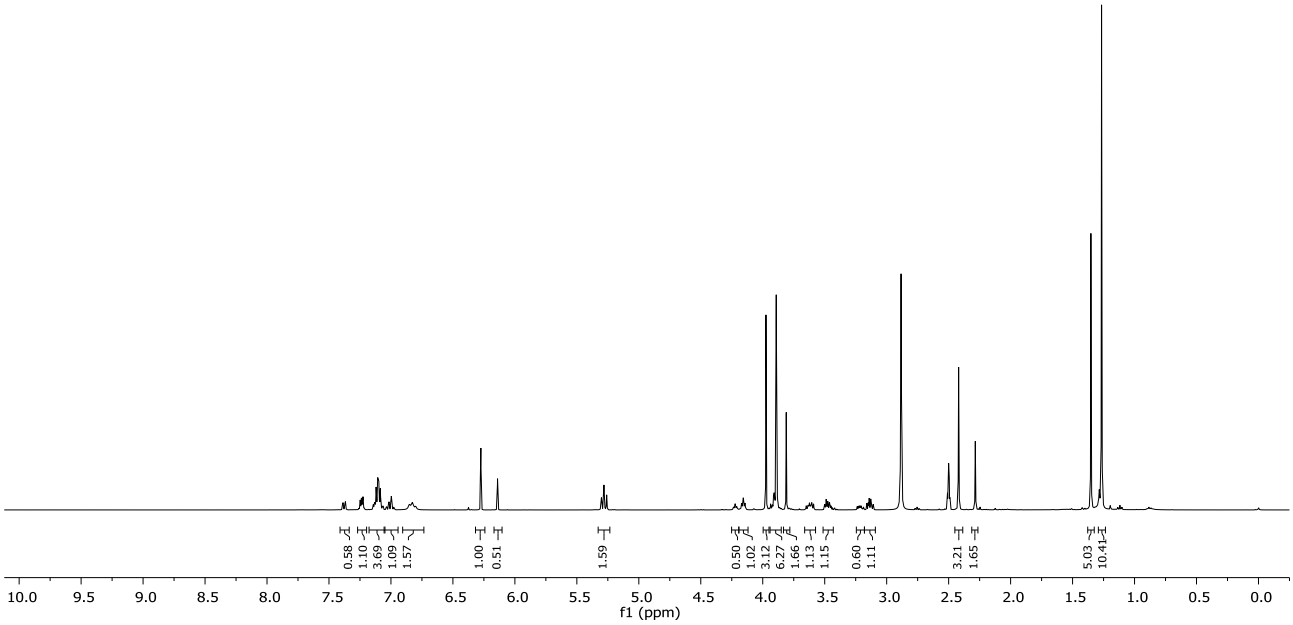
4g

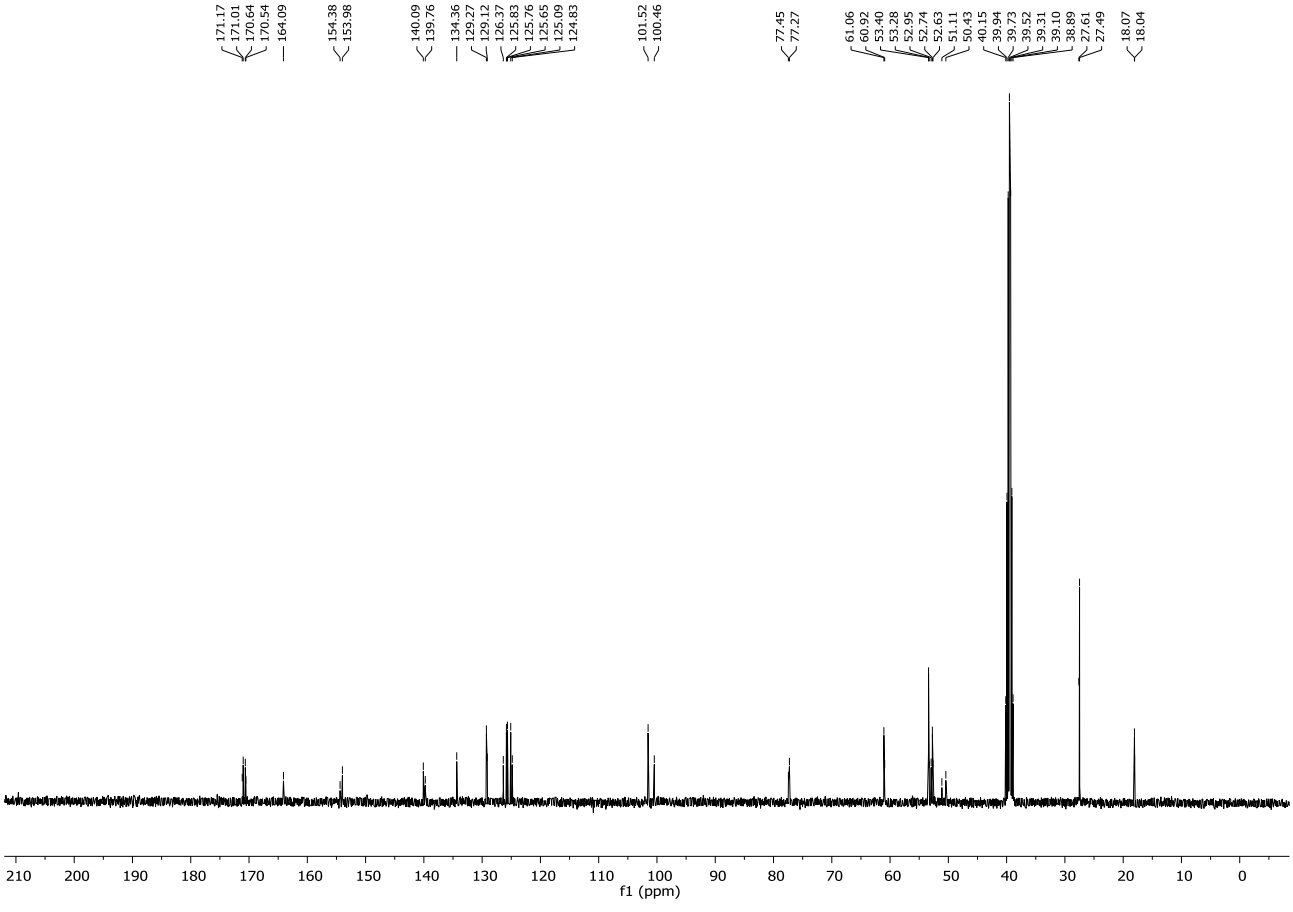
0.97
2.79
0.96
0.90
1.00
0.94
2.80
2.88
1.06
1.06
1.05
2.86
8.80
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

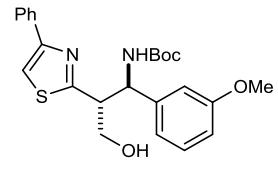

171.01
170.63
164.09
153.97
140.09
134.36
129.26
125.83
125.65
125.09
101.52
77.25
61.05
53.39
52.73
50.41
40.15 DMSO
39.94 DMSO
39.73 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
38.89 DMSO
27.48
18.06
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



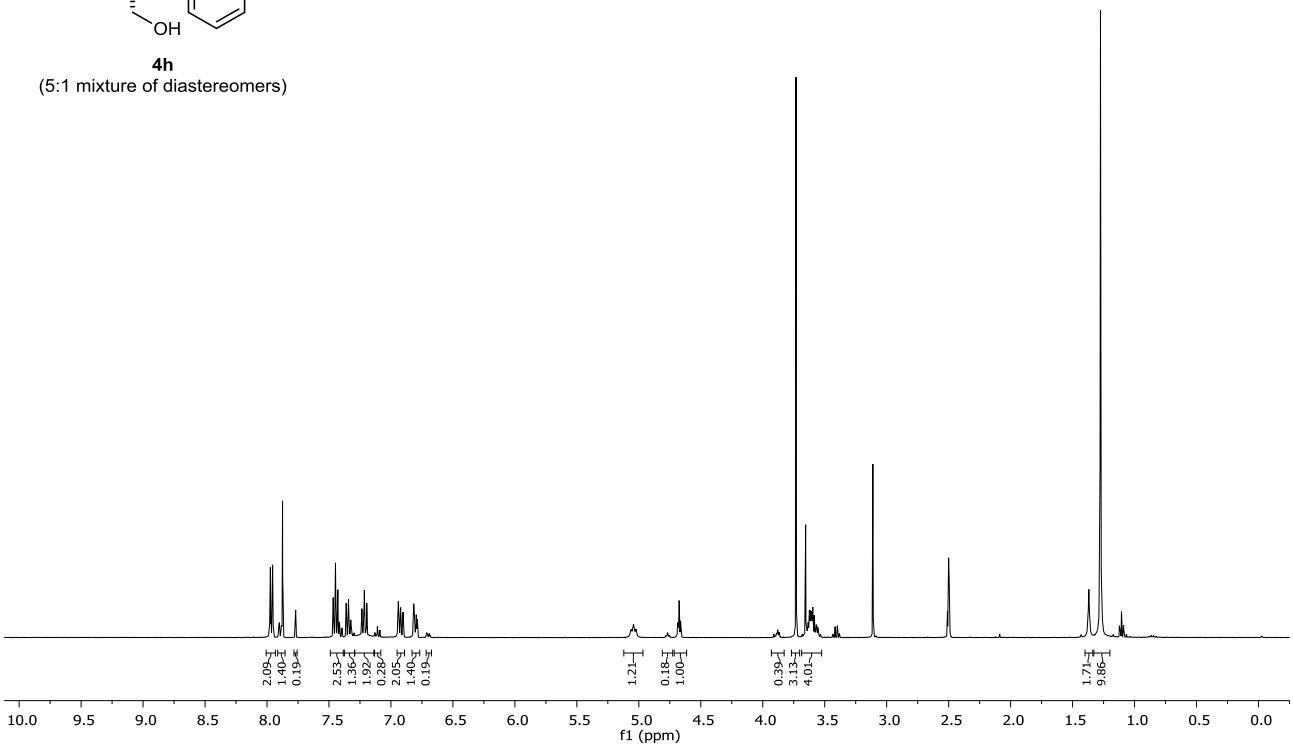
4g 2:1 mixture

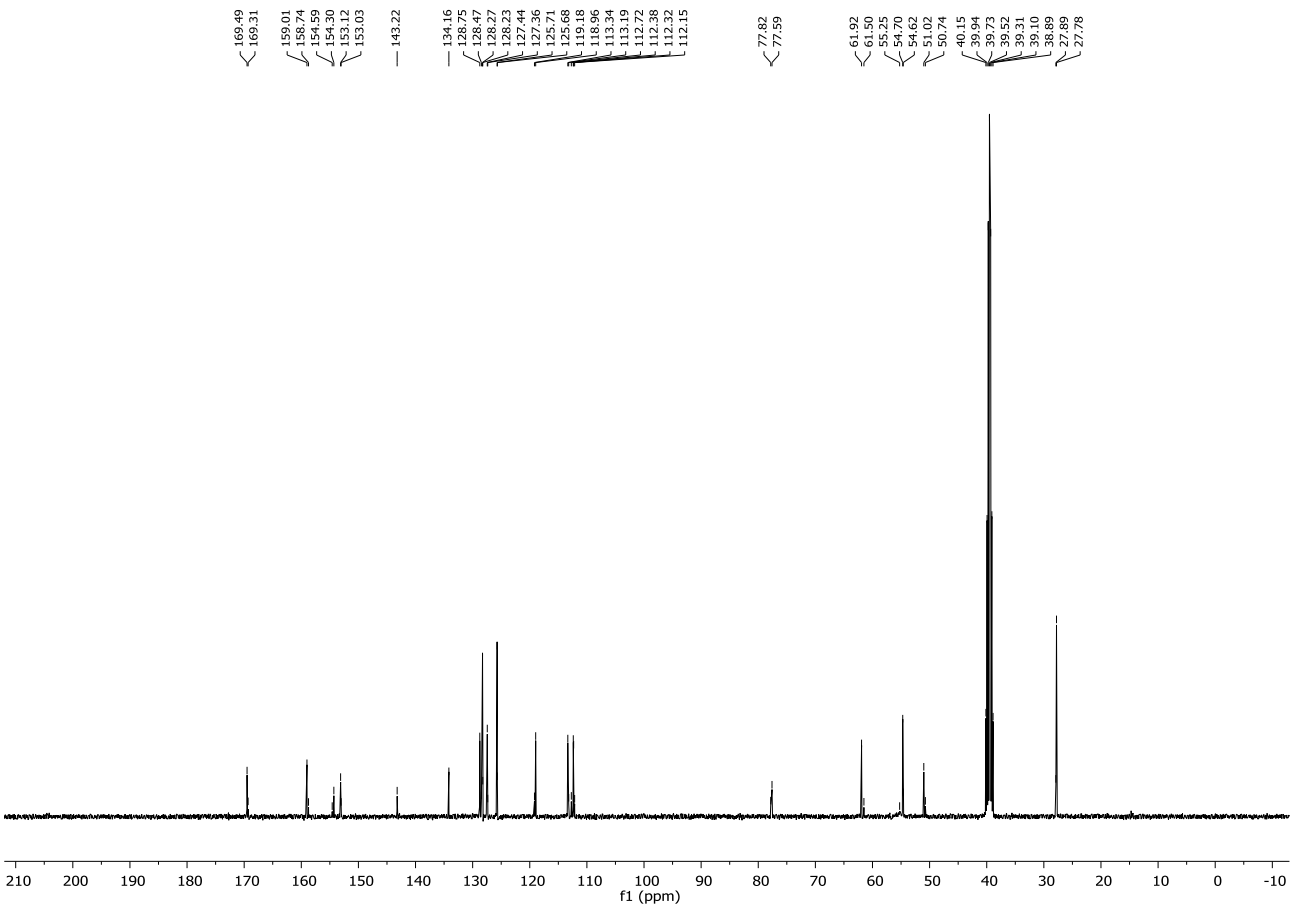


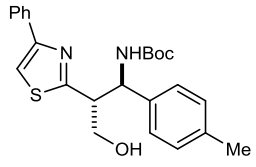




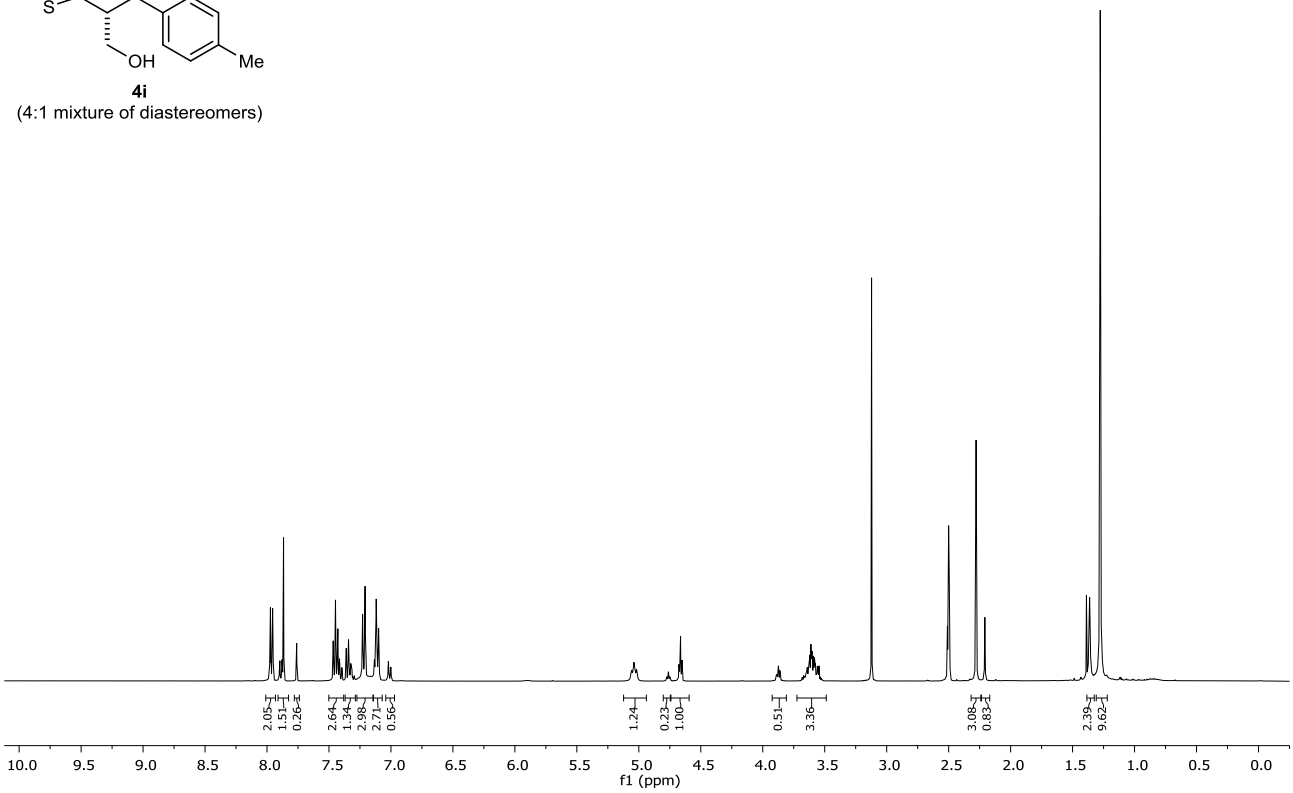
4h
(5:1 mixture of diastereomers)

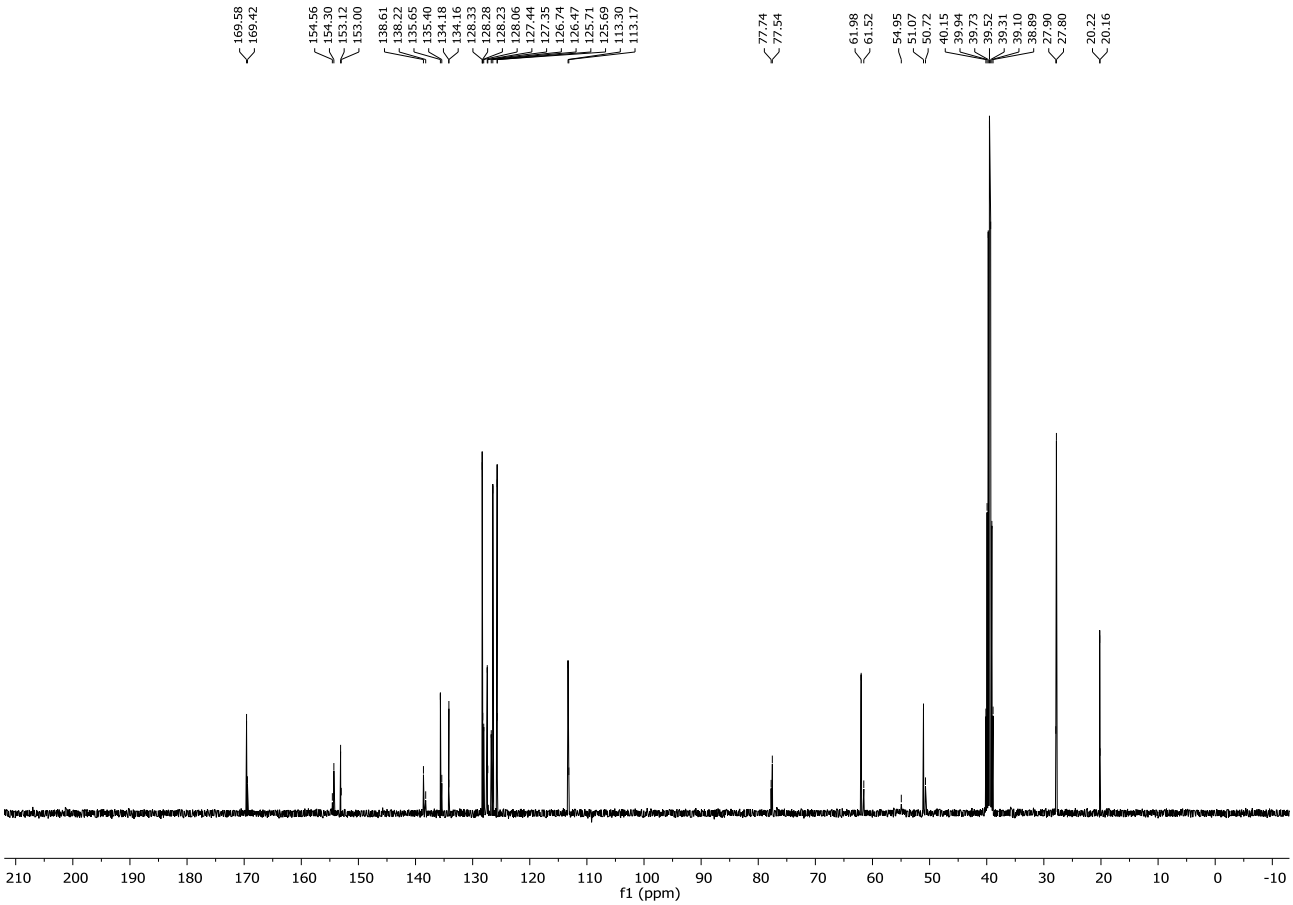


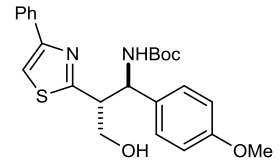




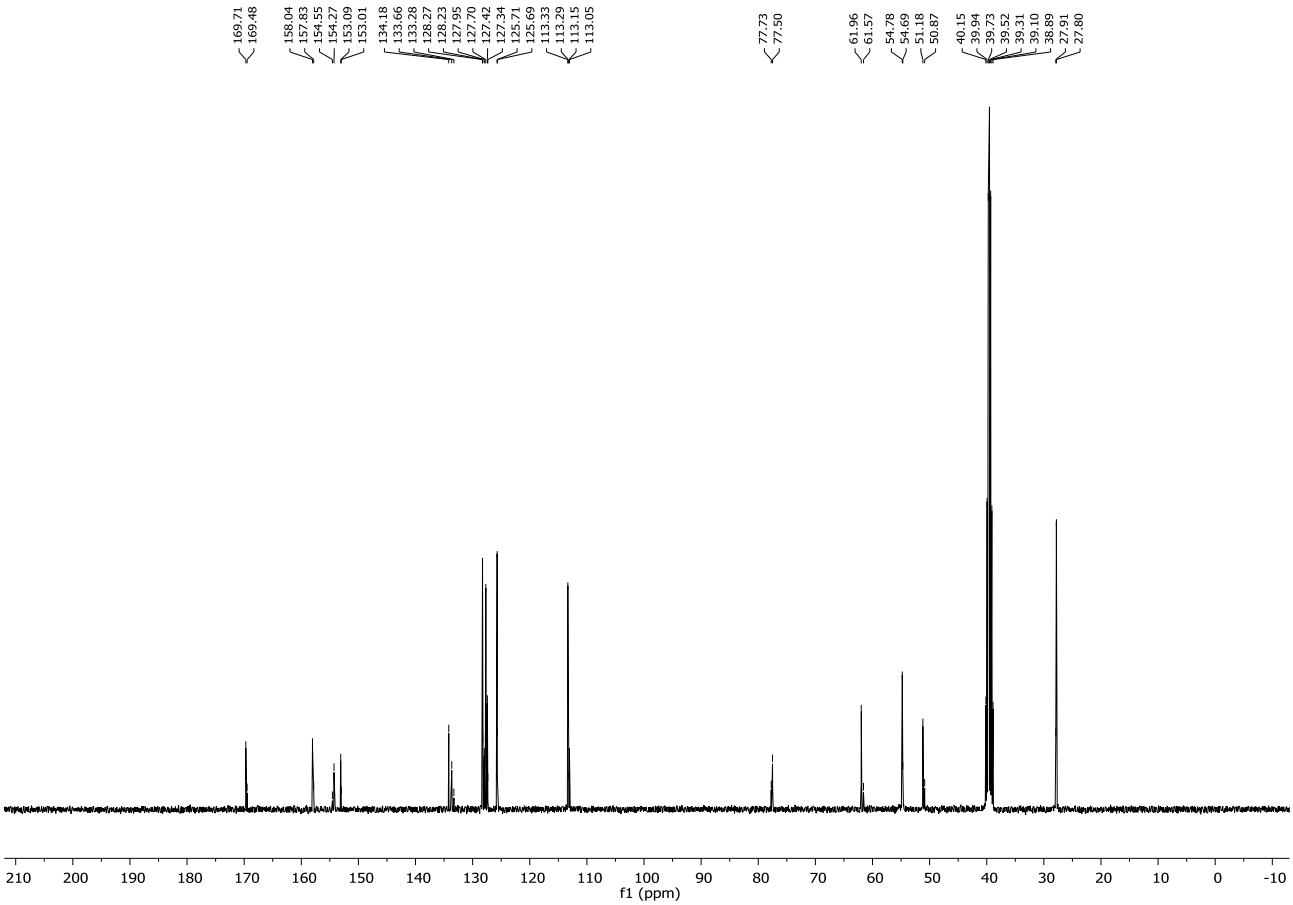
4i
(4:1 mixture of diastereomers)

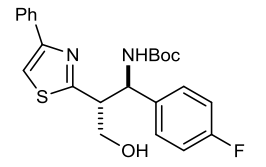




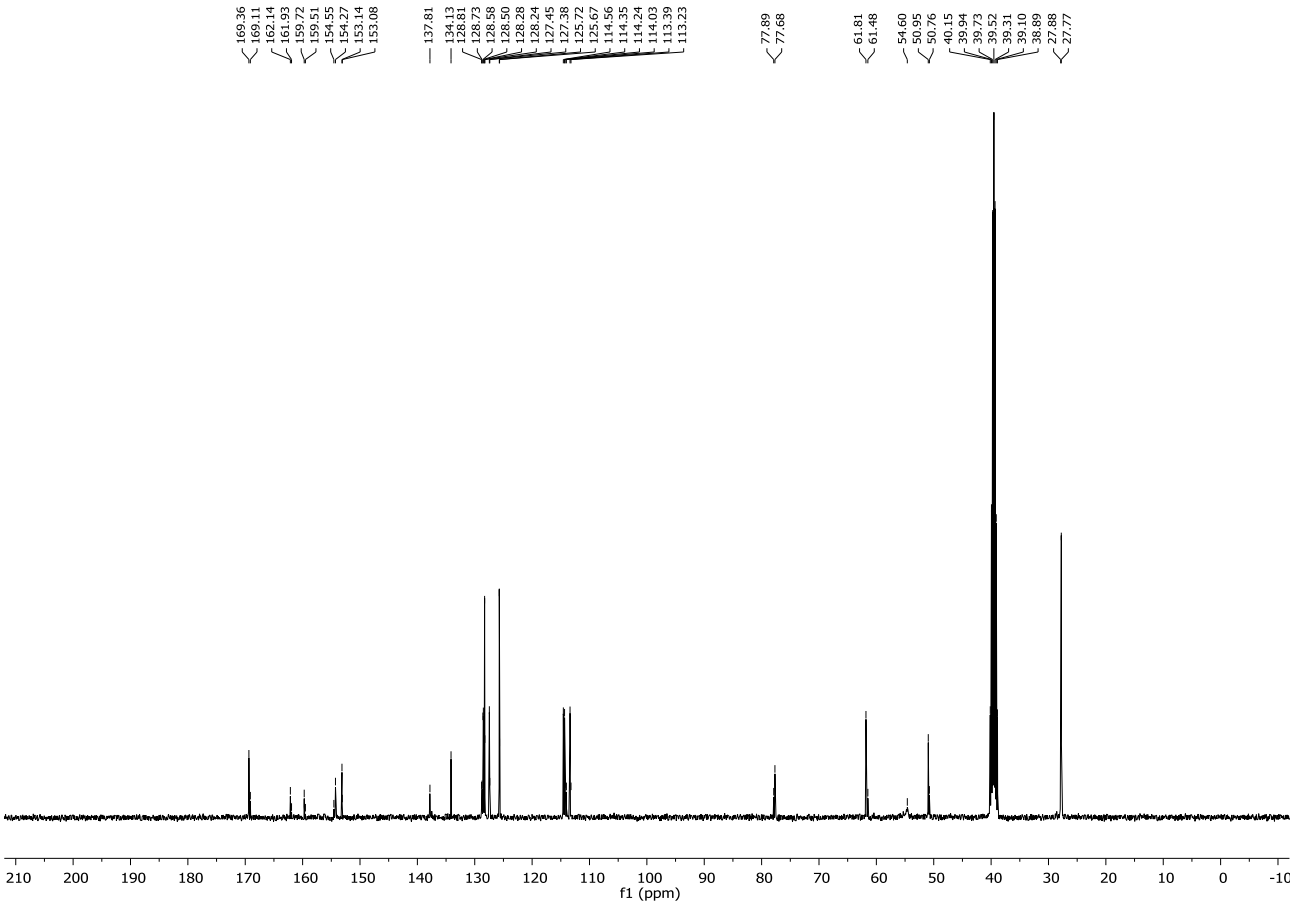


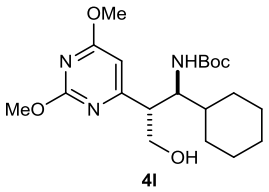
4j
(4:1 mixture of diastereomers)





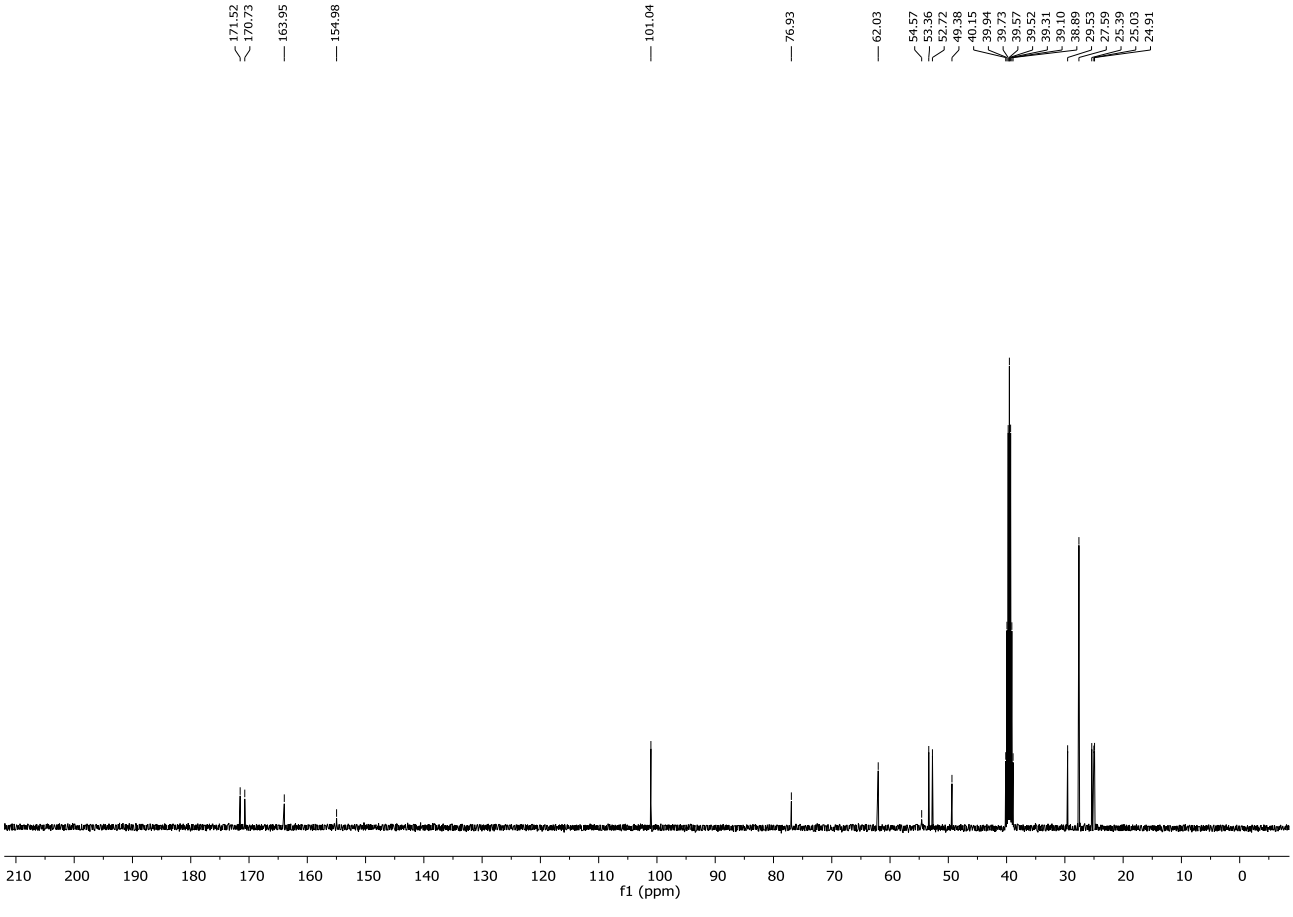
4k
(3.5:1 mixture of diastereomers)

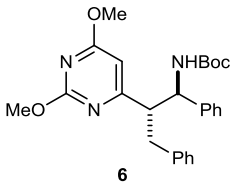



OMe
N
NHBoc
MeO
N
OH

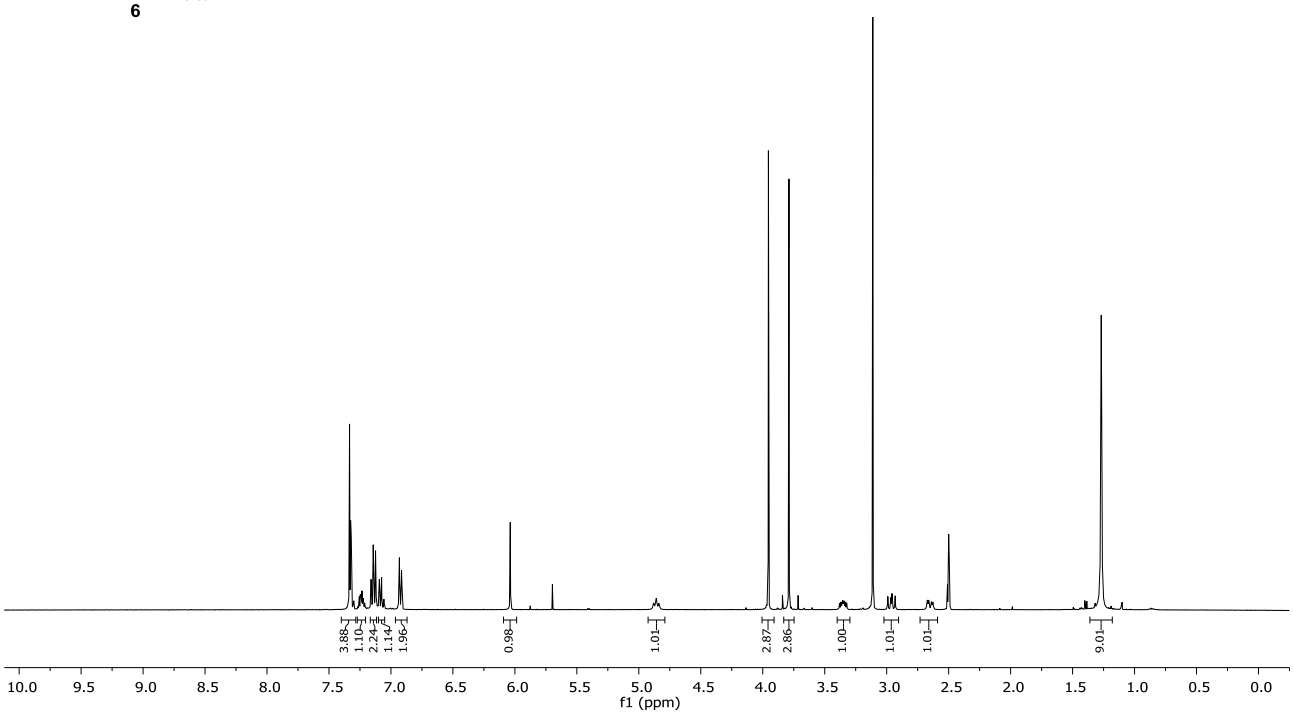
4l

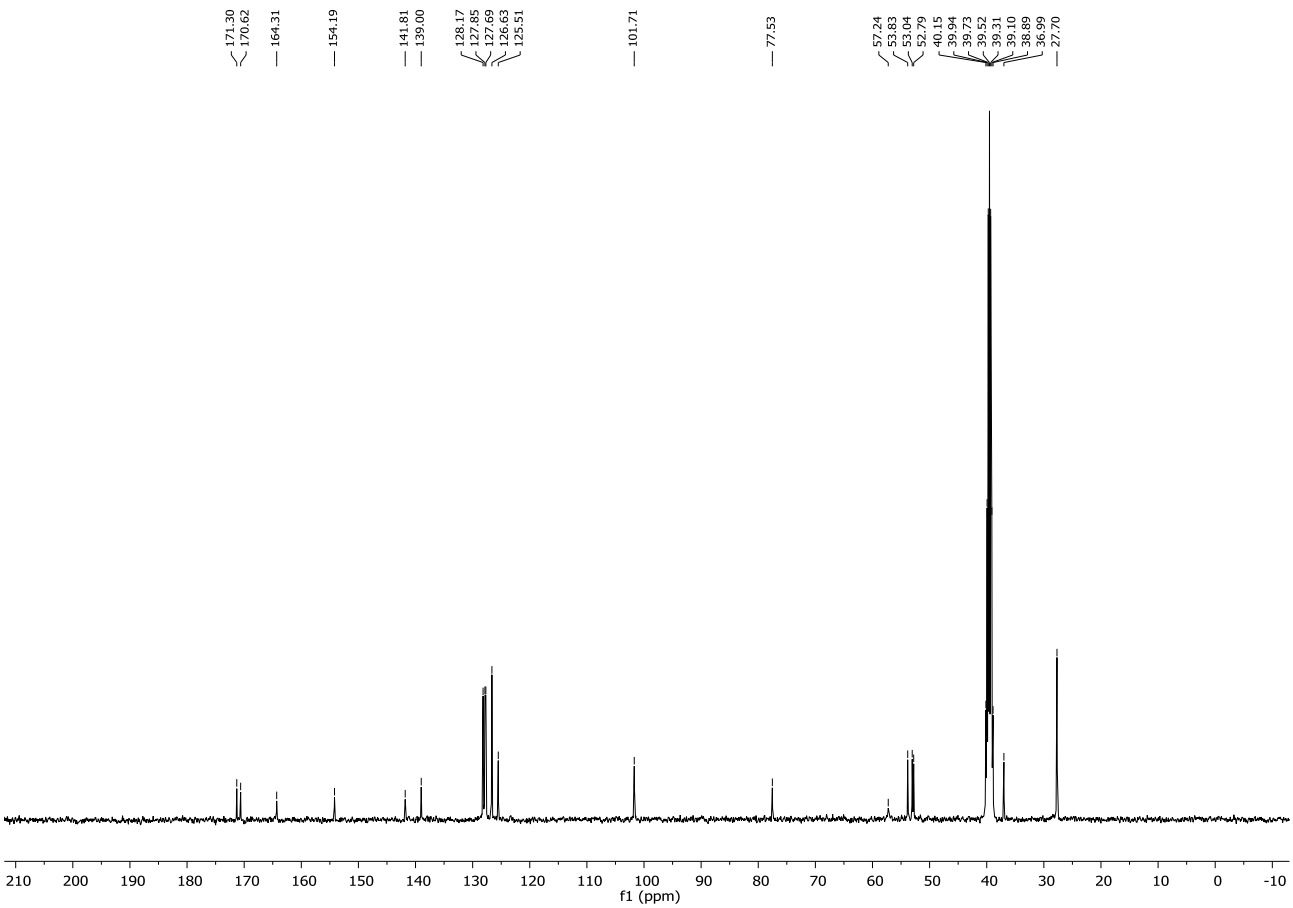
0.96
0.88
0.70
2.71
2.74
1.08
1.84
1.09
4.28
1.27
10.24
3.22
2.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

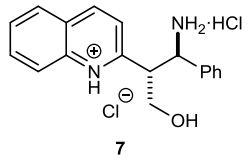

171.52
170.73
163.95
154.98
101.04
76.93
62.03
54.57
53.36
52.72
49.38
40.15
39.94
39.73
39.57
39.52
39.31
39.10
38.89
29.53
27.59
25.39
25.03
24.91
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OMe
N
NHBoc
MeO
N
Ph
Ph

6

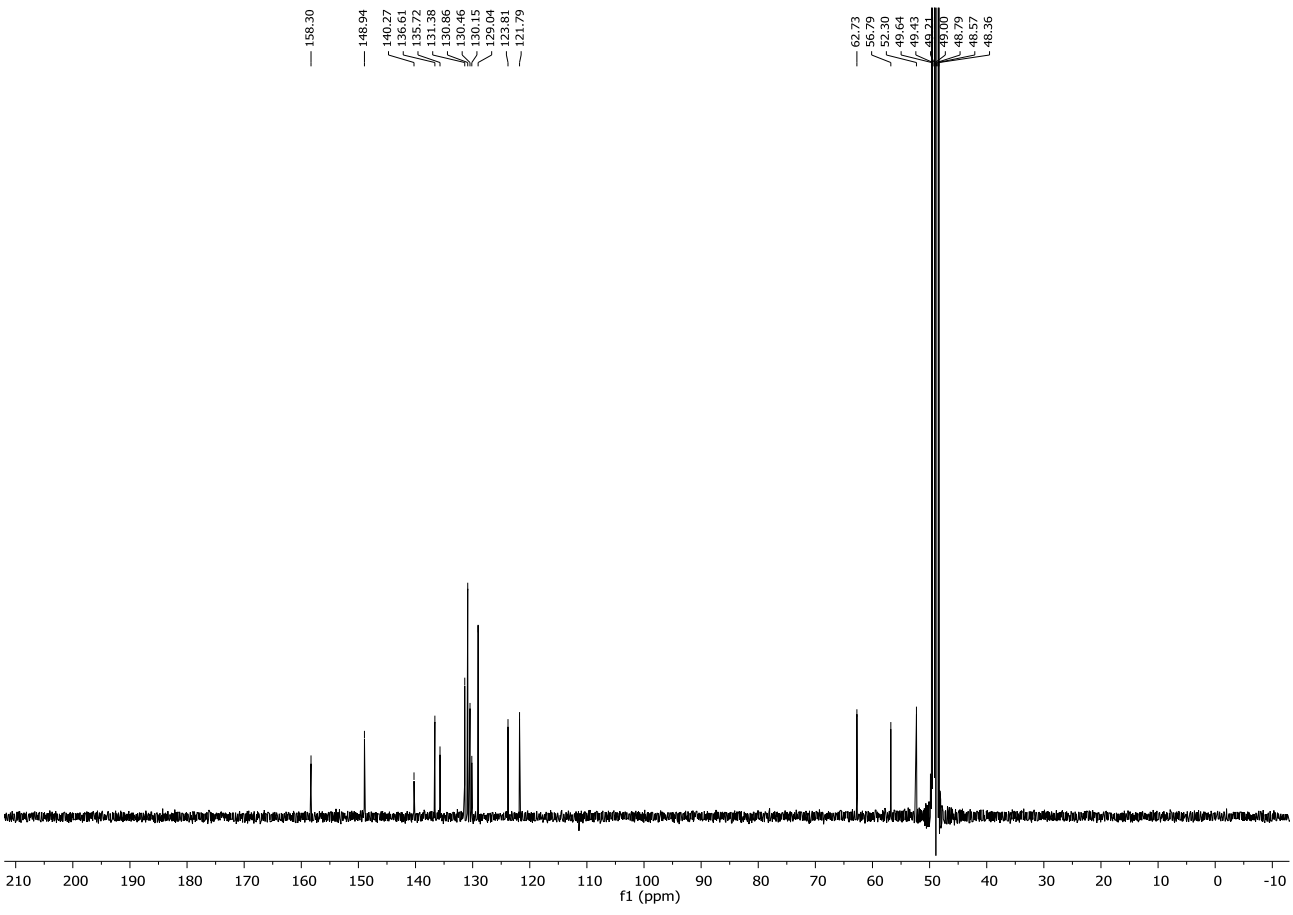

3.88
1.10
2.24
1.14
1.96
0.98
1.01
2.87
2.86
1.00
1.01
1.01
9.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


171.30
170.62
164.31
154.19
141.81
139.00
128.17
127.85
127.69
126.63
125.51
101.71
77.53
57.24
53.83
53.04
52.79
40.15
39.94
39.73
39.52
39.31
39.10
38.89
36.99
27.70
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


NH2·HCl
Ph
N
H
Cl
OH

7

1.00
0.99
1.98
1.03
1.02
1.97
3.00
1.02
1.02
1.05
1.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


158.30
148.94
140.27
136.61
135.72
131.38
130.86
130.46
130.15
129.04
123.81
121.79
62.73
56.79
52.30
49.64
49.43
49.21
49.00
48.79
48.57
48.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)