Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

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Chemodivergence in Enantioselective Desymmetrization of Diazabicycles: Ring-Opening *versus* Reductive Arylation

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General Experimental Procedures. Unless otherwise noted, reactions were carried out under argon atmosphere, in flame-dried, single-neck, round bottom flasks fitted with a rubber septum, with magnetic stirring. Air- or water-sensitive liquids and solutions were transferred via syringe or stainless steel canula. Where necessary (so noted), solutions were deoxygenated by successive freeze-pump-thaw cycles (≥ three iterations). Organic solutions were concentrated by rotary evaporation at 23–40 °C under 40 Torr (house vacuum). Analytical thin layer chromatography (TLC) was performed with Silicycle™ normal phase glass plates (0.25 mm, 60-A pore size, 230-400 mesh). Visualization was done under a 254 nm UV light source and generally by immersion in acidic aqueous-ethanolic vanillin solution, or in potassium permanganate ($KMnO_4$), followed by heating using a heat gun. Purification of reaction products was generally done by flash chromatography with Silicycle™ Ultra-Pure 230-400 mesh silica gel, as described by Still *et al.*[1]

Materials. $[Rh(cod)OH]_2$ was conveniently prepared from $[Rh(cod)Cl]_2$ by a literature procedure.[2] Supplies of chiral bisphosphine ligands were generously provided by the following companies: Josiphos and Walphos families from Solvias Inc., *(R)*-Segphos from Takasago, and P-Phos families from Digital Chemical Specialty. Other chiral phosphine ligands were purchased from Strem Chemicals Inc. Unless otherwise indicated, boronic acids were obtained from Aldrich and used without further purification. Tetrahydrofuran, 1,4-dioxane and toluene were purified by distillation under N_2 from Na/benzophenone

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[2] Uson, R.; Oro, L.A.; Cabeza, J. A. *Inorg. Synth.* **1985**, *23*, 129.

immediately prior to use. Ether and dichloromethane were purified by the method of Pangborn *et al*.[3] Hexanes used for chromatography was purified by simple distillation before use. Diaza-bicyclo[2.2.1]hept-5-ene-dicarbamates **1a**,[4] **1b**,[5] **1c**[4] and **1d**[6] were prepared in quantitative yields by Diels-Alder reactions between cyclopentadiene[7] and the corresponding azodicarbamates at r.t. according to literature procedures and characterization data was fully consistent with that previously reported.

Instrumentation. Proton nuclear magnetic resonance spectra (^{1}H NMR) spectra and carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 23 °C with a Varian Mercury 400 (400 MHz/100 MHz) NMR spectrometer equipped with a Nalorac4N-400 probe, or a Varian 400 (400 MHz/100 MHz) NMR spectrometer equipped with ATB8123-400 probe. Recorded shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents ($CHCl_3$: δ 7.26, $CHDCl_2$: δ 5.29, C_6HD_5: δ 7.15, CD_2HOD: δ 3.30). Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0, CH_2Cl_2: δ 53.8, C_6D_6: δ 128.0, CD_3OD: δ 49.2). Data are represented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet,, qn = quintuplet, sx = sextet, sp = septuplet, m = multiplet, br = broad), and coupling constant (*J*, Hz). Doubling of signals due to carbamate rotamers was often observed: the word 'and' is used specifically to signify extra peaks arising from rotamers in the spectra. Infrared (IR) spectra were obtained using a Perkin-Elmer Spectrum 1000 FT-IR spectrometer as a neat film on a NaCl plate. Data is presented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). High resolution mass spectra were obtained from a SI2 Micromass 70S-250 mass spectrometer (EI) or an ABI/Sciex Qstar mass spectrometer (ESI). Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were measured in a 10.0 cm cell with a Rudolph Autopol IV polarimeter digital polarimeter equipped with a sodium lamp source (589 nm), and are reported as follows: $[\alpha]_D^{T\,^\circ C}$ (c = g/100 mL, solvent).

Determination of the Enantiomeric Excesses by HPLC Analysis. The enantiomeric excess (ee) of the ring-opened products was determined by HPLC analysis after chromatographic purification on silica-gel (see following section for details). Unless otherwise noted, enantiomeric excesses of the bis-protected hydrazine products were determined using analytical chiral columns from Daicel Chemical Industries Ltd, (fitted with a matching 5.0 cm guard column), at 30ºC with 4.0 uL injections of sample solution of approximately 2 mg/mL. The HPLC system was a HP 1100 Series modular system from Agilent, operated by a ChemStation LC 3D software, v. 10.02.

Crytallographic Data: Crystal structure data for **3b** can be retrieved from the Cambridge Crystallographic Data Centre (CCDC) under deposition numbers CCDC 66 1282. These data can be obtained free of charge via **www.ccdc.cam.ac.uk/data_requests/cif**, or by e-mailing **data_request@ccdc.cam.ac.uk**, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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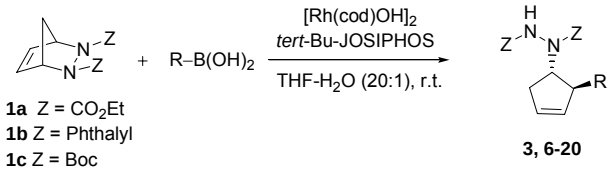
[3] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[4] Diels, O.; Bolm, J. H.; Knoll, W. *Justus Liebigs Ann. Chem.* **1925**, *443*, 242.
[5] Heyman, M. L.; Snyder, J. P. *Tetrahedron Lett.*, **1973**, *14*, 2859.
[6] **1c** was prepared in a one-pot reaction with: cyclopentadiene, commercial 1,2-dihydro-1,4-phthalazinedione and its *in situ* oxidation to the diazoprecuror by lead tetraacetate in dichloromethane. See: Raasch, M. S., *J. Org. Chem*. **1975**, *40*, 161, and Clement, R. A. *J. Org. Chem*. **1962**, *27*, 1115.
[7] Moffett, B. R. *Org. Syntheses*, **1952**, *32*, 41.



General procedure for the Desymmetrization of Diaza-bicyclo[2.2.1]heptenes (1) by Rhodium-catalyzed Allylic Substitution with Organoboron Nucleophiles.

In a representative example: to a 10 mL round-bottom flask equiped with a magnetic stir bar was added $[Rh(cod)OH]_2$ (3.1 mg, 0.0067 mmol), *tert*-Bu-JOSIPHOS (8.8 mg, 0.016 mmol). The vial was flushed with argon (balloon) and distilled THF (1.0 mL) was added. The clear orange solution was stirred at room temperature for 15-20 min, then 0.08 mL H_2O was added.[8] Diazabicyclo[2.2.1]heptene dicarbamate **1c** (40 mg, 0.135 mmol) and the arylboronic acid (0.20–0.27 mmol, 1.5–2.0 equiv) were added *together as a solution*[9] in distilled THF (0.80 mL of a freshly prepared stock solution) and the darkening reaction mixture allowed to react at r.t. (or 0 °C).[10] After 16 h, TLC showed full consumption of **1c** (20% EtOAc/Hex; acidic vanillin stain). The reaction mixture was filtered on a short silica gel pad (~2 g), washing with four portions of Et_2O. The filtrate was concentrated under reduced pressure, then was applied to the top of a column of silica gel and purified by column chromatography (5-10-20% EtOAc/hexane as elution gradient). The ring-opened hydrazine **3c** was recovered as a colourless oil, 43 mg (85%). The enantiomeric excess was determined on the purified product (*vide infra*).

Note 1: NMR analysis displayed very broad peaks for all ring-opened products **3**–**20** due to: (i) rotamers of the bis-carbamate hydrazine moiety, (ii) confomers equilibrium for some products, and (iii) atropisomers for some compounds bearing aromatic *ortho*-substituents. Resolution for both ^1H and ^{13}C NMR spectra did not improve significantly when temperature was varied; most likely due to differential coalescence temperature of the multiple conformers. Doubling of signals was often observed: the word 'and' is used specifically to signify extra peaks arising from rotamers in the spectra.

Note 2: We arbitrarily opted to represent all products **3**–**20** with the *(1R,2S)*-stereochemistry in the paper for consistency and to avoid unnecessary complications for the readers. The depicted (–) enantiomers result from the use of (S_{Fe},*R*)-*tert*-Bu-JOSIPHOS ligand. The use of (R_{Fe},*S*)-*tert*-Bu-JOSIPHOS yielded the (+) enantiomers, having the opposite stereochemistry of that represented.

Expanded references from the manuscript:

Reference [9]: P. E. Finke, M Maccoss, L. C. Meurer, S. G. Mills, C. G. Caldwell, P. Chen, P. L. Durette, J. Hale, E. Holson, I. Kopka, A. Robichaud (Merck & Co Inc.),WO 9714671, **1997**.

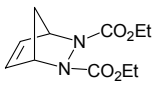
[8] In most cases, the reaction could be run without added water; moisture from either the atmosphere or the boronic acids was sufficient to carry out the reaction (equimolar water to boronic acid = 5 μL H_2O). Generally, no special precautions were taken since we wanted a robust process. However, a referree comment made us realize that the presence of a small amount of water is crucial for the reaction yield. To ensure reproducibility, we opted for the addition of a known amount of water, as described above.

[9] If the alkene is added *before* the boronic acid, a slight erosion in ee occurs (4–9% ee).

[10] The reaction vessel must remain unopened, as the active catalyst in solution appears sensitive to oxygen traces.

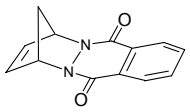
Characterization Data

(1a): 2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-diethyl dicarboxylate.



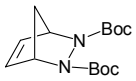
Prepared according to a general procedure.[4] To a freshly distilled cyclopentadiene (1.5–2.0 equiv) solution in CH_2Cl_2 kept at 0 °C, was added the azobis(carbamate) compound. The reaction was allowed to warm up to room temperature and stirred until full consumption of the azo starting material, as observed by TLC. The solvent was evaporated under reduced pressure. The crude clear oil was purified by silica-gel chromatography with EtOAc/hexanes as eluent (20-40% gradient). The diazabicycle was obtained quantitatively as a clear fluid oil. The characterization data was fully concordant with that already reported in the literature. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.51 (2H, br.s), 5.15 (2H, br.s), 4.25-4.15 (4H, m), 1.77-1.71 (2H, m), 1.28 (6H, t, *J* = 7.1 Hz).

(1b): 2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-phthalazide.



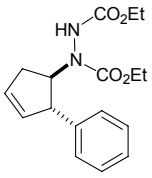
Prepared according to the procedure described for **1a**, where cylopentadiene was reacted with the azophthalazide *in situ* after its oxidation from the commercial phthalyhydrazine.[6] The diazabicycle was obtained as a white solid in 61% yield (5.95 g). The characterization data was fully concordant with that already reported in the literature. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.27 (2H, dd, *J* = 3.7, 5.9 Hz), 7.75 (2H, ddd, *J* = 0.5, 3.7, 5.9 Hz), 6.72 (2H, t, *J* = 1.9 Hz), 5.94-5.92 (2H, m), 2.17 (1H, dt, *J* = 1.6, 8.8 Hz), 2.07 (1H, dt, *J* = 1.6, 8.8 Hz).

(1c): 2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-di-*tert*-butyl dicarboxylate.



To an ice-cooled solution of DtBAD in CH_2Cl_2 (10 g in 500 mL) was added neat cyclopentadiene (1.5 equiv). The clear orange solution was allowed to stir overnight at rt. After 16h, the colorless solution showed full conversion by TLC. The solvent was evaporated under reduced pressure to yield a white solid which had a strong Cp odor. The crude solid was recrystallized in 100 mL hexanes under vigourous stirring. After filtration on fritted funnel and drying, the diazabicycle was obtained quantitatively as a white free-flowing powder (12.8 g, 99%). The characterization data was fully concordant with that already reported in the literature.[5] **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.51 (2H, br.s), 5.21 and 4.96 (2H, coalescing br.s), 1.72-168 (2H, m), 1.57-1.42 (18H, m).

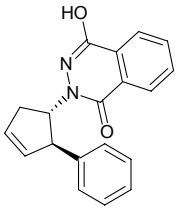
(3a): *trans*-*N,N'*-(2-Phenylcyclopent-3-enyl)-diethylhydrazine dicarboxylate.



Using (S_{Fe},*R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 96% yield (51 mg). The characterization data was fully concordant with that already reported in the literature.[11] **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.32-7.20 (5H, m), 6.40 and 6.20 (1H, coalescing br. s), 5.87 (1H, ddd, *J* = 2.0, 4.4, 6.0 Hz), 5.71 (1H, ddd, *J* = 2.0, 3.9, 6.0 Hz), 4.76 (1H, br. s), 4.23 (2H, dd, *J* = 7.1, 14.2 Hz), 4.15-3.95 (3H, br. m), 2.75-2.65 (1H, m), 2.63-2.49 (1H, m), 1.35-1.22 (3H, m), 1.17-0.92 (3H, m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.2, 156.3, 143.5, 132.9 (2), 130.0 (2), 128.6, 127.7, 126.7, 67.5, 62.7, 62.4, 54.0, 35.4, 14.6, 14.4. The enantiomeric ratio was 87.5:12.5, as determined by HPLC analysis: (Chiralcel OD-H, gradient 1-7% iPrOH/hexane, 1.0 mL/min, 215 nm); t_R = 16.4 min [minor], t_R = 19.6 min [major]. Alternatively, the reaction could be carried out in toluene/water (9:1) to obtain **3a** in 93% yield (49 mg), with the same enantioselectivity (76% ee). The absolute configuration was assigned by analogy with compound **3c**.

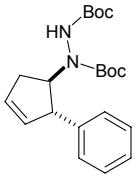
[11] John, J.; Sajisha, V. S.; Mohanlal, S.; Radhakrishnan, K. V. *Chem. Commun.* **2006**, 3510.

(3b): *trans*-4-Hydroxy-2-(2'-phenylcyclopent-3'-enyl)-2*H*-phthalazin-1-one.



Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the phthalazide was obtained as a white solid in quantitative yield (53 mg, m.p.:135-138 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.60 (1H, br.s), 8.42 (1H, d, *J* = 6.7 Hz), 8.06 (1H, d, *J* = 7.6 Hz), 7.79(1H, t, *J* = 7.2 Hz), 7.74 (1H, t, *J* = 7.6 Hz), 7.17-7.14 (2H, m), 7.10-7.05 (3H, m), 5.76-5.70 (2H, m), 5.65-5.60 (1H, m), 4.21-4.17 (1H, m), 2.87-2.77 (1H, dd, *J* = 8.9, 16.5 Hz), 2.57-2.47 (1H, m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.9 (2), 151.6, 143.0, 133.2, 133.0, 132.6, 129.4, 128.7 (2), 127.8, 127.5 (2), 126.8, 124.9, 124.8, 64.5, 55.3, 37.6. **IR** (NaCl, neat film): 3058, 3026, 2930, 2853, 1617, 1573 (s), 1556 (s), 1493, 1385, 1263, 1178, 1091, 693 cm^{-1}. **MS** (EI): *m/z* (rel. intensity): 304 (M^+, 4), 163 (84), 142 (100), 130 (17), 115 (15), 77 (8). **HRMS** (EI): calculated for $C_{19}H_{16}N_2O_2$ [M^+]: 304.1212; found = 304.1205. **$[\alpha]_D^{24.3}$** = +112 (*c* 1.88, $CHCl_3$) for 85:15 er, as determined by HPLC analysis: (Chiralcel AD, elution gradient 0-10% iPrOH/hexane, 0.80 mL/min, 235 nm); t_R = 49.6 min [major], t_R = 52.9 min [minor]. The absolute configuration was assigned by analogy with compound **3c**.

(3c): *trans-N,N'*-(2-Phenylcyclopent-3-enyl)-di-*tert*-butylhydrazine dicarboxylate.



Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 85% yield (43 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.17 (5H, m), 6.26 and 6.06 (1H, coalescing br.s), 5.89-5.83 (1H, m), 5.74-5.66 (1H, br.m), 4.70 (1H, br.s), 3.95 (br.s), 2.72-2.51 (2H, br.m), 1.55-1.05 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.0, 155.1, 143.9, 132.9 (2), 130.2 (2), 128.6, 127.8, 126.6, 81.4 (2), 68.2 and 66.4 (br, rotamers), 54.0, 35.4, 28.4 (3), 28.2 (3). **IR** (NaCl, neat film): 3263 (br), 3056, 3025, 2977, 2930, 2865, 1744-1700 (br.), 1493, 1453, 1392, 1366, 1283, 1249, 1155, 1049, 952, 757, 699 cm^{-1}. **MS** (ESI): *m/z* (rel. intensity): 375.2 (MH^+, 5), 319 (3), 297 (5), 263 (15), 219 (35), 143 (100), 128 (5). **HRMS** (ESI): calculated for $C_{21}H_{31}N_2O_4$ [MH^+]: 375.2278; found = 375.2294. **$[\alpha]_D^{24.3}$** = –75 (*c* 1.33, $CHCl_3$) for 81.2:18.8 er, as determined by HPLC analysis: (Chiralcel AD, gradient 5-10% iPrOH/hexane, 0.80 mL/min, 220 nm); t_R = 39.2 min [major], t_R = 42.7 min [minor]. The absolute configuration was assigned by derivatization to (–)-**21** and comparison to litterature optical rotation values.

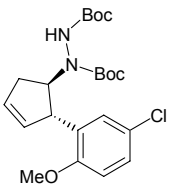
(6): *trans-N,N'*-[2-(2'-Fluorophenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 43% yield (23 mg). Alternatively, the reaction could be carried out in toluene/THF/water (7:2:1) to obtain the ring-opened product in 53% yield (28 mg), with the same enantioselectivity. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.25-7.13 (2H, m), 7.08 (1H, dt, *J* = 1.0, 7.4 Hz), 6.97 (1H, t, *J* = 9.6 Hz), 6.27 and 6.03 (1H, coalescing br.s), 5.91-5.85 (1H, m), 5.67-5.60 (1H, br.m), 4.73 (1H, br.s), 4.25 (br.s), 2.80-2.47 (2H, br.m), 1.56-1.02 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.3 (d, *J* = 244 Hz), 156.0, 154.9, 131.2, 130.3, 128.9, 128.2, 128.1, 124.6, 115.3 (d, *J* = 18.3 Hz), 81.3 (2), 67.8 and 66.0 (br, rotamers), 46.0, 35.3, 28.4 (3), 28.1 (3). **IR** (NaCl, neat film): 3318 (br), 3058, 2977, 2932, 1738-1698 (br.), 1491, 1455, 1393, 1367, 1247, 1156, 1049, 950 cm^{-1}. **MS** (ESI): *m/z* (rel. intensity): 393.2 (MH^+, 15), 281 (13), 237 (96), 161 (100). **HRMS** (ESI): calculated for $C_{21}H_{30}FN_2O_4$ [MH^+]: 393.2184; found = 393.2198. **$[\alpha]_D^{25.6}$** = –121 (*c* 1.00, $CHCl_3$) for 99.8:0.2 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 8% iPrOH/hexane, 1.00 mL/min, 225 nm); t_R = 19.5 min [minor], t_R = 30.8 min [major]. The absolute configuration was assigned by analogy with compound **3c**.

(7): ***trans*-*N,N'*-[2-(2'-Methylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate**. Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, and a mixture of toluene/THF/water (7:2:1) as solvent, the bis-protected hydrazine was obtained as a colourless oil in 99% yield (52 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.19-7.05 (4H, m), 6.17 and 5.93 (1H, coalescing br.s), 5.92-5.83 (1H, m), 5.64 (1H, br.s), 4.75 (1H, br.s), 4.26-4.07 (1H, m), 2.80-2.48 (2H, m), 2.35 (3H, s), 1.58-1.06 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ156.1, 154.9, 141.7, 136.1, 133.1, 131.0, 130.5, 130.0, 127.2, 126.5, 81.4 (2), 67.6 and 64.2 (br, rotamers), 50.6, 35.9, 28.4 (3), 28.2 (3), 20.0. **IR** (NaCl, neat film): 3316 (br), 3055, 3003, 2977, 2929, 2866, 1740-1681 (br.), 1454, 1392, 1367, 1333, 1251, 1157, 1050, 951, 756 cm^{-1}. **MS ESI** , *m/z* (rel. intensity): 389 (MH^+, 5), 333 (7), 277 (17), 232 (67), 156 (58), 69 (14), 57 (100). **HRMS** (ESI^+): calculated for $C_{22}H_{32}N_2O_4$ [MH^+]: 388.2362; found = 388.2358. **$[\alpha]_D^{24.2}$** = –119 (*c* 1.30, $CHCl_3$) for 98.4:1.6 er, as determined by HPLC analysis: (Chiralcel AD, gradient 5-10% iPrOH/hexane, 0.80 mL/min, 220 nm); t_R = 28.4 min [major], t_R = 33.6 min [minor]. The absolute configuration was assigned by analogy with compound **3c**.

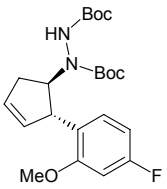
(8): ***trans*-*N,N'*-[2-(2'-Methyl-4'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate**. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand and dioxane as solvent, the bis-protected hydrazine was obtained as a colourless oil in 55% yield (31 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.03 (1H, d, *J* = 8.9 Hz), 6.72-6.67 (2H, m), 6.16 and 5.90 (1H, coalescing br.s), 5.88-5.84 (1H, m), 5.66-5.58 (1H, m), 4.70 (1H, br.s), 4.12 (1H, br.s), 3.77 (3H, s), 2.79-2.61 (1H, m), 2.61-2.49 (1H, m), 2.32 (3H, s), 1.61-1.11 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.1, 156.1, 154.9, 137.4, 133.9, 133.4, 129.7, 128.2, 116.1, 111.6, 81.4 (2), 67.5 and 65.0 (br, rotamers), 55.4, 49.9, 35.7, 28.4 (3), 28.2 (3), 20.2. **IR** (NaCl, neat film): 3319 (br), 3055, 3002, 2977, 2930, 2834, 1745-1700 (br.), 1608, 1578, 1500, 1392, 1367, 1333, 1285, 1253, 1159, 1050, 951, 755 cm^{-1}. **MS ESI** , *m/z* (rel. intensity): 419.5 (MH^+, 5), 363 (8), 307 (8), 263 (13), 187 (15), 185 (100), 141 (45). **HRMS** (ESI^+): calculated for $C_{23}H_{35}N_2O_5$ [MH^+]: 419.2540; found = 419.2554. **$[\alpha]_D^{23.9}$** = +85.5 (*c* 1.54, $CHCl_3$) for 99.3:0.7 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 10% iPrOH/hexane, 1.00 mL/min, 225 nm); t_R = 15.3 min, t_R = 21.9 min. The absolute configuration was assigned by analogy with compound **3c**.

(9): ***trans*-*N,N'*-[2-(2'-Methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate**. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand the bis-protected hydrazine was obtained as a colourless oil in 75% yield (41 mg). On a 1 mmol scale, 347 mg were obtained (86%, >99% ee). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.21-7.15 (2H, m), 6.93 (1H, t, *J* = 7.2 Hz), 6.81 (1H, d, *J* = 8.1 Hz), 6.38 and 6.24 (1H, coalescing br.s), 5.90-5.84 (1H, m), 5.70-5.62 (1H, m), 4.75-4.47 (1H, br.m), 4.42-4.31 (1H, m), 3.82 (3H, s), 2.70-2.48 (2H, m), 1.57-1.00 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ157.3, 156.2, 155.8, 132.3, 130.6, 127.8, 127.7, 121.3, 115.7, 110.4, 81.1 (2), 68.9 and 66.2 (br, rotamers), 55.8, 44.8 (br), 35.4 (br), 28.4 (3), 28.0 (3). **IR** (NaCl, neat film): 3326 (br), 3053, 2976, 2931, 2858, 1745, 1709, 1691, 1598, 1461, 1366, 1243, 1156, 1049, 1026, 951 cm^{-1}. **MS** (ESI): *m/z* (rel. intensity): 405.2 (MH^+, 7), 293 (7), 249 (80), 205 (31), 173 (100), 131 (12), 107 (7). **HRMS** (ESI): calculated for $C_{22}H_{33}N_2O_5$ [MH^+]: 405.2383; found = 405.2400. **$[\alpha]_D^{24.6}$** = +51.0 (*c* 1.47, $CHCl_3$) for 99.7:0.3 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 10% iPrOH/hexane, 1.00 mL/min, 225 nm); t_R = 7.3 min [minor], t_R = 9.1 min [major]. The absolute configuration was assigned by analogy with compound **3c**.

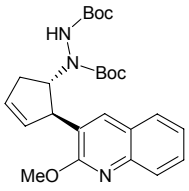
(10): *trans*-*N,N'*-[2-(5'-Chloro-2'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butyl-hydrazine dicarboxylate. Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 96% yield (59 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.16-7.09 (2H, m), 6.72 (1H, d, *J* = 8.6 Hz), 6.30 and 6.14 (1H, coalescing br.s), 5.92-5.85 (1H, m), 5.65-5.56 (1H, m), 4.75-4.50 (1H, br.m), 4.37-4.28 (1H, m), 3.78 (3H, s), 2.72-2.49 (2H, m), 1.57-1.04 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.0, 155.1 (br), 134.0, 131.5, 131.4, 128.5, 127.9, 127.2, 126.2, 111.6, 81.2 (2), 68.6 and 66.1 (br, rotamers), 56.2, 44.8, 35.4, 28.4 (3), 28.1 (3). **IR** (NaCl, neat film): 3316 (br), 3050, 3002, 2976, 2929, 1750-1707 (br), 1489, 1463, 1392, 1366, 1330, 1243, 1155, 1127, 1024, 954 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 439.3 (MH^+, 15), 385 (3), 383 (10), 327 (45), 285 (30), 283 (100), 239 (9), 207 (6). **HRMS** (ESI): calculated for $C_{22}H_{32}N_2O_5$ [MH^+]: 439.1994; found = 439.2013. **$[\alpha]_D^{23.5}$** = –101 (*c* 1.36, $CHCl_3$) for 99.4:0.6 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 10% iPrOH/hexane, 1.0 mL/min, 235 nm); t_R = 12.3 min [minor], t_R = 20.4 min [major]. The absolute configuration was assigned by analogy with compound **3c**.



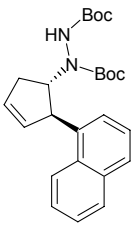
(11): *trans*-*N,N'*-[2-(4'-Fluoro-2'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 54% yield (31 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.08 (1H, t, *J* = 7.0 Hz), 6.61 (1H, dt, *J* = 2.0, 8.3 Hz), 6.54 (1H, dd, *J* = 2.0, 10.9 Hz), 6.29 and 6.12 (1H, coalescing br.s), 5.88-5.82 (1H, m), 5.65-5.56 (1H, m), 4.65 and 4.55 (1H, coalescing br.s), 4.32-4.22 (1H, m), 3.78 (3H, s), 2.68-2.46 (2H, br.m), 1.60-1.04 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (d, *J* = 244 Hz), 158.2, 156.1, 155.1 (br), 132.0, 130.8, 128.4, 127.6, 107.3 (d, *J* = 17.6 Hz), 98.8 (d, *J* = 25.7 Hz), 81.1 (2), 68.6 and 66.3 (br, rotamers), 56.1, 44.7 (br), 35.4, 28.4 (3), 28.1 (3). **IR** (NaCl, neat film): 3315 (br), 3052, 3002, 2976, 2932, 2869, 1748-1694 (br), 1603, 1502, 1456, 1393, 1367, 1331, 1277, 1255, 1152, 1103, 1033, 949, 834 cm^{-1}. **MS** (EI), *m/z* (rel. intensity): 423 (MH^+, 3), 367 (5), 311 (15), 267 (18), 222 (24), 190 (100), 165 (39), 83 (24). **$[\alpha]_D^{23.9}$** = +44.2 (*c* 1.00, $CHCl_3$) for 99.9:0.1 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 10% iPrOH/hexane, 1.0 mL/min, 272 nm); t_R = 11.6 min [major], t_R = 16.0 min [minor]. The absolute configuration was assigned by analogy with compound **3c**.



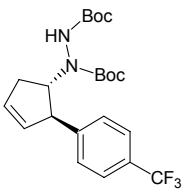
(12): *trans*-*N,N'*-[2-(2'-Methoxy-3'-quinolino)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 91% yield (56 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88-7.77 (2H, m), 7.67 (1H, d, *J* = 7.9 Hz), 7.56 (1H, t, *J* = 7.0 Hz), 7.35 (1H, t, *J* = 7.1 Hz), 6.36 and 6.21 (1H, coalescing br.s), 5.96 (1H, br.s), 5.73 (1H, br.s), 4.83 and 4.69 (1H, coalescing br.s), 4.45-4.31 (1H, m), 4.09 (3H, s), 2.82-2.54 (2H, m), 1.67-0.90 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.7, 156.0, 155.0, 145.6, 135.1, 131.4, 128.9, 128.1, 127.2, 127.1, 125.9, 124.2 (2), 81.2 (2), 68.3 and 65.7 (br, rotamers), 53.9, 46.8, 35.8, 28.4 (3), 28.2 (3). **IR** (NaCl, neat film): 3293 (br), 3054, 3001, 2977, 2929, 2856, 1741-1701 (br.), 1624, 1473, 1443, 1401, 1366, 1256, 1155, 1016, 952, 756 cm^{-1}. **MS** (ESI): *m/z* (rel. intensity): 456.3 (MH^+, 100), 400 (33), 344 (72), 300 (10). **HRMS** (ESI): calculated for $C_{25}H_{34}N_3O_5$ [MH^+]: 456.2492; found = 456.2504. **$[\alpha]_D^{24.9}$** = +162 (*c* 1.31, $CHCl_3$) for 98:2 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 8% iPrOH/hexane, 1.00 mL/min, 225 nm); t_R = 11.3 min [major], t_R = 15.0 min [minor]. The absolute configuration was assigned by analogy with compound **3c**.



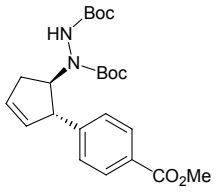
(13): *trans-N,N'*-[2-(2'-Naphthyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand as solvent, the bis-protected hydrazine was obtained as a colourless oil in 68% yield (39 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (1H, br.s), 7.85 (1H, d, *J* = 9.1 Hz), 7.73 (1H, d, *J* = 8.3 Hz), 7.52-7.32 (4H, m), 6.25 (1H, 1H, br.s), 5.99-5.94 (1H, m), 5.86-5.80 (1H, m), 4.88 (1H, br.s), 4.73 (1H, br.s), 2.86-2.60 (2H, m), 1.59-0.80 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ156.2, 154.8, 139.7, 134.3, 133.2, 132.4, 130.2, 129.0, 127.3, 126.1, 125.7, 124.0 (3), 81.4 (2), 67.2 and 64.9 (br, rotamers), 50.7, 36.0, 28.4 (6). **IR** (NaCl, neat film): 3271 (br), 3049, 2977, 2927, 1739-1702 (br.), 1511, 1477, 1392, 1366, 1331, 1251, 1156, 1050, 1023, 950, 778 cm^{-1}. **MS** (ESI): *m/z* (rel. intensity): 425.2 (MH^+, 7), 347 (11), 313 (41), 269 (100), 193 (91), 141 (27). **HRMS** (ESI): calculated for $C_{25}H_{33}N_2O_4$ [MH^+]: 425.2434; found = 425.2422. **$[\alpha]_D^{23.9}$** = +41.2 (*c* 1.40, $CHCl_3$) for 99.0:1.0 er, as determined by HPLC analysis: (Chiralcel AD, gradient 1-5% iPrOH/hexane, 1.0 mL/min, 225 nm); t_R = 23.8 min [minor], t_R = 24.9 min [major]. The absolute configuration was assigned by analogy with compound **3c**.



(14): *trans-N,N'*-[2-(4'-Trifluoromethylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 49% yield (29 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.55 (2H, d, *J* = 7.7 Hz), 7.42 (2H, br.s), 6.21 (1H, br.s), 5.91 (1H, br.s), 5.69 (1H, br.s), 4.70 (1H, br.s), 4.06 (1H, br.s), 2.73-2.50 (2H, m), 1.60-1.01 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.0, 154.9, 148.3, 132.0 (2), 130.9 (2), 128.9 (d, *J* = 31.9 Hz), 128.2, 125.5, 124.6 (d, *J* = 272 Hz), 81.6, 81.5, 68.3 and 65.9 (br, rotamers), 53.8, 35.6, 28.4 (3), 28.1 (3). **IR** (NaCl, neat film): 3261 (br), 3055, 3004, 2978, 2931, 2867, 1738-1681 (br.), 1477, 1392, 1367, 1326, 1249, 1161, 1068, 1018, 951, 851 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 465.2 (MNa^+, 12), 365 (4), 331 (13), 287 (100), 211 (24). **HRMS** (ESI): calculated for $C_{22}H_{29}F_3N_2O_4Na$ [MNa^+]: 465.1971; found = 465.1980. **$[\alpha]_D^{25.4}$** = +116 (*c* 1.45, $CHCl_3$) for 92.0:8.0 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 3% iPrOH/hexane, 0.75 mL/min, 225 nm); t_R = 30.5 min [major], t_R = 35.7 min [minor]. The absolute configuration was assigned by analogy with compound **3c**.



(15): *trans-N,N'*-[2-(4'-Methoxycarbonylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate. Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 58% yield (34 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (2H, d, *J* = 8.3 Hz), 7.32 (2H, br.s), 6.24 (1H, br.s), 5.90-5.84 (1H, m), 5.69-5.63 (1H, m), 4.69 (1H, br.s), 4.09-3.97 (1H, br.m), 3.88 (3H, s), 2.70-2.49 (2H, m), 1.55-0.99 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 167.3, 156.0, 154.9, 149.6, 132.2 (2), 130.8, 129.9 (2), 128.5, 127.9, 81.6, 81.4, 67.8 and 66.0 (br, rotamers), 54.1, 52.2, 35.5, 28.4 (3), 28.2 (3). **IR** (NaCl, neat film): 3316 (br), 3051, 3004, 2977, 2931, 2857, 1744-1710 (br.), 1610, 1476, 1436, 1392, 1367, 1280, 1154, 1111, 1020, 951, 758 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 455.2 (MNa^+, 40), 355 (10), 277 (100), 245 (50), 201 (46), 169 (31). **HRMS** (ESI): calculated for $C_{23}H_{32}N_2O_6Na$ [MNa^+]: 455.2152; found = 455.2170. The enantiomeric ratio was 92.8:7.2, as determined by HPLC analysis: (Chiralcel AD, isocratic 4% iPrOH/hexane, 0.75 mL/min, 225 nm); t_R = 64.2 min [minor], t_R = 71.8 min [major].



(16): *trans*-*N,N'*-[2-(3',4'-Dimethoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butyl-hydrazine dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a white amorphous solid in 80% yield (47 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.94-6.70 (3H, m), 6.20 and 5.94 (1H, coalescing br.s), 5.87-5.82 (1H, m), 5.73-5.66 (1H, m), 4.68 (1H, br.s), 3.98-3.83 (1H, br.m), 3.87 (3H, s), 3.85 (3H, s), 2.73-2.47 (2H, m), 1.55-1.08 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.0, 155.0, 149.2, 147.8, 136.6, 133.0, 130.0, 119.6, 111.4, 110.6, 81.3 (2), 68.4 and 66.2 (br, rotamers), 56.2, 56.0, 53.4, 35.3, 28.4 (3), 28.2 (3). **IR** (NaCl, neat film): 3319 (br), 3050, 2976, 2934, 2857, 1738 (br), 1707, 1590, 1515, 1454, 1393, 1367, 1249, 1157, 1028, 953, 756 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 452.3 (MNa^+, 13), 357 (8), 323 (71), 279 (100), 203 (96), 185 (31), 141 (42). **HRMS** (ESI): calculated for $C_{23}H_{34}N_2O_6Na$ [MNa^+]: 457.2309; found = 457.2323. **$[\alpha]_D^{25.4}$** = +62.2 (*c* 1.40, $CHCl_3$) for 75.0:25.0 er, as determined by HPLC analysis: (Chiralcel OD-H, isocratic 4% iPrOH/hexane, 0.75 mL/min, 232 nm); t_R = 11.1 min [major], t_R = 12.5 min [minor].

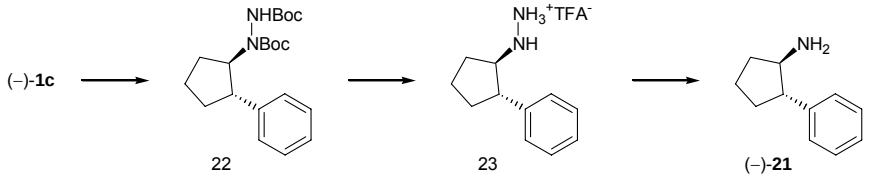
(17): 5-(3'-Thiophenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 89% yield (46 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34-7.26 (1H, m), 7.04-6.92 (2H, m), 4.74-4.30 (2H, br.m), 3.52-3.25 (1H, br.m), 2.51-2.12 (1H, br.m), 2.12-1.58 (3H, br.m), 1.58-1.40 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.1 (br.), 155.7 (br), 143.5, 127.5, 126.5, 120.1, 81.7, 81.5, 65.6 and 64.7 (br, rotamers), 61.1 and 60.4 (br, rotamers), 42.3, 41.1, 36.6 (br, rotamers), 35.6 and 34.3 (br, rotamers), 28.4 (6). **IR** (NaCl, neat film): 3099, 3002, 2976, 2930, 2883, 1733 (br), 1696 (br.), 1590, 1475, 1457, 1367, 1339, 1256, 1161, 1140, 1106, 1048, 1011, 912, 774 cm^{-1}. **MS** (EI), *m/z* (rel. intensity): 380 (M^+, 4), 280 (10), 251 (11), 224 (54), 149 (16), 113 (21), 69 (57), 57 (100). **HRMS** (EI): calculated for $C_{19}H_{28}N_2O_4S$ [M^+]: 380.1770; found = 380.1780. **$[\alpha]_D^{24.6}$** = +22.2 (*c* 1.20, $CHCl_3$) for 81:19 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 5% iPrOH/hexane, 0.80 mL/min, 235 nm); t_R = 12.7 min [minor], t_R = 16.7 min [major].

(18): 5-(2',4'-Dimethoxypyrimidin-5-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 69% yield (41 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (1H, s), 4.79-4.35 (2H, br.m), 4.02 (3H, s), 3.98 (3H, s), 3.41-3.19 (1H, br.m), 2.49-2.18 (1H, br.m), 1.72 (2H, br.s), 1.59 (1H, br.s), 1.63-1.39 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.4, 164.4, 157.1 (br.), 154.6 (br), 154.1, 115.5, 81.7, 81.5, 63.4 and 61.9 (br, rotamers), 61.2 and 60.2 (br, rotamers), 54.9, 54.2, 38.1 and 37.1 (br, rotamers), 35.7, 35.0 and 34.1 (br, rotamers), 28.3 (6). **IR** (NaCl, neat film): 3004, 2979, 2933, 2901, 1734 (br), 1699, 1601, 1567, 1473, 1404, 1368, 1333, 1301, 1257, 1156, 1140, 1106, 1075, 1016, 914, 860, 800, 757 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 437 (MH^+, 3), 307 (11), 280 (21), 236 (27), 167 (93), 69 (23), 57 (100). **$[\alpha]_D^{25.4}$** = –25.5 (*c* 1.37, $CHCl_3$) for 99.9:0.1 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 20% iPrOH/hexane, 1.0 mL/min, 220 nm); t_R = 7.1 min [minor], t_R = 15.4 min [major].

(*d*-18): 5-(6'-Deuterio-2',4'-dimethoxypyrimidin-5-yl)-2,3-diazabicyclo-[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate. Modifications from **18**: after premixing the catalyst in 0.80 mL THF, 0.80 mL D_2O was added. To the orange heterogeneous mixture was added the solution containing **1c** and the boronic acid in THF (0.80 mL). The bis-protected hydrazine was obtained as a colourless oil in 69% yield (41 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): Same as for **18**, with the exception of the singlet at 7.96 ppm, which was significantly decreased (signal was 9% according to integration). **MS** (ESI), *m/z* (rel. intensity): 438.3 (MH^+, 100), 382 (4), 338 (4), 282 (6), 238 (5). **HRMS** (ESI): calculated for $C_{21}H_{32}DN_4O_6$ [MH^+]: 438.2457; found = 438.2478.

(19): 5-(2'-Fluorophenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate. Using (*S,R*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 47% yield (25 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.30-7.17 (1H, m), 7.17-7.01 (3H, m), 4.90-4.33 (2H, br.m), 3.66-3.40 (1H, br.m), 2.60-1.91 (2H, br.m), 1.86-1.63 (2H, br.m), 1.63-1.19 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.2 (d, *J* = 247 Hz), 157.5 (br.), 155.6 (br), 129.7, 128.4, 127.0 (br), 124.3, 115.8 (d, *J* = 22 Hz), 81.7 (2), 64.9 and 63.9 and 62.9 (br, rotamers), 61.8 and 60.2 (br, rotamers), 39.7 and 39.1 and 38.7 (br, rotamers), 36.0 and 35.1 (br, rotamers), 32.7, 28.3 (6). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -114.9 and -115.7 (rotamers). **IR** (NaCl, neat film): 3069, 2978, 2932, 1733 (br), 1699 (br), 1491, 1455, 1367, 1336 (br), 1300, 1258, 1228, 1158, 1141, 1111, 1047, 1005, 970, 859, 757 cm^{-1}. **MS** (EI), *m/z* (rel. intensity): 392 (M^{+}, 3), 263 (11), 236 (71), 192 (7), 161 (13), 113 (42), 69 (67), 57 (100). **HRMS** (EI): calculated for $C_{21}H_{29}N_2O_4F$ [M^{+}]: 392.2111; found = 392.2108. **$[\alpha]_D^{25.6}$** = –38.9 (*c* 1.30, $CHCl_3$) for 99.0:1.0 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 8% iPrOH/hexane, 1.0 mL/min, 225 nm); t_R = 7.31 min [major], t_R = 11.1 min [minor].

(20): 5-(4'-Trifluoromethylphenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate. Using (*R,S*)-*tert*-Bu-Josiphos as chiral ligand, the bis-protected hydrazine was obtained as a colourless oil in 39% yield (23 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.60 (2H, d, *J* = 7.4 Hz), 7.33 (2H, d, *J* = 7.4 Hz), 4.83-4.30 (2H, br.m), 3.55 and 3.39 (1H, coalesc. br.m), 2.64-2.01 (2H, br.m), 1.92-1.63 (2H, br.m), 1.63-1.40 (18H, br.m). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.9 (br.), 155.1 (br), 146.0 (d, *J* = 72.1 Hz), 128.8 (q, *J* = 31.8 Hz),127.5 (2), 125.8 (2), 121.6 (d, *J* = 271.8 Hz), 81.9, 81.8 65.9 and 65.1 (br, rotamers), 61.3 and 60.5 (br, rotamers), 46.2 and 45.0 (br, rotamers), 36.8 and 35.9 (br, rotamers), 34.7 and 32.8 (br, rotamers), 28.4 (6). **IR** (NaCl, neat film): 3001, 2977, 2932, 2887, 1734 (br.), 1700 (br.), 1618, 1476, 1458, 1368, 1326, 1257, 1162, 1125, 1070, 969, 840, 770 cm^{-1}. **MS** (ESI), *m/z* (rel. intensity): 465.2 (MNa^+, 24), 365 (6), 287 (100), 241 (3). **HRMS** (ESI): calculated for $C_{22}H_{29}N_2O_4F_3Na$ [MNa^+]: 465.1971; found = 465.1970. **$[\alpha]_D^{25.4}$** = +23.7 (*c* 1.65, $CHCl_3$) for 92:8 er, as determined by HPLC analysis: (Chiralcel AD, isocratic 3% iPrOH/hexane, 0.75 mL/min, 225 nm); t_R = 14.7 min [minor], t_R = 17.2 min [major].



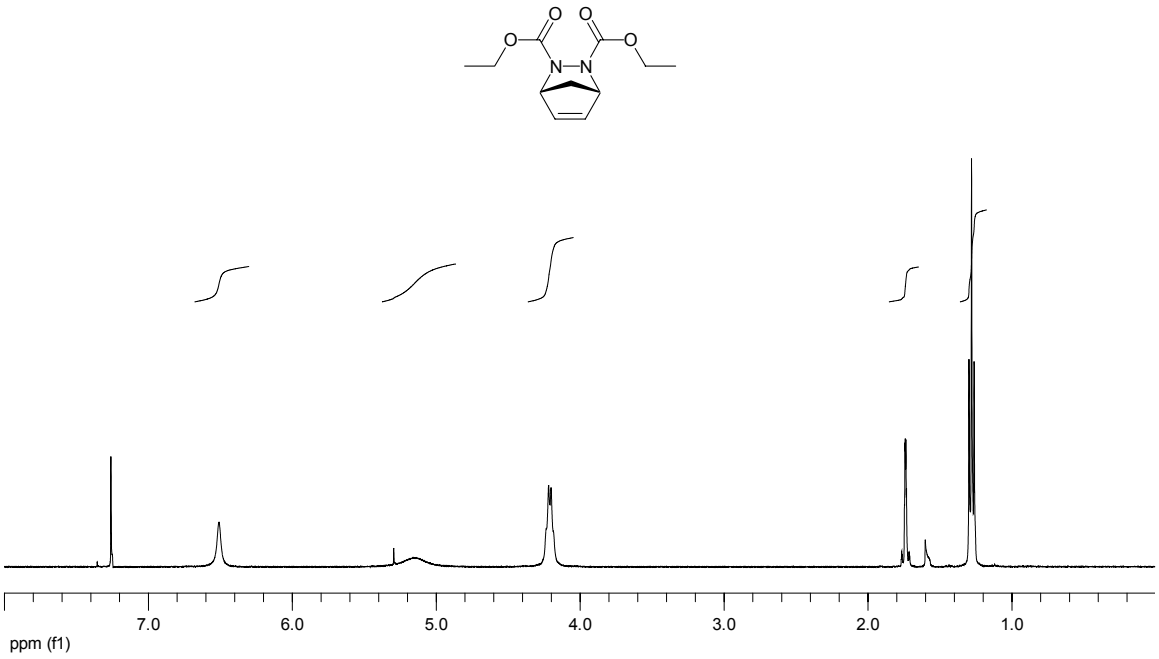
(-)-(*1R,2S*-21): *trans-(1R,2S)*-2-Phenylcyclopentylamine. In a 10 mL RB flask was diluted diazabicycle **1c** (104 mg, 0.277 mmol) in EtOH 95% (3.0 mL). The mixture was stirred for 16 h under a hydrogen atmosphere (balloon). The reaction mixture was filtered on celite, waqshed with methanol. Solvents were remove under reduced pressure, residual methanol was azeotroped with CH_2Cl_2. Recovered 111 mg crude colorless oil. If needed, the 1,2-substituted cyclopentane **22** could be purified by chromatography with 5-20% EtOAc/hexanes gradient. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.30-7.14 (5H, m), 6.06 and 5.81 (1H, br, rotamers), 4.68 and 4.53 (1H, br, rotamers),3.25 and 3.04 (1H, br, rotamers), 2.16-1.90 (2H, br.m), 1.90-1.58 (4H, br.m), 1.58-1.00 (18H, br.m).

The crude $(Boc)_2$-hydrazine **22** was retaken in CH_2Cl_2 (1.0 mL), transferred to a 10 mL flask, then trifluoroacetic acid (1.0 mL) was added at rt. The reaction was stirred for 4 h. After full consumption of starting material by TLC, the reaction mixture was transferred to a 25 mL flask with benzene and TFA was azeotroped under reduced pressure. **23** was recovered as a colorless ionic liquid (84 mg); $[\alpha]_D^{25.4} = -29.2$ (*c* 1.25, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.35-7.18 (5H, m), 6.59 (4H, br.s., hydrazinium), 3.68-3.60 (1H, m), 3.19 (1H, dd, *J* = 17.6, 8.2 Hz), 2.30-2.15 (2H, m), 1.96-1.70 (4H, m). **^{19}F NMR** (375 MHz, $CDCl_3$): δ -76.02 (s).

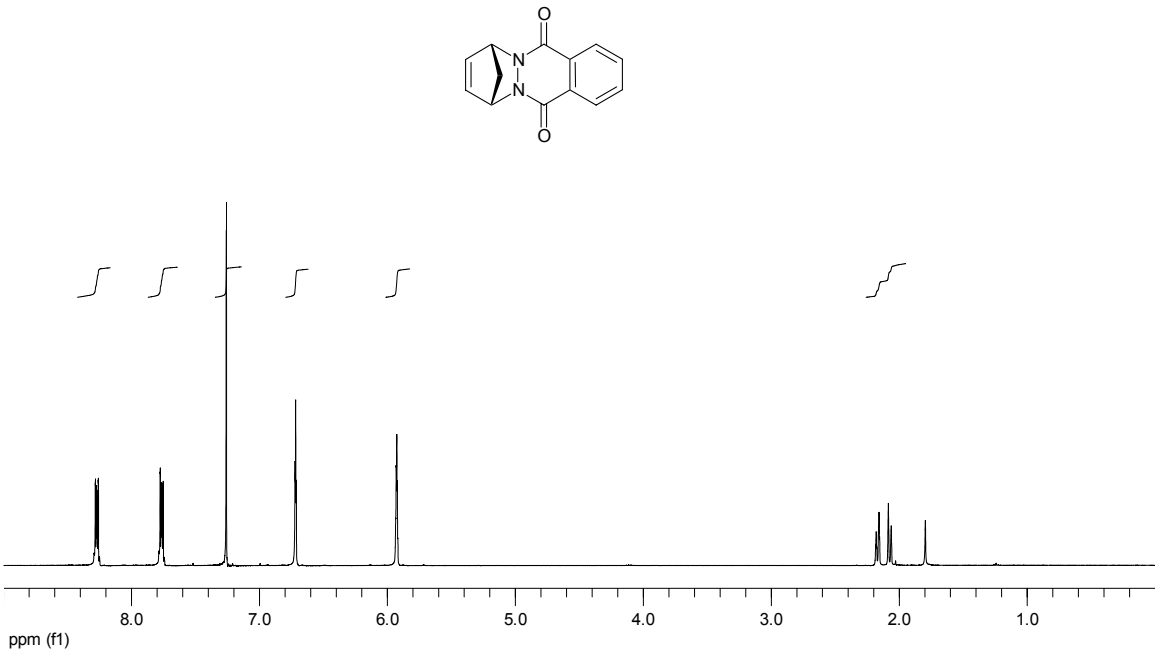
The crude salt **23** was diluted in 2.5 mL EtOH in a 25 mL RB flask, to which was added Raney nickel 2800 in suspension in 0.80 mL EtOH (834 mg of slurry 50% in water, pre-washed with 2 x 2 mL water, 2 x 2 mL methanol, 1 x 2 mL EtOH). The reaction mixture was filtered on celite, waqshed with methanol. Solvents were remove under reduced pressure, residual methanol was azeotroped with CH_2Cl_2. Recovered 31 mg crude colorless oil (69% from **1c**). The characterization data for (+)-(*1R,2S*)-**21** was fully concordant with that already reported in the literature.[12] $[\alpha]_D^{24.5} = -36.5$ (*c* 1.40, $CHCl_3$) for 81:19 er, as determined by HPLC analysis: (Chiralcel OD-H, isocratic 1% iPrOH/hexane, 0.75 mL/min).

[12] a) A. Dahnz, G. Helmchen, *Synlett* **2006**, 697. $[\alpha]_D^{20}$ +56.6 reported for (+)-(*1S,2R*)-**21**·HCl (93% ee). b) Brown, H. C. *et al*, *J. Am. Chem. Soc.* **1986**, *108*, 6761.

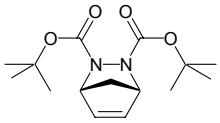
(1a): *meso*-2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-diethyl dicarboxylate

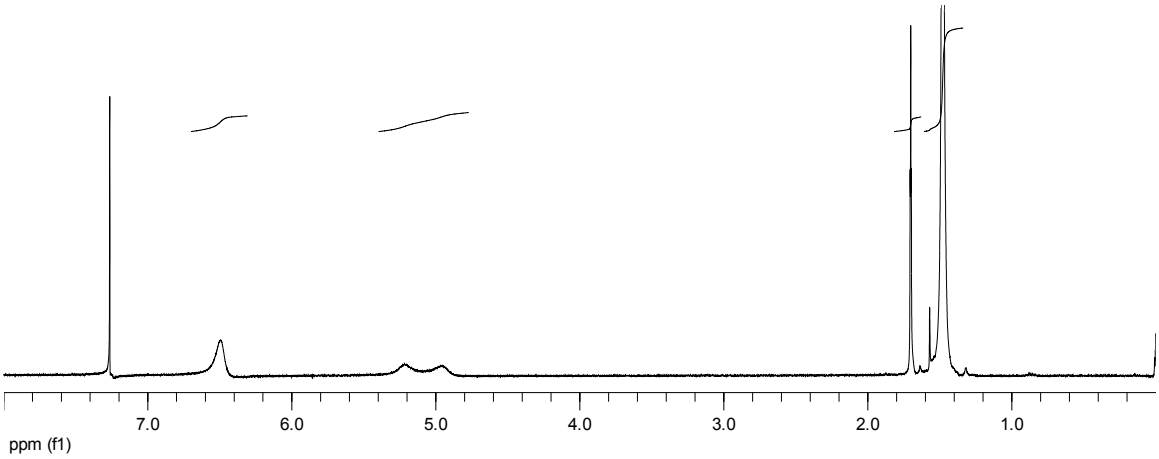


(1b): *meso*-2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-phthalazide

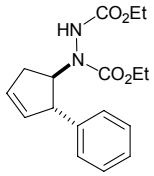


(1c): *meso*-2,3-Diazabicyclo[2.2.1]hept-5-ene-*N,N'*-di-*tert*-butyl dicarboxylate

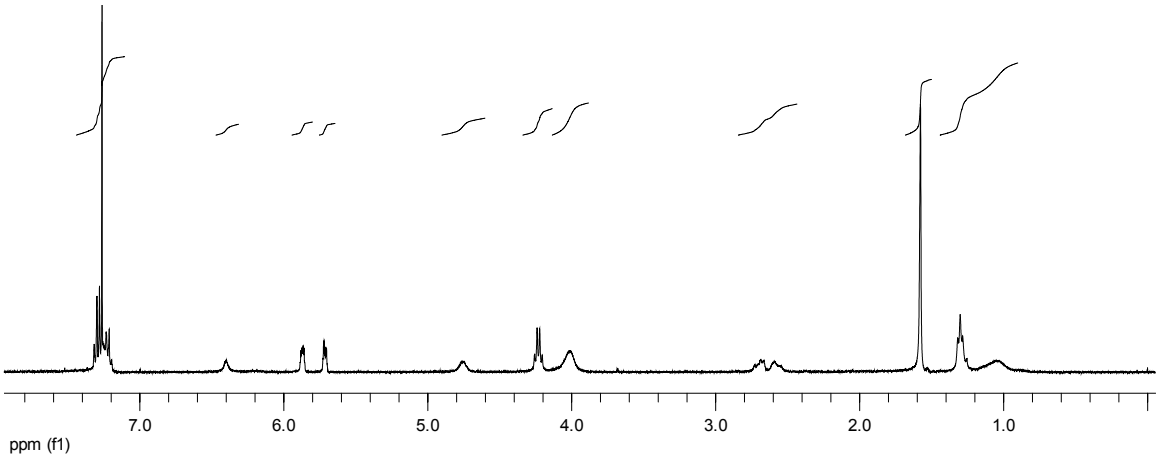




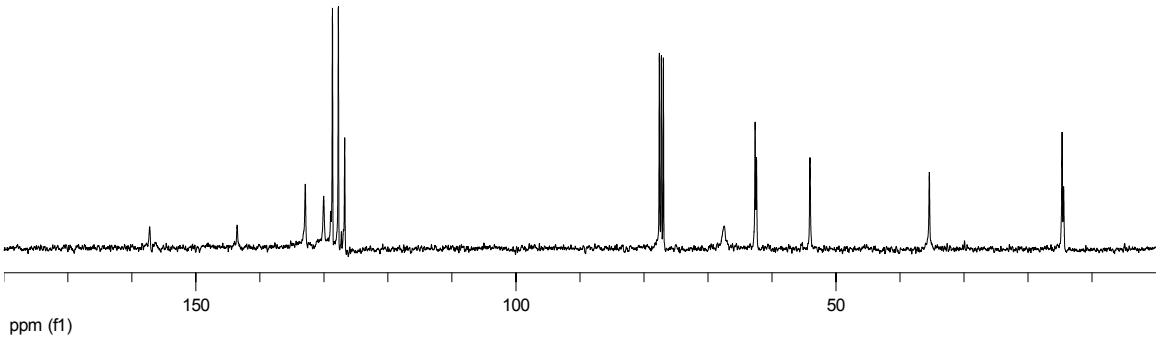
(3a): *trans-N,N'*-(2-Phenylcyclopent-3-enyl)-diethylhydrazine dicarboxylate.



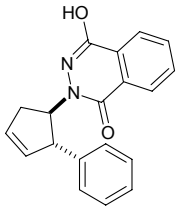
^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):



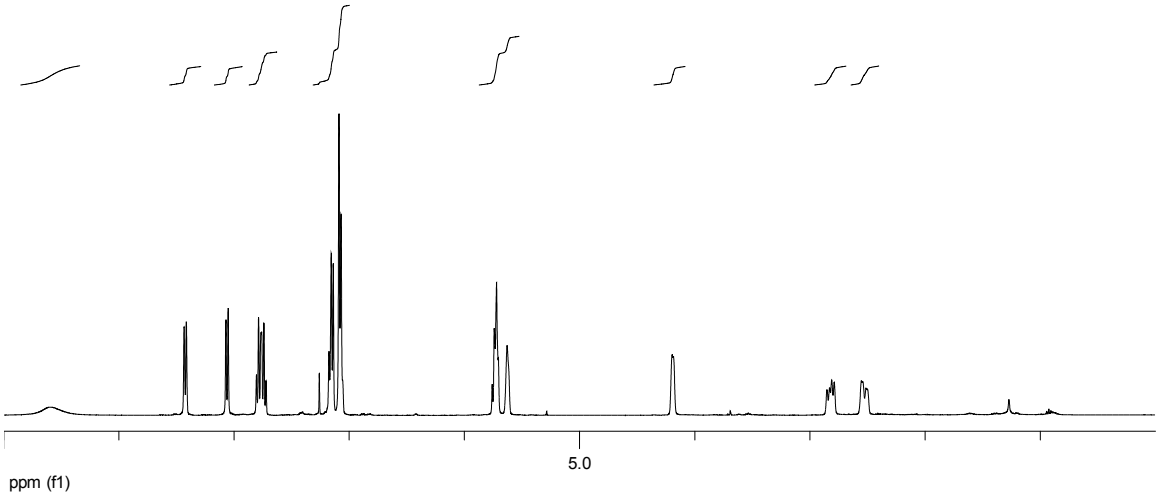
^{13}C NMR *100 MHz* ($CDCl_3$, 25 °C):



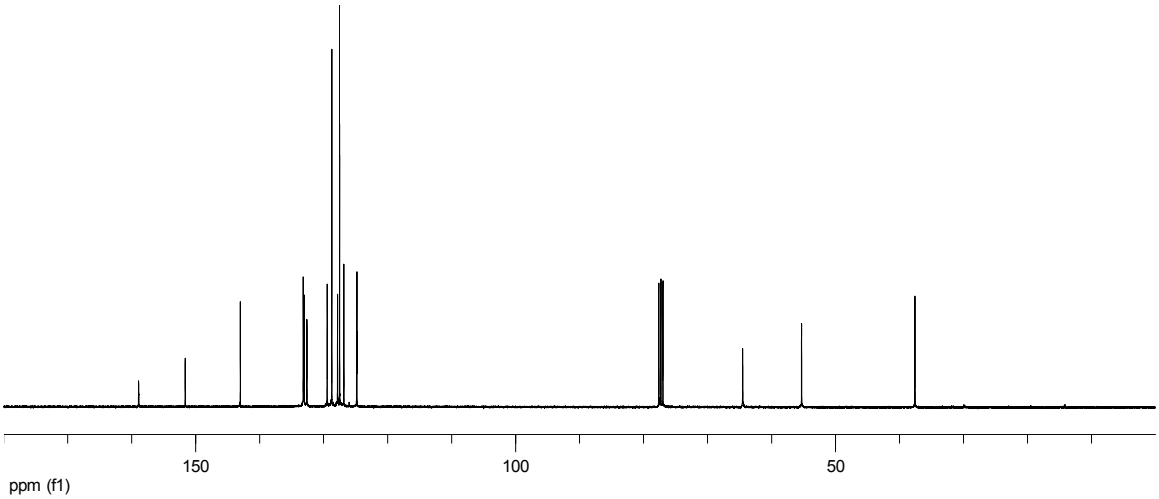
(3b): *trans*-4-Hydroxy-2-(2'-phenylcyclopent-3'-enyl)-2*H*-phthalazin-1-one.



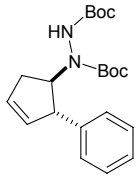
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



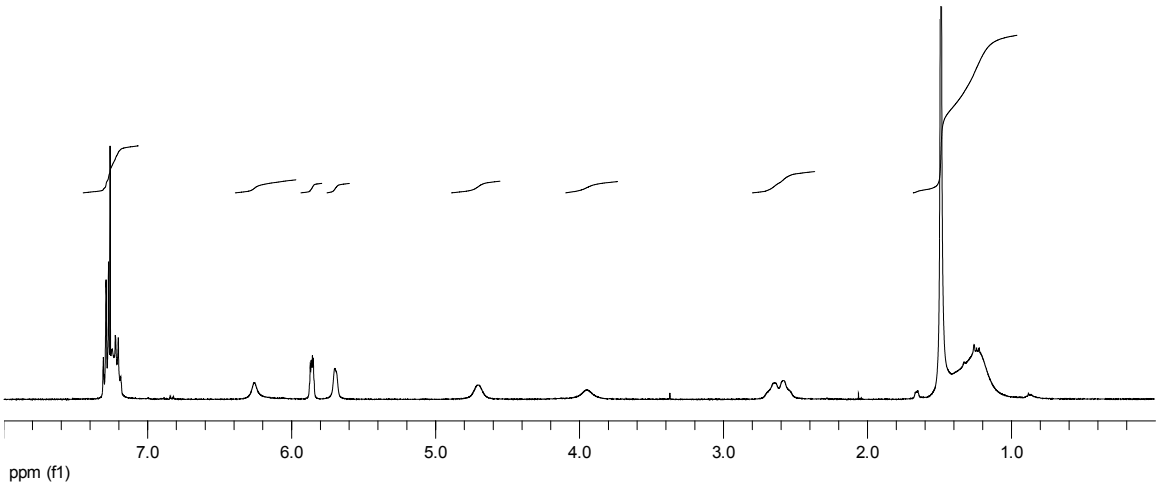
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



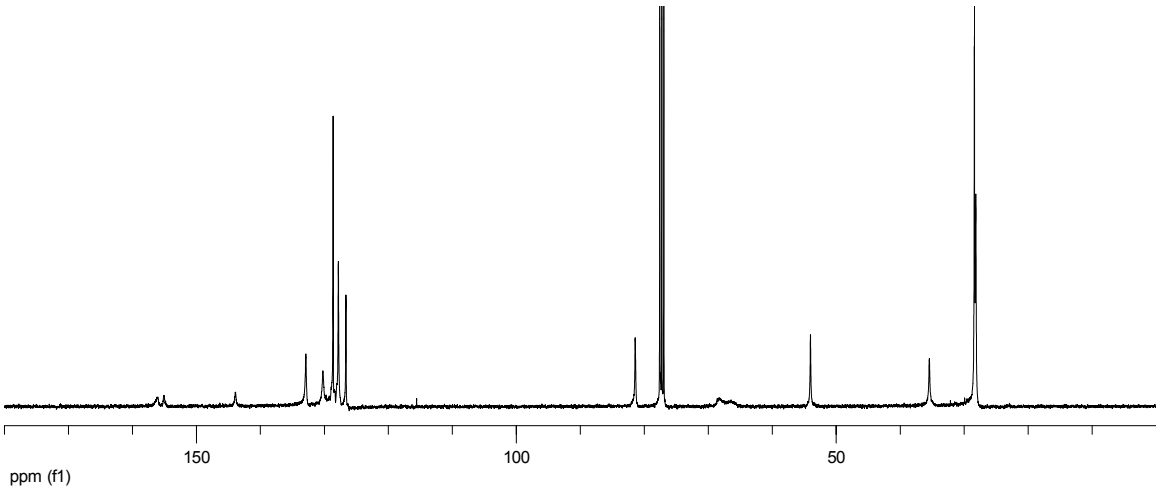
(3c): *trans*-*N,N'*-(2-Phenylcyclopent-3-enyl)-di-*tert*-butylhydrazine dicarboxylate.



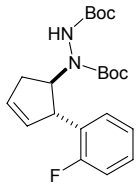
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



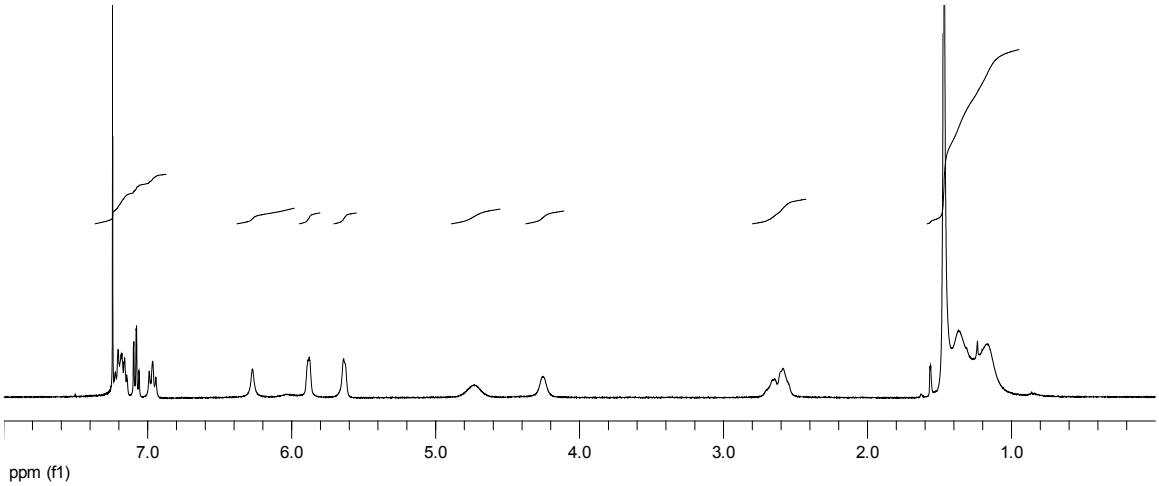
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



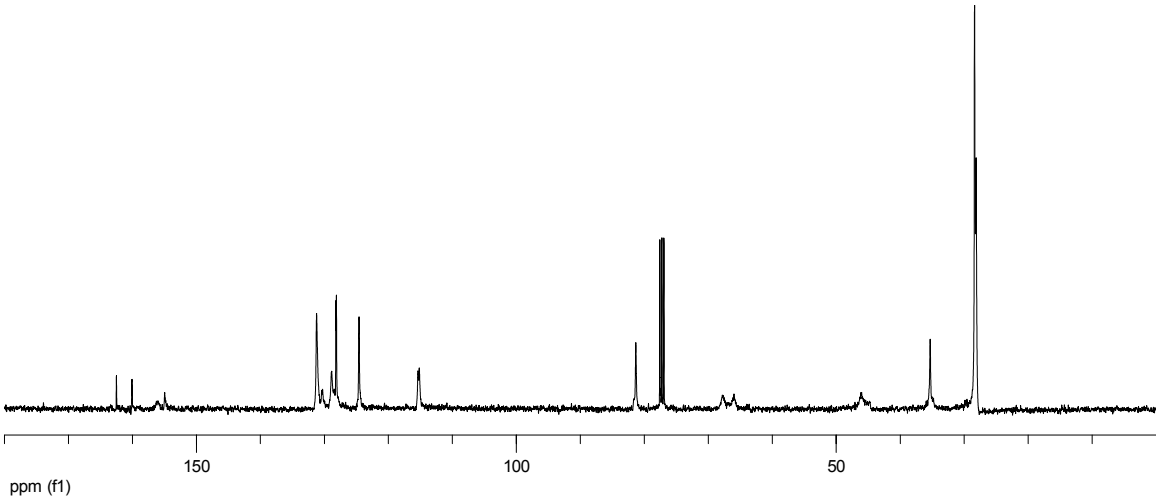
(6): *trans*-*N,N'*-[2-(2'-Fluorophenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate



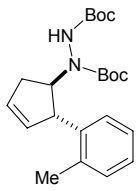
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



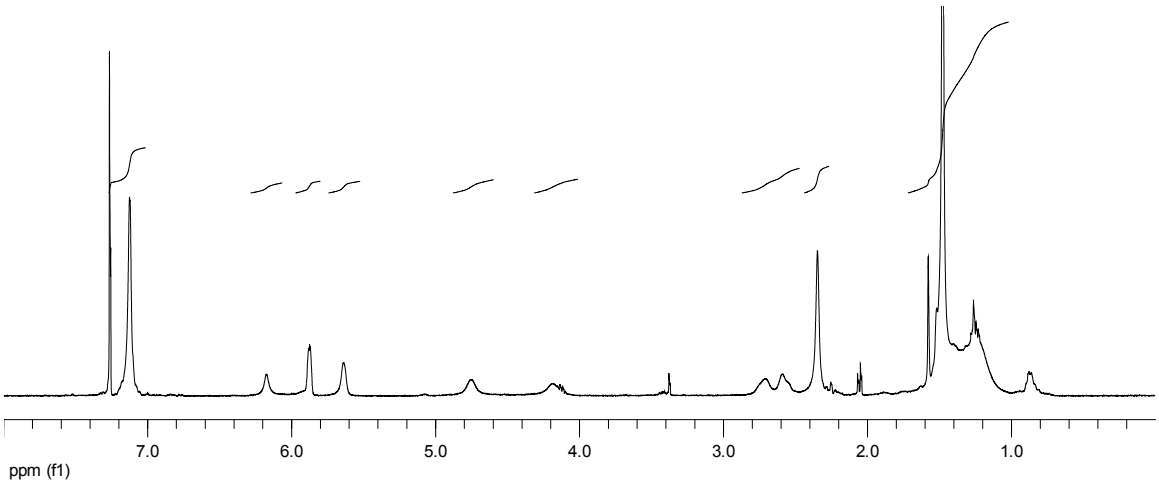
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



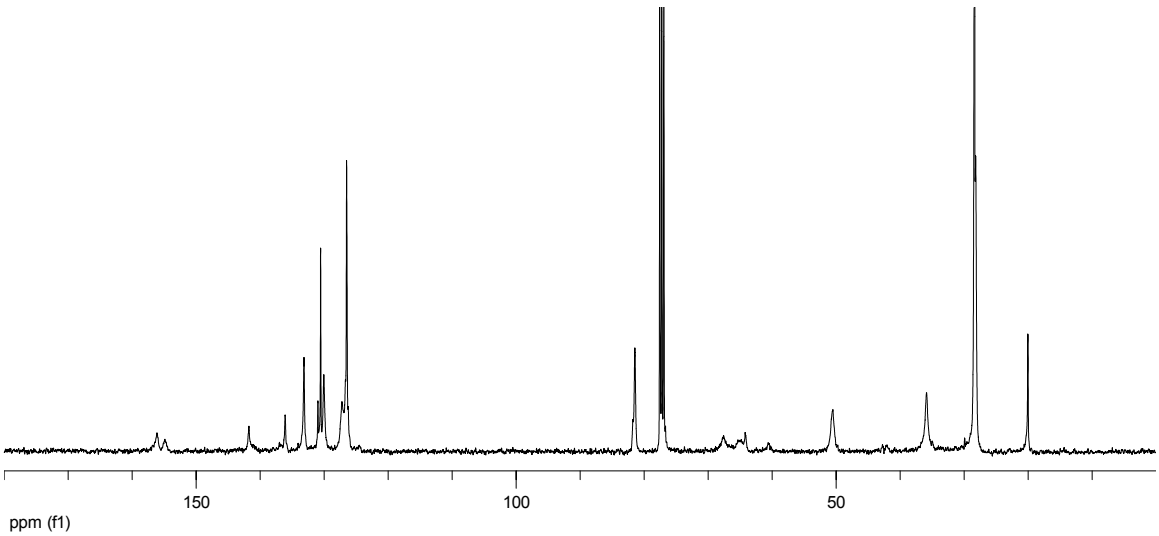
(7): *trans*-*N,N'*-[2-(2'-Methylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



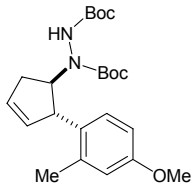
^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):



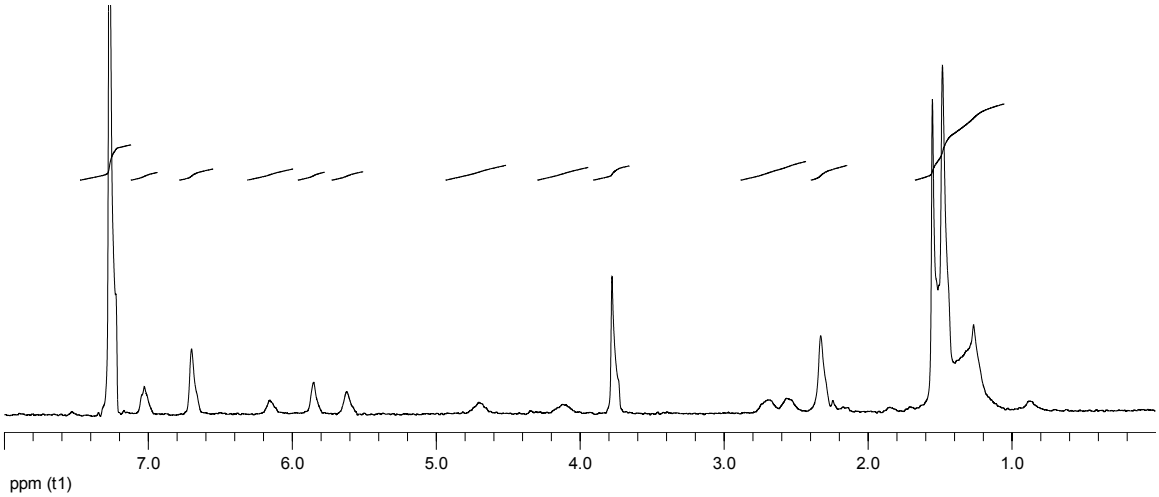
^{13}C NMR *100 MHz* ($CDCl_3$, 25 °C):



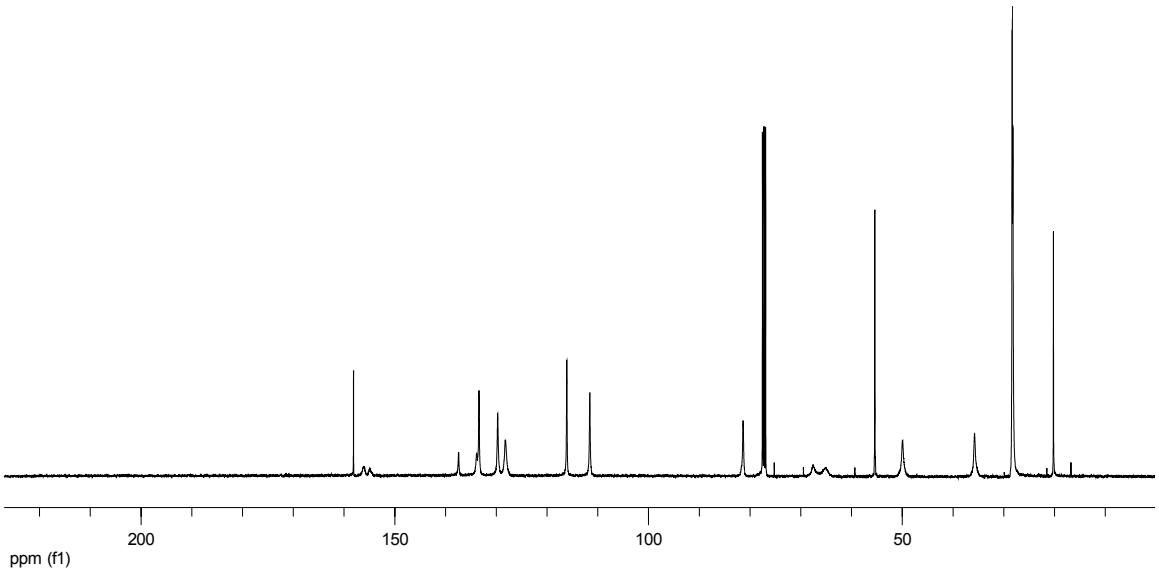
(8): *trans*-*N,N'*-[2-(2'-Methyl-4'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



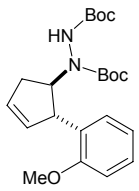
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



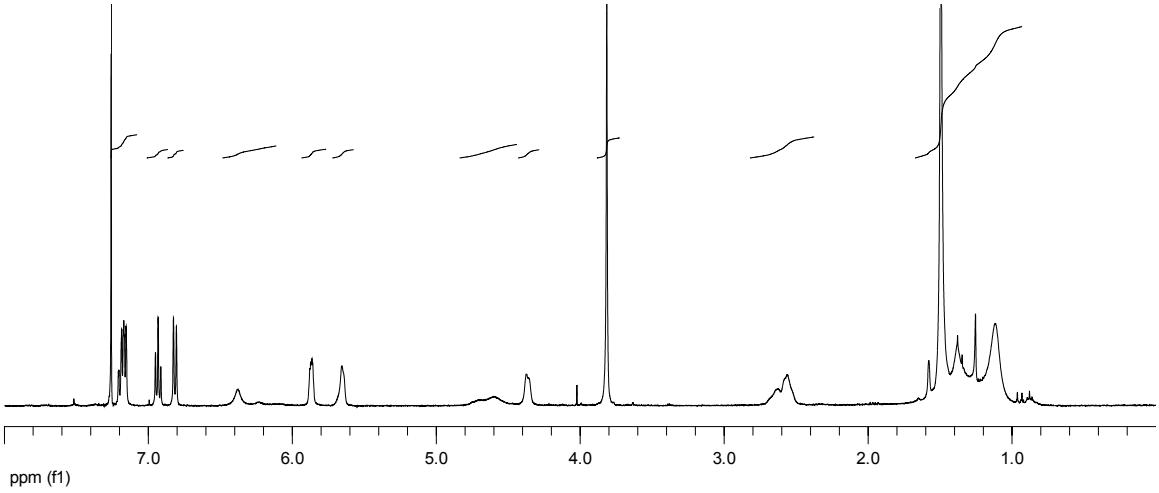
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



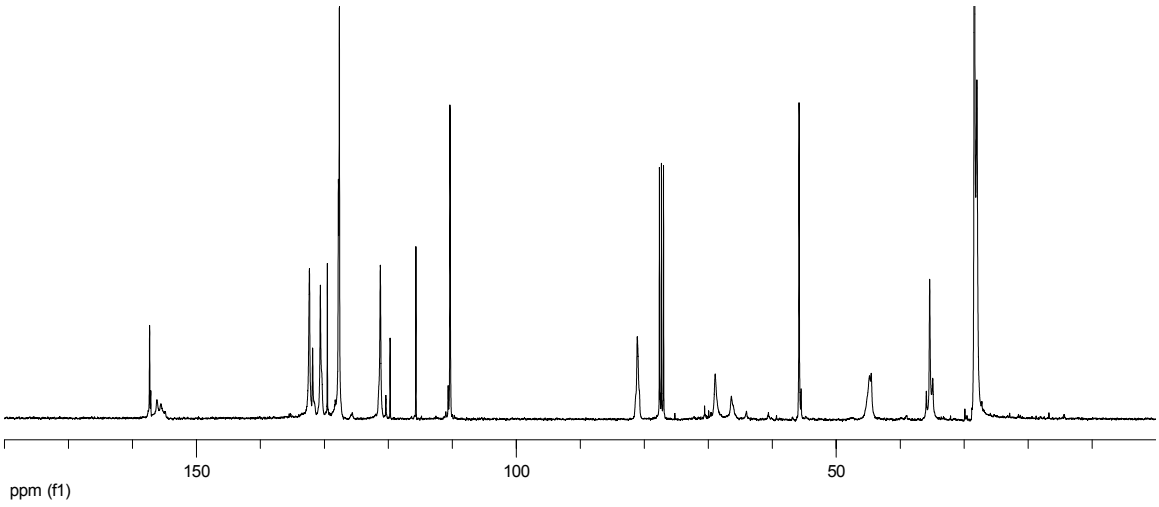
(9): *trans*-*N,N'*-[2-(2'-Methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



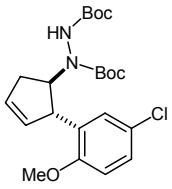
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



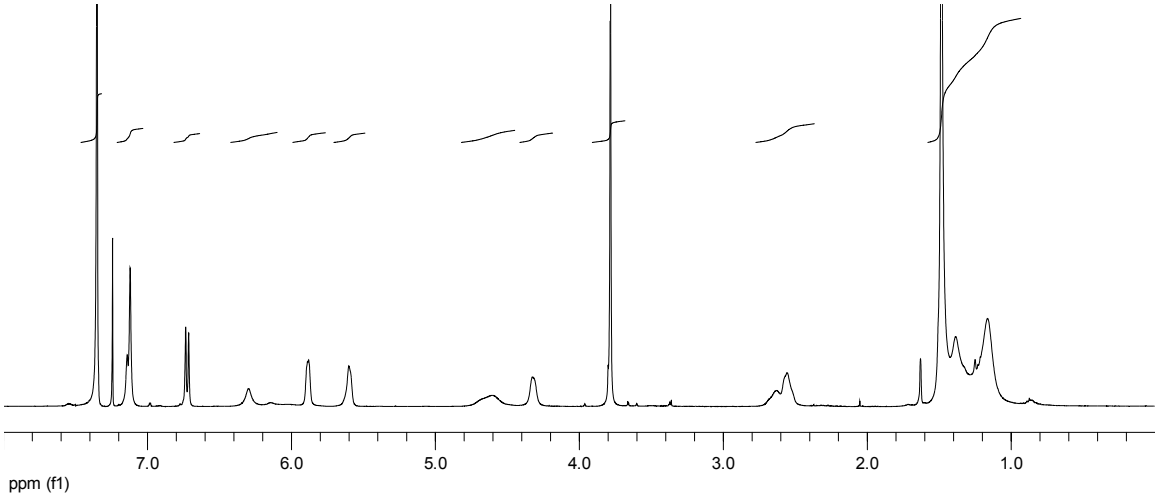
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



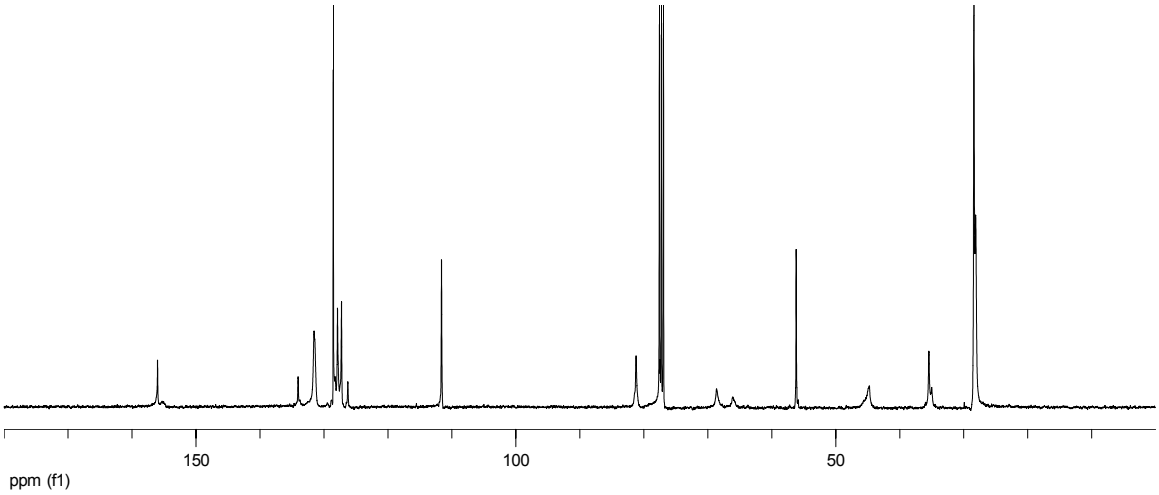
(10): *trans*-*N,N'*-[2-(5'-Chloro-2'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



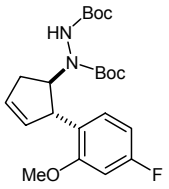
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



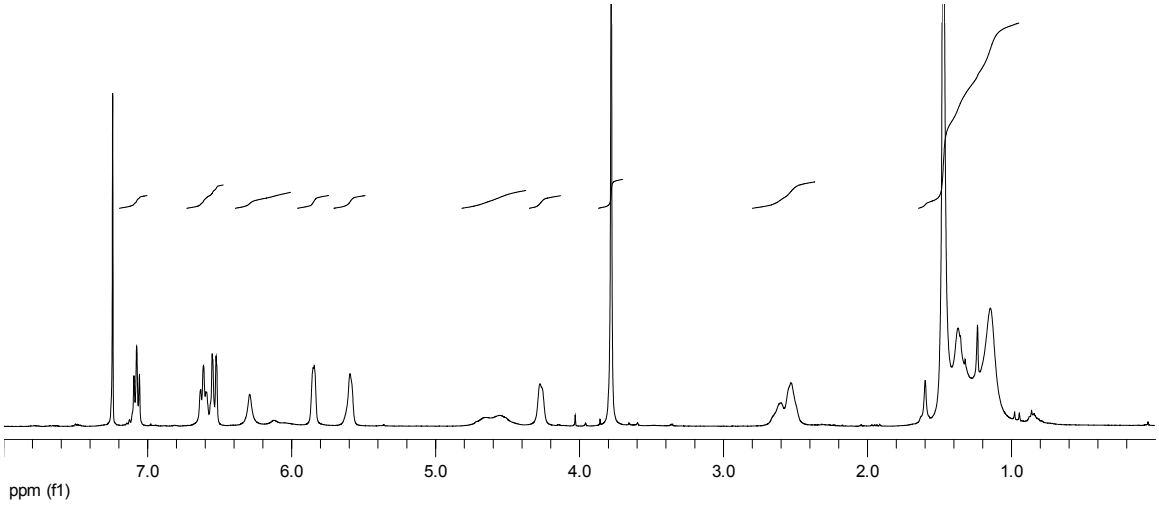
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



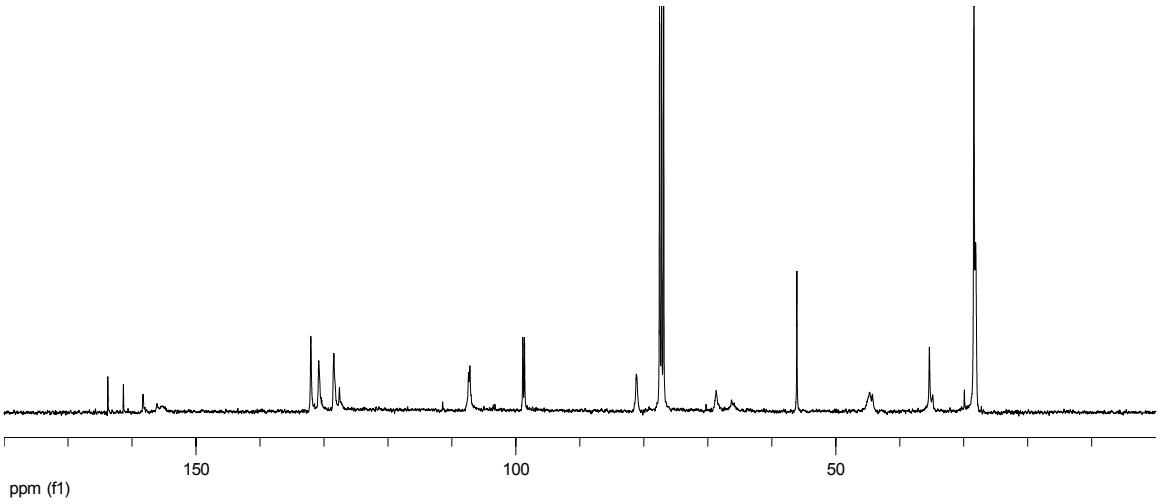
(11): *trans*-*N,N'*-[2-(4'-Fluoro-2'-methoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



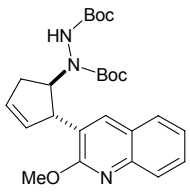
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



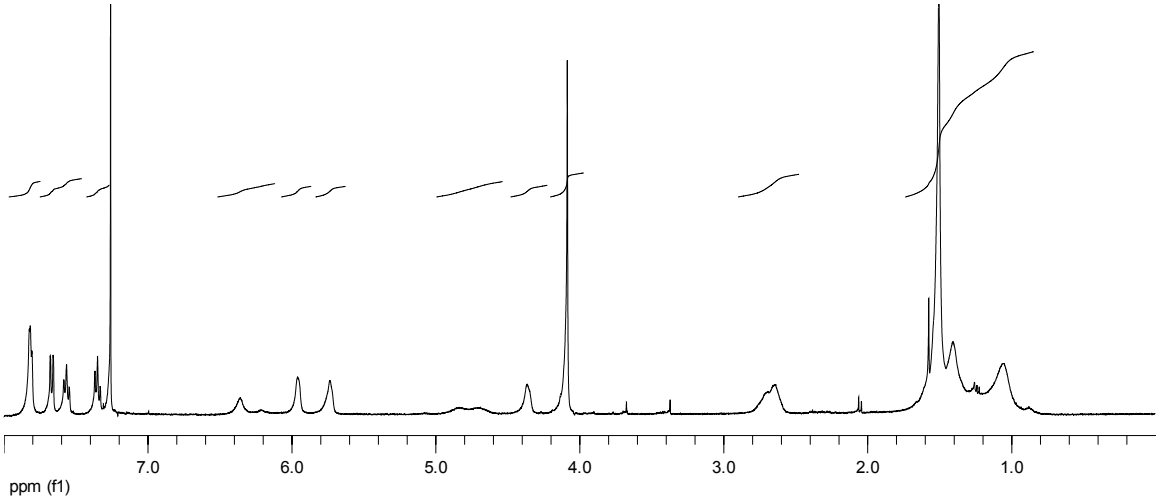
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



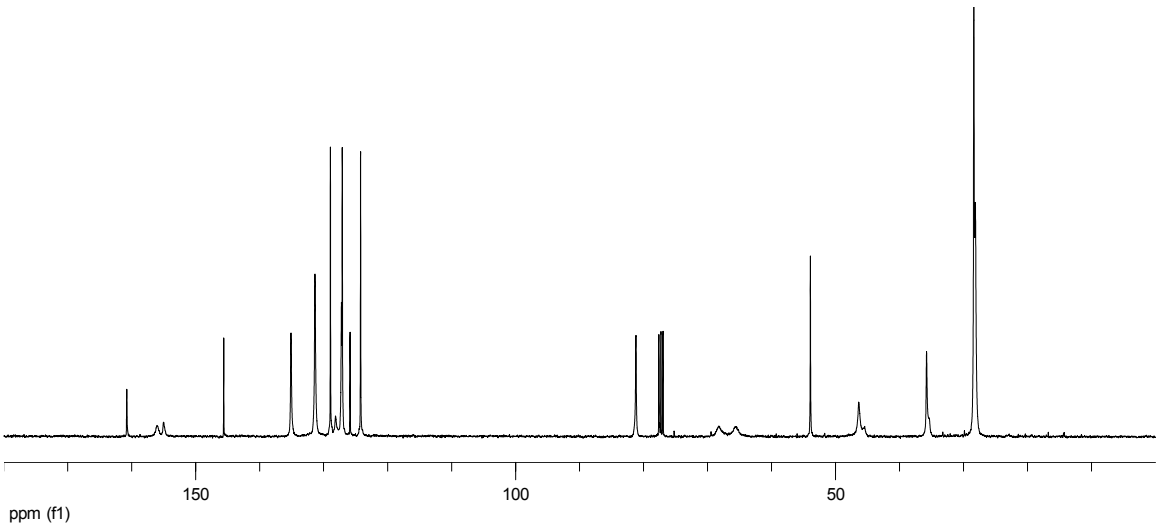
(12): *trans*-*N,N'*-[2-(2'-Methoxy-3'-quinolino)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



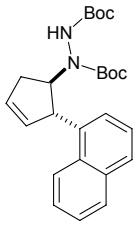
^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):



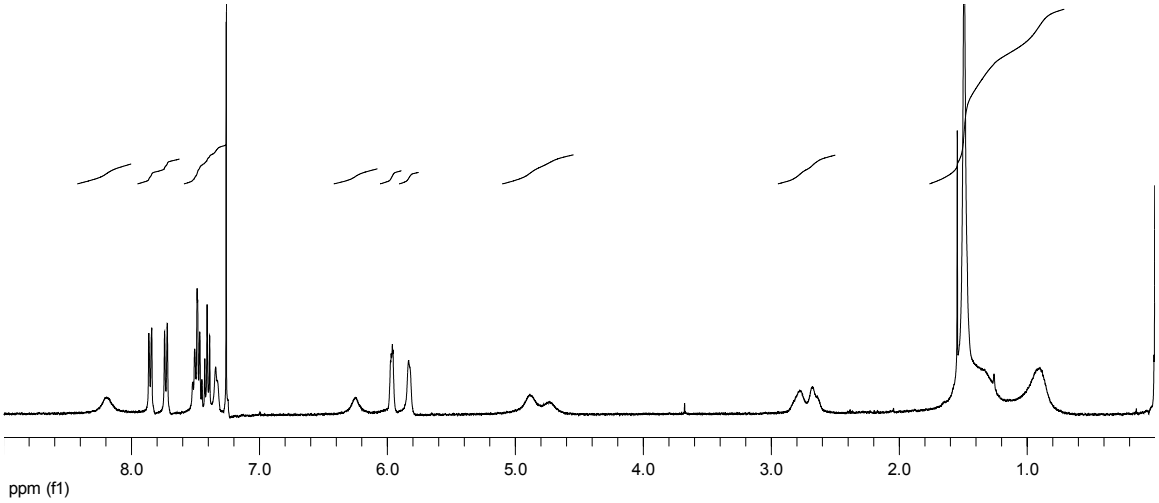
^{13}C NMR *100 MHz* ($CDCl_3$, 25 °C):



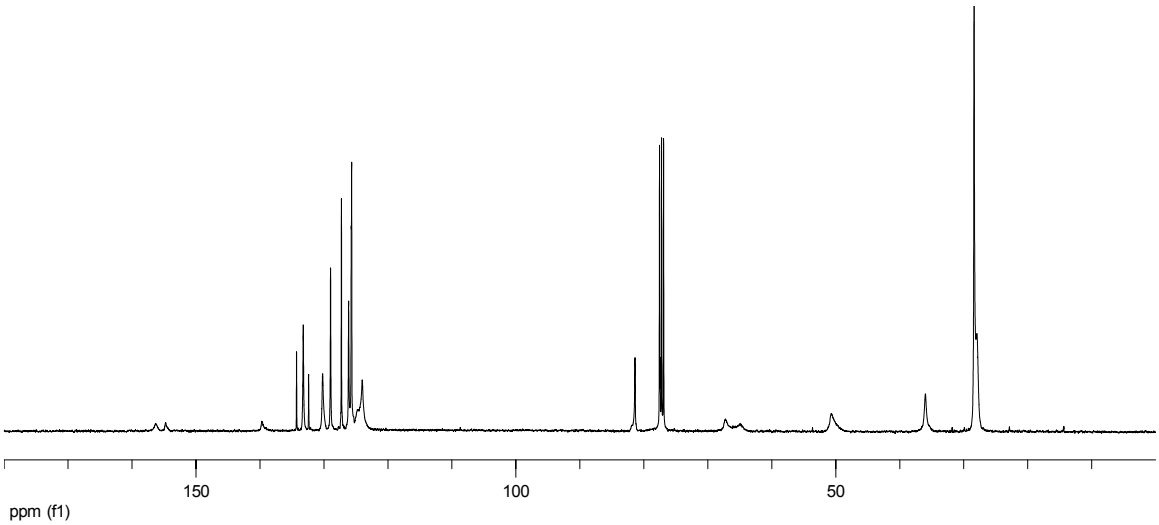
(13): *trans*-*N,N'*-[2-(2'-Naphthyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



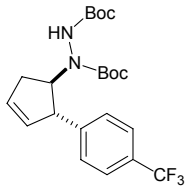
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



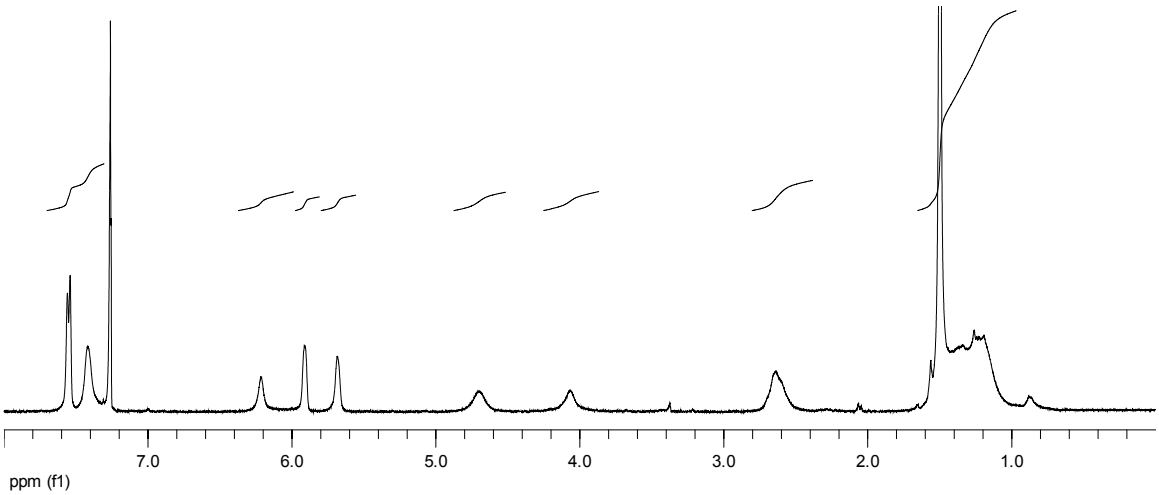
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



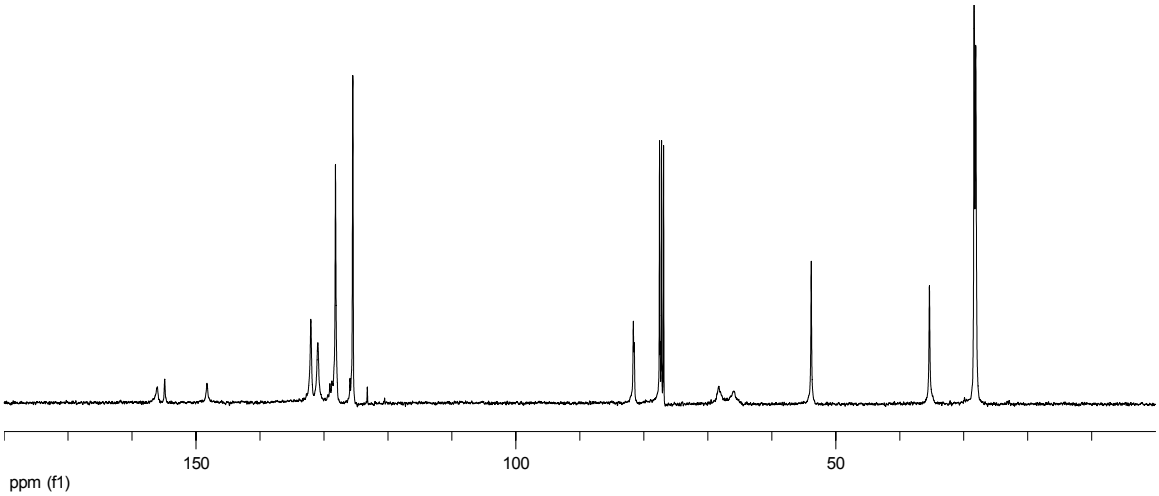
(14): *trans*-*N,N'*-[2-(4'-Trifluoromethylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



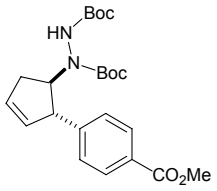
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



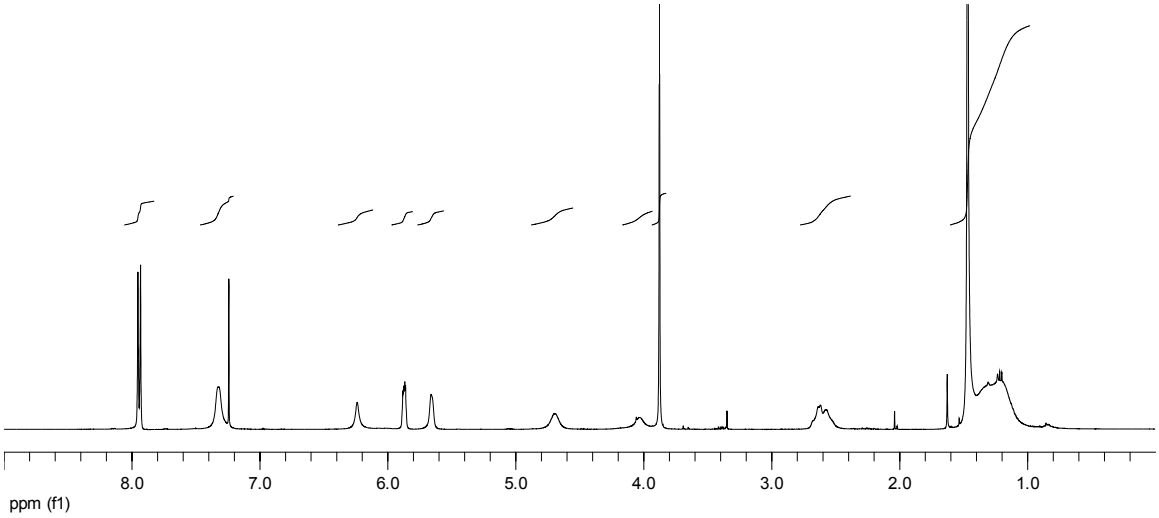
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



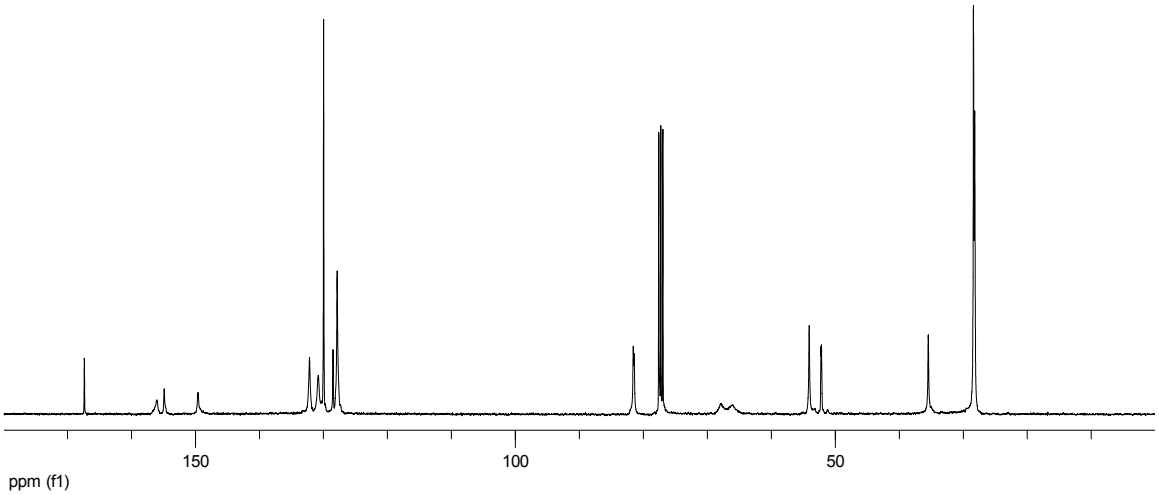
(15): *trans*-*N,N'*-[2-(4'-Methoxycarbonylphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



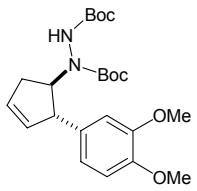
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



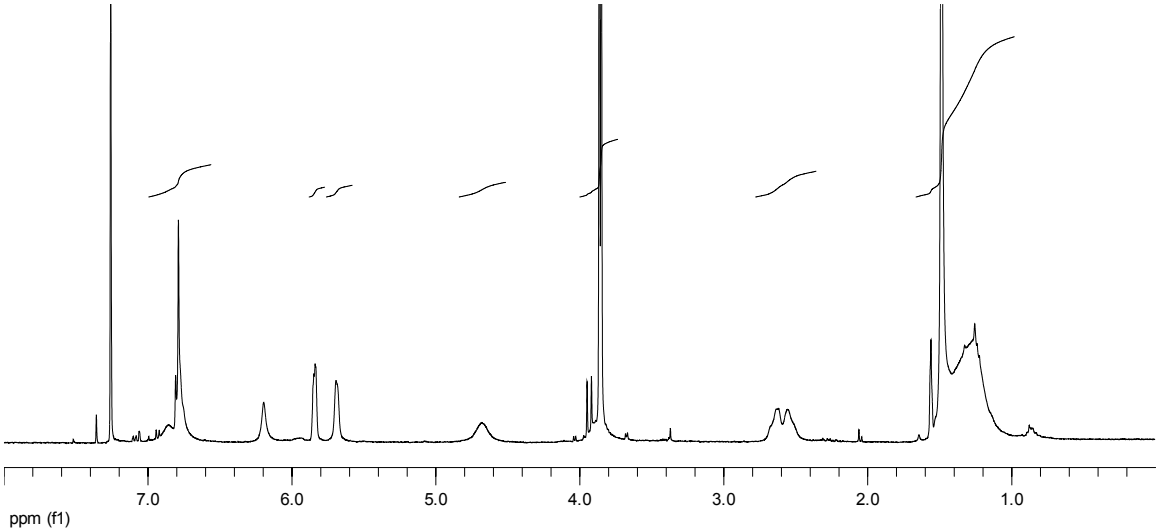
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



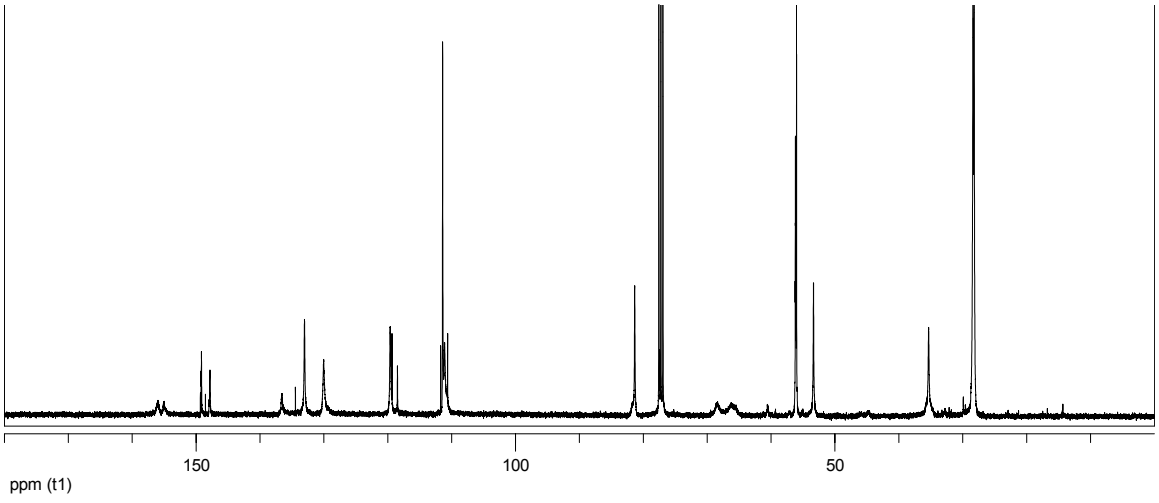
(16): *trans*-*N,N'*-[2-(3',4'-Dimethoxyphenyl)-cyclopent-3-enyl]-di-*tert*-butylhydrazine dicarboxylate.



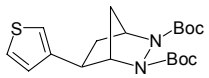
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



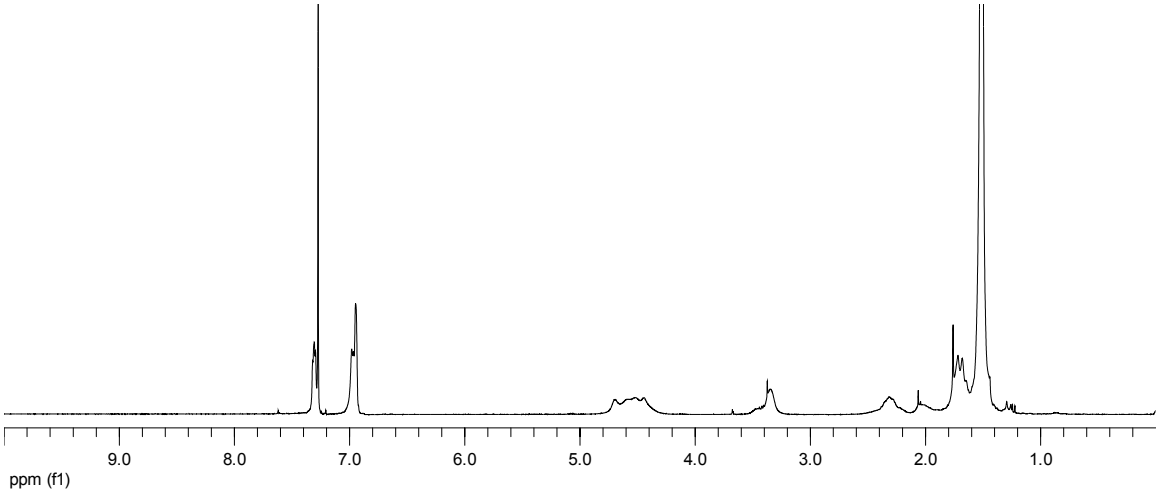
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



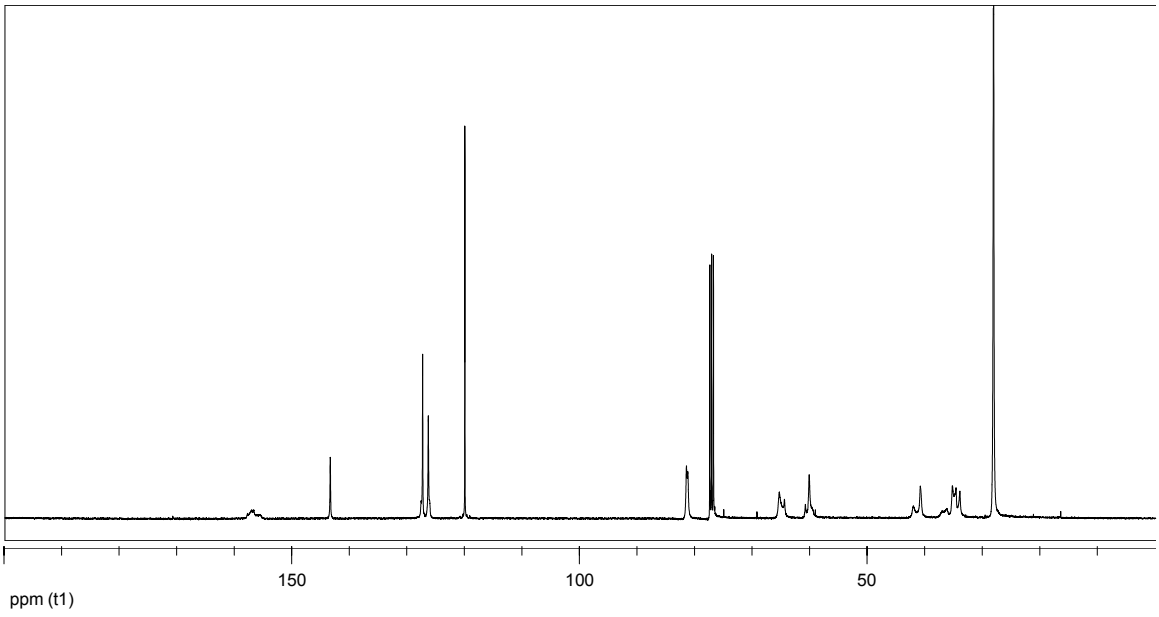
(17): 5-(3'-Thiophenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate.



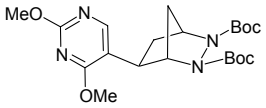
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



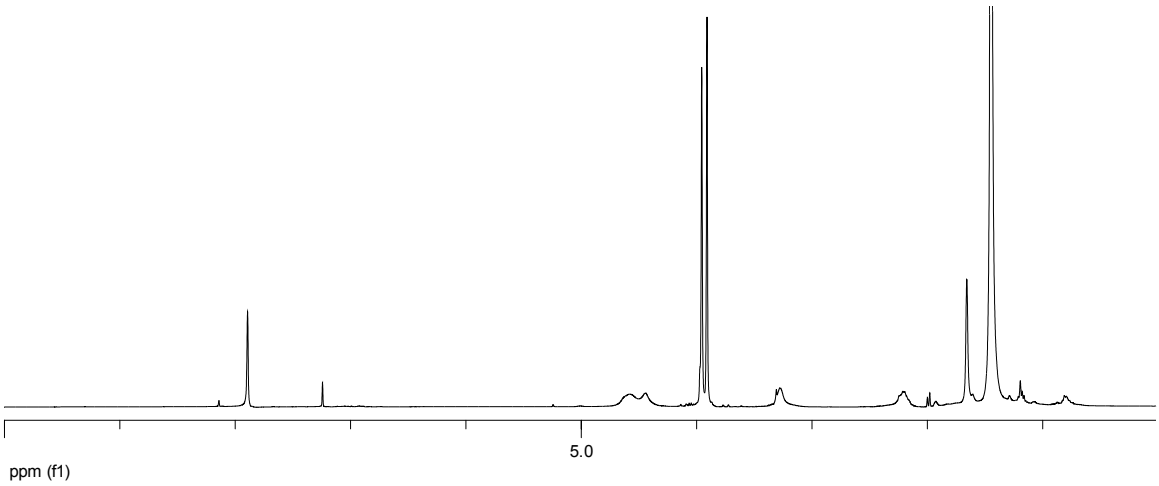
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



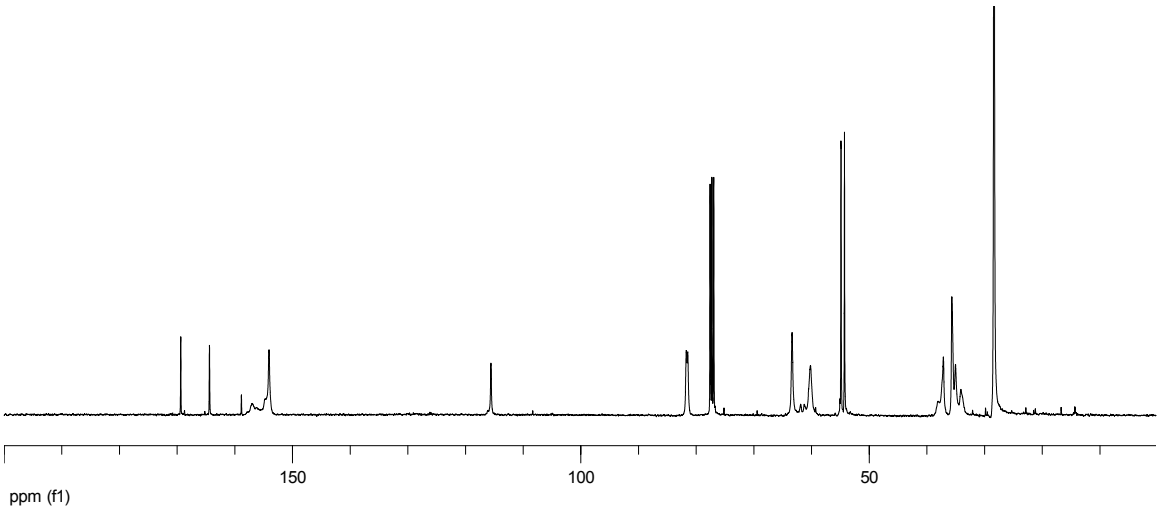
(18): 5-(2',4'-Dimethoxypyrimidin-5-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate.



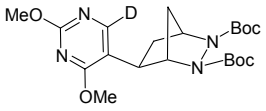
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



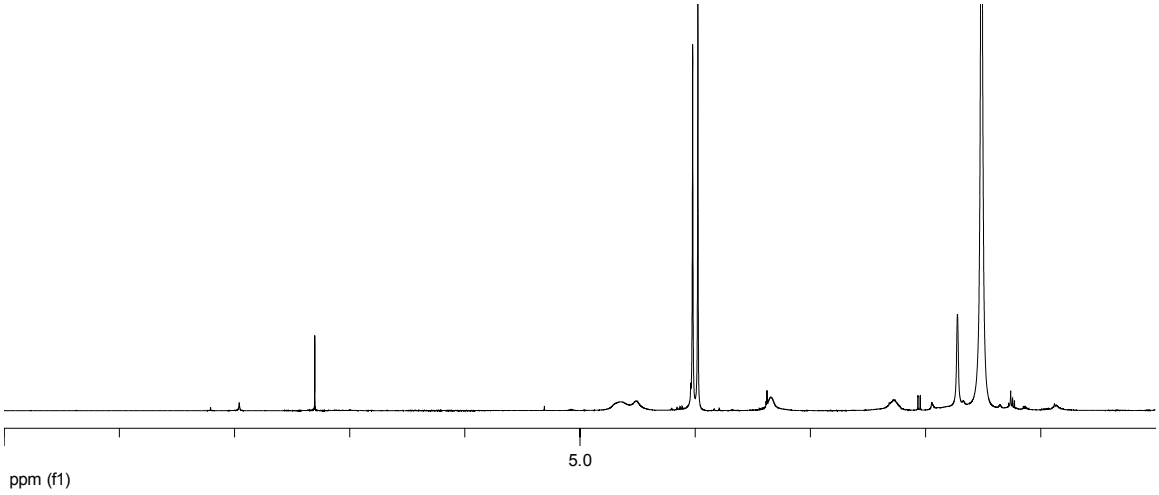
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



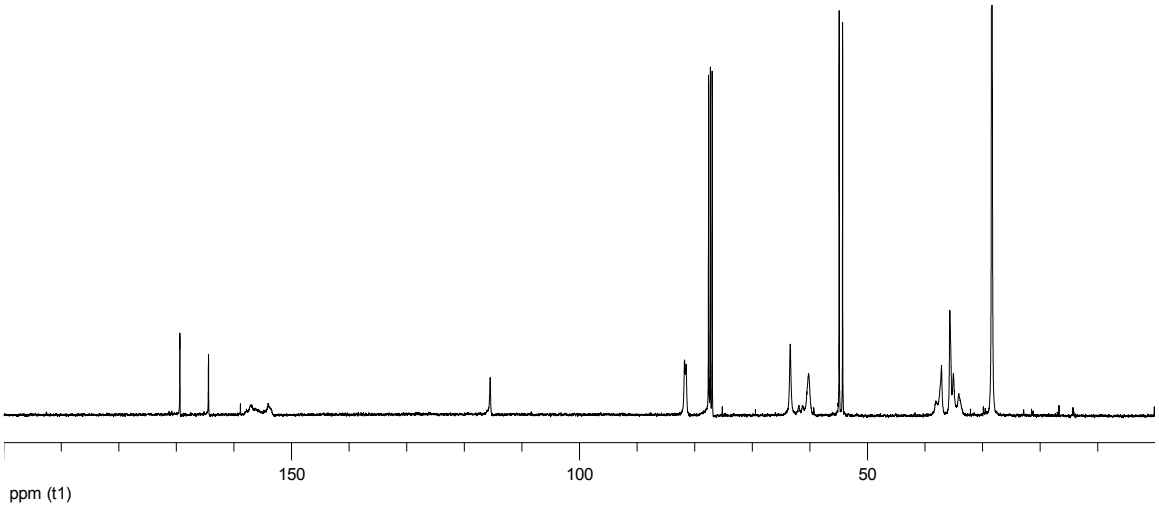
(*d*-18): 5-(6'-Deuterio-2',4'-dimethoxypyrimidin-5-yl)-2,3-diazabicyclo-[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate.



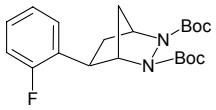
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



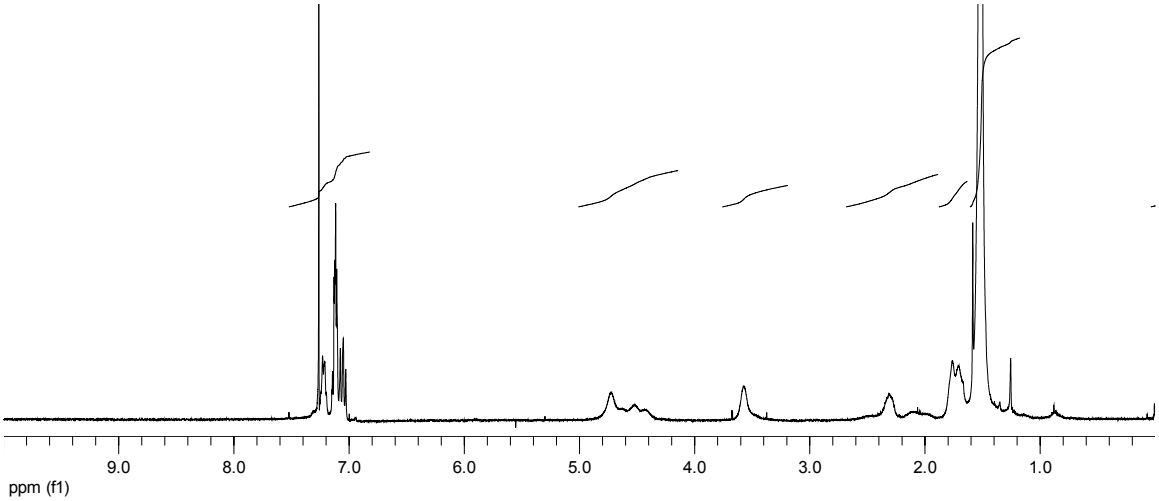
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



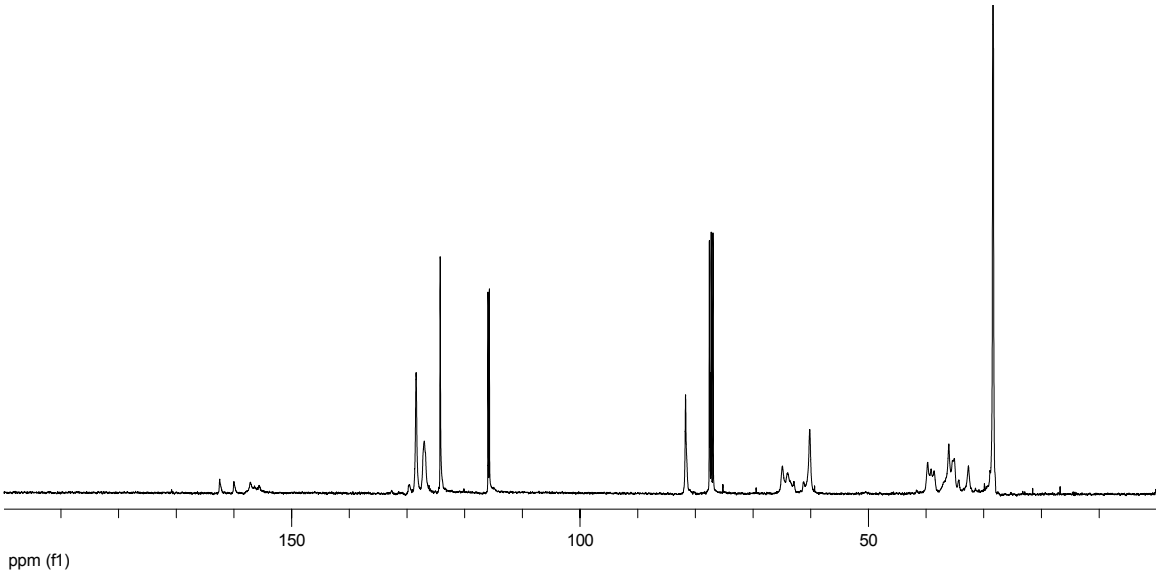
(19): 5-(2'-Fluorophenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate.



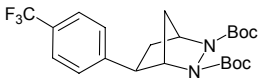
^{1}H NMR *400 MHz* ($CDCl_3$, 25 ^{o}C):



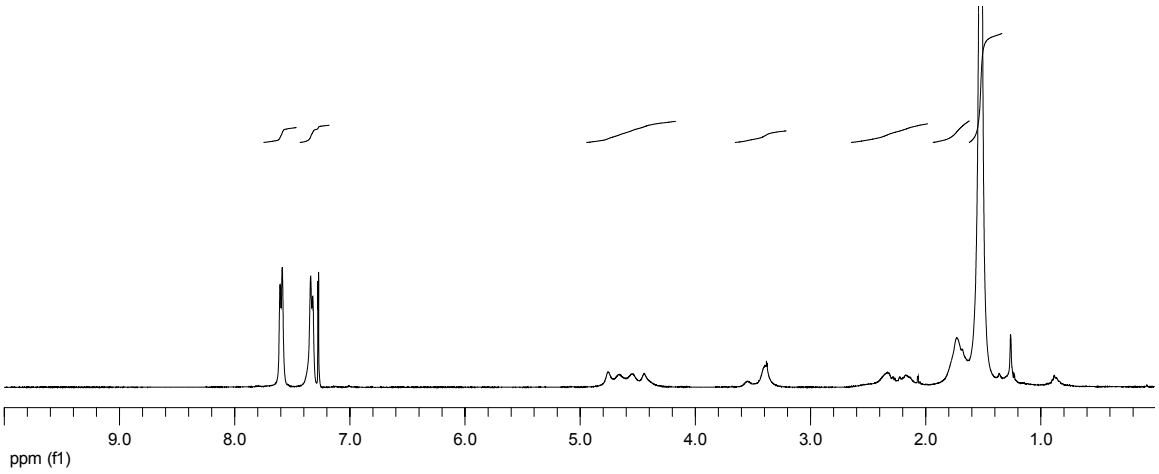
^{13}C NMR *100 MHz* ($CDCl_3$, 25 ^{o}C):



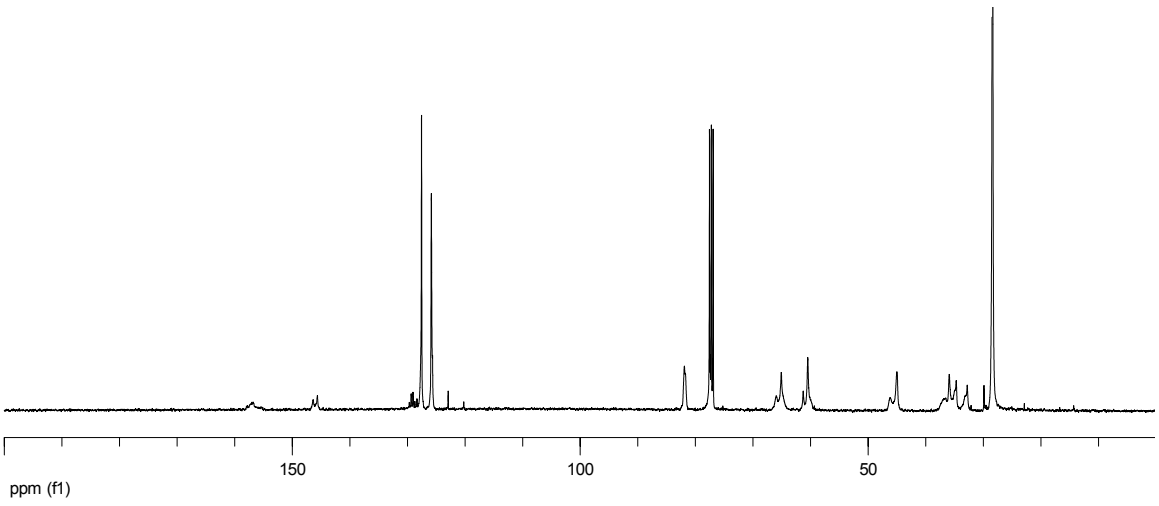
(20): 5-(4'-Trifluoromethylphenyl)-2,3-diazabicyclo[2.2.1]heptane-2,3-di-*tert*-butyl dicarboxylate.



^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):

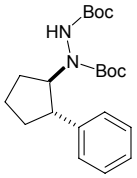


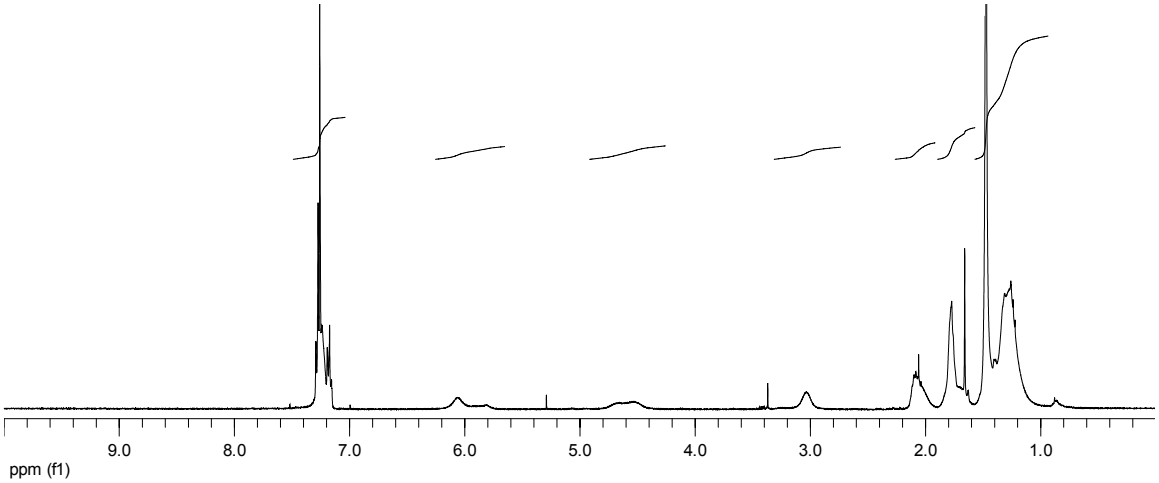
^{13}C NMR *100 MHz* ($CDCl_3$, 25 °C):



***trans*-*N,N'*-(2-Phenylcyclopentyl)-di-*tert*-butylhydrazine dicarboxylate**.

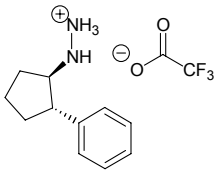
^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):

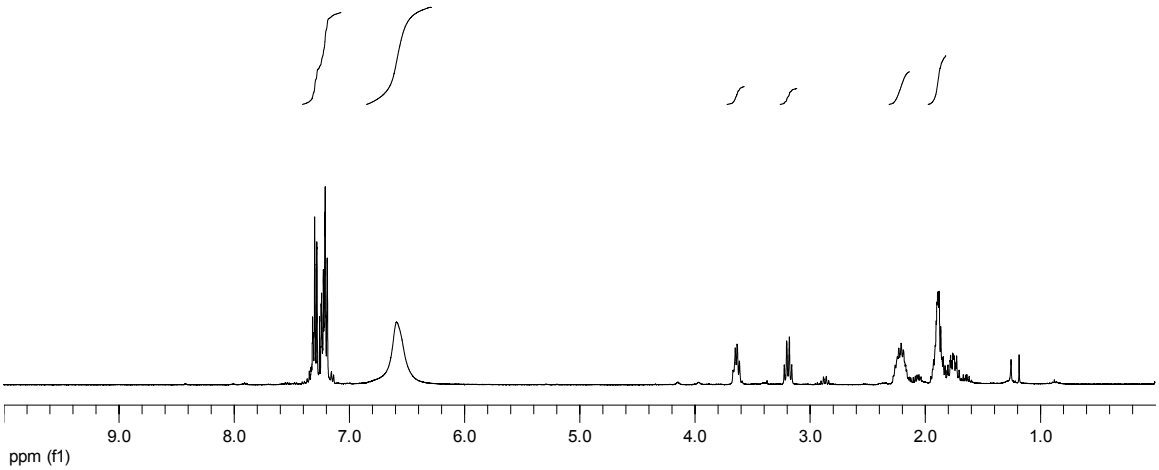




***trans*-(2-Phenylcyclopentyl)-hydrazinium trifluoroacetate**.

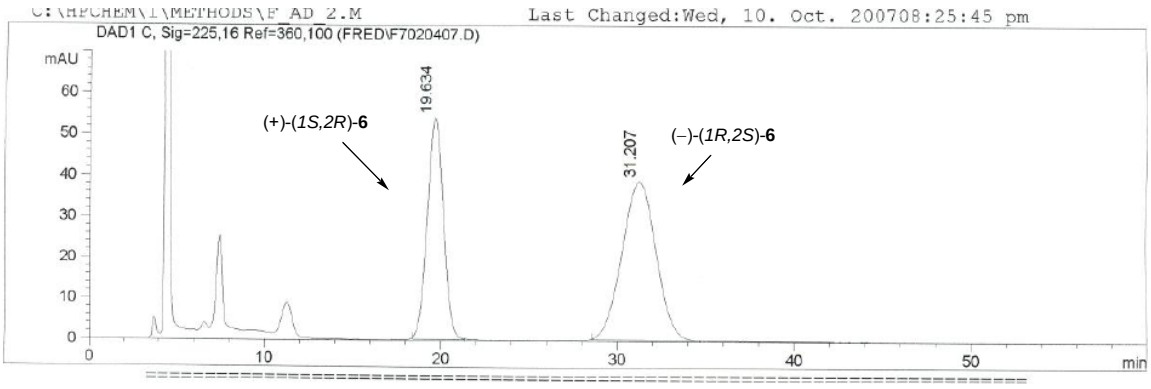
^{1}H NMR *400 MHz* ($CDCl_3$, 25 °C):



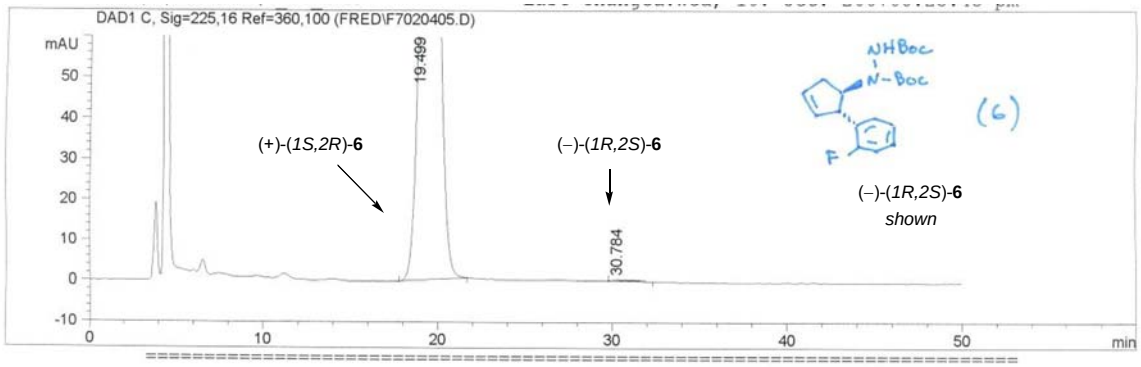


HPLC Representative Traces

HPLC Trace for racemic-**6**:



HPLC Trace for enantiomerically enriched-**6**:



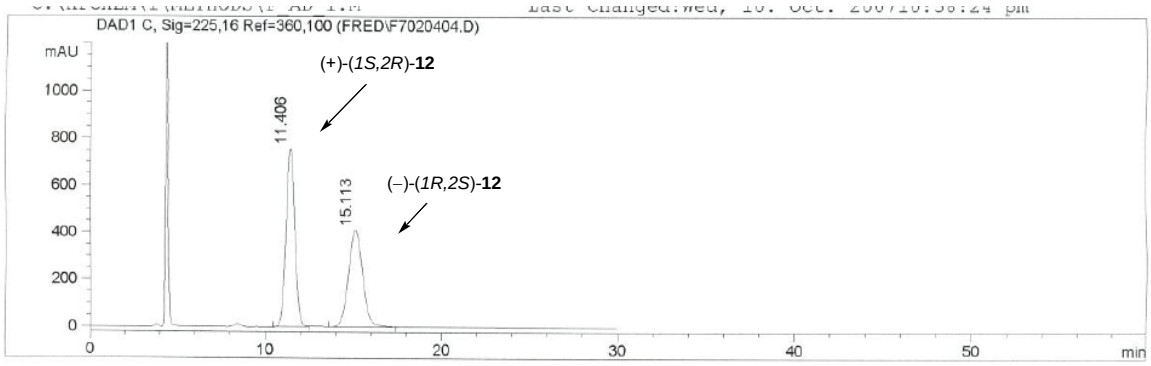
Signal 1: DAD1 C, Sig=225,16 Ref=360,100

Peak #	RT [min]	Height [mAU]	Area [mAU*s]	Area %
1	19.50	203	12991	99.80
2	30.78	0	26	0.20

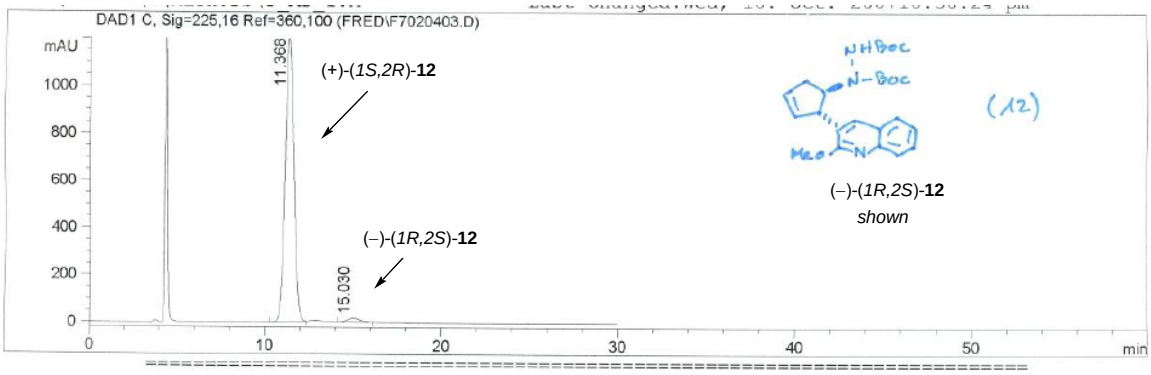
99.6 % ee

HPLC System	Agilent 1100 Series
Column:	Daicel Chiralcel AD
Eluent:	8:92, 2-Propanol:Hexane
Flow:	1.0 mL/min
Injection:	4.0 µL (~1 mg/mL)
Temp. col.:	305°C
Detector freq.:	220 nm

HPLC Trace for racemic-**12**:



HPLC Trace for enantiomerically enriched-**12**:



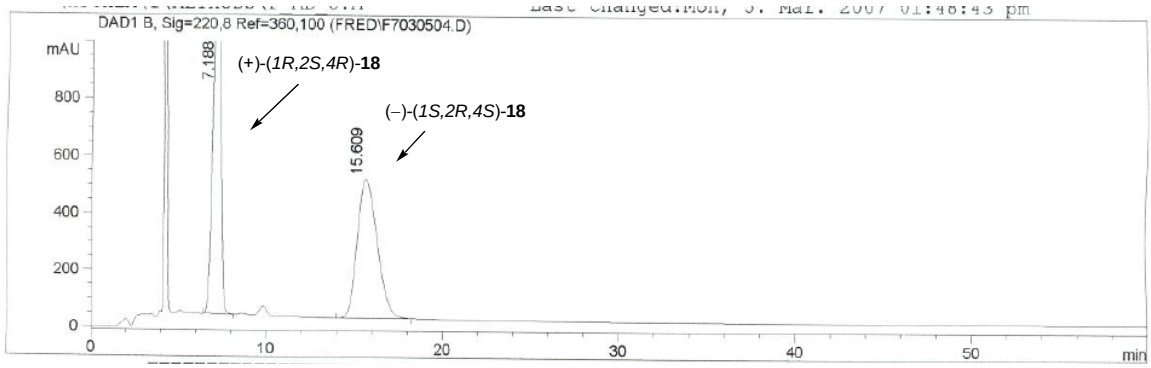

```
Signal  1: DAD1 C, Sig=225,16 Ref=360,100

Peak   RT      Height     Area      Area
 #     [min]    [mAU]   [mAU*s]      %
|---|---------|------|---------|------
   1     11.37   1203      41739  97.88
   2     15.03     17        904   2.12
-------------------------------------
```

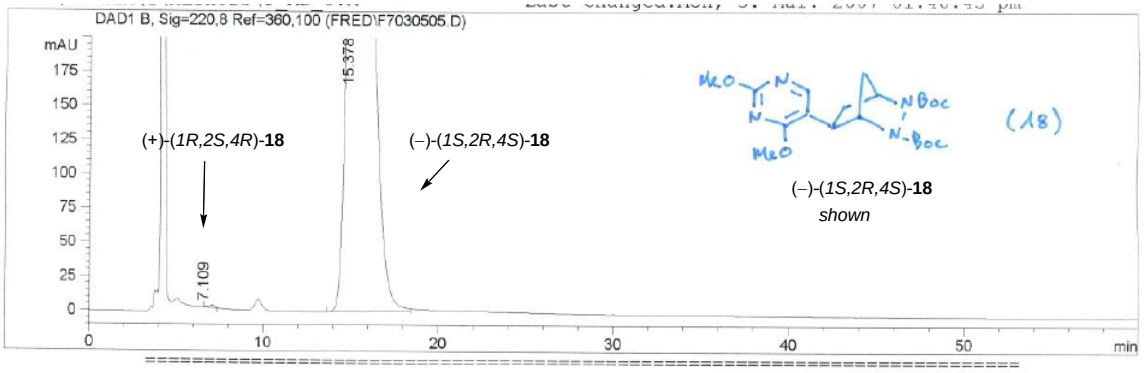
95.8 % ee

HPLC System	Agilent 1100 Series
Column:	Daicel Chiralcel AD
Eluent:	8:92, 2-Propanol:Hexane
Flow:	1.0 mL/min
Injection:	4.0 µL (~1 mg/mL)
Temp. col.:	30 °C
Detector freq.:	225 nm

HPLC Trace for racemic-**18**:



HPLC Trace for enantiomerically enriched-**18**:



Signal 1: DAD1 B, Sig=220,8 Ref=360,100

Peak #	RT [min]	Height [mAU]	Area [mAU*s]	Area %
1	7.11	2	55	0.10
2	15.38	626	52483	99.90

99.8 % ee

HPLC System	Agilent 1100 Series
Column:	Daicel Chiralcel AD
Eluent:	20:80, 2-Propanol:Hexane
Flow:	1.0 mL/min
Injection:	4.0 µL (~1 mg/mL)
Temp. col.:	30 °C
Detector freq.:	220 nm