SUPPORTING INFORMATION

Cycloadditions of Aromatic Azomethine Imines with 1,1-Cyclopropanediesters

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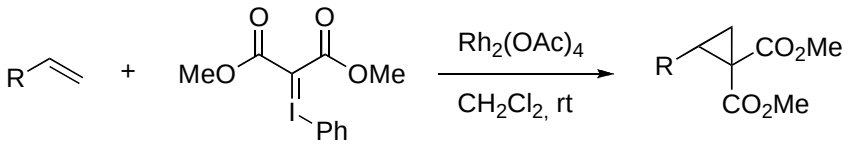
General: All non-aqueous reactions were run under an inert atmosphere (nitrogen or argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.[1] All glassware was stored in the oven and/or was flame-dried prior to use under an inert atmosphere of gas. Anhydrous solvents were obtained either by filtration through drying columns (THF, ether, CH_2Cl_2, benzene, DMF, CH_3CN, toluene, hexane, methanol) on a GlassContour system (Irvine, CA), by distillation over calcium hydride (Et_3N, $ClCH_2CH_2Cl$, pyridine, diisopropylamine, isopropanol) or by distillation over sodium/benzophenone (DME). Microwave experiments were done using a microwave apparatus. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel. Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, or aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica of the indicated solvent system according to standard technique.[2] Melting points were obtained on a melting point apparatus and are uncorrected. Infrared spectra were taken on a FTIR apparatus and are reported in reciprocal centimeters (cm^{-1}). Nuclear magnetic resonance spectra (^1H, ^{13}C, DEPT 135, COSY, HMQC, NOESY) were recorded either on a 300 or 400 MHz spectrometer. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, and assignment. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (77.00 ppm) as the internal standard. All spectra were obtained with complete proton decoupling. When ambiguous, proton and carbon assignments were established using COSY, HMQC and DEPT experiments. Optical rotations were determined with a polarimeter at 589 nm. Data are reported as follows: $[\alpha]_\lambda^{temp}$, concentration (c in g/100 mL), and solvent. High resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal. Combustion analyses were performed by the Laboratoire d'analyse élémentaire de l'Université de Montréal. Preparative High Performance Liquid Chromatography was performed on on a system equipped with a diode array UV detector and using Zorbax Eclipse XDB columns. Data are reported as follows: (column type, eluent, flow rate). Preparative and Analytical Supercritical Fluid Chromatography were performed on an instrument equipped with a UV/Vis detector. Data are reported as follows: (column type, eluent, flow rate, pressure, temperature: retention time (t_r)).

Reagents: Starting alkenes, cyclopropane **2g**, deuterated methanol and acid chlorides (**11** and **12)** were commercially available. Compounds **1a**[3], **7**[3], and **13**[4] were synthesized as described in the literature.

General procedure for the synthesis of 1,1-cyclopropanediesters:

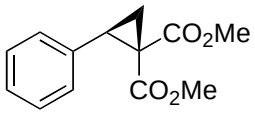
Cyclopropanes **2a-g** were prepared according to the following general procedure, which was slightly modified from literature.[4]



13 **2a-g**

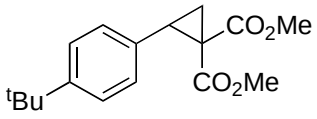
[1] Shriver, D. F.; Drezdzon, M. A. *The manipulation of air-sensitive compounds*; 2nd Edition ed.; Wiley: New York, 1986.
[2] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[3] Legault, C.; Charette, A. B. *J. Org. Chem.* **2003**, *68*, 7119.
[4] Müller, P.; Fernandez, D. *Helv. Chim. Acta* **1995**, *78*, 947.

In a dry flask under argon were added the alkene, anhydrous CH_2Cl_2 and $Rh_2(OAc)_4$. The iodonium ylide **13** was added in small portion over 1 hour. Heat was generated during the reaction. Reaction mixture was stirred an additional 1h. Reaction was concentrated and purified by chromatography on silica gel (10% EtOAc/hexane). In function of the value and the accessibility of the alkene, an excess of alkene or an excess of iodonium ylide were used. Generally, very small amount of $Rh_2(OAc)_4$ was used (~1 mg, the tip of a small spatula). Yields are between 50-90% (calculated from the limiting reagent) except for the 4-nitrostyrene (20% yield using an excess of iodonium ylide).



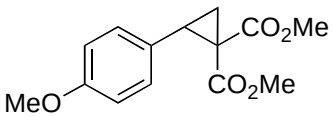
2a

Dimethyl (2*R*)-2-phenylcyclopropane-1,1-dicarboxylate (2a). Colorless oil: R_f 0.53 (20% EtOAc/hexane); $[\alpha]_D^{20}$ +130.6° (c 1.40, $CHCl_3$) and $[\alpha]_D^{20}$ +131.3° (c 2.30, C_6H_6)), lit: -93.4 (*c* 0.8, C_6H_6)[5]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.17 (m, 5H), 3.77 (s, 3H), 3.34 (s, 3H), 3.23 (t, *J* = 8.6 Hz, 1H), 2.19 (dd, *J* = 8.0, 5.2 Hz, 1H), 1.73 (dd, *J* = 9.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 166.9, 134.5, 128.3 (2), 128.0 (2), 127.3, 52.6, 52.0, 37.1, 32.4, 19.0; IR (neat) 2953, 1726, 1436, 1332, 1277, 1217, 1130 cm^{-1}. The ee (99%) was determined by SFC analysis (Chiralcel OB-H, 1% i-PrOH/CO_2, 1.5 mL/min, 150 bar, rt: (–)-**2a** t_r = 7.22 min, (+)-**2a** t_r = 8.47 min). The spectral data were consistent with that previously reported.[6]



2b

Dimethyl 2-(4-tert-butylphenyl)cyclopropane-1,1-dicarboxylate (2b). Colorless oil: R_f 0.24 (10% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H), 7.11-7.06 (m, 2H), 3.75 (s, 3H), 3.32 (s, 3H), 3.17 (t, *J* = 8.6 Hz, 1H), 2.15 (dd, *J* = 8.1, 5.1 Hz, 1H), 1.70 (dd, *J* = 9.3, 5.1 Hz, 1H), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 167.0, 150.2, 131.4, 128.0 (2), 125.0 (2), 52.7, 52.0, 37.1, 34.4, 32.2, 31.2 (3), 19.1; IR (neat) 2953, 1724, 1435, 1329, 1275, 1217, 1125 cm^{-1}; HRMS(ESI) calcd for $C_{17}H_{22}O_4$ $[M+H]^+$: 291.1596, found 291.1599.



2c

Dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (2c). Colorless oil: R_f 0.41 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12-7.09 (m, 2H), 6.81-6.77 (m, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.38 (s, 3H), 3.17 (t, *J* = 8.8 Hz, 1H), 2.14 (dd, *J* = 8.0, 5.2 Hz, 1H), 1.71 (dd, *J* = 9.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 167.1, 158.8, 129.5 (2), 126.3, 113.5 (2), 55.1, 52.7, 52.2, 37.0, 32.1, 19.2; IR (neat) 3002, 2953, 2838, 1721, 1612, 1516, 1435, 1276, 1247, 1216, 1174, 1128 cm^{-1}. The spectral data were consistent with that previously reported.[7]

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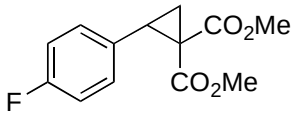
[5] Korotkov, V. S.; Larionov, O. V.; Hofmeister, A.; Magull, J.; de Meijere, A. *J. Org. Chem.* **2007**, *72*, 7504.

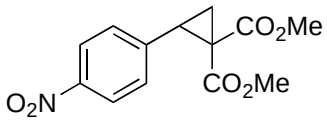
[6] Müller, P.; Ghanem, A. *Org. Lett.* **2004**, *6*, 4347.

[7] Davies, H. M. L.; Panaro, S. A. *Tetrahedron* **2000**, *56*, 4871.



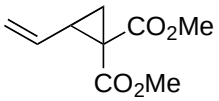
2d

Dimethyl 2-(4-fluorophenyl)cyclopropane-1,1-dicarboxylate (2d). Colorless oil**:** R_f 0.25 (10% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.14 (m, 2H), 6.99-6.93 (m, 2H), 3.79 (s, 3H), 3.39 (s, 3H), 3.19 (t, *J* = 8.8 Hz, 1H), 2.15 (dd, *J* = 8.0, 5.6 Hz, 1H), 1.74 (dd, *J* = 9.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 166.9, 162.1 (d, *J* = 240 Hz), 130.3, 130.2 (d, *J* = 10 Hz, 2C), 115.1 (d, *J* = 20 Hz, 2C), 52.8, 52.3, 37.0, 31.7, 19.2.; IR (neat) 2954, 1723, 1514, 1436, 1277, 1217, 1129 cm^{-1}; HRMS(ESI) calcd for $C_{13}H_{13}FO_4$ [M+Na]$^+$: 275.0690, found 275.0695.



2e

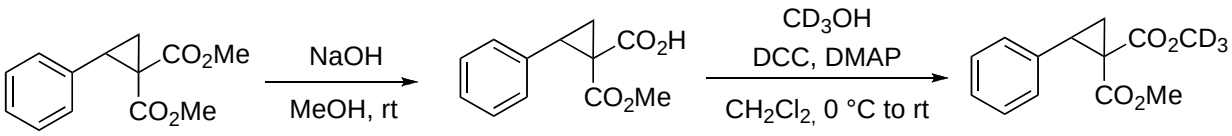
Dimethyl 2-(4-nitrophenyl)cyclopropane-1,1-dicarboxylate (2e). White solid: mp 127-129 °C; R_f 0.17 (10% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dt, *J* = 9.2, 2.2 Hz, 2H), 7.36 (dd, *J* = 11.2, 2.4 Hz, 2H), 3.81 (s, 3H), 3.42 (s, 3H), 3.28 (t, *J* = 8.4 Hz, 1H), 2.22 (dd, *J* = 8.0, 5.6 Hz, 1H), 1.83, (dd, *J* = 9.0, 5.4, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 166.5, 147.2, 142.4, 129.3, 123.4, 53.1, 52.6, 37.7, 31.5, 19.3; IR (neat) 3115, 3086, 2958, 2847, 1731, 1599, 1516, 1437, 1343, 1278, 1212, 1135 cm^{-1}; HRMS(ESI) calcd for $C_{13}H_{13}NO_6$ [M+H]$^+$: 280.0829, found 280.0816.



2f

Dimethyl 2-vinylcyclopropane-1,1-dicarboxylate (2f). Colorless oil: R_f 0.59 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47-5.38 (m, 1H), 5.30 (dd, *J* = 17.0, 1.8 Hz, 1H), 5.14 (dd, *J* = 10.4, 1.2 Hz, 1H), 3.74 (s, 3H), 2.59 (q, *J* = 8.0 Hz, 1H), 1.72 (dd, *J* = 7.6, 4.8 Hz, 1H), 1.59 (dd, *J* = 9.0, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 167.8, 132.9, 118.7, 52.7, 52.6, 35.7, 31.5, 20.6; IR (neat) 2955, 1726, 1437, 1330, 1273, 1210, 1130 cm^{-1}. The spectral data were consistent with that previously reported.[8]

Synthesis of deuterated dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (4):
The preparation of labeled cyclopropane **4** consists of a two-step sequence, where the first step is the selective saponification of the *trans* ester of cyclopropane **2a**, and the second step is a DCC coupling with deuterated methanol.



2a **9** **4**

*Step one: selective saponification of the trans ester of cyclopropane **2a***

(1*R*,2*R*)-1-(methoxycarbonyl)-2-phenylcyclopropanecarboxylic acid (9):

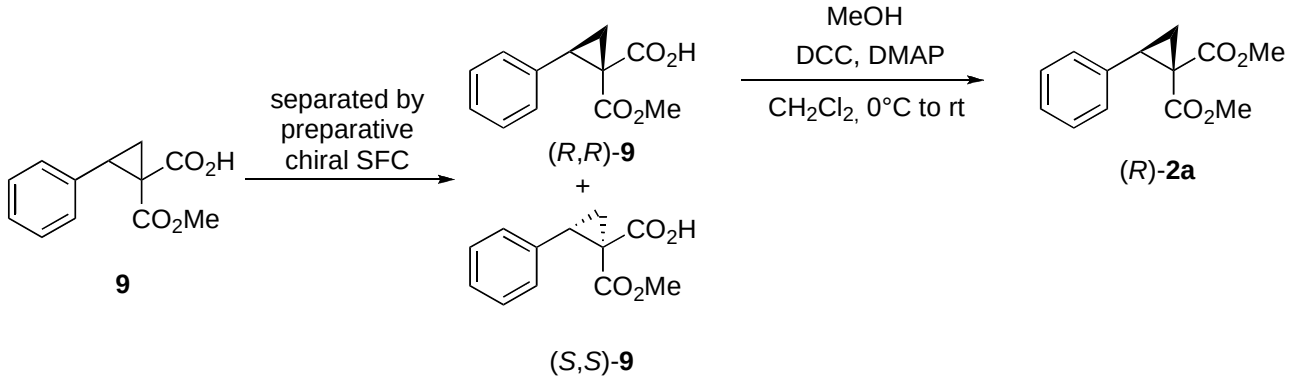
[8] Burgess, K. *J. Org. Chem.* **1987**, *52*, 2046.

In a dry 25 mL flask under argon were added 1,1-cyclopropanediesters **2a** (1.0 g, 4.3 mmol), MeOH (3.0 mL) and 1.7 N aqueous NaOH (3.0 mL, 5.1 mmol). Reaction mixture was stirred for 1.5 h then was diluted with EtOAc and water and layers were separated. The pH 14 aqueous solution was washed one more time with EtOAc. The aqueous layer was then acidified with HCl 10% to reach pH 2 then extracted three times with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated to yield yellow solid. The crude product was then filtered through a silica pad (80% EtOAc/hexane) then concentrated to yield 0.92 g (98%) of white solid. mp 96-98 °C, lit: 60-62 °C[9]; R_f 0.38 (100% CH_2Cl_2); $[\alpha]_D^{20}$ +107.84° (c 1.14, $CHCl_3$), 142.9° (c 1.09, PhH), lit. for ent.: -146.2° (c 1.1, PhH)[9]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 3.43 (t, *J* = 9.0 Hz, 1H), 3.28 (s, 3H), 2.43 (dd, *J* = 8.4, 4.8 Hz, 1H), 2.30 (dd, *J* = 9.2, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.8, 134.0, 129.1, 128.2, 127.9, 52.5, 40.4, 33.7, 21.1; IR (neat) 3030, 2953, 1730, 1694, 1436, 1332, 1293, 1217, 1139 cm^{-1}. The ee (99%) was determined by SFC analysis (Chiralpak AD-H, 5% i-PrOH/CO_2, 3.0 mL/min, 210 bar, 40 °C: (+)-**9** t_r = 6.02 min, (–)-**9** t_r = 8.53 min). The spectral data were consistent with that previously reported.[9]

Step two: DCC coupling with deuterated methanol

In a dry 10 mL flask under argon were added cyclopropane **9** (150 mg, 0.68 mmol), DMAP (98 mg, 0.54 mmol), CH_2Cl_2 (1.4 mL), and CD_3OD (80 μL, 2.0 mmol). The mixture was stirred for 10 min at rt then it was cooled to 0 °C. DCC (155 mg, 0.75 mmol) was slowly added and the reaction mixture was stirred for 30 min. Reaction mixture was allowed to reach rt then stirred for 16 h. Reaction mixture was cooled to 0 °C and filtered through a pad of silica gel (100% CH_2Cl_2 and 100% EtOAc) and concentrated. The crude product was purified by chromatography on silica gel (100% CH_2Cl_2 to 20% EtOAc/CH_2Cl_2) to yield 151 mg (94%) of colorless oil. R_f 0.53 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.17 (m, 5H), 3.34 (s, 3H), 3.23 (t, *J* = 8.6 Hz, 1H), 2.19 (dd, *J* = 8.0, 5.2 Hz, 1H), 1.73 (dd, *J* = 9.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 166.9, 134.5, 128.3 (2), 128.0 (2), 127.3, 52.6, 52.0, 37.1, 32.4, 19.0; IR (neat) 2953, 1726, 1436, 1332, 1277, 1217, 1130 cm^{-1}.

Synthesis of (*R*)-dimethyl 2-phenylcyclopropane-1,1-dicarboxylate ((*R*)-2a):
The procedure for the preparation of the enantiopure cyclopropane (*R*)-**2a** consists of the separation of the two enantiomers of cyclopropane **9** followed by a DCC coupling with methanol.



Step one : separation of the two enantiomers

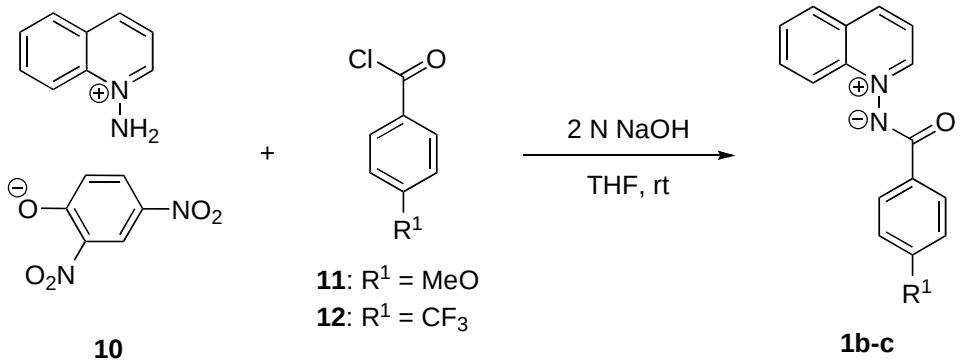
[9] Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.*, **1996**, *118*, 6897.

The two enantiomers of **9** were separated by preparative chiral SFC (Chiralpak AD-H, 16% i-PrOH/CO_2, 62 g/min, 210 bar, rt).

Step two: DCC coupling with methanol

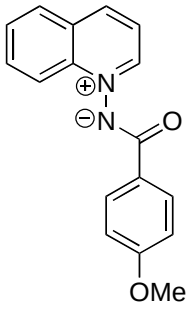
In a dry 10 mL flask under argon were added cyclopropane **9** (226 mg, 1.03 mmol), DMAP (110 mg, 0.80 mmol), CH_2Cl_2 (2.5 mL), and MeOH (140 μL, 3.4 mmol). The mixture was stirred for 10 min at rt then it was cooled to 0 °C. DCC (258 mg, 1.25 mmol) was slowly added and the reaction mixture was stirred for 30 min. Reaction mixture was allowed to reach rt then stirred for 16 h. Reaction mixture was concentrated. The crude product was purified by chromatography on silica gel (100% CH_2Cl_2 to 20% EtOAc/CH_2Cl_2) to yield 181 mg (75%, 99% ee) of colorless oil (see **2a**).

General procedure for the synthesis of the quinolinium ylides: Compounds **1b-c** were prepared according to the following general procedure.



10 **11**: R^1 = MeO; **12**: R^1 = CF_3 **1b-c**

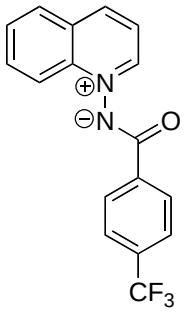
In a 100 mL flask were added the quinolinium salt **10** (3.0 mmol), anhydrous THF (20 mL) and the acid chloride (3.7 mmol, 1.2 equiv). Reaction mixture was stirred for 5 min then 2 N aqueous NaOH (10 mL) was added. Reaction mixture was stirred for an additional 1 h then water and CH_2Cl_2 were added. Layers were separated and aqueous layer was extracted twice. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The crude solid was purified by chromatography on silica gel (5% MeOH/CH_2Cl_2).



1b

***N*-(4-methoxybenzoyl)iminoquinolinium ylide (1b).** Yellow solid (611 mg, 73% from **11**): mp 138-140 °C; R_f 0.23 (10% MeOH/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, J = 6.0 Hz, 1H), 8.82 (d, J = 8.8 Hz, 1H), 8.40 (d, J = 8.40 Hz, 1H), 8.29-8.25 (m, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.90 (dd, J = 8.4, 7.6 Hz, 1H), 7.76 (dd, J = 8.0, 7.2 Hz, 1H), 7.68 (dd, J = 8.4, 6.0 Hz, 1H), 6.99-6.95 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 161.3, 145.7, 139.8, 137.8, 133.1, 130.0, 129.9, 129.7 (2), 129.2, 128.5, 120.4, 120.3, 113.1 (2); IR (neat) 3398, 3072, 2837, 1592,

1543, 1508, 1334, 1301, 1248, 1175 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}N_2O_2$ $[M+H]^+$: 279.1128, found 279.1128.

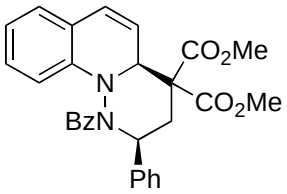


1c

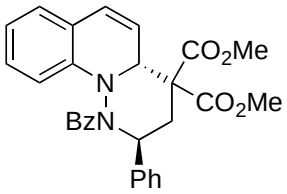
***N*-[4-(trifluoromethyl)benzoyl]iminoquinolinium ylide (1c).** Yellow solid (774 mg, 82% from **12**): mp 166-168 °C; R_f 0.56 (10% MeOH/CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 9.18 (dd, *J* = 6.0, 1.2 Hz, 1H), 8.73 (d, *J* = 8.8 Hz, 1H), 8.41-8.37 (m, 3H), 7.96 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.86 (ddd, *J* = 8.8, 6.8, 1.4 Hz, 1H), 7.73-7.61 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 145.3, 141.0, 139.3, 138.4, 133.3, 131.5 (q, *J* = 32 Hz), 129.9, 129.3, 128.5, 128.4 (2), 124.7 (q, *J* = 3.5 Hz, 2C), 124.2 (q, *J* = 271 Hz), 120.2, 119.9; IR (neat) 3401, 3072, 1600, 1557, 1516, 1318, 1298, 1154, 1112, 1098, 1065 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{11}N_2O_1F_3$ $[M+Na]^+$: 339.0716, found 339.0715.

General procedure for the synthesis of the dihydroquinolines derivatives: Compounds **3a-i** were prepared according to the following general procedure.

In a dry 10 mL micro-wave tube under argon were added the cyclopropane **2a-g** (0.40 mmol), the quinolinium ylide **1a-c** (0.40 mmol), $Ni(ClO_4)_2{\cdot}H_2O$ (0.04 mmol), molecular sieves 3 Å (200 mg), and THF (4 mL). Reaction mixture was stirred for 16 h at rt. Reaction mixture is then filtered on a short pad of silica gel, eluted with CH_2Cl_2, and concentrated. The crude product was purified by chromatography on silica gel (20% EtOAc/hexane).



(*S*)-*cis*-**3a**

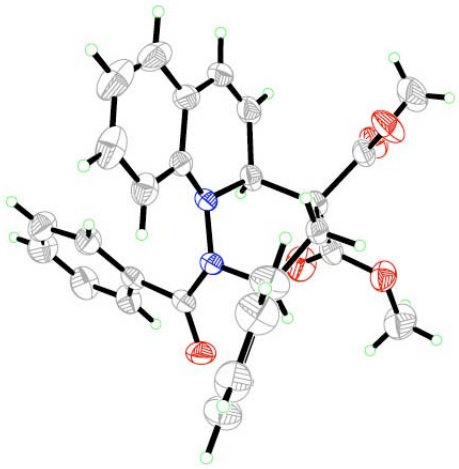


(*S*)-*trans*-**3a**

(4a*S*)-Dimethyl 1-benzoyl-2-phenyl- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate ((*S*)-3a). 153 mg (79%) was obtained in a *cis*/*trans* ratio of 3.3:1 (determined by ^1H NMR). Diastereoisomers were separated by preparative HPLC for characterization (C8, 40% MeCN/water to 100% MeCN, 20 mL/min). *cis*-**3a**: White solid; mp 184-187 °C; R_f 0.21 (30% AcOEt/hexane); $[\alpha]_D^{20}$ –216.9° (c 4.34, $CHCl_3$); ^1H RMN (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 6.7 Hz, 2H), 7.24-7.41 (m, 6H), 6.83-6.86 (m, 2H), 6.68 (td, *J* = 7.4, 1.0 Hz, 1H), 6.58 (d, *J* = 8.5, 1H), 6.28 (d, *J* = 10.0 Hz, 1H), 5.44 (d, *J* = 5.96 Hz, 1H), 5.41 (dd, *J* = 13.2, 4.4 Hz, 1H), 5.31 (dd, *J* = 10.0, 5.1 Hz, 1H), 3.85 (s, 3H), 3.68 (s, 3H), 3.05 (t, *J* = 13.9 Hz, 1H), 2.70 (dd, *J* = 14.3, 4.7 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) δ 175.3, 170.3, 169.2, 143.6, 140.0, 135.0,

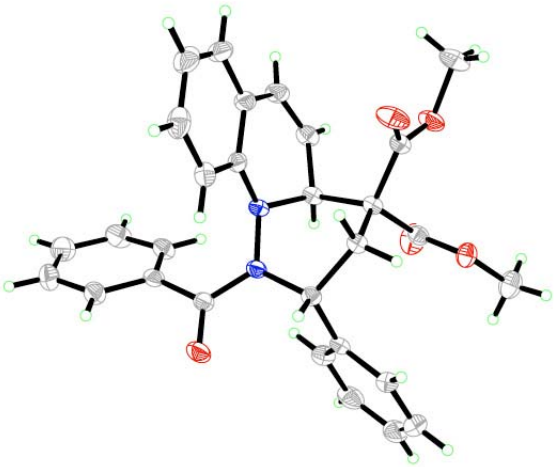
130.7, 129.3, 128.4, 128.0, 127.9, 127.6, 127.4, 127.3, 120.1, 120.0, 119.9, 112.8, 77.3, 61.2, 60.1, 55.2, 53.5, 52.7, 31.6 (4); IR (neat) 3031, 2952, 1730, 1664, 1486, 1455, 1271, 1211, 729, 697 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}N_2O_5$ $[M+H]^+$: 483.1914, found 483.1899. The ee (99%) was determined by SFC analysis (Chiralpak AD-H, 20% i-PrOH/CO_2, 3.0 mL/min, 210 bar, rt: (+)-*cis*-**3a** t_r = 4.36 min, (–)-*cis*-**3a** t_r = 5.05 min). An X-ray crystal structure of compound *cis*-**3a** was obtained to establish its relative configuration.

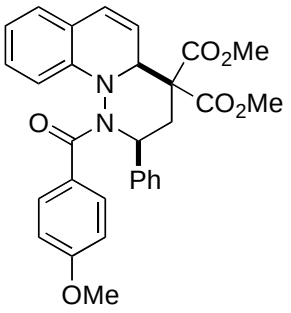
Figure 1. ORTEP representation of compound *cis*-**3a**



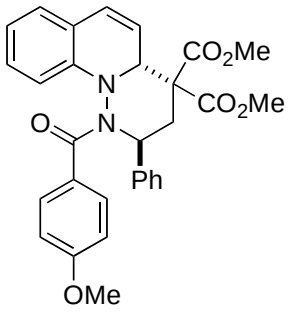
trans-**3a**: White solid; mp 214-216 °C; R_f 0.23 (30% AcOEt/Hex); $[\alpha]_D^{20}$ +240.5° (c 1.19, $CHCl_3$); ^1H RMN (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.34-7.40 (m, 3H), 7.21-7.28 (m, 4H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 7.4, 1.2 Hz, 1H), 6.79 (td, *J* = 7.4, 0.9 Hz, 1H), 6.35 (d, *J* = 9.9 Hz, 1H), 5.90 (dd, *J* = 9.9, 5.7 Hz, 1H), 5.56 (dd, *J* = 8.0, 4.2 Hz, 1H), 5.16 (d, *J* = 5.8 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H), 2.99 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.82 (dd, *J* = 14.2, 8.1 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) δ 172.9, 170.3, 170.2, 143.4, 138.9, 134.0, 131.6, 129.9, 128.5, 128.2, 128.0, 127.3, 126.9, 126.3, 122.9, 122.1, 120.5, 110.4, 77.4, 59.9, 57.3, 53.5, 52.8, 52.5, 33.3 (3); IR (neat) 3030, 2953, 1732, 1662, 1352, 1264, 1240, 911, 730, 699 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}N_2O_5$ $[M+H]^+$: 483.1914. Found 483.1909. The ee (99%) was determined by SFC analysis (Chiralpak AD-H, 30% i-PrOH/CO_2, 3.0 mL/min, 210 bar, 40 °C: (–)-*trans*-**3a** t_r = 2.72 min, (+)-*trans*-**3a** t_r = 6.46 min). An X-ray crystal structure of compound *trans*-**3a** was obtained to establish its relative configuration.

Figure 2. ORTEP representation of compounds *trans*-**3a**





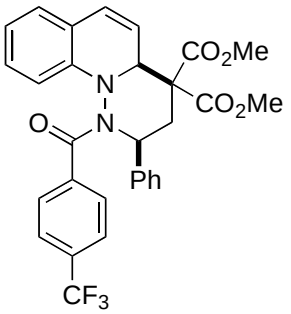
cis-**3b**



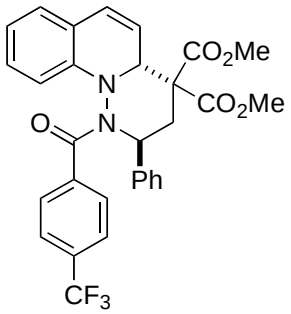
trans-**3b**

Dimethyl 1-(4-methoxybenzoyl)-2-phenyl- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (3b). 111 mg (54%) was obtained in a *cis*/*trans* ratio of 3.8:1 (determined by ^{1}H NMR). Diastereoisomers were separated by preparative HPLC for characterization (C8, 40% MeCN/water to 100% MeCN, 20 mL/min). *cis*-**3b**: White solids; mp 78-81 °C; R_f 0. (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 9.6, 2.8 Hz, 2H), 7.53 (dd, *J* = 10, 3.2 Hz, 2H), 7.34-7.28 (m, 3H), 6.88-6.84 (m, 2H), 6.76 (dt, *J* = 9.6, 2.8 Hz, 2H), 6.69 (td, *J* = 8.2, 0.8 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.32 (d, *J* = 10 Hz, 1H), 5.44 (dd, *J* = 13.4, 5.0 Hz, 2H), 5.36 (dd, *J* = 10, 5.2 Hz, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 3.67 (s, 3H), 3.04 (t, *J* = 13.8 Hz, 1H), 2.70 (dd, *J* = 14.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 170.0, 169.0, 161.5, 143.6, 140.1, 129.7 (2), 129.2, 128.1 (4), 127.6, 127.4, 127.1, 126.3, 120.1, 119.8 (2), 113.0 (2), 112.4, 61.1, 59.7, 55.1, 54.8, 53.2, 52.4, 31.4; IR (neat) 2953, 2839, 1733, 1656, 1603, 1254, 1174 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{28}N_2O_6$ $[M+H]^+$: 513.2020, found 513.2020. The relative configuration was assigned by analogy with compound **3a**.

trans-**3b**: White solids; mp 230-233 °C; R_f 0.10 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dt, *J* = 9.6, 2.8 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H) 7.27-7.22 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.92 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.79 (td, *J* = 8.0, 0.4 Hz, 1H), 6.74 (dt, *J* = 9.8, 2.8 Hz, 2H), 5.92 (dd, *J* = 10.0, 5.6 Hz, 1H), 5.52 (dd, *J* = 8.2, 3.8 Hz, 1H), 3.76 (s, 3H), 3.51 (s, 3H), 3.40 (s, 3H), 2.96 (dd, *J* = 14.4, 4.0 Hz, 1H), 2.82 (dd, *J* = 14.4, 8.4, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.2, 170.1, 162.2, 143.3, 139.1, 130.4 (2), 129.8, 128.3 (2), 127.2, 127.0, 126.7, 126.1 (2), 125.8, 122.9, 121.9, 120.2, 113.1 (2), 110.2, 59.7, 57.2, 55.2, 53.4, 52.6, 52.3, 32.9; IR (neat) 3030, 2952, 2840, 1728, 1664, 1602, 1294, 1254, 1211, 1174 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{28}N_2O_6$ $[M+H]^+$: 513.2020, found 513.2029. The relative configuration was assigned by analogy with compound **3a**.



cis-**3c**

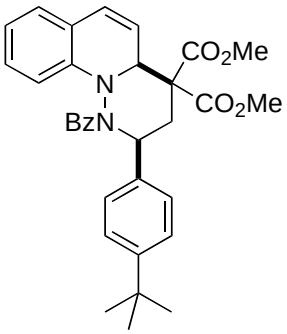


trans-**3c**

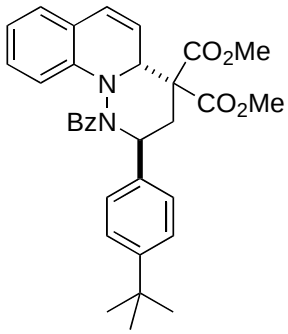
Dimethyl 1-[4-(trifluoromethyl)benzoyl]-2-phenyl- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (3c). 185 mg (84%) was obtained in a *cis*/*trans* ratio of 4.3:1 (determined by ^{1}H NMR). Diastereoisomers were separated by preparative HPLC for characterization (Column C8, 40% MeCN/water to 100% MeCN, 20 mL/min). *cis*-**3c**: White solids; mp 70-73 °C; R_f 0.19 (20%

EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.55-7.51 (m, 4H), 7.36-7.28 (m, 3H), 6.87-6.81 (m, 2H), 6.69 (t, *J* = 7.2 Hz, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.29 (d, *J* = 10.0 Hz, 1H), 5.45-5.36 (m, 2H), 5.31 (dd, J = 10.0, 5.2 Hz, 1H), 3.86 (s, 3H), 3.70 (s, 3H), 3.08 (t, *J* = 14.0 Hz, 1H), 2.72 (dd, *J* = 14.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 170.2, 168.7, 143.1, 139.4, 138.6, 132.1 (t, *J* = 32 Hz), 129.2, 128.3 (4), 128.0, 127.6, 127.3 (3), 124.8 (t, *J* = 3.4 Hz, 2C), 123.8 (q, *J* = 271 Hz), 120.3, 119.8, 119.7, 112.6, 60.9, 60.0, 55.2, 53.3, 52.5, 31.1; IR (neat) 3035, 2954, 1732, 1666, 1321, 1263, 1240, 1210, 1168, 1126, 1110, 1066 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{25}F_3N_2O_5$ $[M+H]^+$: 551.1788, found 551.1788. The relative configuration was assigned by analogy with compound **3a**.

trans-**3c**: White solids; mp 89-92 °C; R_f 0.14 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 8.4 Hz, 4H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.31-7.23 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.92 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.82 (td, *J* = 7.6, 0.8 Hz, 1H), 6.37 (d, *J* = 10.0 Hz, 1H), 5.91 (dd, *J* = 9.8, 5.8 Hz, 1H), 5.58 (dd, *J* = 8.0, 4.4 Hz, 1H), 5.13 (d, *J* = 5.6 Hz, 1H), 3.49 (s, 3H), 3.41 (s, 3H), 2.99 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.80 (dd, *J* = 14.0, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.0, 169.8, 143.0, 138.3, 137.4, 132.8 (q, *J* = 32 Hz), 129.8, 128.4 (2), 128.2 (2) 127.4 (2), 126.8, 126.2 (2), 124.9 (q, *J* = 3.4 Hz, 2C), 123.7 (q, *J* = 272 Hz), 122.7, 122.1, 120.8, 110.1, 59.8, 57.0, 53.6, 52.7, 52.3, 33.4; IR (neat) 3031, 2953, 1728, 1668, 1322, 1298, 1240, 1211, 1167, 1125, 1064 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{25}F_3N_2O_5$ $[M+H]^+$: 551.1788, found 551.1788. The relative configuration was assigned by analogy with compound **3a**.



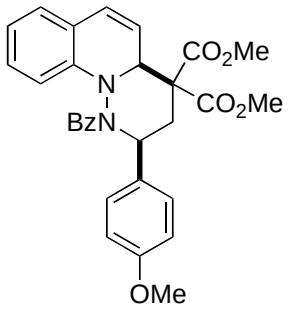
cis-**3d**



trans-**3d**

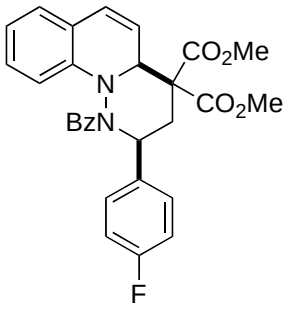
Dimethyl 1-benzoyl-2-(4-tert-butylphenyl)- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (3d). 163 mg (76%) was obtained in a *cis*/*trans* ratio of 3.3:1 (determined by ^{1}H NMR). Diastereoisomers were separated by preparative HPLC for characterization (Column C8, 60% MeCN/water to 100% MeCN, 20 mL/min). *cis*-**3d**: White solid; mp 113-114 °C; R_f 0.22 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.57 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.38-7.22 (m, 3H), 6.90-6.84 (m, 3H), 6.71-6.63 (m, 2H), 6.28 (d, *J* = 10.0 Hz, 1H), 5.43-5.31 (m, 3H), 3.84 (s, 3H), 3.67 (s, 3H), 3.04 (t, *J* = 13.8 Hz, 1H); 2.67 (dd, *J* = 14.4, 4.4 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 170.2, 169.0, 150.8, 143.6, 136.8, 134.9, 130.5, 129.1, 128.0 (2), 127.7 (2), 127.4, 127.2, 127.1 (2), 125.1, 120.1, 119.8 (2), 112.7, 61.2, 59.9, 54.9, 53.2, 52.5, 34.5, 31.7, 31.3 (3); IR (neat) 2954, 1733, 1661, 1263, 1240, 1209, 1172 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{34}N_2O_5$ $[M+H]^+$: 539.2546, found 539.2564. The relative configuration was assigned by analogy with compound **3a**.

trans-**3d**: White solids; mp 130-131 °C; R_f 0.23 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dt, J = 9.2, 1.0 Hz, 2H), 7.44-7.34 (m, 5H), 7.27-7.20 (m, 3H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.77 (td, *J* = 8.4, 0.8 Hz, 1H), 6.35 (d, *J* = 10.0 Hz, 1H), 5.90 (dd, *J* = 9.8, 5.8 Hz, 1H), 5.54 (dd, *J* = 7.8, 4.2 Hz, 1H), 5.19 (d, *J* = 5.6 Hz, 1H); 3.46 (s, 3H), 3.39 (s, 3H), 2.97 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.81 (dd, *J* = 14.2, 7.8 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.2, 170.0, 149.8, 143.3, 135.6, 133.9, 131.3, 129.7, 128.0 (2), 127.7 (2), 127.1 126.7, 125.8 (2), 125.2 (2), 122.7, 121.9, 120.2, 110.2, 59.7, 57.3, 53.2, 52.5, 52.2, 34.4, 33.3, 31.3 (3); IR (neat) 2953, 1729, 1670, 1293, 1269, 1241, 1209, 1179 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{34}N_2O_5$ $[M+H]^+$: 539.2546, found 539.2564. The relative configuration was assigned by analogy with compound **3a**.

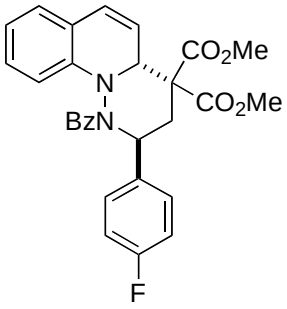


cis-**3e**

Dimethyl 1-benzoyl-2-(4-methoxyphenyl)- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (*cis*-3e). 179 mg (87%) was obtained in a *cis*/*trans* ratio of 6.6:1 (determined by ^{1}H NMR). Diastereoisomers were separated by preparative HPLC for characterization (Column C8, 40% MeCN/water to 100% MeCN, 20 mL/min). White solids, mp 190-192 °C; R_f 0.14 (20% EtOAc/hexane); ^{1}H RMN (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.1 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.38 (tt, *J* = 7.4, 1.8 Hz, 1H), 7.24-7.28 (m, 2H), 6.89 (t, *J* = 8.3 Hz, 1H), 6.83-6.86 (m, *J* = 7.6, 3H), 6.69 (td, *J* = 7.4, 0.9 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.28 (d, *J* = 10.0 Hz, 1H), 5.44 (d, *J* = 5.0Hz, 1H), 5.35 (dd, *J* = 14.0, 4.2 Hz, 1H), 5.31 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.69 (s, 3H), 3.04 (t, *J* = 14.0 Hz, 1H), 2.65 (dd, *J* = 14.3, 4.6 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) 175.2, 170.4, 169.3, 159.3, 143.8, 135.1, 132.2, 130.7, 129.9, 129.4, 128.0, 127.7, 127.5, 127.3, 120.2, 120.1, 119.9, 113.6, 112.8, 61.5, 60.1, 55.5, 54.8, 53.5, 52.7, 31.8 (4); IR (neat) 3002, 2953, 2838, 1731, 1659, 1513, 1266, 1238, 1209, 1171 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{28}N_2O_6$ $[M+H]^+$: 513.2026, found 513.2033. The relative configuration was assigned by analogy with compound **3a**.



cis-**3f**

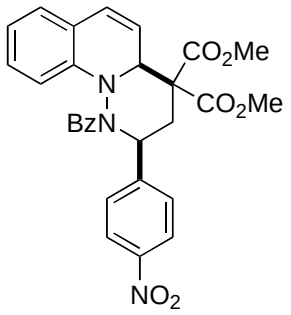


trans-**3f**

Dimethyl 1-benzoyl-2-(4-fluorophenyl)- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (3f). 162 mg (81%) was obtained in a *cis*/*trans* ratio of 4.4:1 (determined by ^{1}H NMR). Diastereoisomers were separated by preparative HPLC for characterization (Column C8, 40% MeCN/water to 100% MeCN, 20 mL/min). *cis*-**3f**: White solids; mp 144-148 °C; R_f 0.11 (100% CH_2Cl_2); ^{1}H RMN (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.2 Hz, 2H), 7.51 (dd, *J* = 8.3, 5.4 Hz, 2H), 7.37 (t, *J* = 6.2 Hz, 1H), 7.25 (t, *J* = 7.9 Hz, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 6.85 (t, *J* = 7.6, 2H), 6.68 (td, *J* = 7.4, 0.6 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.27 (d, *J* = 10.0 Hz, 1H), 5.42 (d, *J* = 4.6 Hz, 1H), 5.37 (dd, *J* = 13.6, 4.5 Hz, 1H), 5.29 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.84 (s, 3H), 3.68 (s, 3H), 3.01 (t, *J* = 13.9 Hz, 1H), 2.66 (dd, *J* = 14.2, 4.7 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) 175.3, 170.3, 169.1, 163.6, 161.2, 143.6, 135.9, 135.8, 134.8, 130.8, 130.4, 129.4, 128.0, 127.7, 127.5, 127.3, 120.2, 120.1, 119.8, 115.3, 115.1, 112.6, 77.4, 61.2, 60.0, 54.5, 53.6, 52.7, 31.5; IR (neat) 2953, 1732,

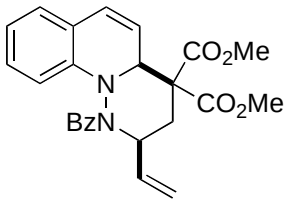
1660, 1510, 1352, 1262, 1227, 909, 847, 728 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{25}N_2O_5F$ $[M+H]^+$: 501.1826, found 501. 1813. The relative configuration was assigned by analogy with compound **3a**.

trans-**3f**: White solid; mp 157-159 °C; R_f 0.09 (100% CH_2Cl_2); ^1H RMN (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.2 Hz, 2H), 7.48 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 2H), 7.05-7.09 (m, 3H), 6.90 (dd, *J* = 7.4, 1.2 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.35 (d, *J* = 10.0 Hz, 1H), 5.90 (dd, *J* = 9.9, 5.7 Hz, 1H), 5.50 (dd, *J* = 8.5, 3.8 Hz, 1H), 5.10 (d, *J* = 5.7 Hz, 1H), 3.55 (s, 3H), 3.41 (s, 3H), 2.94 (dd, *J* = 14.1, 4.0 Hz, 1H), 2.79 (dd, *J* = 14.1, 8.5 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) δ 173.2, 170.3, 170.1, 163.2, 160.7, 143.2, 134.7, 134.7, 133.8, 131.7, 130.0, 128.2, 128.1, 128.0, 127.4, 126.9, 122.8, 122.1, 120.6, 115.5, 115.2, 110.3, 77.4, 59.9, 57.2, 53.2, 52.9, 52.5, 33.3; IR (neat) 3029, 2952, 1728, 1667, 1600, 1510, 1238, 1214, 911, 728 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{25}N_2O_5F$ $[M+H]^+$: 501.1826, found 501. 1816. The relative configuration was assigned by analogy with compound **3a**.

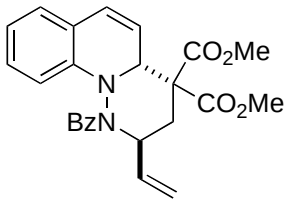


cis-**3g**

Dimethyl 1-benzoyl-2-(4-nitrophenyl)- 2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (*cis*-3g). 24 mg (11%) was obtained in a *cis*/*trans* ratio of 5.9:1 (determined by ^1H NMR). Diastereoisomers were separated by preparative HPLC for characterization (Column C8, 40% MeCN/water to 100% MeCN, 20 mL/min). Yellow solids: mp 208-210 °C; R_f 0.11 (20% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (dt, *J* = 9.2, 2.2 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 2H), 7.62-7.59 (m, 2H), 7.43-7.39 (m, 1H), 7.32-7.25 (5H), 6.89-6.83 (m, 2H), 6.71 (td, *J* = 8.4, 1.2 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 6.30 (d, *J* = 10.4 Hz, 1H), 5.50-5.43 (m, 2H), 5.34 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 3.03 (t, *J* = 13.8 Hz, 1H), 2.73 (dd, *J* = 14.0, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 169.9, 168.7, 147.4, 147.1, 143.2, 134.1, 131.0 (2), 129.3 (2), 128.3, 127.9, 127.8, 127.4, 127.3 (2), 123.5 (2), 120.4, 120.0, 112.1, 60.7, 59.9, 54.6, 53.5, 52.7, 31.2; IR (neat) 2954, 1732, 1663, 1521, 1345, 1265, 1241, 1210, 1172 cm^{-1}**;** HRMS (ESI) calcd for $C_{29}H_{25}N_3O_7$ $[M+H]^+$: 528.1771, found 528.1764. The relative configuration was assigned by analogy with compound **3a**.



cis-**3h**

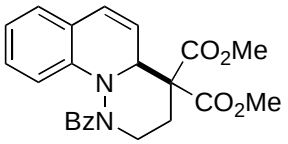


trans-**3h**

Dimethyl 1-benzoyl-2-vinyl- 2,3-dihydro-1 *H*-pyridazino[1,6-a]quinoline-4,4(4a*H*)-dicarboxylate (3h). 54 mg (31%) was obtained in a *cis*/*trans* ratio of 2.6:1 (determined by ^1H NMR). Diastereoisomers were separated by chromatography on silica gel for characterization (20% EtOAc/hexane). *cis*-**3h**: White solids: mp 64-66 °C; R_f 0.15 (20% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61-7.57 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.29-7.10 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.86 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.30-6.28 (m, 1H), 6.11-6.02 (m, 1H),

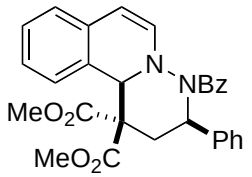
5.44-5.33 (m, 3H), 5.26 (d, J = 10.4 Hz, 1H), 4.75 (qn, J = 6.0 Hz, 1H), 3.82 (s, 3H), 3.65 (s, 3H) 2.60-2.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 170.1, 169.1, 144.1, 137.1, 134.7, 130.5, 129.4, 127.8 (2), 127.5, 127.2, 127.0 (2), 120.3, 120.1, 118.1, 111.9, 60.1, 59.9, 54.4, 53.3, 52.4, 32.1, 29.7; IR (neat) 2952, 1731, 1658, 1263, 1240, 1210, 1177 cm^{-1}**;** HRMS (ESI) calcd for $C_{25}H_{24}N_2O_5$ [M+H]$^+$: 433.1764, found 433.1775. The relative configuration was assigned by analogy with compound **3a**.

trans-**3h**: Colorless oil; R_f 0.21 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.55 (m, 2H), 7.38-7.34 (m, 1H), 7.25-7.20 (m, 3H), 6.97 (d, J = 8.0 Hz, 1H), 6.87 (dd, J = 7.4, 1.4 Hz, 1H), 6.77 (dd, J = 8.4, 0.8 Hz, 1H), 6.50-6.27 (m, 1H), 5.84 (dd, J = 10.0, 5.6 Hz, 1H), 5.37 (dt, J = 17.2, 1.2 Hz, 1H), 5.26 (dt, J = 10.2, 1.2 Hz, 1H), 4.84-4.75 (m, 2H), 3.73 (s, 3H), 3.37 (s, 3H), 2.52 (dd, J = 14.0, 3.6 Hz, 1H), 2.45 (dd, J = 13.8, 10.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 170.1 (2), 142.4, 136.4, 134.3, 131.2, 129.7, 127.8 (2), 127.6 (2), 127.0, 126.5, 122.9, 121.6, 120.1, 115.9, 110.6, 59.9, 56.3, 54.4, 52.7, 52.1, 33.2; IR (neat) 2952, 1726, 1666, 1290, 1251, 1211 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{24}N_2O_5$ [M+H]$^+$: 433.1764, found 433.1775. The relative configuration was assigned by analogy with compound **3a**.



3i

Dimethyl 1-benzoyl-2,3-dihydro-1 *H*-pyridazino[1,6-*a*]quinoline-4,4(4a*H*)-dicarboxylate (3i). Colorless oil (52 mg, 32%); R_f 0.28 (40% EtOAc/hexane); ^{1}H RMN (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.23-7.27 (m, 2H), 7.18 (t, J = 7.8 Hz, 1H), 6.90 (d, J = 7.3 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.77 (t, J = 7.4 Hz, 1H), 6.35 (d, J = 10.0 Hz, 1H), 5.92 (dd, J = 10.0, 5.6 Hz, 1H), 4.70 (d, J = 5.5 Hz, 1H), 4.61 (dd, J = 13.5, 3.3 Hz, 1H), 3.85 (td, J = 12.7, 3.0 Hz, 1H), 3.73 (s, 3H), 3.28 (s, 3H), 2.44 (d(br), J = 13.8 Hz, 1H), 2.12 (td, J = 12.9, 5.1 Hz, 1H); ^{13}C RMN (100 MHz, $CDCl_3$) 172.5, 170.4, 169.9, 142.7, 133.7, 131.0, 129.8, 127.9, 127.6, 127.1, 126.9, 123.0, 122.0, 120.4, 110.8, 60.7, 54.2, 53.0, 52.2, 34.9, 30.0 (2); IR (neat) 2952, 1725, 1653, 1436, 1256, 1216, 1052, 1000, 916, 727 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}N_2O_5$ [M+H]$^+$: 407.1607, found 407.1607.

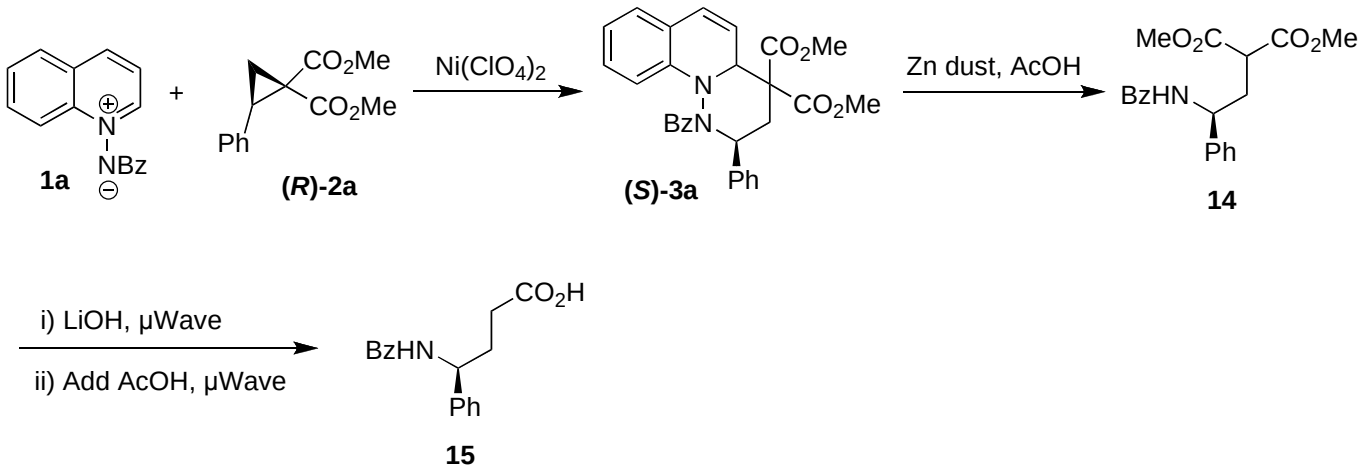


8

Dimethyl (3*R,11b*R**)-4-benzoyl-3-phenyl-3,4-dihydro-2 *H*-pyridazino[6,1-*a*]isoquinoline-1,1(11b*H*)-dicarboxylate (8).** 41 mg (21%) was obtained in a *cis*/*trans* ratio >20:1 (determined by ^{1}H NMR). Colorless oil: R_f 0.23 (100% CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (m, 2H), 7.50 (d, J = 7.6 Hz, 2H), 7.42-7.29 (m, 6H), 7.09 (td, J = 7.2, 1.6 Hz, 1H), 6.97-6.89 (m, 2H), 6.86 (d, J = 7.6 Hz, 1H), 6.53 (d, J = 7.6 Hz, 1H), 5.78 (s, 1H), 5.38 (d, J = 7.6 Hz, 1H), 5.30 (dd, J = 13.6, 4.8 Hz, 1H), 3.91 (s, 3H), 3.24 (q, J = 14.0 Hz, 1H), 3.12 (s, 3H), 2.86 (dd, J = 14.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 170.6, 169.2, 140.8, 137.1, 134.6, 131.3, 130.5, 128.7 (2), 128.5, 128.1 (2), 127.9 (2), 127.8, 127.7 (2), 126.7 (2), 125.2, 124.1, 102.1, 62.3, 61.8, 55.7, 53.4, 52.3, 35.5; IR (neat) 3030, 2952, 1729, 1662, 1349, 1267, 1241, 1221, 1176 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{26}N_2O_5$ [M+H]$^+$: 483.1920, found 483.1911. The relative configuration was assigned by analogy with compound **3a**.

Determination of the absolute stereochemistry of (*S*)-3a
The absolute stereochemistry of (*S*)-**3a** was determined by comparing the chiral SFC chromatogram of the acid **15** synthesized from (*S*)-**3a** with the chromatogram of the acid **15** synthesized from D-(–)-phenylglycine.

Synthesis of (4*S*)- 4-(benzoylamino)-4-phenylbutanoïc acid (15) from (*S*)-3a:
The procedure for the preparation of the acid **15** consists of a two-step sequence, where the first step is the cleavage of the N-N bond, which produced the malonate **14**, and the second step is a saponification-decarboxylation reaction.



Step one : cleavage of the N-N bond

Dimethyl [(2*S*)-2-(benzoylamino)-2-phenylethyl]malonate (14):
At room temperature, 1.0 g of zinc dust (< 10 µm) (1.0 g, 15 mmol) was added to a solution of (*S*)-**3a** (500 mg, 1.0 mmol) dissolved in glacial acetic acid (20 mL). After 20 h of stirring, the reaction mixture was filtered through a celite pad. The filtrate was diluted with ethyl acetate. The solution was washed with water, with a saturated aqueous solution of $NaHCO_3$ and then with a saturated aqueous solution of NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by flash chromatography (eluent: 30% EtOAc/hexanes) to afford 200 mg (54%) of a white solid. mp 139 °C; R_f 0.34 (40% EtOAc/hexanes); $[\alpha]_D^{20}$ +7.5° (c 0.84, acetone); ^{1}H NMR (300 MHz, DMSO d_6): 8.89 (d, *J* = 8.5 Hz, 1H), 7.90-7.88 (m, 2H), 7.51-7.20 (m, 8H), 5.08 (dt, *J* = 8.9, 5.5 Hz) 3.63 (s, 3H), 3.62 (s, 3H), 3.57 (dd, *J* = 8.7, 6.3 Hz, 1H), 2.48-2.24 (m, 2H); ^{13}C NMR (75 MHz, DMSO d_6): 169.3, 169.0, 166.0, 143.0 134.3 131.3, 128.5, 128.3, 127.4, 127.1, 126.5, 52.5, 52.5, 51.1, 48.9, 34.9; IR (neat): 3352, 3032, 2951, 1731, 16490, 1526, 1251, 1159, 701 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{21}NO_5$ $[M+H]^+$: 356.1492. Found 356.1483.

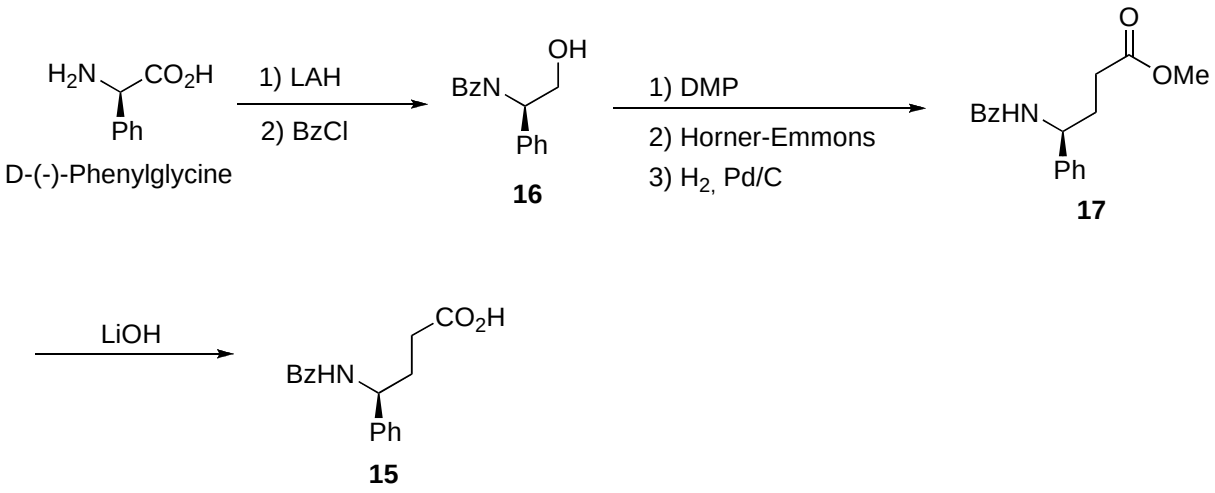
Step two: saponification-decarboxylation

(4*S*)- 4-(benzoylamino)-4-phenylbutanoïc acid (15):

In a 5 mL microwave flask was added **14** (200 mg, 0.56 mmol), iPrOH (1.0 mL) and 1.0 N aqueous LiOH (1.13 mL, 1.13 mmol). Reaction was heated in the microwave apparatus at 120 °C for 5 min. AcOH (1.0 mL) was then added at room temperature and the reaction mixture was heated in the microwave apparatus at 160 °C for 5 min. The cooled solution was then diluted with water and diethyl ether then washed twice with diethyl ether. Aqueous layer was extracted three times with 2

N aqueous NaOH then the combined aqueous layers were acidified with a solution of HCl 50% in water and extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude beige solid was purified by triturating in dichloromethane to yield 158 mg (79%) of a white solid. mp 150 °C; R_f 0.21 (50% EtOAc/hexanes); $[\alpha]_D^{20}$ +15.8° (c 0.30, acetone); ^{1}H NMR (400 MHz, $CDCl_3$): 12.11 (s, 1H), 8.80 (d, J = 8.4 Hz, 1H), 7.90-7.87 (m, 2H), 7.55-7.22 (m, 8H), 5.04 (td, J = 8.8, 5.9 Hz, 1H), 2.33-2.27 (m, 2H), 2.11-2.00 (m, 2H); ^{13}C NMR (100 Hz, DMSO d_6): 174.1, 166.0, 143.7, 135.5, 131.1, 127.4, 126.8, 126.5, 52.6, 31.2, 31.0; IR (neat): 3287, 3061, 3029, 2935, 1706, 1633, 1602, 1576, 1531, 1489, 1447, 1405, 1291, 1208, 1075, 1027, 696 cm^{-1}; HRMS (ESI) Calcd for $C_{17}H_{17}NO_3$ $[M+H]^+$: 284.1281. Found 284.1283. The ee (92%) was determined by SFC analysis (Chiralcel OJ-H, 10% iPrOH/CO_2, 5.0 mL/min, 150 bar, (*R*)- **15** t_r = 2.69 min, (*S*)- **15** t_r = 3.86 min [major product]).

Synthesis of (4*S*)- 4-(benzoylamino)-4-phenylbutanoïc acid (15) from D-(–)-phenylglycine:
The procedure for the preparation of the acid **15** consists of a six-step sequence, which is represented in the next scheme.



Step one-two : LAH reduction- benzoylation of the amine

***N*-[(1*R*)-2-hydroxy-1-phenylethyl]benzamide (16):**
The alcohol **16** was synthesized as described in the literature[10] from D-(–)-phenylglycine. mp 148 °C, lit: 178-180 °C[10]; R_f 0.18 (50% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): 7.83 (d, J = 7.4 Hz, 2H), 7.56-7.33 (m, 8H), 6.94 (d, J = 5.4, 1H), 5.28 (dd, J = 11.0, 4.8 Hz, 1H), 4.01 (d, J = 3.9 Hz, 2H), 2.79 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): 167.7, 138.8, 133.9, 131.7, 128.8, 128.5, 127.8, 126.9, 126.6, 66.5, 56.1; IR (neat): 3335, 1628, 1524, 1490, 1305, 1292, 1034, 1024, 698 cm^{-1}.

Step two-three-four : DMP oxidation- Horner-Emmons olefination

Methyl (4*S*)-4-(benzoylamino)-4-phenylbutanoate (17):
To **16** (664 mg, 2.75 mmol) in dichloromethane (40 mL) was added Dess-Martin periodinane[11] (1.75 g, 4.13 mmol). The reaction mixture was stirred 4 h at room temperature. Then the crude mixture was filtered through a silica gel pad and concentrated under reduced pressure.

[10] Denis, J.-N.; Correa, A.; Greene, A. E. *J. Org. Chem.* **1991**, *56*, 6939.
[11] Boeckman, R. K. Jr.; Shao, P.; Mullins, J. J. *Org. Synth., Coll. Vol.* **2004**, *10*, 696; *Org. Synth.* **2000**, *77*, 141.

To trimethylphosphonoacetate (668 μL, 4.13 mmol) in THF (20 mL) at 0°C (ice-water bath) was added NaH (60% in oil) (165 mg, 4.13 mmol) over 5 min. The white mixture was stirred for 30 min. In another flask, the aldehyde was taken up in THF (10 mL) and added via cannula to the phosphonium ylide mixture and the reaction was stirred at room temperature for 4 h. The reaction was quenched with a saturated aqueous solution of NH_4Cl. The mixture was extracted with diethyl ether. The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of NaCl. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (20% EtOAc/hexanes) to give 282 mg of a white solid. ^{1}H NMR showed the presence of the undesired product **18** (see below) in a 3:1 ratio where the desired product is the major constituent.

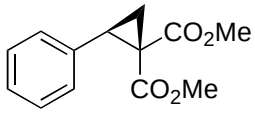
The white solid was dissolved in MeOH (10 mL) and Pd/C (10% w/w) (270 mg) was added to the reaction mixture. Reaction mixture was put under vacuum (water trump) alternate with H_2 three times and was then stirred for 1 h. The reaction mixture was filtered through a silica gel pad and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc/hexanes) to give 157 mg (19% yield over three steps) of a white solid. mp 117 °C; R_f 0.48 (50% EtOAc/hexanes); $[\alpha]_D^{20}$ +6.03° (c 0.70, acetone), ^{1}H NMR (400 MHz, $CDCl_3$): 7.81-7.79 (m, 2H), 7.50-7.43 (m, 2H), 7.36-7.23 (m, 6H), 5.19 (dd, *J* = 14.3, 8.0 Hz, 1H), 3.61 (s, 3H), 2.43-2.38 (m, 2H), 2.27-2.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 173.8, 166.7, 141.4, 133.8, 131.0, 128.2, 128.0, 127.0, 126.8, 126.1, 53.2, 51.4, 30.7, 30.4; IR (neat) : 3311, 3061, 2950, 2342, 1736, 1635, 1602, 1579, 1532, 1490 1438, 1293, 1168, 1075, 1028, 765, 700 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}NO_3$ $[M+H]^+$: 298.1438. Found 284.1430.

Step six : saponification

(4*S*)- 4-(benzoylamino)-4-phenylbutanoïc acid (15):
17 (142 mg, 0.477 mmol) was dissolved in a 1:1 mixture of THF and aqueous NaOH 2N (40 mL). The solution was stirred 16 h. The solution was then washed with diethylether. The aqueous layer was acidified with HCl conc. until pH = 1 and extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield 135 mg (quant.). See page S15 for spectral data. $[\alpha]_D^{20}$ +7.58° (c 1.28, acetone). The ee (65%) was determined by SFC analysis (Chiralcel OJ-H, 10% iPrOH/CO_2, 5.0 mL/min, 147 bar, (*R*)-**15** t_r = 2.62 min, (*S*)-**15** t_r = 3.75 min [major product]).

Methyl 4-(benzoylamino)-4-phenylbut-3-enoate (18):
Light orange solid: mp 125-129 °C; R_f 0.52 (50% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): 8.34 (br, 1H), 7.96 (d, *J* = 7.4 Hz, 2H), 7.61-7.34 (m, 8H), 5.97 (t, *J* = 7.1 Hz, 1H), 3.76 (s, 3H), 3.30 (d, *J* = 7.1, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.63, 165.2, 137.7, 137.1, 133.6, 132.0, 128.7, 128.4, 127.3, 125.9, 114.7, 52.1, 33.6; IR (neat): 3280, 3058, 2950, 1735, 1644, 1601, 1579, 1509, 1480, 1446, 1436, 1322, 1278, 1196, 1168, 1075, 1027, 949, 757, 710, 693 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}NO_3$ $[M+H]^+$: 296.1281. Found 296.1278.

^{1}H and ^{13}C NMR Spectra of selected compounds


CO2Me
CO2Me

2a

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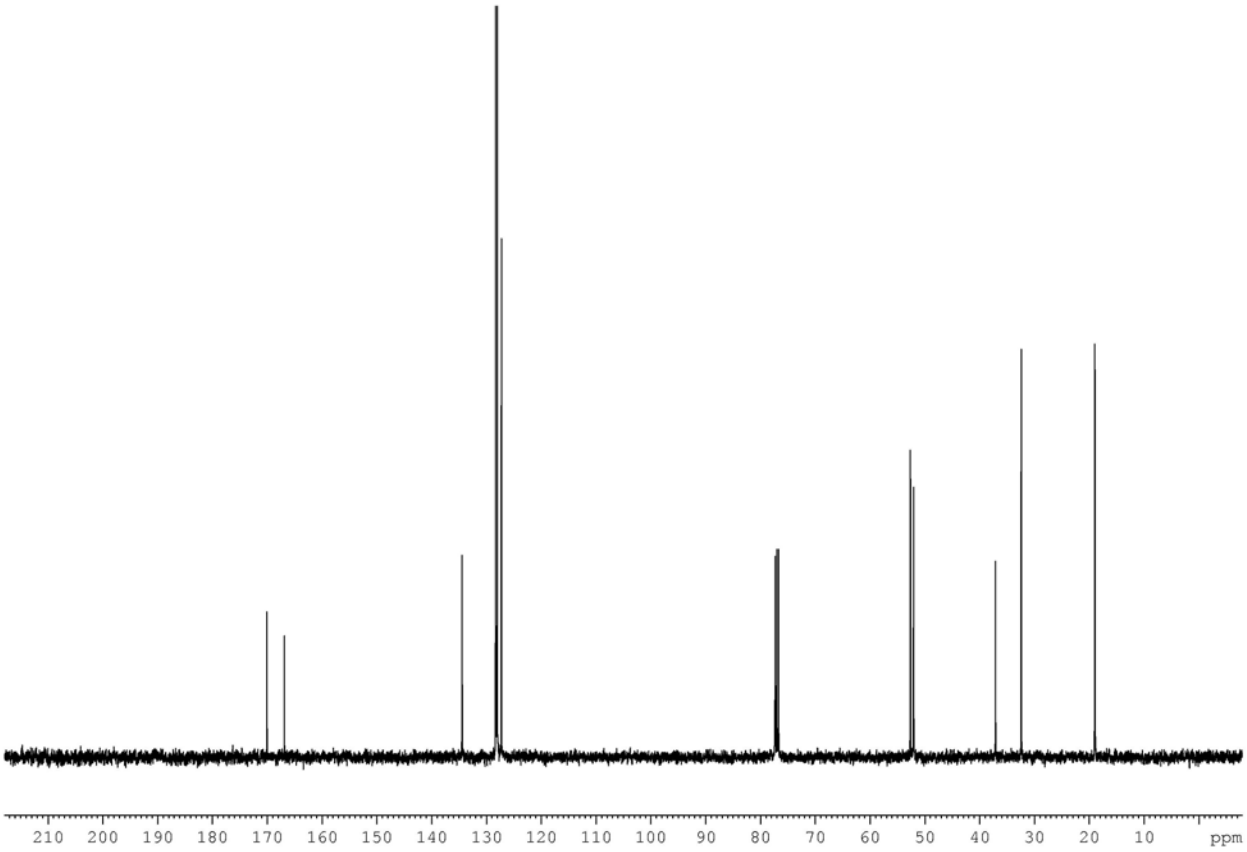
8
7
6
5
4
3
2
1
0
ppm
4.85
3.00
2.94
0.93
1.08
1.14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80
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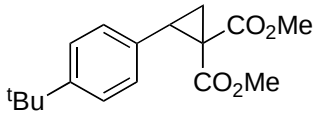
30
20
10
ppm


CO2Me
CO2Me
tBu

2b

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7
6
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0
ppm
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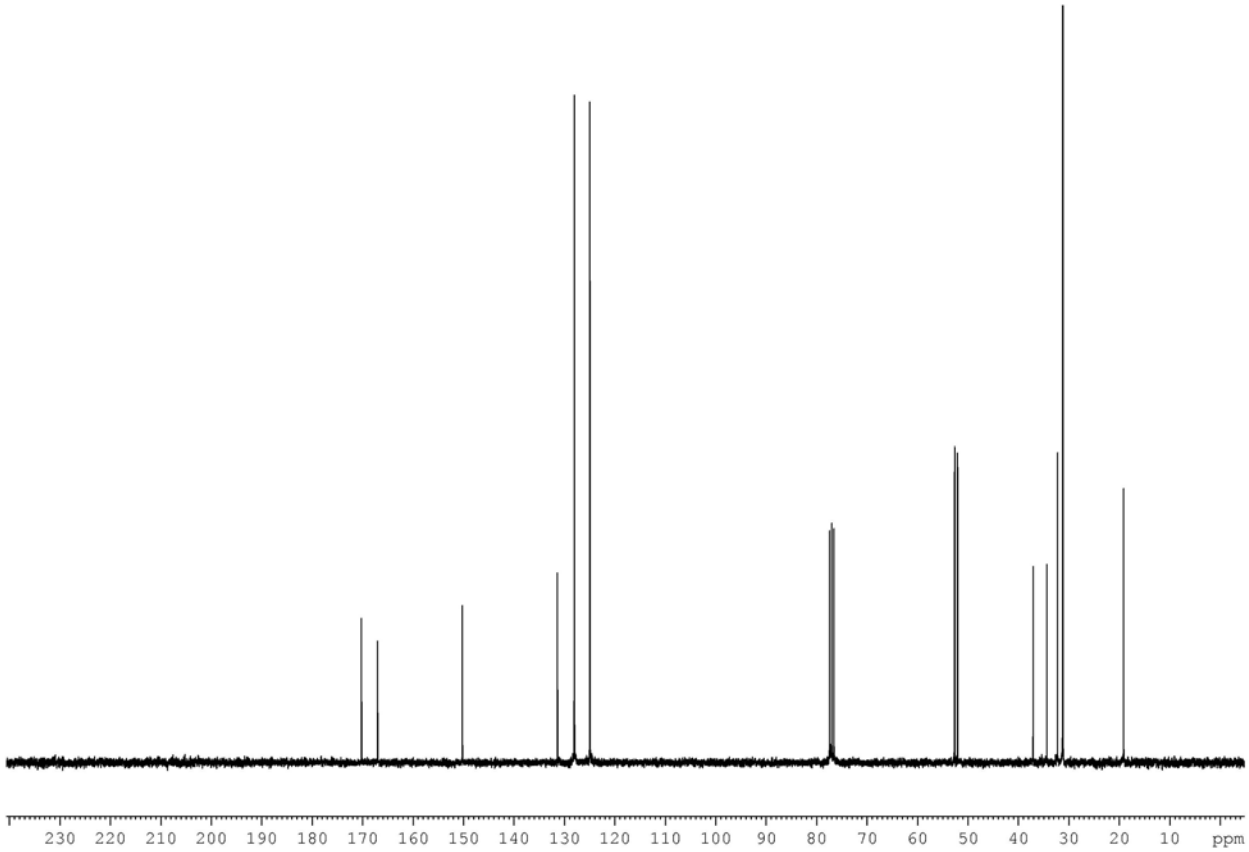
3.06
3.00
0.99
1.04
1.09
9.46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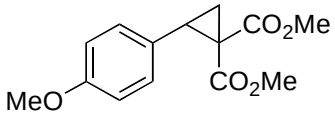
30
20
10
ppm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CO2Me
MeO

2c

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8
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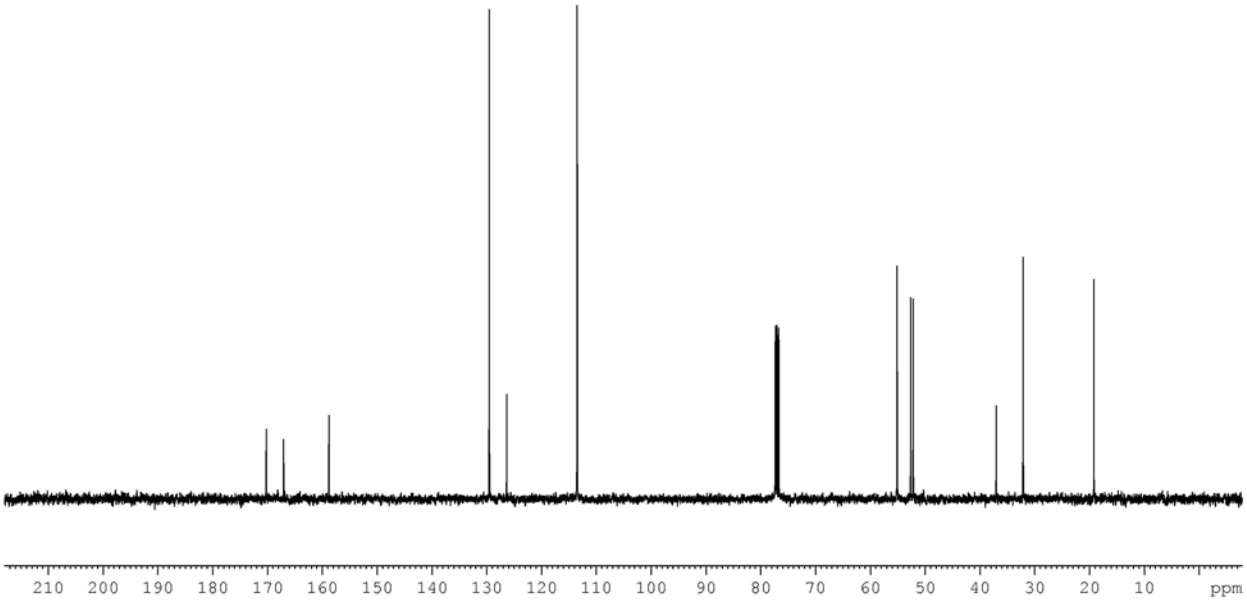
0
ppm
1.93
1.91
5.89
2.86
0.91
1.00
1.00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90
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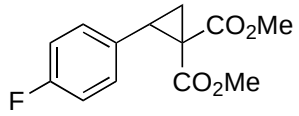
30
20
10
ppm


CO2Me
CO2Me
F

2d

9
8
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5
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1
0
ppm
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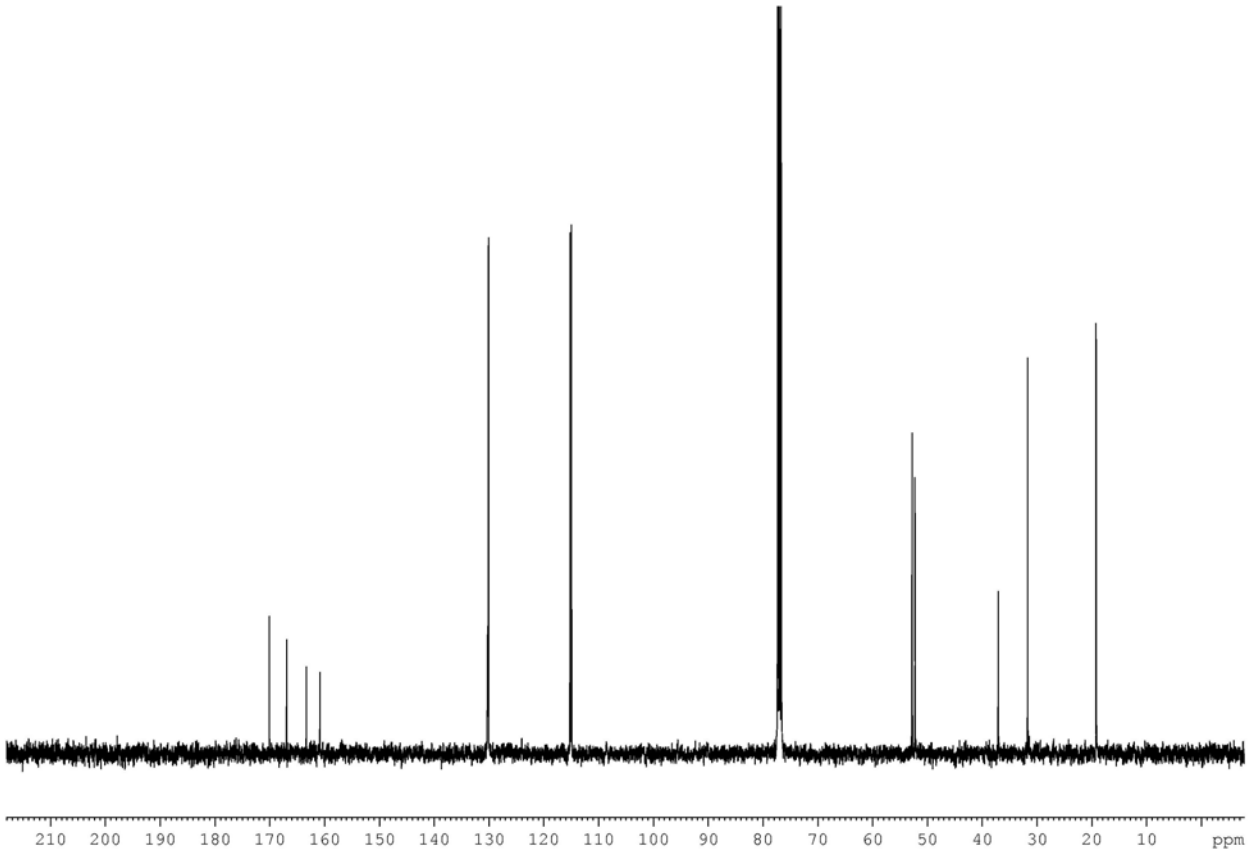
1.91
3.00
2.93
0.99
1.09
1.09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30
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10
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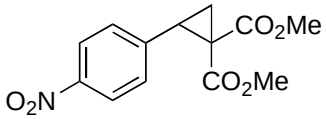
CO2Me
CO2Me
O2N

2e

9
8
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6
5
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3
2
1
0
ppm
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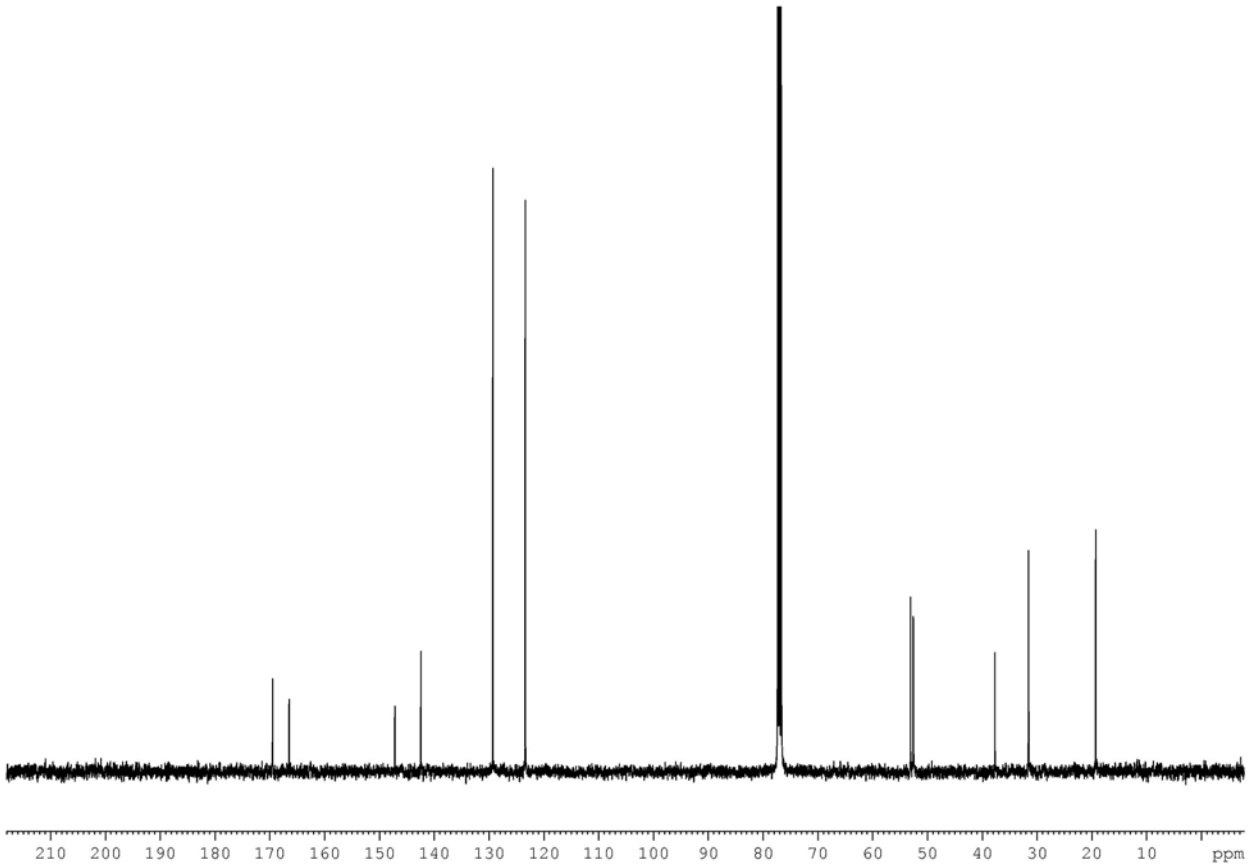
3.00
2.91
0.93
1.06
1.04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80
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30
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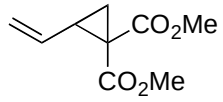
10
ppm


CO2Me
CO2Me

2f

9
8
7
6
5
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3
2
1
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ppm
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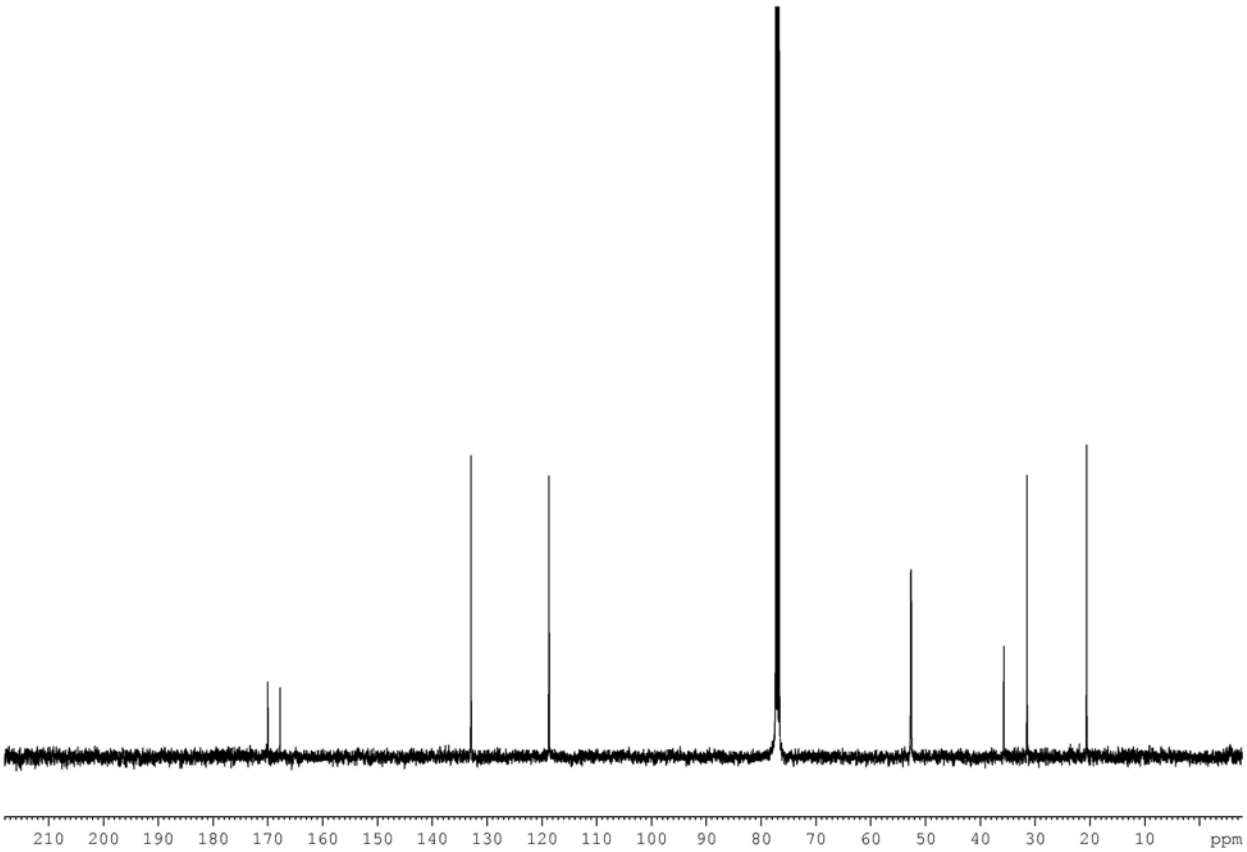
0.91
1.08
1.37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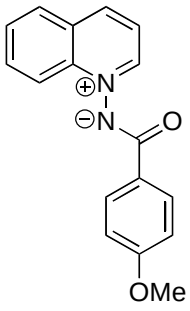
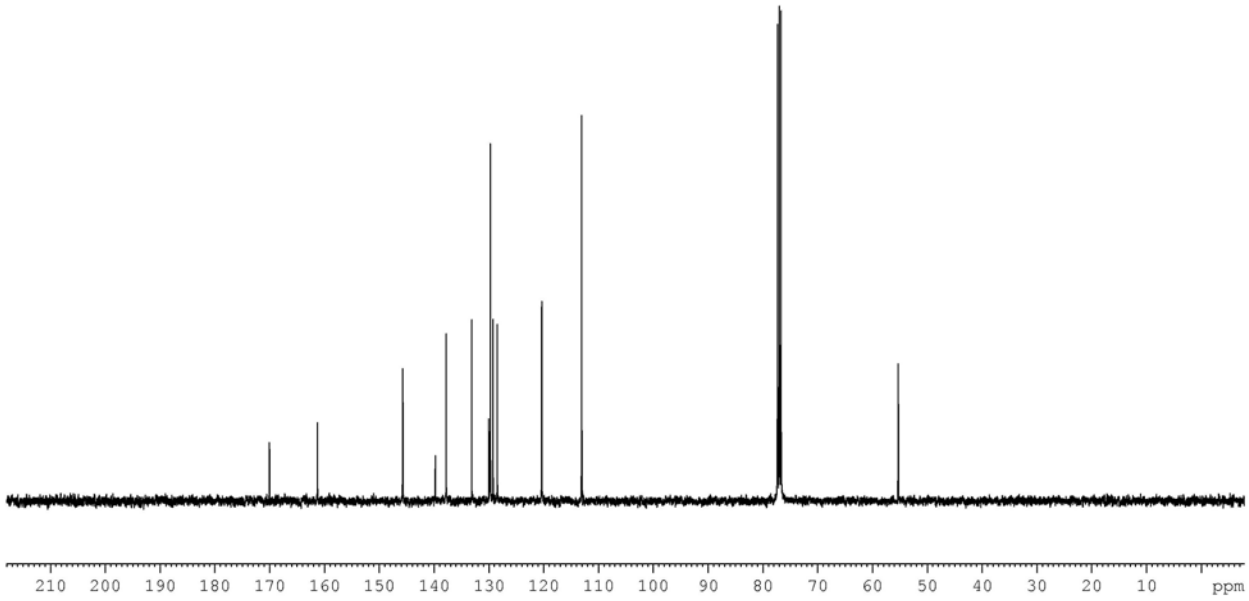
30
20
10
ppm


N
N
O
OMe

1b

9
8
7
6
5
4
3
2
1
0
ppm
0.78
0.80
0.87
1.76
0.90
0.95
0.94
0.95
1.92
3.00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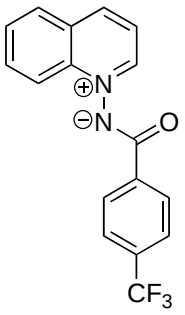
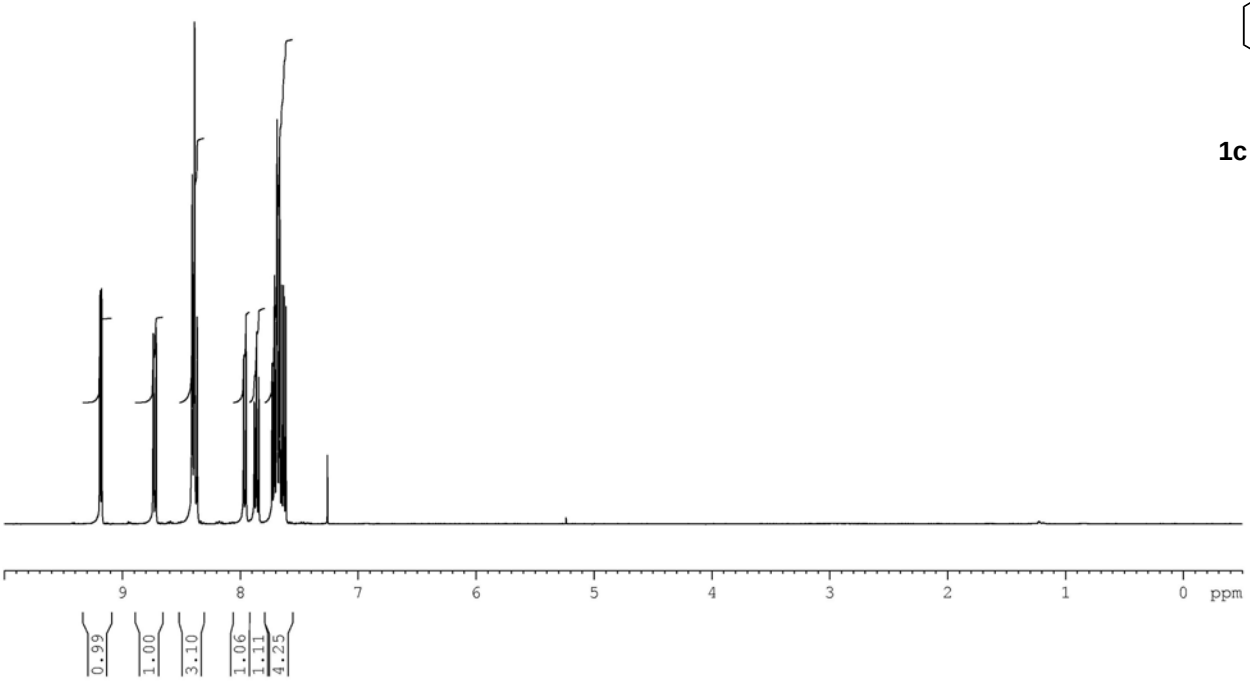
30
20
10
ppm



1c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7
6
5
4
3
2
1
0
ppm
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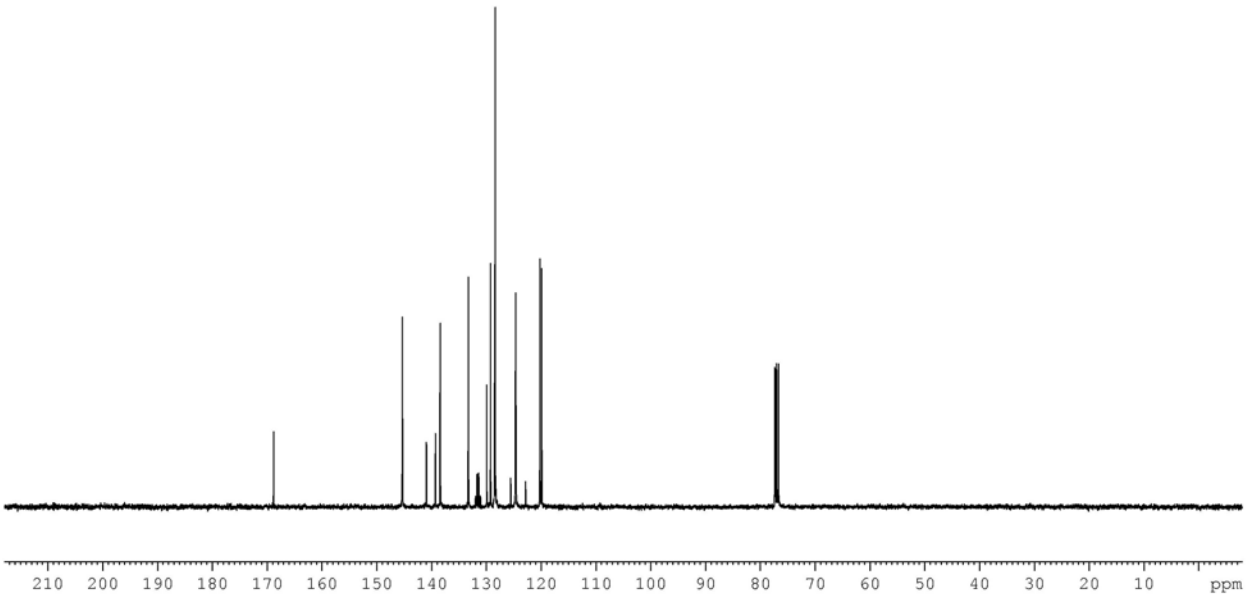
1.00
3.10
1.06
1.11
4.25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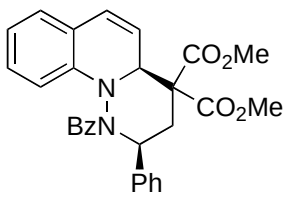
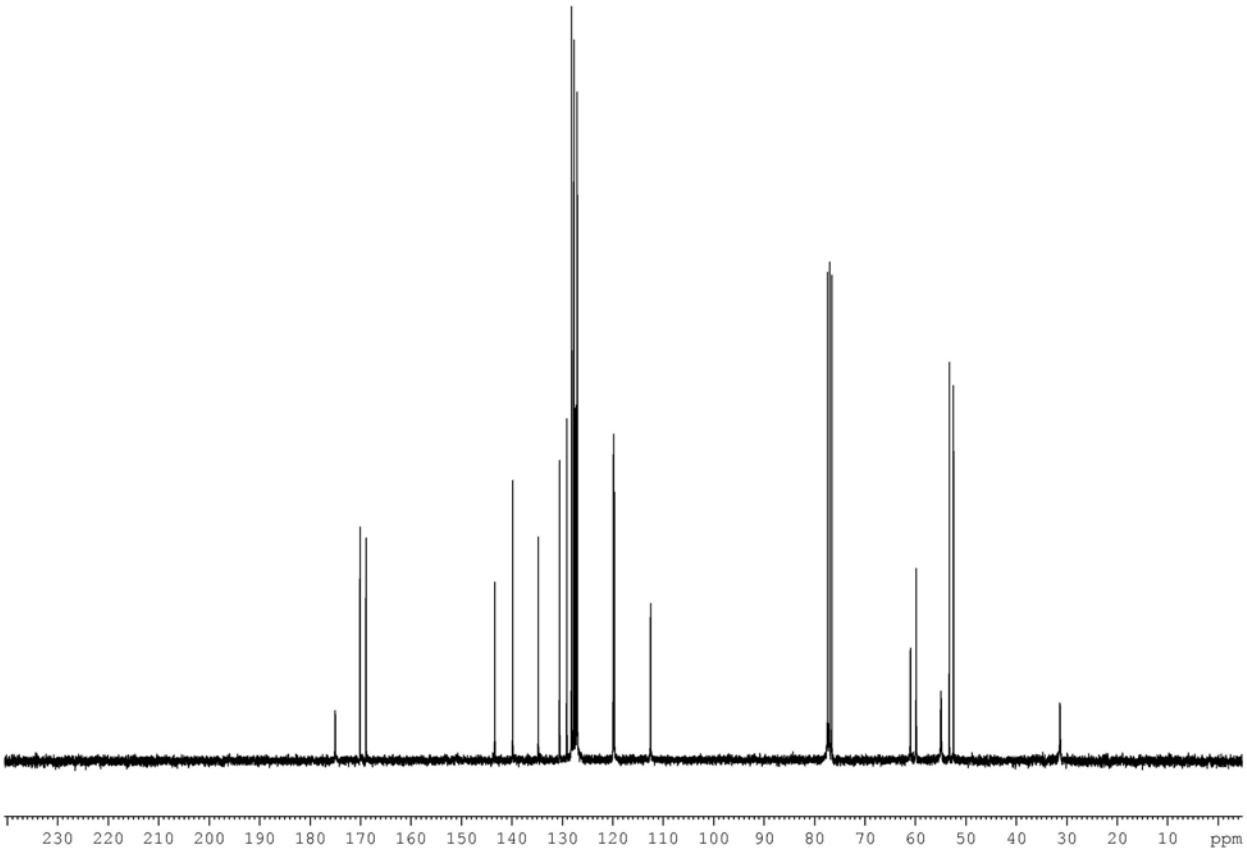
20
10
ppm


CO2Me
CO2Me
N
BzN
Ph

(*S*)-*cis*-**3a**

9
8
7
6
5
4
3
2
1
0
ppm
4.08
6.23
2.00
1.00
1.02
1.00
1.95
1.04
3.02
2.99
1.01
1.01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70
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30
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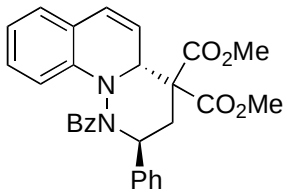
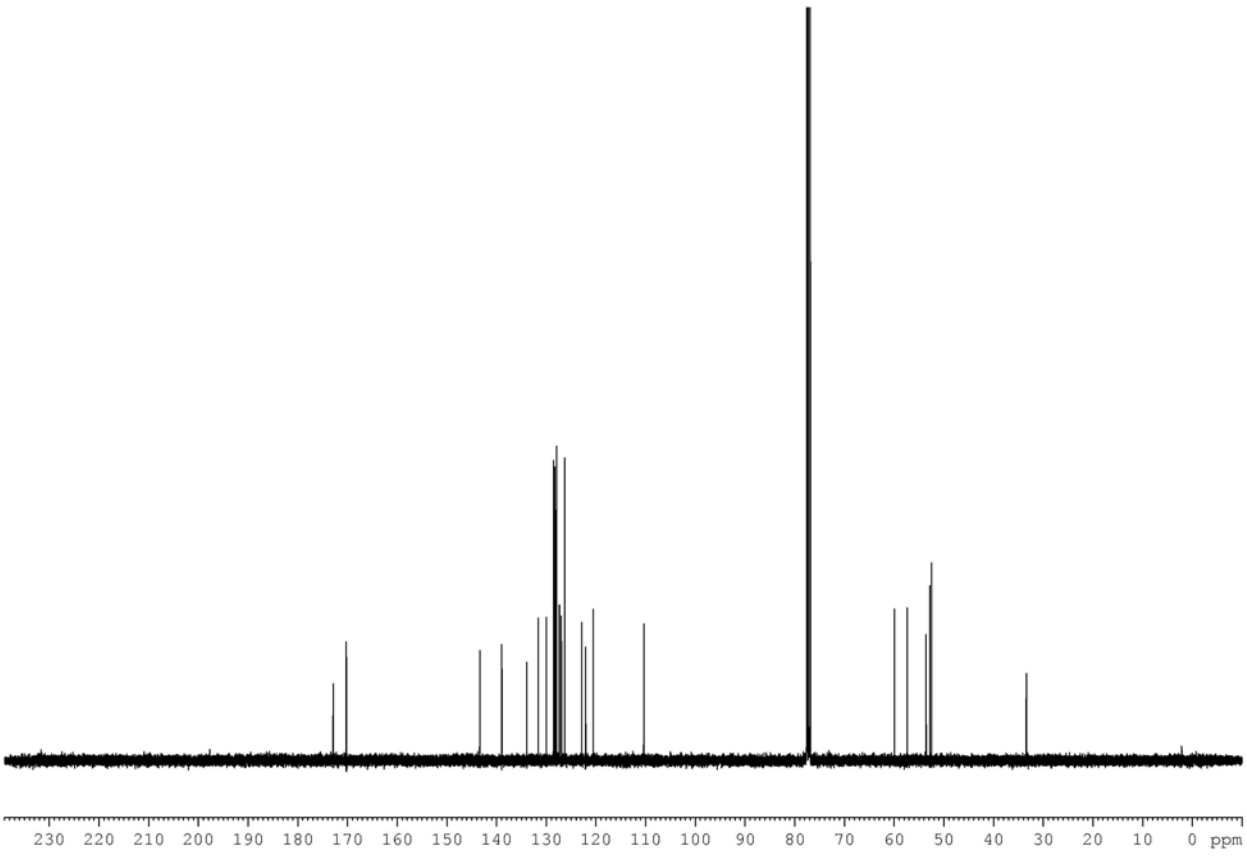
10
ppm


CO2Me
CO2Me
N
BzN
Ph

(*S*)-*trans*-**3a**

9
8
7
6
5
4
3
2
1
0
ppm
2.01
2.12
3.12
4.65
1.03
1.01
1.00
1.00
1.00
1.00
1.00
3.02
2.99
1.02
1.02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200
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100
90
80
70
60
50
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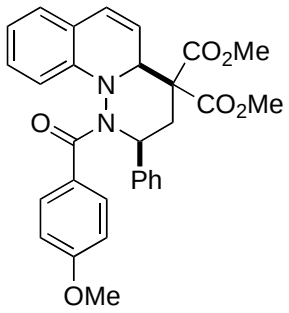
30
20
10
0
ppm


CO2Me
CO2Me
N
N
O
Ph
OMe

cis-**3b**

9
8
7
6
5
4
3
2
1
0
ppm
2.02
1.95
3.34
2.02
1.97
1.00
0.96
0.95
1.94
0.96
3.04
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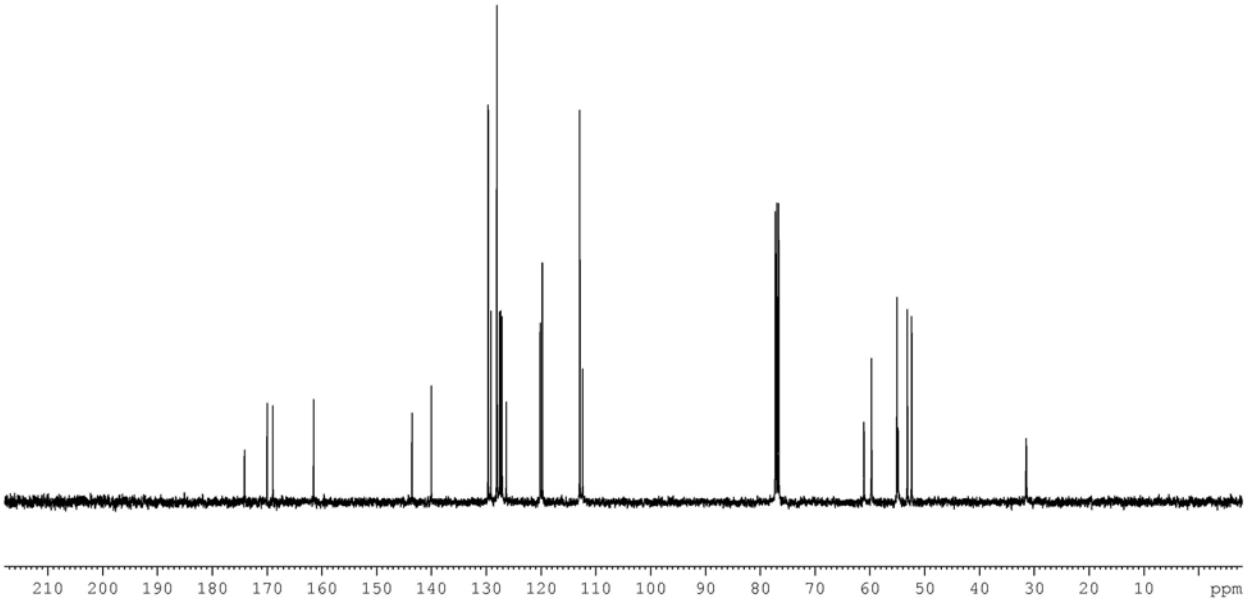
2.83
0.99
0.99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90
80
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50
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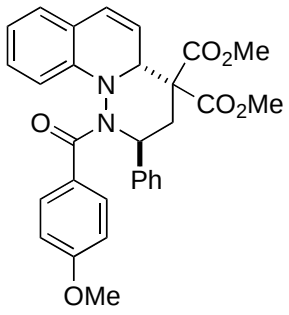
30
20
10
ppm


CO2Me
CO2Me
N
N
O
Ph
OMe

trans-**3b**

9
8
7
6
5
4
3
2
1
0
ppm
2.02
2.13
2.22
3.43
1.05
1.02
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1.00
1.00
1.01
1.00
3.23
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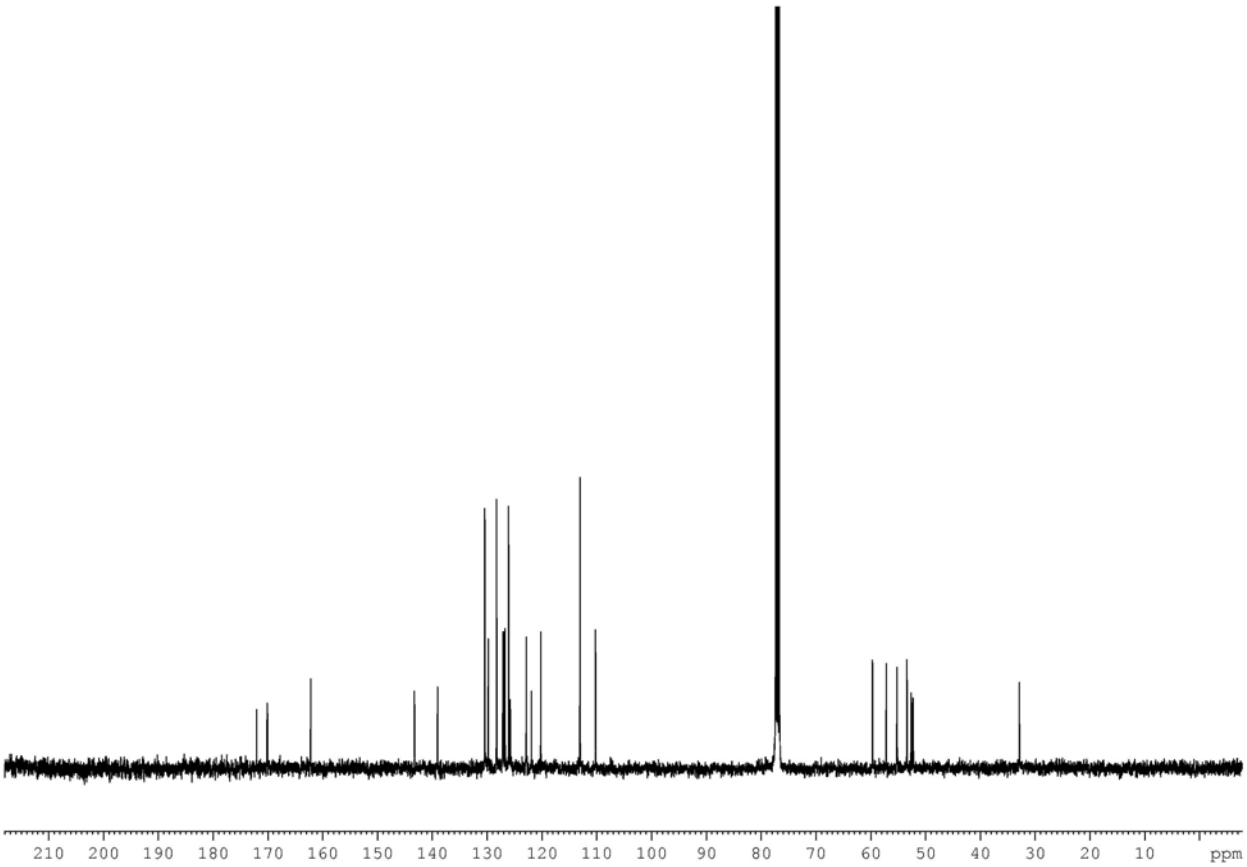
1.02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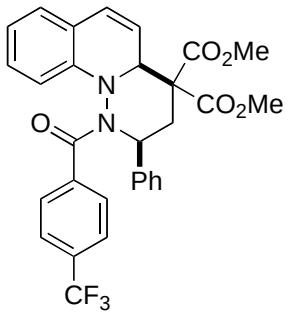
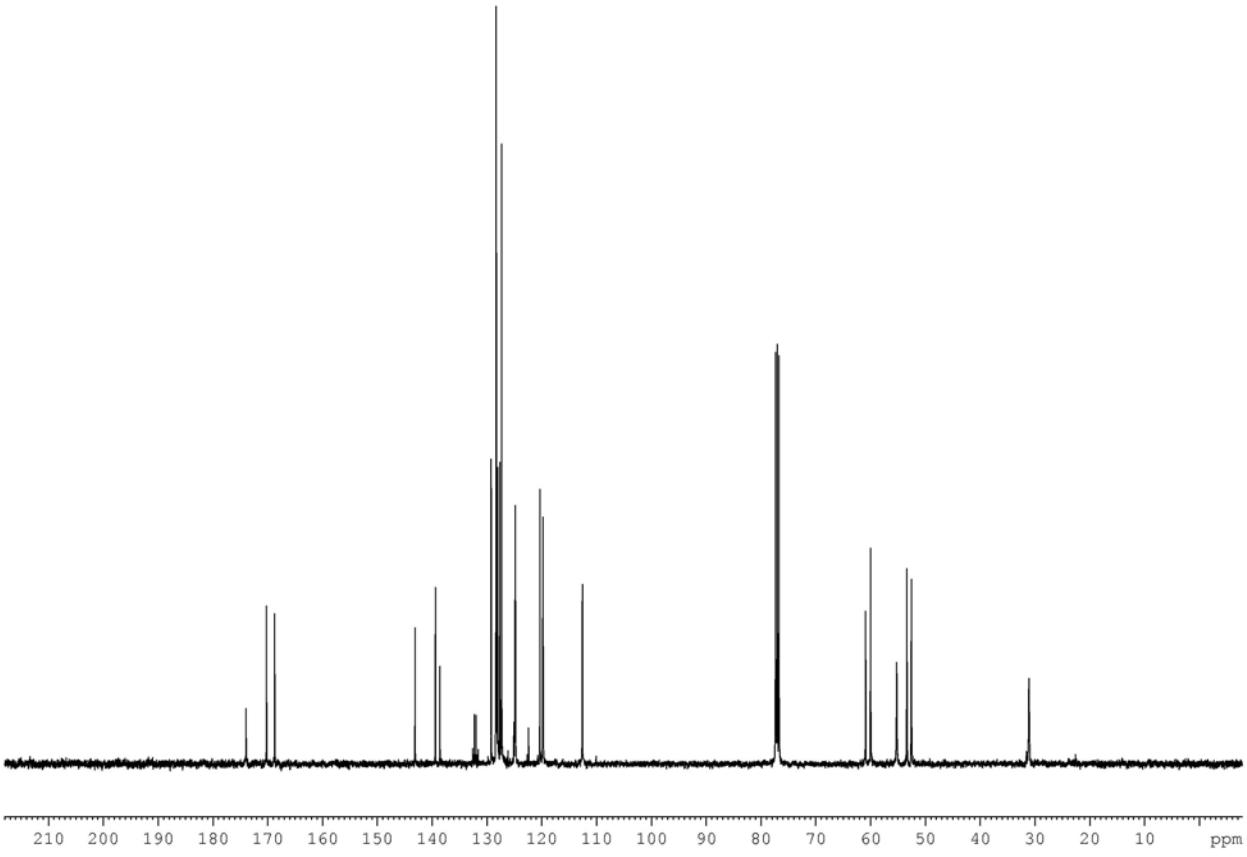
10
ppm


CO2Me
CO2Me
N
N
O
Ph
CF3

cis-**3c**

9
8
7
6
5
4
3
2
1
0
ppm
2.01
4.23
3.19
2.08
1.04
1.03
1.04
1.98
1.04
3.15
3.00
1.05
1.06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90
80
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60
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30
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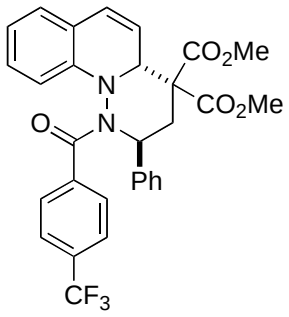
10
ppm


CO2Me
CO2Me
N
N
O
Ph
CF3

trans-**3c**

9
8
7
6
5
4
3
2
1
0
ppm
2.09
4.30
2.15
3.58
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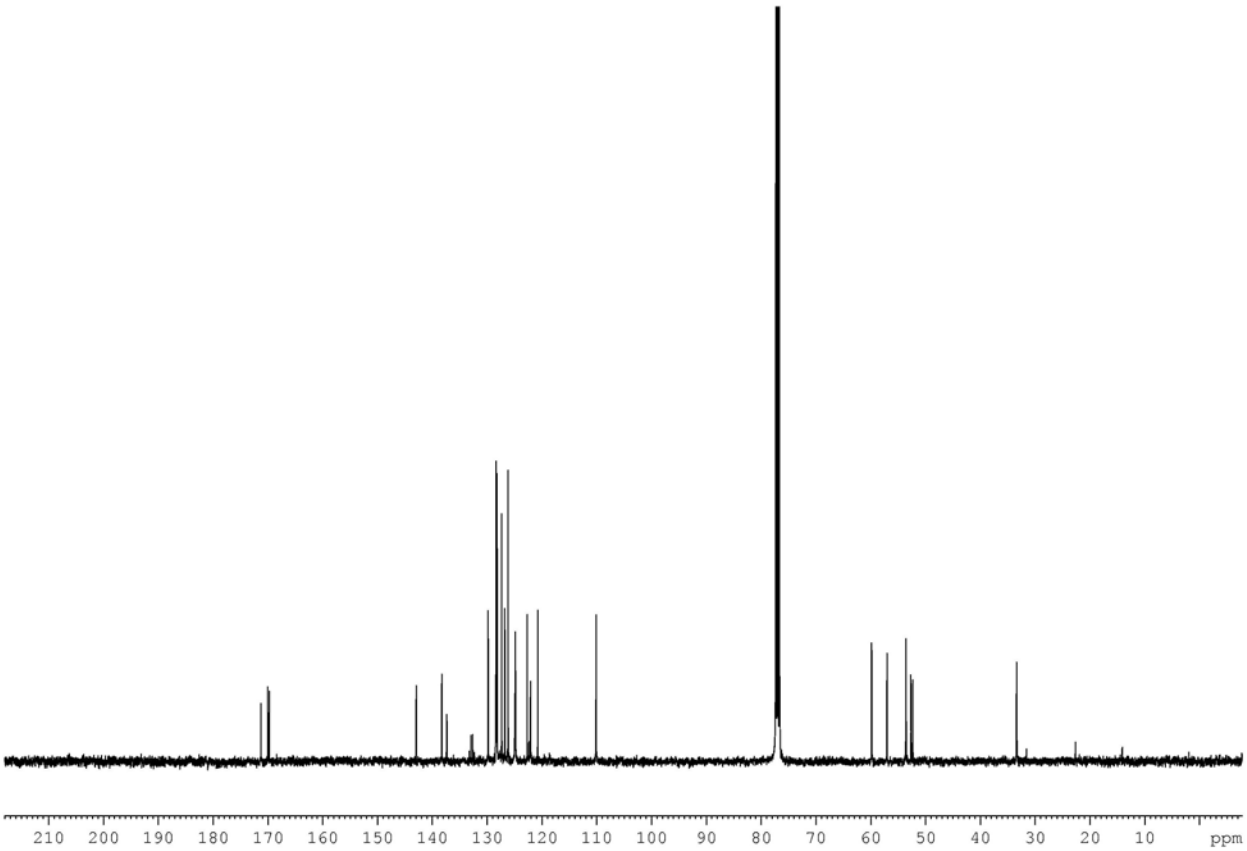
1.05
1.02
1.00
1.00
1.02
1.01
3.11
3.01
1.06
1.08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100
90
80
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60
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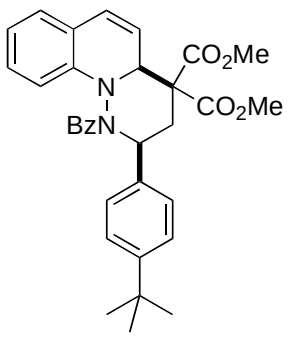
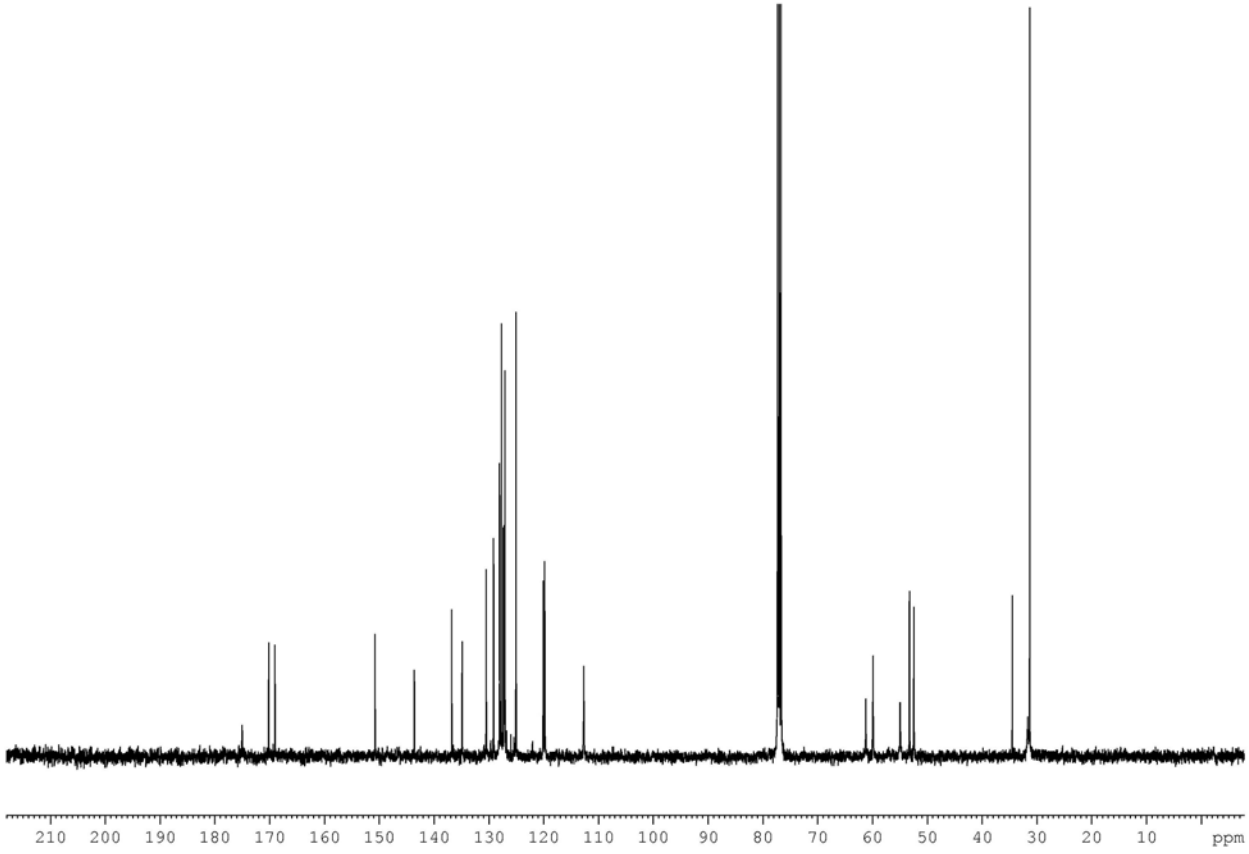
20
10
ppm


CO2Me
CO2Me
N
BzN

cis-**3d**

9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.00
3.45
3.36
2.00
2.00
0.96
3.00
2.81
2.76
1.02
1.01
10.08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90
80
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60
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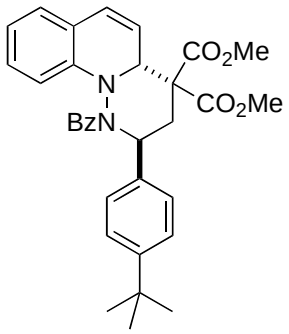
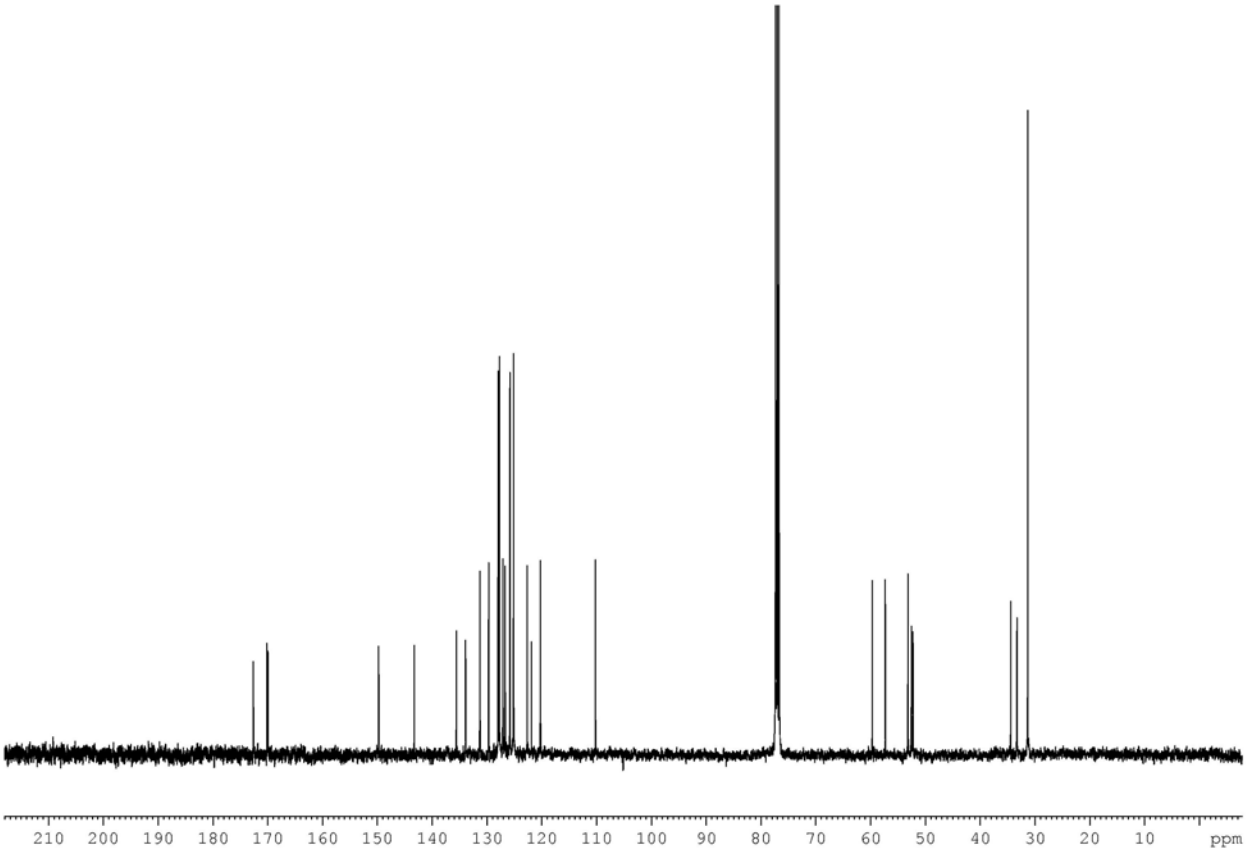
40
30
20
10
ppm


CO2Me
CO2Me
N
BzN

trans-**3d**

9
8
7
6
5
4
3
2
1
0
ppm
2.10
5.23
4.63
1.04
1.03
1.03
1.00
1.01
1.02
1.00
3.21
2.97
1.05
1.04
10.07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80
70
60
50
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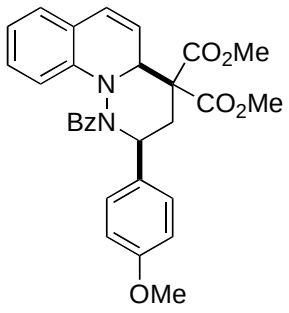
30
20
10
ppm


CO2Me
CO2Me
N
BzN
OMe

cis-**3e**

9
8
7
6
5
4
3
2
1
0
ppm
2.02
2.11
1.41
2.96
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2.09
1.01
1.01
2.05
3.39
2.87
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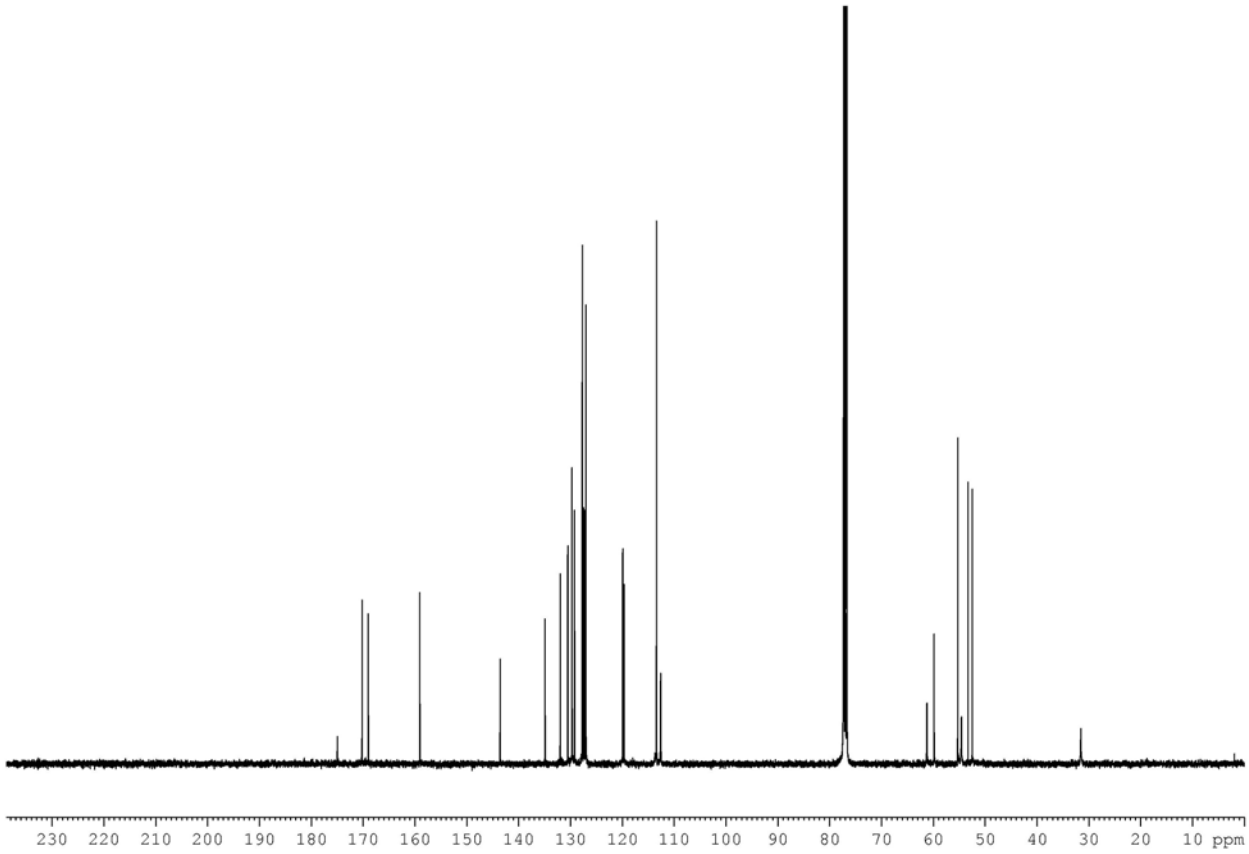
1.04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30
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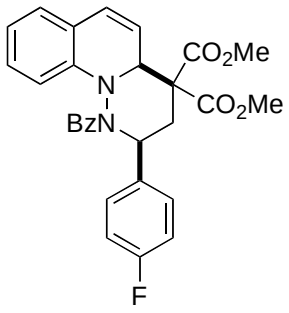
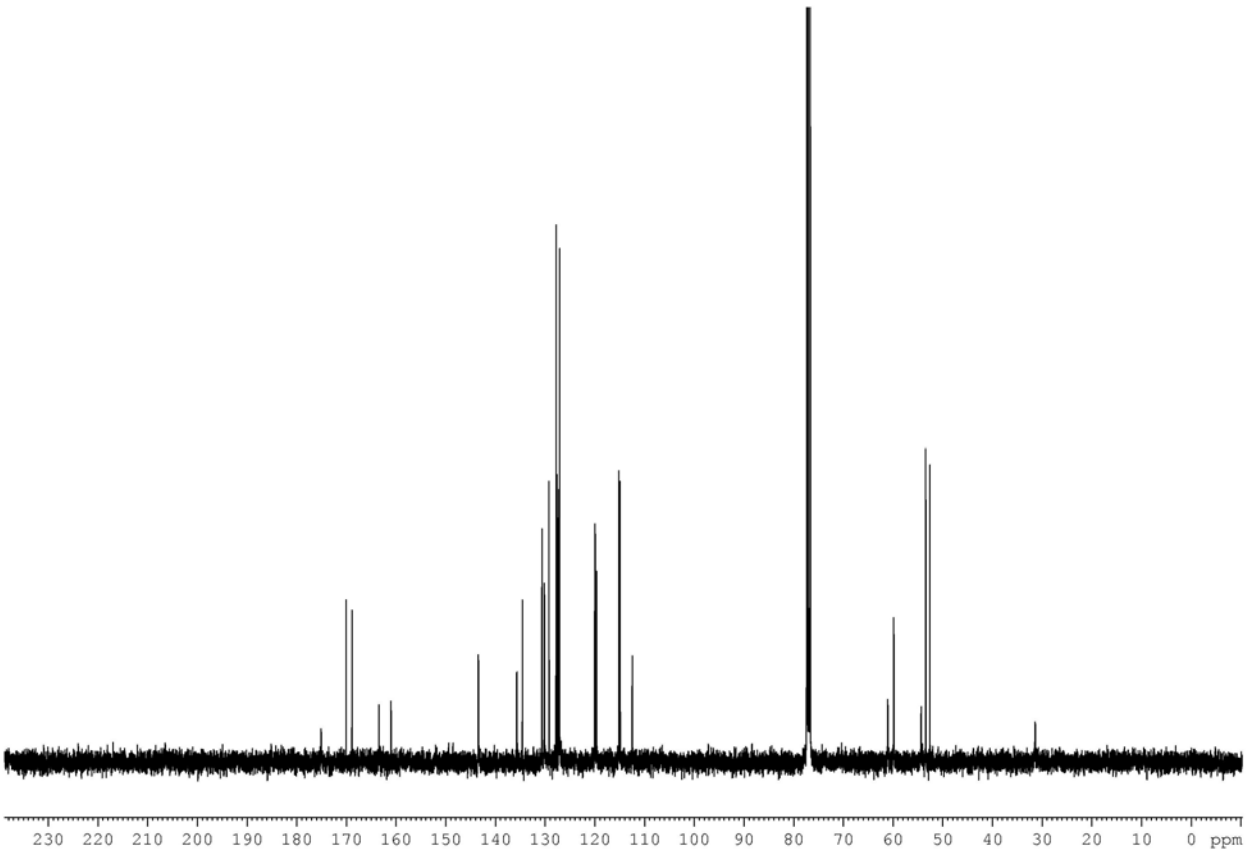
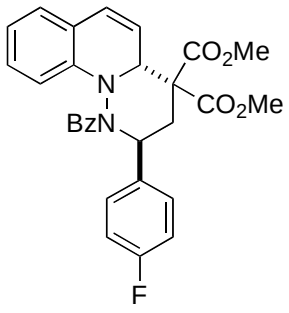
10
ppm


CO2Me
CO2Me
N
BzN
F

cis-**3f**

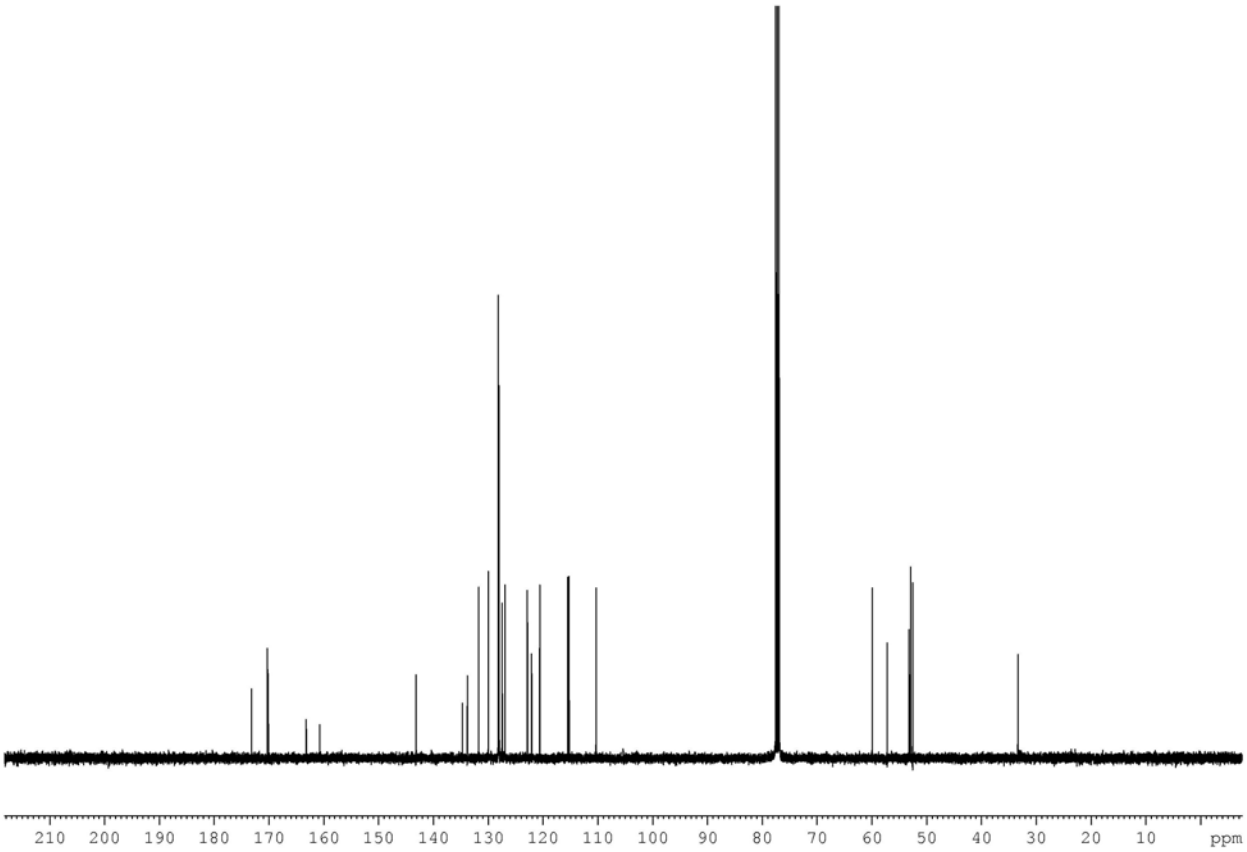
9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.01
1.11
2.53
2.06
2.02
1.02
1.00
0.99
0.98
0.98
1.02
3.03
3.00
1.00
1.00

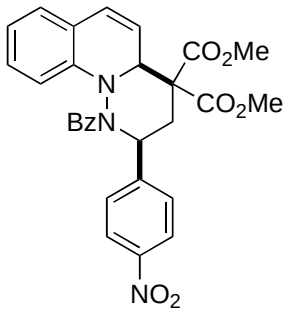

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO2Me
CO2Me
N
BzN
F

trans-**3f**

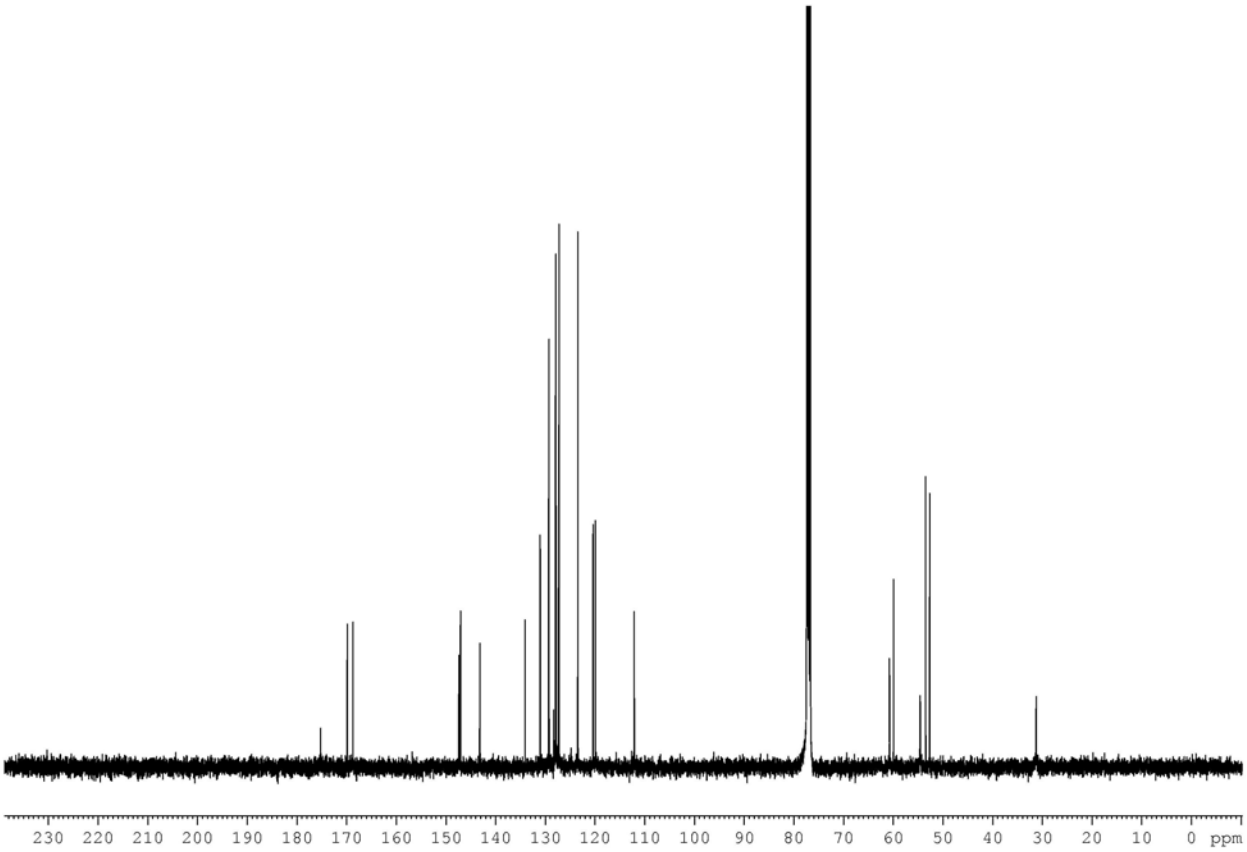
9
8
7
6
5
4
3
2
1
0
ppm
2.01
2.07
1.04
4.01
3.06
1.06
1.02
1.00
1.00
1.00
1.00
3.00
3.00
1.02
1.00

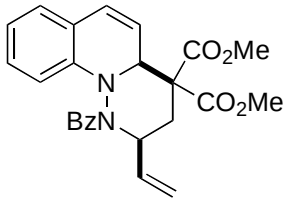

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


CO2Me
CO2Me
N
BzN
NO2

cis-**3g**

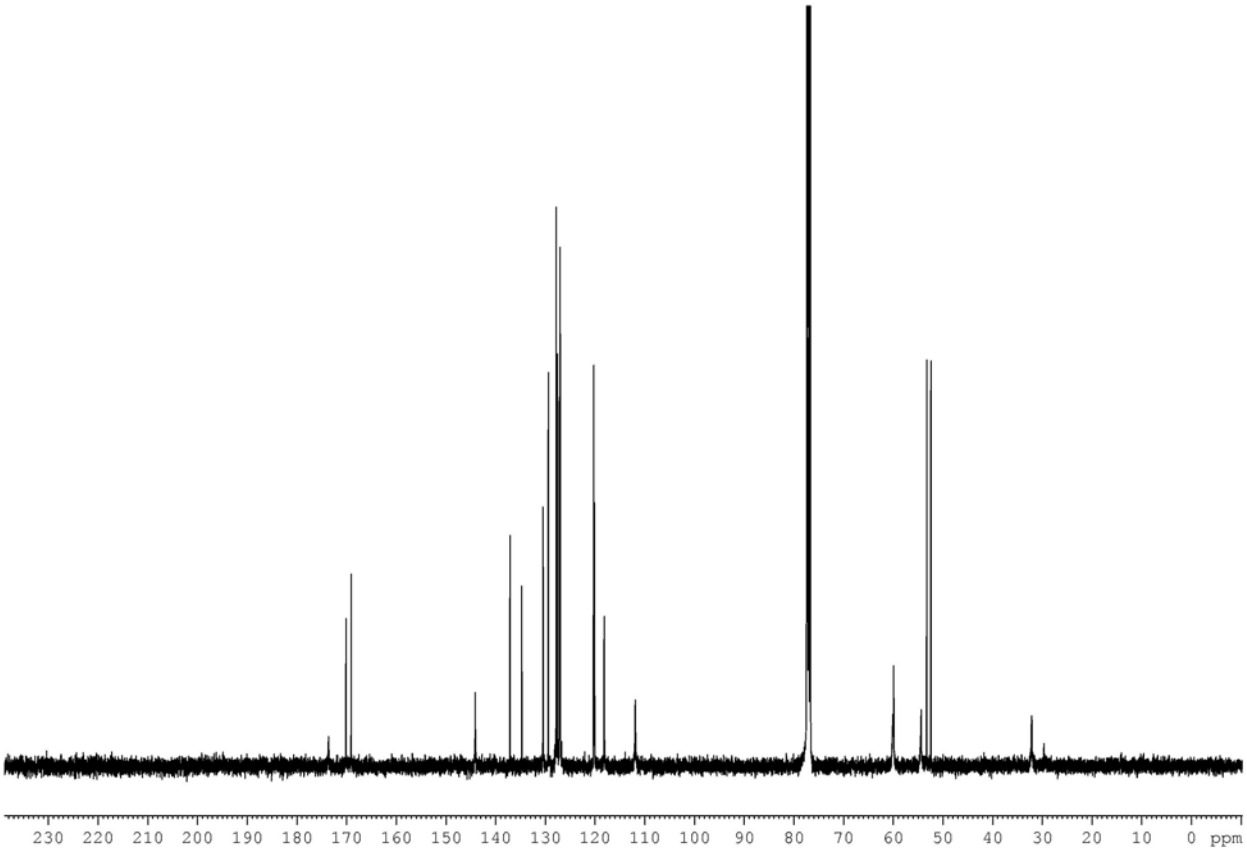
9
8
7
6
5
4
3
2
1
0
ppm
1.76
4.02
1.05
5.21
2.07
1.04
1.00
1.02
3.08
3.14
3.00
1.01
0.99

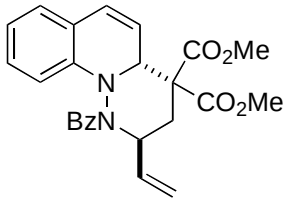

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO2Me
CO2Me
N
BzN

cis-**3h**

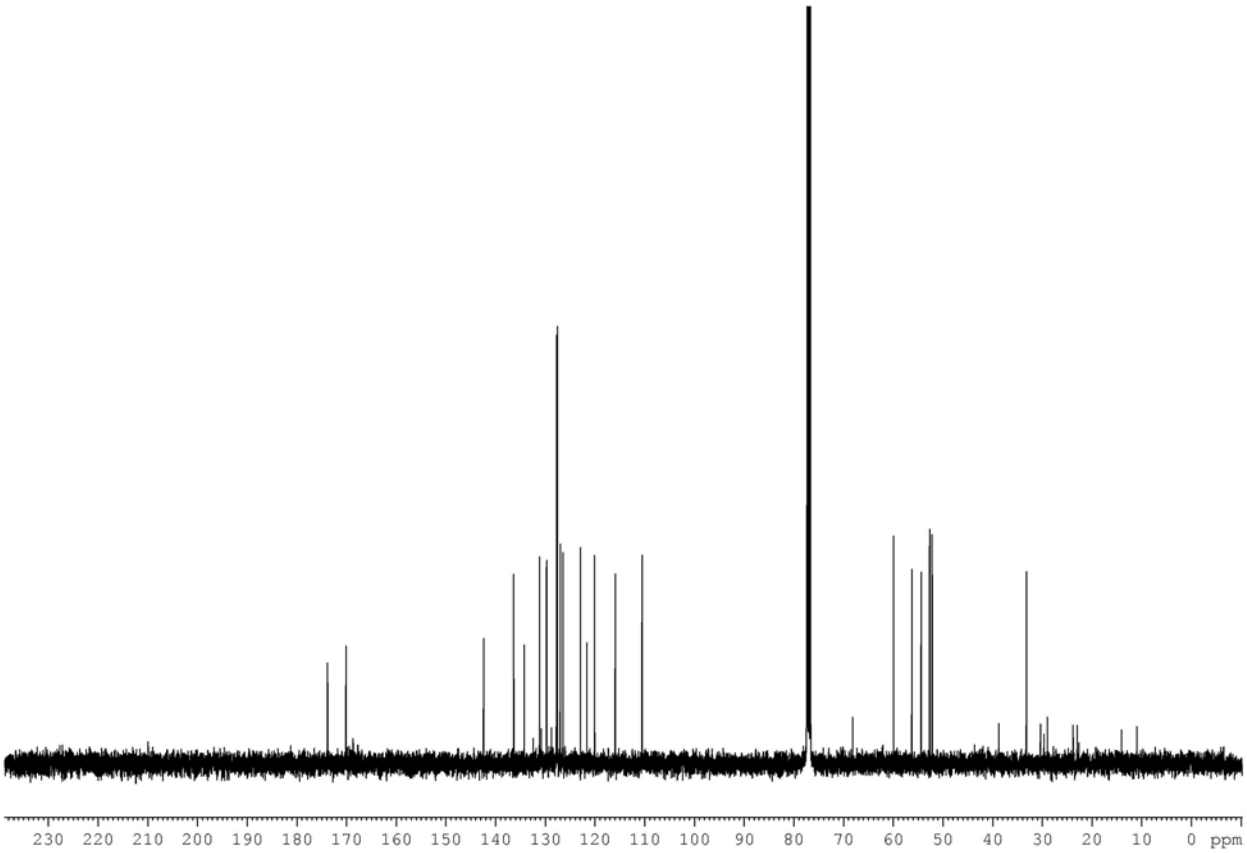
9
8
7
6
5
4
3
2
1
0
ppm
1.91
1.04
3.50
1.07
0.99
1.01
0.99
0.97
0.97
2.97
1.03
0.94
3.00
2.96
2.04

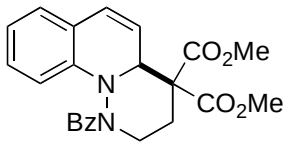

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO2Me
CO2Me
N
BzN

trans-**3h**

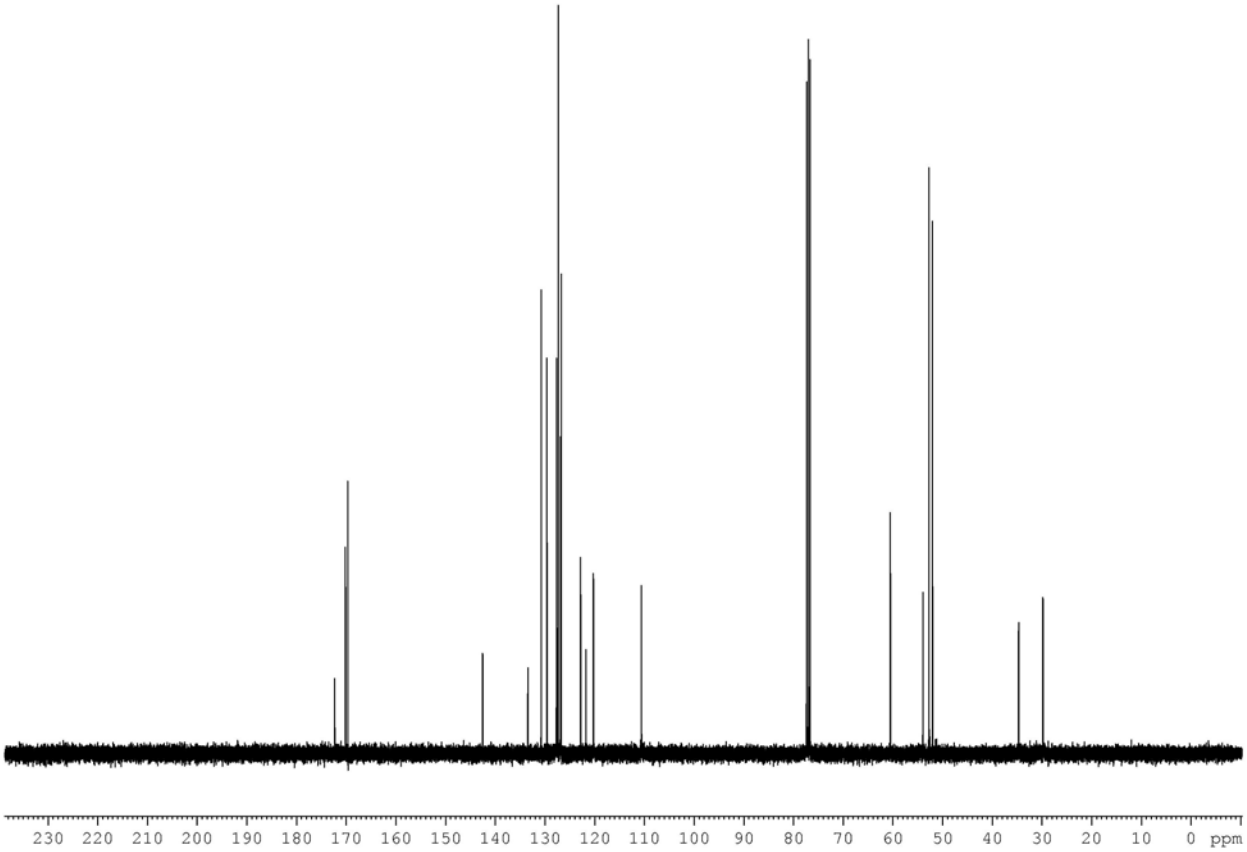
9
8
7
6
5
4
3
2
1
0
ppm
8.21
4.20
12.63
4.28
4.17
4.20
4.07
4.16
4.11
4.32
4.20
8.25
12.45
12.30
8.45

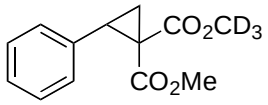

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO2Me
CO2Me
N
BzN

3i

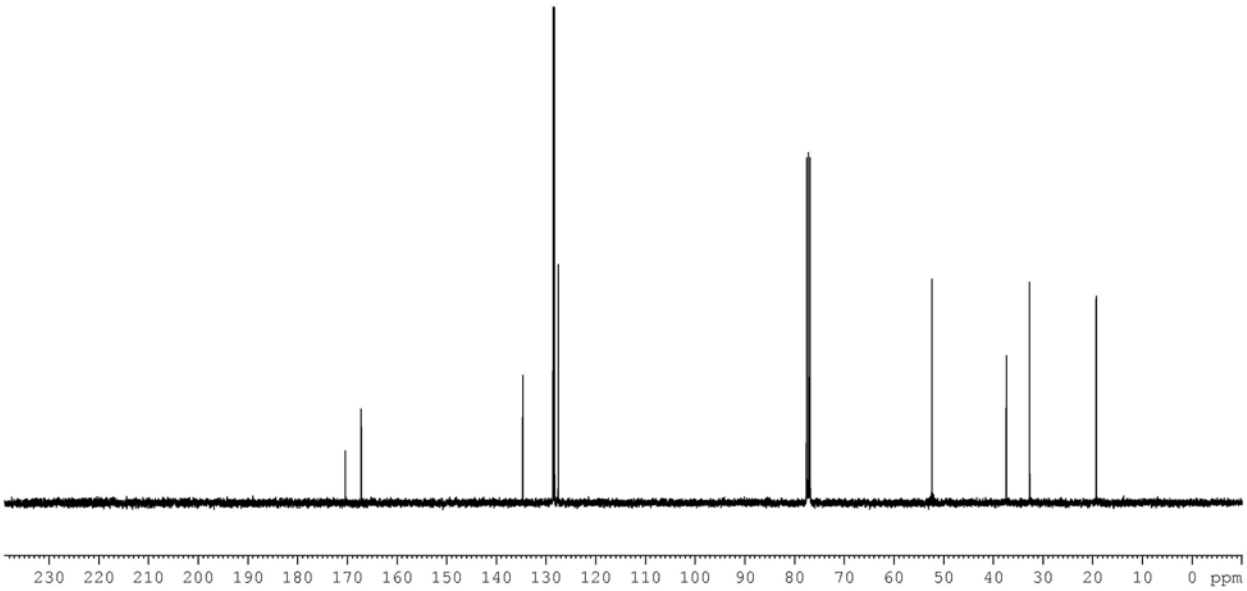
9
8
7
6
5
4
3
2
1
0
ppm

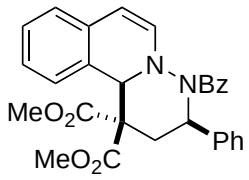

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO_2CD_3
CO_2Me

4

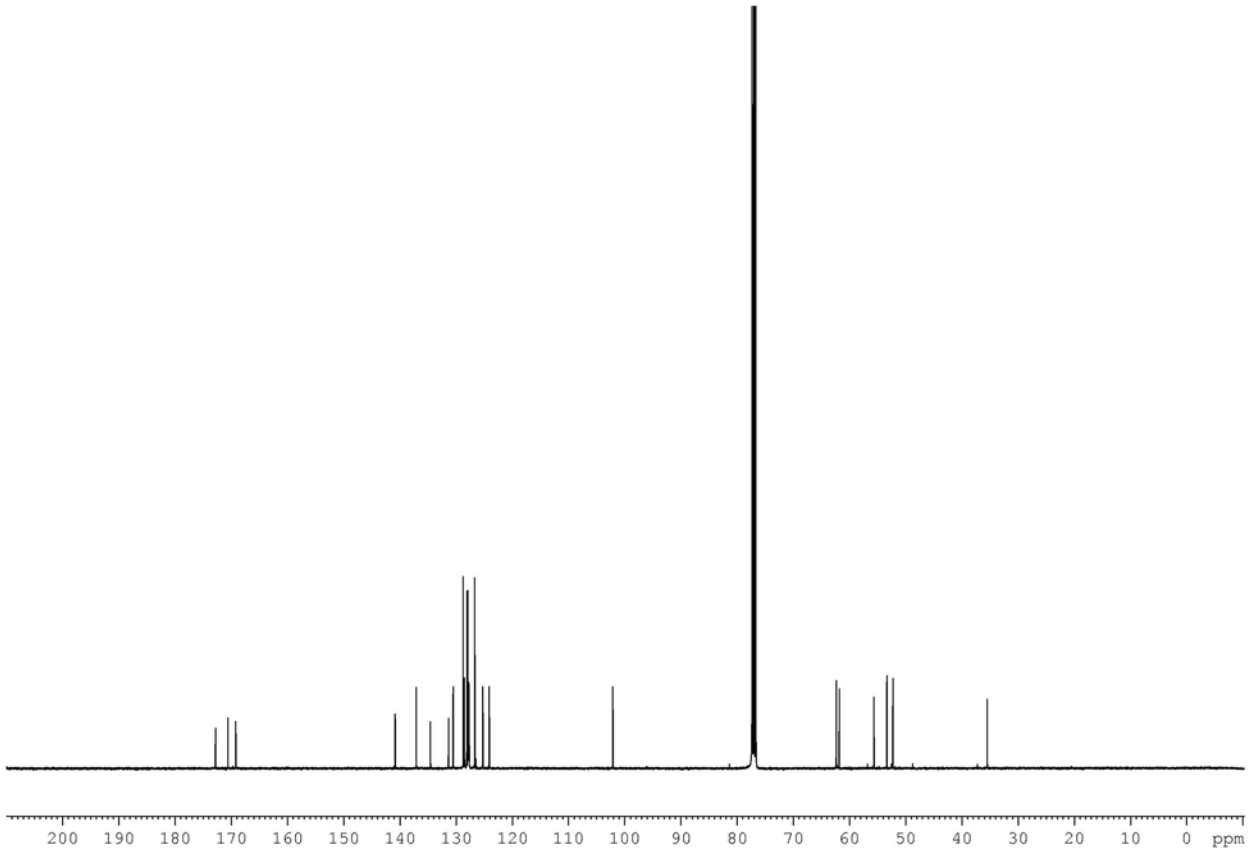
9
8
7
6
5
4
3
2
1
0
ppm
5.10
3.00
1.00
1.04
1.03

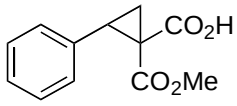

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


N
NBz
MeO2C
Ph
MeO2C

8

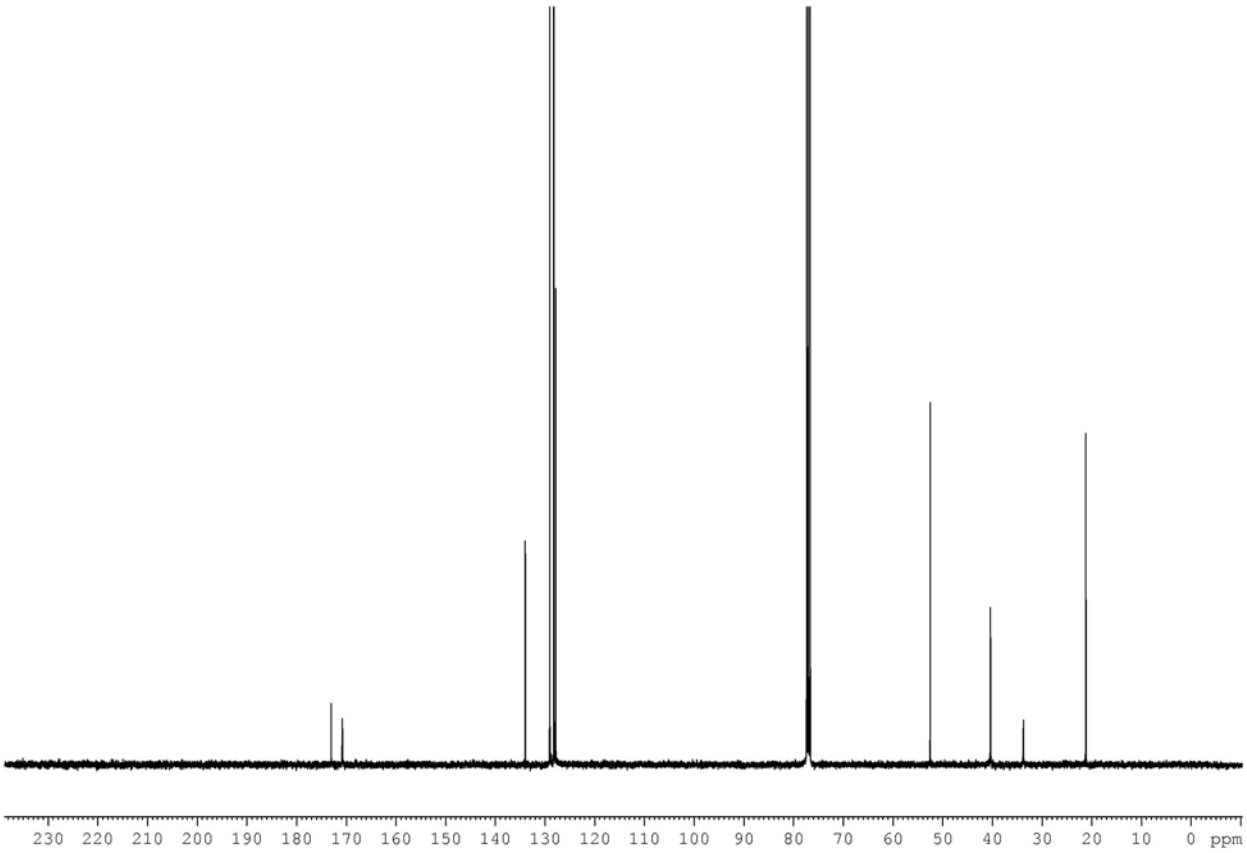
9
8
7
6
5
4
3
2
1
0
ppm
2.02
2.04
6.33
1.06
2.03
1.02
1.01
0.99
1.00
1.03
3.00
1.17
3.01
1.02

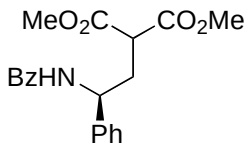

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


CO2H
CO2Me

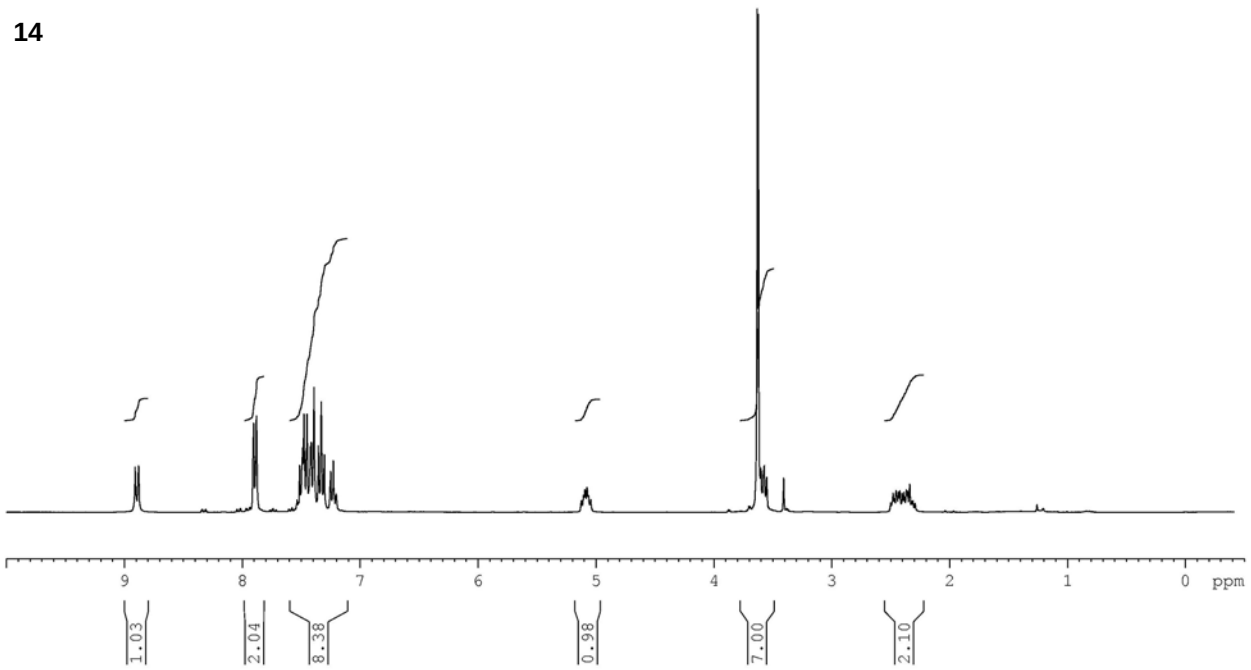
9

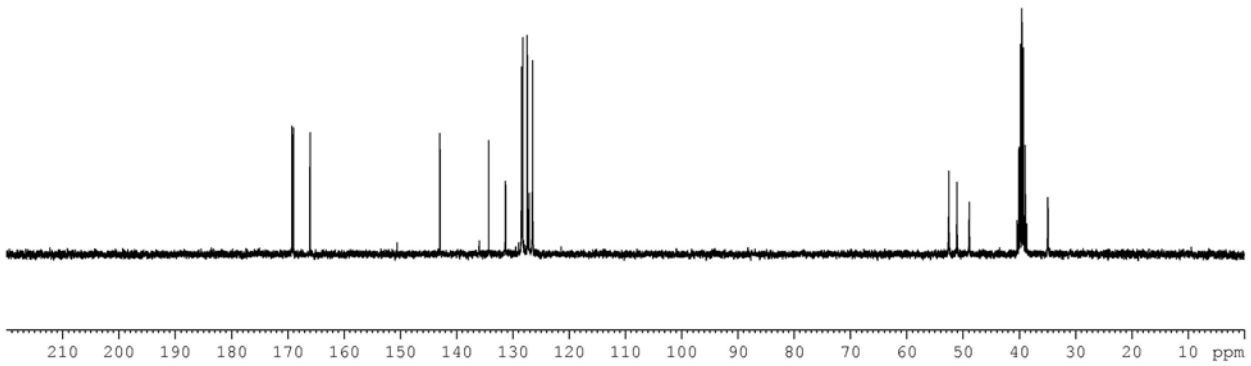
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
5.18
1.04
3.00
1.02
1.00

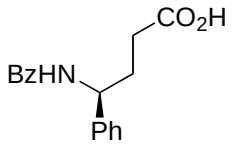

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


MeO2C
CO2Me
BzHN
Ph

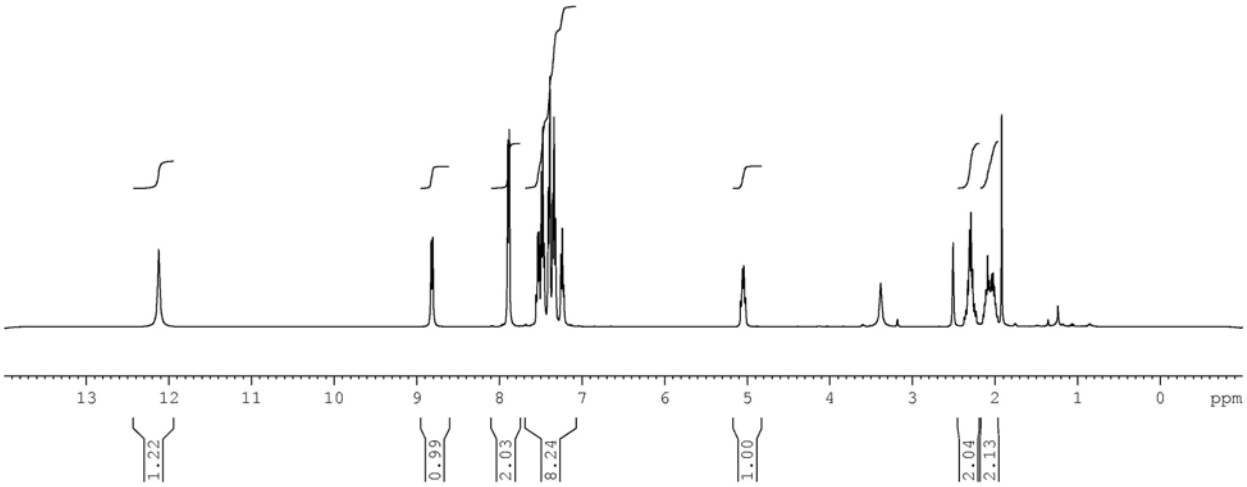
14

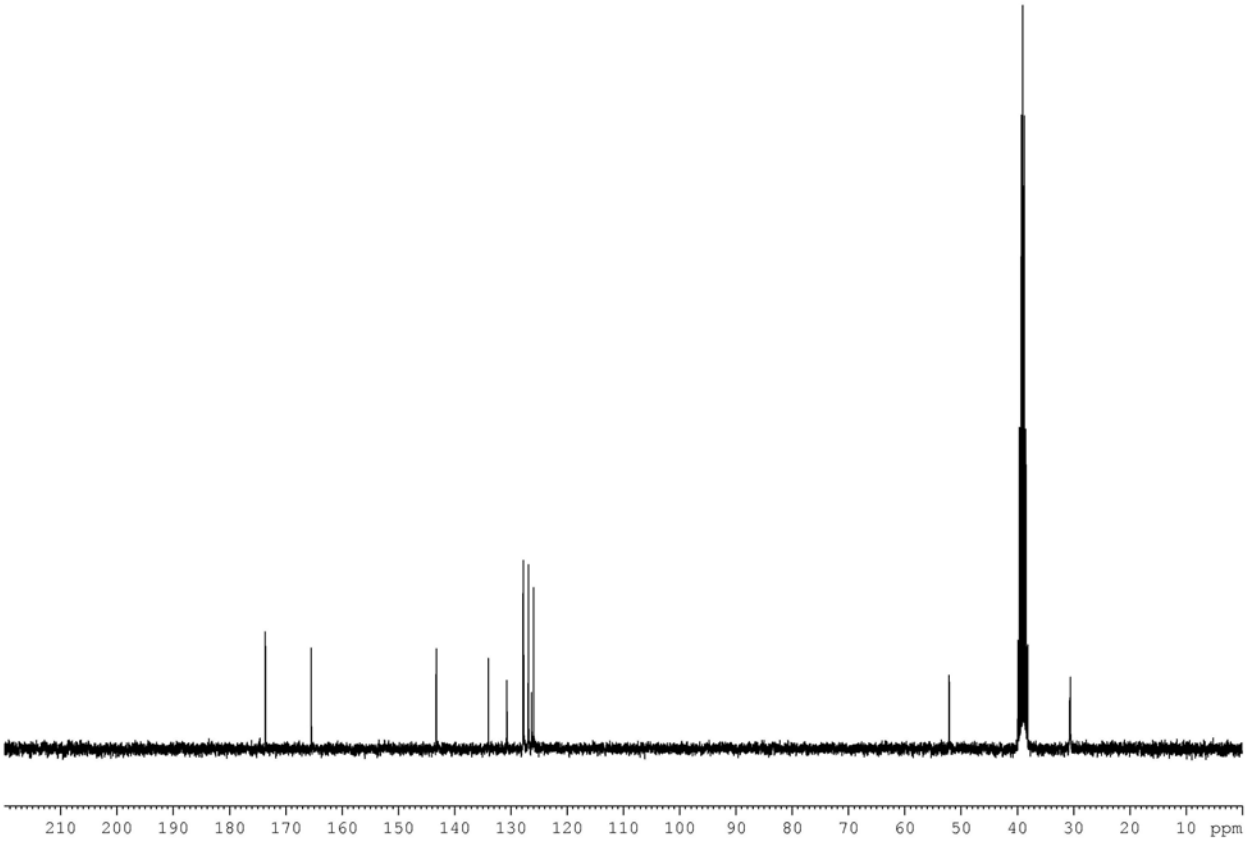

9
8
7
6
5
4
3
2
1
0
ppm
1.03
2.04
8.38
0.98
7.00
2.10

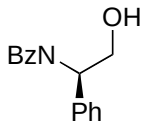

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


CO2H
BzHN
Ph

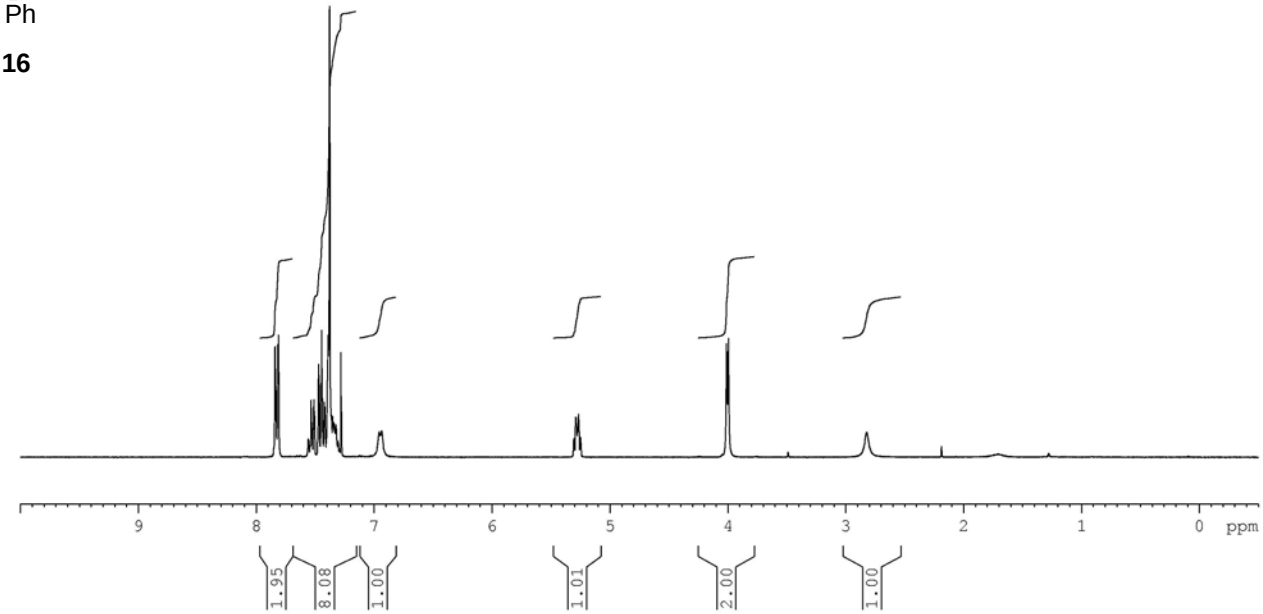
15

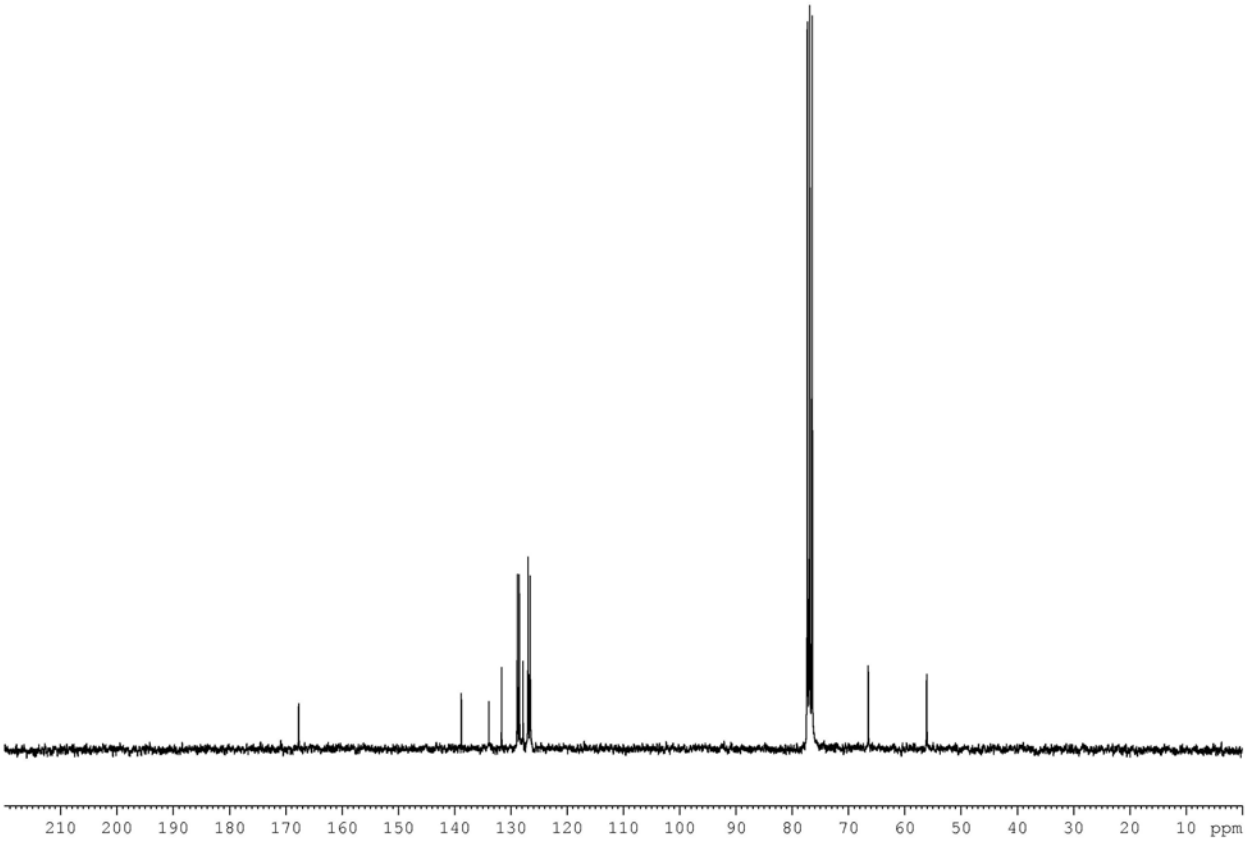

13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.22
0.99
2.03
8.24
1.00
2.04
2.13

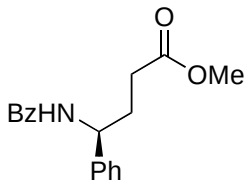

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OH
BzN
Ph

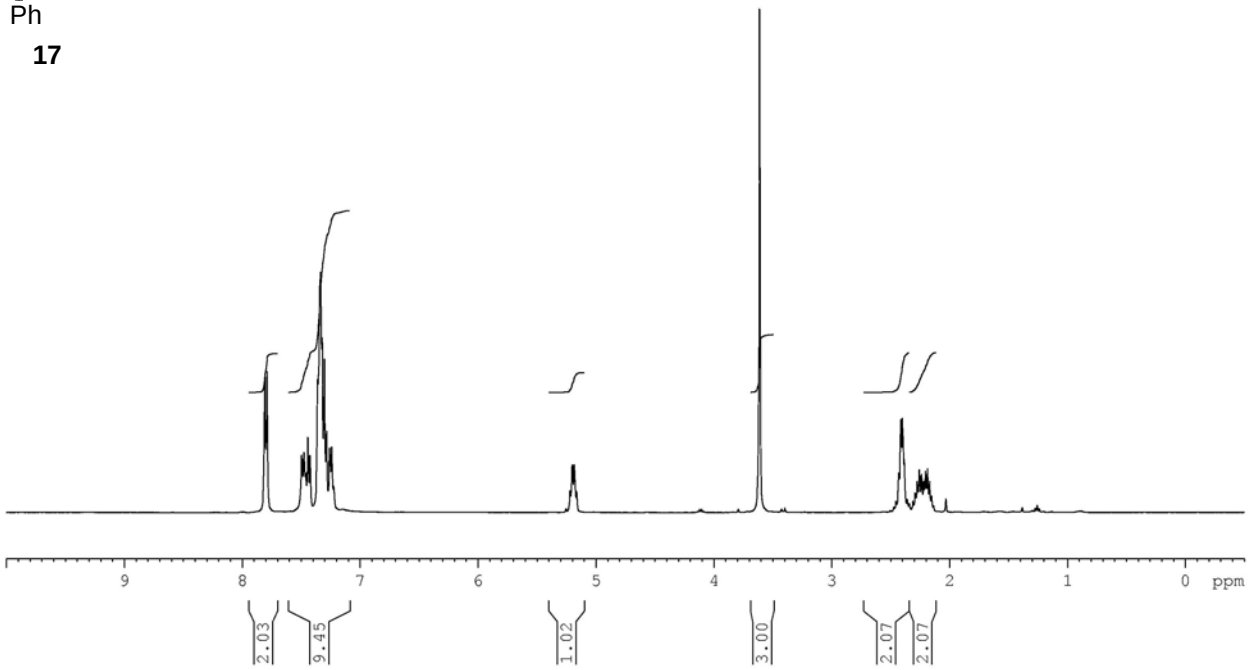
16

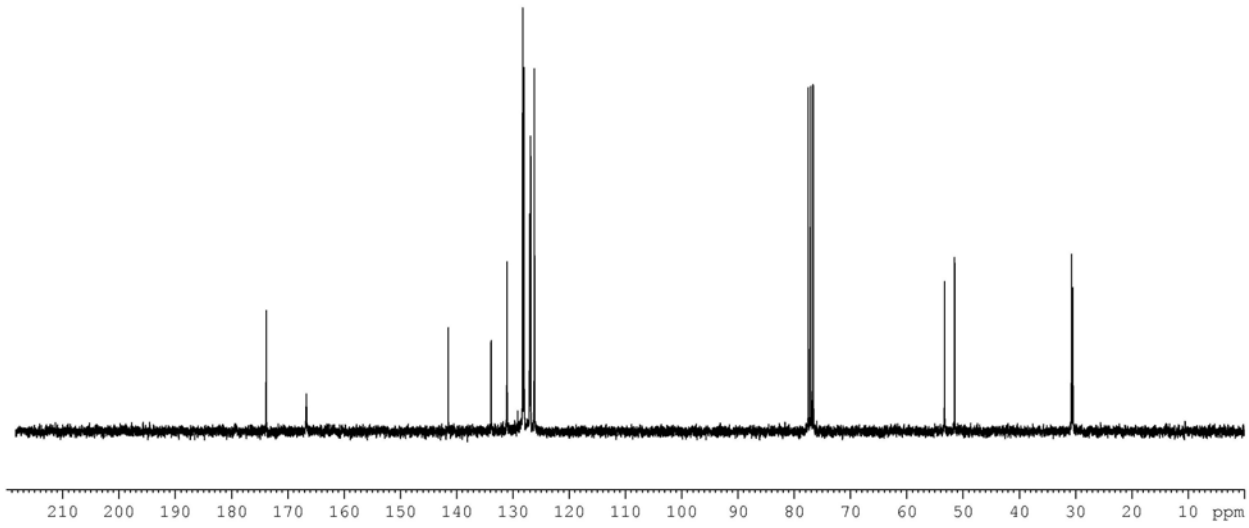

9
8
7
6
5
4
3
2
1
0
ppm
1.95
8.08
1.00
1.01
2.00
1.00

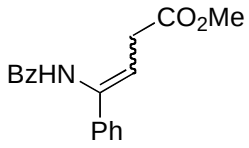

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


O
OMe
BzHN
Ph

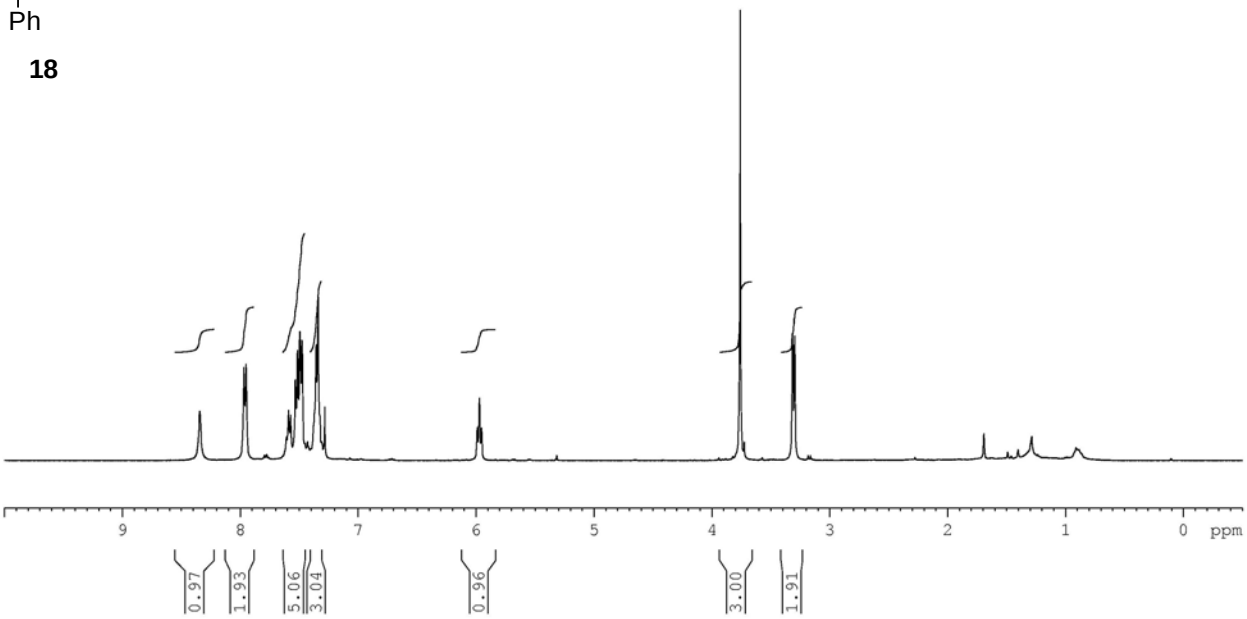
17

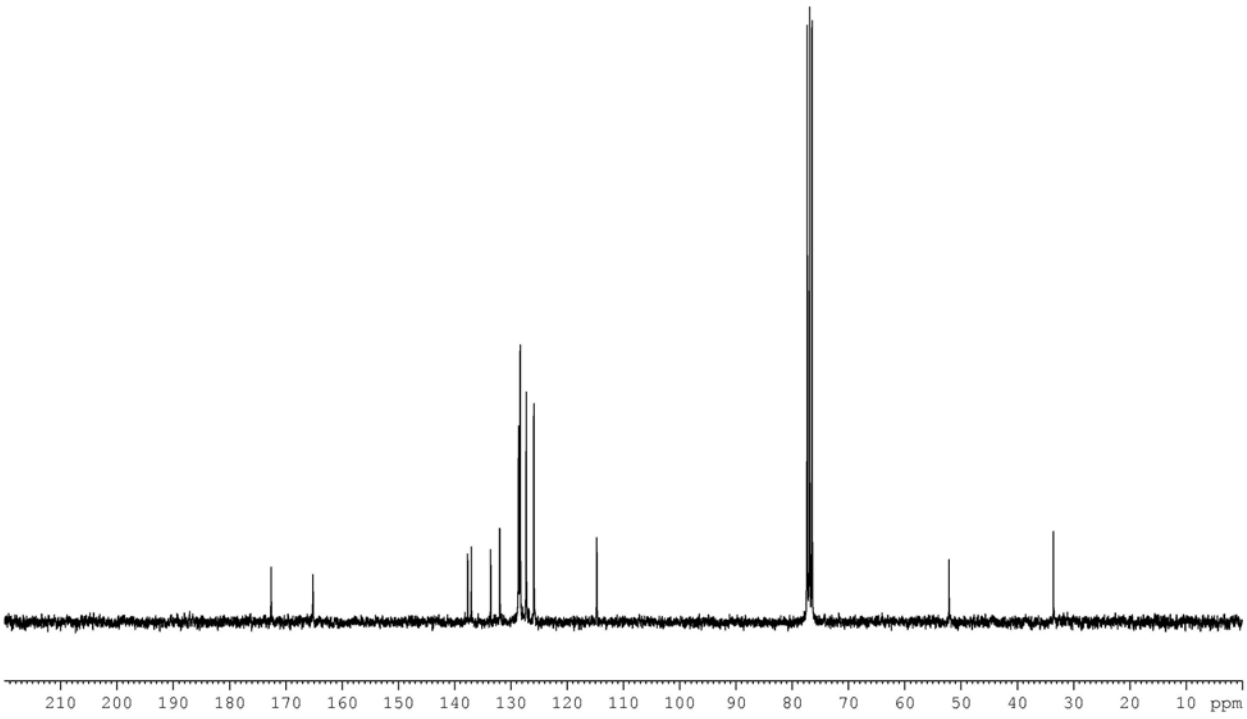

9
8
7
6
5
4
3
2
1
0
ppm
2.03
9.45
1.02
3.00
2.07
2.07


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


CO2Me
BzHN
Ph

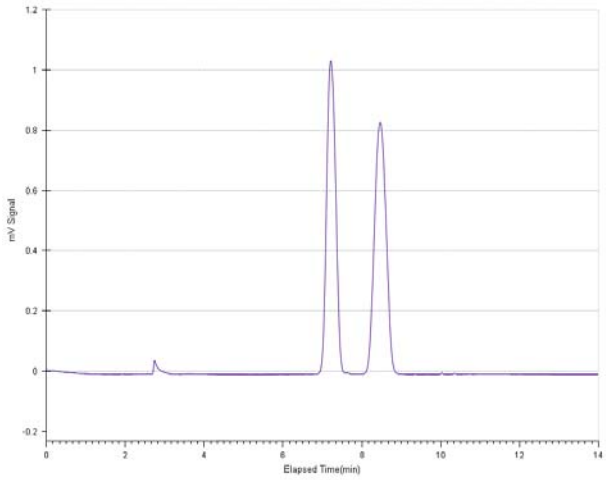
18

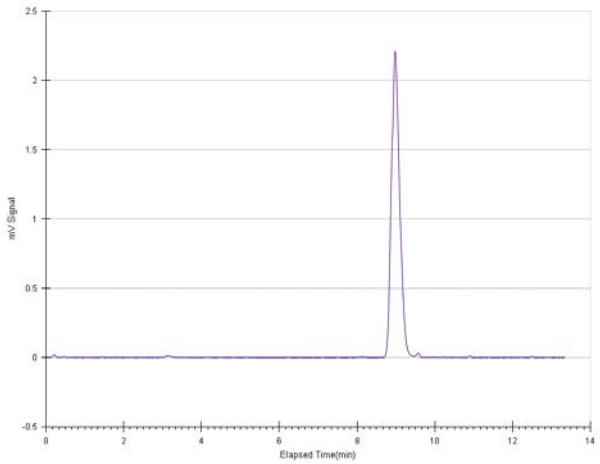

9
8
7
6
5
4
3
2
1
0
ppm
0.97
1.93
5.06
3.04
0.96
3.00
1.91


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

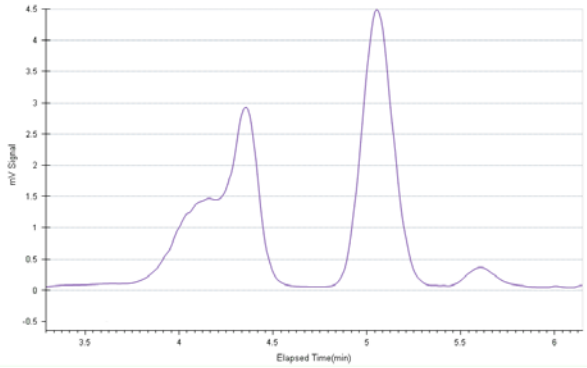
SFC Traces of 1:1 mixtures and enantioenriched compounds

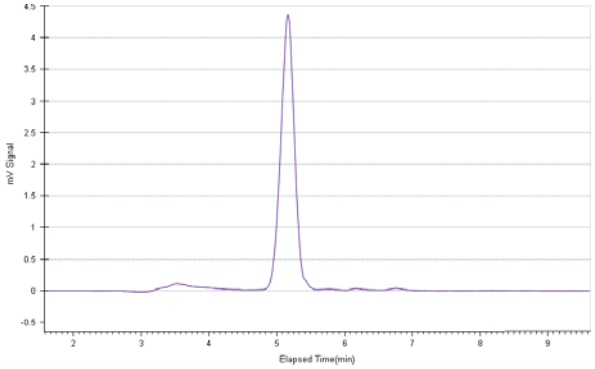
Compound **2a** (1:1 and enantioenriched):



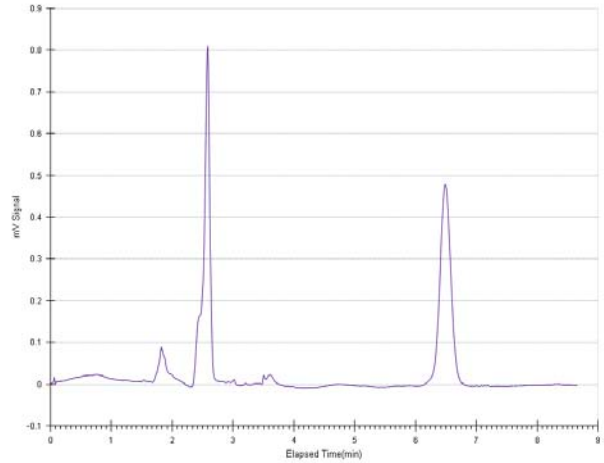


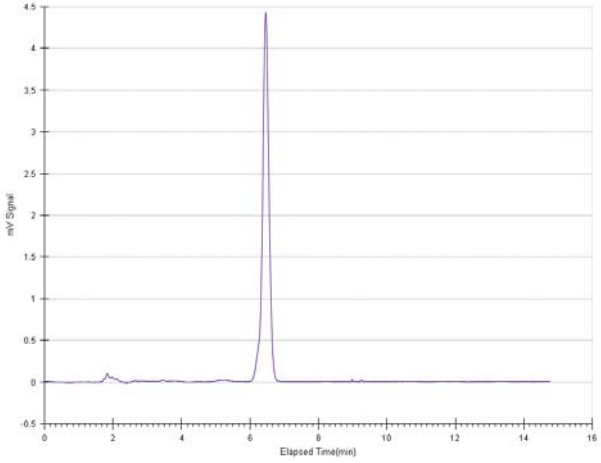
Compound *cis*-**3a** (1:1 and enantioenriched):



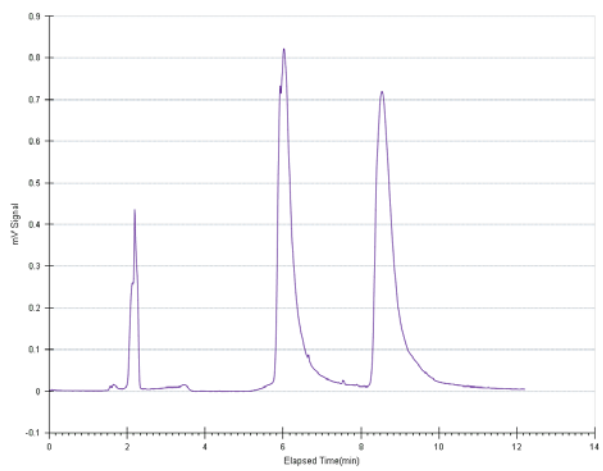


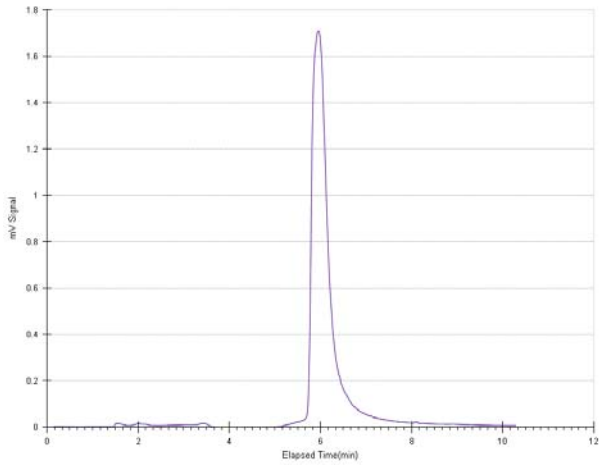
Compound *trans*-**3a** (1:1 and enantioenriched):



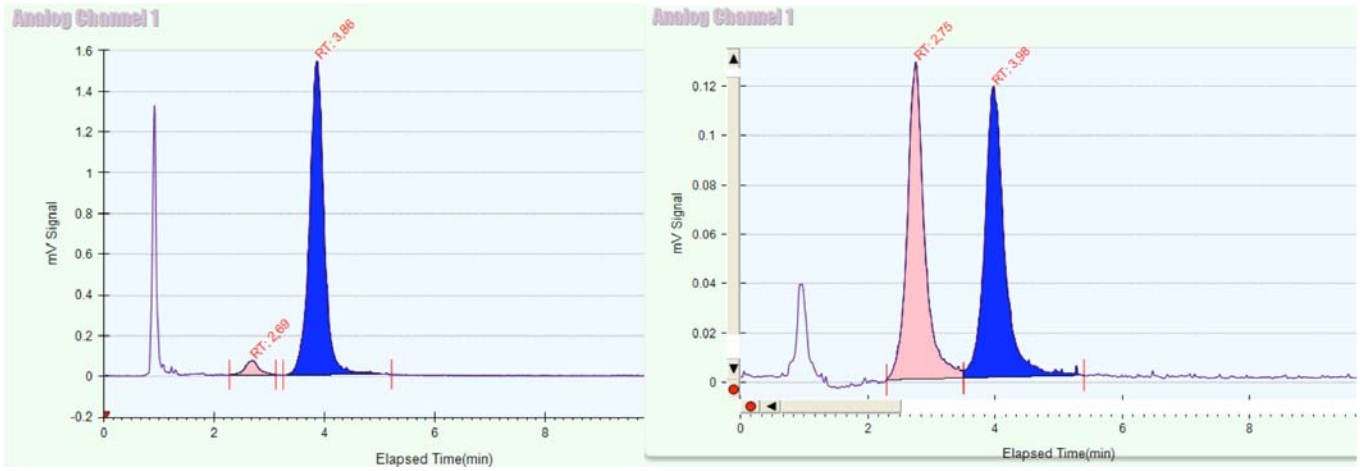


Compound **9** (1:1 and enantioenriched):





Compound **15** (1:1 and from (*S*)-**3a**)



Compound **15** (from D-(**–**)-phenylglycine)