Urea Catalyzed Construction of Oxazinanes

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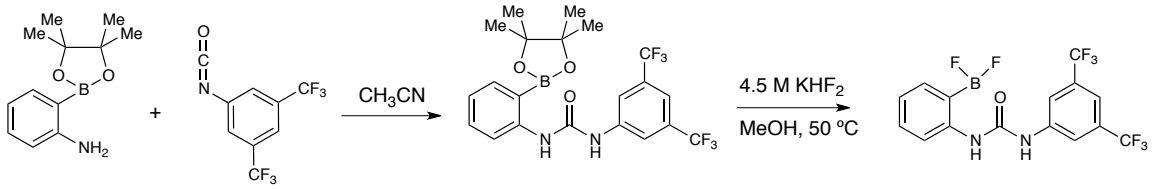
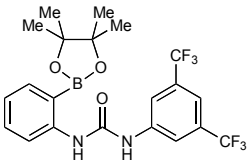
General Methods: Methylene chloride was purified by passage through a bed of activated alumina.[1] Purification of reaction products was carried out by flash chromatography using Aldrich 60 Å (40 - 63 μm). Analytical thin layer chromatography was performed on EMD Chemicals 0.25 μm silica gel 60-F_{254} plates. Visualization was accomplished with UV light and ceric ammonium molybdate stains followed by heating. Melting points (**mp**) were obtained on a Thermo Scientific Mel-temp apparatus and are uncorrected. Infrared spectra (**IR**) were obtained on a Perkin Elmer Spectrum 100R spectrophotometer. Infrared spectra for liquid products were obtained as a thin film on a NaCl disk and spectra for solid products were collected by preparing a NaBr pellet containing the title compound. Proton nuclear magnetic resonances (**^{1}H NMR**) were recorded in deuterated solvents on a Bruker Avance AVIII 400 (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm, δ) using the solvent as internal standard ($CDCl_3$, δ 7.26 and DMSO, δ 2.50). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m) or broad (br). Coupling constants are reported in Hertz (Hz). Proton-decoupled carbon (**^{13}C NMR**) spectra were recorded on a Bruker Avance AVIII 400 (100 MHz) spectrometer and are reported in ppm using the solvent as an internal standard ($CDCl_3$, δ 77.0; DMSO, δ 39.5). Proton decoupled fluorine (**^{19}F NMR**) spectra were recorded on a Bruker Avance AVIII 400 (376 MHz) spectrometer and are reported in ppm using

$CF_3C_6H_5$ as an external standard (-63.72). Boron spectra (**^{11}B NMR**) were recorded on a Bruker Avance DPX 500 (160 MHz) or Bruker Avance AVIII 400 (128 MHz) spectrometer and are reported in ppm using BF_3•OEt_2 as an external standard (0.00). Electrospray mass spectra (**ESI-MS**) were obtained using a Bruker MicrOTOF Mass Spectrometer. Unless otherwise noted, all other commercially available reagents and solvents were purchased from Aldrich and used without further purification.

Procedure for the Preparation of Boronate Urea 9a:

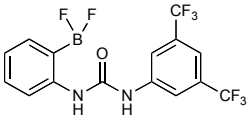


Synthesis of boronate urea pinacol ester:[2]



A flame-dried round bottom flask under N_2 was charged with 2-aminophenyl boronic acid pinacol ester (600 mg, 2.74 mmol). Dry acetonitrile (30 mL) was added to create a clear and colorless solution. Last, 3,5-*bis*-trifluoromethylphenyl isocyanate (473 μL, 2.74 mmol) was introduced to the reaction flask dropwise by syringe. Shortly after addition of the isocyanate, a white precipitate began to form. The reaction was allowed to stir at 23 °C for 4 h. The pure boronate urea pinacol ester was isolated as a white solid after vacuum filtration followed by washing with hexanes. The solid was dried under vacuum (83%). R_f = 0.94 (4:4:1 ethyl acetate/hexanes/methanol); mp 215.2 – 216.9 ºC; IR (NaBr) 3415, 3132, 2985, 1640, 1600, 1581, 1476, 1184, 1129 cm^{-1}; ^{1}H NMR (400 MHz, DMSO d_6) δ 9.93 (br s, 1H); 9.19 (br s, 1H); 8.16 (s, 2H); 7.69 (s, 1H); 7.52-7.50 (m, 1H); 7.42-7.34 (m, 2H); 7.08-7.04 (m, 1H); 1.24 (s, 12H); ^{13}C NMR (100 MHz, DMSO d_6) δ 154.0, 142.2, 141.7, 134.7, 131.2 (q, J = 33 Hz, CCF_3), 130.8, 123.8 (q, J = 271 Hz, CF_3), 123.4, 119.7, 119.4 (d, J = 6 Hz, CF_3), 155.61-155.5 (m), 83.0, 25.5 (the carbon bonded to boron was not seen due to broadening)[3]; ^{11}B NMR (160 MHz, DMSO d_6) δ 26.0 (br s); HRMS (ESI): Mass calculated for $C_{21}H_{21}BF_6N_2O_3$ $[M+H]^+$, 475.1622. Found $[M+H]^+$, 475.1614.

Synthesis of difluoroboronate urea 9a:[2]

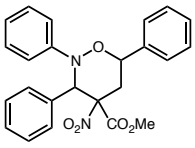


9a: A flame-dried round bottom flask under N_2 was charged with boronate urea pinacol ester (4.6 mmol) and freshly distilled MeOH (30 mL). Aqueous KHF_2 (4.5 M, 18.4 mmol) was introduced to the reaction flask dropwise by syringe, resulting in a white heterogenous mixture, and the reaction was heated to 50 °C. Shortly after heating, the reaction became a clear and colorless solution. After 2 h at 50 °C, the reaction was cooled to 23 °C and concentrated. The white solid was filtered and washed with water to afford the potassium trifluoroboryl urea salt (92%). The urea salt (1.95 g, 4.29 mmol) was dissolved in ethyl acetate (15 mL) and extracted twice with water (5 mL). The organic layer was dried and concentrated to afford a white solid, which was then dissolved in a minimal volume of hot acetonitrile. The solution was allowed to cool to room temperature and then placed in an ice bath. The precipitate was filtered off and the filtrate was concentrated to afford difluoroboryl urea **9a** (1.23 g, 3.11 mmol, 72%) as a white powder. R_f = 0.74 (4:4:1 ethyl acetate/hexanes/methanol); mp 205.3 – 205.9 ºC; IR (NaBr) 3628, 3345, 2986, 1741, 1671, 1585, 1479, 1187, 1128 cm^{-1}; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.27 (br s,

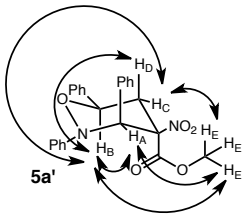
1H); 10.65 (br s, 1H); 8.11 (s, 2H); 7.96 (s, 1H); 7.42-7.40 (m, 1H); 7.32-7.28 (m, 1H); 7.15-7.10 (m, 2H); ^{13}C NMR (100 MHz, DMSO d_6) δ 154.5, 138.1, 137.4, 131.5, 131.2, 130.9, 130.6, 128.2, 124.7, 123.0, 123.0 (q, J = 267 Hz, CF_3), 118.4, 115.4; ^{11}B NMR (160 MHz, DMSO d_6) δ 3.63 (br s); ^{19}F NMR (376 MHz, DMSO d_6) δ –61.7 (s, 6F), –132.8 (s, 1F), –132.9 (s, 1F); HRMS (ESI): Mass calculated for $C_{21}H_{21}BF_6N_2O_3$ $[M+H]^+$, 419.0572. Found $[M+H]^+$, 419.0580.

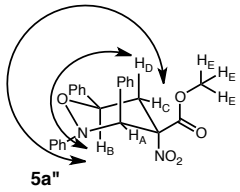
General procedure for the preparation of nitrones:
Nitrones were synthesized following a known procedure.[4] A flame-dried 1000 mL round bottom flask containing a stirbar was charged with aldehyde (98.379 mmol), nitro compound (2.0 eq), and zinc dust (3.0 eq) in 500 mL 95% EtOH under an argon atmosphere. After the solution was cooled to 0 ºC, glacial acetic acid (6.0 eq) was added dropwise. The reaction was warmed to room temperature and stirred for 24 hours. The mixture was filtered through a Celite pad and the crude nitrone was concentrated under reduced pressure. Nitrones were purified via recrystallization.

General procedure for the cycloaddition of nitrocyclopropane carboxylates and nitrones:
A dry, screw-capped reaction vial containing a magnetic stir bar was charged with nitrocyclopropane carboxylate (0.136 mmol) and catalyst **9a** (0.0204 mmol). The vial was fitted with a cap and septa and placed under a positive pressure of argon. Dry toluene (272 μL) was added followed immediately by a nitrone (0.203 mmol). The reaction was allowed to stir at 80 °C for 24 hours. The reaction was allowed to cool to room temperature and then was immediately purified by flash column chromatography with silica gel. Select oxazinane products were further purified by recrystallization when noted.

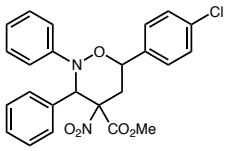


5a: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 52.3 mg of **5a** (91%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.42 (m, 10H); 7.26-7.08 (m, 11H); 6.89-6.84 (m, 1.5H); 6.07 (s, 0.5H); 5.98 (s, 1H); 5.08-5.00 (m, 1.5H); 4.01-4.01 (m, 3H); 3.54-3.54 (m, 1.5H); 3.26-3.01 (m, 3H). Recrystallization (20:80 ethyl acetate/hexanes) yielded the major diastereomer. The following characterization is for the major diastereomer: mp 187.5- 188.8 °C; FTIR (film) 3054, 2987, 1559, 1421, 1265, 1180, 739, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.56 (m, 4H); 7.52-7.42 (m, 3H); 7.25-7.16 (m, 5H); 7.12-7.09 (m, 2H); 6.90-6.85 (m, 1H); 5.99 (s, 1H); 5.04 (dd, J = 11.6, 2 Hz, 1H); 4.01 (s, 3H); 3.17 (dd, J = 14, 12 Hz, 1H); 3.01 (ddd, J = 13.6, 2.4, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.6, 137.9, 132.0, 128.9, 128.9, 128.7, 128.4, 126.5, 122.4, 116.1, 93.4, 78.5, 66.6, 54.5, 32.9; HRMS (ESI): Mass calculated for $C_{24}H_{22}N_2O_5$ $[M+Na]^+$, 441.1421. Found $[M+Na]^+$, 441.1439.

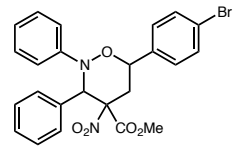




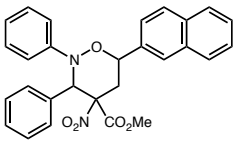
A NOESY experiment was performed in an attempt to assign the relative stereochemistry of the major diastereomer (**5a'**) and minor diastereomer (**5a"**) of oxazinane **5a**. nOe correlations of **5a'** were seen between H_A/H_B, H_A/H_E, H_B/H_C, H_B/H_D, H_B/H_E, H_C/H_D, and, H_C/H_E. Similar NOESY experimentation was performed with the minor diastereomer (**5a"**) which gave nOe correlations between H_B/H_C, H_B/H_D, and H_C/H_D. Based on the nOe signals it was determined that the diastereomers were epimeric at the stereogenic carbon containing the nitro group due to the fact that H_E does not show a nOe with any other proton in **5a"**. Therefore, we propose that the ester functionality is equatorial in **5a"**. Crystal structures grown from racemic product of the major diastereomer **5a'** and minor diastereomer **5a"** were obtained to confirm the relative stereochemistry.



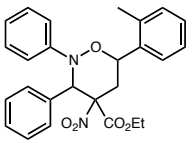
5b: The reaction was allowed to stir at 80 °C for 24 hours with methyl 2-(4-chlorophenyl)-1-nitrocyclopropanecarboxylate (34.8 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 41.3 mg of **5b** (67%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: FTIR (film) 3054, 2956, 1758, 1598, 1559, 1492, 1265, 1091, 824, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58-7.49 (m, 3H); 7.47-7.41 (m, 6H); 7.30 (s, 1.5H); 7.24-7.15 (m, 9H); 7.09-7.06 (m, 3H); 6.90-6.86 (m, 1.5H); 6.02 (s, 0.5H); 5.97 (s, 1H); 5.05-4.99 (m, 1.5H); 4.01 (s, 3H); 3.54 (s, 1.5H); 3.29-3.20 (m, 1H); 3.14-3.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2; 164.0; 147.5; 147.5; 136.7; 136.3; 134.8; 132.5; 131.9; 130.6; 130.2; 130.0; 129.1; 129.0; 129.0; 128.8; 128.7; 128.7; 128.6; 128.5; 128.4; 128.0; 127.9; 127.7; 127.7; 127.5; 122.6; 116.2; 94.9; 93.2; 77.8; 66.7; 54.6; 53.7; 32.9; 32.8; HRMS (ESI): Mass calculated for $C_{24}H_{21}ClN_2O_5$ $[M+Na]^+$, 475.1031. Found $[M+Na]^+$, 475.1033.



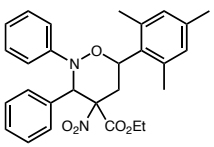
5c: The reaction was allowed to stir at 80 °C for 24 hours with methyl 2-(4-bromophenyl)-1-nitrocyclopropanecarboxylate (39.4 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 diethyl ether/hexanes to 20:80 diethyl ether/hexanes) yielding 49.2 mg of **5c** (73%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: FTIR (film) 3054, 2986, 2958, 1759, 1597, 1558, 1491, 1454, 1256, 1047, 1012, 909, 738, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64–7.55 (m, 5H); 7.42-7.40 (m, 4H); 7.27-7.16 (m, 8H); 7.10-7.08 (m, 3H); 7.00-6.87 (m, 2H); 6.07 (s, 0.5H); 5.99 (s, 1H); 5.05-4.99 (m, 1H); 4.01 (s, 3H); 3.54 (s, 1.5H); 3.31-3.21 (m, 1H); 3.15-3.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.0, 147.5, 147.5, 138.0, 137.2, 126.9, 132.0, 132.0, 131.5, 130.6, 130.2, 130.0, 129.0, 128.8, 128.7, 128.7, 128.5, 128.4, 128.1, 128.0, 128.0, 127.8, 122.9, 122.7, 116.2, 94.9, 93.2, 77.99, 66.7, 66.2, 54.6, 53.7, 53.5, 32.8, 32.8; HRMS (ESI): Mass calculated for $C_{24}H_{21}ClN_2O_5$ $[M+Na]^+$, 519.0526. Found $[M+Na]^+$, 519.0527.



5d: The reaction was allowed to stir at 80 °C for 24 hours with methyl 2-(naphthalen-2-yl)-1-nitrocyclopropanecarboxylate (36.8 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 64.9 mg of **5d** (99%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.89 (m, 5.8H), 7.68-7.61 (m, 4.2H), 7.57-7.53 (m, 2.7H), 7.27-7.27 (m, 1.1H), 7.24-7.12 (m, 9.4H), 6.90-6.86 (m, 1.4H), 6.11 (s, 0.4H), 6.02 (s, 1H), 5.25-5.18 (m, 1.4H), 4.03 (s, 3H), 3.55 (s, 1.2H), 3.55-3.13 (m, 3.2H). The following characterization is for a mixture that contains 91% major diastereomer: mp 132.9-135.6 °C; FTIR (film) 3059, 2956, 1758, 1558, 1492, 1453, 1265, 1062, 738, 620 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.88 (m, 4.4H); 7.68 -7.61 (m, 3.3H); 7.58-7.53 (m, 2.2H); 7.24-7.11 (m, 7.6H); 6.09-6.86 (m, 1.1H); 610 (s, 0.1H); 6.02 (s, 1H); 5.24-5.18 (m, 1.1H); 4.04 (s, 3H); 3.55 (s, 0.3H); 3.31-3.24 (m, 1.1H); 3.17-3.13 (m, 1.1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 164.2 147.7, 147.7, 138.7, 135.6, 135.2, 133.4, 133.3, 133.2, 130.6, 130.2, 129.6, 129.2, 129.1, 128.9. 128.7, 128.7, 128.7, 128.2, 127.8, 126.6, 126.6, 126.5, 125.5, 125.4, 124.3, 124.2, 122.4, 116.1, 95.2, 93.5, 78.5, 77.8, 66.5, 65.9, 54.5, 53.6, 32.9, 32.8, 31.5, 22.6, 21.0 14.1; HRMS (ESI): Mass calculated for $C_{29}H_{26}N_2O_5$ $[M+Na]^+$, 491.1578. Found $[M+Na]^+$, 491.1578.

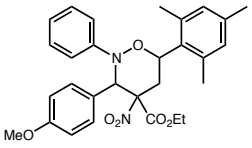


5e: The reaction was allowed to stir at 80 °C for 24 hours with ethyl 1-nitro-2-(*o*-tolyl)cyclopropanecarboxylate (33.9 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (100% hexanes to 50:50 dichloromethane/hexanes) yielding 29.8 mg of **5e** (49%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: mp 134.0-138.0 °C; FTIR (film) 3054, 2986, 1753, 1559, 1492, 1453, 1265, 739, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.61 (m, 3.4H); 7.41-7.31 (m, 3H); 7.28-7.28 (m, 1H); 7.25-7.22 (m, 3H); 7.19-7.10 (m, 5.5H); 6.89-6.85 (m, 1.2H); 6.10 (s, 0.2H); 6.23 (s, 1H); 5.24-5.18 (m, 1.2H); 4.55-4.43 (m, 2H); 3.97 (q, J = 7.2 Hz, 0.4H); 3.25-3.00 (m, 2.5H); 2.41-2.40 (m, 3.6H); 1.42 (t, J = 7.2 Hz, 3H); 1.01 (t, J = 7.2 Hz, 0.6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 163.7, 147.7, 147.7, 36.6, 136.4, 135.9, 135.7, 132.6, 132.1, 130.8, 130.7, 130.5, 128.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 126.6, 126.4, 125.1, 124.9, 122.3, 116.1, 116.0, 95.2, 93.4, 75.8, 75.2, 66.9, 66.6, 63.9, 63.3, 32.4, 32.3, 19.0, 18.9, 14.1, 13.9; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 469.1734. Found $[M+Na]^+$, 469.1749.

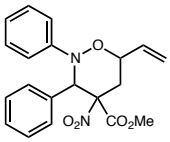


5f: The reaction was allowed to stir at 80 °C for 24 hours with ethyl 2-mesityl-1-nitrocyclopropanecarboxylate (37.7 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (100% hexanes to 50:50 dichloromethane/hexanes) yielding 25.8 mg of **5f** (40%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: mp 161.7-166.6 °C; FTIR (film) 3054, 2986, 1754, 1597, 1558, 1491, 1421, 1265, 896, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.46 (m, 0.3H); 7.53-7.51 (m,

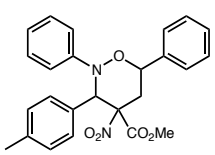
2H); 7.24-7.15 (m, 5.6H); 7.06-7.04 (m, 2.3H); 6.90-6.84 (m, 3.6H); 6.23 (s, 0.16H); 6.16 (s, 1H); 5.38-5.31 (m, 1.2H); 4.54-4.40 (m, 2H); 4.05-3.93 (m, 0.3H); 3.29-3.18 (m, 1.2H); 3.07-3.03 (m; 0.2H); 2.85-2.81 (m, 1H); 2.49-2.47 (m, 7.1H); 2.29 (s, 3.6H); 1.40 (t, J = 7.2 Hz, 3H); 1.01 (t, J = 7.2 Hz, 0.5H). The following characterization is for the major diastereomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.5, 137.9, 136.0, 132.3, 131.4, 130.4, 129.7, 128.7, 128.5, 128.2, 121.9, 115.5, 93.7, 78.4, 65.3, 64.0, 32.0, 21.3, 20.7, 13.9; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 497.2047. Found $[M+Na]^+$, 497.2048.



5g: The reaction was allowed to stir at 80 °C for 24 hours with ethyl 2-mesityl-1-nitrocyclopropanecarboxylate (37.7 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-(4-methoxybenzylidene)aniline oxide (46.2 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (100% hexanes to 50:50 dichloromethane/hexanes) yielding 52.2 mg of **5g** (76%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.44 (m, 2.5H); 7.19-7.15 (m, 2.5H); 7.05-7.05 (m, 2.5H); 6.90-6.84 (m, 4H); 6.76-6.72 (m, 2.5H); 6.17 (s, 0.3H); 6.10 (s, 1H); 5.37-5.28 (m, 1.3H); 4.53-4.39 (m, 2H); 4.06-3.94 (m, 0.6H); 3.73-3.72 (m, 3.9H); 3.28-3.18 (m, 1.3H); 3.06-3.02 (m, 0.3H); 2.82-2.79 (m, 1H); 2.48 (s, 7.9H); 2.29 (s, 4H); 1.39 (t, J = 7.2 Hz, 3H): 1.04 (t, J = 7.2 Hz, 1H). The following characterization is for the major diastereomer. mp 160.3-164.3 °C; FTIR (film) 3054, 2985, 2937, 1754, 1611, 1558, 1513, 1490, 1298, 1265, 1181, 1092, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.44 (m, 2H); 7.25-7.15 (m, 2H); 7.05-7.03 (m, 2H); 6.90-6.83 (m, 3H); 6.74-6.72 (m, 2H); 6.09 (s, 1H); 5.32-5.29 (d, J = 12 Hz, 1H); 4.52-4.39 (m, 2H); 3.72 (s, 3H); 3.28-3.21 (m, 1H); 2.83-2.79 (m, 1H); 2.48 (s, 6H); 2.29 (s, 3H); 1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 159.5, 147.6, 137.8, 136.0, 131.4, 131.1, 130.4, 128.7, 124.1, 121.9, 115.5, 113.6, 93.8, 78.4, 65.0, 63.9, 55.0, 31.9, 21.4, 20.7, 13.9; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 527.2153. Found $[M+Na]^+$, 527.2151.

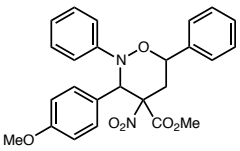


5h: The reaction was allowed to stir at 80 °C for 24 hours with (23.3 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylideneaniline oxide (40.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (100% hexanes to 50:50 dichloromethane/hexanes) yielding 12.5 mg of **5h** (25%) as a mixture of diastereomers as an oil. The following characterization is for the mixture of diastereomers: FTIR (film) 3054, 2987, 1758, 1598, 1560, 1421, 1265, 896, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.53-7.49 (m, 2.8H); 7.20-7.14 (m, 7.4H); 7.07-7.04 (m, 2.8H); 6.88-6.84 (m, 1.4H); 6.12-6.01 (m, 1.4H), 5.95 (d, J = 1.2 Hz, 0.4H); 5.87 (s, 1H); 5.57-5.50 (m, 1.4H); 5.44-5.38 (m, 1.4H); 4.54-4.47 (m, 1.4H); 3.97 (s, 3H); 3.51 (s, 1.2H); 3.06-3.01 (m, 0.5H); 2.90-2.79 (m, 2.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 164.1, 147.6, 147.6, 134.7, 134.6, 131.9, 130.8, 130.3, 128.8, 128.7, 128.6, 128.4, 128.3, 122.5, 122.4, 118.4, 118.3, 116.2, 116.2, 94.7, 93.0, 76.8, 76.1, 66.8, 54.4, 53.5, 31.7, 31.6, 29.7; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 391.1264. Found $[M+Na]^+$, 391.1263.

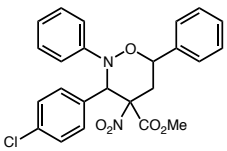


5i: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-(4-methylbenzylidene)aniline oxide (43.0 mg, 0.203

mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 60.1 mg of **5i** (99%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.53 (m, 2.5H); 7.50-7.42 (m, 5.5H); 7.40-7.30 (m, 1.5H); 7.21-7.15 (m, 3.5H); 7.15-7.01 (m, 5H); 6.89-6.85 (m, 1H); 6.04 (s, 0.4H); 5.93 (s, 1H); 5.07-5.00 (m, 1.2H); 4.01 (s, 3H); 3.51 (s, 1H); 3.24-3.00 (m, 3H); 2.25 (s, 1H); 2.23 (s, 3H). Recrystallization (1:3 dichloromethane/hexanes) yielded the major diastereomer. The following characterization is for the major diastereomer. mp 195.0-196.0 °C; FTIR (film) 3054, 2986, 1758, 1559, 1421, 1059, 735, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.54 (m, 2H); 7.50-7.43 (m, 5H); 7.19-7.15 (m, 2H); 7.11-7.08 (m, 2H); 7.03-7.01 (m, 2H); 6.88-6.85 (m, 1H); 5.95 (s, 1H); 5.02 (dd, *J* = 12, 2.4 Hz, 1H); 4.00 (s, 3H); 3.18-3.12 (m, 1H); 3.04-3.00 (m, 1H); 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.7, 138.6. 138.0, 130.5, 129.1, 128.9, 128.8, 128.7, 126.5, 122.3, 116.0, 93.5, 78.5, 66.4, 54.4, 32.9, 21.0; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 433.1758. Found $[M+Na]^+$, 433.1743.

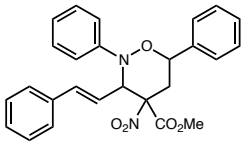


5j: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-(4-methoxybenzylidene)aniline oxide (46.2 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 57.7 mg of **5j** (95%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.41 (m, 8H); 7.20-7.15 (m, 3H); 7.10-7.07 (m, 3H); 6.89-6.85 (m, 1H); 6.77-6.68 (m, 3H); 6.01 (s, 0.25H); 5.94 (s, 1H); 5.07-5.00 (m, 1.3H); 4.00 (m, 3H); 3.89 (s, 1H); 3.73 (s, 1H); 3.71 (3H); 3.29-3.01 (m, 3H). The following characterization is for the major diastereomer. mp 186.1-188.5 °C; FTIR (film) 3054, 2987, 1758, 1559, 1512, 1265, 1032, 896, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.42 (m, 7H); 7.28-7.16 (m, 2H); 7.11–7.09 (m, 2H); 6.90-6.86 (m, 1H); 6.75-6.73 (m, 2H); 5.94 (s, 1H); 5.03 (dd, *J* = 12, 2.4 Hz, 1H); 4.01 (s, 3H); 3.71 (s, 3H); 3.18-3.12 (m, 1H); 3.06-3.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 159.7, 147.7, 137.9, 131.9, 128.8, 128.8, 128.6, 126.4, 123.8, 122.3, 116.1, 113.7, 93.4, 78.4, 66.2, 54.9, 54.4, 32.7; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_6$ $[M+Na]^+$, 471.1527. Found $[M+Na]^+$, 471.1535.

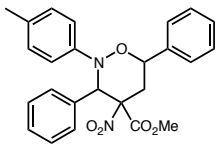


5k: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-(4-chlorobenzylidene)aniline oxide (47.0 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 53.7 mg of **5k** (87%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.44 (m, 9H); 7.36-7.32 (m, 2H); 7.22-7.16 (m, 6H); 7.09-7.07 (m, 3H); 6.92-6.88 (m, 1H); 6.05 (s, 0.5H); 5.97 (s, 1H); 5.09-5.02 (m, 1.5H); 4.01 (s, 3H); 3.58 (s, 1.3H); 3.29-3.24 (m, 0.5H); 3.13-3.00 (m, 2H); Recrystallization (hexanes) yielded the major diastereomer. The following characterization is for the major diastereomer. mp 159.5-160.1°C; FTIR (film) 3054, 2987, 1758, 1560, 1492, 1421, 1265, 1093, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.44 (m, 7H); 7.25-7.17 (m, 4H); 7.09-7.06 (m, 2H); 6.92-6.87 (m, 1H); 5.96 (s, 1H); 5.03 (dd, *J* = 10, 4.4, Hz, 1H);

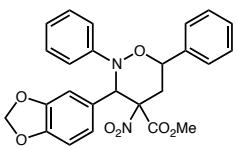
4.01 (s, 3H); 3.09-3.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 147.4, 137.6, 135.1, 131.9, 130.5, 128.9, 128.9, 128.8, 128.6, 126.4, 122.7, 166.1, 93.2, 78.4, 66.1, 54.6, 54.6, 32.7; HRMS (ESI): Mass calculated for $C_{24}H_{21}ClN_2O_5$ $[M+Na]^+$, 475.1031. Found $[M+Na]^+$, 475.1011.



5l: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-((*E*)-3-phenylallylidene)aniline oxide (48.4 mg, 0.203 mmol). The reaction was immediately purified by flash column chromatography with silica gel (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 56.3 mg of **5l** (93%) as a mixture of diastereomers. The following characterization is for the mixture of diastereomers: FTIR (film) 3054, 2987, 1755, 1599, 1558, 1494, 1422, 1265, 1058, 909, 737, 650 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.40 (m, 8H); 7.29-7.27 (m, 6H); 7.25-7.22 (m, 4H); 7.16-7.14 (m, 3H); 6.99-6.95 (m, 1.5H); 6.58 (s, 0.5H); 6.54 (s, 1H); 6.47-6.37 (m, 1.5H); 5.50-5.44 (m, 1.5H); 5.07-5.01 (m, 1.5H); 4.01 (s, 3H); 3.75 (s, 1.5H) 3.25-3.20 (m, 0.5H); 3.10-3.06 (m, 1H); 2.90-2.73 (m, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 164.3, 147.8, 139.0, 138.3, 138.1, 128.1, 135.7, 135.6, 128.8, 128.8, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 126.8, 126.7, 126.4, 126.3, 122.9, 122.9, 118.4, 117.1, 116.6, 116.6, 94.2, 93.2, 78.7, 77.9, 67.7, 67.1, 54.4, 53.9, 33.7, 33.6; HRMS (ESI): Mass calculated for $C_{26}H_{24}N_2O_5$ $[M+Na]^+$, 467.1577. Found $[M+Na]^+$, 467.1562.



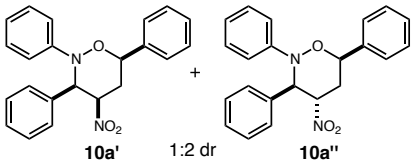
5m: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol), and *N*-benzylidene-4-methylaniline oxide (43.1 mg, 0.203 mmol). The reaction was immediately purified by flash column chromatography with of silica gel (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 33.1 mg of **5m** (56.3%) as a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.53 (m, 6H), 7.51-7.42 (m, 4.5H), 7.27-7.21 (m, 4H), 7.01-6.95 (m, 6H); 6.02-6.02 (m, 0.5H), 5.93 (s, 1H), 5.08-5.02 (m, 1.5H), 4.01 (s, 3H), 3.53 (s, 1.5H), 3.53-3.02 (m, 3H), 2.19, (s, 4.5H). The following characterization is for the major diastereomer. mp 181.3-183.9 °C; FTIR (film) 3054, 2987, 1759, 1558, 1454, 1422, 1265, 1059, 745, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.54 (m, 4H); 7.50-7.41 (m, 3H); 7.23-7.31 (m, 3H); 7.00-6.95 (m, 4H); 5.92 (s, 1H); 5.03 (dd, J = 12, 2 Hz, 1H); 4.01 (s, 1H); 3.17-3.11 (m, 1H); 3.05-3.01 (m; 1H); 2.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 145.3, 138.0, 132.2, 131.9, 130.7, 129.2, 128.8, 128.8, 128.3, 126.5, 116.3, 93.5, 78.4, 66.8, 54.5, 32.9, 20.5, 14.1; HRMS (ESI): Mass calculated for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$, 455.1578. Found $[M+Na]^+$, 455.1571.



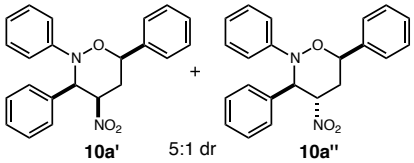
5n: The reaction was allowed to stir at 80 °C for 24 hours with methyl 1-nitro-2-phenylcyclopropanecarboxylate (30.0 mg, 0.136 mmol), catalyst **9a** (8.08 mg, 0.0204 mmol) and (*N*-(benzo[*d*][1,3]dioxol-5-ylmethylene)aniline oxide (49.1 mg, 0.203 mmol). The reaction was immediately purified by silica gel flash column chromatography with (5:95 ethyl acetate/hexanes to 20:80 ethyl acetate/hexanes) yielding 29.3 mg of **5n** (47%) as a mixture of diastereomers. The following characterization is for the major diastereomer. mp 203.3-204.7 °C; FTIR (film) 3054, 2987, 1759, 1559, 1489, 1421, 1264, 1041, 898, 739 cm $^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.40 (m, 5H); 7.23-7.17 (m, 3H); 7.10-7.08 (m, 2H); 6.97-

6.94 (m, 1H); 6.90-6.87 (m, 1H); 6.63-6.61 (m, 1H); 5.89-5.87 (m, 3H); 4.99 (dd, *J* = 12, 2 Hz, 1H); 3.99 (s, 3H); 3.17-3.10 (m, 1H); 3.03-3.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 148.0, 147.6, 147.5, 137.7, 128.9, 128.7, 126.5, 126.3, 125.4, 125.0, 122.4, 116.1, 110.7, 108.1, 101.1, 93.5, 78.4, 66.2, 54.5, 32.7; HRMS (ESI): Mass calculated for $C_{25}H_{22}N_2O_7$ $[M+Na]^+$, 485.1319. Found $[M+Na]^+$, 485.1311.

Procedures for the decarboxylation of oxazinane 5a to 10a:[2a]



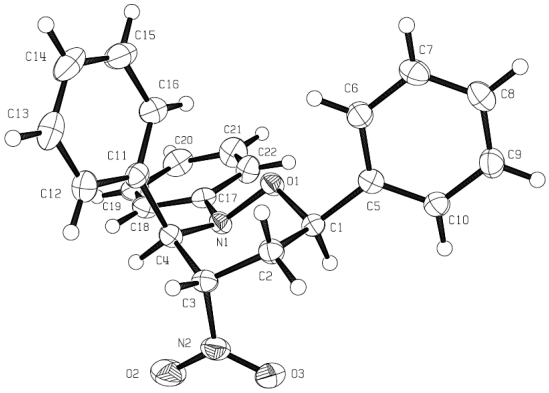
*To obtain a 1:2 (**10a' : 10a''**) mixture of diastereomers:* **5a** as a 2:1 mixture of diastereomers (50 mg, 0.120 mmol) was placed in a screw-capped reaction vial containing a magnetic stir bar followed by LiOH•H_2O (15.1 mg, 0.360 mmol, 3.0 eq). The mixture was dissolved in 2:1 dioxanes: H_2O (2.25 mL) and heated to 80 ^oC for 96 h. The reaction was neutralized with 3M HCl, extracted with DCM, and dried over Na_2SO_4. The product contained a mixture of diastereomers in a 1 to 2 ratio based on a crude ^{1}H NMR. The product was immediately purified by silica gel column chromatography (100% hexanes to 50:50 hexanes/dichloromethane) yielding 30.6 mg (71%) of **10a** as an oil. A crystal structure was obtained from racemic **10a''** to confirm the relative stereochemistry of **10a''**.

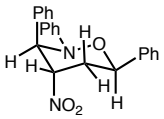


*To obtain a 5:1 (**10a' : 10a''**) mixture of diastereomers:* **5a** as a mixture of diastereomers (75 mg, 0.179 mmol) was placed in a round bottom flask containing a magnetic stir bar followed by LiOH•H_2O (113 mg, 2.685 mmol, 15.0 eq). The mixture was dissolved in 2:1 dioxanes: H_2O (3.60 mL) and heated to 100 ^oC for 18 h. The reaction was neutralized with 3M HCl, extracted with DCM, and dried over Na_2SO_4. The product contained a mixture of diastereomers in a 5 to 1 ratio based on a crude ^{1}H NMR. The product was immediately purified by silica gel column chromatography (100% hexanes to 50:50 hexanes/dichloromethane) yielding 38.6 mg (60%) of **10a** as an oil. The following characterization is for the major diastereomer **10a'** (oil): FTIR (film) 3055, 2981, 1595, 1551, 1495, 1421, 1376, 1263, 895, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.53 (m, 4H); 7.50-7.40 (m, 3H): 7.25-7.23 (m, 3H); 7.22-7.17 (m, 2H); 7.08-7.05 (m, 2H); 6.90-6.83 (m, 1H); 5.63 (d, *J* = 5.6 Hz, 1H); 5.44 (ddd, *J* = 12.4, 5.6, 4.4 Hz, 1H); 5.14 (dd, *J* = 11.6, 2 Hz, 1H); 2.83 (apparent quartet, ddd, *J* = 12.4 Hz, 1H); 2.47 (ddd, *J* = 13.2, 4.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ147.6, 138.1, 132.7, 130.2, 128.8, 128.6, 128.4, 126.6, 122.2, 115.8, 83.6, 78.9, 63.7, 30.2; (only 14 carbons appear; overlap in aromatic region); HRMS (ESI): Mass calculated for $C_{22}H_{20}N_2O_3$ $[M+Na]^+$, 383.1366. Found $[M+Na]^+$, 383.1367. The following characterization is for the diastereomer **10a''** (pale yellow solid): mp 154.6-155.2 °C; FTIR (film) 3054, 2987, 1598, 1552, 1421, 1265, 896, 739, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.61 (m, 2H); 7.48-7.36 (m, 5H): 7.34-7.30 (m, 2H); 7.28-7.26 (m, 0.7H); 7.25-7.24 (m, 0.2H); 7.22-7.17 (m, 2H); 7.05-7.02 (m, 2H); 6.90-6.85 (m, 1H); 5.96 (d, *J* = 1.2 Hz, 1H); 5.40 (dd, *J* = 11.2 Hz, 2.4 Hz, 1H); 4.94 (ddd, *J* = 4.8, 2.8, 2,8, 1H); 2.84 (dddd, *J* = 15.2, 2.8, 2.4, 1.2 Hz, 1H); 2.313 (ddd, *J* = 15.6, 11.6, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 139.0, 135.7, 128.8, 128.7, 128.7, 128.6, 128.5, 127.8, 126.4, 121.8, 115.2, 84.7, 77.8, 62.9, 29.9; HRMS (ESI): Mass calculated for $C_{22}H_{20}N_2O_3$ $[M+Na]^+$, 383.1366. Found $[M+Na]^+$, 383.1372.

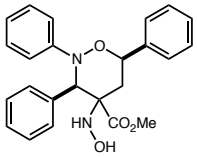
Crystal structure of 10a'':

A crystal was obtained of the racemic diastereomer of **10a''** to determine the relative configuration. The nitro group of **10a''** was found to be on the opposite side of the ring from the two aromatic rings. Due to the nitro group being trans to the two aromatic rings, this diastereomer is named **10a''** for consistency of numbering throughout this text.



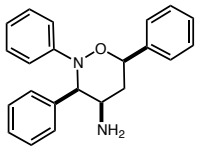


Reduction of oxazinane 5a:



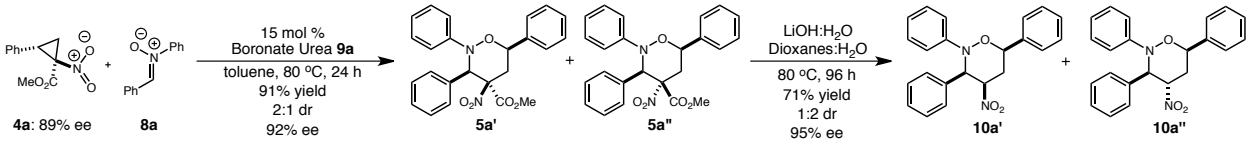
11a: Diastereomers of **5a** (2:1 dr) (50 mg, 0.120 mg) were placed in a round bottom flask containing a magnetic stir bar, 2-propanol (0.05 M) and powdered zinc (45 eq). The flask was fitted with a septa and put under an argon atmosphere. Glacial acetic acid (66 eq) was slowly added to the flask. The mixture was stirred at room temperature for 3 hours and then quenched with aqueous saturated sodium bicarbonate. The mixture stirred vigorously for 15 minutes. After this time, the mixture was filtered through a fritted funnel with Celite, washed with water, DCM, and MeOH to ensure isolation of all material from the crude reaction mixture. The filtrate was then extracted with DCM (3x). The organic layers were combined, dried with sodium sulfate, and the solvent removed under reduced pressure. The crude material was isolated cleanly after filtration and extraction with DCM as a pale yellow solid in 94% yield (45 mg). If necessary, **11a** can be purified further by silica gel flash column chromatography (20/80 ethyl acetate/hexanes to 50/50 ethyl acetate/hexanes after treatment of silica gel with 1:5:19 triethylamine/ethyl acetate/hexanes) yielding 75% (36 mg) of **11a** as a 3:1 mixture of diastereomers. Relative configuration is tentatively assigned based on *J* values of the ^{1}H NMR and analysis of substrates leading to this molecule. The following characterization is for the major diastereomer: mp 172.9-176.1 °C; FTIR (film) 3413, 3055, 2987, 1715 1597, 1491, 1454, 1422, 1265, 1098, 895, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.67 (m, 2H); 7.56-7.53 (m, 2H): 7.48-7.44 (m, 2H); 7.41-7.37 (m, 1H); 7.28-7.22 (m, 0.3H); 7.16-7.11 (m, 2H); 7.07-7.04 (m, 2H); 6.83-6.78 (m, 1H); 5.56 (s, 1H); 5.25 (dd, *J* = 12 Hz, 2.4 Hz, 1H); 5.19 (bs, 1H); 4.63 (bs, 1H); 3.94 (s, 3H); 2.75 (ddd, *J* = 13.6, 2.4, 0.8 Hz, 1H); 2.18 (dd, *J* =13.2, 12.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ173.3, 148.4, 139.5, 134.9, 130.6, 128.6, 128.5, 128.2, 128.2, 128.1, 126.3, 121.5, 115.8, 78.8, 68.5, 65.9, 53.0, 33.2; HRMS (ESI): Mass calculated for $C_{24}H_{24}N_2O_4$ $[M+Na]^+$, 427.1628. Found $[M+Na]^+$, 427.1622.

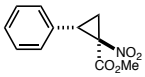
Reduction of oxazinane 10a':



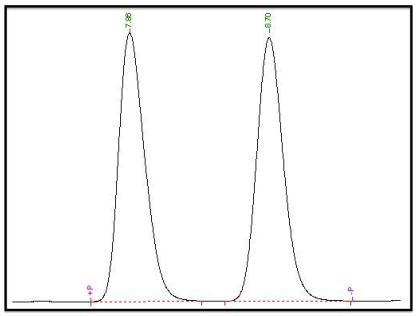
12a': Oxazinane **10a'** (30 mg, 0.083 mmol) was placed in a 5 mL round bottom flask equipped with a magnetic stir bar, 2-propanol (0.05 M) and powdered zinc (20 eq). The flask was fitted with a septa and put under an argon atmosphere. Concentrated HCl (10 eq) was slowly added to the flask. The mixture was stirred at room temperature for 2 hours and then quenched with aqueous saturated sodium bicarbonate. The mixture stirred vigorously for 15 minutes. After this time, the mixture was filtered through a fritted funnel with Celite, washed with water, DCM, and MeOH to ensure isolation of all material from the crude reaction mixture. The filtrate was then extracted with DCM (3x). The organic layers were combined, dried with sodium sulfate, and the solvent removed under reduced pressure to afford **12a'** in 97% yield (27 mg) as an oil. Relative configuration is tentatively assigned based on *J* values of the ^{1}H NMR and analysis of substrates leading to this molecule. FTIR (film) 3365, 3295, 3061, 3031, 2922, 2852, 1597, 1492, 1451, 1265, 1057, 1031, 909 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.65 (m, 2H); 7.53-7.51 (m, 2H); 7.46-7.42 (m, 2H); 7.39-7.36 (m, 1H); 7.28-7.27 (m, 1.6H); 7.23-7.19 (m, 1.3H); 7.16-7.12 (m, 2H); 7.04-7.02 (m, 2H); 6.80-6.76 (m, 1H); 5.12 (dd, *J* = 11.6, 2 Hz, 1H); 4.96 (d, *J* = 5.6 Hz, 1H); 3.78 (ddd, *J* = 12, 10.4, 5.2 Hz, 1H); 2.11 (ddd, *J* = 12.8, 4.4, 2.4 Hz, 1H); 1.94 (apparent quartet, ddd, *J* = 12 Hz, 1H); 1.68 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 139.9, 135.6, 130.8, 128.6, 128.6, 128.15, 128.0, 127.5, 126.4, 120.8, 115.2, 80.5, 67.5, 50.9, 37.9; HRMS (ESI): Mass calculated for $C_{22}H_{22}N_2O_5$ $[M+H]^+$, 331.1805. Found $[M+H]^+$, 331.1803.

Chirality transfer studies:

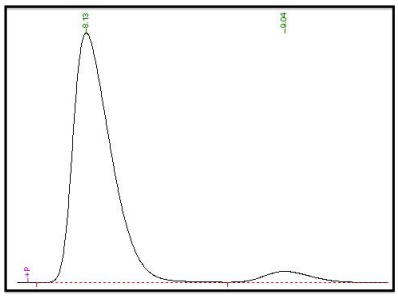




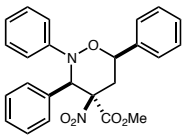
(1*R*,2*S*)-methyl 1-nitro-2-phenylcyclopropanecarboxylate (**4a**) was prepared as previously reported.[6] HPLC (OD-H Chiralcel, 5% IPA in hexanes, 1 mL/min) t_r 8.0 min (major), t_r 8.9 min (minor).



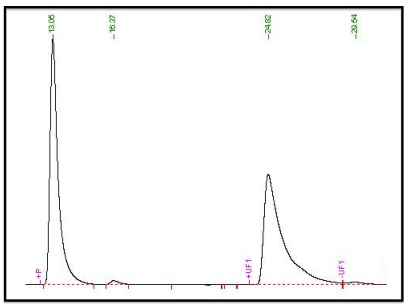
Ret. Time (min)	% Area
7.86	49.9
8.70	50.1



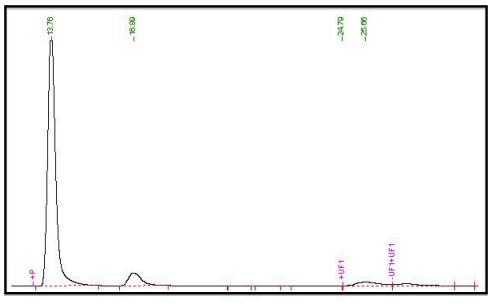
Ret. Time (min)	% Area
8.13	94.5
9.04	5.5



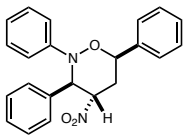
5a': **5a'** and **5a''** were prepared as reported. **5a'** was isolated from **5a''** via crystallization (IPA/hexanes) to afford an 11:1 mixture of **5a'**: **5a''**. Relative stereochemistry was determined by crystal structure for both **5a'** and **5a''**. The enantiomeric excess of **5a'** and was determined by HPLC (AD-H Chiralcel, 3% IPA in hexanes, 0.5 mL/min) t_t 13.4 min (major) t_r 25.2 min (minor).



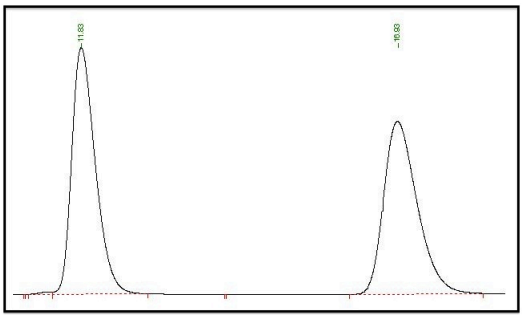
Ret. Time (min)	% Area
13.05	51.0
24.82	49.0



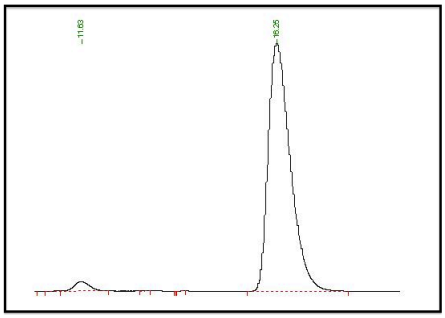
Ret. Time (min)	% Area
13.77	95.8
25.67	4.2



10a'': **10a** was prepared as reported above from a mixture of **5a'** and **5a''** (2:1) and isolated as a single diastereomer. Relative stereochemistry was determined by x-ray crystallographic analysis. The enantiomeric excess of **10a''** was determined by HPLC (OD-H Chiralcel, 3% IPA in hexanes, 1.0 mL/min) t_r 11.7 min (minor), t_r 16.6 min (major).

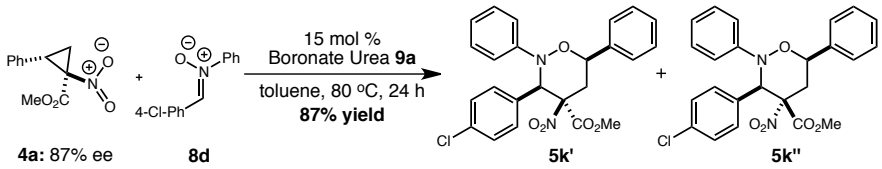


Ret. Time (min)	% Area
11.83	49.7
16.93	50.3

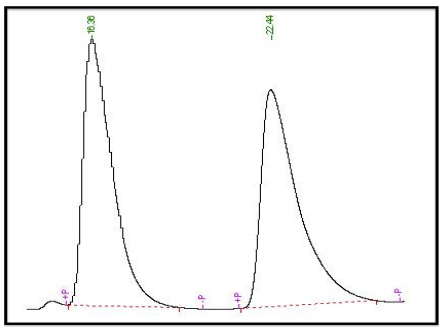


Ret. Time (min)	% Area
11.63	2.5
16.26	97.5

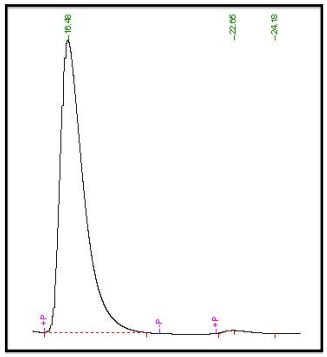
Mechanism studies:



5k was prepared as previously reported using enantioenriched **4a** and nitrone **8d** to give **5k** as an enantioenriched mixture of diastereomers according to the scheme above. Major diastereomer **5k'** was recrystallized (IPA) from this mixture and subjected to HPLC analysis. The major enantiomer of **5k'** was determined by HPLC (AD-H Chiralcel, 3% IPA in hexanes, 0.5 mL/min) t_r 16.42 min (major), t_r 22.55 min (minor).



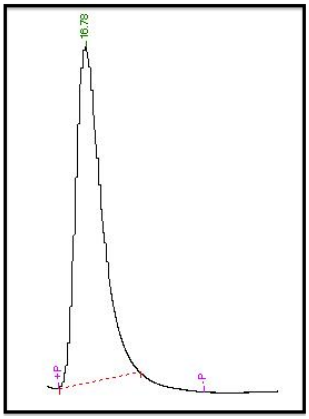
Ret. Time (min)	% Area
16.35	49.46
22.44	50.54



Ret. Time (min)	% Area
16.48	99.94
22.65	0.06

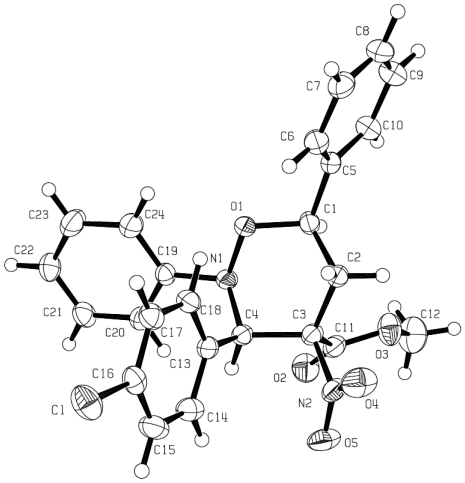
A crystal structure containing one enantiomer and the major diastereomer (**5k'**) was obtained from the initial mixture of diastereomers. The exact crystal was then tested by HPLC showing that the major enantiomer was used during the acquisition of the crystal structure and absolute configuration of **5k'**. From this data, it was determined that inversion of configuration occurs during the initial ring opening of the nitrocyclopropane carboxylate.

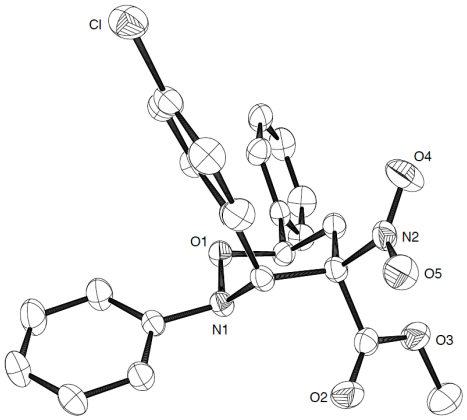
HPLC trace of crystal 5k':

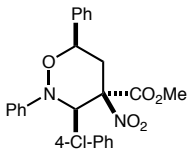


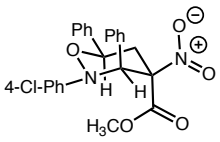
Ret. Time (min)	% Area
16.78	100.00

Crystal structure of 5k' (two Ortep plots)**:**



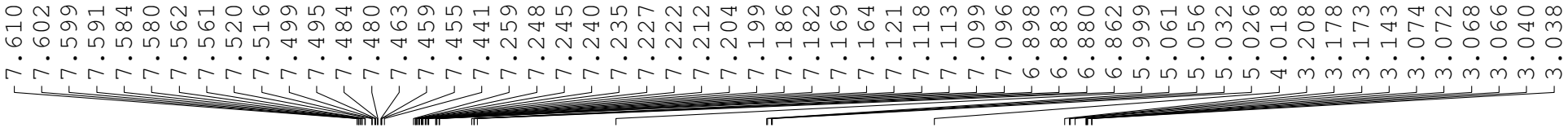


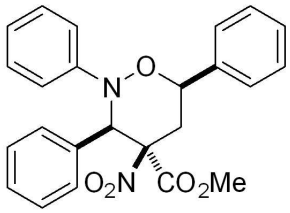




References:

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.
[2] a) So, S. S; Auvil, T. J.; Garza, V. J.; Mattson, A. E. *Org. Lett.* **2012,** *14*, 444. b) Hughes, M. P.; Smith, B. D. *J. Org. Chem.* **1997**, *62*, 4492.
[3] Wrackmeyer, B. *Modern Magnetic Resonance*; Webb, G. A., Ed.; Springer: Netherlands: 2006; Part 1, pp 455-457.
[4] Ganton, M.D.; Kerr, M.A. *J. Org. Chem.* **2004**, *69*, 8554.
[5] Lifchits, O.; Charette, A. B. Org. Lett. 2008, 10, 2809.
[6] Moreau, B.; Charette, A. B. J. Am. Chem. Soc. 2005, 127, 18014.

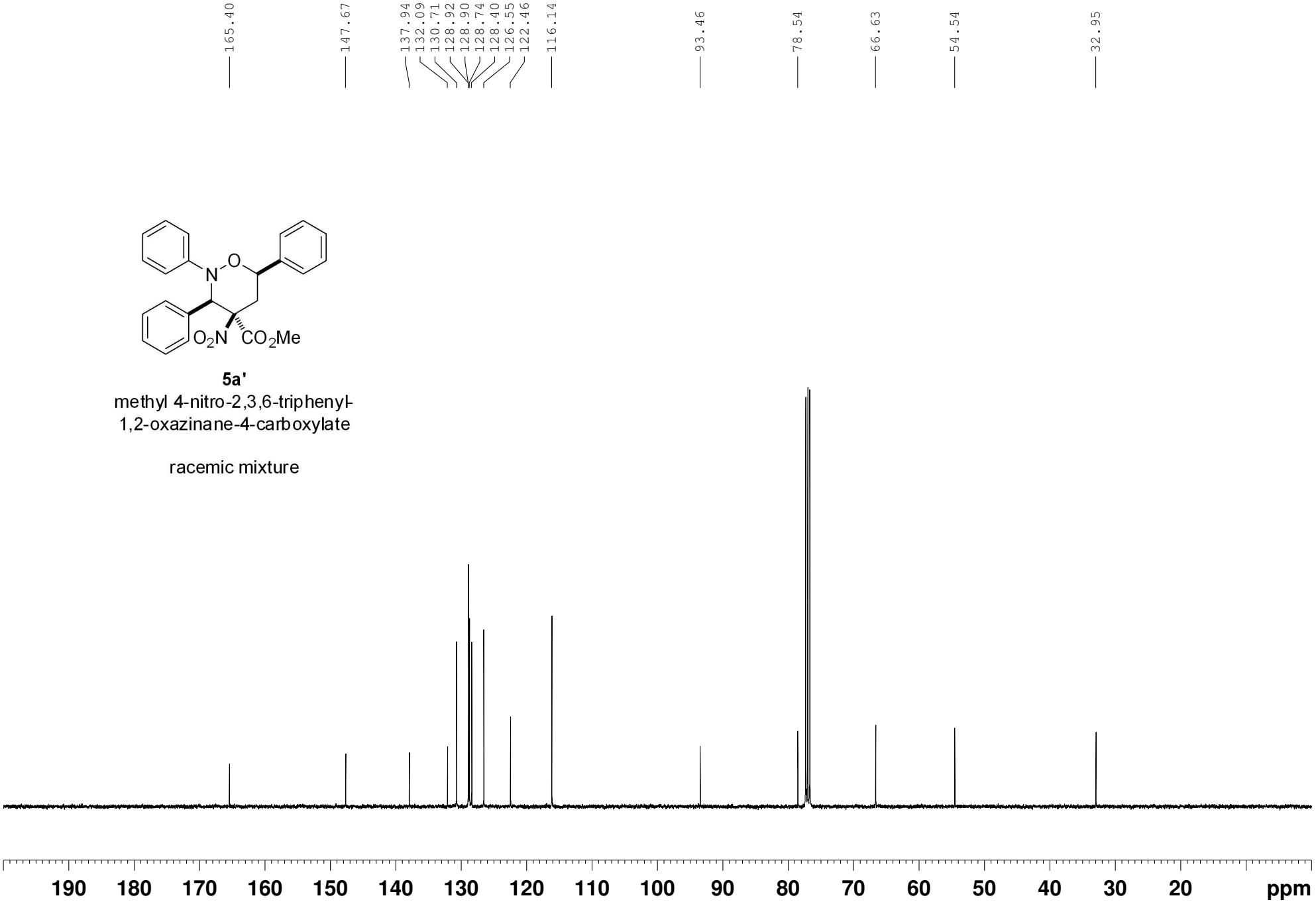




5a'

methyl 4-nitro-2,3,6-triphenyl-1,2-oxazinane-4-carboxylate

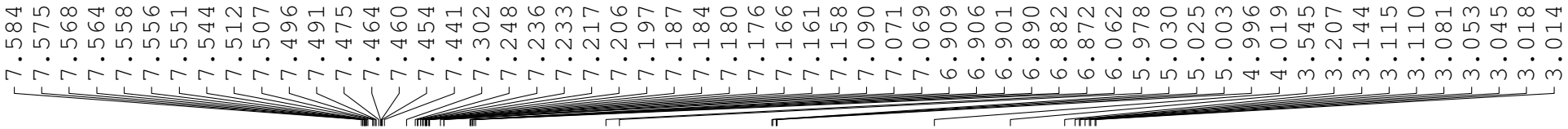
racemic mixture

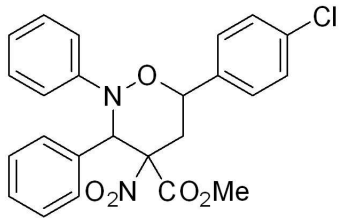


5a'

methyl 4-nitro-2,3,6-triphenyl-1,2-oxazinane-4-carboxylate

racemic mixture

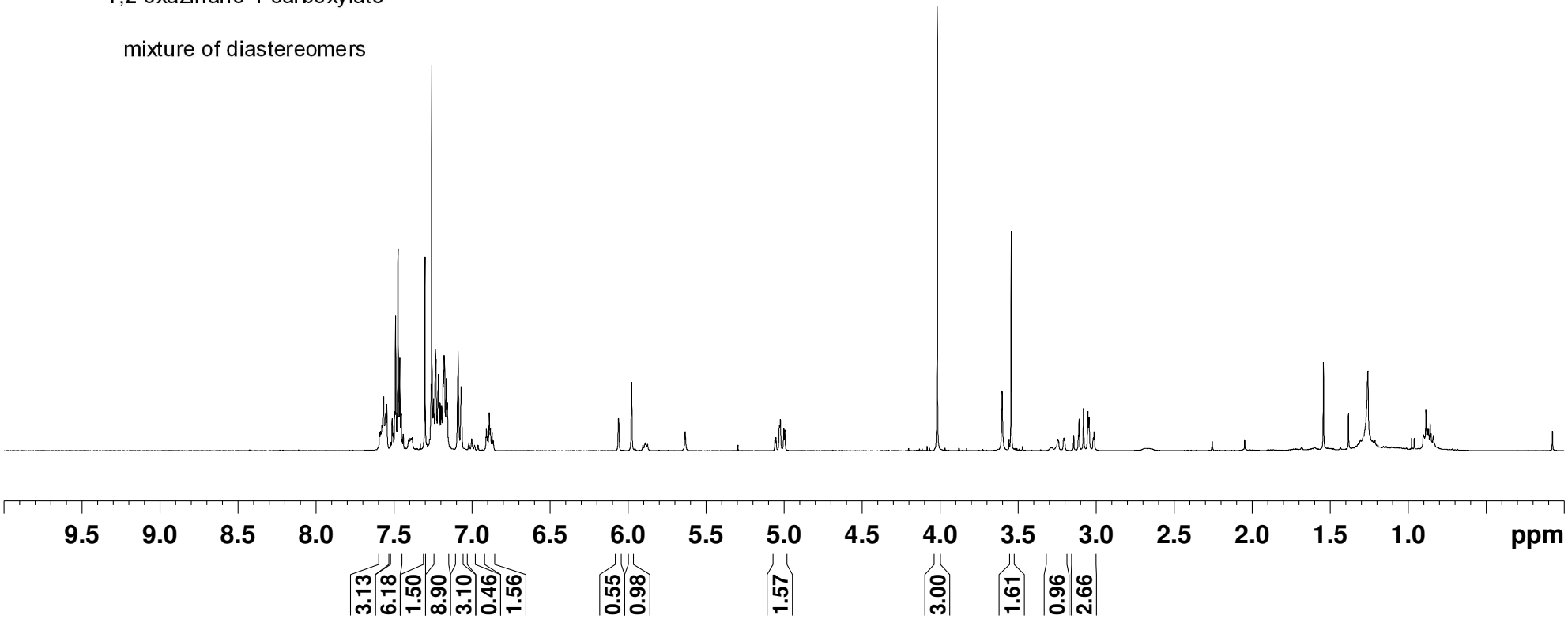


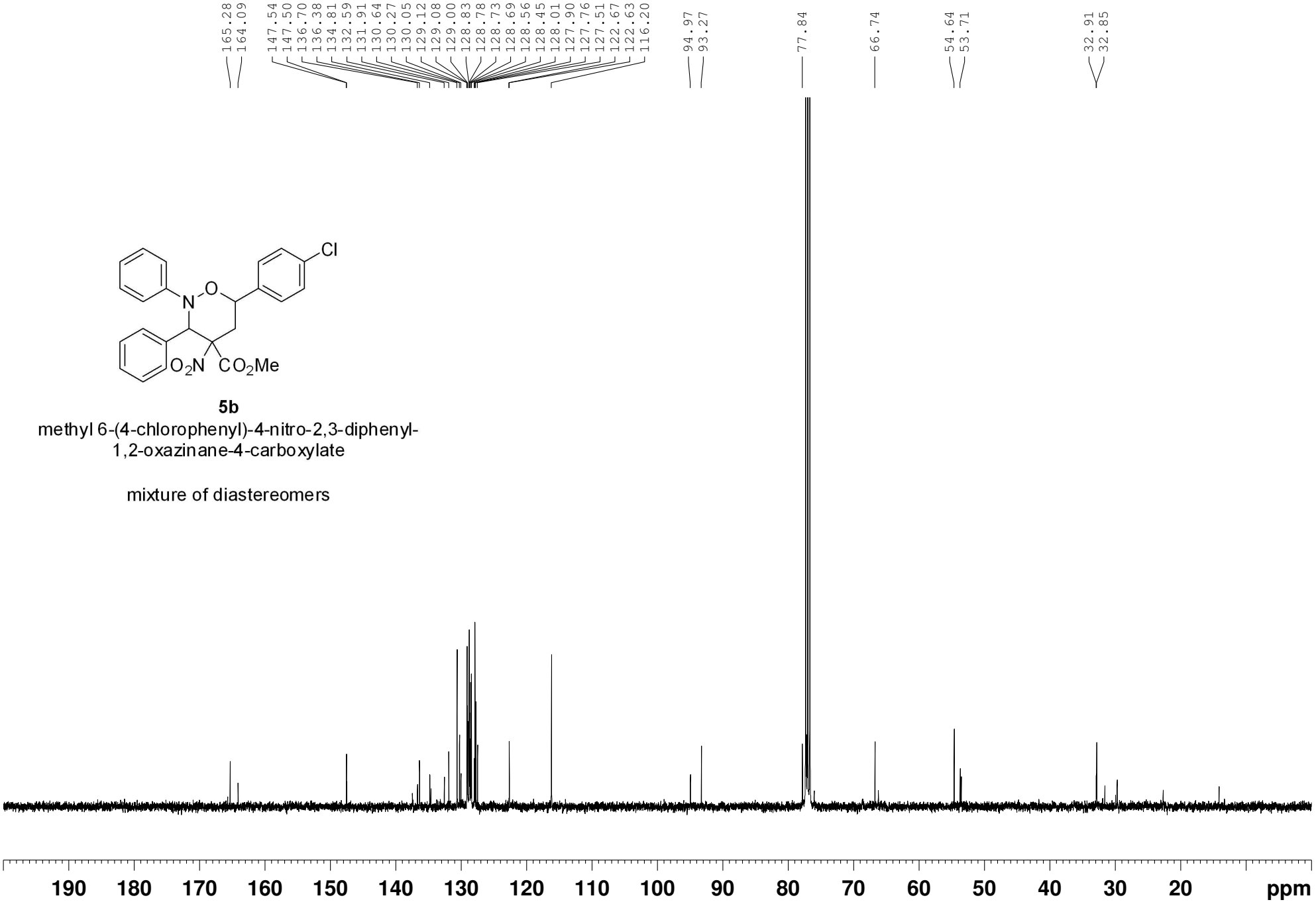


5b

methyl 6-(4-chlorophenyl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers

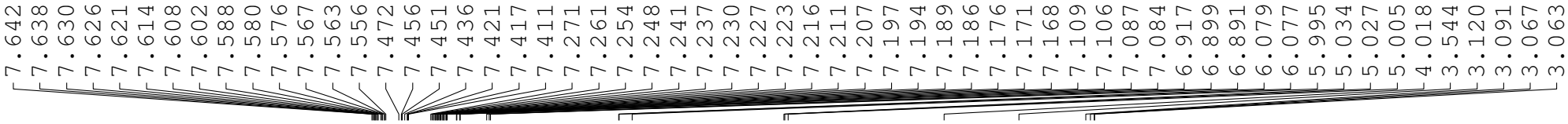


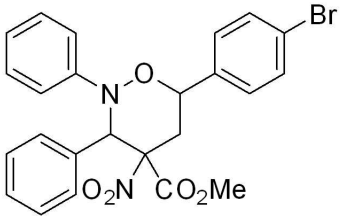


5b

methyl 6-(4-chlorophenyl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers

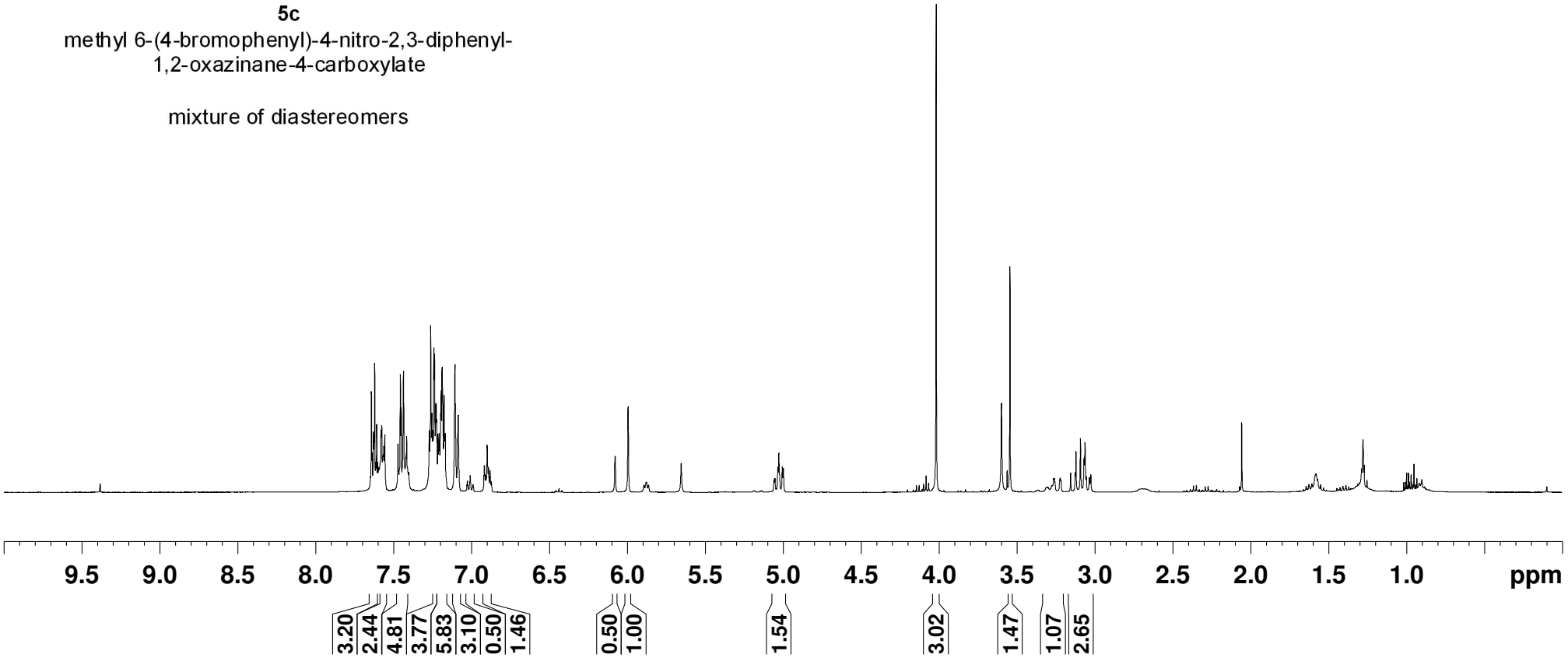


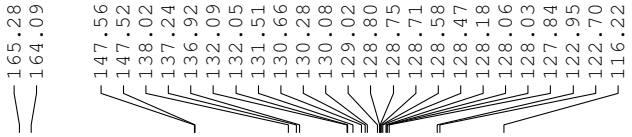


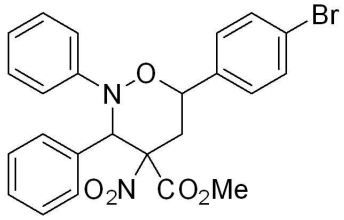
5c

methyl 6-(4-bromophenyl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers



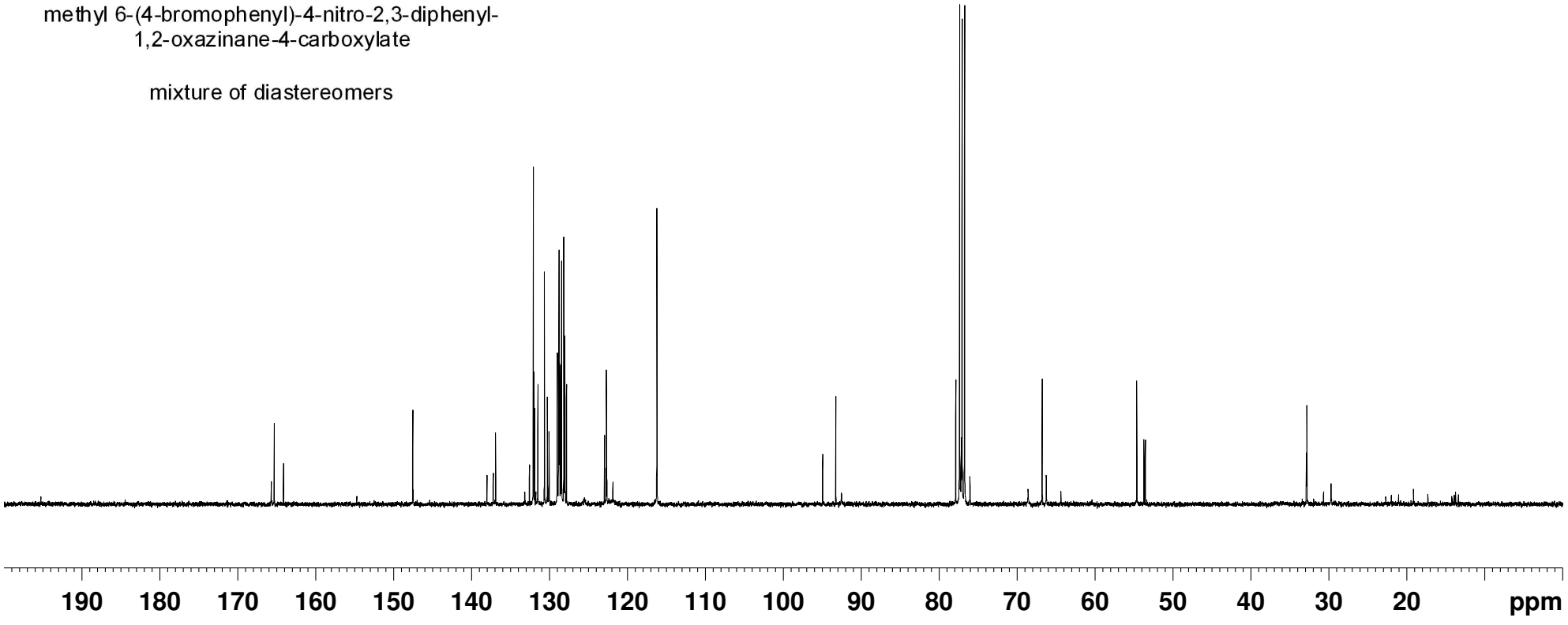


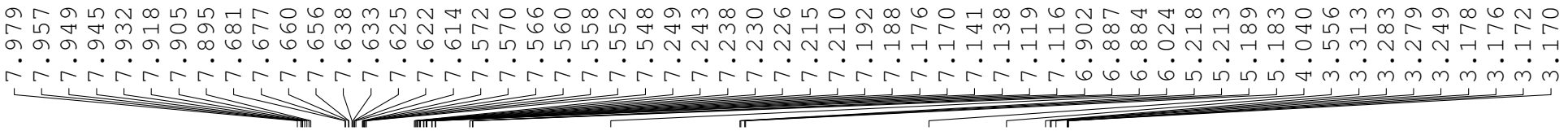


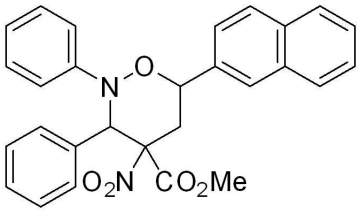
5c

methyl 6-(4-bromophenyl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers



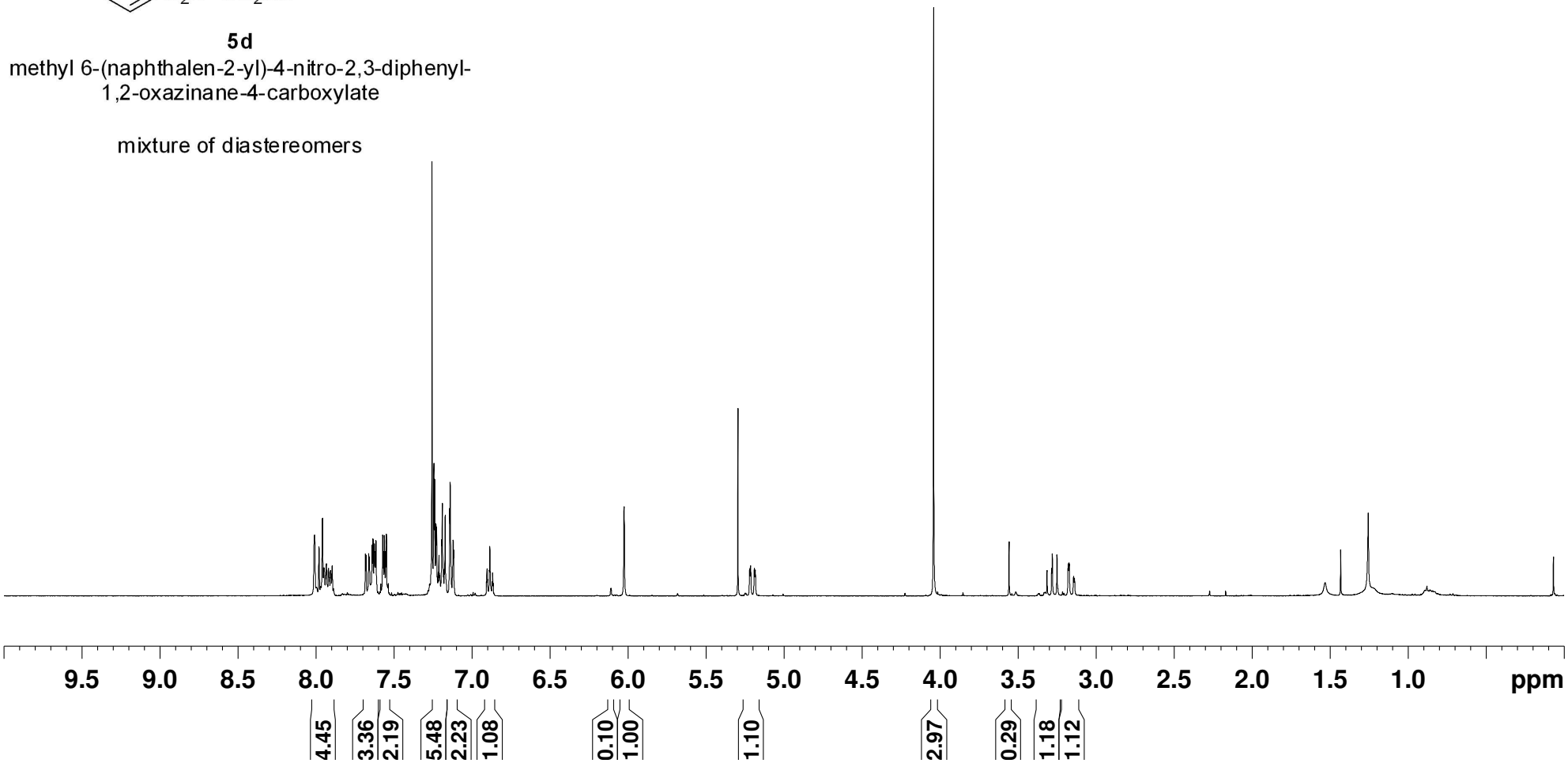


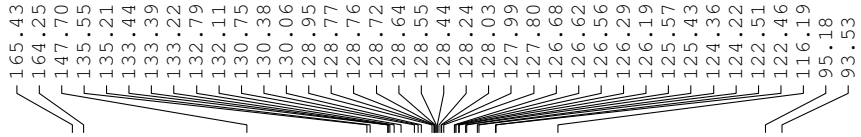


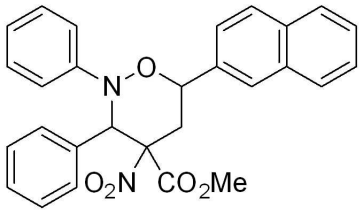
5d

methyl 6-(naphthalen-2-yl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers



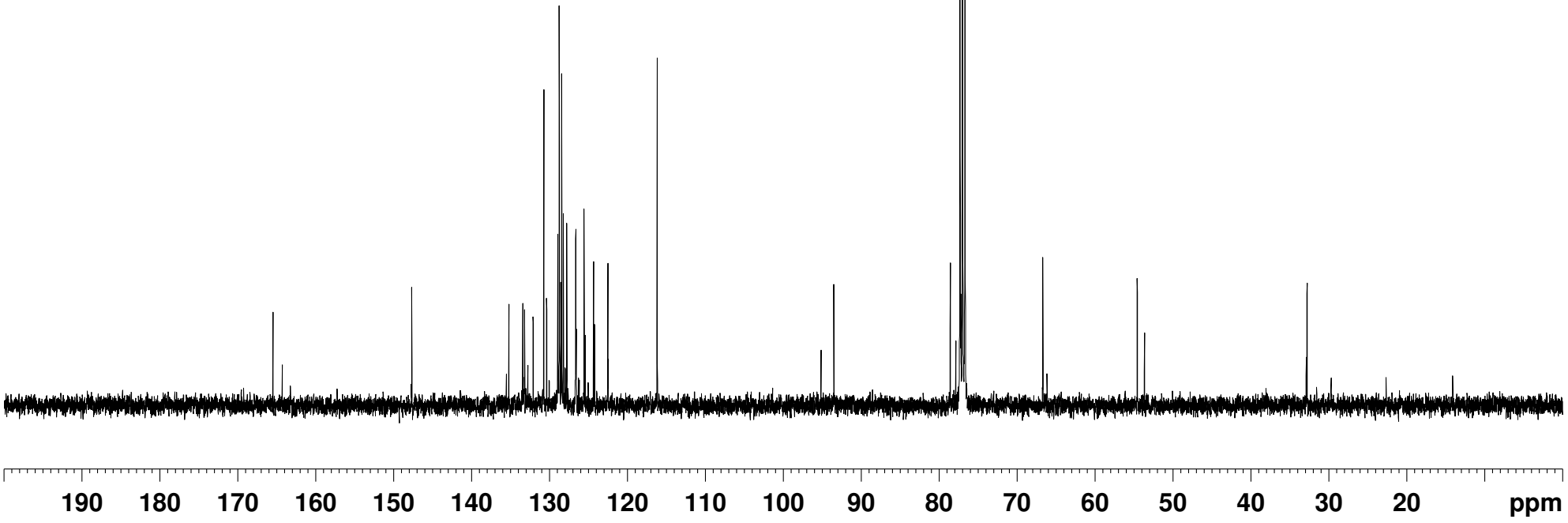


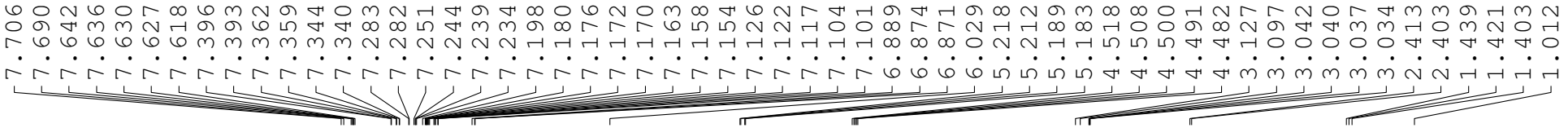


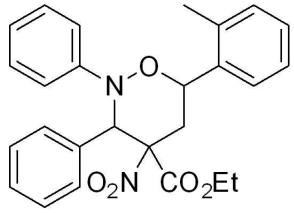
5d

methyl 6-(naphthalen-2-yl)-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers



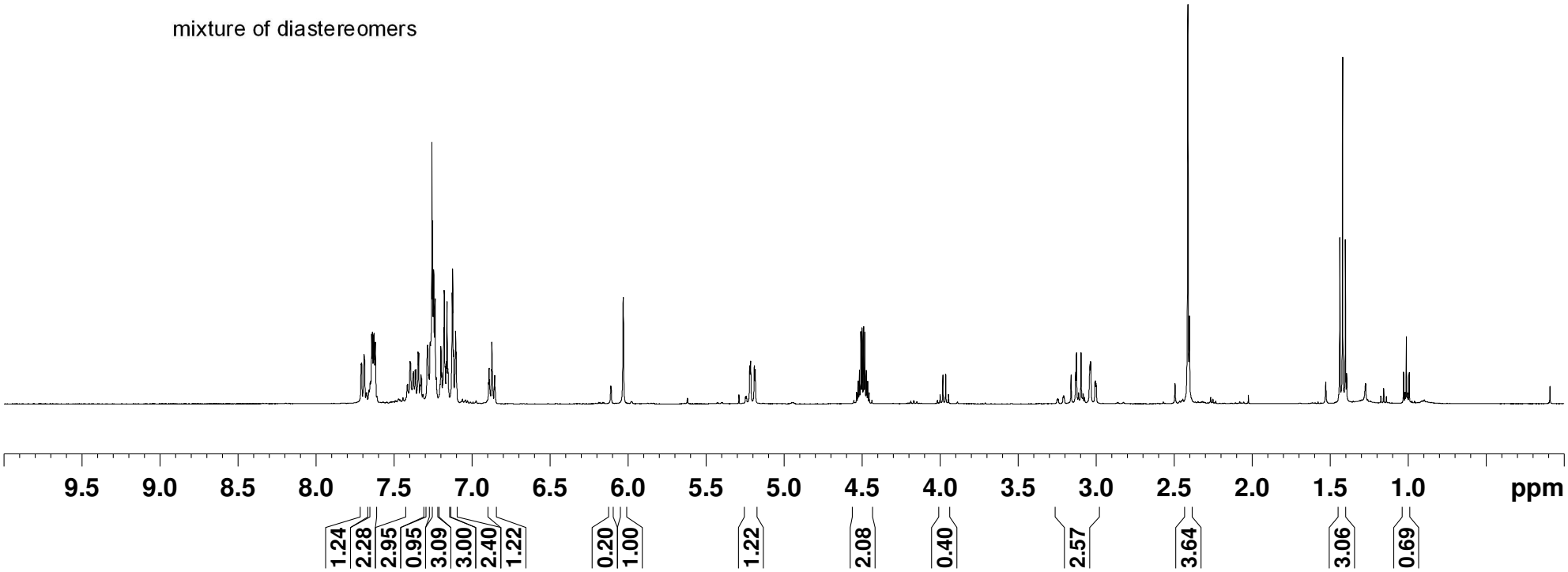


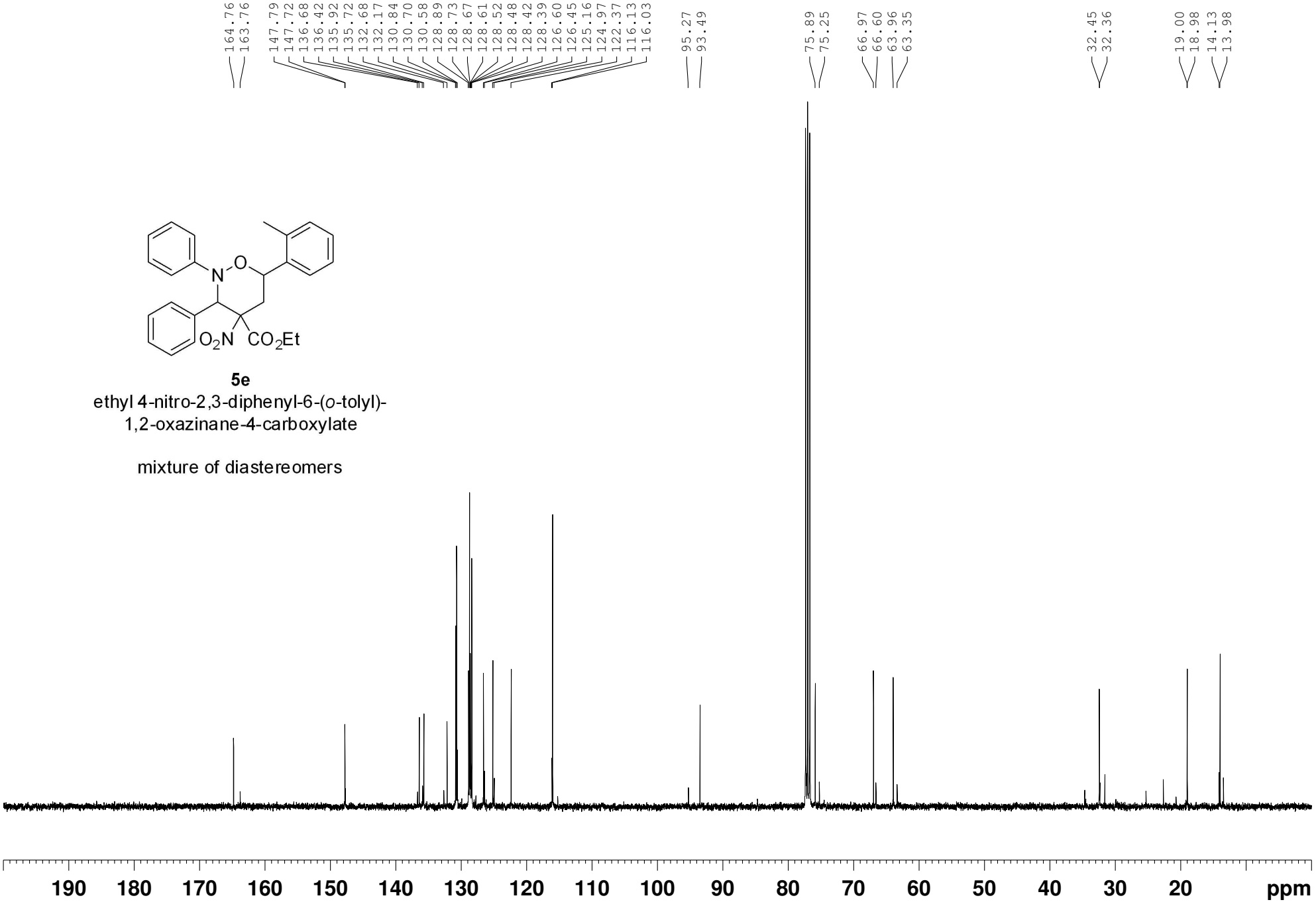


5e

ethyl 4-nitro-2,3-diphenyl-6-(*o*-tolyl)-1,2-oxazinane-4-carboxylate

mixture of diastereomers

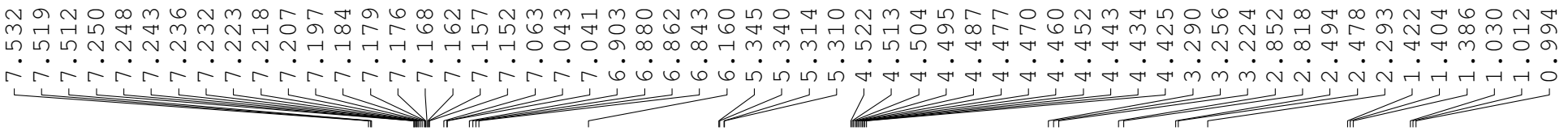


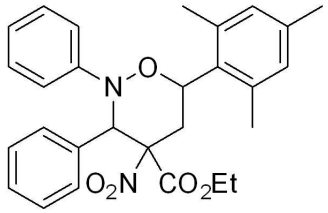


5e

ethyl 4-nitro-2,3-diphenyl-6-(*o*-tolyl)-1,2-oxazinane-4-carboxylate

mixture of diastereomers

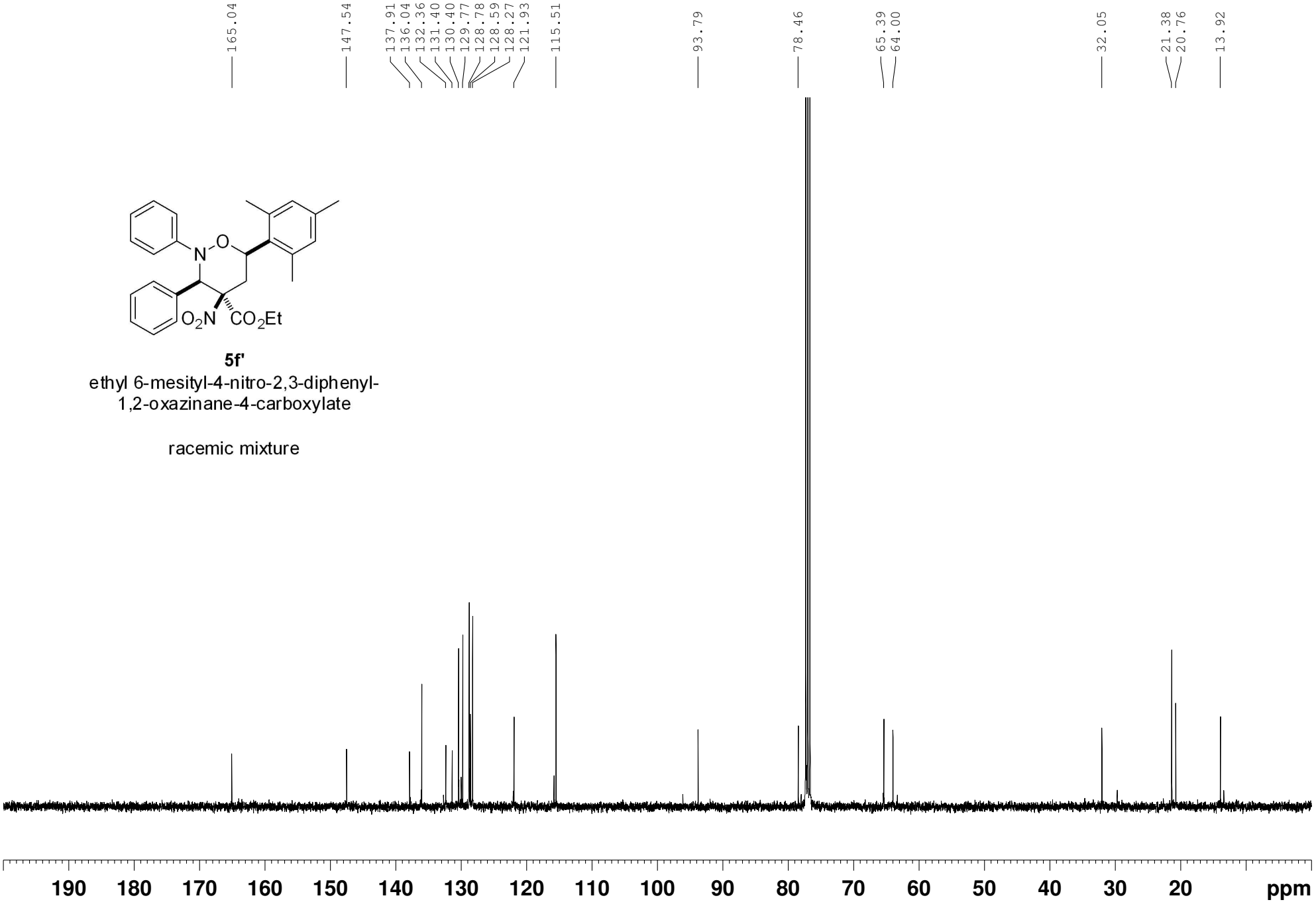




5f

ethyl 6-mesityl-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

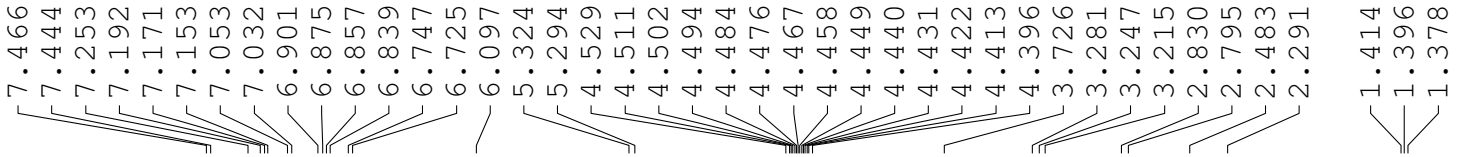
mixture of diastereomers

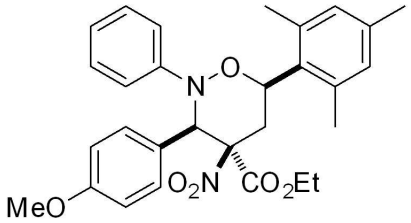


5f'

ethyl 6-mesityl-4-nitro-2,3-diphenyl-1,2-oxazinane-4-carboxylate

racemic mixture

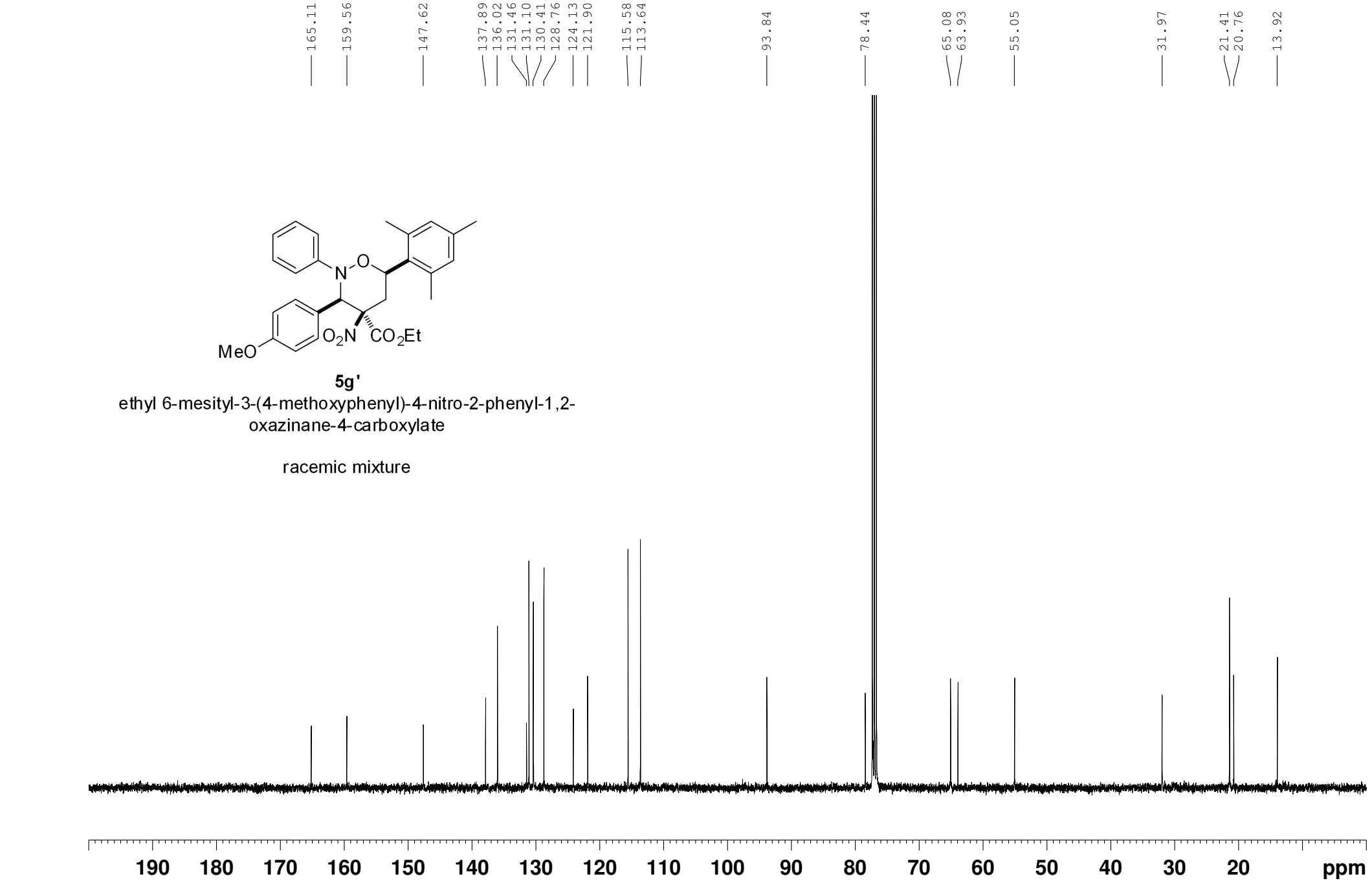




5g'

ethyl 6-mesityl-3-(4-methoxyphenyl)-4-nitro-2-phenyl-1,2-oxazinane-4-carboxylate

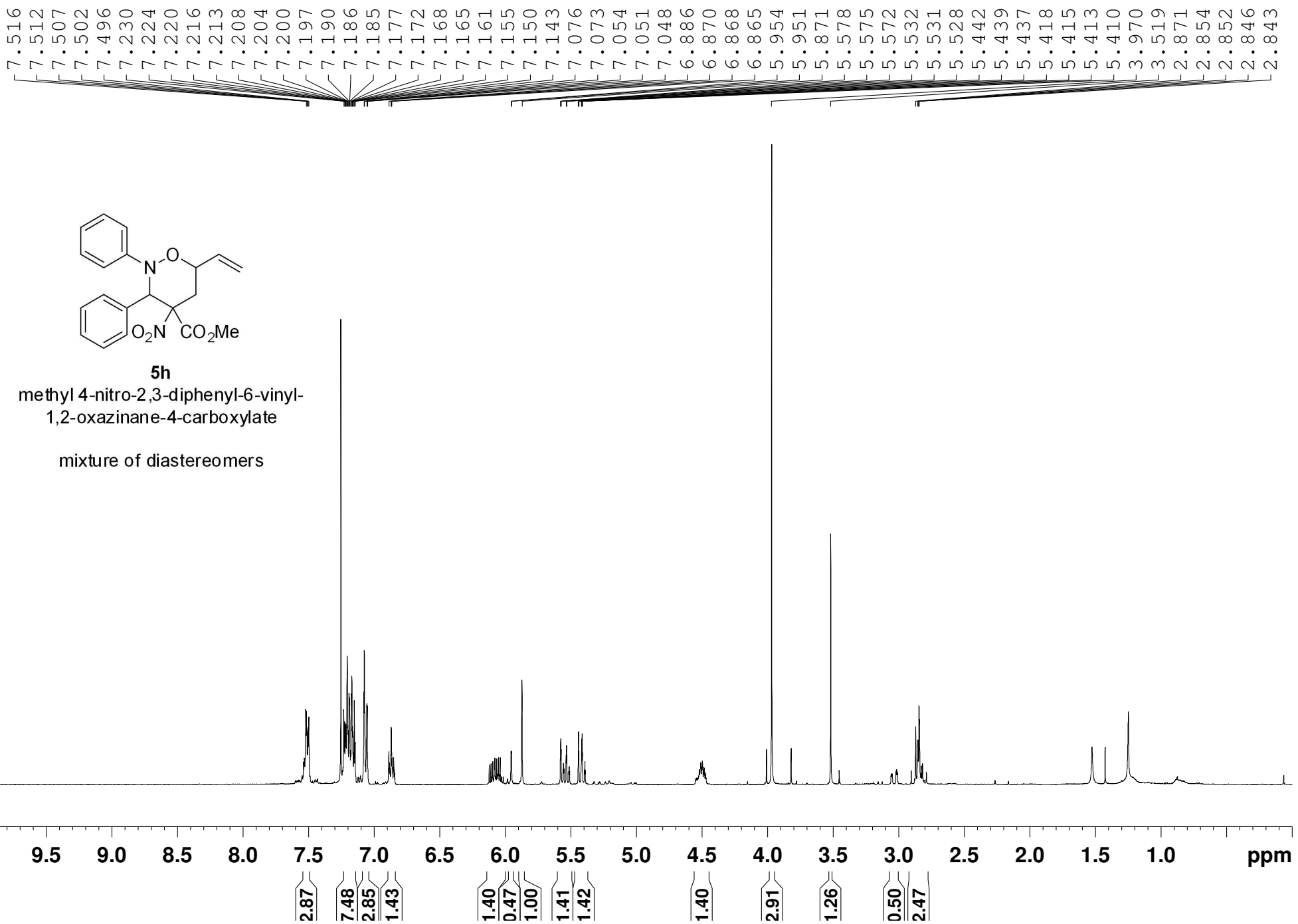
racemic mixture



5g'

ethyl 6-mesityl-3-(4-methoxyphenyl)-4-nitro-2-phenyl-1,2-oxazinane-4-carboxylate

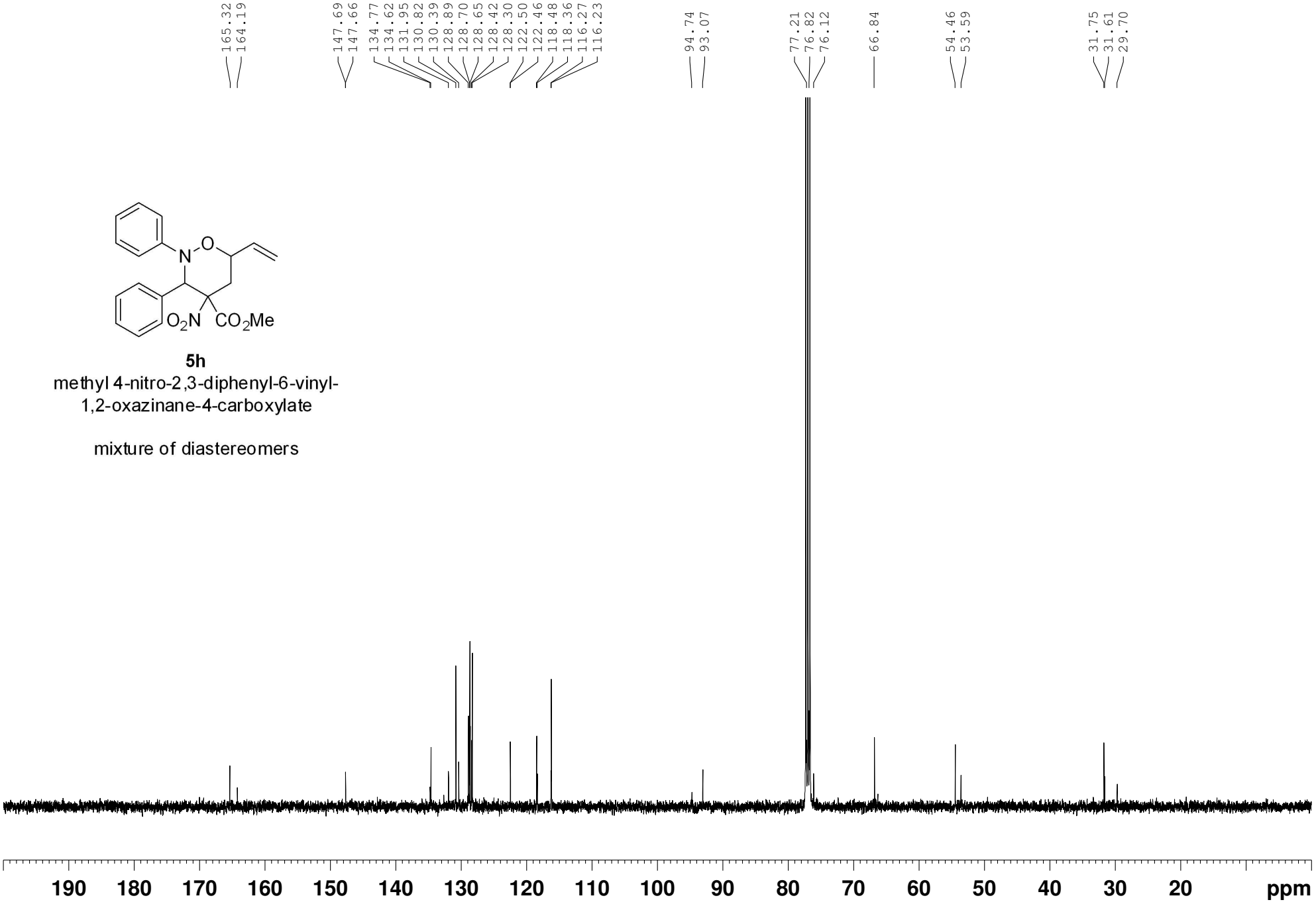
racemic mixture



5h

methyl 4-nitro-2,3-diphenyl-6-vinyl-1,2-oxazinane-4-carboxylate

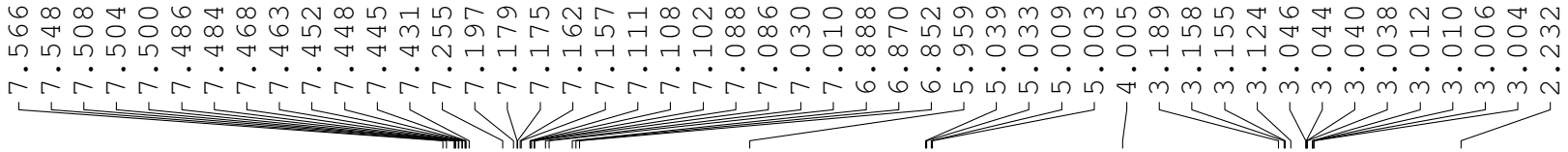
mixture of diastereomers

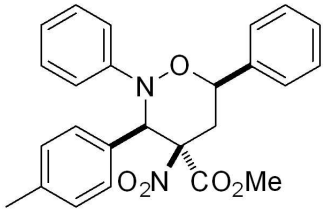


5h

methyl 4-nitro-2,3-diphenyl-6-vinyl-1,2-oxazinane-4-carboxylate

mixture of diastereomers

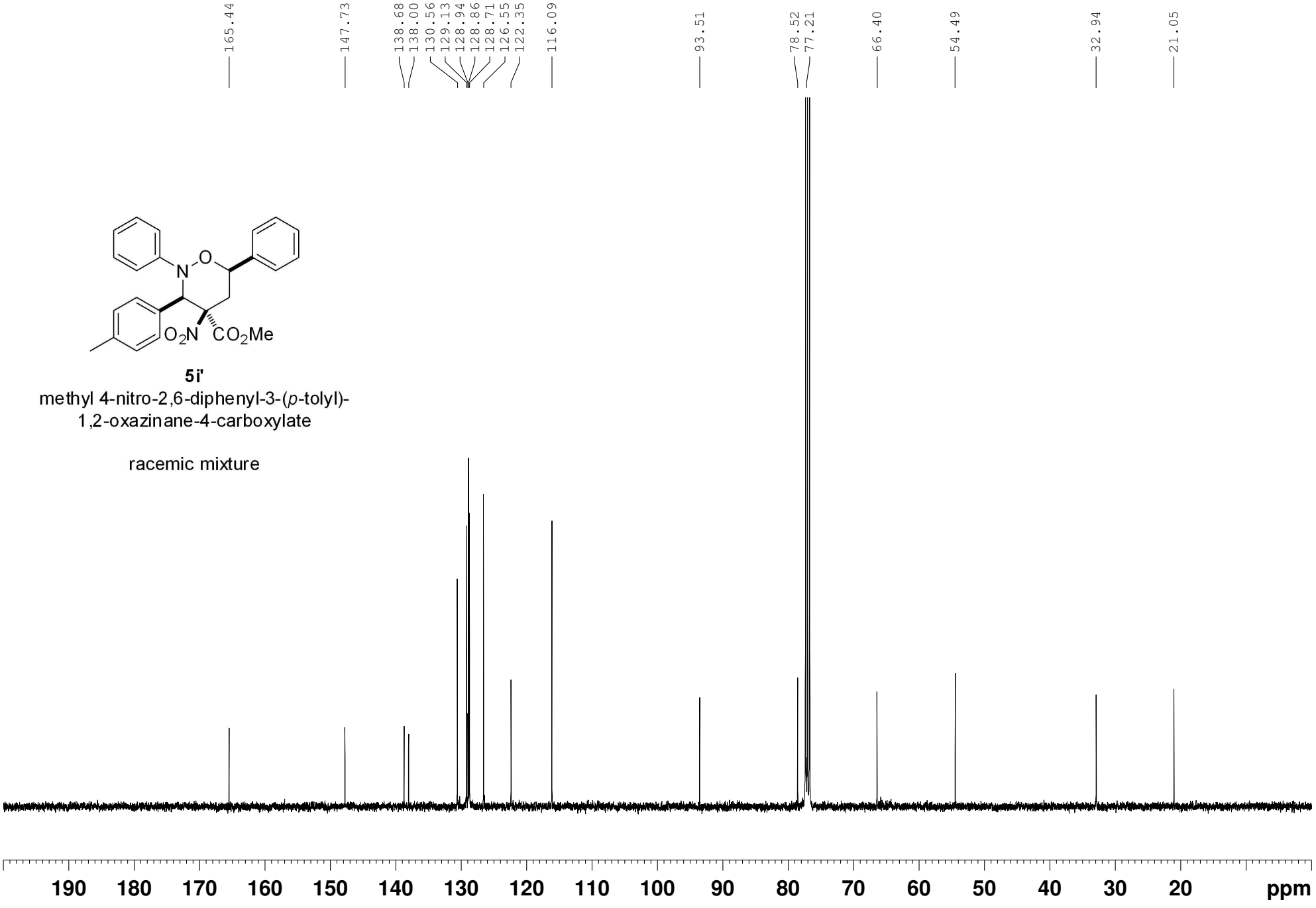




5i'

methyl 4-nitro-2,6-diphenyl-3-(*p*-tolyl)-1,2-oxazinane-4-carboxylate

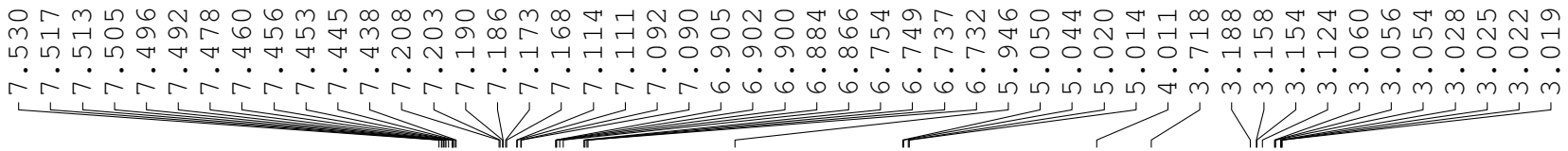
racemic mixture

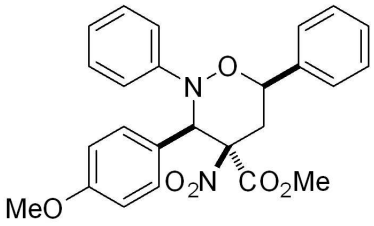


5i'

methyl 4-nitro-2,6-diphenyl-3-(*p*-tolyl)-1,2-oxazinane-4-carboxylate

racemic mixture

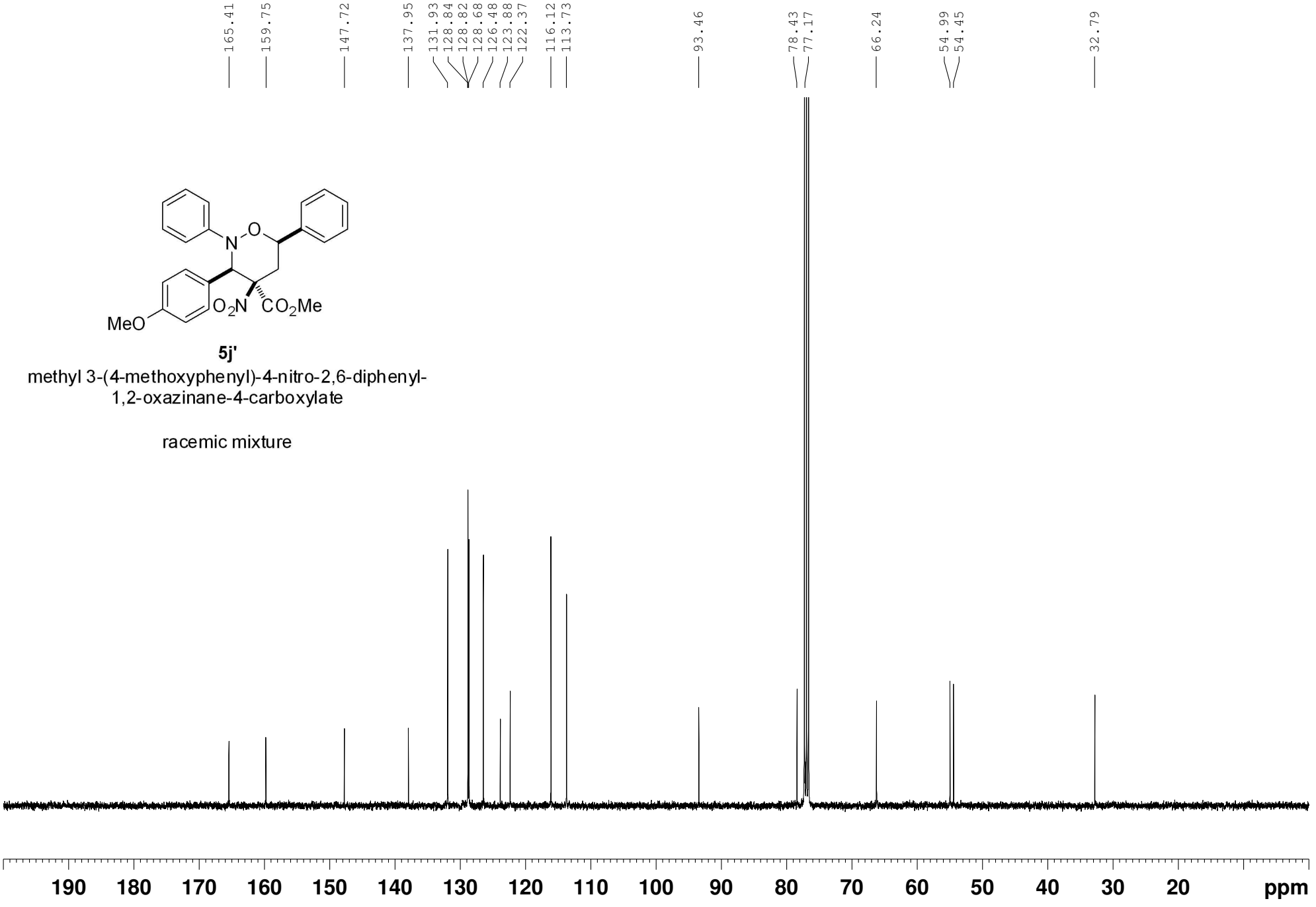




5j'

methyl 3-(4-methoxyphenyl)-4-nitro-2,6-diphenyl-1,2-oxazinane-4-carboxylate

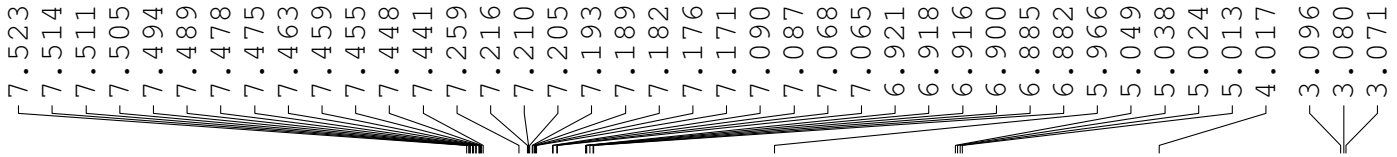
racemic mixture

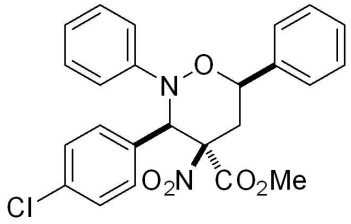


5j'

methyl 3-(4-methoxyphenyl)-4-nitro-2,6-diphenyl-1,2-oxazinane-4-carboxylate

racemic mixture

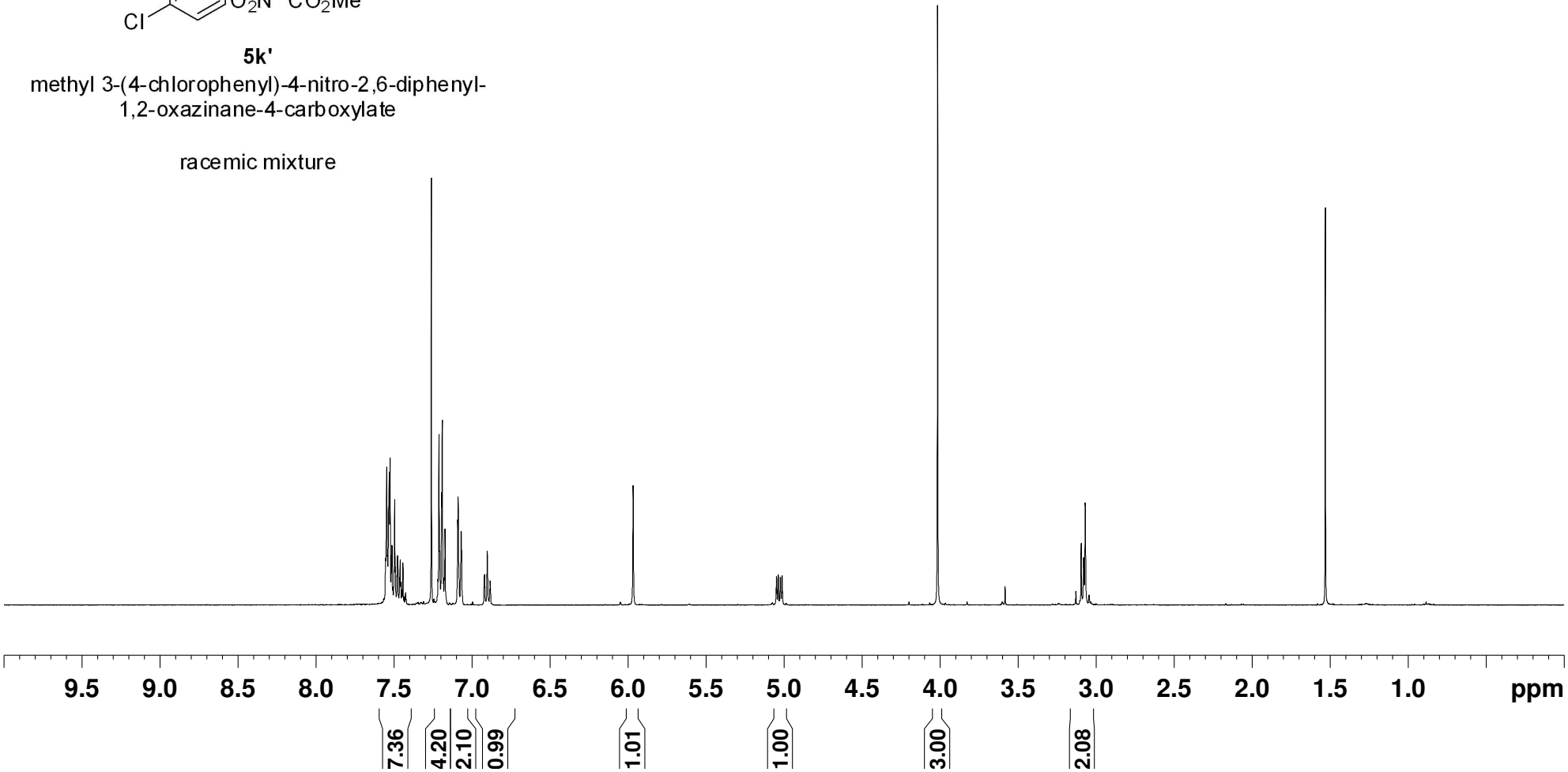


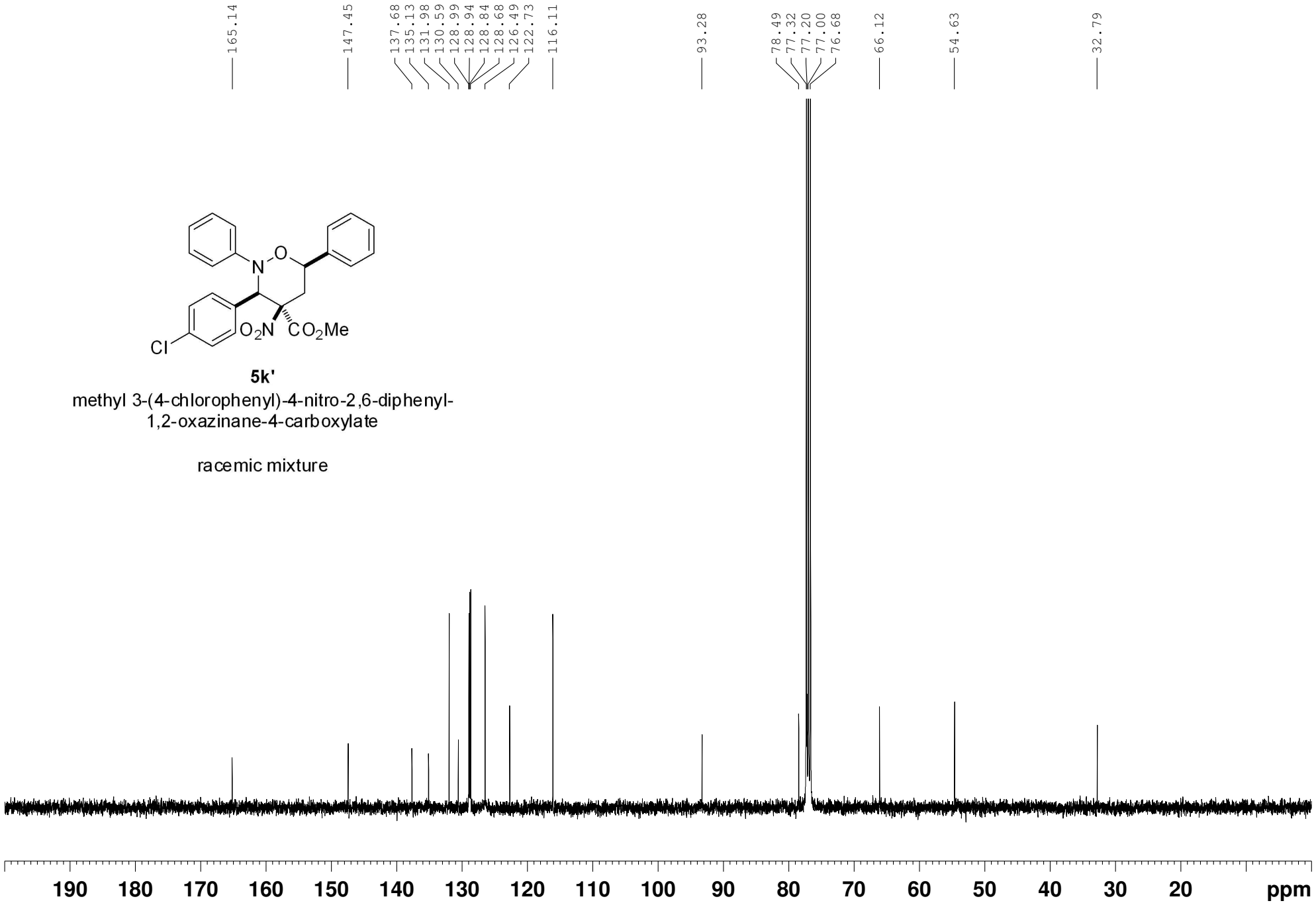


5k'

methyl 3-(4-chlorophenyl)-4-nitro-2,6-diphenyl-1,2-oxazinane-4-carboxylate

racemic mixture

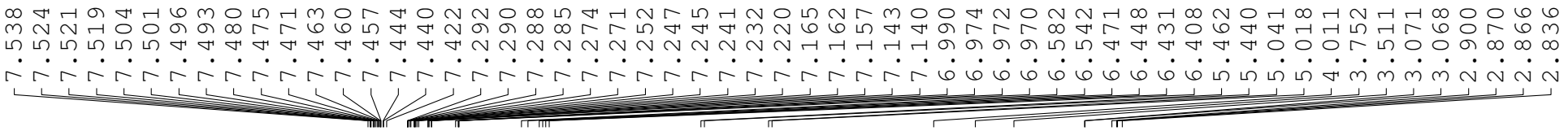


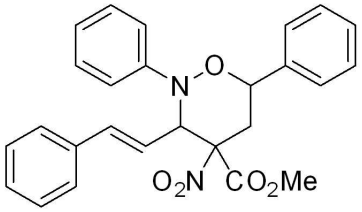


5k'

methyl 3-(4-chlorophenyl)-4-nitro-2,6-diphenyl-1,2-oxazinane-4-carboxylate

racemic mixture

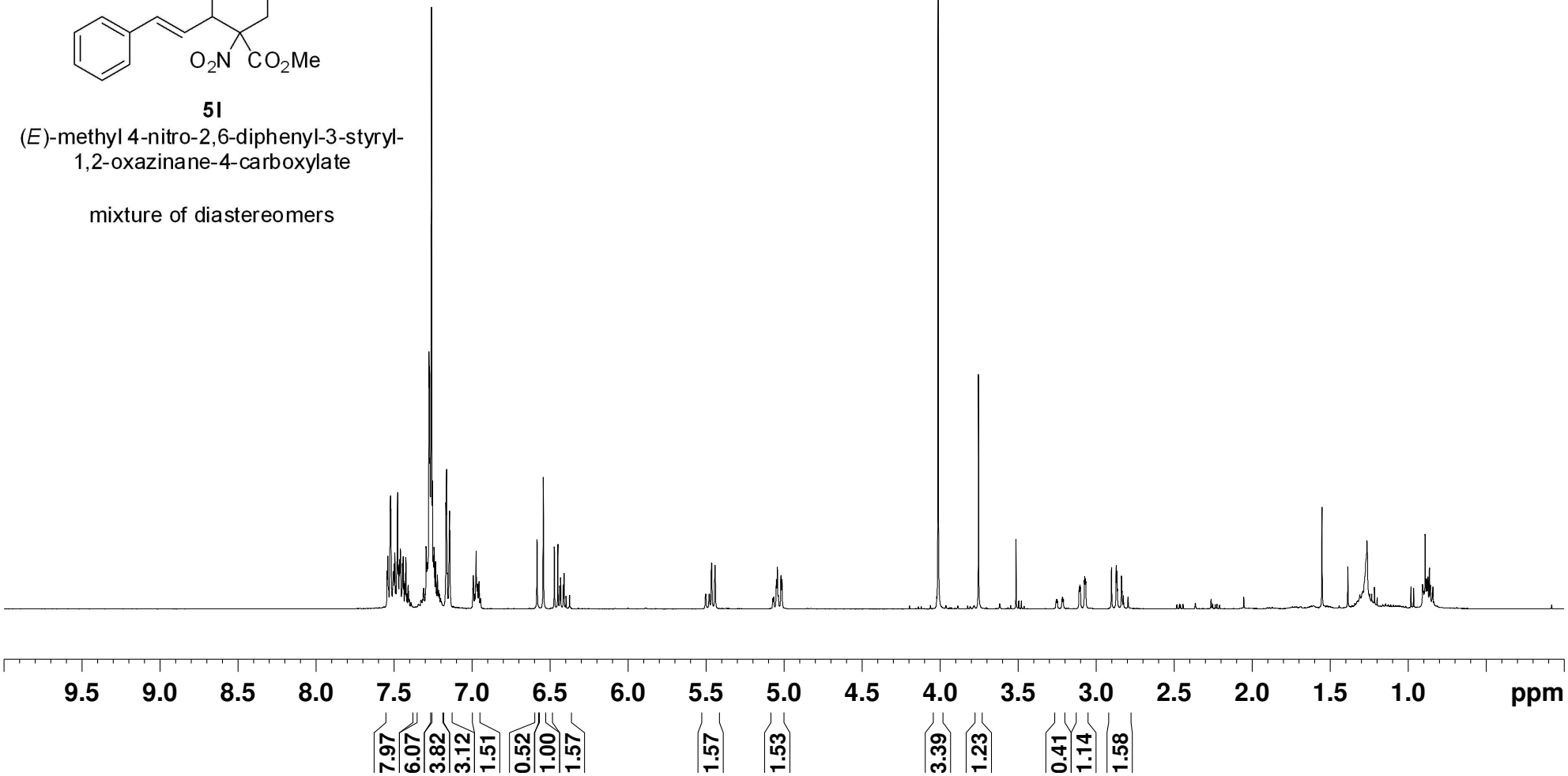


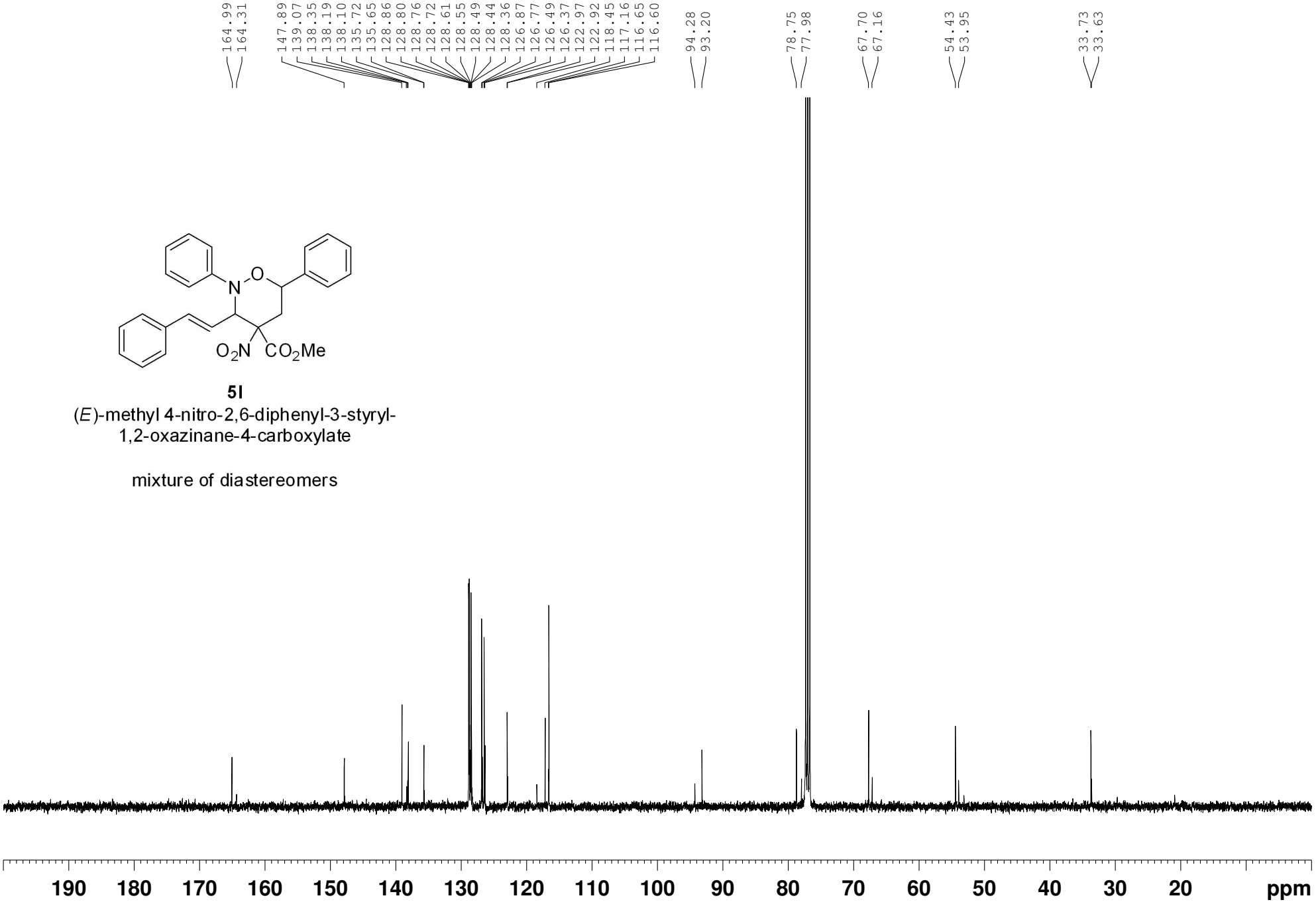


5l

(*E*)-methyl 4-nitro-2,6-diphenyl-3-styryl-1,2-oxazinane-4-carboxylate

mixture of diastereomers

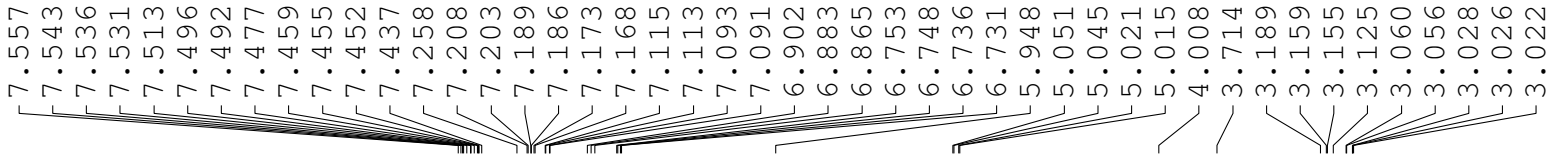


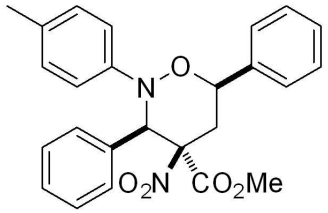


5l

(*E*)-methyl 4-nitro-2,6-diphenyl-3-styryl-1,2-oxazinane-4-carboxylate

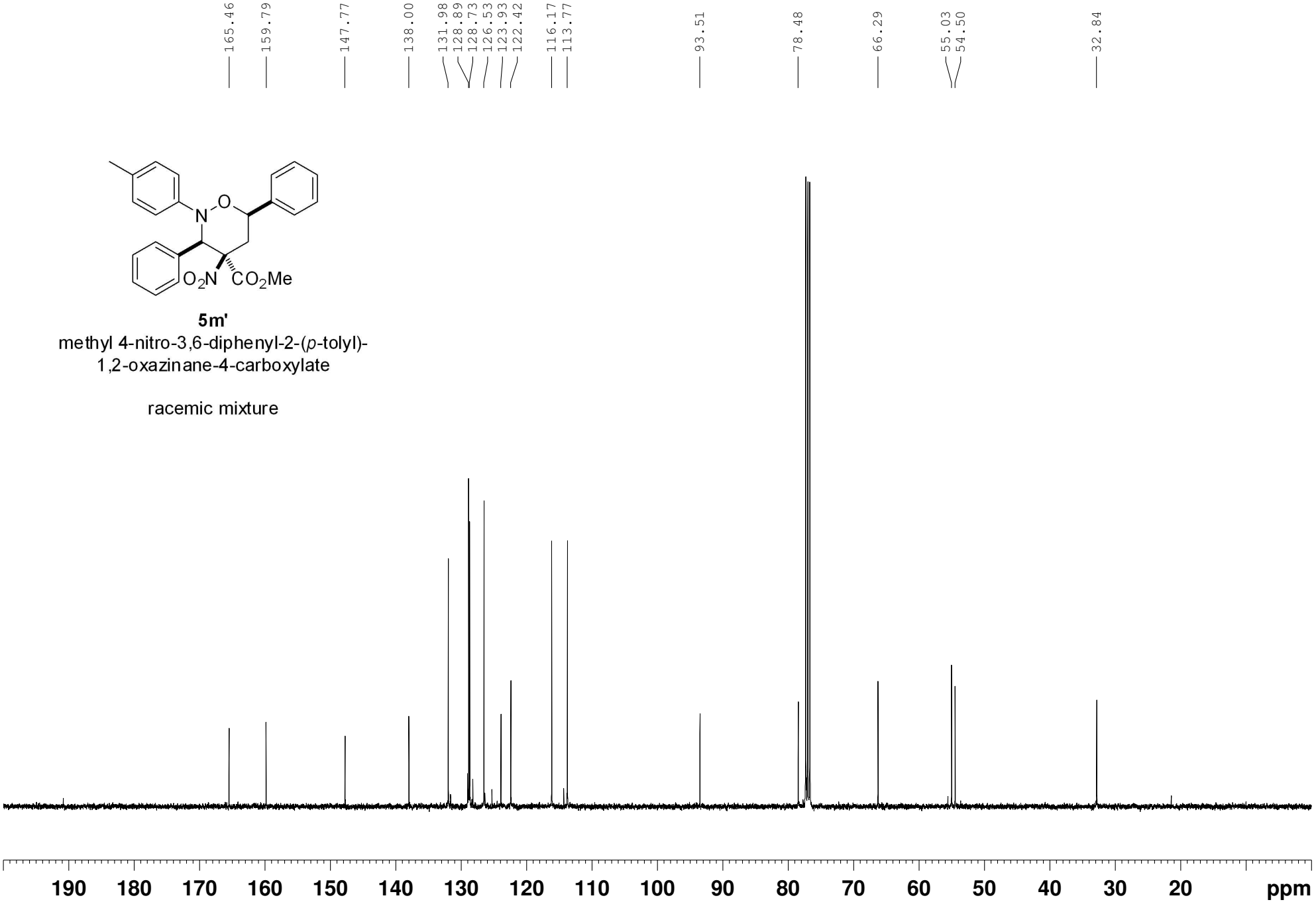
mixture of diastereomers





5m'
methyl 4-nitro-3,6-diphenyl-2-(*p*-tolyl)-1,2-oxazinane-4-carboxylate

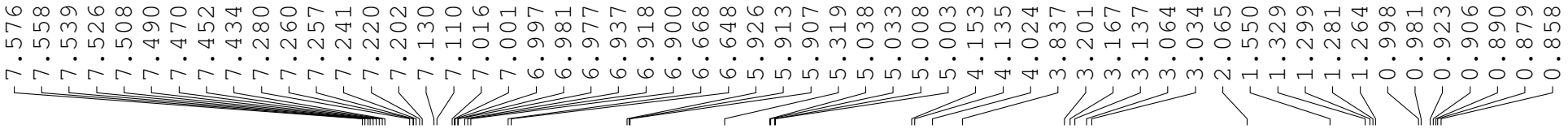
racemic mixture

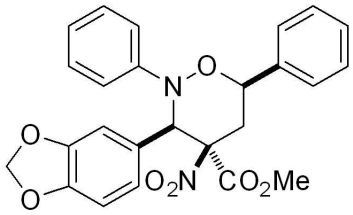


5m'

methyl 4-nitro-3,6-diphenyl-2-(*p*-tolyl)-1,2-oxazinane-4-carboxylate

racemic mixture

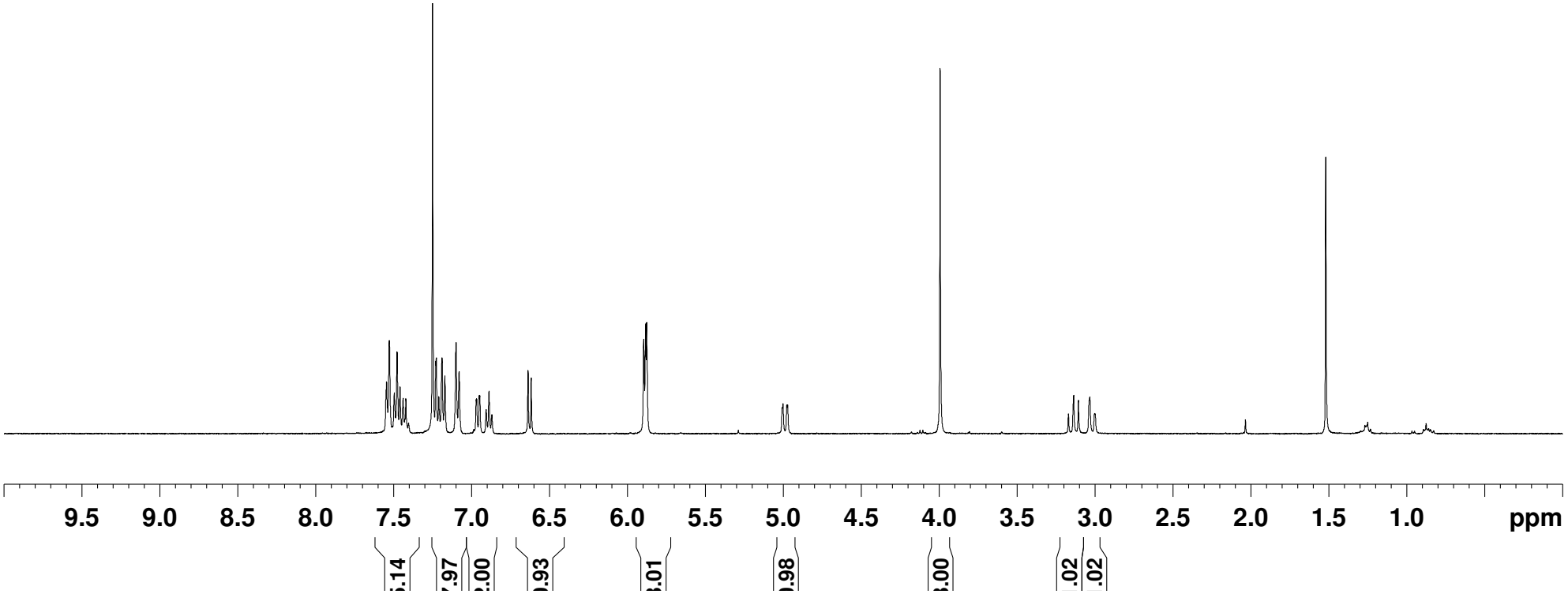


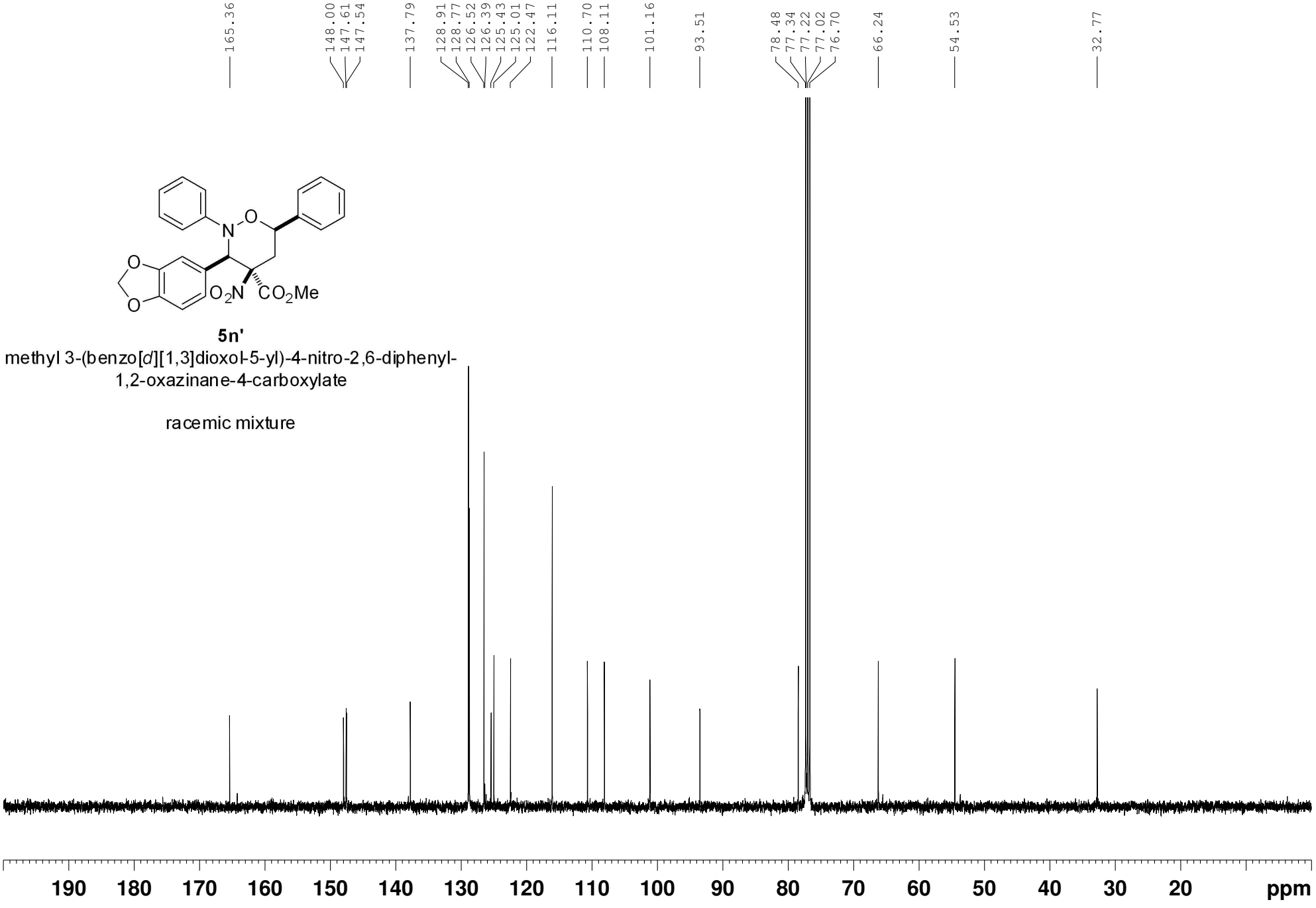


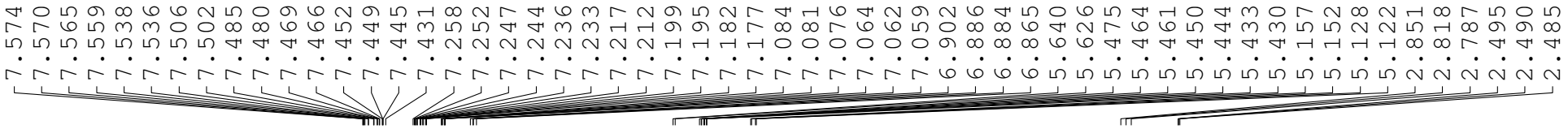
5n'

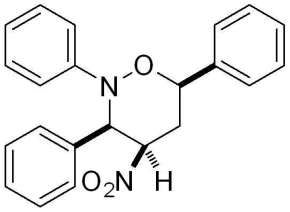
methyl 3-(benzo[*d*][1,3]dioxol-5-yl)-4-nitro-2,6-diphenyl-1,2-oxazinane-4-carboxylate

racemic mixture





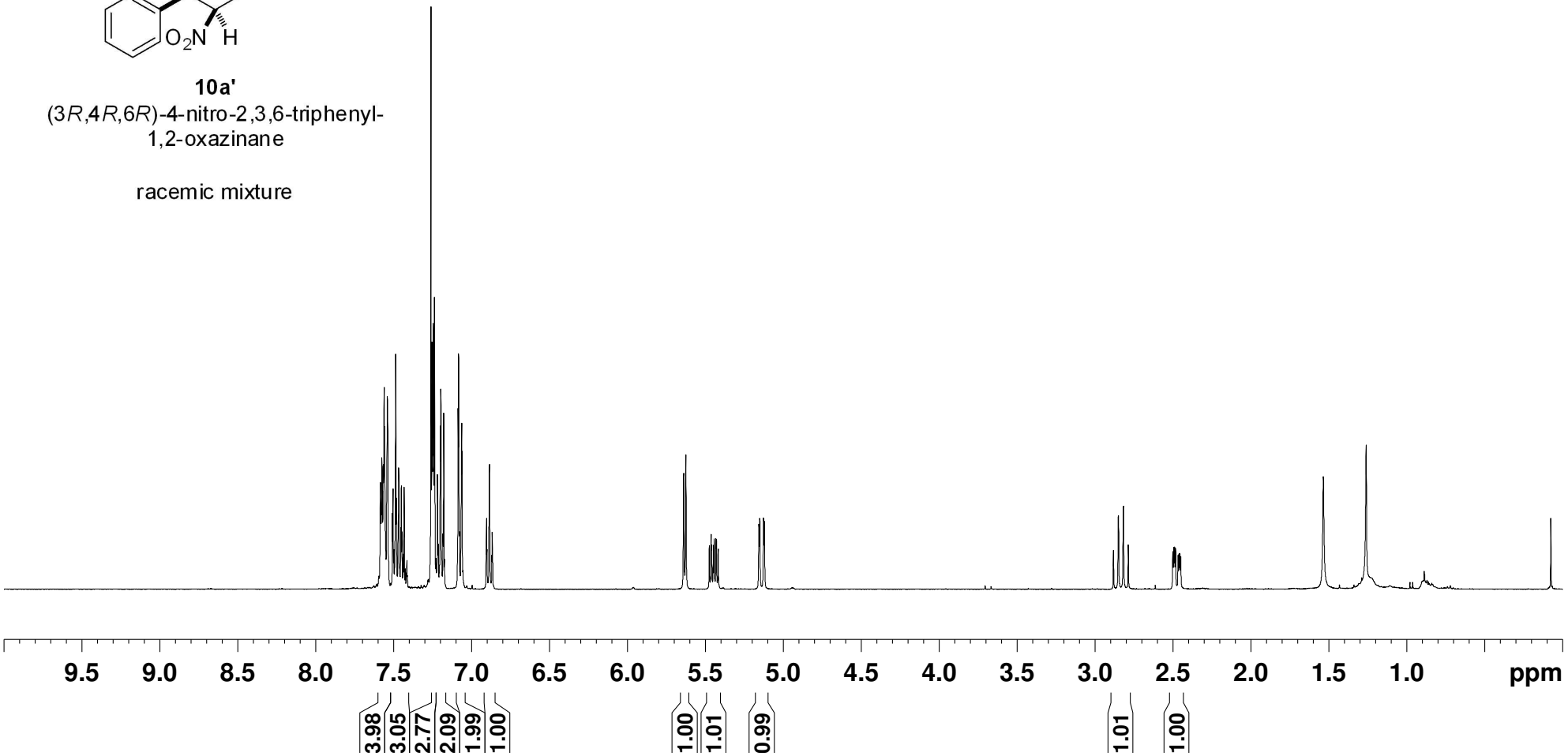


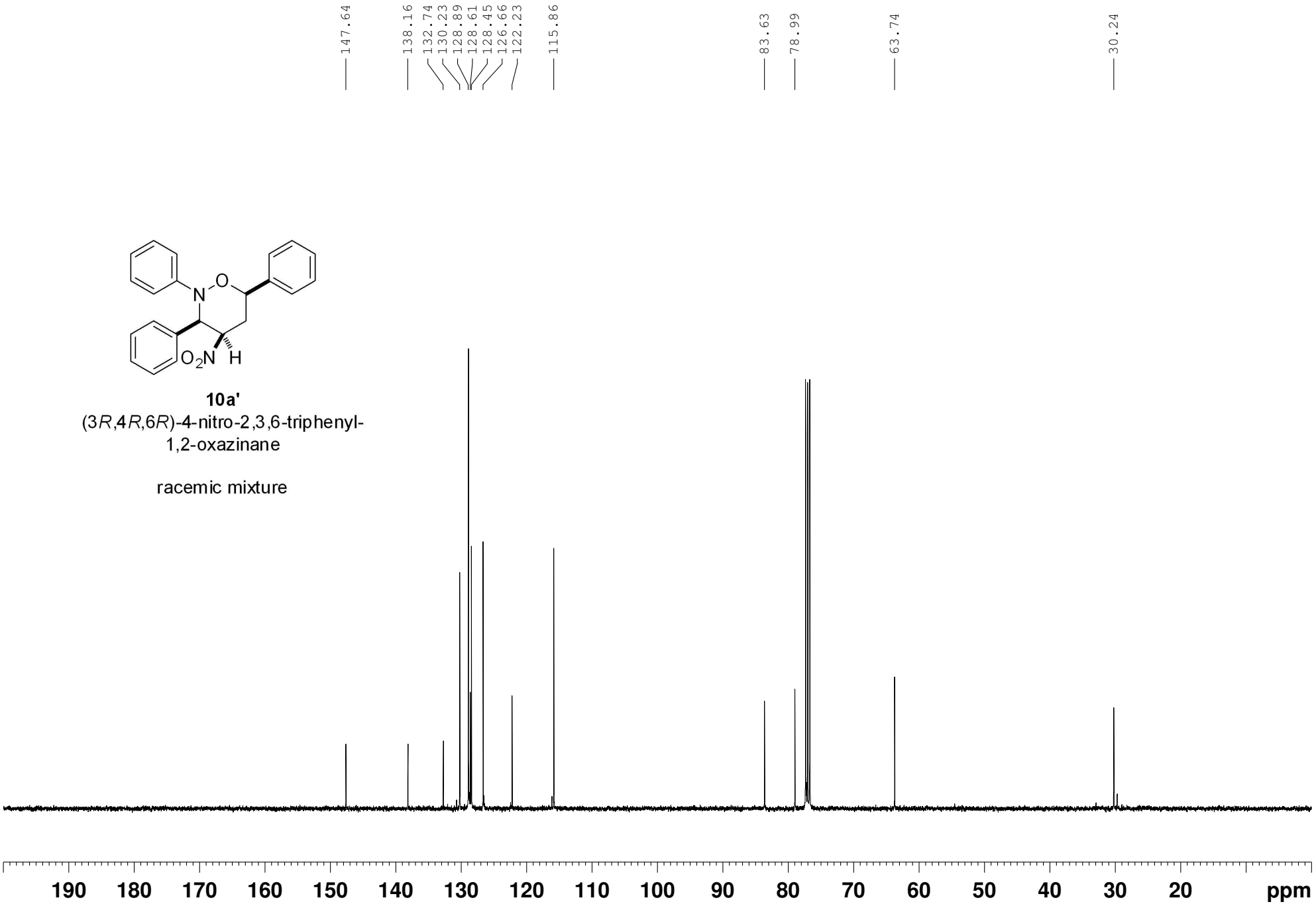


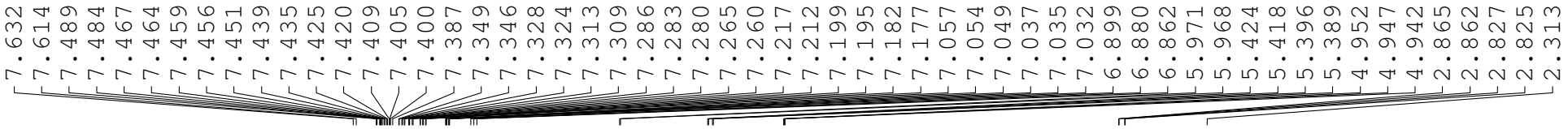
10a'

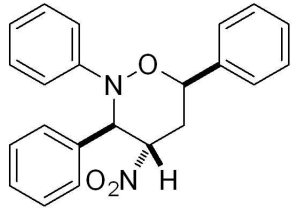
(3*R*,4*R*,6*R*)-4-nitro-2,3,6-triphenyl-1,2-oxazinane

racemic mixture





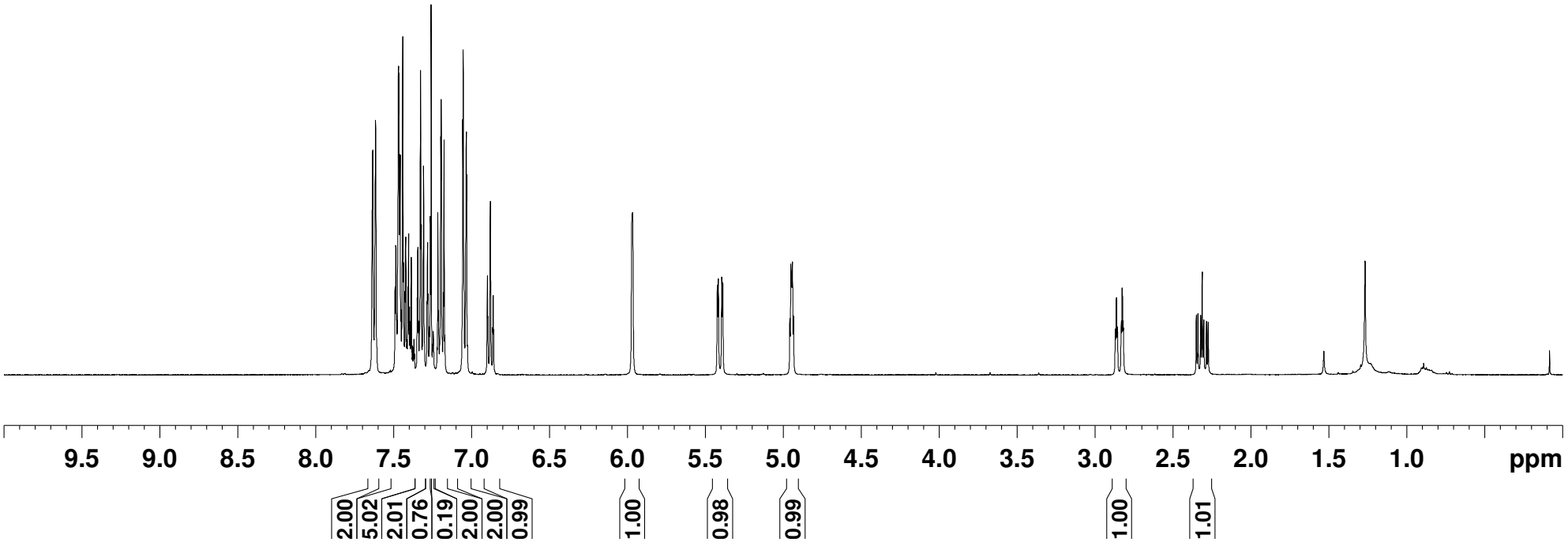


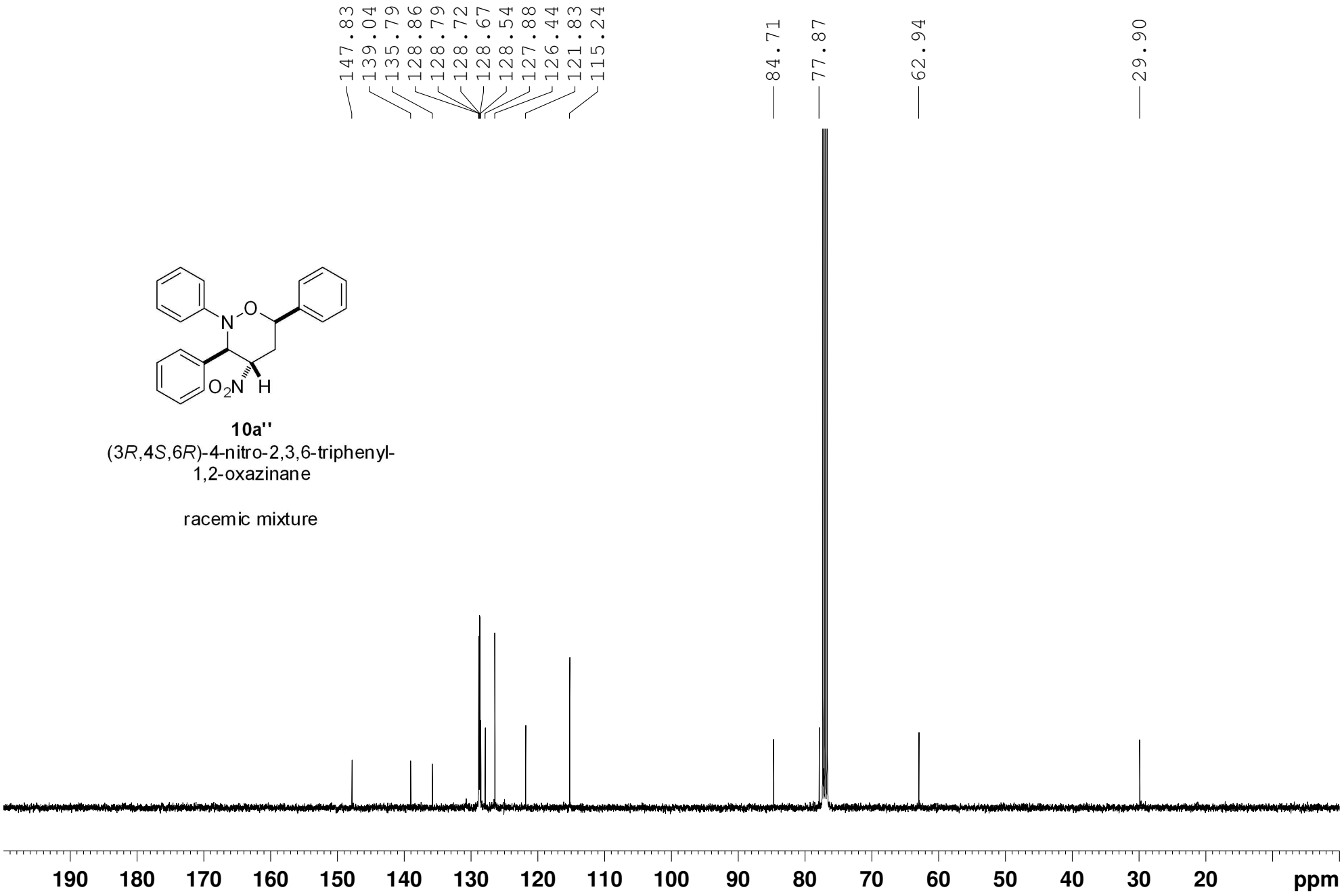


10a''

(3*R*,4*S*,6*R*)-4-nitro-2,3,6-triphenyl-1,2-oxazinane

racemic mixture

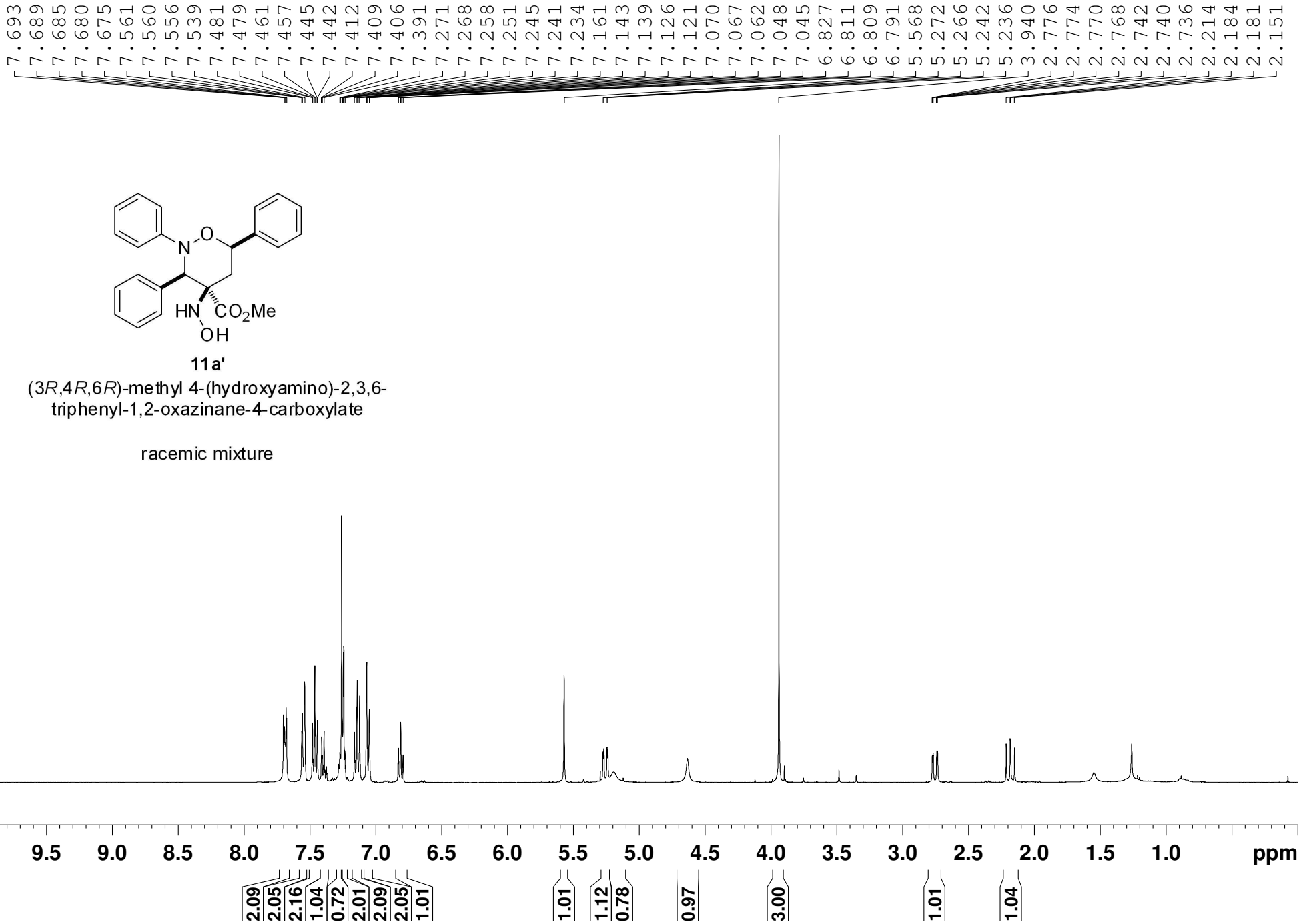


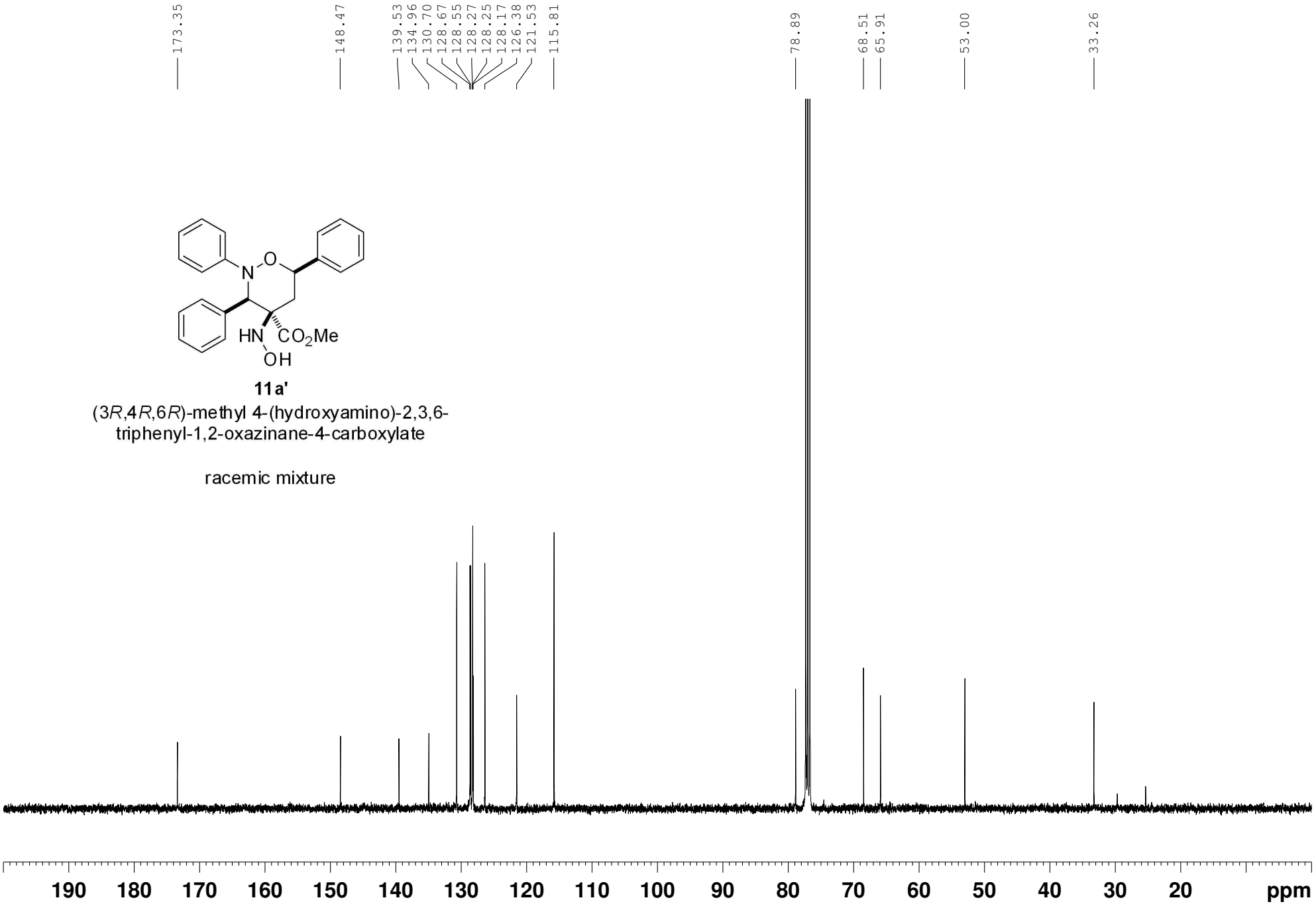


10a''

(3*R*,4*S*,6*R*)-4-nitro-2,3,6-triphenyl-1,2-oxazinane

racemic mixture

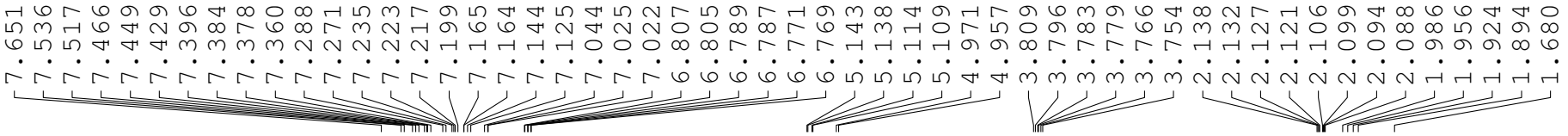


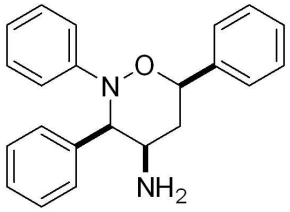


11a'

(3*R*,4*R*,6*R*)-methyl 4-(hydroxyamino)-2,3,6-triphenyl-1,2-oxazinane-4-carboxylate

racemic mixture





12a'

(3*R*,4*R*,6*R*)-2,3,6-triphenyl-1,2-oxazinan-4-amine

racemic mixture