Stereoselective Synthesis of Cyclic Guanidines by Directed Diamination of Unactivated Alkenes

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Supplementary Information

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General Information. All reactions were carried out under an inert atmosphere of dry argon in oven or flame-dried glassware, unless the reaction procedure states otherwise. Dichloromethane, *N*,*N*-diisopropylethylamine and acetonitrile were distilled from calcium hydride in a continuous still under an atmosphere of argon. Reaction temperatures were controlled by IKA ETS-D4 fuzzy thermo couples. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with Silica Gel 60 F_{254} (EMD no. 5715-7) and visualized using combinations of UV, anisaldehyde, ceric ammonium molybdate (CAM), potassium permanganate and iodine staining. Flash column chromatography was preformed using 40-63 μm silica gel (Merck, Geduran, no. 11567-1) as the stationary phase. Proton nuclear magnetic resonance spectra were recorded at 400, 500, and 600 MHz on Varian Unity Inova spectrometers. Carbon nuclear magnetic resonance spectra were recorded at 100 MHz, 125 MHz, and 150 MHz on Varian Unity Inova spectrometers. All Chemical shifts were reported in δ units relative to tetramethylsilane. High Resolution mass spectral data were obtained by the Mass Spectrometry laboratory at the University of California, Santa Barbara. All homoallylic alcohols were synthesized using standard Barbier reaction protocol starting from corresponding readily available aldehydes as described by Wang and co-authors.[1] Homoallylic alcohols **S1q** and **S1r** were prepared as a 1:1 mixture that was separated by HPLC chromatography. The relative *syn* or *anti* stereochemistry was determined by the comparison of ^{1}H NMR data with previously reported assignment.[2] Hydrocinnamaldehyde, cyclohexanecarboxaldehyde, butyraldehyde, isovaleraldehyde, benzaldehyde, 4-bromobenzaldehyde, 2-fluorobenzaldehyde, 4-formylbenzonitrile, anisaldehyde and guanidine hydrochloride were purchased from Sigma-Aldrich, Acros Organics, Alfa Aesar or Fisher Scientific. 3-(Benzyloxy)propanal[3], 3-((4-methoxybenzyl)oxy)propanal[4], 3-((tert-butyldimethylsilyl)oxy)propanal[5], ethyl 6-oxohexanoate[6], hex-5-enal[7], hex-5-ynal[8], 3-(1,3-dioxoisoindolin-2-yl)propanal[9] and tert-butyl (3-oxopropyl)carbamate[10], 3-Phenylhex-5-enoic acid[11] **S2** and 2-phenylhex-5-enoic acid[12] **S3** were prepared according to known literature protocols.

General procedure for the guanidine-containing substrates synthesis:

Method A:

A solution of corresponding alcohol (11.0 mmol) in dichloromethane (22.0 mL, 0.5 M) was cooled to 0 °C and a freshly prepared solution of triphosgene (4.95 mmol) in dichloromethane (10 mL 0.5 M) was added dropwise over 5 min period. During that time no exothermic reaction was observed and then the resultant solution was stirred for 10 min before pyridine (0.88 ml, 11.0 mmol) was added dropwise over 30 min period maintaining the temperature below 5 °C. Upon completion of the addition the stirring was continued for 10 min at 0 °C and then the reaction was diluted

[1] Zhang, Z.; Zhang, J.; Tan, J.; Wang, Z. *J. Org. Chem.*, ***2008***, *73,* 5180.
[2] Kim, H; Ho, S.; Leighton, J, L. *J. Am. Chem. Soc.*, **2011**, 133, 6517-6520.
[3] Mans, D. M.; Pearson, W. H., *Org. Lett.*, ***2004***, *6,* 3305.
[4] Hernández, D.; Lindsay, K. B.; Nielsen, L.; Mittag, T.; Bjerglund, K.; Friis, S.; Mose, R.; Skrydstrup, T. *J. Org. Chem.*, ***2010***, *75,* 3283.
[5] Marshall, J. A.; Van Devender, E. A. *J. Org. Chem.*, **2001**, 66, 8037.
[6] Cloarec, J.-M.; Charette, A. B., *Org. Lett.*, ***2004***, *6,* 4731.
[7] Liniger, M.; Neuhaus, C.; Hofmann, T.; Fransioli-Ignazio, L.; Jordi, M.; Drueckes, P.; Trappe, J.; Fabbro, D.; Altmann, K.-H. *ACS Med. Chem. Lett.*, ***2011***, *2,* 22.
[8] Amoroso, J. W.; Borketey, L. S.; Prasad, G.; Schnarr, N. A. *Org. Lett.*, ***2010***, *12,* 2330.
[9] Storz, M. P.; Allegretta, G.; Kirsch, B.; Empting, M.; Hartmann, R. W. *Org. Biomol. Chem.*, ***2014***, *12,* 6094.
[10] Hequet, A.; Burchak O.N.; Jeanty, M.; Guinchard. X.; Le Pihive, M.; Paris, J.; Denis, J.; Jolivalt, C. *Chem. Med. Chem.*, ***2014***, *9,* 1534.
[11] Stella, L.; Raynier, B.; Surzur, J. M. *Tetrahedron*, **1981**, *37*, 2843-2854.
[12] Barczak, N. T.; Jarvo, E. R. *Chem. Eur. J.*, **2011**, *17*, 12912-12916.

with dichloromethane (40 mL) and poured in water (150 mL). The product was extracted with dichloromethane (3x50 mL) and the combined organic phase was washed with brine (200 mL), dried over Na_2SO_4 and concentrated under reduced pressure providing crude product as yellowish liquid that was used for the next step without further purification.

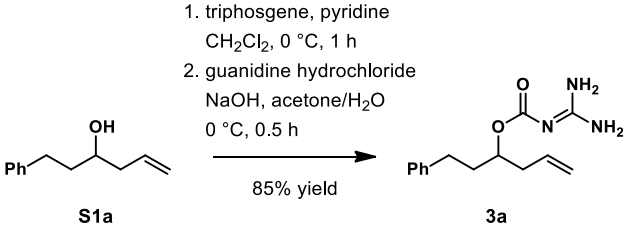
An aqueous solution of free guanidine was prepared by addition of guanidine hydrochloride (4.20 g, 44.0 mmol) to a solution of sodium hydroxide (1.85 g, 46.2 mmol) in water (18.5 mL, 2.5 M) cooled to 0 °C and the resultant homogenous mixture was stirred for 20 min at the same temperature. Then a solution of corresponding chloroformate in acetone (18.5 mL) was added dropwise during 5 min maintaining temperature below 7 °C. After stirring for additional 10 min the mixture was poured into water (100 mL) and the product was extracted with ethyl acetate (3x50 ml). Combined organic phase was washed once with water (100 mL), dried over sodium sulfate and concentrated under reduced pressure to provide crude material that was purified by column chromatography on silica gel (3% methanol in dichloromethane 10% methanol in dichloromethane) or by washing solid material with hexanes and filtration of the pure product.

Method B:

To a solution of corresponding alcohol (5.00 mmol) in tetrahydrofuran (17.0 mL, 0.3 M) 1,1'-carbonyldiimidazole (0.970 g, 6.00 mmol) was added and the resultant mixture was stirred overnight at ambient temperature. After the TLC analysis showed a complete disappearance of the starting alcohol the resultant mixture was directly added dropwise during 20 min to the freshly prepared solution of free guanidine (20.0 mmol) in dimethylformamide (see below). Then the mixture was poured into water (200 mL) and the product was extracted with ethyl acetate (4x70 ml). Combined organic phase was sequentially washed with brine (3x100 ml), saturated aqueous ammonium chloride solution (2x100 mL) and brine (100 mL) again, dried over sodium sulfate and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (3% methanol in dichloromethane 10% methanol in dichloromethane) or by washing solid material with hexanes and filtration of the pure product.

Preparation of free guanidine solution in DMF:

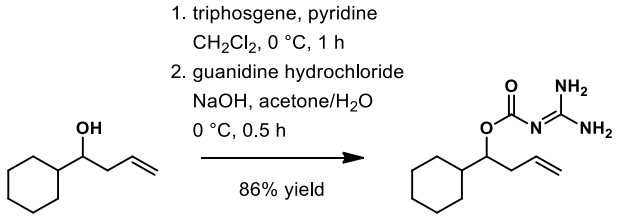
A solution of free guanidine was prepared in separate flask by initial dissolution of sodium (0.460 g, 20.0 mmol) in methanol (15.0 mL) followed by addition of guanidine hydrochloride (1.91 g, 20.0 mmol) into the resulting solution. The resultant cloudy mixture was stirred for 30 min before evaporation to dryness under reduced pressure. To make sure that most portion of MeOH was removed the residue was dried for 30 min under vacuum (failure to do so may result in formation of significant amount of corresponding methyl carbonate). The dry residue was dissolved in dimethylformamide (34.0 mL).



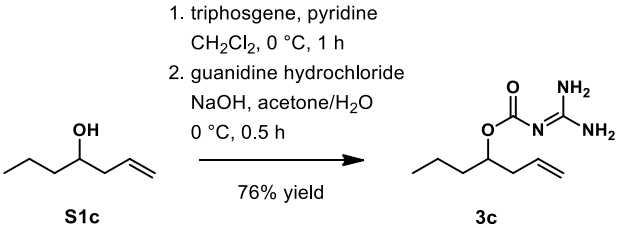
S1a **3a**

Compound 3a. The title compound was prepared according to general method **A** using alcohol **S1a** (1.94 g, 11.0 mmol), triphosgene (1.46 g, 4.95 mmol) and pyridine

(0.88 mL, 11.0 mmol) in 32.0 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (18.5 mL) with a solution of free guanidine in 18.5 mL of water prepared from guanidine hydrochloride (4.20 g, 44.0 mmol) and sodium hydroxide (1.85 g, 46.2 mmol). Compound **3a** (2.50 g, 9.6 mmol, 85% yield) was obtained as white solid after washing with hexanes and filtration. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 2H), 7.16 (m, 3H), 6.58 (br. s, 4H), 5.87 – 5.70 (m, 1H), 5.17 – 5.01 (m, 2H), 4.87 – 4.74 (m, 1H), 2.82 – 2.66 (m, 1H), 2.65 – 2.54 (m, 1H), 2.47 – 2.30 (m, 2H), 1.98 – 1.81 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 162.9, 141.9, 133.9, 128.5, 128.5, 126.0, 117.8, 73.1, 39.0, 35.7, 31.9. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{19}N_3O_2Na$, 284.1375; found, 284.1367. Also compound **3a** was also prepared using method **B** in 87% yield.

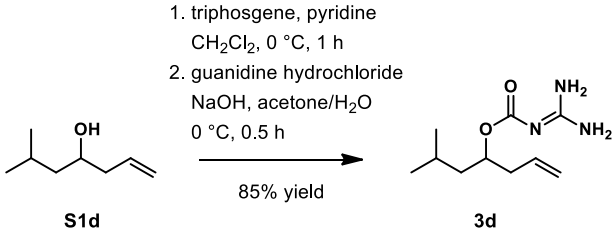


Compound 3b. The title compound was prepared according to general method **A** using alcohol **S1b** (1.46 g, 9.50 mmol), triphosgene (1.26 g, 4.27 mmol) and pyridine (0.76 mL, 9.50 mmol) in 28 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (16.0 mL) with a solution of free guanidine in 16.0 mL of water prepared from guanidine hydrochloride (3.62 g, 38.0 mmol) and sodium hydroxide (1.60 g, 39.9 mmol). Compound **3b** (1.95 g, 8.17 mmol, 86% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (br. s, 4H), 5.85 – 5.68 (m, 1H), 5.15 – 4.93 (m, 2H), 4.69 – 4.51 (m, 1H), 2.47 – 2.22 (m, 2H), 1.84 – 1.58 (m, 5H), 1.57 – 1.40 (m, 1H), 1.25 – 0.91 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 162.8, 134.6, 117.1, 41.0, 35.9, 29.3, 29.0, 28.2, 26.4, 26.1, 26.0. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{21}N_3O_2Na$, 262.1531; found, 262.1527.



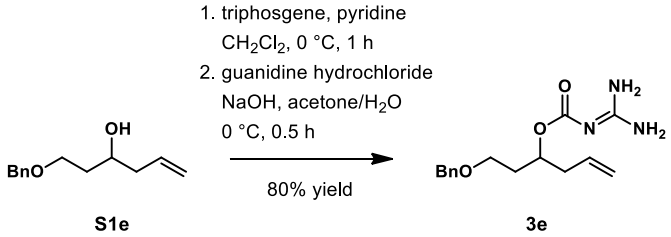
Compound 3c. The title compound was prepared according to general method **A** using alcohol **S1c** (1.50 g, 13.2 mmol), triphosgene (1.74 g, 5.94 mmol) and pyridine (1.06 mL, 13.2 mmol) in 38 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (22.0 mL) with a solution of free guanidine in 22.0 mL of water prepared from guanidine hydrochloride (5.04 g, 52.8 mmol) and sodium hydroxide (2.20 g, 55.4 mmol). Compound **3c** (1.99 g, 10.03 mmol, 76% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (br. s, 4H), 5.85 – 5.69 (m, 1H), 5.15 – 4.99 (m, 2H), 4.83 – 4.73 (m, 1H), 2.36 – 2.23 (m, 2H), 1.61

— 1.45 (m, 2H), 1.44 — 1.26 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 162.9, 134.3, 117.5, 73.5, 39.0, 36.1, 18.8, 14.1. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_9H_{17}N_3O_2Na$, 222.1218; found, 222.1215. Compound **3c** was also prepared using method **B** in 77% yield.



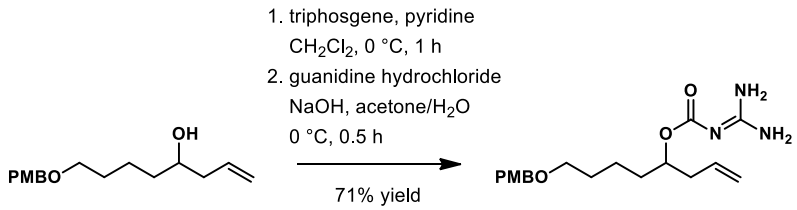
S1d **3d**

Compound 3d. The title compound was prepared according to general method **A** using alcohol **S1d** (1.30 g, 10.2 mmol), triphosgene (1.35 g, 4.59 mmol) and pyridine (0.82 mL, 10.2 mmol) in 30.0 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (17.0 mL) with a solution of free guanidine in 17.0 mL of water prepared from guanidine hydrochloride (3.9 g, 40.8 mmol) and sodium hydroxide (1.70 g, 42.98 mmol). Compound **3d** (1.85 g, 8.67 mmol, 85% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.66 (br. s, 4H), 5.87 — 5.66 (m, 1H), 5.13 — 4.96 (m, 2H), 4.93 — 4.77 (m, 1H), 2.36 — 2.21 (m, 2H), 1.70 — 1.55 (m, 1H), 1.54 — 1.40 (m, 1H), 1.36 — 1.22 (m, 1H), 0.87 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.5, 162.9, 134.2, 117.6, 72.0, 43.1, 39.5, 24.7, 23.2, 22.4. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{10}H_{19}N_3O_2Na$, 236.1375; found, 236.1365.



S1e **3e**

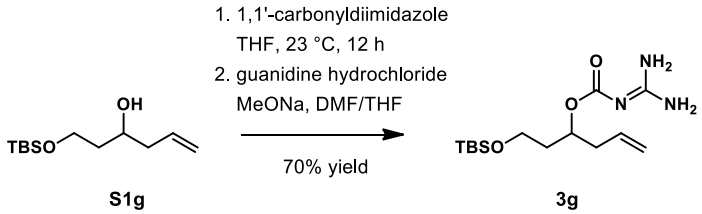
Compound 3e. The title compound was prepared according to general method **A** using alcohol **S1e** (0.900 g, 4.37 mmol), triphosgene (0.580 g, 1.97 mmol) and pyridine (0.35 mL, 4.37 mmol) in 13 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (7.0 mL) with a solution of free guanidine in 7.0 mL of water prepared from guanidine hydrochloride (1.67 g, 17.5 mmol) and sodium hydroxide (0.730 g, 18.35 mmol). Compound **3e** (1.02 g, 3.50 mmol, 80% yield) was obtained as yellowish oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 — 7.20 (m, 5H), 6.24 (br. s, 4H), 5.87 — 5.75 (m, 1H), 5.16 — 5.01 (m, 2H), 5.01 — 4.89 (m, 1H), 4.48 (s, 2H), 3.56 (t, *J* = 6.4 Hz, 2H), 2.48 — 2.31 (m, 2H), 1.99 — 1.81 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3, 162.6, 138.4, 134.0, 128.5, 127.9, 127.8, 117.8, 73.1, 71.0, 67.0, 39.2, 33.9. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{15}H_{21}N_3O_3Na$, 314.1481; found, 314.1479.



S1f 3f

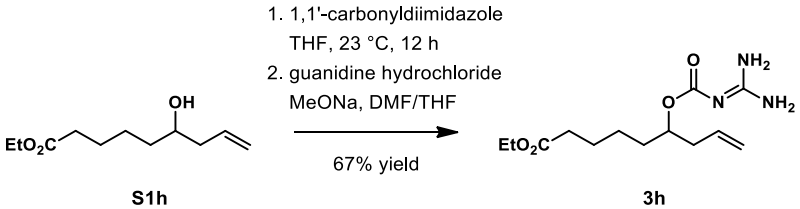
Compound 3f. The title compound was prepared according to general method **A** using alcohol **S1f** (1.20 g, 4.55 mmol), triphosgene (0.600 g, 2.05 mmol) and pyridine (0.36 mL, 4.55 mmol) in 13.0 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (8.0 mL) with a solution of free guanidine in 8.0 mL of water prepared from guanidine hydrochloride (1.74 g, 18.2 mmol) and sodium hydroxide (0.760 g, 19.11 mmol). Compound **3f** (1.13 g, 3.23 mmol, 71% yield) was obtained as yellowish oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.29 (br. s, 4H), 5.86 – 5.69 (m, 1H), 5.16 – 4.98 (m, 2H), 4.82 – 4.68 (m, 1H), 4.42 (s, 2H), 3.80 (s, 3H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.40 – 2.24 (m, 2H), 1.70 – 1.53 (m, 4H), 1.51 – 1.33 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5, 162.6, 159.3, 134.3, 130.6, 129.5, 117.5, 114.0, 73.4, 72.6, 70.2, 55.4, 38.9, 33.5, 29.6, 22.1. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{27}N_3O_4Na$, 372.1899; found, 372.1893.

Compound **3f** was also prepared using method **B** in 86% yield.



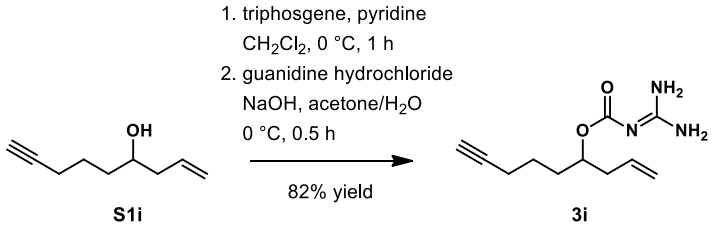
S1g 3g

Compound 3g. The title compound was prepared according to general method **B** using alcohol **S1g** (0.500 g, 2.17 mmol) and 1,1′-carbonyldiimidazole (0.420 g, 2.60 mmol) in 7.0 mL of tetrahydrofuran followed by the reaction of the resulting product solution with free guanidine solution in 14.0 mL of dimethylformamide prepared from guanidine hydrochloride (0.830 g, 8.70 mmol). Compound **3g** (0.480 g, 1.52 mmol, 70% yield) was obtained as yellowish oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.18 – 5.00 (m, 2H), 3.69 (t, *J* = 6.5 Hz, 2H), 2.38 (t, *J* = 6.6 Hz, 2H), 1.80 (dt, *J* = 8.0, 6.3 Hz, 2H), 0.88 (s, 9H), 0.03 (d, *J* = 0.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8, 133.9, 117.3, 70.6, 59.5, 38.9, 36.6, 25.8, 18.1, 5.6. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{29}N_3O_3SiNa$, 338.1876; found, 338.1861.

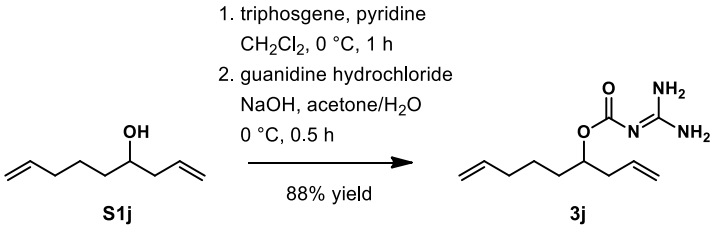


S1h 3h

Compound 3h. The title compound was prepared according to general method **B** using alcohol **S1h** (1.20 g, 6.0 mmol) and 1,1′-carbonyldiimidazole (1.17 g, 7.2 mmol) in 20.0 mL of tetrahydrofuran followed by the reaction of the resulting product solution with free guanidine solution in 40.0 mL of dimethylformamide prepared from guanidine hydrochloride (2.30 g, 24.0 mmol). Compound **3h** (1.09 g, 4.02 mmol, 67% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.89 – 5.71 (m, 1H), 5.17 – 4.98 (m, 2H), 4.80 – 4.69 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.45 – 2.34 (m, 1H), 2.30 (td, *J* = 7.2, 3.9 Hz, 3H), 1.73 – 1.52 (m, 4H), 1.46 – 1.30 (m, 2H), 1.25 (td, *J* = 7.2, 0.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.2, 161.6, 161.2, 133.7, 117.7, 73.9, 60.4, 38.5, 34.1, 33.2, 24.7, 14.14. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_{23}N_3NaO_4$, 308.1586; found, 308.1592.

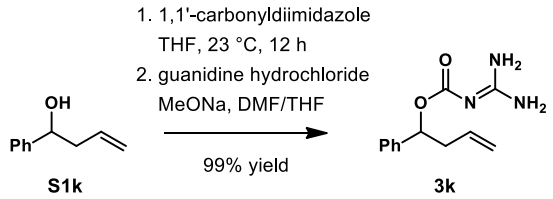


Compound 3i. The title compound was prepared according to general method **A** using alcohol **S1i** (1.00 g, 7.25 mmol), triphosgene (0.960 g, 3.26 mmol) and pyridine (0.58 mL, 7.25 mmol) in 21 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (12.0 mL) with a solution of free guanidine in 12.0 mL of water prepared from guanidine hydrochloride (2.77 g, 29.0 mmol) and sodium hydroxide (1.22 g, 30.5 mmol). Compound **3i** (1.32 g, 5.94 mmol, 82% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (br. s, 4H), 5.88 – 5.75 (m, 1H), 5.16 – 5.00 (m, 2H), 4.87 – 4.75 (m, 1H), 2.45 – 2.28 (m, 2H), 2.25 – 2.17 (m, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.76 – 1.46 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 162.5, 134.0, 117.5, 84.3, 72.9, 68.6, 38.9, 32.8, 24.3, 18.3. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{10}H_{19}N_3O_2Na$, 246.1218; found, 246.1215.

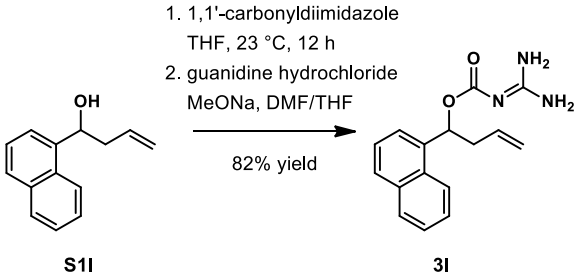


Compound 3j. The title compound was prepared according to general method **A** using alcohol **S1j** (1.10 g, 7.86 mmol), triphosgene (1.04 g, 3.54 mmol) and pyridine (0.63 mL, 7.86 mmol) in 23.0 mL of dichloromethane followed by standard work up procedure and the reaction of the resultant chloroformate dissolved in acetone (13.0 mL) with a solution of free guanidine in 13.0 mL of water prepared from guanidine hydrochloride (3.00 g, 31.4 mmol) and NaOH (1.32 g, 33.0 mmol). Compound **3j** (1.55 g, 6.92 mmol, 88% yield) was obtained as colorless oil after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.63 (br. s, 4H), 5.87 – 5.65 (m, 2H), 5.14 – 4.87 (m, 4H), 4.82 – 4.67 (m, 1H), 2.39 – 2.22 (m, 2H), 2.09 – 1.94 (m,

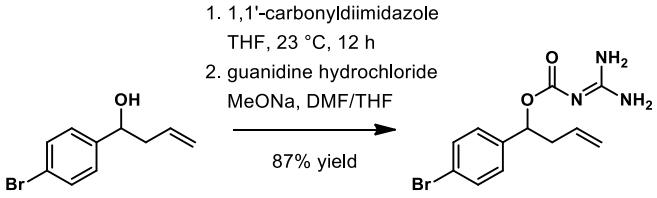
2H), 1.59 – 1.49 (m, 2H), 1.50 – 1.30 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 162.9, 138.6, 134.1, 117.6, 114.8, 73.5, 38.9, 33.6, 33.4, 24.8. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_{19}N_3O_2Na$, 248.1375; found, 248.1371.



Compound 3k. The title compound was prepared according to general method **B** using alcohol **S1k** (1.00 g, 6.76 mmol) and 1,1′-carbonyldiimidazole (1.31 g, 8.11 mmol) in 23.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 46.0 mL of dimethylformamide prepared from guanidine hydrochloride (2.58 g, 27.0 mmol). Compound **3k** (1.56 g, 6.69 mmol, 99% yield) was obtained as white solid after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 7.26 – 7.21 (m, 1H), 6.22 (br. s, *J* = 87.1 Hz, 4H), 5.78 – 5.66 (m, 1H), 5.65 – 5.55 (m, 1H), 5.08 – 4.98 (m, 2H), 2.71 – 2.58 (m, 1H), 2.56 – 2.40 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.3, 162.8, 141.4, 134.0, 128.5, 127.8, 126.3, 117.8, 75.9, 41.3. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{15}N_3O_2Na$, 256.1062; found, 256.1050.

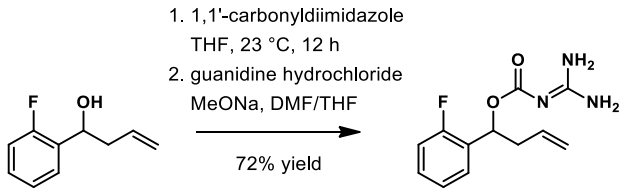


Compound 3l. The title compound was prepared according to general method **B** using alcohol **S1l** (0.560 g, 2.83 mmol) and 1,1′-carbonyldiimidazole (0.550 g, 3.40 mmol) in 10.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 20.0 mL of dimethylformamide prepared from guanidine hydrochloride (1.08 g, 11.3 mmol). Compound **3l** (0.656 g, 2.32 mmol, 82% yield) was obtained as white solid after column chromatography. ^{1}H NMR (600 MHz, DMSO-D_6) δ 8.17 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.61 – 7.45 (m, 4H), 6.92 (br. s, 4H), 6.36 – 6.28 (m, 1H), 5.90 – 5.77 (m, 1H), 5.05 (d, *J* = 17.2 Hz, 1H), 5.00 (d, *J* = 10.1 Hz, 1H), 2.69 – 2.57 (m, 2H). ^{13}C NMR (151 MHz, DMSO-D_6) δ 163.0, 162.7, 138.2, 134.6, 133.3, 129.9, 128.7, 127.5, 126.1, 125.5, 125.4, 123.3, 123.1, 117.3, 70.8, 40.4. HRMS-EI (*m/z*): $[M+Na]^+$ calcd for $C_{16}H_{17}N_3O_2Na$, 306.1218; found, 306.1212.



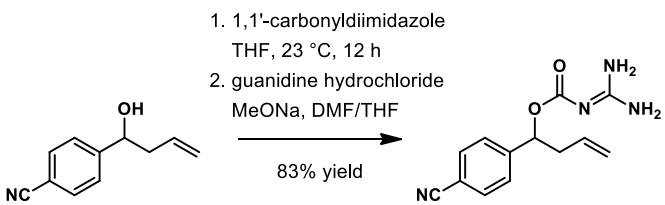
S1m 3m

Compound 3m. The title compound was prepared according to general method **B** using alcohol **S1m** (0.700 g, 3.08 mmol) and 1,1′-carbonyldiimidazole (0.600 g, 3.70 mmol) in 10.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 20.0 mL of dimethylformamide prepared from guanidine hydrochloride (1.18 g, 12.3 mmol). Compound **3m** (0.840 g, 2.68 mmol, 87% yield) was obtained as white solid after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.46 (br. s, 4H), 5.76 – 5.61 (m, 1H), 5.61 – 5.48 (m, 1H), 5.07 – 4.99 (m, 2H), 2.67 – 2.54 (m, 1H), 2.53 – 2.41 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 162.8, 140.4, 133.5, 131.7, 128.1, 121.6, 118.2, 75.2, 41.1. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{12}H_{14}BrN_3O_2Na$, 334.0167; found, 334.0163.



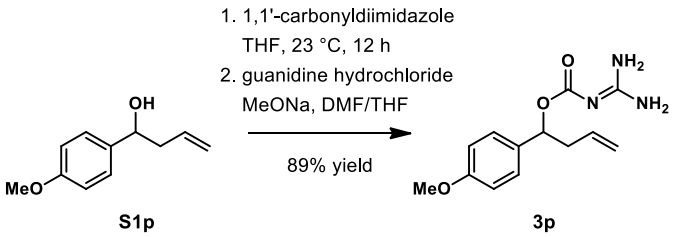
S1n 3n

Compound 3n. The title compound was prepared according to general method **B** using alcohol **S1n** (0.480 g, 2.89 mmol) and 1,1′-carbonyldiimidazole (0.560 g, 3.47 mmol) in 10.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 20.0 mL of dimethylformamide prepared from guanidine hydrochloride (1.10 g, 11.6 mmol). Compound **3n** (0.520 g, 2.08 mmol, 72% yield) was obtained as white solid after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (td, *J* = 7.5, 1.5 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.07 (td, *J* = 7.6, 0.8 Hz, 1H), 6.98 (dt, *J* = 25.5, 8.5 Hz, 1H), 6.48 (br. s, 4H), 5.96 – 5.85 (m, 1H), 5.83 – 5.64 (m, 1H), 5.03 (d, *J* = 17.1 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 2.70 – 2.59 (m, 1H), 2.58 – 2.48 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 162.9, 159.8 (d, *J* = 246.2 Hz), 133.5, 129.3 (d, *J* = 8.2 Hz), 128.5 (d, *J* = 13.3 Hz), 127.7 (d, *J* = 4.2 Hz), 124.4 (d, *J* = 3.5 Hz), 118.1, 115.50 (d, *J* = 21.7 Hz), 69.9, 40.1. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{12}H_{14}FN_3O_2Na$, 274.0968; found, 274.0953.



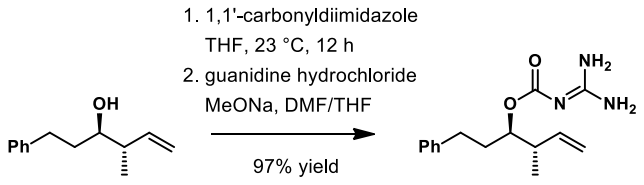
S1o 3o

Compound 3o. The title compound was prepared according to general method **B** using alcohol **S1o** (1.25 g, 7.23 mmol) and 1,1′-carbonyldiimidazole (1.40 g, 8.67 mmol) in 25.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 50.0 mL of dimethylformamide prepared from guanidine hydrochloride (4.99 g, 52.27 mmol). Compound **3o** (1.55 g, 6.0 mmol, 83% yield) was obtained as white solid after column chromatography. ^{1}H NMR (500 MHz, DMSO-D_6) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 6.96 (br. s, 4H), 5.80 – 5.64 (m, 1H), 5.64 – 5.57 (m, 1H), 5.08 – 4.95 (m, 2H), 2.58 – 2.41 (m, 2H). ^{13}C NMR (126 MHz, DMSO-D_6) δ 162.9, 162.3, 147.9, 133.7, 132.1, 126.9, 118.8, 117.9, 109.9, 73.0, 40.4. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{13}H_{14}N_4O_2Na$, 281.1014; found, 281.1017.



S1p 3p

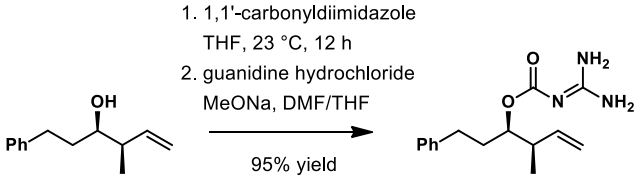
Compound 3p. The title compound was prepared according to general method **B** using alcohol **S1p** (1.00 g, 5.62 mmol) and 1,1′-carbonyldiimidazole (1.09 g, 6.74 mmol) in 19.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 38.0 mL of dimethylformamide prepared from guanidine hydrochloride (2.15 g, 22.5 mmol). Compound **3p** (1.32 g, 5.00 mmol, 89% yield) was obtained as colorless liquid after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.43 (br. s, 4H), 5.77 – 5.62 (m, 1H), 5.61 – 5.48 (m, 1H), 5.03 (d, *J* = 17.2 Hz, 1H), 4.99 (d, *J* = 10.3 Hz, 1H), 3.75 (s, 3H), 2.67 – 2.55 (m, 1H), 2.55 – 2.44 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.3, 162.8, 159.2, 134.0, 133.4, 127.7, 117.8, 113.9, 75.6, 55.4, 41.2. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{13}H_{17}N_3O_3Na$, 286.1168; found, 286.1159.



S1q 3q

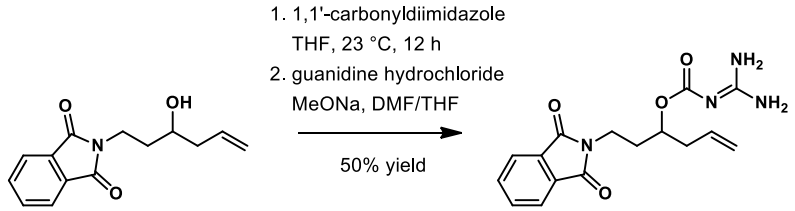
Compound 3q. The title compound was prepared according to general method **B** using alcohol **S1q** (0.100 g, 0.525 mmol) and 1,1′-carbonyldiimidazole (98.0 mg, 0.604 mmol) in 1.80 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 5.30 mL of dimethylformamide prepared from guanidine hydrochloride (0.100 g, 1.05 mmol). Compound **3q** (0.140 g, 0.509 mmol, 97% yield) was obtained as yellowish oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 1H), 7.16 (ddd, *J* = 6.2, 3.2, 1.9 Hz, 1H), 5.78 (ddd, *J* = 17.0, 10.4, 7.7 Hz, 1H), 5.10 – 4.96 (m, 2H), 4.79 (dt, *J* = 8.8, 4.3 Hz, 1H), 2.70 (ddd, *J* = 13.6, 10.5, 5.4 Hz, 1H), 2.58 (ddd, *J* = 13.7, 10.3, 6.2 Hz, 1H), 2.51 – 2.43 (m, 1H), 1.93 – 1.74 (m, 2H), 1.02 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 162.2, 141.9, 139.6, 128.4, 128.3, 125.8,

115.4, 41.6, 33.4, 32.1, 15.6. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{15}H_{21}N_3NaO_2$, 298.1531; found, 298.1508.



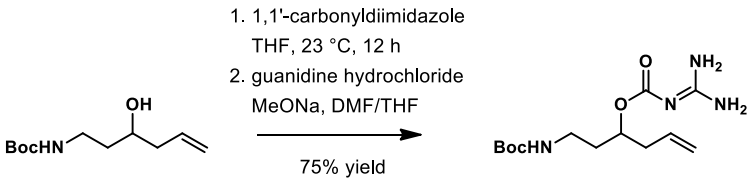
S1r **3r**

Compound 3r. The title compound was prepared according to general method **B** using alcohol **S1r** (97.0 mg, 0.509 mmol) and 1,1′-carbonyldiimidazole (95.0 mg, 0.586 mmol) in 1.70 mL of tetrahydrofurane followed by the reaction of the resultant product solution with free guanidine solution in 5.10 mL of dimethylformamide prepared from guanidine hydrochloride (97.0 mg, 1.02 mmol). Compound **3r** (0.138 g, 1.52 mmol, 95% yield) was obtained as yellowish oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.24 (m, 2H), 7.20 – 7.13 (m, 3H), 5.80 (ddd, *J* = 17.7, 10.4, 7.7 Hz, 1H), 5.15 – 4.96 (m, 2H), 4.74 (q, *J* = 6.4 Hz, 1H), 2.81 – 2.70 (m, 1H), 2.58 (dt, *J* = 13.7, 8.1 Hz, 1H), 2.49 (p, *J* = 6.9 Hz, 1H), 1.86 (ddd, *J* = 8.5, 7.6, 6.2 Hz, 2H), 1.05 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 162.2, 141.2, 139.6, 128.4, 128.3, 125.8, 115.4, 41.6, 33.4, 32.1, 15.6. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{15}H_{21}N_3NaO_2$, 298.1531; found, 298.1526.



S1s **3s**

Compound 3s. The title compound was prepared according to general method **B** using alcohol **S1s** (0.150 g, 0.612 mmol) and 1,1′-carbonyldiimidazole (0.159 g, 0.978 mmol) in 6.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 4.0 mL of dimethylformamide prepared from guanidine hydrochloride (0.117 g, 1.20 mmol). Compound **3s** (0.100 g, 3.03 mmol, 50% yield) was obtained as white solid after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 5.4 Hz, 2H), 7.72 (d, *J* = 5.5 Hz, 2H), 7.26 (br. s, 4H), 5.79-5.72 (m, 1H), 5.18 – 4.99 (m, 2H), 4.79 – 4.63 (m, 1H), 3.91 – 3.61 (m, 2H), 2.58 – 2.42 (m, 1H), 2.42 – 2.29 (m, 1H), 2.06 – 1.91 (m, 1H), 1.90 – 1.77 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.53, 162.28, 162.07, 134.07, 133.24, 131.99, 123.30, 118.08, 70.92, 38.81, 34.82, 32.26. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{16}H_{18}N_4O_4Na$, 353.1226; found, 353.1219.



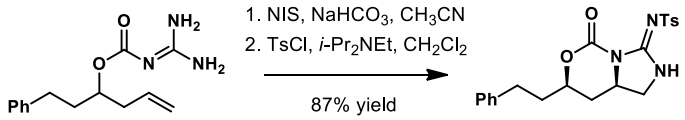
S1t **3t**

Compound 3t. The title compound was prepared according to general method **B** using alcohol **S1t** (0.300 g, 1.39 mmol) and 1,1'-carbonyldiimidazole (0.362 g, 2.23 mmol) in 14.0 mL of tetrahydrofuran followed by the reaction of the resultant product solution with free guanidine solution in 9.0 mL of dimethylformamide prepared from guanidine hydrochloride (0.273 g, 2.86 mmol). Compound **3t** (0.319 g, 1.06 mmol, 75% yield) was obtained as white solid after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (br. s, 4H), 5.78-5.61 (m, 1H), 5.17 – 4.99 (m, 3H), 4.85 – 4.73 (m, 1H), 3.32 – 3.17 (m, 1H), 3.10 – 2.93 (m, 1H), 2.42 – 2.22 (m, 2H), 1.81 – 1.59 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.76, 161.38, 156.28, 133.49, 117.89, 79.43, 71.41, 38.97, 36.95, 34.25, 28.42. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{13}H_{24}N_4O_4Na$, 323.1695; found, 323.1707.

General procedure for guanidilation of unactivated alkenes:

A solution of corresponding guanidine derivative (0.400 mmol) in acetonitrile (8.0 mL, 0.05 M) was placed in a 20 mL round bottom flask equipped with argon inlet and stirring bar. Then sodium bicarbonate (0.336 g, 4.0 mmol) was added and the reaction mixture was cooled to 0 °C (ice bath). N-Iodosuccinimide (0.189 g, 0.840 mmol) was added in one portion and the mixture was stirred for 5 hours at 0 °C. Then it was quenched by addition of 30% aqueous solution of sodium sulfite (10 mL) and the product was extracted once with ethyl acetate (50.0 mL). The organic phase was separated and concentrated under reduced pressure to remove acetonitrile, the residue was again dissolved in ethyl acetate. This solution was washed again with the same aqueous solution of sodium sulfite to ensure complete reduction of iodinated compounds. The organic layer was separated and the aqueous layer was additionally extracted with ethyl acetate (3x30 mL). Combined organic phase was dried over sodium sulfate and concentrated under reduced pressure to provide the crude product that was used for the next step without father purification.

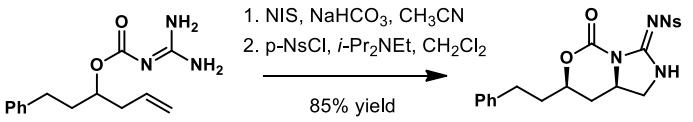
The crude product was dissolved in dichloromethane (5.0 mL), then Hunig's base (0.14 mL, 0.80 mmol) and corresponding sulfonyl chloride (0.48 mmol) were added sequentially at room temperature. The mixture was stirred for 10 min and then was directly fractionated by column chromatography to produce the desired product.



3a **5a**

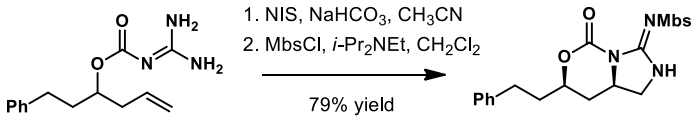
Compound 5a. The title compound was prepared according to general procedure using compound **3a** (0.100 g, 0.383 mmol), N-iodosuccinimide (0.181 g, 0.805 mmol) and sodium bicarbonate (0.321 g, 3.83 mmol) in 7.5 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (88.0 mg, 0.460 mmol) and Hunig's base

(0.13 mL, 0.766 mmol) in dichloromethane (5 mL). Compound **5a** (0.146 g, 0.354 mmol, 87% yield) was obtained as white solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (br. s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 7.0 Hz, 2H), 4.39 – 4.29 (m, 1H), 4.19 (dd, *J* = 9.0, 6.9 Hz, 1H), 4.10 – 4.01 (m, 1H), 3.20 (dd, *J* = 10.3, 9.3 Hz, 1H), 2.87 – 2.77 (m, 1H), 2.76 – 2.64 (m, 1H), 2.41 (s, 3H), 2.21 (dt, *J* = 13.5, 2.9 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.94 – 1.84 (m, 1H), 1.62 – 1.48 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 145.9, 145.2, 140.3, 133.9, 129.5, 128.7, 128.6, 128.4, 126.3, 78.1, 51.8, 49.5, 36.6, 31.3, 30.7, 21.7. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{21}H_{24}N_3O_4S$, 414.1488; found, 414.1479.



3a **5b**

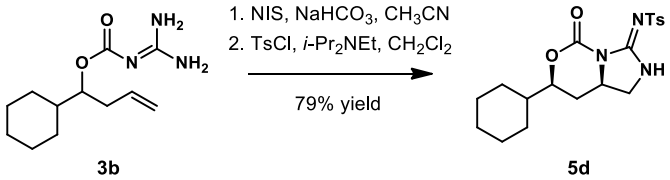
Compound 5b. The title compound was prepared according to general procedure using compound **3a** (0.100 g, 0.383 mmol), N-iodosuccinimide (0.181 g, 0.805 mmol) and sodium bicarbonate (0.321 g, 3.83 mmol) in 7.5 mL of acetonitrile followed by the reaction with p-nitrobenzenesulfonyl chloride (0.101 g, 0.460 mmol) and Hunig's base (0.13 mL, 0.766 mmol) in dichloromethane (5.0 mL). Compound **5b** (0.144 g, 0.324 mmol, 85% yield) was obtained as yellowish solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, DMSO-D_6) δ 8.43 (d, *J* = 8.8 Hz, 2H), 8.27 (d, *J* = 8.8 Hz, 2H), 7.99 (s, 1H), 7.32 – 7.26 (m, 2H), 7.26 – 7.16 (m, 3H), 4.53 – 4.43 (m, 1H), 4.33 – 4.19 (m, 2H), 3.50 (dd, *J* = 9.5, 8.7 Hz, 1H), 2.75 – 2.67 (m, 1H), 2.67 – 2.57 (m, 1H), 2.29 (d, *J* = 13.5 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.80 – 1.70 (m, 1H). ^{13}C NMR (151 MHz, DMSO-D_6) δ 150.5, 149.5, 146.3, 142.1, 140.9, 130.2, 128.4, 128.3, 126.0, 124.1, 78.5, 51.7, 49.2, 36.0, 30.2, 29.6. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{20}N_4O_6SNa$, 467.1001; found, 467.0991.



3a **5c**

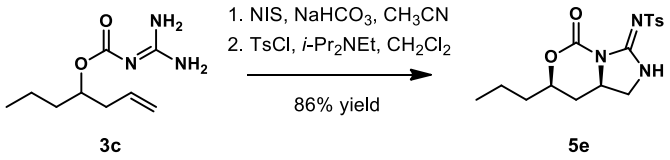
Compound 5c. The title compound was prepared according to general procedure using compound **3a** (0.100 g, 0.383 mmol), N-iodosuccinimide (0.181 g, 0.805 mmol) and sodium bicarbonate (0.321 g, 3.83 mmol) in 7.50 mL of acetonitrile followed by the reaction with p-methoxybenzenesulfonyl chloride (95.0 mg, 0.460 mmol) and Hunig's base (0.133 mL, 0.766 mmol) in dichloromethane (5.0 mL). Compound **5c** (0.130 g, 0.303 mmol, 79% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (br. s, 1H), 8.01 (d, *J* = 9.0 Hz, 2H), 7.27 (t, *J* = 8.7 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 7.1 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.41 – 4.27 (m, 1H), 4.19 (dd, *J* = 9.0, 6.9 Hz, 1H), 4.14 – 3.99 (m, 1H), 3.86 (s, 3H), 3.19 (dd, *J* = 10.3, 9.3 Hz, 1H), 2.86 – 2.78 (m, 1H), 2.77 – 2.68 (m, 1H), 2.26 – 2.17 (m,

1H), 2.07 – 1.96 (m, 1H), 1.95 – 1.84 (m, 1H), 1.62 – 1.50 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 149.2, 146.0, 140.3, 131.1, 128.7, 128.5, 128.3, 126.4, 114.1, 78.1, 55.8, 51.8, 49.6, 36.7, 31.4, 30.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{21}H_{23}N_3O_5SNa$, 452.1256; found, 452.1259.



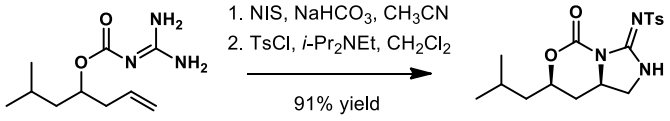
3b **5d**

Compound 5d. The title compound was prepared according to general procedure using compound **3b** (0.100 g, 0.418 mmol), N-iodosuccinimide (0.200 g, 0.879 mmol) and sodium bicarbonate (0.351 g, 4.18 mmol) in 8.5 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (95.0 mg, 0.500 mmol) and Hunig's base (0.15 mL, 0.837 mmol) in dichloromethane (5.0 mL). Compound **5d** (0.129 g, 0.330 mmol, 79% yield) was obtained as white solid after column chromatography (dichloromethane 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (br. s, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 4.20 (dd, *J* = 9.0, 6.9 Hz, 1H), 4.17 – 4.11 (m, 1H), 4.11 – 4.03 (m, 1H), 3.24 – 3.15 (m, 1H), 2.39 (s, 3H), 2.19 (dt, *J* = 13.5, 2.8 Hz, 1H), 1.84 – 1.78 (m, 1H), 1.75 – 1.67 (m, 2H), 1.65 – 1.57 (m, 2H), 1.57 – 1.46 (m, 2H), 1.24 – 1.13 (m, 2H), 1.12 – 0.92 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.4, 145.9, 145.1, 133.9, 129.5, 128.7, 83.2, 51.9, 49.6, 41.8, 28.4, 27.8, 27.8, 26.0, 25.7, 25.6, 21.6. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{19}H_{25}N_3O_4SNa$, 414.1463; found, 414.1450.



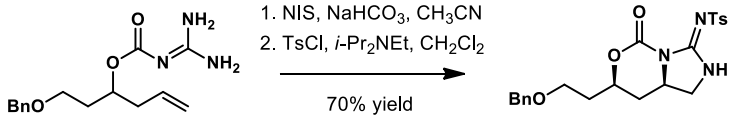
3c **5e**

Compound 5e. The title compound was prepared according to general procedure using compound **3c** (0.100 g, 0.503 mmol), N-iodosuccinimide (0.237 g, 1.06 mmol) and sodium bicarbonate (0.421 g, 5.03 mmol) in 10.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.115 g, 0.603 mmol) and Hunig's base (0.17 mL, 1.00 mmol) in dichloromethane (5.0 mL). Compound **5e** (0.152 g, 0.433 mmol, 86% yield) was obtained as yellowish solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (br. s, 1H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 4.44 – 4.32 (m, 1H), 4.21 (dd, *J* = 9.0, 6.8 Hz, 1H), 4.17 – 4.06 (m, 1H), 3.20 (dd, *J* = 10.3, 9.1 Hz, 1H), 2.41 (s, 3H), 2.24 (dt, *J* = 13.5, 3.0 Hz, 1H), 1.73 – 1.63 (m, 1H), 1.61 – 1.41 (m, 3H), 1.42 – 1.32 (m, 1H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 146.0, 145.2, 133.9, 129.6, 128.8, 79.0, 51.9, 49.6, 37.1, 31.3, 21.7, 17.9, 13.71. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{16}H_{21}N_3O_4SNa$, 374.1150; found, 374.1143.



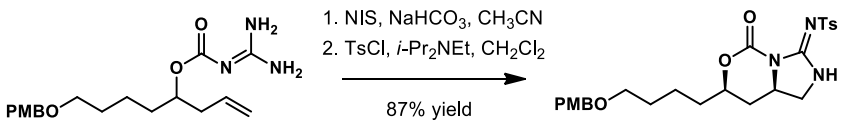
3d 5f

Compound 5f. The title compound was prepared according to general procedure using compound **3d** (0.100 mg, 0.470 mmol), N-iodosuccinimide (0.222 g, 0.986 mmol) and sodium bicarbonate (0.395 g, 4.70 mmol) in 9.4 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.115 g, 0.603 mmol) and Hunig's base (0.16 mL, 0.940 mmol) in dichloromethane (0.5 mL). Compound **5f** (0.156 g, 0.427 mmol, 91% yield) was obtained as yellowish solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (br. s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 4.47 – 4.38 (m, 1H), 4.20 (dd, *J* = 8.9, 6.8 Hz, 1H), 4.17 – 4.07 (m, 1H), 3.19 (dd, *J* = 10.2, 9.0 Hz, 1H), 2.39 (s, 3H), 2.23 (dt, *J* = 13.6, 2.9 Hz, 1H), 1.92 – 1.75 (m, 1H), 1.66 – 1.57 (m, 1H), 1.53 – 1.44 (m, 1H), 1.38 – 1.25 (m, 1H), 0.88 (d, *J* = 2.7 Hz, 3H), 0.87 (d, *J* = 2.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 146.0, 145.2, 133.9, 129.5, 128.7, 77.6, 51.9, 49.6, 44.2, 31.8, 23.9, 22.9, 21.9, 21.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{17}H_{23}N_3O_4SNa$, 388.1307; found, 388.1297.



3e 5g

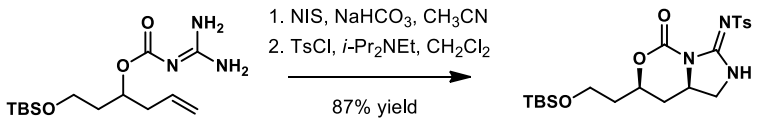
Compound 5g. The title compound was prepared according to general procedure using compound **3e** (0.100 g, 0.344 mmol), N-iodosuccinimide (0.162 g, 0.722 mmol) and sodium bicarbonate (0.289 g, 3.44 mmol) in 7.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (78.0 mg, 0.412 mmol) and Hunig's base (0.12 mL, 0.688 mmol) in dichloromethane (5.0 mL). Compound **5g** (0.117 g, 0.264 mmol, 70% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (br. s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.22 (m, 7H), 4.61 – 4.54 (m, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.19 (dd, *J* = 9.0, 6.8 Hz, 1H), 4.11 – 4.02 (m, 1H), 3.68 – 3.60 (m, 1H), 3.59 – 3.53 (m, 1H), 3.18 (dd, *J* = 10.3, 9.2 Hz, 1H), 2.41 (s, 3H), 2.23 (dt, *J* = 13.6, 2.9 Hz, 1H), 2.00 – 1.83 (m, 2H), 1.58 – 1.47 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 145.9, 145.2, 138.0, 133.9, 129.5, 128.7, 128.5, 127.8, 127.7, 76.7, 73.2, 65.1, 51.9, 49.5, 35.3, 31.4, 21.7. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{22}H_{26}N_3O_5S$, 444.1593; found, 444.1578.



3f 5h

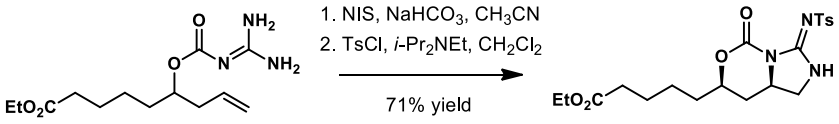
Compound 5h. The title compound was prepared according to general procedure using compound **3f** (0.100 g, 0.287 mmol), N-iodosuccinimide (0.135 g, 0.602 mmol) and sodium bicarbonate (0.241 g, 2.87 mmol) in 5.7 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (65.0 mg, 0.344 mmol) and Hunig's base

(0.10 mL, 0.574 mmol) in dichloromethane (5.0 mL). Compound **5h** (0.126 g, 0.251 mmol, 87% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.38 (s, *J* = 6.7 Hz, 2H), 4.37 – 4.30 (m, 1H), 4.19 (dd, *J* = 8.8, 7.0 Hz, 1H), 4.11 – 4.01 (m, 1H), 3.77 (s, 3H), 3.41 (t, *J* = 6.1 Hz, 2H), 3.18 (dd, *J* = 10.2, 9.3 Hz, 1H), 2.41 (s, 3H), 2.18 (dt, *J* = 13.5, 2.9 Hz, 1H), 1.73 – 1.65 (m, 1H), 1.63 – 1.54 (m, 3H), 1.54 – 1.37 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 149.2, 145.9, 145.2, 133.9, 130.5, 129.5, 129.3, 128.7, 113.8, 79.1, 72.6, 69.5, 55.3, 51.8, 49.5, 34.8, 31.2, 29.3, 21.7, 21.4. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{25}H_{31}N_3O_6SNa$, 524.1831; found, 524.1811.



3g **5i**

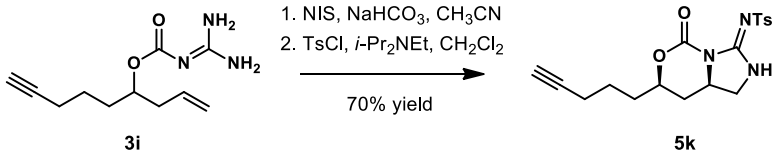
Compound **5i.** The title compound was prepared according to general procedure using compound **3g** (0.100 g, 0.316 mmol), N-iodosuccinimide (0.149 g, 0.665 mmol) and sodium bicarbonate (0.266 g, 3.16 mmol) in 6.3 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (73.0 mg, 0.380 mmol) and Hunig's base (0.10 mL, 0.633 mmol) in dichloromethane (5.0 mL). Compound **5i** (0.120 mg, 0.256 mmol, 87% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.58 (dddd, *J* = 12.0, 7.5, 4.8, 2.6 Hz, 1H), 4.24 (dd, *J* = 9.0, 6.8 Hz, 1H), 4.21 – 4.06 (m, 1H), 3.78 (ddd, *J* = 10.4, 8.3, 4.2 Hz, 1H), 3.70 (dt, *J* = 10.4, 5.2 Hz, 1H), 3.22 (dd, *J* = 10.4, 9.0 Hz, 1H), 2.42 (s, 3H), 2.30 (dt, *J* = 13.7, 3.0 Hz, 1H), 1.88 (dddd, *J* = 14.2, 7.4, 5.2, 4.2 Hz, 1H), 1.84 – 1.76 (m, 1H), 1.60 (dt, *J* = 13.6, 11.7 Hz, 1H), 0.85 (s, 9H), 0.02 (d, *J* = 3.0 Hz, 6H).^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 145.8, 145.1, 134.0, 129.5, 128.8, 76.4, 58.1, 51.9, 49.5, 38.0, 31.7, 25.9, 21.7, 18.2, 5.4. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{21}H_{33}N_3O_5SSiNa$, 490.1808; found, 490.1790.



3h **5j**

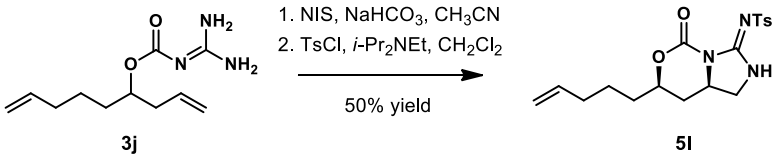
Compound **5j.** The title compound was prepared according to general procedure using compound **3h** (0.100 g, 0.47 mmol), N-iodosuccinimide (0.166 g, 0.735 mmol) and sodium bicarbonate (0.294 g, 3.50 mmol) in 7.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (80.0 mg, 0.420 mmol) and Hunig's base (0.12 mL, 0.701 mmol) in dichloromethane (4.0 mL). Compound **5j** (0.109 g, 0.334 mmol, 71% yield) was obtained as yellowish solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (br. s, 1H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.29 (m, 2H), 4.39 (dddd, *J* = 11.8, 7.4, 4.8, 2.5 Hz, 1H), 4.24 (dd, *J* = 9.0, 6.8 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 3H), 3.22 (dd, *J* = 10.4, 9.1 Hz, 1H), 2.43 (s, 3H), 2.29 (t, *J* = 7.3 Hz, 2H), 2.24

(dt, *J* = 13.6, 3.0 Hz, 1H), 1.73 (dddd, *J* = 14.0, 10.3, 7.3, 5.3 Hz, 1H), 1.69 – 1.59 (m, 3H), 1.59 – 1.48 (m, 2H), 1.47 – 1.37 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 149.1, 145.7, 145.1, 133.9, 129.5, 128.8, 78.7, 60.4, 51.8, 49.5, 34.7, 33.9, 31.3, 24.4, 24.1, 21.7, 14.2. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{27}N_3O_6SNa$, 460.1618; found, 460.1501.



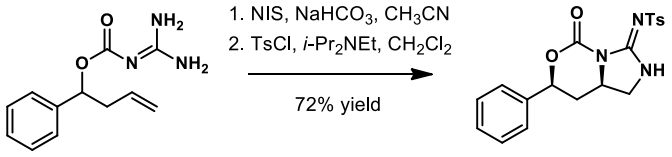
3i **5k**

Compound 5k. The title compound was prepared according to general procedure using compound **3i** (0.100 g, 0.448 mmol), N-iodosuccinimide (0.212 g, 0.942 mmol) and sodium bicarbonate (0.379 g, 4.48 mmol) in 9.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.102 g, 0.538 mmol) and Hunig's base (0.16 mL, 0.896 mmol) in dichloromethane (5.0 mL). Compound **5k** (0.117 g, 0.312 mmol, 70% yield) was obtained as yellowish oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.46 – 4.35 (m, 1H), 4.25 – 4.17 (m, 1H), 4.18 – 4.07 (m, 1H), 3.25 – 3.12 (m, 1H), 2.39 (s, 3H), 2.26 (dt, *J* = 13.5, 2.9 Hz, 1H), 2.22 – 2.15 (m, 2H), 1.92 (t, *J* = 2.6 Hz, 1H), 1.80 – 1.63 (m, 3H), 1.62 – 1.46 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 146.0, 145.2, 133.8, 129.5, 128.7, 83.3, 78.7, 69.3, 51.8, 49.6, 33.9, 31.3, 23.4, 21.7, 18.0. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{18}H_{21}N_3O_4SNa$, 398.1150; found, 398.1156.



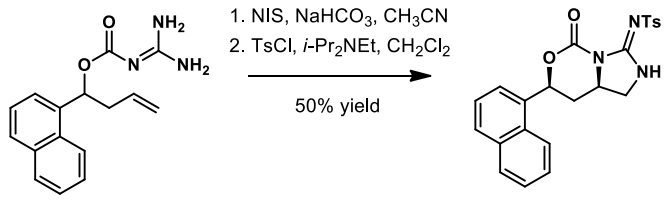
3j **5l**

Compound 5l. The title compound was prepared according to general procedure using compound **3j** (0.100 g, 0.444 mmol), N-iodosuccinimide (0.210 g, 0.933 mmol) and sodium bicarbonate (0.373 g, 4.44 mmol) in 9.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.101 g, 0.533 mmol) and Hunig's base (0.16 mL, 0.888 mmol) in dichloromethane (5.0 mL). Compound **5l** (84.0 mg, 0.223 mmol, 50% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.78 – 5.67 (m, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 4.43 – 4.33 (m, 1H), 4.26 – 4.18 (m, 1H), 4.16 – 4.06 (m, 1H), 3.24 – 3.14 (m, 1H), 2.41 (s, 3H), 2.24 (dt, *J* = 13.6, 2.9 Hz, 1H), 2.09 – 1.99 (m, 2H), 1.77 – 1.65 (m, 1H), 1.64 – 1.47 (m, 3H), 1.47 – 1.38 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.3, 146.0, 145.2, 137.8, 133.9, 129.6, 128.8, 115.4, 79.1, 51.9, 49.6, 34.4, 33.2, 31.3, 23.7, 21.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{18}H_{23}N_3O_4SNa$, 400.1307; found, 400.1296.



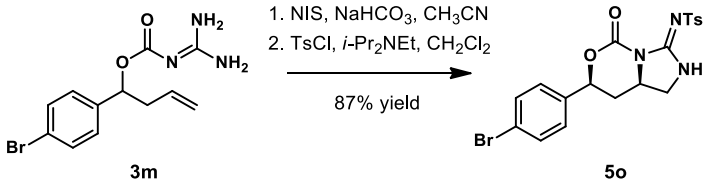
3k **5m**

Compound 5m. The title compound was prepared according to general procedure with different reaction time (5 hours at 0 °C followed by 5 hours at ambient temperature) using compound **3k** (0.100 g, 0.429 mmol), N-iodosuccinimide (0.203 g, 0.901 mmol) and sodium bicarbonate (0.361 g, 4.29 mmol) in 8.6 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.980 g, 0.515 mmol) and Hunig's base (0.15 mL, 0.858 mmol) in dichloromethane (5.0 mL). Compound **5m** (0.119 g, 0.309 mmol, 72% yield) was obtained as white solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (br. s, 1H), 7.96 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.26 (m, 7H), 5.38 (dd, *J* = 11.9, 2.6 Hz, 1H), 4.33 – 4.22 (m, 2H), 3.29 – 3.20 (m, 1H), 2.47 (dt, *J* = 13.8, 2.8 Hz, 1H), 2.41 (s, 3H), 1.88 – 1.77 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.1, 145.9, 145.3, 137.2, 133.9, 129.6, 129.3, 128.9, 128.9, 125.9, 80.3, 52.1, 49.6, 33.7, 21.8. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{19}H_{19}N_3O_4SNa$, 408.0994; found, 408.0979.

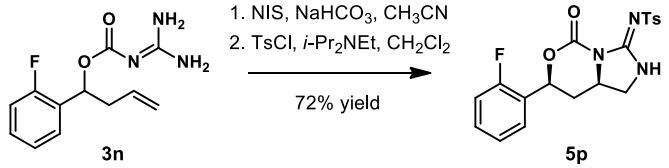


3l **5n**

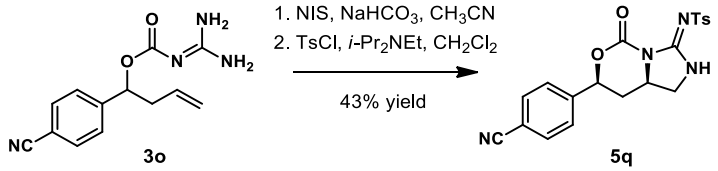
Compound 5n. The title compound was prepared according to general procedure with different reaction time (5 hours at 0°C followed by 5 hours at ambient temperature) using compound **3l** (0.100 g, 0.353 mmol), N-iodosuccinimide (0.167 g, 0.742 mmol) and sodium bicarbonate (0.297 g, 3.53 mmol) in 7.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (81.0 mg, 0.424 mmol) and Hunig's base (0.12 mL, 0.706 mmol) in dichloromethane (5.0 mL). Compound **5n** (77.0 mg, 0.177 mmol, 50% yield) was obtained as white solid after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, DMSO-D_6) δ 8.14 (d, *J* = 8.3 Hz, 1H), 8.07 (s, 1H), 8.02 – 7.91 (m, 4H), 7.65 – 7.51 (m, 4H), 7.45 (d, *J* = 8.1 Hz, 2H), 6.48 – 6.37 (m, 1H), 4.67 – 4.50 (m, 1H), 4.32 – 4.21 (m, 1H), 3.59 – 3.44 (m, 1H), 2.65 – 2.53 (m, 1H), 2.41 (s, 3H), 2.36 – 2.24 (m, 1H). ^{13}C NMR (126 MHz, DMSO-D_6) δ 149.7, 146.4, 144.6, 134.2, 133.5, 133.2, 129.8, 129.4, 129.1, 128.7, 128.5, 126.6, 126.0, 125.4, 123.8, 123.0, 76.6, 52.0, 49.2, 30.7, 21.1. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{23}H_{21}N_3O_4SNa$, 458.1150; found, 458.1131.



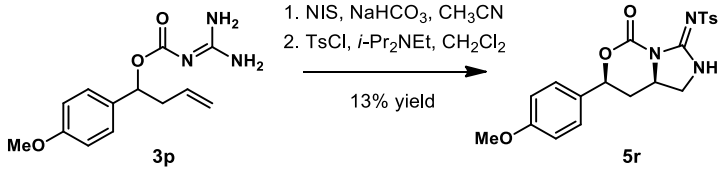
Compound 5o. The title compound was prepared according to general procedure with different reaction time (5 hours at 0 °C followed by 5 hours at ambient temperature) using compound **3m** (0.100 g, 0.321 mmol), N-iodosuccinimide (0.151 g, 0.673 mmol) and $NaHCO_3$ (0.270 g, 3.21 mmol) in 7.4 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (73.0 mg, 0.385 mmol) and Hunig's base (0.11 mL, 0.640 mmol) in dichloromethane (5.0 mL). Compound **5o** (0.126 g, 0.272 mmol, 87% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, cdcl$_3$) δ 8.35 (br. s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 5.38 (dd, *J* = 11.9, 2.5 Hz, 1H), 4.36 – 4.28 (m, 1H), 4.26 (dd, *J* = 8.8, 6.9 Hz, 1H), 3.25 (dd, *J* = 9.9, 9.3 Hz, 1H), 2.52 – 2.45 (m, 1H), 2.42 (s, 3H), 1.87 – 1.73 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 145.8, 145.4, 136.3, 133.8, 132.1, 129.7, 128.8, 127.6, 123.2, 79.5, 52.0, 49.5, 33.5, 21.8. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{19}H_{18}BrN_3O_4SNa$, 486.0099; found, 486.0076.



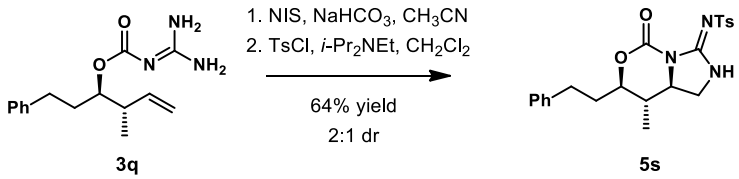
Compound 5p. The title compound was prepared according to general procedure with different reaction time (5 hours at 0 °C followed by 5 hours at ambient temperature) using compound **3n** (0.100 g, 0.398 mmol), N-iodosuccinimide (0.188 g, 0.837 mmol) and sodium bicarbonate (0.334 g, 3.98 mmol) in 8.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (91.0 mg, 0.476 mmol) and Hunig's base (0.138 mL, 0.796 mmol) in dichloromethane (5.0 mL). Compound **5p** (0.123 g, 0.305 mmol, 72% yield) was obtained as yellowish oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (br. s, 1H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.39 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36 – 7.30 (m, 3H), 7.15 (dd, *J* = 16.5, 8.8 Hz, 1H), 7.06 (dd, *J* = 10.0, 8.8 Hz, 1H), 5.67 (dd, *J* = 11.8, 2.7 Hz, 1H), 4.38 – 4.26 (m, 2H), 3.31 – 3.25 (m, 1H), 2.60 – 2.51 (m, 1H), 2.43 (s, 3H), 1.94 – 1.82 (m, 1H). ^{13}C NMR (151 MHz, cdcl$_3$) δ 160.4, 158.7, 148.9, 145.5 (d, J = 59.2 Hz), 134.0, 130.9 (d, J = 8.3 Hz), 129.6, 128.9, 127.3 (d, J = 3.2 Hz), 124.8 (d, J = 3.5 Hz), 124.6 (d, J = 12.3 Hz), 115.9 (d, J = 21.0 Hz), 74.9 (d, J = 3.3 Hz), 52.0, 49.5, 32.5, 21.8. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{19}H_{18}FN_3O_4SNa$, 426.0900; found, 426.0883.



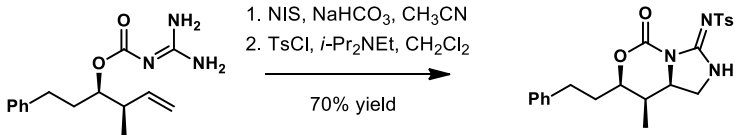
Compound 5q. The title compound was prepared according to general procedure with different reaction time (5 hours at 0 °C followed by 2 hours at ambient temperature) using compound **3o** (0.100 g, 0.388 mmol), N-iodosuccinimide (0.183 g, 0.814 mmol) and sodium bicarbonate (0.326 g, 3.88 mmol) in 7.8 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (88.0 mg, 0.465 mmol) and Hunig's base (0.14 mL, 0.776 mmol) in dichloromethane (5.0 mL). Compound **5q** (69.0 mg, 0.169 mmol, 43% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.62 – 5.40 (m, 1H), 4.48 – 4.35 (m, 1H), 4.29 (dd, *J* = 8.7, 7.1 Hz, 1H), 3.34 – 3.20 (m, 1H), 2.64 – 2.50 (m, 1H), 2.42 (s, 3H), 1.90 – 1.70 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 145.7, 145.5, 142.4, 133.7, 132.8, 129.7, 128.8, 126.5, 118.2, 113.0, 78.96 (s), 51.91 (s), 49.47 (s), 33.50 (s), 21.78 (s). HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{18}N_4O_4SNa$, 433.0946; found, 433.0926.



Compound 5r. The title compound was prepared according to general procedure with different reaction time (5 hours at 0 °C followed by 5 hours at ambient temperature) using compound **3p** (0.100 g, 0.380 mmol), N-iodosuccinimide (0.180 g, 0.798 mmol) and sodium bicarbonate (0.320 g, 3.80 mmol) in 7.6 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (87.0 mg, 0.456 mmol) and Hunig's base (0.13 mL, 0.760 mmol) in dichloromethane (5.0 mL). Significant amount of material insoluble in dichloromethane was obtained after the first step. Compound **5r** (20.0 mg, 50.0 μmol, 13% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.35 (dd, *J* = 11.9, 2.4 Hz, 1H), 4.35 – 4.24 (m, 2H), 3.80 (s, 3H), 3.33 – 3.25 (m, 1H), 2.50 – 2.42 (m, 4H), 1.95 – 1.84 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 145.8, 145.3, 134.1, 129.7, 129.2, 128.0, 127.5, 125.9, 114.4, 80.2, 55.5, 52.2, 49.6, 33.7, 21.8. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{21}N_3O_5SNa$, 438.1100; found, 438.1085.

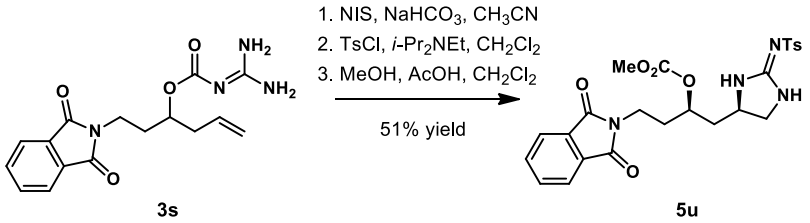


Compound 5s. The title compound was prepared according to general procedure using compound **3q** (0.139 g, 0.505 mmol), N-iodosuccinimide (0.239 g, 1.06 mmol) and sodium bicarbonate (0.424 g, 5.05 mmol) in 5.70 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.115 g, 6.06 mmol) and Hunig's base (0.18 mL, 1.01 mmol) in dichloromethane (4.0 mL). Compound **5s** (0.137 g, 0.323 mmol, mixture of diastereomers (dr 2:1), 64% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.2 Hz, 1H), 4.24 (dd, J = 9.0, 6.9 Hz, 1H), 4.04 – 3.98 (m, 1H), 3.72 (td, J = 10.4, 6.9 Hz, 1H), 3.23 (dd, J = 10.5, 9.1 Hz, 1H), 2.89 (ddt, J = 14.9, 9.9, 5.2 Hz, 1H), 2.79 – 2.68 (m, 1H), 2.04 (ddd, J = 14.5, 9.7, 7.2 Hz, 1H), 1.83 (dtd, J = 14.2, 9.2, 4.7 Hz, 1H), 1.76 – 1.64 (m, 1H), 0.99 (dd, J = 6.9, 2.1 Hz, 3H). Minor diastereomer: 8.34 (s, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 4.29-4.25 (m, 1H), 4.11 – 4.04 (m, 1H), 3.46 (t, J = 9.8 Hz, 1H), 2.89 (ddt, J = 14.9, 9.9, 5.2 Hz, 1H), 2.79 – 2.68 (m, 1H), 2.17 – 2.09 (m, 1H), 1.83 (dtd, J = 14.2, 9.2, 4.7 Hz, 1H), 1.76 – 1.64 (m, 1H), 0.99 (dd, J = 6.9, 2.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ major diastereomer: 149.0, 145.9, 140.5, 139.4, 134.0, 129.5, 128.8, 128.6, 128.4, 126.3, 56.7, 49.0, 36.0, 33.9, 30.5, 30.3, 21.7, 12.0. Minor diastereomer: 148.8, 145.8, 139.9, 134.2, 129.5, 128.8, 128.7, 128.4, 126.5, 83.7, 51.3, 45.8, 36.6, 31.4, 30.5, 21.7, 12.1.HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{22}H_{25}N_3NaO_4S$, 450.1463; found, 450.1451.

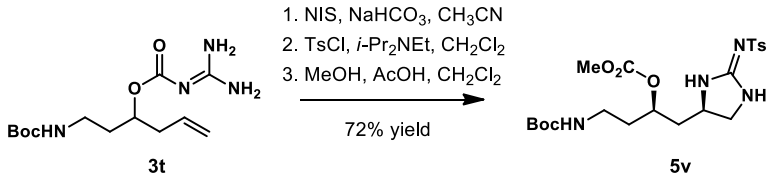


3r 5t

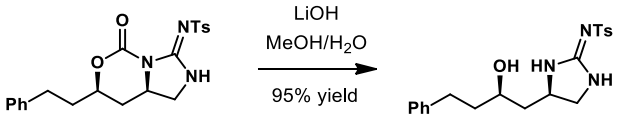
Compound 5t. The title compound was prepared according to general procedure using compound **3r** (0.138 g, 0.501 mmol), N-iodosuccinimide (0.236 g, 1.05 mmol) and sodium bicarbonate (0.421 g, 5.01 mmol) in 10.0 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (0.115 g, 0.601 mmol) and Hunig's base (0.18 mL, 1.00 mmol) in dichloromethane (4.0 mL). Compound **5t** (0.149 g, 0.351 mmol, 70% yield) was obtained as colorless oil after column chromatography (dichloromethane → 20% ethyl acetate in dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.27 (m, 4H), 7.24 – 7.15 (m, 3H), 4.33 (ddd, *J* = 9.0, 4.4, 2.2 Hz, 1H), 4.19 (ddd, *J* = 10.6, 7.4, 3.4 Hz, 1H), 4.19 (ddd, *J* = 10.6, 7.4, 3.4 Hz, 1H), 3.46 (t, *J* = 9.9 Hz, 1H), 2.86 (ddd, *J* = 14.2, 9.0, 5.4 Hz, 1H), 2.71 (dt, *J* = 13.9, 8.1 Hz, 1H), 2.44 (s, 3H), 2.19 – 2.03 (m, 2H), 1.85 – 1.74 (m, 1H), 0.87 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 145.8, 140.1, 129.5, 128.7, 128.7, 128.4, 126.4, 81.5, 56.0, 45.6, 33.7, 31.2, 30.3, 21.7, 5.2. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{22}H_{25}N_3NaO_4S$, 450.1463; found, 450.1458.



Compound 5u. The title compound was prepared according to general procedure using compound **3s** (0.100 g, 0.287 mmol), N-iodosuccinimide (0.135 g, 0.602 mmol) and sodium bucarbonate (0.241 g, 2.87 mmol) in 5.7 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (65 mg, 0.344 mmol) and Hunig's base (0.10 mL, 0.574 mmol) in dichloromethane (5.0 mL). The mixture of corresponding product and succinimide obtained after the column chromatography was treated with methanol (1.0 mL) in acetic acid (0.30 mL) and dichloromethane (3 mL). Compound **5u** (80.0 mg, 0.155 mmol, 51% yield) was obtained as yellowish oil after column chromatography (50% ethyl acetate in dichloromethane → 10% methanol in dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.80 (m, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.72 – 7.65 (m, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 5.79 (br. s, 2H), 4.78 – 4.64 (m, 1H), 3.82 – 3.58 (m, 7H), 3.36 – 3.26 (m, 1H), 2.42 (s, 3H), 2.01 – 1.84 (m, 2H), 1.82 – 1.70 (m, 1H), 1.47 – 1.34 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 155.5, 151.8, 145.1, 134.1, 133.7, 132.1, 130.2, 127.8, 123.4, 73.5, 56.3, 54.9, 53.0, 40.9, 34.3, 32.8, 21.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{24}H_{26}N_4O_7SNa$, 537.1420; found, 537.1431.



Compound 5v. The title compound was prepared according to general procedure using compound **3t** (73.0 mg, 0.242 mmol), N-iodosuccinimide (0.115 mg, 0.509 mmol) and sodium bicarbonate (0.204 g, 2.42 mmol) in 4.9 mL of acetonitrile followed by the reaction with p-toluenesulfonyl chloride (60.0 mg, 0.315 mmol) and Hunig's base (84.0 μL, 0.485 mmol) in dichloromethane (5 mL). The mixture of corresponding product and succinimide obtained after the column chromatography was treated with methanol (1.0 mL) in acetic acid (0.30 mL) and dichloromethane (3 mL). Compound **5v** (85.0 mg, 0.175 mmol, 72% yield) was obtained as yellow oil after column chromatography (50% ethyl acetate in dichloromethane 10% methanol in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.39 (br. s, 3H), 5.03 – 4.87 (m, 1H), 4.81 – 4.68 (m, 1H), 3.75 - 3.69 (m, 4H), 3.34 – 3.28 (m, 1H), 3.23 – 3.15 (m, 1H), 3.05 – 2.92 (m, 1H), 2.42 (s, 3H), 1.79 – 1.61 (m, 3H), 1.47 (d, J = 6.6 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.99, 155.70, 151.88, 145.19, 133.57, 130.18, 127.75, 79.32, 73.68, 56.06, 54.93, 52.96, 40.89, 36.63, 34.60, 28.47, 21.70. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{21}H_{32}N_4O_7SNa$, 507.1889; found, 507.1868.

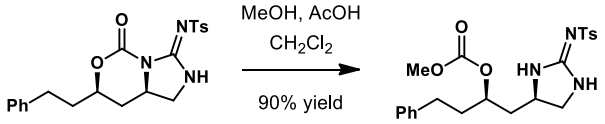


5a **6**

Compound 6. Compound **5a** (69.0 mg, 0.168 mmol) was dissolved in a mixture of methanol (2.5 mL) and water (2.5 mL) then lithium hydroxide (70.0 mg, 1.68 mmol) was added at ambient temperature. The reaction was stirred at room temperature for 30 min. Then it was poured in water (10 mL) and the product was extracted with ethyl acetate (3x15 mL). Combined organic phase was washed with brine, dried over sodium sulfate and concentrated under reduced pressure to produce compound **6** (62.0 mg, 0.160 mmol, 95% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.23 (m, 2H), 7.17 (d, *J* = 7.4 Hz, 3H), 5.30 (br. s, 3H), 3.91 – 3.73 (m, 3H), 3.18 (dd, *J* = 9.0, 6.5 Hz, 1H), 2.75 – 2.67 (m, 1H), 2.66 – 2.58 (m, 1H), 2.44 (s, 3H), 1.78 – 1.67 (m, 1H), 1.66 – 1.57 (m, 1H), 1.53 (ddd, *J* = 13.7, 3.8, 1.8 Hz, 1H), 1.28 – 1.18 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.87, 145.07, 142.19, 133.49, 130.03, 128.35, 128.24, 127.55, 125.62, 70.57, 59.65, 53.66, 43.30, 39.27, 31.61, 21.57. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{20}H_{26}N_3O_3S$, 388.1695; found, 388.1700.

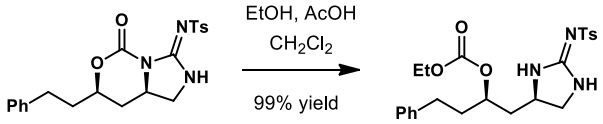
General procedure for ring opening reaction:

To a solution of compound **5** (0.194 mmol) in a mixture of dichloromethane (3 mL) and acetic acid (0.3 mL) corresponding alcohol (4.85 mmol) was added at ambient temperature and the reaction mixture was stirred until full consumption of the starting material was observed by TLC analysis (2-24 h). The solvent was evaporated under reduced pressure and the dry residue was co-evaporated with toluene (10.0 mL) to remove acetic acid. Then the crude product was dissolved in CH_2Cl_2 (20 ml) and the solution was washed with saturated aqueous sodium bicarbonate (10 ml). The organic phase was dried over sodium sulfate and concentrated to provide crude product that was purified by column chromatography (3% methanol in dichloromethane 10% methanol in dichloromethane).



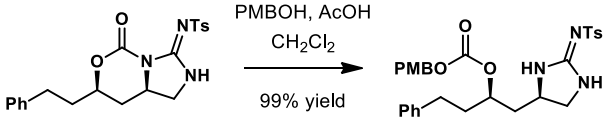
5a **7a**

Compound 7a. The title compound was prepared according to general procedure using substrate **5a** (0.135 g, 0.327 mmol) and methanol (0.33 mL, 8.16 mmol). The product **7a** was obtained (0.130 g, 0.292 mmol, 90% yield) as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 2H), 5.71 (br. s, 2H), 4.83 – 4.72 (m, 1H), 3.82 – 3.68 (m, 5H), 3.35 – 3.24 (m, 1H), 2.71 – 2.50 (m, 2H), 2.41 (s, 3H), 1.99 – 1.73 (m, 3H), 1.47 – 1.35 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.6, 151.9, 144.8, 141.1, 133.8, 130.0, 128.5, 128.3, 127.7, 126.1, 75.5, 56.5, 54.8, 52.9, 41.1, 36.0, 31.4, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{22}H_{28}N_3O_5S$, 446.1750; found, 446.1743.



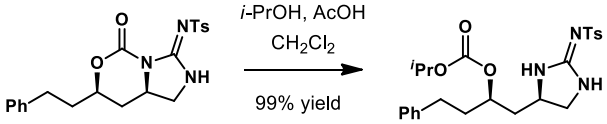
5a **7b**

Compound 7b. The title compound was prepared according to general procedure using substrate **5a** (80.0 mg, 0.194 mmol) and ethanol (0.28 mL, 4.84 mmol). The product **7b** was obtained (88.0 mg, 0.194 mmol, 99% yield) as colorless oil after column chromatography. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.25 (t, *J* = 6.7 Hz, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H), 5.57 (br. s, 2H), 4.78 – 4.69 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.78 – 3.68 (m, 2H), 3.32 – 3.24 (m, 1H), 2.63 (ddd, *J* = 14.0, 10.6, 5.6 Hz, 1H), 2.55 (ddd, *J* = 14.0, 10.4, 5.9 Hz, 1H), 2.39 (s, 3H), 1.93 – 1.84 (m, 1H), 1.83 – 1.75 (m, 2H), 1.39 – 1.32 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.0, 151.7, 144.8, 141.1, 133.7, 130.0, 128.5, 128.3, 127.7, 126.0, 75.1, 64.0, 56.5, 52.9, 41.1, 36.0, 31.5, 21.6, 14.2. HRMS-EI (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{30}N_3O_5S$, 460.1906; found, 460.1896.



5a **7c**

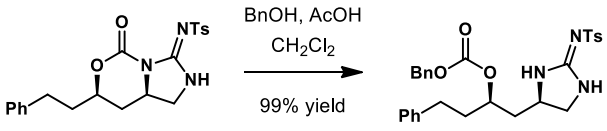
Compound 7c. The title compound was prepared according to general procedure using substrate **5a** (80.0 mg, 0.194 mmol) and 4-methoxybenzyl alcohol (0.60 mL, 4.84 mmol). The product **7c** was obtained (0.106 g, 0.192 mmol, 99% yield) as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.41 (br. s, 2H), 5.09 (s, 2H), 4.83 – 4.71 (m, 1H), 3.80 (s, 3H), 3.77 – 3.70 (m, 2H), 3.33 – 3.26 (m, 1H), 2.67 – 2.59 (m, 1H), 2.59 – 2.51 (m, 1H), 2.42 (s, 3H), 1.94 – 1.85 (m, 1H), 1.83 – 1.75 (m, 2H), 1.43 – 1.32 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9, 154.9, 151.7, 144.8, 141.1, 133.8, 130.3, 130.0, 128.5, 128.3, 127.7, 127.4, 126.1, 114.0, 75.4, 69.5, 56.5, 55.3, 52.9, 41.1, 36.0, 31.4, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{29}H_{34}N_3O_6S$, 552.2168; found, 552.2163.



5a **7d**

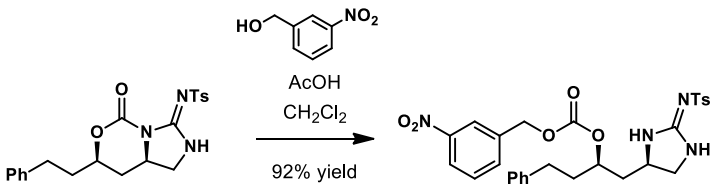
Compound 7d. The title compound was prepared according to general procedure using substrate **5a** (80.0 mg, 0.194 mmol) and isopropanol (0.37 mL, 4.84 mmol). The product **7d** was obtained (90 mg, 0.190 mmol, 99% yield) as a colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 7.3 Hz, 2H), 5.16 (br. s, 1H), 4.92 – 4.79 (m, 1H), 4.77 – 4.71 (m, 1H), 3.81 –

3.70 (m, 2H), 3.35 – 3.26 (m, 1H), 2.65 (ddd, *J* = 13.9, 10.5, 5.5 Hz, 1H), 2.57 (ddd, *J* = 13.9, 10.2, 6.0 Hz, 1H), 2.42 (s, 3H), 1.96 – 1.85 (m, 1H), 1.85 – 1.75 (m, 2H), 1.42 – 1.33 (m, 1H), 1.30 (d, *J* = 6.1 Hz, 3H), 1.29 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.5, 151.6, 144.8, 141.1, 133.8, 130.0, 128.5, 128.3, 127.7, 126.1, 74.8, 71.9, 56.6, 53.0, 41.2, 36.1, 31.5, 21.8, 21.8, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{24}H_{32}N_3O_5S$, 474.2063; found, 474.2054.



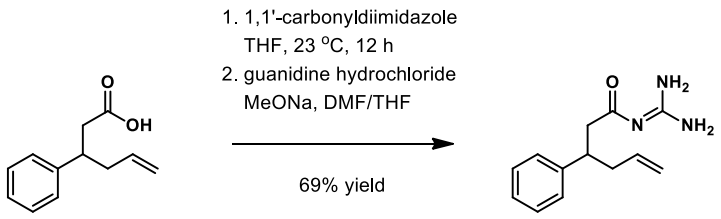
5a **7e**

Compound 7e. The title compound was prepared according to general procedure using substrate **5a** (80.0 mg, 0.194 mmol) and benzyl alcohol (0.50 mL, 4.84 mmol). The product **7e** was obtained (0.100 g, 0.192 mmol, 99% yield) as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.24 (m, 9H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.1 Hz, 2H), 5.47 (br. s, 2H), 5.16 (s, 2H), 4.85 – 4.73 (m, 1H), 3.81 – 3.69 (m, 2H), 3.35 – 3.27 (m, 1H), 2.65 (ddd, *J* = 13.8, 10.4, 5.7 Hz, 1H), 2.57 (ddd, *J* = 13.8, 10.2, 6.1 Hz, 1H), 2.42 (s, 3H), 1.97 – 1.87 (m, 1H), 1.87 – 1.76 (m, 2H), 1.46 – 1.34 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 151.7, 144.8, 141.1, 135.3, 133.8, 130.0, 128.6, 128.5, 128.5, 128.28, 128.29, 127.7, 126.1, 75.6, 69.6, 56.5, 52.9, 41.1, 36.0, 31.4, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{28}H_{32}N_3O_5S$, 522.2063; found, 522.2054.



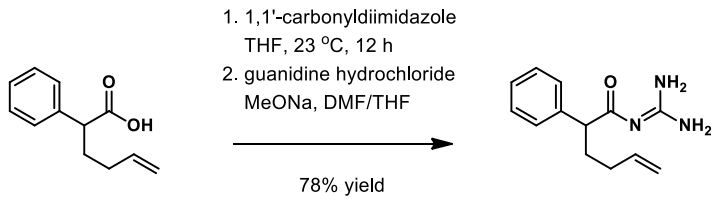
5a **7f**

Compound 7f. The title compound was prepared according to general procedure using substrate **5a** (80.0 mg, 0.194 mmol) and 3-nitrobenzyl alcohol (0.574 mL, 4.84 mmol). The product **7f** was obtained (0.107 g, 0.189 mmol, 92% yield) as colorless oil after column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.0 Hz, 2H), 5.23 (s, 2H), 5.08 (br. s, 2H), 4.86 – 4.79 (m, 1H), 3.82 – 3.67 (m, 2H), 3.35 – 3.27 (m, 1H), 2.70 – 2.54 (m, 2H), 2.42 (s, 3H), 2.00 – 1.78 (m, 3H), 1.50 – 1.41 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 151.6, 148.37, 144.9, 140.9, 137.4, 133.9, 133.7, 130.0, 129.7, 128.5, 128.2, 127.7, 126.1, 123.4, 122.9, 76.2, 68.0, 56.6, 53.0, 40.9, 35.9, 31.4, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{28}H_{31}N_4O_7S$, 567.1913; found, 567.1903.



S2 **8a**

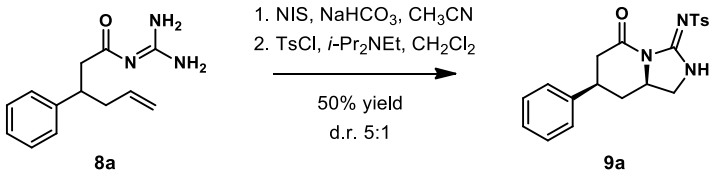
Compound 8a. To a solution of acid **S2** (0.900 g, 4.41 mmol) in 18.0 mL of THF was added 1,1'-carbonyldiimidazole (0.900 g, 5.29 mmol) at room temperature and the mixture was stirred for 20 min. After the TLC analysis showed a complete disappearance of acid **S2** the solution was directly added dropwise to the freshly prepared free guanidine (1.70 g, 17.6 mmol) in 54.0 mL of dimethylformamide (see above). 10 min after the mixture was poured into water (200 mL) and the product was extracted with ethyl acetate (4x70 mL). Combined organic phase was sequentially washed with brine (3x100 mL), saturated aqueous ammonium chloride solution (2x100 mL) and brine (100 mL) again, dried over sodium sulfate and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (3% methanol in dichloromethane → 10% methanol in dichloromethane). Compound **8a** (0.710 g, 3.04 mmol, 69% yield) was obtained as white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.10 (m, 5H), 5.66 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.03 – 4.79 (m, 2H), 3.27 (p, *J* = 7.4 Hz, 1H), 2.68 (dd, *J* = 15.1, 7.0 Hz, 1H), 2.58 (dd, *J* = 15.1, 7.9 Hz, 1H), 2.49 – 2.28 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 185.6, 161.7, 144.7, 136.5, 128.3, 127.6, 126.1, 116.4, 46.8, 42.3, 40.8. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{13}H_{17}N_3O$, 232.1450; found, 232.1451.



S3 **8b**

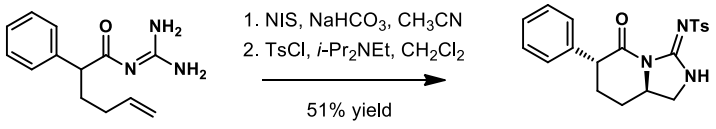
Compound 8b. To a solution of acid **S3** (1.39 g, 7.34 mmol) in 24.0 mL of THF was added 1,1'-carbonyldiimidazole (1.37 g, 8.44 mmol) at room temperature and the mixture was stirred for 20 min. After the TLC analysis showed a complete disappearance of acid **S3** the resultant mixture was directly added dropwise to the freshly prepared solution of free guanidine (1.40 g, 14.68 mmol) in 54.0 mL of dimethylformamide (see above). 10 min after the mixture was poured into water (200 mL) and the product was extracted with ethyl acetate (4x70 mL). Combined organic phase was sequentially washed with brine (3x100 mL), saturated aqueous ammonium chloride solution (2x100 mL) and brine (100 mL) again, dried over sodium sulfate and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (3% methanol in dichloromethane → 10% methanol in dichloromethane). Compound **8b** (1.32 g, 5.72 mmol, 78% yield) was obtained as white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.03 (m, 5H), 5.81 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.12 – 4.82 (m, 2H), 3.51 (t, *J* = 7.5 Hz, 1H), 2.24 – 2.10 (m, 1H), 2.07 – 1.92 (m, 2H), 1.91 – 1.73 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.9, 162.3,

141.4, 138.3, 128.4, 128.1, 126.7, 114.9, 56.0, 32.9, 31.8. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{13}H_{17}N_3O$, 232.1450; found, 232.1449.



8a **9a**

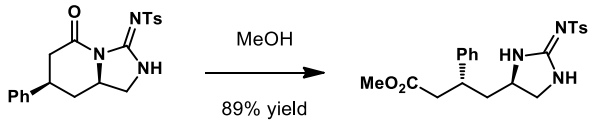
Compound 9a. The title compound was prepared according to general procedure with different reaction time (1.5 hours at 0°C) using compound **8a** (0.100 g, 0.432 mmol), N-iodosuccinimide (0.204 g, 0.907 mmol) and $NaHCO_3$ (0.363 g, 4.32 mmol) in 9.0 ml of acetonitrile followed by the quench with sodium sulfite solution. The organic layer was immediately treated with p-toluenesulfonyl chloride (99.0 mg, 0.518 mmol) and Hunig's base (0.15 ml, 0.864 mmol), 10 minutes after it was washed with brine, dried over sodium sulfate and concentrated under reduced pressure. Compound **9a** (83.0 mg, 0.216 mmol, 50% yield, dr 5:1) was obtained as yellowish oil after column chromatography (dichloromethane → 20% EtOAc in dichloromethane). Major diastereomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.00 (d, J = 8.5 Hz, 2H), 7.33 (dt, *J* = 7.7, 3.4 Hz, 4H), 7.29 – 7.24 (m, 1H), 7.17 – 7.13 (m, 2H), 4.22 (dd, *J* = 8.9, 6.6 Hz, 1H), 4.14 (tdt, *J* = 9.8, 6.6, 3.1 Hz, 1H), 3.28 (dd, *J* = 10.7, 8.9 Hz, 1H), 3.19 – 3.11 (m, 1H), 2.78 (ddd, *J* = 18.3, 5.9, 1.8 Hz, 1H), 2.44 (s, 3H), 2.31 (dtd, *J* = 13.1, 3.1, 1.6 Hz, 1H), 1.70 (td, *J* = 12.8, 11.4 Hz, 1H). Minor diastereomer: 8.70 (s, 1H), 7.97 (d, *J* = 6.5 Hz, 2H), 7.33 (dt, *J* = 7.7, 3.4 Hz, 4H), 7.29 – 7.24 (m, 1H), 7.13 – 7.10 (m, 2H), 4.04 (dd, J = 8.9, 6.8 Hz, 1H), 3.77 (tdd, *J* = 10.8, 6.8, 3.8 Hz, 0H), 3.47 (p, *J* = 4.8 Hz, 1H), 3.28 (dd, *J* = 10.7, 8.9 Hz, 1H), 2.78 (ddd, *J* = 18.3, 5.9, 1.8 Hz, 1H), 2.51 (dd, *J* = 18.3, 12.1 Hz, 1H), 2.44 (s, 3H), 1.70 (td, *J* = 12.8, 11.4 Hz, 1H), 1.91 (ddd, *J* = 13.3, 11.3, 4.9 Hz, 1H). Major diastereomer: ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1, 146.5, 144.5, 141.9, 134.2, 129.5, 129.1, 128.8, 127.5, 126.3, 54.5, 50.2, 40.6, 38.5, 33.7, 21.7. Minor diastereomer: 170.1, 145.0, 141.7, 134.2, 129.4, 129.1, 128.8, 127.4, 126.7, 50.3, 49.8, 37.5, 35.9, 33.7, 21.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{21}N_3O_3S$, 406.1201; found, 406.1206.



8b **9b**

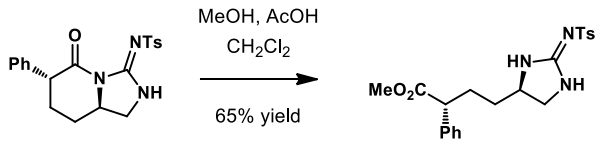
Compound 9b. The title compound was prepared according to general procedure with different reaction time (1.5 hours at 0°C) using compound **8b** (0.100 g, 0.432 mmol), N-iodosuccinimide (0.204 g, 0.907 mmol) and $NaHCO_3$ (0.363 g, 4.32 mmol) in 9 ml of acetonitrile followed by the quench with sodium sulfite solution. The organic layer was immediately treated with p-toluenesulfonyl chloride (99.0 mg, 0.518 mmol) and Hunig's base (0.15 ml, 0.864 mmol), 10 minutes after it was washed with brine, dried over sodium sulfate and concentrated under reduced pressure. Compound **9b** (84.0 mg, 0.216 mmol, 51% yield) was obtained as yellowish oil after column chromatography (dichloromethane → 20% EtOAc in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.07 – 7.88 (m, 2H), 7.34 (ddd, J = 7.7, 4.9, 2.9 Hz, 4H),

7.31 – 7.27 (m, 1H), 7.22 – 7.12 (m, 2H), 4.22 (dd, J = 8.7, 6.7 Hz, 1H), 4.20 – 4.08 (m, 1H), 3.62 (dd, J = 11.8, 6.5 Hz, 1H), 3.28 (dd, J = 10.5, 8.7 Hz, 1H), 2.44 (s, 3H), 2.26 (dddd, J = 25.0, 13.2, 6.9, 3.5 Hz, 2H), 2.11 – 1.98 (m, 1H), 1.72 – 1.59 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.9, 146.5, 144.9, 138.8, 134.3, 129.4, 128.9, 128.8, 128.3, 127.5, 55.4, 50.4, 49.9, 30.0, 26.8, 21.7. HRMS-EI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{21}N_3O_3S$, 406.1201; found, 406.1201.



9a **10a**

Compound 10a. The title compound (5:1 diastereomeric mixture) was prepared using substrate **9a** (40.0 mg, 0.104 mmol) dissolved in a mixture of methanol and dichloromethane (1:1, 2.0 mL) and stirred for 12 h at room temperature. The crude mixture was concentrated by reduce pressure and product **10a** was obtained (38.5 mg, 0.093 mmol, 89% yield) as a white solid after column chromatography on silica gel (10% methanol in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ major diastereomer: 7.73 – 7.68 (m, 2H), 7.29 – 7.24 (m, 4H), 7.22 – 7.18 (m, 2H), 7.14 (dd, J = 7.0, 1.7 Hz, 1H), 5.48 (bs, 2H), 3.54 (s, 3H), 3.50 – 3.44 (m, 2H), 3.31 – 3.22 (m, 1H), 3.03 (p, J = 5.3, 4.6 Hz, 1H), 2.61 – 2.51 (m, 2H), 2.43 (s, 3H), 1.65 (ddd, J = 13.0, 7.8, 4.6 Hz, 1H), 1.52 (ddd, J = 13.1, 10.0, 4.5 Hz, 1H). Minor diastereomer: 7.81 – 7.76 (m, 2H), 7.37-7.33 (m, 4H), 7.22 – 7.18 (m, 2H), 7.11 (dd, J = 7.0, 1.7 Hz, 1H), 5.48 (bs, 2H), 3.54 (s, 3H), 3.50 – 3.44 (m, 2H), 3.31 – 3.22 (m, 1H), 3.03 (p, J = 5.3, 4.6 Hz, 1H), 2.61 – 2.51 (m, 2H), 2.43 (s, 3H), 1.65 (ddd, J = 13.0, 7.8, 4.6 Hz, 1H), 1.52 (ddd, J = 13.1, 10.0, 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ major diastereomer: 172.2, 145.1, 142.8, 130.1, 130.0, 128.7, 127.7, 127.5, 126.9, 51.5, 41.7, 39.22, 21.63. Minor diastereomer: 172.2, 145.1, 142.8, 133.4, 130.1, 128.7, 127.7, 127.2, 126.9, 53.0, 43.6, 41.2, 21.6. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{21}H_{25}N_3O_4S$; 416.1644 found, 416.1640.



9b **10b**

Compound 10b. The title compound was prepared according to general procedure using substrate **9b** (40.0 mg, 0.104 mmol), methanol (0.28 mL, 4.84 mmol) and acetic acid (50.0 μL, 0.874 mmol). The product **10b** was obtained (28.0 mg, 67.6 μmol, 65% yield) as colorless oil after column chromatography on silica gel (10% methanol in dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, J = 10.1, 8.2 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.30 – 7.26 (m, 3H), 7.22 – 7.19 (m, 2H), 3.76 - 3.74 (m, 1H), 3.62 (s, 3H), 3.45 (t, J = 7.3 Hz, 1H), 3.26 – 3.22 (m, 1H), 2.46 (s, 3H), 2.09 – 1.92 (m, 1H), 1.77 – 1.58 (m, 1H), 1.43 – 1.32 (m, 1H), 1.29 – 1.16 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 145.4, 133.3, 130.2, 130.2, 128.7, 127.8., 127.6, 127.4, 52.0, 51.2, 33.3, 29.2, 21.7. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{21}H_{25}N_3O_4S$; 416.1644 found, 416.1634.

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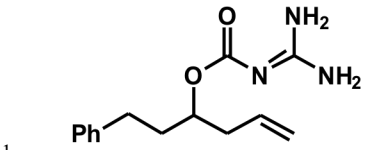
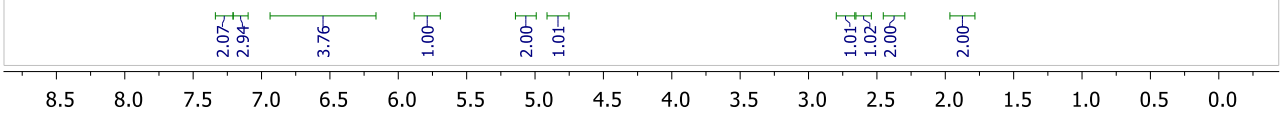


^{1}H NMR spectra of compound **3a**



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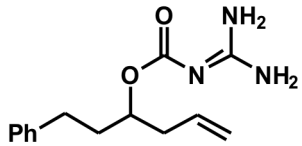
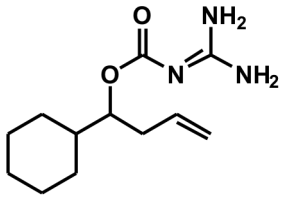
5 Number of Scans	84
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-03-10T22:22:21
8 Spectrometer Frequency	125.70

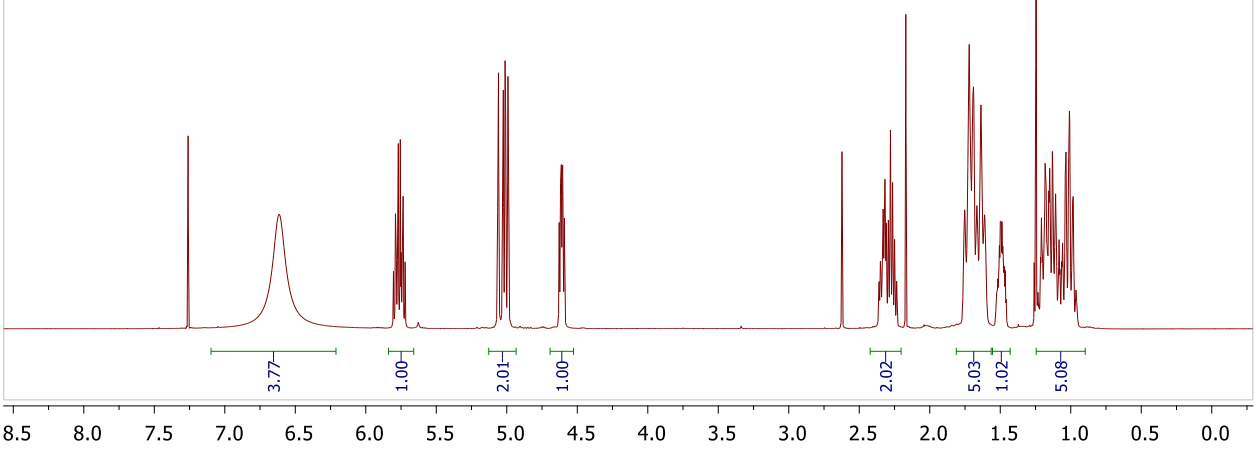


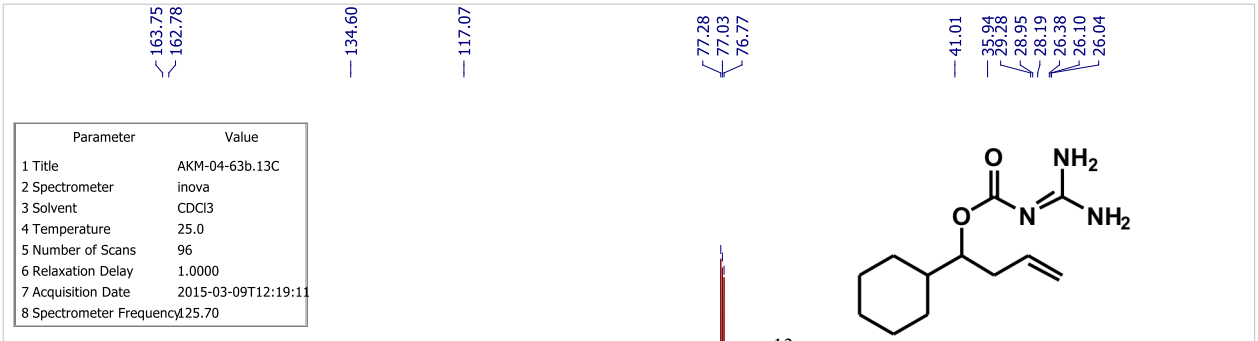
^{13}C NMR spectra of compound **3a**

Parameter	Value
1 Title	AKM-04-63b
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-03-09T12:16:24
8 Spectrometer Frequency	499.86



^{1}H NMR spectra of compound **3b**

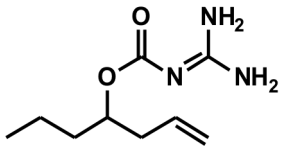




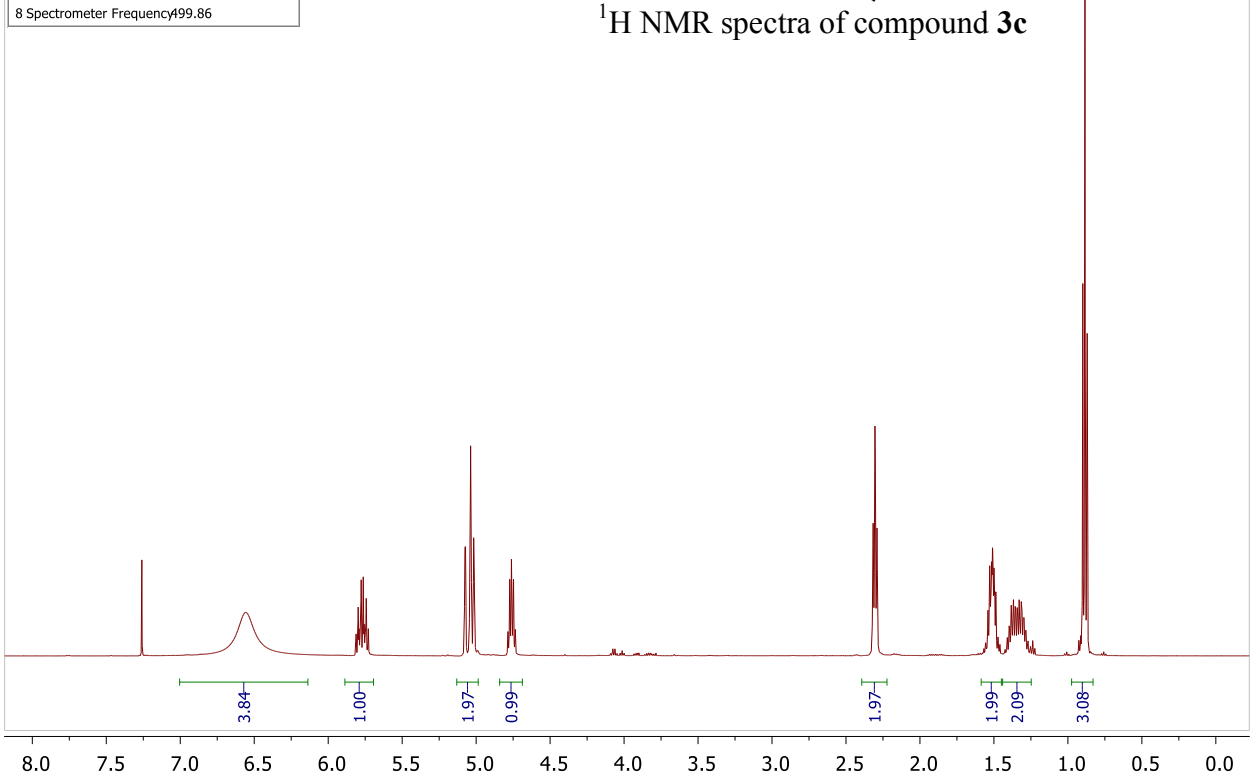
Parameter	Value
1 Title	AKM-04-63b.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	96
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-03-09T12:19:11
8 Spectrometer Frequency	125.70

^{13}C NMR spectra of compound **3b**

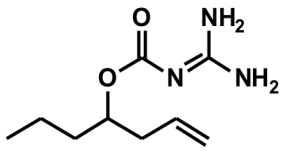
Parameter	Value
1 Title	AKM-04-81
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-03-16T21:16:16
8 Spectrometer Frequency	499.86



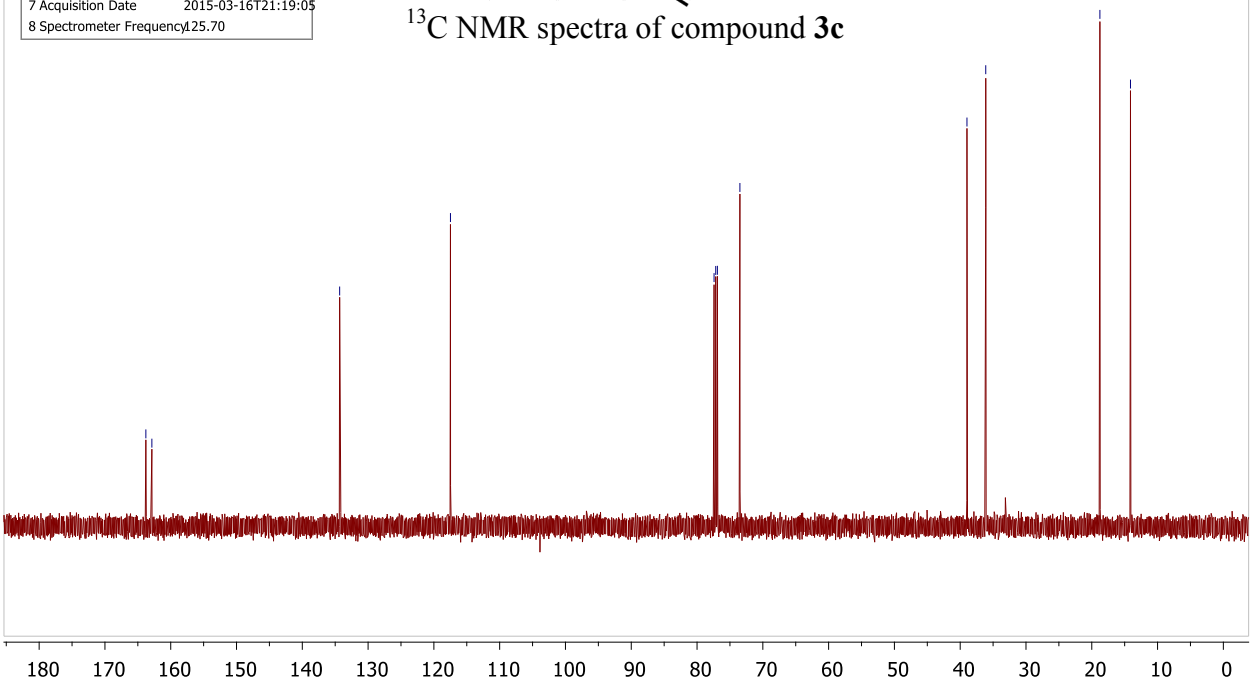
^{1}H NMR spectra of compound **3c**



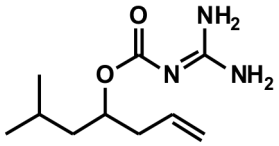
Parameter	Value
1 Title	AKM-04-81.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	60
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-03-16T21:19:05
8 Spectrometer Frequency	125.70



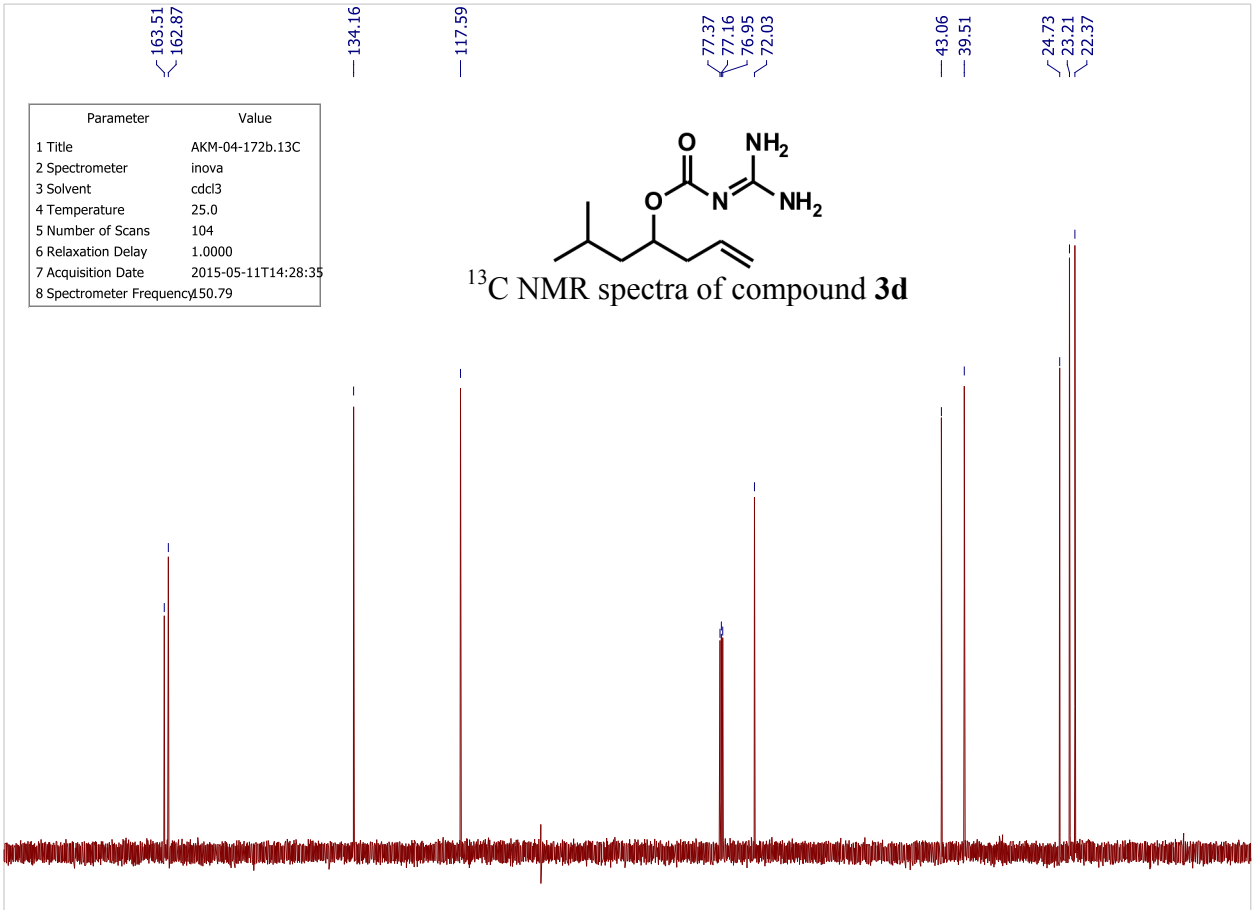
^{13}C NMR spectra of compound **3c**



Parameter	Value
1 Title	AKM-04-172b
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-11T14:25:13
8 Spectrometer Frequency	599.64



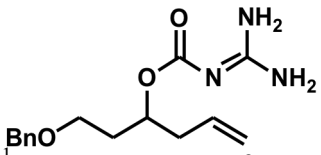
^{1}H NMR spectra of compound **3d**



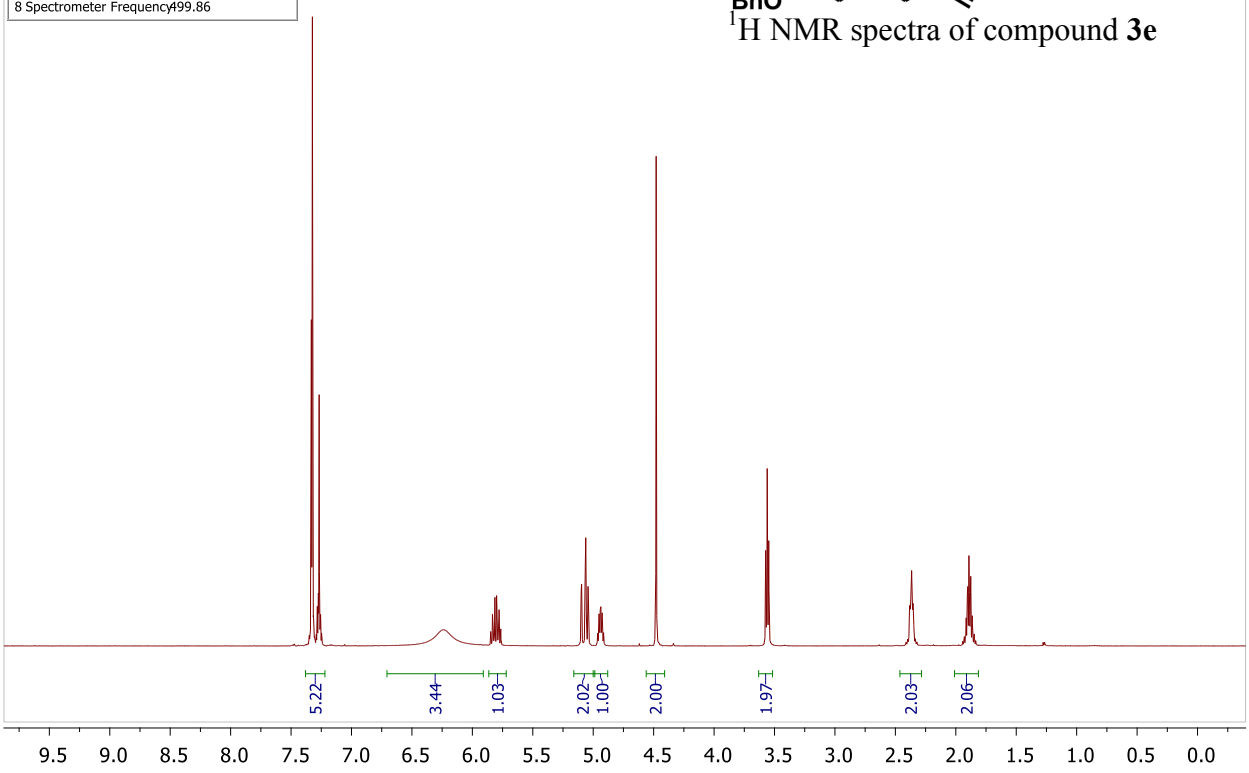
Parameter	Value
1 Title	AKM-04-172b.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	104
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-11T14:28:35
8 Spectrometer Frequency	150.79

^{13}C NMR spectra of compound **3d**

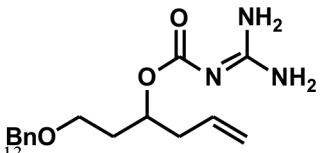
Parameter	Value
1 Title	AKM-03-172.1
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2014-11-06T13:14:18
8 Spectrometer Frequency	499.86



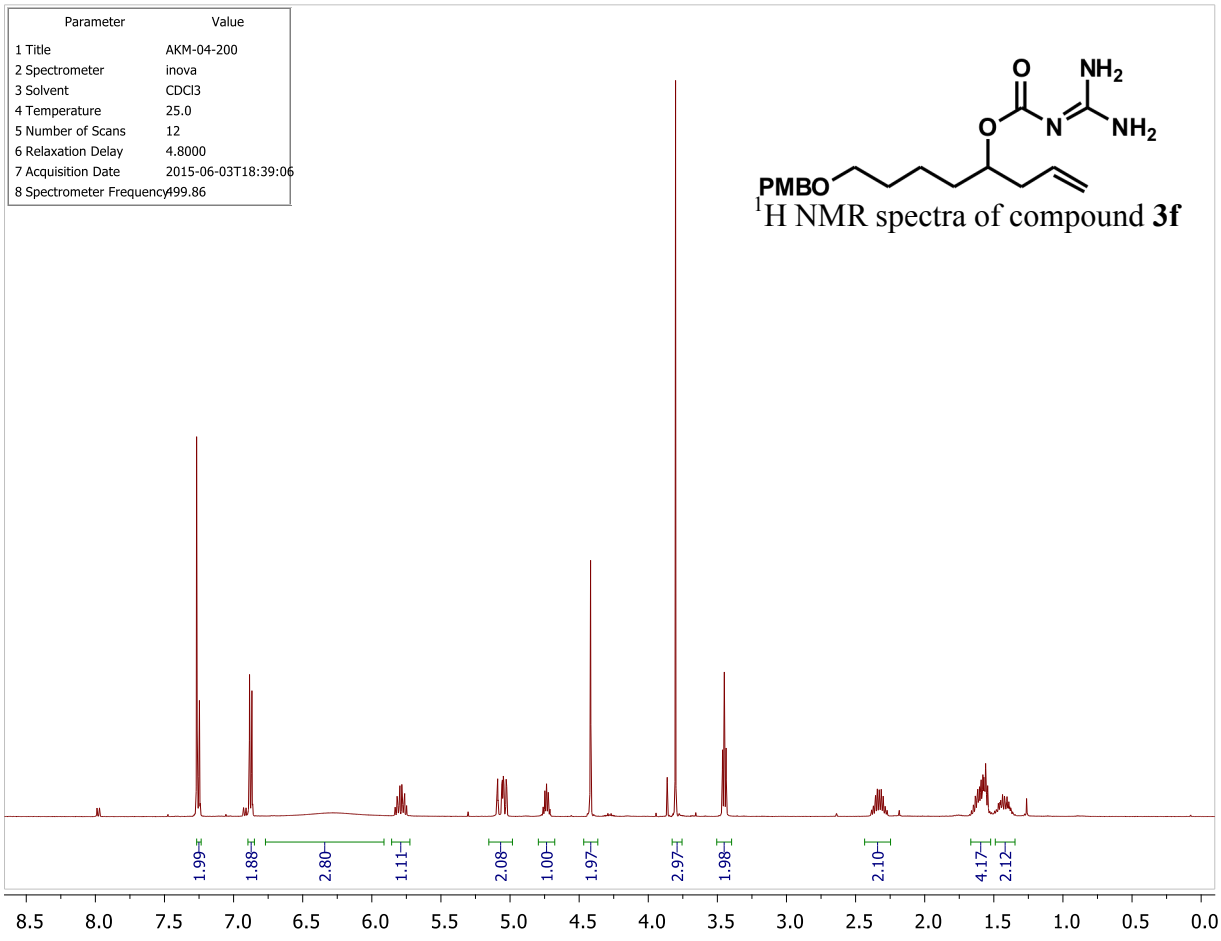
^{1}H NMR spectra of compound **3e**



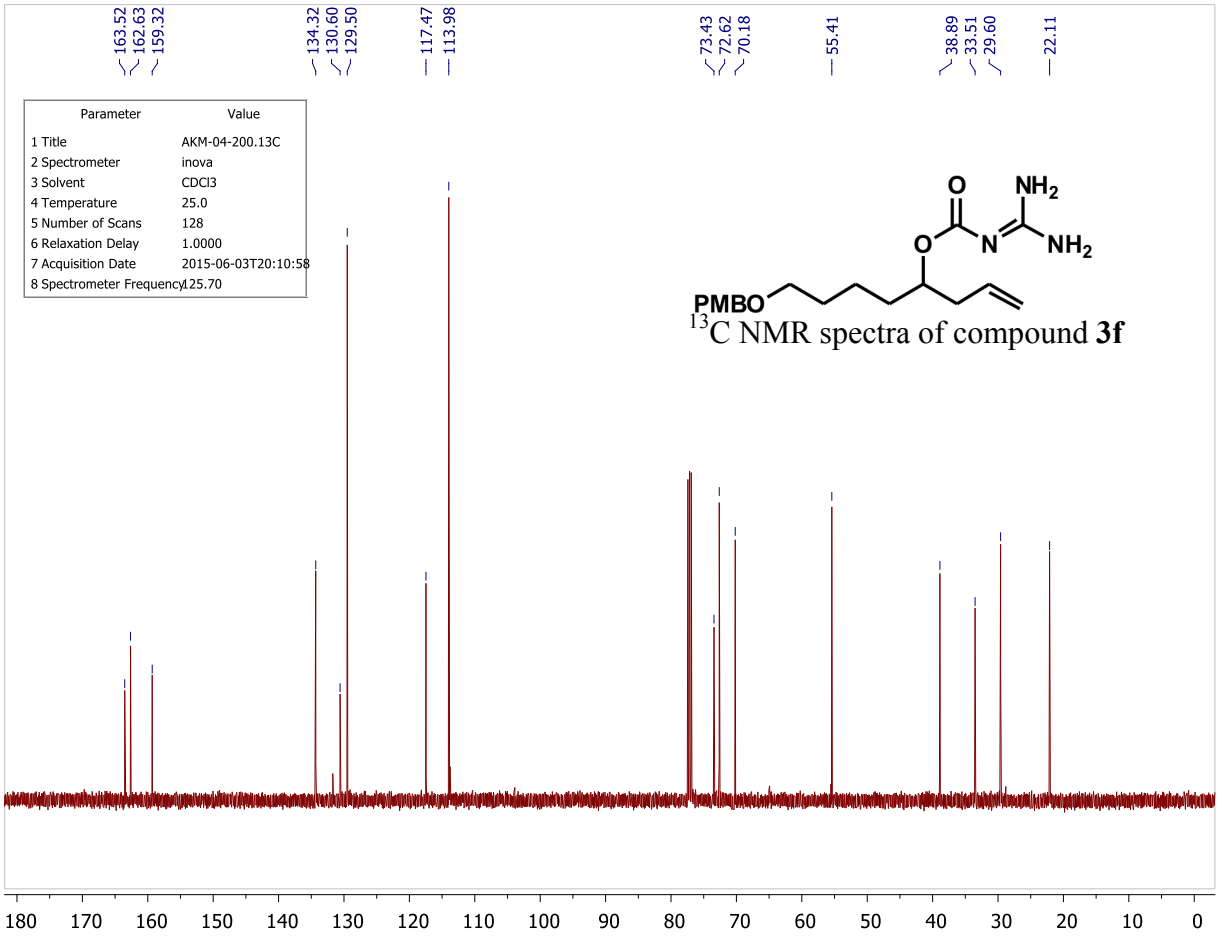
Parameter	Value
1 Title	AKM-04-168.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	132
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-08T12:05:54
8 Spectrometer Frequency	125.70



^{13}C NMR spectra of compound **3e**

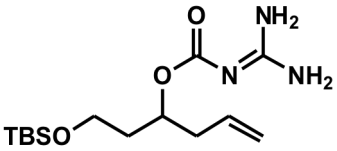


^{1}H NMR spectra of compound **3f**

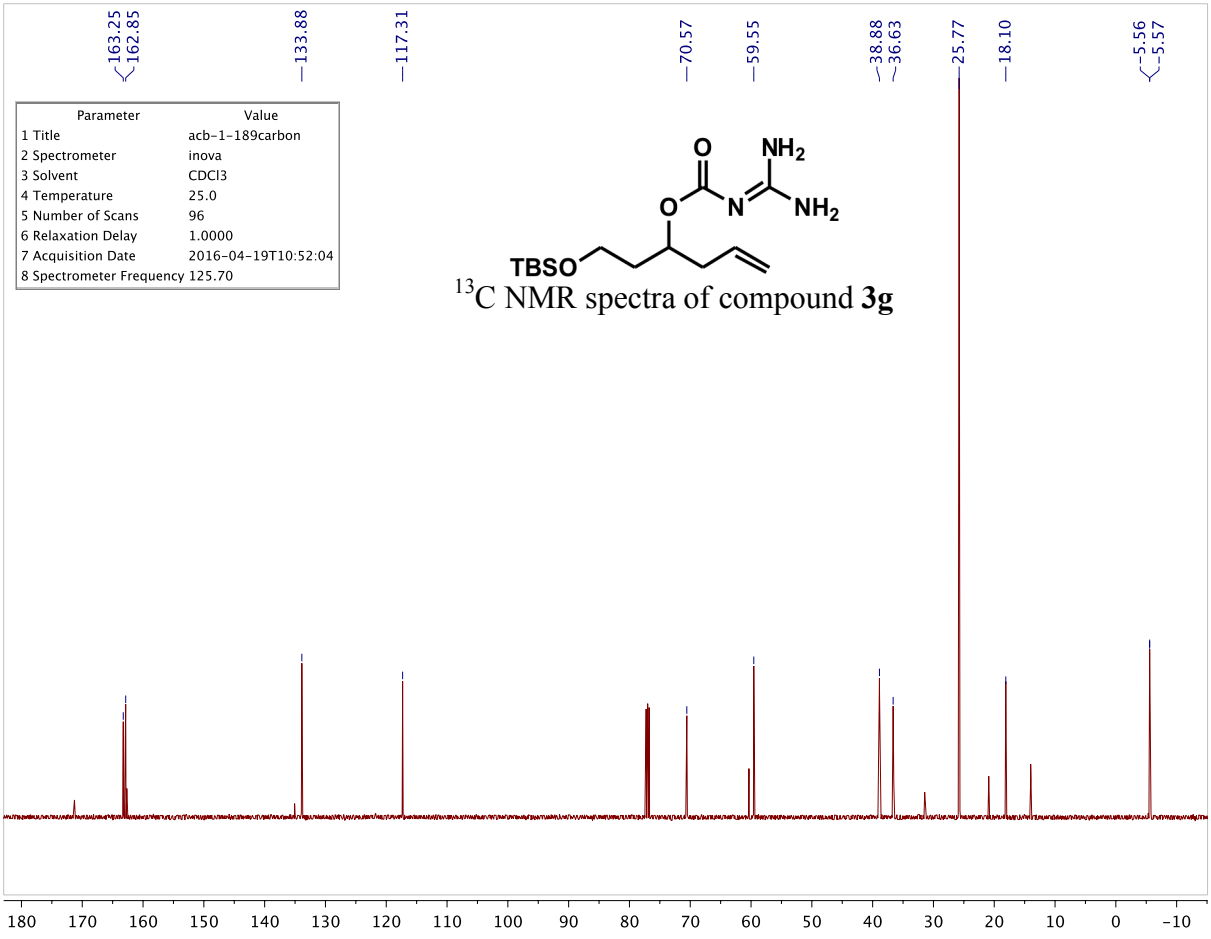


^{13}C NMR spectra of compound **3f**

Parameter	Value
1 Title	acb-01-189-aa
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-10-09T10:55:28
8 Spectrometer Frequency	599.64



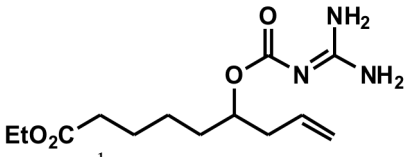
^{1}H NMR spectra of compound **3g**



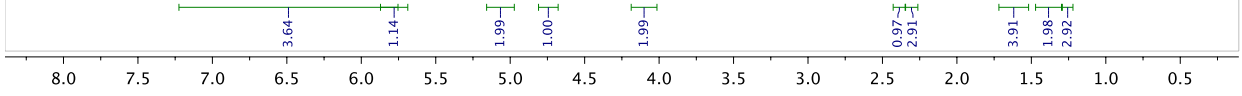
Parameter	Value
1 Title	acb-1-189carbon
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	96
6 Relaxation Delay	1.0000
7 Acquisition Date	2016-04-19T10:52:04
8 Spectrometer Frequency	125.70

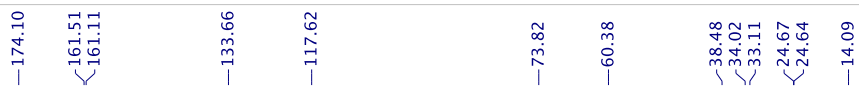
^{13}C NMR spectra of compound **3g**

Parameter	Value
1 Title	acb-01-181-b-2
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-09-30T10:30:26
8 Spectrometer Frequency	499.86

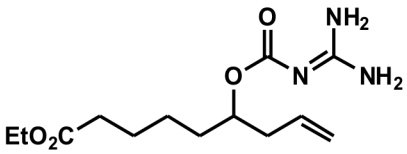


^{1}H NMR spectra of compound **3h**

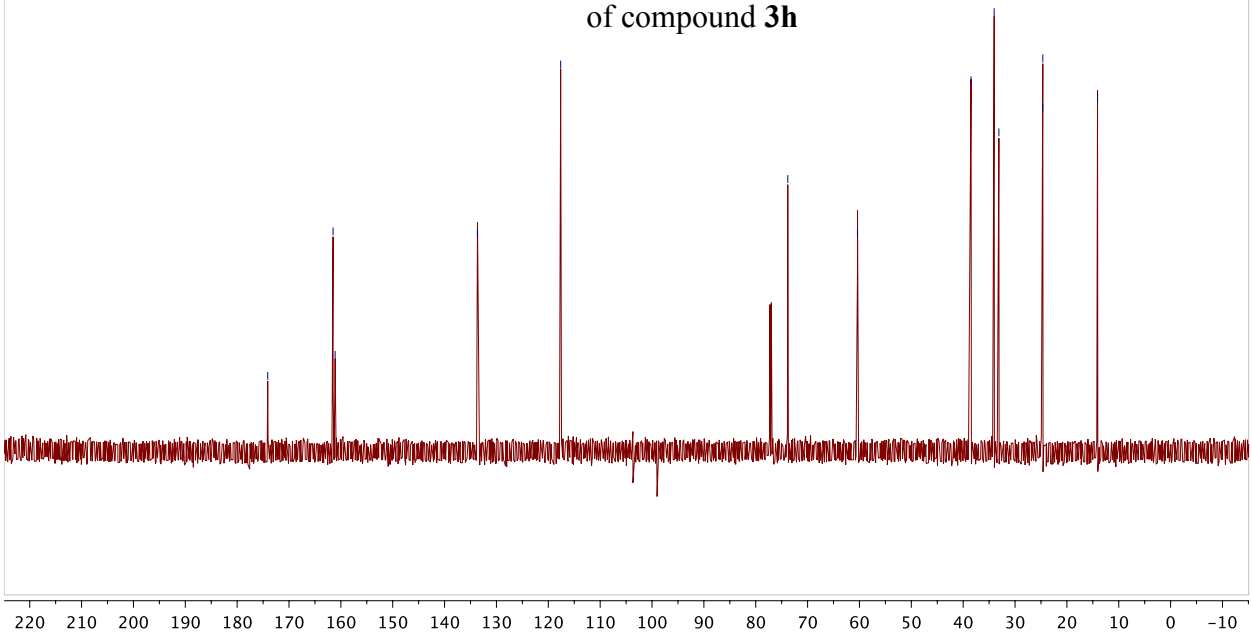




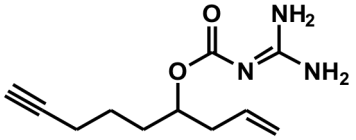
Parameter	Value
1 Title	acb-01-181-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	36
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-09-29T12:16:50
8 Spectrometer Frequency	125.70



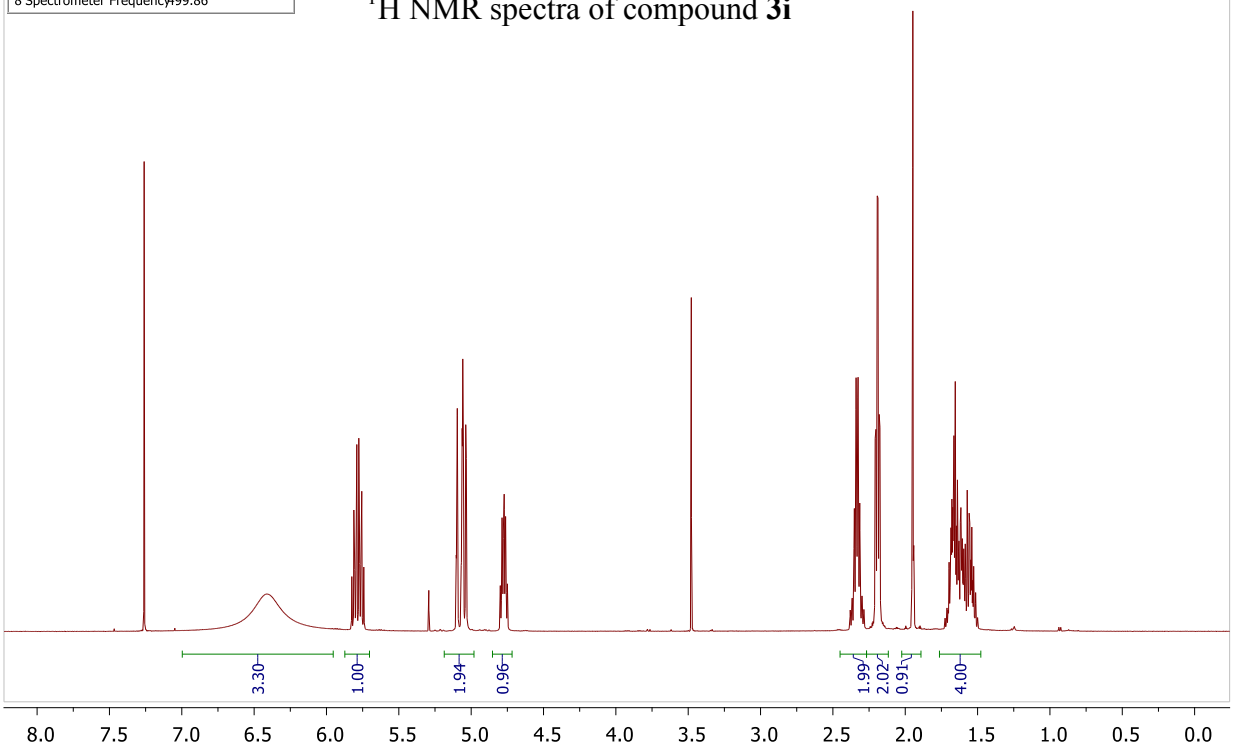
^{13}C NMR spectra of compound **3h**



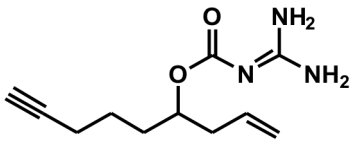
Parameter	Value
1 Title	AKM-04-163
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	20
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-06T21:25:41
8 Spectrometer Frequency	499.86



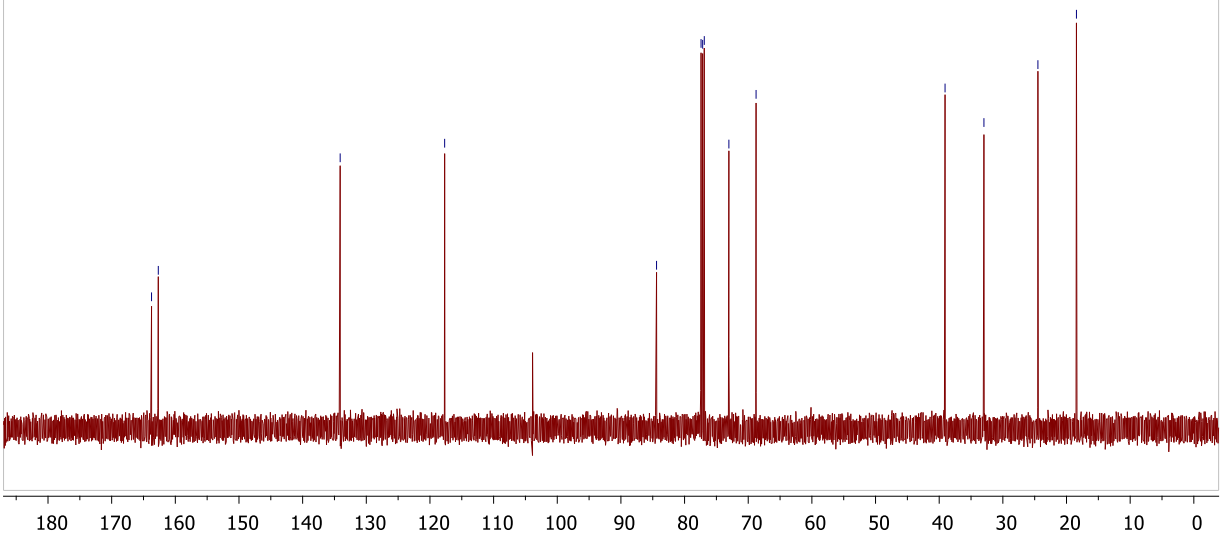
^{1}H NMR spectra of compound **3i**



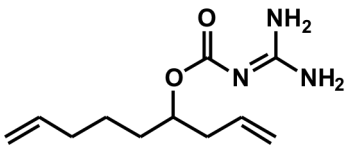
Parameter	Value
1 Title	AKM-04-163.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	68
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-06T21:29:26
8 Spectrometer Frequency	125.70



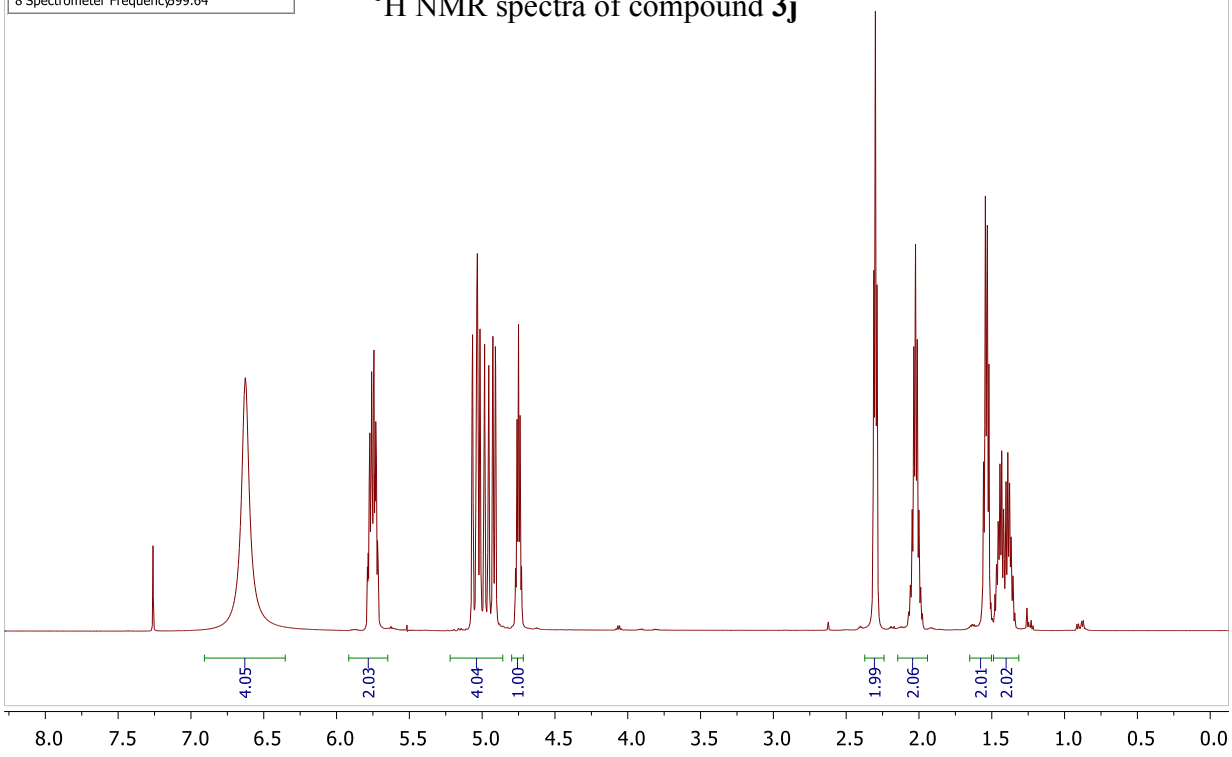
^{13}C NMR spectra of compound **3i**



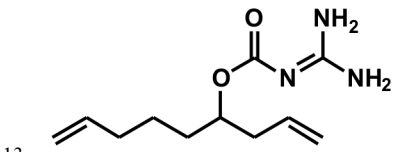
Parameter	Value
1 Title	AKM-04-174
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-11T14:36:19
8 Spectrometer Frequency	599.64



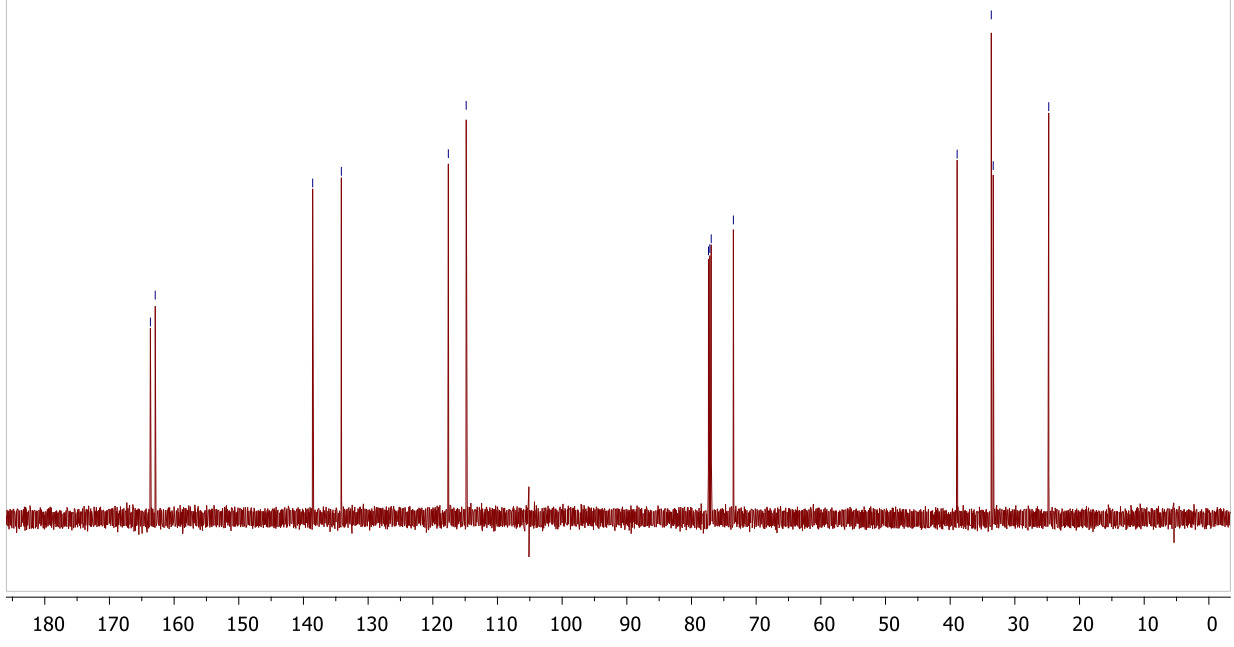
^{1}H NMR spectra of compound **3j**



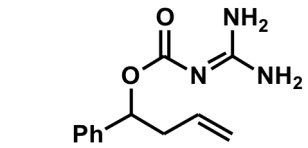
Parameter	Value
1 Title	AKM-04-174.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	108
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-11T14:40:07
8 Spectrometer Frequency	150.79



^{13}C NMR spectra of compound **3j**

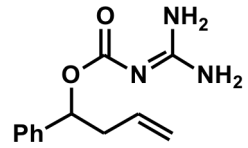


Parameter	Value
1 Title	AKM-04-120a_repurified
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-16T11:54:15
8 Spectrometer Frequency	599.64

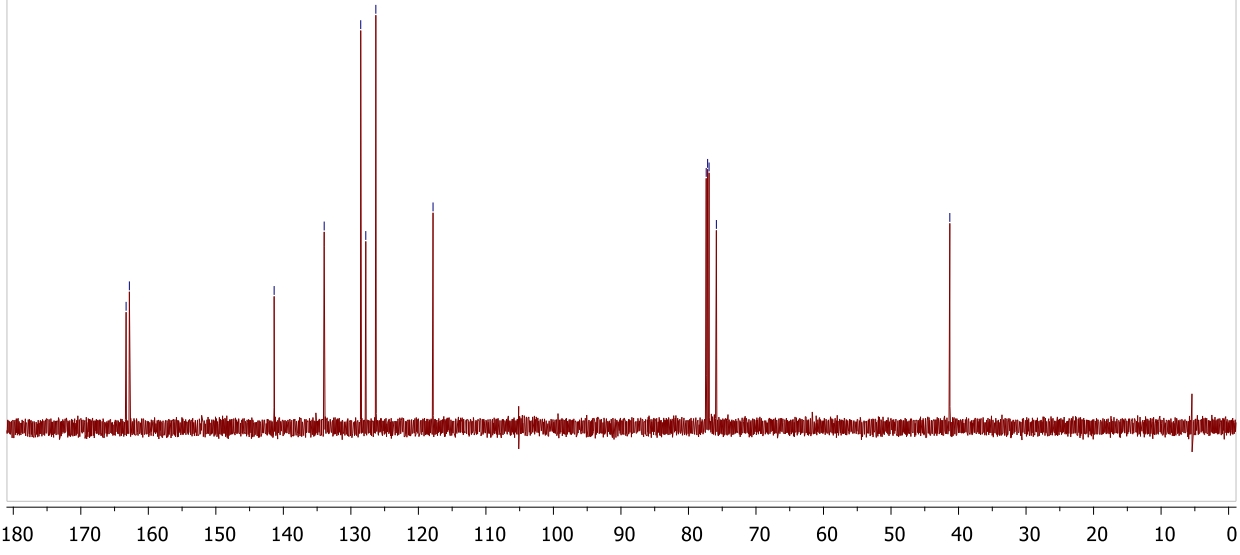


^{1}H NMR spectra of compound **3k**

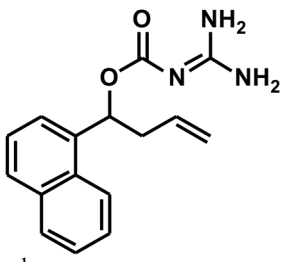
Parameter	Value
1 Title	AKM-04-120a.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	228
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-04-06T11:57:20
8 Spectrometer Frequency	150.79



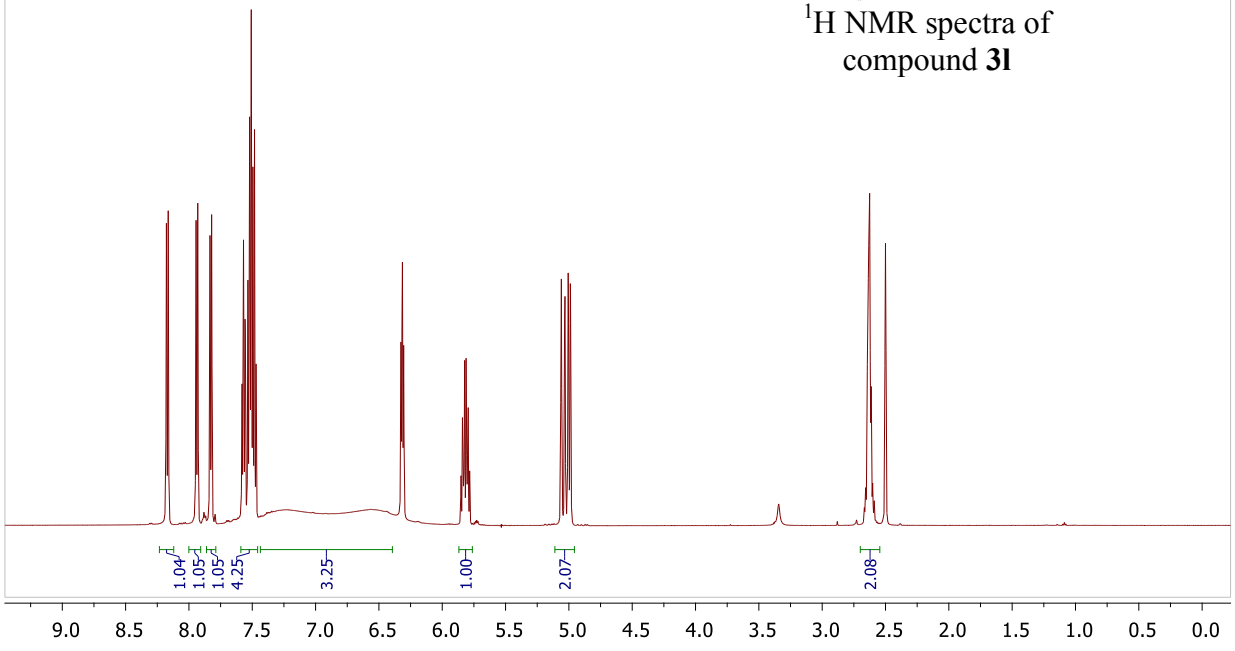
^{13}C NMR spectra of compound **3k**

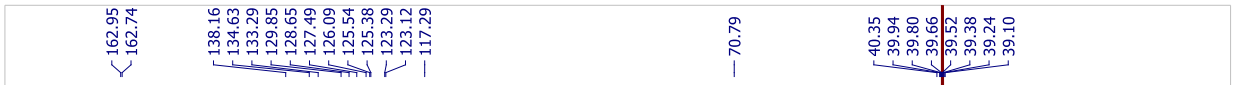


Parameter	Value
1 Title	AKM-04-119a.DMSO
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-04-06T15:41:47
8 Spectrometer Frequency	599.64

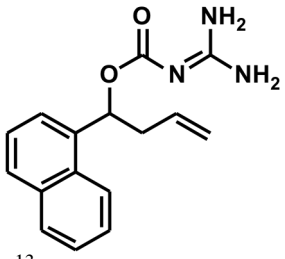


^{1}H NMR spectra of compound **3l**

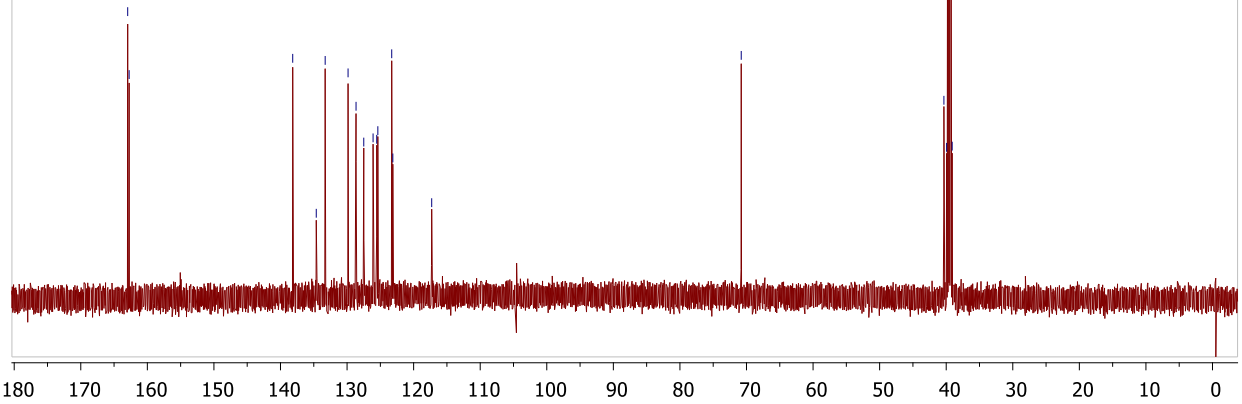


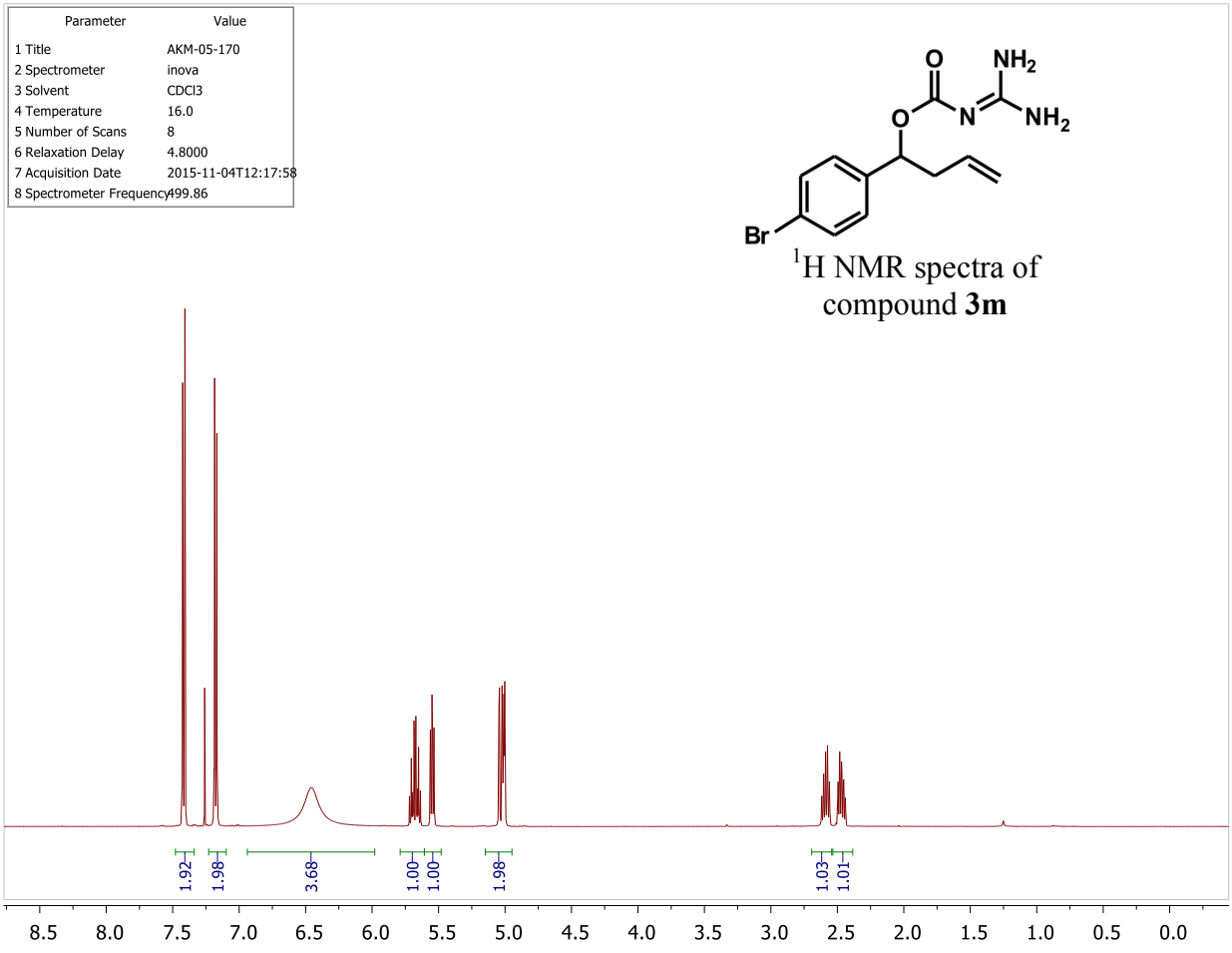


Parameter	Value
1 Title	AKM-04-119a.DMSO.13C
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	376
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-04-06T15:45:03
8 Spectrometer Frequency	150.79

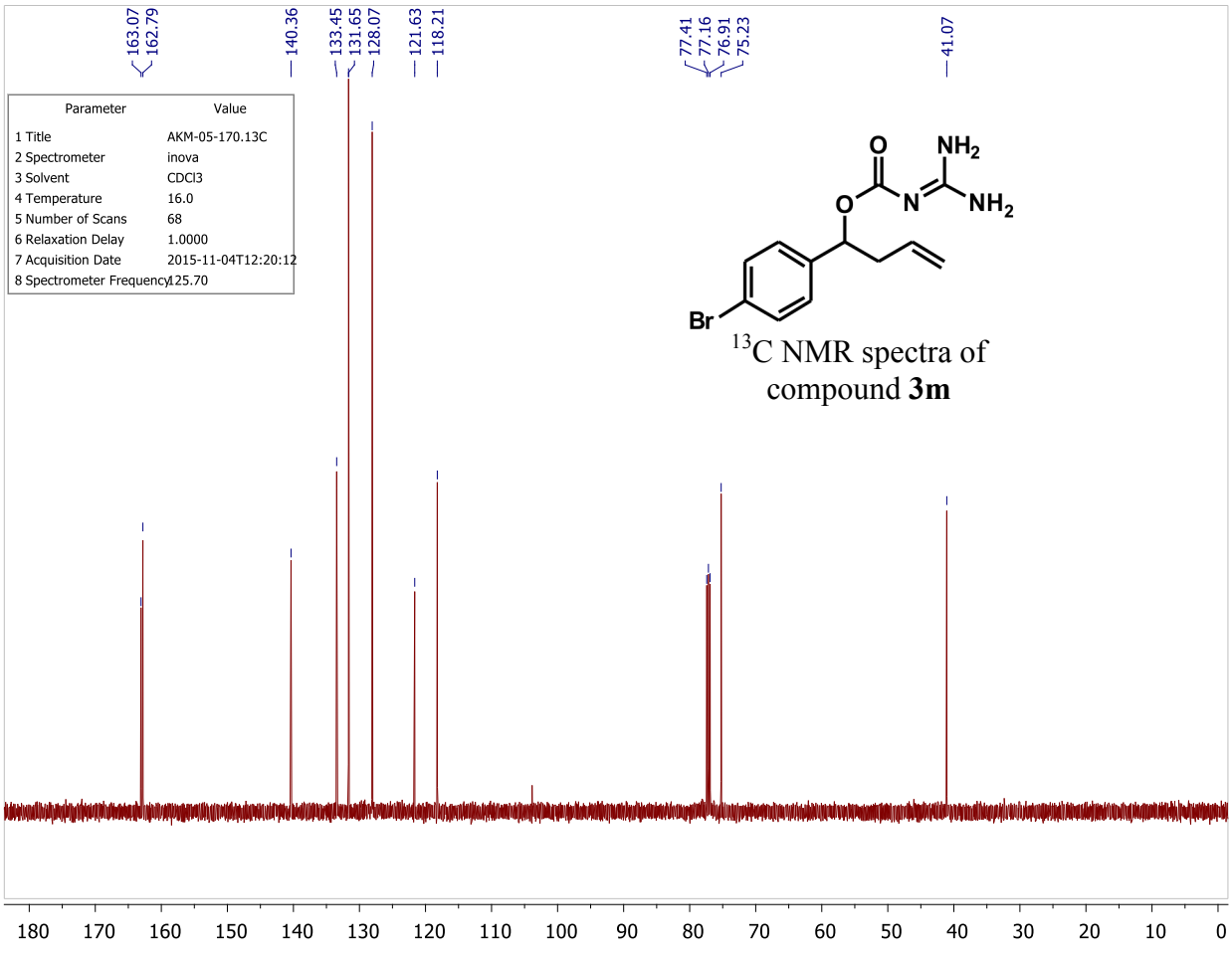


^{13}C NMR spectra of compound **3l**



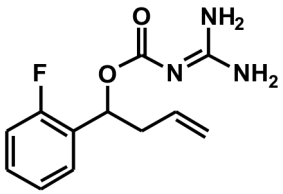


^{1}H NMR spectra of compound **3m**

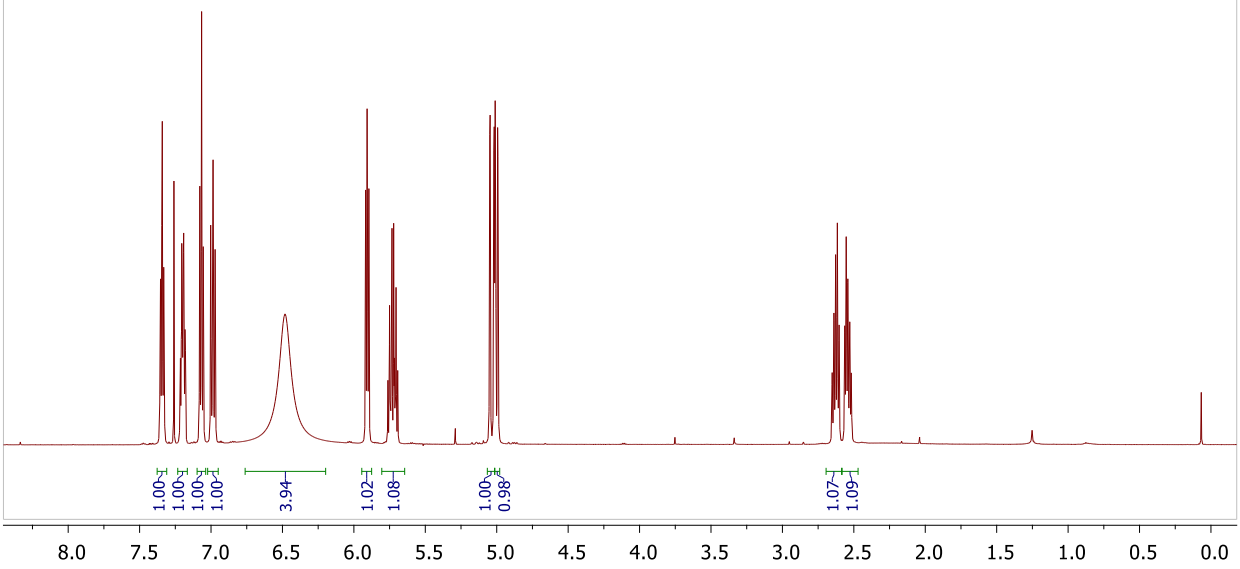


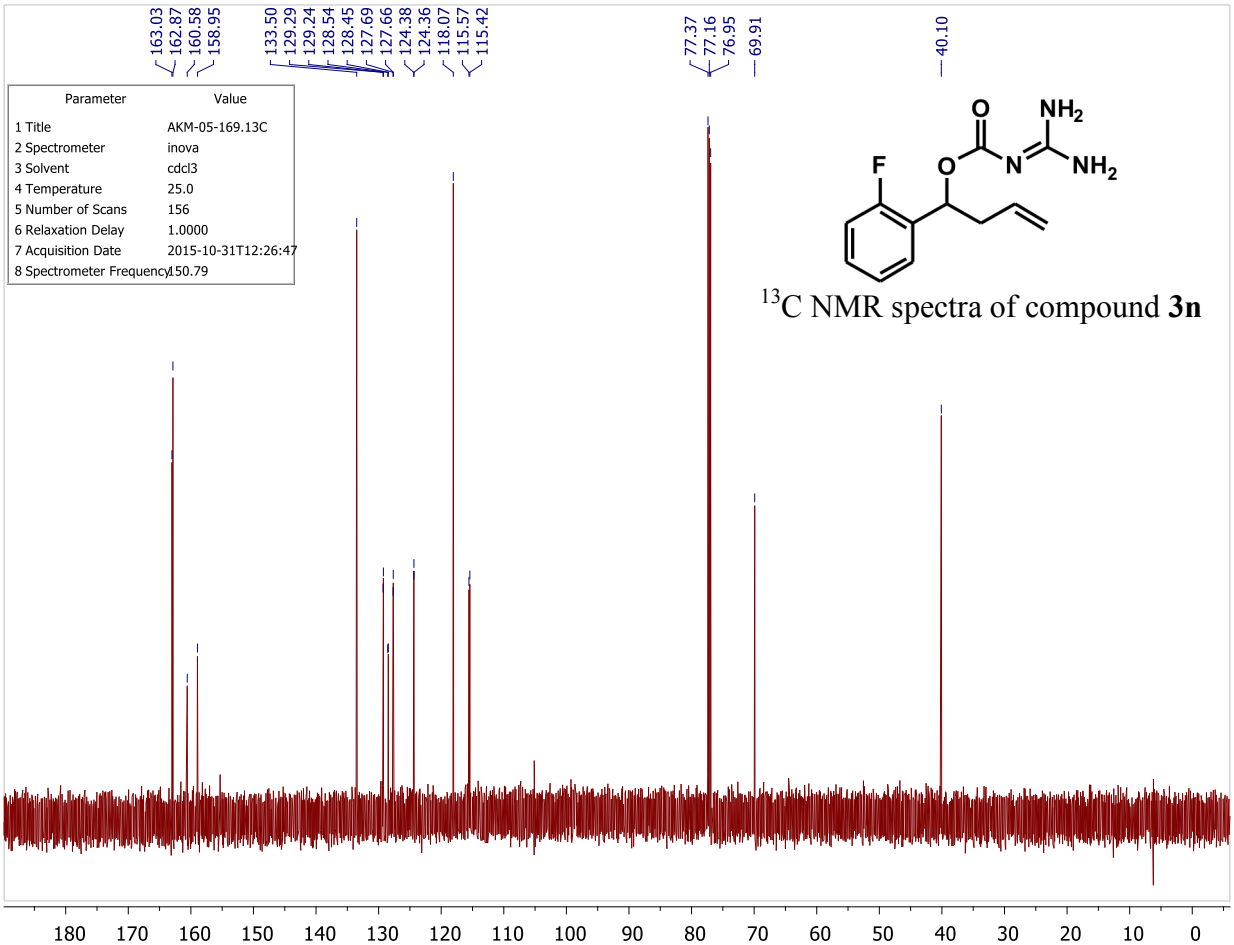
^{13}C NMR spectra of compound **3m**

Parameter	Value
1 Title	AKM-05-169
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-31T12:24:13
8 Spectrometer Frequency	599.64



^{1}H NMR spectra of compound **3n**

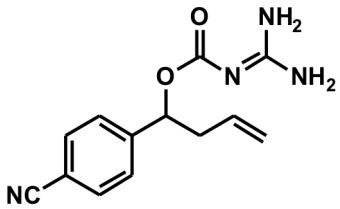




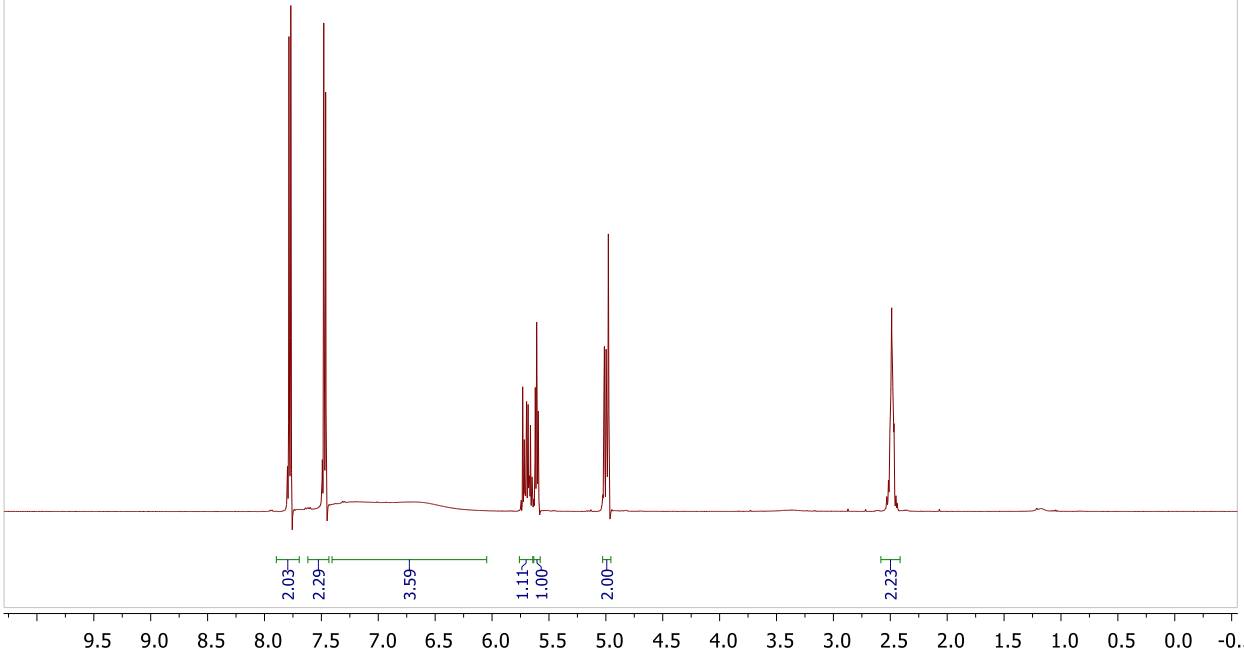
Parameter	Value
1 Title	AKM-05-169.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	156
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-31T12:26:47
8 Spectrometer Frequency	150.79

^{13}C NMR spectra of compound **3n**

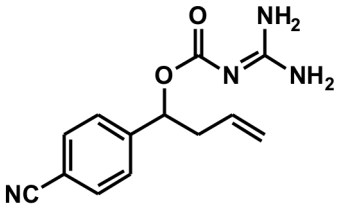
Parameter	Value
1 Title	AKM-05-151
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-25T00:36:12
8 Spectrometer Frequency	499.86



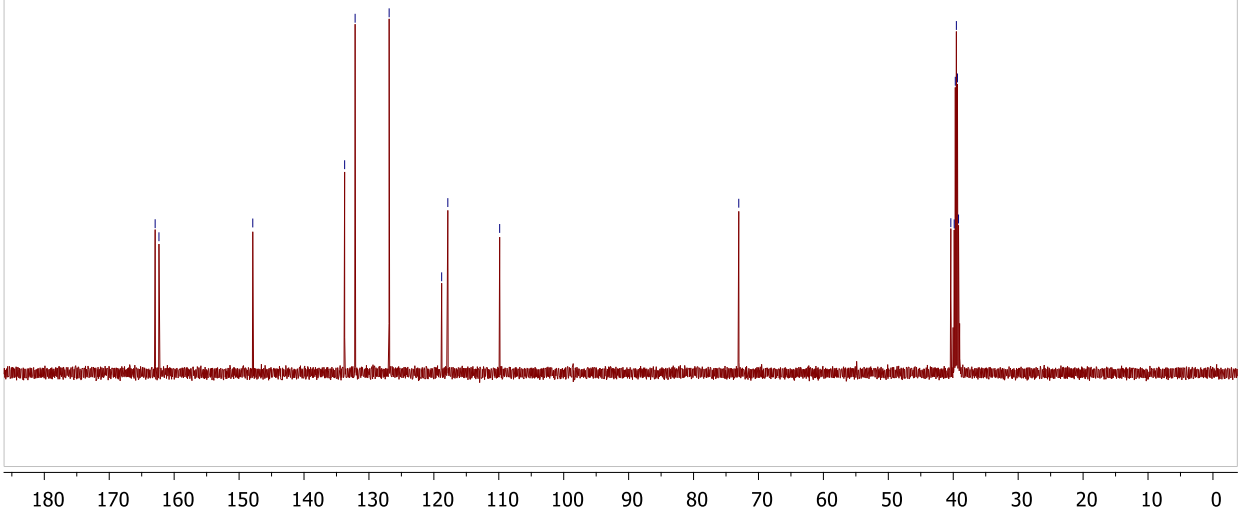
^{1}H NMR spectra of compound **3o**



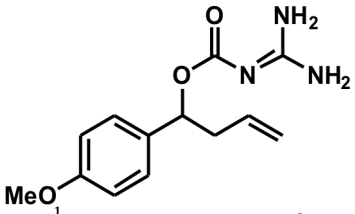
Parameter	Value
1 Title	AKM-05-151.13C
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	100
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-25T00:39:08
8 Spectrometer Frequency	125.70



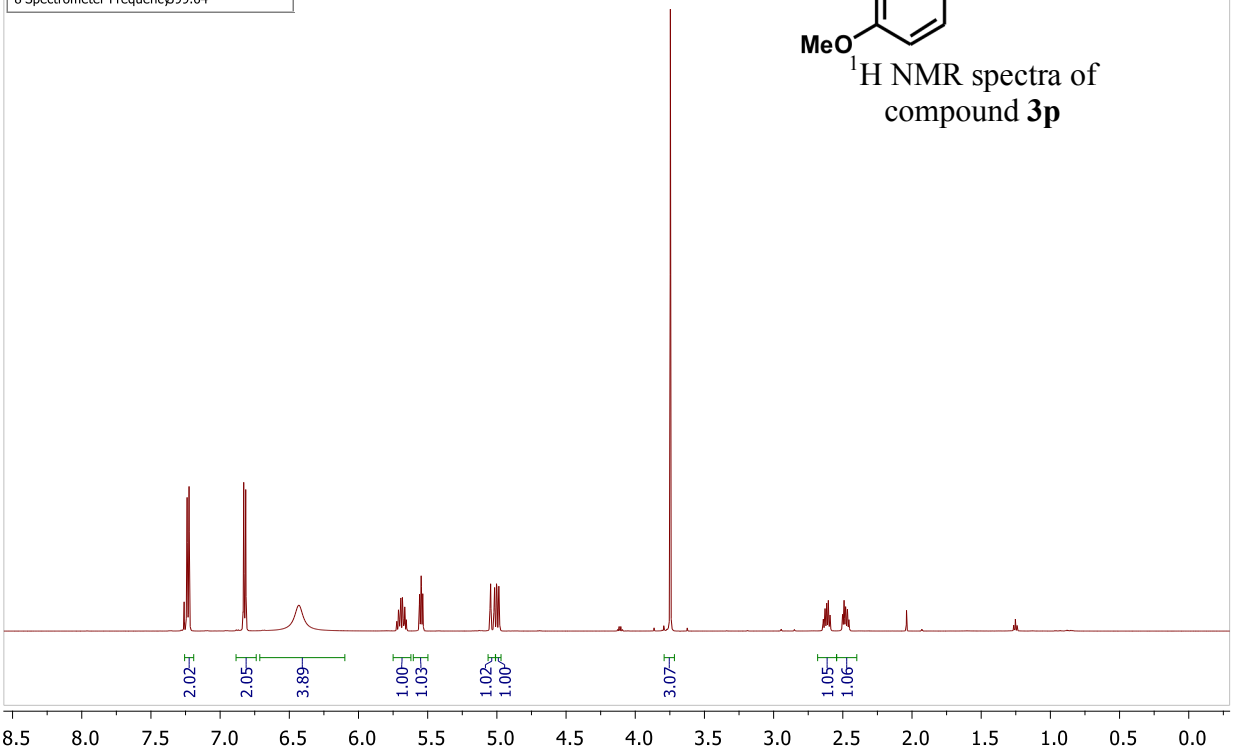
^{13}C NMR spectra of compound **3o**



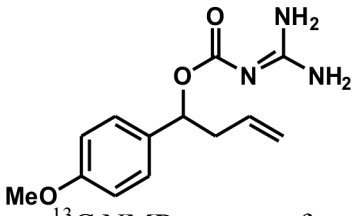
Parameter	Value
1 Title	AKM-04-121
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-04-06T21:15:54
8 Spectrometer Frequency	599.64



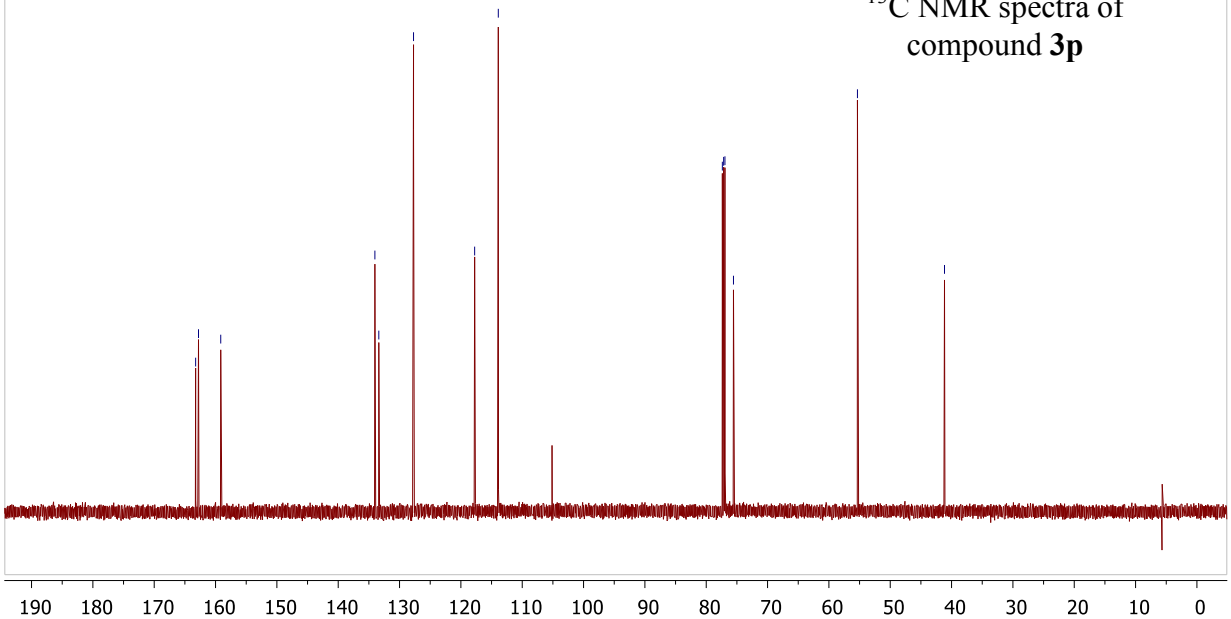
^{1}H NMR spectra of compound **3p**



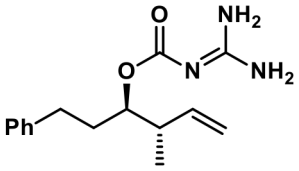
Parameter	Value
1 Title	AKM-04-121.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	348
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-04-06T21:18:57
8 Spectrometer Frequency	150.79



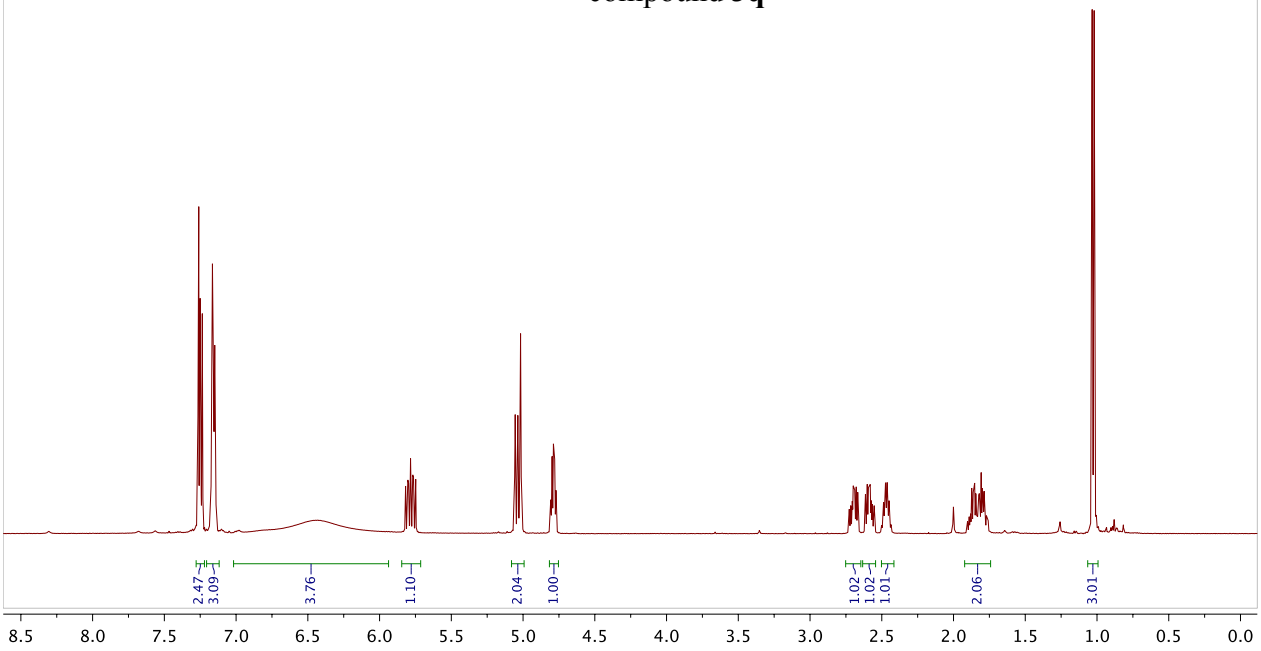
^{13}C NMR spectra of compound **3p**



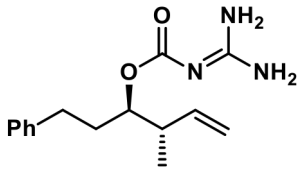
Parameter	Value
1 Title	ky-4-153-b
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-09-30T10:12:03
8 Spectrometer Frequency	499.86



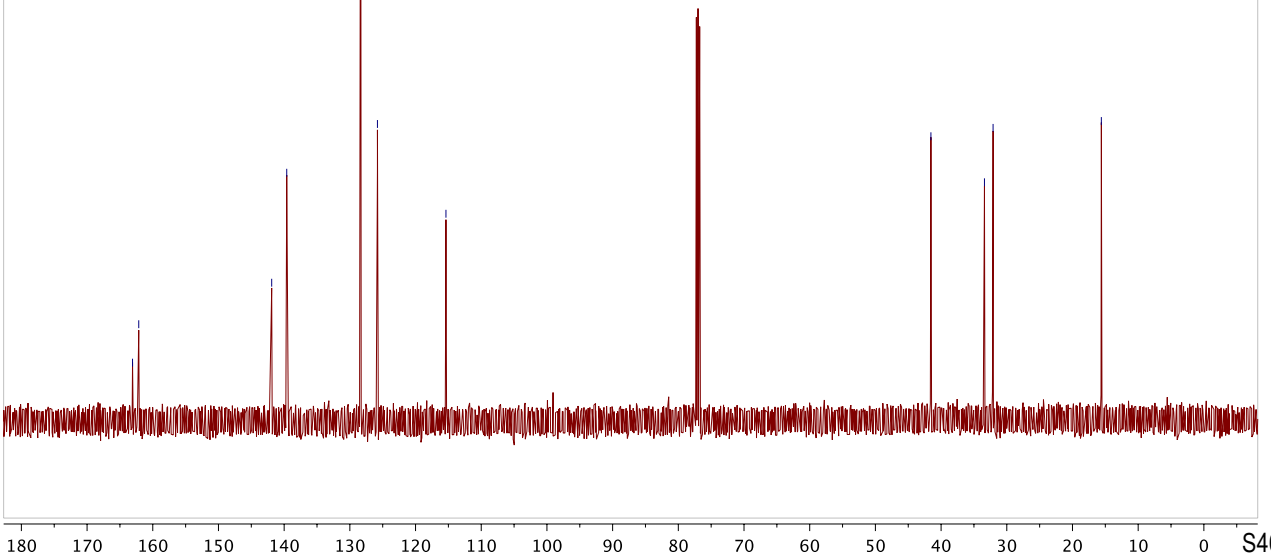
^{1}H NMR spectra of compound **3q**



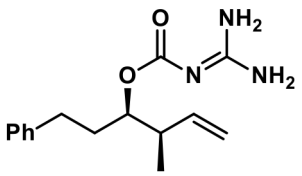
Parameter	Value
1 Title	ky-4-153-b-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	100
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-09-30T10:13:48
8 Spectrometer Frequency	125.70



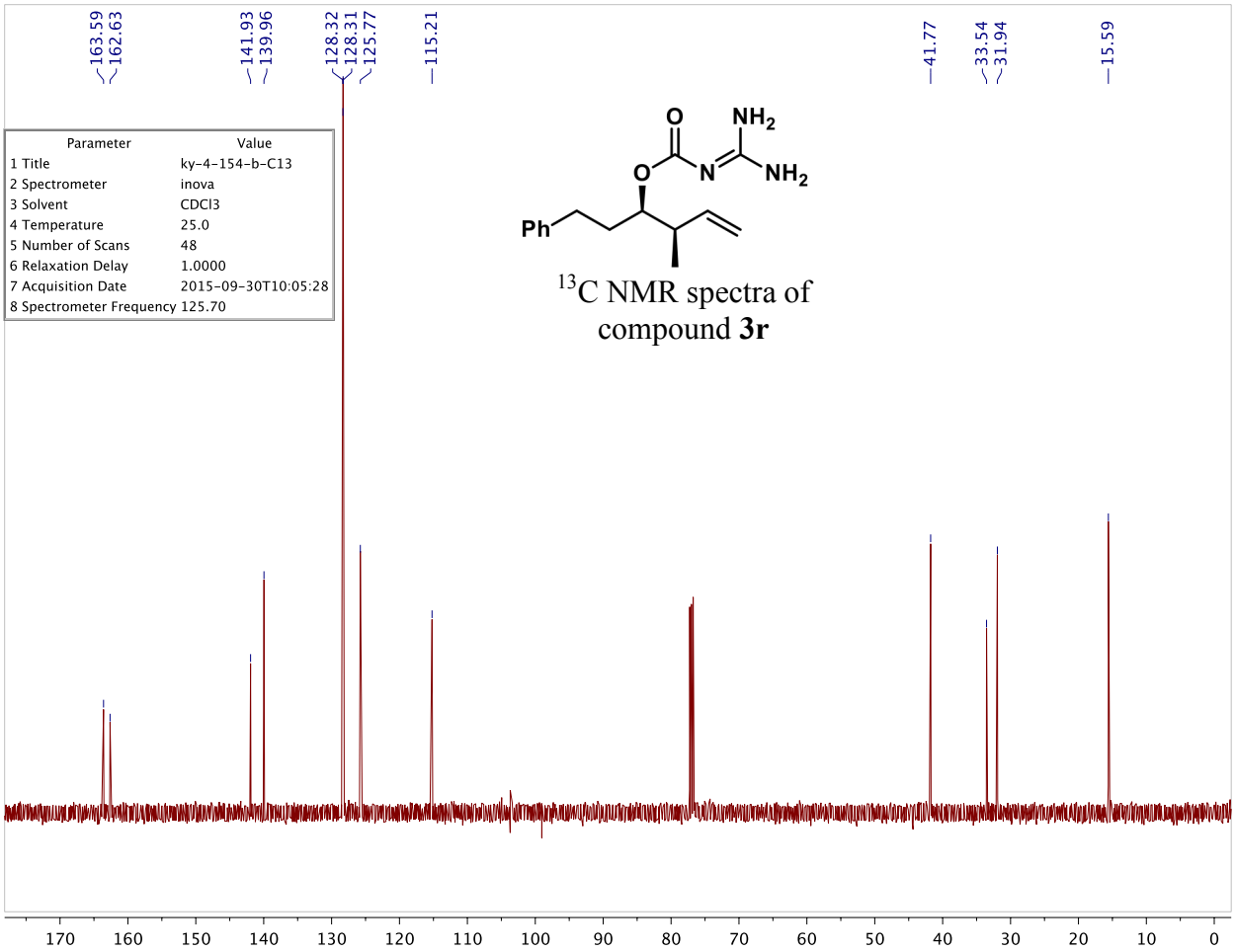
^{13}C NMR spectra of compound **3q**



Parameter	Value
1 Title	ky-4-154-bx
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-10-07T16:13:19
8 Spectrometer Frequency	499.86



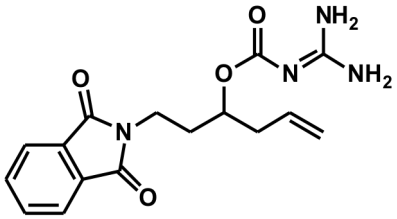
^{1}H NMR spectra of compound **3r**



Parameter	Value
1 Title	ky-4-154-b-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	48
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-09-30T10:05:28
8 Spectrometer Frequency	125.70

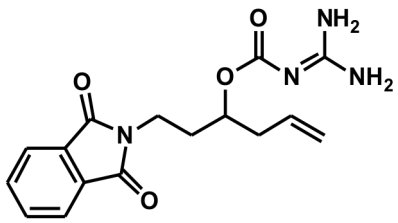
^{13}C NMR spectra of compound **3r**

Parameter	Value
1 Title	jlc-1-066proton1
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-28T12:48:08
8 Spectrometer Frequency	499.86

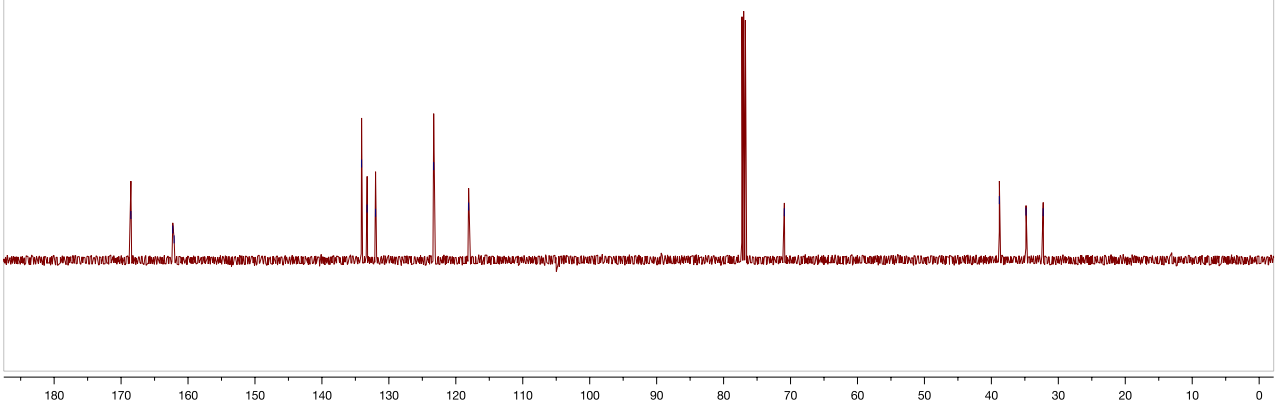


^{1}H NMR spectra of compound **3s**

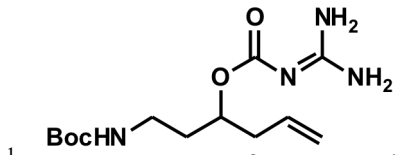
Parameter	Value
1 Title	jlc-1-066carbon
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	180
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-28T12:51:50
8 Spectrometer Frequency	125.70



^{13}C NMR spectra of compound **3s**

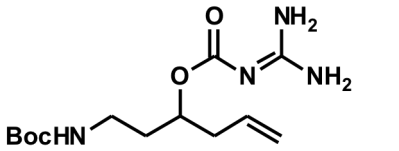


Parameter	Value
1 Title	jlc-1-068proton
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-21T12:13:13
8 Spectrometer Frequency	499.86

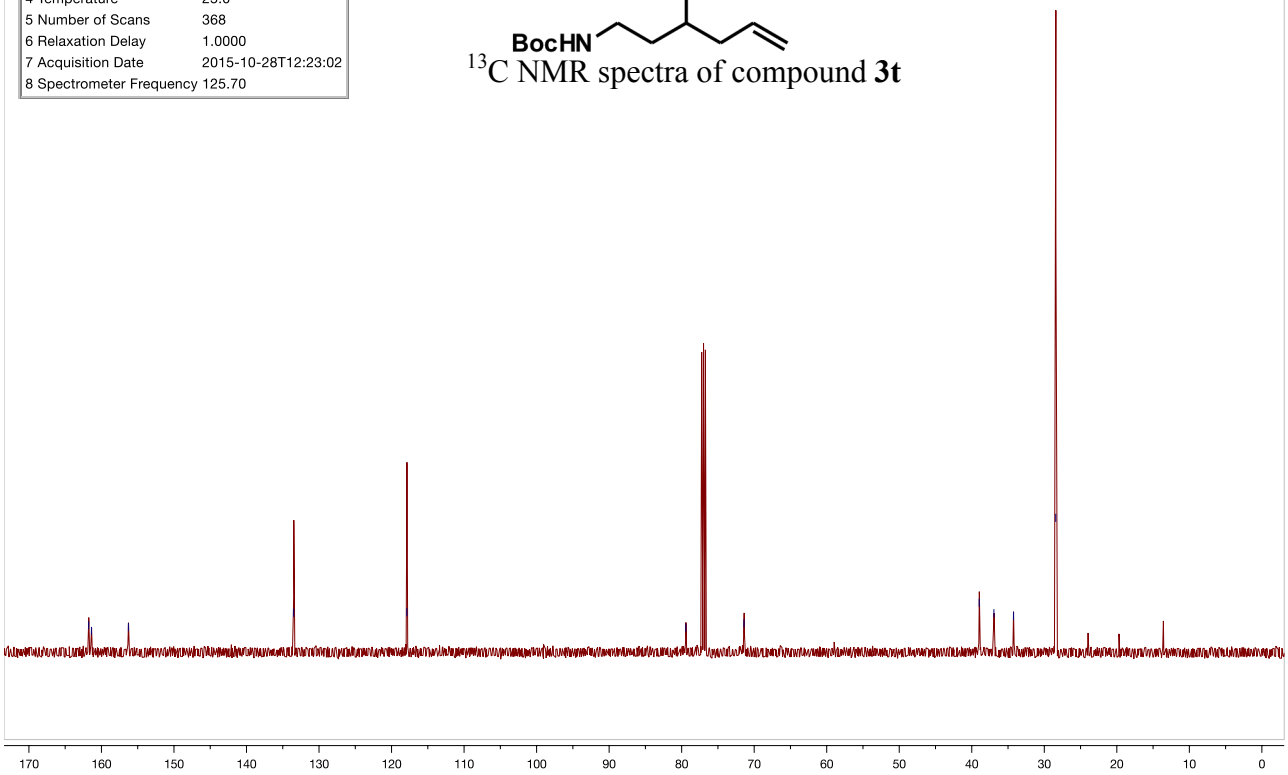


^{1}H NMR spectra of compound **3t**

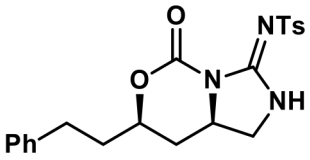
Parameter	Value
1 Title	jlc-1-068carbon
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	368
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-28T12:23:02
8 Spectrometer Frequency	125.70



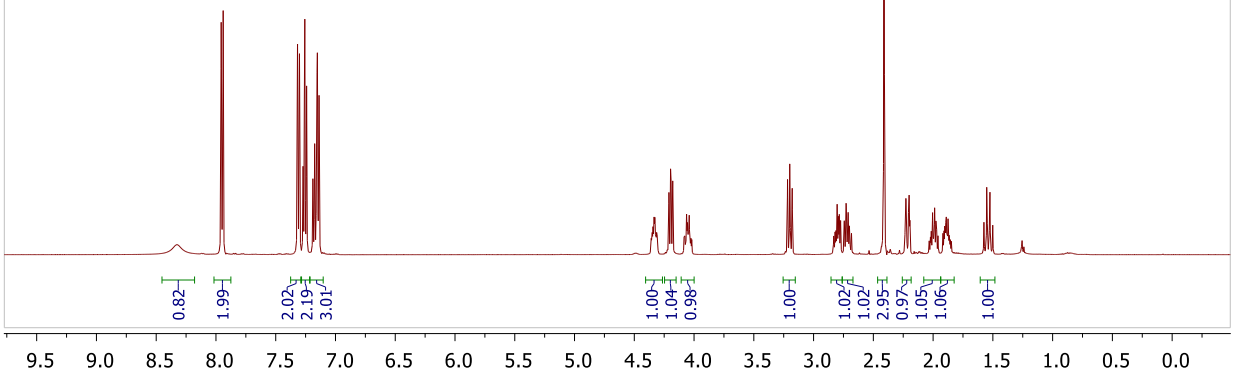
^{13}C NMR spectra of compound **3t**

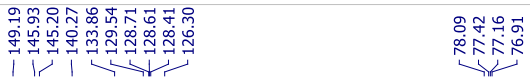


Parameter	Value
1 Title	AKM-04-185a.1
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-28T12:11:07
8 Spectrometer Frequency	499.86

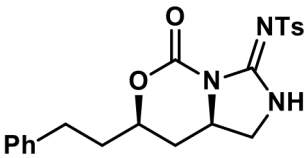


^{1}H NMR spectra of compound **5a**

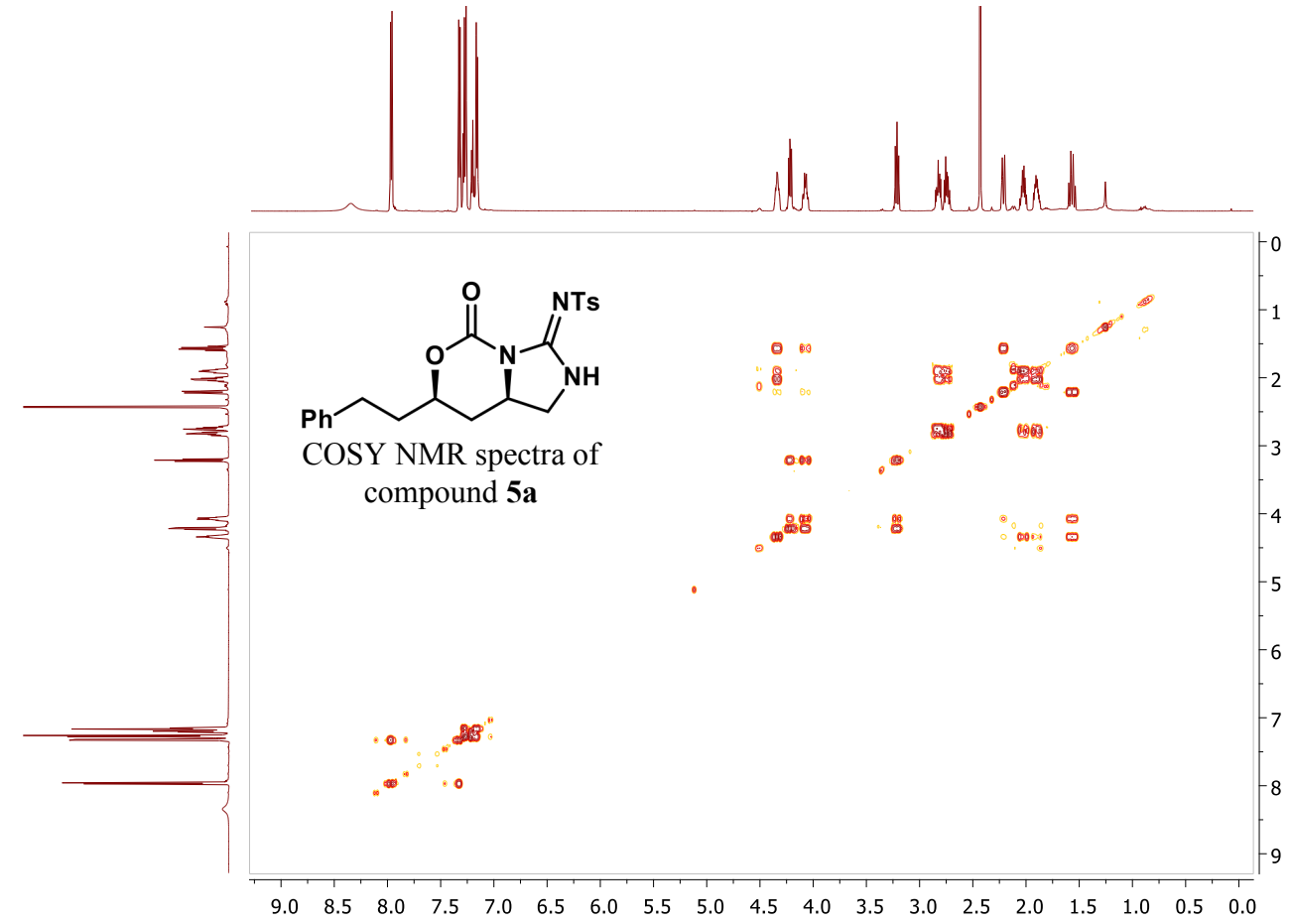




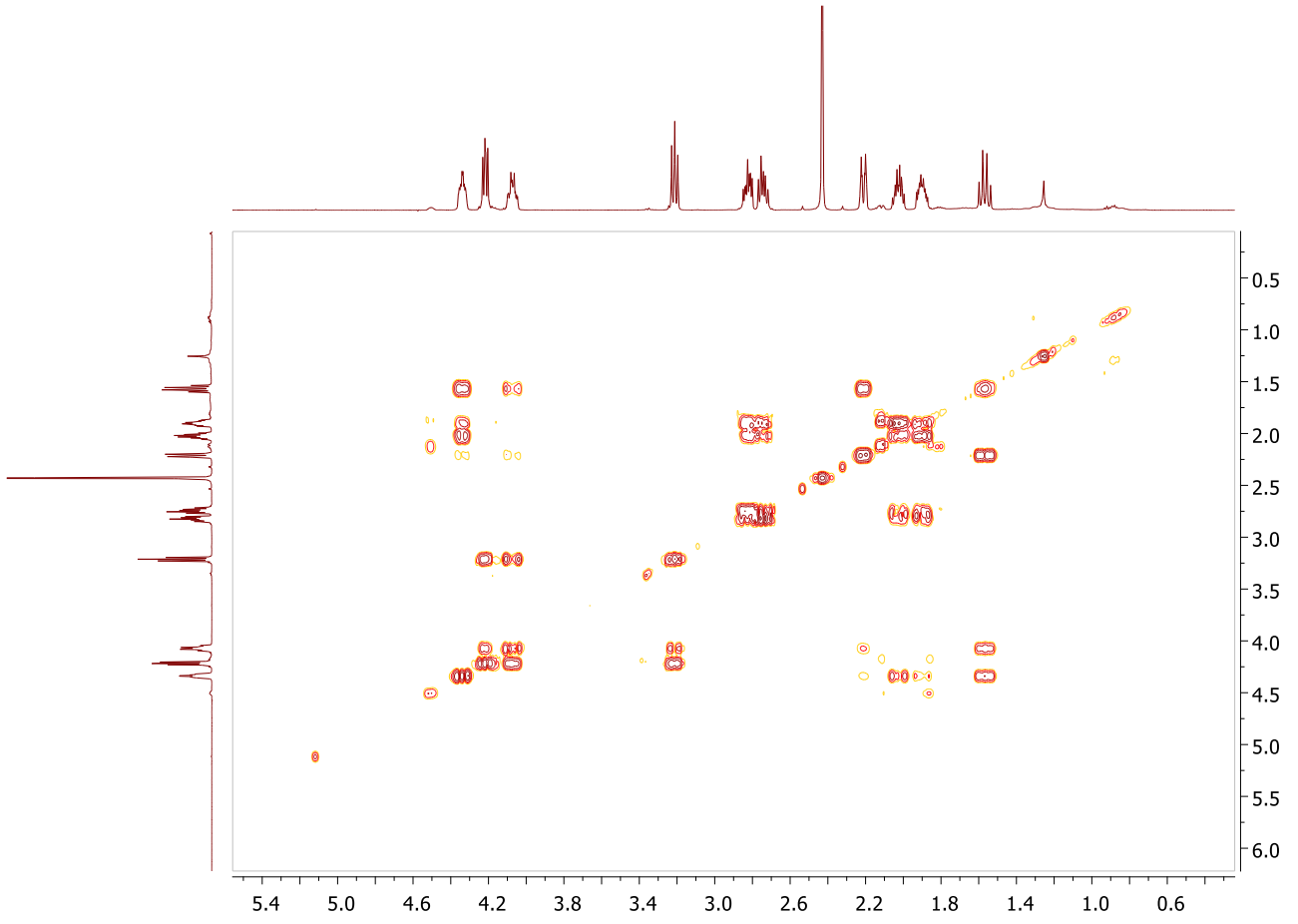
Parameter	Value
1 Title	AKM-04-185a.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	68
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-28T12:13:43
8 Spectrometer Frequency	125.70

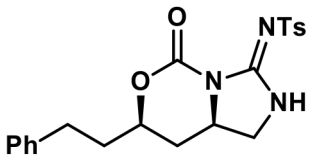


^{13}C NMR spectra of compound **5a**

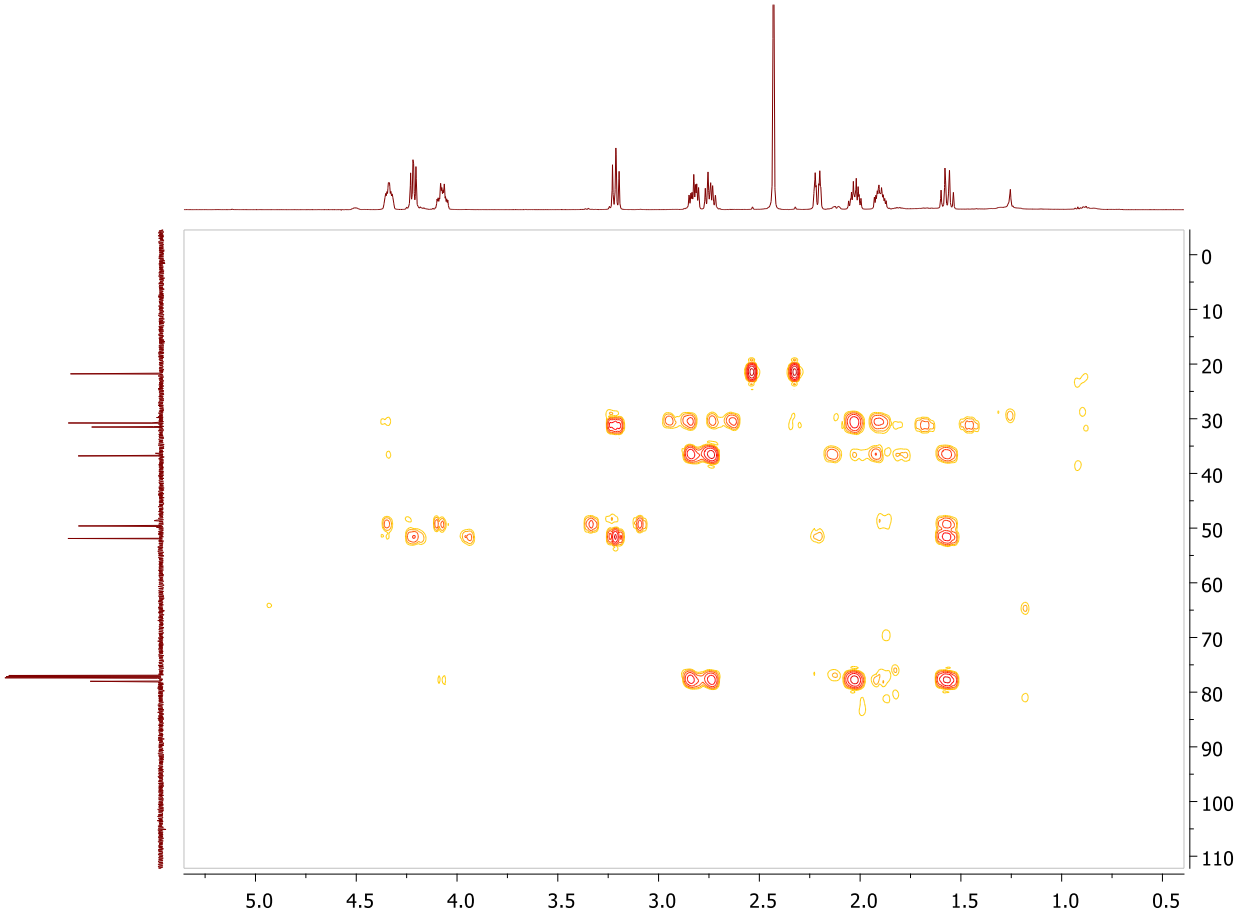


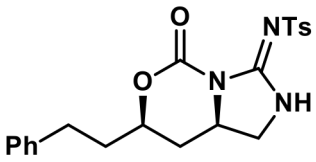
COSY NMR spectra of compound **5a**





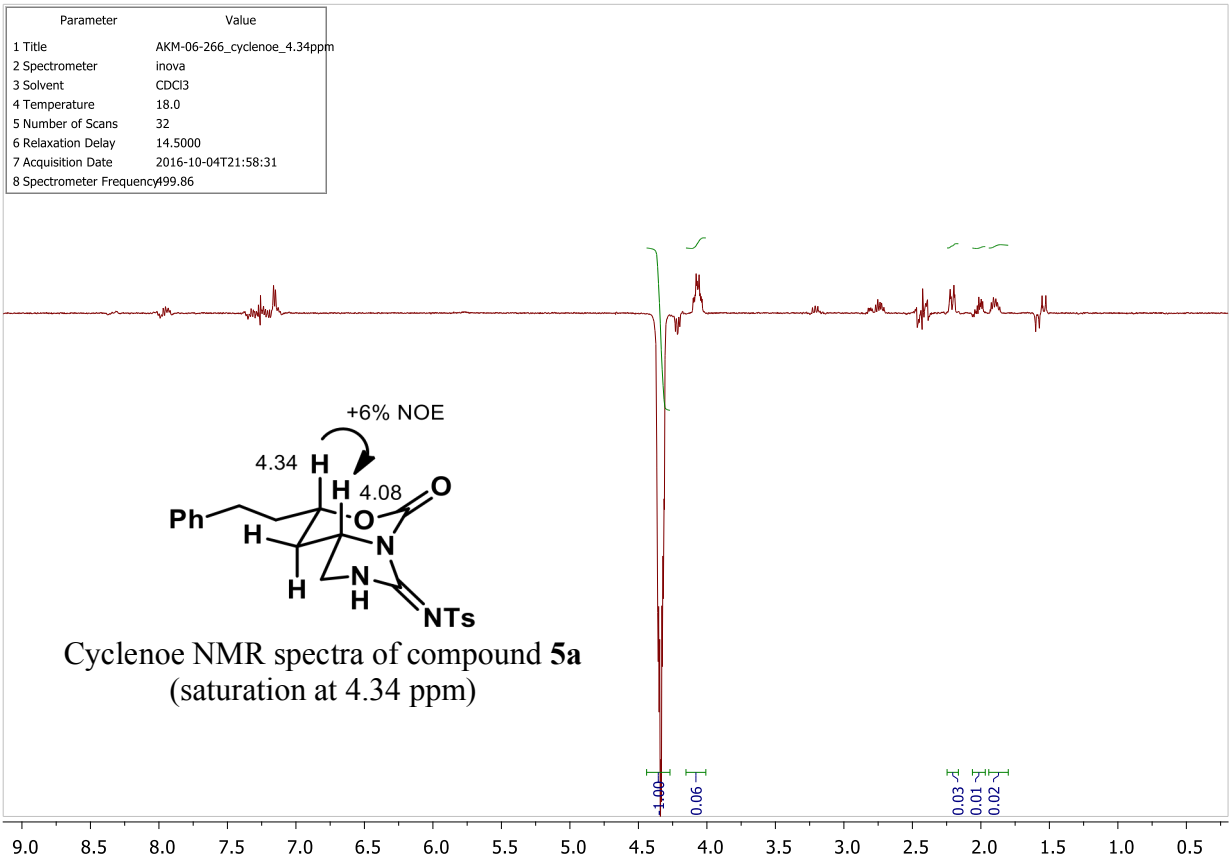
HMBC NMR spectra of compound **5a**





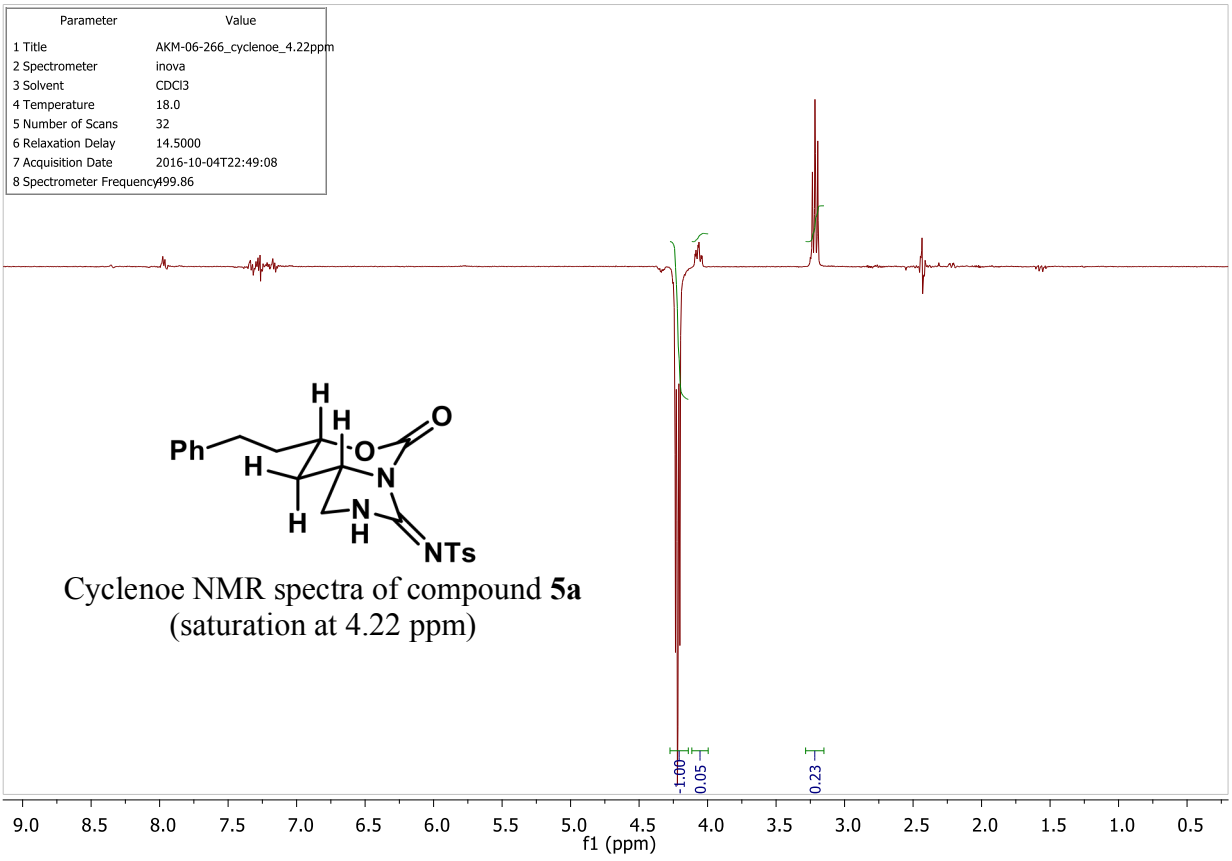
HSQC NMR spectra of compound **5a**

Parameter	Value
1 Title	AKM-06-266_cyclenoe_4.34ppm
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	18.0
5 Number of Scans	32
6 Relaxation Delay	14.5000
7 Acquisition Date	2016-10-04T21:58:31
8 Spectrometer Frequency	499.86

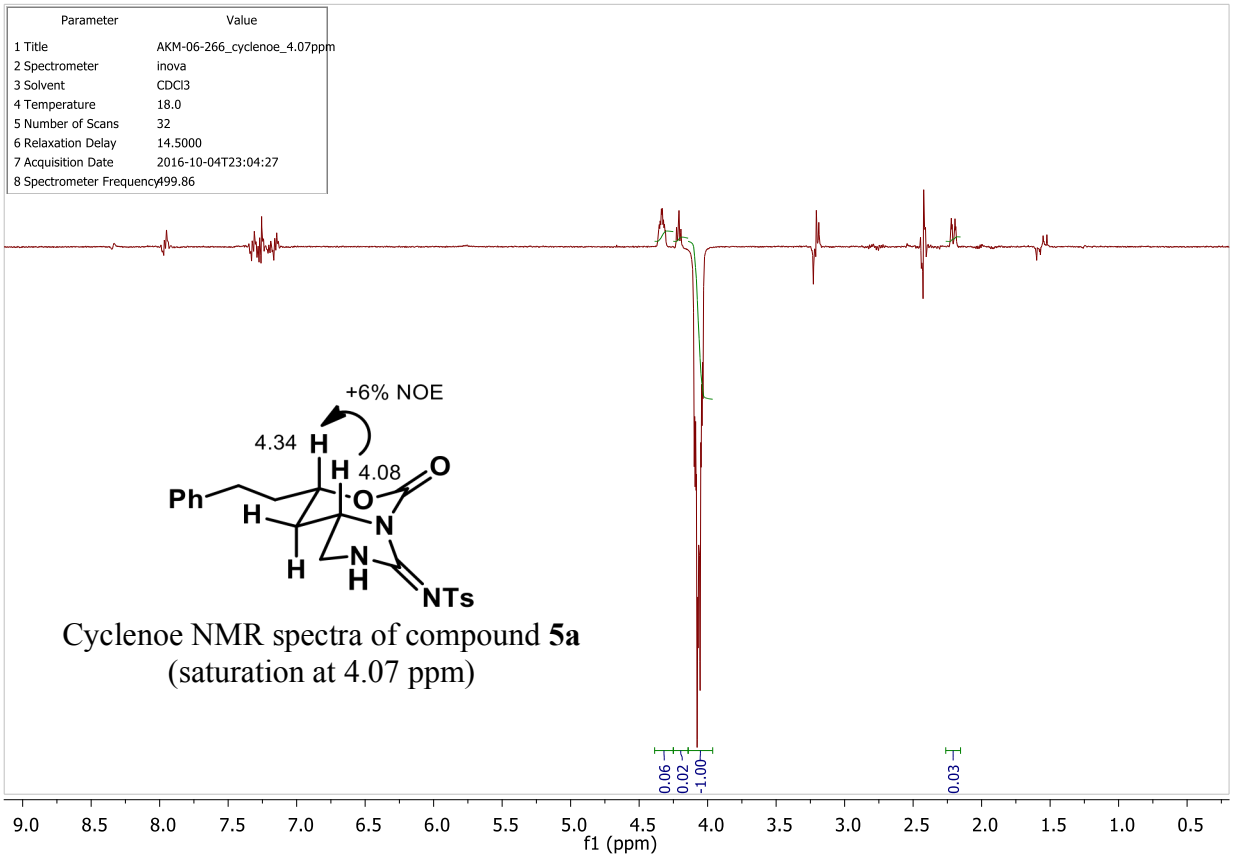


Cyclenoe NMR spectra of compound **5a**
(saturation at 4.34 ppm)

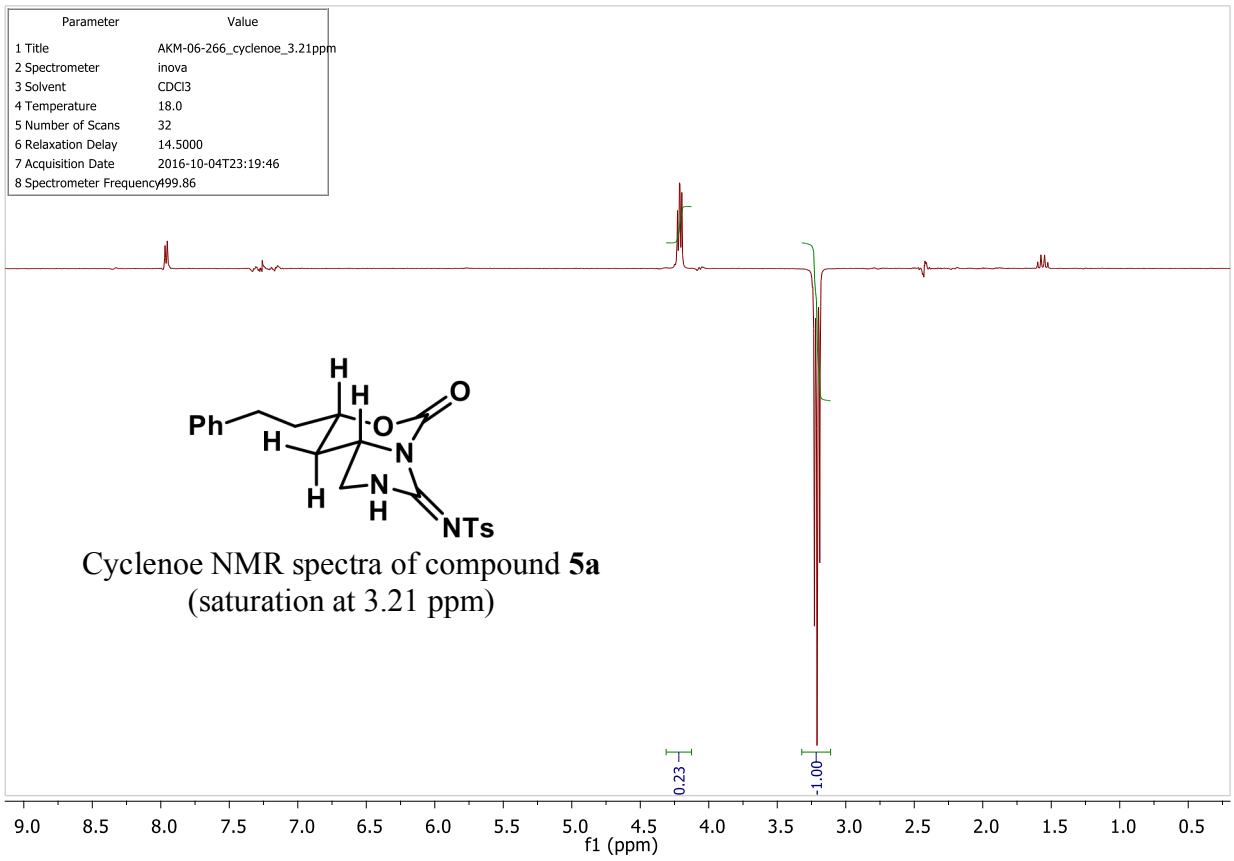
Parameter	Value
1 Title	AKM-06-266_cyclenoe_4.22ppm
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	18.0
5 Number of Scans	32
6 Relaxation Delay	14.5000
7 Acquisition Date	2016-10-04T22:49:08
8 Spectrometer Frequency	499.86



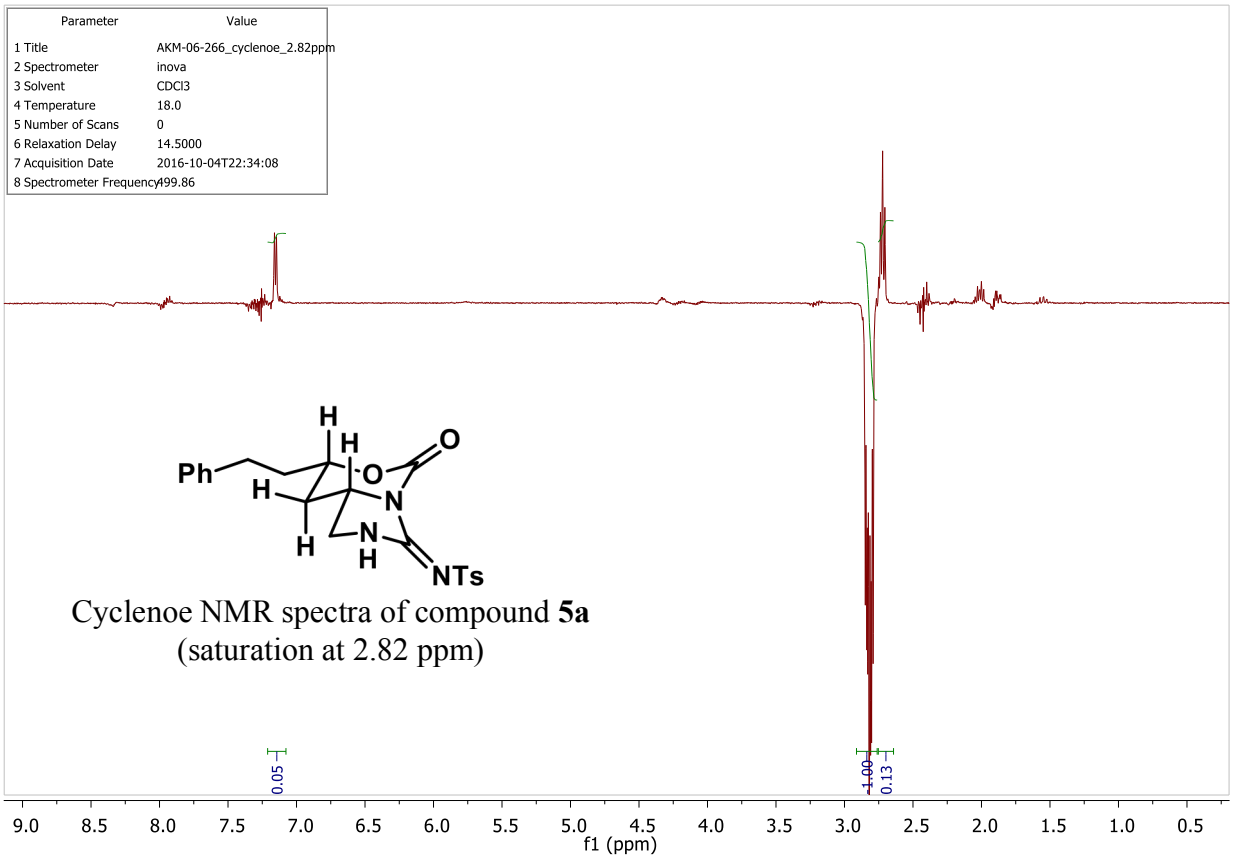
Cyclenoe NMR spectra of compound **5a**
(saturation at 4.22 ppm)



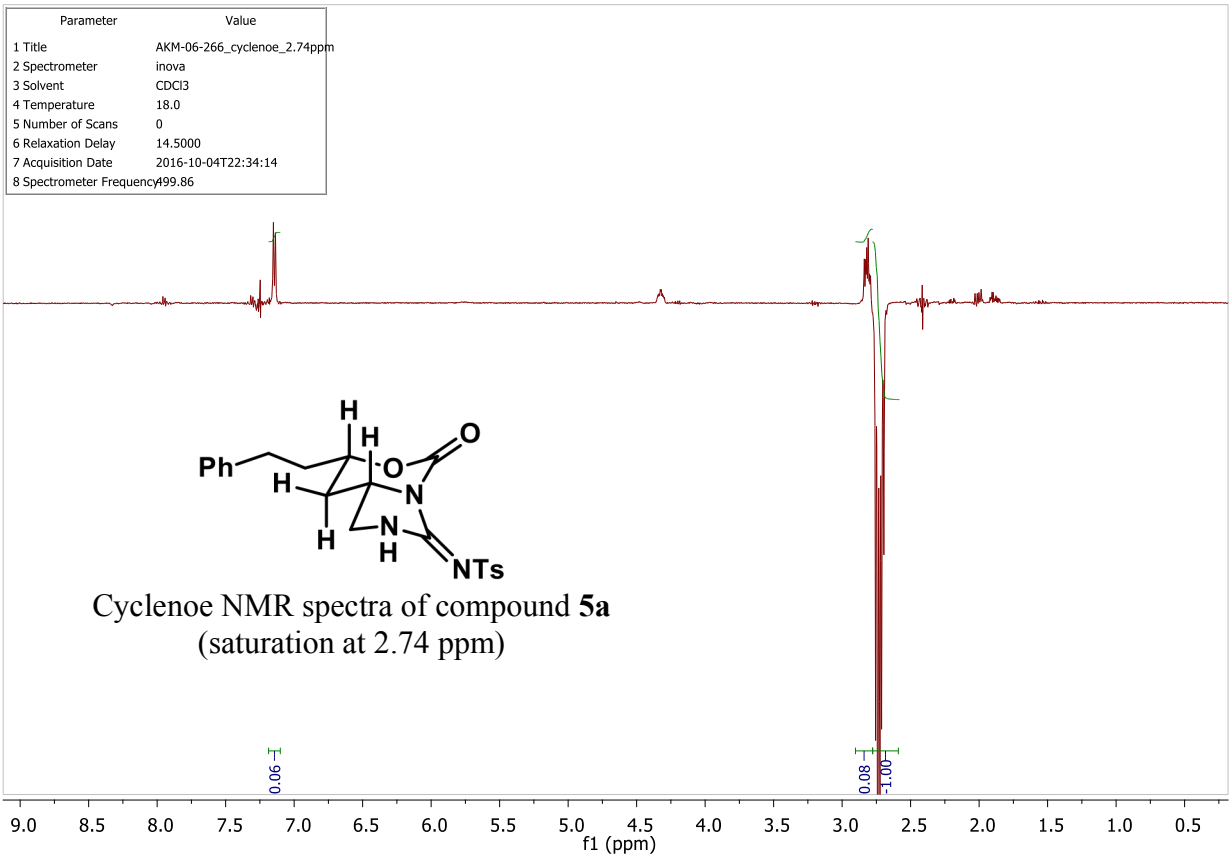
Cyclenoe NMR spectra of compound **5a**
(saturation at 4.07 ppm)



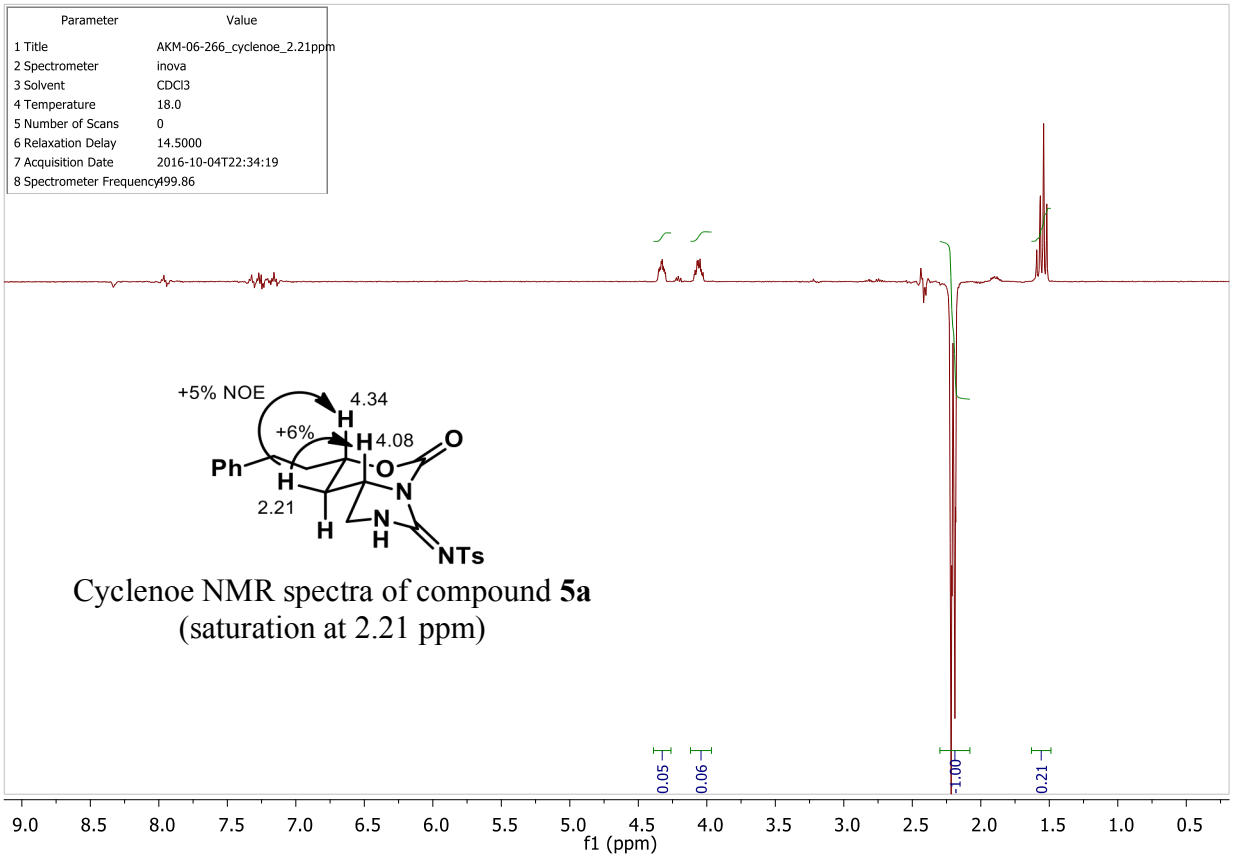
Cyclenoe NMR spectra of compound **5a**
(saturation at 3.21 ppm)



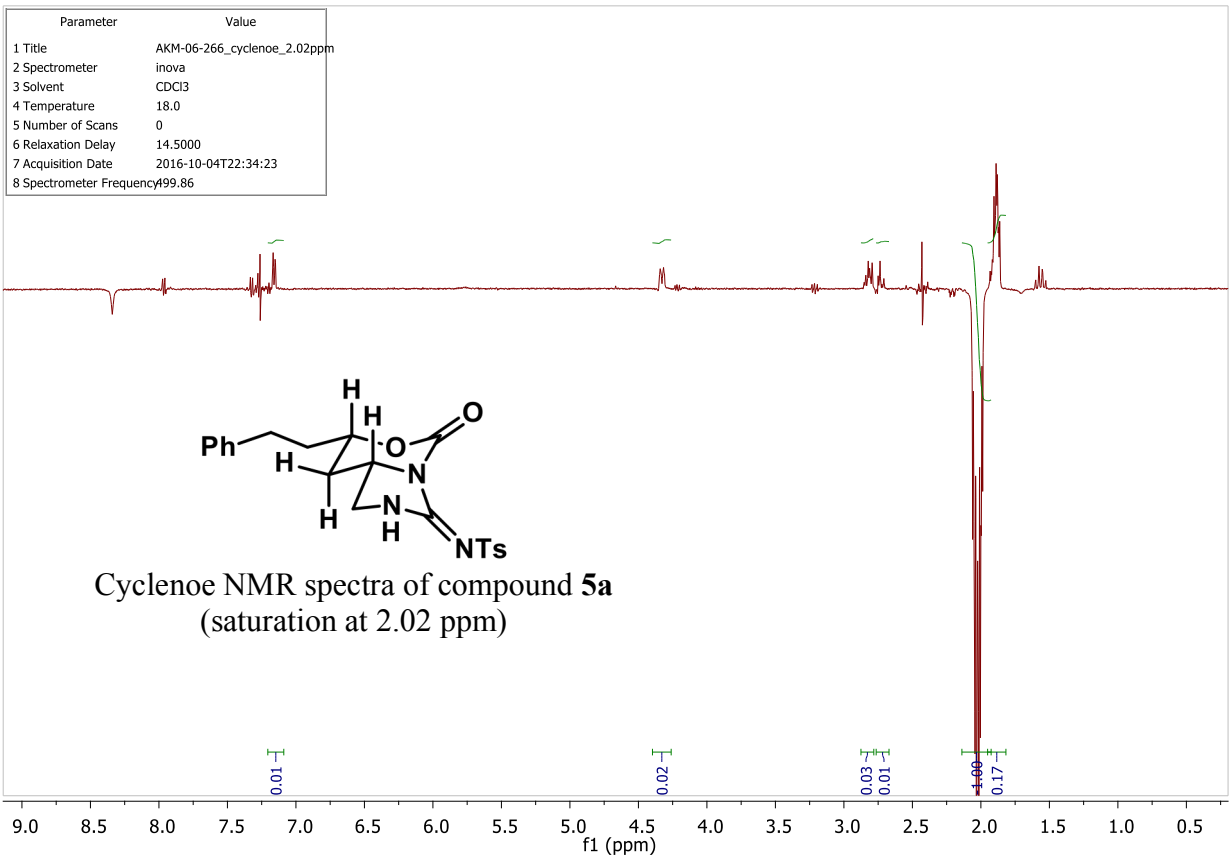
Cyclenoe NMR spectra of compound **5a**
(saturation at 2.82 ppm)



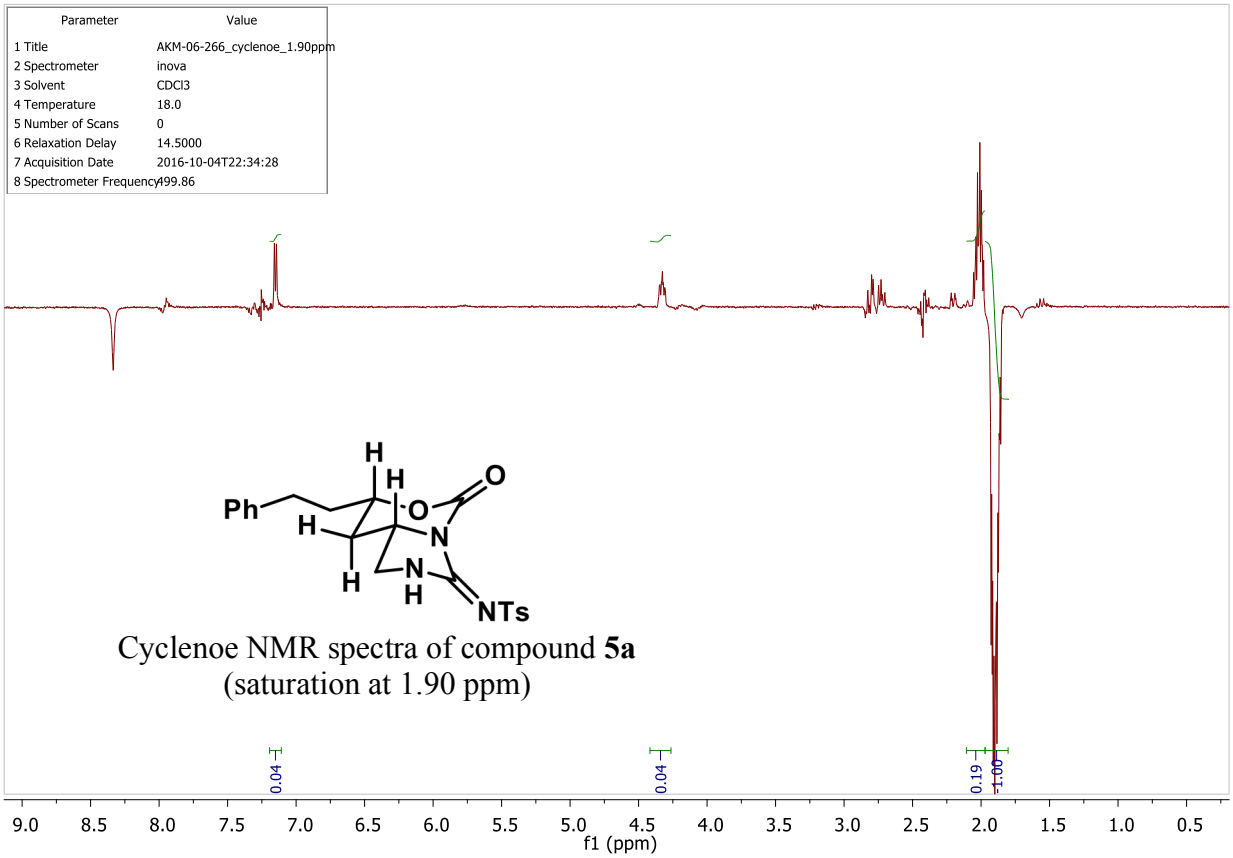
Cyclenoe NMR spectra of compound **5a**
(saturation at 2.74 ppm)



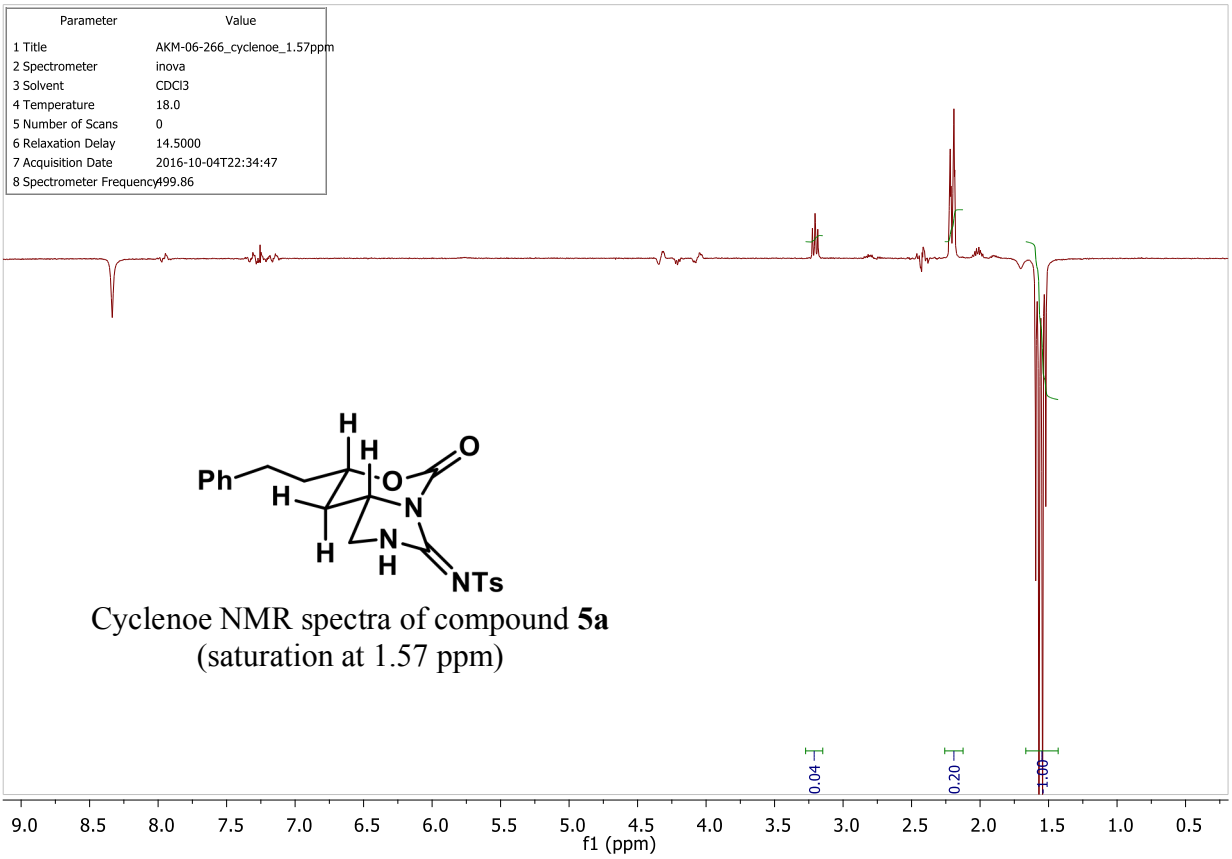
Cyclenoe NMR spectra of compound **5a**
(saturation at 2.21 ppm)



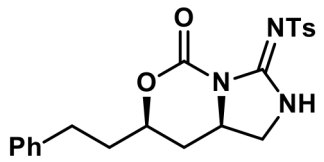
Cyclenoe NMR spectra of compound **5a**
(saturation at 2.02 ppm)



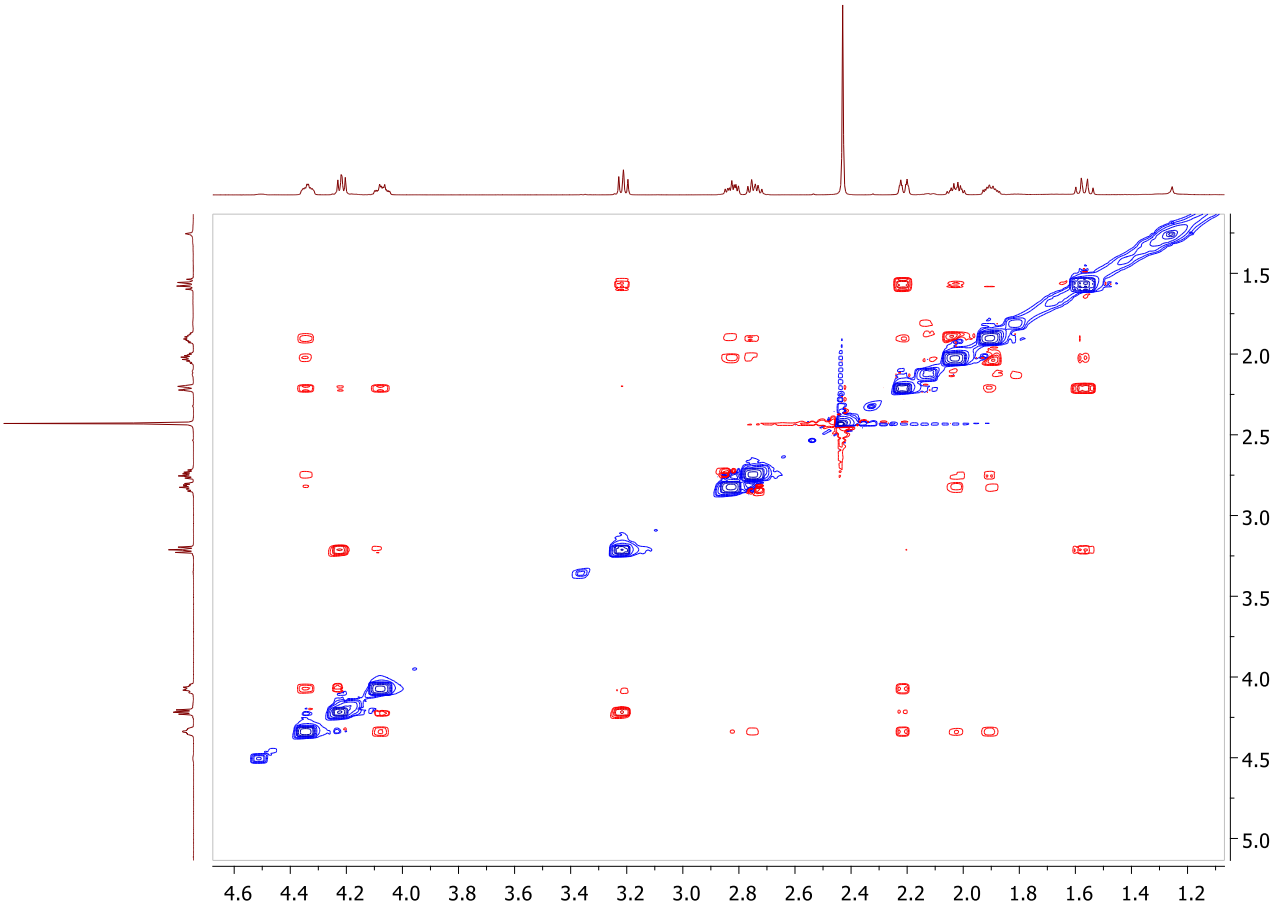
Cyclenoe NMR spectra of compound **5a**
(saturation at 1.90 ppm)

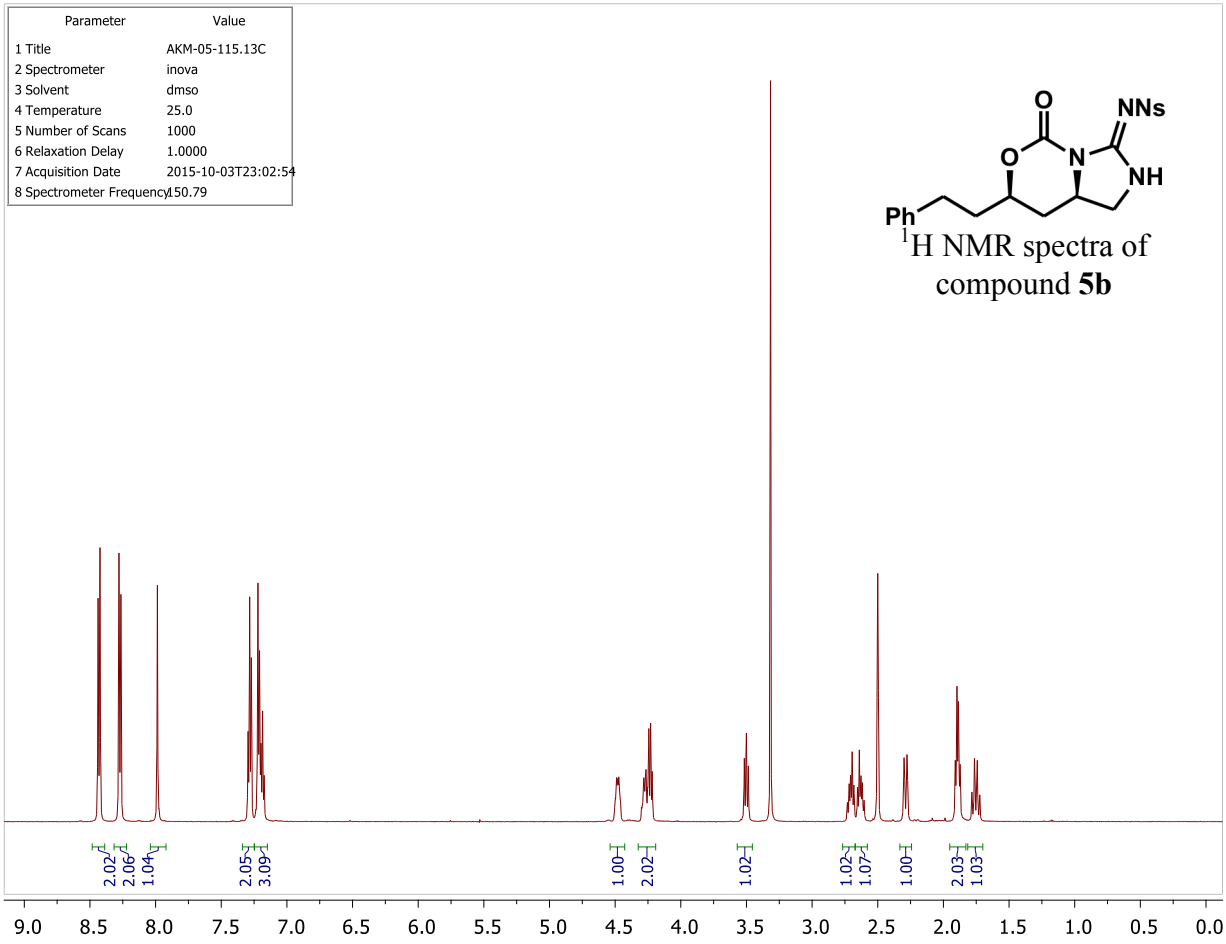


Cyclenoe NMR spectra of compound **5a**
(saturation at 1.57 ppm)

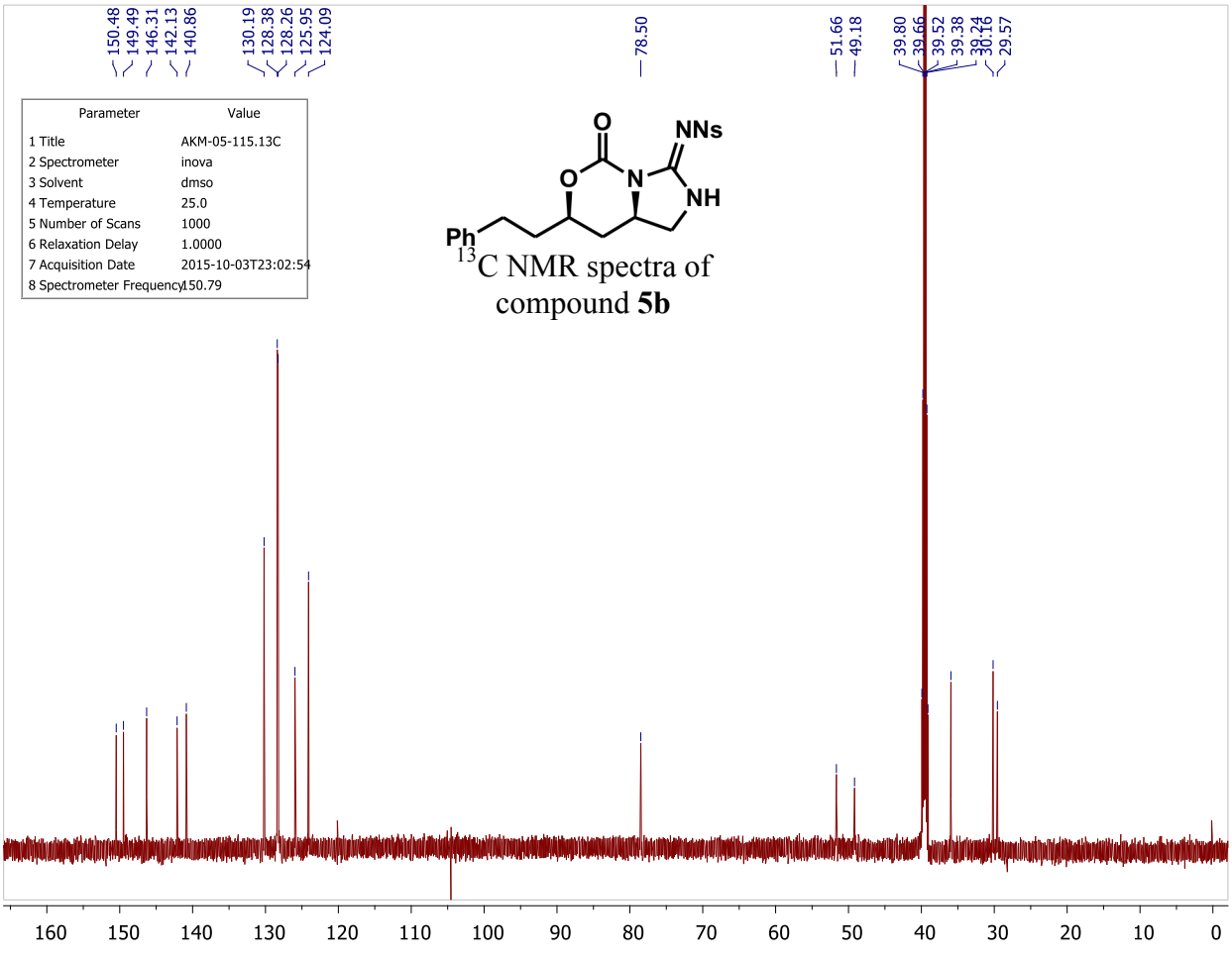


NOESY NMR spectra of compound **5a**



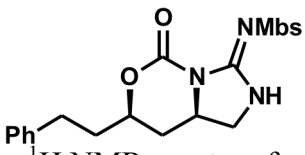


^{1}H NMR spectra of compound **5b**

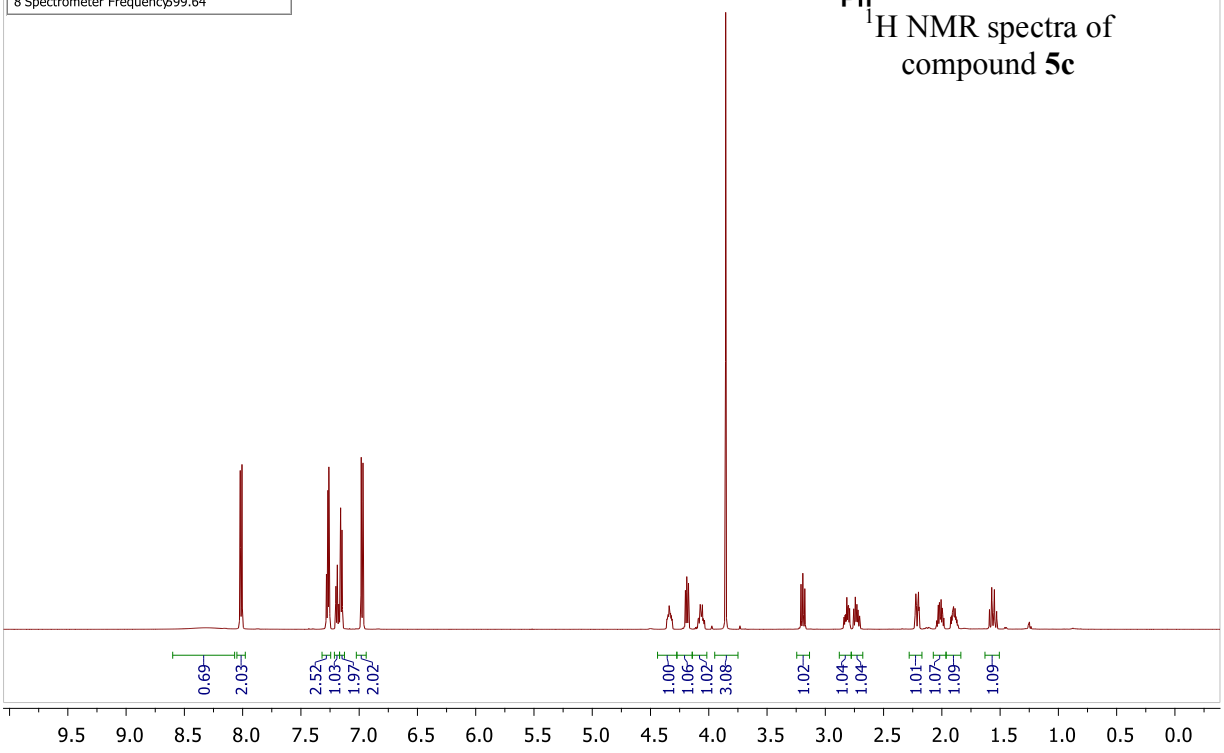


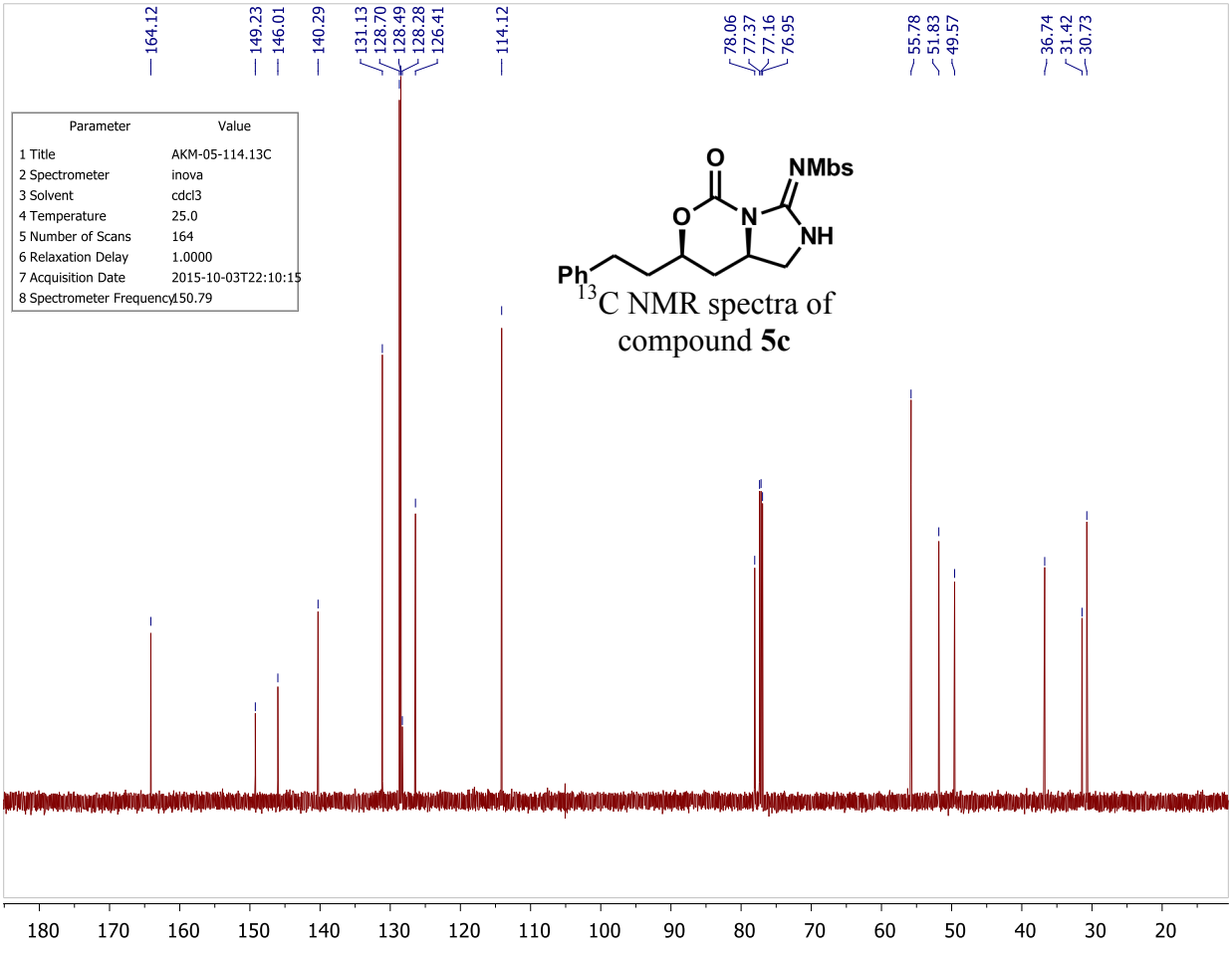
^{13}C NMR spectra of compound **5b**

Parameter	Value
1 Title	AKM-05-114
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	28
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-03T22:05:14
8 Spectrometer Frequency	599.64



^{1}H NMR spectra of compound **5c**

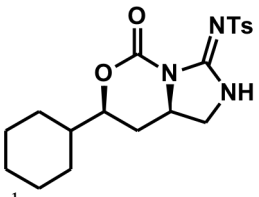




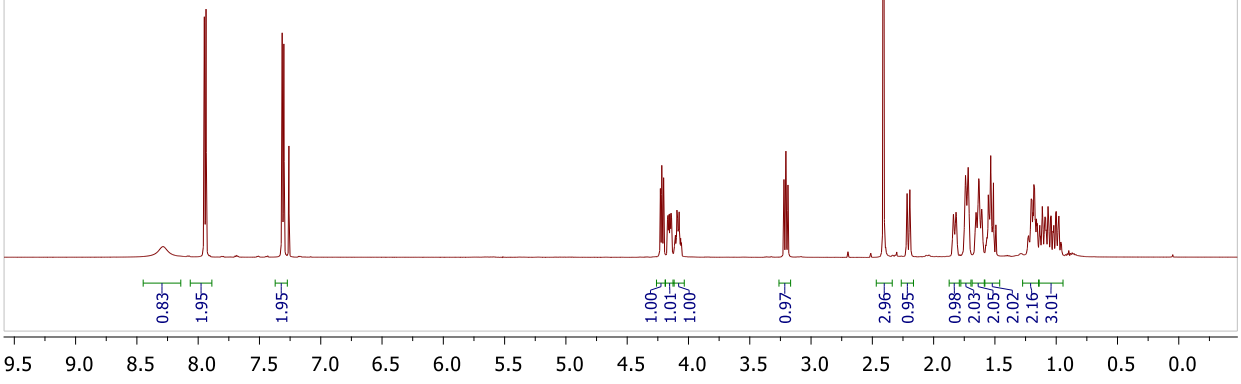
Parameter	Value
1 Title	AKM-05-114.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	164
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-03T22:10:15
8 Spectrometer Frequency	150.79

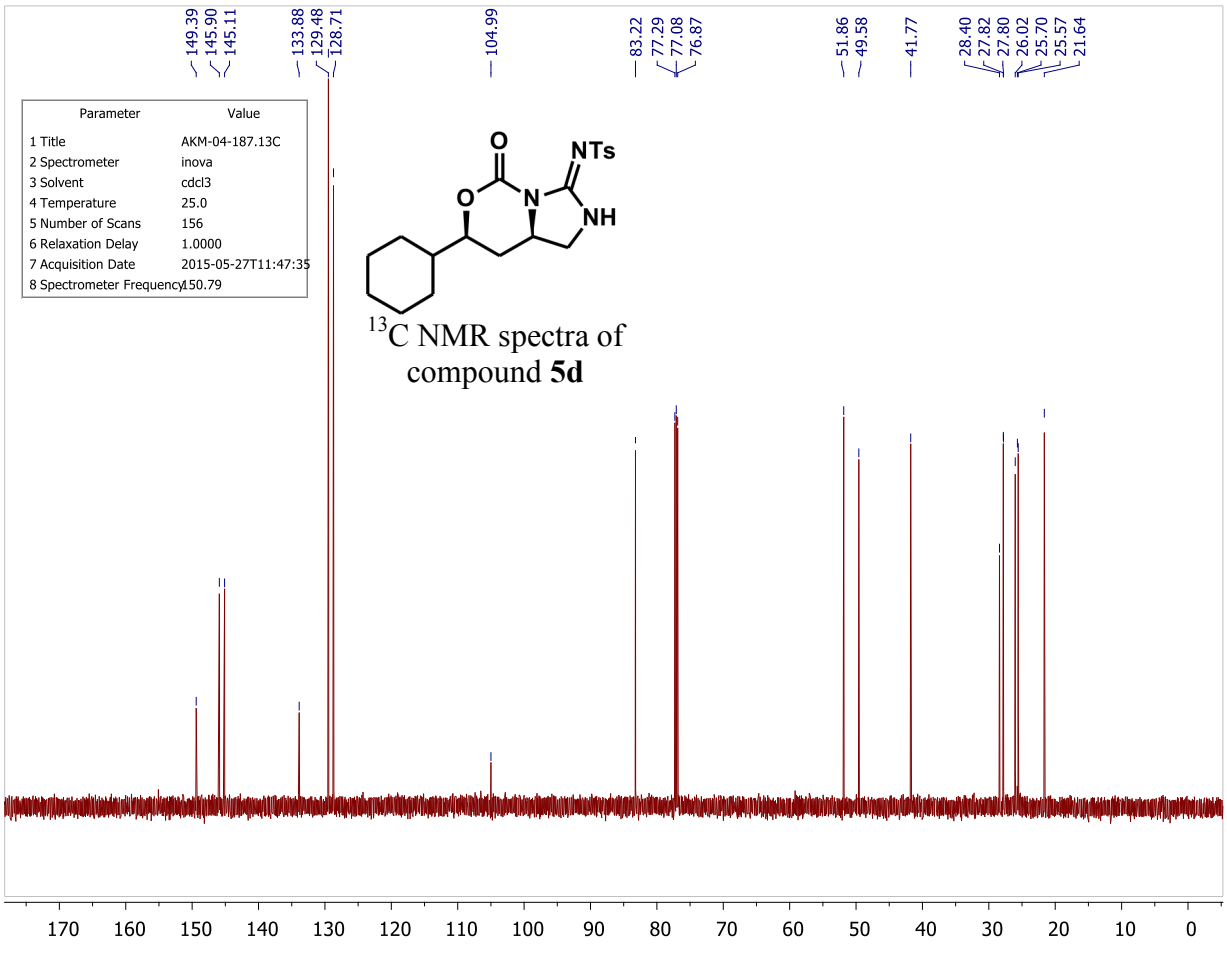
^{13}C NMR spectra of compound **5c**

Parameter	Value
1 Title	AKM-04-187
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-27T11:44:11
8 Spectrometer Frequency	599.64



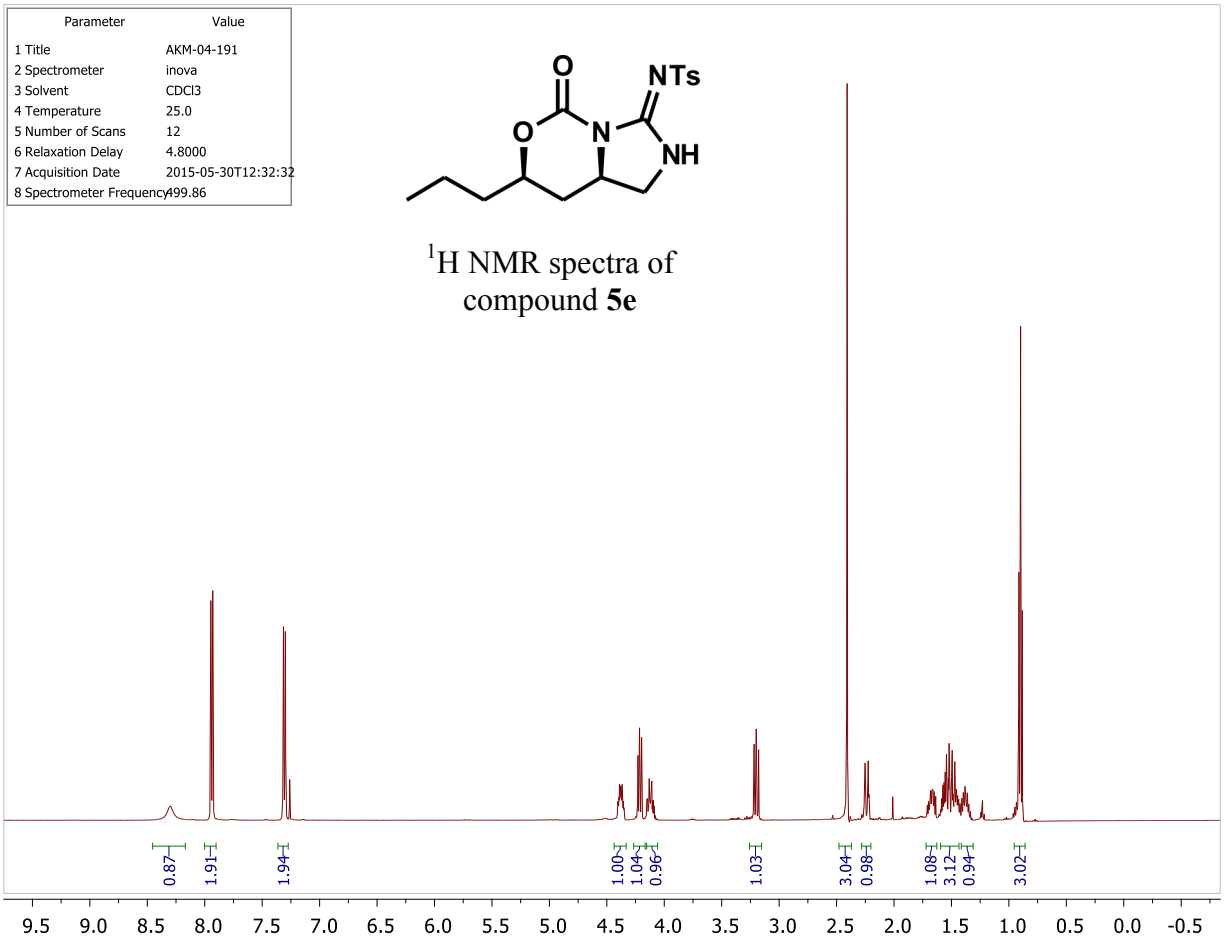
^{1}H NMR spectra of compound **5d**



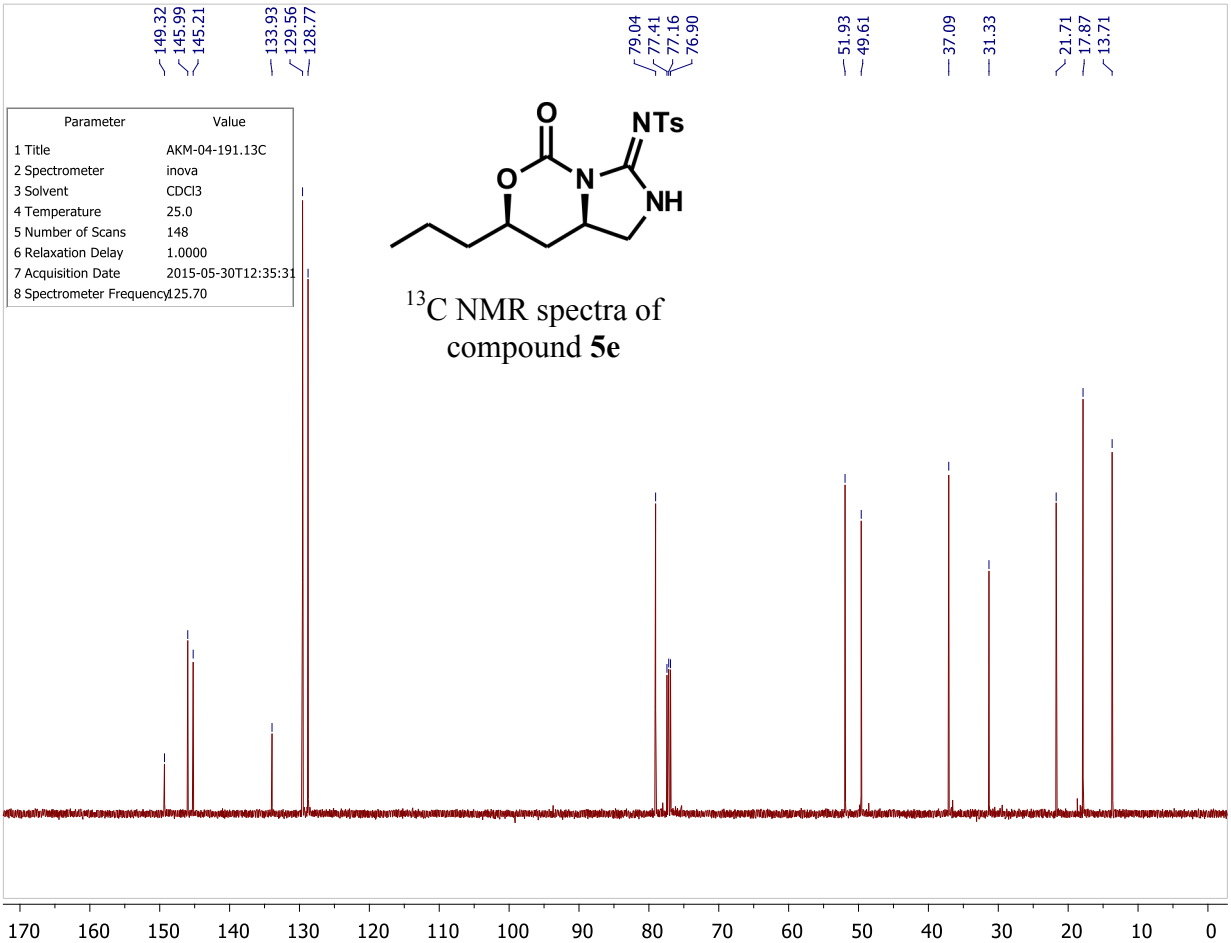


Parameter	Value
1 Title	AKM-04-187.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	156
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-27T11:47:35
8 Spectrometer Frequency	150.79

^{13}C NMR spectra of compound **5d**

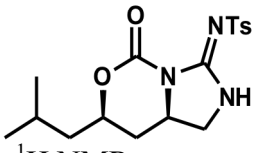


^{1}H NMR spectra of compound **5e**

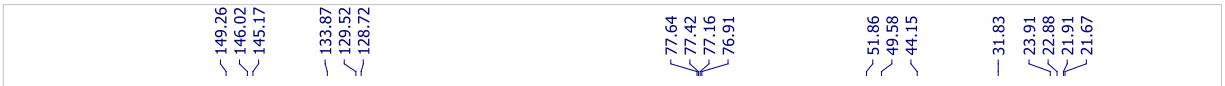


^{13}C NMR spectra of compound **5e**

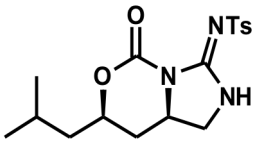
Parameter	Value
1 Title	AKM-04-192
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-29T11:34:53
8 Spectrometer Frequency	499.86



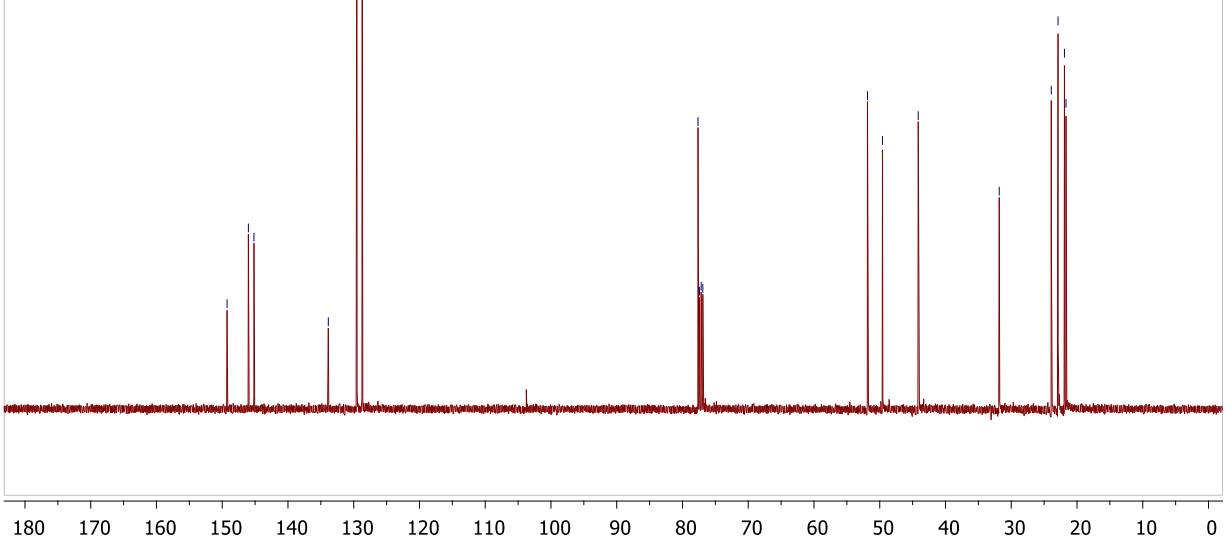
^{1}H NMR spectra of compound **5f**



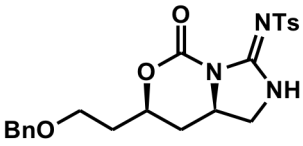
Parameter	Value
1 Title	AKM-04-192.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	80
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-29T11:38:05
8 Spectrometer Frequency	125.70



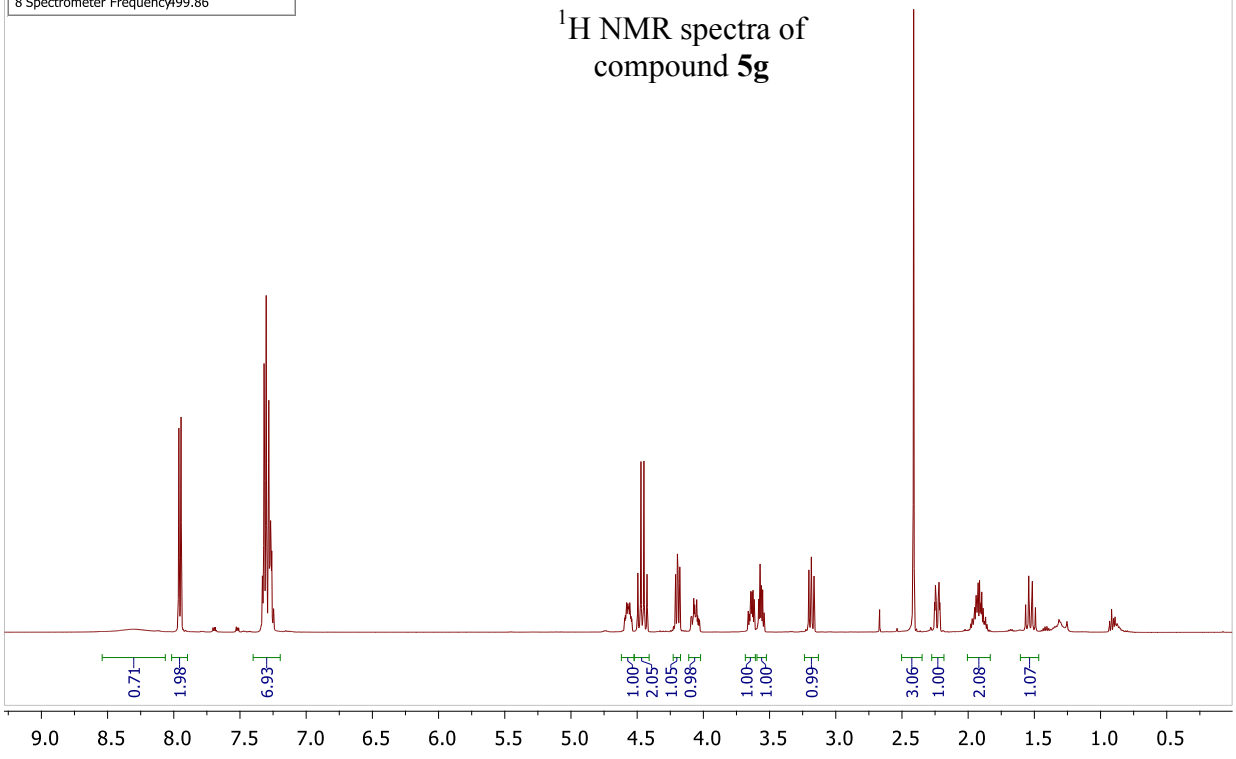
^{13}C NMR spectra of compound **5f**



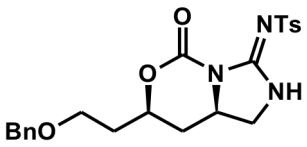
Parameter	Value
1 Title	AKM-04-189
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-28T12:03:24
8 Spectrometer Frequency	499.86



^{1}H NMR spectra of compound **5g**

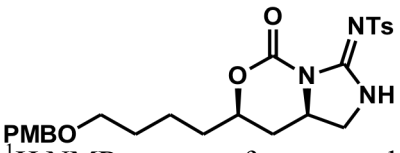


Parameter	Value
1 Title	AKM-04-189.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	60
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-28T12:06:30
8 Spectrometer Frequency	125.70

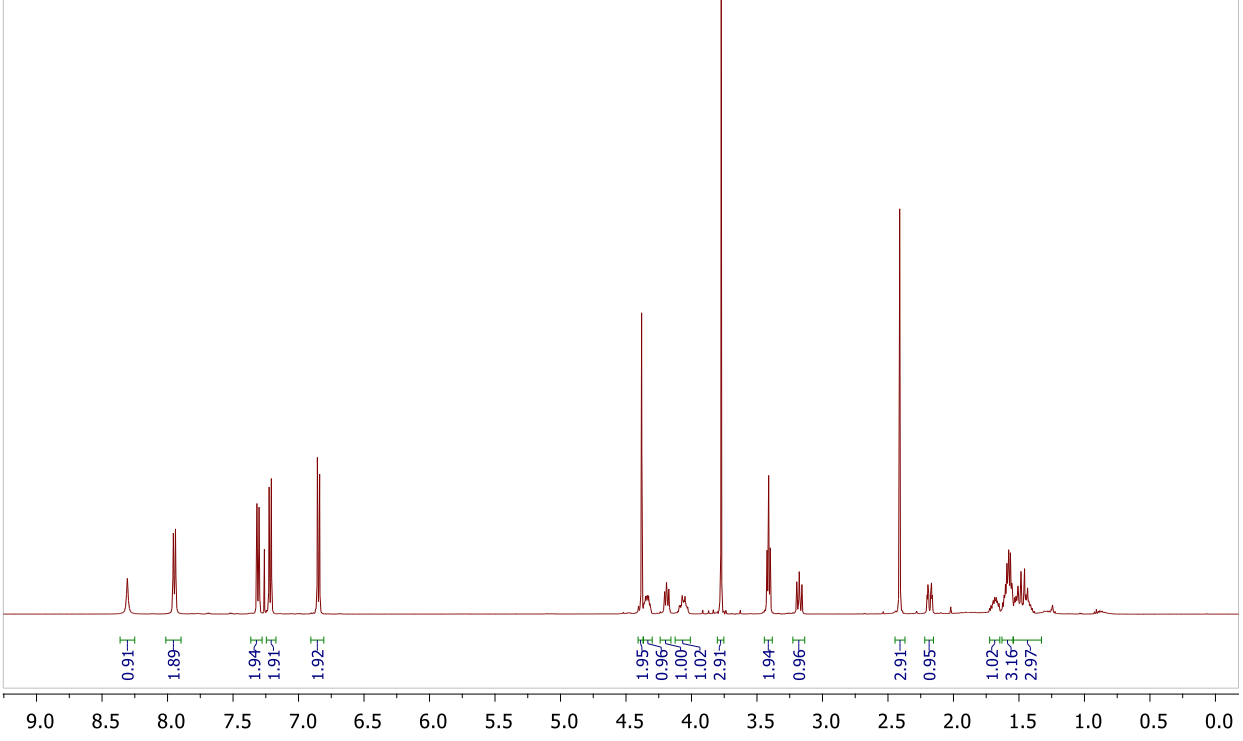


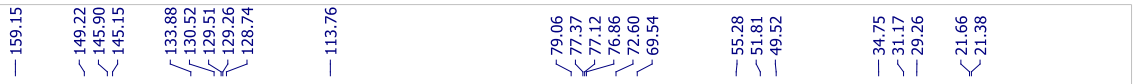
^{13}C NMR spectra of compound **5g**

Parameter	Value
1 Title	AKM-04-197
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-30T12:55:43
8 Spectrometer Frequency	499.86

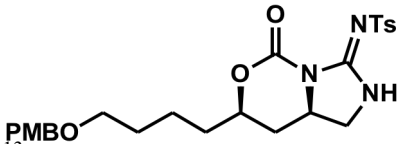


^{1}H NMR spectra of compound **5h**



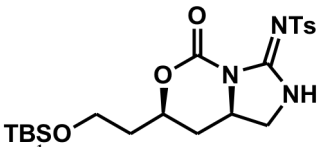


Parameter	Value
1 Title	AKM-04-197.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	164
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-30T12:58:58
8 Spectrometer Frequency	125.70



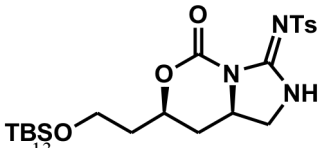
^{13}C NMR spectra of compound **5h**

Parameter	Value
1 Title	ky-4-166-a
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	100.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-10-09T09:58:53
8 Spectrometer Frequency	499.86



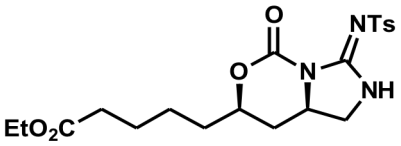
^{1}H NMR spectra of compound **5i**

Parameter	Value
1 Title	ky-4-166-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	100.0
5 Number of Scans	104
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-09T10:00:31
8 Spectrometer Frequency	125.70

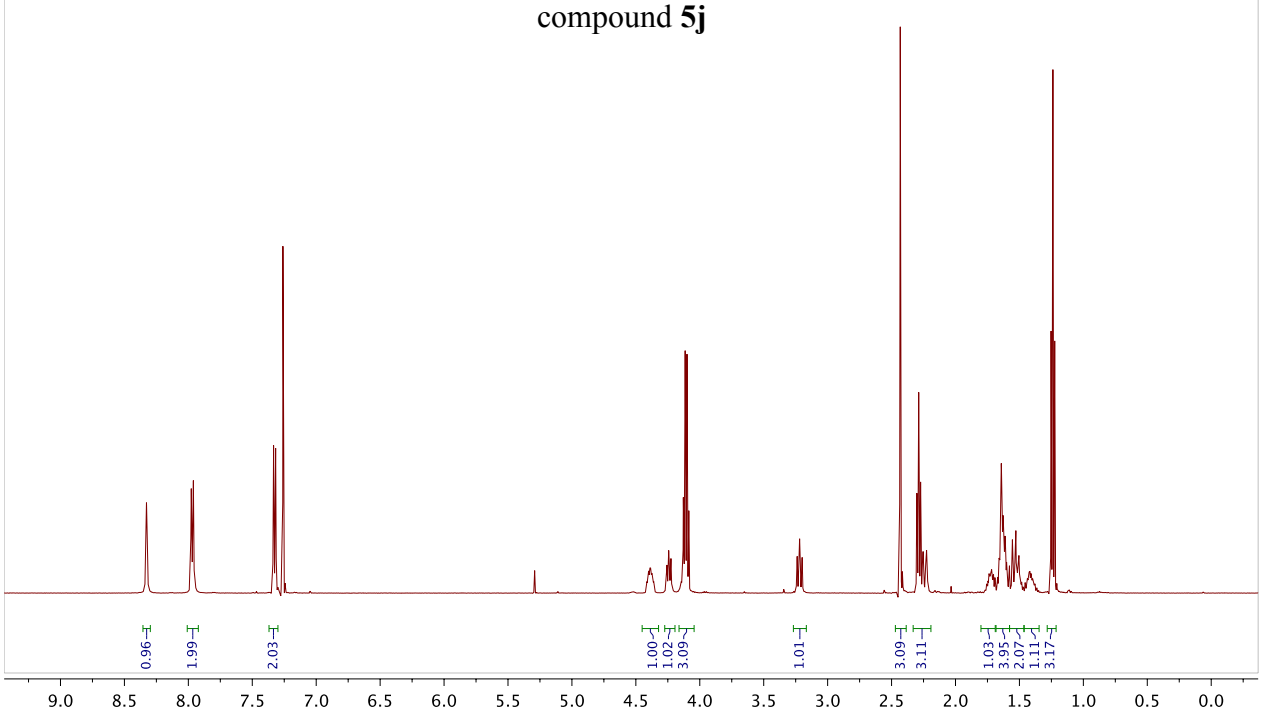


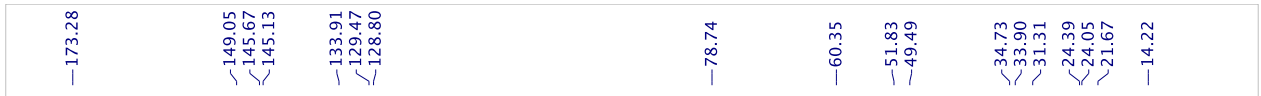
^{13}C NMR spectra of compound **5i**

Parameter	Value
1 Title	ky-4-164-a
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-10-07T16:27:49
8 Spectrometer Frequency	499.86

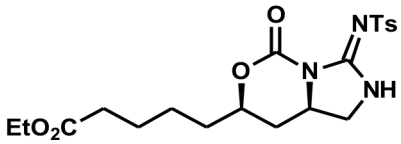


^{1}H NMR spectra of compound **5j**

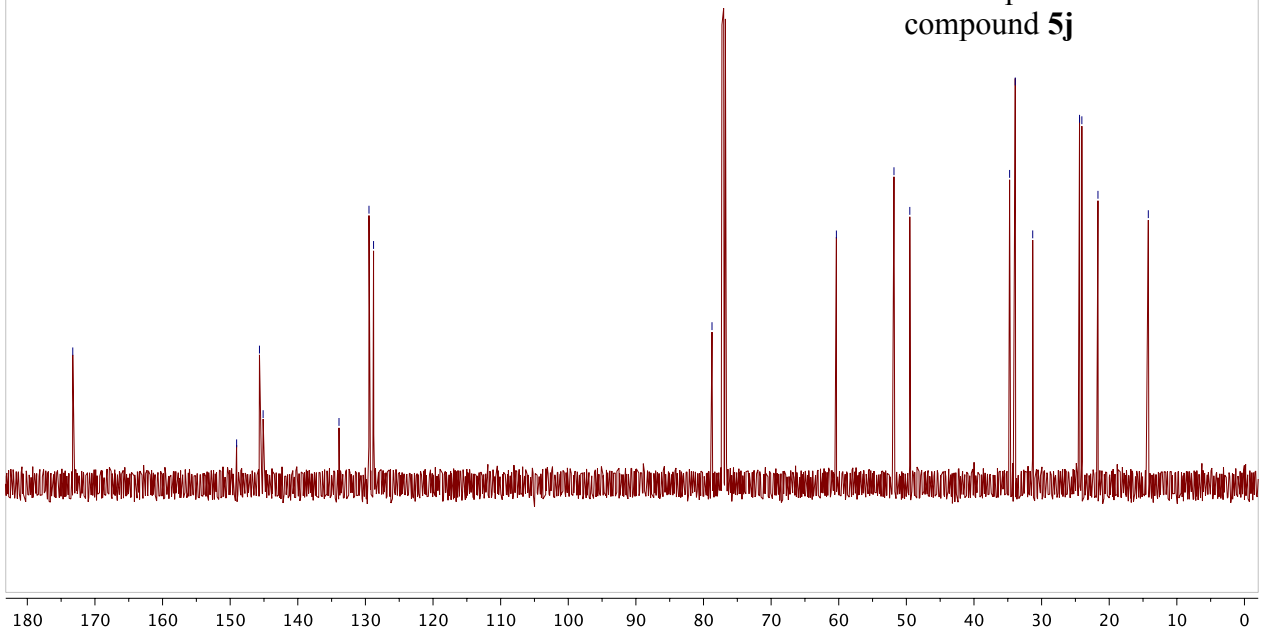




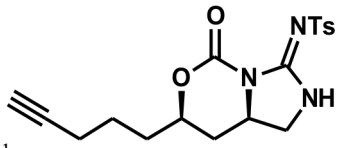
Parameter	Value
1 Title	ky-4-164-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	168
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-07T16:30:14
8 Spectrometer Frequency	125.70



^{13}C NMR spectra of compound **5j**

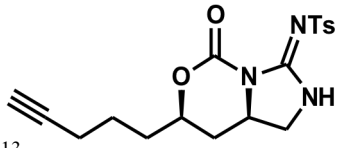


Parameter	Value
1 Title	AKM-04-194
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-29T12:02:28
8 Spectrometer Frequency	499.86



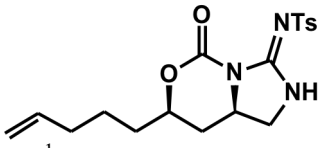
^{1}H NMR spectra of compound **5k**

Parameter	Value
1 Title	AKM-04-194.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	100
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-29T12:05:02
8 Spectrometer Frequency	125.70



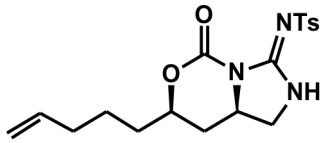
^{13}C NMR spectra of compound **5k**

Parameter	Value
1 Title	AKM-04-188
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-05-27T11:57:15
8 Spectrometer Frequency	599.64

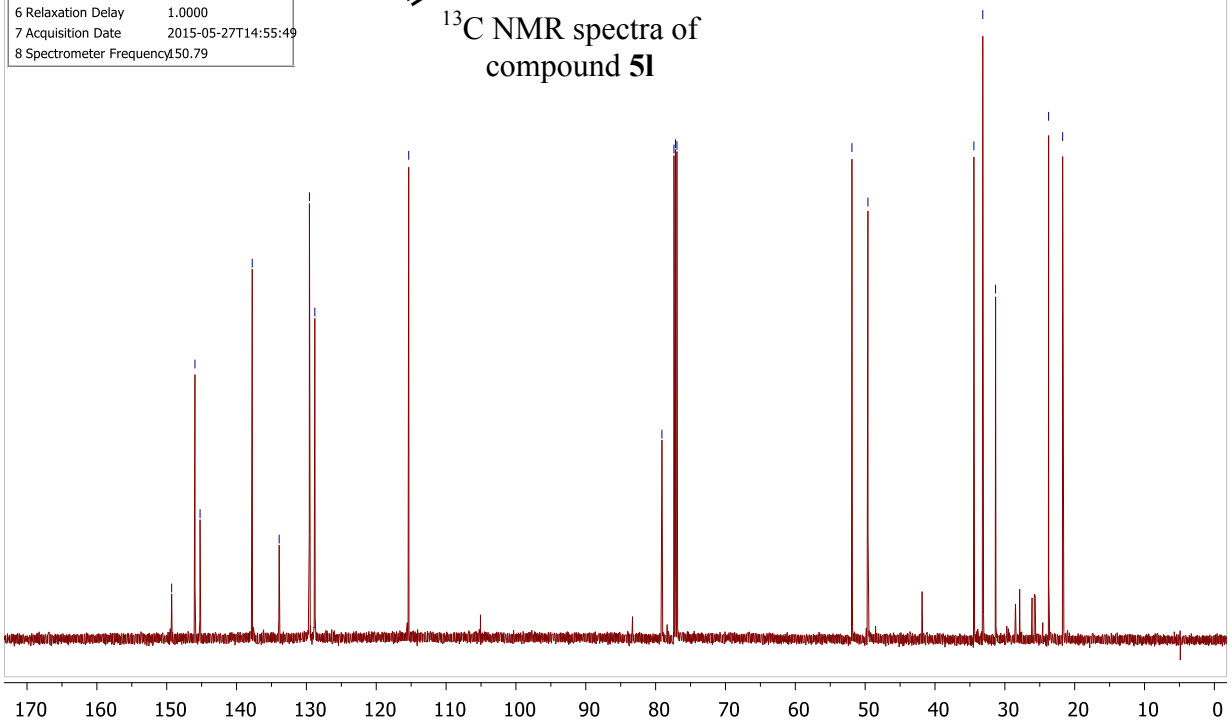


^{1}H NMR spectra of compound **5l**

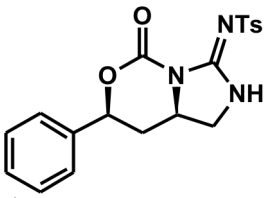
Parameter	Value
1 Title	AKM-04-188.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	1044
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-05-27T14:55:49
8 Spectrometer Frequency	150.79



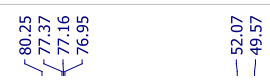
^{13}C NMR spectra of compound **5l**



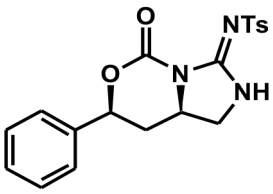
Parameter	Value
1 Title	AKM-05-136
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-19T11:36:29
8 Spectrometer Frequency	599.64



^{1}H NMR spectra of compound **5m**

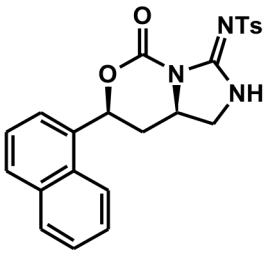


Parameter	Value
1 Title	AKM-05-136.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	204
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-19T11:39:44
8 Spectrometer Frequency	150.79



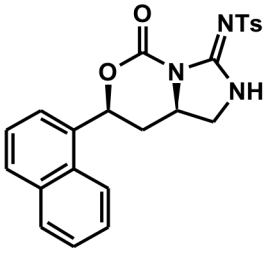
^{13}C NMR spectra of compound **5m**

Parameter	Value
1 Title	AKM-05-141
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-21T11:30:19
8 Spectrometer Frequency	499.86



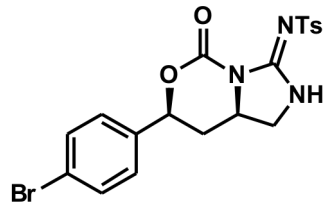
^{1}H NMR spectra of compound **5n**

Parameter	Value
1 Title	AKM-05-141.13C
2 Spectrometer	inova
3 Solvent	dmso
4 Temperature	25.0
5 Number of Scans	280
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-21T11:33:51
8 Spectrometer Frequency	125.70

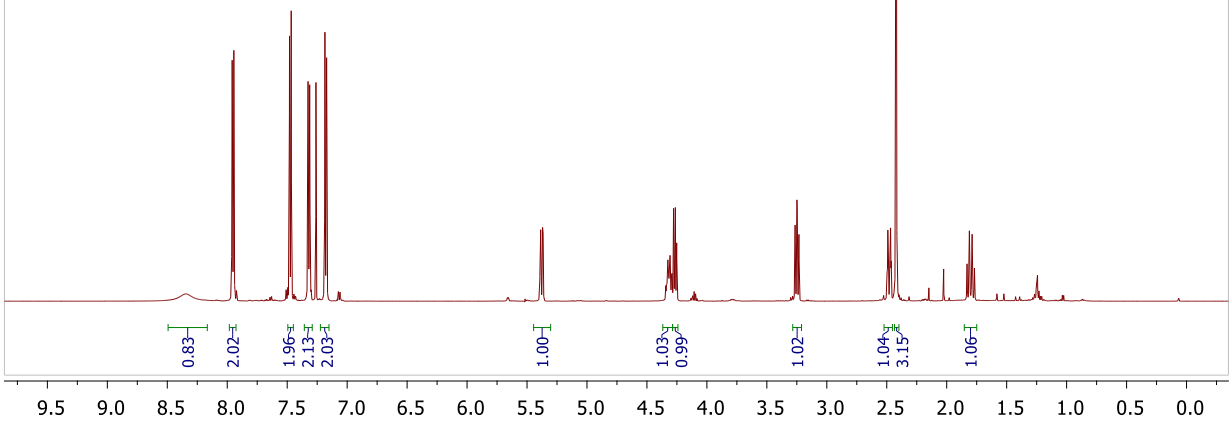


^{13}C NMR spectra of compound **5n**

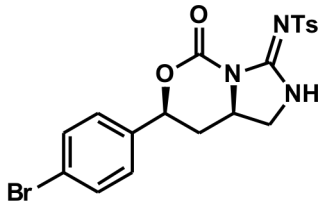
Parameter	Value
1 Title	AKM-05-172a
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-11-04T10:38:07
8 Spectrometer Frequency	599.64



^{1}H NMR spectra of compound **5o**

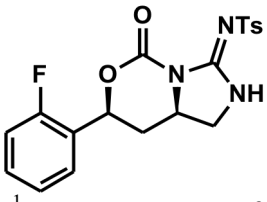


Parameter	Value
1 Title	AKM-05-172a.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	16.0
5 Number of Scans	208
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-04T12:07:35
8 Spectrometer Frequency	125.70

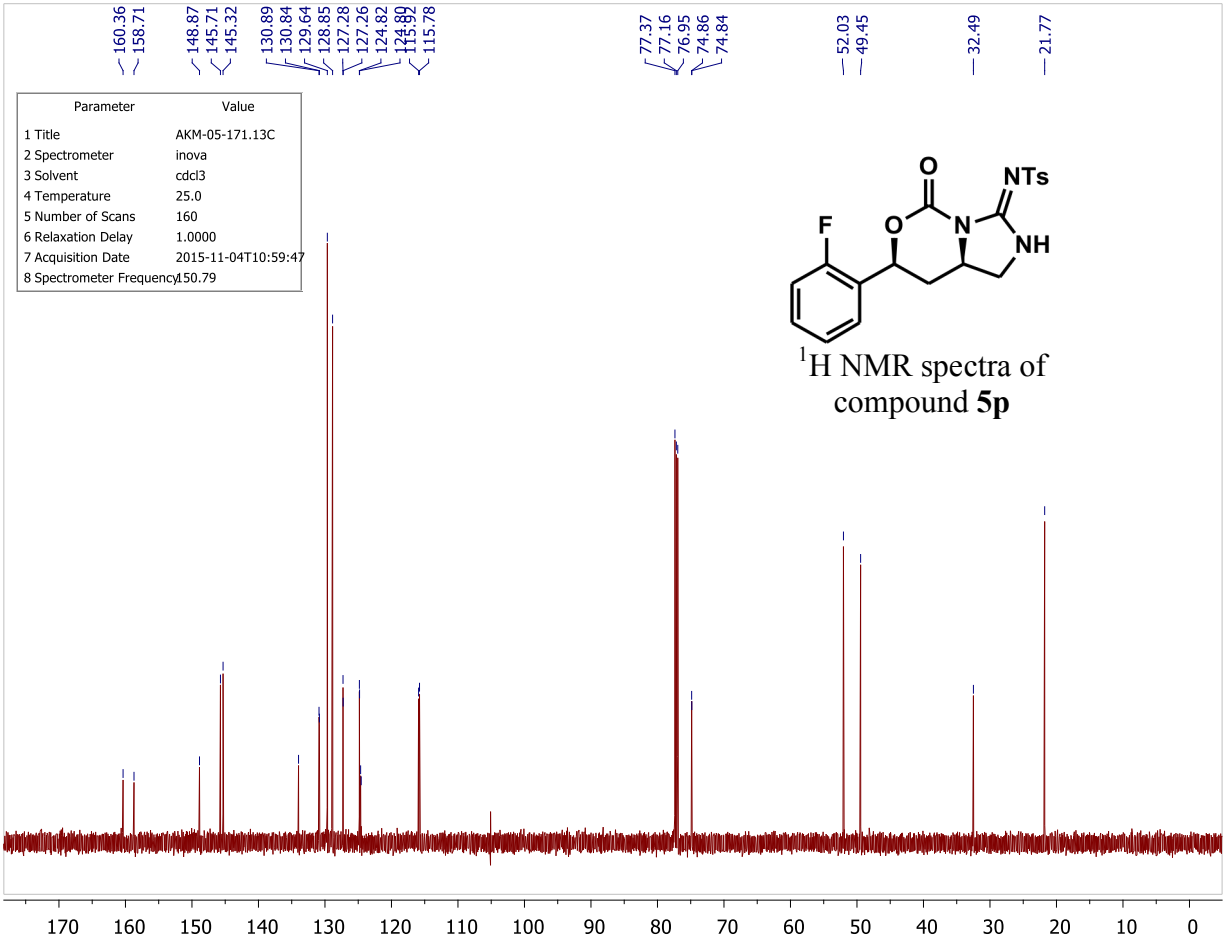


^{13}C NMR spectra of compound **5o**

Parameter	Value
1 Title	AKM-05-171
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-11-04T10:56:41
8 Spectrometer Frequency	599.64



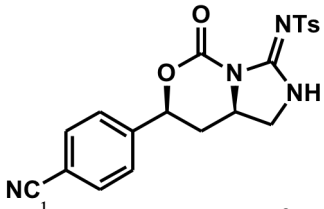
^{1}H NMR spectra of compound **5p**



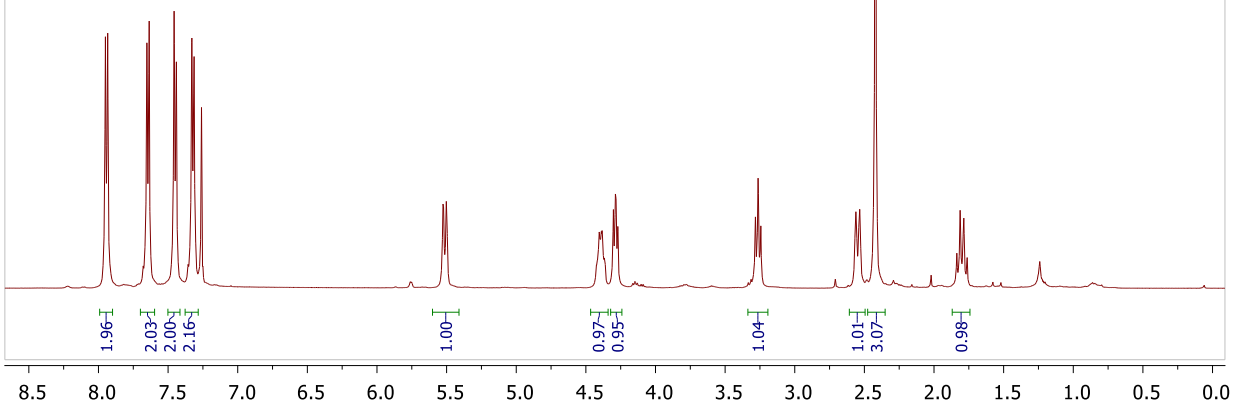
Parameter	Value
1 Title	AKM-05-171.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	160
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-04T10:59:47
8 Spectrometer Frequency	150.79

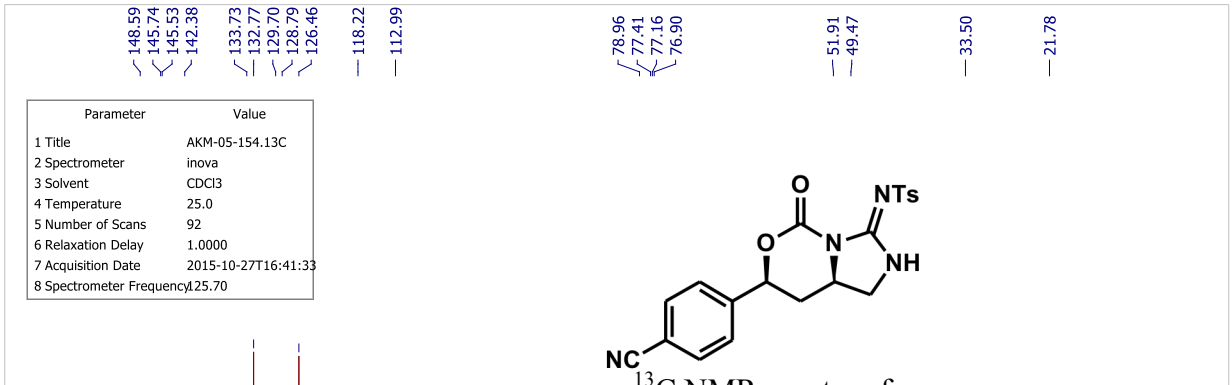
^{1}H NMR spectra of compound **5p**

Parameter	Value
1 Title	AKM-05-154
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-27T16:38:46
8 Spectrometer Frequency	499.86



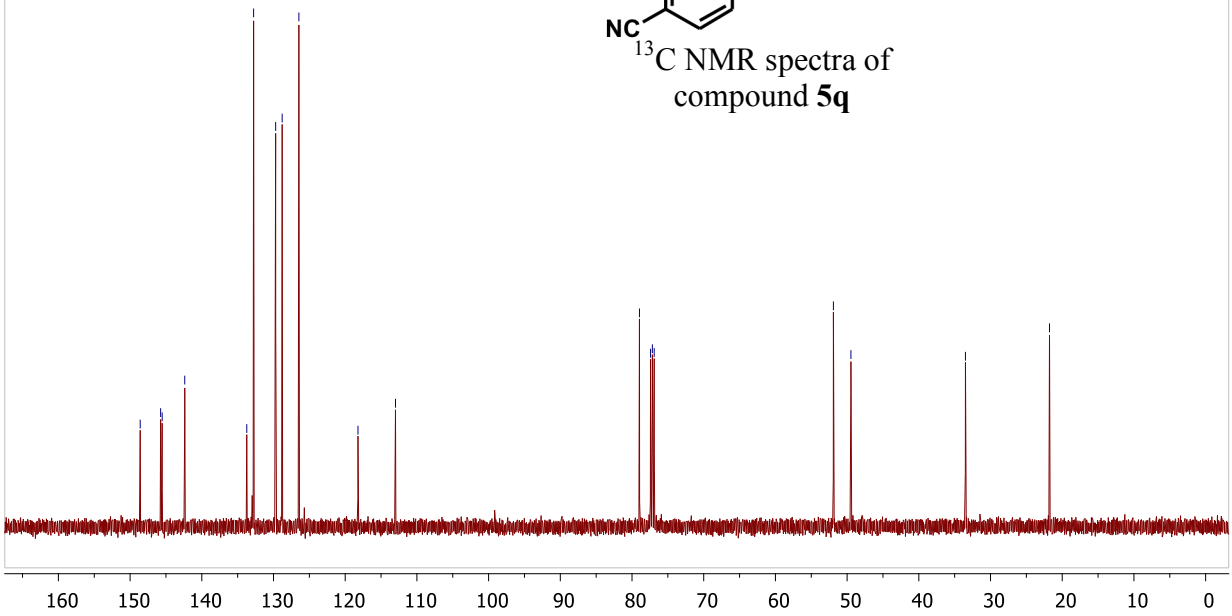
^{1}H NMR spectra of compound **5q**



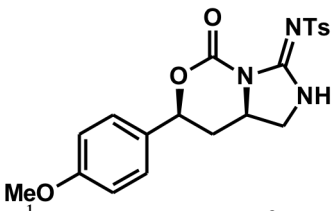


Parameter	Value
1 Title	AKM-05-154.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	92
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-27T16:41:33
8 Spectrometer Frequency	125.70

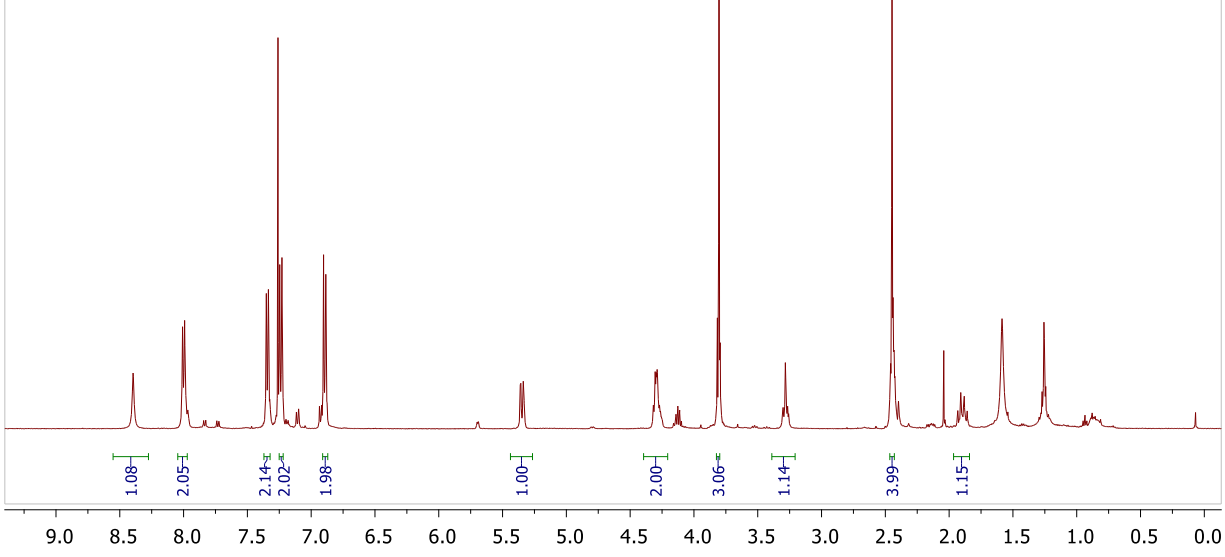
^{13}C NMR spectra of compound **5q**

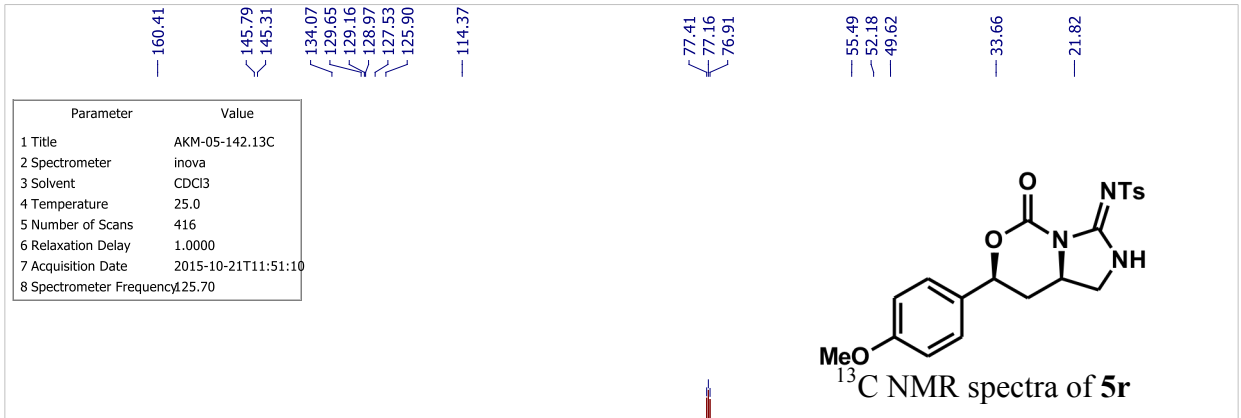


Parameter	Value
1 Title	AKM-05-142repurified
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-27T16:29:10
8 Spectrometer Frequency	499.86



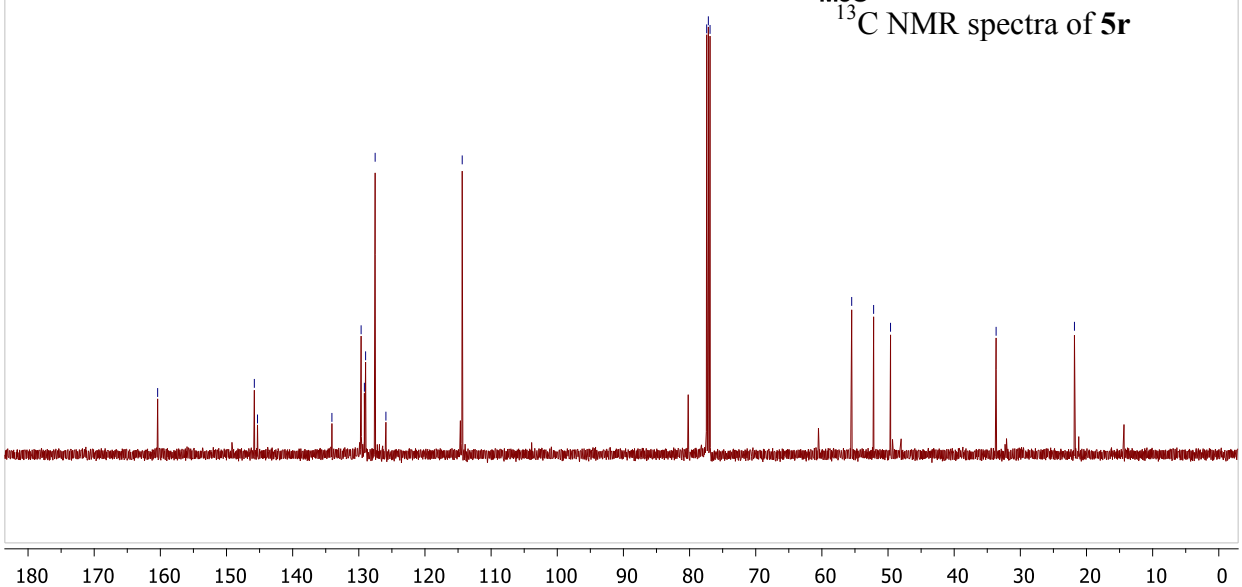
^{1}H NMR spectra of **5r**

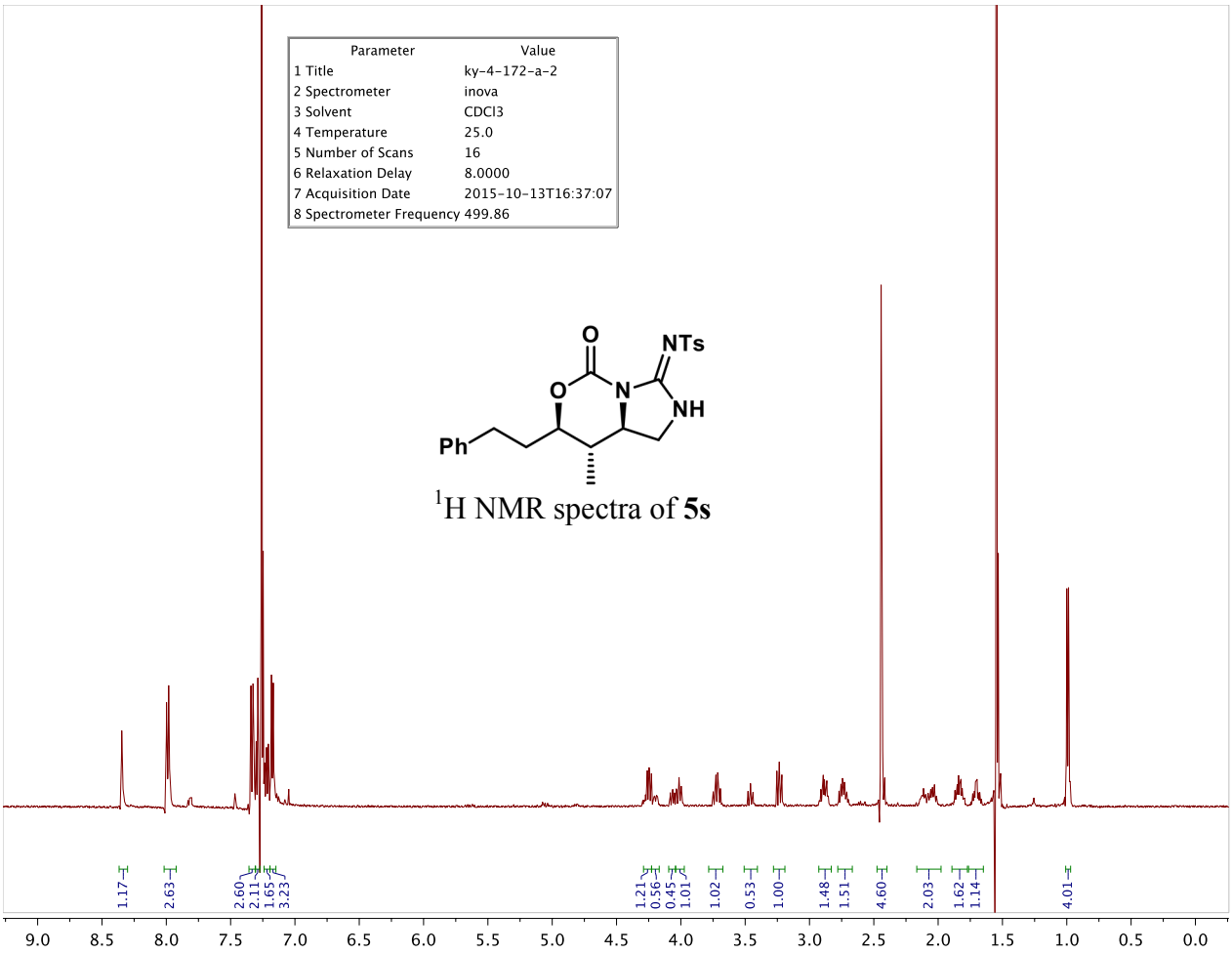




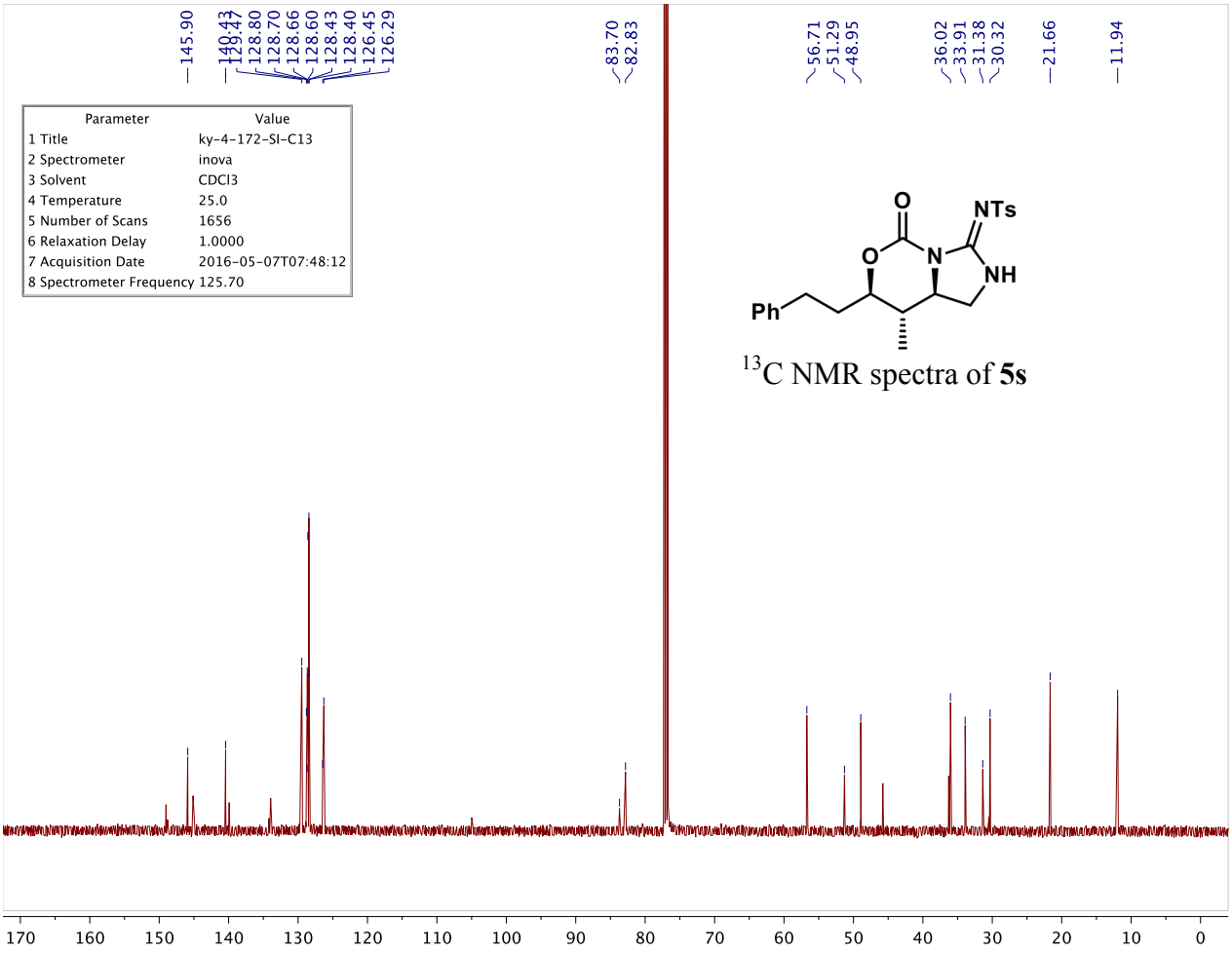
Parameter	Value
1 Title	AKM-05-142.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	416
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-21T11:51:10
8 Spectrometer Frequency	125.70

^{13}C NMR spectra of **5r**

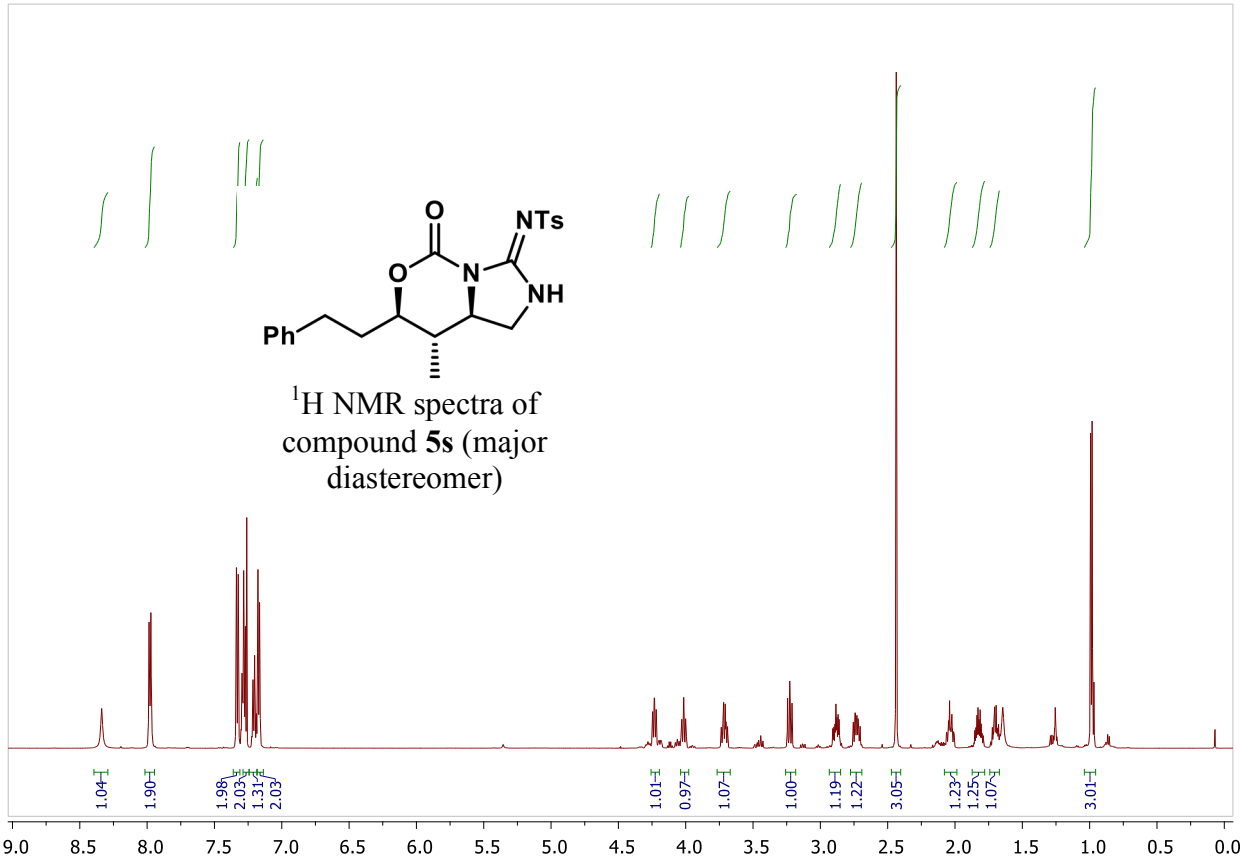




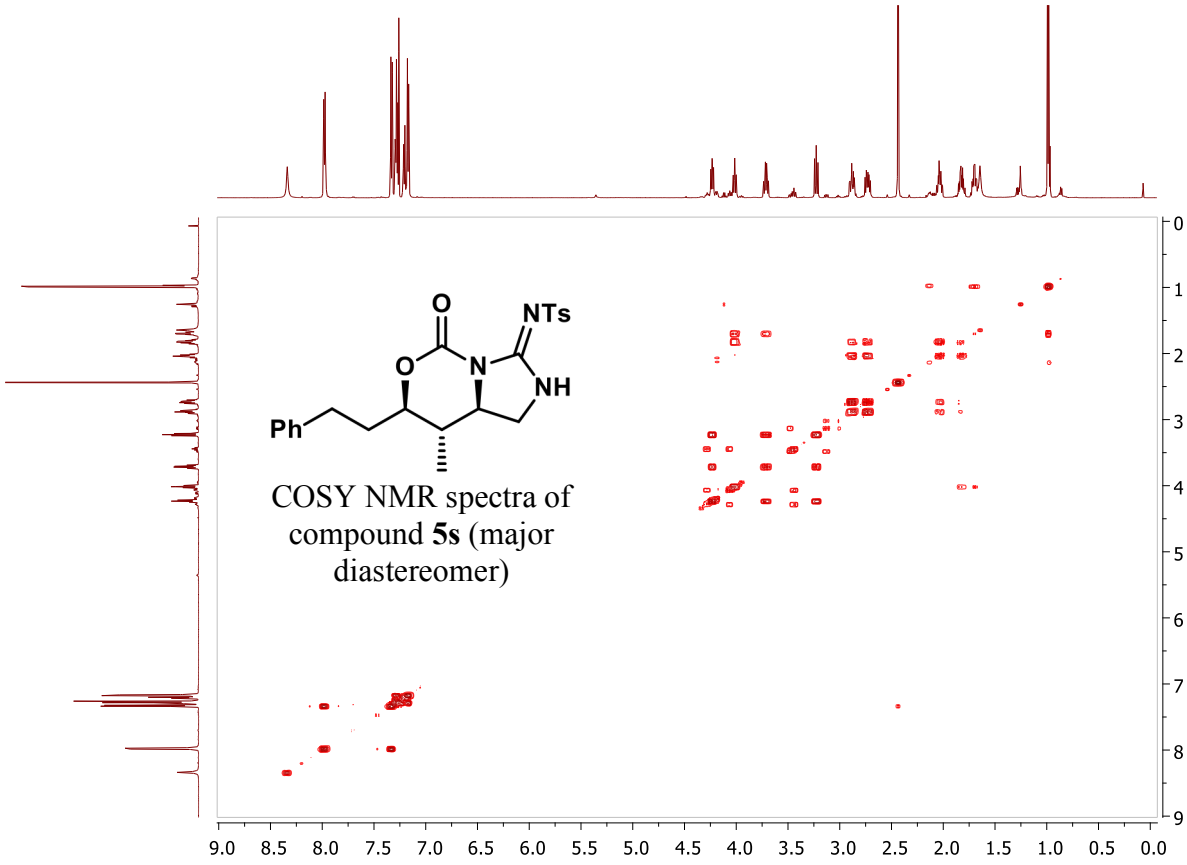
^{1}H NMR spectra of **5s**



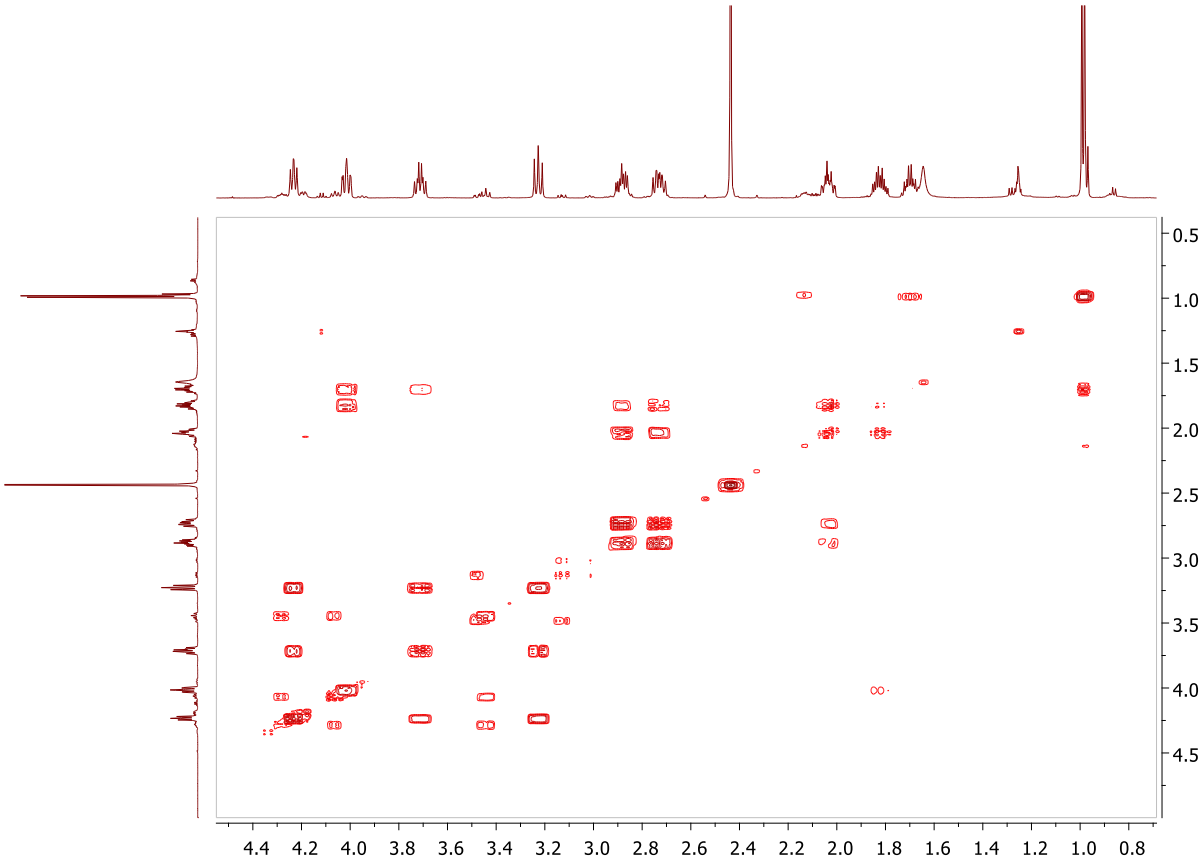
^{13}C NMR spectra of **5s**

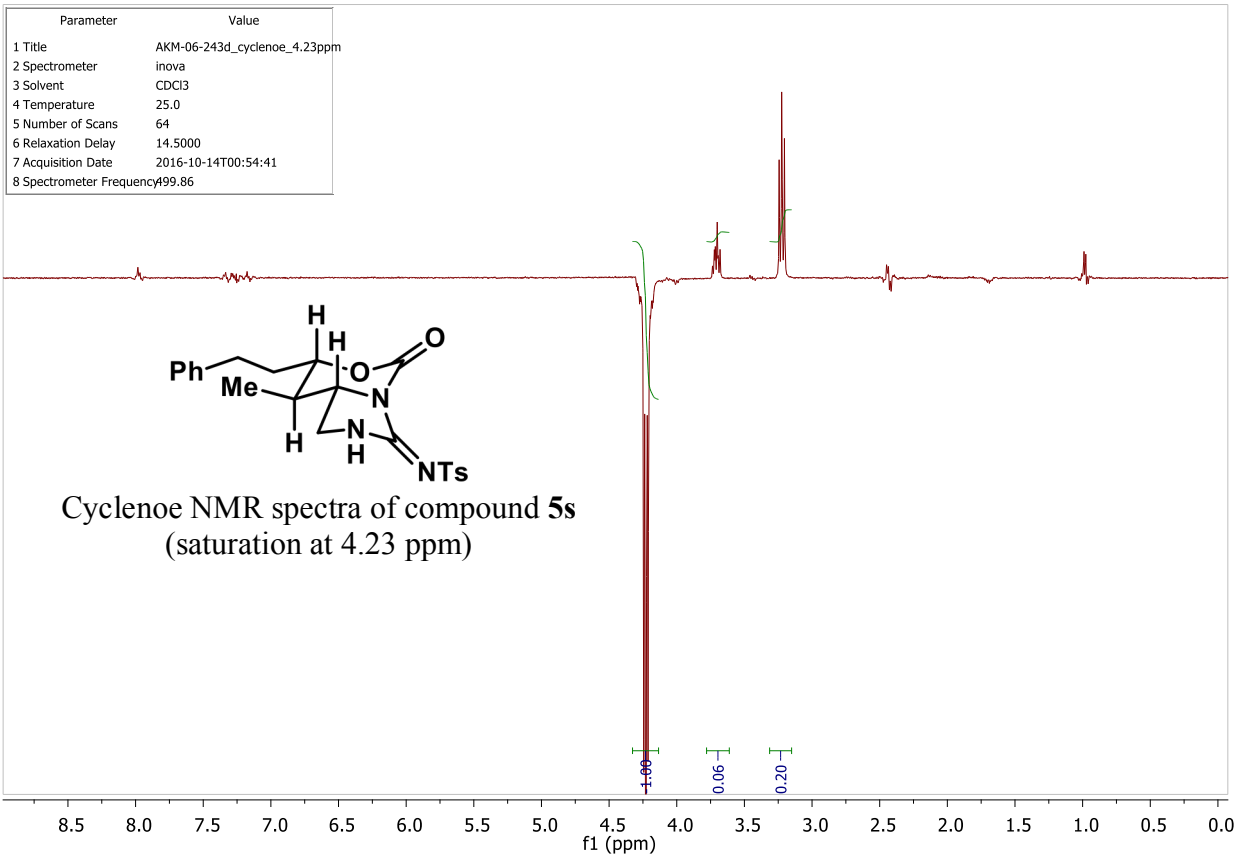


^{1}H NMR spectra of compound **5s** (major diastereomer)



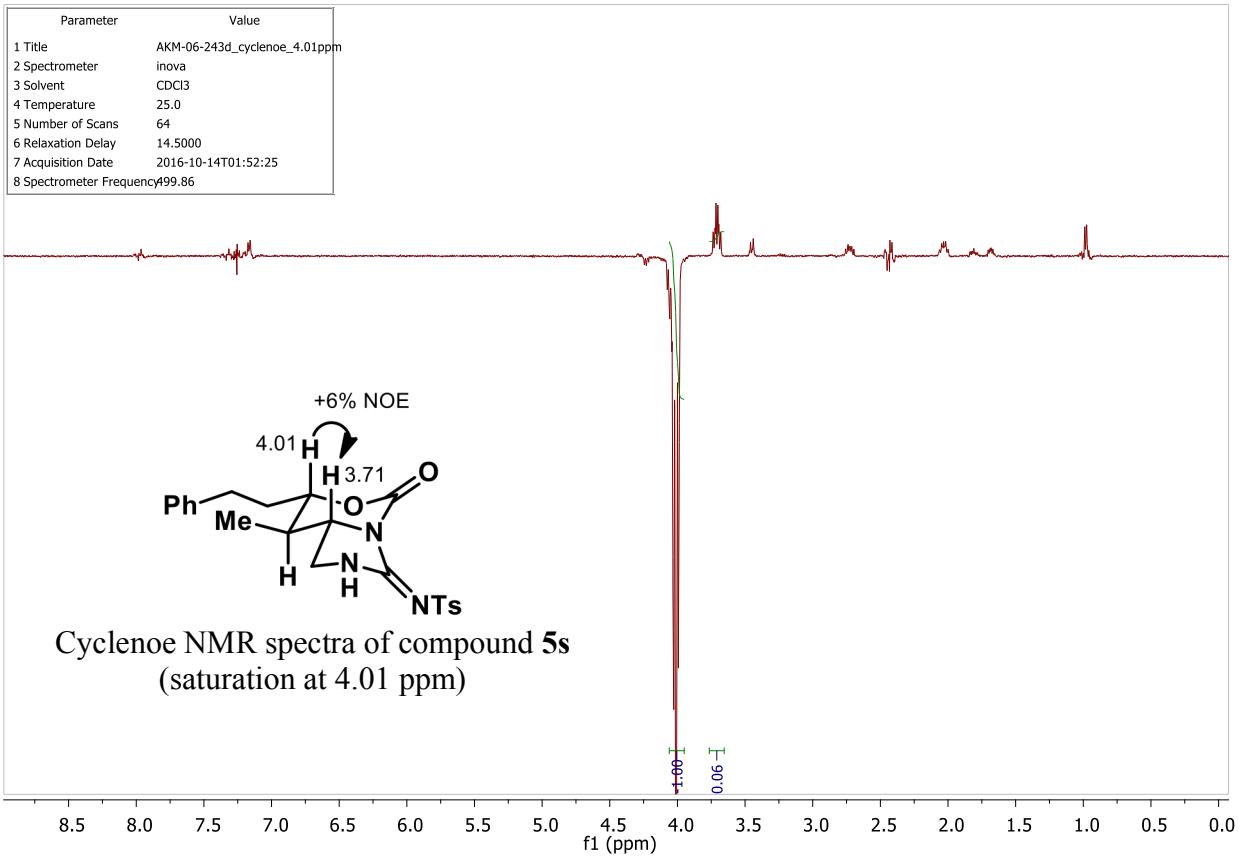
COSY NMR spectra of compound **5s** (major diastereomer)





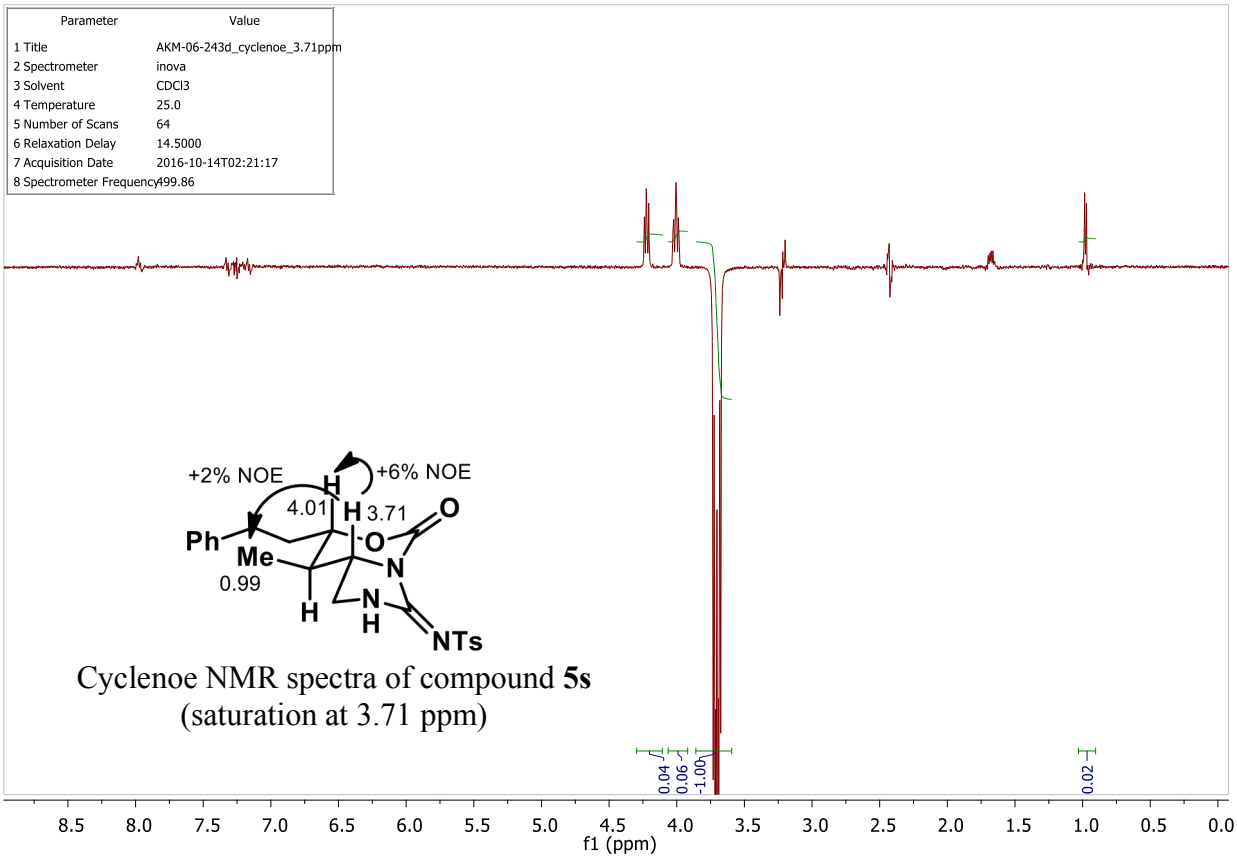
Cyclenoe NMR spectra of compound **5s**
(saturation at 4.23 ppm)

Parameter	Value
1 Title	AKM-06-243d_cyclenoe_4.01ppm
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	64
6 Relaxation Delay	14.5000
7 Acquisition Date	2016-10-14T01:52:25
8 Spectrometer Frequency	499.86

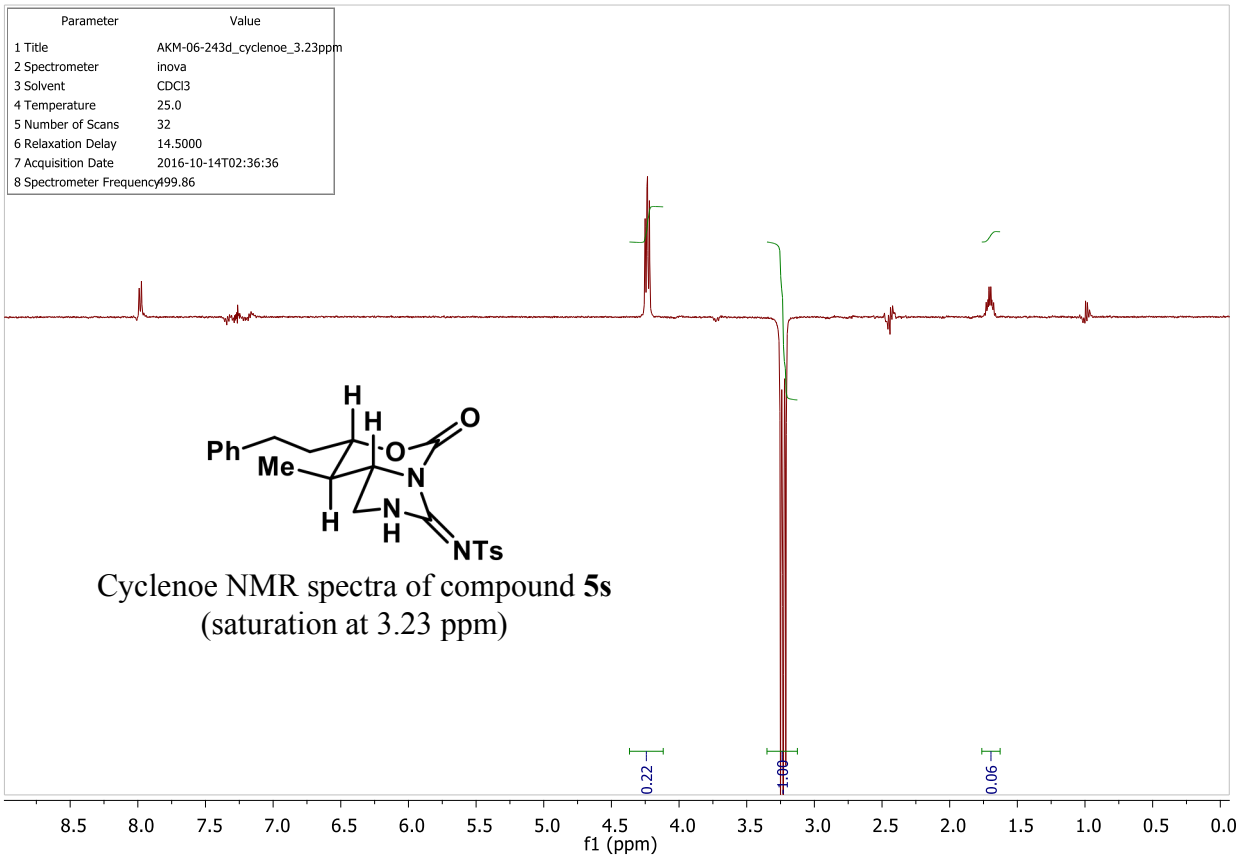


Cyclenoe NMR spectra of compound **5s**
(saturation at 4.01 ppm)

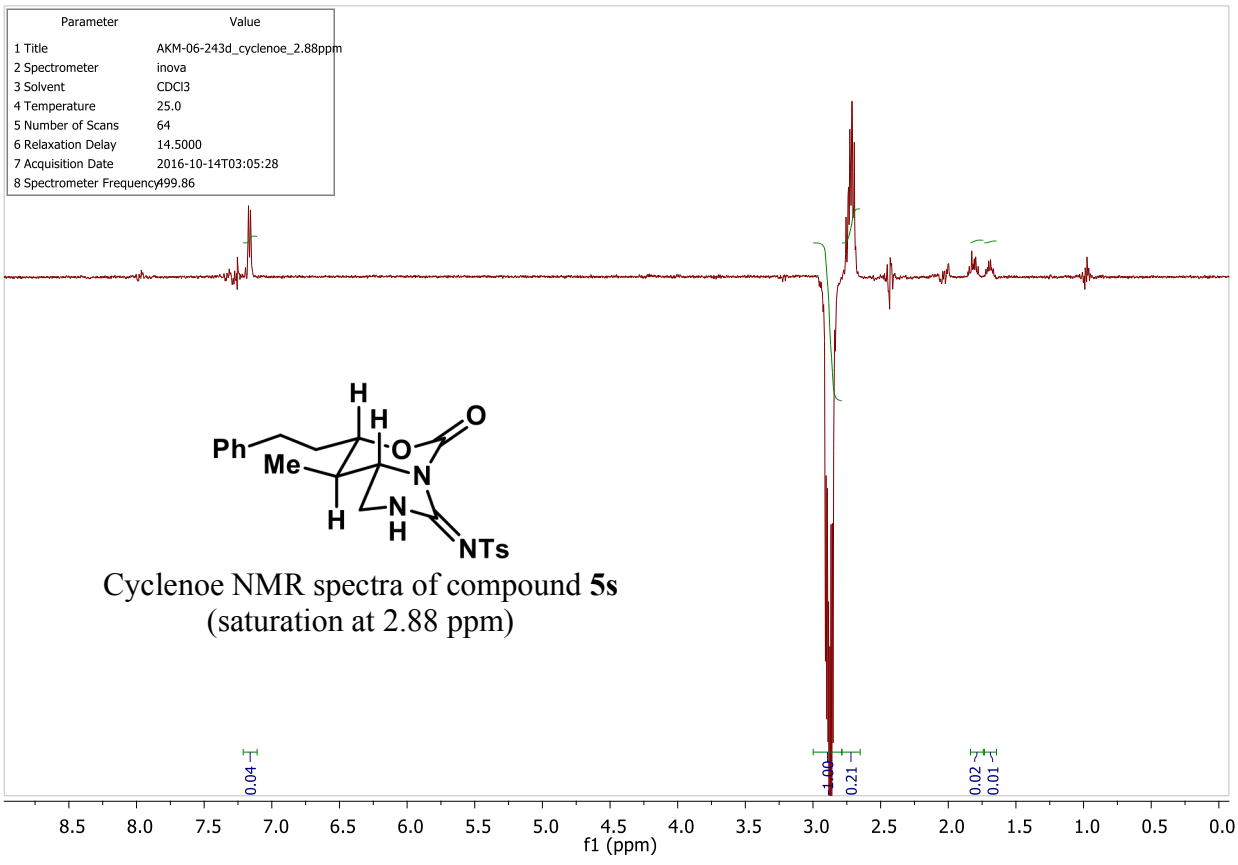
Parameter	Value
1 Title	AKM-06-243d_cyclenoe_3.71ppm
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	64
6 Relaxation Delay	14.5000
7 Acquisition Date	2016-10-14T02:21:17
8 Spectrometer Frequency	499.86



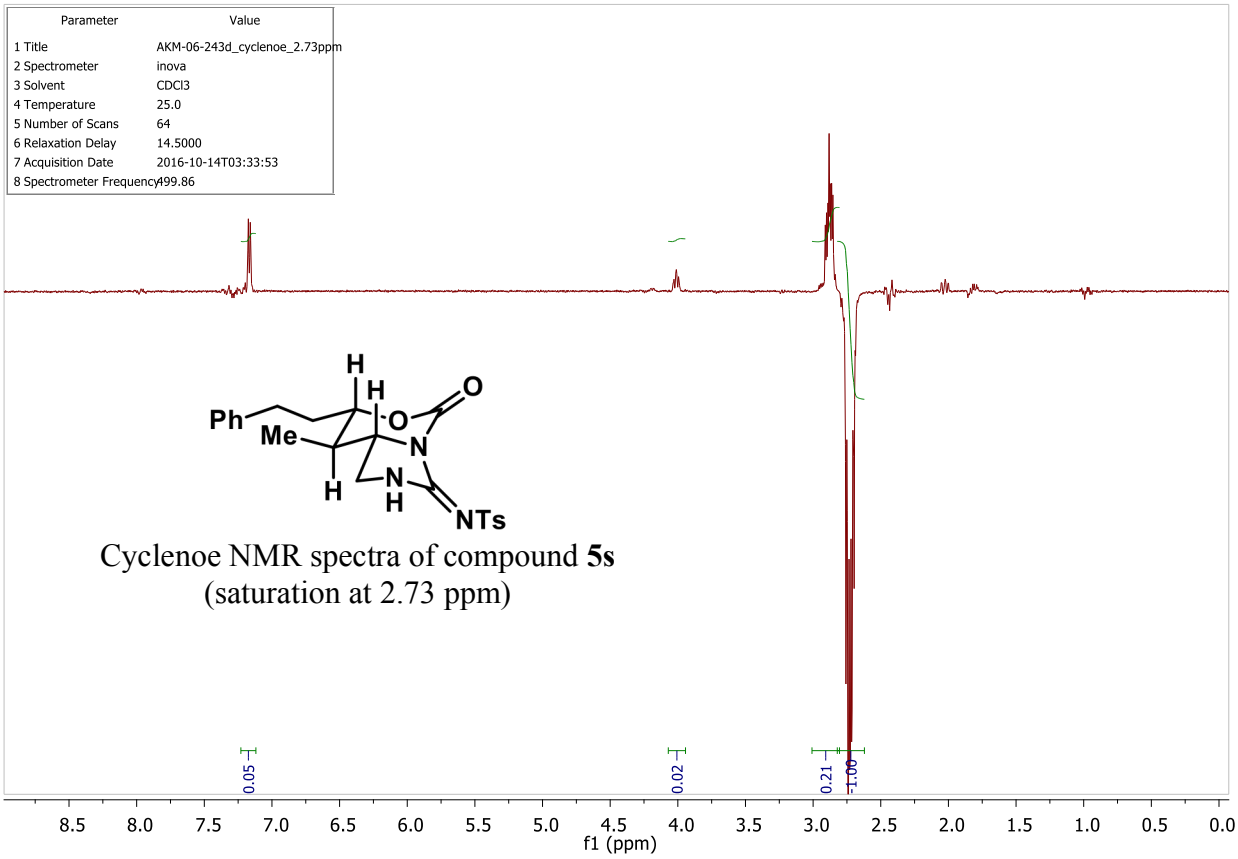
Cyclenoe NMR spectra of compound **5s**
(saturation at 3.71 ppm)



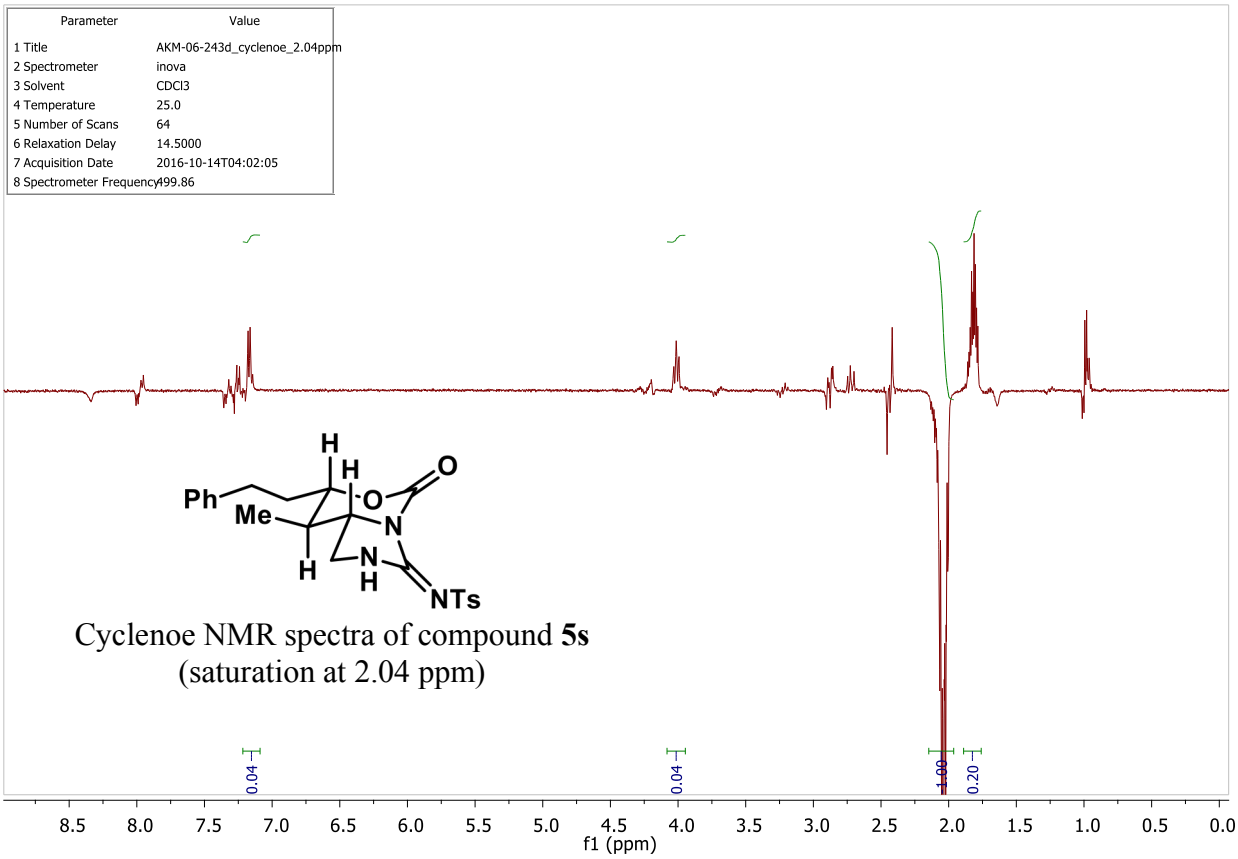
Cyclenoe NMR spectra of compound **5s**
(saturation at 3.23 ppm)



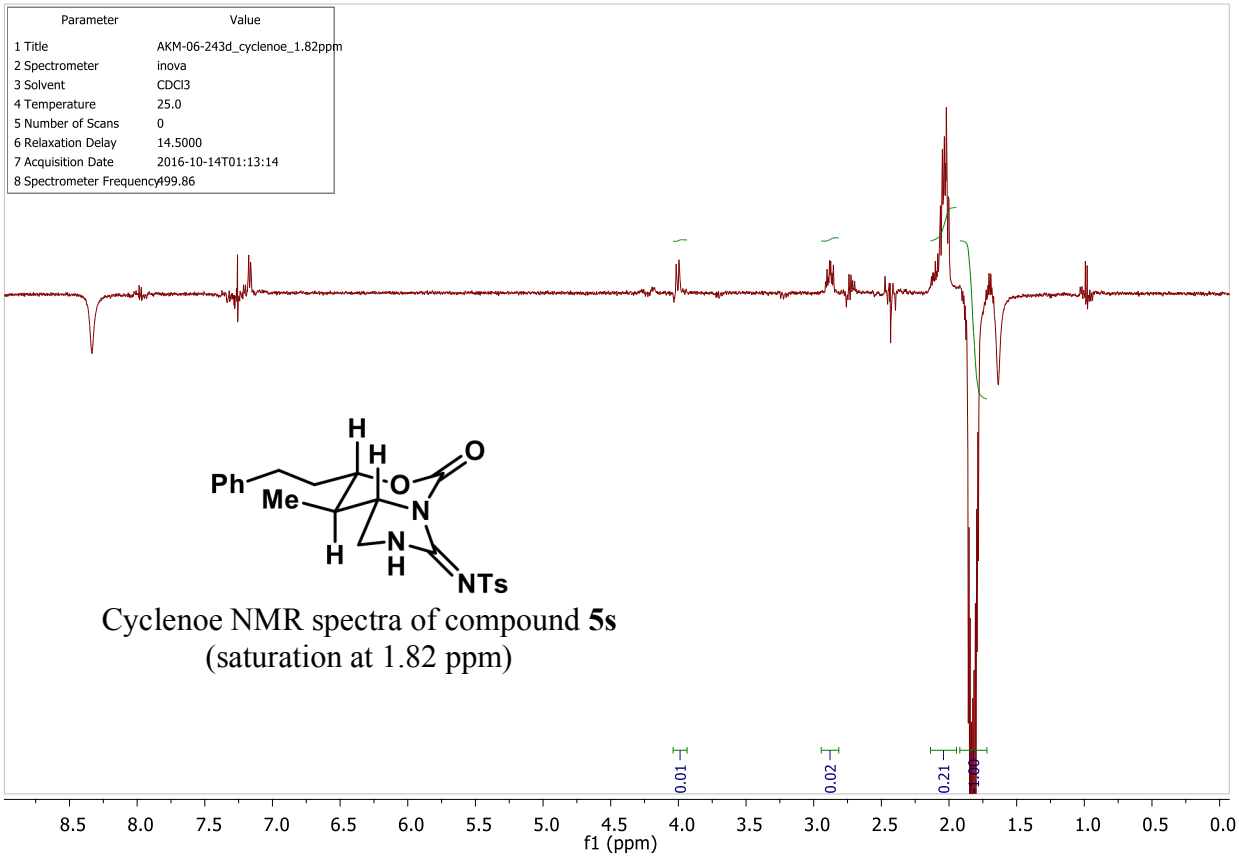
Cyclenoe NMR spectra of compound **5s**
(saturation at 2.88 ppm)



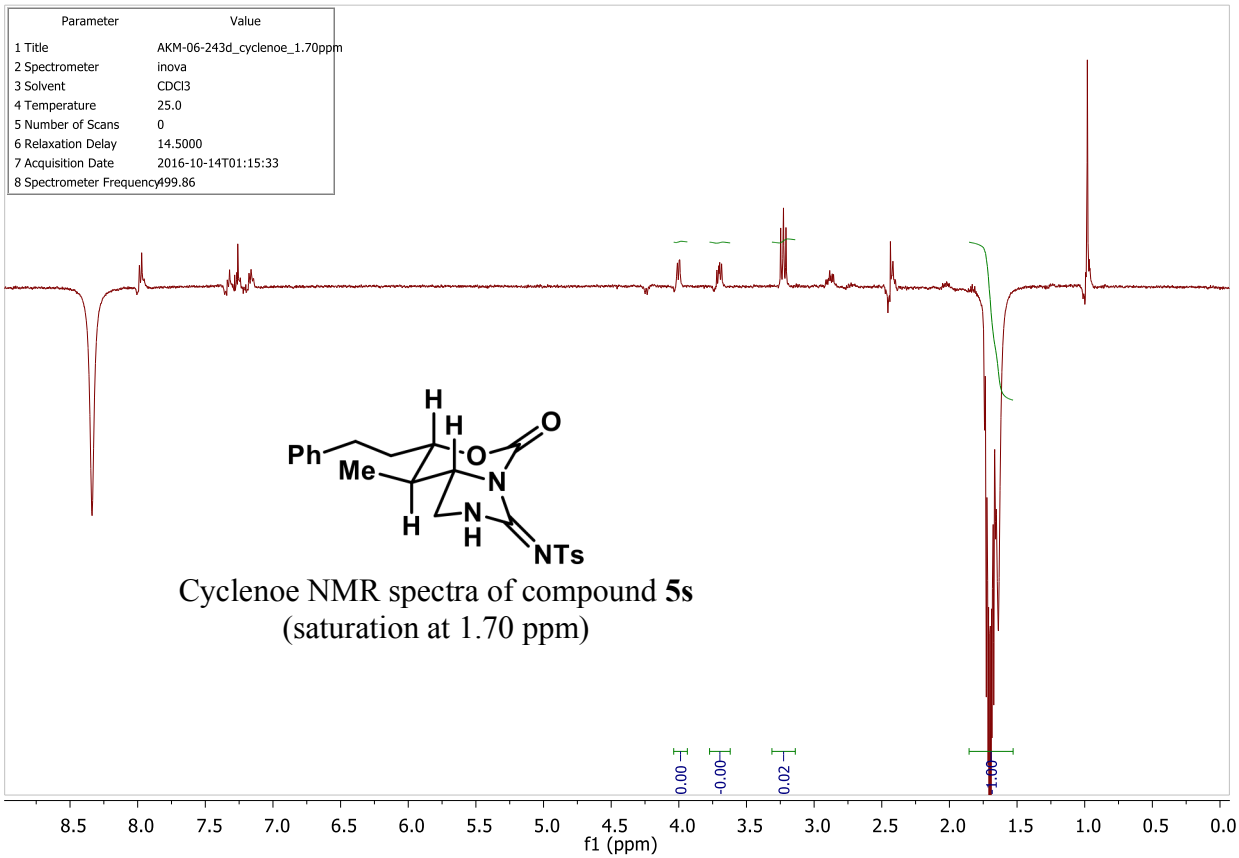
Cyclenoe NMR spectra of compound **5s**
(saturation at 2.73 ppm)



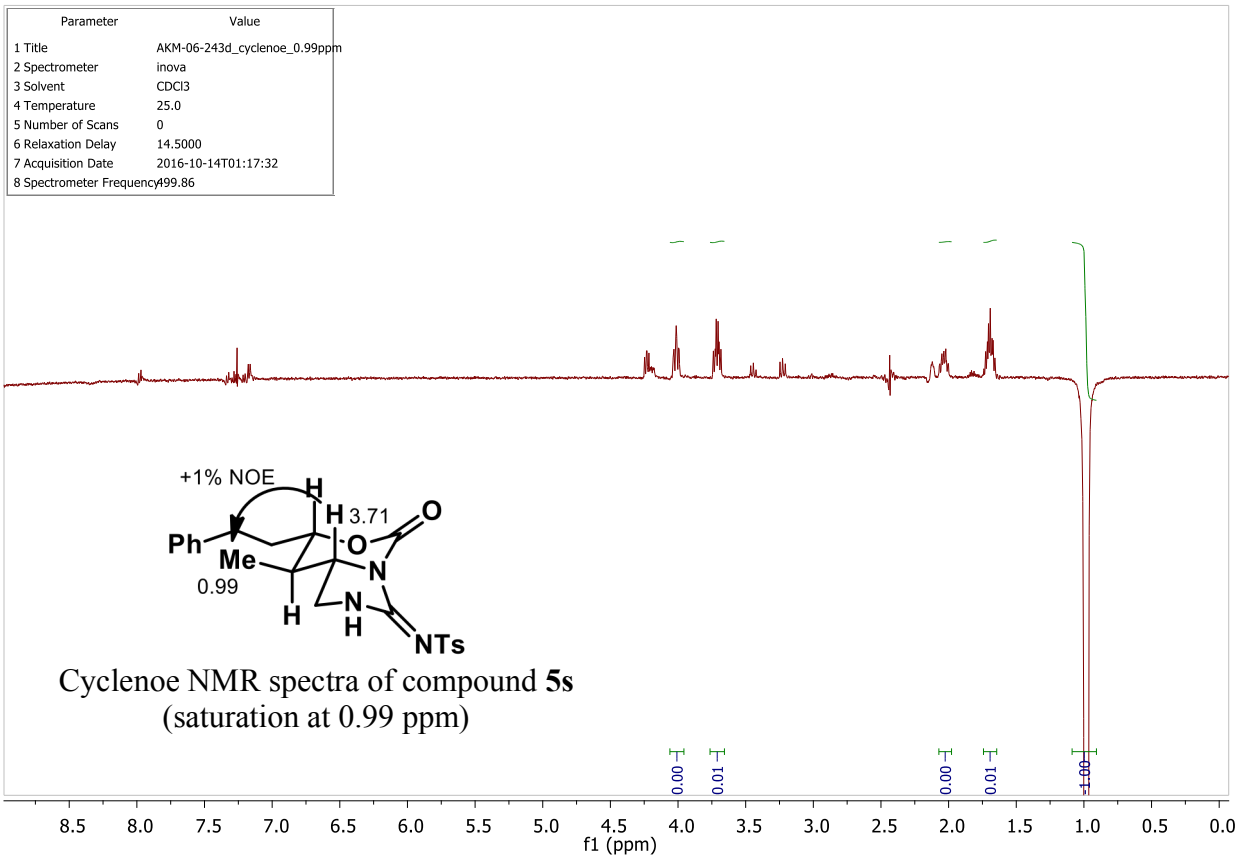
Cyclenoe NMR spectra of compound **5s**
(saturation at 2.04 ppm)



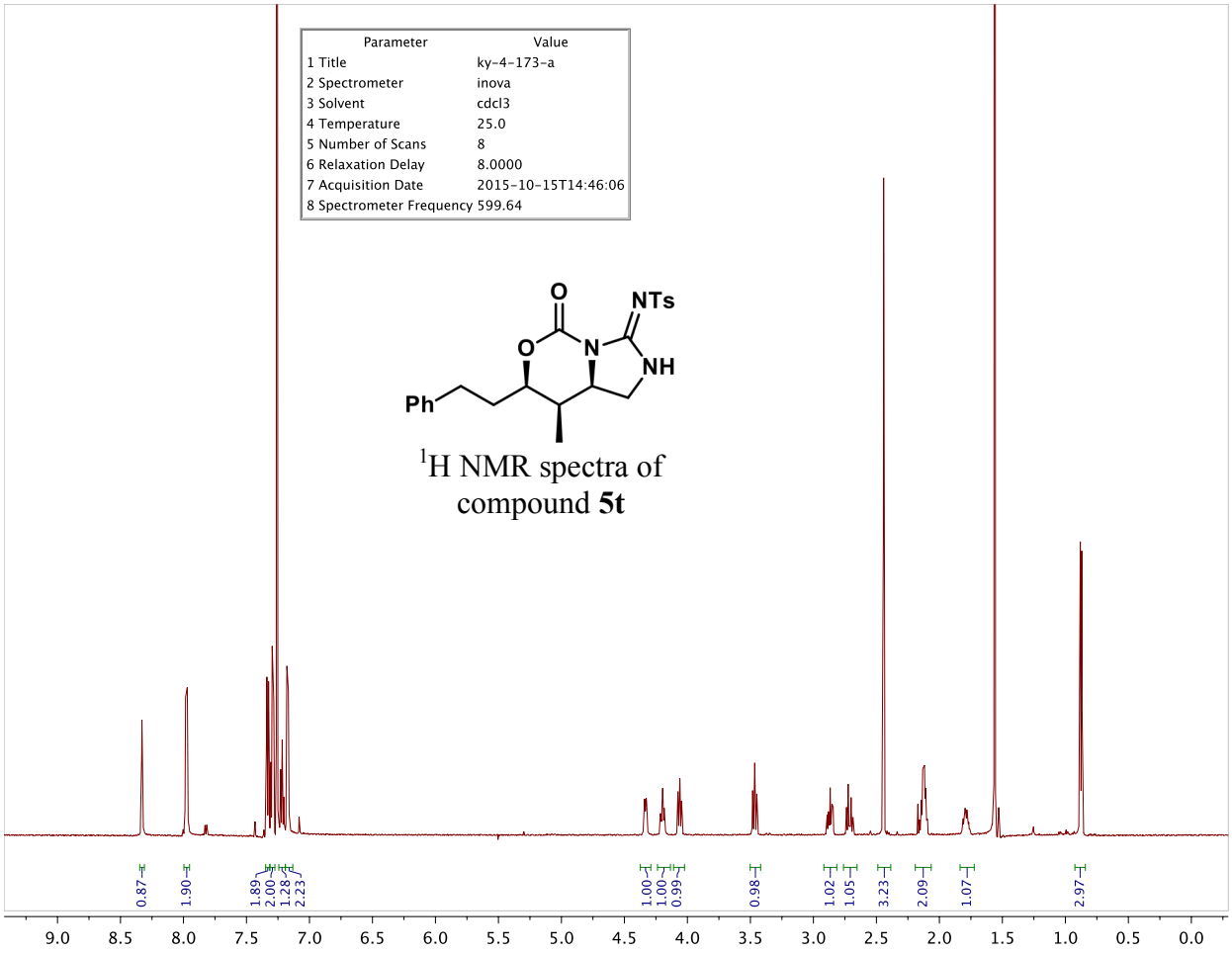
Cyclenoe NMR spectra of compound **5s**
(saturation at 1.82 ppm)



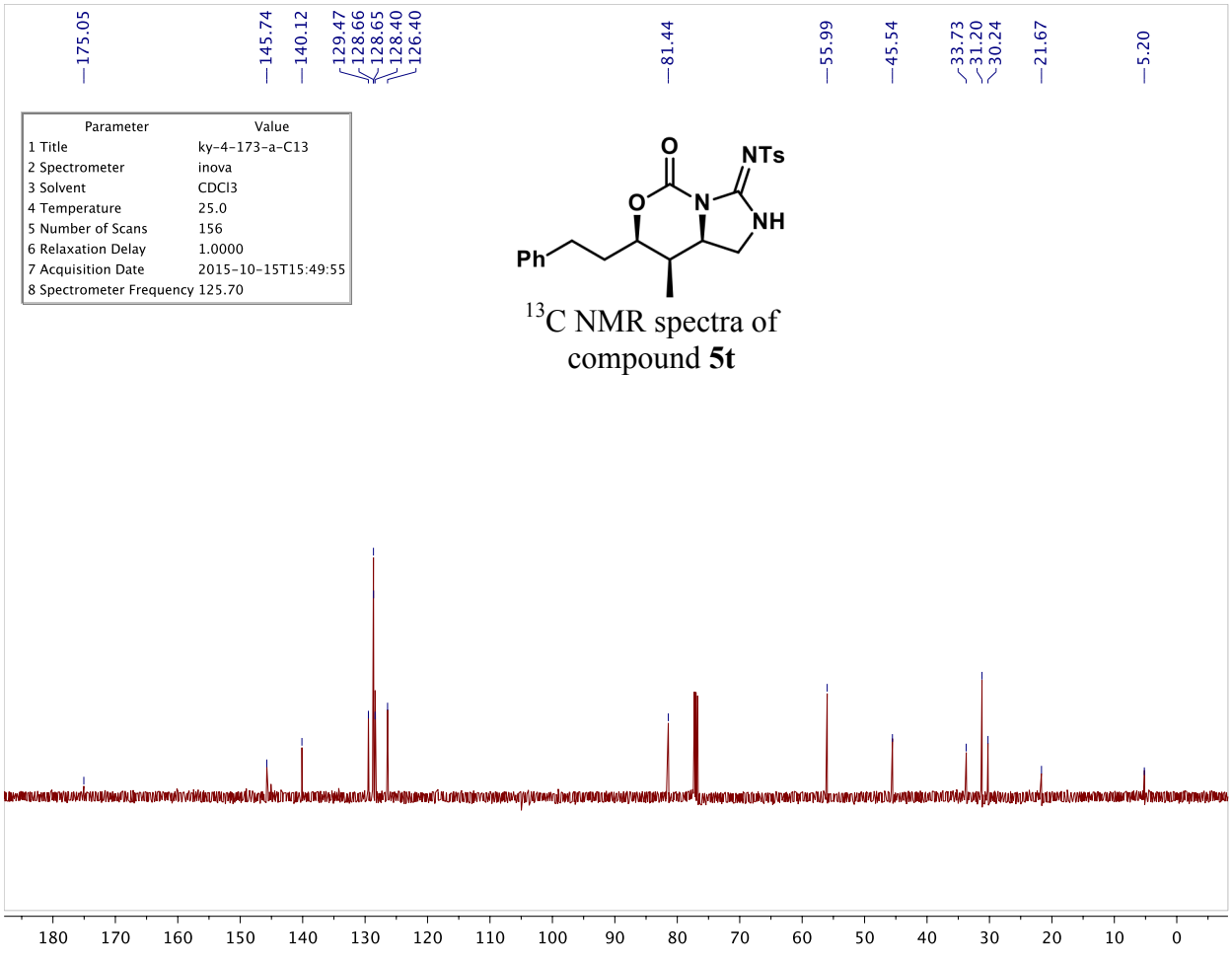
Cyclenoe NMR spectra of compound **5s**
(saturation at 1.70 ppm)



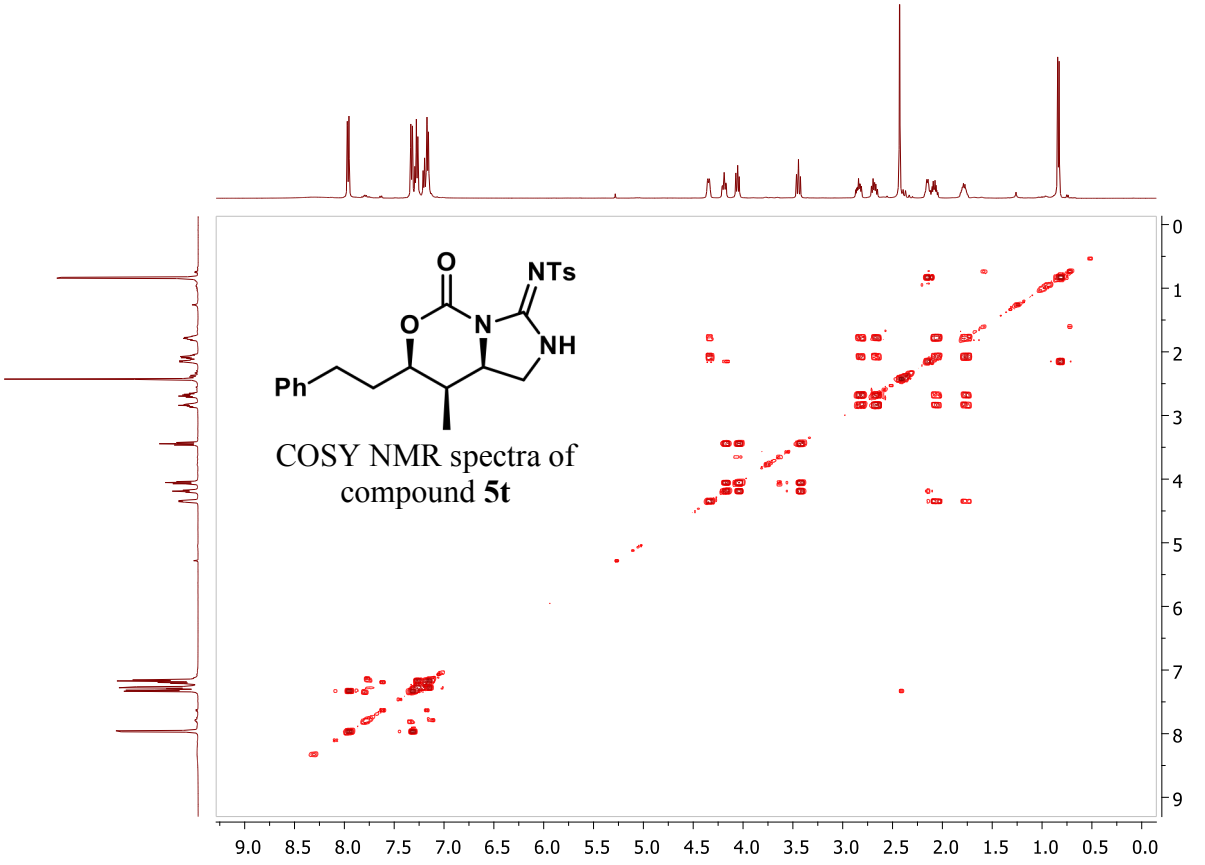
Cyclenoe NMR spectra of compound **5s**
(saturation at 0.99 ppm)



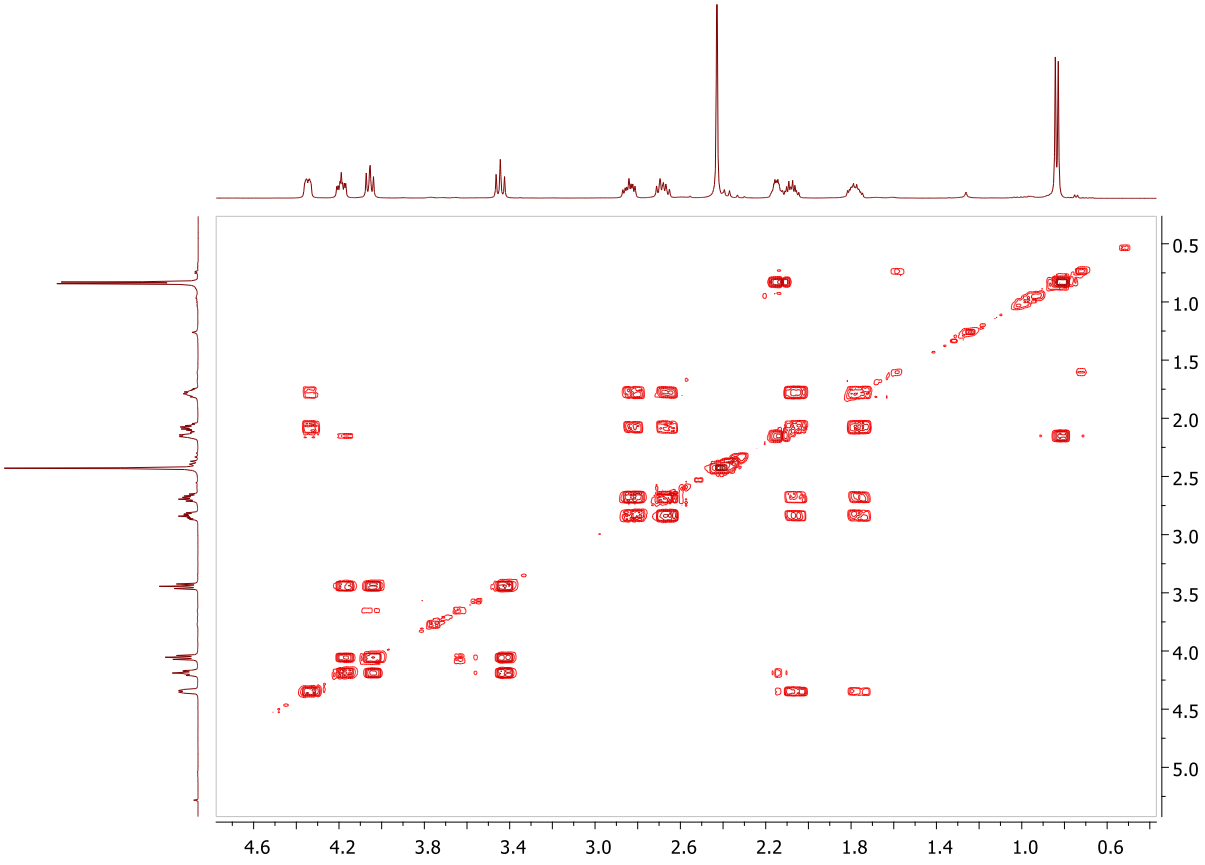
^{1}H NMR spectra of compound **5t**

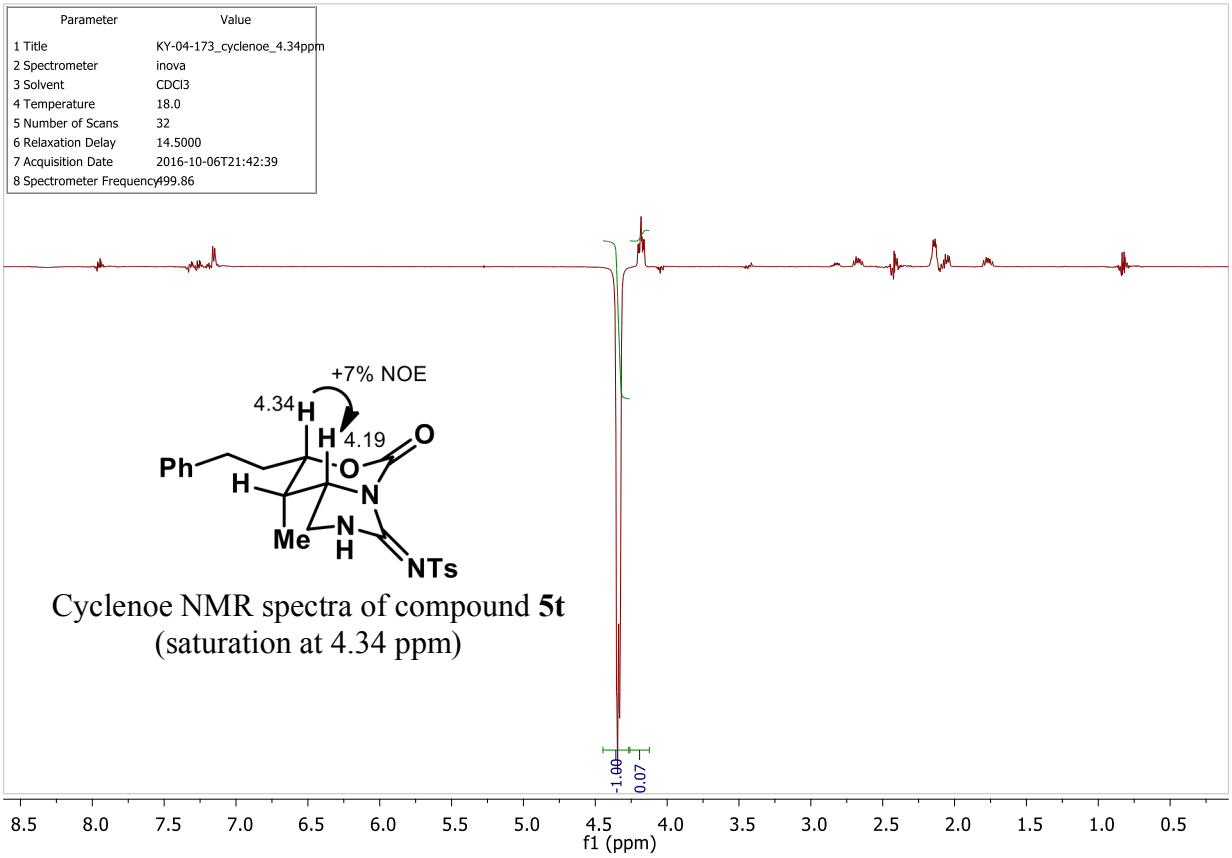


^{13}C NMR spectra of compound **5t**

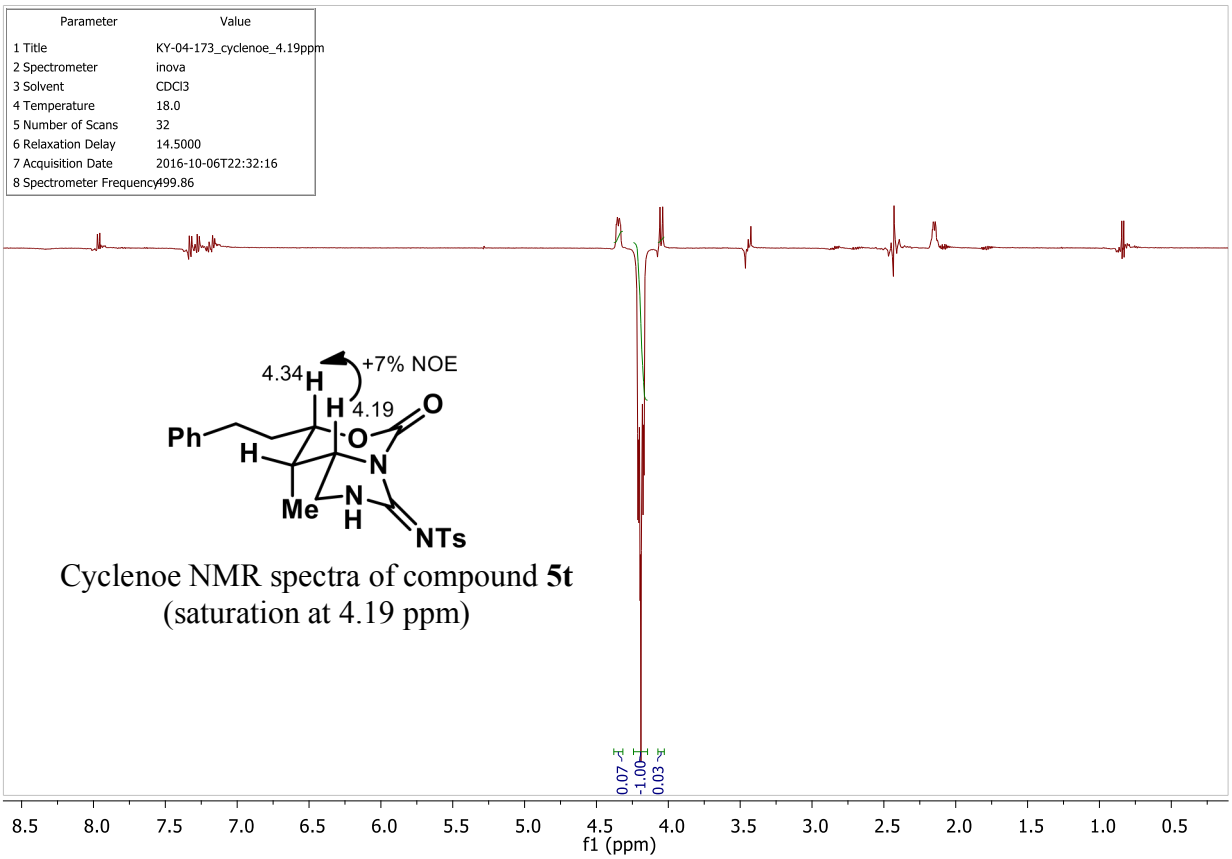


COSY NMR spectra of compound **5t**

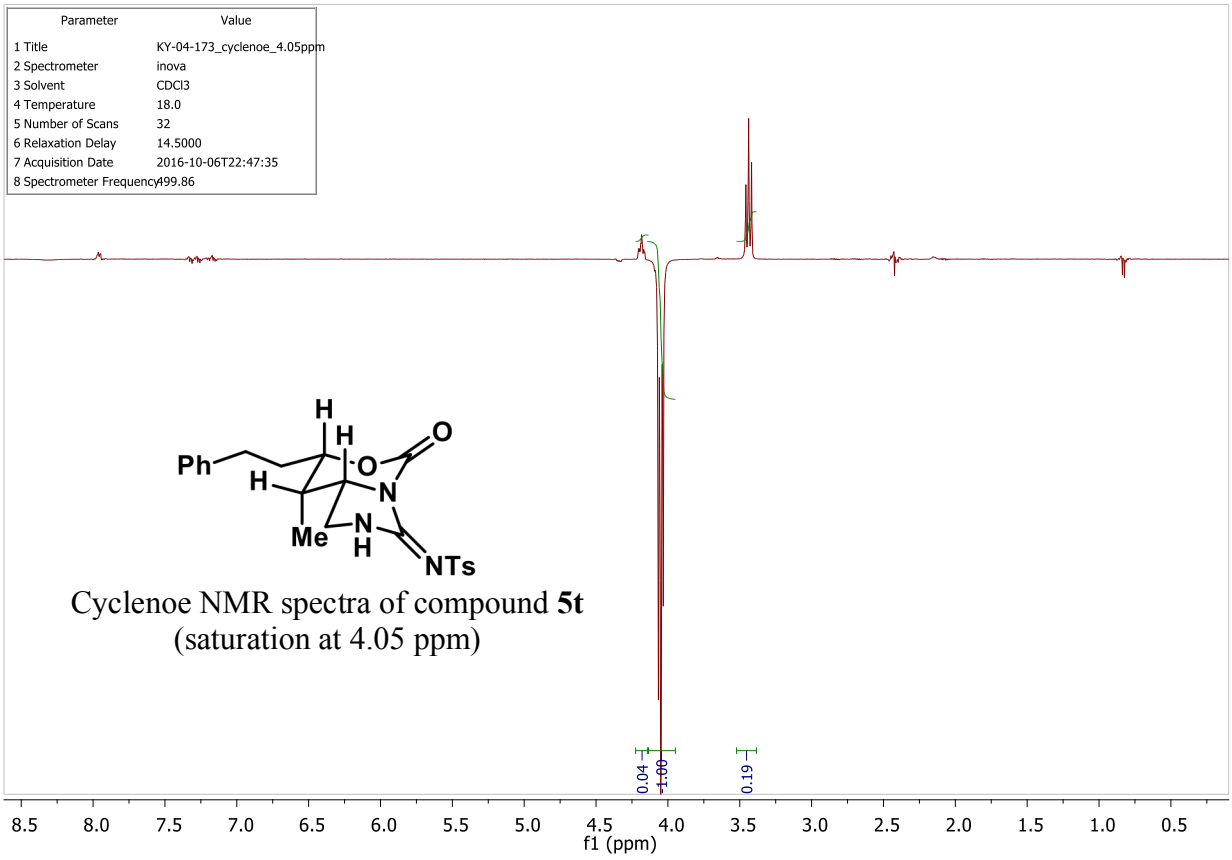




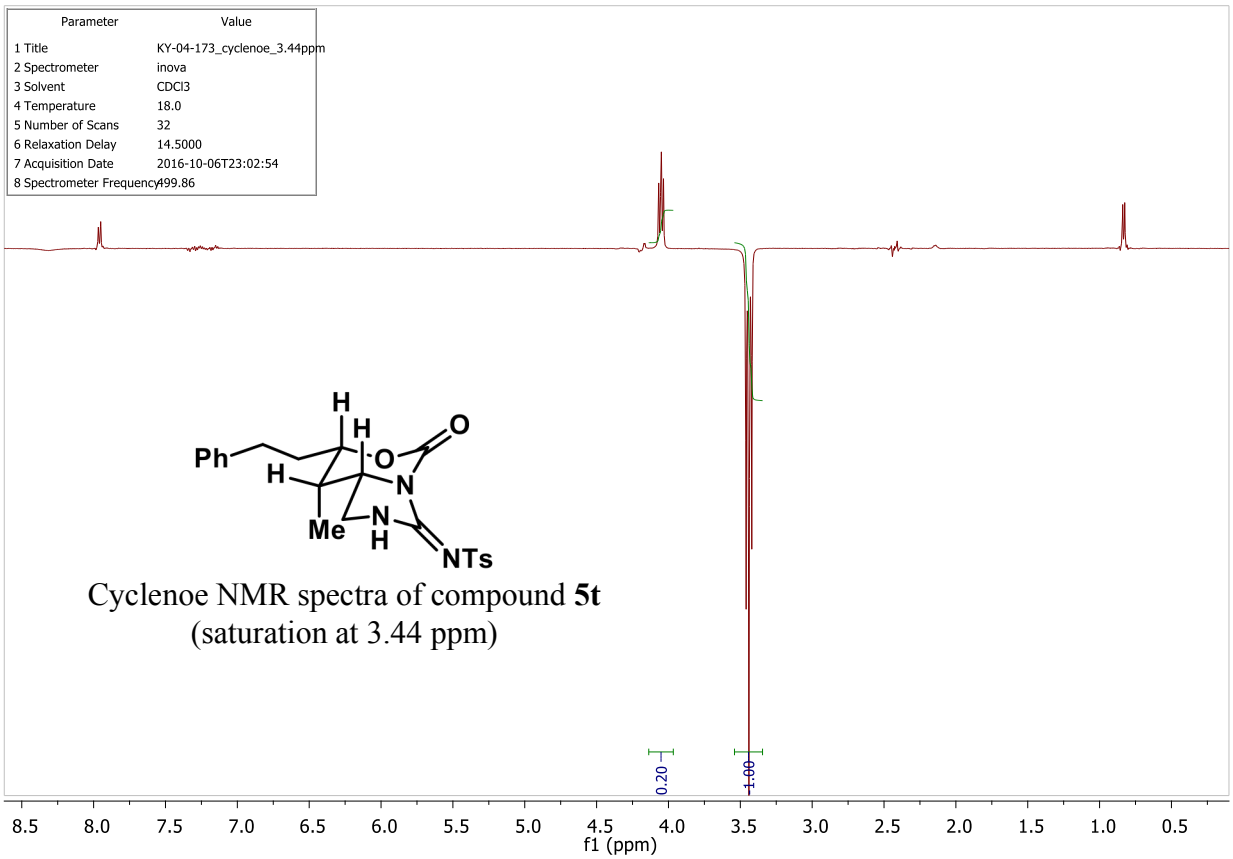
Cyclenoe NMR spectra of compound **5t**
(saturation at 4.34 ppm)



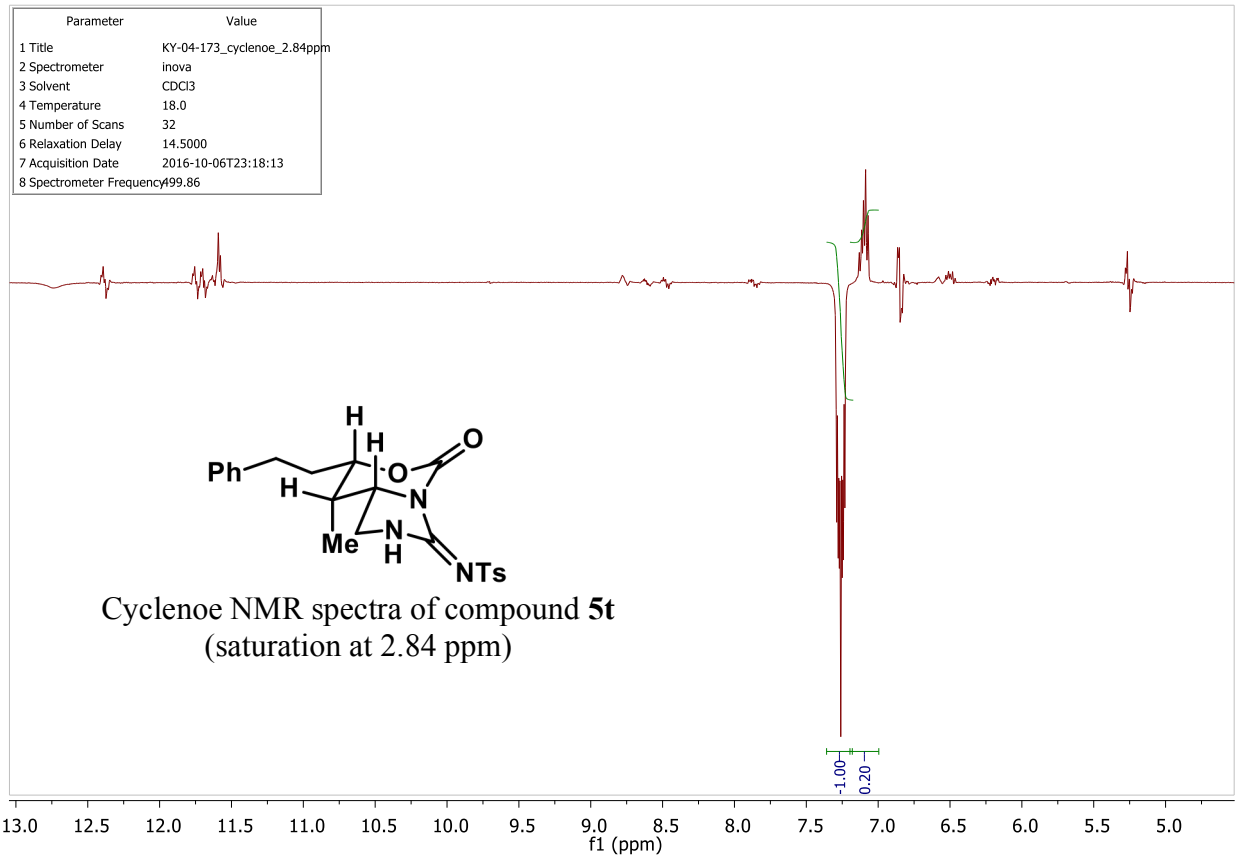
Cyclenoe NMR spectra of compound **5t**
(saturation at 4.19 ppm)



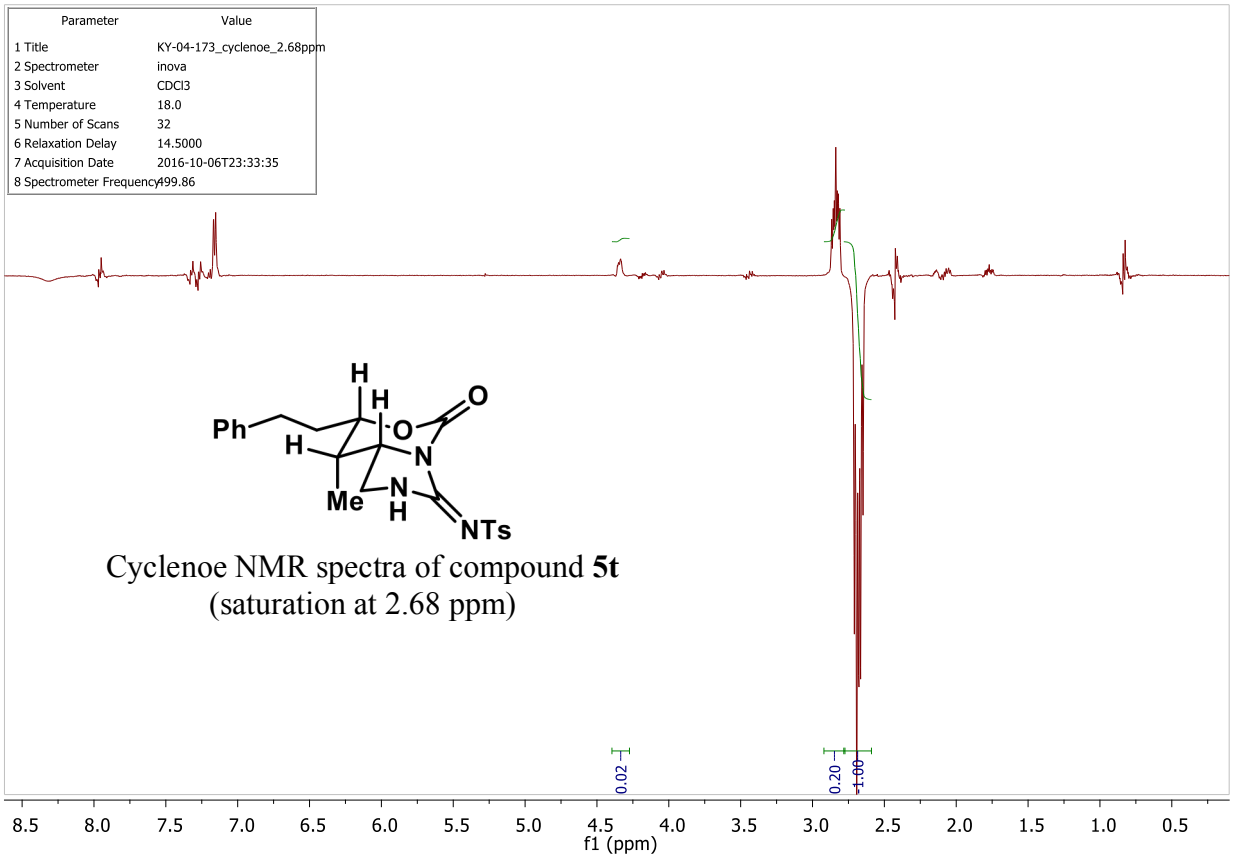
Cyclenoe NMR spectra of compound **5t**
(saturation at 4.05 ppm)



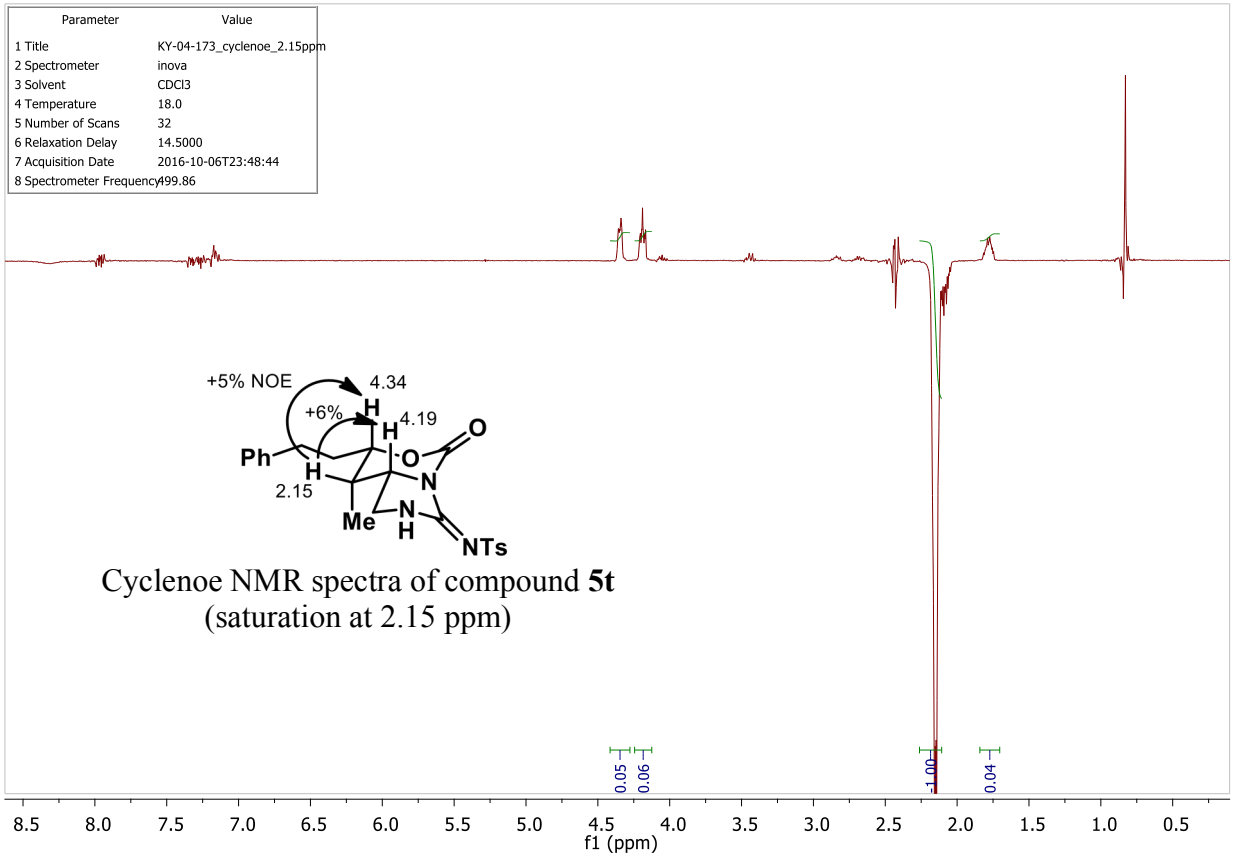
Cyclenoe NMR spectra of compound **5t**
(saturation at 3.44 ppm)



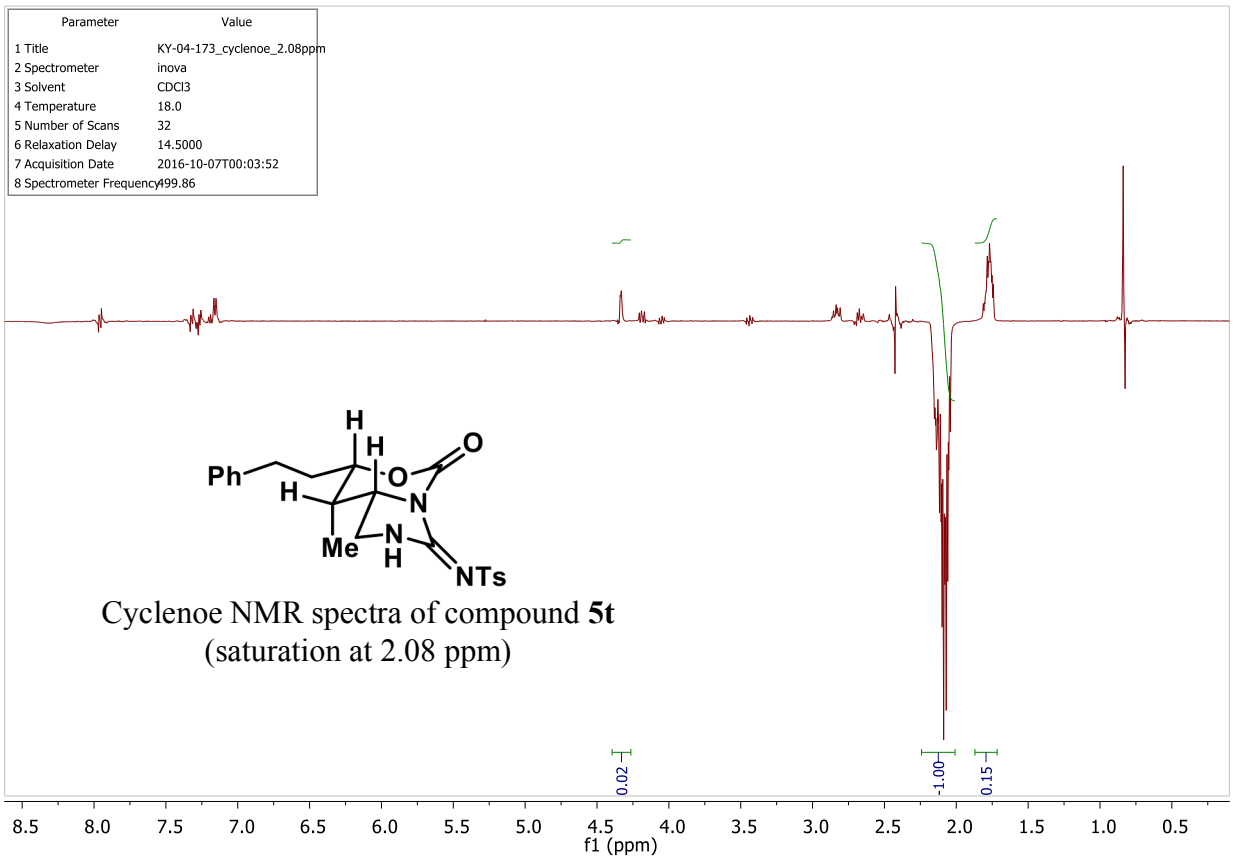
Cyclenoe NMR spectra of compound **5t**
(saturation at 2.84 ppm)



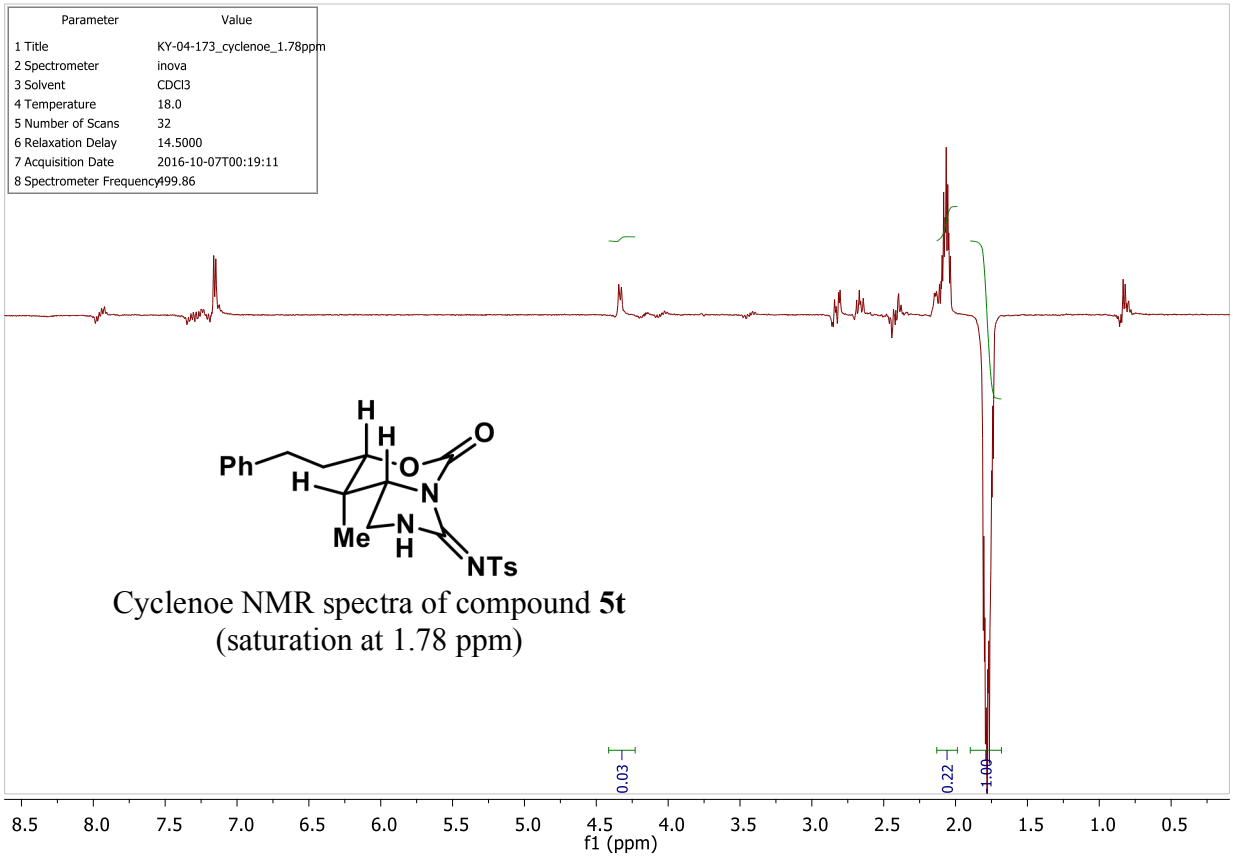
Cyclenoe NMR spectra of compound **5t**
(saturation at 2.68 ppm)



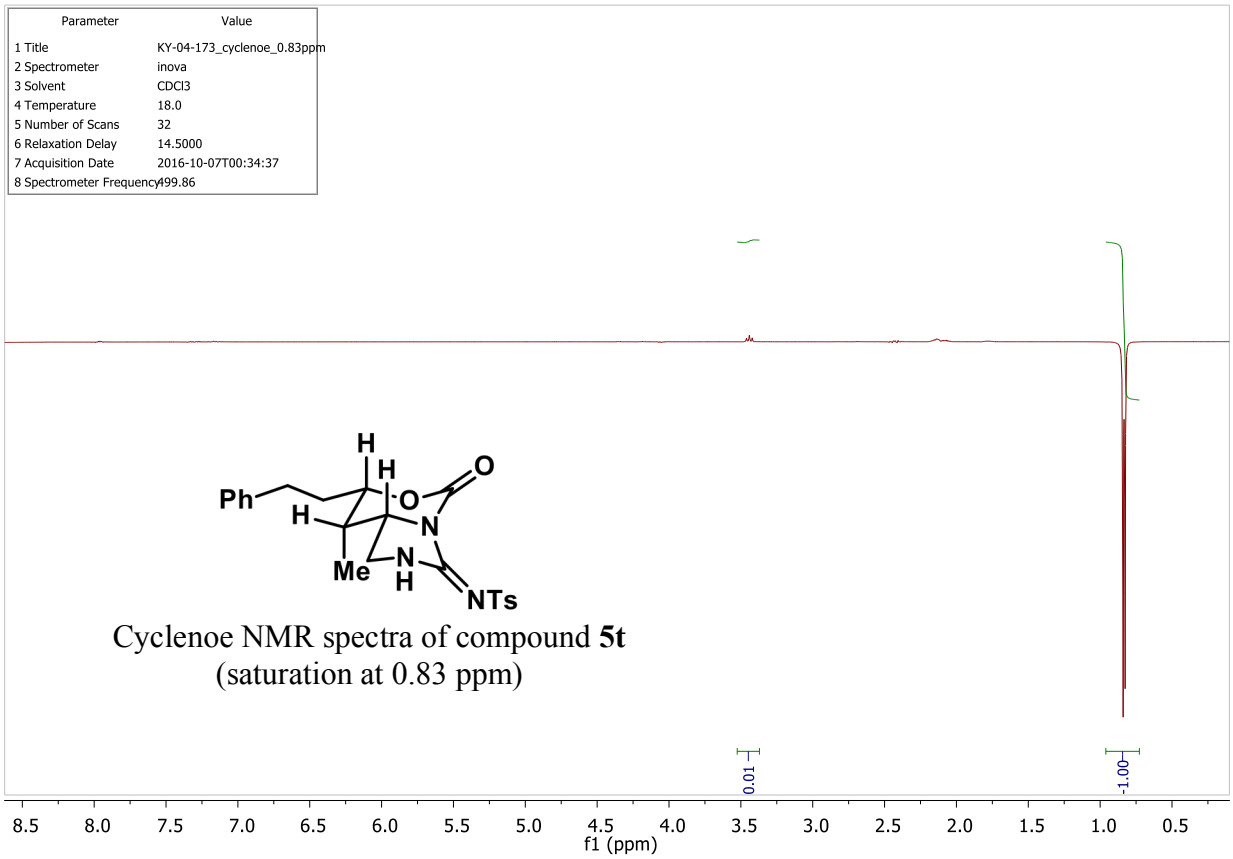
Cyclenoe NMR spectra of compound **5t**
(saturation at 2.15 ppm)



Cyclenoe NMR spectra of compound **5t**
(saturation at 2.08 ppm)

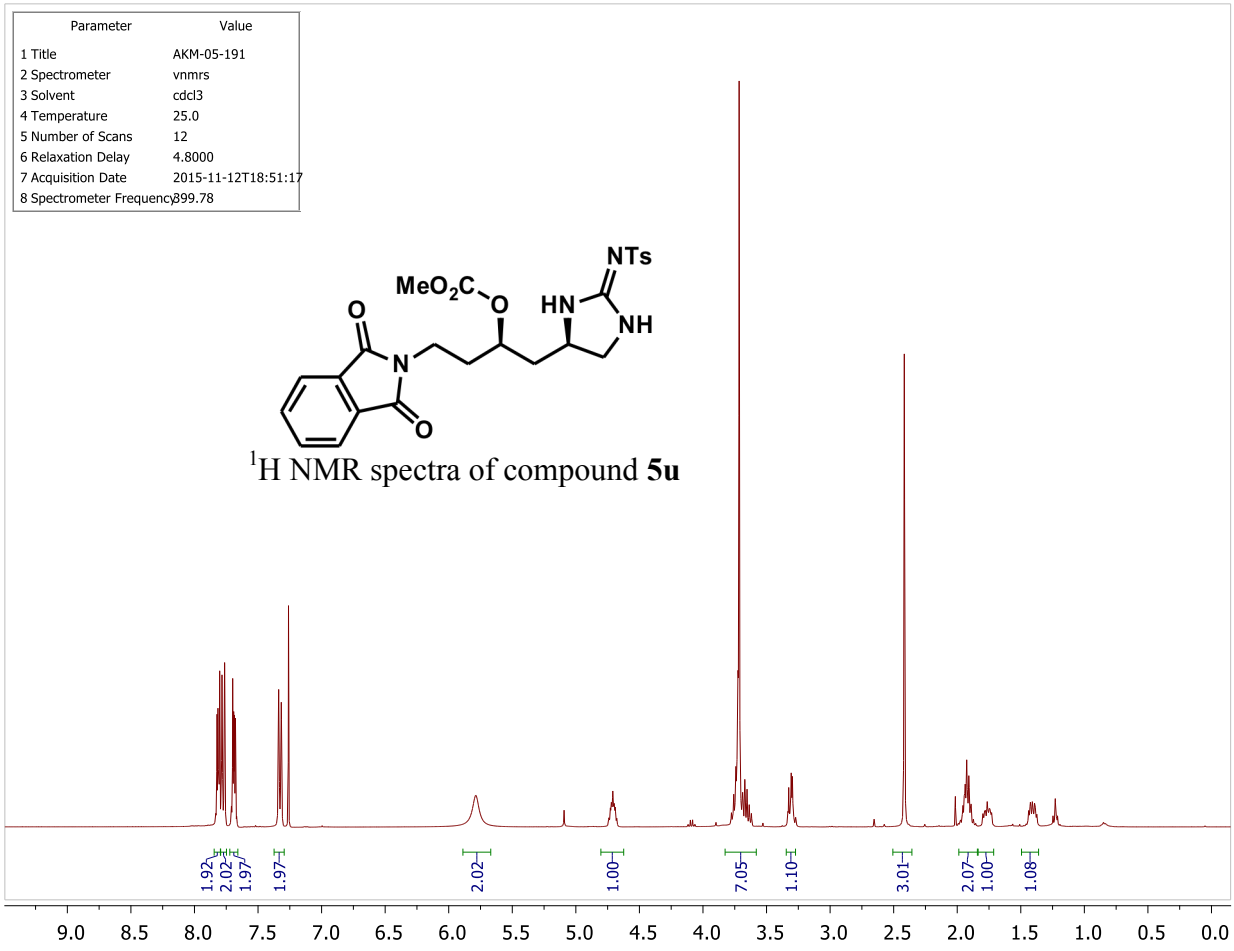


Cyclenoe NMR spectra of compound **5t**
(saturation at 1.78 ppm)

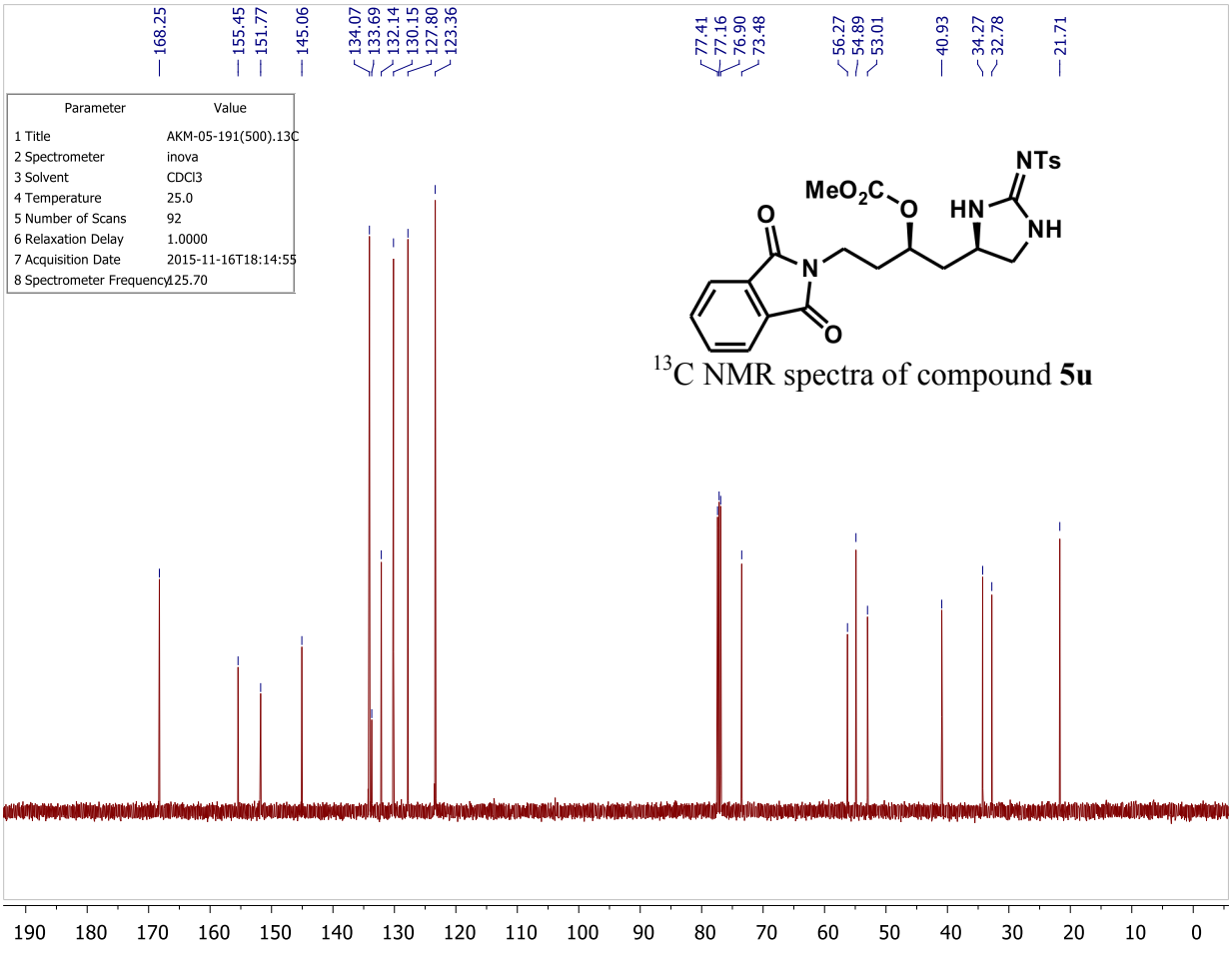


Cyclenoe NMR spectra of compound **5t**
(saturation at 0.83 ppm)

Parameter	Value
1 Title	AKM-05-191
2 Spectrometer	vnmrs
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-11-12T18:51:17
8 Spectrometer Frequency	399.78



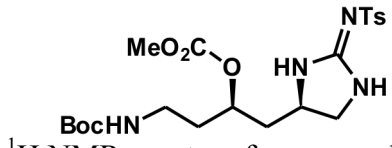
^{1}H NMR spectra of compound **5u**



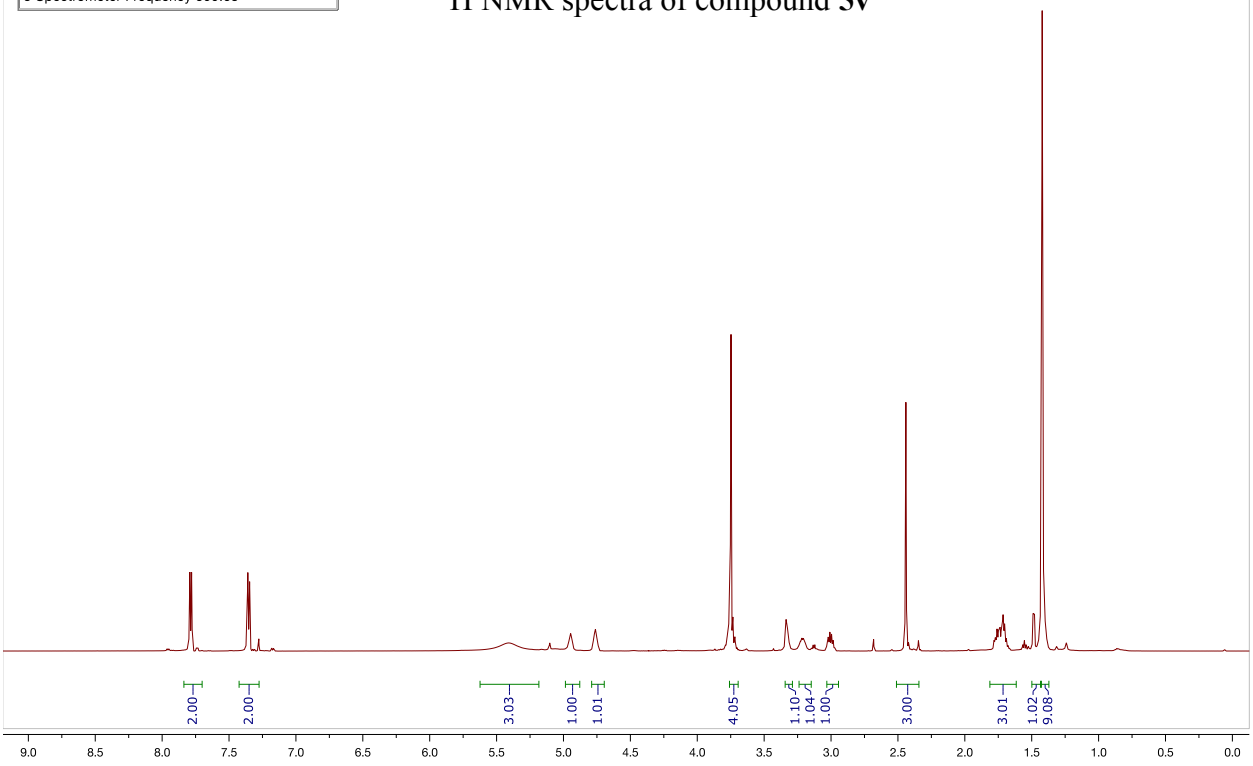
Parameter	Value
1 Title	AKM-05-191(500).13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	92
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-16T18:14:55
8 Spectrometer Frequency	125.70

^{13}C NMR spectra of compound **5u**

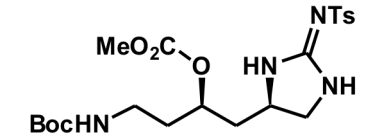
Parameter	Value
1 Title	jlc-1-090proton600
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-11-23T15:41:34
8 Spectrometer Frequency	599.63



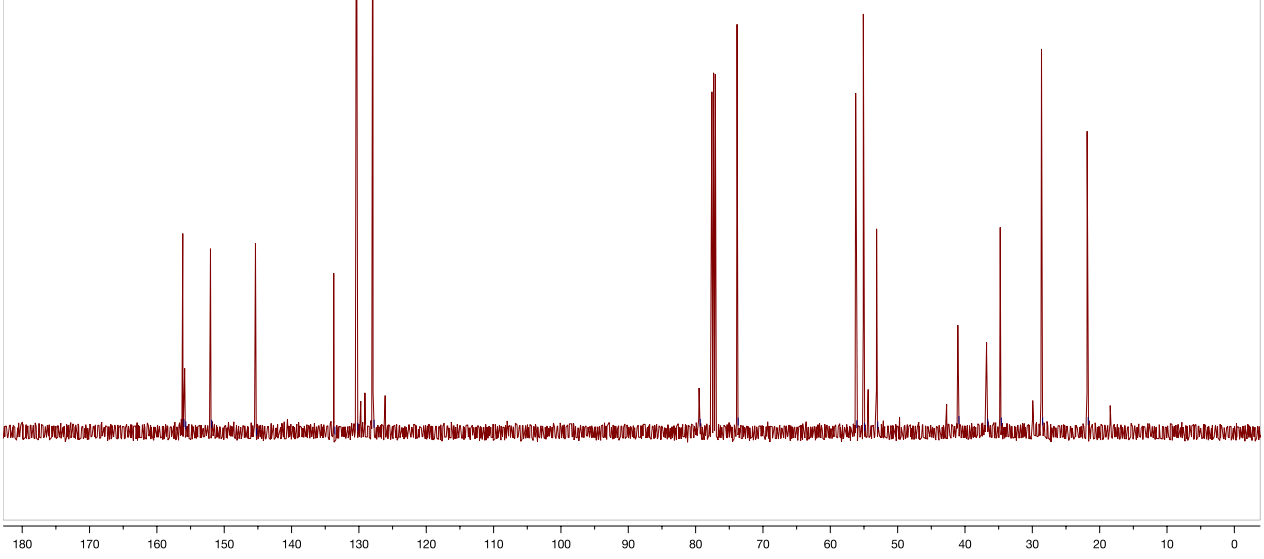
^{1}H NMR spectra of compound **5v**



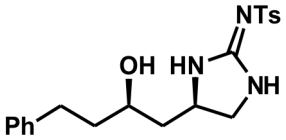
Parameter	Value
1 Title	jlc-1-090carbon1
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	232
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-25T12:29:03
8 Spectrometer Frequency	125.70



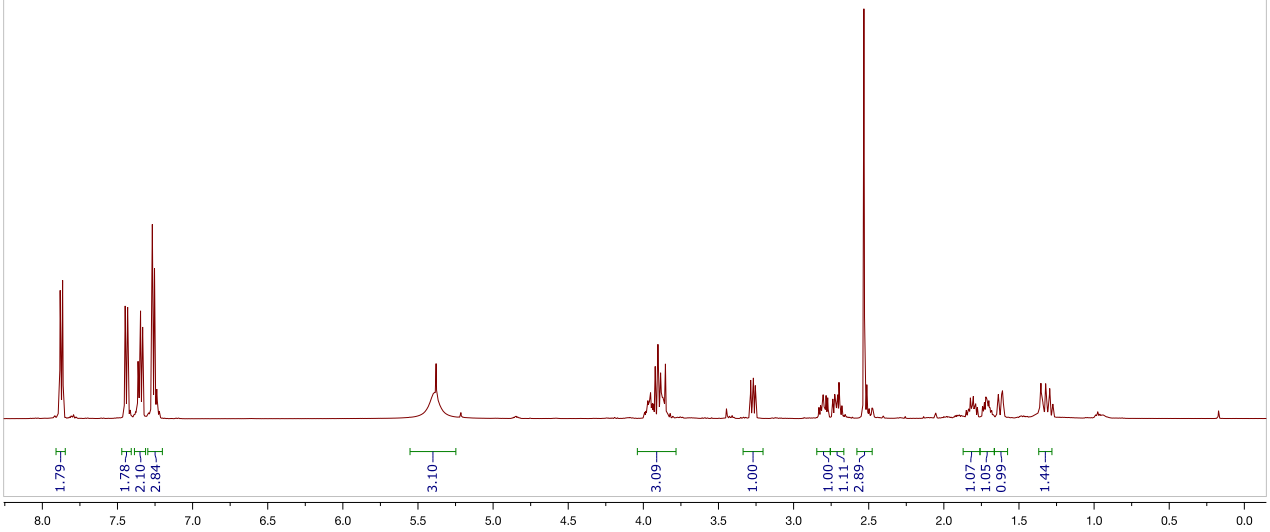
^{13}C NMR spectra of compound **5v**



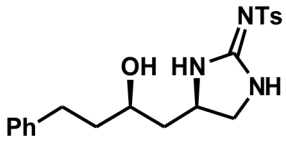
Parameter	Value
1 Title	jlc-1-085proton
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-11-16T14:39:49
8 Spectrometer Frequency	499.86



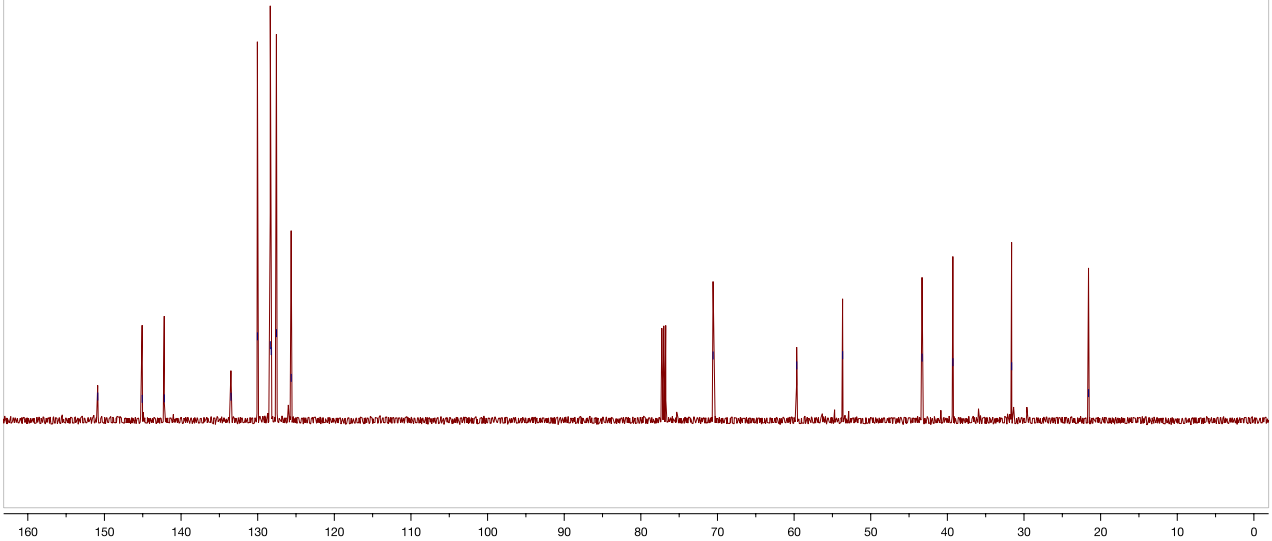
^{1}H NMR spectra of compound **6**



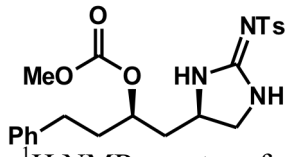
Parameter	Value
1 Title	jlc-1-085carbon
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	128
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-16T14:32:12
8 Spectrometer Frequency	125.70



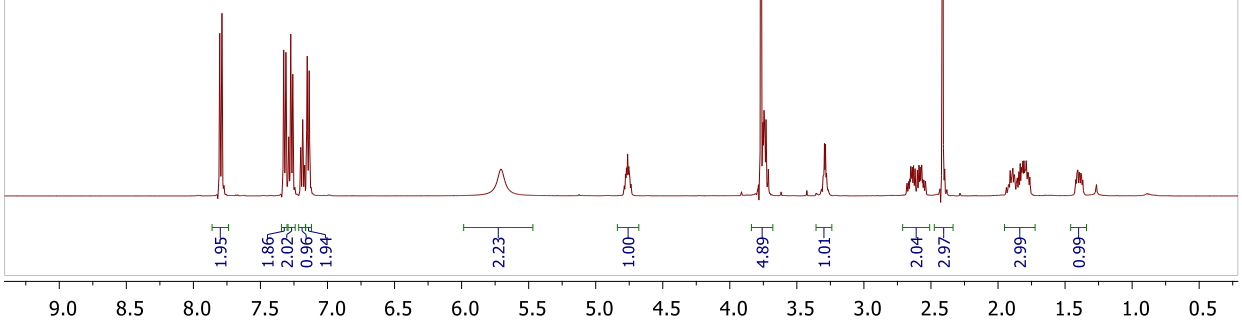
^{13}C NMR spectra of compound **6**



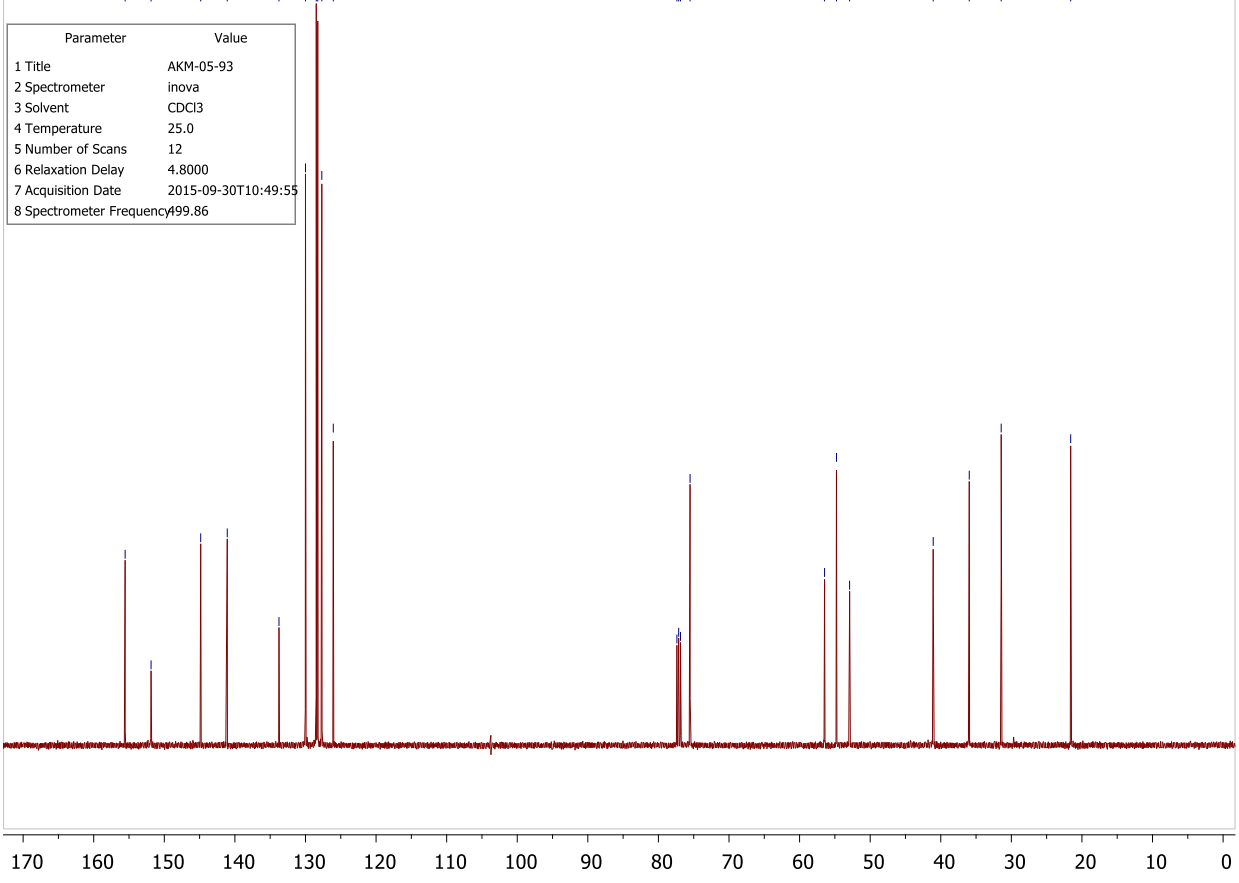
Parameter	Value
1 Title	AKM-05-93
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-09-30T10:49:55
8 Spectrometer Frequency	499.86



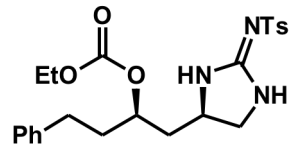
^{1}H NMR spectra of compound **7a**



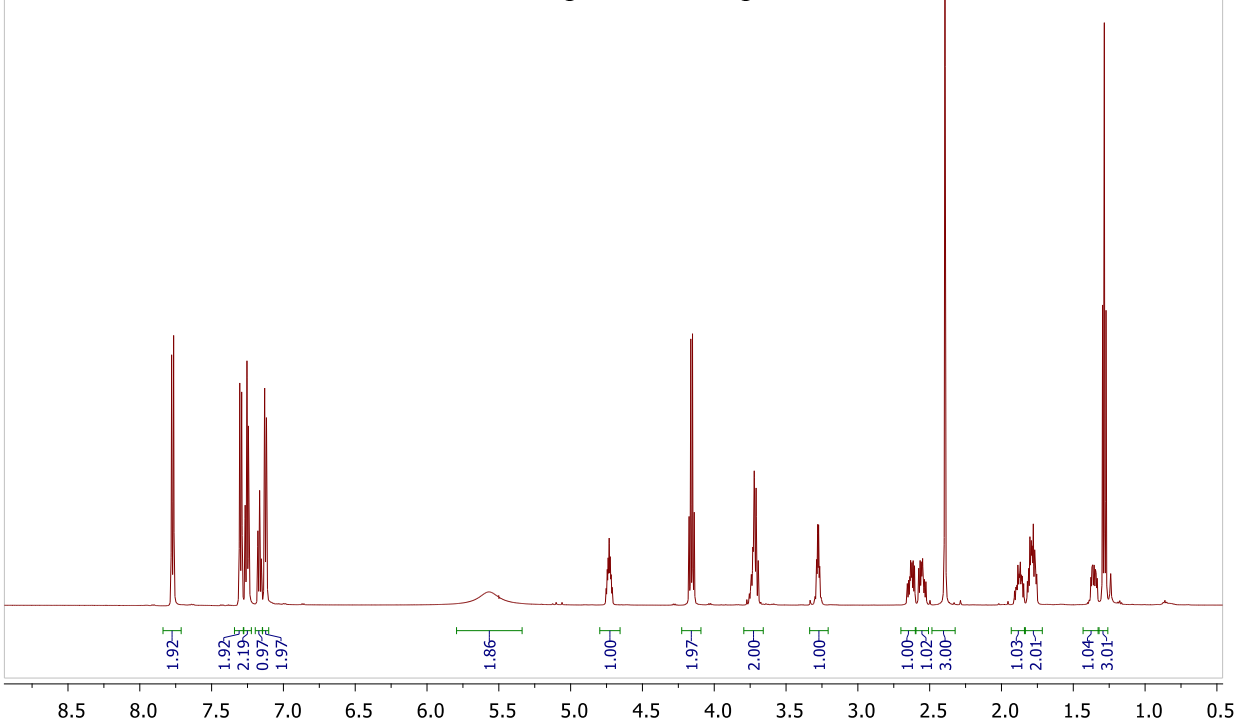
Parameter	Value
1 Title	AKM-05-93
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-09-30T10:49:55
8 Spectrometer Frequency	499.86

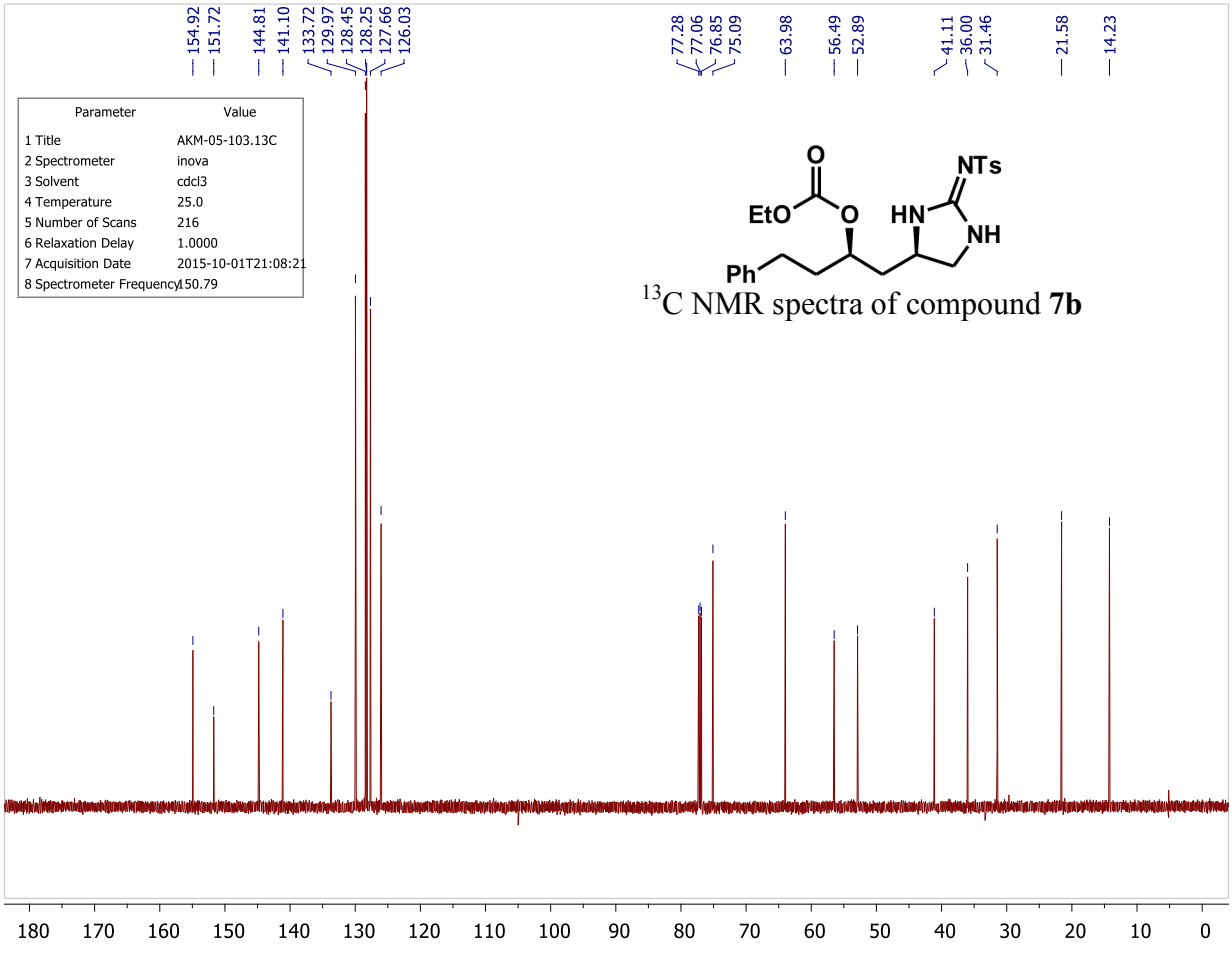


Parameter	Value
1 Title	AKM-05-103
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-01T21:04:51
8 Spectrometer Frequency	599.64



^{1}H NMR spectra of compound **7b**

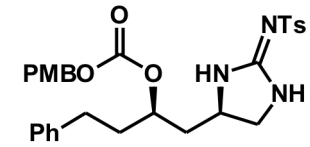




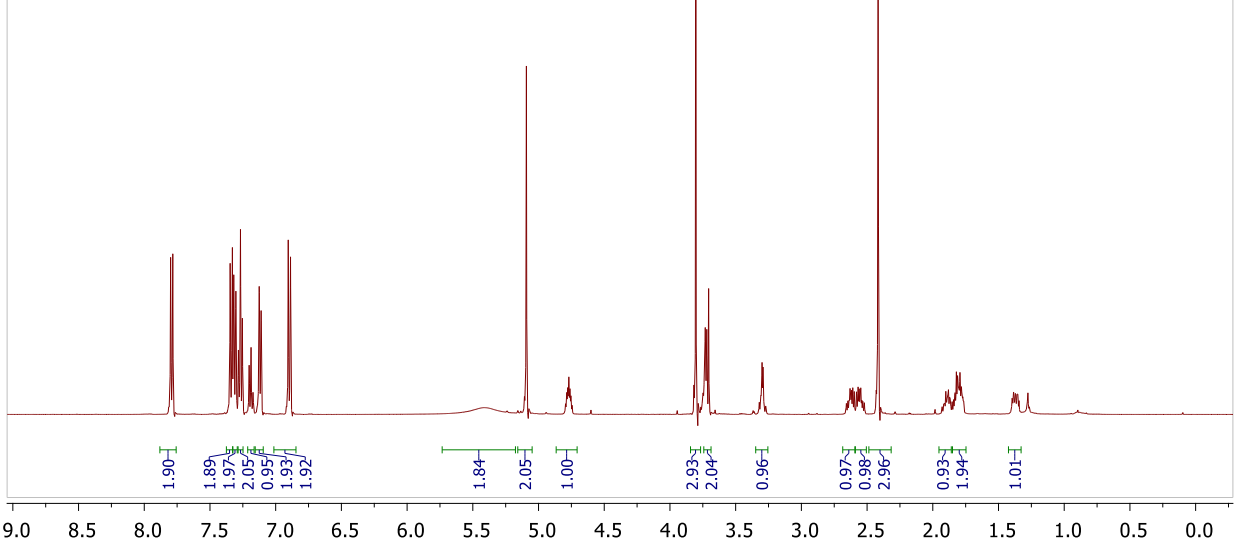
Parameter	Value
1 Title	AKM-05-103.13C
2 Spectrometer	inova
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	216
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-01T21:08:21
8 Spectrometer Frequency	150.79

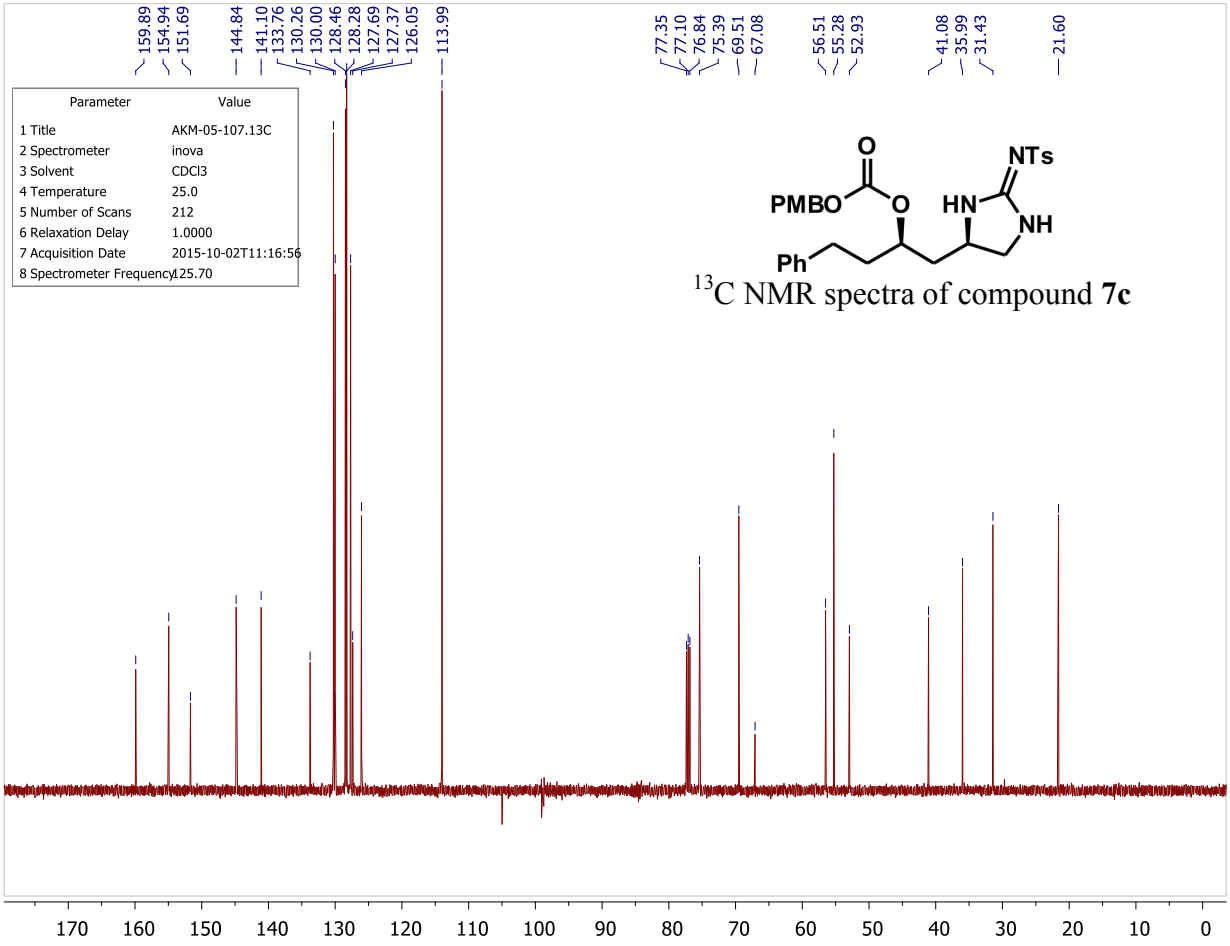
^{13}C NMR spectra of compound **7b**

Parameter	Value
1 Title	AKM-05-107
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	16
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-02T11:12:55
8 Spectrometer Frequency	499.86



^{1}H NMR spectra of compound **7c**

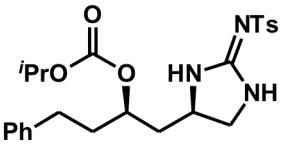




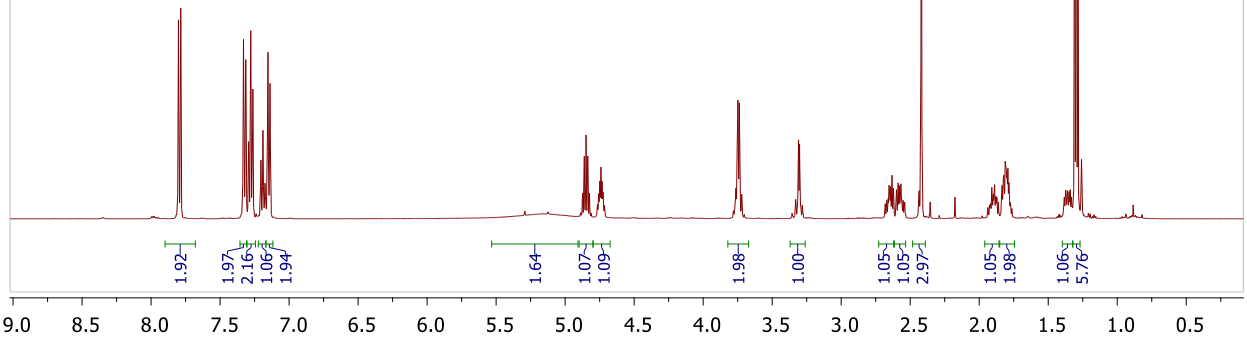
Parameter	Value
1 Title	AKM-05-107.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	212
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-02T11:16:56
8 Spectrometer Frequency	125.70

^{13}C NMR spectra of compound **7c**

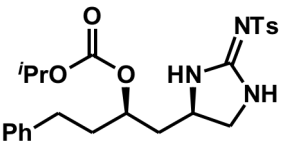
Parameter	Value
1 Title	AKM-05-105b
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	20
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-05T11:36:00
8 Spectrometer Frequency	499.86



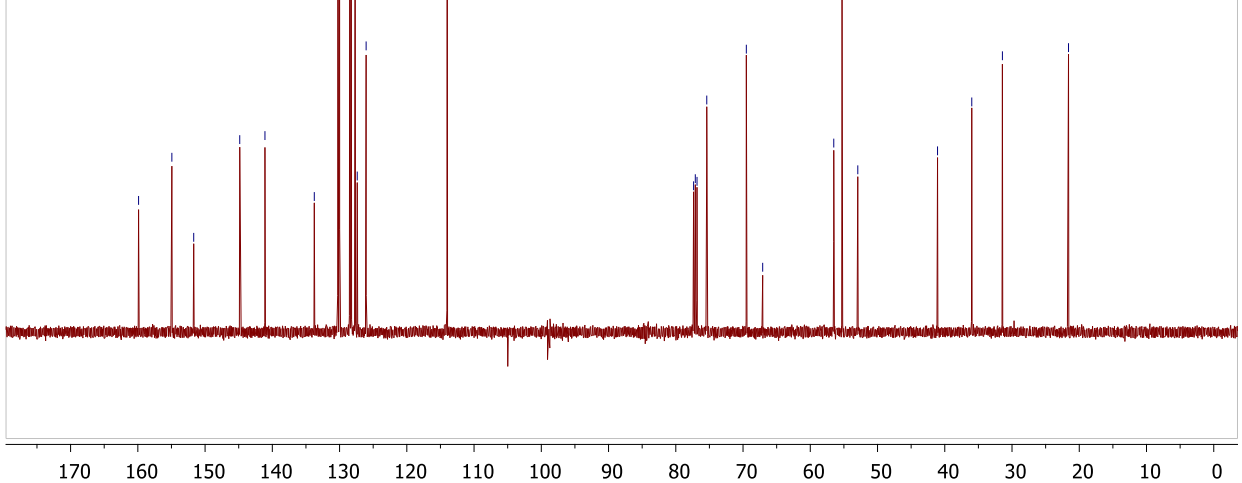
^{1}H NMR spectra of compound **7d**



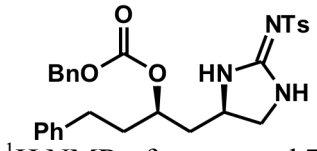
Parameter	Value
1 Title	AKM-05-107.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	212
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-02T11:16:56
8 Spectrometer Frequency	125.70



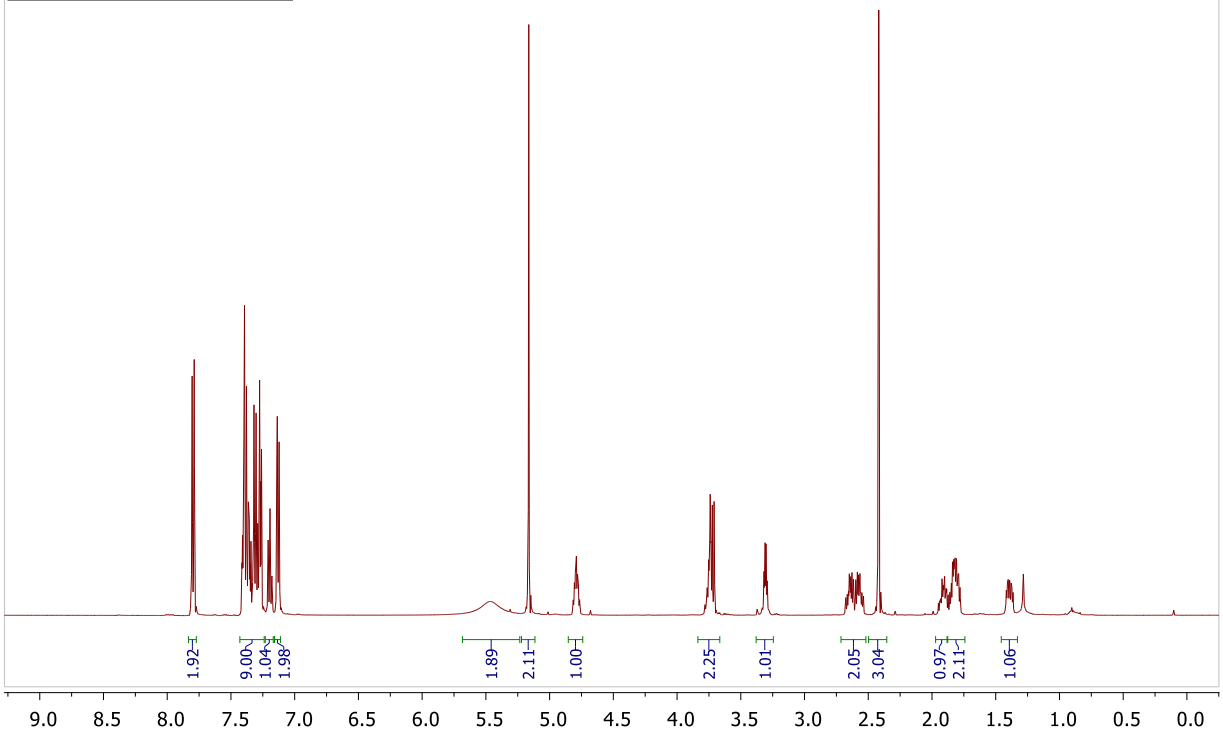
^{13}C NMR spectra of compound **7d**



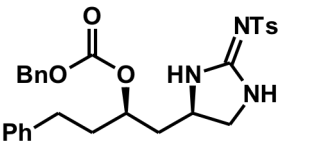
Parameter	Value
1 Title	AKM-05-106
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	20
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-02T11:27:32
8 Spectrometer Frequency	499.86



^{1}H NMR of compound **7e**

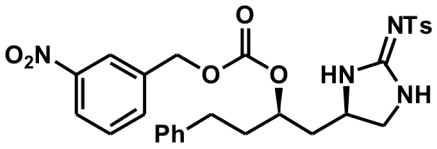


Parameter	Value
1 Title	AKM-05-106.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	172
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-02T11:31:28
8 Spectrometer Frequency	125.70

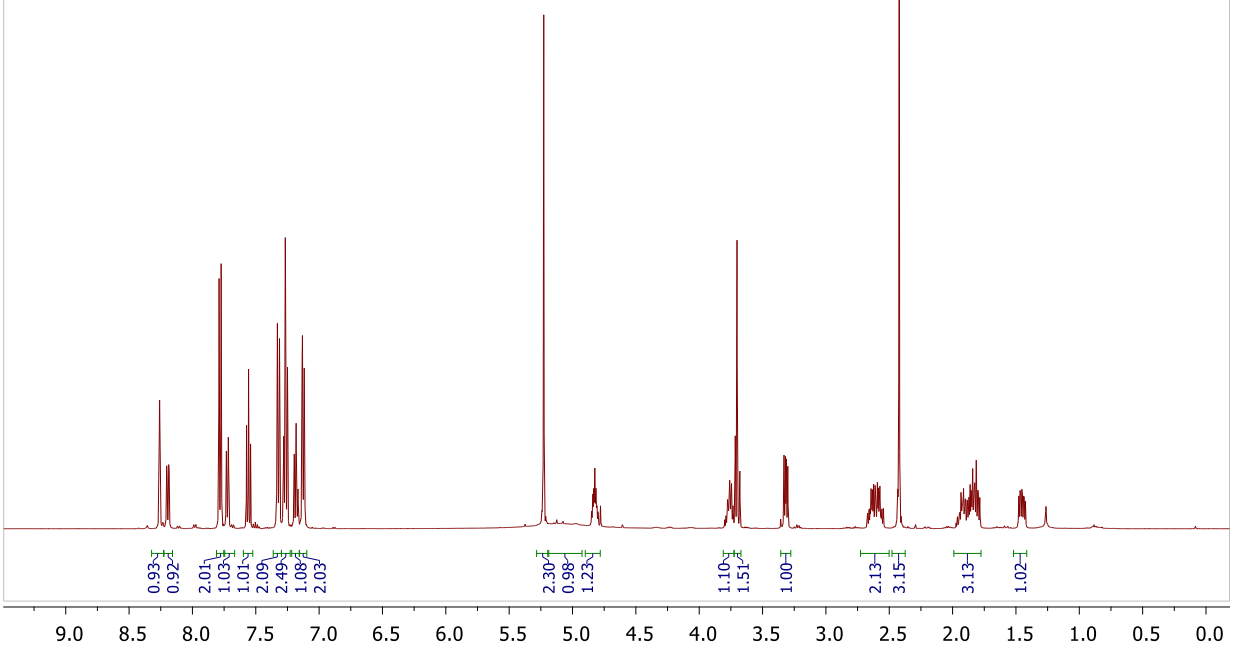


^{13}C NMR of compound **7e**

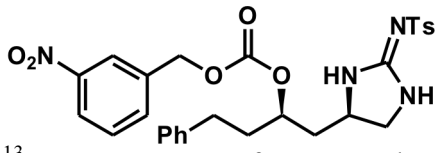
Parameter	Value
1 Title	AKM-05-108
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	28
6 Relaxation Delay	4.8000
7 Acquisition Date	2015-10-02T11:40:34
8 Spectrometer Frequency	499.86



^{1}H NMR spectra of compound **7f**

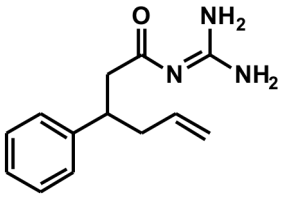


Parameter	Value
1 Title	AKM-05-108.13C
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	328
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-02T11:45:28
8 Spectrometer Frequency	125.70

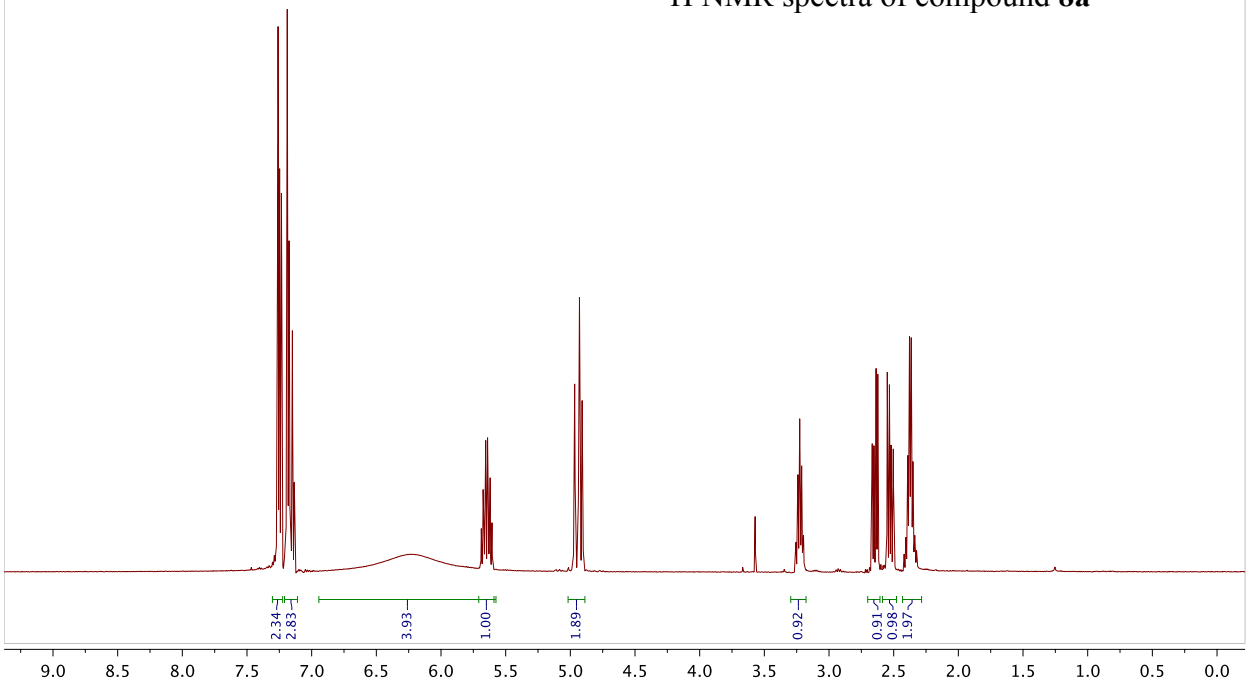


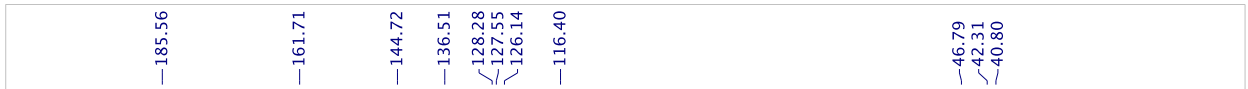
^{13}C NMR spectra of compound **7f**

Parameter	Value
1 Title	ky-4-209-a-SI
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	4.8000
7 Acquisition Date	2016-03-29T12:34:58
8 Spectrometer Frequency	499.86

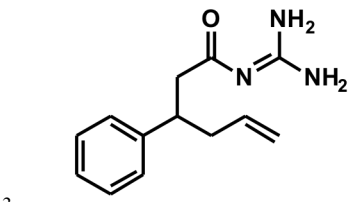


^{1}H NMR spectra of compound **8a**

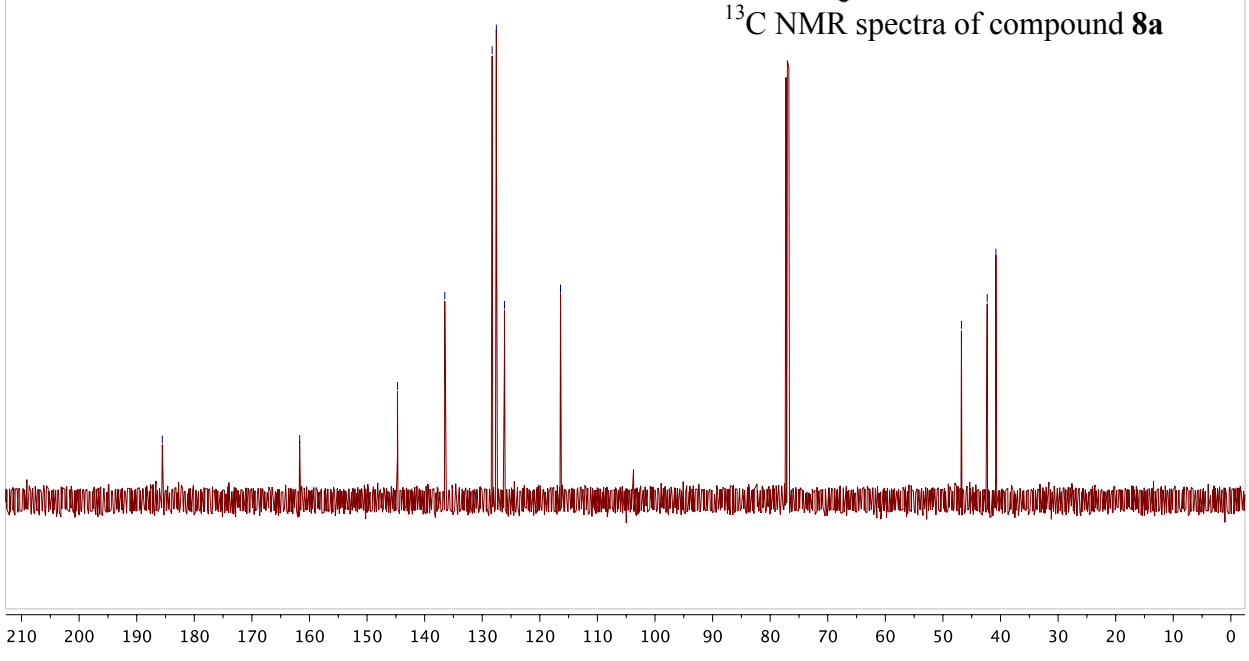




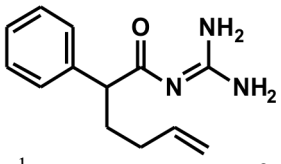
Parameter	Value
1 Title	ky-4-209-a-SI-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	-20.0
5 Number of Scans	148
6 Relaxation Delay	1.0000
7 Acquisition Date	2016-03-29T12:37:18
8 Spectrometer Frequency	125.70



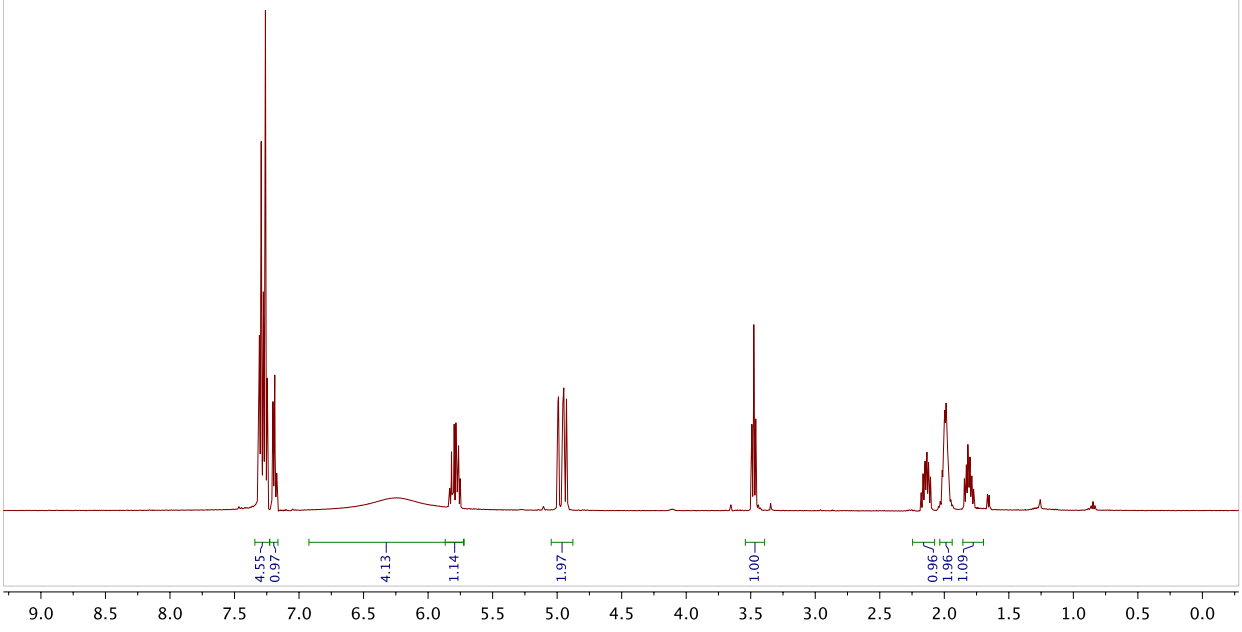
^{13}C NMR spectra of compound **8a**



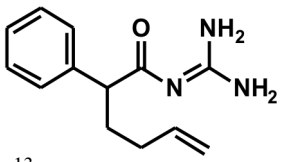
Parameter	Value
1 Title	ky-4-193-a
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-10-30T08:49:57
8 Spectrometer Frequency	499.86



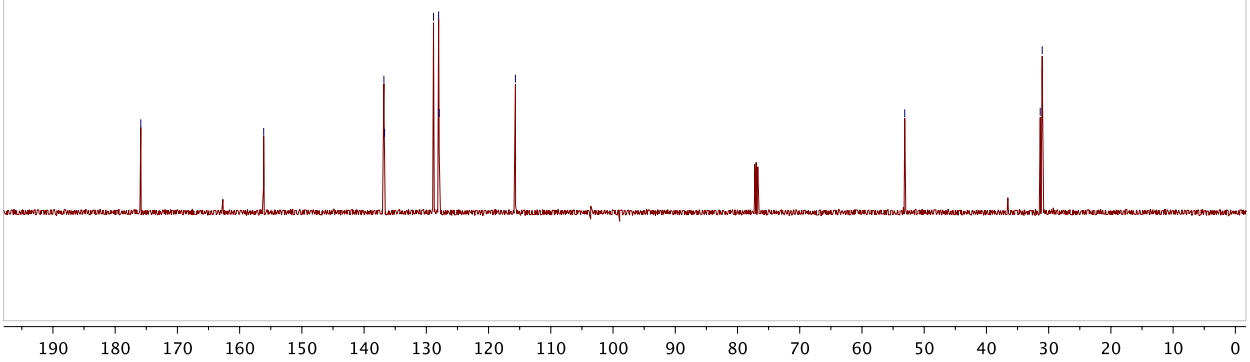
^{1}H NMR spectra of compound **8b**



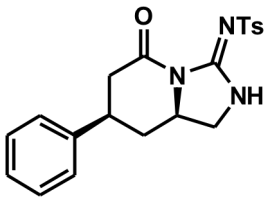
Parameter	Value
1 Title	ky-4-193-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	32
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-10-29T12:52:45
8 Spectrometer Frequency	125.70



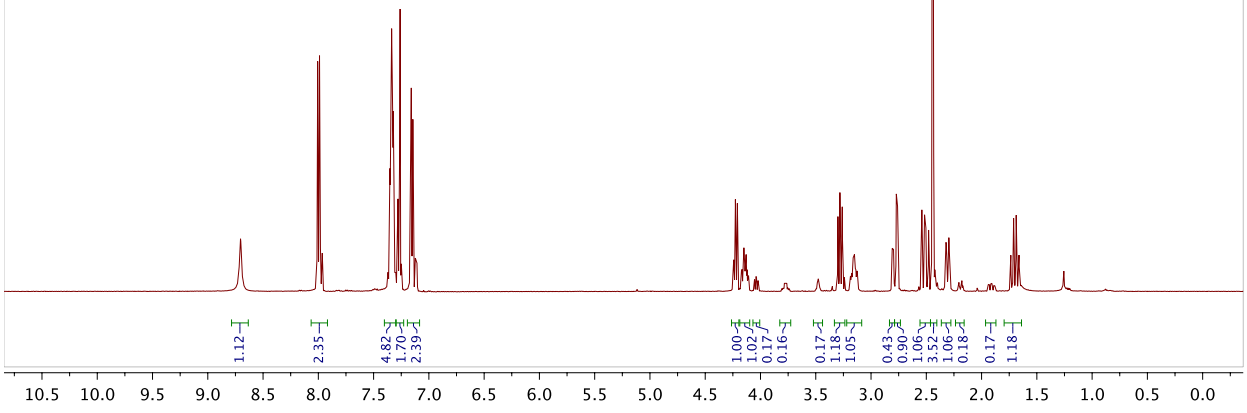
^{13}C NMR spectra of compound **8b**



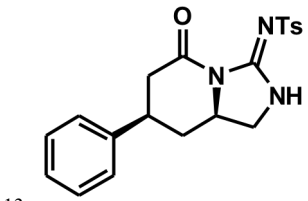
Parameter	Value
1 Title	ky-4-210-a-2
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	16.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-11-06T09:12:42
8 Spectrometer Frequency	499.86



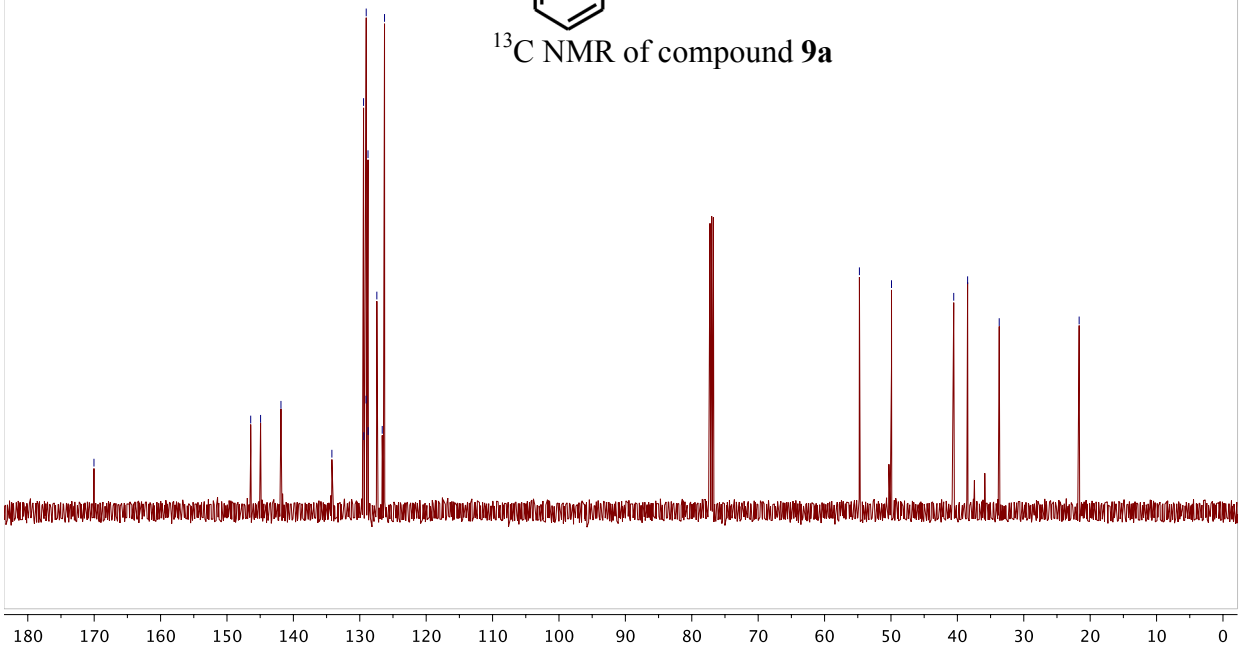
^{1}H NMR of compound **9a**

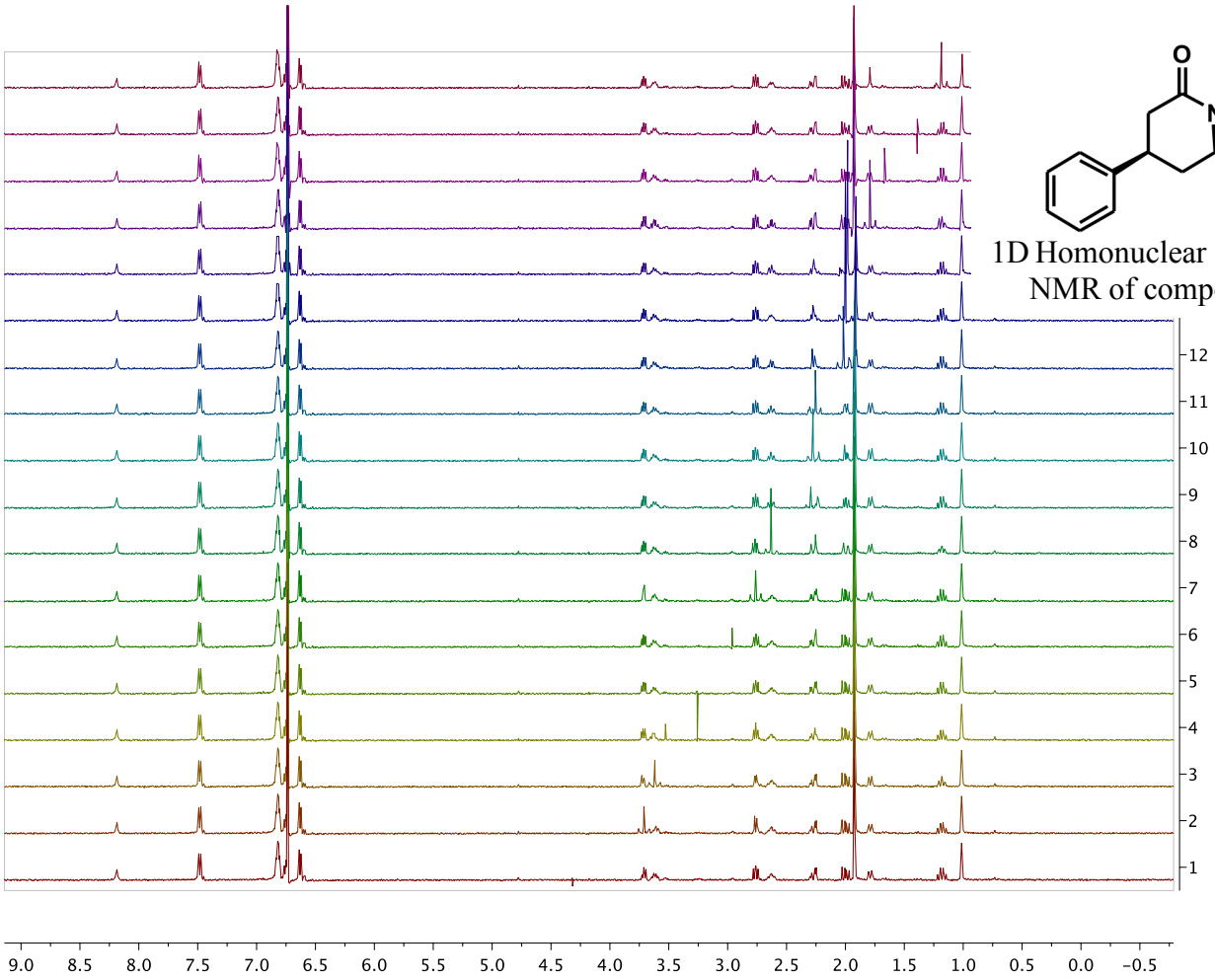


Parameter	Value
1 Title	ky-4-210-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	16.0
5 Number of Scans	124
6 Relaxation Delay	1.0000
7 Acquisition Date	2015-11-06T09:14:14
8 Spectrometer Frequency	125.70

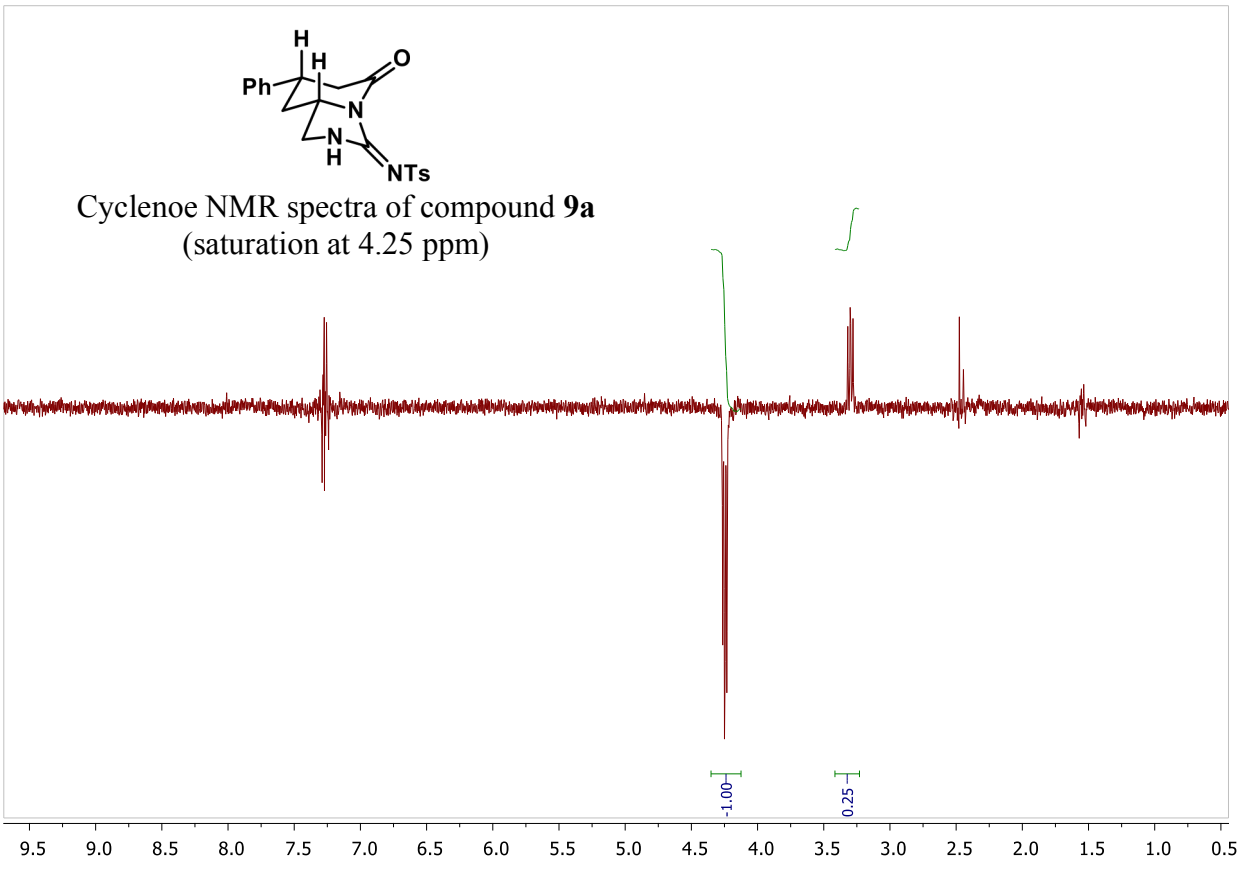


^{13}C NMR of compound **9a**

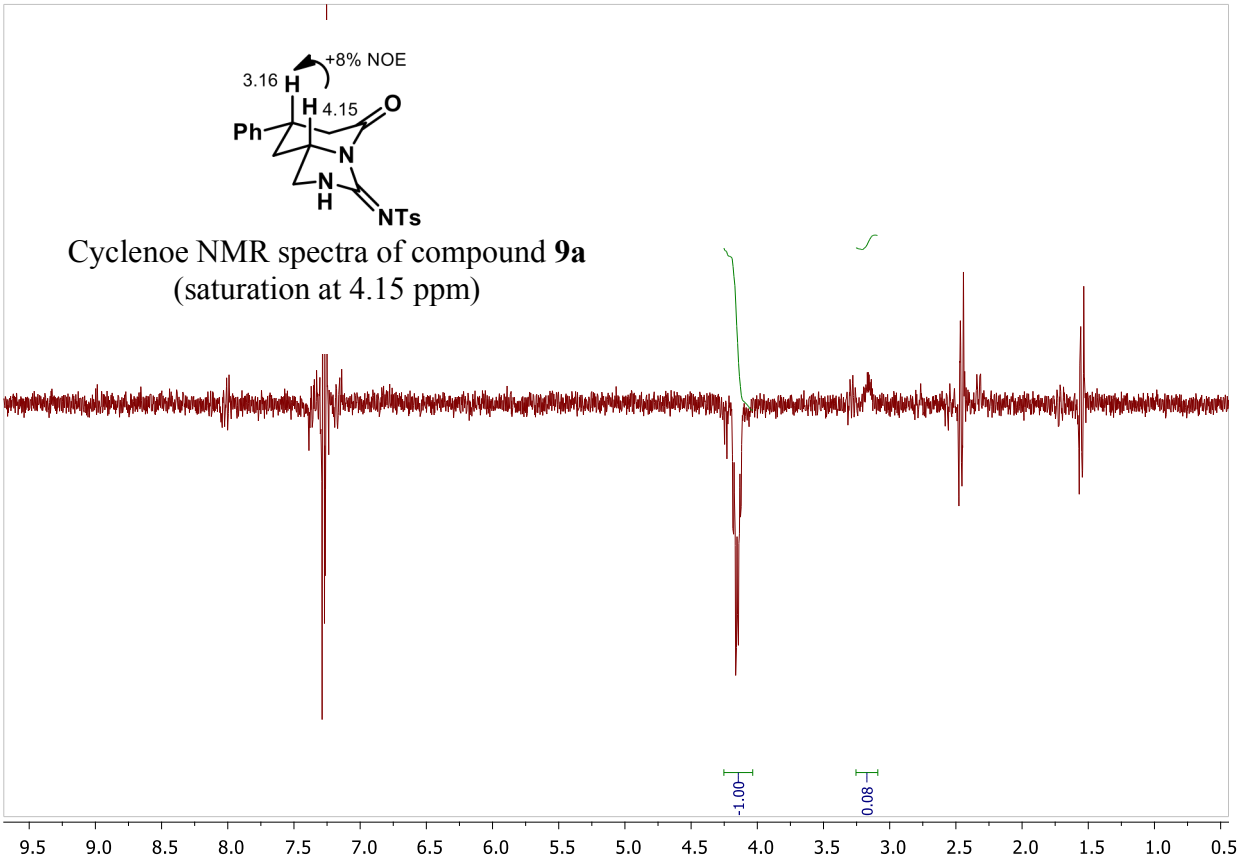




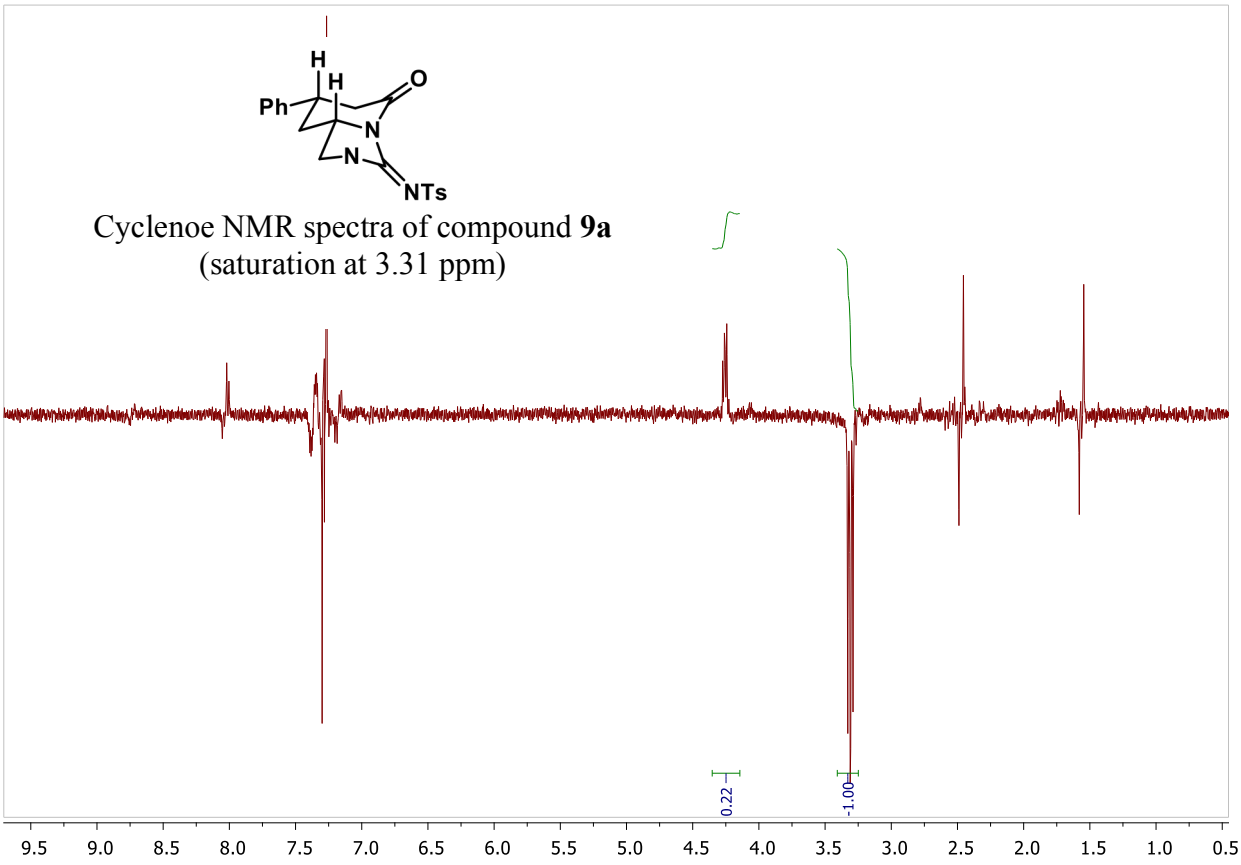
1D Homonuclear decoupling NMR of compound **9a**



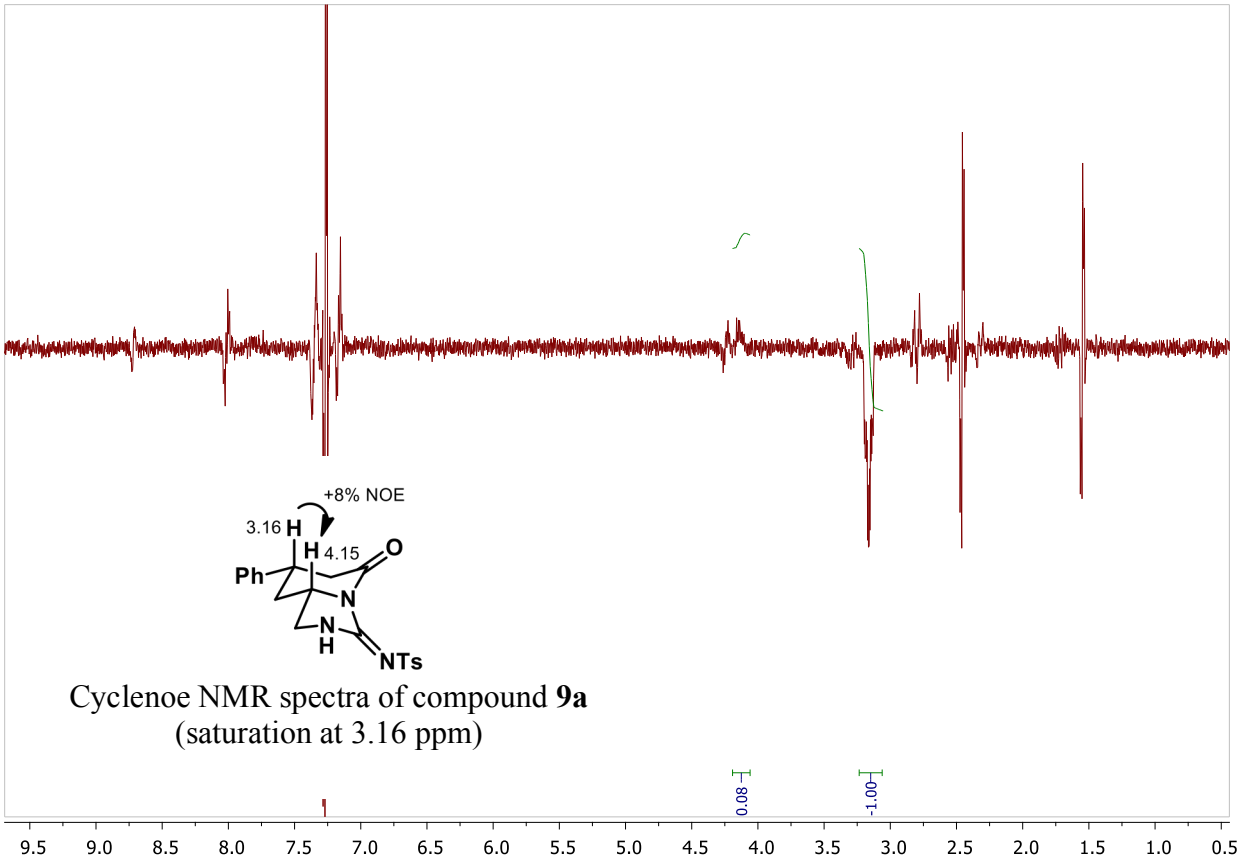
Cyclenoe NMR spectra of compound **9a** (saturation at 4.25 ppm)



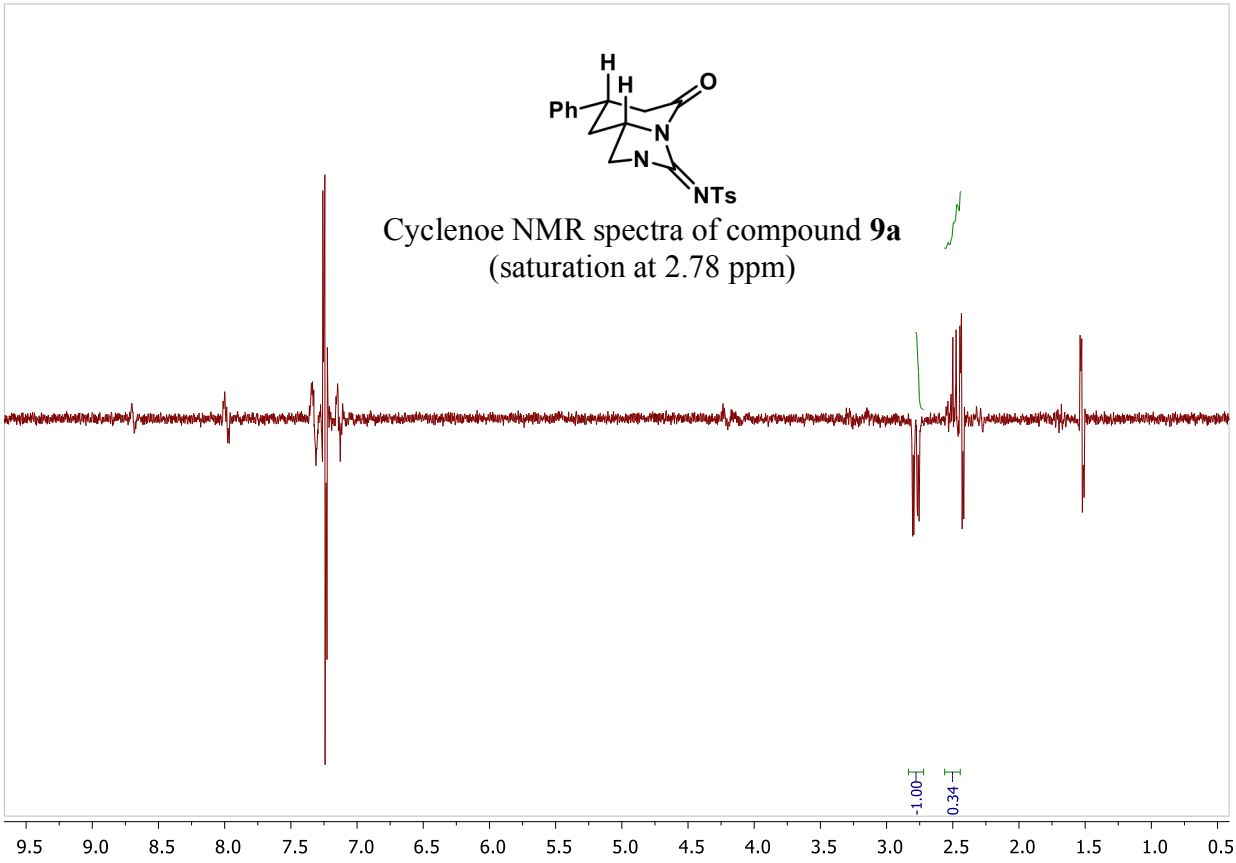
Cyclenoe NMR spectra of compound **9a**
(saturation at 4.15 ppm)



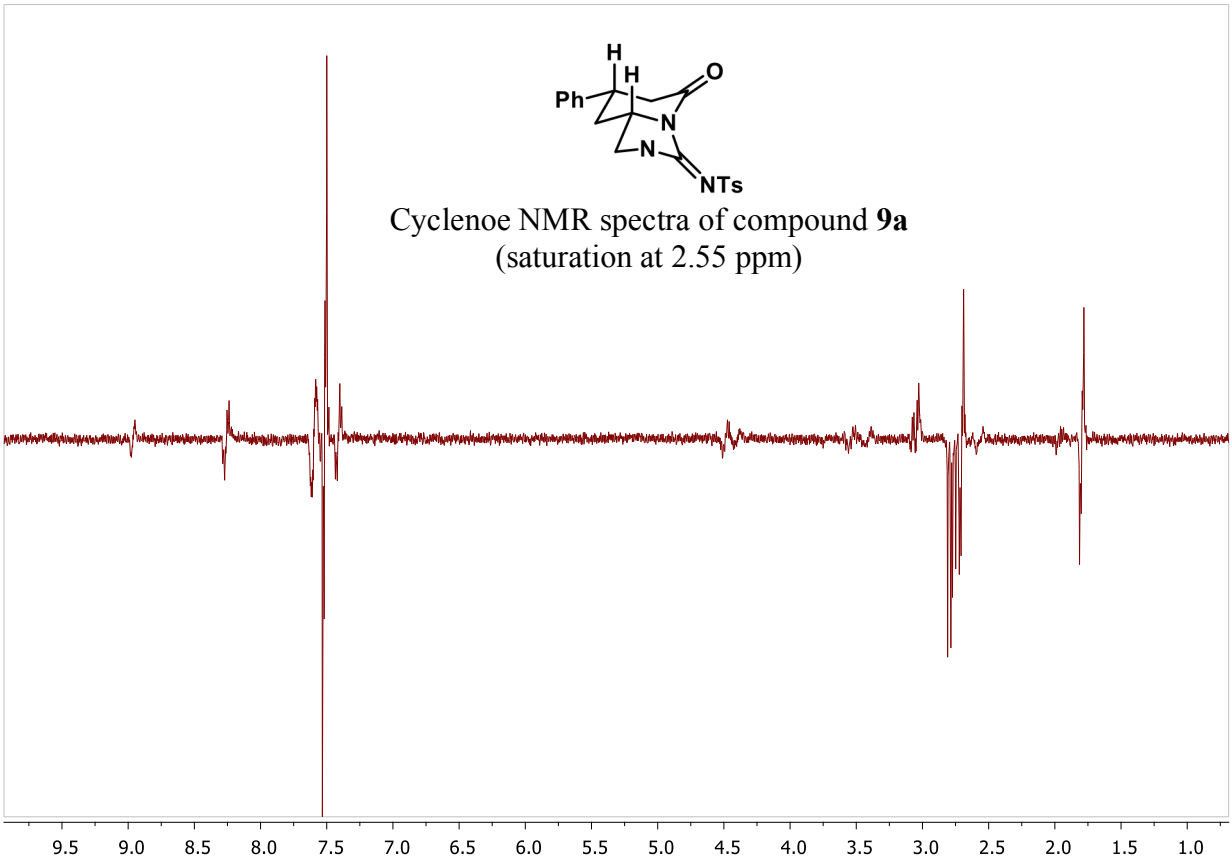
Cyclenoe NMR spectra of compound **9a**
(saturation at 3.31 ppm)

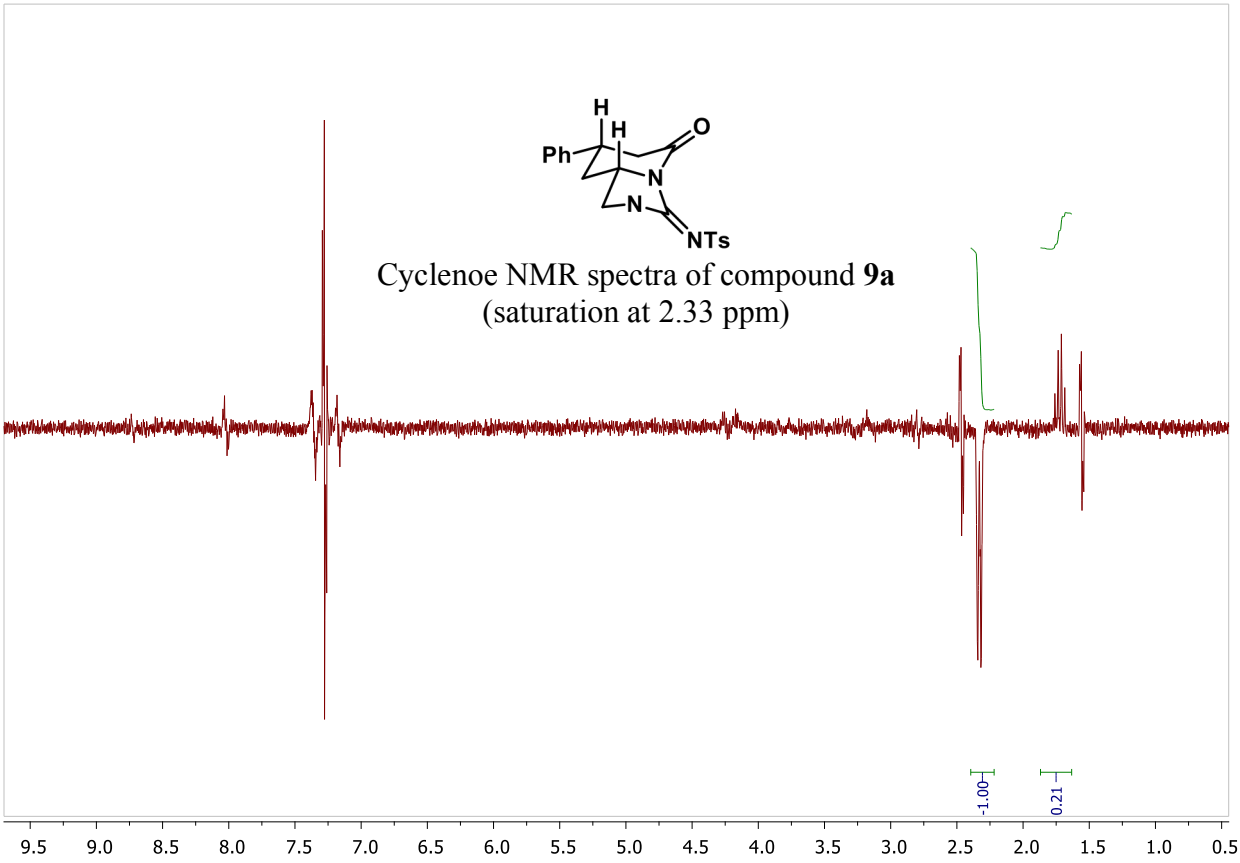


Cyclenoe NMR spectra of compound **9a**
(saturation at 3.16 ppm)

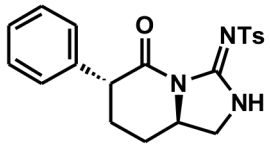


Cyclenoe NMR spectra of compound **9a**
(saturation at 2.78 ppm)


H
H
O
Ph
N
N
NTs
Cyclenoe NMR spectra of compound **9a**
(saturation at 2.55 ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0

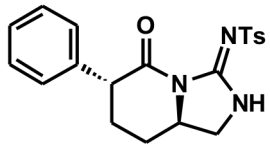

H
H
O
Ph
N
N
NTs
Cyclenoe NMR spectra of compound **9a**
(saturation at 2.33 ppm)
-1.00
0.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

Parameter	Value
1 Title	ky-4-207-a
2 Spectrometer	vnmrs
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	8
6 Relaxation Delay	8.0000
7 Acquisition Date	2015-11-02T18:06:51
8 Spectrometer Frequency	399.78

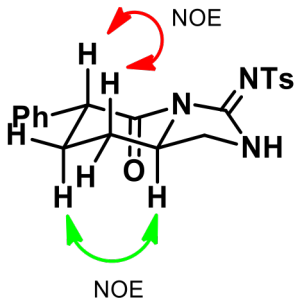


^{1}H NMR of compound **9b**

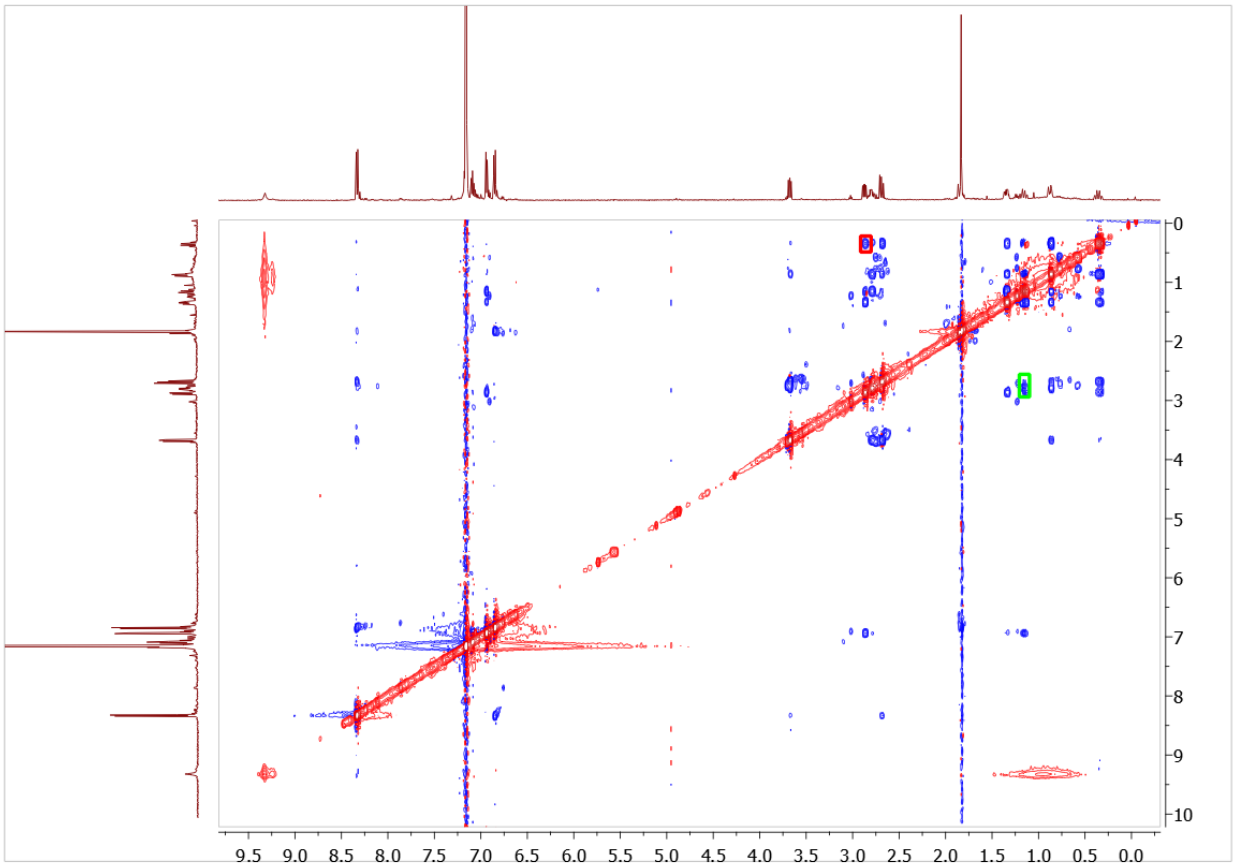
Parameter	Value
1 Title	ky-4-207-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	904
6 Relaxation Delay	1.0000
7 Acquisition Date	2016-05-05T18:12:55
8 Spectrometer Frequency	125.70

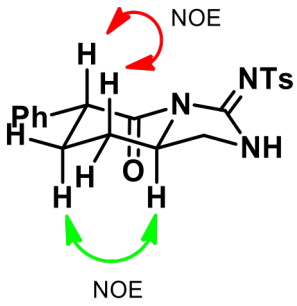


^{13}C NMR of compound **9b**

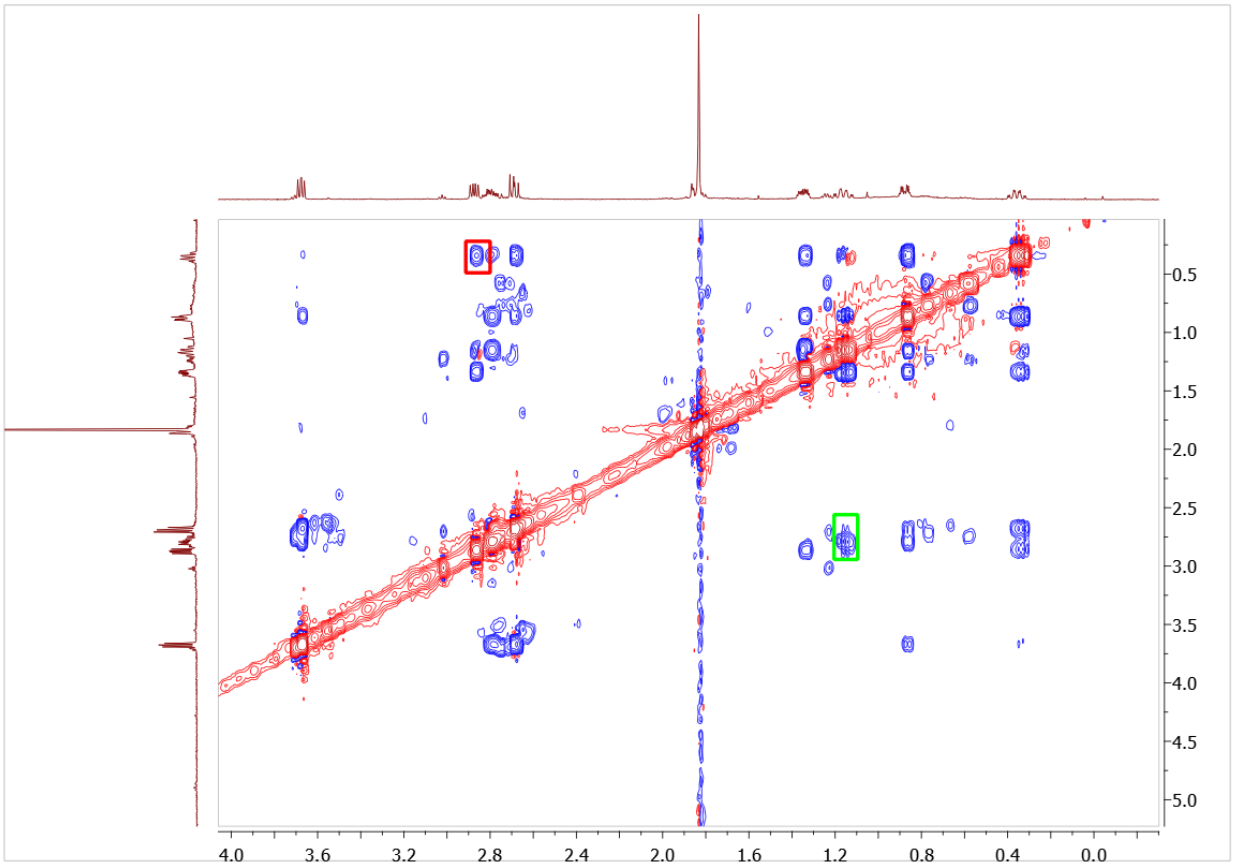


2D NOESY NMR spectra of compound **9b**

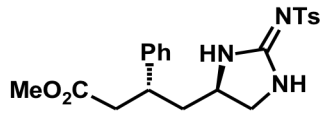




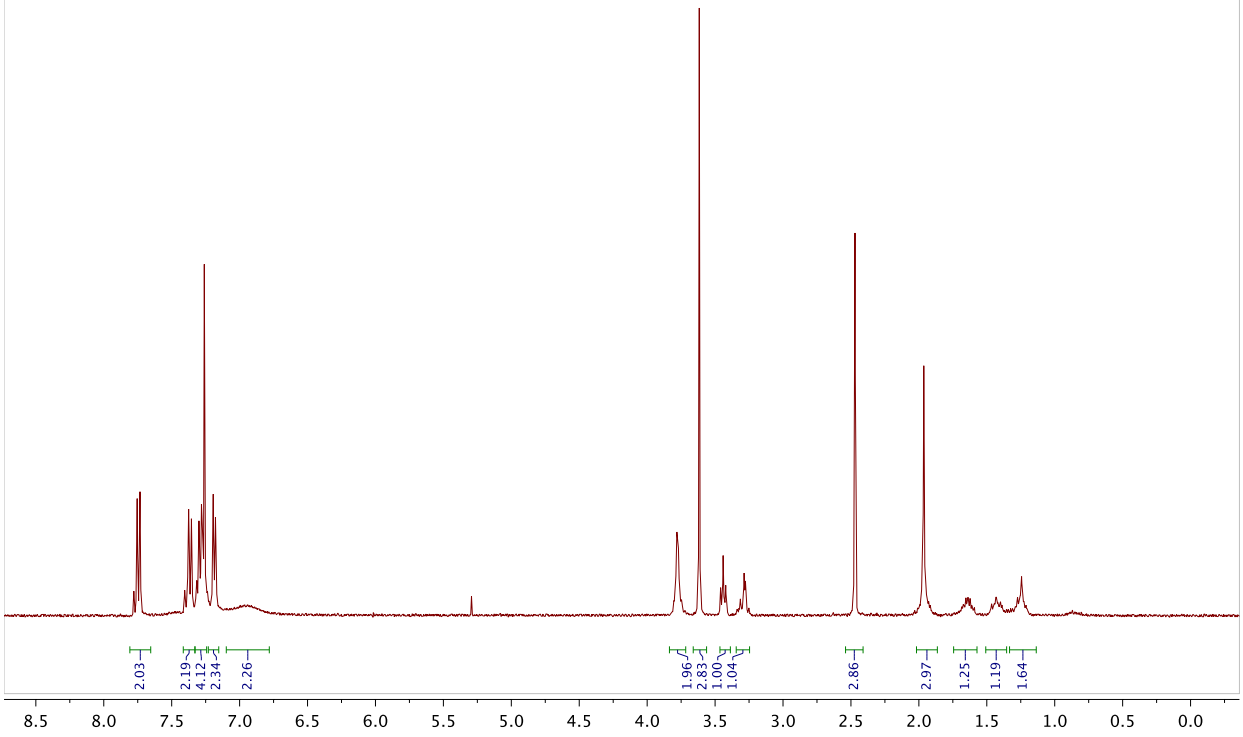
Fragment of 2D NOESY NMR spectra of compound **9b**



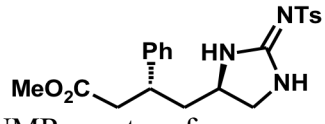
Parameter	Value
1 Title	ky-5-98-a-4
2 Spectrometer	vnmrs
3 Solvent	cdcl3
4 Temperature	25.0
5 Number of Scans	4
6 Relaxation Delay	8.0000
7 Acquisition Date	2016-04-05T21:04:05
8 Spectrometer Frequency	399.78



^{1}H NMR spectra of compound **10a**

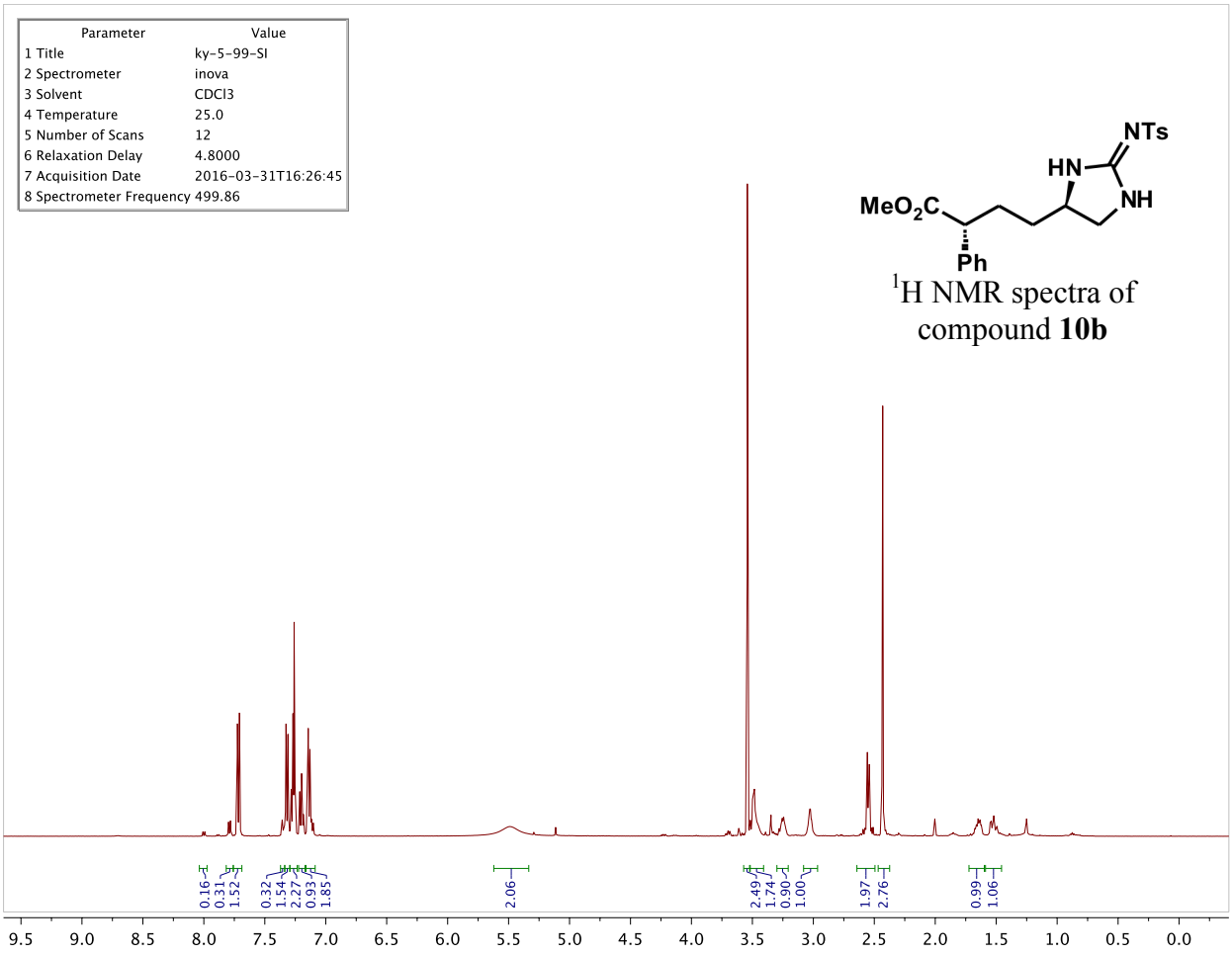


Parameter	Value
1 Title	ky-5-98-a-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	-20.0
5 Number of Scans	364
6 Relaxation Delay	1.0000
7 Acquisition Date	2016-03-31T13:44:38
8 Spectrometer Frequency	125.70



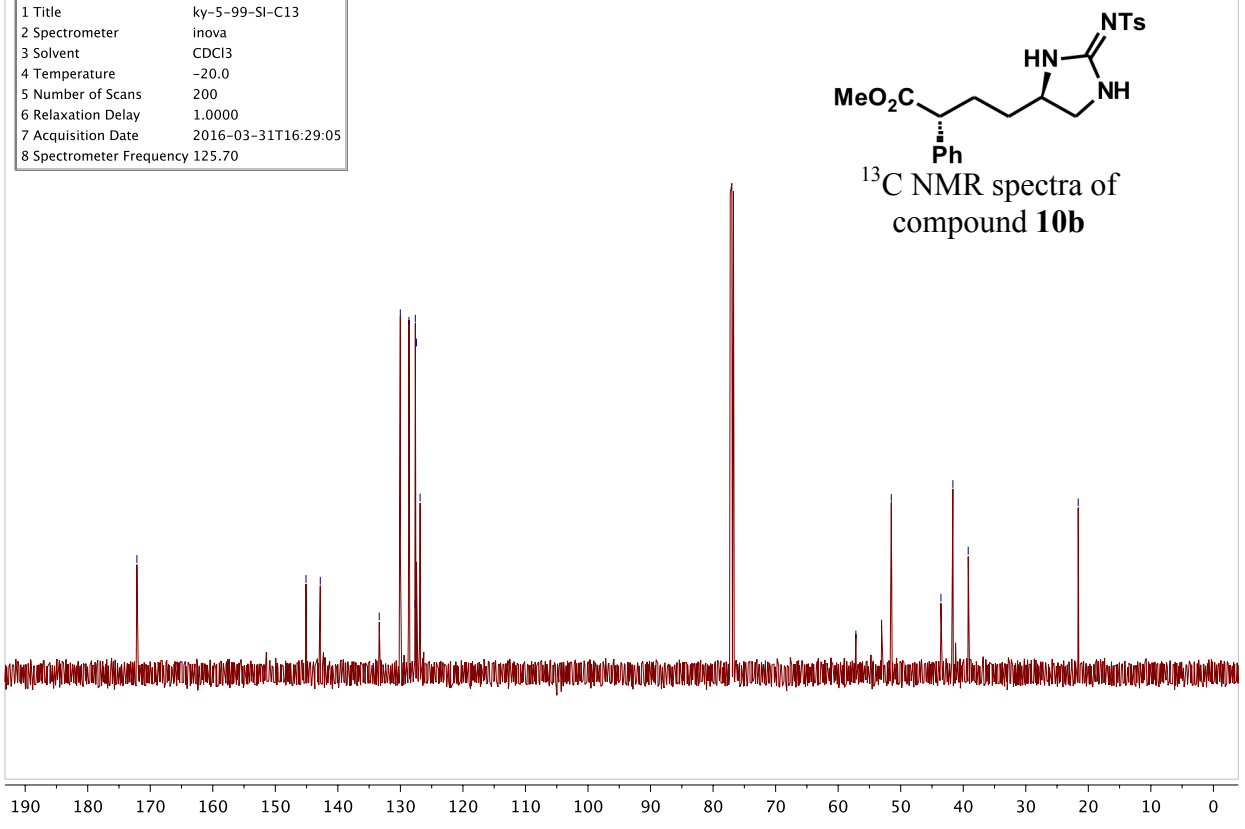
^{13}C NMR spectra of compound **10a**

Parameter	Value
1 Title	ky-5-99-SI
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	25.0
5 Number of Scans	12
6 Relaxation Delay	4.8000
7 Acquisition Date	2016-03-31T16:26:45
8 Spectrometer Frequency	499.86



^{1}H NMR spectra of compound **10b**

Parameter	Value
1 Title	ky-5-99-SI-C13
2 Spectrometer	inova
3 Solvent	CDCl3
4 Temperature	-20.0
5 Number of Scans	200
6 Relaxation Delay	1.0000
7 Acquisition Date	2016-03-31T16:29:05
8 Spectrometer Frequency	125.70



^{13}C NMR spectra of compound **10b**