Development of a simple system for the oxidation of electron-rich diazo compounds to ketones

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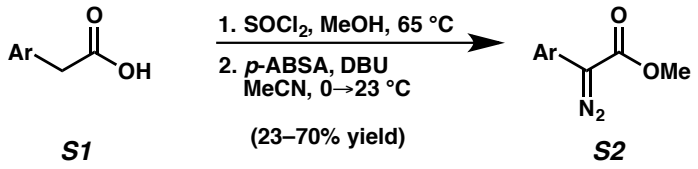
Materials and Methods

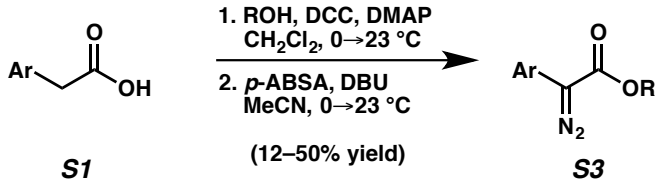
Unless noted in the specific procedure, reactions were performed in non-dry glassware under an air atmosphere. Dried and deoxygenated solvents were prepared by passage through columns of activated alumina before use.[1] Commercial reagents were used as received. *p*-Acetamidobenzenesulfonyl azide (*p*-ABSA) was prepared following a literature procedure.[2] Brine is defined as a saturated aqueous solution of sodium chloride. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Reaction progress was monitored by thin-layer chromatography (TLC). TLC was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 spectrometer (500 MHz and 126 MHz, respectively) and are reported in terms of chemical shift relative to residual $CHCl_3$ (δ 7.26 and δ 77.16 ppm, respectively) or $D_3CS(O)CHD_2$ (δ 2.50 and δ 39.52 ppm, respectively). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Abbreviations are used as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = complex multiplet. Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer using thin film samples on NaCl plates, or a Thermo Scientific Nicolet iS5 attenuated total reflectance spectrometer using solid samples, and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra (HRMS) were obtained form the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer with fast atom bombardment (FAB+) ionization mode or were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+) ionization mode.

General Experimental Procedures



General Procedure A. *Synthesis of aryl diazoacetates by Fischer esterification and diazo transfer.*
To a solution of the aryl acetic acid (12.0 mmol, 1.00 equiv) in methanol (60 mL) was added thionyl chloride (2.63 mL, 36.0 mmol, 3.00 equiv). The solution was heated to reflux. Upon completion (as determined by TLC analysis), the solution was concentrated in vacuo and the crude residue was used without further purification.

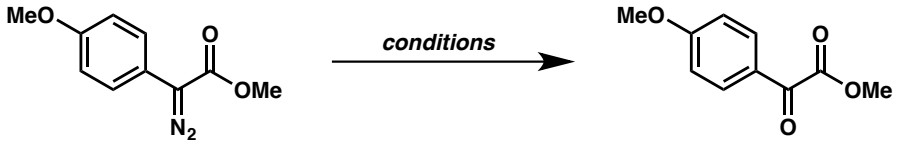
To a flame-dried round-bottom flask with a magnetic stir bar were added the aryl acetic acid ester (12.0 mmol, 1.00 equiv), *p*-ABSA (3.46 g, 14.4 mmol, 1.20 equiv), and dry acetonitrile (50 mL). The solution was stirred under nitrogen and cooled to 0 °C using an ice water bath. DBU (1.97 mL, 13.2 mmol, 1.10 equiv) was added by syringe rapidly in one portion, and the reaction mixture was allowed to warm to 23 °C and stir overnight. Upon completion (as determined by TLC analysis) or after 24 hours, whichever came first, the reaction mixture was quenched with saturated aqueous ammonium chloride (50 mL) and extracted with ether (3 x 50 mL). The combined organic layers were washed with brine (1 x 100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate as eluent. The aryl diazoacetates were obtained in 23–70% yield over two steps.



General Procedure B. *Synthesis of aryl diazoacetates by Steglich esterification and diazo transfer.*
To a flame-dried round-bottom flask with a magnetic stir bar were added the aryl acetic acid (12.0 mmol, 1.00 equiv) and dry dichloromethane (13 mL). The solution was stirred under nitrogen while DMAP (approx. 50 mg) and the alcohol (12.0 mmol, 1.00 equiv) were added. The solution was cooled to 0 °C using an ice water bath and DCC (2.72 g, 13.2 mmol, 1.10 equiv) was added. The mixture was allowed to stir for five minutes at 0 °C, and then the ice water bath was removed and the mixture was allowed to warm to 23 °C. Upon completion (as determined by TLC analysis), the heterogeneous mixture was filtered through Celite, rinsing with dichloromethane (20 mL). The filtrate was concentrated, suspended in dichloromethane, and filtered through Celite, washing with dichloromethane (20 mL). The filtrate was washed with 0.5 M aqueous hydrochloric acid (2 x 50 mL) and saturated aqueous sodium bicarbonate (1 x 50 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude residue

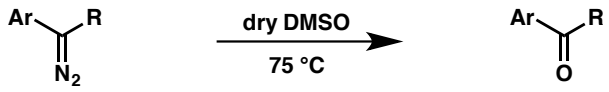
was purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate as eluent.

To a flame-dried round-bottom flask with a magnetic stir bar were added the aryl acetic acid ester (10.0 mmol, 1.00 equiv), *p*-ABSA (2.88 g, 12.0 mmol, 1.20 equiv), and dry acetonitrile (35 mL). The solution was stirred under nitrogen and cooled to 0 °C using an ice water bath. DBU (1.65 mL, 11.0 mmol, 1.10 equiv) was added by syringe rapidly in one portion, and the reaction mixture was allowed to warm to 23 °C and stir overnight. Upon completion (as determined by TLC analysis) or after 24 hours, whichever came first, the reaction mixture was quenched with saturated aqueous ammonium chloride (50 mL) and extracted with ether (3 x 50 mL). The combined organic layers were washed with brine (1 x 100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate as eluent. The aryl diazoacetates were obtained in 12–50% yield over two steps.



2 ***4***

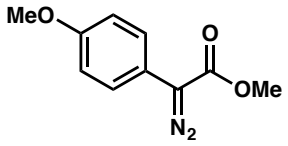
General Procedure C. *Optimization of the diazo oxidation reaction.*
To an oven-dried 1-dram vial equipped with a magnetic stir bar were added methyl 2-diazo-2-(4-methoxyphenyl)acetate (**2**, 21 mg, 0.10 mmol, 1.00 equiv), the appropriate oxidant (see Table 1, 0.20 mmol, 2.00 equiv), and the appropriate solvent (0.5 mL or 0.25 mL, see Table 1). The vial was sealed with a Teflon-lined plastic cap and placed in a metal heating block at the appropriate temperature (see Table 1). Upon completion (as determined by TLC analysis) or after 72 hours, whichever came first, the solution was allowed to cool to room temperature and the mixture was loaded directly onto a silica gel column, eluting with a mixture of hexanes and ethyl acetate.



S4 ***S5***

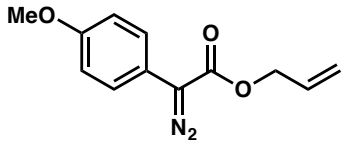
General Procedure D. *Oxidation of diazo compounds.*
To an oven-dried 1-dram vial equipped with a magnetic stir bar were added the appropriate diazo compound (0.40 mmol, 1.00 equiv) and anhydrous DMSO (0.5 mL). The vial was sealed with a Teflon-lined plastic cap and placed in a metal heating block at 75 °C. Upon completion (as determined by TLC analysis), the solution was allowed to cool to room temperature and the mixture was loaded directly onto a silica gel column, eluting with a mixture of hexanes and ethyl acetate.

Substrate Synthesis and Characterization Data



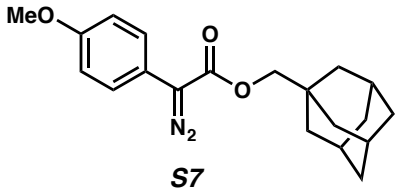
2

methyl 2-diazo-2-(4-methoxyphenyl)acetate (2):
Diazoacetate **2** was prepared from 4-methoxyphenylacetic acid using General Procedure A. Characterization data match those reported in the literature.[3]



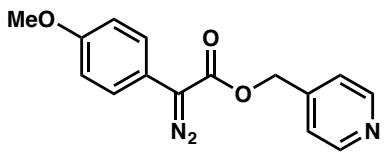
S6

allyl 2-diazo-2-(4-methoxyphenyl)acetate (S6):
Diazoacetate **S6** was prepared from 4-methoxyphenylacetic acid using General Procedure B. Characterization data (^{1}H NMR, ^{13}C NMR, IR) match those reported in the literature.[4] HRMS (FAB+) *m/z* calc'd for $C_{12}H_{12}N_2O_3$ $[M]^+$: 232.0848, found 232.0838.



S7

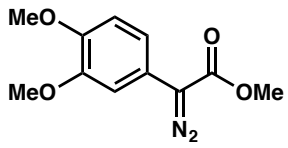
((1*s*,3*s*)-adamantan-1-yl)methyl 2-diazo-2-(4-methoxyphenyl)acetate (S7):
Diazoacetate **S7** was prepared from 4-methoxyphenylacetic acid using General Procedure B. R*f* = 0.30 (5% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.43–7.36 (m, 2H), 6.98–6.90 (m, 2H), 3.86 (s, 2H), 3.82 (s, 3H), 2.01 (p, *J* = 3.0 Hz, 3H), 1.75 (dt, *J* = 12.2, 3.0 Hz, 3H), 1.66 (dddt, *J* = 12.5, 3.8, 2.3, 1.2 Hz, 3H), 1.57 (d, *J* = 2.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 166.0, 158.1, 126.0, 117.2, 114.7, 74.4, 55.5, 39.4, 37.1, 33.5, 28.1 (the diazo carbon is not observed); IR (Neat Film, NaCl) 2911, 2847, 2088, 1688, 1514, 1386, 1346, 1253, 1234, 1164, 1049, 1024, 823, 739 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{20}H_{24}N_2O_3$ $[M]^+$: 340.1787, found 340.1785.



S8

pyridin-4-ylmethyl 2-diazo-2-(4-methoxyphenyl)acetate (S8):
Diazoacetate **S8** was prepared from 4-methoxyphenylacetic acid using General Procedure B. R*f* = 0.30 (50% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.67–8.55 (m, 2H), 7.43–7.33 (m, 2H), 7.31–7.21 (m, 2H), 7.00–6.90 (m, 2H), 5.45–5.15 (m, 2H),

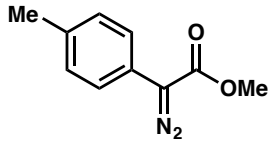
3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.3, 158.4, 150.2, 145.0, 126.2, 121.9, 116.4, 114.8, 64.5, 55.5 (the diazo carbon is not observed); IR (Neat Film, NaCl) 3013, 2935, 2836, 2085, 1703, 1606, 1513, 1415, 1382, 1346, 1297, 1256, 1151, 1026, 828, 737 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{14}N_3O_3$ $[M+H]^+$: 284.1030, found 284.1020.



S9

methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (S9):

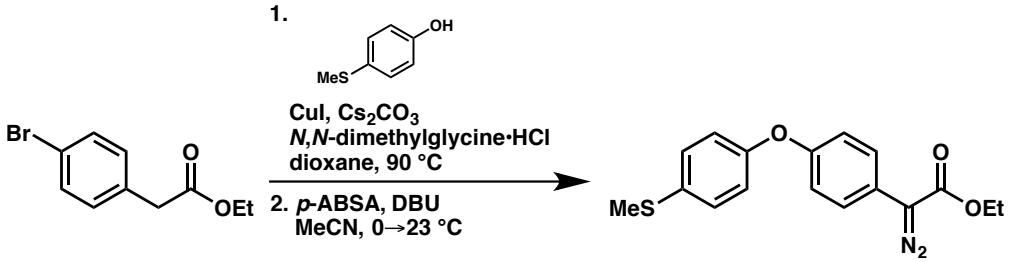
Diazoacetate **S9** was prepared from 4-methoxyphenylacetic acid using General Procedure A. R*f* = 0.4 (25% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.18 (d, *J* = 2.0, 1H), 6.89 (d, *J* = 8.4, 1H), 6.87 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 166.2, 149.6, 147.5, 117.5, 116.6, 111.8, 108.4, 56.1, 56.0, 52.1 (the diazo carbon is not observed); IR (Neat Film, NaCl) 2944, 2841, 2087, 1689, 1581, 1519, 1438, 1356, 1320, 1256, 1136, 1023, 863, 825, 793, 764, 736 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{12}N_2O_4$ $[M]^+$: 236.0797, found 236.0786. Characterization data (^{1}H NMR and ^{13}C NMR) also match those reported in the literature.[5]



S10

methyl 2-diazo-2-(*p*-tolyl)acetate (S10):

Diazoacetate **S10** was prepared from 4-methylphenylacetic acid using General Procedure A. Characterization data match those reported in the literature.[6]



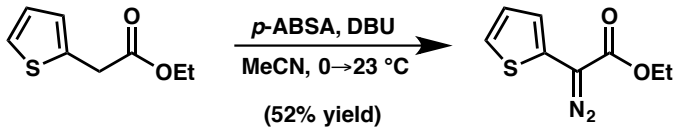
S11 (44% yield over two steps) ***S12***

ethyl 2-diazo-2-(4-(4-(methylthio)phenoxy)phenyl)acetate (S12):

C–O bond formation: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added **S11** (1.00 g, 4.11 mmol, 1.00 equiv), 4-(methylmercapto)phenol (866 mg, 6.17 mmol, 1.50 equiv), copper(I) iodide (78 mg, 0.41 mmol, 0.10 equiv), and cesium carbonate (2.68 g, 8.22 mmol, 2.00 equiv). The Schlenk tube was capped with a rubber septum and evacuated and backfilled with nitrogen three times. Dry dioxane (9 mL) was added by syringe. The septum was replaced with a glass stopper and the Schlenk tube

was placed in a 90 °C oil bath. Upon completion (as determined by TLC analysis, approx. 24 hours), the contents were diluted with water (100 mL), and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with water (1 x 100 mL) and brine (1 x 100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to provide the diaryl ether as a colorless oil (681 mg, 55% yield).

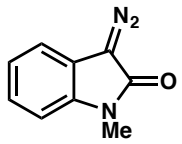
Diazo transfer: To a flame-dried round-bottom flask with a magnetic stir bar were added the diaryl ether (681 mg, 2.25 mmol, 1.00 equiv), *p*-ABSA (649 mg, 2.70 mmol, 1.20 equiv), and dry acetonitrile (8 mL). The solution was stirred under nitrogen and cooled to 0 °C using an ice water bath. DBU (370 µL, 2.48 mmol, 1.10 equiv) was added by syringe rapidly in one portion, and the reaction mixture was allowed to warm to 23 °C and stir overnight. Upon completion (as determined by TLC analysis, approx. 12 hours), the reaction mixture was quenched with saturated aqueous ammonium chloride (25 mL) and extracted with ether (3 x 25 mL). The combined organic layers were washed with brine (1 x 50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to provide diazoacetate **S12** as an orange solid (592 mg, 80% yield). R*f* = 0.6 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47–7.37 (m, 2H), 7.30–7.20 (m, 2H), 7.07–6.99 (m, 2H), 6.99–6.92 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.48 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 165.5, 155.5, 155.1, 132.6, 129.2, 125.9, 120.2, 119.6, 119.4, 61.1, 17.1, 14.6 (the diazo carbon is not observed); IR (Neat Film, NaCl) 2981, 2920, 2085, 1698, 1589, 1506, 1488, 1370, 1341, 1246, 1170, 1093, 1046, 1012, 872, 828, 740, 655 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{17}H_{17}N_2O_4S$ $[M+OH]^+$: 345.0904, found 345.0910.



S13 ***S14***

ethyl 2-diazo-2-(thiophen-2-yl)acetate (S14):

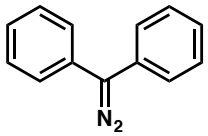
To a flame-dried round-bottom flask with a magnetic stir bar were added ethyl 2-thiopheneacetate (1.50 mL, 10.0 mmol, 1.00 equiv), *p*-ABSA (2.88 g, 12.0 mmol, 1.20 equiv), and dry acetonitrile (35 mL). The solution was stirred under nitrogen and cooled to 0 °C using an ice water bath. DBU (1.65 mL, 11.0 mmol, 1.10 equiv) was added by syringe rapidly in one portion, and the reaction mixture was allowed to warm to 23 °C and stir overnight. Upon completion (as determined by TLC analysis, approx. 4 hours), the reaction mixture was quenched with saturated aqueous ammonium chloride (100 mL) and extracted with ether (3 x 50 mL). The combined organic layers were washed with brine (1 x 100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to provide diazoacetate **S14** as a red solid (1.01 g, 52% yield). Characterization data match those reported in the literature.[7]



S15

3-diazo-1-methylindolin-2-one (S15):

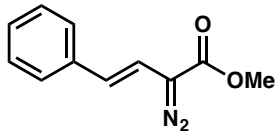
Diazooxindole **S15** was prepared using the procedure of Hu.[8] Characterization data match those reported in the literature.[7]



S16

(diazomethylene)dibenzene (S16):

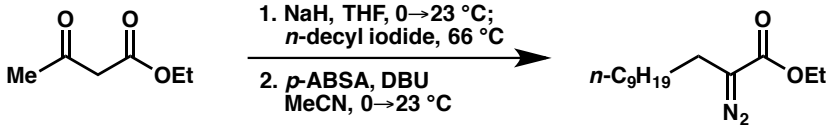
To vial equipped with a magnetic stir bar were added benzophenone hydrazine (1.00 g, 5.10 mmol, 1.00 equiv), activated manganese(IV) oxide (1.15 g, 13.3 mmol, 2.60 equiv), and chloroform (16 mL). The suspension was stirred at 23 °C. Upon completion (as determined by TLC analysis), the suspension was filtered through Celite, washing with dichloromethane. The filtrate was concentrated, and the resulting purple oil was passed through a plug of basic activated alumina, washing with pentane. The filtrate was concentrated and stored at –20 °C to provide **S16** as dark red/purple crystals (585 mg, 59% yield). Characterization data (^{1}H NMR, ^{13}C NMR, IR) match those reported in the literature.[7] HRMS (FAB+) *m/z* calc'd for $C_{13}H_{10}N_2$ $[M]^+$: 194.0844, found 194.0843.



14

methyl (*E*)-2-diazo-4-phenylbut-3-enoate (14):

Vinyl diazoacetate **14** was prepared using the procedure of Davies.[9] Characterization data match those reported in the literature.[9]



S17 **(87% yield over two steps)** ***16***

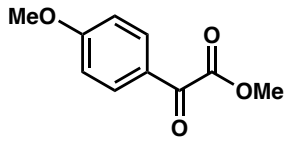
ethyl 2-diazododecanoate (16):

Alkylation: To a flame-dried round-bottom flask equipped with a magnetic stir bar were added sodium hydride (60% suspension in mineral oil, 600 mg, 15.0 mmol, 1.50 equiv) and dry THF (15 mL). The contents were stirred under nitrogen and cooled to 0 °C using an ice water bath. Ethyl acetoacetate (**S17**, 1.90 mL, 15.0 mmol, 1.50 equiv) was added dropwise by syringe, and the suspension was allowed to warm to 23 °C and stir for 10

minutes. *n*-Decyl iodide (2.13 mL, 10.0 mmol, 1.00 equiv) was added dropwise by syringe, and the suspension heated to reflux overnight. Upon completion (as determined by TLC analysis), the reaction mixture was quenched with saturated aqueous ammonium chloride (100 mL) and extracted with dichloromethane (3 x 100 mL). The combined organic layers were washed with brine (1 x 100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to provide the alkylation product as a colorless oil (2.65 g, 98% yield).

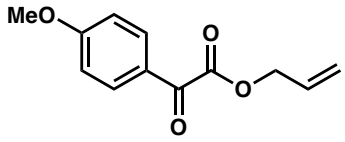
Diazo transfer and deacetylation: Using a procedure similar to that reported by Wulff.[10] To a flame-dried round-bottom flask with a magnetic stir bar were added the alkylation product of the previous step (1.00 g, 3.70 mmol, 1.00 equiv), *p*-ABSA (1.33 g, 5.55 mmol, 1.50 equiv), and dry acetonitrile (8 mL). The solution was stirred under nitrogen and cooled to 0 °C using an ice water bath. DBU (1.66 mL, 11.1 mmol, 3.00 equiv) was added by syringe rapidly in one portion, and the reaction mixture was allowed to warm to 23 °C. Upon completion (as determined by TLC analysis, approx. 3 hours), the reaction mixture was quenched with 1 M aqueous hydrochloric acid (50 mL) and extracted with hexanes (3 x 50 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (1 x 50 mL) and brine (1 x 50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (3% ethyl acetate in hexanes) to provide diazoacetate **16** as a yellow oil (838 mg, 89% yield, 87% yield over two steps). R*f* = 0.7 (10% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.21 (q, *J* = 7.1 Hz, 2H), 2.40–2.16 (m, 2H), 1.55–1.43 (m, 2H), 1.41–1.20 (m, 17H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 60.8, 32.0, 29.7, 29.7, 29.5, 29.4, 28.9, 27.7, 23.1, 22.8, 14.7, 14.3 (the diazo carbon is not observed). The carbonyl carbon was not directly observed, however HMBC analysis showed a clear ^{3}J coupling between the proton signal at 4.21 ppm and a peak at 167.4 ppm; IR (Neat Film, NaCl) 2925, 2855, 2080, 1696, 1465, 1370, 1304, 1171, 1133, 1097, 739 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{27}N_2O_2$ $[M+H]^+$: 255.2073, found 255.2077.

Oxidation Product Characterization Data



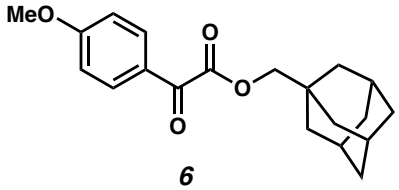
4

methyl 2-(4-methoxyphenyl)-2-oxoacetate (4):
Ketoester **4** was prepared from diazoacetate **2** using General Procedure D. 91% isolated yield. Characterization data match those reported in the literature.[11]



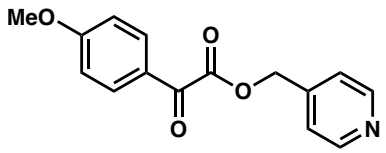
5

allyl 2-(4-methoxyphenyl)-2-oxoacetate (5):
Ketoester **5** was prepared from diazoacetate **S6** using General Procedure D. 90% isolated yield. Characterization data match those reported in the literature.[12]



6

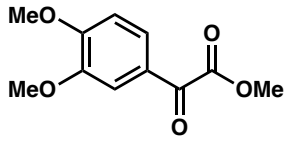
((1*s*,3*s*)-adamantan-1-yl)methyl 2-(4-methoxyphenyl)-2-oxoacetate (6):
Ketoester **6** was prepared from diazoacetate **S7** using General Procedure D. 85% isolated yield. R*f* = 0.5 (25% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.05–7.91 (m, 2H), 7.05–6.92 (m, 2H), 3.98 (s, 2H), 3.90 (s, 3H), 2.00 (p, *J* = 3.1 Hz, 3H), 1.73 (dt, *J* = 12.1, 3.0 Hz, 3H), 1.70–1.62 (m, 3H), 1.60 (d, *J* = 2.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 185.3, 165.1, 164.8, 132.6, 125.7, 114.4, 75.4, 55.8, 39.2, 36.9, 33.5, 28.0; IR (Neat Film, NaCl) 2902, 2848, 1732, 1674, 1597, 1573, 1511, 1309, 1266, 1204, 1162, 989, 846, 618 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{20}H_{25}O_4$ $[M+H]^+$: 329.1747, found 329.1761.



7

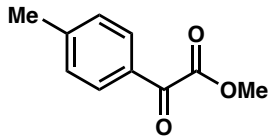
pyridin-4-ylmethyl 2-(4-methoxyphenyl)-2-oxoacetate (7):
Ketoester **7** was prepared from diazoacetate **S8** using General Procedure D. After silica gel column chromatography, a pyridinium compound with an unknown counterion was obtained. The fractions containing this salt were stirred over solid potassium carbonate (1.00 g) for 30 minutes at 23 °C before filtration and concentration furnished the freebase

7 in 74% isolated yield. R*f* = 0.15 (50% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.72–8.57 (m, 2H), 8.05–7.92 (m, 2H), 7.40–7.28 (m, 2H), 7.05–6.88 (m, 2H), 5.40 (s, 2H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 183.9, 165.4, 163.6, 150.4, 143.7, 132.8, 125.4, 125.1, 114.5, 65.5, 55.9; IR (Neat Film, NaCl) 2936, 2842, 1738, 1674, 1598, 1511, 1267, 1202, 1161, 1011, 848, 798 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{14}NO_4$ $[M+H]^+$: 272.0917, found 272.0930.



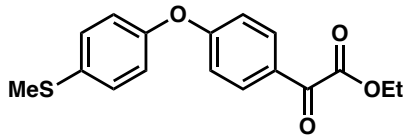
8

methyl 2-(3,4-dimethoxyphenyl)-2-oxoacetate (8):
Ketoester **8** was prepared from diazoacetate **S9** using General Procedure D. 78% isolated yield. Characterization data match those reported in the literature.[13]



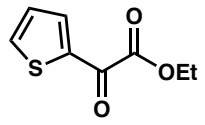
9

methyl 2-oxo-2-(*p*-tolyl)acetate (9):
Ketoester **9** was prepared from diazoacetate **S10** using General Procedure D. 62% isolated yield. Characterization data match those reported in the literature.[13]



10

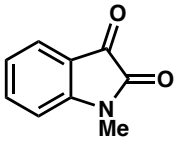
ethyl 2-(4-(4-(methylthio)phenoxy)phenyl)-2-oxoacetate (10):
Ketoester **10** was prepared from diazoacetate **S12** using General Procedure D. 68% isolated yield. R*f* = 0.45 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13–7.90 (m, 2H), 7.36–7.27 (m, 2H), 7.09–6.93 (m, 4H), 4.44 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 184.9, 164.0, 163.8, 152.6, 135.1, 132.7, 128.8, 127.1, 121.3, 117.2, 62.4, 16.7, 14.3; IR (Neat Film, NaCl) 2983, 2921, 1734, 1680, 1603, 1583, 1488, 1248, 1201, 1158, 1013, 872, 836 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{17}H_{17}O_5S$ $[M+OH]^+$: 333.0791, found 333.0806.



11

ethyl 2-oxo-2-(thiophen-2-yl)acetate (11):

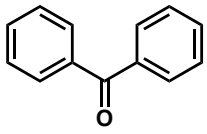
Ketoester **11** was prepared from diazoacetate **S14** using General Procedure D. 75% isolated yield. Characterization data (^{1}H NMR, ^{13}C NMR, IR) match those reported in the literature.[14] HRMS (FAB+) *m/z* calc'd for $C_8H_9O_3S$ $[M+H]^+$: 185.0272, found 185.0276.



12

1-methylindoline-2,3-dione (12):

Isatin **12** was prepared from diazoacetate **15** using General Procedure D. 52% isolated yield. Characterization data match those reported in the literature.[15]

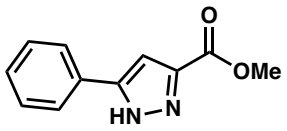


13

benzophenone (13):

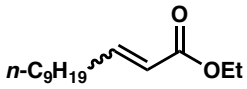
Benzophenone (**13**) was prepared from diazoacetate **S16** using General Procedure D. 56% isolated yield. Characterization data match those reported in the literature.[16]

Characterization of 15 and 17



15

methyl 5-phenyl-1*H*-pyrazole-3-carboxylate (15):
Pyrazole **15** was prepared from diazoacetate **14** using General Procedure D. >99% isolated yield. R*f* = 0.1 (25% ethyl acetate in hexanes); ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.89–7.79 (m, 2H), 7.50–7.40 (m, 2H), 7.40–7.31 (m, 1H), 7.26 (s, 1H), 3.84 (s, 3H) (the *N–H* peak is not observed); ^{13}C NMR (DMSO-d_6, 126 MHz) δ 161.3, 146.6, 140.4, 130.1, 129.0, 128.4, 125.3, 105.2, 51.7. Detection of two pyrazole carbons required a line broadening setting of 10 Hz. These peaks are clearly shown without baseline correction in the spectral expansion; ATR-IR (Neat) 3206, 3138, 3063, 3018, 2955, 1731, 1492, 1245, 1195, 1134, 1011, 761 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{11}H_{11}N_2O_2$ $[M+H]^+$: 203.0815, found 203.0820.



17

ethyl dodec-2-enoate (17):
Enoate **17** was prepared from diazoacetate **16** using General Procedure D. 59% isolated yield, 1:1 *E*:*Z*. Characterization data match those reported in the literature.[17]

Notes and References

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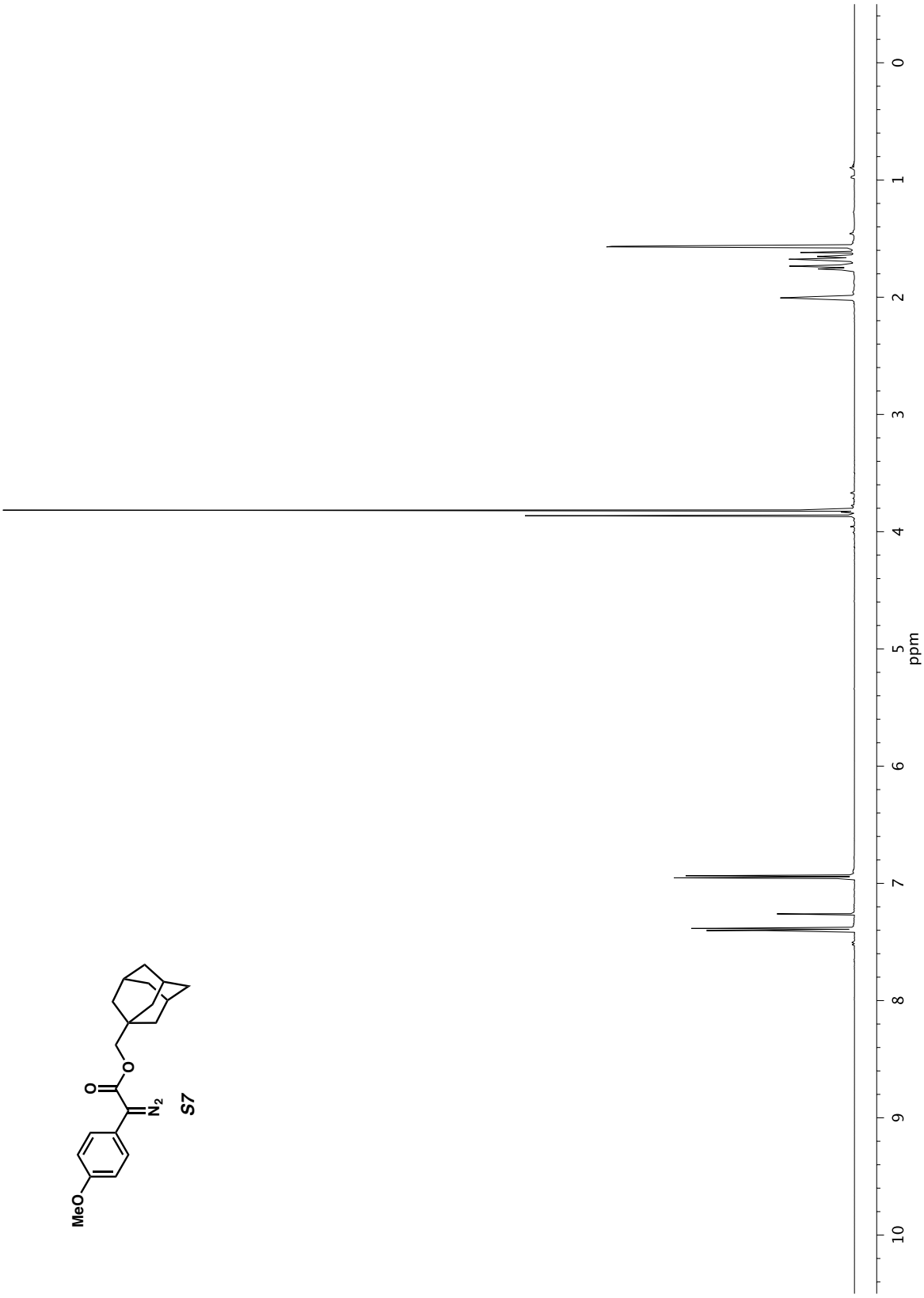
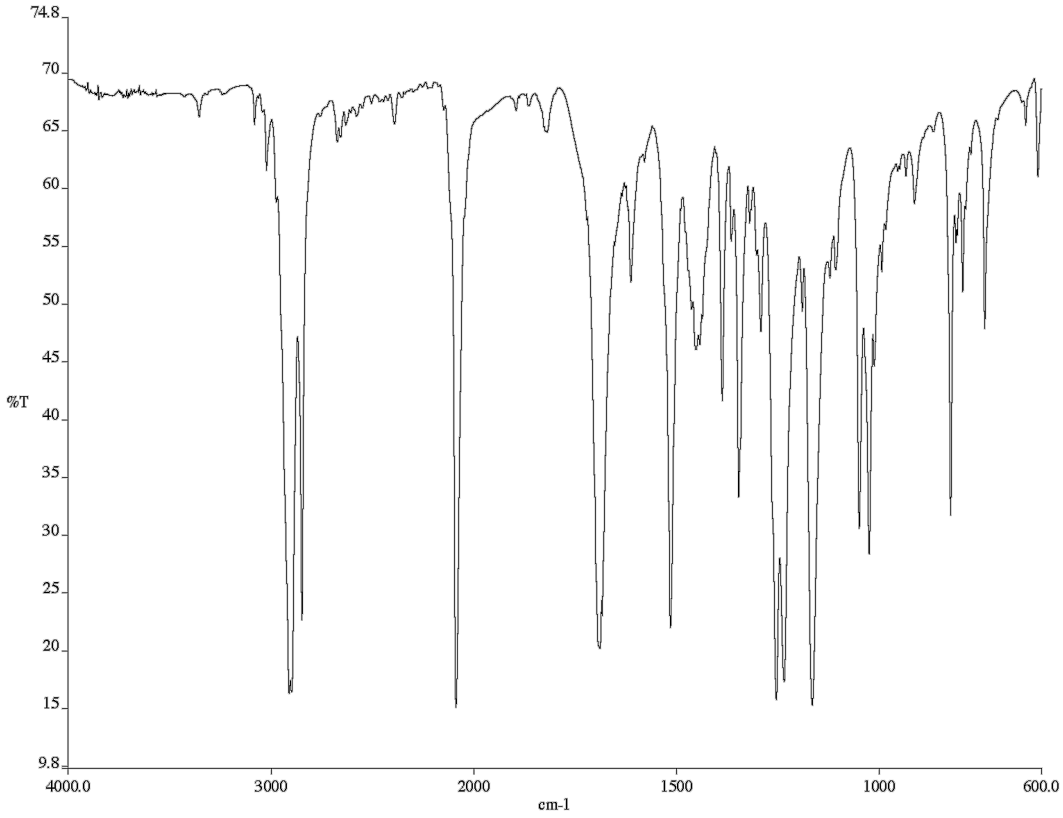
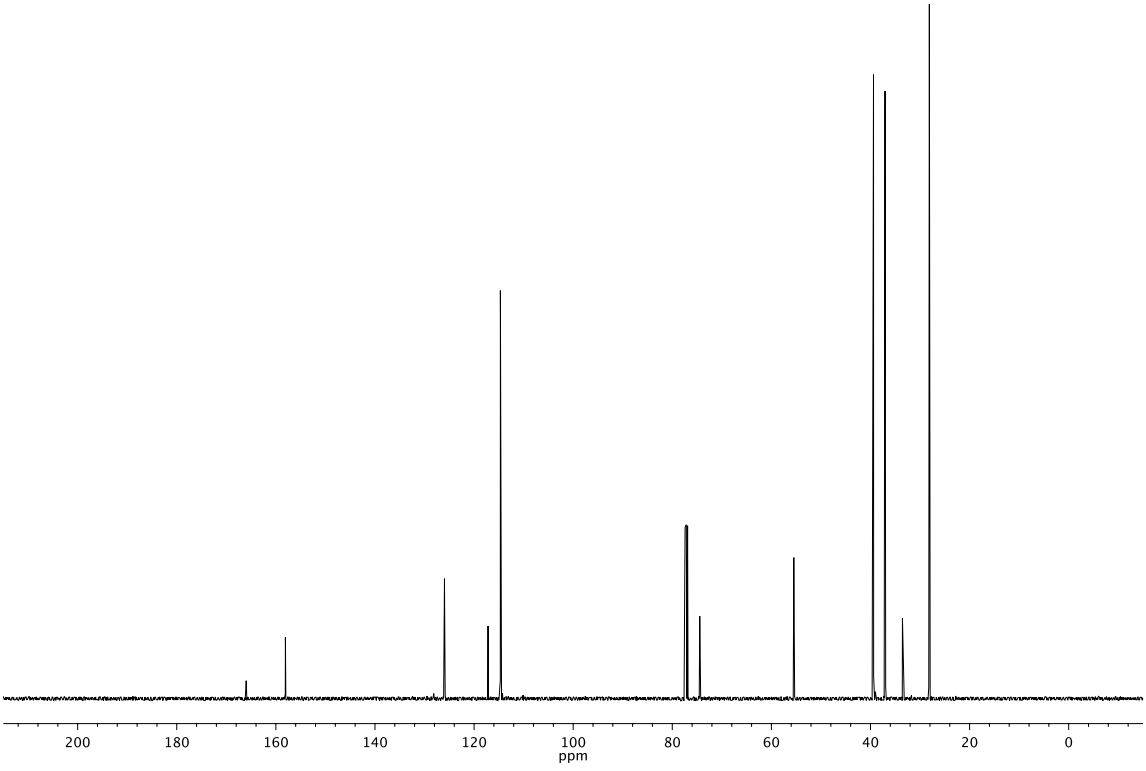


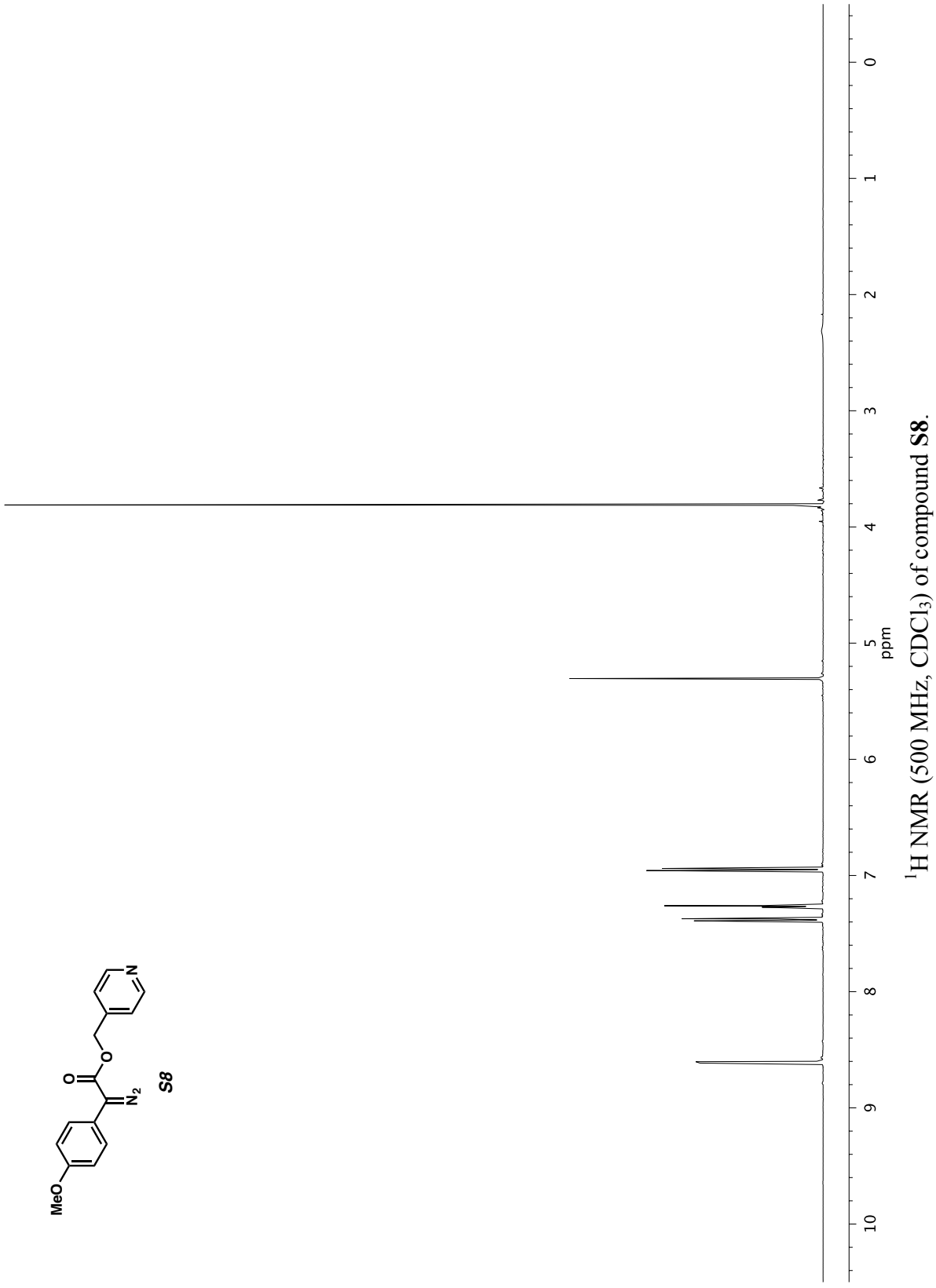
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S7**.



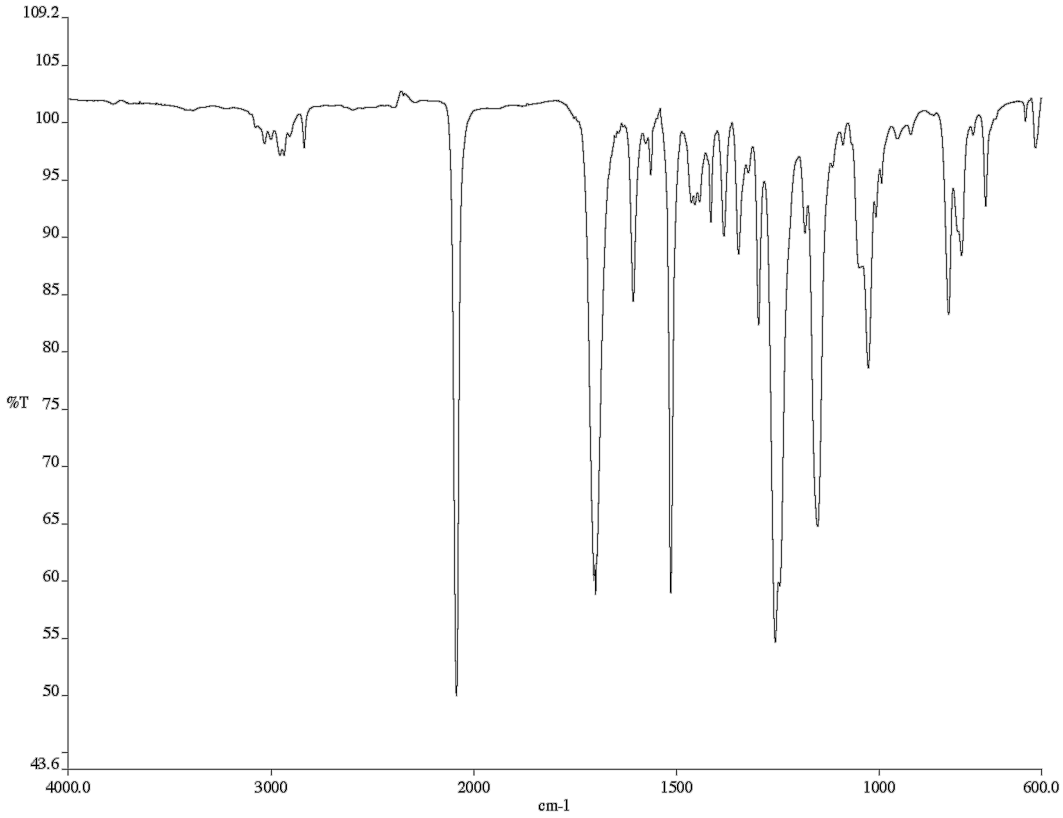
Infrared spectrum (Thin Film, NaCl) of compound **S7**.



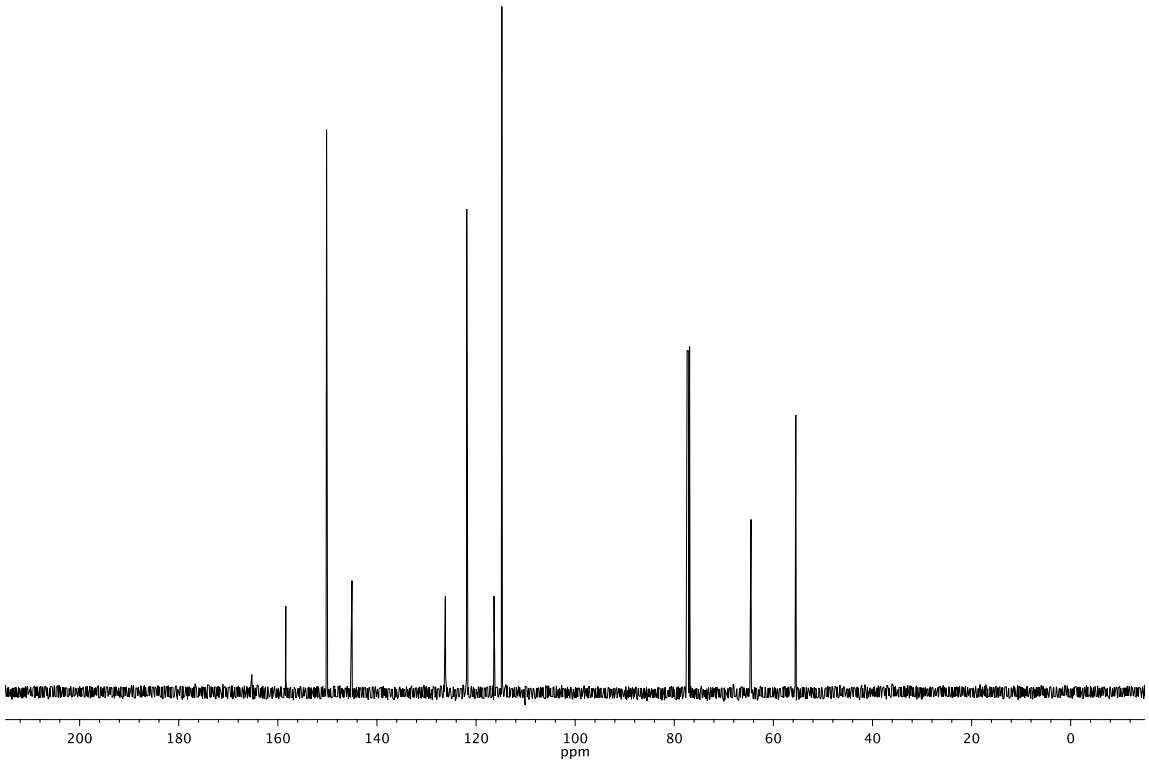
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S7**.



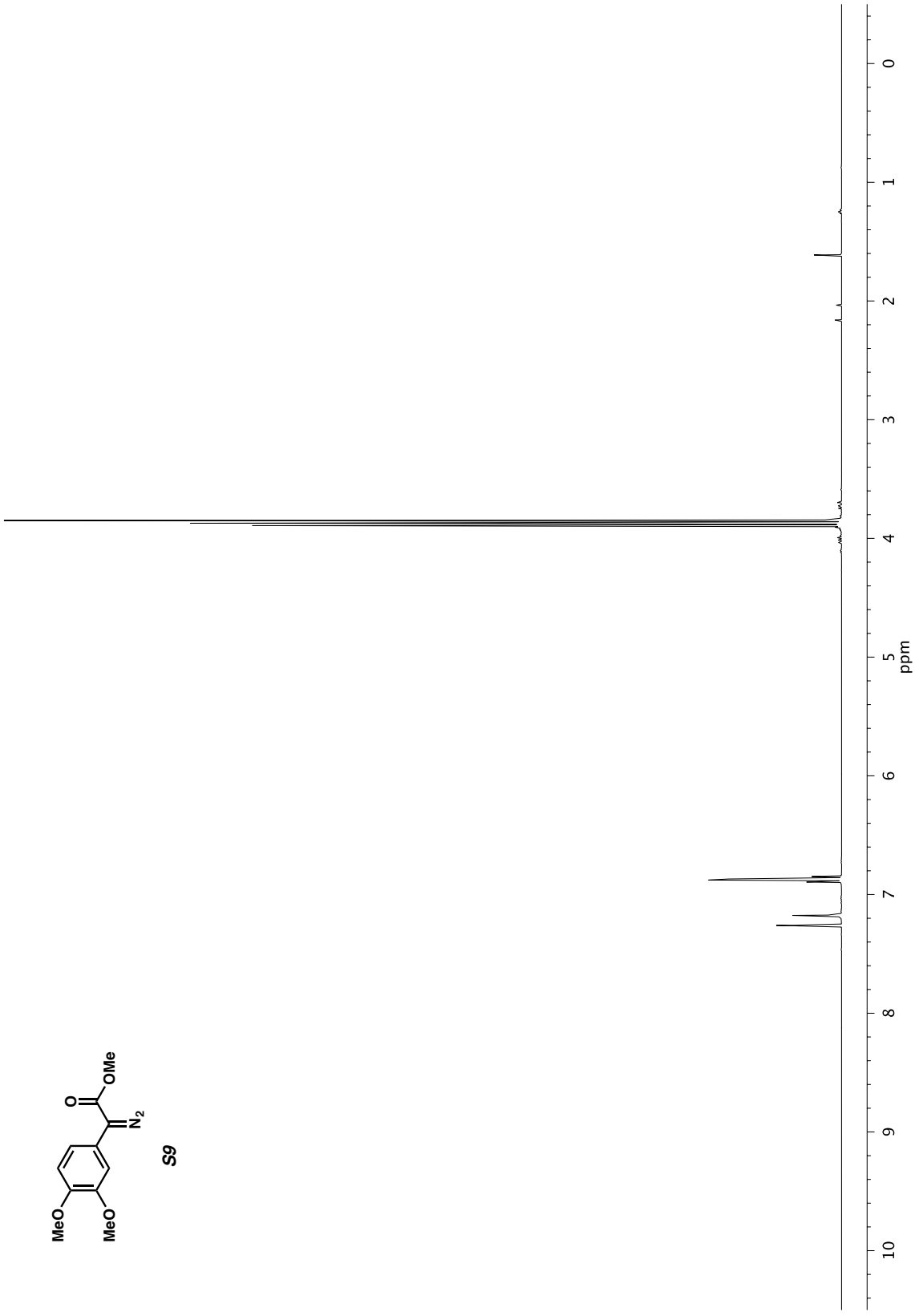
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S8**.



Infrared spectrum (Thin Film, NaCl) of compound **S8**.

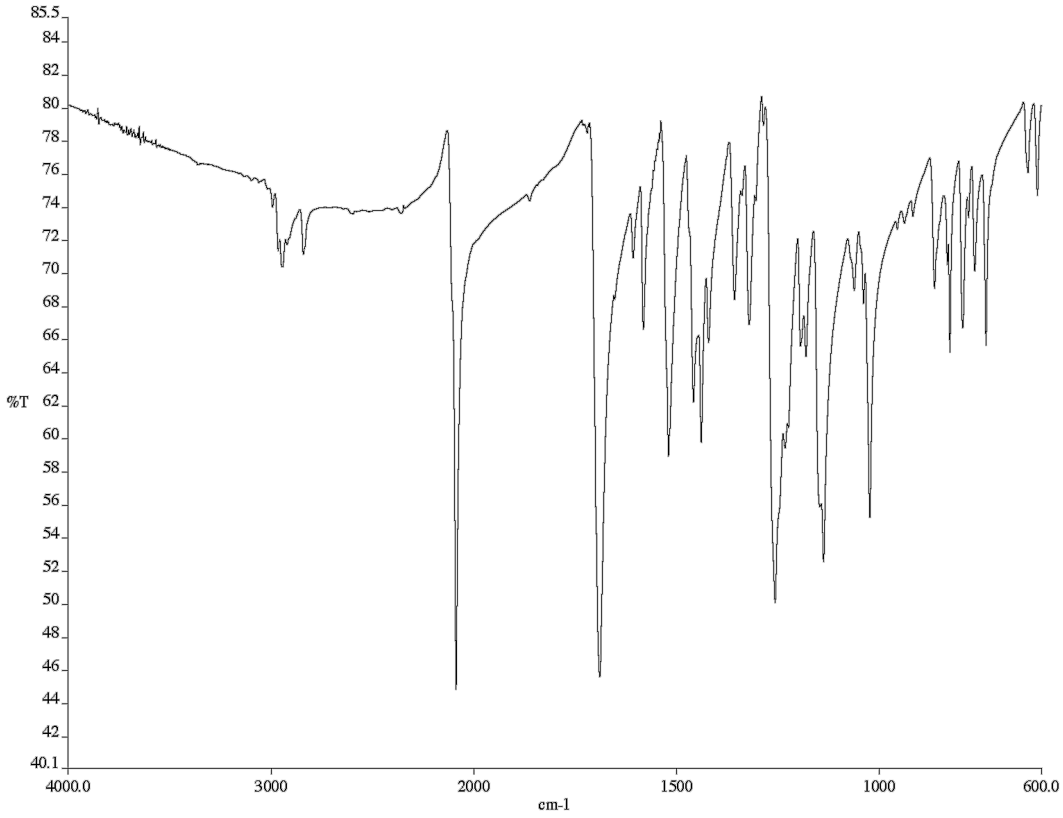


^{13}C NMR (126 MHz, $CDCl_3$) of compound **S8**.

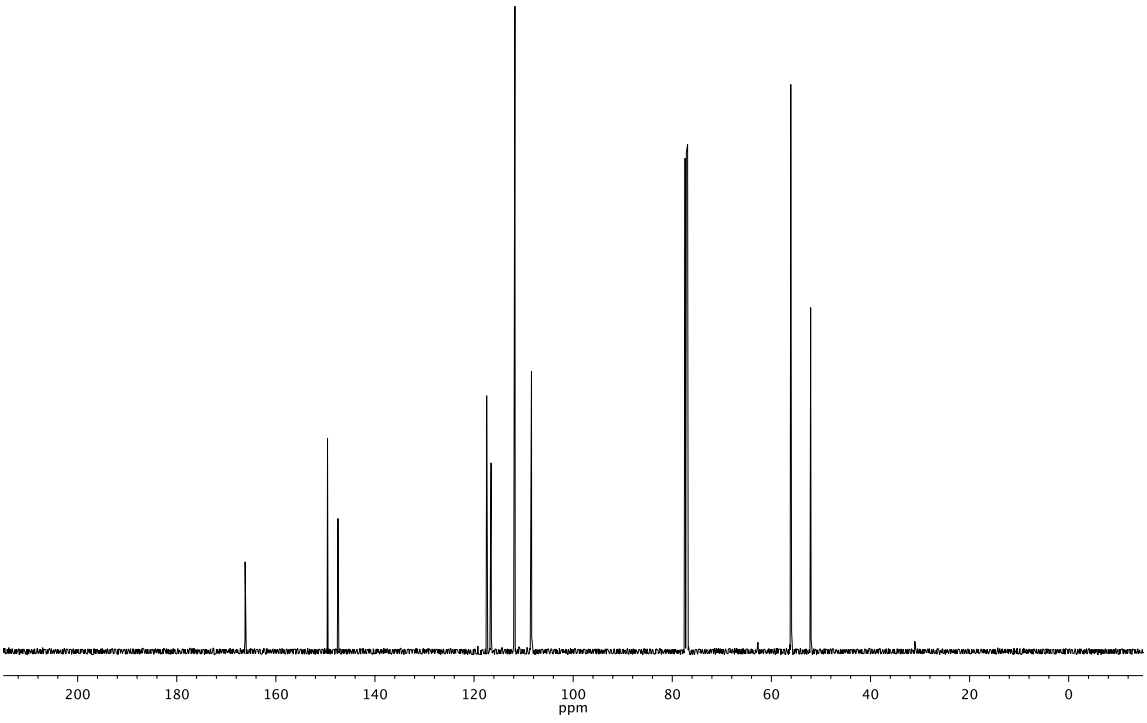


^{1}H NMR (500 MHz, $CDCl_3$) of compound **S9**.

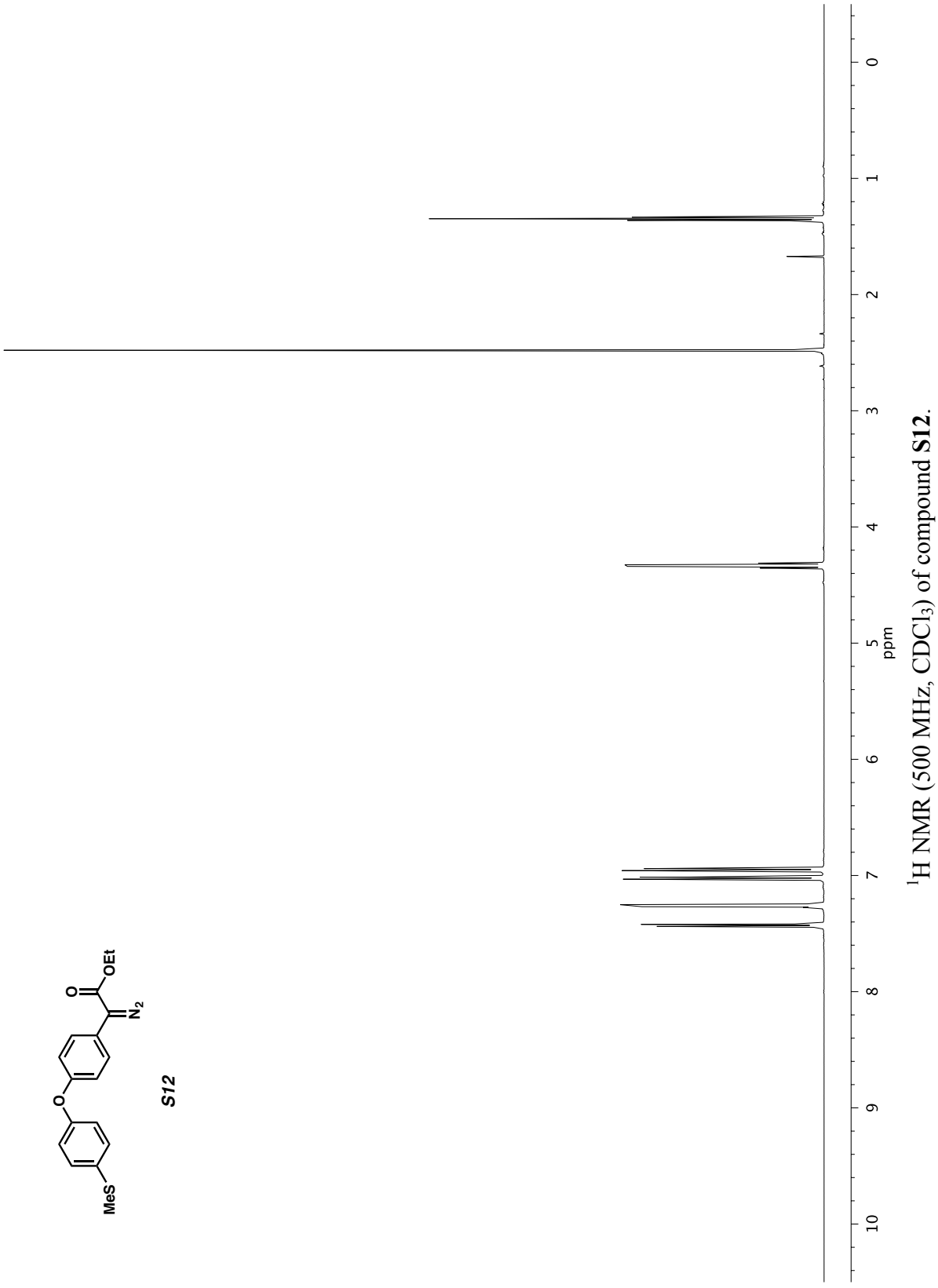
S9



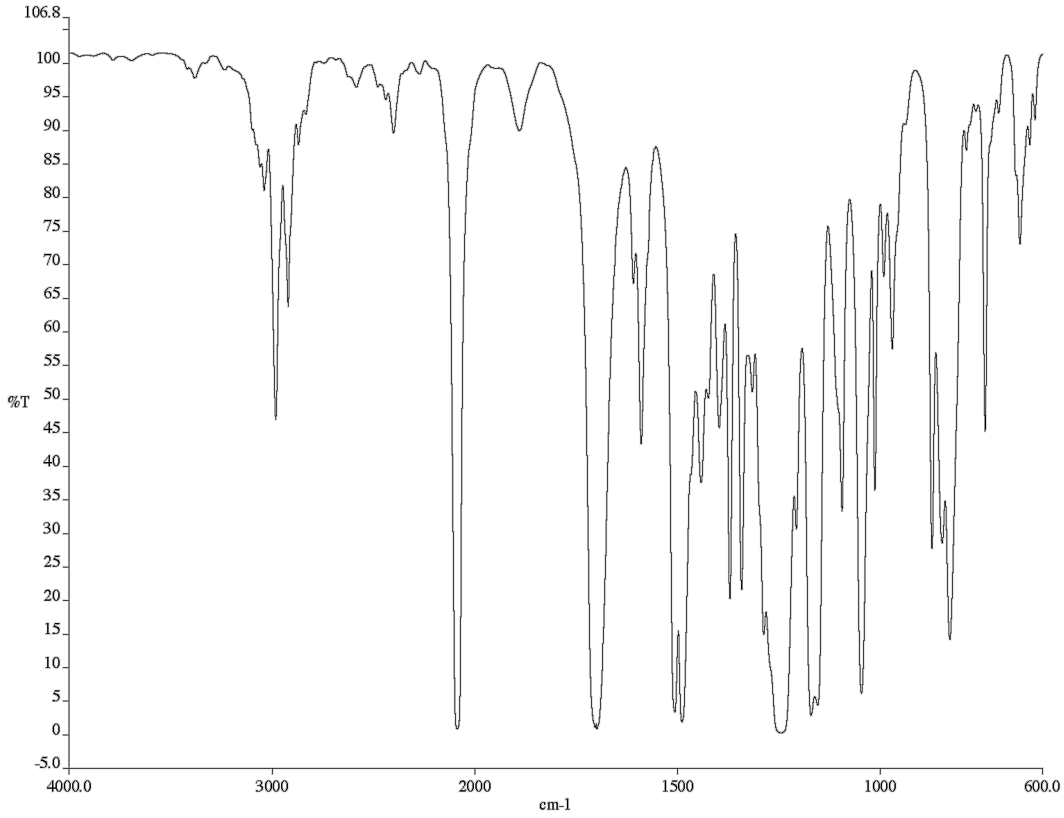
Infrared spectrum (Thin Film, NaCl) of compound **S9**.



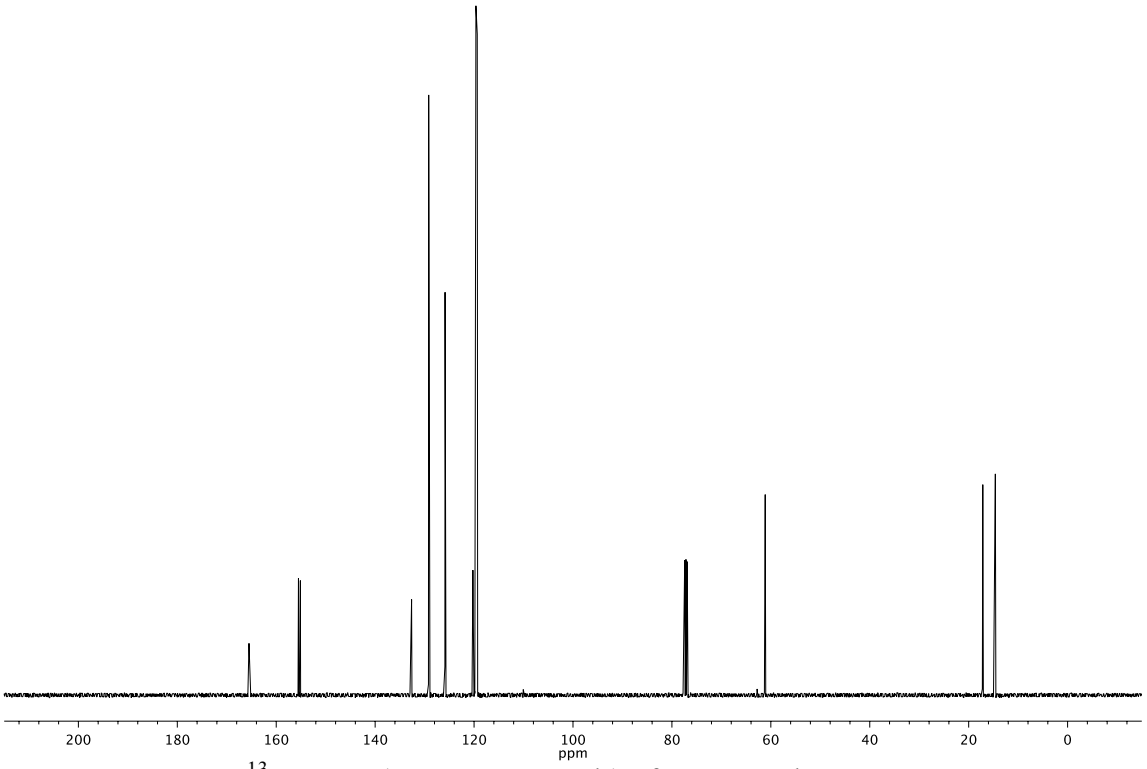
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S9**.



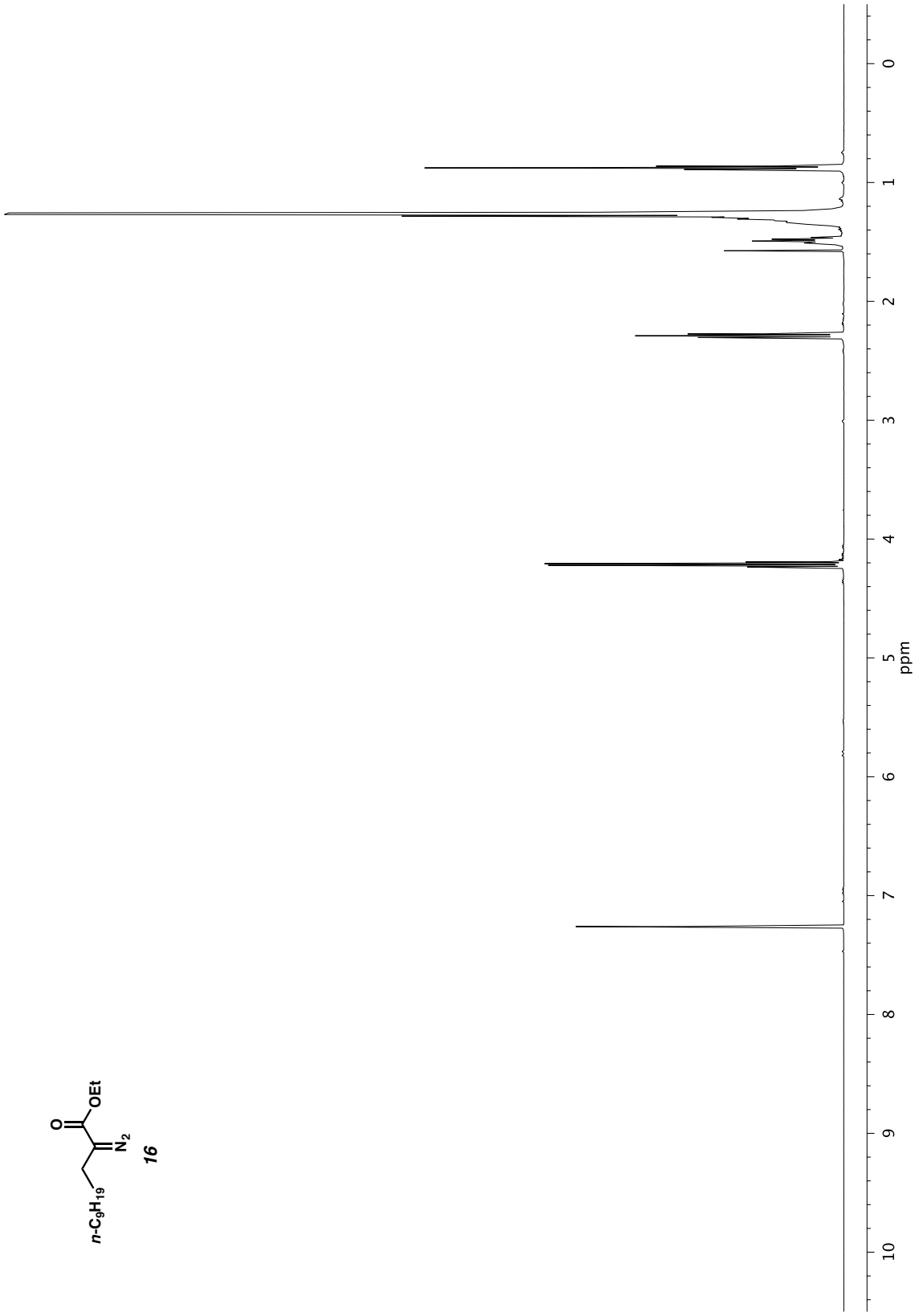
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S12**.



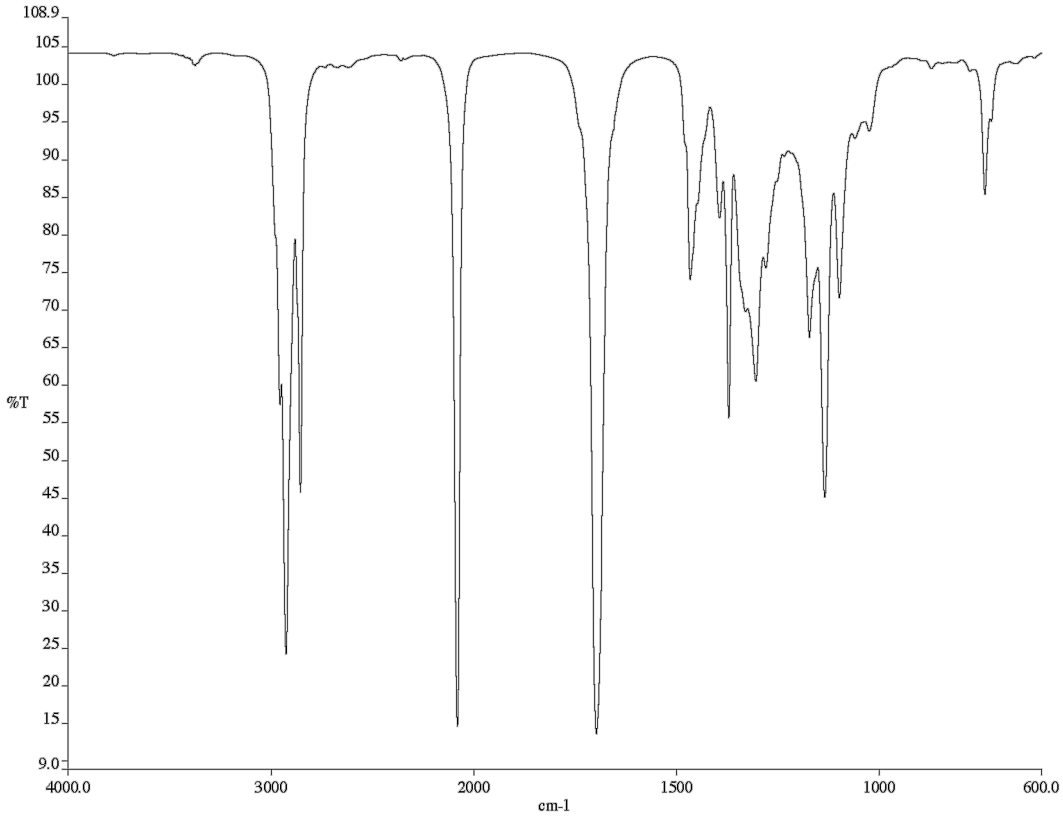
Infrared spectrum (Thin Film, NaCl) of compound **S12**.



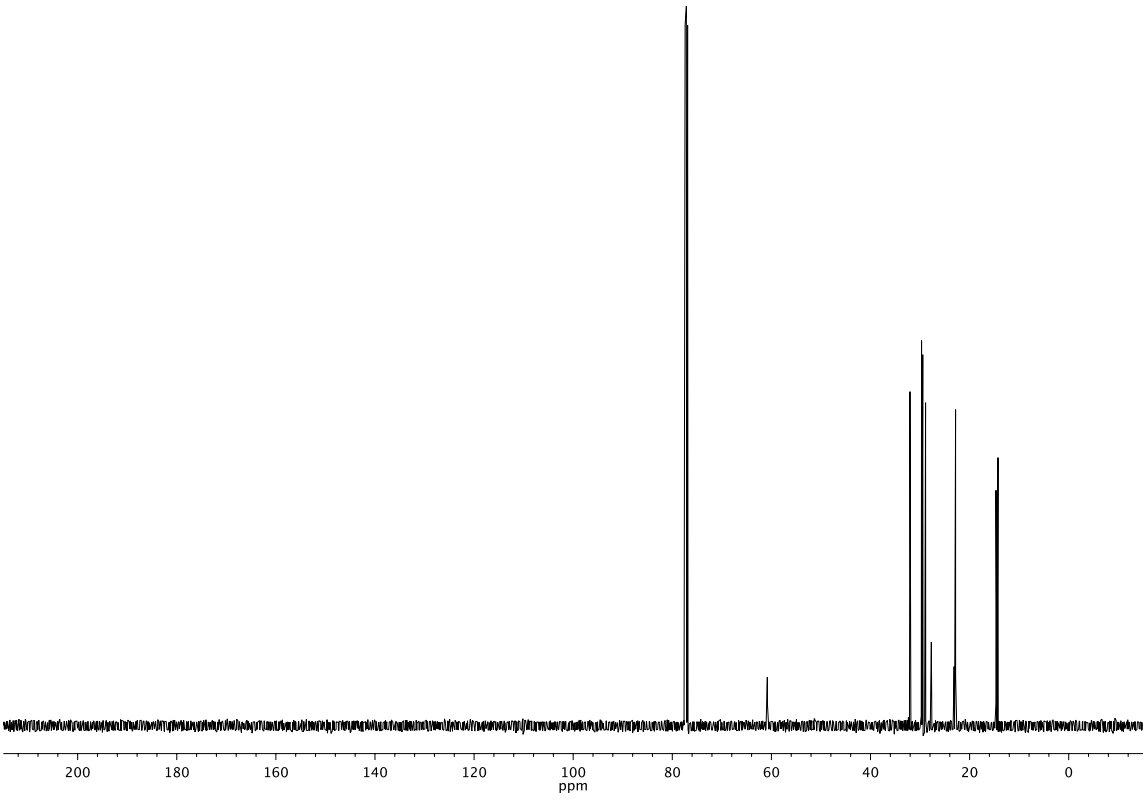
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S12**.



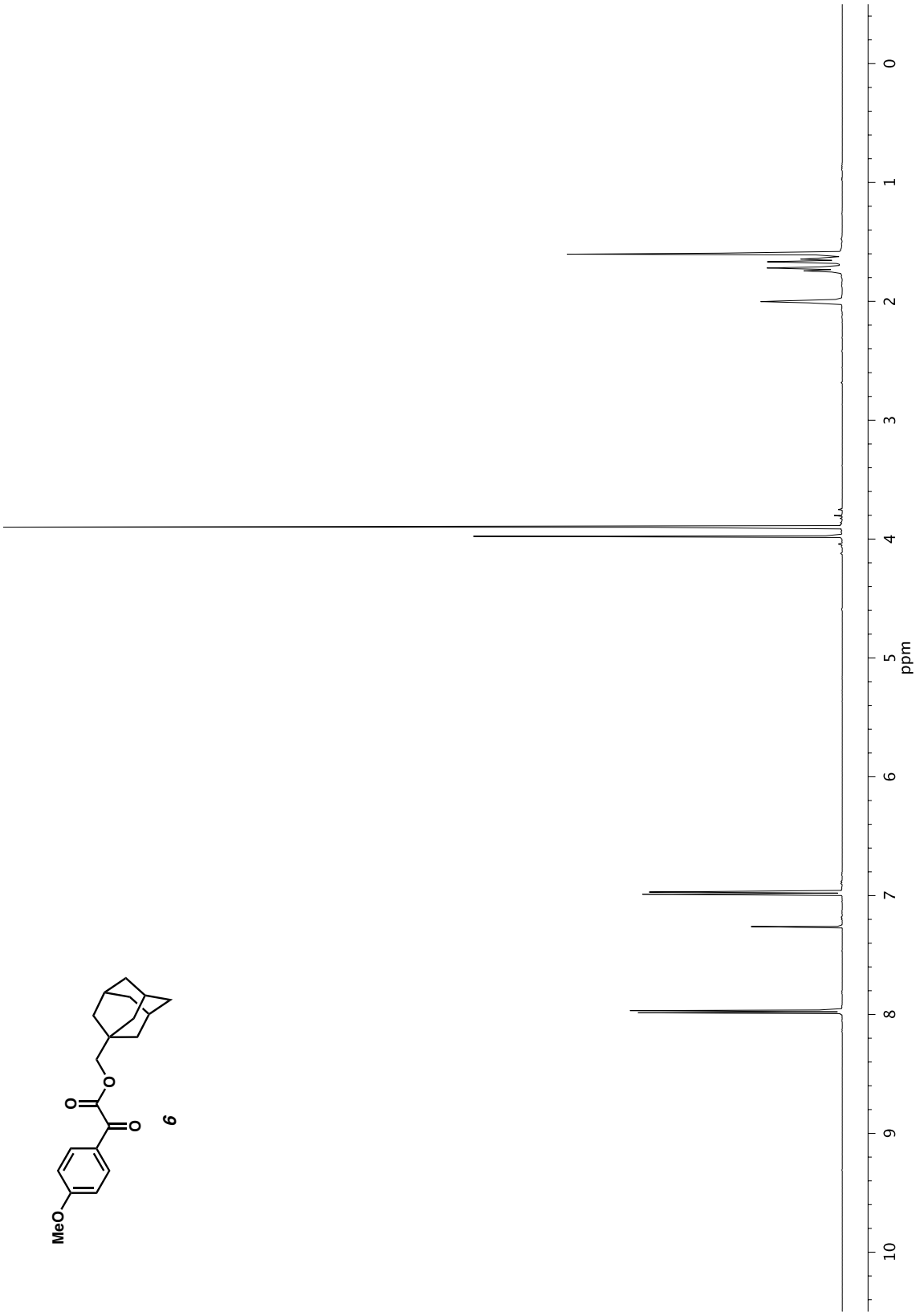
^{1}H NMR (500 MHz, $CDCl_3$) of compound **16**.



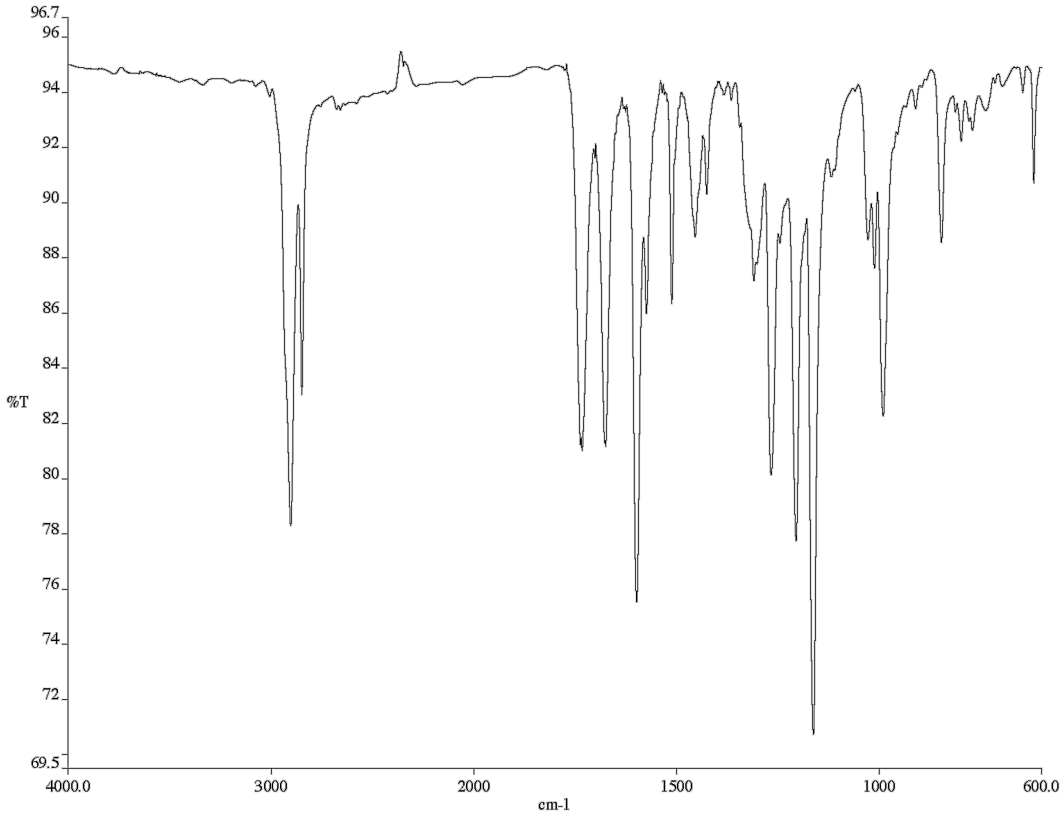
Infrared spectrum (Thin Film, NaCl) of compound **16**.



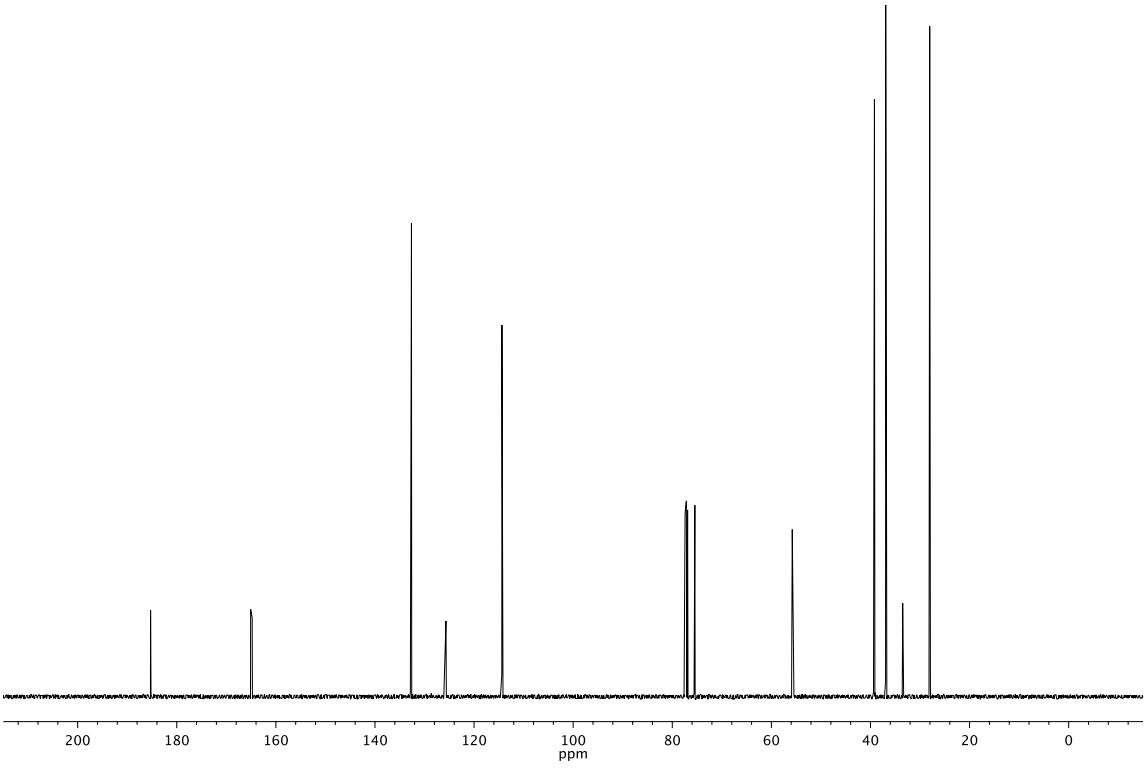
^{13}C NMR (126 MHz, $CDCl_3$) of compound **16**.



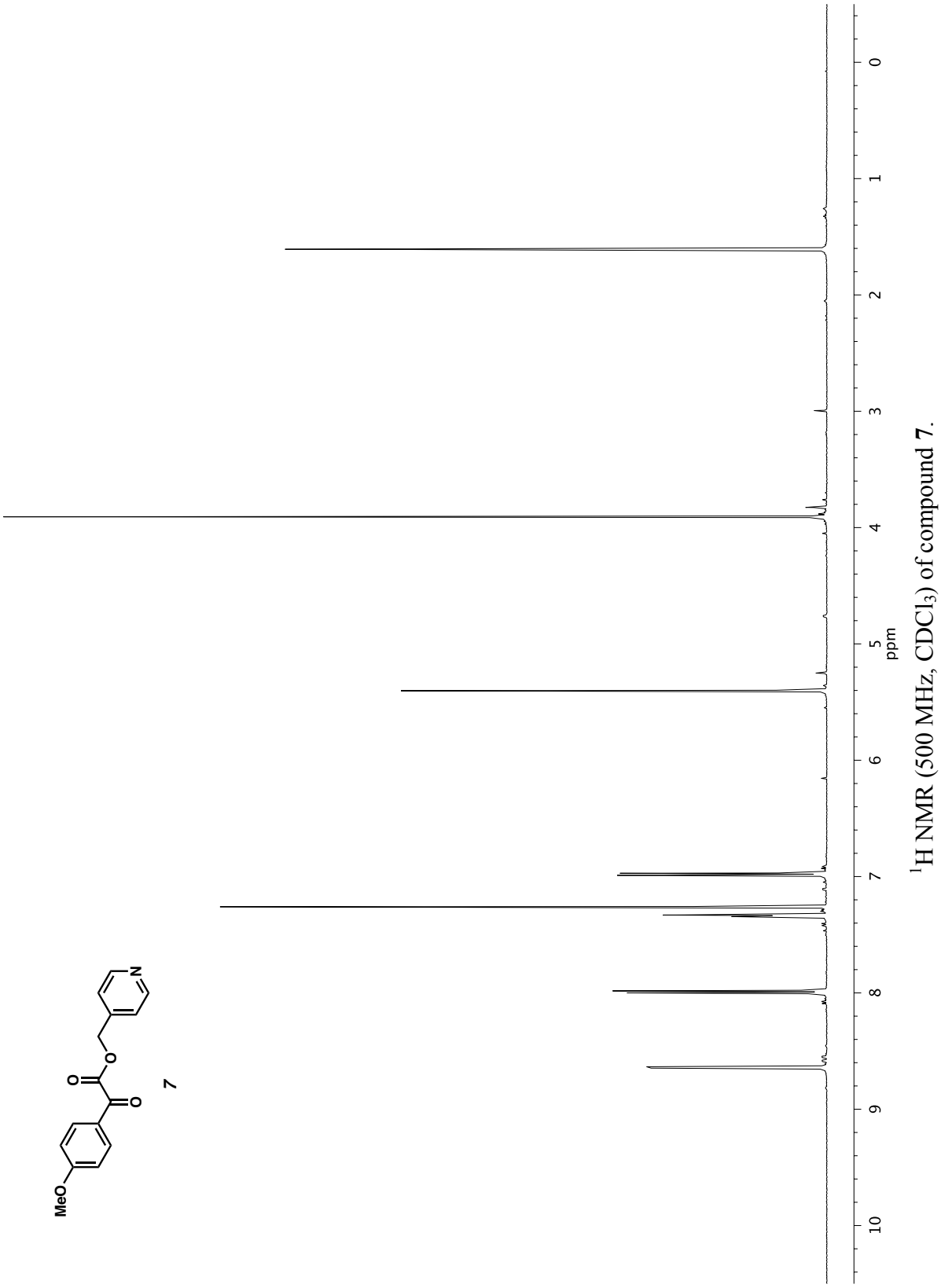
^{1}H NMR (500 MHz, $CDCl_3$) of compound **6**.



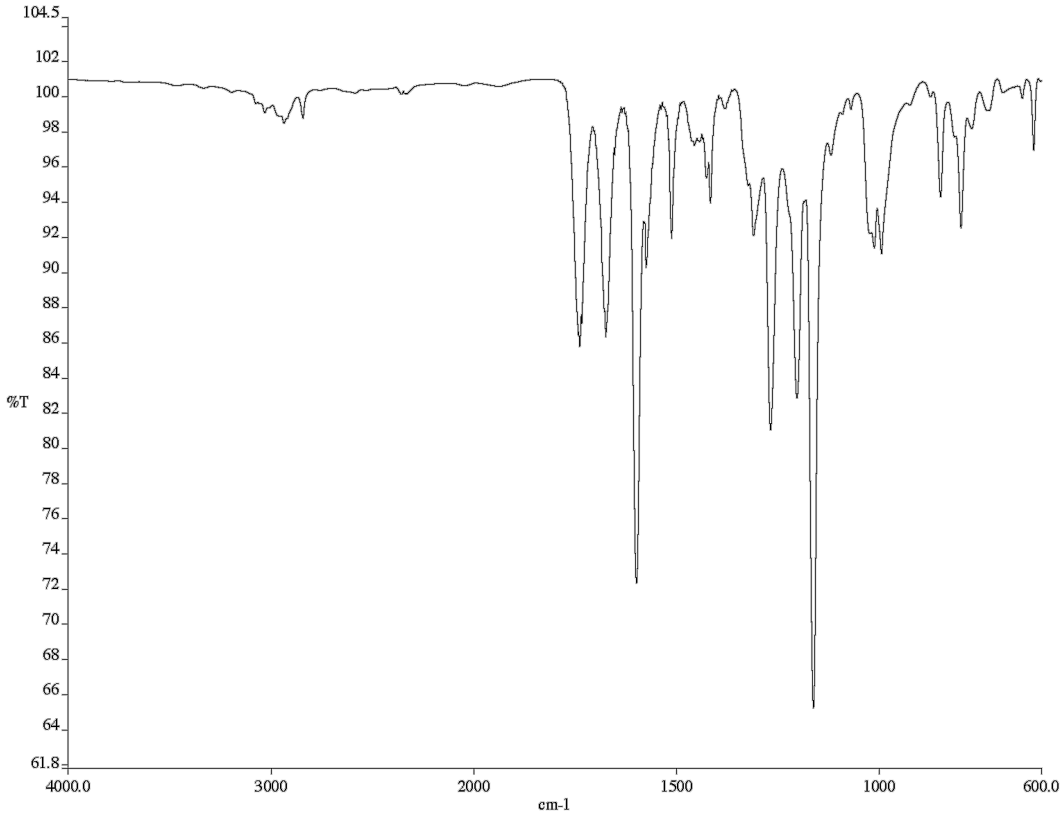
Infrared spectrum (Thin Film, NaCl) of compound **6**.



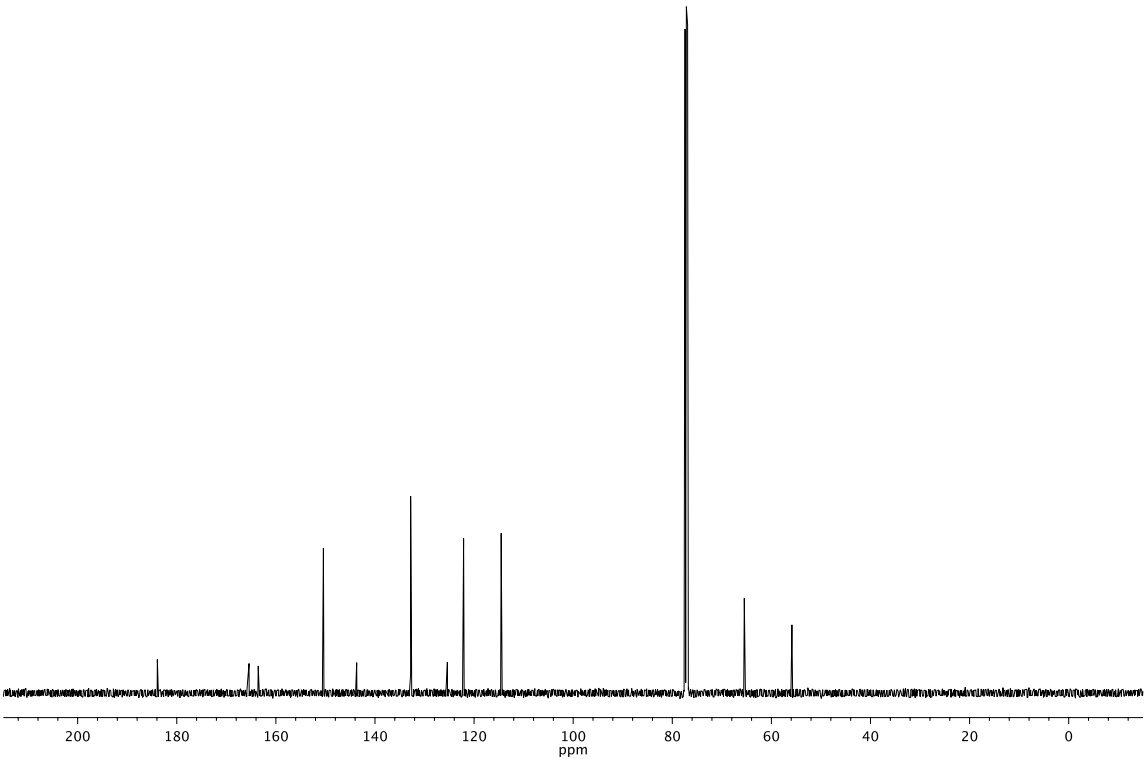
^{13}C NMR (126 MHz, $CDCl_3$) of compound **6**.



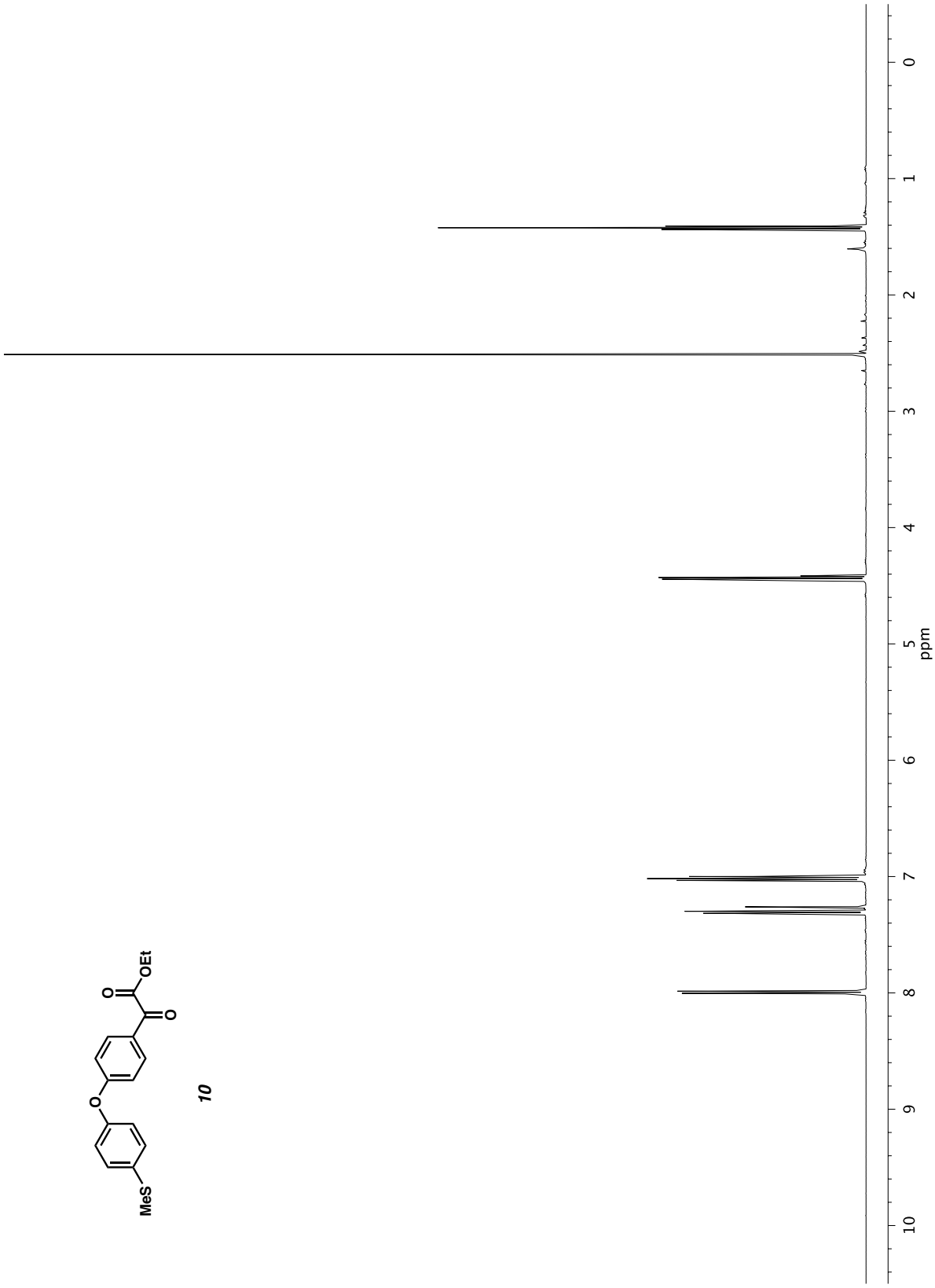
^{1}H NMR (500 MHz, $CDCl_3$) of compound **7**.



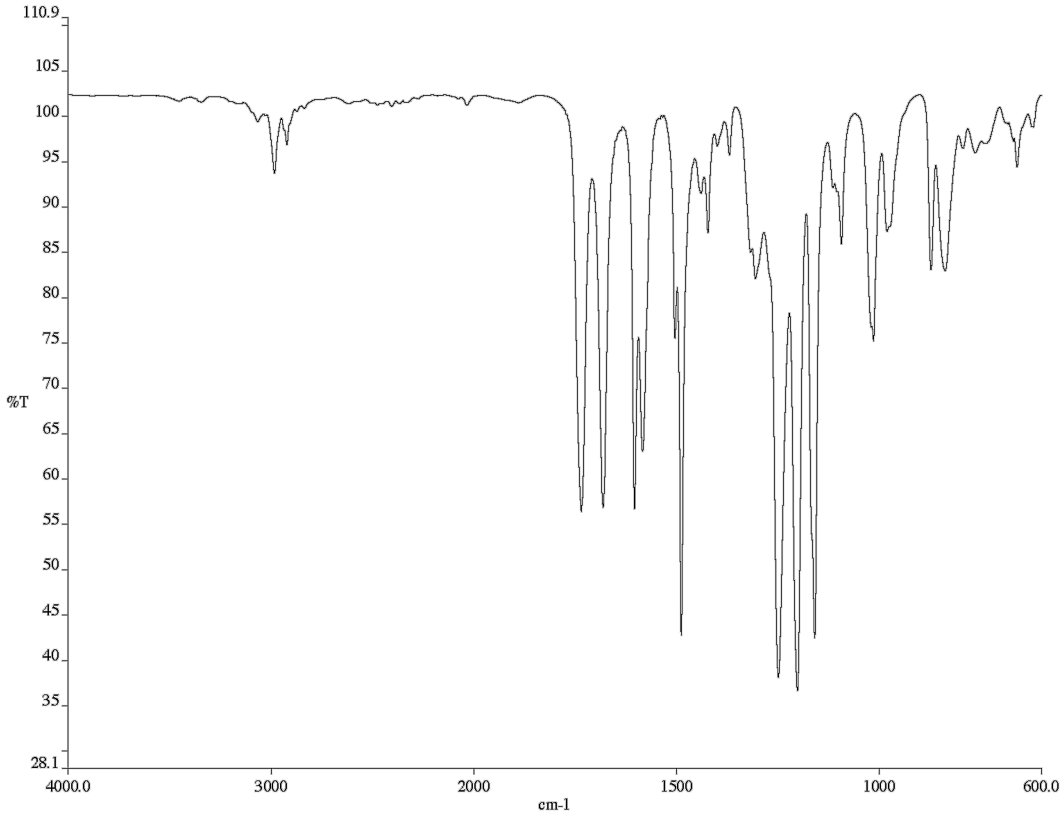
Infrared spectrum (Thin Film, NaCl) of compound **7**.



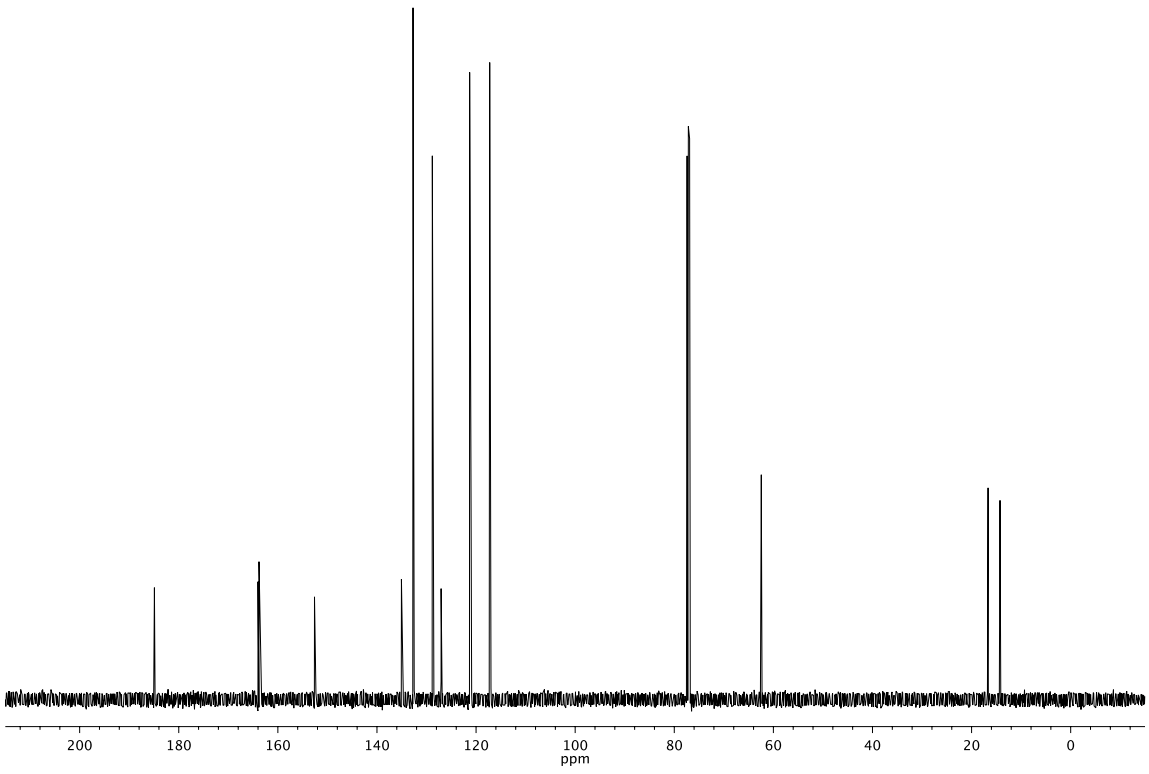
^{13}C NMR (126 MHz, $CDCl_3$) of compound **7**.



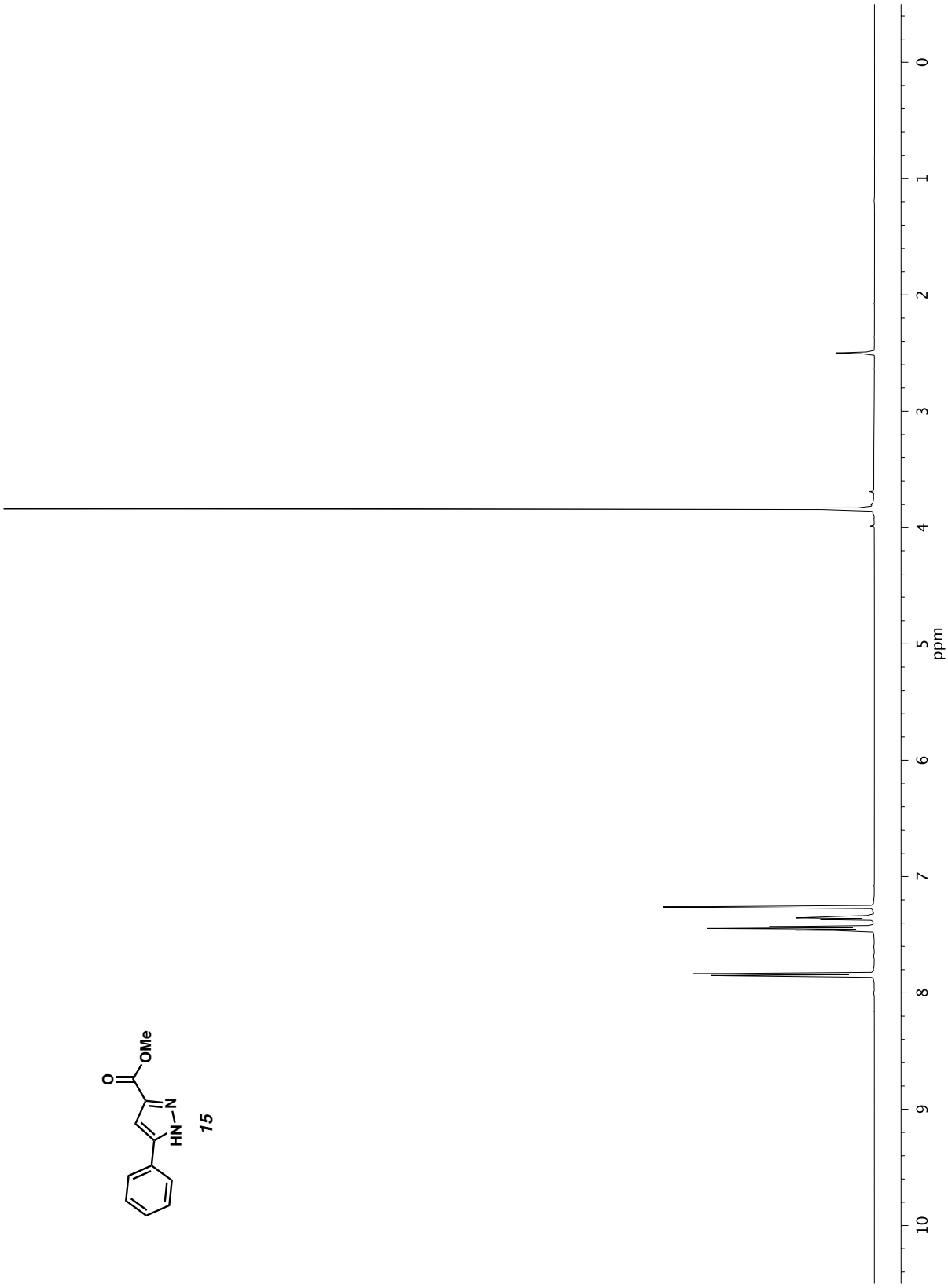
^{1}H NMR (500 MHz, $CDCl_3$) of compound **10**.



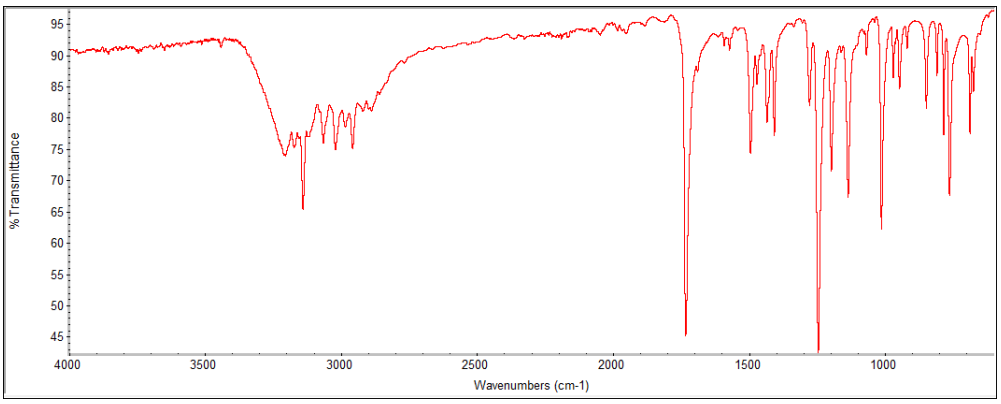
Infrared spectrum (Thin Film, NaCl) of compound **10**.



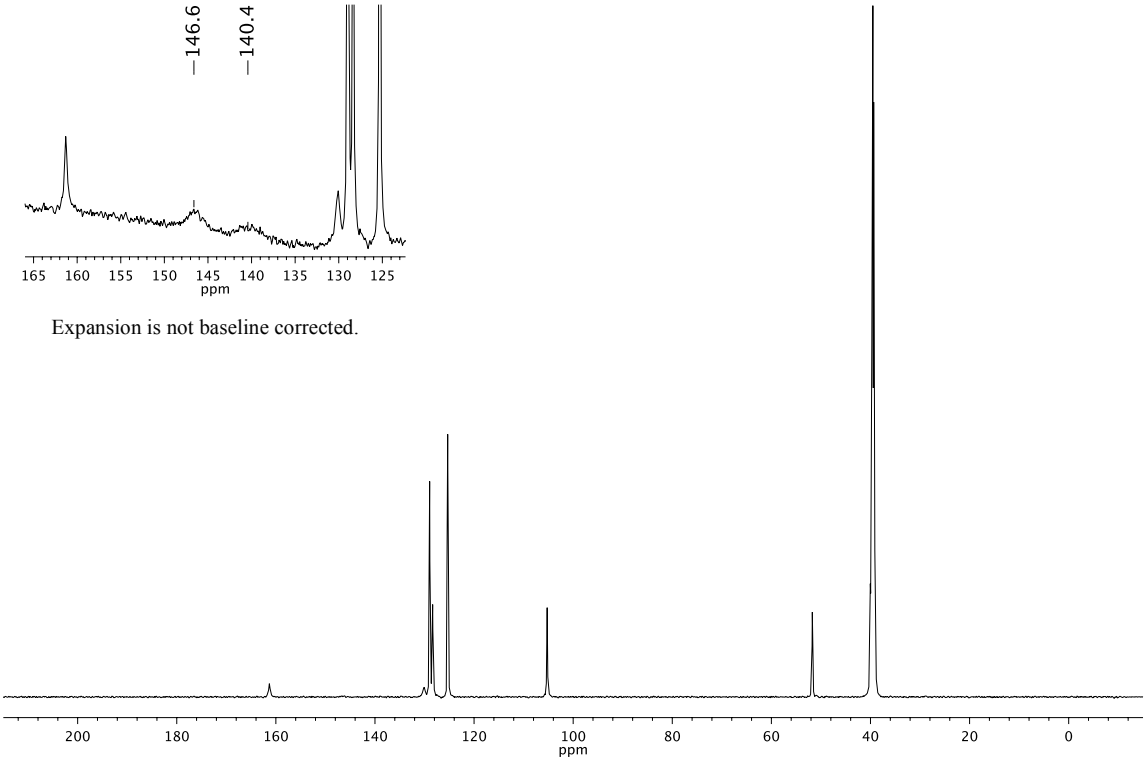
^{13}C NMR (126 MHz, $CDCl_3$) of compound **10**.



^{1}H NMR (500 MHz, DMSO-d_6) of compound **15**.



ATR-Infrared spectrum (Neat) of compound **15**.



^{13}C NMR (126 MHz, DMSO-d_6) of compound **15**.