Supplementary Material

One-Pot Synthesis of Highly Functionalized Pyridines via a Rhodium Carbenoid Induced Ring Expansion of Isoxazoles

James R. Manning and Huw M. L. Davies*

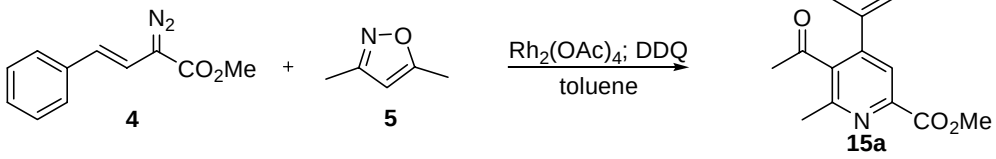
Department of Chemistry, University at Buffalo, The State University of New York,

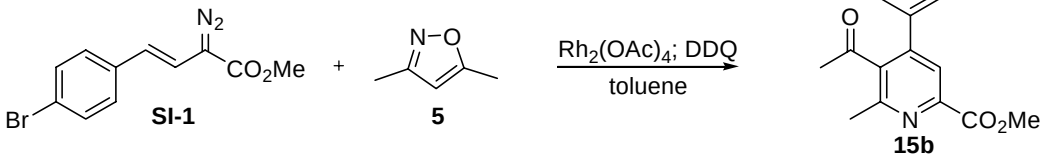
Buffalo, New York, 14260-3000

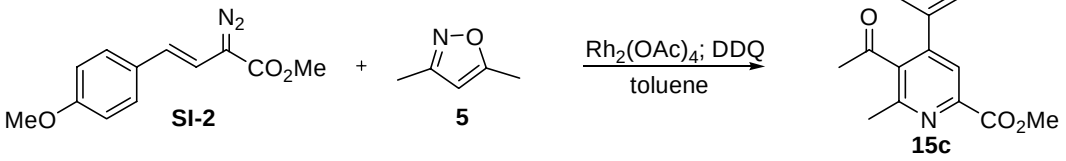
hdavies@buffalo.edu

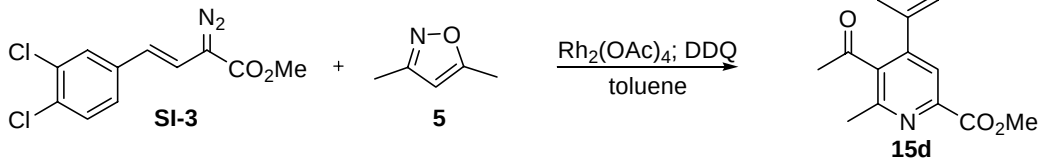
Table of Contents

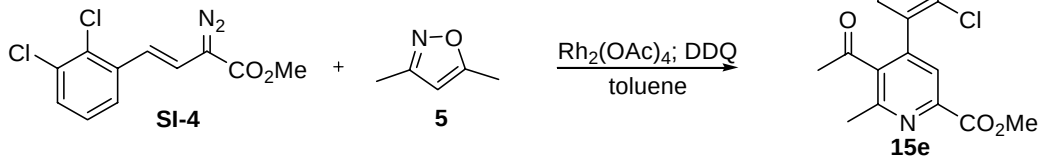
Reaction Equations for Table 1 Products:

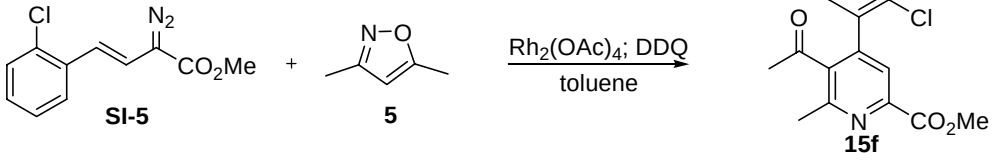
1) 

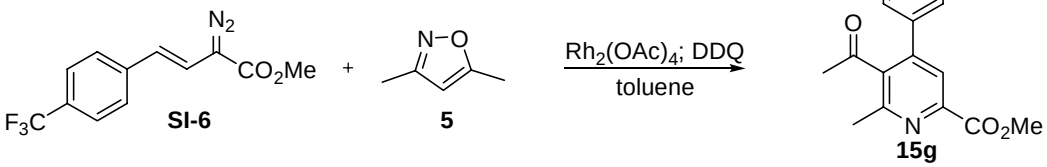
2) 

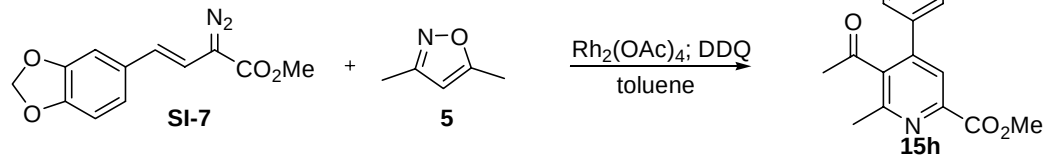
3) 

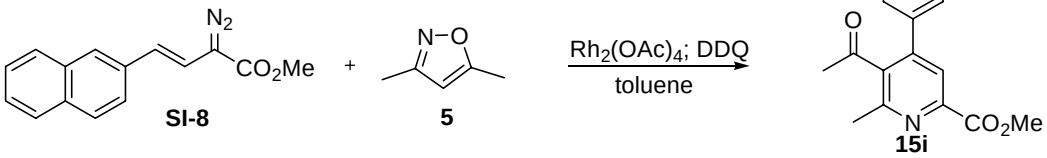
4) 

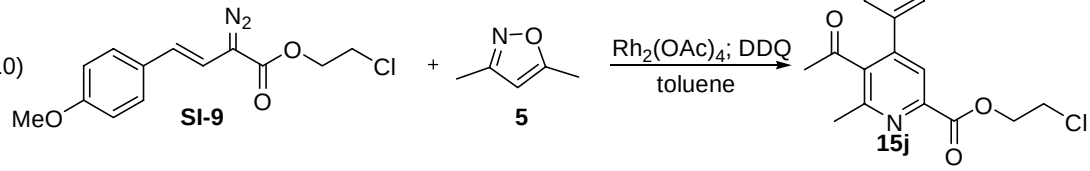
5) 

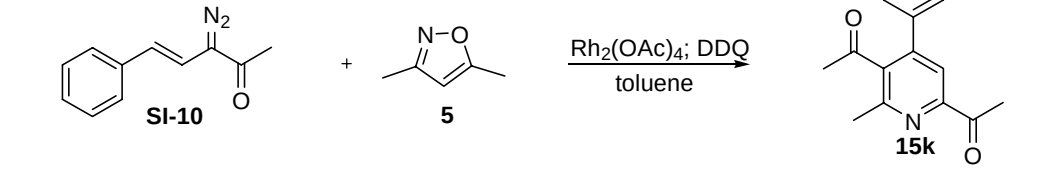
6) 

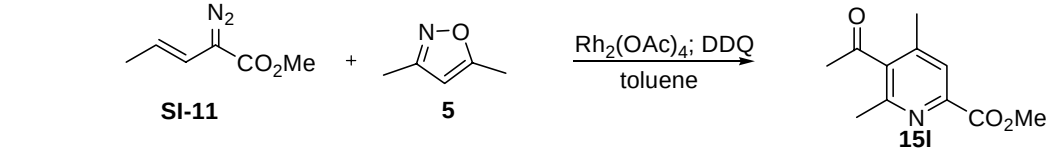
7) 

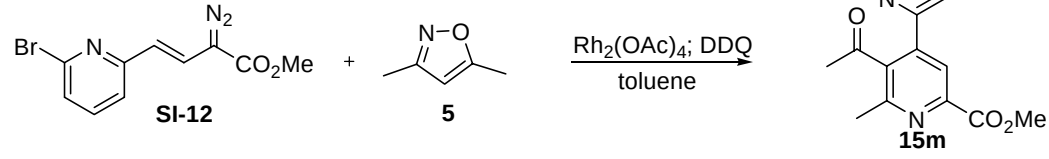
8) 

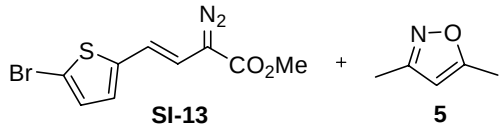
9) 

10) 

11) 

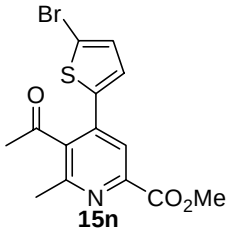
12) 

13) 

14) 

SI-13 + **5**

$Rh_2(OAc)_4$; DDQ, toluene



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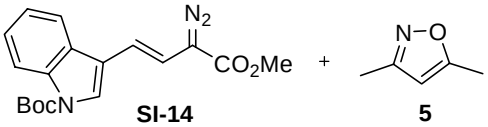
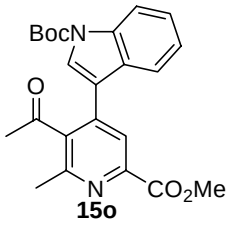
15) 

SI-14 + **5**

$Rh_2(OAc)_4$; DDQ, toluene



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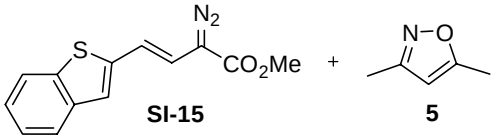
16) 

SI-15 + **5**

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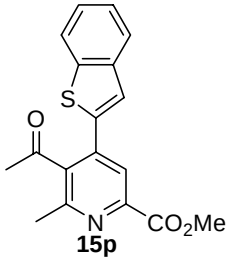

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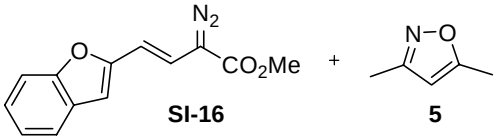
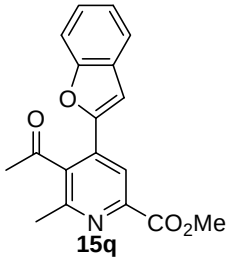
17) 

SI-16 + **5**

$Rh_2(OAc)_4$; DDQ, toluene



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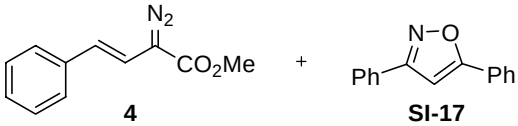
18) 

4 + **SI-17**

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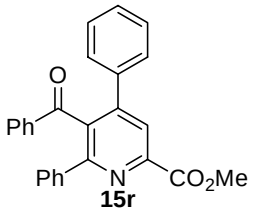

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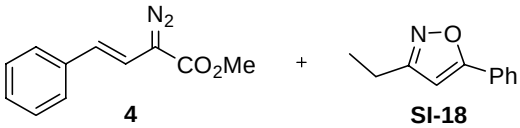
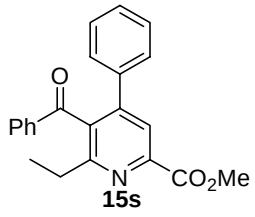
19) 

4 + **SI-18**

$Rh_2(OAc)_4$; DDQ, toluene



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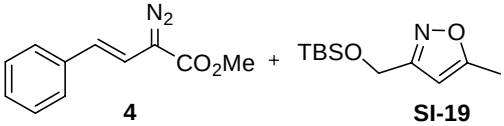
20) 

4 + **SI-19**

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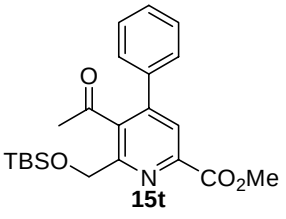

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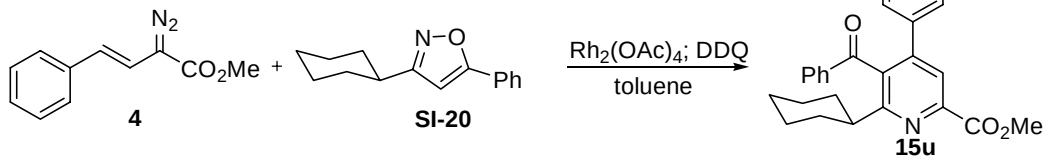
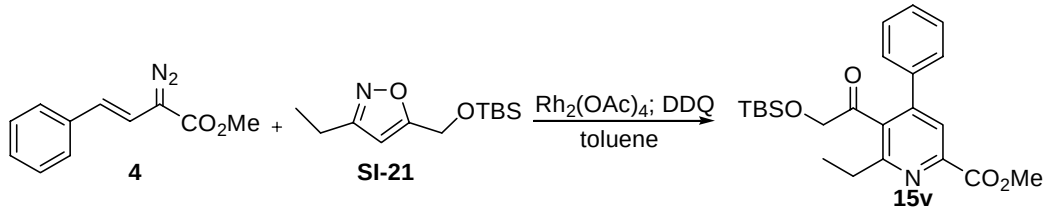
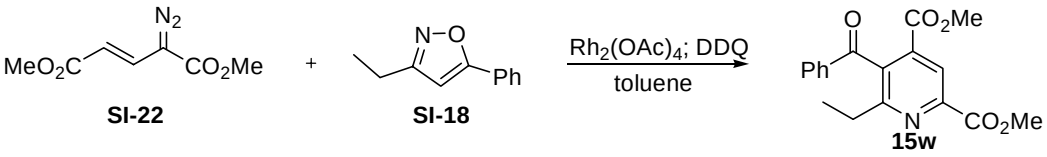
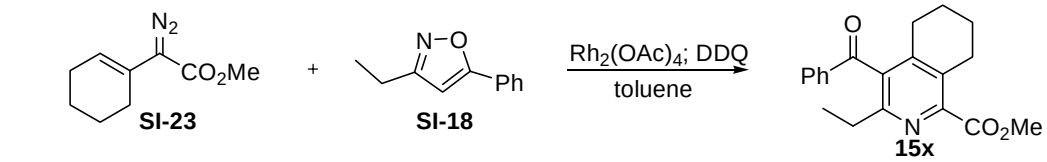
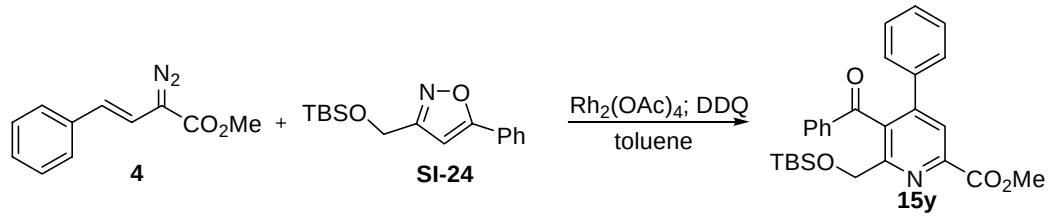
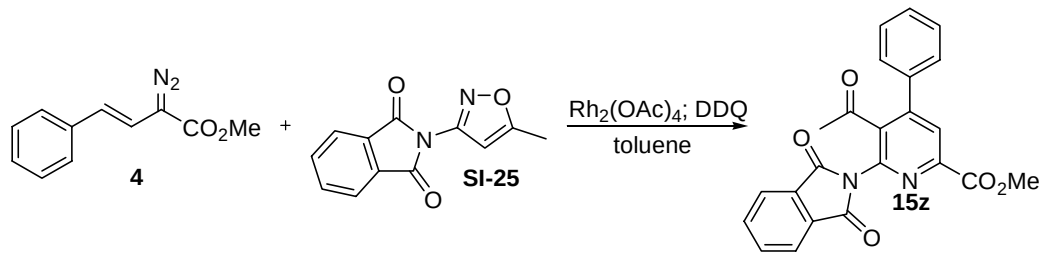
21) 

22) 

23) 

24) 

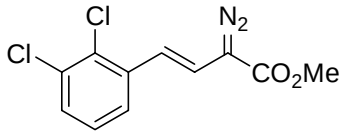
25) 

26) 

General: All experiments were performed under anhydrous conditions in an atmosphere of argon except where stated, using flame-dried glassware. Acetonitrile, THF, and toluene were dried by a solvent purification system (passed through activated alumina columns). Aqueous solutions of ammonium chloride (NH_4Cl) and sodium bicarbonate ($NaHCO_3$) were saturated. Unless otherwise noted, all other reagents were obtained from commercial sources and used as received. ^1H Nuclear Magnetic Resonance (NMR) spectra were recorded at 300, 400 or 500 MHz. Data are presented as follows: chemical shift (in ppm on the δ scale relative to δH 7.26 for the residual protons in $CDCl_3$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, b = broad), coupling constant (J/Hz), integration. Coupling constants were taken directly from the spectra and are uncorrected. ^{13}C NMR spectra were recorded at 75 or 125 MHz, and all chemical shift values are reported in ppm on the δ scale, with an internal reference of δC 77.0 for $CDCl_3$. Mass spectral determinations were carried out by LC-MS (ESI), or electron impact ionization (EI). Melting points are uncorrected. Infrared spectral data are reported in units of cm^{-1}. Analytical TLC was performed on silica gel plates using UV light or potassium permanganate stain if stated. Flash column chromatography was performed on silica gel 60A (230-400 mesh). Compounds **4**,[1] **SI-1**,[2] **SI-2**,[2] **SI-3**,[2] **SI-8**,[2] **SI-10**,[3] **SI-11**,[4] **SI-14**,[2] **SI-16**,[2] **SI-17**,[5] **SI-18**,[5] **SI-20**,[5] **SI-22**,[6] **SI-23**[7] and **SI-25**[8] were prepared according to their respective literature procedures.

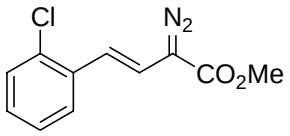
Synthesis of starting materials

(*E*)-Methyl 2-diazo-4-(2,3-dichlorophenyl)but-3-enoate (SI-4)



Prepared according to a modified literature procedure[1,2] using 2,3-dichlorobenzaldehyde as the aromatic aldehyde component (5.25 g, 30 mmol). Purified by flash chromatography (silica gel, 9:1 pentane:diethyl ether) to give the product as a pink solid (3.43 g, 42% yield). R_f 0.24 (9:1 pentane:diethyl ether); FTIR (neat): 3062, 2953, 2083, 1709, 1621, 1437, 1415, 1349 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.17 (*appt* t, *J* = 8.0 Hz, 1H), 6.59 (d, *J* = 16.5 Hz, 1H), 6.53 (d, *J* = 16.5 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8 (C), 136.9 (C), 133.3 (C), 130.2 (C), 128.3 (CH), 127.0 (CH), 124.1 (CH), 118.3 (CH), 115.6 (CH), 52.3 (CH_3), missing C attributed to $C=N_2$; LRMS (EI) m/z (relative intensity): 270 $[M]^+$ (67); HRMS (EI) Calcd for $[C_{11}H_8Cl_2N_2O_2]^+$ 269.9957, Found 269.9957.

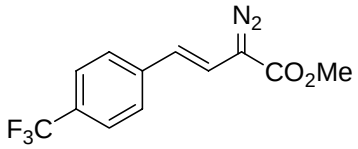
(*E*)-Methyl 2-diazo-4-(2-chlorophenyl)but-3-enoate (SI-5)



Prepared according to a modified literature procedure[1,2] using 2-chlorobenzaldehyde as the aromatic aldehyde component (4.22 g, 30 mmol). Purified by flash chromatography (silica gel, 12:1 pentane:diethyl ether) to give the product as a red oil that became solid upon storage in the freezer (4.68 g, 66% yield). R_f 0.31 (9:1 pentane:diethyl ether); FTIR (neat): 3065, 3026, 2953, 2081, 1705, 1621, 1472, 1438 cm^{-1}; ^1H NMR (500 MHz,

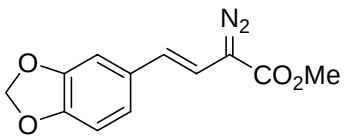
$CDCl_3$) δ 7.55 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.34 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.23 (*appt* t, *J* = 8.0 Hz, 1H), 7.14 (td, *J* = 8.0, 1.5 Hz, 1H), 6.58 (d, *J* = 16.5 Hz, 1H), 6.52 (d, *J* = 16.5 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6 (C), 134.4 (C), 131.9 (C), 129.3 (CH), 127.6 (CH), 126.6 (CH), 125.7 (CH), 118.2 (CH), 113.6 (CH), 51.9 (CH_3), missing C attributed to C=N_2; LRMS (EI) m/z (relative intensity): 236 $[M]^+$ (70); HRMS (EI) Calcd for $[C_{11}H_9ClN_2O_2]^+$ 236.0347, Found 236.0349.

(*E*)-Methyl 2-diazo-4-(4-(trifluoromethyl)phenyl)but-3-enoate (SI-6)



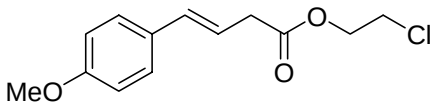
Prepared according to a modified literature procedure[1,2] using 4-(trifluoromethyl)benzaldehyde (1.74 g, 10 mmol) as the aromatic aldehyde component. Purified by flash chromatography (silica gel, 10:1 pentane:diethyl ether) to give the product as an orange solid (1.25 g, 46% yield). The ^{1}H NMR, IR, and MS data were consistent with the published values.[9] R_f 0.33 (9:1 pentane:diethyl ether); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0 (C), 140.2 (C), 128.6 (q, *J* = 33 Hz, C), 125.8 (CH), 125.6 (q, *J* = 4 Hz, CH), 124.2 (q, *J* = 271 Hz, CF_3), 121.2 (CH), 114.4 (CH), 52.3 (CH_3), missing C attributed to C=N_2.

(*E*)-Methyl 2-diazo-4-(benzo[*d*][1,3]dioxol-5-yl)but-3-enoate (SI-7)



Prepared according to a modified literature procedure[1,2] using piperonal (4.50 g, 30 mmol) as the aromatic aldehyde component. Purified by flash chromatography (silica gel, 9:1 pentane:diethyl ether) to give the product as a red solid (3.99 g, 54% yield). R_f 0.23 (9:1 pentane:diethyl ether); FTIR (neat): 2068, 1690, 1500, 1438 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.75 (s, 2H), 6.26 (d, *J* = 16.5 Hz, 1H), 6.11 (d, *J* = 16.5 Hz, 1H), 5.95 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5 (C), 148.1 (C), 146.8 (C), 131.3 (C), 122.8 (CH), 120.3 (CH), 109.1 (CH), 108.2 (CH), 105.0 CH), 101.0 (CH_2), 52.1 (CH_3), missing C attributed to C=N_2; LRMS (ESI) m/z (relative intensity): 269 $[M+Na]^+$ (100); HRMS (ESI) Calcd for $[C_{12}H_{11}N_2O_4]^+$ 247.0713, Found 247.0718.

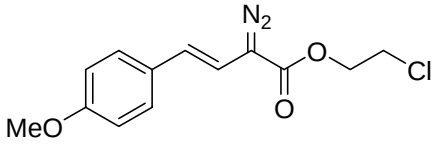
(*E*)-2-Chloroethyl 4-(4-methoxyphenyl)but-3-enoate (SI-26)



To a flame dried round-bottomed flask charged with a stir bar and under argon was added *p*-anisaldehyde (6.81 g, 50 mmol), 2-carboxyethyltriphenylphosphonium chloride[1] (22.2 g, 60 mmol) and THF (125 mL). The solution was cooled to 0 ºC in an ice bath and a solution of potassium *tert*-butoxide (14.0 g, 125 mmol) in THF (125 mL) was added via cannula over 20 min. The solution was stirred for another 15 min at 0 °C and then for 1 h at room temperature. The solution was then poured into a 1:1 mixture of ice water:saturated $NaHCO_3$ solution (200 mL) and washed with diethyl ether (2 x 50 mL). The aqueous layer was then acidified to pH 2 by the careful addition of 10% HCl solution and then extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were

dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was then dissolved in 2-chloroethanol (200 mL) and 1 mL of concentrated H_2SO_4 was added. The solution was stirred overnight at room temperature, then quenched with saturated $NaHCO_3$ solution and transferred to a separatory funnel. Diethyl ether (200 mL) and saturated $NaHCO_3$ solution (200 mL) were added and the layers were separated. The organic layer was washed with a 1:1 mixture of brine:saturated $NaHCO_3$ solution (2 x 100 mL), dried over $MgSO_4$, filtered and concentrated by evaporation. The residue was purified by flash chromatography (silica gel, 4:1 pentane:diethyl ether) to give the product as a white solid (7.15 g, 56% yield). mp = 64-65 °C, R_f 0.23 (5:1 pentane:diethyl ether); FTIR (neat): 2955, 2835, 1733, 1607, 1513 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.46 (d, *J* = 16.0 Hz, 1H), 6.15 (dt, *J* = 16.0, 7.0 Hz, 1H), 4.37 (t, *J* = 5.5 Hz, 2H), 3.81 (s, 3H), 3.70 (t, *J* = 5.5 Hz, 2H), 3.28 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (C), 158.9 (C), 132.7 (CH), 129.2 (C), 127.2 (CH), 118.7 (CH), 113.6 (CH), 63.9 (CH_2), 54.8 (CH_3), 41.3 (CH_2), 37.7 (CH_2); LRMS (EI) m/z (relative intensity): 254 $[M]^+$ (42); HRMS (EI) Calcd for $[C_{13}H_{15}ClO_3]^+$ 254.0704, Found 254.0710.

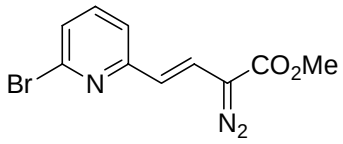
(*E*)-2-Chloroethyl 2-diazo-4-(4-methoxyphenyl)but-3-enoate (SI-9)



Prepared by a modified literature procedure.[10] To a dry round-bottomed flask charged with a stir bar and under argon was added **SI-26** (6.80 g, 27.0 mmol), *p*-acetamidobenzenesulfonyl azide[10] (9.73 g, 40.5 mmol) and acetonitrile (150 mL). The

solution was cooled to 0 °C in an ice bath and DBU (6.17 g, 40.5 mmol) was added rapidly by syringe. The solution was stirred for 3 hours at 0 °C, then quenched with saturated NH_4Cl solution (100 mL). The solution was extracted with diethyl ether (2 x 100 mL). The combined extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, 4:1 pentane:diethyl ether) to give the product as a dark red oil, which became solid upon storage in the freezer (5.44 g, 72% yield). R_f 0.22 (5:1 pentane:diethyl ether); FTIR (neat): 3003, 2958, 2836, 2082, 1701, 1606, 1251 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.28 (d, *J* = 16.5 Hz, 1H), 6.17 (d, *J* = 16.5 Hz, 1H), 4.49 (t, *J* = 6.0 Hz, 2H), 3.80 (s, 3H), 3.72 (t, *J* = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5 (C), 158.7 (C), 129.3 (C), 126.8 (CH), 122.9 (CH), 113.9 (CH), 107.9 (CH), 64.2 (CH_2), 54.9 (CH_3), 41.4 (CH_2), missing C attributed to $C{=}N_2$; LRMS (EI) m/z (relative intensity): 280 $[M]^+$ (18); HRMS (EI) Calcd for $[C_{13}H_{13}ClN_2O_3]^+$ 280.0609, Found 280.0613.

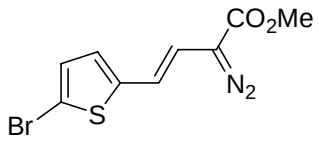
(*E*)-Methyl 2-diazo-4-(6-bromopyridin-2-yl)but-3-enoate (SI-12)



Prepared according to a modified literature procedure[1,2] using 6-bromopyridine-2-carboxaldehyde (5.2 g, 28 mmol) as the aromatic aldehyde component. Purified by flash chromatography (silica gel, 5:1 pentane:diethyl ether) to give the product as an orange solid (2.60 g, 33% yield). R_f 0.28 (5:1 pentane:diethyl ether); FTIR (neat): 3064, 2954, 2093, 1697, 1623, 1571, 1370, 1291 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (t, *J* = 8.0

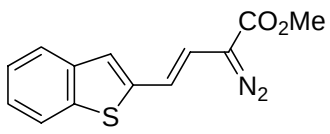
Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 15.5 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 6.38 (d, J = 15.5 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4 (C), 156.1 (C), 141.8 (C), 138.6 (CH), 125.1 (CH), 120.4 (CH), 119.7 (CH), 118.3 (CH), 52.2 (CH_3), missing C attributed to C=N_2); LRMS (EI) m/z (relative intensity): 281 $[M]^+$ (52); HRMS (ESI) Calcd for $[C_{10}H_8BrN_3O_2]^+$ 280.9794, Found 280.9800.

(*E*)-methyl 2-diazo-4-(5-bromothiophen-2-yl)but-3-enoate (SI-13)



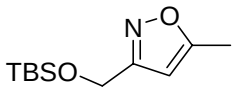
Prepared according to a modified literature procedure[1,2] using 5-bromo-2-thiophenecarboxaldehyde (7.80 g, 40.9 mmol) as the aromatic aldehyde component. Purified by flash chromatography (silica gel, 10:1 pentane:diethyl ether) to give the product as an red solid (5.72 g, 49% yield). R_f 0.28 (9:1 pentane:diethyl ether); FTIR (neat): 2959, 2069, 1691, 1438, 1305, 1244, 1117, 924, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, J = 4.0 Hz, 1H), 6.63 (d, J = 4.0 Hz, 1H), 6.31 (d, J = 16.0 Hz, 1H), 6.17 (d, J = 16.0 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0 (C), 143.7 (C), 130.3 (CH), 124.6 (CH), 116.0 (CH), 111.1 (CH), 110.7 (C), 52.3 (CH_3), missing C attributed to C=N_2; LRMS (EI) m/z (relative intensity): 288.0 $[M]^+$ (18), 200.9 (30), 179 (100); HRMS (EI) Calcd for $[C_9H_7N_2O_2Br^{81}S]^+$ 287.9386, Found 287.9390.

(*E*)-Methyl 2-diazo-4-(benzo[*b*]thiophen-2-yl)but-3-enoate (SI-15)



Prepared according to a modified literature procedure[1,2] using benzo[b]thiophene-2-carboxaldehyde (5.00 g, 30.8 mmol) as the aromatic aldehyde component. Purified by flash chromatography (silica gel, 10:1 pentane:diethyl ether) to give the product as a red solid (3.0 g, 38% yield). R_f 0.29 (9:1 pentane:diethyl ether); FTIR (neat): 3056, 3000, 2951, 2080, 1710, 1434, 1237, 930, 751 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.31-7.25 (m, 2H), 7.07 (s, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (C), 142.1 (C), 140.1 (C), 138.8 (C), 124.4 (CH), 124.3 (CH), 123.2 (CH), 122.0 (CH), 121.4 (CH), 117.0 (CH), 113.2 (CH), 52.3 (CH_3), missing C attributed to $C=N_2$; LRMS (EI) m/z (relative intensity): 258 $[M]^+$ (42); HRMS (EI) Calcd for $[C_{13}H_{10}N_2O_2S]^+$ 258.0457, Found 258.0466.

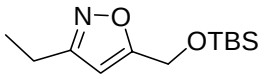
3-((*tert*-Butyldimethylsilyloxy)methyl)-5-methylisoxazole (SI-19)



To a flame dried round-bottomed flask charged with a stir bar and under argon was added (5-methylisoxazol-3-yl)methanol (0.396 g, 3.5 mmol), DCM (15 mL) and DMAP (0.021 g, 0.175 mmol). The solution was cooled to 0 °C in an ice bath and TBSCl (0.580 g, 3.85 mmol) followed by imidazole (0.262 g, 3.85 mmol) was added. The solution was stirred overnight at room temperature and then washed with brine (2X), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, 9:1 pentane:diethyl ether) to give the product as a clear oil (0.713 g, 90% yield). R_f 0.26 (15:1 pentane:diethyl ether); FTIR (neat): 2956, 2930, 2866, 2858, 1608, 1485, 1473, 1464, 1258, 1131, 1103, 839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03 (s,

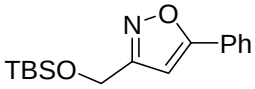
1H), 4.72 (s, 2H), 2.41 (s, 3H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0 (C), 164.0 (C), 100.5 (CH), 57.3 (CH_2), 25.6 (CH_3), 18.1 (C), 12.0 (CH_3), -5.5 (CH_3); LRMS (ESI) m/z (relative intensity): 228 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{11}H_{21}NO_2SiNa]^+$ 250.1234, Found 250.1236.

5-((*tert*-Butyldimethylsilyloxy)methyl)-3-ethylisoxazole (SI-21)



Prepared by a modified literature procedure[5] using propionaldehyde (1.16 g, 20 mmol) and *tert*-butyldimethyl(2-propynyloxy)silane as the components. Purified by flash chromatography (silica gel, 15:1 pentane:diethyl ether) to give the product as a colorless oil (2.25 g, 47% yield). R_f 0.32 (15:1 pentane:diethyl ether, $KMnO_4$ stain); FTIR (neat): 2956, 2931, 2885, 2858, 1609, 1463, 1384, 1257, 1137, 1098 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.05 (s, 1H), 4.74 (s, 2H), 2.68 (q, J = 7.5 Hz, 2H), 1.27 (t, J = 7.5 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4 (C), 164.7 (C), 100.6 (CH), 57.2 (CH_2), 25.5 (CH_3), 19.3 (CH_2), 18.0 (C), 12.4 (CH_3), -5.7 (CH_3); LRMS (ESI) m/z (relative intensity): 242 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{12}H_{24}NO_2Si]^+$ 242.1571, Found 242.1565.

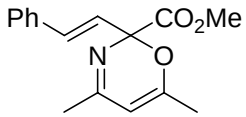
3-((*tert*-Butyldimethylsilyloxy)methyl)-5-phenylisoxazole (SI-24)



Prepared by the same procedure as for **SI-19** except using (5-phenylisoxazol-3-yl)methanol (0.500 g, 2.85 mmol). Purified by flash chromatography (silica gel, 12:1

pentane:diethyl ether) to give the product as a colorless oil (0.740 g, 90% yield). R_f 0.35 (15:1 pentane:diethyl ether); FTIR (neat): 2954, 2929, 2884, 2857, 1575, 1469, 1452, 1257, 1106, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79-7.77 (m, 2H), 7.46-7.42 (m, 3H), 6.56 (s, 1H), 4.80 (s, 2H), 0.94 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5 (C), 164.3 (C), 129.8 (CH), 128.6 (CH), 127.3 (C), 125.5 (CH), 98.3 (CH), 57.3 (CH_2), 25.6 (CH_3), 18.0 (C), -5.6 (CH_3); LRMS (ESI) m/z (relative intensity): 290 $[M+H]^+$ (100); Anal. Calcd for $C_{16}H_{23}NO_2Si$: C, 66.39; H, 8.01; N, 4.84. Found: C, 66.65; H, 8.13; N, 4.85.

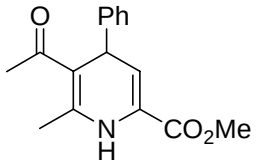
(*E*)-Methyl 4,6-dimethyl-2-styryl-2*H*-1,3-oxazine-2-carboxylate (6)



To a flame dried round-bottomed flask charged with a stir bar and under argon was added 3,5-dimethylisoxazole **5** (0.049 g, 0.50 mmol), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol) and toluene (1.5 mL). A condenser was attached to the flask and the solution was heated to 60 °C in an oil bath. A solution of (*E*)-methyl 2-diazo-4-phenylbut-3-enoate **4** (0.202 g, 1.0 mmol) in toluene (1.5 mL) was then added dropwise into the solution by syringe pump over 30 min. The solution was then concentrated *in vacuo* and the residue purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a sticky yellow oil (0.107 g, 79% yield). R_f 0.13 (1:1 pentane:diethyl ether); FTIR (neat): 2952, 1742, 1659, 1578, 1237, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.0 Hz, 2H), 7.35-7.28 (m, 3H), 7.06 (broad d, J = 15.5 Hz, 1H), 6.47 (broad d, J = 15.5 Hz, 1H), 5.35 (s, 1H), 3.81 (s, 3H), 2.09 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

135.5 (C), 128.5 (CH), 127.1 (CH), 52.9 (CH_3), 23.9 (CH_3), missing resonances attributed to peak broadening; LRMS (EI) m/z (relative intensity): 271 $[M]^+$ (10); HRMS (EI) Calcd for $[C_{16}H_{17}NO_3]^+$ 271.1203, Found 271.1205.

Methyl 5-acetyl-6-methyl-4-phenyl-1,4-dihydropyridine-2-carboxylate (7)

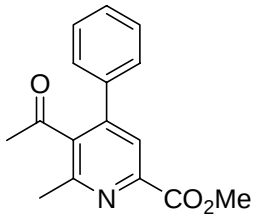


6 was dissolved in toluene and heated at reflux for 2.5 h. ^{1}H NMR analysis at this point showed complete conversion to **7**. R_f 0.28 (1:2 pentane:diethyl ether); FTIR (neat): 2978, 2870, 1717, 1668, 1561, 1479, 1437, 1278, 1139, 756, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.23-7.22 (m, 3H), 6.35 (bs, 1H), 6.09 (d, *J* = 5.5 Hz, 1H), 4.70 (d, *J* = 5.5 Hz, 1H), 3.77 (s, 3H), 2.43 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0 (C), 163.0 (C), 146.8 (C), 146.1 (C), 128.9 (CH), 127.3 (CH), 126.8 (CH), 125.4 (C), 116.0 (CH), 106.2 (C), 52.4 (CH_3), 41.8 (CH), 29.4 (CH_3), 21.2 (CH_3); LRMS (EI) m/z (relative intensity): 271 $[M]^+$ (45), 211 $[M\text{-}HCO_2Me]^+$ (100), 194 $[M\text{-}C_6H_5]^+$ (65); HRMS (EI) Calcd for $[C_{16}H_{17}NO_3]^+$ 271.1203, Found 271.1199.

Typical Procedure for the One-Pot Synthesis of Pyridines

To a flame dried round-bottomed flask charged with a stir bar and under argon was added 3,5-dimethylisoxazole **5** (0.049 g, 0.50 mmole), $Rh_2(OAc)_4$ (1.1 mg, 0.0025 mmol, 0.005 equiv) and toluene (1.5 mL). A reflux condenser was attached to the flask and the solution was heated in an oil bath to 60 °C. A solution of (*E*)-methyl 2-diazo-4-phenylbut-3-enoate **4** (0.202 g, 1.0 mmol) in toluene (1.5 mL) was then added dropwise into the solution by syringe pump over 30 min. The solution was then immediately transferred to a heating mantle and heated at reflux for 4 h. The solution was then allowed to cool to room temperature and DDQ (0.114 g, 0.5 mmol) was added. The solution was stirred for 30 min at room temperature, then diluted with a solution of diethyl ether containing 1% triethylamine (v/v, 10 mL). The solution was vacuum filtered through a plug of silica gel (1.5" x 1.5") using the 1% triethylamine solution in diethyl ether to wash through (200 mL). The filtrate was concentrated *in vacuo* and purified by flash chromatography to give **15a** as a yellow solid (0.093 g, 69% yield).

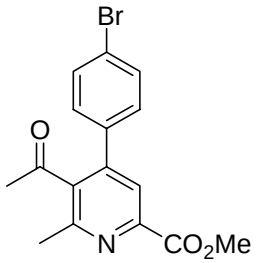
Methyl 5-acetyl-6-methyl-4-phenylpicolinate (15a)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a yellow solid (0.093 g, 69% yield). mp = 95-96 ºC; R_f 0.24 (1:2 pentane:diethyl ether); FTIR (neat): 2953, 1745, 1722, 1698, 1578, 1547, 1437, 1379, 1339, 1241, 1143, 778, 753, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.48-

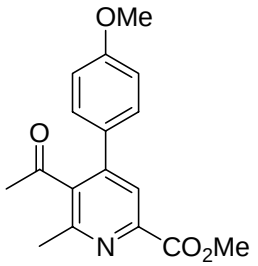
7.40 (m, 3H), 7.39-7.38 (m, 2H), 4.03 (s, 3H), 2.64 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3 (C), 165.3 (C), 154.6 (C), 147.3 (C), 138.7 (C), 136.9 (C), 129.4 (CH), 129.1 (CH), 128.5 (CH), 123.5 (CH), 53,1 (CH_3), 31.7 (CH_3), 22.9 (CH_3), missing C attributed to accidental equivalence; LRMS (ESI) m/z (relative intensity): 561 $[2M+Na]^+$ (100), 270 $[M+H]^+$ (29); Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.16; H, 5.67; N, 5.09.

Methyl 5-acetyl-4-(4-bromophenyl)-6-methylpicolinate (15b)



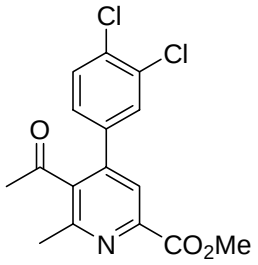
Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a light yellow solid (0.129 g, 74% yield). mp = 136-137 ºC; R_f 0.27 (1:1 pentane:diethyl ether); FTIR (neat): 2947, 1744, 1724, 1701, 1244, 1145, 1011 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 4.03 (s, 3H), 2.64 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0 (C), 165.1 (C), 154.7 (C), 147.4 (C), 145.8 (C), 138.5 (C), 135.7 (C), 132.3 (CH), 130.0 (CH), 124.1 (C), 123.1 (CH), 53.1 (CH_3), 31.8 (CH_3), 22.8 (CH_3); LRMS (ESI) m/z (relative intensity): 350 $[M(^{81}Br)+H]^+$ (100); Anal. Calcd for $C_{16}H_{14}BrNO_3$: C, 55.19; H, 4.05; N, 4.02. Found: C, 55.18; H, 4.08; N, 4.03.

Methyl 5-acetyl-4-(4-methoxyphenyl)-6-methylpicolinate (15c)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a yellow solid (0.096 g, 64% yield). mp = 129-130 ºC; R_f 0.23 (1:2 pentane:diethyl ether); FTIR (neat): 2952, 2839, 1722, 1699, 1514, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 4.02 (s, 3H), 3.86 (s, 3H), 2.62 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5 (C), 165.2 (C), 160.5 (C), 154.3 (C), 147.0 (C), 146.7 (C), 138.3 (C), 129.7 (CH), 128.8 (C), 123.2 (CH), 114.4 (CH), 55.2 (CH_3), 52.9 (CH_3), 31.4 (CH_3), 22.7 (CH_3); LRMS (ESI) m/z (relative intensity): 300 $[M+H]^+$ (100); Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 67.94; H, 5.97; N, 4.52.

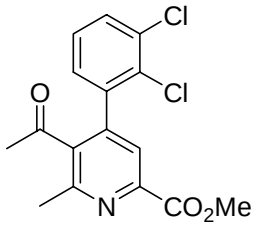
Methyl 5-acetyl-4-(3,4-dichlorophenyl)-6-methylpicolinate (15d)



Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as an off-white solid (0.119 g, 70% yield). mp = 141-142 ºC; R_f 0.13 (1:1 pentane:diethyl ether); FTIR (neat): 2951, 1724, 1702, 1242, 1139 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 2.0 Hz, 1H), 7.21 (dd,

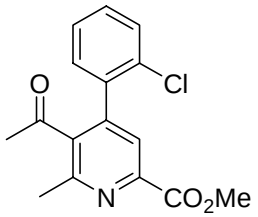
J = 8.5, 2.0 Hz, 1H), 4.04 (s, 3H), 2.64 s, 3H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6 (C), 165.0 (C), 154.8 (C), 147.6 (C), 144.5 (C), 138.5 (C), 136.7 (C), 134.1 (C), 133.6 (C), 131.1 (CH), 130.3 (CH), 127.8 (CH), 123.0 (CH), 53.2 (CH_3), 31.9 (CH_3), 22.8 (CH_3); LRMS (EI) m/z (relative intensity): 337 $[M]^+$ (7); Anal. Calcd for $C_{16}H_{13}Cl_2NO_3$: C, 56.82; H, 3.87; N, 4.14. Found: C, 56.95; H, 3.93; N, 4.05.

Methyl 5-acetyl-4-(2,3-dichlorophenyl)-6-methylpicolinate (15e)



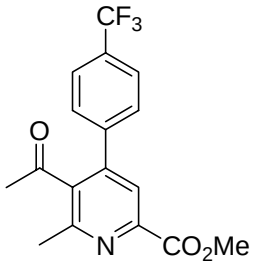
Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a yellow solid (0.129 g, 76% yield). mp = 119-120 °C; R_f 0.22 (1:2 pentane:diethyl ether); FTIR (neat): 2951, 1746, 1725, 1703, 1438, 1413, 1246, 1150 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.57 (dd, J = 8.0, 1.5 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.09 (dd, J = 8.0, 1.5 Hz, 1H), 4.03 (s, 3H), 2.67 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4 (C), 164.8 (C), 154.7 (C), 146.9 (C), 144.2 (C), 138.9 (C), 137.3 (C), 133.9 (C), 131.2 (CH), 130.6 (C), 129.1 (CH), 127.5 (CH), 123.9 (CH), 53.0 (CH_3), 31.3 (CH_3), 22.9 (CH_3); LRMS (ESI) m/z (relative intensity): 338 $[M+H]^+$ (100); Anal. Calcd for $C_{16}H_{13}Cl_2NO_3$: C, 56.82; H, 3.87; N, 4.14. Found: C, 56.88; H, 3.88; N, 4.10.

Methyl 5-acetyl-4-(2-chlorophenyl)-6-methylpicolinate (15f)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a light yellow solid (0.116 g, 76% yield). mp = 158-159 ºC; R_f 0.27 (1:2 pentane:diethyl ether); FTIR (neat): 2951, 1745, 1724, 1702, 1437, 1240 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.40 (td, *J* = 8.0, 1.5 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.0, 1.5 Hz, 1H), 4.03 (s, 3H), 2.66 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5 (C), 164.8 (C), 154.5 (C), 146.6 (C), 144.5 (C), 139.0 (C), 135.1 (C), 131.9 (C), 130.8 (CH), 130.4 (CH), 129.8 (CH), 126.9 (CH), 124.1 (CH), 52.8 (CH_3), 31.0 (CH_3), 22.8 (CH_3); LRMS (ESI) m/z (relative intensity): 304 $[M+H]^+$ (100); Anal. Calcd for $C_{16}H_{14}ClNO_3$: C, 63.27; H, 4.65; N, 4.61. Found: C, 63.44; H, 4.71; N, 4.58.

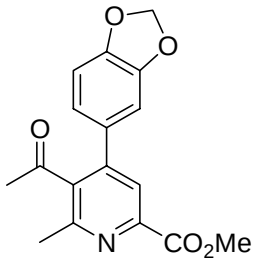
Methyl 5-acetyl-6-methyl-4-(4-(trifluoromethyl)phenyl)picolinate (15g)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a yellow solid (0.123 g, 73% yield). mp = 99-101 ºC; R_f 0.29 (1:2 pentane:diethyl ether); FTIR (neat): 2954, 1746, 1725, 1703, 1326, 1245, 1168, 1127, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.52 (d,

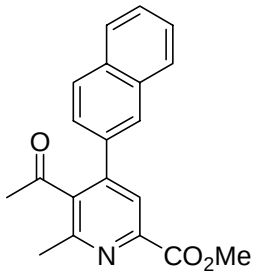
J = 8.0 Hz, 2H), 4.04 (s, 3H), 2.65 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6 (C), 164.9 (C), 154.7 (C), 147.5 (C), 145.5 (C), 140.3 (C), 138.6 (C), 131.4 (q, J = 33 Hz, C), 128.9 (CH), 125.9 (q, J = 3.5 Hz, CH), 123.6 (q, J = 271 Hz, CF_3), 123.1 (CH), 53.0 (CH_3), 31.8 (CH_3), 22.7 (CH_3); LRMS (ESI) m/z (relative intensity): 697 $[2M+Na]^+$ (30), 338 $[M+H]^+$ (100); Anal. Calcd for $C_{17}H_{14}F_3NO_3$: C, 60.54; H, 4.18; N, 4.15. Found: C, 60.40; H, 4.23; N, 4.08.

Methyl 5-acetyl-4-(benzo[*d*][1,3]dioxol-5-yl)-6-methylpicolinate (15h)



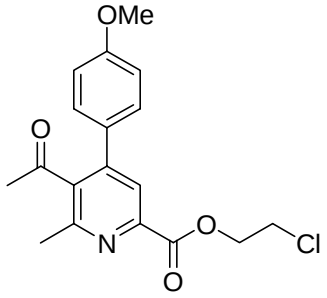
Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a light yellow solid (0.086 g, 55% yield). mp = 151-152 ºC; R_f 0.23 (1:2 pentane:diethyl ether); FTIR (neat): 2951, 2911, 1723, 1701, 1504, 1491, 1445, 1231, 1037 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (s, 1H), 6.91-6.83 (m, 3H), 6.06 (s, 2H), 4.03 (s, 3H), 2.62 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3 (C), 165.3 (C), 154.6 (C), 148.8 (C), 148.4 (C), 147.2 (C), 146.8 (C), 138.5 (C), 130.6 (C), 123.3 (CH), 122.8 (CH), 108.8 (CH), 108.7 (CH), 101.6 (CH_2), 53.0 (CH_3). 31.6 (CH_3), 22.8 (CH_3); LRMS (ESI) m/z (relative intensity): 314 $[M+H]^+$ (100); Anal. Calcd for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 65.07; H, 4.78; N, 4.39.

Methyl 5-acetyl-6-methyl-4-(naphthalen-2-yl)picolinate (15i)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a yellow solid (0.104 g, 65% yield). mp = 95-96 °C; R_f 0.13 (1:1 pentane:diethyl ether); FTIR (neat): 3057, 2951, 2858, 1744, 1723, 1700, 1578, 1437, 1392, 1249, 1232, 1143 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.90-7.86 (m, 3H), 7.58-7.56 (m, 2H), 7.48 (d, *J* = 8.5 Hz, 1H), 4.04 (s, 3H), 2.67 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2 (C), 165.2 (C), 154.5 (C), 147.2 (C), 147.1 (C), 138.7 (C), 134.1 (C), 133.1 (C), 132.9 (C), 129.0 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 127.2 (CH), 126.9 (CH), 125.4 (CH), 123.6 (CH), 52.9 (CH_3), 31.6 (CH_3), 22.8 (CH_3); LRMS (ESI) m/z (relative intensity): 320 $[M+H]^+$ (100); Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.13; H, 5.36; N, 4.36.

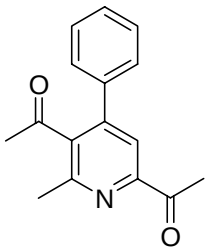
2-Chloroethyl 5-acetyl-4-(4-methoxyphenyl)-6-methylpicolinate (15j)



Purified by flash chromatography (silica gel, 1:3 pentane:diethyl ether) to give the product as a yellow solid (0.095 g, 55% yield). mp = 118-119 °C; R_f 0.16 (1:2

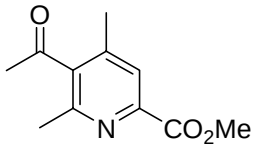
pentane:diethyl ether); FTIR (neat): 2960, 2839, 1745, 1723, 1699, 1609, 1515, 1253, 1239 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 4.68 (t, *J* = 6.0 Hz, 2H), 3.87 (s, 3H), 3.86 (t, *J* = 6.0 Hz, 2H), 2.62 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4 (C), 164.1 (C), 160.4 (C), 154.5 (C), 146.7 (C), 146.5 (C), 138.4 (C), 129.7 (CH), 128.7 (C), 123.4 (CH), 114.4 (CH), 64.9 (CH_2), 55.1 (CH_3), 41.0 (CH_2), 31.4 (CH_3), 22.6 (CH_3); LRMS (ESI) m/z (relative intensity): 348 $[M+H]^+$ (100); Anal. Calcd for $C_{18}H_{18}ClNO_4$: C, 62.16; H, 5.22; N, 4.03. Found: C, 62.23; H, 5.29; N, 3.91.

1-(5-(Acetyl)-6-methyl-4-phenylpyridin-2-yl)ethanone (15k)



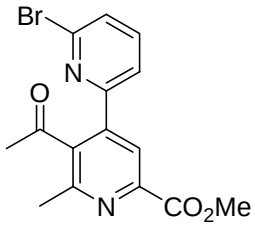
Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a white solid (0.081 g, 64% yield). mp = 125-126 ºC; R_f 0.24 (5:1 pentane:diethyl ether); FTIR (neat): 2991, 1707, 1698, 1379, 1352, 1228 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.46-7.45 (m, 3H), 7.38-7.36 (m, 2H), 2.76 (s, 3H), 2.60 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7 (C), 199.8 (C), 153.7 (C), 152.7 (C), 147.1 (C), 138.6 (C), 137.3 (C), 129.2 (CH), 129.0 (CH), 128.5 (CH), 119.7 (CH), 31.7 (CH_3), 25.8 (CH_3), 22.7 (CH_3); LRMS (ESI) m/z (relative intensity): 254 $[M+H]^+$ (100); Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.98; H, 5.97; N, 5.34.

Methyl 5-acetyl-4,6-dimethylpicolinate (15l)



Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as an oil (0.032 g, 31% yield). R_f 0.18 (1:2 pentane:diethyl ether); FTIR (neat): 2954, 1720, 1701, 1584, 1564, 1439, 1235, 1143 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (s, 1H), 4.01 (s, 3H), 2.56 (s, 3H), 2.54 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3 (C), 165.4 (C), 153.0 (C), 147.0 (C), 143.5 (C), 140.5 (C), 124.6 (CH), 53.0 (CH_3), 31.7 (CH_3), 22.6 (CH_3), 18.8 (CH_3); LRMS (ESI) m/z (relative intensity): 437 $[2M+Na]^+$ (98), 208 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{11}H_{14}NO_3]^+$ 208.0968, Found 208.0969.

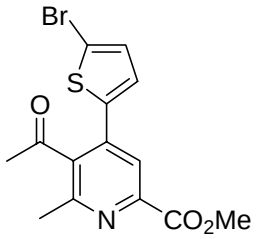
Methyl 5-acetyl-4-(6-bromopyridin-2-yl)-6-methylpicolinate (15m)



Purified by flash chromatography (silica gel, diethyl ether) to give the product as a yellow solid (0.079 g, 45% yield). mp = 135-136 °C, R_f 0.22 (diethyl ether); FTIR (neat): 3070, 2952, 1742, 1723, 1701, 1563, 1544, 1436, 1250, 1147, 1120 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H), 7.53 (d, J = 7.5 Hz, 1H), 4.05 (s, 3H), 2.67 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.2 (C), 165.1 (C), 155.0 (C), 154.3 (C), 147.4 (C), 143.1 (C), 141.3 (C), 139.6 (CH),

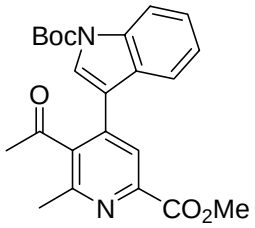
139.2 (C), 128.5 (CH), 121.0 (CH), 53.2 (CH_3), 32.1 (CH_3), 22.7 (CH_3), missing CH attributed to accidental equivalence; LRMS (ESI) m/z (relative intensity): 349 $[M+H]^+$ (72); Anal. Calcd for $C_{15}H_{13}BrN_2O_3$: C, 51.60; H, 3.75; N, 8.02. Found: C, 51.60; H, 3.84; N, 7.95.

Methyl 5-acetyl-4-(5-bromothiophen-2-yl)-6-methylpicolinate (15n)



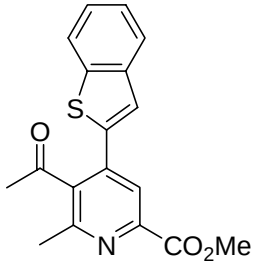
Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a sticky yellow solid (0.057 g, 32% yield). R_f 0.24 (1:2 pentane:diethyl ether); FTIR (neat): 2951 1745, 1723, 1701, 1580, 1438, 1239, 1145 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.09 (d, J = 4.0 Hz, 1H), 6.95 (d, J = 4.0 Hz, 1H), 4.03 (s, 3H), 2.61 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.1 (C), 165.0 (C), 154.8 (C), 147.6 (C), 139.0 (C), 138.4 (C), 137.5 (C), 131.4 (CH), 129.6 (CH), 122.6 (CH), 116.2 (C), 53.1 (CH_3), 31.5 (CH_3), 22.7 (CH_3); LRMS (EI) m/z (relative intensity): 353 $[M]^+$ (9), 274 $[M-Br]^+$ (100); HRMS (EI) Calcd for $[C_{14}H_{12}BrNO_3S]^+$ 352.9716, Found 352.9728.

***tert*-Butyl 3-(3-acetyl-6-(methoxycarbonyl)-2-methylpyridin-4-yl)-1*H*-indole-1-carboxylate (15o)**



Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a yellow solid (0.153 g, 75% yield). R_f 0.24 (1:2 pentane:diethyl ether); FTIR (neat): 2980, 2952, 1740, 1703, 1591, 1545, 1452, 1370, 1302, 1239, 1154, 1080 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.0 Hz, 1H), 8.20 (s, 1H), 7.63 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.43 (*appt* t, *J* = 8.0 Hz, 1H), 7.33 (*appt* t, *J* = 7.5 Hz, 1H), 4.04 (s, 3H), 2.66 (s, 3H), 2.17 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2 (C), 165.3 (C), 154.7 (C), 149.0 (C), 147.3 (C), 139.1 (C), 135.4 (C), 128.1 (C), 126.0 (CH), 125.5 (CH), 123.61 (CH), 123.56 (CH), 119.4 (CH), 116.4 (C), 115.5 (CH), 84.7 (C), 53.0 (CH_3), 31.4 (CH_3), 28.0 (CH_3), 22.8 (CH_3), missing C attributed to accidental equivalence; LRMS (ESI) m/z (relative intensity): 409 $[M+H]^+$ (100); Anal. Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.91; H, 6.01; N, 6.53.

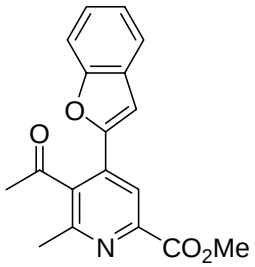
Methyl 5-acetyl-4-(benzo[*b*]thiophen-2-yl)-6-methylpicolinate (15p)



Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a light yellow solid (0.099 g, 61% yield). R_f 0.21 (1:2 pentane:diethyl ether); FTIR (neat): 3059, 3000, 2951, 2852, 1743, 1724, 1702, 1579, 1436, 1235, 1145, 749,

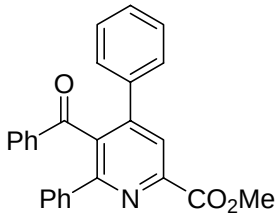
727 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.89-7.87 (m, 1H), 7.85-7.83 (m, 1H), 7.45-7.41 (m, 3H), 4.05 (s, 3H), 2.65 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4 (C), 165.1 (C), 154.8 (C), 147.5 (C), 140.7 (C), 139.8 (C), 139.7 (C), 138.2 (C), 137.5 (C), 126.3 (CH), 125.8 (CH), 125.1 (CH), 124.6 (CH), 123.3 (CH), 122.3 (CH), 53.2 (CH_3), 31.7 (CH_3), 22.8 (CH_3); LRMS (EI) m/z (relative intensity): 325 $[M]^+$ (82); Anal. Calcd for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N, 4.30; S, 9.85. Found: C, 66.24; H, 4.66; N, 4.24; S, 9.78.

Methyl 5-acetyl-4-(benzofuran-2-yl)-6-methylpicolinate (15q)



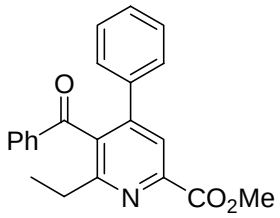
Purified by flash chromatography (silica gel, 1:3 pentane:diethyl ether) to give the product as a yellow solid (0.061 g, 39% yield). mp = 122-123 ºC; R_f 0.26 (1:3 pentane:diethyl ether); FTIR (neat): 3000, 2952, 1744, 1724, 1705, 1587, 1438, 1252, 1145, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.40 (dd, *J* = 8.5, 7.5 Hz, 1H), 7.31 (dd, *J* = 8.5, 7.5 Hz, 1H), 7.24 (s, 1H), 4.06 (s, 3H), 2.64 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7 (C), 165.1 (C), 155.3 (C), 154.7 (C), 150.2 (C), 147.5 (C), 135.8 (C), 134.6 (C), 128.0 (C), 126.4 (CH), 123.8 (CH), 121.9 (CH), 119.9 (CH), 111.5 (CH), 108.4 (CH), 53.1 (CH_3), 31.5 (CH_3), 22.6 (CH_3); LRMS (EI) m/z (relative intensity): 309 $[M]^+$ (52); Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 70.00; H, 5.01; N, 4.40.

Methyl 5-benzoyl-4,6-diphenylpicolinate (15r)



Purified by flash chromatography (silica gel, 2:1 pentane:diethyl ether) to give the product as a yellow solid (0.071 g, 36% yield). mp = 191-192 ºC; R_f 0.22 (2:1 pentane:diethyl ether); FTIR (neat): 3058, 3027, 2947, 1724, 1670, 1247 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.52-7.46 (m, 4H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.32-7.22 (m, 10H), 4.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6 (C), 165.5 (C), 157.6 (C), 150.4 (C), 148.0 (C), 138.7 (C), 137.1 (C), 137.0 (C), 136.4 (C), 133.4 (CH), 129.4 (CH), 129.2 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 124.5 (CH), 53.1 (CH_3); LRMS (ESI) m/z (relative intensity): 394 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{26}H_{20}NO_3]^+$ 394.1438, Found 394.1453.

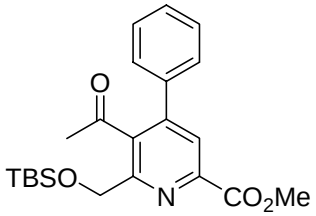
Methyl 5-benzoyl-6-ethyl-4-phenylpicolinate (15s)



Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as a sticky white solid (0.145 g, 84% yield). R_f 0.31 (1:1 pentane:diethyl ether); FTIR (neat): 3061, 3031, 2975, 2951, 2876, 1746, 1724, 1670, 1579, 1449, 1244 cm^{-1}; ^1H

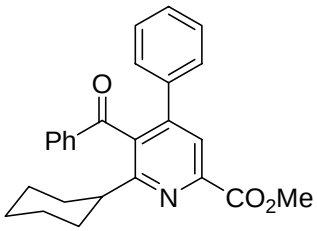
NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.31-7.27 (m, 4H), 7.24-7.23 (m, 3H), 4.06 (s, 3H), 2.83 (bs, 2H), 1.26 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2 (C), 165.5 (C), 160.9 (C), 148.8 (C), 147.8 (C), 136.9 (C), 136.5 (C), 136.0 (C), 133.8 (CH), 129.1 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 123.3 (CH), 52.9 (CH_3), 29.6 (CH_2), 14.3 (CH_3); LRMS (ESI) m/z (relative intensity): 345 $[M]^+$ (40); Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.47; H, 5.65; N, 4.02.

Methyl 5-acetyl-6-((*tert*-butyldimethylsilyloxy)methyl)-4-phenylpicolinate (15t)



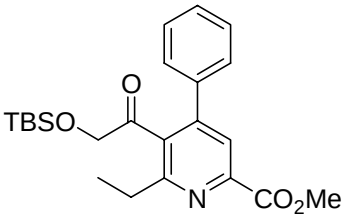
Purified by flash chromatography (silica gel, 3:1 pentane:diethyl ether) to give the product as a yellow oil (0.095 g, 48% yield). R_f 0.26 (3:1 pentane:diethyl ether); FTIR (neat): 2952, 2930, 2857, 1748, 1726, 1704, 1256, 1237, 1142, 839 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.47-7.46 (m, 3H), 7.38-7.36 (m, 2H), 5.04 (s, 2H), 4.02 (s, 3H), 2.03 (s, 3H), 0.90 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1 (C), 165.1 (C), 157.4 (C), 147.7 (C), 146.3 (C), 138.4 (C), 136.8 (C), 129.2 (CH), 128.9 (CH), 128.5 (CH), 125.1 (CH), 66.6 (CH_2), 53.0 (CH_3), 32.2 (CH_3), 25.9 (CH_3), 18.5 (C), -5.6 (CH_3); LRMS (ESI) m/z (relative intensity): 400 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{22}H_{30}NO_4Si]^+$ 400.1939, Found 400.1937.

Methyl 5-benzoyl-6-cyclohexyl-4-phenylpicolinate (15u)



Purified by flash chromatography (silica gel, 5:1 pentane:diethyl ether) to give the product as an off-white solid (0.160 g, 80% yield). mp = 169-170 ºC; R_f 0.32 (3:1 pentane:diethyl ether); FTIR (neat): 2928, 2853, 1747, 1724, 1670, 1449, 1249, 1239 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.56 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.26-7.21 (m, 5H), 4.03 (s, 3H), 2.62 (tt, *J* = 11.5, 3.5 Hz, 1H), 1.93-1.61 (m, 7H), 1.35-1.06 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6 (C), 165.8 (C), 163.6 (C), 148.6 (C), 148.0 (C), 137.3 (C), 137.1 (C), 135.6 (C), 133.7 (CH), 129.1 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 123.2 (CH), 52.8 (CH_3), 44.0 (CH), 32.6 (CH_2), 26.2 (CH_2), 25.5 (CH_2); LRMS (EI) m/z (relative intensity): 399 $[M]^+$ (29); Anal. Calcd for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.25; H, 6.32; N, 3.61 .

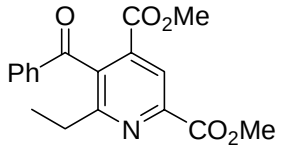
Methyl 5-(2-(*tert*-butyldimethylsilyloxy)acetyl)-6-ethyl-4-phenylpicolinate (15v)



Purified by flash chromatography (silica gel, 7:5:1 hexanes:dichloromethane:ethyl acetate) to give the product as a colorless oil (0.100 g, 48% yield). R_f 0.27 (7:5:1 hexanes:dichloromethane:ethyl acetate); FTIR (neat): 2953, 2931, 2885, 2857, 1749,

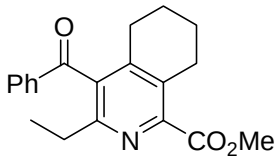
1722, 1255, 1133 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.45-7.44 (m, 3H), 7.39-7.37 (m, 2H), 4.03 (s, 3H), 4.00 (s, 2H), 2.86 (q, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.5 Hz, 3H), 0.70 (s, 9H), -0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9 (C), 165.4 (C), 160.4 (C), 148.0 (C), 147.7 (C), 137.0 (C), 135.8 (C), 129.2 (CH), 128.9 (CH), 128.7 (CH), 123.0 (CH), 69.6 (CH_2), 53.0 (CH_3), 29.5 (CH_2), 25.5 (CH_3), 18.0 (C), 14.5 (CH_3), -5.9 (CH_3); LRMS (ESI) m/z (relative intensity): 414 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{23}H_{32}NO_4Si]^+$ 414.2095, Found 414.2095.

Dimethyl 5-benzoyl-6-ethylpyridine-2,4-dicarboxylate (15w)



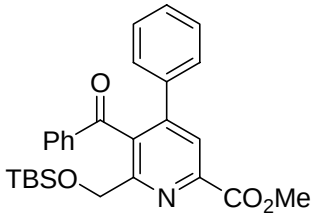
Purified by flash chromatography (silica gel, 1:1 pentane:diethyl ether) to give the product as an off-white solid (0.108 g, 66% yield). mp = 113-114 ºC; R_f 0.28 (1:1 pentane:diethyl ether); FTIR (neat): 2954, 1733, 1676, 1440, 1252 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 4.07 (s, 3H), 3.75 (s, 3H), 2.77 (q, *J* = 7.5 Hz, 2H), 1.22 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4 (C), 164.7 (C), 164.1 (C), 161.8 (C), 148.7 (C), 137.3 (C), 137.1 (C), 136.6 (C), 133.8 (CH), 128.8 (CH), 128.6 (CH), 122.2 (CH), 53.1 (CH_3), 52.8 (CH_3), 29.4 (CH_2), 13.8 (CH_3); LRMS (ESI) m/z (relative intensity): 328 $[M+H]^+$ (50); Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.93; H, 5.28; N, 4.28.

Methyl 4-benzoyl-3-ethyl-5,6,7,8-tetrahydroisoquinoline-1-carboxylate (15x)



Purified by flash chromatography (silica gel, 2:1 pentane:diethyl ether) to give the product as a colorless oil (0.050 g, 31% yield). R_f 0.23 (2:1 pentane:diethyl ether); FTIR (neat): 2938, 2865, 1732, 1670, 1558, 1449, 1437, 1206, 1166 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 3.99 (s, 3H), 2.99-2.97 (m, 2H), 2.64-2.36 (m, 4H), 1.78-1.70 (m, 4H), 1.15 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9 (C), 167.2 (C), 155.5 (C), 148.6 (C), 144.9 (C), 136.4 (C), 136.0 (C), 134.3 (CH), 130.6 (C), 129.3 (CH), 129.1 (CH), 52.7 (CH_3), 29.2 (CH_2), 27.0 (CH_2), 25.9 (CH_2), 22.0 (CH_2), 21.5 (CH_2), 14.1 (CH_3); LRMS (ESI) m/z (relative intensity): 346 $[M+Na]^+$ (100), 324 $[M+H]^+$ (45); HRMS (ESI) Calcd for $[C_{20}H_{22}NO_3]^+$ 324.1594, Found 324.1591.

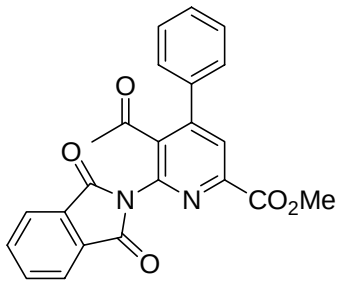
Methyl 5-benzoyl-6-((*tert*-butyldimethylsilyloxy)methyl)-4-phenylpicolinate (15y)



Purified by flash chromatography (silica gel, 3:1 pentane:diethyl ether) to give the product as a sticky light yellow solid (0.111 g, 48% yield). R_f 0.18 (3:1 pentane:diethyl ether); FTIR (neat): 2952, 2929, 2880, 2856, 1747, 1726, 1672, 1450, 1245, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.52 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.22-7.18 (m, 7H), 5.05 (bs, 2H), 4.05 (s, 3H), 0.64 (s, 9H), -0.23 (s, 6H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 196.0 (C), 165.3 (C), 159.1 (C), 149.6 (C), 146.7 (C), 137.3 (C), 136.8 (C), 136.1 (C), 132.9 (CH), 129.2 (CH), 128.6 (CH), 128.3 (CH), 127.9 (CH), 125.0 (CH), 66.5 (CH_2), 53.0 (CH_3), 25.6 (CH_3), 18.3 (C), -6.2 (CH_3), missing CH attributed to accidental equivalence; LRMS (ESI) m/z (relative intensity): 462 $[M+H]^+$ (100); HRMS (ESI) Calcd for $[C_{27}H_{32}NO_4Si]^+$ 462.2095, Found 462.2078.

Methyl 5-acetyl-6-(1,3-dioxoisoindolin-2-yl)-4-phenylpicolinate (15z)



Purified by flash chromatography (silica gel, 1:2 pentane:diethyl ether) to give the product as a white solid (0.117 g, 58% yield). mp = 213-214 °C; R_f 0.18 (1:2 pentane:diethyl ether); FTIR (neat): 2951, 2919, 1726, 1700, 1396, 1375, 1248 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.94-7.93 (m, 2H), 7.81-7.79 (m, 2H), 7.53-7.52 (m, 3H), 7.44-7.43 (m, 2H), 4.04 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7 (C), 166.6 (C), 164.2 (C), 150.8 (C), 148.2 (C), 142.8 (C), 137.5 (C), 136.2 (C), 134.6 (CH), 131.8 (C), 130.0 (CH), 129.4 (CH), 128.5 (CH), 126.8 (CH), 124.0 (CH), 53.3 (CH_3), 30.7 (CH_3); LRMS (ESI) m/z (relative intensity): 401 $[M+H]^+$ (82); HRMS (ESI) Calcd for $[C_{23}H_{16}N_2O_5Na]^+$ 423.0951, Found 423.0953.

X-Ray Analysis

A crystal of **15b** suitable for X-ray analysis was grown as follows: In a small vial, 50 mg of **15b** was dissolved in a minimal amount of ethyl acetate. The solution was allowed to slowly evaporate over 2 days at which time a crystal suitable for X-ray analysis had formed.

Figure S1. X-ray structure of **15b**.[11]

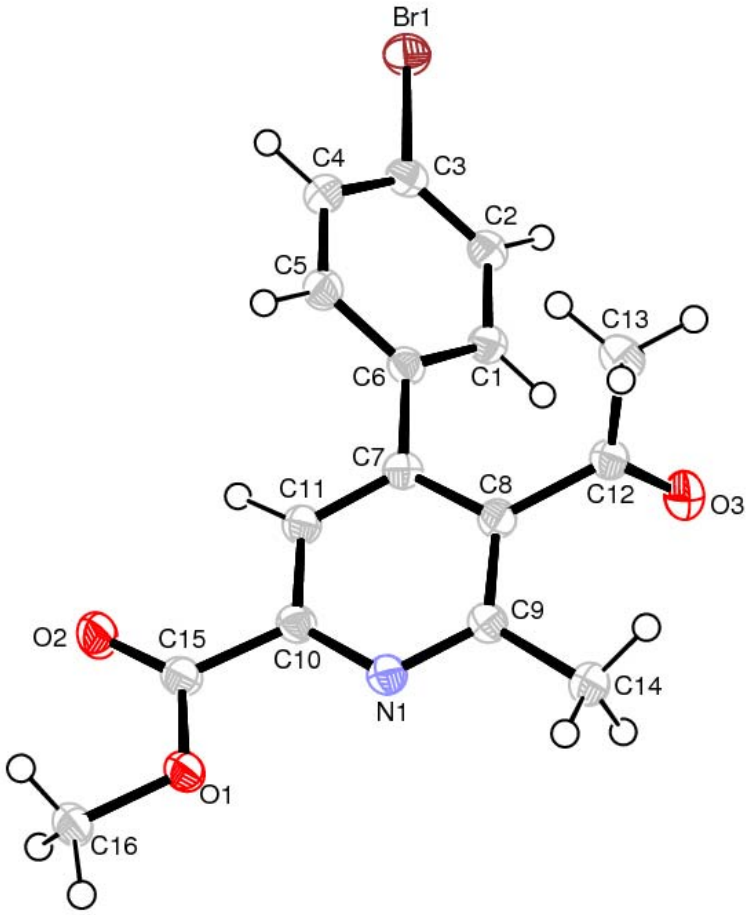


Fig S1. Ortep representation of **15b**. Thermal ellipsoids - 50% probability.

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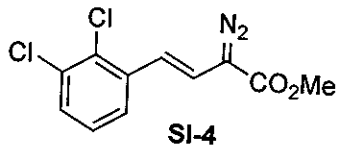
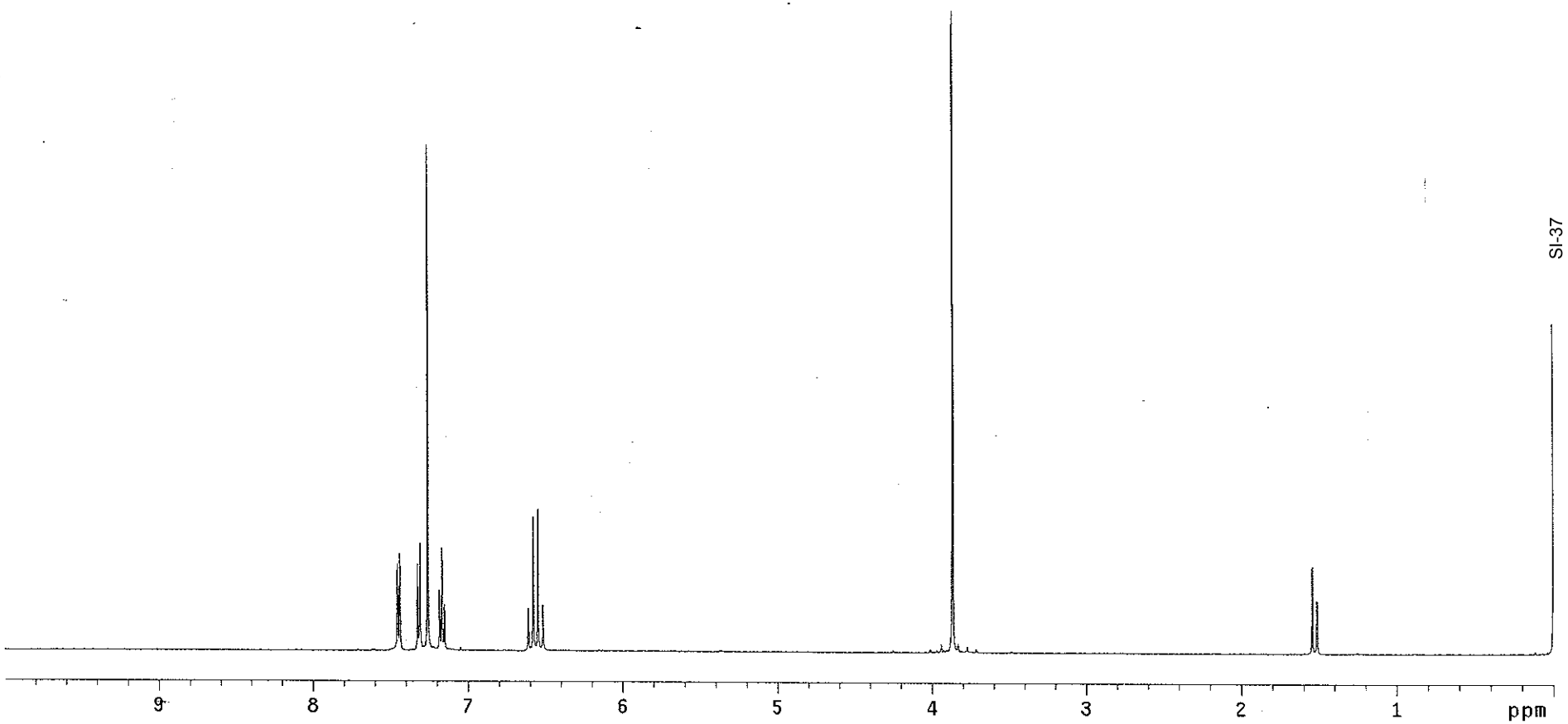
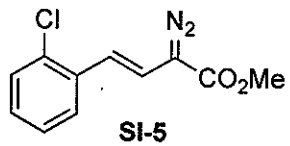
(11) The X-ray crystallographic data have been submitted to the Cambridge Structure Database [Pitak, M.; Gembicky, M.; Coppens, P. *Private Communication* 2008, CCDC 675737].

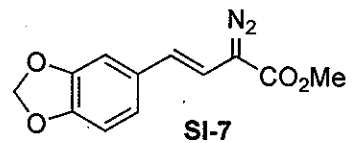


SI-4

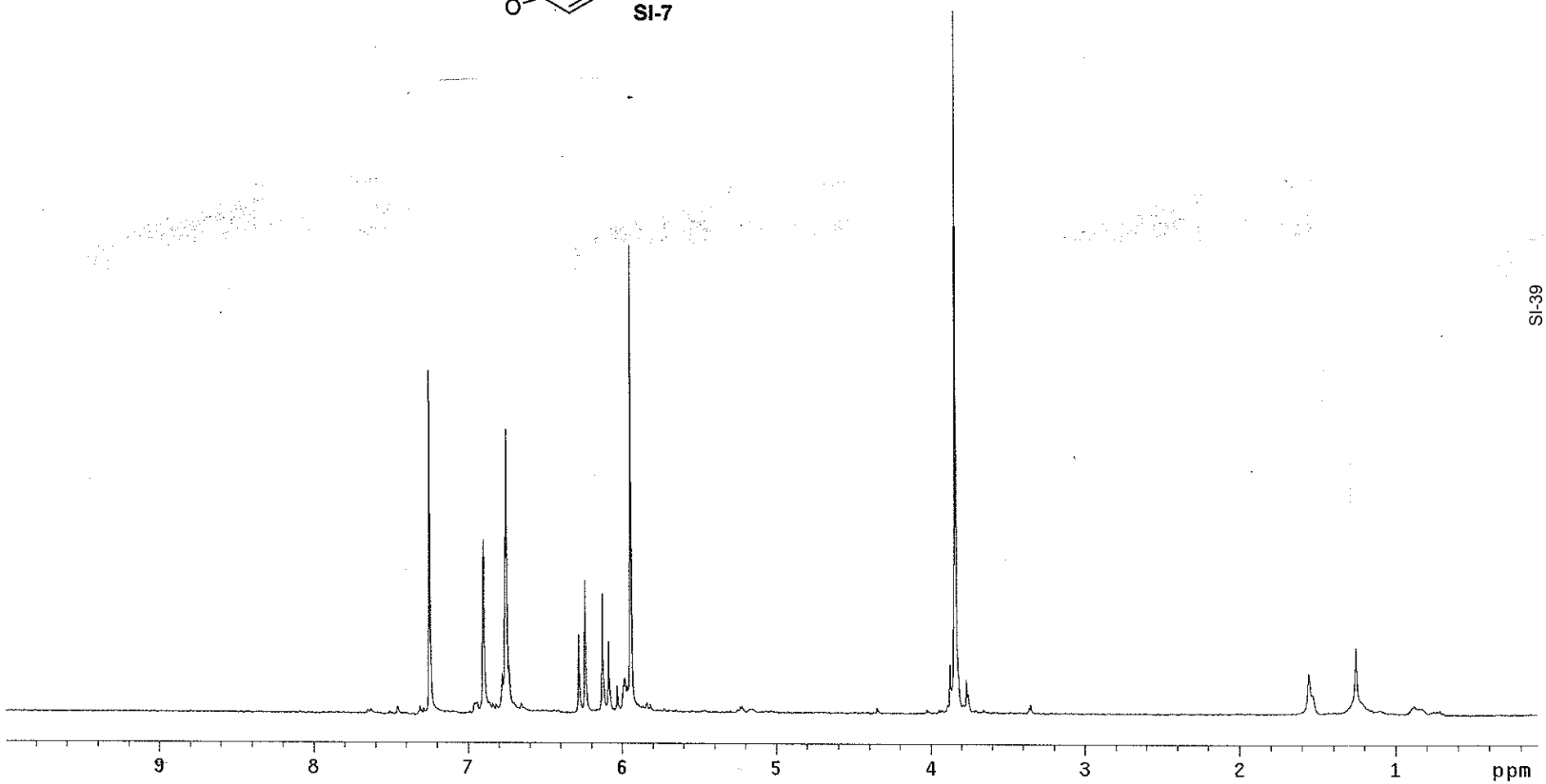


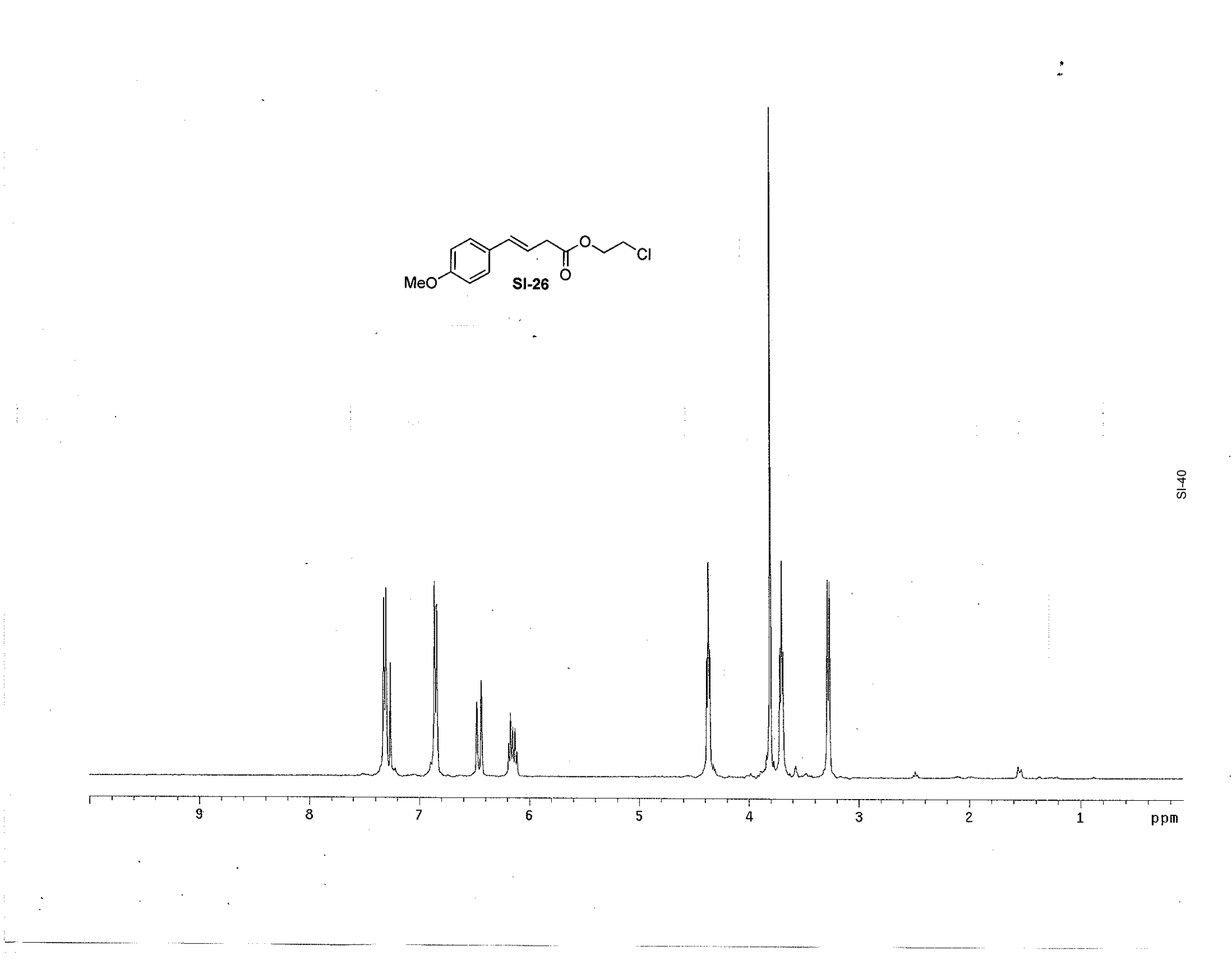


SI-5



SI-7

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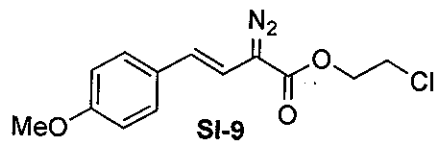
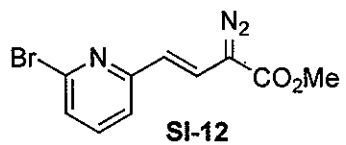
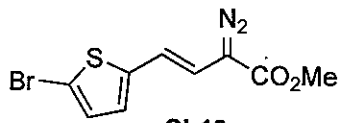


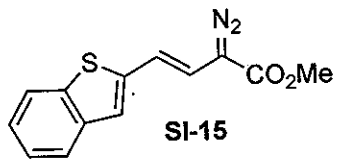
SI-9



SI-12



SI-13



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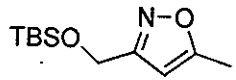
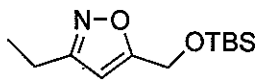


SI-19



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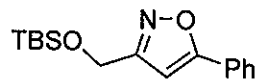

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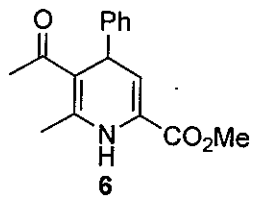

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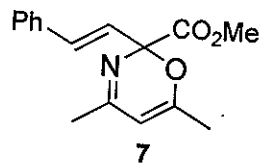

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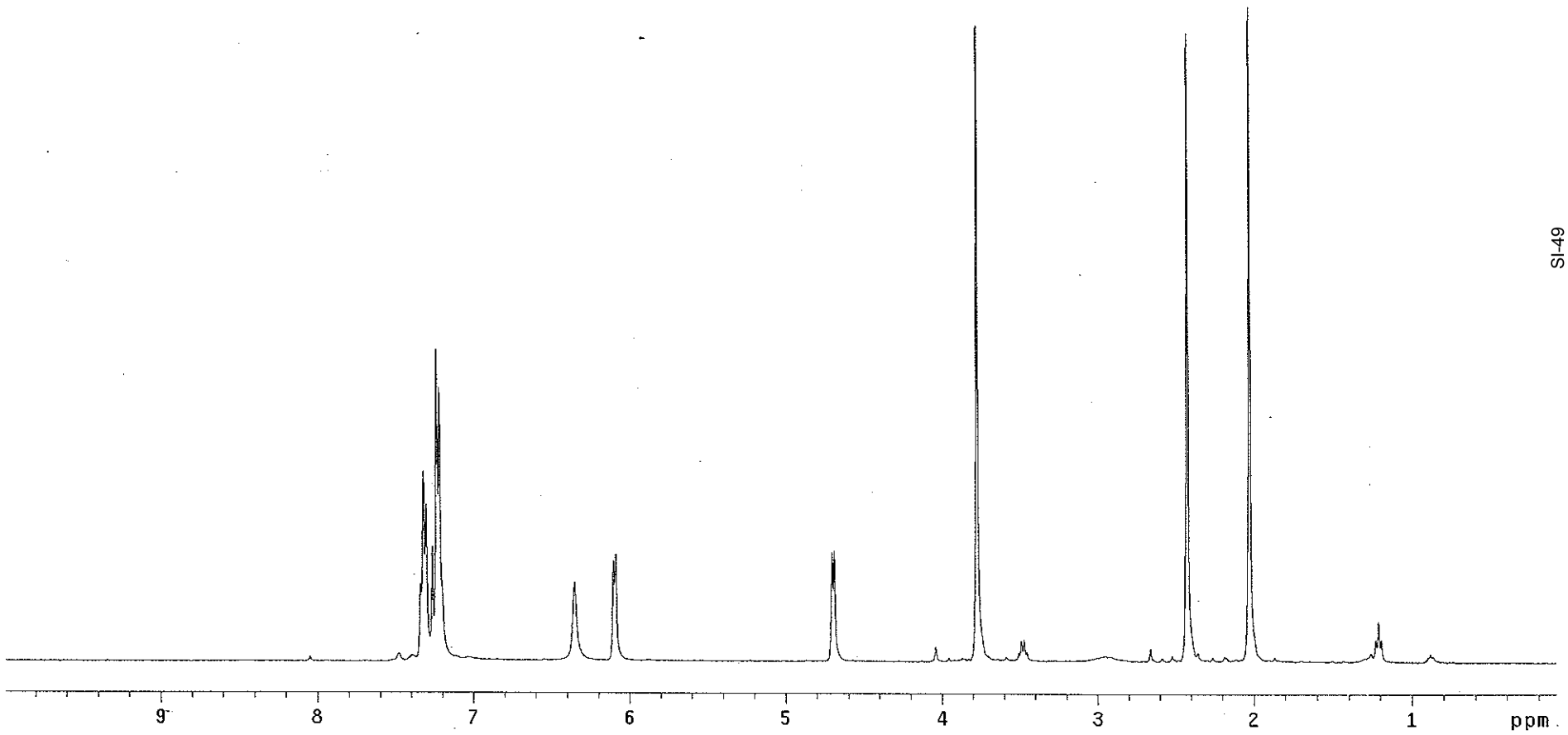

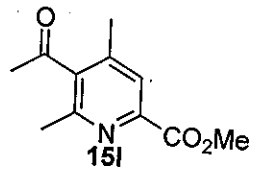

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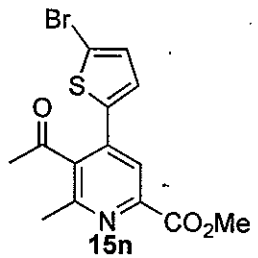

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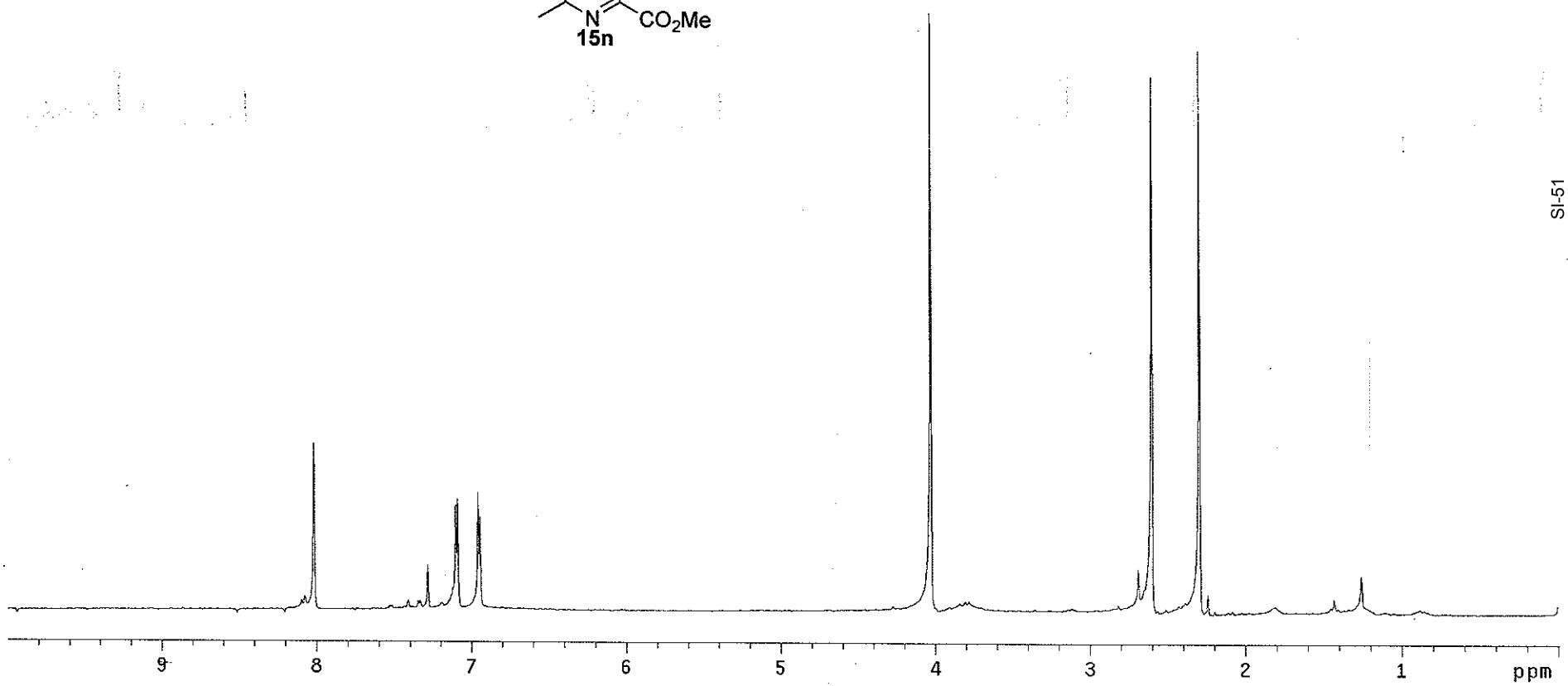

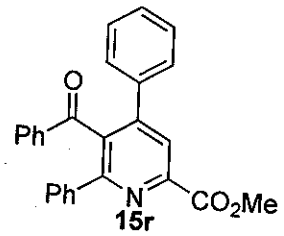

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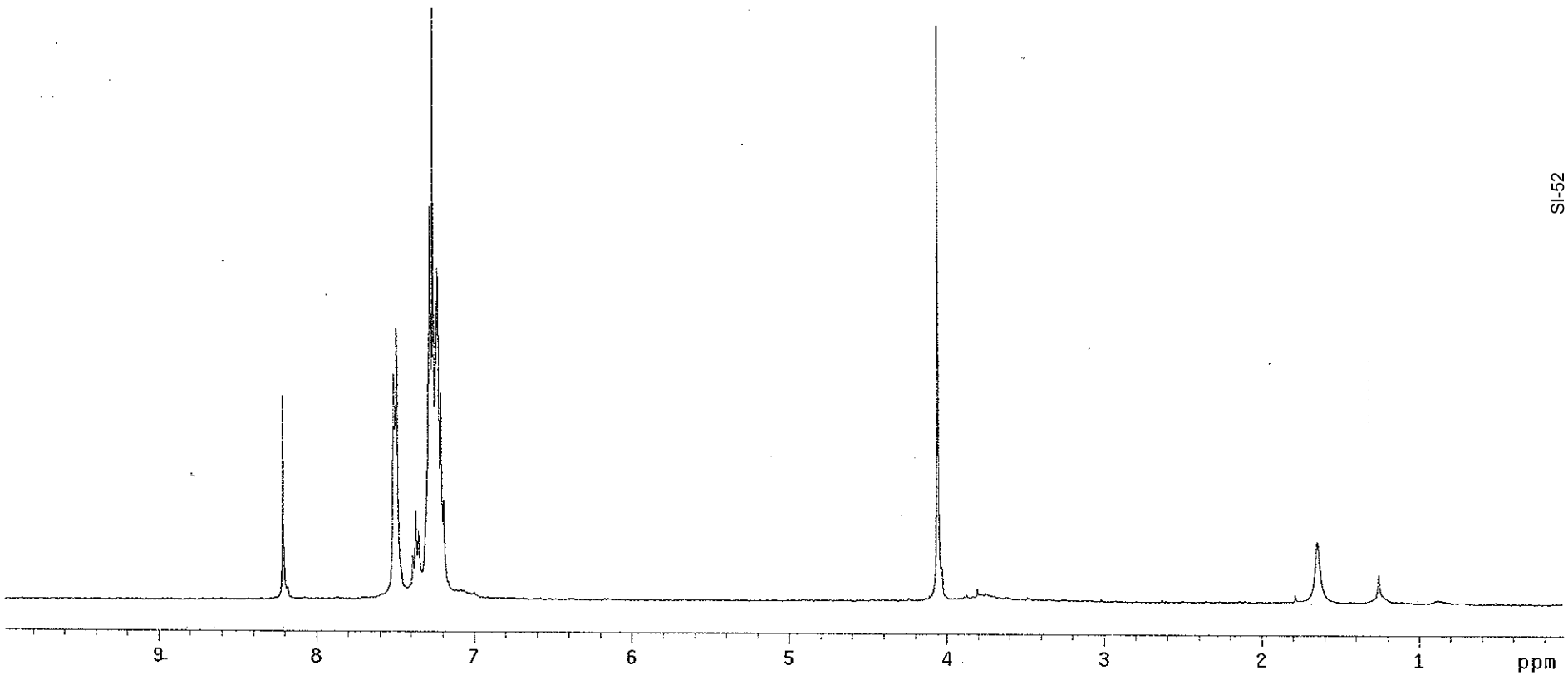

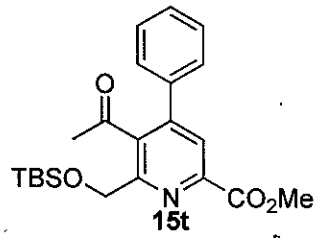

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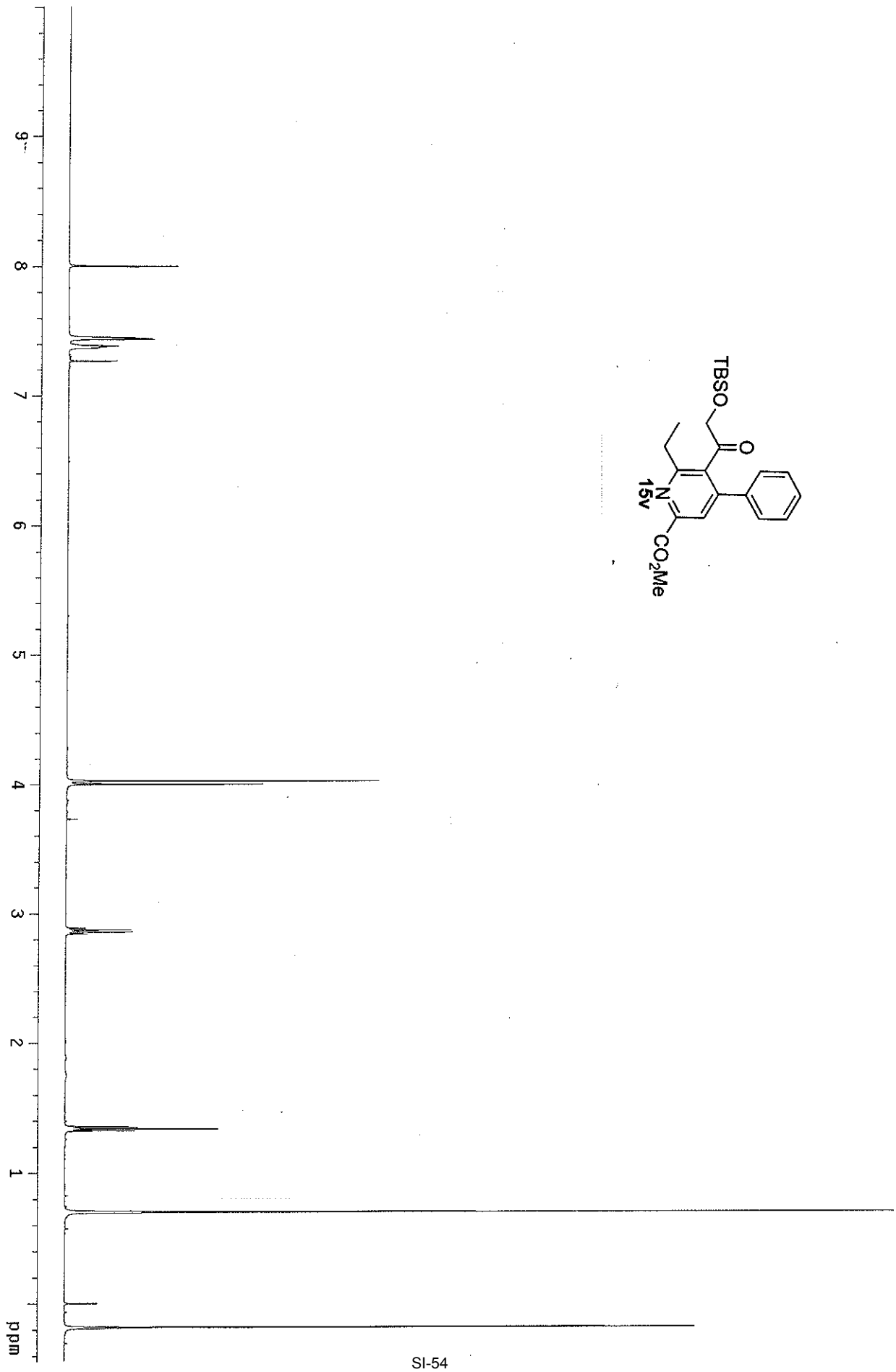
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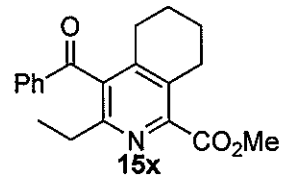

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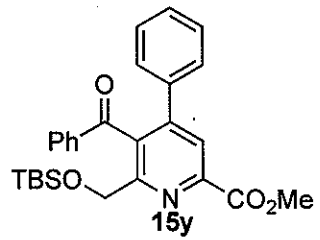

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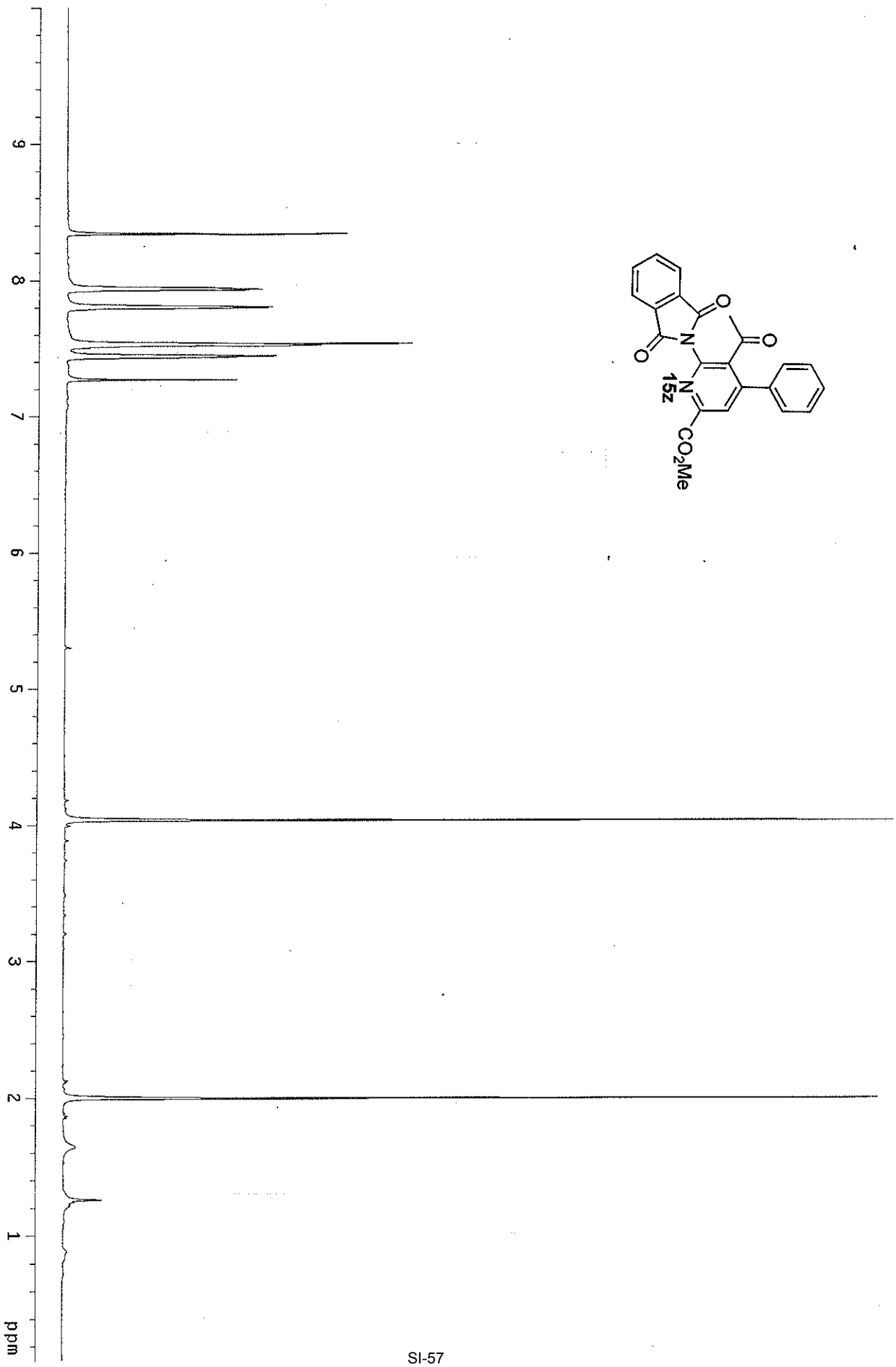
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