Supporting Information:

Diversity-Oriented Synthesis of Acyclic Nucleosides via Ring-Opening of Vinyl Cyclopropanes with Purines

Hong-Ying Niu,*[a,b] Cong Du,[a] Ming-Sheng Xie,[a] Yong Wang,[a] Qian Zhang,[a] Gui-Rong Qu,[a] and Hai-Ming Guo*[a]

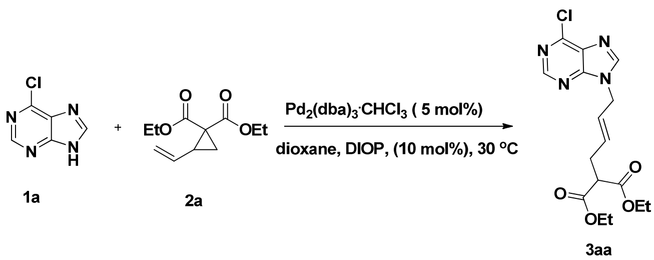
[a] *Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang 453007, P. R. China*
[b] *School of Chemistry and Chemical Engineering, Henan Institute of Science and Technology, Xinxiang 453003, China.*
E-mail: niu_hy@163.com; guohm518@hotmail.com

Contents

1. General information:

All reactions were carried out in oven-dried Schlenk tube filled nitrogen, and monitored by thin layer chromatography (TLC). All reagents were reagent grade quality and purchased from commercial sources unless otherwise indicated. Anhydrous dioxane was freshly distilled from sodium/ benzophenone before used. NMR spectra were recorded with a 400 MHz spectrometer for ^{1}H NMR, 100 MHz for ^{13}C NMR. Chemical shifts δ are given in ppm relative to tetramethylsilane as internal standard. Multiplicities are reported as follows: singlet(s), doublet(d), doublet of doublets(dd), triplet(t), quartet(q), multiplet(m). High resolution mass spectra were taken with a 3000 mass spectrometer, using Waters Q-TofMS/MS system. For column chromatography silica gel (200-300 mesh) was used as the stationary phase. **1c**[1], **1d-f**[2], **1g-h**[3], **1m**[4], **2a-e**[5] were synthesized following reported methods.

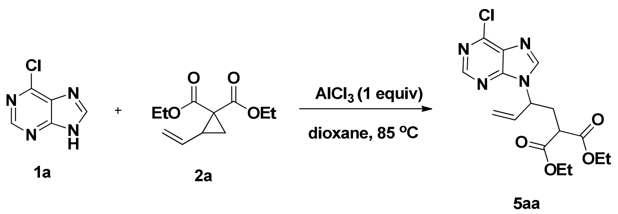
2. General procedure for the 1,5-ring-opening reaction of $Pd_2(dba)_3 \cdot CHCl_3$:



Scheme S1 General procedure for the 1,5-ring-opening reaction of $Pd_2(dba)_3$•CHCl.

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester **2a** (0.1 mmol, 21.2 mg), 6-chloropurine **1a** (0.15 mmol, 23.2 mg), $Pd_2(dba)_3 \cdot CHCl_3$ (5.2 mg, 5 mol%), DIOP (5.0 mg, 10 mol%). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with $\mathbf{N_2}$ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 30 ^{o}C for **18 h**, it was then filtered through Celite and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product **3aa** (82 %).

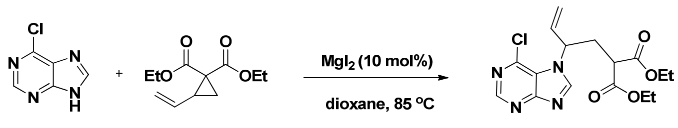
3. General procedure for the 1,3-ring-opening reaction of $AlCl_3$:



Scheme S2 General procedure for the 1,3-ring-opening reaction of $AlCl_3$.

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester **2a** (0.3 mmol, 63.6 mg), 6-chloropurine **1a** (0.1 mmol, 15.5 mg), $AlCl_3$ (0.1 mmol, 13.4 mg). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with $\mathbf{N_2}$ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 85 ^{o}C for **18 h**, it was then filtered through Celite and the organic phase was washed with cooled water. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product **5aa** (79 %).

4. General procedure for the 1,3-ring-opening reaction of MgI_2:

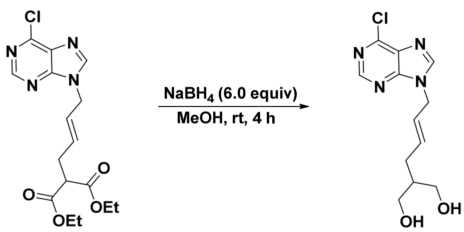


1a 2a 6aa

Scheme S3 General procedure for the 1,3-ring-opening reaction of MgI_2.

To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added 2-vinylcyclopropane-1,1-dicarboxylic acid diethyl ester **2a** (0.5 mmol, 106.1 mg), 6-chloropurine **1a** (0.1 mmol, 15.5 mg), MgI_2 (2.8 mg, 10 mol%). The Schlenk tube sealed with threaded stopper was evacuated and backfilled with $\mathbf{N_2}$ (this process was repeated for 3 times), and then dioxane (2.0 mL) were added via syringe. The mixture stirred at 85 ^{o}C for **18 h**, it was then filtered through Celite and the organic phase was washed with cooled water. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The resulted residue was purified by flash chromatography over silica gel (ethyl acetate / petroleum ether) to give the desired product **6aa** (72 %).

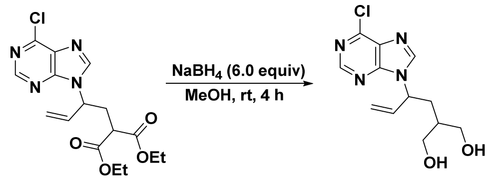
5. Hydrogenation of adduct 3aa and 5aa.



3aa 7aa

Scheme S4 Hydrogenation of adduct **3aa**.

To a solution of acyclic nucleoside analogue **3aa** (110.0 mg, 0.3 mmol) in MeOH (10.0 mL) at 0 ºC, $NaBH_4$ (68.0 mg, 1.8 mmol) was added. After **3aa** was consumed (determined by TLC), saturated NH_4Cl aq. (10.0 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (10.0 mL×3) and the combined organic phases were dried and concentrated. The residue was purified by silica gel flash chromatography (CH_2Cl_2/MeOH) to afford product **7aa** (53 %).



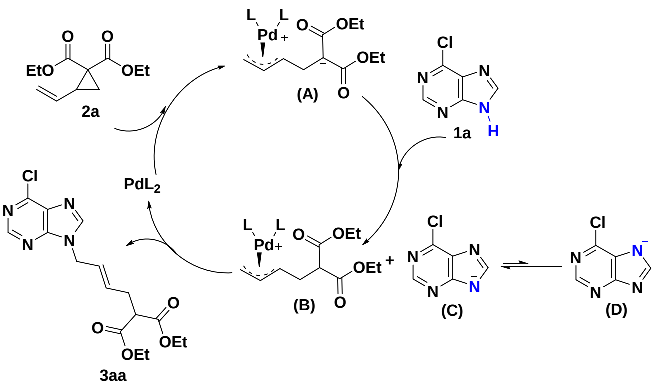
5aa 8aa

Scheme S5 Hydrogenation of adduct **5aa**.

To a solution of acyclic nucleoside analogue **5aa** (110.0 mg, 0.3 mmol) in MeOH (10.0 mL) at 0 ºC, $NaBH_4$ (68.0 mg, 1.8 mmol) was added. After **5aa** was consumed (determined by TLC), saturated NH_4Cl aq. (10.0 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (10.0 mL×3) and the combined organic phases were dried and concentrated. The residue was purified by silica gel flash chromatography (CH_2Cl_2/MeOH) to afford product **8aa** (47 %).

6. Proposed mechanism for Pd-catalyzed ring-opening reaction

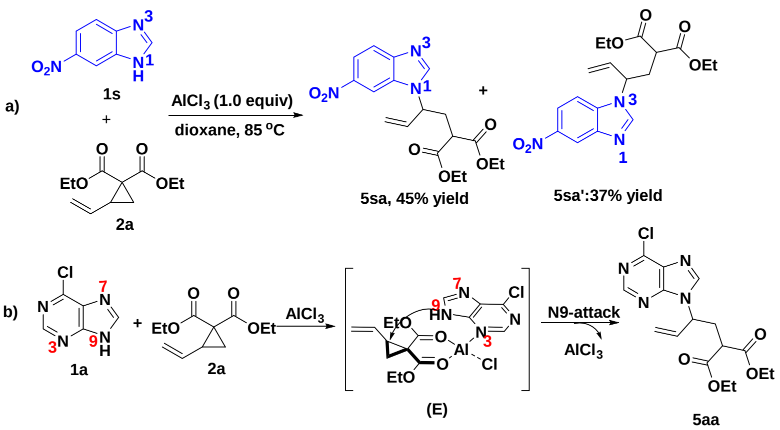
A possible catalytic cycle for the palladium-catalyzed 1,5-ring-opening of vinyl cyclopropane **2a** with 6-chloro-purine **1a** was shown in Scheme S6. Initially, palladium (0) coordinated with the vinyl cyclopropane **2a** to genarate the zwitterionic π-allylpalladium complex **A** by cleavage of the three-membered ring. Subsequently, the proton transfer from the 6-chloro-purine **1a** to intermediate **A** afforded nucleophilic anions **C** and **D**. The anion **C** attacked the less substituted carbon of the π-allyl moiety in intermediate **B** will produce the 1,5-ring-opening N9-adduct **3aa**. Meanwhile, the nucleophilic addition between anion **D** with less substituted carbon of intermediate **B** will generate 1,5-ring-opening N7 adduct **4aa**. If the anions **C** or **D** attacted the more substituted carbon of the intermediate **B**, the 1,3-ring-opening N9 adduct **5aa** and N7 adduct **6aa** will be obtained, respectively.



Scheme S6 The proposed mechanism for the palladium-catalyzed ring-opening reaction

7. Control experiment and proposed mechanism for Al-catalyzed ring-opening reaction

The control experiment with 6-nitro-benzoimidazole **1s** as a nucleophilie was carried out in the presence of $AlCl_3$, and the 1,3-ring-opening products were afforded in 82% total yield, in which the ratio of the N1 to N3 adducts was 45:37 (Scheme S7a). Thus, we proposed that the N3 in purine participated in the coordination with aluminium and resulted in the high regioselectivity.[6] As shown in Scheme S7b, the bidentate vinyl cyclopropane **2a** and N3 in 6-chloro-purine **1a** coordinated with aluminium to form complex **E**. Thus, the N9 position was close to vinyl cyclopropane **2a** to procced with 1,3-ring-opening reaction to generate the 1,3-ring-opening N9-adduct **5aa**.

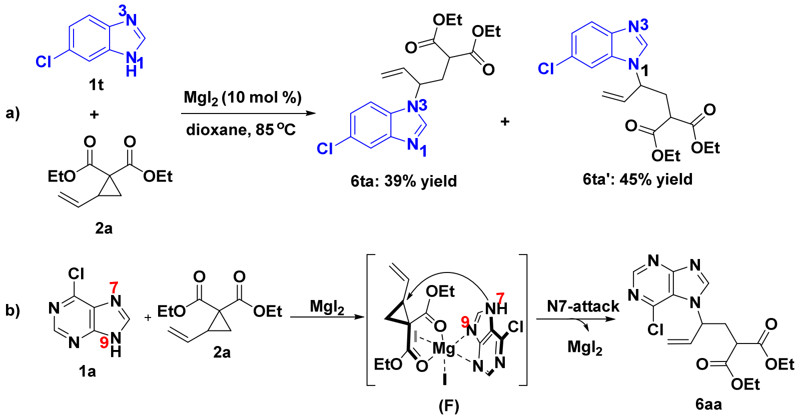


Scheme S7 (a) The control experiment; (b) The proposed mechanism for the aluminium-catalyzed ring-opening reaction.

8. Control experiment and proposed mechanism for Mg-catalyzed ring-opening reaction

The control experiments with 6-chloro-benzoimidazole **1t** as nucleophiles was explored, and the corresponding 1,3-ring-opening products were obtained in a poor ratio of N1 to N3 adducts

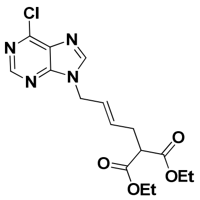
(Scheme 8a). Thus, we proposed that the N3 in purine also participated in the coordination with magnesium and resulted in the high regioselectivity.[7] As shown in Scheme 8b, the bidentate vinyl cyclopropane **2a** and bidentate N3, N9 in 6-chloro-purine **1a** coordinated with magnesium to form an octahedral geometry as the intermediate **F**. Thus, the N7 position could attack vinyl cyclopropane **2a** to afford the N7-adduct **6aa**.



Scheme S8 (a) The control experiment; (b) The proposed mechanism for the magnesium-catalyzed ring-opening reaction

9. Characterization of compounds

(*E*)-Diethyl 2-(4-(6-chloro-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3aa)

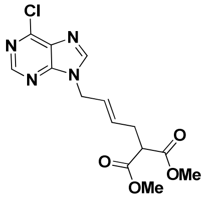


3aa

Colorless oil; 82% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.12 (s, 1H), 5.88-5.75 (m, 2H), 4.84 (d, *J* = 5.2 Hz, 2H), 4.21-4.14 (m, 4H), 3.42 (t, *J* = 7.2 Hz, 1H), 2.68 (t, *J* = 6.4 Hz, 2H), 1.24 (t, *J* = 6.8 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.3, 151.7, 151.4, 150.7, 144.7, 132.7, 131.3, 125.5, 61.4, 51.0, 45.4, 31.0, 13.9 ppm. HRMS: calcd for $C_{16}H_{19}ClN_4O_4Na$ $[M+Na]^+$ 389.0987, found 389.0987.

(*E*)-Dimethyl 2-(4-(6-chloro-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ab)

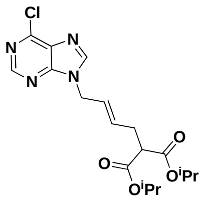


3ab

Colorless oil; 82% yield.

^{1}**H NMR** (400 MHz, DMSO): δ 8.78 (s, 1H), 8.63 (s, 1H), 5.83-5.76 (m, 1H), 5.67-5.60 (m, 1H), 4.85 (d, *J* = 6.0 Hz, 2H), 3.63 (t, *J* = 7.6 Hz, 1H), 3.58 (s, 6H), 2.49 (m, 2H) ppm. ^{13}**C NMR** (100 MHz, DMSO): δ 169.3, 152.1, 152.0, 149.5, 147.6, 131.2, 131.1, 127.1, 52.8, 50.8, 45.6, 31.3 ppm. HRMS: calcd for $C_{14}H_{15}ClN_4O_4Na$ $[M+Na]^+$ 361.0674, found 361.0677.

(*E*)-Diisopropyl 2-(4-(6-chloro-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ac)

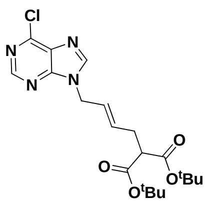


3ac

Colorless oil; 75% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.12 (s, 1H), 5.88-5.74 (m, 2H), 5.07-4.98 (m, 2H), 4.83 (d, *J* = 5.6 Hz, 2H), 3.34 (t, *J* = 7.2 Hz, 1H), 2.65 (t, *J* = 6.4 Hz, 2H), 1.21 (t, *J* = 3.2 Hz, 12H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.0, 152.0, 151.6, 151.0, 144.8, 133.1, 131.6, 125.4, 69.2, 51.5, 45.6, 31.1, 21.6, 21.5 ppm. HRMS: calcd for $C_{18}H_{23}ClN_4O_4Na$ $[M+Na]^+$ 417.1300, found 417.1301.

(*E*)- Di-tert-butyl 2-(4-(6-chloro-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ad)

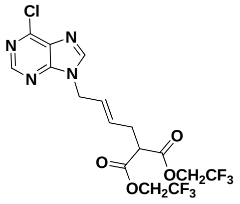


3ad

Colorless oil; 56% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.13 (s, 1H), 5.87-5.74 (m, 2H), 4.84 (d, *J* = 5.2 Hz, 2H), 3.22 (t, *J* = 7.2 Hz, 1H), 2.59 (t, *J* = 6.4 Hz, 2H), 1.42 (s, 18H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 167.9, 152.0, 151.0, 144.8, 133.4, 125.0, 81.8, 53.1, 45.7, 31.2, 27.9 ppm. HRMS: calcd for $C_{20}H_{27}ClN_4O_4Na$ $[M+Na]^+$ 445.1613, found 445.1606.

(*E*)-Bis(2,2,2-trifluoroethyl) 2-(4-(6-chloro-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ae)

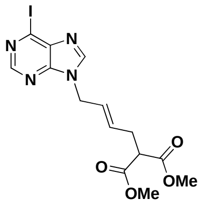


3ae

Colorless oil; 37% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.09 (s, 1H), 5.88-5.72 (m, 2H), 4.85 (d, *J* = 5.6 Hz, 2H), 4.53 (q, *J* = 8.0 Hz, 4H), 3.67 (t, *J* = 7.2 Hz, 1H), 2.76 (t, *J* = 6.8 Hz, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 166.1, 152.1, 151.2, 144.7, 130.6, 127.2, 61.3, 60.9, 50.3, 45.4, 31.0 ppm. HRMS: calcd for $C_{16}H_{13}ClF_6N_4O_4Na$ $[M+Na]^+$ 497.0422, found 497.0412.

(*E*)-Dimethyl 2-(4-(6-iodo-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3bb)

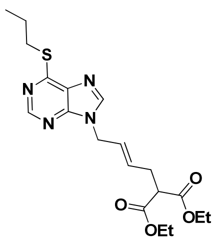


3bb

Colorless oil; 63% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.12 (s, 1H), 5.80 (q, *J* = 5.3 Hz, 2H), 4.81 (d, *J* = 4.6 Hz, 2H), 3.72 (s, 6H), 3.46 (t, *J* = 7.2 Hz, 1H), 2.68 (t, *J* = 6.2 Hz, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.9, 152.0, 147.8, 144.1, 138.6, 132.6, 125.8, 122.1, 52.7, 50.9, 45.6, 31.2 ppm. HRMS: calcd for $C_{14}H_{15}IN_4O_4Na$ $[M+Na]^+$ 453.0030, found 453.0032.

(*E*)-Diethyl 2-(4-(6-(propylthio)-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ca)

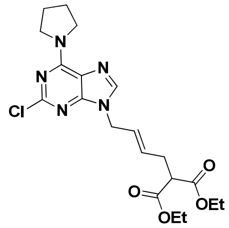


3ca

Colorless oil; 92% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.69 (s, 1H), 7.91 (s, 1H), 5.81-5.71 (m, 2H), 4.77 (d, *J* = 4.4 Hz, 2H), 4.22-4.10 (m, 4H), 3.41-3.34 (m, 3H), 2.66 (t, *J* = 6.4 Hz, 2H), 1.86-1.77 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 6H) , 1.07 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 161.6, 151.9, 148.1, 142.0, 131.9, 131.3, 126.3, 61.6, 51.3, 45.0, 31.2, 30.6, 22.9, 14.0, 13.4 ppm. HRMS: calcd for $C_{19}H_{26}N_4O_4SNa$ $[M+Na]^+$ 429.1567, found 429.1569.

(*E*)-Diethyl 2-(4-(2-chloro-6-(pyrrolidin-1-yl)-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3da)

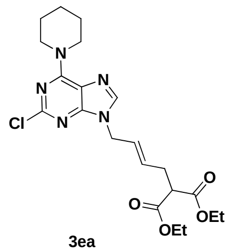


3da

Colorless oil; 67% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.63 (s, 1H), 5.77-5.69 (m, 2H), 4.68 (s, 2H), 4.17-4.16 (m, 6H), 3.74 (s, 2H), 3.39 (t, *J* = 7.2 Hz, 1H), 2.64 (t, *J* = 6.4 Hz, 2H), 2.06-1.97 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 154.2, 153.3, 151.1, 138.6, 131.4, 126.7, 119.0, 61.5, 51.4, 48.9, 47.7, 44.8, 31.2, 26.1, 24.1, 14.0 ppm. HRMS: calcd for $C_{20}H_{26}ClN_5O_4Na$ $[M+Na]^+$ 458.1566, found 458.1563.

(*E*)-Diethyl 2-(4-(2-chloro-6-(piperidin-1-yl)-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ea)

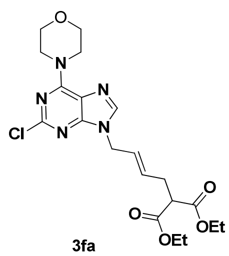


3ea

Colorless oil; 89% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.63 (s, 1H), 5.78-5.66 (m, 2H), 4.66 (d, *J* = 4.8 Hz, 2H), 4.23-4.141(m, 4H), 3.39 (t, *J* = 7.2 Hz, 1H), 2.65 (t, *J* = 6.4 Hz, 2H), 1.70 (s, 6H), 1.23 (t, *J* = 7.2 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 154.0, 153.9, 151.8, 137.8, 131.4, 126.6, 118.5, 61.5, 51.3, 44.8, 31.2, 26.1, 24.6, 14.0 ppm. HRMS: calcd for $C_{21}H_{28}ClN_5O_4Na$ $[M+Na]^+$ 472.1722, found 472.1728.

(*E*)-Diethyl 2-(4-(2-chloro-6-morpholino-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3fa)

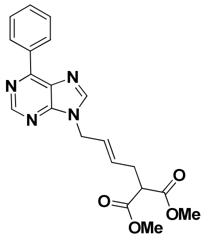


3fa

Colorless oil; 89% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 5.73 (dd, *J* = 7.6, 5.0 Hz, 2H), 4.68 (d, *J* = 4.3 Hz, 2H), 4.22-4.15 (m, 8H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.40 (t, *J* = 7.2 Hz, 1H), 2.70-2.60 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 154.0, 153.9, 152.0, 138.4, 131.7, 126.5, 118.7, 66.9, 61.6, 51.4, 44.9, 31.2, 14.1 ppm. HRMS: calcd for $C_{20}H_{26}ClN_5O_5Na$ $[M+Na]^+$ 474.1515, found 474.1518.

(*E*)-Dimethyl 2-(4-(6-phenyl-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3gb)

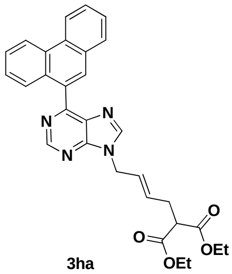


3gb

Colorless oil; 67% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.77 (d, *J* = 7.6 Hz, 2H), 8.10 (s, 1H), 7.60-7.51 (m, 3H), 5.87-5.75 (m, 2H), 4.86 (d, *J* = 4.4 Hz, 2H), 3.71 (s, 6H), 3.47 (t, *J* = 7.2 Hz, 1H), 2.69 (t, *J* = 6.4 Hz, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.9, 154.9, 152.4, 152.2, 143.9, 135.6, 131.8, 131.0, 131.0, 129.7, 128.6, 126.5, 52.7, 51.0, 45.0, 31.3 ppm. HRMS: calcd for $C_{20}H_{20}N_4O_4Na$ $[M+Na]^+$ 403.1377, found 403.1371.

(*E*)-Diethyl 2-(4-(6-(phenanthren-9-yl)-9*H*-purin-9-yl)but-2-en-1-yl)malonate (3ha)

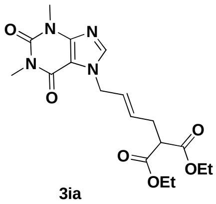


3ha

Colorless oil; 69% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.77 (dd, *J* = 19.6, 8.4 Hz, 2H), 8.27 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.11 (s, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.75-7.55 (m, 4H), 5.92-5.83 (m, 2H), 4.92 (d, *J* = 3.2 Hz, 2H), 4.23-4.14 (m, 4H), 3.45 (t, *J* = 7.2 Hz, 1H), 2.71 (t, *J* = 5.6 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 158.0, 152.3, 151.9, 144.4, 132.9, 132.3, 131.3, 131.3, 131.1, 130.9, 129.6, 129.6, 128.5, 127.7, 126.8, 126.8, 126.7, 126.5, 126.2, 122.9, 122.6, 61.6, 51.3, 45.2, 31.2, 14.1 ppm. HRMS: calcd for $C_{30}H_{28}N_4O_4Na$ $[M+Na]^+$ 531.2003, found 531.2002.

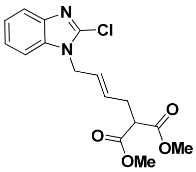
(*E*)-Diethyl 2-(4-(1,3-dimethyl-2,6-dioxo-2,3-dihydro-1*H*-purin-7(6*H*)-yl)but-2-en-1-yl) malonate (3ia)


3ia

Colorless oil; 94% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 7.53 (s, 1H), 5.84-5.73 (m, 2H), 4.87 (d, *J* = 4.0 Hz, 2H), 4.21-4.13 (m, 4H), 3.58 (s, 3H), 3.42-3.38 (m, 4H), 2.66 (t, *J* = 6.4 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 155.2, 151.7, 148.8, 140.5, 132.2, 126.8, 106.8, 61.6, 51.3, 48.3, 31.2, 29.8, 28.0, 14.1 ppm. HRMS: calcd for $C_{18}H_{24}N_4O_6Na$ [M+Na$^+$] 415.1588, found 415.1587.

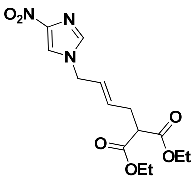
(*E*)-Dimethyl 2-(4-(2-chloro-1*H*-benzo[*d*]imidazol-1-yl)but-2-en-1-yl)malonate (3jb)


3jb

Yellow oil; 68% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 7.71-7.69 (m, 1H), 7.30-7.26 (m, 3H), 5.71-5.56 (m, 2H), 4.76 (d, *J* = 5.2 Hz, 2H), 3.66 (s, 6H), 3.41 (t, *J* = 7.2 Hz, 1H), 2.64 (t, *J* = 7.2 Hz, 2H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.9, 141.7, 140.3, 134.8, 130.2, 126.1, 123.2, 122.7, 119.5, 109.6, 52.5, 51.1, 45.8, 31.2 ppm. HRMS: calcd for $C_{16}H_{17}ClN_2O_4Na$ [M+Na]$^+$ 359.0769, found 359.0763.

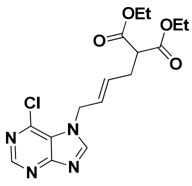
(*E*)-Diethyl 2-(4-(4-nitro-1*H*-imidazol-1-yl)but-2-en-1-yl)malonate (3ka)


3ka

Yellow oil; 75% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.58 (s, 1H), 5.79-5.68 (m, 2H), 4.91 (d, *J* = 4.4 Hz, 2H), 4.22-4.14 (m, 4H), 3.39 (t, *J* = 6.4 Hz, 1H), 2.65 (t, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 140.7, 133.5, 132.7, 125.9, 61.6, 51.2, 49.4, 31.1, 14.0 ppm. HRMS: calcd for $C_{14}H_{19}N_3O_6Na$ [M+Na]$^+$ 348.1166, found 348.1174.

(*E*)-Diethyl 2-(4-(6-chloro-7*H*-purin-7-yl)but-2-en-1-yl)malonate (4aa)

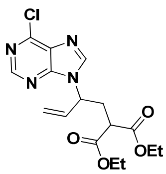


4aa

Colorless oil; 2% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.26 (s, 1H), 5.72-5.70 (m, 2H), 5.02 (d, *J* = 5.2 Hz, 2H), 4.27-4.18 (m, 4H), 3.50 (t, *J* = 7.2 Hz, 1H), 2.86 (t, *J* = 6.4 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.7, 151.9, 151.7, 150.9, 145.3, 131.6, 130.9, 125.3, 61.8, 51.1, 40.9, 26.8, 14.1 ppm. HRMS: calcd for $C_{16}H_{19}ClN_4O_4Na$ $[M+Na]^+$ 389.0988, found 389.0987.

Diethyl 2-(2-(6-chloro-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5aa)

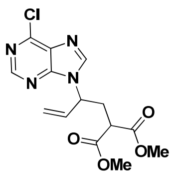


5aa

Colorless oil; 79% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.12 (s, 1H), 6.23-6.22 (m, 1H), 5.38 (d, *J* = 10.4 Hz, 1H), 5.32-5.28 (m, 2H), 4.23-4.03 (m, 4H), 3.20 (t, *J* = 7.4 Hz, 1H), 2.73 (t, *J* = 8.0 Hz, 2H), 1.26-1.17 (m, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.1, 168.1, 151.8, 151.5, 151.0, 143.8, 134.1, 131.6, 119.6, 61.9, 61.8, 56.5, 48.6, 32.6, 13.9, 13.8 ppm. HRMS: calcd for $C_{16}H_{19}ClN_4O_4Na$ $[M+Na]^+$ 389.0987, found 389.0978.

Dimethyl 2-(2-(6-chloro-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ab)

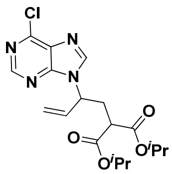


5ab

Colorless oil; 87% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.12 (s,1H), 6.23-6.14 (m, 1H), 5.38 (d, *J* = 10.4 Hz, 1H), 5.32-5.28 (m, 2H), 3.73 (s, 3H), 3.63 (s, 3H), 3.24 (t, *J* = 7.2 Hz, 1H), 2.75 (t, *J* = 7.6 Hz, 2H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 168.5, 151.9, 151.5, 151.2, 143.8, 134.0, 131.7, 119.8, 56.5, 52.9, 52.9, 48.3, 32.8 ppm. HRMS: calcd for $C_{14}H_{16}ClN_4O_4Na$ $[M+Na]^+$ 361.0674, found 361.0664.

Diisopropyl 2-(2-(6-chloro-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ac)

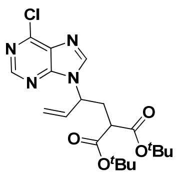


5ac

Colorless oil; 67% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.13 (s, 1H), 6.23-6.14 (m, 1H), 5.37 (dd, *J* = 10.4, 0.7 Hz, 1H), 5.31-5.27 (m, 2H), 5.10-5.00 (m, 1H), 4.98-4.89 (m, 1H), 3.11 (t, *J* = 7.2 Hz, 1H), 2.70 (t, *J* = 7.2 Hz, 2H), 1.24-1.14 (m, 12H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 167.8, 167.7, 151.9, 151.5, 151.2, 143.8, 134.2, 131.7, 119.7, 69.7, 69.6, 56.6, 49.0, 32.6, 21.6, 21.5, 21.5, 21.4 ppm. HRMS: calcd for $C_{18}H_{23}ClN_4O_4Na$ $[M+Na]^+$ 417.1300, found 417.1292.

Di-tert-butyl 2-(2-(6-chloro-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ad)

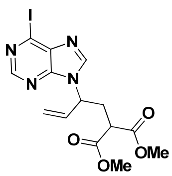


5ad

Colorless oil; 63% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.13 (s, 1H), 6.23-6.14 (m, 1H), 5.36 (d, *J* = 10.0 Hz, 1H), 5.30-5.26 (m, 2H), 2.99 (t, *J* = 7.2 Hz, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.45 (s, 9H), 1.39 (s, 9H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 167.6, 167.5, 151.9,151.6, 151.2, 143.8, 134.4, 131.8, 119.5, 82.4, 82.4, 56.6, 50.5, 32.8, 27.8, 27.8 ppm. HRMS: calcd for $C_{20}H_{27}ClN_4O_4Na$ $[M+Na]^+$ 445.1613, found 445.1605.

Dimethyl 2-(2-(6-iodo-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5bb)

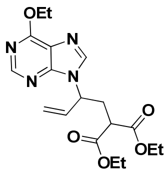


5bb

Colorless oil; 44% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.62 (s, 1H), 8.12 (s, 1H), 6.22-6.14 (m, 1H), 5.39-5.24 (m, 3H), 3.73 (s, 3H), 3.63 (s, 3H), 3.23 (t, *J* = 7.4 Hz, 1H), 2.74 (t, *J* = 7.4 Hz, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 168.5, 152.0, 147.8, 143.1, 138.7, 134.0, 122.4, 119.8, 56.6, 53.0, 52.9, 48.3, 32.8 ppm. HRMS: calcd for $C_{14}H_{15}IN_4O_4Na$ $[M+Na]^+$ 453.0030, found 453.0029.

Diethyl 2-(2-(6-ethoxy-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5la)

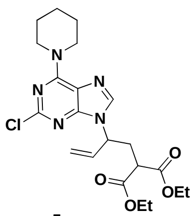


5la

Colorless oil; 48% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.90 (s, 1H), 6.22-6.13 (m, 1H), 5.33-5.21 (m, 3H), 4.66 (q, J = 7.2 Hz, 2H), 4.22-4.03 (m, 4H), 3.17 (t, J = 7.2 Hz, 1H), 2.70 (t, J = 7.4 Hz, 2H), 1.51 (t, J = 7.2 Hz, 3H), 1.21 (dt, J = 19.9, 7.1 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.3, 160.9, 152.1, 151.8, 140.6, 134.8, 121.6, 118.8, 63.1, 61.9, 61.9, 55.8, 48.6, 32.9, 14.5, 14.0, 13.9 ppm. HRMS: calcd for $C_{18}H_{24}N_4O_5Na$ $[M+Na]^+$ 399.1639, found 399.1642.

Diethyl 2-(2-(2-chloro-6-(piperidin-1-yl)-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ea)

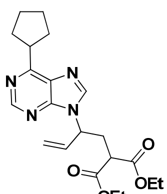


5ea

Colorless oil; 89% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 6.15-6.06 (m, 1H), 5.32-5.21 (m, 2H), 5.19-5.15 (m, 1H), 4.28-4.01 (m, 8H), 3.16 (dd, J = 8.0, 6.4 Hz, 1H), 2.70-2.51 (m, 2H), 1.72-1.69 (m, 6H), 1.26 (t, J = 7.4 Hz, 3H), 1.19 (t, J = 7.4 Hz, 3H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.3, 154.0, 153.8, 151.9, 136.5, 135.0, 118.5, 61.9, 61.8, 54.7, 48.6, 33.1, 26.1, 24.6, 13.9, 13.9 ppm. HRMS: calcd for $C_{21}H_{28}ClN_5O_4Na$ $[M+ Na^+]$ 472.1722, found 472.1713.

Diethyl 2-(2-(6-cyclopentyl-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ma)



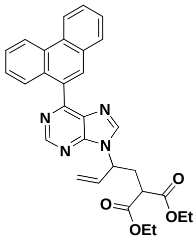
5ma

Colorless oil; 62% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.87 (s, 1H), 8.00 (s, 1H), 6.24-6.15 (m, 1H), 5.35-5.25 (m, 3H), 4.22-4.14 (m, 2H), 4.11-3.99 (m, 2H), 3.93-3.84 (m, 1H), 3.22 (t, J = 7.2 Hz, 1H), 2.79-2.67 (m, 2H), 2.17-1.76 (m, 8H), 1.23 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H) ppm. ^{13}**C NMR** (100

MHz, $CDCl_3$): δ 168.4, 168.3, 166.4, 152.5, 150.4, 142.0, 134.8, 132.3, 119.0, 61.9, 61.8, 55.7, 48.8, 42.6, 32.8, 32.8, 26.3,14.0, 13.9 ppm. HRMS: calcd for $C_{21}H_{28}N_4O_4Na$ $[M+Na]^+$ 423.2003, found 423.1996.

Diethyl 2-(2-(6-(phenanthren-9-yl)-9*H*-purin-9-yl)but-3-en-1-yl)malonate (5ha)

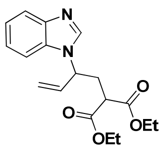


5ha

Colorless oil; 82% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 9.16 (s, 1H), 8.77 (dd, J = 20.0, 8.0 Hz, 2H), 8.29-8.25 (m, 2H), 8.12 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.73-7.56 (m, 4H), 6.32-6.24 (m, 1H), 5.44-5.35 (m, 3H), 4.27-4.07 (m, 4H), 3.33 (t, J = 7.2 Hz, 1H), 2.88-2.76 (m, 2H), 1.29-1.20 (m, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.3, 158.2, 152.3, 151.9, 143.3, 143.3, 134.6, 132.9, 131.3, 131.2, 131.2, 131.0, 131.0, 129.6, 127.8, 126.8, 126.8, 126.7, 126.5, 122.9, 122.6, 119.4, 62.0, 61.9, 56.0, 48.8, 32.8, 14.0, 14.0 ppm. HRMS: calcd for $C_{30}H_{29}N_4O_4$ $[M+H]^+$ 509.2183, found 509.2174.

Diethyl 2-(2-(1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate 5na

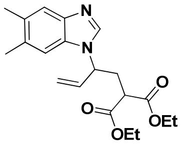


5na

Yellow oil; 61% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.83-7.80 (m, 1H), 7.42-7.40 (m, 1H), 7.31-7.28 (m, 2H), 6.12-6.04 (m, 1H), 5.35 (dd, J = 10.4, 1.2 Hz, 1H), 5.23 (dd, J = 17.2, 1.2 Hz, 1H), 5.06-5.01 (m, 1H), 4.21-4.03 (m, 4H), 3.18 (dd, J = 8.0, 6.4 Hz, 1H), 2.73-2.59 (m, 2H), 1.24-1.18 (m, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 168.4, 144.0, 141.4, 135.0, 133.1, 123.0, 122.4, 120.6, 118.7, 110.5, 61.9, 61.8, 56.1, 48.5, 32.6, 14.0, 13.9 ppm. HRMS: calcd for $C_{18}H_{22}N_2O_4Na$ $[M+Na]^+$ 353.1472, found 353.1467.

Diethyl 2-(2-(5,6-dimethyl-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate 5oa

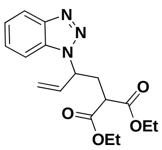


5oa

Yellow oil; 35% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.55 (s, 1H), 7.13 (s, 1H), 6.09-6.01 (m, 1H), 5.30 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.18 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.98-4.93 (m, 1H), 4.21-4.05 (m, 4H), 3.16-3.13 (m, 1H), 2.69-2.56 (m, 2H), 2.36-2.35 (m, 6H), 1.23-1.16 (m, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 168.3, 142.4, 140.6, 135.1, 132.0, 131.4, 131.3, 120.3, 118.2, 110.5, 61.7, 61.7, 55.9, 48.4, 32.4, 20.5, 20.1, 13.8, 13.8 ppm. HRMS: calcd for $C_{20}H_{27}N_2O_4$ [M+H$^+$] 359.1965, found 359.1957

Diethyl 2-(2-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)but-3-en-1-yl)malonate 5pa

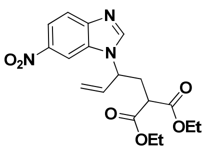


5pa

Yellow oil; 87% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.52-7.44(m, 2H), 7.39-7.35 (m, 1H), 6.22-6.14 (m, 1H), 5.50-5.44 (m, 1H), 5.32 (d, *J* = 10.4 Hz, 1H), 5.23 (dd, *J* = 16.8, 0.8 Hz, 1H), 4.20-4.03 (m, 4H), 3.22 (dd, *J* = 8.4, 6.4 Hz, 1H), 2.96-2.88 (m, 1H), 2.80-2.73 (m, 1H), 1.22-1.17 (m, 6H) ppm. 13**C NMR** (100 MHz, CDCl3): δ 168.6, 168.4, 146.1, 134.8, 132.5, 127.3, 124.1, 120.1, 118.9, 109.7, 61.7, 61.7, 59.7, 48.4, 32.4, 13.9 ppm. HRMS: calcd for $C_{17}H_{21}N_3O_4Na$ [M+Na]+ 354.1424, found 354.1419.

Diethyl 2-(2-(6-nitro-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate (5sa)



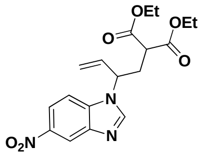
5sa

Yellow oil; 45% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 2.0 Hz, 1H), 8.23 (dd, *J* = 9.2, 2.0 Hz,1H), 8.17 (s, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 6.13-6.05 (m, 1H), 5.46 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.31 (dd, *J* =

17.2, 1.6 Hz, 1H), 5.15-5.10 (m, 1H), 4.24-4.09 (m, 4H), 3.20 (t, J = 7.2 Hz, 1H), 2.69 (t, J = 7.6 Hz, 2H), 1.25-1.20 (m, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.3, 168.1, 148.2, 145.8, 143.9, 134.1, 132.5, 120.8, 119.8, 118.3, 107.5, 62.1, 62.1, 56.8, 48.5, 32.7, 13.9, 13.9 ppm. HRMS: calcd for $C_{18}H_{22}N_3O_6$ [M+H$^+$] 354.1424, found 354.1424.

Diethyl 2-(2-(5-nitro-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate (5sa')

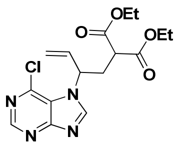


5sa'

Yellow oil; 37% yield.

^{1}**H NMR** (400 MHz, CDCl3): δ 8.73 (d, J = 2.0 Hz, 1H), 8.24 (dd, J = 8.8, 2.0 Hz, 1H), 8.11 (s, 1H), 7.52 (d, J = 9.2 Hz,1H), 6.12-6.04 (m,1H), 5.44 (dd, J = 10.4, 1.2 Hz,1H), 5.28 (dd, J = 17.2, 1.2 Hz, 1H), 5.14-5.08 (m, 1H), 4.21-4.07 (m, 4H), 3.20 (t, J = 7.2 Hz, 1H), 2.72-2.59 (m, 2H), 1.22 (q, J = 7.2 Hz, 6H) ppm. ^{13}**C NMR** (100 MHz, CDCl3): δ 168.2, 168.2, 144.7, 143.8, 143.2, 137.2, 134.0, 119.8, 118.8, 117.2, 110.6, 62.0, 62.0, 56.7, 48.3, 32.5, 13.9, 13.9 ppm. HRMS: calcd for $C_{18}H_{21}N_3O_6Na$ [M+Na]+ 398.1323, found 398.1323.

Diethyl 2-(2-(6-chloro-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6aa)

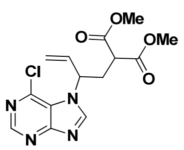


6aa

Colorless oil; 72% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.35 (s, 1H), 6.12-6.03 (m, 1H), 5.74 (q, J = 7.2 Hz, 1H), 5.41 (d, J = 10.4 Hz, 1H), 5.22 (d, J = 17.2 Hz, 1H), 4.23-4.05 (m, 4H), 3.31 (t, J = 7.2 Hz, 1H), 2.77-2.68 (m, 2H), 1.25-1.19 (m, 6H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.0, 167.9, 161.6, 152.3, 146.9, 142.7, 134.8, 122.1, 119.8, 62.1, 62.0, 57.3, 48.5, 33.5, 13.8 ppm. HRMS: calcd for $C_{16}H_{19}ClN_4O_4Na$ $[M+Na]^+$ 389.0987, found 389.0978.

Dimethyl 2-(2-(6-chloro-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6ab)

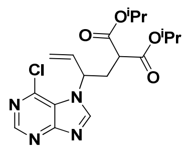


6ab

Colorless oil; 84% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.93(s, 1H), 8.36 (s, 1H), 6.13-6.05 (m, 1H), 5.76 (d, *J* = 7.6 Hz, 1H), 5.44 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.25 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.38 (t, *J* = 7.2 Hz, 1H), 2.78-2.67 (m, 2H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.3, 161.6, 152.5, 146.8, 142.8, 134.7, 122.1, 120.0, 57.3, 53.1, 53.0, 48.2, 33.7 ppm. HRMS: calcd for $C_{14}H_{15}ClN_4O_4Na$ $[M+Na]^+$ 361.0674, found 361.0668.

Diisopropyl 2-(2-(6-chloro-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6ac)

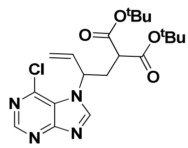


6ac

Colorless oil; 64% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.36 (s, 1H), 6.11-6.03 (m, 1H), 5.76-5.07 (m, 1H), 5.40 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.20 (dd, *J* = 16.8, 1.2 Hz, 1H), 5.07-4.91 (m, 2H), 3.24 (t, *J* = 7.2 Hz, 1H), 2.76-2.63 (m, 2H), 1.22-1.15(m, 12H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 167.6, 161.7, 152.5, 146.9, 142.8, 135.0, 122.2, 119.7, 69.9, 69.9, 57.5, 48.9, 33.4, 21.5, 21.5, 21.4 ppm. HRMS: calcd for $C_{18}H_{23}ClN_4O_4Na$ $[M+Na]^+$ 417.1300, found 417.1290.

Di-tert-butyl 2-(2-(6-chloro-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6ad)

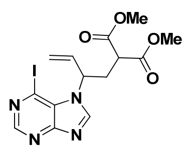


6ad

Colorless oil; 41% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.36 (s, 1H), 6.10-6.01 (m, 1H), 5.70 (q, *J* = 7.2 Hz, 1H), 5.38 (dd, *J* = 10.4, 0.8 Hz, 1H), 5.17 (dd, *J* = 17.2, 0.8 Hz, 1H), 3.15 (t, *J* = 7.2 Hz, 1H), 2.68-2.59 (m, 2H), 1.44 (s, 3H), 1.40 (s, 3H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 167.5, 167.4, 161.7, 152.4, 146.9, 142.9, 135.3, 122.3, 119.5, 82.7, 57.7, 50.5, 33.4, 27.9, 27.8 ppm. HRMS: calcd for $C_{20}H_{27}ClN_4O_4Na$ $[M+Na]^+$ 445.1613, found 445.1606.

Dimethyl 2-(2-(6-iodo-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6bb)

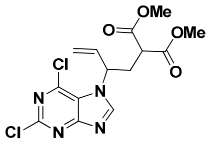


6bb

Colorless oil; 31% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.37 (s, 1H), 6.09-6.03 (m, 2H), 5.40 (d, *J* = 9.2 Hz, 1H), 5.16 (d, *J* = 15.6 Hz, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 3.39 (t, *J* = 7.2 Hz, 1H), 2.83-2.71 (m, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.4, 159.0, 152.7, 146.9, 135.0, 127.6, 119.6, 108.3, 55.0, 53.2, 53.1, 48.2, 33.5 ppm. HRMS: calcd for $C_{14}H_{15}IN_4O_4Na$ $[M+Na]^+$ 453.0030, found 453.0023.

Dimethyl 2-(2-(2,6-dichloro-7*H*-purin-7-yl)but-3-en-1-yl)malonate (6qb)

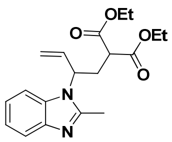


6qb

Colorless oil; 33% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.35 (s, 1H), 6.10-6.01 (m, 1H), 5.68 (q, *J* = 6.8 Hz, 1H), 5.44 (dd, *J* = 9.2, 1.2 Hz, 1H), 5.23 (dd, *J* = 15.6, 1.2 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.35 (t, *J* = 7.2 Hz, 1H), 2.74-2.69 (m, 2H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.3, 168.3, 163.3, 153.3, 148.1, 143.6, 134.4, 121.4, 120.3, 57.6, 53.2, 53.1, 48.1, 33.6 ppm. HRMS: calcd for $C_{14}H_{14}Cl_2N_4O_4Na$ $[M+Na]^+$ 395.0284, found 395.0277.

Diethyl 2-(2-(2-methyl-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate (6ra)

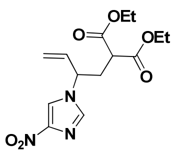


6ra

Yellow oil; 71% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.70-7.67 (m, 1H), 7.35-7.33 (m, 1H), 7.23-7.16 (m, 2H), 6.14-6.06 (m, 1H), 5.29 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.13-5.06 (m, 2H), 4.23-4.06 (m, 2H), 3.98 (q, *J* = 7.2 Hz, 2H), 3.12-3.01 (m, 1H), 2.84-2.76 (m, 1H), 2.72-2.64 (m, 1H), 2.57 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 168.6, 168.3, 151.6, 142.7, 1346, 133.5, 122.1, 122.0, 119.3, 118.0, 111.1, 61.8, 61.8, 55.6, 48.5, 31.2, 14.6, 13.9, 13.8 ppm. HRMS: calcd for $C_{19}H_{25}N_2O_4$ $[M+H^+]$ 345.1809, found 345.1800.

Diethyl 2-(2-(4-nitro-1*H*-imidazol-1-yl)but-3-en-1-yl)malonate (6ka)

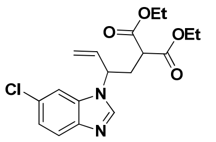


6ka

Yellow oil; 95% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.48 (s, 1H), 5.99-5.91 (m, 1H), 5.44 (d, *J* = 10.4 Hz, 1H), 5.30 (d, *J* = 17.2 Hz, 1H), 4.83-4.77 (m, 1H), 4.23-4.17 (m, 4H), 3.21 (t, *J* = 7.2 Hz, 1H), 2.53-2.48 (m, 2H), 1.29-1.25 (m, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.1, 168.0, 135.1, 134.1, 120.4, 117.6, 62.2, 62.2, 59.1, 48.2, 33.4, 14.0, 14.0 ppm. HRMS: calcd for $C_{14}H_{219}N_3O_6Na$ [M+Na$^+$] 348.1166, found 348.1165.

Diethyl 2-(2-(6-chloro-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate (6ta)

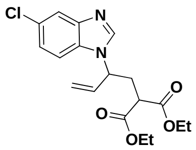


6ta

Yellow oil; 45% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 1.2 Hz, 1H), 7.24 (d, *J* = 1.6 Hz, 1H), 6.10-6.01 (m, 1H), 5.38 (d, *J* = 10.4 Hz, 1H), 5.24 (d, *J* = 17.2 Hz, 1H), 5.00-4.96 (m, 1H), 4.23-4.07 (m, 4H), 3.15 (t, *J* = 7.2 Hz, 1H), 2.63 (t, *J* = 7.2 Hz, 2H), 1.25-1.19 (m, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.5, 168.3, 142.6, 142.2, 134.6, 133.7, 128.9, 123.2, 121.4, 119.0, 110.6, 62.0, 61.9, 56.2, 48.5, 32.6, 13.9, 13.9 ppm. HRMS: calcd for $C_{18}H_{22}ClN_2O_4Na$ [M+Na$^+$] 387.1082, found 387.1080.

Diethyl 2-(2-(5-chloro-1*H*-benzo[*d*]imidazol-1-yl)but-3-en-1-yl)malonate (6ta')

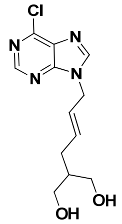


6ta'

Yellow oil; 39% yield.

[1]**H NMR** (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.79 (d, *J* = 1.6 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.24 (s, 1H), 6.10-6.01 (m, 1H), 5.37 (dd, *J* = 10.4, 0.8 Hz, 1H), 5.22 (dd, *J* = 17.2, 0.8 Hz, 1H), 5.04-4.99 (m, 1H), 4.21-4.05 (m, 4H), 3.18-3.14 (m, 1H), 2.70-2.57 (m, 2H), 1.24-1.18 (m, 6H) ppm. [13]**C NMR** (100 MHz, $CDCl_3$): δ 168.4, 168.3, 144.8, 142.6, 134.6, 131.7, 128.1, 123.6, 120.3, 119.0, 111.3, 61.9, 61.9, 56.4, 48.4, 32.5, 14.0, 13.9 ppm. HRMS: calcd for $C_{18}H_{22}ClN_2O_4$ [M+H$^+$] 365.1263, found 365.1266.

(*E*)-2-(4-(6-Chloro-9*H*-purin-9-yl)but-2-en-1-yl)propane-1,3-diol (7aa)

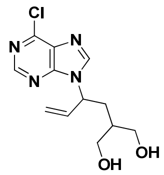


7aa

Colorless oil; 53% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.14 (s, 1H), 5.89-5.70 (m, 2H), 4.87 (d, J = 6.4 Hz, 2H), 3.81-3.77 (m, 2H), 3.69-3.65 (m, 2H), 2.16 (t, J = 7.2 Hz, 4H), 1.88-1.61 (m, 1H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 152.0, 144.9, 135.0, 131.7, 124.4, 65.3, 46.0, 41.7, 31.0 ppm. HRMS: calcd for $C_{12}H_{15}ClN_4O_2Na$ $[M+Na]^+$ 305.0776, found 305.0776.

2-(2-(6-Chloro-9*H*-purin-9-yl)but-3-en-1-yl)propane-1,3-diol (8aa)



8aa

Colorless oil; 47% yield.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.19 (s, 1H), 6.20-6.12 (m, 1H), 5.43-5.26 (m, 3H), 3.80-3.64 (m, 4H), 2.46 (d, J = 19.1 Hz, 2H), 2.30-2.16 (m, 2H), 1.58-1.52 (m, 1H) ppm. ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 151.8, 151.5, 151.2, 143.9, 135.2, 131.6, 119.1, 64.4, 64.4, 56.3, 38.8, 32.7 ppm. HRMS: calcd for $C_{12}H_{15}ClN_4O_2Na$ $[M+Na]^+$ 305.0776, found 305.0776.

10. References:

[1] H. C. Koppel , D. E. O'Brien and R. K. Robins, *J. Org. Chem.*, 1959, **24**, 259.

[2] G.-R. Qu, L. Zhao, D.-C. Wang, J. Wu and H.-M. Guo, *Green Chem.*, 2008, **10**, 287.

[3] M. Hocek, D. Hocková and H. Dvořáková, *Synthesis*, 2004, **6**, 889.

[4] H. Dvořáková, D. Dvořák and A. Ho1ý, *Tetrahedron Lett.*, 1996, **37**, 1285.

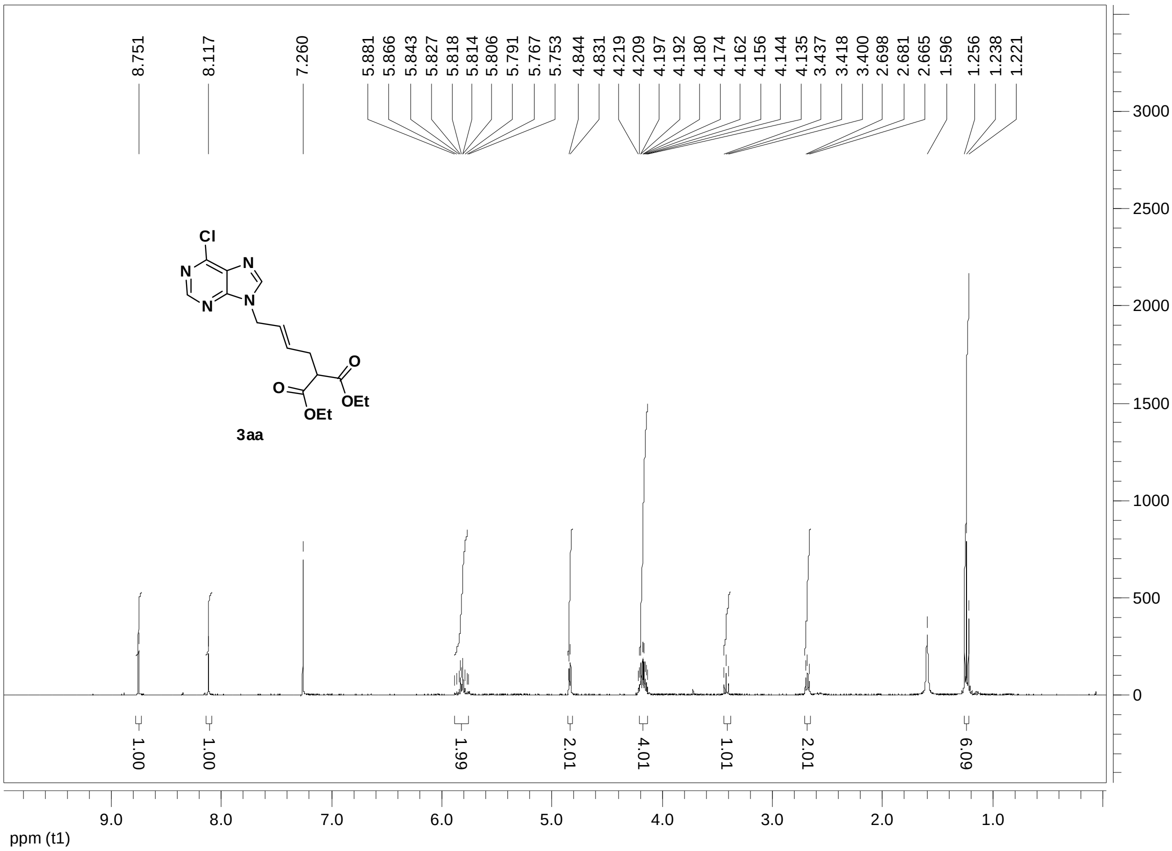
[5] A. T. Parsons, M. J. Campbell and J. S. Johnson, *Org. Lett.*, 2008, 10, 2541.

[6] (*a*) Y. Hamashima, D. Sawada, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 1999, **121**, 2641; (*b*) J. Casas, C. Nájera, J. M. Sansano and J. M. Saá, *Org. Lett.*, 2002, **4**, 2589; (*c*) Y. Hamashima, D. Sawada, H. Nogami, M. Kanai and M. Shibasaki, *Tetrahedron*, 2001, **57**, 805; (*d*) J. Casas, C. Nájera, J. M. Sansano and J. M. Saá, *Tetrahedron*, 2004, **60**, 10487.

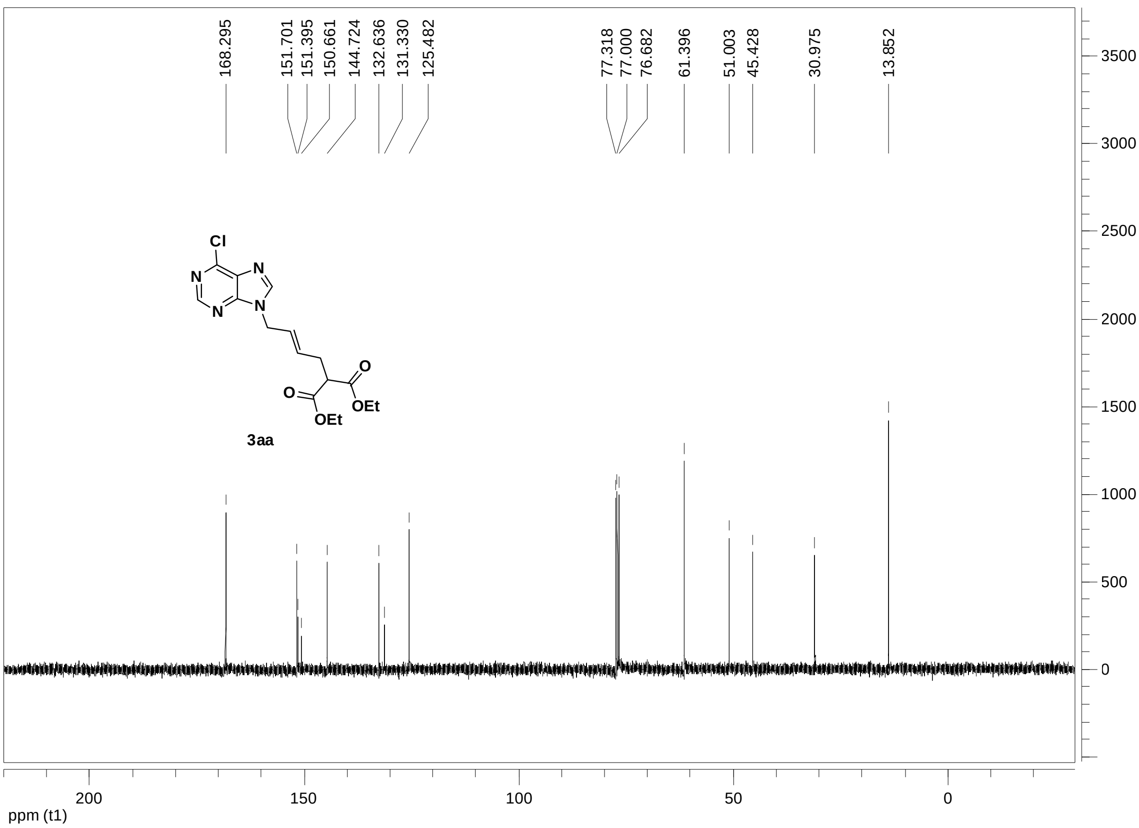
[7] (*a*) M. P. Sibi, K. Itoh and C. P. Jasperse, *J. Am. Chem. Soc.*, 2004, **126**, 5366; (*b*) M. P. Sibi, G. Petrovic, and J. Zimmerman, *J. Am. Chem. Soc.*, 2005, **127**, 2390, (*c*) M. P. Sibi, N. Prabagaran, S. G. Ghorpade and C. P. Jasperse, *J. Am. Chem. Soc.*, 2003, **125**, 11796.

11. Copies of ^{1}H NMR and ^{13}C NMR spectra

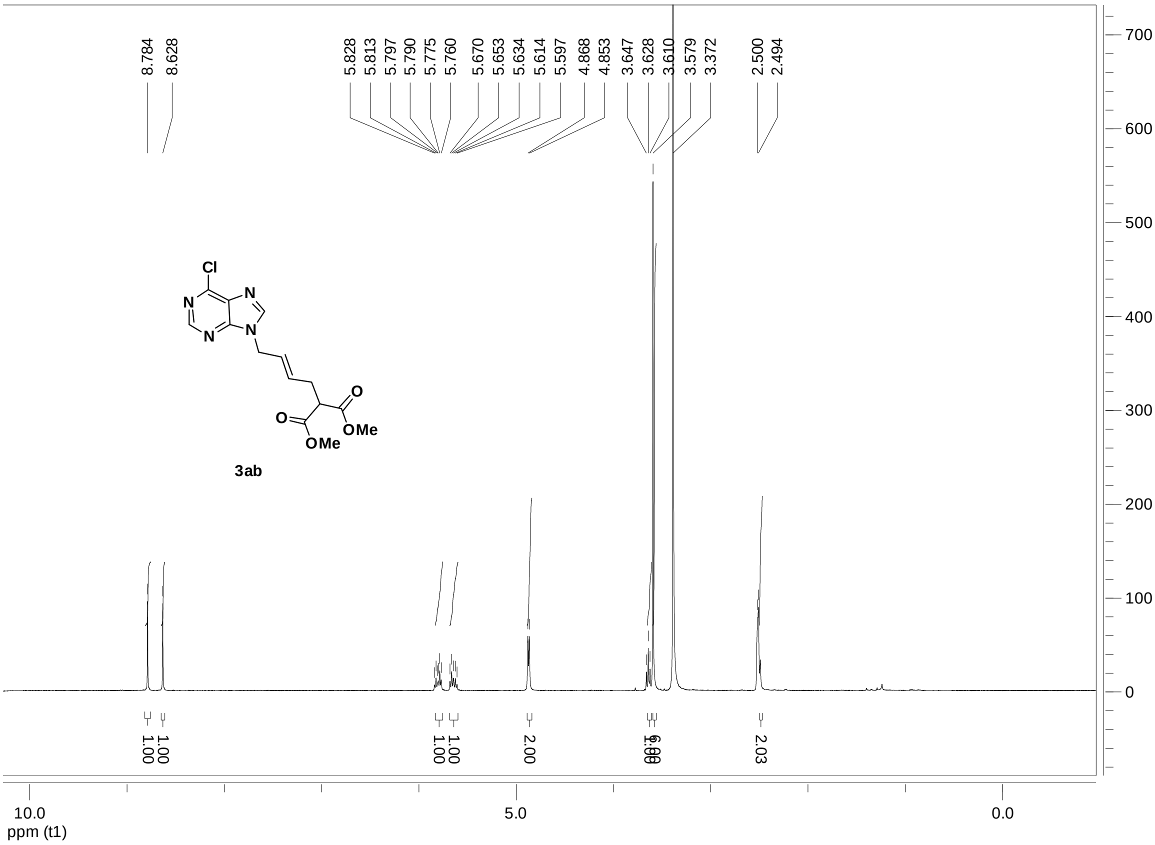
^{1}H-NMR for 3aa



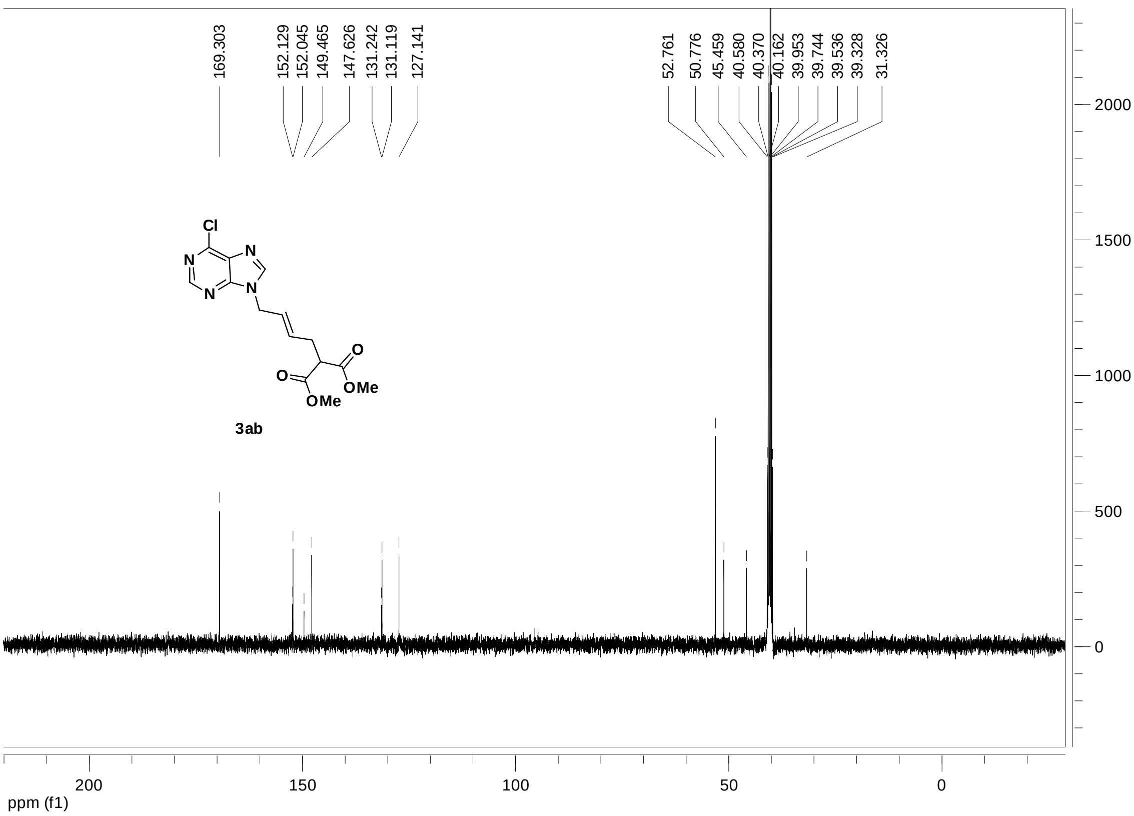
^{13}C-NMR for 3aa



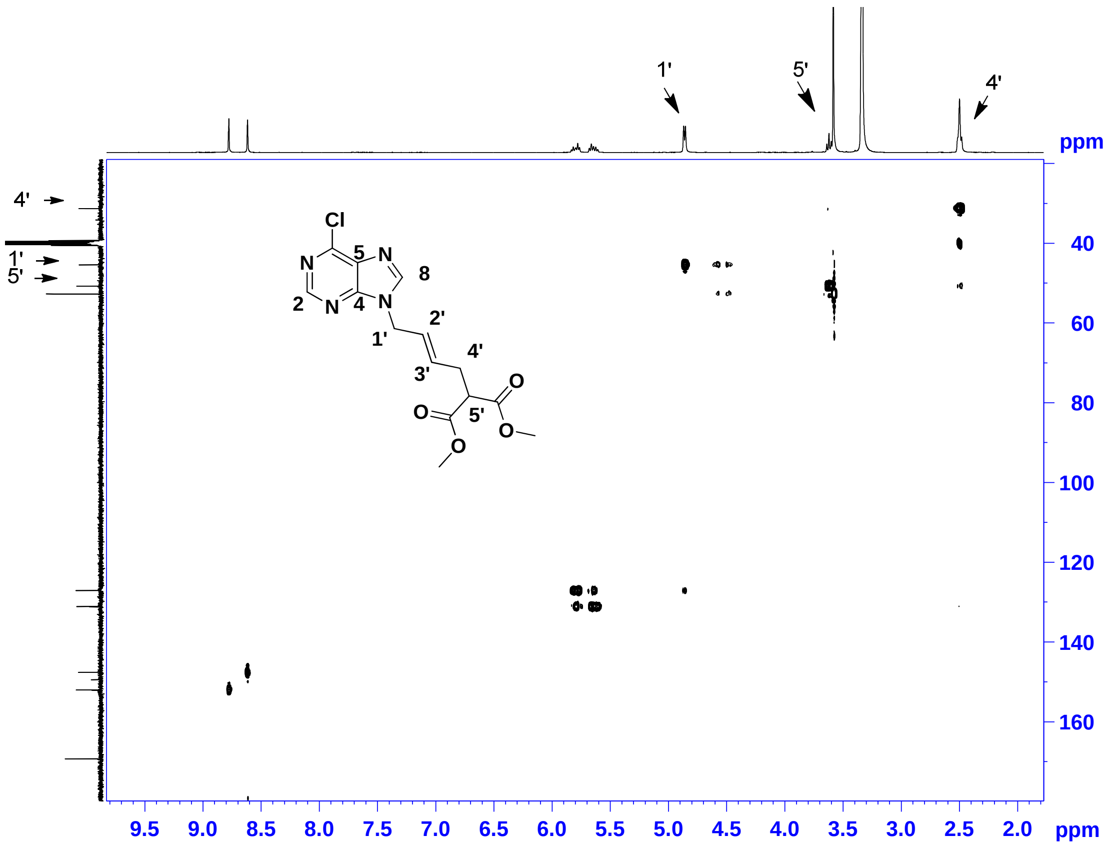
^{1}H-NMR for 3ab



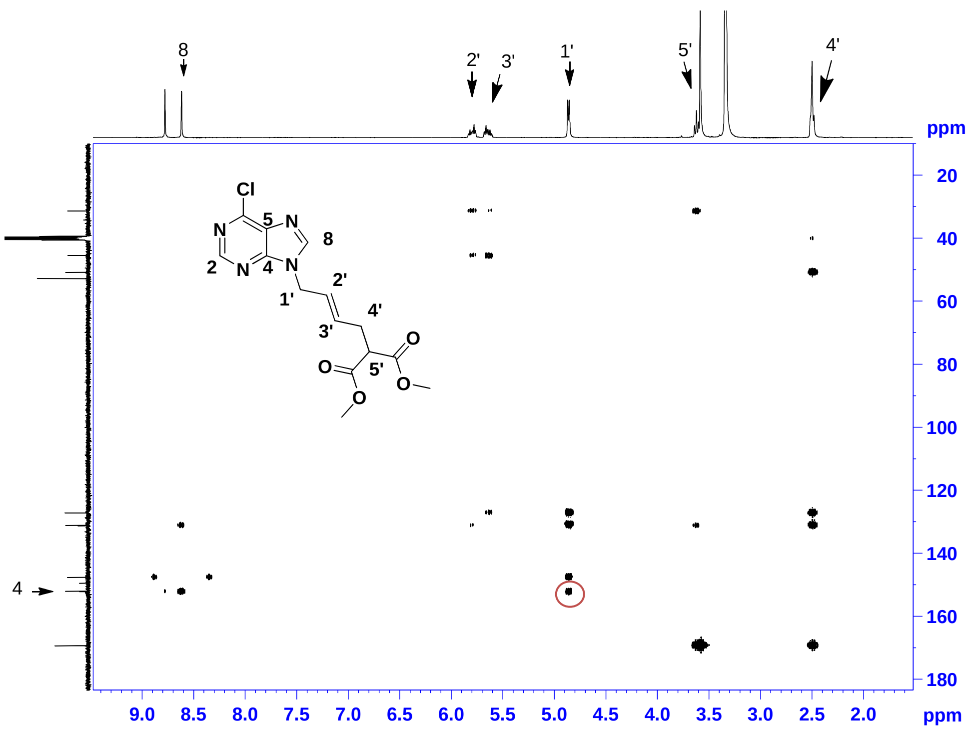
^{13}C-NMR for 3ab



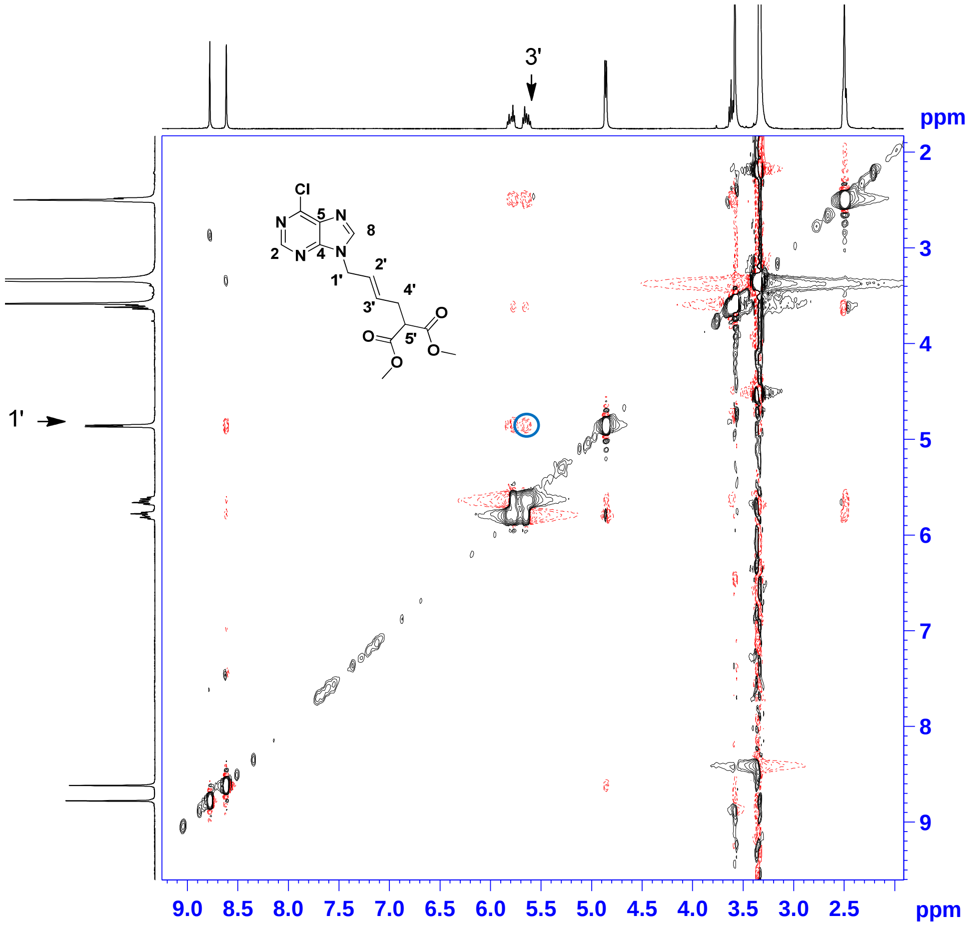
HSQC for 3ab



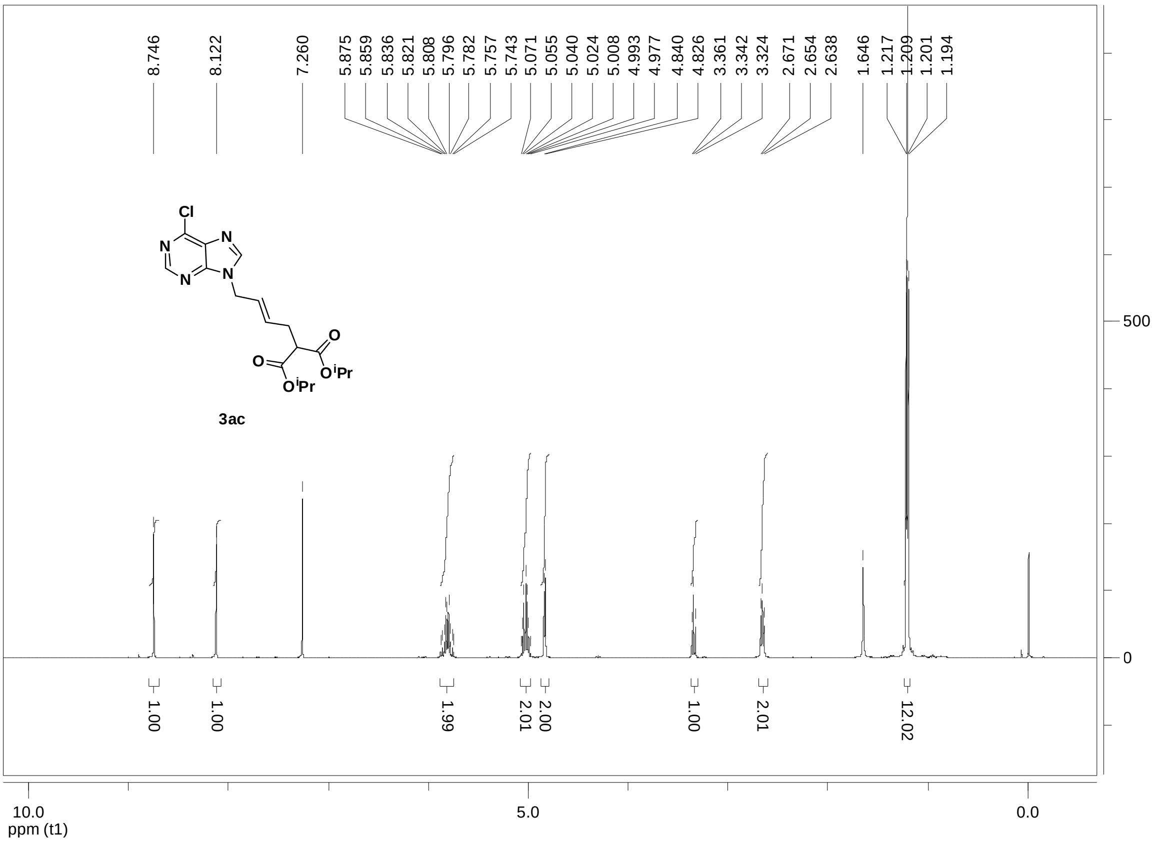
HMBC for 3ab



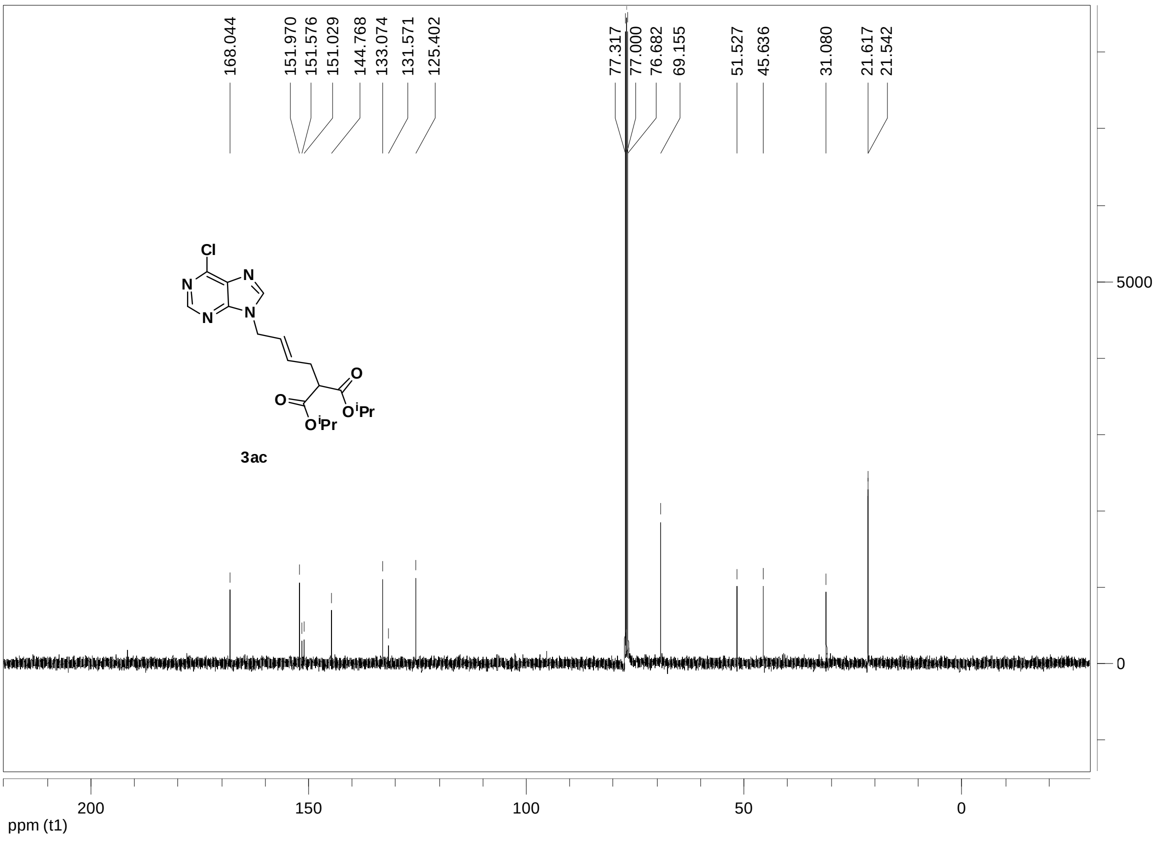
Noesy for 3ab



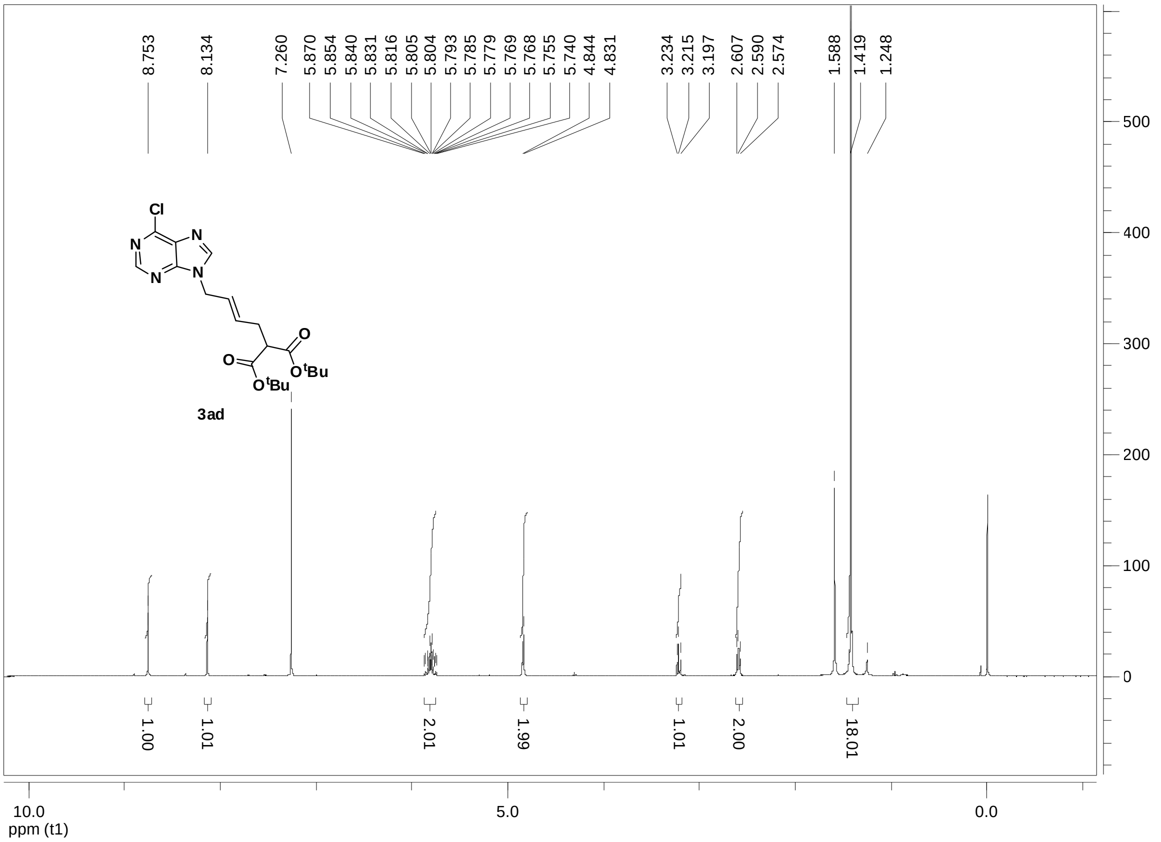
^{1}H-NMR for 3ac



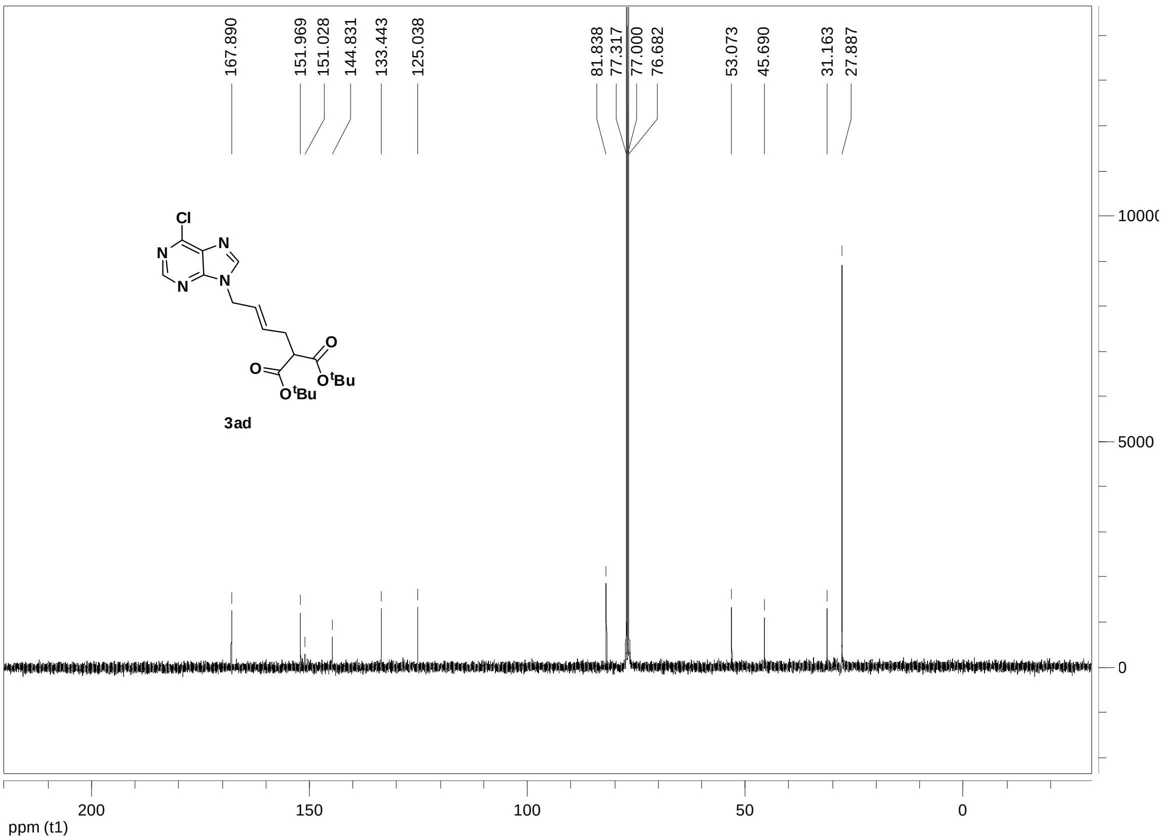
^{13}C-NMR for 3ac



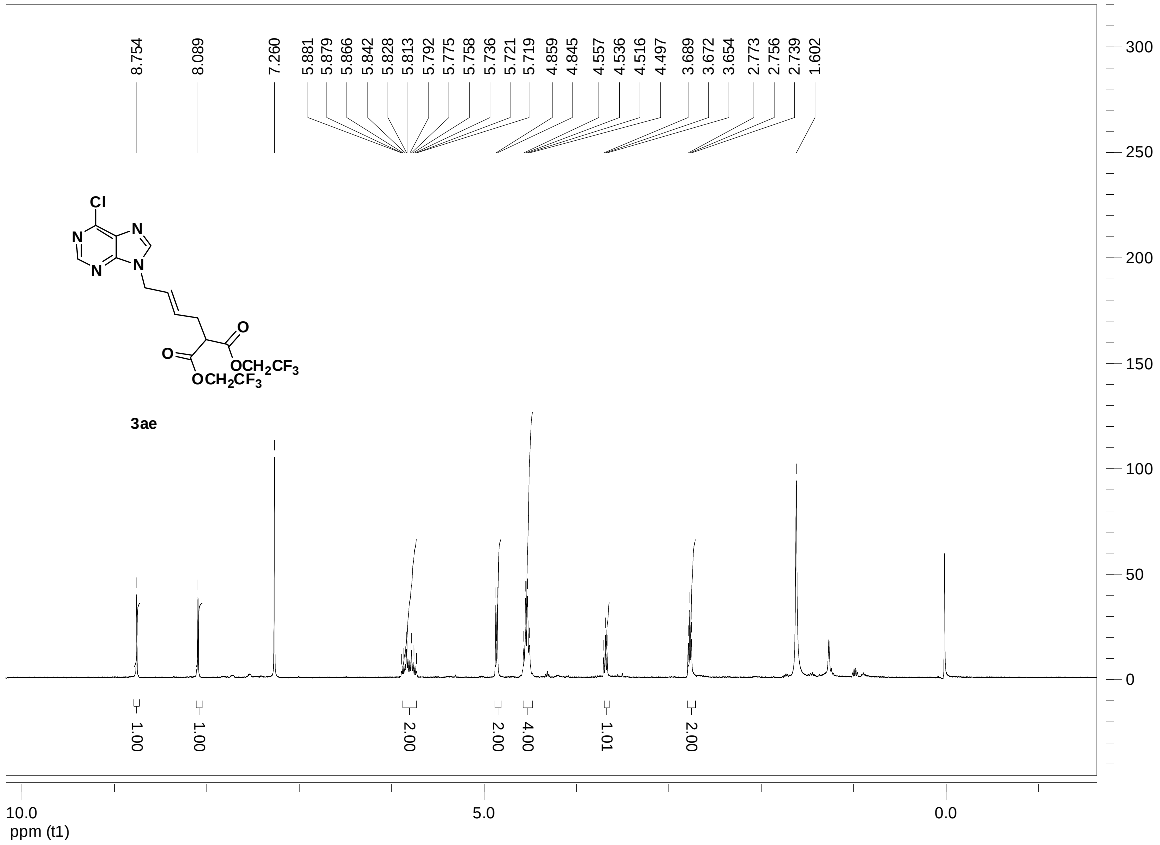
^{1}H-NMR for 3ad



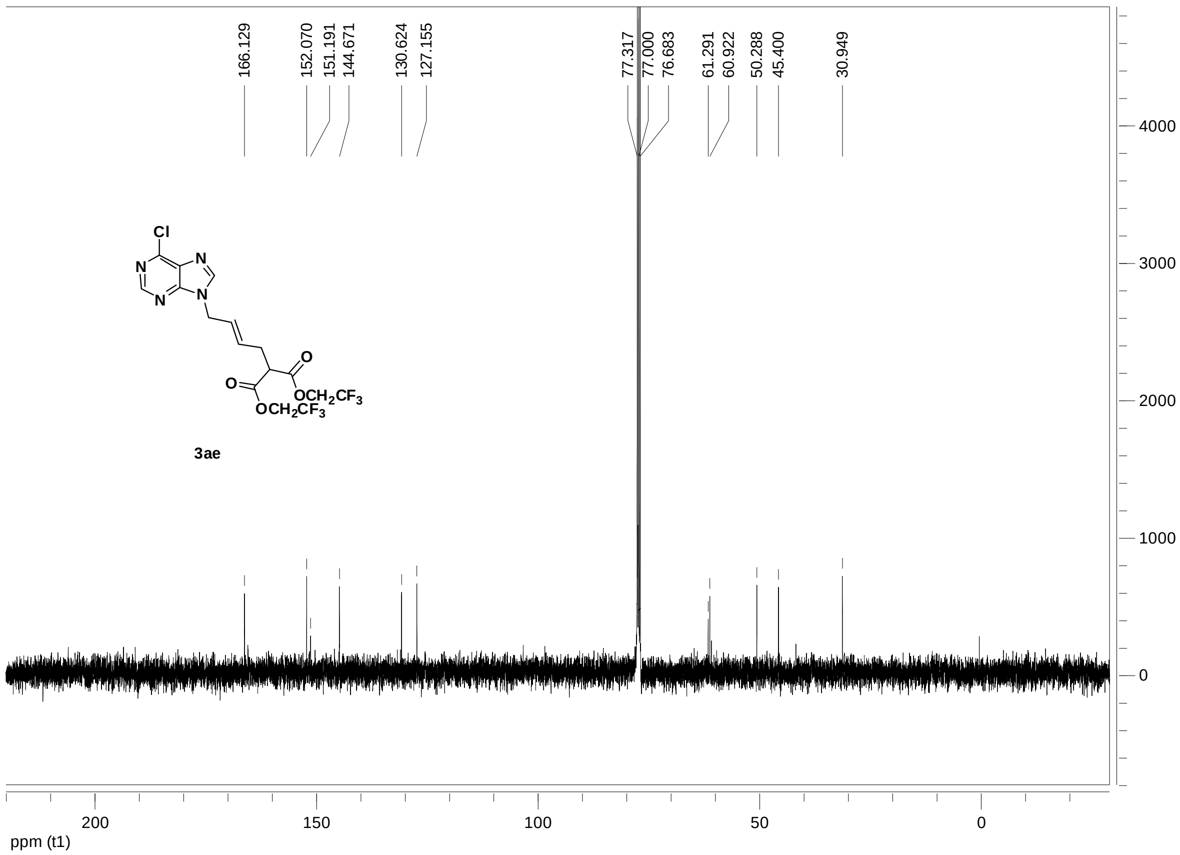
^{13}C-NMR for 3ad



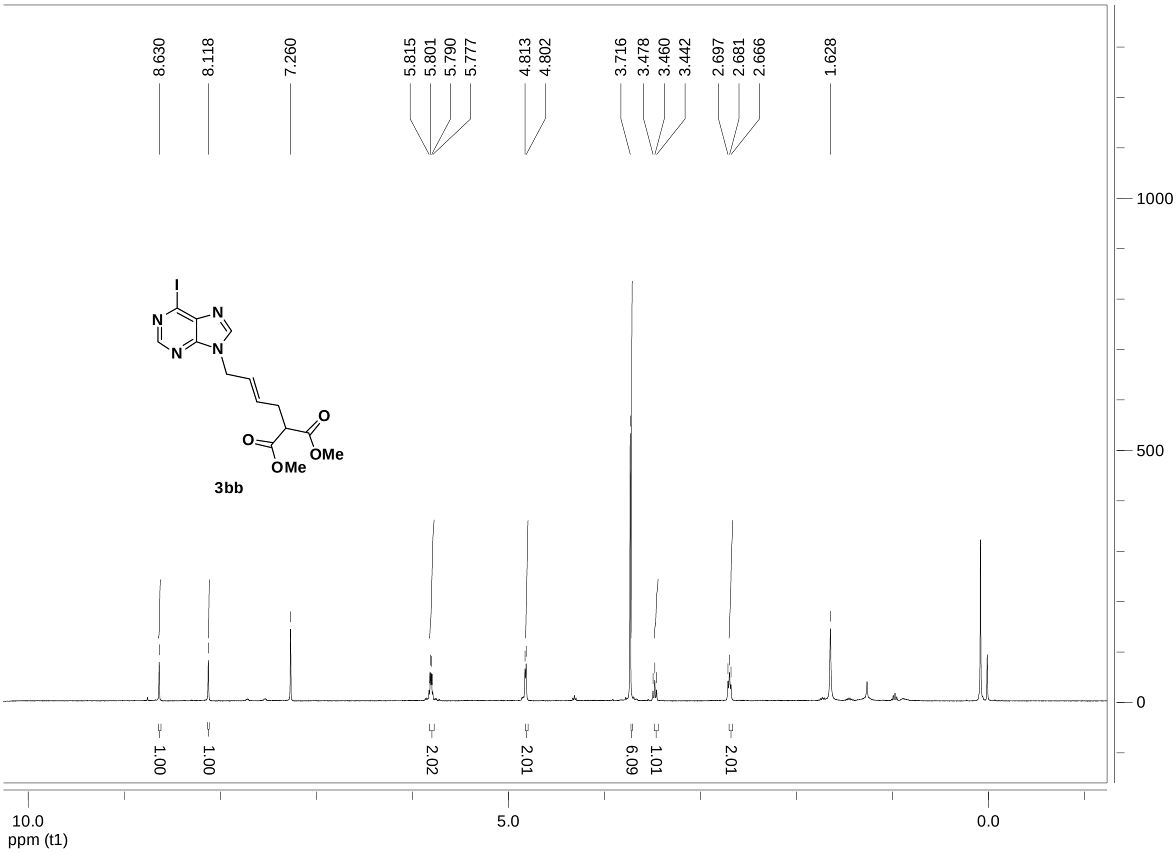
^{1}H-NMR for 3ae



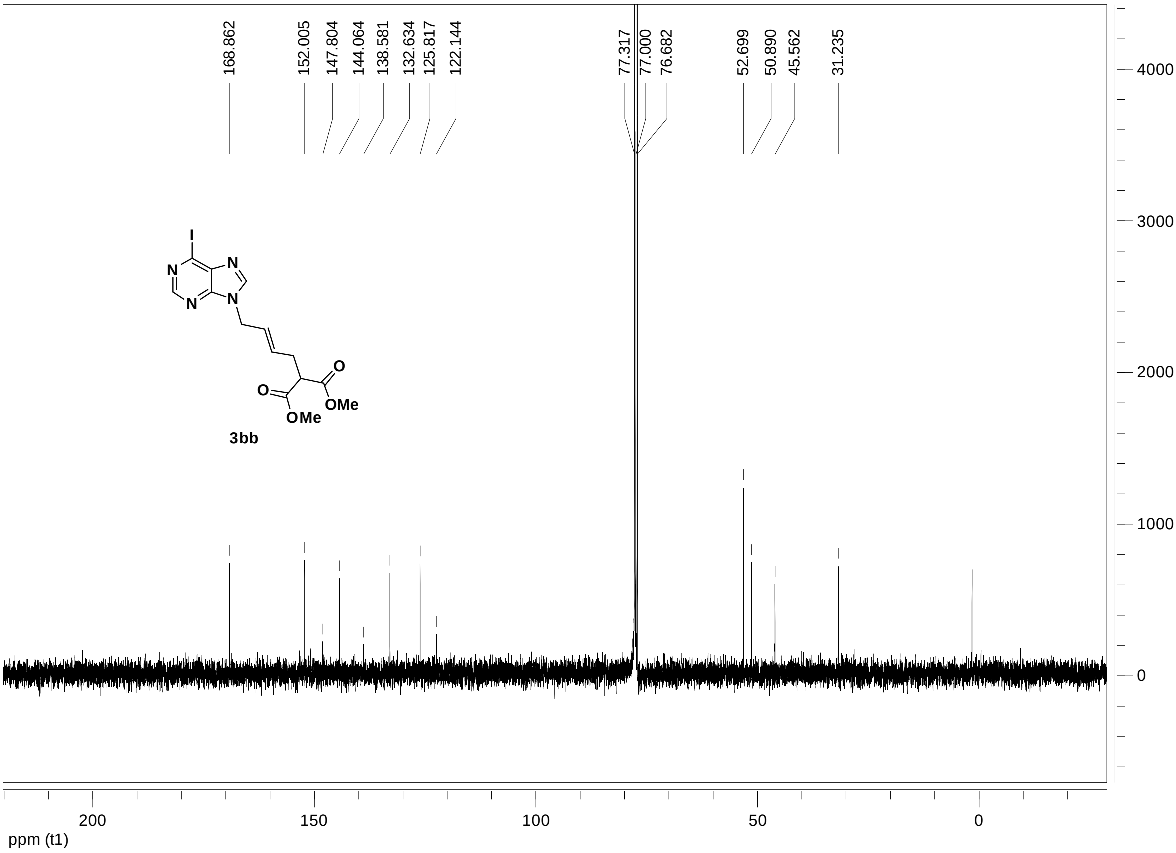
^{13}C-NMR for 3ae



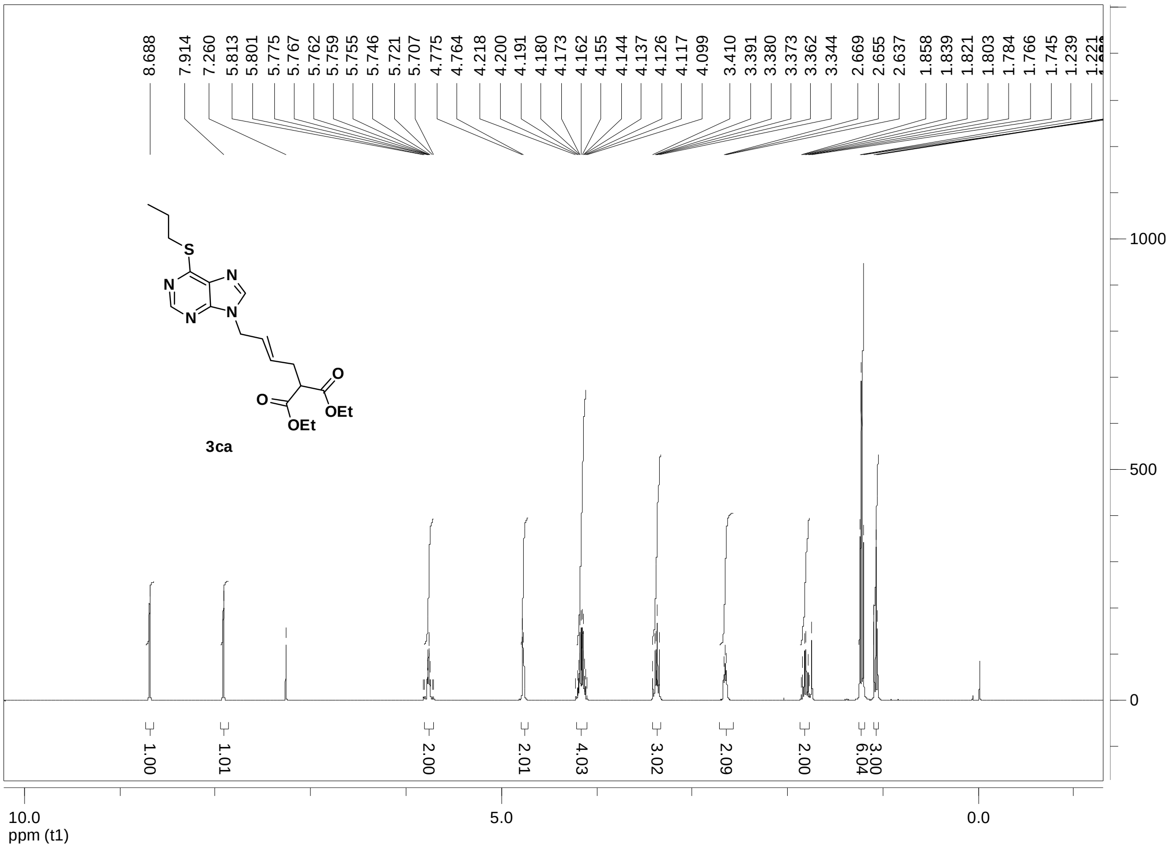
^{1}H-NMR for 3bb



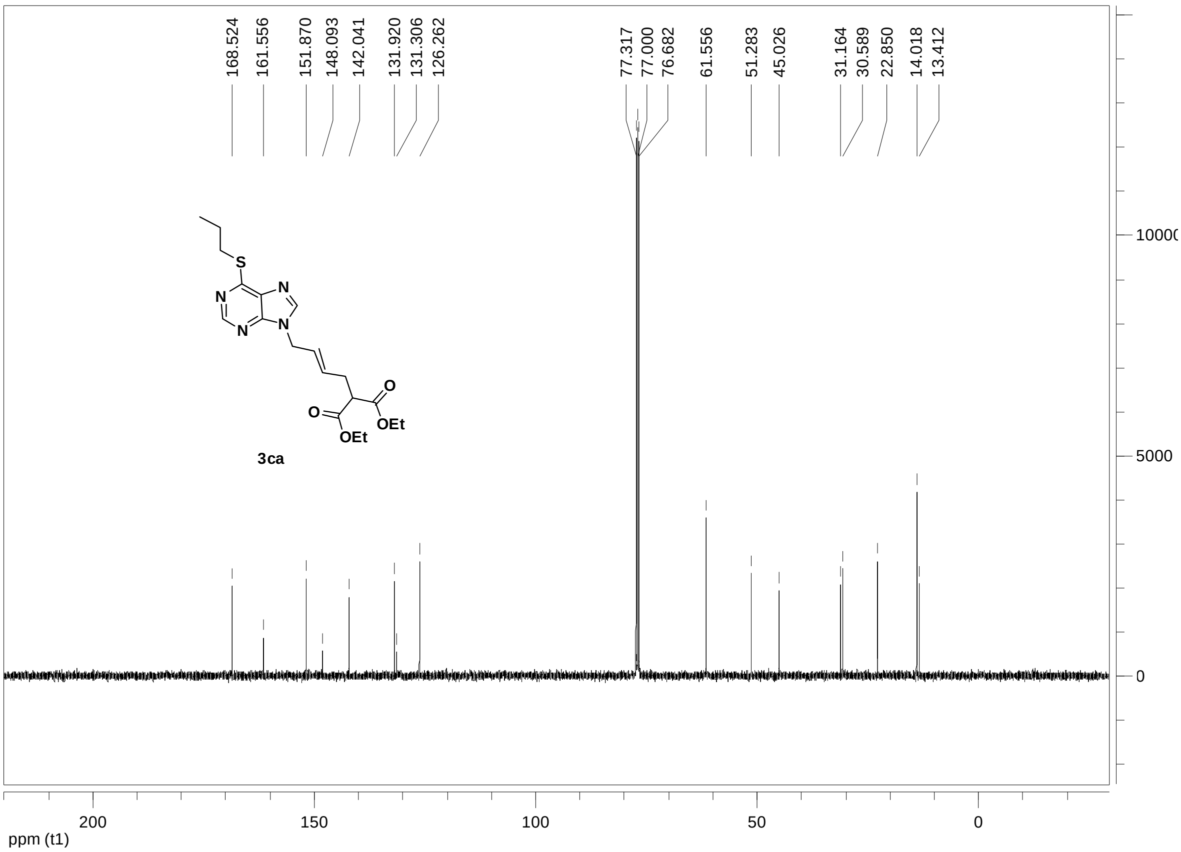
^{13}C-NMR for 3bb



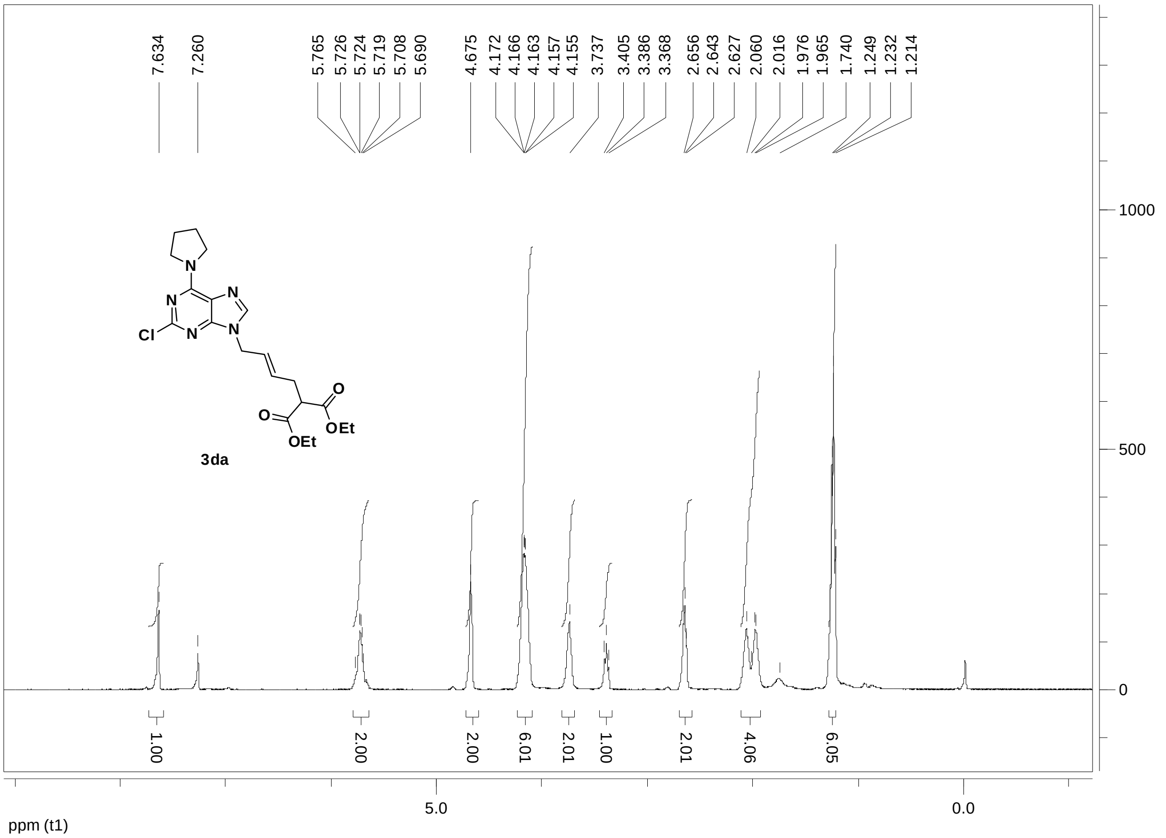
^{1}H-NMR for 3ca



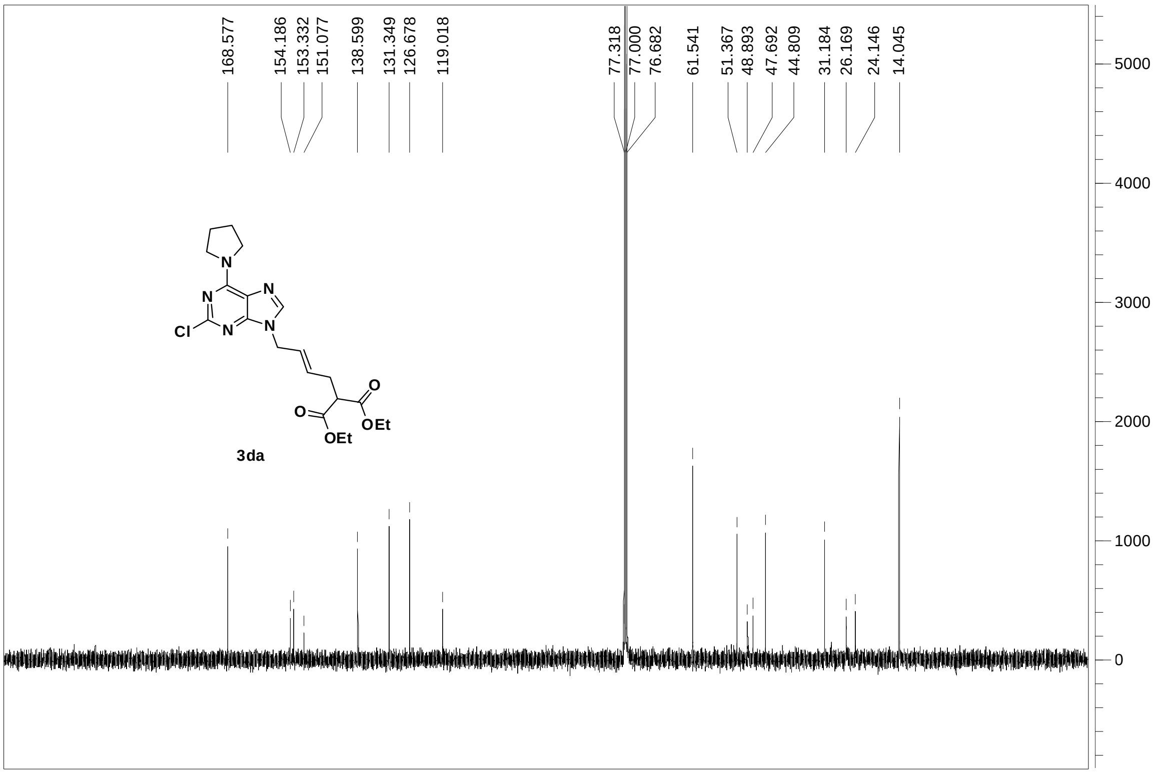
^{13}C-NMR for 3ca



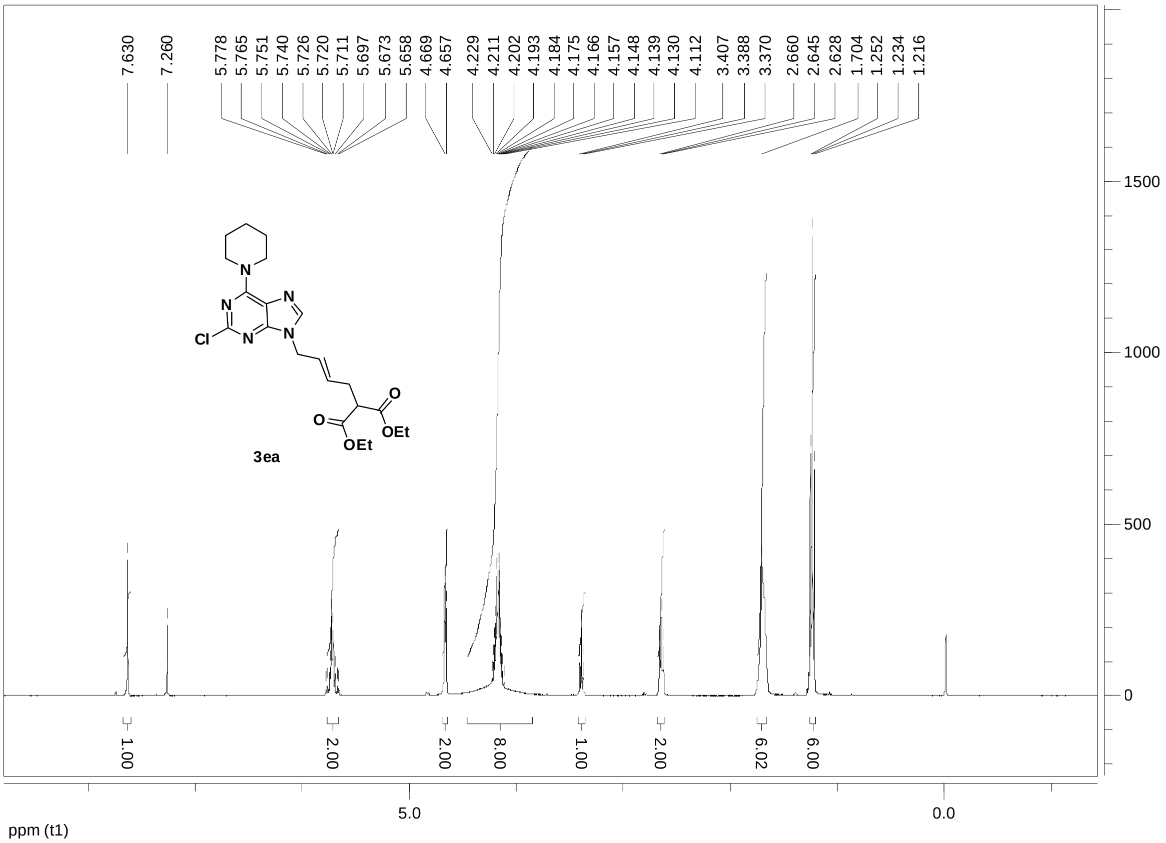
^{1}H-NMR for 3da



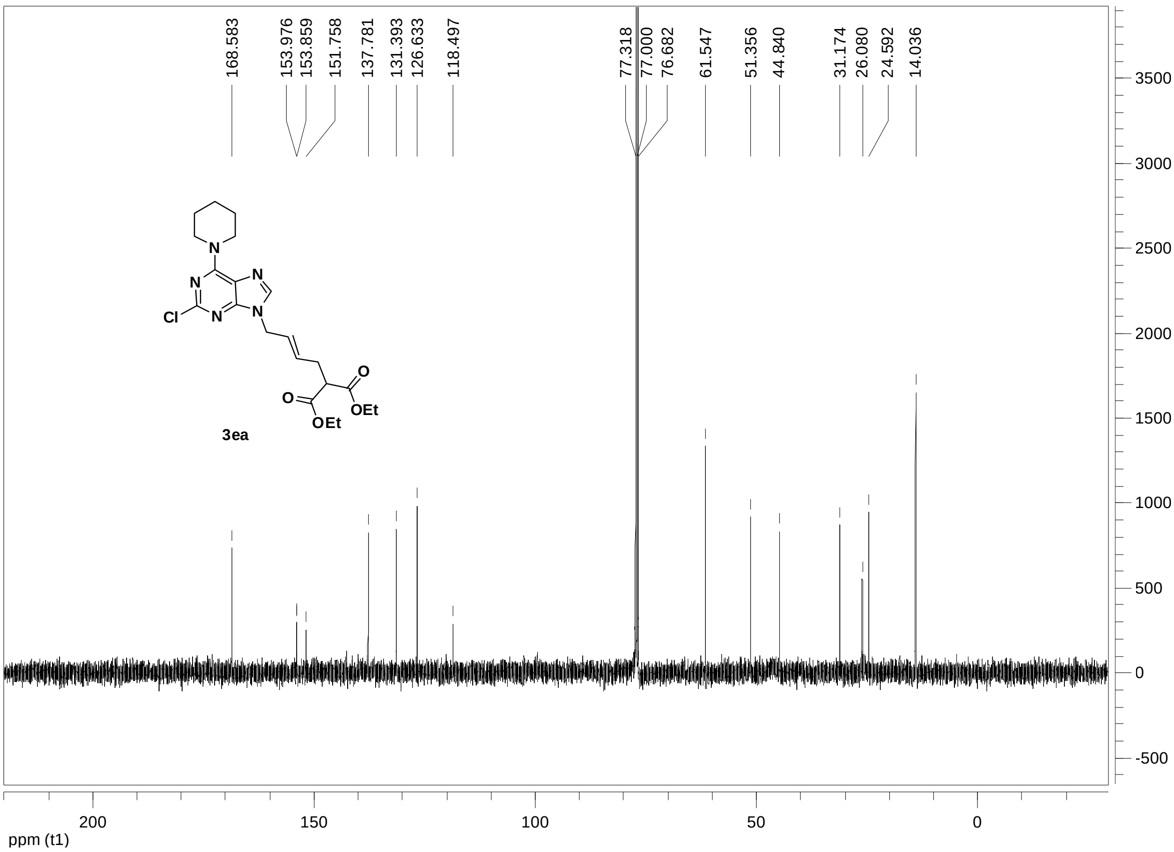
^{13}C-NMR for 3da



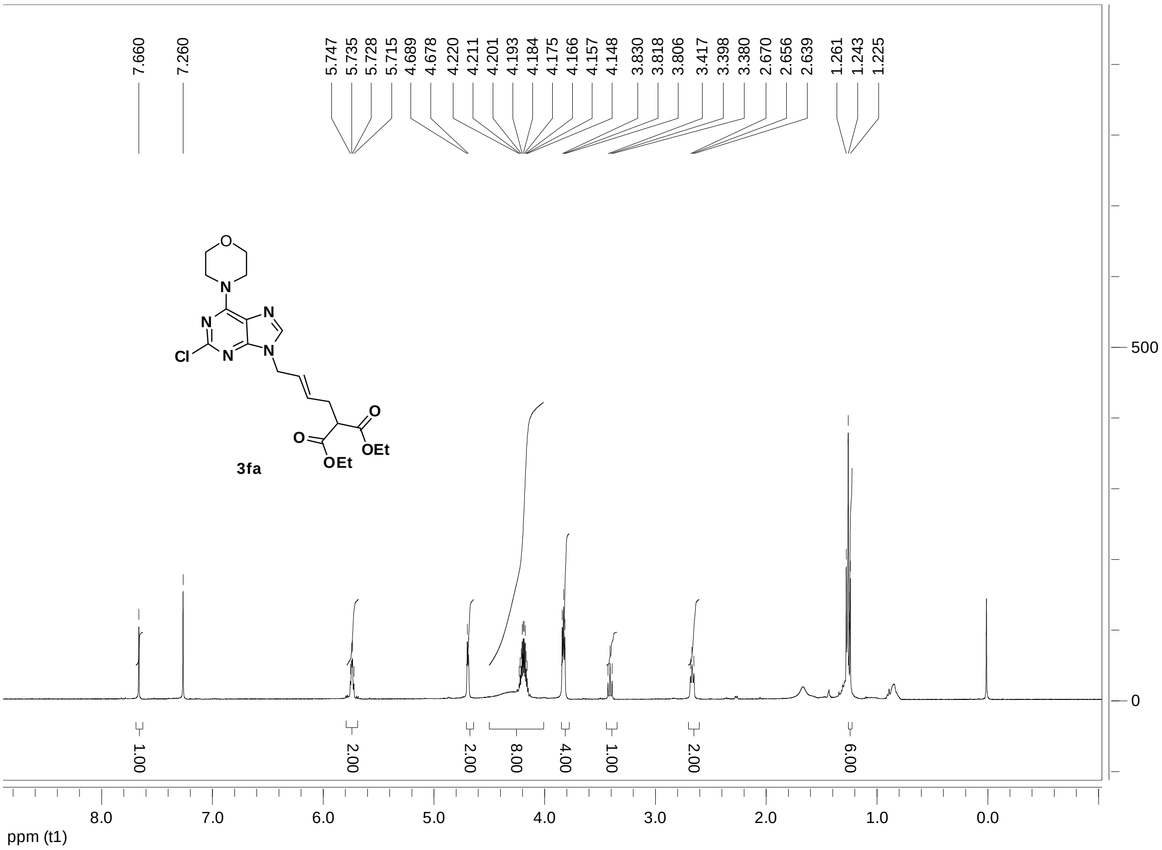
[1]H-NMR for 3ea



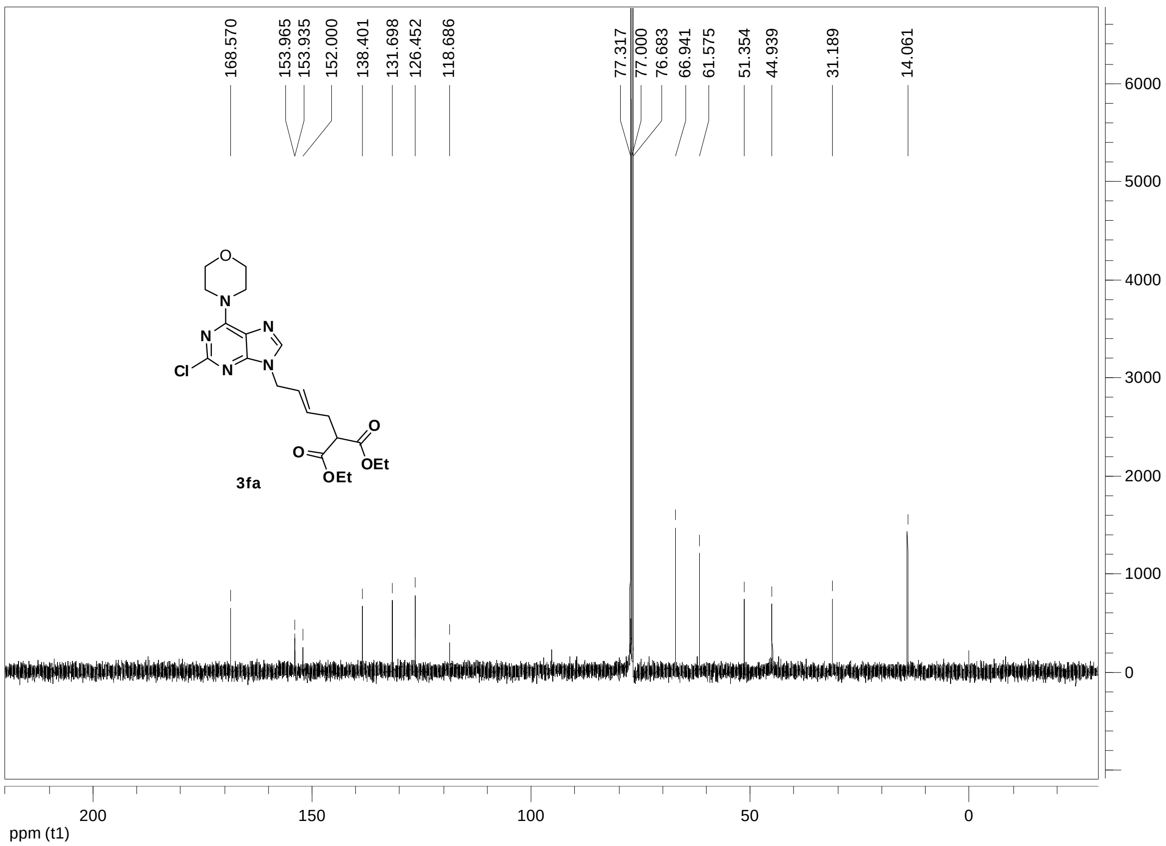
[13]C-NMR for 3ea



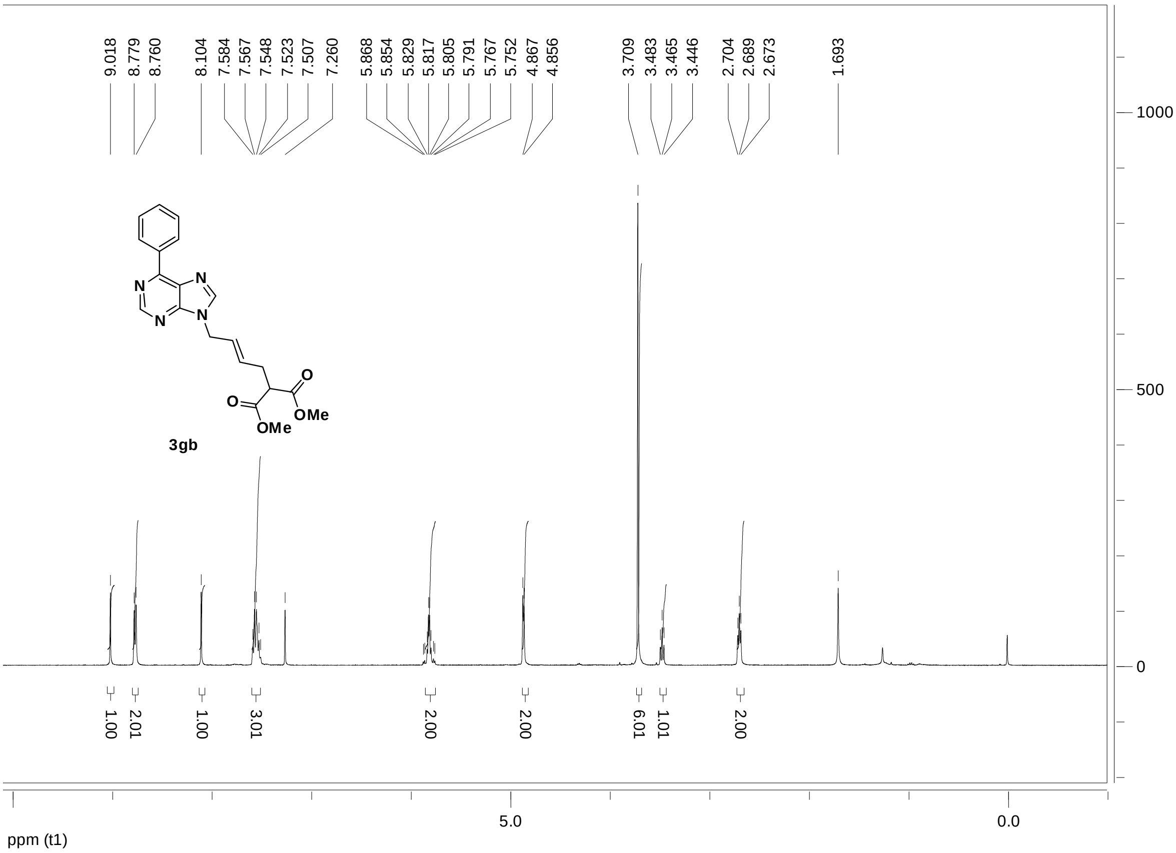
^{1}H-NMR for 3fa



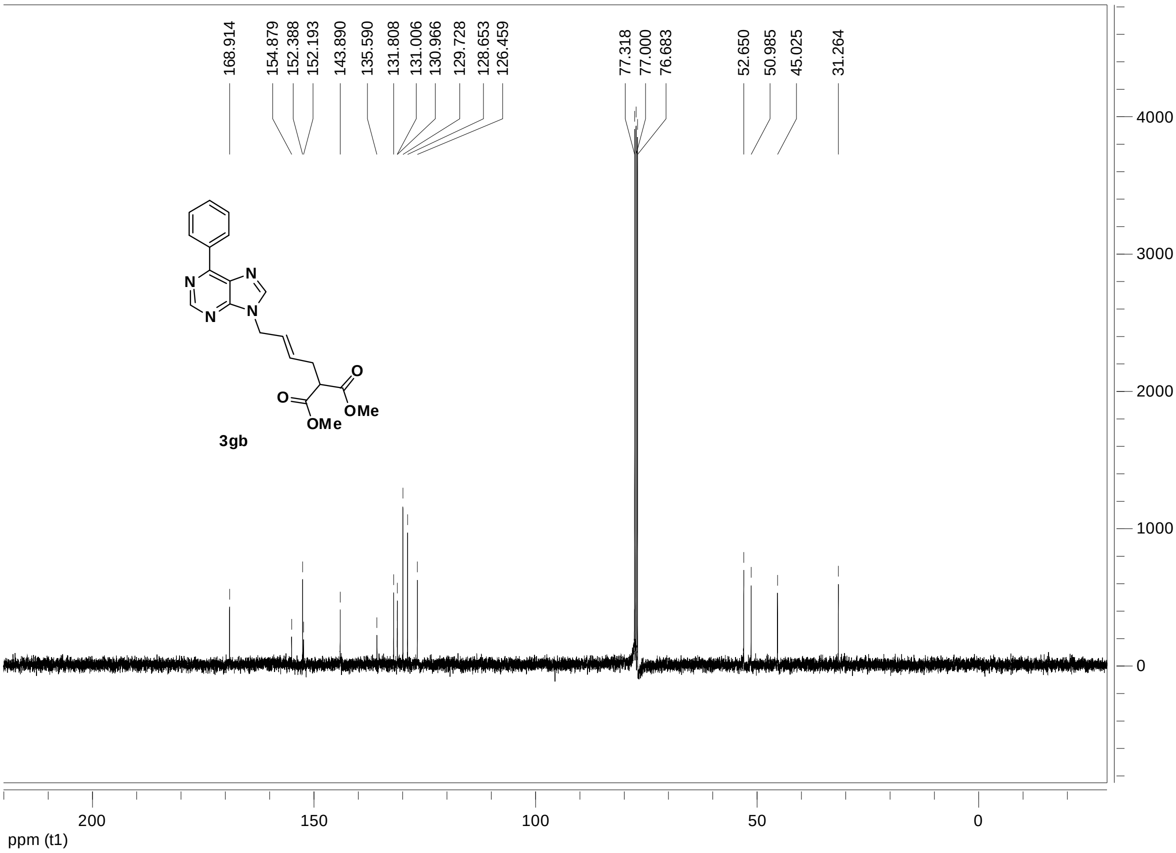
^{13}C-NMR for 3fa



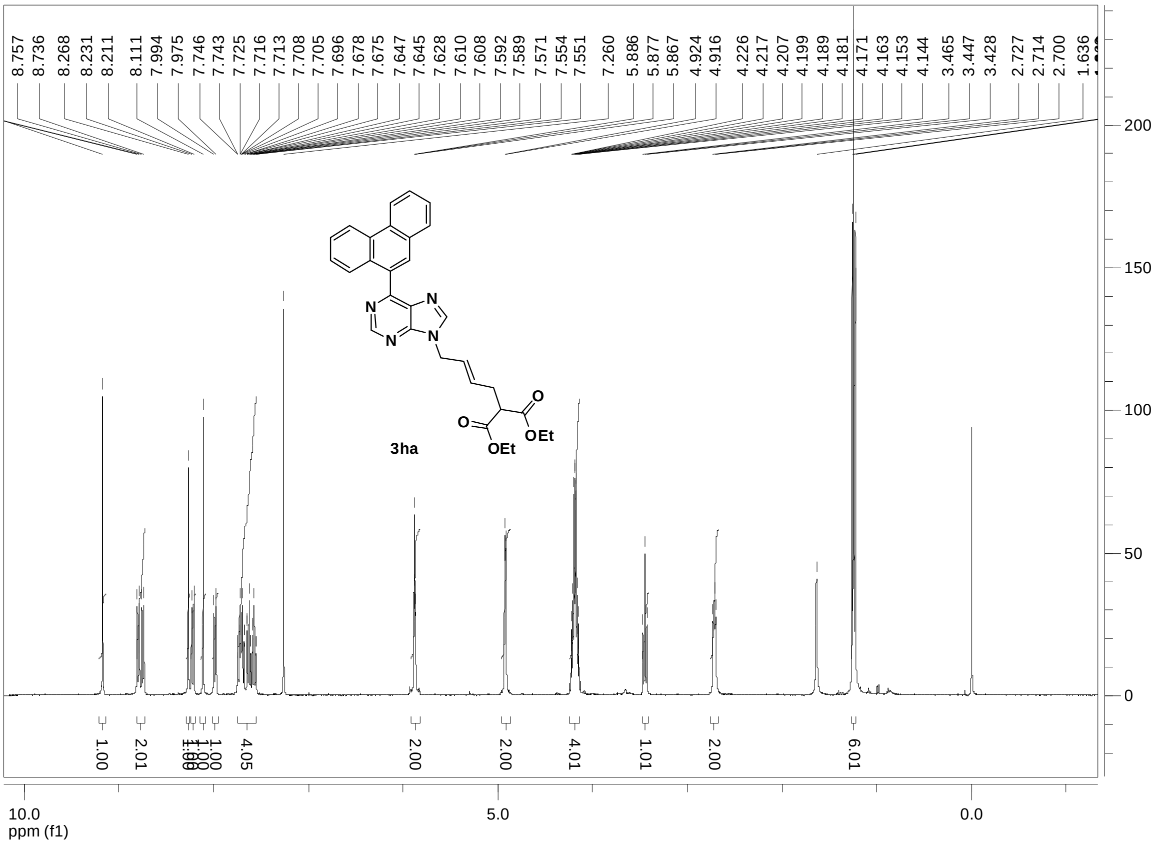
^{1}H-NMR for 3gb



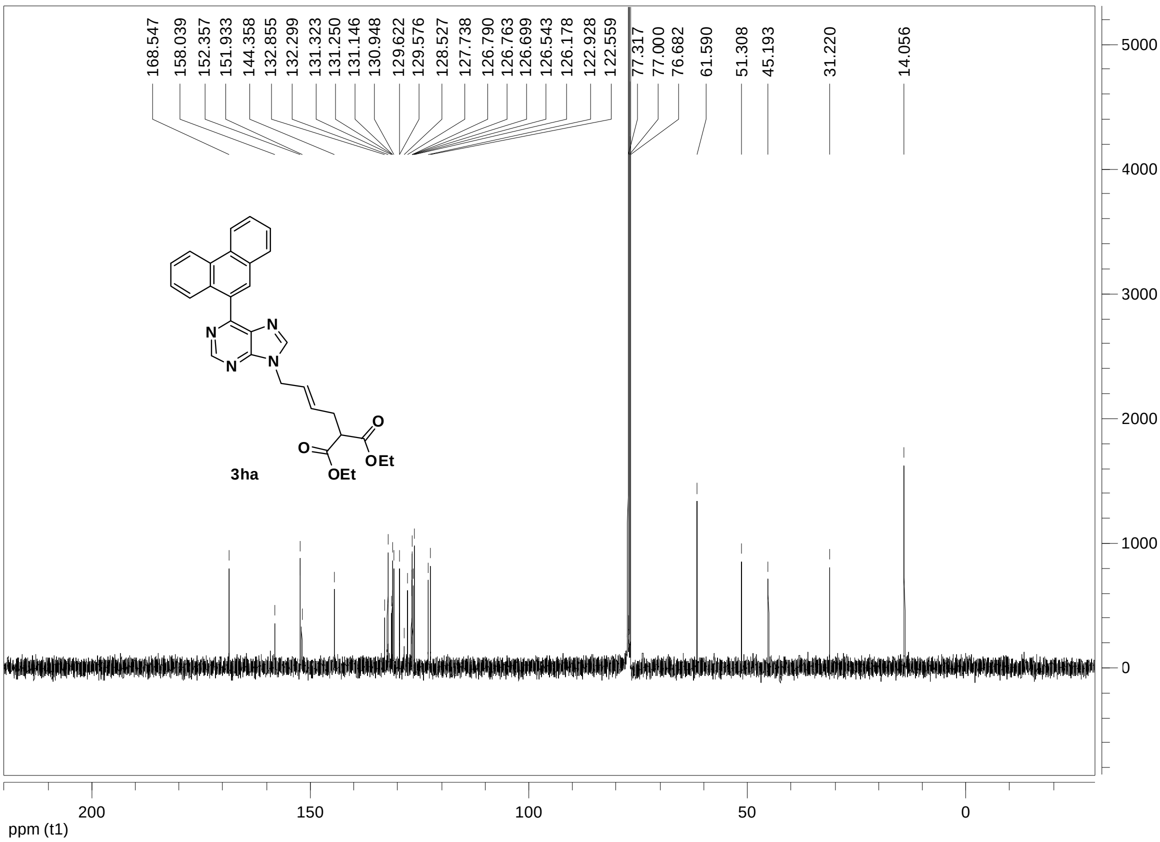
^{13}C-NMR for 3gb



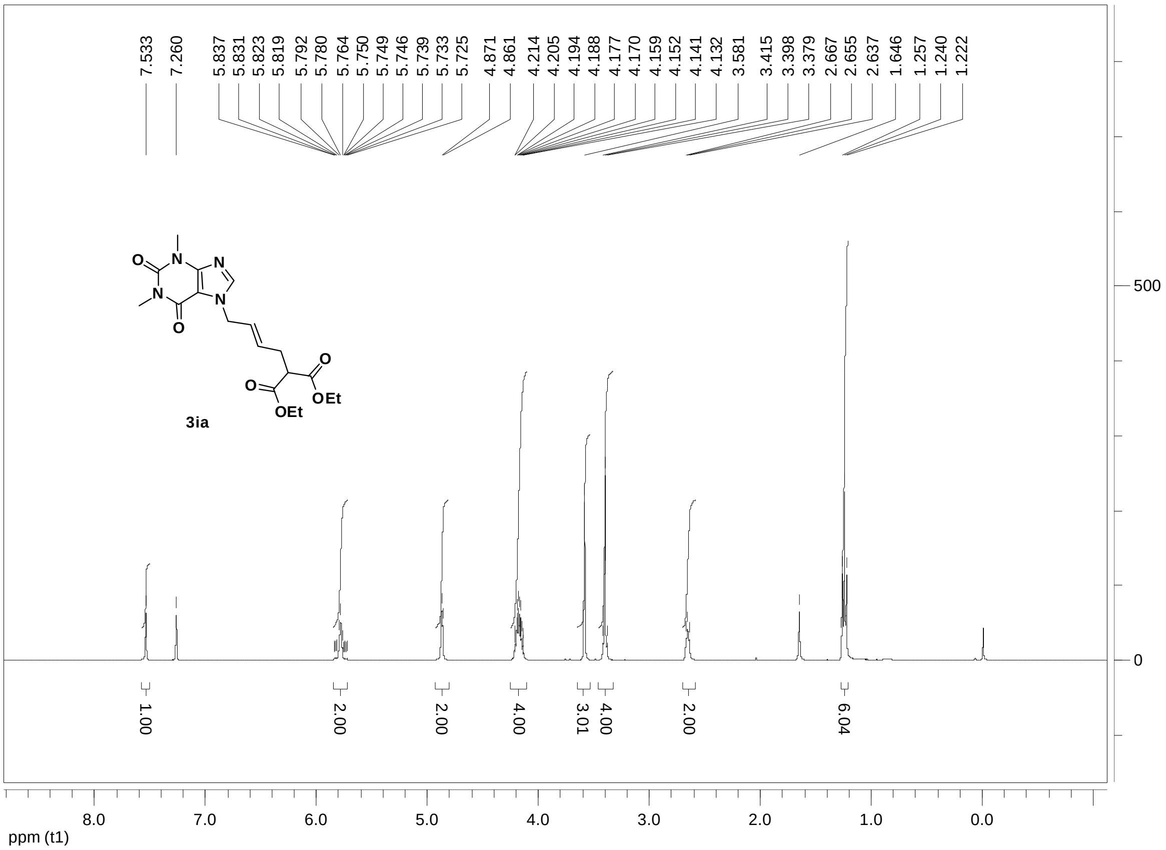
^{1}H-NMR for 3ha



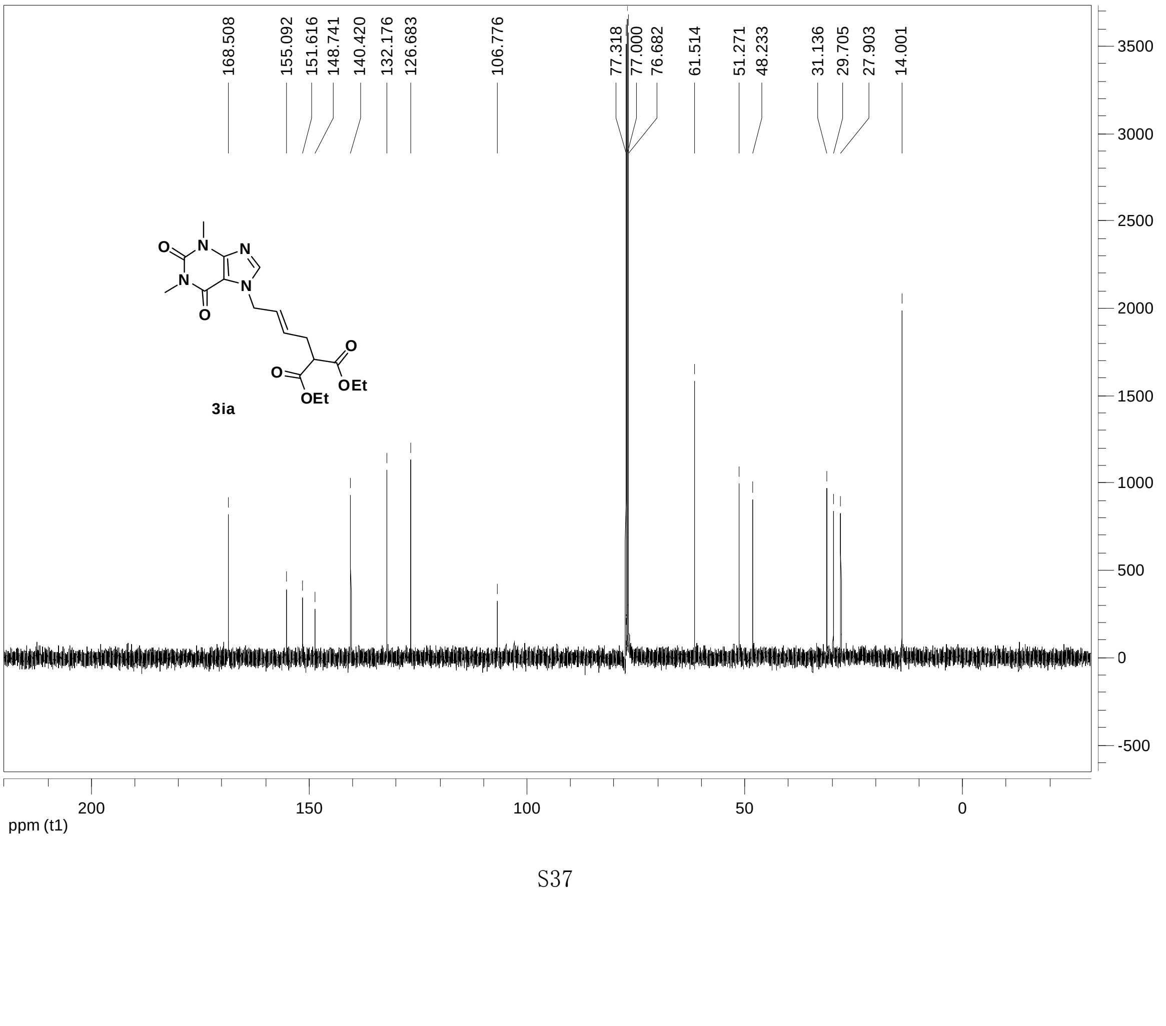
^{13}C-NMR for 3ha



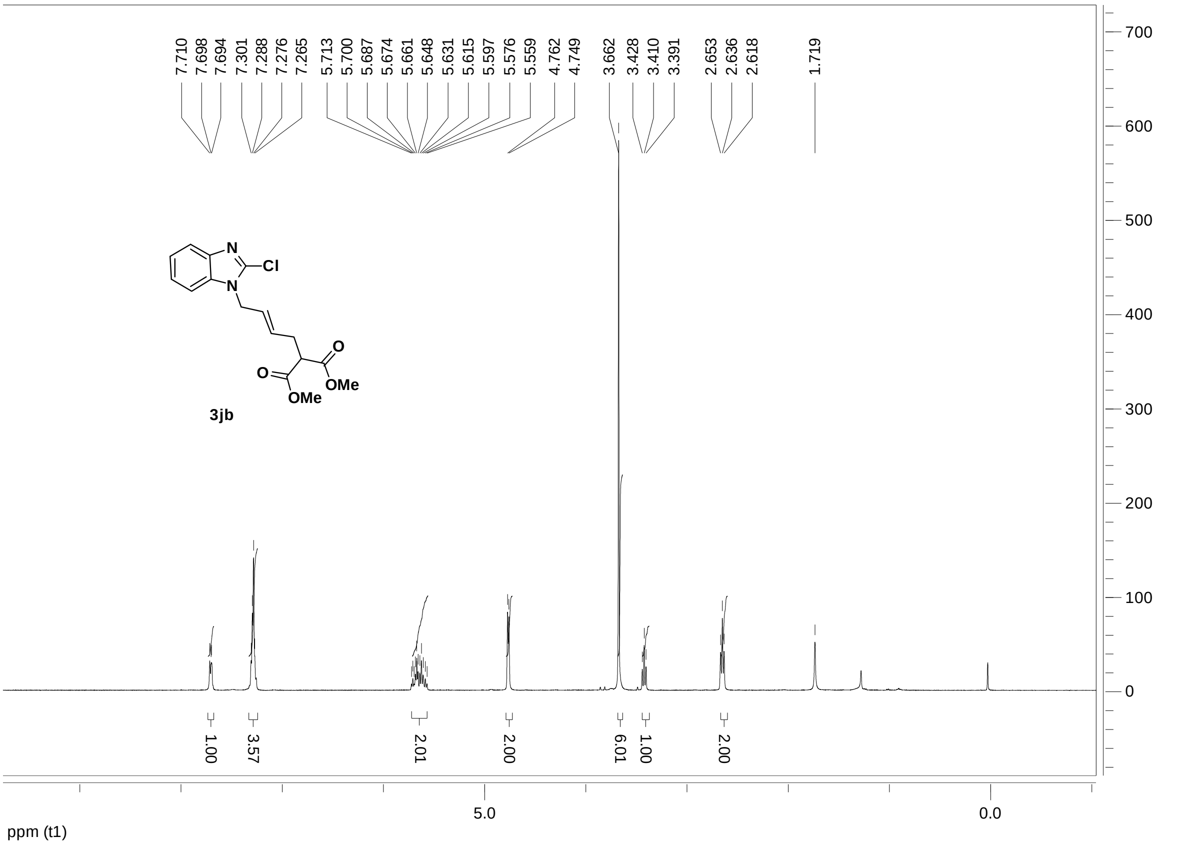
[1]H-NMR for 3ia



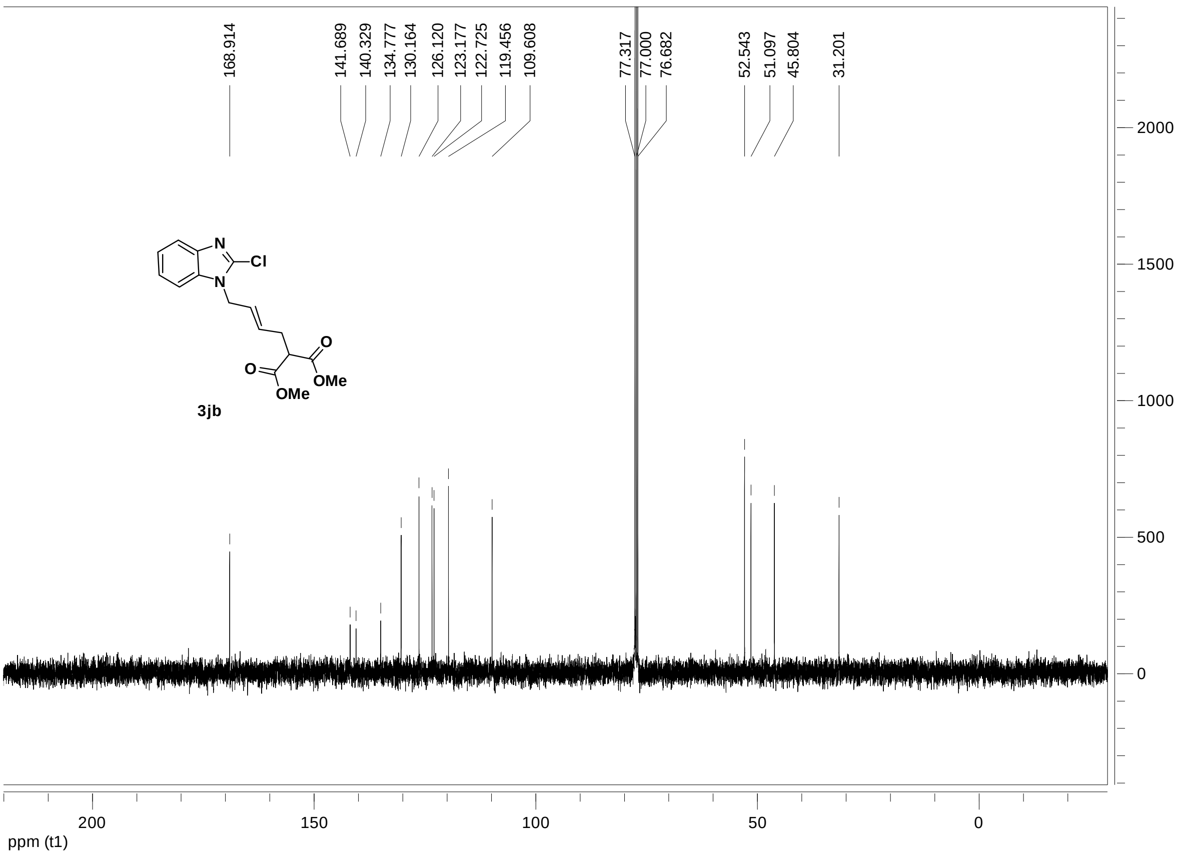
[13]C-NMR for 3ia



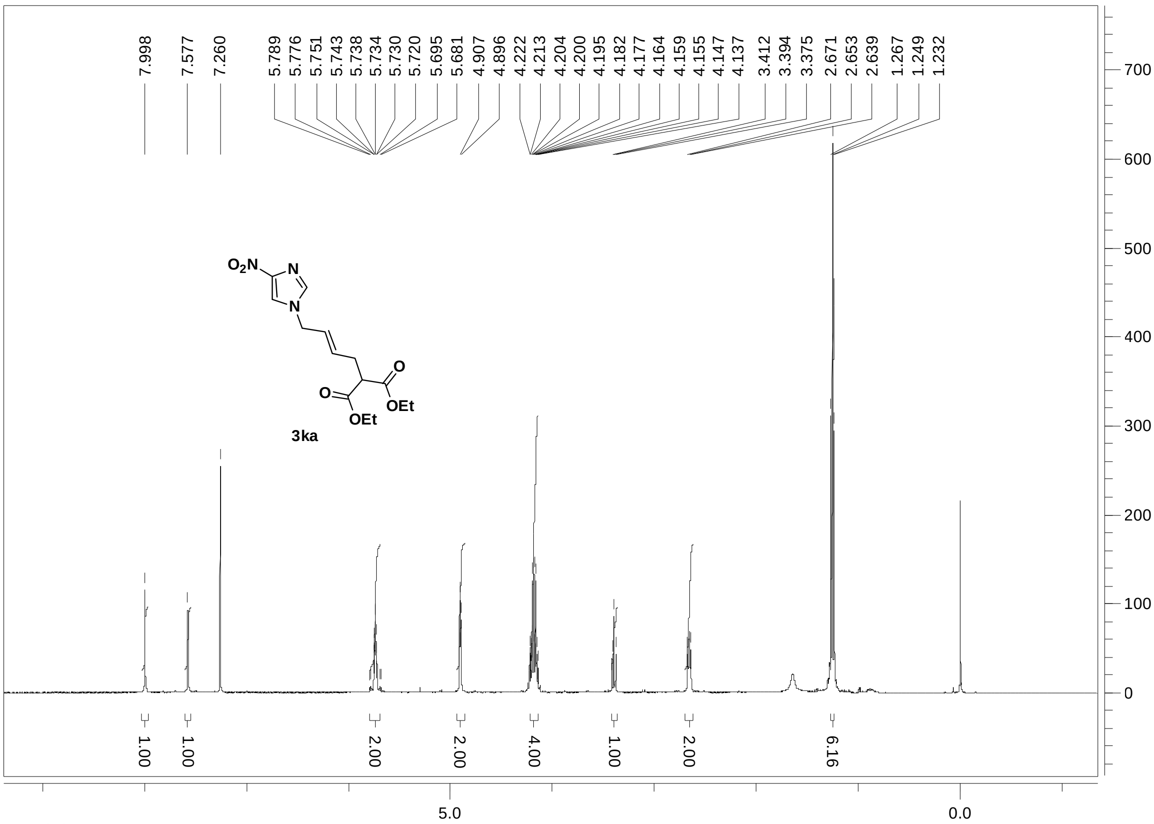
^{1}H-NMR for 3jb



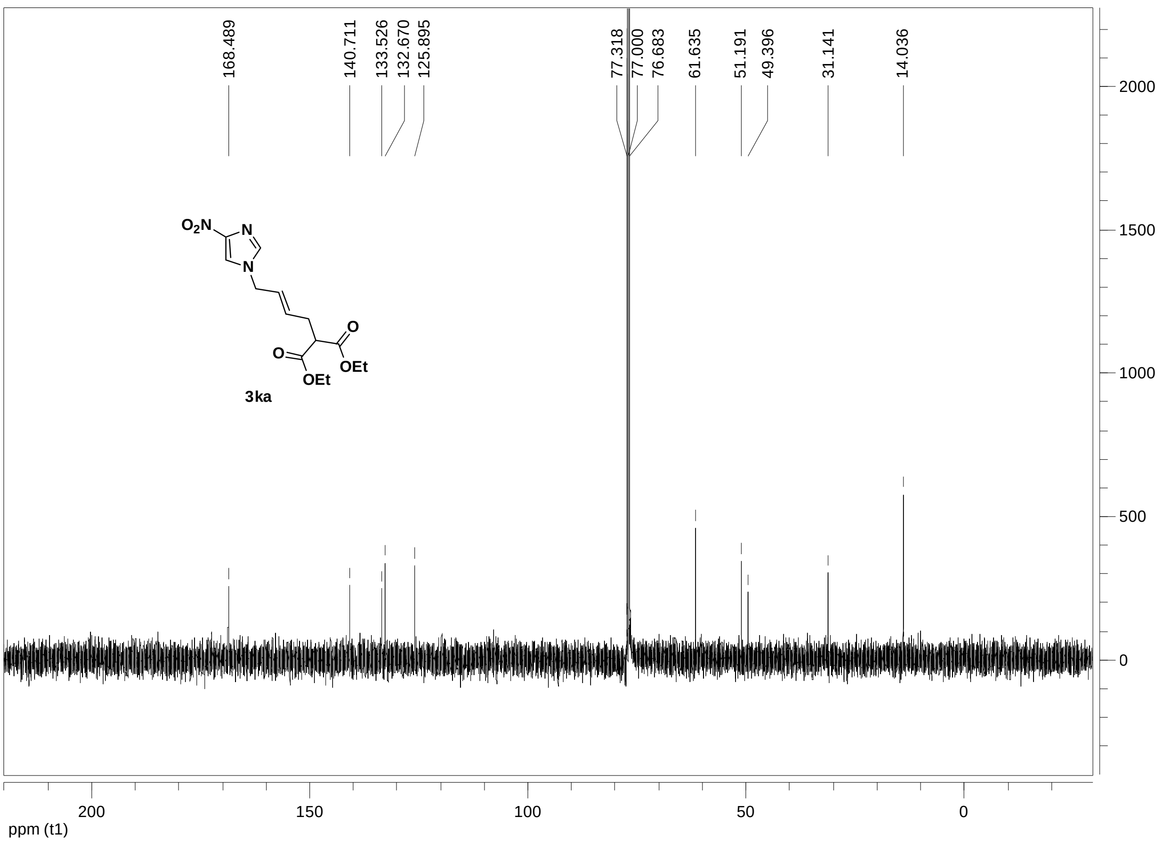
^{13}C-NMR for 3jb



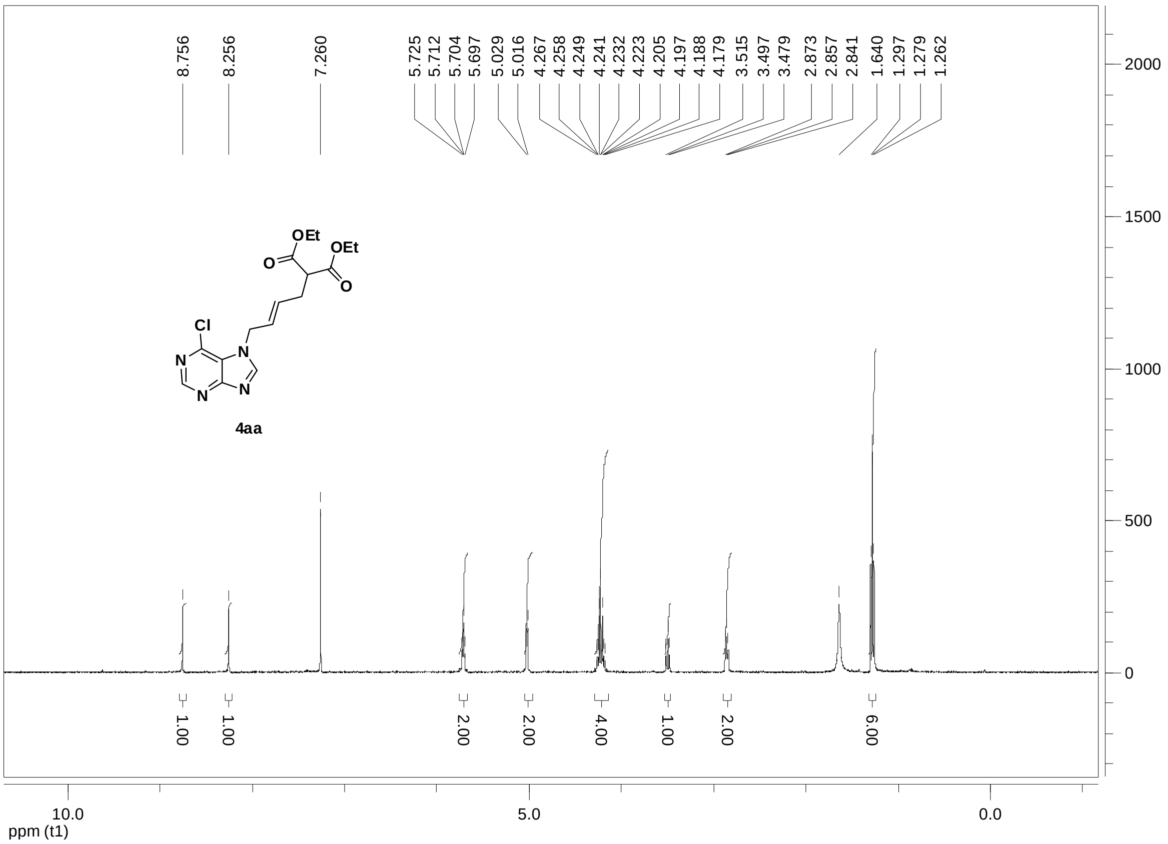
^{1}H-NMR for 3ka



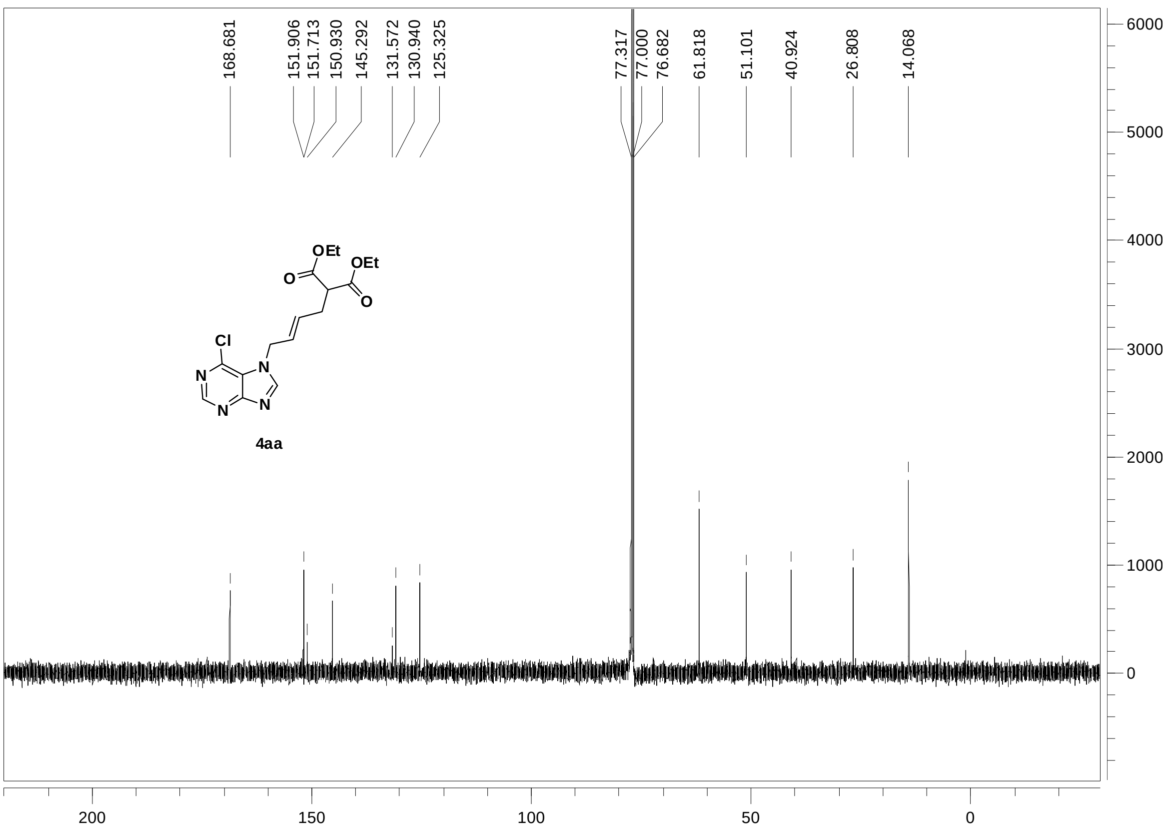
^{13}C-NMR for 3ka



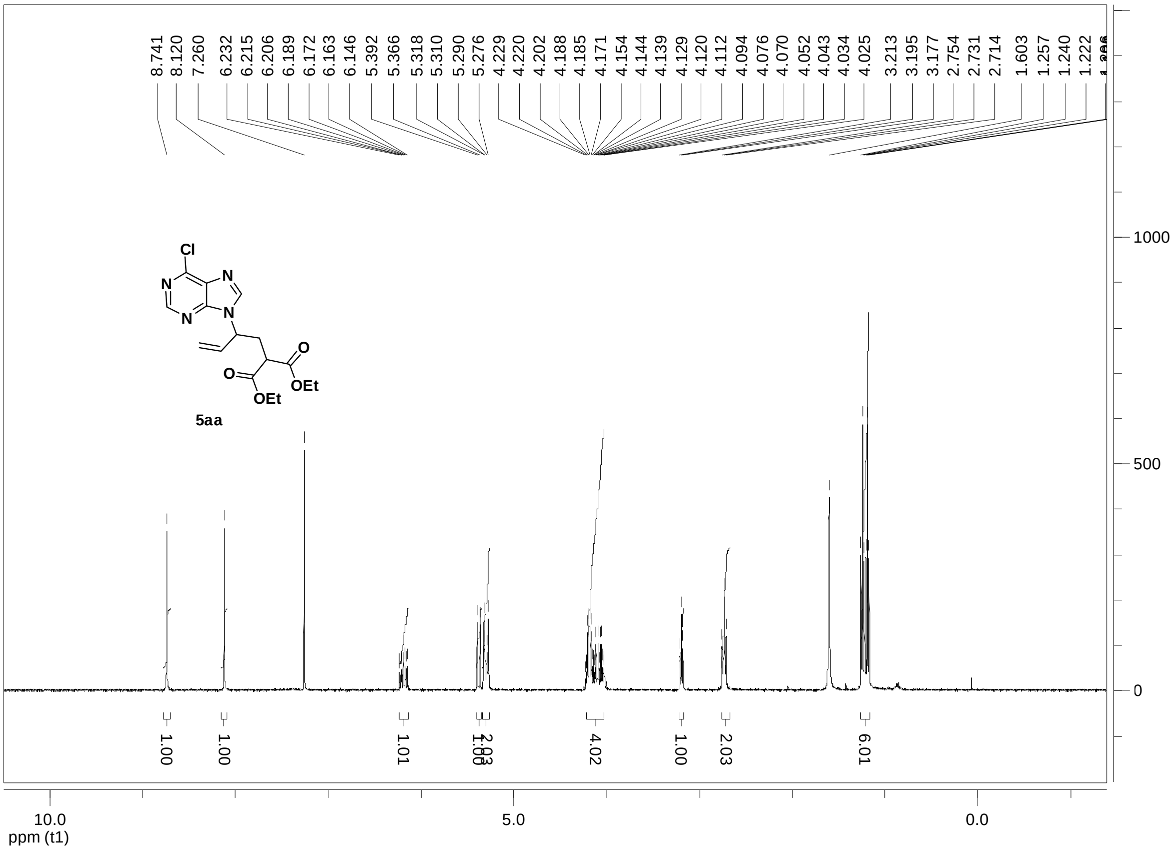
^{1}H-NMR for 4aa



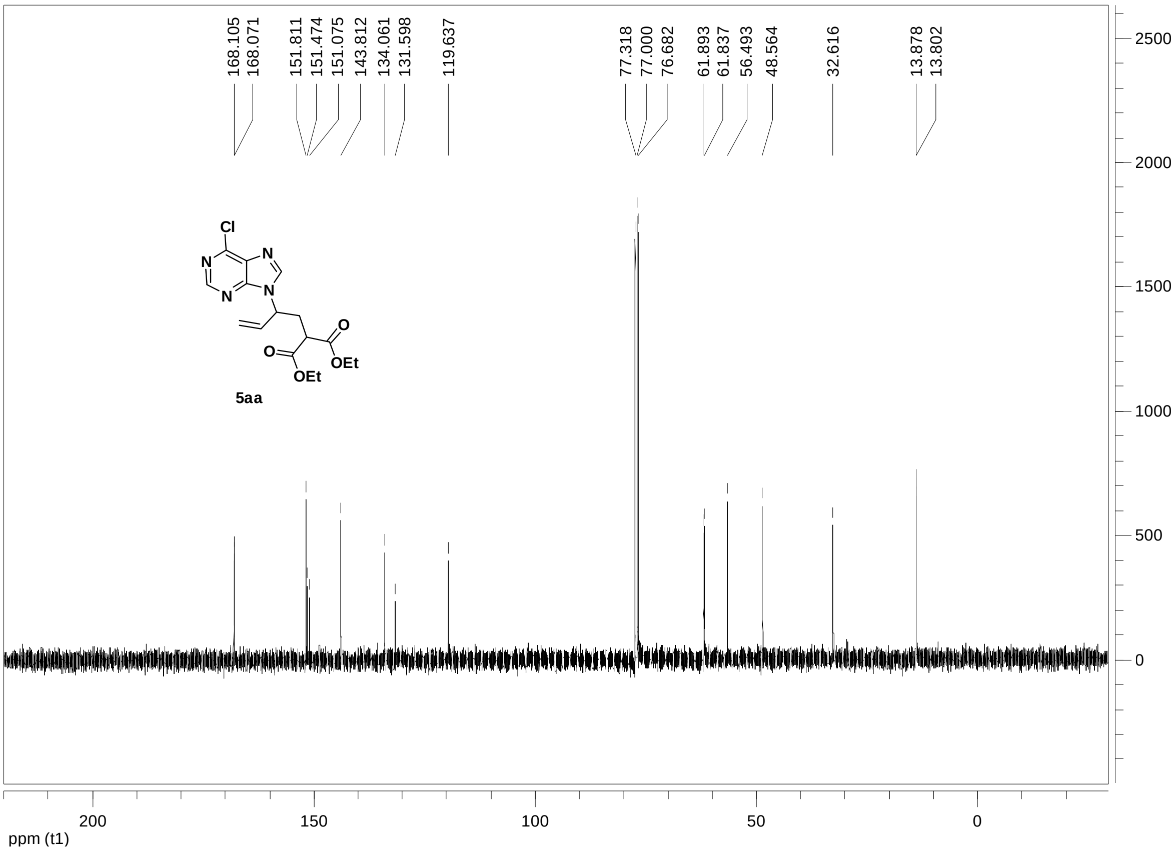
^{13}C-NMR for 4aa



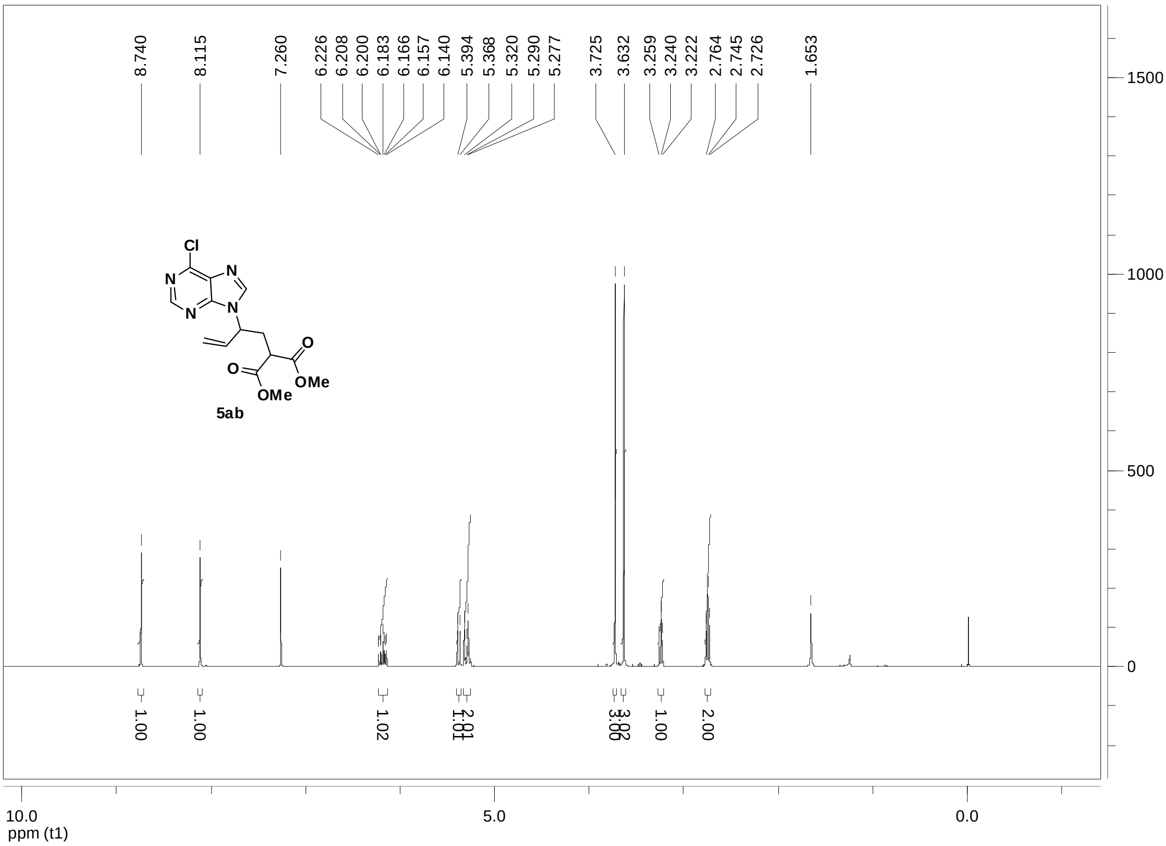
^{1}H-NMR for 5aa



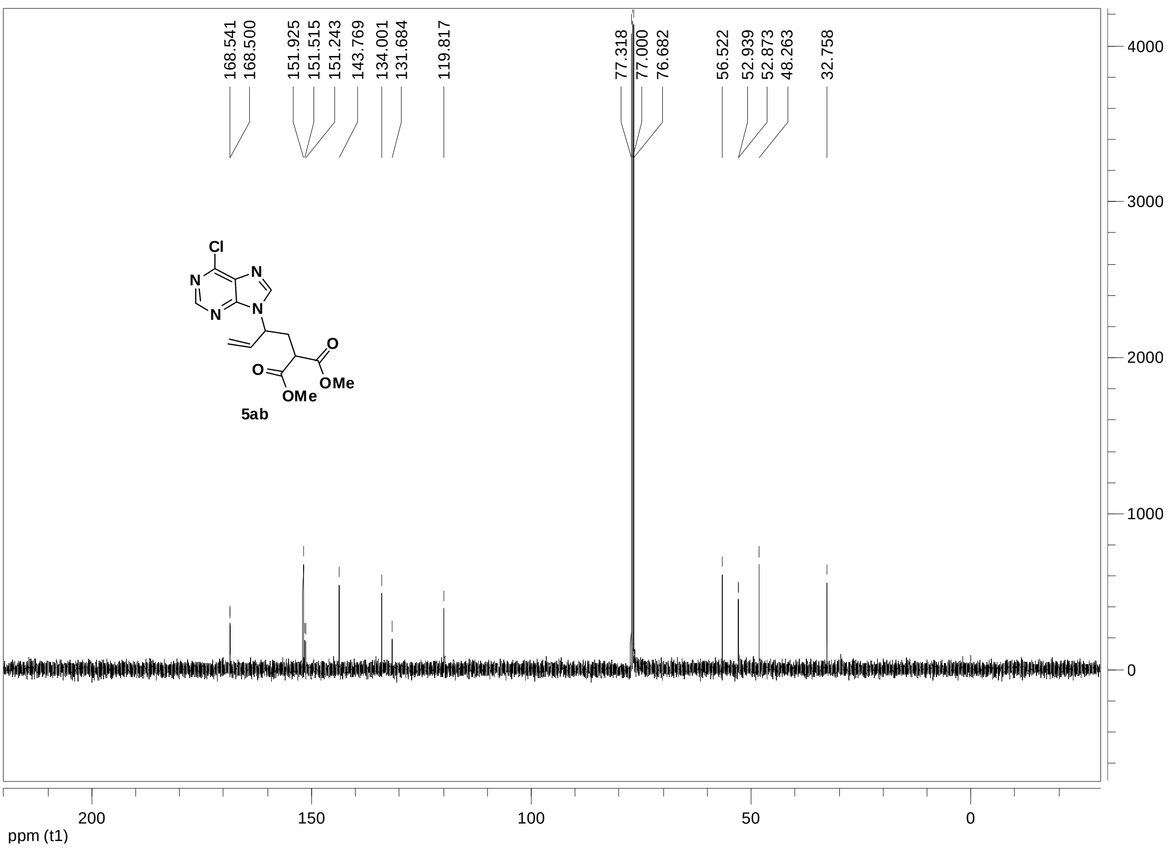
^{13}C-NMR for 5aa



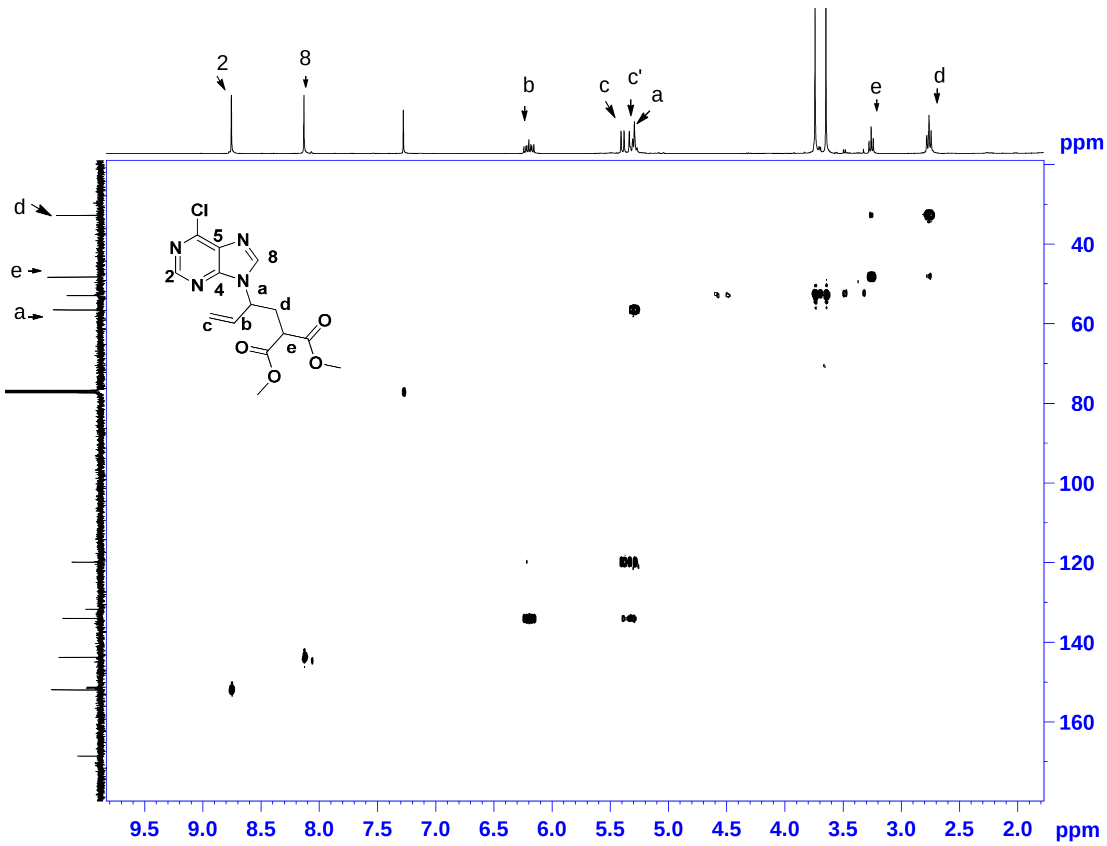
[1]H-NMR for 5ab



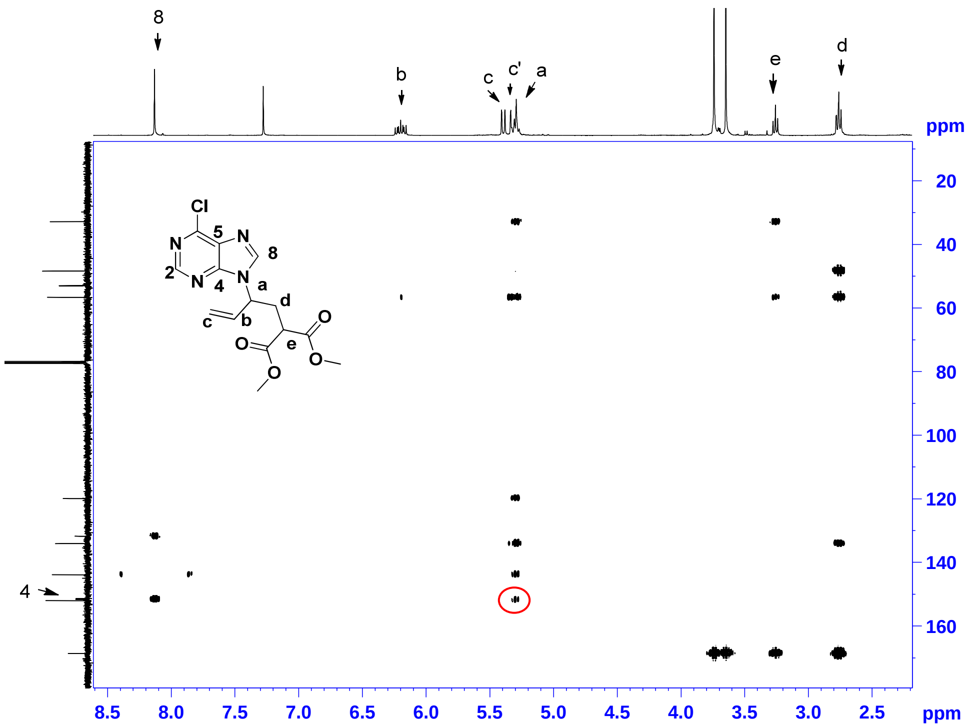
[13]C-NMR for 5ab



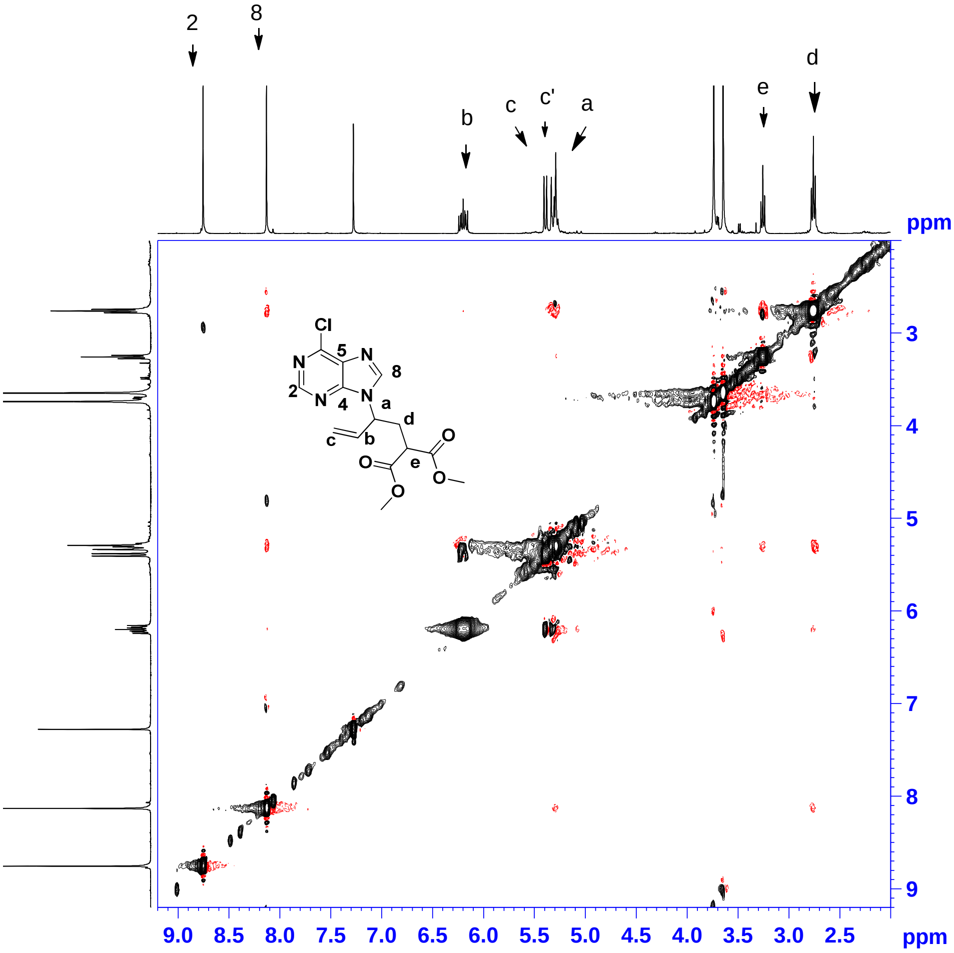
HSQC for 5ab



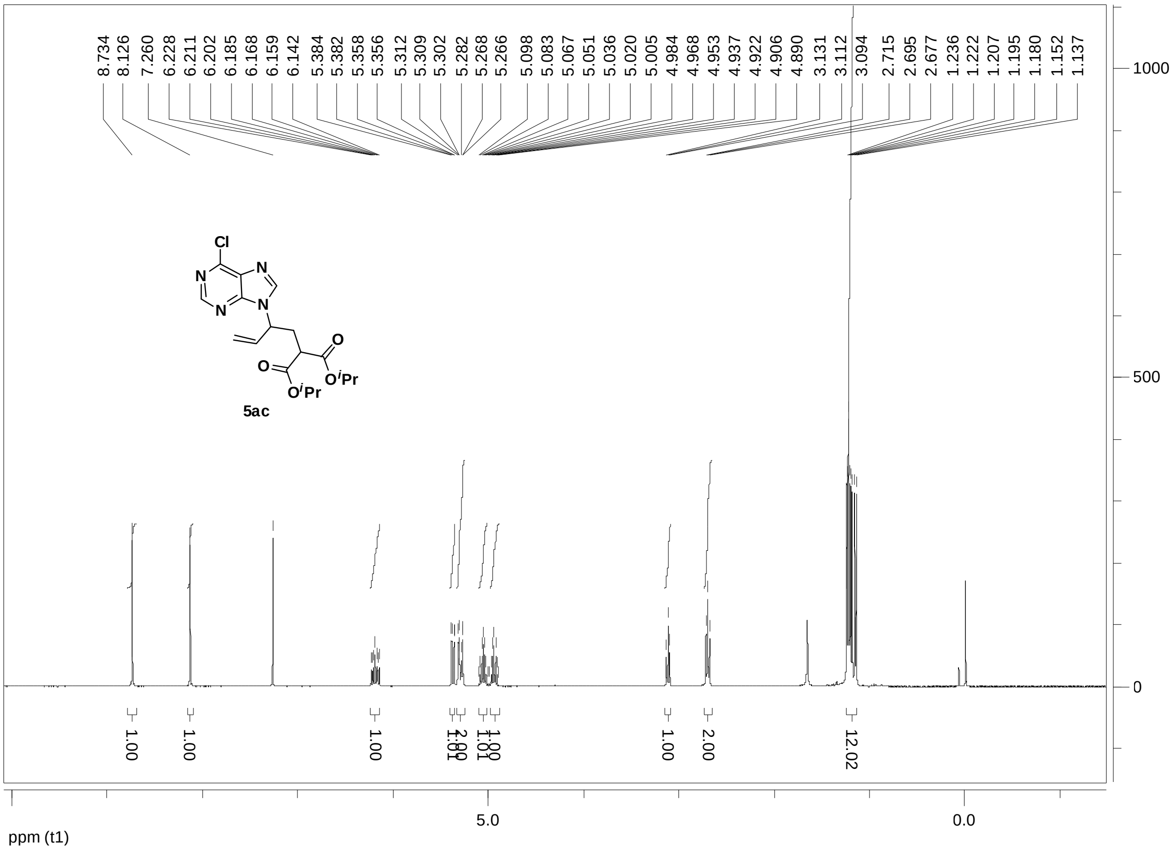
HMBC for 5ab



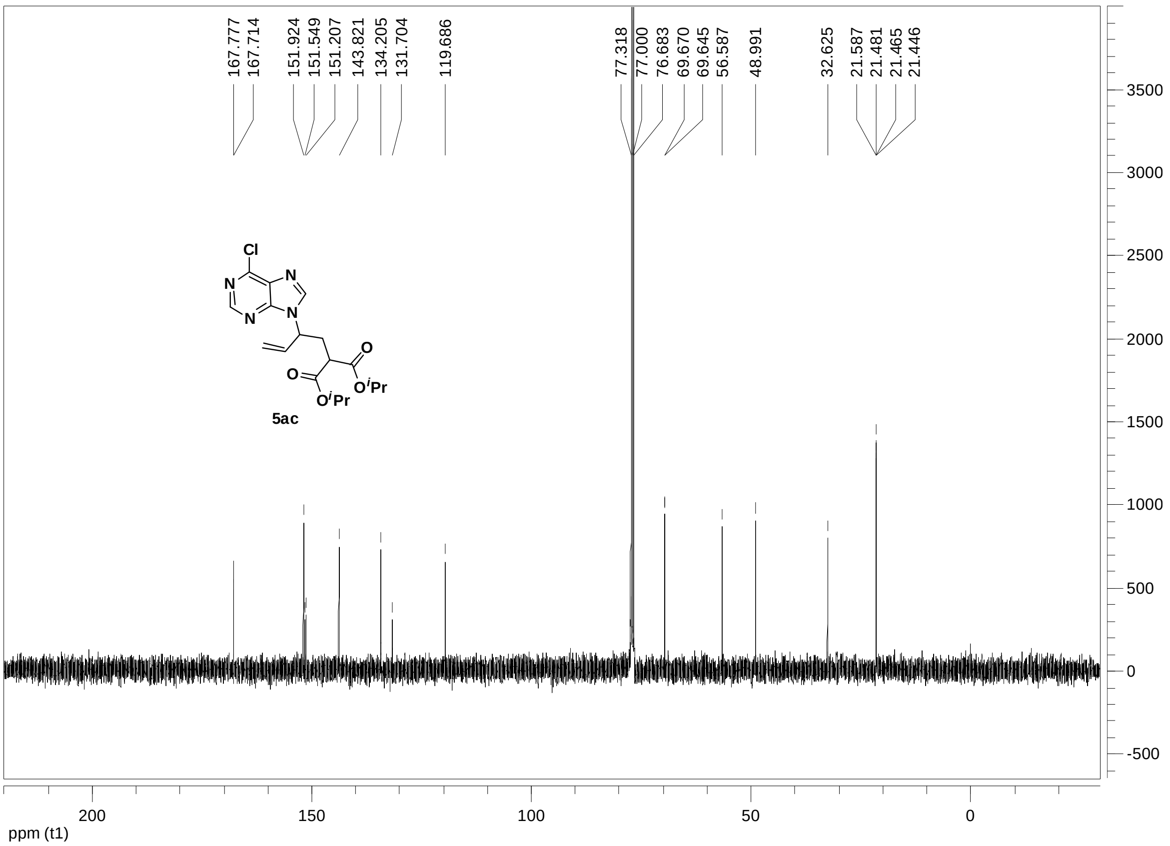
Noesy for 5ab



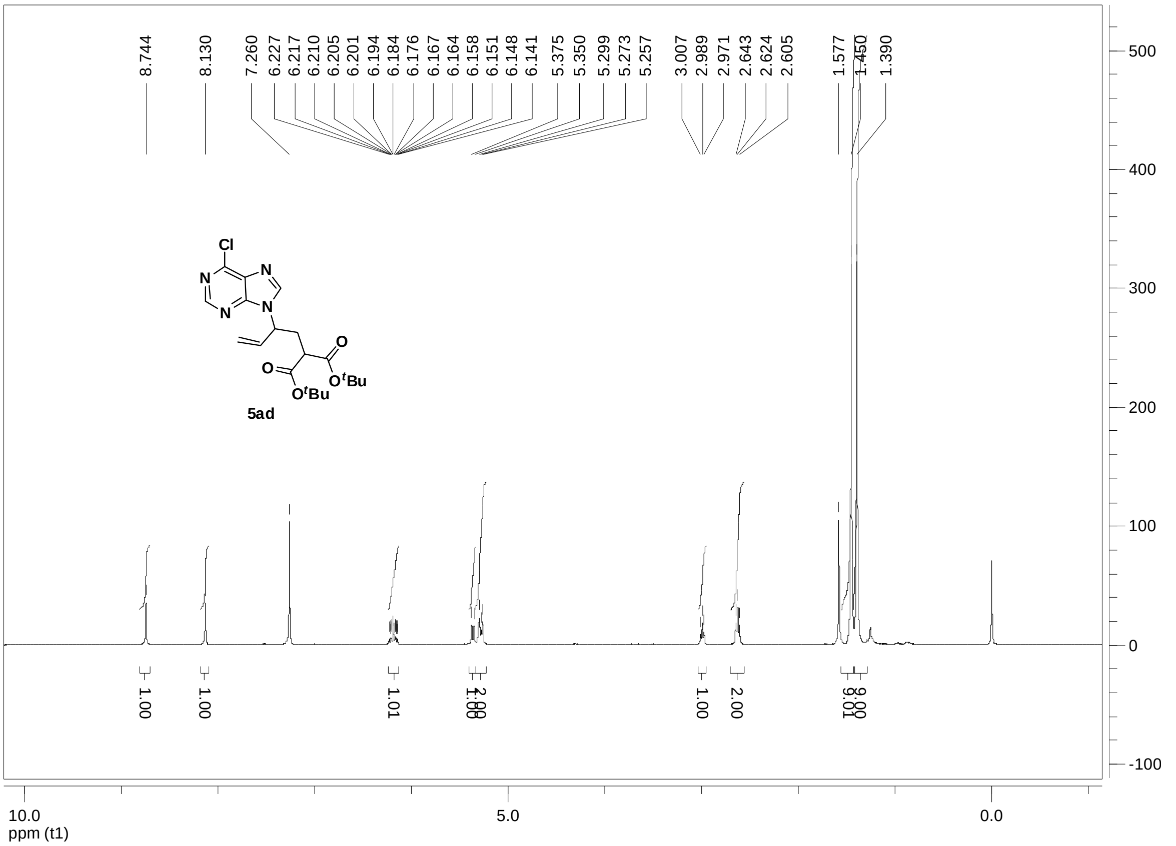
[1]H-NMR for 5ac



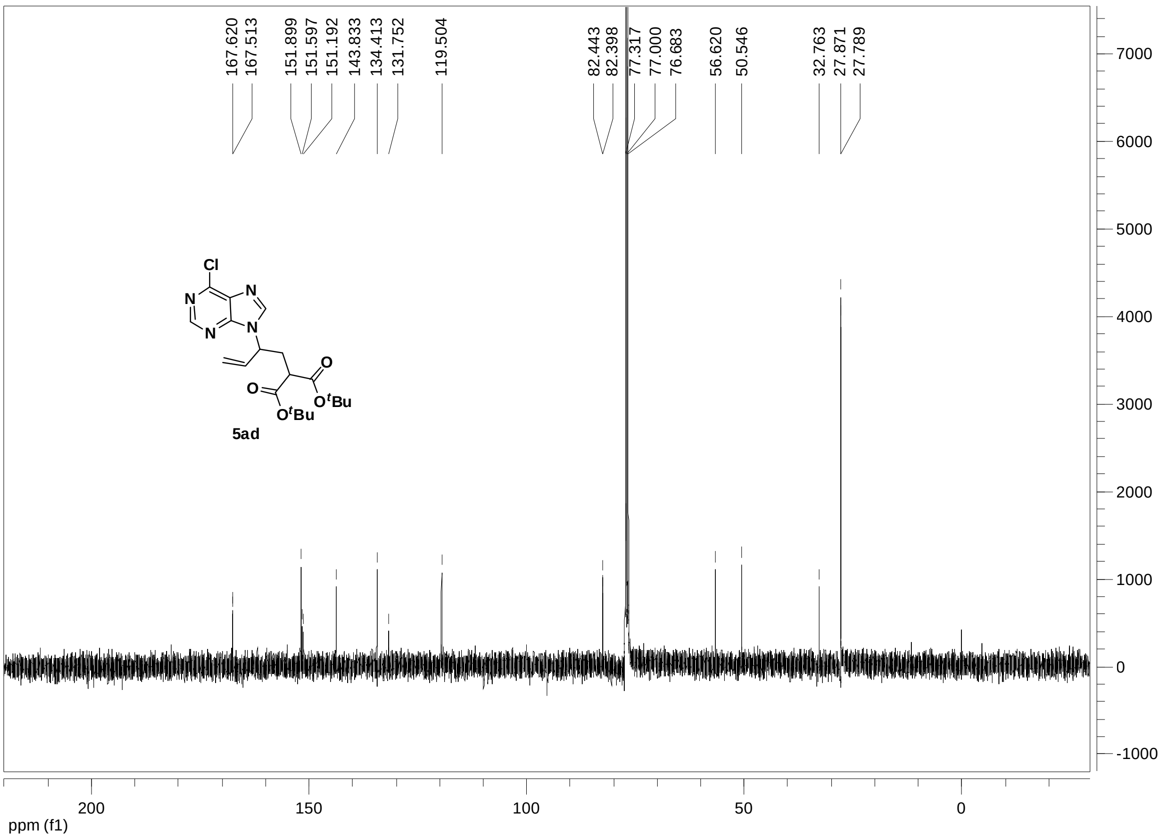
[13]C-NMR for 5ac



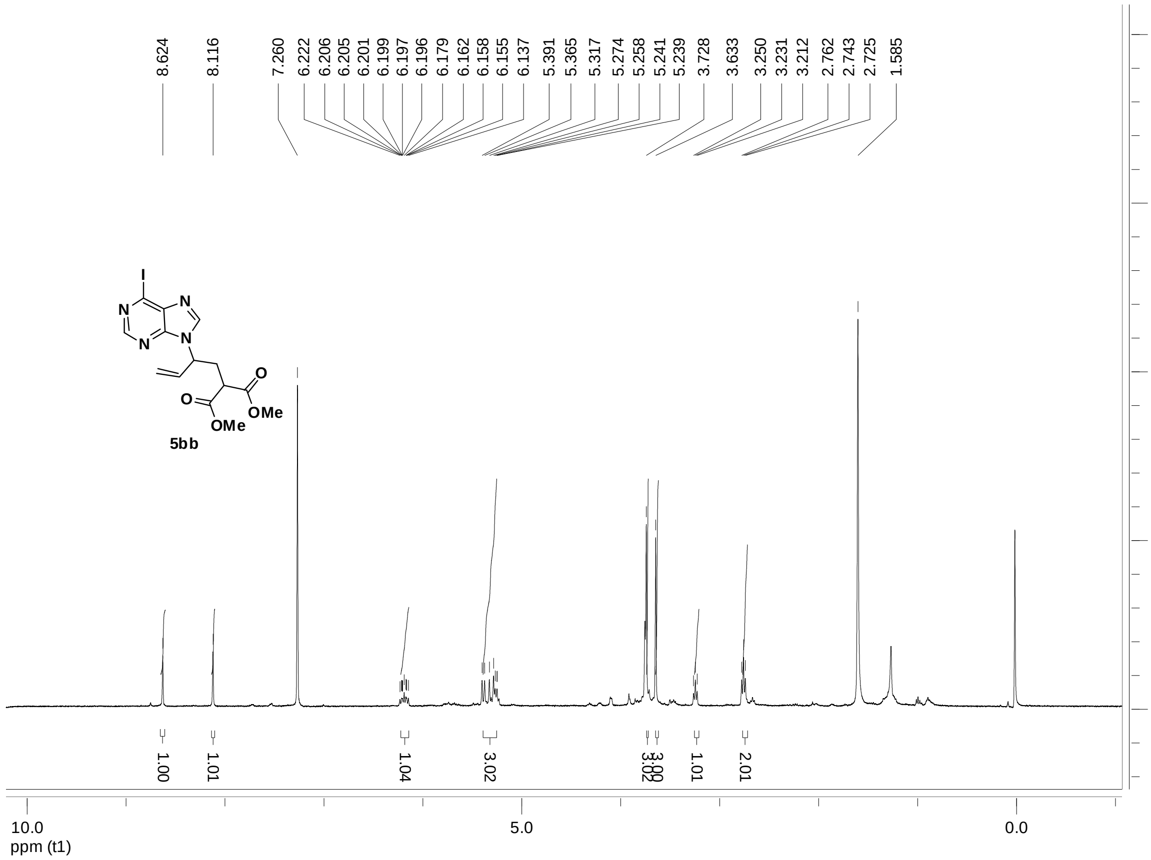
^{1}H-NMR for 5ad



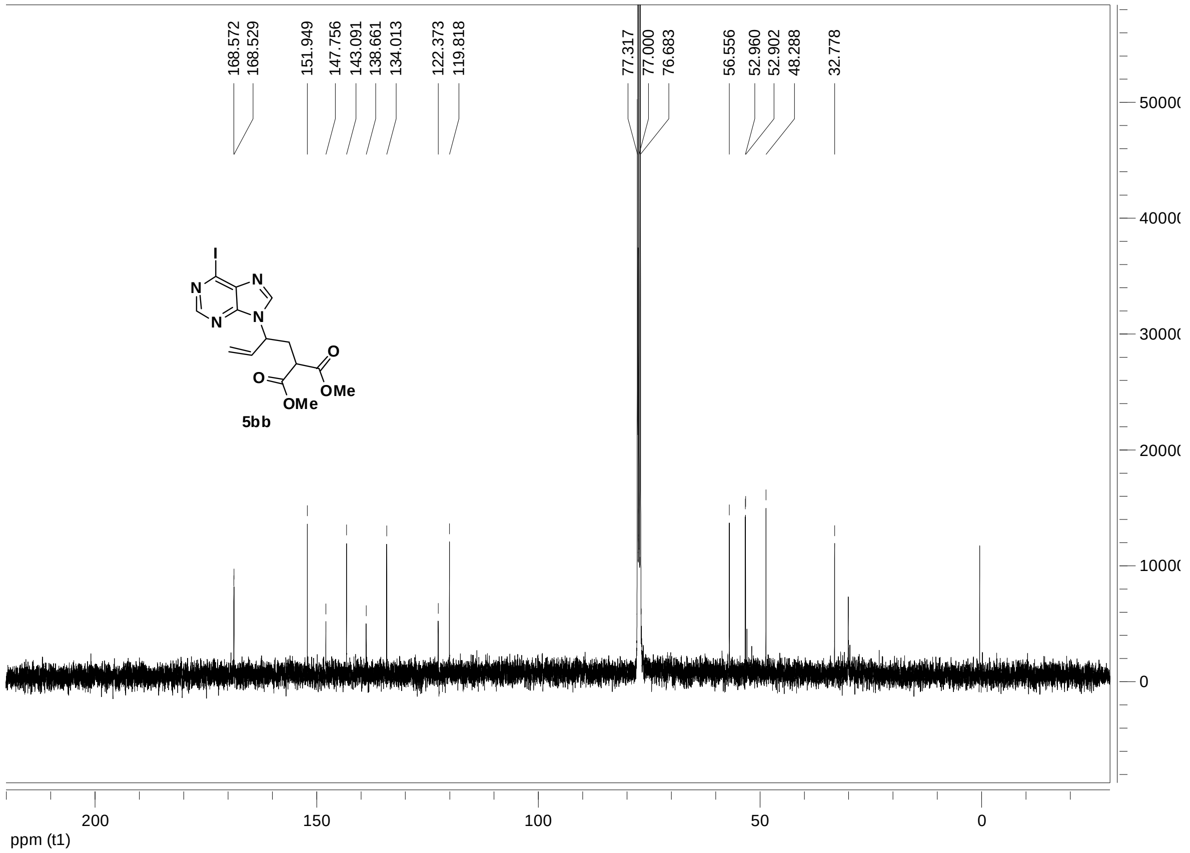
^{13}C-NMR for 5ad



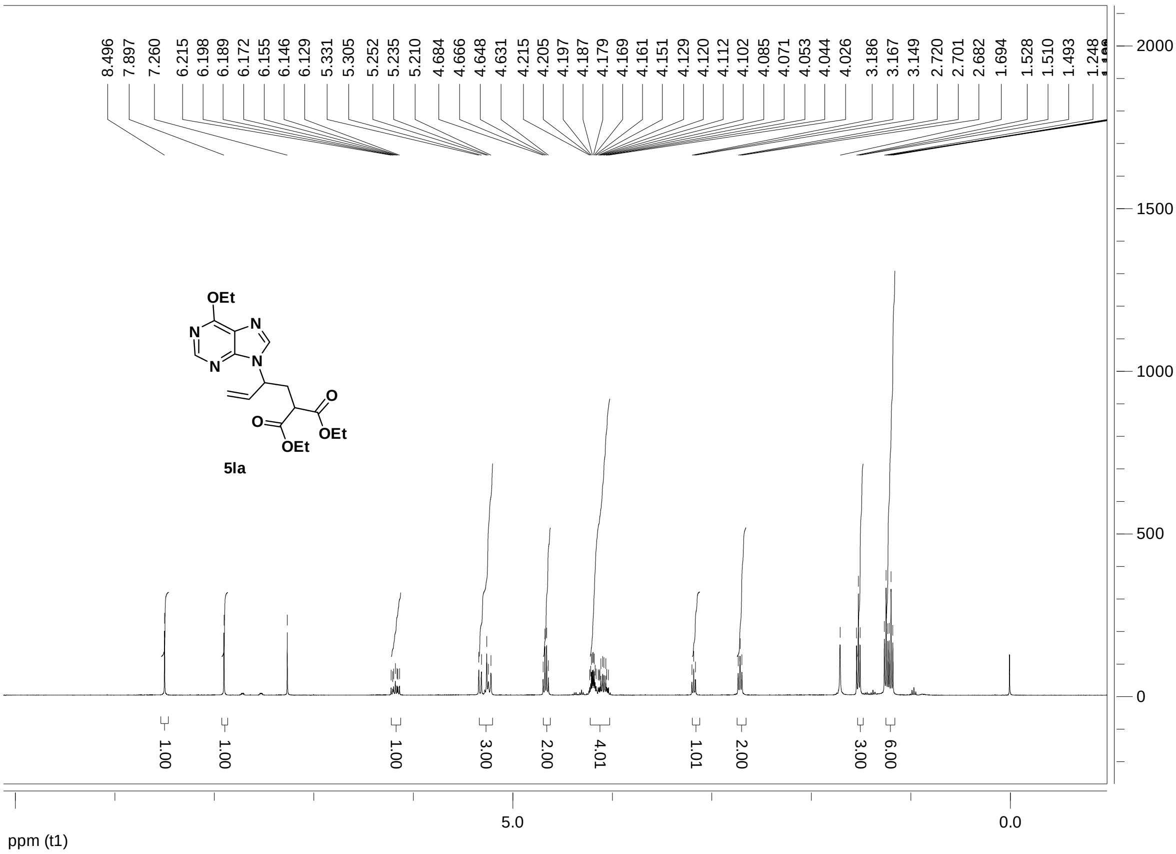
^{1}H-NMR for 5bb



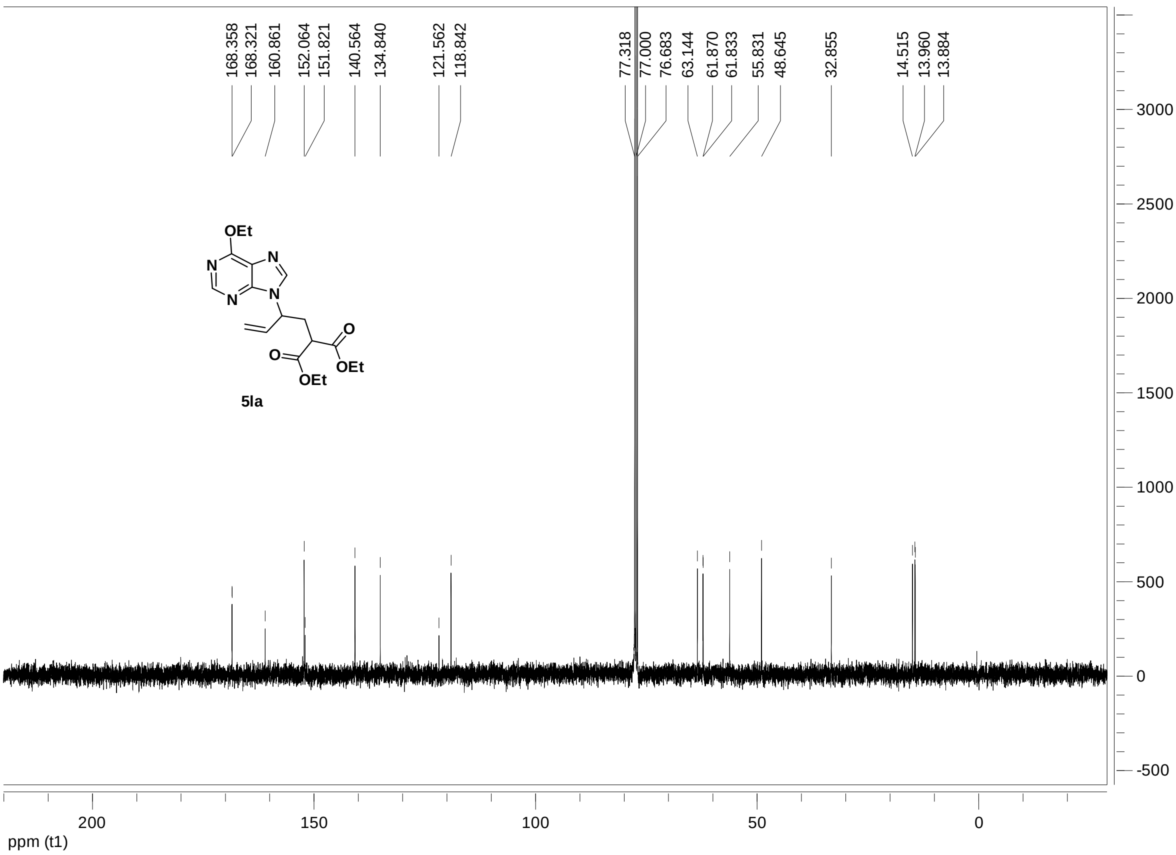
^{13}C-NMR for 5bb



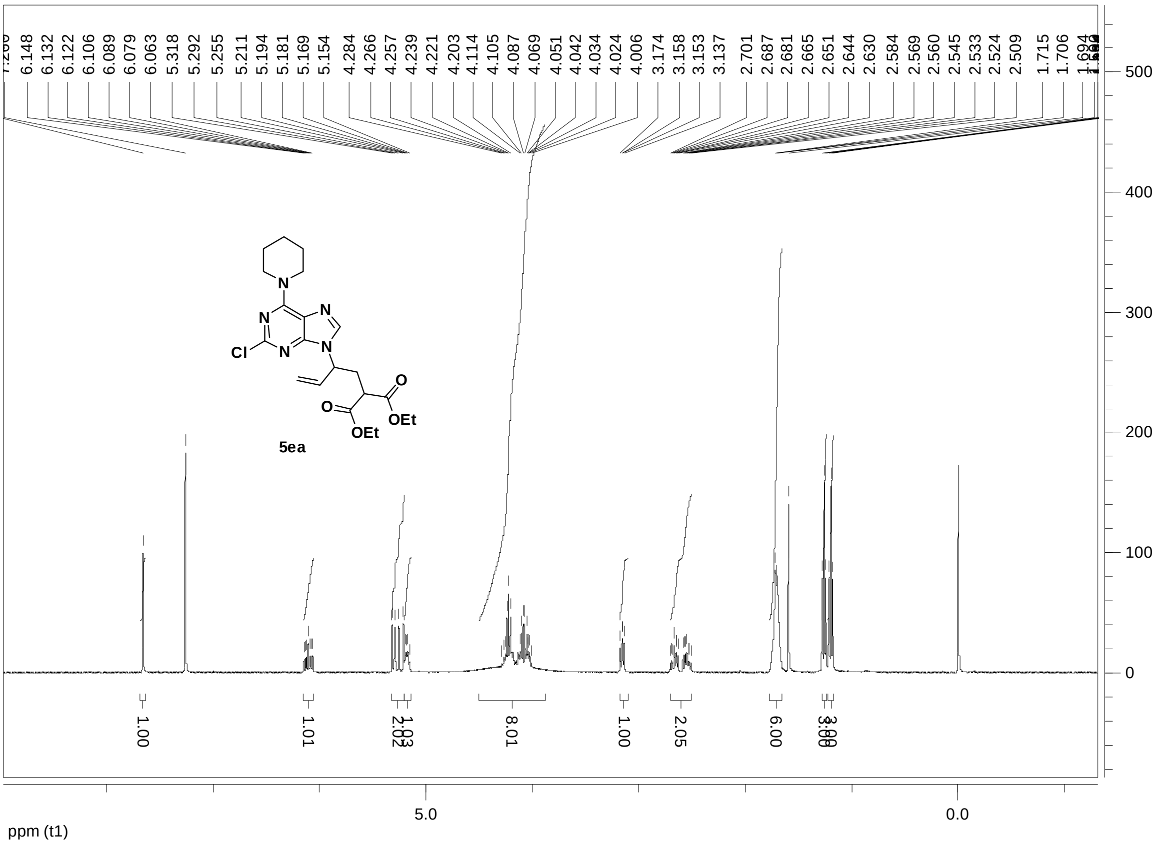
^{1}H-NMR for 5la



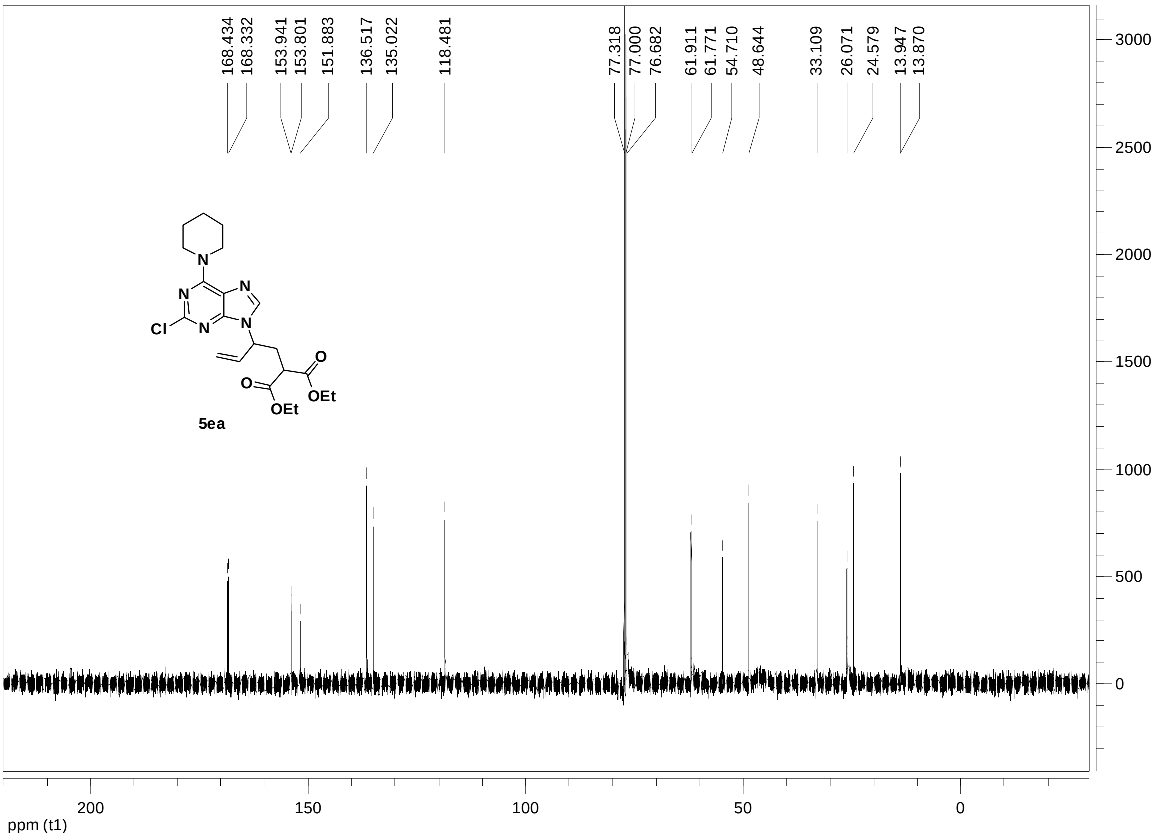
^{13}C-NMR for 5la



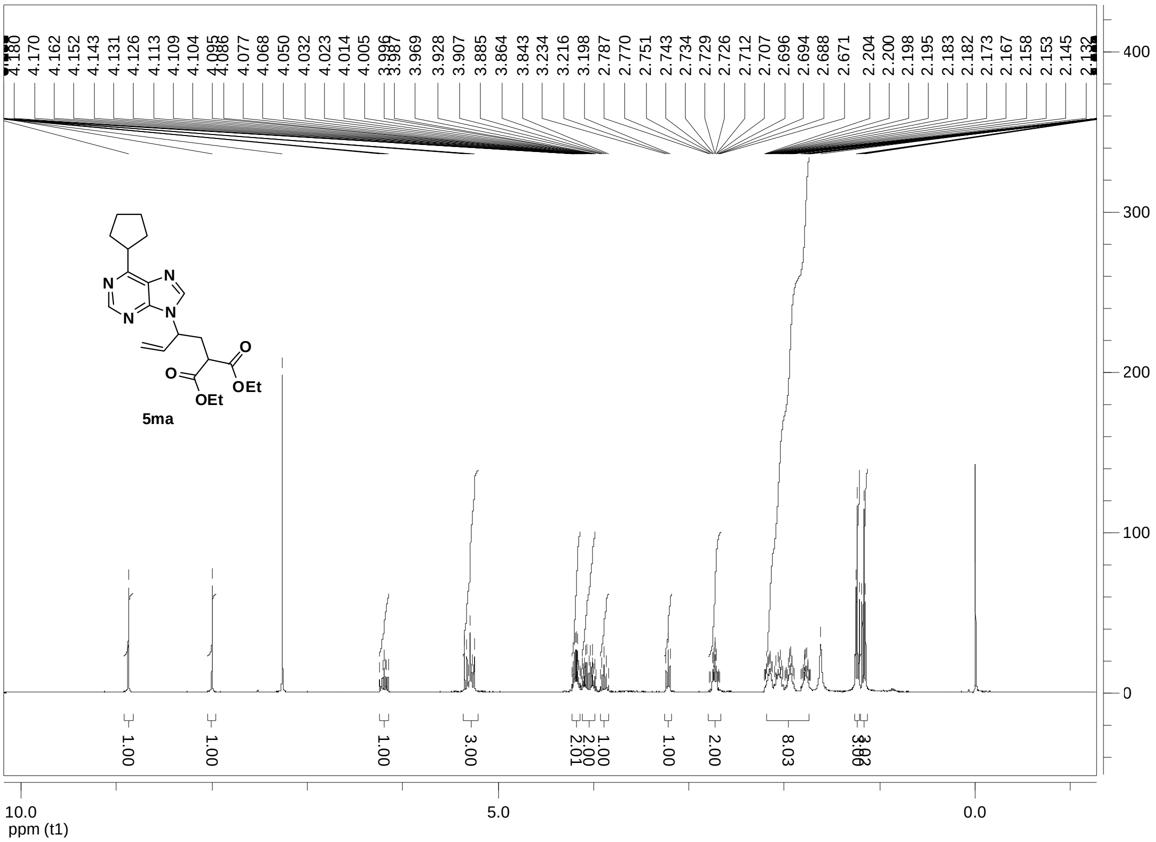
[1]H-NMR for 5ea



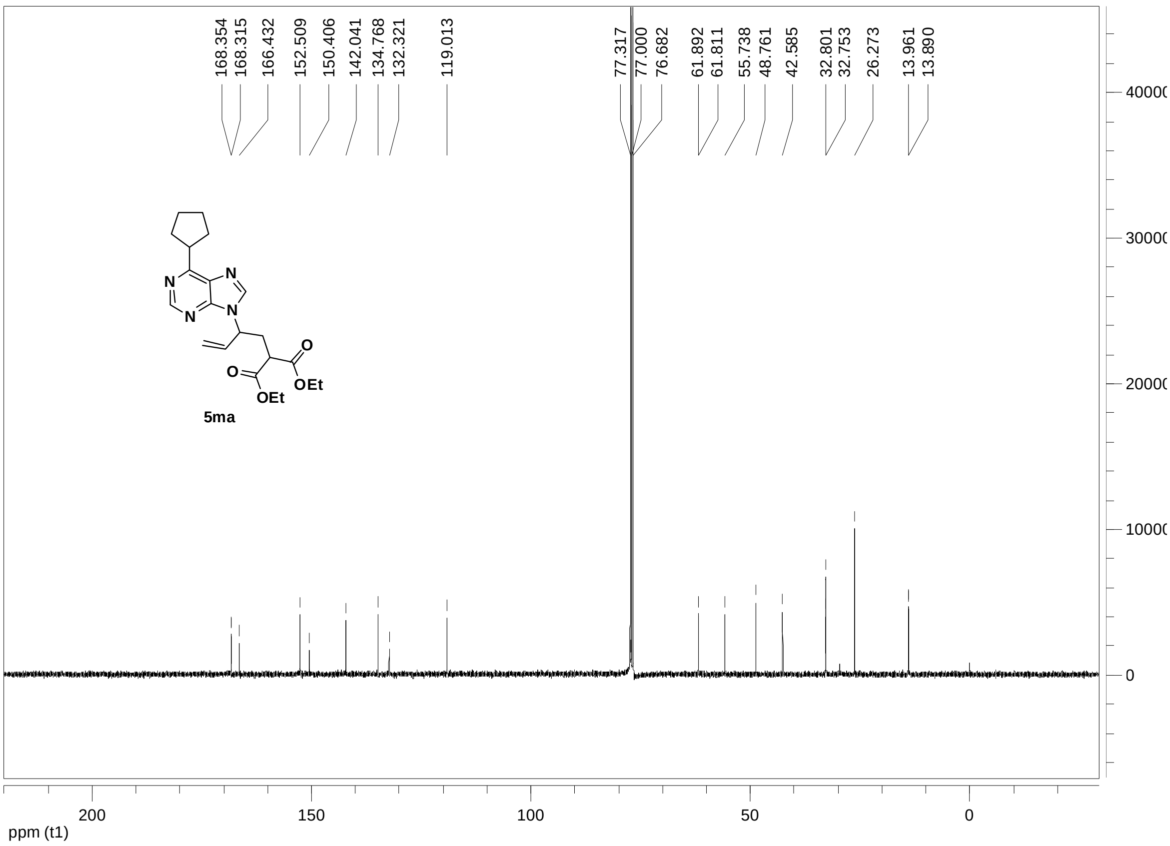
[13]C-NMR for 5ea



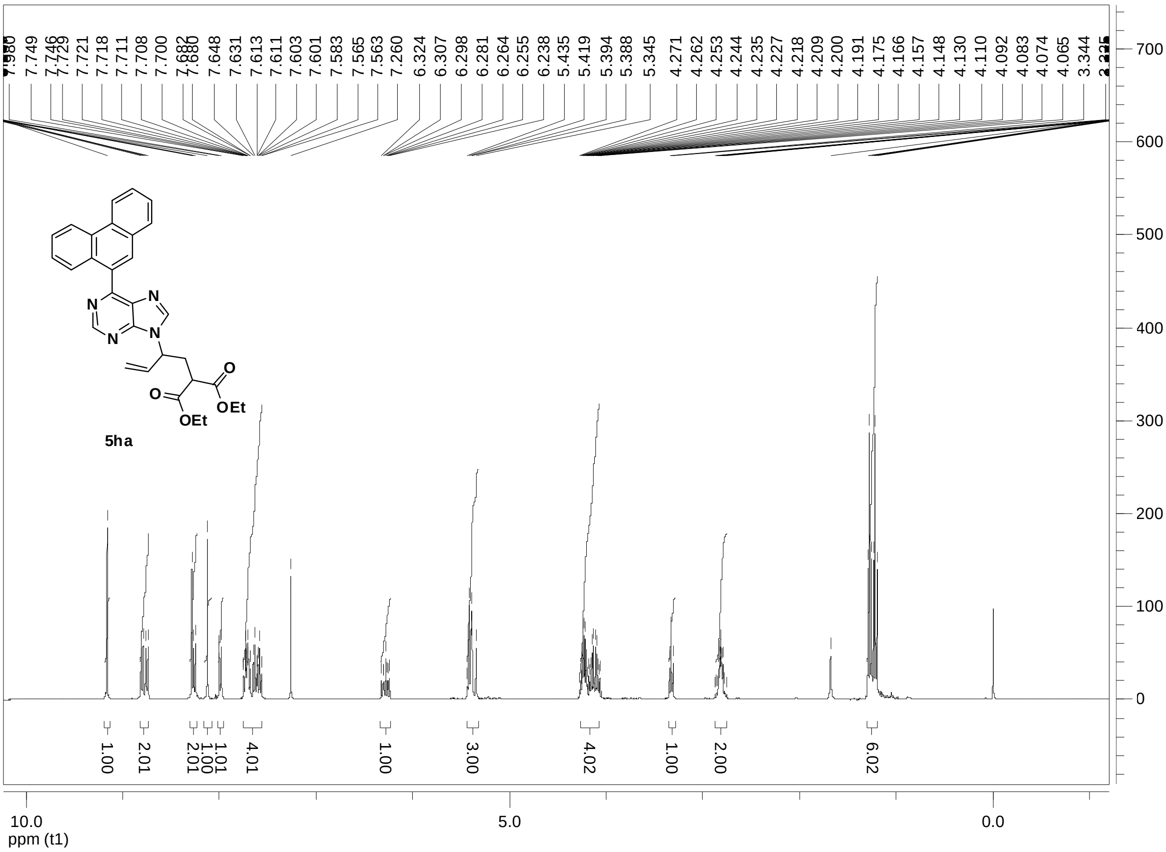
[1]H-NMR for 5ma



[13]C-NMR for 5ma

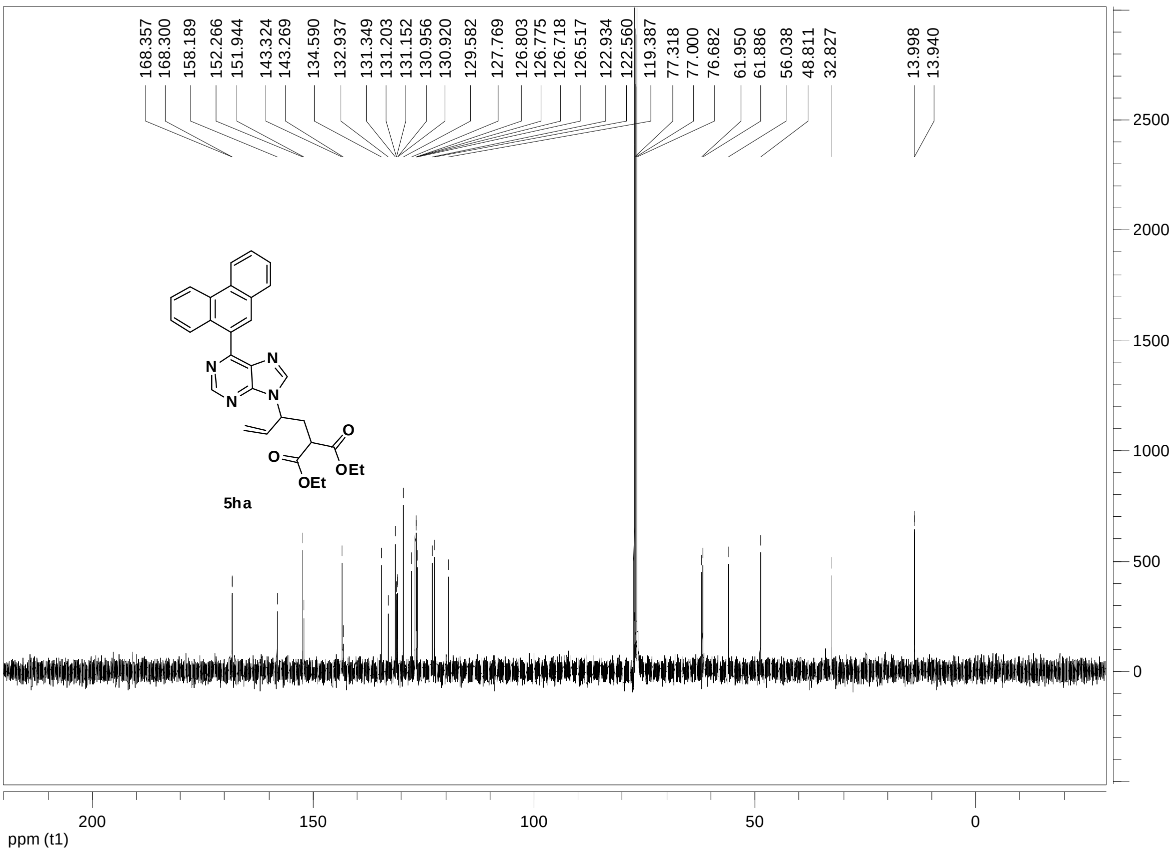


[1]H-NMR for 5ha



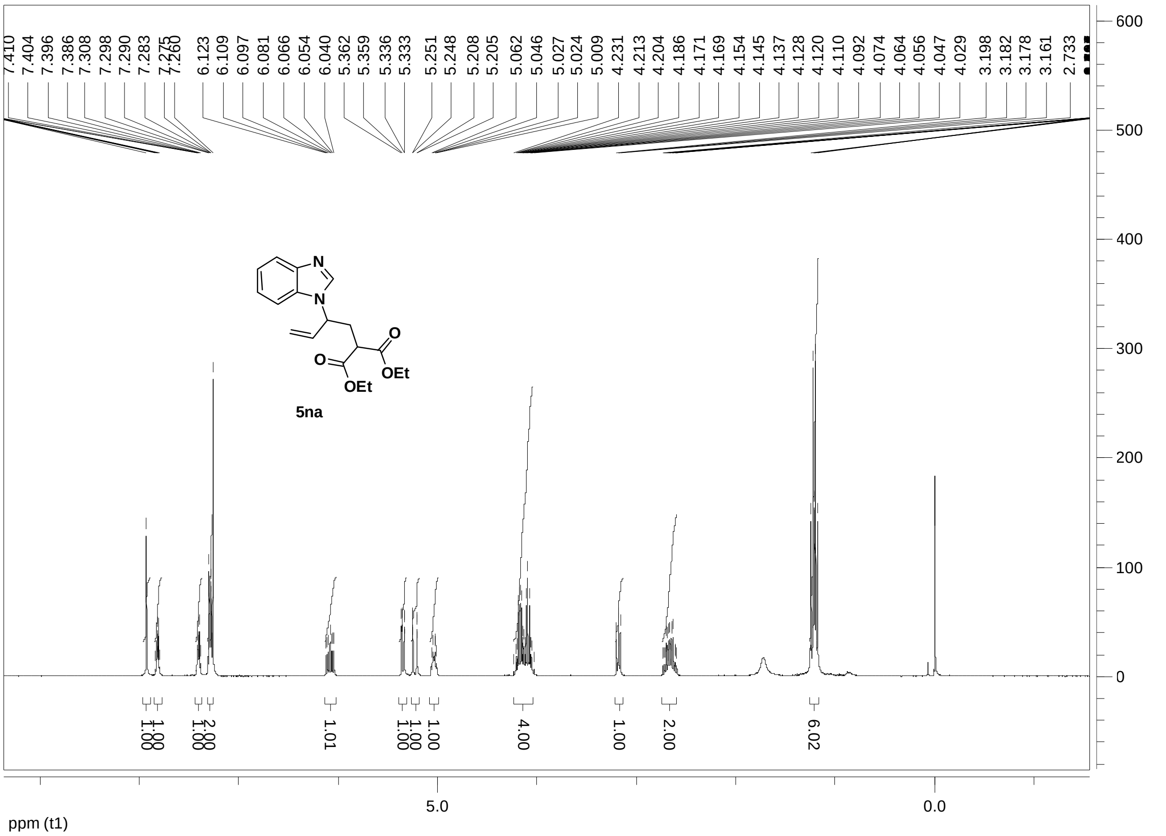
5ha

[13]C-NMR for 5ha

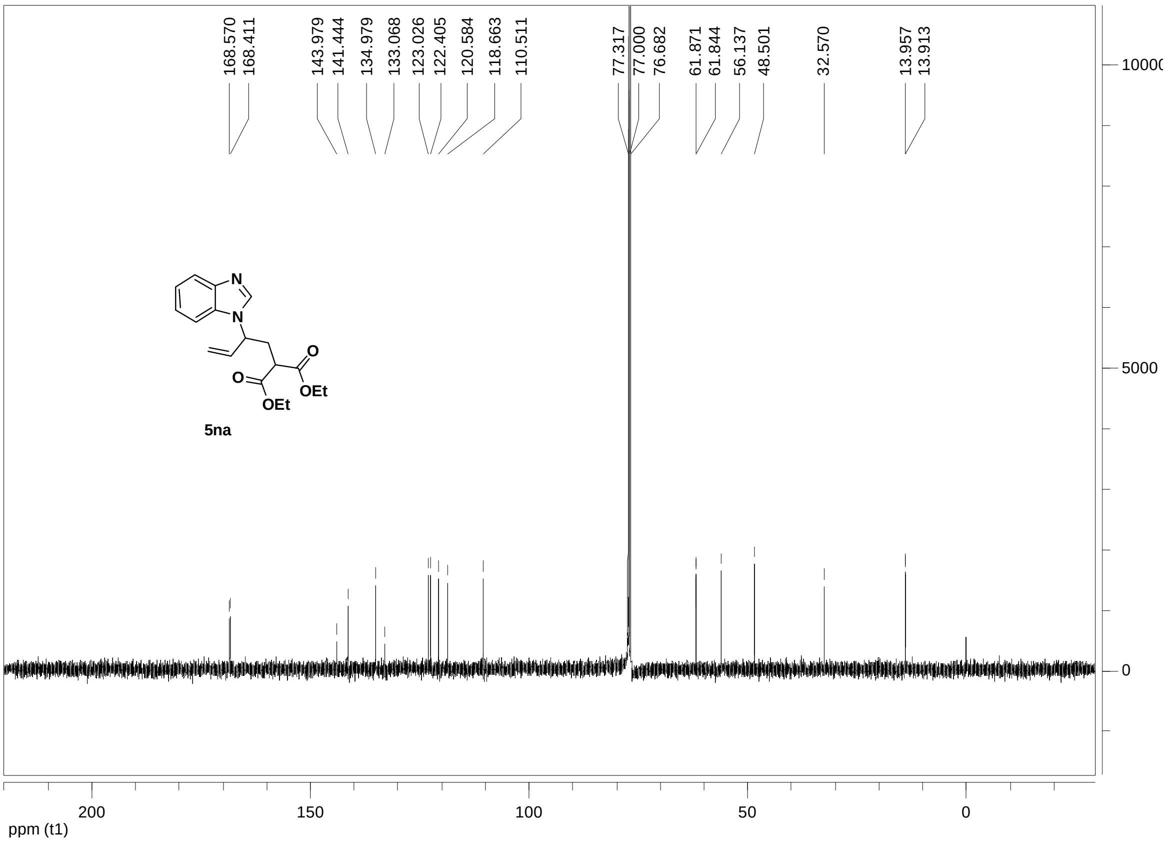


5ha

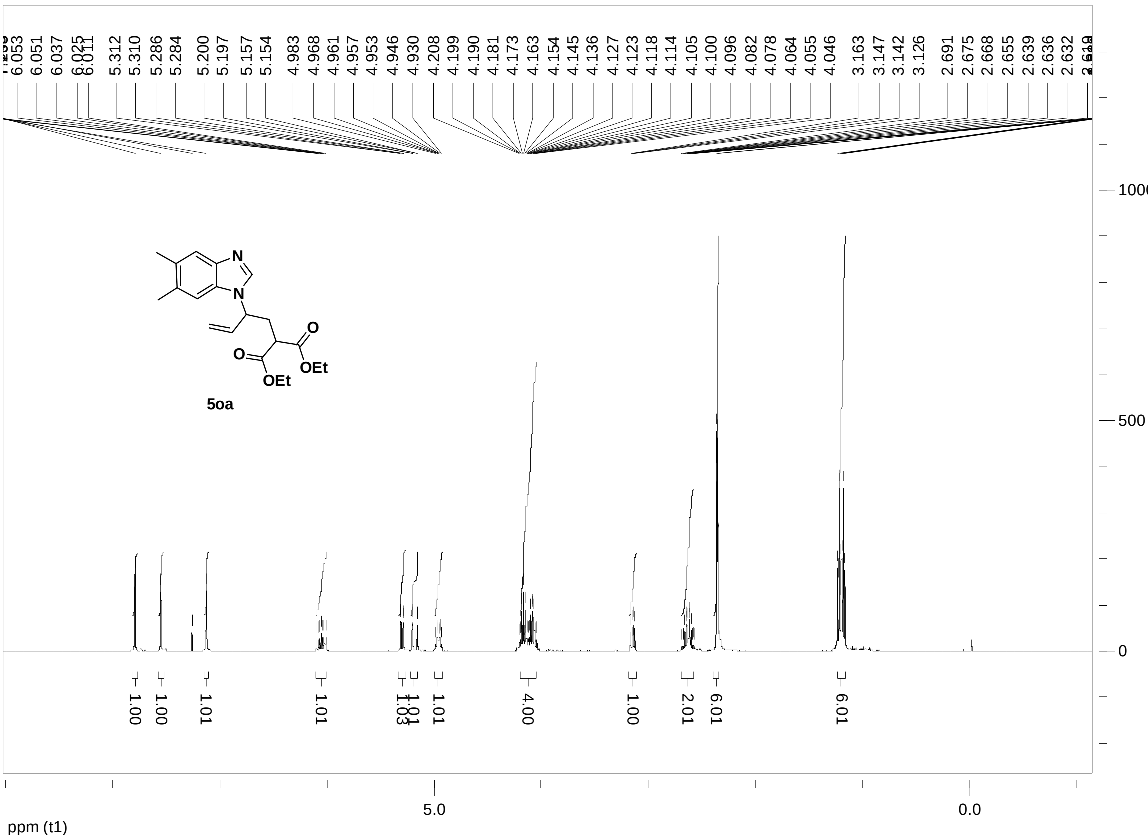
^{1}H-NMR for 5na



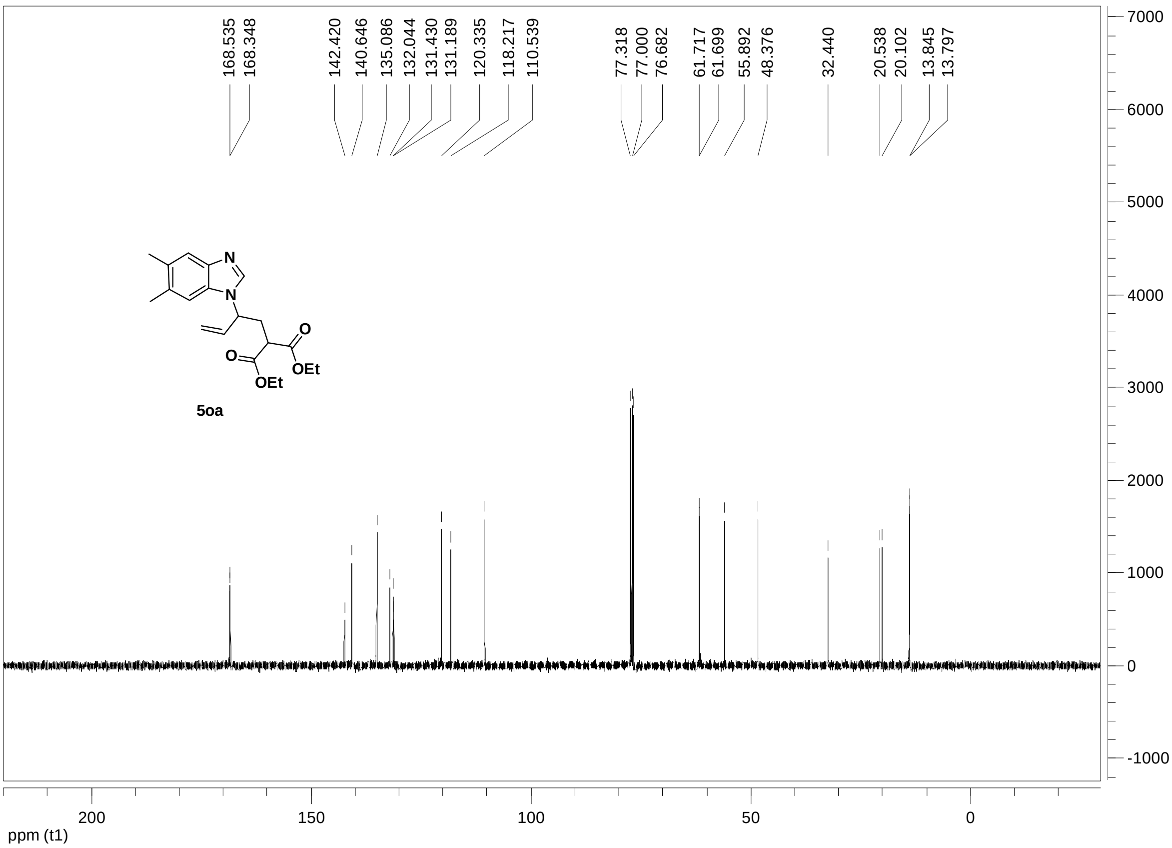
^{13}C-NMR for 5na



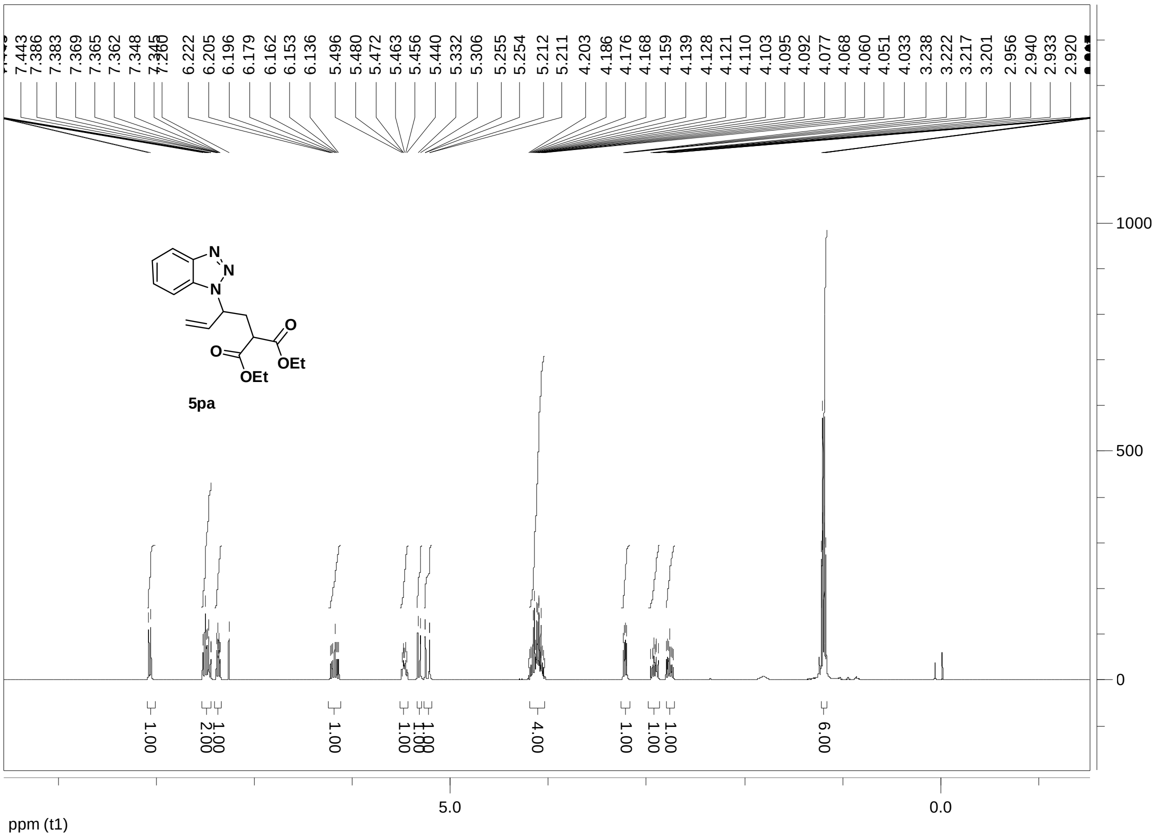
[1]H-NMR for 5oa



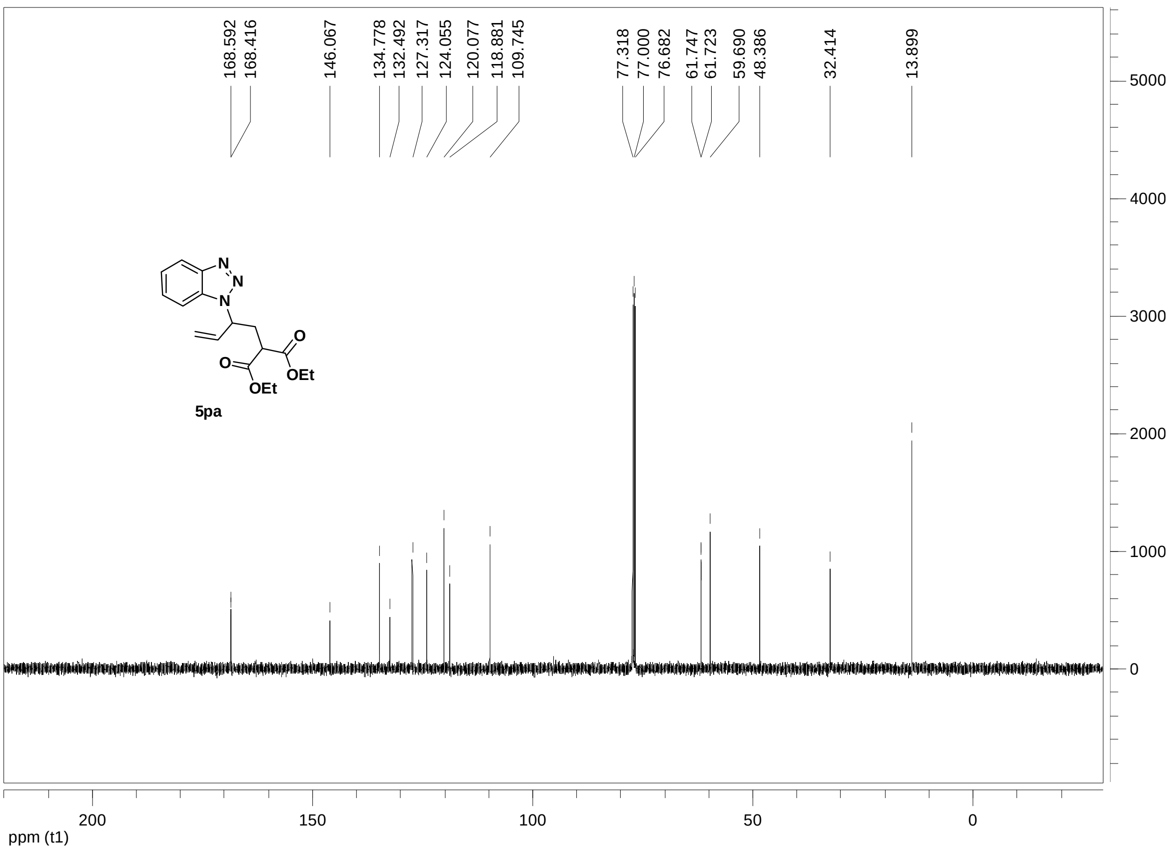
[13]C-NMR for 5oa



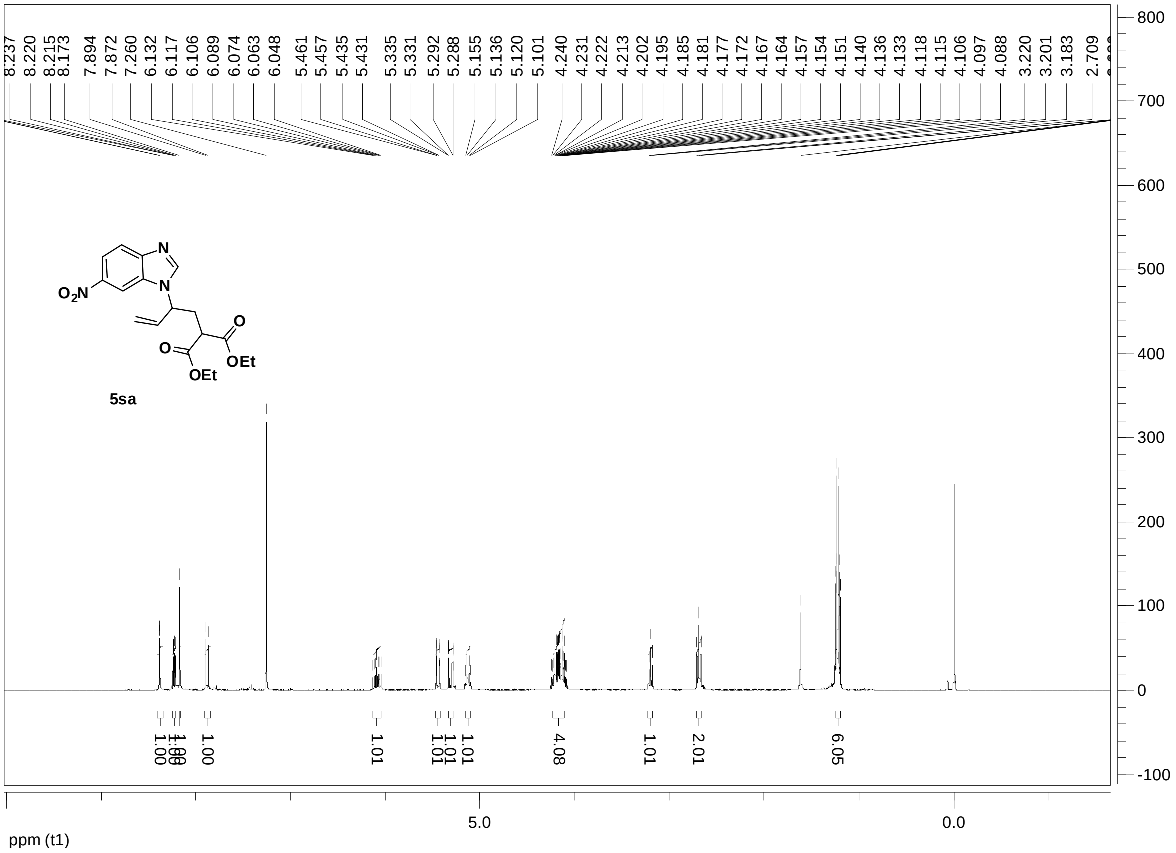
^{1}H-NMR for 5pa



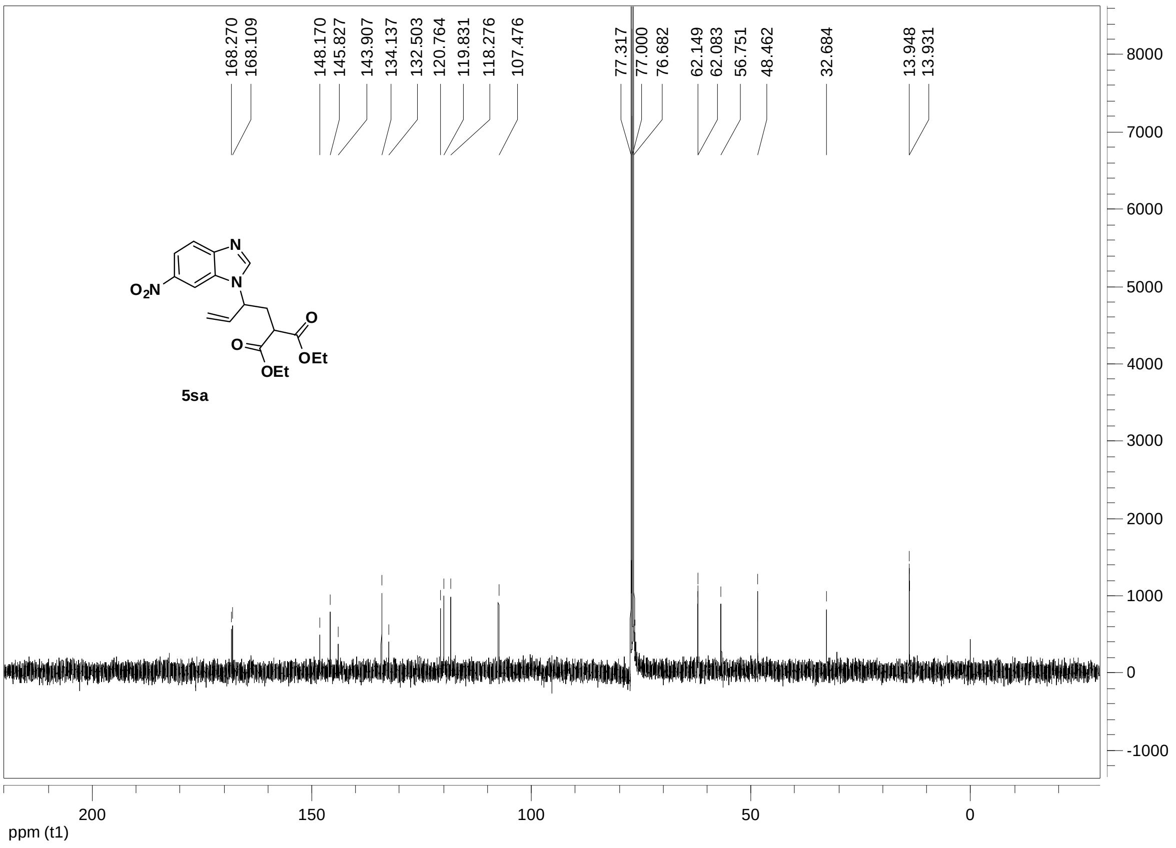
^{13}C-NMR for 5pa



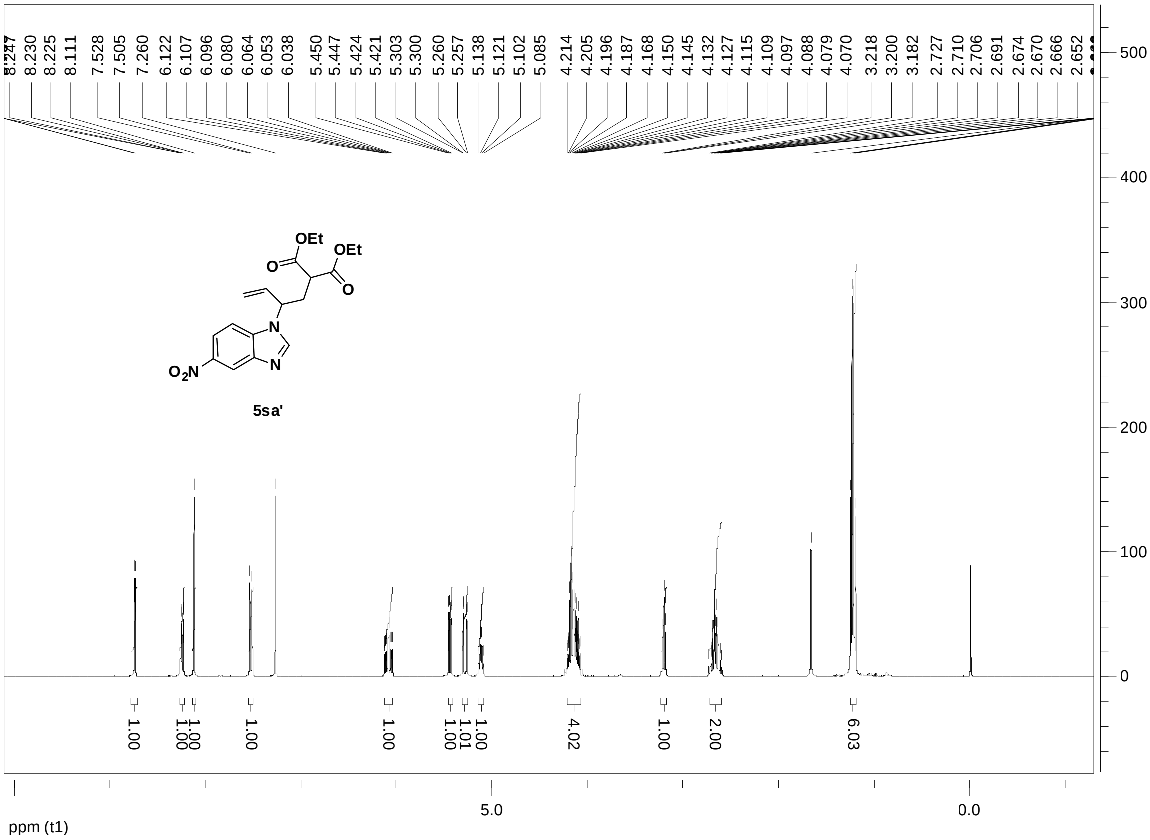
^{1}H-NMR for 5sa



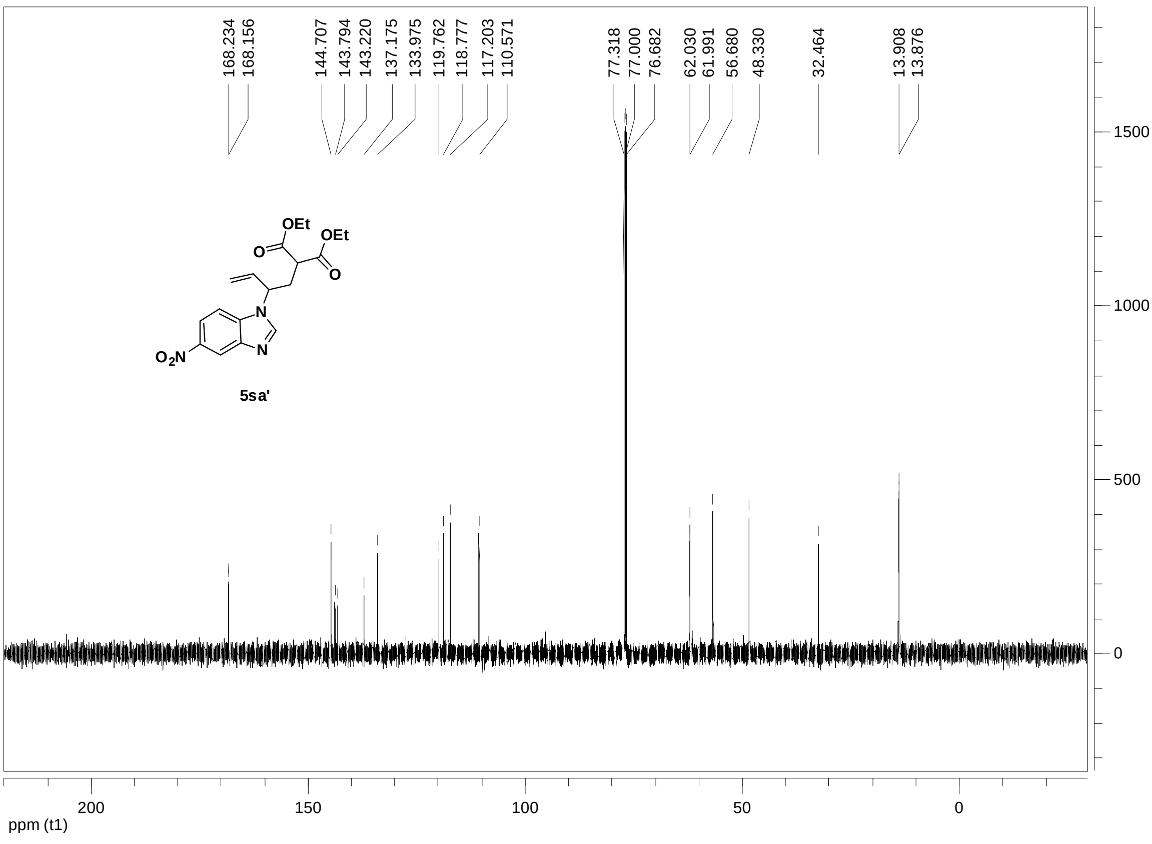
^{13}C-NMR for 5sa



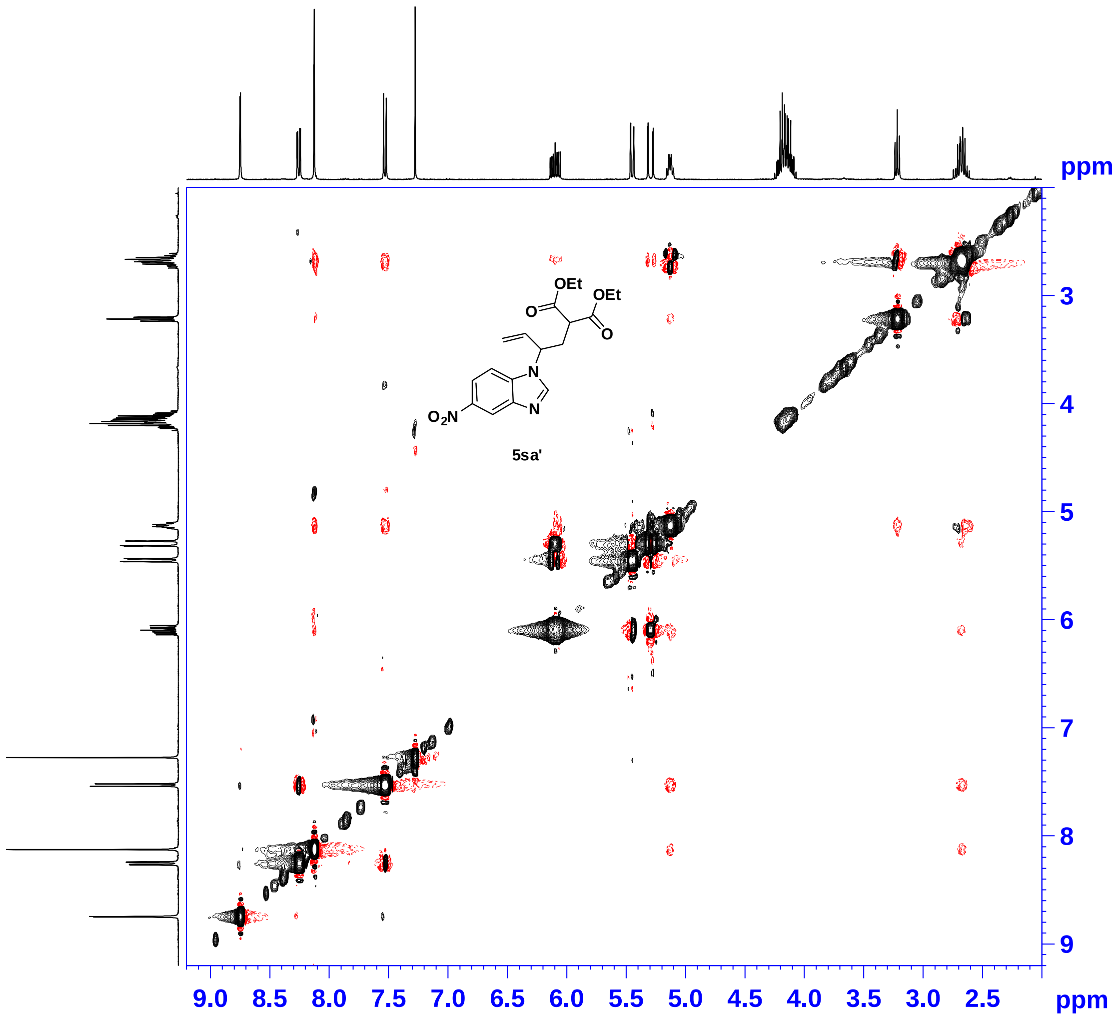
^{1}H-NMR for 5sa'



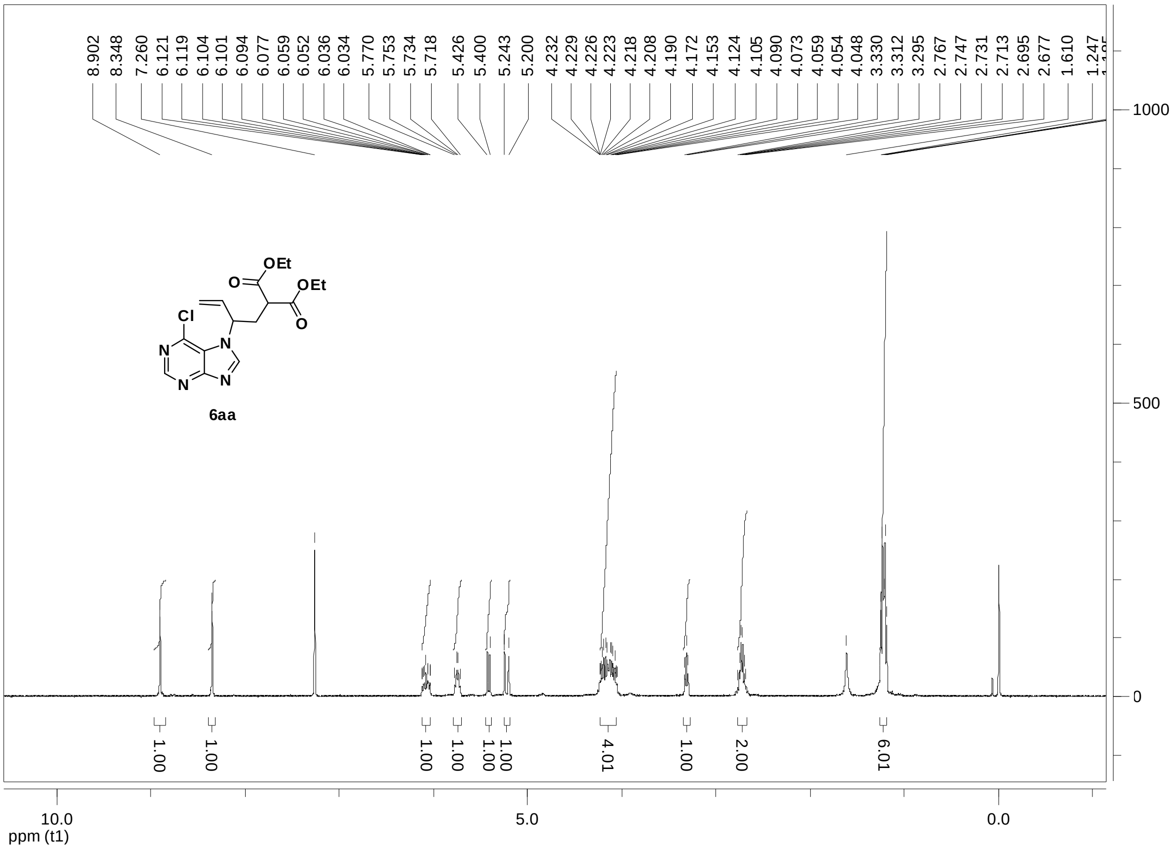
^{13}C-NMR for 5sa'



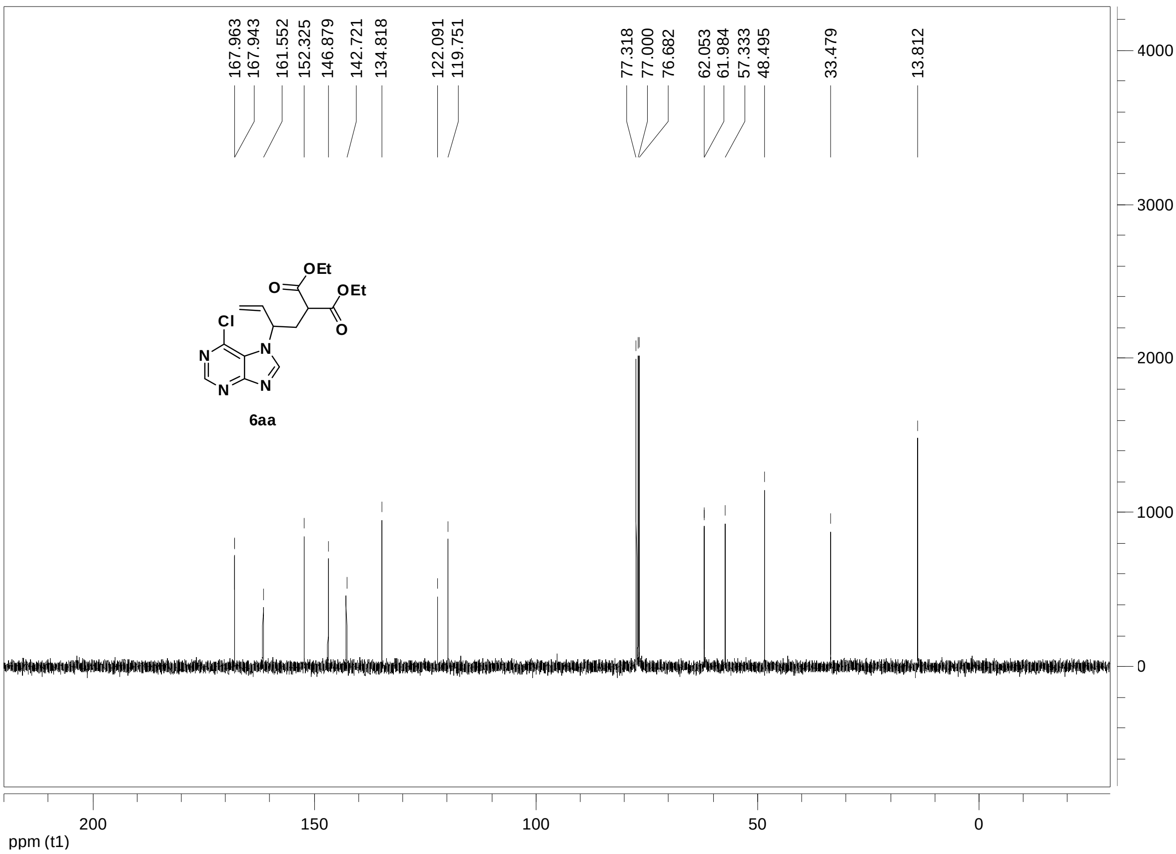
Noesy for 5sa'



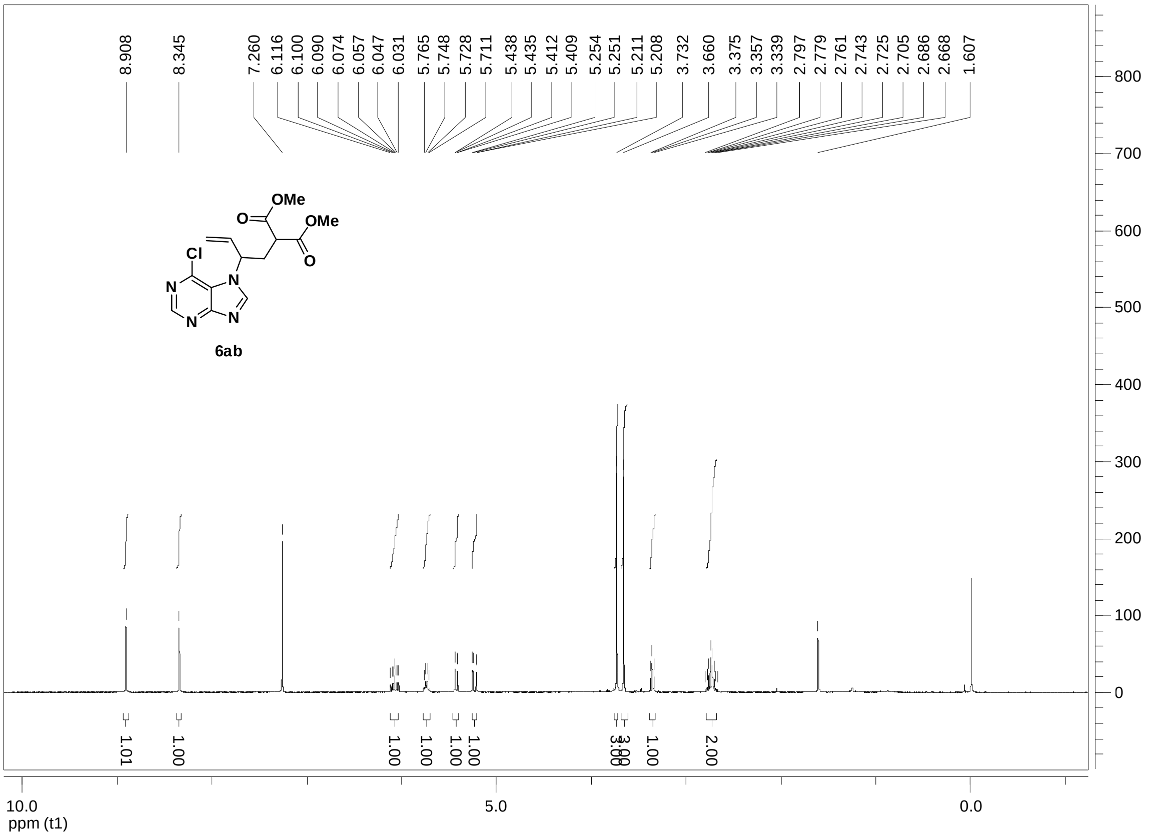
^{1}H-NMR for 6aa



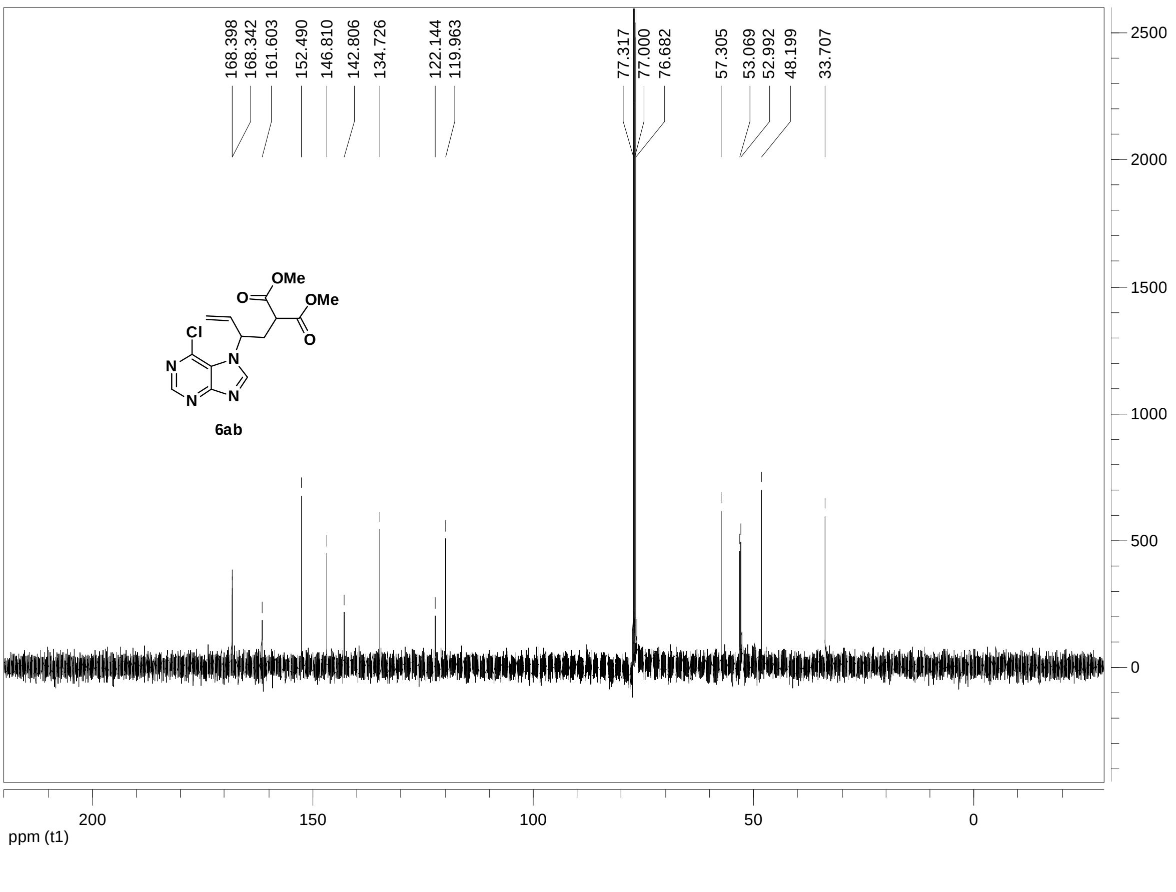
^{13}C-NMR for 6aa



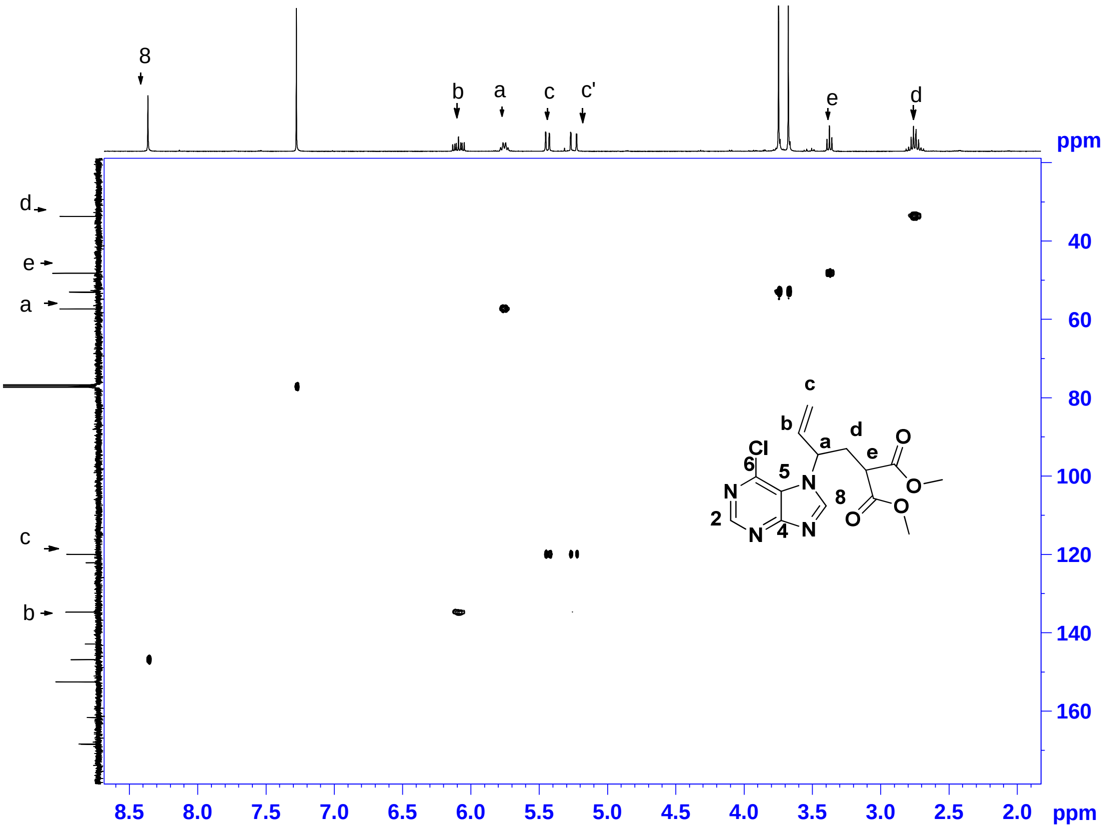
[1]H-NMR for 6ab



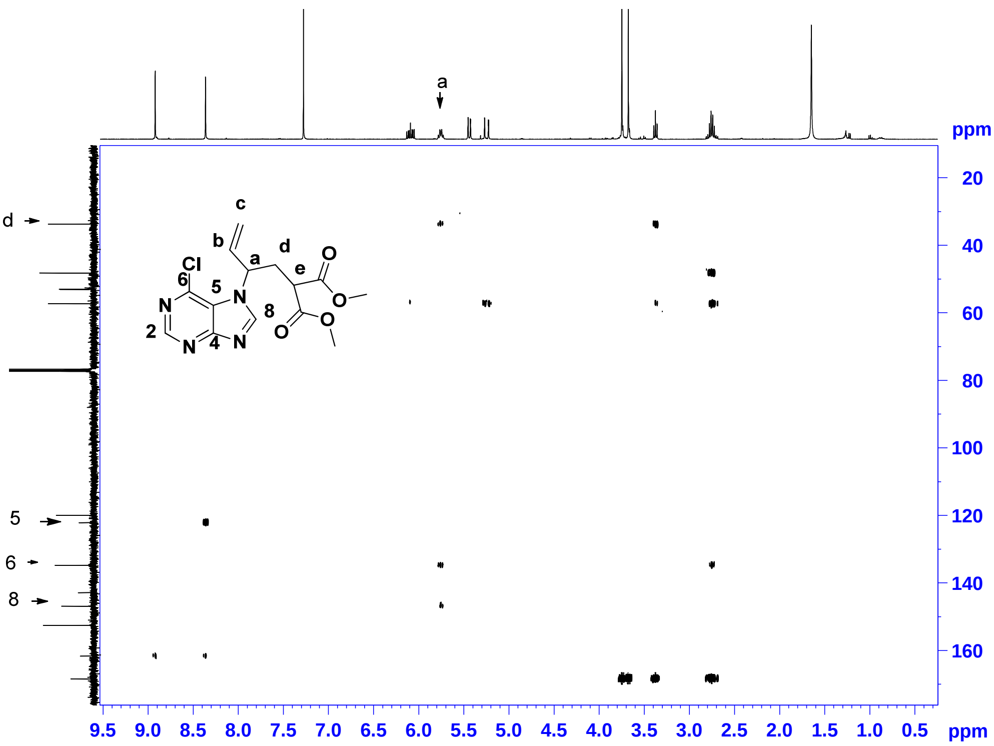
[13]C-NMR for 6ab



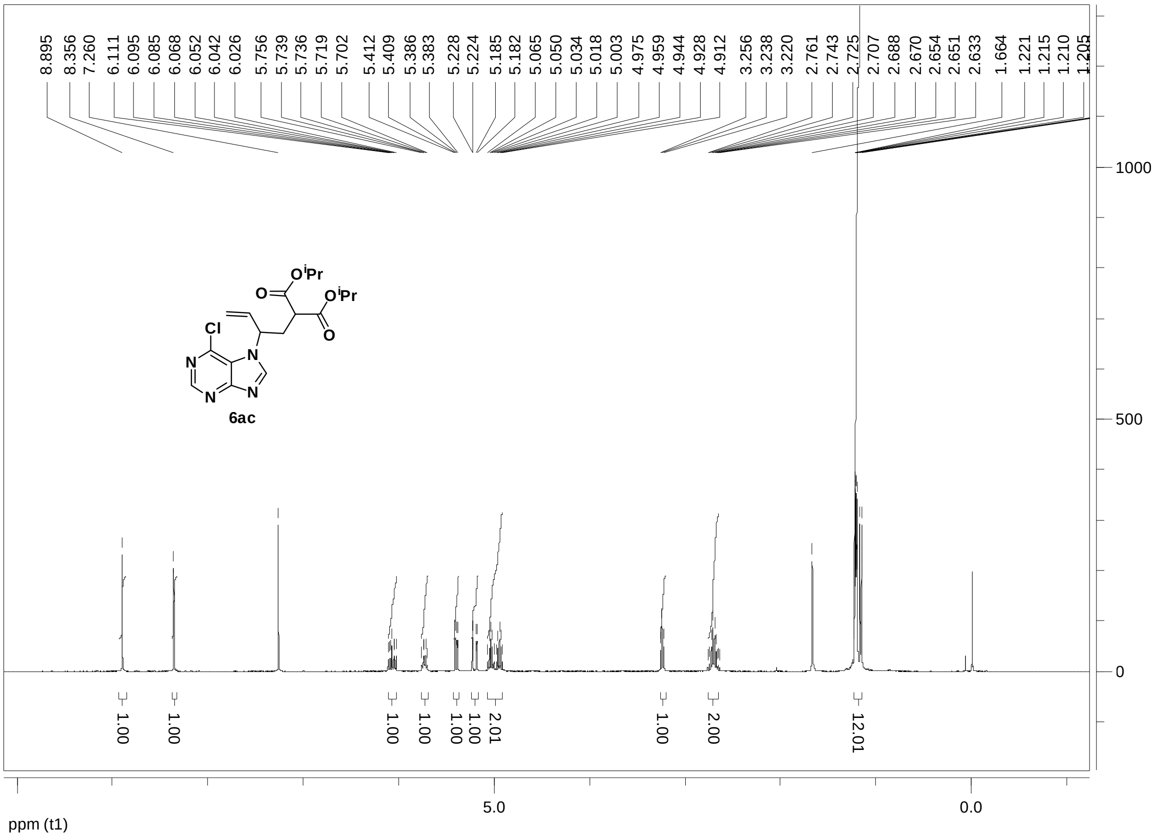
HSQC for 6ab



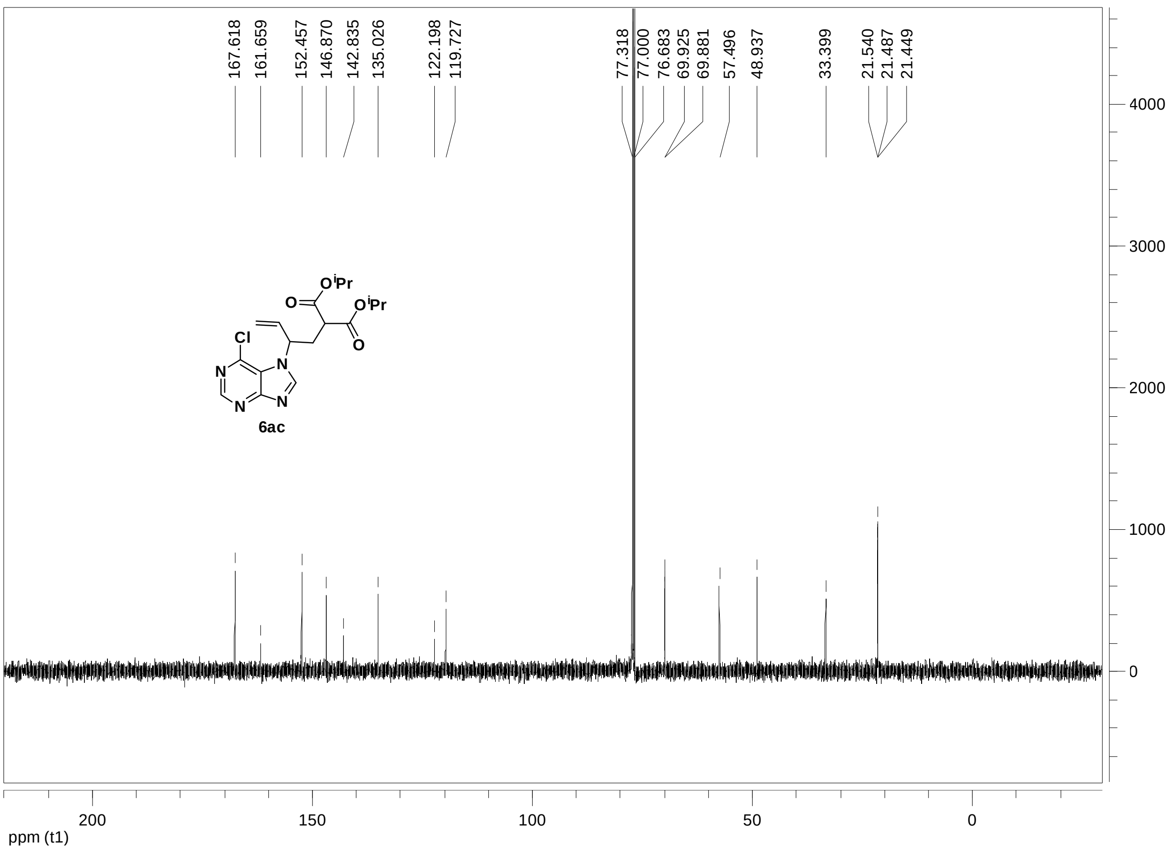
HMBC for 6ab



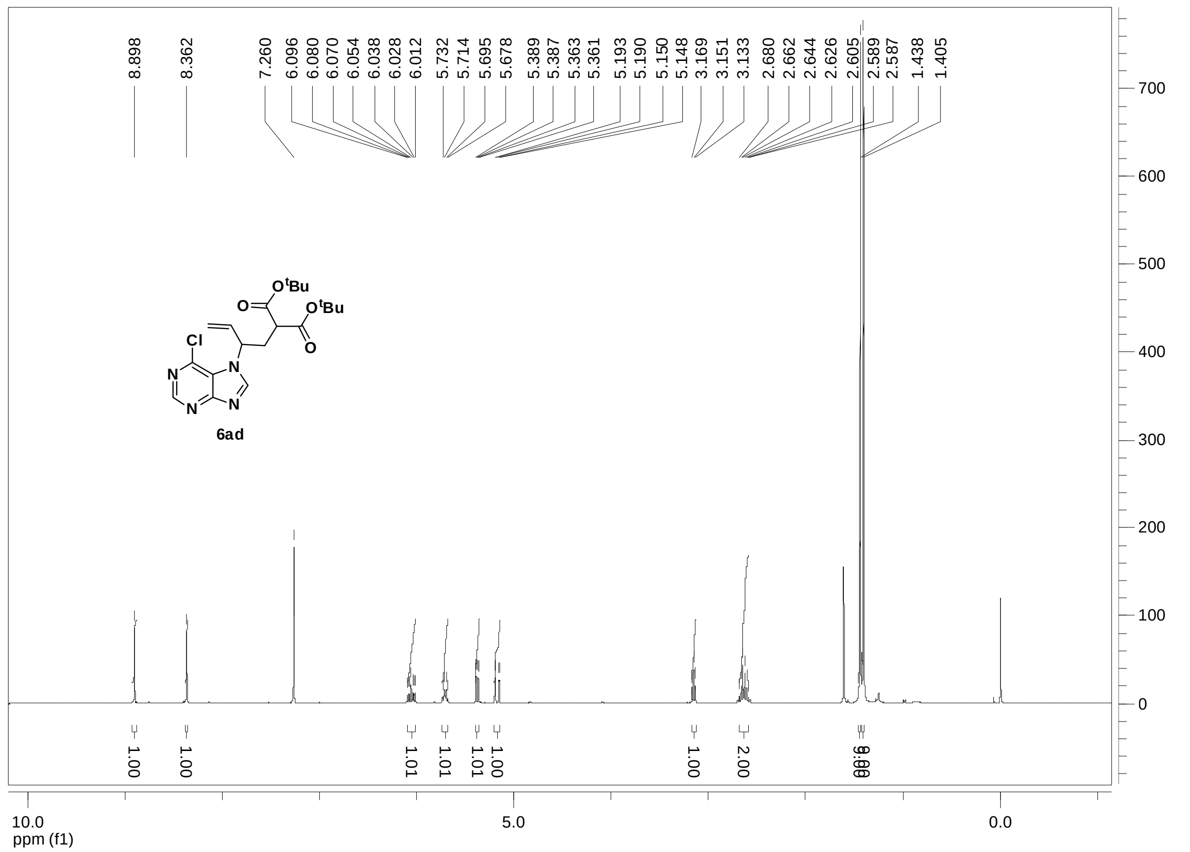
^{1}H-NMR for 6ac



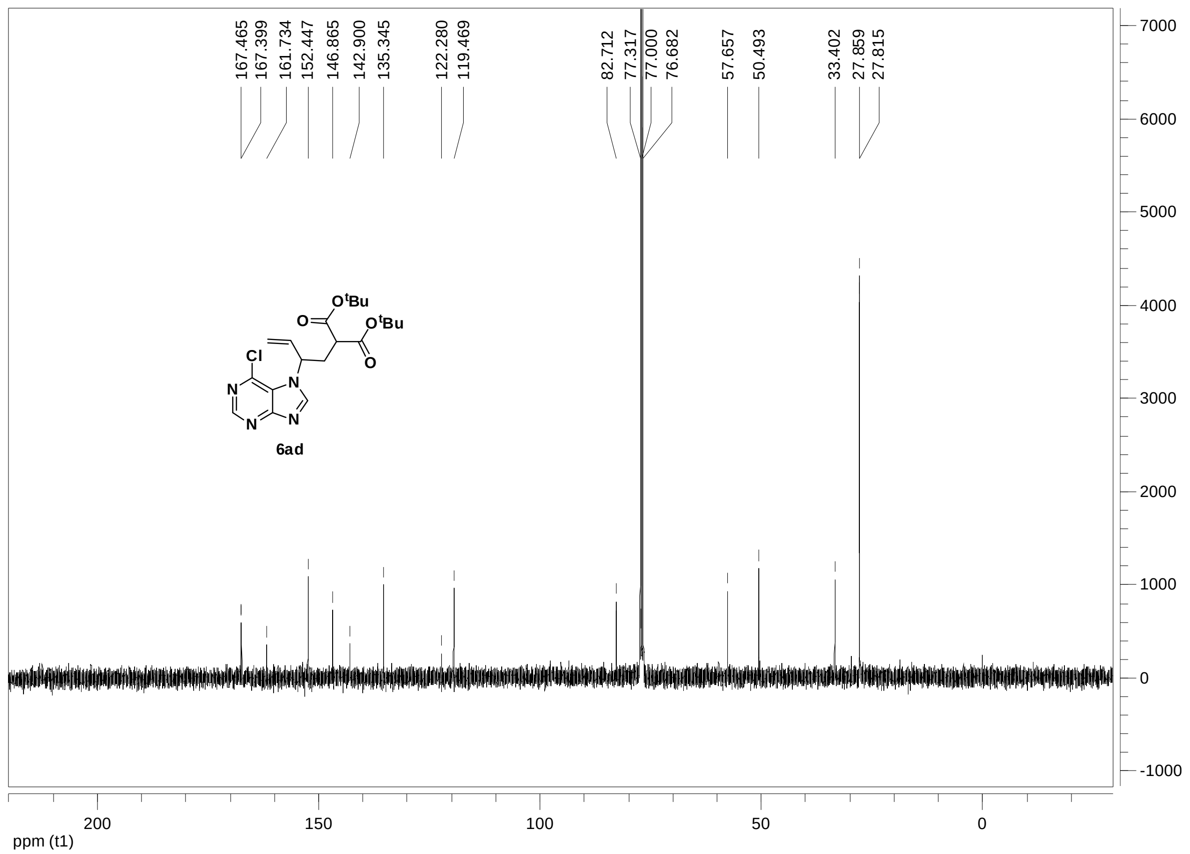
^{13}C-NMR for 6ac



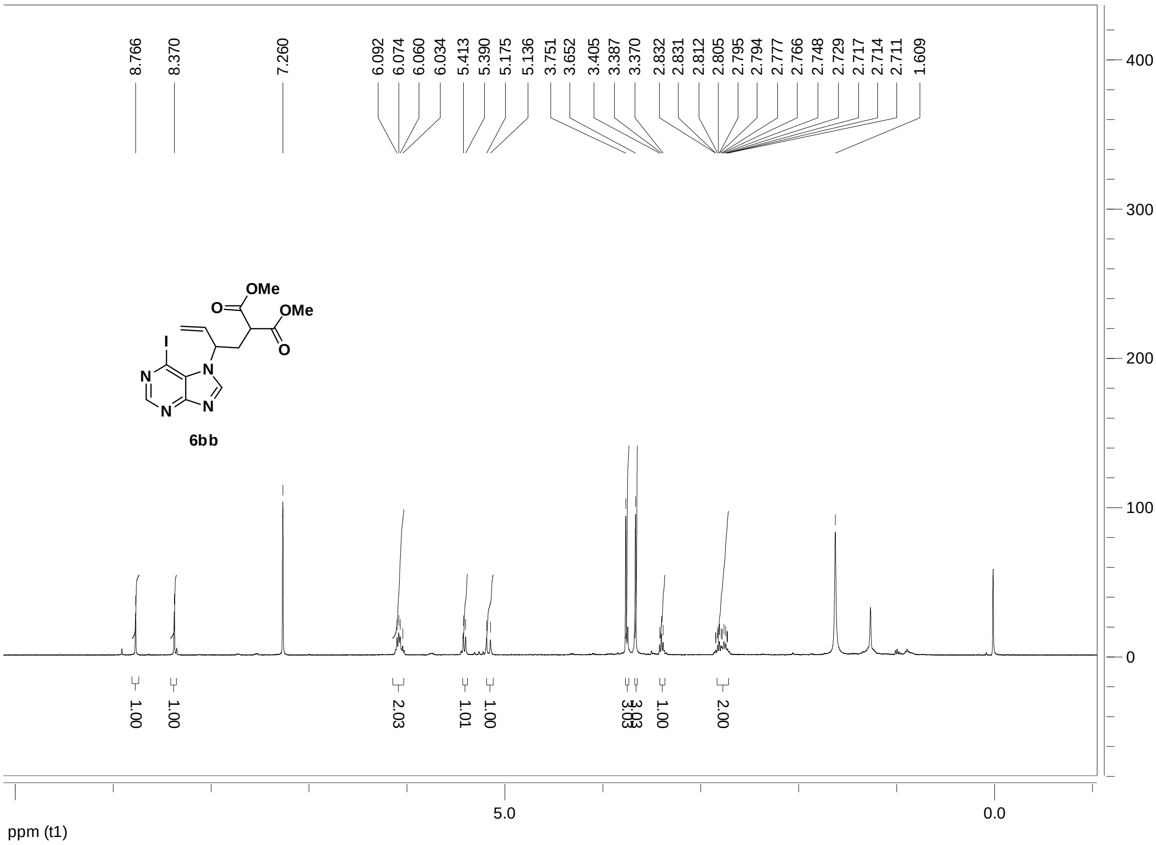
^{1}H-NMR for 6ad



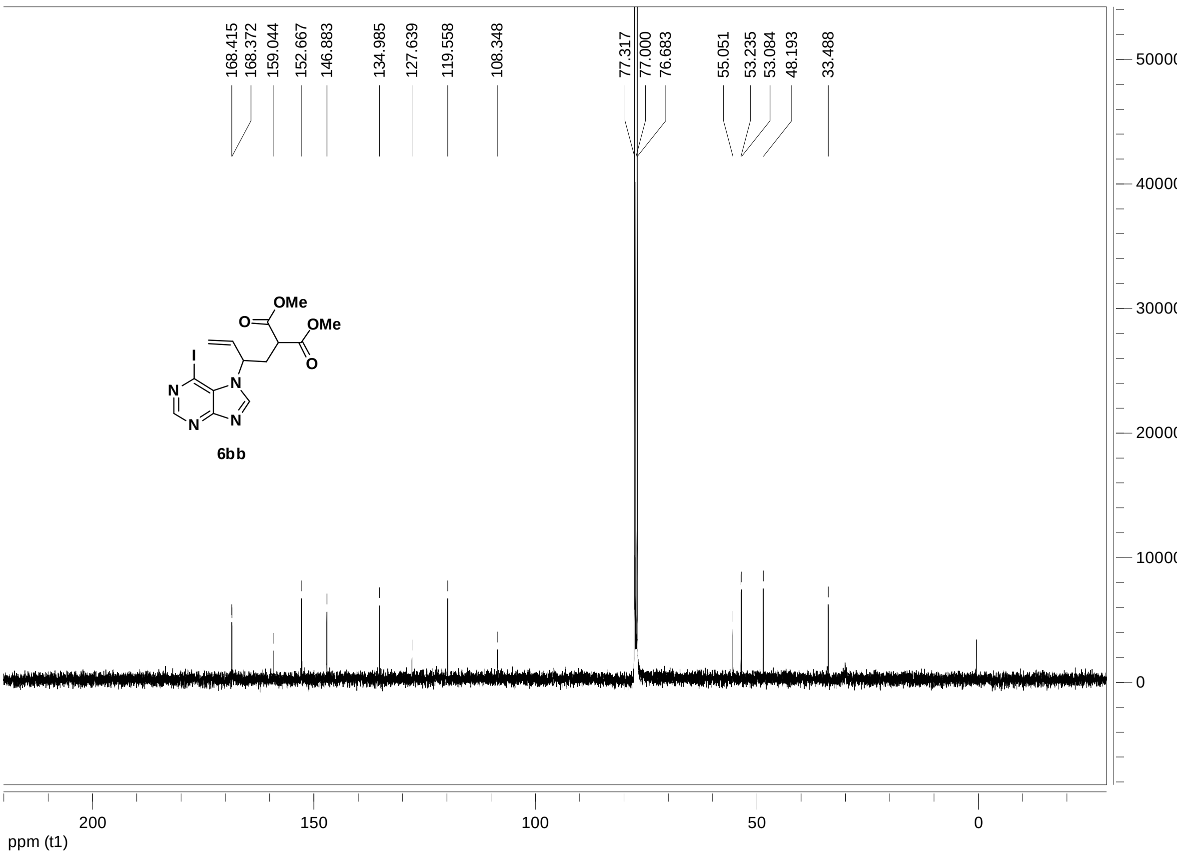
^{13}C-NMR for 6ad



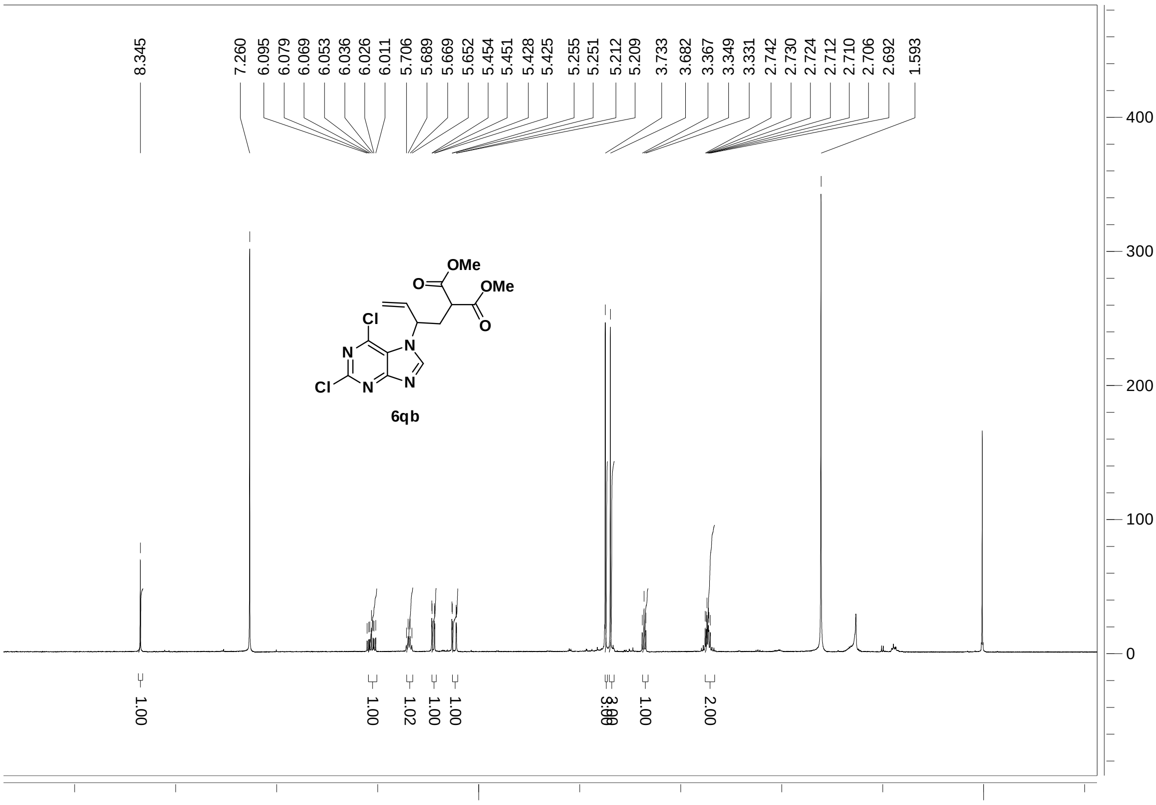
[1]H-NMR for 6bb



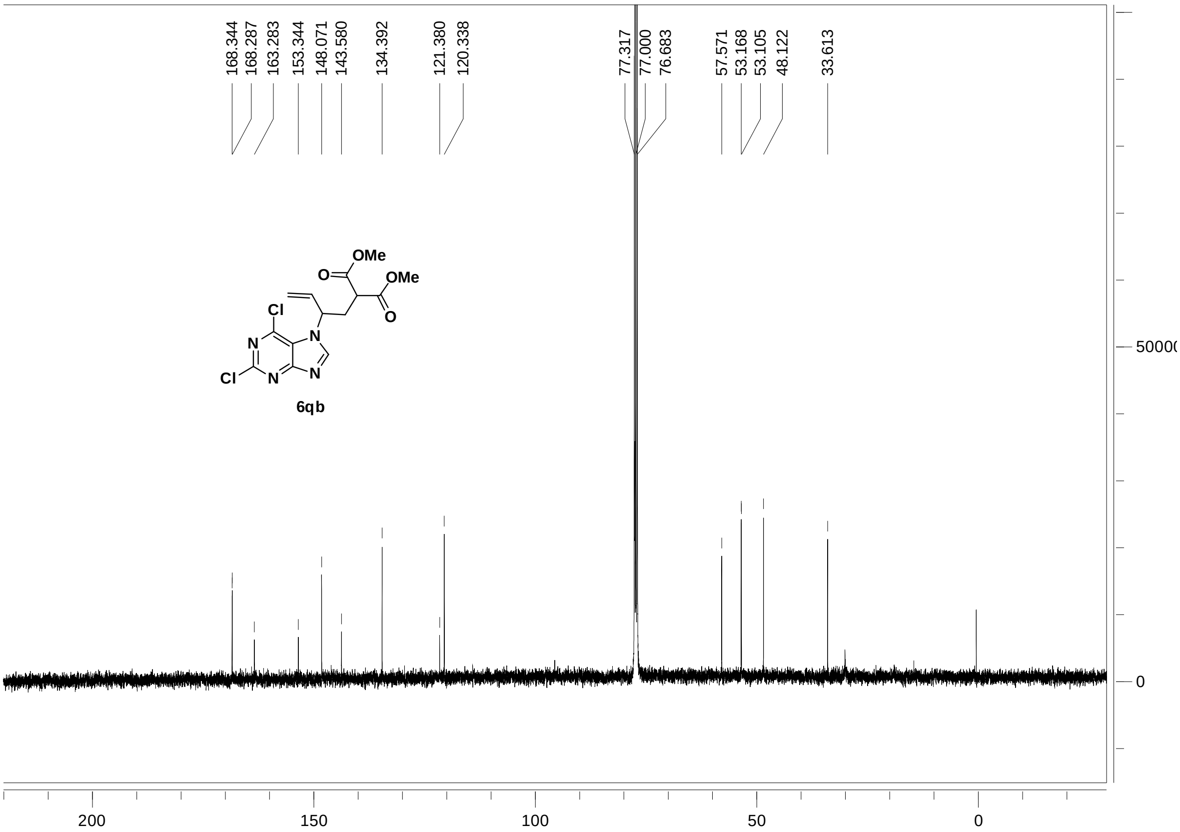
[13]C-NMR for 6bb



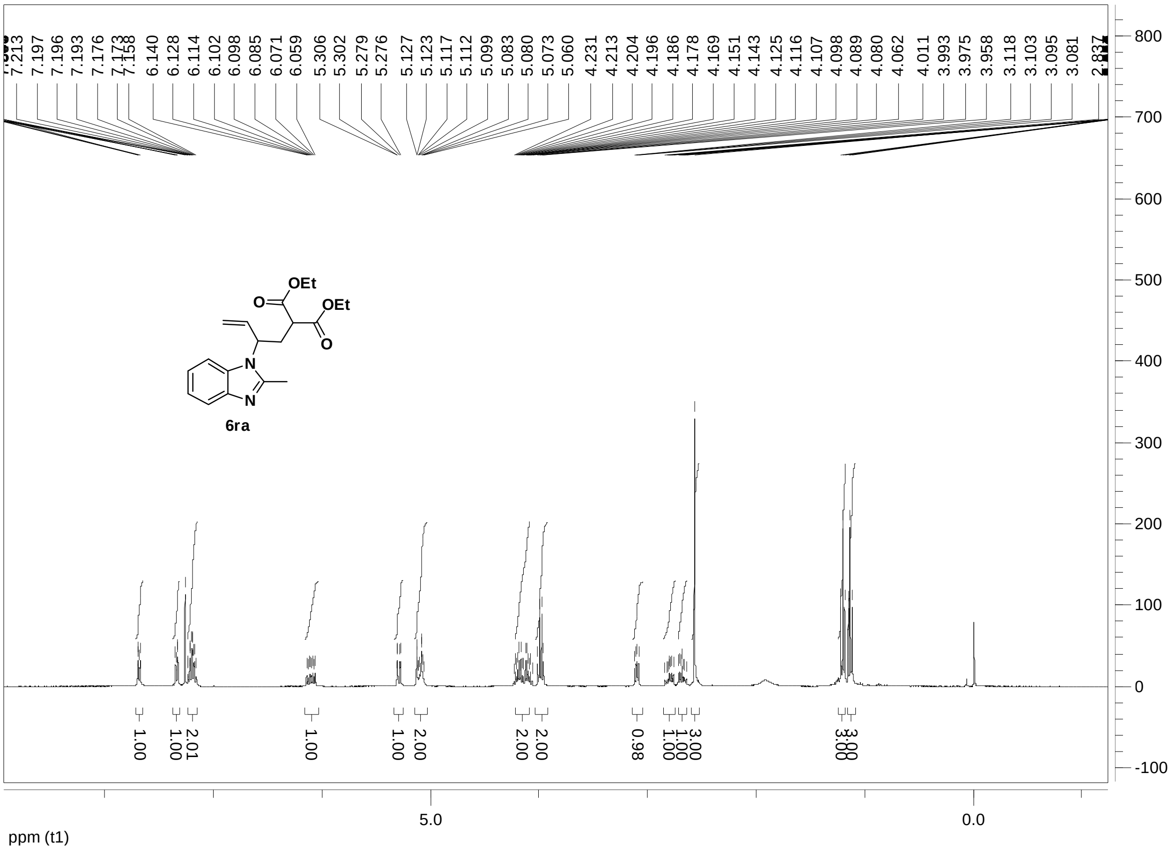
[1]H-NMR for 6qb



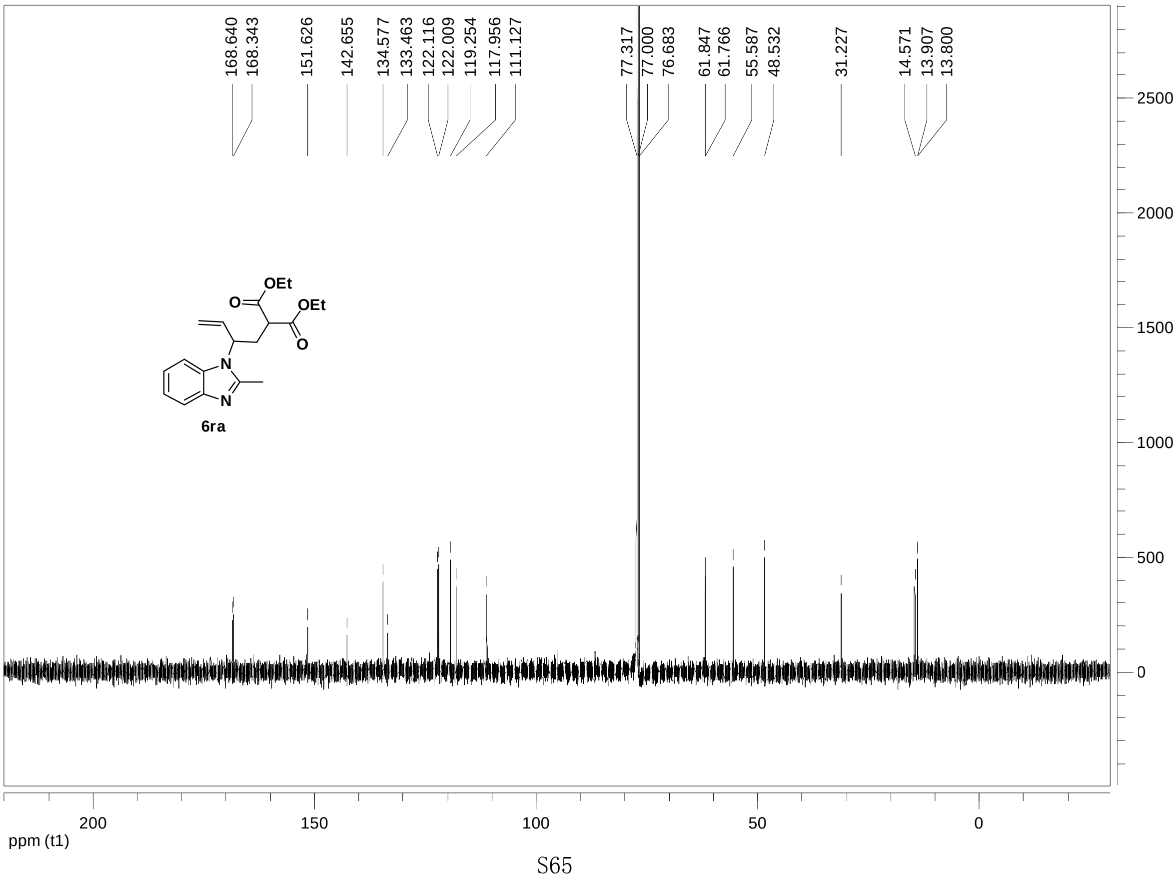
[13]C-NMR for 6qb



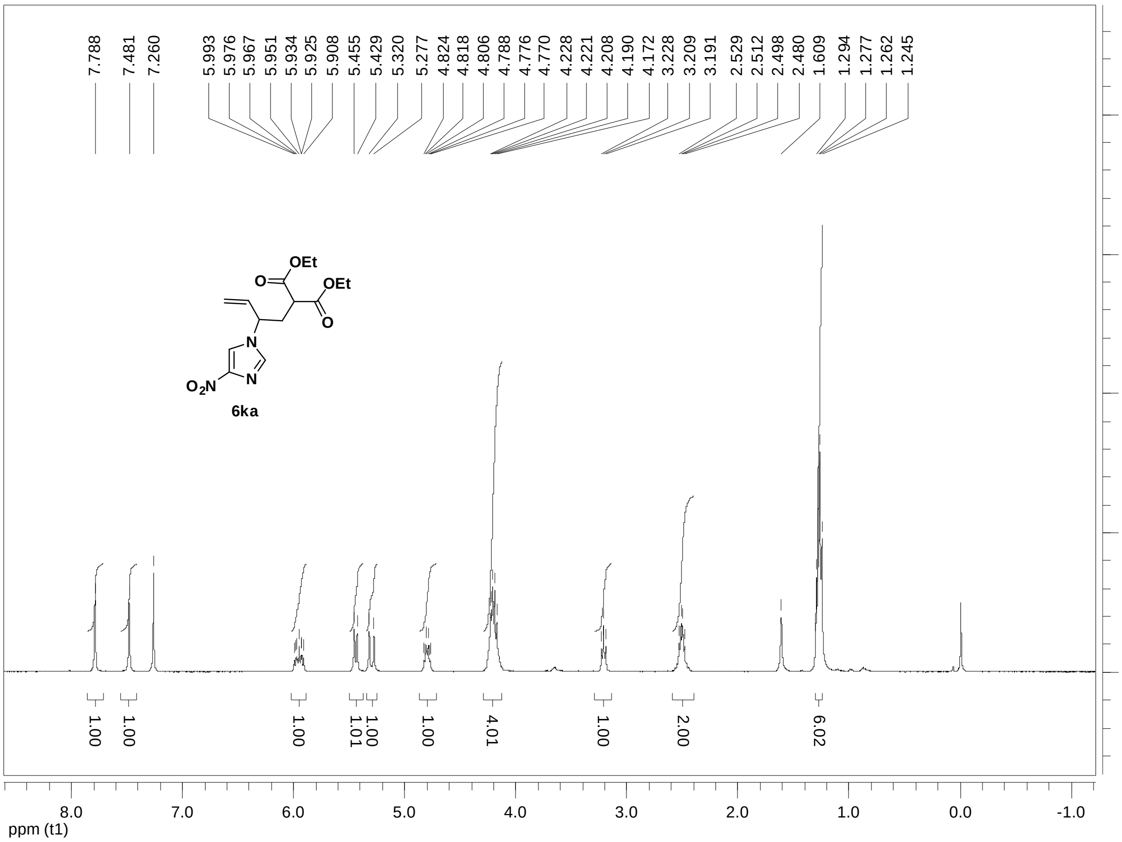
^{1}H-NMR for 6ra



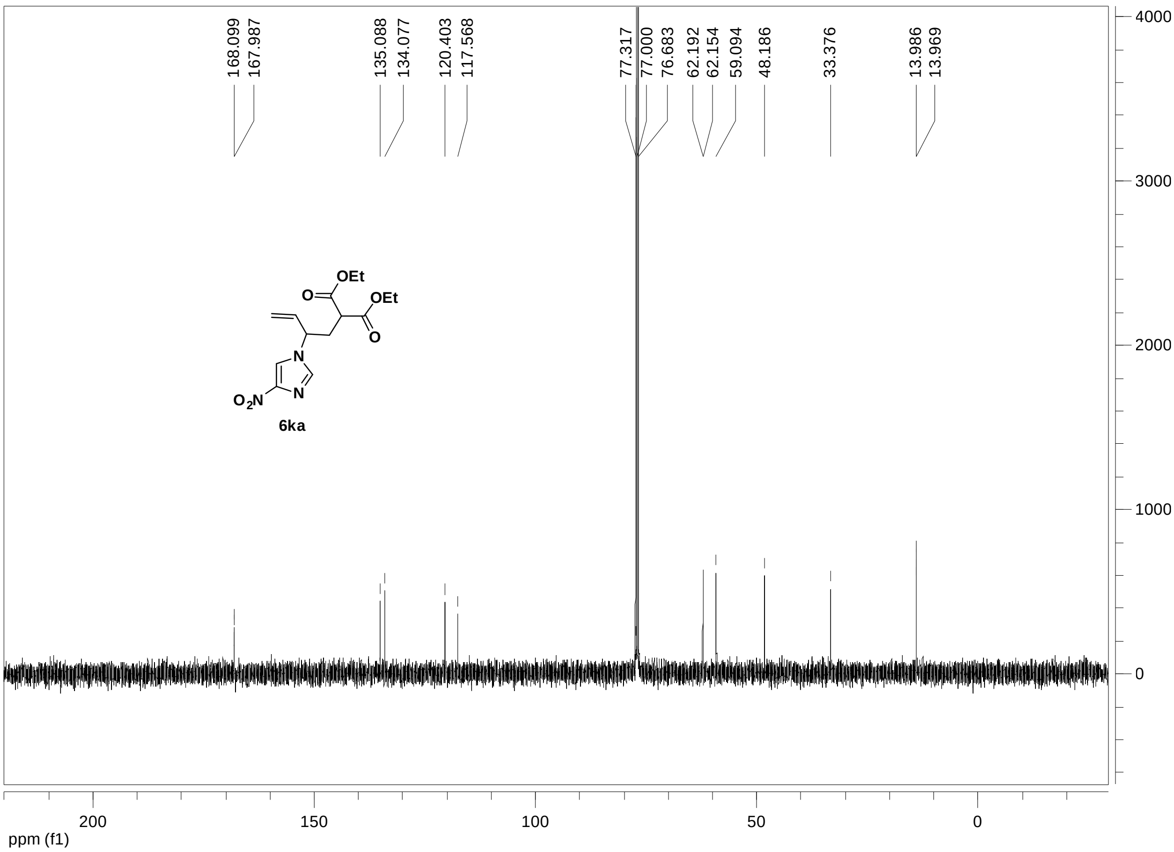
^{13}C-NMR for 6ra



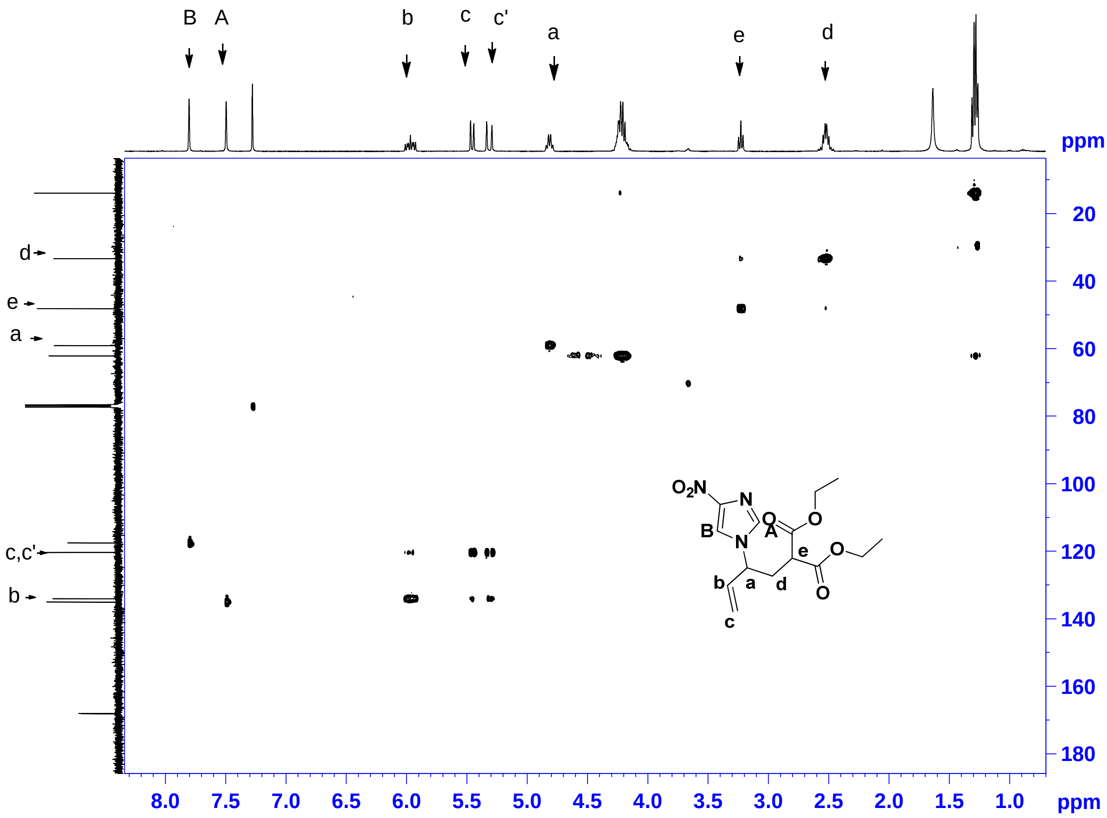
^{1}H-NMR for 6ka



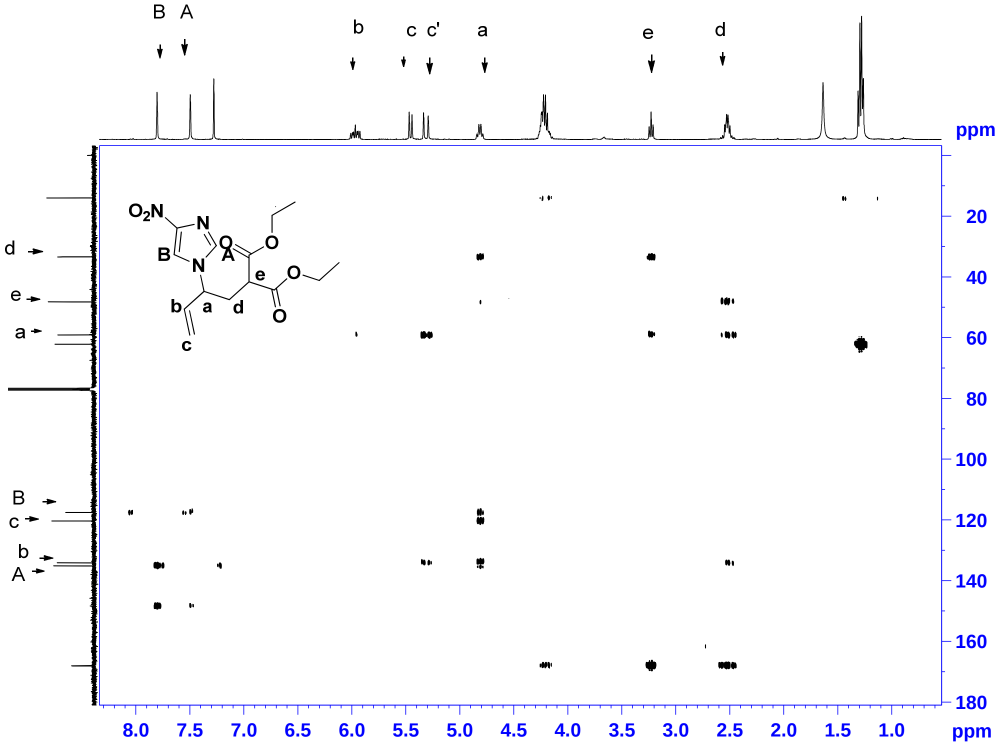
^{13}C-NMR for 6ka



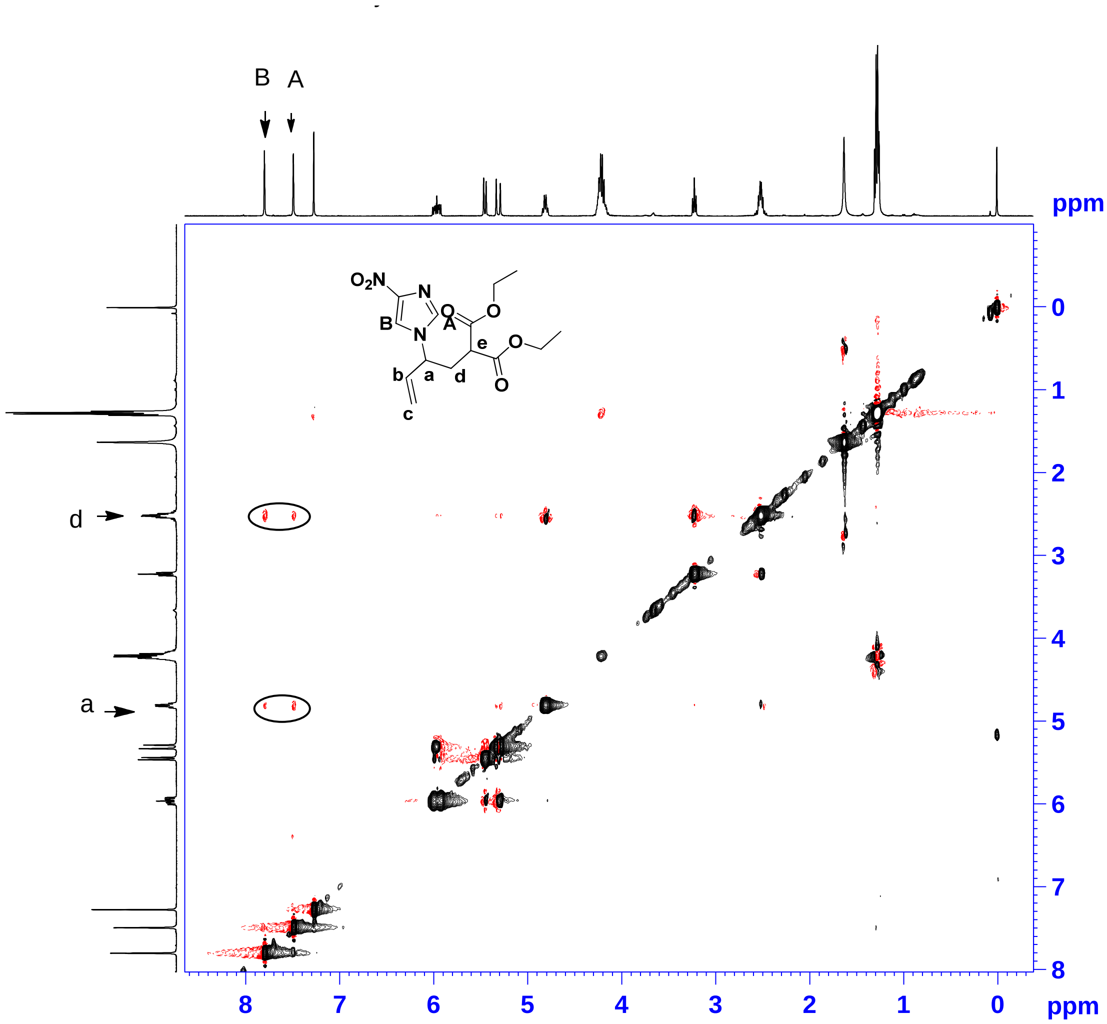
HSQC for 6ka



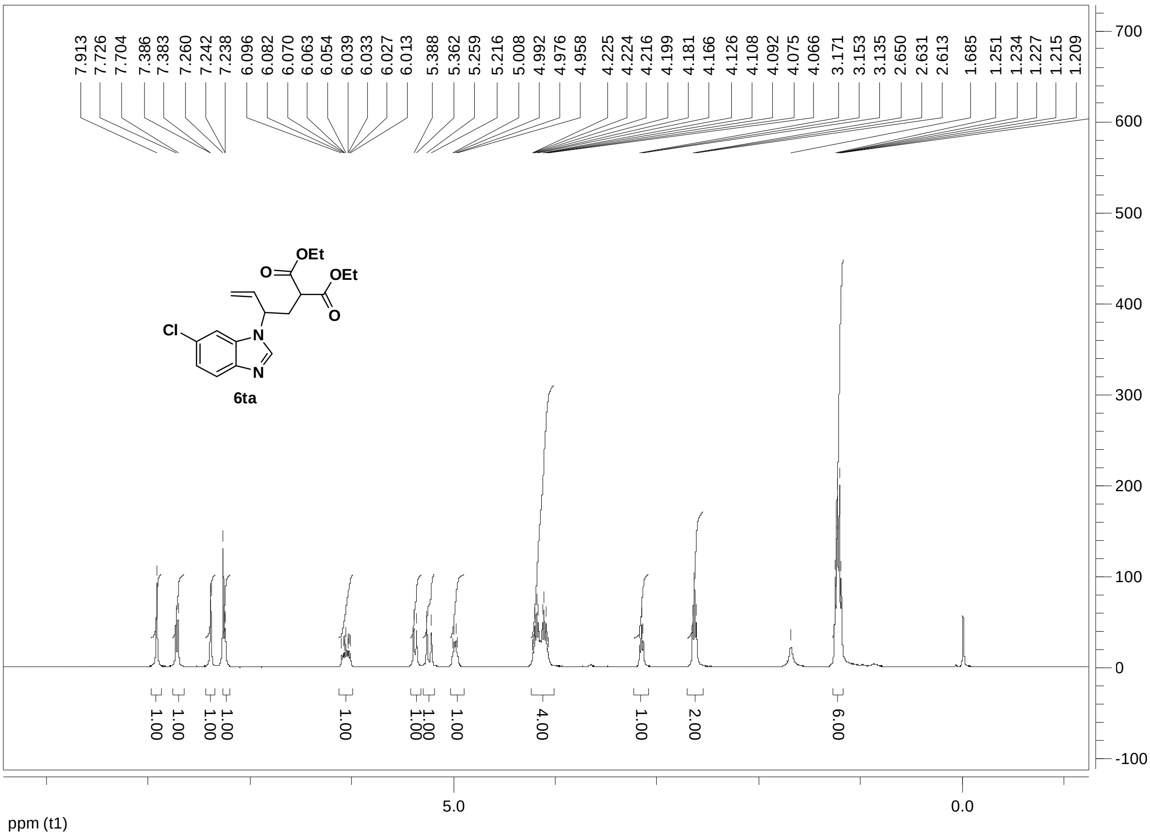
HMBC for 6ka



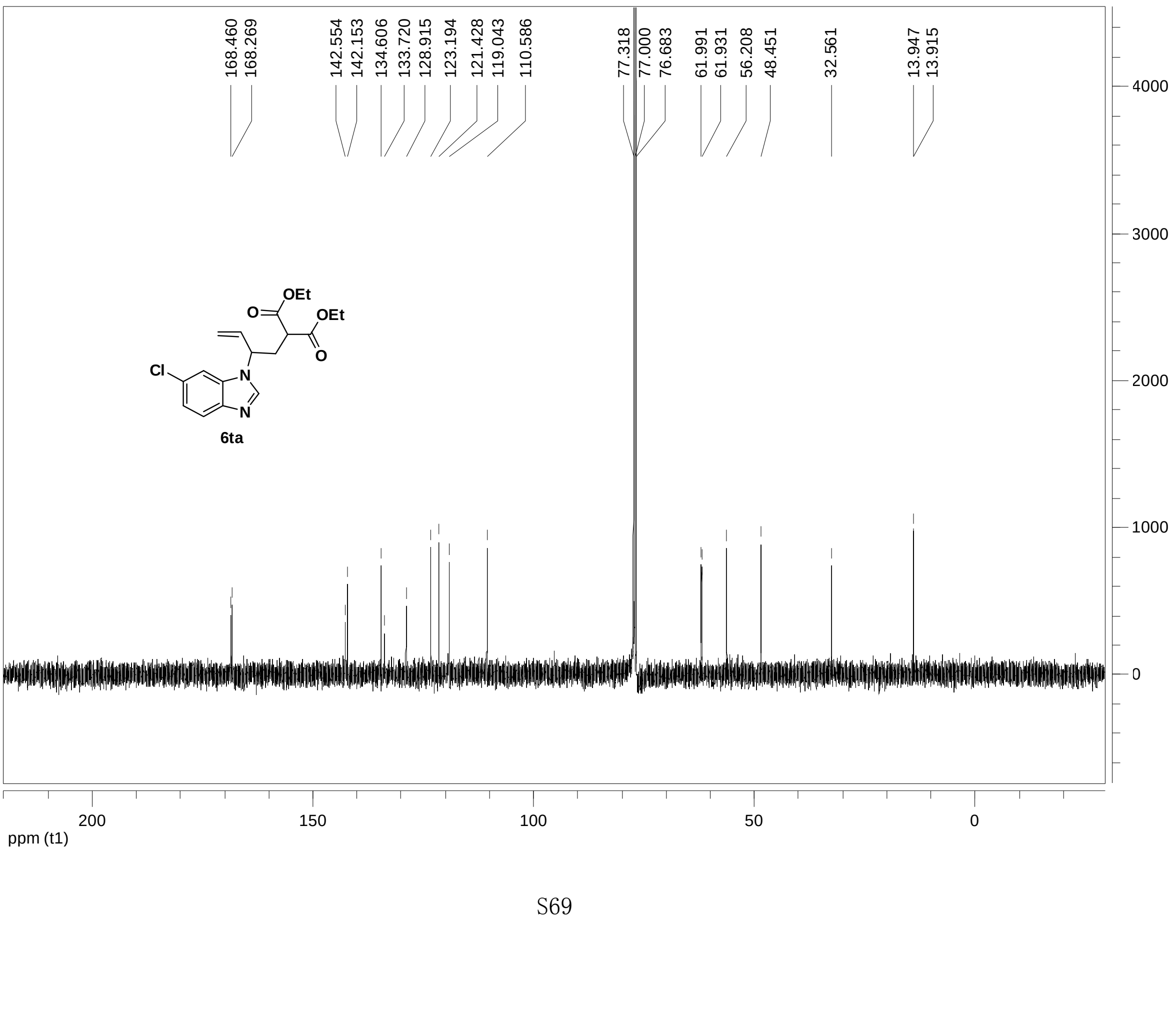
Noesy for 6ka



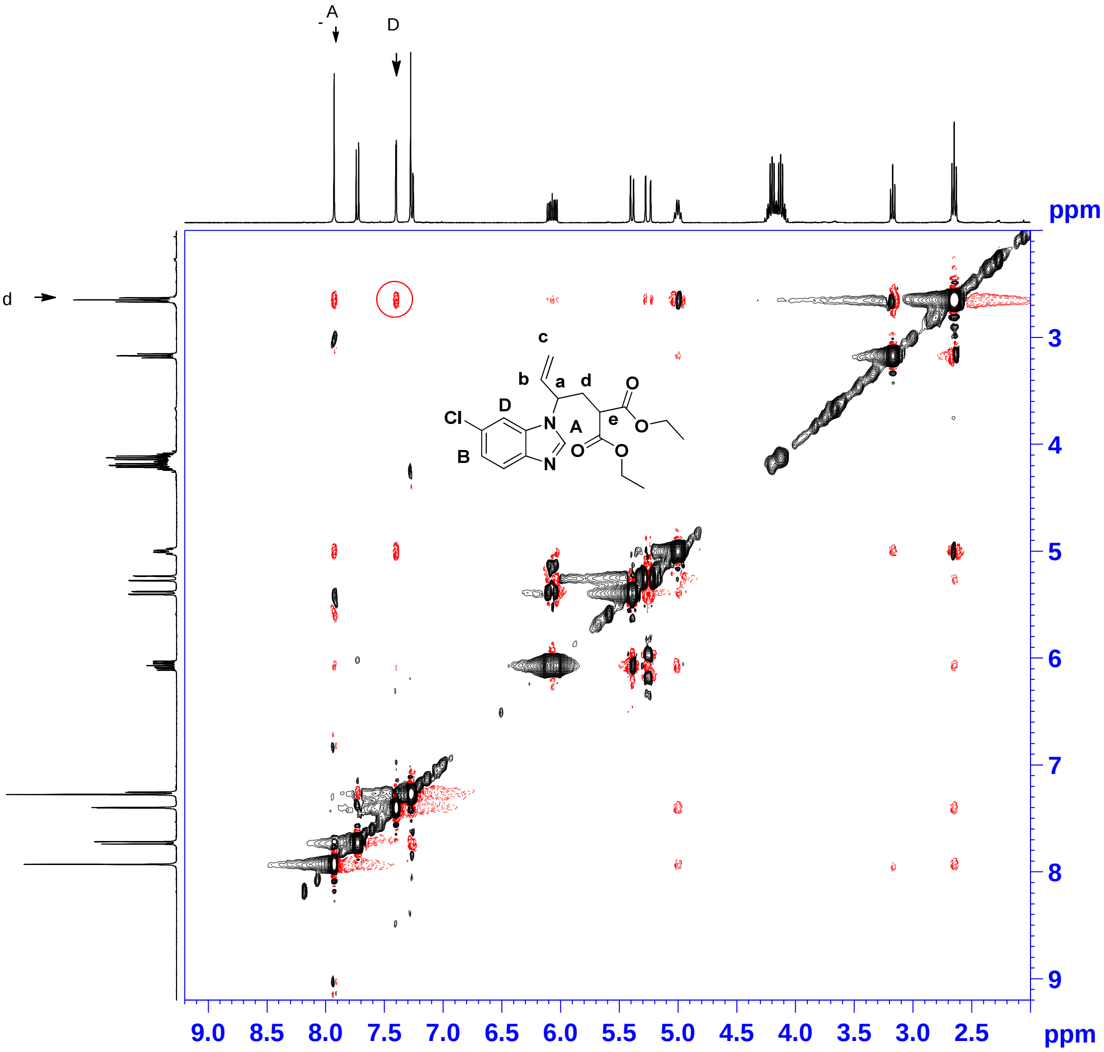
^{1}H-NMR for 6ta



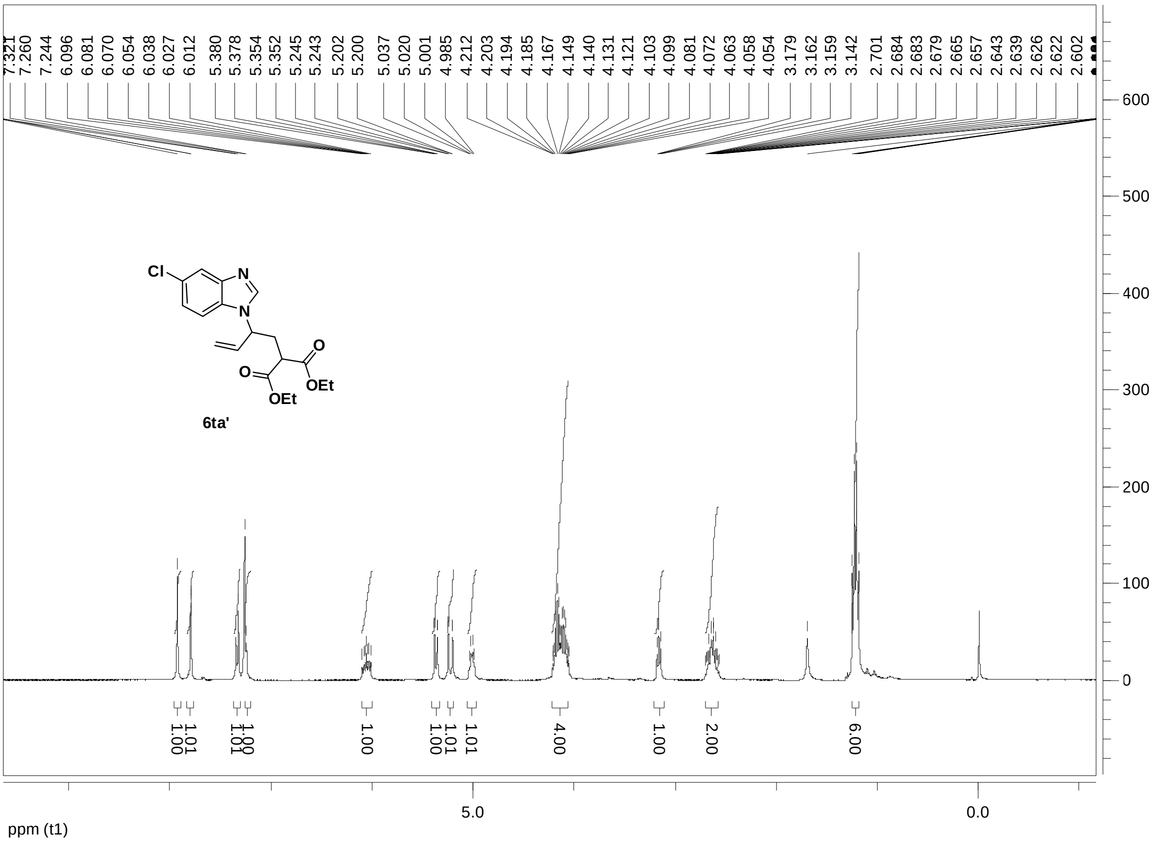
^{13}C-NMR for 6ta



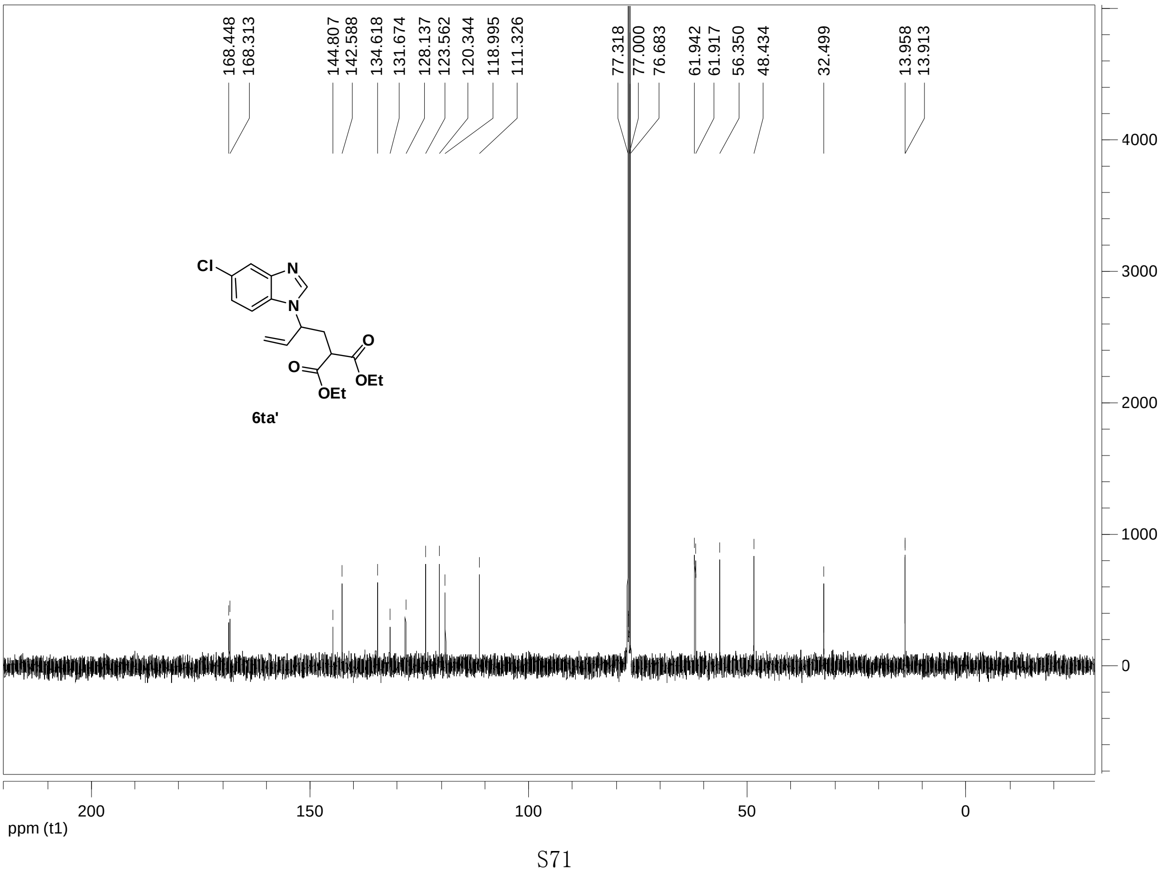
Noesy for 6ta



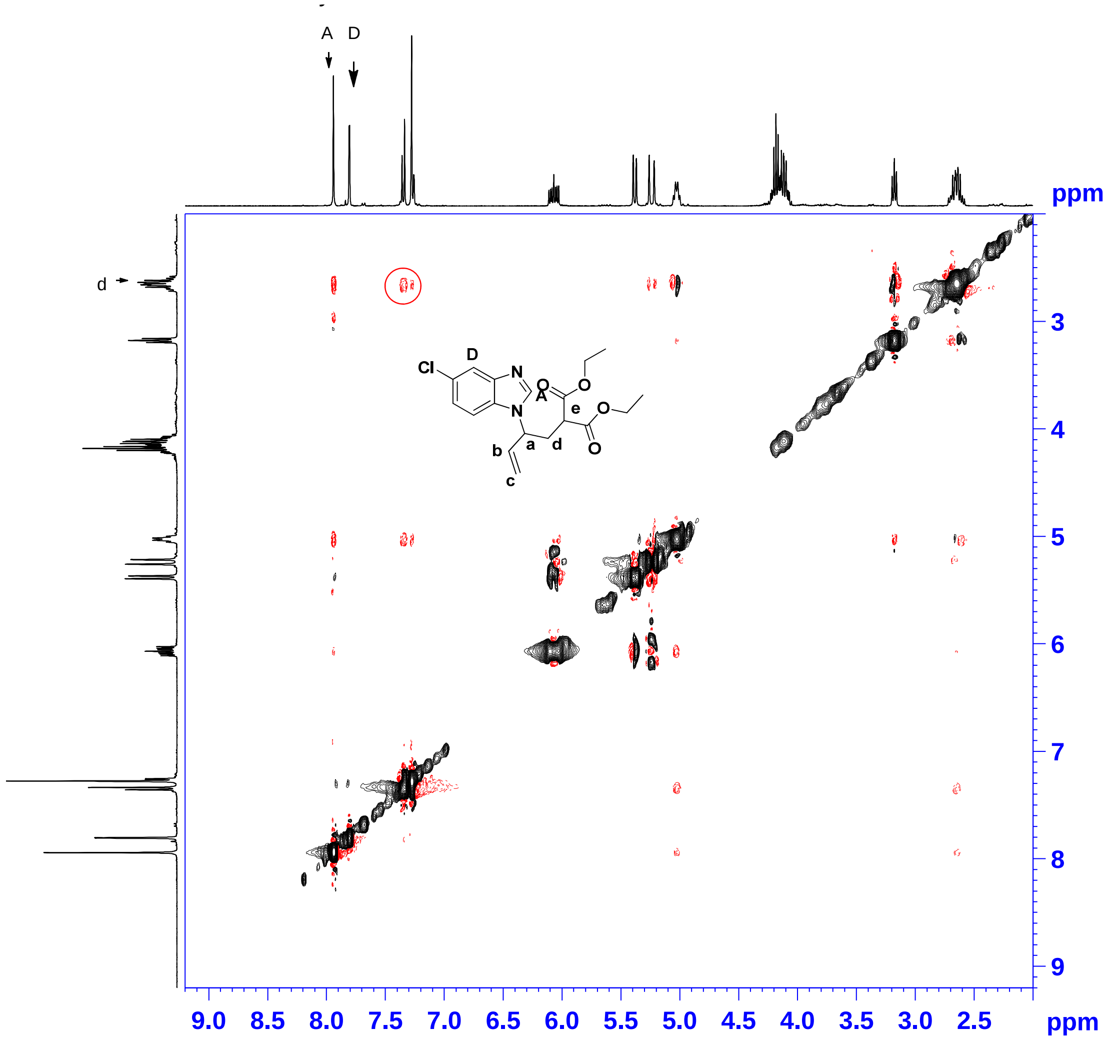
[1]H-NMR for 6ta'



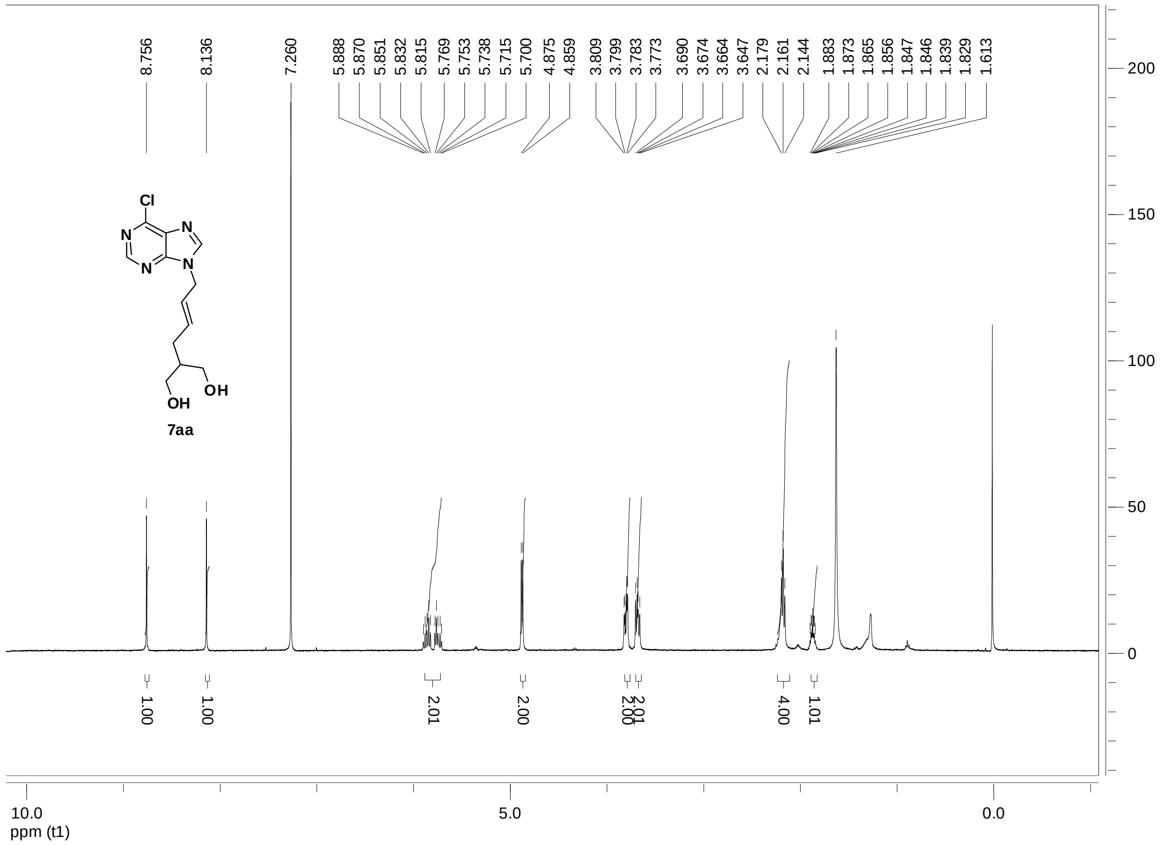
[13]C-NMR for 6ta'



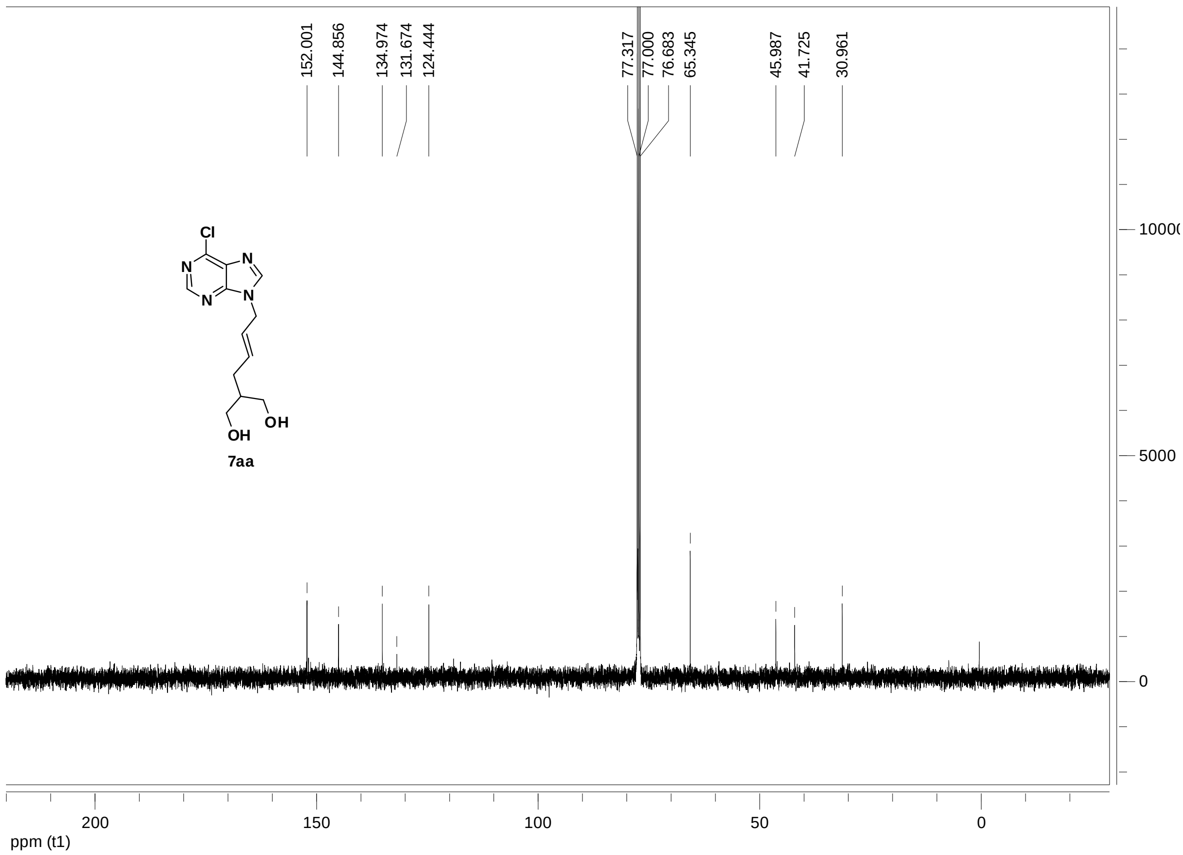
Noesy for 6ta'



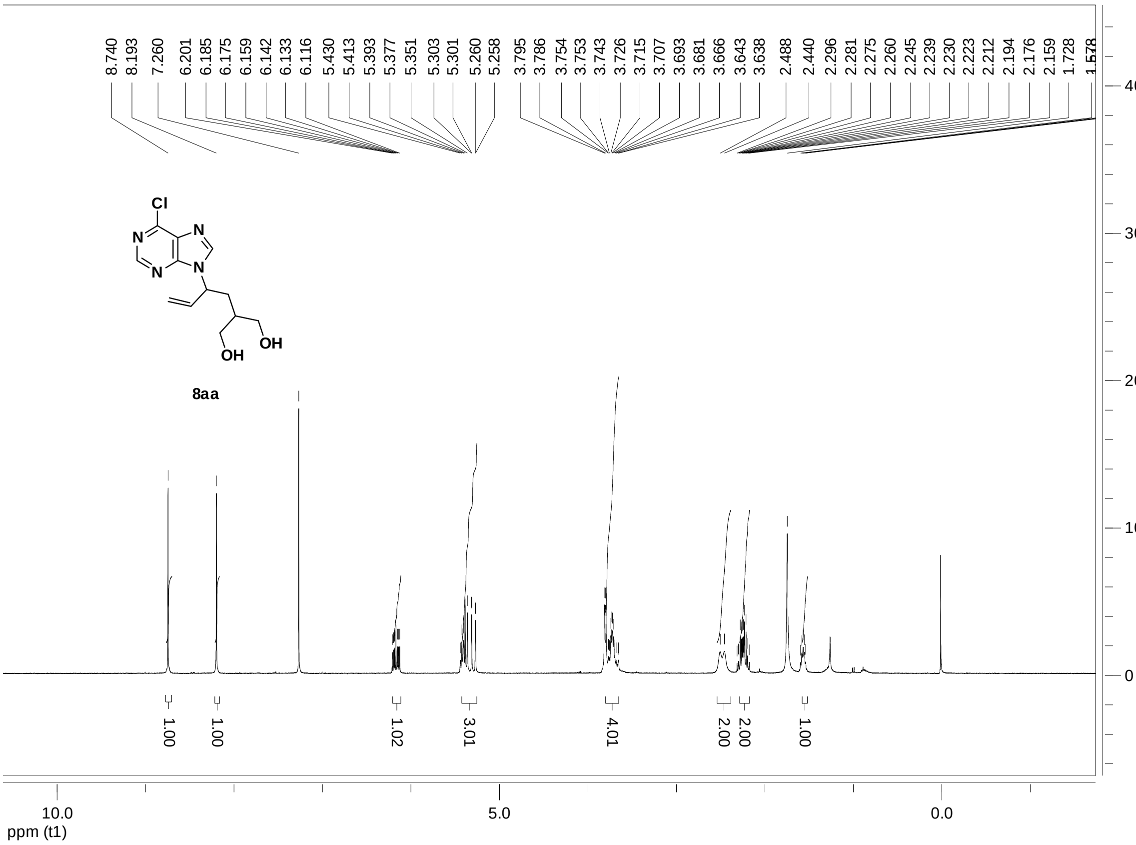
^{1}H-NMR for 7aa



^{13}C-NMR for 7aa



^{1}H-NMR for 8aa



^{13}C-NMR for 8aa