Supporting Information for

A convenient Michael addition of imidazoles to acrylates catalyzed by Lipozyme TL IM from *Thermomyces lanuginosus* in a continuous-flow microreactor

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Materials

Unless otherwise stated, all chemicals were obtained from commercial sources and used without further purification. Lipozyme TL IM from Thermomyces lanuginosus was purchased from Novo Nordisk. Imidazole, acrylates and all other chemicals were of the highest purity commercially available and without further purification. Harvard Apparatus PHD 2000 syringe pumps were purchased from Harvard apparatus.

Experimental setup

The enzymatic Michael addition of imidazole derivatives with acrylates is described in Fig. 1. The micro-flow reactor was composed of a syringe pump (Harvard Apparatus PHD 2000), reactant injector, Y-shaped mixer, microchannel reactor and product collector. Syringe pumps were used to deliver reagents from reactant injectors to Y-shaped mixer and then to the microchannel reactor. Reagent feed **1** (10 mL) with the imidazole derivatives in DMSO solution and reagent feed **2** (10 mL) with acrylates in DMSO solution were fully mixed in Y-shaped mixer. Lipozyme TL IM (catalyst reactivity: 250 IUN.g^{-1}) were filled in microchannel reactor made of a PFA reactor coil (inner diameter ID = 1.8 mm, length = 1 m). The microchannel reactor with catalyst in it was submerged into a thermostatic water bath to control the temperature. Feed **1** and **2** were mixed together at a flow rate of 7.3 µL min^{-1} in a Y-mixer at 45 °C and the resulting stream (14.6 µL min^{-1}) was connected to a sample vial which was used to collect the final mixture.

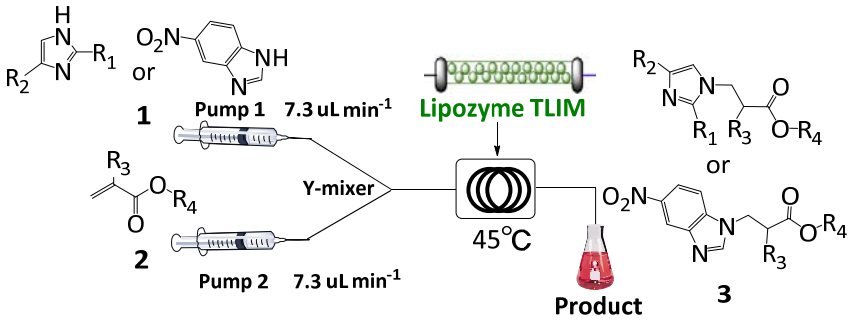


Fig. 1 Experimental setup for Michael addition of imidazole derivatives with acrylates catalyzed by lipase TL IM in a continuous flow microreactor.

General Procedure for Michael addition reaction in Continuous Flow Microreactors

Method B: 1.0 mmol of the imidazole derivatives was dissolved in 10 mL DMSO (feed 1, ~0.1 M) and 4.0 mmol acrylates were dissolved in 10 mL DMSO (feed 2; ~0.4 M). Lipozyme TL IM (0.87 g) were filled in PFA reactor coil (inner diameter ID= 1.8 mm, length = 1m. We filled the silica gel-loaded enzyme granules in a pipe by physical filling, and then filled the enzyme evenly with an ultrasonic oscillator.). Streams 1 and 2 were mixed together at a flow rate of. 7.3 µL min^{-1} in a Y-mixer at 45 °C and the resulting stream (14.6 µL min^{-1}) was connected to a sample vial which was used to collect the final mixture. The final mixture was then evaporated, and the residue was submitted to column chromatography on silica gel (200-300 mesh). The products were eluted with a gradient of petroleum ether /ethyl acetate (4:1, by vol). The purification was monitored by TLC. The fractions containing the main products were pooled, the solvent evaporated, and the residue analyzed by ^{1}H NMR, ^{13}C NMR and ESI-MS.

General Procedure for Michael addition reaction under Shaker Conditions.

Method A: imidazole derivatives (0.25 mmol) and acrylates (1.0 mmol) were added to 5 mL DMSO. The biocatalyst lipozyme TL IM (40 mg/mL, 0.20 g) was then added and the suspension maintained at 45 °C for 24 h under Shaker Conditions. The mixture was cooled and filtered. Then evaporated under reduced pressure and the residue was submitted to column chromatography on silica gel (200– 300 mesh). The products were eluted with a gradient of normal petroleum ether/ethyl acetate (4:1, by vol). The purification was monitored by TLC. The fractions containing the main products were pooled, the solvent evaporated, and the residue analyzed by ^{1}H NMR, ^{13}C NMR and ESI-MS.

Thin-Layer Chromatography

Analytical TLC was performed on silica gel 60 plates (Merck) using petroleum ether /ethyl acetate(2:1, by vol) as developing solvent. Spots were detected by ultraviolet irradiation at 254 nm.

High Performance Liquid Chromatography (HPLC)

The reaction was monitored by HPLC analysis using a Shim-Pack VP-ODS column (4.6×150 mm) and a UV detector (285 nm). MeOH/NaH_2PO_4 solution (7.5×10^{-3} M) (25:75) was used as eluant at 1.0 mL min^{-1} for imidazole and acrylates. MeOH/H_2O solution (30:70) was used as eluant at 1.0 mL min^{-1} for nitroimidazole and acrylates. The yield was defined as the ratio between the molar concentration of N-substituted imidazole derivatives and the initial molar concentration of the imidazole derivatives used.

In order to examine the reproducibility of the method, we repeated the reaction five times, the result are illustrate in Figure 2.

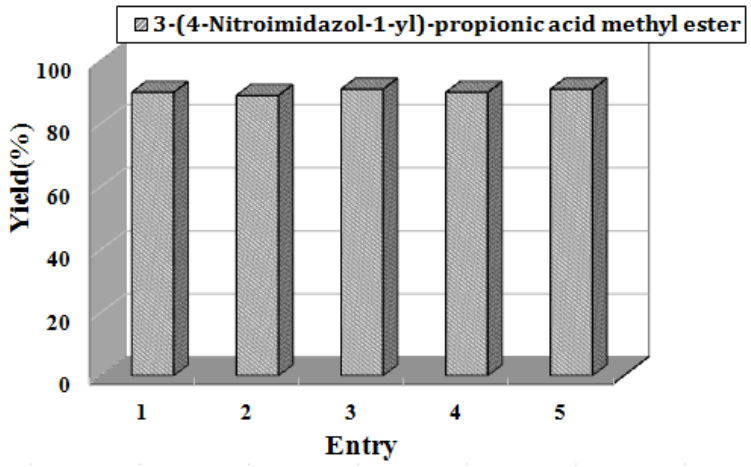


Figure 2.The reproducibility of the reaction on the conversion of 3-(4-Nitroimidazol-1-yl)-propionic acid

methyl ester by Lipozyme TL IM in a continuous flow microreactor.

The reaction time is calculated in two ways:

(1) Actual reaction time: We use the timer calculated the reaction time: the start time of the reaction begin from the two reaction solution first contact with the catalyst in microreactor to the first droplet of product flow out of the tube of microreactor.

(2) Theoretical reaction time: There is a display data on the microreactor injection pump and the data will increase with the continuous injection. For example, we choose a flow rate (0.0073 mL/min), when the two reaction solution first contact with the catalyst in microreactor, a data display(0.0670 mL), another data is got at the time the first droplet of product flow out of the tube of microreactor (0.3223 mL). So the reaction time is: (0.3223-0.0670)/0.0073= 34.9 min.

We have five flow rates: 0.0127 mL/min, 0.0102 mL/min, 0.0085 mL/min, 0.0073 mL/min, 0.0064 mL/min. From the Table 1, we can see that no matter which flow rate we test, the two data on the microreactor is almost the same. The Actual time and the Theoretical time are almost the same as well.

Table 1

First data (mL)	Second data (mL)	Flow rate (mL/min)	Actual time (min) way 1	Theoretical time (min) way 2
0.0673	0.3220	0.0127	20	20.05
0.0672	0.3220	0.0102	25	24.98
0.0673	0.3222	0.0085	30	29.98
0.0670	0.3223	0.0073	35	34.97
0.0671	0.3225	0.0064	40	39.91

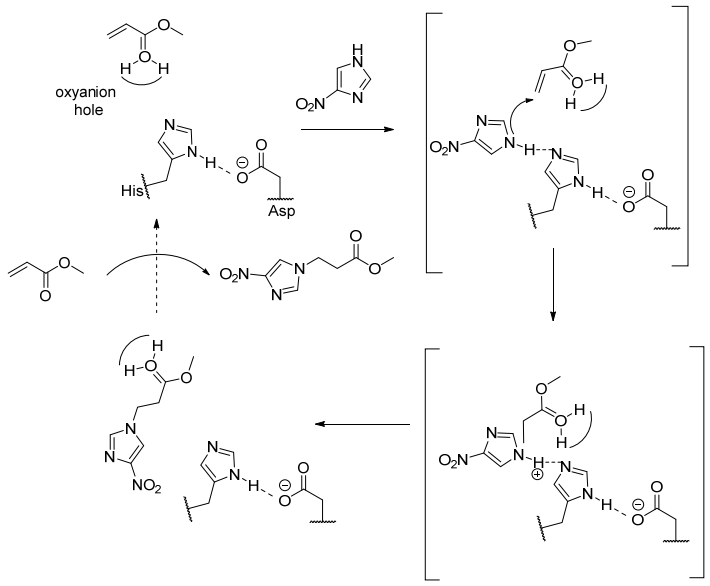
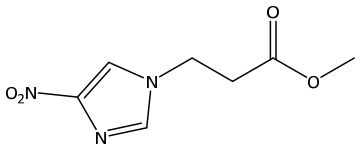


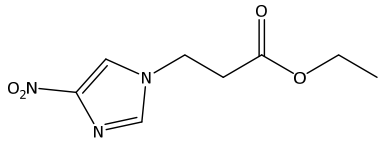
Figure 3 Mechanism of lipase catalyzed Michael addition.

Nuclear magnetic resonance (NMR) analysis

After purification of the synthesized products by column chromatography, the chemical structures of imidazoles were determined by ^{1}H NMR, ^{13}C NMR and ESI-MS.

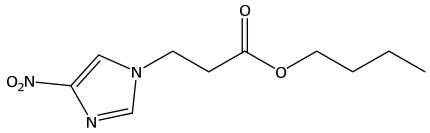


3-(4-Nitroimidazol-1-yl)-propionic acid methyl ester (3a)[1]. White solid, mp: 109°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (d, 1H, *J* = 1.1 Hz, N=CHN), 7.52 (d, 1H, *J* = 1.1 Hz, NCH=C), 4.36 (t, 2H, *J* = 6.1 Hz, NCH_2), 3.73 (s, 3H, OCH_3), 2.87 (t, 2H, *J* = 6.1 Hz, CH_2C=O); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.38 (C=O), 148.71 (C_4),136.34 (C_2), 119.33 (C_5), 52.46 (OCH_3), 43.55 (NCH_2), 35.08 (CH2C=O). ESI-MS (m/z): 200 (M+1); IR (KBr): 3079, 3042, 1729, 1526, 1485, 1336, 1204, 1179, 1153,991, 822, 760, 656 cm^{-1}.

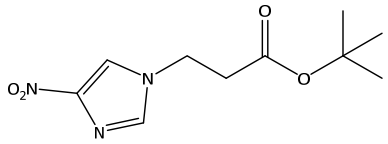


3-(4-Nitroimidazol-1-yl)-propionic acid ethyl ester (3b)[1]. White solid, mp: 36°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, 1H, *J* = 1.1 Hz, N=CHN), 7.57 (d, 1H, *J* = 1.1 Hz, NCH=C), 4.37 (t, 2H, *J* = 6.1 Hz, NCH_2), 4.14 (q, 2H, *J* = 7.1 Hz, OCH_2), 2.85 (t, 2H, *J* = 6.1 Hz, CH_2C=O), 1.23 (t, 3H, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR(125 MHz, $CDCl_3$): δ = 169.98 (C=O), 147.83 (C_4), 136.46 (C_2), 119.64 (C_5), 61.48 (OCH_2), 43.63 (NCH_2), 35.18 (CH_2C=O), 13.98 (CH_2CH_3); ESI-MS (m/z): 214 (M+1); IR (KBr): 3079, 2979, 1732, 1525, 1486, 1455,1339, 1201, 990, 880, 824,

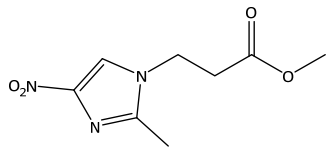
654 cm^{-1}.



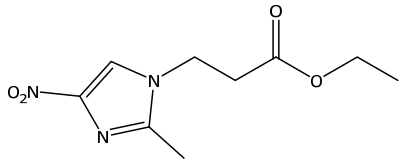
3-(4-Nitroimidazol-1-yl)-propionic acid butyl ester (3c)[1]. White solid, mp: 48°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, 1H, *J* = 1.1 Hz, N=CHN), 7.58 (d, 1H, *J* = 1.1 Hz, NCH=C), 4.37 (t, 2H, *J* = 6.1 Hz, NCH_2), 4.09 (t, 2H, J = 6.6 Hz, OCH_2), 2.86 (t, 2H, *J* = 6.1 Hz, CH_2C=O), 1.57 (m, 2H, $CH_2CH_2CH_2$), 1.31 (m, 2H, $CH_2CH_2CH_3$), 0.89 (t, 3H, J = 7.4 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.08 (C=O), 147.82 (C_4), 136.45 (C_2), 119.62 (C_5), 65.36 (OCH_2), 43.66 (NCH_2), 35.16 (CH_2C=O), 30.37 ($CH_2CH_2CH_2$), 18.92 (CH_2CH_3), 13.50 (CH_2CH_3); ESI-MS (m/z): 242 (M+1); IR (KBr): 2963, 1727, 1524, 1488, 1338, 1296, 1205, 990, 880, 823, 655 cm^{-1}.



3-(4-Nitroimidazol-1-yl)-propionic acid *tert*-butyl ester (3d)[1]. White solid, mp: 50°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, 1H, *J* = 1.1 Hz, N=CHN), 7.51 (d, 1H, *J* = 1.1 Hz, NCH=C), 4.31 (t, 2H, *J* = 6.1 Hz, NCH_2), 2.76 (t, 2H, *J* = 6.1 Hz, CH_2C=O), 1.43 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.12 (C=O), 147.71 (C_4), 136.34 (C_2), 119.38 (C_5), 82.51 ($OC(CH_3)_3$), 43.83 (NCH_2), 36.37 (O=CCH_2), 27.97 ($C(CH_3)_3$); ESI-MS (m/z): 242 (M+1); IR (KBr): 2976, 1728, 1526, 1486, 1342, 1167, 991, 882, 824, 759, 654 cm^{-1}.

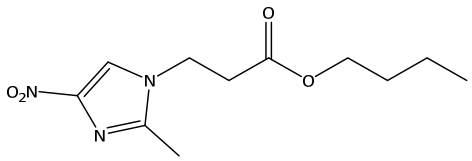


3-(2-Methyl-4-nitroimidazol-1-yl)-propionic acid methyl ester (3f)[2]. Syrupy liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 (s, 1H, NCH=C), 4.23 (t, 2H, *J* = 6.4 Hz, NCH_2), 3.66 (s, 3H, OCH_3), 2.81 (t, 2H, *J* = 6.4 Hz, CH_2C=O), 2.43 (s, 3H, N=CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.21 (C=O), 146.35 (C_4), 144.81 (C_2), 119.82 (C_5), 52.20 (OCH_3), 42.24 (NCH_2), 34.25 (CH_2C=O), 12.87 (N=CCH_3); ESI-MS (m/z): 214(M+1); IR (KBr): 3104, 1737, 1540, 1496, 1329, 1212, 1145, 997, 848, 826, 758, 677, 561 cm^{-1}.

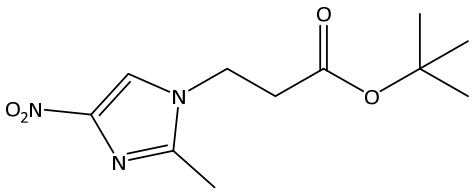


3-(2-Methyl-4-nitroimidazole-1-yl)-propionic acid Ethyl ester (3g)[2]. Syrupy liquid; ^{1}H NMR (500 MHz,

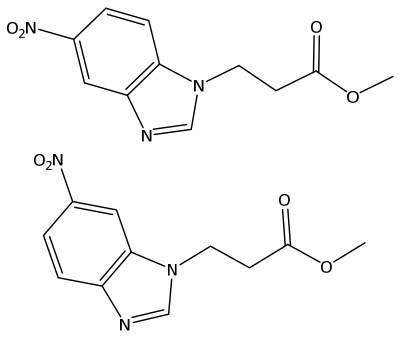
$CDCl_3$): δ = 7.74 (s, 1H, NCH=C), 4.20 (t, 2H, *J* = 6.4 Hz, NCH_2), 4.07 (q, 2H, *J* = 7.1 Hz, OCH_2), 2.77 (t, 2H, *J* = 6.4 Hz, $O=CCH_2$), 2.40 (s, 3H, $N=CCH_3$), 1.16 (t, 3H, *J* = 7.1 Hz, $CH_2\underline{C}H_3$). ^{13}CNMR (125 MHz, $CDCl_3$): δ = 169.71 (C=O), 146.21 (C_4), 144.77 (C_2), 119.87 (C_5), 61.24 (OCH_2), 42.23 (NCH_2), 34.40 ($O=C\underline{C}H_2$), 13.82 ($N=C\underline{C}H_3$), 12.79 ($CH_2\underline{C}H_3$). ESI–MS (*m/z*): 228 (*M* + 1); IR (KBr): 3142, 2991, 1729, 1537, 1500, 1408, 1322, 1292, 1202, 1024, 945, 826, 805, 754, 556 cm^{-1}.



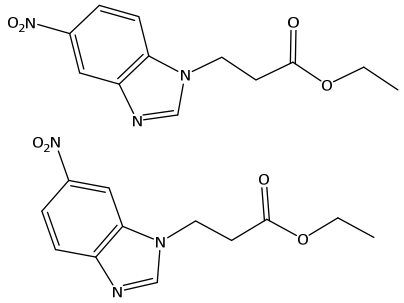
3-(2-Methyl-4-nitroimidazole-1-yl)-propionic acid butyl ester (3h)[2]. Hazel columnar crystal, mp: 41°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (s, 1H, NCH=C), 4.14 (t, 2H, *J* = 6.4 Hz, NCH_2), 3.92 (t, 2H, *J* = 6.7 Hz, OCH_2), 2.71 (t, 2H, *J* = 6.4 Hz, $O=CCH_2$), 2.31 (s, 3H, $N=CCH_3$), 1.41 (m, 2H, $CH_2\underline{C}H_2CH_2$), 1.14 (m, 2H, $C\underline{H}_2CH_3$), 0.72 (t, 3H, *J* = 7.4 Hz, $CH_2\underline{C}H_3$). ^{13}CNMR (125 MHz, $CDCl_3$): δ = 169.95 (O=C), 146.08 (C_4), 144.91 (C_2), 120.11 (C_5), 65.02 (OCH_2), 42.32 (NCH_2), 34.37 ($O=C\underline{C}H_2$), 30.24 ($OCH_2\underline{C}H_2$), 18.77 ($\underline{C}H_2CH_3$), 13.35 ($N=C\underline{C}H_3$), 12.76 ($CH_2\underline{C}H_3$). ESI–MS (*m/z*): 256 (*M* + 1); IR (KBr): 3102, 2963, 2937, 1729, 1542, 1505, 1415, 1325, 1292, 1209, 1146, 999, 826, 758, 562 cm^{-1}.



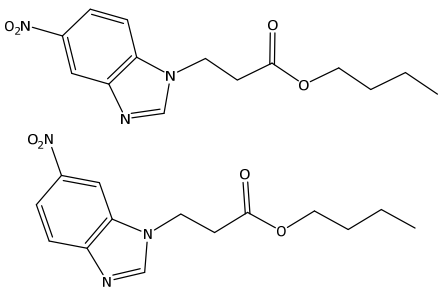
3-(2-Methyl-4-nitroimidazole-1-yl)-propionic acid *tert*-butyl ester (3i). Hazel columnar crystal, mp: 45°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75(s, 1H, NCH=C), 4.18 (t, 2H, *J* = 6.4 Hz, NCH_2), 2.71 (t, 2H, *J* = 6.4 Hz, $O=CCH_2$), 2.45 (s, 3H, $N=CCH_3$), 1.40 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.95 (O=C), 146.11 (C_4), 144.77 (C_2), 119.74 (C_5), 82.35 ($O\underline{C}(CH_3)_3$), 42.56 (NCH_2), 35.70 ($O=C\underline{C}H_2$), 27.90 ($OC(\underline{C}H_3)_3$), 13.01 ($N=C\underline{C}H_3$). ESI–MS (*m/z*): 256 (*M* + 1); IR (KBr): 3109, 2979, 1727, 1537, 1499, 1415, 1318, 1290, 1143, 999, 828, 758 cm^{-1}.



3-(6-nitro-benzimidazole-1-yl)-propionic acid methyl ester and 3-(5-nitro-benzimidazole-1-yl)-propionic acid methyl ester (3p). Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.71 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.40 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.27-8.20 (m, 4H, Ar-H), 7.87 (d, 1H, *J* = 8.9 Hz, Ar-H), 7.50 (d, 1H, *J* = 8.9 Hz, Ar-H), 4.60 (m, 4H, NCH_2), 3.69 (s, 6H, OCH_3), 2.94 (m, 4H, $O{=}CCH_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.71, 147.97, 146.78, 143.99, 143.90, 143.09, 137.54, 132.77, 120.66, 118.96, 118.19, 117.25, 109.45, 106.47, 52.32, 40.82, 40.77, 34.09. ESI–MS (*m*/*z*): 250 (*M* + 1); IR (KBr): 2957, 1726, 1519, 1435, 1340, 1205, 1176, 980, 935, 788, 739 cm^{-1}.

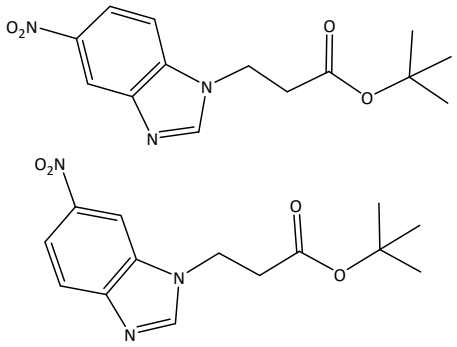


3-(6-nitro-benzimidazole-1-yl)-propionic acid Ethyl ester and 3-(5-nitro-benzimidazole-1-yl)-propionic acid Ethyl ester (3q). yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.52 (d, 1H, *J* = 2.1 Hz, Ar-H), 8.32 (d, 1H, *J* = 2.1 Hz, Ar-H), 8.24 (s, 1H, Ar-H), 8.16 (s, 1H, Ar-H), 8.06 (m, 2H, Ar-H), 7.72 (d, 1H, *J* = 8.9 Hz, Ar-H), 7.45 (d, 1H, *J* = 8.9 Hz, Ar-H) 4.54 (m, 4H, NCH_2), 4.02 (m, 4H, OCH_2), 2.87 (m, 4H, $O{=}CCH_2$), 1.10 (m, 6H, $OCH_2C\underline{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.20, 147.59, 146.68, 145.78, 144.28, 144.05, 141.75, 137.25, 132.47, 119.98, 119.16, 118.73, 116.67, 109.90, 106.99, 61.45, 41.20, 34.25, 13.99. ESI–MS (*m*/*z*): 264 (*M* + 1); IR (KBr): 3095, 2976, 1716, 1510, 1337, 1295, 1199, 1167, 1061, 1013, 889, 824, 740 cm^{-1}.



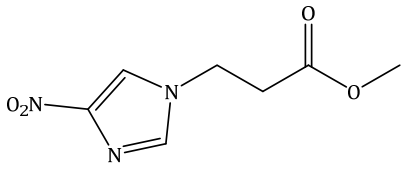
3-(6-nitro-benzimidazole-1-yl)-propionic acid Butyl ester and 3-(5-nitro-benzimidazole-1-yl)-propionic acid Butyl ester (3r)[3]. Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.89 (s, 1H, Ar-H), 8.75 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.63 (s, 1H, Ar-H), 8.51 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.30 (m, 2H, Ar-H), 7.96 (d, 1H, *J* = 8.9 Hz, Ar-H), 7.60 (d, 1H, *J*

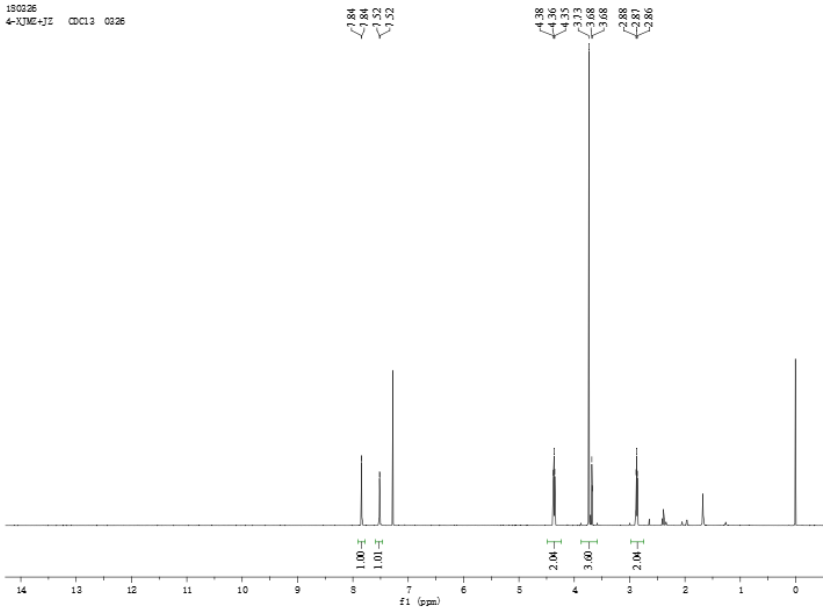
= 8.9 Hz, Ar-H), 4.68 (m, 4H, NCH_2), 4.07 (m, 4H, OCH_2), 2.98 (m, 4H, $O=CCH_2$), 1.67 (m, 4H, $OCH_2C\underline{H_2}$), 1.28 (m, 4H, $C\underline{H_2}CH_3$), 0.90 (t, *J* = 7.2 Hz, 6H, $CH_2C\underline{H_3}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.36, 147.35, 146.57, 144.30, 140.94, 137.04, 132.28, 119.71, 119.44, 119.21, 116.49, 110.17, 107.28, 65.43, 41.39, 34.25, 30.40, 18.97, 13.58. ESI–MS (*m*/*z*): 292 (*M* + 1); IR (KBr): 3436, 3093, 1725, 1518, 1435, 1384, 1341, 1206, 1176, 788, 739 cm^{-1}.



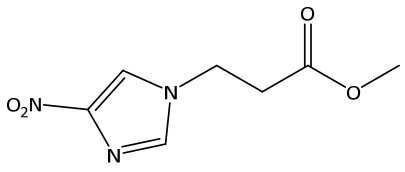
3-(6-nitro-benzimidazole-1-yl)-propionic acid *tert*-butyl ester and 3-(5-nitro-benzimidazole-1-yl)-propionic acid *tert*-butyl ester (3s). Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.42 (d, 1H, *J* = 2.0 Hz, Ar-H), 8.29-8.21 (m, 4H, Ar-H), 7.88 (d, 1H, *J* = 8.9 Hz, Ar-H), 7.51 (d, 1H, *J* = 8.9 Hz, Ar-H), 4.55 (m, 4H, NCH_2), 2.84 (m, 4H, $O=CCH_2$), 1.39 (s, 18H, $OC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.48, 147.91, 146.77, 143.98, 142.94, 137.57, 132.78, 120.53, 118.90, 118.21, 117.17, 109.61, 106.65, 82.28, 82.25, 41.09, 41.03, 35.46, 35.39, 27.96. ESI–MS (*m*/*z*): 292 (*M* + 1); IR (KBr): 2978, 1725, 1517, 1371, 1345, 1231, 1157, 1061, 884, 843, 796, 741 cm^{-1}.

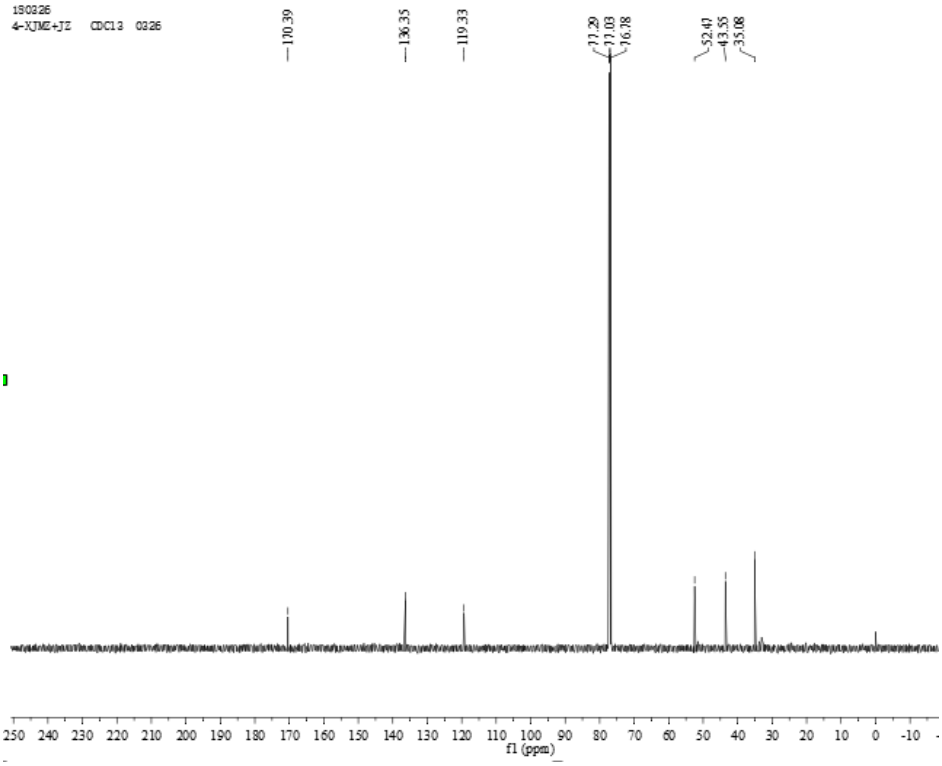
^{1}H-NMR of compound 3a



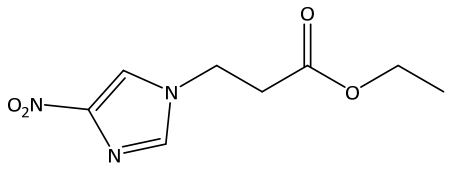


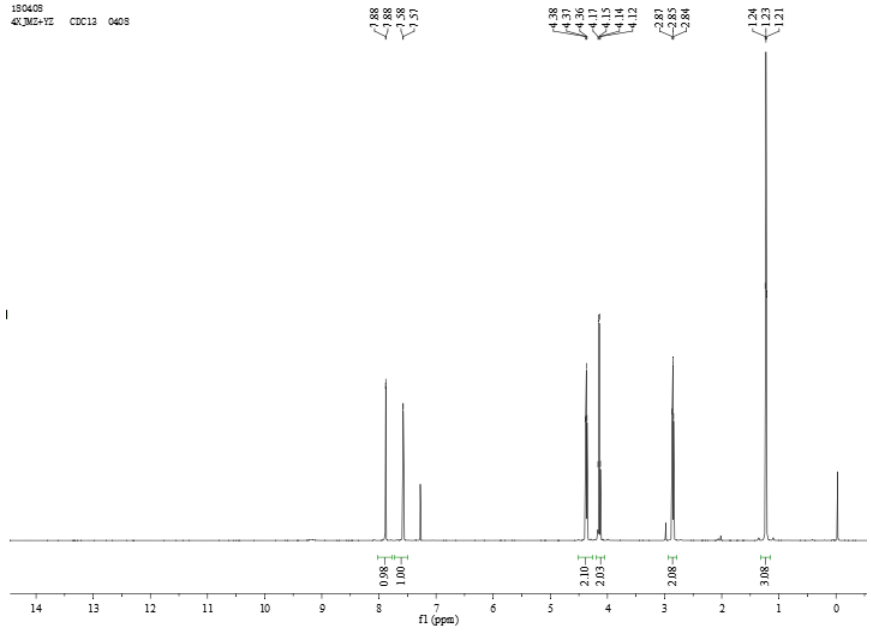
^{13}C-NMR of compound 3a



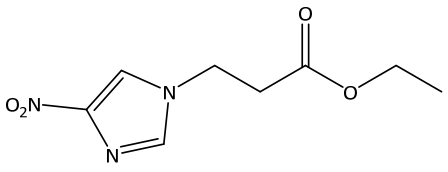


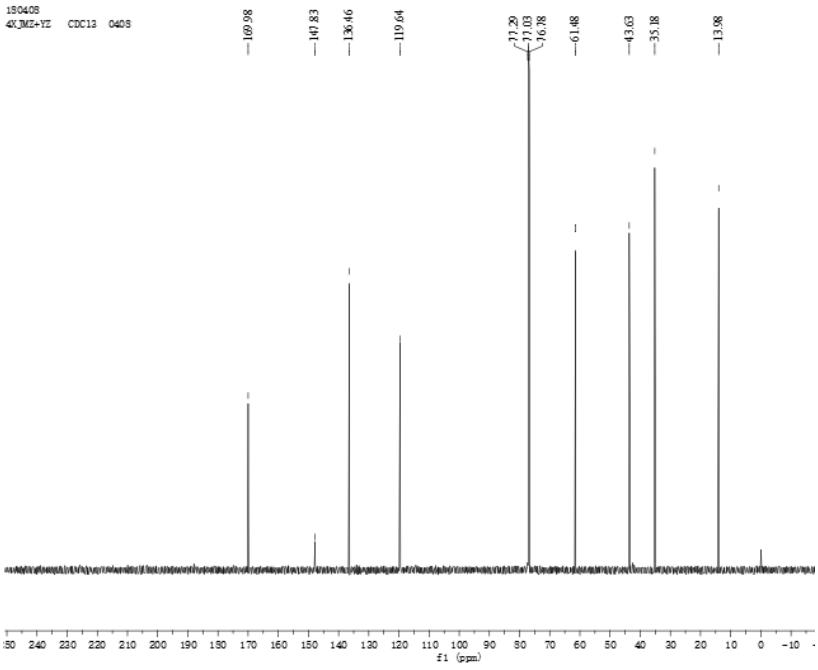
^{1}H-NMR of compound 3b



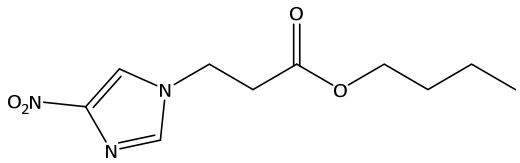


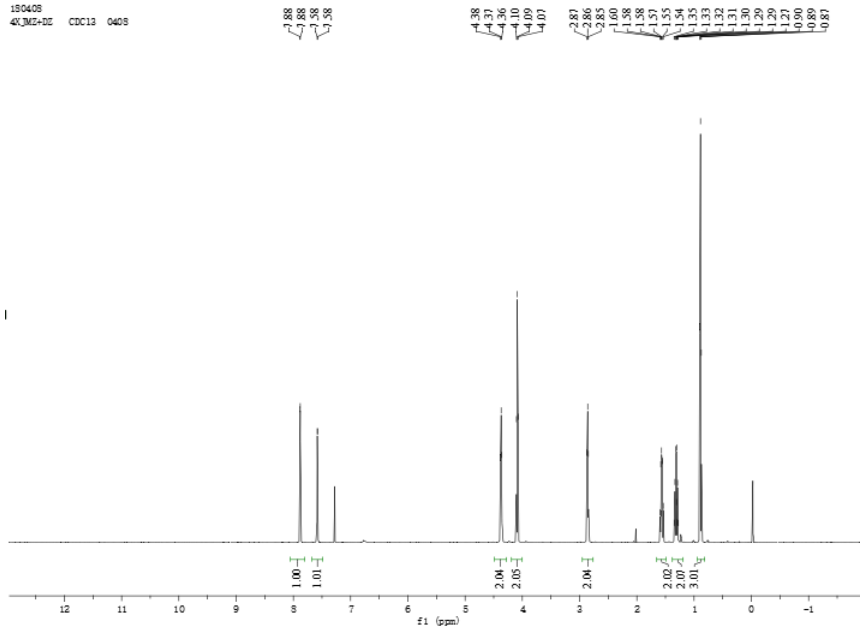
^{13}C-NMR of compound 3b



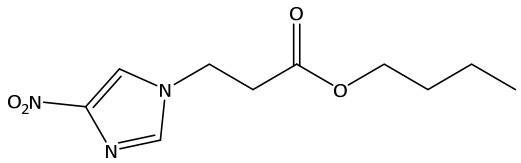


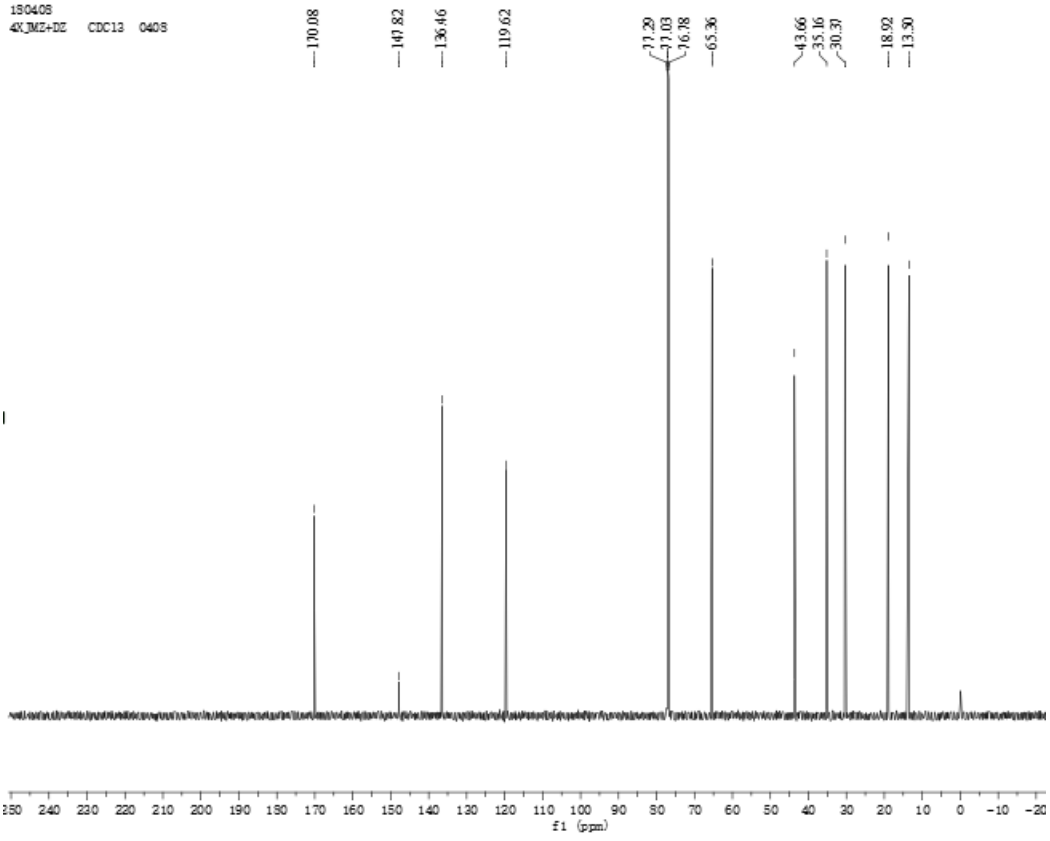
^{1}H-NMR of compound 3c



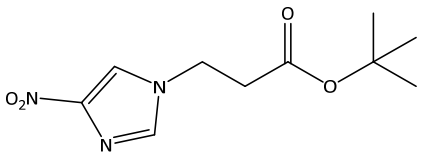


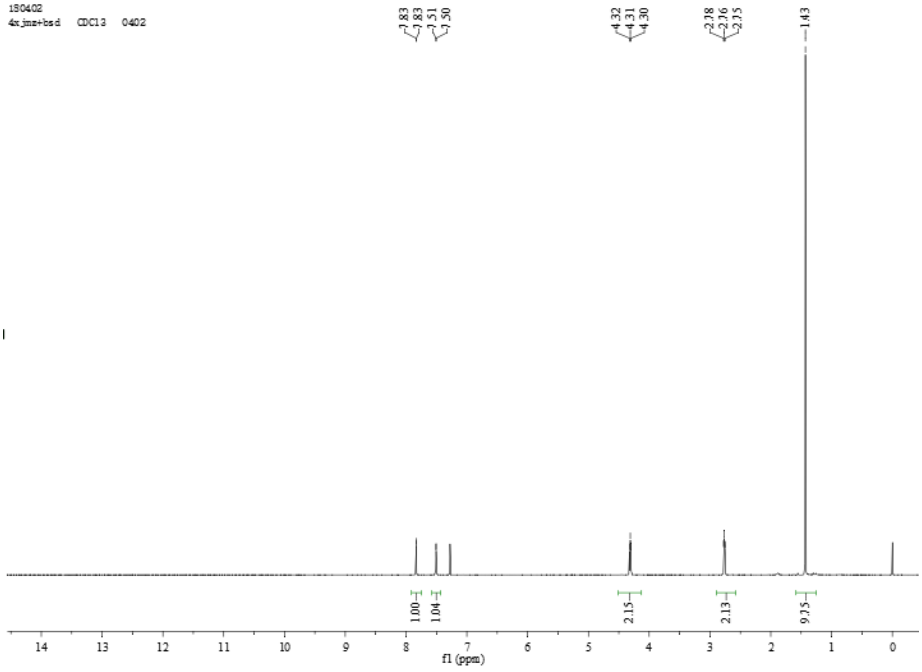
^{13}C-NMR of compound 3c



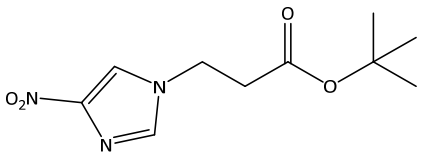


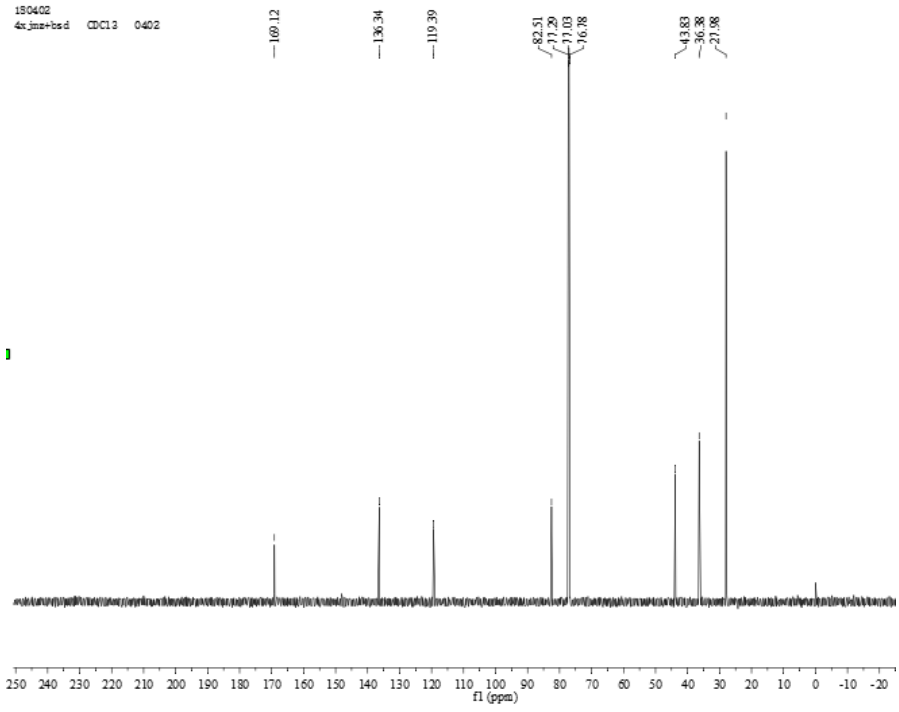
^{1}H-NMR of compound 3d



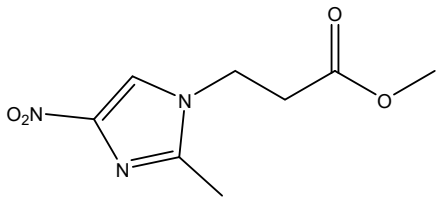


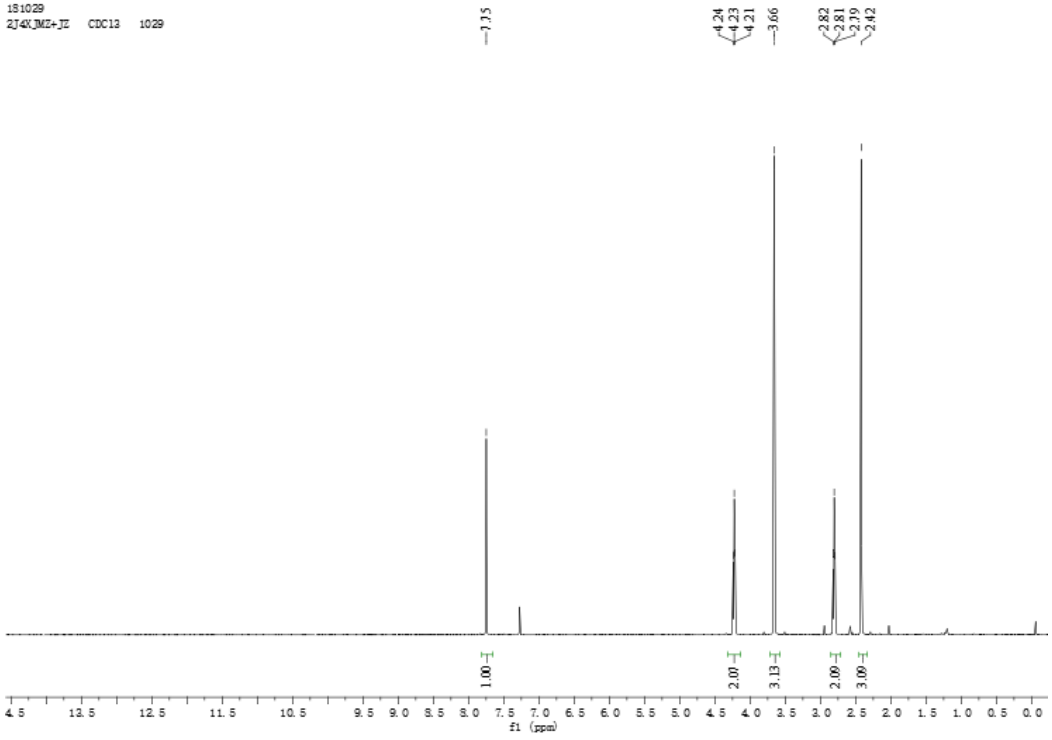
^{13}C-NMR of compound 3d





^{1}H-NMR of compound 3f





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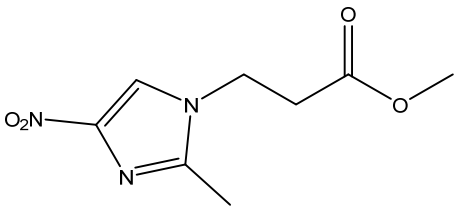
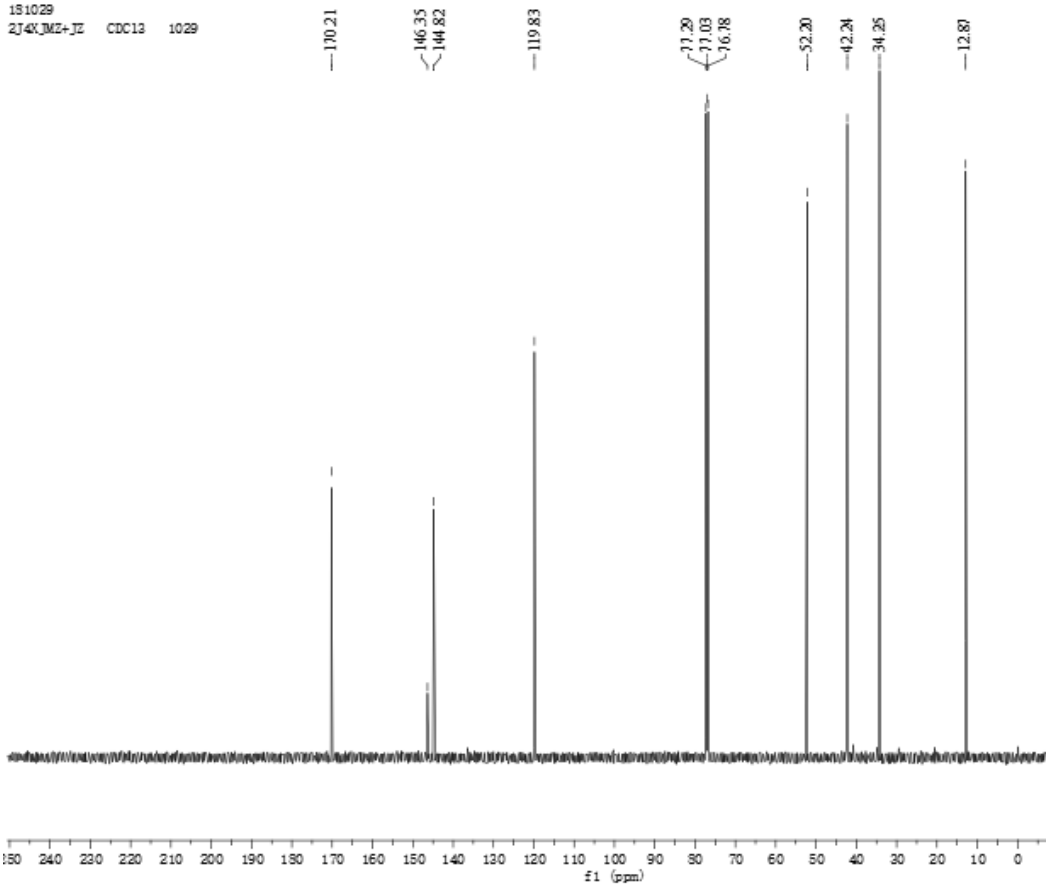
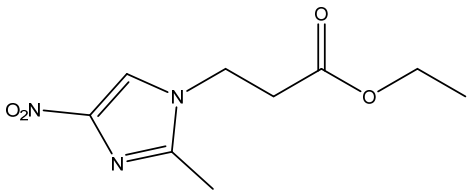
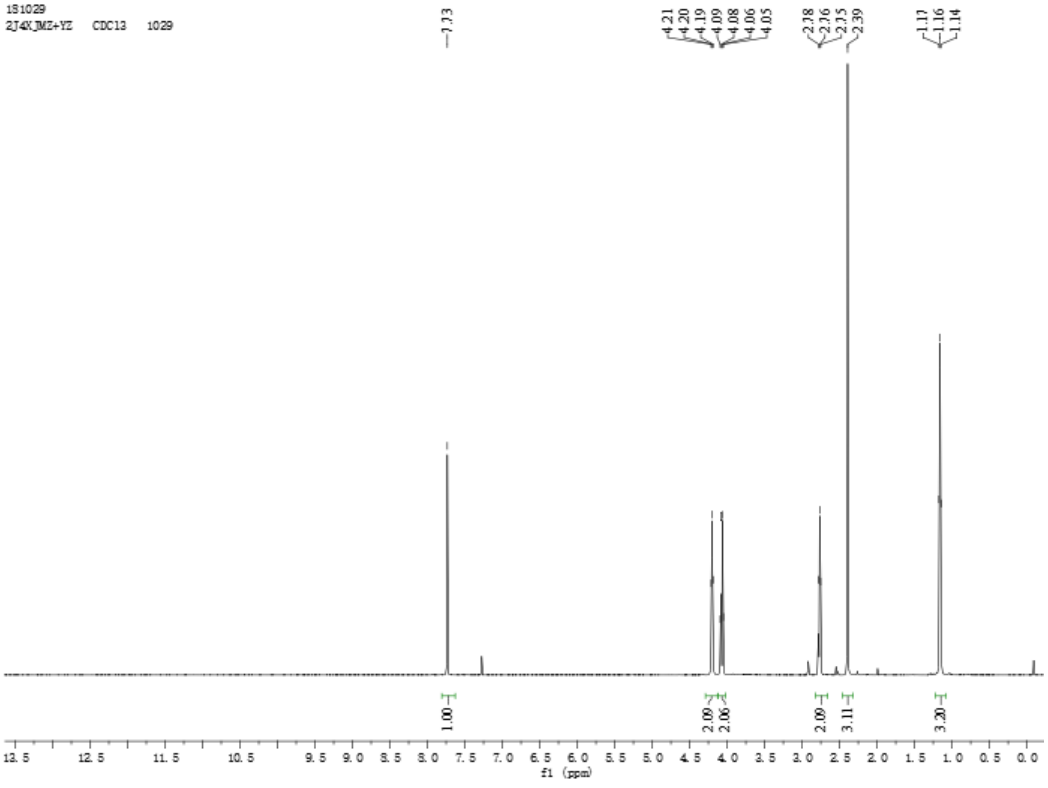


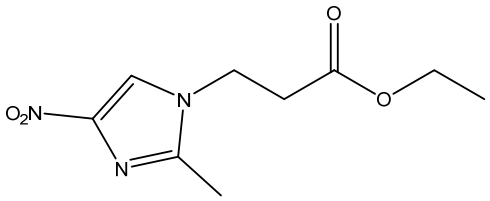


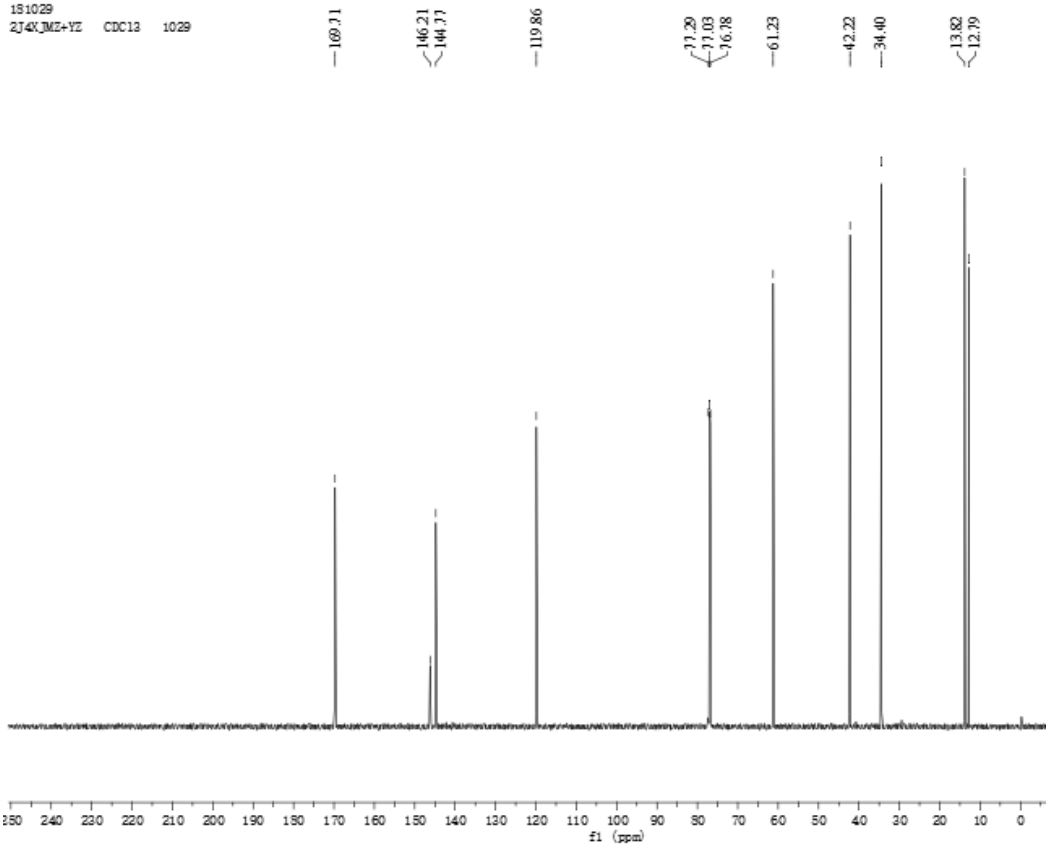
^{1}H-NMR of compound 3g



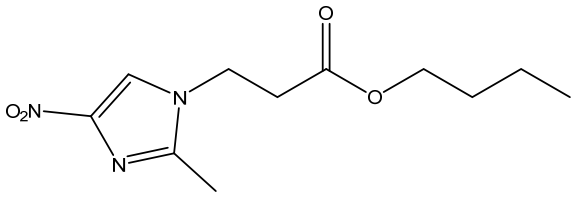


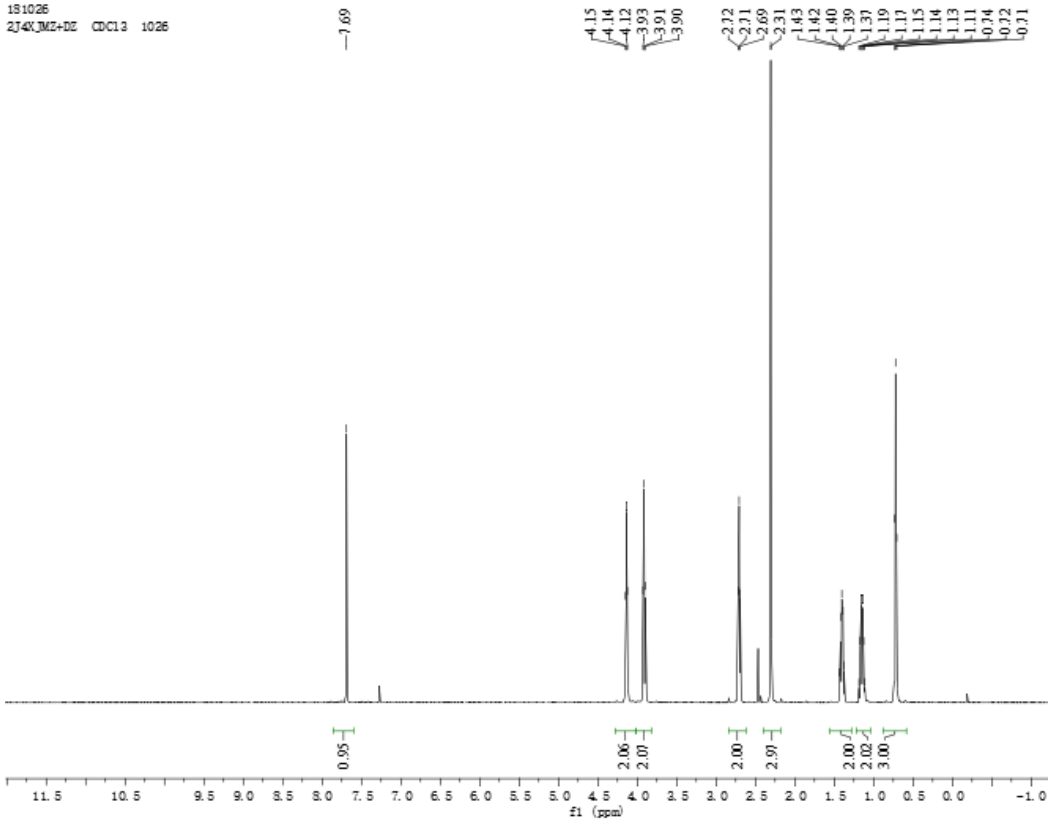
^{13}C-NMR of compound 3g



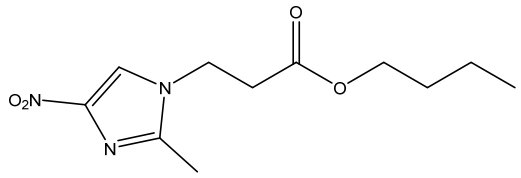


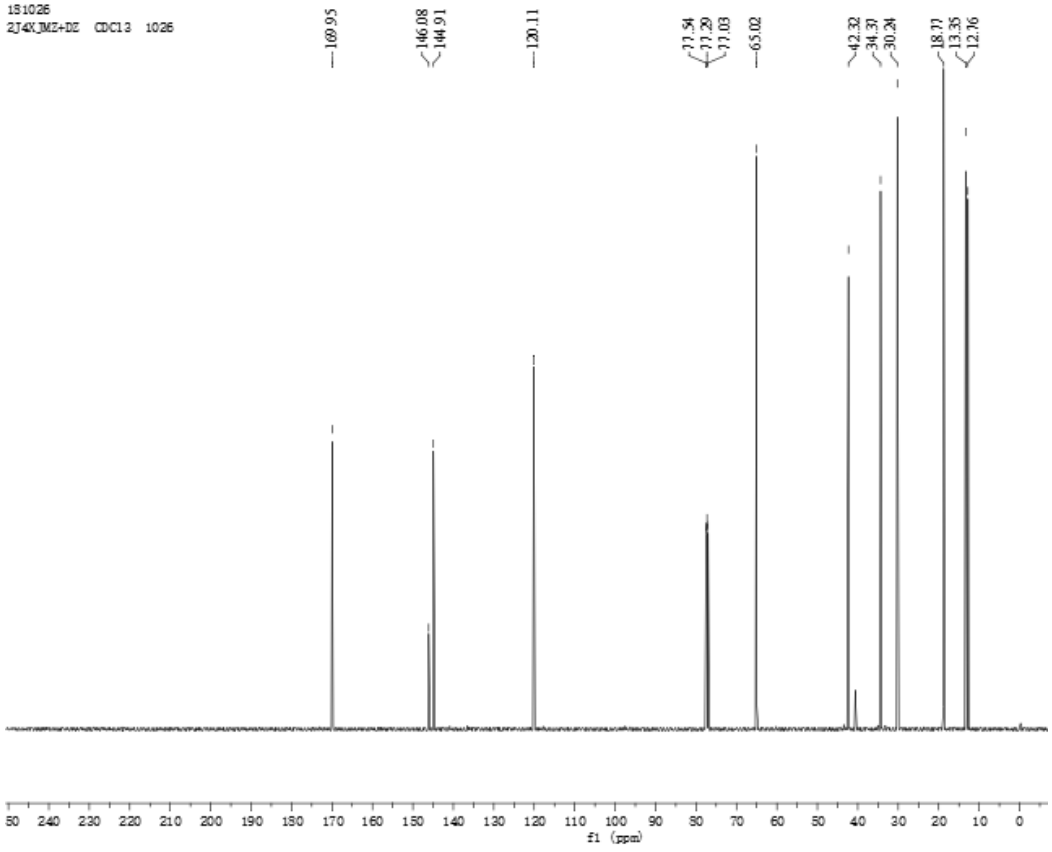
^{1}H-NMR of compound 3h



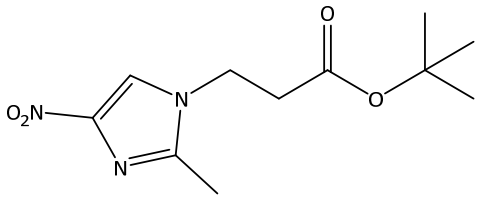


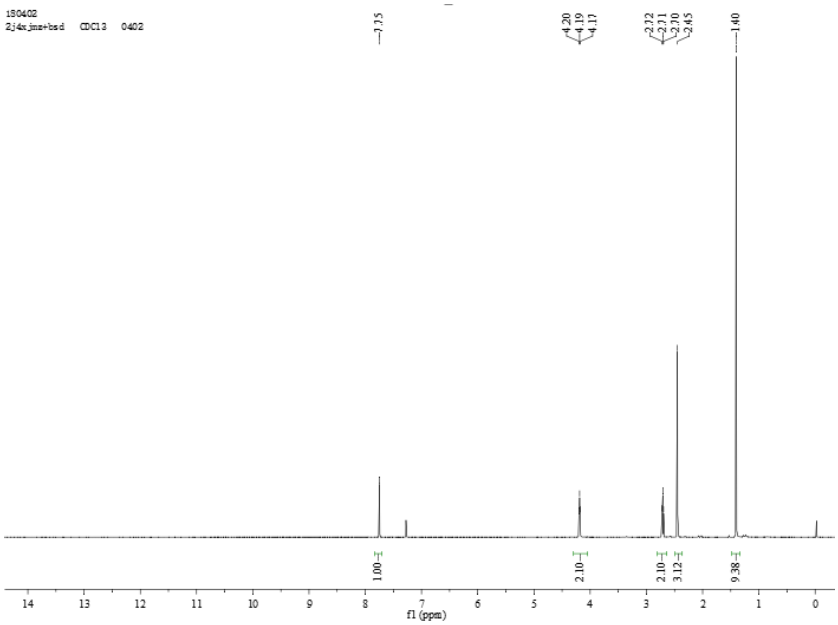
^{13}C-NMR of compound 3h



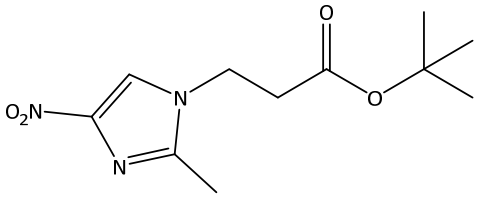


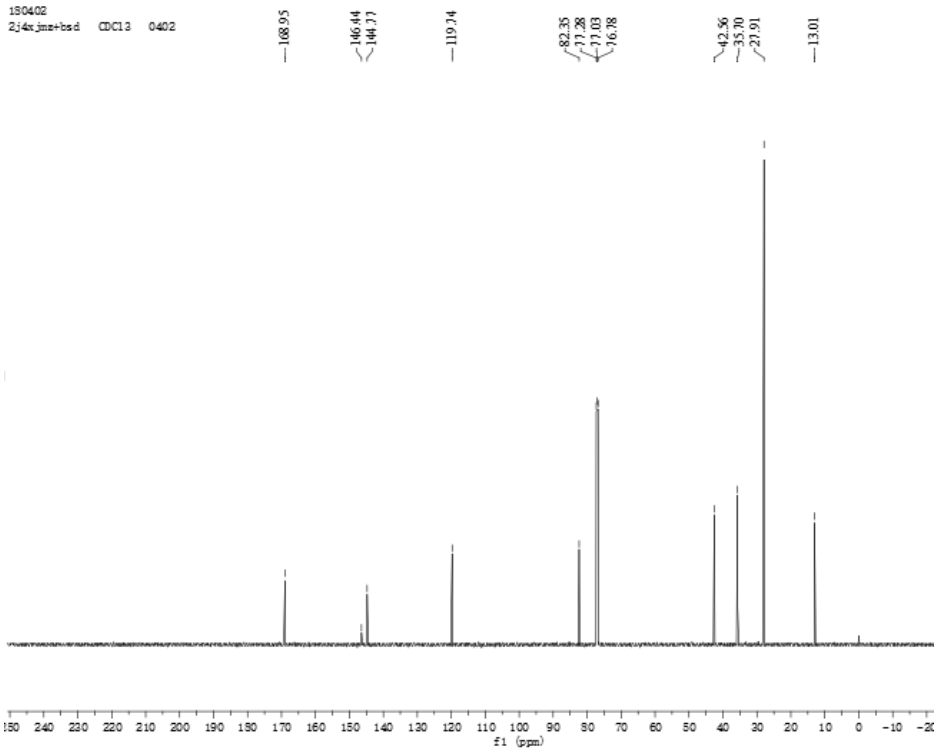
^{1}H-NMR of compound 3i



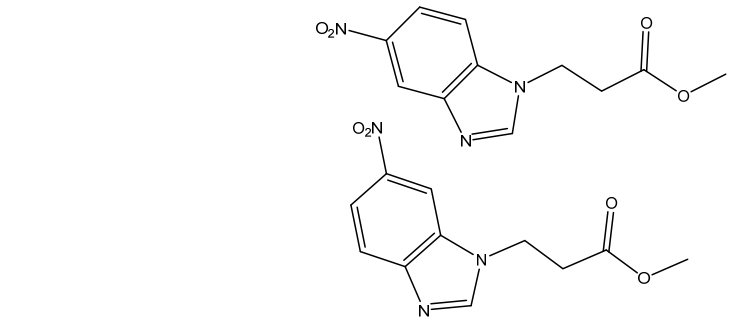


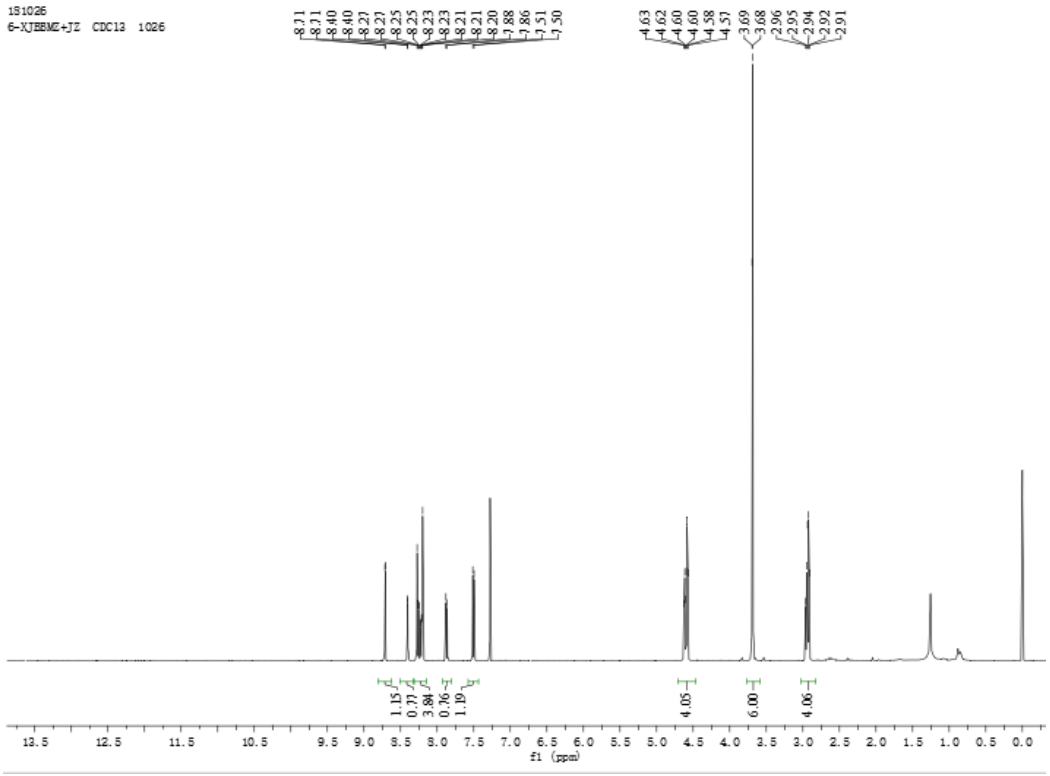
^{13}C-NMR of compound 3i



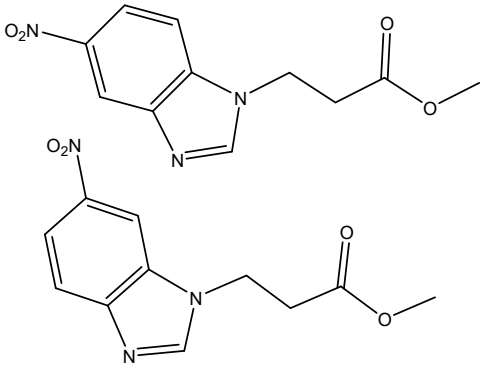


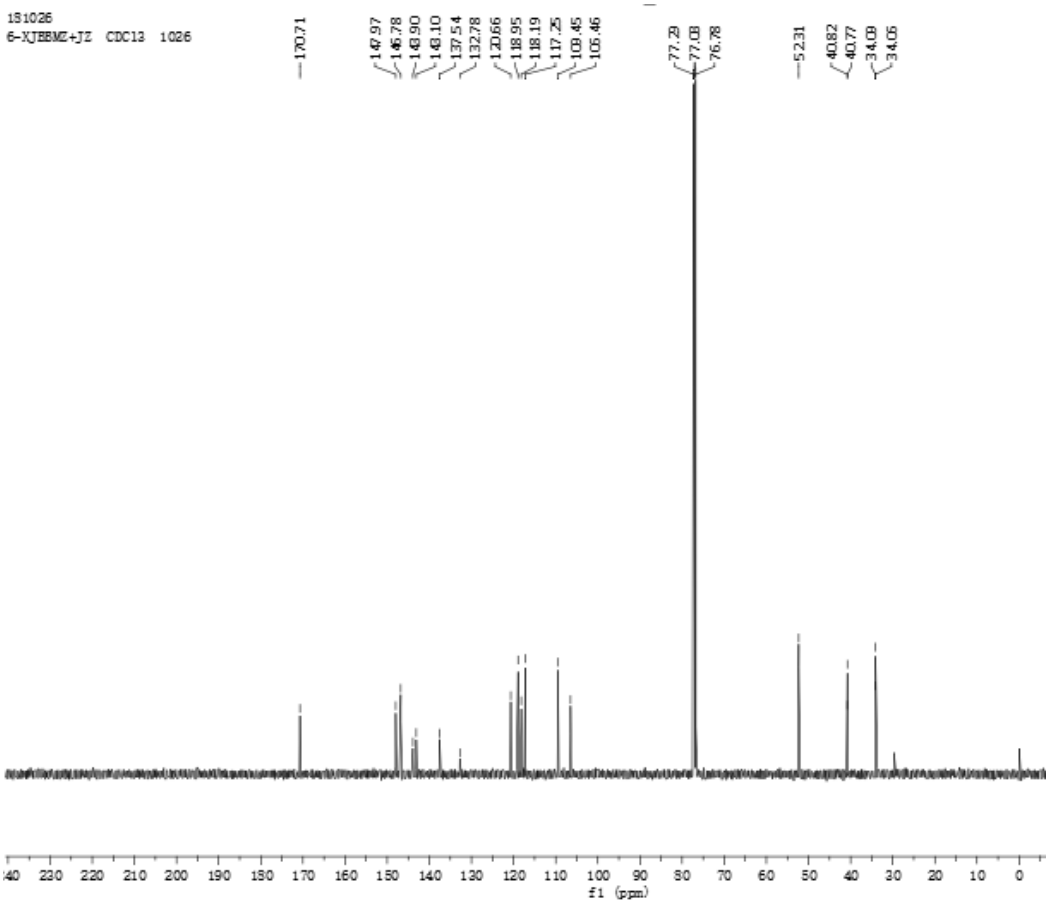
^{1}H-NMR of compound 3p



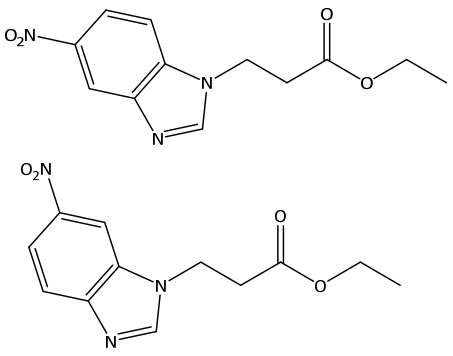


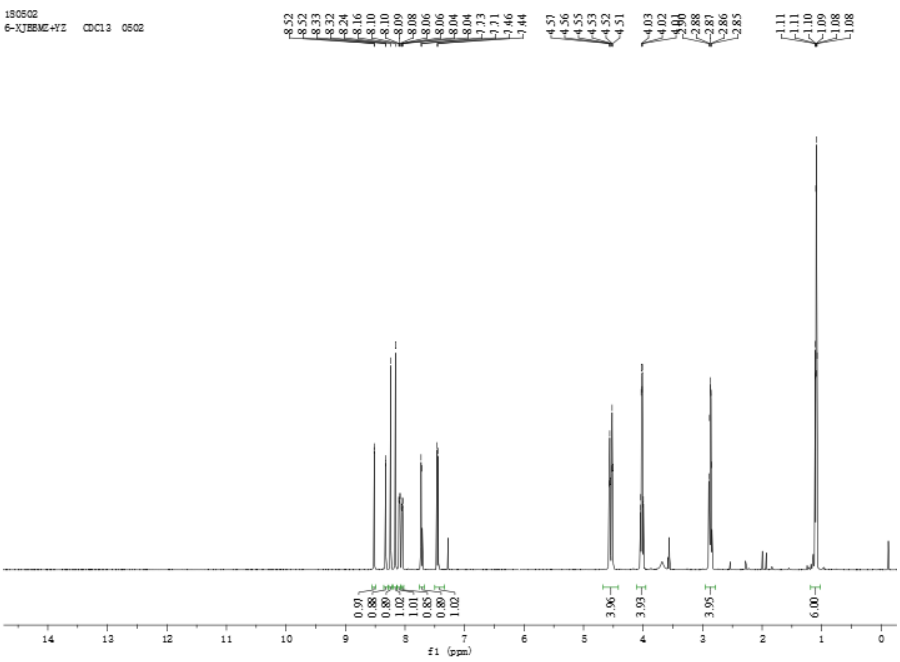
^{13}C-NMR of compound 3p



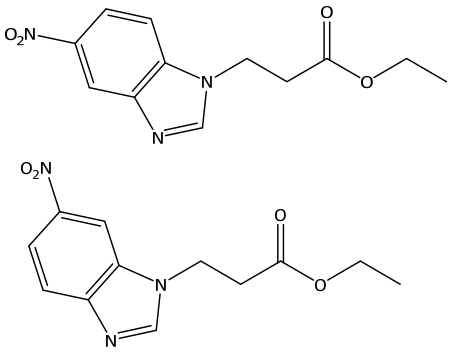


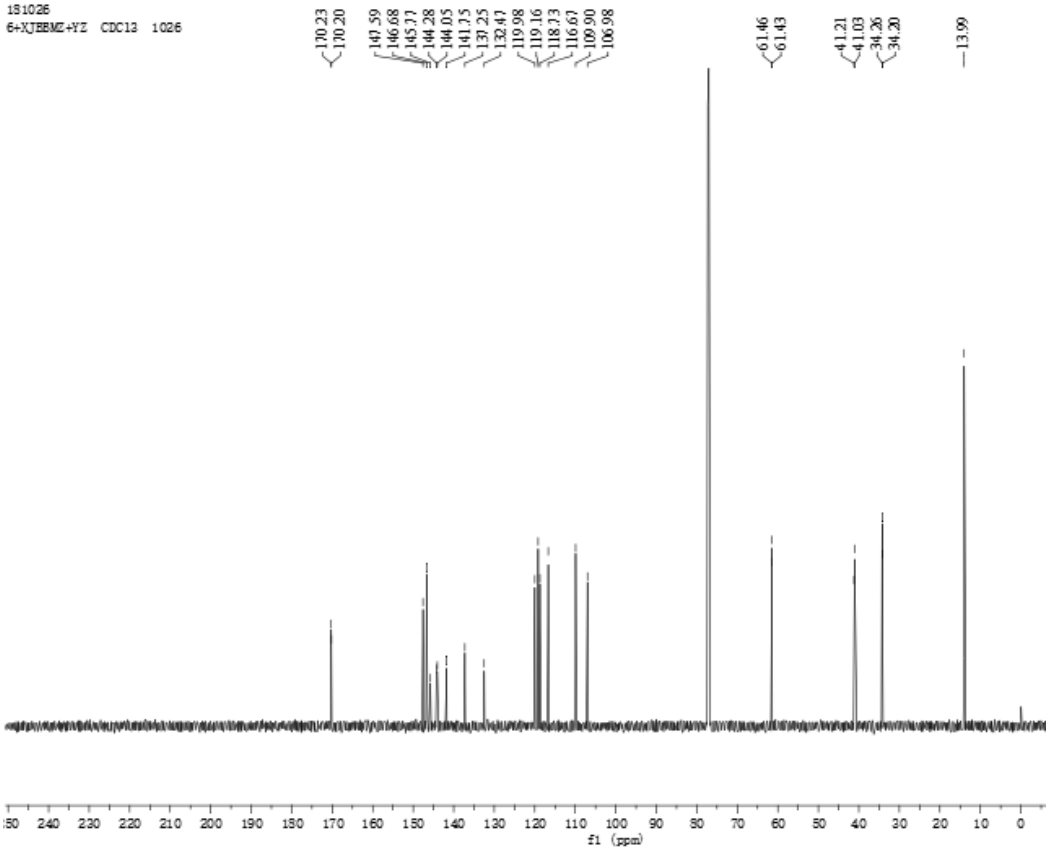
^{1}H-NMR of compound 3q



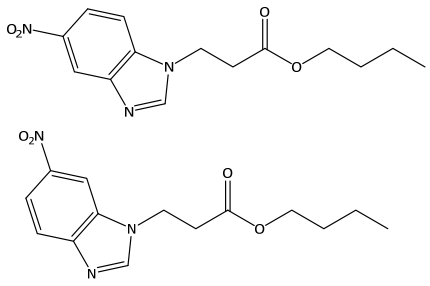


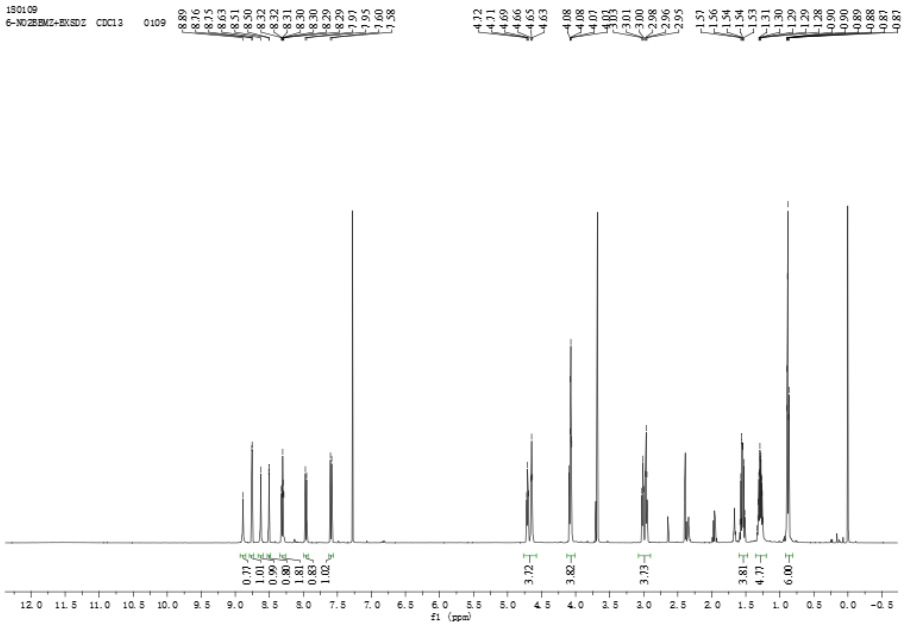
^{13}C-NMR of compound 3q



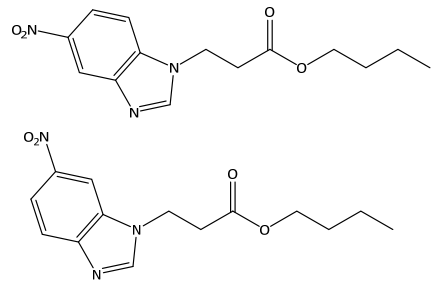


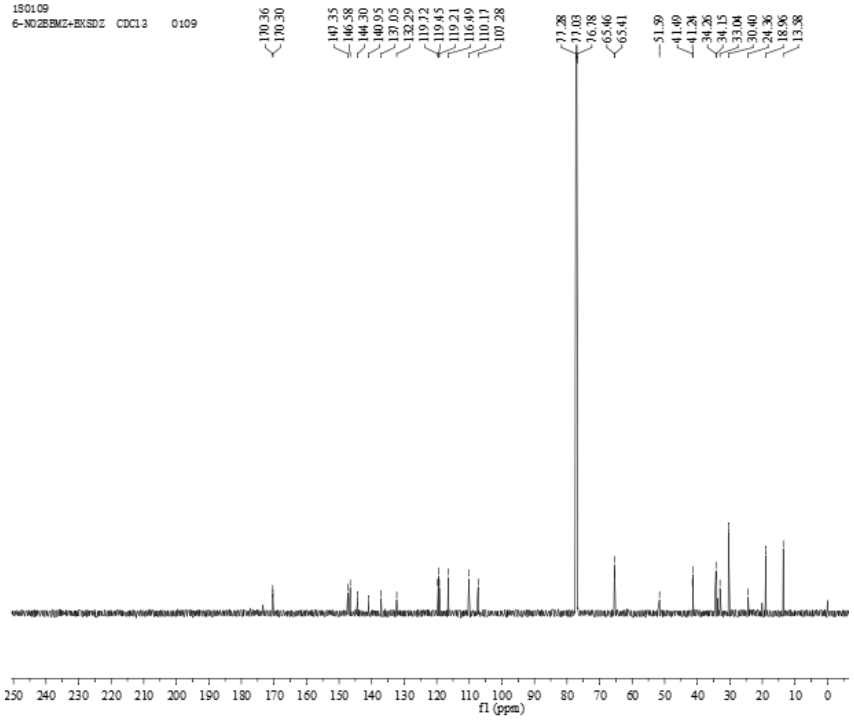
^{1}H-NMR of compound 3r



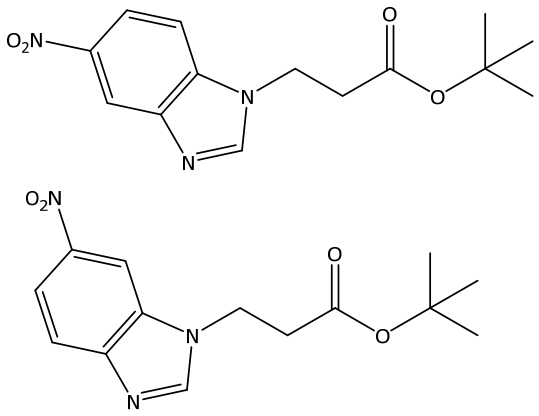


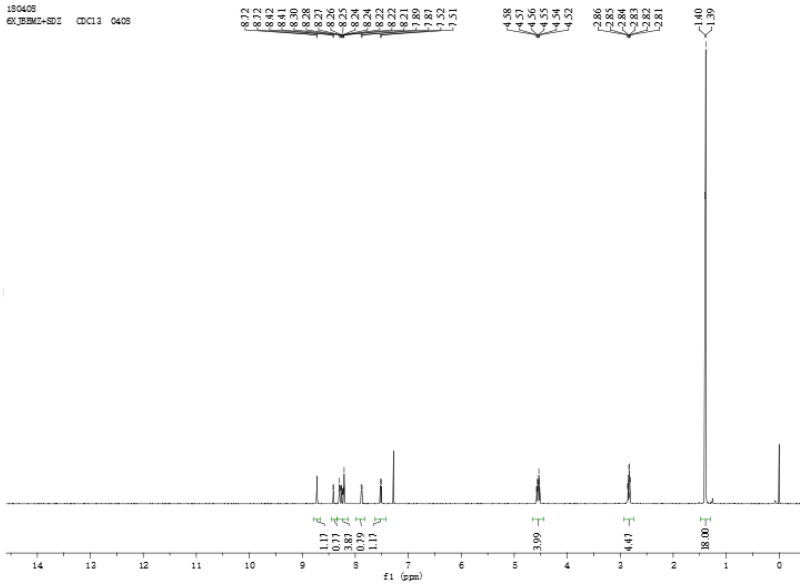
^{13}C-NMR of compound 3r



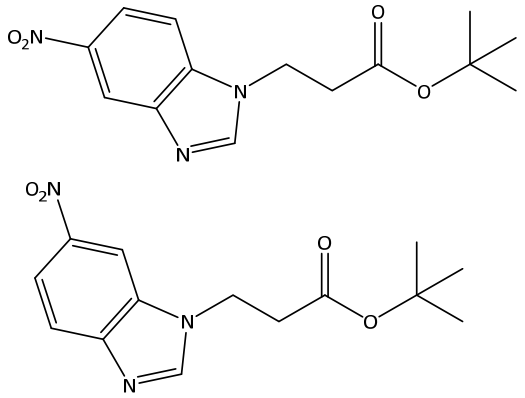


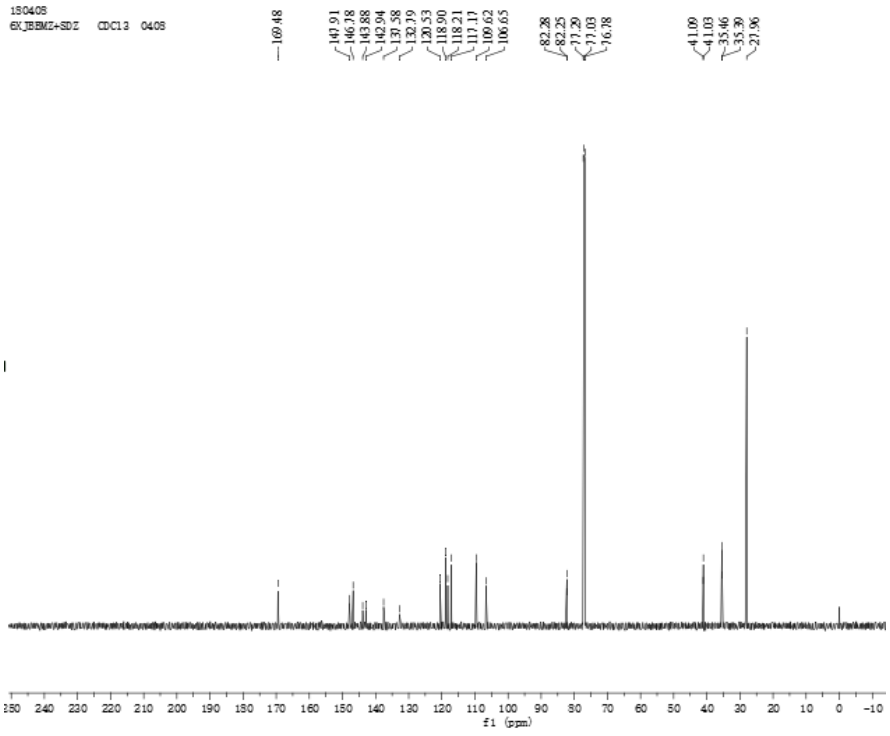
^{1}H-NMR of compound 3s





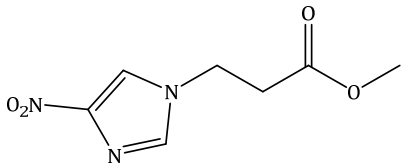
^{13}C-NMR of compound 3s

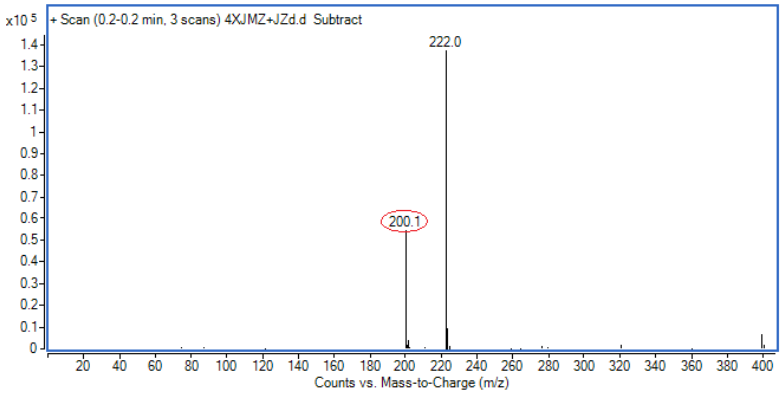




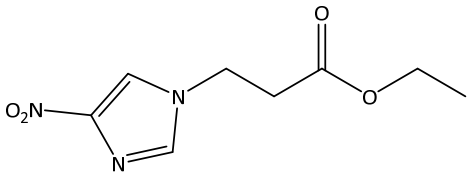
The Mass spectrum of compound

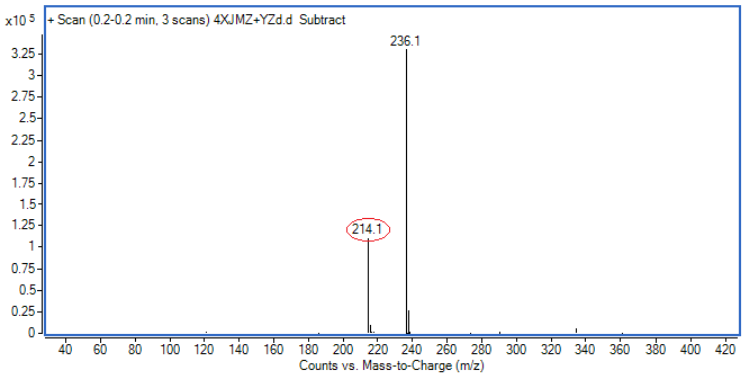
compound 3a



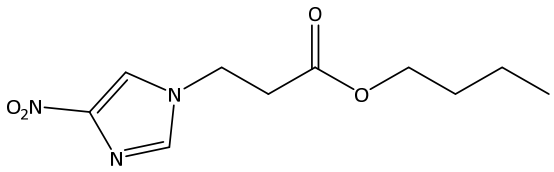


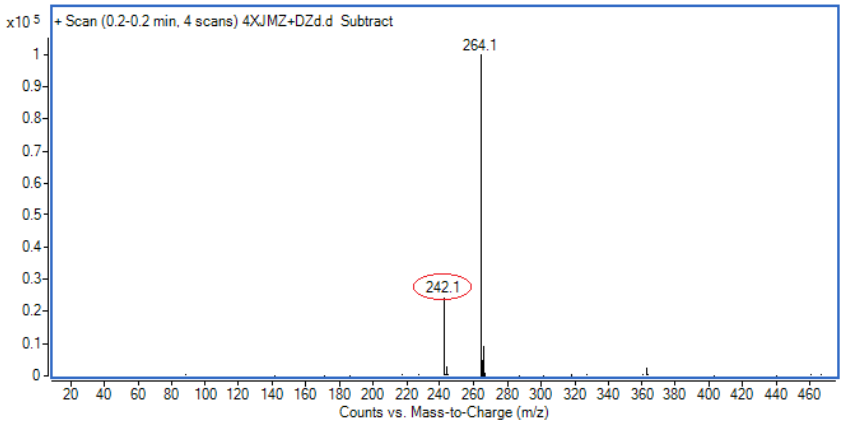
compound 3b



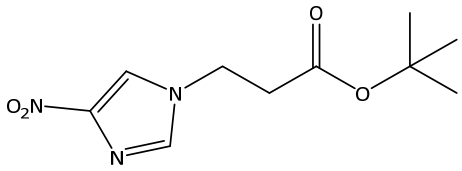


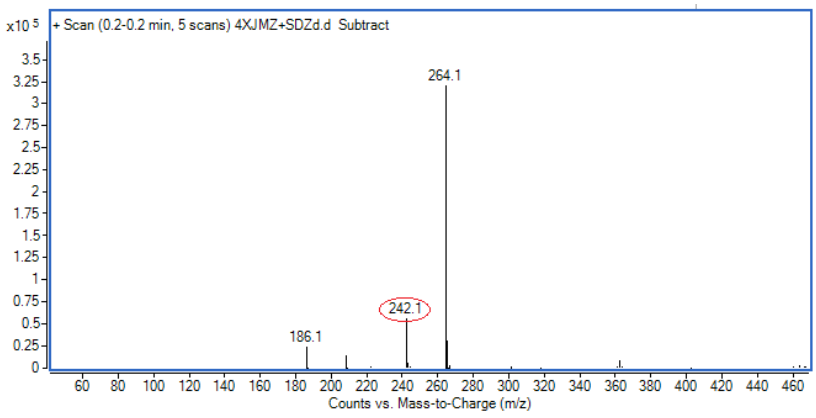
compound 3c



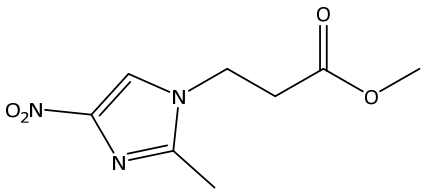


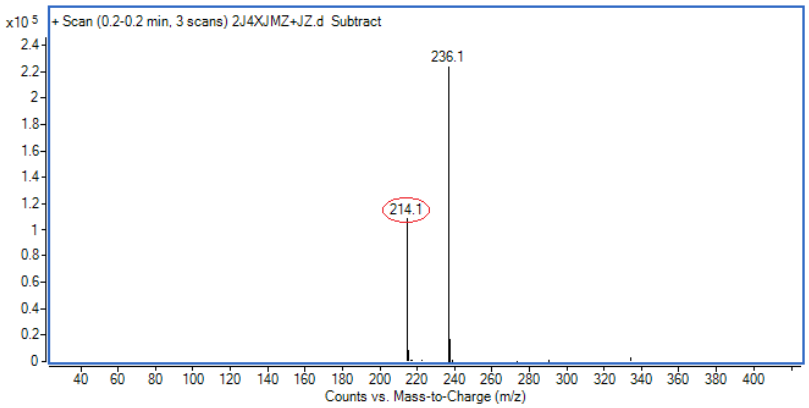
compound 3d



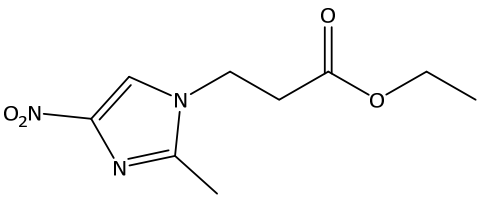


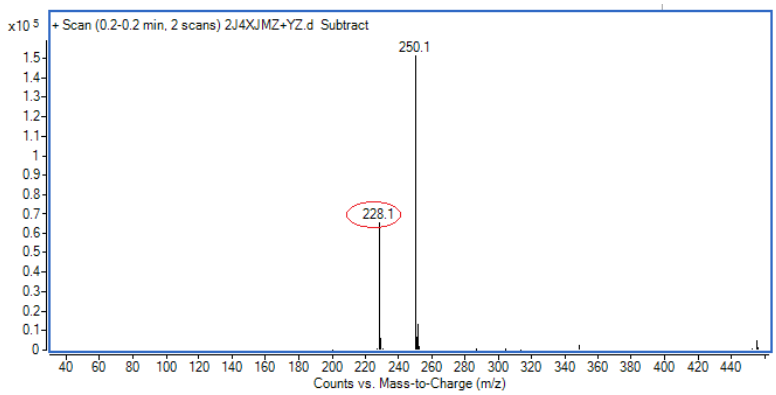
compound 3f



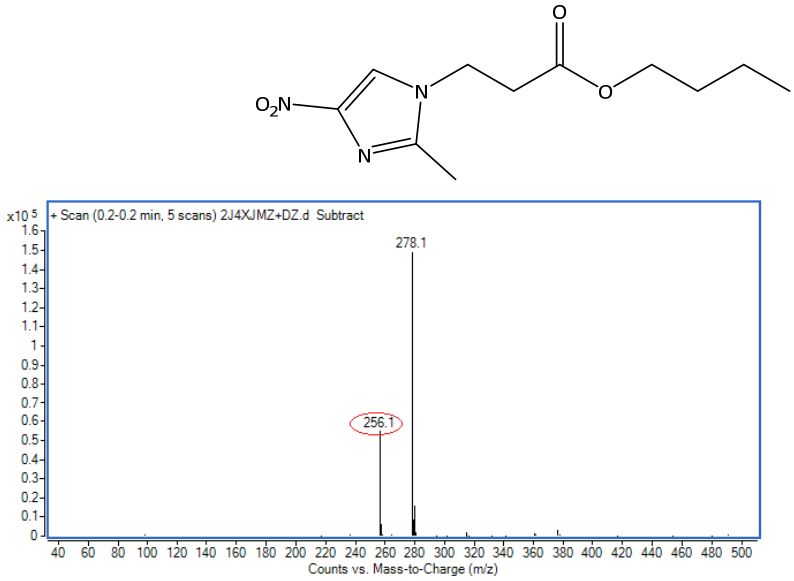


compound 3g

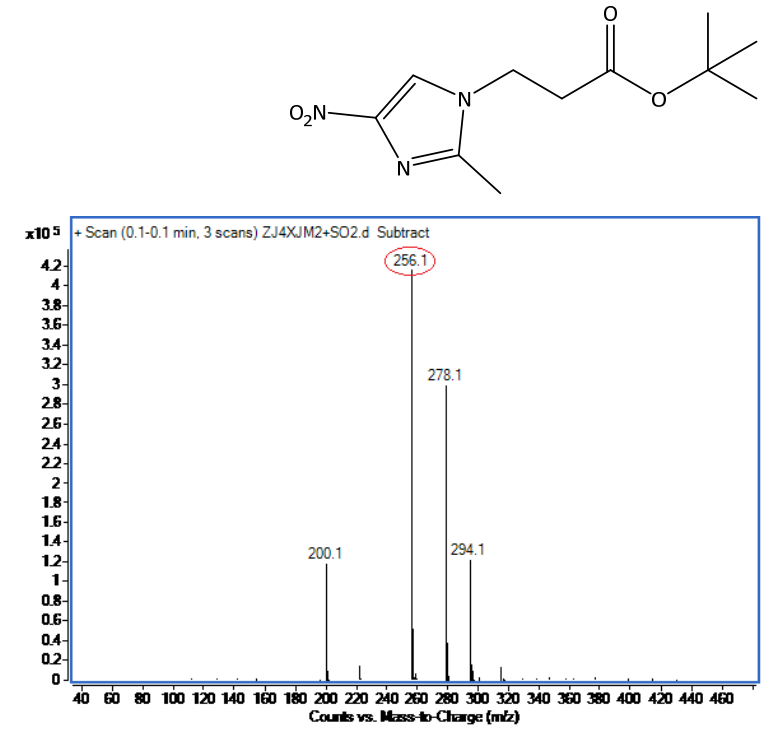




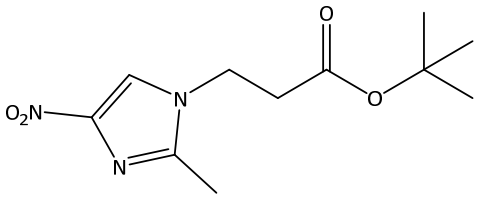
compound 3h

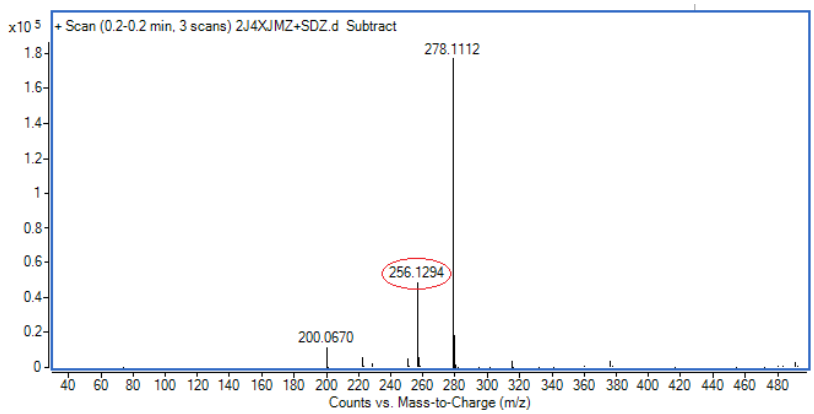


compound 3i



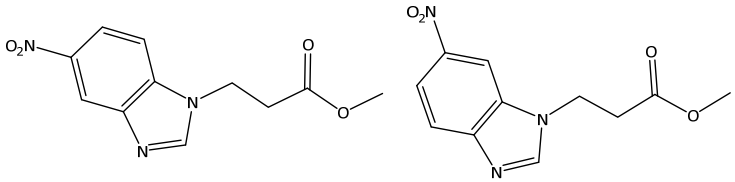
compound 3i

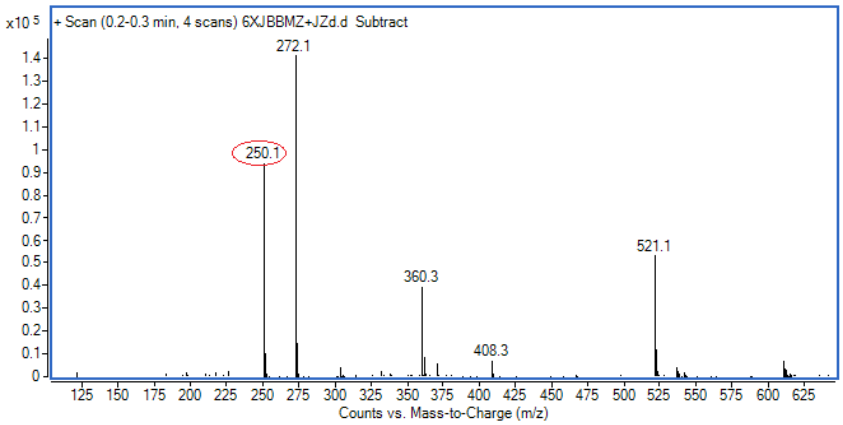




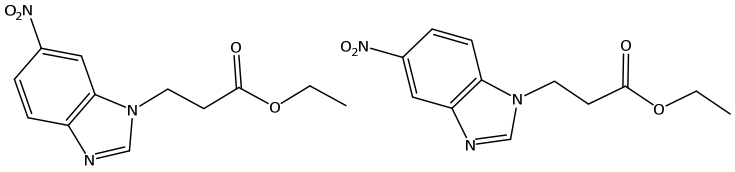
Formula (M)	Ion Formula	m/z	Calc m/z	Diff (ppm)
C11 H17 N3 O4	C11 H17 N3 Na O4	278.1112	278.1111	-0.29

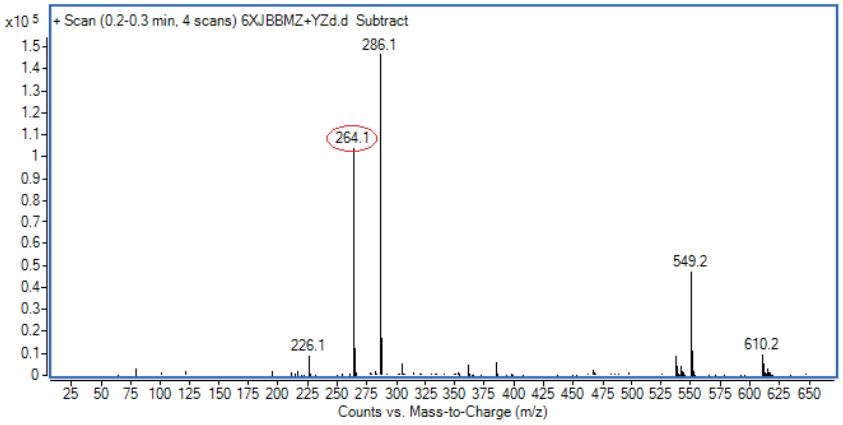
compound 3p



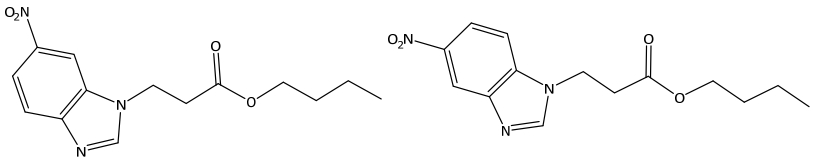


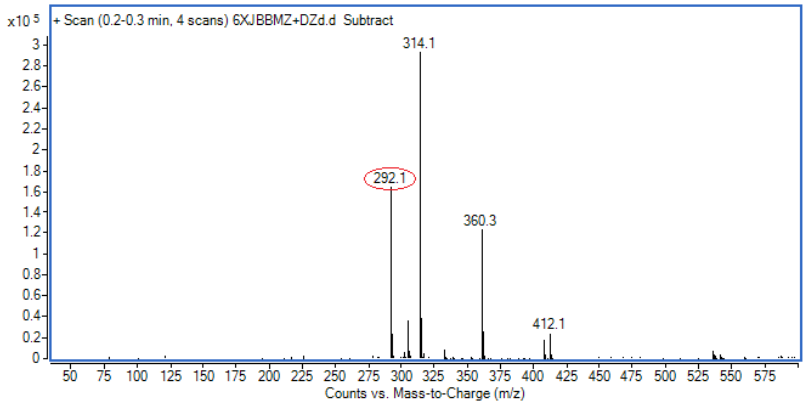
compound 3q



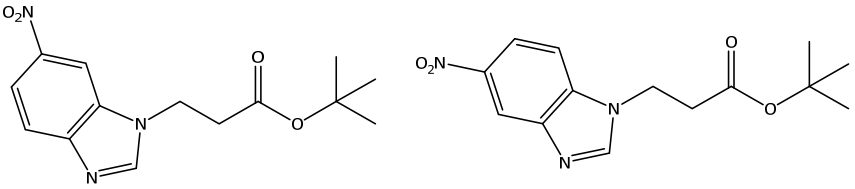


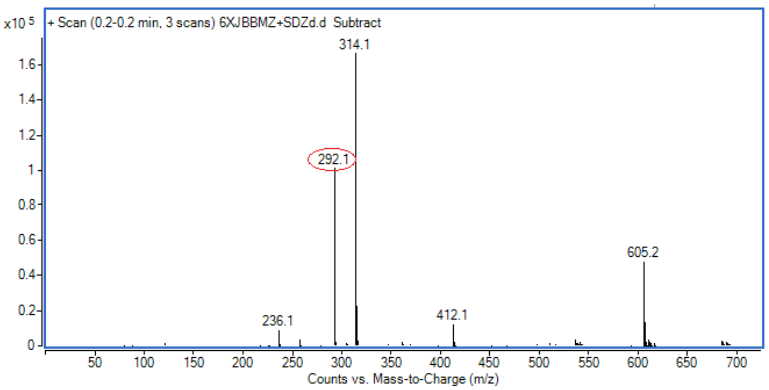
compound 3r





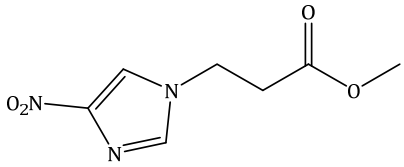
compound 3s

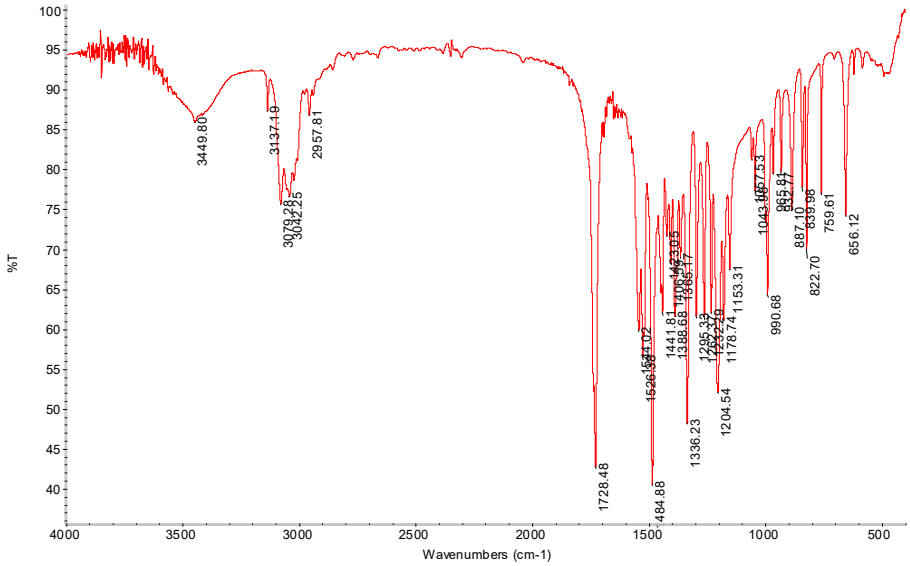




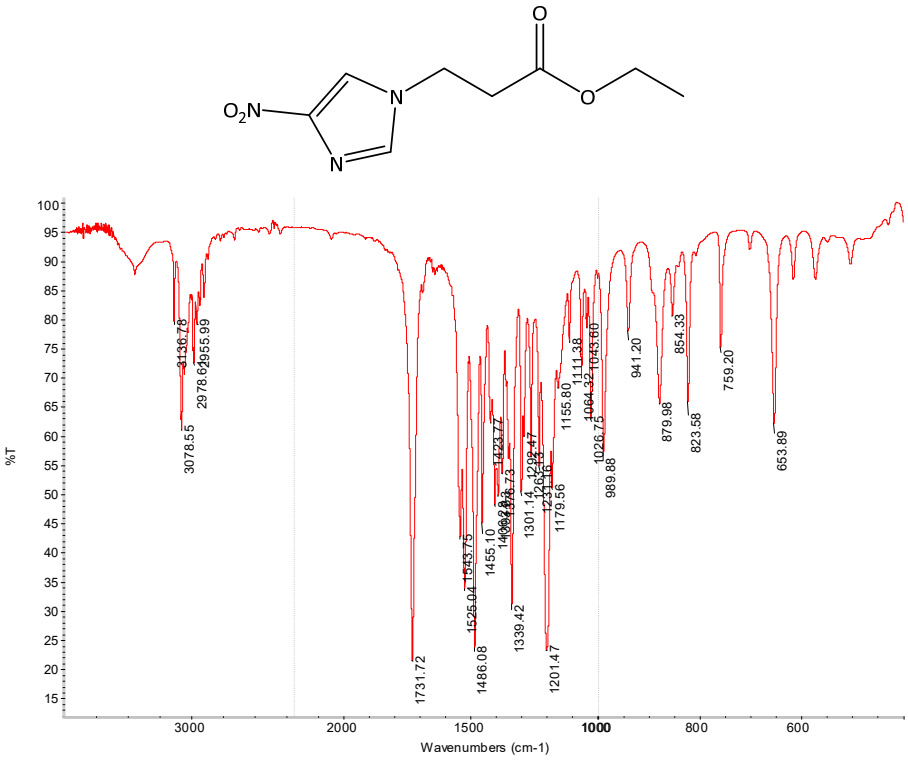
The IR spectra of compound

compound 3a

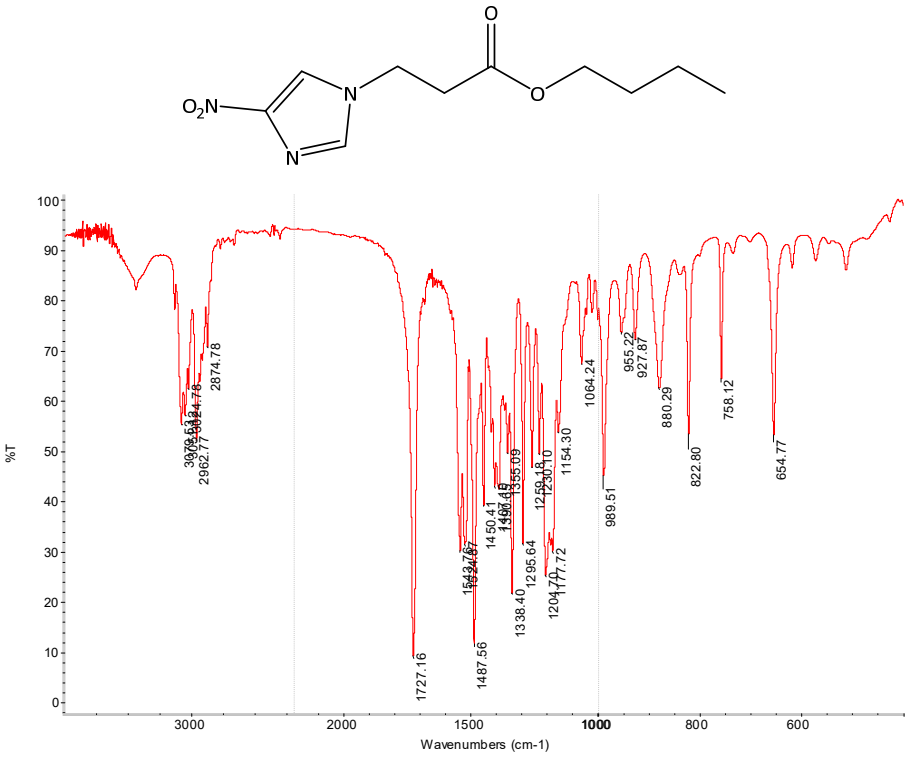




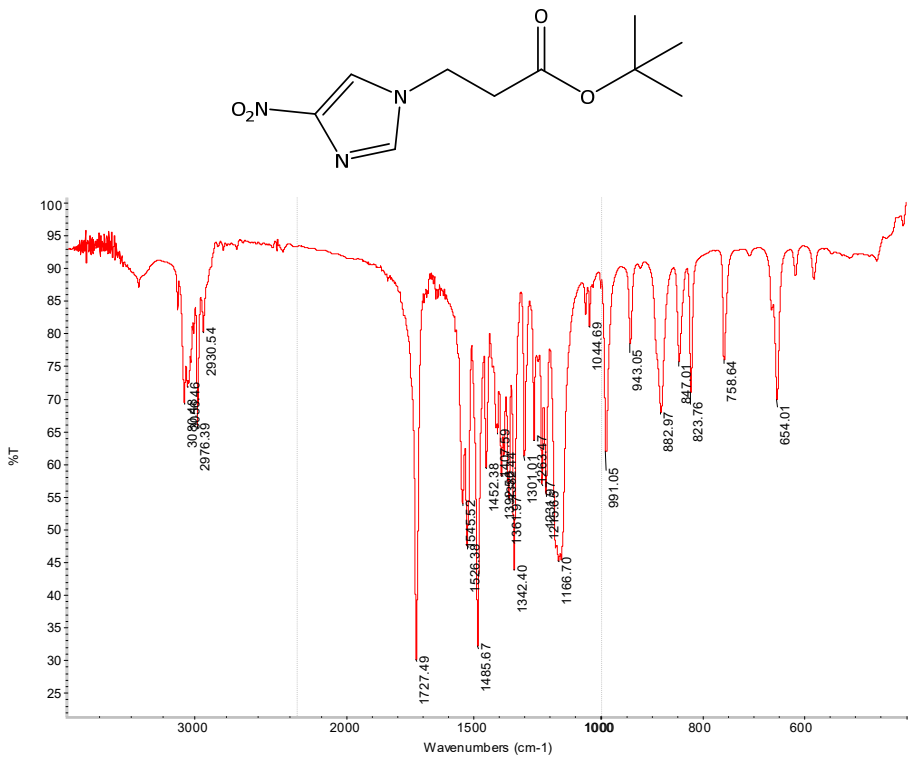
compound 3b



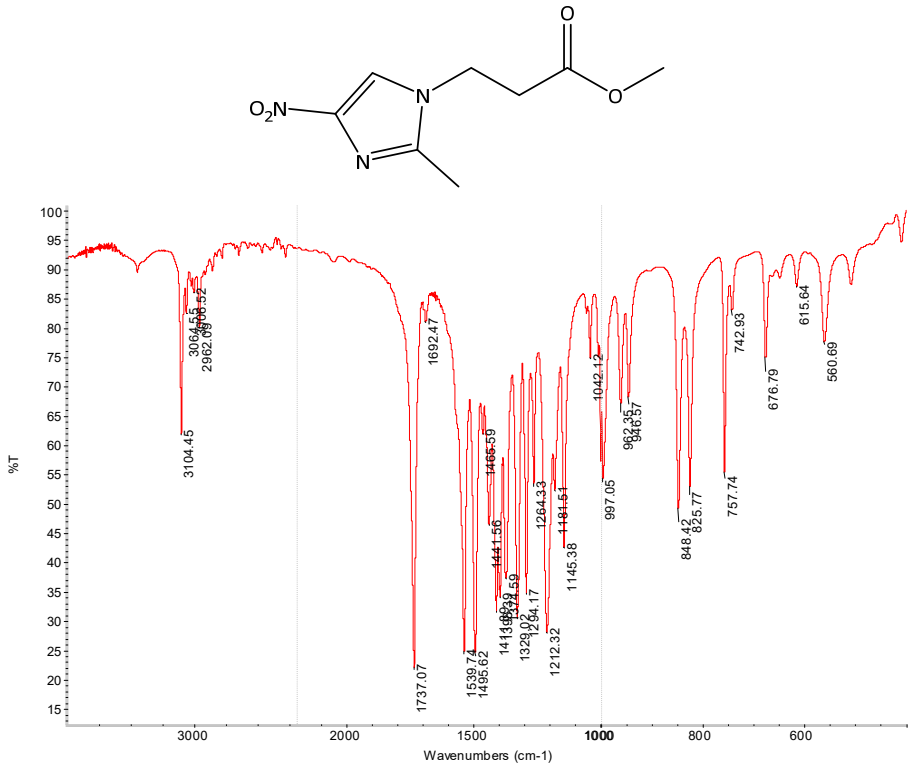
compound 3c



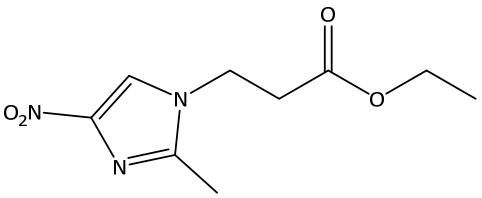
compound 3d

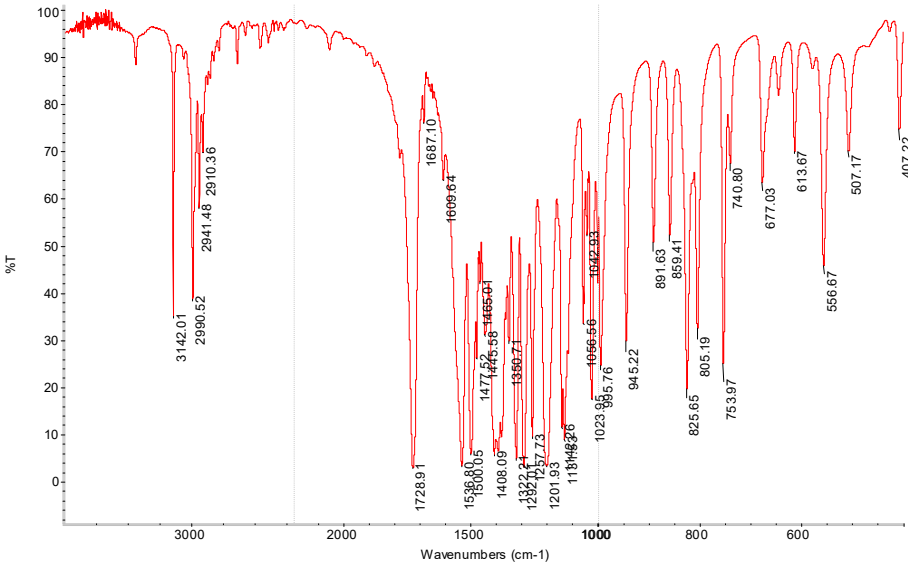


compound 3f

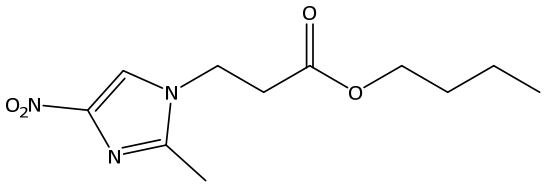


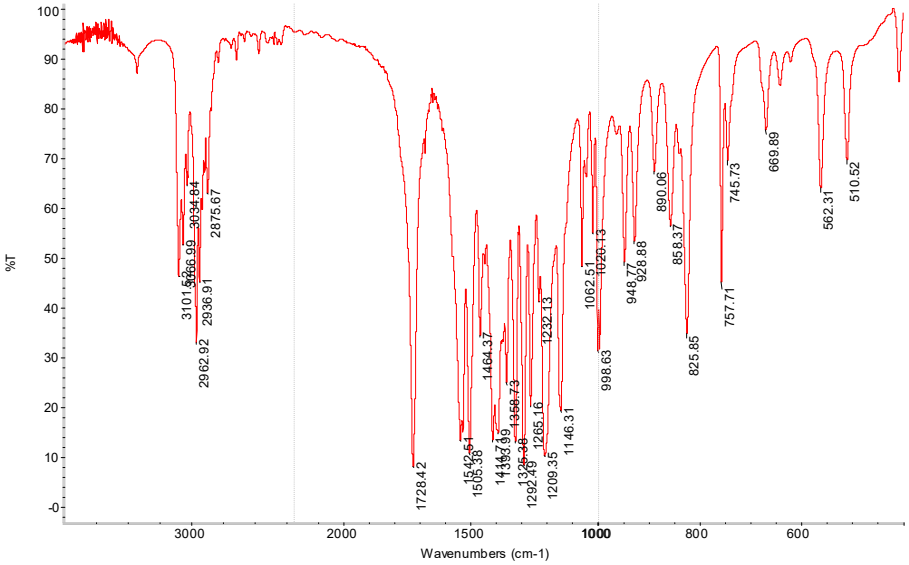
compound 3g



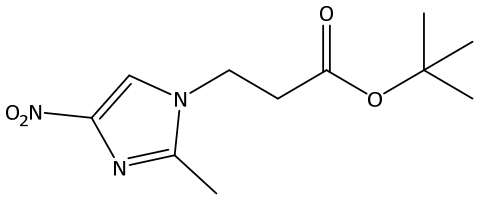


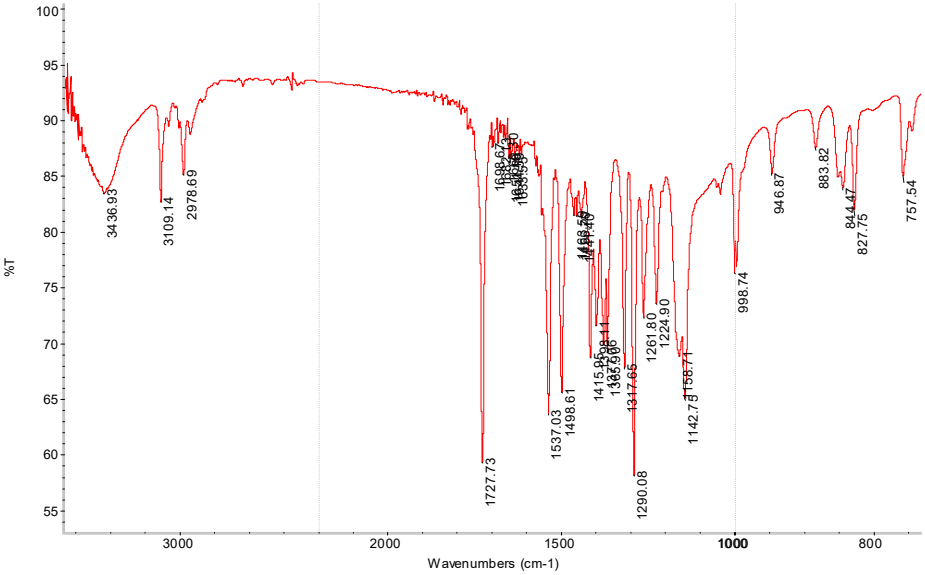
compound 3h



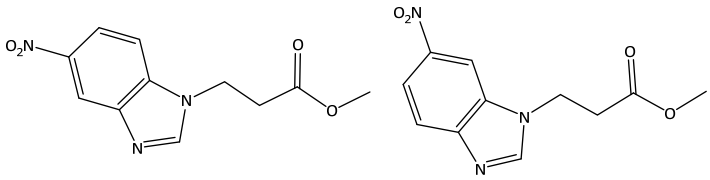


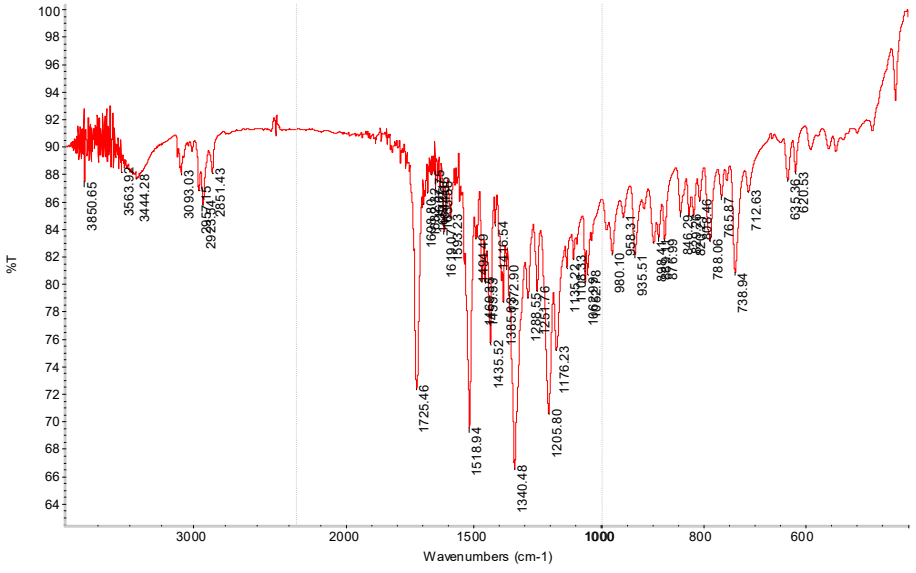
compound 3i



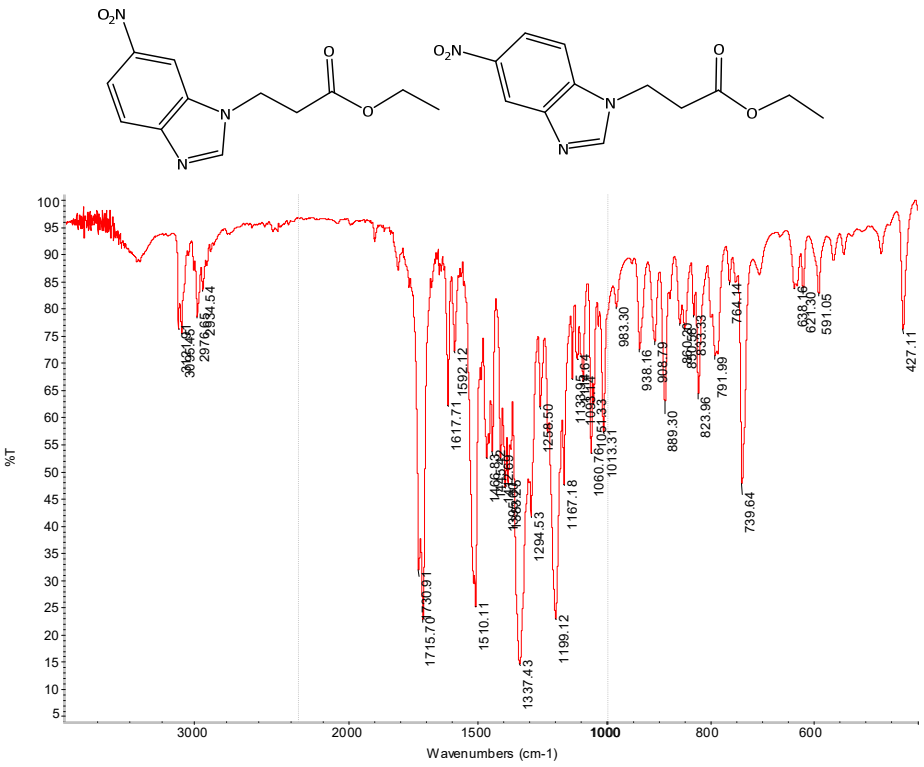


compound 3p

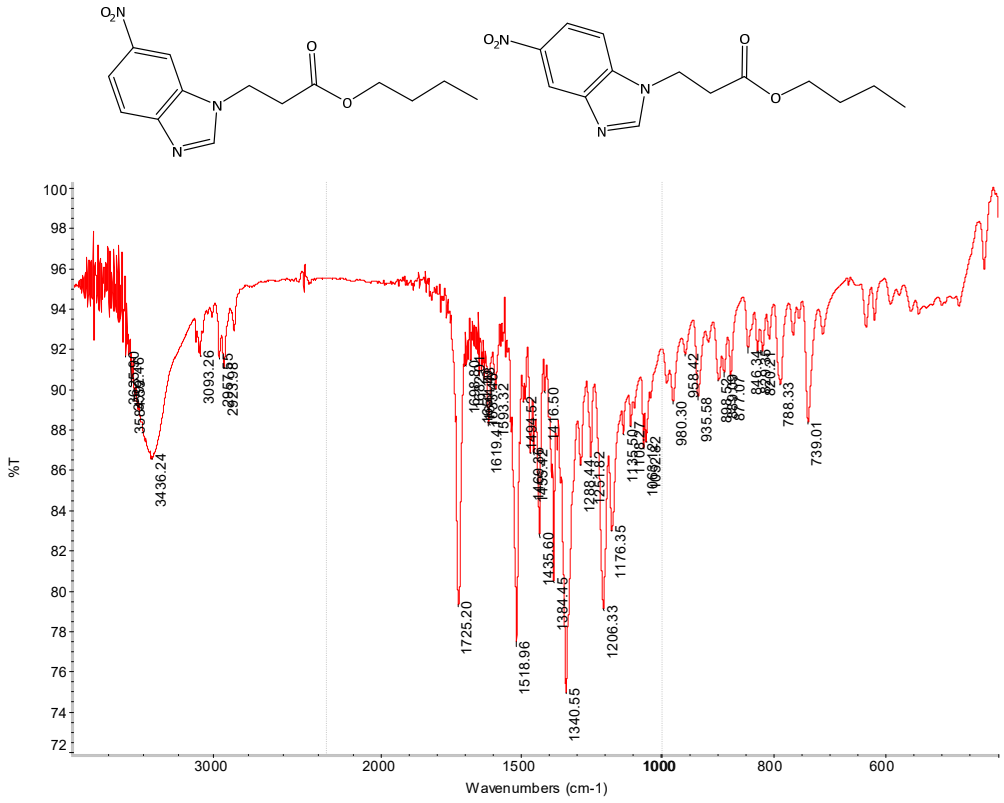




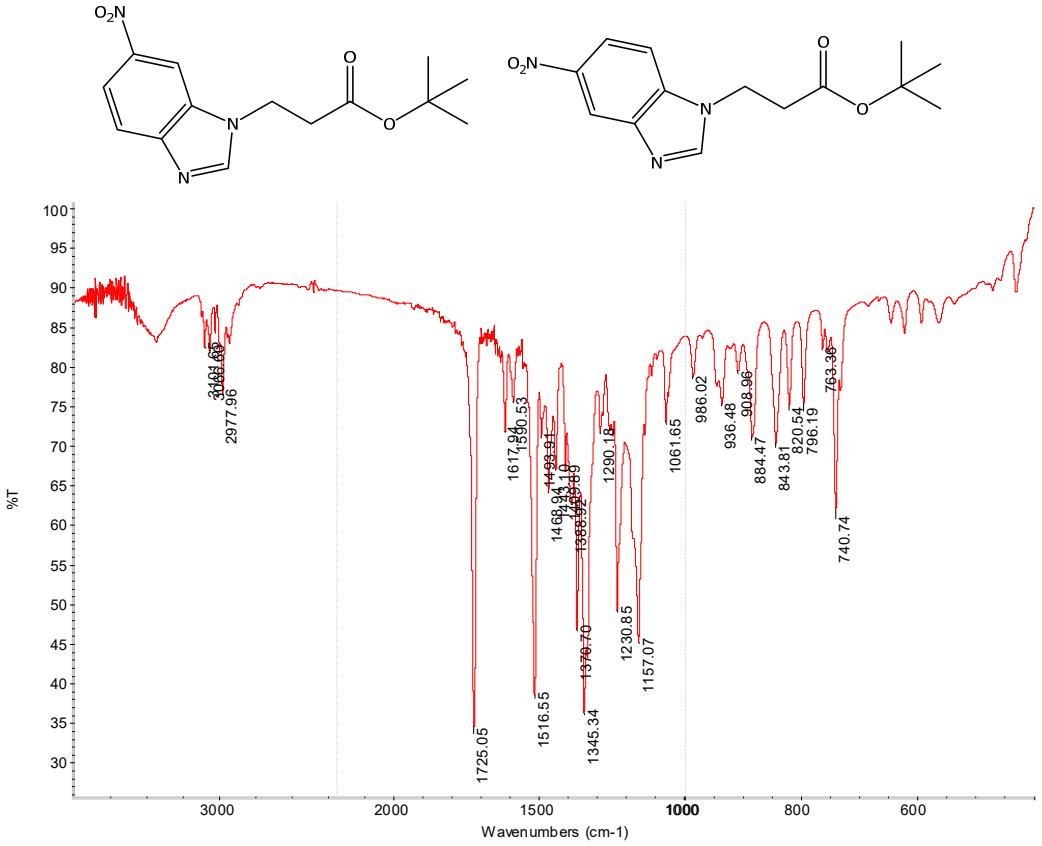
compound 3q



compound 3r



compound 3s



[1] J. Xu, C. Qian, B. Liu, Q. Wu and X. Lin, *Tetrahedron*, 2007, **63**, 986-990.

[2] Y. Cai, Q. Wu, Y. Xiao, D. Lv, X. Lin, J. Biotechnol., 2006, 121, 330-337.

[3] J. Wen, Y. Luo, H. Zhang, H. Zhao, C. Zhou, G. Cai, *Chin. Chem. Lett.*, 2016, **27**, 391-394.