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Electronic Supplementary Information

Synthesis of aliphatic α-ketoamides from α-substituted methyl ketones via a Cu-catalyzed aerobic oxidative amidation

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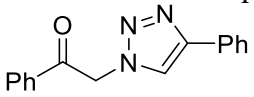
1) General information

All chemicals were purchased from commercial source and used without further purification. Flash chromatography was carried out using MPLC Biotage, Merck silica gel 60 (230-400 mesh) and visualized by UV-lamp and suitable staining reagents. ^{1}H and ^{13}C NMR spectra were recorded using a Varian INOVA (400 MHz). Chemical shifts were reported as parts per million (ppm) relative to the solvent residual peak ($CDCl_3$ = 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR) as an internal standard. All melting point values were monitored by Kruss KSP1D automatic melting point meter. High resolution mass spectra were obtained from Thermo Scientific LTQ Orbitrap XL and Bruker compact UHPLC-quadrupole time-of-flight (Q-TOF) MS system using ESI+ mass ionization method at Organic Chemistry Research Center in Sogang University. GC-MS spectra were obtained from Agilent 5977A GC/MSD system at Organic Chemistry Research Center in Sogang University. The elemental analysis was acquired from Thermo-Finnigan Flash EA2000 system at Organic Chemistry Research Center in Sogang University.

2) Experimental procedures for the synthesis of starting materials

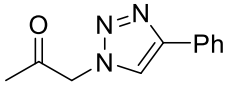
a) Preparation of α-1,2,3-triazoyl-ketones by click chemistry

1-Phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one (7)[1]



Prepared according to the procedure reported in the literature.[1] All analytical data were in good accordance with data reported in the literature.

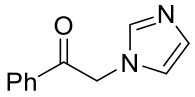
1-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)propan-2-one (14).



Phenylacetylene (1.50 mL, 13.7 mmol) and α-azidoacetone (1.23 g, 12.4 mmol) were suspended in CH_3CN (24 mL). DIPEA (321 mg, 2.48 mmol) was added, followed by CuI (236 mg, 1.24 mmol). After the heterogeneous mixture was stirred at room temperature for 12 h, the reaction mixture was diluted with water (100 mL). The crude product was extracted with EtOAc (80 mL x 2), and dried over $MgSO_4$. After removal of solvent, the crude mixture was purified by flash column chromatography (silica gel, hexane/EtOAc = 60/40) to obtain **14** as pure white solid (1.94 g, 78%): mp = 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.82 (m, 3H), 7.42 (t, J = 8.0 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 5.24 (s, 2H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 130.4, 129.0, 128.4, 125.9, 121.3, 58.6, 27.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{12}N_3O$ 202.0975; Found 202.0975.

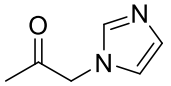
b) Preparation of α-imidazolyl-ketones by alkylation with imidazole

2-(1*H*-Imidazol-1-yl)-1-phenylethan-1-one (11).[2]



To imidazole (1.44 g, 21.1 mmol) in a 100 mL round-bottom flask was added CH_2Cl_2 (16.8 mL). After stirring, 2-bromoacetophenone (2.0 g, 10.1 mmol) was added in portions, and the mixture was stirred at room temperature for 23.5 h. The reaction mixture was treated with brine (120 mL) and extracted with CH_2Cl_2 (5 x 120 mL). The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dissolved in EtOAc (500 mL), filtered and dried in vacuum to afford the product as a yellow solid (1.45 g, 78%): mp = 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.65 (t, *J* = 7.0 Hz, 1H), 7.54-7.48 (m, 3H), 7.13 (s, 1H), 6.94 (s, 1H), 5.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 138.3, 134.5, 134.3, 129.8, 129.2, 128.1, 120.4, 52.6. Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.98; H, 5.45; N, 14.98. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{11}N_2O$ 187.0866; Found 187.0865

1-(1*H*-Imidazol-1-yl)propan-2-one (13).

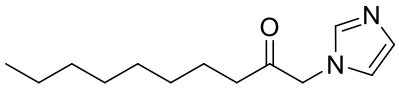


To imidazole (2.21 g, 32.4 mmol) in a pressure tube was added CH_3CN (21 mL). After stirring, chloroacetone (0.89 mL, 10.8 mmol) was added, and the reaction mixture was stirred at 80 °C for 3.5 h. The mixture was transferred to a 250 mL round-bottom flask and evaporated under reduced pressure. Et_2O (200 mL) was added and the Et_2O solution was stirred for 5 min. The Et_2O solution was transferred to a second round-bottom flask, and CH_2Cl_2 (200 mL) was added to the Et_2O-insoluble residue in the 250 mL round-bottom flask. The CH_2Cl_2 solution was stirred for 10 min, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography (10:90 MeOH/Et_2O) to afford the product as a yellow viscous liquid (811 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.09 (s, 1H), 6.86 (s, 1H), 4.73 (s, 2H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 137.9, 129.9, 120.0, 56.0, 27.0. Anal. Calcd for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.03; H, 6.62; N, 22.59. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_6H_9N_2O$ 125.0709; Found 125.0708.

c) General procedure for the synthesis of compounds (16)-(21)

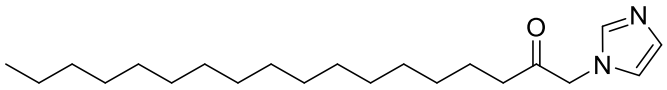
Method A: To imidazole (3 equiv) and α-chloro-long aliphatic ketone (1 equiv) in a pressure tube was added CH_3CN (0.5 M), and the mixture was stirred at 80 °C for the stipulated time. After concentrated under reduced pressure, the mixture was treated with saturated aqueous $NaHCO_3$ solution (120 mL) and extracted with CH_2Cl_2 (5 x 120 mL) unless otherwise specified. The combined organic phases were poured to a 1000 mL separatory funnel and extracted with water (1 x 300 mL). The organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. The crude mixture was purified by MPLC unless otherwise specified.

1-(1*H*-Imidazol-1-yl)decan-2-one (16).



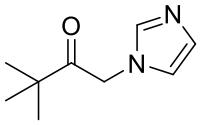
Method A was followed using 1-chlorodecan-2-one (1.60 g, 8.39 mmol), imidazole (1.71 g, 25.2 mmol) and CH_3CN (16.8 mL) for 4 h at 80 °C. Purification by MPLC (5:95-15:75 MeOH/EtOAc) afforded the product as a white solid (1.29 g, 69%): mp = 57-58 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.10 (s, 1H), 6.86 (s, 1H), 4.71 (s, 2H), 2.41 (t, *J* = 7.2 Hz, 2H), 1.59 (quint, *J* = 7.2 Hz, 2H), 1.28-1.22 (m, 10H), 0.86 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 137.9, 129.7, 120.0, 55.3, 39.6, 31.8, 29.3, 29.1 (2C), 23.3, 22.6, 14.1. Anal. Calcd for $C_{13}H_{22}N_2O$: C, 70.23; H, 9.97; N, 12.60. Found: C, 70.22; H, 9.95; N, 12.65. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{23}N_2O$ 223.1805; Found 223.1805.

1-(1*H*-Imidazol-1-yl)octadecan-2-one (17).



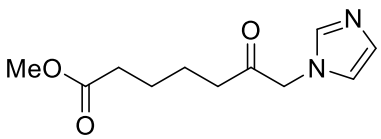
Method A was followed using 1-chlorooctadecan-2-one (1.00 g, 3.30 mmol), imidazole (674 mg, 9.90 mmol) and CH_3CN (6.6 mL) for 3.5 h at 80 °C. After work-up the product was obtained as a white solid (722 mg, 66%): mp = 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.12 (s, 1H), 6.88 (s, 1H), 4.72 (s, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 1.60 (quint, J = 6.8 Hz, 2H), 1.29-1.21 (m, 26H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 138.0, 129.8, 120.0, 55.4, 39.7, 32.0, 29.76 - 29.70 (m), 29.6, 29.5, 29.43, 29.39, 29.1, 23.4, 22.8, 14.2. Anal. Calcd for $C_{21}H_{38}N_2O$: C, 75.39; H, 11.45; N, 8.37. Found: C, 75.43; H, 11.44; N, 8.28. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{39}N_2O$ 335.3057; Found 335.3056.

1-(1*H*-Imidazol-1-yl)-3,3-dimethylbutan-2-one (18).



Method A was followed using 1-chloropinacolin (1 mL, 7.62 mmol), imidazole (1.56 g, 22.9 mmol and CH_3CN (15 mL) for 3.5 h at 80 °C. After work-up the product was obtained as a white solid (698 mg, 55%): mp = 37-40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.06 (s, 1H), 6.82 (s, 1H), 4.89 (s, 2H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4, 138.1, 129.5, 120.2, 50.6, 43.6, 26.3 (3C). Anal. Calcd for $C_9H_{14}N_2O$: C, 65.03; H, 8.49; N, 16.85. Found: C, 65.09; H, 8.57; N, 16.79. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_{15}N_2O$ 167.1179; Found 167.1178.

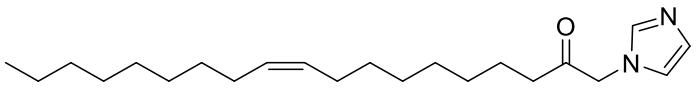
Methyl 7-(1*H*-imidazol-1-yl)-6-oxoheptanoate (19).



Method A was followed using methyl 7-chloro-6-oxoheptanoate (1.00 g, 5.19 mmol), imidazole (1.06 g, 15.6 mmol) and CH_3CN (10 mL) for 4 h at 80 °C. After concentrated under reduced pressure, the mixture was treated with water and extracted with CH_2Cl_2. After work-up the product was obtained as a yellow solid (862 mg, 74%): mp = 36-37 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.02 (s, 1H), 6.81 (s, 1H), 4.69 (s, 2H), 3.59 (s, 3H), 2.39 (t, *J* = 6.6 Hz, 2H), 2.25 (t, *J* = 6.6 Hz, 2H), 1.57-1.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 173.6, 137.9, 129.6,

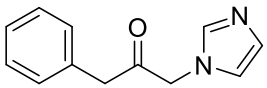
120.0, 55.2, 51.6, 39.1, 33.5, 24.1, 22.6. Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.98; H, 7.09; N, 12.41. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{17}N_2O_3$ 225.1234; Found 225.1234.

_(Z)_-1-(1_H_-Imidazol-1-yl)nonadec-10-en-2-one (20).



Method A was followed using *(Z)*-1-chlorononadec-10-en-2-one (1.00 g, 3.18 mmol), imidazole (650 mg, 9.54 mmol) and CH_3CN (6.4 mL) for 5 h at 80 °C. After concentrated under reduced pressure, the mixture was treated with saturated aqueous $NaHCO_3$ solution and extracted with EtOAc. Purification by MPLC (10:90 MeOH/EtOAc) afforded the product as a yellow solid (717 mg, 65%): mp = 39-40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.04 (s, 1H), 6.82 (s, 1H), 5.34-5.25 (m, 2H), 4.68 (s, 2H), 2.37 (t, *J* = 7.4 Hz, 2H), 1.96 (q, *J* = 6.4 Hz, 4H), 1.55 (quint, *J* = 7.2 Hz, 2H), 1.27-1.17 (m, 20H), 0.83 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 137.9, 130.1, 129.7 (2C), 120.0, 55.4, 39.7, 32.0, 29.8, 29.7, 29.6, 29.4 (2C), 29.3, 29.1 (2C), 27.3, 27.2, 23.4, 22.7, 14.2. Anal. Calcd for $C_{22}H_{38}N_2O$: C, 76.25; H, 11.05; N, 8.08. Found: C, 76.26; H, 11.03; N, 8.11. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{39}N_2O$ 347.3057; Found 347.3056.

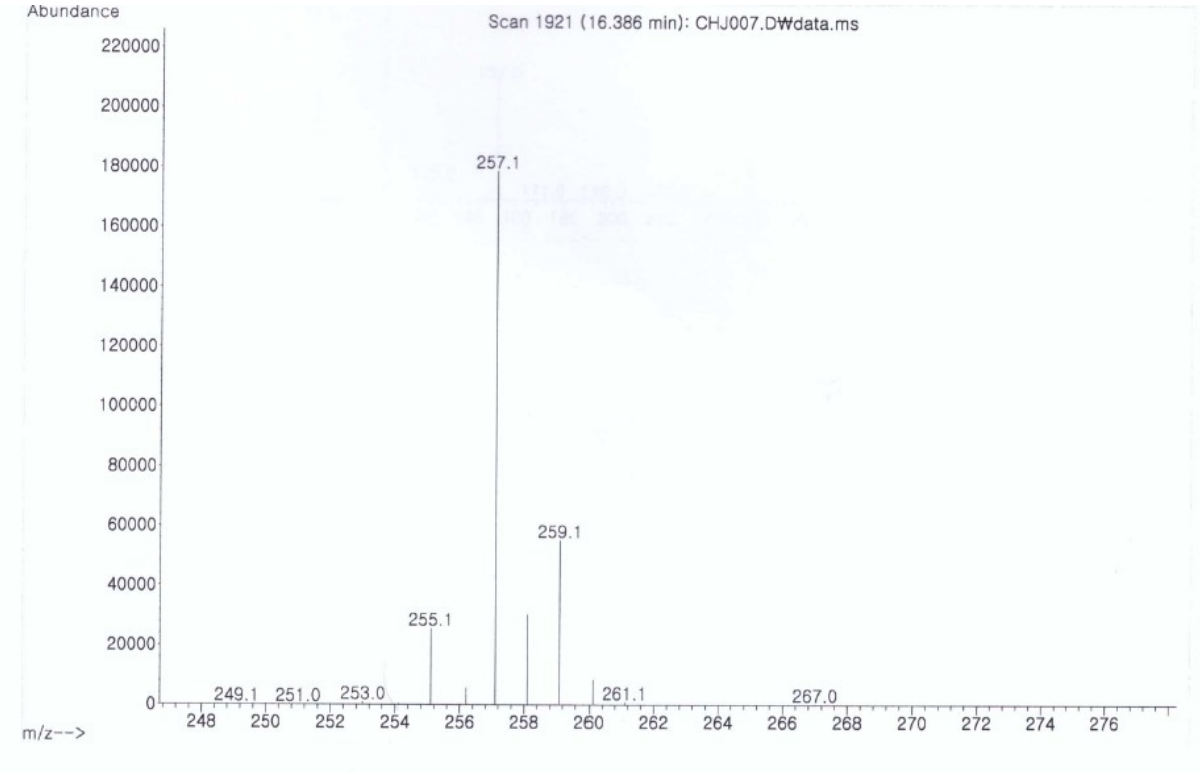
1-(1_H_-Imidazol-1-yl)-3-phenylpropan-2-one (21).

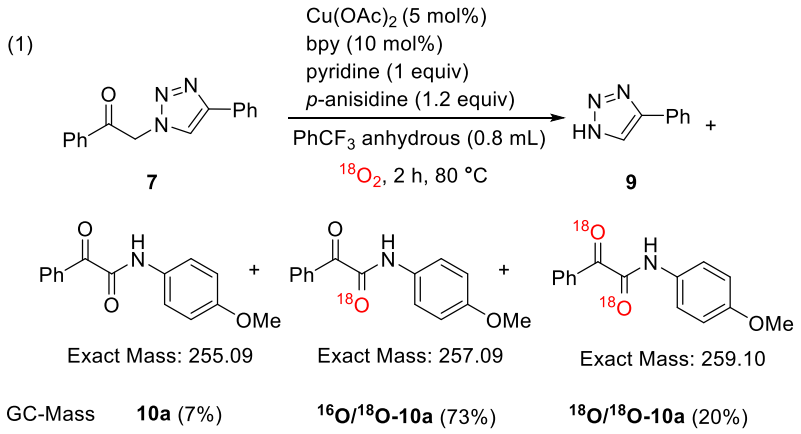


Method A was followed using 1-chloro-3-phenylpropan-2-one (1.00 g, 5.93 mmol), imidazole (1.21 g, 17.8 mmol) and CH_3CN (11 mL) for 3.5 h at 80 °C. After concentrated under reduced pressure, the mixture was treated with water and extracted with CH_2Cl_2. Purification by MPLC (5:95 MeOH/EtOAc) afforded the product as a white solid (657 mg, 55%): mp = 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 4H), 7.18 (d, *J* = 7.6 Hz, 2H), 7.08 (s, 1H), 6.80 (s, 1H), 4.74 (s, 2H), 3.73 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 138.0, 132.4, 129.9, 129.4, 129.3, 127.8, 120.0, 54.5, 47.3. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.82; H, 6.04; N, 14.07. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}N_2O$ 201.1022; Found 201.1022.

3) Preliminary investigation for synthesis of α-ketoamide by using isotope

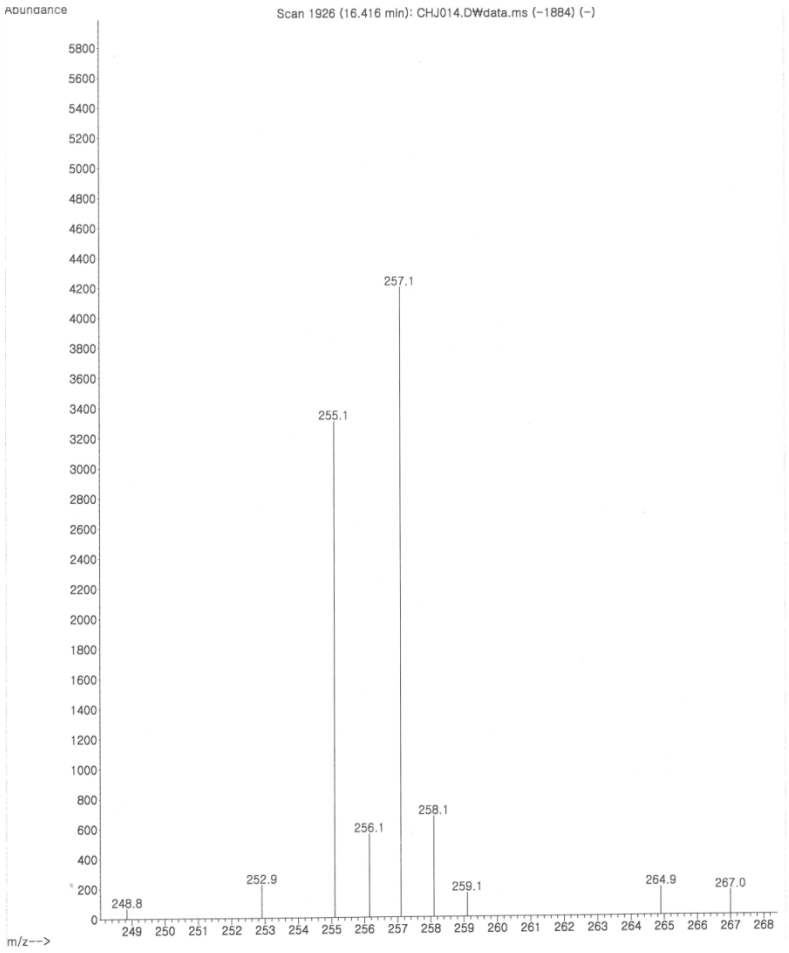
(1) Labeling experiment: synthesis of 10a by using isotope $^{18}O_2$ gas

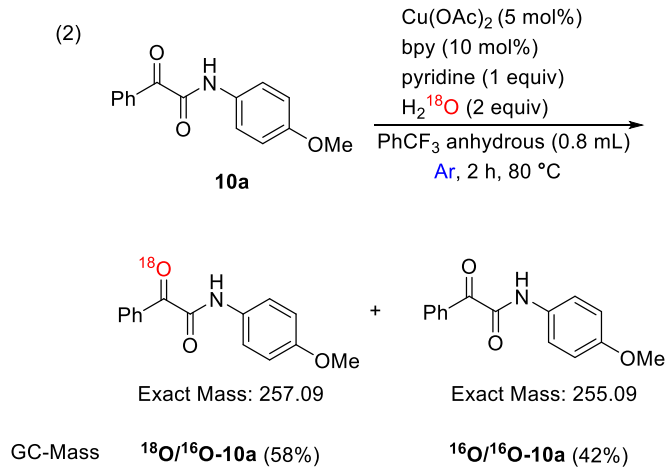




Method L: A solution of 1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one (**7**, 53 mg, 0.2 mmol) and *p*-anisidine (30 mg, 0.24 mmol) in anhydrous $PhCF_3$ (0.8 mL) was treated with $Cu(OAc)_2$ (2 mg, 0.01 mmol), bpy (3 mg, 0.02 mmol) and pyridine (16 mg, 0.2 mmol). The reaction mixture under $^{18}O_2$ was stirred at 80 °C for 2 h. After cooling down to room temperature, the crude mixture was analyzed by GC-MS.

(2) Labeling experiment: scrambling investigation of 10a by using isotope $H_2{}^{18}O$



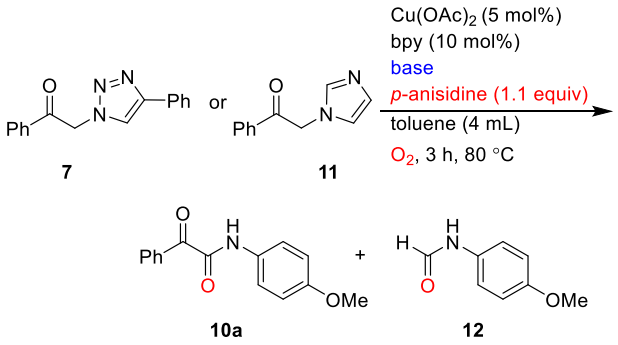


Method M: *N*-(4-Methoxyphenyl)-2-oxo-2-phenylacetamide (**10a**, 51 mg, 0.2 mmol) in a reaction vial was treated with $Cu(OAc)_2$ (2 mg, 0.01 mmol) and bpy (3 mg, 0.02 mmol). The vial was flushed with argon. The reaction mixture was injected with anhydrous $PhCF_3$ (0.8 mL), pyridine (16 mg, 0.2 mmol) and $H_2{}^{18}O$ (8 mg, 0.4 mmol) in sequence. The reaction mixture under argon was stirred at 80 °C for 2 h in the sealed vial. After cooling down to room temperature, the crude mixture was analyzed by GC-MS.

4) Optimization of the synthesis of aromatic α-ketoamides

(1) Synthesis of α-ketoamides from acetophenone and optimization of the conditions

Table S1. Investigation of the selectivity of two pathways depending on the presence of an imidazoyl or triazoyl group and the base[a]



entry	sm	variation from the standard conditions	**10a**[b] (%)	**12**[b] (%)
1	**7**	Ar instead of O_2, imidazole (3 equiv)	0	0
2	**7**	pyridine (1 equiv)	67	32
3	**7**	$Cu(OAc)_2$ (10 mol%), pyridine (1 equiv)	48	50
4	**11**	pyridine (1 equiv)	62	23
5	**11**	DMAP (1 equiv)	25	62
6	**11**	2,6-lutidine (1 equiv)	43	50
7	**11**	imidazole (1 equiv)	60	5
8[c]	**7**	imidazole (3 equiv)	62	5
9	**11**	imidazole (3 equiv)	78	1

[a]Reaction conditions: ketone (1 mmol) scale, O_2 balloon.

[b]Isolated yield. [c]Reaction time = 18 h.

As mentioned earlier, 4-phenyl-1,2,3-triazole was obtained via a copper-catalyzed aerobic oxidative C-N bond cleavage of **7**, as shown in Scheme 2 (a).[1] When the reaction was performed under Ar instead of molecular oxygen, the reaction did not proceed as expected (Table S1, entry 1). When we repeated a similar reaction in the presence of *p*-anisidine as the amine, α-ketoamide **10a** was isolated in 67% yield (Table S1, entry 2).

This is consistent with our hypothesis that phenylglyoxylic acid is formed when hydroxide attacks the key triazol-1-yl-1,2-diketo intermediate.[1] However, although starting material **7** was completely consumed and 4-phenyl-1,2,3-triazole was obtained in high yield, only 67% of desired compound **10a** was obtained along with byproduct formamide **12** in 32% yield. Increasing the catalyst loading ($Cu(OAc)_2$, 10 mol%) was not successful

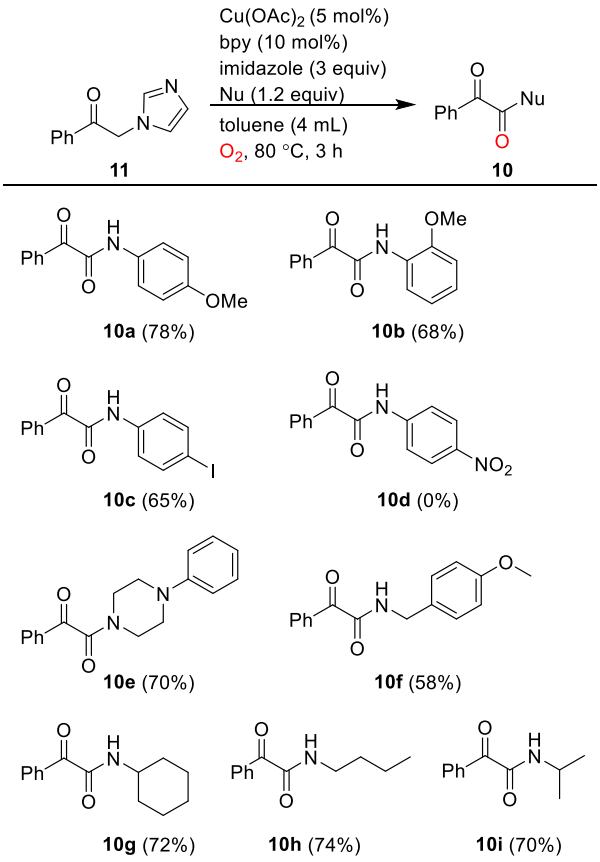
as it afforded desired product **10a** (48%, Table S1, entry 3) with lower selectivity. Based on various controlled experiments, another heterocycle, imidazole instead of 1,2,3-triazole, and various bases were tested for the selective aerobic oxidative amidation, and other parameters were optimized as well.

When α-imidazol-1-yl-acetophenone (**11**) was used as the starting material instead of α-(1,2,3-triazo-1-yl)-acetophenone **7**, the yield of formamide **12** as a byproduct (23%, entry 4) was lower. Reactions with α-imidazoyl acetophenone **11** afforded lower yields of desired product **10a** in the presence of DMAP (25%, entry 5) and 2,6-lutidine (43%, entry 6). Although one equivalent of imidazole could inhibit the formation of byproduct formamide **12** (although it was still obtained in a low yield (5%, entry 7)), the yield of the desired product (60%) was not improved. However, the reaction with 3 equiv of imidazole resulted in a high yield of desired compound **10a** (78%), while the formation of undesired byproducts was suppressed (entry 9). The reaction of α-triazoyl acetophenone **7** under the same optimized conditions was not only slower (18 h) but also unsatisfactory in terms of yield (entry 8). We reached the following two conclusions. 1) Along with the kind of heteroaryl group, such as imidazoyl or triazoyl groups, the selectivity of the reaction varies and provides different ratios of desired product **10** and undesired product **12**. 2) Imidazole, a weaker base, gave the desired α-ketoamide product with high selectivity and yield.

(2) Investigation of amines to prepare α-ketoamides from acetophenone

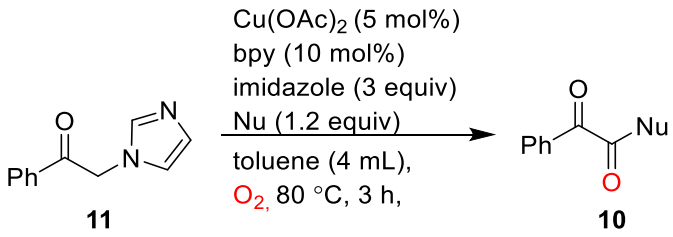
Under the optimal conditions, the scope of the copper-catalyzed aerobic oxidative amidation leading to α-ketoamides was further expanded to a range of substituted amines and anilines (Table S2). Both anilines and alkyl amines proceeded well and provided the corresponding products **10a-10c** and **10g-10i** in moderate to excellent yields. Notably, secondary amine and benzyl amine could be transformed into the desired products **10e** and **10f** in moderate yields. However, due to the electron-withdrawing group on the substrate, desired product **10d** could not be obtained. The results show that amines bearing electron-donating groups afford higher yields than those bearing electron-withdrawing groups. Because electron-rich amines can easily form radical cations in the case of Cu-catalyzed aerobic oxidation, they can react to give azo compounds. Although this side reaction leads to a low yield of the desired product, aerobic oxidation of the ketone, which is activated by the imidazole group, is sufficiently faster such that the radical cations of electron-rich amines do not form. As a result, desired products **10g-10i** were isolated in high yields.

Table S2. The scope of amines in the copper-catalyzed aerobic oxidative amidation to prepare aromatic α-ketoamides[a,b]



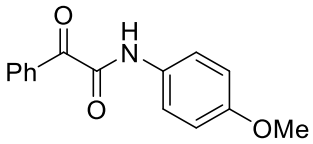
[a]Reaction conditions: ketone (1.0 mmol) scale, O_2 balloon. [b]Isolated yields.

5) General procedure for the synthesis of compounds (10a)-(10c) and (10e)-(10i)



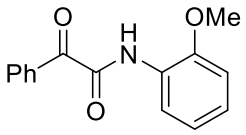
Method B: A solution of the α-imidazol-1-yl acetophenone (186 mg, 1.0 mmol) and amine compounds (1.2 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 3 h and quenched with water (10 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC.

***N*-(4-Methoxyphenyl)-2-oxo-2-phenylacetamide (10a).**



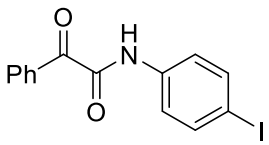
Method B was followed using *p*-anisidine (148 mg) as starting material. Purification by MPLC (hexane/EtOAc = 70/30) obtained the product as a yellow powder (199 mg, 78%): mp 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.41 (d, J = 4.0 Hz, 2H), 7.67-7.61 (m, 3H), 7.50 (t, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.7, 158.8, 157.1, 134.7, 133.3, 131.6, 129.9, 128.7, 121.6, 114.5, 55.6. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{13}NO_3Na$ 278.0788; Found 278.0787.

***N*-(2-Methoxyphenyl)-2-oxo-2-phenylacetamide (10b).**



Method B was followed using *o*-anisidine (148 mg) as starting material. Purification by MPLC (hexane/EtOAc = 75/25) obtained the product as a yellow powder (173 mg, 68%): mp 80-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.50 (d, J = 4.0 Hz, 1H), 8.41 (d, J = 8.0 Hz, 2H), 7.64 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 7.13 (t, J = 8.0 Hz, 1H), 7.02 (t, J = 8.0 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 159.0, 148.8, 134.5, 132.2, 131.4, 128.5, 126.4, 125.1, 121.0, 119.8, 110.2, 55.8. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{13}NO_3Na$ 278.0788; Found 278.0790.

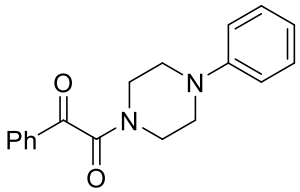
***N*-(4-Iodophenyl)-2-oxo-2-phenylacetamide (10c).**



Method B was followed using 4-iodooaniline (263 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained the product as a yellow powder (228 mg, 65%): mp 145-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.39 (d, J = 8.0 Hz,

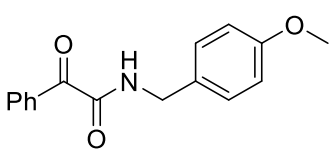
2H), 7.70-7.64 (m, 3H), 7.52-7.47 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 158.9, 138.3, 136.5, 134.9, 133.0, 131.6, 128.7, 121.8, 89.0. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{10}INO_2Na$ 373.9648; Found 373.9648.

1-Phenyl-2-(4-phenylpiperazin-1-yl)ethane-1,2-dione (10e).



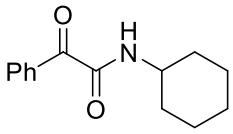
Method B was followed using 1-phenylpiperazine (195 mg) as starting material. Purification by MPLC (hexane/EtOAc = 30/70) obtained the product as a red oil (205 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 2H), 6.77-6.75 (m, 3H), 3.76 (br, 2H), 3.35 (br, 2H), 3.12 (br, 2H), 2.97 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.5, 165.5, 150.8, 135.1, 133.2, 129.8, 129.4, 129.2, 121.1, 117.1, 50.0, 49.7, 45.9, 41.4. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{18}N_2O_2$ Na 317.1261; Found 317.1261.

***N*-(4-Methoxybenzyl)-2-oxo-2-phenylacetamide (10f).**



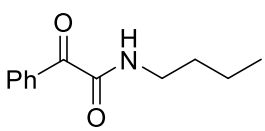
Method B was followed using 4-methoxybenzylamine (164 mg) as starting material. Purification by MPLC (hexane/EtOAc = 40/60) obtained the product as a yellow oil (156 mg, 58%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.36 (s, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 4.50 (d, *J* = 8.0 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.8, 161.6, 159.4, 134.6, 133.4, 131.4, 129.5, 129.3, 128.6, 114.3, 55.4, 43.1. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{15}NO_3Na$ 292.0944; Found 292.0945.

***N*-Cyclohexyl-2-oxo-2-phenylacetamide (10g).**



Method B was followed using cyclohexylamine (119 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained the product as a white powder (166 mg, 72%): mp 100-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 6.98 (s, 1H), 3.89-3.91 (m, 1H), 1.98 (d, *J* = 8.0 Hz, 2H), 1.78-1.74 (m, 2H), 1.64 (d, *J* = 12.0 Hz, 1H), 1.40 (q, *J* = 12.0 Hz, 2H), 1.31-1.20 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 161.0, 134.4, 133.5, 131.3, 128.6, 48.6, 32.8, 25.5, 24.9. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_2Na$ 254.1152; Found 254.1152.

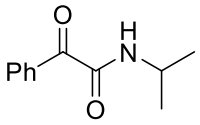
***N*-Butyl-2-oxo-2-phenylacetamide (10h).**



Method B was followed using *n*-butylamine (88 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained the product as a yellow oil (151 mg, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.4 Hz, 2H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.13 (s, 1H), 3.38 (q, *J* = 8.0 Hz, 2H), 1.57 (quint, *J* = 8.0 Hz, 2H), 1.39 (sextet, *J* = 8.0 Hz, 2H),

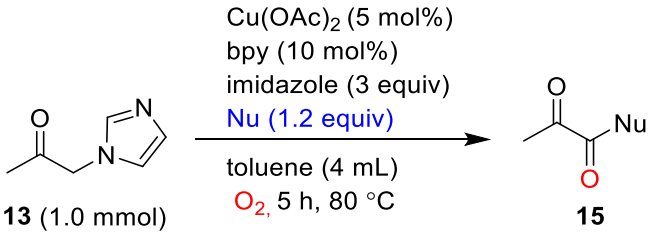
0.94 (t, J = 8.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.1, 161.9, 134.4, 133.5, 131.3, 128.5, 39.3, 31.4, 20.2, 13.8. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{15}NO_2Na$ 228.0995; Found 228.0994.

***N*-Isopropyl-2-oxo-2-phenylacetamide (10i).**



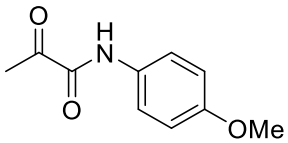
Method B was followed using isopropylamine (71 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained the product as a yellow oil (133 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 6.92 (br, 1H), 4.16 (octet, J = 8.0, 1H), 1.27 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 161.0, 134.4, 133.5, 131.3, 128.6, 41.8, 22.6. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{11}H_{13}NO_2Na$ 214.0839; Found 214.0838.

6) General procedure for the synthesis of compounds (15a)-(15f) and (15i)



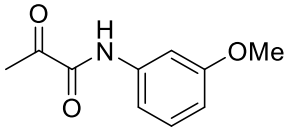
Method C: A solution of the α-imidazol-1-yl acetone (124 mg, 1.0 mmol) and amine compounds (1.2 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h and quenched with 0.5 N HCl aqueous (10 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC.

***N*-(4-Methoxyphenyl)-2-oxopropanamide (15a).**



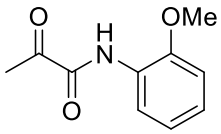
Method C was followed using *p*-anisidine (148 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained the product as a brown powder (131 mg, 68%): mp 118-119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (br, 1H), 7.56 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 3.80 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 157.5, 157.2, 129.6, 121.4, 114.5, 55.6, 24.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{10}H_{11}NO_3Na$ 216.0631; Found 216.0631.

***N*-(3-Methoxyphenyl)-2-oxopropanamide (15b).**



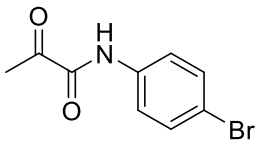
Method C was followed using *m*-anisidine (148 mg) as starting material. Purification by MPLC (hexane/EtOAc = 85/15) obtained the product as an orange powder (125 mg, 65%): mp 91-92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (br, 1H), 7.38 (s, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 160.4, 157.7, 137.5, 130.1, 112.1, 111.4, 105.4, 55.5, 24.2. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{10}H_{11}NO_3Na$ 216.0631; Found 216.0630.

***N*-(2-Methoxyphenyl)-2-oxopropanamide (15c).**



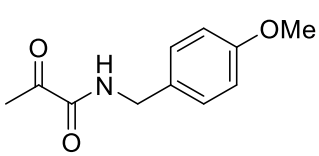
Method C was followed using *o*-anisidine (148 mg) as starting material. Purification by MPLC (hexane/EtOAc = 90/10) obtained the product as a yellow oil (92 mg, 48%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (br, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.91 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 157.7, 148.9, 126.1, 125.2, 121.1, 119.7, 110.2, 55.9, 24.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{10}H_{11}NO_3Na$ 216.0631; Found 216.0633.

***N*-(4-Bromophenyl)-2-oxopropanamide (15d).**



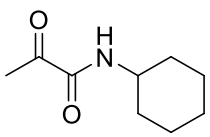
Method C was followed using 4-bromoaniline (205 mg) as starting material. Purification by MPLC (hexane/EtOAc = 90/10) obtained the product as an orange powder (139 mg, 58%): mp 157-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (br, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 157.6, 135.4, 132.4, 121.4, 118.2, 24.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_9H_9BrNO_2$ 241.9811; Found 241.9811.

***N*-(4-Methoxybenzyl)-2-oxopropanamide (15e).**



Method C was followed using 4-methoxybenzylamine (164 mg) as starting material. Purification by MPLC (hexane/EtOAc = 70/30) obtained the product as a white powder (134 mg, 65%): mp 70-71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 4.40 (d, *J* = 4.0 Hz, 2H), 3.79 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 159.9, 159.4, 129.5, 129.1, 114.3, 55.4, 43.1, 24.7. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{11}H_{13}NO_3Na$ 230.0788; Found 230.0787.

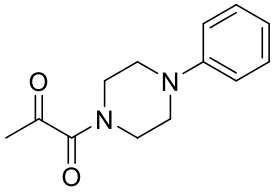
***N*-Cyclohexyl-2-oxopropanamide (15f).**



Method C was followed using cyclohexylamine (119 mg) as starting material. Purification by MPLC (hexane/EtOAc = 85/15) obtained the product as a white powder (104 mg, 62%): mp 73-74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (br, 1H), 3.74-3.67 (m, 1H), 2.45 (s, 3H), 1.88

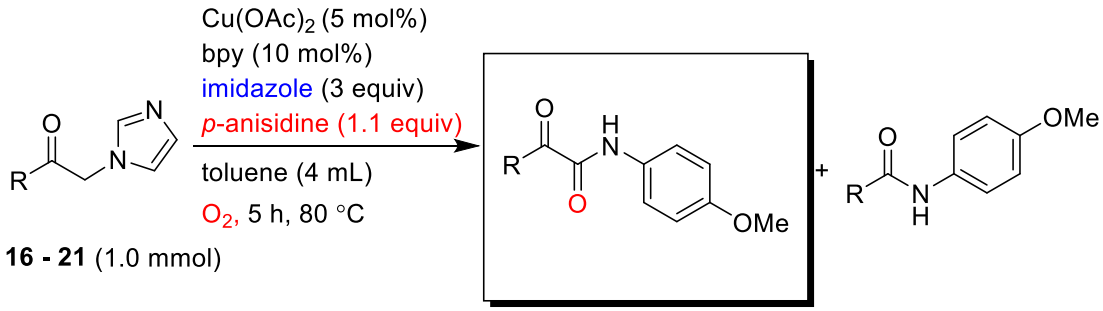
(d, J = 10.4 Hz, 2H), 1.72 (d, J = 13.2 Hz, 2H), 1.61 (d, J = 12.4 Hz, 1H), 1.36 (q, J = 12.0 Hz, 2H), 1.24-1.16 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 159.3, 48.5, 32.8, 25.5, 24.8, 24.6. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_9H_{15}NO_2Na$ 192.0995; Found 192.0996.

1-(4-Phenylpiperazin-1-yl)propane-1,2-dione (15i).



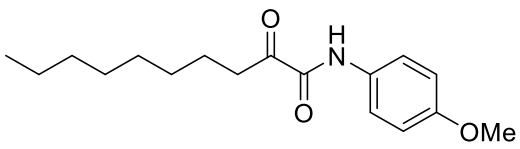
Method C was followed using 1-phenylpiperazine (195 mg) as starting material. Purification by MPLC (hexane/EtOAc = 20/80) obtained the product as an orange oil (171 mg, 74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 3H), 3.78 (t, J = 4.0 Hz, 2H), 3.65 (t, J = 4.0 Hz, 2H), 3.22-3.19 (m, 4H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 164.9, 150.8, 129.4, 120.9, 117.0, 50.1, 49.5, 45.7, 41.7, 28.0. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{16}N_2O_2Na$ 255.1104; Found 255.1105.

7) General procedure for the synthesis of compounds (22)-(26)



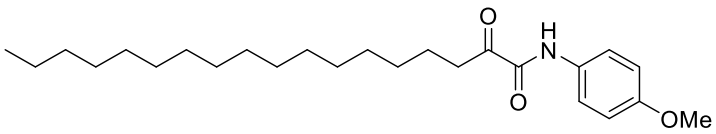
Method D: A solution of the α-imidazol-1-yl-long aliphatic chain compounds (1.0 mmol) and *p*-anisidine (135 mg, 1.1 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h and quenched with 0.5 N HCl aqueous (10 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC unless otherwise specified.

***N*-(4-Methoxyphenyl)-2-oxodecanamide (22).**



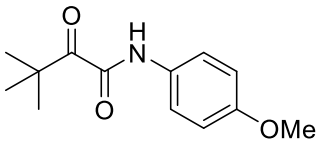
Method D was followed using 1-(1*H*-imidazol-1-yl)decan-2-one (**16**, 222 mg) as starting material. Purification by MPLC (hexane/EtOAc = 90/10) obtained **22** as a white powder (180 mg, 62%): mp 110-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (br, 1H), 7.57 (d, J = 12.0 Hz, 2H), 6.90 (d, J = 12.0 Hz, 2H), 3.80 (s, 3H), 2.99 (t, J = 8.0 Hz, 2H), 1.65 (quint, J = 6.8 Hz, 2H), 1.32-1.27 (m, 10H), 0.88 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 157.5, 157.1, 129.7, 121.4, 114.5, 55.6, 36.6, 31.9, 29.4, 29.24, 29.23, 23.5, 22.8, 14.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{25}NO_3Na$ 314.1727; Found 314.1728.

***N*-(4-Methoxyphenyl)-2-oxooctadecanamide (23).**



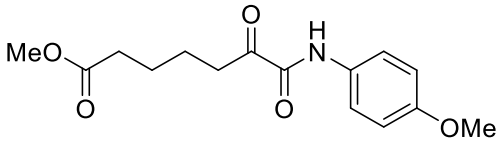
Method D was followed using 1-(1*H*-imidazol-1-yl)octadecan-2-one (**17**, 334 mg) as starting material. Purification by MPLC (hexane/EtOAc = 90/10) obtained **23** as a white powder (274 mg, 68%): mp 69-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (br, 1H), 7.57 (d, *J* = 12.0 Hz, 2H), 6.90 (d, *J* = 12.0 Hz, 2H), 3.80 (s, 3H), 2.99 (t, *J* = 8.0 Hz, 2H), 1.65 (quint, *J* = 8.0 Hz, 2H), 1.32-1.27 (m, 26H), 0.88 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 157.5, 157.1, 129.7, 121.4, 114.5, 55.6, 36.6, 32.1, 29.84-29.79 (m), 29.7, 29.6, 29.51, 29.48, 29.2, 23.5, 22.8, 14.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{41}NO_3Na$ 426.2979; Found 426.2978.

***N*-(4-Methoxyphenyl)-3,3-dimethyl-2-oxobutanamide (24).**



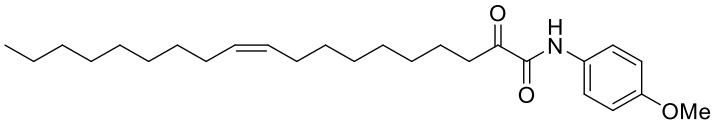
Method D was followed using 1-(1*H*-imidazol-1-yl)-3,3-dimethylbutan-2-one (**18**, 166 mg) as starting material. Purification by MPLC (hexane/EtOAc = 80/20) obtained **24** as a brown powder (197 mg, 84%): mp 70-71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (br, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 3.80 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 157.0, 156.7, 129.8, 121.4, 114.4, 55.6, 43.3, 26.6. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{17}NO_3Na$ 258.1101; Found 258.1101.

Methyl 7-((4-methoxyphenyl)amino)-6,7-dioxoheptanoate (25).



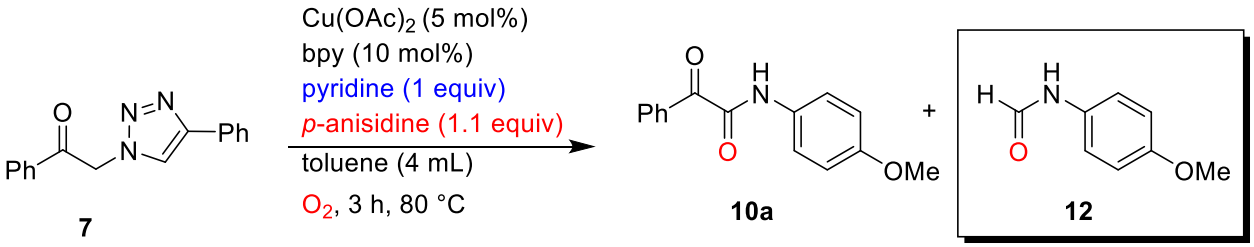
Method E: A solution of methyl 7-(1*H*-imidazol-1-yl)-6-oxoheptanoate (**19**, 224 mg, 1.0 mmol) and *p*-anisidine (135 mg, 1.1 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h and quenched slowly with cooled 0.05 N HCl aqueous (10 mL) in an ice bath. Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC (hexane/EtOAc = 40/60) to obtain **25** as a brown powder (170 mg, 58%): mp 108-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (br, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 3.81 (s, 3H), 3.67 (s, 3H) 3.04 (t, *J* = 6.0 Hz, 2H), 2.37 (t, *J* = 6.8 Hz, 2H), 1.72-1.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.2, 173.9, 157.3, 157.1, 129.6, 121.4, 114.5, 55.6, 51.8, 36.2, 33.9, 24.4, 22.8. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{19}NO_5Na$ 316.1155; Found 316.1155.

(*Z*)-*N*-(4-Methoxyphenyl)-2-oxononadec-10-enamide (26).



Method D was followed using *(Z)*-1-(1*H*-imidazol-1-yl)nonadec-10-en-2-one (**20**, 346 mg) as starting material. Purification by MPLC (hexane/EtOAc = 90/10) obtained **26** as a brown powder (299 mg, 72%): mp 86-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (br, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 5.37-5.33 (m, 2H), 3.80 (s, 3H), 2.99 (t, *J* = 8.0 Hz, 2H), 2.05-1.96 (m, 4H), 1.65 (quint, *J* = 7.2 Hz, 2H), 1.32-1.25 (m, 20H), 0.87 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 157.4, 157.1, 130.1, 129.8, 129.7, 121.3, 114.4, 55.6, 36.5, 32.0, 29.9, 29.8, 29.7, 29.5 (m), 29.4, 29.21, 29.19, 27.34, 27.29, 23.5, 22.8, 14.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{26}H_{41}NO_3Na$ 438.2979; Found 438.2980.

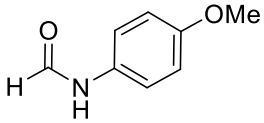
8) Side products



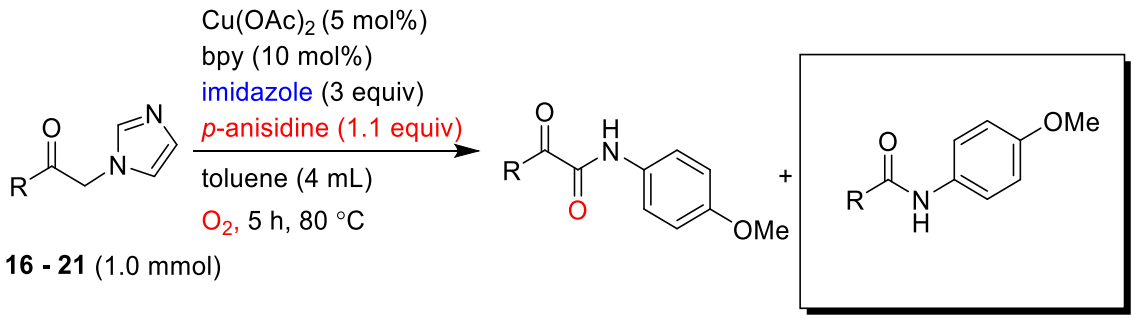
Method F: A solution of 1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one (**7**, 263 mg, 1.0 mmol) and *p*-anisidine (135 mg, 1.1 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and pyridine (79.1 mg, 1.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 3 h and quenched with water (10 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC to obtain **12**.

***N*-(4-Methoxyphenyl)formamide (12).**

This compound **12** is the side product in the **synthesis of compound 10a.**

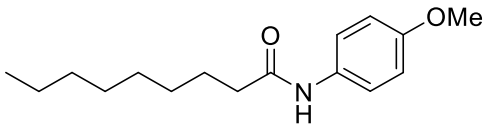


Method F was followed to obtain **12**. Purification by MPLC (hexane/EtOAc = 20/80) obtained **12** as a red solid (48 mg, 32%): mp 79-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (br, 1H), 8.49 (d, *J* = 12.0 Hz, 1H), 8.22-8.20 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H) 6.86-6.79 (m, 4H), 3.77-3.74 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 159.5, 157.5, 156.6, 130.2, 129.7, 121.9, 121.4, 114.9, 114.1, 55.54, 55.46. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_8H_{10}NO_2$ 152.0706; Found 152.0706.



_N_-(4-Methoxyphenyl)nonanamide (30).

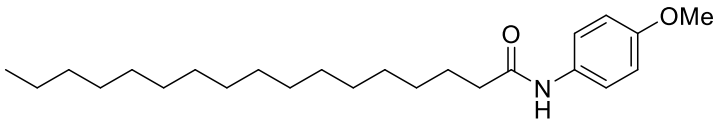
This compound **30** is the side product in the **synthesis of 22** **(Method D).**



Isolated as a brown powder (99.8 mg, 38%): mp 92-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.0 Hz, 2H), 7.16 (s, 1H), 6.85 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 2.32 (t, J = 8.0 Hz, 2H), 1.71 (quint, J = 8.0 Hz, 2H), 1.36-1.25 (m, 10H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 131.2, 121.9, 114.2, 55.6, 37.8, 32.0, 29.5, 29.4, 29.3, 25.9, 22.8, 14.2. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{25}NO_2Na$ 286.1778; Found 286.1779.

_N_-(4-Methoxyphenyl)heptadecanamide (31).

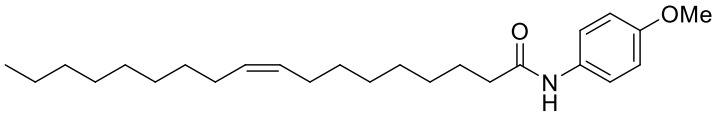
This compound **31** is the side product in the **synthesis of 23** **(Method D).**



Isolated as a white powder (119 mg, 32%): mp 108-109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.19 (s, 1H), 6.84 (d, J = 8.0 Hz, 2H), 3.78 (s, 3H), 2.31 (t, J = 8.0 Hz, 2H) 1.70 (quint, J = 8.0 Hz, 2H), 1.37-1.21 (m, 26H), 0.87 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 131.2, 121.8, 114.2, 55.6, 37.8, 32.1, 29.84-29.80 (m), 29.76, 29.6, 29.53, 29.51, 29.4, 25.9, 22.8, 14.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{41}NO_2Na$ 398.3030; Found 398.3036.

***N*-(4-Methoxyphenyl)oleamide (34).**

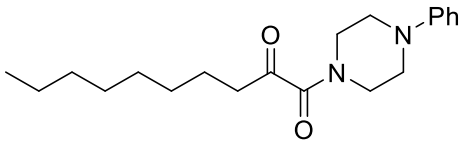
This compound **34** is the side product in the **synthesis of 26** **(Method D).**



Isolated as a white powder (108 mg, 28%): mp 76-78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0 Hz, 2H), 7.16 (s, 1H), 6.84 (d, J = 8.0 Hz, 2H), 5.44-5.28 (m, 2H), 3.78 (s, 3H), 2.32 (t, J = 8.0 Hz, 2H), 2.11-1.93 (m, 4H), 1.71 (quint, J = 6.8 Hz, 2H), 1.31-1.26 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 131.2, 130.1, 129.9, 121.8, 114.2, 55.6, 37.8, 32.0, 29.9, 29.8, 29.7, 29.5 (m), 29.4, 29.3, 27.4, 27.3, 25.8, 22.8, 14.3. HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{41}NO_2Na$ 410.3030; Found 410.3027.

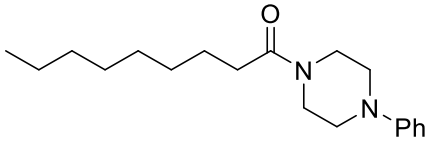
9) Three additional experiments to elucidate acyl amides from α-ketoamides

1-(4-Phenylpiperazin-1-yl)decane-1,2-dione (28).



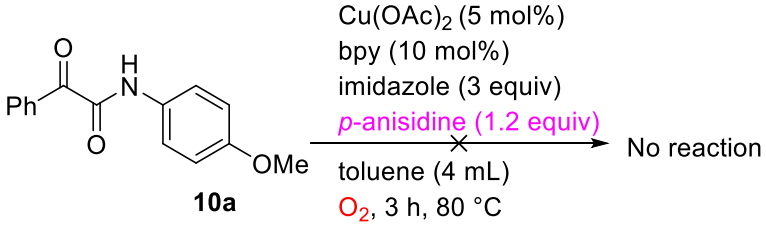
Method G: Method D was followed using 1-(1*H*-imidazol-1-yl)decan-2-one (**16**, 222 mg) as starting material. 1-Phenylpiperazine (178 mg, 1.1 mmol) was used instead of *p*-anisidine (1.1 mmol). The crude product was purified by glass column chromatography on silica gel (hexane/EtOAc/TEA = 85/10/5) to obtain the product as a yellow oil (204 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 8.0 Hz, 2H), 6.94-6.90 (m, 3H), 3.79 (t, *J* = 4.0 Hz, 2H), 3.61 (t, *J* = 4.0 Hz, 2H), 3.23-3.17 (m, 4H), 2.79 (t, *J* = 8.0 Hz, 2H), 1.64 (quint, *J* = 8.0 Hz, 2H), 1.36-1.26 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 165,6, 150.9, 129.4, 121.0, 117.0, 50.1, 49.6, 45.7, 41.6, 40.3, 31.9, 29.4, 29.23, 29.21, 23.0, 22.7, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{31}N_2O_2$ 331.2380; Found 331.2380.

1-(4-Phenylpiperazin-1-yl)nonan-1-one (29).



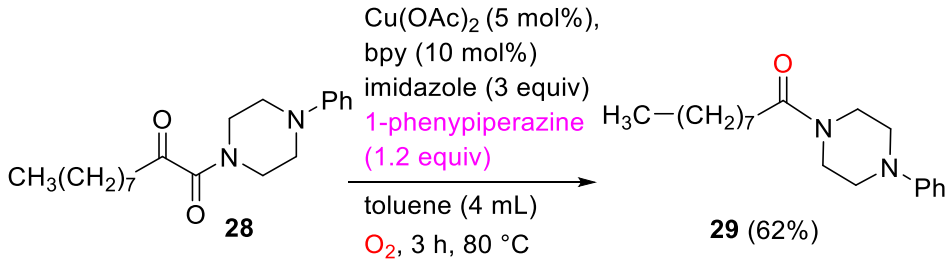
This compound **29** (87 mg, 29%) was also isolated from **Method G** as a white solid: mp 48-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 8.0 Hz, 2H), 6.95-6.89 (m, 3H), 3.78 (t, *J* = 5.2 Hz, 2H), 3.63 (t, *J* = 5.2 Hz, 2H), 3.19-3.14 (m, 4H), 2.36 (t, *J* = 8.0 Hz, 2H), 1.65 (quint, *J* = 8.0 Hz, 2H), 1.37-1.27 (m, 10H), 0.88 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 151.0, 129.4, 120.9, 116.9, 50.1, 49.7, 45.6, 41.5, 33.5, 32.0, 29.6, 29.5, 29.3, 25.5, 22.8, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{31}N_2O$ 303.2431; Found 303.2431.

(1) No reaction



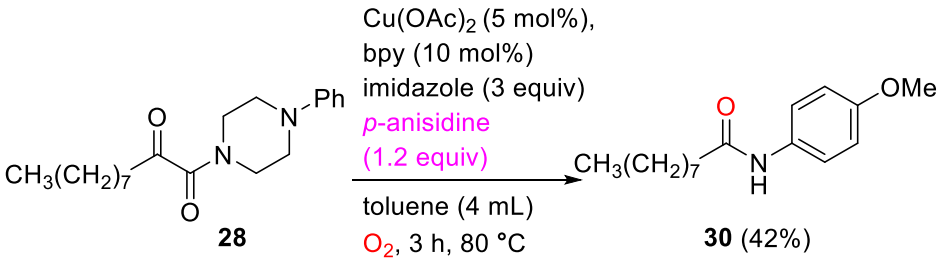
A solution of *N*-(4-methoxyphenyl)-2-oxo-2-phenylacetamide (**10a**, 255 mg, 1.0 mmol) and *p*-anisidine (148 mg, 1.2 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 3 h. **10a** 100% as starting material was recovered.

(2) The synthesis of 1-(4-phenylpiperazin-1-yl)nonan-1-one (29) from 28



Method H: A solution of 1-(4-phenylpiperazin-1-yl)decane-1,2-dione (**28**, 330 mg, 1.0 mmol) and 1-phenylpiperazine (195 mg, 1.2 mmol) in toluene (4 mL) was treated with $Cu(OAc)_2$ (9 mg, 0.05 mmol), bpy (16 mg, 0.1 mmol) and imidazole (204 mg, 3.0 mmol). The reaction mixture under O_2 balloon was stirred at 80 °C for 3 h and quenched with water (10 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC (hexane/EtOAc = 70/30) to obtain **29** as a white solid (187 mg, 62%).

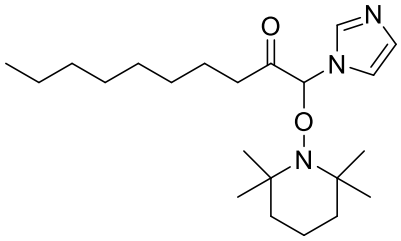
(3) The synthesis of *N*-(4-methoxyphenyl)nonanamide (30) from 28



Method H was followed using *p*-anisidine (148 mg, 1.2 mmol) as starting material instead of 1-phenylpiperazine (1.2 mmol). The crude product was purified by MPLC (hexane/EtOAc = 70/30) to obtain the product as a brown powder (110 mg, 42%).

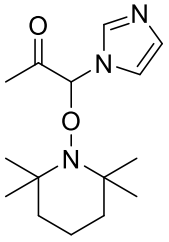
10) General procedure of TEMPO experiments (35)-(39)

1-(1*H*-Imidazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)decan-2-one (35).



Method I: A solution of 1-(1*H*-imidazol-1-yl)decan-2-one (**16**, 111 mg, 0.5 mmol) in toluene (1 mL) was treated with $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), bpy (8 mg, 0.05 mmol) and imidazole (34 mg, 0.5 mmol). TEMPO (78 mg, 0.5 mmol) was added to the mixture and rinsed with toluene (1 mL). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h. The neat solution (0.5 mL) was transferred to an 8 mL vial. Toluene was removed from the neat solution with high vacuum for 2 h. ^{1}H NMR sample was prepared with $CDCl_3$ (0.5 mL) to investigate the ratio of TEMPO trapped products. After ^{1}H NMR spectra were recorded, extra crude mixture was combined with ^{1}H NMR sample. The extra solvents were evaporated under reduced pressure and the crude mixture was transferred into a 50 mL separatory funnel with EtOAc (4 mL) and water (4 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 4 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC (hexane/EtOAc = 70/30) to obtain the product as a colorless oil (162 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.09 (s, 1H), 6.97 (s, 1H), 5.79 (s, 1H), 2.61-2.46 (m, 2H), 1.57-1.23 (m, 21H), 1.11 (s, 3H), 1.05 (s, 3H), 0.86 (t, *J* = 6.8 Hz, 3H), 0.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 137.3, 130.3, 117.3, 93.6, 61.5, 59.9, 40.3, 40.0, 38.7, 33.2, 31.9, 31.6, 29.4, 29.2, 29.1, 23.2, 22.7, 20.4 (m), 17.0, 14.2. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{40}N_3O_2$ 378.3115; Found 378.3115.

1-(1*H*-Imidazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-one (36).

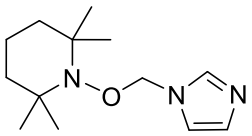


Method J: A solution of 1-(1*H*-imidazol-1-yl)propan-2-one (**13**, 62 mg, 0.5 mmol) in toluene (1 mL) was treated with $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), bpy (8 mg, 0.05 mmol) and imidazole (34 mg, 0.5 mmol). TEMPO (78 mg, 0.5 mmol) was added to the mixture and rinsed with toluene (1 mL). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h. The neat solution (0.5 mL) was transferred to an 8 mL vial. Toluene was removed from the neat solution with high vacuum for 2 h. ^{1}H NMR sample was prepared with $CDCl_3$ (0.5 mL) to investigate the ratio of TEMPO trapped products. After ^{1}H NMR spectra were recorded, extra crude mixture was combined with ^{1}H NMR sample. The extra solvents were evaporated under reduced pressure and the crude mixture was transferred into a 50 mL separatory funnel with EtOAc (4 mL) and water (4 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 4 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC (EtOAc/MeOH = 98/2) to obtain the product as a white powder (98 mg, 71%): mp 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.10 (s, 1H), 6.99 (s, 1H), 5.77 (s, 1H), 2.28 (s, 3H), 1.54-1.30 (m, 6H), 1.23 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H), 0.46 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 200.1, 137.2, 130.5, 117.1, 93.9, 61.5, 59.9, 40.3, 40.0, 33.2, 31.6, 26.1, 20.42, 20.35, 17.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{26}N_3O_2$ 280.2020; Found 280.2018.

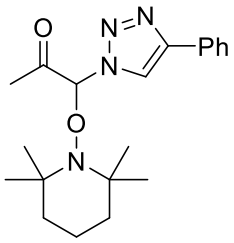
1-((1*H*-Imidazol-1-yl)methoxy)-2,2,6,6-tetramethylpiperidine (37).

This compound **37** is the common side product in the both **Method I** and **Method J.**



Method I: The crude product was purified by MPLC (hexane/EtOAc = 70/30) to obtained **37** (4 mg, 4%). **Method J**: The crude product was purified by MPLC (EtOAc/MeOH = 98/2) 2 times to separate **37** from **36** (14 mg, 12%). Isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.07 (br, 2H), 5.44 (s, 2H), 1.47-1.45 (m, 4H), 1.35-1.31 (m, 2H), 1.06 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 129.7, 119.5, 81.1, 60.2, 39.8, 33.0, 20.2, 17.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{24}N_3O$ 238.1914; Found 238.1914.

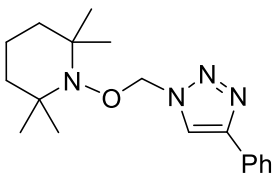
1-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-one (38).



Method K: A solution of 1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)propan-2-one (**14**, 101 mg, 0.5 mmol) in toluene (1 mL) was treated with $Cu(OAc)_2$ (4.5 mg, 0.025 mmol), bpy (8 mg, 0.05 mmol) and imidazole (34 mg, 0.5 mmol). TEMPO (78 mg, 0.5 mmol) was added to the mixture and rinsed with toluene (1 mL). The reaction mixture under O_2 balloon was stirred at 80 °C for 5 h. The neat solution (0.5 mL) was transferred to an 8 mL vial. Toluene was removed from the neat solution with high vacuum for 2 h. ^{1}H NMR sample was prepared with $CDCl_3$ (0.5 mL) to investigate the ratio of TEMPO trapped products. After ^{1}H NMR spectra were recorded, extra crude mixture was combined with ^{1}H NMR sample. The extra solvents were evaporated under reduced pressure and the crude mixture was transferred into a 50 mL separatory funnel with EtOAc (4 mL) and water (4 mL). Phases were separated and the aqueous layer was extracted with EtOAc (3 x 4 mL), dried separated organic phases with Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by MPLC (hexane/EtOAc = 80/20) to obtain **38** as a white powder (64 mg, 36%): mp 105-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 6.30 (s, 1H), 2.43 (s, 3H), 1.53-1.41 (m, 6H), 1.27 (s, 3H), 1.20 (s, 3H), 1.08 (s, 3H), 0.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 147.9, 130.1, 128.9, 128.5, 125.9, 119.7, 95.1, 61.6, 60.0, 40.1, 39.9, 33.0, 31.7, 27.0, 20.39, 20.37, 16.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{29}N_4O_2$ 357.2285; Found 357.2285.

2,2,6,6-Tetramethyl-1-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methoxy)piperidine (39).

This compound **39** is the side product in the synthesis of **38.** **(Method K)**



The crude product was purified by MPLC (hexane/EtOAc = 80/20) to obtain **39** as a white powder (48 mg, 31%): mp 75-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 5.90 (s, 2H), 1.53-1.47 (m, 4H), 1.37-1.33 (m, 2H), 1.09 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 130.6, 129.0, 128.4, 126.0, 120.3, 83.5, 60.4, 39.8, 33.0, 20.3, 17.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{27}N_4O$ 315.2179; Found 315.2179.

11) Comparison of crude mixture (Method I-K) ^{1}H NMR and compound (35-39) ^{1}H NMR

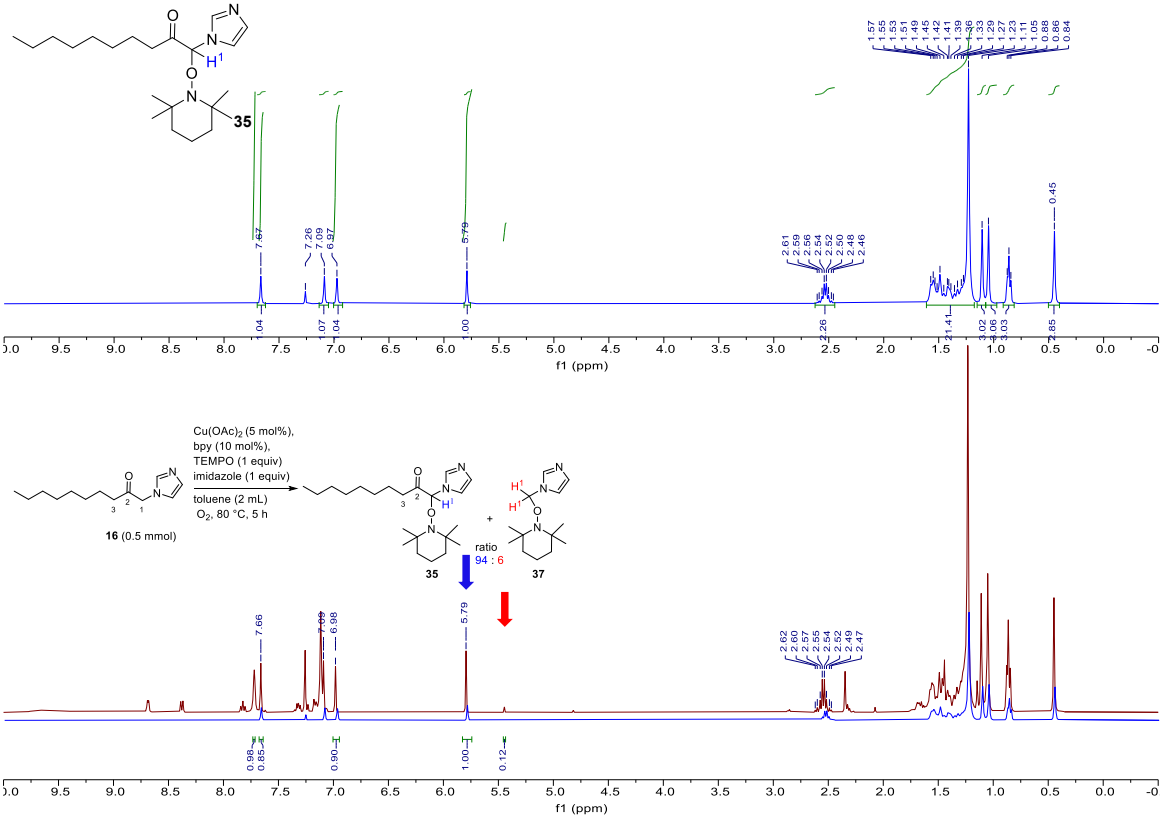


Fig. S1. Comparison of Crude ^{1}H NMR **Method I** and ^{1}H NMR of **35.**

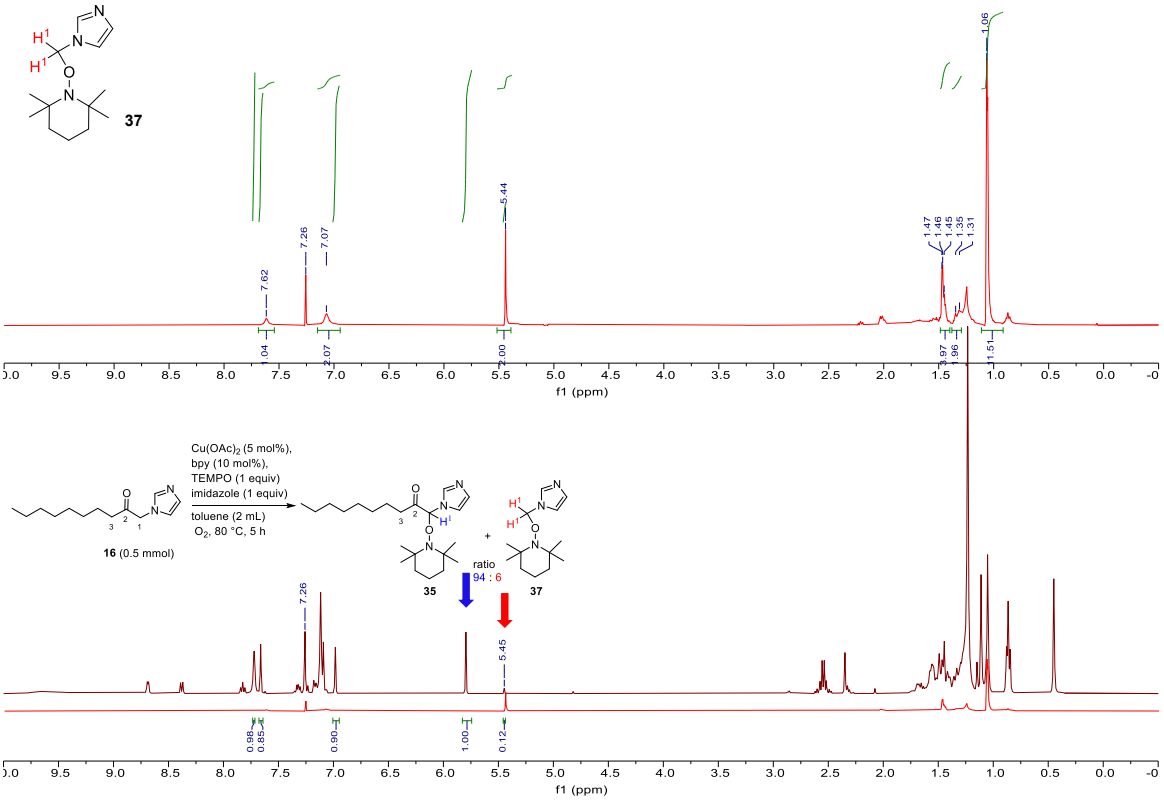


Fig. S2. Comparison of Crude ^{1}H NMR **Method I** and ^{1}H NMR of **37.**

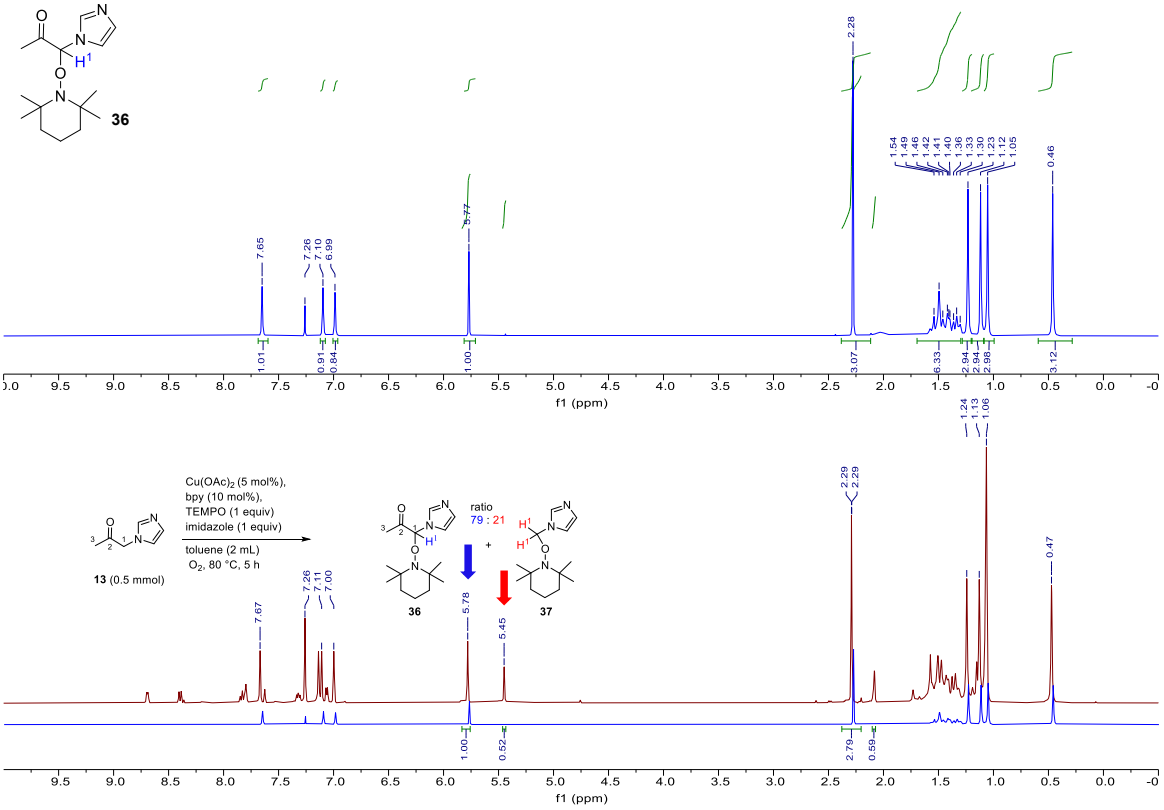


Fig. S3. Comparison of Crude ^{1}H NMR **Method J** and ^{1}H NMR of **36.**

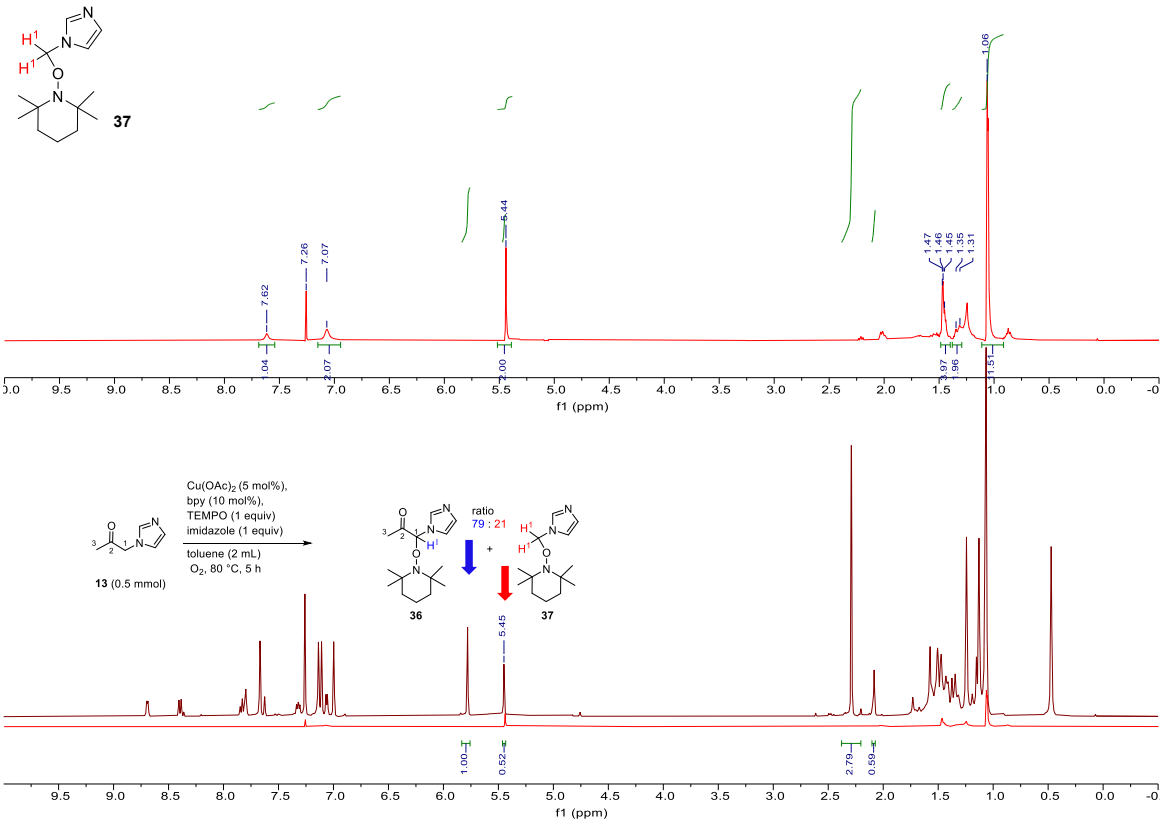


Fig. S4. Comparison of Crude ^{1}H NMR **Method J** and ^{1}H NMR of **37.**

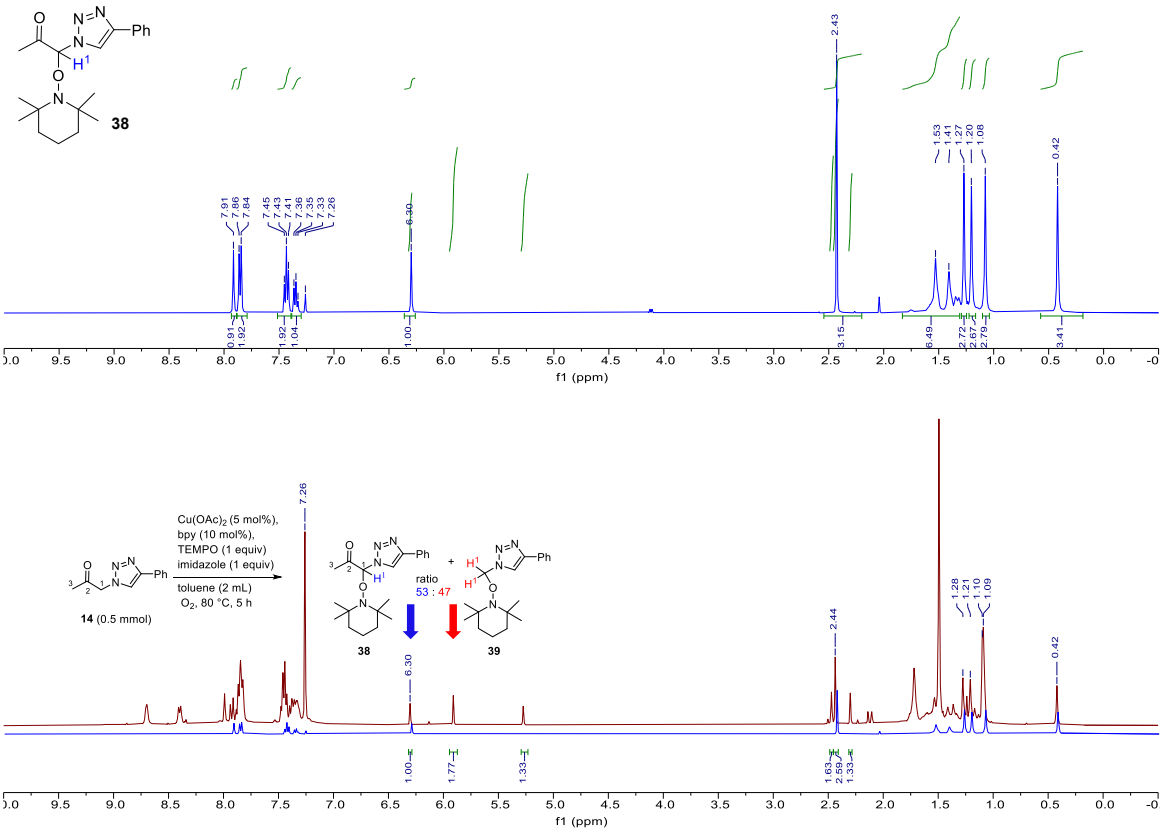


Fig. S5. Comparison of Crude ^{1}H NMR **Method K** and ^{1}H NMR of **38.**

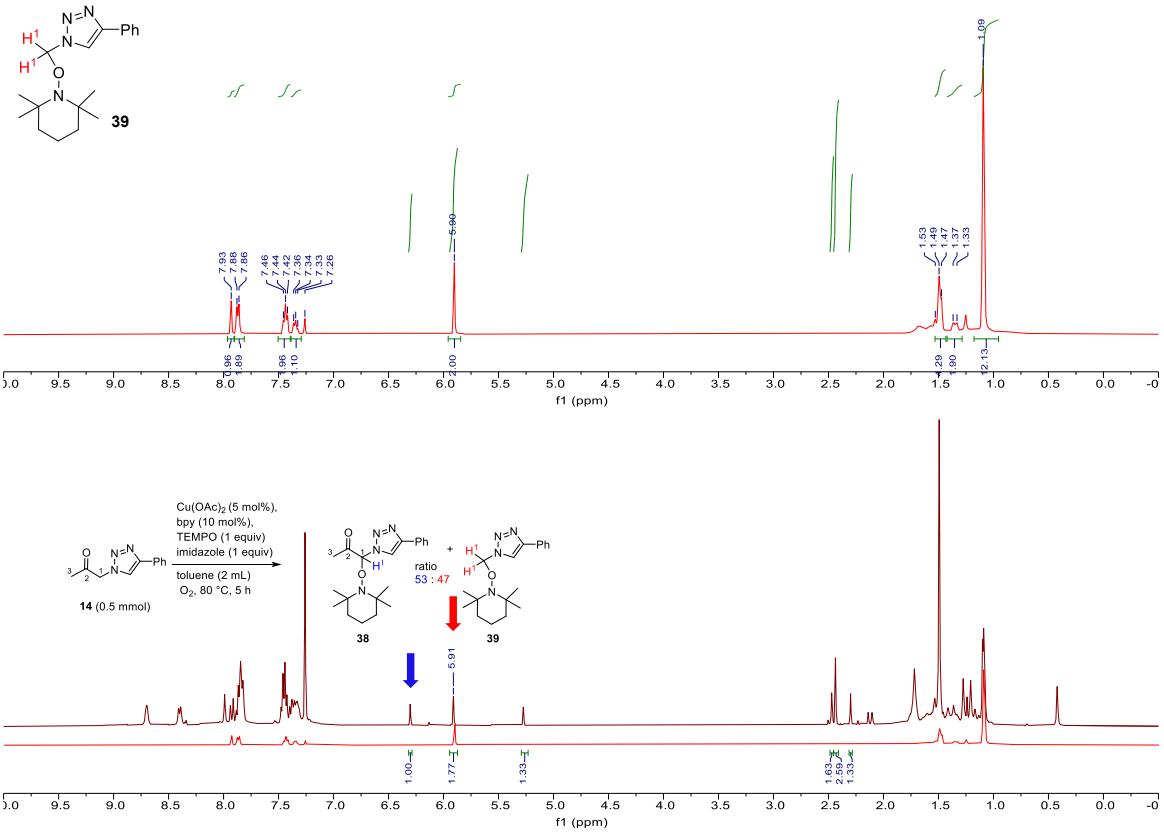
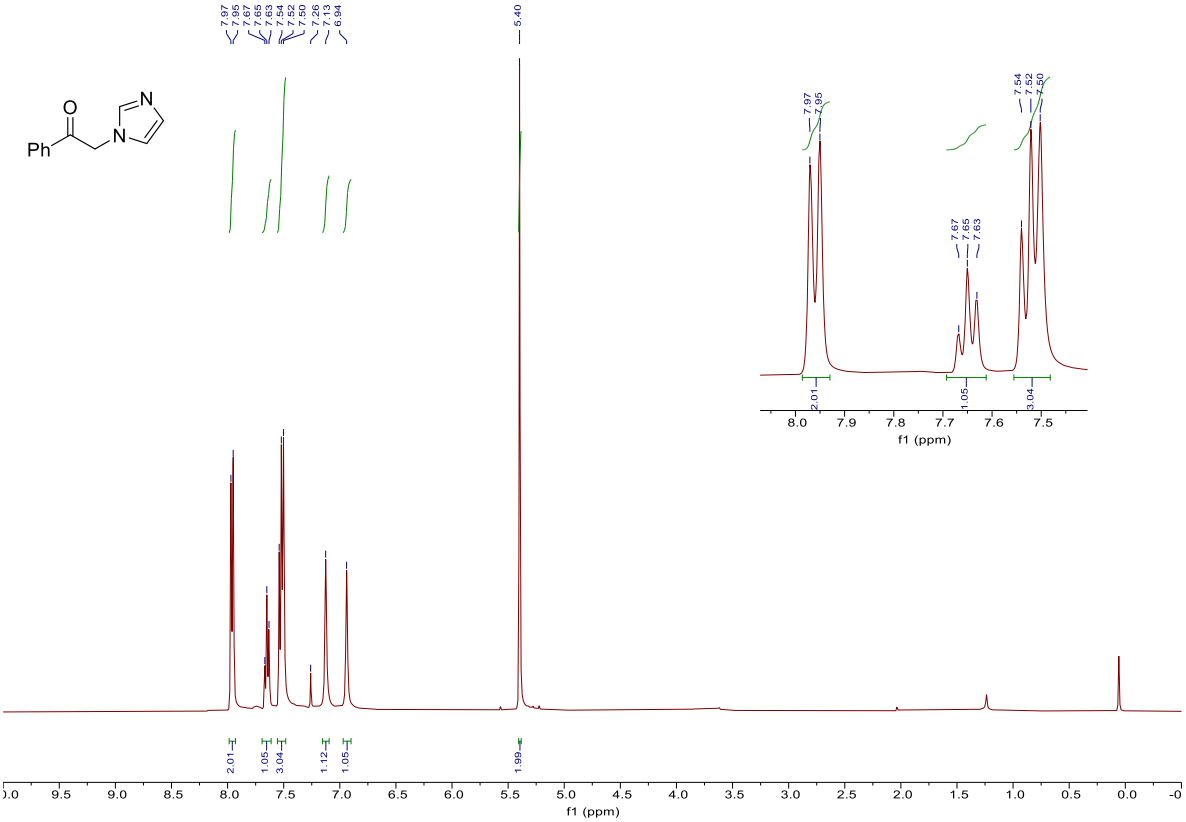


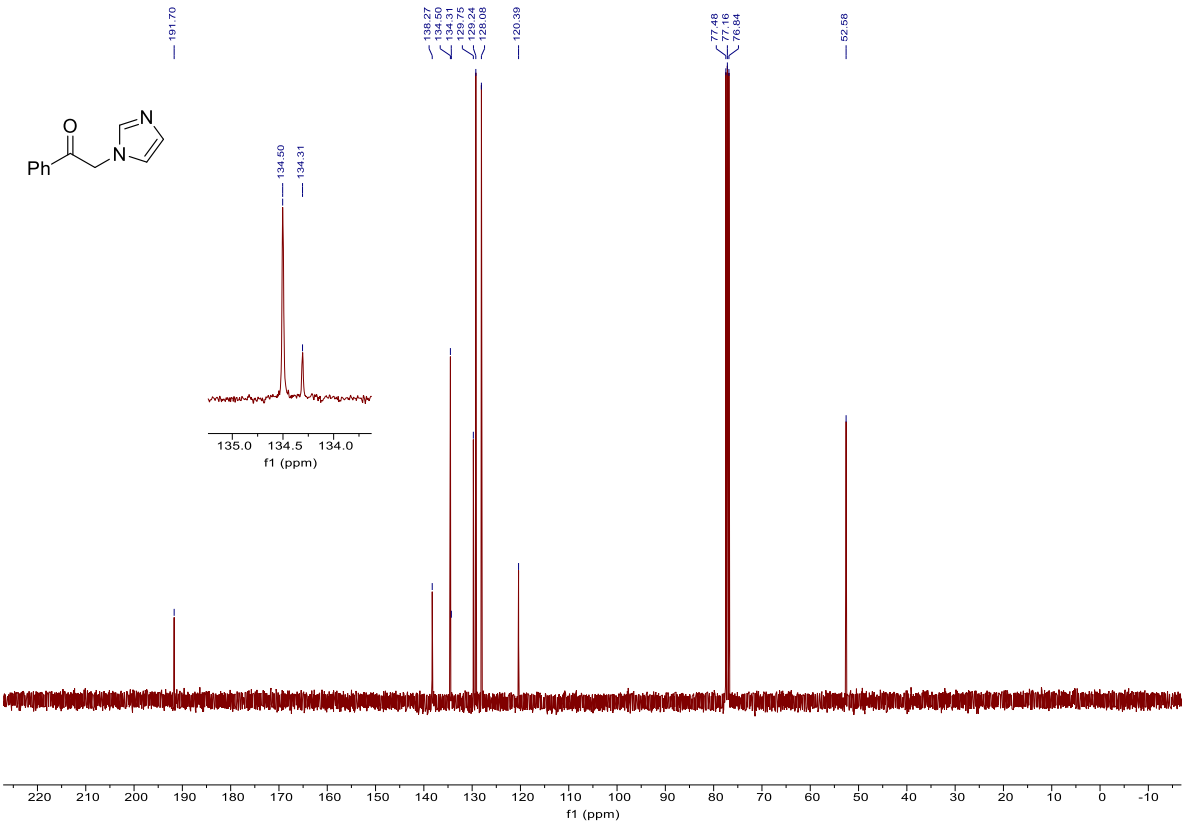
Fig. S6. Comparison of Crude ^{1}H NMR **Method K** and ^{1}H NMR of **39.**

12) Copies of ^{1}H NMR and ^{13}C NMR spectra

2-(1*H*-Imidazol-1-yl)-1-phenylethan-1-one (11).

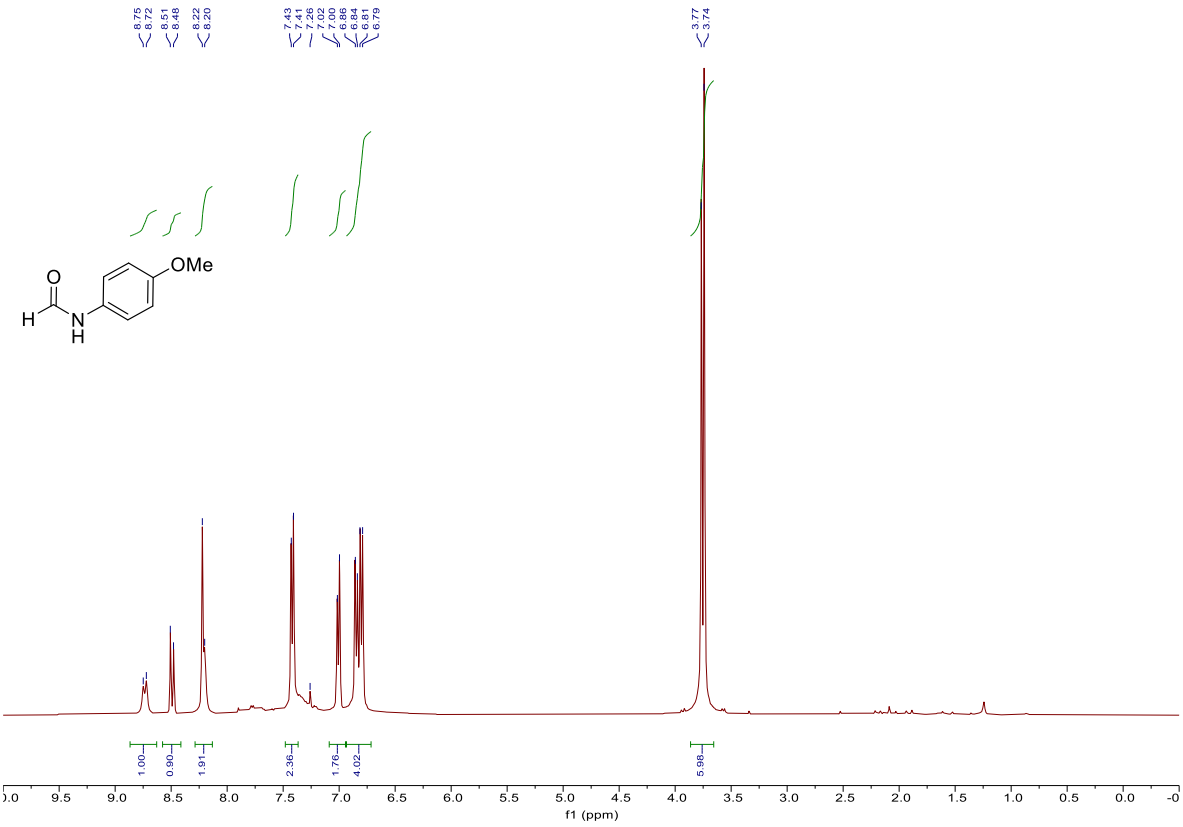
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

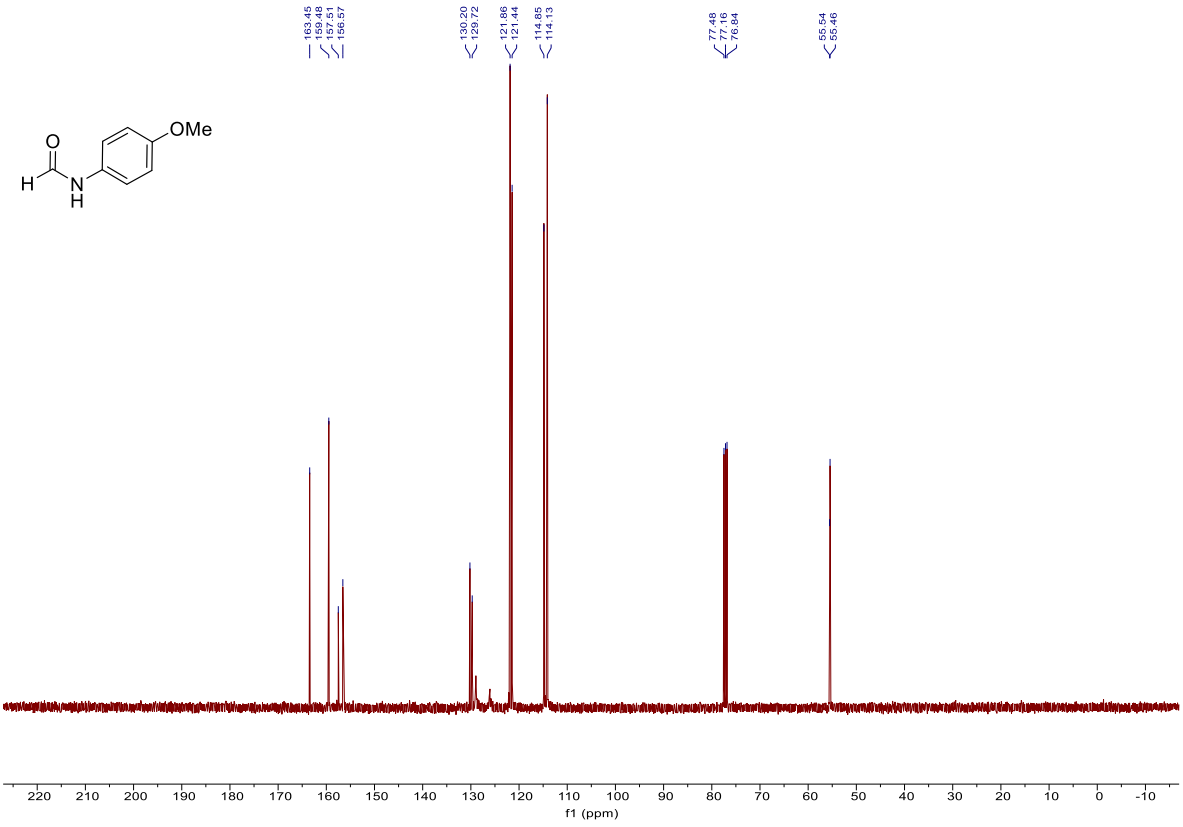




_N_-(4-Methoxyphenyl)formamide (12).

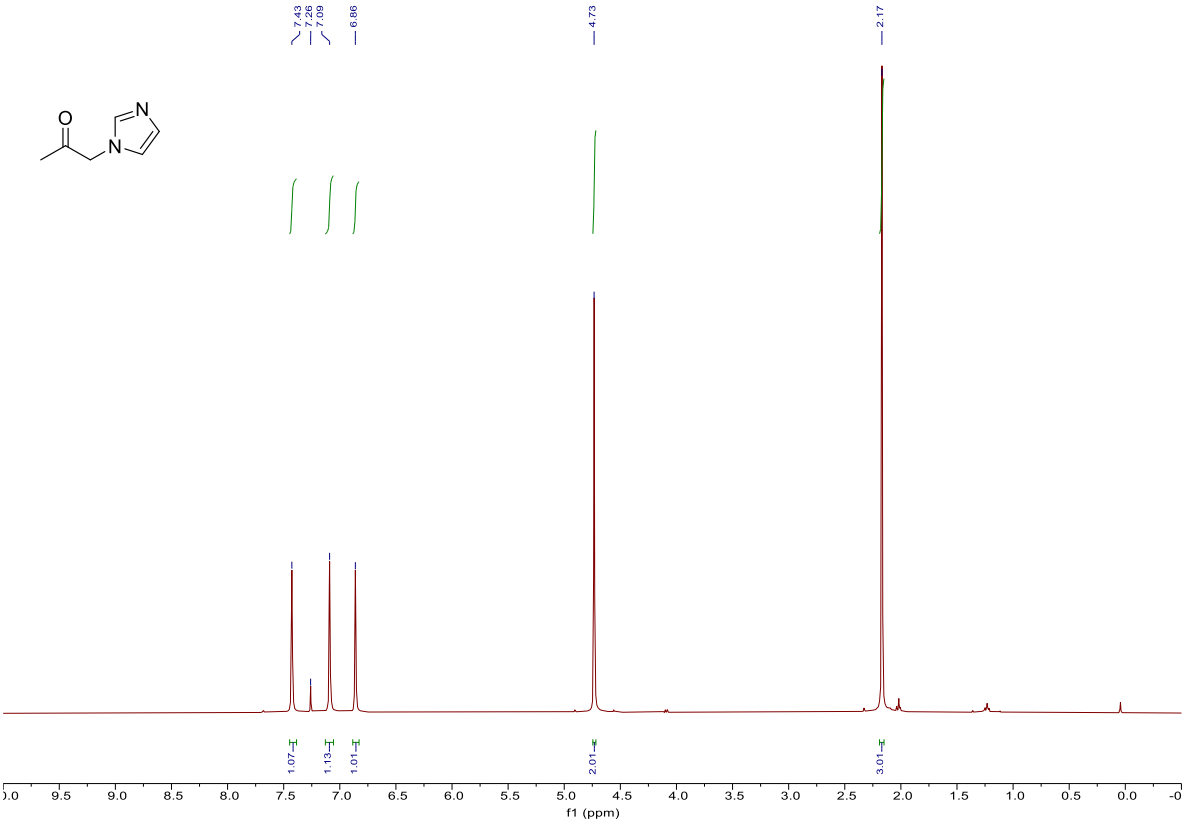
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

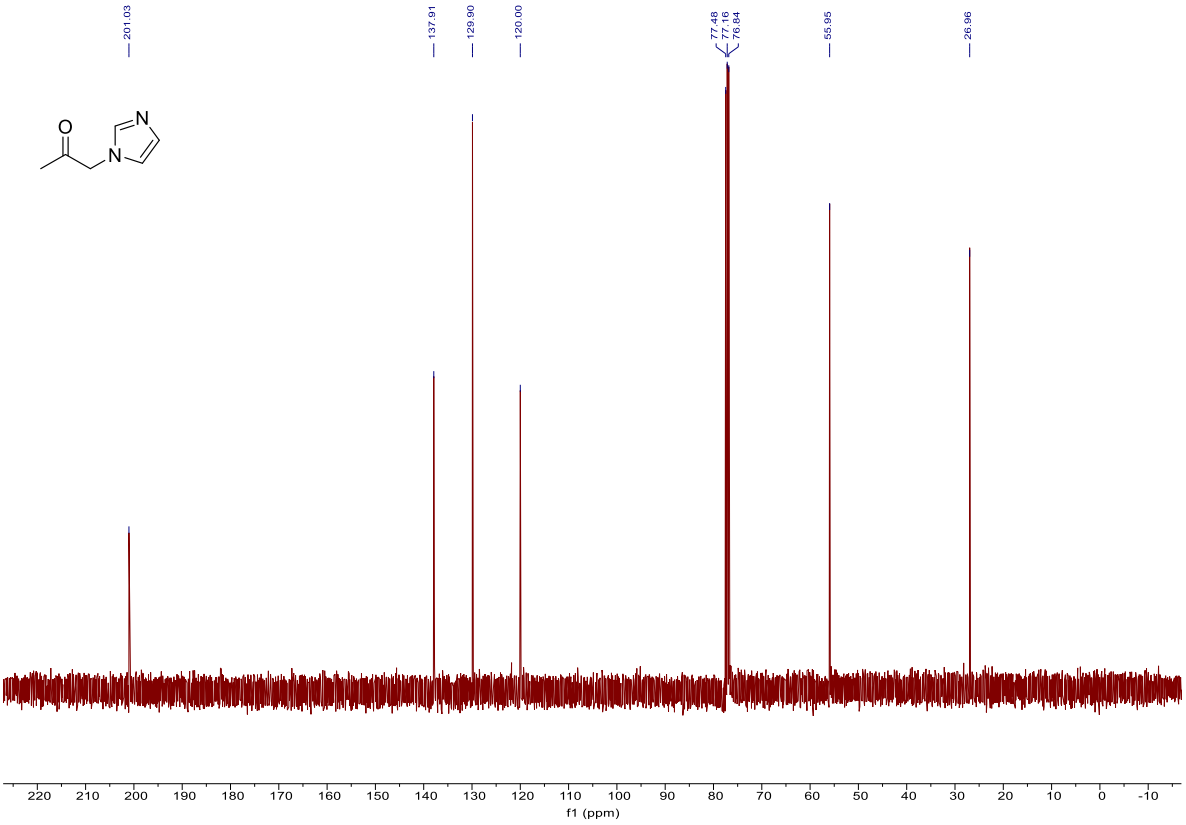




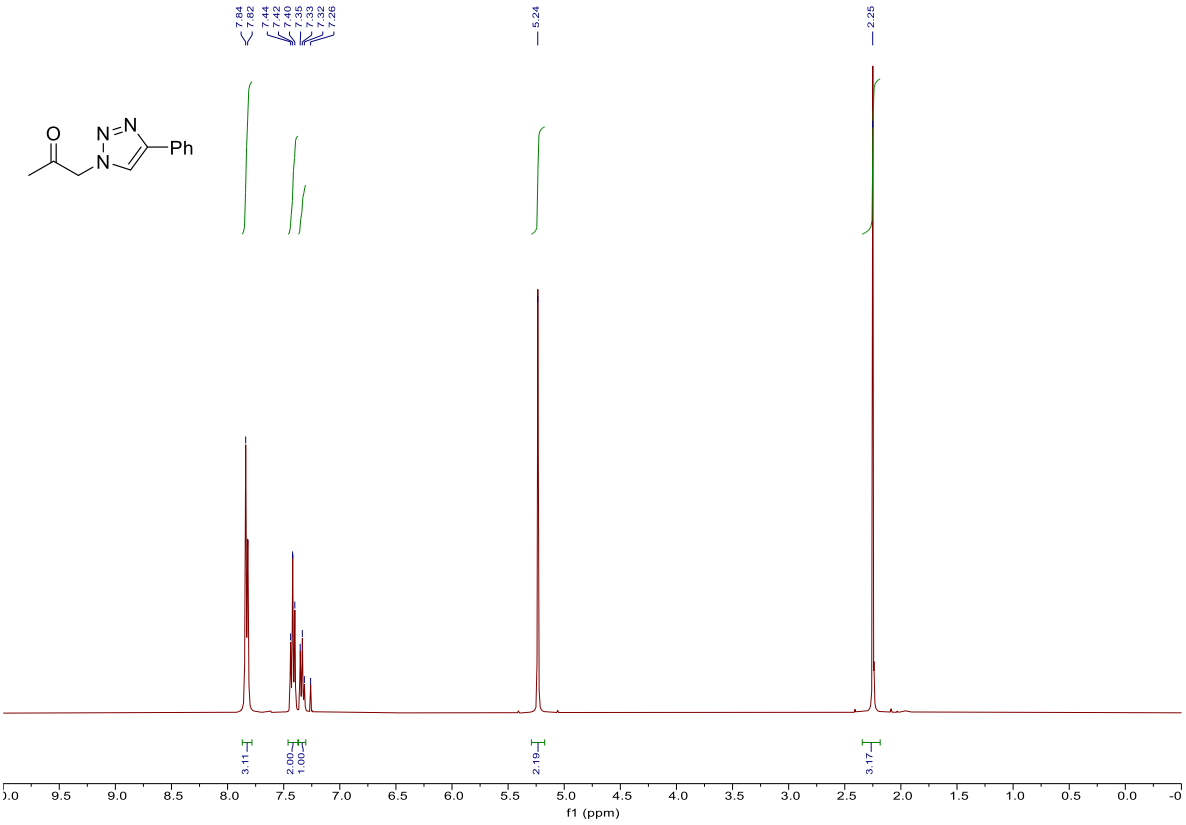
1-(1*H*-Imidazol-1-yl)propan-2-one (13).

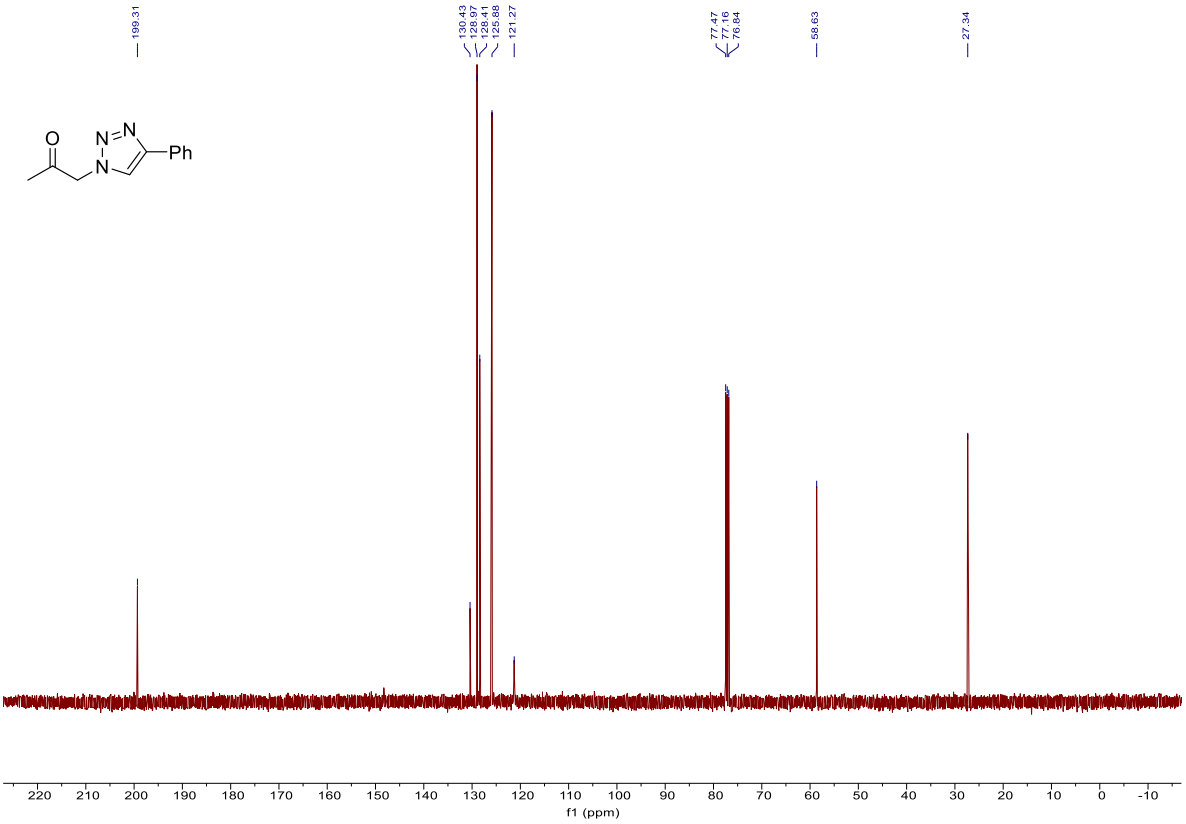
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).





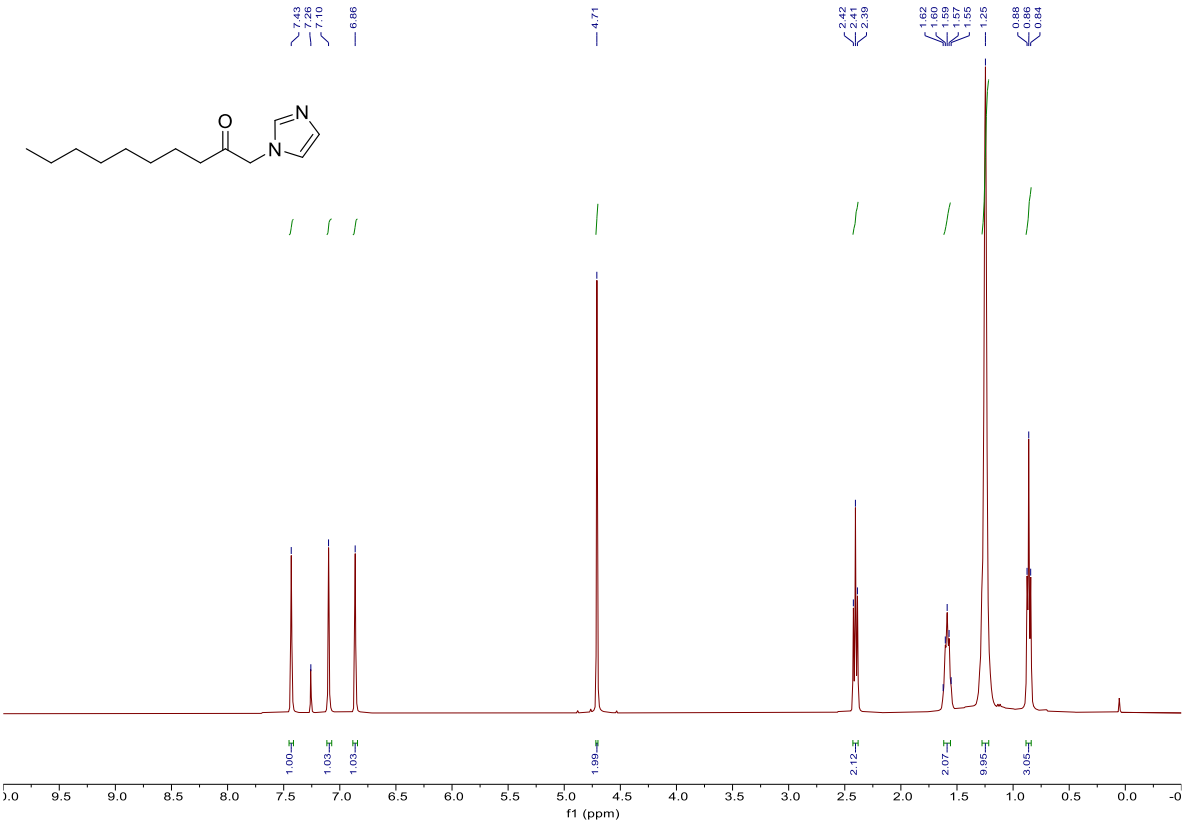
1-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)propan-2-one (14).
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

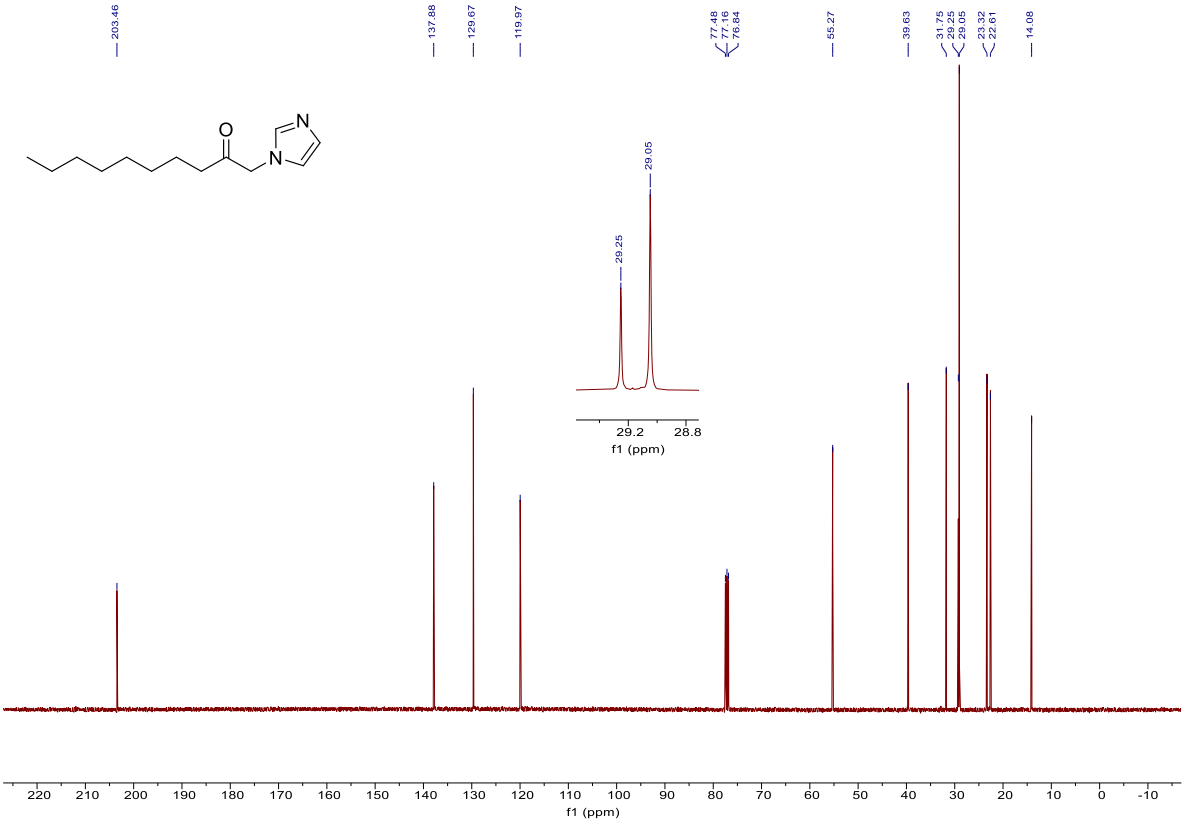




1-(1*H*-Imidazol-1-yl)decan-2-one (16).

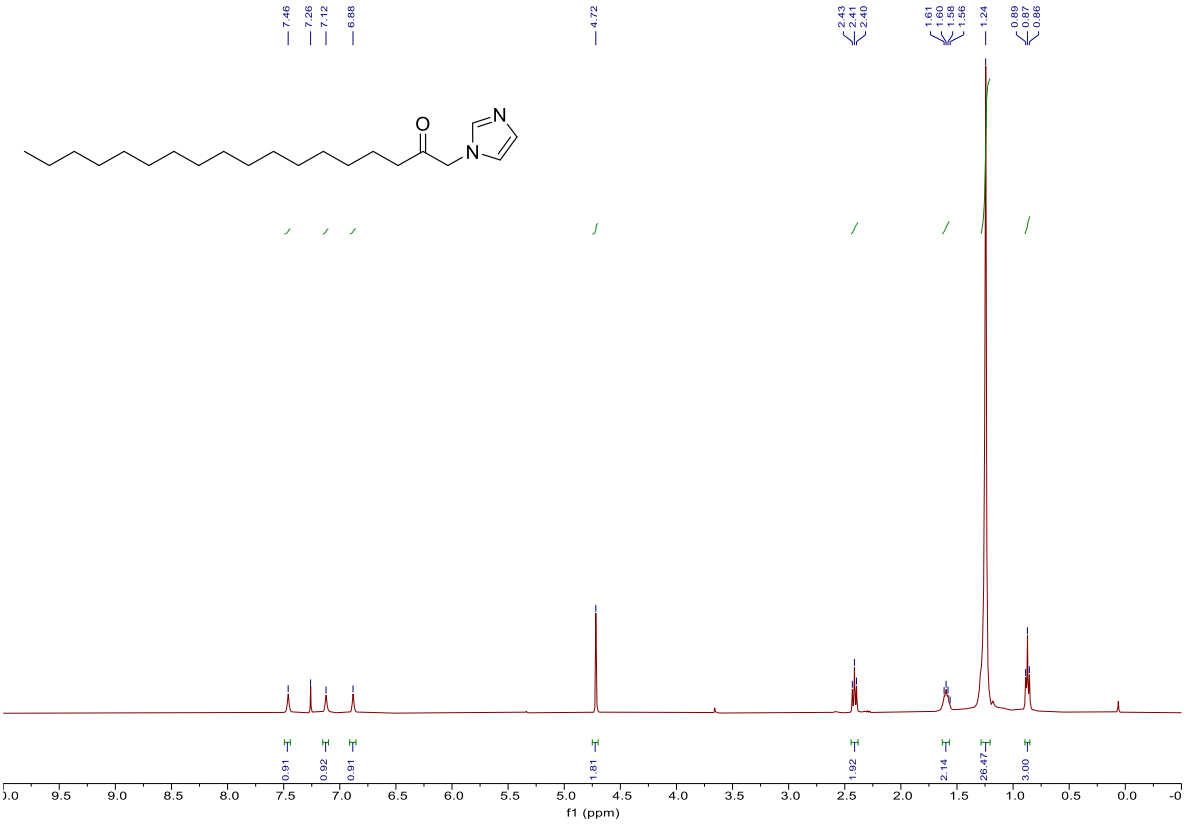
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

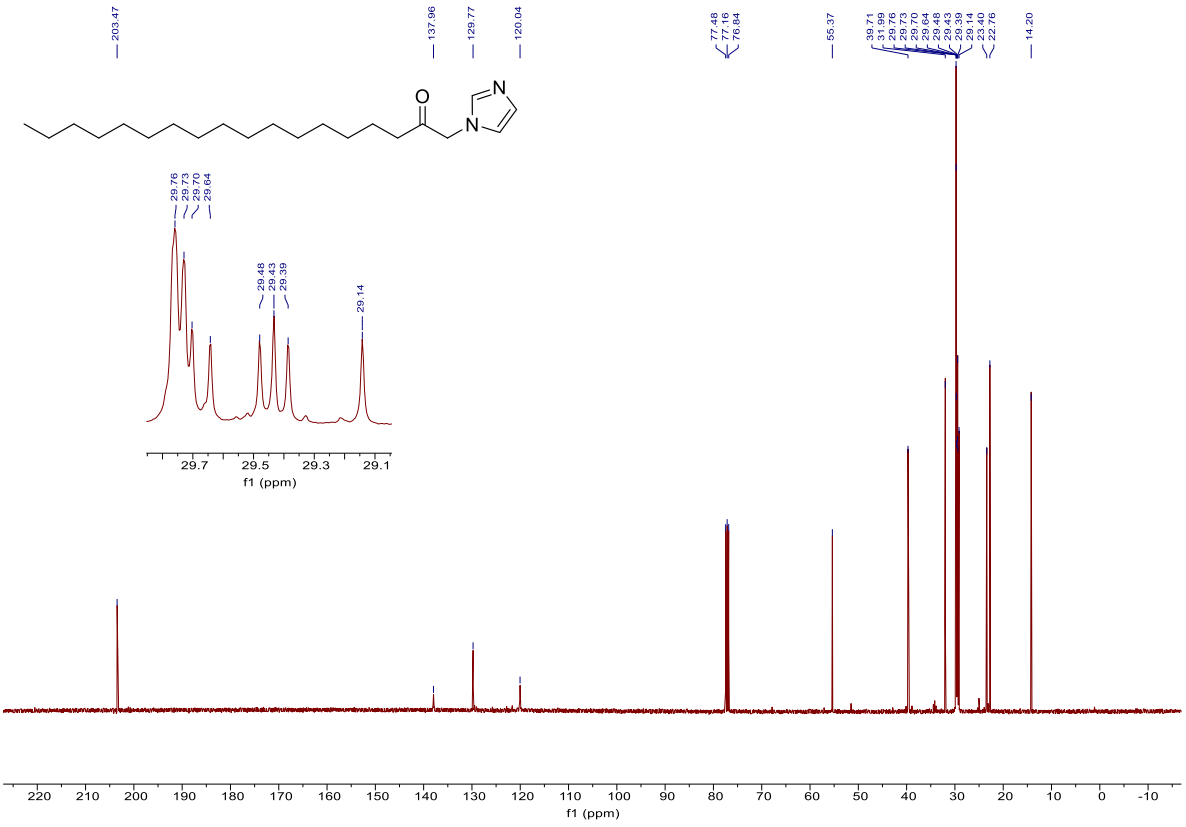




1-(1*H*-Imidazol-1-yl)octadecan-2-one (17).

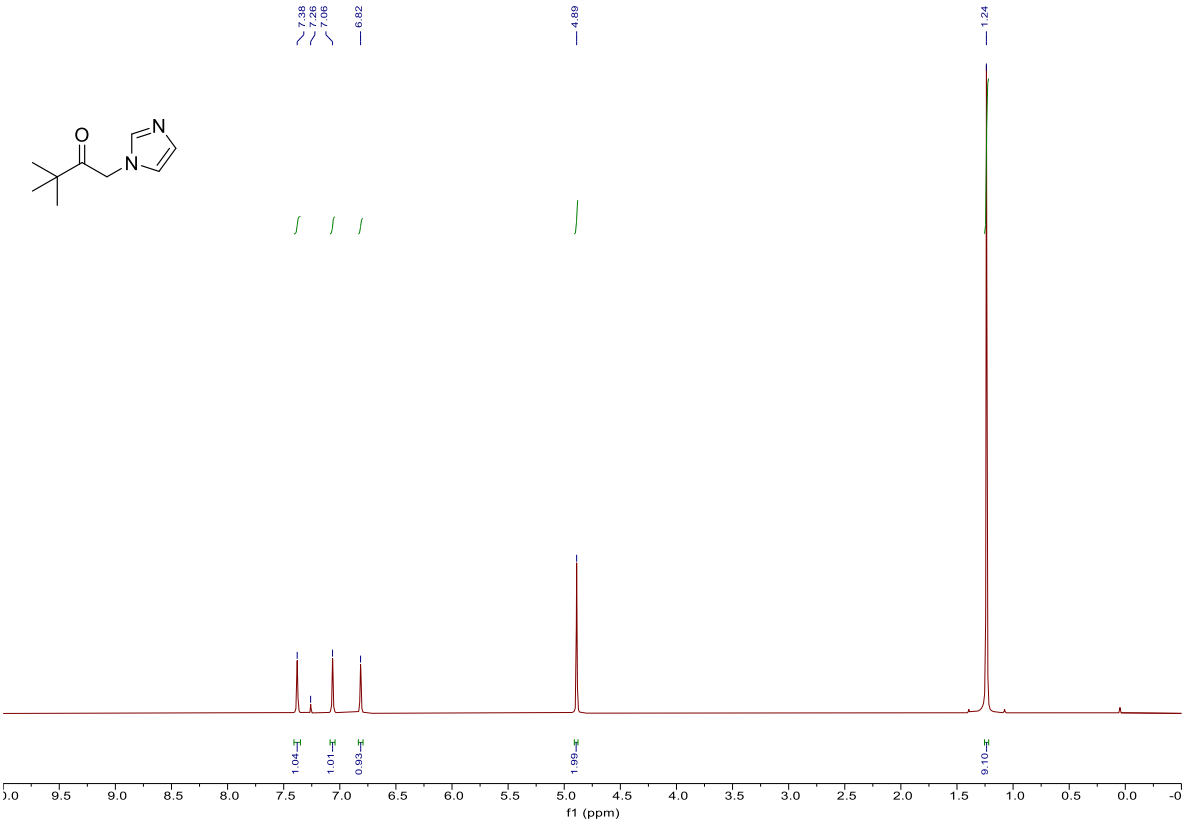
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

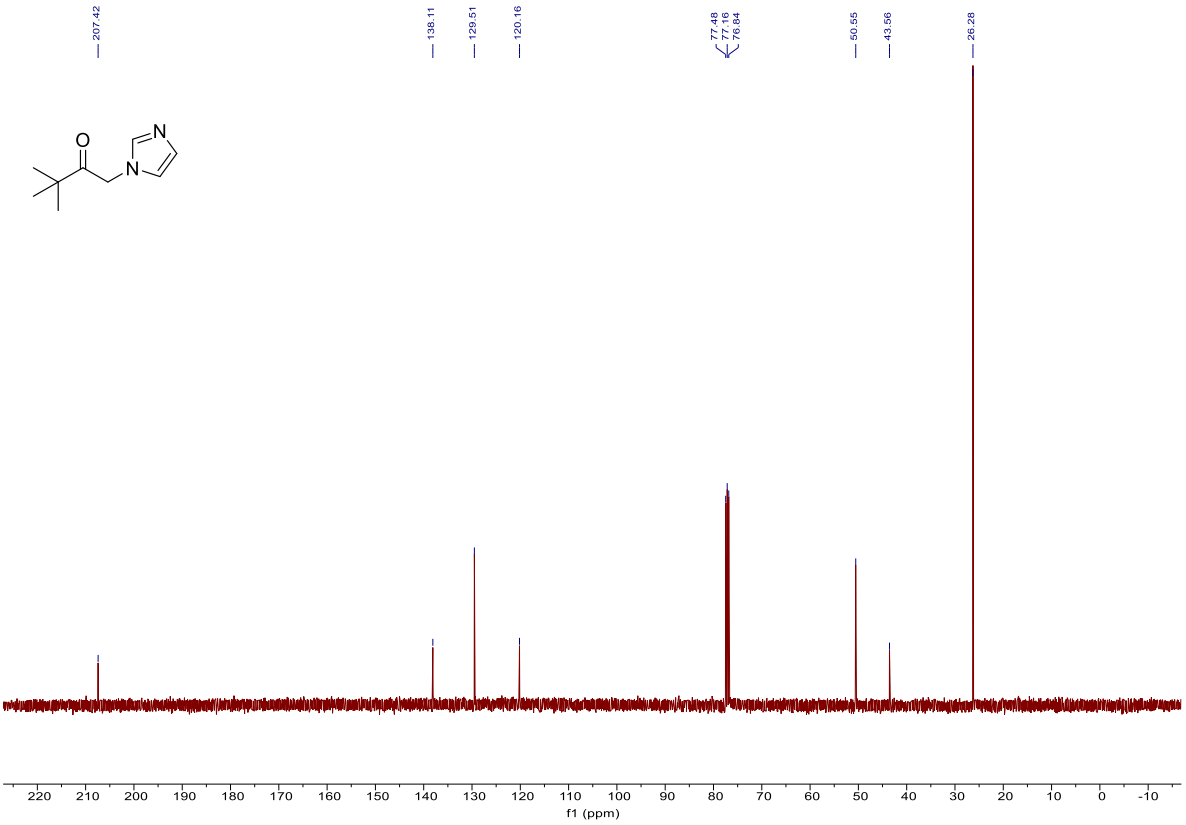




1-(1*H*-Imidazol-1-yl)-3,3-dimethylbutan-2-one (18).

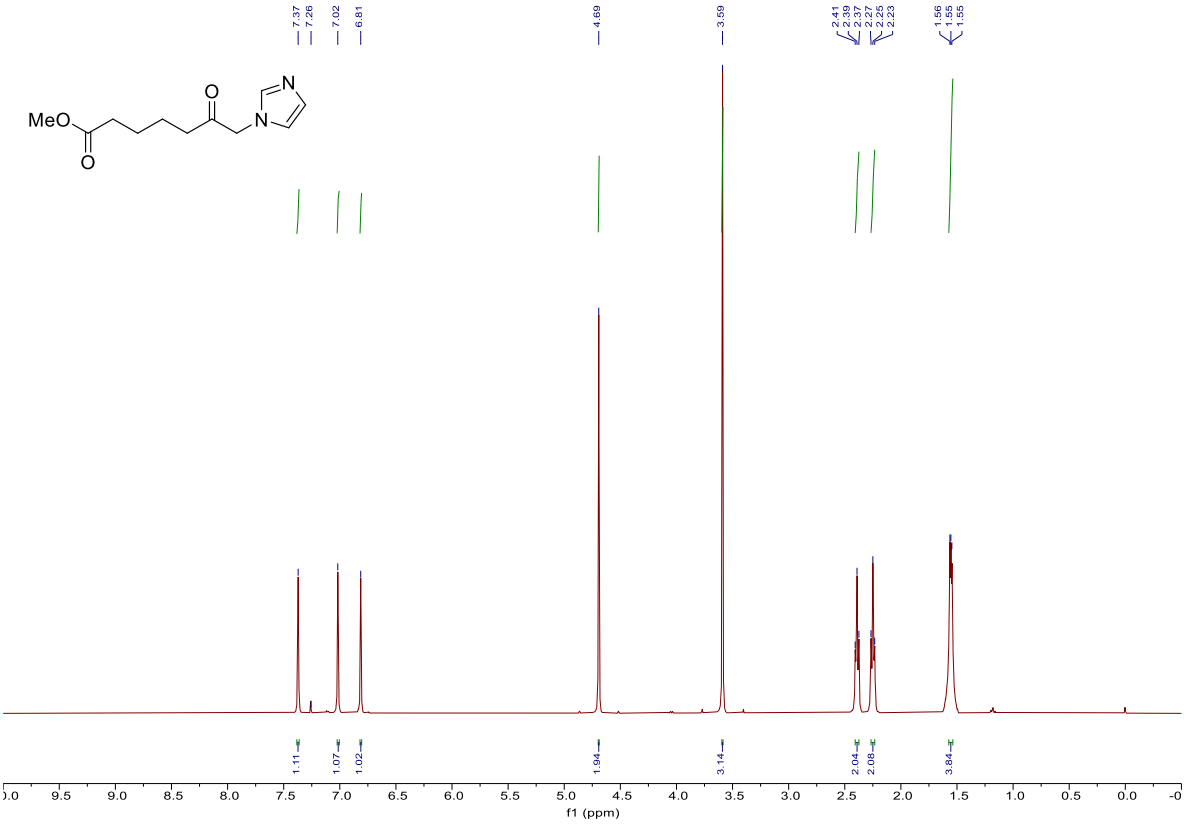
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

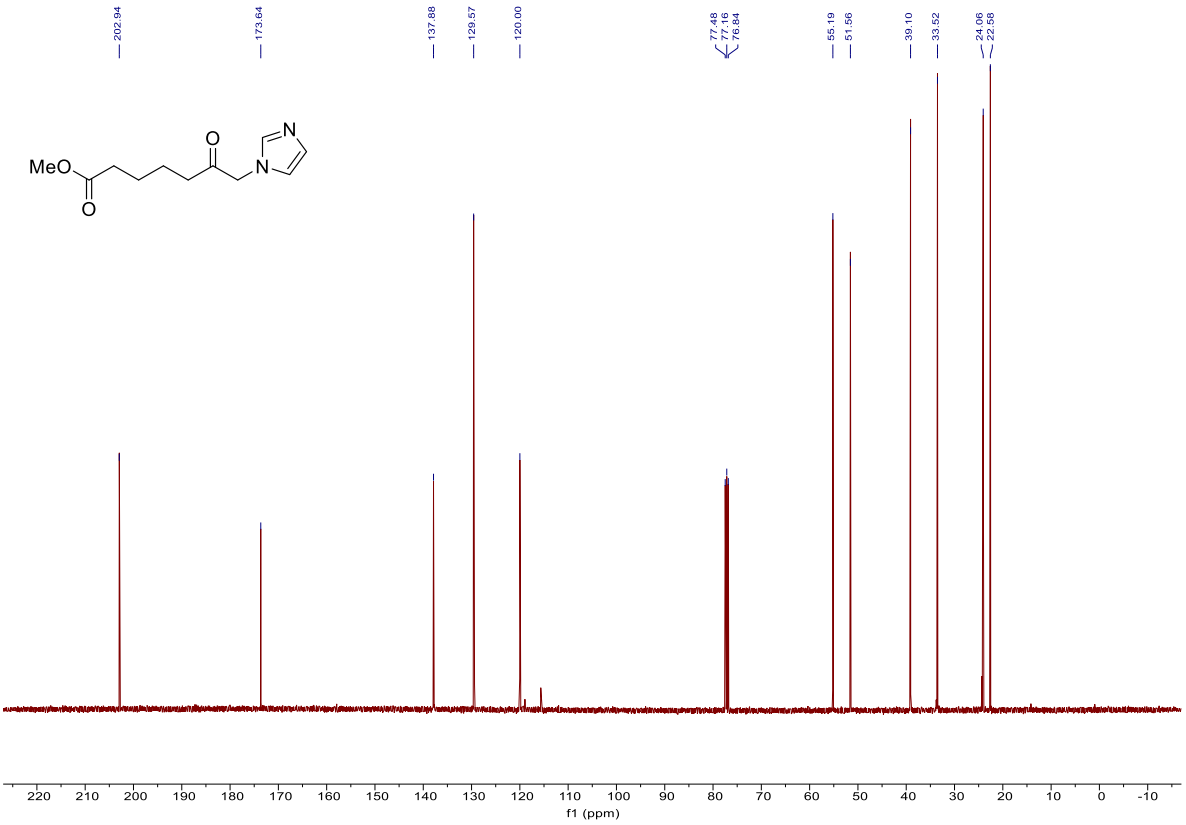




Methyl 7-(1*H*-imidazol-1-yl)-6-oxoheptanoate (19).

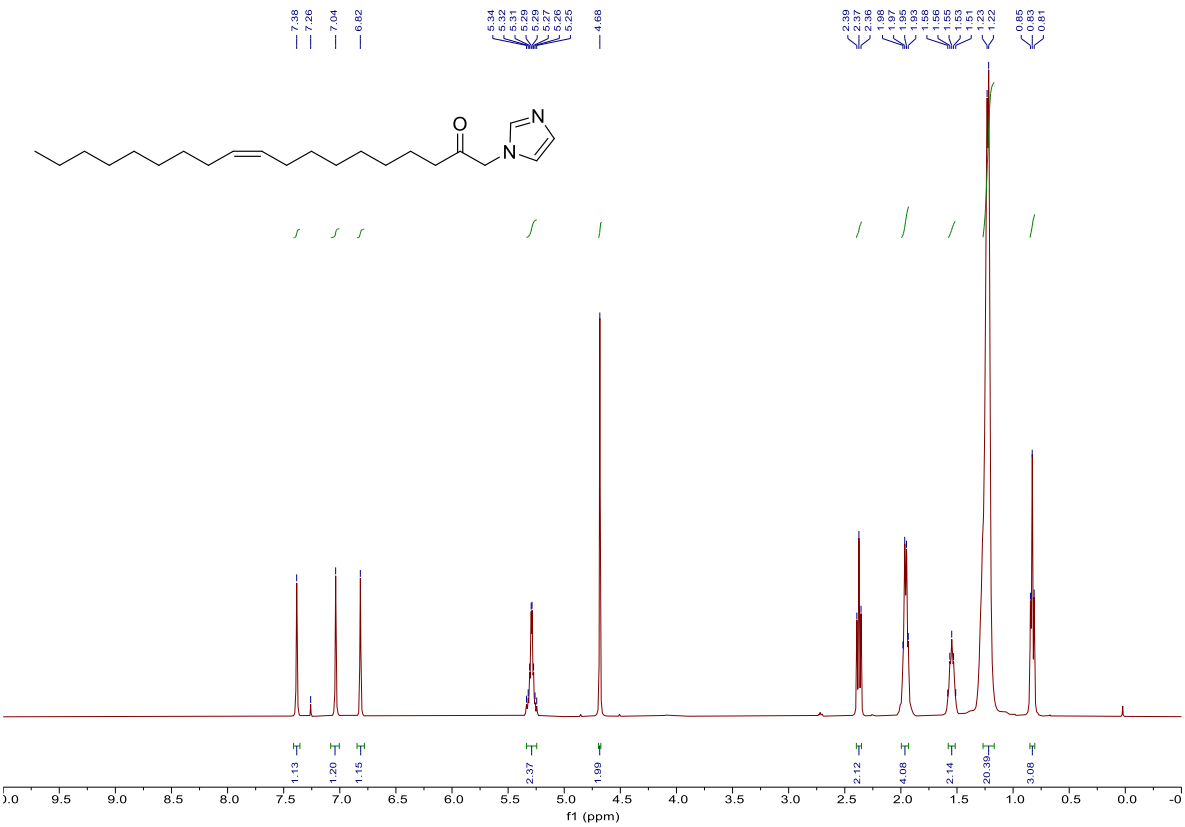
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

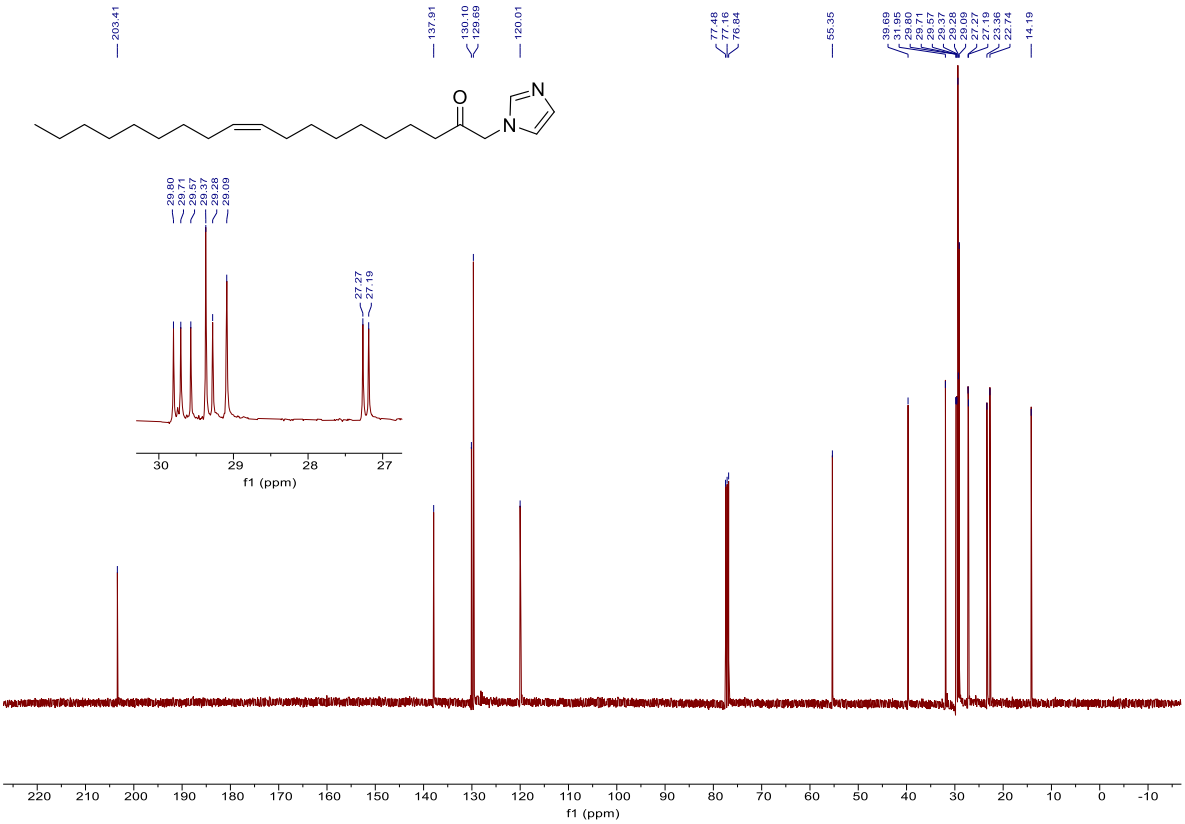




***(Z)*-1-(1*H*-Imidazol-1-yl)nonadec-10-en-2-one (20).**

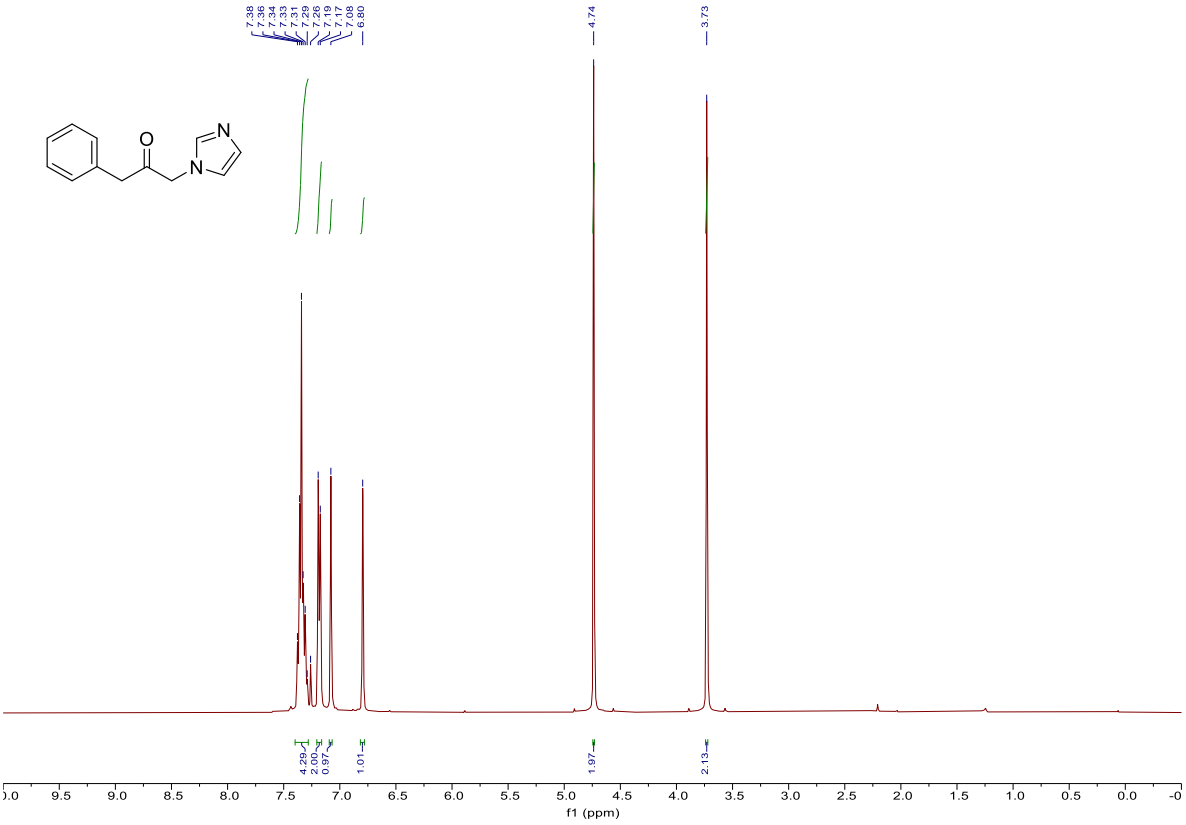
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

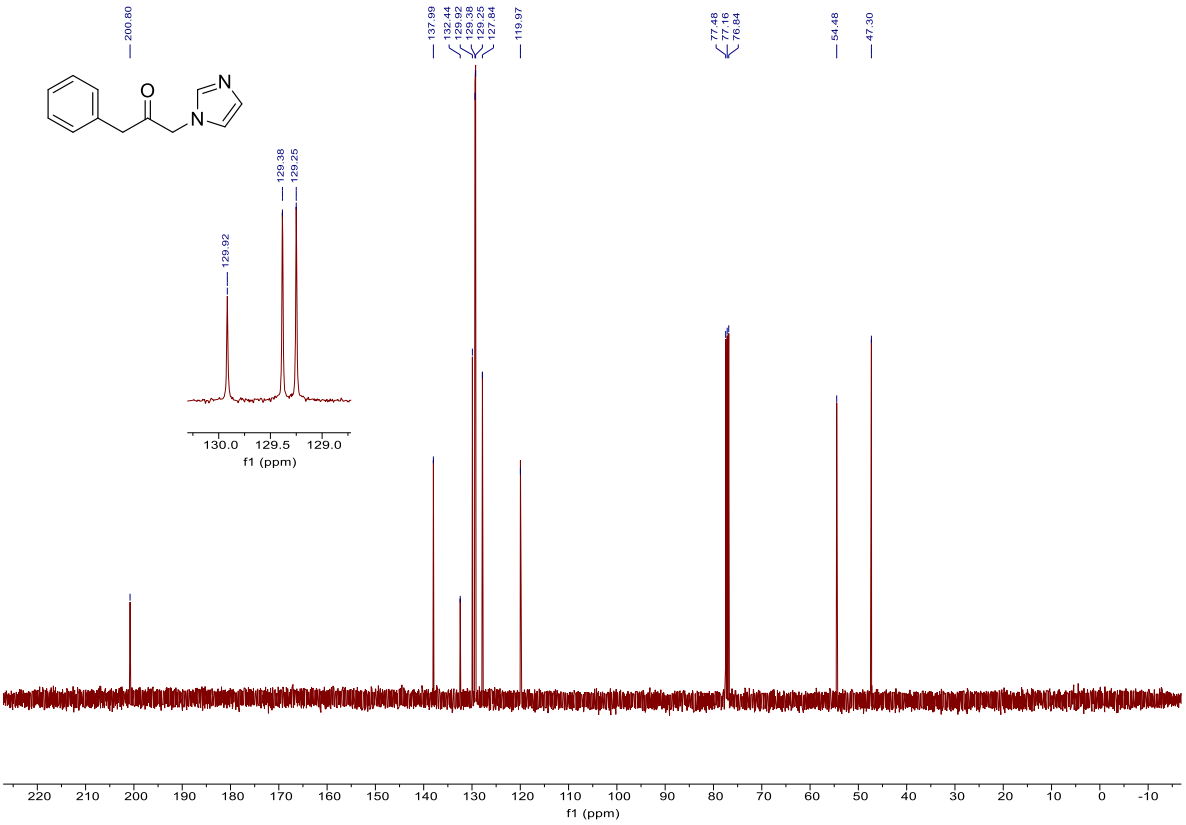




1-(1*H*-Imidazol-1-yl)-3-phenylpropan-2-one (21).

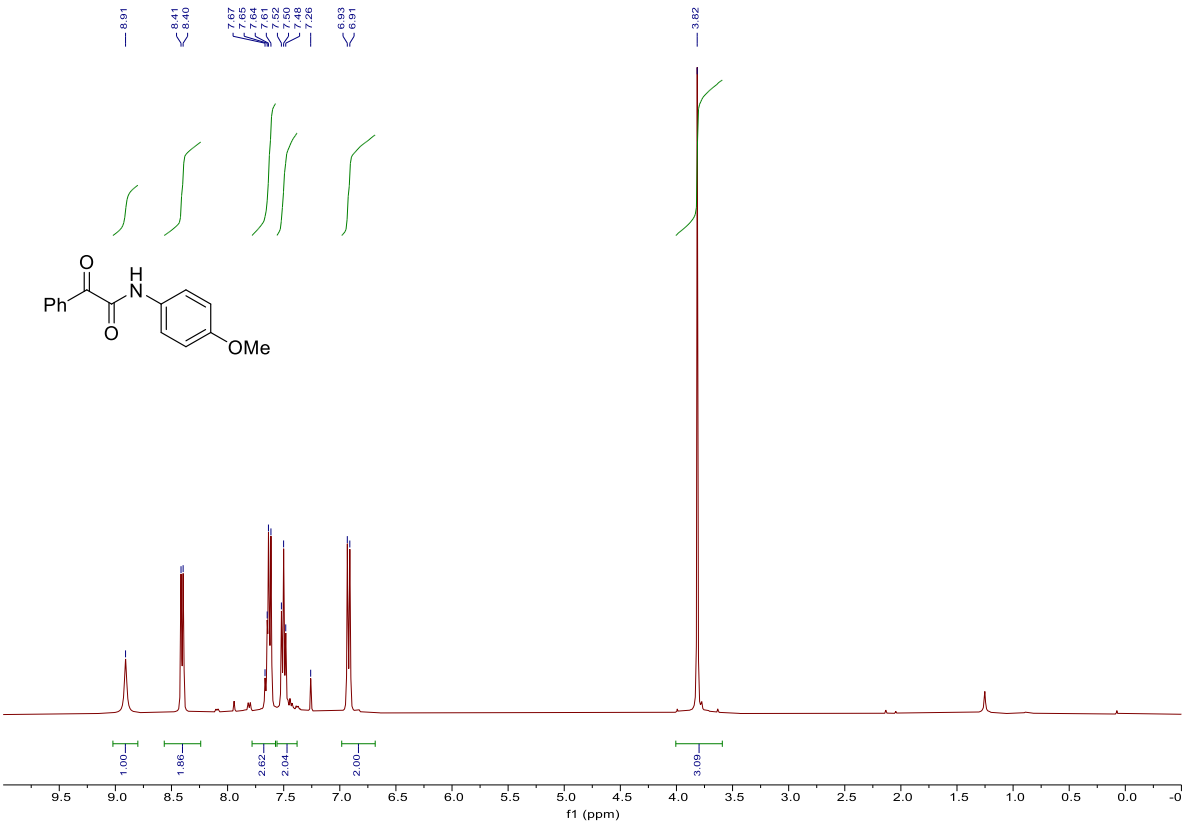
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

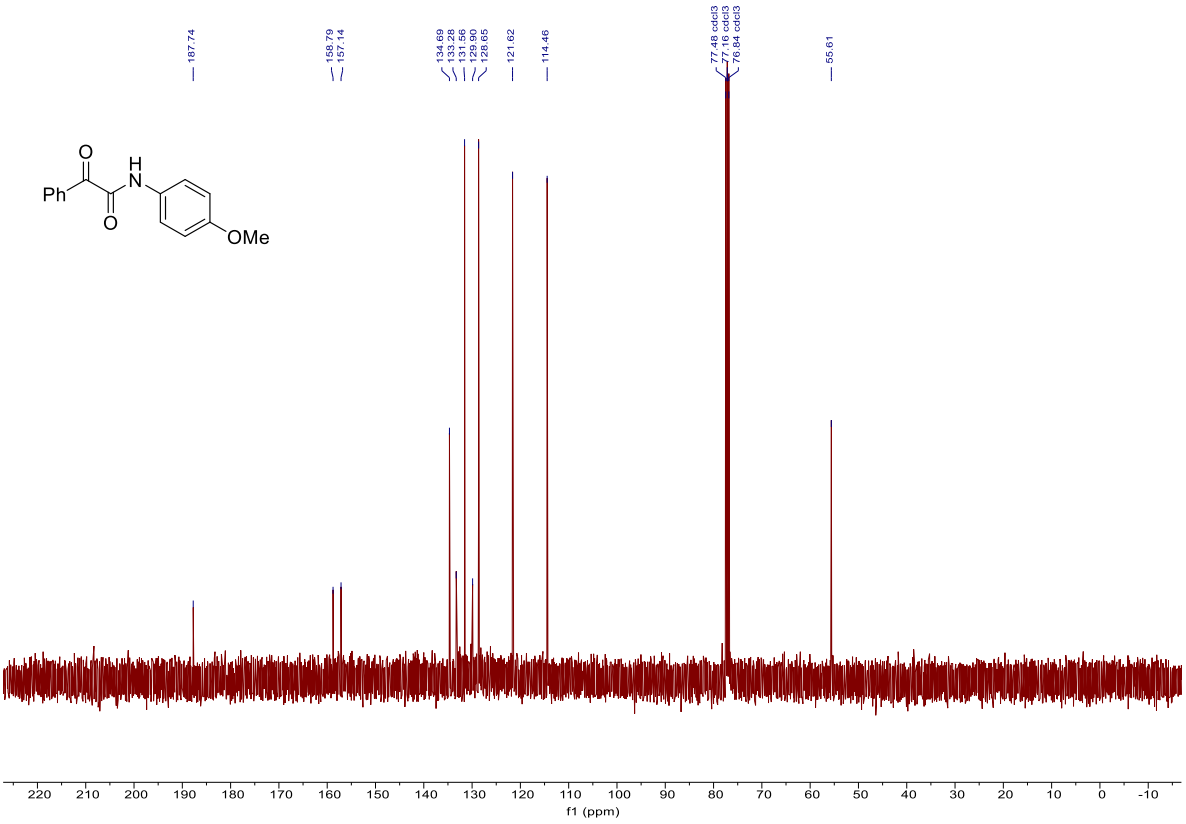




_N_-(4-Methoxyphenyl)-2-oxo-2-phenylacetamide (10a).

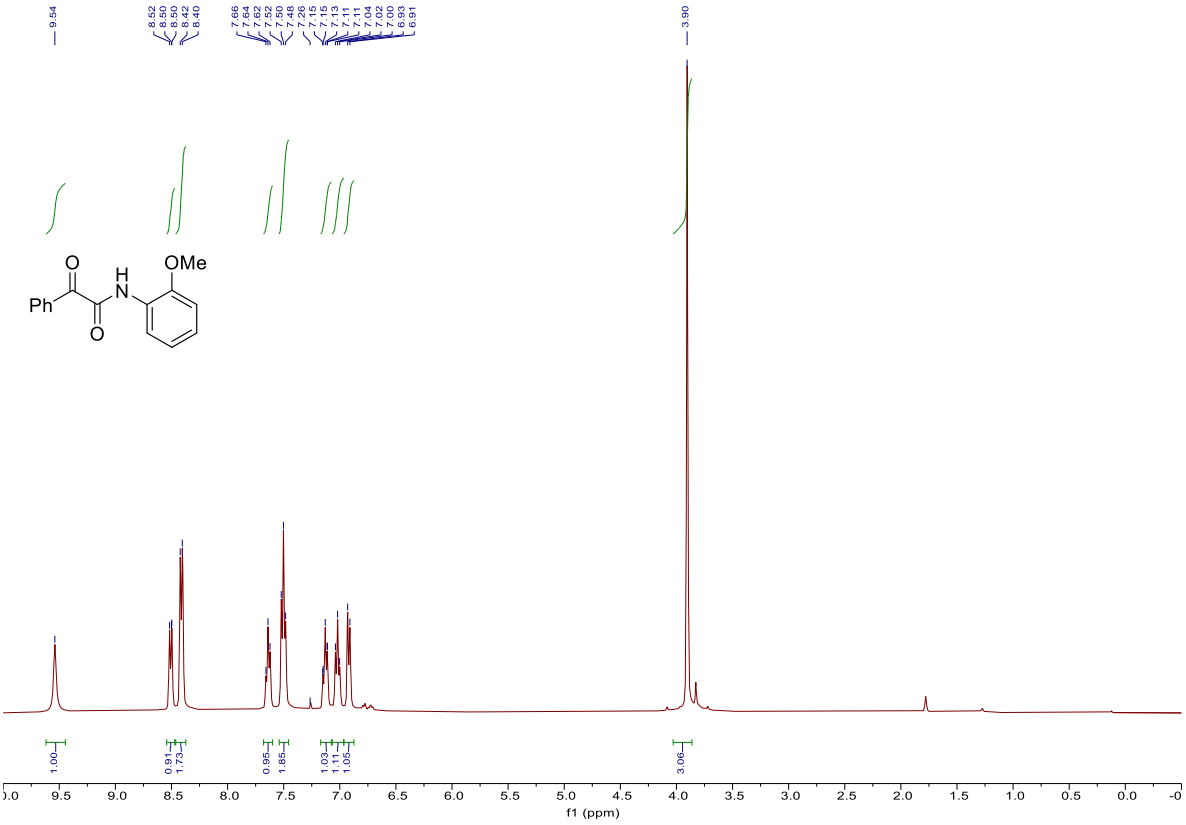
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

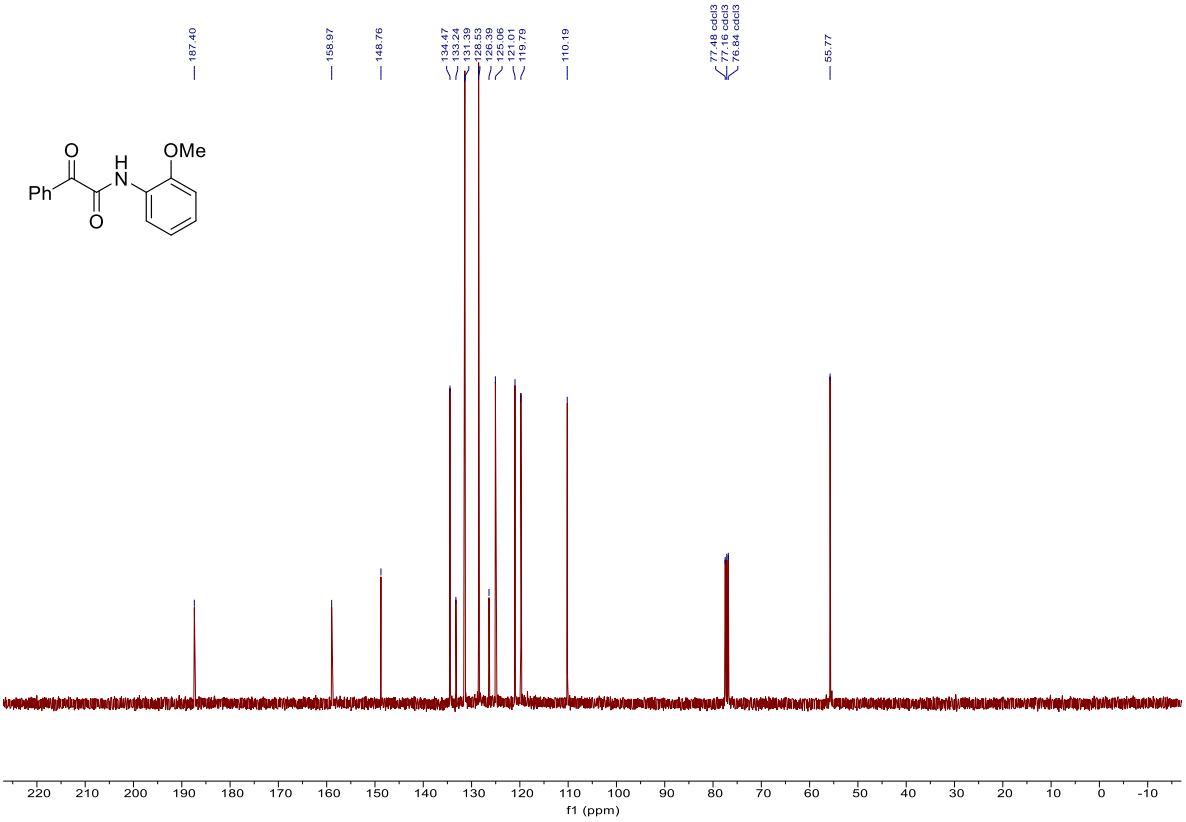




_N_-(2-Methoxyphenyl)-2-oxo-2-phenylacetamide (10b).

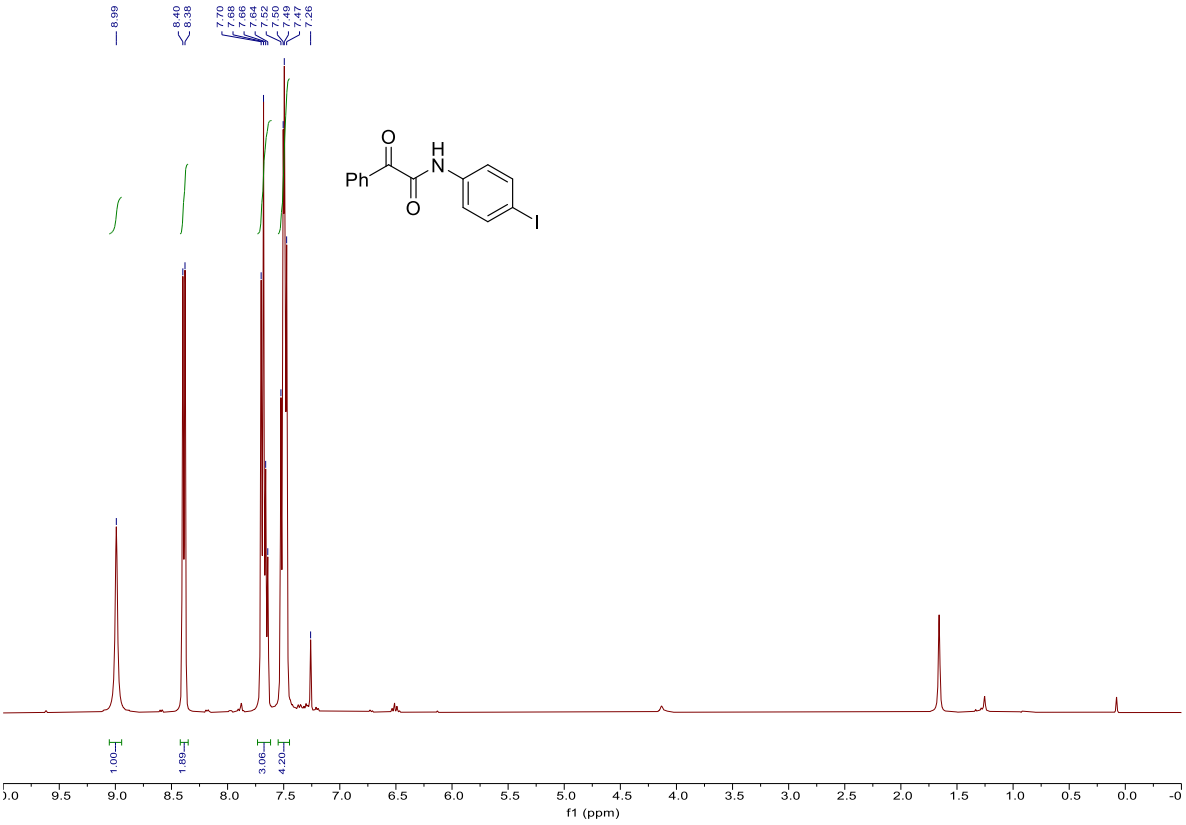
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

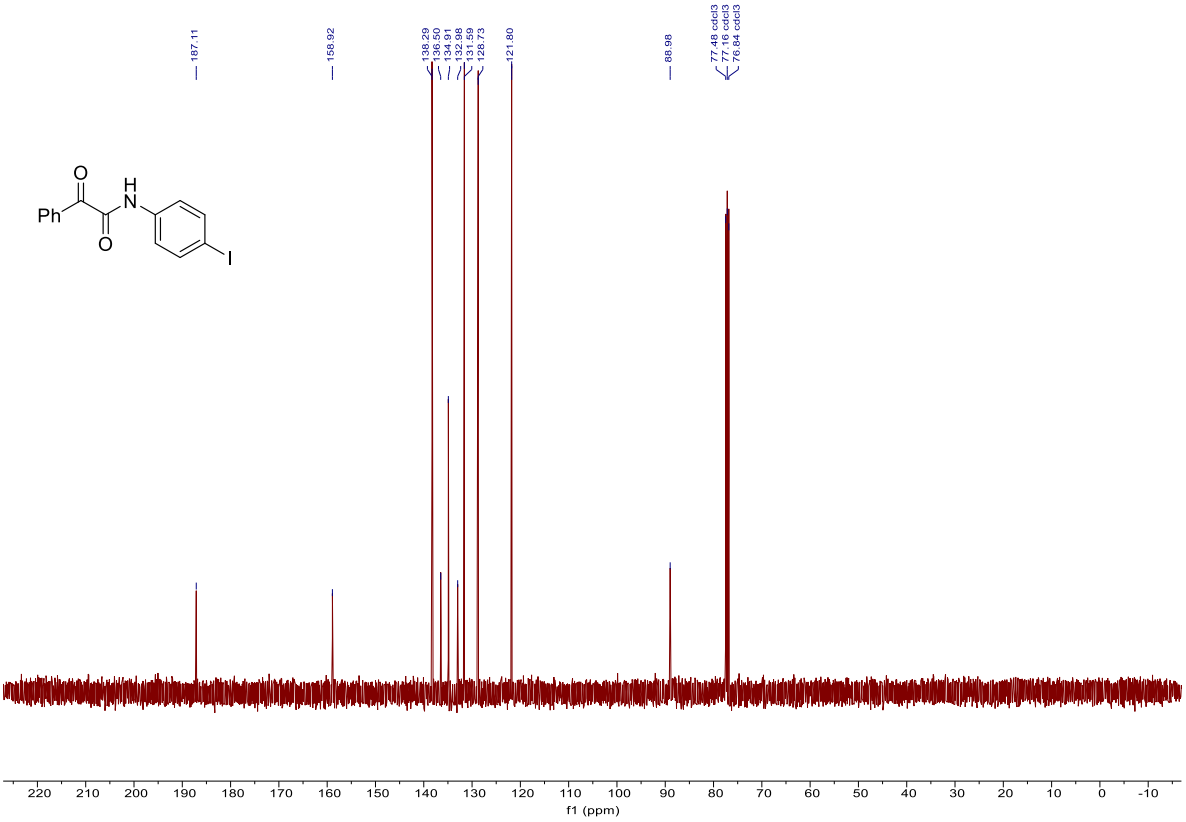




_N_-(4-Iodophenyl)-2-oxo-2-phenylacetamide (10c).

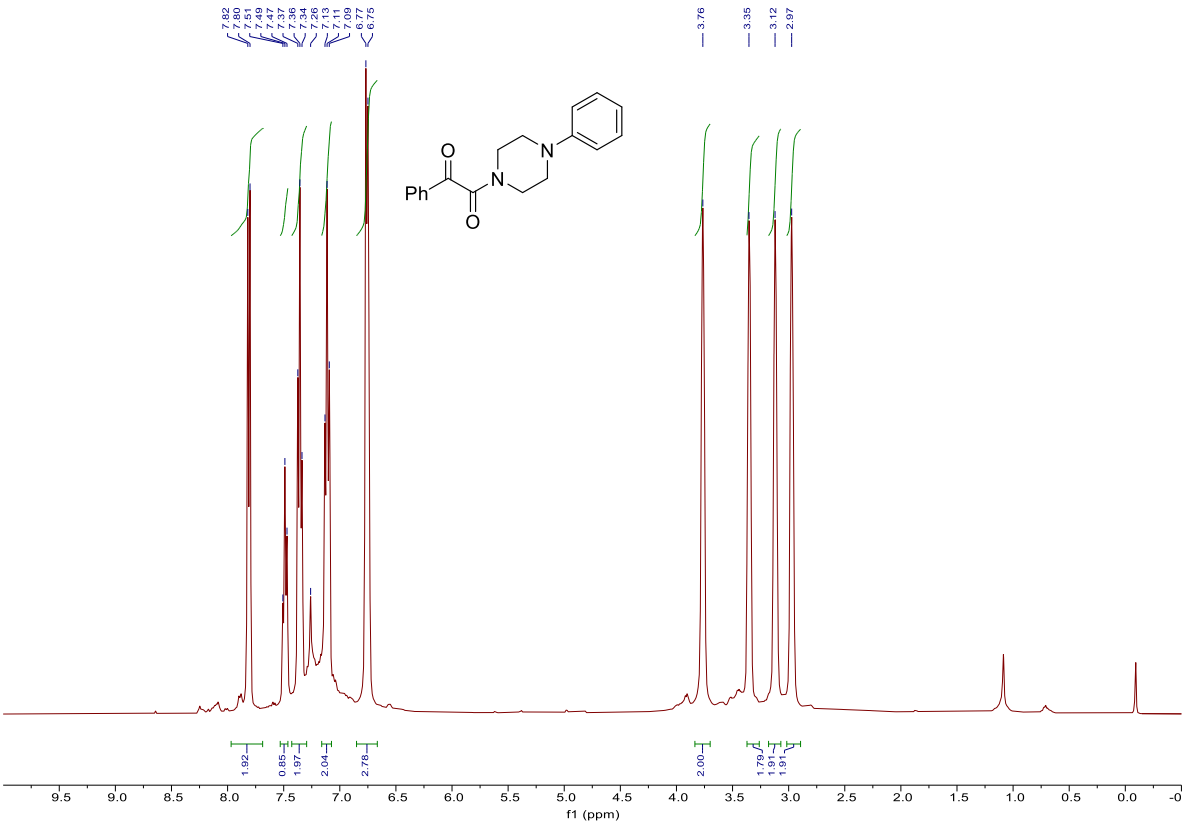
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

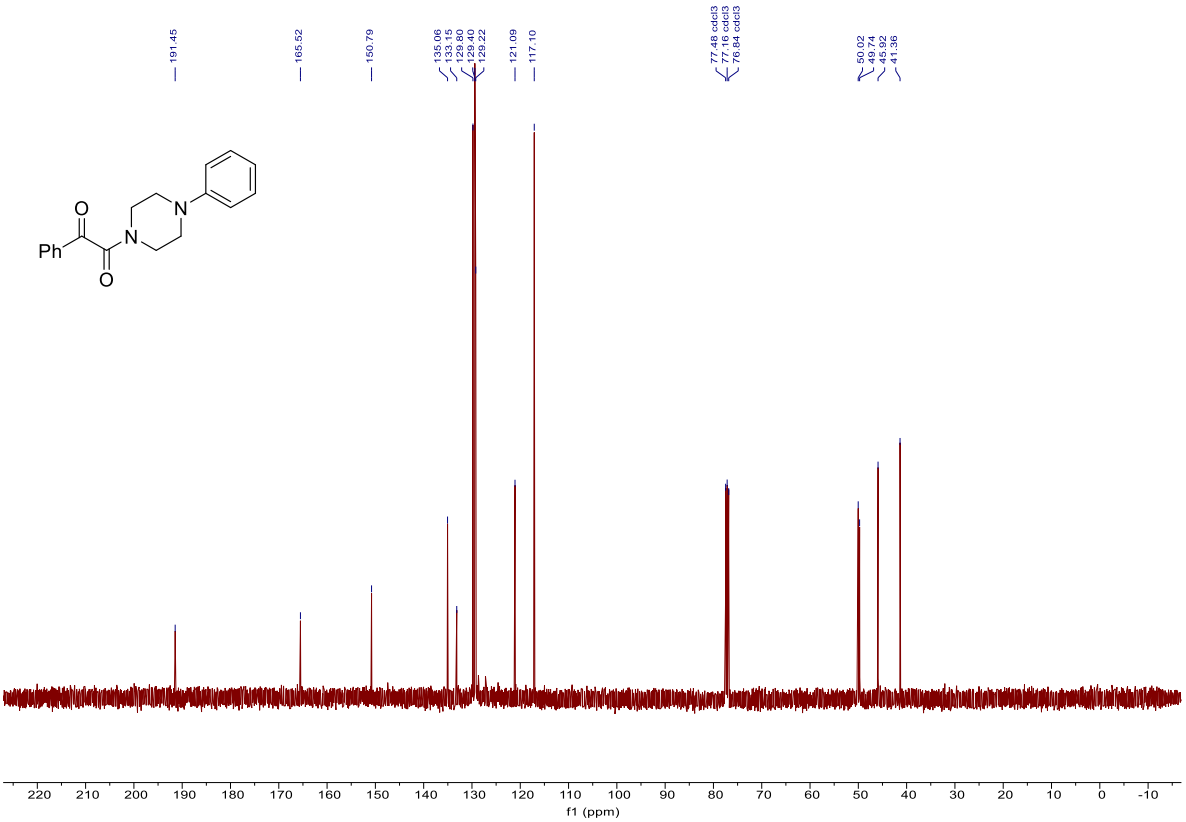




1-Phenyl-2-(4-phenylpiperazin-1-yl)ethane-1,2-dione (10e).

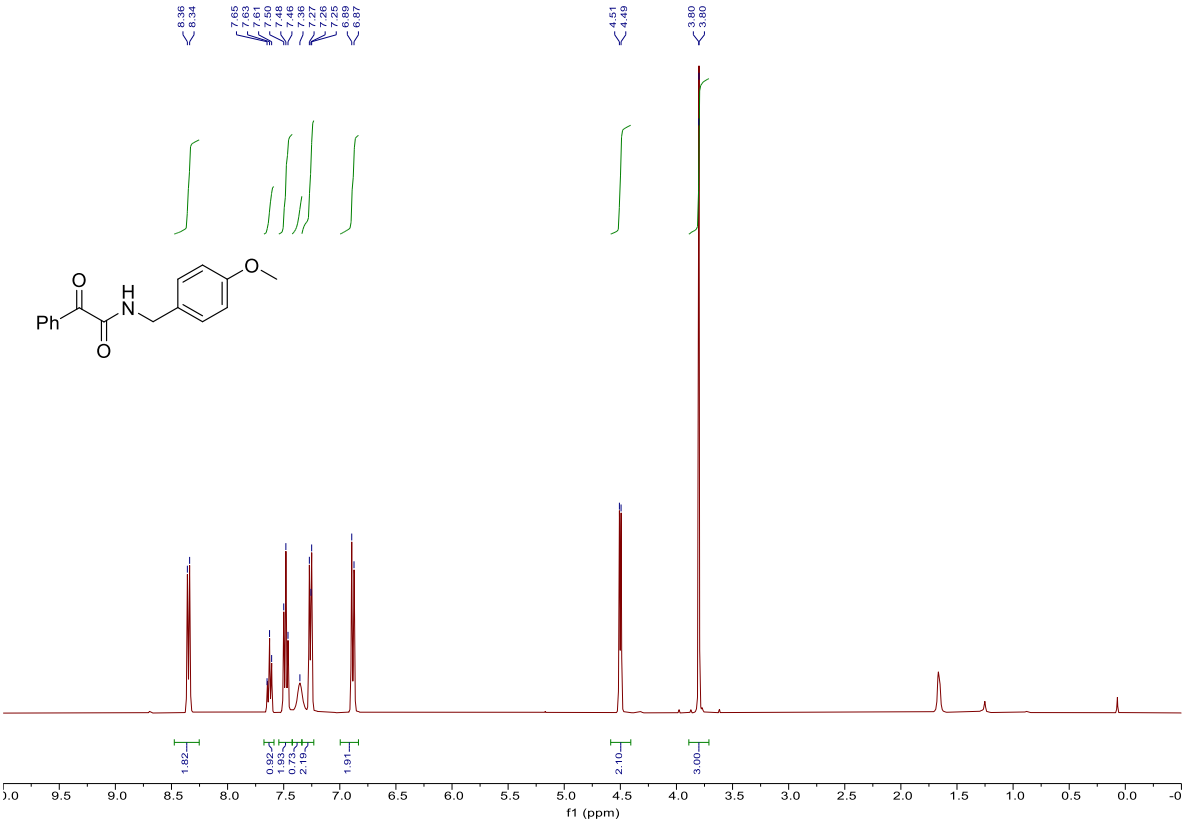
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

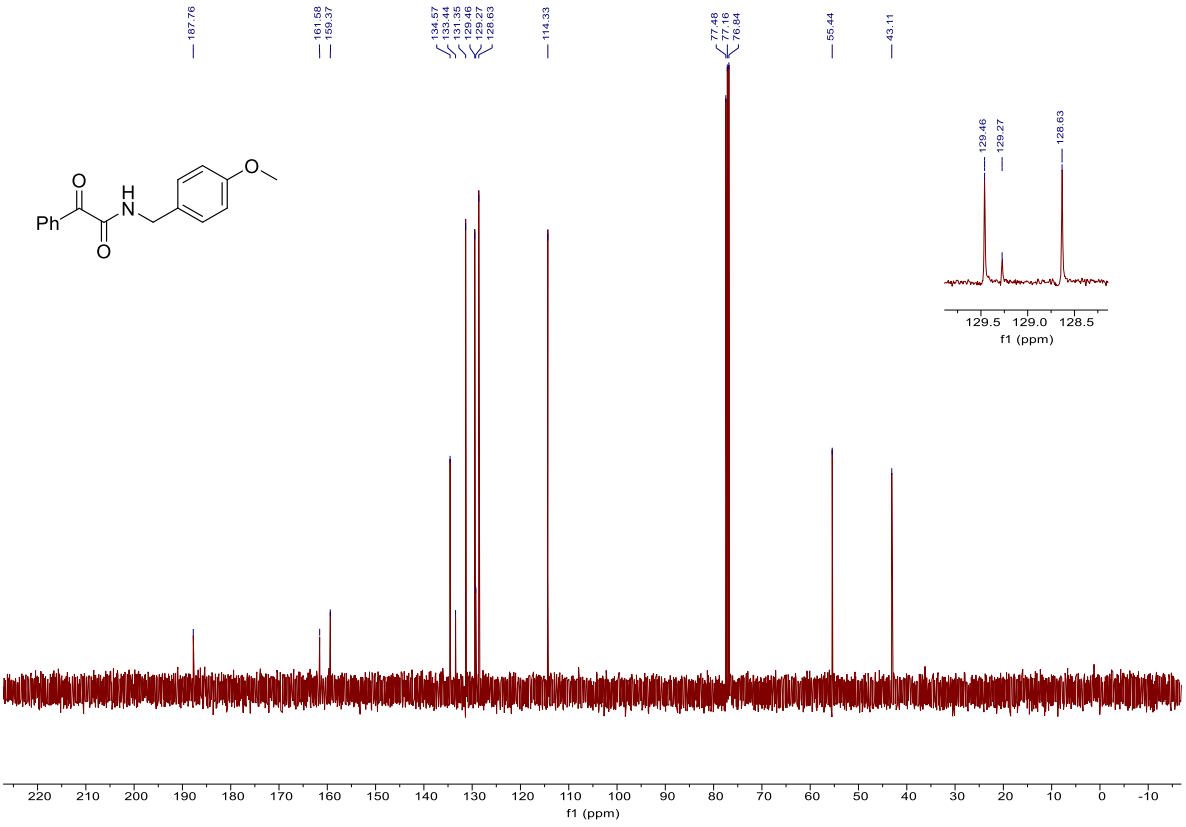




_N_-(4-Methoxybenzyl)-2-oxo-2-phenylacetamide (10f).

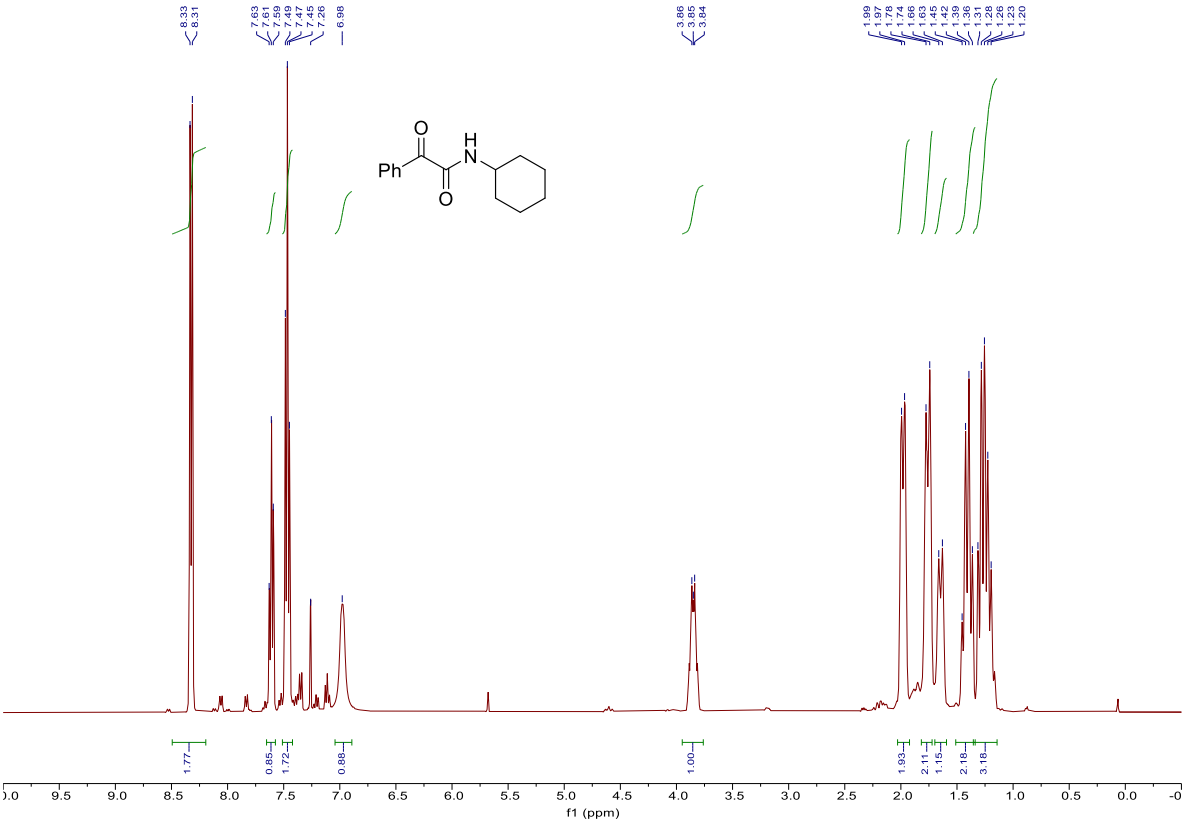
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

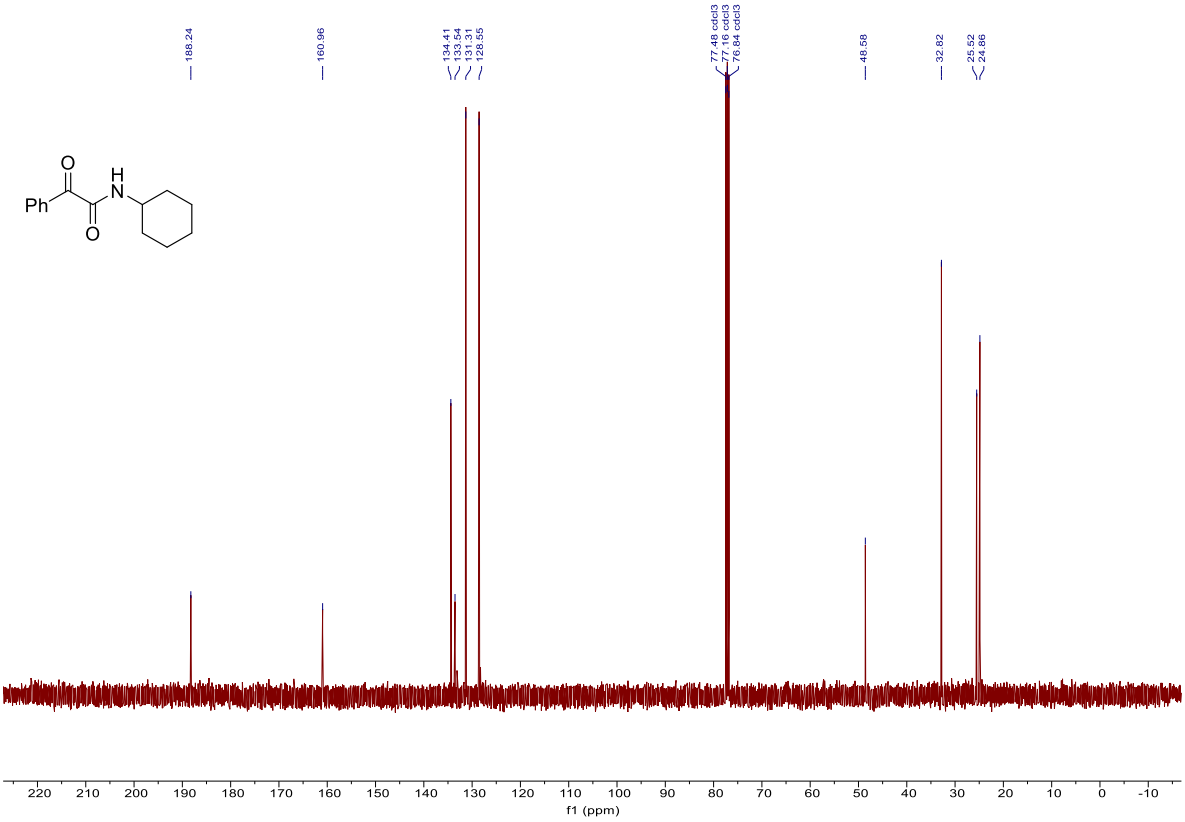




_N_-Cyclohexyl-2-oxo-2-phenylacetamide (10g).

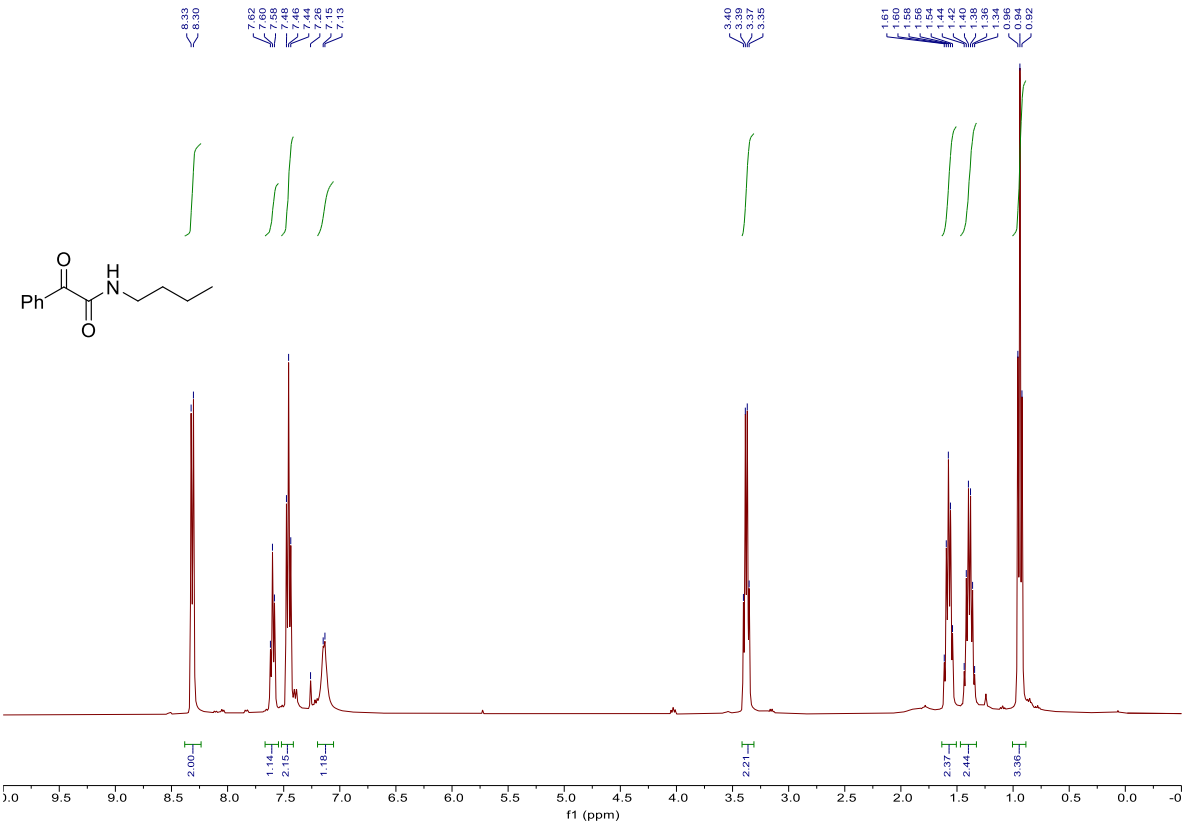
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

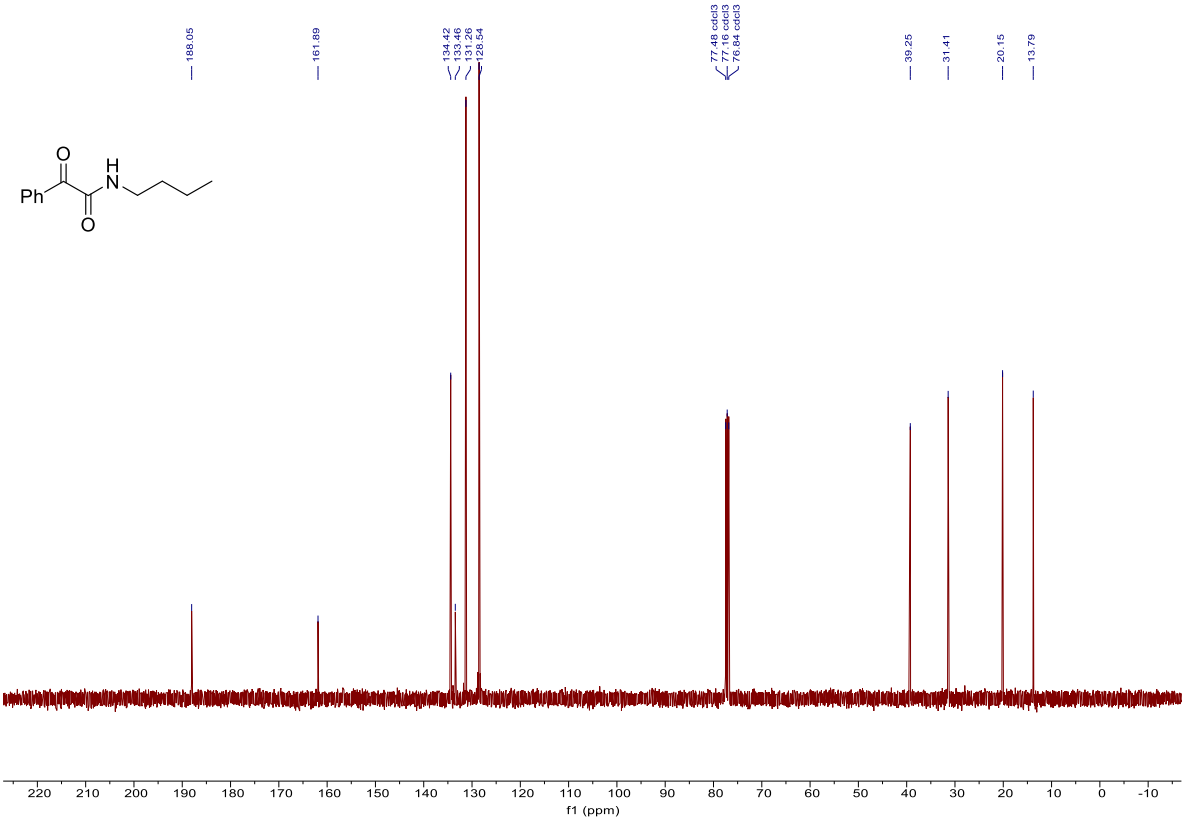




_N_-Butyl-2-oxo-2-phenylacetamide (10h).

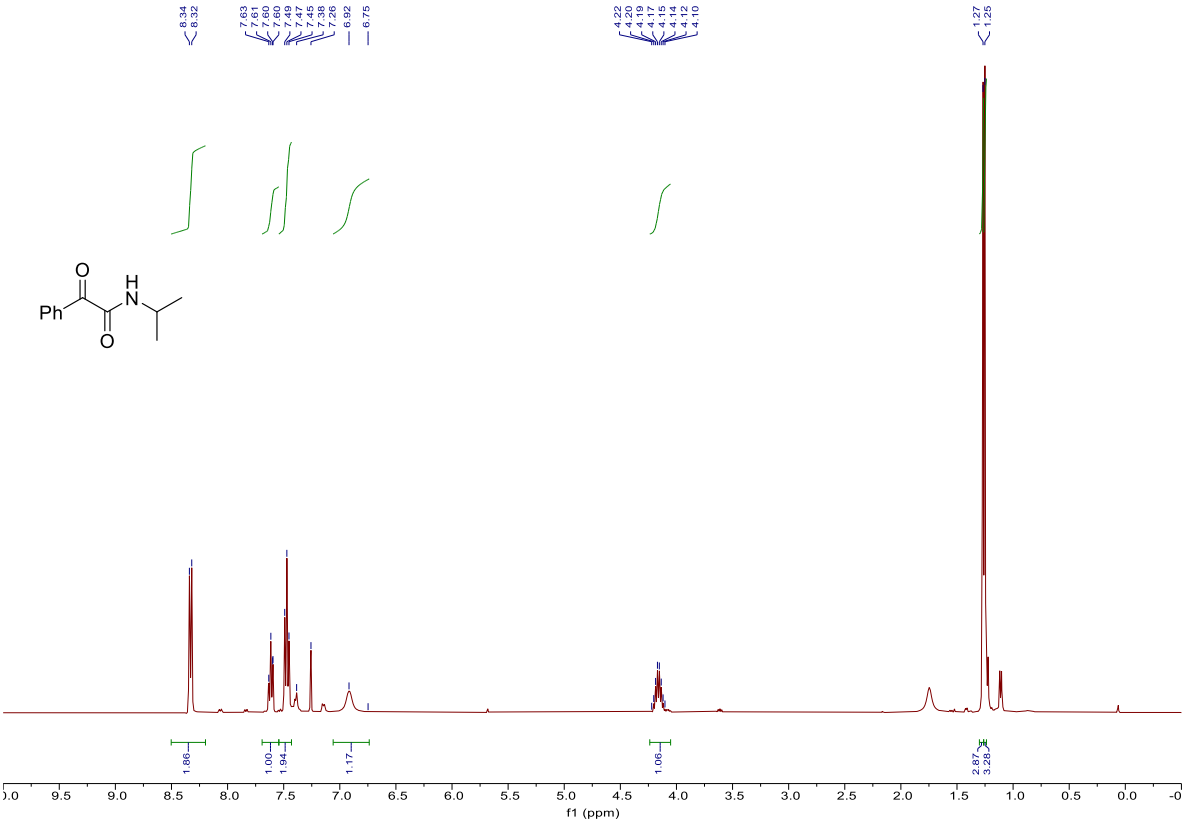
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

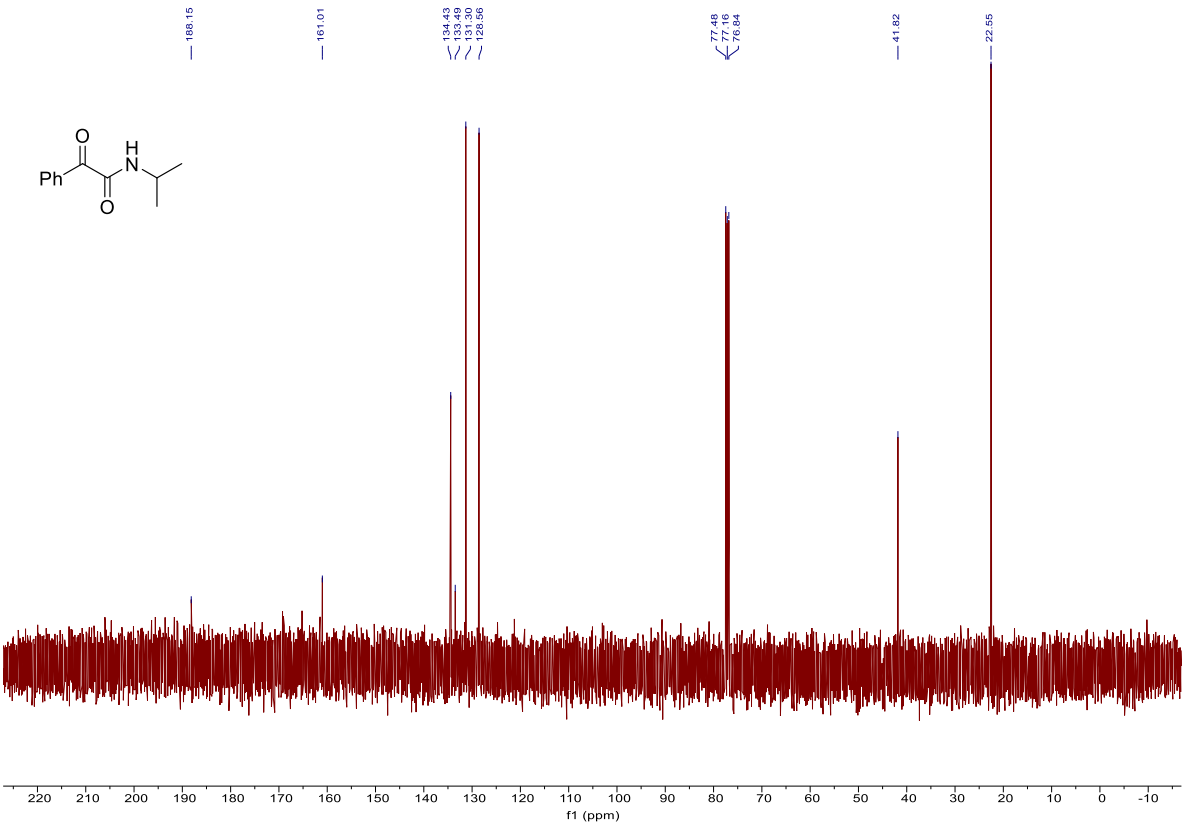




_N_-Isopropyl-2-oxo-2-phenylacetamide (10i).

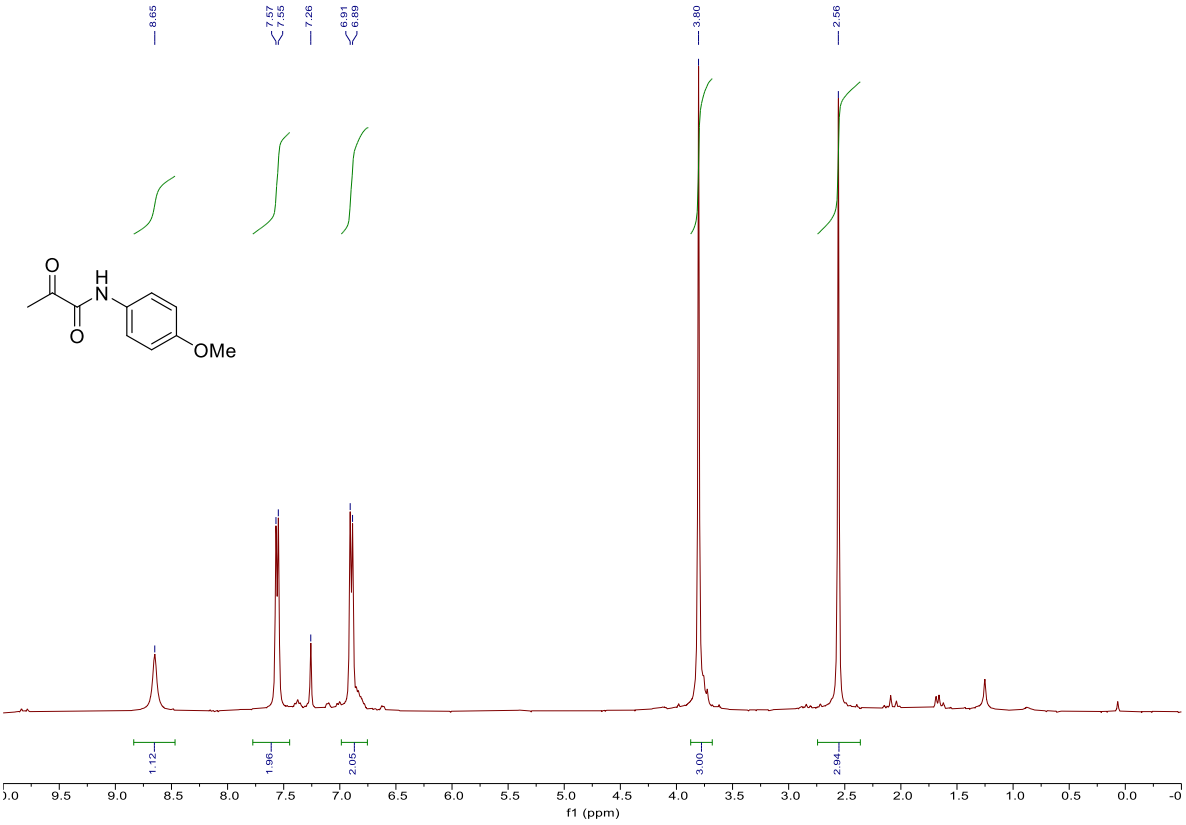
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

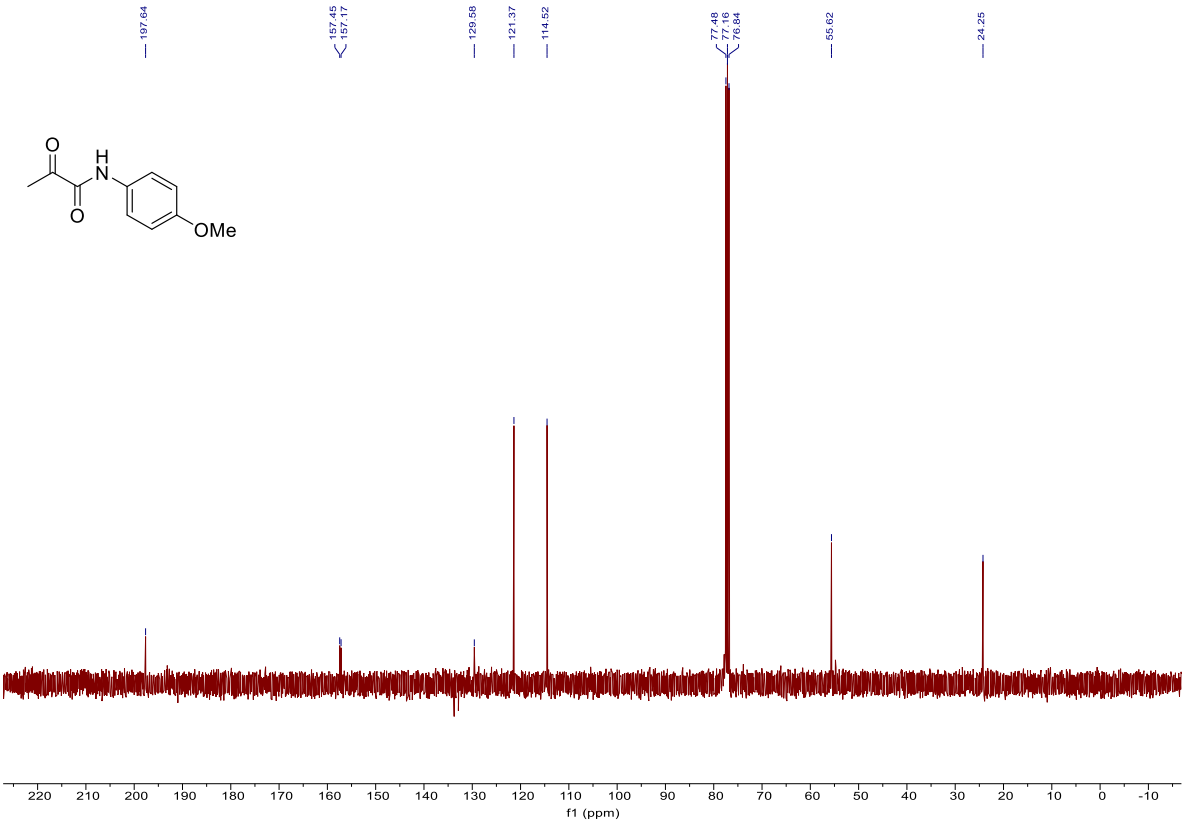




_N_-(4-Methoxyphenyl)-2-oxopropanamide (15a).

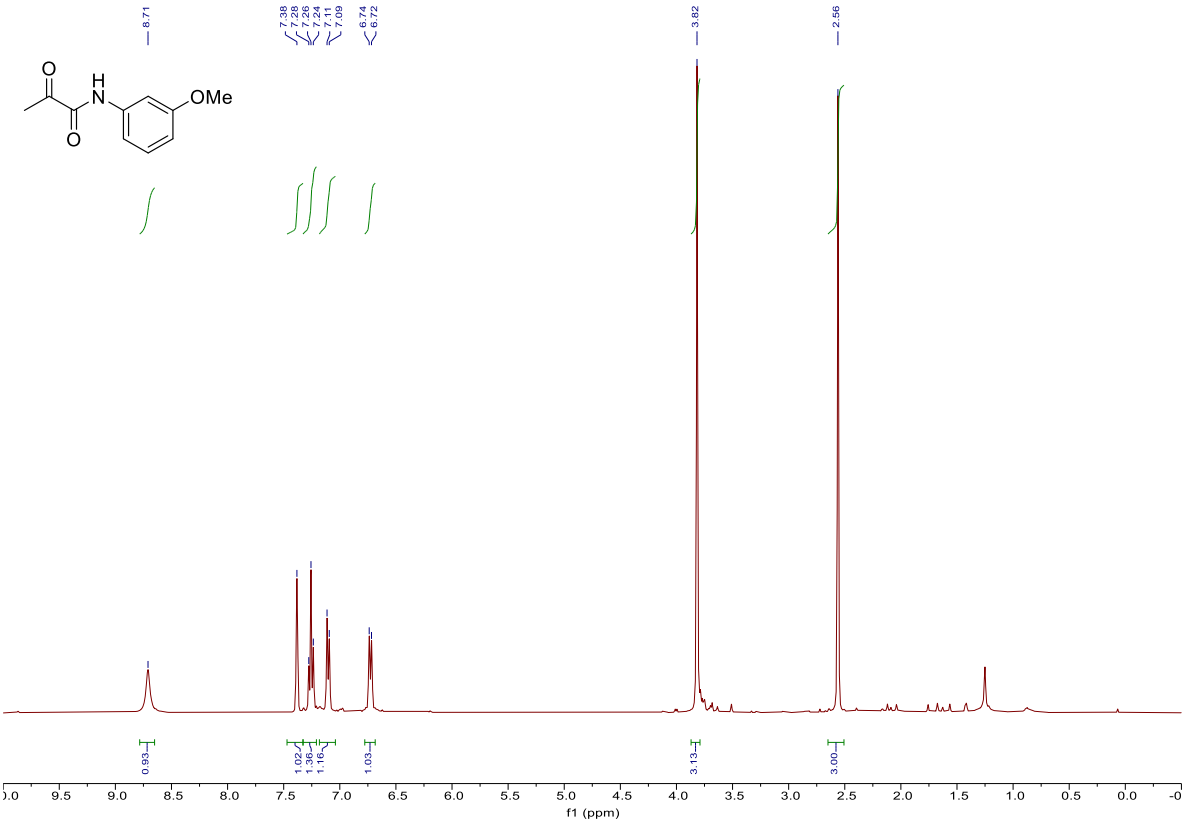
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

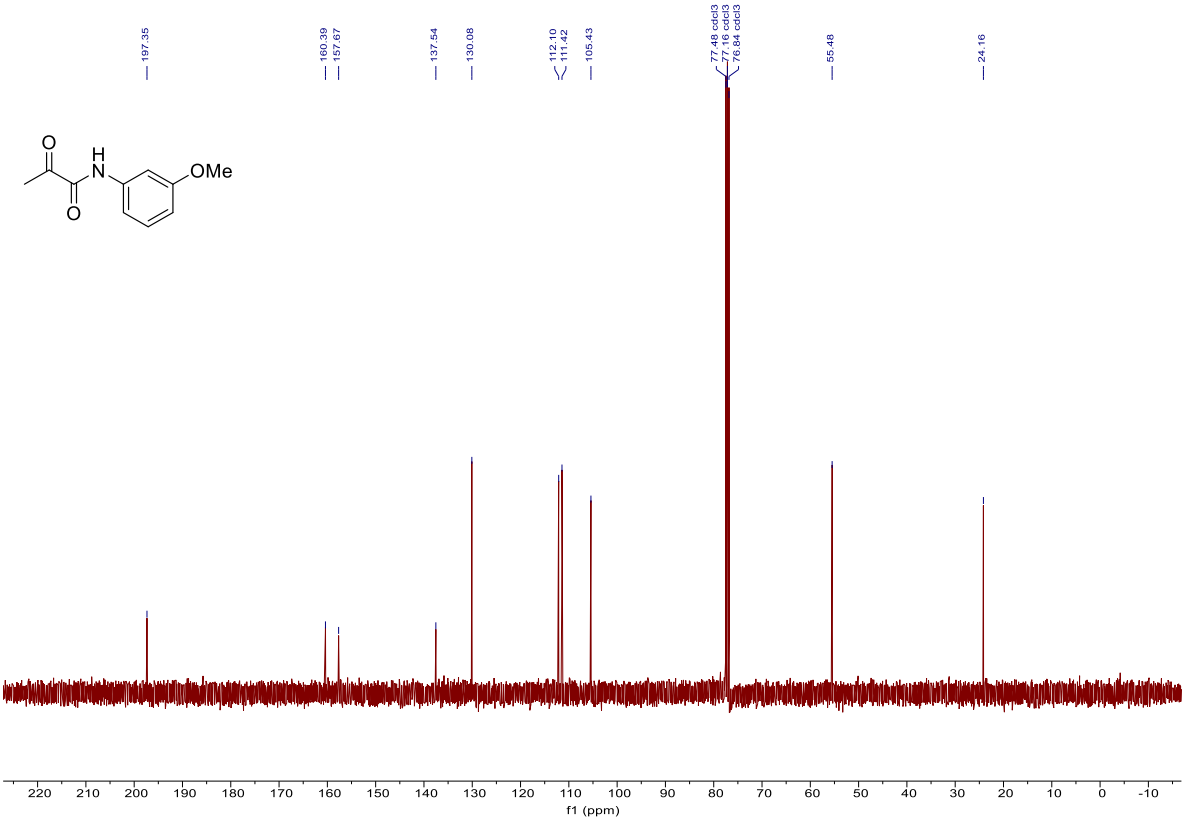




_N_-(3-Methoxyphenyl)-2-oxopropanamide (15b).

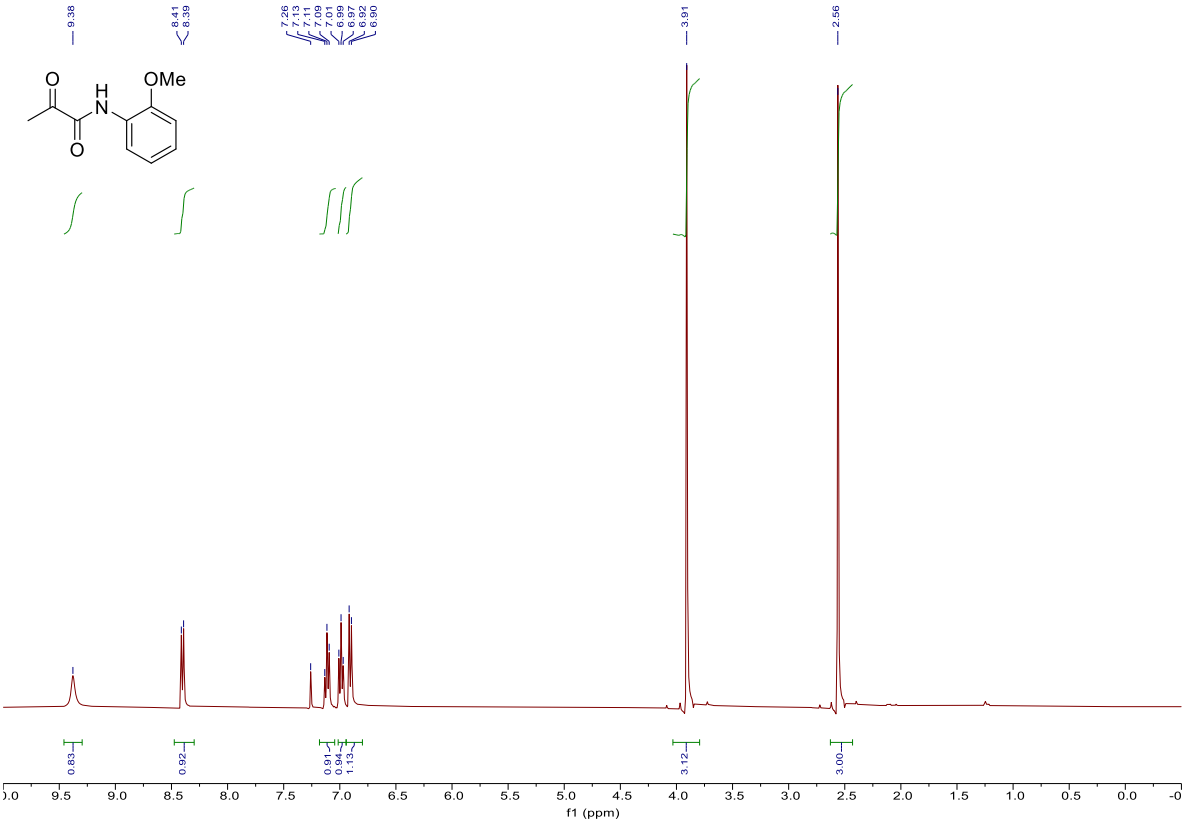
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

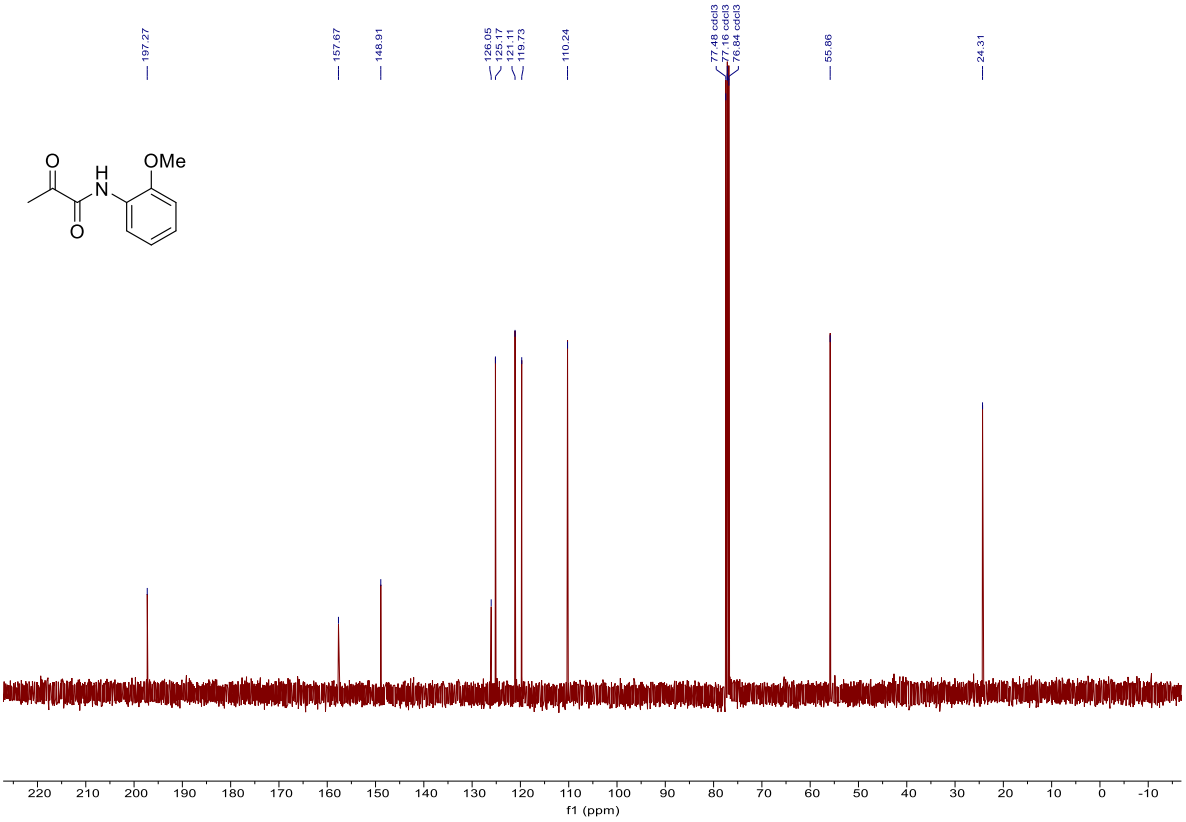




_N_-(2-Methoxyphenyl)-2-oxopropanamide (15c).

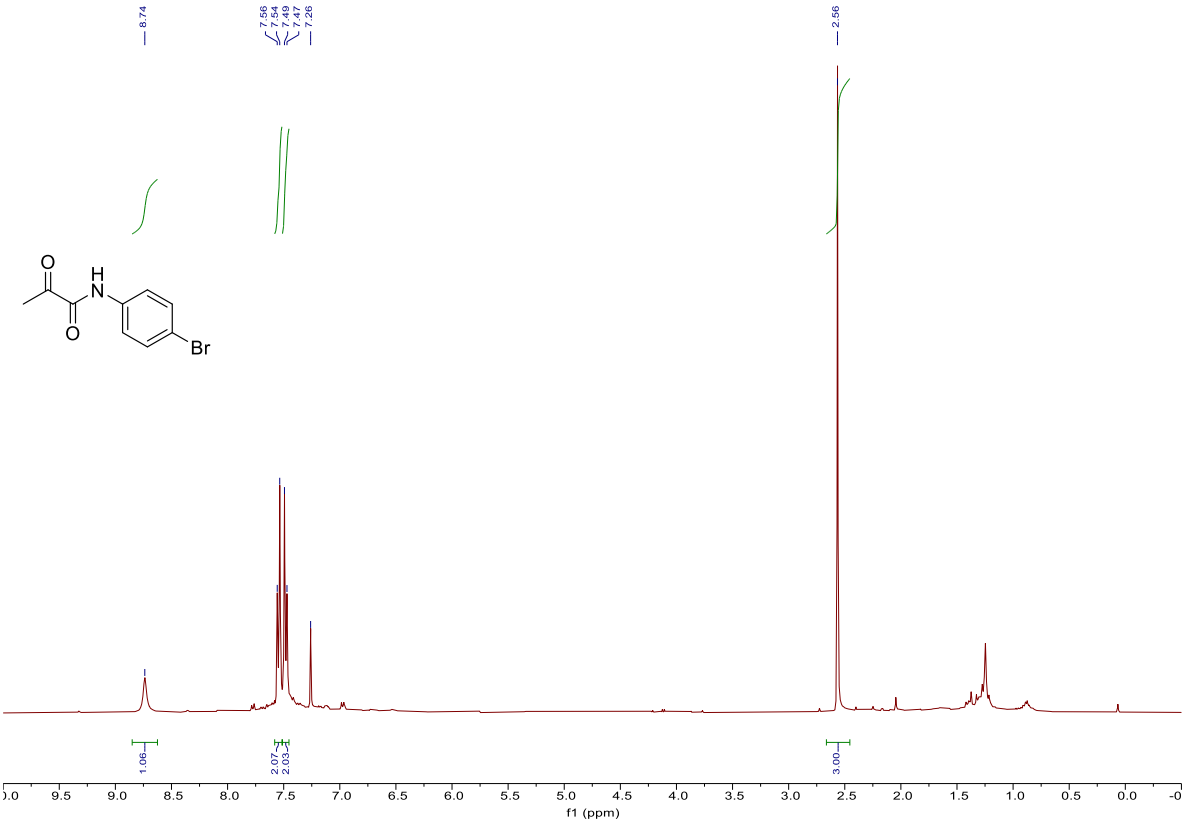
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

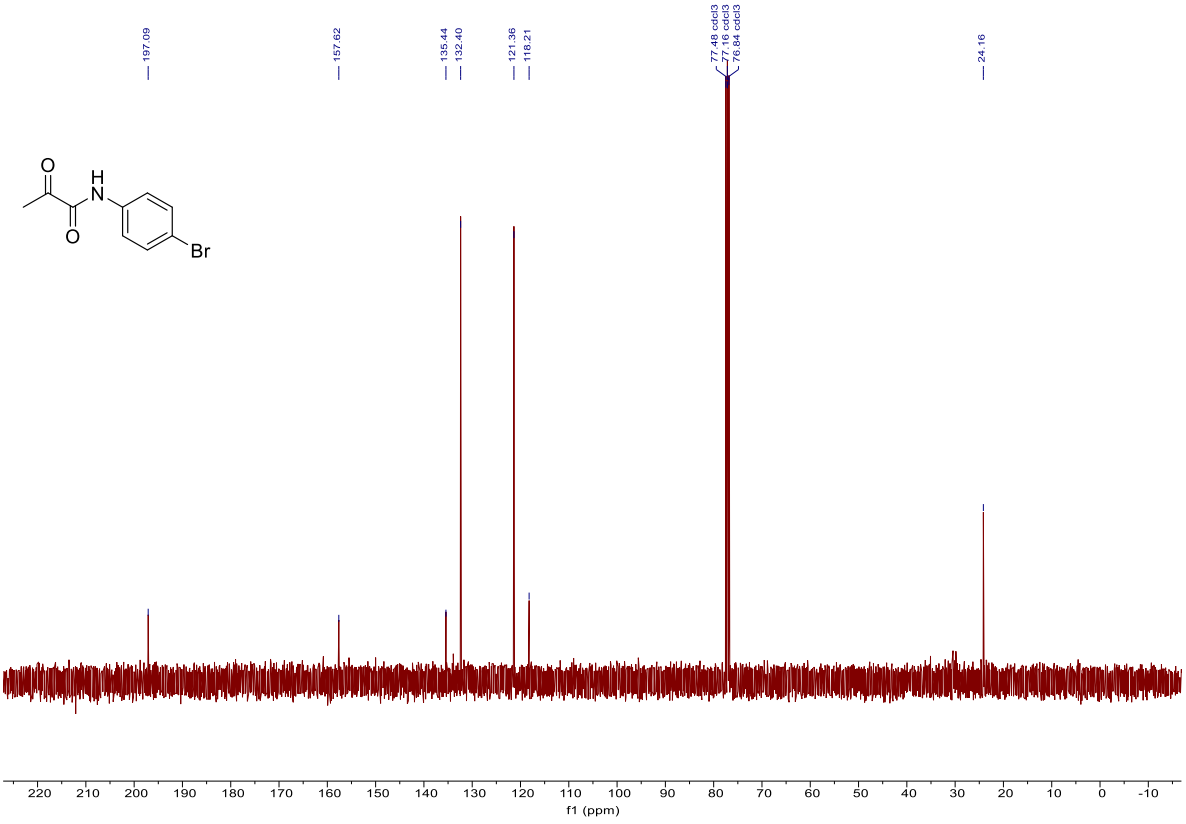




_N_-(4-Bromophenyl)-2-oxopropanamide (15d).

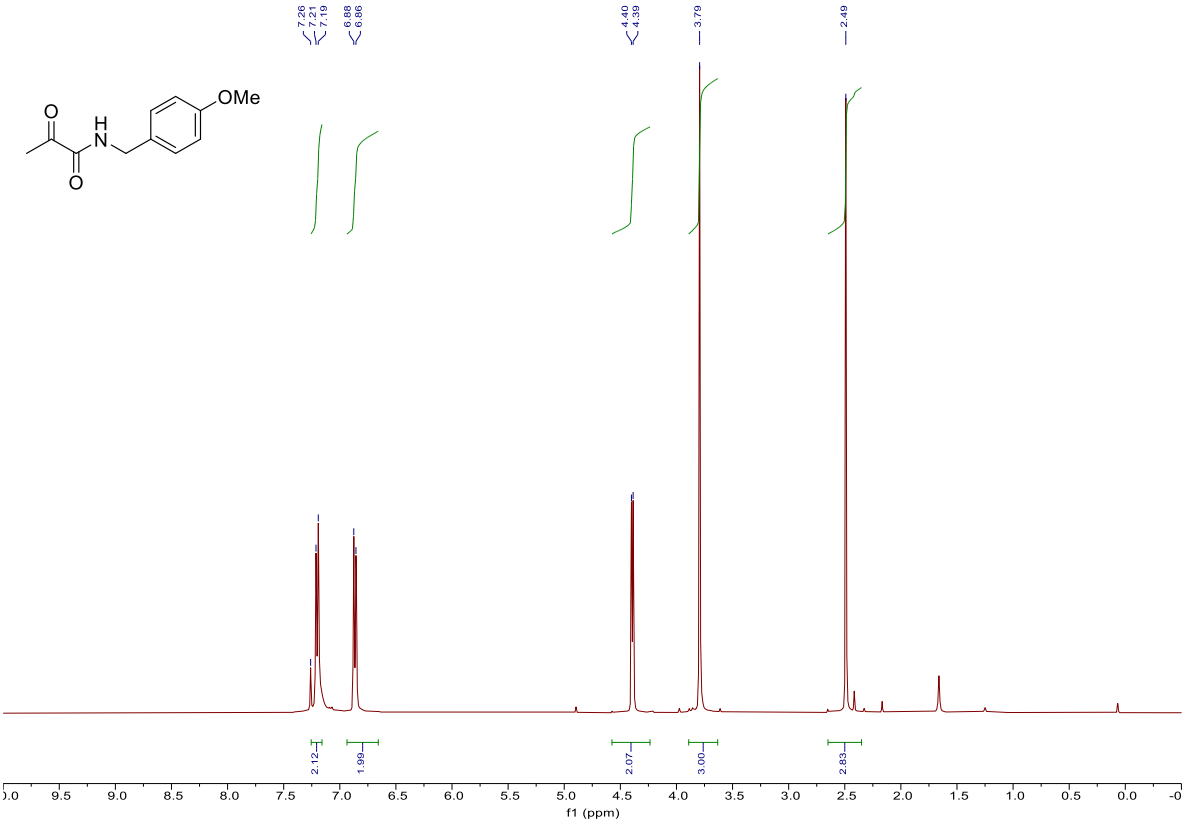
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

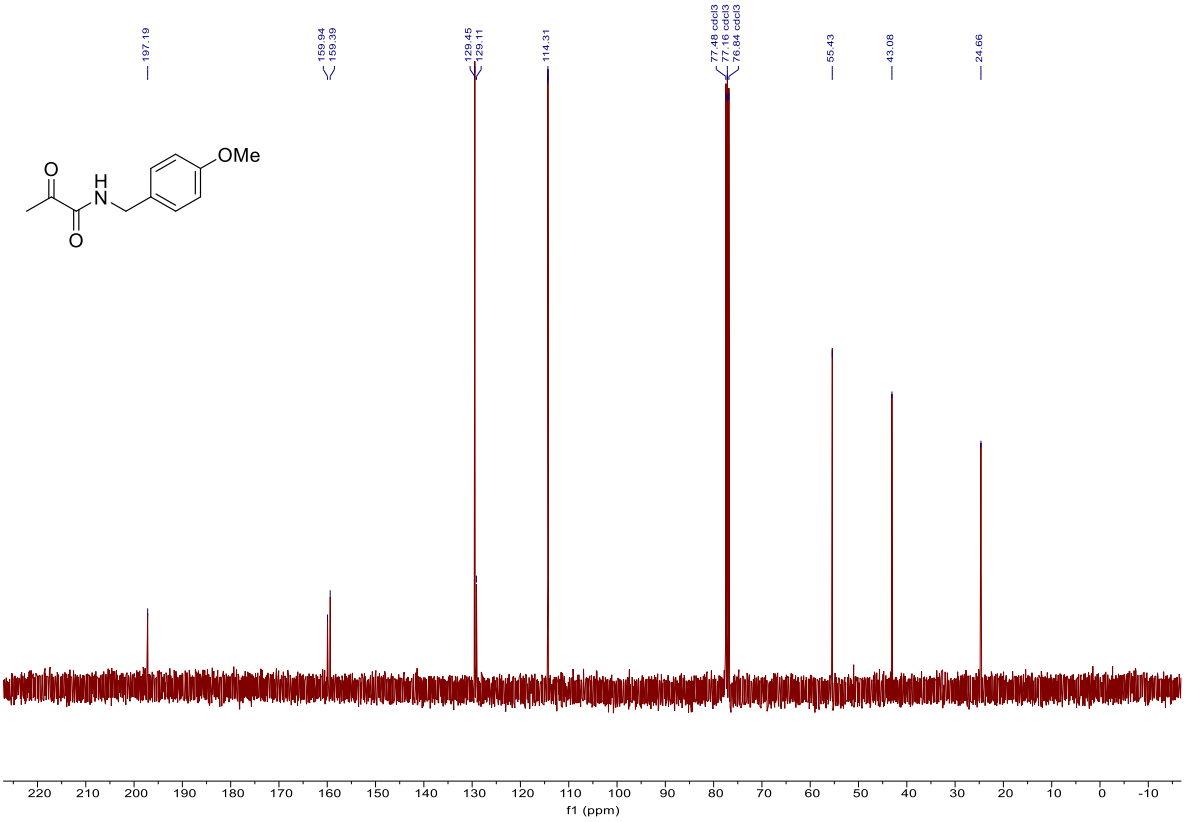




_N_-(4-Methoxybenzyl)-2-oxopropanamide (15e).

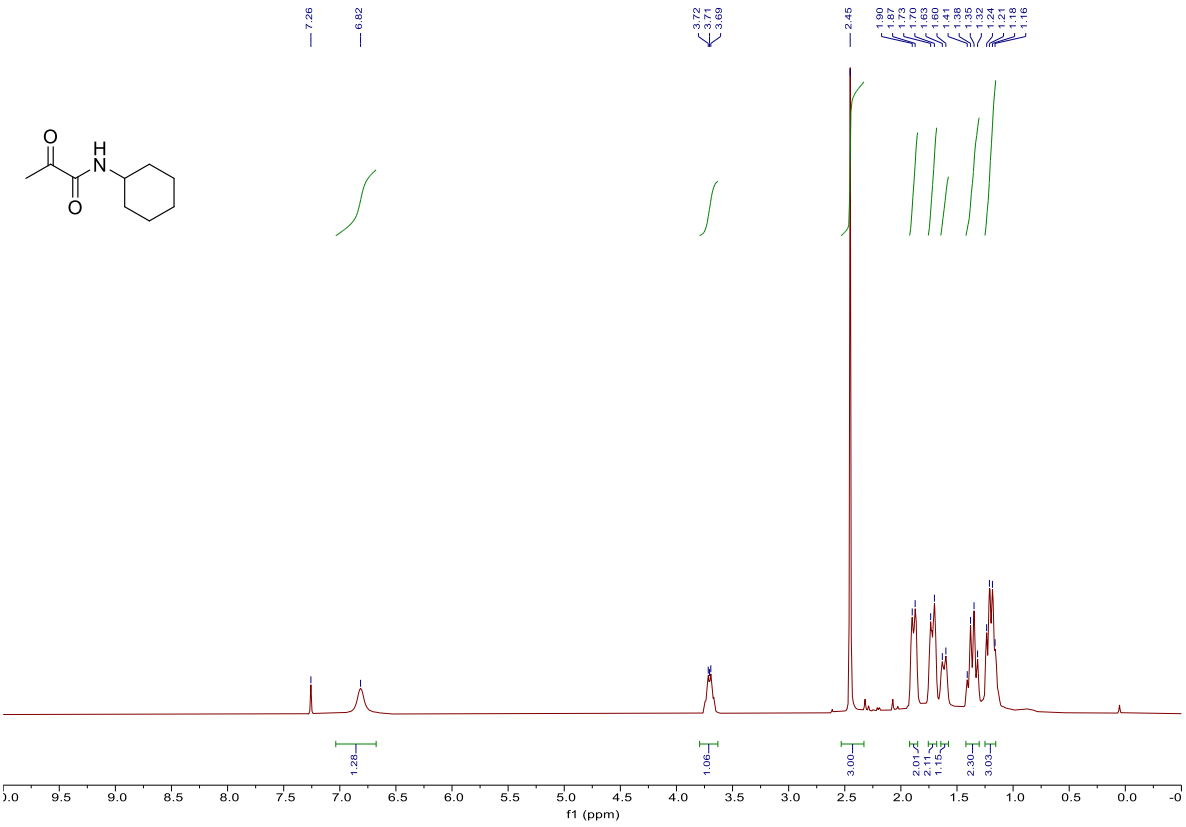
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

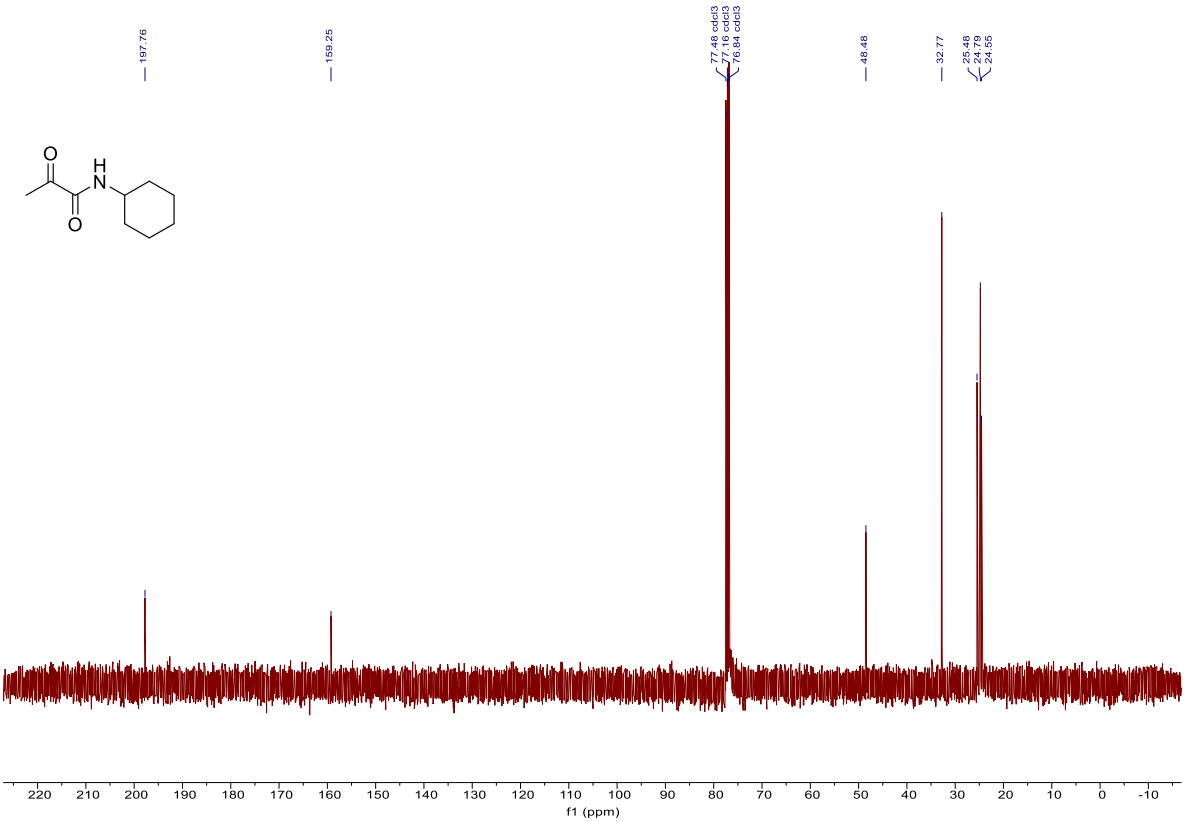




_N_-Cyclohexyl-2-oxopropanamide (15f).

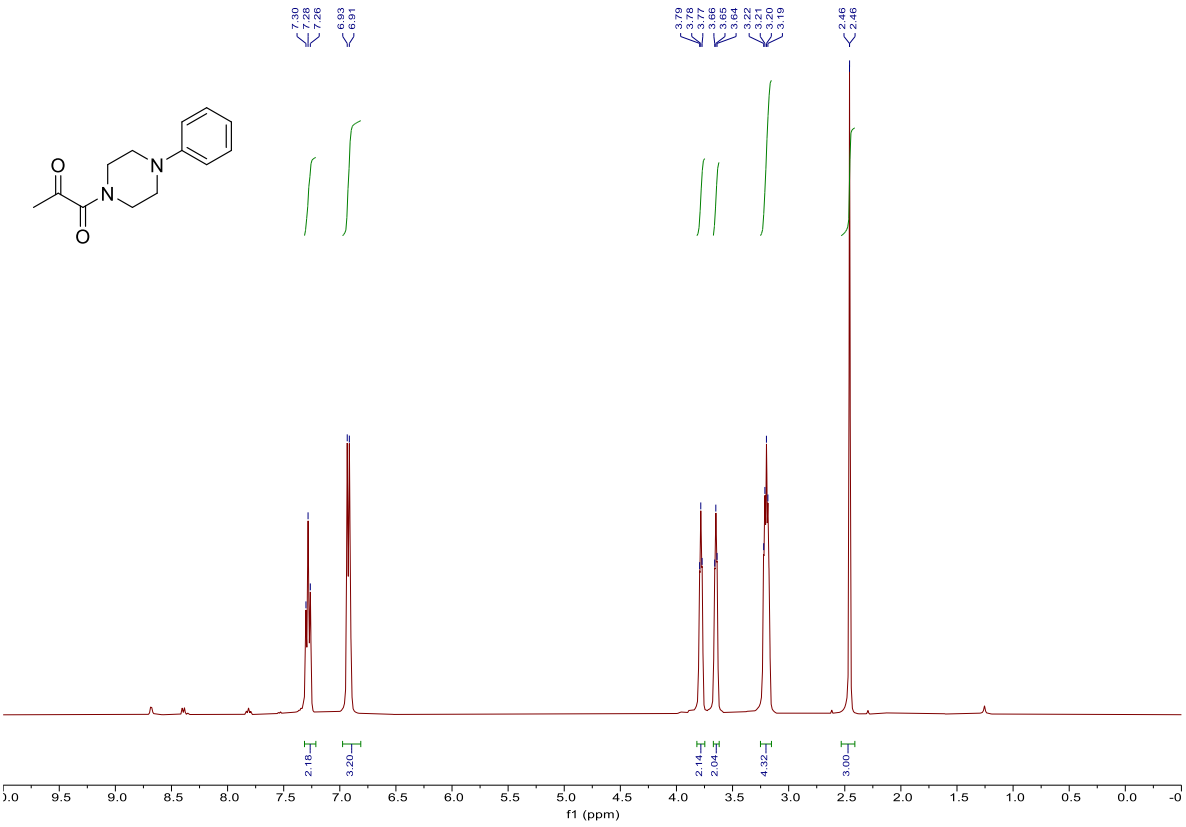
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

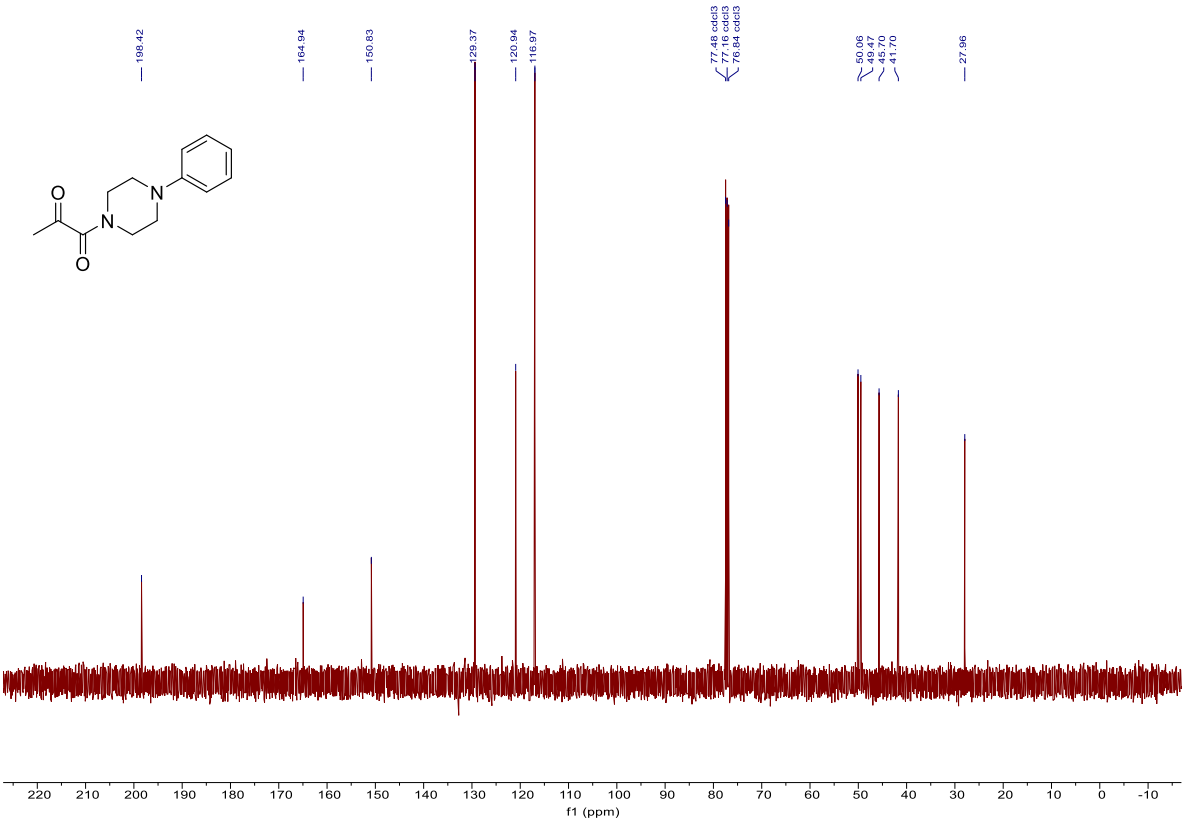




1-(4-Phenylpiperazin-1-yl)propane-1,2-dione (15i).

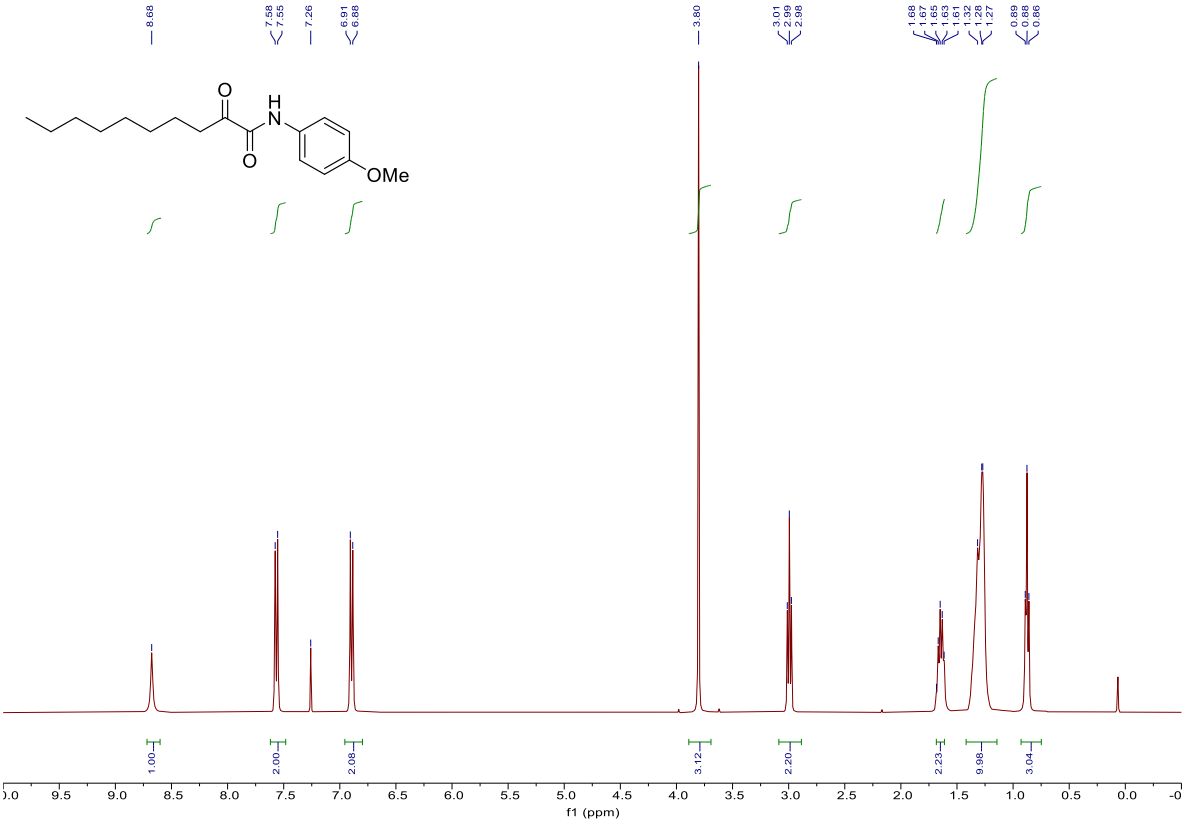
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

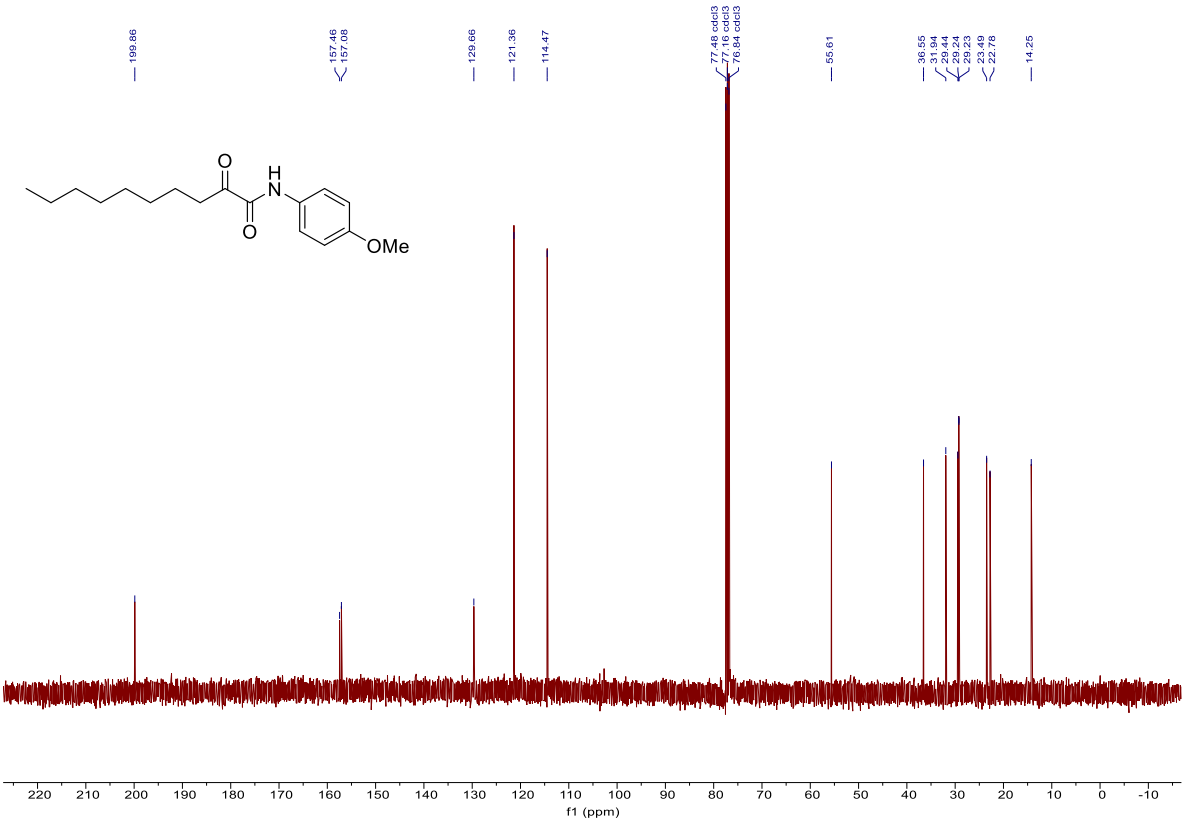




_N_-(4-Methoxyphenyl)-2-oxodecanamide (22).

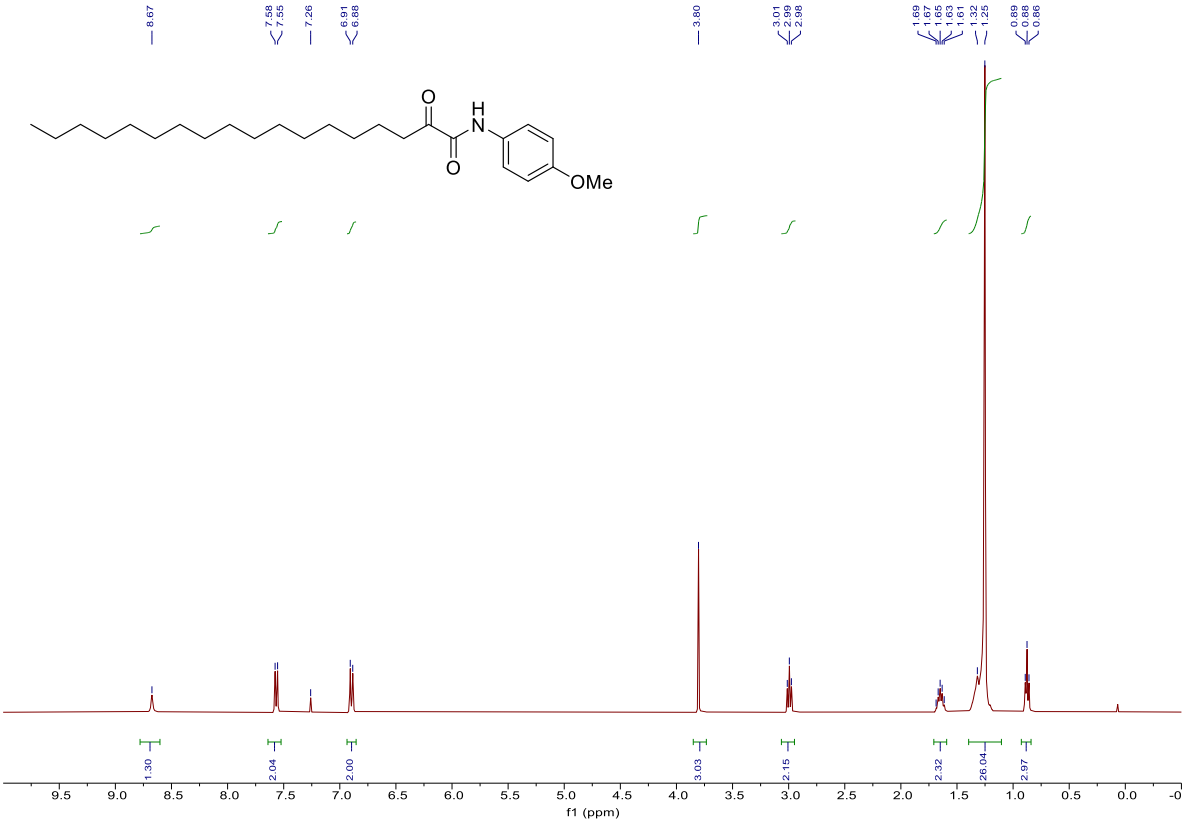
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

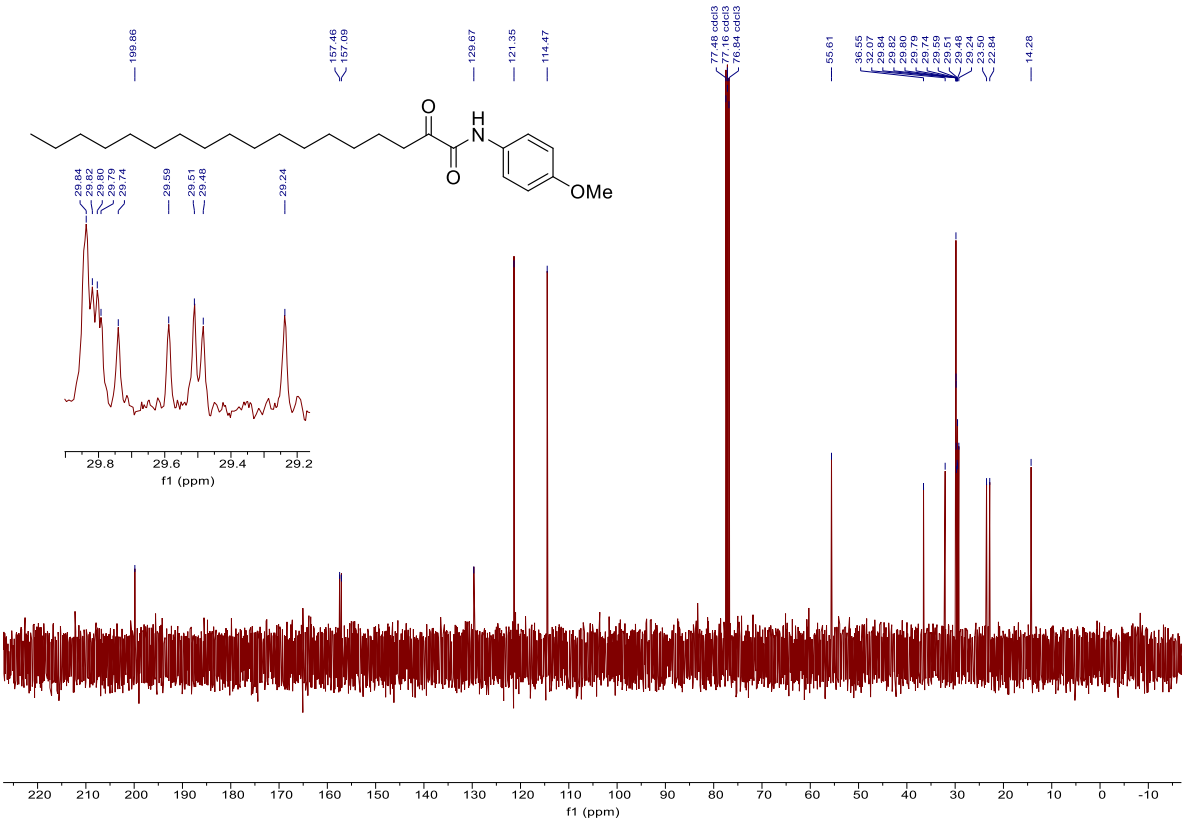




_N_-(4-Methoxyphenyl)-2-oxooctadecanamide (23).

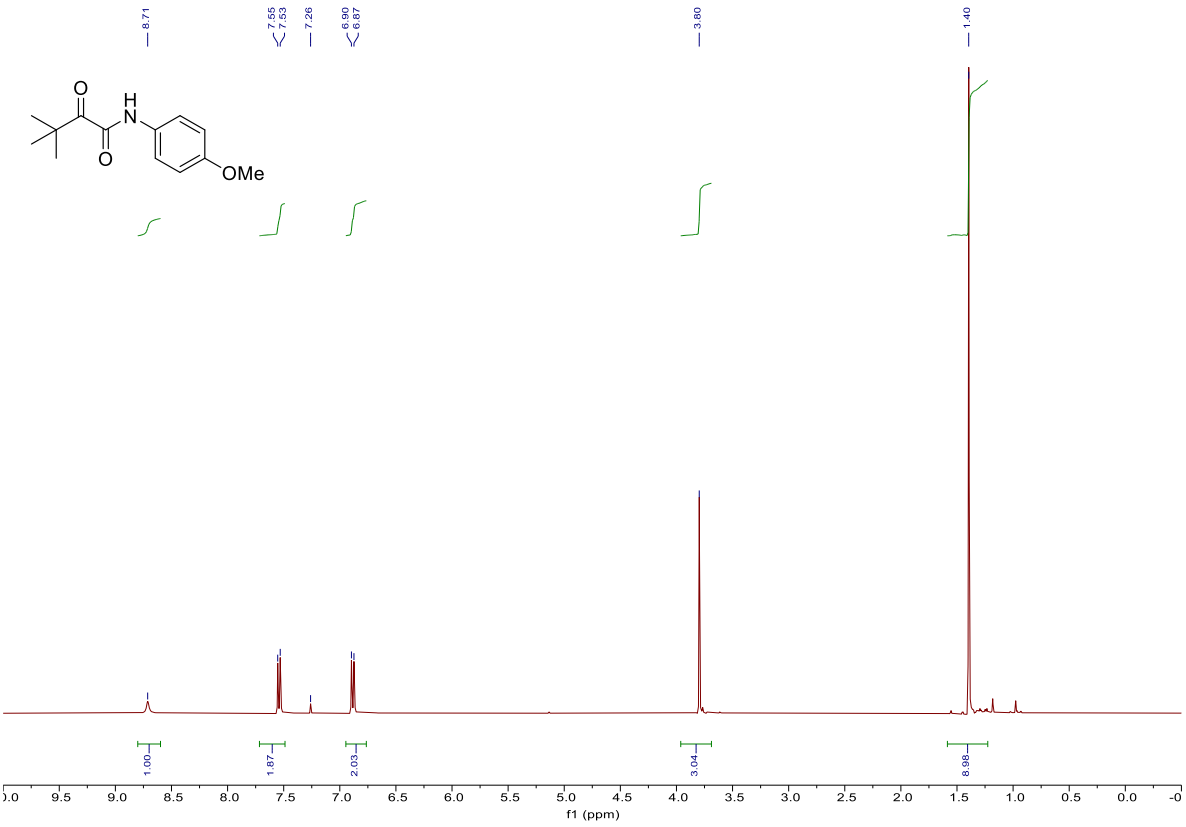
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

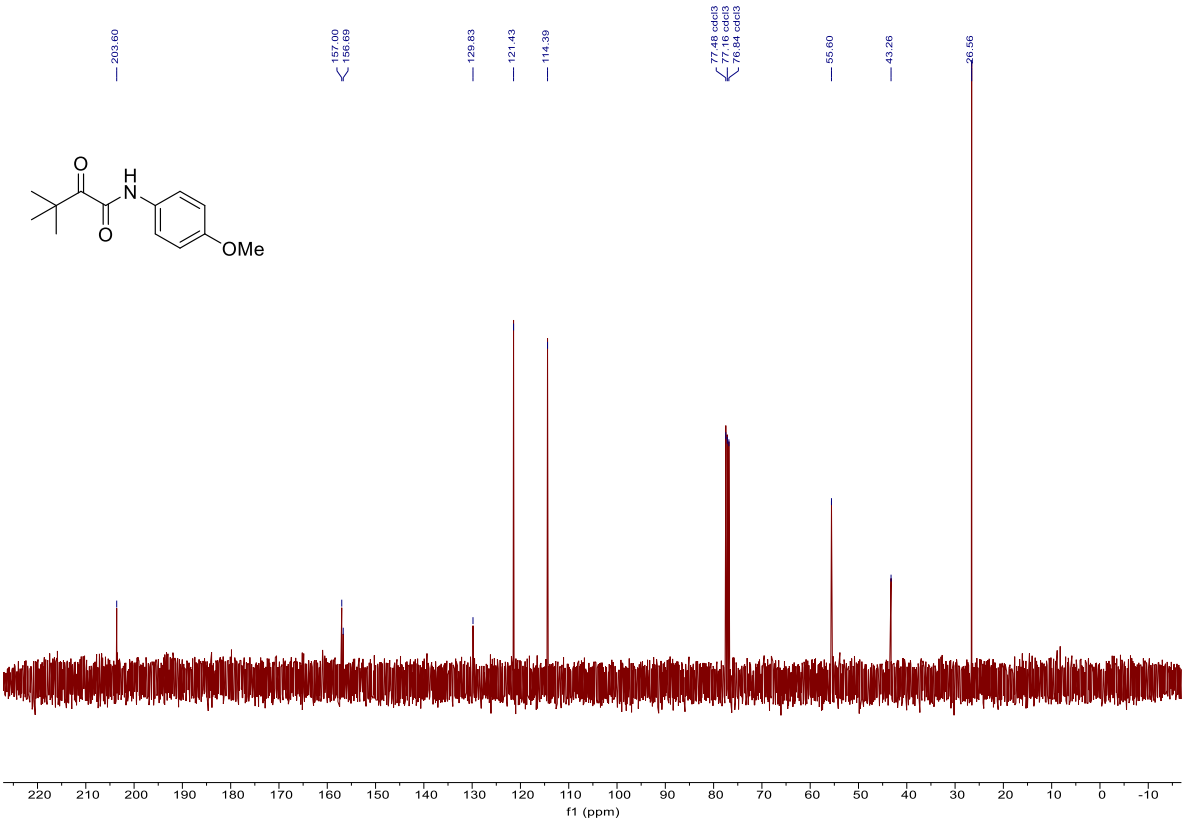




_N_-(4-Methoxyphenyl)-3,3-dimethyl-2-oxobutanamide (24).

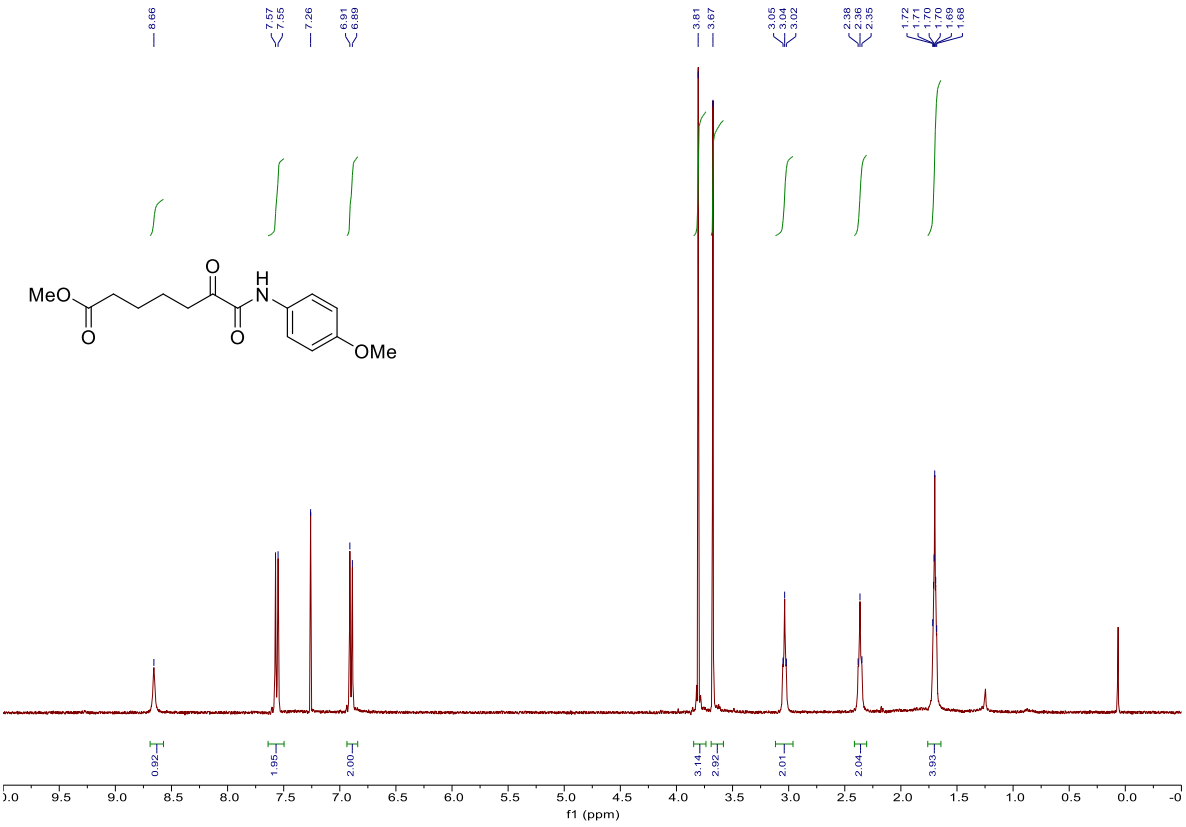
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

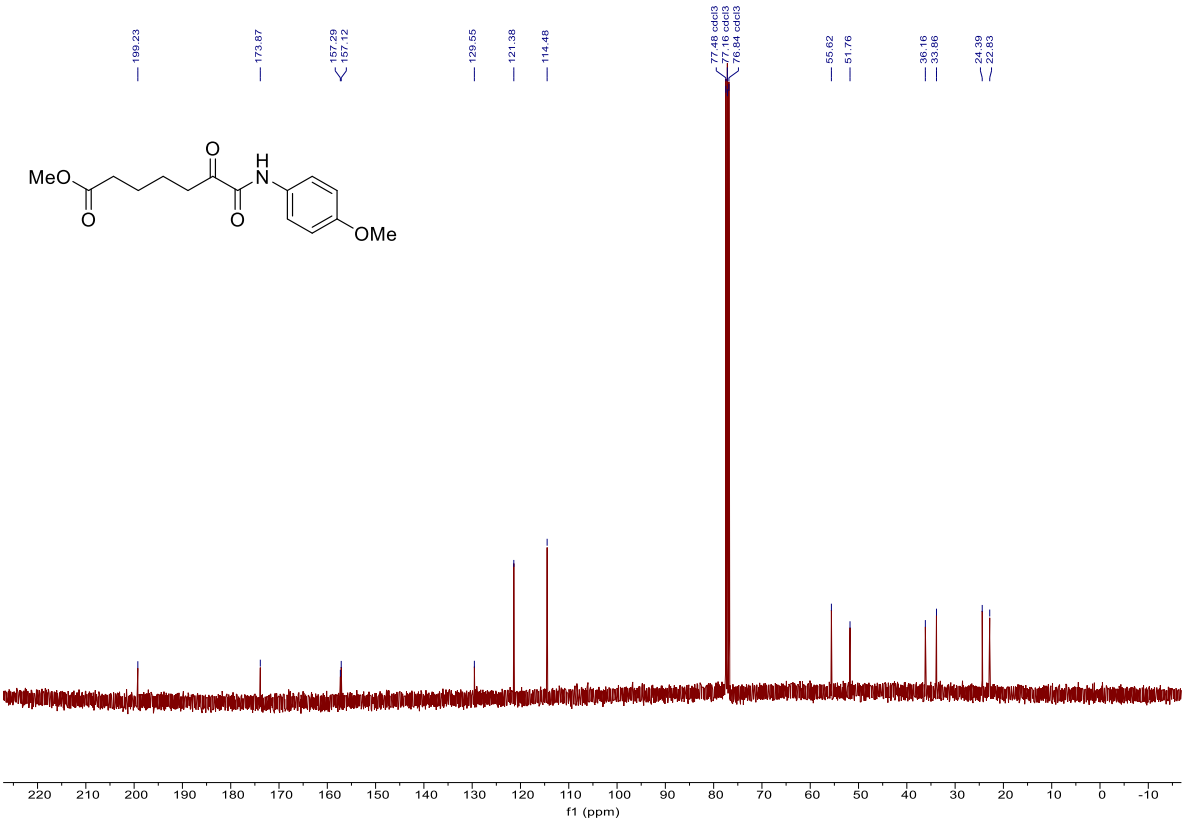




Methyl 7-((4-methoxyphenyl)amino)-6,7-dioxoheptanoate (25).

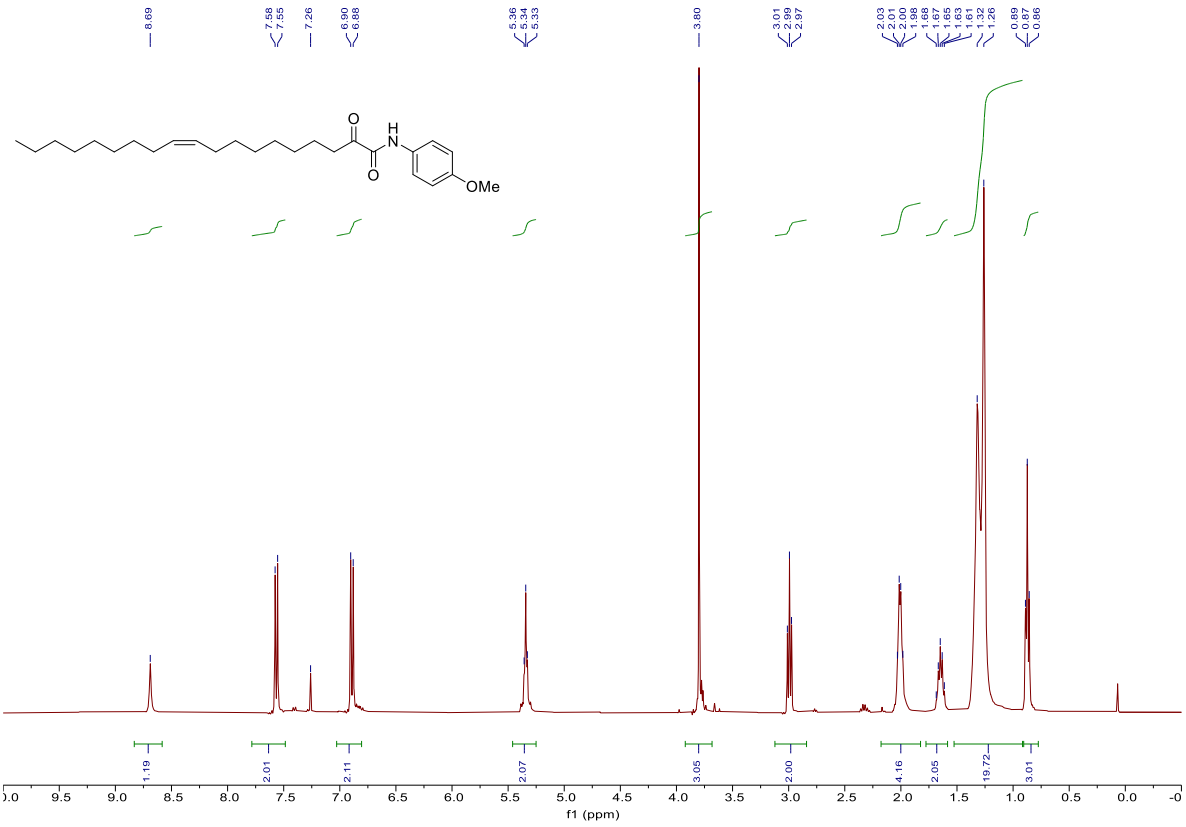
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

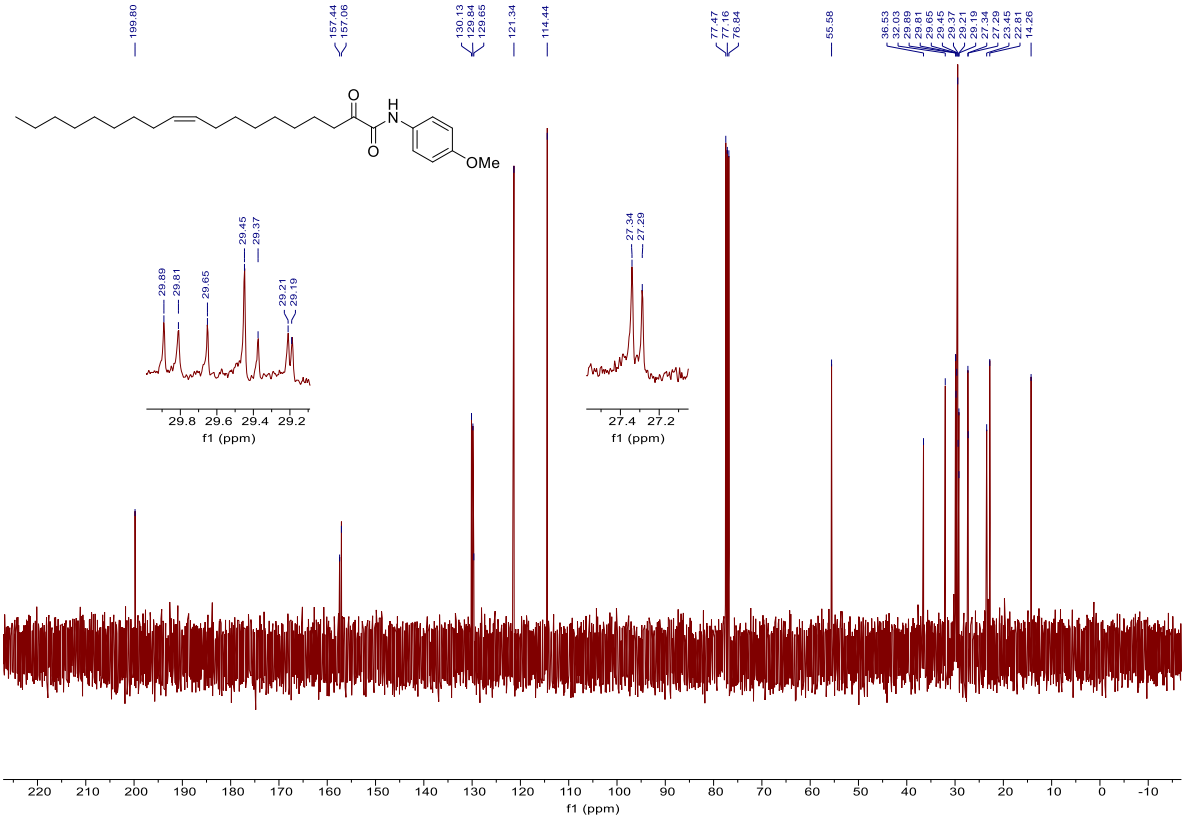




(*Z*)-*N*-(4-Methoxyphenyl)-2-oxononadec-10-enamide (26).

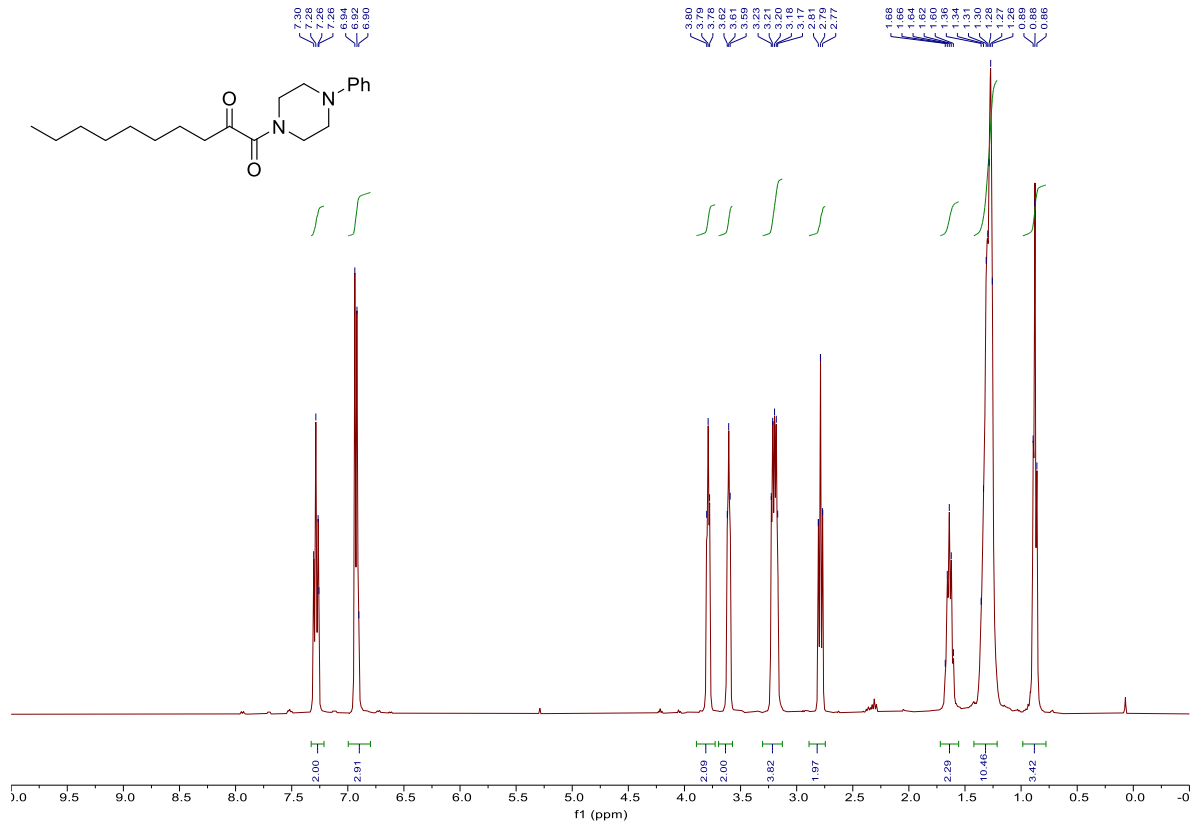
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

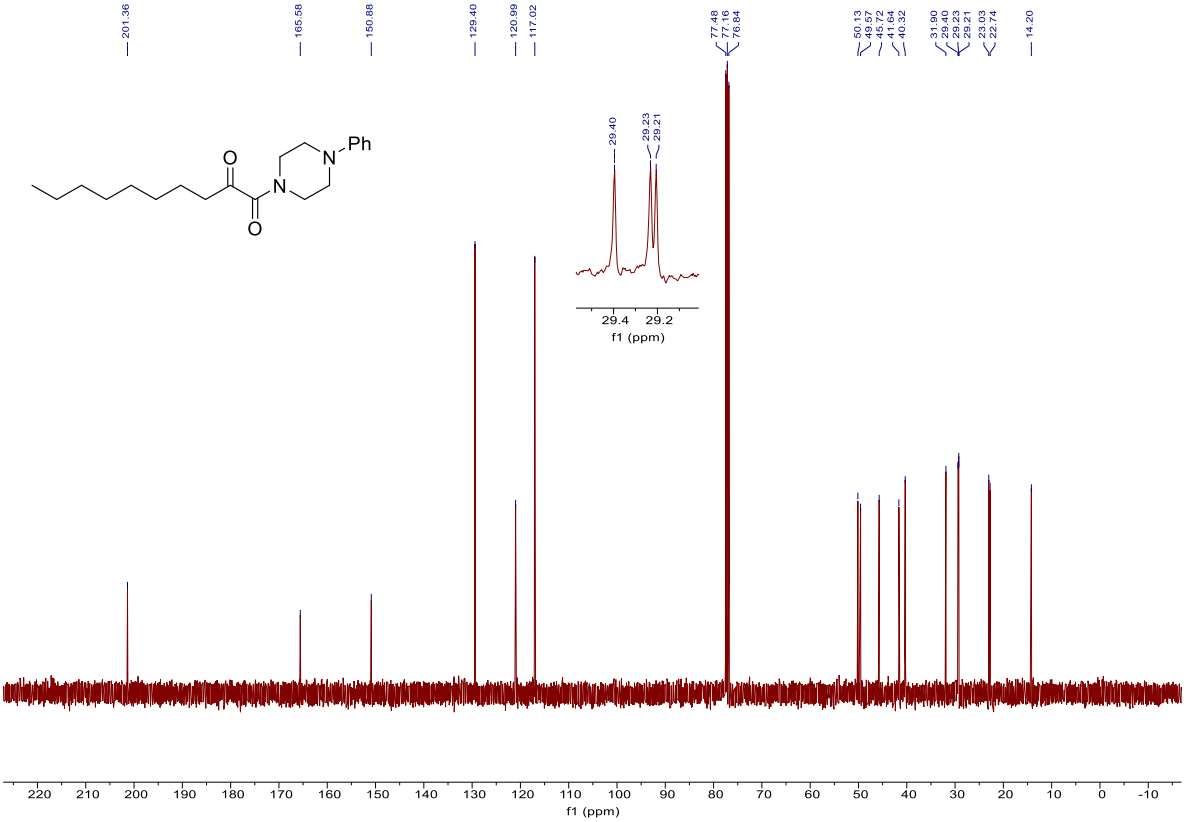




1-(4-Phenylpiperazin-1-yl)decane-1,2-dione (28).

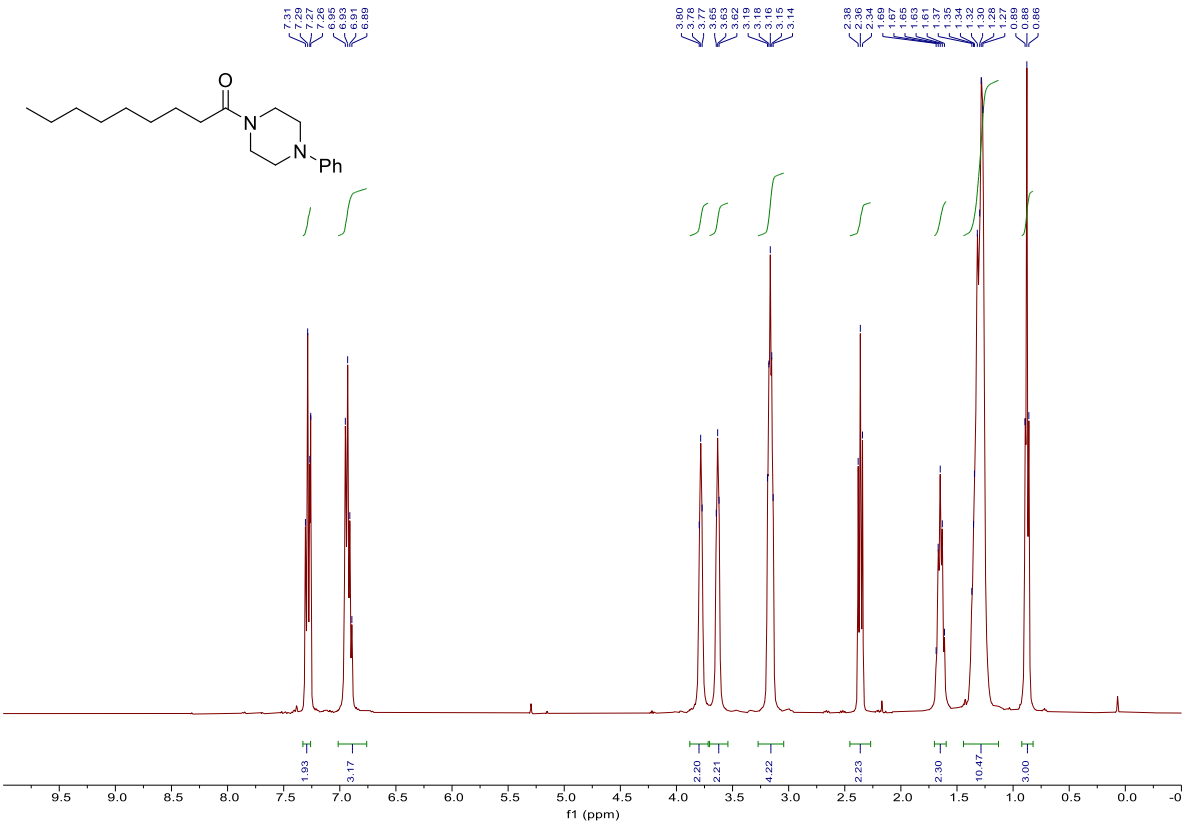
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

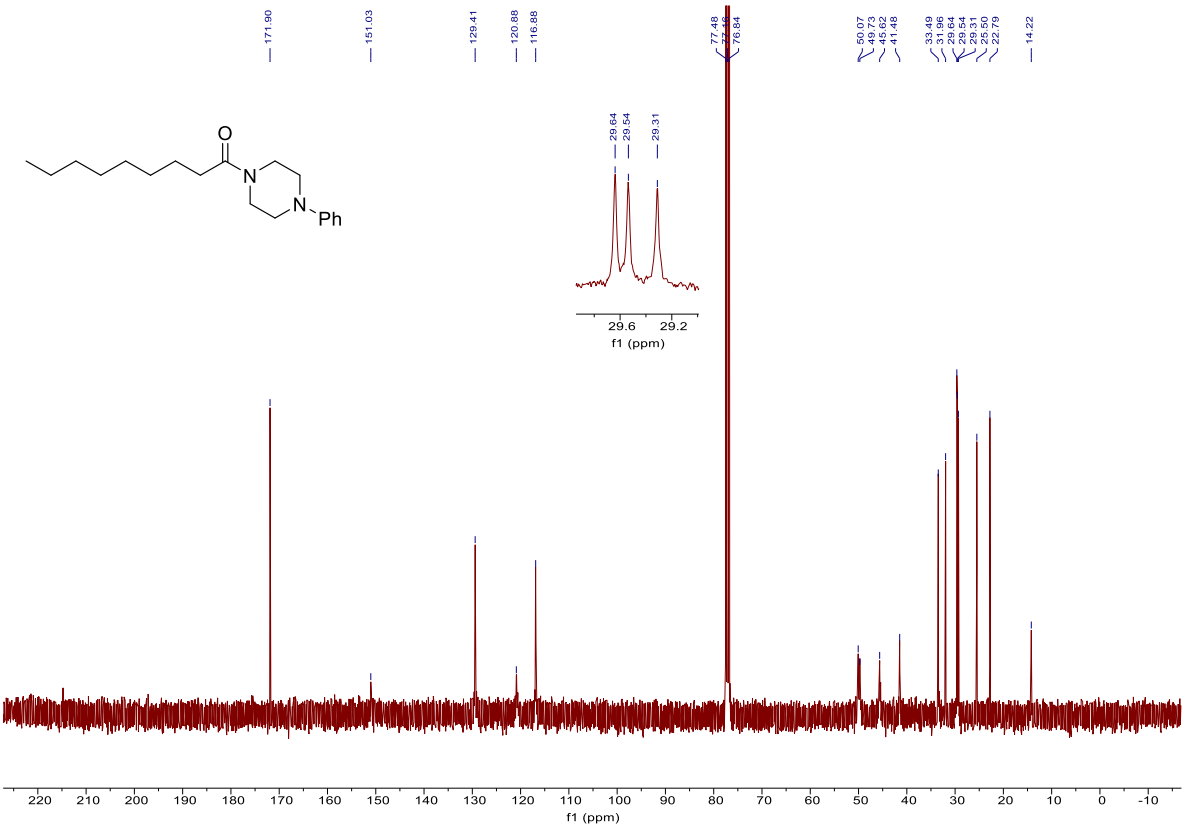




1-(4-Phenylpiperazin-1-yl)nonan-1-one (29).

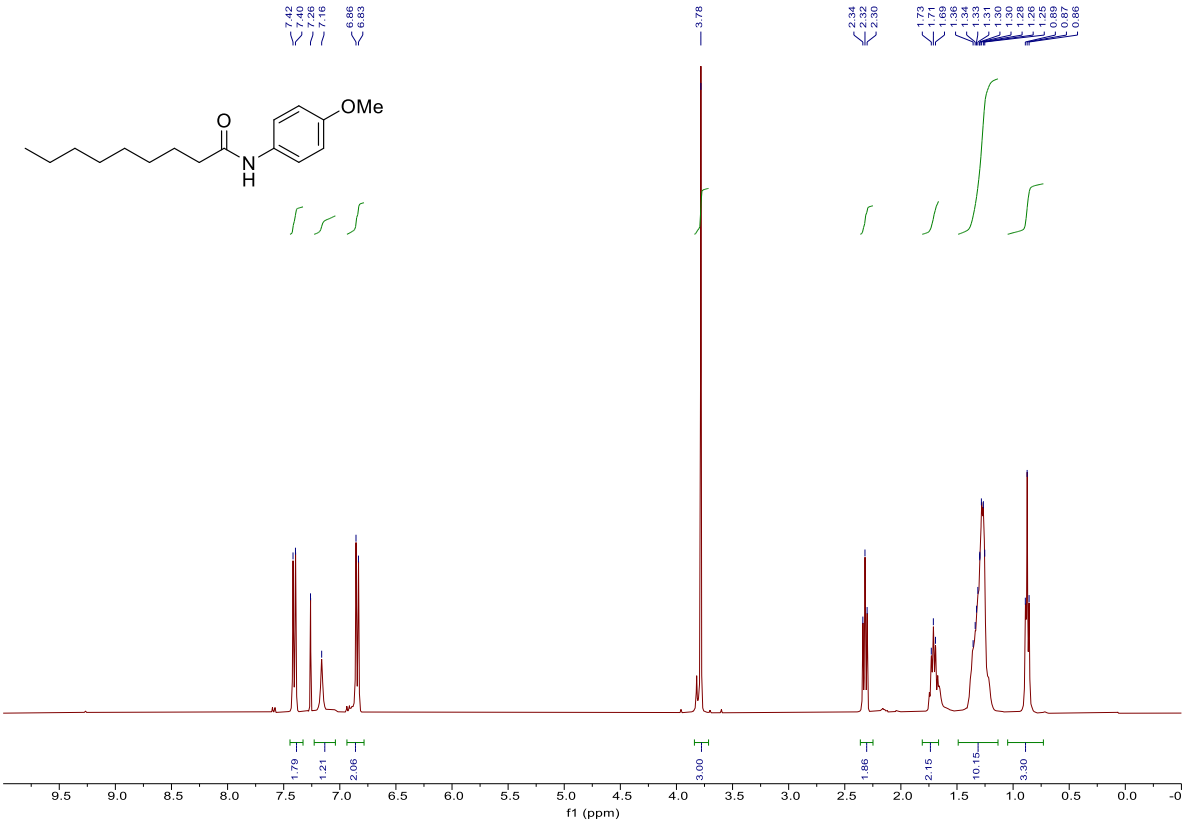
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

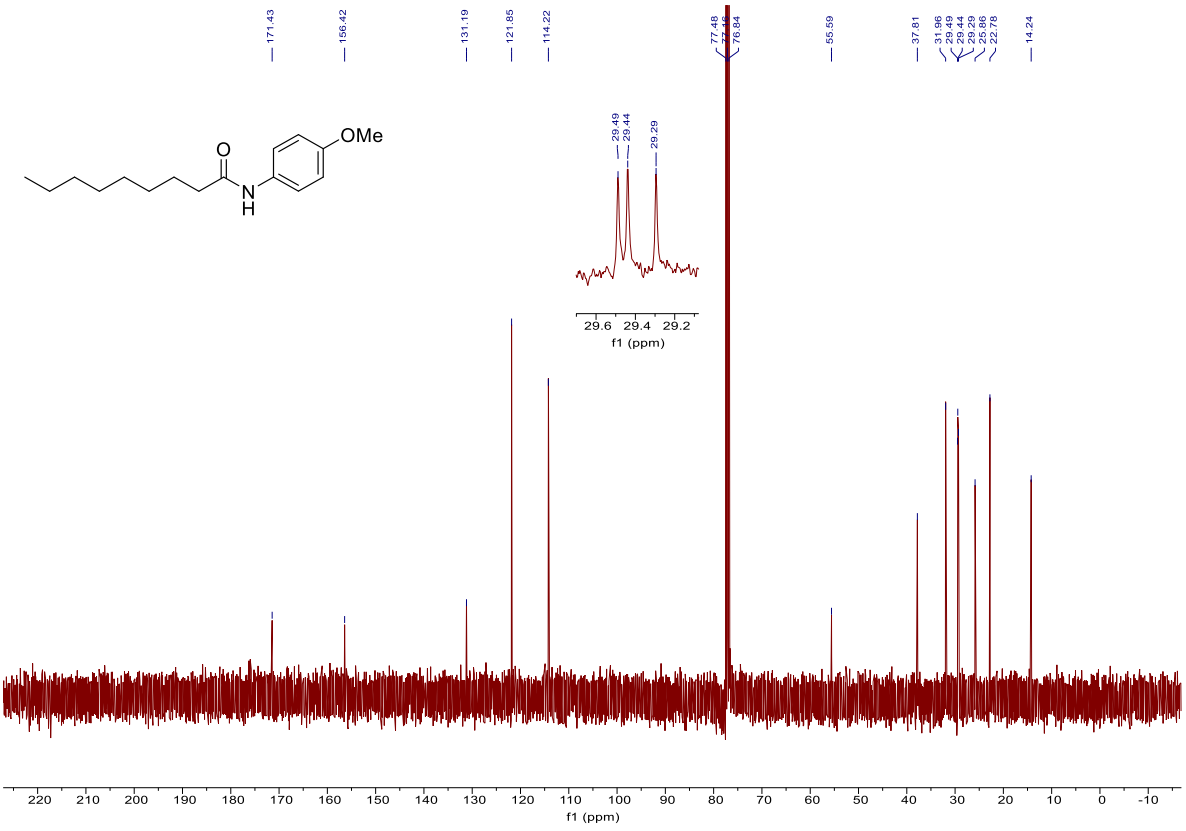




_N_-(4-Methoxyphenyl)nonanamide (30).

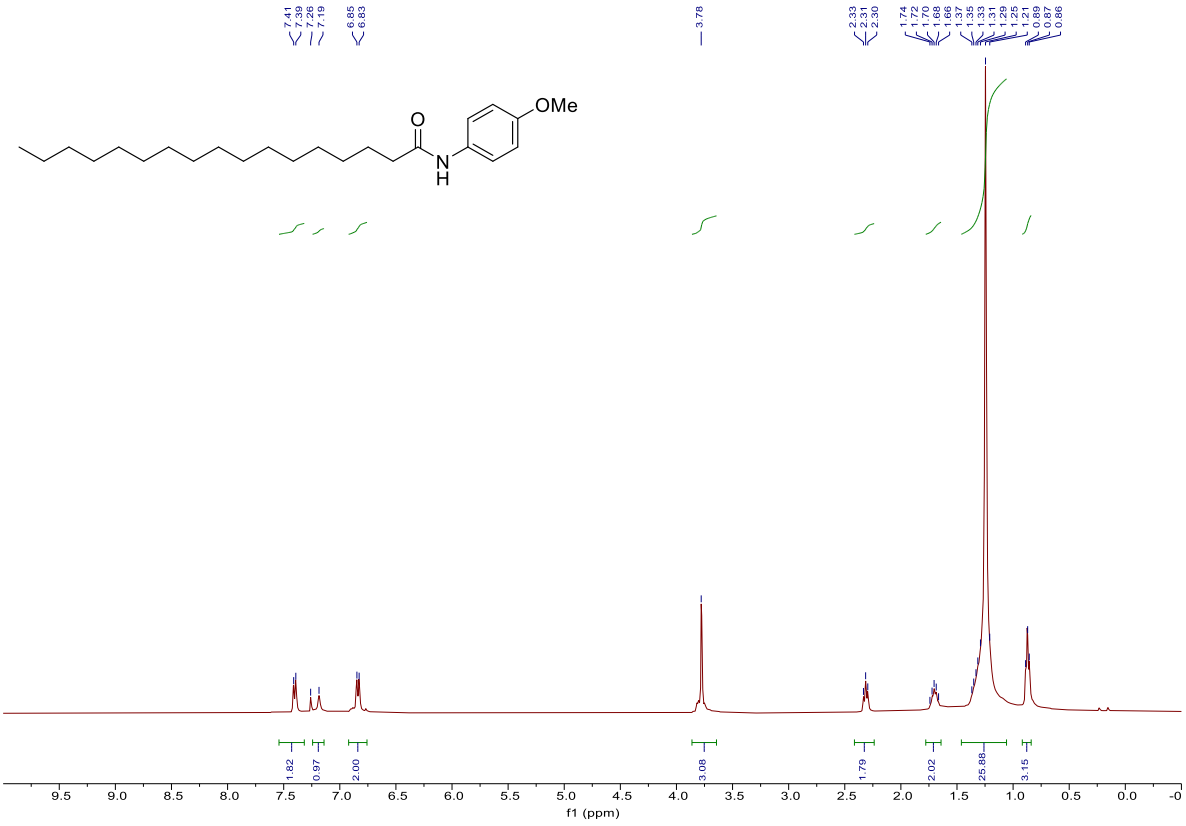
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

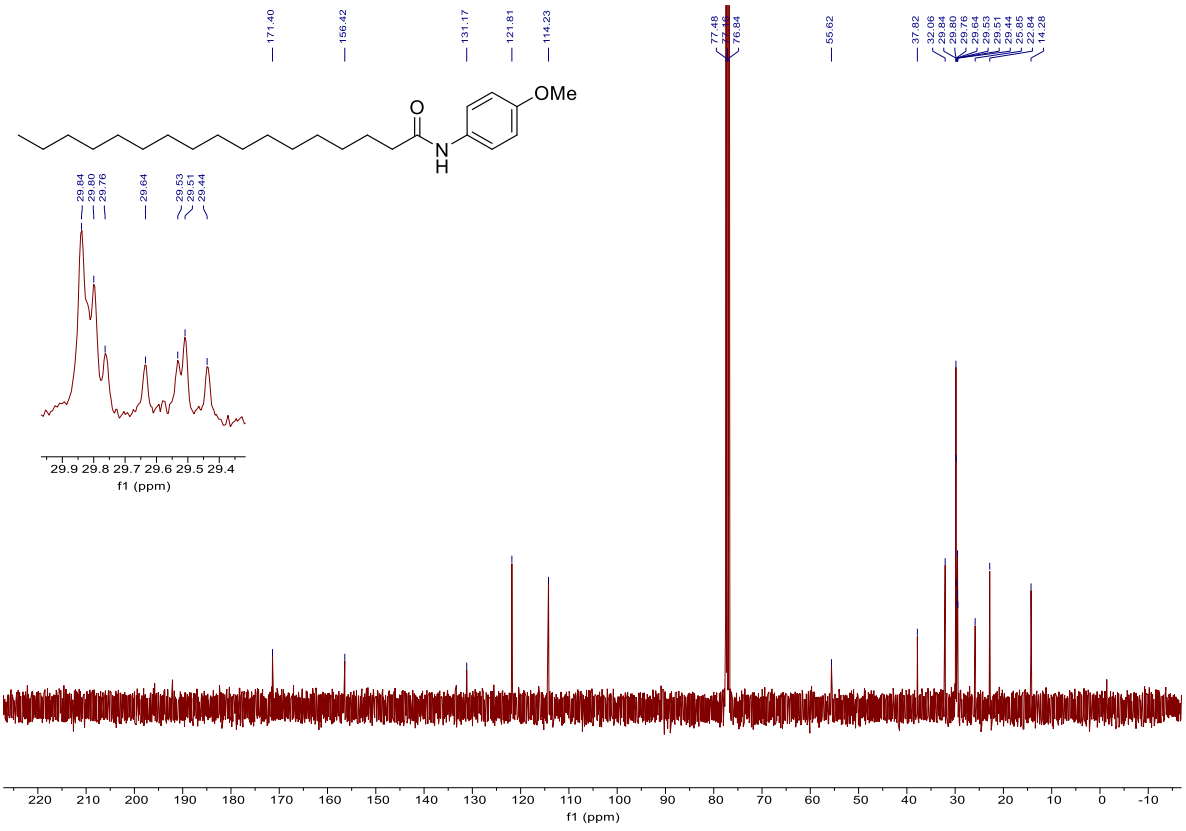




N-(4-Methoxyphenyl)heptadecanamide (31).

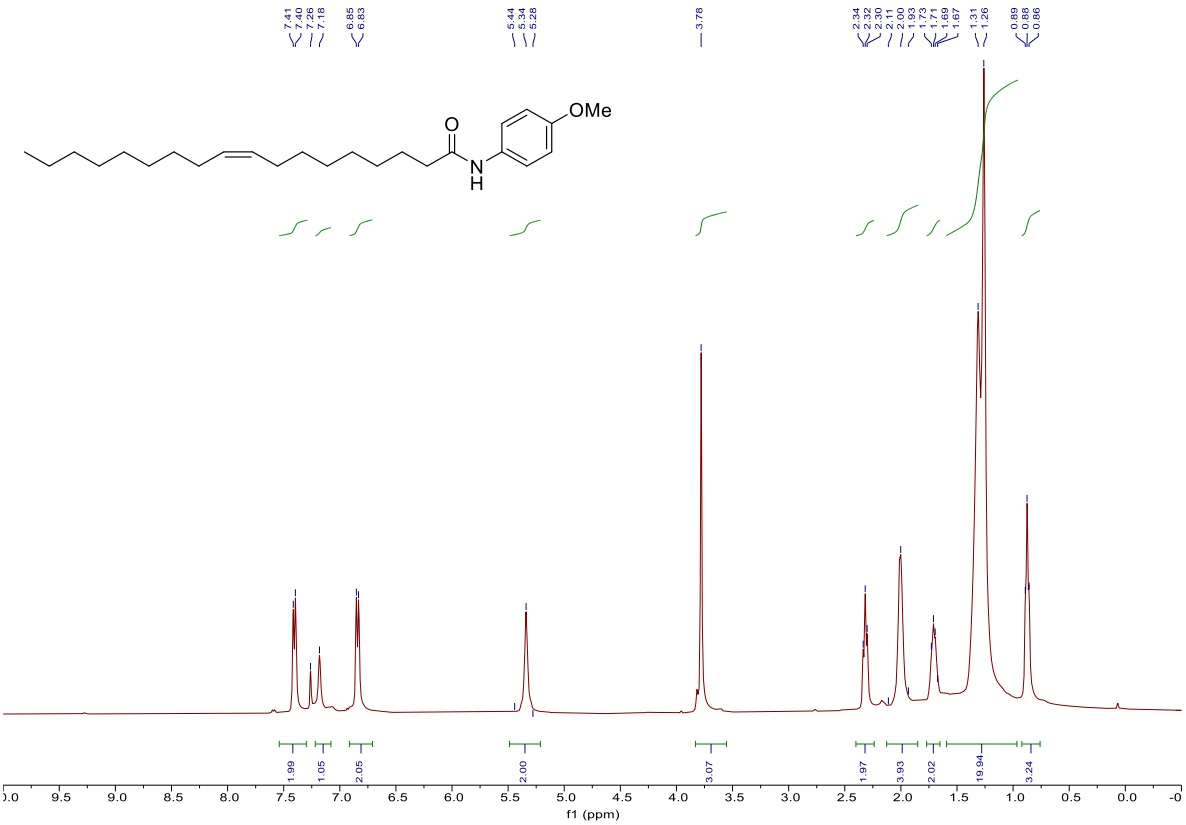
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

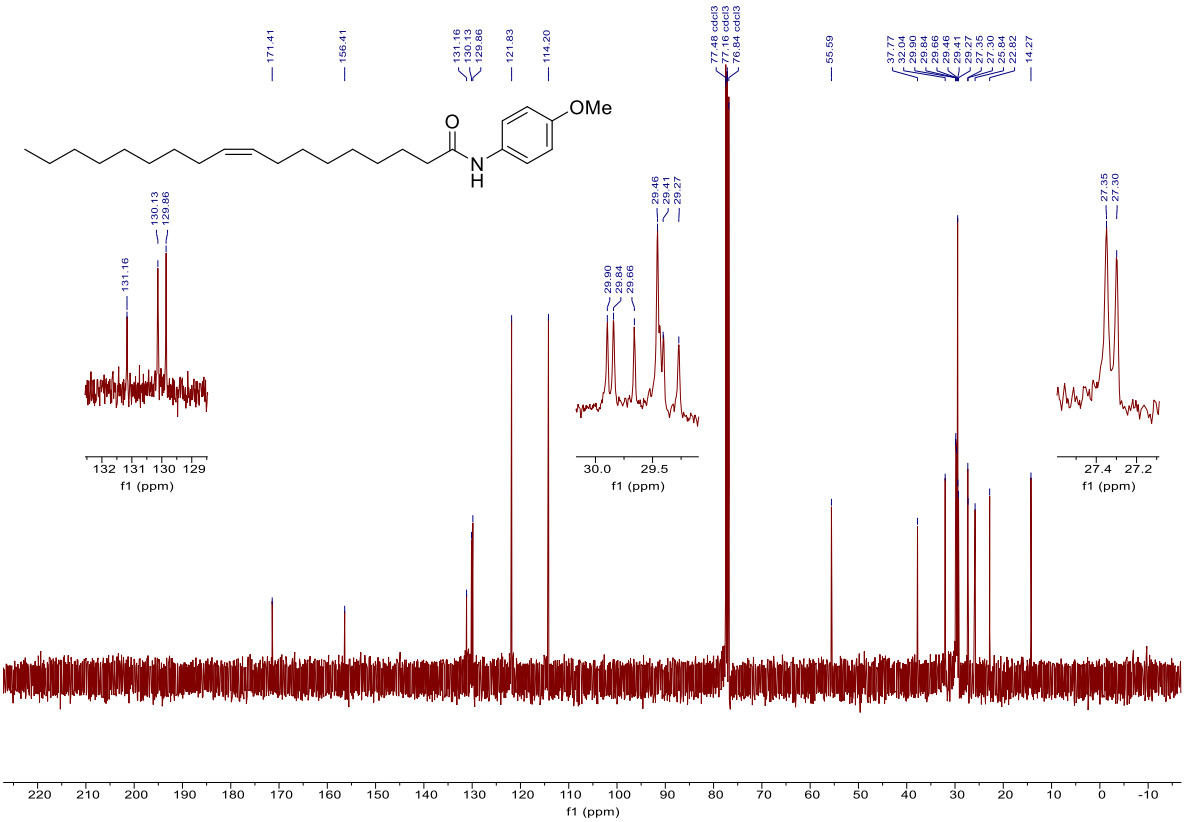




_N_-(4-Methoxyphenyl)oleamide (34).

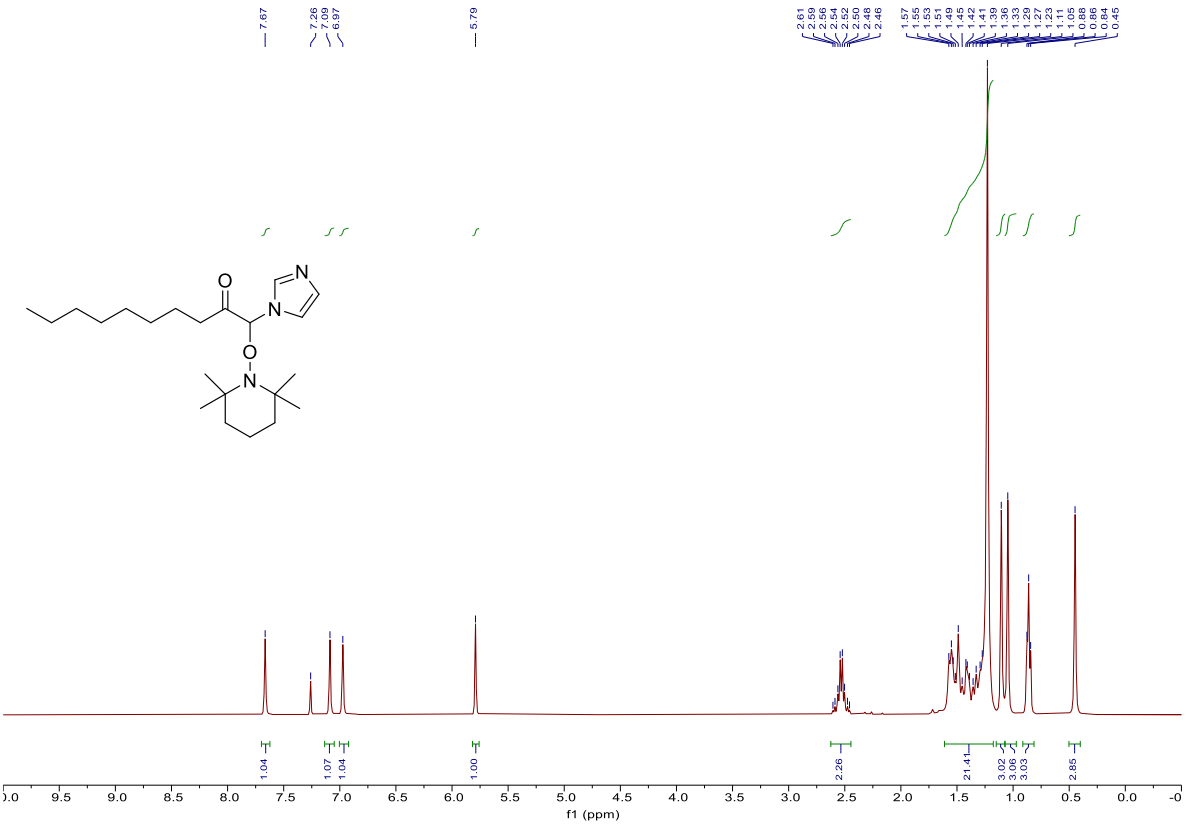
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

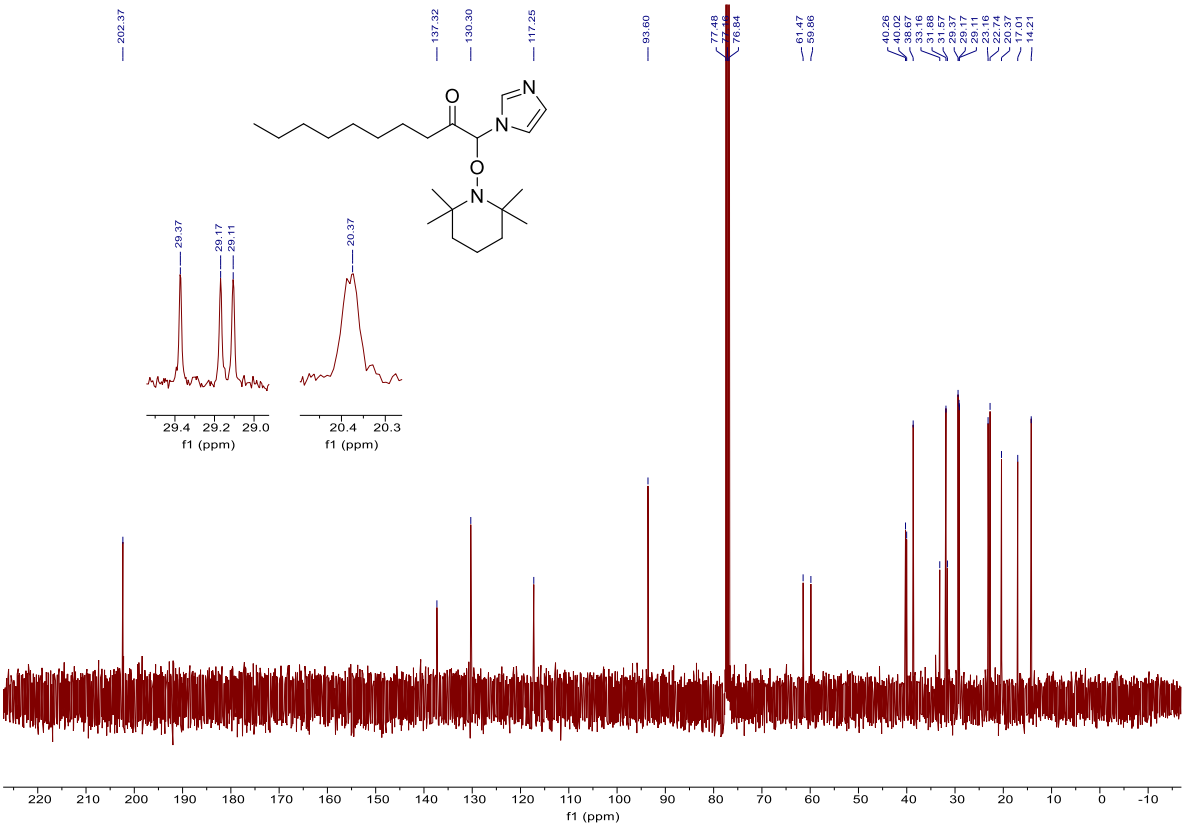




1-(1*H*-Imidazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)decan-2-one (35).

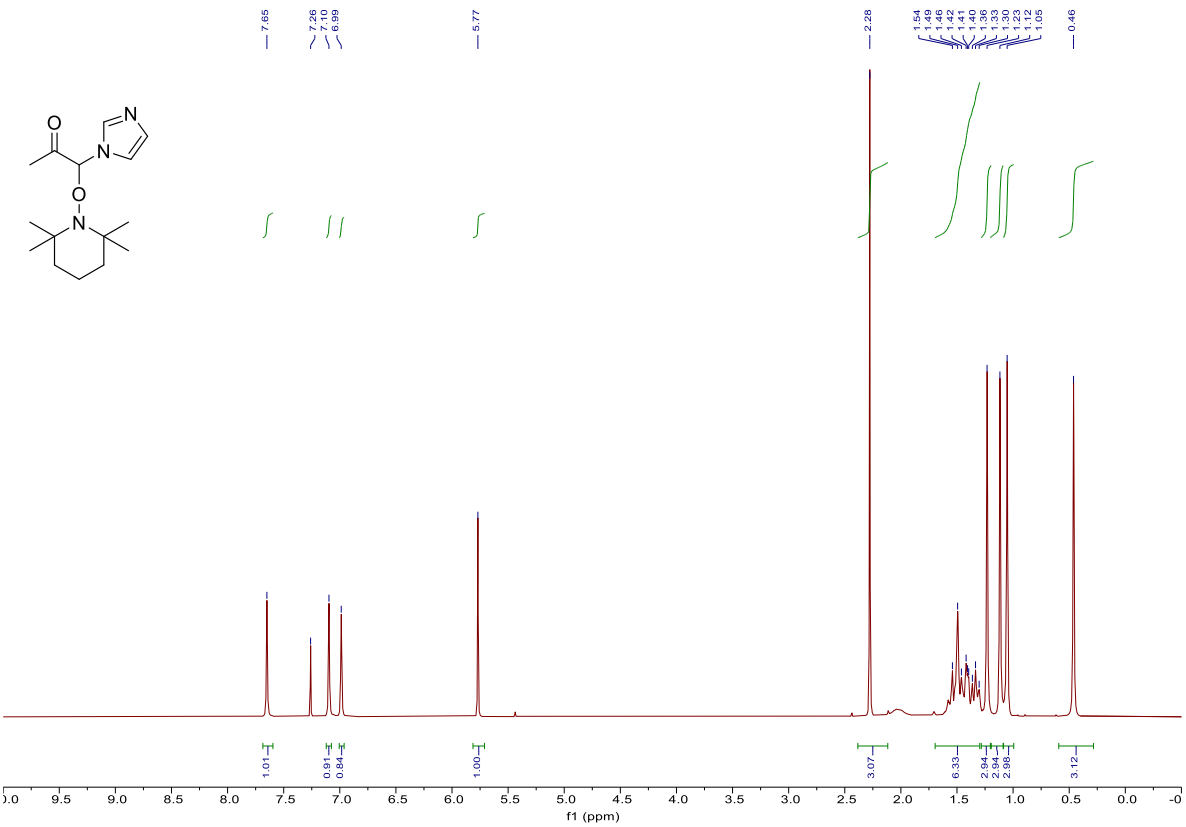
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

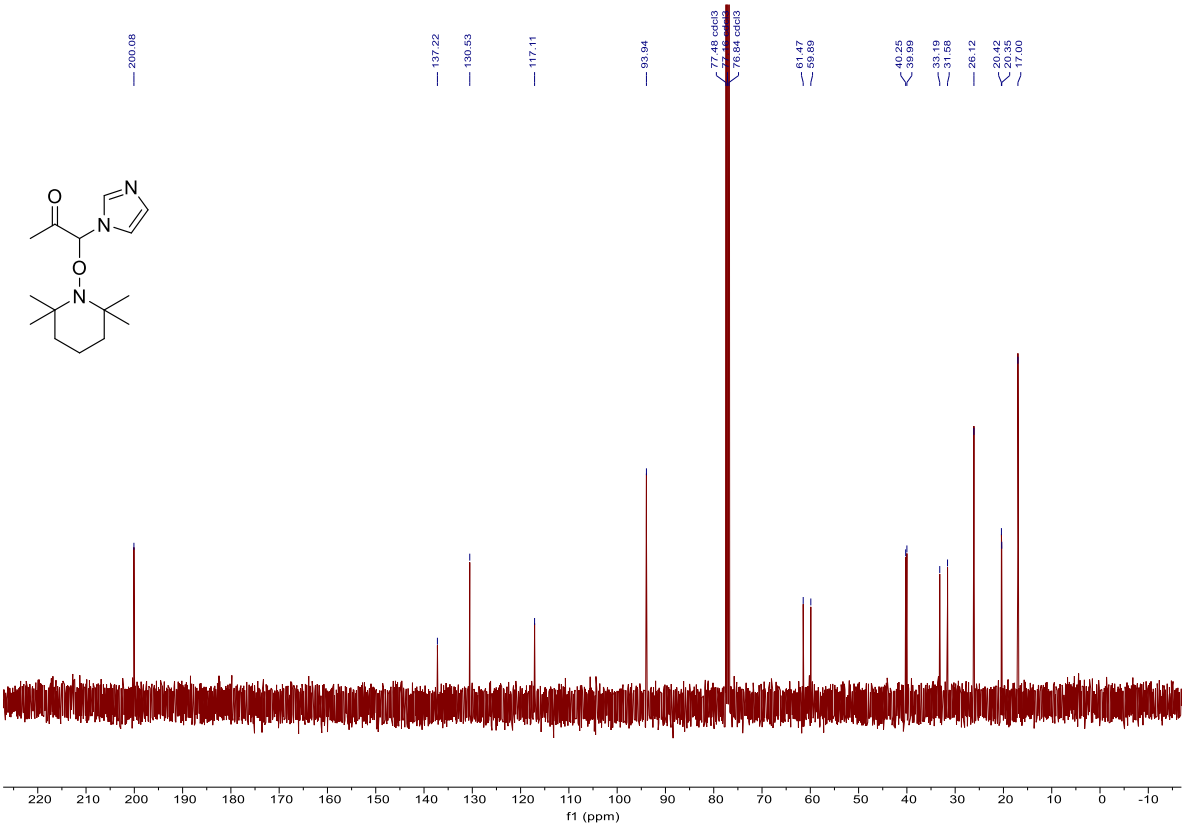




1-(1*H*-Imidazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-one (36).

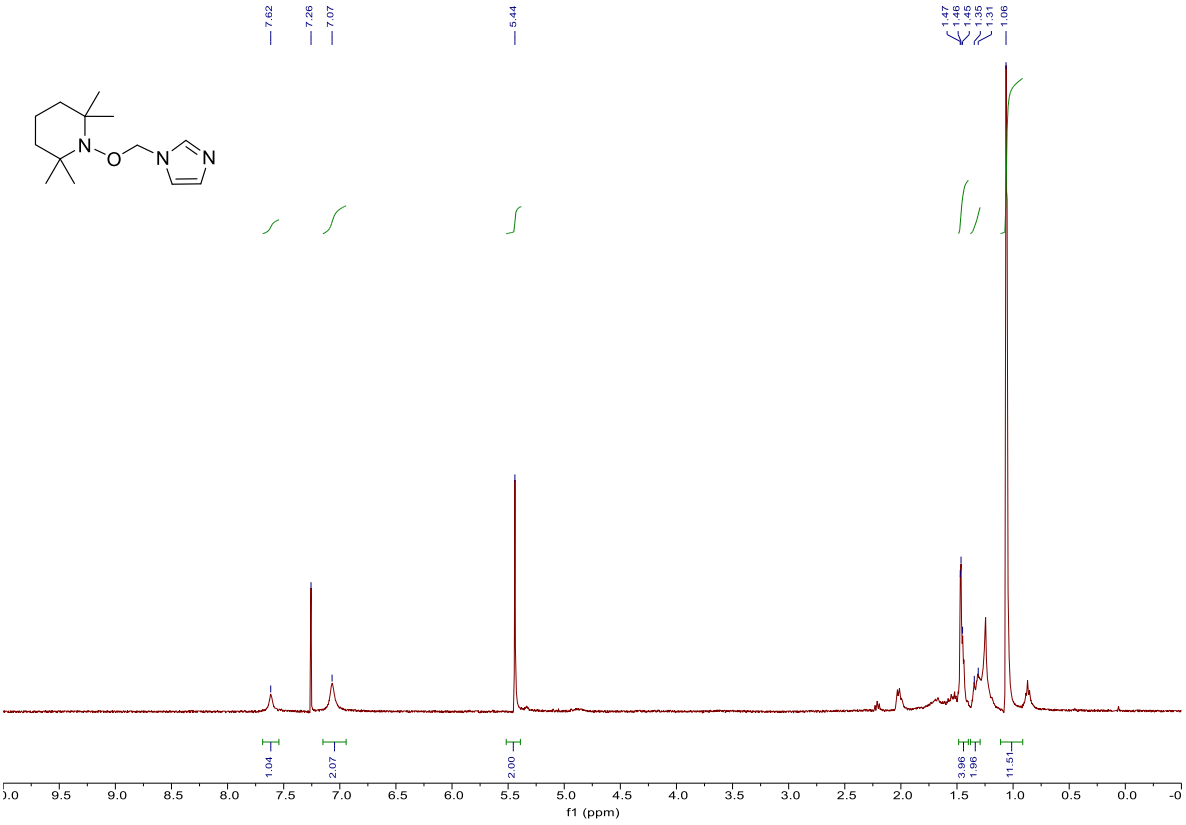
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

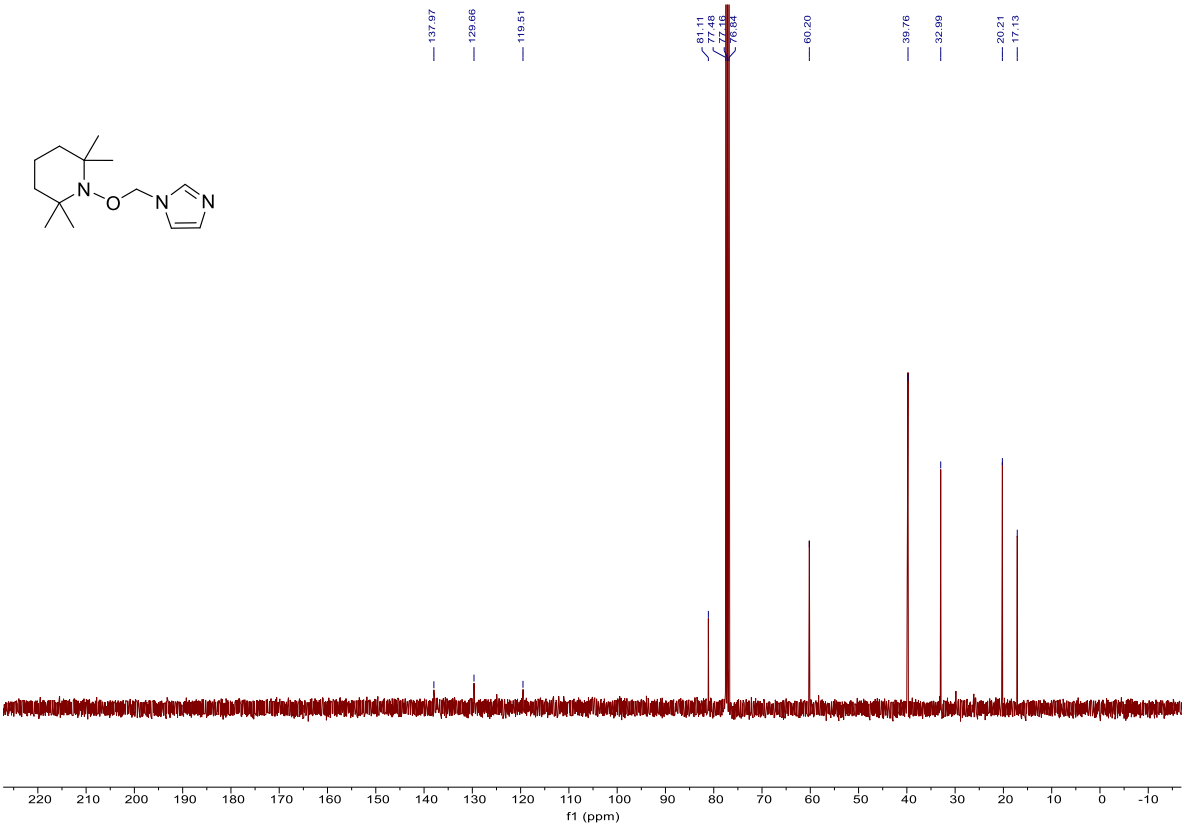




1-((1*H*-Imidazol-1-yl)methoxy)-2,2,6,6-tetramethylpiperidine (37).

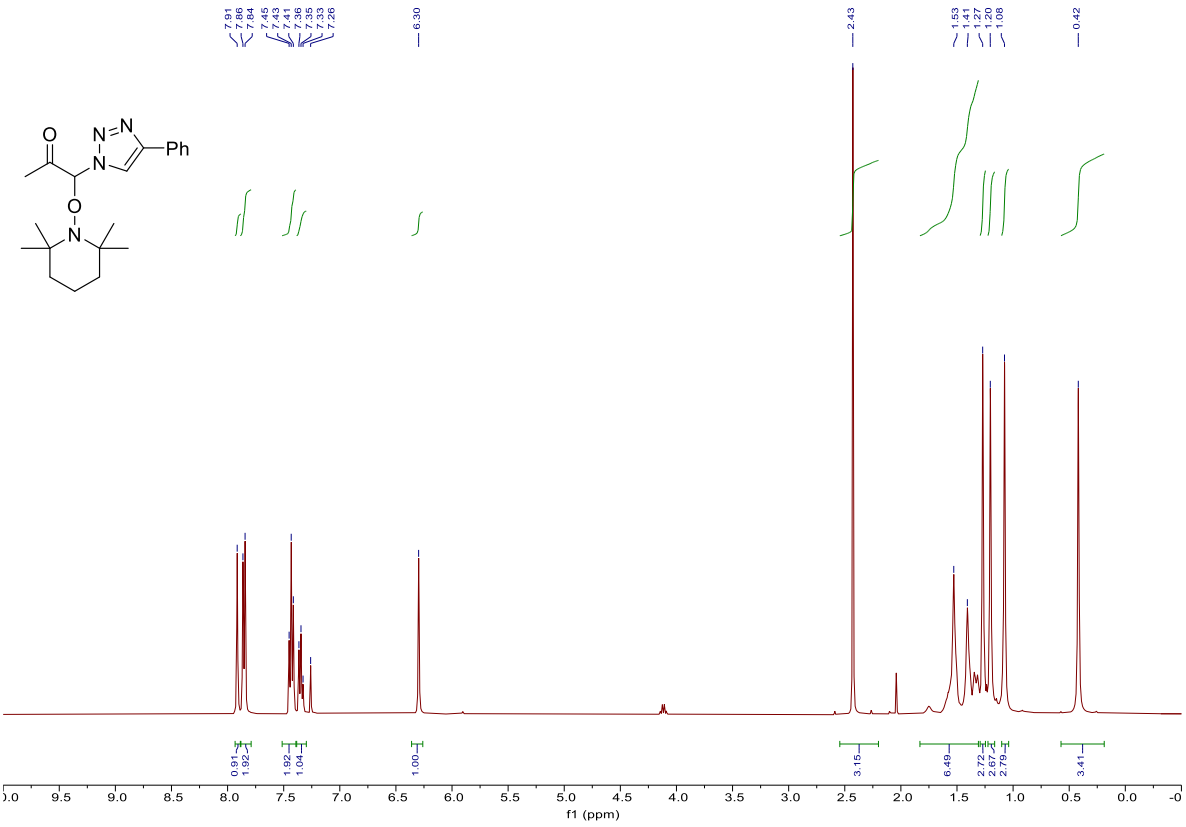
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

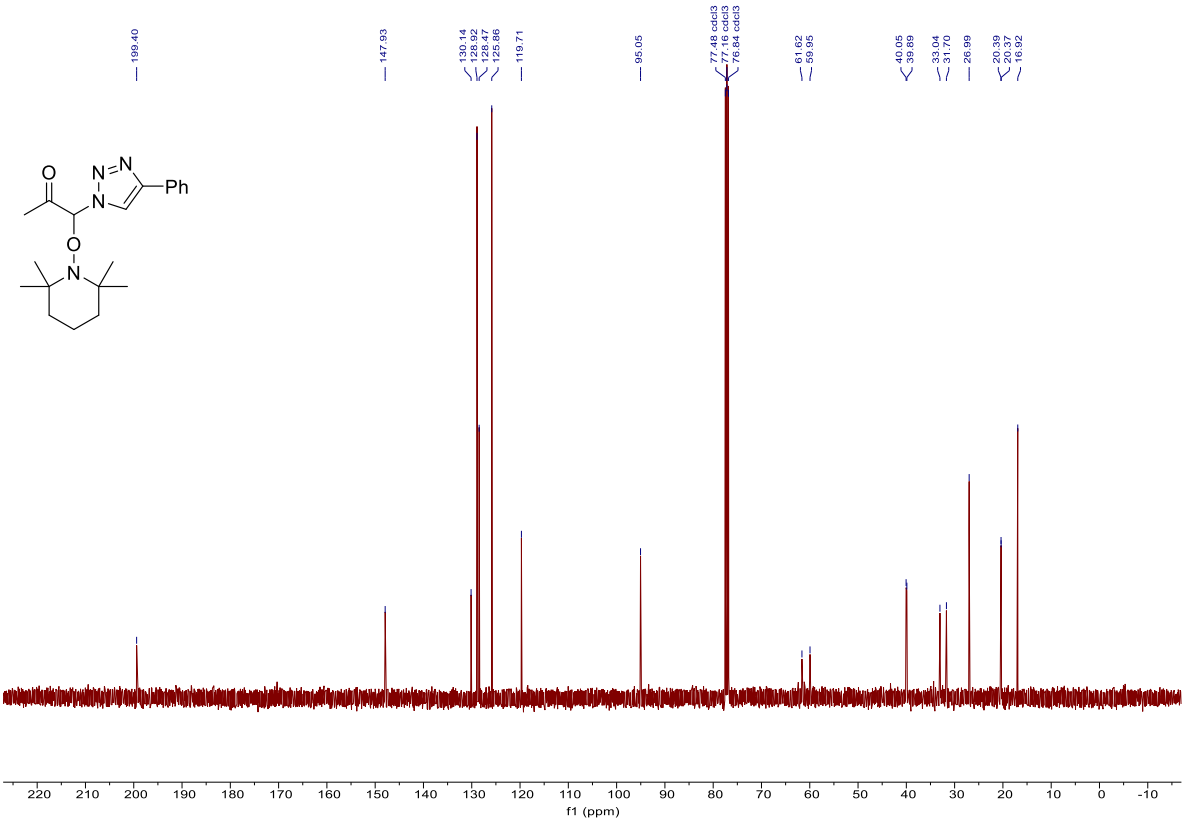




1-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-one (38).

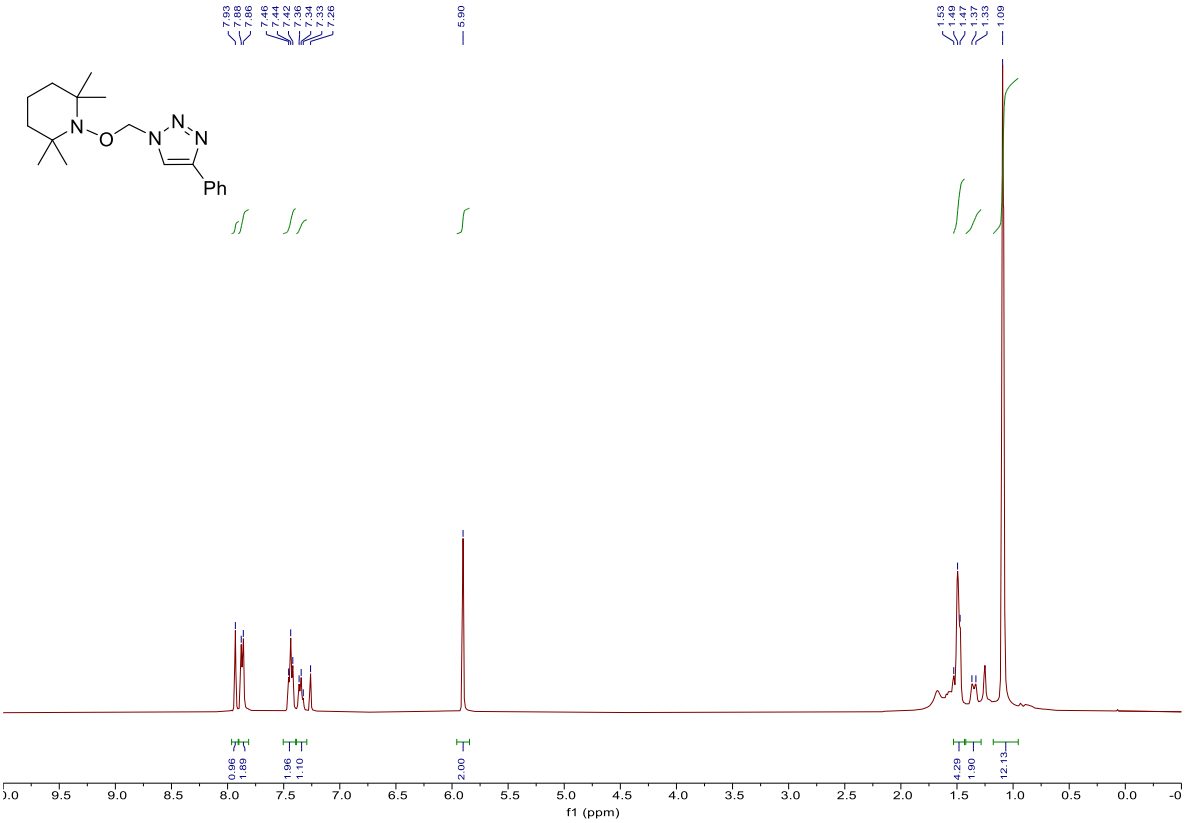
^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).

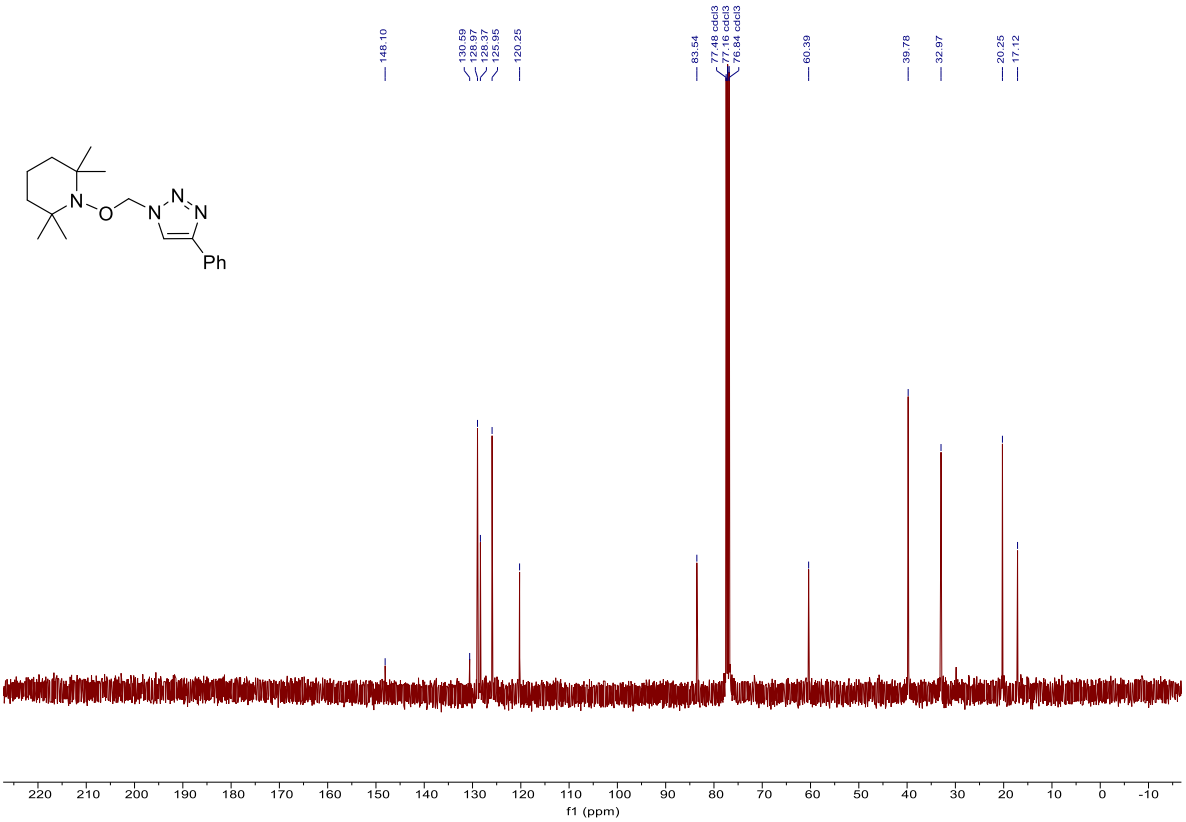




2,2,6,6-Tetramethyl-1-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methoxy)piperidine (39).

^{1}H NMR and ^{13}C NMR (400, 100 MHz, $CDCl_3$).





13) References

1) H. Cha, K. Lee and D. Y. Chi, *Tetrahedron*, 2017, **73**, 2878–2885.

2) I. C. Lennon and J. A. Ramsden, *Org. Process Res. Dev*., 2005, **9**, 110–112.