# Supporting Information

# Copper-catalyzed synthesis of α-ketoamides using water and dioxygen as the oxygen source

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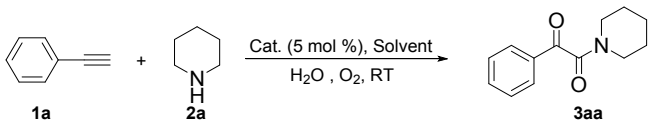
## 1. General remarks

All commercially available reagent grade chemicals were purchased from Aldrich, Acros and Alfa Aesar Chemical Company and used as received without further purification unless otherwise stated. NMR spectra were recorded in $CDCl_3$ or $CD_3COCD_3$ on a Bruker Avance 600 spectrometer with TMS as internal standard (600 MHz $^1H$, 150 MHz $^{13}C$) at room temperature, and the chemical shifts (δ) were expressed in ppm and J values were given in Hz. The following abbreviations are used to indicate the multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m) or broad (br). Mass analyses and HRMS were obtained on a Finnigan-LCQDECA mass spectrometer and a Bruker Daltonics Bio-TOF-Q mass spectrometer by the ESI method, respectively. Column chromatography was performed on silica gel (200-300 mesh).

## 2. Optimization of reaction conditions

**Table 1:** Reaction of **1a** and **2a** under various conditions [a]



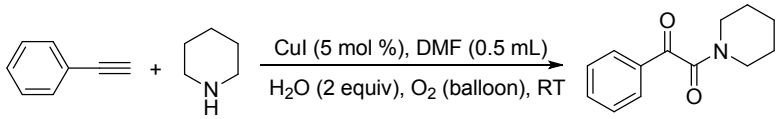

**1a** **2a** **3aa**

| Entry | Catalyst | Solvent | $H_2O$ | temperture | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | CuBr | THF | 2 equiv | rt | 21 |
| 2 | CuBr | THF | 2 equiv | rt | 0[c] |
| 3 | CuBr | THF | - | rt | 0[d] |
| 4 | $CuBr_2$,$CuCl_2$,$Cu(OTf)_2$ ,CuCl | THF | 2 equiv | rt | <20 |
| 5 | $(CH_3CN)_4CuPF_6$ | THF | 2 equiv | rt | 24 |
| 6 | CuI | THF | 2 equiv | rt | 46 |
| 7 | AgOTf, $RhCl_3$, $InBr_3$,$BiBr_3$, $NiCl_2$ | THF | 2 equiv | rt | 0 |
| 8 | $AuBr_3$ | THF | 2 equiv | rt | trace |
| 9 | - | THF | 2 equiv | rt | 0 |
| 10 | CuI | THF | 1 equiv | rt | 40 |
| 11 | CuI | THF | 3 equiv | rt | 43 |
| 12 | CuI | Dioxane | 2 equiv | rt | 25 |
| 13 | CuI | MeOH | 2 equiv | rt | 0 |
| 14 | CuI | DMSO | 2 equiv | rt | 37 |

| | | | | | |
|---|---|---|---|---|---|
| 15 | CuI | $CH_3CN$ | 2 equiv | rt | 35 |
| **16** | **CuI** | **DMF** | **2 equiv** | **rt** | **71** |
| 17 | CuI | DMF | 2 equiv | rt | 39 |
| 18 | CuI | DMF | 2 equiv | 50°C | 51 |
| 19 | CuI | DMF | 2 equiv | 80°C | 36 |

[a] Reaction conditions: **1a** (2 mmol), **2a** (0.5 mmol), catalyst (5 mol %), $H_2O$ (indicated amount), $O_2$ (balloon), solvent (0.5 mL), 12 h. [b] Isolated yields based on **2a**. [c] Under $N_2$. [d] Dry THF was used and 4Å molecular sieve was added continually. [e] Under air.

***Table 2:*** Screening of additives and ligands [a]




**1a** **2a** **3aa**

| Entry | Ligand or Additive | Yield (%)[b] |
|---|---|---|
| 1 | $Et_3N$ (10 mol %) | 41 |
| 2 | Pyridine (10 mol %) | 32 |
| 3 | $K_2CO_3$ (10 mol %) | 19 |
| 4 | $Zn(OTf)_2$ (10 mol %) | 51 |
| 5 | $PPh_3$ (10 mol %) | 39 |
| 6 | 2,2'-Bipyridine (10 mol %) | 36 |

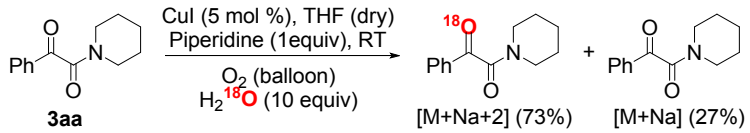
[a] Reaction conditions: **1a** (2 mmol), **2a** (0.5 mmol), CuI (5 mol %), $H_2O$ (2 equiv), $O_2$ (balloon), DMF (0.5 mL), at room temperature, 12 h. [b] Isolated yields based on **2a**.

## 3. General procedure for the synthesis of *α*-ketoamides

Alkyne **1** (2 mmol) was added to a mixture of CuI (0.025 mmol), $H_2O$ (1.0 mmol), and amine **2** (0.5 mmol) in DMF (0.5mL) at room temperature under $O_2$ (balloon). The reaction mixture was stirred at room temperature. After the completion of the reaction (monitored by TLC), the reaction solution was submitted to flash chromatographic separation on silica gel using petroleum ether/ethyl acetate as an eluent to give the corresponding product.

## 4. Labeling experiments

**4.1** Isotope labeling experiment of **3aa** using $H_2{}^{18}O$ indicated that only one oxygen atom of $\alpha$-ketoamide would occur exchange with $H_2O$

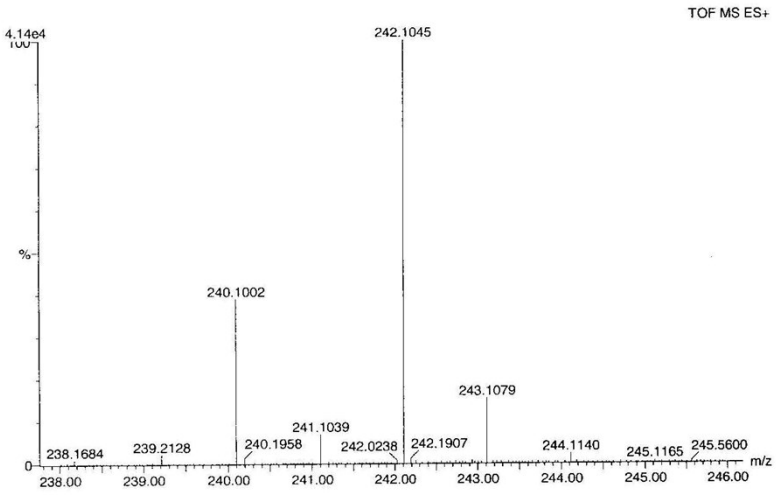



**3aa** (108.5 mg, 0.5 mmol) was added to a mixture of CuI (4.8 mg, 0.025 mmol), $H_2{}^{18}O$ (90 μL, 5.0 mmol), and piperdine (50 μL, 0.5 mmol) in dry THF (0.5 mL) at room temperature under $O_2$ (balloon). After stirring at room temperature for 48 h, the solution was immediately measured by HRMS.

**Elemental Composition Report** **Page 1**

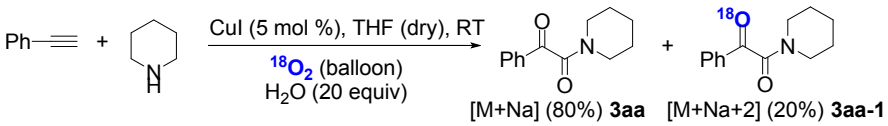
**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
915 formula(e) evaluated with 5 results within limits (up to 2 closest results for each mass)
Elements Used:
C: 12-100 H: 0-100 N: 0-4 16O: 0-10 18O: 0-10 Na: 0-1




| | | | | | | |
|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | |
| Maximum: | | 5.0 | 10.0 | 50.0 | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Formula |
| 240.1002 | 240.1000 | 0.2 | 0.8 | 6.5 | 20507.1 | C13 H15 N 16O2 Na |
| | 240.0999 | 0.3 | 1.2 | 7.5 | 606.2 | C12 H13 N3 18O Na |
| 242.1045 | 242.1043 | 0.2 | 0.8 | 6.5 | 829.7 | C13 H15 N 16O 18O Na |
| | 242.1050 | -0.5 | -2.1 | 6.5 | 17694032.0 | C12 H14 N 16O 18O3 |

**4.2** Isotope labeling experiment using $^{18}O_2$ to investigate the origination of the carbonyl oxygen atom of **3aa.**




Phenylacetylene (219 μL, 2.0 mmol) was added to a mixture of CuI (4.8 mg, 0.025 mmol), $H_2O$ (180 μL, 10 mmol), and piperdine (50 μL, 0.5 mmol) in dry THF (0.5 mL) at room temperature under $^{18}O_2$ (balloon). After stirring at room temperature for 12 h, the reaction solution was submitted to flash chromatographic separation on a short silica gel using petroleum ether/ethyl acetate (5:1) as an eluent. Then the product was immediately measured by HRMS.

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
686 formula(e) evaluated with 34 results within limits (up to 3 closest results for each mass)
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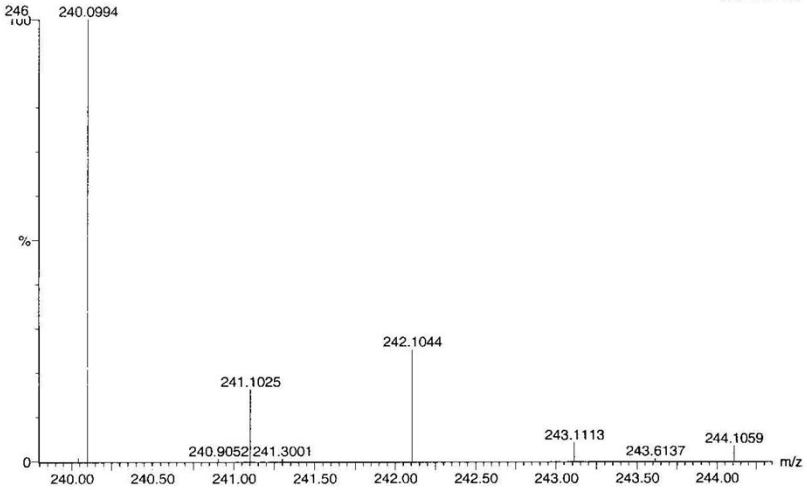
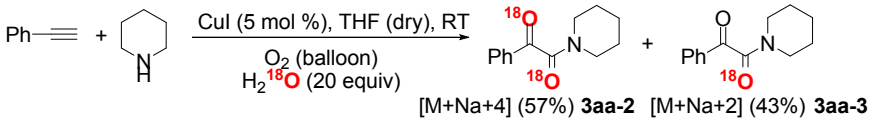
TOF MS ES+




| | | | | | | |
|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | |
| Maximum: | | 5.0 | 100.0 | 50.0 | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Formula |
| 240.0994 | 240.1000 | -0.6 | -2.5 | 6.5 | 27.6 | C13 H15 N 16O2 Na |
| 242.1044 | 242.1043 | 0.1 | 0.4 | 6.5 | 1.6 | C13 H15 N 16O 18O Na |

**4.3** Isotope labeling experiment using $H_2{}^{18}O$ to investigate the origination of the

carbonyl oxygen atom of **3aa.**




[M+Na+4] (57%) **3aa-2** [M+Na+2] (43%) **3aa-3**

Phenylacetylene (219 μL, 2 mmol) was added to a mixture of CuI (4.8 mg, 0.025 mmol), $H_2{}^{18}O$ (180 μL, 10 mmol), and piperdine (50 μL, 0.5 mmol) in dry THF (0.5 mL) at room temperature under $O_2$ (balloon). After stirring at room temperature for 12h, the reaction solution was submitted to flash chromatographic separation on a short silica gel using petroleum ether/ethyl acetate (5:1) as an eluent. Then the product was immediately measured by HRMS.

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
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Selected filters: None

Monoisotopic Mass, Even Electron Ions
1583 formula(e) evaluated with 80 results within limits (up to 1 closest results for each mass)
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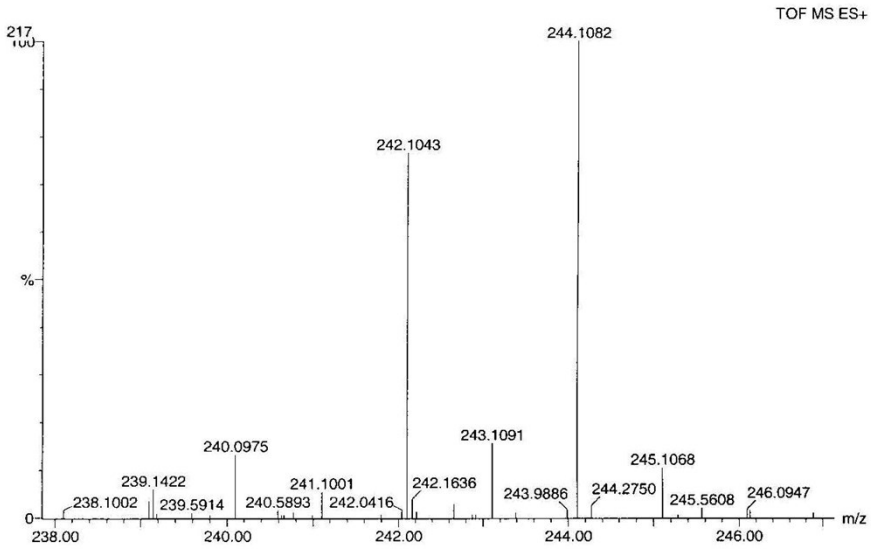
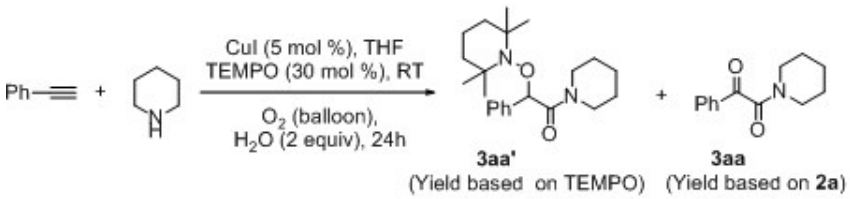



| | | | | | | |
|---|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | | |
| Maximum: | | 5.0 | 100.0 | 50.0 | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Formula |
| 242.1045 | 242.1043 | 0.2 | 0.8 | 6.5 | 6.8 | C13 H15 N Na 16O 18O |
| 244.1082 | 244.1085 | -0.3 | -1.2 | 6.5 | 10092.1 | C13 H15 N Na 18O2 |

## 5. Radical capture experiments




**General procedure:**

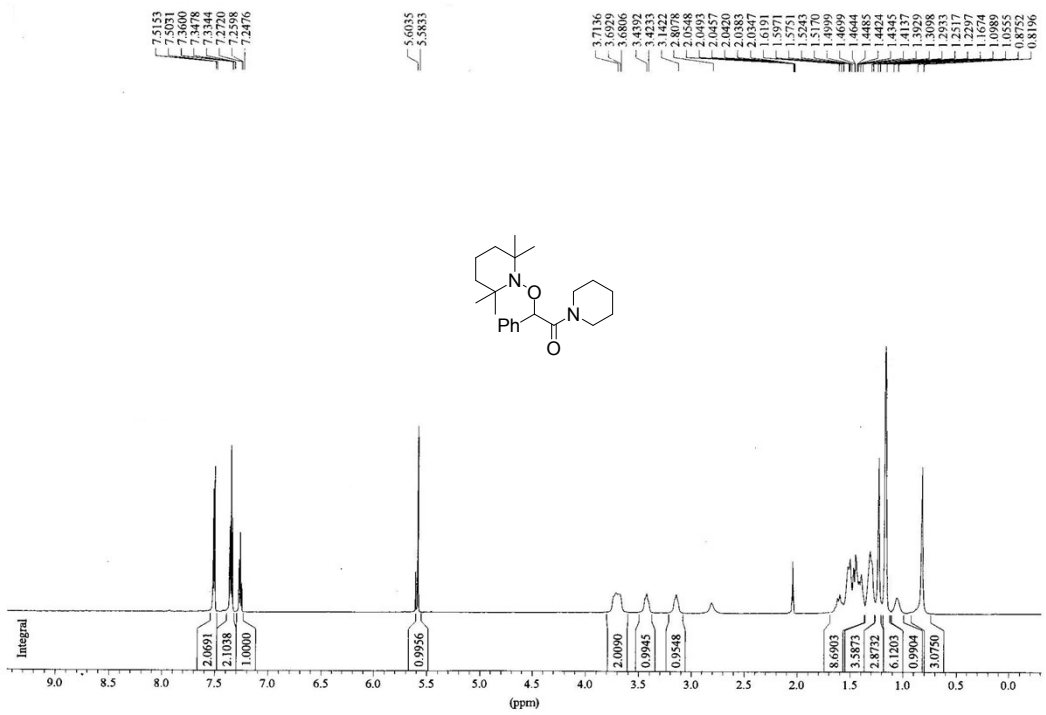
Phenylacetylene (438 μL, 4.0 mmol) was added to a mixture of CuI (9.6 mg, 0.05 mmol), $H_2O$ (2.0 mmol), piperdine (100 μL, 1.0 mmol) and 2,2,6,6-tetramethylpiperidine-1-oxy (46.8 mg, 0.3 mmol) in THF (1.0 mL) under $O_2$ (balloon). The mixture was stirred at room temperature. After the completion of the reaction (monitored by TLC), the reaction solution was submitted to flash chromatographic separation on silica gel using petroleum ether/ethyl acetate (20:1) as an eluent affording a white solid 72 mg (68%, yield based on TEMPO) **3aa'** and 10 mg **3aa** (5 %, yield based on **2a**).

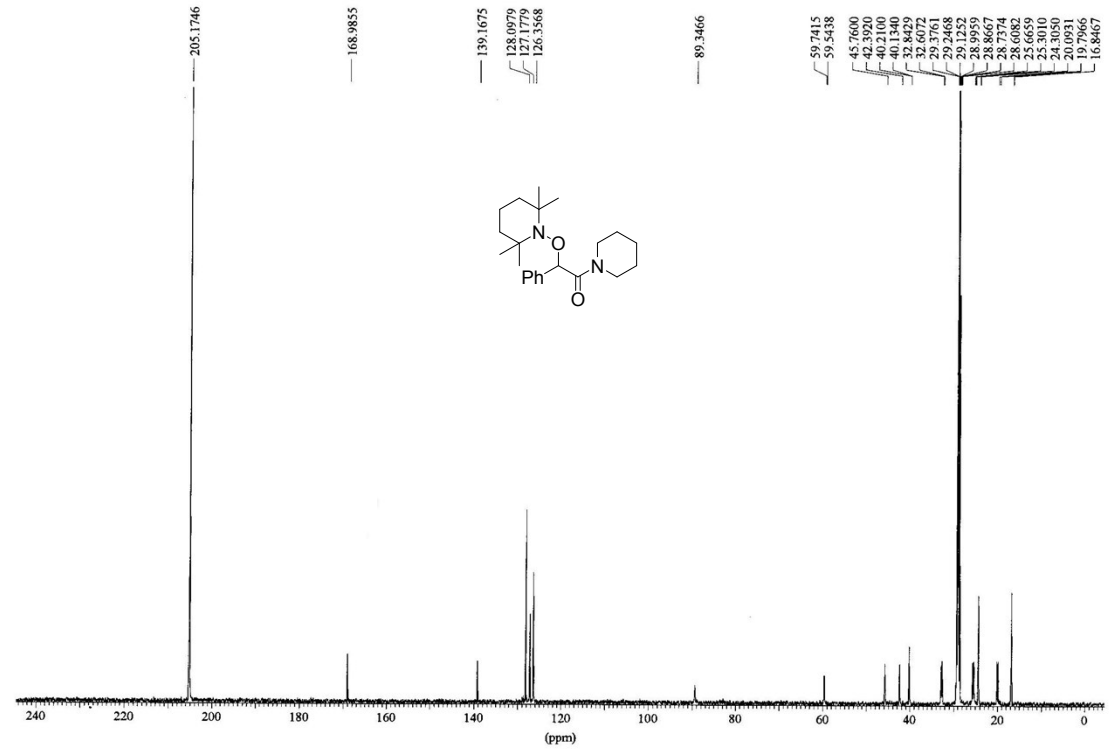
**Analytical data for compounds 3aa':**

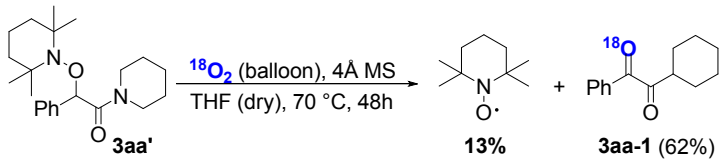
**$^1$HNMR (600 MHz, $CD_3COCD_3$):** δ (ppm) = 7.51 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 5.58 (s, 1H), 3.71-3.68 (m, 2H), 3.44-3.42 (m, 1H), 3.14 (brs, 1H), 1.61-1.39 (m, 8H), 1.30-1.29 (m, 3H), 1.23 (brs, 3H), 1.1 (s, 6H), 1.05 (brs, 1H), 0.82 (s, 3H); **$^{13}$CNMR (150 MHz, $CD_3COCD_3$):** δ (ppm) = 169.0, 139.2, 128.1, 127.2, 126.4, 89.3, 59.7, 59.5, 45.8, 42.4, 40.2, 40.1, 32.8, 32.6, 25.7, 25.3, 24.3, 20.1, 19.8, 16.8. HRMS calcd for $C_{22}H_{35}N_2O_2$ $(M + H)^+$: 359.2699, found: 359.2690.

**$^{1}$H and $^{13}$C spectra of 3aa'**

**2-phenyl-1-(piperidin-1-yl)-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)ethanone**



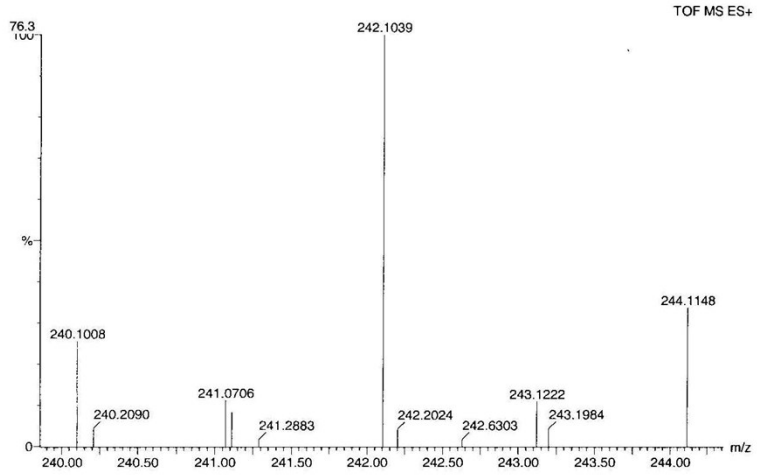



To a 25-mL flask equipped with a magnetic stirrer, in which the air was replaced by $^{18}O$-labeled $O_2$, was added **3aa'** (190 mg, 0.5 mmol), dry THF (4.0 mL), 4Å molecular sieve (400 mg). After stirring at 70ºC for 48 h, the reaction solution was filtered, washed with dry $CH_2Cl_2$, concentrated, then the residue was submitted to flash chromatographic separation on a short silica gel using petroleum ether/ethyl acetate (20:1) as an eluent affording a colorless oil 72 mg (62%) **3aa-1** and 11 mg (13%) TEMPO. Then the product **3aa-1** was immediately measured by HRMS. (The $\alpha$-ketone at $\alpha$-ketoamide is very easy to undergo oxygen exchange with water in air or silica gel, thus the signal of unlabelled product, 240.1008, was detected.)

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
701 formula(e) evaluated with 31 results within limits (up to 1 closest results for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-4 16O: 0-10 18O: 0-10 Na: 1-1




| | | | | | | |
|---|---|---|---|---|---|---|
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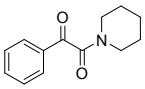
| Maximum: | | 5.0 | 100.0 | 50.0 | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Formula |
| 242.1039 | 242.1043 | -0.4 | -1.7 | 6.5 | 0.5 | C13 H15 N 16O 18O Na |

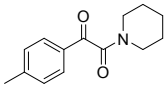
## 6. Analytical data for compounds 3aa-3af

### 1-phenyl-2-(piperidin-1-yl) ethane-1,2-dione (3aa)



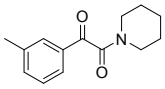
The crude reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3aa** as a colorless oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.95 (d, *J* = 8.0 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 3.71 (brs, 2H), 3.29 (t, *J* = 5.7 Hz, 2H), 1.71-1.70 (m, 4H), 1.55 (brs, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.9, 165.5, 134.6, 133.3, 129.6, 129.0, 47.0, 42.2, 26.2, 25.5, 24.4. HRMS calcd for $C_{13}H_{15}NNaO_2$ $(M + Na)^+$: 240.0995, found: 240.1002.

### 1-(piperidin-1-yl)-2-*p*-tolyllethane-1,2-dione (3ba)



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ba** as a colorless oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.84 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 3.71-3.70 (m, 2H), 3.28 (t, *J* = 5.6 Hz, 2H), 2.43 (s, 3H), 1.69 (brt, *J* = 2.8 Hz, 4H), 1.55-1.54 (m, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.7, 165.7, 145.8, 130.9, 129.7, 47.0, 42.1, 26.2, 25.5, 24.4, 21.9. HRMS calcd for $C_{14}H_{17}NNaO_2$ $(M + Na)^+$: 254.1151, found: 254.1145.

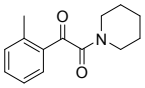
### 1-(piperidin-1-yl)-2-*m*-tolylethane-1,2-dione (3ca)



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ca** as a colorless oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.76-7.74 (m, 2H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 3.71 (brs, 2H), 3.29 (t, *J* = 5.6 Hz, 2H), 2.42 (s, 3H), 1.70 (brt, *J* = 2.9 Hz, 4H), 1.56-1.55 (m, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 192.2, 165.6, 138.9, 135.5, 133.3, 129.9,

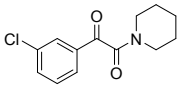
128.9, 126.9, 47.1, 42.1, 26.2, 25.5, 24.4, 21.3. HRMS calcd for $C_{14}H_{17}NNaO_2$ (M + Na)$^+$: 254.1151, found: 254.1160.

**1-(piperidin-1-yl)-2-*o*-tolyethane-1,2-dione (3da)**



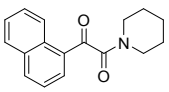
The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 4:1) affording **3da** as a colorless oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.71 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.32-7.29 (m, 2H), 3.70-3.68 (m, 2H), 3.31 (t, *J* = 5.7 Hz, 2H), 1.70 (brt, *J* = 2.6 Hz ,4H), 1.57-1.55 (m, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 193.9, 166.2, 141.5, 133.6, 132.7, 132.6, 131.7, 126.1, 47.0, 42.2, 26.1, 25.4, 24.4, 21.8. HRMS calcd for $C_{14}H_{17}NNaO_2$ (M + Na)$^+$: 254.1151, found: 254.1155.

**1-(3-chlorophenyl)-2-(piperidin-1-yl) ethane-1,2-dione (3ea)**



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ea** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.93 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 3.71-3.70 (m, 2H), 3.29 (t, *J* = 5.6 Hz, 2H), 1.71 (brt, *J* = 2.6 Hz, 4H), 1.59 (brs, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 190.4, 164.7, 135.4, 134.9, 134.5, 130.3, 129.3, 127.8, 47.1, 42.3, 26.2, 25.4, 24.4. HRMS calcd for $C_{13}H_{14}ClNNaO_2$ (M+Na)$^+$: 274.0605, Found: 274.0611.

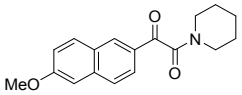
**1-(naphthalen-1-yl)-2-(piperidin-1-yl) ethane-1,2-dione (3fa)**



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 8:1) affording **3fa** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 9.28 (d, *J* = 8.6 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 8.03 (dd, *J* = 1.1, 7.4 Hz, 1H), 7.91

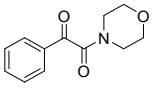
(d, *J* = 8.0 Hz, 1H), 7.71-7.68 (m, 1H), 7.61-7.58 (m, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 3.75-3.73 (m, 2H), 3.35 (t, *J* = 5.6 Hz, 2H), 1.71 (brt, *J* = 2.9 Hz, 4H), 1.57-1.55 (m, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 194.4, 166.0, 135.8, 134.3, 134.1, 131.0, 129.3, 128.7, 128.6, 127.0, 125.9, 124.5, 47.2, 42.3, 26.1, 25.4, 24.4. HRMS calcd for $C_{17}H_{17}NNaO_2$ $(M+Na)^+$: 290.1151, Found: 290.1162.

**1-(6-methoxynaphthalen-2-yl)-2-(piperidin-1-yl) ethane-1,2-dione (3ga)**



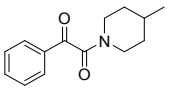

The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ga** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 8.36 (s, 1H), 7.98 (dd, *J* = 1.7, 8.6 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.21 (dd, *J* = 2.6, 8.9 Hz, 1H), 7.17 (d, *J* = 2.4 Hz, 1H), 3.95 (s, 3H), 3.76-3.75 (m, 2H), 3.33 (t, *J* = 5.5 Hz, 2H), 1.72 (brt, *J* = 2.6 Hz, 4H), 1.57-1.54 (brs, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.8, 165.8, 160.5, 138.2, 132.6, 131.5, 128.8, 127.8, 127.7, 124.6, 120.0, 106.0, 55.5, 47.2, 42.2, 26.3, 25.5, 24.4. HRMS calcd for $C_{18}H_{19}NNaO_3$ $(M+Na)^+$: 320.1257, Found: 320.1251.

**1-morpholino-2-phenylethane-1,2-dione (3ab)**



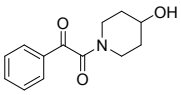

The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 4:1) affording **3ab** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.97 (d, *J* = 8.1 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 2H), 3.80 (brs, 4H), 3.66 (t, *J* = 4.8 Hz, 2H), 3.39 (t, *J* = 4.8 Hz, 2H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.1, 165.5, 134.9, 133.1, 129.7, 129.1, 66.8, 66.7, 46.3, 41.6. HRMS: calcd for $C_{12}H_{13}NNaO_3$ $(M+Na)^+$: 242.0788, Found: 242.0783.

**1-(4-methylpiperdin-1-yl)-2-phenylethane-1,2-dione (3ac)**



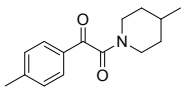
The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ac** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.95 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 4.65-4.62 (m, 1H), 3.54-3.52 (m, 1H), 3.08-3.04 (m, 1H), 2.83-2.78 (m, 1H), 1.81-1.79 (m, 1H), 1.70-1.61 (m, 2H), 1.26 (m, 1H), 1.15 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.9, 165.5, 134.6, 133.3, 129.6, 129.0, 46.3, 41.5, 34.3, 33.6, 31.0, 21.6. HRMS calcd for $C_{14}H_{17}NNaO_2$ $(M+Na)^+$: 252.1151, Found: 252.1155.

**1-(4-hydroxypiperidin-1-yl)-2-phenylethane-1,2-dione (3ad)**



The reaction mixture was purified by column chromatography (petroleum ether/ ethyl acetate 1:1) affording **3ad** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.95 (d, *J* = 7.7 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 4.12-4.08 (m, 1H), 4.04-4.00 (m, 1H), 3.59-3.55 (m, 1H), 3.53-3.49 (m, 1H), 3.21-3.17 (m, 1H), 2.02-1.98 (m, 1H), 1.89-1.84 (m, 1H), 1.70-1.64 (m, 2H), 1.57-1.52 (m, 1H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.7, 165.5, 134.8, 133.2, 129.6, 129.1, 66.6, 43.0, 38.3, 34.2, 33.6. HRMS calcd for $C_{13}H_{15}NNaO_3$ $(M+Na)^+$: 256.0944, Found: 256.0942.

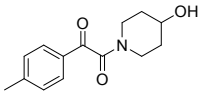
**1-(4-methylpiperidin-1-yl)-2-(p-tolyl)ethane-1,2-dione (3bc)**



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3bc** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.83 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.63-4.60 (m, 1H), 3.53-3.49 (m, 1H), 3.06-3.01 (m, 1H), 2.81-2.76 (m, 1H), 2.43 (s, 3H), 1.79-1.77 (m, 1H), 1.67-1.65

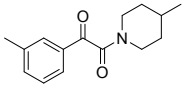
(m, 1H), 1.62-1.59 (m, 1H), 1.27-1.20 (m, 1H), 1.16-1.09 (m, 1H), 0.97 (d, $J$ = 6.5 Hz, 3H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.7, 165.7, 145.8, 130.9, 129.70, 129.69, 46.3, 41.5, 34.3, 33.6, 31.0, 21.9, 21.6. HRMS calcd for $C_{15}H_{19}NNaO_2$ $(M+Na)^+$: 268.1308, Found: 268.1312.

**1-(4-hydroxypiperidin-1-yl)-2-(p-tolyl)ethane-1,2-dione (3bd)**



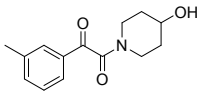

The reaction mixture was purified by column chromatography (petroleum ether/ ethyl acetate 1:1) affording **3bd** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.83 (d, $J$ = 8.0 Hz, 2H), 7.30 (d, $J$ = 8.0 Hz, 2H), 4.10-4.06 (m, 1H), 4.01-3.98 (m, 1H), 3.56-3.52 (m, 1H), 3.50-3.45 (m, 1H), 3.18-3.14 (m, 1H), 2.43 (s, 3H), 1.99-1.95 (m, 1H), 1.85-1.81 (m, 1H), 1.68-1.62 (m, 1H), 1.55-1.49 (m, 1H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.4, 165.7, 146.1, 130.8, 129.8, 129.7, 66.6, 43.0, 38.2, 34.1, 33.6, 21.9. HRMS calcd for $C_{14}H_{17}NNaO_3$ $(M+Na)^+$: 270.1101, Found: 270.1107.

**1-(4-methylpiperidin-1-yl)-2-(m-tolyl)ethane-1,2-dione (3cc)**



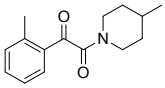

The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3cc** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.75-7.72 (m, 2H), 7.44 (d, $J$ = 7.5 Hz, 1H), 7.38 (t, $J$ = 7.6 Hz, 1H), 4.64-4.60 (m, 1H), 3.53-3.49 (m, 1H), 3.07-3.02 (m, 1H), 2.82-2.77 (m, 1H), 2.41 (s, 3H), 1.80-1.78 (m, 1H), 1.67-1.66 (m, 1H), 1.63-1.60 (m, 1H), 1.28-1.21 (m, 1H), 1.17-1.11 (m, 1H), 0.97 (d, $J$ = 6.5 Hz, 3H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 192.2, 165.6, 138.9, 135.5, 133.3, 129.9, 128.9, 126.9, 46.3, 41.5, 34.3, 33.6, 31.0, 21.6, 21.3. HRMS calcd for $C_{15}H_{19}NNaO_2$ $(M+Na)^+$: 268.1308, Found: 268.1313.

**1-(4-hydroxypiperidin-1-yl)-2-(m-tolyl)ethane-1,2-dione (3cd)**



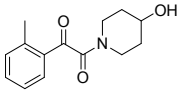
The reaction mixture was purified by column chromatography (petroleum ether/ ethyl acetate 1:1) affording **3cd** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.74-7.72 (m, 2H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 4.10-4.06 (m, 1H), 4.02-3.98 (m, 1H), 3.56-3.52 (m, 1H), 3.51-3.47 (m, 1H), 3.18-3.14 (m, 1H), 2.41 (s, 3H), 2.00-1.95 (m, 1H), 1.86-1.82 (m, 1H), 1.68-1.63 (m, 1H), 1.55-1.50 (m, 1H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 192.0, 165.6, 139.0, 135.7, 133.1, 129.8, 128.9, 126.9, 66.5, 43.0, 38.3, 34.1, 33.5, 21.3. HRMS calcd for $C_{14}H_{17}NNaO_3$ $(M+Na)^+$: 270.1101, Found: 270.1105.

**1-(4-methylpiperidin-1-yl)-2-(o-tolyl)ethane-1,2-dione (3dc)**



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3dc** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.70 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.32-7.29 (m, 2H), 4.62-4.59 (m, 1H), 3.57-3.54 (m, 1H), 3.09-3.05 (m, 1H), 2.82-2.77 (m, 1H), 2.67 (s, 3H), 1.80-1.78 (m, 1H), 1.68-1.62 (m, 2H), 1.29-1.22 (m, 1H), 1.20-1.14 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 193.8, 166.2, 141.5, 133.6, 132.7, 132.6, 131.7, 126.1, 46.3, 41.5, 34.2, 33.5, 31.1, 21.8, 21.6. HRMS calcd for $C_{15}H_{19}NNaO_2$ $(M+Na)^+$: 268.1308, Found: 268.1313.

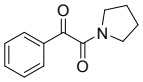
**1-(4-hydroxypiperidin-1-yl)-2-(o-tolyl)ethane-1,2-dione (3dd)**



The reaction mixture was purified by column chromatography (petroleum ether/ ethyl acetate 1:1) affording **3dd** as a yellow oil. $^{1}$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.69 (d, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 4.10-4.06 (m, 1H), 4.02-3.98 (m, 1H), 3.59-3.55 (m, 1H), 3.50-3.45 (m, 1H), 3.21-3.17 (m, 1H),

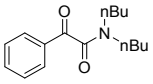
2.66 (s, 3H), 2.00-1.95 (m, 1H), 1.88-1.84 (m, 1H), 1.68-1.62 (m, 1H), 1.57-1.52 (m, 1H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 193.6, 166.2, 141.6, 133.8, 132.7, 131.6, 126.2, 66.6, 43.0, 38.3, 34.0, 33.5, 21.8. HRMS calcd for $C_{14}H_{17}NNaO_3$ $(M+Na)^+$: 270.1101, Found: 270.1107.

**1-phenyl-2-(pyrrolidin-1-yl) ethane-1,2-dione (3ae)**



The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3ae** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.99 (d, *J* = 8.1 Hz, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 2H), 3.65 (t, *J* = 6.6 Hz, 2H), 3.42 (t, *J* = 6.6 Hz, 2H), 1.98-1.91 (m, 4H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.6, 164.9, 134.6, 133.0, 129.9, 128.9, 46.7, 45.2, 25.9, 24.0. HRMS calcd for $C_{12}H_{13}NNaO_2$ $(M+Na)^+$: 226.0838, Found: 226.0845.

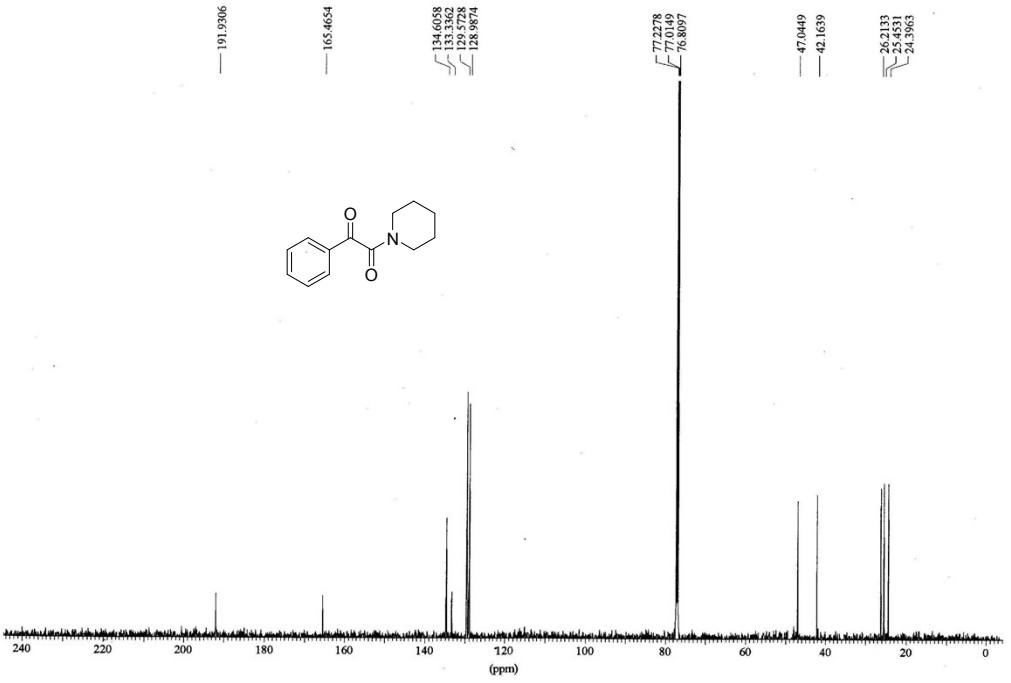
**N,N-dibutyl-2-oxo-2-phenylacetamide (3af)**



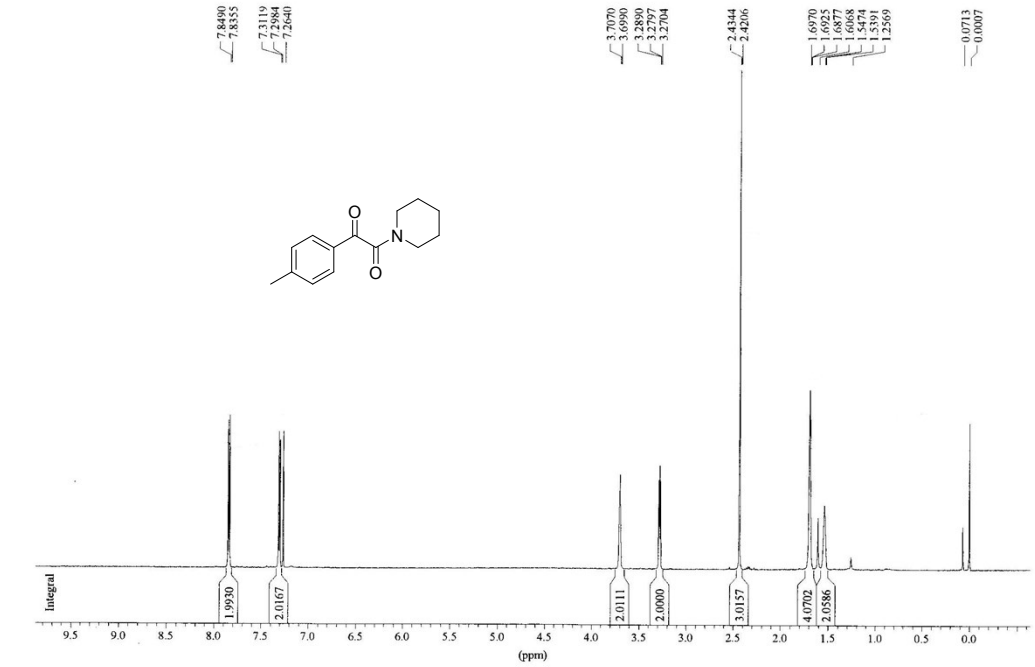
The reaction mixture was purified by column chromatography (petroleum ether/ethyl acetate 5:1) affording **3af** as a yellow oil. $^1$HNMR (600 MHz, $CDCl_3$): δ (ppm) = 7.94 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 3.50 (t, *J* = 7.7 Hz, 2H), 3.15 (t, *J* = 7.9 Hz, 2H) 1.70-1.65 (m, 2H), 1.56-1.51 (m, 2H), 1.45-1.40 (m, 2H), 1.22-1.17 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.82 (t, *J* = 7.4 Hz, 3H); $^{13}$CNMR (150 MHz, $CDCl_3$): δ (ppm) = 191.6, 167.1, 134.4, 133.4, 129.6, 128.9, 47.4, 44.0, 30.6, 29.5, 20.2, 19.8, 13.8, 13.5. HRMS calcd for $C_{16}H_{23}NNaO_2$ $(M+Na)^+$: 284.1621, Found: 284.1617.

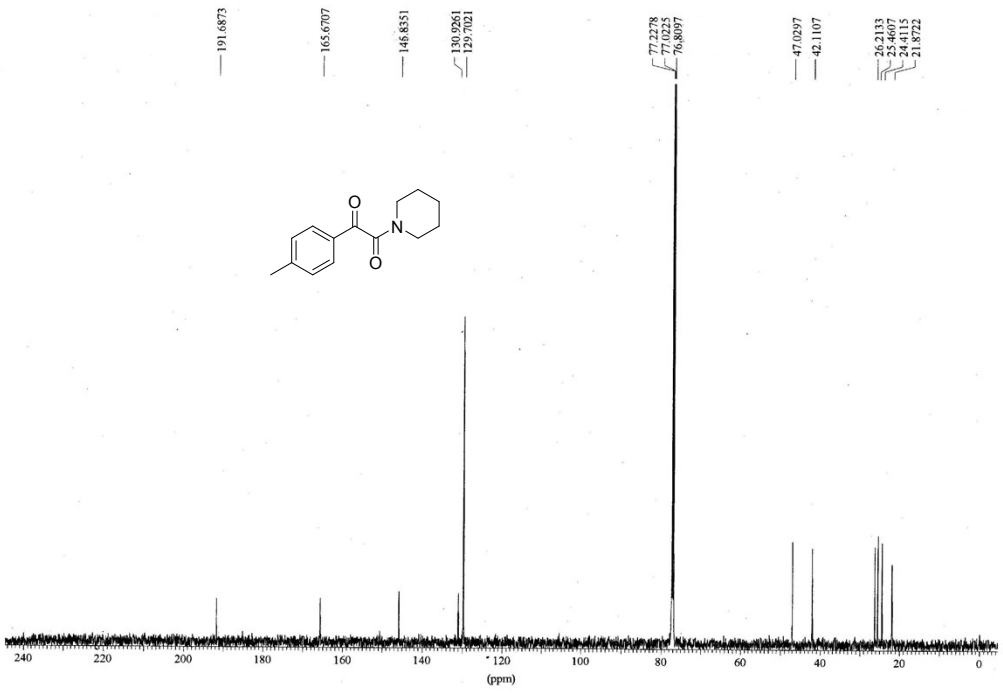
## 7. $^{1}H$ and $^{13}C$ spectra

## 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3aa)

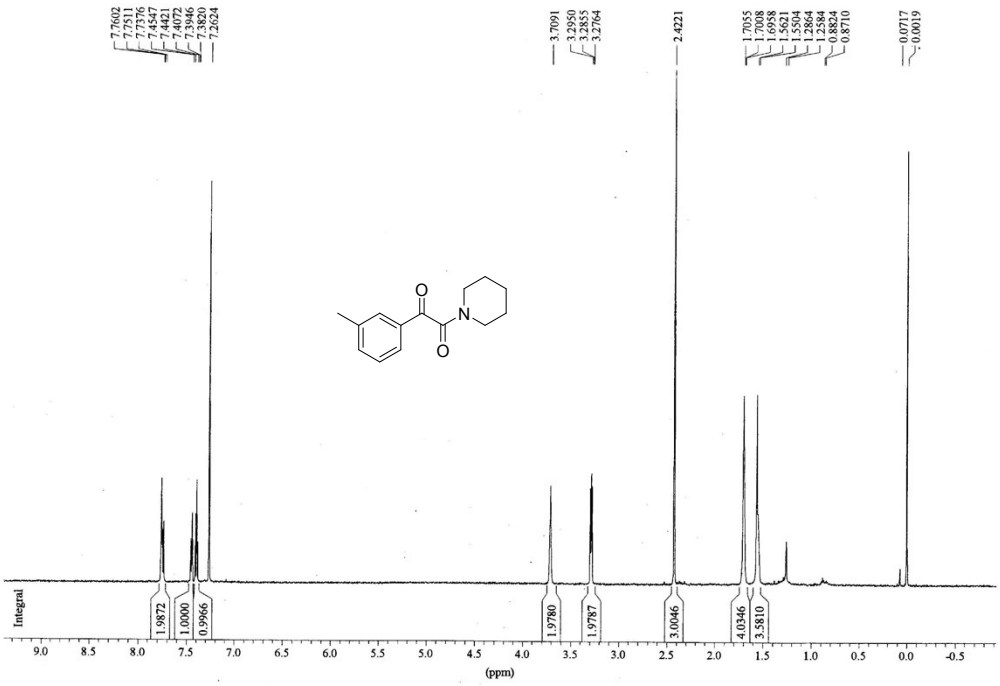



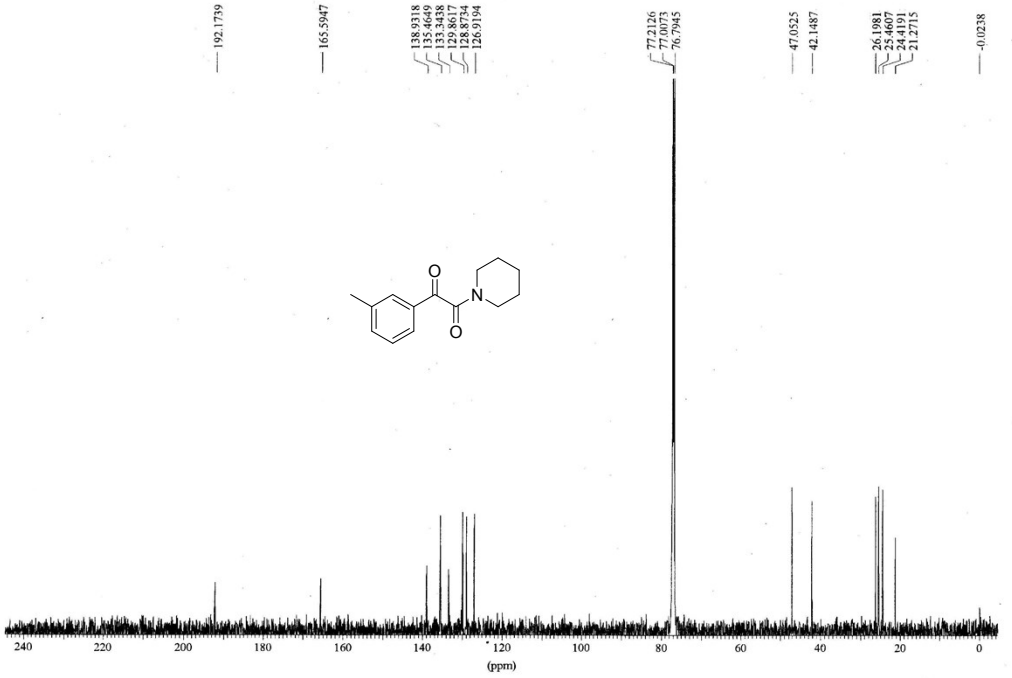
**1-(piperidin-1-yl)-2-*p*-tolyllethane-1,2-dione (3ba)**



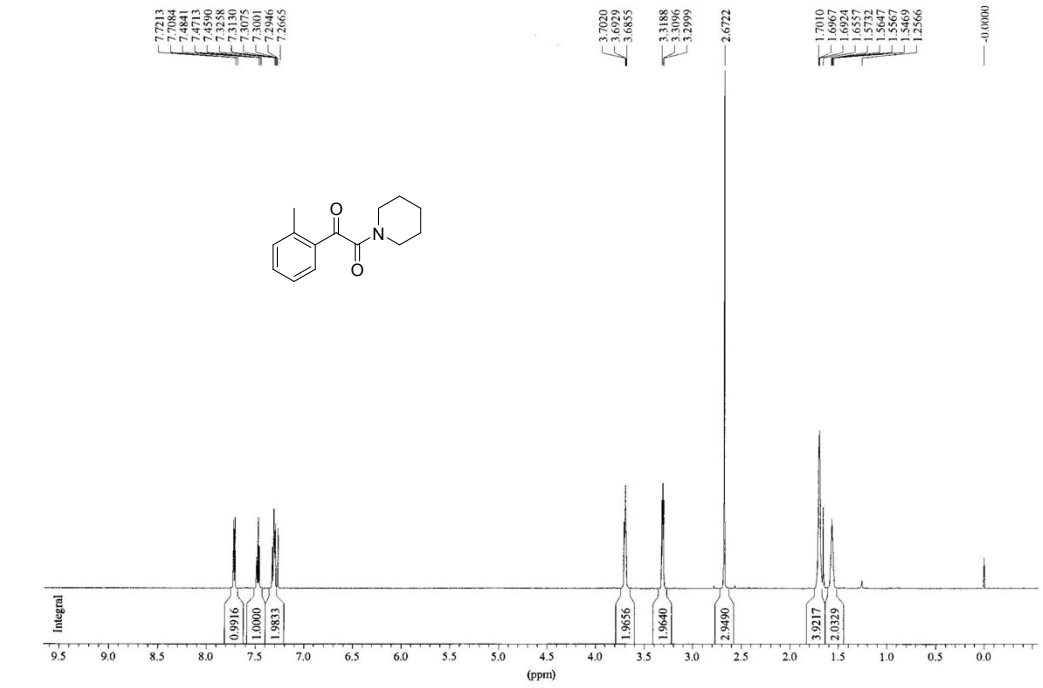



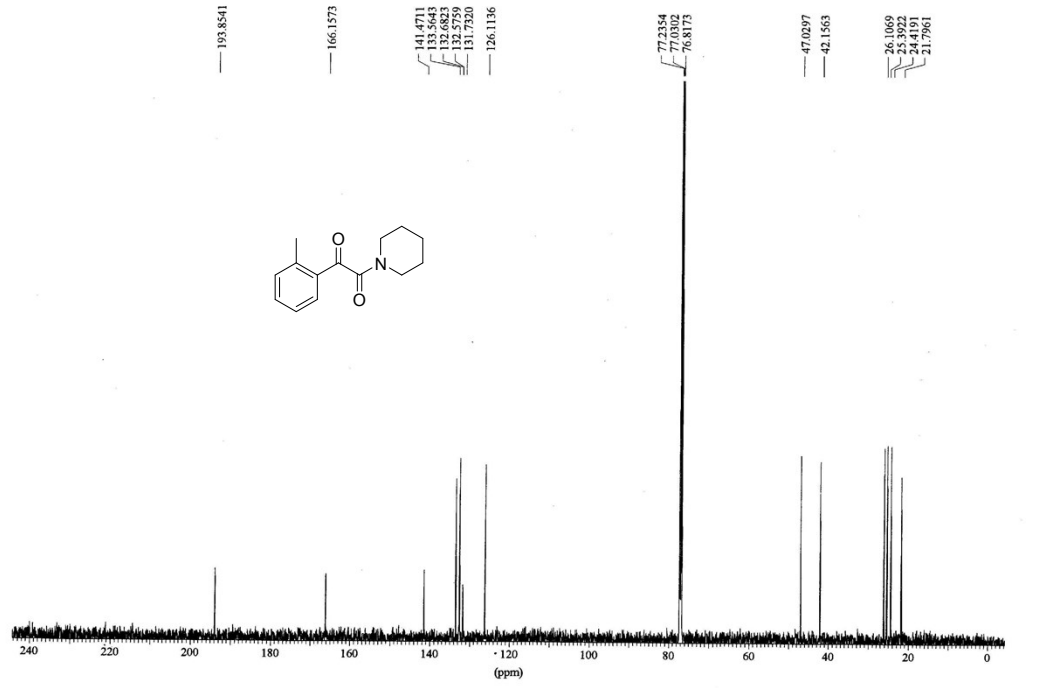
**1-(piperidin-1-yl)-2-*m*-tolylethane-1,2-dione (3ca)**



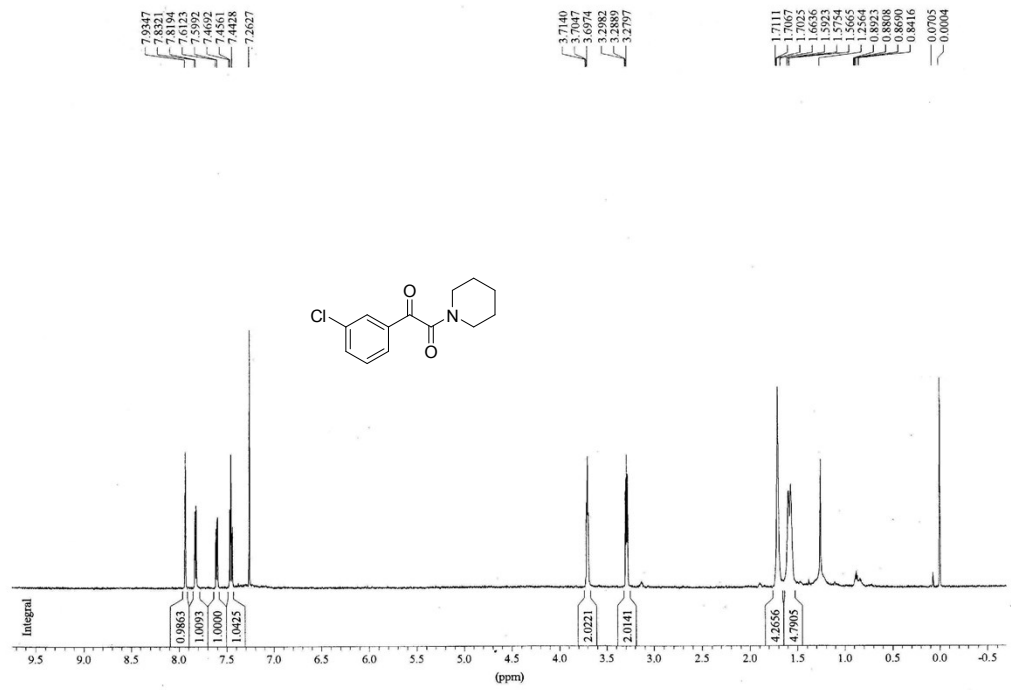



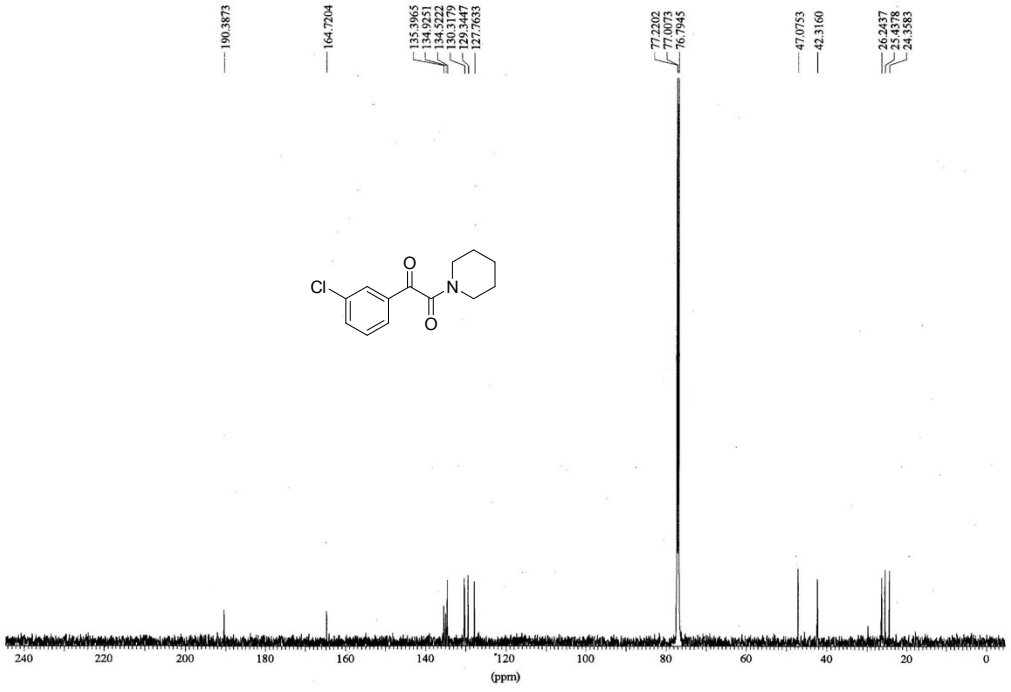
## 1-(piperidin-1-yl)-2-tolylethane-1,2-dione (3da)



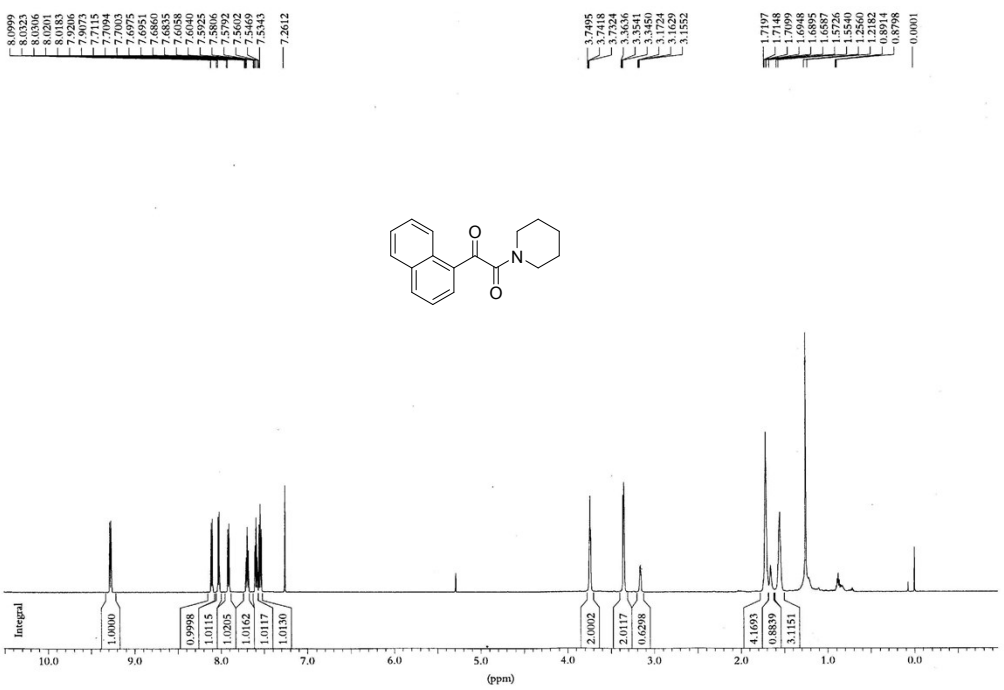



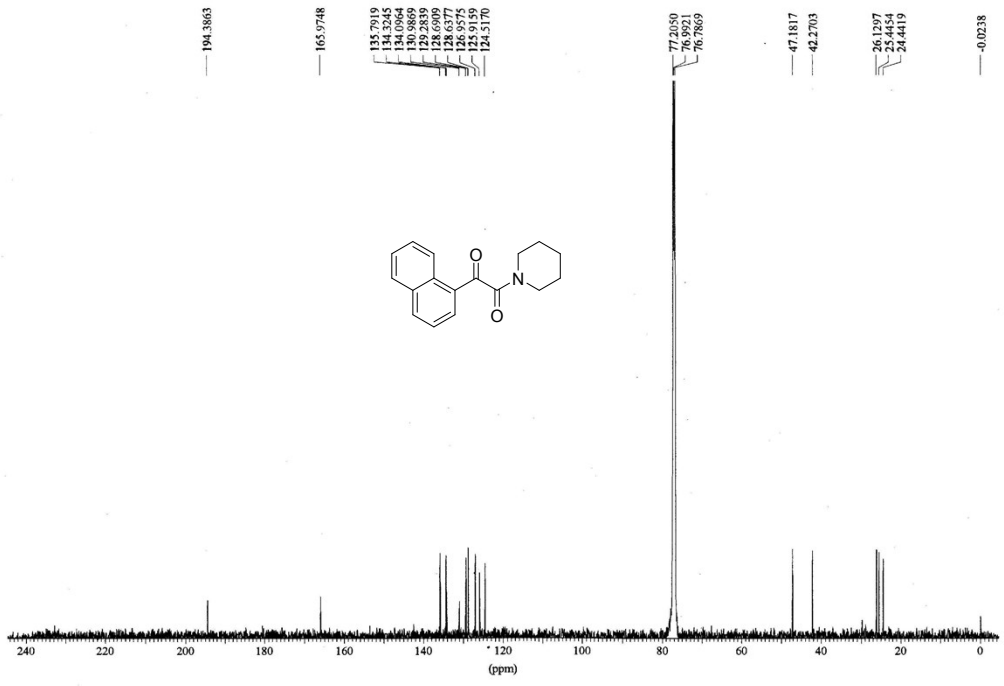
## 1-(3-chlorophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3ea)



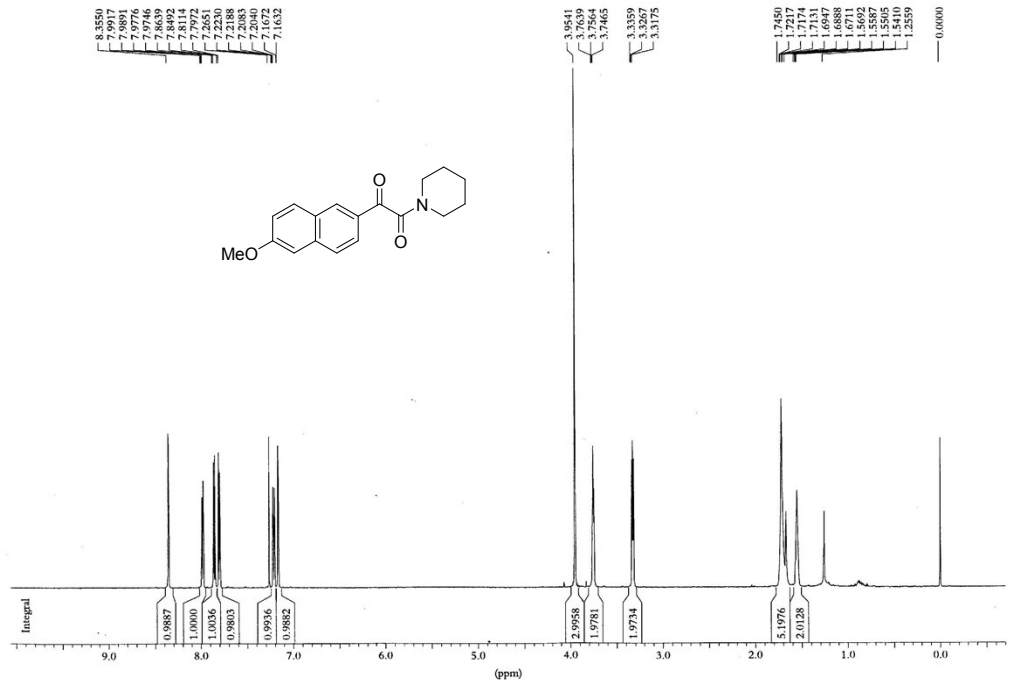



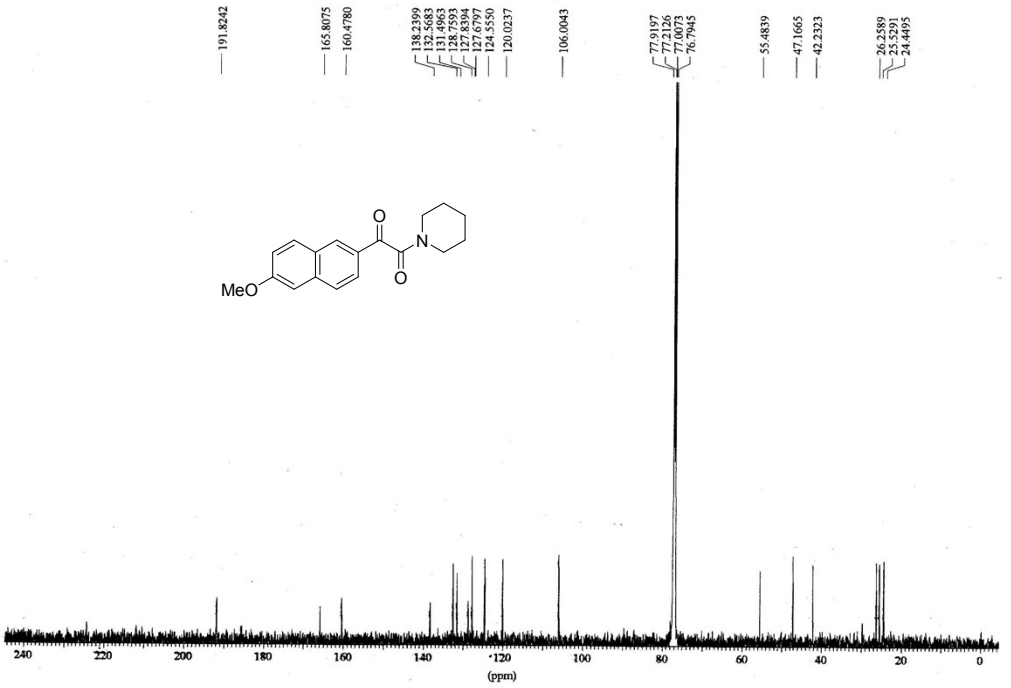
## 1-(naphthalen-1-yl)-2-(piperidin-1-yl)ethane-1,2-dione (3fa)



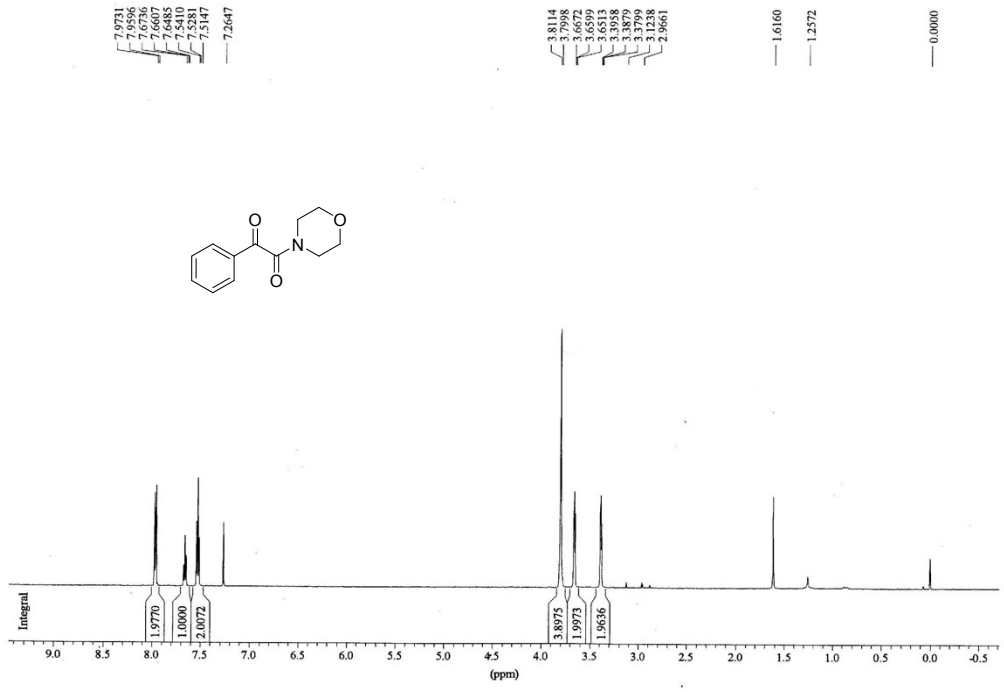



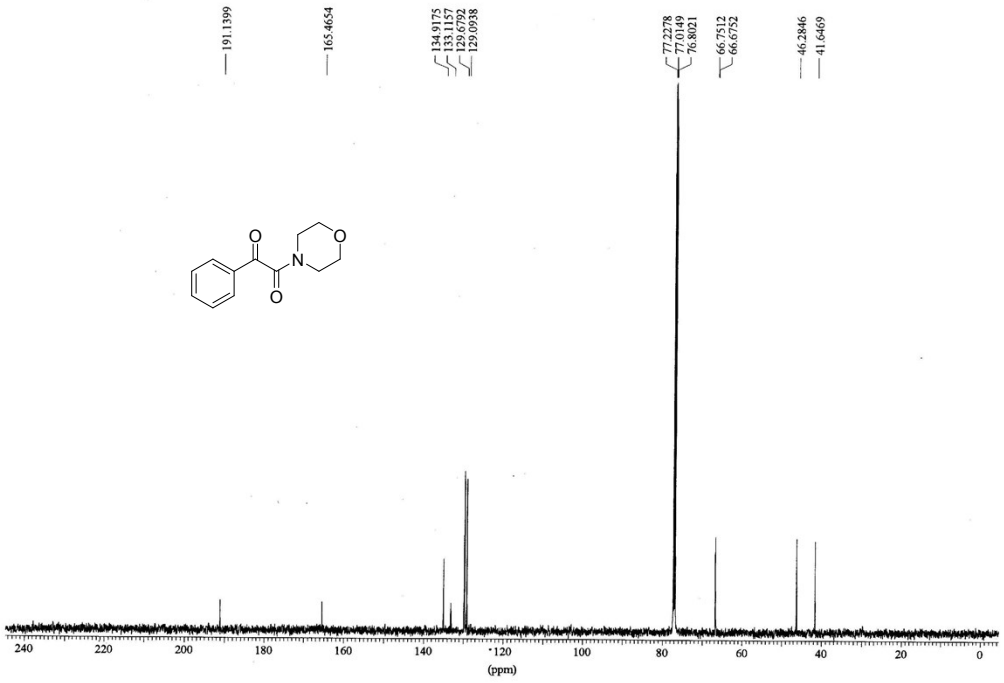
**1-(6-methoxynaphthalen-2-yl)-2-(piperidin-1-yl)ethane-1,2-dione (3ga)**



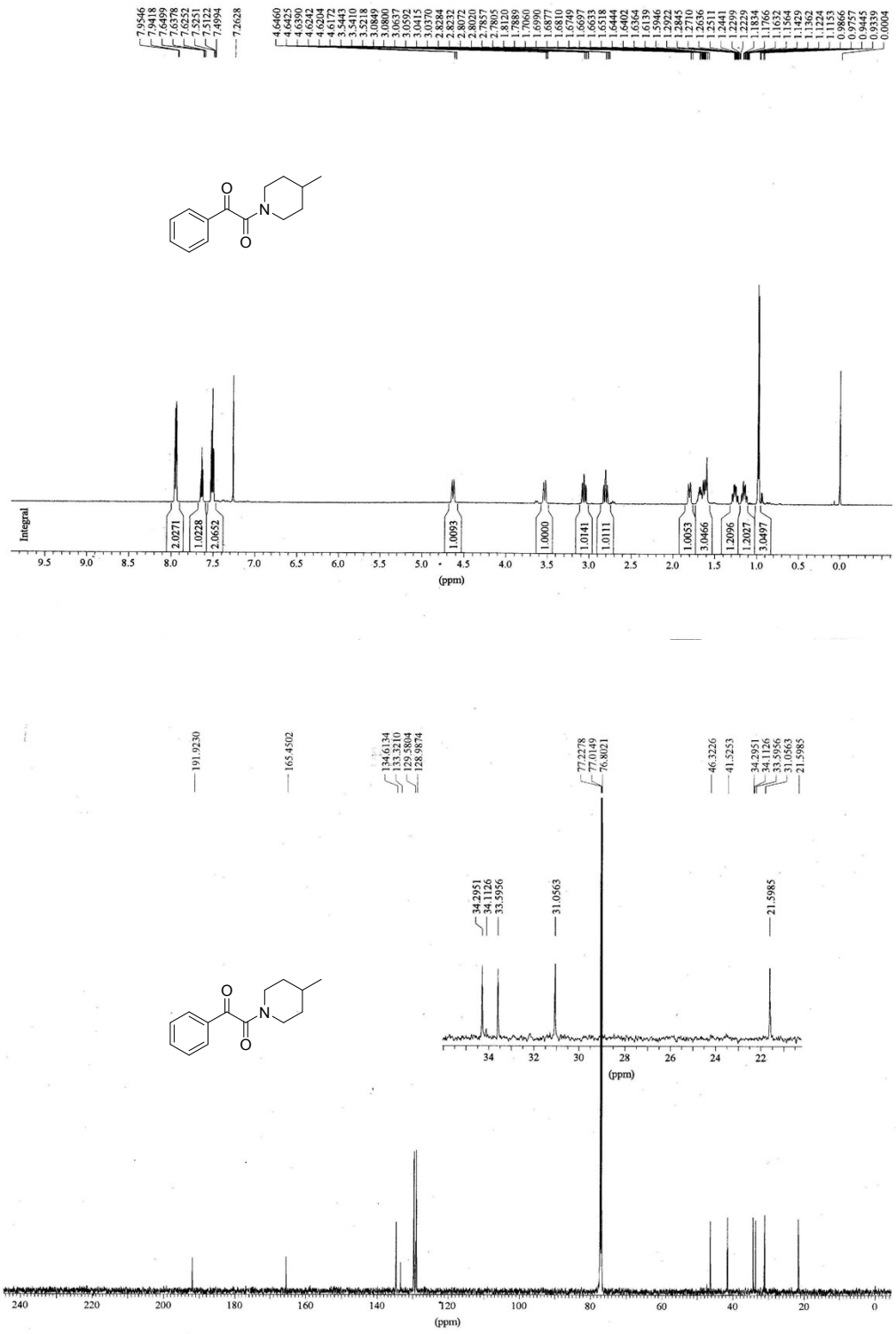



## 1-morpholino-2-phenylethane-1,2-dione (3ab)

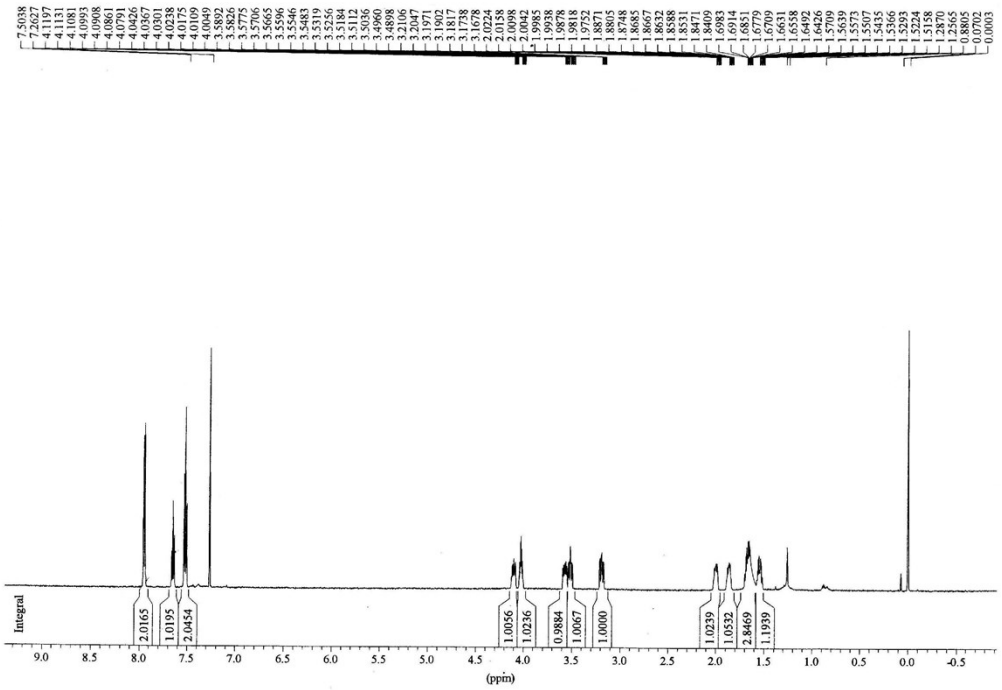


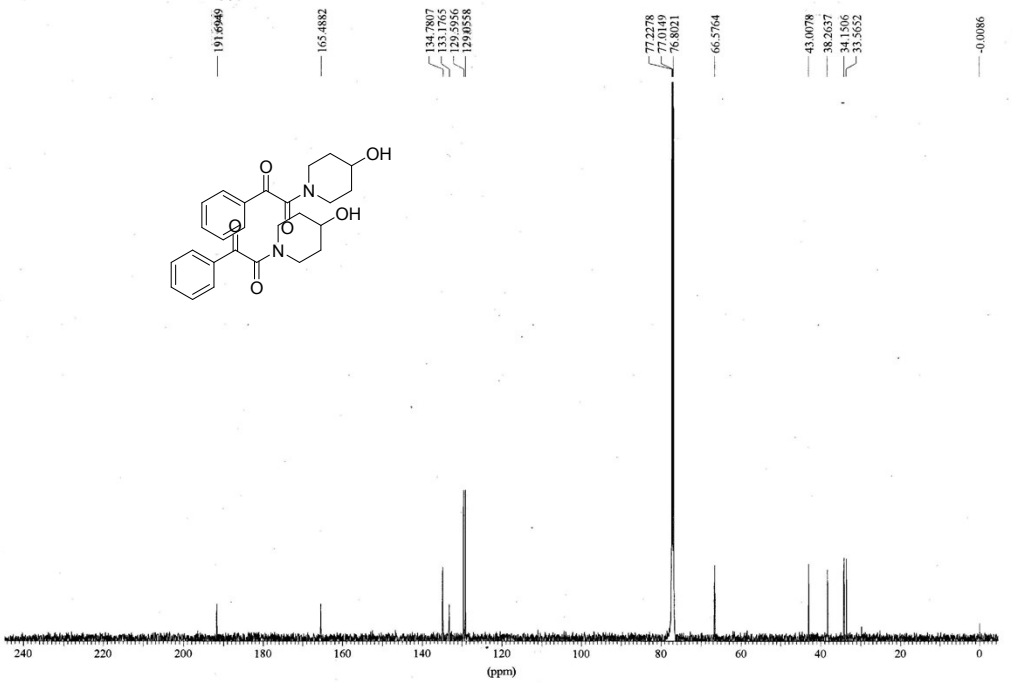



## 1-(4-methylpiperdin-1-yl)-2-phenylethane-1,2-dione (3ac)

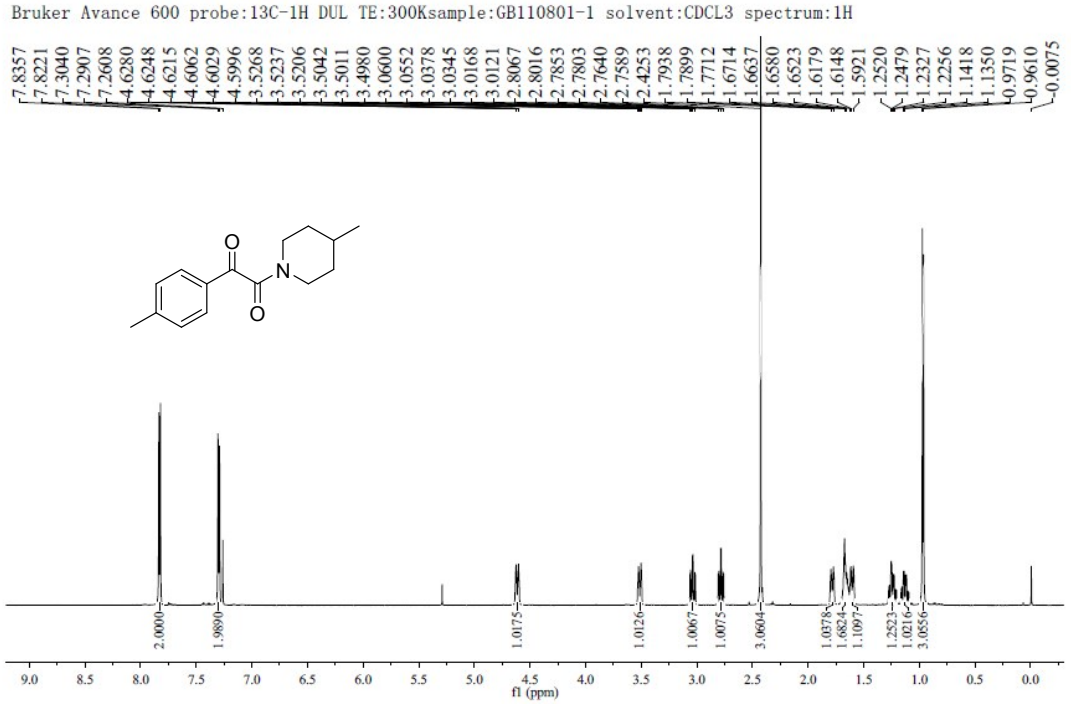


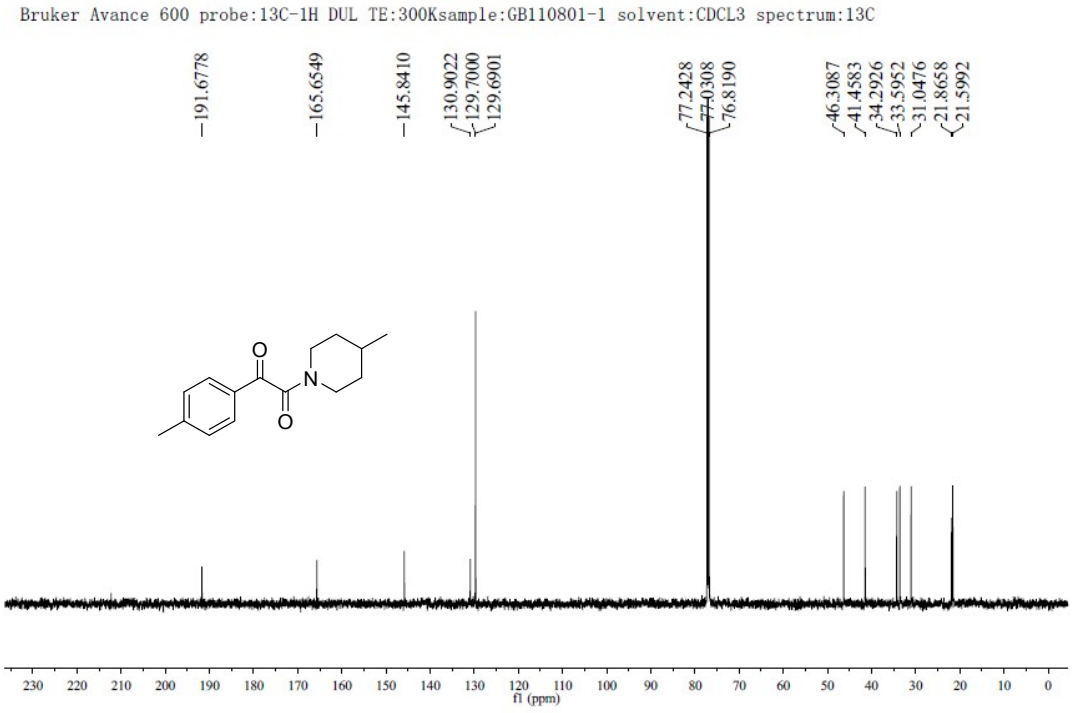
1-**(4-hydroxypiperidin-1-yl)-2-phenylethane-1,2-dione (3ad)**



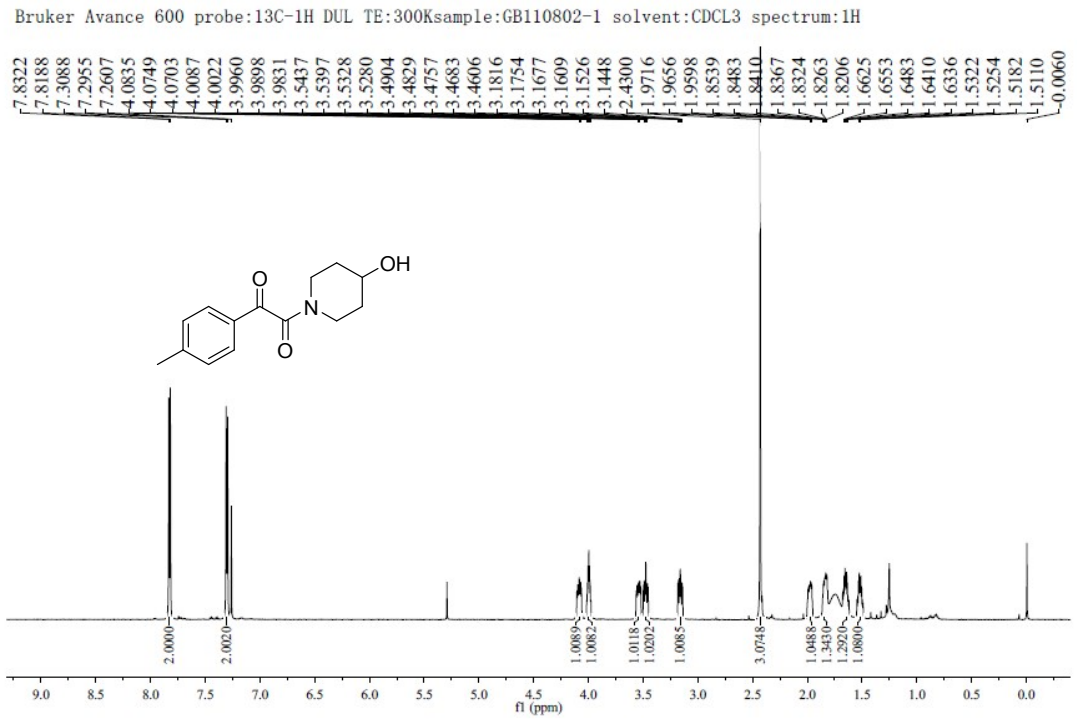



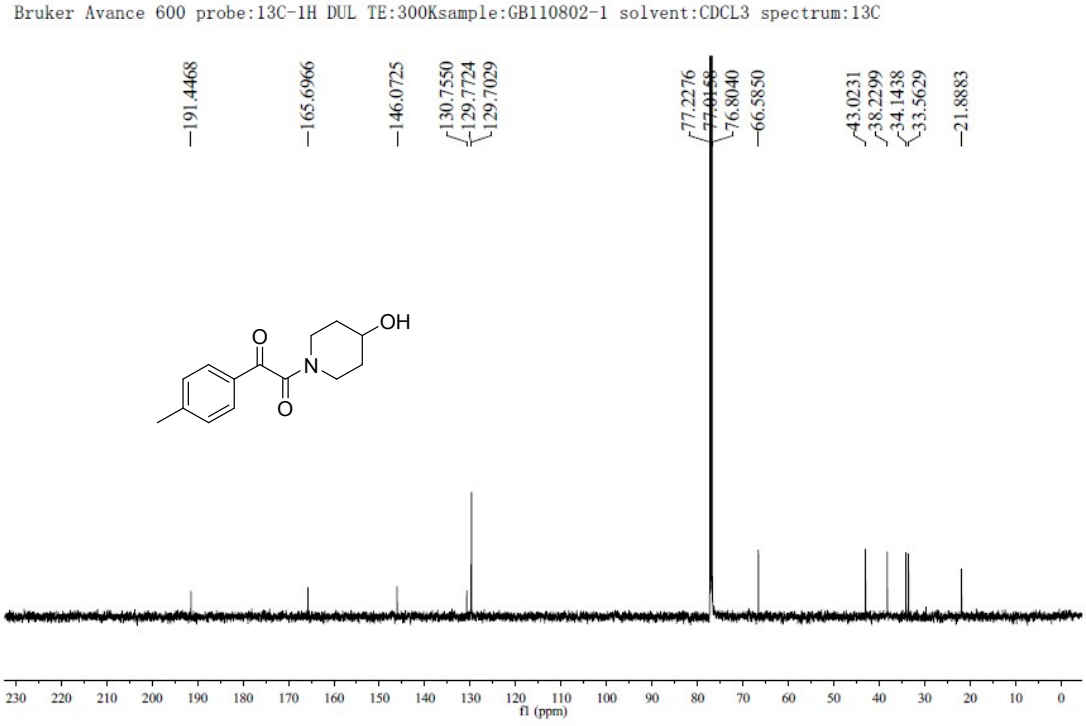
## 1-(4-methylpiperidin-1-yl)-2-(p-tolyl)ethane-1,2-dione (3bc)



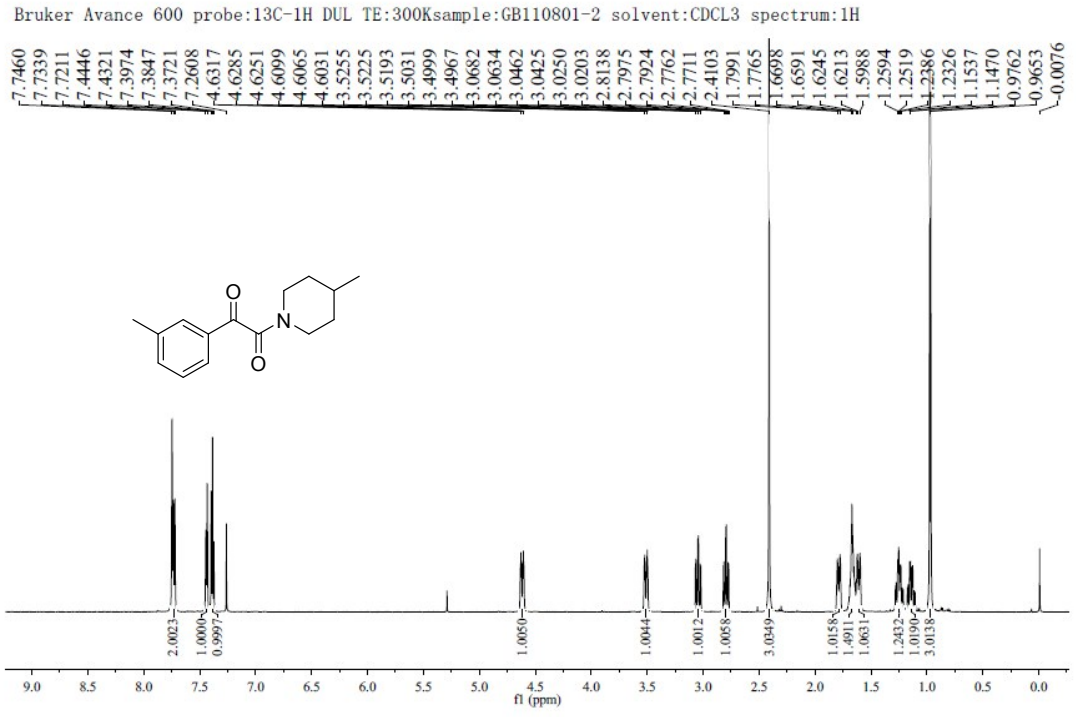



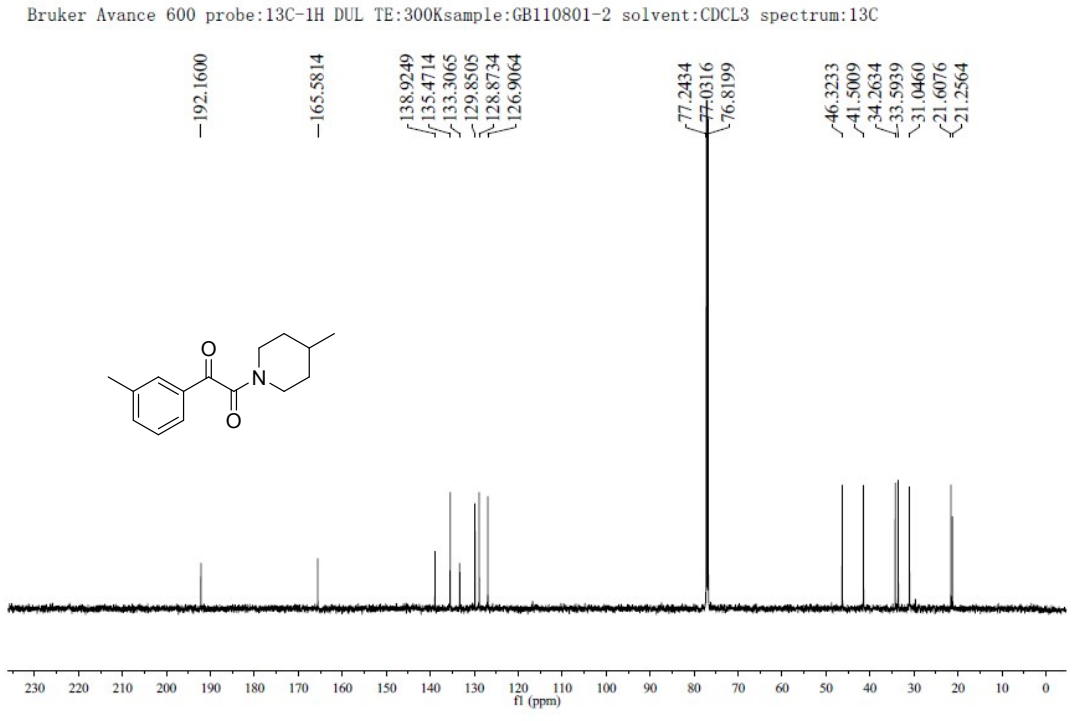
## 1-(4-hydroxypiperidin-1-yl)-2-(p-tolyl)ethane-1,2-dione (3bd)



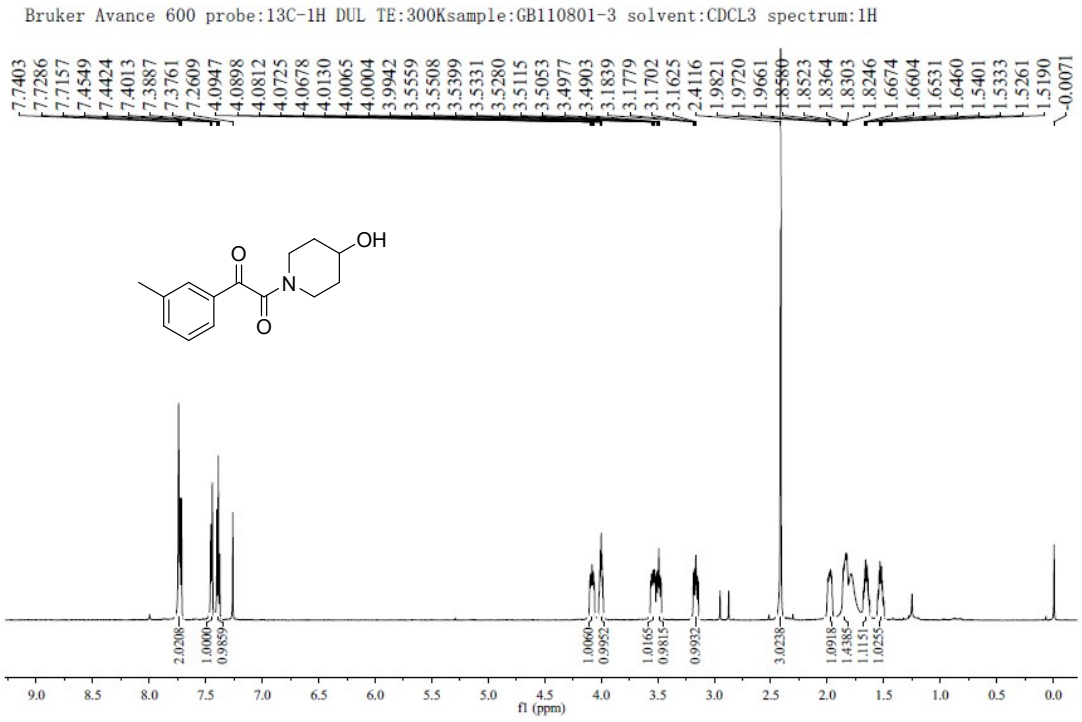



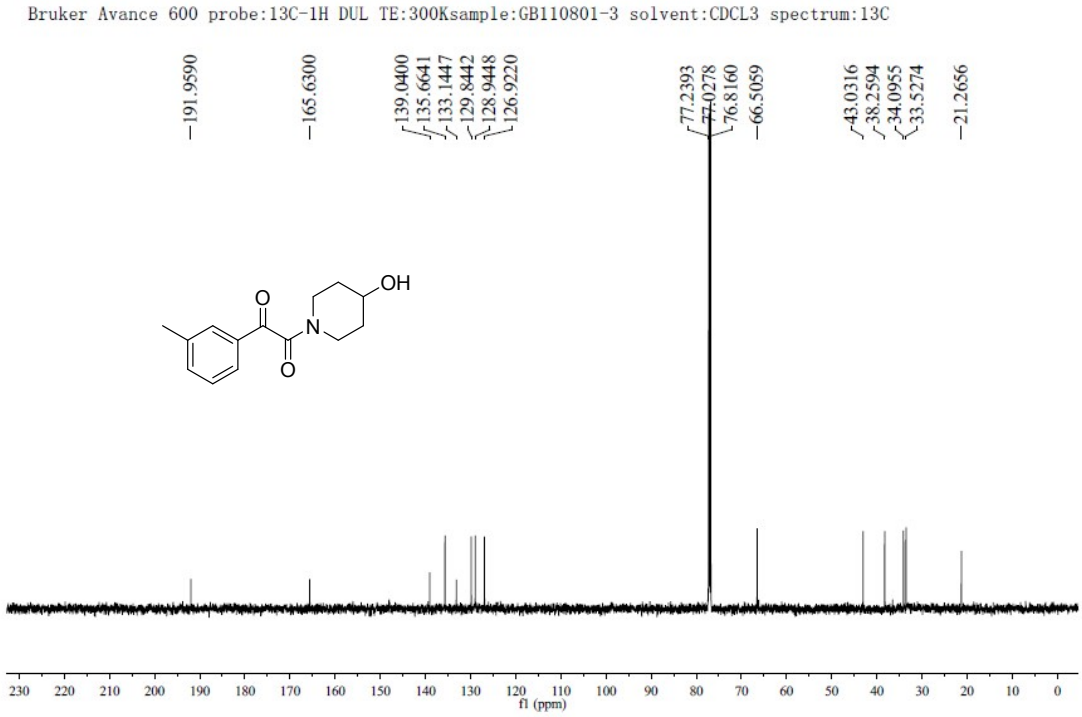
## 1-(4-methylpiperidin-1-yl)-2-(m-tolyl)ethane-1,2-dione (3cc)



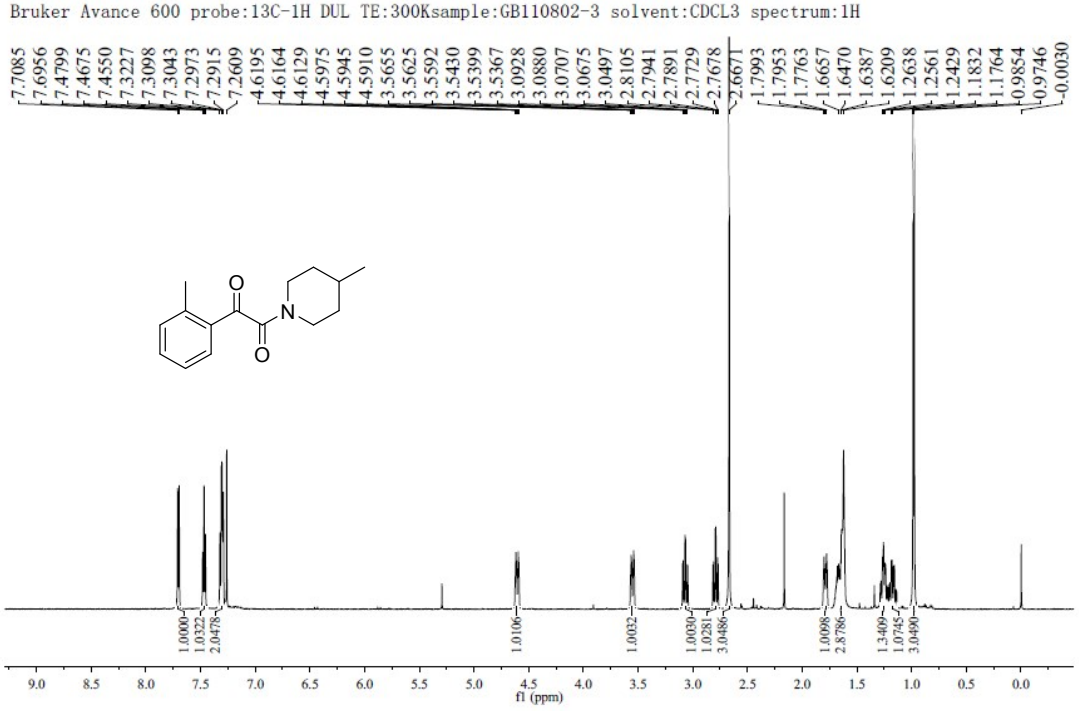



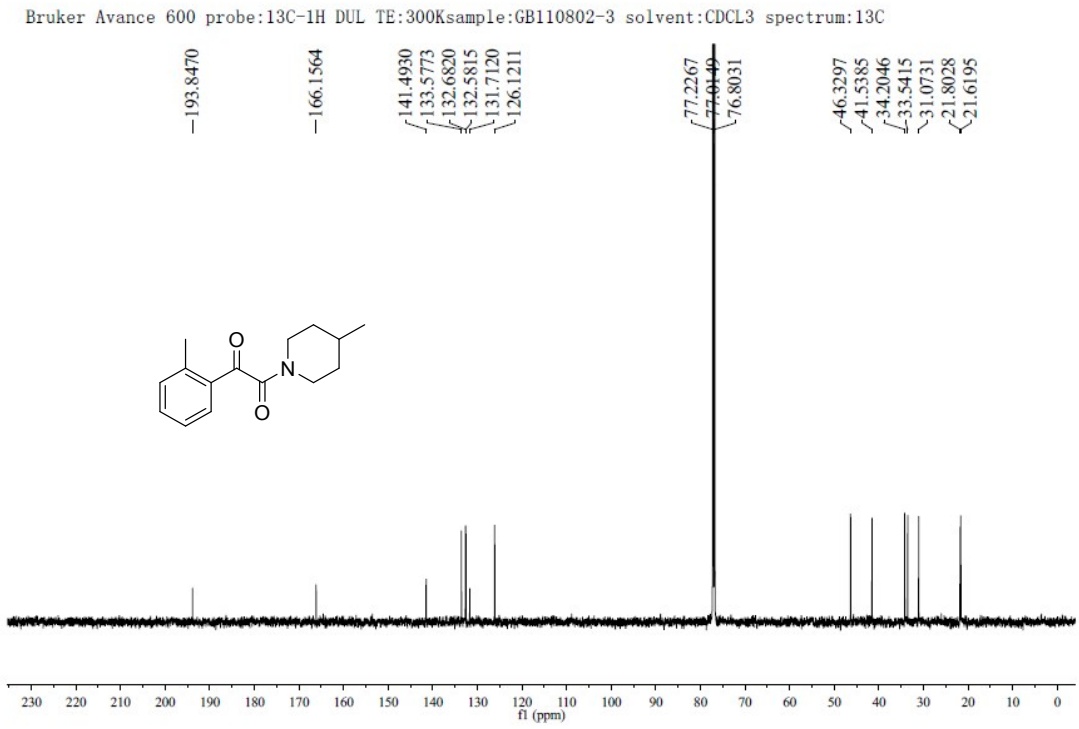
## 1-(4-hydroxypiperidin-1-yl)-2-(m-tolyl)ethane-1,2-dione (3cd)



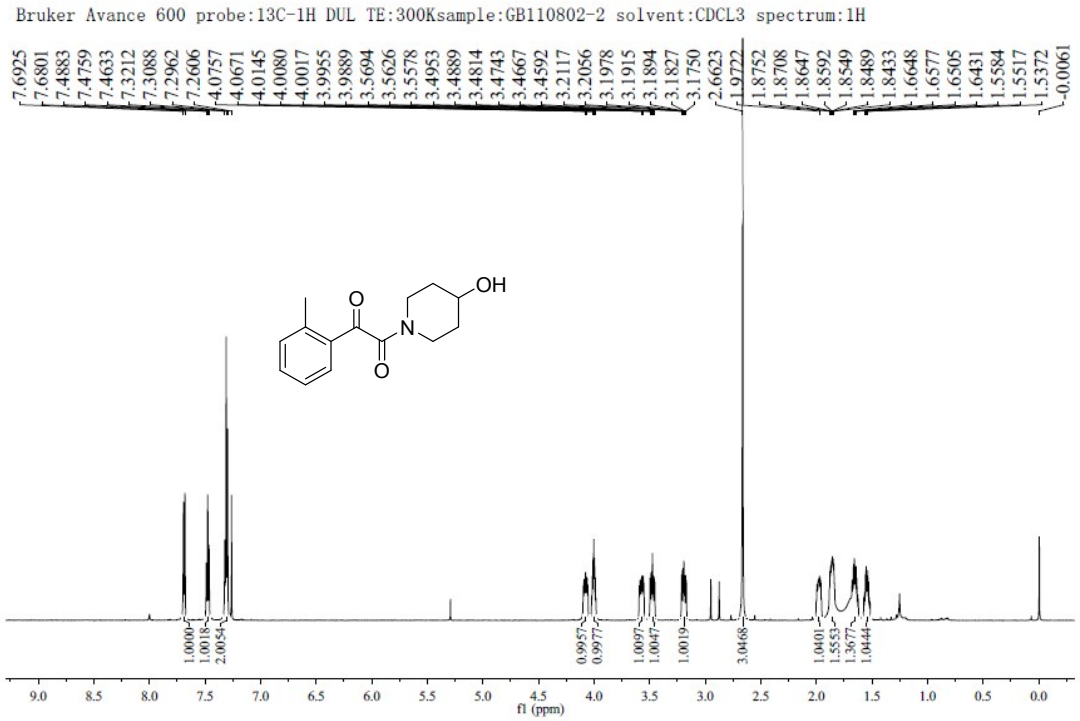



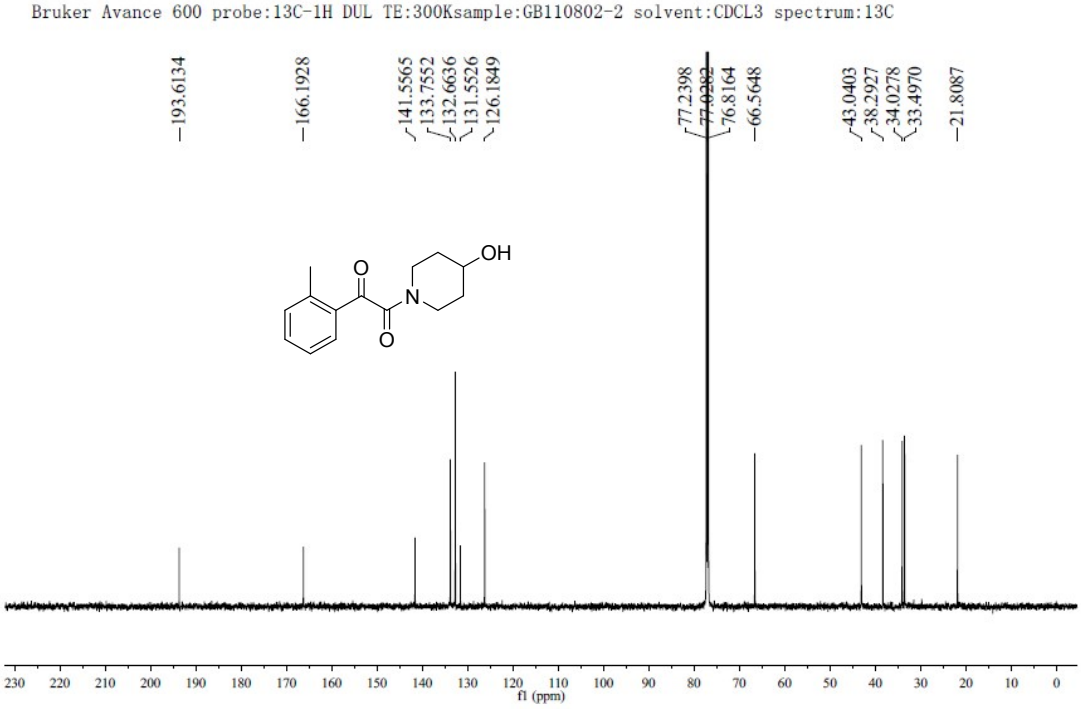
## 1-(4-methylpiperidin-1-yl)-2-(o-tolyl)ethane-1,2-dione (3dc)



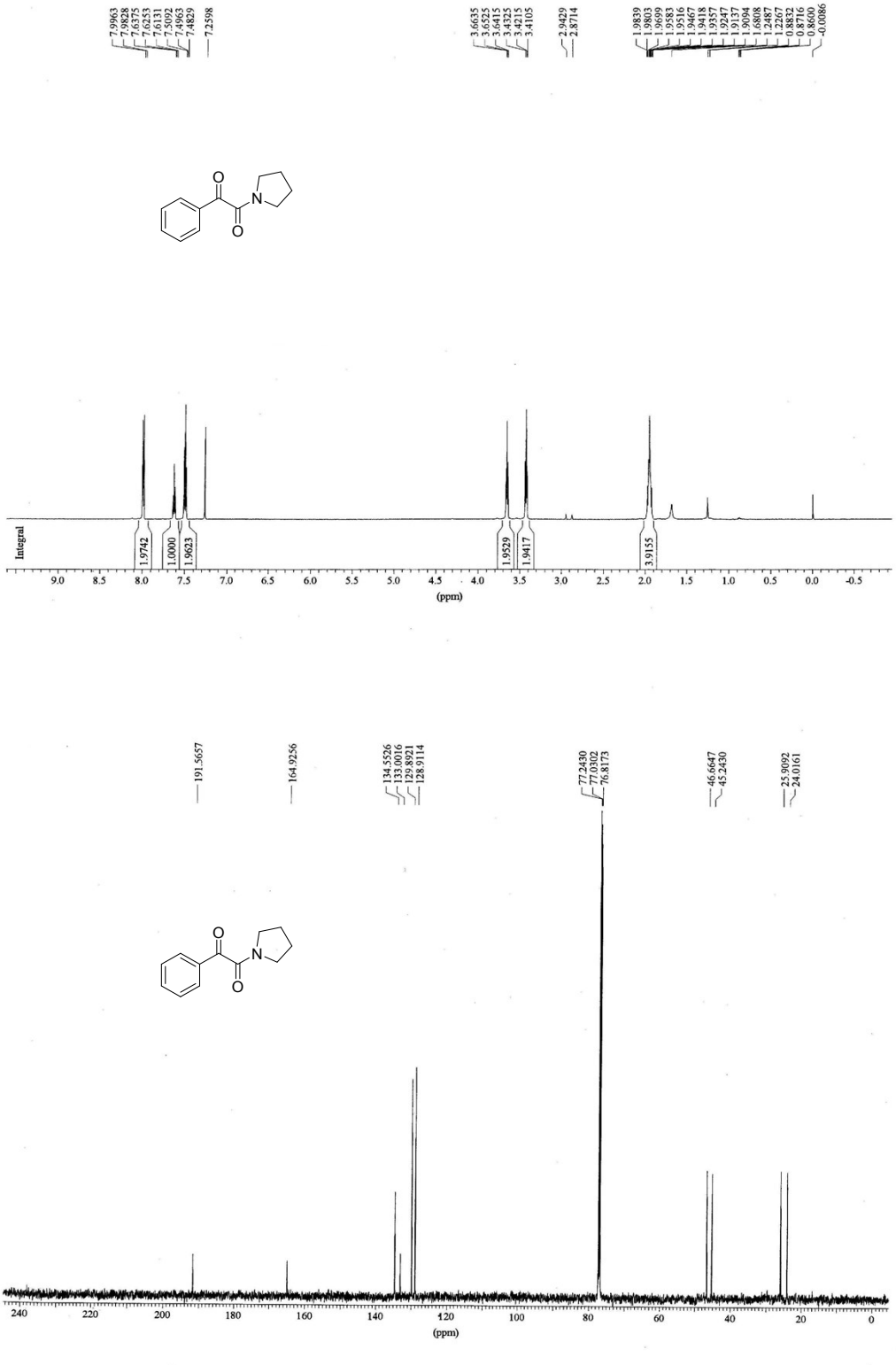



## 1-(4-methylpiperidin-1-yl)-2-(o-tolyl)ethane-1,2-dione (3dd)



## 1-phenyl-2-(pyrrolidin-1-yl) ethane-1,2-dione (3ae)



## N,N-dibutyl-2-oxo-2-phenylacetamide (3af)