

# Direct Synthesis of 1,3-Diketones by Rh-catalyzed Reductive $\alpha$ -Acylation of Enones

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## Supporting Information

General Information .....	S2
Experimental Section .....	S2
Materials .....	S2
Typical procedure for reductive $\alpha$ -acylation reaction .....	S2
Spectroscopic Data .....	S3-S6
Typical procedure for one-pot synthesis of a 1,3-diketone .....	S7
Typical procedure for one-pot synthesis of a pyrazole. ....	S7
Spectroscopic Data .....	S7
References .....	S8
<sup>1</sup> H NMR Charts.....	S9-S21

## General Information:

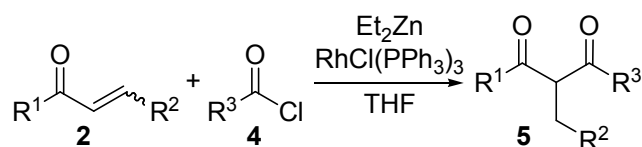
$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on JNM-GX400 and JEOL-ECA-600SN spectrometers.  $^{19}\text{F}$  NMR spectrum was recorded on Hitachi FT-NMR R-90H spectrometer. Chemical shifts of  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR are reported in ppm from tetramethylsilane (TMS) as an internal standard. Chemical shifts of  $^{19}\text{F}$  NMR are reported in ppm from benzotrifluoride (BTF) as an internal standard. All data are reported as follows: chemical shifts, relative integration value, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). Mass spectra were obtained on JEOL JMS-700T spectrometer. IR spectra were recorded on Hitachi 270-30 Infrared spectrophotometer. Melting points were measured on Yanagimoto micro melting point apparatus MP-S3. Analytical gas-liquid chromatography (GLC) was carried out on Hitachi 263-50 gas chromatograph (column; 5% SE-30 3 mm x 2 m, carrier;  $\text{N}_2$  at 30 ml/min). Peak areas were calculated on Hitachi D-2500 Chromato-Integrator.

## Experimental Section:

### Materials

Tetrahydrofuran (THF) was distilled over benzophenone ketyl sodium just before use. All commercially available acid chlorides were distilled just before use. Other commercially available reagents were used without further purification. All experiments were carried out under argon atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents unless otherwise noted.

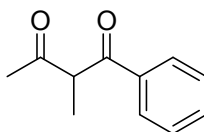
### Typical procedure for reductive $\alpha$ -acylation reaction.



$\alpha,\beta$ -Unsaturated ketone (**2**; 4 mmol) and acid chloride (**4**; 2 mmol) were added to a solution of  $\text{RhCl}(\text{PPh}_3)_3$  (2 mol%) in THF (5 mL) at 0 °C. Then 1.0 M  $\text{Et}_2\text{Zn}$  in hexane (3 mmol) was gradually added to the mixture at 0 °C, and was stirred at same temperature for the reaction time shown in Table 2. The mixture was quenched with 10% HCl, and extracted with AcOEt. The AcOEt layer was washed with sat. NaCl and dried over  $\text{MgSO}_4$ . The solvent was removed *in vacuo* and the residue was purified by column chromatography to give the corresponding 1,3-diketone (**5**).

### Spectroscopic Data:

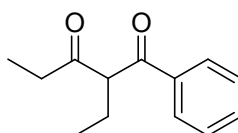
#### 2-Methyl-1-phenylbutane-1,3-dione (5a)<sup>1</sup>



The title product (**5a**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 62% yield (216.8 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.46 (3H, d, *J* = 7.0 Hz), 2.17 (3H, s), 4.50 (1H, q, *J* = 7.0 Hz), 7.50 (2H, m), 7.61 (1H, m), 7.98 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.62, 27.90, 56.77, 128.61, 128.80, 133.62, 135.83, 197.20, 204.94; MS *m/z*: 176 (M<sup>+</sup>); HRMS Calcd. for C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>: 176.084 (M<sup>+</sup>), Found: 176.084; IR (neat) cm<sup>-1</sup>: 3072, 2992, 2944, 1726, 1678.

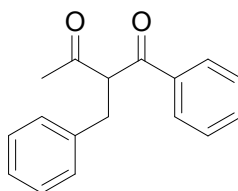
#### 2-Ethyl-1-phenylpentane-1,3-dione (5c)



The title product (**5c**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 79% yield (321.4 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.94 (3H, t, *J* = 7.3 Hz), 1.00 (3H, t, *J* = 7.4 Hz), 2.04 (2H, m), 2.47 (2H, m), 4.39 (1H, t, *J* = 7.1 Hz), 7.48 (2H, m), 7.60 (1H, m), 7.99 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 7.65, 12.30, 22.52, 34.01, 64.17, 128.55, 128.77, 133.52, 136.57, 196.52, 206.72; MS *m/z*: 204 (M<sup>+</sup>); HRMS Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: 204.115 (M<sup>+</sup>), Found: 204.114; IR (neat) cm<sup>-1</sup>: 2980, 2944, 1726, 1682.

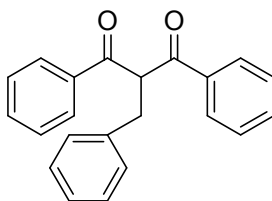
#### 2-Benzyl-1-phenylbutane-1,3-dione (5d)<sup>2</sup>



The title product (**5d**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 64% yield (321.0 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 2.13 (3H, s), 3.32 (2H, m), 4.80 (1H, t, *J* = 7.2 Hz), 7.16-7.27 (5H, m), 7.45 (2H, m), 7.57 (1H, m), 7.92 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 28.58, 34.75, 64.78, 126.58, 128.55, 128.61, 128.69, 128.74, 133.63, 136.30, 138.27, 195.62, 203.14; MS *m/z*: 252 (M<sup>+</sup>); HRMS Calcd. for C<sub>17</sub>H<sub>16</sub>O<sub>2</sub>: 252.115 (M<sup>+</sup>), Found: 252.115; IR (neat) cm<sup>-1</sup>: 3068, 3036, 2928, 1722, 1684.

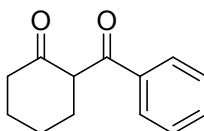
### **2-Benzyl-1,3-diphenylpropane-1,3-dione (5e)<sup>2</sup>**



The title product (**5e**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 74% yield (468.2 mg).

Colorless crystals; M.p. 105.0-106.0 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 3.45 (2H, d, *J* = 6.7 Hz), 5.52 (1H, t, *J* = 6.7 Hz), 7.14-7.26 (5H, m), 7.40 (4H, m), 7.53 (2H, m), 7.89 (4H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 35.16, 58.91, 126.52, 128.50, 128.73, 128.88, 133.41, 135.82, 138.94, 195.25; MS *m/z* : 314 (M<sup>+</sup>); HRMS Calcd. for C<sub>22</sub>H<sub>18</sub>O<sub>2</sub>: 314.131 (M<sup>+</sup>), Found: 314.132; IR (KBr) cm<sup>-1</sup>: 1698, 1668.

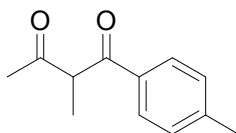
### **2-Benzoylcyclohexanone (5g) and its tautomer<sup>3</sup>**



The title product (**5g**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 81% yield (327.2 mg) as a mixture of the tautomers.

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.58-1.64 (1H, m), 1.71-1.81 (1.5H, m), 1.87-2.05 (1.5H, m), 2.07-2.15 (0.5H, m), 2.28-2.36 (0.5H, m), 2.39-2.42 (1H, m), 2.47-2.61 (2H, m), 4.38 (0.6H, m), 7.40-7.48 (2.5H, m), 7.52-7.58 (1.5H, m), 7.89-7.91 (1H, m), 16.76 (0.4H, s); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 21.84, 23.06, 23.42, 26.44, 27.27, 29.97, 32.66, 42.24, 58.75, 107.00, 127.47, 127.98, 128.39, 128.55, 130.30, 133.17, 136.40, 137.34, 189.38, 191.26, 197.40, 208.49; MS *m/z* : 202 (M<sup>+</sup>); HRMS Calcd. for C<sub>13</sub>H<sub>14</sub>O<sub>2</sub>: 202.099 (M<sup>+</sup>), Found: 202.100; IR (neat) cm<sup>-1</sup>: 2936, 2864, 1712, 1676, 1602, 1584.

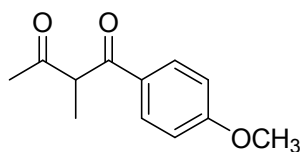
### **2-Methyl-1-*p*-tolylbutane-1,3-dione (5h)**



The title product (**5h**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 57% yield (215.0 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.44 (3H, d, *J* = 7.0 Hz), 2.15 (3H, s), 2.42 (3H, s), 4.47 (1H, q, *J* = 7.0 Hz), 7.29 (2H, m), 7.88 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.62, 21.65, 27.83, 56.69, 128.74, 129.48, 133.36, 144.60, 196.80, 205.10; MS *m/z*: 190 (M<sup>+</sup>); HRMS Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>: 190.099 (M<sup>+</sup>), Found: 190.100; IR (neat) cm<sup>-1</sup>: 2988, 2940, 1724, 1676.

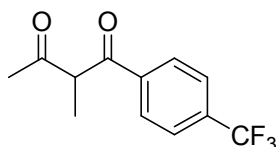
### **1-(4-Methoxyphenyl)-2-methylbutane-1,3-dione (5i)**<sup>4</sup>



The title product (**5i**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 51% yield (210.4 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.44 (3H, d, *J* = 7.0 Hz), 2.14 (3H, s), 3.88 (3H, s), 4.43 (1H, q, *J* = 7.0 Hz), 6.96 (2H, m), 7.97 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.68, 27.64, 55.52, 56.70, 113.98, 128.89, 131.03, 163.88, 195.54, 205.31; MS *m/z*: 206 (M<sup>+</sup>); HRMS Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>: 206.094 (M<sup>+</sup>), Found: 206.094; IR (neat) cm<sup>-1</sup>: 2980, 2940, 1724, 1670, 1600, 1264.

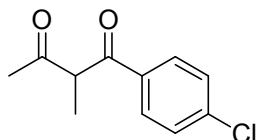
### **1-[4-(Trifluoromethyl)phenyl]-2-methylbutane-1,3-dione (5i) and its tautomer**



The title product (**5a**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 74% yield (361.0 mg) as a mixture of the tautomers.

Colorless crystals; M.p. 48.0-50.0 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.49 (2.55H, d, *J* = 7.0 Hz), 1.92 (0.45H, s), 2.19 (2.55H, s), 2.29 (0.45H, s), 4.49 (0.85H, q, *J* = 7.0 Hz), 7.62 (0.3H, m), 7.70 (0.3H, m), 7.76 (1.7H, m), 8.08 (1.7H, m), 16.5 (0.15H, s); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ: 13.48, 14.34, 25.87, 27.85, 57.25, 105.23, 123.49 (q, *J* = 272.3 Hz), 123.80 (q, *J* = 272.3 Hz), 125.25 (q, *J* = 4.2 Hz), 125.98 (q, *J* = 4.2 Hz), 128.56, 129.04, 131.87 (q, *J* = 32.8 Hz), 134.93 (q, *J* = 32.8 Hz), 138.68, 139.62, 179.34, 196.32, 199.67, 204.60; <sup>19</sup>F NMR (90 MHz, CDCl<sub>3</sub>) δ: -0.51 (3F, s); MS *m/z*: 244 (M<sup>+</sup>); HRMS Calcd. for C<sub>12</sub>H<sub>11</sub>F<sub>3</sub>O<sub>2</sub>: 244.071 (M<sup>+</sup>), Found: 244.071; IR (KBr) cm<sup>-1</sup>: 1716, 1692, 1336, 1170, 1112.

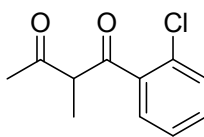
### **1-(4-Chlorophenyl)-2-methylbutane-1,3-dione (5k)**



The title product (**5k**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 70% yield (295.3 mg).

A colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.46 (3H, d, *J* = 7.0 Hz), 2.16 (3H, s), 4.44 (1H, q, *J* = 7.0 Hz), 7.46 (2H, m), 7.92 (2H, m); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 13.54, 27.75, 56.91, 129.13, 130.01, 134.16, 140.18, 195.86, 204.70; MS *m/z*: 210 (M<sup>+</sup>); HRMS Calcd. for C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>Cl: 210.05 (M<sup>+</sup>), Found: 210.04; IR (neat) cm<sup>-1</sup>: 2992, 2940, 1728, 1686, 1592.

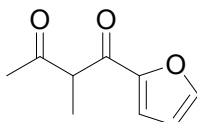
### **1-(2-Chlorophenyl)-2-methylbutane-1,3-dione (5l) and its tautomer**



The title product (**5l**) was purified by column chromatography (AcOEt : hexane = 1:9) and was obtained in 57% yield (242.2 mg) as a mixture of the tautomers.

A colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.42 (0.75H, d,  $J = 7.2$  Hz), 1.69 (2.25H, s), 2.23 (0.75H, s), 2.26 (2.25H, s), 4.48 (0.25H, q,  $J = 7.2$  Hz), 7.28-7.46 (5H, m), 16.20 (0.75H, s);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 13.15, 13.42, 25.41, 28.92, 59.94, 106.41, 126.78, 127.03, 128.70, 129.36, 129.62, 130.38, 130.43, 131.24, 132.02, 135.51, 138.47, 180.19, 197.84, 200.33, 204.28; MS  $m/z$ : 210 ( $\text{M}^+$ ); HRMS Calcd. for  $\text{C}_{11}\text{H}_{11}\text{O}_2\text{Cl}$ : 210.05 ( $\text{M}^+$ ), Found: 210.04; IR (neat)  $\text{cm}^{-1}$ : 2932, 1728, 1696.

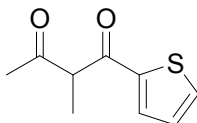
### **1-(Furan-2-yl)-2-methylbutane-1,3-dione (5m)**



The title product (**5m**) was purified by column chromatography (AcOEt : hexane = 2:3) and was obtained in 66% yield (217.9 mg).

A colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.43 (3H, d,  $J = 7.0$  Hz), 2.21 (3H, s), 4.28 (1H, q,  $J = 7.0$  Hz), 6.58 (1H, m), 7.29 (1H, m), 7.62 (1H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 12.85, 28.26, 56.87, 112.66, 118.46, 146.91, 151.81, 185.61, 204.26; MS  $m/z$ : 166 ( $\text{M}^+$ ); HRMS Calcd. for  $\text{C}_9\text{H}_{10}\text{O}_3$ : 166.06 ( $\text{M}^+$ ), Found: 166.06; IR (neat)  $\text{cm}^{-1}$ : 3144, 2992, 2944, 1728, 1670.

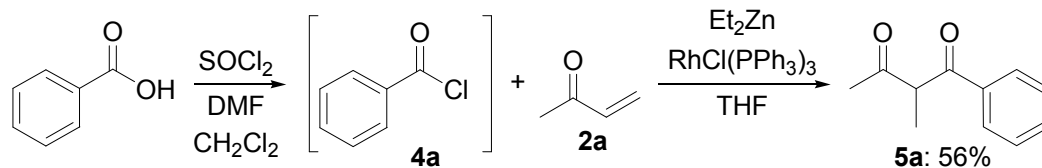
### **2-Methyl-1-(thiophen-2-yl)butane-1,3-dione (5n)**



The title product (**5n**) was purified by column chromatography (AcOEt : hexane = 2:3) and was obtained in 55% yield (200.6 mg).

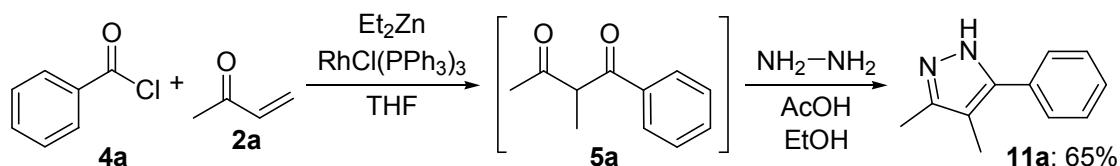
A colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.48 (3H, d,  $J = 7.1$  Hz), 2.19 (3H, s), 4.32 (1H, q,  $J = 7.1$  Hz), 7.17 (1H, m), 7.72 (1H, m), 7.79 (1H, m);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 13.67, 27.62, 58.26, 128.41, 133.17, 134.93, 143.19, 189.58, 204.27; MS  $m/z$ : 182 ( $\text{M}^+$ ); HRMS Calcd. for  $\text{C}_9\text{H}_{10}\text{O}_2\text{S}$ : 182.04 ( $\text{M}^+$ ), Found: 182.03; IR (neat)  $\text{cm}^{-1}$ : 3108, 2992, 2940, 1726, 1664.

### Typical procedure for one-pot synthesis of a 1,3-diketone.



To a solution of benzoic acid (2 mmol) of  $\text{CH}_2\text{Cl}_2$  (5 mL) was added  $\text{SOCl}_2$  (2.6 mmol) and DMF (2 drops) at room temperature, and was stirred for 20h. The solvent was removed *in vacuo*, then  $\text{RhCl}(\text{PPh}_3)_3$  (2 mol%) and THF (5 mL) were added to the residue. Methyl vinyl ketone (4 mmol) was added to the THF solution at 0 °C, then 1.0 M  $\text{Et}_2\text{Zn}$  in hexane (3 mmol) was gradually added to the mixture. The mixture was stirred at the same temperature for 1h, then it was quenched with 10% HCl, and extracted with AcOEt. The AcOEt layer was washed with sat. NaCl and dried over  $\text{MgSO}_4$ . The solvent was removed *in vacuo* and the residue was purified by column chromatography to give **5a** (197.1 mg, 56%).

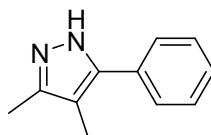
### Typical procedure for one-pot synthesis of a pyrazole.



Methyl vinyl ketone (**2a**, 4 mmol) and benzoyl chloride (**4a**, 2 mmol) were added to a solution of  $\text{RhCl}(\text{PPh}_3)_3$  (2 mol%) in THF (5 mL) at 0 °C. Then 1.0 M  $\text{Et}_2\text{Zn}$  in hexane (3 mmol) was gradually added to the mixture at 0 °C, and was stirred at the same temperature for 1h. AcOH (2mL), EtOH (10mL) and hydrazine monohydrate (20 mmol) were added to the mixture, and it was stirred at room temperature for 1h. The mixture was quenched with 10% NaOH, and extracted with AcOEt. The AcOEt layer was washed with sat. NaCl and dried over  $\text{MgSO}_4$ . The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : hexane = 2:3) to give the pyrazole (**11a**; 224.4 mg, 65%).

### Spectroscopic Data:

#### 3,4-Dimethyl-5-phenyl-1H-pyrazole (11a)



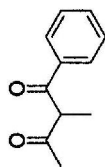
The title product (**11a**) was purified by column chromatography (AcOEt : hexane = 2:3) and was obtained in 65% yield (224.4 mg).

A colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 2.12 (3H, s), 2.18 (3H, s), 7.32 (1H, m), 7.39 (2H, m), 7.55 (2H, m), 10.57 (1H, brs);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.80, 10.57, 110.61, 127.43, 127.58, 128.51, 132.37, 142.68, 145.80; MS  $m/z$ : 172 ( $\text{M}^+$ ); HRMS Calcd. for  $\text{C}_{11}\text{H}_{12}\text{N}_2$ : 172.100 ( $\text{M}^+$ ), Found: 172.100; IR (neat)  $\text{cm}^{-1}$ : 2952, 1596, 1496, 1448, 770, 700.

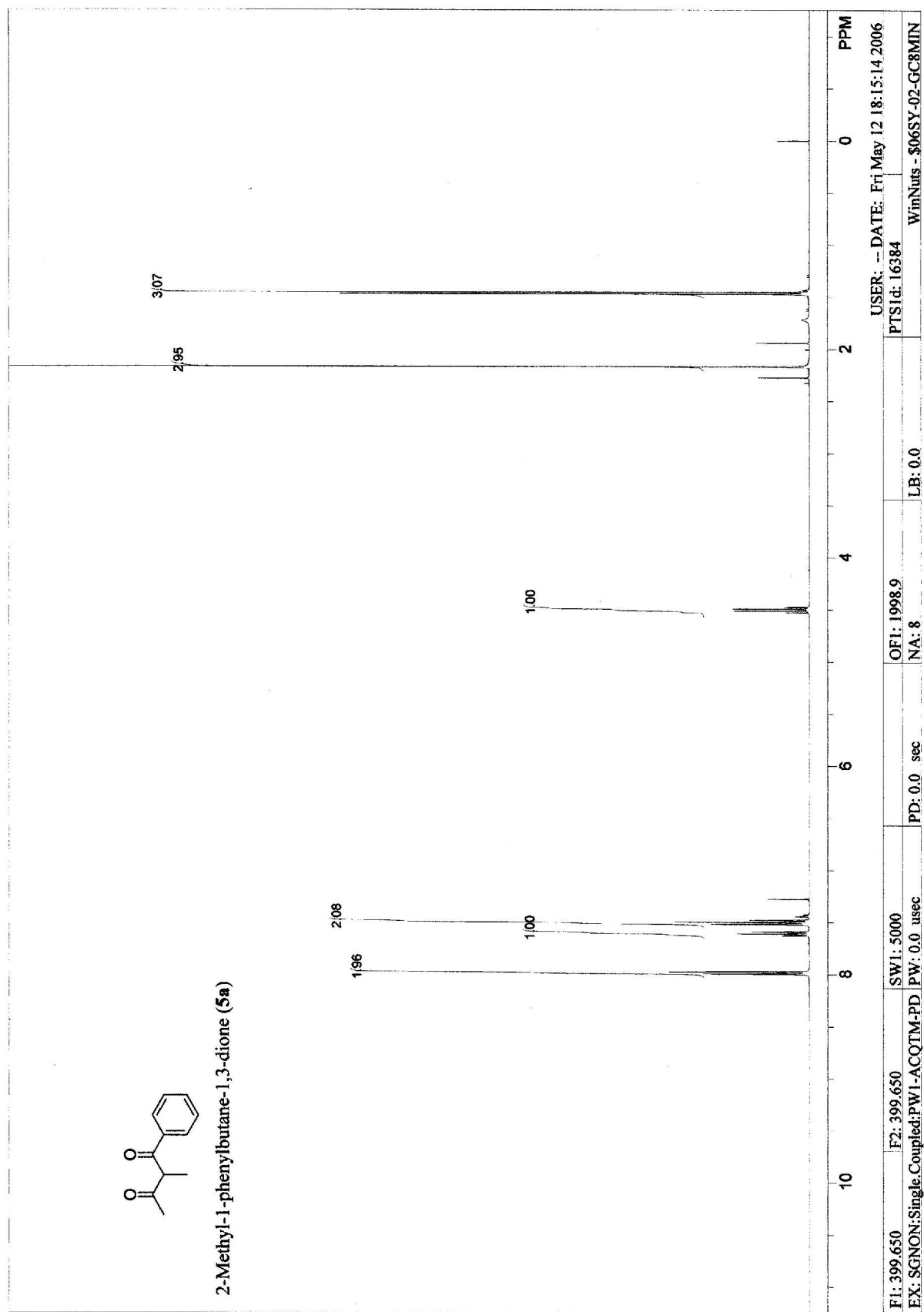
### **References.**

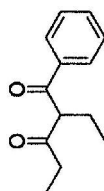
1. Dalgaard, L.; Jensen, L.; Lawesson, S. -O. *Tetrahedron* **1974**, *30*, 93-104.
2. Rueping, M.; Nachtsheim, B. J.; Kuenkel, A. *Org. Lett.* **2007**, *9*, 825-828.
3. Nishimura, Y., Miyake, Y., Amemiya, R., Yamaguchi, M. *Org. Lett.* **2006**, *8*, 5077-5080.
4. Davis, B. R.; Hinds, M. G.; Ting, P. P. C. *Aust. J. Chem.* **1992**, *45*, 865-875.



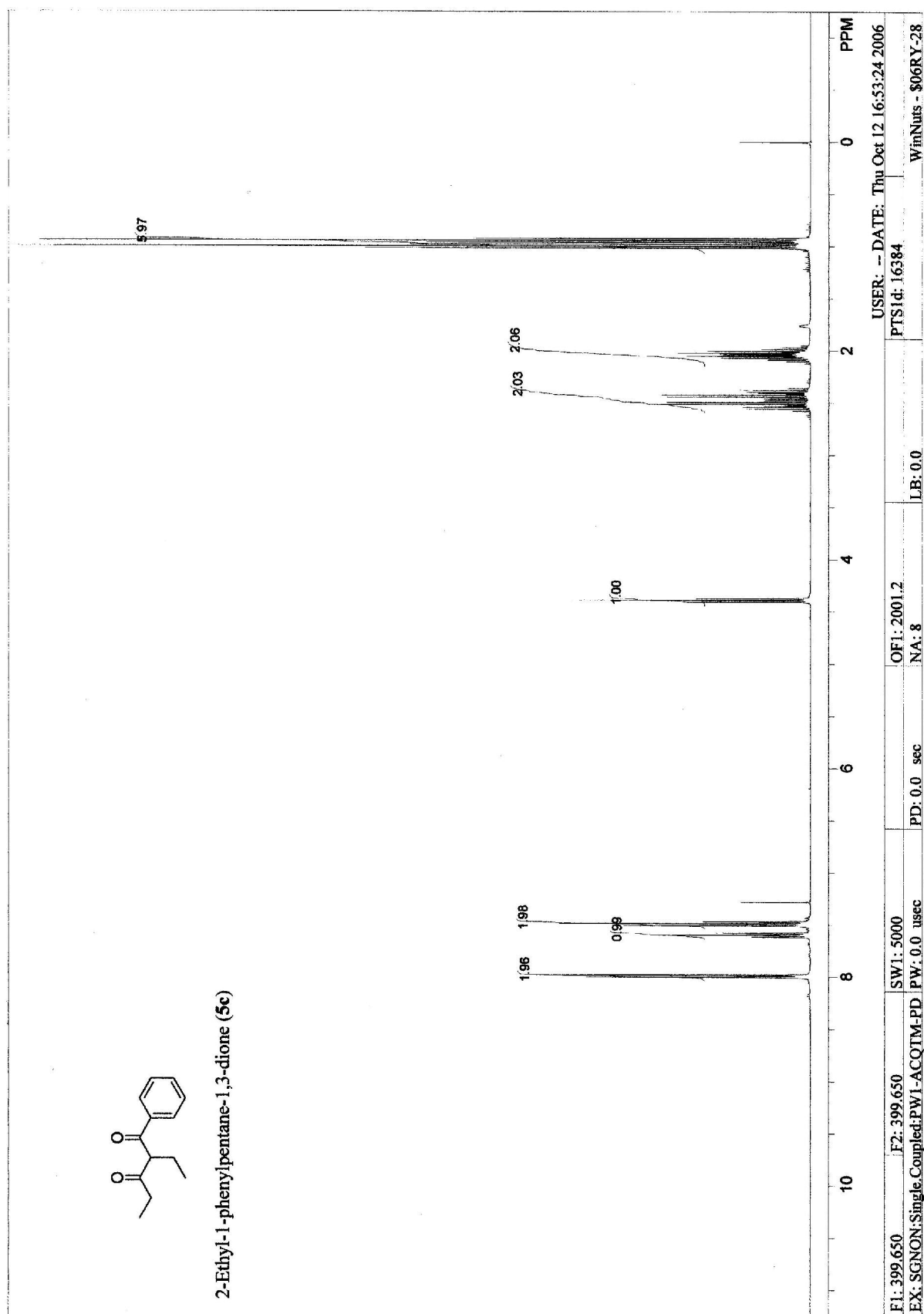


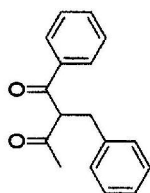
2-Methyl-1-phenylbutane-1,3-dione (5a)



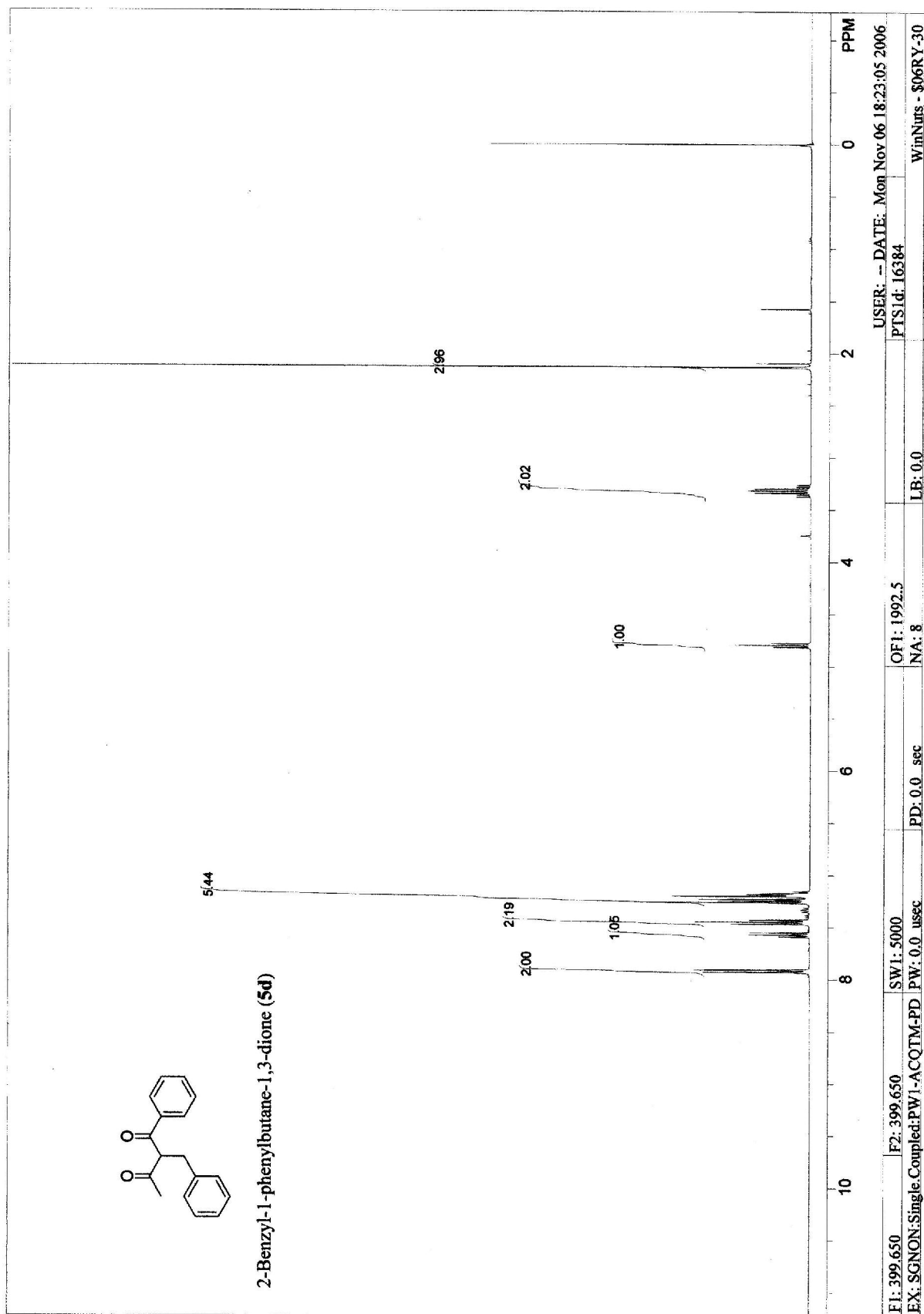


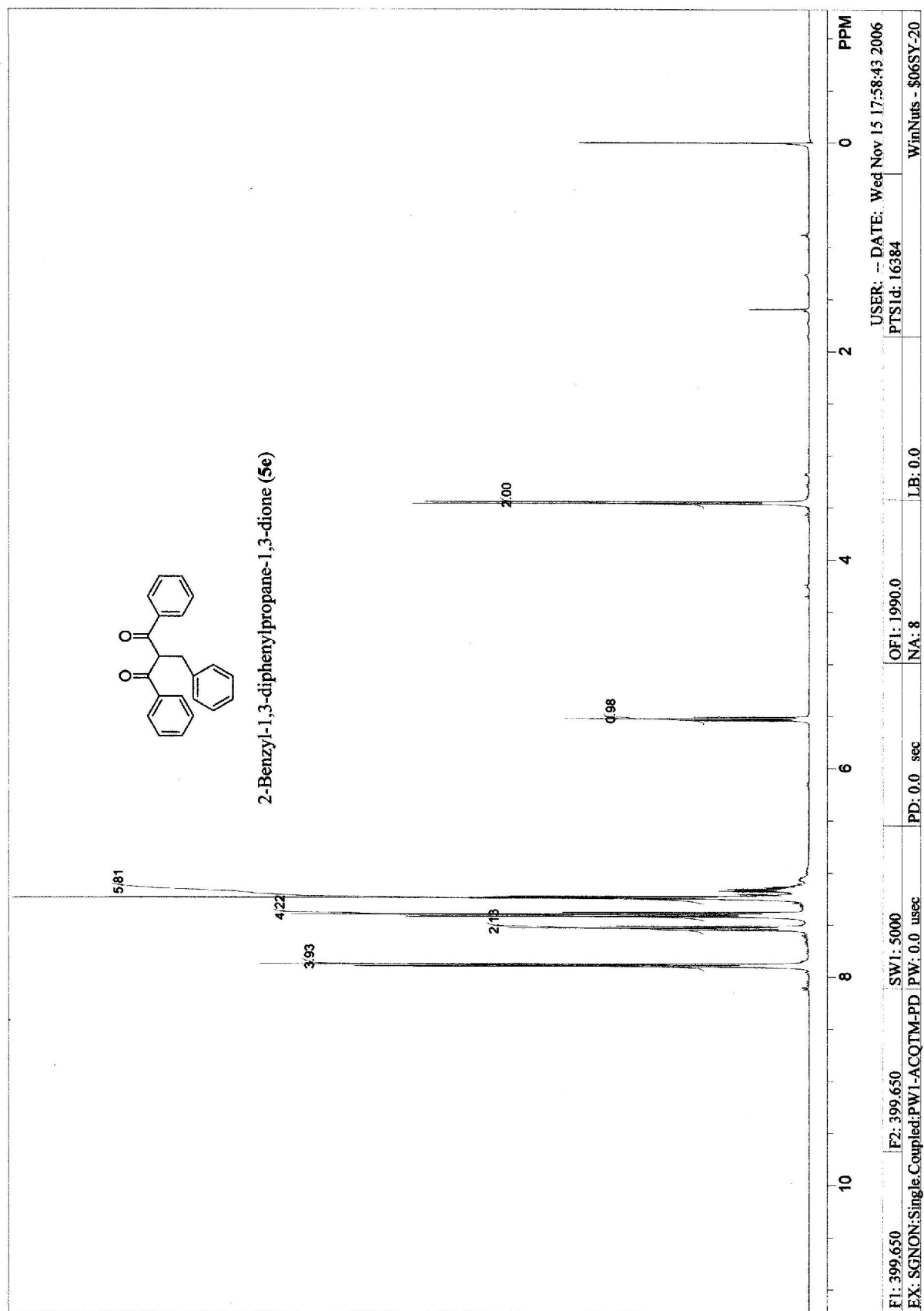
2-Ethyl-1-phenylpentane-1,3-dione (5c)

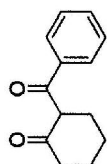




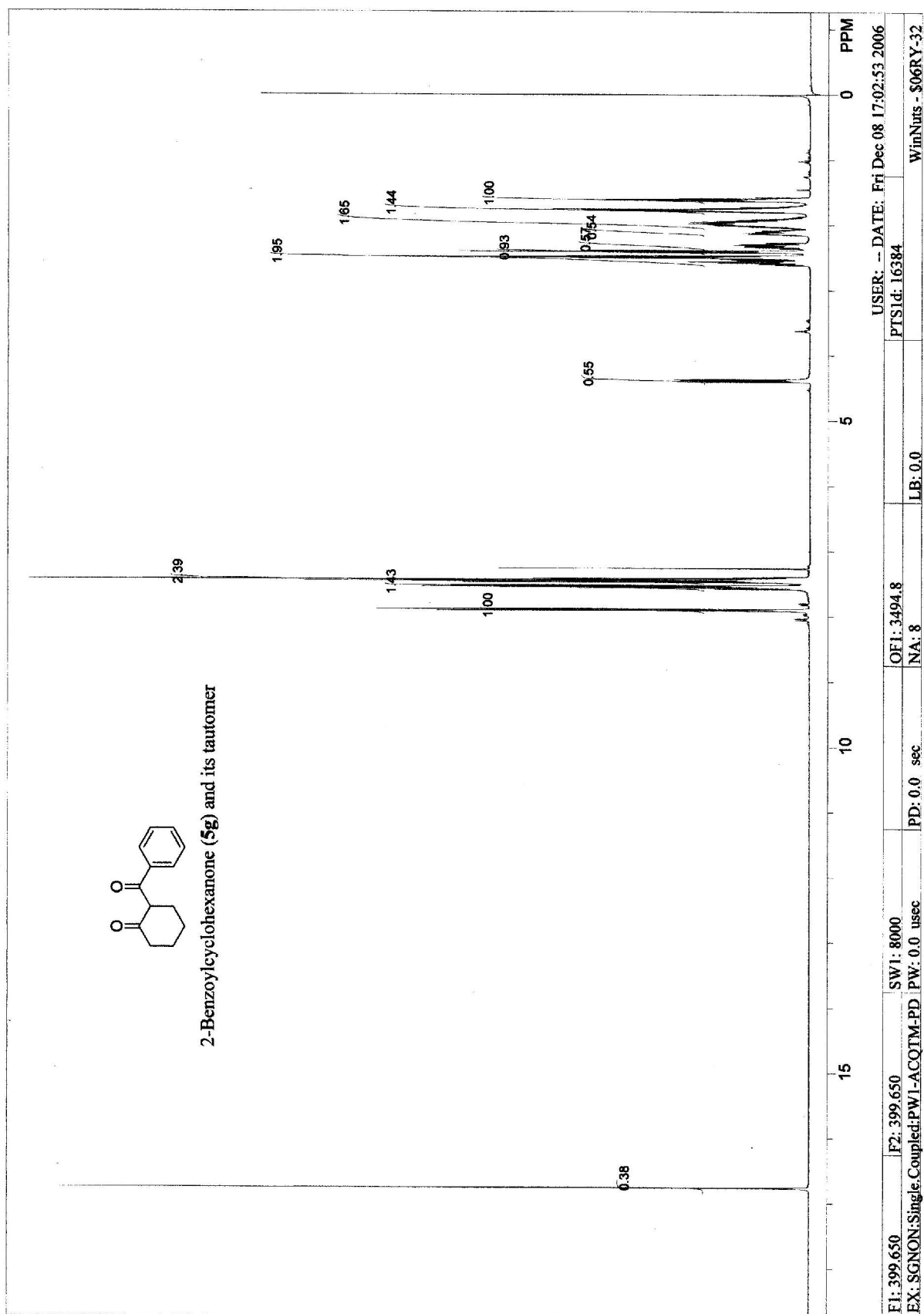
2-Benzyl-1-phenylbutane-1,3-dione (**5d**)

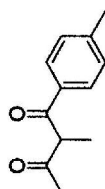




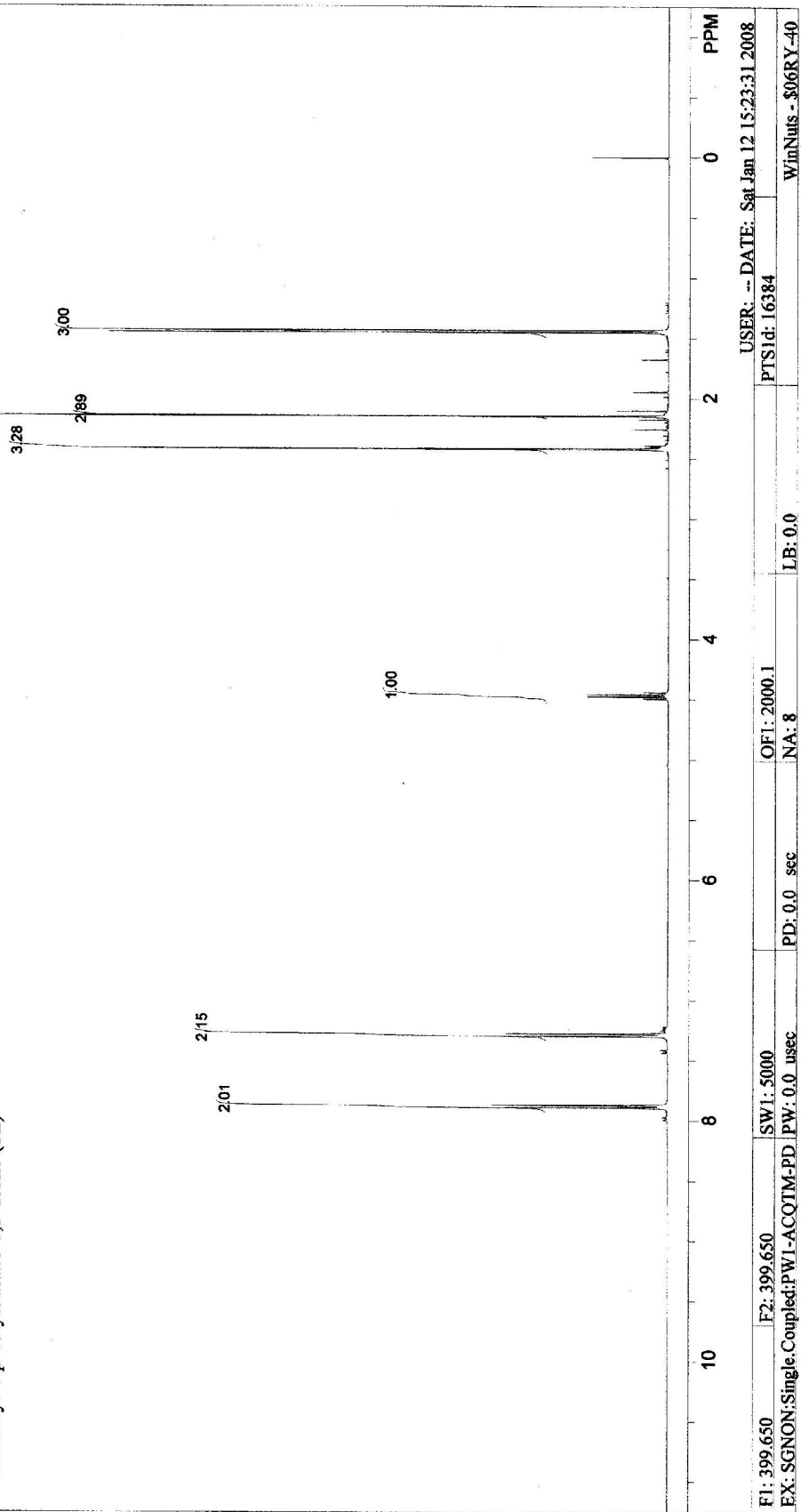


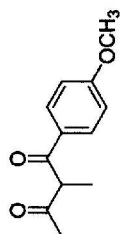
2-Benzoylcyclohexanone (**5g**) and its tautomer



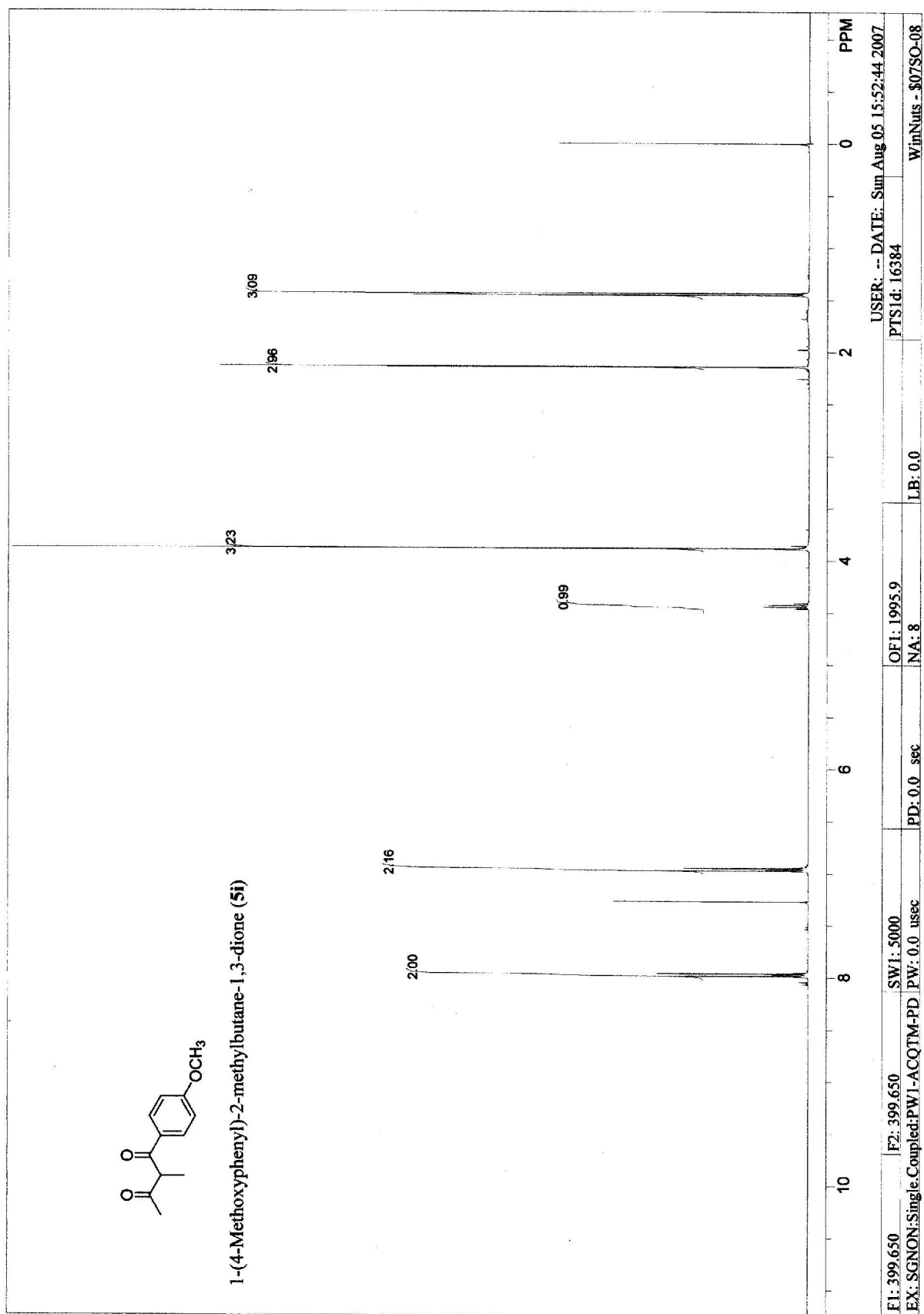


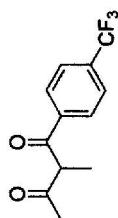
2-Methyl-1-*p*-tolylbutane-1,3-dione (**5h**)



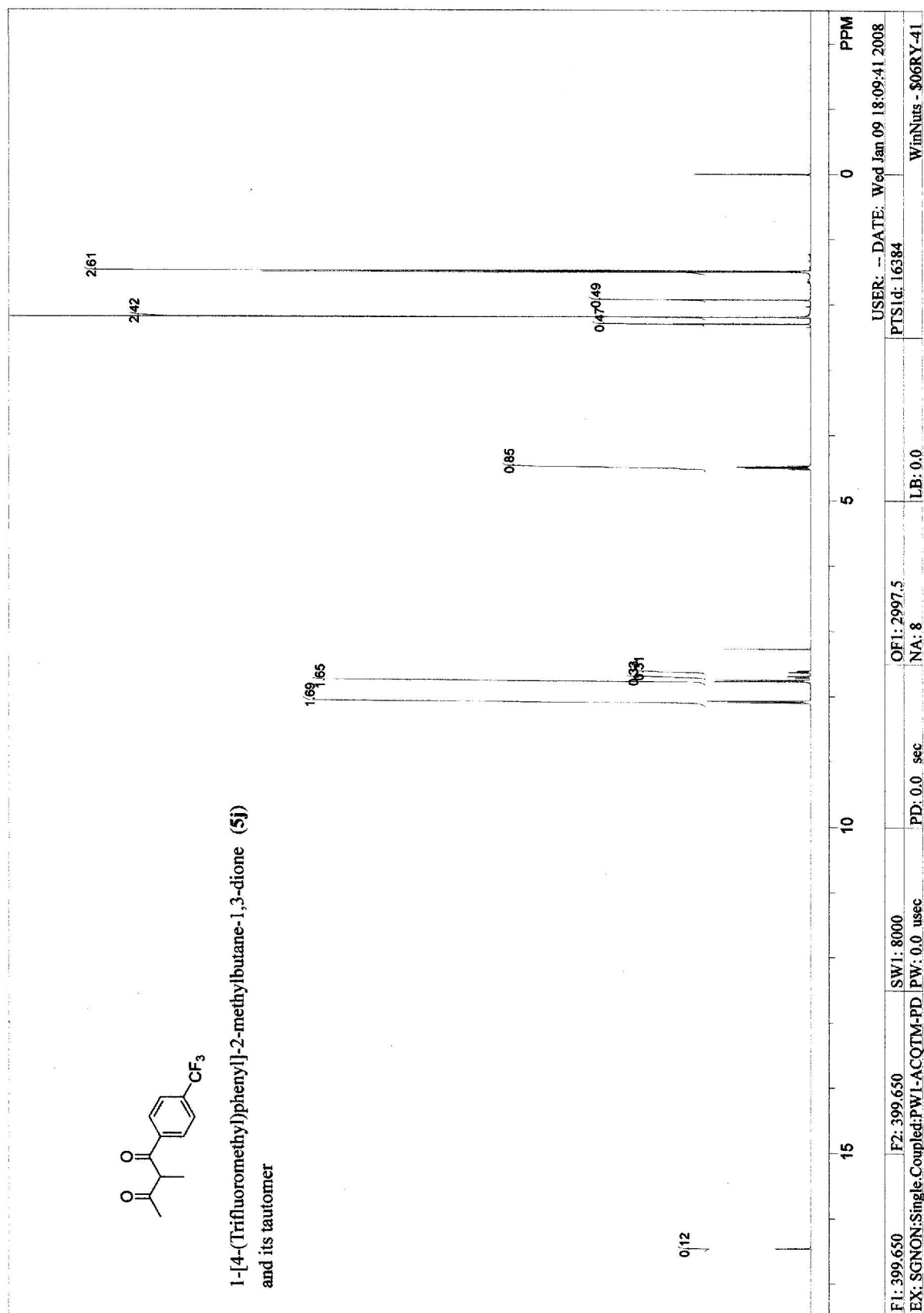


1-(4-Methoxyphenyl)-2-methylbutane-1,3-dione (5i)

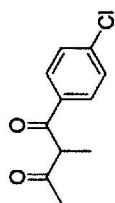




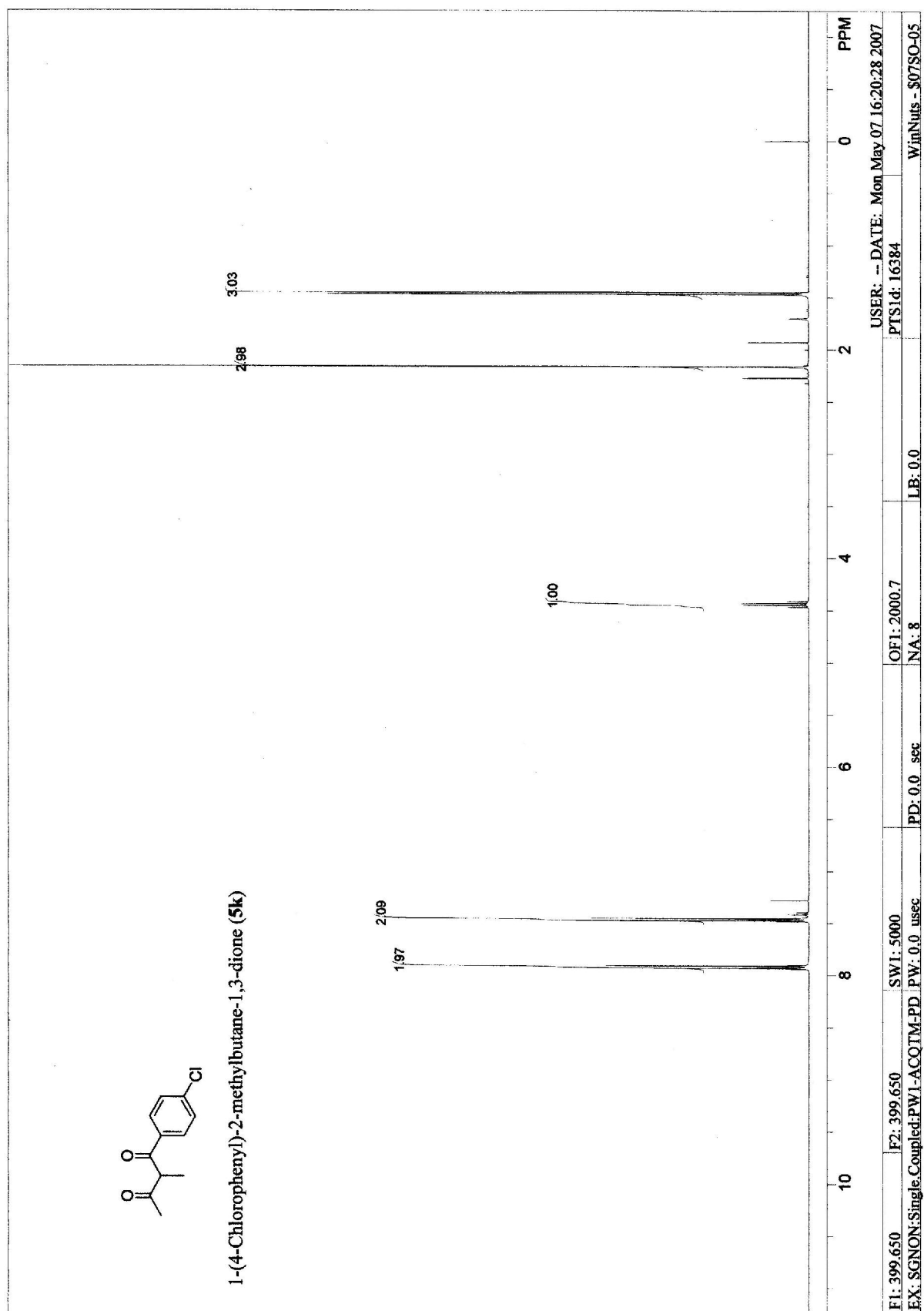
1-[4-(Trifluoromethyl)phenyl]-2-methylbutane-1,3-dione (5j)  
and its tautomer

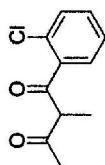




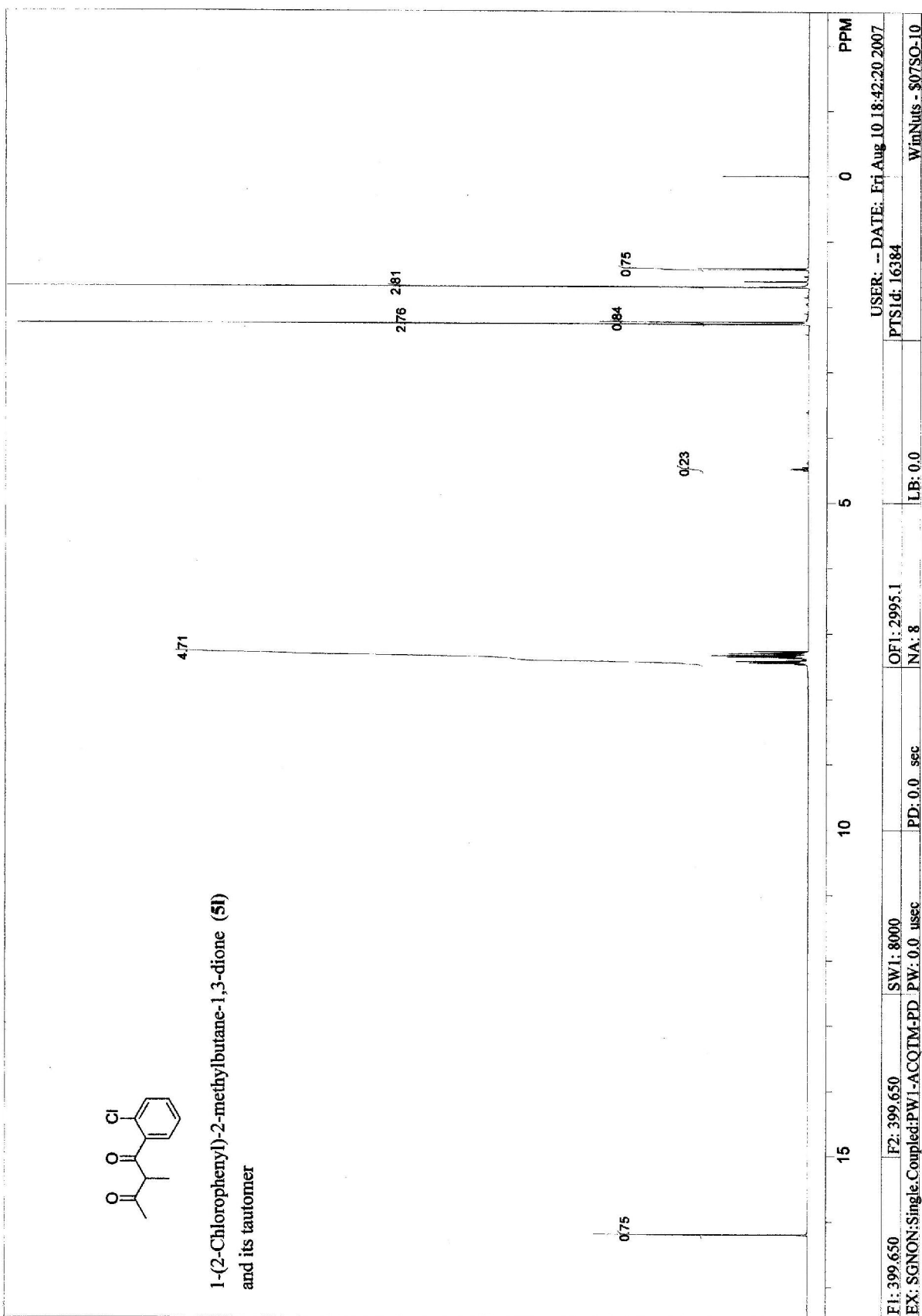


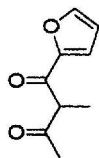
1-(4-Chlorophenyl)-2-methylbutane-1,3-dione (5k)



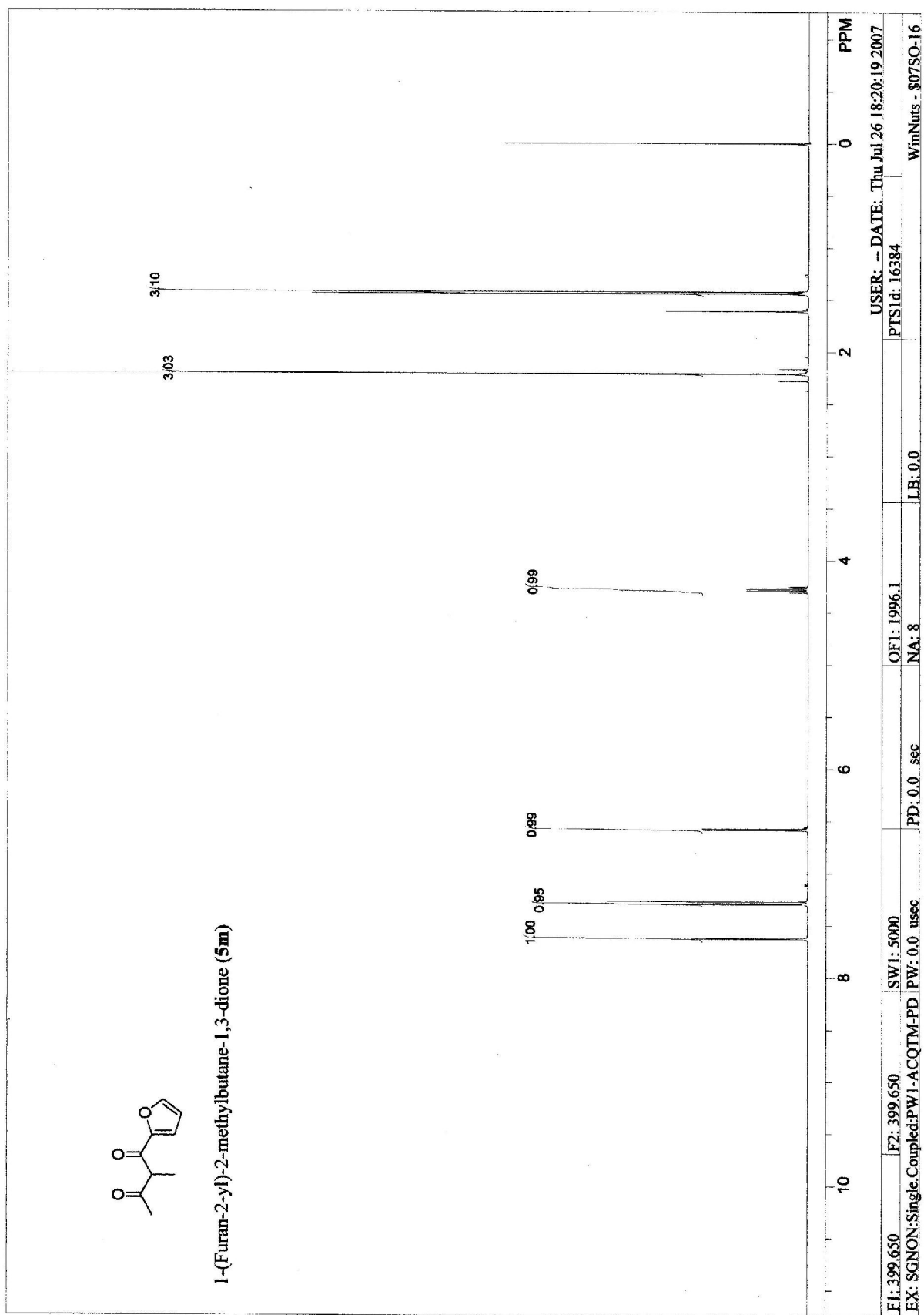


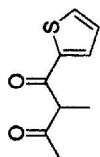
1-(2-Chlorophenyl)-2-methylbutane-1,3-dione (**5I**)  
and its tautomer



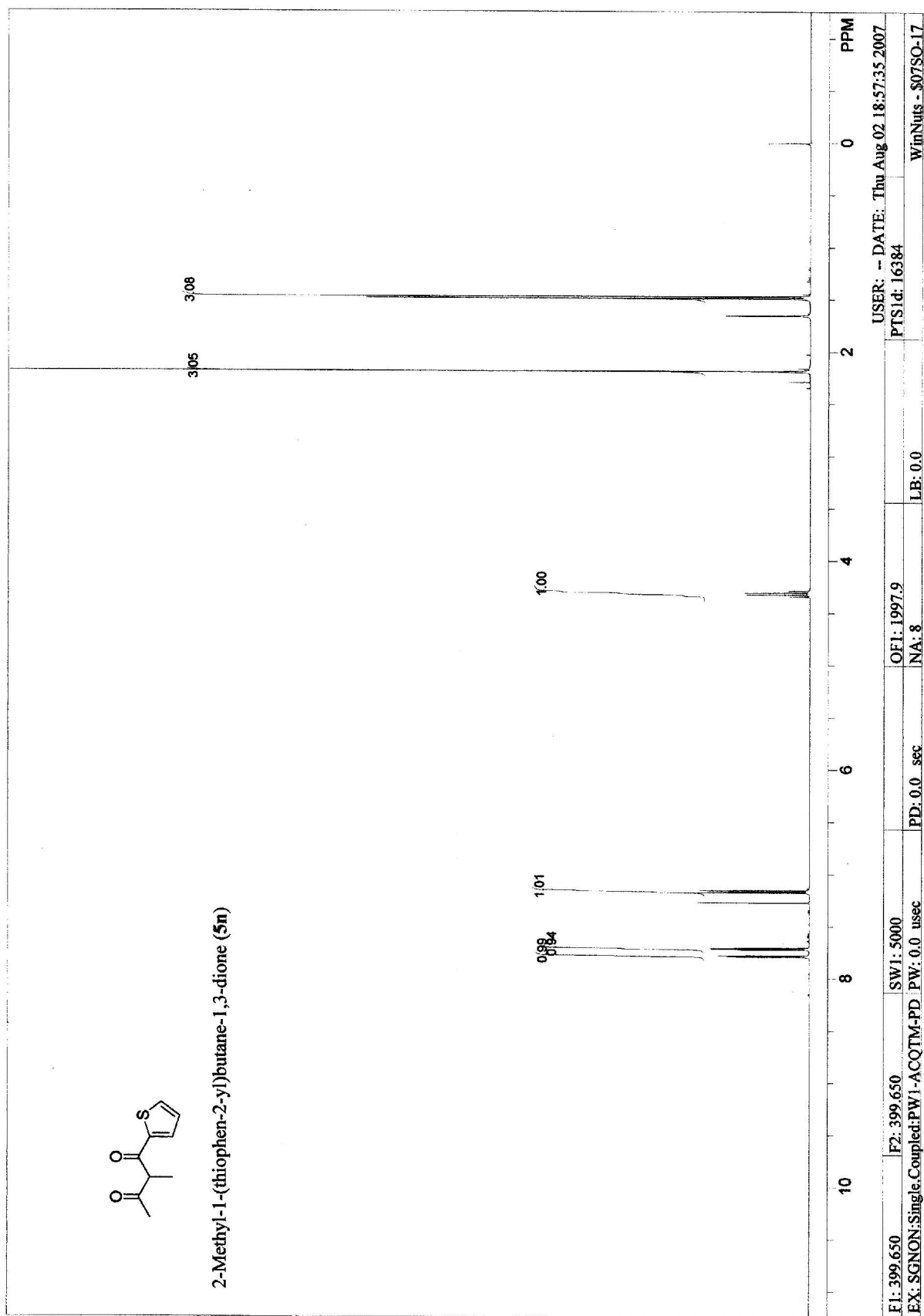


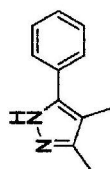
1-(Furan-2-yl)-2-methylbutane-1,3-dione (5m)





2-Methyl-1-(thiophen-2-yl)butane-1,3-dione (**5n**)





3,4-Dimethyl-5-phenyl-1H-pyrazole (11a)

