

# One-pot Synthesis of Substituted 2,5-Dihydrofurans from $\beta$ -Oxo Amides and Cinnamaldehydes

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## I. General

All reagents and substrates **1** and **2** were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded at 25 °C at 300 MHz and 100 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on FTIR-spectrophotometer in the range of 400-4000  $\text{cm}^{-1}$ .

### . Synthesis of substrates 1

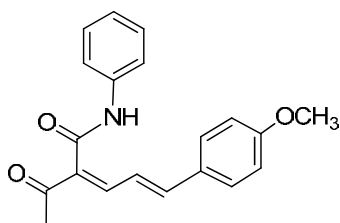
Substrates **1a-1k** were purchased from commercial sources and used without treatment. For the preparation of **1l**, see: Z. Zhang, Y. Liu, L. Ling, Y. Li, Y. Dong, M. Gong, X. Zhao, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* 2011, **133**, 4330. For the preparation of **1m** and **1p**, see: M. Sechi, U. Azzena, M. P. Delussu, R. Dallochio, A. Dessì, A. Cosseddu, N. Pala, N. Neamati, *Molecules* 2008, **13**, 2442. For the preparation of **1n** and **1o**, see: M. Habash, M. O. Taha, *Bioorg. Med. Chem.* 2011, **19**, 4746.

## III. Synthesis and analytical data of substrate 3

### 1. Preparation of substrate 3aa.

Typical procedure for the synthesis of substituted Knoevenagel condensation adducts **3** (**3aa** as an example): To a 100 mL round-bottomed flask was added 3-oxo-*N*-(*p*-tolyl)butanamide **1a** (10.0 mmol), 3-(4-methoxyphenyl)acrylaldehyde **2a** (10.0 mmol), piperidine (5 % mmol 0.5 mmol) and ethyl acetate (30 mL). Then the mixture was heated under reflux for 3.5 h, and cooled to room temperature. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL), and extracted with dichloromethane ( $3 \times 20$  mL). The combined organic phase was washed with water and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 10:1, v/v) to give 84% yield of **3aa** as yellow solid.

### 2. Analytical data of substrate 3aa



#### 2-Acetyl-5-(4-methoxyphenyl)-*N*-phenylpenta-2,4-dienamide (**3aa**)

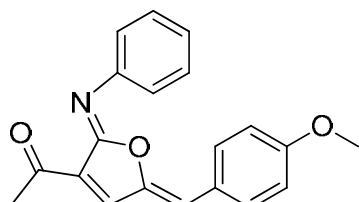
Yellow solid: m.p. 127-128 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.55 (s, 3H), 3.86 (s, 3H), 6.92 (d,  $J = 8.7$  Hz, 2H), 7.11 (d,  $J = 6.0$  Hz, 1H), 7.15 (s, 1H), 7.36 (t,  $J = 8.7$  Hz, 2H), 7.59 (d,  $J = 8.7$  Hz, 2H), 7.64-7.68 (m, 3H), 8.25-8.34 (dd,  $J_1 = 15.3$  Hz,  $J_2 = 3.9$  Hz, 1H), 10.41 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.6, 55.4, 114.4, 120.6, 123.56, 124.2, 128.6, 128.9, 130.2, 138.1, 148.0, 153.2, 161.6, 162.8, 200.4; Anal. Calcd for  $\text{C}_{20}\text{H}_{19}\text{NO}_3$ : C, 74.75; H, 5.96; N, 4.36; Found: C, 74.43; H, 5.77; N, 4.75.

## . Synthesis and analytical data of products 4

### 1. Preparation of products 4aa-fe.

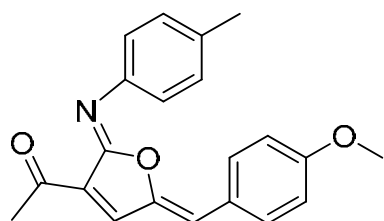
Typical procedure for the synthesis of substituted dihydrofurans **4** (**4aa** as an example): To a 100 mL round-bottomed flask was added 3-oxo-*N*-(*p*-tolyl)butanamide **1a** (1.0 mmol), 3-(4-methoxyphenyl)acrylaldehyde **2a** (1.0 mmol), piperidine (5 % mmol 0.05 mmol) and 1,3-dichloropropane (10 mL). Then the mixture was heated under reflux for 3.5 h, and cooled to room temperature. To a solution of mixture was added dropwise a solution of PIDA (0.386 g, 1.2 mmol) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (0.32ml, 3.0 mmol) in dry  $\text{CH}_2\text{ClCH}_2\text{Cl}$  (10.0 mL) at 0 °C under stirring. Then the mixture was stirred at room temperature for 5.0 h when **3aa** was consumed (monitored by TLC). The reaction mixture was then poured into aqueous  $\text{NaHCO}_3$  (50 mL), and extracted with  $\text{CH}_2\text{Cl}_2$  (3 × 20 mL). The combined organic phase was washed with water (3 × 20 mL), dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, petroleum ether: diethyl ether = 8:1) to give **4aa** (0.236 g, 74 %).

### 2. Analytical data of products 4aa-fe.



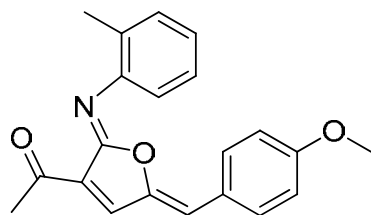
#### 1-(5-(4-Methoxybenzylidene)-2-(phenylimino)-2,5-dihydrofuran-3-yl)ethanone (**4aa**)

Orange solid; m.p. 133-134 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.74 (s, 3H), 3.84 (s, 3H), 6.03 (s, 1H), 6.85 (d,  $J = 9.0$  Hz, 2H), 7.17-7.22 (m, 1H), 7.42 (m, 4H), 7.64 (d,  $J = 9.0$  Hz, 2H), 7.73 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  29.7, 55.3, 113.8, 114.4, 123.5, 124.8, 126.4, 128.7, 131.9, 132.1, 141.6, 145.8, 148.5, 154.7, 160.5, 193.3; IR (KBr,  $\text{cm}^{-1}$ ): 2924, 2854, 1668, 1543, 1290, 1166, 769, 606; Anal. Calcd for  $\text{C}_{20}\text{H}_{17}\text{NO}_3$ : C, 75.22; H, 5.37; N, 4.39; Found: C, 75.43; H, 5.29; N, 4.26.



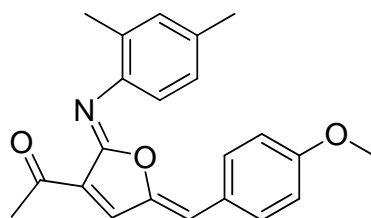
#### 1-(5-(4-Methoxybenzylidene)-2-(*p*-tolylimino)-2,5-dihydrofuran-3-yl)ethanone (**4ba**)

Orange solid; m.p. 155-156 °C;  $^1\text{H}$  NMR (400 MHz, DMSO):  $\delta$  2.35 (s, 3H), 2.62 (s, 3H), 3.81 (s, 3H), 6.41 (s, 1H), 6.98 (d,  $J = 8.8$  Hz, 2H), 7.25-7.30 (m, 4H), 7.69 (d,  $J = 8.8$  Hz, 2H), 8.10 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  21.1, 29.9, 55.4, 113.4, 114.5, 123.8, 126.5, 129.4, 131.8, 132.4, 134.7, 141.3, 142.9, 148.7, 154.1, 160.4, 193.6; IR (KBr,  $\text{cm}^{-1}$ ): 2923, 2854, 1677, 1658, 1600, 1542, 1257, 1165, 821; Anal. Calcd for  $\text{C}_{21}\text{H}_{19}\text{NO}_3$ : C, 75.66; H, 5.74; N, 4.20; Found: C, 76.31; H, 5.83; N, 4.35.



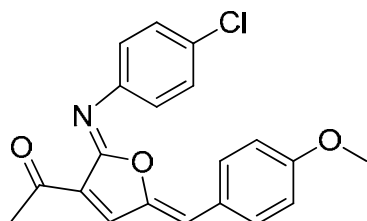
**1-(5-(4-Methoxybenzylidene)-2-(*o*-tolylimino)-2,5-dihydrofuran-3-yl)ethanone (4ca)**

Orange solid: m.p. 129-130 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.35 (s, 3H), 2.77 (s, 3H), 3.82 (s, 3H), 6.02 (s, 1H), 6.83 (d, *J* = 9.0 Hz, 2H), 7.08-7.13 (m, 1H), 7.21-7.27 (m, 2H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.60 (d, *J* = 9.0 Hz, 2H), 7.74 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 18.5, 29.7, 30.0, 55.3, 113.8, 114.4, 121.4, 124.7, 125.9, 126.4, 130.4, 131.9, 132.0, 141.7, 144.6, 148.5, 154.1, 160.4, 193.4; IR (KBr, cm<sup>-1</sup>): 2924, 2854, 1660, 1542, 1253, 1167, 830; Anal. Calcd for C<sub>21</sub>H<sub>19</sub>NO<sub>3</sub>: C, 75.66; H, 5.74; N, 4.20; Found: C, 75.01; H, 5.63; N, 4.07.



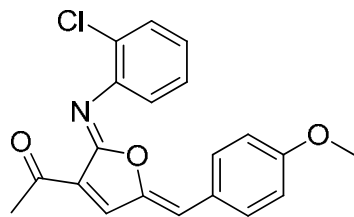
**1-(2-(2,4-Dimethylphenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4da)**

Orange solid: m.p. 112-113 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.33 (s, 3H), 2.37 (s, 3H), 2.76 (s, 3H), 3.83 (s, 3H), 6.00 (s, 1H), 6.86 (d, *J* = 9.0 Hz, 2H), 7.08 (t, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 9.0 Hz, 2H), 7.72 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 18.5, 21.0, 30.00, 55.3, 113.4, 114.4, 121.4, 126.5, 131.2, 131.8, 132.2, 132.7, 134.4, 141.3, 141.6, 148.6, 153.6, 160.3, 193.6; IR (KBr, cm<sup>-1</sup>): 2922, 2854, 1663, 1540, 1249, 1165, 972, 815; Anal. Calcd for C<sub>22</sub>H<sub>21</sub>NO<sub>3</sub>: C, 76.06; H, 6.09; N, 4.03; Found: C, 75.55; H, 6.15; N, 4.16.



**1-(2-(4-Chlorophenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4ea)**

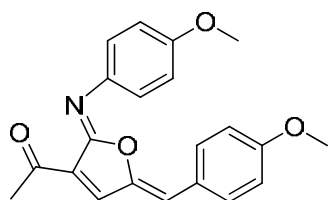
Orange solid: m.p. 152-153 °C; <sup>1</sup>H NMR (400 MHz, DMSO): δ 2.61 (s, 3H), 3.81 (s, 3H), 6.46 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 2H), 8.14 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.8, 55.4, 114.4, 114.5, 124.9, 126.2, 128.8, 130.0, 131.9, 141.9, 144.3, 148.3, 155.0, 160.7, 193.1; IR (KBr, cm<sup>-1</sup>): 2924, 2853, 1662, 1584, 1257, 1169, 998, 806; Anal. Calcd for C<sub>20</sub>H<sub>16</sub>ClNO<sub>3</sub>: C, 67.90; H, 4.56; N, 3.96; Found: C, 68.54; H, 4.48; N, 4.21.



**1-(2-(2-Chlorophenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fa)**

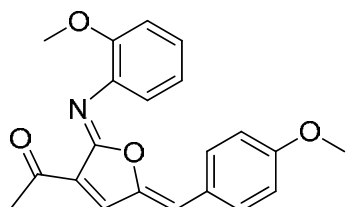
Orange solid: m.p. 169-170 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.79 (s, 3H), 3.83 (s, 3H), 6.08 (s, 1H), 6.83(d, *J* = 9.0 Hz, 2H), 7.09-7.15 (m, 1H), 7.28-7.31 (m, 1H), 7.43-7.47 (m, 2H), 7.57 (d, *J* = 9.0 Hz, 2H), 7.77 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.7, 30.0, 55.3, 114.4, 114.9, 123.1, 125.4, 126.2, 126.9, 129.9, 131.6, 132.1, 142.3, 143.4, 148.3, 160.6, 193.3; IR (KBr, cm<sup>-1</sup>): 2924, 2854, 1660, 1540, 1254, 1166, 869, 756; Anal. Calcd for C<sub>20</sub>H<sub>16</sub>ClNO<sub>3</sub>: C, 67.90; H, 4.56; N, 3.96; Found: C, 67.03; H, 4.42; N, 4.01.

Crystal data for **4fa**: C<sub>20</sub>H<sub>16</sub>ClNO<sub>3</sub>, Red crystal, *M* = 353.08, Orthorhombic, Pca21, *a* = 13.1628(8) Å, *b* = 11.5556(7) Å, *c* = 22.0722(13) Å, α = 90.00°, β = 90.00°, γ = 90.00°, *V* = 3357.3(3) Å<sup>3</sup>, *Z* = 8, *T* = 293(2) K, F<sub>000</sub> = 1569. CCDC deposition number: 794625. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).



**1-(5-(4-Methoxybenzylidene)-2-((4-methoxyphenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ga)**

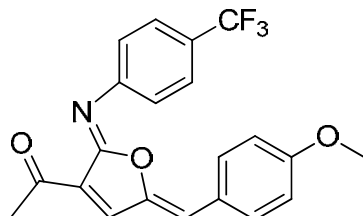
Red solid: m.p. 126-128 °C; <sup>1</sup>H NMR (300 MHz, DMSO): δ 2.62 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 6.36 (s, 1H), 7.01 (d, *J* = 4.8 Hz, 2H), 7.04 (d, *J* = 4.8 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 2H), 7.72 (d, *J* = 9.0 Hz, 2H), 8.07 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.5, 55.3, 55.4, 113.2, 114.1, 114.6, 125.1, 126.2, 131.2, 131.5, 138.1, 141.9, 148.4, 153.2, 156.7, 160.0, 192.5; Anal. Calcd for C<sub>21</sub>H<sub>19</sub>NO<sub>4</sub>: C, 72.19; H, 5.48; N, 4.01; Found: C, 73.01; H, 5.32; N, 4.11.



**1-(5-(4-Methoxybenzylidene)-2-((2-methoxyphenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ha)**

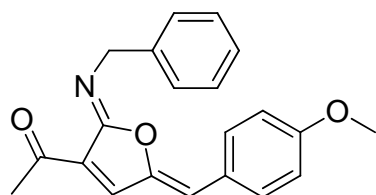
Red solid: m.p. 155-157 °C; <sup>1</sup>H NMR (300 MHz, DMSO): δ 2.62 (s, 3H), 3.76 (s, 3H), 3.78 (s, 3H),

6.38(s, 1H), 6.89 (d,  $J = 8.7$  Hz, 2H), 6.98-7.03 (m, 1H), 7.11-7.20 (m, 3H), 7.54 (d,  $J = 8.7$  Hz, 2H), 8.11(s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  29.4, 55.3, 55.4, 111.9, 113.7, 114.4, 120.4, 122.4, 125.2, 126.1, 130.0, 131.7, 135.3, 143.0, 148.0, 150.9, 154.8, 160.0, 192.2; Anal. Calcd for  $\text{C}_{21}\text{H}_{19}\text{NO}_4$ : C, 72.19; H, 5.48; N, 4.01; Found: C, 72.77; H, 5.36; N, 4.17.



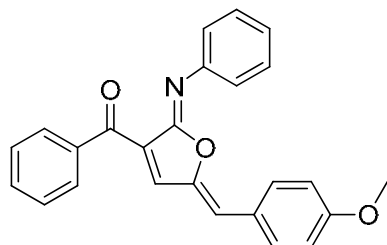
**1-(5-(4-Methoxybenzylidene)-2-((4-(trifluoromethyl)phenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ia)**

Red solid: m.p. 120-122 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.72 (s, 3H), 3.84 (s, 3H), 6.09(s, 1H), 6.85(d,  $J = 9.0$  Hz, 2H), 7.42(d,  $J = 9.0$  Hz, 2H), 7.58(d,  $J = 9.0$  Hz, 2H), 7.67(d,  $J = 9.0$  Hz, 2H), 7.78(s, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO):  $\delta$  29.4, 55.3, 114.6, 115.2, 123.3, 124.5 (q,  $^2J_{\text{CF}} = 31$  Hz), 124.7 (q,  $^1J_{\text{CF}} = 270$  Hz), 126.0 (d,  $^3J_{\text{CF}} = 3$  Hz), 130.2, 131.9, 143.7, 147.9, 149.6, 155.8, 160.3, 191.9; Anal. Calcd for  $\text{C}_{21}\text{H}_{16}\text{F}_3\text{NO}_3$ : C, 65.12; H, 4.16; N, 3.62; Found: C, 64.82; H, 4.09; N, 3.30.



**1-(2-(Benzylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4ja)**

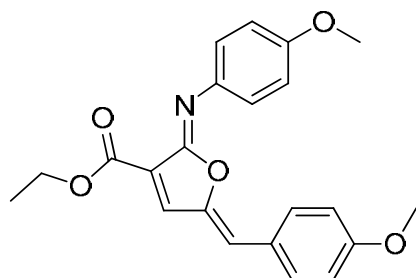
Orange solid: m.p. 76-78 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.68 (s, 3H), 3.87 (s, 3H), 4.90 (s, 2H), 6.20 (s, 1H), 6.97 (d,  $J = 9.0$  Hz, 2H), 7.30 (s, 1H), 7.37 (t,  $J = 7.5$  Hz, 2H), 7.49 (d,  $J = 7.5$  Hz, 2H), 7.70 (d,  $J = 9.0$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  29.6, 51.9, 55.0, 112.4, 113.7, 114.2, 126.4, 127.2, 128.1, 128.3, 131.6, 141.5, 159.9, 193.2; Anal. Calcd for  $\text{C}_{21}\text{H}_{19}\text{NO}_3$ : C, 75.66; H, 5.74; N, 4.20; Found: C, 75.87; H, 5.68; N, 4.15.



**(5-(4-Methoxybenzylidene)-2-(phenylimino)-2,5-dihydrofuran-3-yl)(phenyl)methanone (4ka)**

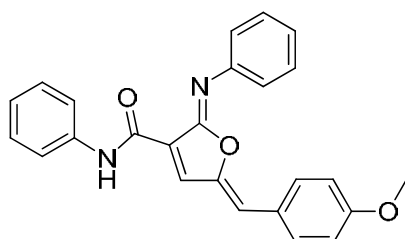
Red solid: m.p. 133-134 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.84 (s, 3H), 5.99 (s, 1H), 6.86 (d,  $J = 8.0$  Hz, 2H), 7.17 (q,  $J = 4.0$  Hz, 1H), 7.38 (d,  $J = 4.0$  Hz, 4H), 7.45 (s, 1H), 7.51 (t,  $J = 8.0$  Hz, 2H), 7.61-7.66 (m, 3H), 7.99 (d,  $J = 8.0$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.3, 112.6, 114.4, 123.6, 124.8, 126.4, 128.4, 128.6, 129.8, 131.6, 132.0, 133.5, 137.0, 141.0, 145.8, 148.7, 154.9, 160.3, 188.8; Anal. Calcd for  $\text{C}_{25}\text{H}_{19}\text{NO}_3$ : C, 78.72; H, 5.02; N, 3.67; Found: C,

78.53; H, 5.11; N, 3.49.



**Ethyl 5-(4-methoxybenzylidene)-2-((4-methoxyphenyl)imino)-2,5-dihydrofuran-3-carboxylate (4la)**

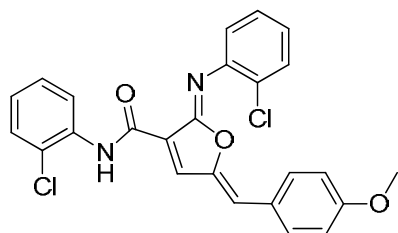
Orange solid; m.p. 140-142 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.40 (t, *J* = 7.2 Hz, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 4.39 (q, *J* = 7.2 Hz, 2H), 5.96 (s, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 14.2, 55.4(1), 55.4(2), 61.3, 112.6, 113.8, 114.4, 125.0, 125.4, 126.4, 131.6, 139.0, 142.4, 148.4, 157.0, 160.3, 161.0; Anal. Calcd for C<sub>22</sub>H<sub>21</sub>NO<sub>5</sub>: C, 69.64; H, 5.58; N, 3.69; Found: C, 70.07; H, 5.61; N, 3.53.



**5-(4-Methoxybenzylidene)-N-phenyl-2-(phenylimino)-2,5-dihydrofuran-3-carboxamide (4ma)**

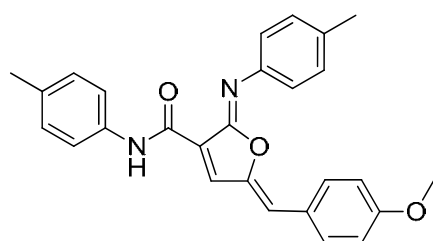
Orange solid; m.p. 214-215 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 3.78 (s, 3H), 6.10 (s, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 7.08 (t, *J* = 8.0 Hz, 1H), 7.19-7.22 (m, 1H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 1H), 11.17 (s, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 55.4, 114.4, 114.5, 119.9, 124.0, 124.5, 125.7, 126.1, 127.0, 129.0, 129.0, 132.0, 138.0, 141.3, 144.1, 148.4, 156.0, 157.9, 160.7; IR (KBr, cm<sup>-1</sup>): 3482, 1784, 1677, 1600, 1510, 1498, 1255, 754; Anal. Calcd for C<sub>25</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>: C, 75.74; H, 5.08; N, 7.07. Found: C, 75.46; H, 4.89; N, 6.91.

Crystal data for **4ma**: C<sub>25</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>, Red crystal, *M* = 396.43, triclinic, P-1, *a* = 5.4633(7) Å, *b* = 11.7064(14) Å, *c* = 15.7002(19) Å, α = 86.485(2)°, β = 85.610(2)°, γ = 81.447(2)°, *V* = 988.8(2) Å<sup>3</sup>, *Z* = 2, *T* = 293(2) K, *F*(000) = 296. CCDC deposition number: 884905. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).



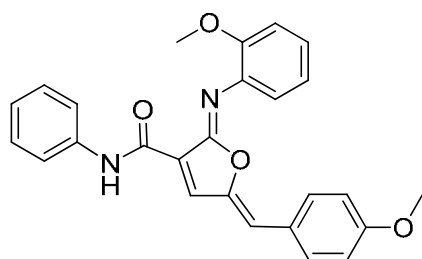
***N*-(2-chlorophenyl)-2-((2-chlorophenyl)imino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-carboxamide (4na)**

Orange solid: m.p. 203-204 °C; <sup>1</sup>H NMR (400 MHz, DMSO): δ 3.79 (s, 3H), 6.62 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.53-7.62 (m, 5H), 8.37 (s, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 11.08 (s, 1H); <sup>13</sup>C NMR (100 MHz, DMSO): δ 55.4, 114.7, 116.2, 122.1, 123.0, 123.7, 124.9, 125.5, 126.3, 127.7, 127.8, 129.5, 129.8, 132.2, 134.5, 144.2, 150.7, 157.1, 157.5, 160.6; Anal. Calcd for C<sub>25</sub>H<sub>18</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>: C, 64.53; H, 3.90; N, 6.02; Found: C, 64.81; H, 3.75; N, 5.86.



**5-(4-Methoxybenzylidene)-*N*-(*p*-tolyl)-2-(*p*-tolylimino)-2,5-dihydrofuran-3-carboxamide (4oa)**

Orange solid: m.p. 191-193 °C; <sup>1</sup>H NMR (300 MHz, DMSO): δ 2.30 (s, 3H), 2.38 (s, 3H), 3.83 (s, 3H), 6.55 (s, 1H), 7.06 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 9.0 Hz, 2H), 7.34 (d, *J* = 9.0 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.63 (d, *J* = 9.0 Hz, 2H), 7.75 (d, *J* = 9.0 Hz, 2H), 8.20 (s, 1H), 11.08 (s, 1H); <sup>13</sup>C NMR (100 MHz, DMSO): δ 19.5, 19.7, 54.8, 113.2, 114.2, 119.1, 123.0, 125.4, 126.2, 128.6, 128.7, 130.9, 132.8, 134.3, 134.8, 140.5, 140.8, 147.8, 154.6, 156.5, 159.9; Anal. Calcd for C<sub>27</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>: C, 76.39; H, 5.70; N, 6.60; Found: C, 76.25; H, 5.79; N, 6.77.

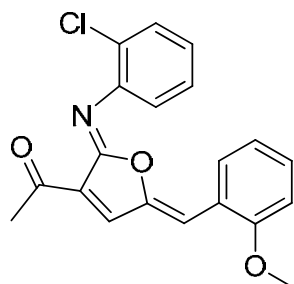


**5-(4-Methoxybenzylidene)-2-((2-methoxyphenyl)imino)-*N*-phenyl-2,5-dihydrofuran-3-carboxamide (4pa)**

Orange solid: m.p. 209-210 °C; <sup>1</sup>H NMR (400 MHz, DMSO): δ 3.83 (s, 3H), 3.92 (s, 3H), 6.57 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 7.11-7.21 (m, 3H), 7.27-7.31 (m, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.73-7.75 (m, 5H), 8.22 (s, 1H), 11.60 (s, 1H); <sup>13</sup>C NMR (100 MHz, DMSO): δ 55.0, 55.5, 112.2, 113.9, 114.3, 119.0, 120.2, 122.5, 123.6, 125.5, 125.9, 126.2, 128.5, 131.3, 137.7, 141.0, 148.0, 152.8, 154.8, 156.9, 160.0; Anal. Calcd for C<sub>26</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: C, 73.23; H, 5.20; N, 6.57; Found: C,

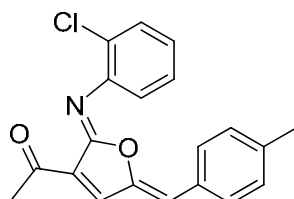


72.59; H, 5.12; N, 6.73.



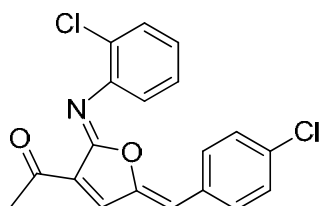
**1-(2-((2-Chlorophenyl)imino)-5-(2-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fb)**

Red solid: m.p. 147-149 °C;  $^1\text{H NMR}$  (400 MHz, DMSO):  $\delta$  2.65 (s, 3H), 3.85 (s, 3H), 6.79 (s, 1H), 6.82 (t,  $J = 8.0$  Hz, 1H), 7.07(d,  $J = 8.0$  Hz, 1H), 7.18-7.22 (m, 1H), 7.31-7.35 (m, 1H), 7.39-7.44 (m, 2H), 7.55 (d,  $J = 8.0$  Hz, 1H), 7.71 (d,  $J = 8.0$  Hz, 1H), 8.33 (s, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  29.7, 30.0, 55.6, 108.6, 110.6, 121.0, 122.4, 123.1, 125.4, 126.9, 129.8, 130.7, 130.9, 132.1, 142.7, 143.3, 149.5, 157.6, 193.3; IR (KBr,  $\text{cm}^{-1}$ ): 2924, 2853, 1668, 1555, 1248, 1021, 750; Anal. Calcd for  $\text{C}_{20}\text{H}_{16}\text{ClNO}_3$ : C, 67.90; H, 4.56; N, 3.96. Found: C, 69.77; H, 4.62; N, 3.82.



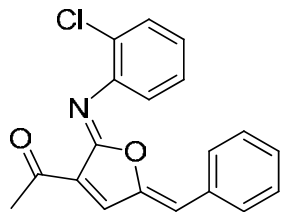
**1-(2-((2-Chlorophenyl)imino)-5-(4-methylbenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fc)**

Red solid: m.p. 111-113 °C;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.35 (s, 3H), 2.80 (s, 3H), 6.10 (s, 1H), 7.11-7.16(m, 3H), 7.28-7.34(m, 1H), 7.44-7.50(m, 3H), 7.53(s, 1H), 7.79(s, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  21.5, 30.0, 114.9, 123.1, 125.5, 126.9, 129.6, 129.9, 130.3, 132.4, 140.0, 142.3, 143.4, 149.7, 155.6, 193.2; Anal. Calcd for  $\text{C}_{20}\text{H}_{16}\text{ClNO}_2$ : C, 71.11; H, 4.77; N, 4.15. Found: C, 70.81; H, 4.85; N, 4.29.



**1-(5-(4-Chlorobenzylidene)-2-((2-chlorophenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4fd)**

Orange solid: m.p. 127-129 °C;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.79 (s, 3H), 6.05 (s, 1H), 7.11-7.17 (m, 1H), 7.25-7.28 (m, 2H), 7.31-7.34 (m, 1H), 7.38-7.42 (m, 1H), 7.46-7.49 (m, 2H), 7.52 (s, 1H), 7.78 (s, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  30.1, 113.0, 122.9, 125.8, 127.0, 129.1, 130.0, 131.3, 131.7, 133.1, 135.2, 142.0, 143.2, 149.9, 155.2, 193.0; Anal. Calcd for  $\text{C}_{19}\text{H}_{13}\text{Cl}_2\text{NO}_2$ : C, 63.71; H, 3.66; N, 3.91; Found: C, 63.06; H, 3.41; N, 4.14.



### 1-(5-Benzylidene-2-(2-chlorophenylimino)-2,5-dihydrofuran-3-yl)ethanone (**4fe**)

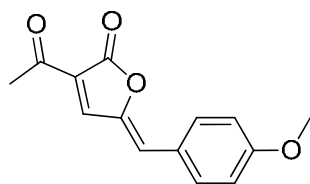
Orange solid: m.p. 109-110 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.80 (s, 3H), 6.11 (s, 1H), 7.11-7.16 (m, 1H), 7.30 (d, *J* = 3.0 Hz, 2H), 7.31-7.34 (m, 2H), 7.45-7.51 (m, 2H), 7.61 (d, *J* = 3.0 Hz, 1H), 7.63 (d, *J* = 3.0 Hz, 1H), 7.80 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 30.1, 114.6, 123.1, 125.6, 126.9, 128.2, 128.8, 129.3, 129.9, 130.3, 132.8, 133.2, 142.3, 143.2, 149.6, 155.3, 193.2; IR (KBr, cm<sup>-1</sup>): 2924, 2854, 1660, 1555, 1177, 971, 748, 680; Anal. Calcd for C<sub>22</sub>H<sub>23</sub>NO<sub>3</sub>: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.47; H, 6.75; N, 4.55.

## V. Synthesis and analytical data of products **5**

### 1. Preparation of products **5fa-pa**.

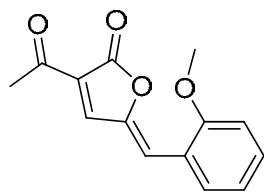
Typical procedure for the synthesis of substituted furan-2(*5H*)-ones **5** (**5fa** as an example): To a 50 mL round-bottomed flask was added 1-(2-((2-chlorophenyl)imino)-5-(2-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone **4fa** (1.0 mmol), tetrahydrofuran (5 ml), HCl (aq, 37.5 %, 2.5 mmol). Then the mixture was stirred at room temperature for 2.0 h. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL), and extracted with dichloromethane (3 × 20 mL). The combined organic phase was washed with water and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 10:1, v/v) to give 89% yield of **5fa** as yellow solid.

### 3. Analytical data of products **5fa-pa**



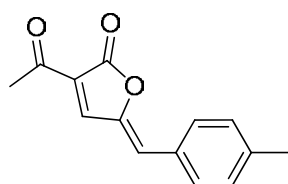
### 3-Acetyl-5-(4-methoxybenzylidene)furan-2(*5H*)-one (**5fa**)

Yellow solid: m.p. 164-166 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.60 (s, 3H), 3.88 (s, 3H), 6.30 (s, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 8.04 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.0, 55.5, 114.8, 121.1, 125.4, 131.4, 133.9, 144.8, 148.1, 161.9, 167.2, 192.0; Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>4</sub>: C, 68.85; H, 4.95; Found: C, 69.01; H, 4.87.



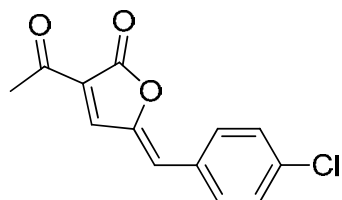
**3-Acetyl-5-(2-methoxybenzylidene)furan-2(5H)-one (5fb)**

Yellow solid: m.p. 172-175 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.60 (s, 3H), 3.91 (s, 3H), 6.92 (t, *J* = 6.0 Hz, 2H), 7.05 (t, *J* = 6.0 Hz, 1H), 7.36-7.42 (m, 1H), 8.07 (s, 1H), 8.24-8.27 (dd, *J*<sub>1</sub> = 6.0 Hz, *J*<sub>2</sub> = 3.0 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.0, 55.7, 110.7, 114.81, 121.3, 121.5, 126.1, 132.5, 145.9, 148.6, 158.34, 167.1, 191.9; IR (KBr, cm<sup>-1</sup>): 1783, 1594, 1673, 1484, 1367, 1251, 1185, 923, 760; Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>4</sub>: C, 68.85; H, 4.95; Found: C, 68.70; H, 5.03.



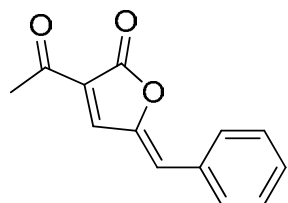
**3-Acetyl-5-(4-methylbenzylidene)furan-2(5H)-one (5fc)**

Yellow solid: m.p. 145-147 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.40 (s, 3H), 2.60 (s, 3H), 6.32 (s, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 8.05 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 21.7, 29.0, 121.0, 126.5, 129.8, 129.9, 131.8, 141.7, 145.6, 148.3, 167.0, 191.9; IR (KBr, cm<sup>-1</sup>): 1759, 1686, 1568, 1366, 1178, 1092, 810; Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>3</sub>: C, 73.67; H, 5.30; Found: C, 73.41; H, 5.24.



**3-Acetyl-5-(4-chlorobenzylidene)furan-2(5H)-one (5fd)**

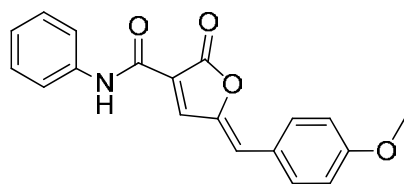
Yellow solid: m.p. 132-135 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 2.61 (s, 3H), 6.28 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 8.05 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.0, 119.0, 127.3, 129.4, 130.7, 132.7, 136.9, 146.3, 148.1, 166.6, 191.7; Anal. Calcd for C<sub>13</sub>H<sub>9</sub>ClO<sub>3</sub>: C, 62.79; H, 3.65; Found: C, 63.01; H, 3.59.



**3-Acetyl-5-benzylidenefuran-2(5H)-one (5fe)**

Yellow solid: m.p. 157-159 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.60 (s, 3H), 6.33 (s, 1H), 7.44 (d, *J* = 6.0 Hz, 3H), 7.84-7.86 (m, 2H), 8.07 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 29.1,

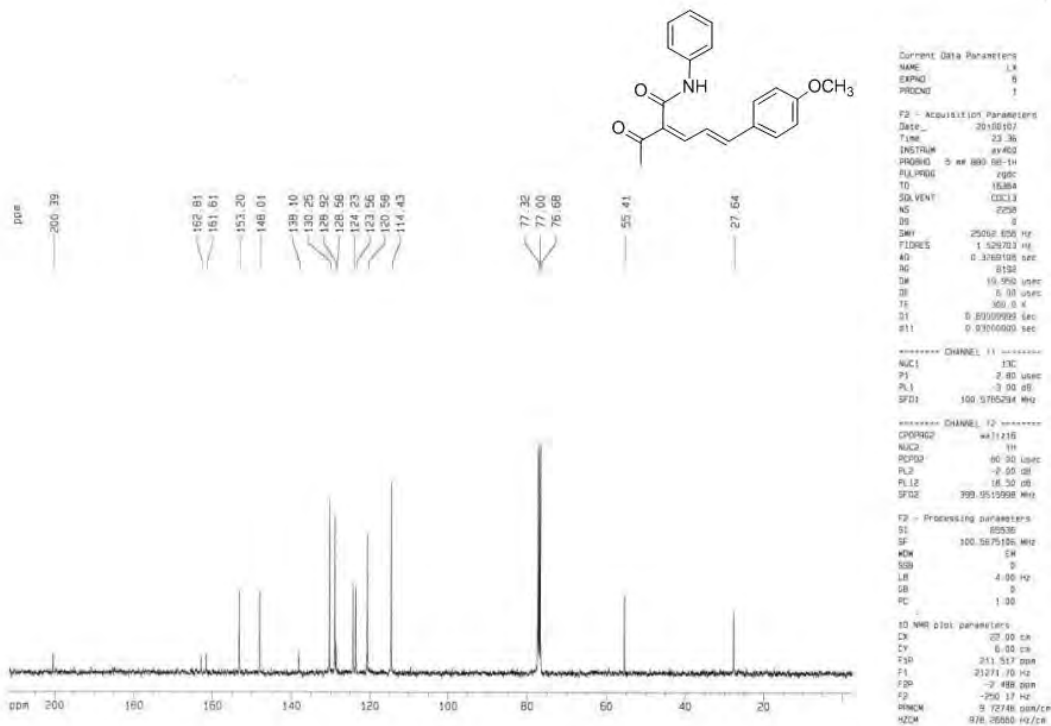
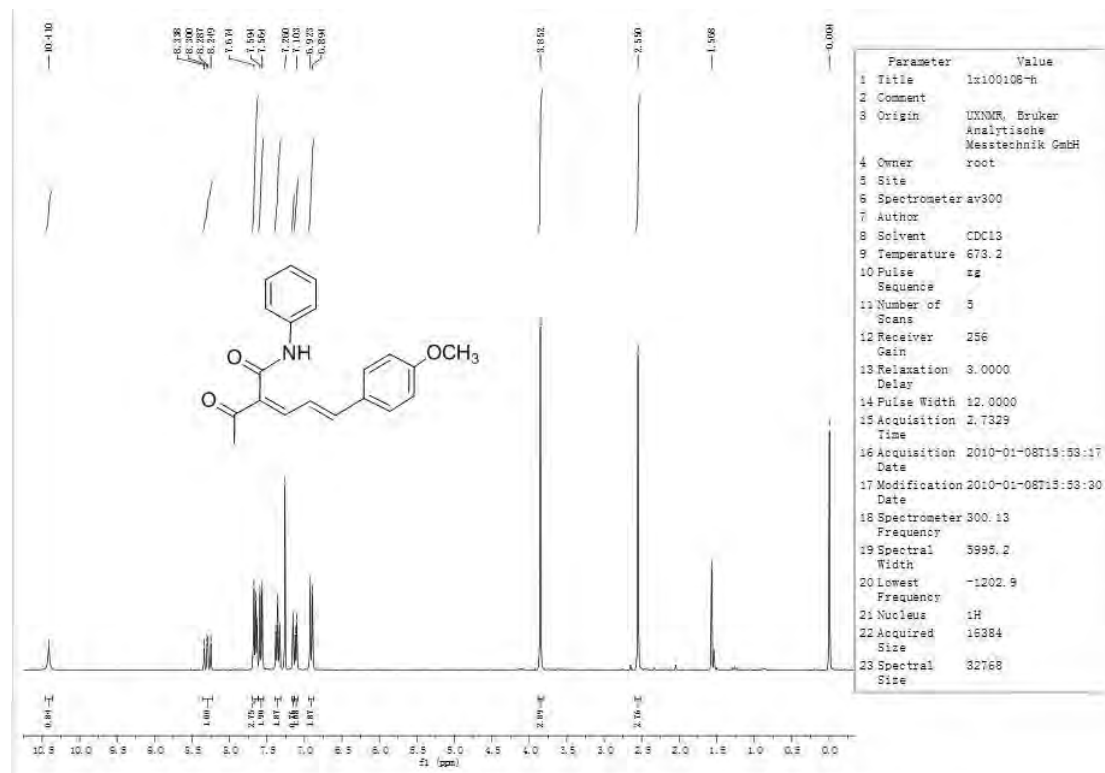
120.6, 127.1, 129.1, 130.8, 131.7, 132.4, 146.1, 148.3, 166.9, 191.8; Anal. Calcd for C<sub>13</sub>H<sub>10</sub>O<sub>3</sub>:  
C, 72.89; H, 4.71; Found: C, 72.74; H, 4.66.



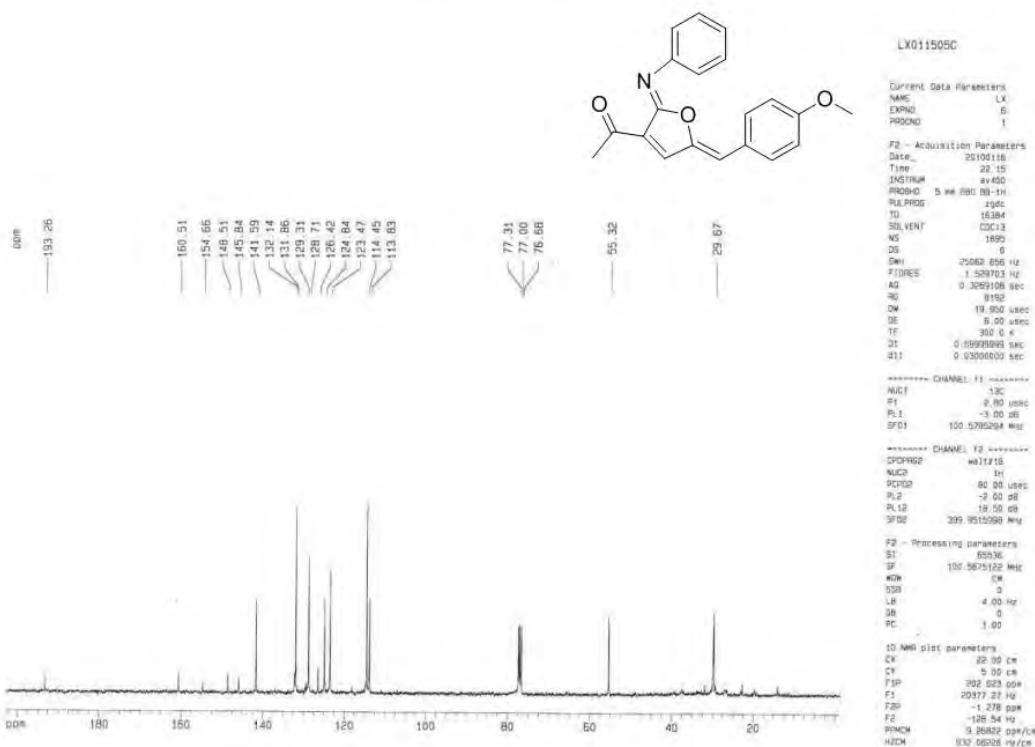
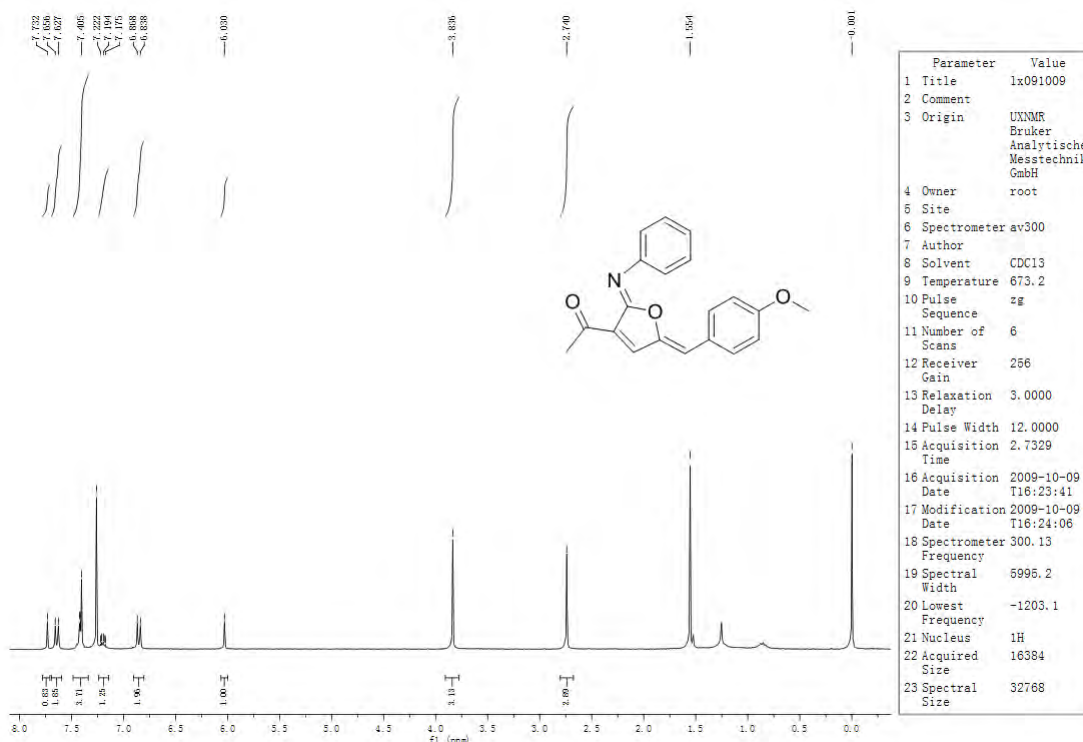
**5-(4-methoxybenzylidene)-2-oxo-N-phenyl-2,5-dihydrofuran-3-carboxamide (5pa)**

Yellow solid: m.p. 194-196 °C; <sup>1</sup>H NMR (400 MHz, DMSO): δ 3.84 (s, 3H), 6.75 (s, 1H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 8.8 Hz, 2H), 8.47 (s, 1H), 9.81 (s, 1H); <sup>13</sup>C NMR (100 MHz, DMSO): δ 55.4, 114.9, 119.5, 119.8, 121.6, 124.3, 125.2, 128.9, 133.2, 137.8, 144.5, 147.7, 157.6, 161.1, 167.6; IR (KBr, cm<sup>-1</sup>): 1784, 1776, 1601, 1498, 1252, 960, 764; Anal. Calcd for C<sub>19</sub>H<sub>15</sub>NO<sub>4</sub>: C, 71.02; H, 4.71; N, 4.36; Found: C, 70.80; H, 4.64; N, 4.51.

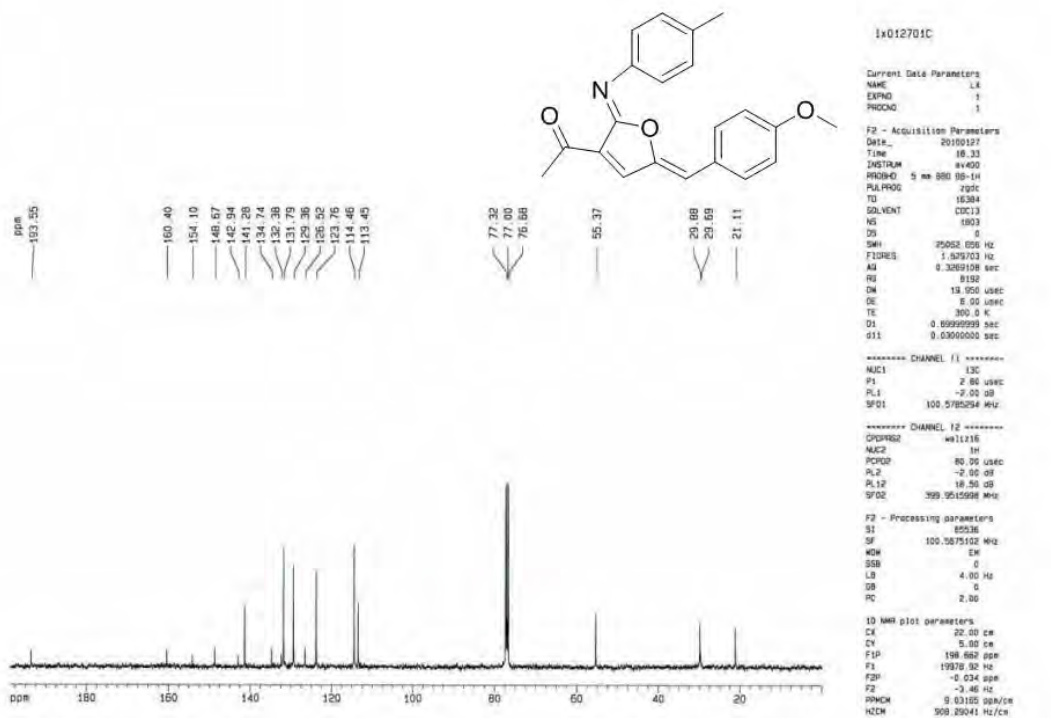
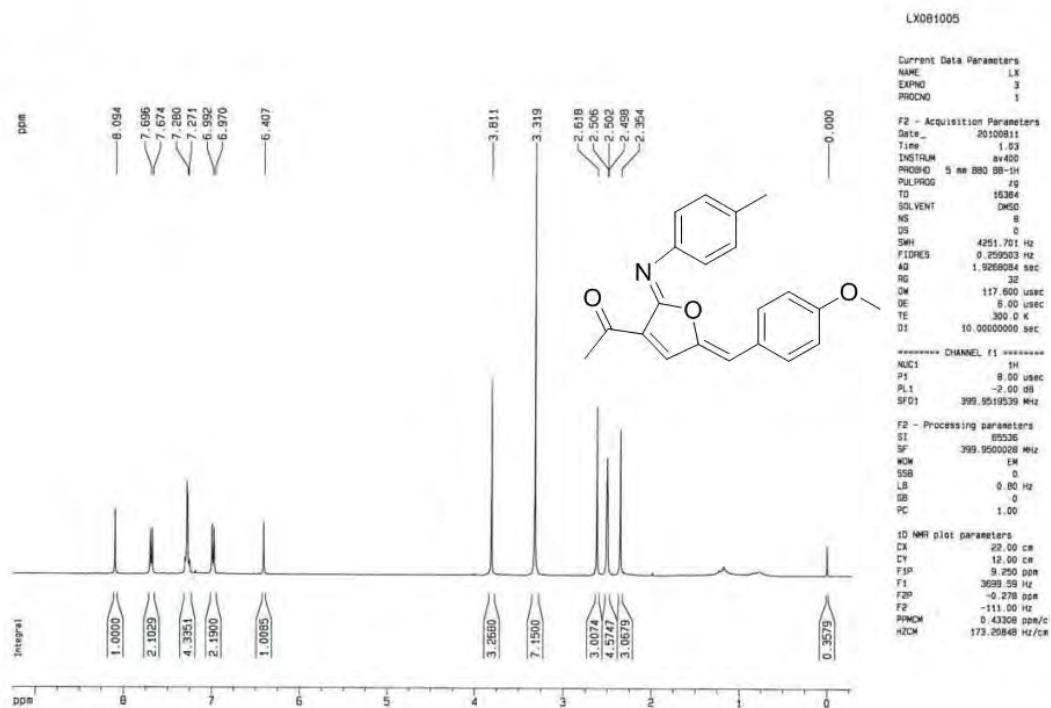
**VI. Copies of NMR spectra of substrate 3 and products 4, 5**  
**3aa**



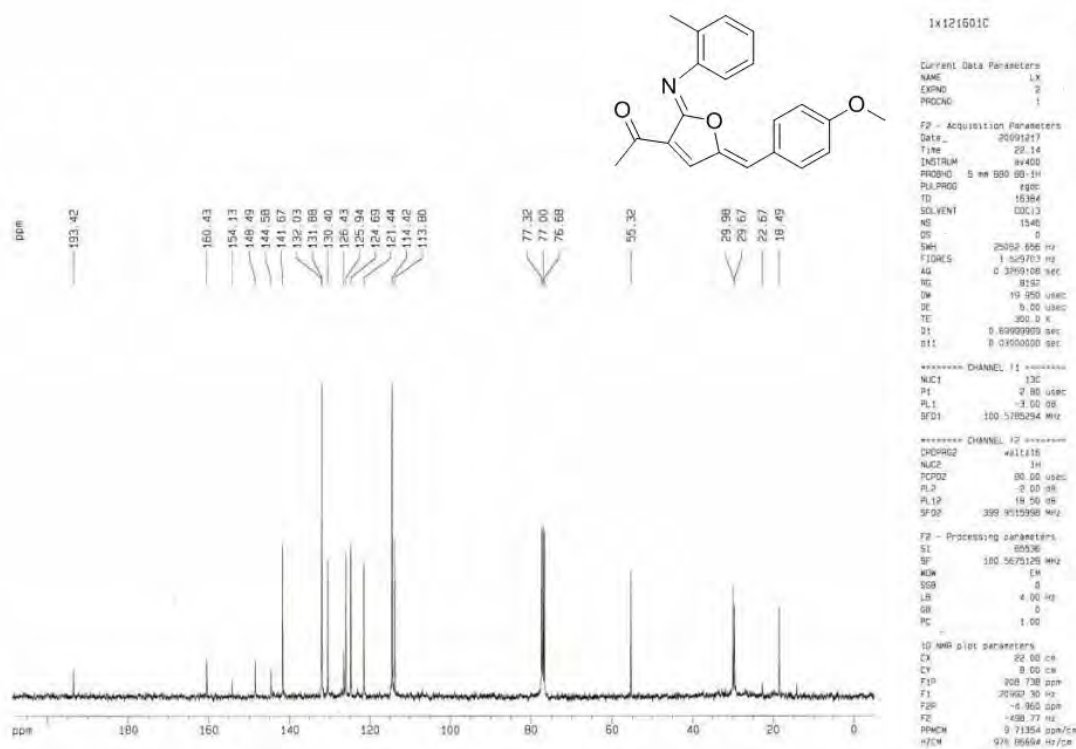
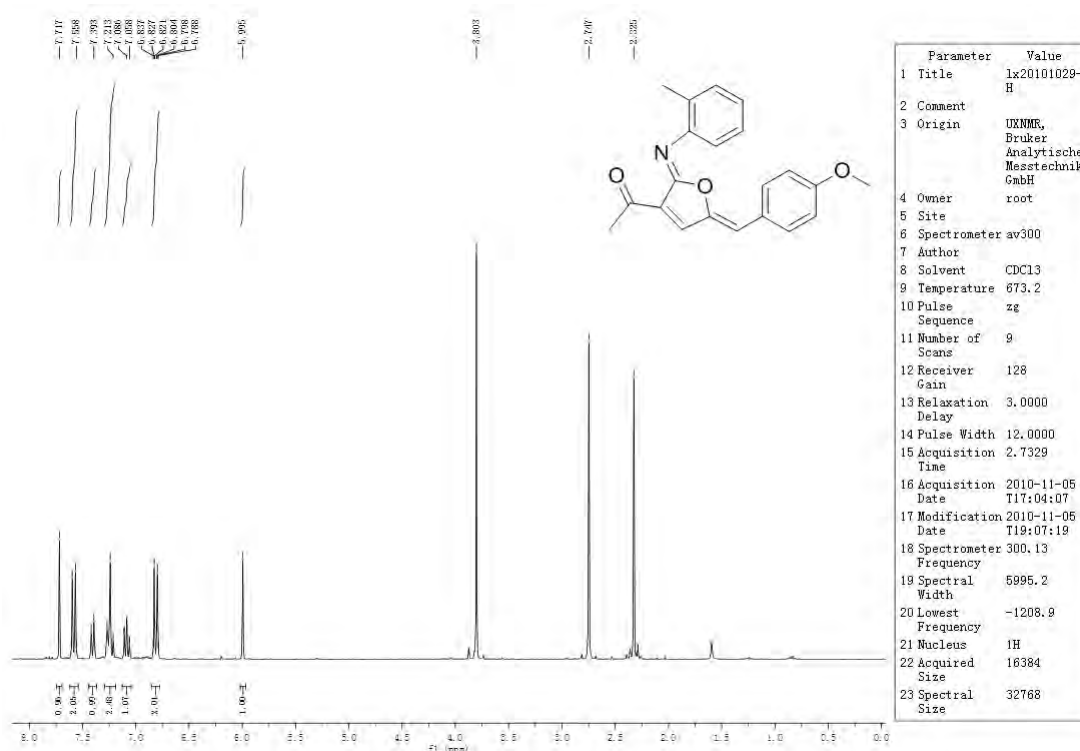
4aa



4ba

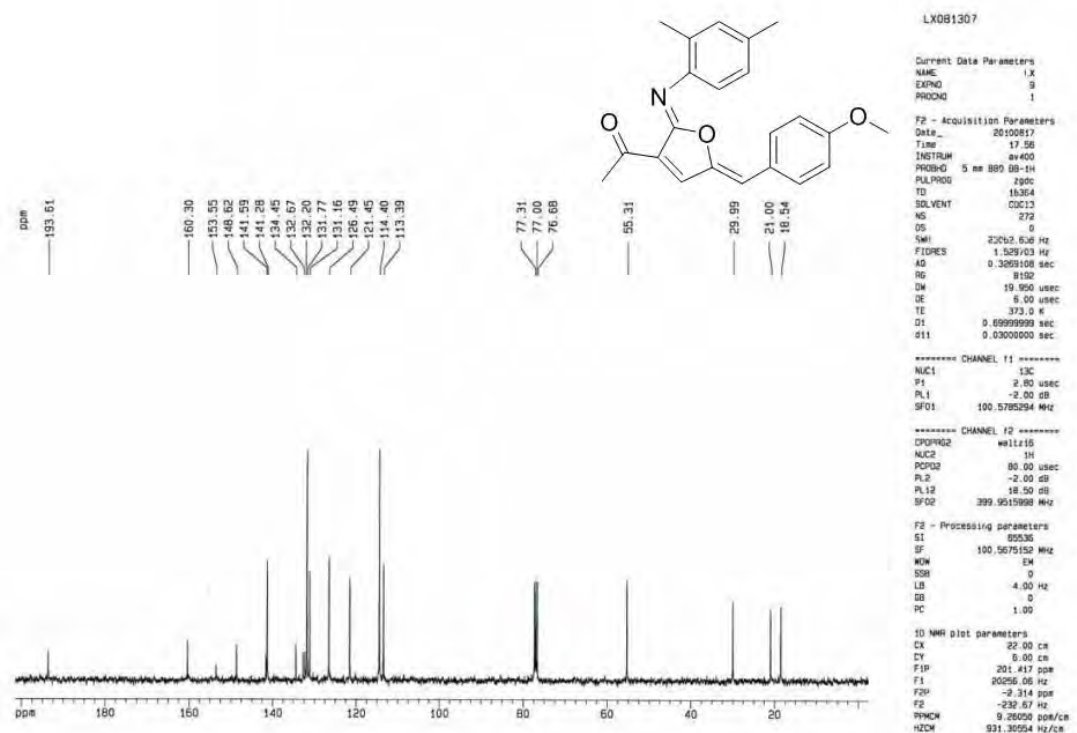
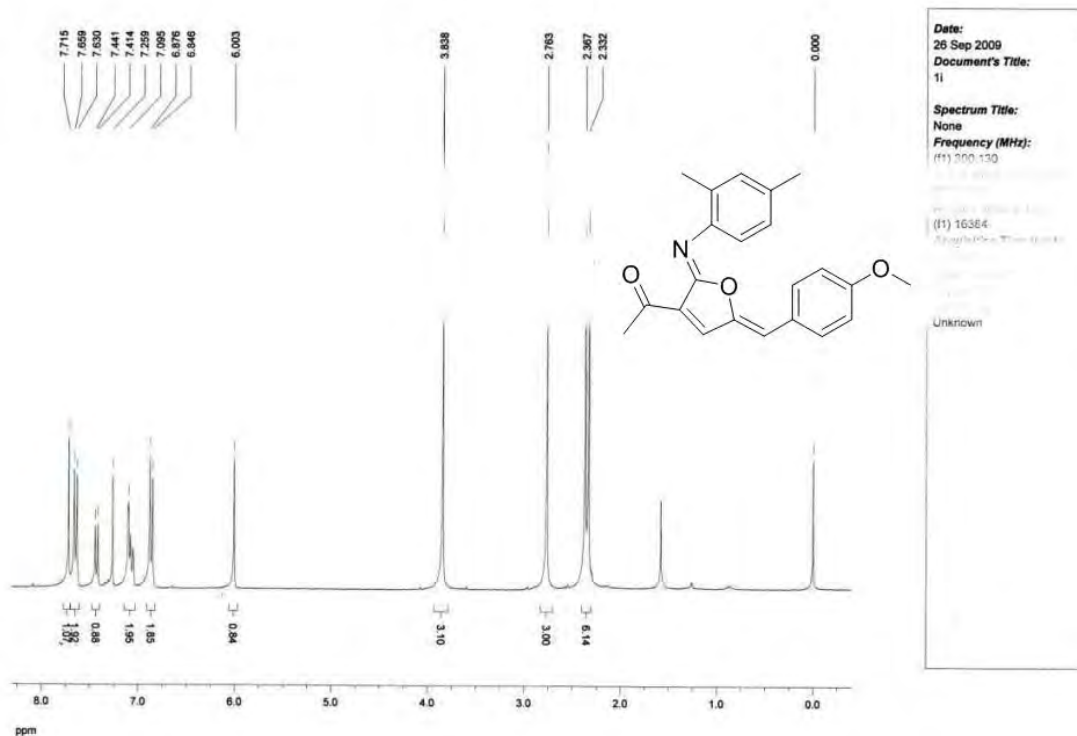


4ca

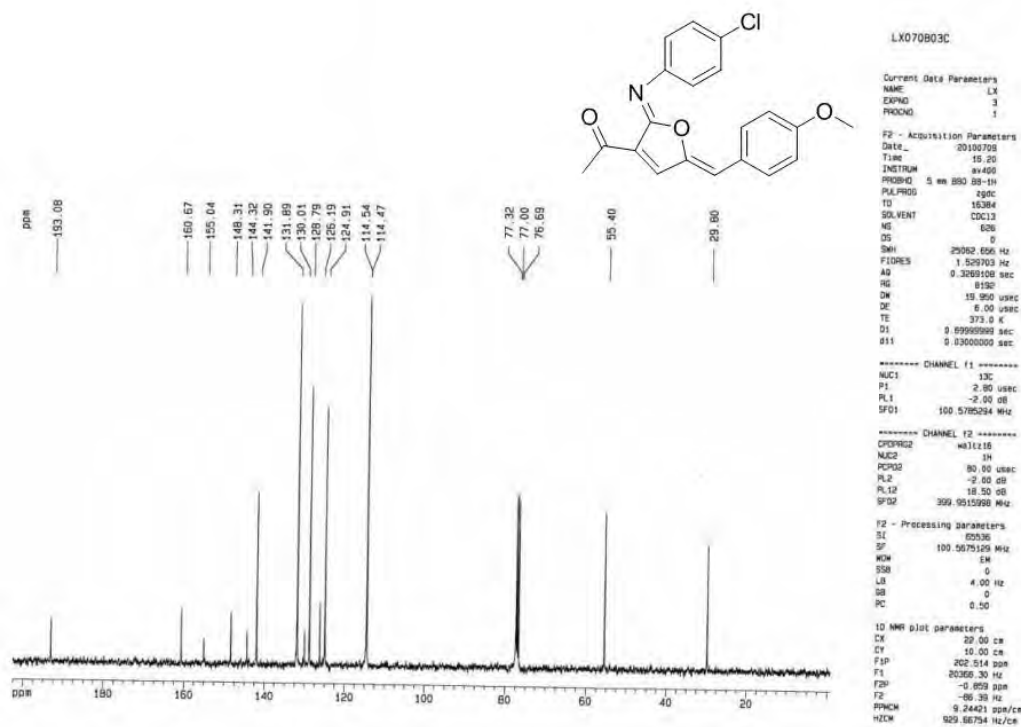
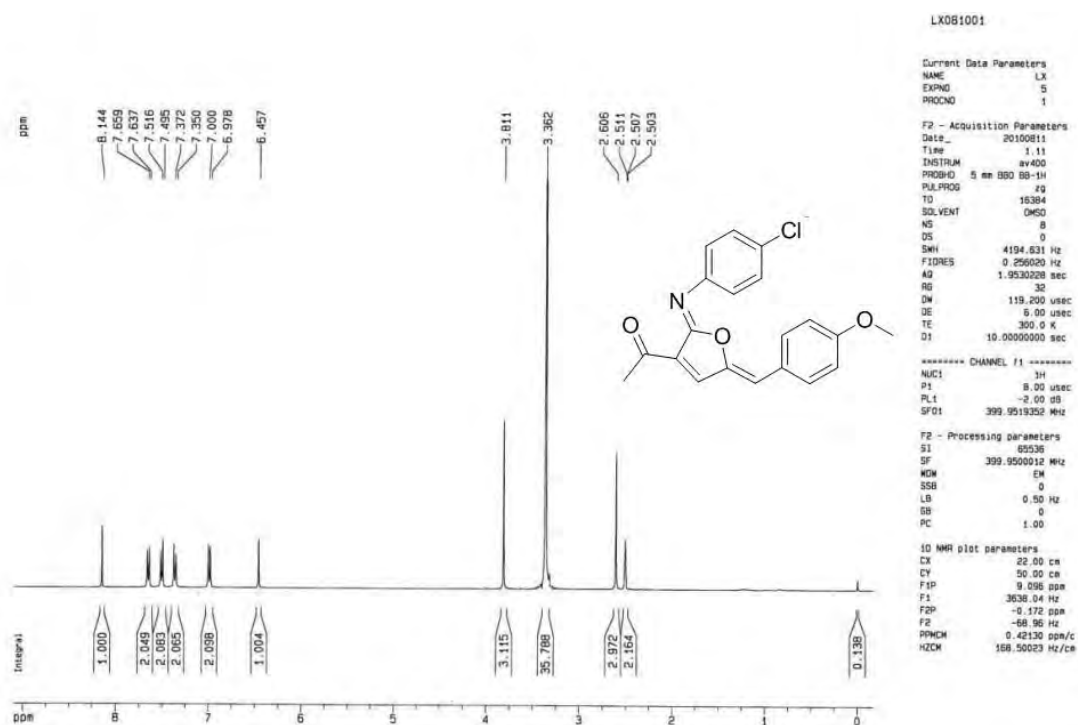




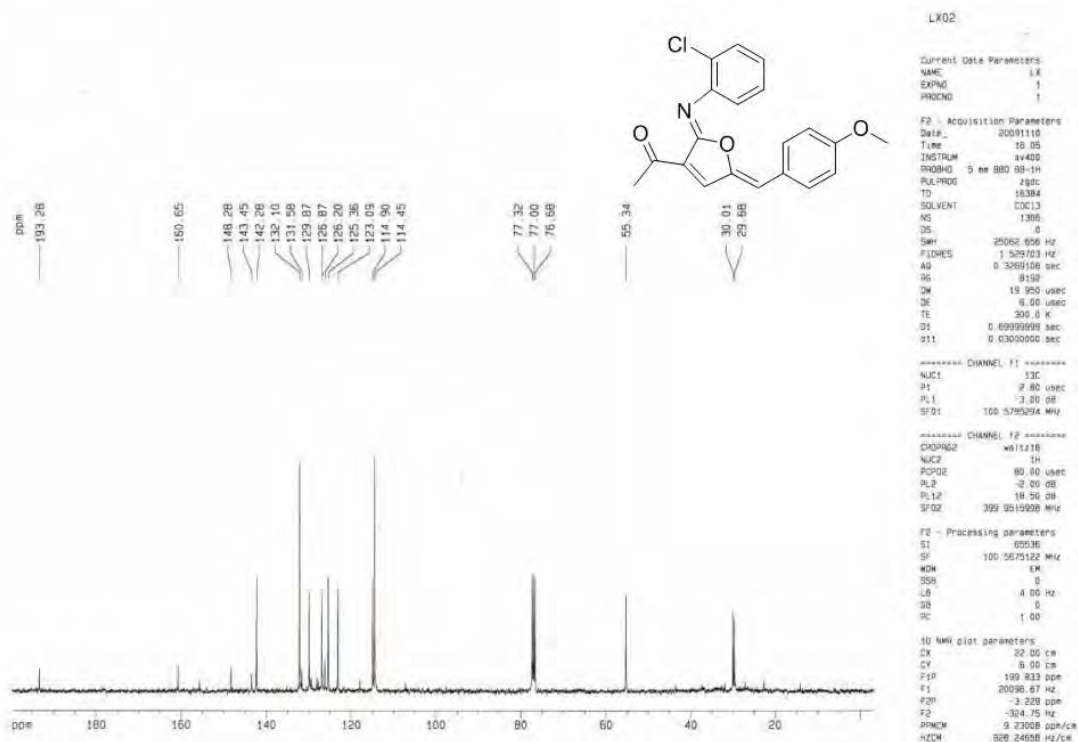
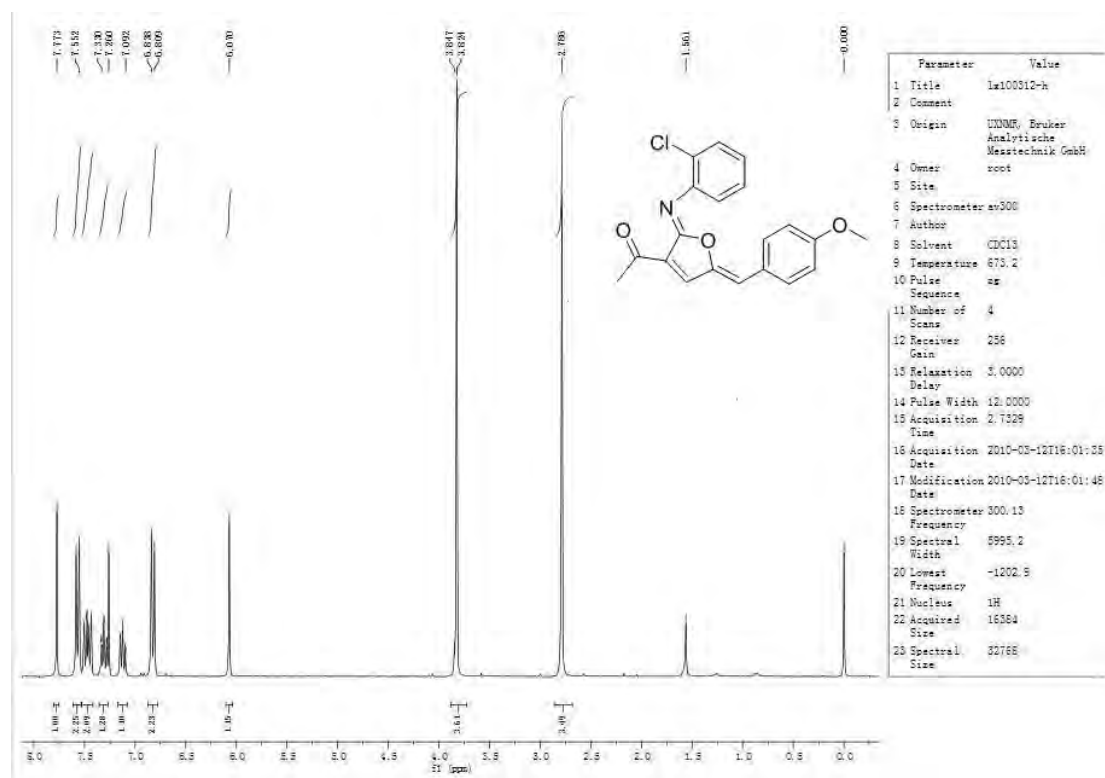
4da



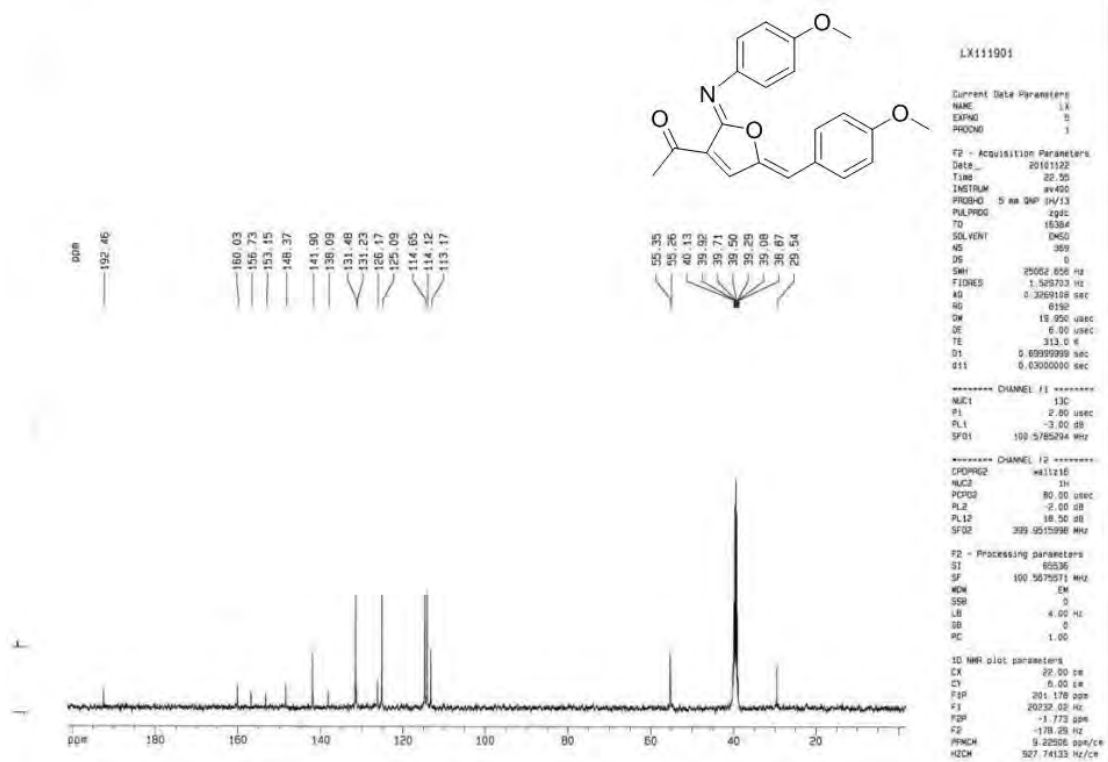
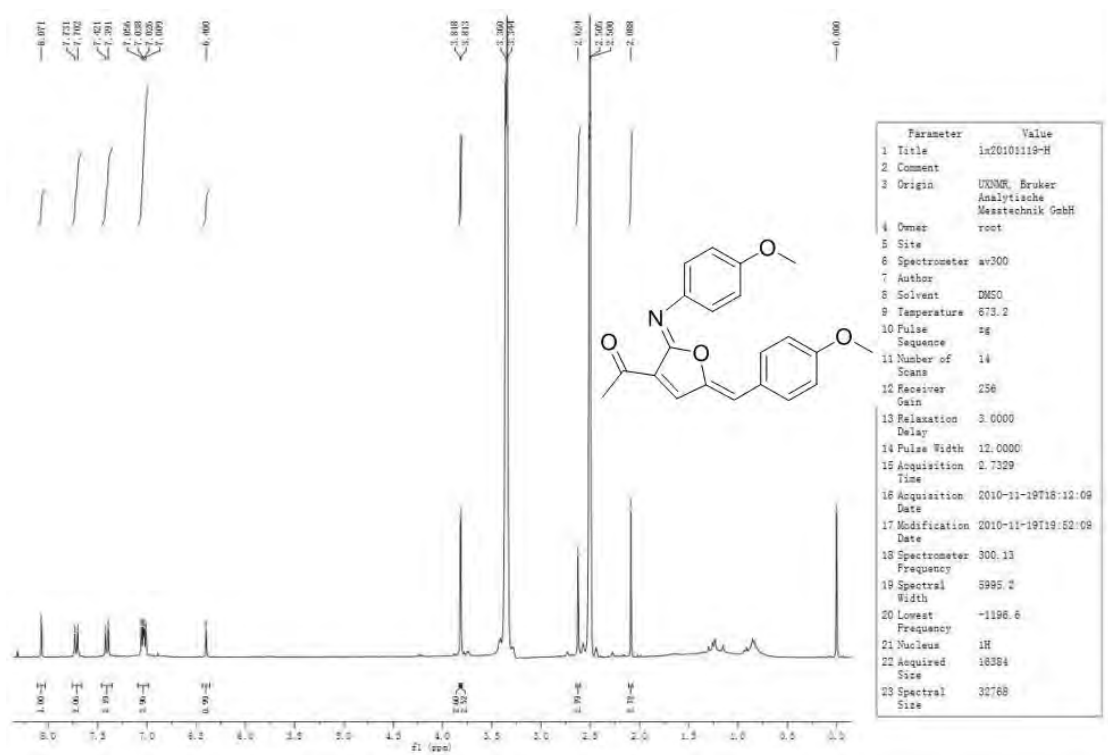
4ea



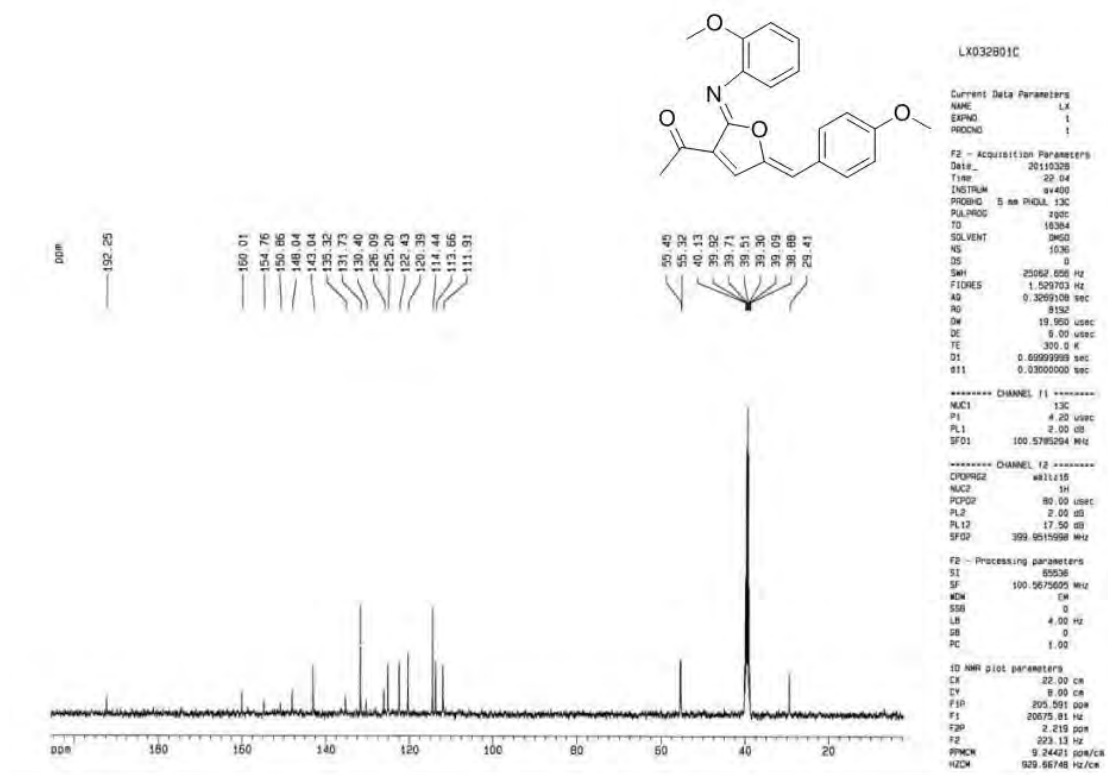
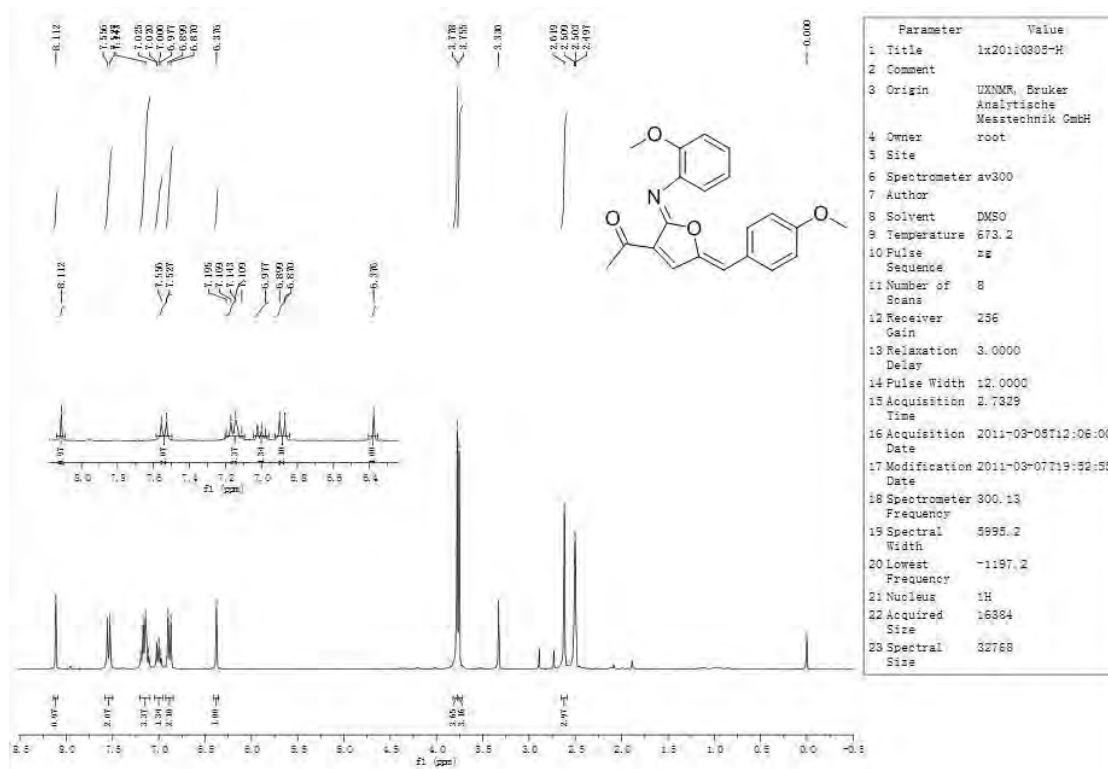
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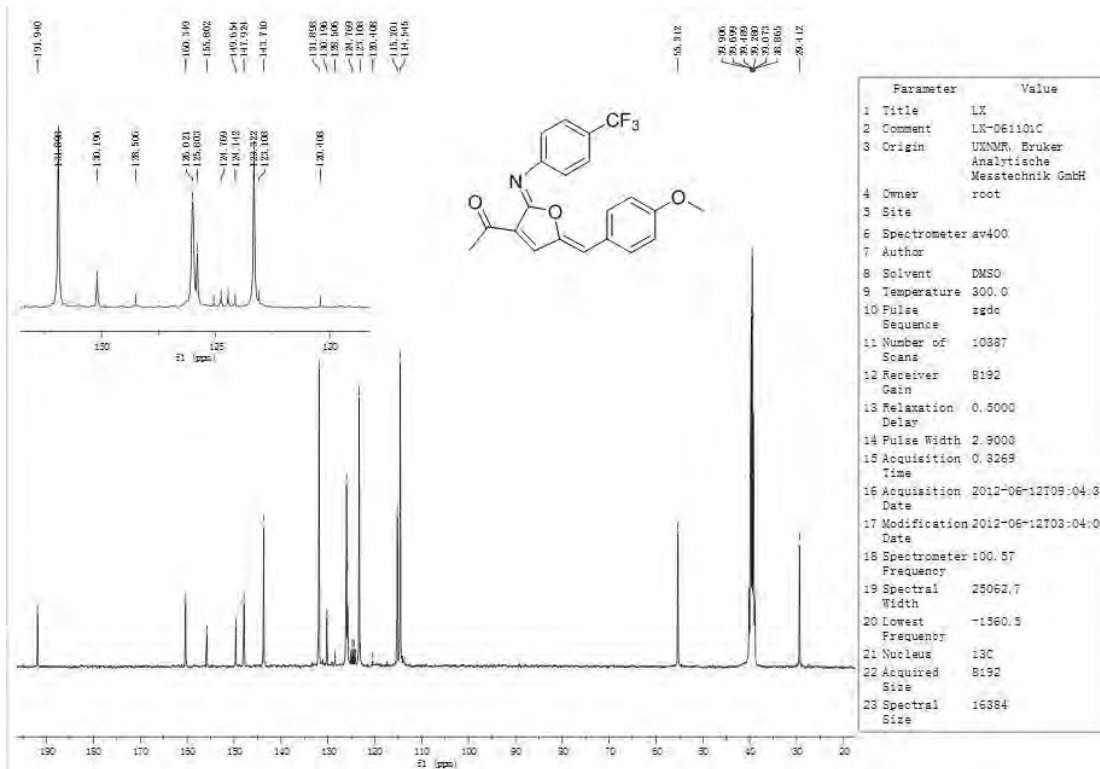
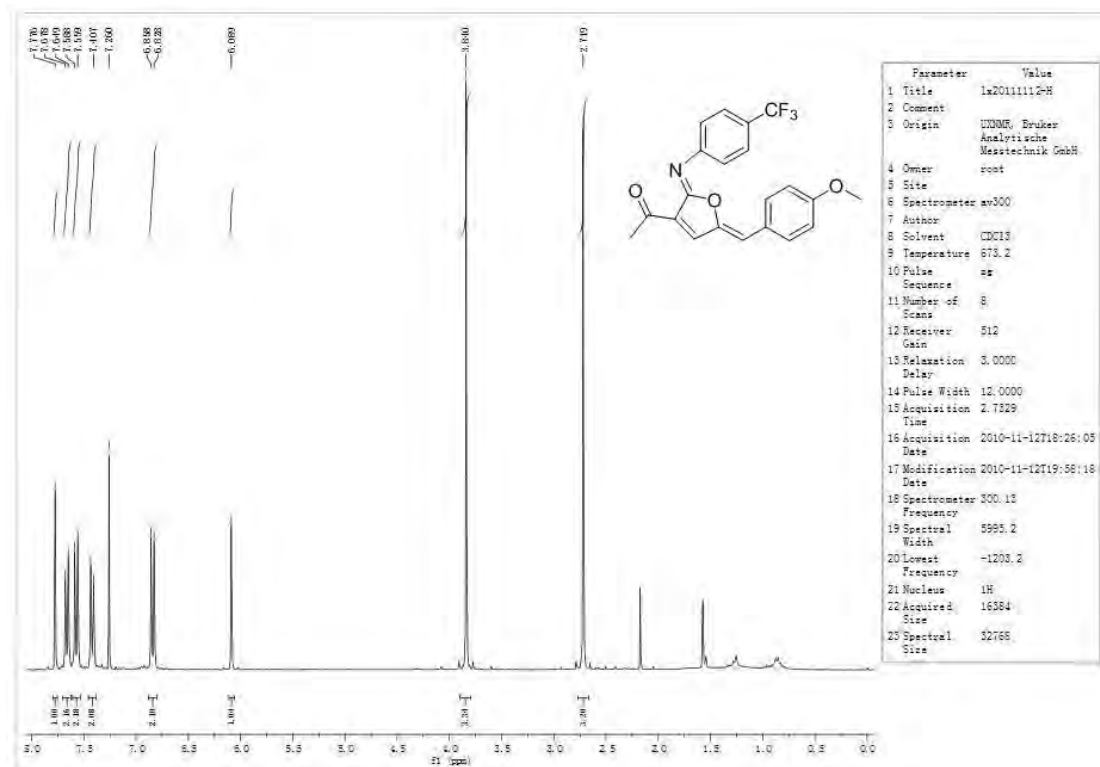
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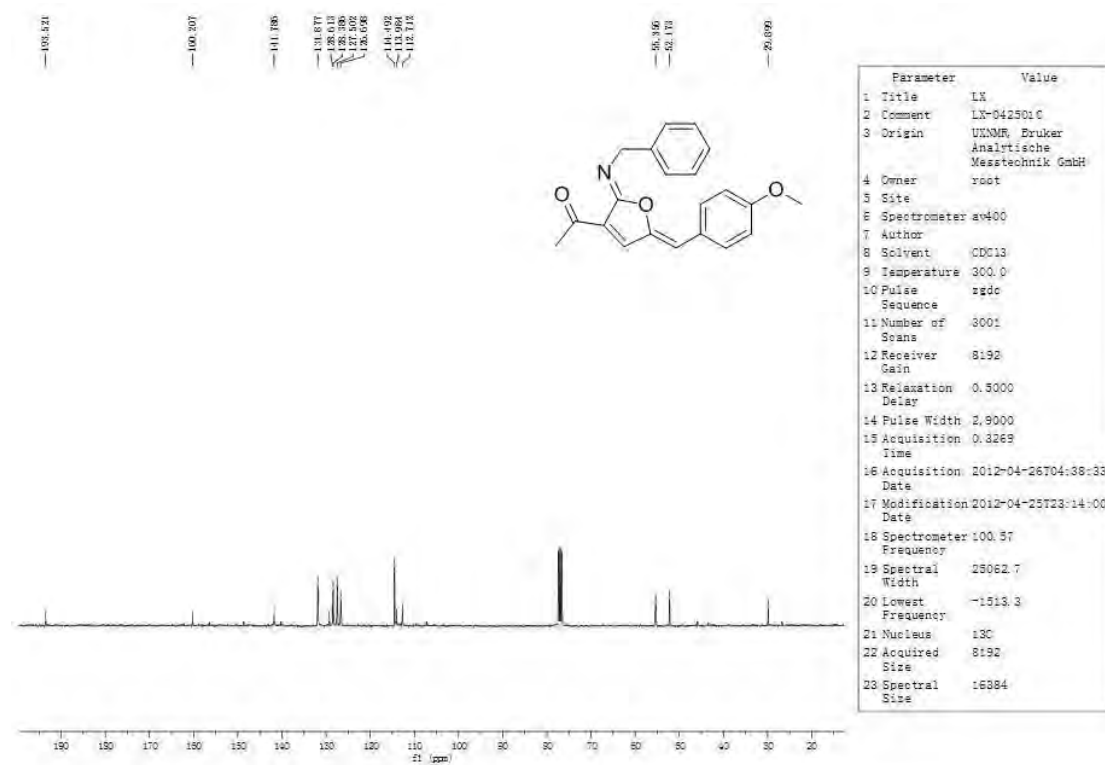
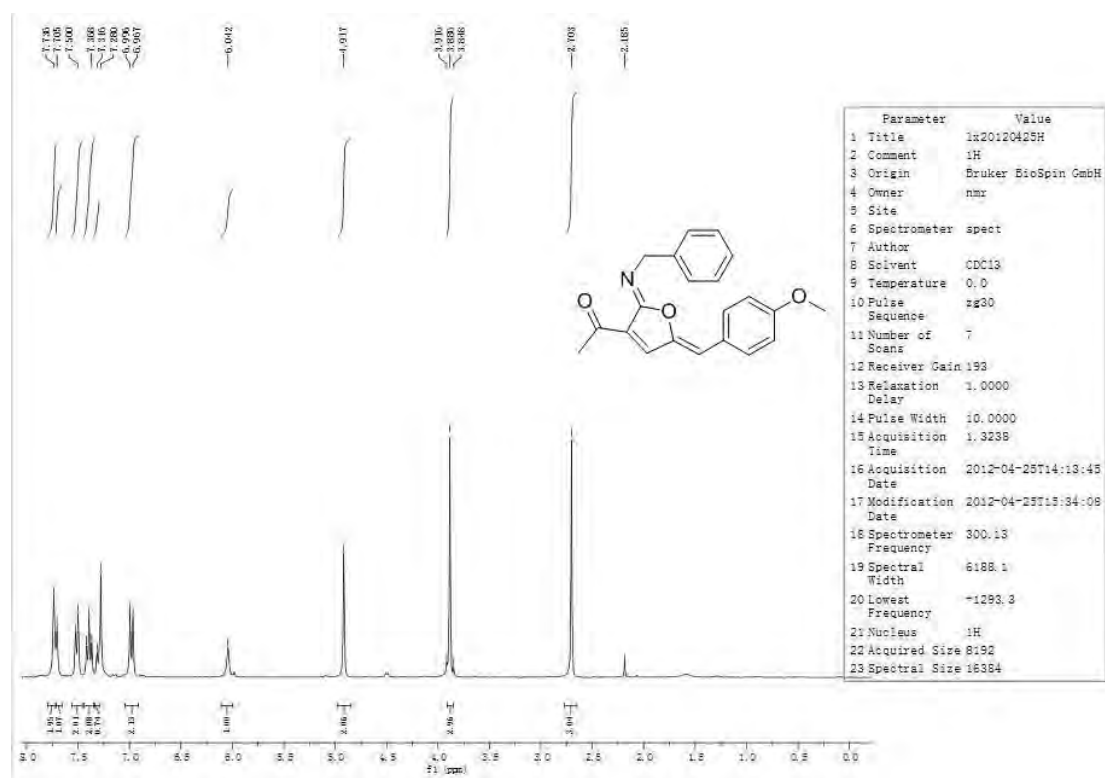
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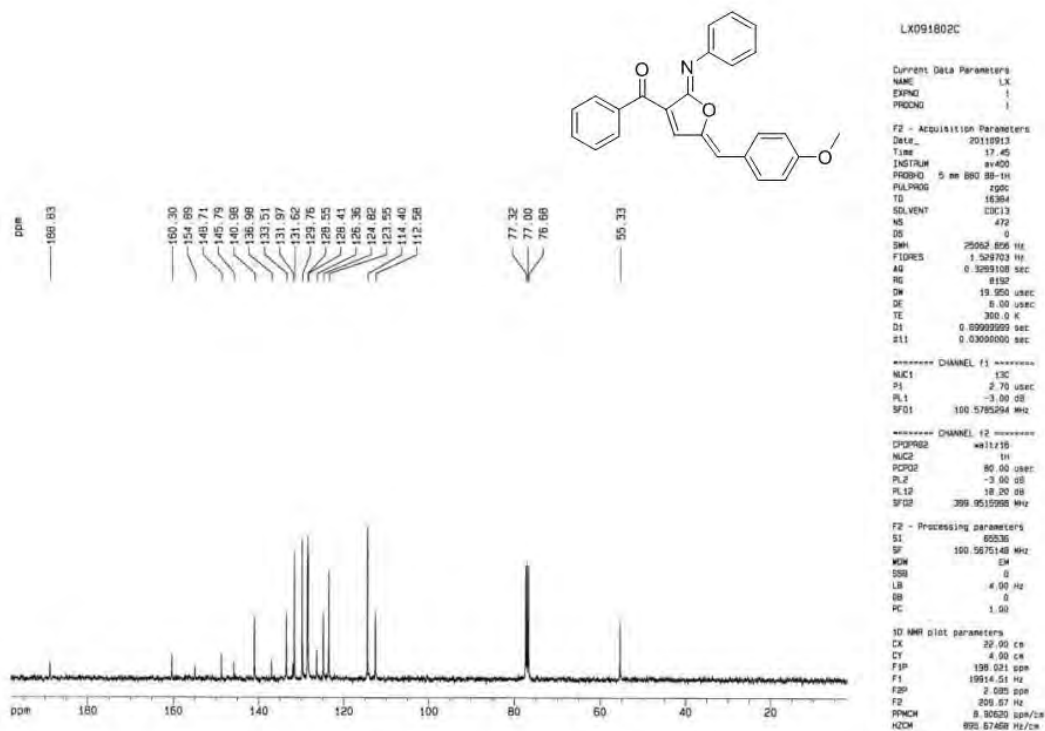
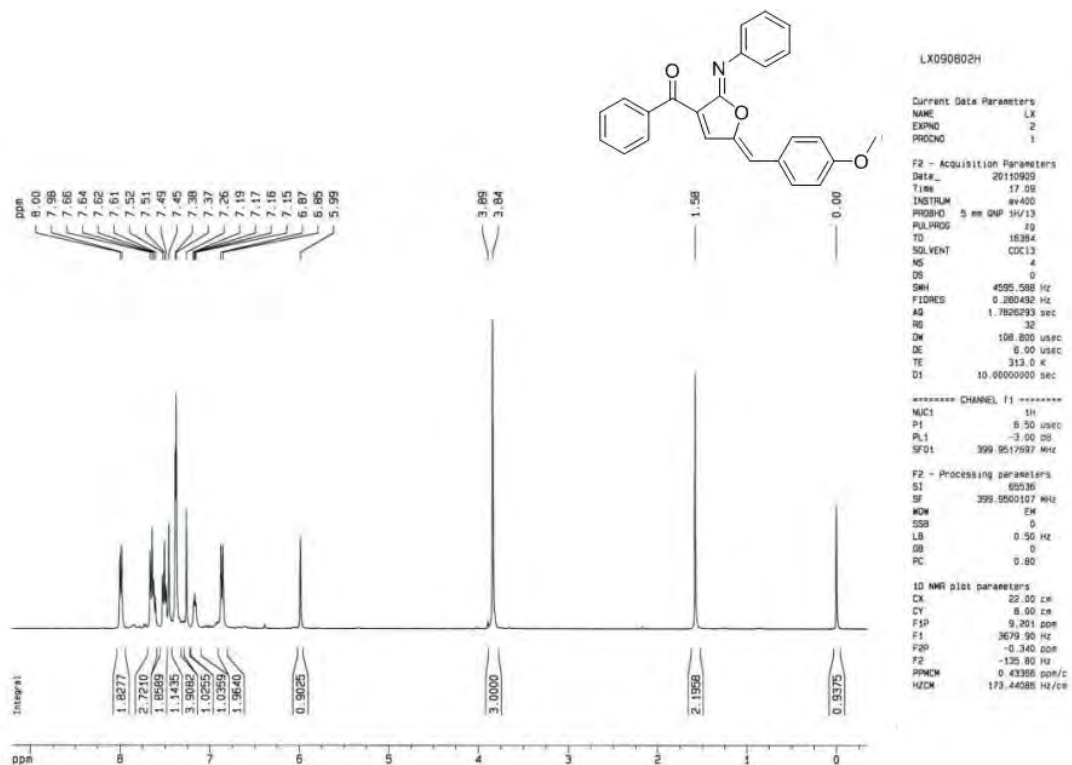
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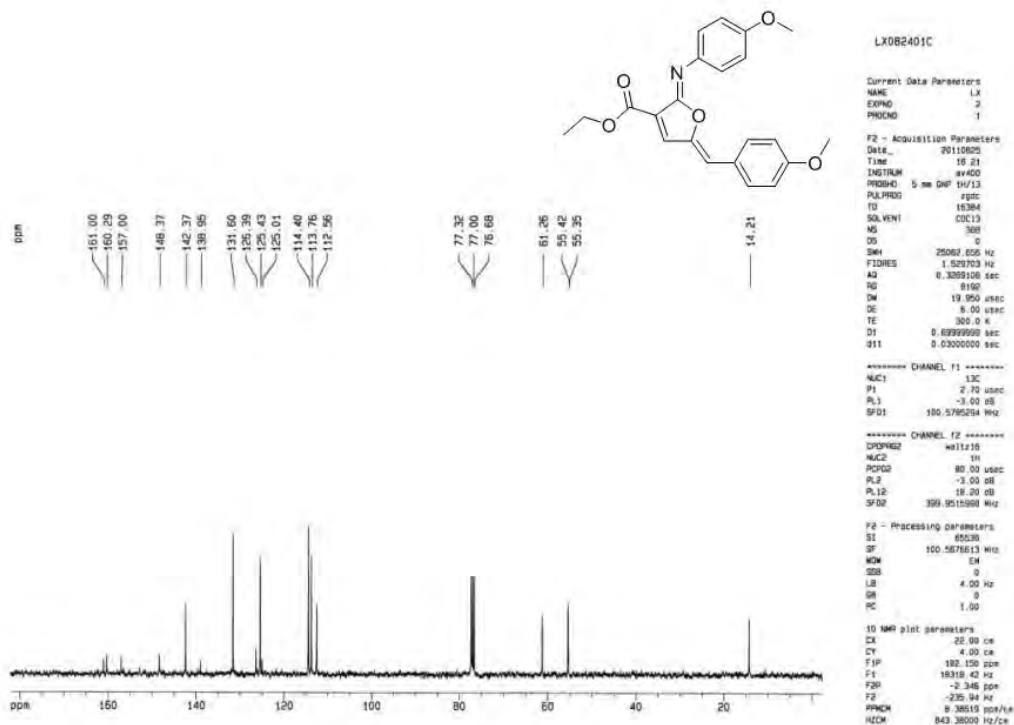
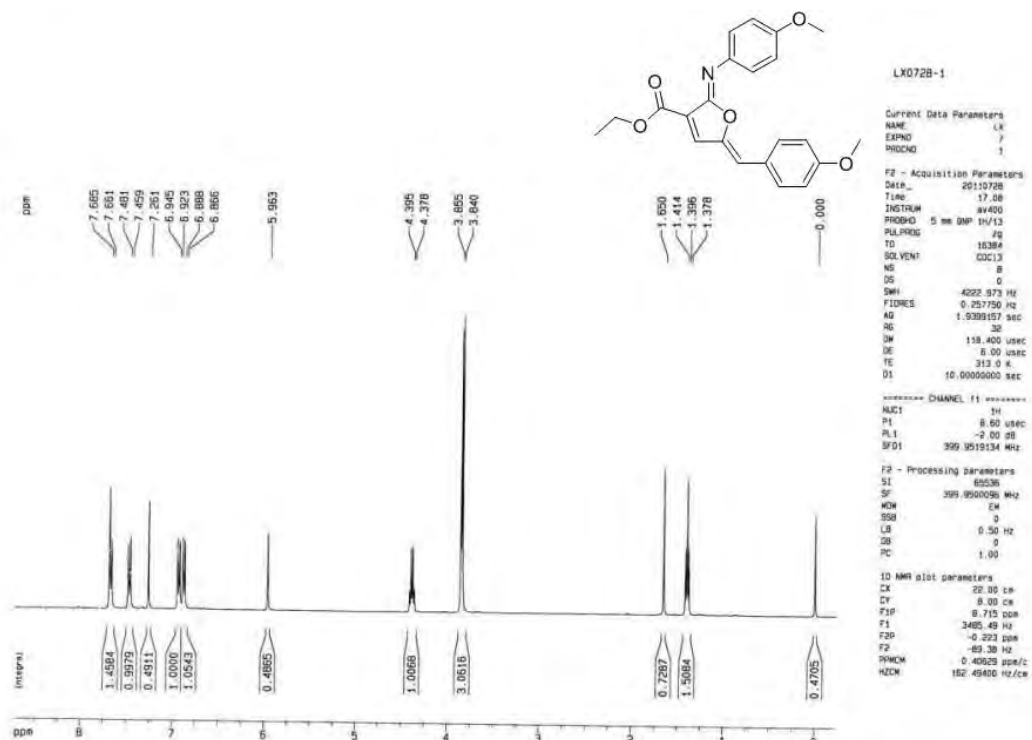


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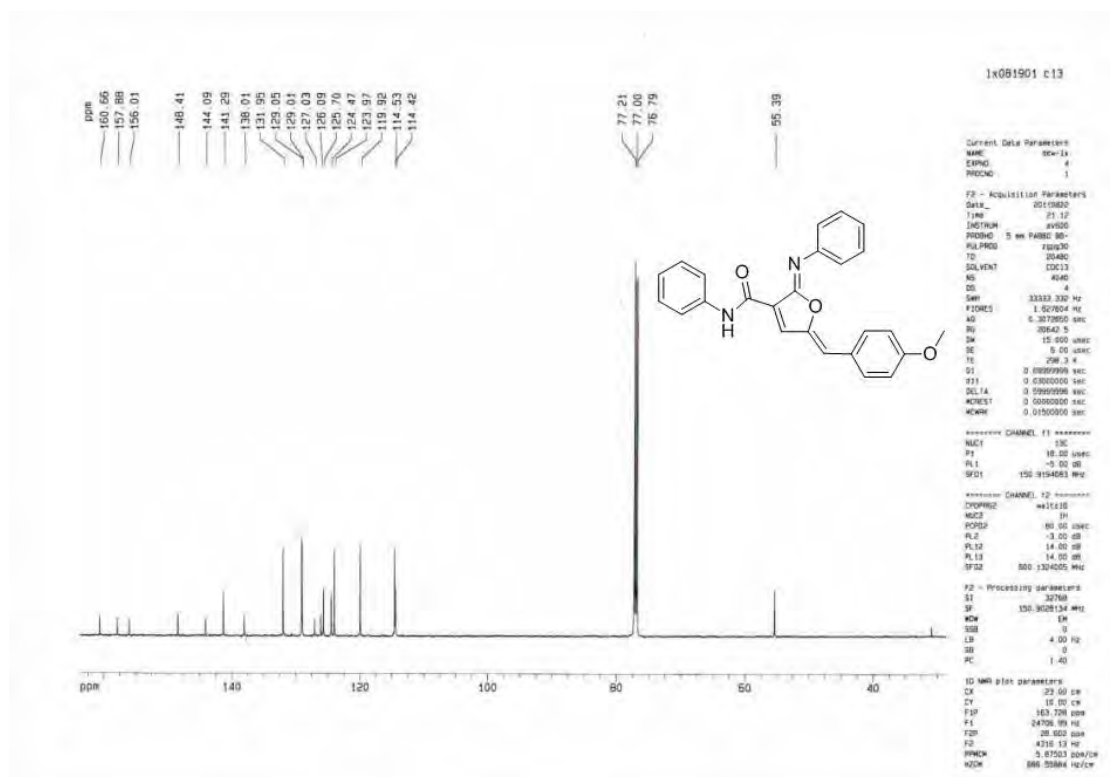
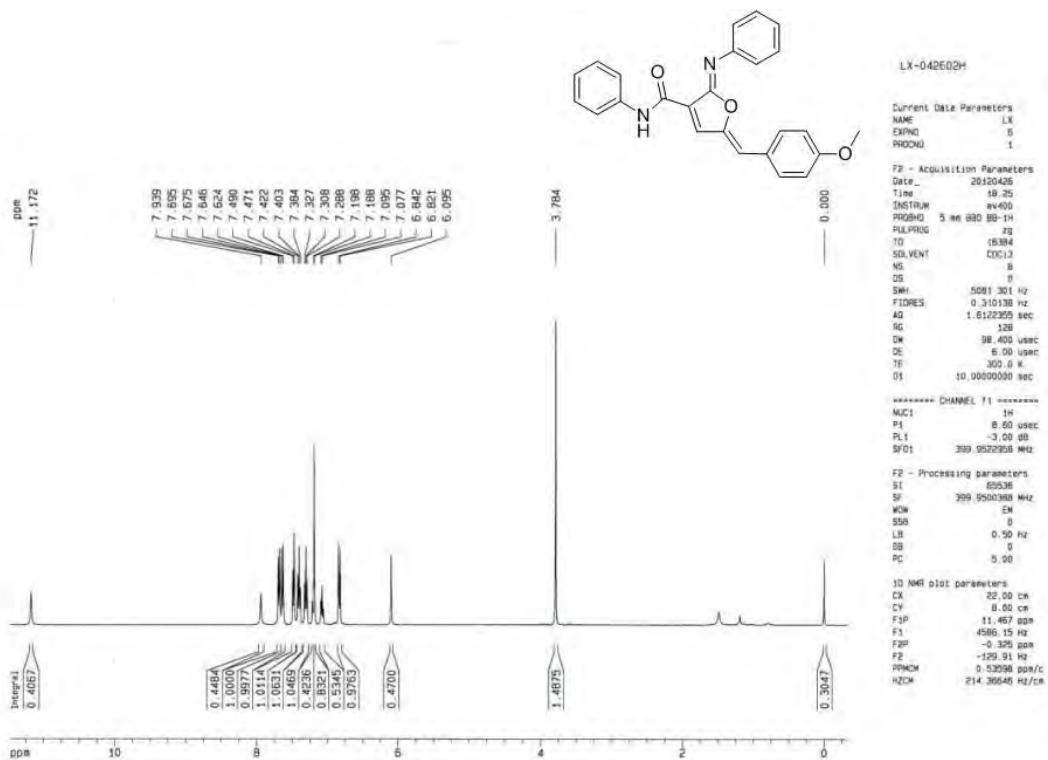




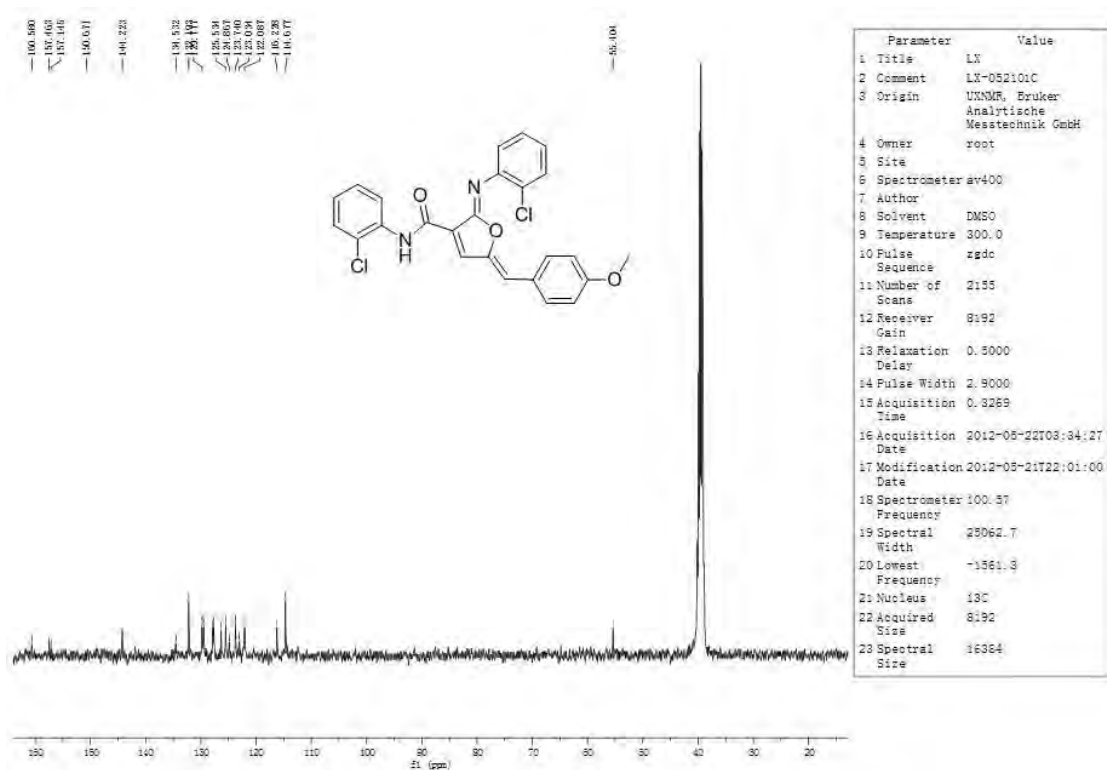
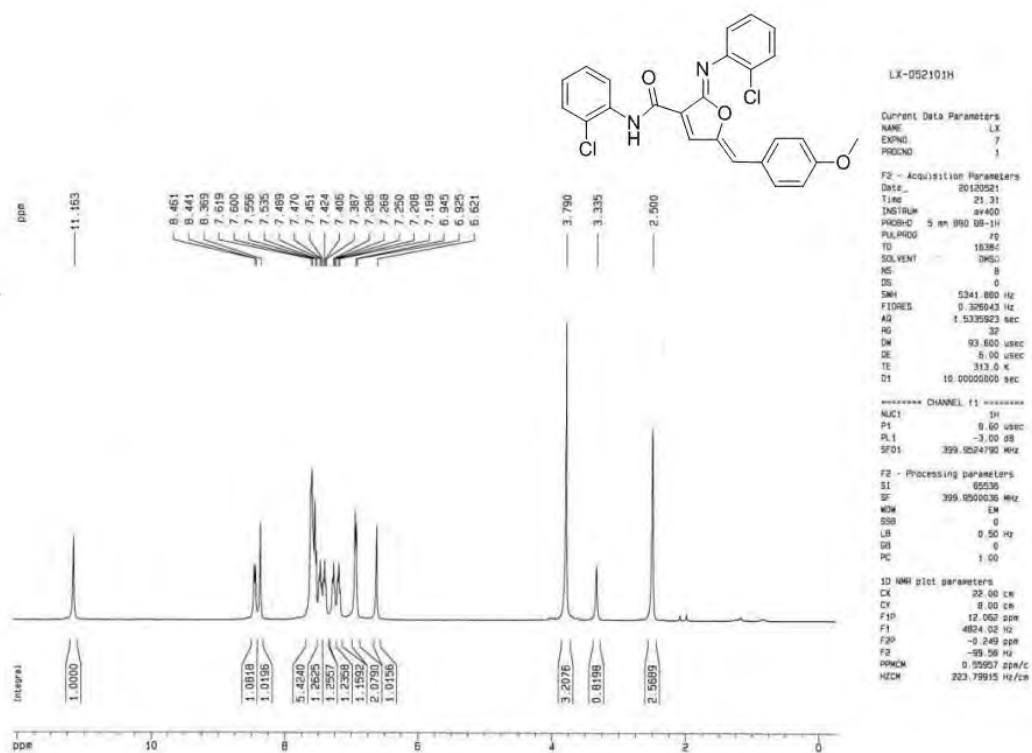
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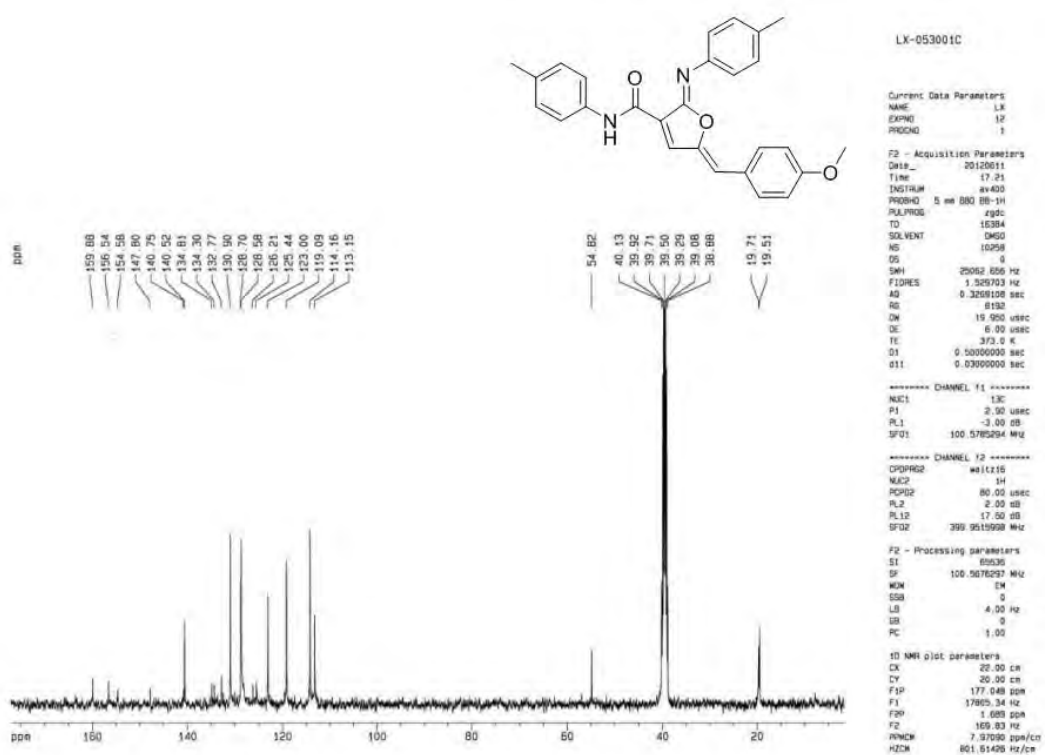
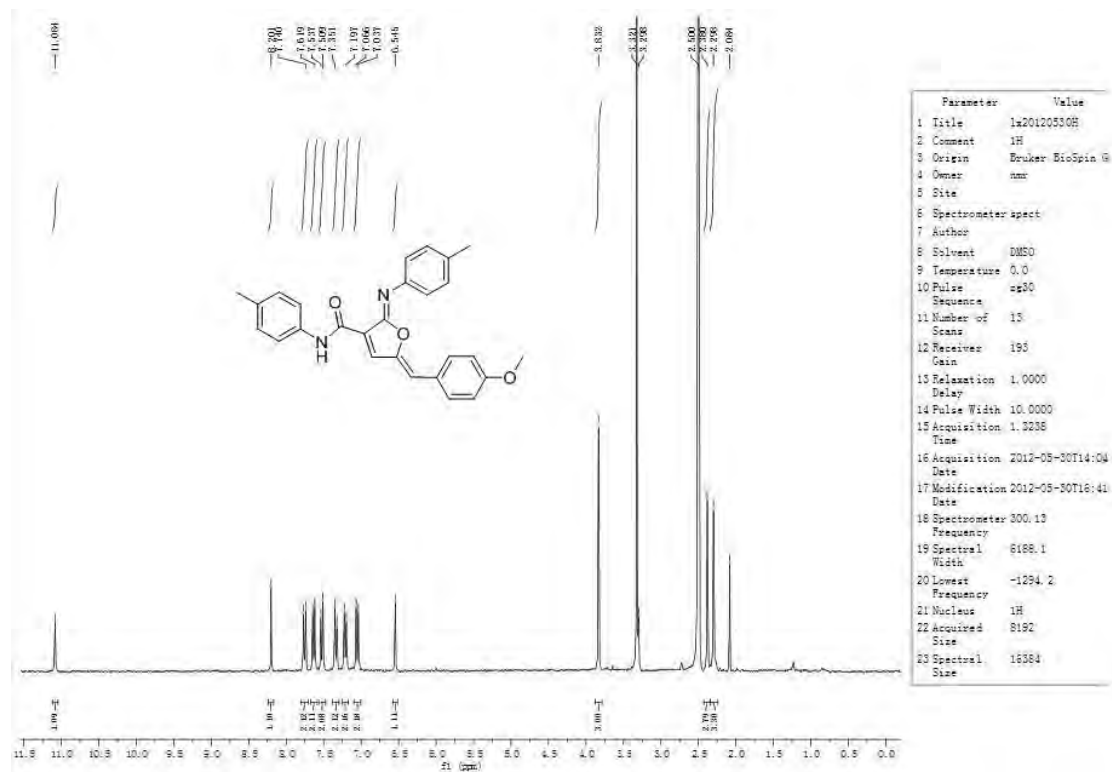
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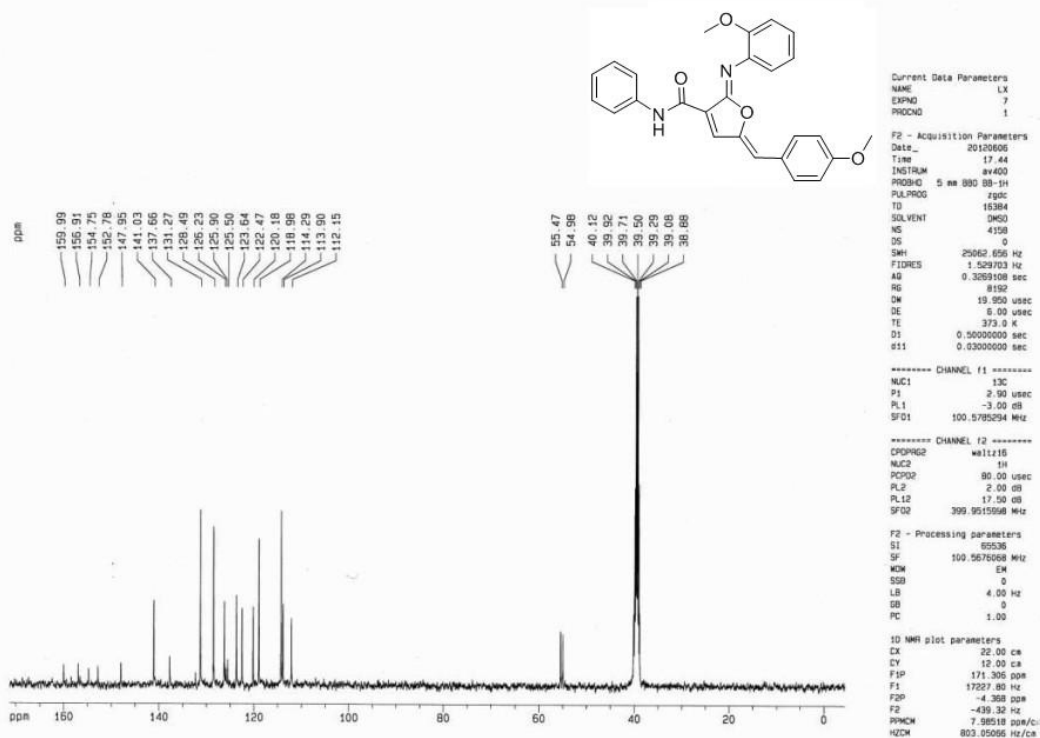
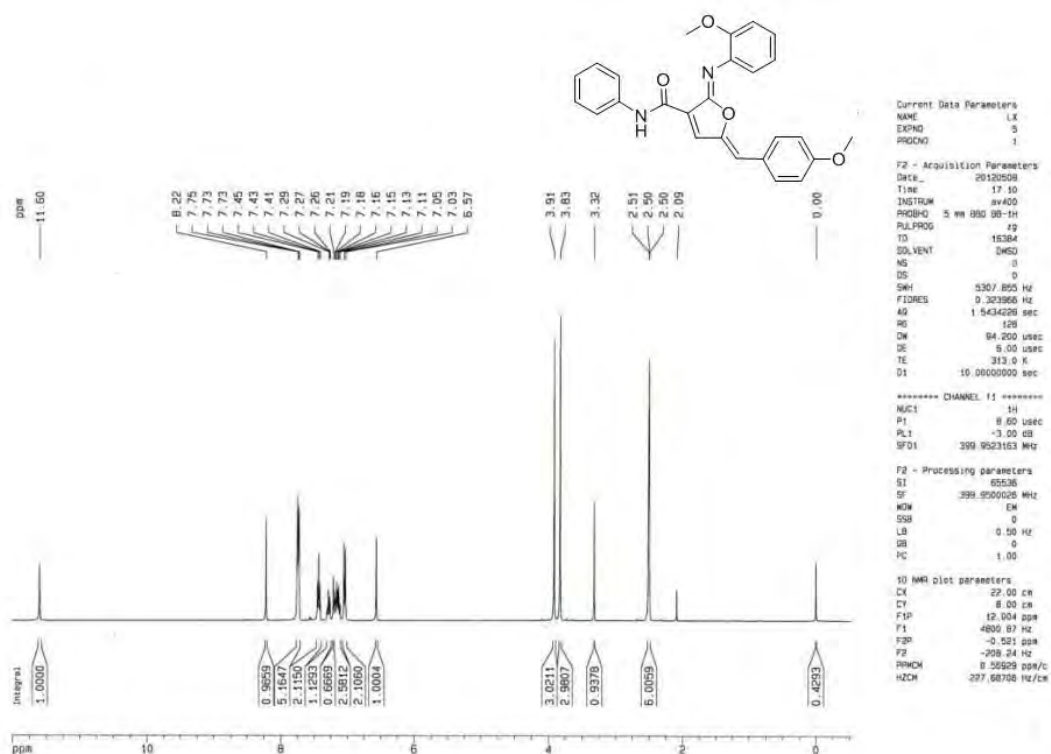
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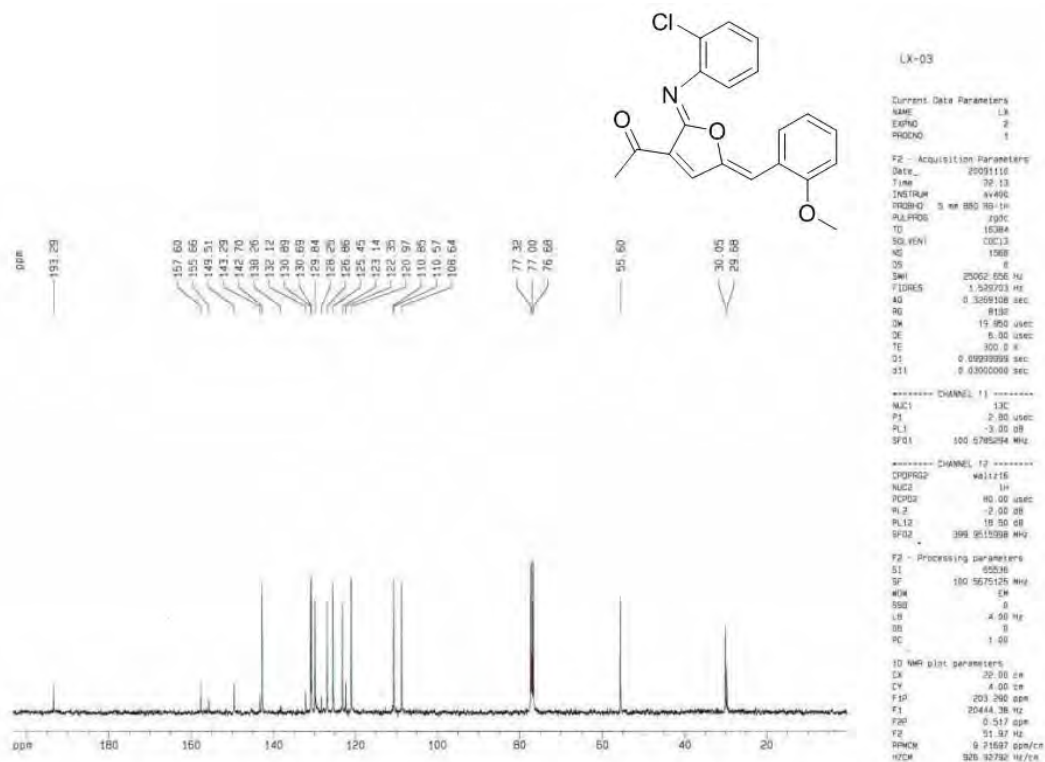
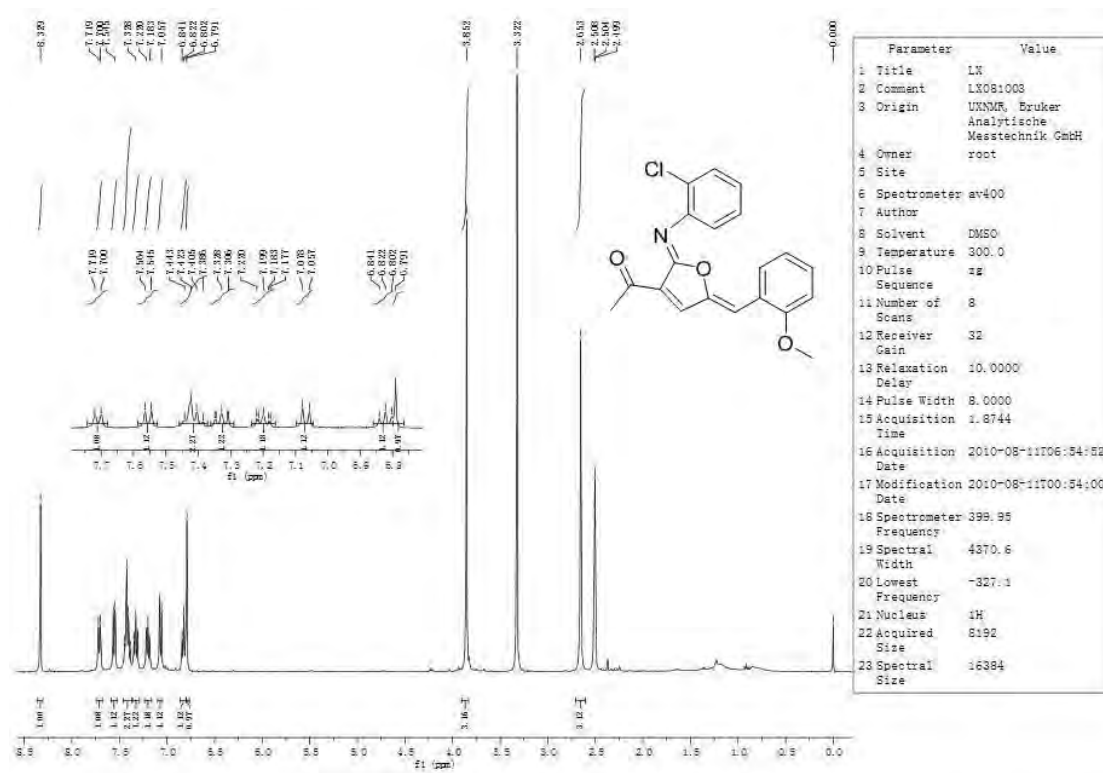
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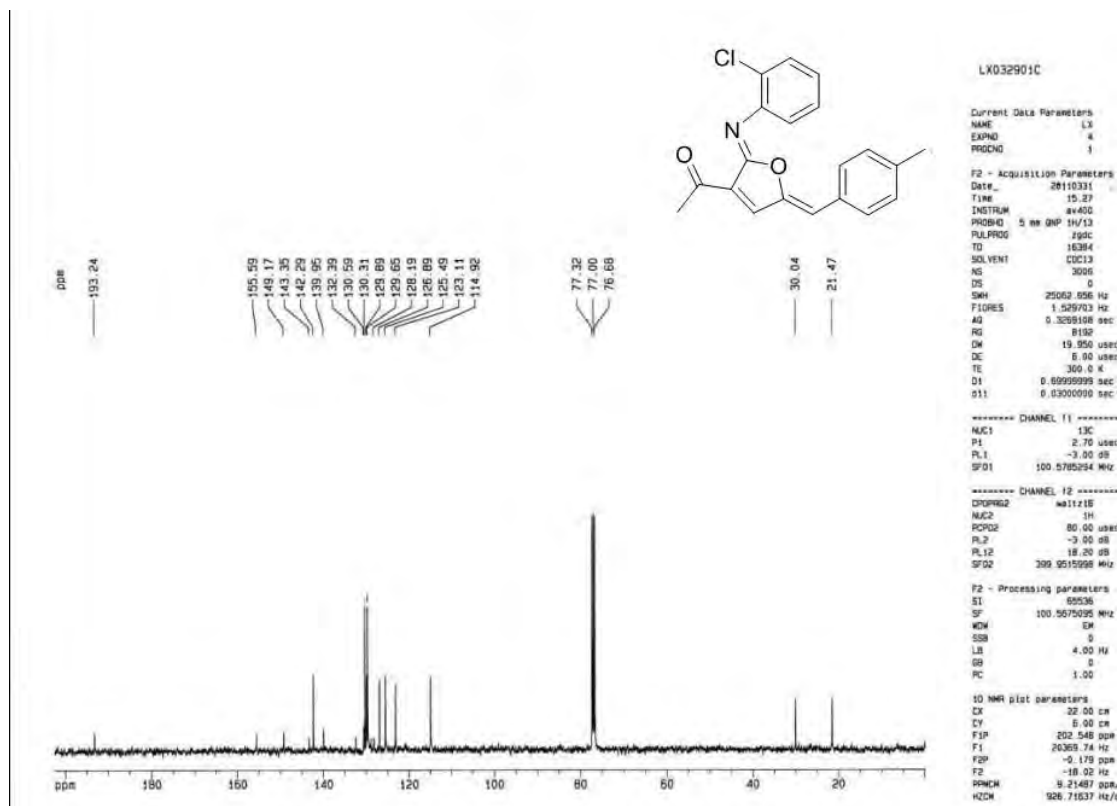
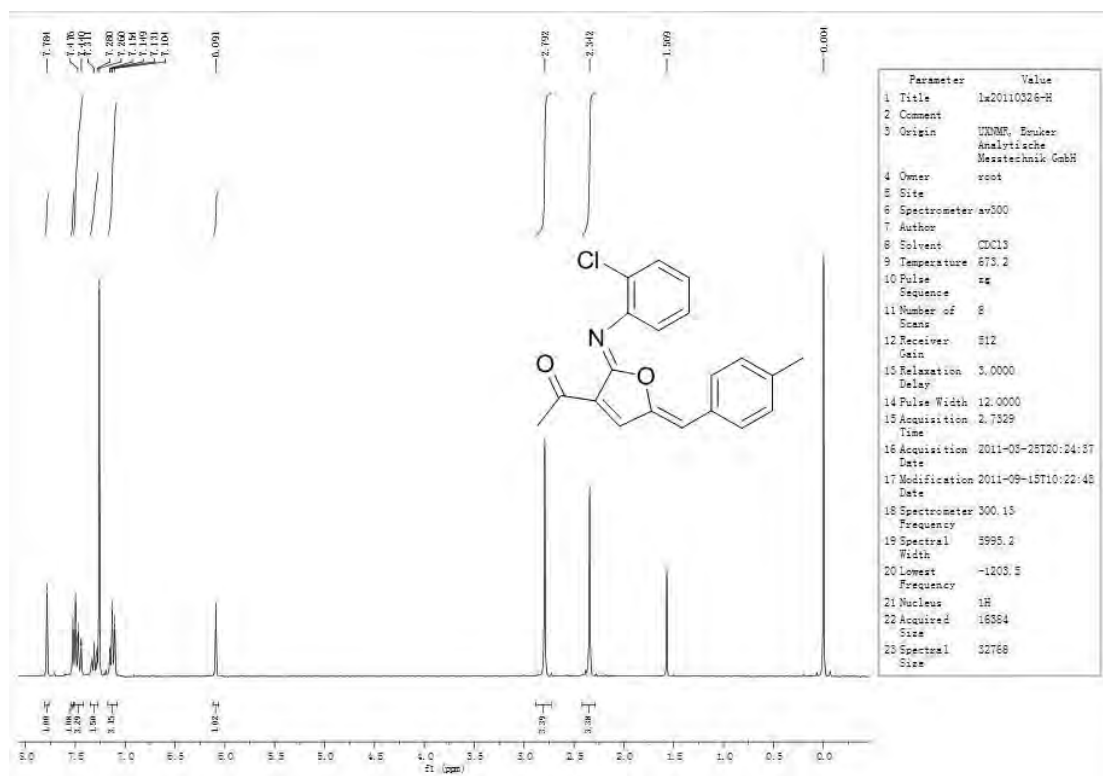
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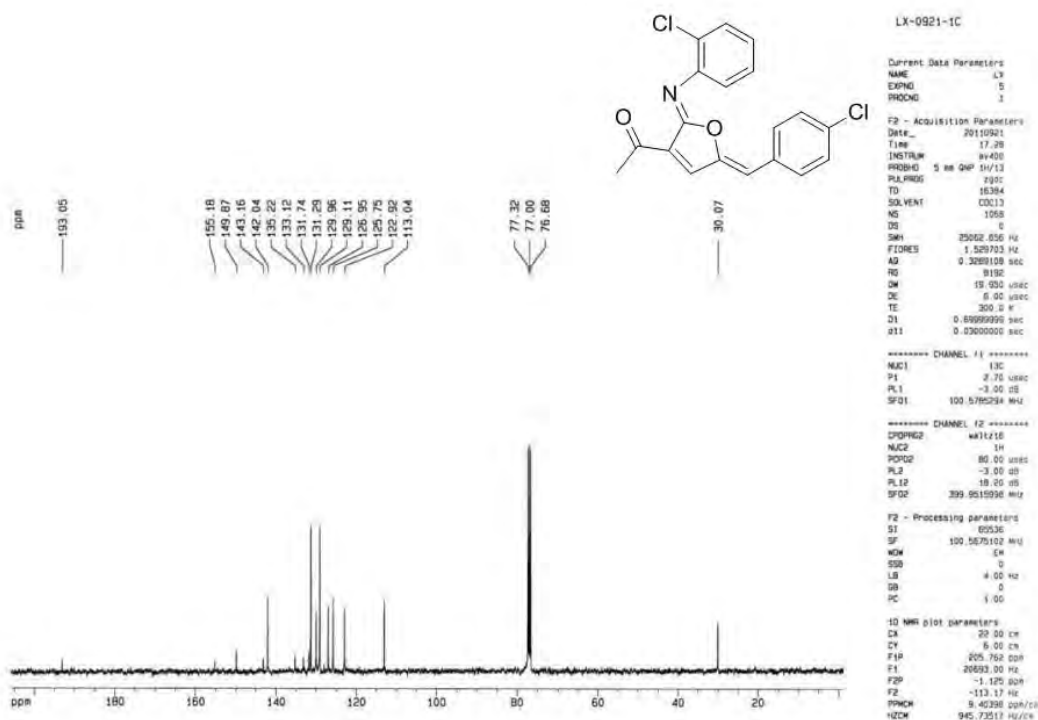
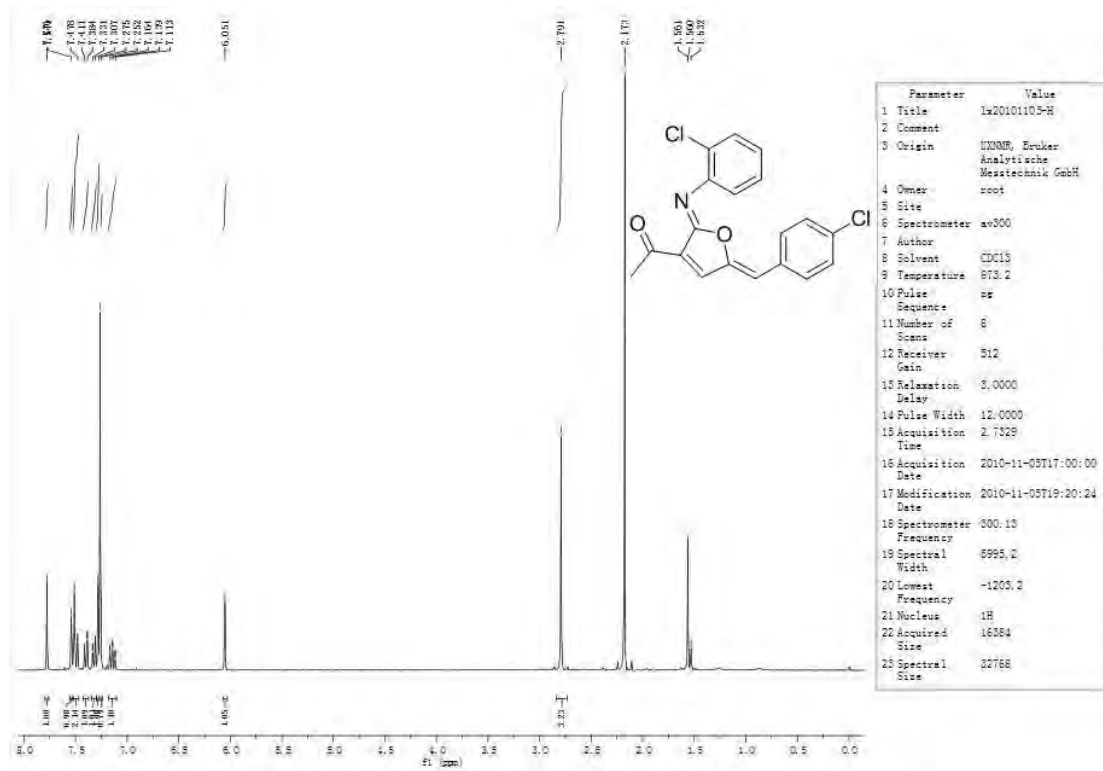
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4fc

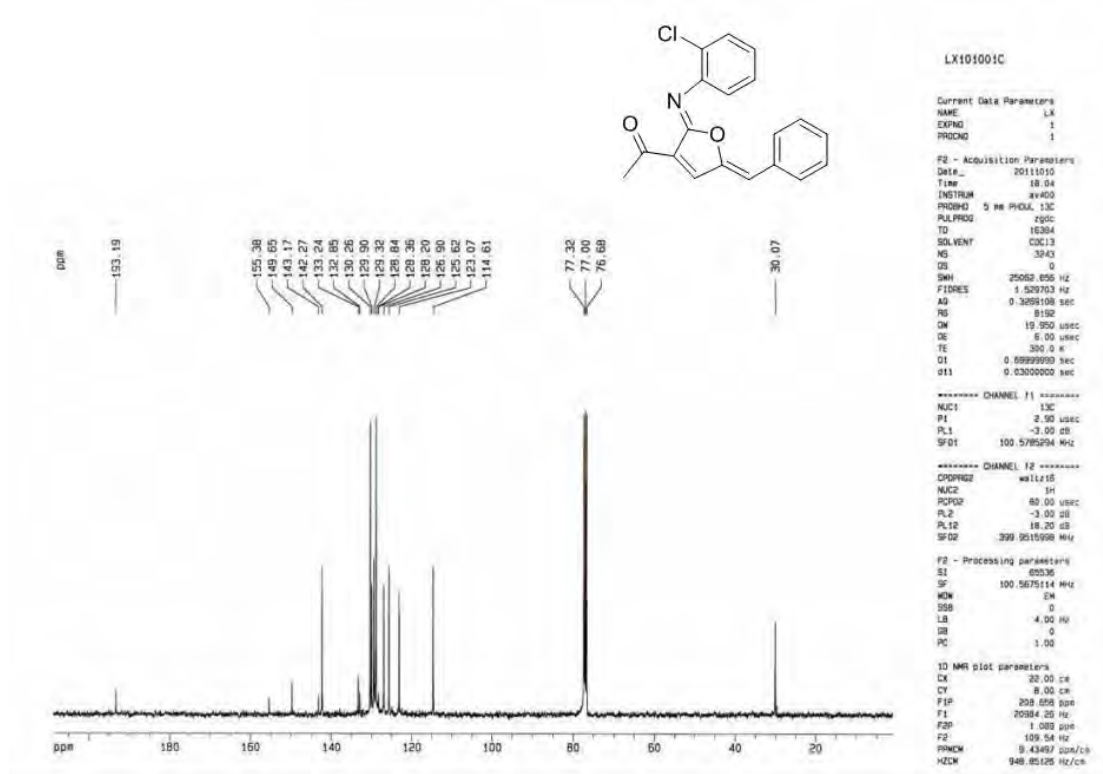
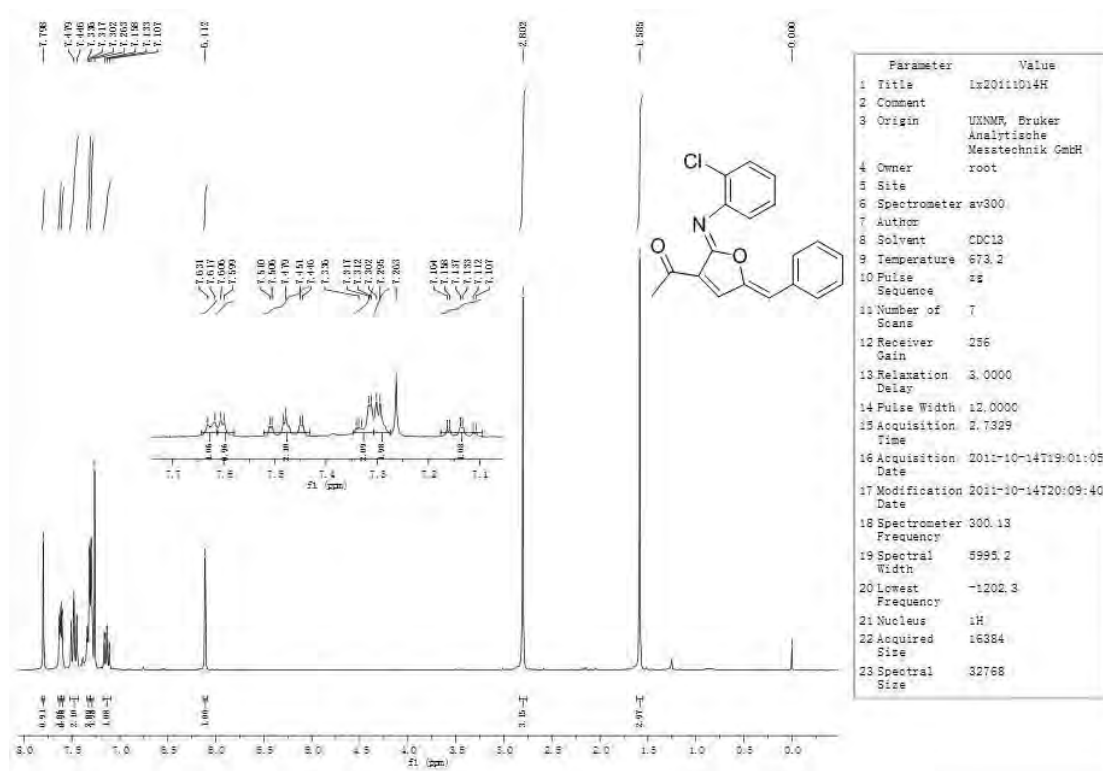


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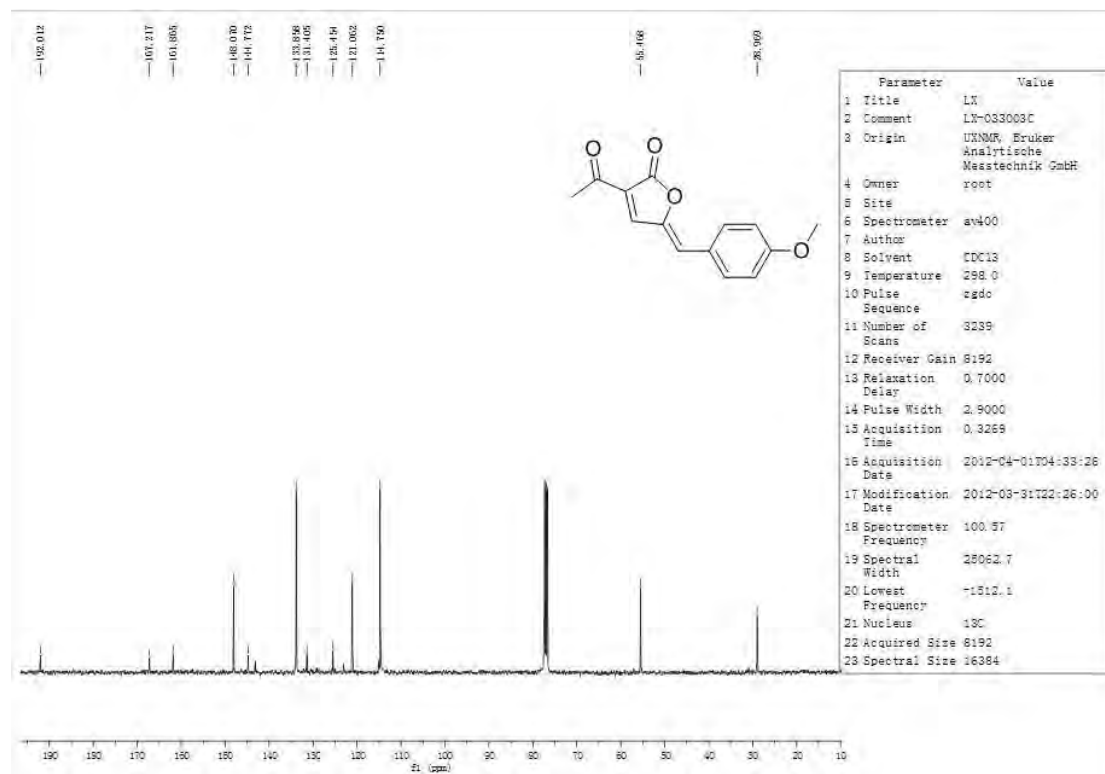
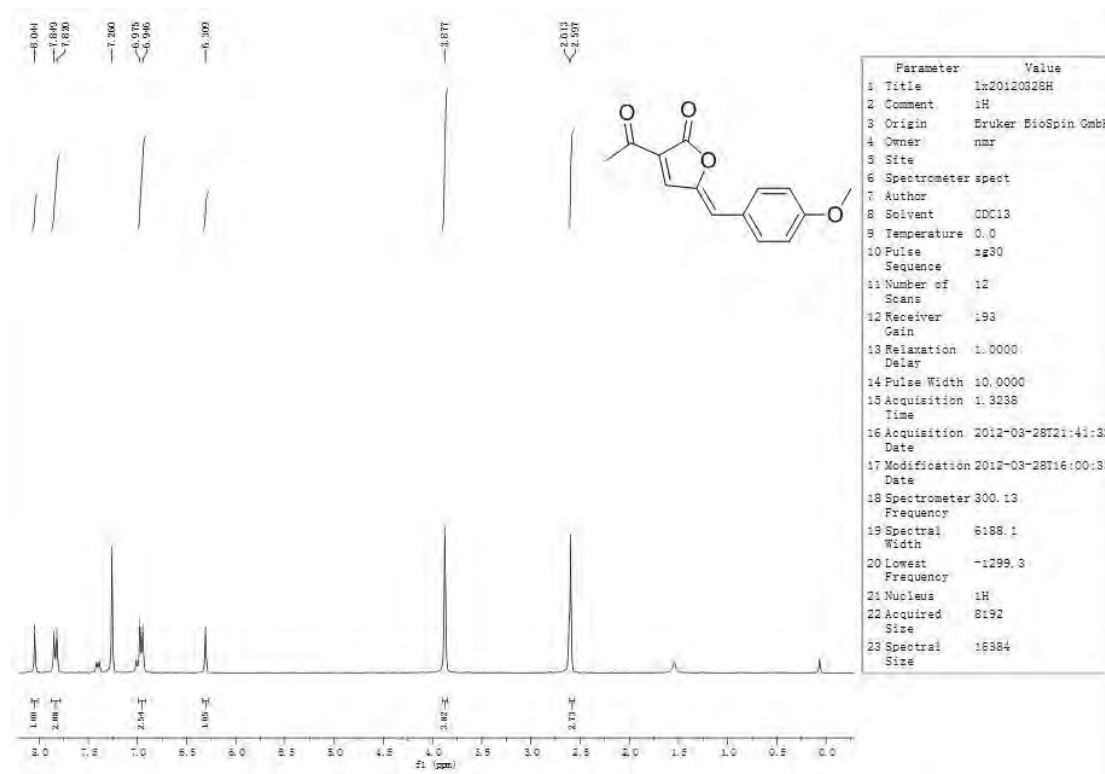




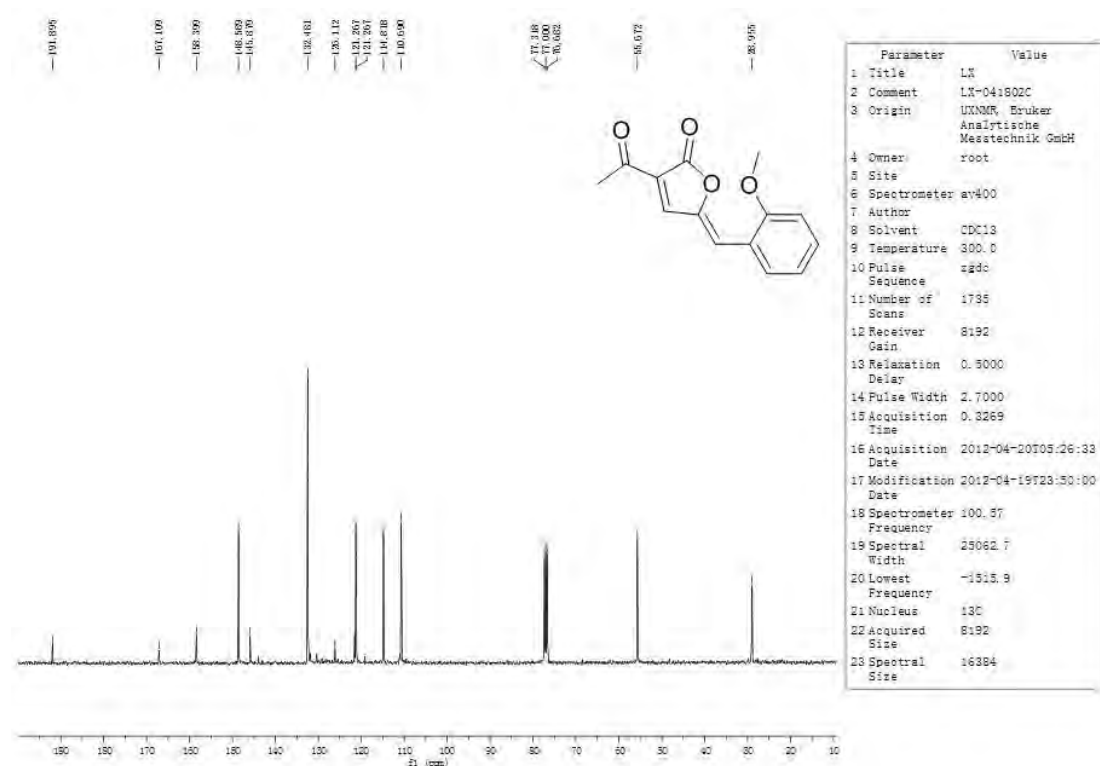
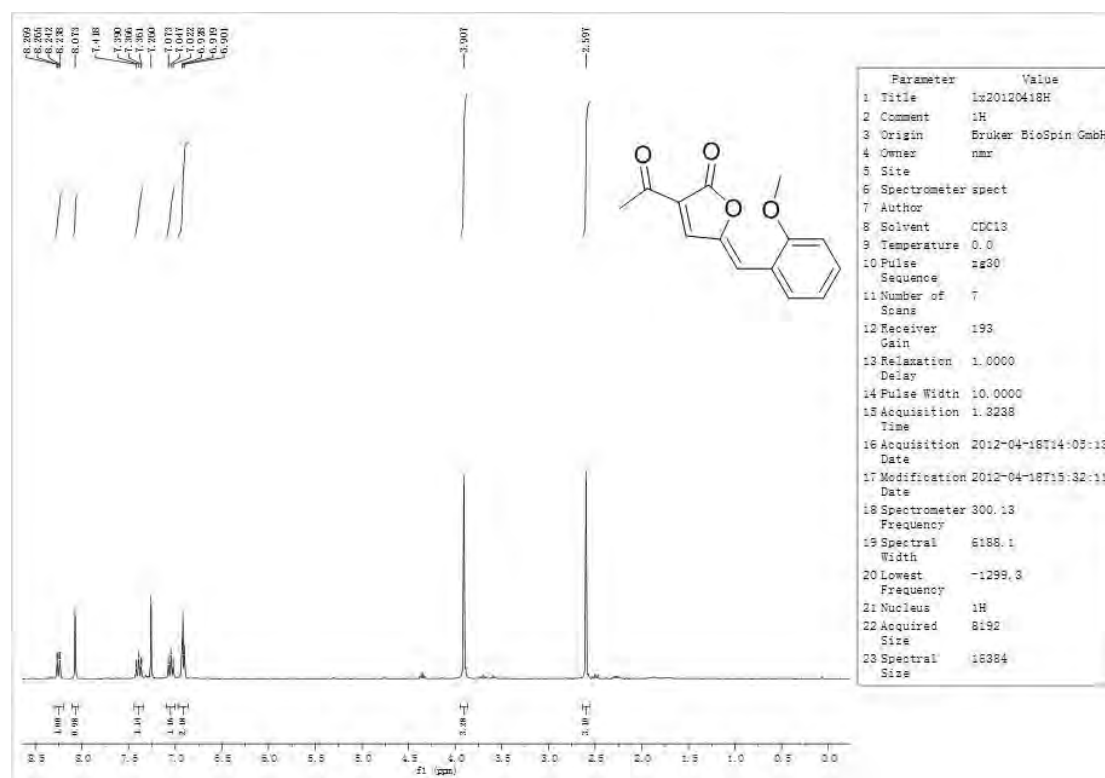
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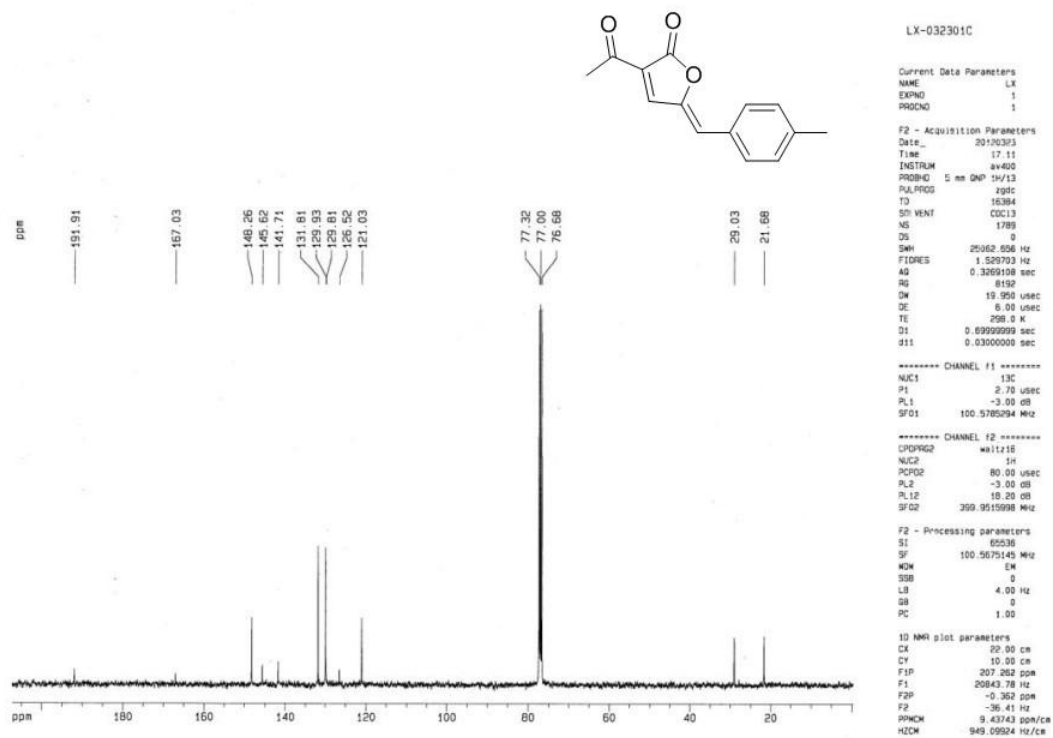
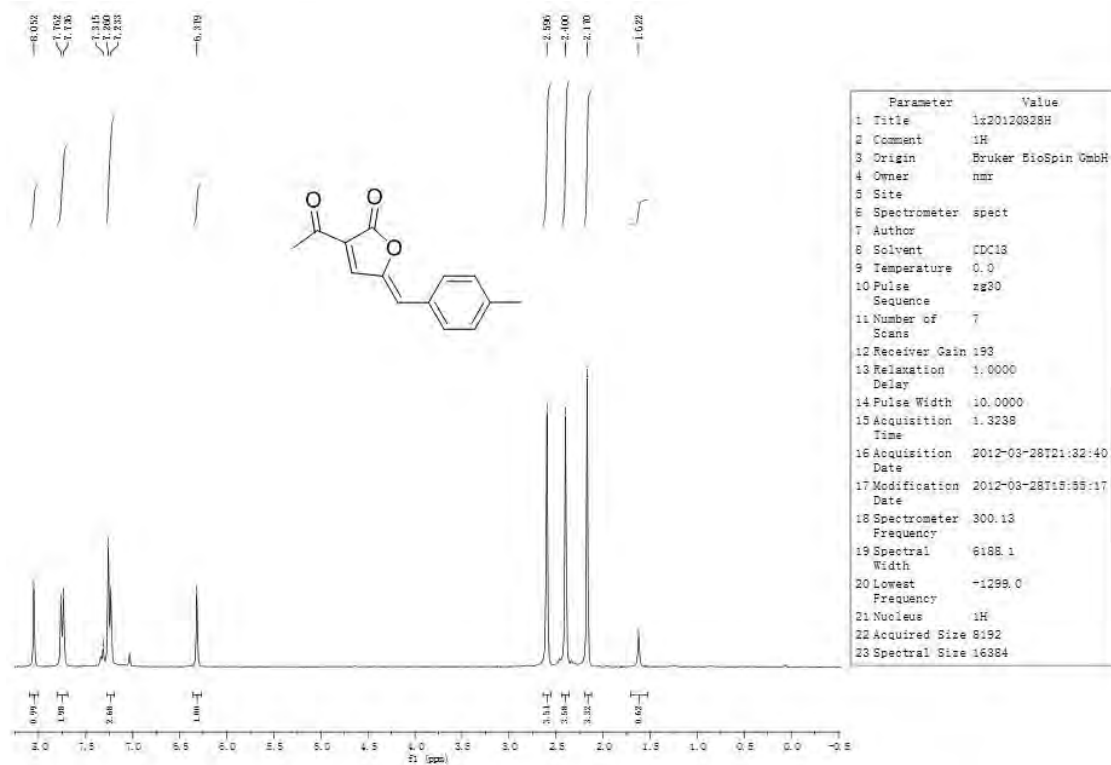
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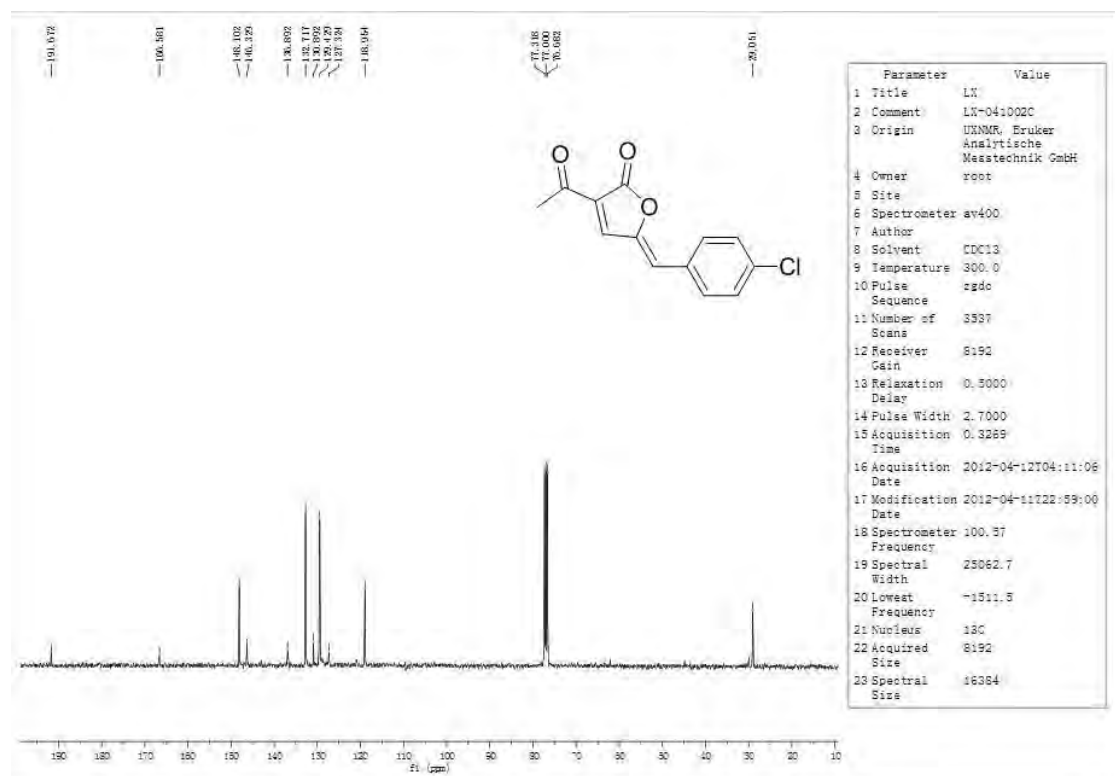
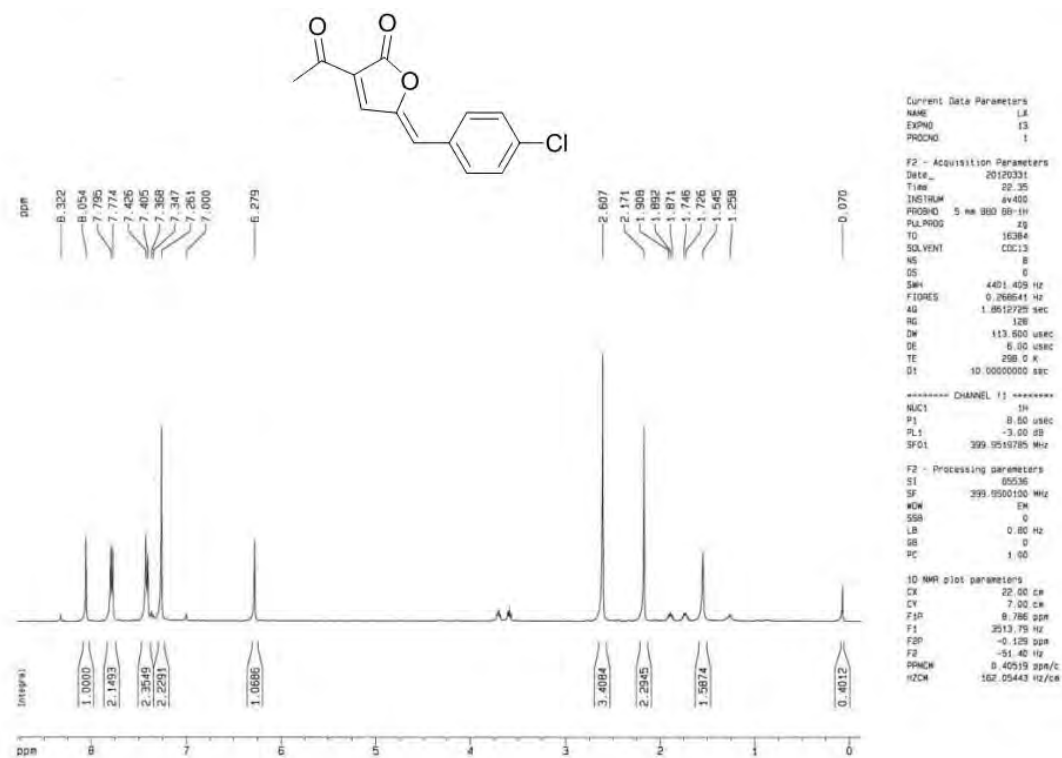
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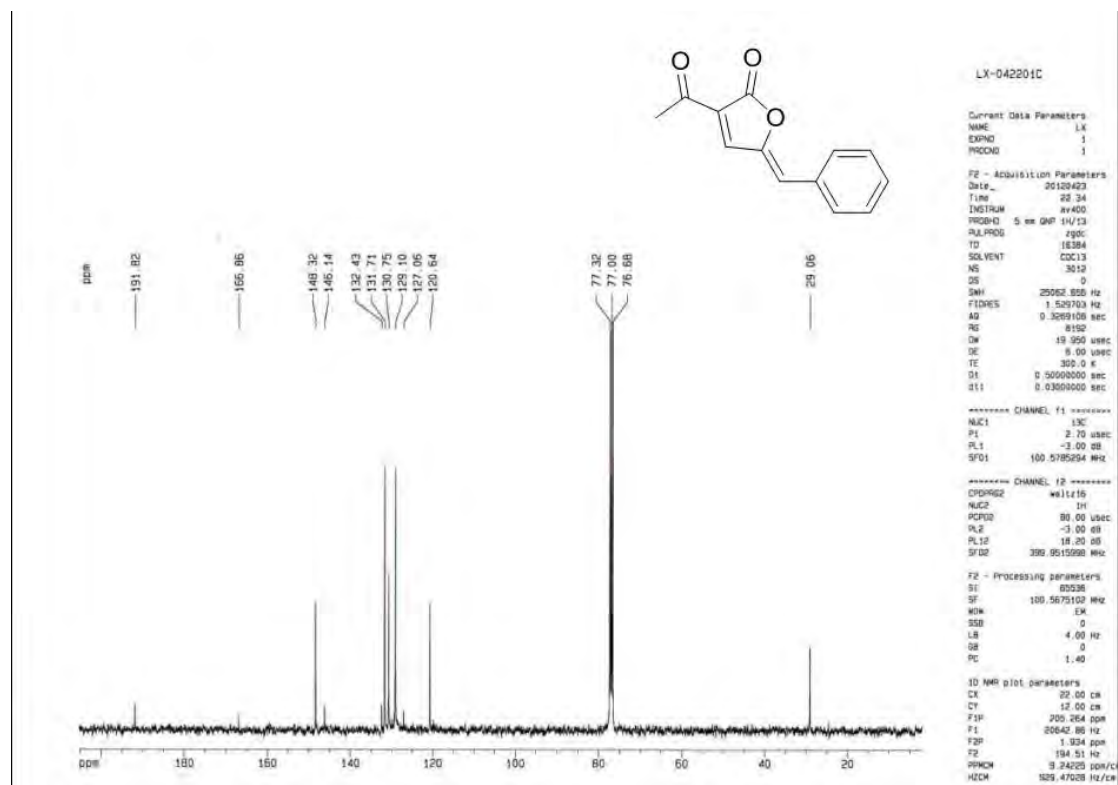
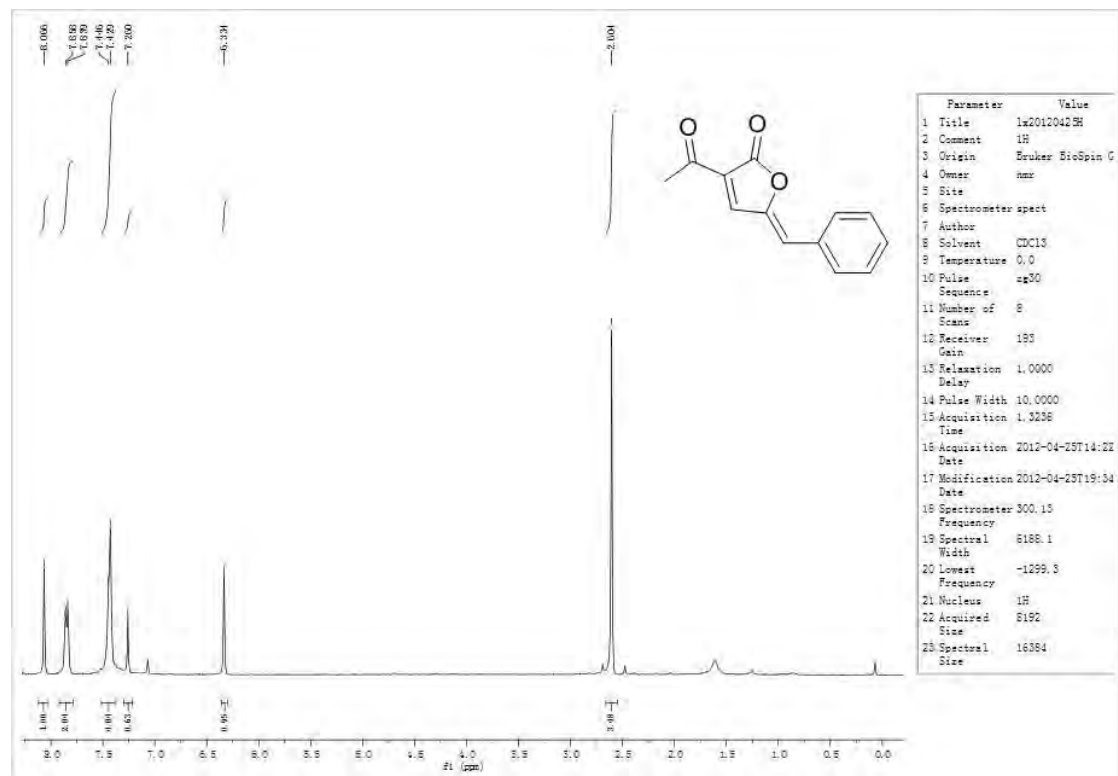
5fc



5fd



5fe



5pa

