

FeCl₃ or MeSO₃H-Promoted Multicomponent Reactions for Facile Synthesis of Structurally Diverse Furan Analogues

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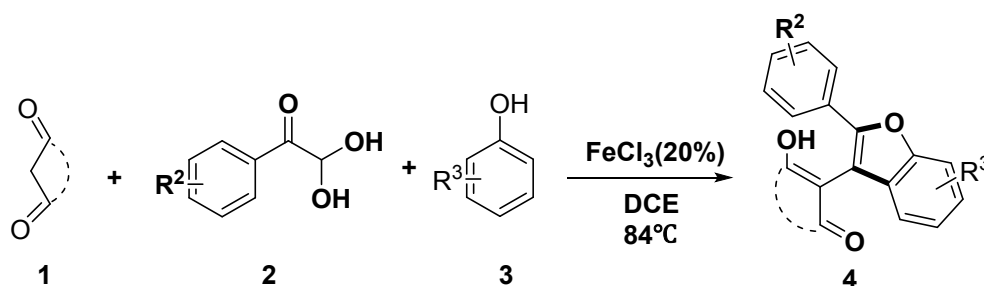
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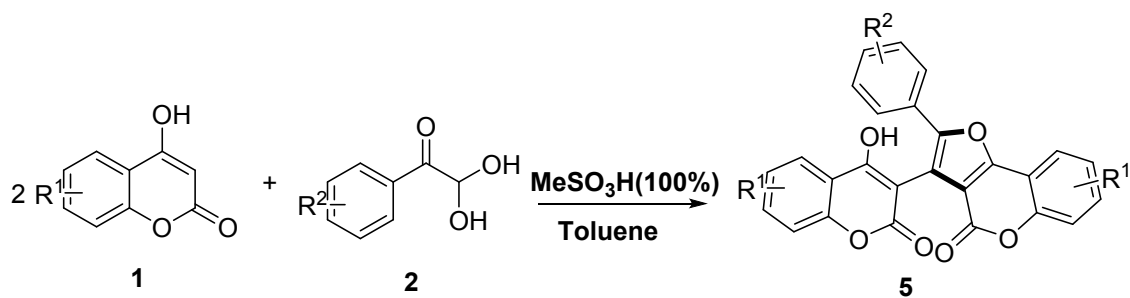
1. General Information

All reagents were obtained from commercial sources (purity > 99%) and used without further purification, unless otherwise indicated. Melting points were determined with a Büchi B-540 capillary melting point apparatus. The ^1H and ^{13}C NMR spectroscopic data were recorded with a Varian instrument at 600 and 150 MHz, respectively, and TMS was used as the internal standard. Mass spectrometry was performed with a Thermo Finnigan LCQ-Advantage instrument. High resolution mass spectral (HRMS) analyze was measured on an Agilent 1290-6540 UHPLC Q-ToF HR-MS System ESI spectrometer. Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. Reactions were stirred using Teflon-coated magnetic stir bars.

2. General procedure for the synthesis of furan analogues 4 and 5



A mixture of the cyclic dicarbonyl compounds **1** (1 mmol), arylglyoxal monohydrate **2** (1mmol), phenol **3** (1mmol) and FeCl₃ (0.2mmol) in DCE (5 mL) was stirred at reflux for 0.5 – 1.0 h. Upon completion of the reaction (progress was monitored by TLC), the mixture was cooled to room temperature and aqueous NH₄Cl (30 mL) was added. The aqueous phase was extracted with ethyl acetate (3 x 25 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding products **4**.

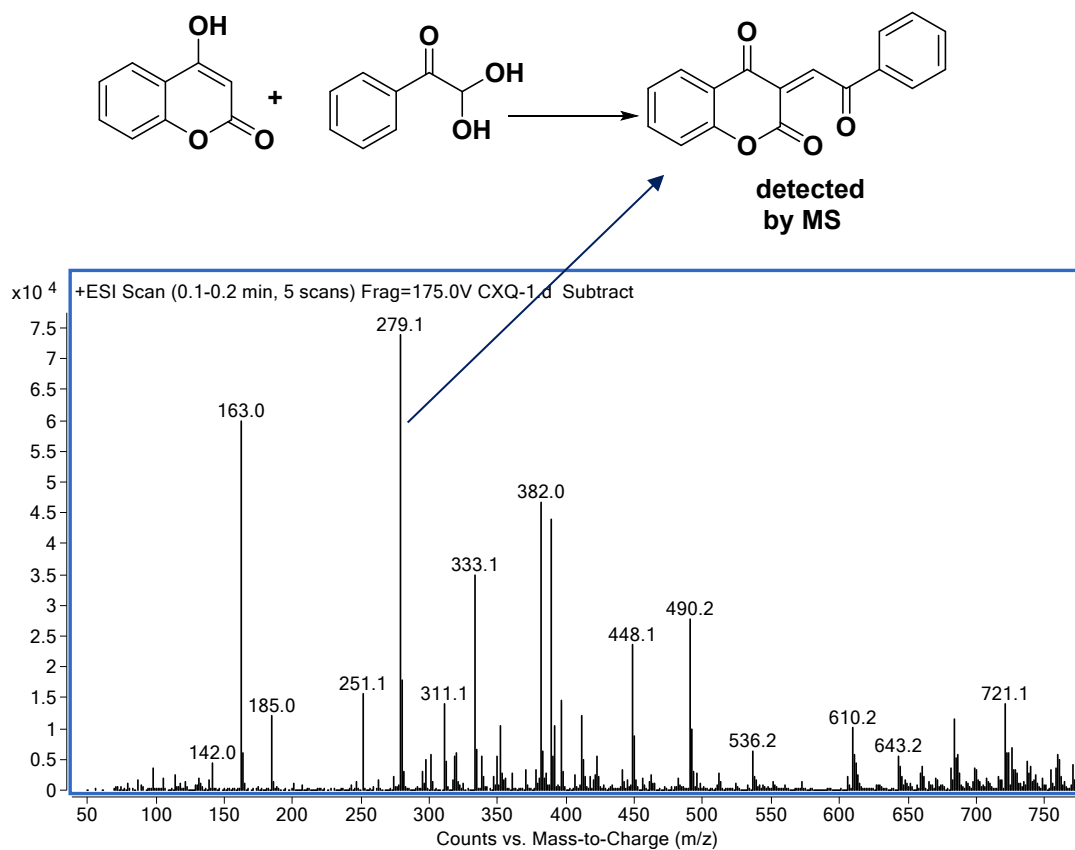


A mixture of the 4-Hydroxycoumarin **1** (1 mmol), arylglyoxal monohydrate **2** (0.5mmol), and MeSO_3H (0.5mmol) in toluene (5 mL) was stirred at reflux for 0.5 – 1.0 h. Upon completion of the reaction (progress was monitored by TLC), the mixture was cooled to room temperature. The solid was removed by filtration, washed with water and a little cold toluene, and then dried to give the pure product **5**.

3. Evidence in support of the mechanism

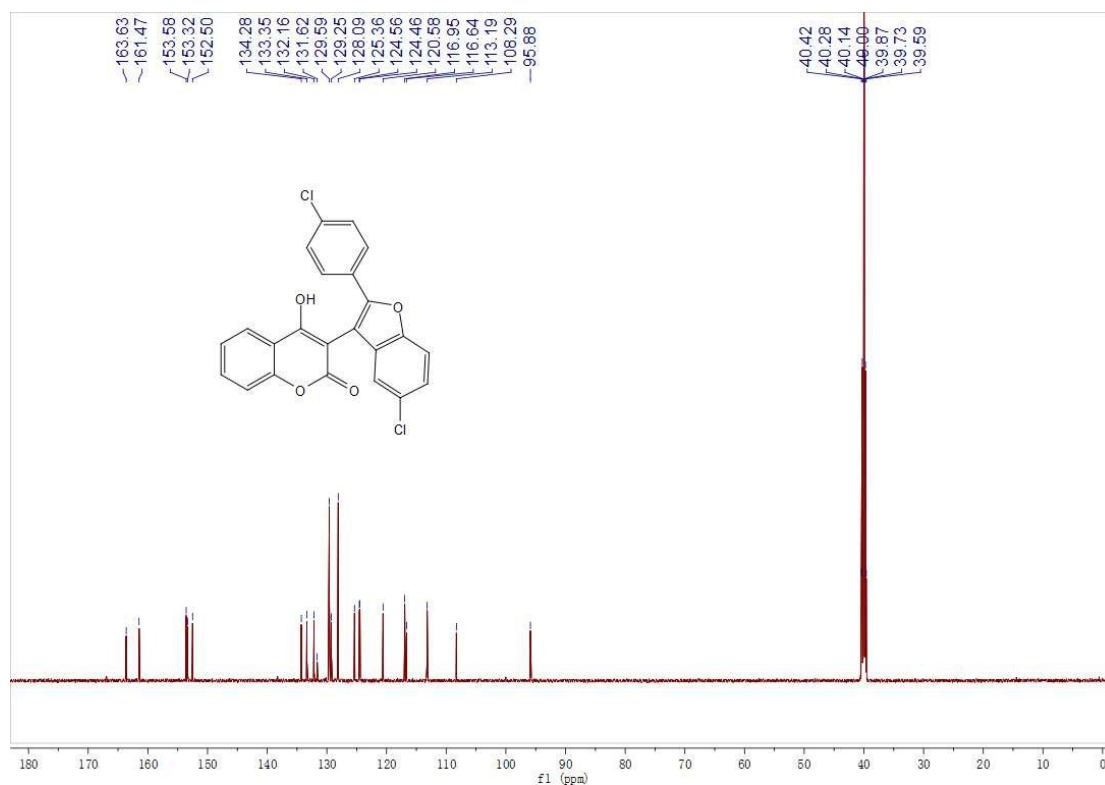
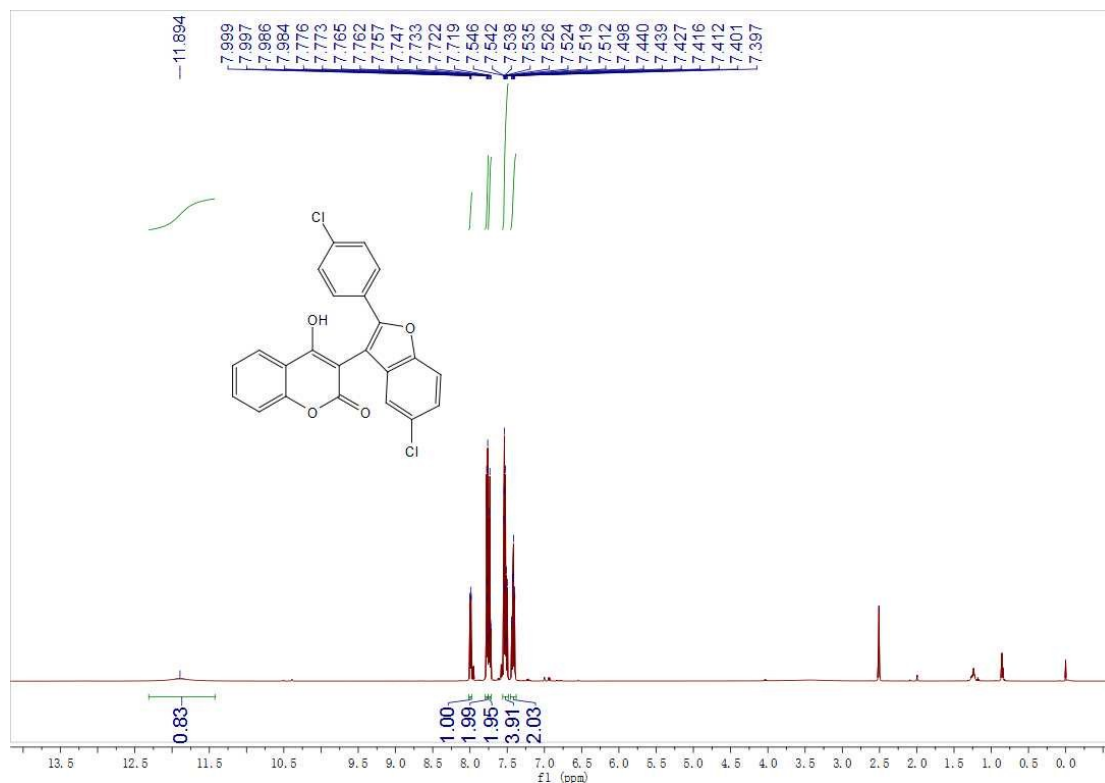
Mass spectrum of the intermediate

We used MS to monitor the reaction, and the possible intermediate was observed (see below).

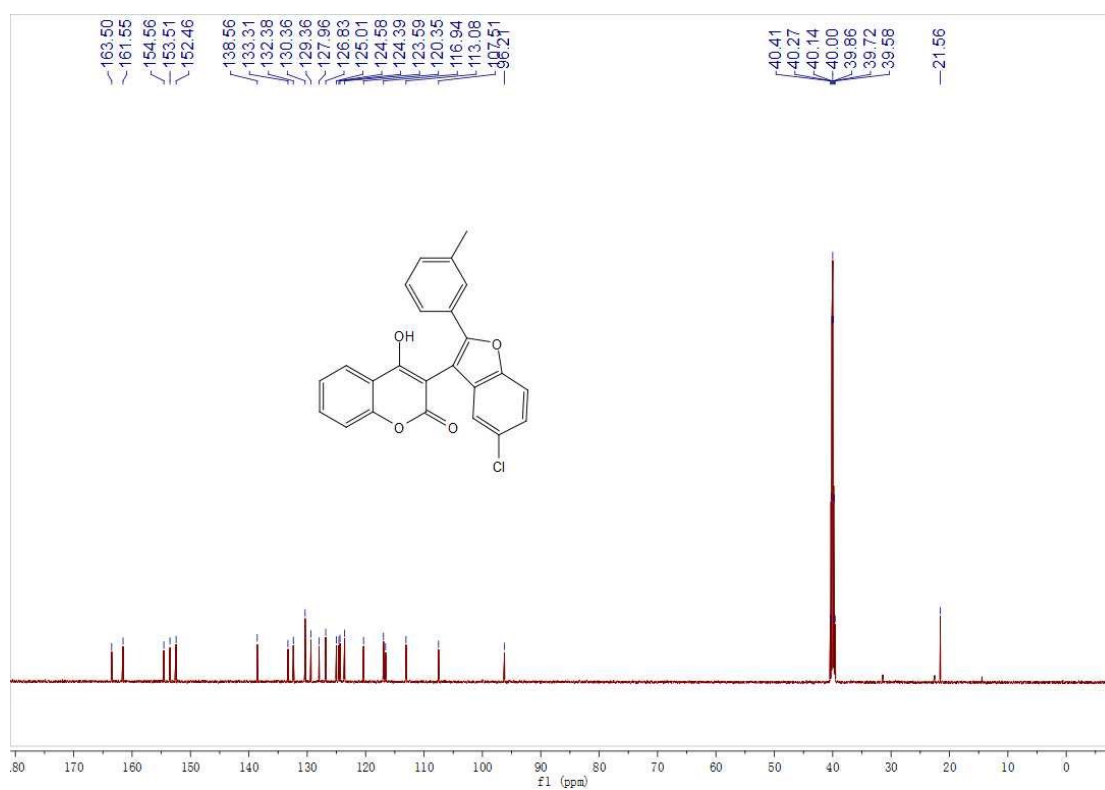
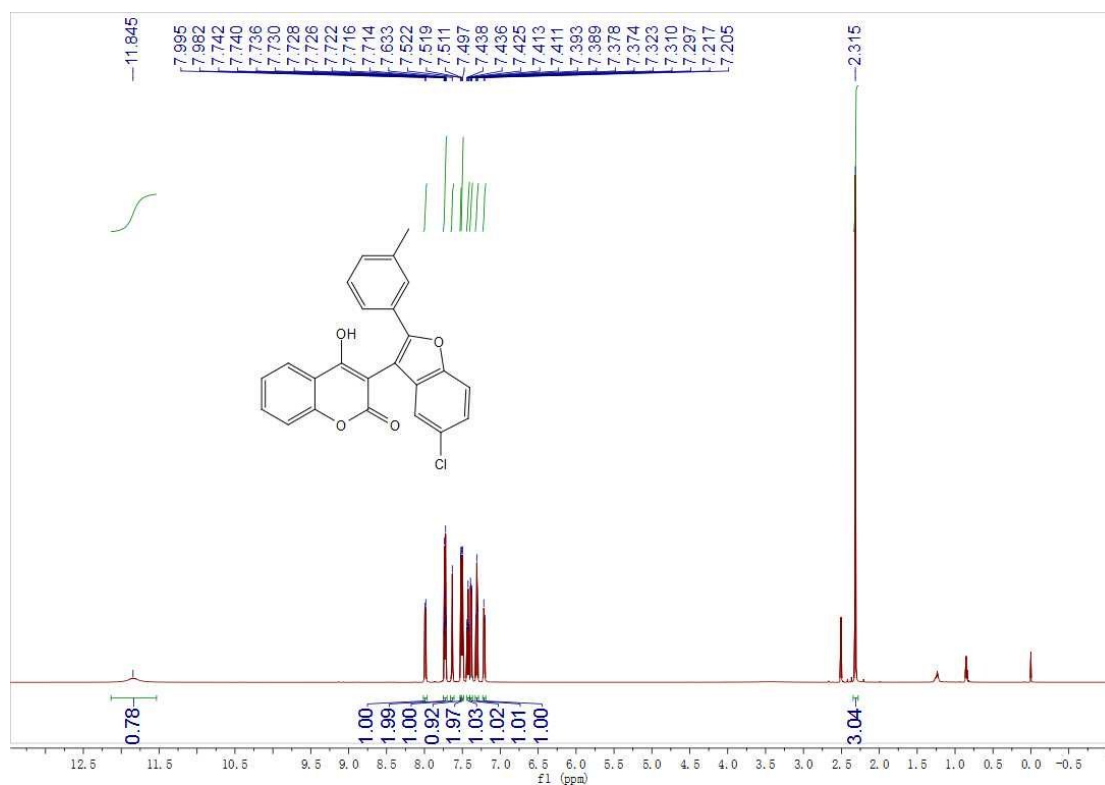


4. ¹H NMR and ¹³C NMR spectra of compounds 4, 5

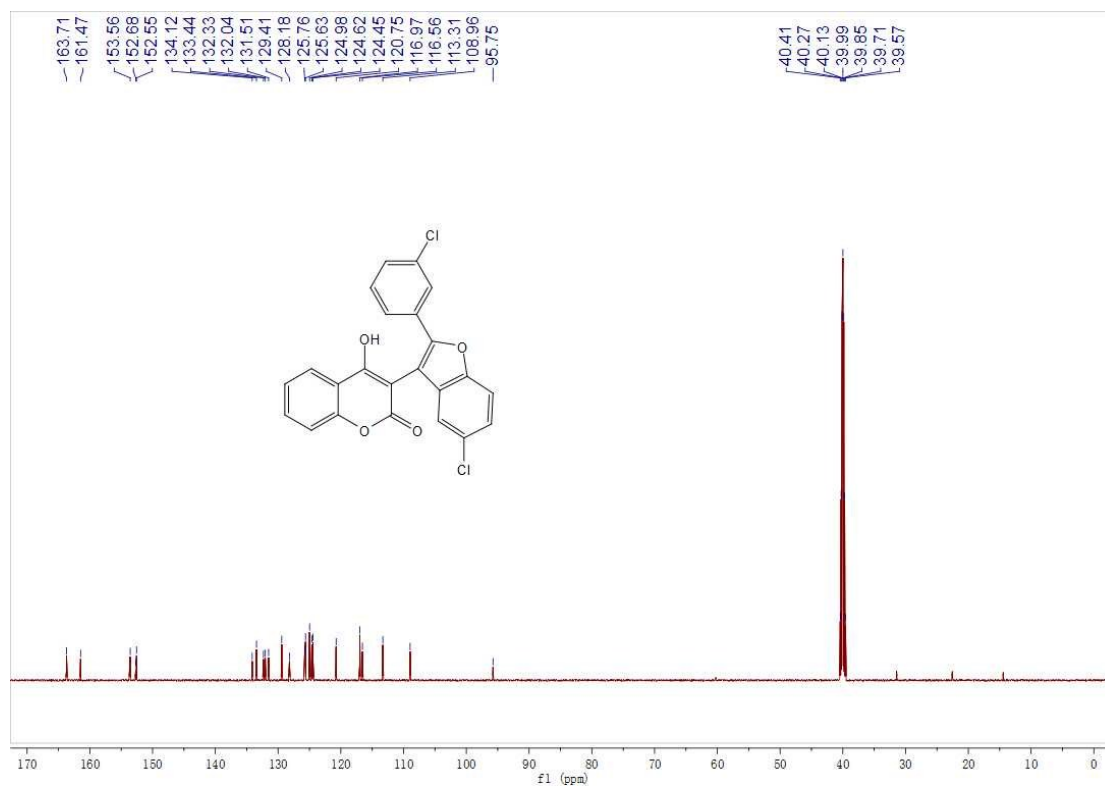
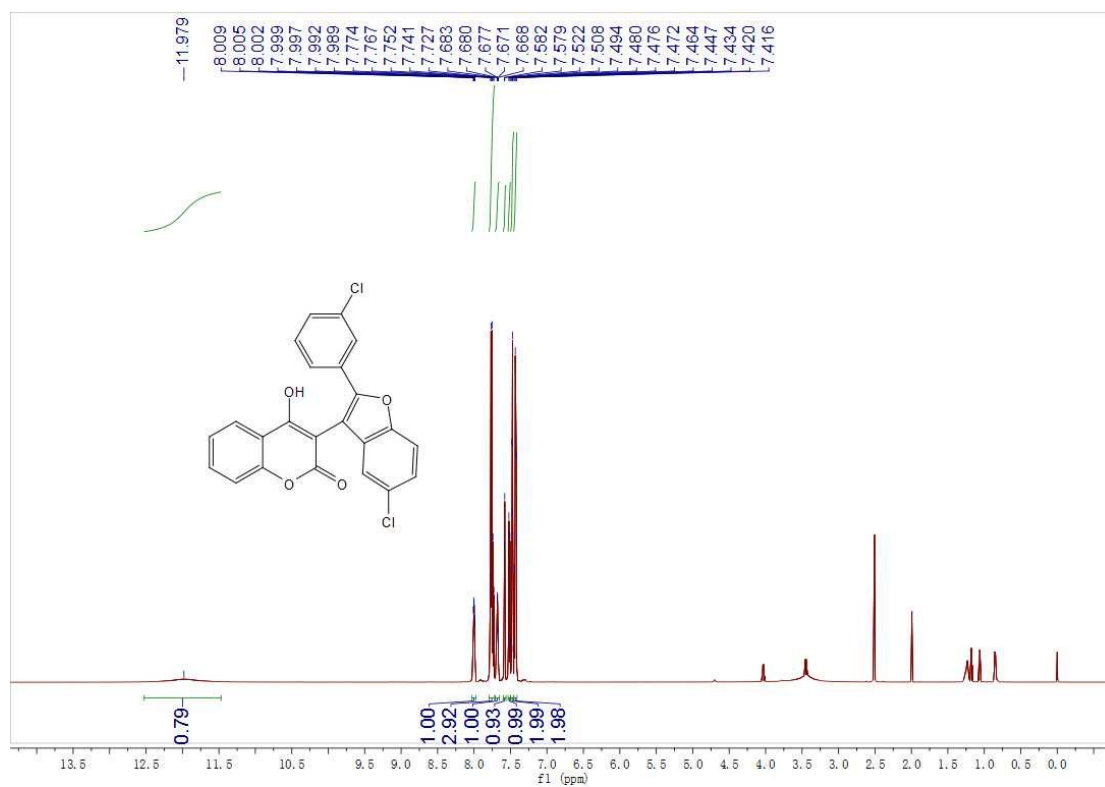
3-(5-chloro-2-(4-chlorophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4a**)



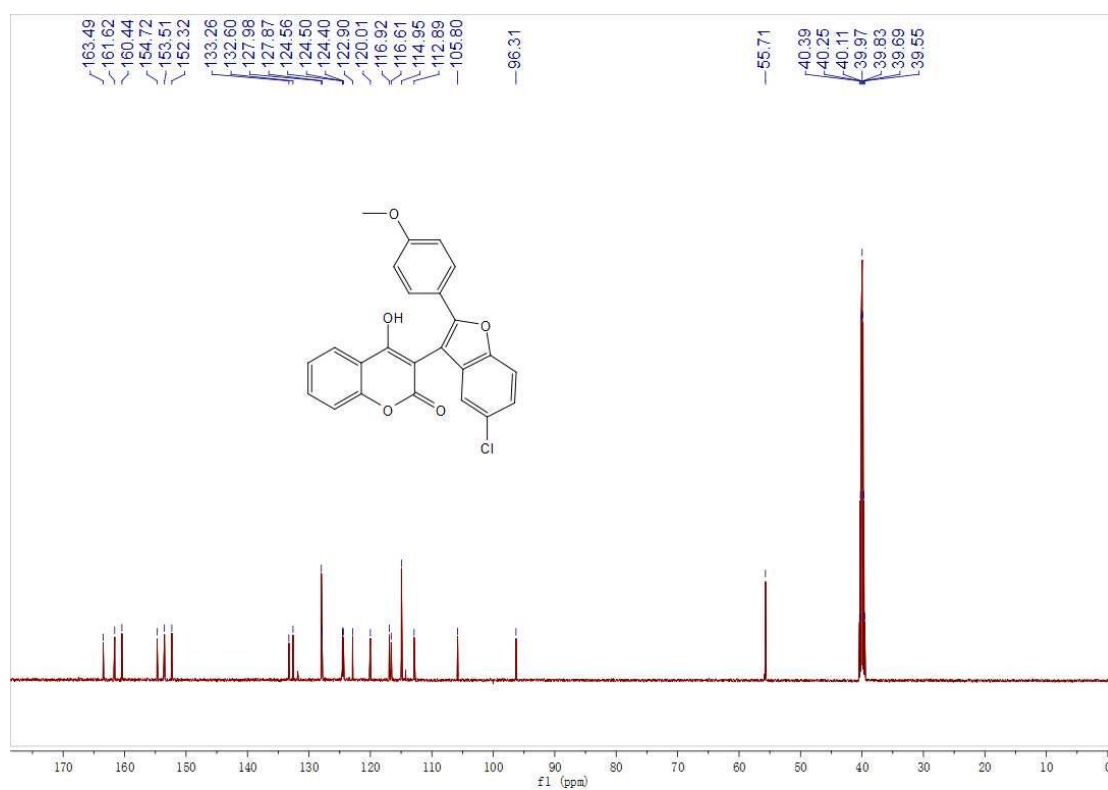
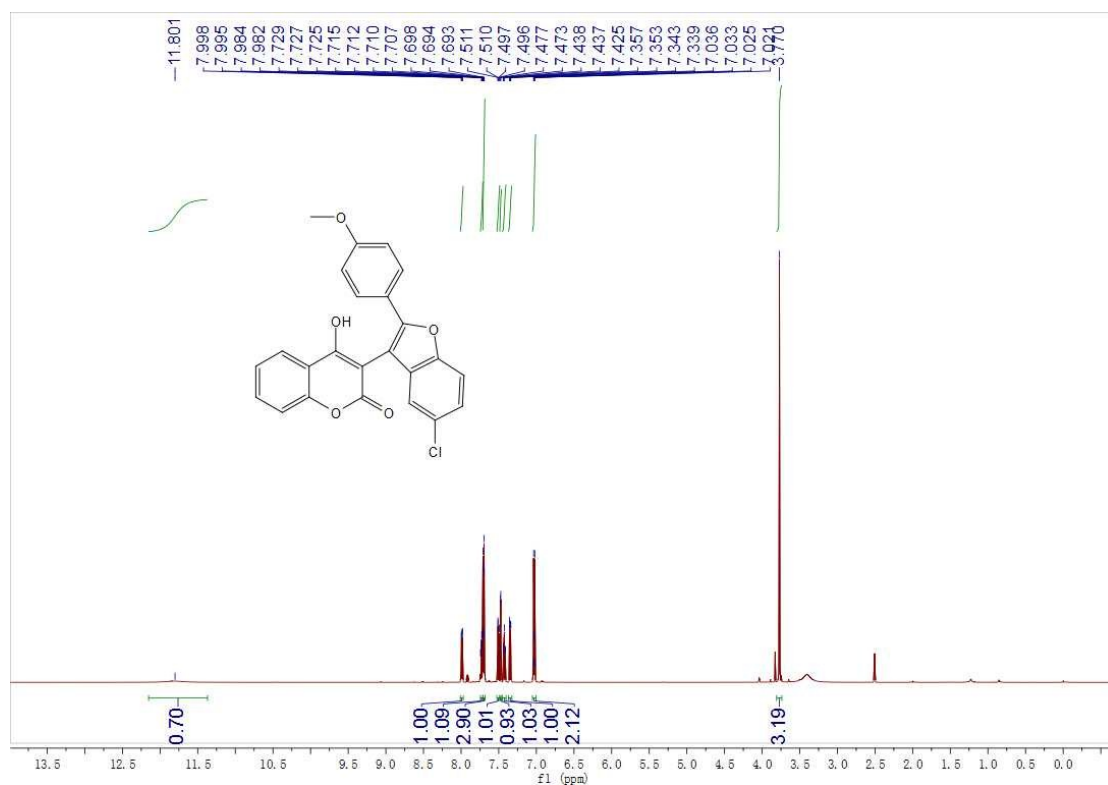
3-(5-chloro-2-(*m*-tolyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4b**).



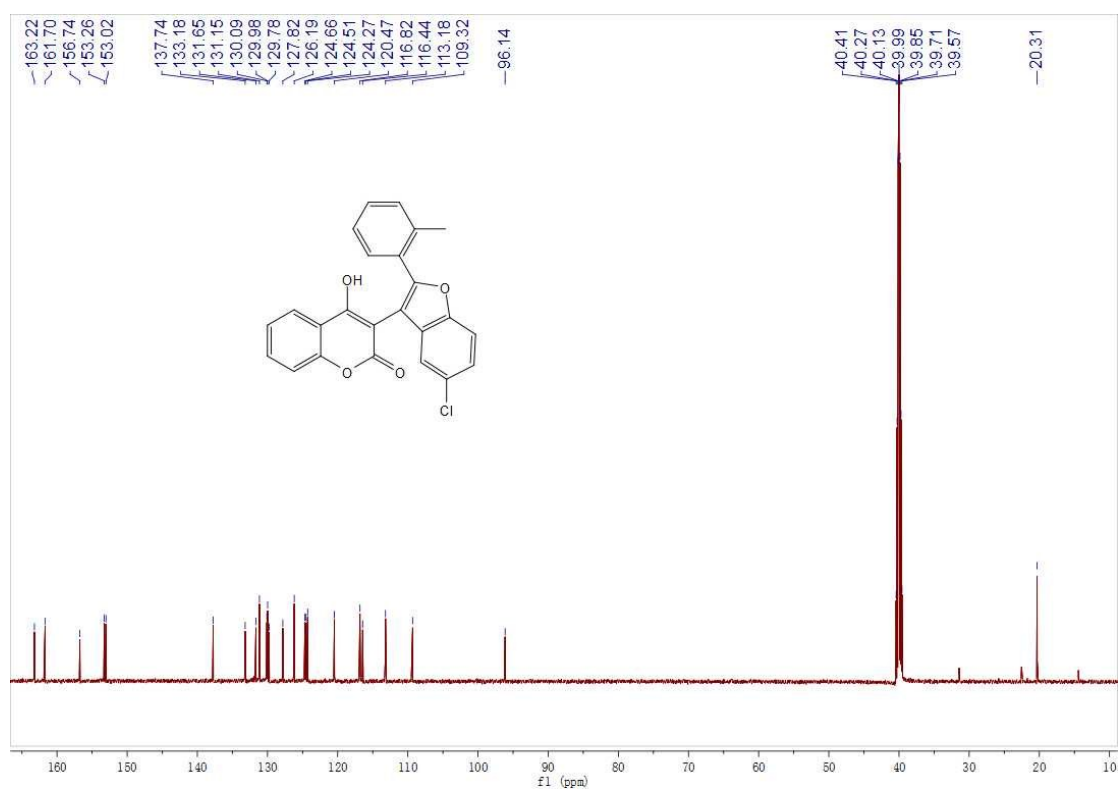
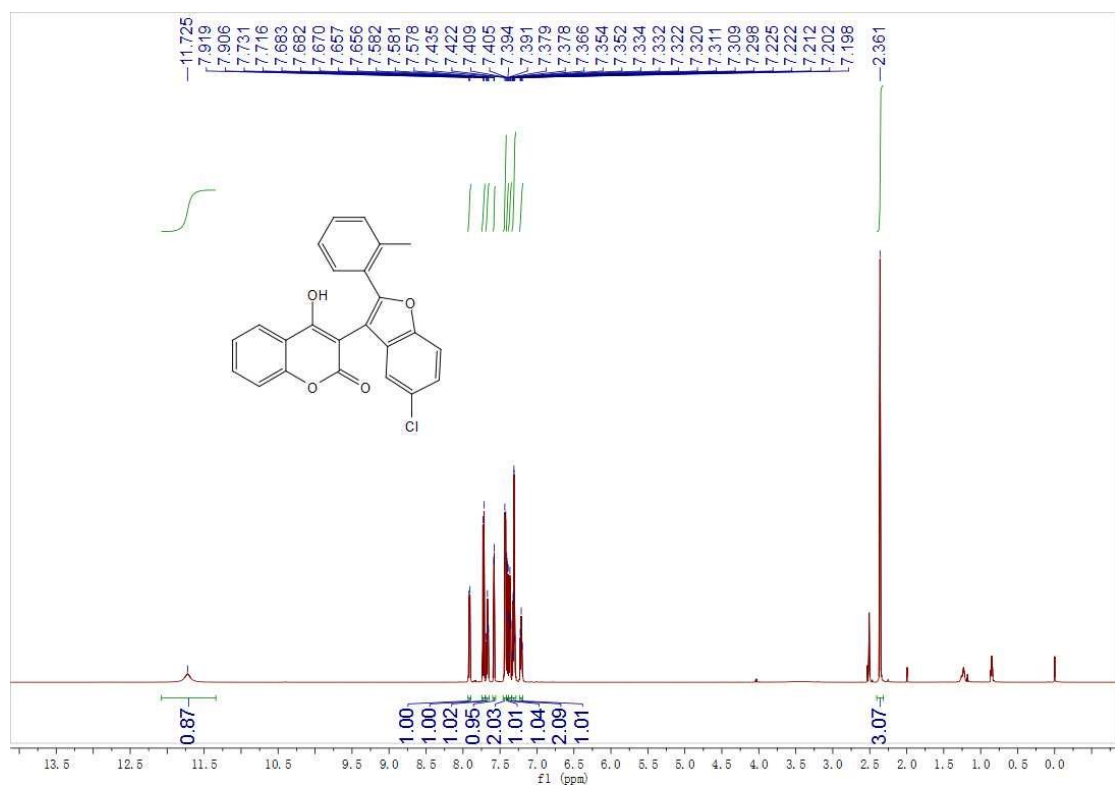
3-(5-chloro-2-(3-chlorophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4c**)



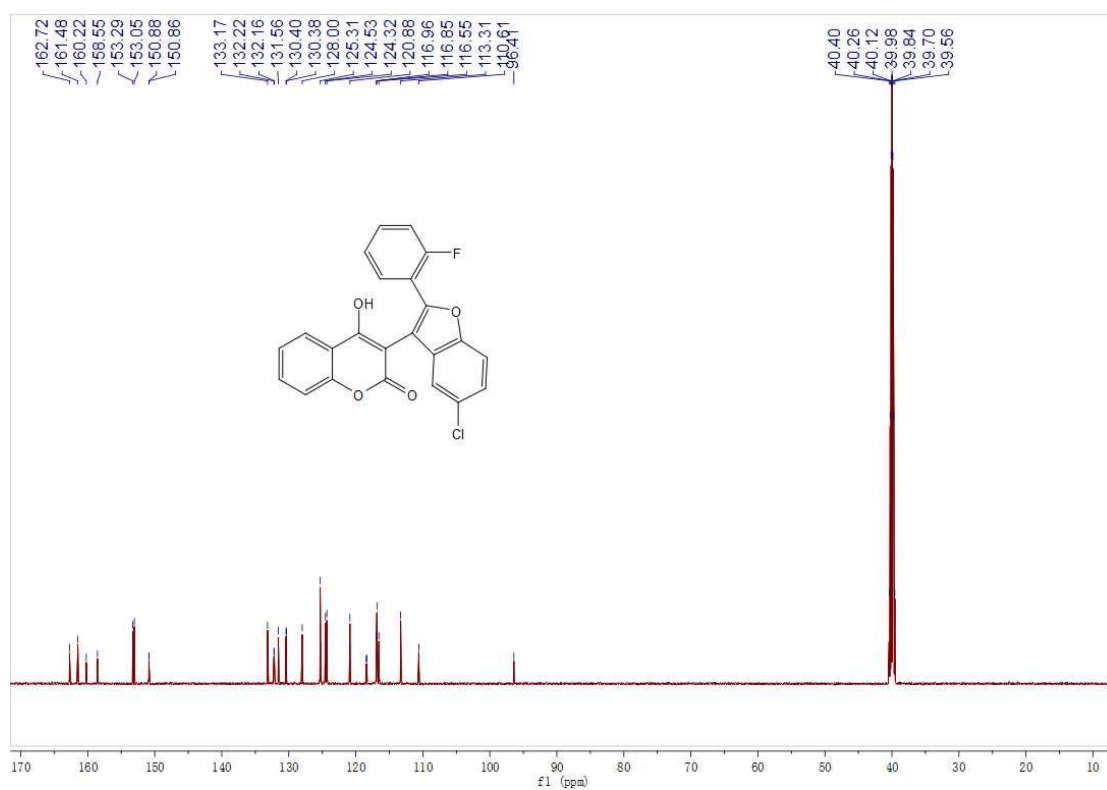
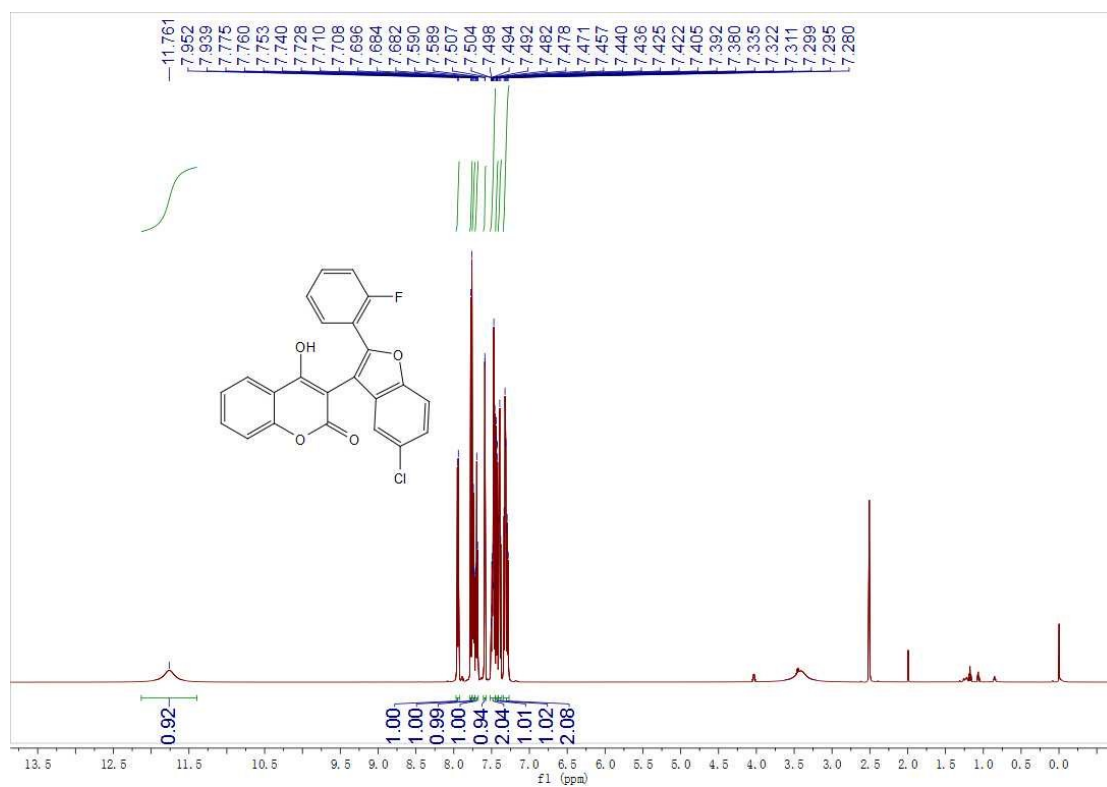
3-(5-chloro-2-(4-methoxyphenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4d**)



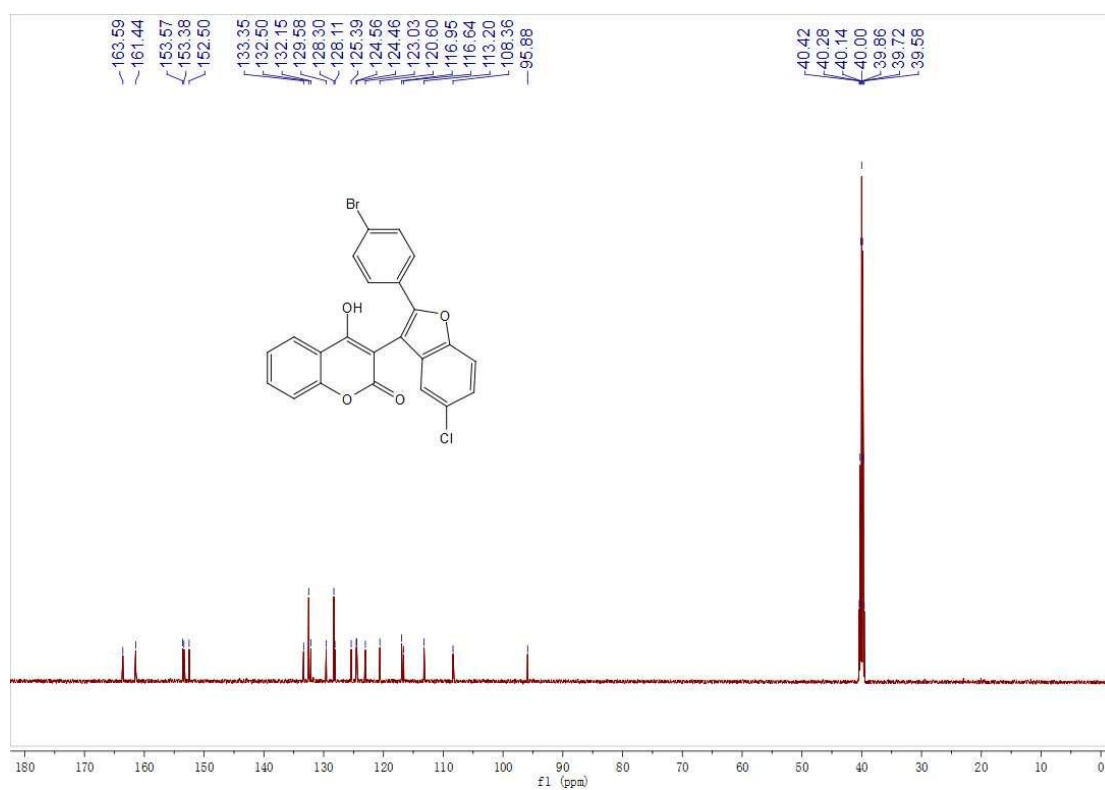
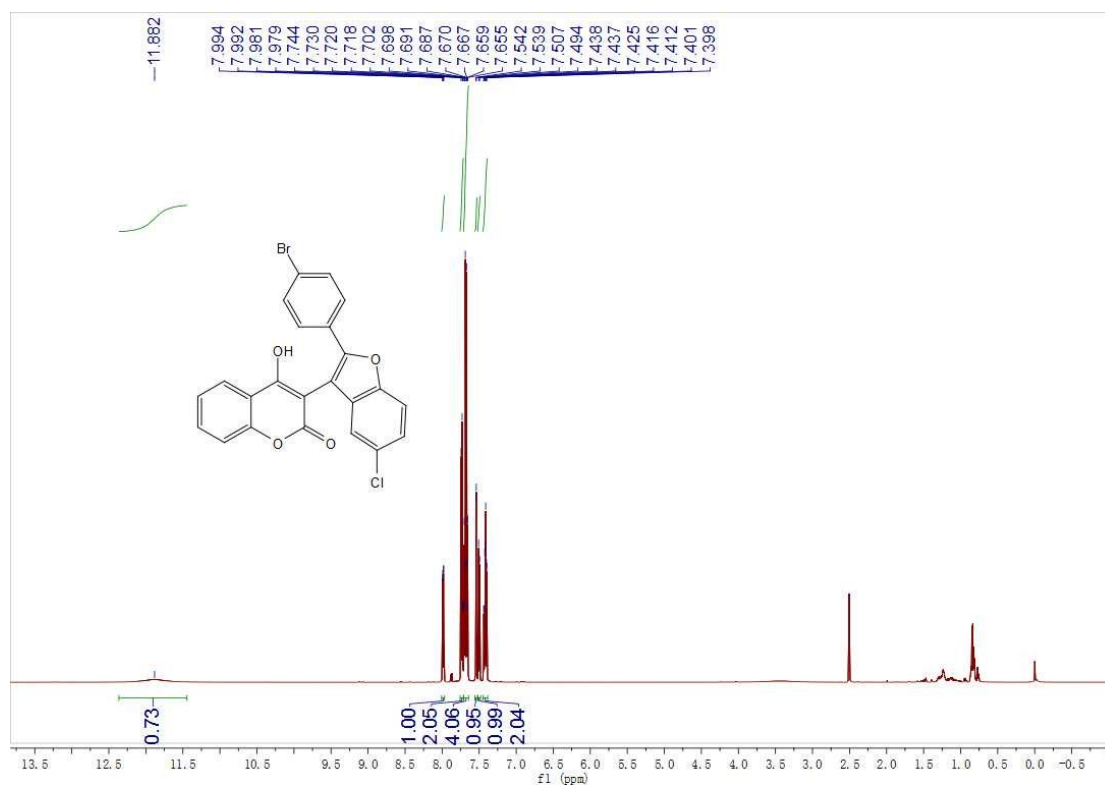
3-(5-chloro-2-(*o*-tolyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4e**)



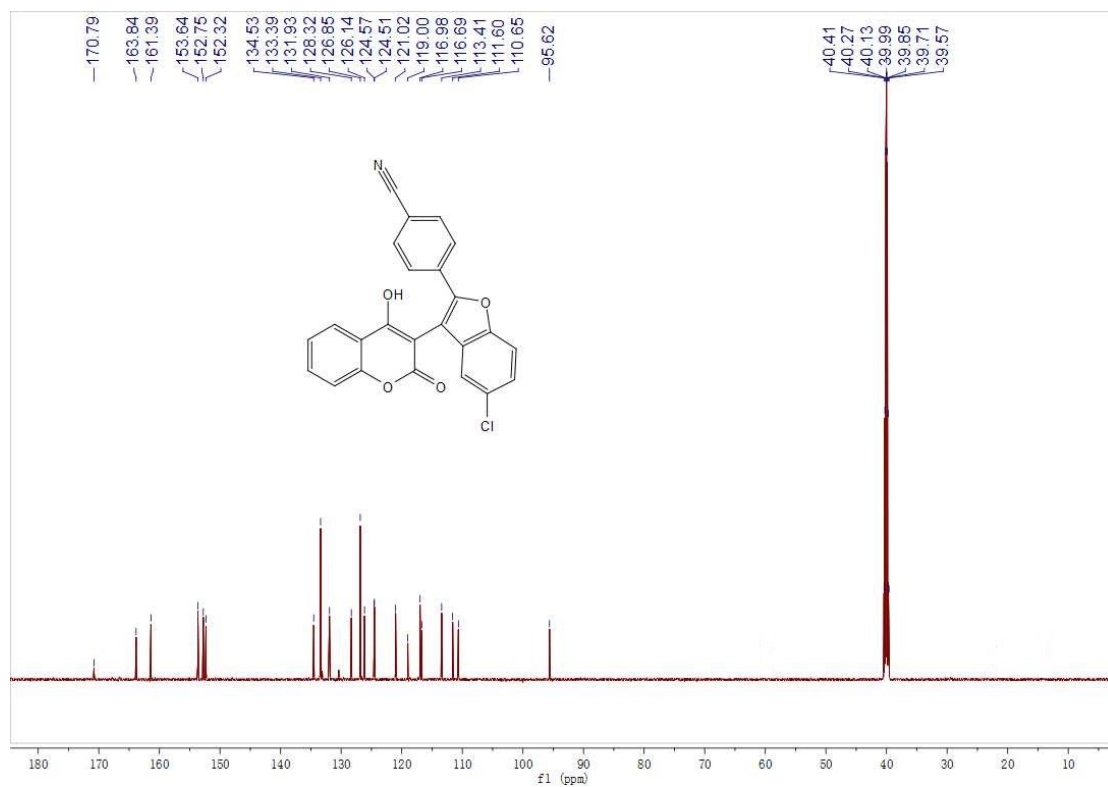
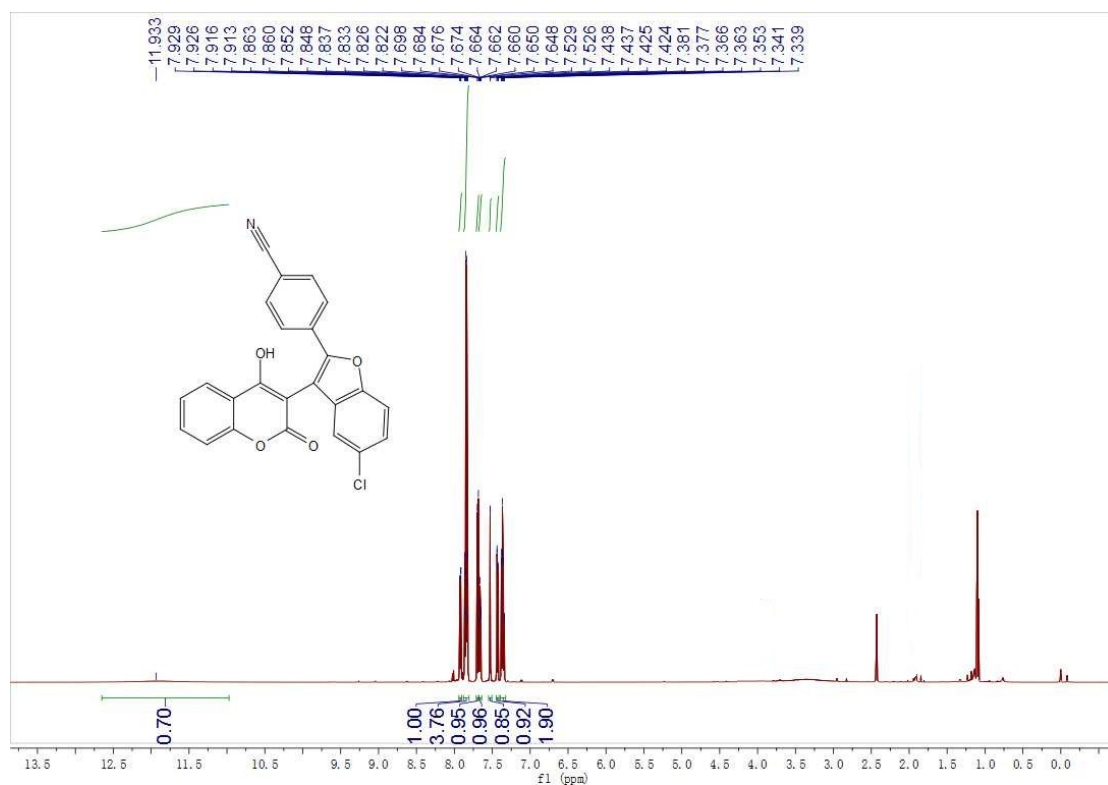
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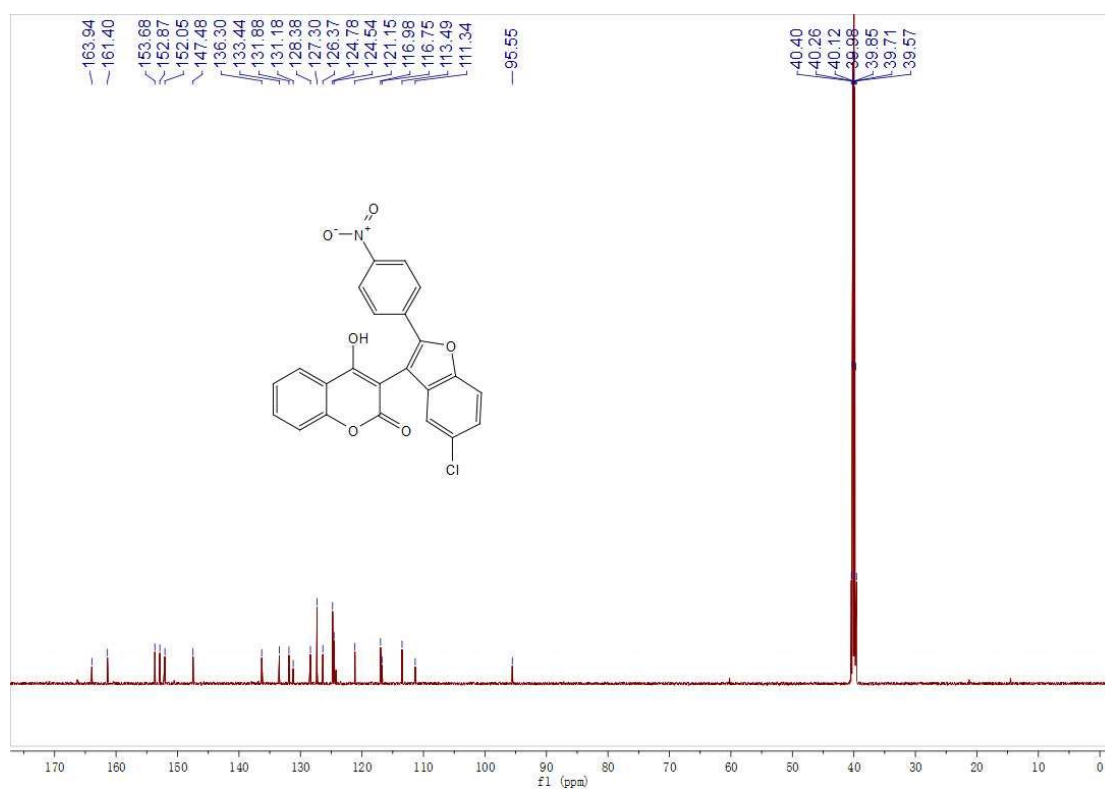
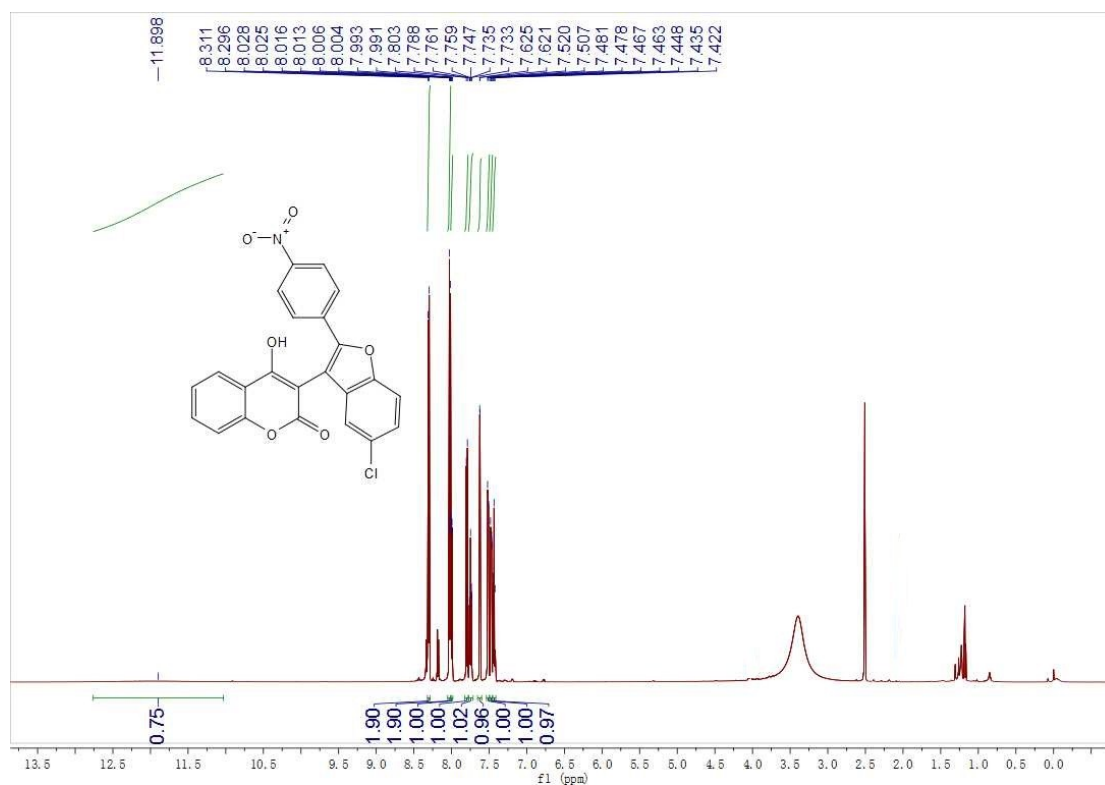
3-(2-(4-bromophenyl)-5-chlorobenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4g**)



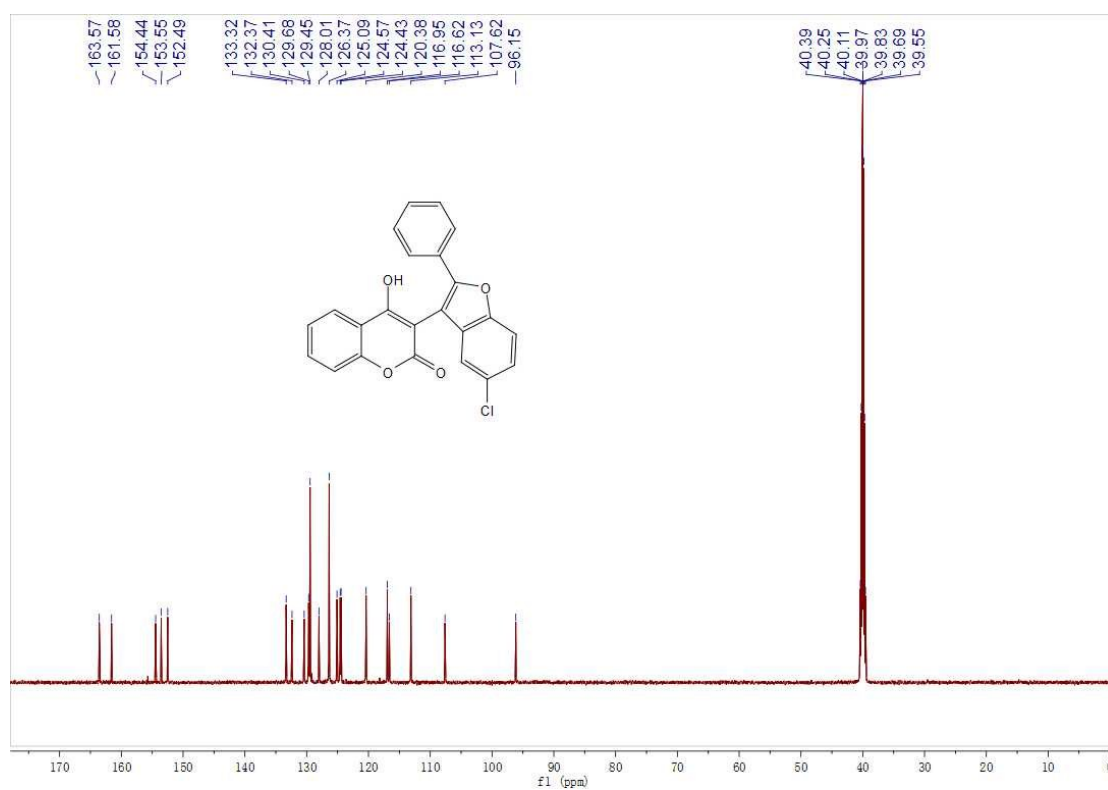
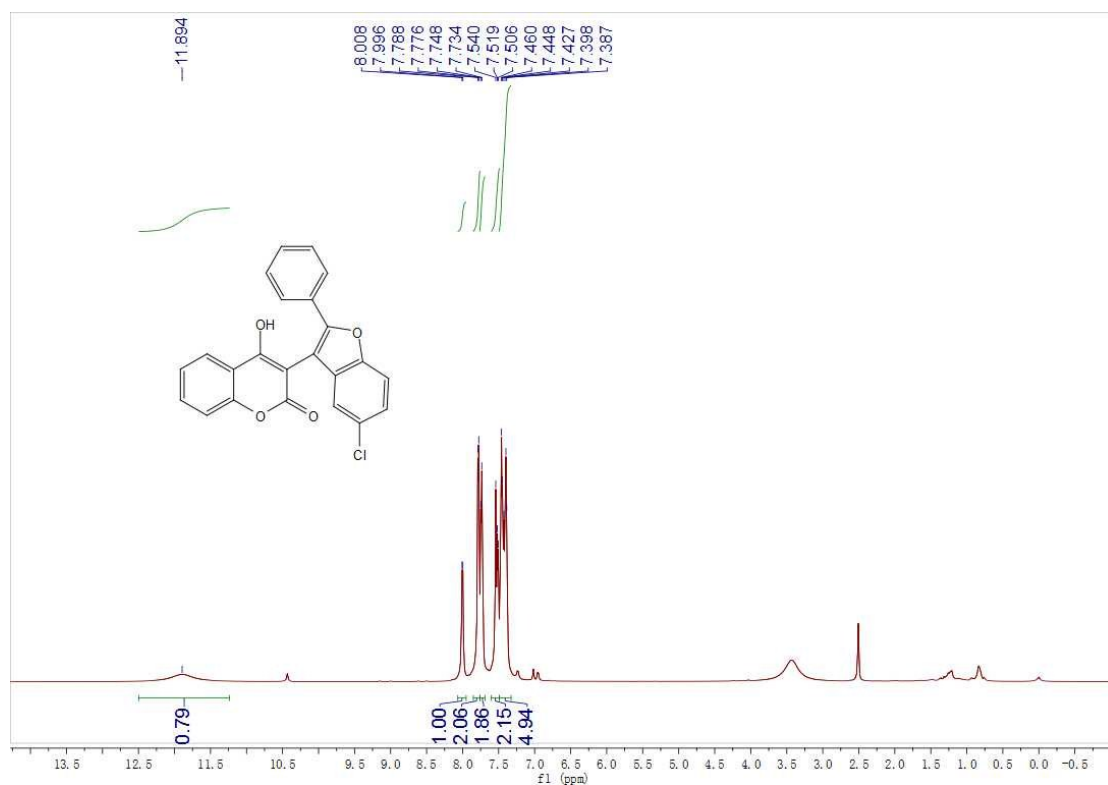
4-(5-chloro-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)benzofuran-2-yl)benzonitrile (**4h**)



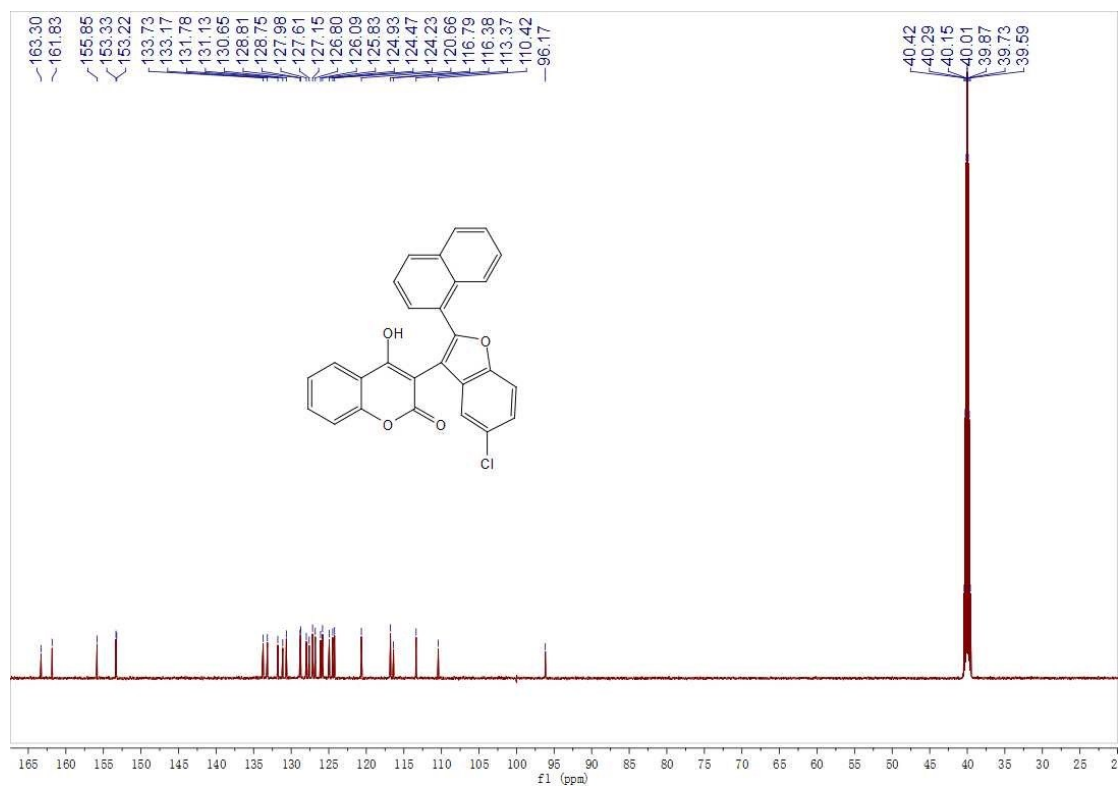
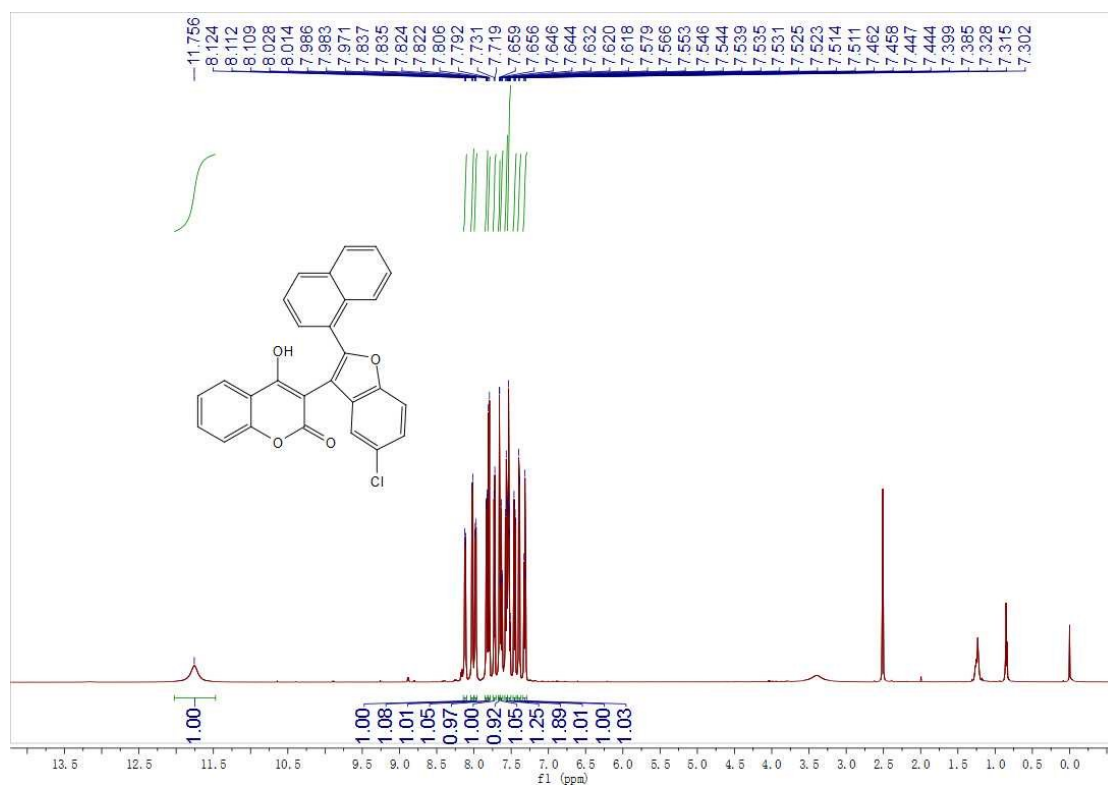
3-(5-chloro-2-(4-nitrophenyl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4i**)



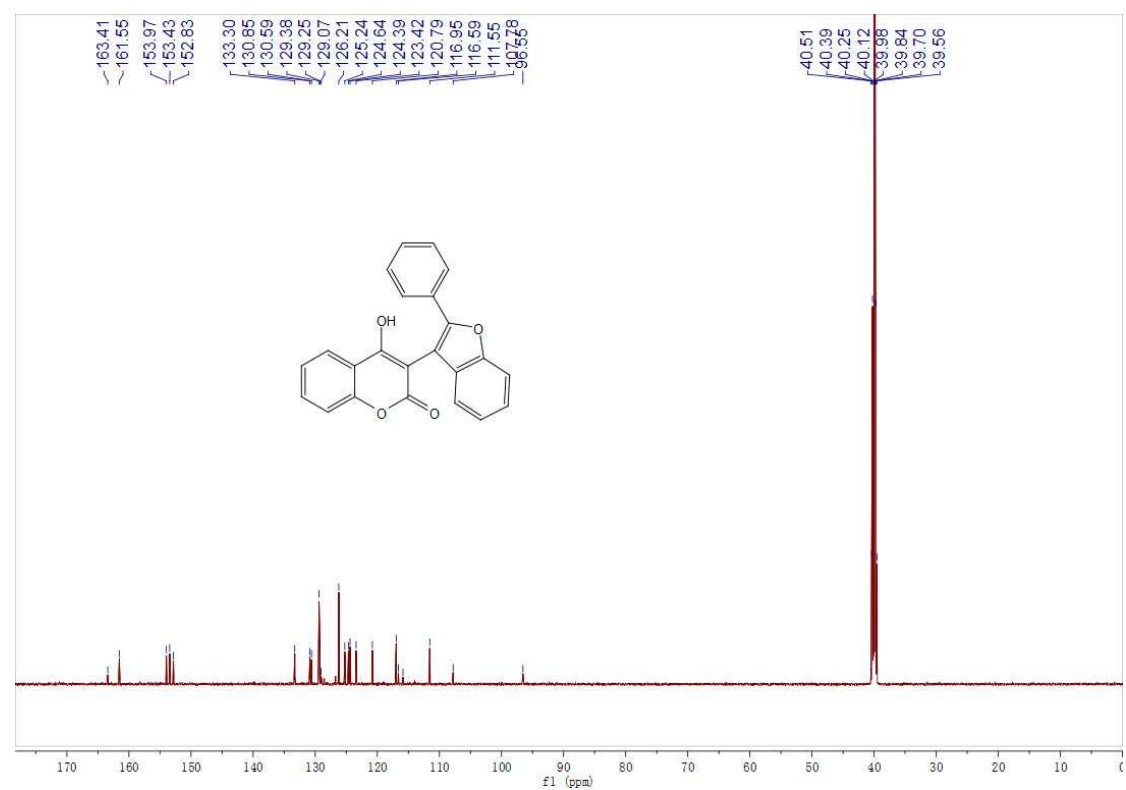
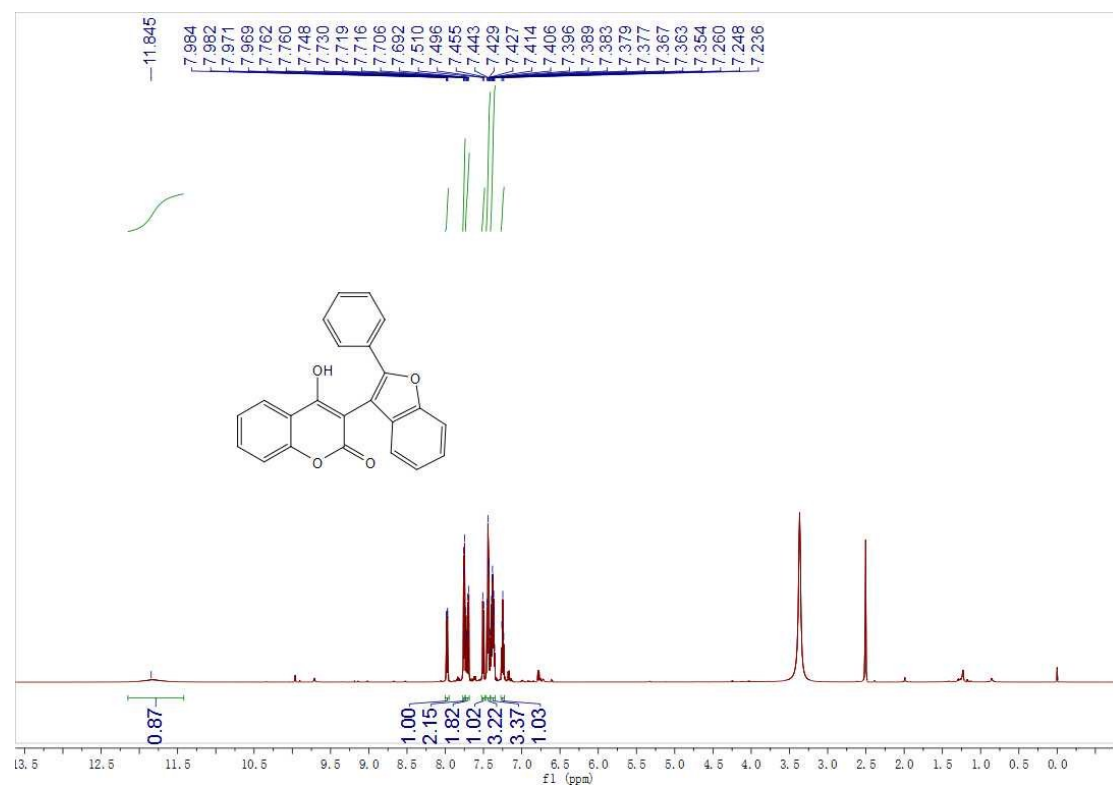
3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4j**)



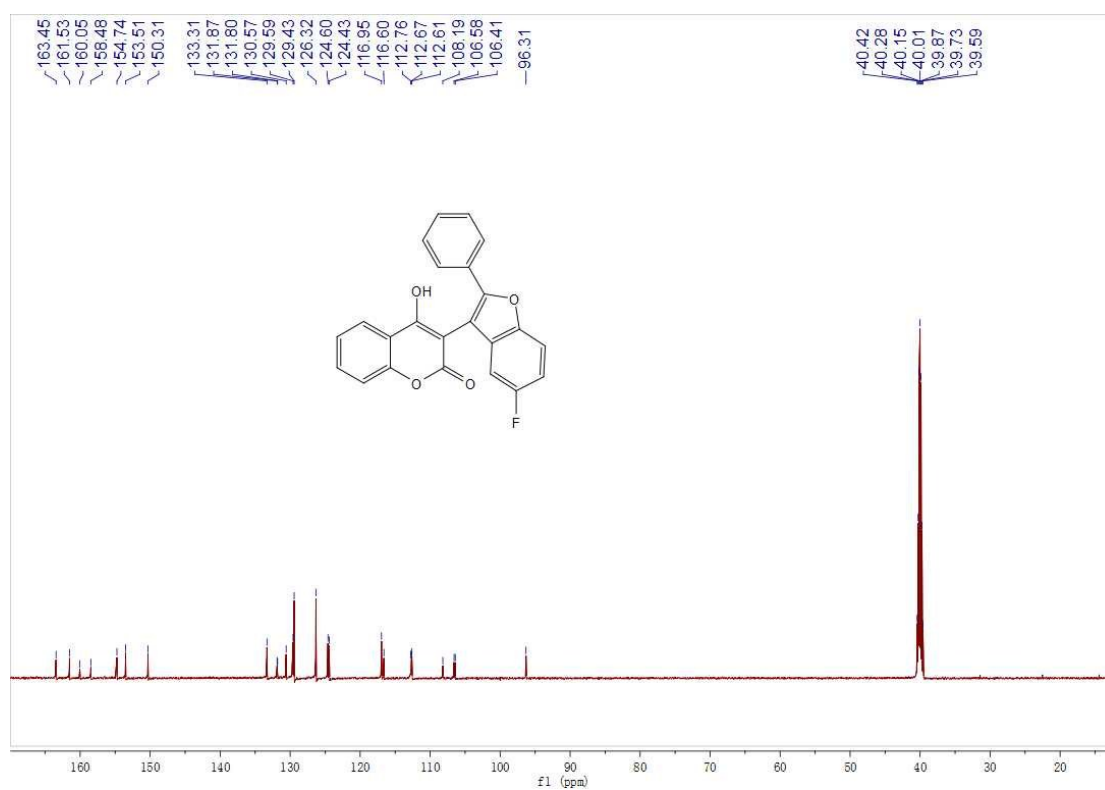
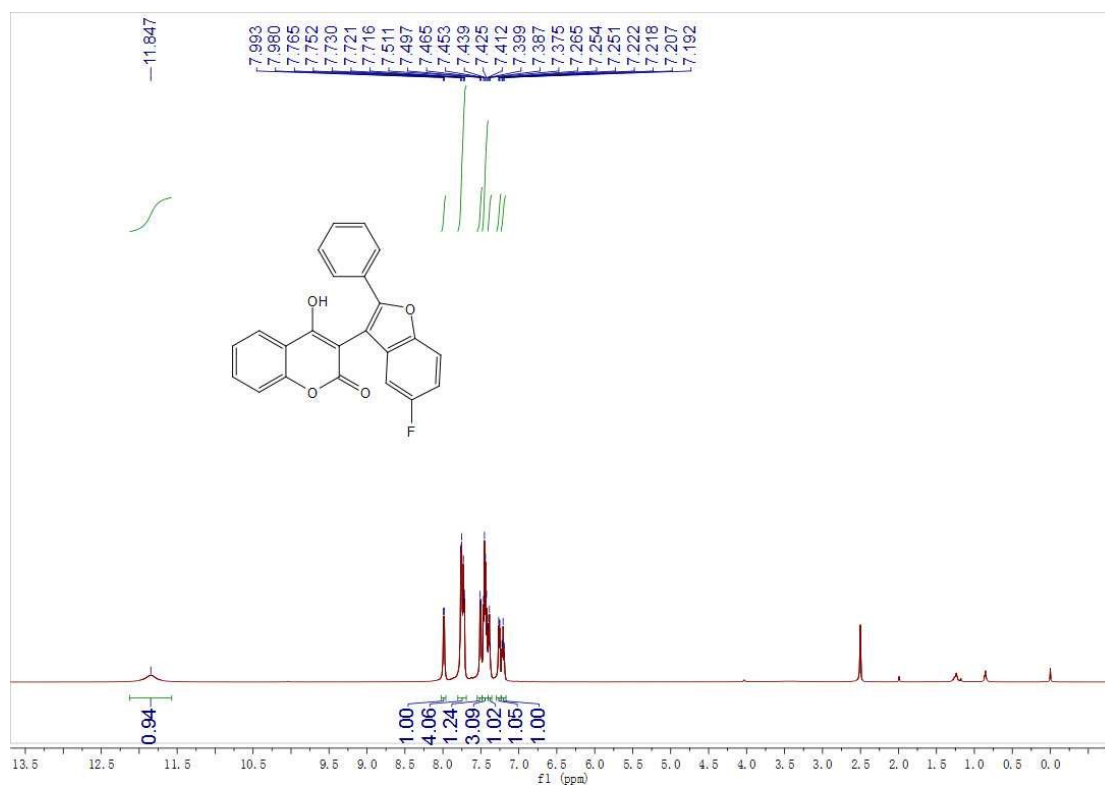
3-(5-chloro-2-(naphthalen-1-yl)benzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4k**)



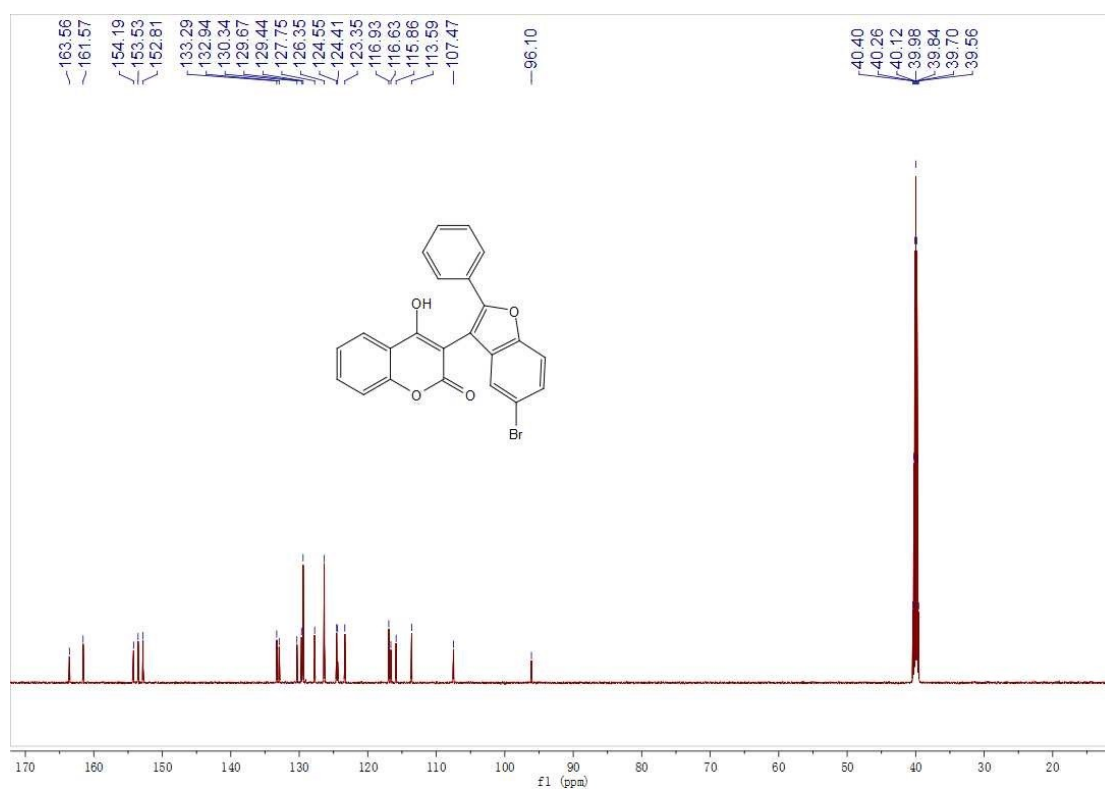
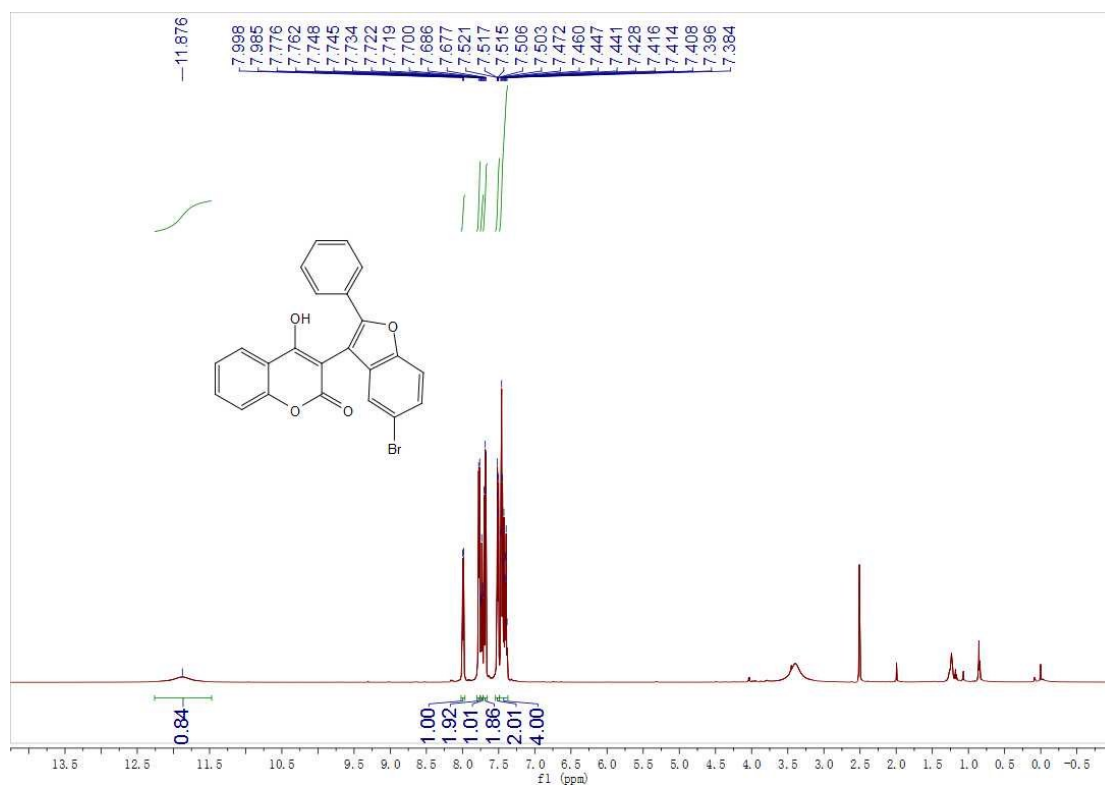
4-hydroxy-3-(2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4l**)



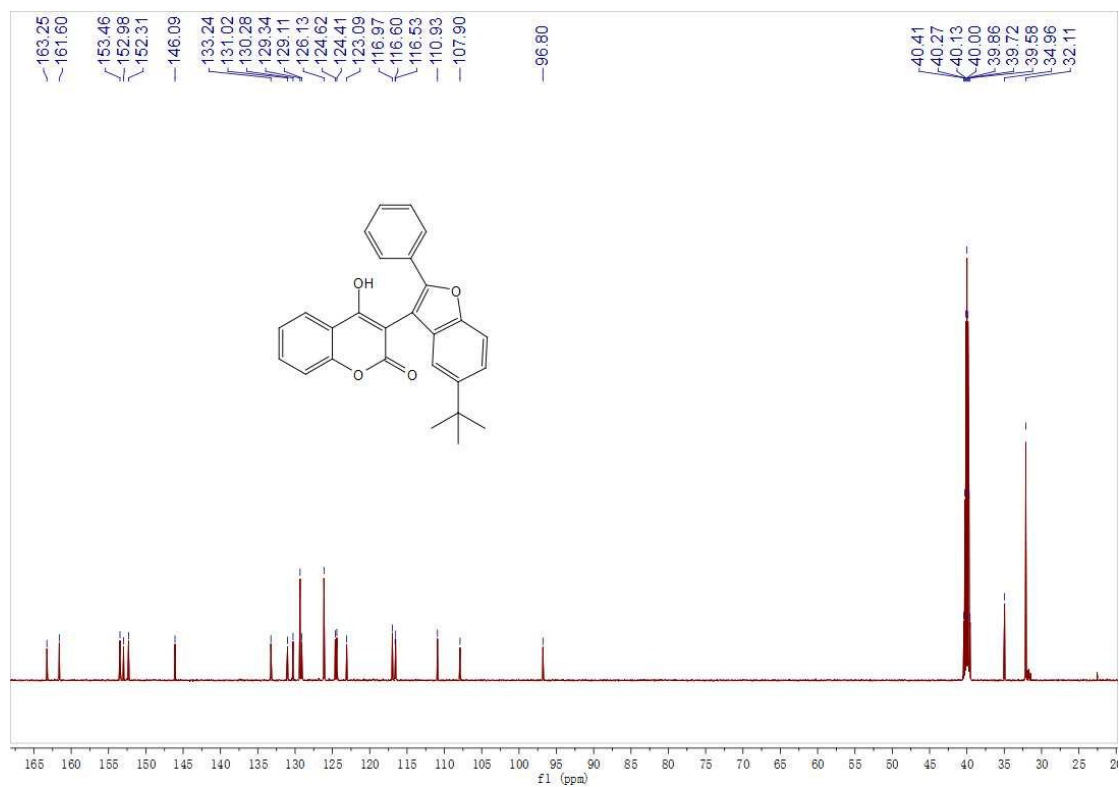
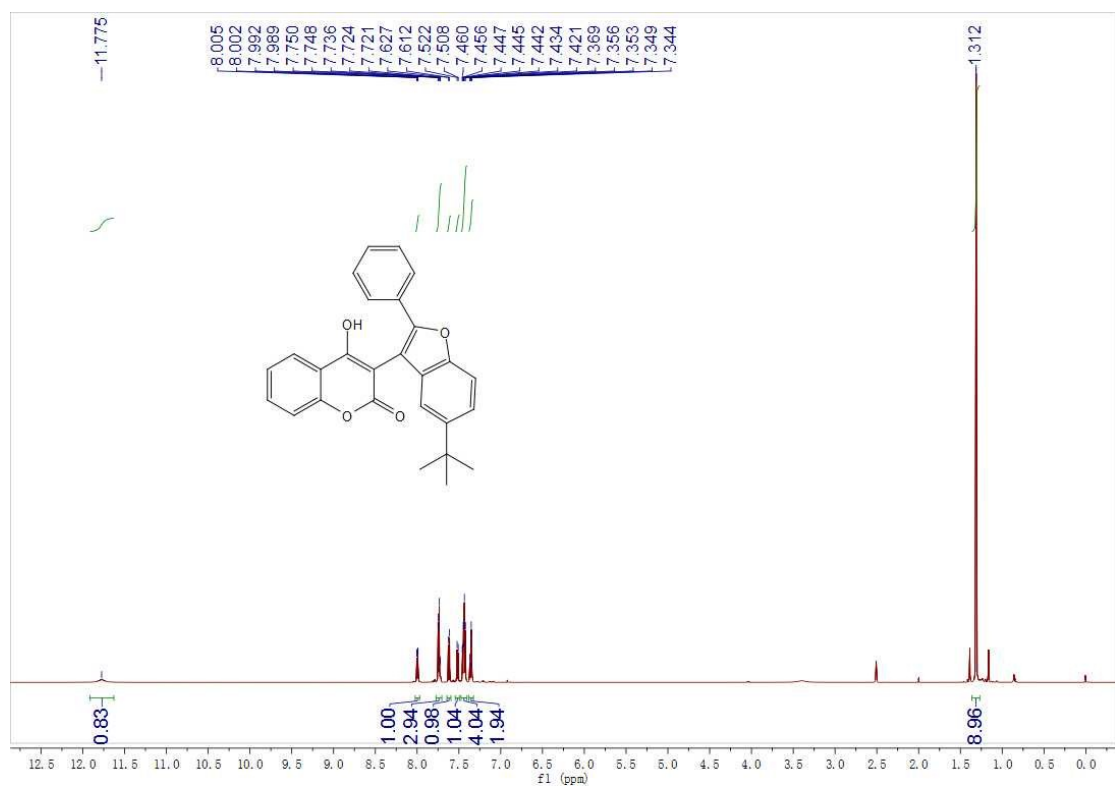
3-(5-fluoro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4m**)



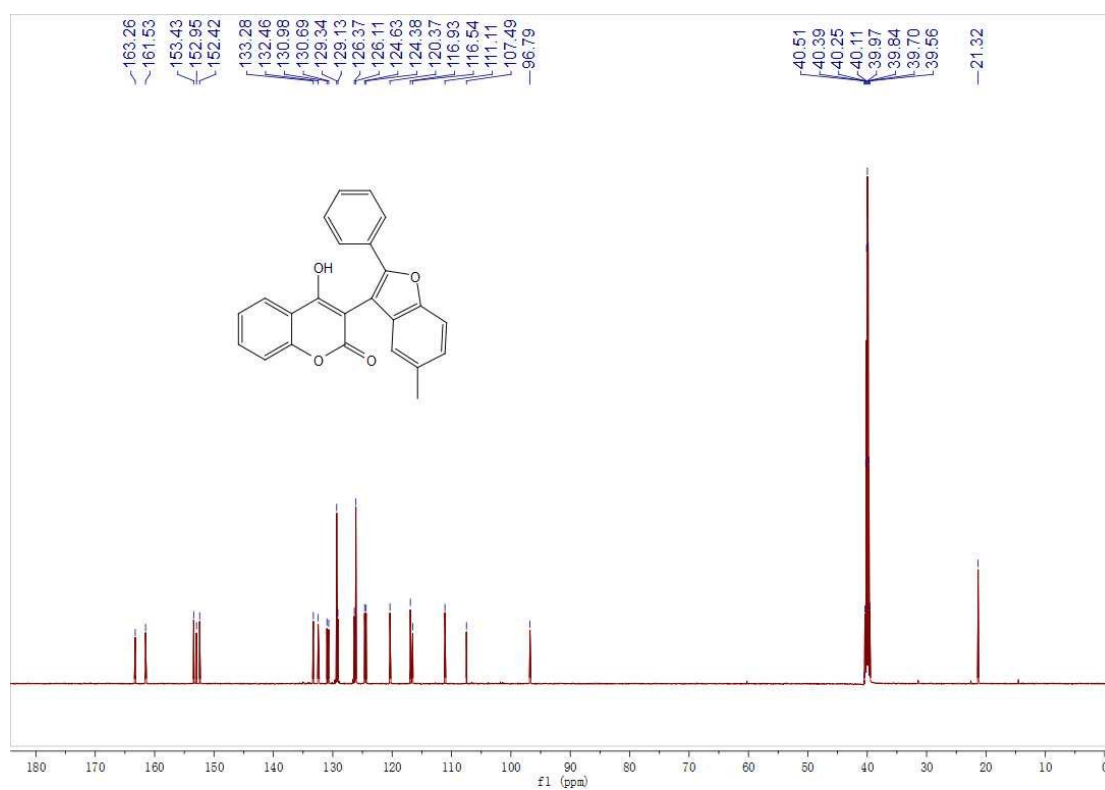
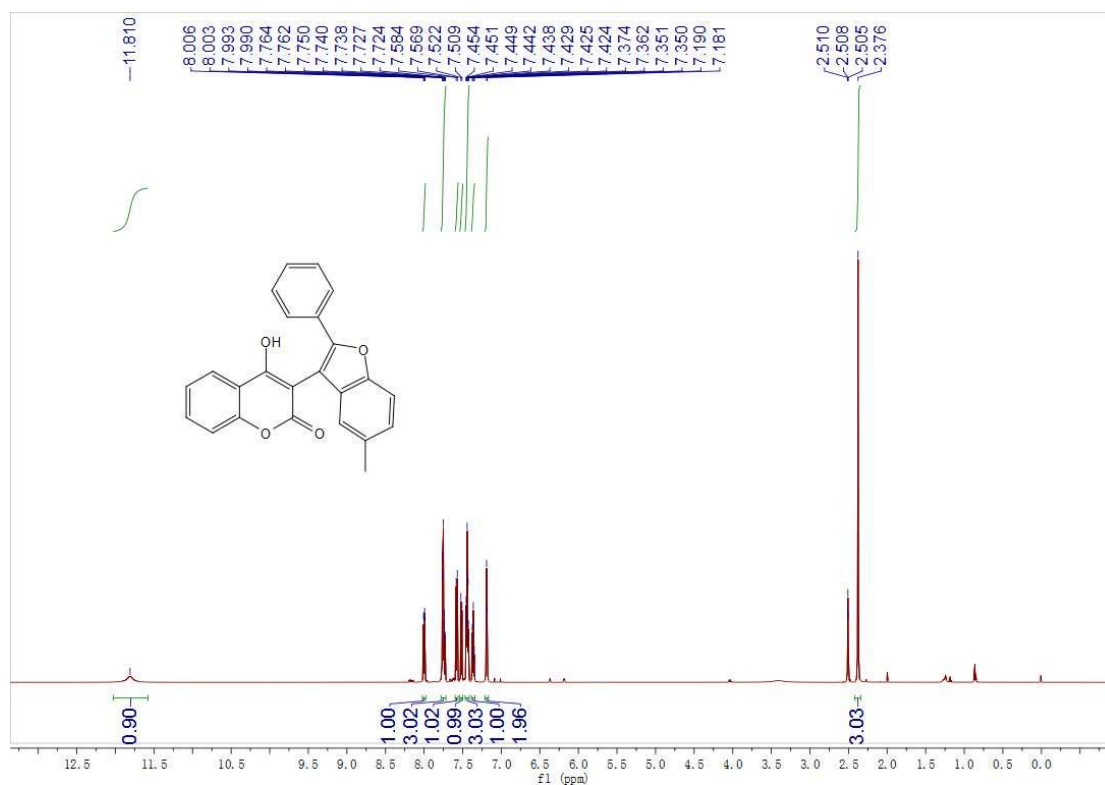
3-(5-bromo-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4n**)



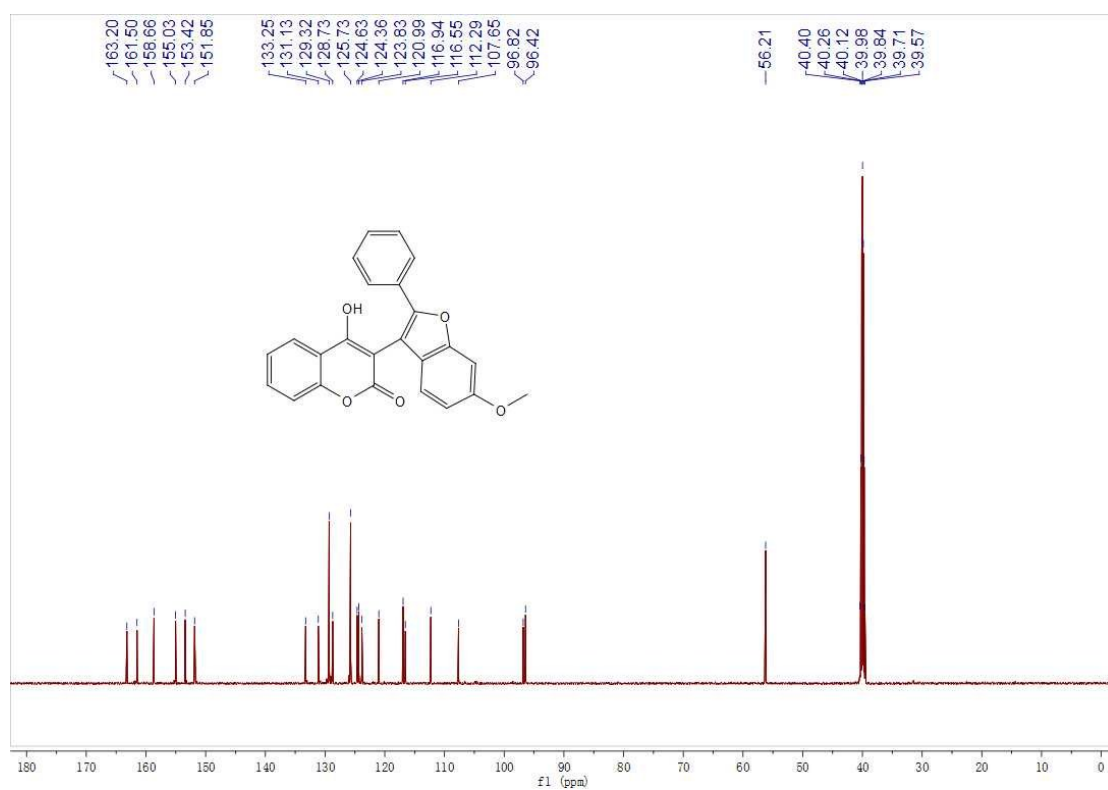
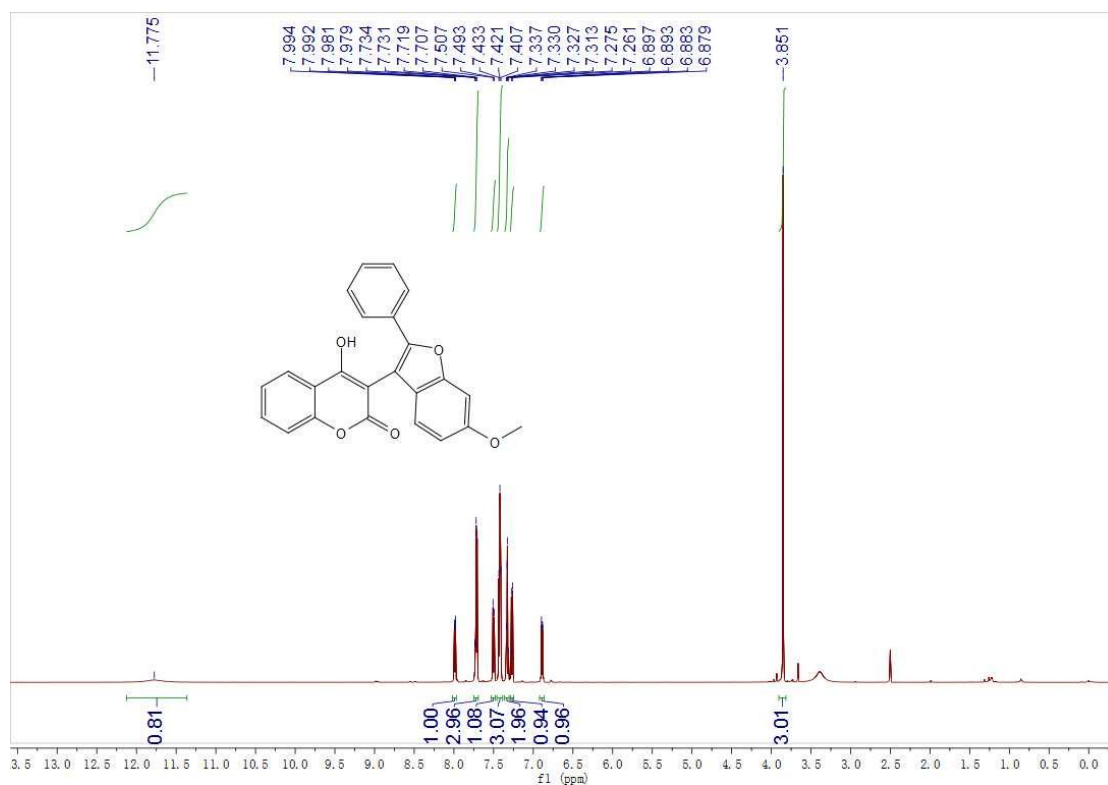
3-(5-(*tert*-butyl)-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4o**)



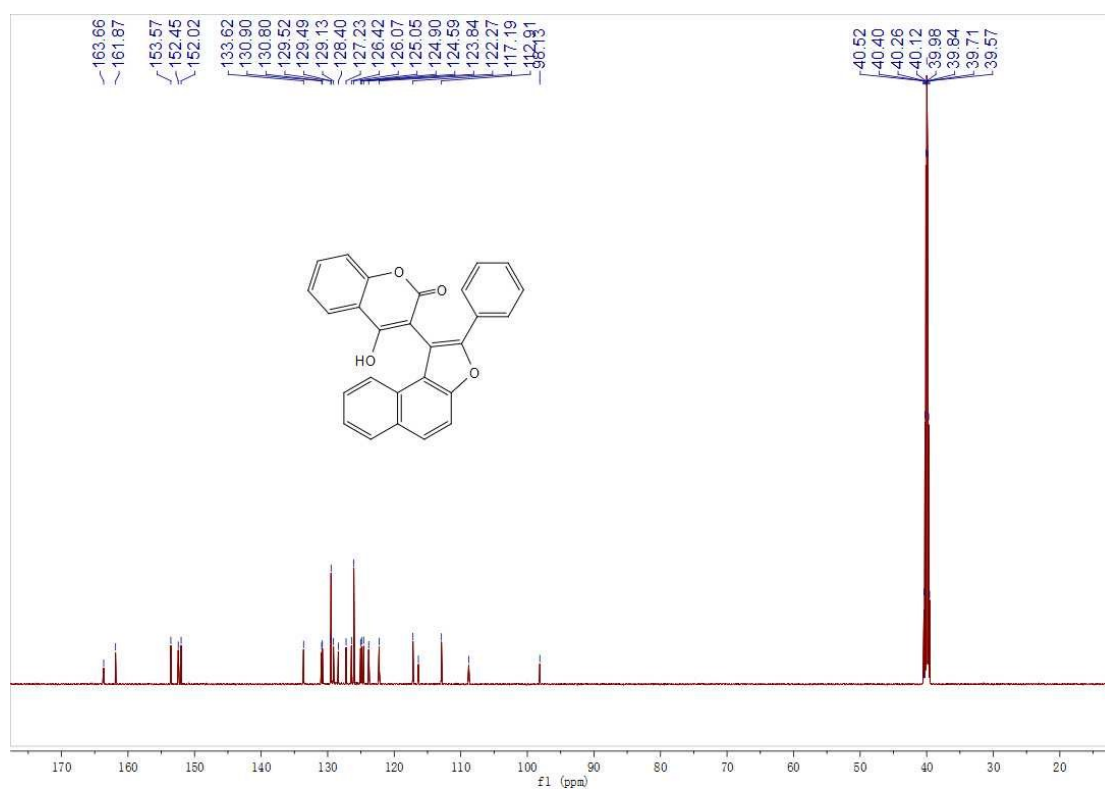
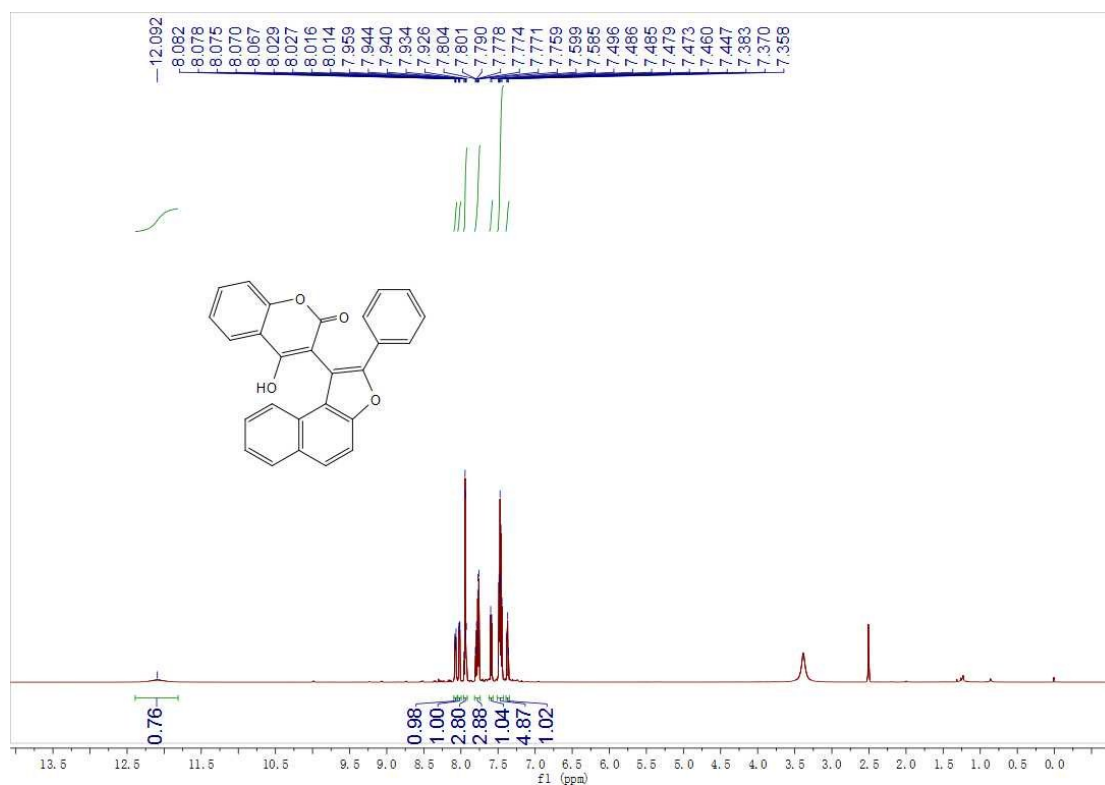
4-hydroxy-3-(5-methyl-2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4p**)



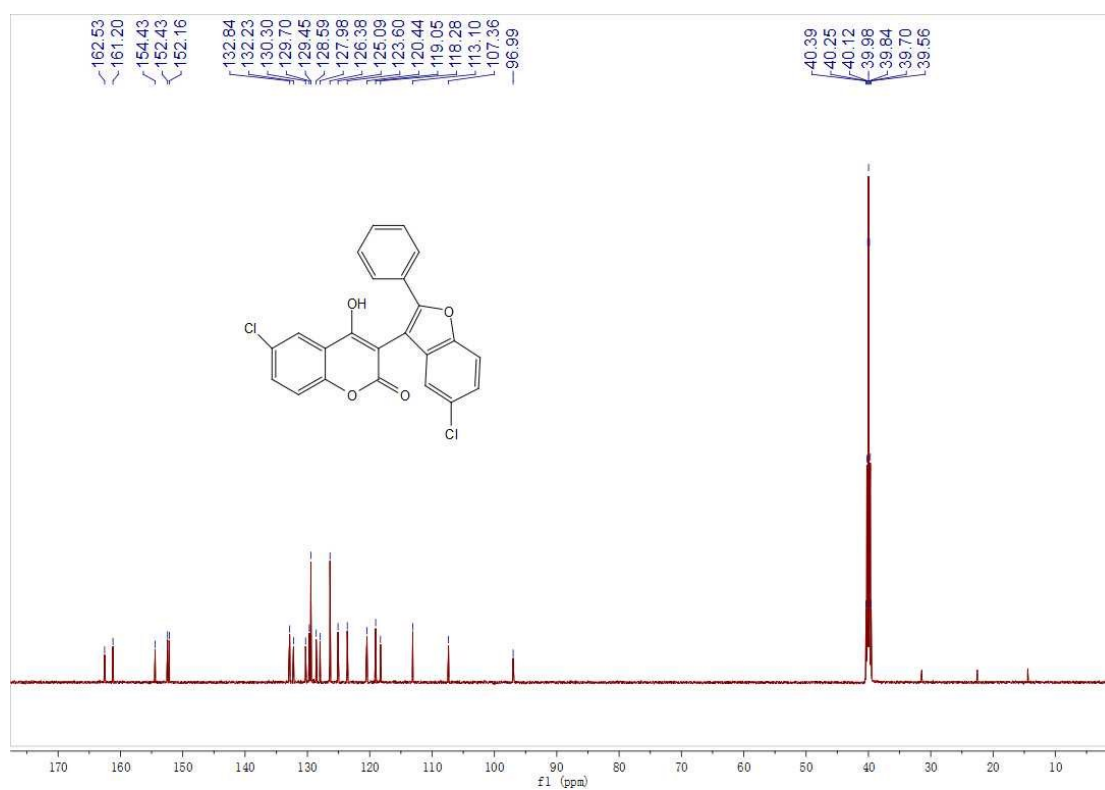
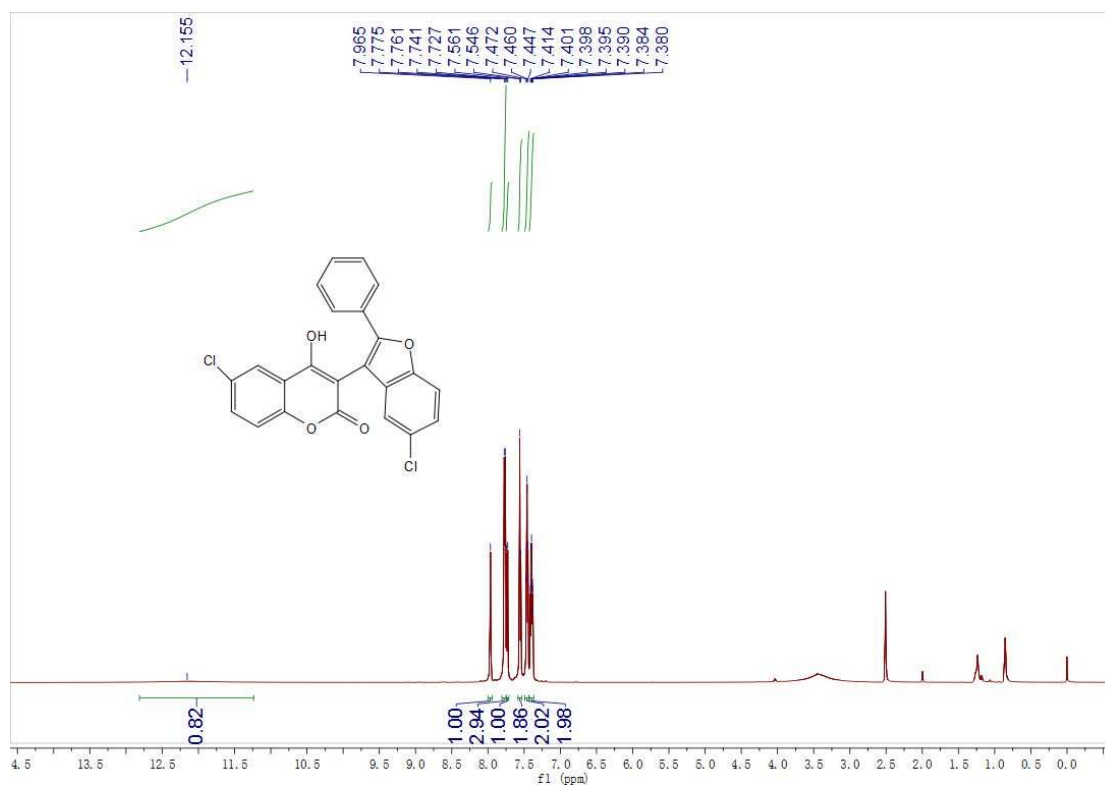
4-hydroxy-3-(6-methoxy-2-phenylbenzofuran-3-yl)-2H-chromen-2-one (**4q**)



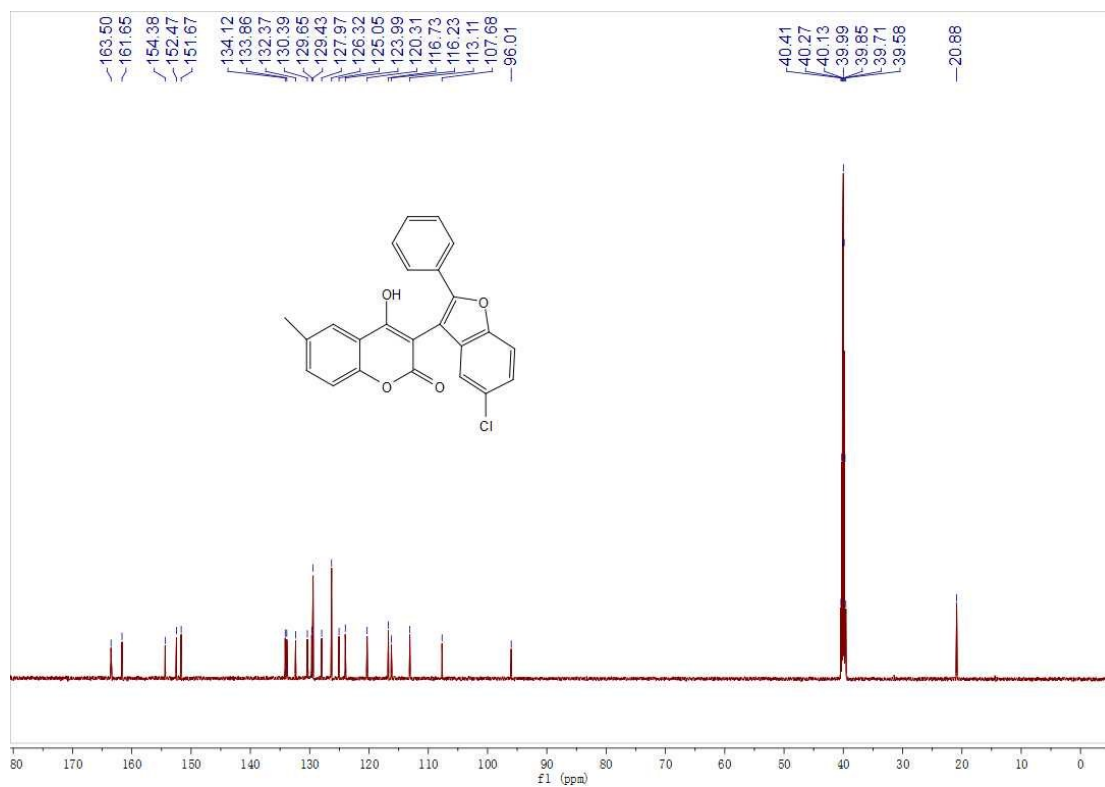
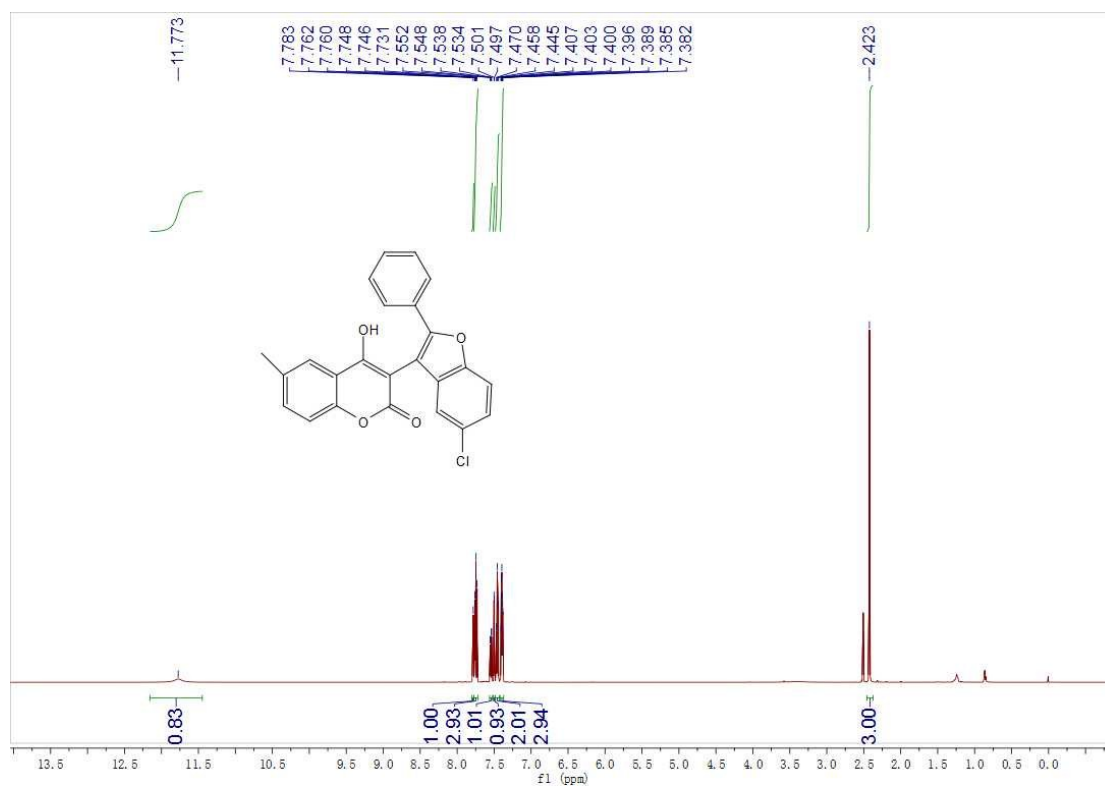
4-hydroxy-3-(2-phenylnaphtho[2,1-b]furan-1-yl)-2H-chromen-2-one (**4r**)



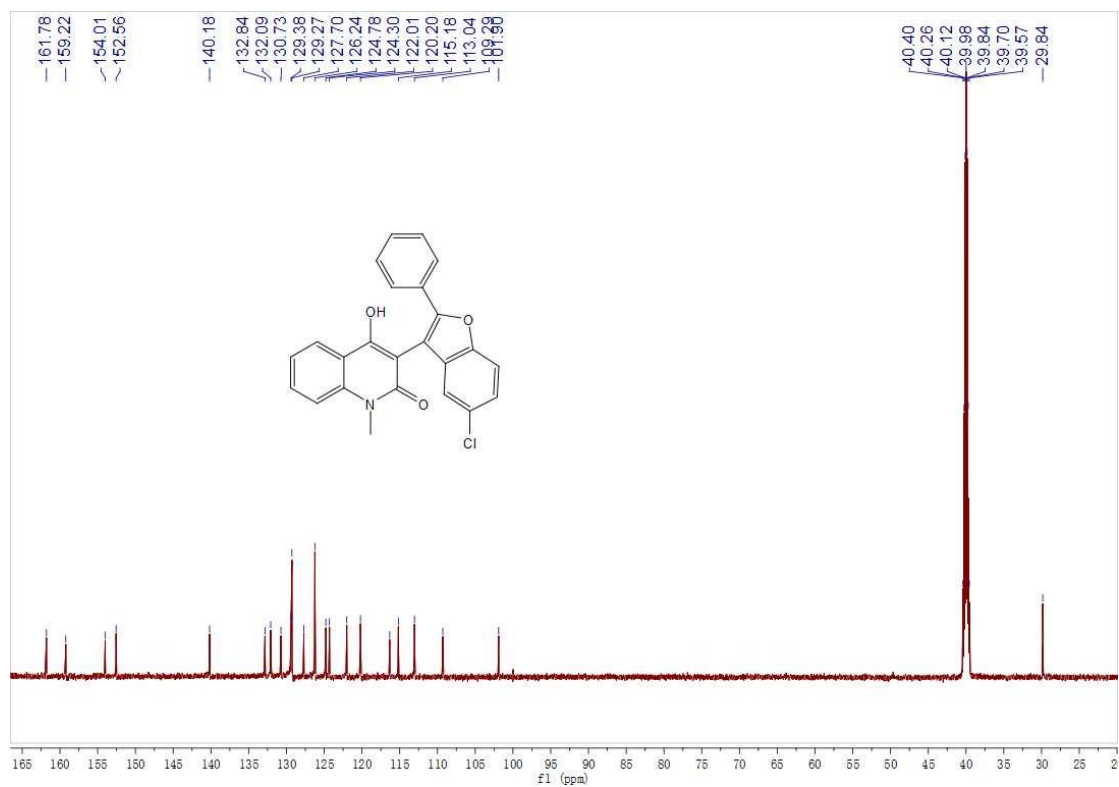
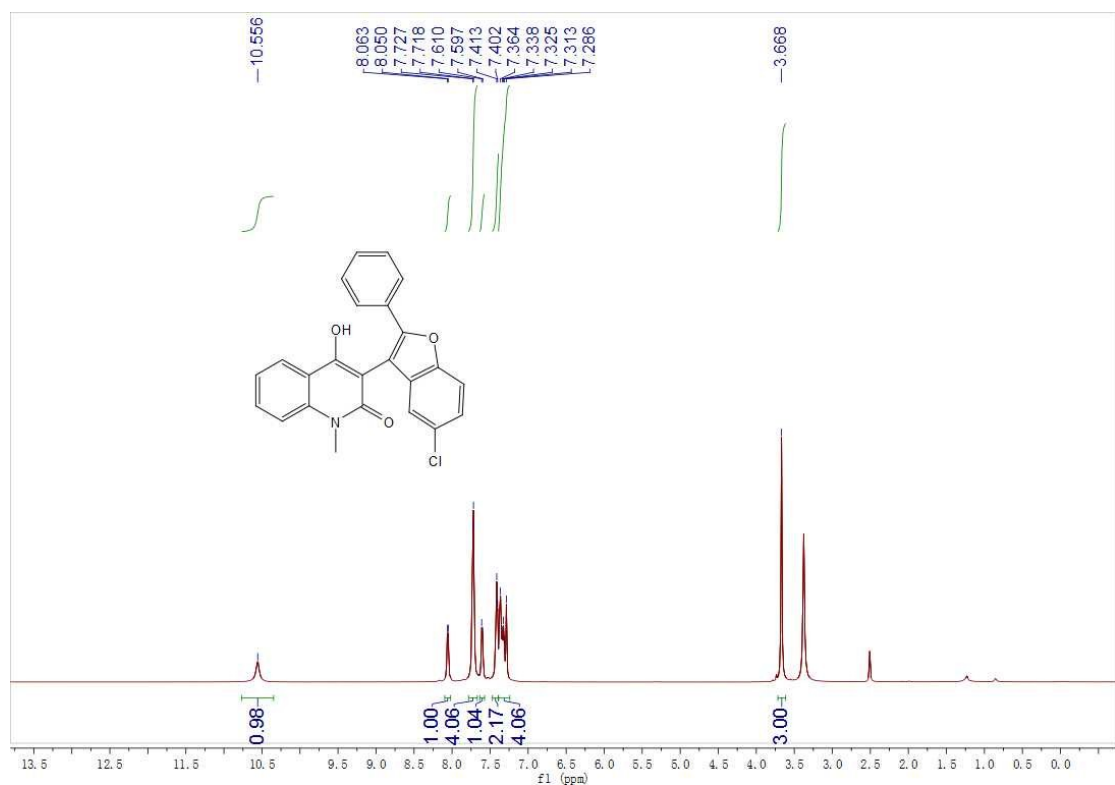
6-chloro-3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-2H-chromen-2-one (**4s**)



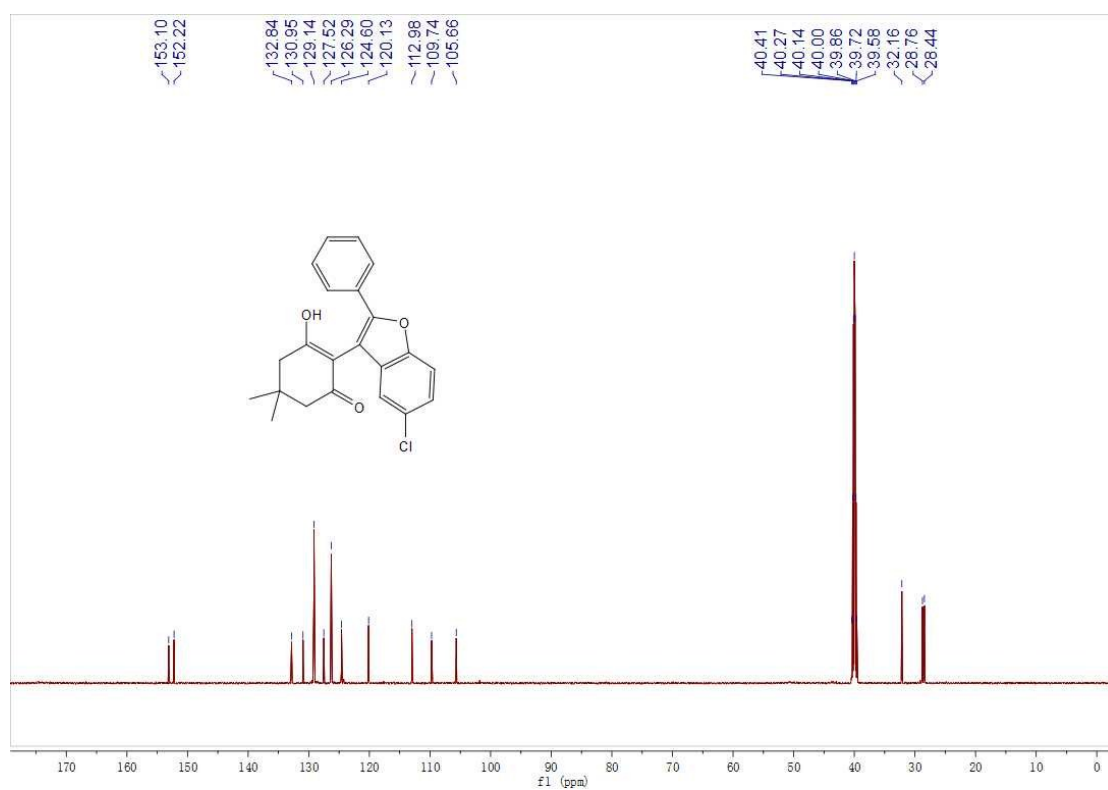
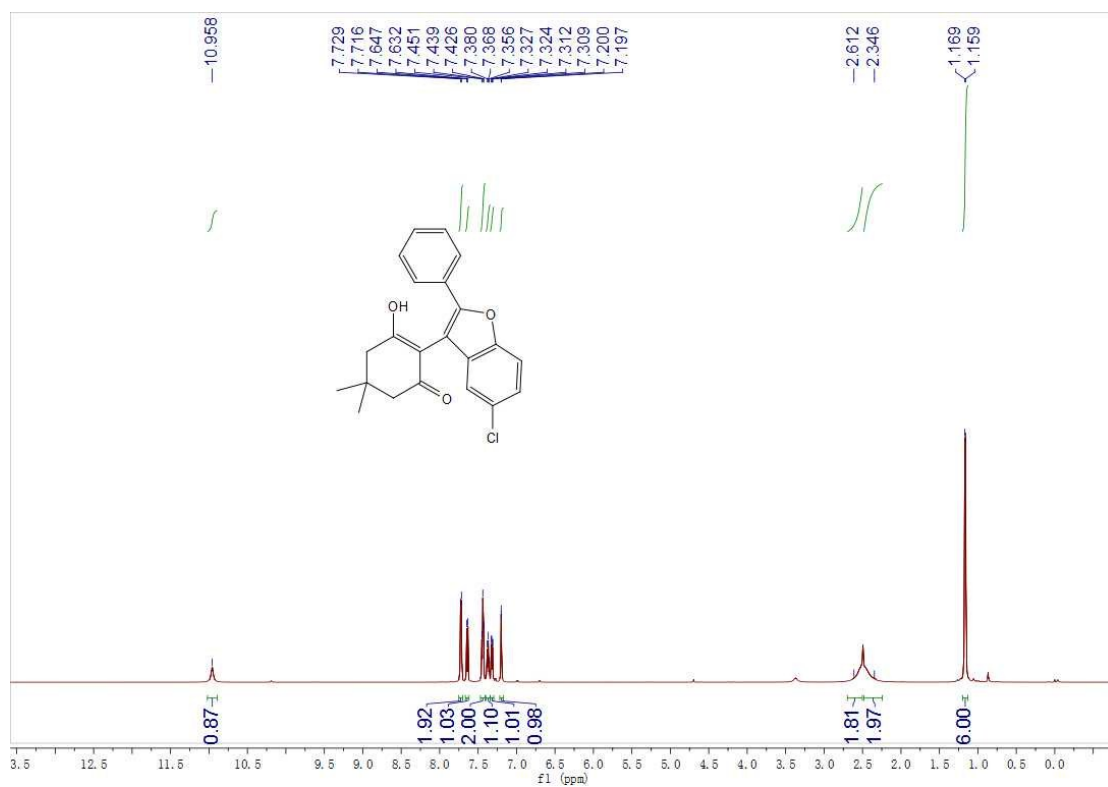
3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-6-methyl-2H-chromen-2-one (**4t**)



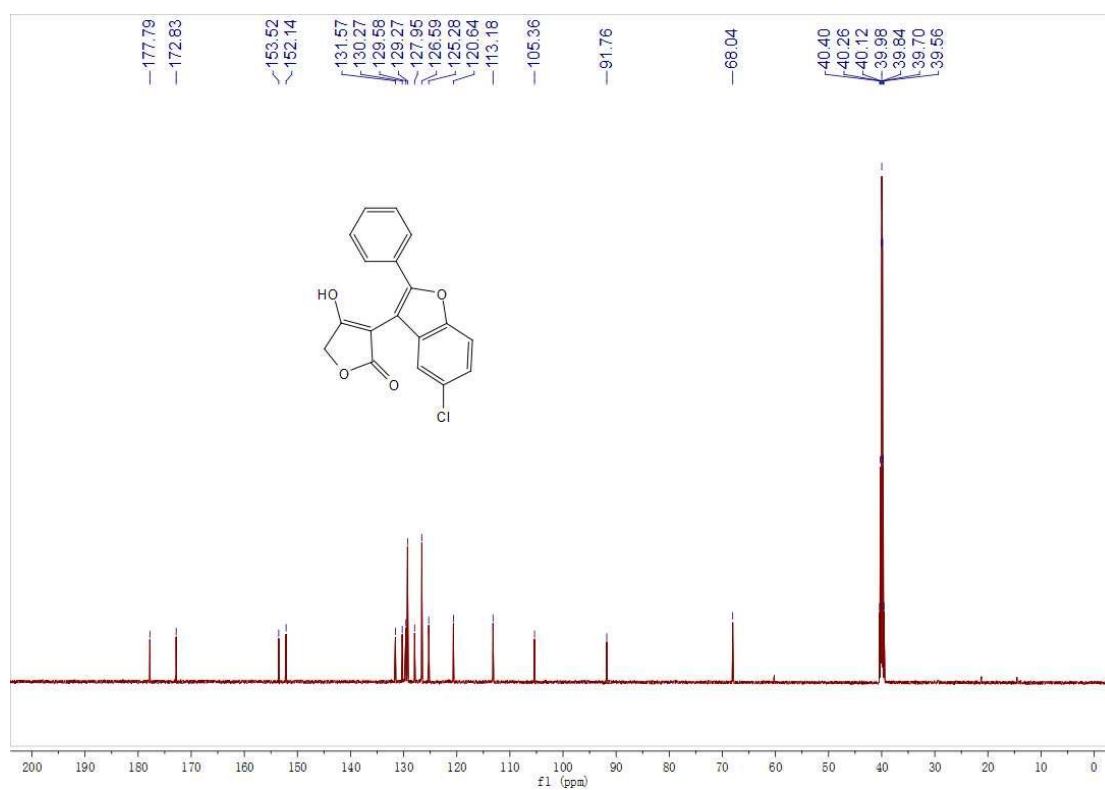
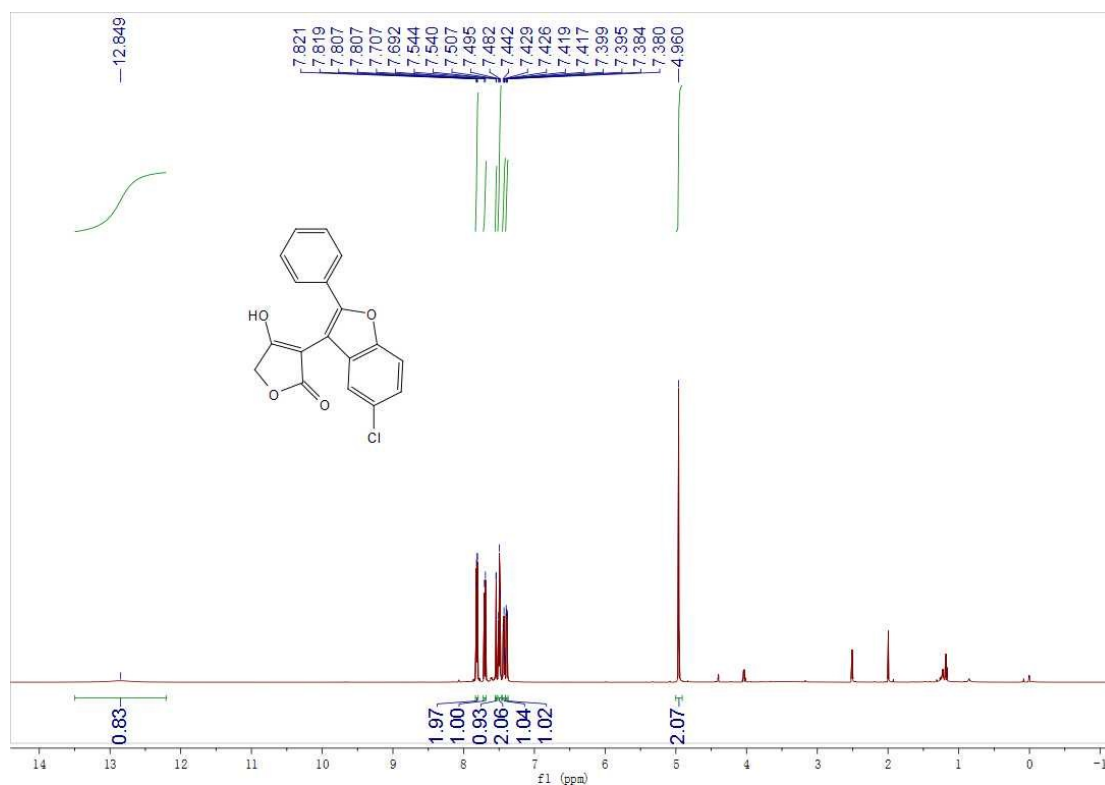
3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxy-1-methylquinolin-2(1H)-one (**4u**)



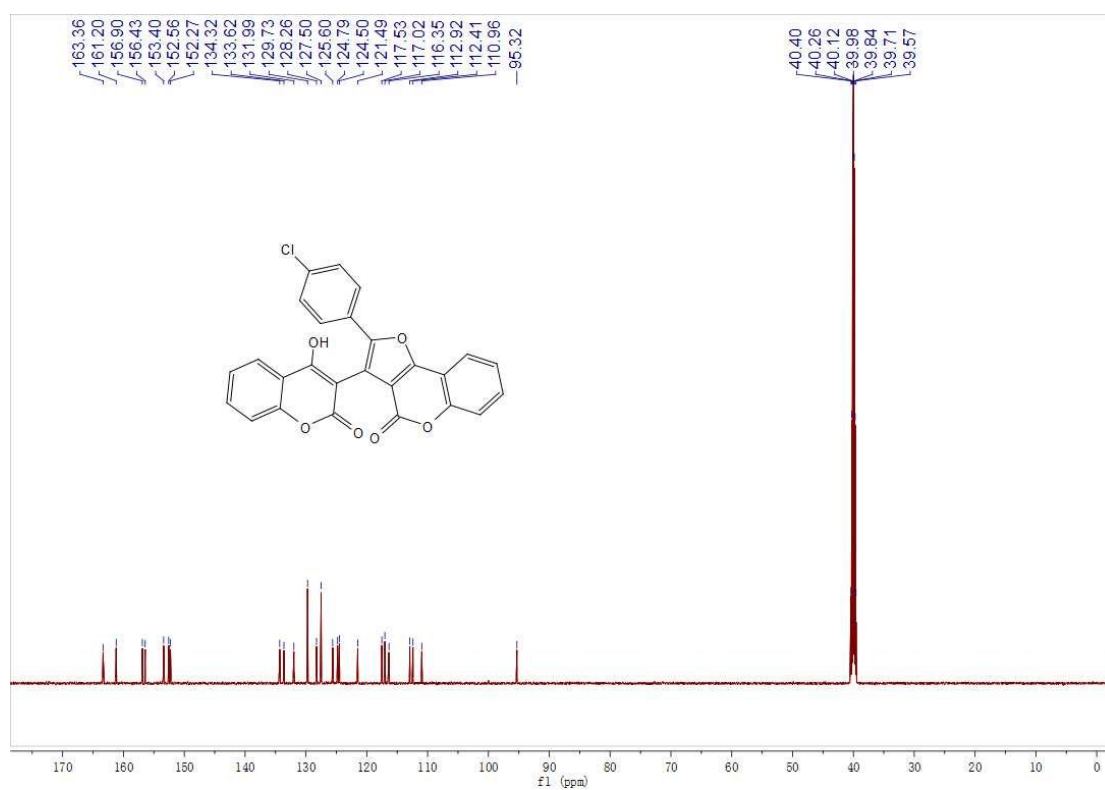
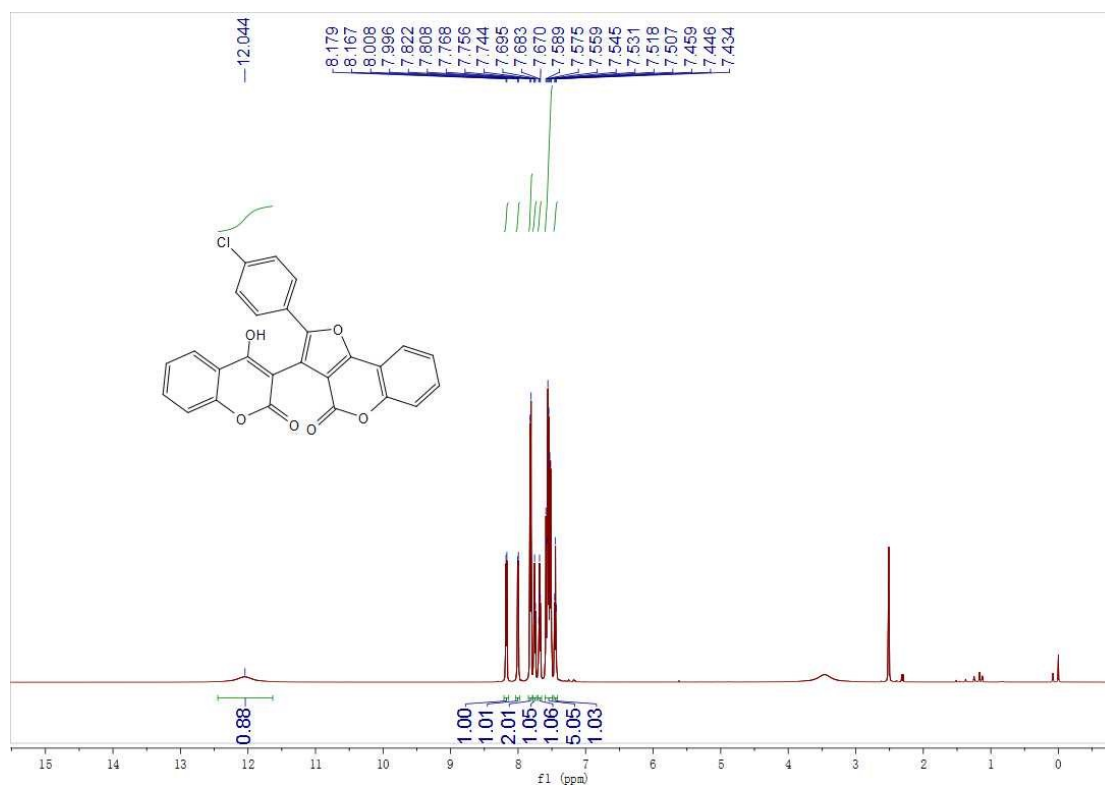
2-(5-chloro-2-phenylbenzofuran-3-yl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (**4v**)



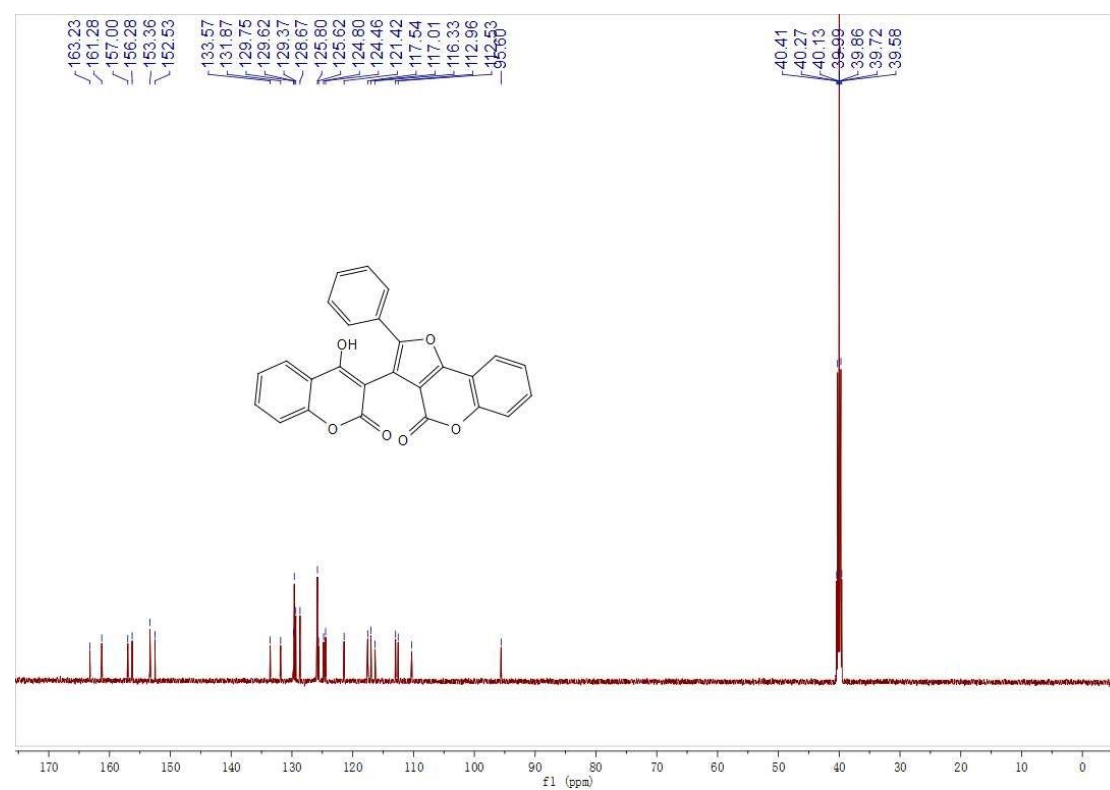
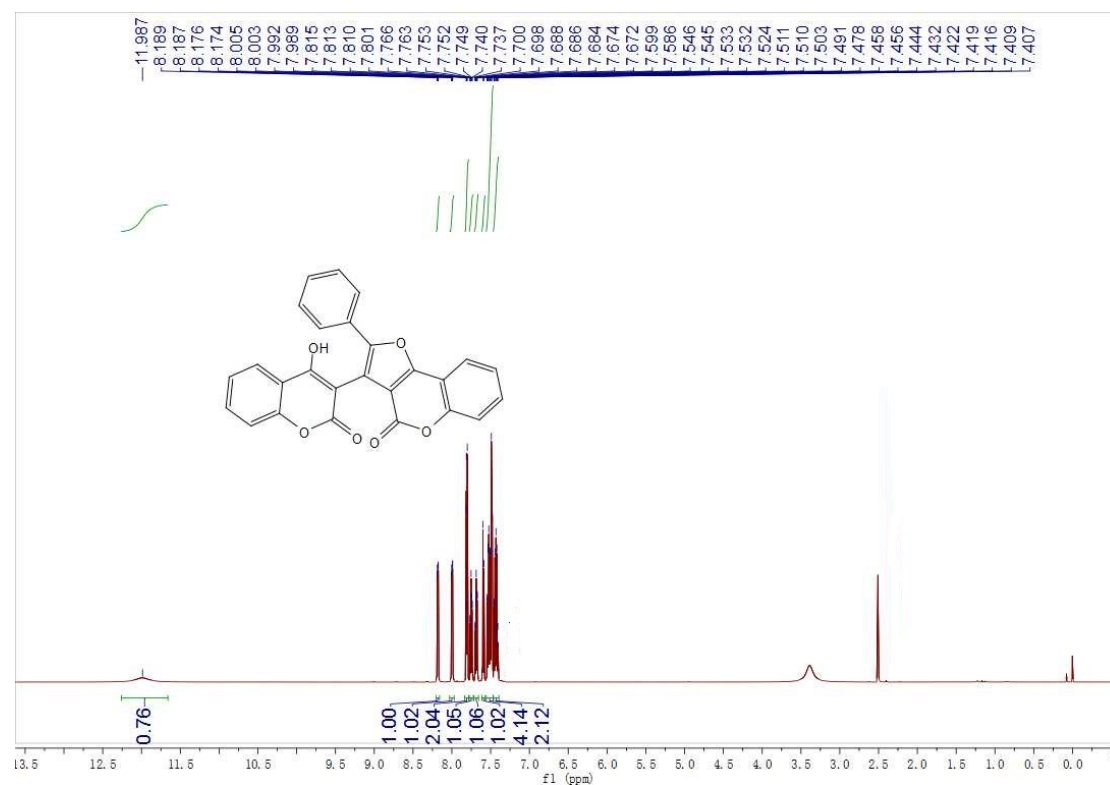
3-(5-chloro-2-phenylbenzofuran-3-yl)-4-hydroxyfuran-2(5H)-one (**4w**)



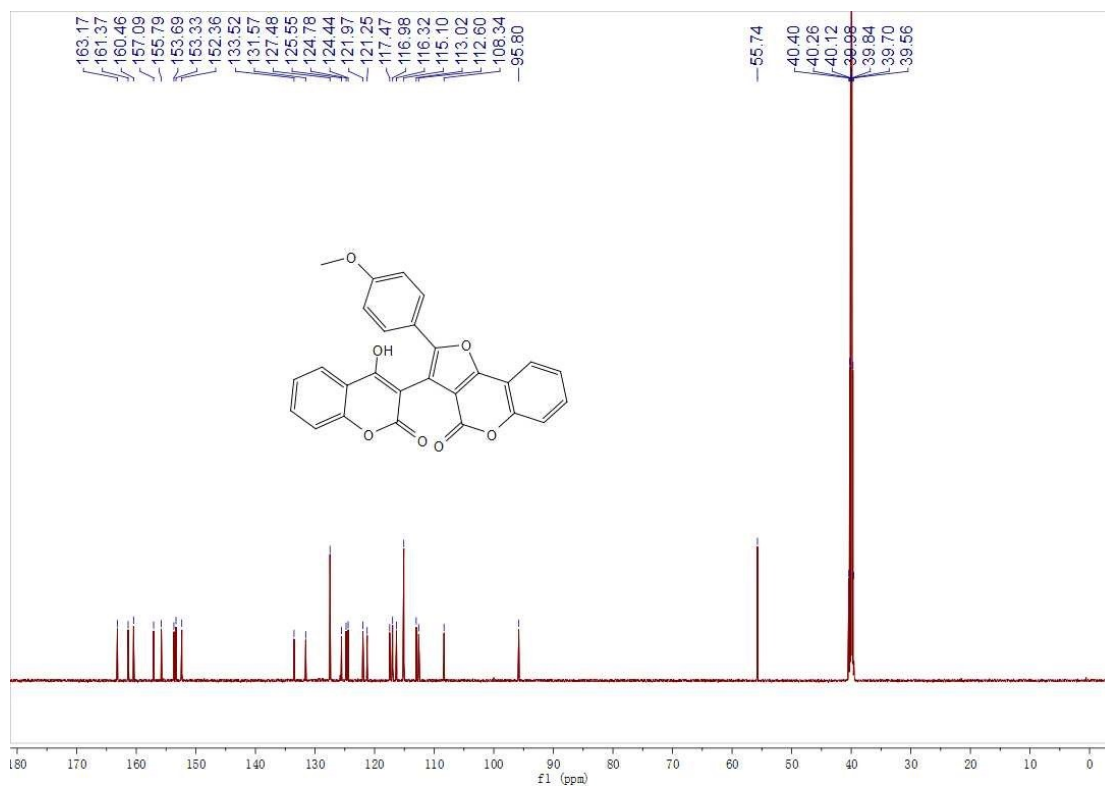
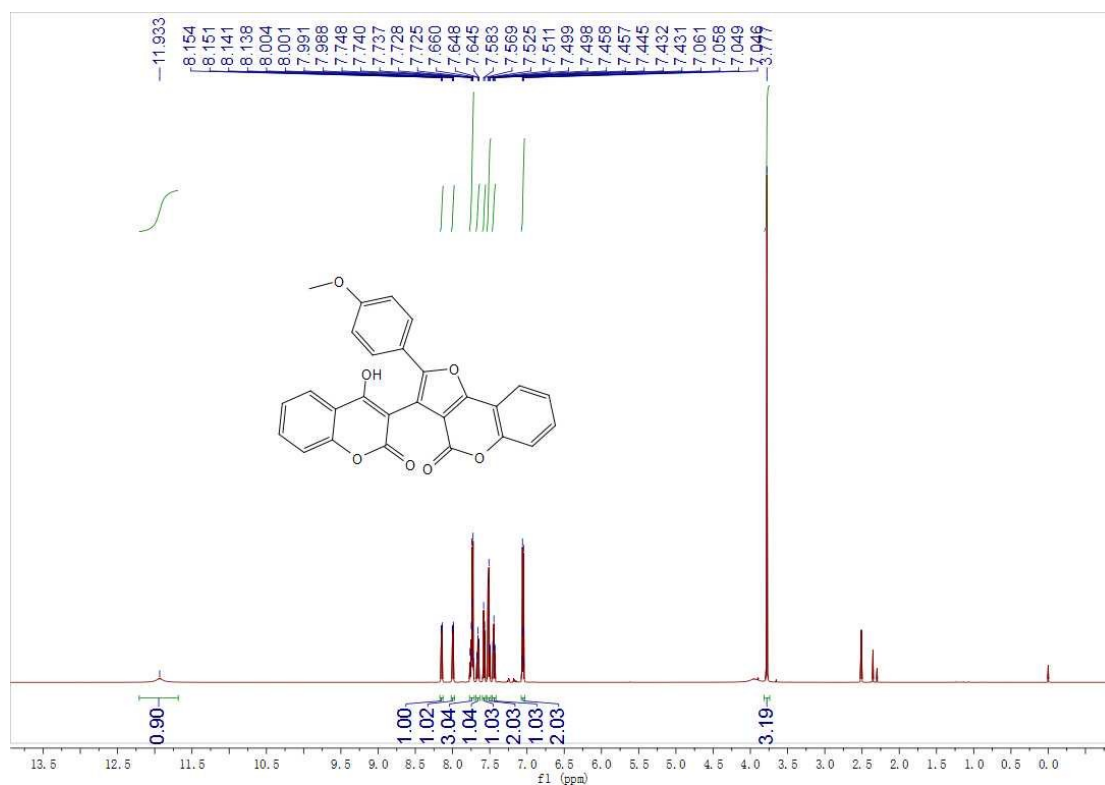
2-(4-chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5a**)



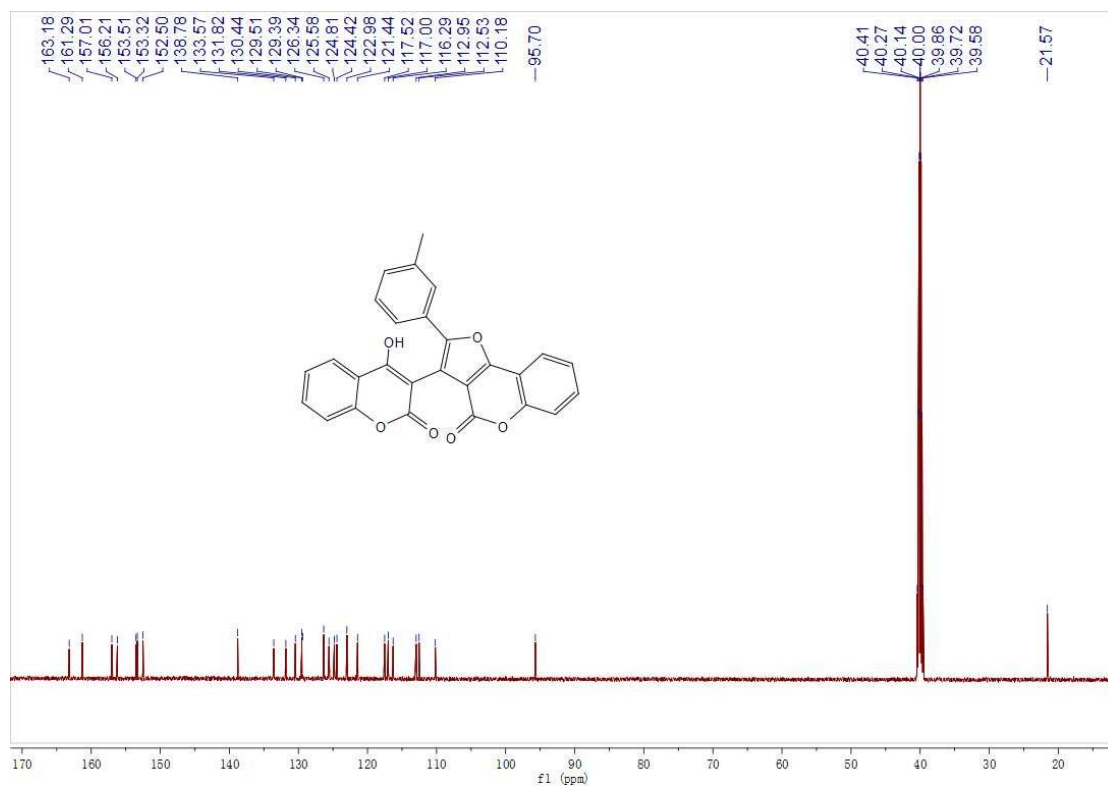
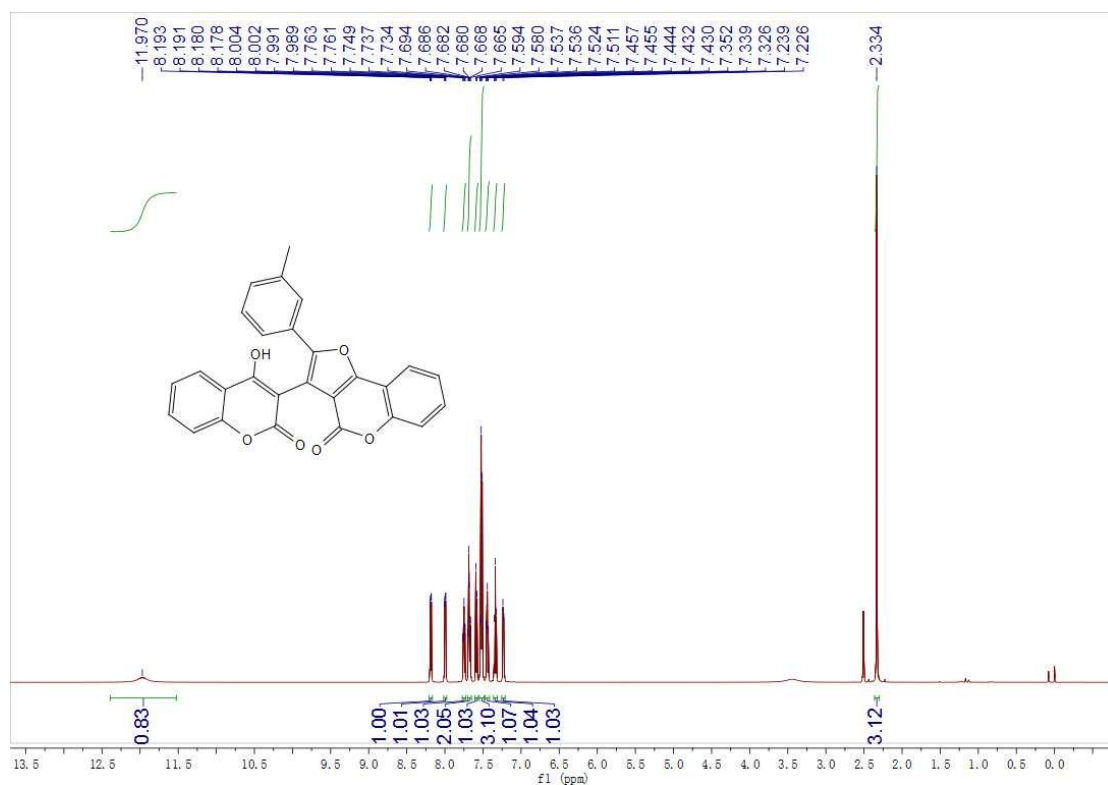
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5b**)



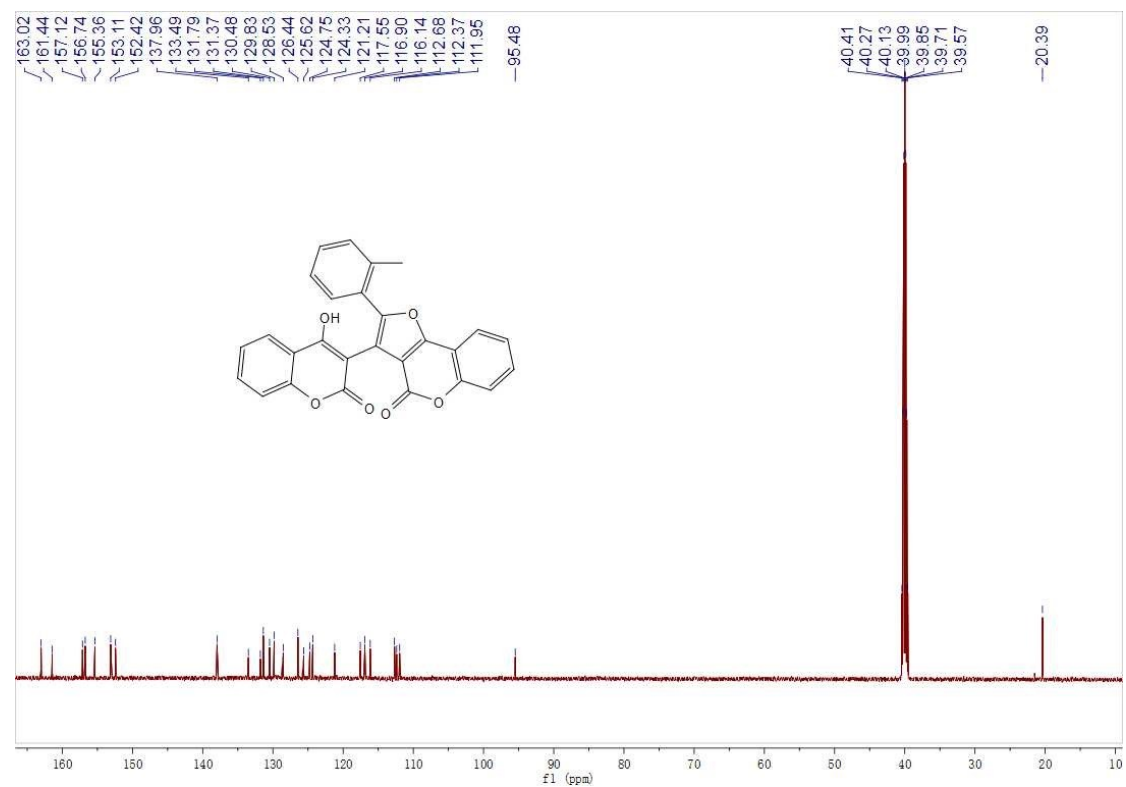
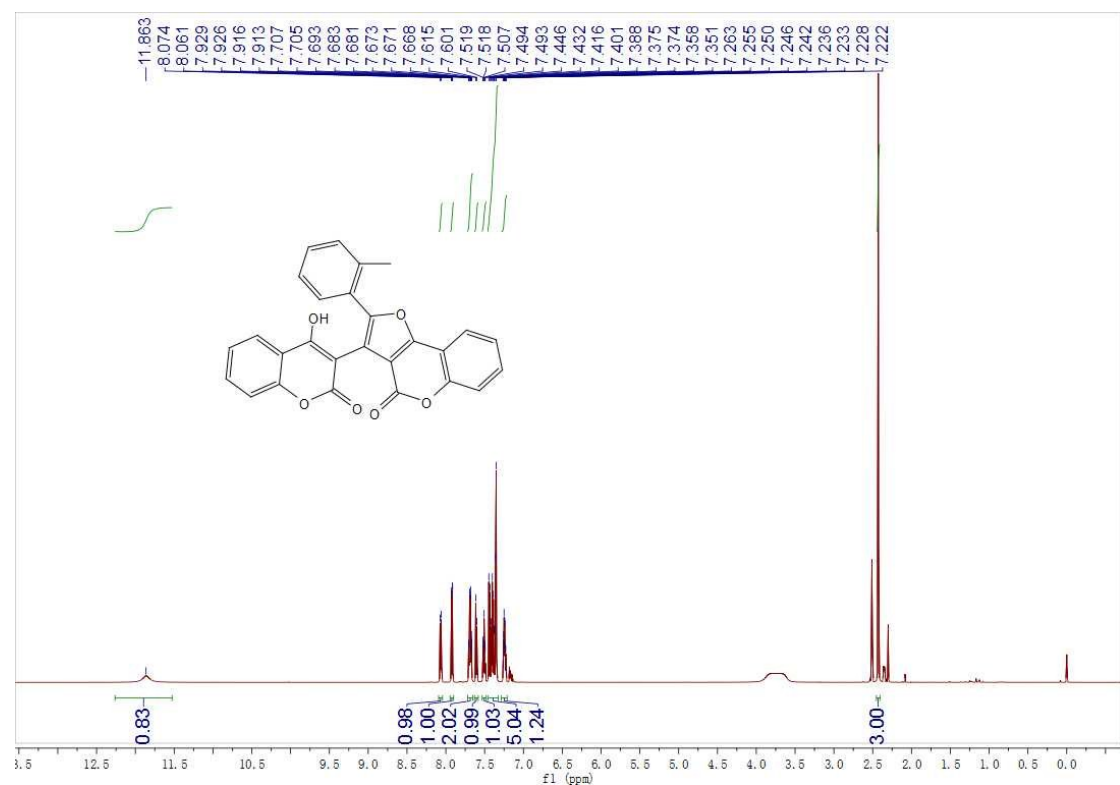
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5c**)



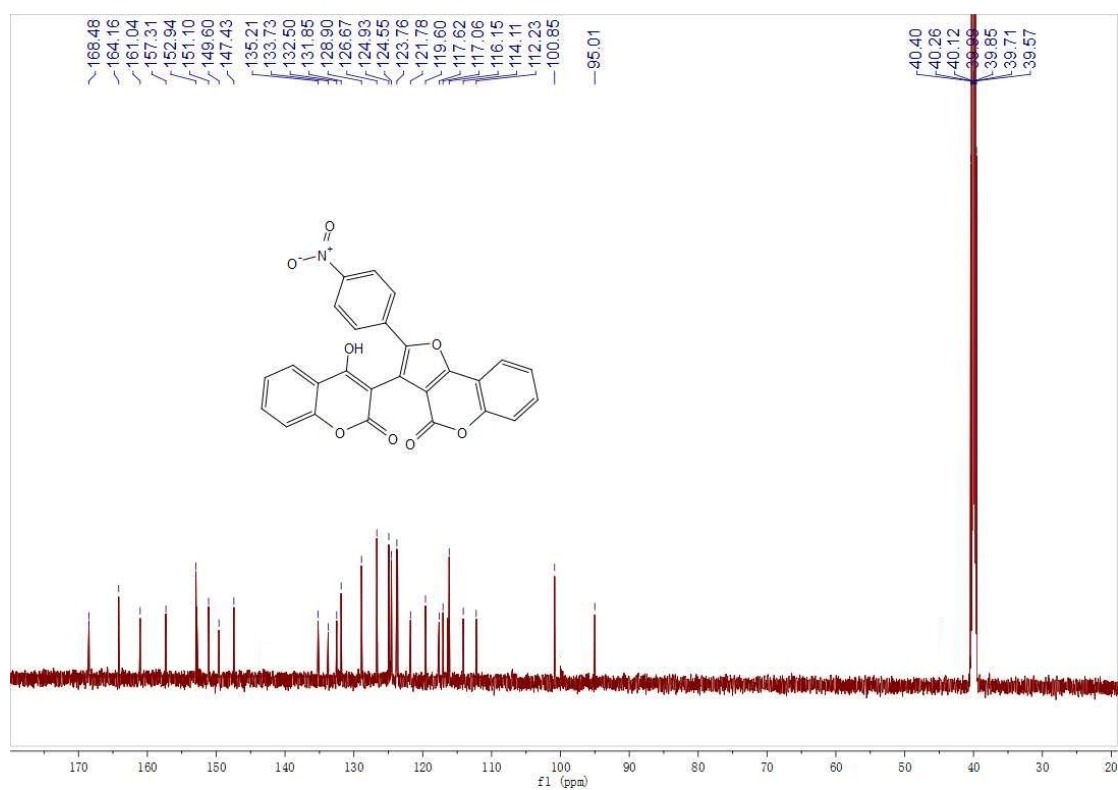
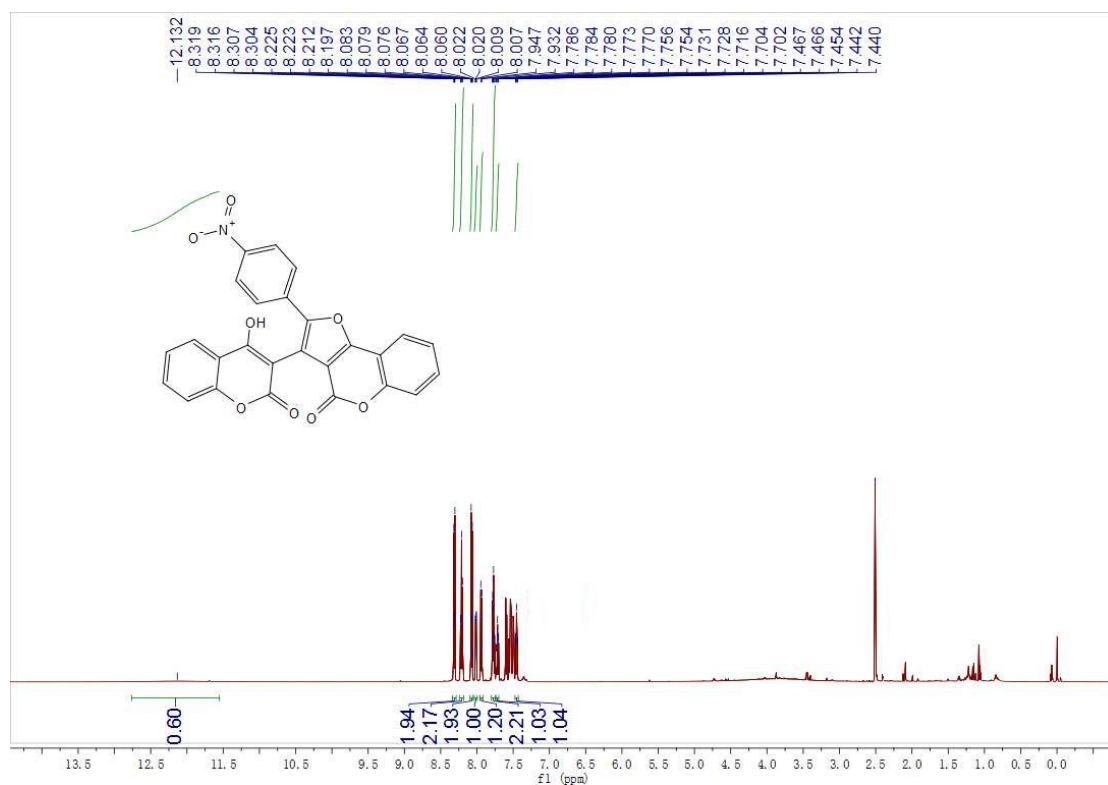
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(m-tolyl)-4H-furo[3,2-c]chromen-4-one (**5d**)



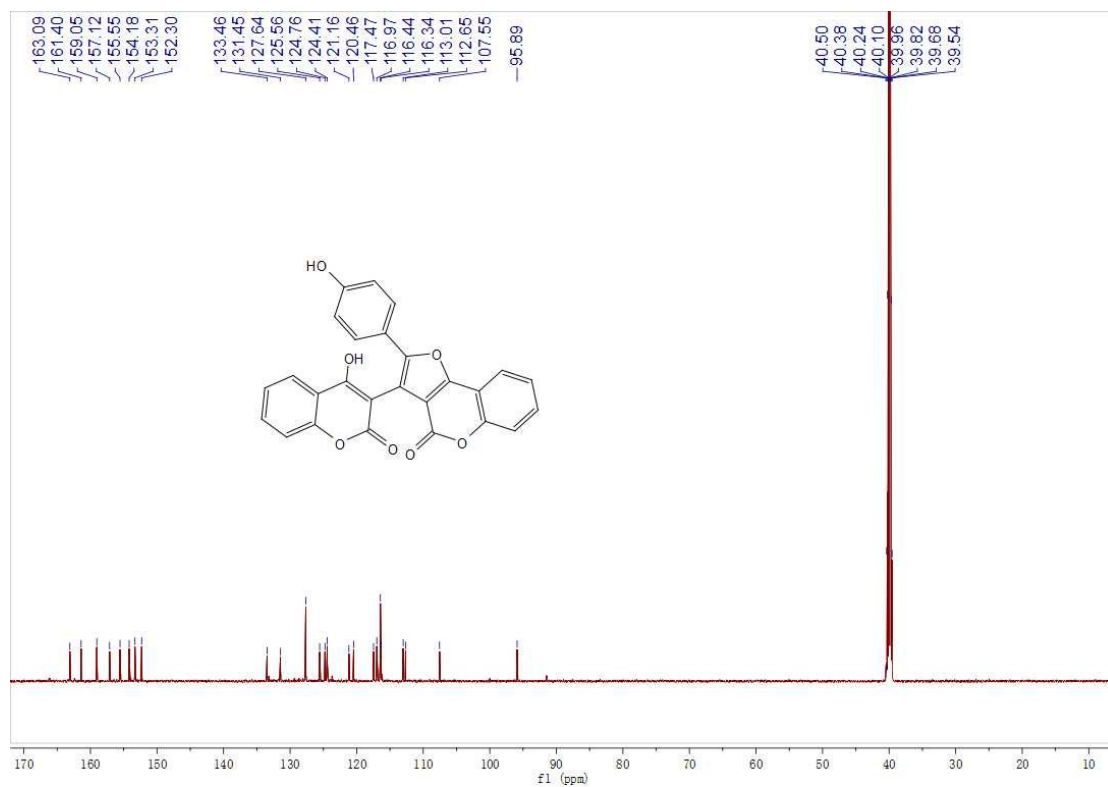
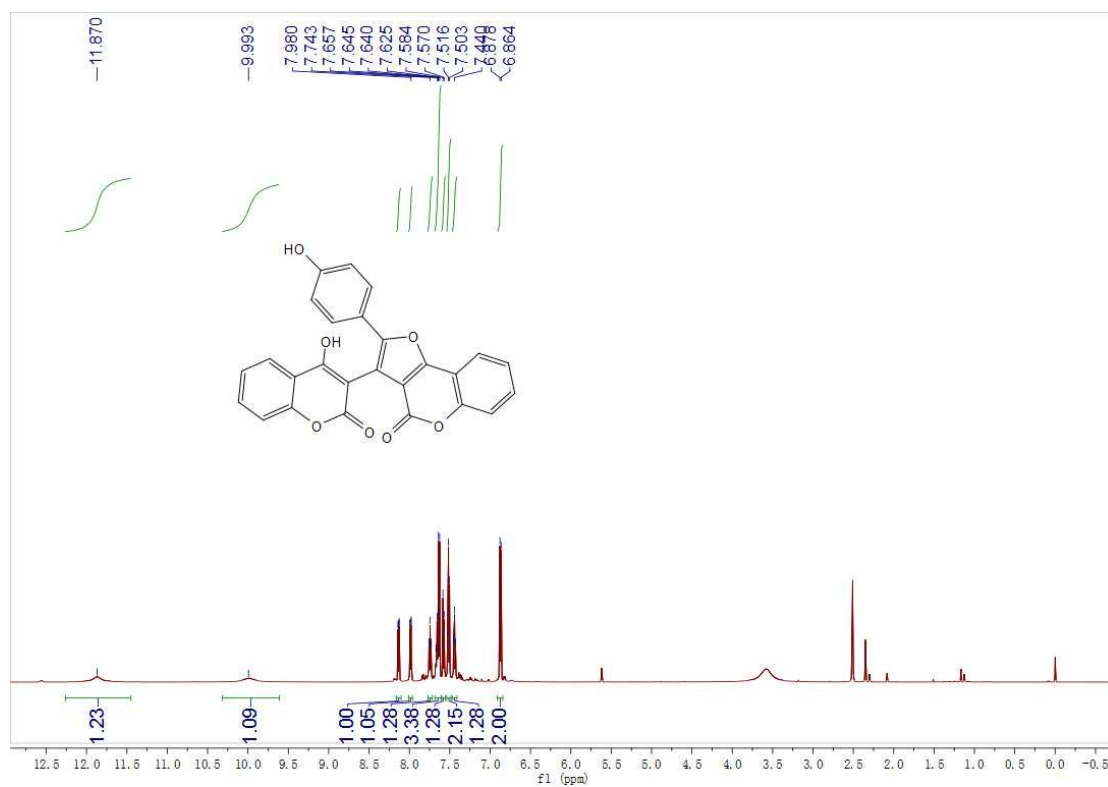
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(o-tolyl)-4H-furo[3,2-c]chromen-4-one (**5e**)



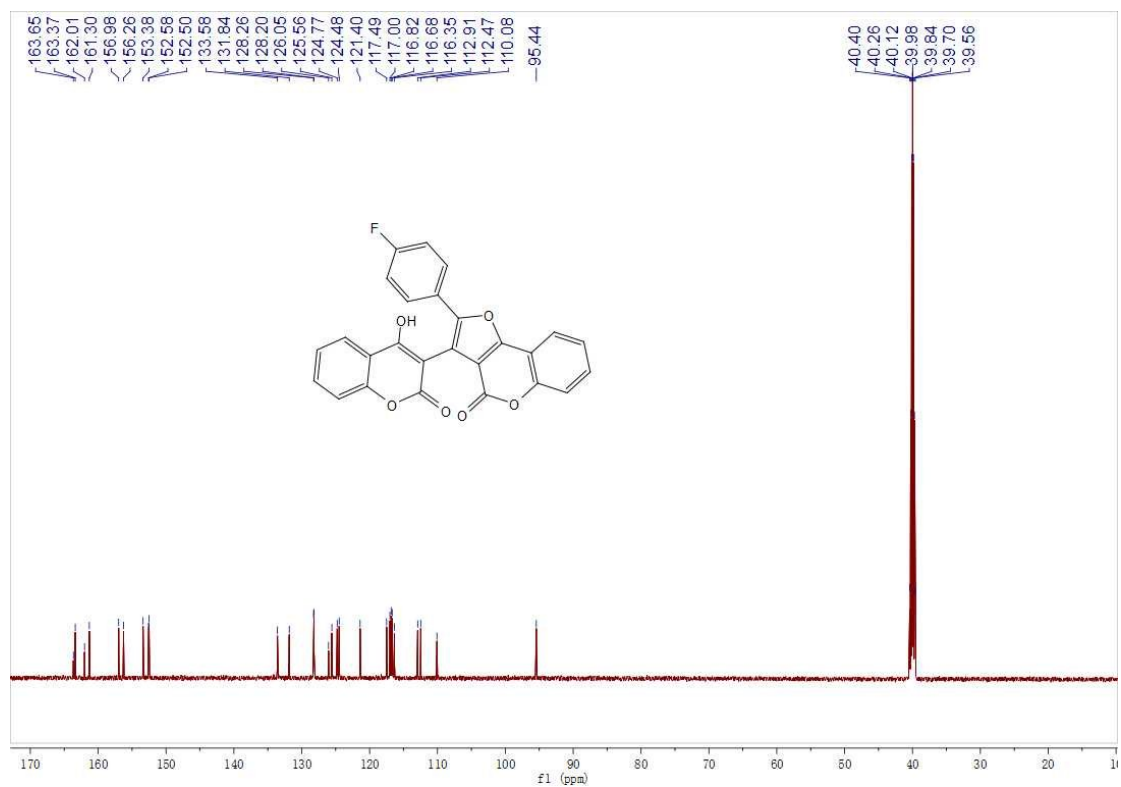
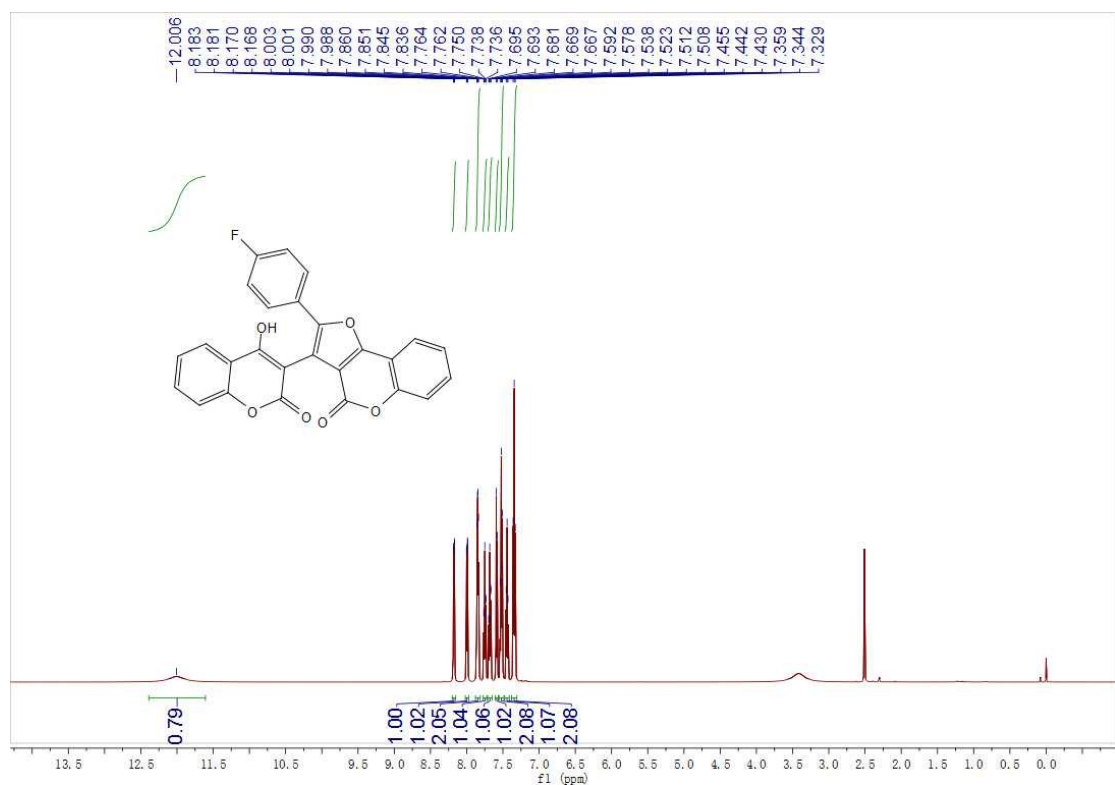
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-nitrophenyl)-4H-furo[3,2-c]chromen-4-one (**5f**)



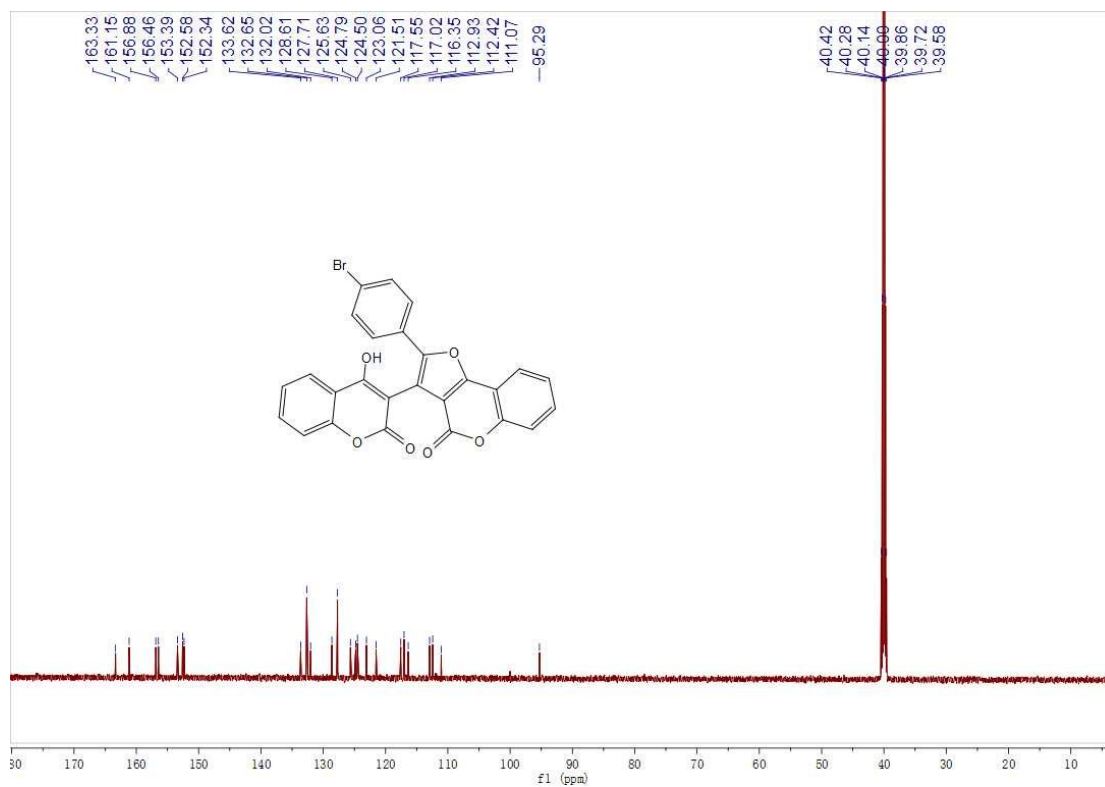
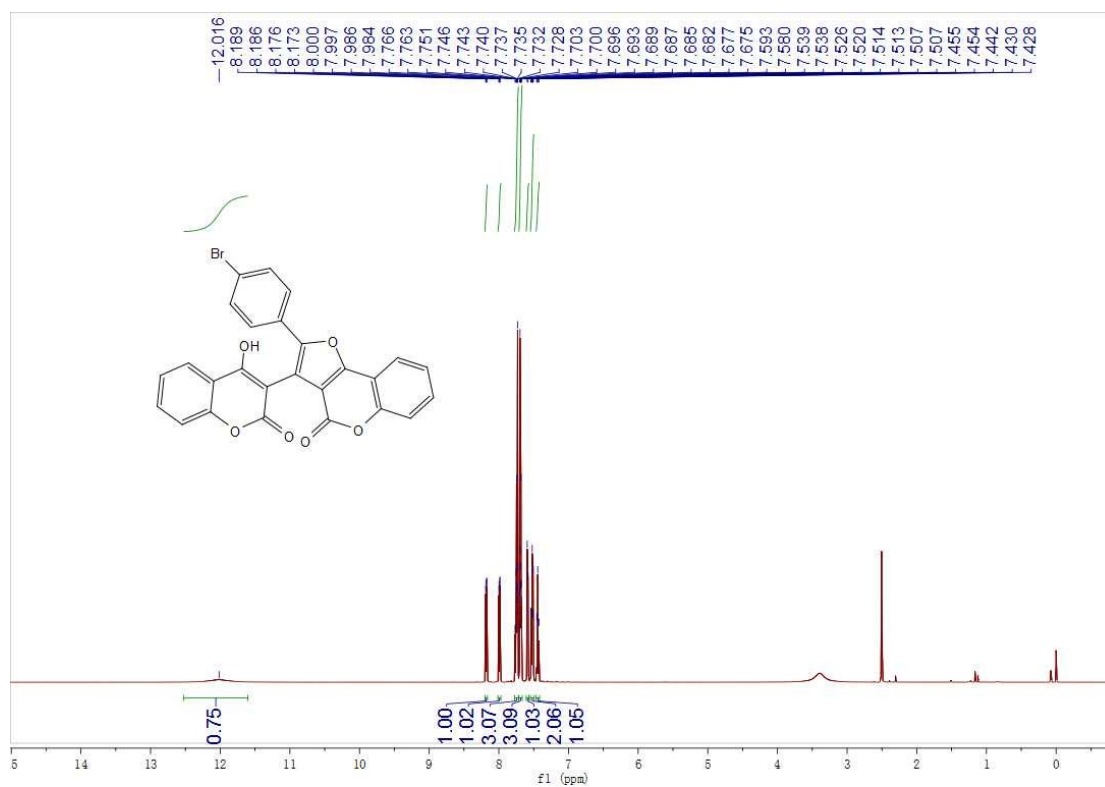
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-hydroxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5g**)



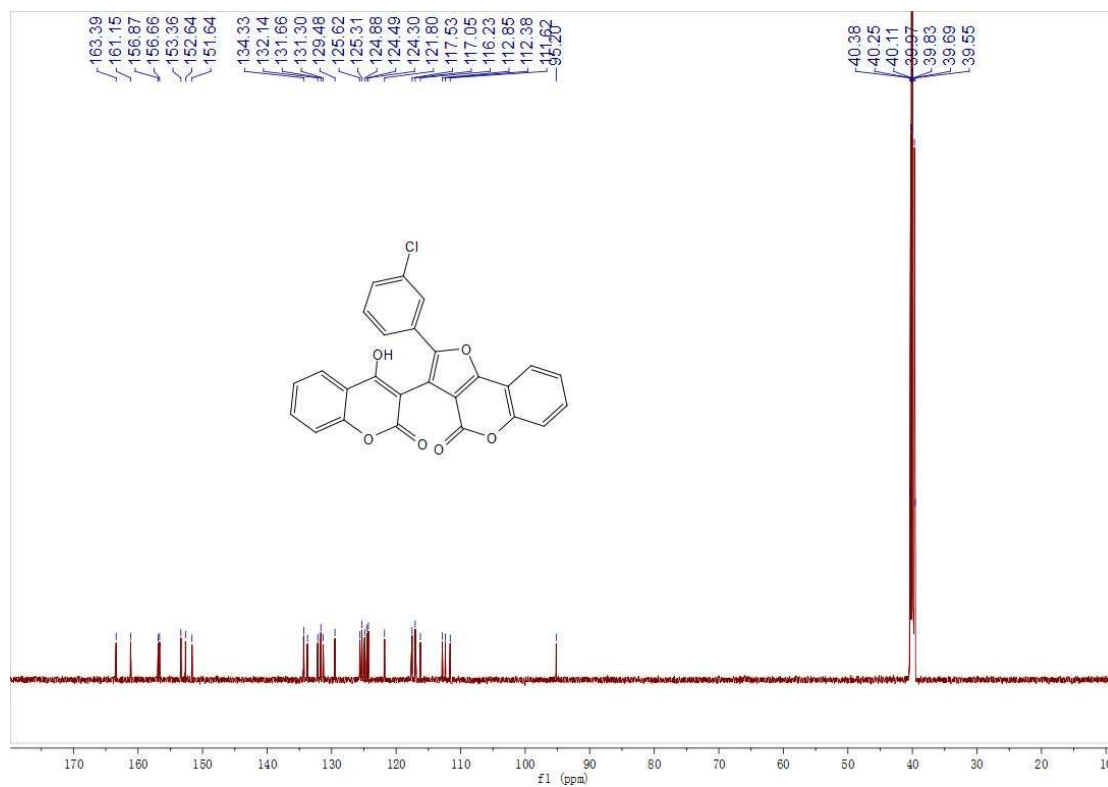
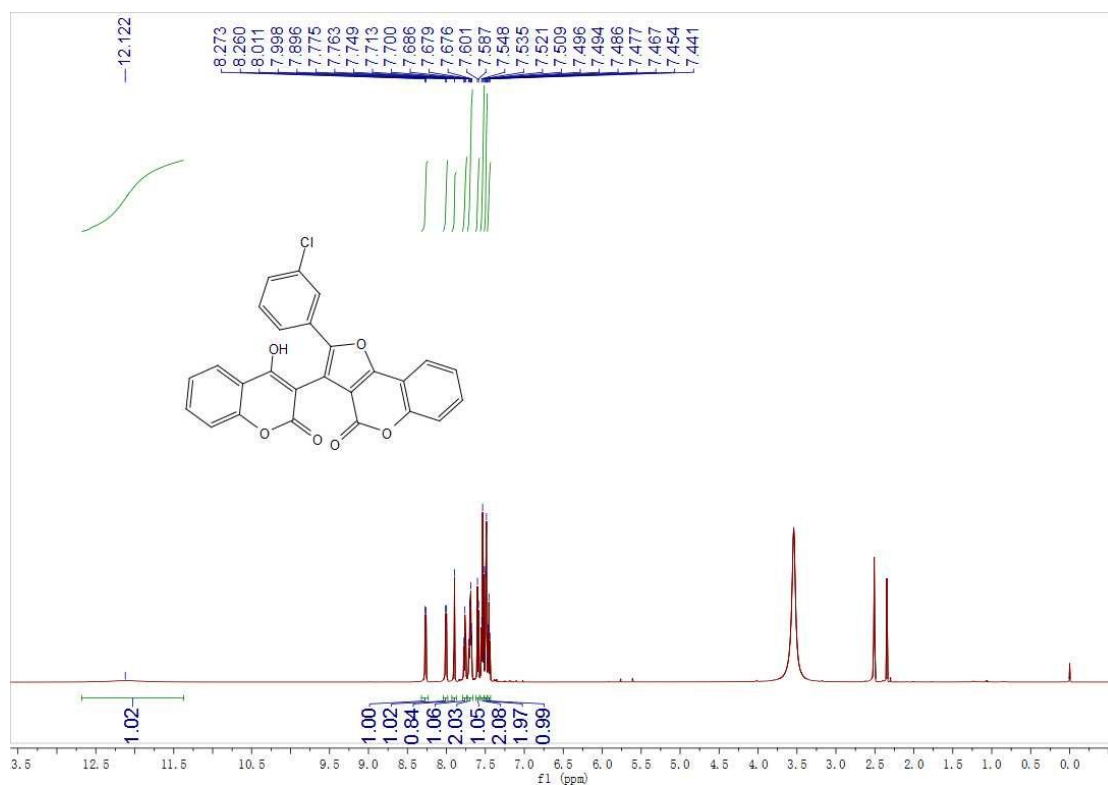
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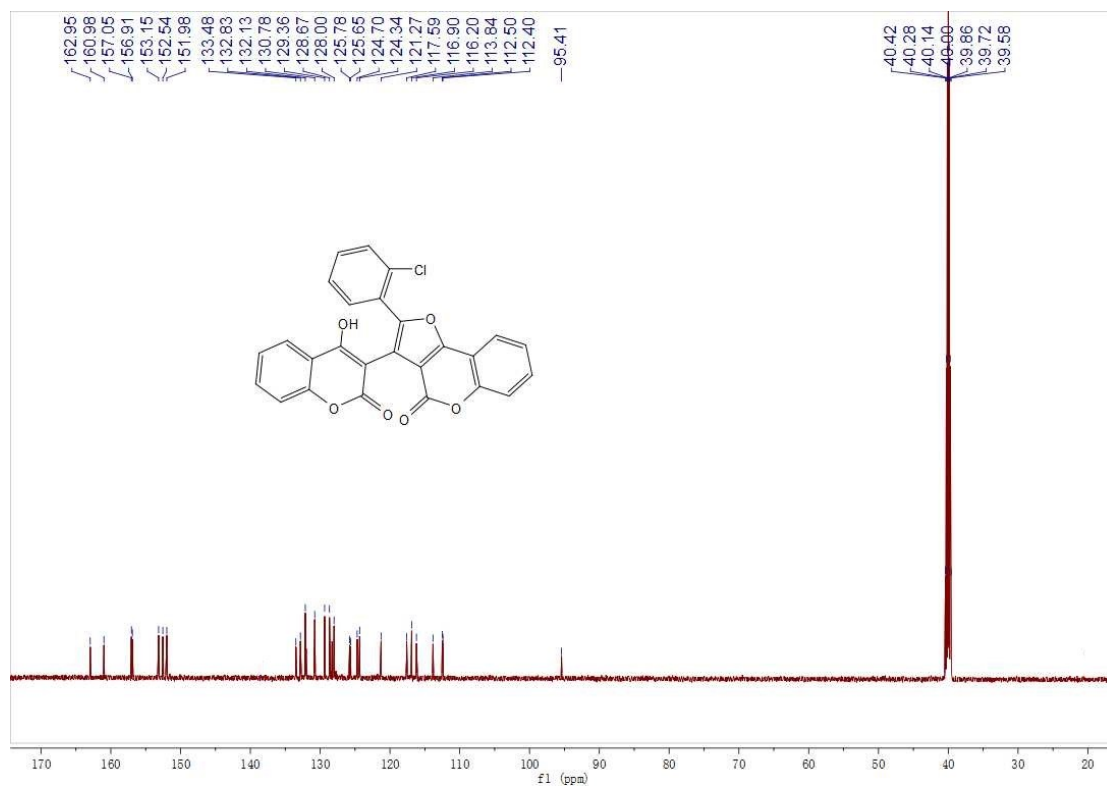
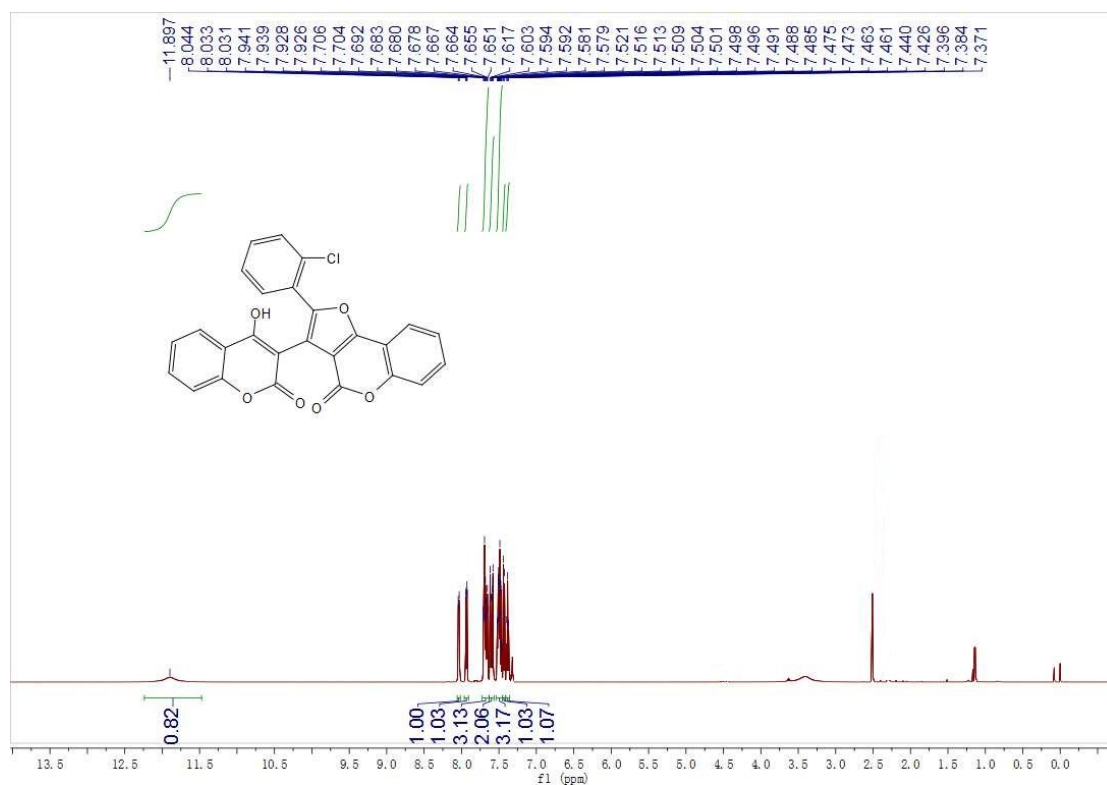
2-(4-bromophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5i**)



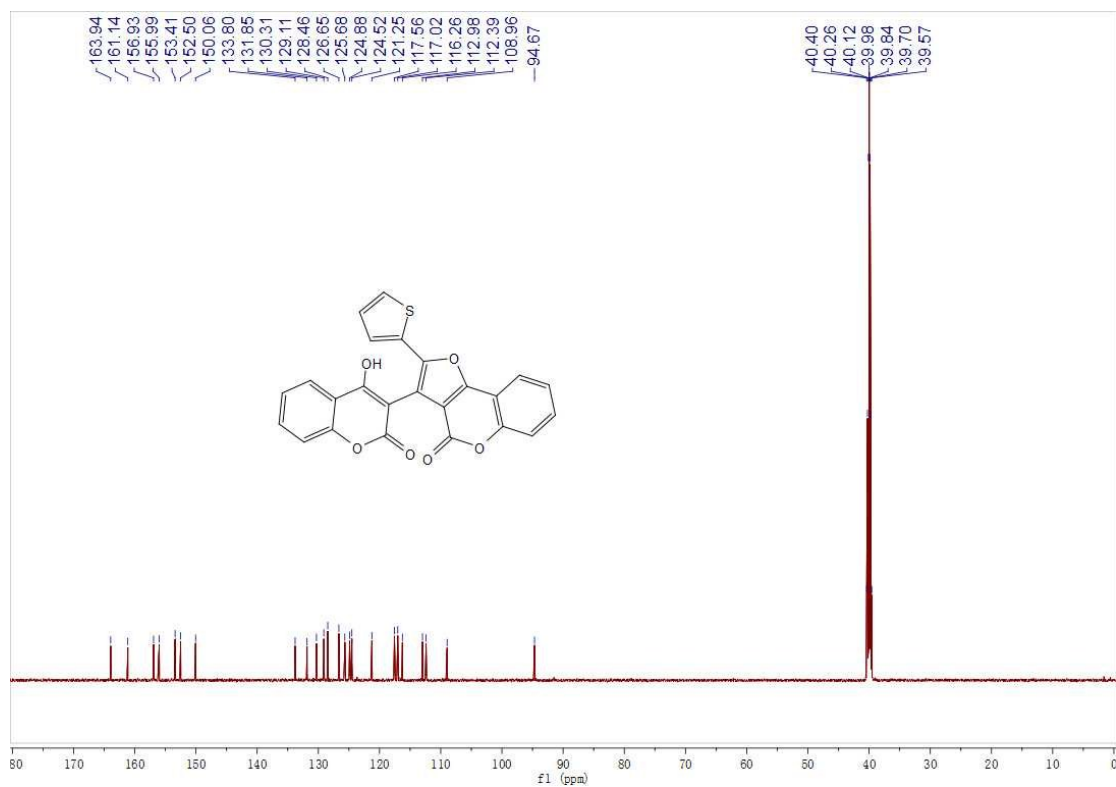
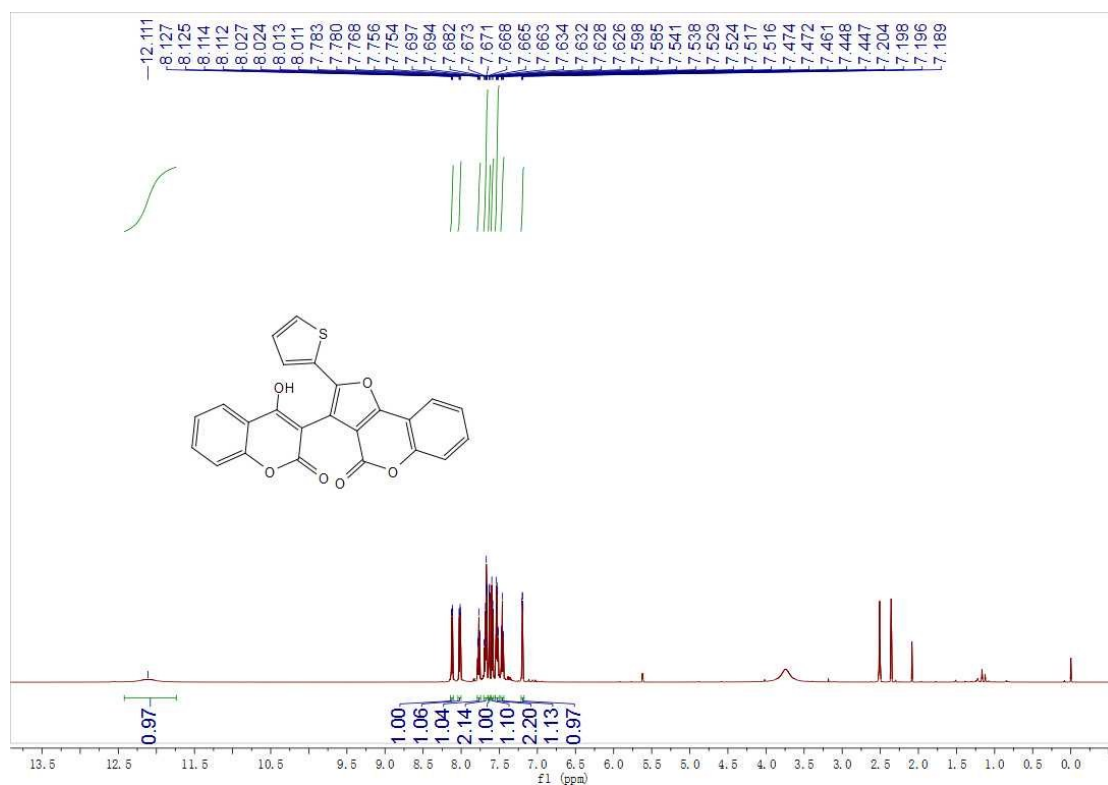
2-(3-chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5j**)



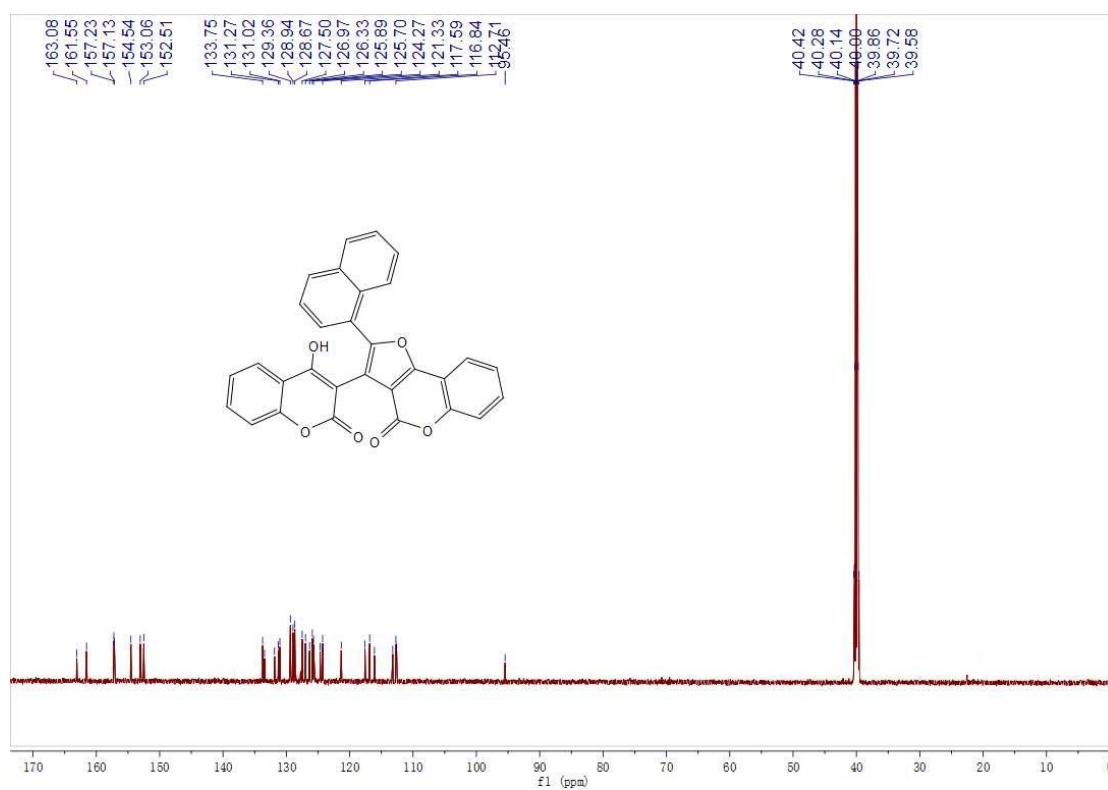
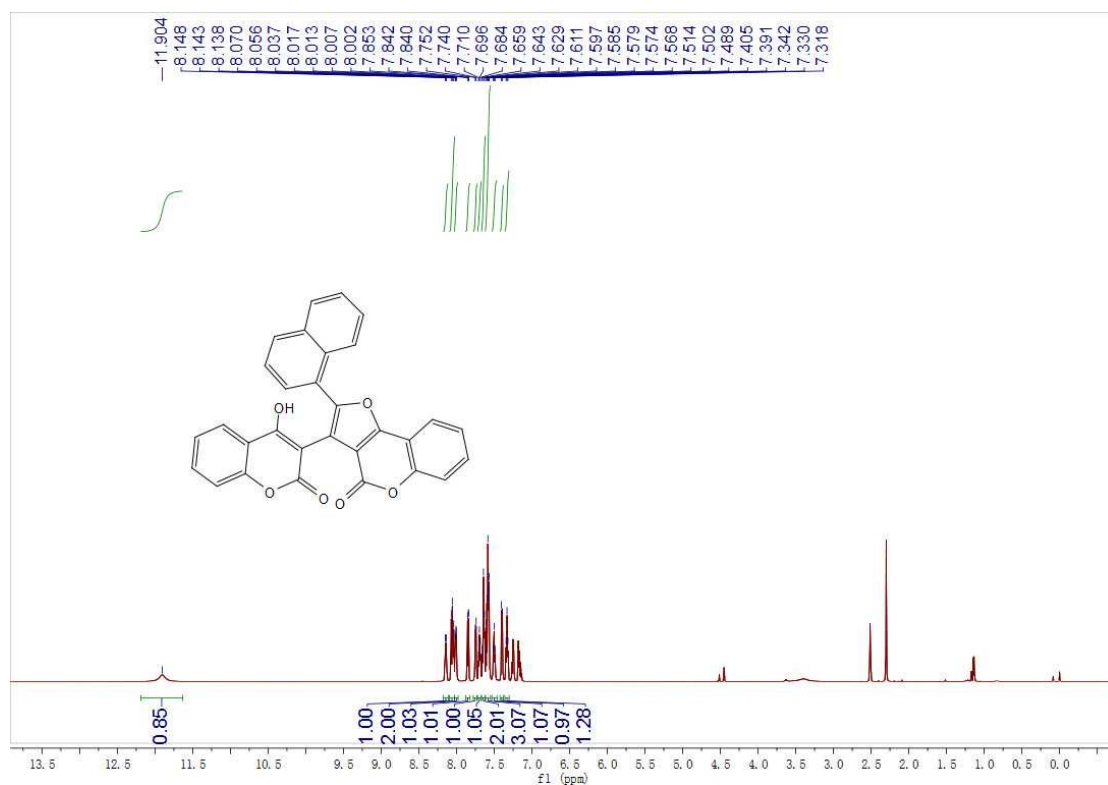
2-(2-chlorophenyl)-3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-4H-furo[3,2-c]chromen-4-one (**5k**)



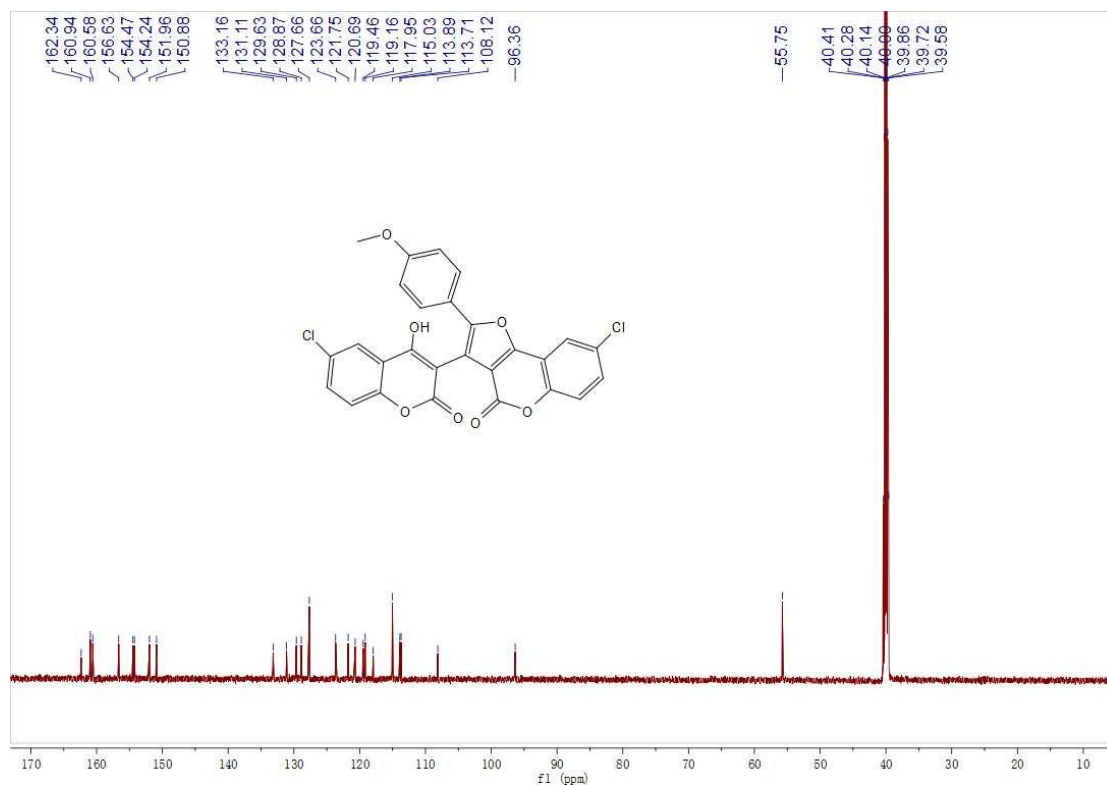
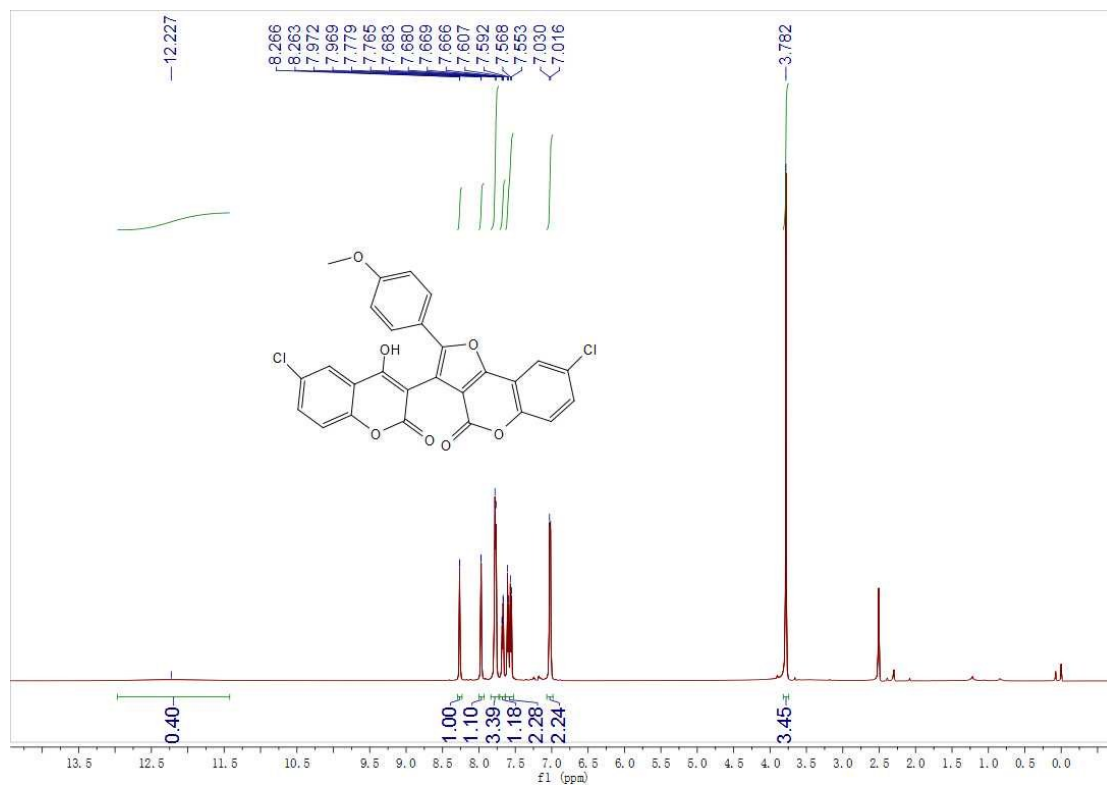
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(thiophen-2-yl)-4H-furo[3,2-c]chromen-4-one (**5I**)



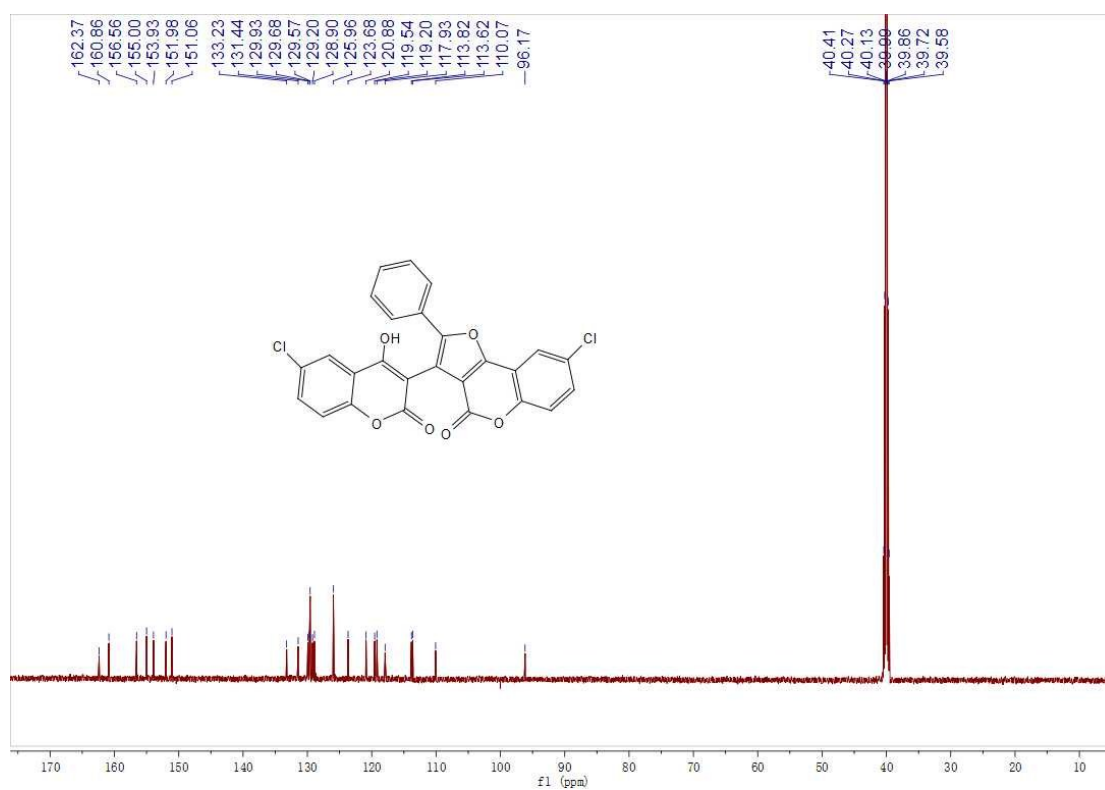
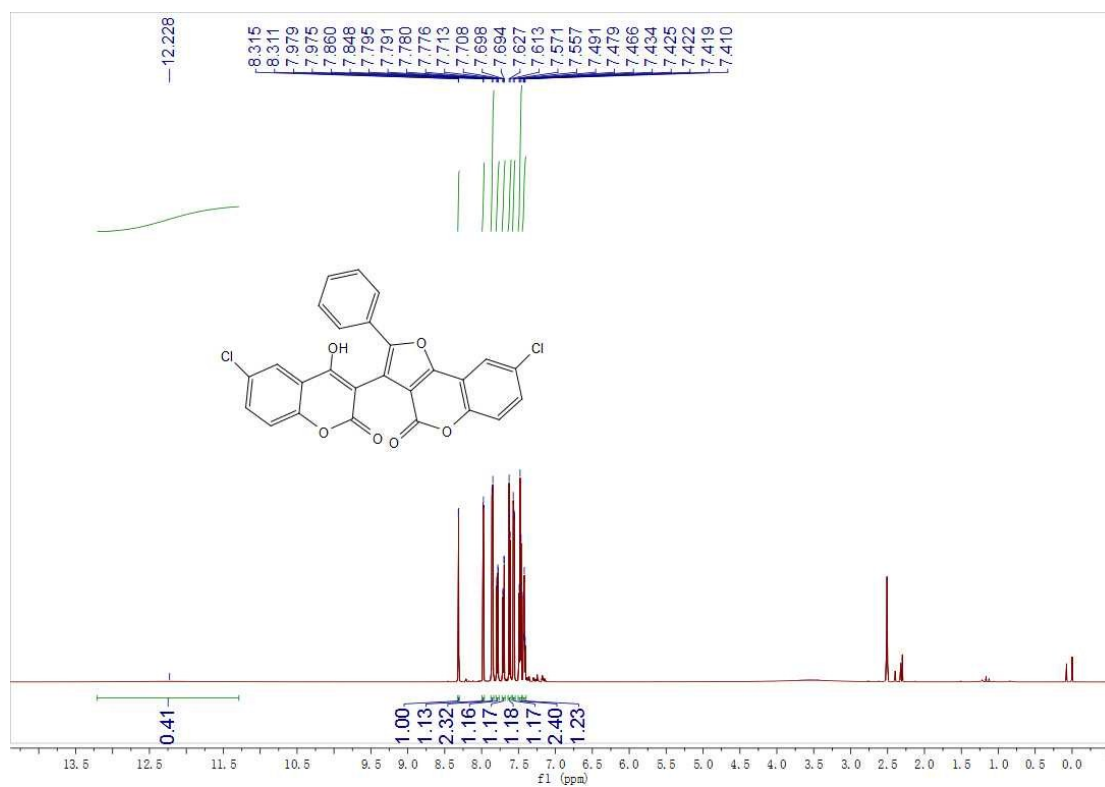
3-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(naphthalen-1-yl)-4H-furo[3,2-c]chromen-4-one (**5m**)



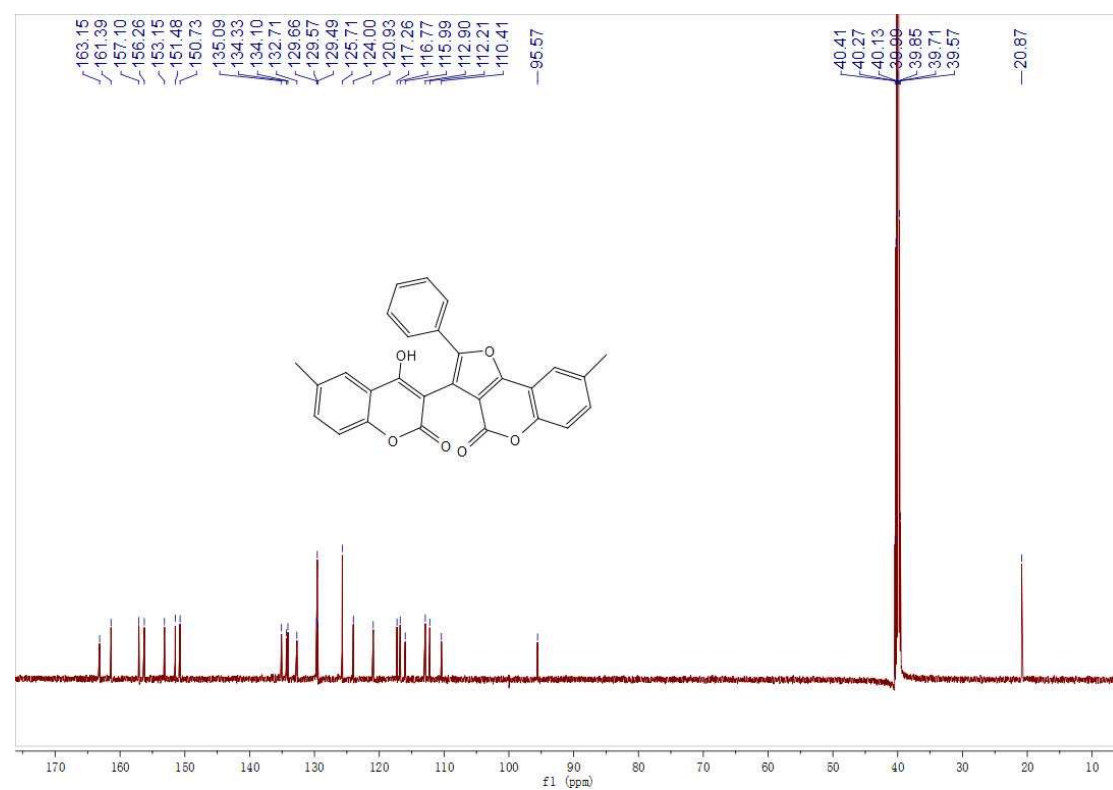
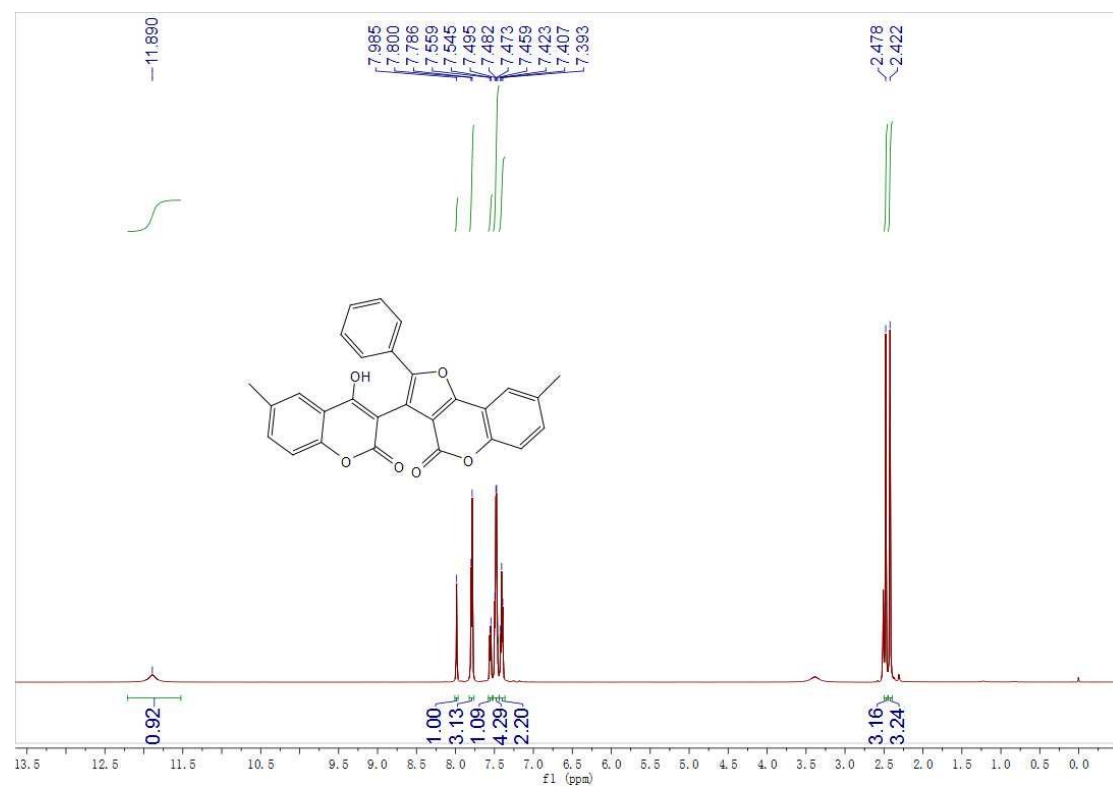
8-chloro-3-(6-chloro-4-hydroxy-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one (**5n**)



8-chloro-3-(6-chloro-4-hydroxy-2-oxo-2H-chromen-3-yl)-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5o**)



3-(4-hydroxy-6-methyl-2-oxo-2H-chromen-3-yl)-8-methyl-2-phenyl-4H-furo[3,2-c]chromen-4-one (**5p**)



3-(4-hydroxy-6-methyl-2-oxo-2H-chromen-3-yl)-2-(4-methoxyphenyl)-8-methyl-4H-furo[3,2-c]chromen-4-one (**5q**)

