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Graphical Abstract

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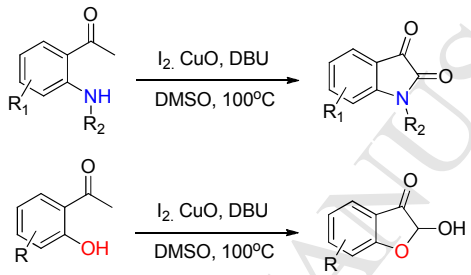

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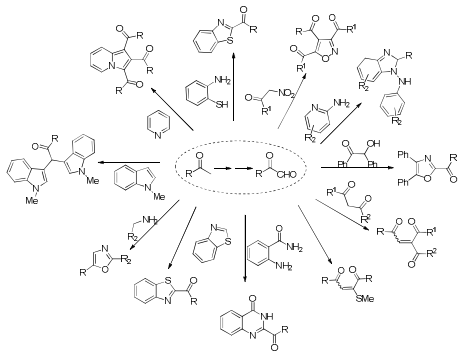
ABSTRACT

A novel and attractive protocol to synthesis indole-2,3-diones and 2-hydroxy-3(2H)-benzofuranones and via copper(II) oxide catalyzed intramolecular cyclization is described. This method possesses functional-group compatibility, easy workup procedure, shorter reaction time and high yields.

1. Introduction

Indole-2,3-diones (isatins) are important heterocycles found in many natural products, pharmaceuticals.[1] Also Indole-2,3-diones are commonly used in organic synthesis to construct new structural frameworks.[2] Traditionally, the most practical approach to this class of compounds is the Sandmeyer method,[3] starting from the requisite aniline, chloral hydrate, hydroxylamine hydrochloride and sulfuric acid, which provided a useful access to construct isatins. However, in more recent years, a wider variety of efficient methods have been developed for the synthesis of indole-2,3-diones. The copper-catalyzed intramolecular C-H oxidation/acylation of formyl-N-arylformamides has also proven successful in the construction of indole-2,3-diones with oxygen as oxidant.[4] In addition, Jadhav and co-workers reported a general catalytic $Cu(OAc)_2$/TEMPO method performed in either air or $Cu(OAc)_2/O_2$ systems for the C-N and C-O cross-coupling reaction to construct indole-2,3-diones.[5] Indoles have also been utilized as substrates for the synthesis of indole-2,3-diones with selected catalyst.[6] Although each existing method has its own merits for the preparation of certain indole-2,3-dione derivative(s), further investigation into a simpler general method remains highly valuable.



Scheme 1. In situ trapping of unstable α-ketoaldehyde intermediates strategy to construct diverse compounds through intermolecular reactions.

In recent years, we reported an efficient in situ trapping of unstable-ketoaldehyde intermediates strategy to construct diverse compounds through intermolecular reactions (Scheme 1).[7] Also, we suspect to design intramolecular reactions in situ capture α-ketoaldehyde as a supplement of intermolecular reactions.

Retrosynthetically (Scheme 2), it was envisioned that 1-methylindoline-2,3-dione could be obtained from 2-(2-(methylamino)phenyl)-2-oxoacetaldehyde **A** through an intramolecular condensation process,[8] while **A** could be furnished from the α-halogenated ketone through Kornblum Oxidation.[9] It was also suggested that **B** could be easily prepared from 1-(2-(methylamino)phenyl)ethanone **1a** through a halogenation process.[10] Based on the retrosynthetic analysis, it was herein

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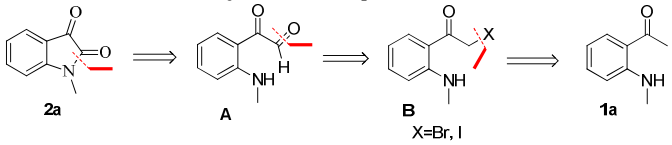
assumed that indole-2,3-diones could be obtained from 1-(2-aminophenyl)ethanones via the integration of iodination/oxidation/cyclization sequences.[11]



Scheme 2. Retrosynthetic analysis and the protocols for one-pot synthesis of 1-methylindoline-2,3-dione through intramolecular cyclization.

2. Results and discussion

Our investigation began this reaction with 1-(2-(phenylamino)phenyl)ethanone **1a** as model substrate in DMSO. The reaction of 1-(2-(methylamino)phenyl)ethanone with I_2/CuO (0.5 equiv/0.5 equiv) could only afford the desired product in very low yield at 100℃ in DMSO (Table 1, entry 1). To improve the yield of the products, the amount of I_2, CuO and various bases were investigated in further detail in DMSO. First, a series of bases, such as NaOH, KOH, Na_2CO_3, K_2CO_3, Cs_2CO_3, Et_3N, DBU and DABCO were screened for the reaction (Table 1, entry 2-9). Much to our satisfaction, the reaction efficiency was much improved to 90% with DBU as the base. When the reaction was conducted without I_2, almost no desired product was obtained (Table 1, entry 10). However, further increases in the additive dose to 0.5 equiv could not enhance the yield beyond 90%. When the reaction was conducted in the absence of the CuO, only 20% of the product **2a** could be obtained (Table 1, entry 15). These results indicated that I_2, DBU and CuO are necessary for the reaction. Moreover, further examination revealed that adjustments in temperature resulted in decreased yields (Table 1, entry 19-22). It was thus determined that the optimum conditions for this reaction were I_2/DBU/CuO (0.5 equiv/0.5 equiv/0.5 equiv) at a temperature of 100 ℃ in DMSO (Table 1, entry 8).

Table 1. Optimization of the reaction conditions[a]

Entry	I_2 (equiv)	Base	CuO (equiv)	Temp (□)	Yield (%)[b]
1[c]	0.5		0.5	100	22
2	0.5	NaOH	0.5	100	35
3	0.5	KOH	0.5	100	58
4	0.5	Na_2CO_3	0.5	100	63
5	0.5	K_2CO_3	0.5	100	80
6	0.5	Cs_2CO_3	0.5	100	83
7	0.5	Et_3N	0.5	100	52
8	**0.5**	**DBU**	**0.5**	**100**	**90**
9	0.5	DABCO	0.5	100	55
10[d]		DBU	0.5	100	Trace
11	0.25	DBU	0.5	100	76
12	0.75	DBU	0.5	100	88
13	1.0	DBU	0.5	100	67
14	1.5	DBU	0.5	100	65
15[e]	0.5	DBU		100	20
16	0.5	DBU	0.75	100	38
17	0.5	DBU	1.0	100	35
18	0.5	DBU	1.25	100	32
19	0.5	DBU	0.5	60	42
20	0.5	DBU	0.5	80	73
21	0.5	DBU	0.5	90	87
22	0.5	DBU	0.5	110	83

[a] Reaction conditions: **1a** (1.0 mmol), CuO (0.5 mmol) were heated in DMSO for 2h.

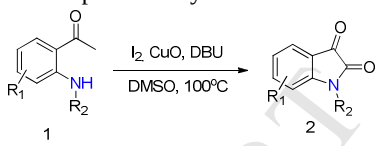
[b] Isolated yields.

[c] Reaction conditions: **1a** (1.0 mmol), I_2 (0.5 mmol), CuO (0.5 mmol) were heated in DMSO at 100 ℃ for 2h.

[d] Reaction conditions: **1a** (1.0 mmol), DBU (0.5 mmol), CuO (0.5 mmol) were heated in DMSO at 100 ℃ for 2h.

[e] Reaction conditions: **1a** (1.0 mmol), I_2 (0.5 mmol), DBU (0.5 mmol) were heated in DMSO at 100 ℃ for 2h.

Table 2. Reaction scope of methyl ketones[a]



Entry	1	2	Yields[b] (%)
1	**1c** (R_1=H, R_2=CH_3)	**2a**	90
2	**1b** (R_1=H, R_2=Ph)	**2b**	83
3	**1c** (R_1=H, R_2=Bn)	**2c**	85
4	**1d** ((R_1=[d][1,3]dioxol-5-yl, R_2=CH_3)	**2d**	82
5	**1e** R_1=5-I, R_2= Ph)	**2e**	91
6	**1g** (R_1=[d][1,3]dioxol-5-yl, R_2= Ph)	**2f**	78
7	**1h** (R_1=H, R_2=H)	**2g**	0

[a] Reaction conditions: **1a** (1.0 mmol), I_2 (0.5 mmol), DBU (0.5 mmol), CuO (0.5 mmol) were heated in DMSO at 100 ℃ for 2h.

[b] Isolated yields.

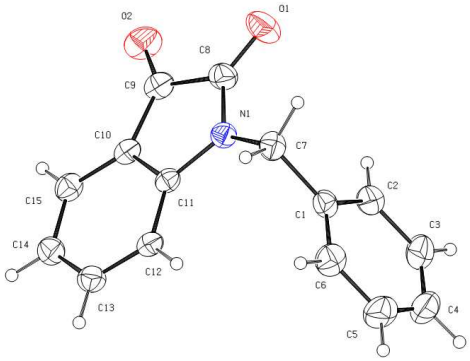
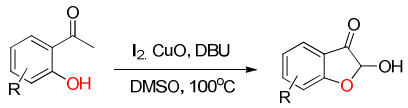


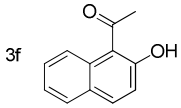
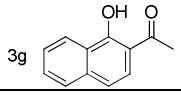
Fig. 1. X-ray crystal structure of compound **2c**

With this optimized result in hand, we next explored the scope of this reaction, diverse Indole-2,3-diones (**2a-2f**) was achieved high yields using optimum condition (Table 2). Much to our surprise when the substrate was 1-(2-aminophenyl)ethanone, no deserved product was obtained. (Table 2, 2g), this may be that 1-(2-aminophenyl)ethanone was oxidized to 1-(2-nitrophenyl)ethanone under the reaction condition. Fortunately the target products **2c** (Fig. 1)[12] and **2e** (in Supplementary data) were further determined by X-ray crystallographic analysis.

2-hydroxybenzofuran-3(2H)-ones are also compounds which are recurrent motifs and subunits in organic molecules with interesting biological activities, such as antimicrobial activity,[13,14] antilammatory,[14] antifungalactivity.[13,16] Therefore, considerable attention has been paid to their efficient synthetic methods.[17] Inspired by the aforementioned results, it was supposed that 2-hydroxybenzofuran-3(2H)-ones could also be constructed from 1-(2-hydroxyphenyl)ethanones by intramolecular cyclization under the standard conditions. As depicted in Table 3, the conditions were mild enough to be compatible with electron-donating and halogenated substrates (68-83%; **4a-4e**). Pleasingly,

Table 3. Reaction scope of methyl ketones and benzylamine derivatives[a,b]



Entry	R	4	Yields[b] (%)
1	**3a** (H)	**4a**	72
2	**3b** (5-F)	**4b**	70
3	**3c** (5-Br)	**4c**	79
4	**3d** (4-F)	**4d**	83
5	**3e** (5-OCH_3)	**4e**	80
6		**4f**	81
7		**4g**	85

[a] Reaction conditions: **1a** (1.0 mmol), I_2 (0.5 mmol), DBU (0.5 mmol), CuO (0.5 mmol) were heated in DMSO at 100 ℃ for 2h.

[b] Isolated yields.

the desired 2-hydroxybenzofuran-3(2H)-ones could be obtained in good yields from steric substrates (80%-85%; **4f**-**4g**). To our delight, product **4e** was also further determined by X-ray crystallographic analysis (Fig. 2).[18]

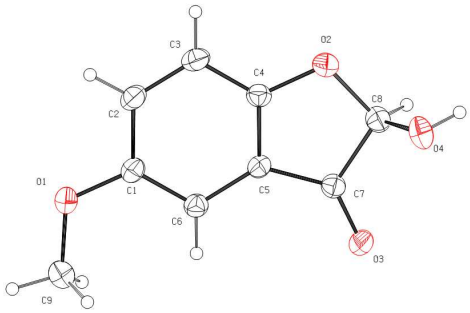
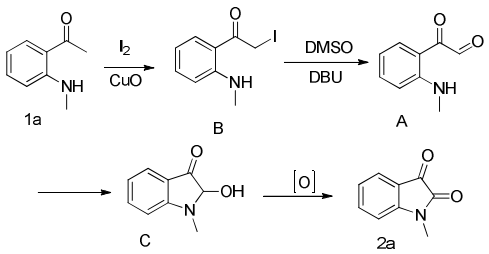


Fig. 2. X-ray crystal structure of compound **4e**

In accordance with the results, a plausible mechanism proposed for the I_2/CuO promoted cyclization reaction is presented in Scheme 3. It is proposed that 1-(2-(methylamino)phenyl)ethanone **1a** with I_2 and CuO initially undertook a halogenation reaction to afford the intermediate α-iodo-1-(2-(methylamino)phenyl)ethanone **B**. Subsequently, **B** was further converted into the intermediate 2-oxo-2-(2-(methylamino)phenyl)acetaldehyde **A** via Kornblum oxidation.[19] The addition of the glyoxal group with amine generates hemiaminal intermediate **C**.[11] Finally, it is proposed that intermediate **C** underwent oxidation to provide the desired product **2a**.



Scheme 3. Plausible mechanism for the reaction.

3. Conclusion

In conclusion, we have reported a new intramolecular cyclization to construct Indole-2,3-diones and 2-hydroxy- 3(2H)-benzofuranones from easily available1-(2-aminophenyl) ethanones and 1-(2-hydroxyphenyl)ethanones via a one-step, one-pot procedure. This reaction provided significant advantages in the use of simple substrates, mild reaction conditions and provision of excellent yields. Further studies on the design of other complicated compounds and investigations toward the applications in organic synthesis are currently underway in our laboratory.

4. Experimental

4.1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-d_6 on 100 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a Bruker 7-tesla FT-ICR MS equipped with an electrospray source. MS was carried out on a Thermo DSQ Ⅱ MS spectrometer (EI, 70 eV). Elemental analyses were performed using a VARIO EL Ⅲ elemental analyzer. The X-ray crystal-structure determinations were obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

4.2. General procedure for synthesis of 2 (2a as an example)

A sealed tube was charged with 1-(2-(methylamino)phenyl)ethanone **1a** (74.6 mg, 0.5 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (38.1 mg, 0.25 mmol), copper (Ⅱ) oxide (20 mg, 0.25 mmol) and iodine (63.5 mg, 0.25 mmol) at room temperature, and then dried solvent DMSO (3mL) was added. The resulting mixture was stirred at 100 ℃ and monitored to completion by TLC analysis. After cooling to room temperature, H_2O (50 ml) was added and the aqueous mixture was extracted with EtOAc 3 times (3 × 50 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the eluent to give the expected product **2a** as yellow solid (90% yield).

4.3. General procedure for synthesis of 4 (4a as an example)

A sealed tube was charged with 1-(2-hydroxyphenyl)ethanone **3a** (75.1 mg, 0.5 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (38.1 mg, 0.25 mmol), copper(Ⅱ) oxide (20 mg, 0.25 mmol) and iodine (63.5 mg, 0.25 mmol) at room temperature, and then dried solvent DMSO (3 mL) was added. The resulting mixture was stirred at 100 ℃ and monitored to completion by TLC analysis. After cooling to room temperature, H_2O (50 ml) was added and the aqueous mixture was extracted with EtOAc 3 times (3 × 50 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the

eluent to give the expected product **4a** as light yellow solid (72% yield).

4.4. Characterization data

4.4.1 *1-methylindoline-2,3-dione (**2a**)*

Yield 90%; red solid; mp 118-120 ^{o}C; IR (KBr): 3451, 1749, 1722, 1601, 1475, 1323, 1114, 831, 702, 470 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.61 (s, 1H), 7.28 (s, 1H), 7.14 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 183.19, 158.01, 151.22, 138.36, 124.94, 123.65, 117.12, 109.89, 26.04; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_9H_7NaNO_2$: 184.0369; found: 184.0371.

4.4.2 *1-phenylindoline-2,3-dione (**2b**)*

Yield 85%; red solid; mp 162-164 ^{o}C; IR (KBr): 3459, 1736, 1609, 1491, 1466, 1471, 1367, 1296, 1193, 926, 854, 810, 760, 698, 485 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) = 7.88 (d, J = 7.8 Hz, 1H), 7.70 (s, 1H), 7.56 (d, J = 7.2 Hz, 2H), 7.42 (d, J = 7.2 Hz, 2H), 7.19 (s, 2H); 6.91 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 138.99, 138.29, 129.84, 128.70, 127.56, 125.86, 125.62, 125.45, 124.47, 124.21, 110.20, 111.06; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_{14}H_9NaNO_2$: 246.0530; found: 246.0526.

4.4.3 *1-benzylindoline-2,3-dione (**2c**)*

Yield 85%; yellow solid; mp 163-165 ^{o}C; IR (KBr): 3450, 1736, 1607, 1491, 1466, 1367, 1296, 1193, 927, 760, 468 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.86 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.35-7.31 (m, 6H), 6.58 (d, J = 8.4 Hz, 1H) , 4.91 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 181.81, 157.15, 149.89, 146.26, 133.95, 133.72, 129.07, 128.26, 127.32, 119.10, 113.11, 86.17, 44.05; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_{15}H_{11}NaNO_2$: 260.0682; found: 260.0685.

4.4.4 *5-methyl-5H-[1,3]dioxolo[4,5-f]indole-6,7-dione (**2d**)*

Yield 85%; red solid; mp 192-194 ^{o}C; IR (KBr): 3426, 1735, 1612, 1479, 1435, 1384, 1344, 1242, 1094, 1036, 934, 807, 487 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.02 (s, 1H), 6.44 (s, H), 6.08 (s, 2H), 3.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 180.66, 159.16, 156.57, 151.13, 144.35, 110.16, 104.84, 102.63, 92.99, 26.25; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_{15}H_{12}NaNO_4$: 228.0270; found: 228.0267.

4.4.5 *1-benzyl-5-iodoindoline-2,3-dione (**2e**)*

Yield 91%; yellow solid; mp 199-201 ^{o}C; IR (KBr): 3448, 1745, 1731, 1603, 1467, 1434, 1325, 1313, 1176, 1127, 818, 713, 517 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.89 (s, 1H), 7.78 (s, 1H), 7.76 (s, 1H), 7.36-7.29 (m, 5H); 6.57 (d, J = 8.4 Hz, 1H), 4.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 181.84, 157.18, 149.92, 146.30, 133.96, 133.80, 129.11, 128.31, 127.35, 119.14, 113.12, 86.20, 44.08; MS (70ev): m/z = 363.21; Anal. Calcd. for $C_{15}H_{10}INO_2$: C, 49.61; H, 2.78; N, 3.86 %. Found: C, 49.75; H, 2.85; N, 3.69 %.

4.4.6 *5-benzyl-5H-[1,3]dioxolo[4,5-f]indole-6,7-dione (**2f**)*

Yield 78%; red solid; mp 191-193 ^{o}C; IR (KBr): 3458, 2926, 1741, 1722, 1612, 1494, 1472, 1410, 1386, 1345, 1325, 1247, 1156, 1031, 896, 832, 798, 710, 697, 600, 488, 460 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.35-7.27 (m, 5H); 7.00 (s, 1H), 6.29 (s, 1H), 6.01 (s, 2H), 4.86 (s, 2H), 6.57 (d, J = 8.4 Hz, 1H), 4.92 (s, 2H); ^{13}C NM.R (100 MHz, $CDCl_3$): δ (ppm) = 220.09, 203.83, 180.43, 159.19, 156.34, 150.25, 144.39, 134.48, 129.02, 128.09, 127.20, 110.39, 104.73, 102.56, 94.00, 43.92; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_{16}H_{11}NNaO_4$: 304.0580; found: 304.0582.

4.4.7 *2-hydroxybenzofuran-3(2H)-one (**4a**)*

Yield 72%; light yellow solid; mp 133–135 ^{o}C; IR (KBr): 3441, 3221, 1704, 1617, 1463, 1322, 1147, 1128, 998, 762 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.65 (d, J = 8.4 Hz, 1H), 7.62 (s, 1H), 7.09 (d, J = 7.2 Hz, 1H), 5.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 198.75, 171.47, 139.45, 125.02, 122.48, 119.00, 113.51, 96.93; MS (70ev): m/z = 150.11; Anal. Calcd. for $C_8H_6O_3$: C, 64.00; H, 4.03 %. Found: C, 63.81; H, 4.15 %.

4.4.8 *5-fluoro-2-hydroxybenzofuran-3(2H)-one (**4b**)*

Yield 70%; brown solid; mp 189-192 ^{o}C; IR (KBr): 3253, 1712, 1493, 1342, 1315, 1245, 1164, 1133, 1109, 1024, 933, 825, 782 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.66-7.61 (m, 1H), 7.48-7.45 (m, 1H), 5.65 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 198.28, 167.01, 126.48 (d, J_{CF} = 25.0 Hz), 119.87, 114.93, 109.50 (d, J_{CF} = 23.0 Hz), 98.62; MS (70ev): m/z = 168.11; Anal. Calcd. for $C_8H_5FO_3$: C, 57.15; H, 3.00 %. Found: C, 57.02; H, 2.89 %.

4.4.9 *5-bromo-2-hydroxybenzofuran-3(2H)-one (**4c**)*

Yield 79%; white solid; mp 124-126 ^{o}C; IR (KBr): 3417, 1716, 1613, 1466, 1272, 1145, 1115, 923, 826 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.87 (d, J = 8.8 Hz, 1H), 7.79 (s, 1H), 7.19 (d, J = 8.8 Hz, 1H), 5.65 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 197.34, 169.50, 141.28, 126.51, 121.37, 115.78, 113.51, 98.45; MS (70ev): m/z = 228.04; Anal. Calcd. for $C_8H_5BrO_3$: C, 41.95; H, 2.20 %. Found: C, 41.66; H, 2.09 %.

4.4.10 *6-fluoro-2-hydroxybenzofuran-3(2H)-one (**4d**)*

Yield 83%; yellow oil; IR (KBr): 3435, 2962, 2831, 1727, 1647, 1509, 1421, 1367, 1259, 1156, 1123, 988, 854, 799, 599, 558 cm^{-1}; ^{1}H NMR (600MHz,): δ (ppm) = 7.39 (d, J = 9.6 Hz ,1H) , 6.85 (t, J = 7.2 Hz, 1H), 6.27 (d, J = 9.6 Hz, 1H), 6.12 (t, J = 9.0 Hz 1H), 4.81 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 196.45, 172.20 (d, J_{CF} = 15.0 Hz), 170.33, 167.79, 126.77 (d, J_{CF} =12.0 Hz), 116.43, 110.47, 100.78 (d, J_{CF} = 26.0 Hz), 98.92 (d, J_{CF} =13.0 Hz); MS (70ev): m/z = 168.08; Anal. Calcd. for $C_8H_5FO_3$: C, 57.15; H, 3.00 %. Found: C, 56.96; H, 2.81 %.

4.4.11 *2-hydroxy-5-methoxybenzofuran-3(2H)-one (**4e**)*

Yield 80%; light brown solid; mp 190-193 ^{o}C; IR (KBr): 3253, 1716, 1492, 1342, 1285, 1245, 1164, 1134, 1110, 1025, 933, 825, 782 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.36 -7.34 (m, 1H), 7.13 (d, J = 6Hz, 1H), 7.06 (s, 1H), 5.56 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 198.63, 165.76, 154.40, 128.05, 119.28, 114.35, 104.90, 98.18; MS (70ev): m/z = 180.13; Anal. Calcd. for $C_9H_8O_4$: C, 60.00; H, 4.48 %. Found: C, 59.72; H, 4.36 %.

4.4.12 *2-hydroxynaphtho[2,1-b]furan-1(2H)-one (**4f**)*

Yield 81%; yellow solid; mp 238-240 ^{o}C; IR (KBr): 3195, 1669, 1578, 1530, 1449, 1286, 1206, 1139, 1095, 929, 824, 751, 576, 465 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 8.55 (d, J = 8.0 Hz ,1H), 8.35 (d, J = 8.8Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 6.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 5.71(s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 197.94, 173.55, 141.09, 130.17, 129.12, 128.70, 128.61, 125.29, 121.89, 114.25, 110.79, 98.61; HRMS (APCI): m/z [M + Na]$^{+}$ calcd for $C_{12}H_8NaO_3$: 223.0366; found: 223.0366.

4.4.13 *2-hydroxynaphtho[1,2-b]furan-3(2H)-one (**4g**)*

Yield 85%; light yellow solid; mp 179-182 ^{o}C; IR (KBr): 3445, 1633, 1467, 1434, 1307, 1284, 1257, 1210, 1091, 792, 764 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ (ppm) = 7.96-7.92 (m, 1H),

7.84 (t, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 173.06, 160.38, 136.82, 131.49, 129.45, 127.68, 125.97, 124.89, 124.13, 123.20, 118.44, 106.05; MS (70ev): m/z = 200.15; Anal. Calcd. for $C_{12}H_8O_3$: C, 72.00; H, 4.03 %. Found: C, 71.83; H, 3.89 %.

Acknowledgments

This work was supported by Central China Normal University, the National Natural Science Foundation of China (Grant 21032001 and 21272085). We thank Dr. Xianggao Meng (Central China Normal University) for performing X-ray crystallographic analysis and Dr. Chuanqi Zhou (Hebei University) for performing the HRMS analysis.

Supplementary data

The X-ray crystal structures of compound **2f** and ^{1}H and ^{13}C NMR spectra of compounds are available in Supplementary data. Supplementary data related to this article can be found online at doi:

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11. During our preparation of this manuscript Deng and co-workers reported the same starting materials as ours: Selenium-Promoted Intramolecular Oxidative Amidation of 2-(Arylamino)-acetophenones for the Synthesis of N-Arylisatins Liu, Y.; Chen, H.; Hu, X.; Zhou, W.; Deng, G. J. *Eur. J. Org. Chem*. **2013**, *20*, 4229–4232.
12. Crystal structure data for compound **2c**: CCDC number 948705, $C_{15}H_{11}NO_2$, Monoclinic, space group P2(1)/c, a = 6.592(4), b = 4.916(3), c = 18.359(10) Å, α = 90°, β = 98.768(7)°, γ = 90°, V = 588.0(6) Å^3, T = 296(2) K, Z = 2, Dc= 1.340 Mg/m^3, μ = 0.090 mm^{-1}, λ = 0.71073 Å, F(000) 248, crystal size 0.12 x 0.10 x 0.10 mm^3, 2191 independent reflections [R(int) = 0.0445], reflections collected 4304, refinement method: Full-matrix least-squares on F^2: goodness-of-fit on F^2 1.055, final R indices [$I > 2\sigma(I)$], R_1 = 0.0472, wR_2 = 0.1286, largest diff. peak and hole 0.188and -0.197e.Å^{-3}.
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18. Crystal structure data for compound **4b**: CCDC number 948707, $C_9H_8O_4$, Orthorhombic, space group Pna2(1), a = 20.870(5), b = 3.9446(9), c = 9.784(2) Å, α = 90°, β = 90 °, γ = 90°, V = 805.3(6) Å^3, T = 296(2) K, Z = 4, Dc = 1.486 Mg/m^3, μ = 0.118 mm^{-1}, λ = 0.71073 Å, F(000) 376, crystal size 0.12 x 0.10 x 0.10 mm^3, 2427 independent reflections [R(int) = 0.0435], reflections collected 4304, refinement method: Full-matrix least-squares on F^2: goodness-of-fit on F^2 1.055, final R indices [$I > 2\sigma(I)$], R_1 = 0.0434, wR_2 = 0.9875, largest diff. peak and hole 0.172 and -0.141e.Å^{-3}.
19. Halogenation reaction and Kornblum oxidation processes are well investigated in our previous studies. See refs 8b-8h and 9b-9d.

Supporting Information

Logical design and synthesis of Indole-2,3-diones and 2-hydroxy-3(2H)-benzofuranones via one-pot intramolecular cyclization

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1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-*d*6 on 100 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a Bruker 7-tesla FT-ICR MS equipped with an electrospray source. MS was carried out on a Thermo DSQ Ⅱ MS spectrometer (EI, 70 eV) Elemental analyses were performed using a VARIO EL Ⅲ elemental analyzer. The X-ray crystal-structure determinations were obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

2. Synthesis of 2a-2g, 4a-4g

2.1. General procedure for synthesis of 2a-2g (2a as an example)

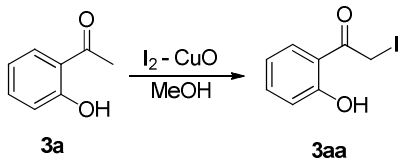
General procedure: A sealed tube was charged with 1-(2-(methylamino)phenyl)ethanone **1a** (80.6 mg, 0.5 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (38.1 mg, 0.25 mmol), copper (Ⅱ) oxide (20 mg, 0.25 mmol) and iodine (63.5 mg, 0.25 mmol) at room temperature, and then dried solvent DMSO (3mL) was added. The resulting mixture was stirred at 110 ℃ and monitored to completion by TLC analysis. After cooling to room temperature, H_2O (50 ml) was added and the aqueous mixture was extracted with EtOAc 3 times (3 × 50 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the eluent to give the expected product **2a** as yellow solid (90% yield).

2.2 . General procedure for synthesis of 4a-4g (4a as an example)

General procedure: A sealed tube was charged with 1-(2-hydroxyphenyl)ethanone **3a** (75.1 mg, 0.5 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (38.1 mg, 0.25 mmol), copper(Ⅱ) oxide (20 mg, 0.25 mmol) and iodine (63.5 mg, 0.25 mmol) at room temperature, and then dried solvent DMSO (3mL) was added. The resulting mixture was stirred at 100 ℃ and monitored to completion by TLC analysis. After cooling to room temperature, H_2O (50 ml) was added and the aqueous mixture was extracted with EtOAc 3 times (3 × 50 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the eluent to give the expected product **4a** as light yellow solid (72% yield).

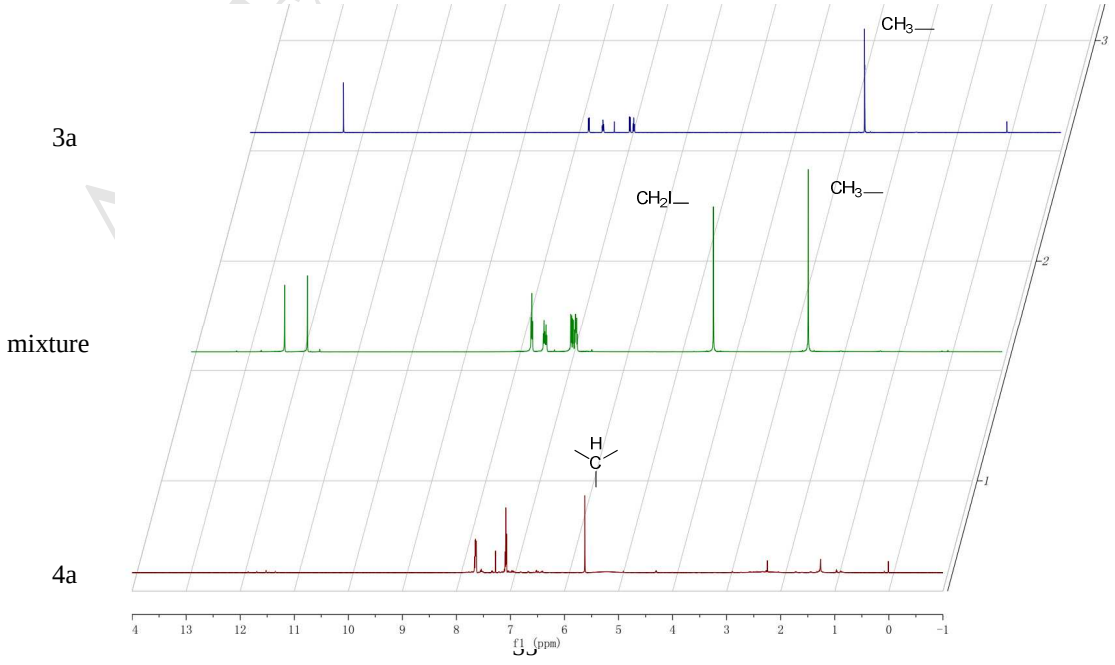
3. Control experimental

To confirm the reaction process, the reaction of intermediate 1-(2-hydroxyphenyl) -2-iodoethanone was carried out. A mixture of 1-(2-hydroxyphenyl)ethanone **3a** (1 equiv), CuO (1 equiv), and iodine (1 equiv) in methanol was heated at 80 °C for 1 h. compound **3aa** was obtained (Scheme s1). Then the reaction was carried out with the mixture as substrate under the optimum condition, we have also gotten the target compound **4a** (Fig. s1).



3a **3aa**

Scheme s1. iodination of 1-(2-hydroxyphenyl)ethanone



3. Crystallographic data and molecular structure of compounds 2e

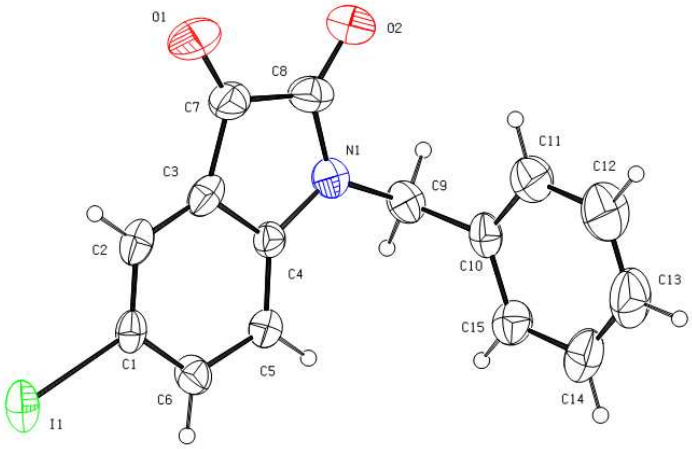
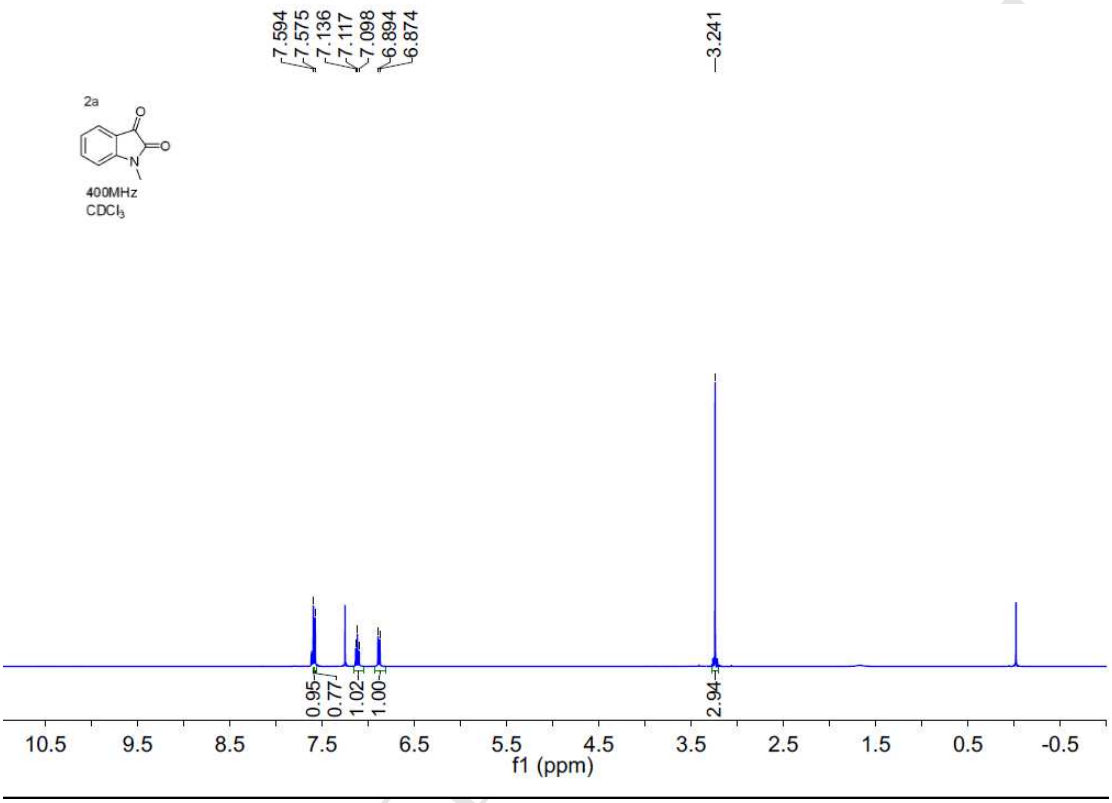
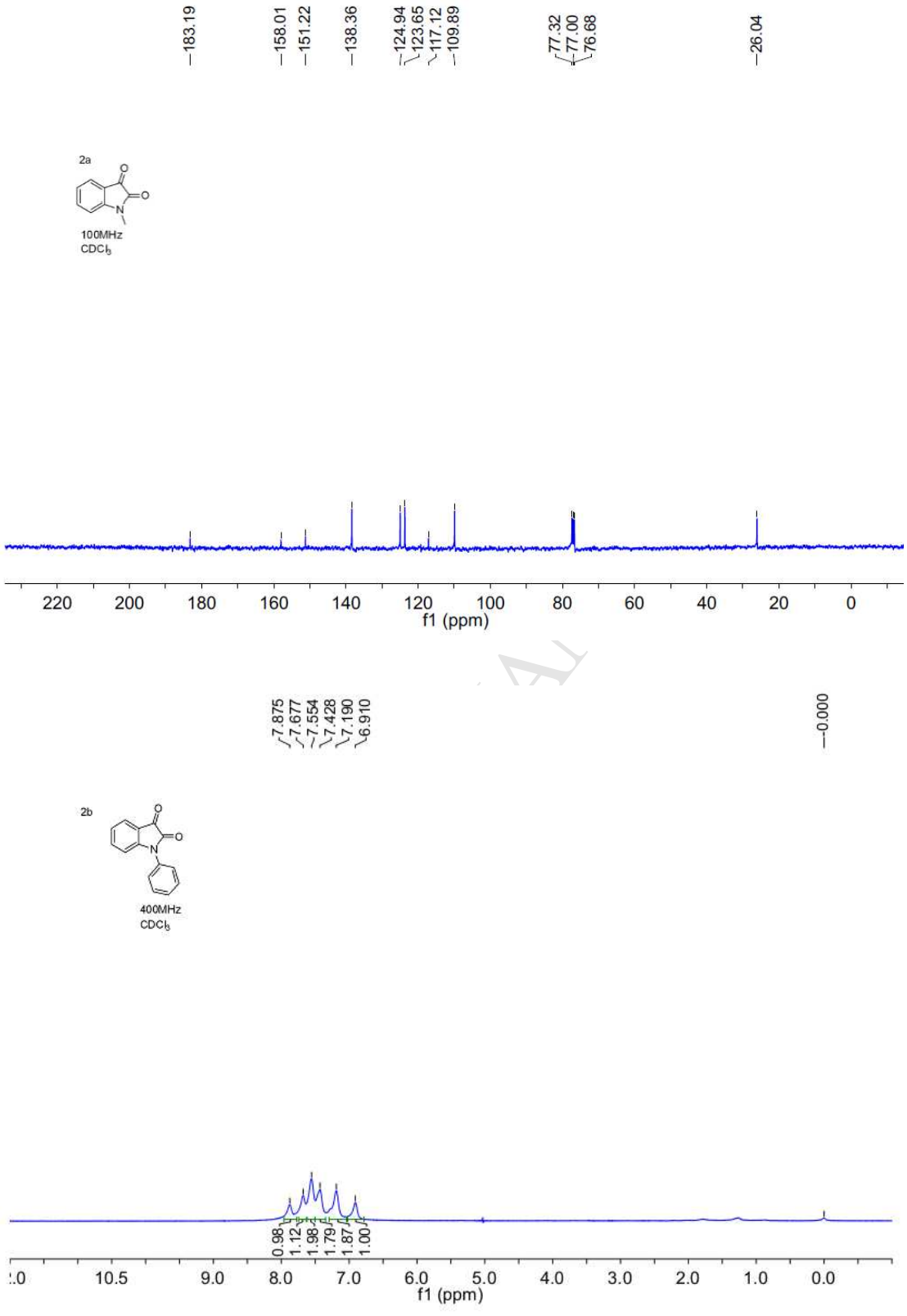


Fig. s2. X-ray crystal structure of compound **2e**

Crystal structure data for compound **2e**: CCDC number: 960539, $C_{15}H_{10}INO_2$, Orthorhombic, space group P2(1)2(1)2(1), a = 4.5682(12), b = 13.600(4), c = 22.338(6) Å, α = 90°, β = 90°, γ = 90°, V = 1387.8(7) $Å^3$, T = 296(2)K, Z = 4, Dc = 1.738Mg/m^3, μ = 2.304 $mm^{-1,}$ λ = 0.71073Å, F(000) 704, crystal size 0.15 x 0.12 x 0.10 mm^3, 2827 independent reflections [R(int) = 0.0726], reflections collected 10305, refinement method: Full-matrix least-squares on F_2: goodness-of-fit on F_2 1.037, final R indices [$I > 2\sigma(I)$], R_1 = 0.0611, wR_2 = 0.1517, largest diff. peak and hole 1.261 and -1.536e.$Å^{-3}$. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4. Appendix: spectral copies of ^{1}H NMR, and ^{13}C NMR

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2a
100MHz
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220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)
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7.677
7.554
7.428
7.190
6.910
0.000
2b
400MHz
CDCl3
0.98
1.12
1.98
1.79
1.87
1.00
10.5
9.0
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4.0
3.0
2.0
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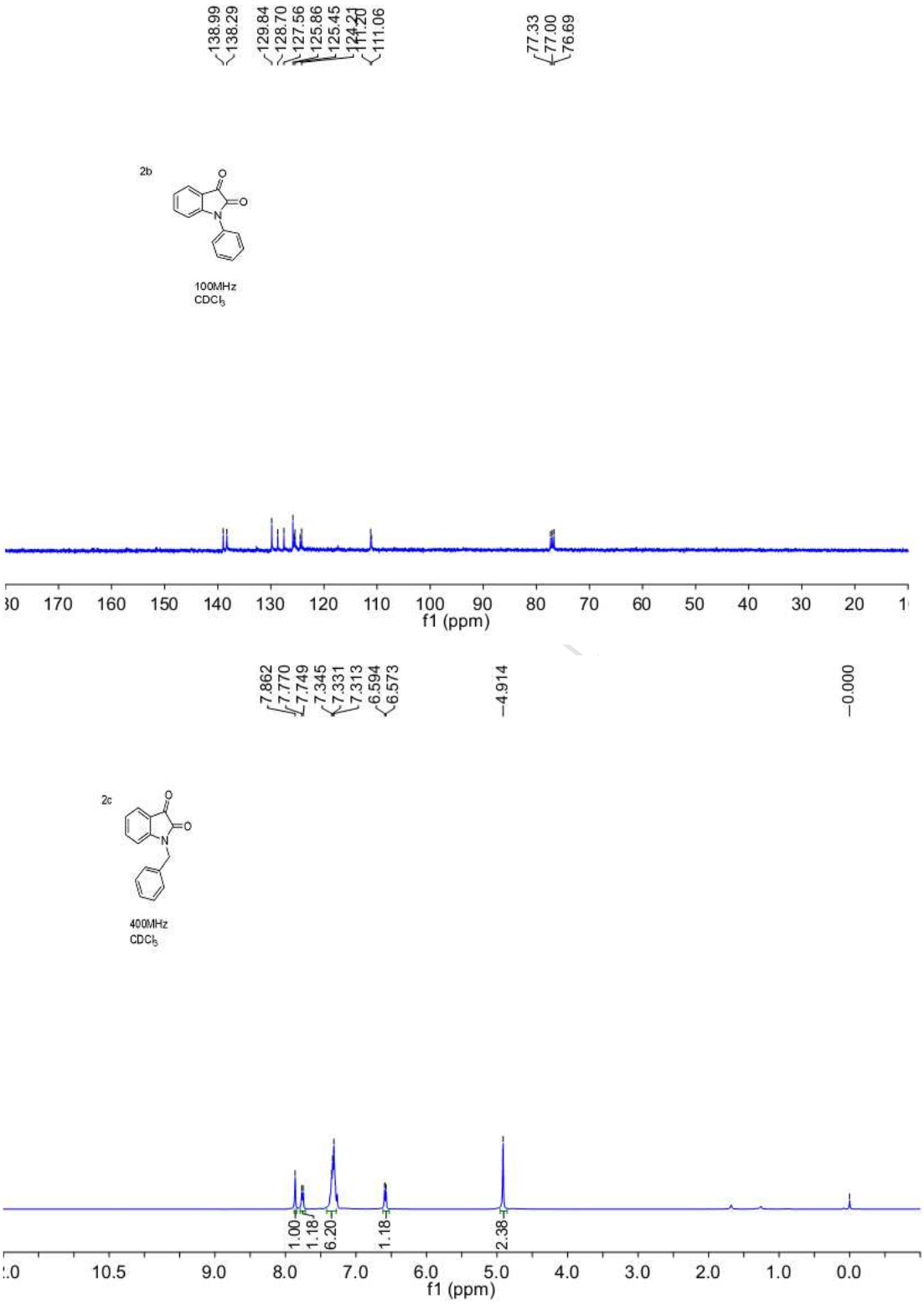
0.0
f1 (ppm)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100MHz
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7.331
7.313
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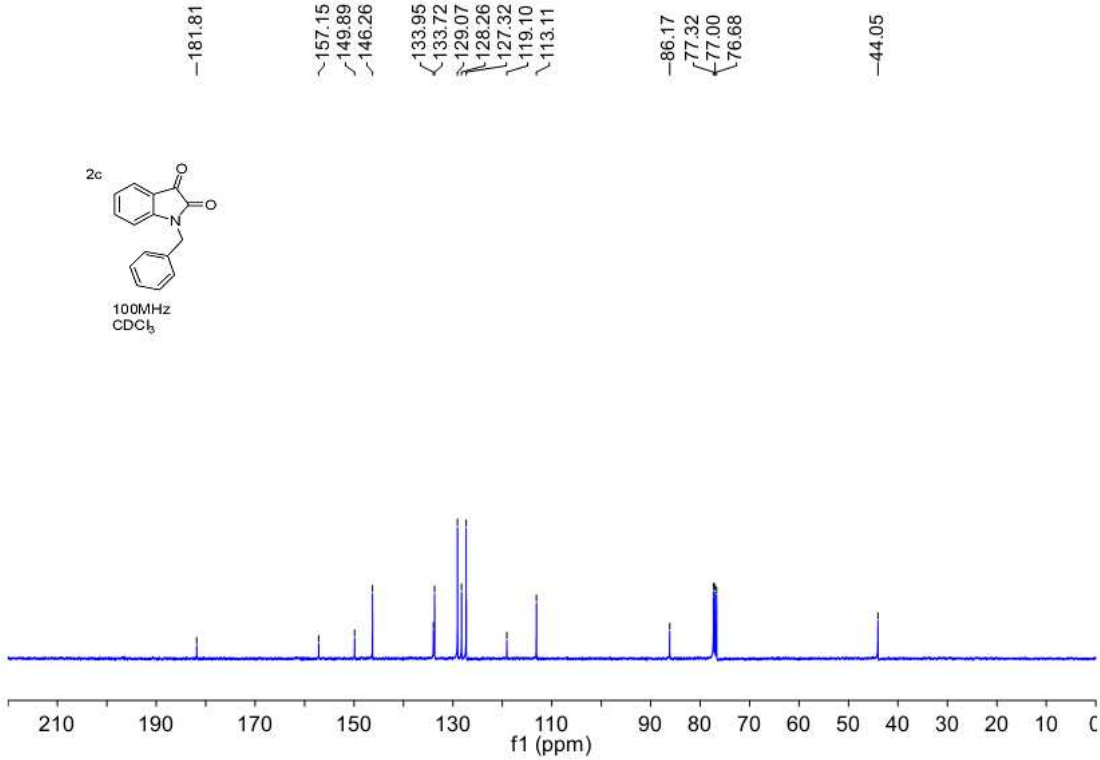
f1 (ppm)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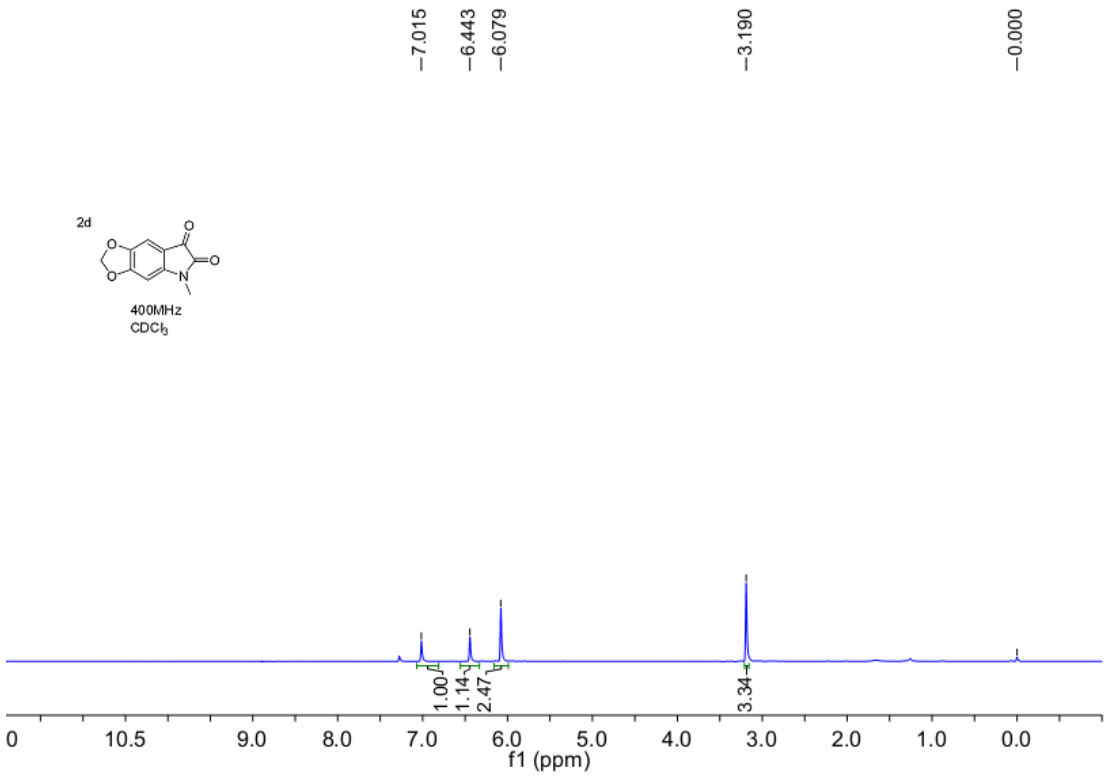
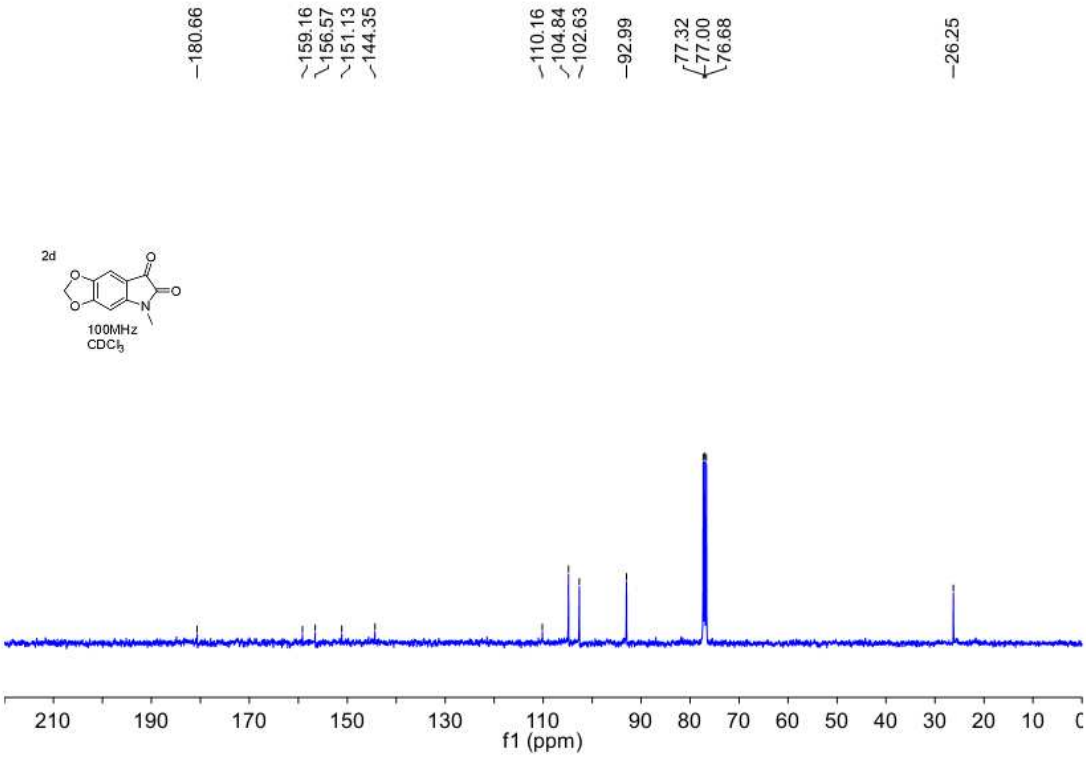
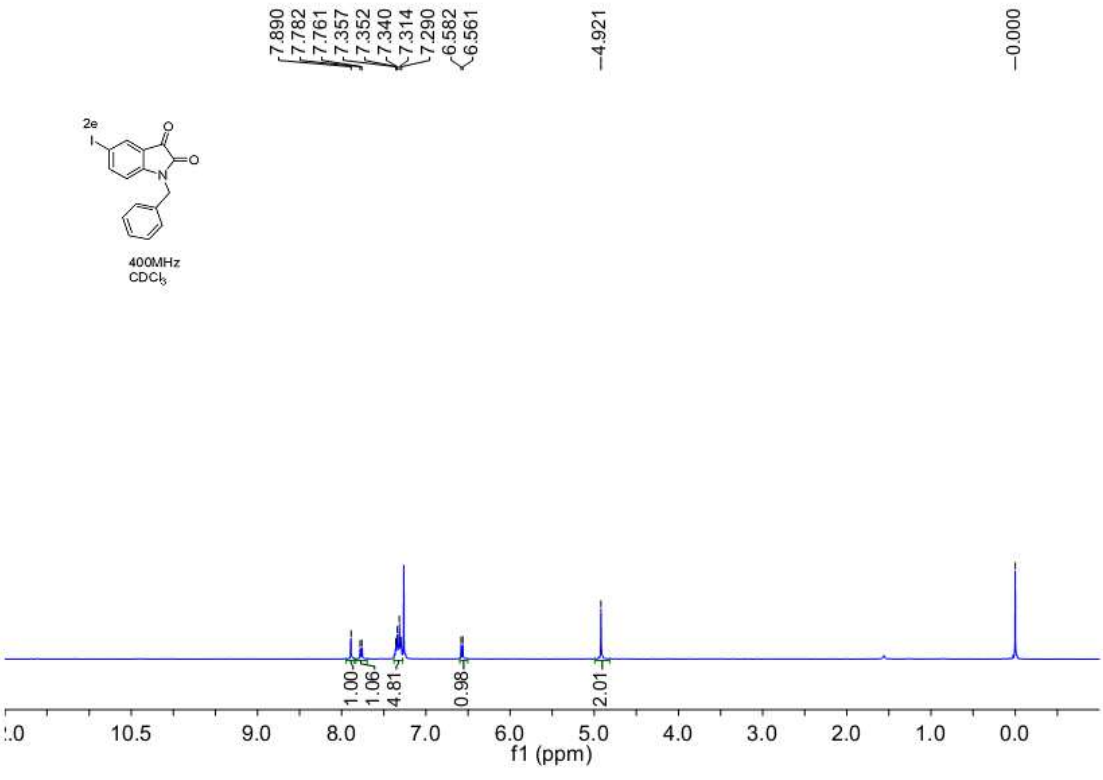
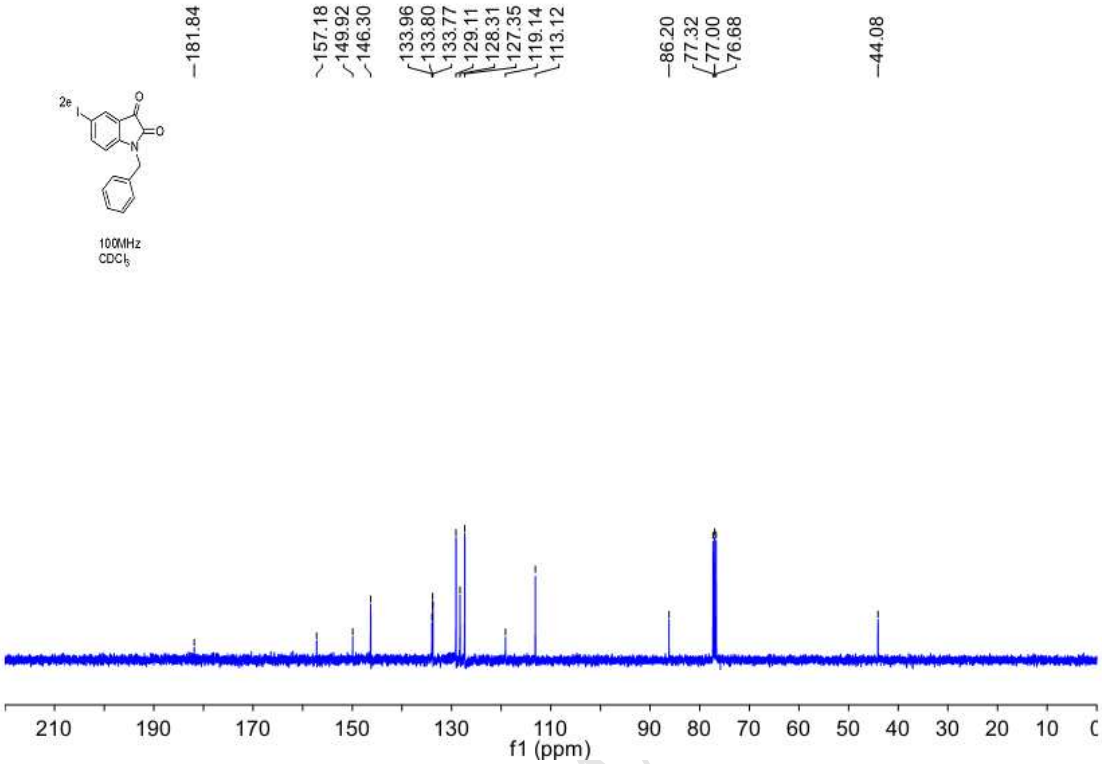
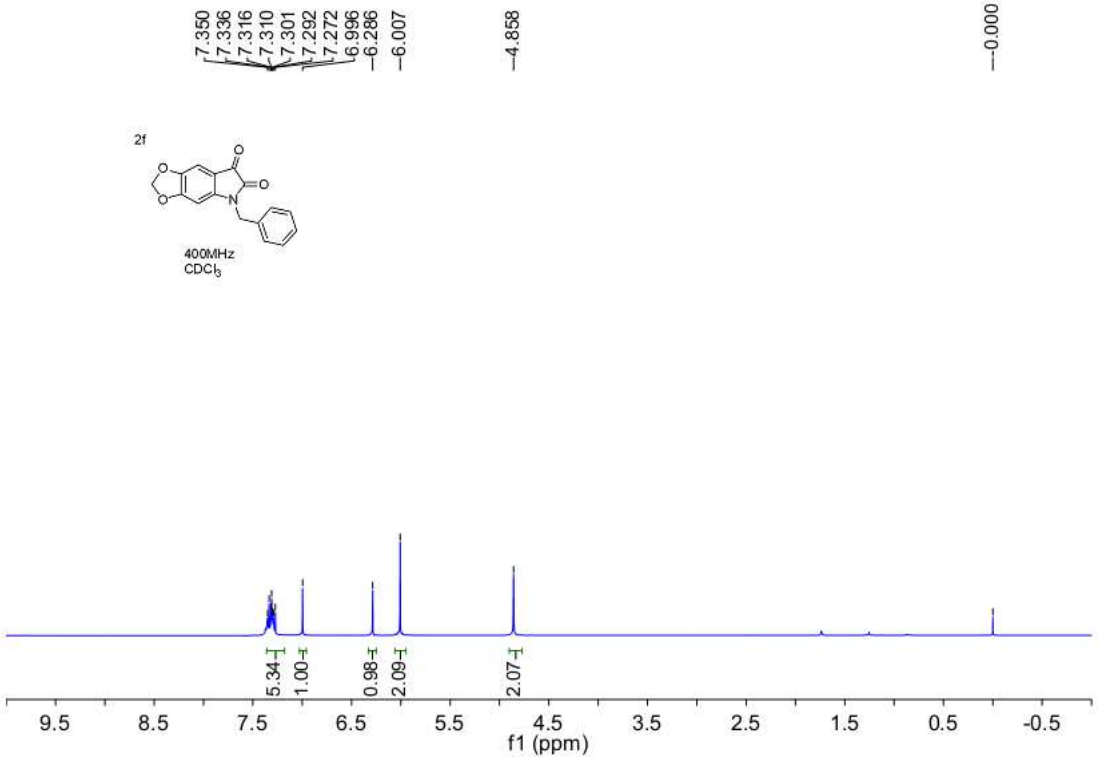
77.00
76.68
44.05
2c
100MHz
CDCl3
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

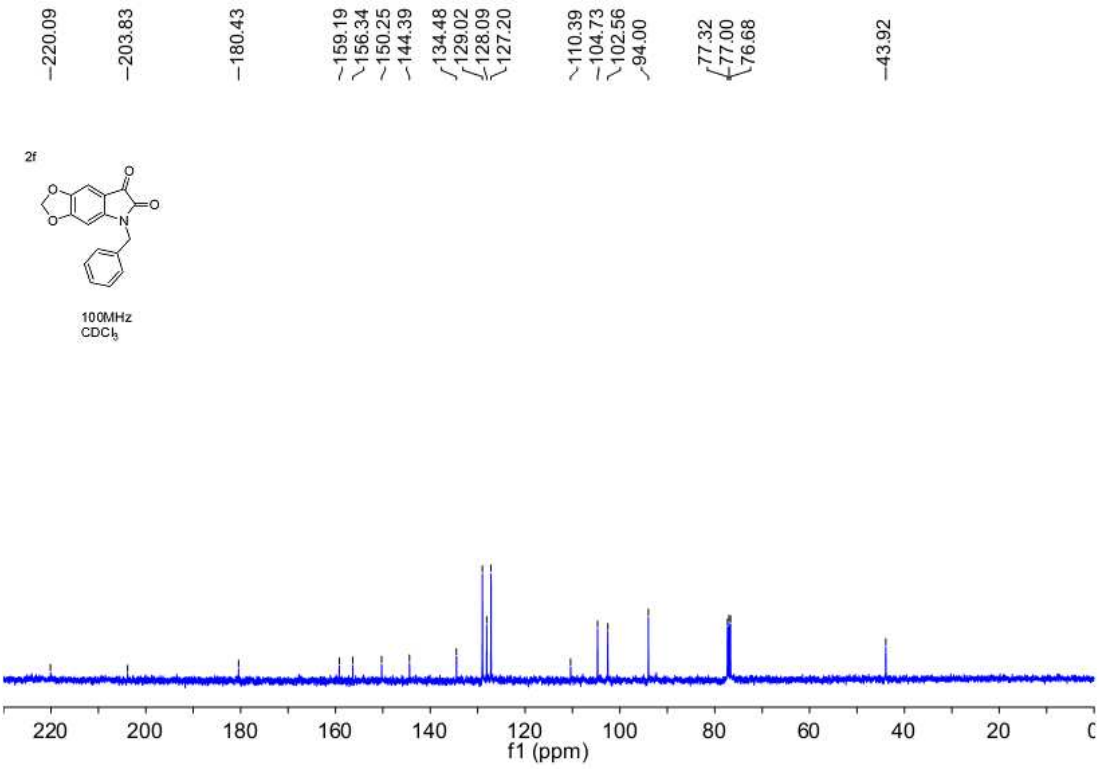

7.015
6.443
6.079
3.190
0.000
2d
400MHz
CDCl3
1.00
1.14
2.47
3.34
0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

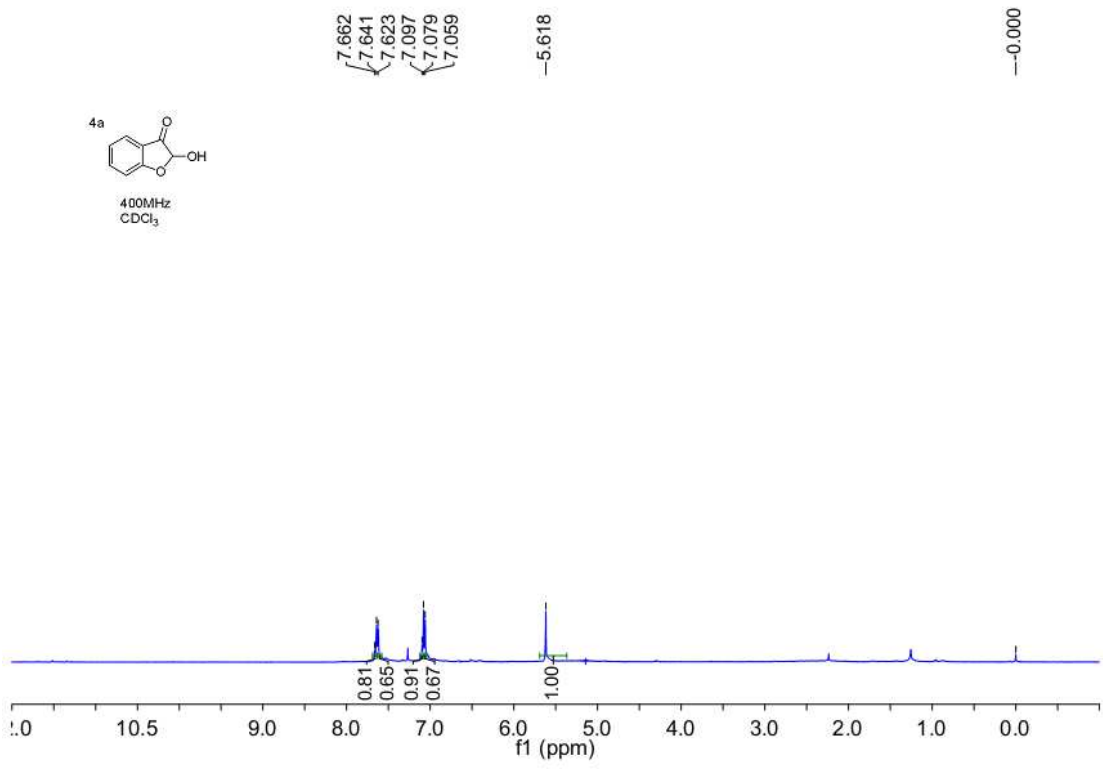

180.66
159.16
156.57
151.13
144.35
110.16
104.84
102.63
92.99
77.32
77.00
76.68
26.25
2d
100MHz
CDCl3
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

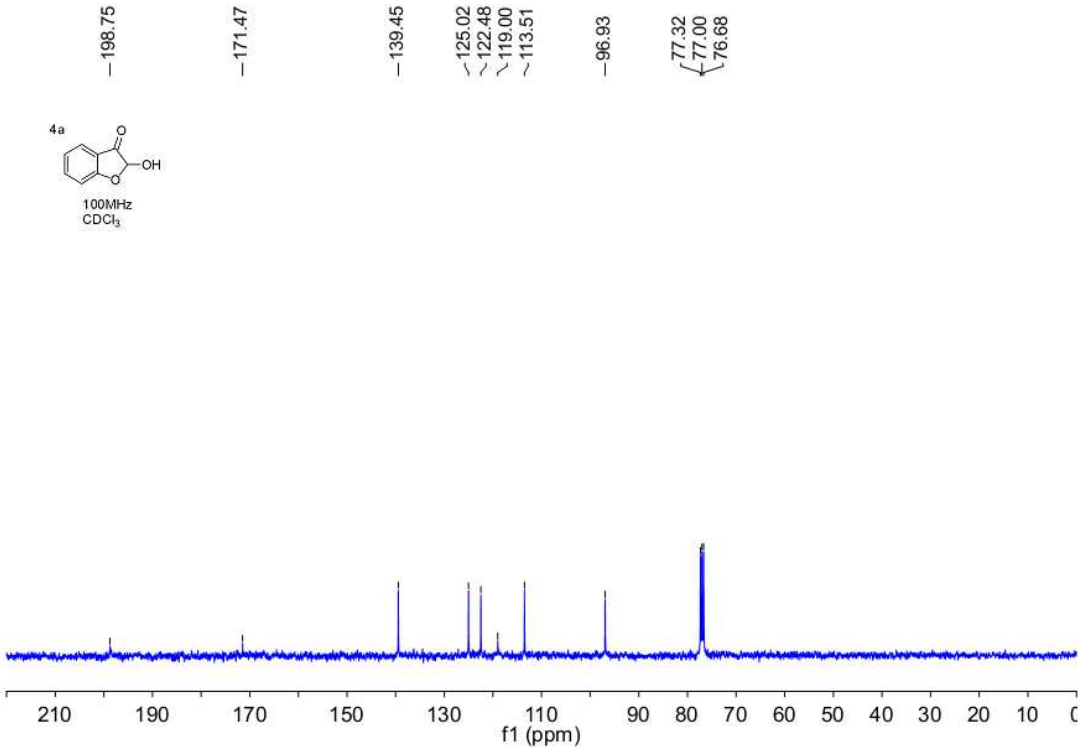

7.890
7.782
7.761
7.357
7.352
7.340
7.314
7.290
6.582
6.561
4.921
0.000
2e
400MHz
CDCl3
1.00
1.06
4.81
0.98
2.01
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

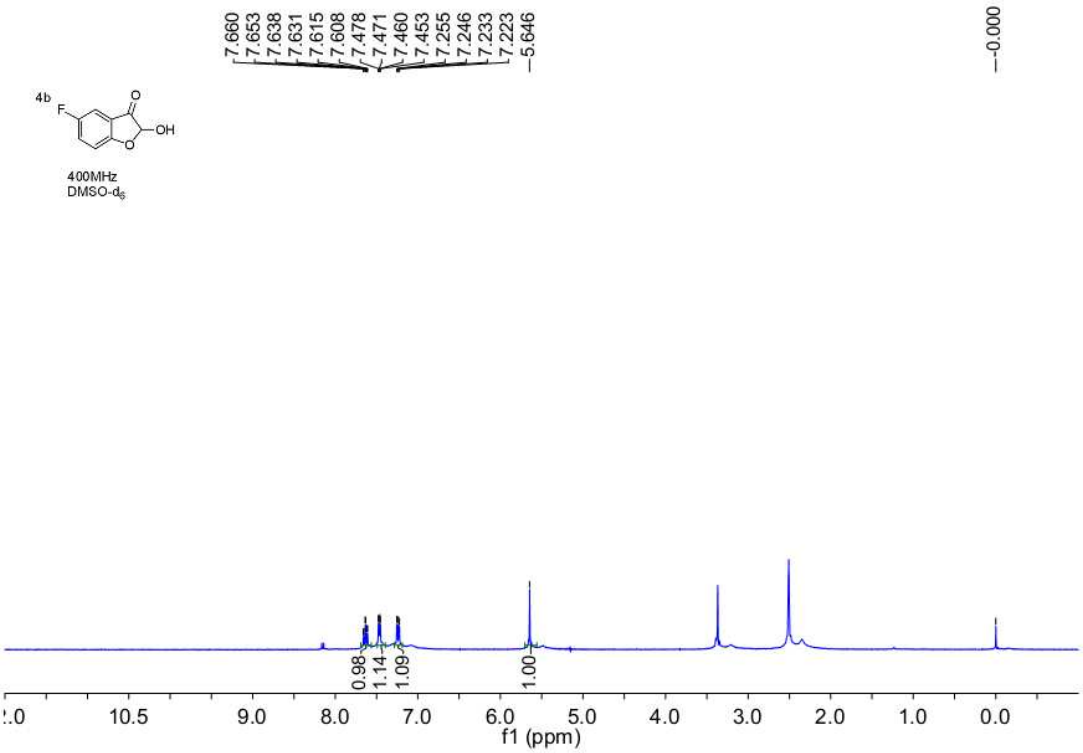

181.84
157.18
149.92
146.30
133.96
133.80
133.77
129.11
128.31
127.35
119.14
113.12
86.20
77.32
77.00
76.68
44.08
2e
100MHz
CDCl3
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

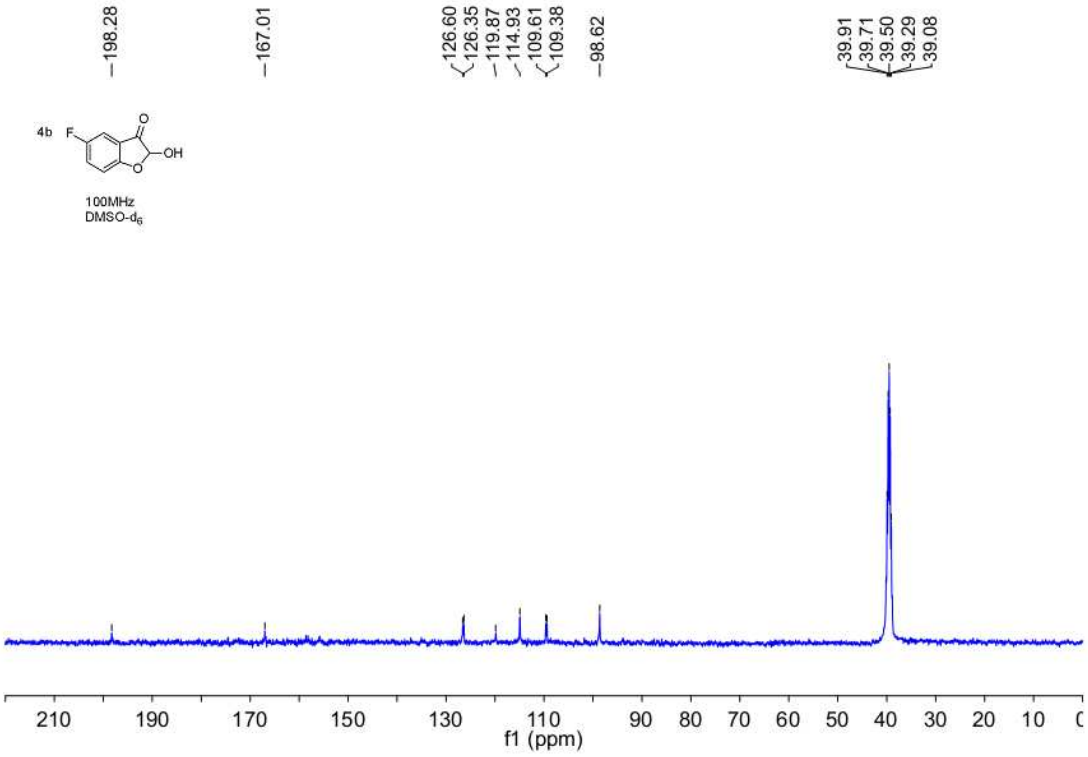

7.350
7.336
7.316
7.310
7.301
7.292
7.272
6.996
6.286
6.007
4.858
0.000
2f
400MHz
CDCl3
5.34
1.00
0.98
2.09
2.07
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

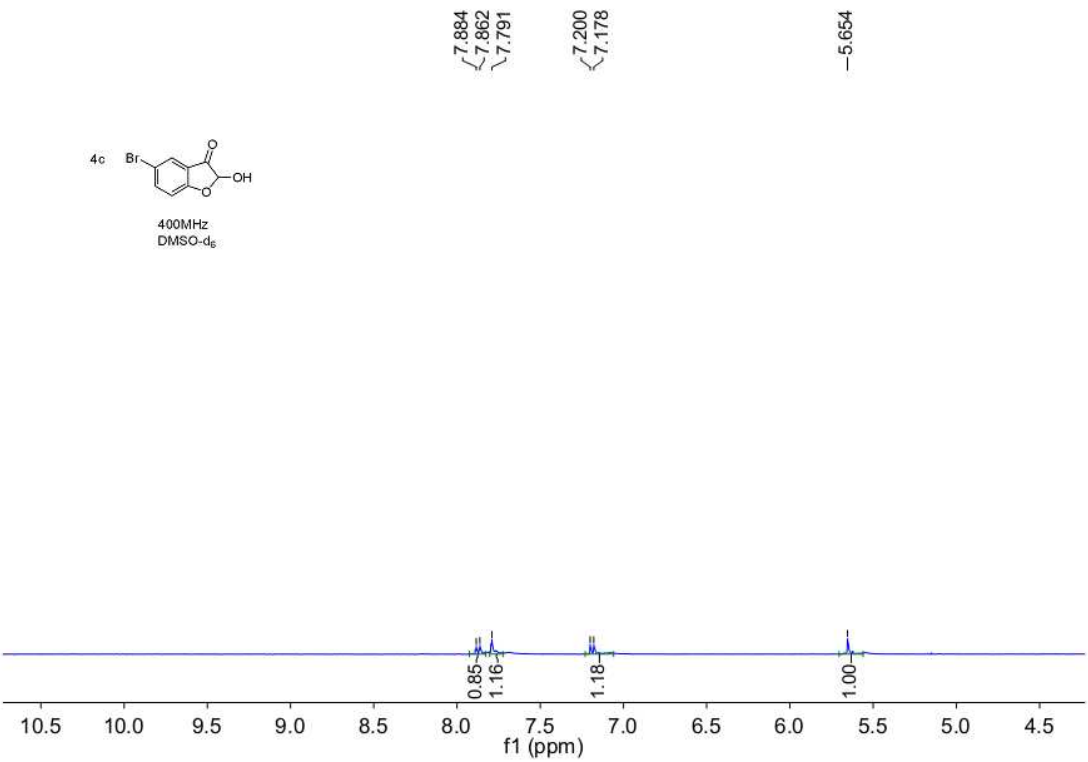

220.09
203.83
180.43
159.19
156.34
150.25
144.39
134.48
129.02
128.09
127.20
110.39
104.73
102.56
94.00
77.32
77.00
76.68
43.92
2f
100MHz
CDCl3
220
200
180
160
140
120
100
80
60
40
20
f1 (ppm)

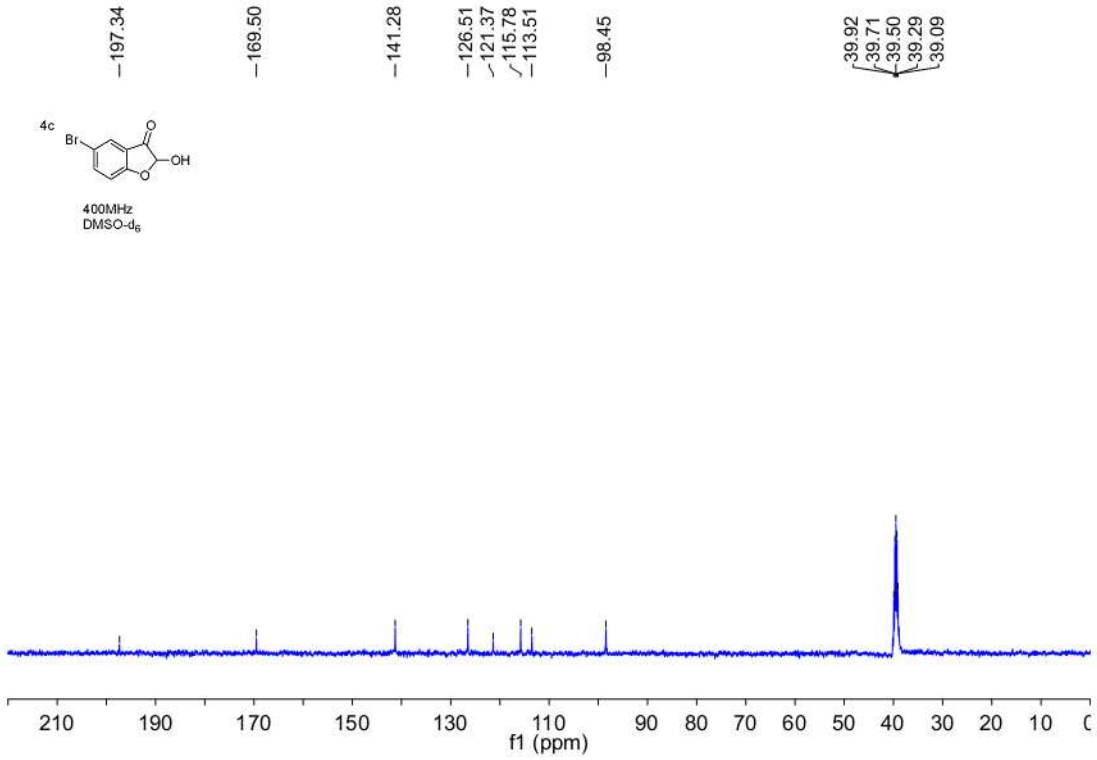

7.662
7.641
7.623
7.097
7.079
7.059
5.618
0.000
4a
OH
400MHz
CDCl3
0.81
0.65
0.91
0.67
1.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

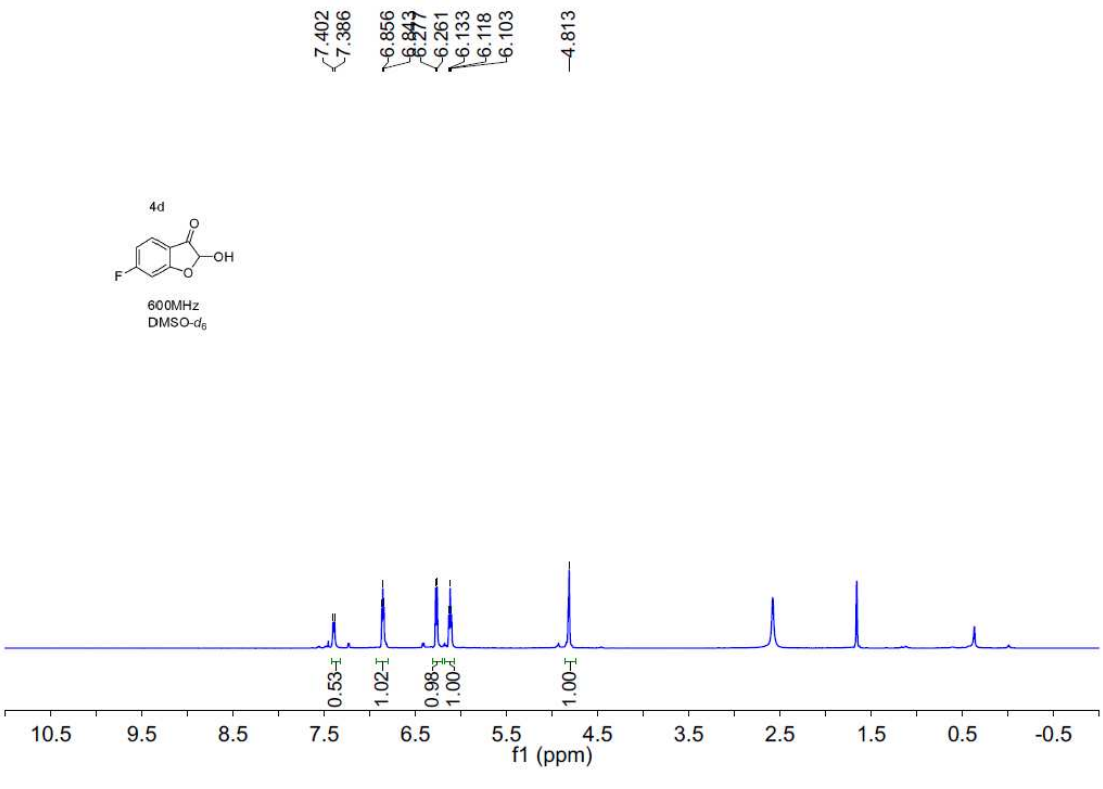

198.75
171.47
139.45
125.02
122.48
119.00
113.51
96.93
77.32
77.00
76.68
4a
OH
100MHz
CDCl3
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

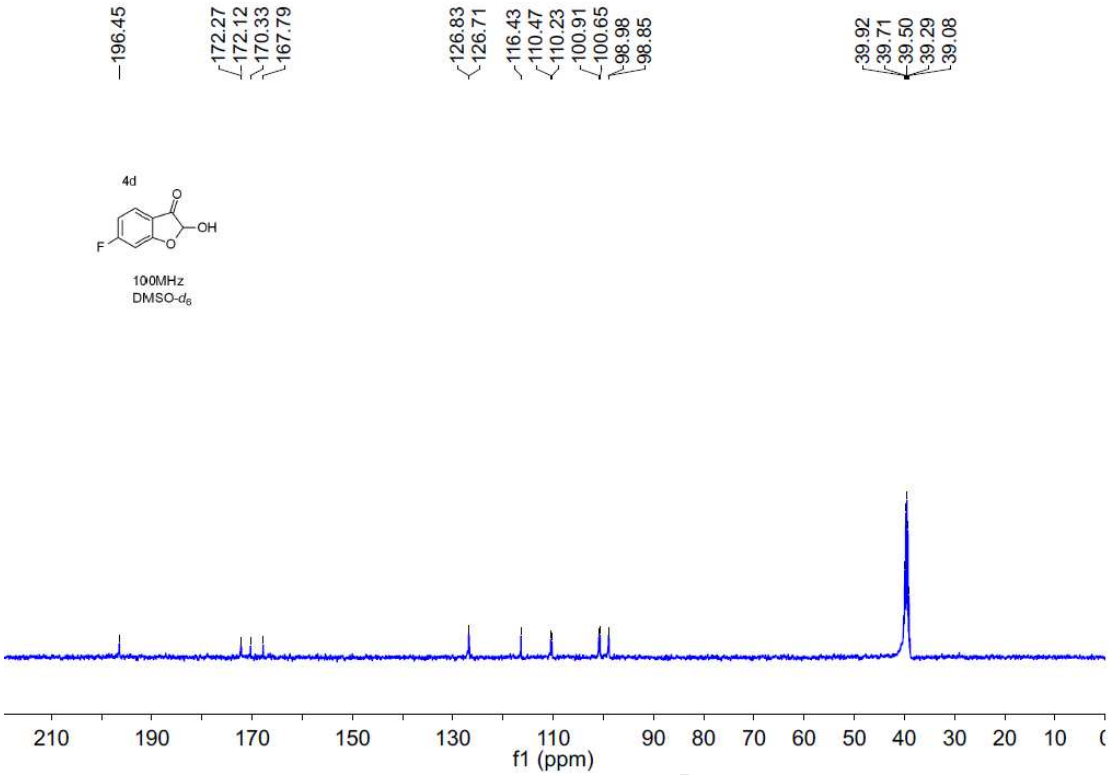

7.660
7.653
7.638
7.631
7.615
7.608
7.478
7.471
7.460
7.453
7.255
7.246
7.233
7.223
5.646
0.000
4b
F
OH
400MHz
DMSO-d6
0.98
1.14
1.09
1.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

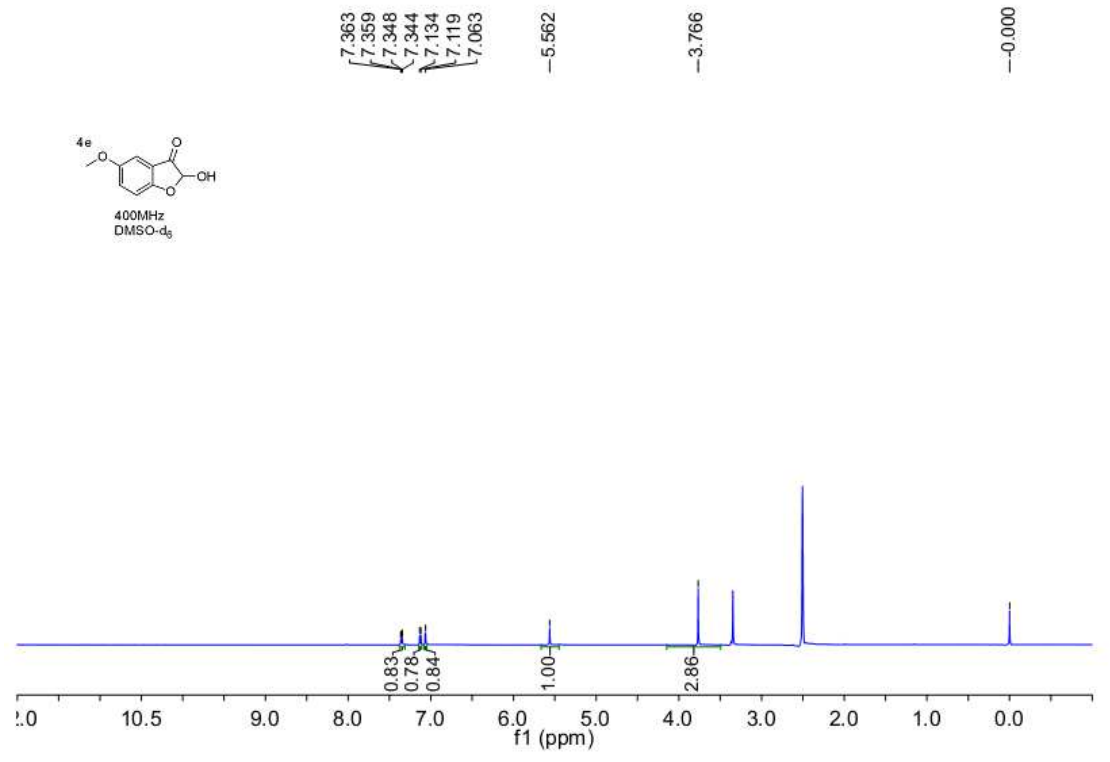

198.28
167.01
126.60
126.35
119.87
114.93
109.61
109.38
98.62
39.91
39.71
39.50
39.29
39.08
4b
F
O
OH
100MHz
DMSO-d6
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

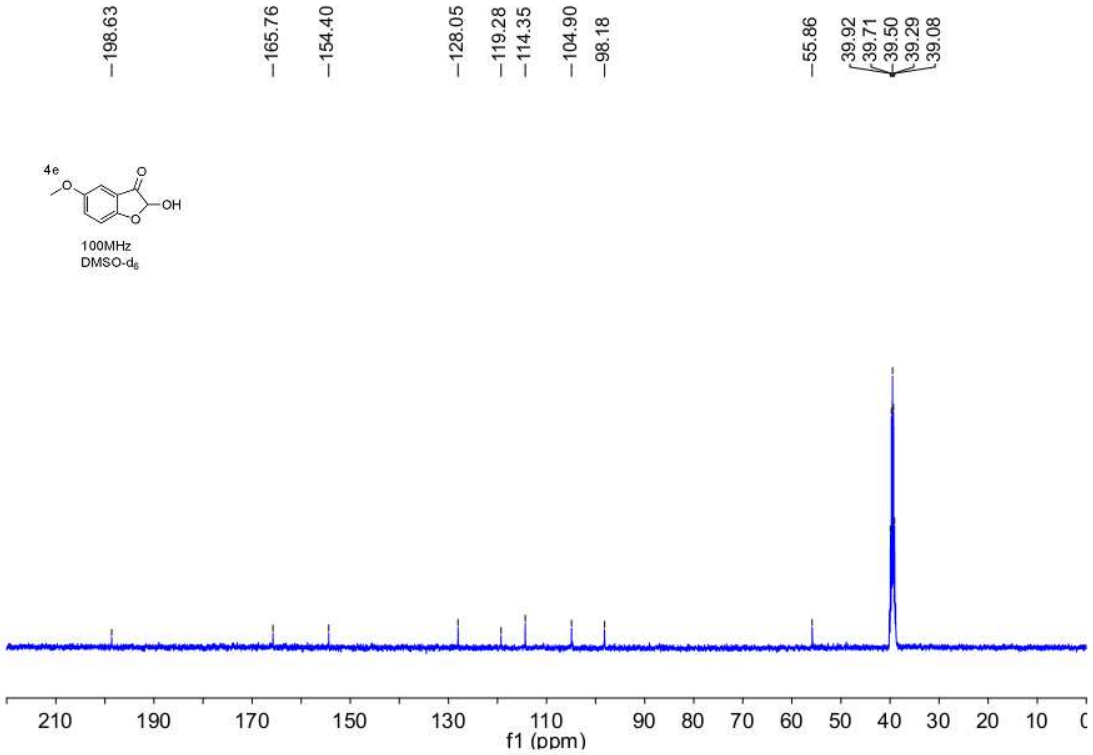

7.884
7.862
7.791
7.200
7.178
5.654
4c
Br
O
OH
400MHz
DMSO-d6
0.85
1.16
1.18
1.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
f1 (ppm)

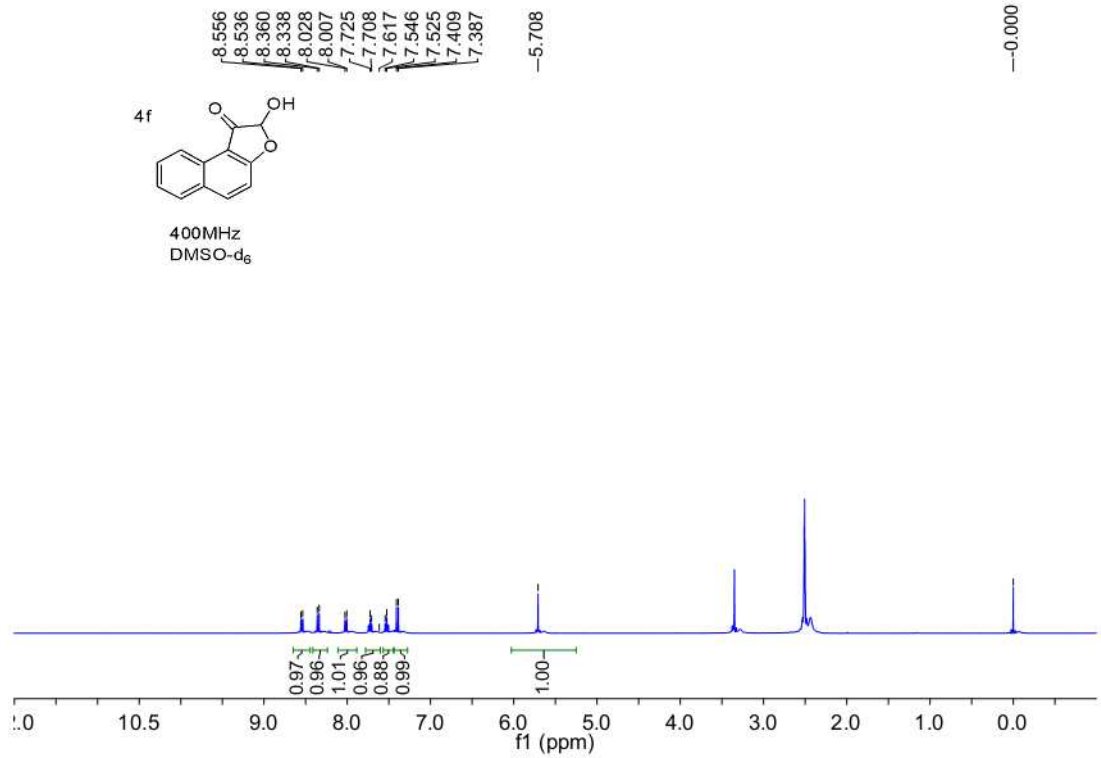

197.34
169.50
141.28
126.51
121.37
115.78
113.51
98.45
39.92
39.71
39.50
39.29
39.09
4c
Br
O
OH
400MHz
DMSO-d6
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)

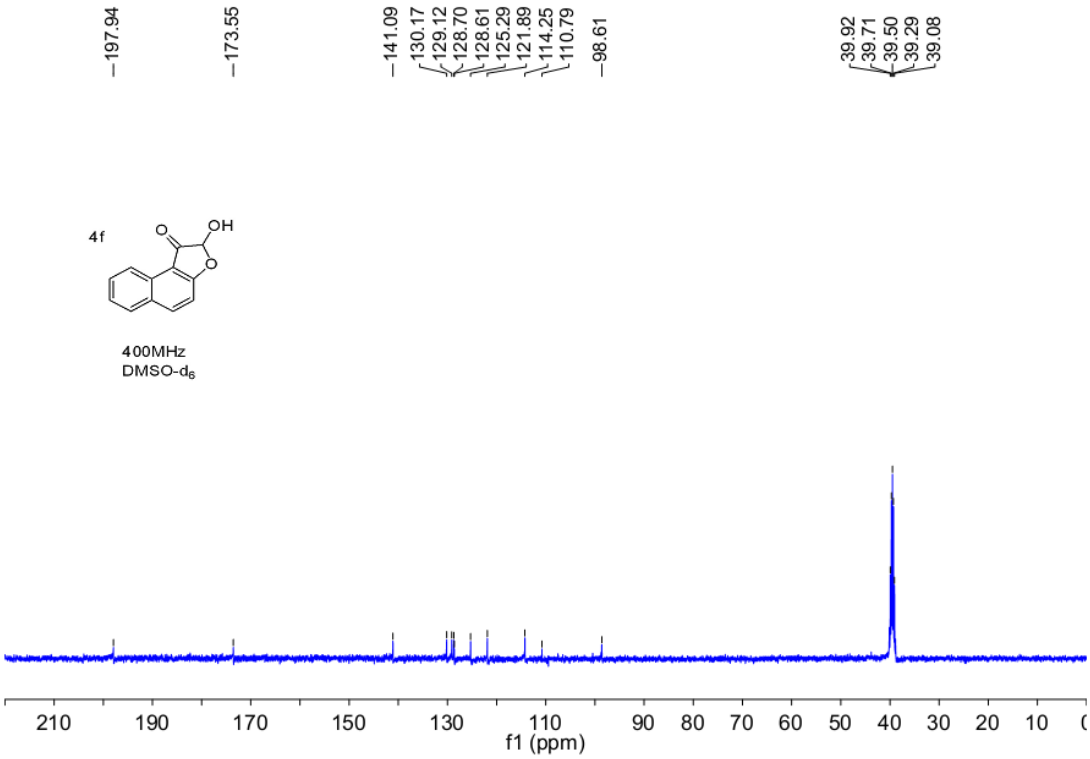

7.402
7.386
6.856
6.261
6.133
6.118
6.103
4.813
4d
O
OH
F
600MHz
DMSO-d6
0.53
1.02
0.98
1.00
1.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

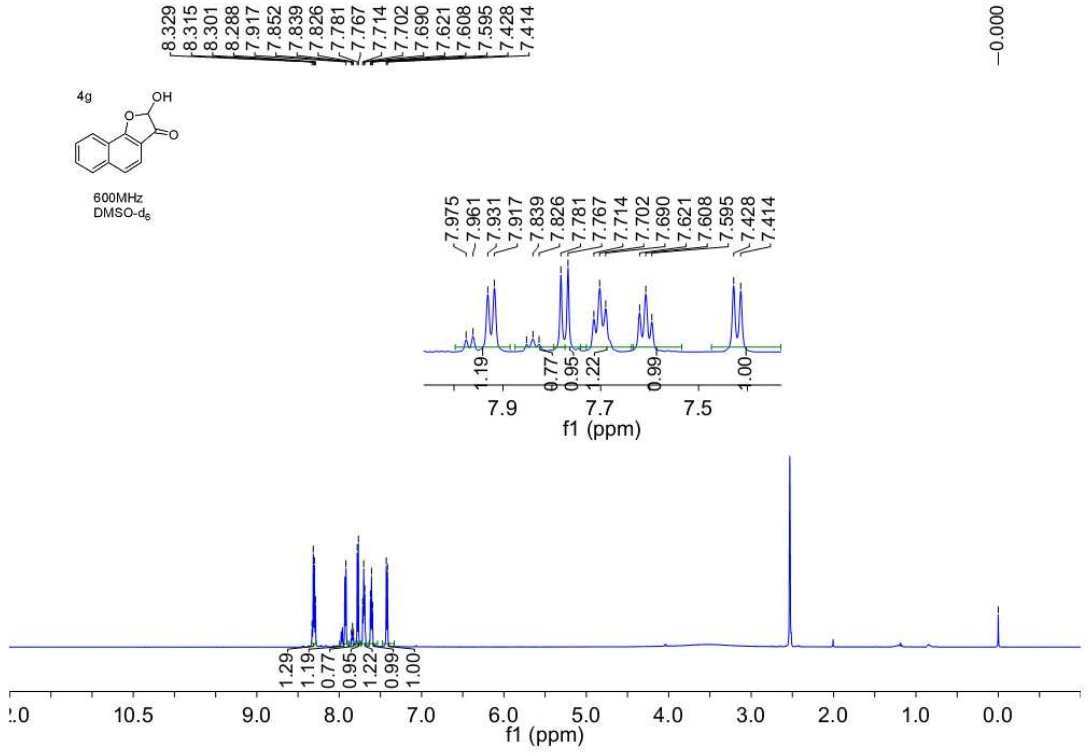

196.45
172.27
172.12
170.33
167.79
126.83
126.71
116.43
110.47
110.23
100.91
100.65
98.98
98.85
39.92
39.71
39.50
39.29
39.08
4d
OH
F
O
100MHz
DMSO-d_6
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.363
7.359
7.348
7.344
7.134
7.119
7.063
5.562
3.766
0.000
4e
OH
O
400MHz
DMSO-d_6
0.83
0.78
0.84
1.00
2.86
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


198.63
165.76
154.40
128.05
119.28
114.35
104.90
98.18
55.86
39.92
39.71
39.50
39.29
39.08
4e
OH
100MHz
DMSO-d6
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.556
8.536
8.360
8.338
8.028
8.007
7.725
7.708
7.617
7.546
7.525
7.409
7.387
5.708
0.000
4f
OH
400MHz
DMSO-d6
0.97
0.96
1.01
0.96
0.88
0.99
1.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


197.94
173.55
141.09
130.17
129.12
128.70
128.61
125.29
121.89
114.25
110.79
98.61
39.92
39.71
39.50
39.29
39.08
4f
OH
O
O
400MHz
DMSO-d6
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.329
8.315
8.301
8.288
7.917
7.852
7.839
7.826
7.781
7.767
7.714
7.702
7.690
7.621
7.608
7.595
7.428
7.414
0.000
4g
OH
O
O
600MHz
DMSO-d6
7.975
7.961
7.931
7.917
7.839
7.826
7.781
7.767
7.714
7.702
7.690
7.621
7.608
7.595
7.428
7.414
1.19
0.77
0.95
1.22
0.99
1.00
7.9
7.7
7.5
f1 (ppm)
1.29
1.19
0.77
0.95
1.22
0.99
1.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)