Supporting Information

Co/Mn-Mediated Oxygenative Cross-Coupling of Indoles with *β*-Keto Esters via Dioxygen Activation: An Efficient Access to Ketonization-Olefination of Indoles

Wenliang Wu, Jing Xu, Shijun Huang and Weiping Su*

State Key Laboratory of Structural Chemistry
Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences
Fuzhou, Fujian 350002 (China)
E-mail: wpsu@fjirsm.ac.cn

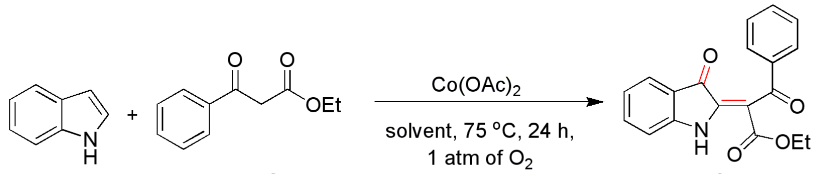
Table of Contents

Contents

General

All reactions were carried out under dry O_2 with dry solvents under anhydrous conditions. $Co(OAc)_2\cdot 4H_2O$ was purchased from Alfa Aesar and converted to the anhydrous salt by drying at 80 °C/1 mmHg for 60 h. Ethyl 3-cyano-benzoyl-acetate,[1] Methyl benzoylacetate,[2] ethyl 3-(naphthalen-3-yl)-3-oxopropanoate[1] **2b,** isopropyl benzoylacetate[2] **2c** , benzyl benzoylacetate[3] and Deuterioindoles[4] were prepared according to the reported procedures. All other reagents were purchased from TCI, Sigma-Aldrich, Alfa Aesar, Acros, and Meryer and used without further purification. DMSO and DMF were distilled from CaH_2 under nitrogen and stored under nitrogen. ^{1}H NMR(400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (377 MHz) spectra were recorded in $CDCl_3$ solutions using a Burker AVANCE 400 spectrometer. Single-crystal X-ray diffraction data were collected on Rigaku Mercury CCD with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) in the ω scanning mode at room temperature. The structure were solved by direct methods and refined by full-matrix least squares on F^2 with the *SHELXTL-97* program. CCDC reference number 763658. Elemental analyses were performed on a Vario EL III elemental analyzer.

Table S1 Screening Results for Co/Mn-Mediated Oxidative Coupling of Indole with Ethyl Benzoylacetate[a]



Entry	**2a** (equiv)	additive (equiv)	acid (equiv)	solvent	Yield (%)[b]
1	1	—	—	DMF	14
2[c]	1	—	—	DMF	<5
3	1	—	—	DMSO	10
4[d]	1	—	—	DMF	0
5[e]	1	—	—	DMF	0
6[d]	1	$Mn(OAc)_2$ (1.0)	—	DMF	<5
7	5	—	—	DMF	13
8	1	—	PivOH (20)	DMF	15
9	5	—	PivOH (20)	DMF	26
10	5	—	PivOH(10)	DMF	17
11	5	—	PivOH (30)	DMF	33
12	5	—	PivOH (40)	DMF	32
13	3	—	PivOH (30)	DMF	18
14	4	—	PivOH (30)	DMF	24
15	6	—	PivOH (30)	DMF	28
16	5	—	AcOH (30)	DMF	23
17	5	—	EtCOOH (30)	DMF	25
18	5	$Mn(OAc)_2$ (0.10)	PivOH (30)	DMF	41
19	5	$Mn(OAc)_2$ (0.25)	PivOH (30)	DMF	52
20	5	$Mn(OAc)_2$ (0.50)	PivOH (30)	DMF	44
21	5	$Mn(OAc)_2$ (0.25)	PivOH (30)	5% DMSO-DMF	58
22	5	$Mn(OAc)_2$ (0.25)	PivOH (30)	10% DMSO-DMF	63
23	5	$Mn(OAc)_2$ (0.25)	PivOH(30)	20% DMSO-DMF	57
24	5	$Mn(OAc)_2$ (0.25)	PivOH (30)	30% DMSO-DMF	51
25	5	$Mn(OAc)_2$ (0.25), NHPI (0.15)	PivOH (30)	10% DMSO-DMF	70
26	5	$Mn(OAc)_2$ (0.25), NHPI (0.30)	PivOH (30)	10% DMSO-DMF	65
27	5	$Mn(OAc)_2$ (0.25), NHPI (0.50)	PivOH (30)	10% DMSO-DMF	63

[a] 0.125 mmol scale, $Co(OAc)_2$ (1.0 equiv), DMF (1 mL, 0.125 M), 1 atm of O_2. [b] Isolated yields. [c] $Co(OAc)_2$ (0.15 equiv). [d] In the absence of $Co(OAc)_2$. [e] N_2 atmosphere.

General procedure

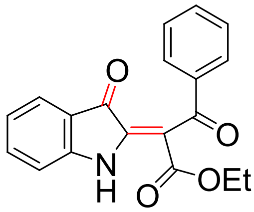
In a glove box, a 30 mL of Schlenk tube equipped with a stir bar was charged with indole **1**, $Co(OAc)_2$ (1 equiv), $Mn(OAc)_2$ (0.25 equiv), NHPI (0.15 equiv), pivalic acid (30 equiv), DMSO (0.1 mL), and DMF (1 mL, 0.125 M). The tube was fitted with a rubber septum and removed out of the glove box. Then, the tube was evacuated and refilled with O_2 for three times. Subsequently, ethyl benzoylacetate **2a** (5 equiv) was added to the Schlenk tube through the rubber septum using syringes, and then the septum was replaced by a Teflon screwcap under an oxygen flow. The reaction mixture was stirred at 75 °C for 24 h. Upon completion, the reaction mixture was diluted with 10 mL of ethyl ether, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the ethyl ether (30 mL). The filtrate was washed with water (3×15 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product **3a**.

Experimental data

Ethyl 3-(naphthalen-3-yl)-3-oxopropanoate 2b, was prepared according to the reported procedures[1], afforded an oil (65% yield). ^{1}H NMR [shows a 18:82 enol/ketone ratio] (400 MHz, $CDCl_3$): δ [keto form] 8.44 (s, 1 H), 8.01 (d, J = 8.6 Hz, 1 H), 7.96 (d, J = 8.0 Hz, 1 H), 7.90 – 7.83 (m, 2 H), 7.63 – 7.51 (m, 2 H), 4.23 (q, J = 7.1 Hz, 2 H), 4.12 (s, 2 H), 1.26 (t, J = 7.1 Hz, 3 H); [enol form] 12.70 (s, 1 H), 8.35 (s, 1 H), 7.77 – 7.75 (m, 1 H), 5.81 (s, 1 H), 4.29 (q, J = 7.1 Hz, 2 H), 1.35 (t, J = 7.1 Hz, 3 H).

Isopropyl benzoylacetate 2c, was prepared according to the reported procedures[2], afforded an oil (35% yield). ^{1}H NMR [shows a 16:84 enol/ketone ratio] (400 MHz, $CDCl_3$): *δ* [keto form] 7.93 (d, *J* = 7.4 Hz, 2 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.7 Hz, 2 H), 5.10 – 5.04 (m, 1 H), 3.95 (s, 2 H), 1.22 (d, *J* = 6.2 Hz, 6 H); [enol form] 12.65 (s, 1 H), 7.77 (d, *J* = 7.6 Hz, 2 H), 7.43 – 7.40 (m, 3 H), 5.63 (s, 1 H), 5.16 – 5.13 (m, 1 H), 1.31 (d, *J* = 6.3 Hz, 6 H).

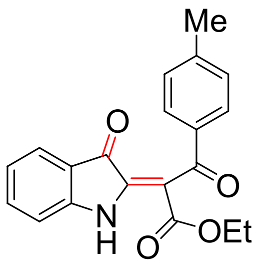
(Z)-ethyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-phenylpropanoate



3a

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.28 (s, 1 H), 7.96 (d, *J* = 7.8 Hz, 2 H), 7.58 – 7.42 (m, 5 H), 6.96 – 6.93 (m, 2 H), 4.22 (q, *J* = 7.1 Hz, 2 H), 1.16 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ, 192.3, 186.1, 166.8, 152.6, 142.9, 137.6, 137.3, 133.4, 128.8, 128.5, 125.6, 122.0, 119.8, 111.9, 107.8, 61.6, 14.0. Anal. Calcd. for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36; Found: C, 70.97; H, 4.50; N, 4.31.

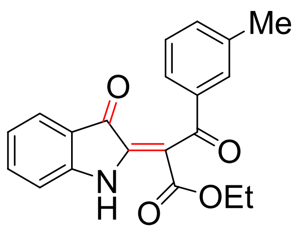
(Z)-ethyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-p-tolylpropanoate



3b

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (69% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1 H), 7.87 (d, J = 8.2 Hz, 2 H), 7.52 – 7.45 (m, 2 H), 7.23 (d, J = 8.1 Hz, 2 H), 6.95 – 6.91 (m, 2 H), 4.21 (q, J = 7.1 Hz, 2 H), 2.39 (s, 3 H), 1.16 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.9, 186.1, 166.9, 152.5, 144.3, 142.8, 137.5, 134.9, 129.3, 128.9, 125.6, 121.9, 119.9, 111.9, 108.1, 61.6, 21.8, 14.0. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.31; H, 4.95; N, 4.05.

(Z)-ethyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-m-tolylpropanoate

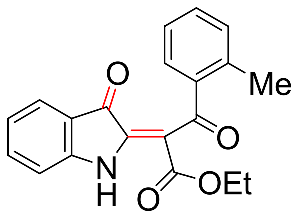


3c

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (68% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1 H), 7.81 (s, 1 H), 7.73 (d, J = 7.6 Hz, 1 H), 7.53 – 7.46 (m, 2 H), 7.38 – 7.29 (m, 2 H), 6.96 – 6.92 (m, 2 H), 4.22 (q, J = 7.1 Hz, 2 H), 2.39 (s, 3 H), 1.16 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

192.4, 186.1, 166.8, 152.6, 142.8, 138.4, 137.5, 137.3, 134.3, 129.2, 128.4, 126.2, 125.6, 122.0, 119.9, 111.9, 108.1, 61.6, 21.4, 14.0. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.52; H, 4.90; N, 4.10.

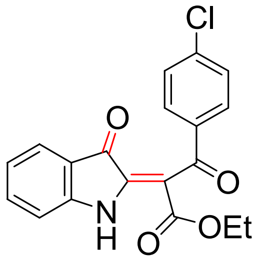
(Z/E)-ethyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-o-tolylpropanoate



3d

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (61% yield). ^{1}H NMR [**Z/E** = 4:1] (400 MHz, $CDCl_3$): *δ* **Z**: 9.28 (s, 1 H), 7.67 – 6.91 (m, 8 H), 4.24 (q, *J* = 7.1 Hz, 2 H), 2.78 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H). **E**: 10.59 (s, 1 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 2.36 (s, 3 H), 1.06 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ **Z**: 193.8, 186.3, 167.0, 152.6, 142.4, 140.8, 137.5, 134.3, 132.0, 132.0, 130.7, 125.5, 125.2, 121.9, 119.9, 111.9, 110.1, 61.6, 21.6, 14.0. **E**: 197.3, 187.0, 167.9, 152.1, 139.5, 137.5, 136.6, 135.3, 132.7, 129.9, 125.9, 125.1, 123.6, 123.0, 119.7, 112.4, 109.0, 67.7, 19.3, 13.5. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.49; H, 5.10; N, 4.15.

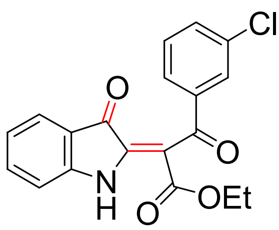
(Z)-ethyl 3-(4-chlorophenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate



3e

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (66% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1 H), 7.90 (d, J = 8.6 Hz, 2 H), 7.53 – 7.47 (m, 2 H), 7.42 (d, J = 8.6 Hz, 2 H), 6.97 – 6.94 (m, 2 H), 4.22 (q, J = 7.1 Hz, 2 H), 1.17 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 186.1, 166.5, 152.5, 143.1, 139.8, 137.7, 135.7, 130.2, 128.9, 125.7, 122.2, 119.8, 112.0, 107.2, 61.7, 14.0. Anal. Calcd. for $C_{19}H_{14}ClNO_4$: C, 64.14; H, 3.97; N, 3.94; Found: C, 64.15; H, 3.87; N, 3.87.

(Z)-ethyl 3-(3-chlorophenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate

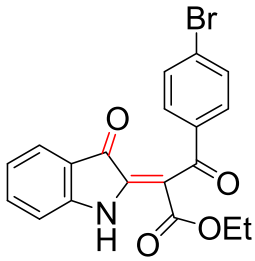


3f

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (65% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.27 (s, 1 H), 7.93 (t, J = 1.8 Hz, 1 H), 7.84 (dt, J = 7.8 Hz, J = 1.2 Hz,1 H), 7.55 – 7.49 (m, 3 H), 7.39 (t, J = 7.8 Hz, 1 H), 6.99 – 6.95 (m, 2

H), 4.24 (q, J = 7.1 Hz, 2 H), 1.18 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 186.1, 166.5, 152.5, 143.2, 138.9, 137.8, 134.9, 133.3, 129.9, 128.7, 126.9, 125.8, 122.2, 119.7, 111.9, 107.0, 61.8, 14.0 .Anal. Calcd. for $C_{19}H_{14}ClNO_4$: C, 64.14; H, 3.97; N, 3.94; Found: C, 64.15; H, 4.01; N, 3.91.

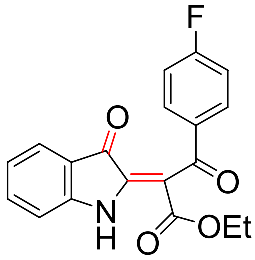
(Z)-ethyl 3-(4-bromophenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate



3g

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (65% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1 H), 7.83 (d, J = 8.8 Hz, 2 H), 7.58 (d, J = 8.6 Hz, 2 H), 7.53 – 7.47 (m, 2 H), 6.97 – 6.93 (m, 2 H), 4.21 (q, J = 7.1 Hz, 2 H), 1.16 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 186.1, 166.5, 152.5, 143.1, 137.7, 136.1, 131.9, 130.2, 128.6, 125.7, 122.2, 119.8, 112.0, 107.1, 61.7, 14.0. Anal. Calcd. for $C_{19}H_{14}BrNO_4$: C, 57.02; H, 3.53; N, 3.50; Found: C, 56.61; H, 3.54; N, 3.33.

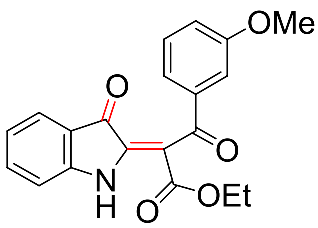
(Z)-ethyl 3-(4-fluorophenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate



3h

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (68% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (s, 1 H), 8.00 – 7.97 (m, 2 H), 7.52 – 7.46 (m, 2 H), 7.12 – 7.08 (m, 2 H), 6.95 – 6.92 (m, 2 H), 4.20 (q, J = 7.1 Hz, 2 H), 1.15 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.1, 186.1, 166.6, 165.9 (d, J = 254.8 Hz), 152.6, 142.9, 137.7, 133.9 (d, J = 2.8 Hz), 131.4 (d, J = 9.5 Hz), 125.6, 122.1, 119.8, 115.7 (d, J = 21.9 Hz), 112.0, 107.4, 61.6, 14.0; ^{19}F NMR (377 MHz, $CDCl_3$): δ -104.79. Anal. Calcd. for $C_{19}H_{14}FNO_4$: C, 67.25; H, 4.16; N, 4.13; Found: C, 66.68; H, 4.73; N, 4.01.

(Z)-ethyl 3-(3-methoxyphenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate

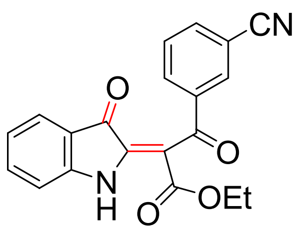


3i

Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (67% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.27 (s, 1 H), 7.58 (t, J = 2.0 Hz, 1 H), 7.52 (d, J = 7.7 Hz, 1 H), 7.50 –

7.46 (m, 2 H), 7.32 (t, *J* = 7.9 Hz, 1 H), 7.11 (dd, *J* = 8.3 Hz, *J* = 2.7 Hz, 1 H), 6.96 – 6.93 (m, 2 H), 4.22 (q, *J* = 7.1 Hz, 2 H), 3.86 (s, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 186.0, 166.8, 159.9, 152.5, 142.9, 138.7, 137.5, 129.5, 125.6, 122.0, 121.8, 120.1, 120.0, 112.6, 111.9, 107.9, 61.6, 55.4, 14.0; Anal. Calcd. for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99; Found: C, 67.87; H, 5.09; N, 3.65.

(Z)-ethyl 3-(3-cyanophenyl)-3-oxo-2-(3-oxoindolin-2-ylidene)propanoate

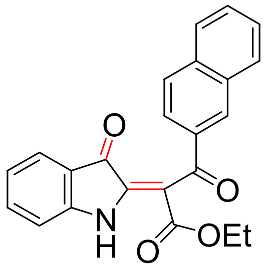


3j

Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (62% yield). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.30 (s, 1 H), 8.22 – 8.20 (m, 2 H), 7.83 (d, *J* = 7.7 Hz, 1 H), 7.60 (t, *J* = 7.7 Hz, 1 H), 7.53 – 7.50 (m, 2 H), 6.99 – 6.96 (m, 2 H), 4.23 (q, *J* = 7.1 Hz, 2 H), 1.17 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 186.2, 166.2, 152.6, 143.5, 138.2, 138.0, 136.1, 132.6, 132.4, 129.7, 125.8, 122.4, 119.6, 119.6, 118.1, 113.1, 112.1, 106.1, 61.8, 14.0 .Anal. Calcd. for $C_{20}H_{14}NO_4$: C, 69.36; H, 4.07; N, 8.09; Found: C, 68.96; H, 4.39; N, 7.85.

(Z)-ethyl 3-(naphthalen-2-yl)-3-oxo-2-(3-

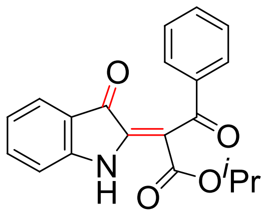
oxoindolin-2-ylidene)propanoate



3k

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (64% yield). [1]H NMR (400 MHz, $CDCl_3$): δ 9.35 (s, 1 H), 8.39 (s, 1 H), 8.14 (dd, J = 8.6 Hz, J = 1.6 Hz, 1 H), 7.93 – 7.86 (m, 3 H), 7.60 – 7.47 (m, 4 H), 6.98 – 6.92 (m, 2 H), 4.23 (q, J = 7.1 Hz, 2 H), 1.15 (t, J = 7.1 Hz, 3 H); [13]C NMR (100 MHz, $CDCl_3$): δ 192.2, 186.1, 166.9, 152.5, 143.1, 137.6, 136.0, 134.9, 132.6, 130.8, 129.6, 128.6, 128.5, 127.9, 126.6, 125.7, 124.3, 122.0, 119.9, 111.9, 107.9, 61.7, 14.0. Anal. Calcd. for $C_{23}H_{17}NO_4$: C, 74.38; H, 4.61; N, 3.77; Found: C, 74.20; H, 4.71; N, 3.73.

(Z)-propyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-phenylpropanoate

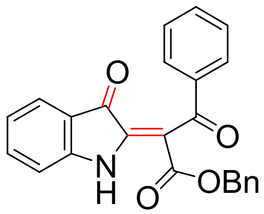


3l

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (61% yield). [1]H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1 H), 7.95 (d, J = 7.8 Hz, 2 H), 7.57 – 7.42 (m, 5 H), 6.96 –

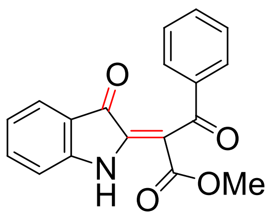
6.93 (m, 2 H), 5.12 (m, 1 H), 1.16 (d, *J* = 6.3 Hz, 6 H), . [13]C NMR (100 MHz, $CDCl_3$): δ 192.2, 186.0, 166.4, 152.5, 142.8, 137.5, 137.4, 133.2, 128.8, 128.5, 125.6, 121.9, 119.9, 111.8, 108.5, 69.5, 21.5. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.55; H, 5.06; N, 4.09.

(Z)-benzyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-phenylpropanoate



3m

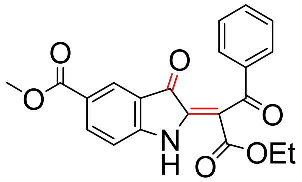
Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (68% yield). [1]H NMR (400 MHz, $CDCl_3$): *δ* 9.30 (s, 1 H), 7.99 (d, *J* = 7.6 Hz, 2 H), 7.61 – 7.44 (m, 5 H), 7.28 – 7.26 (m, 3 H), 7.14 – 7.12 (m, 2 H), 6.99 – 6.94 (m, 2 H), 5.22 (s, 2 H); [13]C NMR (100 MHz, $CDCl_3$): δ 192.1, 186.0, 166.5, 152.4, 143.2, 137.6, 137.3, 135.4, 133.4, 128.9, 128.6, 128.4, 128.1, 127.3, 125.7, 122.1, 119.8, 111.9, 107.4, 66.8. Anal. Calcd. for $C_{24}H_{17}NO_4$: C, 75.19; H, 4.47; N, 3.65; Found: C, 75.58; H, 4.55; N, 3.39. **(Z)-methyl 3-oxo-2-(3-oxoindolin-2-ylidene)-3-phenylpropanoate**



3n

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (69% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1 H), 7.98 (d, J = 7.8 Hz, 2 H), 7.59 – 7.43 (m, 5 H), 6.98 – 6.94(m, 2 H), 3.75(s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 186.0, 167.2, 152.5, 143.0, 137.6, 137.2, 133.5, 128.9, 128.6, 125.7, 122.1, 119.9, 111.9, 107.3, 52.6. Anal. Calcd. for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56; Found: C, 70.09; H, 4.25; N, 4.40.

(Z)-methyl 2-(1-(ethoxycarbonyl)-2-oxo-2-phenylethylidene)-3 oxoindoline-5-carboxylate

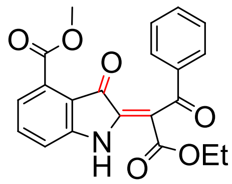


3o

Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (45% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1 H), 8.25 – 8.23 (m, 2 H), 7.98 (d, J = 7.6 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 7.48 (t, J = 7.7 Hz, 2 H), 7.03 (d, J = 8.9 Hz, 1 H), 4.25 (q, J = 7.1 Hz, 2 H), 3.90(s, 3 H), 1.18 (t, J = 7.1 Hz, 3 H),; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6, 185.0, 166.5, 165.8, 155.1, 142.6, 139.0, 137.0, 133.6, 128.8, 128.6, 127.5, 124.2, 119.7, 111.6, 109.7, 61.9, 52.2, 13.9. Anal. Calcd. for $C_{21}H_{17}NO_6$: C, 66.49; H, 4.52; N, 3.69; Found: C, 66.38; H, 4.28; N, 3.62.

(Z)-methyl 2-(1-(ethoxycarbonyl)-2-oxo-2-phenylethylidene)-3-

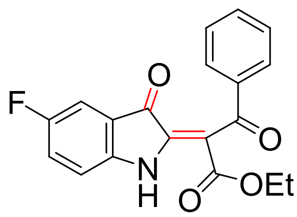
oxoindoline-4-carboxylate



3p

Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (50% yield). [1]H NMR (400 MHz, $CDCl_3$): δ 9.42 (s, 1 H), 7.95 (d, J = 7.6 Hz, 2 H), 7.57 – 7.51 (m, 2 H), 7.44 (d, J = 7.6 Hz, 2 H), 7.26 (d, J = 7.0 Hz, 1 H), 7.07 (d, J = 8.0 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.83(s, 3 H), 1.14 (t, J = 7.1 Hz, 3 H),; [13]C NMR (100 MHz, $CDCl_3$): δ 191.9, 183.1, 166.8, 165.9, 153.0, 142.3, 137.1, 136.8, 133.4, 131.3, 128.9, 128.5, 122.7, 116.9, 114.8, 108.7, 61.7, 52.6, 13.9. Anal. Calcd. for $C_{21}H_{17}NO_6$: C, 66.49; H, 4.52; N, 3.69; Found: C, 66.43; H, 4.61; N, 3.46.

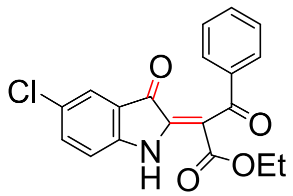
(Z)-ethyl 2-(5-fluoro-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate



3q

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (57% yield). [1]H NMR (400 MHz, $CDCl_3$): δ 9.25 (s, 1 H), 7.96 (d, J = 7.4 Hz, 2 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.25 – 7.19 (m, 2 H), 6.92 (dd, *J* = 8.5 Hz, *J* = 3.6 Hz, 1 H), 4.22 (q, *J* = 7.1 Hz, 2 H), 1.16 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.9, 185.4 (d, *J* = 3.0 Hz), 166.7, 158.2 (d, *J* = 242.8 Hz), 148.8, 143.2, 137.2, 133.5, 128.8, 128.6, 124.6 (d, *J* = 24.9 Hz), 120.5 (d, *J* = 8.1 Hz), 112.7 (d, *J* = 8.1 Hz), 111.7 (d, *J* = 24.2 Hz), 108.7, 61.7, 14.0; ^{19}F NMR (377 MHz, $CDCl_3$): δ -121.1. Anal. Calcd. for $C_{19}H_{14}FNO_4$: C, 67.25; H, 4.16; N, 4.13; Found: C, 66.97; H, 4.37; N, 4.05.

(Z)-ethyl 2-(5-chloro-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate

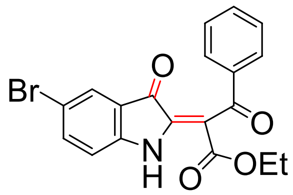


3r

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (56% yield). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.33 (s, 1 H), 7.95 (d, *J* = 7.6 Hz, 2 H), 7.57 (t, *J* = 7.5 Hz, 1 H), 7.47 – 7.42 (m, 4 H), 6.91 (d, *J* = 8.4 Hz, 1 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 1.15 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8, 185.0, 166.6, 150.8, 142.6, 137.1, 137.0, 133.5, 128.8, 128.6, 127.5, 125.2, 120.9, 113.1, 108.9, 61.8, 14.0. Anal. Calcd. for $C_{19}H_{14}ClNO_4$: C, 64.14; H, 3.97; N, 3.94; Found: C, 64.10; H, 3.95; N, 3.67.

(Z)-ethyl 2-(5-bromo-3-oxoindolin-2-ylidene)-3-

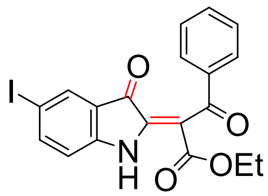
oxo-3-phenylpropanoate



3s

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (60% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (s, 1 H), 7.95 (d, J = 7.4 Hz, 2 H), 7.63 – 7.55 (m, 3 H), 7.45 (t, J = 7.7 Hz, 2 H), 6.87 (d, J = 8.4 Hz, 1 H), , 4.22 (q, J = 7.1 Hz, 2 H), 1.16 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 184.8, 166.6, 151.2, 142.4, 139.8, 137.1, 133.5, 128.8, 128.6, 128.2, 121.4, 114.5, 113.5, 109.0, 61.8, 14.0 Anal. Calcd. for $C_{19}H_{14}BrNO_4$: C, 57.02; H, 3.53; N, 3.50; Found: C, 56.77; H, 3.55; N, 3.49.

(Z)-ethyl 2-(5-iodo-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate

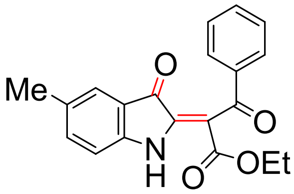


3t

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (51% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (s, 1 H), 7.94 (d, J = 7.8 Hz, 2 H), 7.80 (s, 1 H), 7.75 (dd, J = 8.5

Hz, *J* = 1.8 Hz, 1 H), 7.56 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 7.7 Hz, 2 H), 6.77 (d, *J* = 8.4 Hz, 1 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 1.15 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8, 184.5, 166.6, 151.7, 145.5, 142.0, 137.1, 134.1, 133.5, 128.8, 128.6, 121.9, 113.9, 108.8, 83.7, 61.7, 13.9. Anal. Calcd. for $C_{19}H_{14}INO_4$: C, 51.03; H, 3.16; N, 3.13; Found: C, 50.88; H, 3.01; N, 2.98.

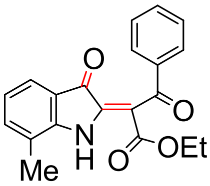
(Z)-ethyl 2-(5-methyl-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate



3u

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.19 (s, 1 H), 7.96 (d, *J* = 7.8 Hz, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.31 – 7.29 (m, 2 H), 6.84 (d, *J* = 8.6 Hz, 1 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 2.27 (s, 3 H),1.16 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 186.2, 166.9, 150.6, 143.4, 138.4, 137.4, 133.3, 131.7, 128.8, 128.5, 125.5, 119.9, 111.6, 107.3, 61.5, 20.6, 14.0. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.56; H, 5.15; N, 4.11.

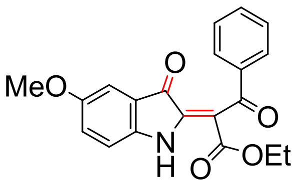
(Z)-ethyl 2-(7-methyl-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate



3v

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (s, 1 H), 7.97 (d, J = 7.8 Hz, 2 H), 7.56 (t, J = 7.4 Hz, 1 H), 7.44 (t, J = 7.7 Hz, 2 H), 7.38 (d, J = 7.6 Hz, 1 H), 7.32 (d, J = 7.4 Hz, 1 H), 6.87 (t, J = 7.5 Hz, 1 H), 4.24 (q, J = 7.1 Hz, 2 H), 2.32 (s, 3 H), 1.18 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 186.4, 167.0, 151.4, 143.2, 138.3, 133.3, 128.8, 128.5, 123.1, 121.9, 120.9, 119.5, 107.9, 61.6, 15.3, 14.0. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found: C, 71.45; H, 5.02; N, 4.15.

(Z)-ethyl 2-(5-methoxy-3-oxoindolin-2-ylidene)-3-oxo-3-phenylpropanoate

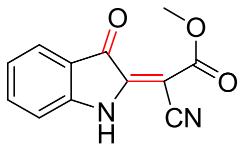


3w

Following the general procedure, using 30% ether in petroleum ether as the eluant afforded a red solid (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.10 (s, 1 H), 7.97 (d, J = 7.4 Hz, 2 H), 7.56 (t, J = 7.4 Hz, 1 H), 7.44 (t, J = 7.6 Hz, 2 H), 7.10 (dd, J = 8.6 Hz, J = 2.6 Hz, 1 H), 7.00 (d, J = 2.6

Hz, 1 H), 6.87 (d, J = 8.6 Hz, 1 H), 4.22 (q, J = 7.1 Hz, 2 H), 3.73(s, 3 H), 1.16 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 186.2, 166.8, 155.3, 147.2, 143.7, 137.4, 133.3, 128.8, 128.5, 125.8, 120.2, 112.8, 107.9, 107.6, 61.5, 55.9, 14.0. Anal. Calcd. for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99; Found: C, 67.82; H, 4.84; N, 3.73.

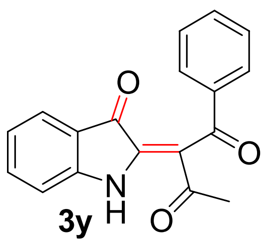
(E)-methyl 2-cyano-2-(3-oxoindolin-2-ylidene)acetate



3x

Following the general procedure, using 40% ether in petroleum ether as the eluant afforded a red solid (50% yield). ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 11.37 (s, 1 H), 7.67 – 7.61 (m, 2 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.13 (t, J = 7.4 Hz, 1 H), 3.85 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1, 165.4, 151.9, 149.9, 138.4, 125.8, 123.9, 119.5, 115.0, 114.3, 75.8, 53.1. Anal. Calcd. for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28; Found: C, 63.07; H, 3.62; N, 12.11.

(E)-2-(1,3-dioxo-1-phenylbutan-2-ylidene)indolin-3-one

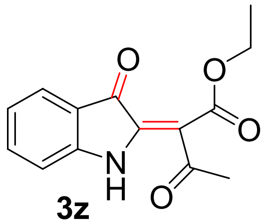


3y

Following the general procedure, but in the absence of $Mn(OAc)_2$. Using 20% ether in petroleum ether as the eluant afforded a red solid (45%

yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.34 (s, 1 H), 8.01 (d, J = 7.4 Hz, 2 H), 7.58 (t, J = 7.4 Hz, 1 H), 7.50 - 7.44(m, 4 H), 6.97 – 6.94 (m, 2 H), 2.20(s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 195.5, 187.8, 152.9, 141.3, 137.6, 137.5, 133.8, 128.9, 125.6, 122.6, 119.4, 113.9, 112.2, 29.3. Anal. Calcd. for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81; Found: C, 73.88; H, 4.52; N, 4.67.

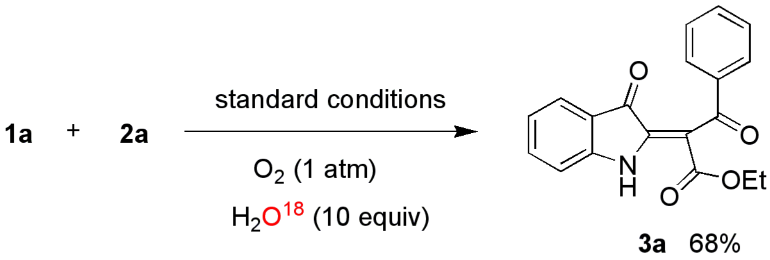
(E/Z)-ethyl 3-oxo-2-(3-oxoindolin-2-ylidene)butanoate

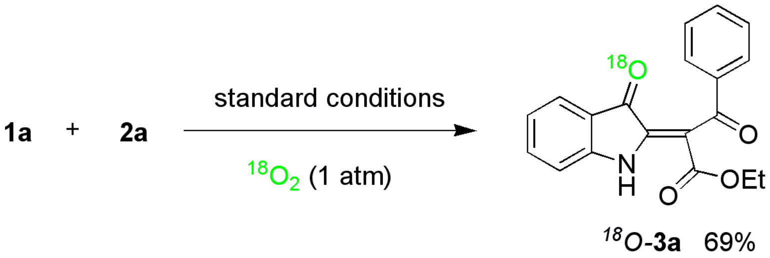


3z

Following the general procedure, using 20% ether in petroleum ether as the eluant afforded a red solid (40% yield). ^{1}H NMR [**E**/**Z** = 3.6:1] (400 MHz, $CDCl_3$): δ **E**: 10.23 (s, 1 H), 7.64 – 7.62 (m, 1 H), 7.51 – 7.47 (m, 1 H), 7.02 (t, J = 7.4 Hz, 1 H), 6.98 – 6.90 (m, 1 H), 4.44 (q, J = 7.2 Hz, 2 H), 2.35 (s, 3 H), 1.40 (t, J = 7.2 Hz, 3 H). **Z**: 9.04 (s, 1 H), 4.29 (q, J = 7.1 Hz, 2 H), 2.50 (s, 3 H), 1.32 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ E: 197.6, 187.2, 167.1, 152.3, 141.2, 137.5, 125.6, 122.7, 119.6, 112.1, 108.2, 62.2, 28.5, 13.8. **Z**: 199.8, 186.6, 166.1, 152.6, 141.3, 137.6, 125.6, 122.0, 119.8, 111.8, 110.6, 61.6, 31.3, 14.1. Anal. Calcd. for $C_{20}H_{17}NO_4$: C, 64.86; H, 5.05; N, 5.40; Found: C, 64.67; H, 5.08; N, 5.21.

Labeling experiments:





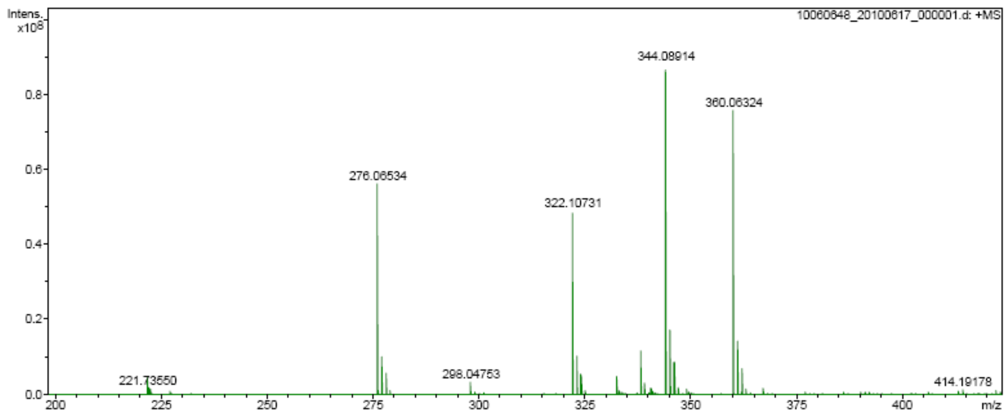
The ^{18}O was determined by HRMS. It should be noted that the labeling product undergoes partial oxygen exchange during the purification process. When the reaction was carried out in the presence of 10 equiv of H_2O^{18}, only normal ^{16}O-product was detected.

The HRMS spectra of **3a** for the reaction in the presence of H_2O^{18}.

Peking University Mass Spectrometry Sample Analysis Report

Analysis Info

Analysis Name	10060648_20100617_000001.d	Acquisition Date	6/17/2010 11:23:27 AM
Sample	wwwl-1616	Instrument	Bruker Apex IV FTMS
Comment	ESI Positive	Operator	Peking University



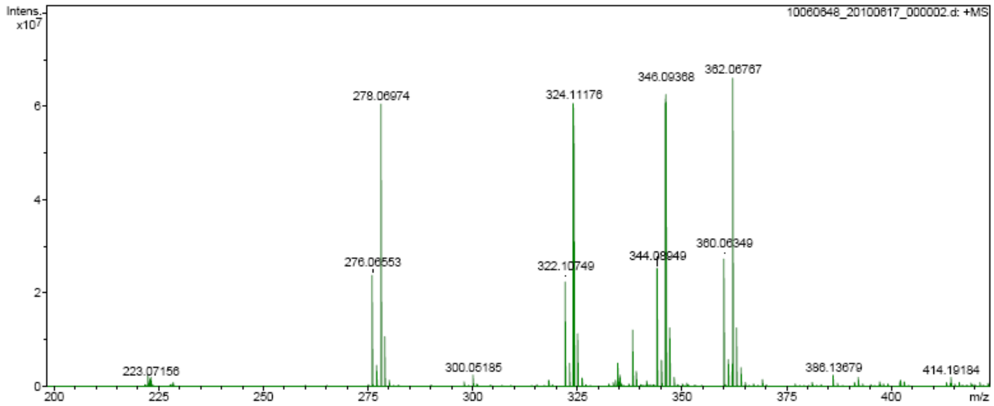
Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
322.10731	1	C 19 H 16 N O 4	100.00	322.10738	0.1	0.2	47.0	12.5	even	ok
344.08914	1	C 19 H 15 N Na O 4	100.00	344.08933	0.2	0.6	42.4	12.5	even	ok

The HRMS spectra of **3a** for the reaction under $^{18}O_2$ (97%).

Peking University Mass Spectrometry Sample Analysis Report

Analysis Info

Analysis Name	10060648_20100617_000002.d	Acquisition Date	6/17/2010 11:24:54 AM
Sample	wwwl-1816	Instrument	Bruker Apex IV FTMS
Comment	ESI Positive	Operator	Peking University



Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
322.10749	1	C 19 H 16 N O 4	100.00	322.10738	-0.1	-0.3	672.5	12.5	even	ok
324.11176	1	C 19 H 16 N O 3 Ot	100.00	324.11163	-0.1	-0.4	145.3	12.5	even	ok
344.08949	1	C 19 H 15 N Na O 4	100.00	344.08933	-0.2	-0.5	659.9	12.5	even	ok
346.09368	1	C 19 H 15 N Na O 3 Ot	100.00	346.09357	-0.1	-0.3	163.3	12.5	even	ok

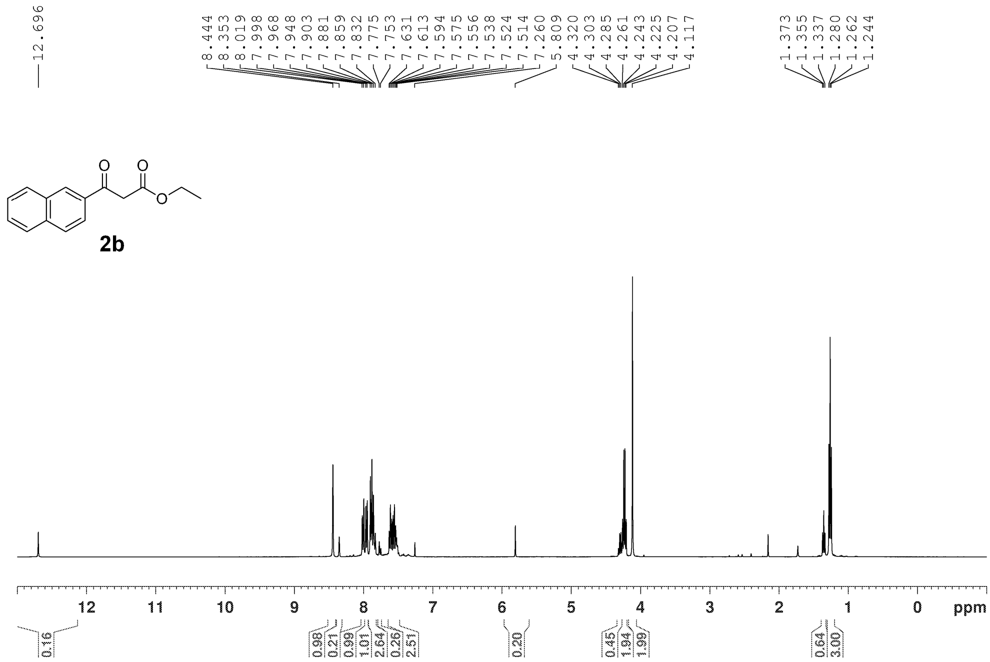
References

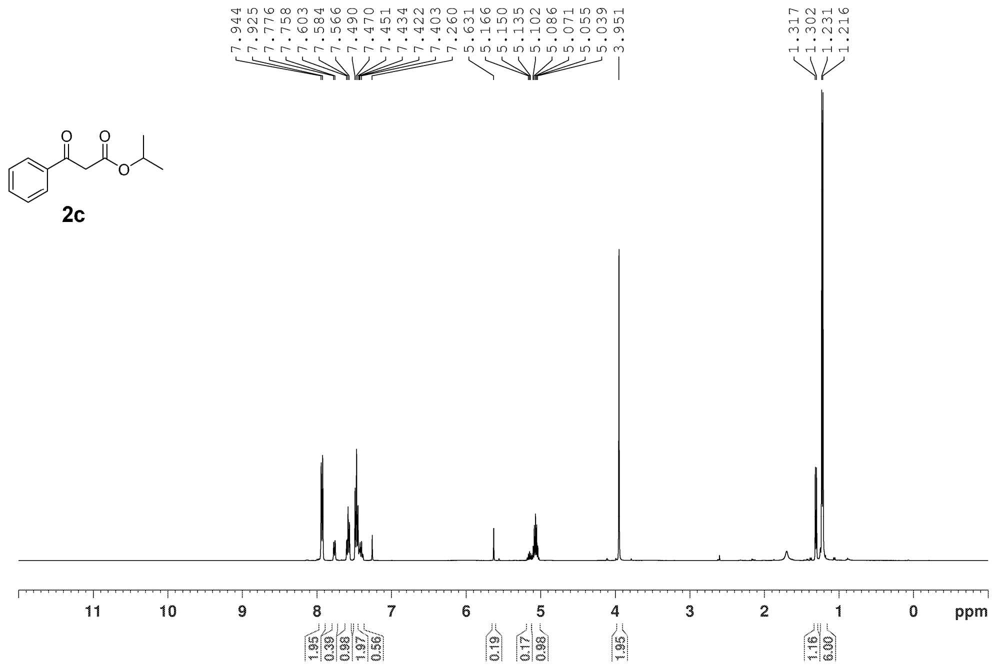
[1] V. Gasparotto, I. Castagliuolo, G. Chiarelotto, V. Pezzi, D.Montanaro, P. Brun, G. Palù, G. Viola, M. G. Ferlin, *J. Med. Chem.* **2006**, *49*, 1910-1915.

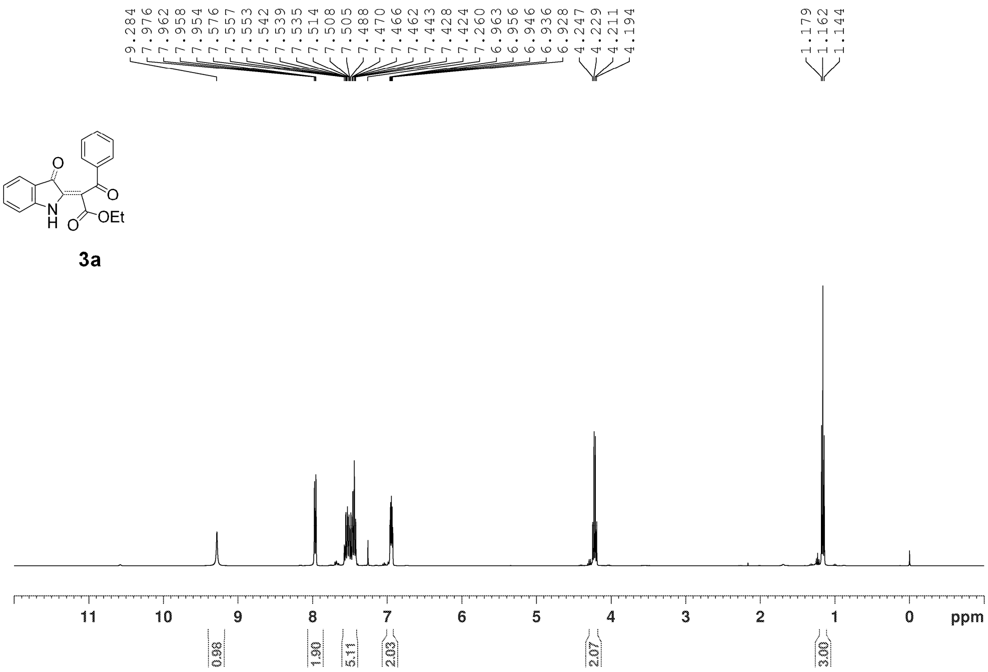
[2] Z. Rappoport, A. Gazit, *J. Org. Chem.* **1986**, *51*, 4112-4131.

[3] K. Yoshizawa, S. Toyota, F. Toda, *Tetrahedron. Lett.* **2001**, *42*, 7983-7985.

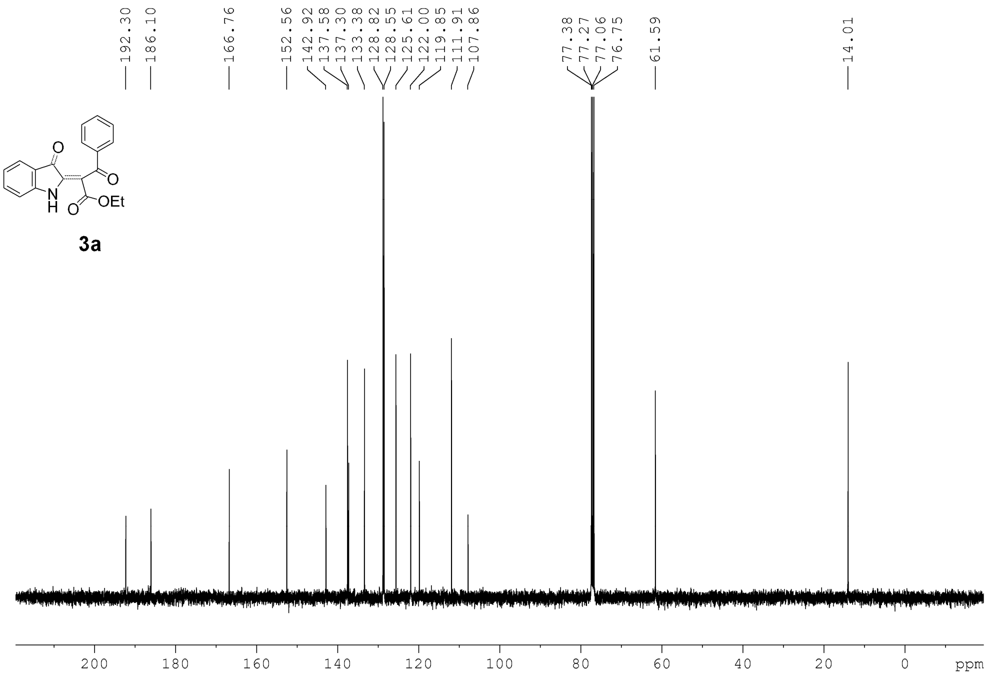
[4] S. L. I.-L. Juana, H. J. Anthony, P. Noojaree, V. R. S. Patrick, *J. Chem. Soc. Perkin trans. II* **1987**, 1221.


12.696
8.444 8.353 8.019 7.998 7.968 7.948 7.903 7.881 7.859 7.832 7.775 7.753 7.631 7.613 7.594 7.575 7.556 7.538 7.524 7.514 7.260 5.809 4.320 4.303 4.285 4.261 4.243 4.225 4.207 4.117
1.373 1.355 1.337 1.280 1.262 1.244
O
O
O
2b
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.16
0.98 0.21 0.99 1.01 2.64 0.26 2.51
0.20
0.45 1.94 1.99
0.64 3.00

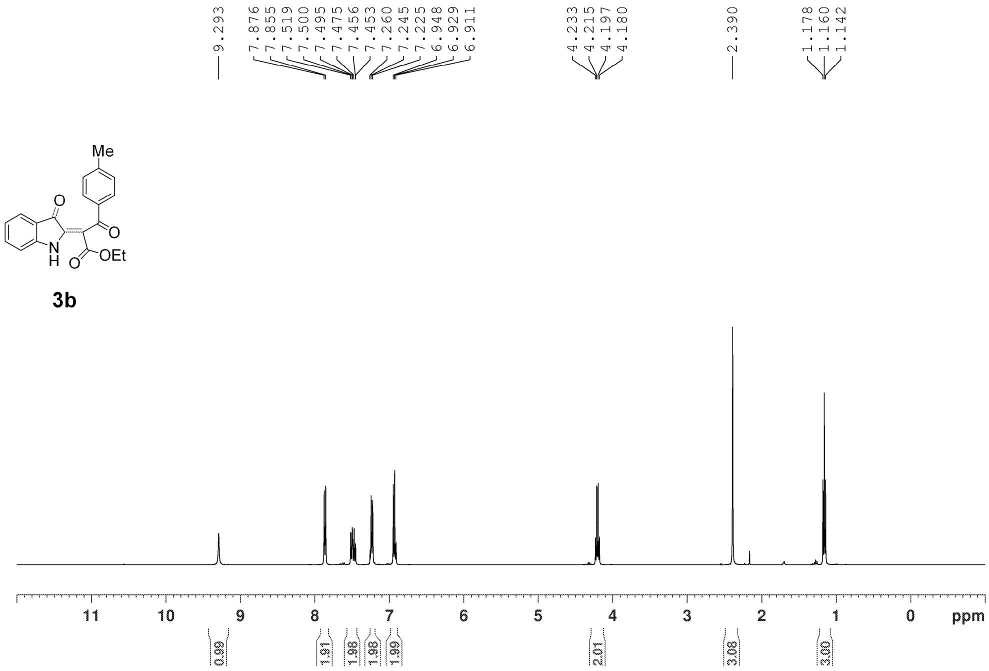

7.944 7.925 7.776 7.758 7.603 7.584 7.566 7.490 7.470 7.451 7.434 7.422 7.403 7.260 5.631 5.166 5.150 5.135 5.102 5.086 5.071 5.055 5.039 3.951
1.317 1.302 1.231 1.216
O
O
O
2c
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.95 0.39 0.98 1.97 0.56
0.19
0.17 0.98
1.95
1.16 6.00

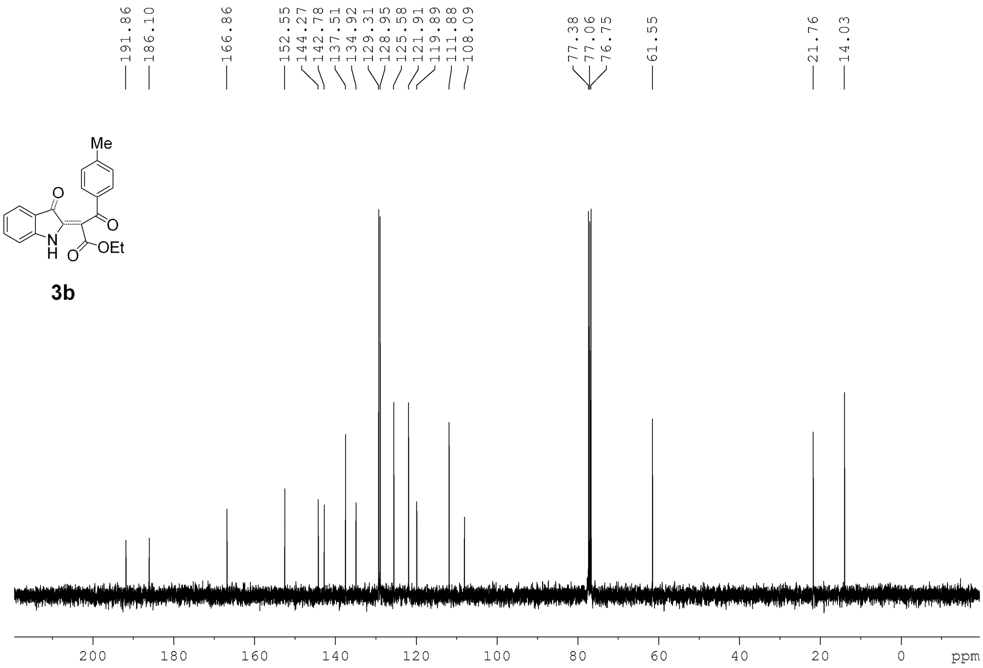


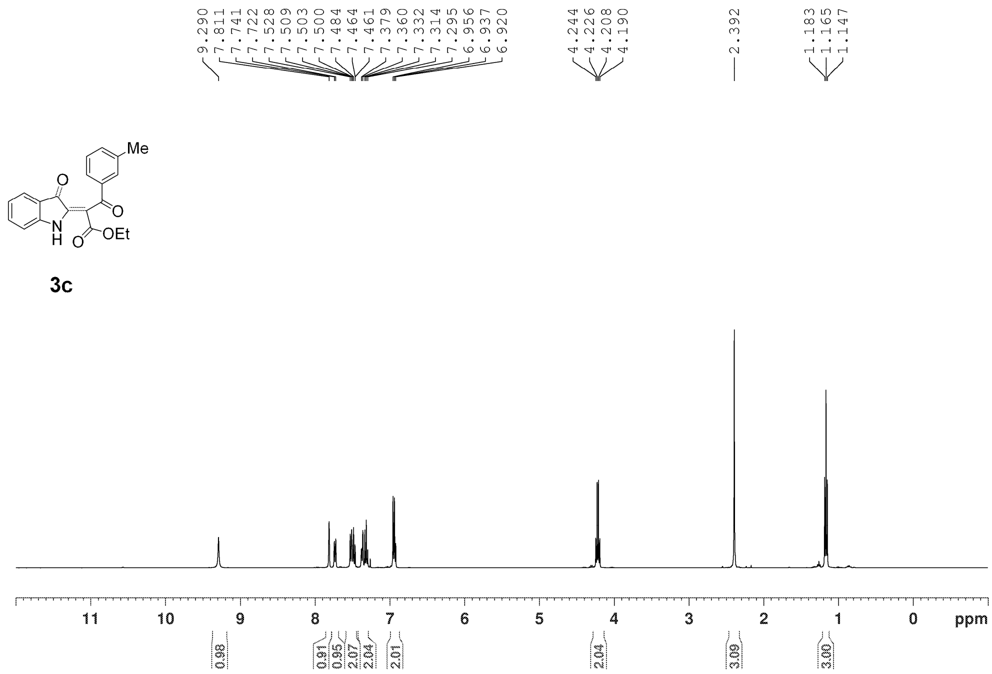
3a



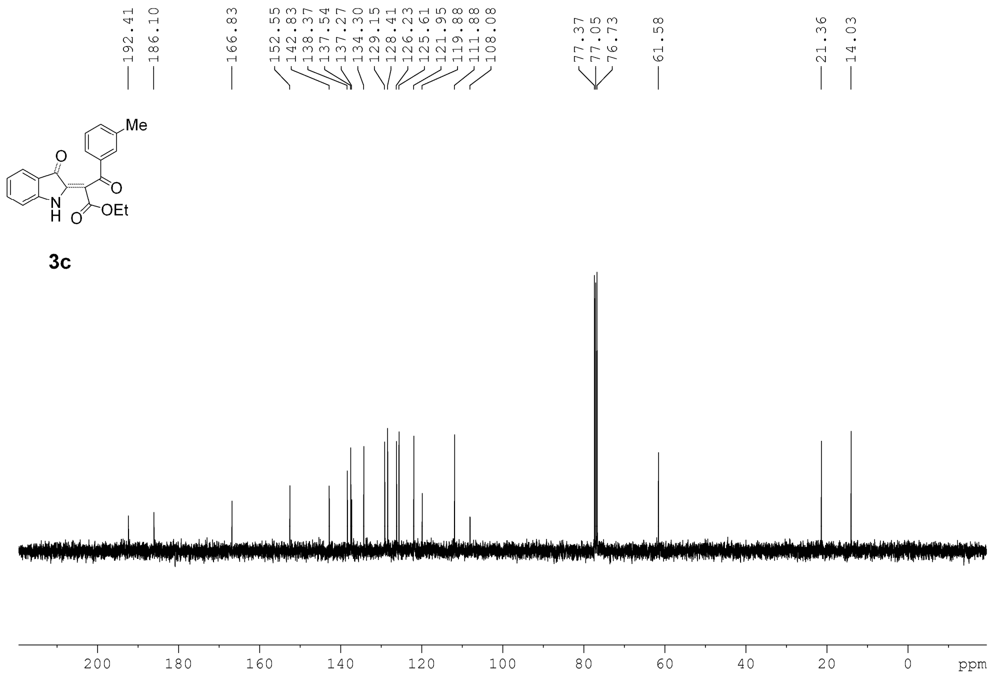
3a


9.293
7.876
7.855
7.519
7.500
7.495
7.475
7.456
7.453
7.260
7.245
7.225
6.948
6.929
6.911
4.233
4.215
4.197
4.180
2.390
1.178
1.160
1.142
Me
O
O
N
H
O
OEt
3b
0.99
1.91
1.98
1.98
1.99
2.01
3.08
3.00
11 10 9 8 7 6 5 4 3 2 1 0 ppm


191.86
186.10
166.86
152.55
144.27
142.78
137.51
134.92
129.31
128.95
125.58
121.91
119.89
111.88
108.09
77.38
77.06
76.75
61.55
21.76
14.03
Me
O
O
N
H
O
OEt
3b
200 180 160 140 120 100 80 60 40 20 0 ppm

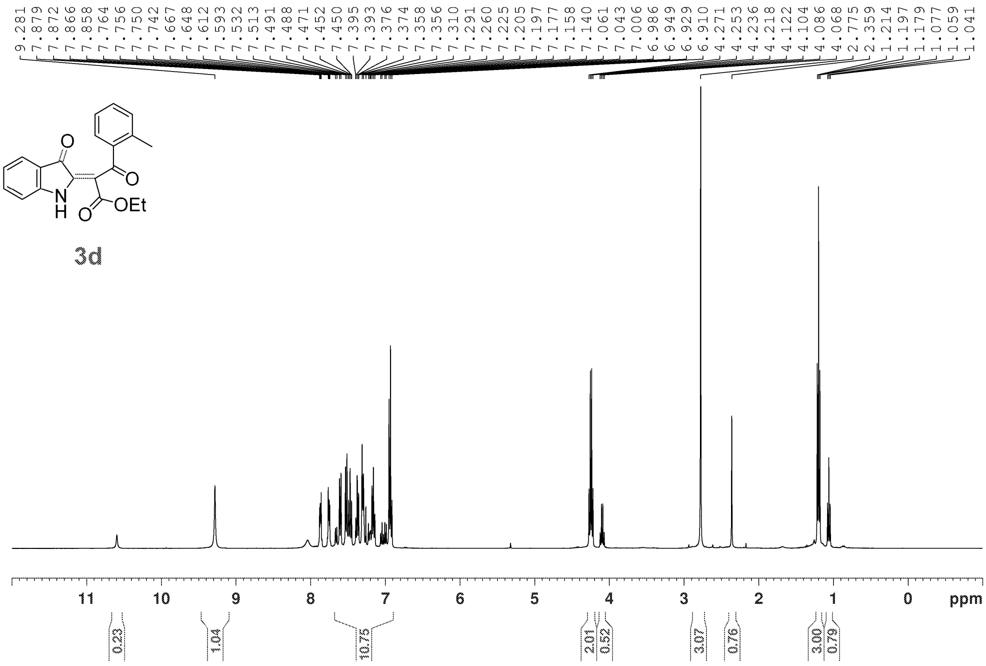

9.290
7.811
7.741
7.722
7.528
7.509
7.503
7.500
7.484
7.464
7.461
7.379
7.360
7.332
7.314
7.295
6.956
6.937
6.920
4.244
4.226
4.208
4.190
2.392
1.183
1.165
1.147
Me
O
O
N
H
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
0.91
0.95
2.07
2.04
2.01
2.04
3.09
3.00

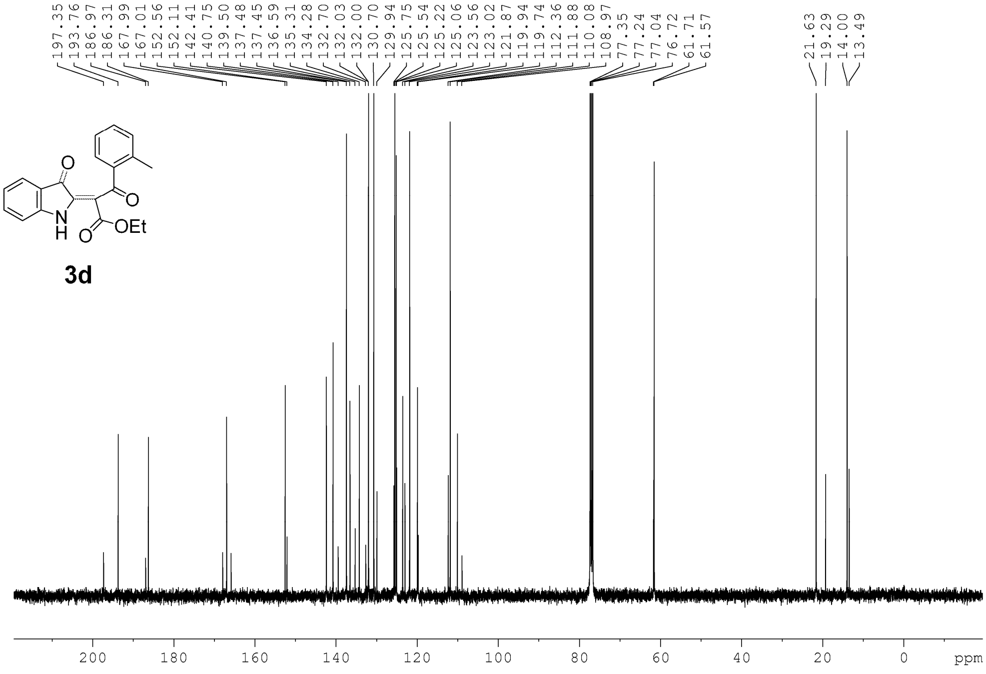
3c

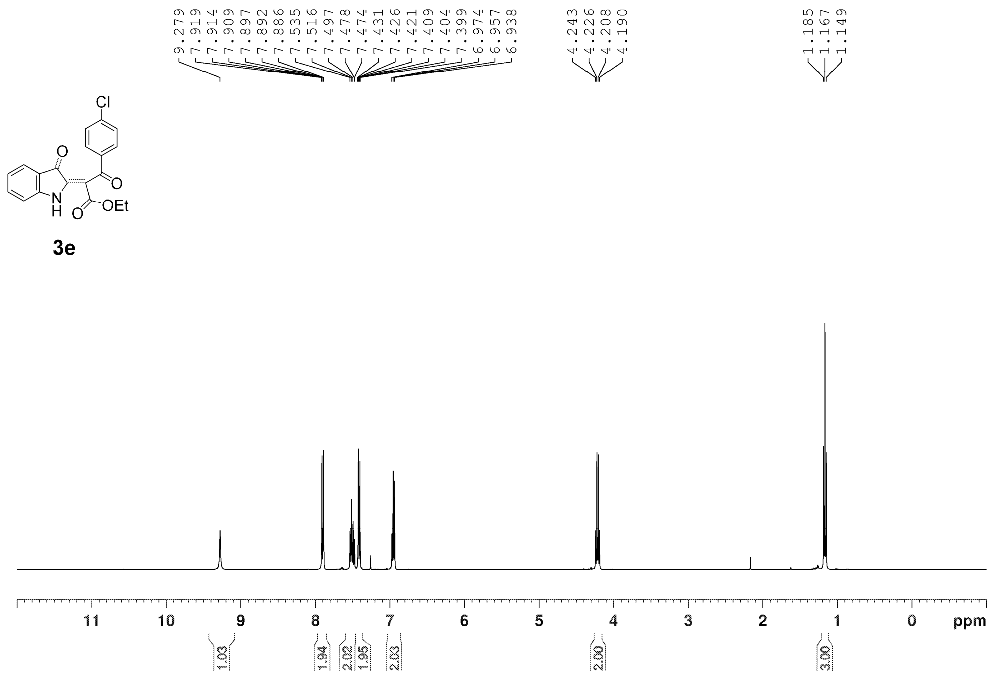

192.41
186.10
166.83
152.55
142.83
138.37
137.54
137.27
134.30
129.15
128.41
126.23
125.61
121.95
119.88
111.88
108.08
77.37
77.05
76.73
61.58
21.36
14.03
Me
O
O
N
H
O
OEt
200
180
160
140
120
100
80
60
40
20
0
ppm

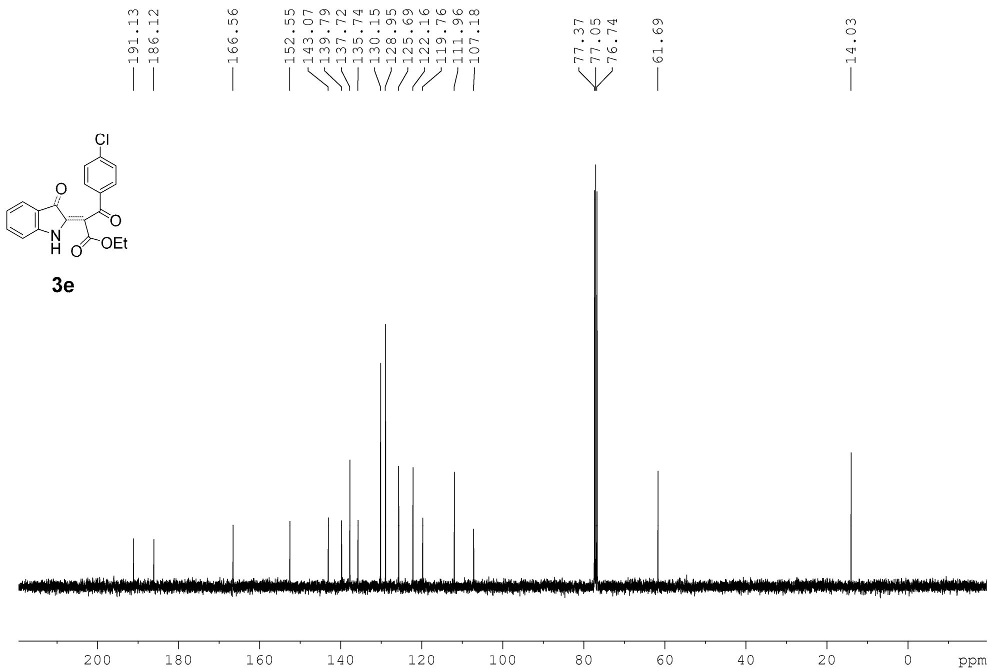
3c

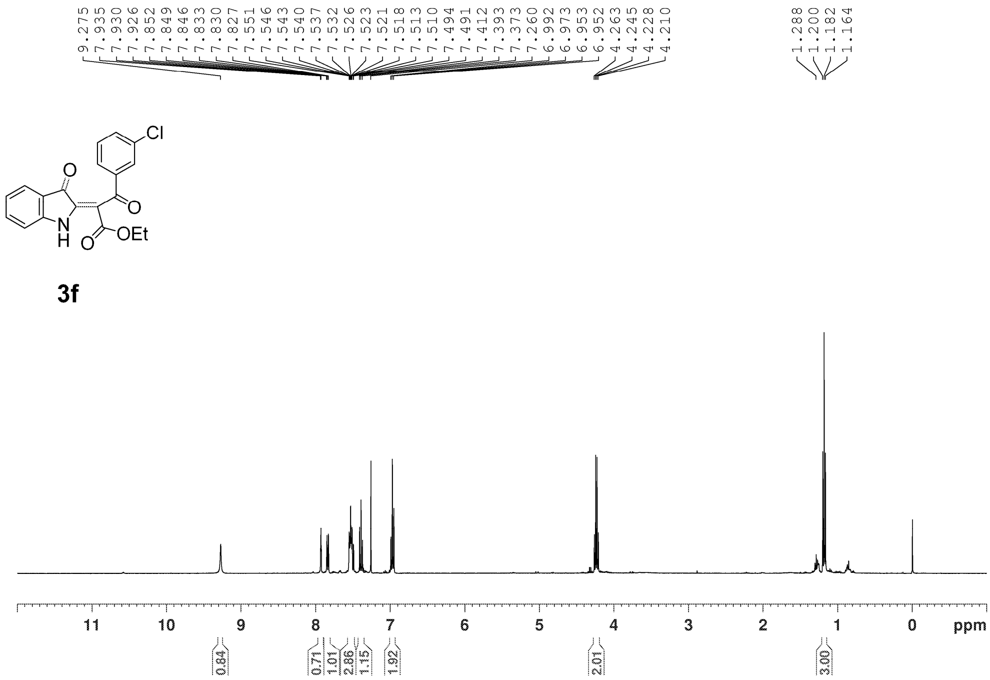
Electronic Supplementary Material (ESI) for Chemical Communications



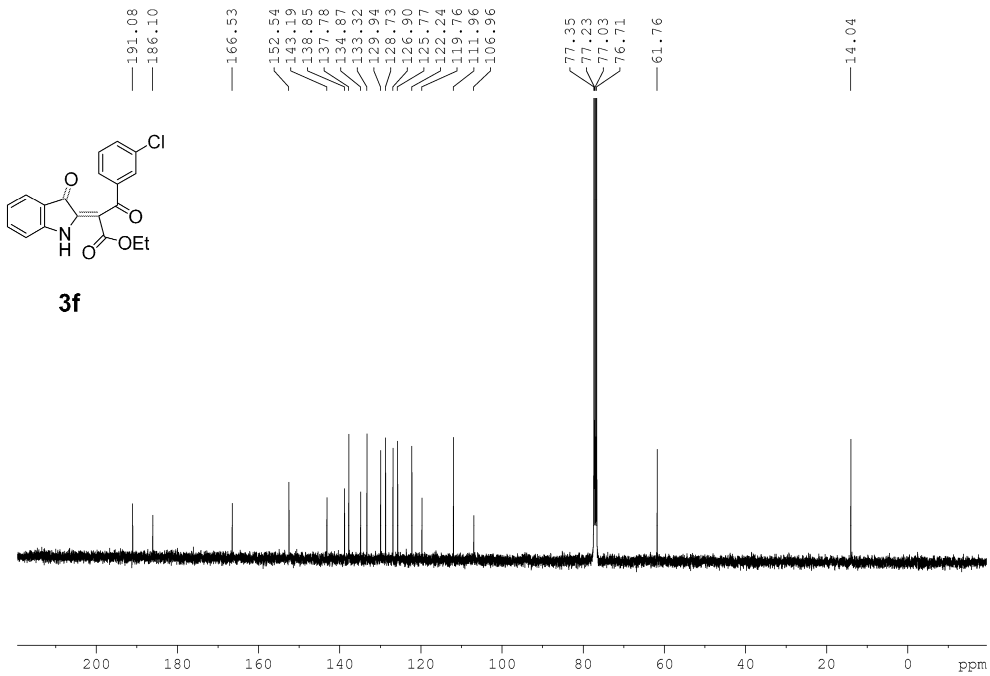



9.279
7.919
7.914
7.909
7.897
7.892
7.886
7.535
7.516
7.497
7.478
7.474
7.431
7.426
7.421
7.409
7.404
7.399
6.974
6.957
6.938
4.243
4.226
4.208
4.190
1.185
1.167
1.149
Cl
O
O
N
H
O
OEt
3e
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
1.94
2.02
1.95
2.03
2.00
3.00

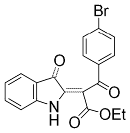

191.13
186.12
166.56
152.55
143.07
139.79
137.72
135.74
130.15
128.95
125.69
122.16
119.76
111.96
107.18
77.37
77.05
76.74
61.69
14.03
Cl
O
O
N
H
O
OEt
3e
200
180
160
140
120
100
80
60
40
20
0
ppm


9.275
7.935
7.930
7.926
7.852
7.849
7.846
7.833
7.830
7.827
7.551
7.546
7.543
7.540
7.537
7.532
7.526
7.523
7.521
7.518
7.513
7.510
7.494
7.491
7.412
7.393
7.373
7.260
6.992
6.973
6.953
6.952
4.263
4.245
4.228
4.210
1.288
1.200
1.182
1.164
Cl
O
O
N
H
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.84
0.71
1.01
2.86
1.15
1.92
2.01
3.00

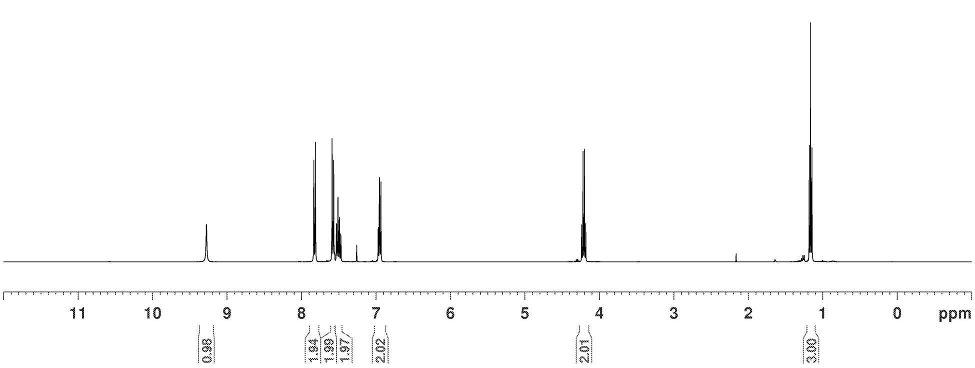
3f

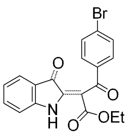

191.08
186.10
166.53
152.54
143.19
138.85
137.78
134.87
133.32
129.94
128.73
126.90
125.77
122.24
119.76
111.96
106.96
77.35
77.23
77.03
76.71
61.76
14.04
Cl
O
O
N
H
O
OEt
200
180
160
140
120
100
80
60
40
20
0
ppm

3f

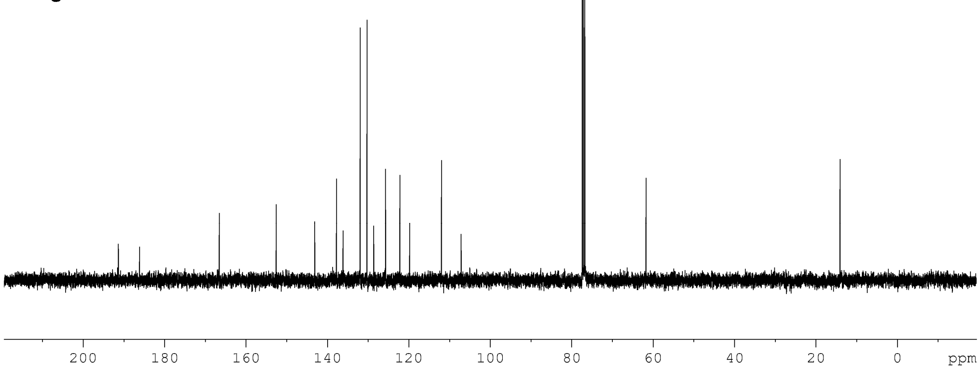

Br
O
O
N
H
O
OEt

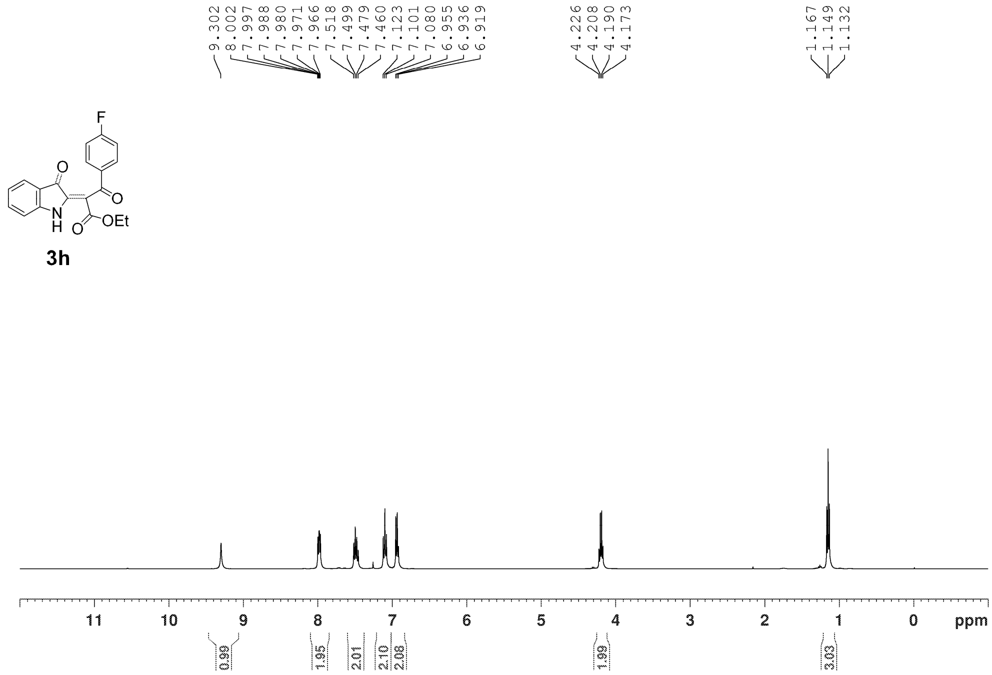
3g

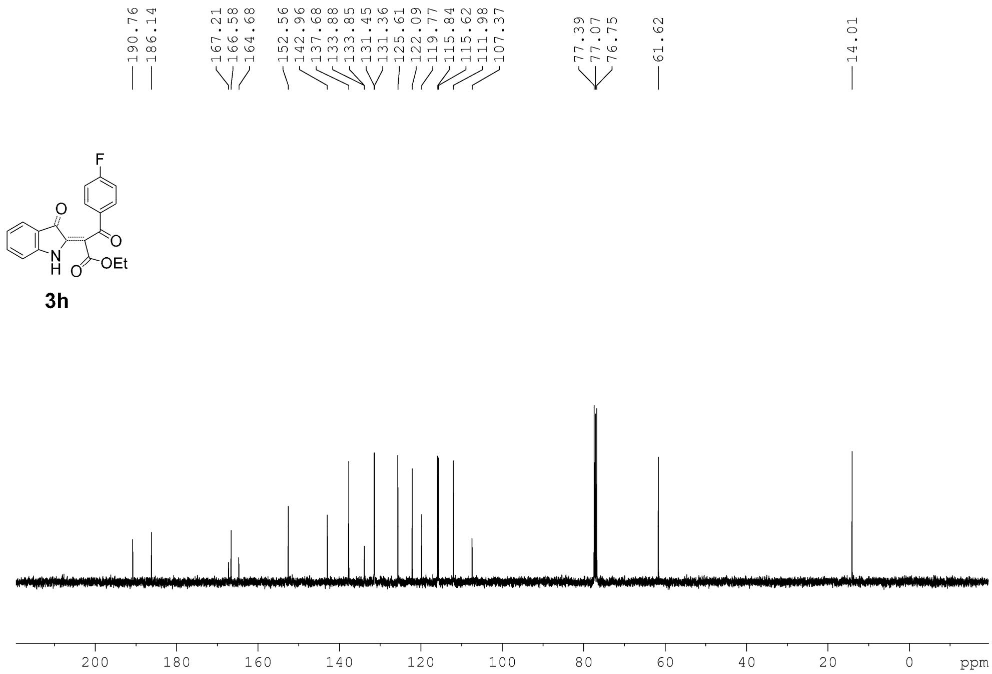

9.278
7.842
7.836
7.832
7.819
7.815
7.809
7.597
7.591
7.587
7.574
7.570
7.564
7.531
7.512
7.493
7.474
7.471
7.260
6.971
6.954
6.935
4.239
4.221
4.203
4.185
1.183
1.165
1.147
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
1.94
1.99
1.97
2.02
2.01
3.00

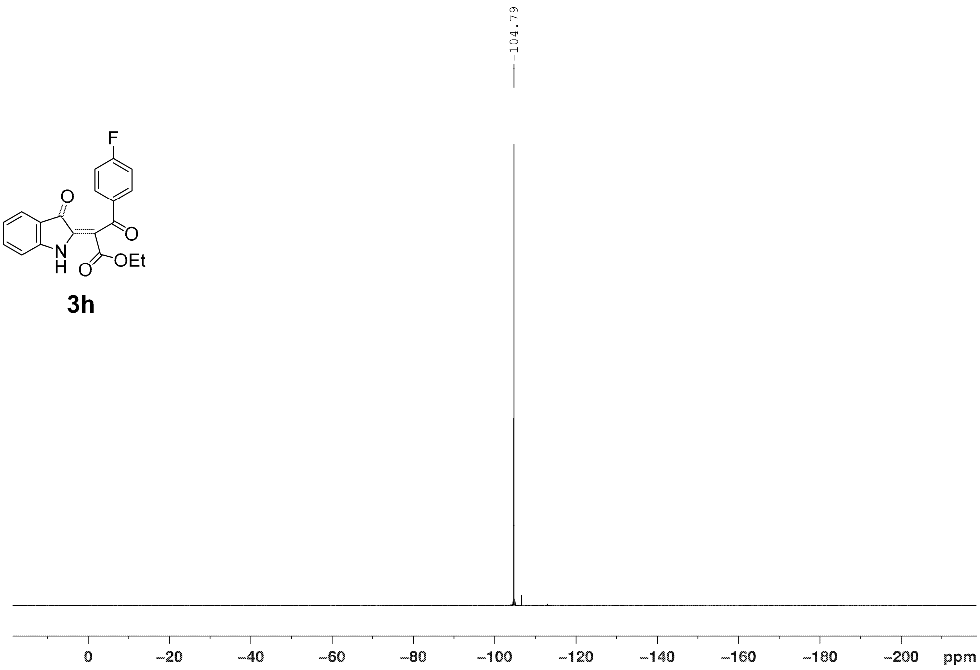

Br
O
O
N
H
O
OEt

3g

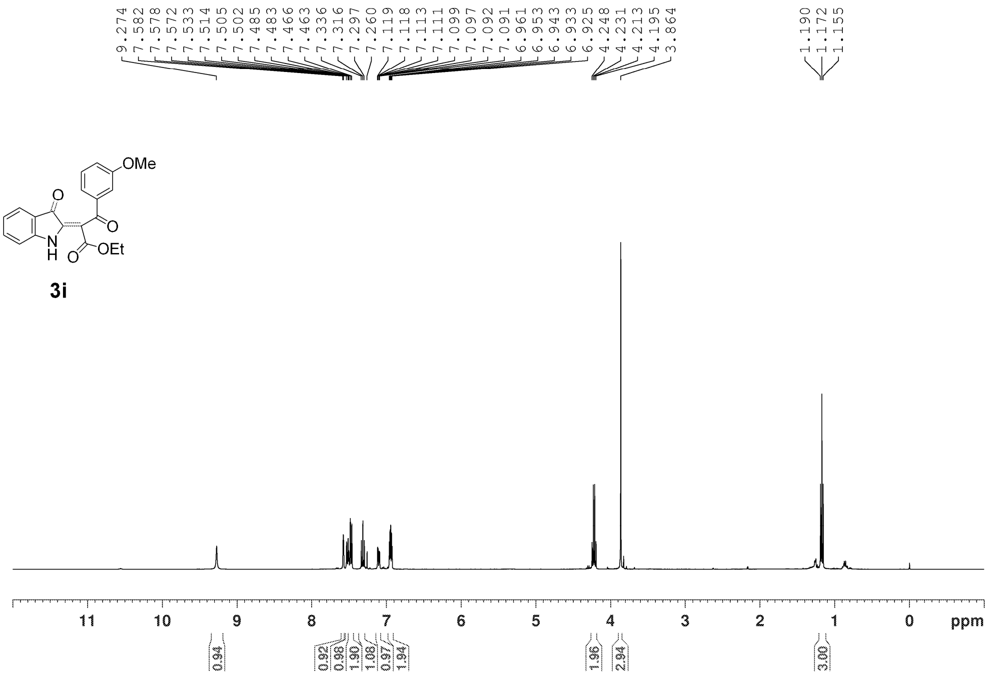

191.32
186.11
166.55
152.54
143.09
137.72
136.14
131.92
130.25
128.59
125.69
122.17
119.76
111.95
107.12
77.36
77.04
76.72
61.69
14.03
200
180
160
140
120
100
80
60
40
20
0
ppm


9.302
8.002
7.997
7.988
7.980
7.971
7.966
7.518
7.499
7.479
7.460
7.123
7.101
7.080
6.955
6.936
6.919
4.226
4.208
4.190
4.173
1.167
1.149
1.132
F
O
O
N
H
O
OEt
3h
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
1.95
2.01
2.10
2.08
1.99
3.03

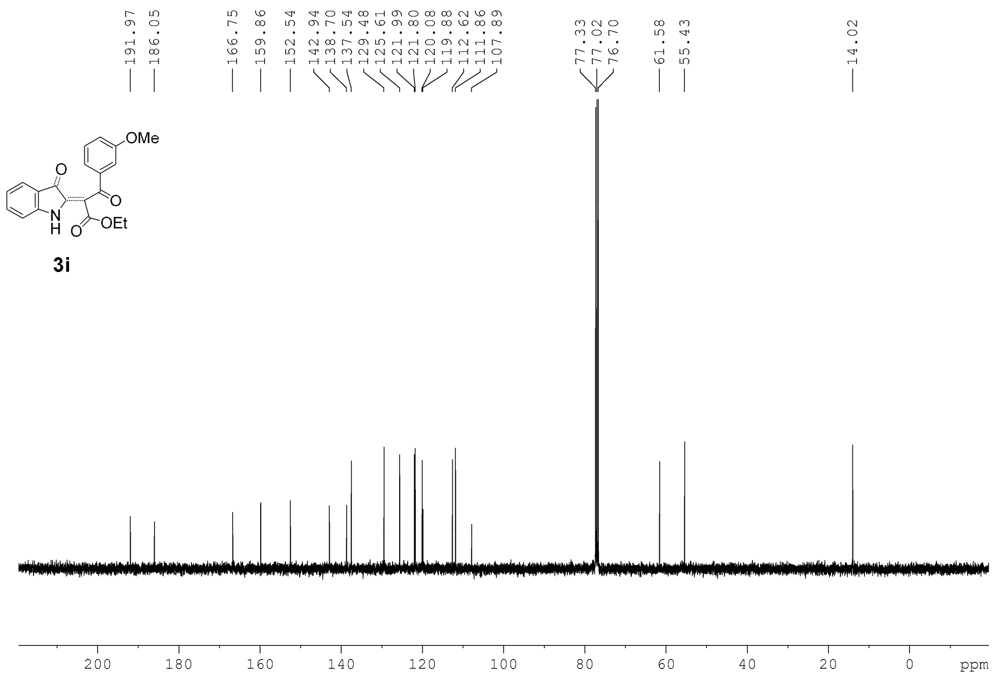

190.76
186.14
167.21
166.58
164.68
152.56
142.96
137.68
133.88
133.85
131.45
131.36
125.61
122.09
119.77
115.84
115.62
111.98
107.37
77.39
77.07
76.75
61.62
14.01
F
O
O
N
H
O
OEt
3h
200
180
160
140
120
100
80
60
40
20
0
ppm


-104.79
F
O
O
N
H
O
OEt
0
−20
−40
−60
−80
−100
−120
−140
−160
−180
−200
ppm

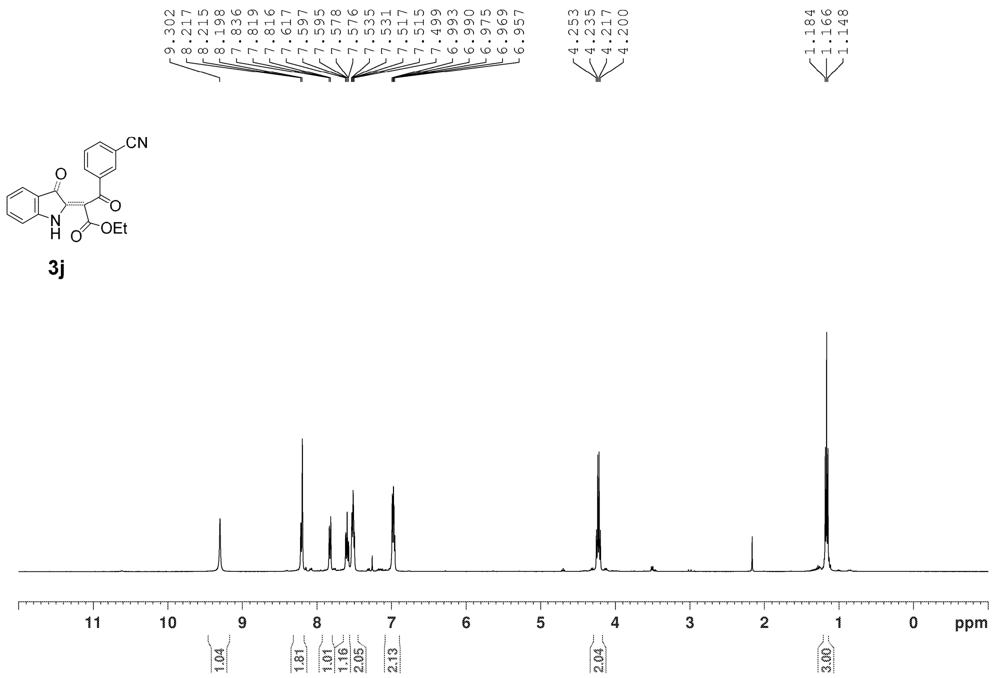
3h


9.274
7.582
7.578
7.572
7.533
7.514
7.505
7.502
7.485
7.483
7.466
7.463
7.336
7.316
7.297
7.260
7.119
7.118
7.113
7.111
7.099
7.097
7.092
7.091
6.961
6.953
6.943
6.933
6.925
4.248
4.231
4.213
4.195
3.864
1.190
1.172
1.155
OMe
O
O
N
H
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.94
0.92
0.98
1.90
1.08
0.97
1.94
1.96
2.94
3.00

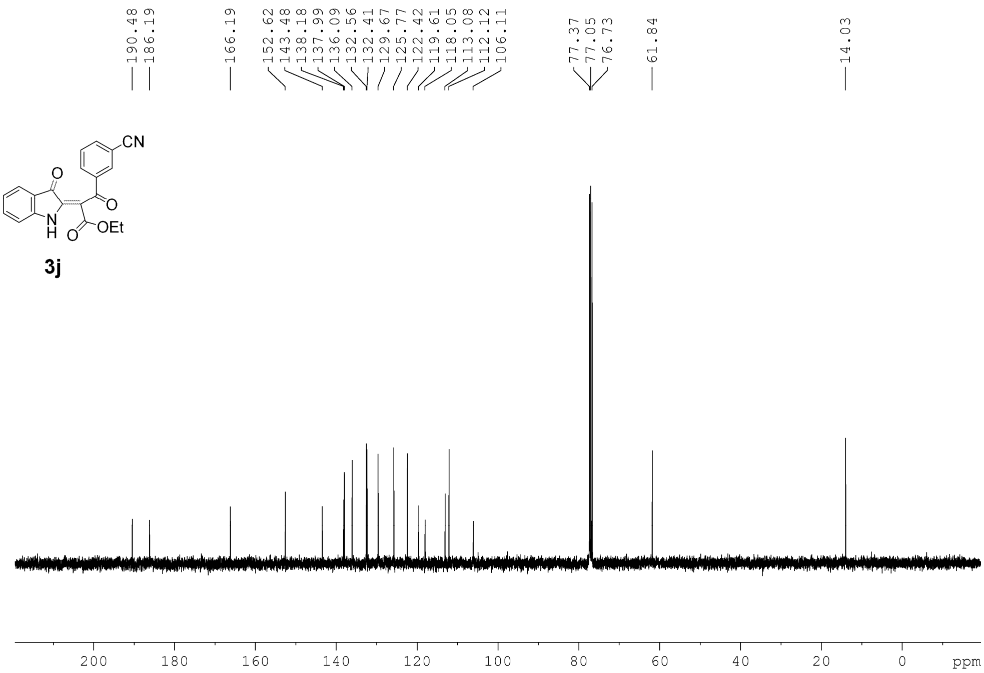
3i


191.97
186.05
166.75
159.86
152.54
142.94
138.70
137.54
129.48
125.61
121.99
121.80
120.08
119.88
112.62
111.86
107.89
77.33
77.02
76.70
61.58
55.43
14.02
OMe
O
O
N
H
O
OEt
200
180
160
140
120
100
80
60
40
20
0
ppm

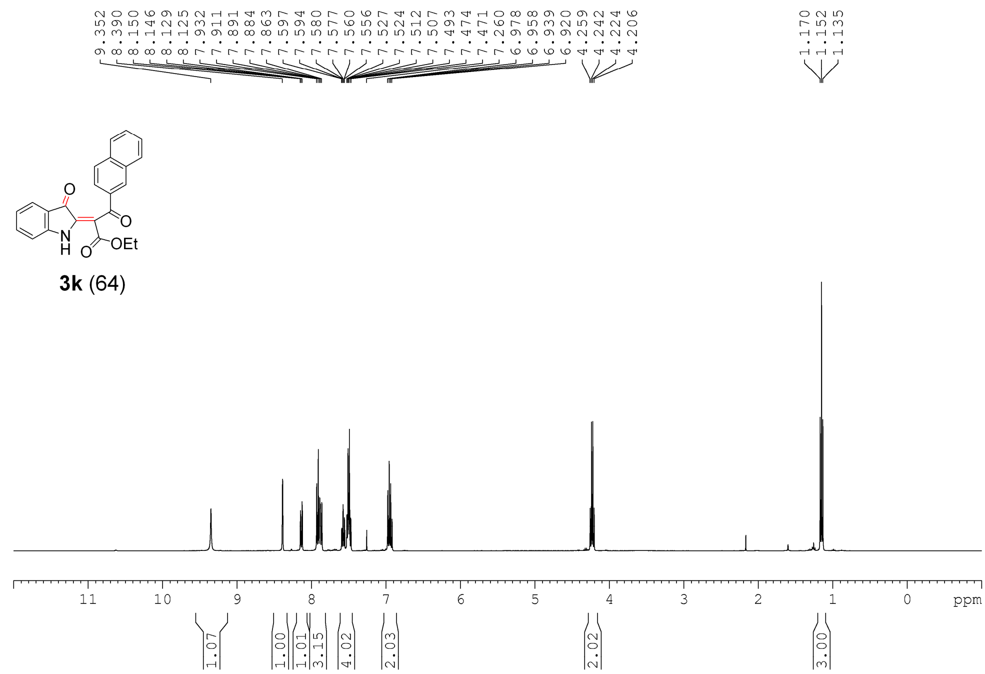
3i


9.302
8.217
8.215
8.198
7.836
7.819
7.816
7.617
7.597
7.595
7.578
7.576
7.535
7.531
7.517
7.515
7.499
6.993
6.990
6.975
6.969
6.957
4.253
4.235
4.217
4.200
1.184
1.166
1.148
CN
O
O
N
H
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.04
1.81
1.01
1.16
2.05
2.13
2.04
3.00

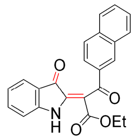
3j


190.48
186.19
166.19
152.62
143.48
138.18
137.99
136.09
132.56
132.41
129.67
125.77
122.42
119.61
118.05
113.08
112.12
106.11
77.37
77.05
76.73
61.84
14.03
CN
O
O
N
H
O
OEt
200 180 160 140 120 100 80 60 40 20 0 ppm

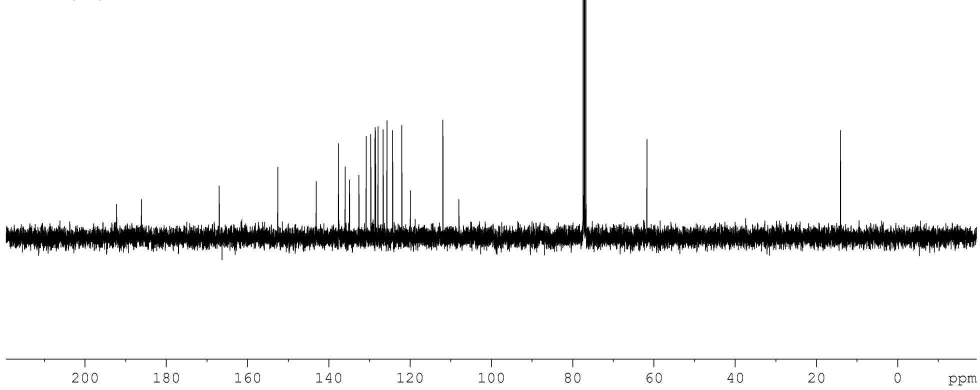
3j

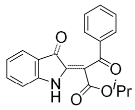

9.352
8.390
8.150
8.146
8.129
8.125
7.932
7.911
7.891
7.884
7.863
7.597
7.594
7.580
7.577
7.560
7.556
7.527
7.524
7.512
7.507
7.493
7.474
7.471
7.260
6.978
6.958
6.939
6.920
4.259
4.242
4.224
4.206
1.170
1.152
1.135
O
O
N
H
O
OEt
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.07
1.00
1.01
3.15
4.02
2.03
2.02
3.00

3k (64)

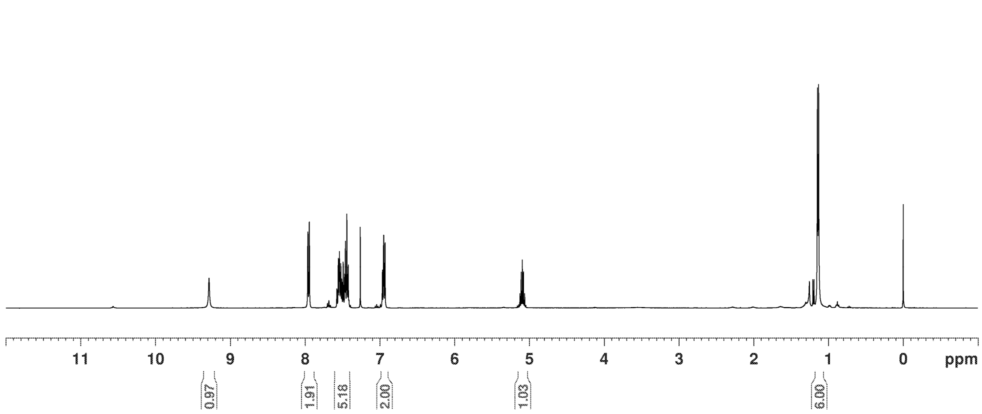

O
O
N
H
O
OEt

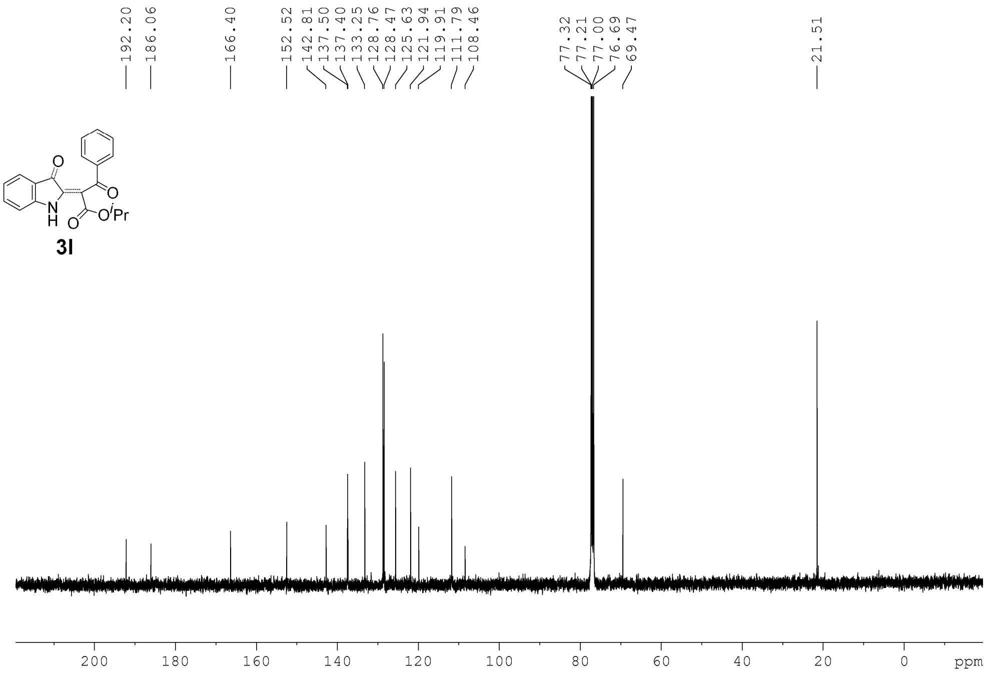
3k (64)


192.22
186.08
166.95
152.53
143.07
137.57
135.95
134.88
132.58
130.78
129.64
128.59
128.48
127.86
126.62
125.66
124.27
122.03
119.90
111.88
107.95
77.35
77.03
76.71
61.66
14.03
200 180 160 140 120 100 80 60 40 20 0 ppm

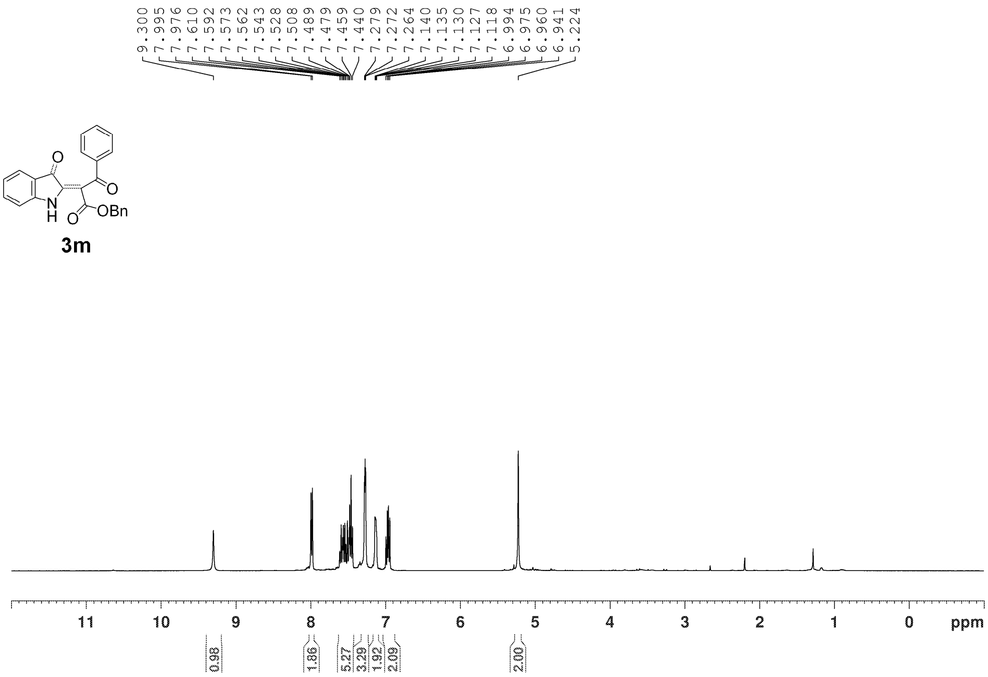

O
O
N
H
O
O^{i}Pr

3l

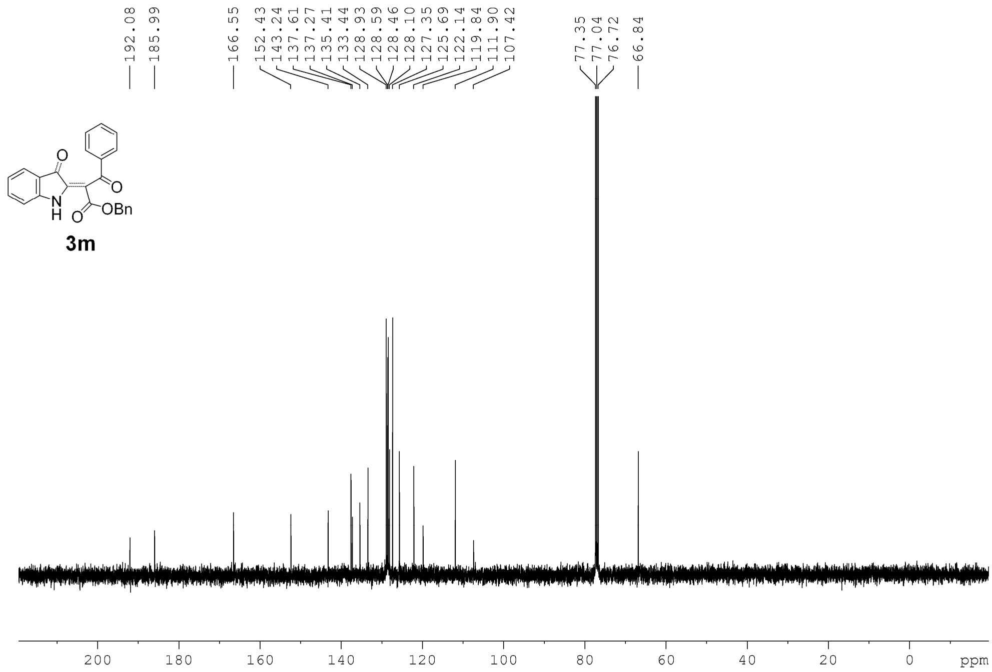

9.283
7.960
7.947
7.943
7.939
7.681
7.576
7.573
7.569
7.559
7.554
7.550
7.539
7.536
7.533
7.522
7.509
7.506
7.498
7.490
7.488
7.471
7.468
7.459
7.456
7.440
7.426
7.421
7.411
7.260
6.966
6.964
6.950
6.947
6.929
5.125
5.109
5.093
5.077
5.062
1.146
1.130
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.97
1.91
5.18
2.00
1.03
6.00


192.20
186.06
166.40
152.52
142.81
137.50
137.40
133.25
128.76
128.47
125.63
121.94
119.91
111.79
108.46
77.32
77.21
77.00
76.69
69.47
21.51
O
N
H
O
O
O^{i}Pr
200 180 160 140 120 100 80 60 40 20 0 ppm

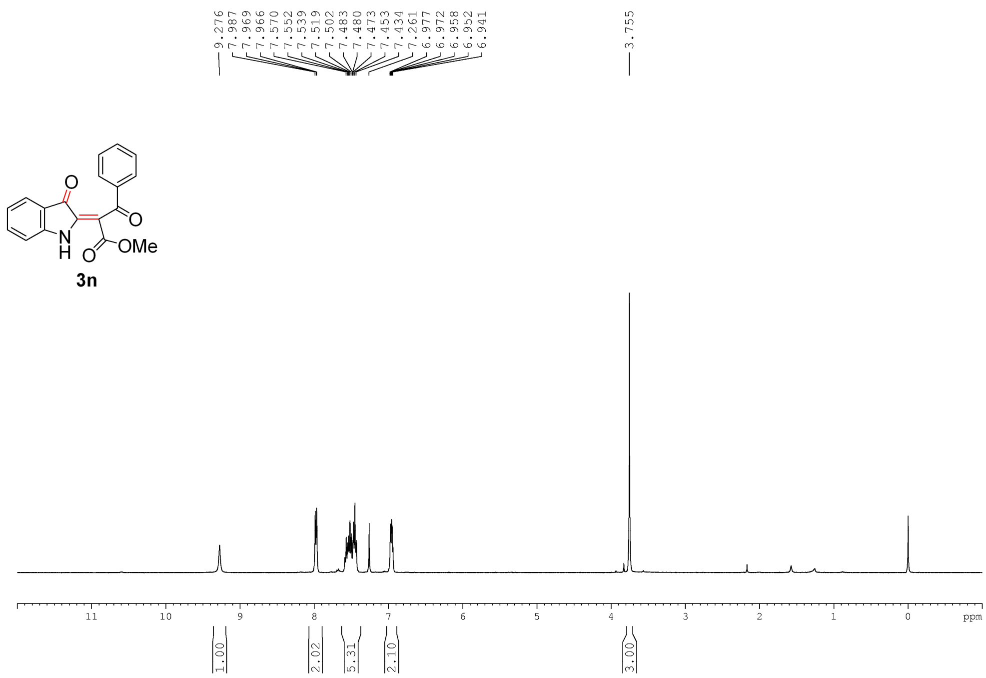
3l


9.300
7.995
7.976
7.610
7.592
7.573
7.562
7.543
7.528
7.508
7.489
7.479
7.459
7.440
7.279
7.272
7.264
7.140
7.135
7.130
7.127
7.118
6.994
6.975
6.960
6.941
5.224
O
N
H
O
O
OBn
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.98
1.86
5.27
3.29
1.92
2.09
2.00

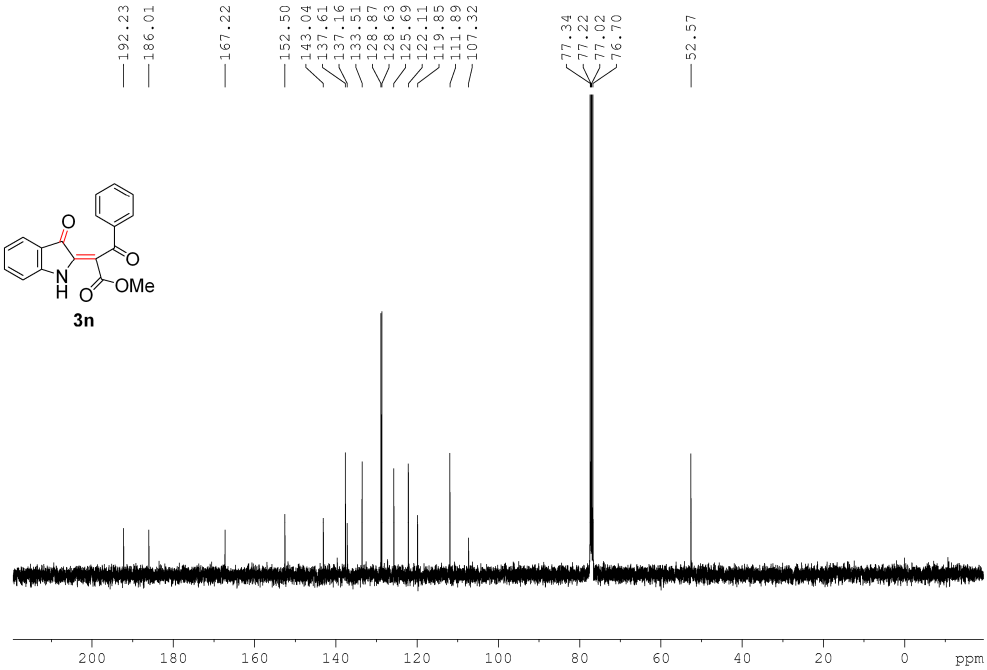
3m


192.08
185.99
166.55
152.43
143.24
137.61
137.27
135.41
133.44
128.93
128.59
128.46
128.10
127.35
125.69
122.14
119.84
111.90
107.42
77.35
77.04
76.72
66.84
O
O
N
H
O
OBn
200
180
160
140
120
100
80
60
40
20
0
ppm

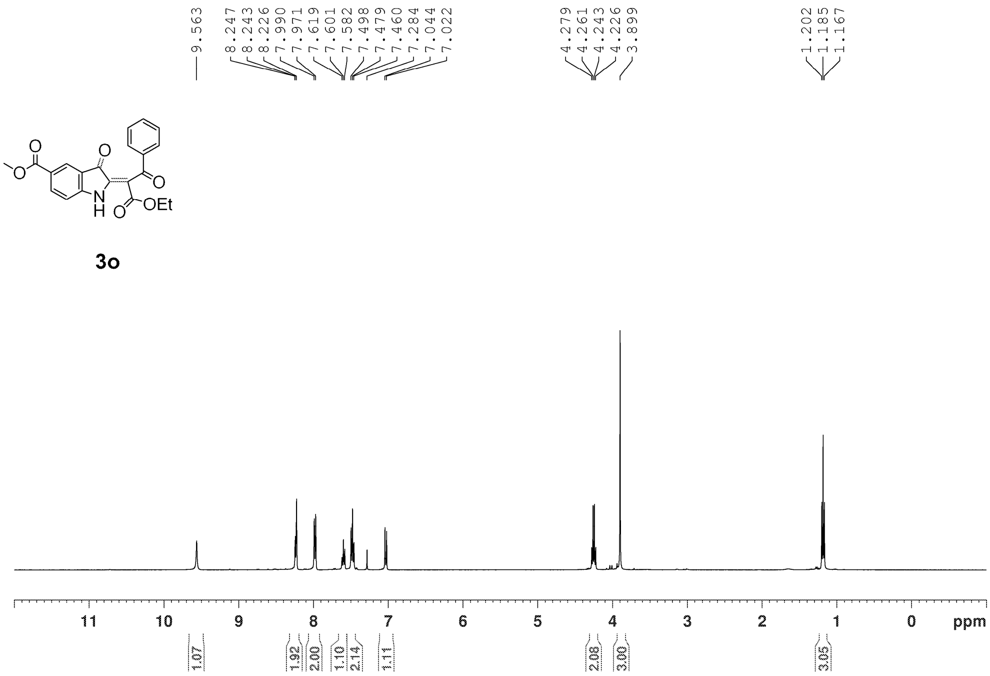
3m


9.276
7.987
7.969
7.966
7.570
7.552
7.539
7.519
7.502
7.483
7.480
7.473
7.453
7.434
7.261
6.977
6.972
6.958
6.952
6.941
3.755
O
O
N
H
O
OMe
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.02
5.31
2.10
3.00

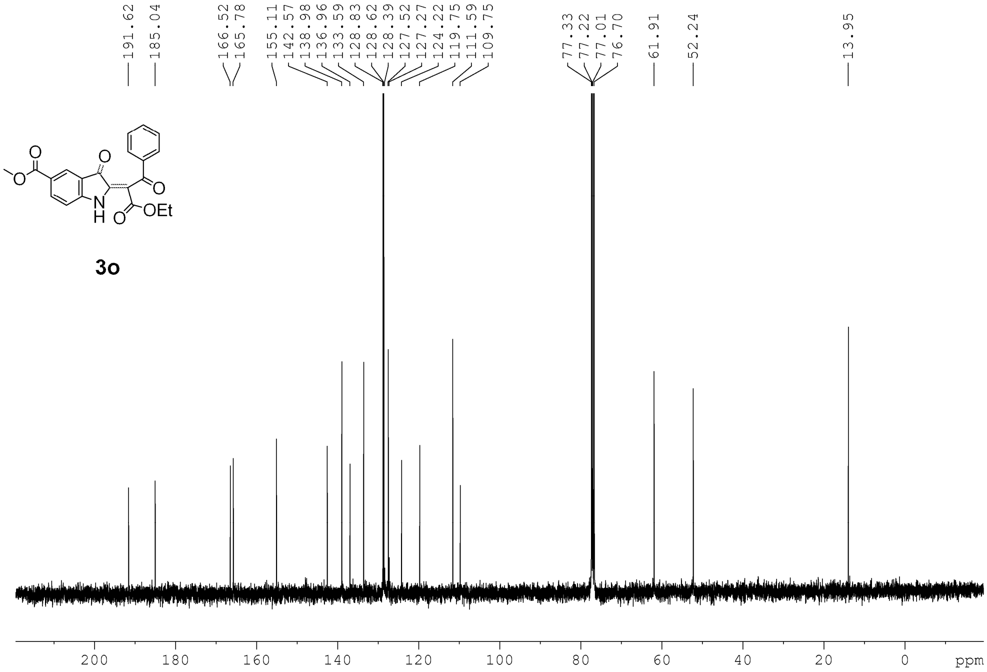
3n


192.23
186.01
167.22
152.50
143.04
137.61
137.16
133.51
128.87
128.63
125.69
122.11
119.85
111.89
107.32
77.34
77.22
77.02
76.70
52.57
O
N
H
O
O
OMe
200
180
160
140
120
100
80
60
40
20
0
ppm

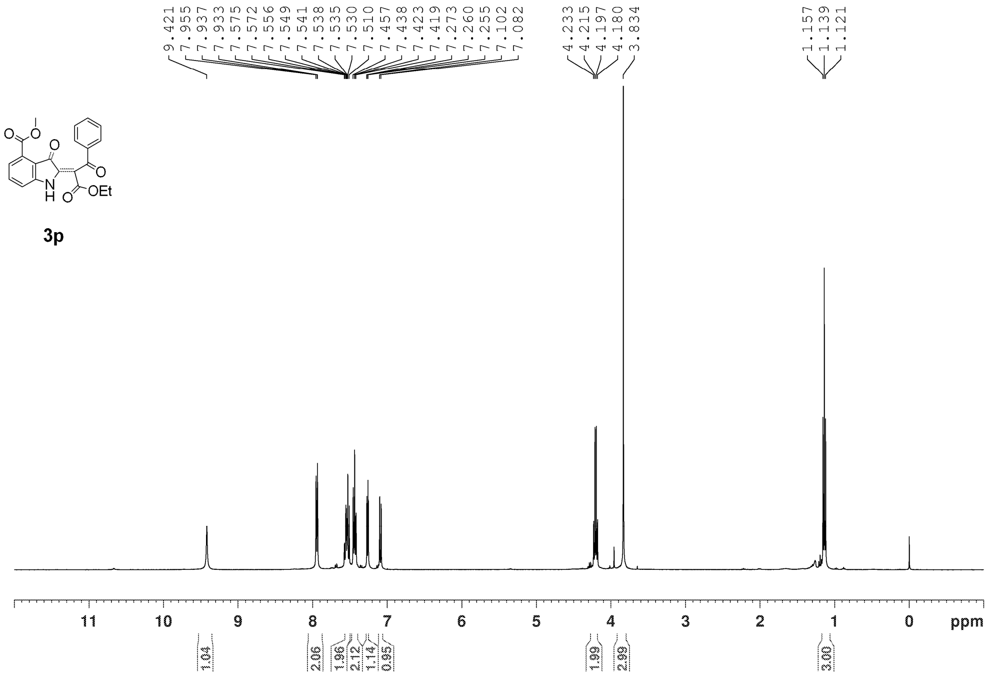
3n


9.563
8.247
8.243
8.226
7.990
7.971
7.619
7.601
7.582
7.498
7.479
7.460
7.284
7.044
7.022
4.279
4.261
4.243
4.226
3.899
1.202
1.185
1.167
O
O
O
N
H
O
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.07
1.92
2.00
1.10
2.14
1.11
2.08
3.00
3.05

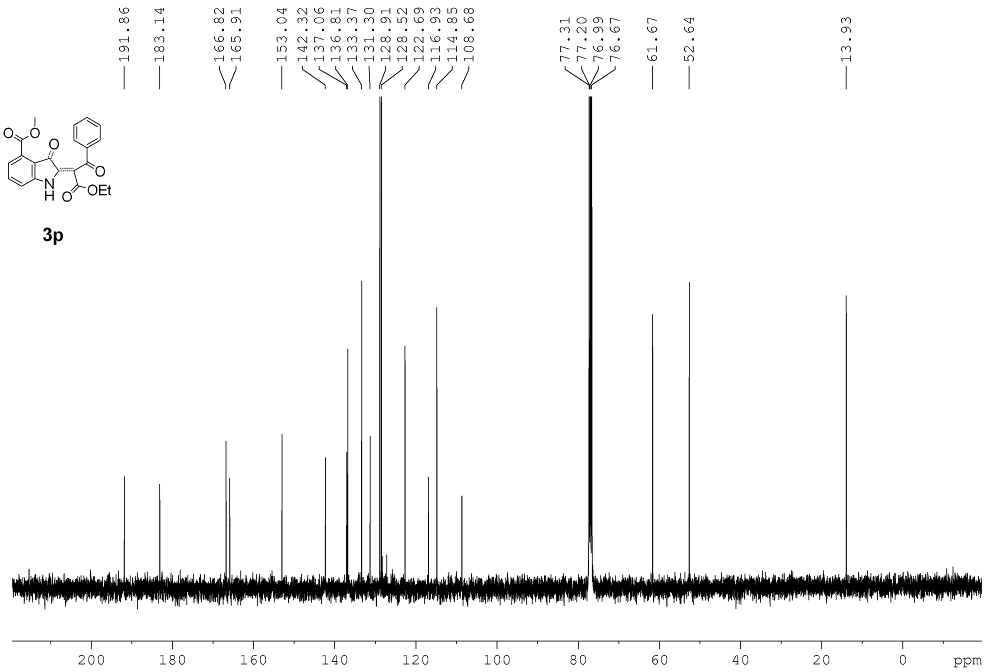
3o

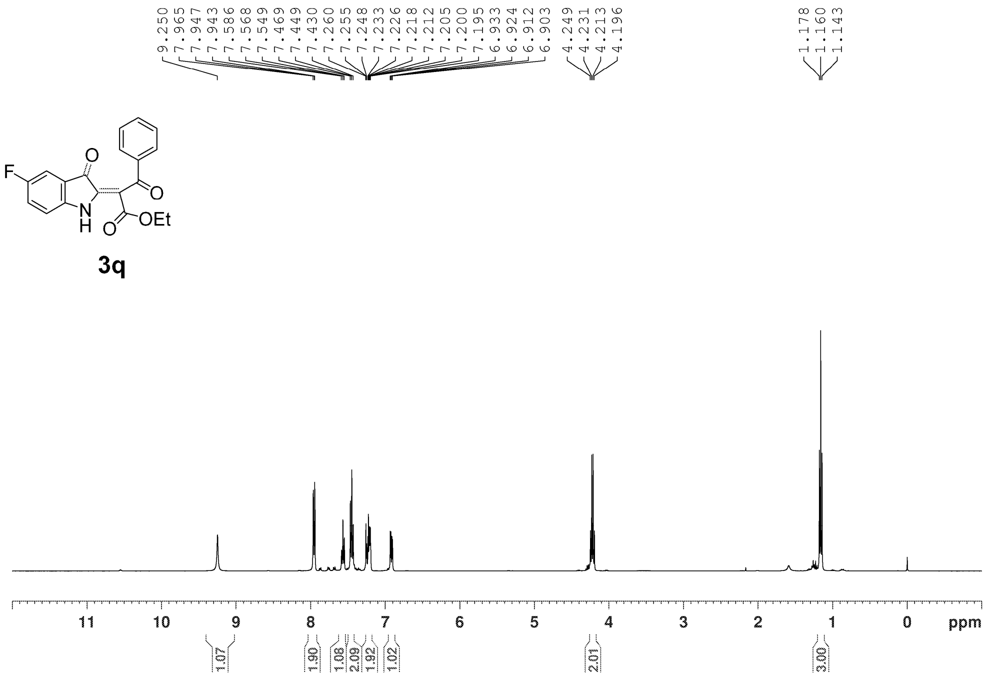

191.62
185.04
166.52
165.78
155.11
142.57
138.98
136.96
133.59
128.83
128.62
128.39
127.52
127.27
124.22
119.75
111.59
109.75
77.33
77.22
77.01
76.70
61.91
52.24
13.95
O
O
O
N
H
O
O
OEt
200
180
160
140
120
100
80
60
40
20
0
ppm

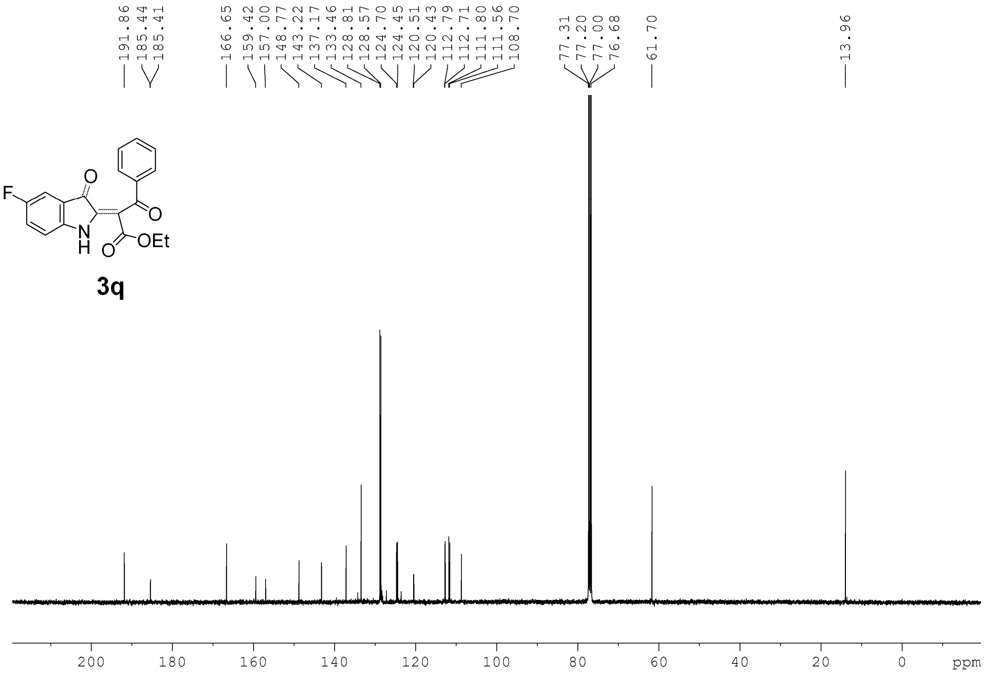
3o

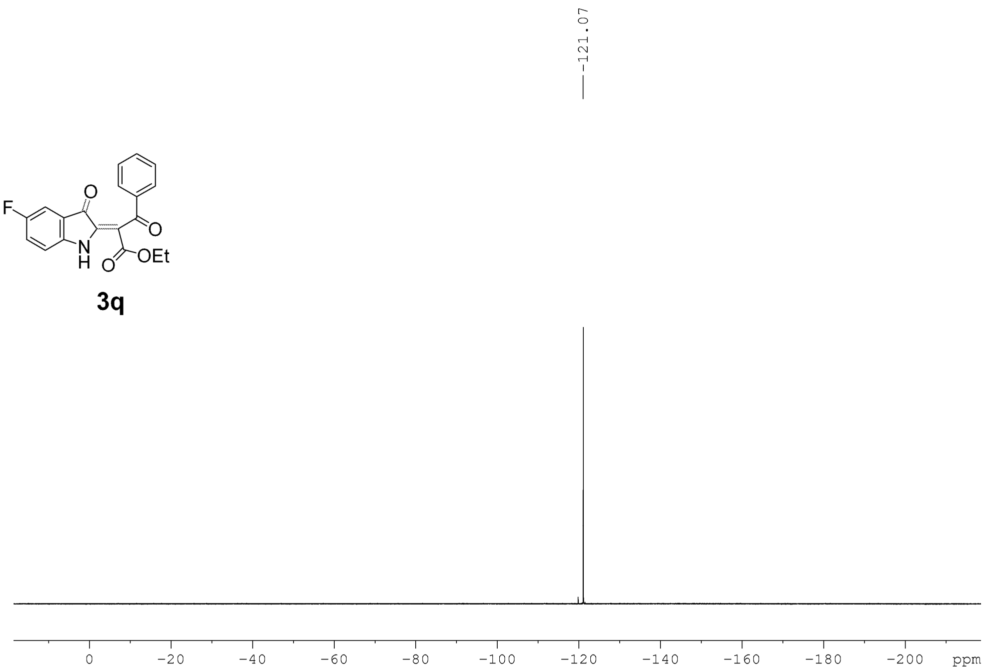

9.421
7.955
7.937
7.933
7.575
7.572
7.556
7.549
7.541
7.538
7.535
7.530
7.510
7.457
7.438
7.423
7.419
7.273
7.260
7.255
7.102
7.082
4.233
4.215
4.197
4.180
3.834
1.157
1.139
1.121
O
O
O
N
H
O
O
OEt
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.04
2.06
1.96
2.12
1.14
0.95
1.99
2.99
3.00

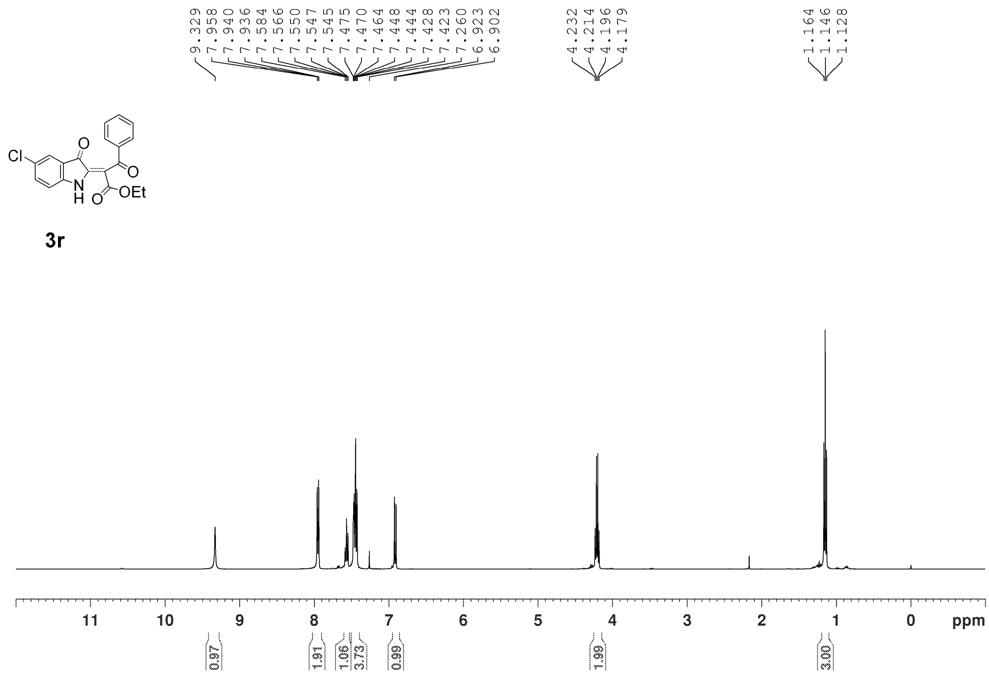
3p

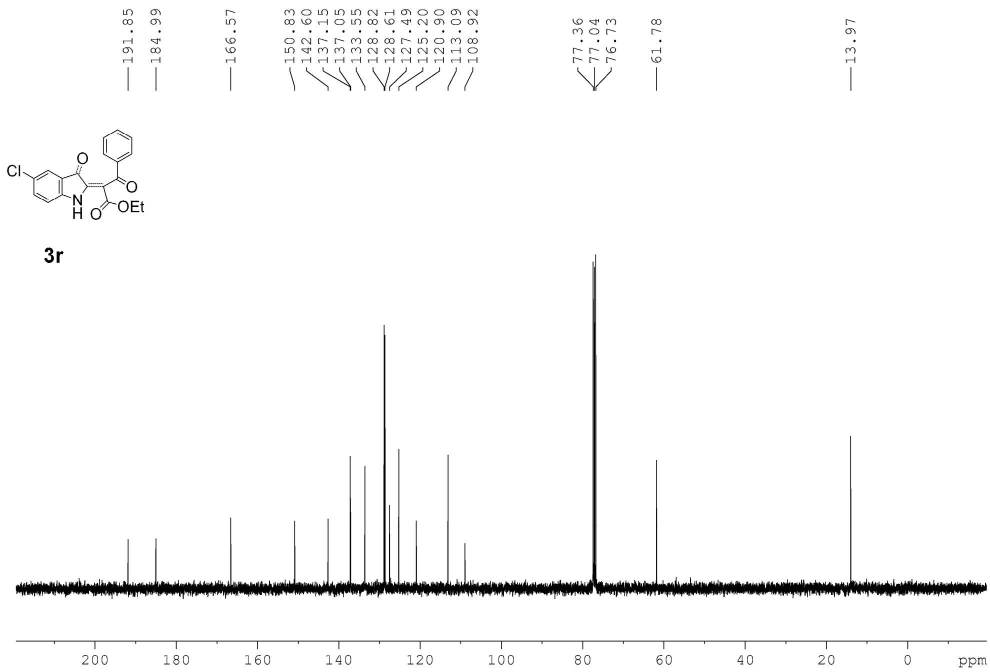

191.86
183.14
166.82
165.91
153.04
142.32
137.06
136.81
133.37
131.30
128.91
128.52
122.69
116.93
114.85
108.68
77.31
77.20
76.99
76.67
61.67
52.64
13.93
O
O
O
O
N
H
O
OEt
3p
200
180
160
140
120
100
80
60
40
20
0
ppm

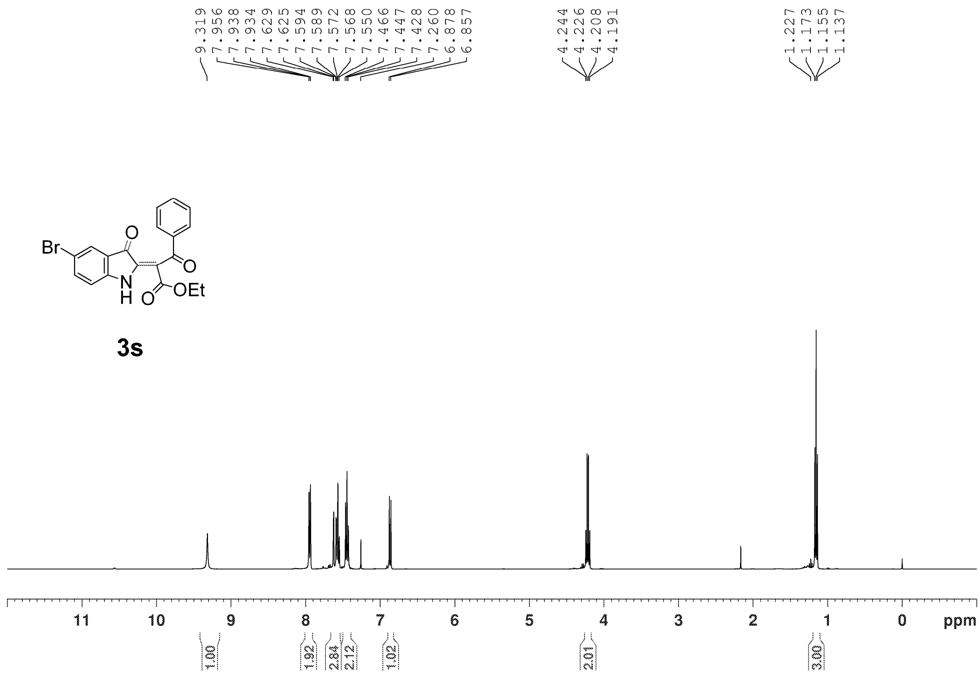

9.250
7.965
7.947
7.943
7.586
7.568
7.549
7.469
7.449
7.430
7.260
7.255
7.248
7.233
7.226
7.218
7.212
7.205
7.200
7.195
6.933
6.924
6.912
6.903
4.249
4.231
4.213
4.196
1.178
1.160
1.143
F
O
O
N
H
O
OEt
3q
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.07
1.90
1.08
2.09
1.92
1.02
2.01
3.00

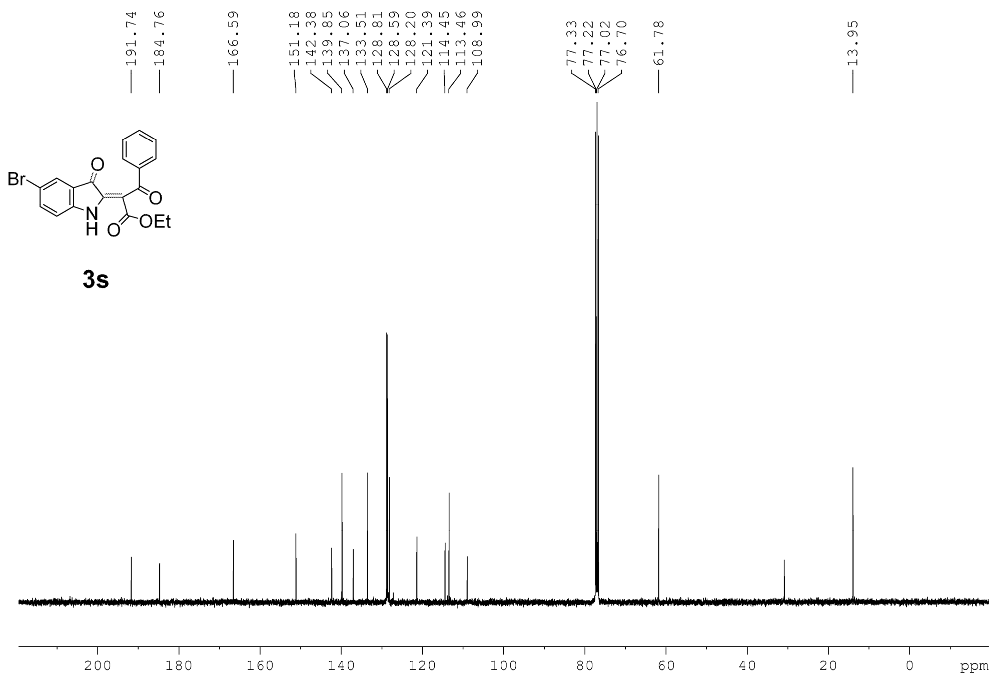

191.86
185.44
185.41
166.65
159.42
157.00
148.77
143.22
137.17
133.46
128.81
128.57
124.70
124.45
120.51
120.43
112.79
112.71
111.80
111.56
108.70
77.31
77.20
77.00
76.68
61.70
13.96
F
O
N
H
O
OEt
O
3q
200
180
160
140
120
100
80
60
40
20
0
ppm

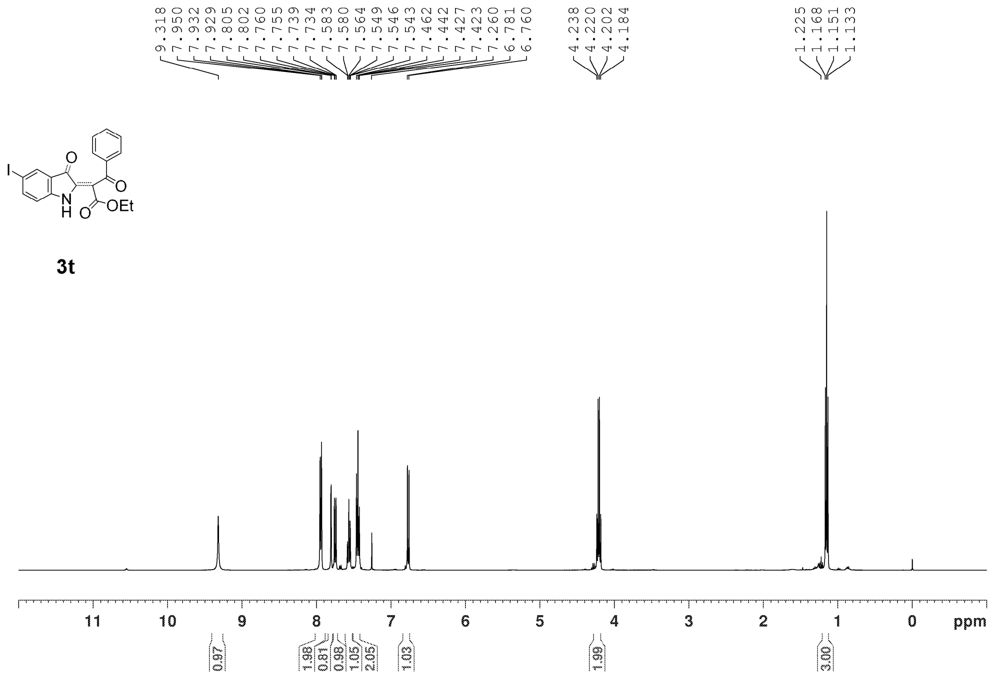

-121.07
F
O
N
H
O
OEt
O
3q
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

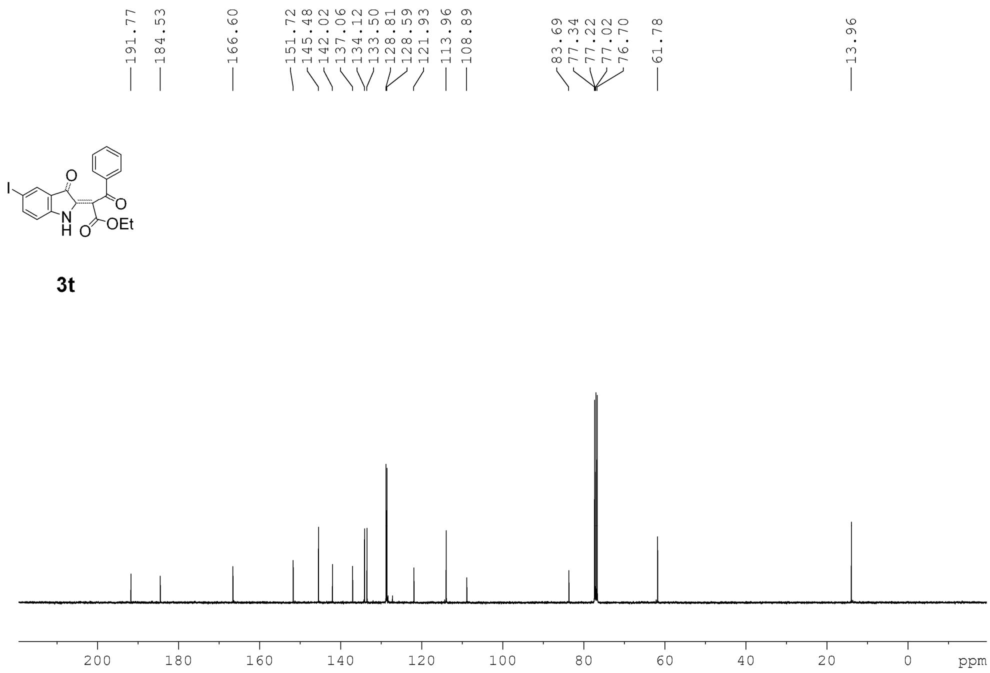

9.329
7.958
7.940
7.936
7.584
7.566
7.550
7.547
7.545
7.475
7.470
7.464
7.448
7.444
7.428
7.423
7.260
6.923
6.902
4.232
4.214
4.196
4.179
1.164
1.146
1.128
3r
0.97
1.91
1.06
3.73
0.99
1.99
3.00
11 10 9 8 7 6 5 4 3 2 1 0 ppm

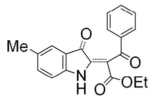

191.85
184.99
166.57
150.83
142.60
137.15
137.05
133.55
128.82
128.61
127.49
125.20
120.90
113.09
108.92
77.36
77.04
76.73
61.78
13.97
3r
200 180 160 140 120 100 80 60 40 20 0 ppm



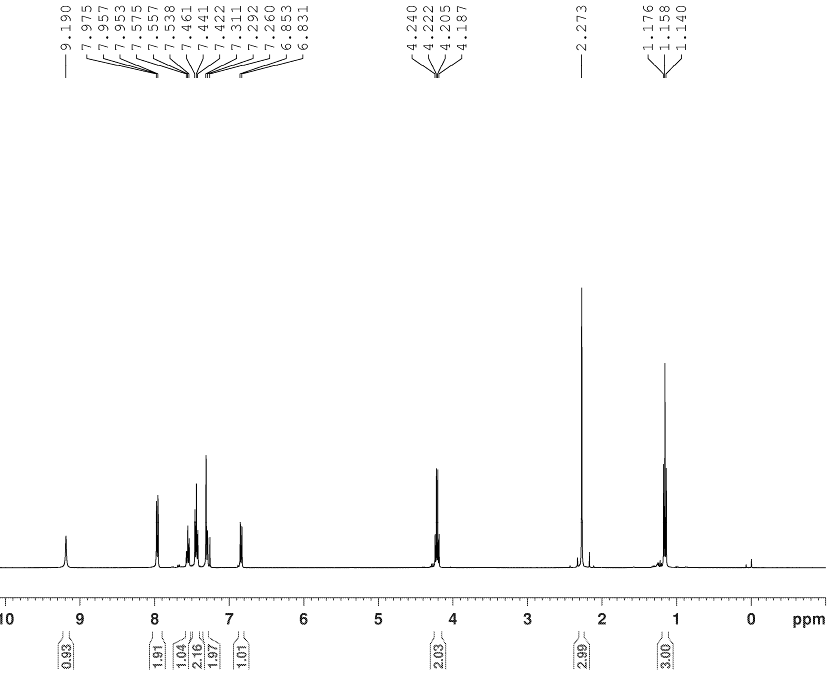


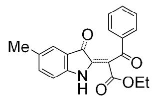

9.318
7.950
7.932
7.929
7.805
7.802
7.760
7.755
7.739
7.734
7.583
7.580
7.564
7.549
7.546
7.543
7.462
7.442
7.427
7.423
7.260
6.781
6.760
4.238
4.220
4.202
4.184
1.225
1.168
1.151
1.133
I
O
O
N
H
O
OEt
3t
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
1.98
0.81
0.98
1.05
2.05
1.03
1.99
3.00


191.77
184.53
166.60
151.72
145.48
142.02
137.06
134.12
133.50
128.81
128.59
121.93
113.96
108.89
83.69
77.34
77.22
77.02
76.70
61.78
13.96
I
O
O
N
H
O
OEt
3t
200
180
160
140
120
100
80
60
40
20
0
ppm

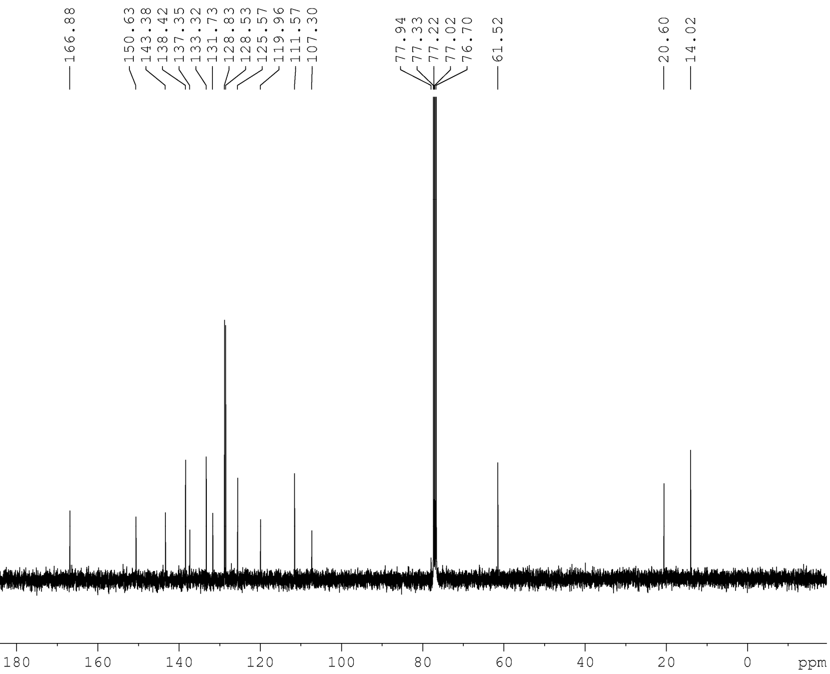

Me
O
N
H
O
O
OEt

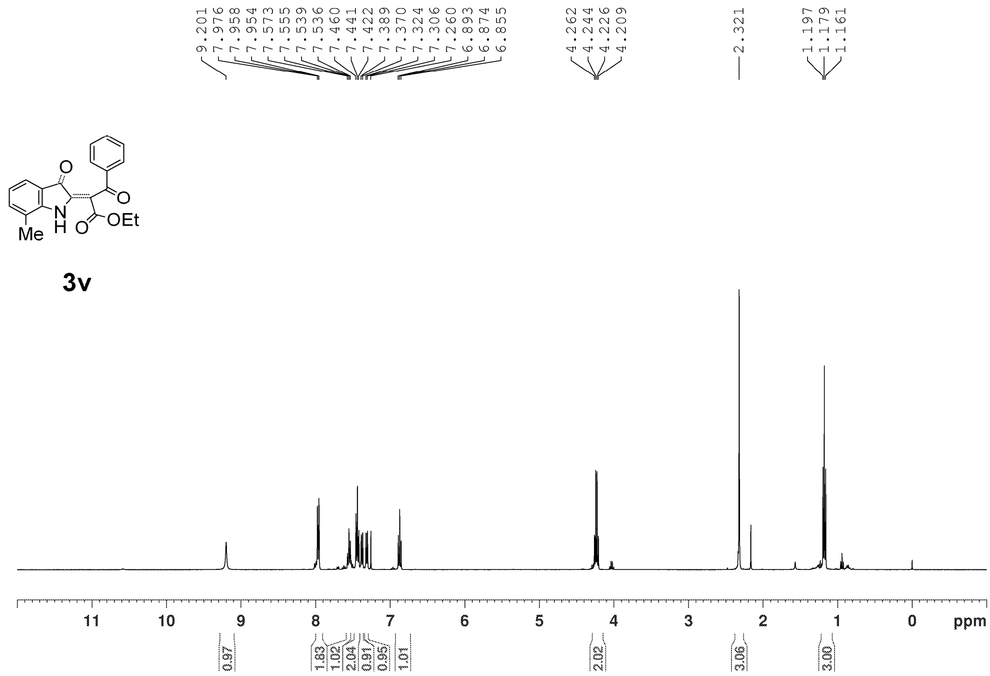
3u

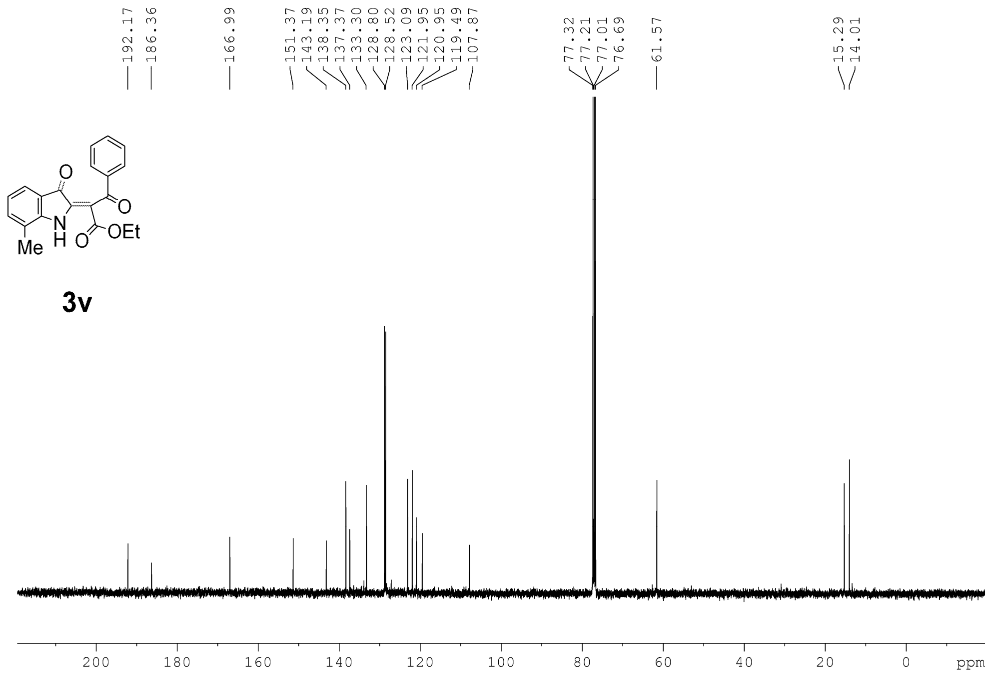

9.190
7.975
7.957
7.953
7.575
7.557
7.538
7.461
7.441
7.422
7.311
7.292
7.260
6.853
6.831
4.240
4.222
4.205
4.187
2.273
1.176
1.158
1.140
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.93
1.91
1.04
2.16
1.97
1.01
2.03
2.99
3.00

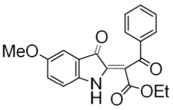

Me
O
N
H
O
O
OEt

3u

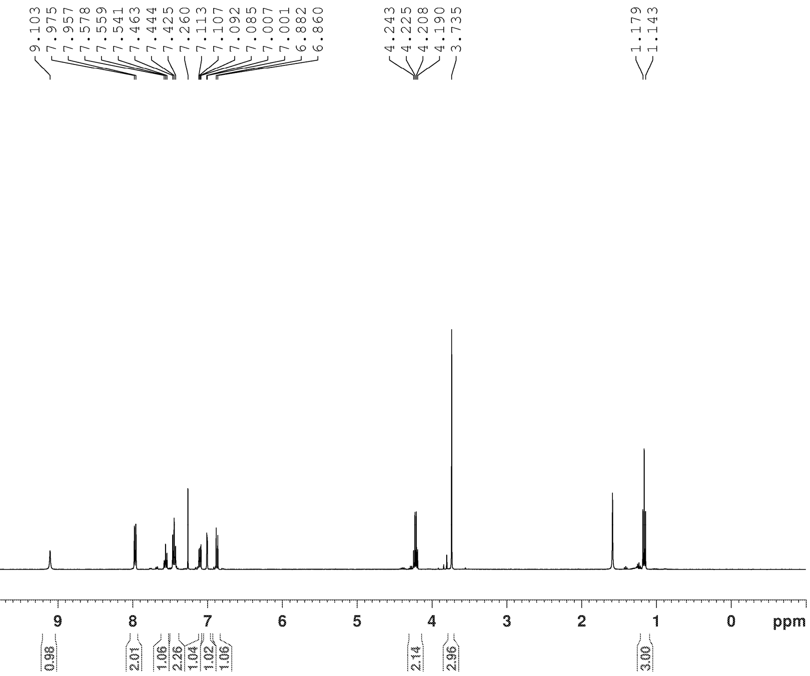

192.42
186.17
166.88
150.63
143.38
138.42
137.35
133.32
131.73
128.83
128.53
125.57
119.96
111.57
107.30
77.94
77.33
77.22
77.02
76.70
61.52
20.60
14.02
200
180
160
140
120
100
80
60
40
20
0
ppm

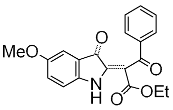

9.201
7.976
7.958
7.954
7.573
7.555
7.539
7.536
7.460
7.441
7.422
7.389
7.370
7.324
7.306
7.260
6.893
6.874
6.855
4.262
4.244
4.226
4.209
2.321
1.197
1.179
1.161
O
O
N
H
O
OEt
Me
3v
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
1.83
1.02
2.04
0.91
0.95
1.01
2.02
3.06
3.00


192.17
186.36
166.99
151.37
143.19
138.35
137.37
133.30
128.80
128.52
123.09
121.95
120.95
119.49
107.87
77.32
77.21
77.01
76.69
61.57
15.29
14.01
O
O
N
H
O
OEt
Me
3v
200
180
160
140
120
100
80
60
40
20
0
ppm

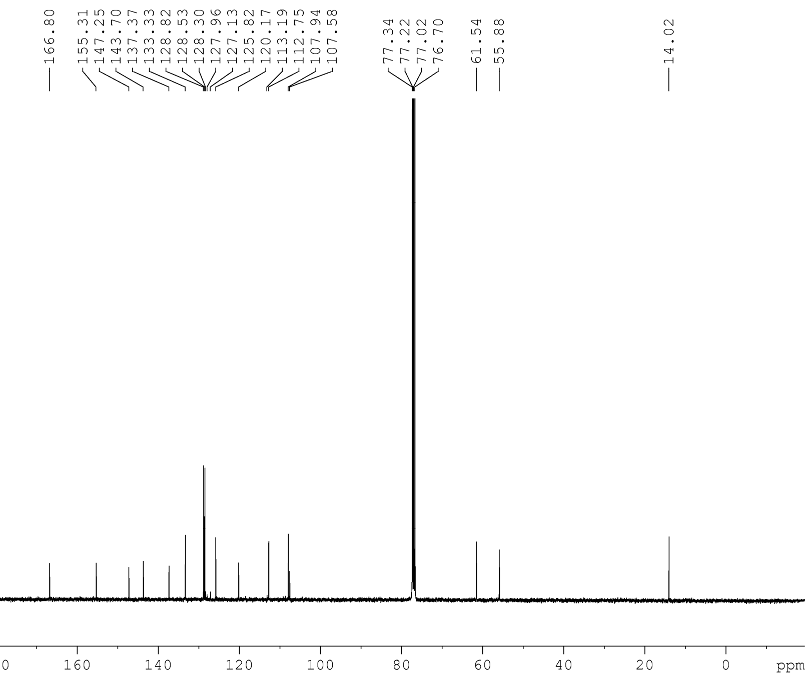

MeO
O
N
H
O
O
OEt

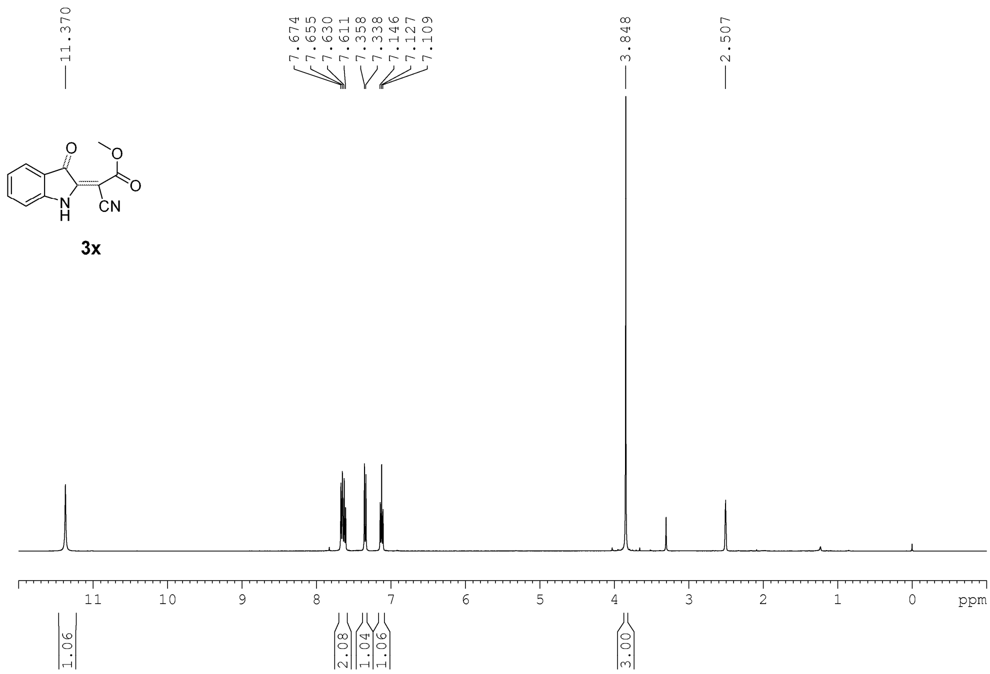
3w

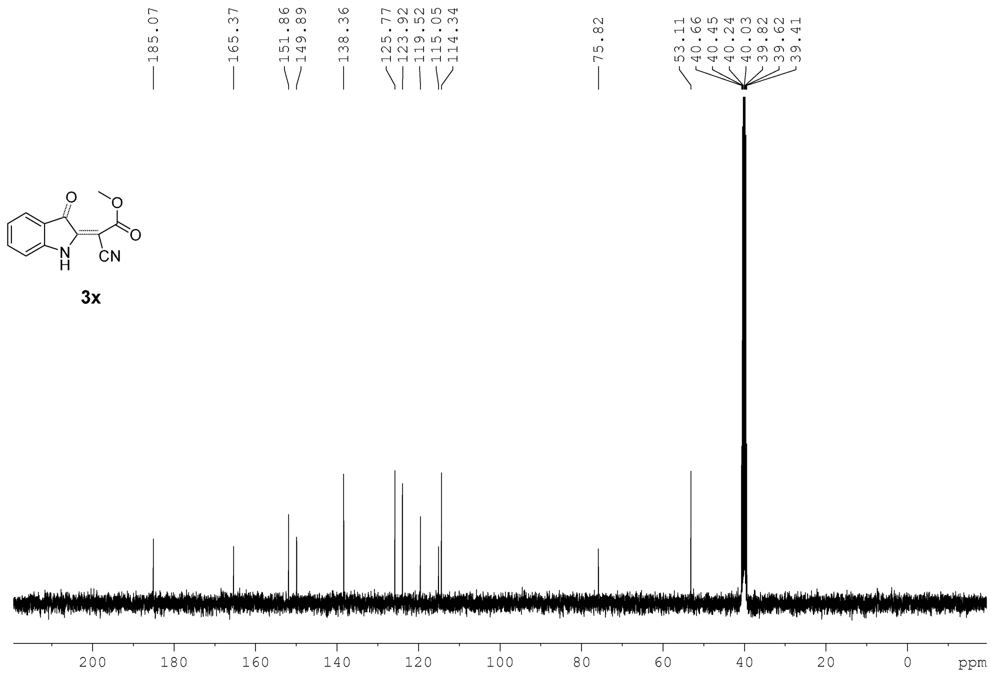

9.103
7.975
7.957
7.578
7.559
7.541
7.463
7.444
7.425
7.260
7.113
7.107
7.092
7.085
7.007
7.001
6.882
6.860
4.243
4.225
4.208
4.190
3.735
1.179
1.143
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
2.01
1.06
2.26
1.04
1.02
1.06
2.14
2.96
3.00

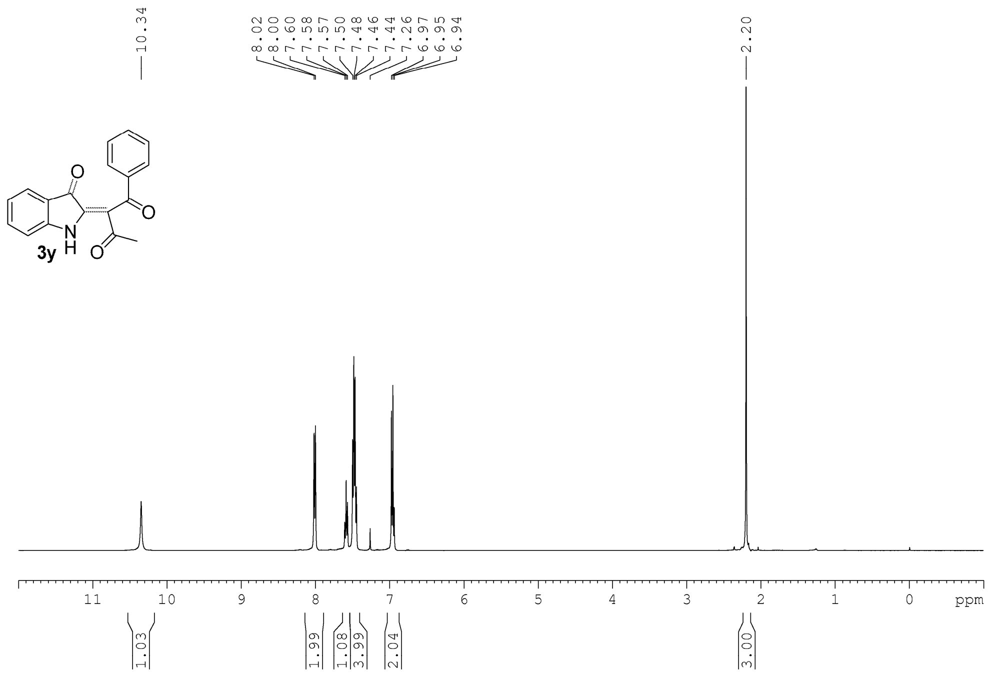

MeO
O
N
H
O
O
OEt

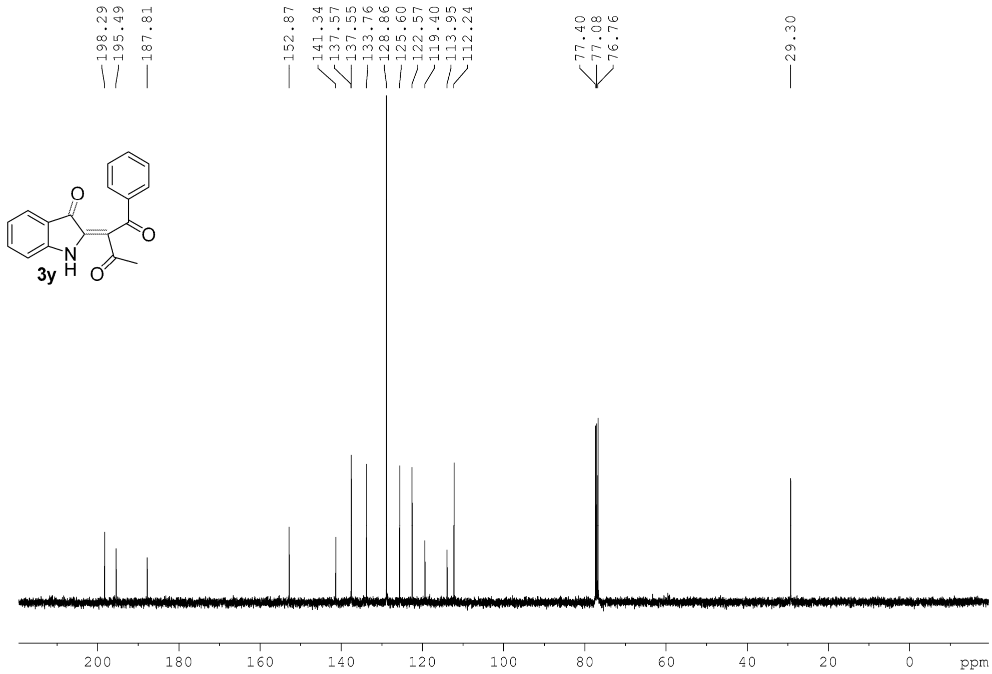
3w

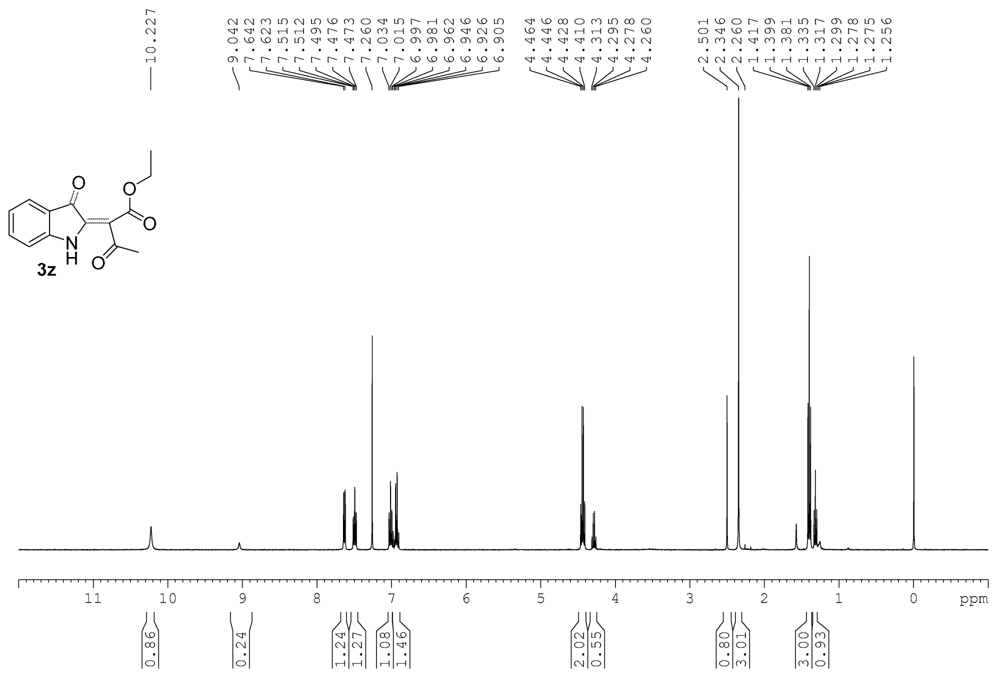

192.38
186.21
166.80
155.31
147.25
143.70
137.37
133.33
128.82
128.53
128.30
127.96
127.13
125.82
120.17
113.19
112.75
107.94
107.58
77.34
77.22
77.02
76.70
61.54
55.88
14.02
200
180
160
140
120
100
80
60
40
20
0
ppm


11.370
7.674
7.655
7.630
7.611
7.358
7.338
7.146
7.127
7.109
3.848
2.507
3x
1.06
2.08
1.04
1.06
3.00
ppm

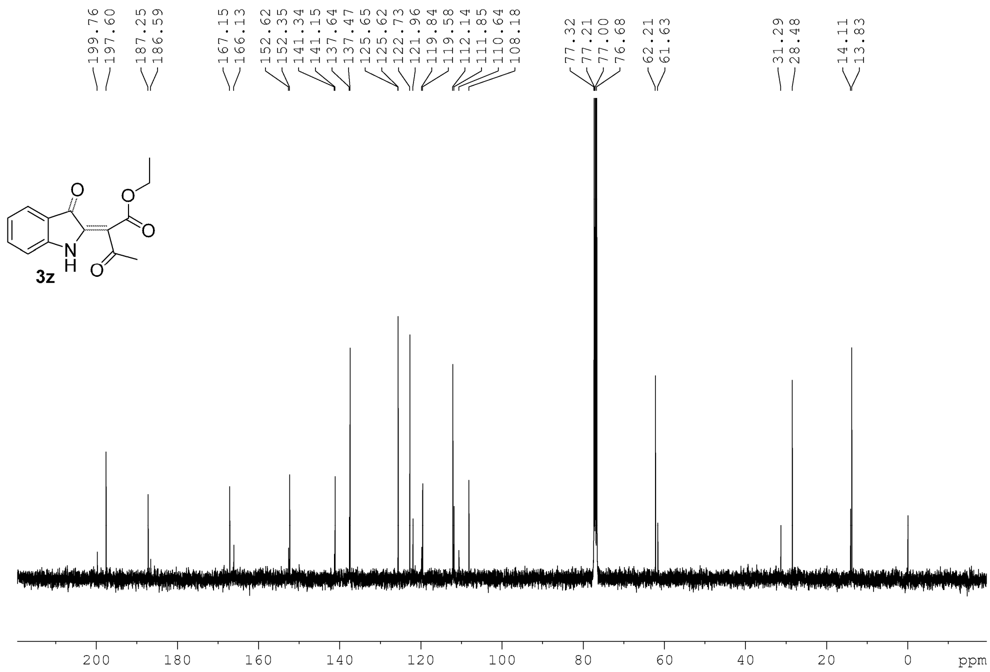

185.07
165.37
151.86
149.89
138.36
125.77
123.92
119.52
115.05
114.34
75.82
53.11
40.66
40.45
40.24
40.03
39.82
39.62
39.41
3x
ppm


10.34
8.02
8.00
7.60
7.58
7.57
7.50
7.48
7.46
7.44
7.26
6.97
6.95
6.94
2.20
3y
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.03
1.99
1.08
3.99
2.04
3.00


198.29
195.49
187.81
152.87
141.34
137.57
137.55
133.76
128.86
125.60
122.57
119.40
113.95
112.24
77.40
77.08
76.76
29.30
3y
200 180 160 140 120 100 80 60 40 20 0 ppm


10.227
9.042
7.642
7.623
7.515
7.512
7.495
7.476
7.473
7.260
7.034
7.015
6.997
6.981
6.962
6.946
6.926
6.905
4.464
4.446
4.428
4.410
4.313
4.295
4.278
4.260
2.501
2.346
2.260
1.417
1.399
1.381
1.335
1.317
1.299
1.278
1.275
1.256
ppm
0.86
0.24
1.24
1.27
1.08
1.46
2.02
0.55
0.80
3.01
3.00
0.93

3z


199.76
197.60
187.25
186.59
167.15
166.13
152.62
152.35
141.34
141.15
137.64
137.47
125.65
125.62
122.73
121.96
119.84
119.58
112.14
111.85
110.64
108.18
77.32
77.21
77.00
76.68
62.21
61.63
31.29
28.48
14.11
13.83
ppm

3z

Table S2. Crystallographic Data for compound **3a**[a]

	compound **1**
chemical formula	$C_{19}H_{15}NO_4$
formula weight (g·mol^{-1})	321.32
space group	P2(1)/c
a (Å)	7.769(5)
b (Å)	11.658(7)
c (Å)	18.192(10)
β (deg)	95.910(12)
V (Å^3)	1639.0(16)
Z	4
T (K)	293(2)
λ (Å)	0.71073 Å
D_{calc} (g·cm^{-1})	1.302
μ (mm^{-1})	0.092
F (000)	672
Crystal size	0.5000 × 0.3000 × 0.2000 mm
Theta range for data collection	2.08 to 27.50 deg.
Limiting indices	-10≤h≤10
	-15≤k≤15
	-23≤l≤22
Reflections collected / unique	12330 / 3726 (R_{int} = 0.0316)
Data / restraints / parameters	3726 / 0 / 218
Goodness-of-fit on F^2	1.004
Final *R* indices ($I>2\sigma(I)$)	*R*1 = 0.0666, *wR*2 = 0.2427
R indices (all data)	*R*1 = 0.0892, *wR*2 = 0.2740

[a] *R* defined as $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and *R*w defined as $(\Sigma[w(Fo^2 - Fc^2)^2]/\Sigma[wFo^4])^{1/2}$.

Table S3. Bond lengths [Å] and angles [deg] for compound **3a**

Bond lengths [Å]			
O(1)-C(7)	1.216(3)	O(2)-C(10)	1.333(3)
O(2)-C(11)	1.451(3)	O(3)-C(10)	1.215(3)
O(4)-C(13)	1.208(3)	N(1)-C(8)	1.366(3)
N(1)-C(1)	1.394(3)	C(1)-C(2)	1.381(4)
C(1)-C(6)	1.396(4)	C(2)-C(3)	1.380(4)
C(3)-C(4)	1.377(4)	C(4)-C(5)	1.368(4)
C(5)-C(6)	1.393(4)	C(6)-C(7)	1.457(4)
C(7)-C(8)	1.518(3)	C(8)-C(9)	1.350(3)
C(9)-C(10)	1.474(3)	C(9)-C(13)	1.514(3)
C(11)-C(12)	1.482(5)	C(13)-C(14)	1.484(3)
C(14)-C(19)	1.383(4)	C(14)-C(15)	1.397(4)
C(15)-C(16)	1.386(4)	C(16)-C(17)	1.377(6)
C(17)-C(18)	1.382(6)	C(18)-C(19)	1.378(4)
Bond angles [deg]			
C(10)-O(2)-C(11)	116.5(2)	C(8)-N(1)-C(1)	110.9(2)
C(2)-C(1)-N(1)	128.5(2)	C(2)-C(1)-C(6)	121.3(2)
N(1)-C(1)-C(6)	110.2(2)	C(3)-C(2)-C(1)	117.1(3)
C(4)-C(3)-C(2)	122.3(3)	C(5)-C(4)-C(3)	120.7(3)
C(4)-C(5)-C(6)	118.5(3)	C(5)-C(6)-C(1)	120.1(2)
C(5)-C(6)-C(7)	132.7(2)	C(1)-C(6)-C(7)	107.3(2)
O(1)-C(7)-C(6)	129.8(2)	O(1)-C(7)-C(8)	125.0(2)
C(6)-C(7)-C(8)	105.2(2)	C(9)-C(8)-N(1)	128.7(2)
C(9)-C(8)-C(7)	124.9(2)	N(1)-C(8)-C(7)	106.4(2)
C(8)-C(9)-C(10)	120.0(2)	C(8)-C(9)-C(13)	122.4(2)
C(10)-C(9)-C(13)	117.6(2)	O(3)-C(10)-O(2)	123.7(2)
O(3)-C(10)-C(9)	124.4(2)	O(2)-C(10)-C(9)	111.9(2)
O(2)-C(11)-C(12)	107.7(3)	O(4)-C(13)-C(14)	122.2(2)
O(4)-C(13)-C(9)	119.1(2)	C(14)-C(13)-C(9)	118.63(19)
C(19)-C(14)-C(15)	119.9(2)	C(19)-C(14)-C(13)	119.0(2)
C(15)-C(14)-C(13)	121.1(2)	C(16)-C(15)-C(14)	119.7(3)
C(17)-C(16)-C(15)	119.7(3)	C(16)-C(17)-C(18)	120.7(3)
C(19)-C(18)-C(17)	119.9(3)	C(18)-C(19)-C(14)	120.0(3)

Table S4. Atomic coordinates (×10^4) and equivalent isotropic displacement parameters (Å^2×10^3) for compound **3a**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	944(3)	5297(2)	8029(1)	72(1)
O(2)	2980(2)	2717(2)	10272(1)	60(1)
O(3)	2825(3)	4463(2)	10784(1)	73(1)
O(4)	121(2)	2929(2)	8809(1)	70(1)
N(1)	1910(3)	6247(2)	9836(1)	55(1)
C(1)	1518(3)	7279(2)	9469(1)	53(1)
C(2)	1551(4)	8376(2)	9757(2)	67(1)
C(3)	1135(5)	9263(3)	9269(2)	78(1)
C(4)	683(4)	9080(3)	8527(2)	79(1)
C(5)	651(4)	7995(3)	8240(2)	69(1)
C(6)	1075(3)	7079(2)	8716(1)	55(1)
C(7)	1174(3)	5846(2)	8599(1)	54(1)
C(8)	1712(3)	5343(2)	9357(1)	50(1)
C(9)	1977(3)	4216(2)	9498(1)	49(1)
C(10)	2634(3)	3837(2)	10248(1)	53(1)
C(11)	3723(4)	2263(3)	10976(2)	70(1)
C(12)	3958(6)	1010(3)	10887(2)	104(1)
C(13)	1577(3)	3301(2)	8916(1)	51(1)
C(14)	3018(3)	2835(2)	8530(1)	50(1)
C(15)	4615(3)	3393(3)	8567(2)	69(1)
C(16)	5947(4)	2921(4)	8214(2)	89(1)
C(17)	5692(5)	1897(4)	7842(2)	97(1)
C(18)	4100(6)	1358(3)	7790(2)	87(1)
C(19)	2761(4)	1830(2)	8129(2)	64(1)

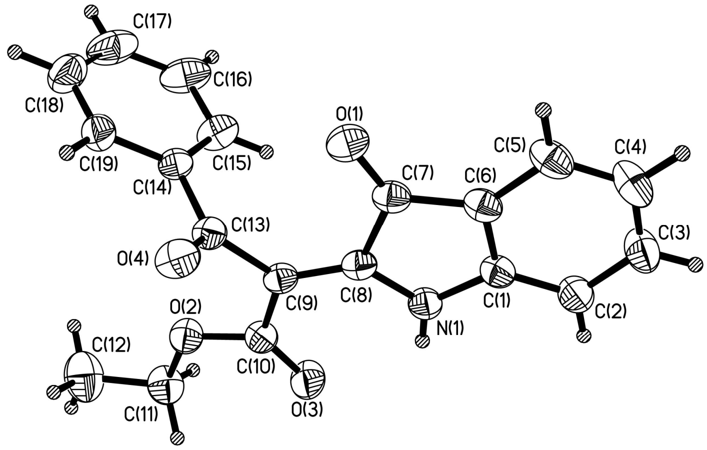


Figure 1. ORTEP diagram of compound **3a** (ellipsoids at 30% probability.)