Supporting Information

Controllable Construction of Isoquinolinedione and Isocoumarin Scaffolds via Rh^{III}-Catalyzed C-H Annulation of *N*-tosylbenzamides with Diazo Compounds

Yanfei Liu, Jiaping Wu,* Baiyang Qian, Yongjia Shang*

Key Laboratory of Functional Molecular Solids, Ministry of Education, Anhui Key Laboratory of Molecule-Based Materials, College of Chemistry and Materials Science, Anhui Normal University, Wuhu 241002, P.R. China

E-mail: *wujiaping@ahnu.edu.cn; shyj@mail.ahnu.edu.cn*

General Information 2

Experimental Procedures 2

1. Synthesis of *N*-tosylbenzamides 2

2. Synthesis of *N*-methoxybenzamide 2-3

3. Synthesis of diazo compounds 3

4. Optimization of reaction conditions 3-7

5. General procedure for the preparation of 3 7

6. General procedure for the preparation of 4 8

References 8

Characterization Data of 3a-q, 8 and 9 9-14

Characterization Data of 4a-p, 4t-z 14-20

NMR (^{1}H NMR and ^{13}C NMR) Spectra 21-62

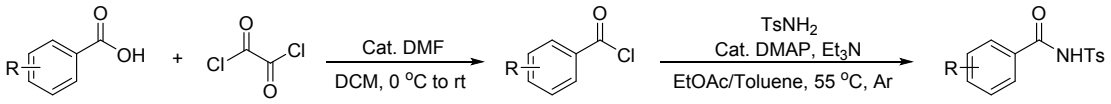
Crystal Structures of 3a 63

I General Information

All reactions were carried under Ar atmosphere unless otherwise noted. All chemicals were used without further purification as commercially available. Reactions were monitored by using thin-layer chromatography (TLC) on commercial silica gel plates (GF 254). Visualization of the developed plates was performed under UV lights (254 and 365 nm). Flash column chromatography was performed on silica gel (200-300 mesh). NMR (500 MHz or 400 MHz for ^{1}H NMR, 125 MHz or 100 MHR for ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard unless otherwise noted. Chemical shifts (δ) were reported in ppm referenced to the $CDCl_3$ residual peak (δ 7.28) for ^{1}H NMR. Chemical shifts of ^{13}C NMR were reported relative to $CDCl_3$ (δ 77.0). The following abbreviations were used to describe peak splitting patterns when appropriate: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m). Coupling constant, *J*, was reported in Hertz unit (Hz). High-resolution mass spectra (HRMS) analysis was measured using ESI techniques. The melting points were measured using X-4 melting point apparatus.

II Experimental Procedures

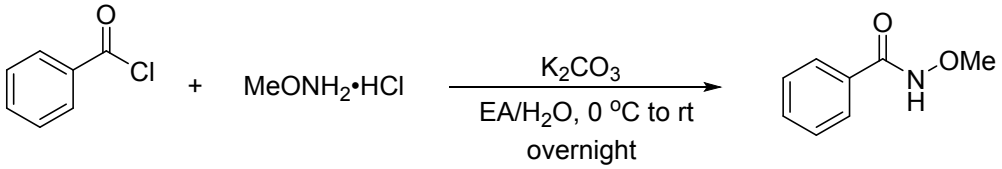
1. Synthesis of *N*-tosylbenzamides [1-5]



A 100mL round-bottom flask was charged with benzoic acid (3 mmol), DCM (10 mL) and catalytic amount of DMF (two drops). The reaction mixture was cooled to 0 °C and stired for 5 minutes. Then $(COCl)_2$ (3.6-9 mmol) was added dropwise to the reaction mixture and stirred for 3-12 h and monitored by TLC (petroleum ether/ethyl acetate 10:1. The resulting mixture was concentrated under reduced pressure to afford acid chloride which was used directly without any further purification for the next step.

A 25mL reaction tube under Ar was filled with *p*-toluene sulfonamide (1.0 eq), DMAP (0.5 mol %), ethyl acetate (2 mL/mmol) and triethylamide (2.5 eq). A solution of acid chloride (1.1 eq) in toluene (0.8 mL/mmol) was added dropwise at room temperature. The mixture was stirred for 1 h at 55 °C under Ar, cooled to room temperature and quenched with a solution of hydrochloric acid (0.5 M).The resulting mixture was then extracted with ethyl acetate (3 times). The combined organic layers were dried on $NaSO_4$, filtered and evaporated. The residue was purified by passing through a pad of silica gel eluting with CH_2Cl_2 or petroleum ether/ethyl acetate 5:1 to 3:1.

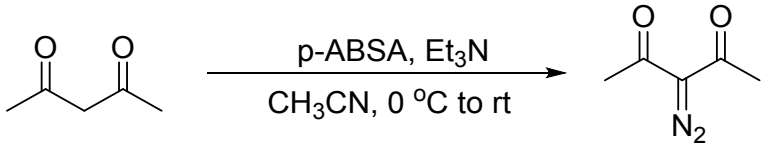
2. Synthesis of N-methoxybenzamide [6]



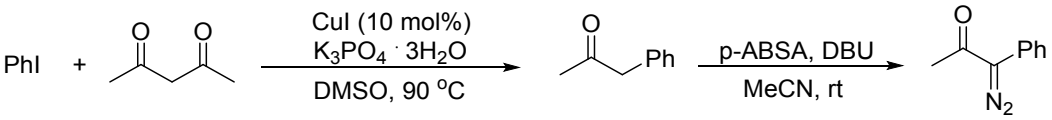
To a solution of K_2CO_3 (6.0 mmol, 2.0 equiv) in a mixture of EA/H2O (30 mL, 2:1) was added O-methylhydroxylamine hydrochloride (3.6 mmol, 1.2 equiv). The resulting solution was cooled to 0 °C, followed by dropwise addition of the benzoyl chloride (3.0 mmol, 1.0 equiv). The reaction mixture was warmed to room temperature and stirred for overnight. The organic phase was separated and the aqueous phase was extracted with EtOAc (20 mL × 3). The combined organic layers were dried over

Na_2SO_4, filtered, and evaporated under reduced pressure. The pure products were obtained by flash column chromatography.

3. Synthesis of diazo compounds [7-9]



A 100 mL round-bottomed flask was charged with acetylacetone (10 mmol) and acetonitrile (60 mL). *p*-Acetamidobenzene sulfonylazide (*p*-ABSA) (11-12 mmol) was added and the reaction was cooled to 0 °C. Trimethylamine (Et_3N) (30 mmol) was added dropwise and the reaction was warmed to room temperature for 1 h. and monitored by TLC. The resulting suspension was filtered through a fritted funnel and concentrated. The obtained residue was triturated with 1:1 ether:petroleum ether and the precipitated white solids were removed via filtration and evaporated. The residue was purified by passing through a pad of silica gel eluting with petroleum ether/ethyl acetate 2:1.

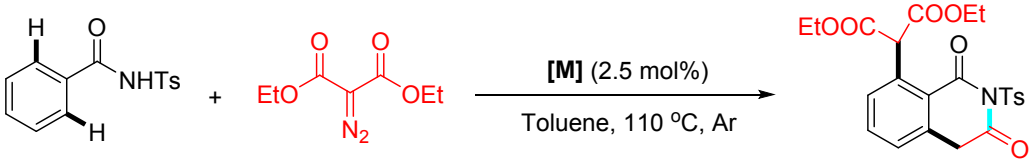


A mixture of iodobenzene (1.0 mmol), acetylacetone (3.0 mmol), CuI (10 mol%) and $K_3PO_4 \cdot 3H_2O$ (3.0 mmol) in DMSO (3 mL) was stirred in Ar at 90 °C. After completion of the reaction, it was monitored by TLC. And then, the mixture was quenched with diluted hydrochloride (2mL, 2M), the solution was extracted with ethyl acetate (3 times). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel eluting with petroleum ether/ethyl acetate 20:1.

And then, the product was dissolved in acetonitrile (2 mL/mmol) and P-ABSA (1.2 eq) was added. The solution was stirred at room temperature for 5 minutes and cooled to 0 °C. DBU (1.3 eq) was added dropwise and the mixture was stirred at room temperature for 3 h and monitored by TLC. The reaction was then quenched with 10 w% NaOH (aq), followed by extraction with EtO_2 (2 times). The combined organic layers were anhydrous sodium sulfate and concentrated under reduced pressure. The yellow crude product was purified by silica gel column chromatography eluting by petroleum ether/ethyl acetate 10:1 to afford product as yellow solid.

4. Optimization of reaction conditions

Screening of Catalyst



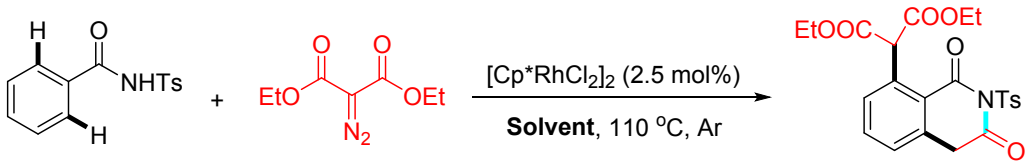
1a **2a** **3a**

Entry[a]	[M]	Yiled[b] %
1	**$[Cp^*RhCl_2]_2$**	**44**
2	$[Rh(OAc)_2]_2$	NR

3	$(PPh_3)_3RuCl_2$	NR
4	$[Cp^*IrCl_2]_2$	Trace
5	$Pd(OAc)_2$	NR

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), **[M]** (0.0025 mmol) in Toluene (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield.

Screening of Solvent I

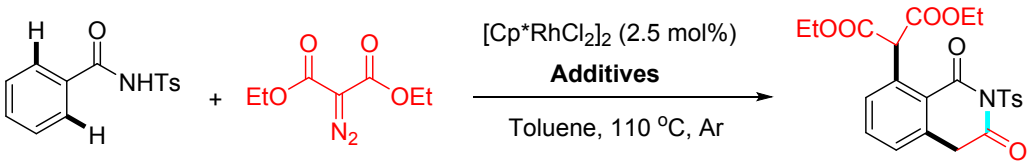


1a **2a** **3a**

Entry[a]	Solvent	Yield[b] %
1	DCE	32
2	THF	19
3	Dioxane	15
4	MeCN	22
5	DMF	0
6	MeOH	0
7	EtOH	0
8	DCM	34
9	EtOAc	41
10	$CHCl_3$	15
11	DMSO	Trace
12	DMA	0
13	CCl_4	Trace
14	TFE	0
15	DME	40
16	**Toluene**	**44**

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in Solvent (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield.

Screening of Additives



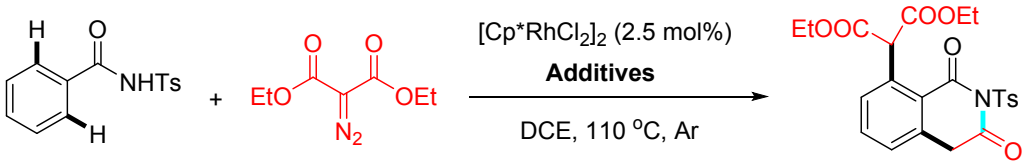
1a **2a** **3a**

Entry[a]	Additives (10 mol%)	Yield[b] %
1	$AgSbF_6$	0
2	$AgBF_4$	0

3	AgOTf	Trace
4	$AgN(Tf)_2$	0
5	LiOAc (2.1 eq)	Trace
6	Li_2CO_3 (2.1 eq)	31
7	*t*-BuOLi (2.1 eq)	Trace
8	LiCl (2.1 eq)	21
9[c]		Trace
10	Na_2CO_3	Trace
11	K_2CO_3	Trace
12	Li_2CO_3	37
13	Cs_2CO_3	14
14	Ag_2CO_3	34
15	H_2O (1.1 eq)	46
16	H_2O (1.1 eq) ,LiCl (2.1 eq)	25
17	H_2O (2.2 eq)	30
18	CsOPiv	10
19	AcOH(1.0 eq)	32
20	AcONa(1.0 eq)	22
21	AgOAc	44
22	CsOAc	15
23	PivOH	36
24	H_2O(1.1 eq) ,AcOH(1.0 eq)	43
25	H_2O(1.1 eq) ,AcONa	34
26	H_2O(1.1 eq) ,Ac_2O(1.0 eq)	55
27	Ac_2O(1.0 eq)	18
28	TFA(1.0 eq)	42
29	**H_2O(1.1 eq), TFA(1.0 eq)**	**61**
30	H_2O(1.1 eq), PivOH(1.0 eq)	47
31	H_2O(1.1 eq), TsOH(1.0 eq)	50
32	H_2O(1.1 eq), $B(OH)_3$(1.0 eq)	50
33	H_2O(1.1 eq) ,HCOOH(1.0 eq)	60
34	H_2O(2.2 eq) ,TFA(1.0 eq)	57
35	H_2O(1.1 eq) ,TFA(2.0 eq)	48
36	H_2O(1.1 eq) ,TOF(1.0 eq)	0

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in Toluene (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield. [c]Air reaction.

Replacement Solvent and Screening Quantity of Additives

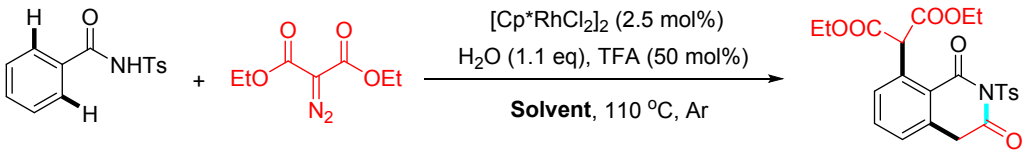


1a **2a** **3a**

Entry[a]	Additives	Yield[b] %
1	H_2O(1.1 eq) ,TFA(1.0 eq)	71
2	H_2O(2.2 eq) ,TFA(1.0 eq)	71
3	H_2O(1.1 eq), TFA(2.0 eq)	52
4	H_2O(1.1 eq) ,TFA(20 mol%)	51
5	**H_2O(1.1 eq) ,TFA(50 mol%)**	**77**

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in DCE (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield.

Screening of Solvent II

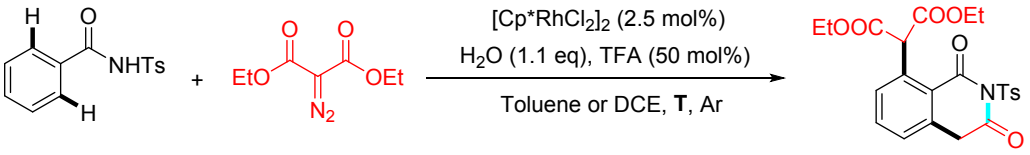


1a **2a** **3a**

Entry[a]	Solvent	Yield[b] %
1	Toluene	49
2	DCM	38
3	CH_3CN	66
4	THF	75
5	1,4-Dioxane	66

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in Solvent (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield.

Screening of Temperature



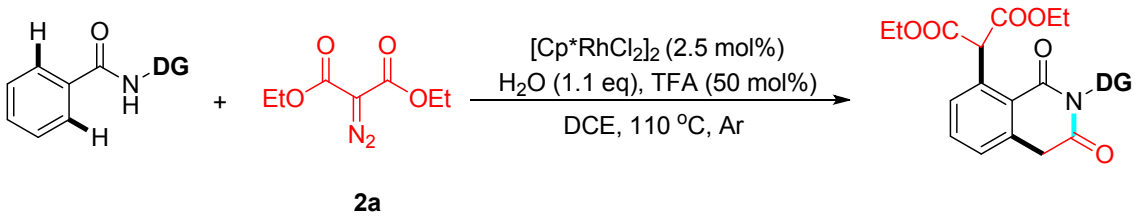
1a **2a** **3a**

Entry[a]	T. (°C)	Yield[b] %
1	90	27
2	100	35
3	**110**	**44**
4	120	33

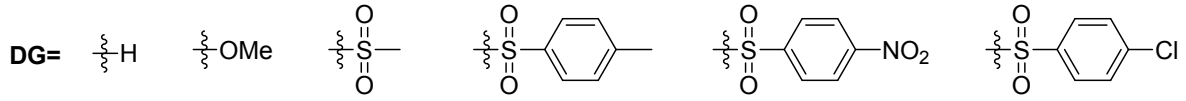
5[c]	90	32

[a]Reactions conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in Solvent (1.0 mL) at selected temperature under Ar for 24 h. [b]Isolated yield. [c]DCE.

Screening of Directing Groups



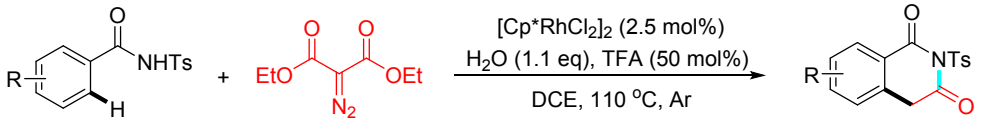
2a



Entry[a]	DG	Yield[b] %
1	H	0
2	OMe	0
3	Ms	NR
4	**Ts**	**77**
5	Ns	0
6	Cs	0

[a]Reactions conditions: **amides** (0.1 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol) in DCE (1.0 mL) at 110 °C under Ar for 24 h. [b]Isolated yield.

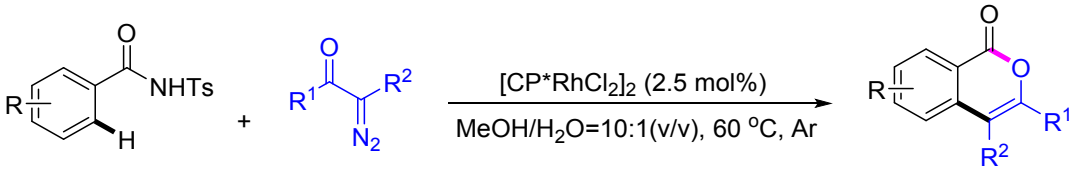
5. General procedure for the preparation of isoquinolinediones



1 **2a** **3**

A reaction tube charged with *N*-tosylcarboxamide (0.1 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%, 1.6 mg） and stir bar. H_2O (1.1 eq, 2.0 μL), TFA (50 mol%, 3.7μL) was added via microsyringe and diazo compounds (0.3 mmol) was added via syringe in the solvent DCE (2.0 mL) under Ar. After that, the mixture was stirred at 110 °C for 24 h. The pure product was obtained by flash column chromatography (silica gel) eluting by petroleum ether/ethyl acetate 6:1 to 3:1.

6. General procedure for the preparation of isocoumarins



1 **2** **4**

A reaction tube was charged with *N*-tosylcarboxamide (0.1 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%, 1.6 mg） and stir bar. Diazo (0.3 mmol) was added via syringe in the solvent MeOH/H_2O 10:1 under Ar. After that, the mixture was stirred at 60 ^oC for 24 h under Ar and monitored by TLC. The pure product was obtained by flash column chromatography (silica gel) eluting by petroleum ether/ethyl acetate 15:1 to 10:1.

Refferences

(1) S. Samanta, T. L. Lim, Y. Lam, *Chem. Med. Chem.* **2013**, *8*, 994.

(2) L.Wang, Y. B. Xie, N. Y. Huang, J. Y. Yan, W. M. Hu, M. G. Liu, M. W. Ding, *ACS Catal.* **2016**, *6*, 4010.

(3) R. Bisht, M. E. Hoque, B. Chattopadhyay, *Angew. Chem. Int. Ed.* **2018**, *57*, 15762.

(4) E. Dubost, V. Babin, F. Benoist, A. Hebert, P. Barbey, C. Chollet, J. P. Bouillon, A. Manrique, G. Pieters, F. Fabis, T. Cailly, *Org. Lett.* **2018**, *20*, 6302.

(5) F. Péron, C. Fossey, T. Cailly, F. Fabis, *Org. Lett.* **2012**, *14*, 1827.

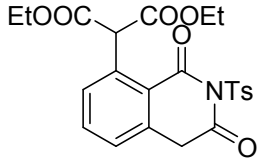
(6) Y. Fukui, P. Liu, Q. Liu, Z.-T. He, N.-Y. Wu, P. Tian, G.-Q. Lin, J. Am. Chem. Soc. ,2014, **136**, 15607.

(7) R. J. Sharpe, J. T. Malinowski, J. S. Johnson, *J. Am. Chem. Soc.* **2013**, *135*, 17990.

(8) C. He, S. Guo, L. Huang, A. W. Lei, *J. Am, Chem. Soc.* **2010**, *132*, 8273.

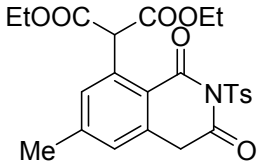
(9) J. Yang, C. Q. Ke, D. Zhang, X. H. Liu, X. M. Feng, *Org. Lett.* **2018**, *20*, 4536.

III Characterization Data of 3a-q, 8 and 9



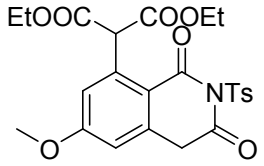
(3a) diethyl 2-(1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate

This compound was purified by column chromatography to afford a white solid in 77% yield (36 mg); Melting point: 119-121 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19-8.16 (m, 2H), 7.59-7.55 (m, 1H), 7.39-7.34 (m, 3H), 7.24-7.22 (m, 1H), 5.75 (s, 1H), 4.28-4.23 (m, 4H), 4.05 (s, 2H), 2.44 (s, 3H), 1.31-1.27 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 166.5, 163.4, 145.9, 136.3, 135.3, 134.1, 133.7, 129.7, 129.5, 127.6, 124.9, 62.0, 55.3, 39.7, 21.8, 14.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}NO_8S$ 474.1217; Found 474.1211.



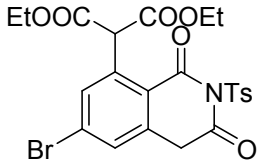
(3b) diethyl 2-(6-methyl-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate

This compound was purified by column chromatography to afford a white solid in 54% yield (26 mg); Melting point: 56-58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19-8.16 (m, 2H), 7.36-7.34 (m, 2H), 7.15 (s, 1H), 7.03 (s, 1H), 5.74 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 4H), 4.02 (s, 2H), 2.44 (s, 3H), 2.39 (s, 3H), 1.31-1.28 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 166.8, 163.3, 145.8, 145.1, 136.3, 135.4, 134.3, 130.7, 129.5, 128.1, 122.1, 62.0, 55.3, 39.7, 21.8, 21.8, 14.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_8S$ 488.1374; Found 488.1382.



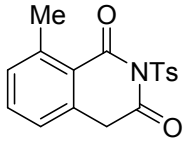
(3c) diethyl 2-(6-methoxy-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate

This compound was purified by column chromatography to afford a white solid in 31% yield (16 mg); Melting point: 142-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.16 (m, 2H), 7.36 - 7.33 (m, 2H), 6.88 (d, *J* = 2.4 Hz, 1H), 6.66 - 6.65 (m, 1H), 5.78 (s, 1H), 4.25 (q, *J* = 7.2 Hz, 4H), 4.04 (s, 2H), 3.85 (s, 3H), 2.44 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 167.2, 163.6, 163.2, 146.1, 139.3, 137.4, 135.8, 129.8, 117.5, 117.2, 111.8, 62.3, 56.1, 55.8, 40.5, 22.2, 14.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{26}NO_9S$ 504.1323; Found 504.1328.



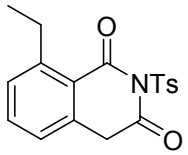
(3d) diethyl 2-(6-bromo-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate.

This compound was purified by column chromatography to afford a white solid in 25% yield (14 mg); Melting point: 145-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.16 (m, 2H), 7.53-7.52 (m, 1H), 7.42-7.41 (m, 1H), 7.37-7.34 (m, 2H), 5.71 (s, 1H), 4.27 (q, *J* = 7.2 Hz, 4H), 4.03 (s, 2H), 2.45 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 165.8, 162.9, 146.1, 138.0, 135.6, 135.0, 133.1, 130.5, 129.6, 129.5, 129.0, 123.8, 62.3, 55.0, 39.2, 21.8, 14.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{23}BrNO_8S$ 552.0322; Found 552.0314.



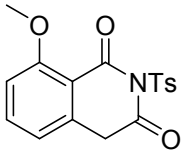
(3e) 8-methyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione.

This compound was purified by column chromatography to afford a white solid in 83% yield (27 mg); Melting point: 183-185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-8.22 (m, 2H), 7.45-7.37 (m, 3H), 7.23 (d, J=7.6 Hz, 1H), 7.07 (d, J=7.6 Hz, 1H), 4.04 (s, 2H), 2.68 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 163.3, 145.8, 142.9, 135.5, 133.7, 133.4, 131.7, 129.6, 129.4, 125.4, 124.7, 39.8, 22.7, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_4S$ 330.0795; Found 330.0803.



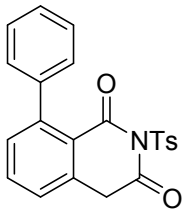
(3f) 8-ethyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 65% yield (22 mg); Melting point: 154-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-8.22 (m, 2H), 7.46 (t, J=7.6 Hz, 1H), 7.38 (d, J=8.0 Hz, 2H), 7.28-7.26 (m, 2H), 7.07 (d, J=7.6 Hz, 1H), 4.00 (s, 2H), 3.11-3.05 (m, 2H), 2.46 (s, 3H), 1.26-1.23 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.3, 148.5, 145.8, 135.5, 133.5, 130.1, 129.6, 129.4, 125.3, 124.9, 39.7, 27.8, 21.8, 15.4. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{18}NO_4S$ 344.0951; Found 344.0947.



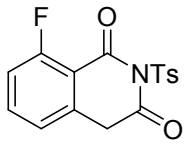
(3g) 8-methoxy-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 51% yield (18 mg); Melting point: 186-188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.24 (m, 2H), 7.53-7.49 (m, 1H), 7.37-7.35 (m, 2H), 6.95-6.93 (m, 1H), 6.80-6.77 (m, 1H), 4.01 (s, 2H), 3.96 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 161.1, 160.7, 145.7, 135.5, 135.3, 135.2, 129.6, 129.5, 119.1, 115.1, 111.1, 56.3, 39.4, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_5S$ 346.0744; Found 346.0741.



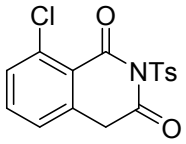
(3h) 8-phenyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 45% yield (18 mg); Melting point: 140-142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.12 (m, 2H), 7.56 (t, J=7.6 Hz, 1H), 7.46-7.38 (m, 3H), 7.34-7.28 (m, 5H), 7.23-7.21 (m, 1H), 4.03 (s, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 162.9, 145.8, 144.4, 139.8, 135.3, 133.0, 132.9, 131.4, 129.5, 129.5, 128.6, 128.3, 127.8, 126.3, 125.8, 39.3, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{18}NO_4S$ 392.0951; Found 392.0959.



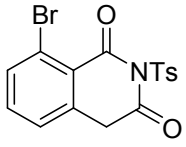
(3i) 8-fluoro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 56% yield (19 mg); Melting point: 185-187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.21 (m, 2H), 7.59-7.54 (m, 1H), 7.39-7.37 (m, 2H), 7.15-7.10 (m, 1H), 7.07-7.04 (m, 1H), 4.10 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 162.8 (d, J=267.2 Hz), 159.4 (d, J=4.8 Hz), 146.0, 135.8 (d, J=10.2 Hz), 135.2, 135.0, 129.6 (d, J=8.2 Hz), 123.2 (d, J=4.3 Hz), 116.7, 116.5, 114.8 (d, J=6.4 Hz), 39.4 (d, J=2.6 Hz), 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}FNO_4S$ 334.0544; Found 334.0541.



(3j) 8-chloro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

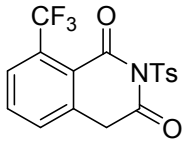
This compound was purified by column chromatography to afford a white solid in 40% yield (14 mg); Melting point: 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.22 (m, 2H), 7.50-7.44 (m, 2H), 7.40-7.38 (m, 2H), 7.17-7.14 (m, 1H), 4.04 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 160.7, 146.0, 136.2, 135.2, 135.2, 133.9, 131.6, 129.7, 129.6, 126.0, 124.2, 39.5, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClNO_4S$ 350.0248; Found 350.0242.



(3k) 8-bromo-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

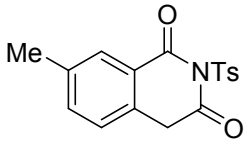
This compound was purified by column chromatography to afford a white solid in 60% yield (24 mg); Melting point: 222-225 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.23 (m, 2H), 7.73-7.71 (m, 1H), 7.40-7.36 (m, 3H), 7.22-7.19 (m, 1H), 4.04 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.1, 146.1,

135.3, 135.2, 135.1, 134.0, 129.7, 129.6, 126.7, 125.7, 123.8, 39.5, 21.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}BrNO_4S$ 393.9743; Found 393.9741.



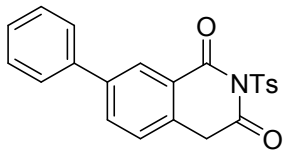
(3l) 2-tosyl-8-(trifluoromethyl)isoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 81% yield (31 mg); Melting point: 187-189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-8.21 (m, 2H), 7.85-7.83 (m, 1H), 7.71-7.67 (m, 1H), 7.47-7.45 (m, 1H), 7.40-7.38 (m, 2H), 4.04 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 171.5, 164.2 (d, J=525.9 Hz), 145.6 (d, J=111.9 Hz), 137.8, 135.7, 134.8 (q, J=210 Hz), 133.9, 132.8, 130.2, 129.2, 129.1 (q, J=173.0 Hz), 127.0 (q, J=6.4 Hz), 125.6, 37.4, 21.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{13}F_3NO_4S$ 384.0512; Found 384.0504.



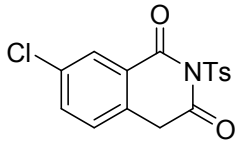
(3m) 7-methyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 68% yield (22 mg); Melting point: 191-193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.20 (m, 2H), 7.93-7.90 (m, 1H), 7.41-7.36 (m, 3H), 7.14-7.12 (m, 1H), 4.07 (s, 2H), 2.44 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 163.0, 145.8, 138.3, 135.8, 135.4, 130.1, 129.7, 129.6, 129.4, 127.3, 125.4, 39.6, 21.8, 21.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_4S$ 330.0795; Found 330.0794.



(3n) 7-phenyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

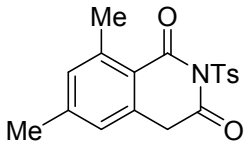
This compound was purified by column chromatography to afford a white solid in 65% yield (25 mg); Melting point: 162-164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 2.0 Hz, 1H), 8.25-8.22 (m, 2H), 7.84-7.81 (m, 1H), 7.59-7.56 (m, 2H), 7.48-7.43 (m, 2H), 7.41-7.37 (m, 3H), 7.33-7.31 (m, 1H), 4.16 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 162.9, 146.0, 141.4, 138.9, 135.3, 133.3, 131.8, 129.7, 129.5, 129.1, 128.3, 127.9, 127.9, 127.0, 126.0, 39.7, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{18}NO_4S$ 392.0951; Found 392.0955.



(3o) 7-chloro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

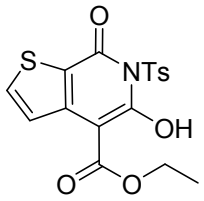
This compound was purified by column chromatography to afford a white solid in 50% yield (17 mg);

Melting point:201-203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.19 (m, 2H), 8.11-8.10 (m, 1H), 7.57-7.55 (m, 1H), 7.40-7.37 (m, 2H), 7.22-7.19 (m, 1H), 4.09 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 161.7, 146.1, 135.1, 134.8, 134.6, 131.3, 129.7, 129.5, 129.4, 128.8, 127.1, 39.3, 21.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClNO_4S$ 350.0248; Found 350.0241.



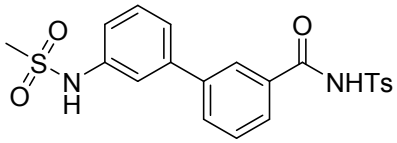
(3p) 6,8-dimethyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

This compound was purified by column chromatography to afford a white solid in 51% yield (18 mg); Melting point: 203-205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-8.21 (m, 2H), 7.39-7.36 (m, 2H), 7.03 (s, 1H), 6.87 (s, 1H), 4.00 (s, 2H), 2.63 (s, 3H), 2.45 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 163.2, 145.6, 144.5, 143.0, 135.7, 133.9, 132.7, 129.6, 129.4, 125.9, 122.0, 39.8, 22.6, 21.8, 21.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{18}NO_4S$ 344.0951; Found 344.0955.



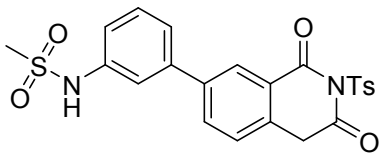
(3q) ethyl 5-hydroxy-7-oxo-6-tosyl-6,7-dihydrothieno[2,3-c]pyridine-4-carboxylate

This compound was purified by column chromatography to afford a white solid in 41% yield (16 mg); Melting point: decomposition. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.35 (s, 1H), 8.15-8.12 (m, 2H), 7.86 (dd, J=5.2 Hz, J=13.6 Hz, 2H), 7.41-7.39 (m, 2H), 4.56-4.50 (m, 2H), 2.46 (s, 3H), 1.51 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 165.0, 153.9, 149.8, 146.0, 136.6, 133.5, 129.7, 129.7, 125.0, 119.0, 99.0, 62.6, 21.9, 14.3.HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_6S_2$ 394.0414; Found 394.0407.



(8) 3'-(methylsulfonamido)-*N*-tosyl-[1,1'-biphenyl]-3-carboxamide

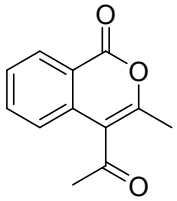
This compound was purified by column chromatography to afford a white solid in 90% yield; Melting point: 186-188 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.64 (s, 1H), 9.85 (s, 1H), 8.13 (s, 1H), 7.93-7.84 (m, 4H), 7.62-7.58 (m, 1H), 7.52-7.45 (m, 5H), 7.29-7.26 (m, 1H), 3.04 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 165.7, 144.8, 140.7, 140.5, 139.6, 137.1, 132.8, 131.8, 130.5, 130.0, 130.0, 128.3, 128.2, 127.0, 123.1, 119.9, 118.8, 39.8, 21.6. HRMS (APCI) *m/z:* $[M+H]^+$ Calcd for $C_{21}H_{20}N_2O_5S_2$ 445.0886; Found 445.0891.



(9) *N*-(3-(1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-7-yl)phenyl)methanesulfonamide

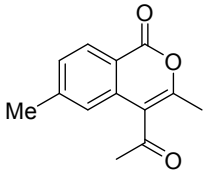
This compound was purified by column chromatography to afford a white solid in 46% yield (22 mg); Melting point: 219-221 °C. ^{1}H NMR (400 MHz, Methylene Chloride-d_2) δ 8.31 (d, J = 2.0 Hz, 1H), 8.19-8.16 (m, 2H), 7.84 (dd, J = 8.0, 2.0 Hz, 1H), 7.49-7.36 (m, 6H), 7.27-7.25 (m, 1H), 6.66 (s, 1H), 4.17 (s, 2H), 3.04 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 167.7, 162.7, 146.2, 140.7, 140.2, 137.7, 135.4, 133.2, 132.6, 130.4, 129.6, 129.3, 128.2, 127.5, 126.2, 123.9, 120.1, 119.1, 39.7, 39.6, 21.5. HRMS (APCI) *m/z:* $[M+H]^+$ Calcd for $C_{23}H_{20}N_2O_6S_2$ 485.0836; Found 485.0842.

IV Characterization Data of 4a-p, 4t-z



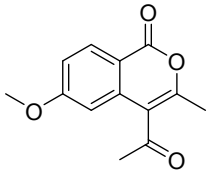
(4a) 4-acetyl-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 77% yield (16 mg); Melting point: 97-99 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33-8.31 (m, 1H), 7.76-7.70 (m, 1H), 7.56-7.50 (m, 1H), 7.33 (d, J = 8.0 Hz, 1H), 2.58 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7, 161.7, 153.0, 135.6, 134.8, 130.5, 128.7, 123.5, 120.2, 119.0, 32.8, 18.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{11}O_3$ 203.0703; Found 203.0700.



(4b) 4-acetyl-3,6-dimethyl-1*H*-isochromen-1-one

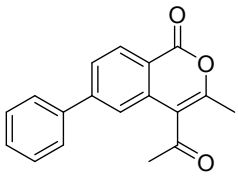
This compound was purified by column chromatography to afford a white solid in 43% yield (9 mg); Melting point: 112-114 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.5 Hz, 1H), 7.08 (s, 1H), 2.57 (s, 3H), 2.46 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 161.8, 152.8, 146.8, 134.8, 130.5, 130.0, 123.5, 118.9, 117.8, 32.9, 22.6, 18.7. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{13}O_3$ 217.0859; Found 217.0854.



(4c) 4-acetyl-6-methoxy-3-methyl-1*H*-isochromen-1-one

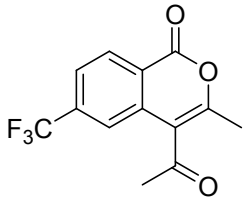
This compound was purified by column chromatography to afford a white solid in 84% yield (20 mg); Melting point: 85-87 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 1H), 7.03-7.01 (m, 1H), 6.68 (d, J = 2.0 Hz, 1H), 3.87 (s, 3H), 2.56 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 165.3,

161.5, 153.8, 136.9, 132.7, 118.8, 116.3, 113.2, 106.6, 56.1, 32.8, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{13}O_4$ 233.0808; Found 233.0800.



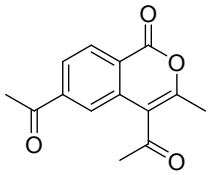
(4d) 4-acetyl-3-methyl-6-phenyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 65% yield (18 mg); Melting point: 149-150 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.75-7.73 (m, 1H), 7.63-7.57 (m, 2H), 7.52-7.42 (m, 4H), 2.61 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7, 161.6, 153.3, 148.5, 139.7, 135.3, 131.0, 129.5, 129.3, 127.9, 127.8, 121.8, 119.1, 118.9, 32.9, 18.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{15}O_3$ 279.1016; Found 279.1013.



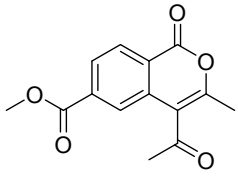
(4e) 4-acetyl-3-methyl-6-(trifluoromethyl)-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 69% yield (19 mg); Melting point: 99-102 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 8.5 Hz, 1H), 7.76-7.74 (m, 1H), 7.62 (s, 1H), 2.61 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 160.5, 155.0, 137.0 (q, J=26.2 Hz), 135.2, 131.5, 125.1 (q, J=3.0 Hz), 123.5 (d, J=217.3 Hz), 122.7, 120.9 (q, J=3.5 Hz), 118.4, 32.9, 19.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{10}F_3O_3$ 271.0577; Found 271.0580.



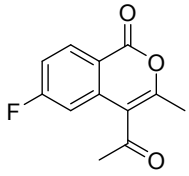
(4f) 1,1'-(3-methyl-1-oxo-1*H*-isochromene-4,6-diyl)bis(ethan-1-one)

This compound was purified by column chromatography to afford a white solid in 51% yield (12 mg); Melting point: 116-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.0 Hz, 1H), 8.05-8.02 (m, 1H), 7.91 (d, J = 1.2 Hz, 1H), 2.68 (s, 3H), 2.63 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 196.9, 160.5, 153.9, 141.9, 134.7, 130.7, 127.3, 123.1, 122.7, 118.4, 32.6, 27.0, 18.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{13}O_4$ 245.0808; Found 245.0811.



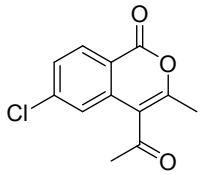
(4g) methyl 4-acetyl-3-methyl-1-oxo-1*H*-isochromene-6-carboxylate

This compound was purified by column chromatography to afford a white solid in 84% yield (22 mg); Melting point: 147-149 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 8.14-8.12 (m, 1H), 8.00 (s, 1H), 3.98 (s, 3H), 2.62 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 165.9, 160.9, 154.0, 136.4, 134.8, 130.8, 129.0, 125.0, 123.2, 118.8, 53.2, 32.9, 18.8. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{13}O_5$ 261.0757; Found 261.0758.



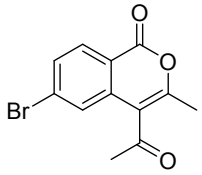
(4h) 4-acetyl-6-fluoro-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 79% yield (17 mg);^{1}H Melting point: 110-112 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35-8.32 (m, 1H), 7.22-7.20 (m, 1H), 7.05-7.02 (m, 1H), 2.58 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 167.2 (d, J=204.5 Hz), 160.7, 154.9, 137.4 (d, J=8.6 Hz), 133.8 (d, J=8.3 Hz), 118.4 (d, J=2.2 Hz), 117.0 (d, J=18.4 Hz), 116.7, 110.0 (d, J=19.3 Hz), 32.8, 19.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}FO_3$ 221.0608; Found 221.0609.



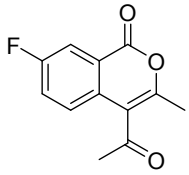
(4i) 4-acetyl-6-chloro-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 82% yield (19 mg); Melting point: 118-120 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 8.5 Hz, 1H), 7.49- 7.47 (m, 1H), 7.34 (d, J = 2.0 Hz, 1H), 2.59 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 160.9, 154.7, 142.5, 136.1, 132.0, 129.2, 123.4, 118.5, 118.1, 32.8, 19.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}ClO_3$ 237.0313; Found 237.0309.



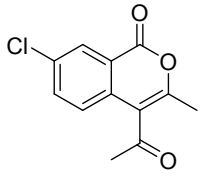
(4j) 4-acetyl-6-bromo-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 74% yield (21 mg); Melting point: 131-133 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.5 Hz, 1H), 7.65- 7.63 (m, 1H), 7.51 (d, J = 1.5 Hz, 1H), 2.59 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 161.0, 154.7, 136.2, 132.1, 132.0, 131.3, 126.5, 118.9, 118.0, 32.8, 19.0. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}BrO_3$ 280.9808; Found 280.9801.



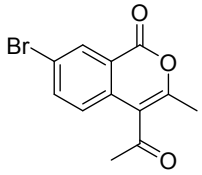
(4k) 4-acetyl-7-fluoro-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 48% yield (11 mg); Melting point: 138-141 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 - 8.13 (m, 1H), 7.54-7.42 (m, 2H), 2.51 (d, J = 3.5 Hz, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 160.2, 155.9 (d, J=249.8 Hz), 152.1, 129.3 (d, J=8.0 Hz), 126.2 (d, J=3.6 Hz), 123.7 (d, J=12.6 Hz), 121.7 (d, J=3.9 Hz), 121.6 (d, J=21.0 Hz), 114.5, 31.8 (d, J=9.2 Hz), 17.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}FO_3$ 221.0608; Found 221.0604.



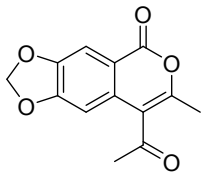
(4l) 4-acetyl-7-chloro-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 62% yield (15 mg); Melting point: 124-126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 1.0 Hz, 1H), 7.69-7.66 (m, 1H), 7.31 (d, J = 8.5 Hz, 1H), 2.57 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 160.5, 153.6, 135.8, 134.7, 133.2, 129.9, 125.2, 121.6, 118.4, 32.8, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}ClO_3$ 237.0313; Found 237.0309.



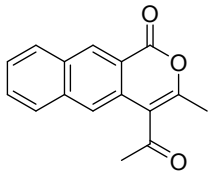
(4m) 4-acetyl-7-bromo-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 69% yield (19 mg); Melting point: 122-124 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.83-7.81 (m, 1H), 7.24 (d, J=8.5 Hz, 1H), 2.57 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 160.3, 153.8, 138.6, 133.5, 133.0, 125.3, 122.4, 121.7, 118.4, 32.8, 18.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{10}BrO_3$ 280.9808; Found 280.9804.



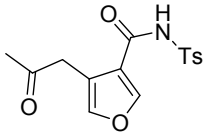
(4n) 8-acetyl-7-methyl-5*H*-[1,3]dioxolo[4,5-g]isochromen-5-one

This compound was purified by column chromatography to afford a white solid in 60% yield (15 mg); Melting point: 144-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.13 (s, 2H), 2.51 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 160.6, 152.8, 151.7, 140.2, 126.7, 117.3, 114.7, 114.1, 109.6, 102.7, 32.3, 17.5. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{11}O_5$ 247.0601; Found 247.0600.



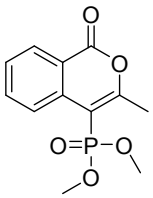
(4o) 4-acetyl-3-methyl-1*H*-benzo[g]isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 92% yield (23 mg); Melting point: 141-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.72 (s, 1H), 7.68-7.65 (m, 1H), 7.60-7.57 (m, 1H), 2.66 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.8, 161.6, 150.7, 136.4, 132.6, 132.1, 129.8, 129.6, 129.1, 128.1, 127.2, 121.8, 118.5, 118.1, 32.5, 18.3. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}O_3$ 253.0859; Found 253.0858.



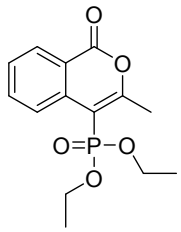
(4p) 4-(2-oxopropyl)-*N*-tosylfuran-3-carboxamide

This compound was purified by column chromatography to afford a white solid in 53% yield (17 mg); Melting point: 175-177 °C. ^{1}H NMR (500 MHz, DMSO) δ 12.17 (s, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 2.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 2.0 Hz, 1H), 4.13 (s, 2H), 2.45 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 203.5, 162.0, 157.5, 145.1, 143.2, 137.5, 130.4, 128.5, 116.3, 110.1, 42.9, 30.5, 21.9. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{16}NO_5S$ 322.0744; Found 322.0743.



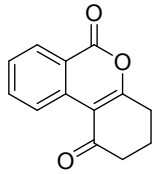
(4t) dimethyl (3-methyl-1-oxo-1*H*-isochromen-4-yl)phosphonate

This compound was purified by column chromatography to afford a white solid in 67% yield (18 mg); Melting point: 70-71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32-8.30 (m, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.77-7.73 (m, 1H), 7.56-7.50 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.77 (d, J = 2.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 165.8, 161.0, 135.6, 135.5, 135.1, 129.6, 128.2, 125.9, 119.8, 119.7, 102.4, 100.8, 52.6, 52.5, 20.6. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}O_5P$ 269.0573; Found 269.0570.



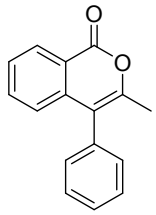
(4u) diethyl (3-methyl-1-oxo-1*H*-isochromen-4-yl)phosphonate

This compound was purified by column chromatography to afford a white solid in 95% yield (28 mg); Melting point: 62-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32-8.29 (m, 1H), 8.22-8.20 (m, 1H), 7.77-7.73 (m, 1H), 7.54-7.50 (m, 1H), 4.28-4.18 (m, 2H), 4.15-4.05 (m, 2H), 2.77 (d, J = 2.4 Hz, 3H), 1.35-1.31 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 165.2, 161.2, 135.8, 135.7, 134.9, 129.5, 128.1, 126.2, 119.9, 119.7, 103.7, 101.8, 62.3, 62.3, 20.6, 16.3, 16.3. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}O_5P$ 297.0886; Found 297.0890.



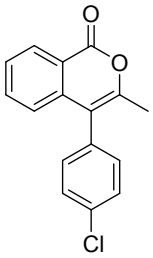
(4v) 3,4-dihydro-1*H*-benzo[c]chromene-1,6(2*H*)-dione

This compound was purified by column chromatography to afford a white solid in 96% yield (21 mg); Melting point: 153-155 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (d, J = 8.5 Hz, 1H), 8.29- 8.27 (m, 1H), 7.83-7.75 (m, 1H), 7.57-7.49 (m, 1H), 2.96-2.93 (m, 2H), 2.68-2.65 (m, 2H), 2.21-2.15 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 169.9, 160.9, 136.0, 134.4, 130.0, 128.8, 126.4, 120.3, 112.0, 39.3, 29.4, 20.4. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{11}O_3$ 215.0703; Found 215.0700.



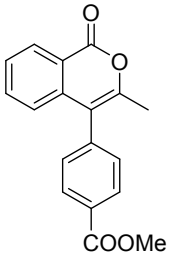
(4w) 3-methyl-4-phenyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 86% yield (20 mg); Melting point: 127-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35-8.32 (m, 1H), 7.61-7.59 (m, 1H), 7.52-7.43 (m, 4H), 7.29-7.26 (m, 3H), 7.01-6.99 (m, 1H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 151.6, 138.7, 134.6, 134.5, 130.6, 129.5, 129.0, 128.2, 127.4, 124.5, 120.0, 116.4, 18.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}O_2$ 237.0910; Found 237.0906.



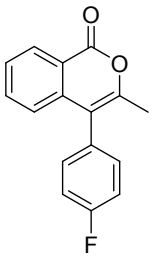
(4x) 4-(4-chlorophenyl)-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 60% yield (16 mg); Melting point: 154-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35-8.32 (m, 1H), 7.63-7.57 (m, 1H), 7.50-7.44 (m, 3H), 7.25-7.21 (m, 2H), 6.97 (d, J = 8.0 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 151.8, 138.3, 134.8, 134.3, 132.9, 132.0, 129.6, 129.3, 127.6, 124.3, 120.0, 115.3, 18.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}ClO_2$ 271.0517; Found 271.0520.



(4y) methyl 4-(3-methyl-1-oxo-1*H*-isochromen-4-yl)benzoate

This compound was purified by column chromatography to afford a white solid in 65% yield (19 mg); Melting point: 152-155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36-8.34 (m, 1H), 8.21-8.15 (m, 2H), 7.63-7.57 (m, 1H), 7.51-7.45 (m, 1H), 7.41-7.35 (m, 2H), 6.94 (d, J = 8.0 Hz, 1H), 3.98 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 162.4, 151.7, 139.4, 138.0, 134.8, 130.8, 130.3, 130.1, 129.7, 127.7, 124.2, 120.0, 115.6, 52.4, 18.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{15}O_4$ 295.0965; Found 295.0964.

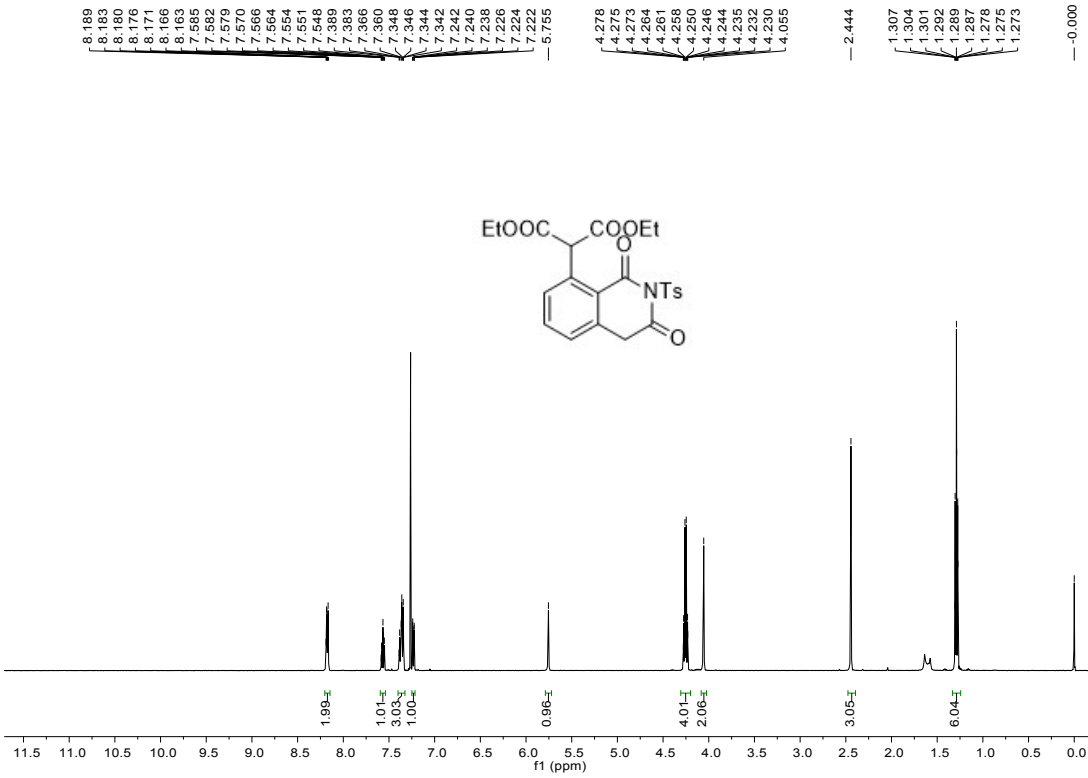


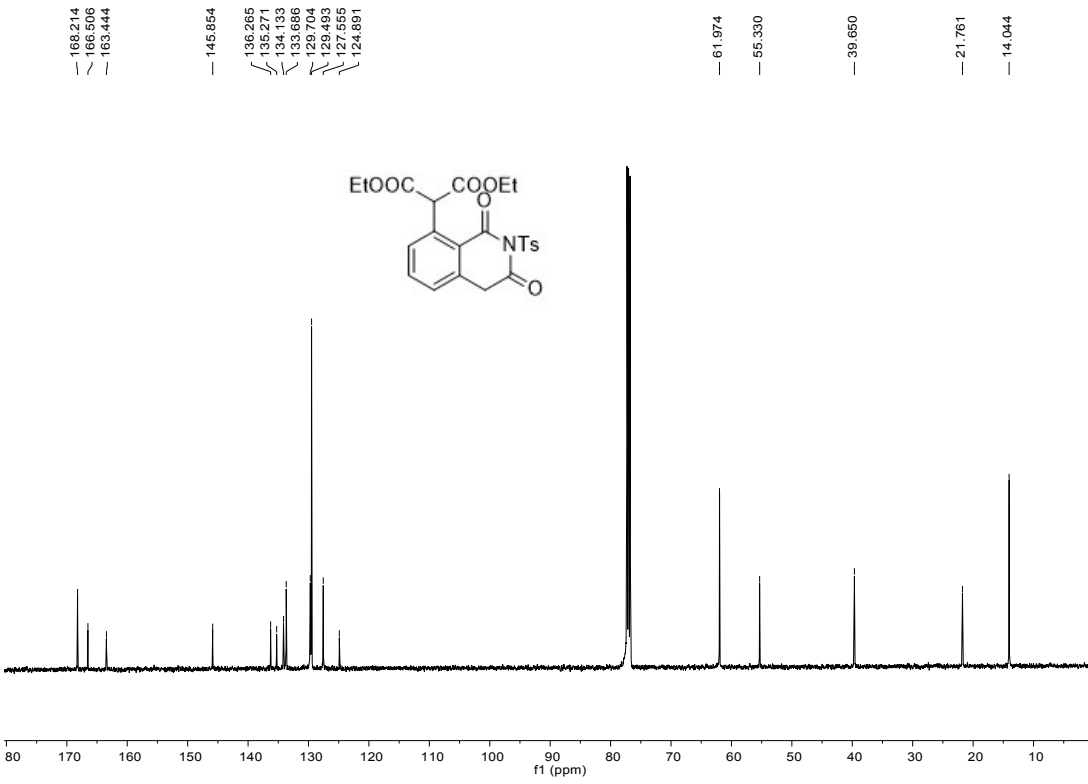
(4z) 4-(4-fluorophenyl)-3-methyl-1*H*-isochromen-1-one

This compound was purified by column chromatography to afford a white solid in 25% yield (6 mg); Melting point: 135-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35-8.33 (m, 1H), 7.65-7.56 (m, 1H), 7.53-7.44 (m, 1H), 7.29-7.17 (m, 6H), 6.97 (d, J = 8.0 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, J=246.3 Hz), 162.5, 151.9, 138.6, 134.7, 132.3 (d, J=8.0 Hz), 130.3, 129.6, 127.5, 124.3, 120.0, 116.1 (d, J=21.5 Hz), 115.4, 18.1. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}FO_2$ 255.0816; Found 255.0821.

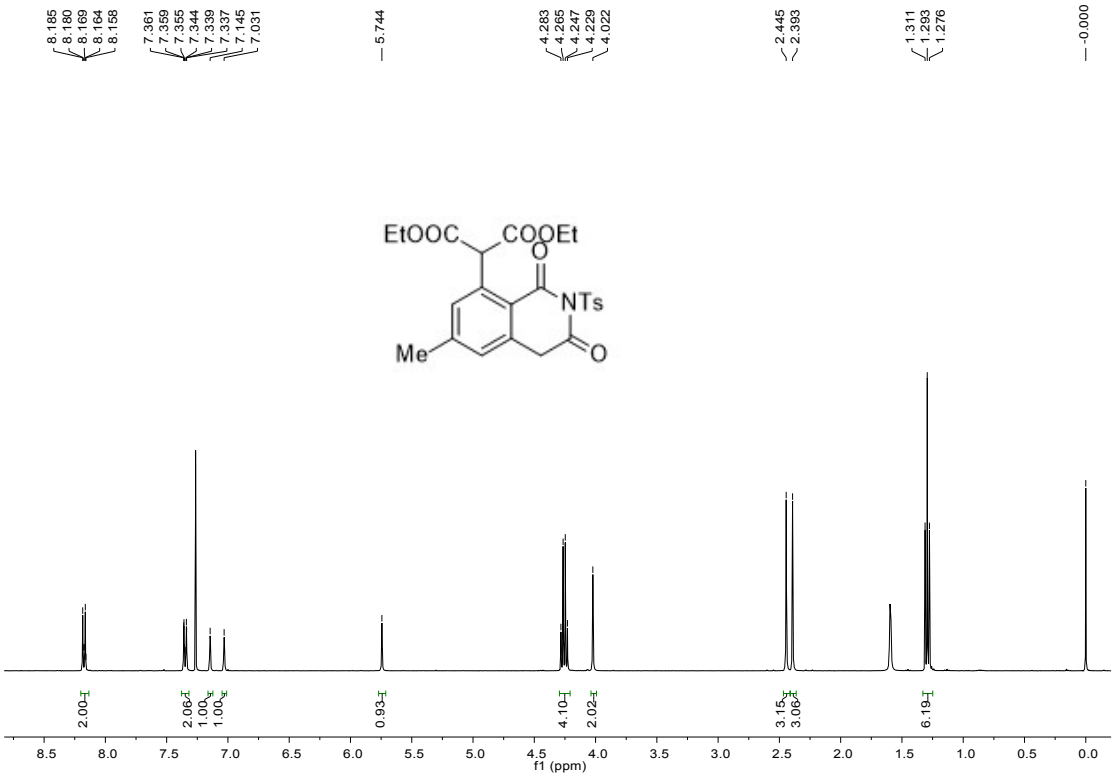
V NMR (^{1}H NMR and ^{13}C NMR) of 3a-q, 4a-p, 4t-z, 8 and 9

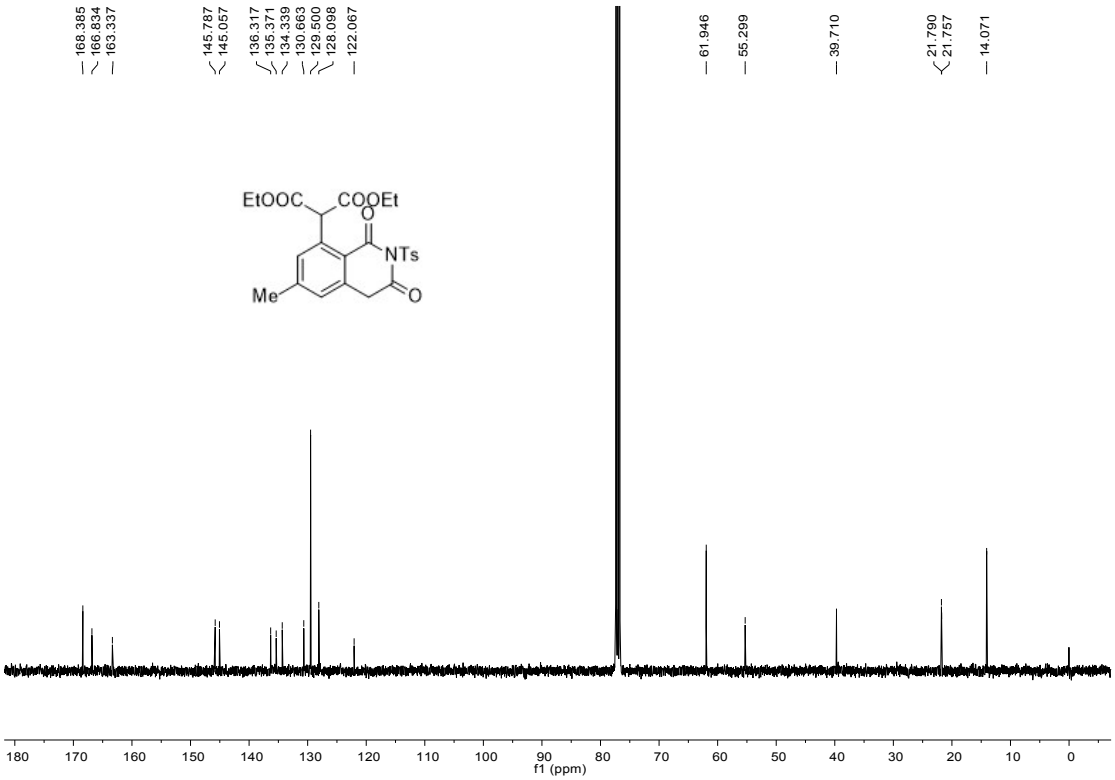
(3a) diethyl 2-(1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate



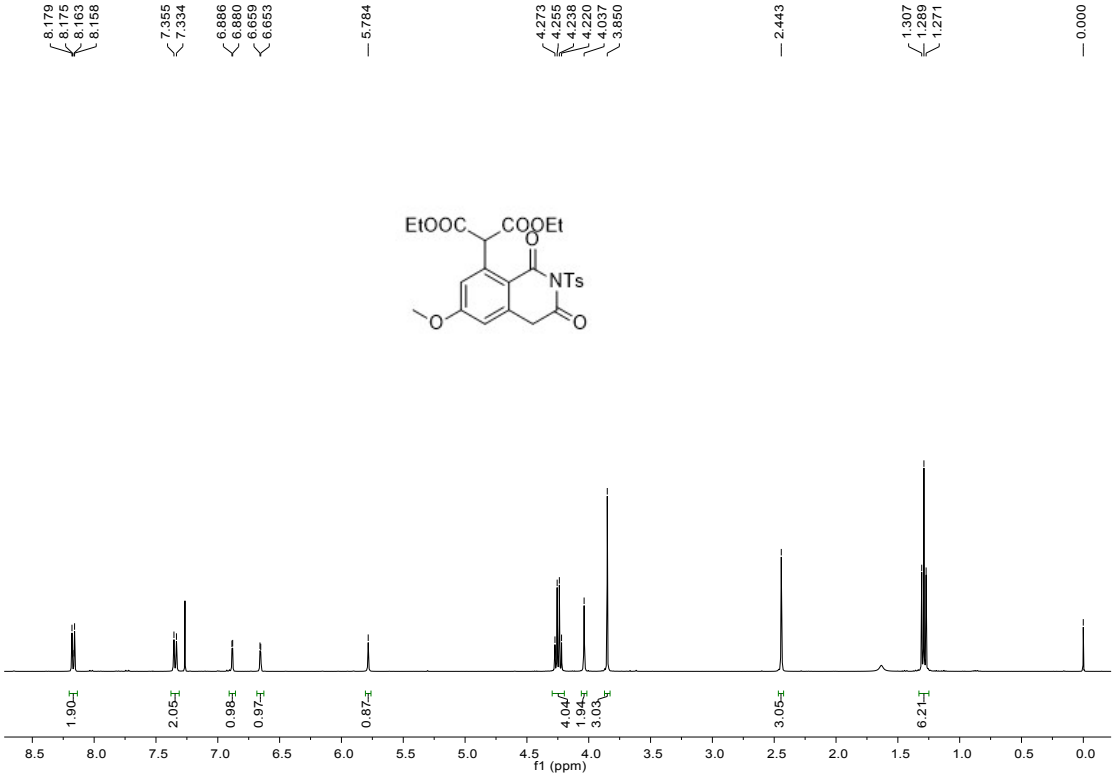


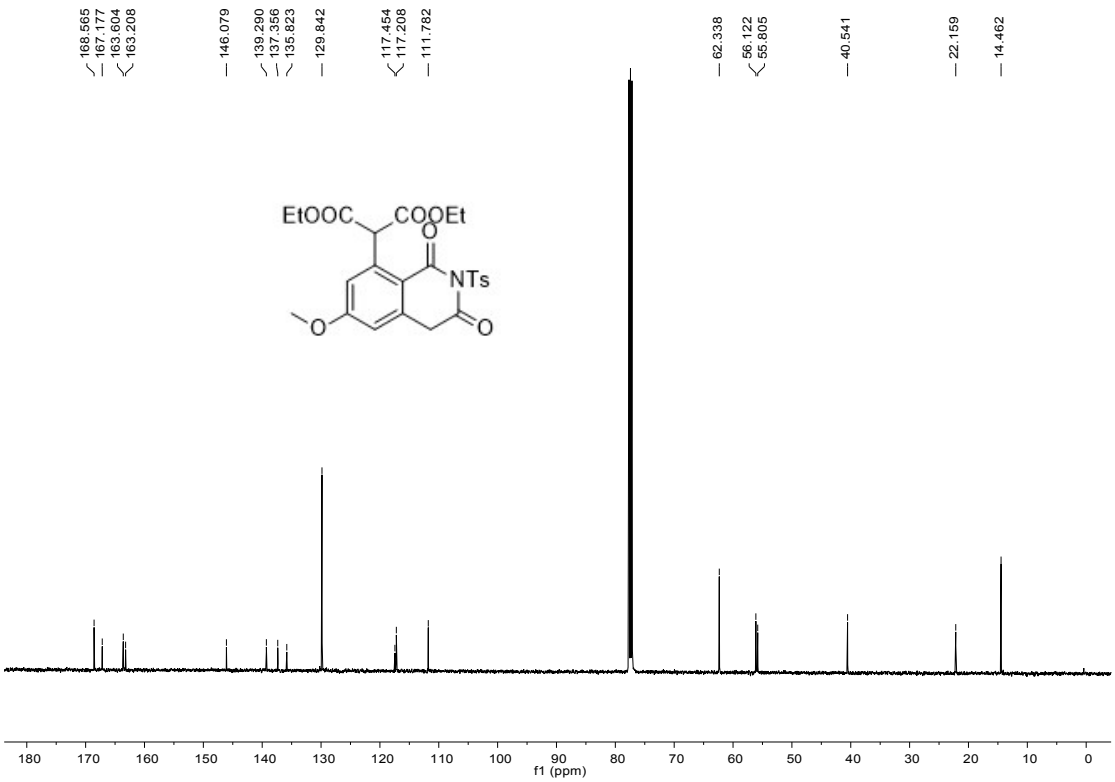
(3b) diethyl 2-(6-methyl-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate





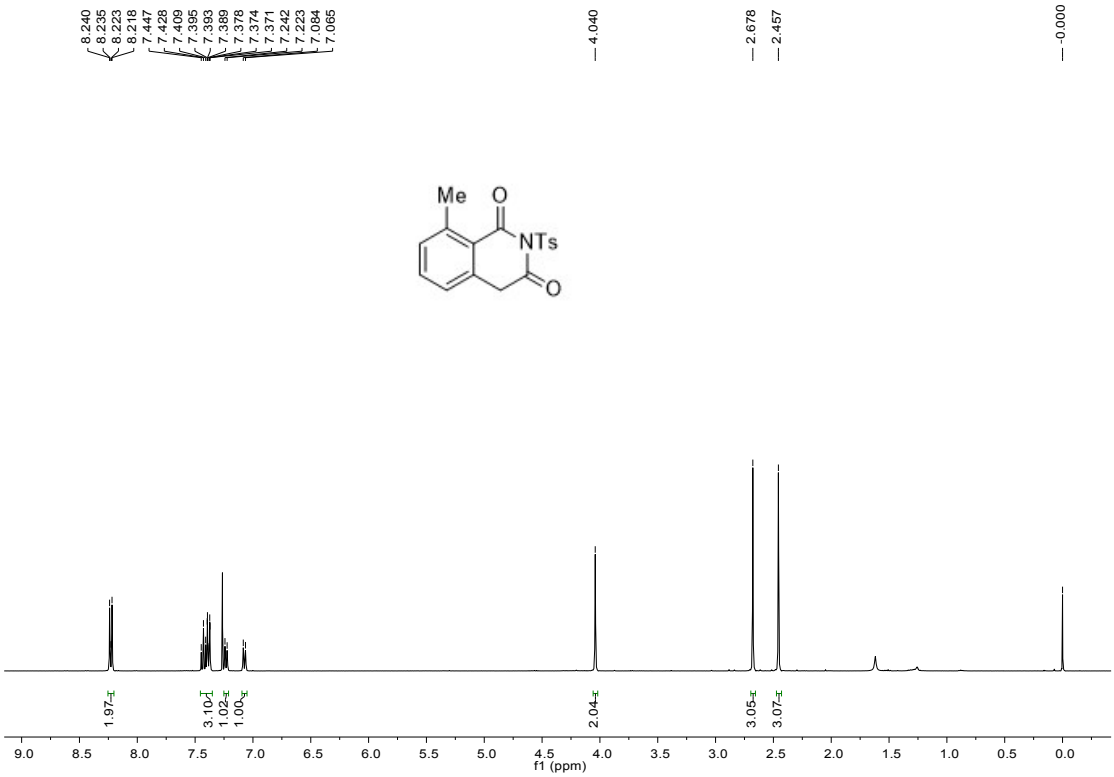
(3c) diethyl 2-(6-methoxy-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate

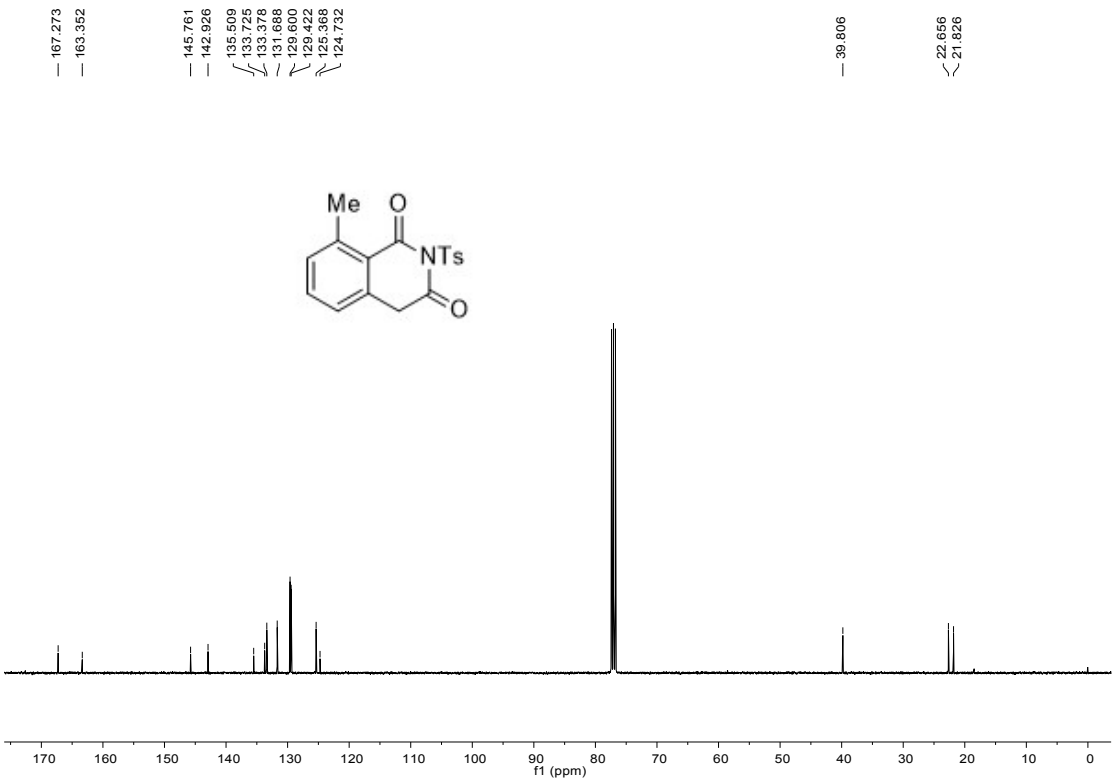




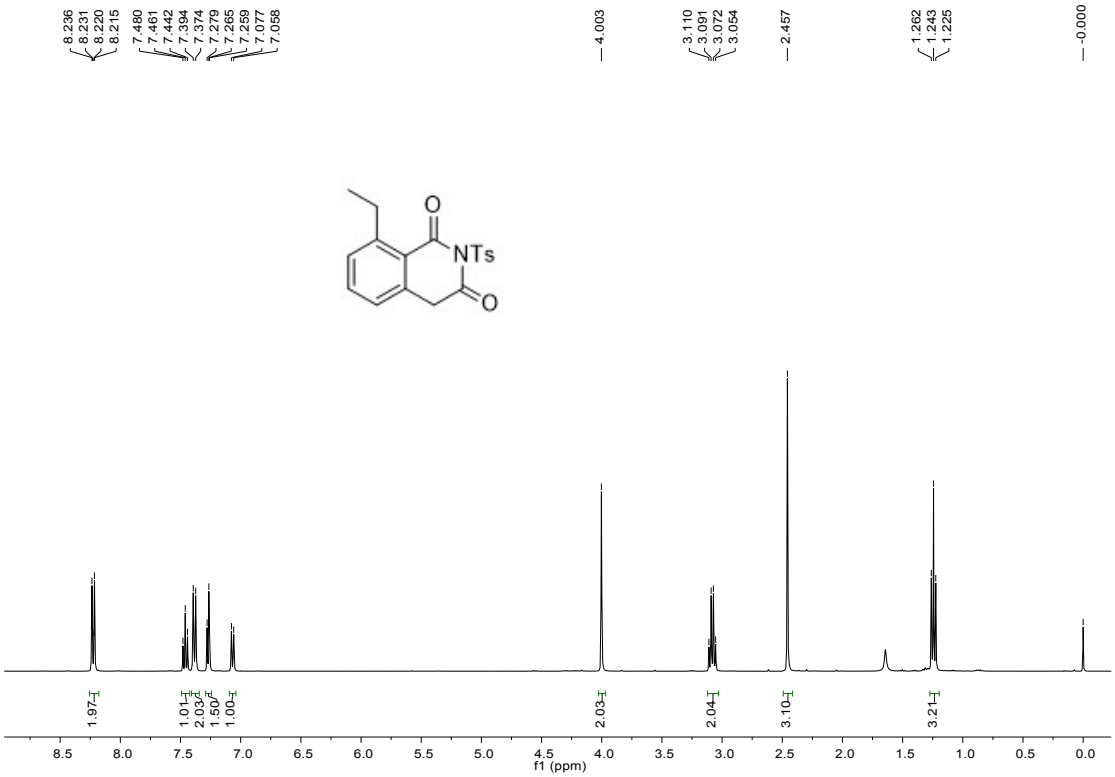
(3d) diethyl 2-(6-bromo-1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-8-yl)malonate.

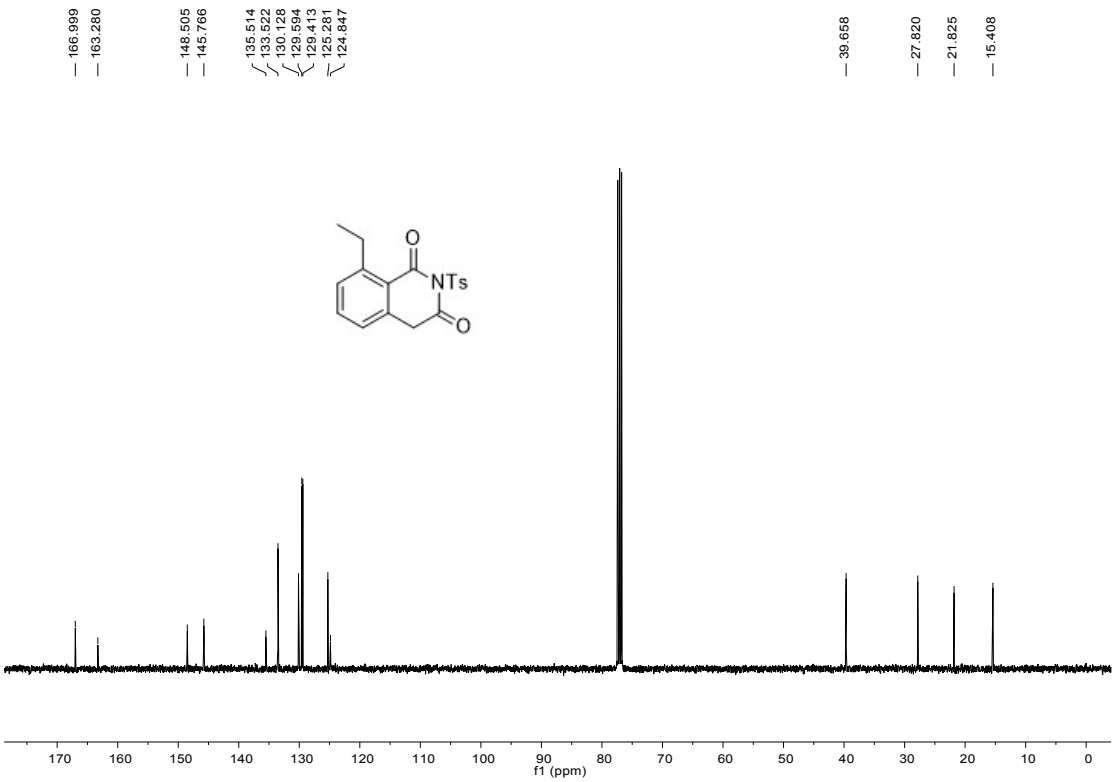
(3e) 8-methyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione.



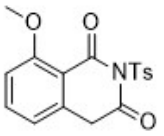


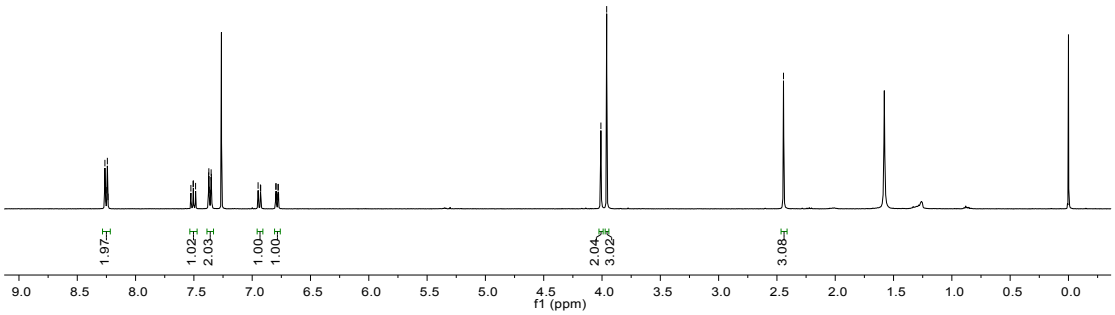
(3f) 8-ethyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

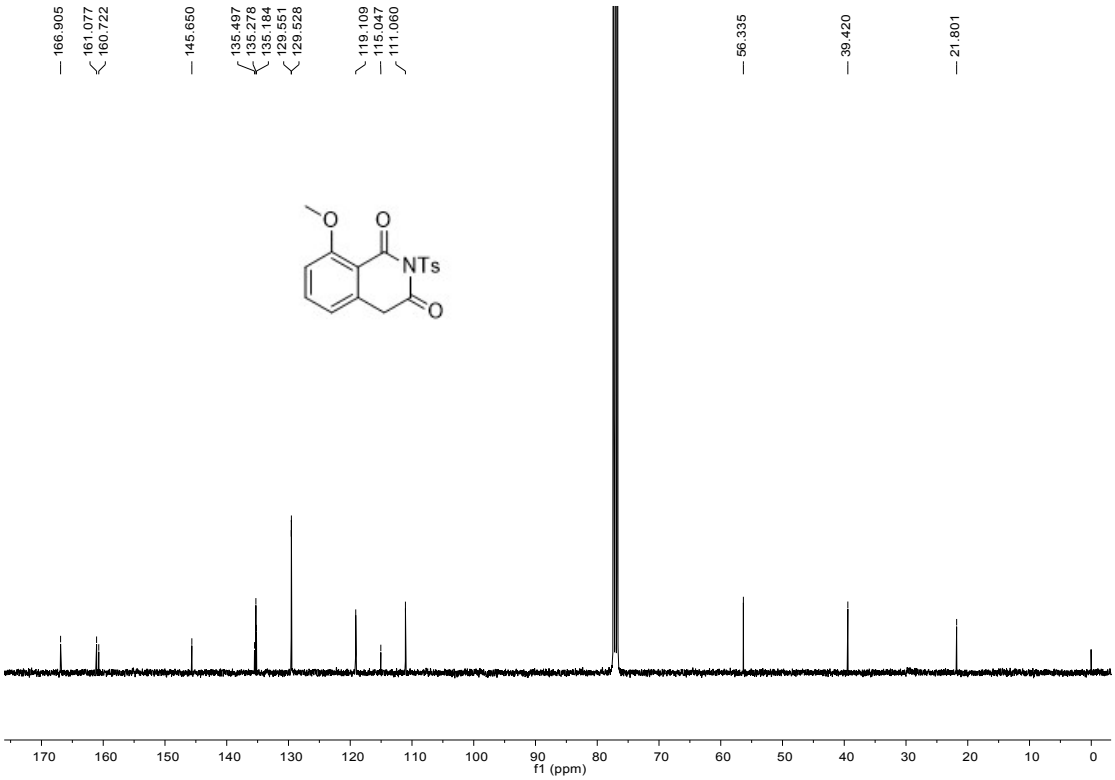




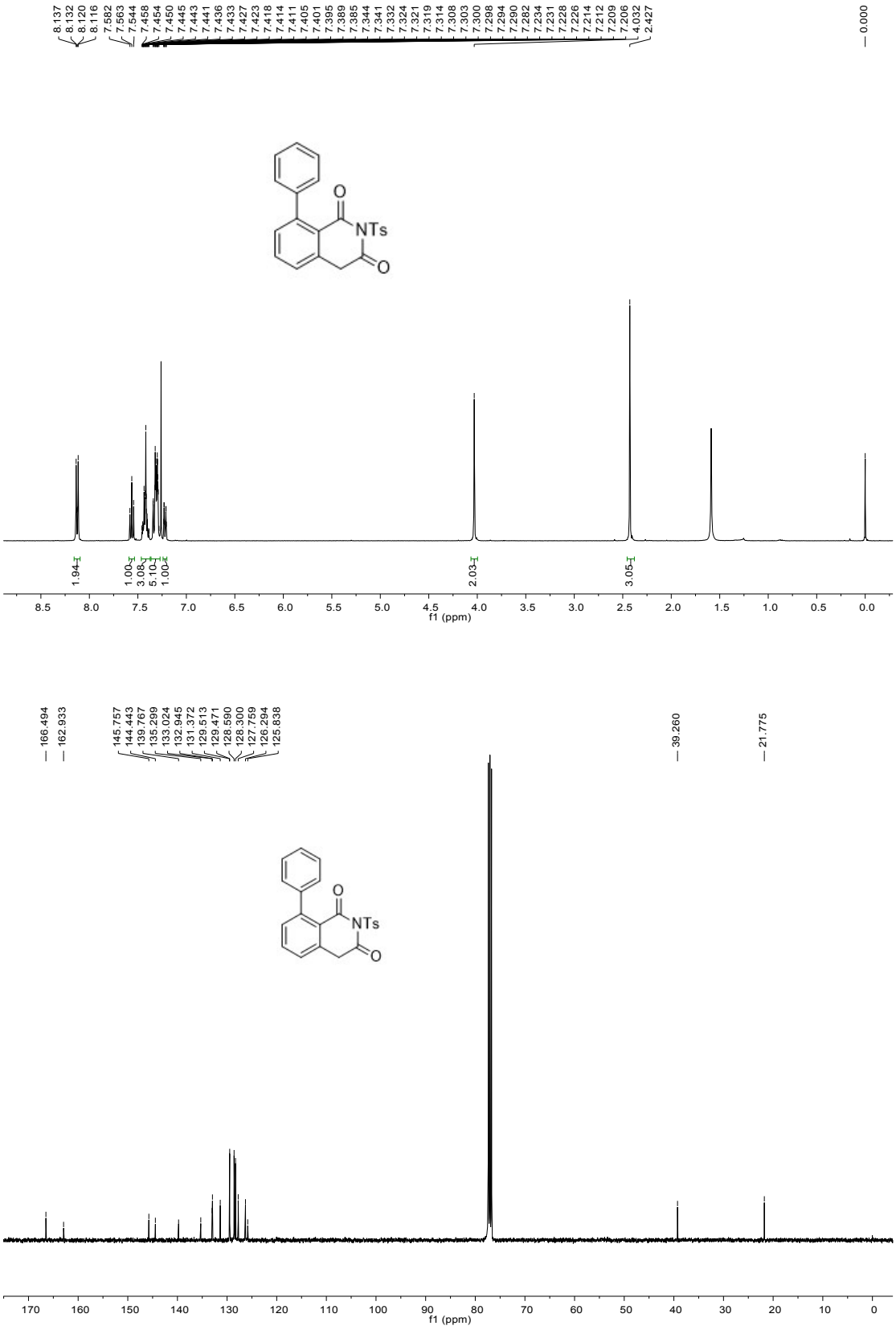
(3g) 8-methoxy-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione



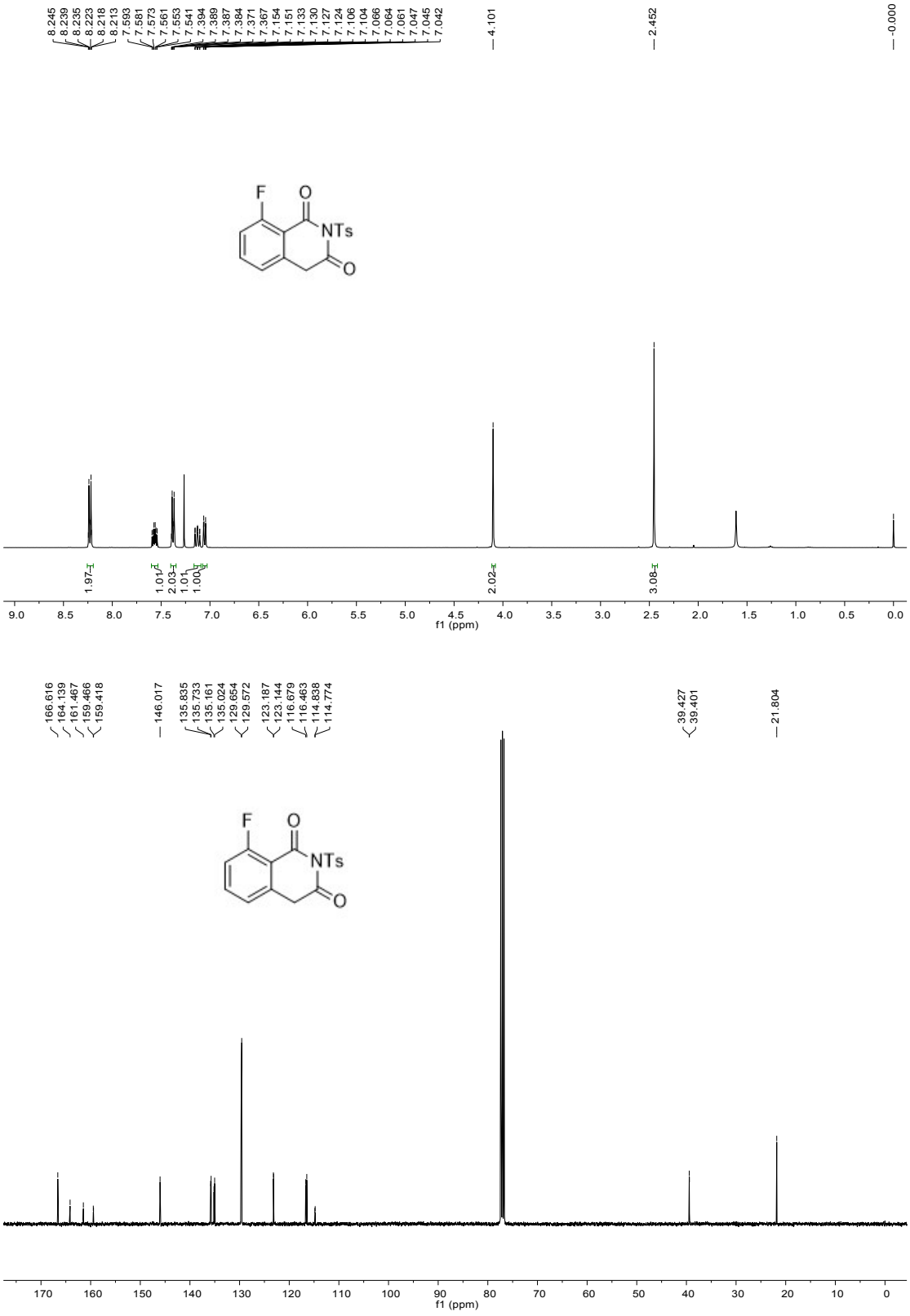




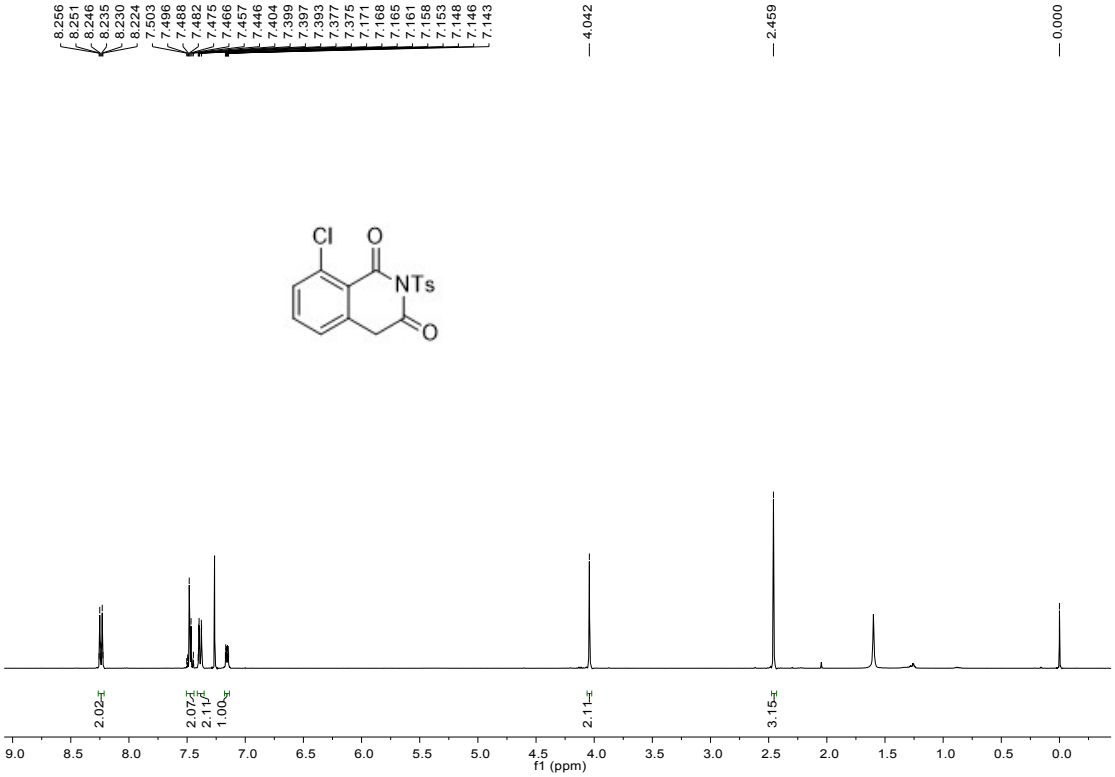
(3h) 8-phenyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

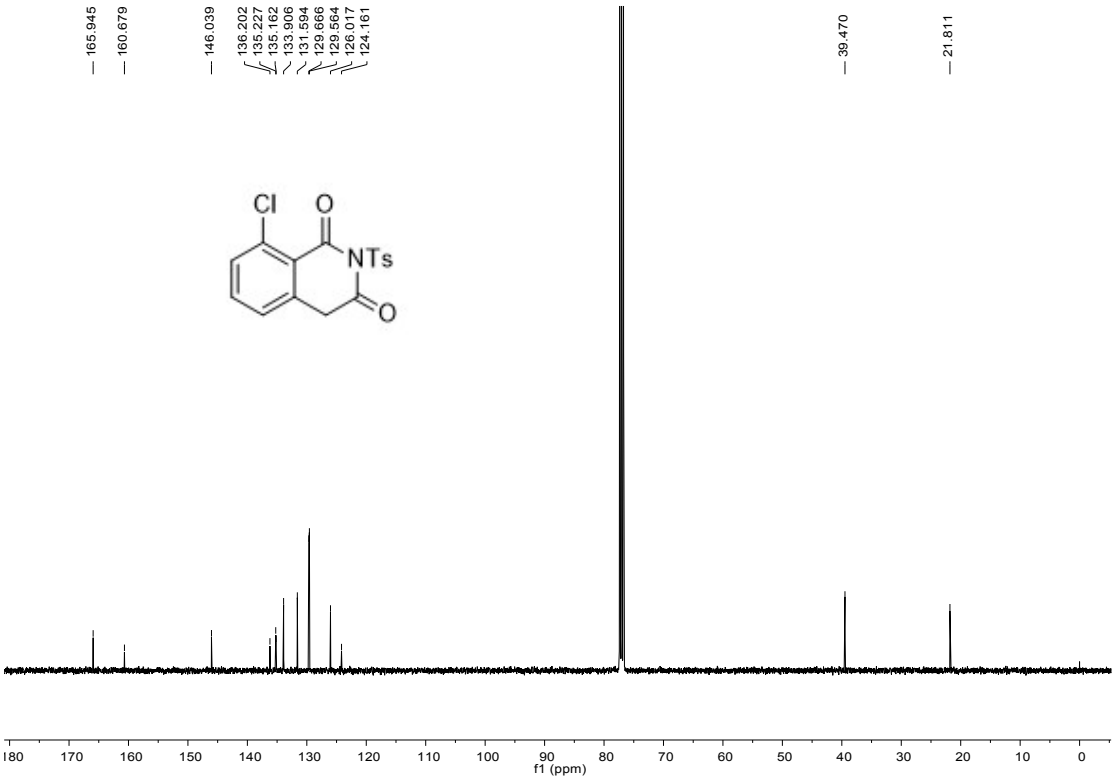


(3i) 8-fluoro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

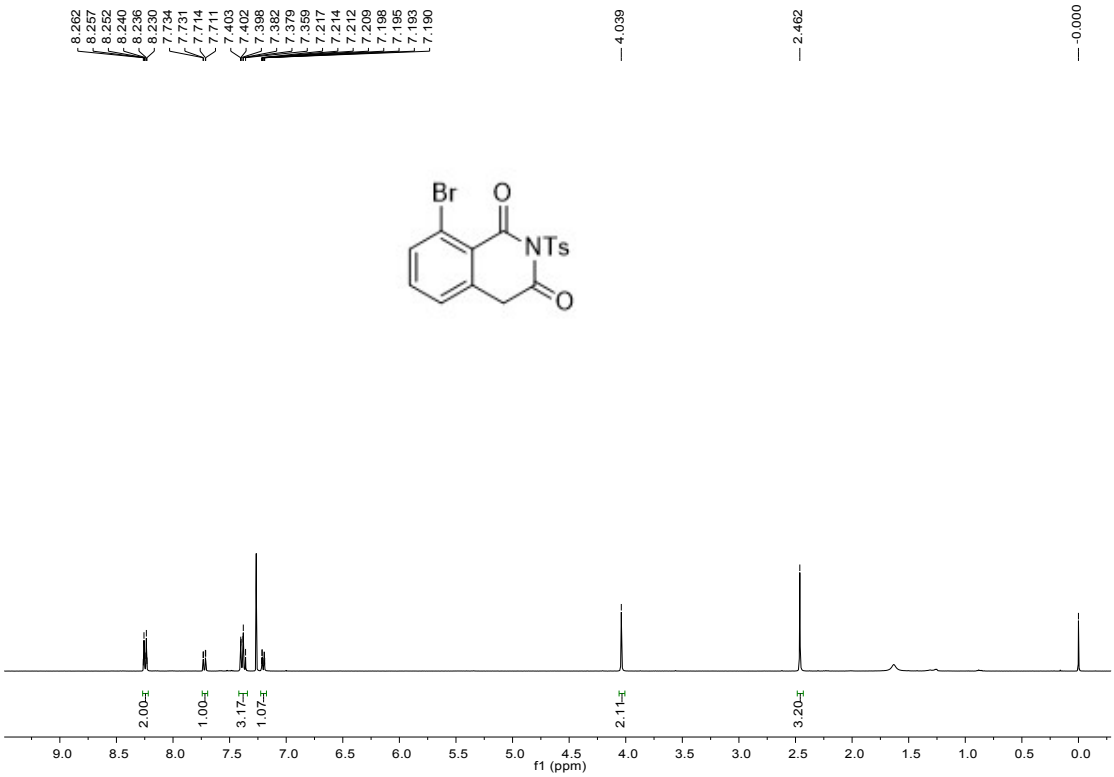


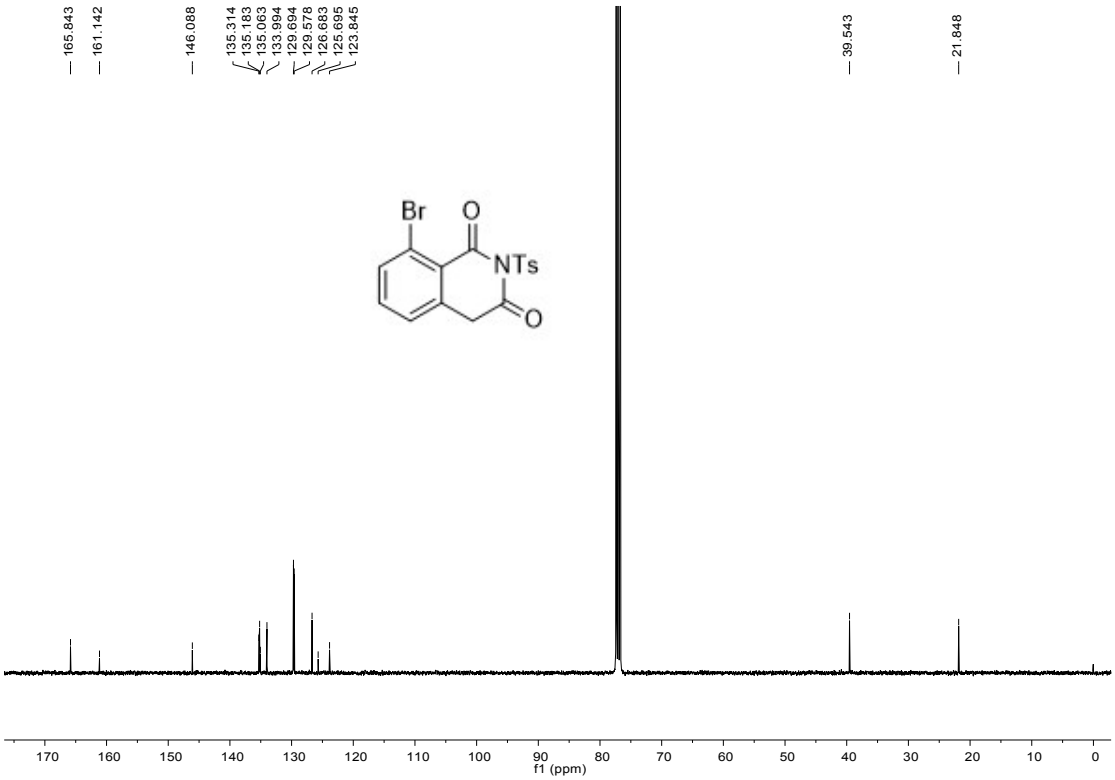
(3j) 8-chloro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione



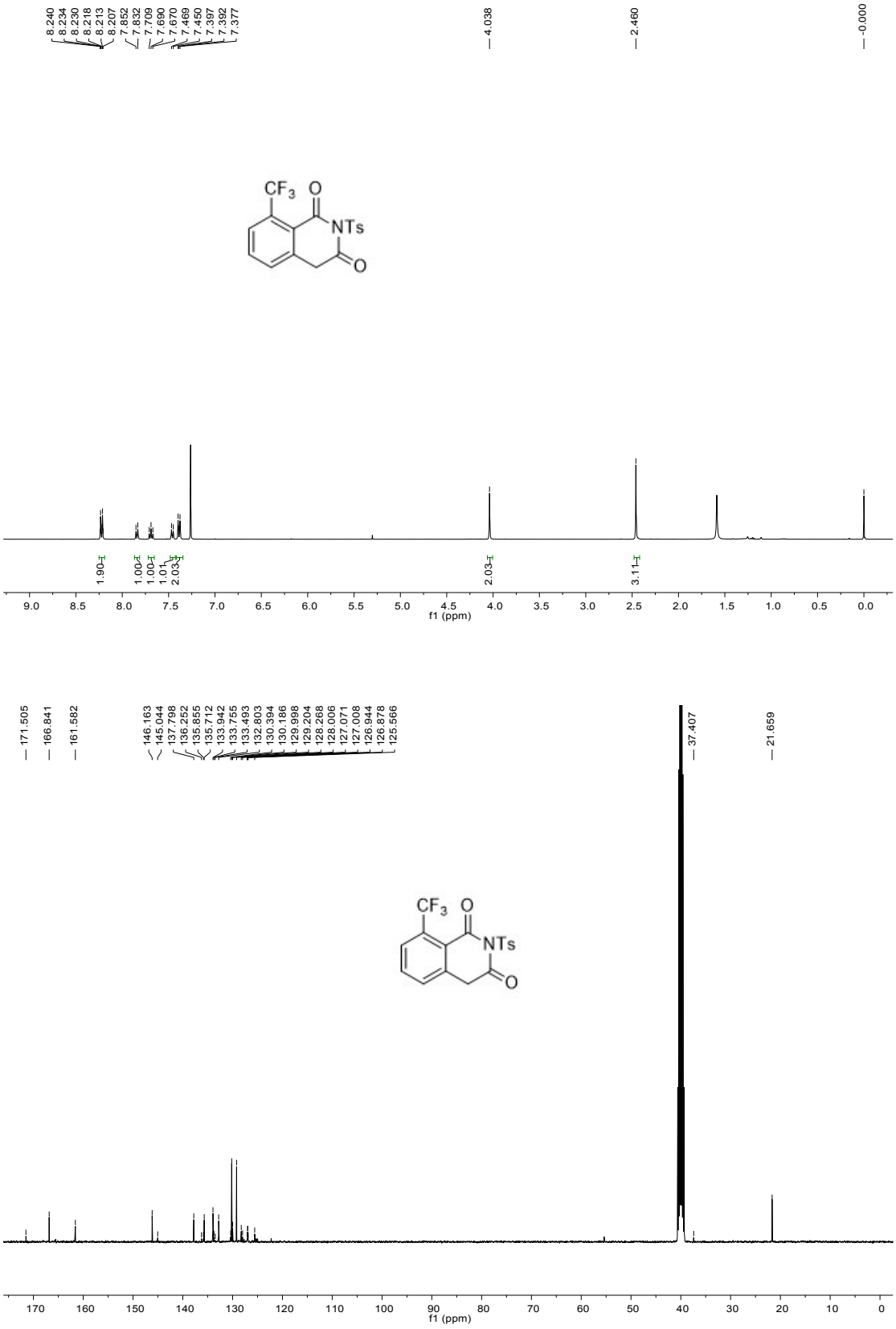


(3k) 8-bromo-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

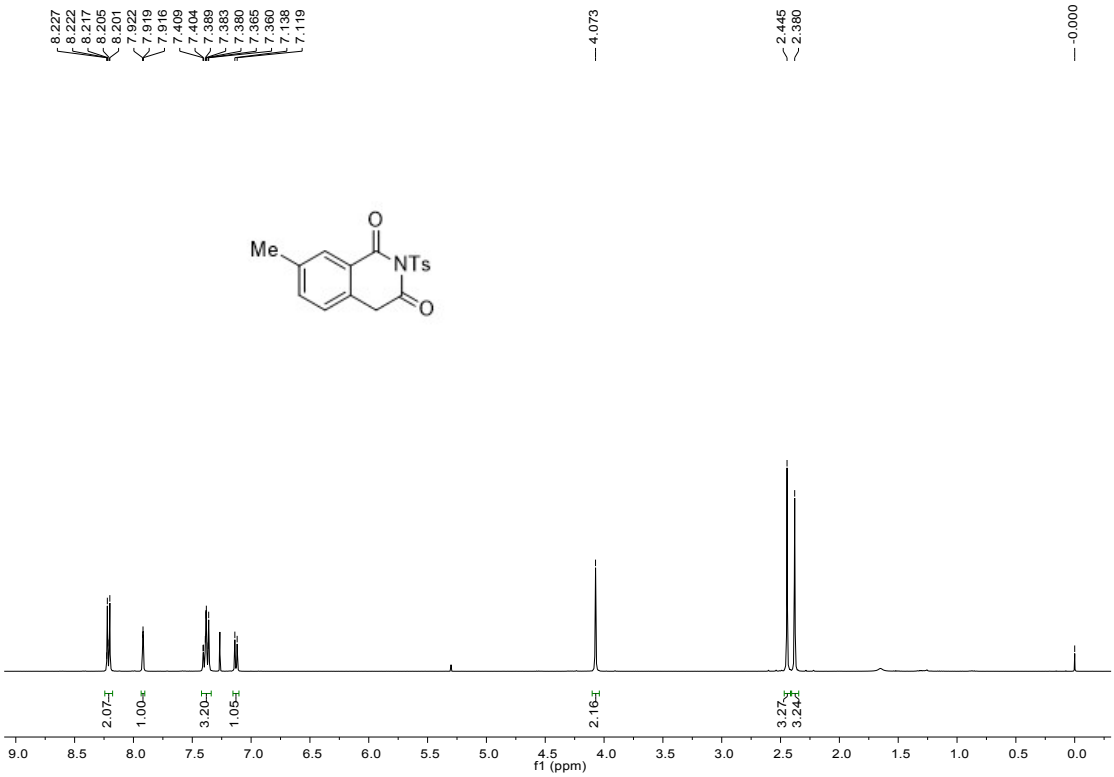


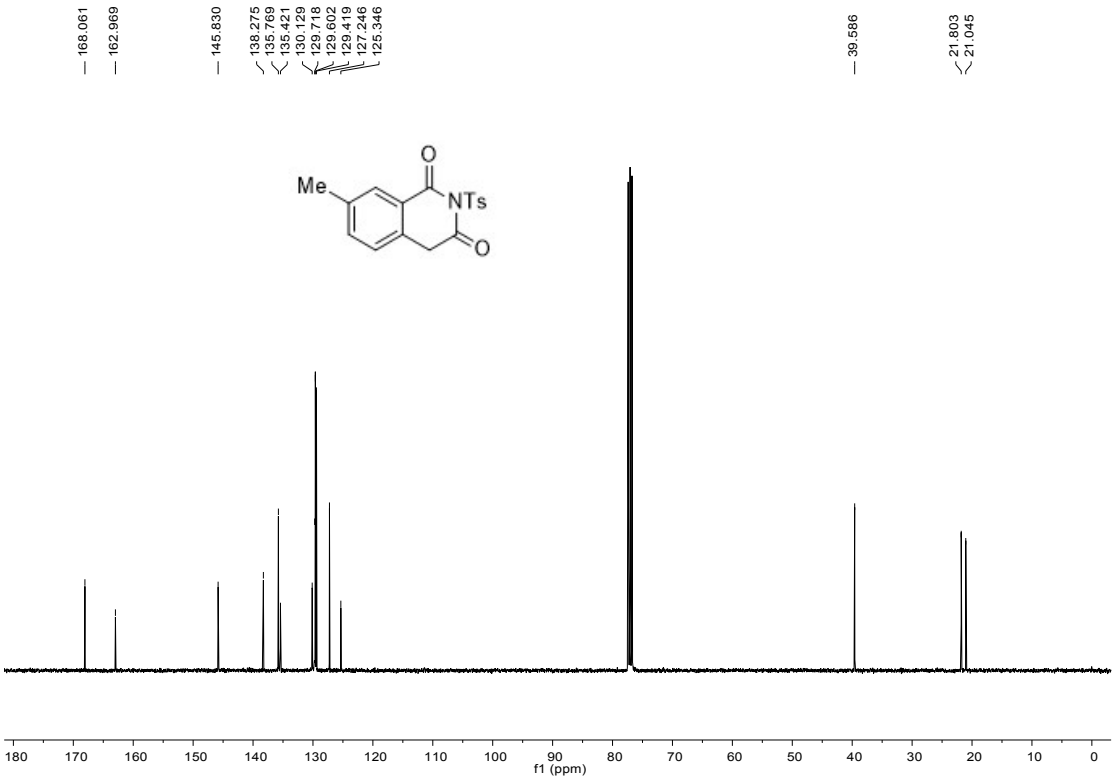


(3l) 2-tosyl-8-(trifluoromethyl)isoquinoline-1,3(2*H*,4*H*)-dione

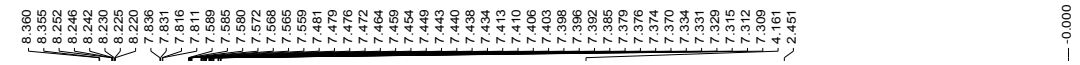


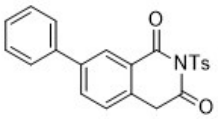
(3m) 7-methyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

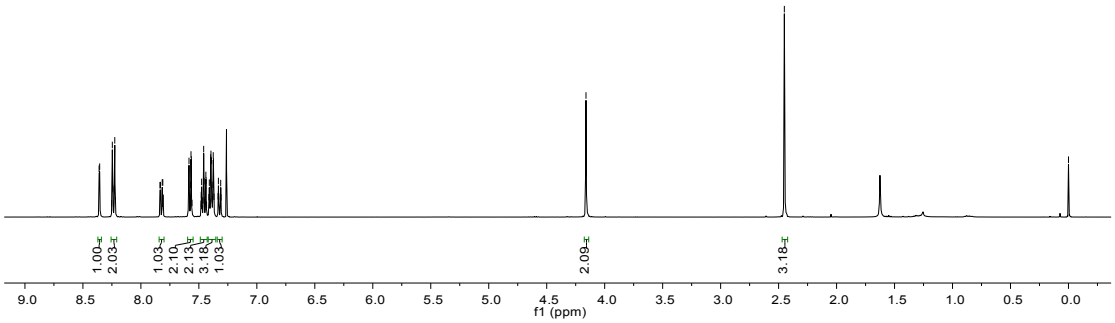


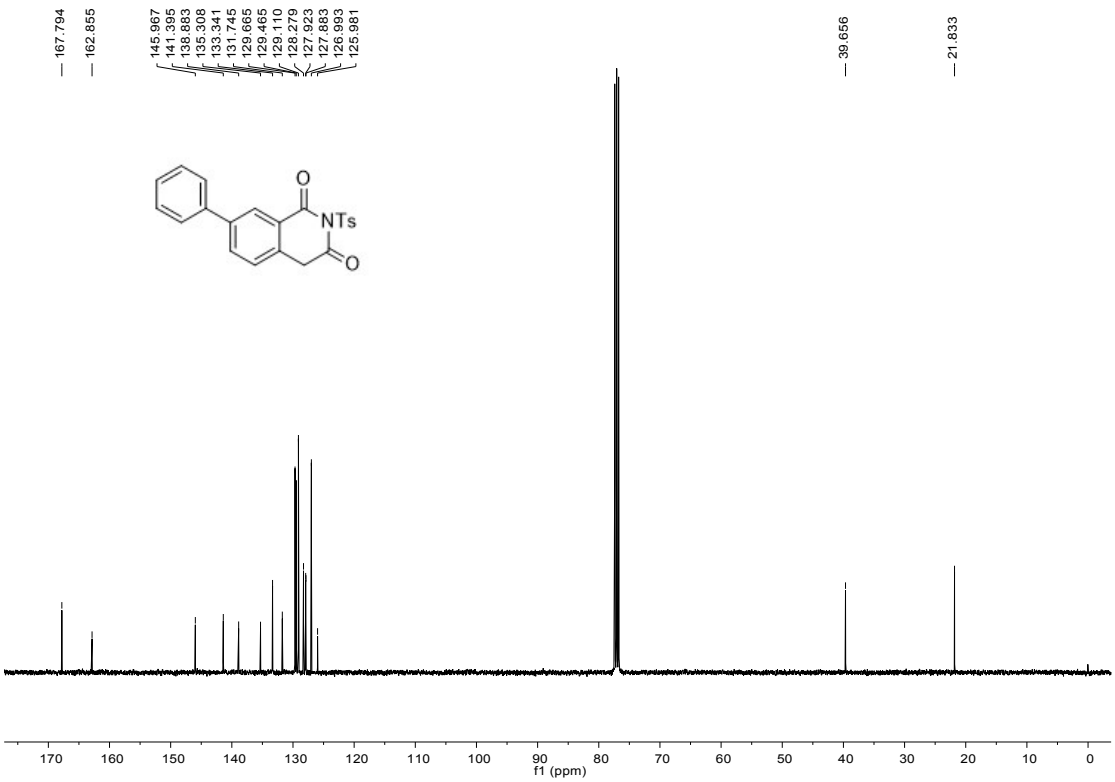


(3n) 7-phenyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

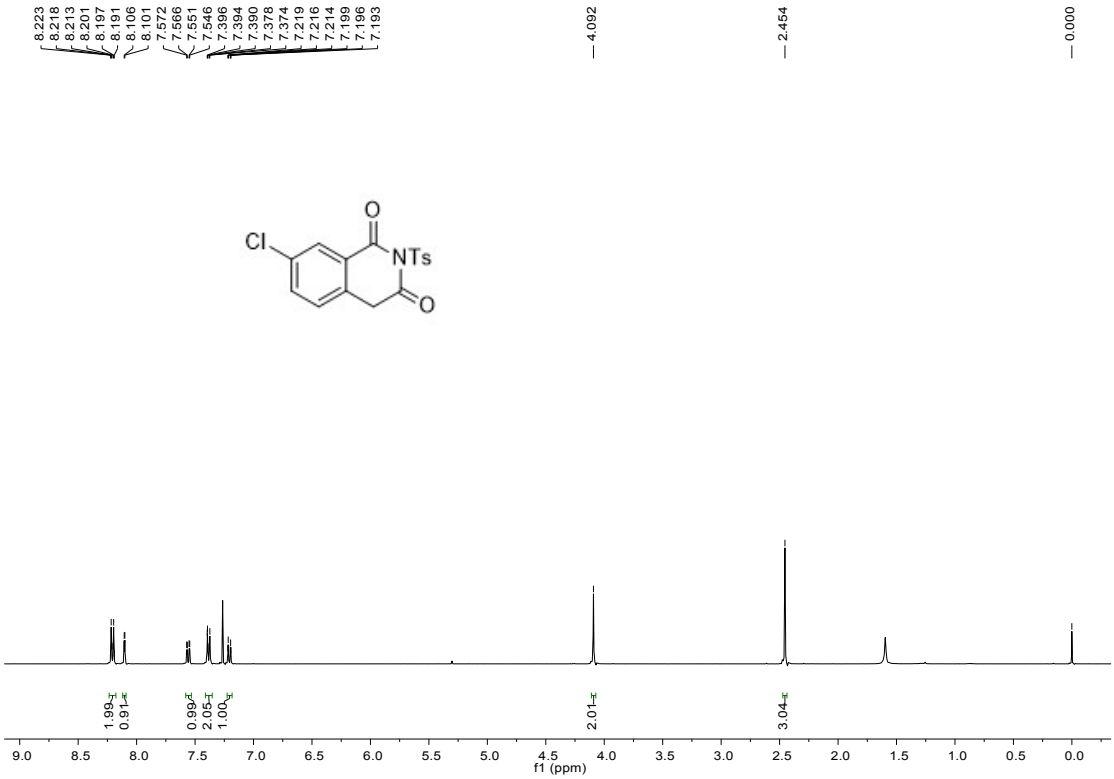


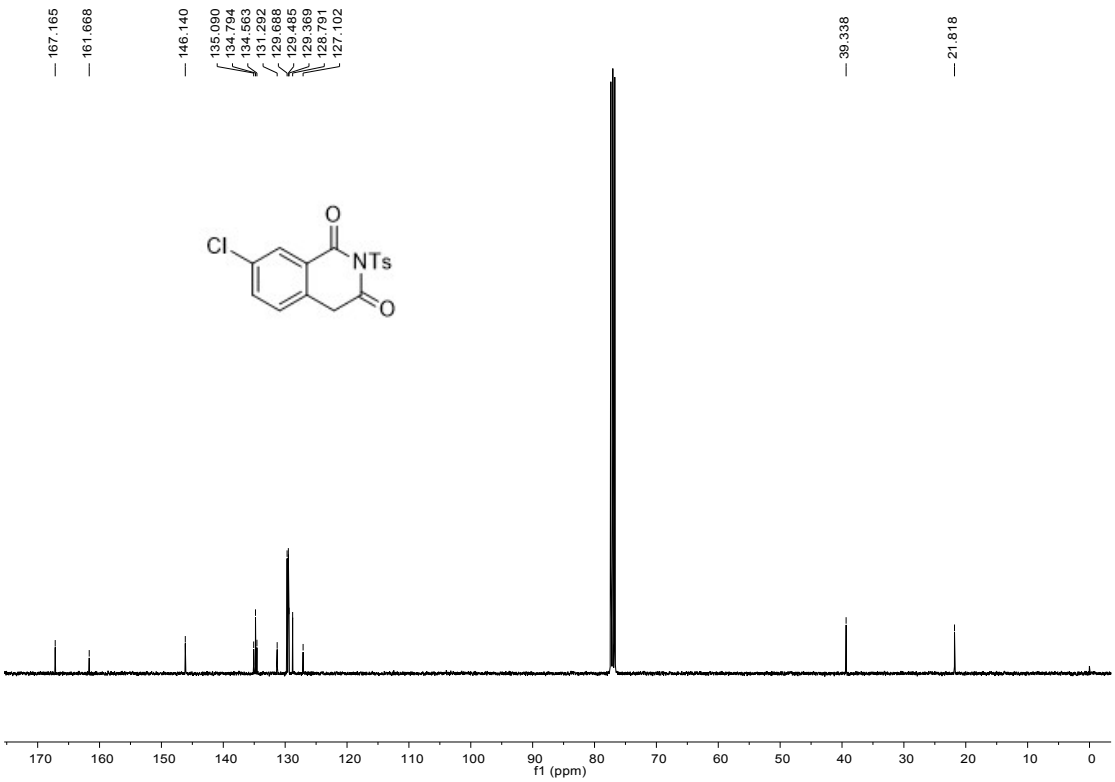




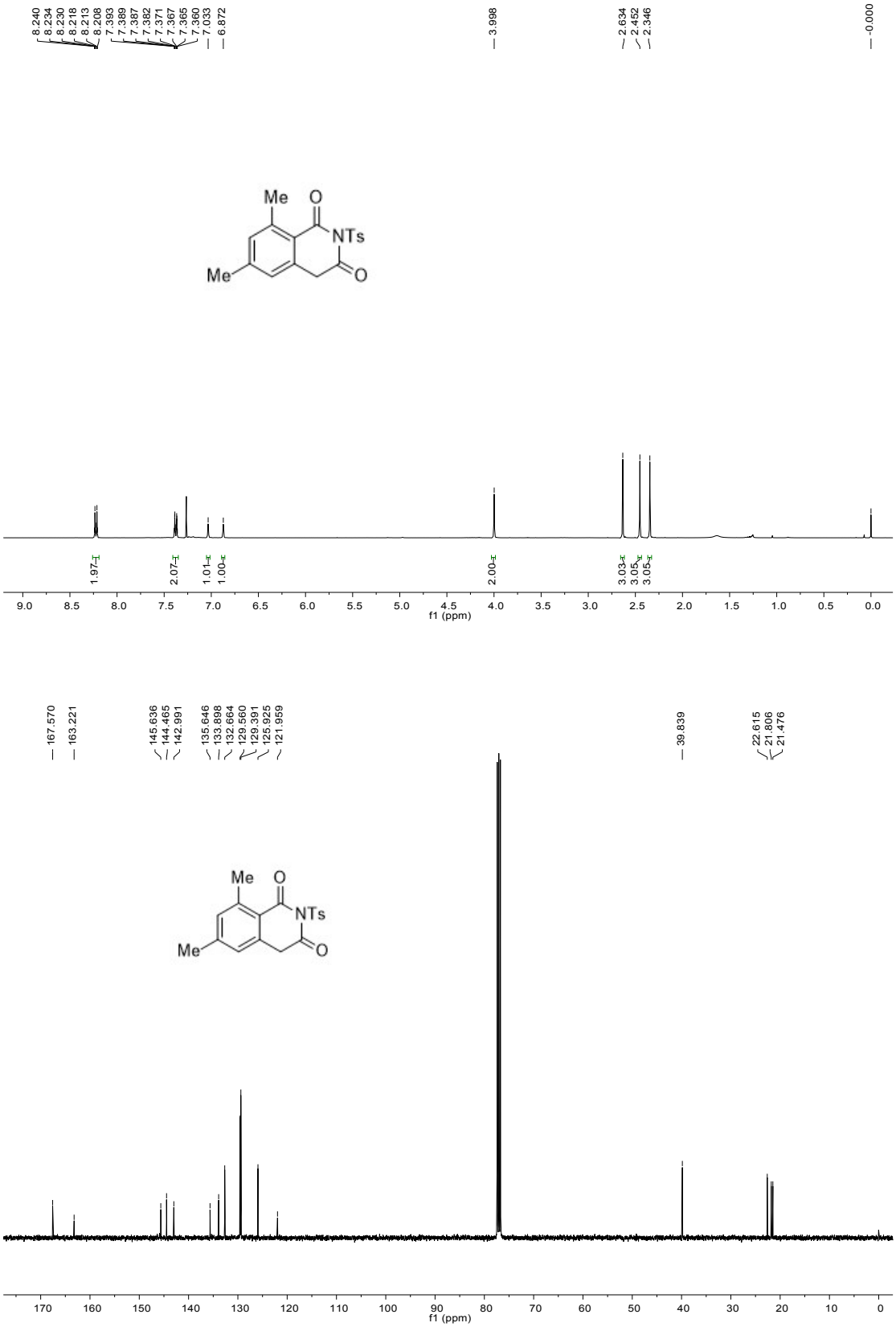


(3o) 7-chloro-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

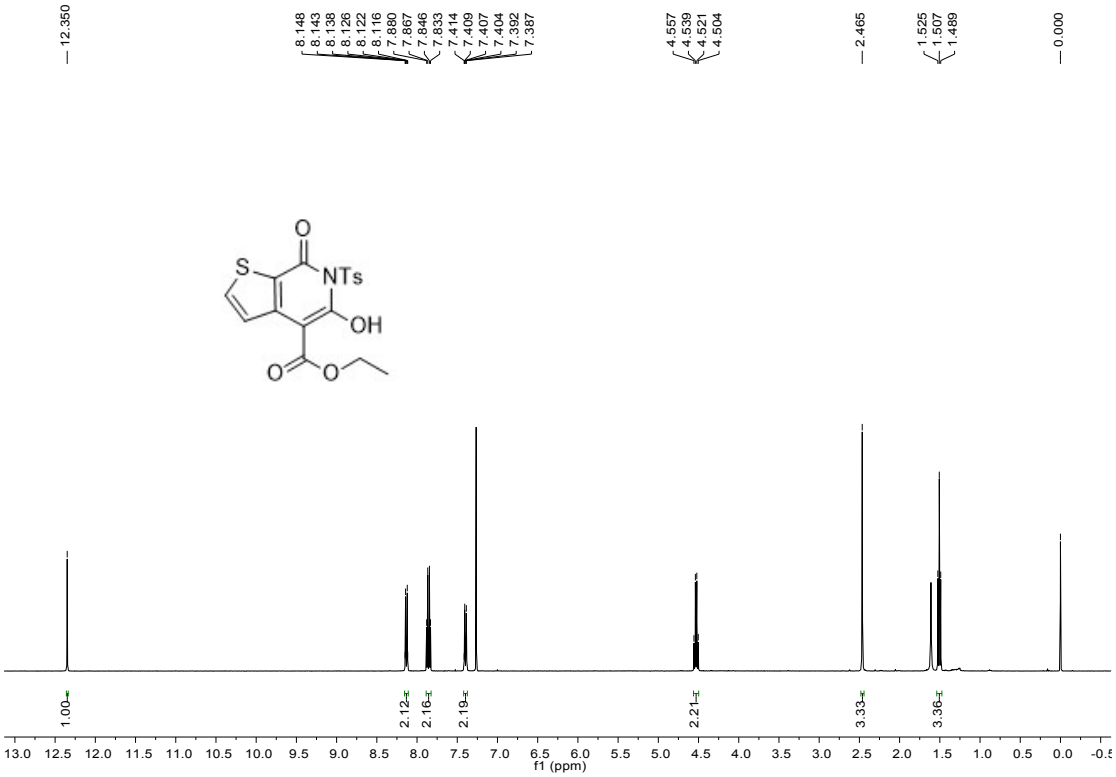


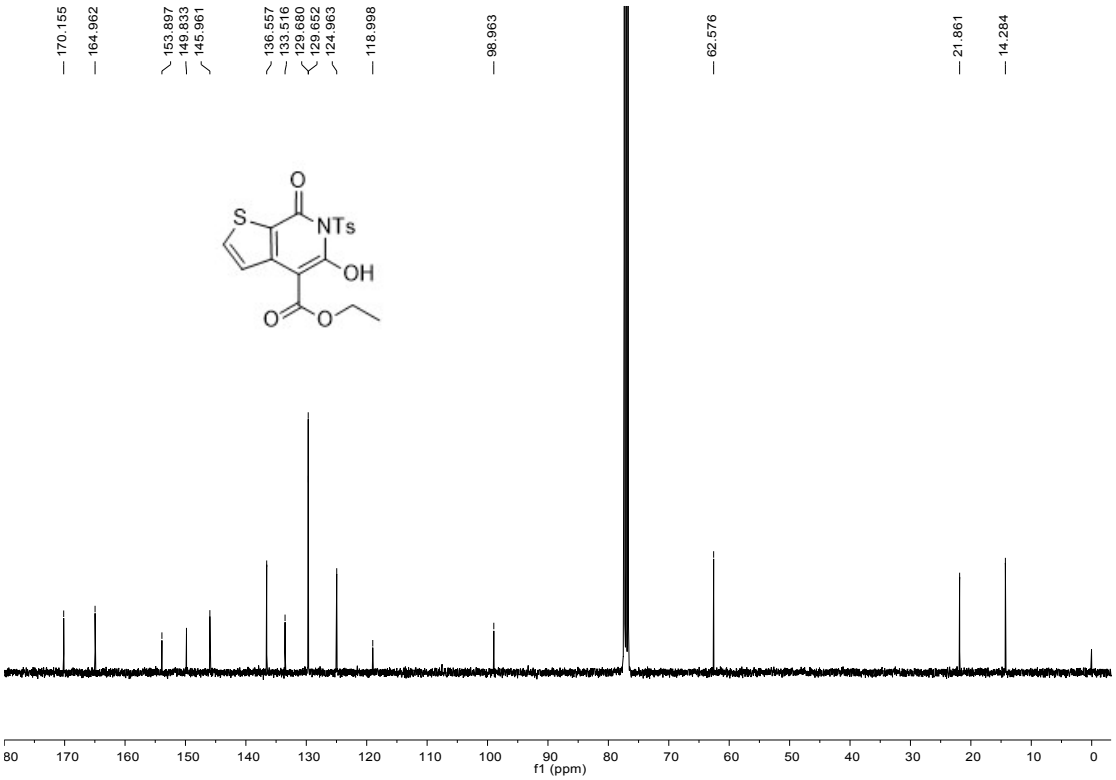


(3p) 6,8-dimethyl-2-tosylisoquinoline-1,3(2*H*,4*H*)-dione

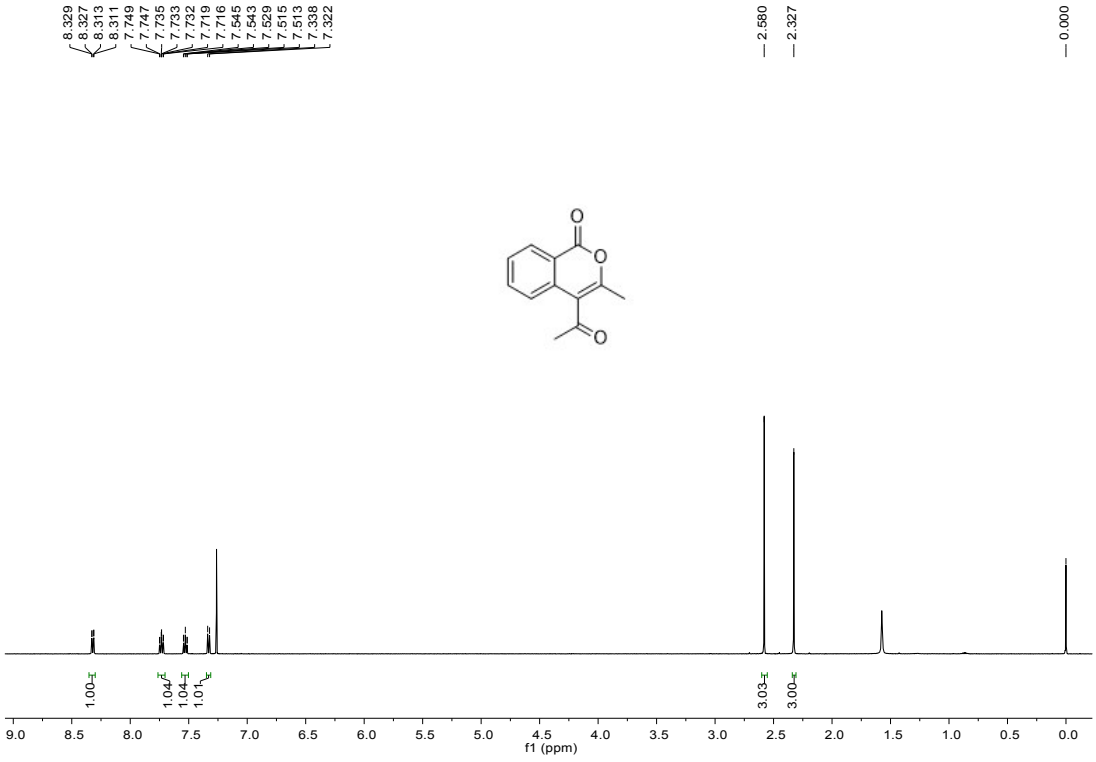


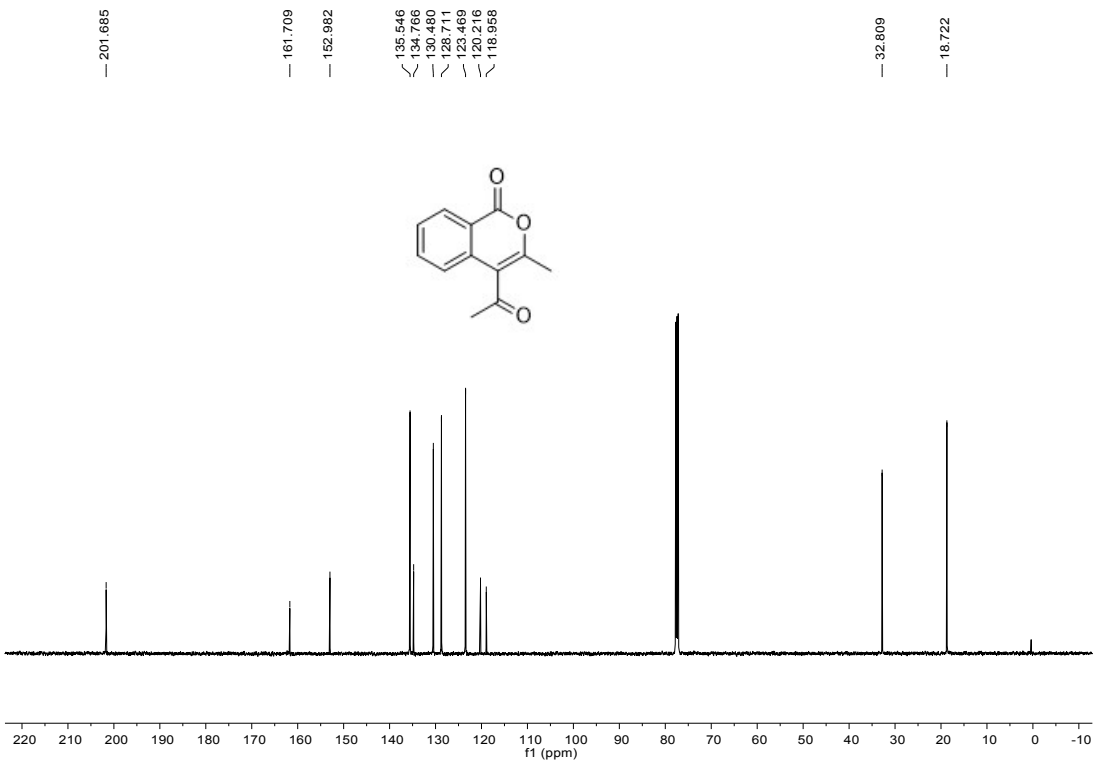
(3q) ethyl 5-hydroxy-7-oxo-6-tosyl-6,7-dihydrothieno[2,3-c]pyridine-4-carboxylate



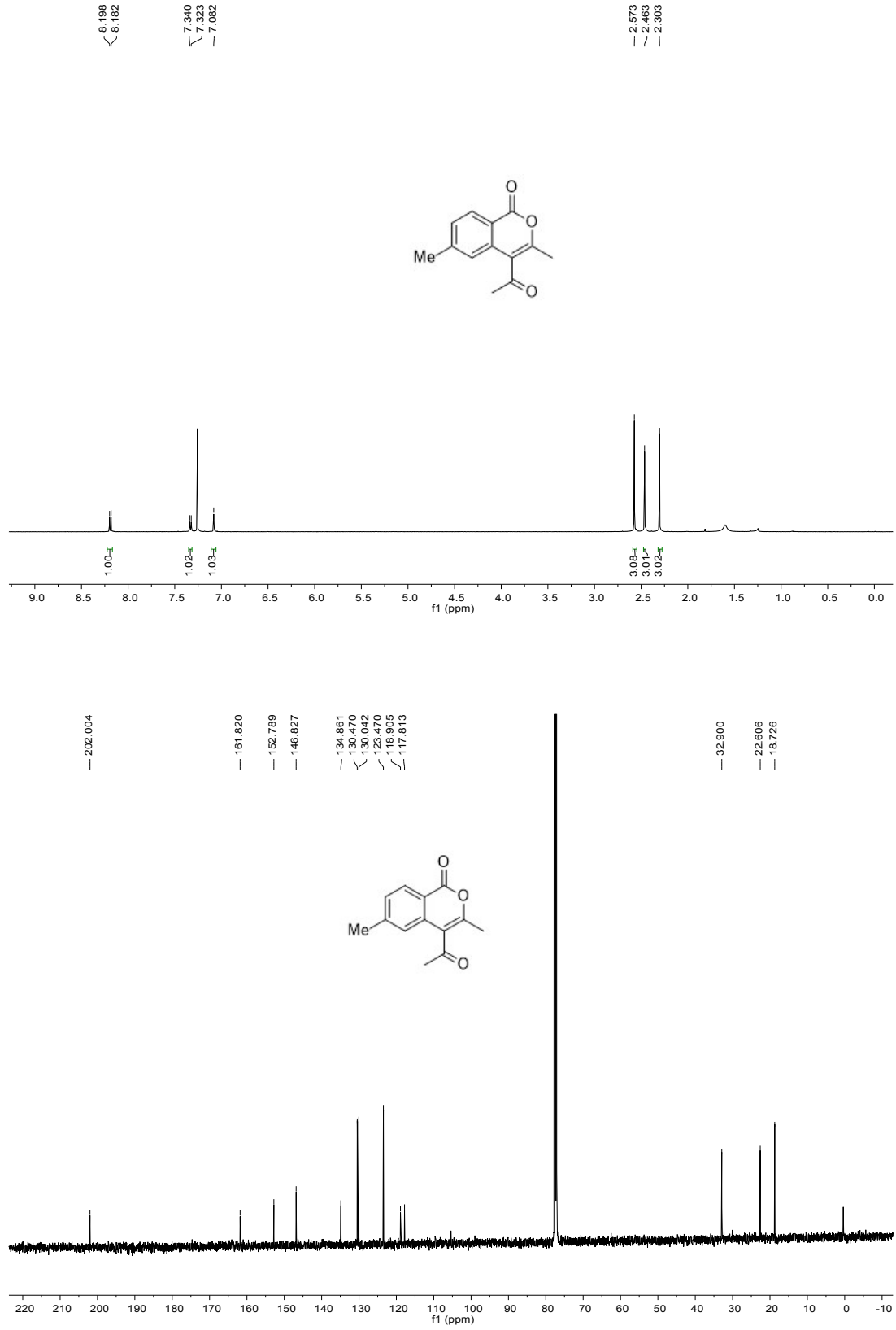


(4a) 4-acetyl-3-methyl-1*H*-isochromen-1-one

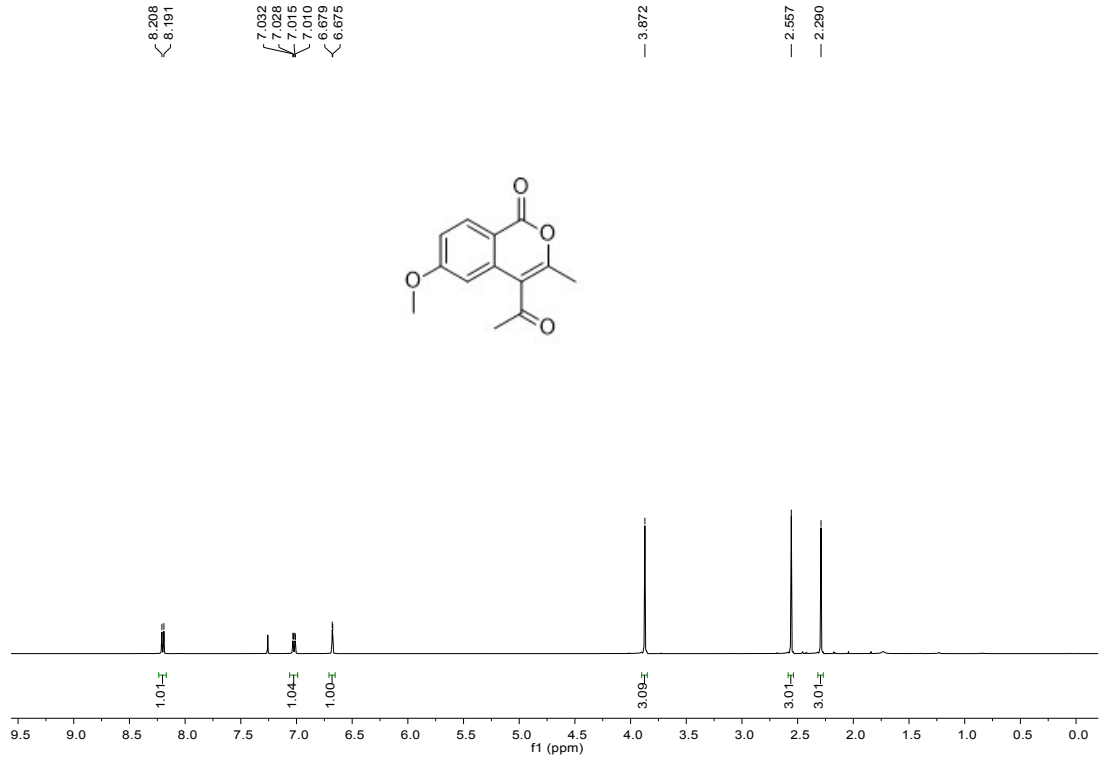


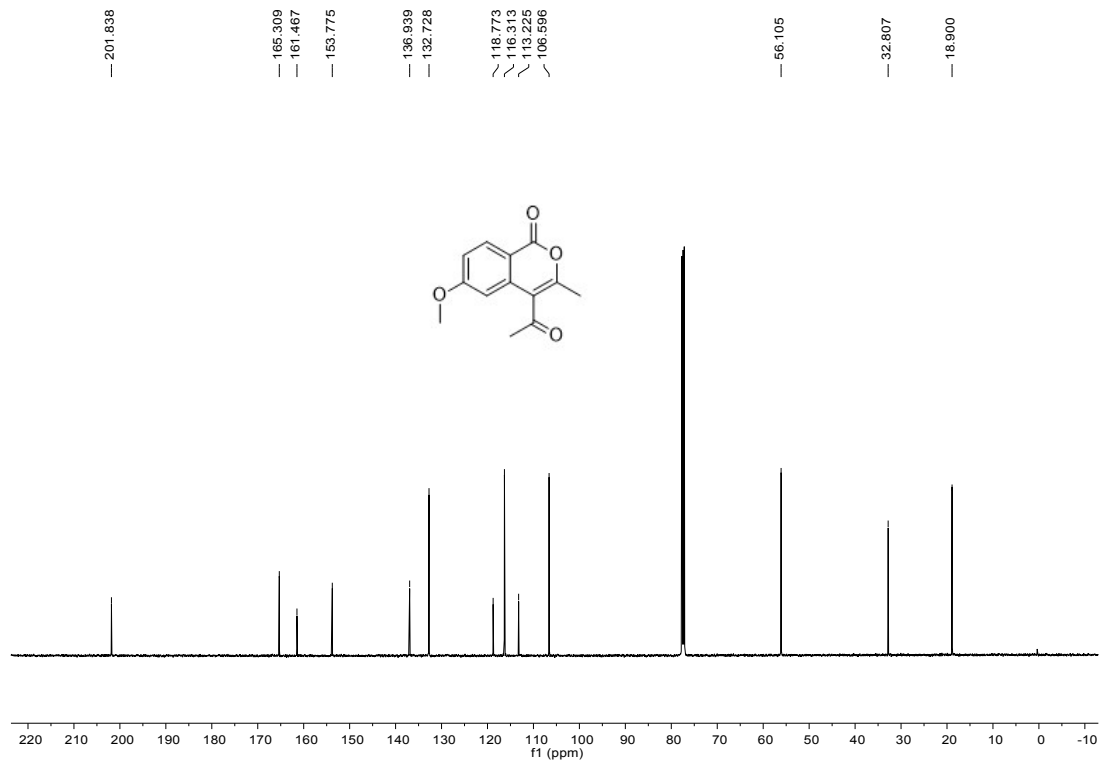


(4b) 4-acetyl-3,6-dimethyl-1*H*-isochromen-1-one

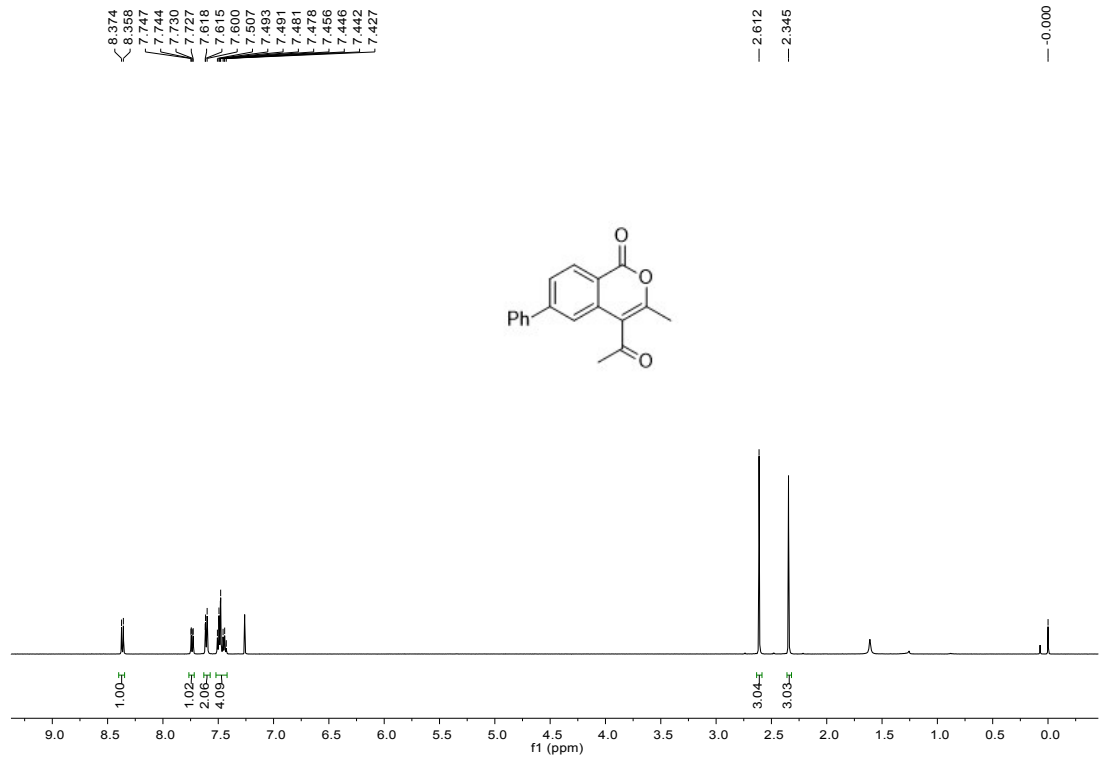


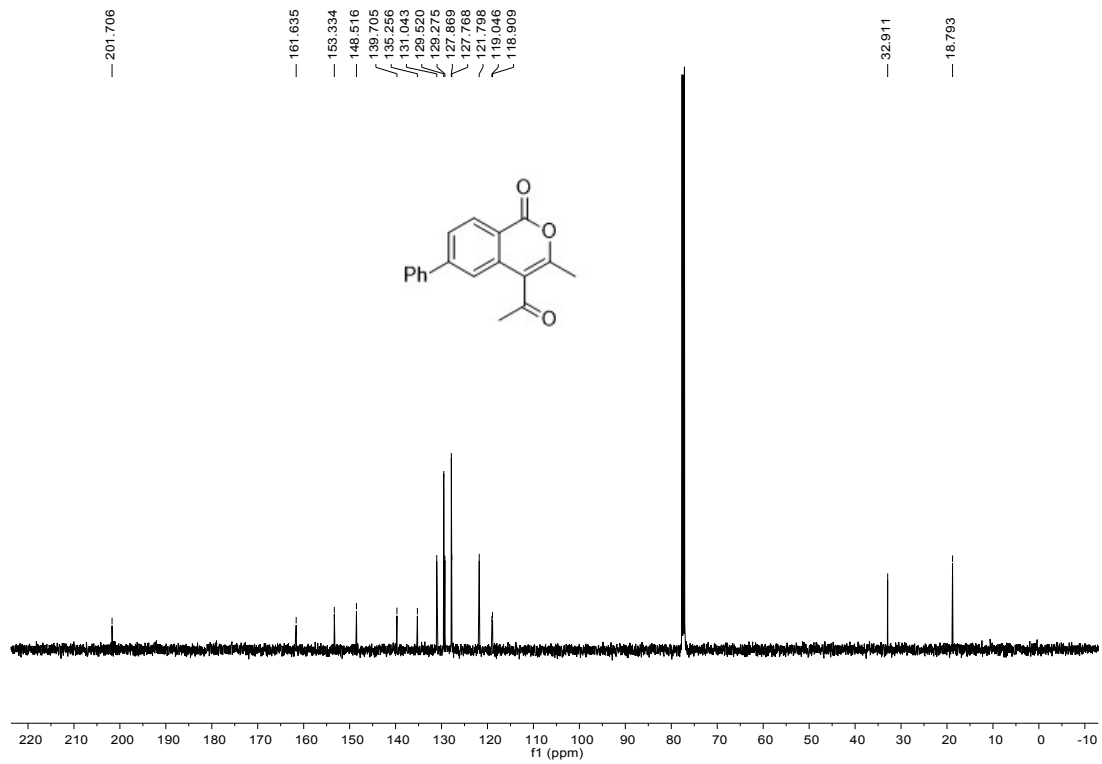
(4c) 4-acetyl-6-methoxy-3-methyl-1*H*-isochromen-1-one



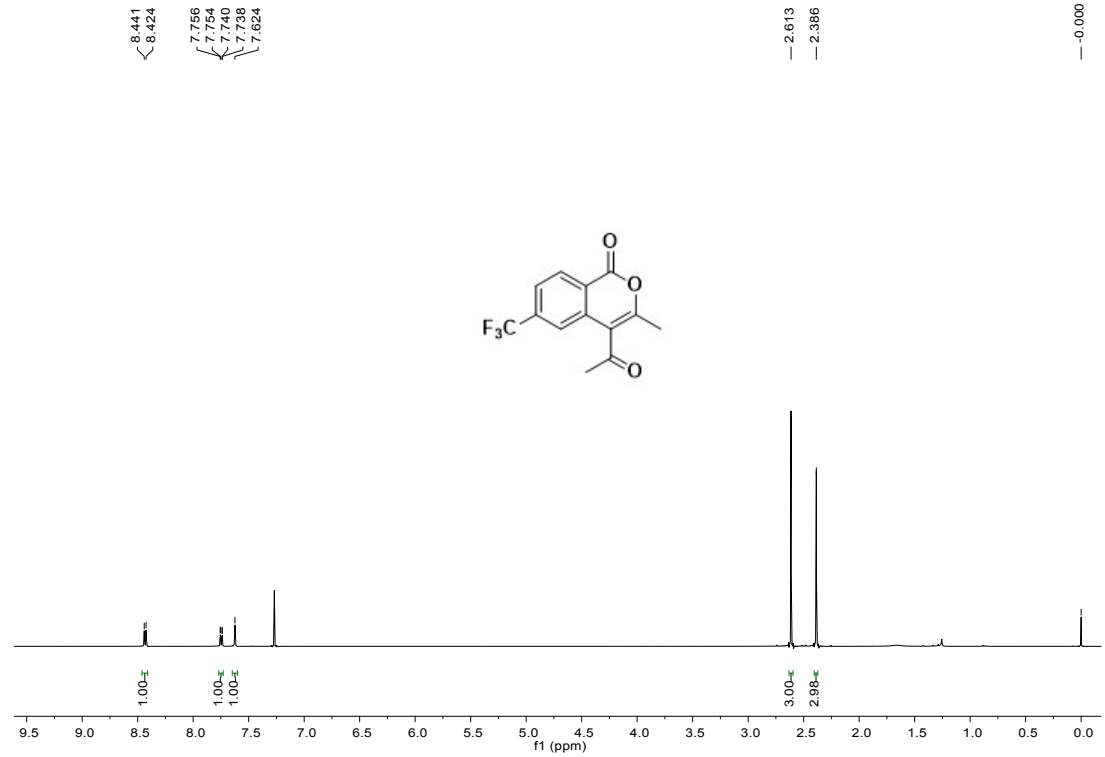


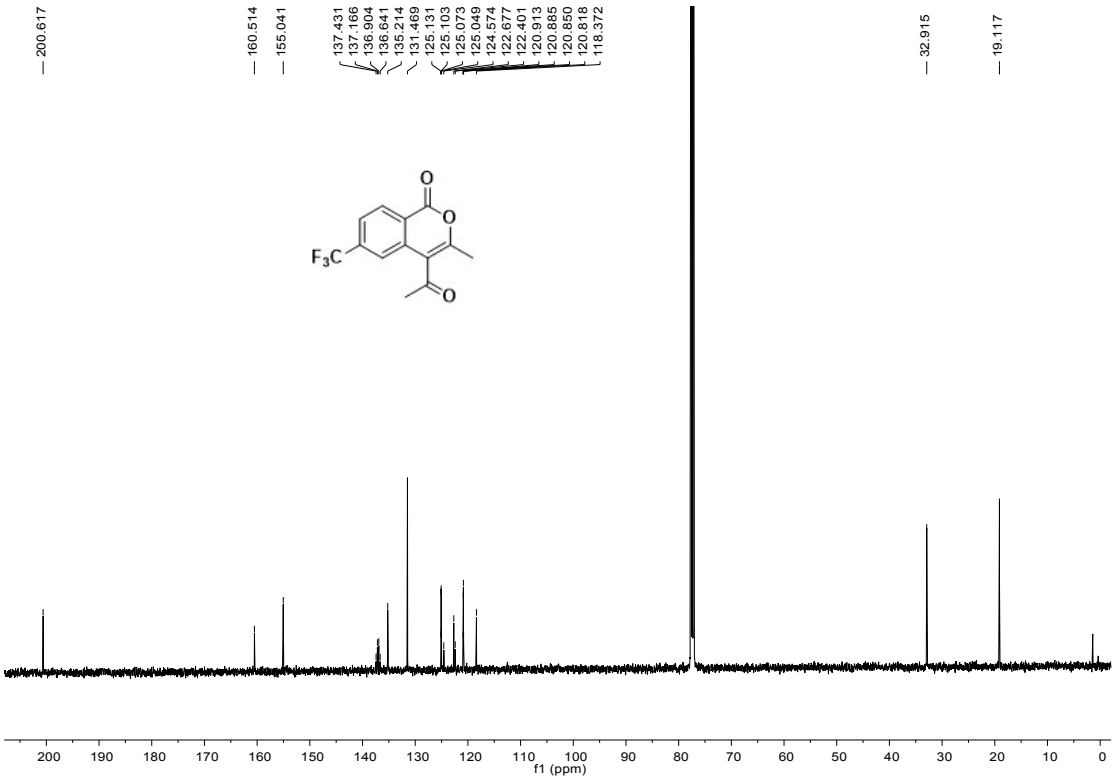
(4d) 4-acetyl-3-methyl-6-phenyl-1*H*-isochromen-1-one



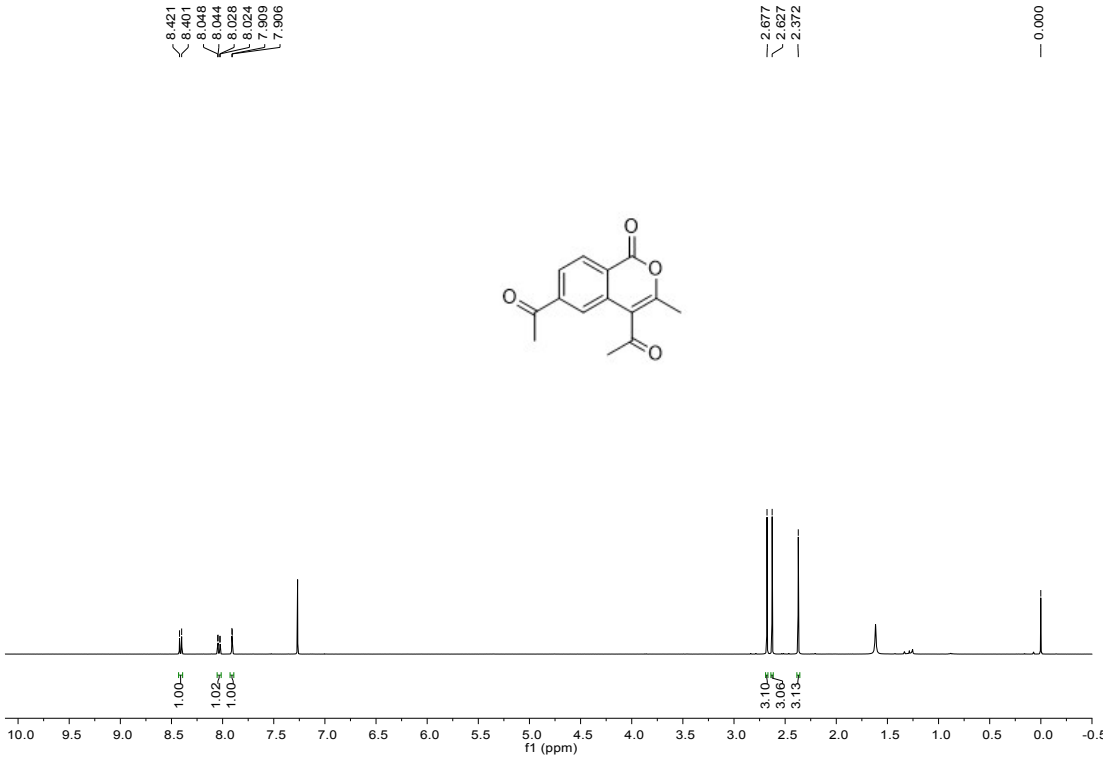


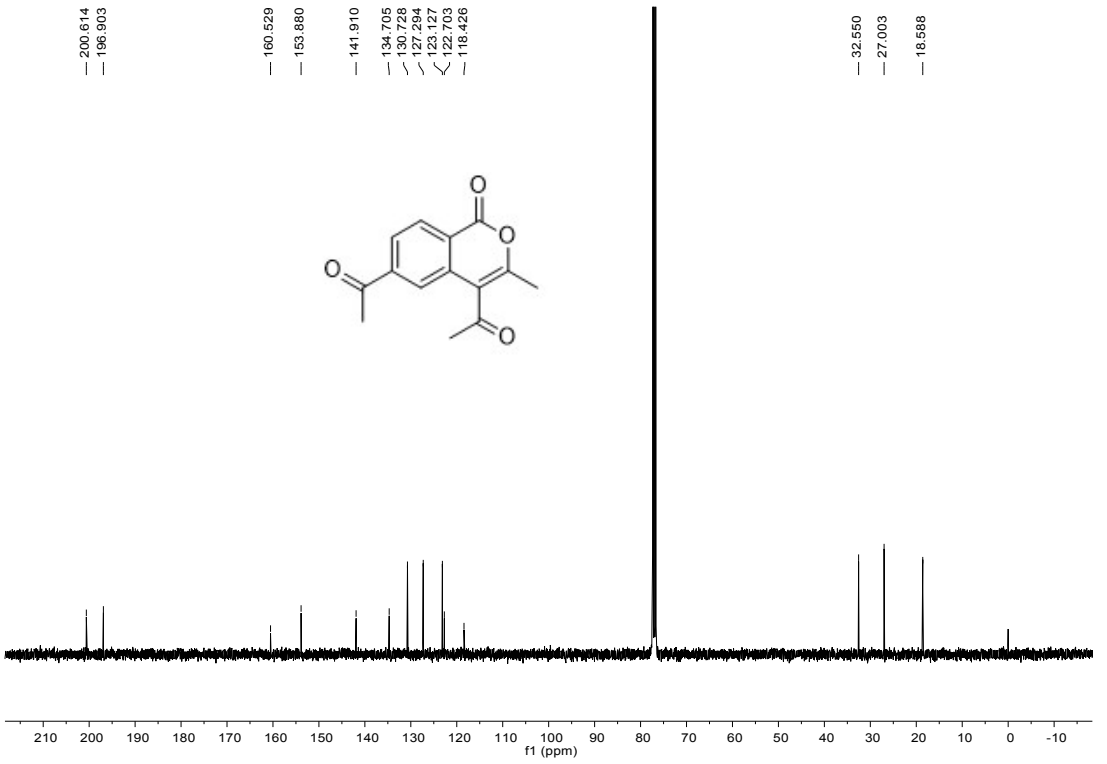
(4e) 4-acetyl-3-methyl-6-(trifluoromethyl)-1*H*-isochromen-1-one



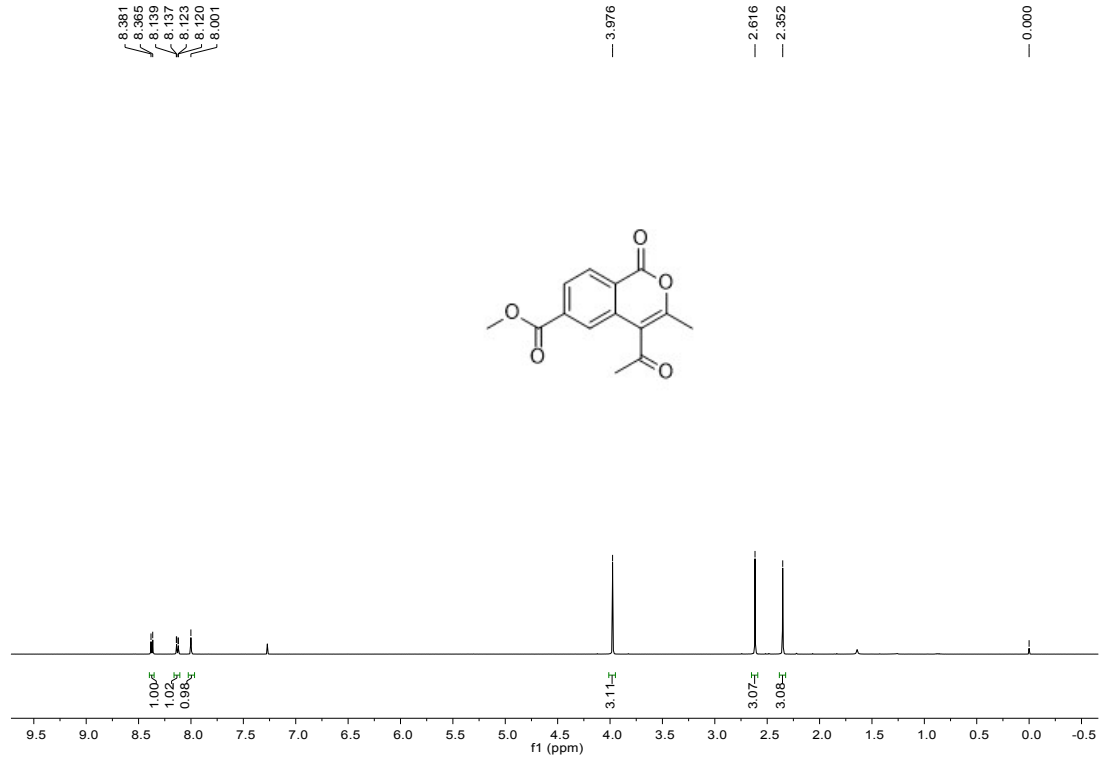


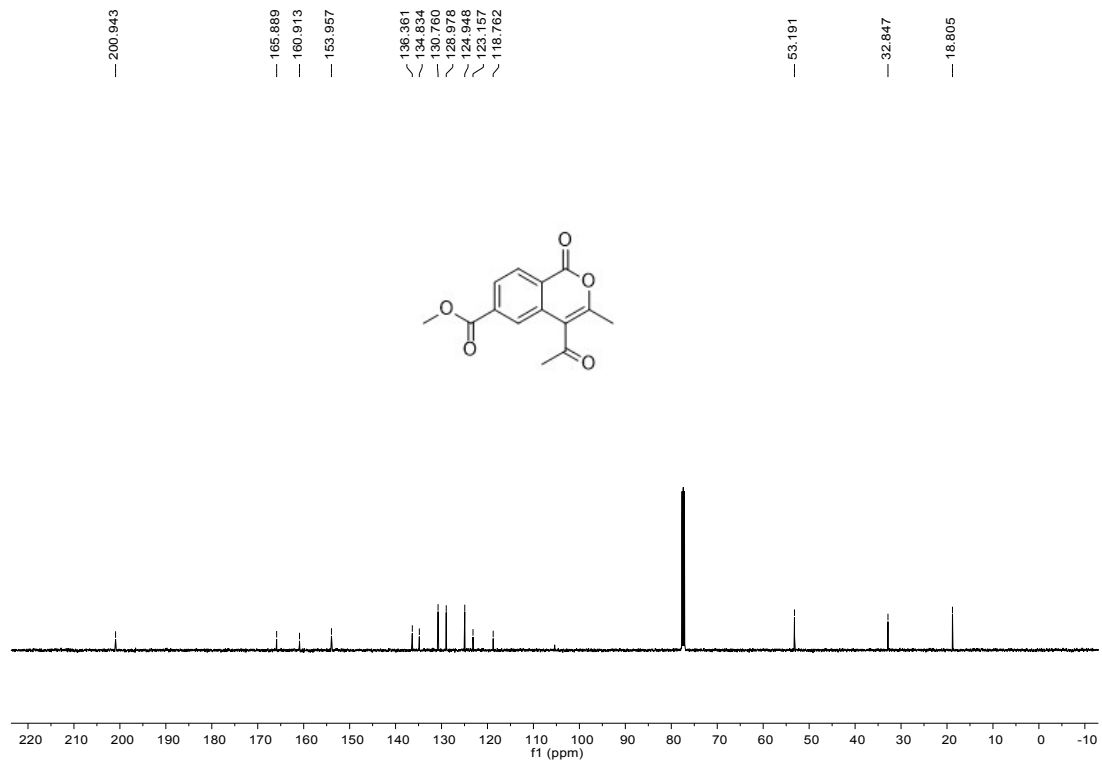
(4f) 1,1'-(3-methyl-1-oxo-1*H*-isochromene-4,6-diyl)bis(ethan-1-one)



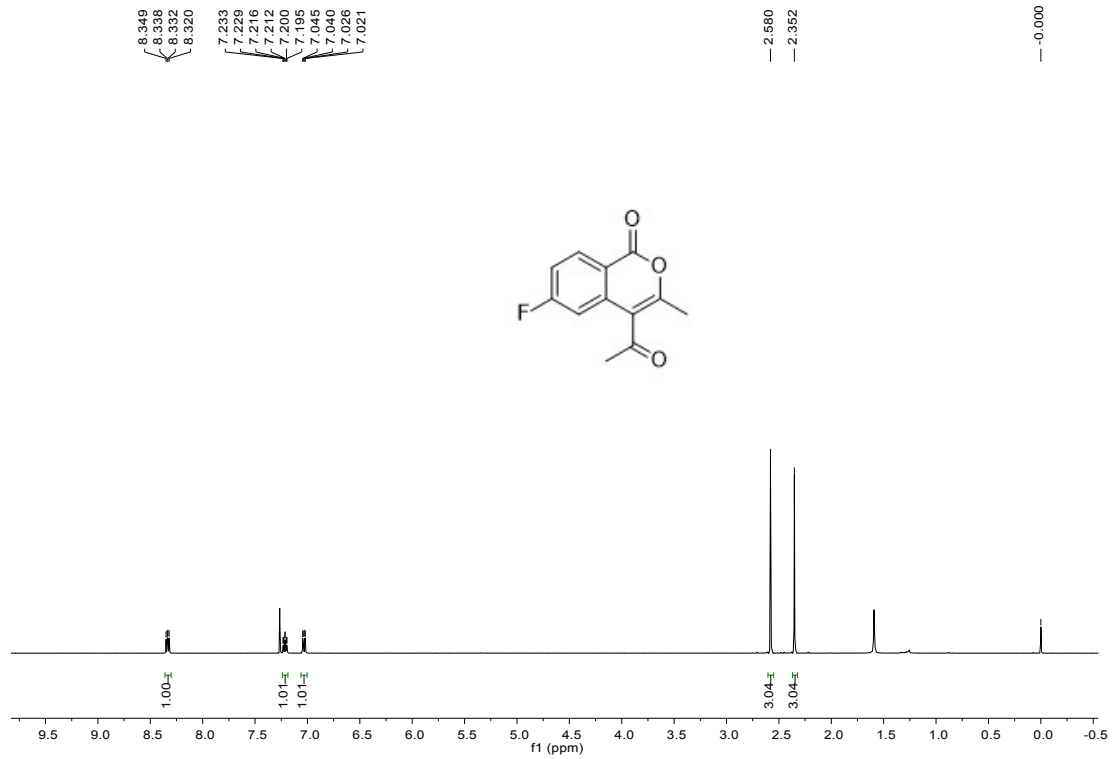


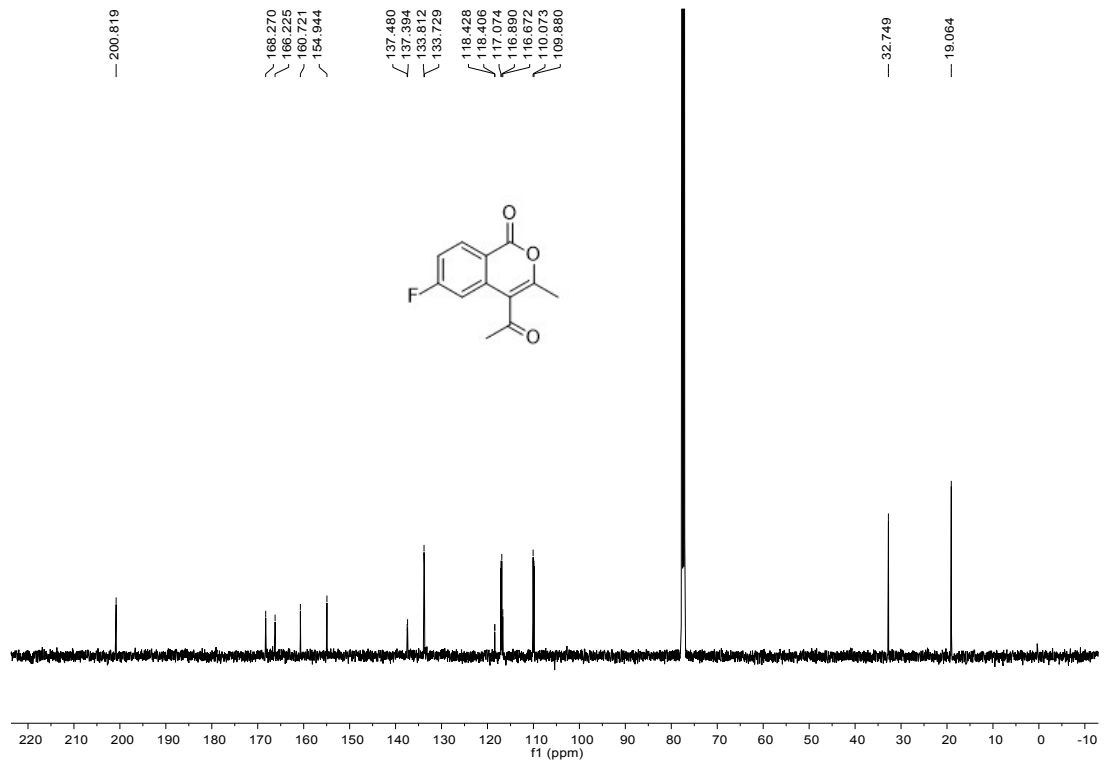
(4g) methyl 4-acetyl-3-methyl-1-oxo-1*H*-isochromene-6-carboxylate



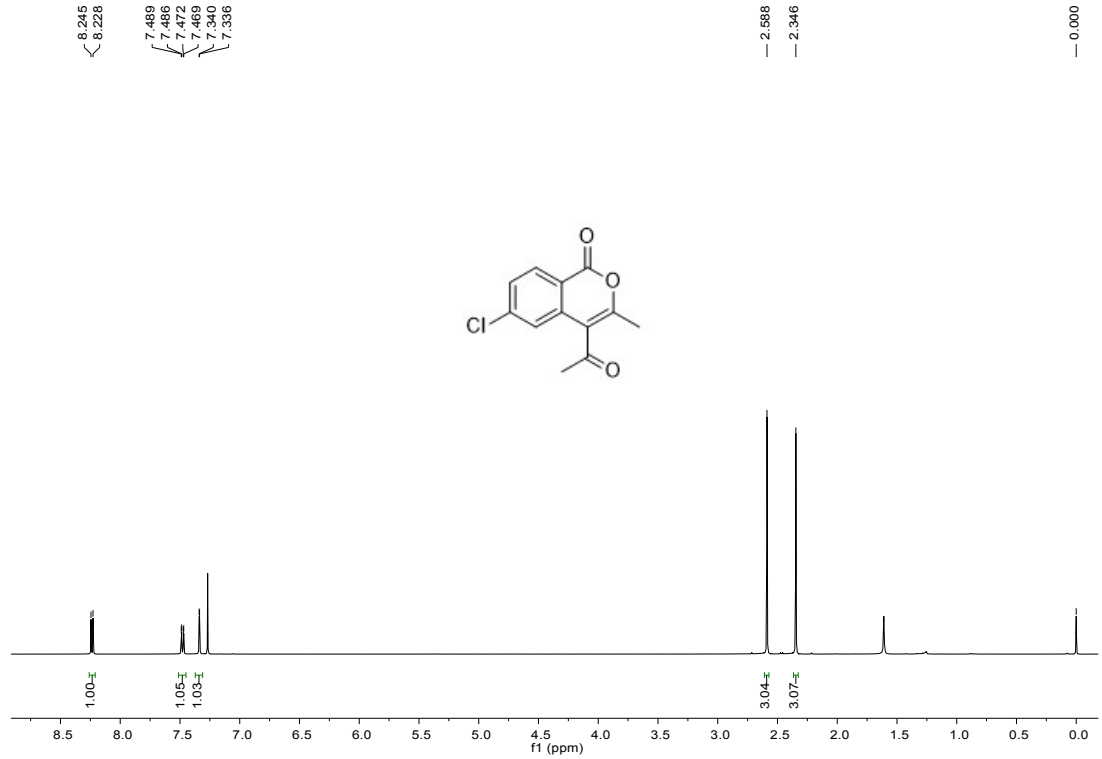


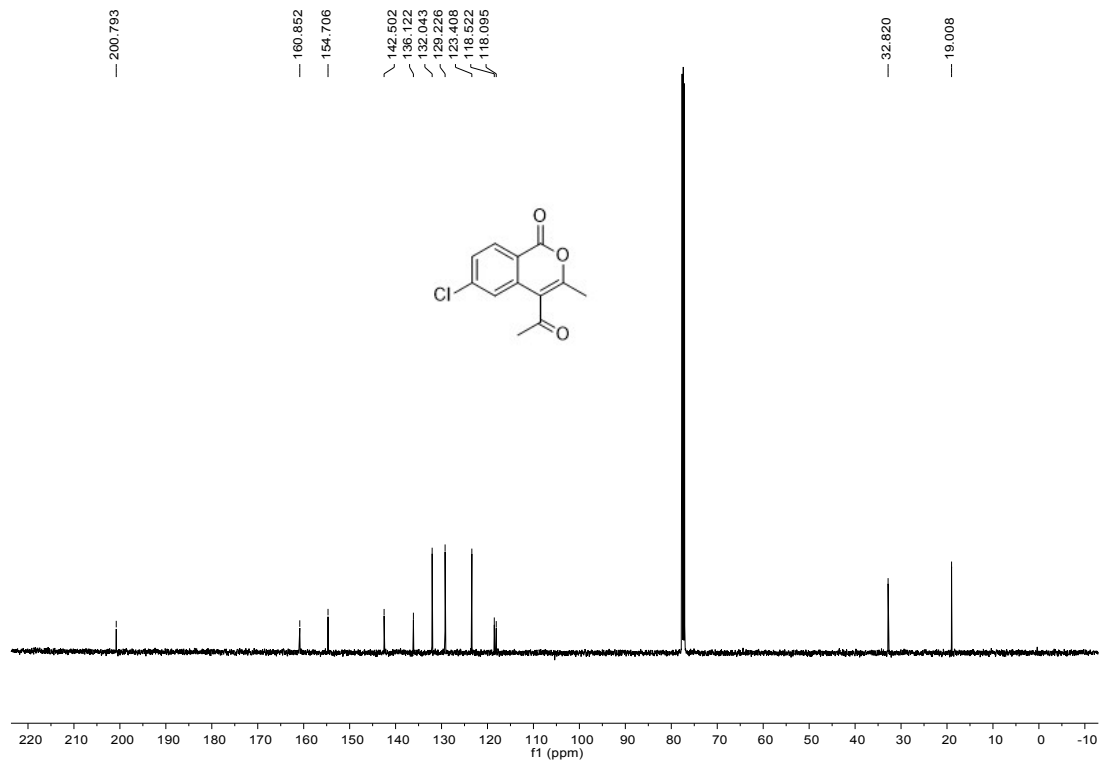
(4h) 4-acetyl-6-fluoro-3-methyl-1*H*-isochromen-1-one



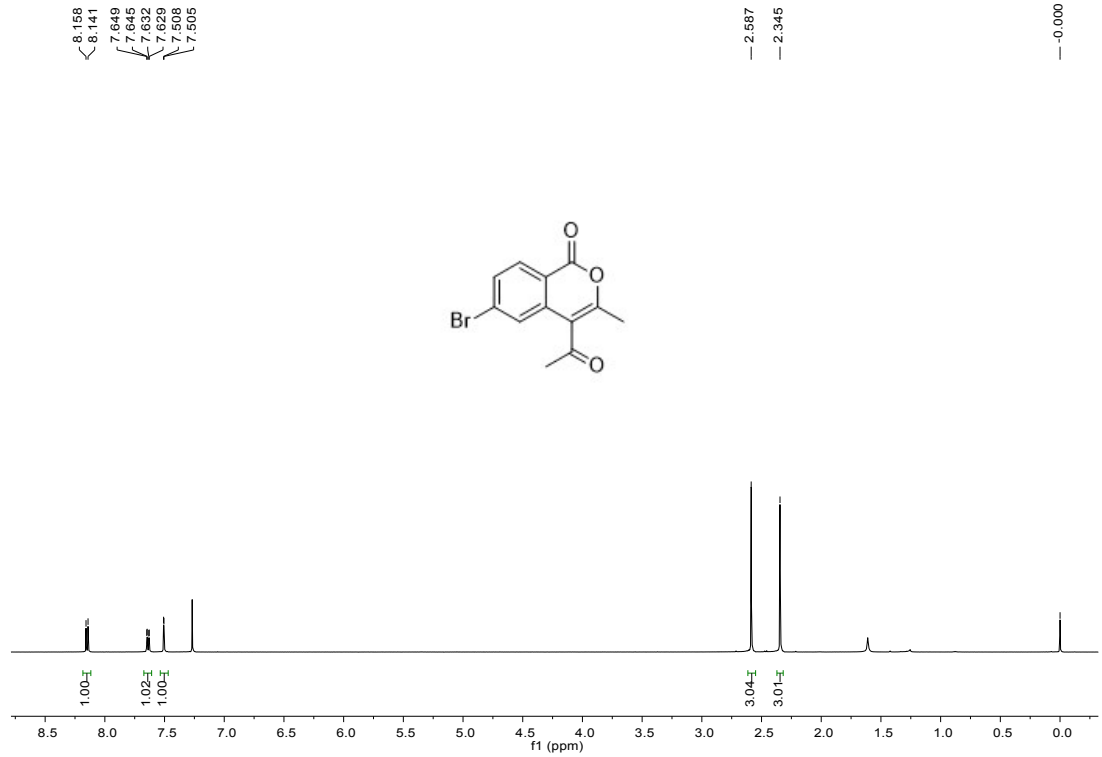


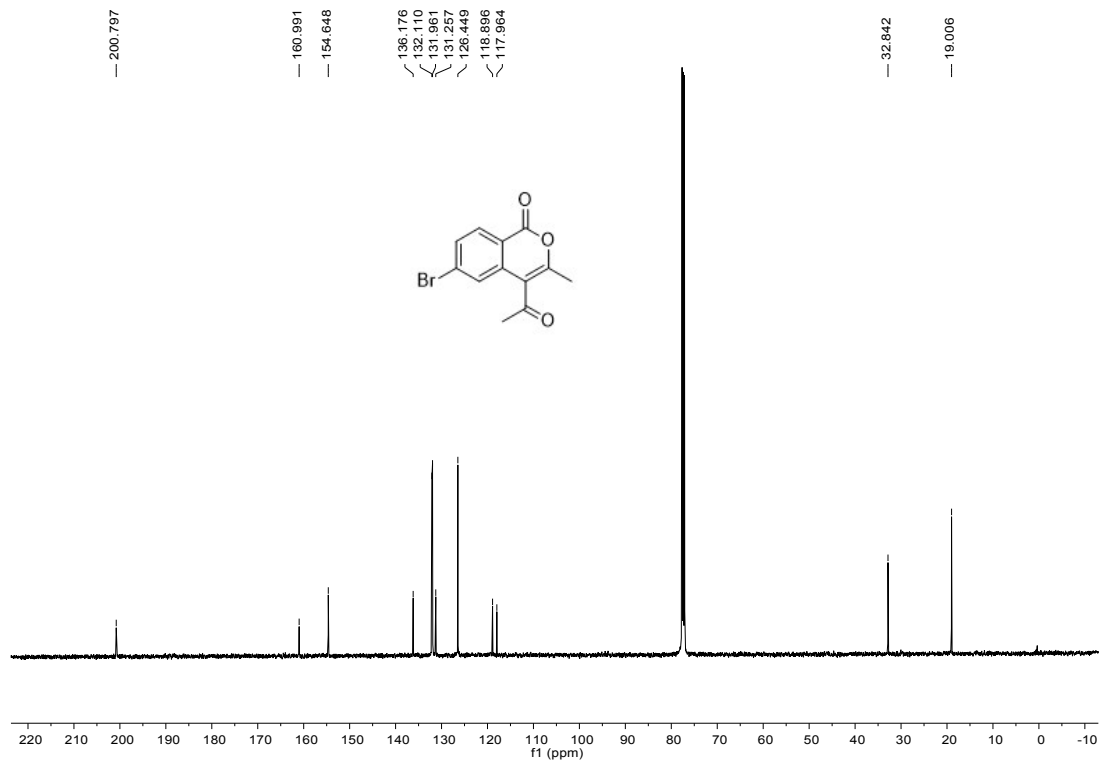
(4i) 4-acetyl-6-chloro-3-methyl-1*H*-isochromen-1-one



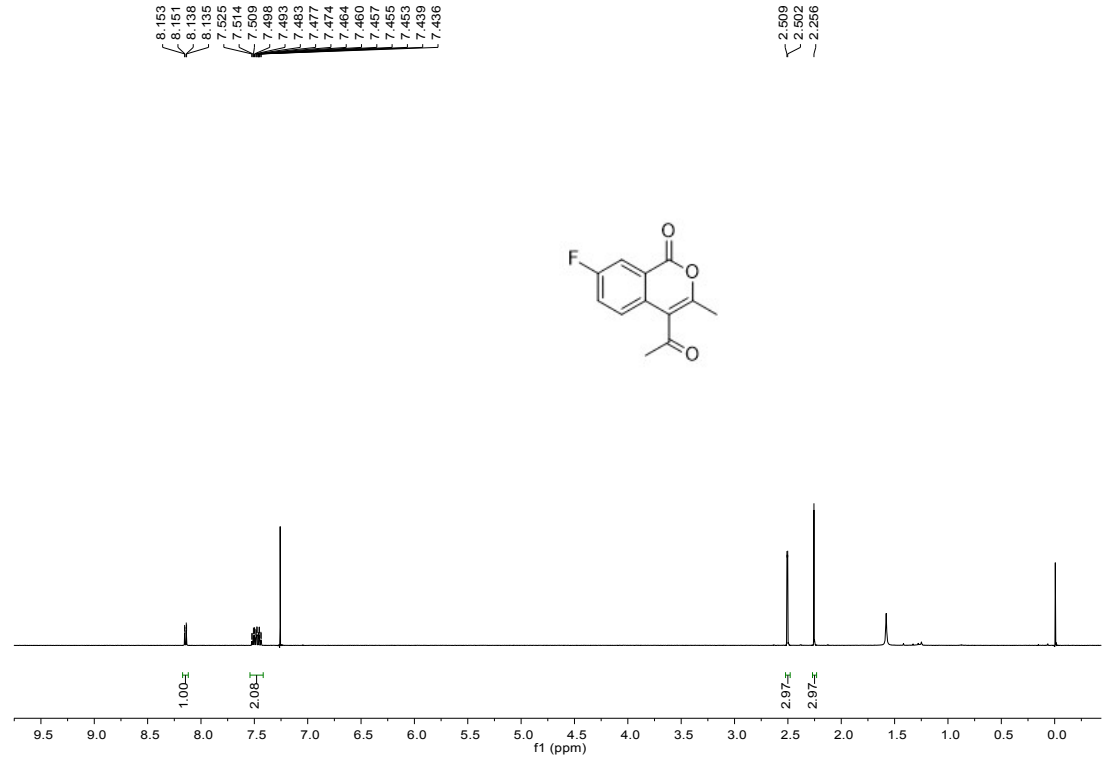


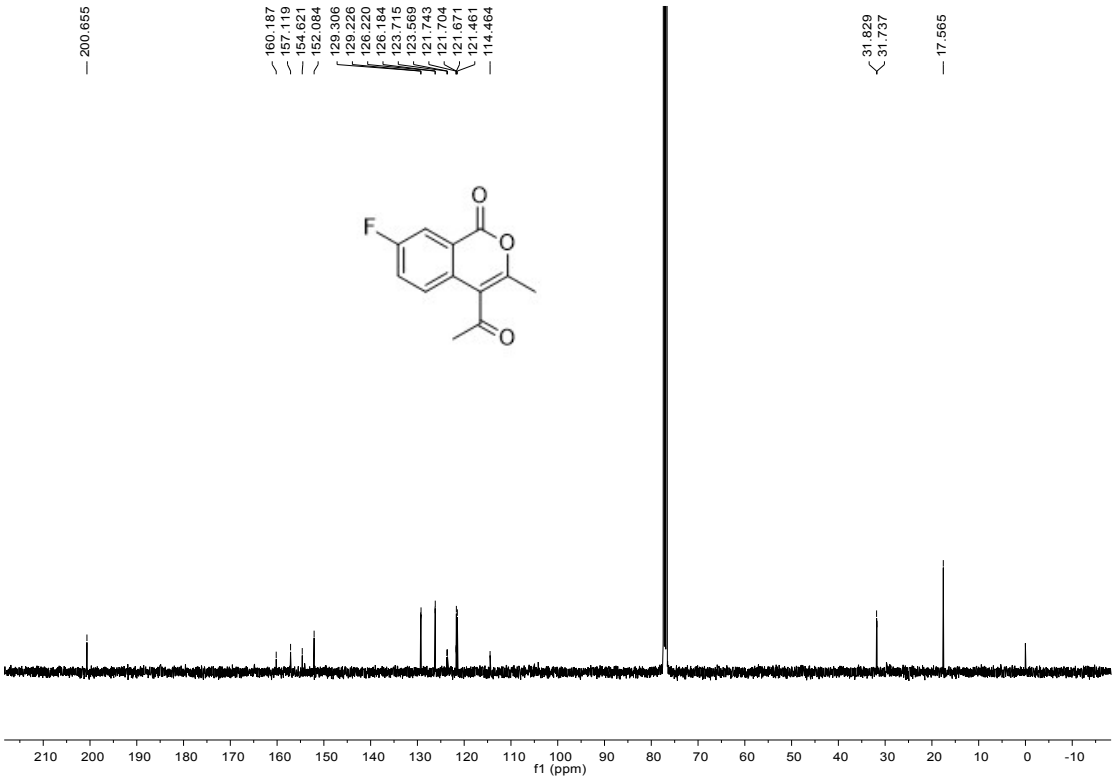
(4j) 4-acetyl-6-bromo-3-methyl-1*H*-isochromen-1-one



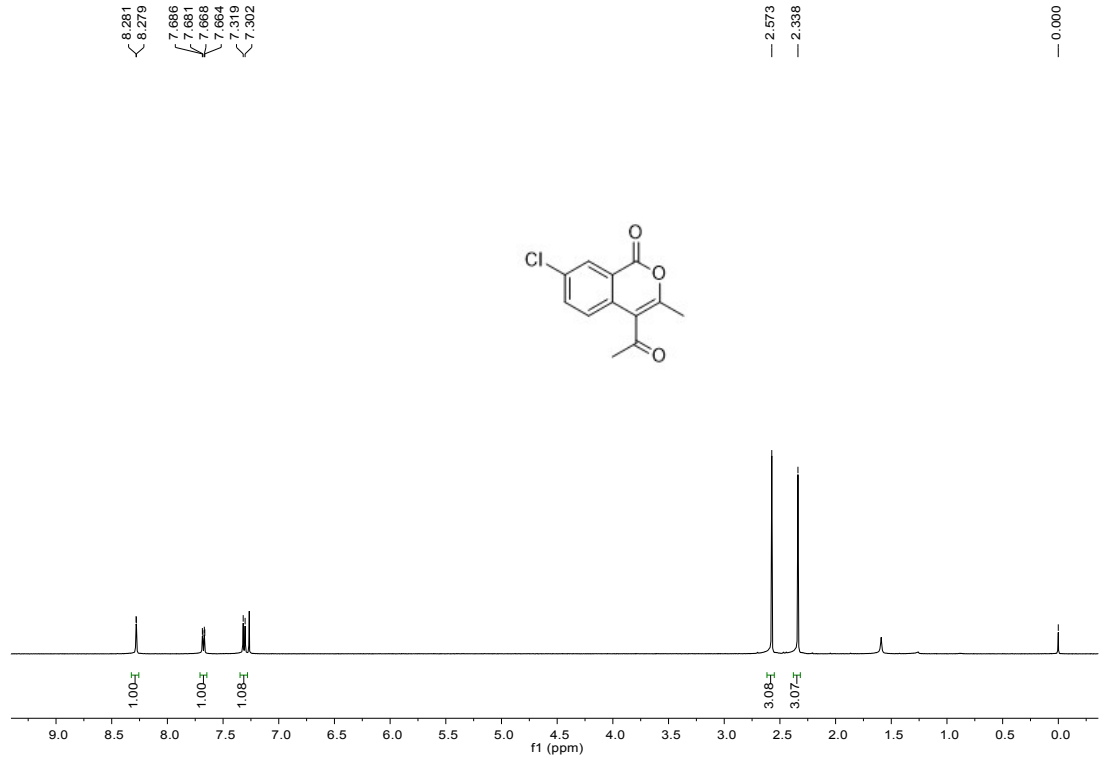


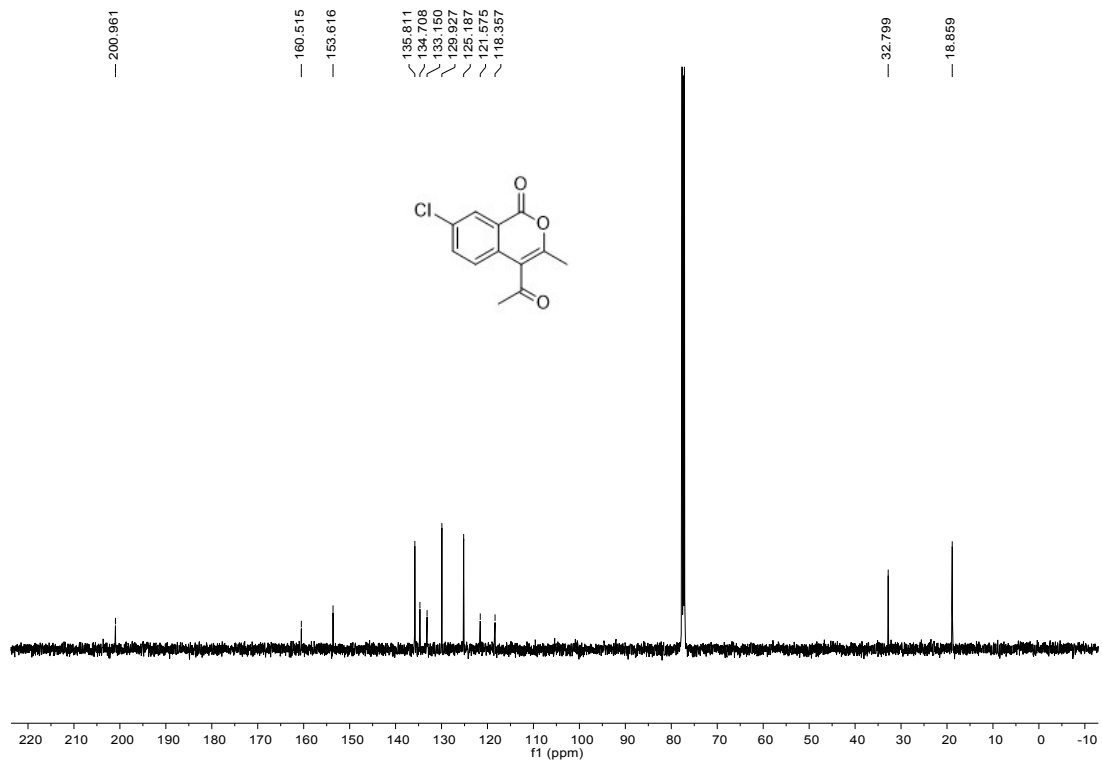
(4k) 4-acetyl-7-fluoro-3-methyl-1*H*-isochromen-1-one



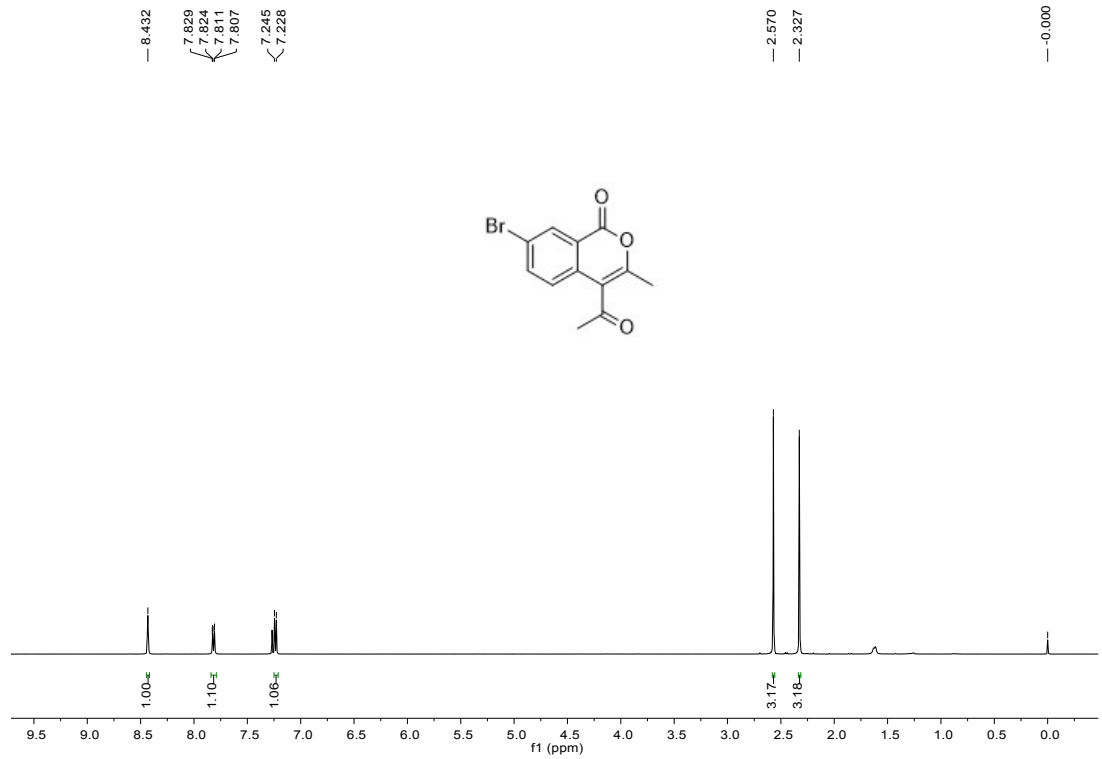


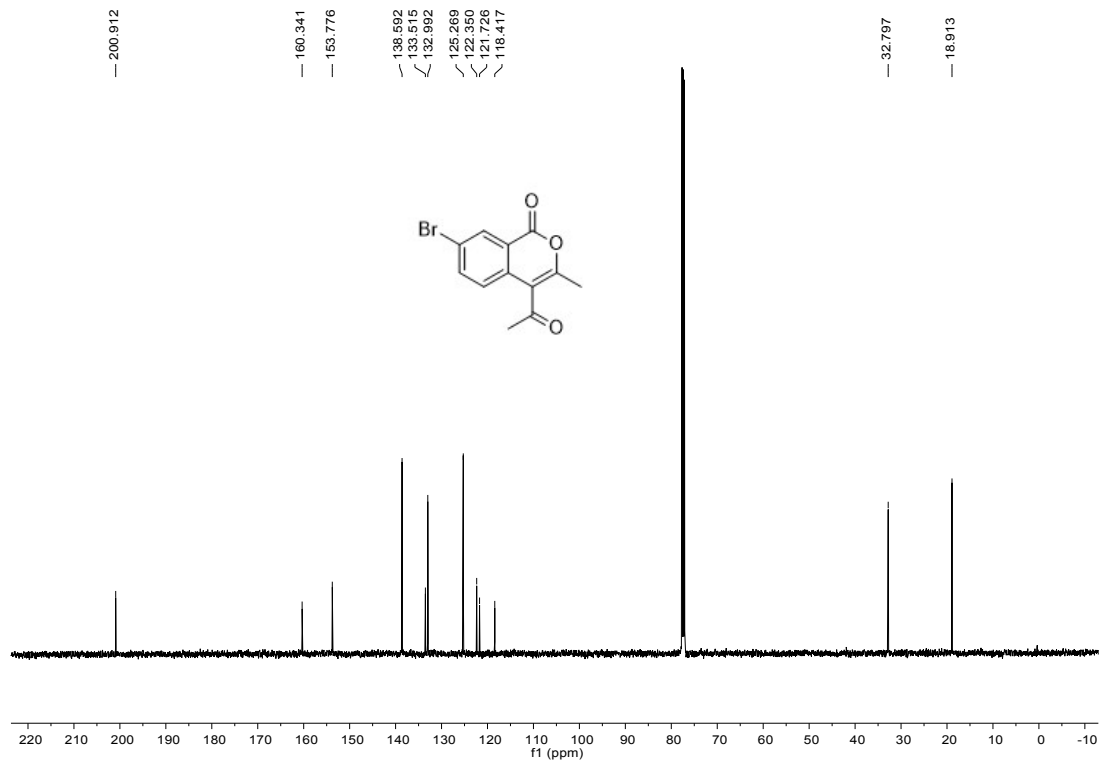
(4l) 4-acetyl-7-chloro-3-methyl-1*H*-isochromen-1-one



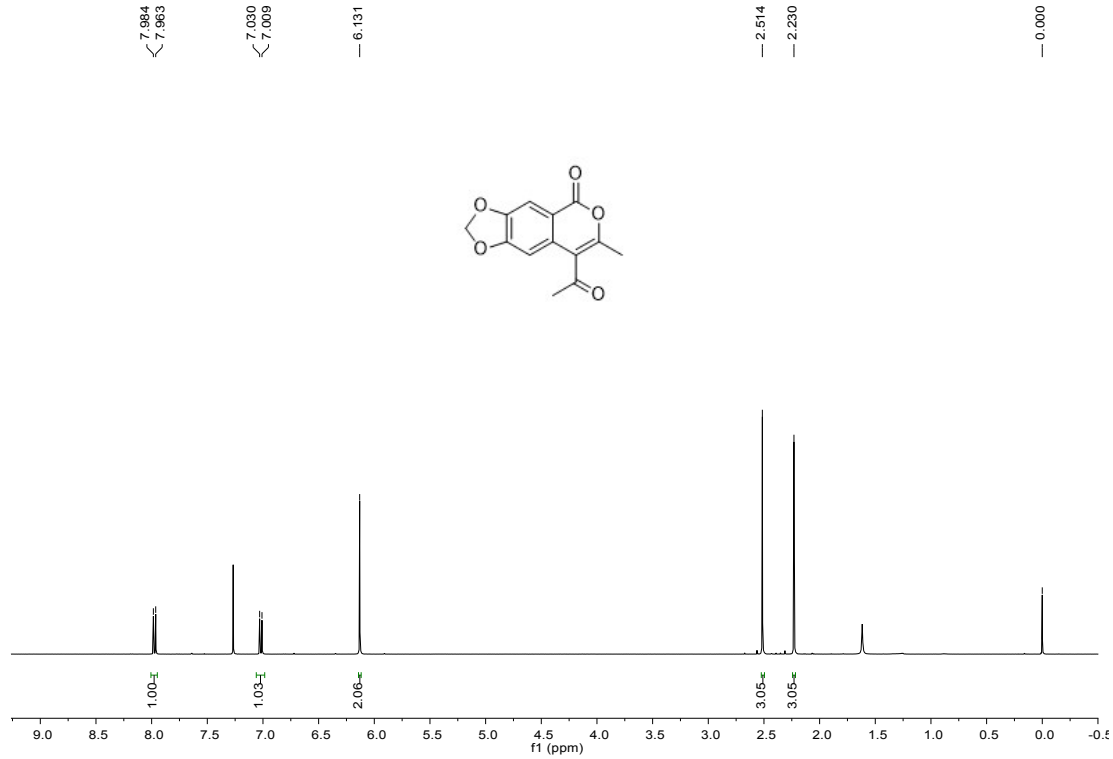


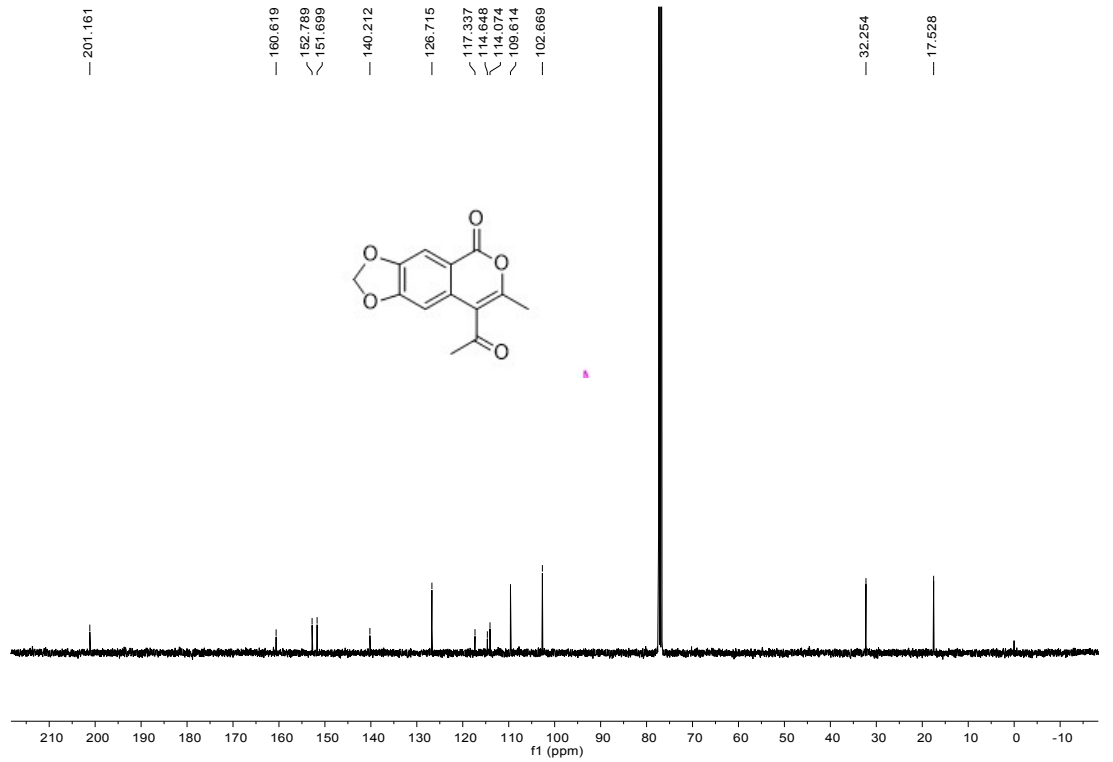
(4m) 4-acetyl-7-bromo-3-methyl-1*H*-isochromen-1-one



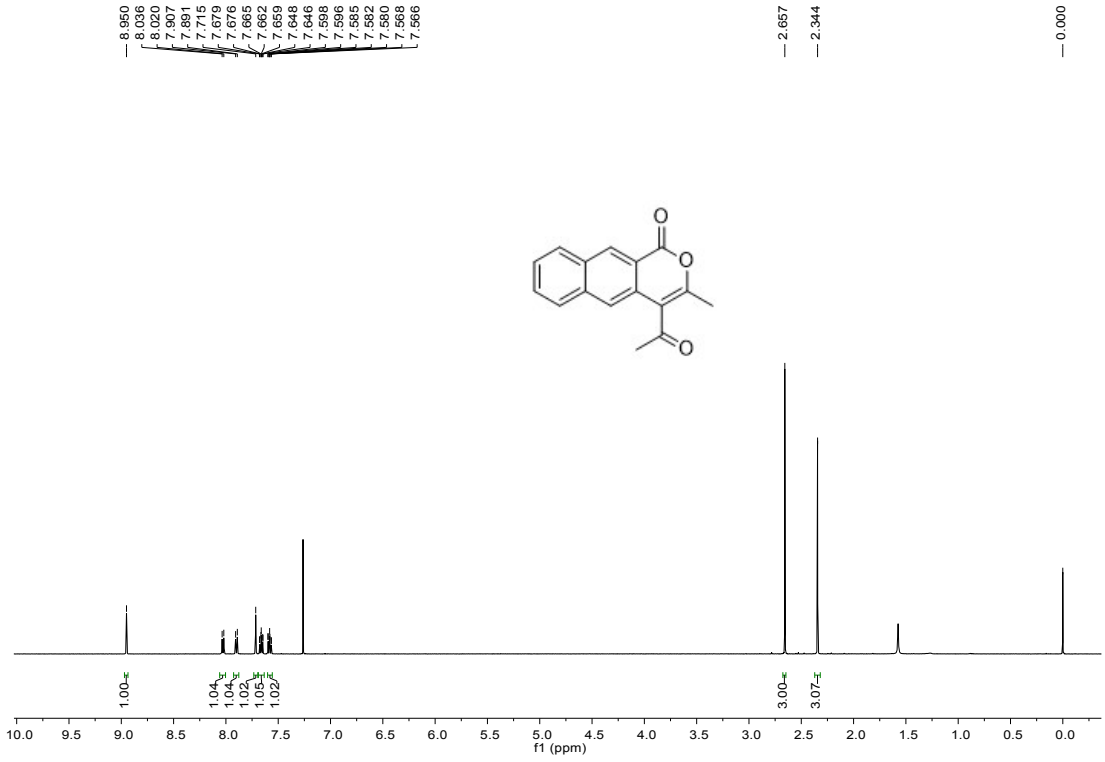


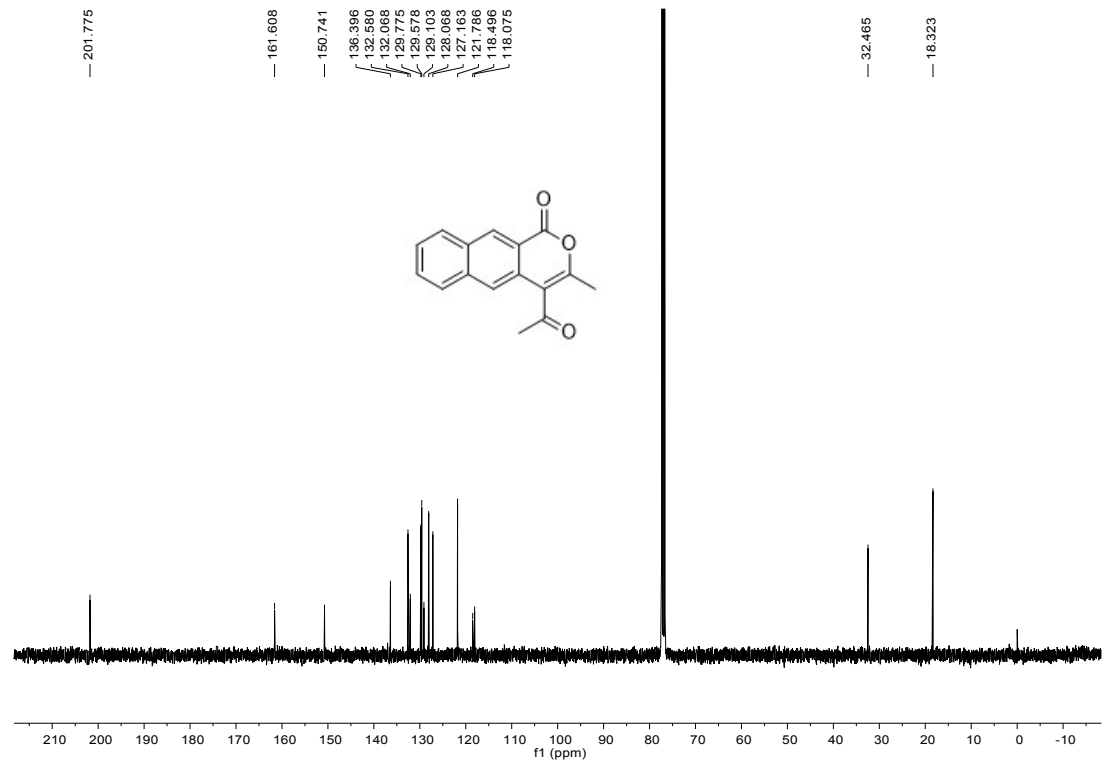
(4n) 8-acetyl-7-methyl-5*H*-[1,3]dioxolo[4,5-g]isochromen-5-one



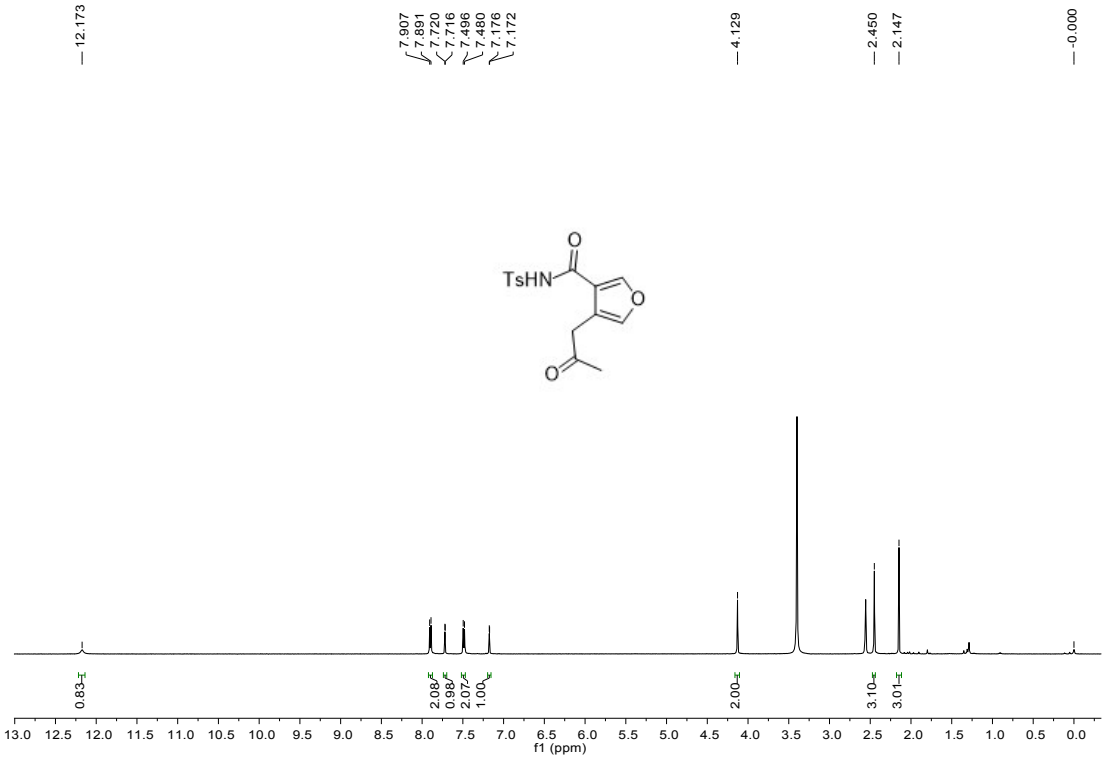


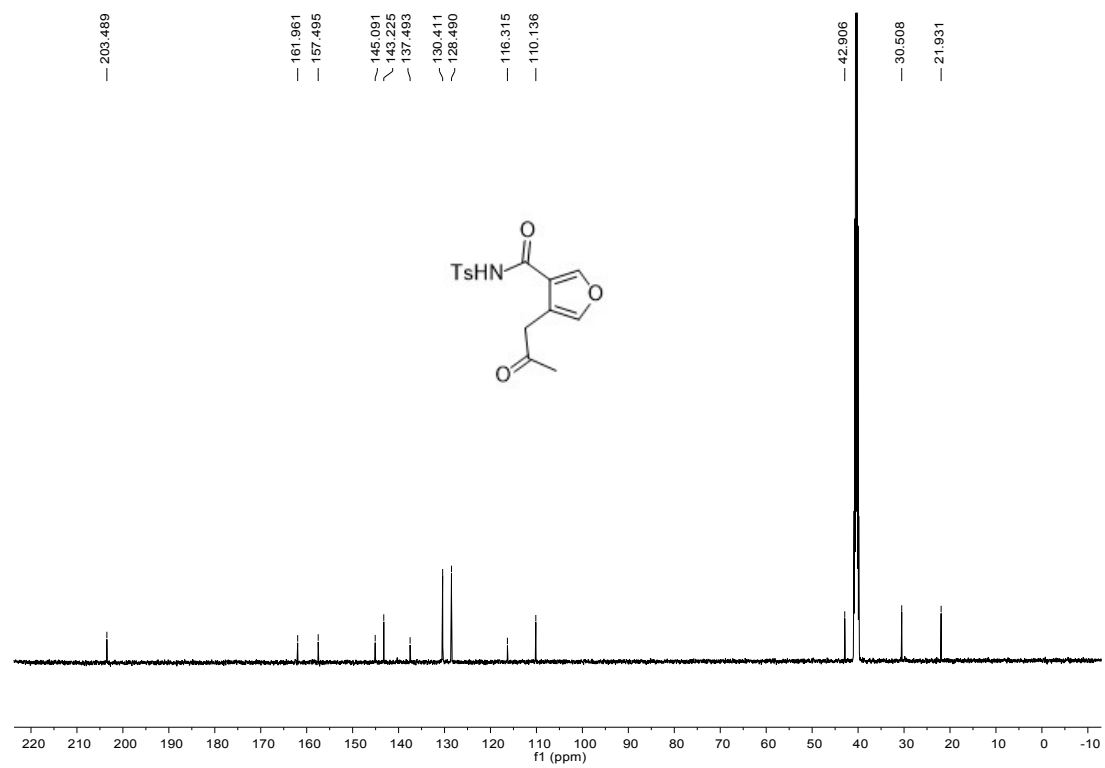
(4o) 4-acetyl-3-methyl-1*H*-benzo[g]isochromen-1-one



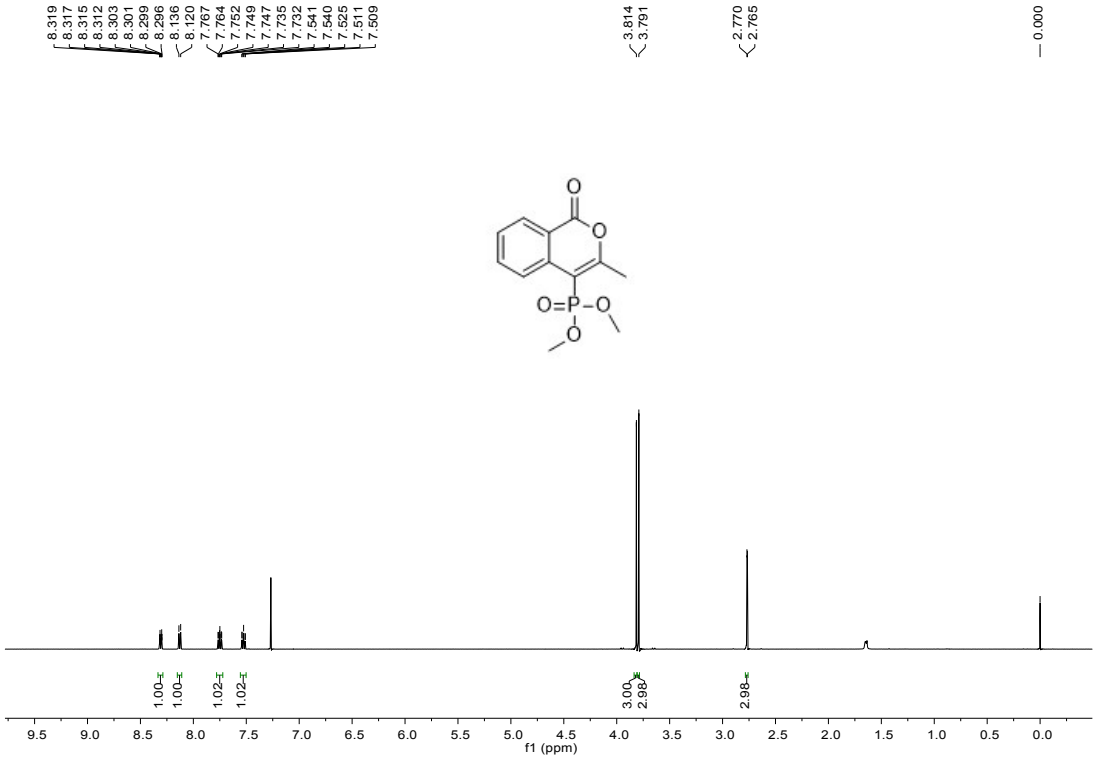


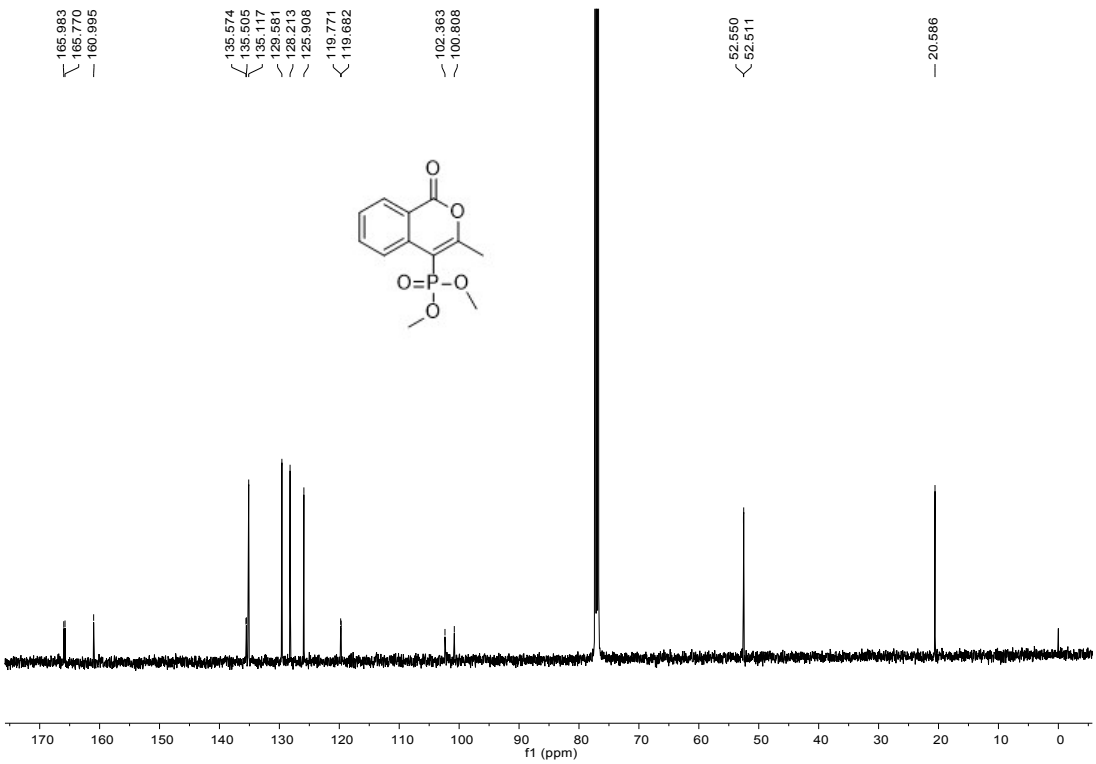
(4p) 4-(2-oxopropyl)-*N*-tosylfuran-3-carboxamide



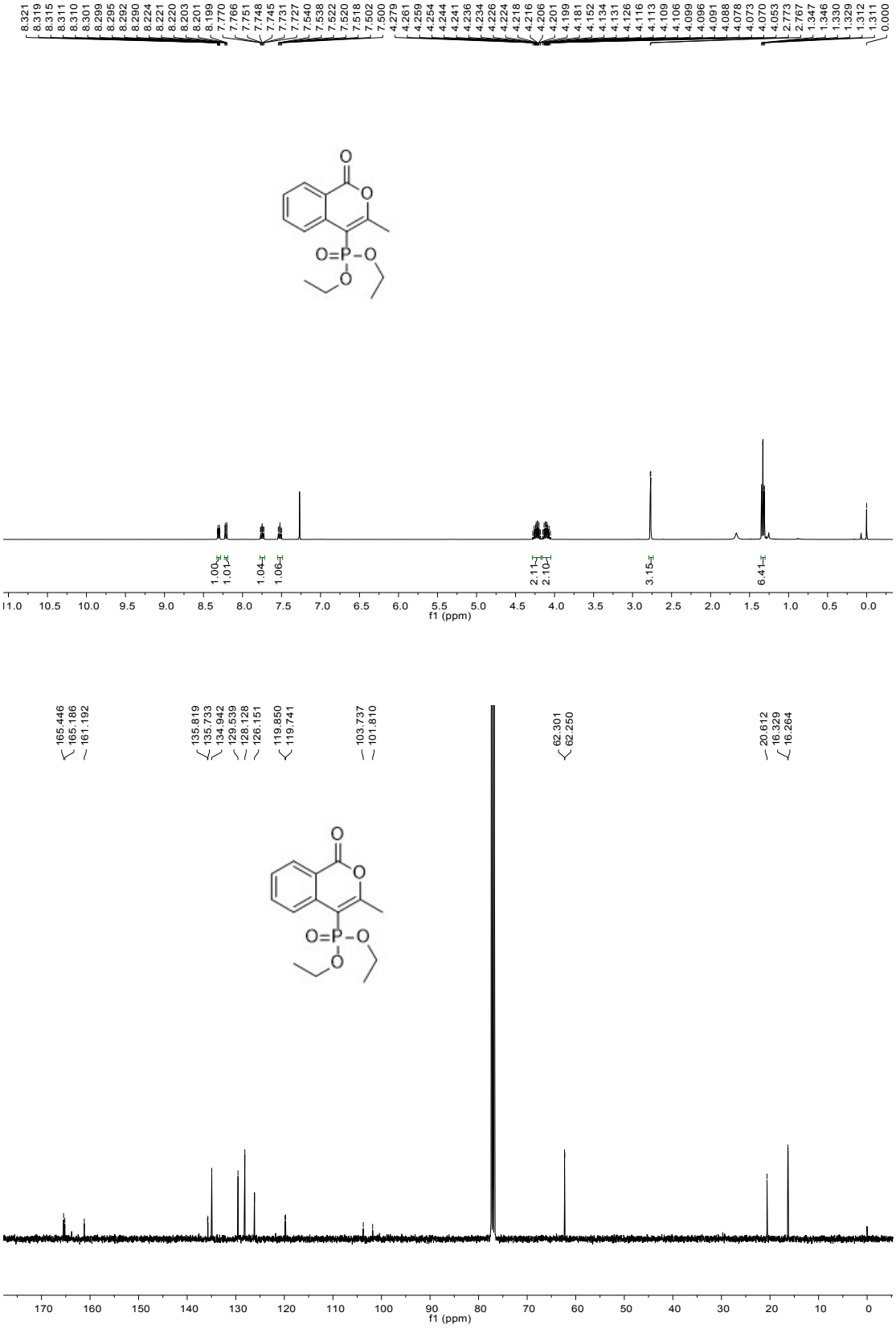


(4t) dimethyl (3-methyl-1-oxo-1*H*-isochromen-4-yl)phosphonate

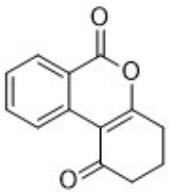


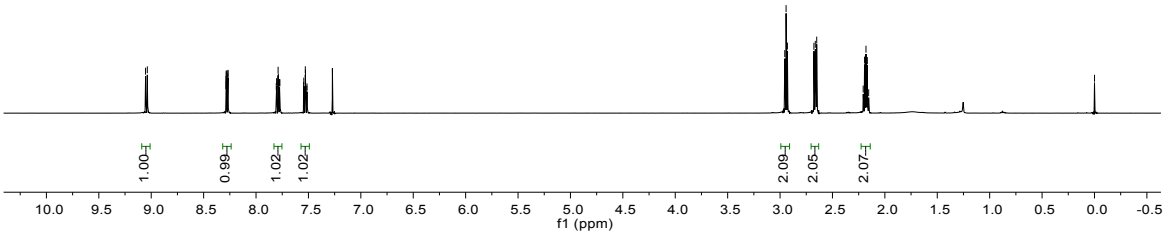


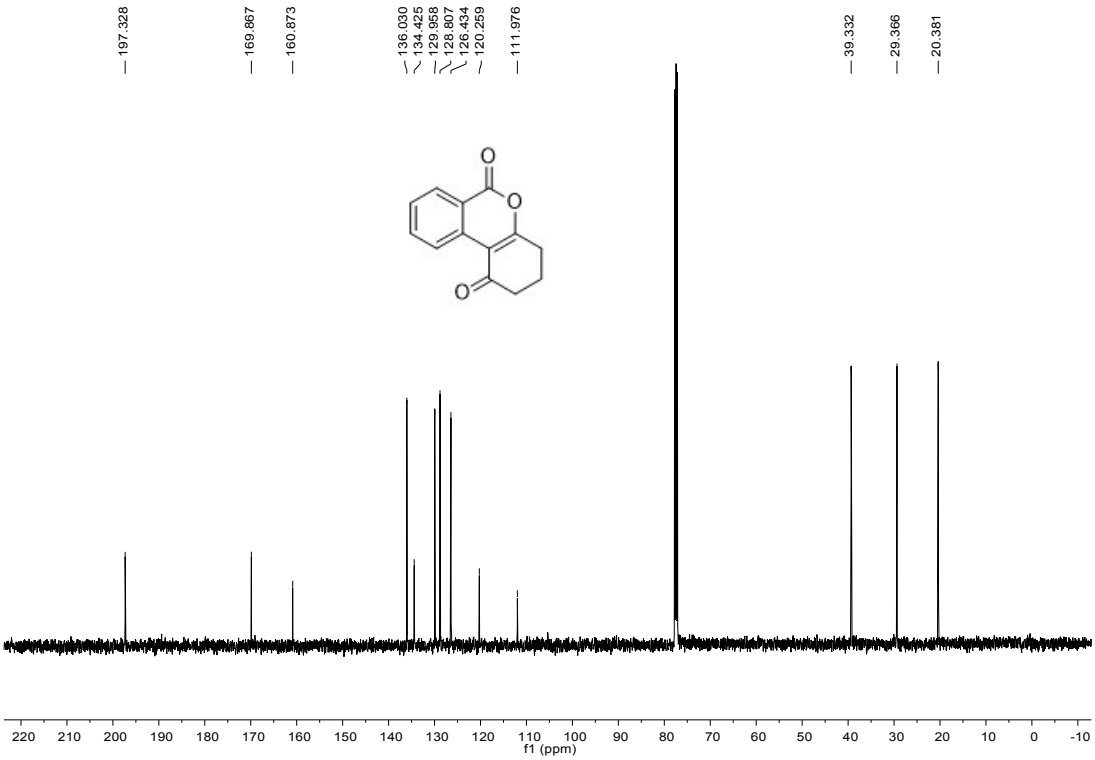
(4u) diethyl (3-methyl-1-oxo-1*H*-isochromen-4-yl)phosphonate



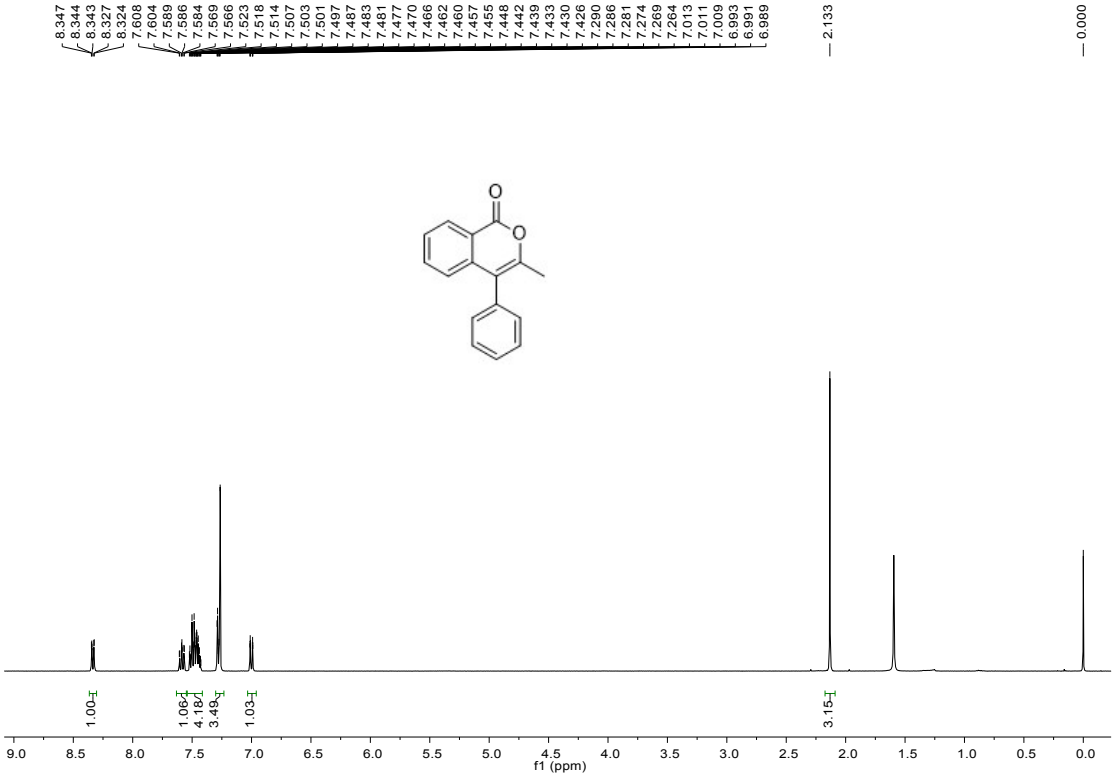
(4v) 3,4-dihydro-1*H*-benzo[c]chromene-1,6(2*H*)-dione

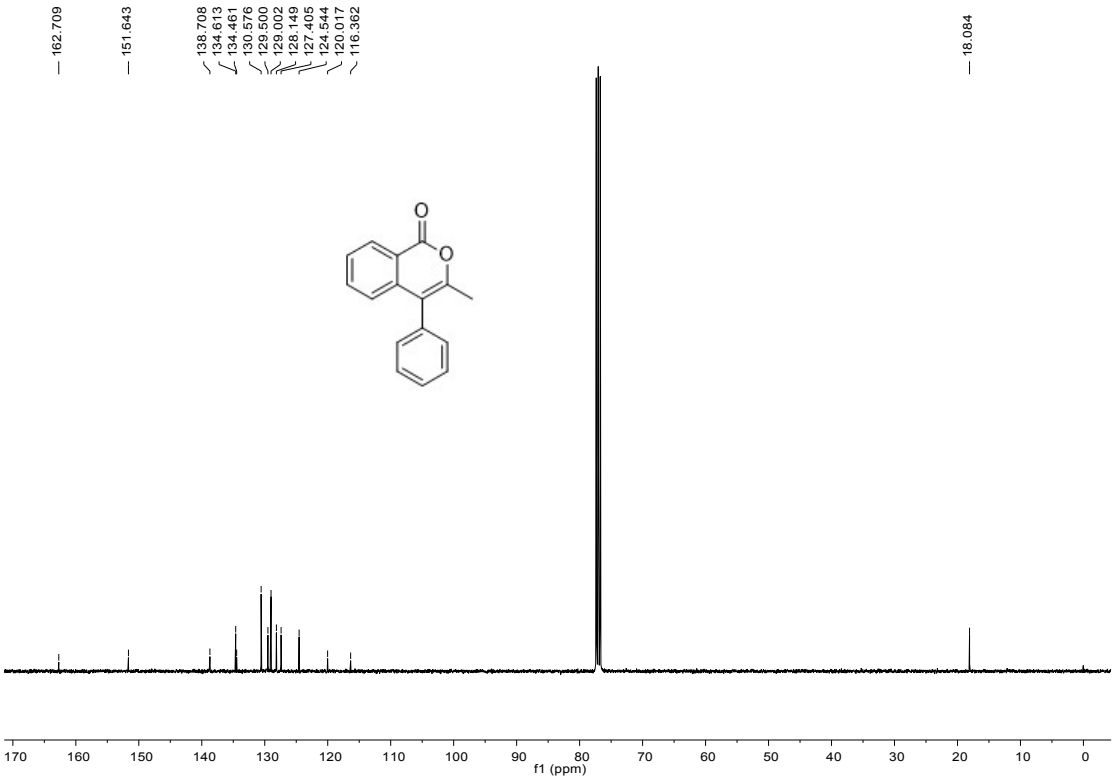




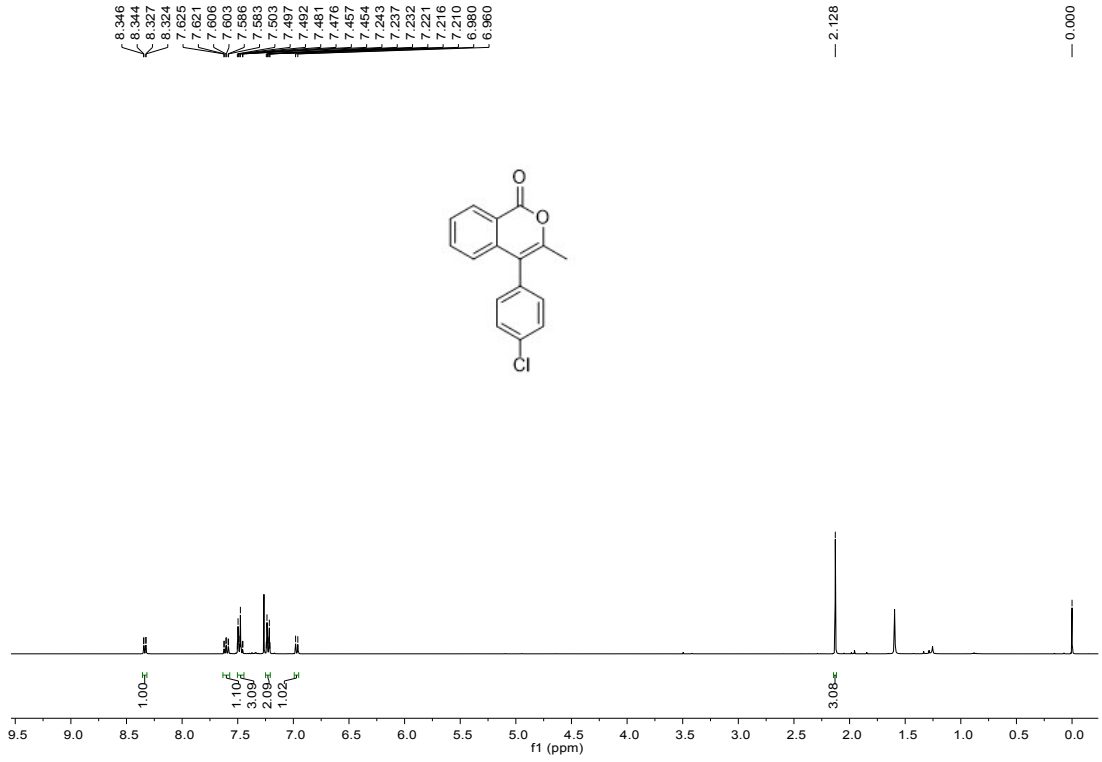


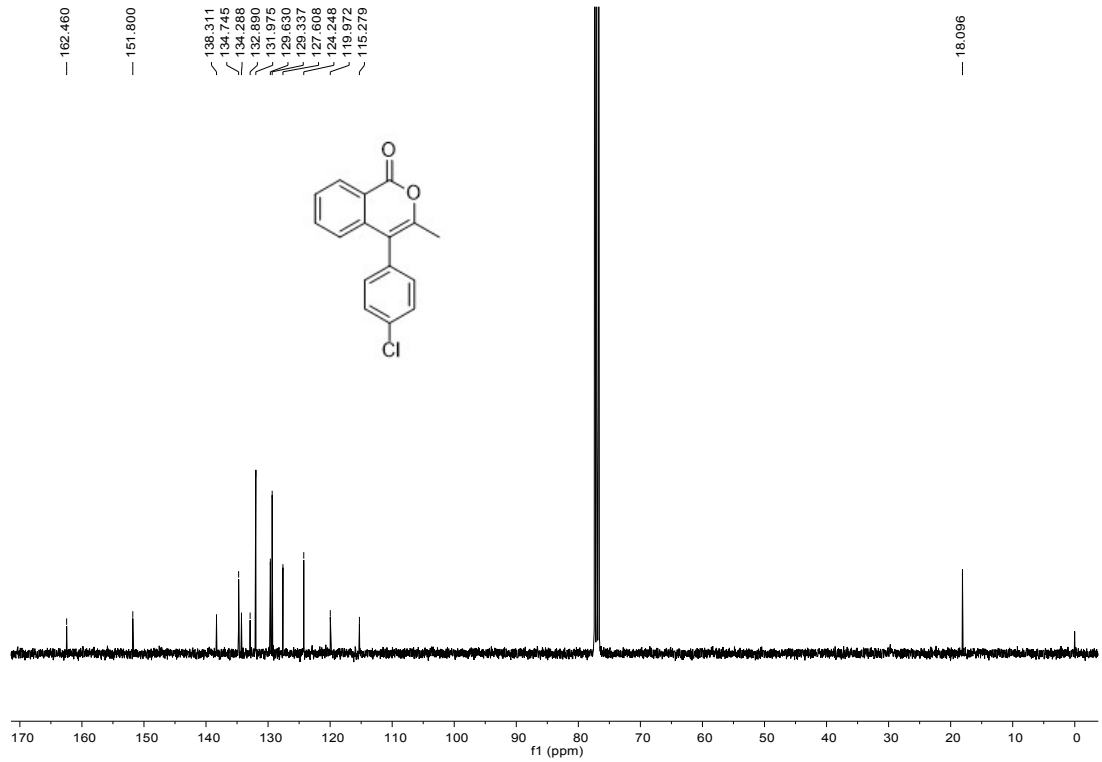
(4w) 3-methyl-4-phenyl-1*H*-isochromen-1-one



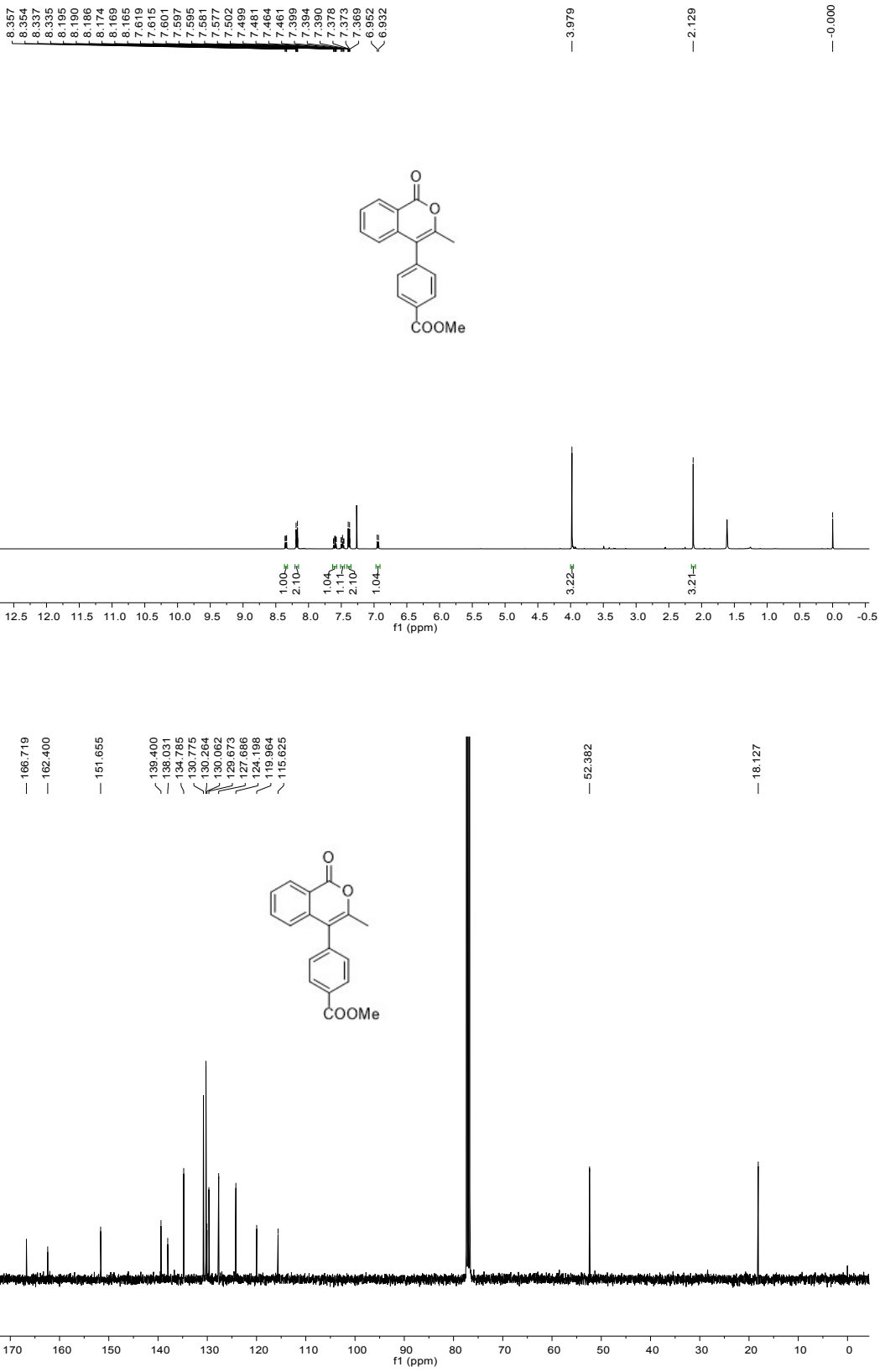


(4x) 4-(4-chlorophenyl)-3-methyl-1*H*-isochromen-1-one

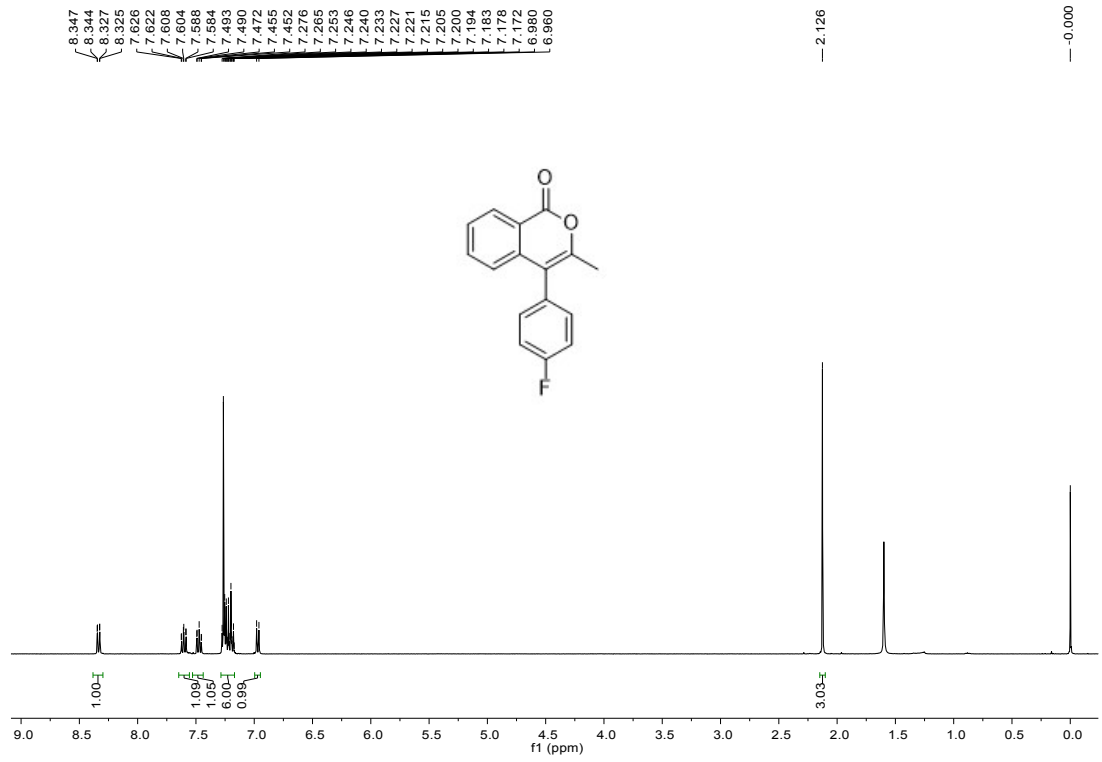


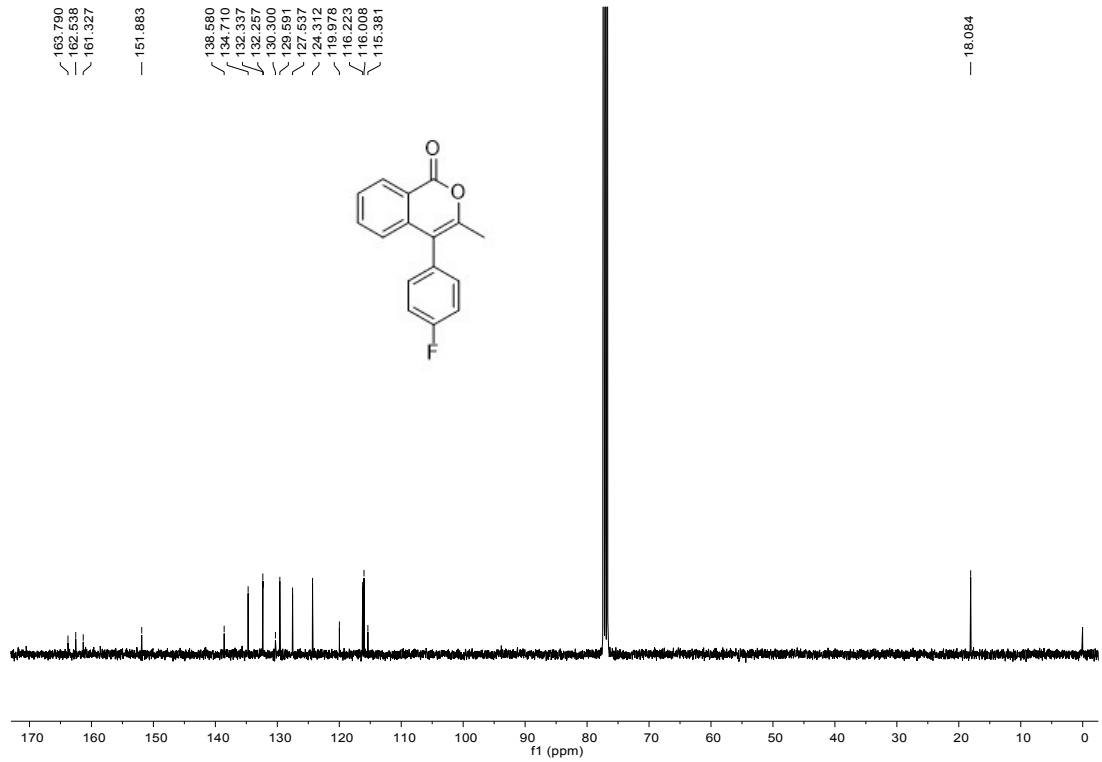


(4y) methyl 4-(3-methyl-1-oxo-1*H*-isochromen-4-yl)benzoate

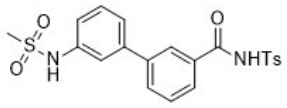


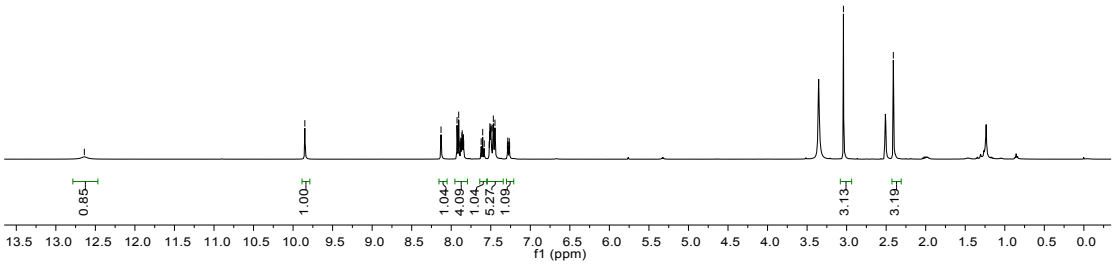
(4z) 4-(4-fluorophenyl)-3-methyl-1*H*-isochromen-1-one

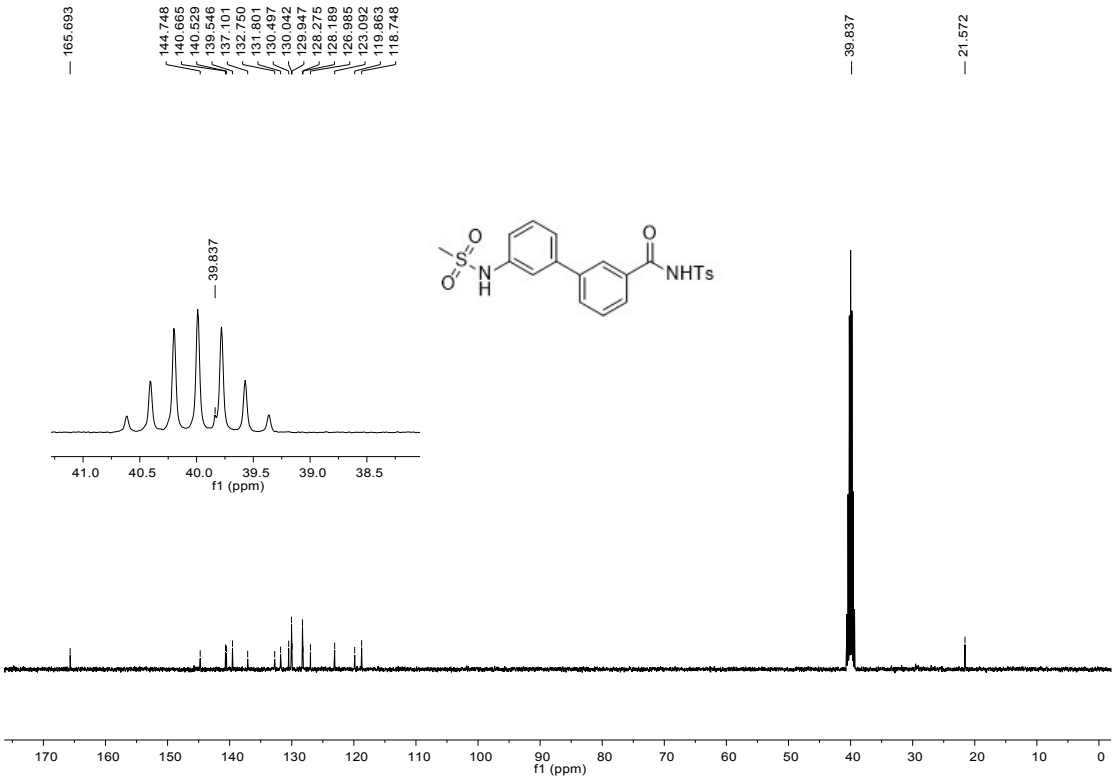




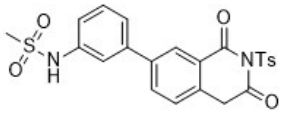
(8) 3'-(methylsulfonamido)-*N*-tosyl-[1,1'-biphenyl]-3-carboxamide

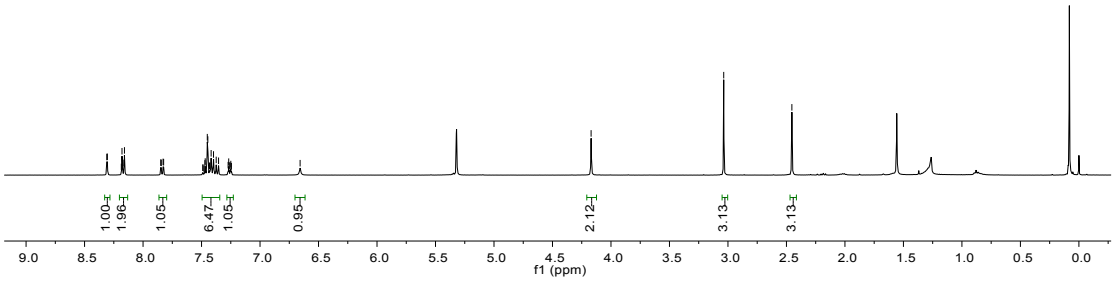


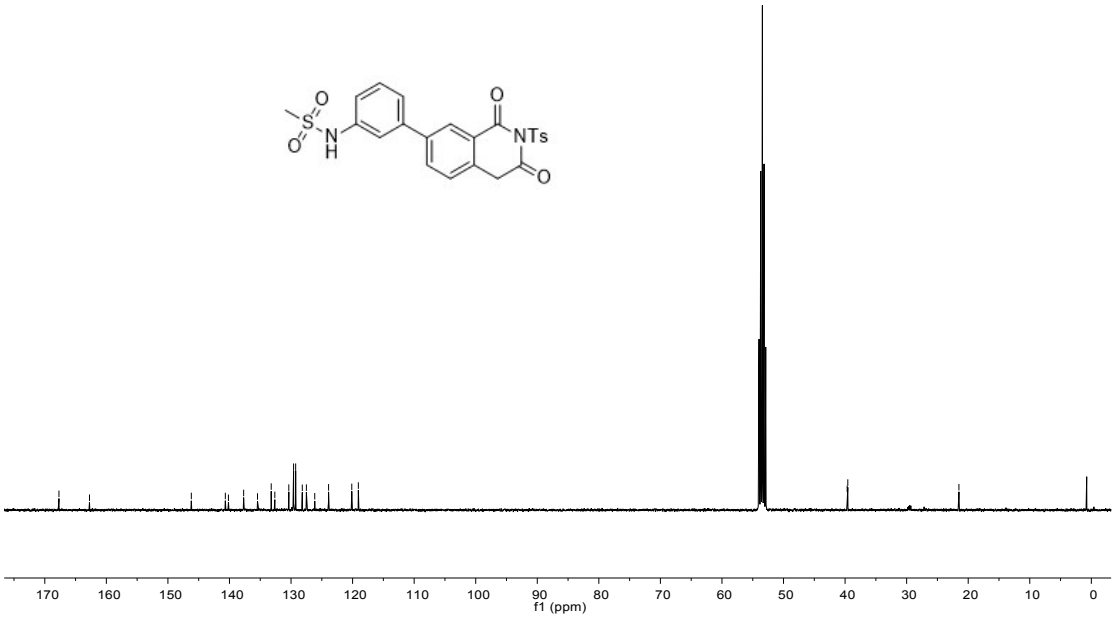




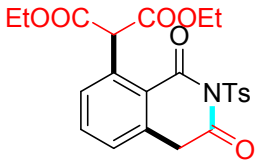
(9) *N*-(3-(1,3-dioxo-2-tosyl-1,2,3,4-tetrahydroisoquinolin-7-yl)phenyl)methanesulfonamide







Crystal Structures of 3a (CCDC 1918352)



3a