Supporting Information

Palladium catalyzed tandem cyclization of acryloylbenzamides and *N*-arylacrylamides with epoxides: Access to functionalized isoquinolinediones and oxindoles

Xiao-Yu Lu,* Fu-Yi Shui, Xiang Zhang, Rui Huang, Zi-Zhen Wang, Yi-Wei Song, Fan Jiang, Gui-Xian Yang and Yan-Xi Sun

E-mail: xiaoyulu@mail.ustc.edu.cn

School of Materials and Chemical Engineering, ChuZhou University, Chu Zhou, 239000, China.

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I. General Information

a. Materials

All the reactions were carried out in oven-dried schlenk tubes under argon atmosphere (purity ≥99.999%). $Pd(PPh_3)_4$ (CAS: 14221-01-3), $PdCl_2(PPh_3)_2$ (CAS: 13965-03-2), dppf (CAS: 548-26-5), xantphos (CAS: 161265-03-8), dpephos (CAS: 166330-10-5), BINAP (CAS: 98327-87-8), dppbz (CAS: 13991-08-7), dppm (CAS: 2071-20-7), dppe (CAS: 1663-45-2), dppp (CAS: 6737-42-4), dppb (CAS: 7688-25-7), 1,5-bis(diphenylphosphino)pentane (CAS: 27721-02-4), 1,1-bis(diisopropylphosphino)ferrocene (CAS: 97239-80-0), 1,1-Bis(di-tert-butylphosphino)ferrocene (CAS: 84680-95-5) and isobutylene oxide (CAS: 558-30-5) were purchased from Adamas. The following chemicals were purchased and used as received: $PhCF_3$ (Adamas), THF (Adamas) and 1,4-dioxane (Adamas) were stored over 4 Å molecular sieves under an argon atmosphere in a septum-capped bottle. All the other reagents and solvents mentioned in this text were purchased from commercial sources and used without purification.

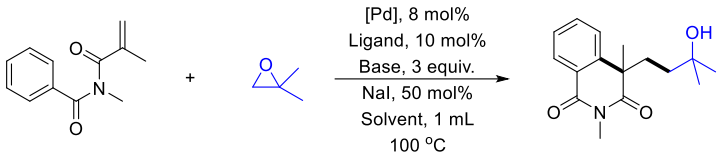
b. Analytical Methods

^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature in Chloroform-*d* unless otherwise noted; Data for ^1H-NMR are reported as follows: chemical shift (δ ppm), multiplicity, integration, and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm), multiplicity, and coupling constant (Hz). Gas chromatographic (GC) analysis was acquired on a Shimadzu GC-2014 Series GC System equipped with a flame-ionization detector. GC-MS analysis was performed on Thermo Scientific AS 3000 Series GC-MS System. HRMS analysis was performed on Finnigan LCQ advantage Max Series MS System. HPLC analysis was performed on Waters-Breeze (2487 Dual Absorbance Detector and 1525 Binary HPLC Pump). Chiralpak IC, AD, AS, KM columns were purchased from Daicel Chemical Industries, LTD. Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Flash column chromatographic purification of products was accomplished using forced-flow chromatography on Silica Gel (200-300 mesh). The mass analyzer type of the HRMS measurements was “LTQ Orbitrap”.

II. General Experimental Procedures

a. Optimization of the reaction conditions

Table S1



1a, 0.2 mmol + **2a**, 0.6 mmol → **3a**

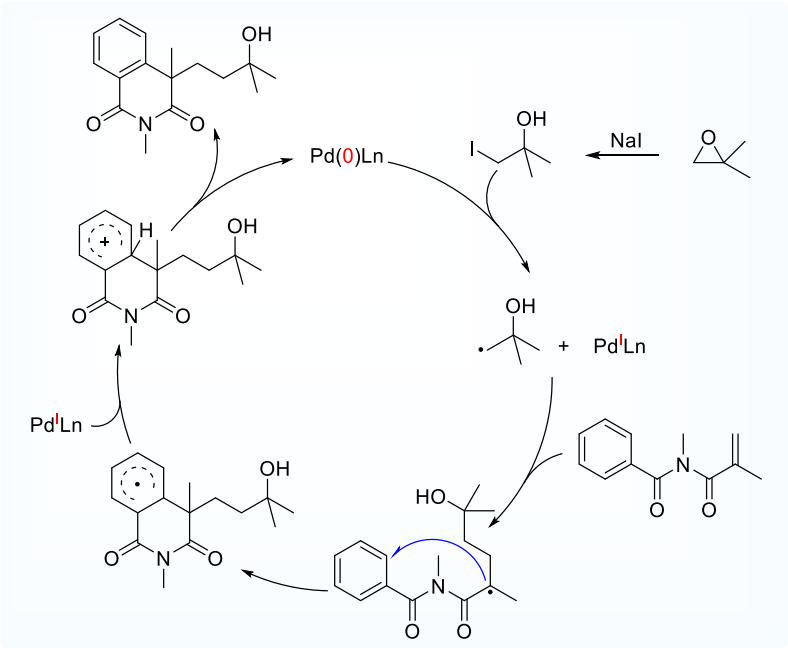
Entry	Catalyst	Ligand	Base	Solvent	Yield%[c]
1[a]	$PdCl_2(PPh_3)_4$	dppf	Cy_2NMe	$PhCF_3$	12
2[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	$PhCF_3$	76
3[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	dioxane	40
4[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	THF	35
5[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	DMAc	Trace
6[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	toluene	31
7[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	DMSO	Trace
8[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	CH_3CN	< 5
9[a]	$Pd(PPh_3)_4$	dppf	Cy_2NMe	DCE	Trace
10[a]	$Pd(PPh_3)_4$	BINAP	Cy_2NMe	$PhCF_3$	33
11[a]	$Pd(PPh_3)_4$	dppm	Cy_2NMe	$PhCF_3$	Trace
12[a]	$Pd(PPh_3)_4$	dppe	Cy_2NMe	$PhCF_3$	Trace
13[a]	$Pd(PPh_3)_4$	dppp	Cy_2NMe	$PhCF_3$	25
14[a]	**$Pd(PPh_3)_4$**	**dppb**	**Cy_2NMe**	**$PhCF_3$**	**93**
15[a]	$Pd(PPh_3)_4$	L1	Cy_2NMe	$PhCF_3$	50
16[a]	$Pd(PPh_3)_4$	DPEphos	Cy_2NMe	$PhCF_3$	75
17[a]	$Pd(PPh_3)_4$	dippf	Cy_2NMe	$PhCF_3$	65
18[a]	$Pd(PPh_3)_4$	xantphos	Cy_2NMe	$PhCF_3$	78
19[a]	$Pd(PPh_3)_4$	L2	Cy_2NMe	$PhCF_3$	71
20[a]	$Pd(PPh_3)_4$	dppb	Et_3N	$PhCF_3$	Trace
21[a]	$Pd(PPh_3)_4$	dppb	K_2CO_3	$PhCF_3$	Trace
22[a]	$Pd(PPh_3)_4$	dppb	Cs_2CO_3	$PhCF_3$	Trace
23[b]	w/o	dppb	Cy_2NMe	$PhCF_3$	Trace

Reaction conditions: [a]**1a** (0.2 mmol), **2a** (3.0 equiv.), base (3.0 equiv.), catalyst (8 mol%), ligand (10 mol%) and NaI (50 mol %) in 1 mL solvent at 100 ℃ for 20 h under Ar. [b]No catalyst. [c]isolated yield. L1 = 1,5-Bis(Diphenylphosphino)Pentane, dippf = 1,1-bis(diisopropylphosphino)ferrocene, L2 = 1,1-Bis(di-*tert*-butylphosphino)ferrocene.

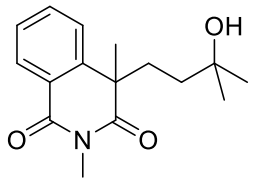
b. Experimental Procedures for Examples Described (General Procedure)

In air, acryloylbenzamide or *N*-arylacrylamide (0.2 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (18 mg, 8 mol%), dppb (9 mg, 10 mol%), and NaI (15 mg, 50 mol%) were added to a schlenk tube equipped with a stir bar. The vessel was evacuated and filled with argon (three cycles). $PhCF_3$ (1.0 mL, 0.5 M), epoxide (3.0 equiv.), and Cy_2NMe (128 μL, 3.0 equiv.) were added in turn by syringe. The resulting reaction mixture was stirred at 100 ℃ for 20 h. (If acryloylbenzamide or *N*-arylacrylamide was a liquid, add it through the syringe after adding the solvent). The residue was purified by silica gel (200-300 mesh) columun chromatography using petroleum ether (PE) and ethyl acetate (EtOAc).

III. Proposed Reaction Mechanism



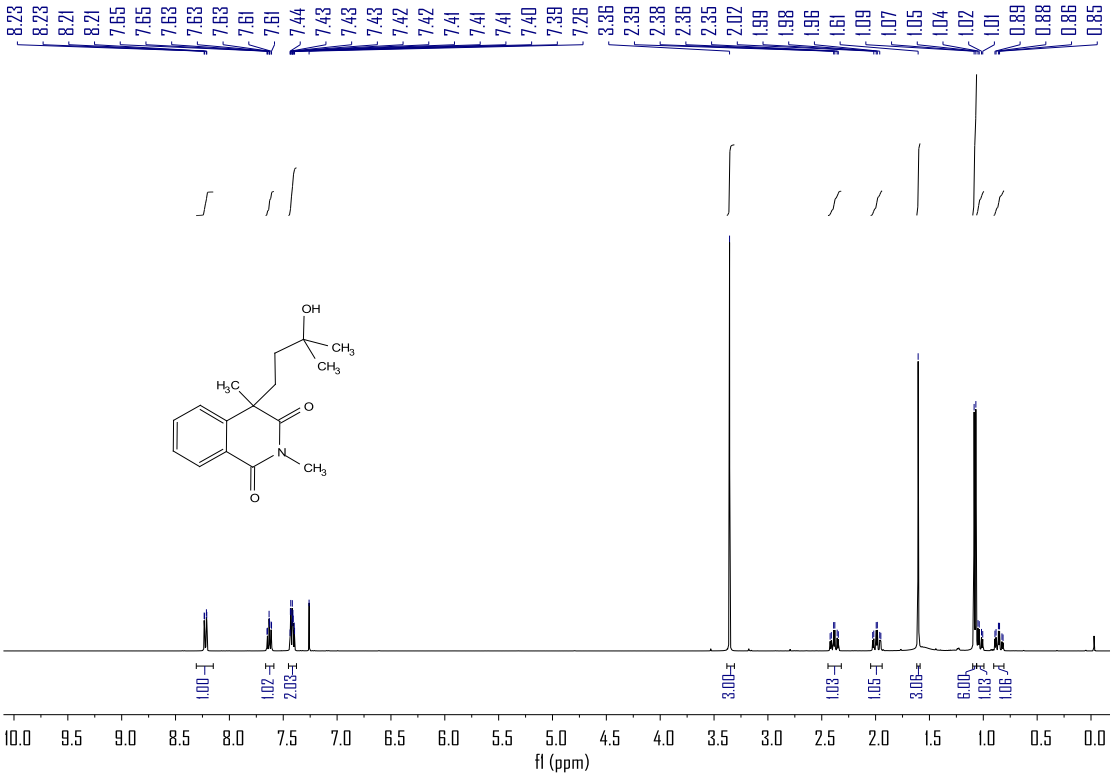
IV. Substrate Scope, Spectral Data and NMR Spectra

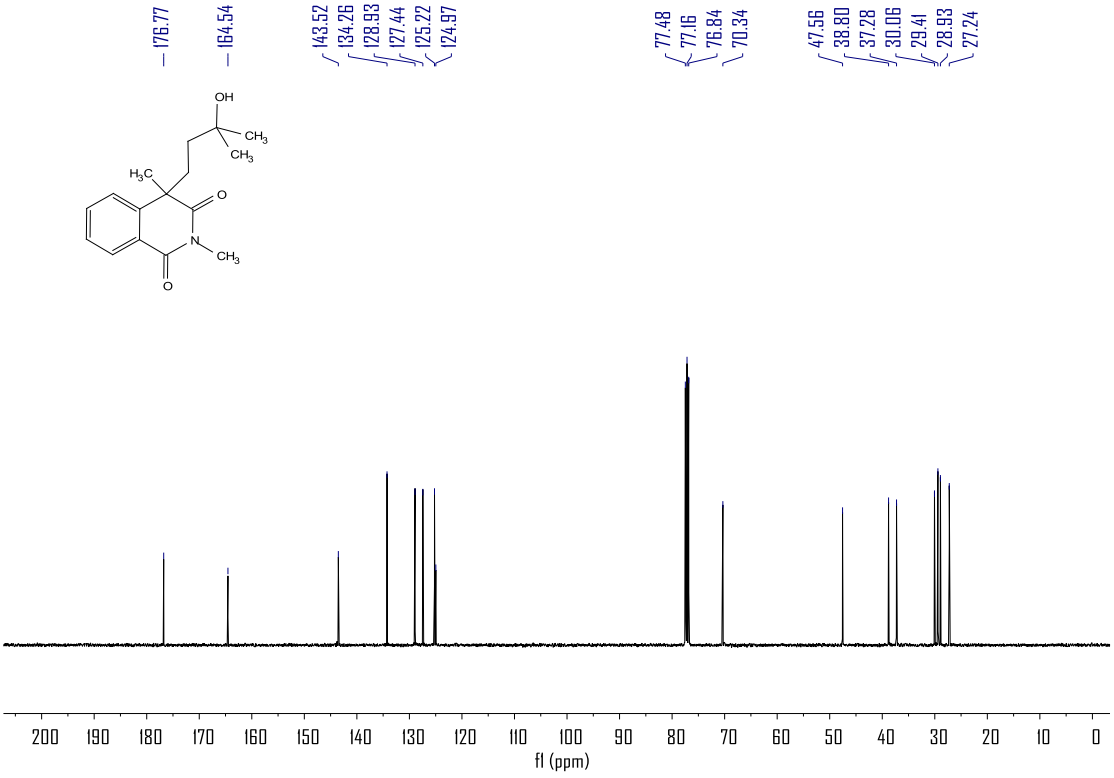


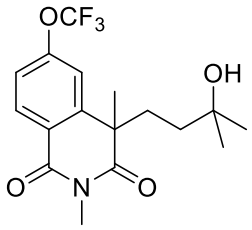
4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3a**, pale-yellow liquid, 51 mg, 93%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.22 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.68 – 7.55 (m, 1H), 7.48 – 7.37 (m, 2H), 3.36 (s, 3H), 2.38 (td, *J* = 13.0, 4.4 Hz, 1H), 1.99 (td, *J* = 13.1, 4.1 Hz, 1H), 1.61 (s, 3H), 1.08 (d, *J* = 6.5 Hz, 6H), 1.03 (dd, *J* = 13.0, 4.5 Hz, 1H), 0.85 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.77, 164.54, 143.52, 134.26, 128.93, 127.44, 125.22, 124.97, 70.34, 47.56, 38.80, 37.28, 30.06, 29.41, 28.93, 27.24.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_3$: 298.1414; found: 298.1418.



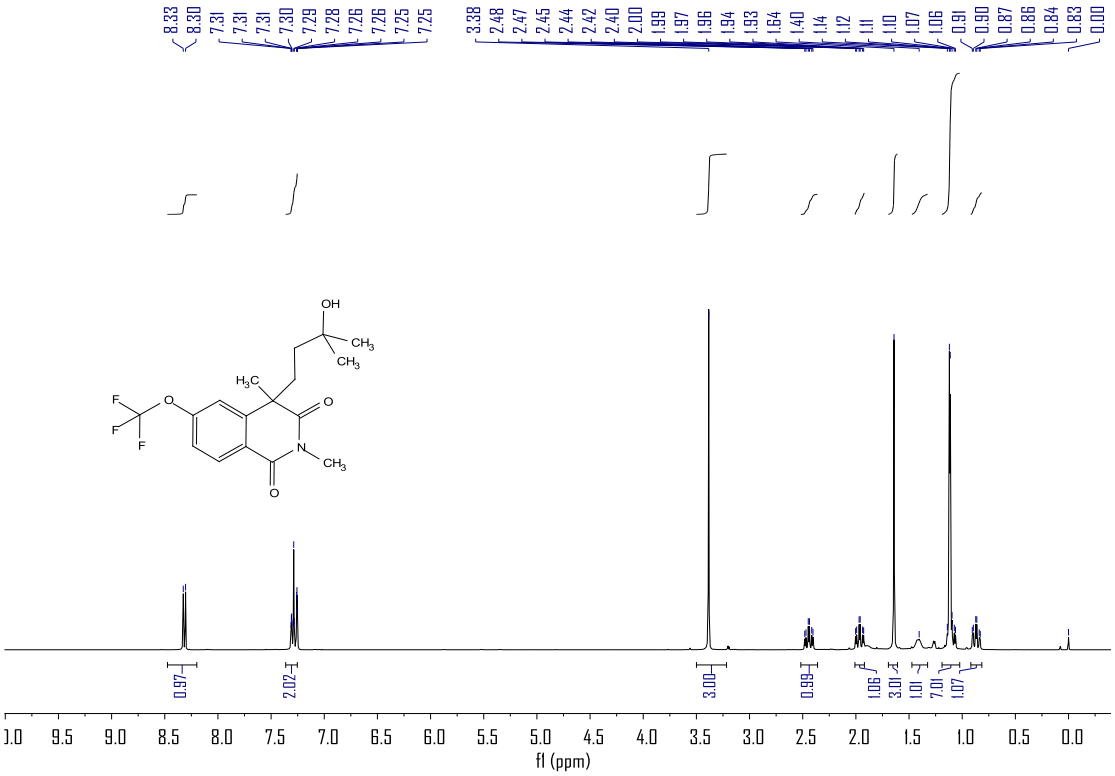




4-(3-hydroxy-3-methylbutyl)-2,4-dimethyl-6-(trifluoromethoxy)isoquinoline-1,3(2H, 4H)-dione

Following the general procedure (**3b**, pale-yellow liquid, 58 mg, 81%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.7 Hz, 1H), 7.36 – 7.24 (m, 2H), 3.38 (s, 3H), 2.44 (td, *J* = 13.1, 4.5 Hz, 1H), 1.96 (td, *J* = 13.1, 3.9 Hz, 1H), 1.64 (s, 3H), 1.40 (s, 1H), 1.16 – 1.04 (m, 7H), 0.87 (td, *J* = 13.0, 3.9 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.05, 163.38, 153.63, 146.06, 131.45, 123.39, 120.33 (q, *J* = 259.6 Hz), 119.62, 117.08, 70.27, 47.83, 38.77, 37.33, 29.97, 29.25, 29.00, 27.35. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -57.59.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{20}F_3NNaO_4$: 382.1237; found: 382.1235.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2.44
2.42
2.40
2.00
1.99
1.97
1.96
1.94
1.93
1.64
1.40
1.14
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1.10
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1.06
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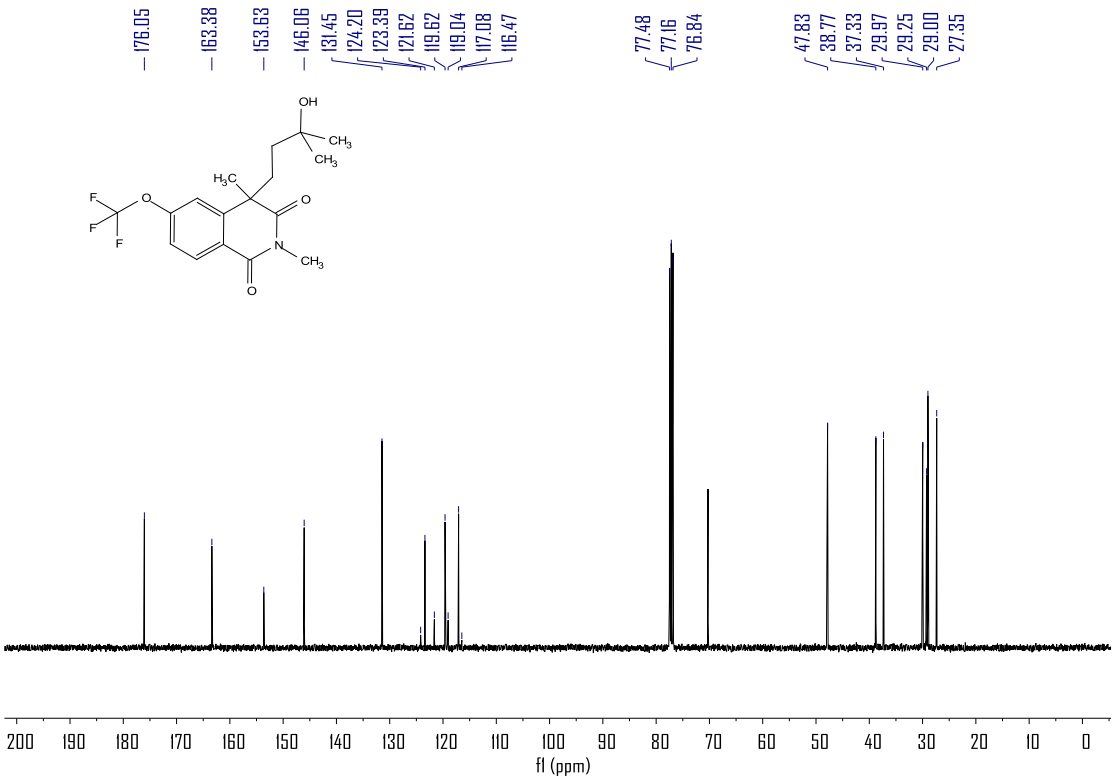
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F
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N
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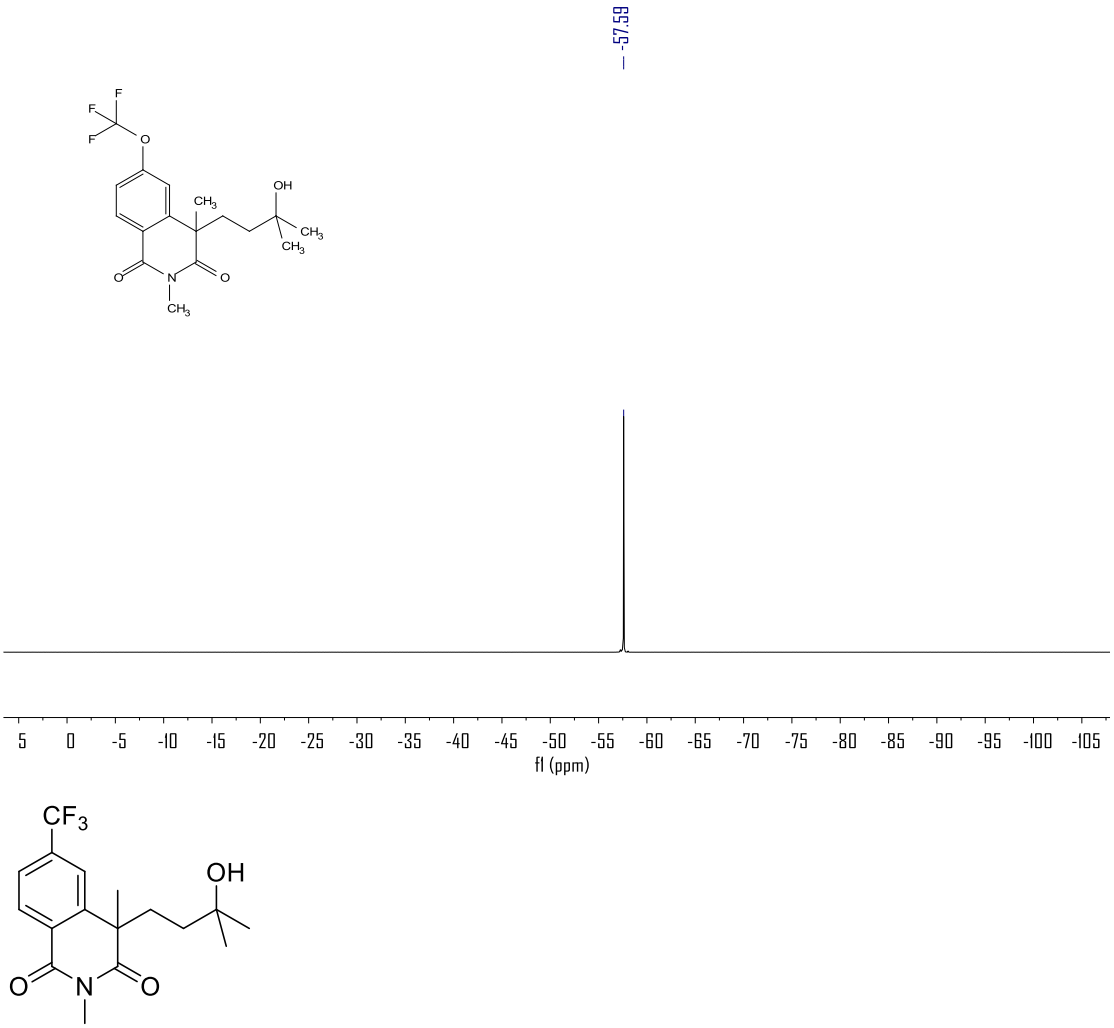
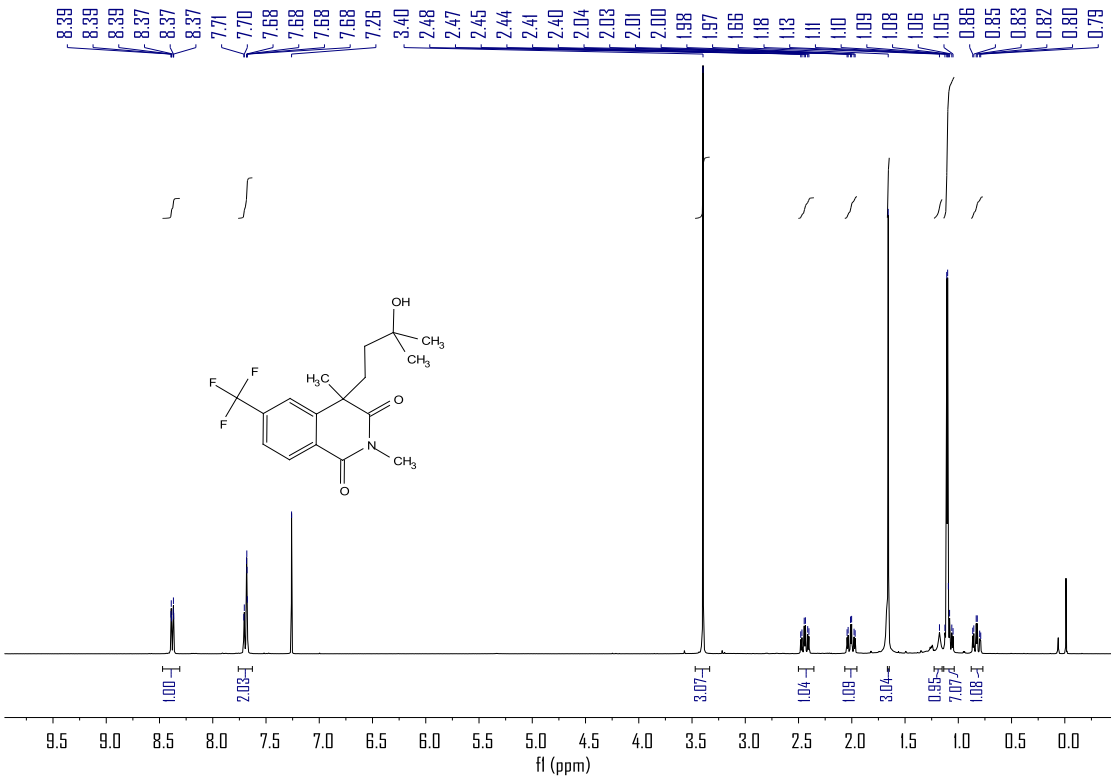
O
f1 (ppm)



4-(3-hydroxy-3-methylbutyl)-2,4-dimethyl-6-(trifluoromethyl)isoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3c**, pale-yellow liquid, 43 mg, 63%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.38 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.75 – 7.65 (m, 2H), 3.40 (s, 3H), 2.44 (td, *J* = 13.1, 4.5 Hz, 1H), 2.01 (td, *J* = 13.1, 4.0 Hz, 1H), 1.66 (s, 3H), 1.18 (s, 1H), 1.13 – 1.05 (m, 7H), 0.83 (td, *J* = 13.0, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 175.90, 163.44, 144.37, 135.77 (q, *J* = 33.0 Hz), 129.89, 127.93, 124.32 (q, *J* = 3.5 Hz), 123.50 (q, *J* = 273.0 Hz), 122.49 (q, *J* = 3.7 Hz), 70.34, 47.82, 38.79, 37.39, 29.88, 29.38, 28.99, 27.51. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -63.13.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{20}F_3NNaO_3$: 366.1287; found: 366.1296.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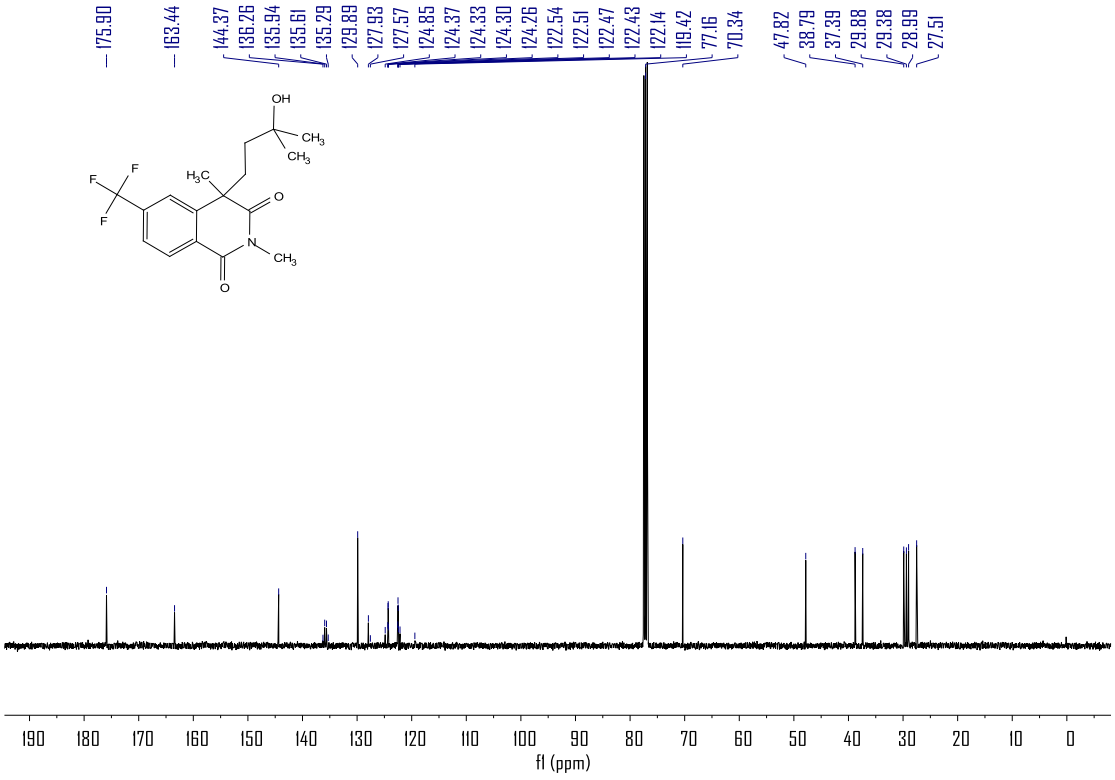
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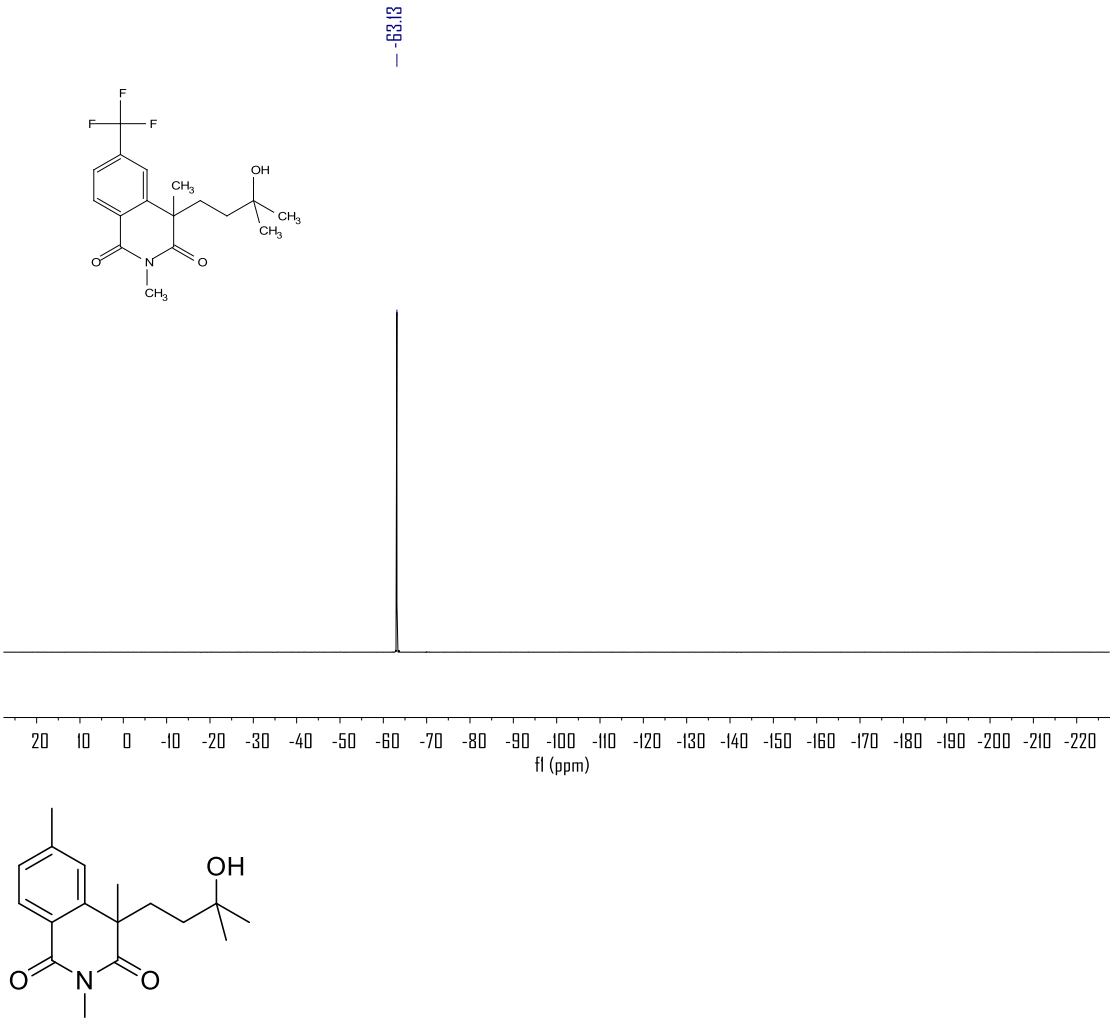
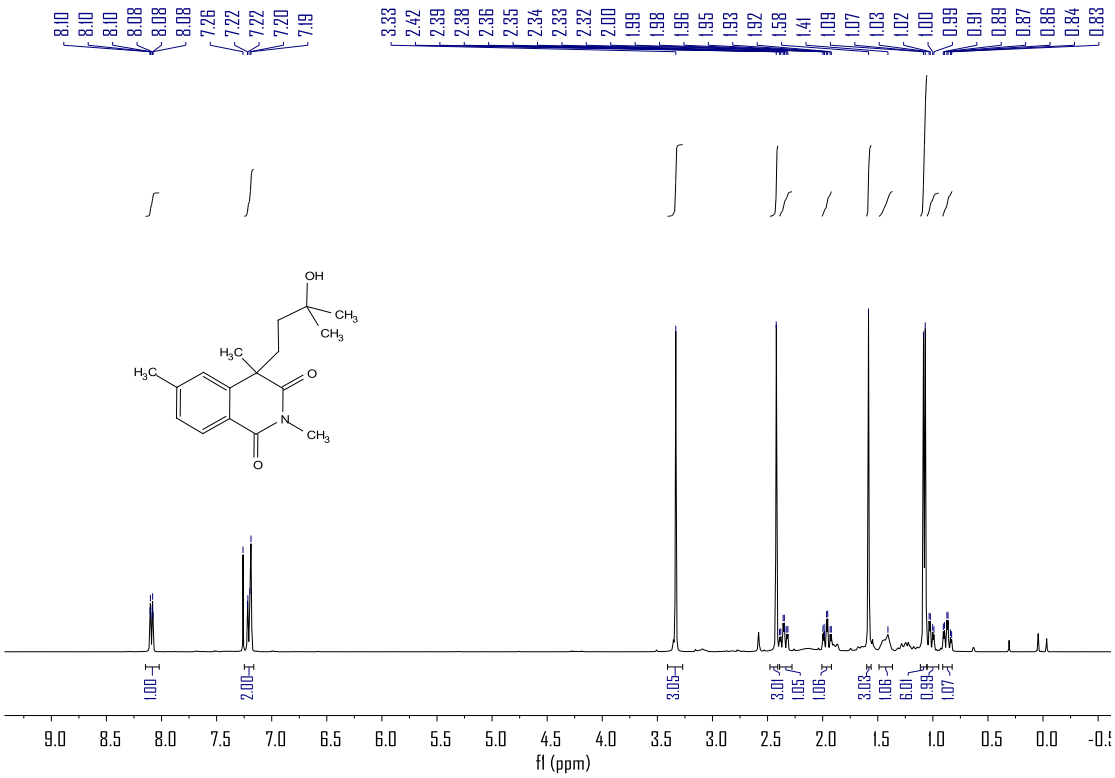


4-(3-hydroxy-3-methylbutyl)-2,4,6-trimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3d**, pale-yellow liquid, 52 mg, 90%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.09 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.30 – 7.11 (m, 2H), 3.33 (t, *J* = 1.7 Hz, 3H), 2.42 (s, 3H), 2.35 (td, *J* = 13.0, 4.3 Hz, 1H), 1.96 (td, *J* = 13.1, 4.2 Hz, 1H), 1.58 (s, 3H), 1.41 (s, 1H), 1.08 (d, *J* = 6.6 Hz, 6H), 1.01 (dd, *J* = 12.9, 4.5 Hz, 1H), 0.87 (td, *J* = 13.1, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.91, 164.54, 145.09, 143.54, 128.91, 128.54, 125.55, 122.47, 70.35, 47.47, 38.79, 37.35, 29.95, 29.40, 28.89, 27.13, 22.09.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_3$: 312.1570; found: 312.1576.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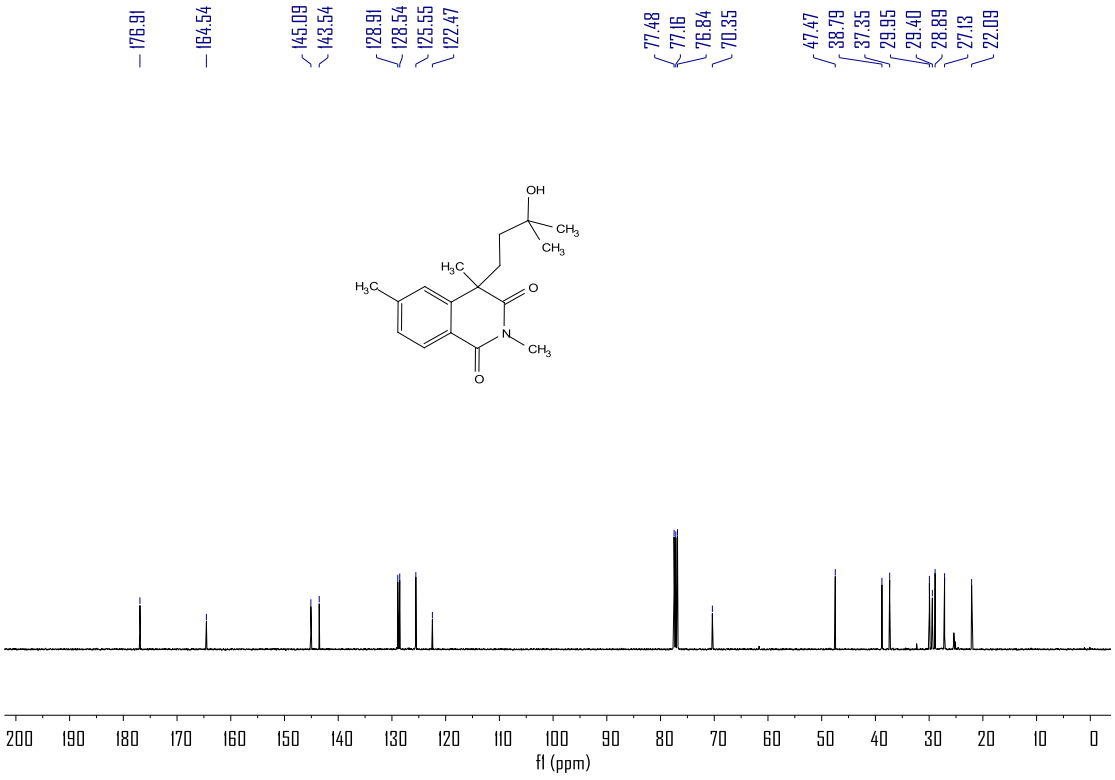
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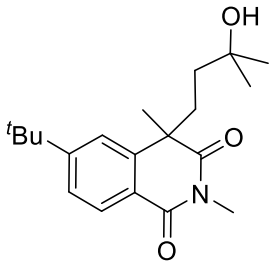
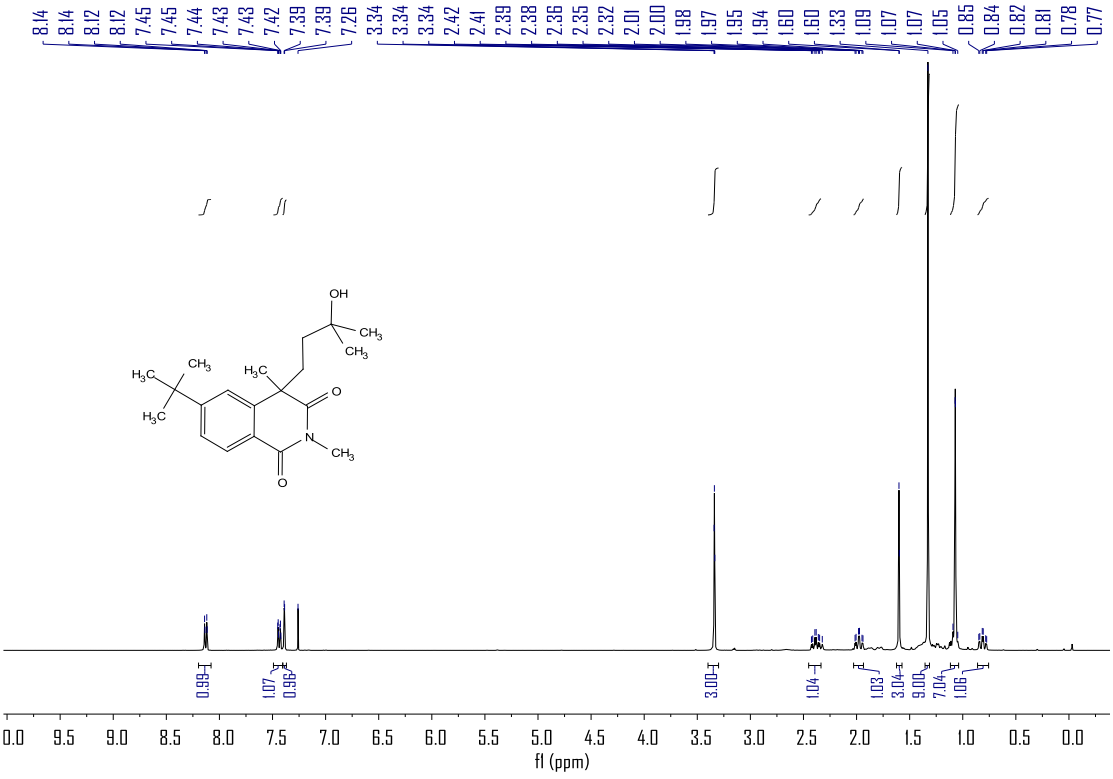
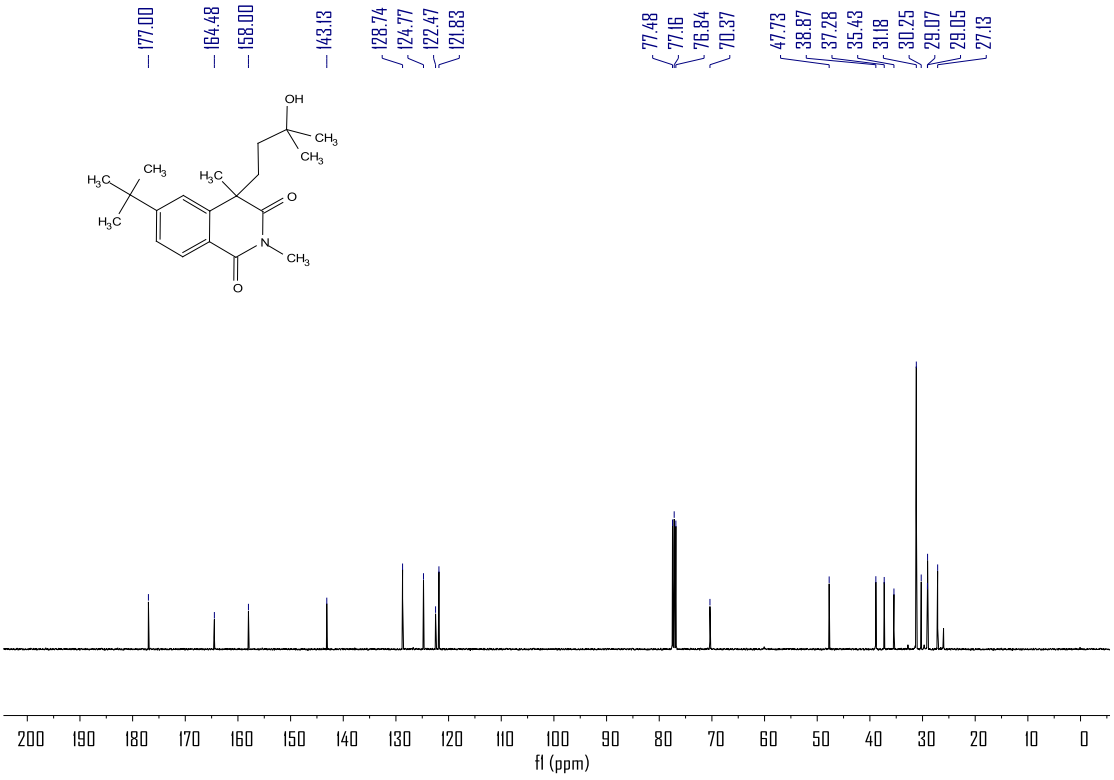


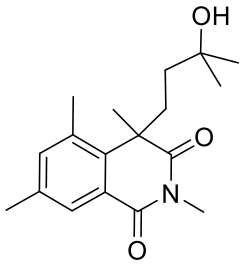
6-(tert-butyl)-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3e**, pale-yellow liquid, 54 mg, 82%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.13 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.44 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.39 (d, *J* = 1.7 Hz, 1H), 3.34 (t, *J* = 1.3 Hz, 3H), 2.44 – 2.30 (m, 1H), 1.98 (td, *J* = 13.0, 3.7 Hz, 1H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.33 (s, 9H), 1.15 – 1.02 (m, 7H), 0.81 (td, *J* = 13.0, 3.6 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 177.00, 164.48, 158.00, 143.13, 128.74, 124.77, 122.47, 121.83, 70.37, 47.73, 38.87, 37.28, 35.43, 31.18, 30.25, 29.07, 29.05, 27.13.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{29}NNaO_3$: 354.2040; found: 354.2045.



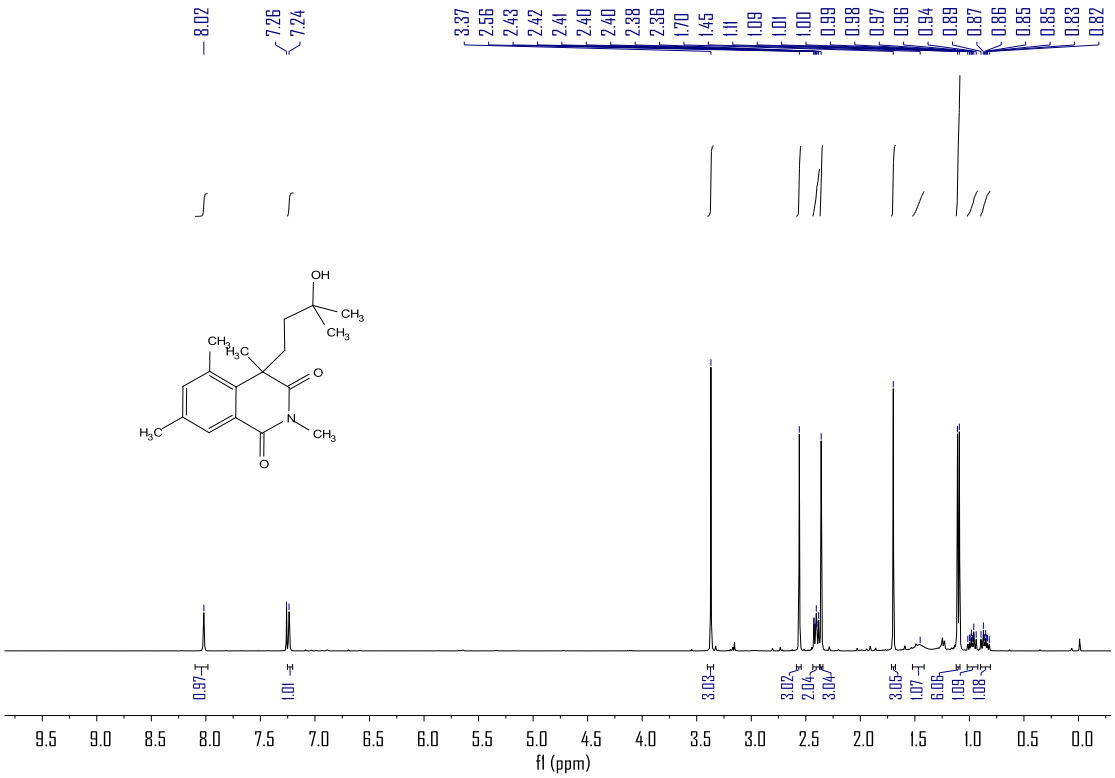


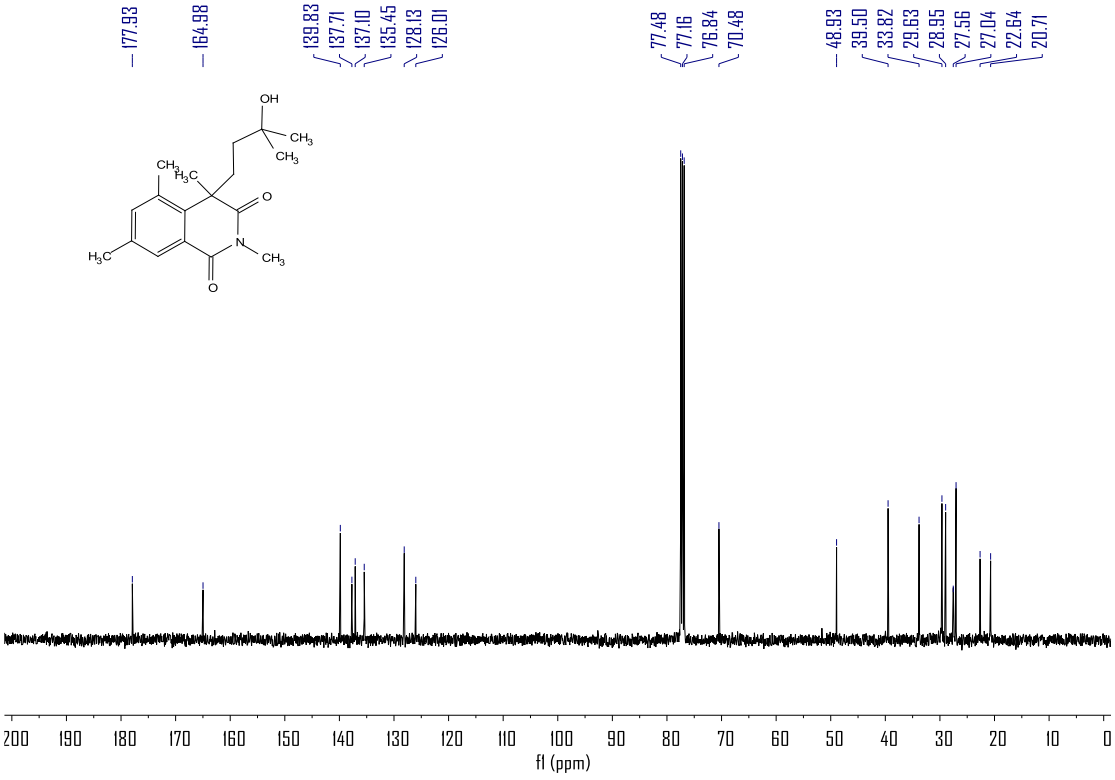


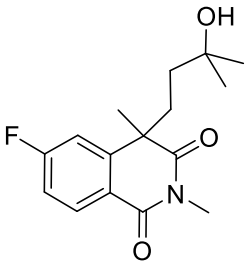
4-(3-hydroxy-3-methylbutyl)-2,4,5,7-tetramethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3f**, pale-yellow liquid, 45 mg, 75%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.02 (s, 1H), 7.24 (s, 1H), 3.37 (s, 3H), 2.56 (s, 3H), 2.44 – 2.38 (m, 2H), 2.36 (s, 3H), 1.70 (s, 3H), 1.45 (s, 1H), 1.10 (d, *J* = 6.6 Hz, 6H), 1.03 – 0.92 (m, 1H), 0.90 – 0.81 (m, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 177.93, 164.98, 139.83, 137.71, 137.10, 135.45, 128.13, 126.01, 70.48, 48.93, 39.50, 33.82, 29.63, 28.95, 27.56, 27.04, 22.64, 20.71.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{25}NNaO_3$: 326.1727; found: 326.1733.


8.02
7.26
7.24
3.37
2.56
2.43
2.42
2.41
2.40
2.40
2.38
2.36
1.70
1.45
1.11
1.09
1.01
1.00
0.99
0.98
0.97
0.96
0.94
0.89
0.87
0.86
0.85
0.85
0.83
0.82
OH
CH3
CH3
CH3
H3C
O
N
CH3
H3C
O
0.97
1.01
3.03
3.02
2.04
3.04
3.05
1.07
6.06
1.09
1.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

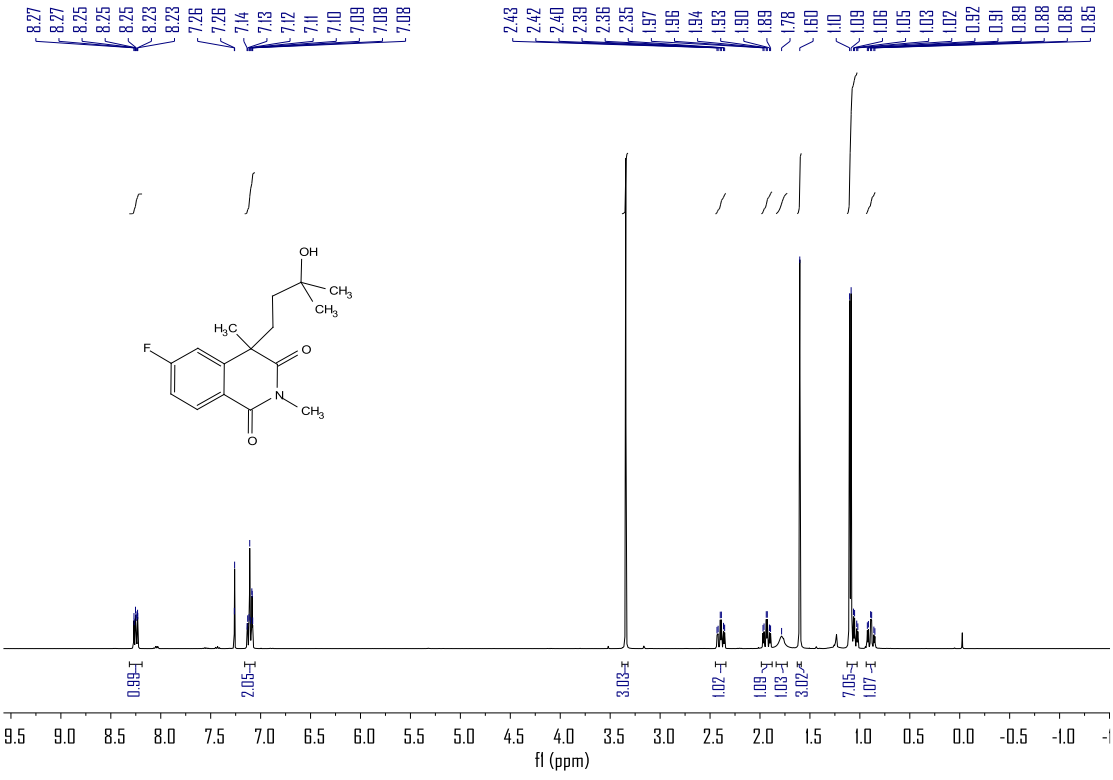

177.93
164.98
139.83
137.71
137.10
135.45
128.13
126.01
77.48
77.16
76.84
70.48
48.93
39.50
33.82
29.63
28.95
27.56
27.04
22.64
20.71
OH
CH3
CH3
CH3
H3C
O
N
CH3
H3C
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

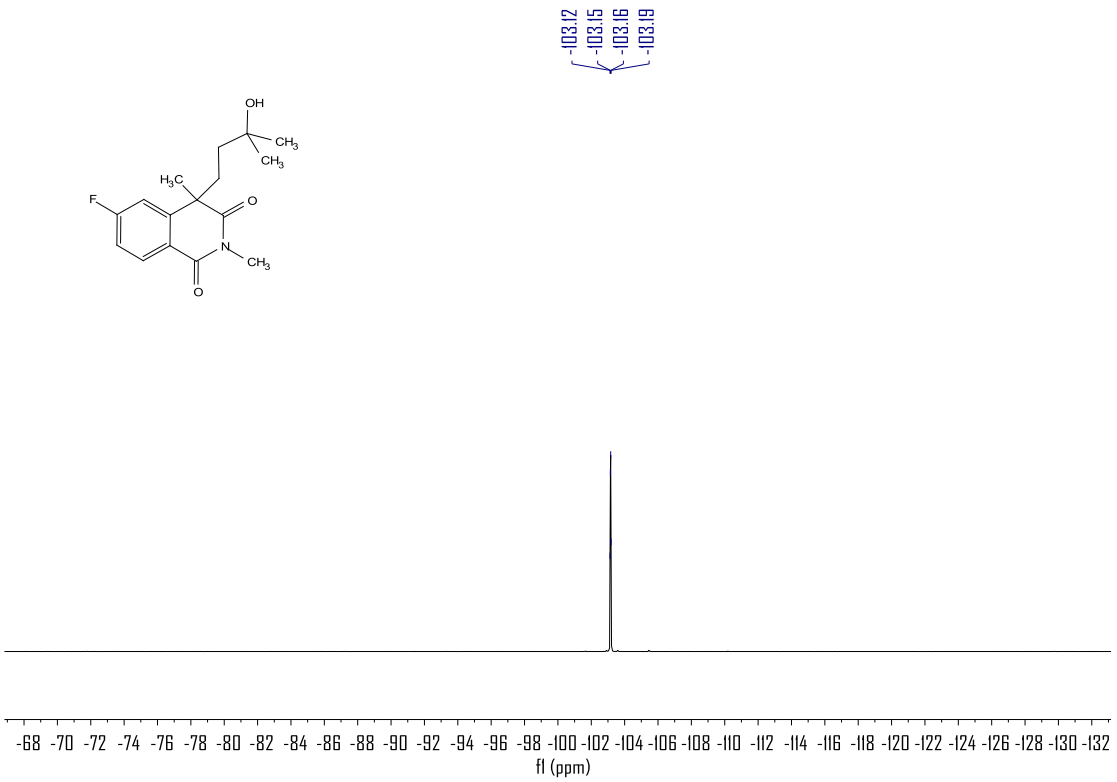


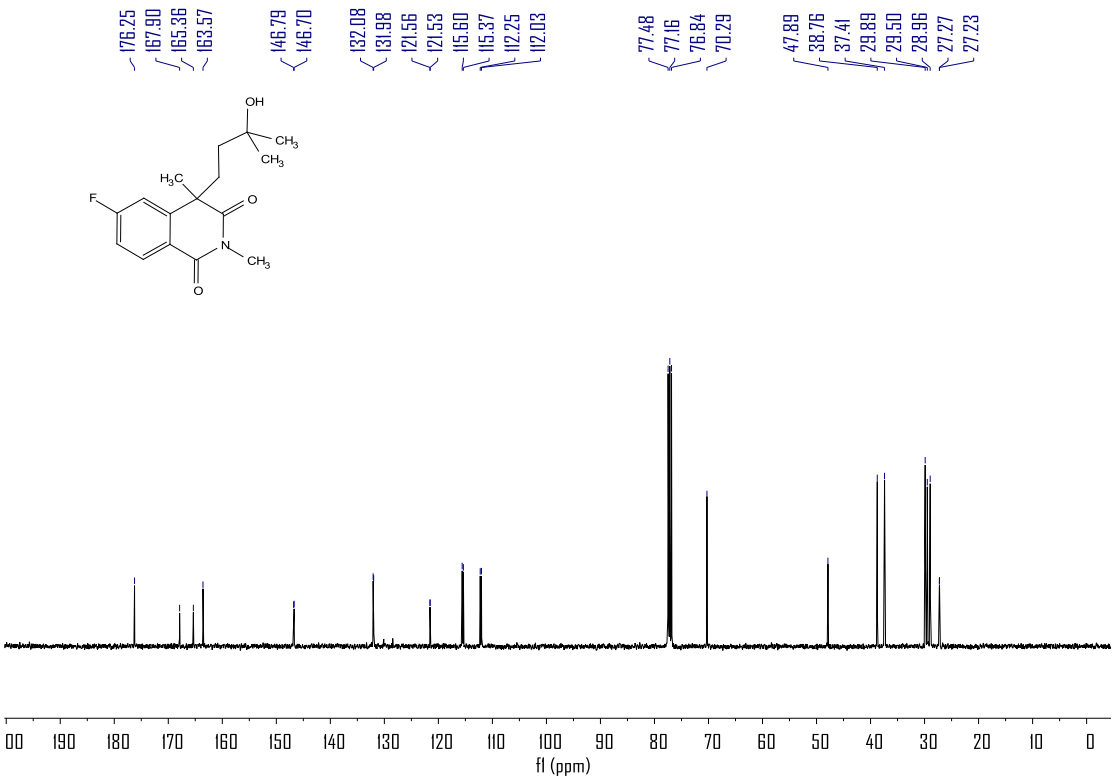
6-fluoro-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

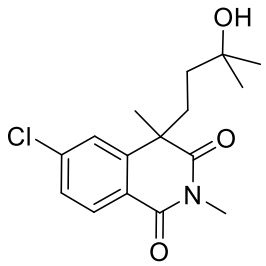
Following the general procedure (**3g**, pale-yellow liquid, 45 mg, 77%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.33 – 8.22 (m, 1H), 7.16 – 7.03 (m, 2H), 3.34 (s, 3H), 2.39 (td, *J* = 13.1, 4.4 Hz, 1H), 1.93 (td, *J* = 13.1, 4.2 Hz, 1H), 1.78 (s, 1H), 1.60 (s, 3H), 1.13 – 1.00 (m, 7H), 0.89 (td, *J* = 13.0, 4.1 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -103.16 (q, *J* = 8.4 Hz). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.25, 166.63 (d, *J* = 255.7 Hz), 163.57, 146.75 (d, *J* = 8.5 Hz), 132.03 (d, *J* = 9.7 Hz), 121.54 (d, *J* = 2.5 Hz), 115.49 (d, *J* = 22.3 Hz), 112.14 (d, *J* = 23.0 Hz), 70.29, 47.89, 38.76, 37.41, 29.89, 29.50, 28.96, 27.23.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}FNNaO_3$: 316.1319; found: 316.1325.




-103.12
-103.15
-103.16
-103.19
OH
CH3
CH3
H3C
F
O
N
CH3
O
-68 -70 -72 -74 -76 -78 -80 -82 -84 -86 -88 -90 -92 -94 -96 -98 -100 -102 -104 -106 -108 -110 -112 -114 -116 -118 -120 -122 -124 -126 -128 -130 -132
f1 (ppm)

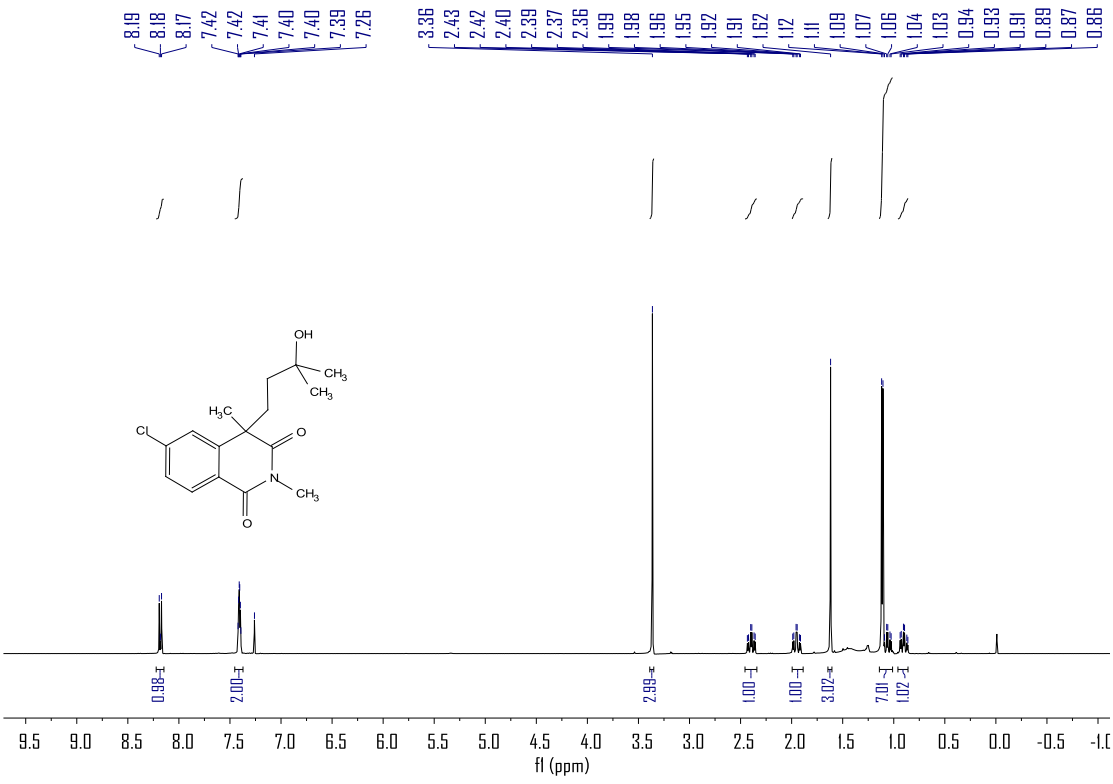

176.25
167.90
165.36
163.57
146.79
146.70
132.08
131.98
121.56
121.53
115.60
115.37
112.25
112.03
77.48
77.16
76.84
70.29
47.89
38.76
37.41
29.89
29.50
28.96
27.27
27.23
OH
CH3
CH3
H3C
F
O
N
CH3
O
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

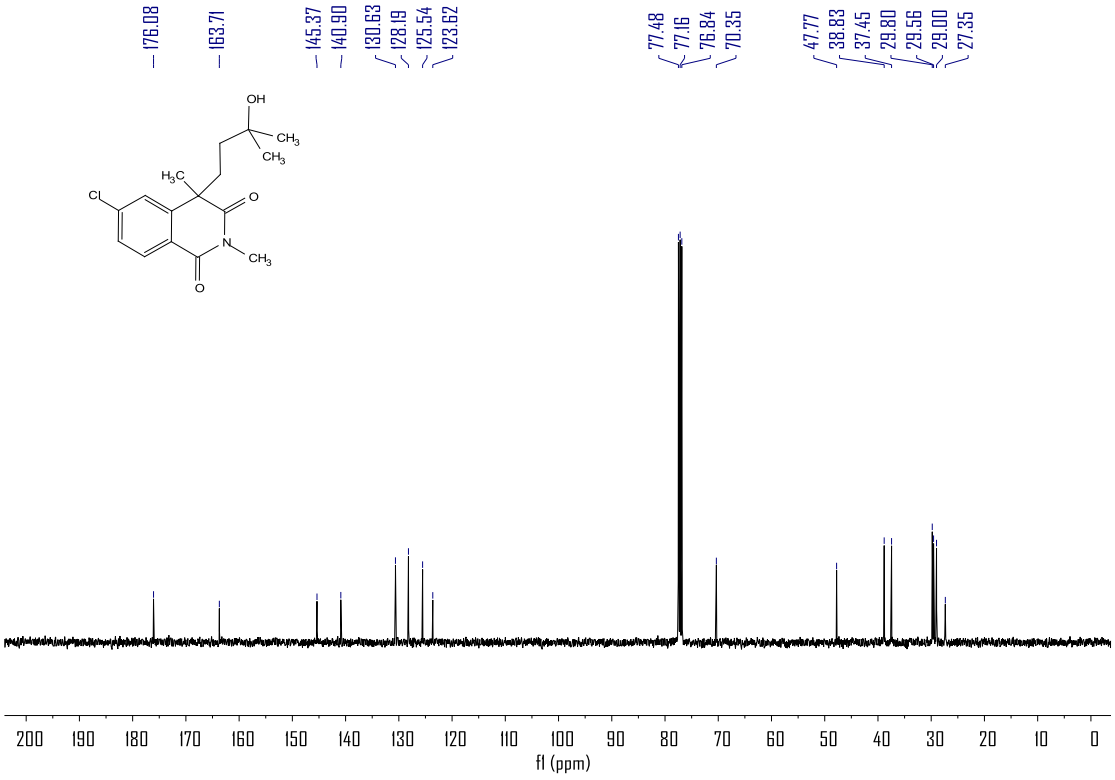


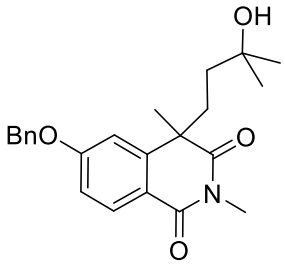
6-chloro-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3h**, pale-yellow liquid, 38 mg, 62%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 9.0 Hz, 1H), 7.46 – 7.36 (m, 2H), 3.36 (s, 3H), 2.40 (td, *J* = 13.0, 4.4 Hz, 1H), 1.95 (td, *J* = 13.0, 4.2 Hz, 1H), 1.62 (s, 3H), 1.16 – 1.01 (m, 7H), 0.90 (td, *J* = 13.0, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.08, 163.71, 145.37, 140.90, 130.63, 128.19, 125.54, 123.62, 70.35, 47.77, 38.83, 37.45, 29.80, 29.56, 29.00, 27.35.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}ClNNaO_3$: 332.1024; found: 332.1027.



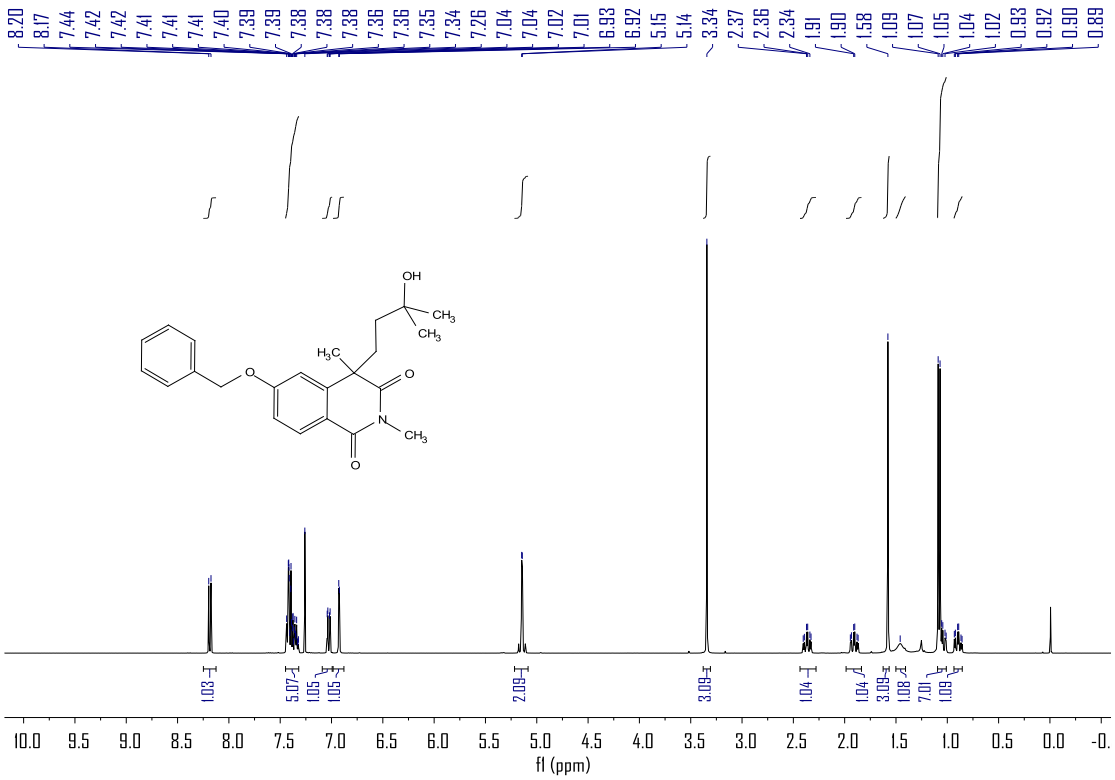


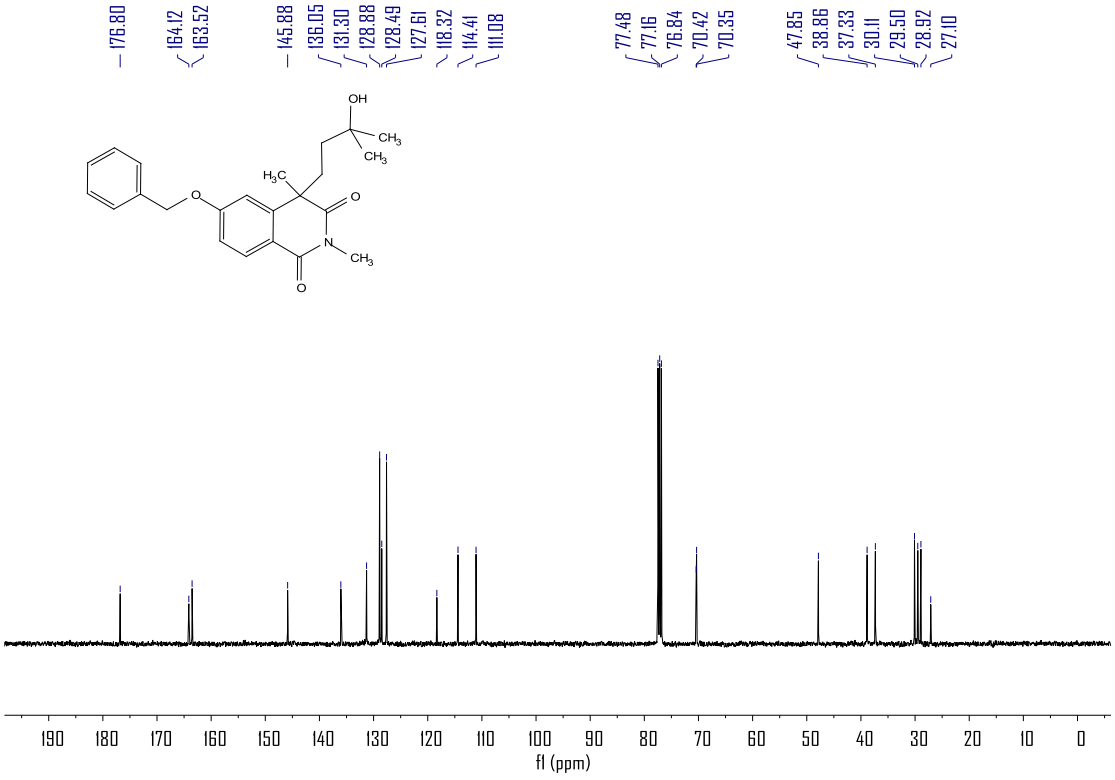


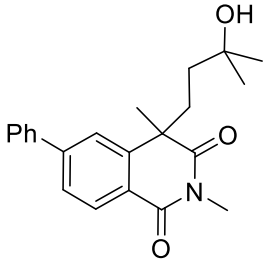
6-(benzyloxy)-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3i**, pale-yellow liquid, 65 mg, 86%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 8.8 Hz, 1H), 7.46 – 7.30 (m, 5H), 7.03 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 5.14 (d, *J* = 2.5 Hz, 2H), 3.34 (s, 3H), 2.37 (td, *J* = 12.9, 4.4 Hz, 1H), 1.91 (td, *J* = 13.0, 4.2 Hz, 1H), 1.58 (s, 3H), 1.46 (s, 1H), 1.08 (d, *J* = 7.4 Hz, 7H), 0.89 (td, *J* = 12.9, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.80, 164.12, 163.52, 145.88, 136.05, 131.30, 128.88, 128.49, 127.61, 118.32, 114.41, 111.08, 70.42, 70.35, 47.85, 38.86, 37.33, 30.11, 29.50, 28.92, 27.10.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{27}NNaO_4$: 404.1832; found: 404.1839.


8.20
8.17
7.44
7.42
7.42
7.41
7.41
7.41
7.40
7.39
7.39
7.38
7.38
7.38
7.36
7.36
7.35
7.34
7.26
7.04
7.04
7.02
7.01
6.93
6.92
5.15
5.14
3.34
2.37
2.36
2.34
1.91
1.90
1.58
1.09
1.07
1.05
1.04
1.02
0.93
0.92
0.90
0.89
OH
CH3
CH3
H3C
O
O
N
CH3
O
1.03
5.07
1.05
1.05
2.09
3.09
1.04
1.04
3.09
1.08
7.01
1.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

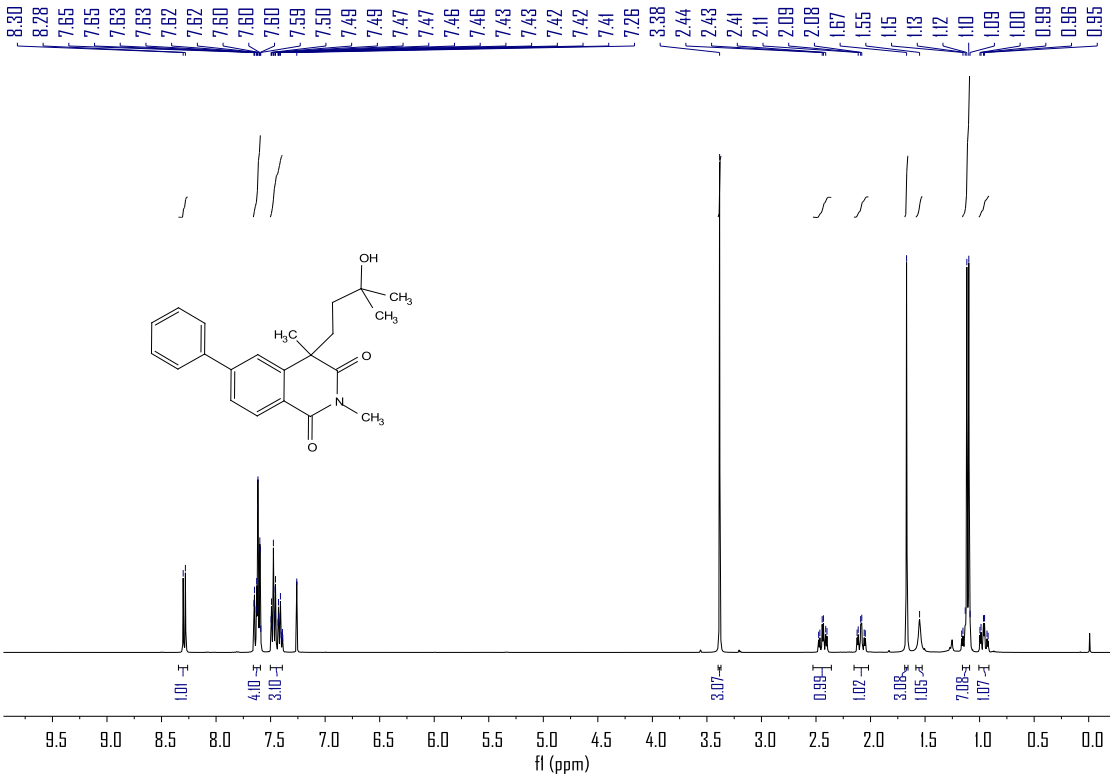

176.80
164.12
163.52
145.88
136.05
131.30
128.88
128.49
127.61
118.32
114.41
111.08
77.48
77.16
76.84
70.42
70.35
47.85
38.86
37.33
30.11
29.50
28.92
27.10
OH
CH3
CH3
H3C
O
O
N
CH3
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

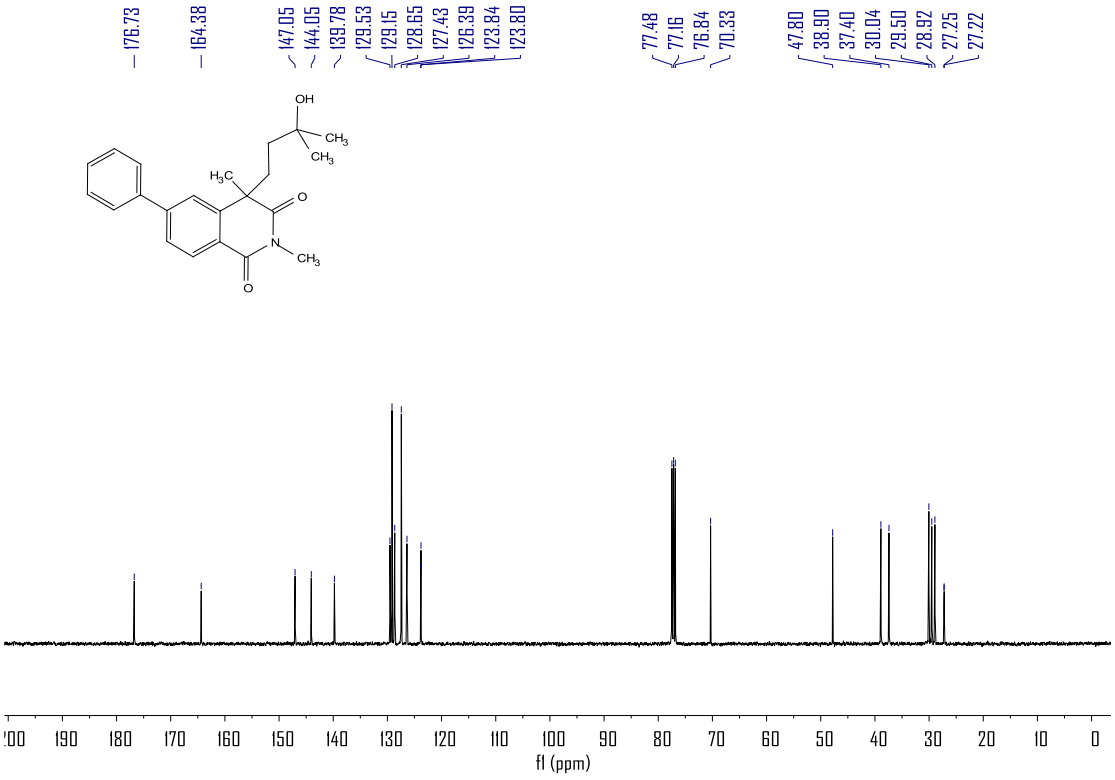


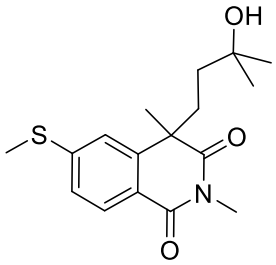
4-(3-hydroxy-3-methylbutyl)-2,4-dimethyl-6-phenylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3j**, pale-yellow liquid, 52 mg, 74%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 8.1 Hz, 1H), 7.68 – 7.58 (m, 4H), 7.53 – 7.40 (m, 3H), 3.38 (s, 3H), 2.44 (td, *J* = 13.0, 4.5 Hz, 1H), 2.09 (td, *J* = 13.0, 4.0 Hz, 1H), 1.67 (s, 3H), 1.55 (s, 1H), 1.11 (d, *J* = 7.2 Hz, 7H), 0.96 (td, *J* = 13.0, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.73, 164.38, 147.05, 144.05, 139.78, 129.53, 129.15, 128.65, 127.43, 126.39, 123.84, 123.80, 70.33, 47.80, 38.90, 37.40, 30.04, 29.50, 28.92, 27.25, 27.22.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{25}NNaO_3$: 374.1727; found: 374.1735.



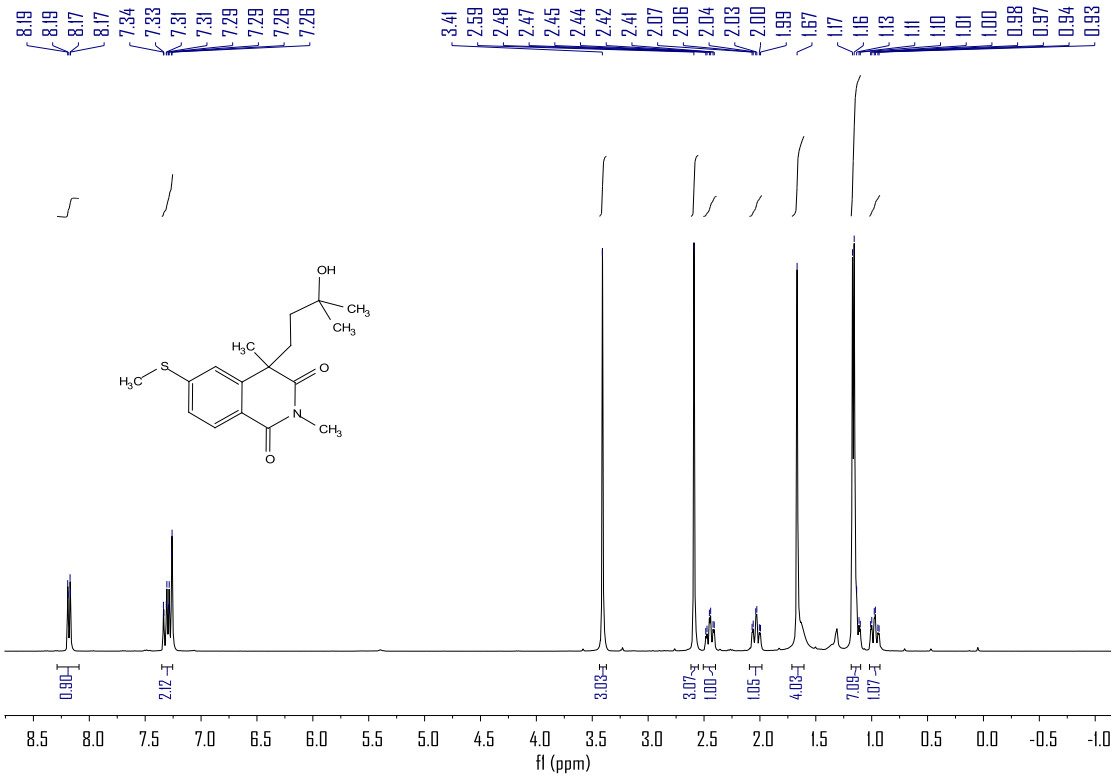




4-(3-hydroxy-3-methylbutyl)-2,4-dimethyl-6-(methylthio)isoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3k**, pale-yellow liquid, 45 mg, 70%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.18 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.38 – 7.22 (m, 2H), 3.41 (s, 3H), 2.59 (s, 3H), 2.45 (td, *J* = 13.0, 4.4 Hz, 1H), 2.03 (td, *J* = 13.1, 4.0 Hz, 1H), 1.72 – 1.54 (m, 4H), 1.16 (d, *J* = 6.2 Hz, 7H), 0.97 (td, *J* = 13.2, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.49, 164.19, 147.33, 143.97, 129.28, 124.14, 121.49, 121.42, 70.33, 47.67, 38.81, 37.24, 30.00, 29.49, 28.91, 27.19, 27.16, 14.90.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_3S$: 344.1291; found: 344.1295.


8.19
8.19
8.17
8.17
7.34
7.33
7.31
7.31
7.29
7.29
7.26
7.26
3.41
2.59
2.48
2.47
2.45
2.44
2.42
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1.99
1.67
1.17
1.16
1.13
1.11
1.10
1.01
1.00
0.98
0.97
0.94
0.93
OH
CH3
CH3
H3C
S
H3C
O
N
CH3
O
0.90
2.12
3.03
3.07
1.00
1.05
4.03
7.09
1.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.5
2.0
1.5
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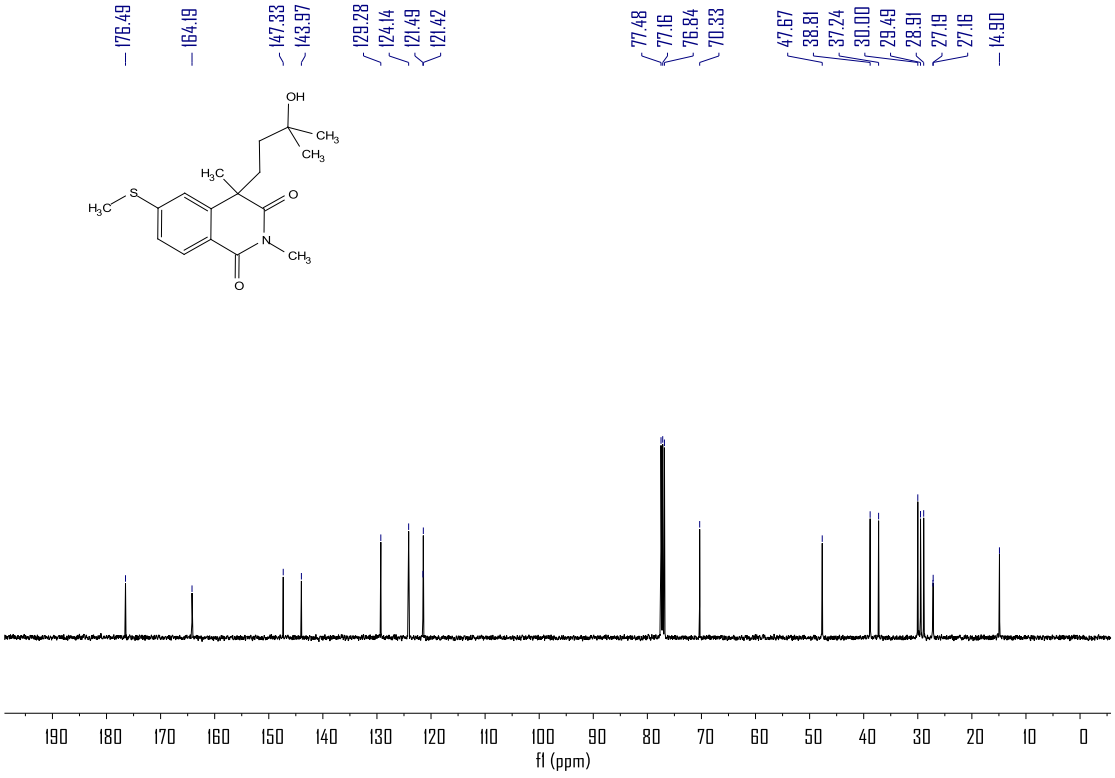
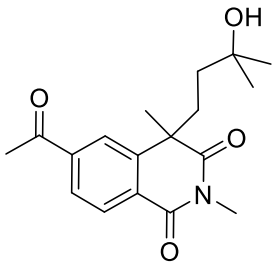
0.5
0.0
-0.5
-1.0
f1 (ppm)

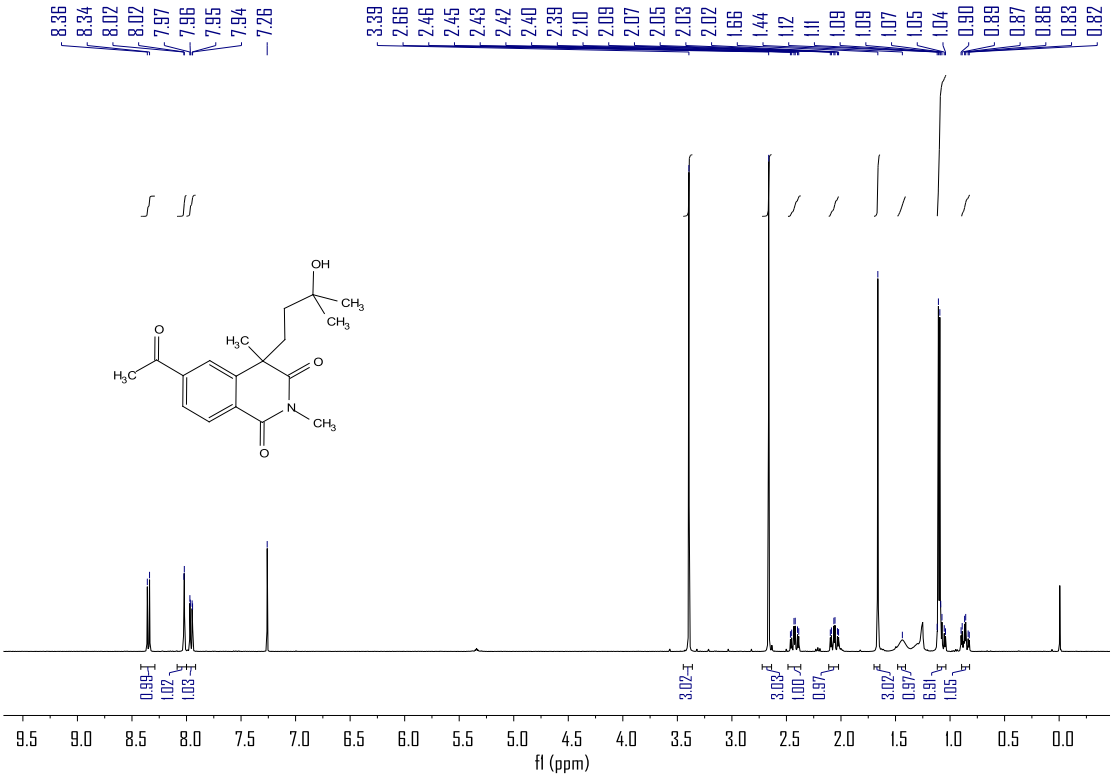

176.49
164.19
147.33
143.97
129.28
124.14
121.49
121.42
77.48
77.16
76.84
70.33
47.67
38.81
37.24
30.00
29.49
28.91
27.19
27.16
14.90
OH
CH3
CH3
H3C
S
H3C
O
N
CH3
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

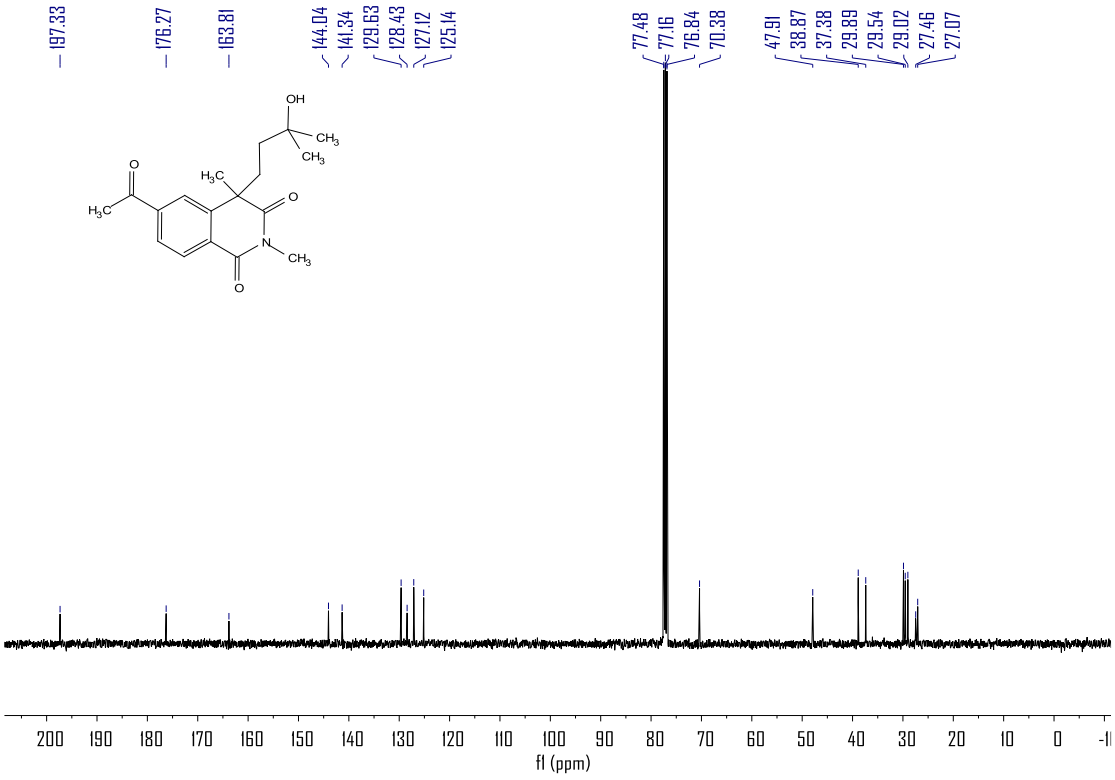


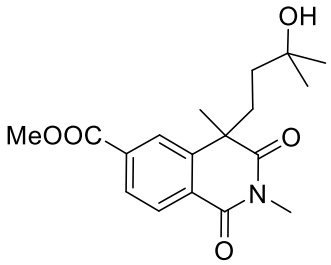
6-acetyl-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3l**, pale-yellow liquid, 24 mg, 37%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 1.5 Hz, 1H), 7.96 (dd, *J* = 8.2, 1.6 Hz, 1H), 3.39 (s, 3H), 2.66 (s, 3H), 2.43 (td, *J* = 13.0, 4.5 Hz, 1H), 2.06 (td, *J* = 13.1, 4.1 Hz, 1H), 1.66 (s, 3H), 1.44 (s, 1H), 1.16 – 0.99 (m, 7H), 0.86 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 197.33, 176.27, 163.81, 144.04, 141.34, 129.63, 128.43, 127.12, 125.14, 70.38, 47.91, 38.87, 37.38, 29.89, 29.54, 29.02, 27.46, 27.07.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_4$: 340.1519; found: 340.1526.



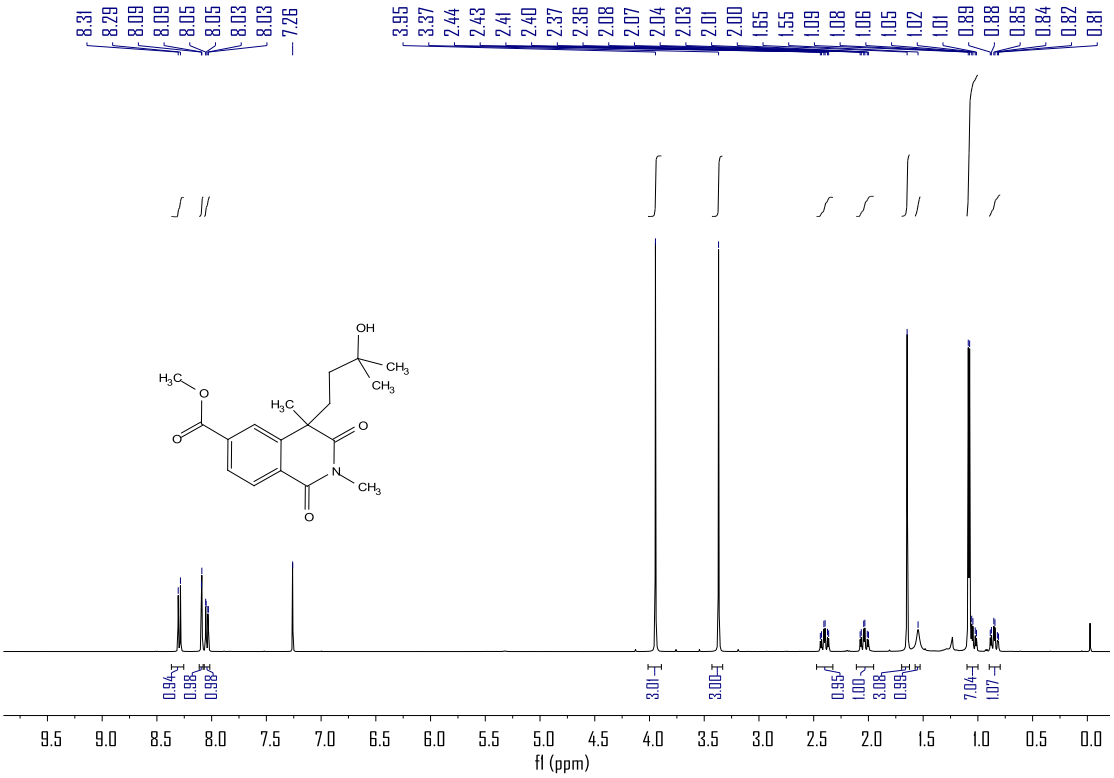


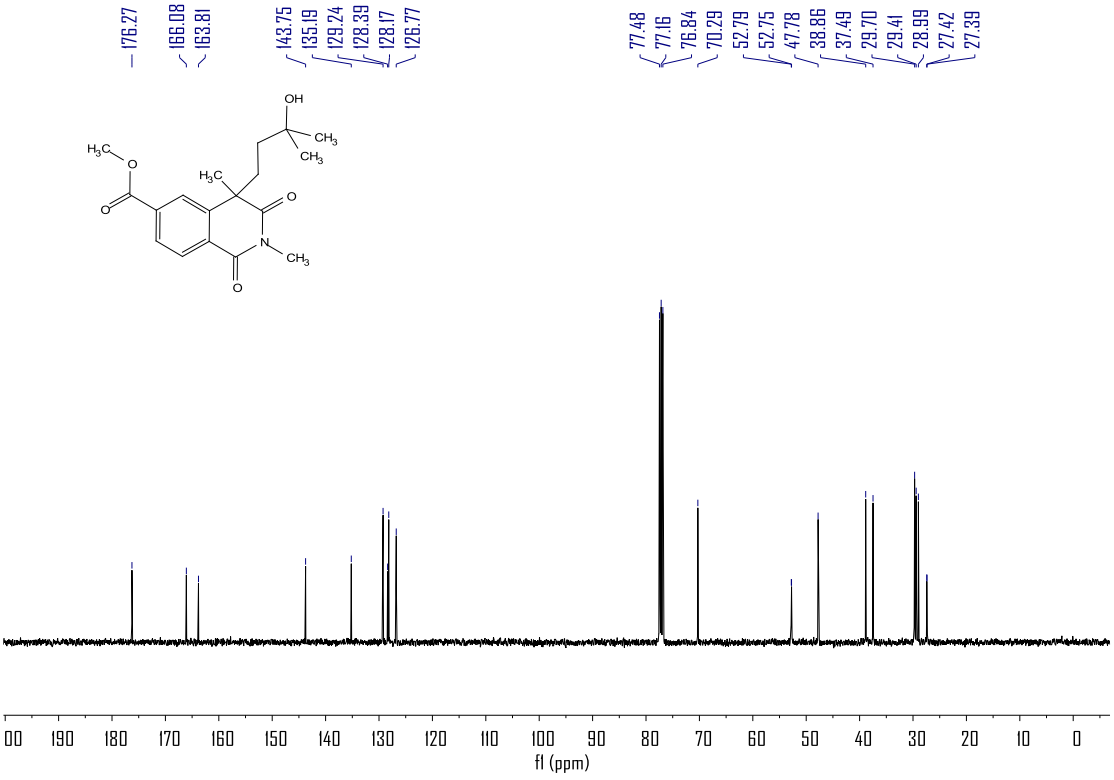


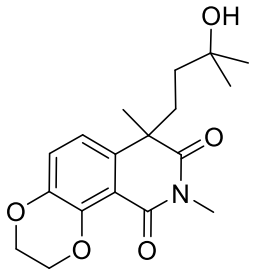
Methyl-4-(3-hydroxy-3-methylbutyl)-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinoline-6-carboxylate

Following the general procedure (**3m**, pale-yellow liquid, 39 mg, 58%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 8.1 Hz, 1H), 8.09 (s, 1H), 8.04 (dd, *J* = 8.2, 1.5 Hz, 1H), 3.95 (s, 3H), 3.37 (s, 3H), 2.40 (td, *J* = 13.0, 4.4 Hz, 1H), 2.04 (td, *J* = 13.1, 4.2 Hz, 1H), 1.65 (s, 3H), 1.55 (s, 1H), 1.14 – 0.98 (m, 7H), 0.85 (td, *J* = 12.9, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.27, 166.08, 163.81, 143.75, 135.19, 129.24, 128.39, 128.17, 126.77, 70.29, 52.79, 52.75, 47.78, 38.86, 37.49, 29.70, 29.41, 28.99, 27.42, 27.39.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_5$: 356.1468; found: 356.1473.


8.31
8.29
8.09
8.09
8.05
8.05
8.03
8.03
7.26
3.95
3.37
2.44
2.43
2.41
2.40
2.37
2.36
2.08
2.07
2.04
2.03
2.01
2.00
1.65
1.55
1.09
1.08
1.06
1.05
1.02
1.01
0.89
0.88
0.85
0.84
0.82
0.81
0.94
0.98
0.98
0.98
3.01
3.00
0.95
1.00
3.08
0.99
7.04
1.07
f1 (ppm)

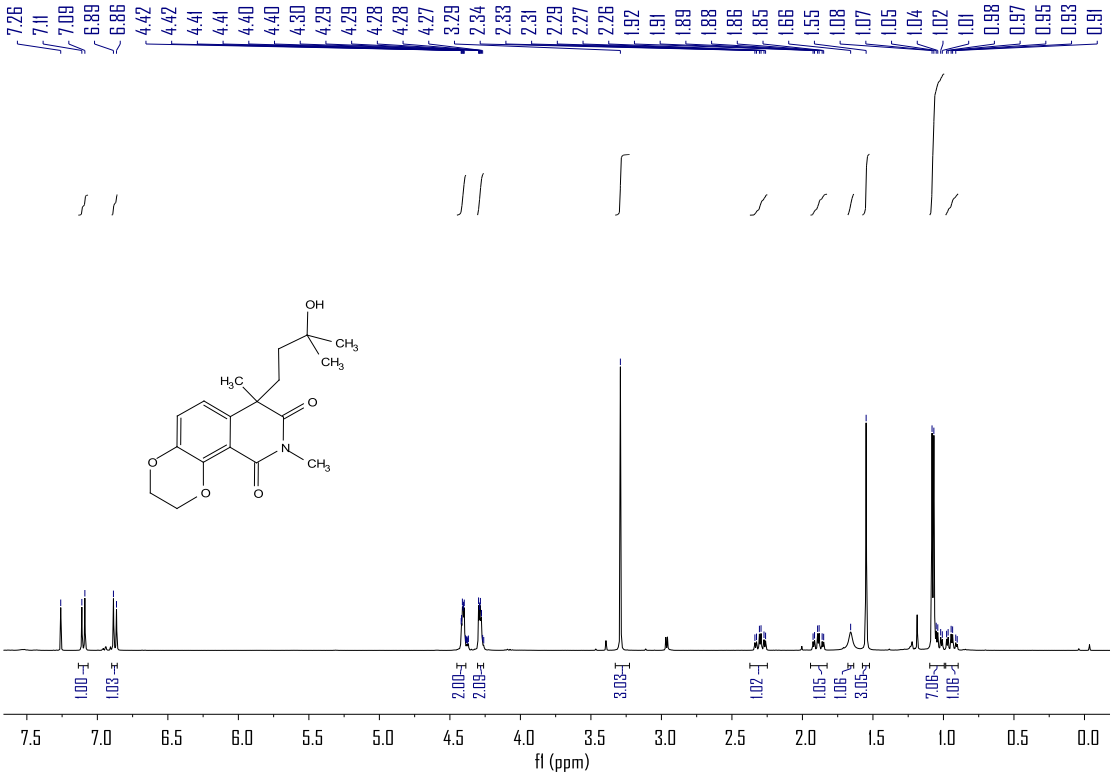

176.27
166.08
163.81
143.75
135.19
129.24
128.39
128.17
126.77
77.48
77.16
76.84
70.29
52.79
52.75
47.78
38.86
37.49
29.70
29.41
28.99
27.42
27.39
f1 (ppm)

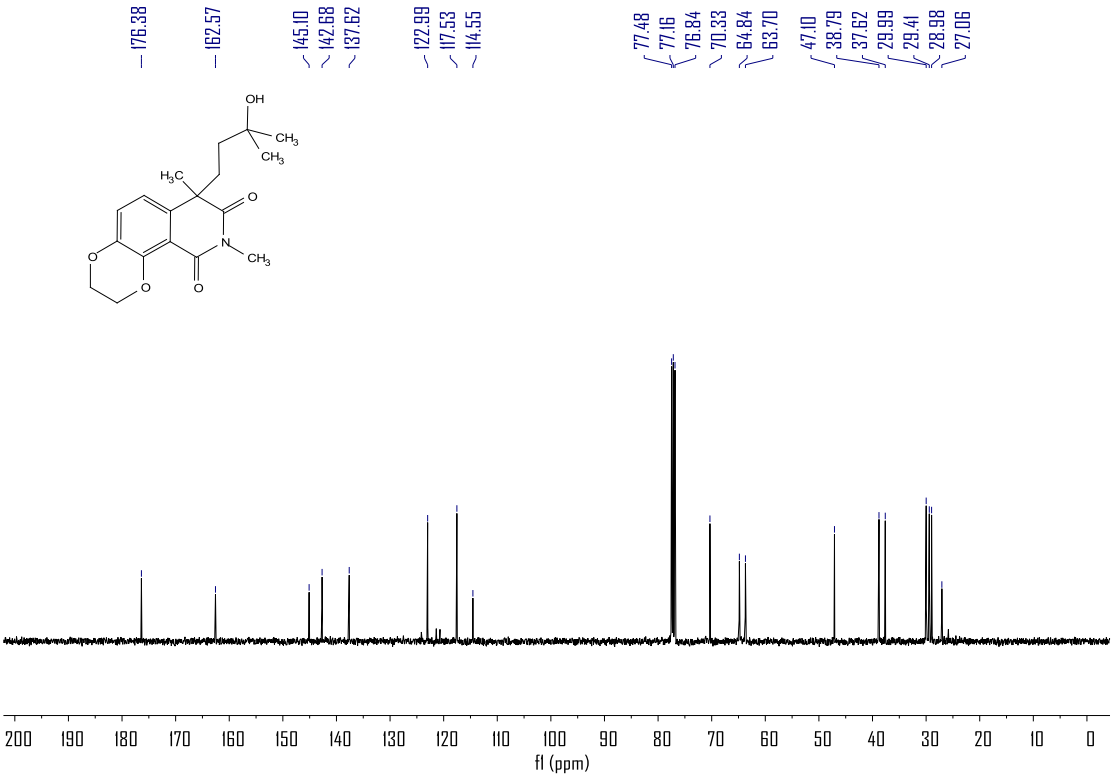


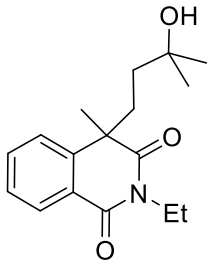
7-(3-hydroxy-3-methylbutyl)-7,9-dimethyl-2,3-dihydro-[1,4]dioxino[2,3-h]isoquinoline-8,10(7H,9H)-dione

Following the general procedure (**3n**, pale-yellow liquid, 34 mg, 51%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.10 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 1H), 4.44 – 4.38 (m, 2H), 4.29 (dd, *J* = 5.6, 2.8 Hz, 2H), 3.29 (s, 3H), 2.30 (td, *J* = 12.9, 4.6 Hz, 1H), 1.89 (td, *J* = 12.9, 4.3 Hz, 1H), 1.66 (s, 2H), 1.55 (s, 3H), 1.10 – 1.00 (m, 7H), 0.94 (td, *J* = 12.9, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.38, 162.57, 145.10, 142.68, 137.62, 122.99, 117.53, 114.55, 70.33, 64.84, 63.70, 47.10, 38.79, 37.62, 29.99, 29.41, 28.98, 27.06.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_5$: 356.1468; found: 356.1477.



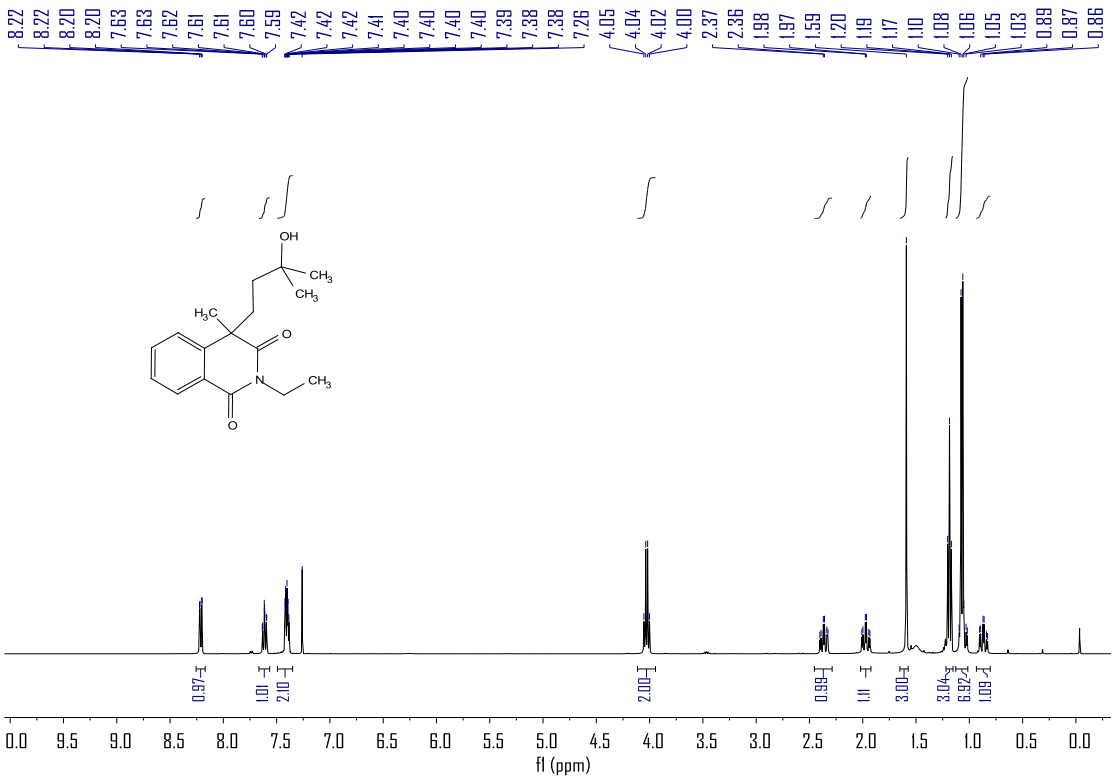


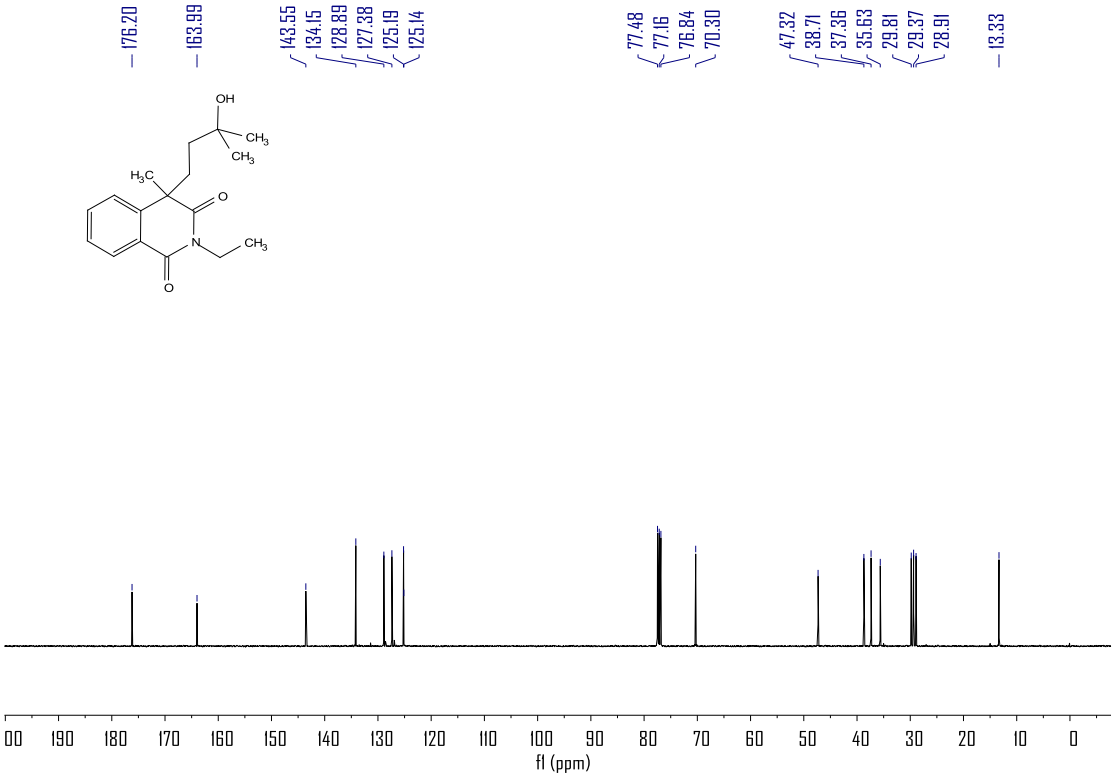


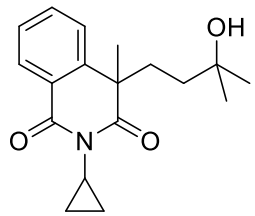
2-ethyl-4-(3-hydroxy-3-methylbutyl)-4-methylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3o**, pale-yellow liquid, 42 mg, 72%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.21 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.69 – 7.56 (m, 1H), 7.47 – 7.35 (m, 2H), 4.03 (q, *J* = 7.0 Hz, 2H), 2.36 (td, *J* = 13.0, 4.4 Hz, 1H), 1.97 (td, *J* = 13.0, 4.1 Hz, 1H), 1.59 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H), 1.07 (d, *J* = 6.6 Hz, 7H), 0.87 (td, *J* = 12.9, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.20, 163.99, 143.55, 134.15, 128.89, 127.38, 125.19, 125.14, 70.30, 47.32, 38.71, 37.36, 35.63, 29.81, 29.37, 28.91, 13.33.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_3$: 312.1570; found: 312.1573.


8.22 8.22 8.20 8.20 7.63 7.63 7.62 7.61 7.61 7.60 7.59 7.42 7.42 7.42 7.41 7.40 7.40 7.40 7.40 7.39 7.38 7.38 7.26 4.05 4.04 4.02 4.00 2.37 2.36 1.98 1.97 1.59 1.20 1.19 1.17 1.10 1.08 1.06 1.05 1.03 0.89 0.87 0.86
OH
CH3
CH3
H3C
O
N
CH3
O
0.97 1.01 2.10 2.00 0.99 1.11 3.00 3.04 6.92 1.09
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

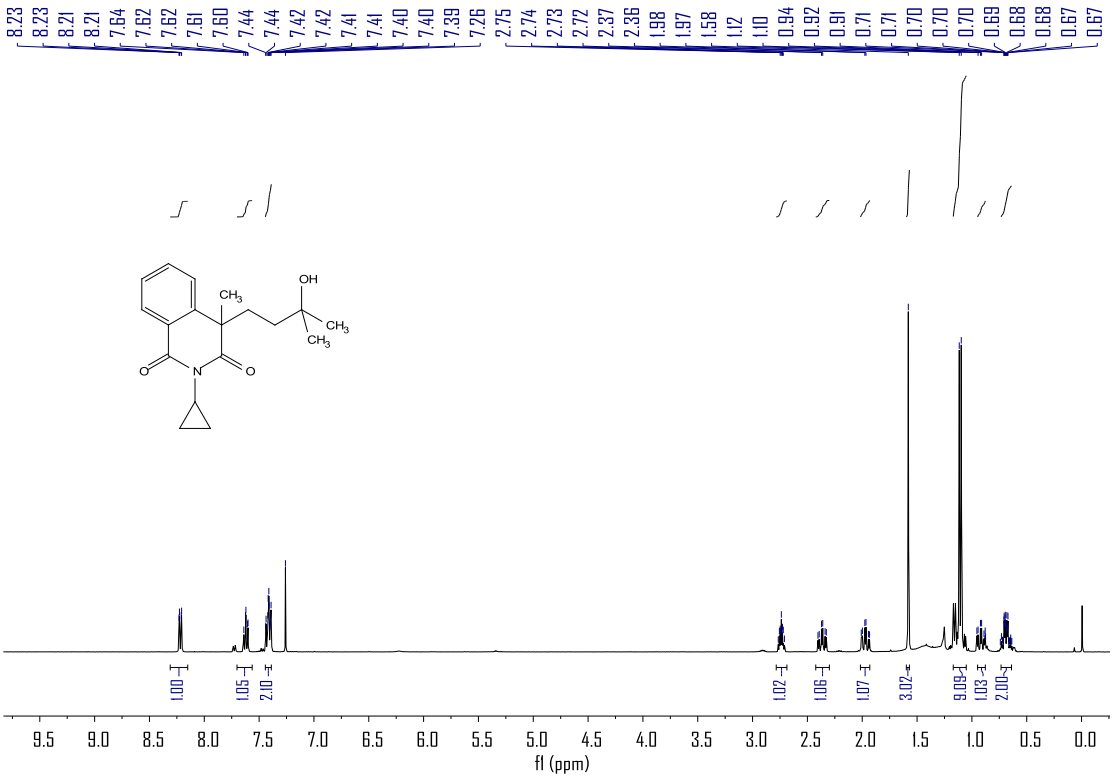

176.20 163.99 143.55 134.15 128.89 127.38 125.19 125.14 77.48 77.16 76.84 70.30 47.32 38.71 37.36 35.63 29.81 29.37 28.91 13.33
OH
CH3
CH3
H3C
O
N
CH3
O
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

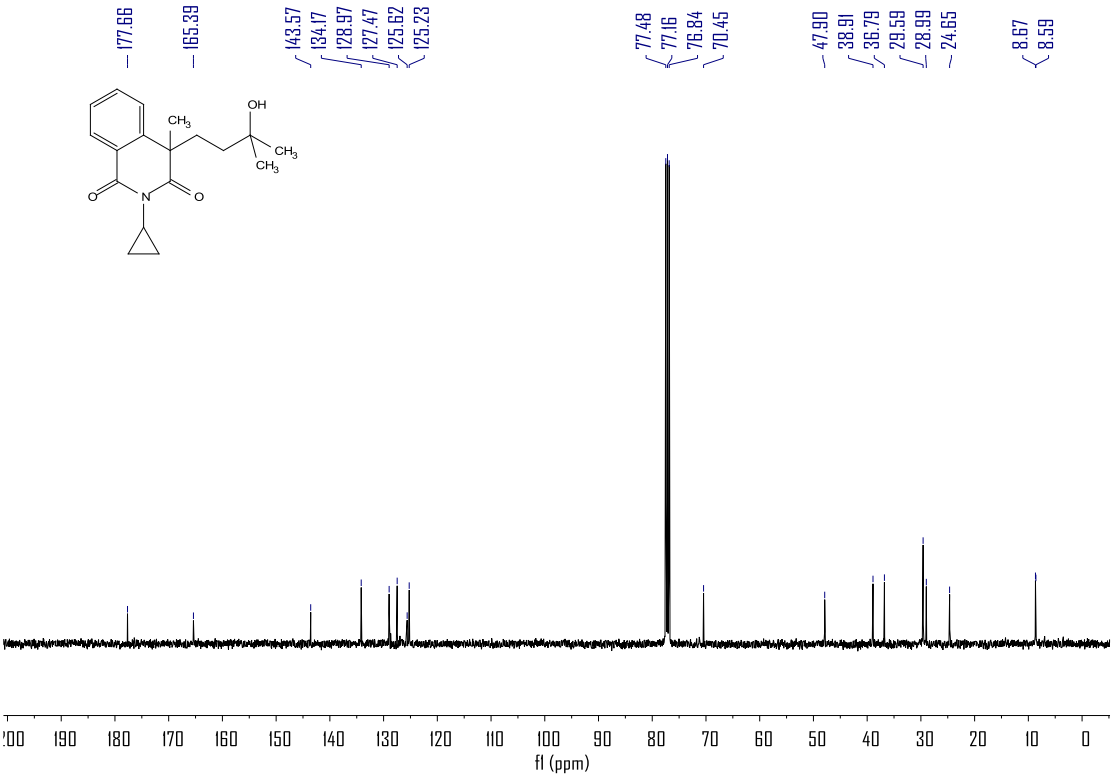


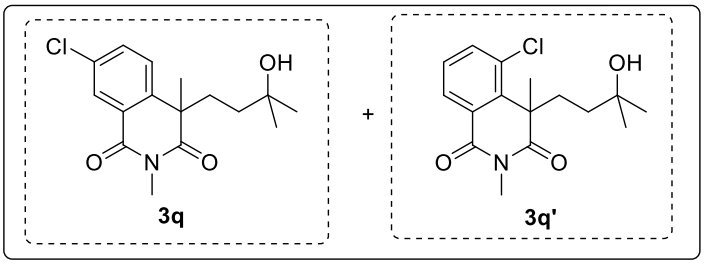
2-cyclopropyl-4-(3-hydroxy-3-methylbutyl)-4-methylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3p**, pale-yellow liquid, 21 mg, 35%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.22 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.67 – 7.57 (m, 1H), 7.47 – 7.33 (m, 2H), 2.74 (tt, *J* = 7.1, 4.1 Hz, 1H), 2.37 (td, *J* = 13.0, 4.4 Hz, 1H), 1.99 (dd, *J* = 13.0, 4.2 Hz, 1H), 1.58 (s, 3H), 1.11 (d, *J* = 7.2 Hz, 9H), 0.92 (td, *J* = 13.0, 4.2 Hz, 1H), 0.76 – 0.56 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 177.66, 165.39, 143.57, 134.17, 128.97, 127.47, 125.62, 125.23, 70.45, 47.90, 38.91, 36.79, 29.59, 28.99, 24.65, 8.67, 8.59.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_3$: 324.1570; found: 324.1573.







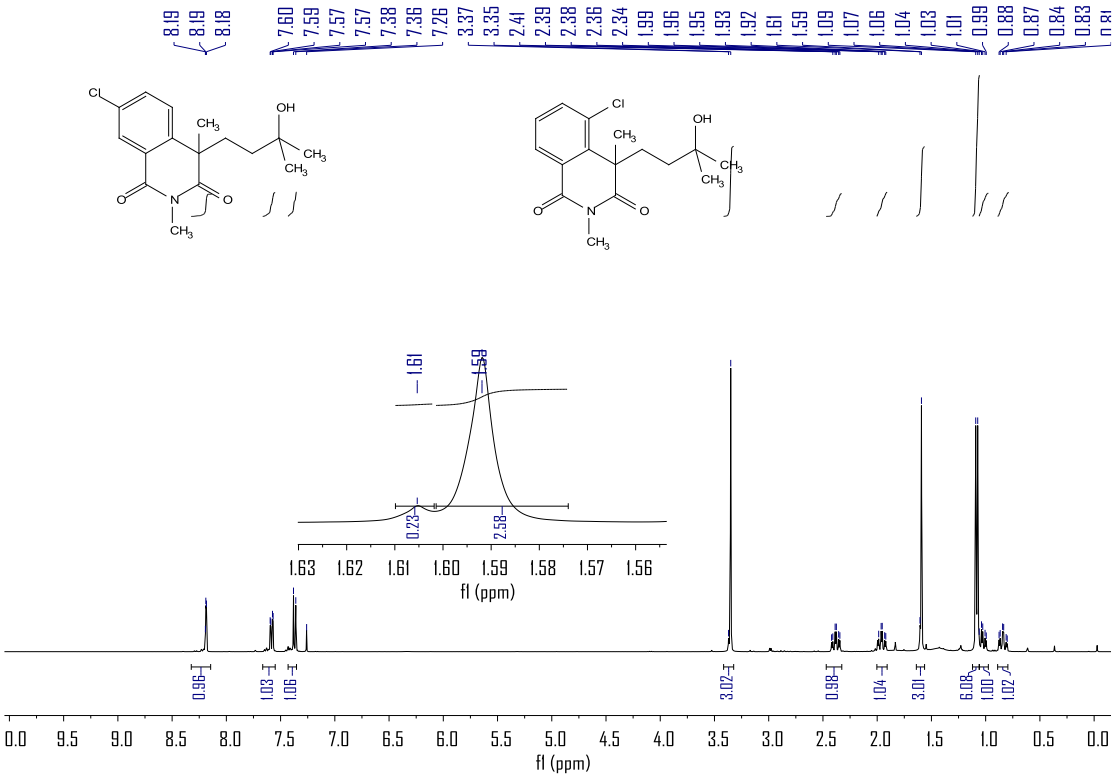
7-chloro-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

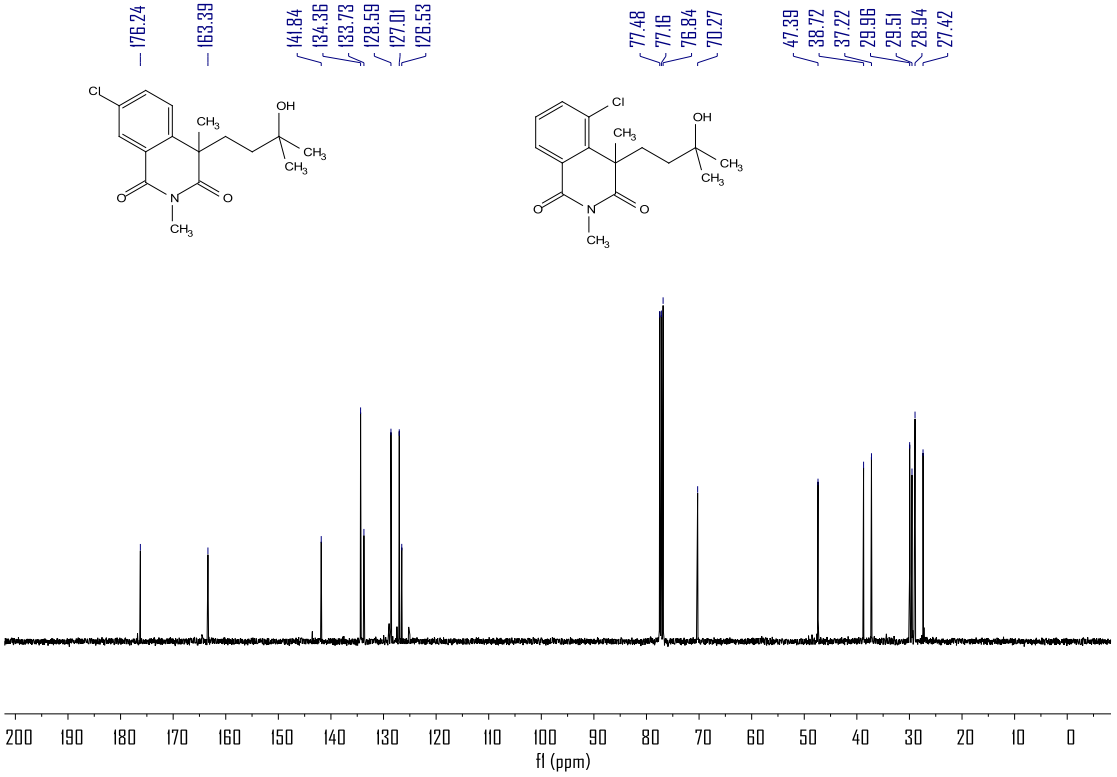
and

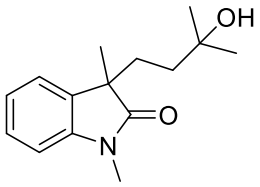
5-chloro-4-(3-hydroxy-3-methylbutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**3q:3q' = 11:1**, pale-yellow liquid, 53 mg, 85%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 2.2 Hz, 1H), 7.58 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 3.35 (s, 3H), 2.38 (td, *J* = 13.0, 4.5 Hz, 1H), 2.05 – 1.91 (m, 1H), 1.59 (s, 3H), 1.08 (d, *J* = 7.3 Hz, 6H), 1.09 – 1.02 (m, 1H), 0.84 (td, *J* = 13.0, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.24, 163.39, 141.84, 134.36, 133.73, 128.59, 127.01, 126.53, 70.27, 47.39, 38.72, 37.22, 29.96, 29.51, 28.94, 27.42.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}ClNNaO_3$: 332.1024; found: 332.1031.


8.19
8.19
8.18
7.60
7.59
7.57
7.57
7.38
7.36
7.26
3.37
3.35
2.41
2.39
2.38
2.36
2.34
1.99
1.96
1.95
1.93
1.92
1.61
1.59
1.09
1.07
1.06
1.04
1.03
1.01
0.99
0.88
0.87
0.84
0.83
Cl
OH
CH3
CH3
CH3
O
N
O
CH3
1.61
1.59
0.23
2.58
1.63 1.62 1.61 1.60 1.59 1.58 1.57 1.56
f1 (ppm)
0.96
1.03
1.06
3.02
0.98
1.04
3.01
6.08
1.00
1.02
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

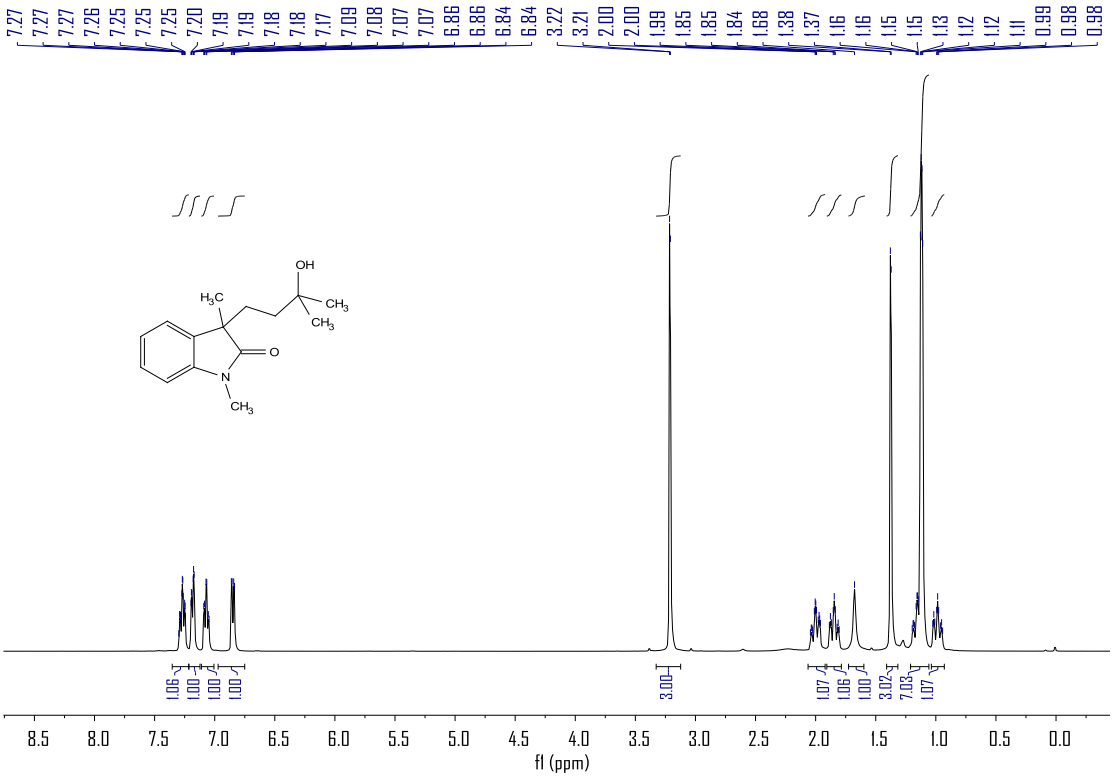

176.24
163.39
141.84
134.36
133.73
128.59
127.01
126.53
77.48
77.16
76.84
70.27
47.39
38.72
37.22
29.96
29.51
28.94
27.42
Cl
OH
CH3
CH3
CH3
O
N
O
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

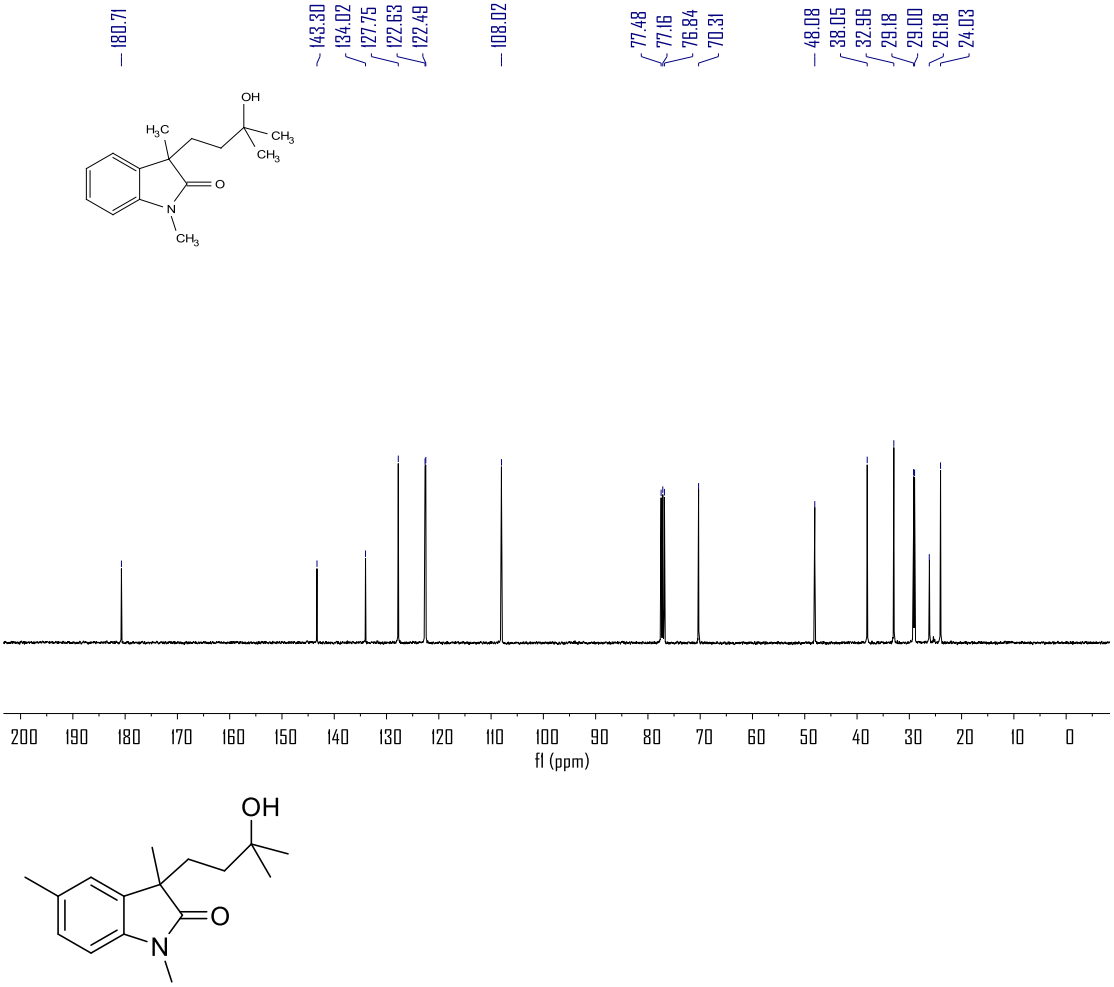


3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4a**, pale-yellow liquid, 47 mg, 95%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 (tdd, *J* = 7.7, 2.9, 1.4 Hz, 1H), 7.22 – 7.15 (m, 1H), 7.07 (td, *J* = 7.5, 2.5 Hz, 1H), 6.85 (dd, *J* = 7.8, 2.6 Hz, 1H), 3.21 (d, *J* = 2.7 Hz, 3H), 2.00 (tdd, *J* = 13.0, 4.7, 2.6 Hz, 1H), 1.85 (tt, *J* = 13.0, 3.4 Hz, 1H), 1.68 (s, 1H), 1.37 (d, *J* = 2.6 Hz, 3H), 1.23 – 1.07 (m, 7H), 0.98 (tt, *J* = 13.0, 3.4 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.71, 143.30, 134.02, 127.75, 122.63, 122.49, 108.02, 70.31, 48.08, 38.05, 32.96, 29.18, 29.00, 26.18, 24.03.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}NNaO_2$: 270.1465; found: 270.1471.

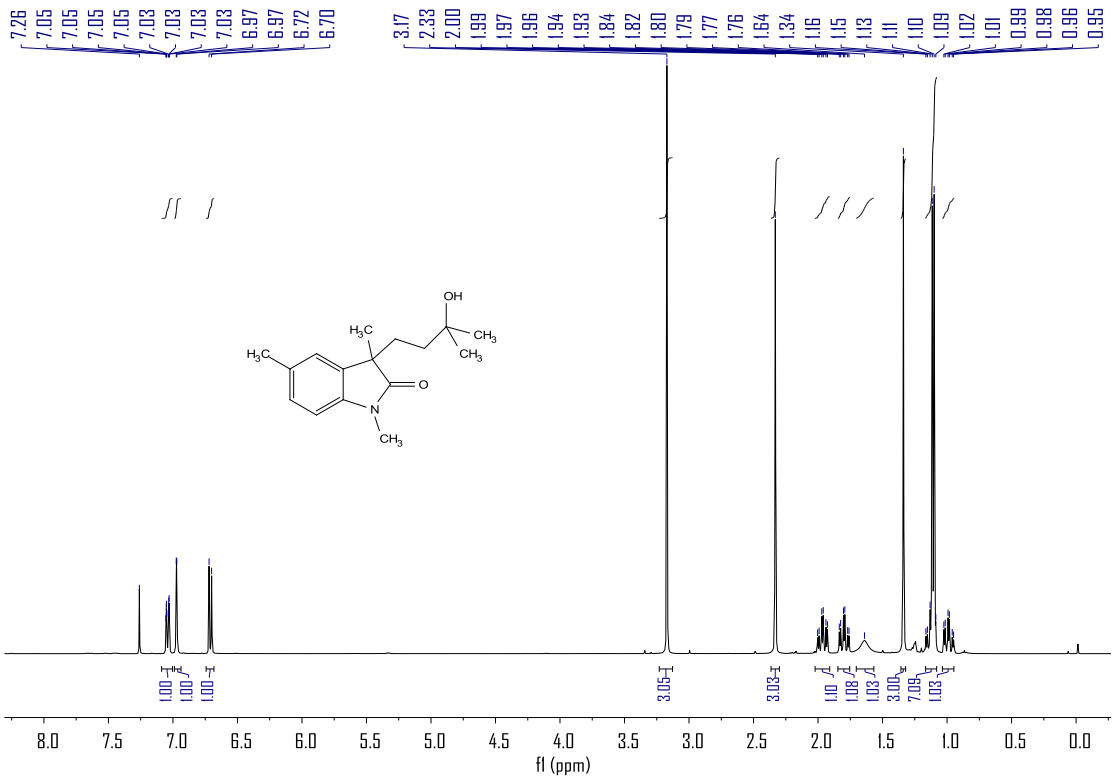


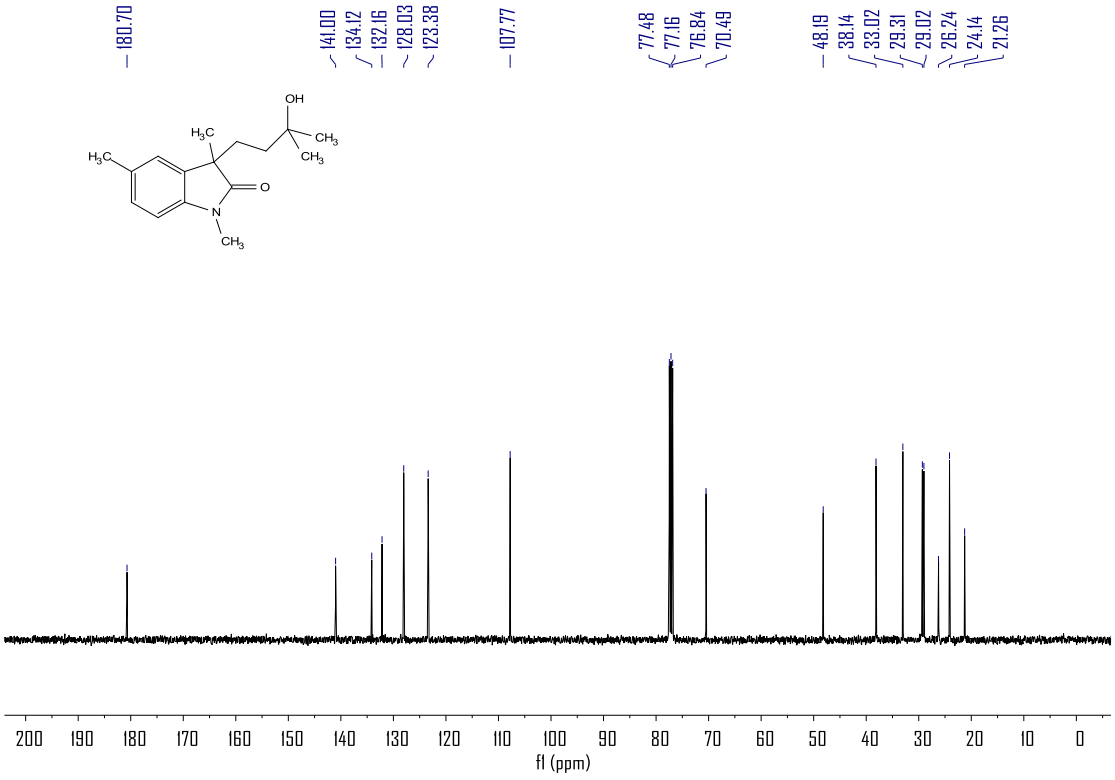


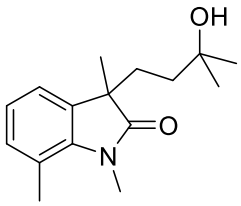
3-(3-hydroxy-3-methylbutyl)-1,3,5-trimethylindolin-2-one

Following the general procedure (**4b**, pale-yellow liquid, 47 mg, 90%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.12 – 7.01 (m, 1H), 6.97 (d, *J* = 1.6 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 3.17 (s, 3H), 2.33 (s, 3H), 1.97 (td, *J* = 12.9, 4.6 Hz, 1H), 1.80 (td, *J* = 13.0, 4.2 Hz, 1H), 1.64 (s, 1H), 1.34 (s, 3H), 1.11 (d, *J* = 5.9 Hz, 7H), 0.99 (td, *J* = 13.0, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.70, 141.00, 134.12, 132.16, 128.03, 123.38, 107.77, 70.49, 48.19, 38.14, 33.02, 29.31, 29.02, 26.24, 24.14, 21.26.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}NNaO_2$: 284.1621; found: 284.1626.


7.26
7.05
7.05
7.05
7.05
7.03
7.03
7.03
7.03
6.97
6.97
6.72
6.70
3.17
2.33
2.00
1.99
1.97
1.96
1.94
1.93
1.84
1.82
1.80
1.79
1.77
1.76
1.64
1.34
1.16
1.15
1.13
1.11
1.10
1.09
1.02
1.01
0.99
0.98
0.96
0.95
OH
H3C
CH3
H3C
CH3
O
N
CH3
1.00
1.00
1.00
3.05
3.03
1.10
1.08
1.03
3.00
7.09
1.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

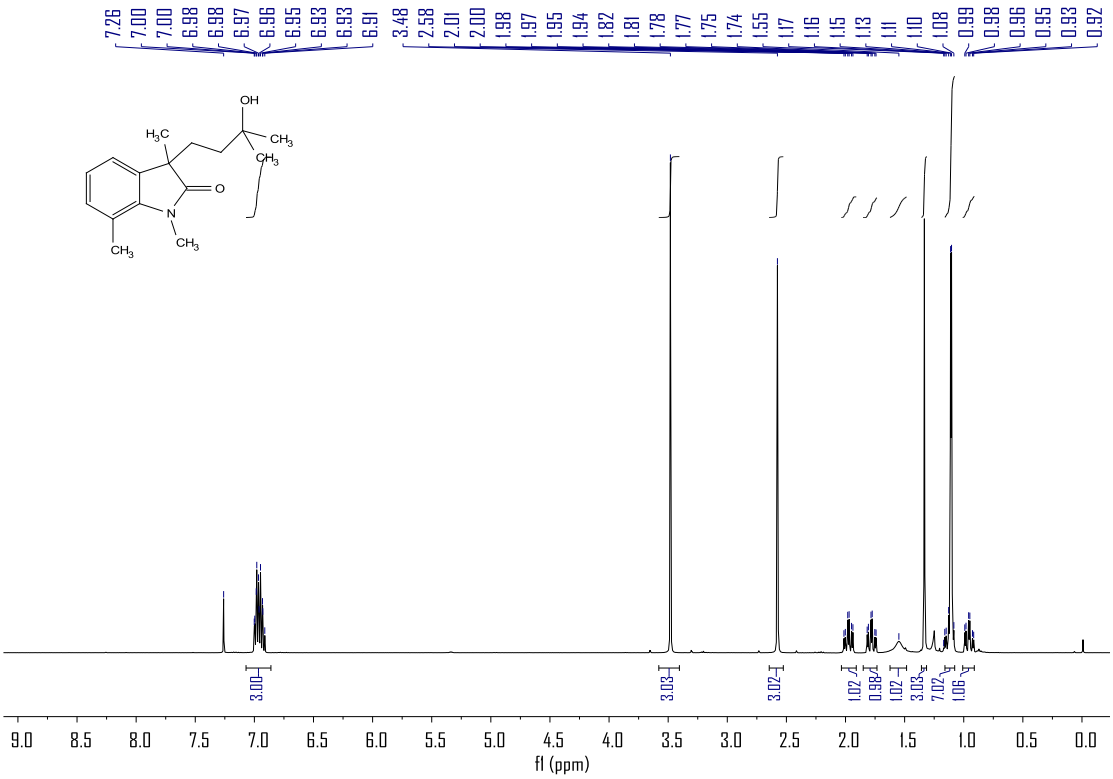

180.70
141.00
134.12
132.16
128.03
123.38
107.77
77.48
77.16
76.84
70.49
48.19
38.14
33.02
29.31
29.02
26.24
24.14
21.26
OH
H3C
CH3
H3C
CH3
O
N
CH3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

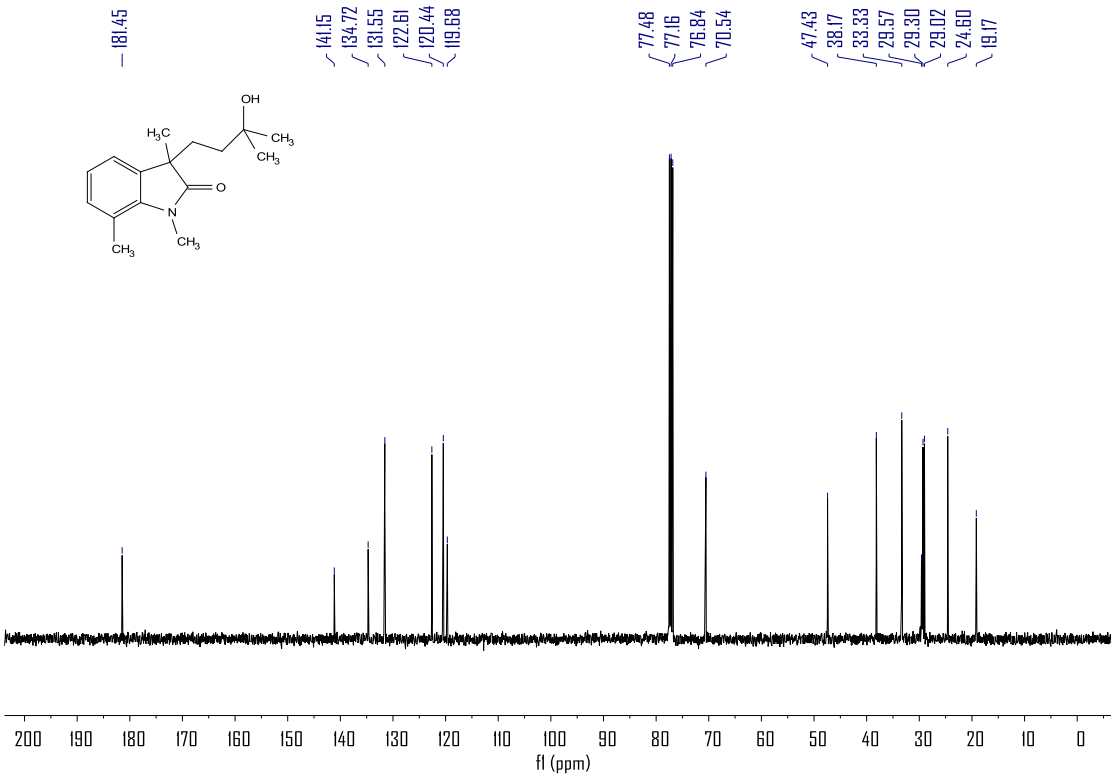


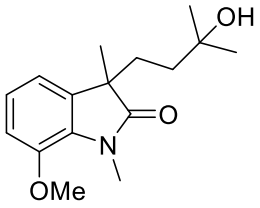
3-(3-hydroxy-3-methylbutyl)-1,3,7-trimethylindolin-2-one

Following the general procedure (**4c**, pale-yellow liquid, 35 mg, 67%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.06 – 6.85 (m, 3H), 3.48 (s, 3H), 2.58 (s, 3H), 1.98 (td, *J* = 12.9, 4.6 Hz, 1H), 1.78 (td, *J* = 13.0, 4.1 Hz, 1H), 1.55 (s, 1H), 1.33 (s, 3H), 1.11 (d, *J* = 3.1 Hz, 7H), 0.95 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.45, 141.15, 134.72, 131.55, 122.61, 120.44, 119.68, 70.54, 47.43, 38.17, 33.33, 29.57, 29.30, 29.02, 24.60, 19.17.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}NNaO_2$: 284.1621; found: 284.1628.



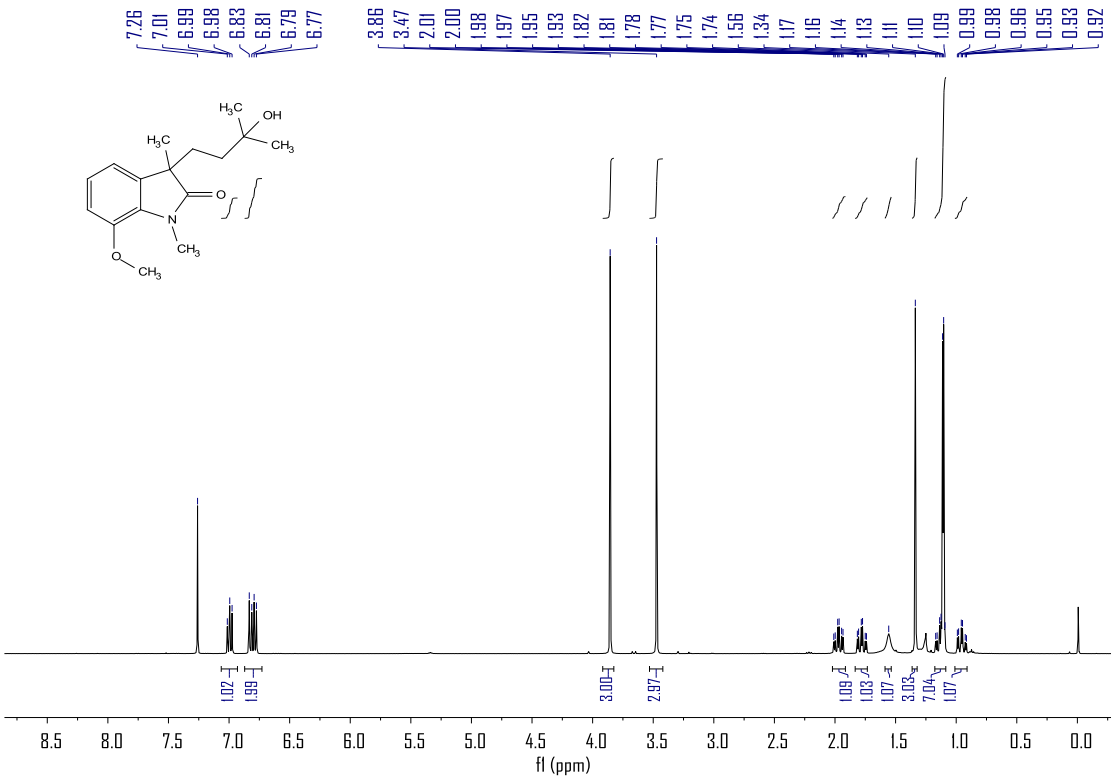


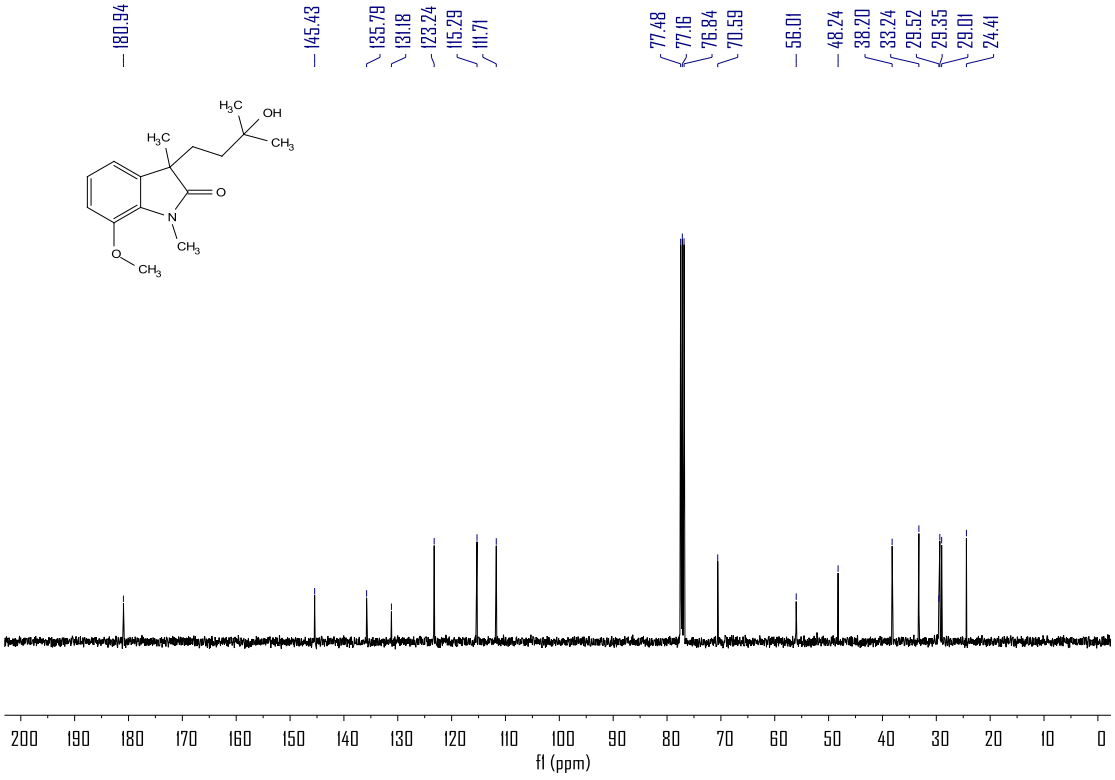


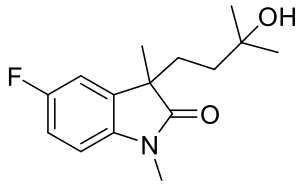
3-(3-hydroxy-3-methylbutyl)-7-methoxy-1,3-dimethylindolin-2-one

Following the general procedure (**4d**, pale-yellow liquid, 39 mg, 70%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.10 – 6.92 (m, 1H), 6.81 (dd, *J* = 15.7, 7.9 Hz, 2H), 3.87 (s, 3H), 3.48 (s, 3H), 1.98 (td, *J* = 12.9, 4.6 Hz, 1H), 1.79 (td, *J* = 13.0, 4.1 Hz, 1H), 1.57 (s, 1H), 1.35 (s, 3H), 1.19 – 1.09 (m, 7H), 0.96 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.94, 145.43, 135.79, 131.18, 123.24, 115.29, 111.71, 70.59, 56.01, 48.24, 38.20, 33.24, 29.52, 29.35, 29.01, 24.41.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}NNaO_3$: 300.1570; found: 300.1577.


7.26
7.01
6.99
6.98
6.83
6.81
6.79
6.77
3.86
3.47
2.01
2.00
1.98
1.97
1.95
1.93
1.82
1.81
1.78
1.77
1.75
1.74
1.56
1.34
1.17
1.16
1.14
1.13
1.11
1.10
1.09
0.99
0.98
0.96
0.95
0.93
0.92
H3C
OH
CH3
H3C
O
N
CH3
O
CH3
1.02
1.99
3.00
2.97
1.09
1.03
1.07
3.03
7.04
1.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

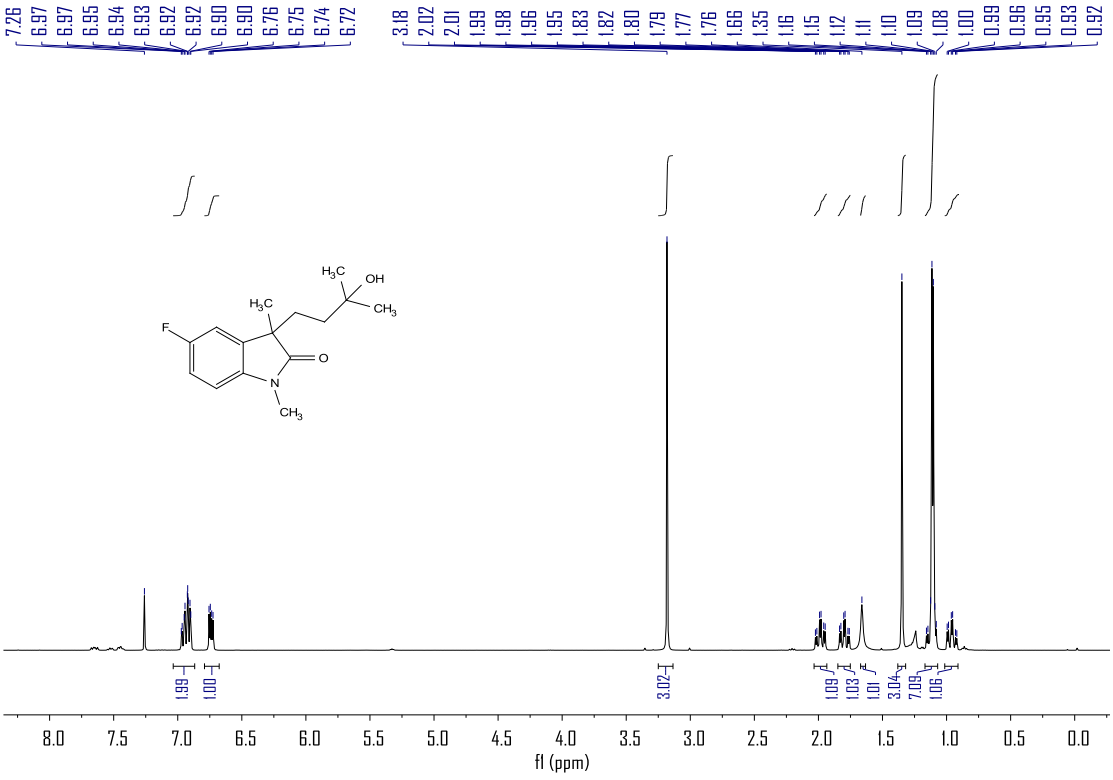

180.94
145.43
135.79
131.18
123.24
115.29
111.71
77.48
77.16
76.84
70.59
56.01
48.24
38.20
33.24
29.52
29.35
29.01
24.41
H3C
OH
CH3
H3C
O
N
CH3
O
CH3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

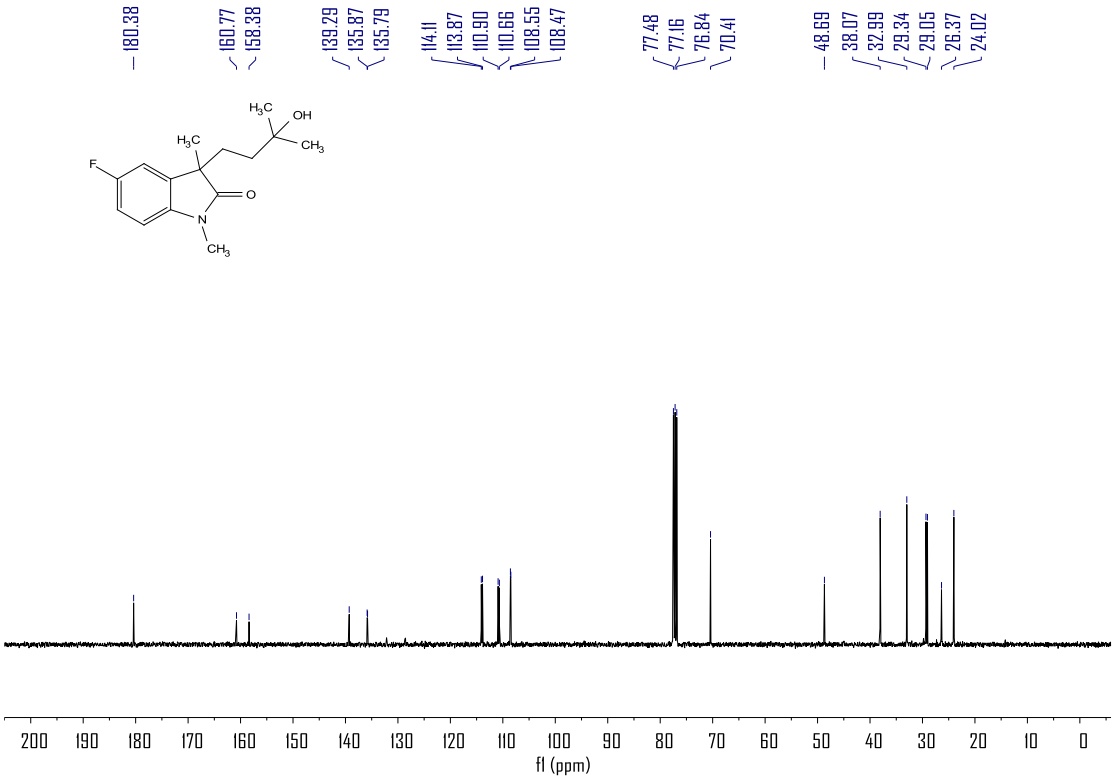


5-fluoro-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4e**, pale-yellow liquid, 44 mg, 84%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.00 – 6.86 (m, 2H), 6.74 (dd, *J* = 8.4, 4.1 Hz, 1H), 3.18 (s, 3H), 1.99 (td, *J* = 13.0, 4.5 Hz, 1H), 1.80 (td, *J* = 13.0, 4.1 Hz, 1H), 1.66 (s, 1H), 1.35 (s, 3H), 1.11 (d, *J* = 4.4 Hz, 7H), 0.96 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.38, 159.58 (d, *J* = 240.6 Hz), 139.29, 135.83 (d, *J* = 7.7 Hz), 113.99 (d, *J* = 23.6 Hz), 110.78 (d, *J* = 24.5 Hz), 108.51 (d, *J* = 8.1 Hz), 70.41, 48.69, 38.07, 32.99, 29.34, 29.05, 26.37, 24.02. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -120.69.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}FNNaO_2$: 288.1370; found: 288.1378.




180.38
160.77
158.38
139.29
135.87
135.79
114.11
113.87
110.90
110.66
108.55
108.47
77.48
77.16
76.84
70.41
48.69
38.07
32.99
29.34
29.05
26.37
24.02
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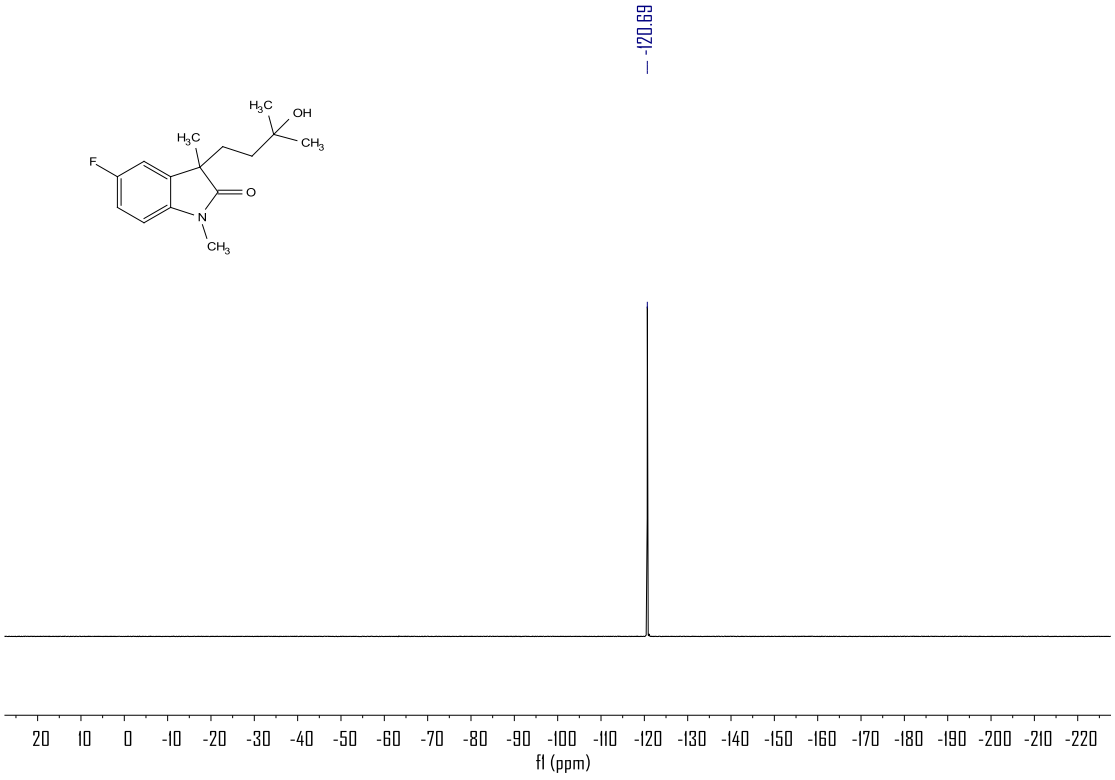
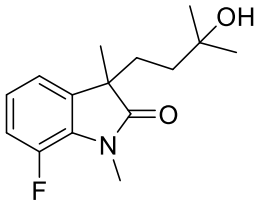
CH3
F
O
N
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

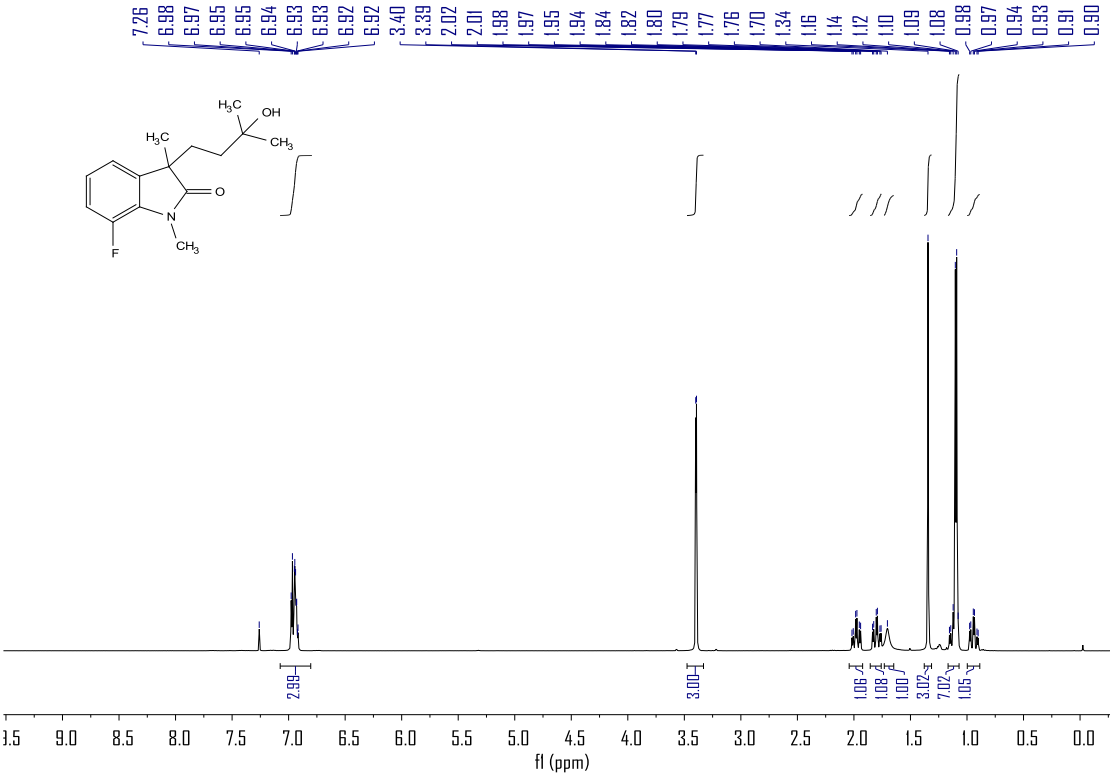

-120.69
H3C
OH
H3C
CH3
F
O
N
CH3
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

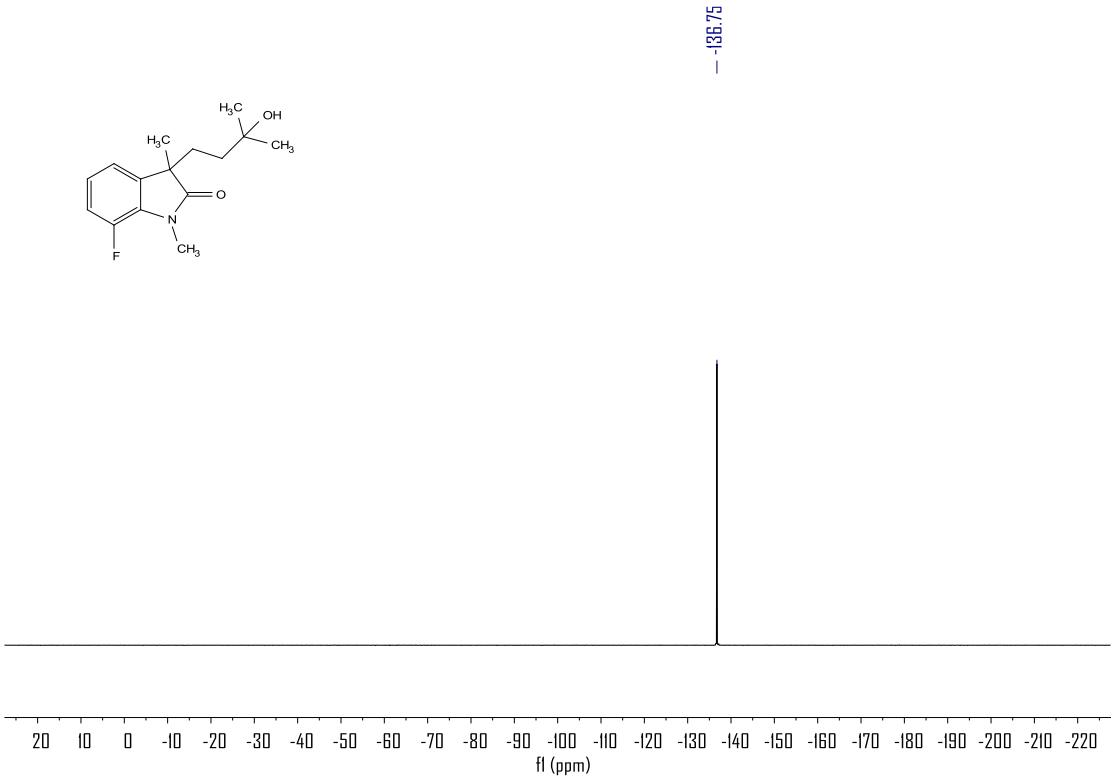


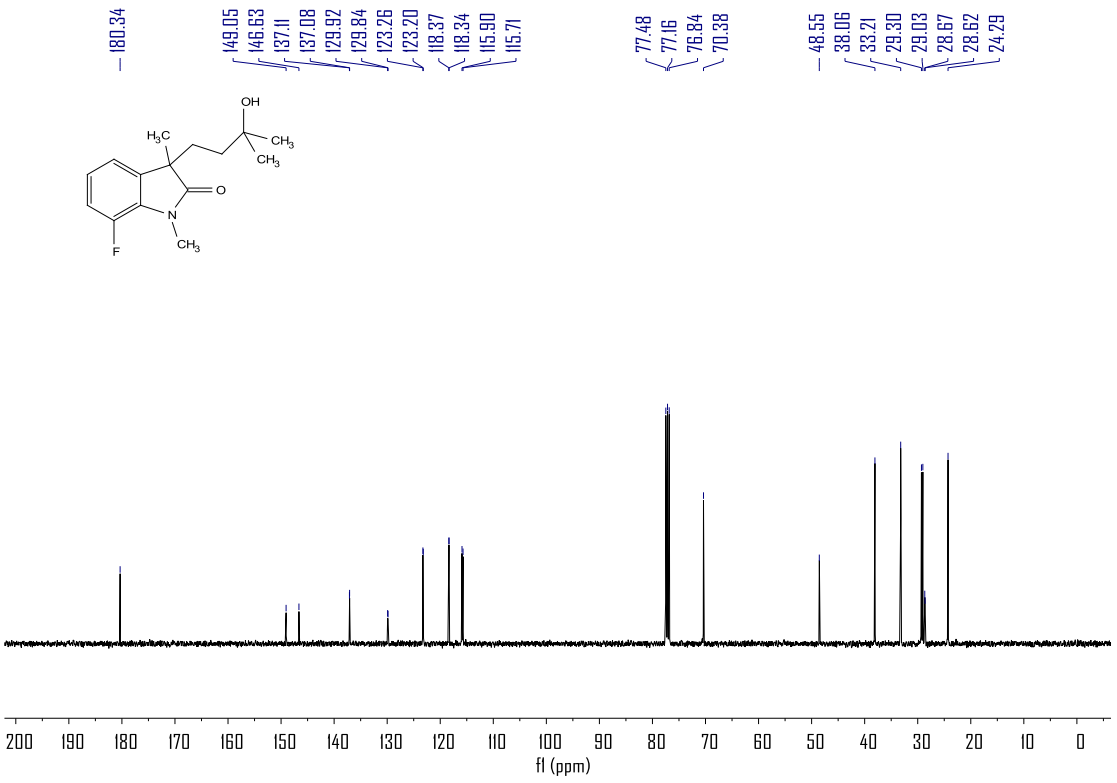
7-fluoro-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4f**, pale-yellow liquid, 39 mg, 73%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.01 – 6.85 (m, 3H), 3.40 (d, *J* = 2.6 Hz, 3H), 1.98 (td, *J* = 13.0, 4.5 Hz, 1H), 1.80 (td, *J* = 13.0, 4.1 Hz, 1H), 1.70 (s, 1H), 1.34 (s, 3H), 1.10 (d, *J* = 4.7 Hz, 7H), 0.94 (td, *J* = 13.0, 4.1 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -136.75. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.34, 147.84 (d, *J* = 243.5 Hz), 137.10 (d, *J* = 2.9 Hz), 129.88 (d, *J* = 7.9 Hz), 123.23 (d, *J* = 6.3 Hz), 118.36 (d, *J* = 3.2 Hz), 115.80 (d, *J* = 19.2 Hz), 70.38, 48.55, 38.06, 33.21, 29.30, 29.03, 28.67, 24.29.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}FNNaO_2$: 288.1370; found: 288.1366.




-136.75
f1 (ppm)


180.34
149.05
146.63
137.11
137.08
129.92
129.84
123.26
123.20
118.37
118.34
115.90
115.71
77.48
77.16
76.84
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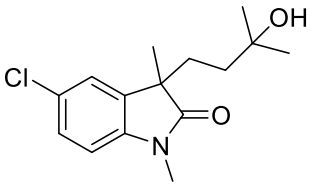
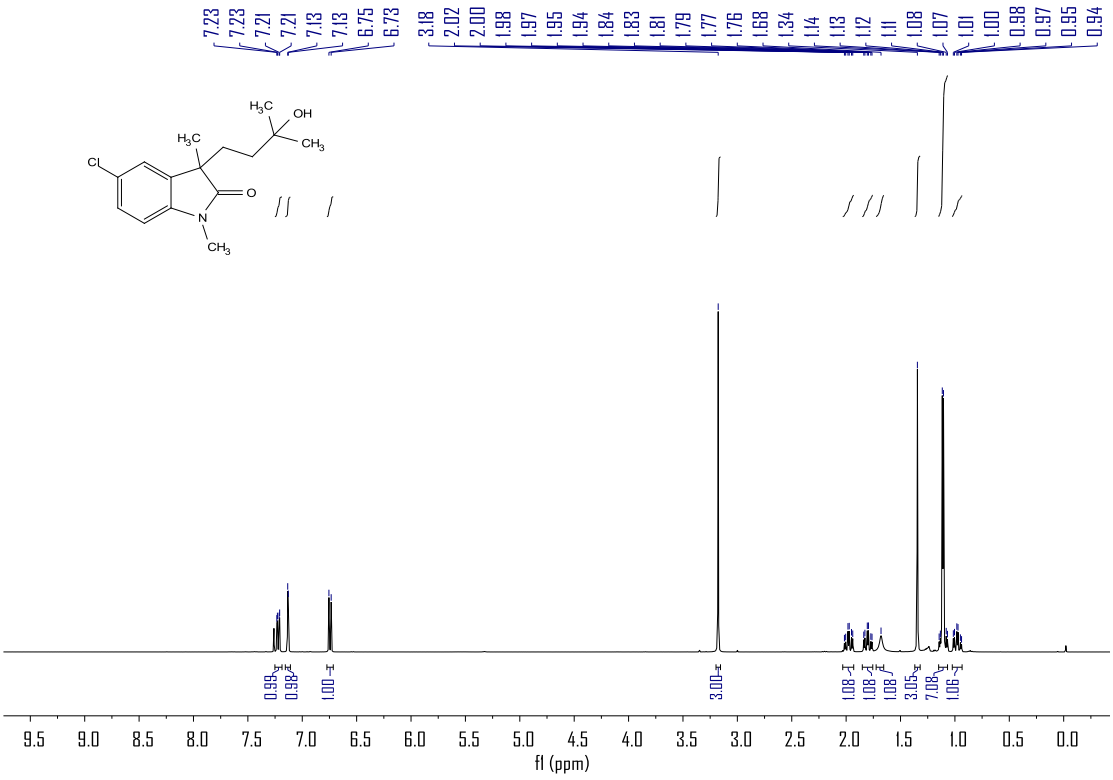
48.55
38.06
33.21
29.30
29.03
28.67
28.62
24.29
f1 (ppm)

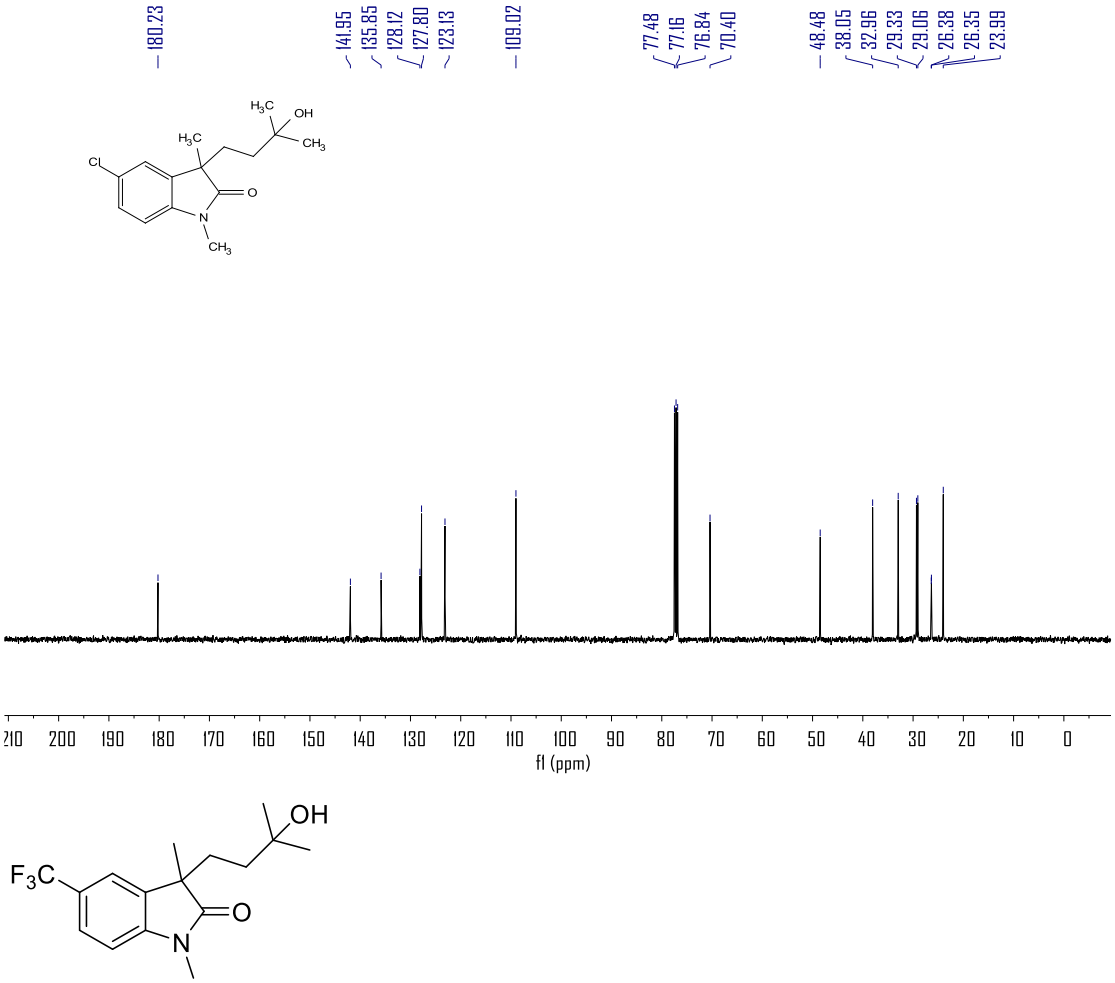


5-chloro-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4g**, pale-yellow liquid, 51 mg, 91%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.37 – 7.32 (m, 1H), 7.26 (s, 1H), 6.88 (dt, *J* = 8.3, 1.3 Hz, 1H), 3.33 – 3.28 (m, 3H), 2.16 – 2.07 (m, 1H), 1.98 – 1.87 (m, 2H), 1.51 – 1.44 (m, 3H), 1.28 – 1.17 (m, 7H), 1.14 – 1.04 (m, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.23, 141.95, 135.85, 128.12, 127.80, 123.13, 109.02, 70.40, 48.48, 38.05, 32.96, 29.33, 29.06, 26.38, 26.35, 23.99.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClNNaO_2$: 304.1075; found: 304.1079.

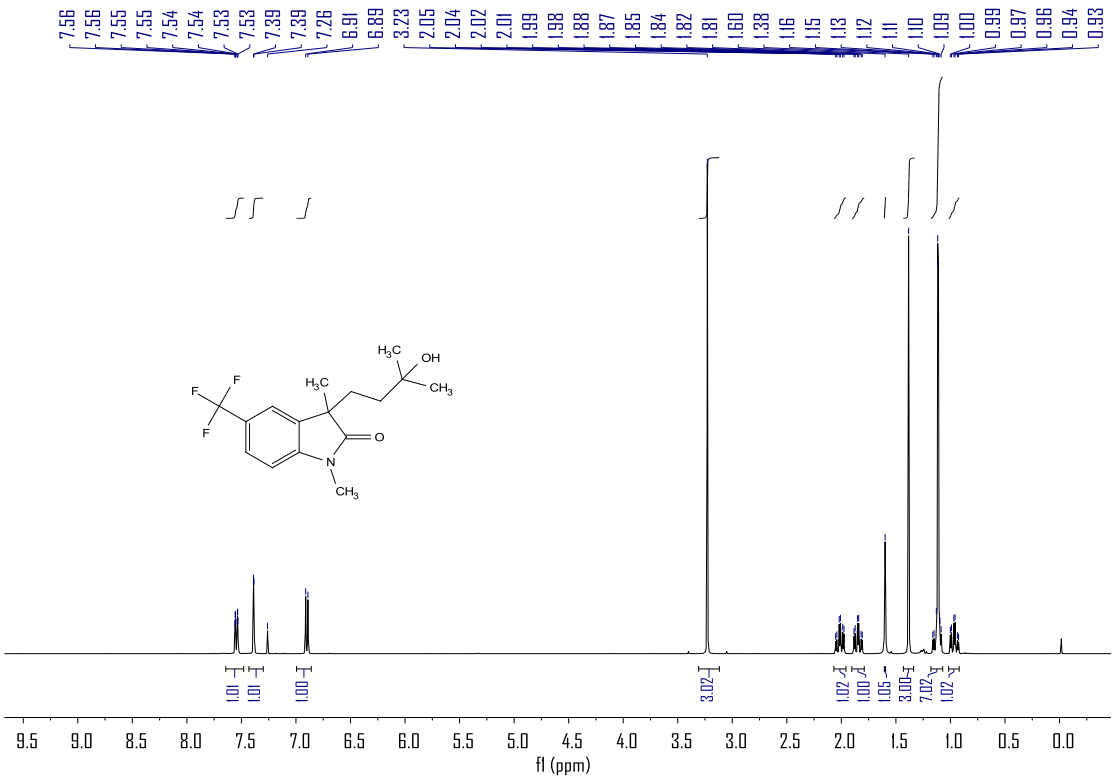


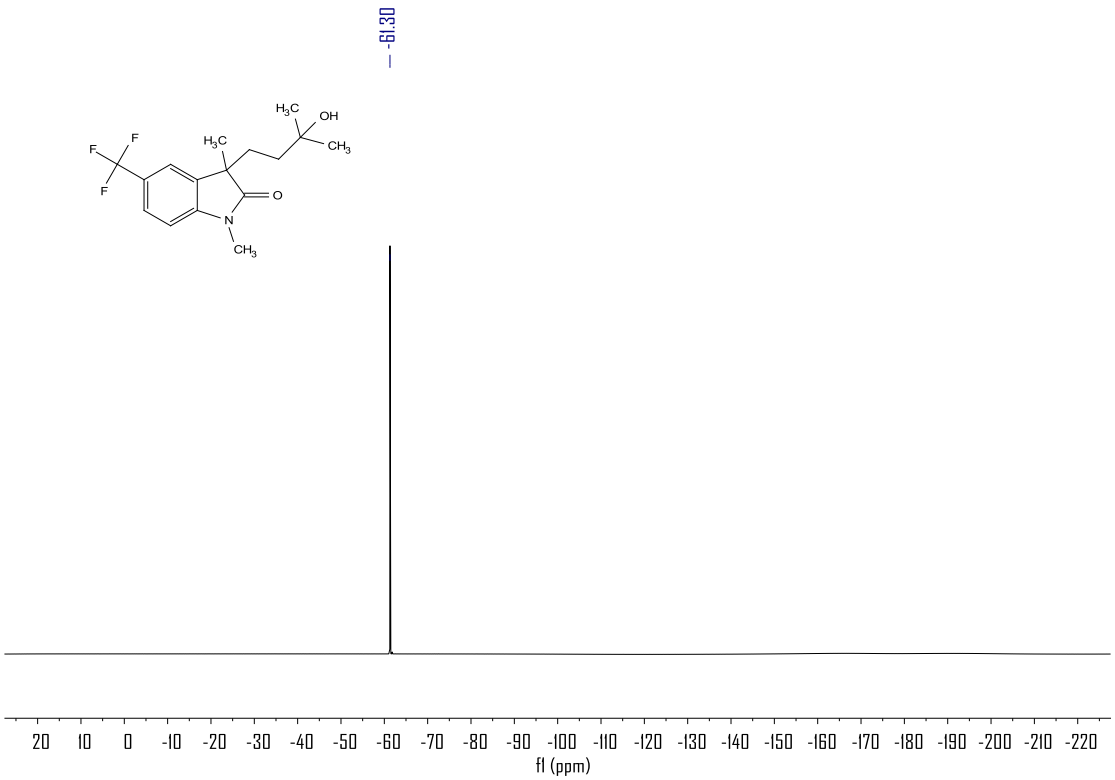


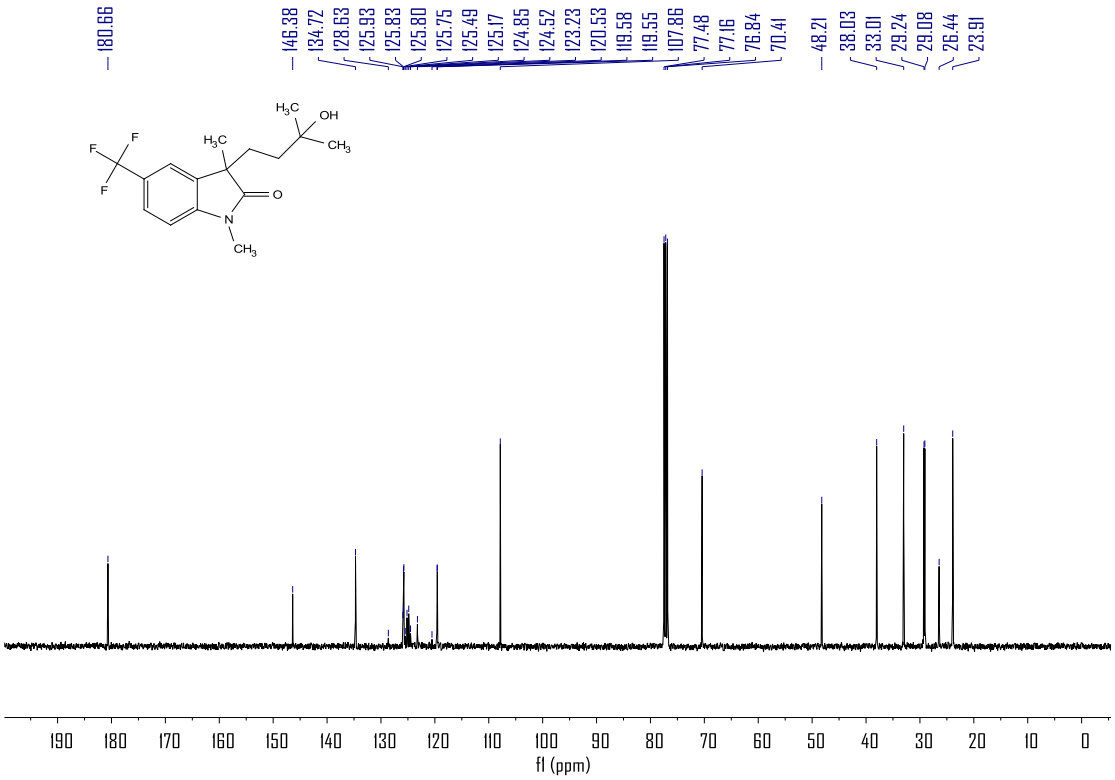
3-(3-hydroxy-3-methylbutyl)-1,3-dimethyl-5-(trifluoromethyl)indolin-2-one

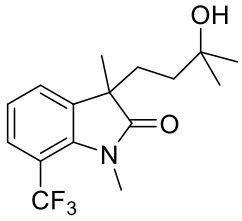
Following the general procedure (**4h**, pale-yellow liquid, 43 mg, 69%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.68 – 7.45 (m, 1H), 7.39 (d, *J* = 1.7 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 3.23 (s, 3H), 2.01 (td, *J* = 13.0, 4.5 Hz, 1H), 1.85 (td, *J* = 13.1, 4.2 Hz, 1H), 1.60 (s, 1H), 1.38 (s, 3H), 1.11 (d, *J* = 2.8 Hz, 7H), 0.96 (td, *J* = 13.0, 4.2 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -61.30. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.66, 146.38, 134.72, 125.79 (q, *J* = 3.9 Hz), 125.01 (q, *J* = 32.6 Hz), 124.58 (q, *J* = 271.3 Hz), 119.57 (q, *J* = 3.0 Hz), 107.86, 70.41, 48.21, 38.03, 33.01, 29.24, 29.08, 26.44, 23.91.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}F_3NNaO_2$: 338.1338; found: 338.1340.


7.56 7.56 7.55 7.55 7.54 7.54 7.53 7.53 7.39 7.39 7.26 6.91 6.89
3.23 2.05 2.04 2.02 2.01 1.99 1.98 1.88 1.87 1.85 1.84 1.82 1.81 1.60 1.38 1.16 1.15 1.13 1.12 1.11 1.10 1.09 1.00 0.99 0.97 0.96 0.94 0.93
1.01 1.01 1.00 3.02 1.02 1.00 1.05 3.00 7.02 1.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-61.30
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

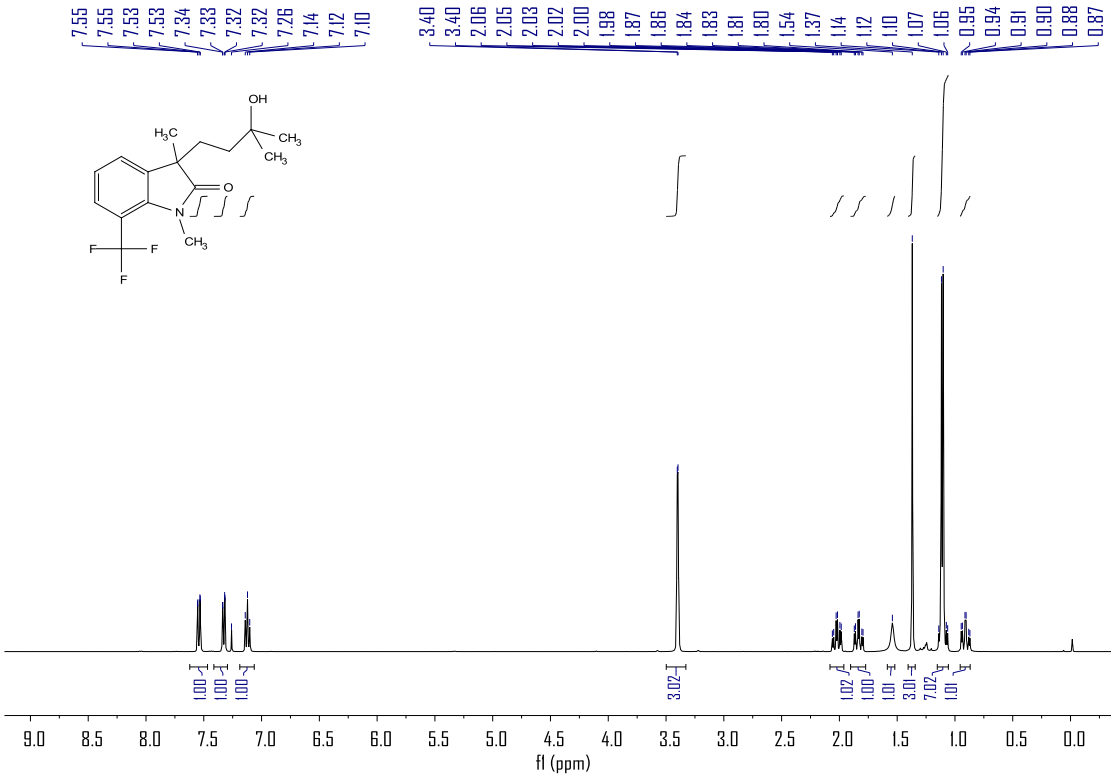


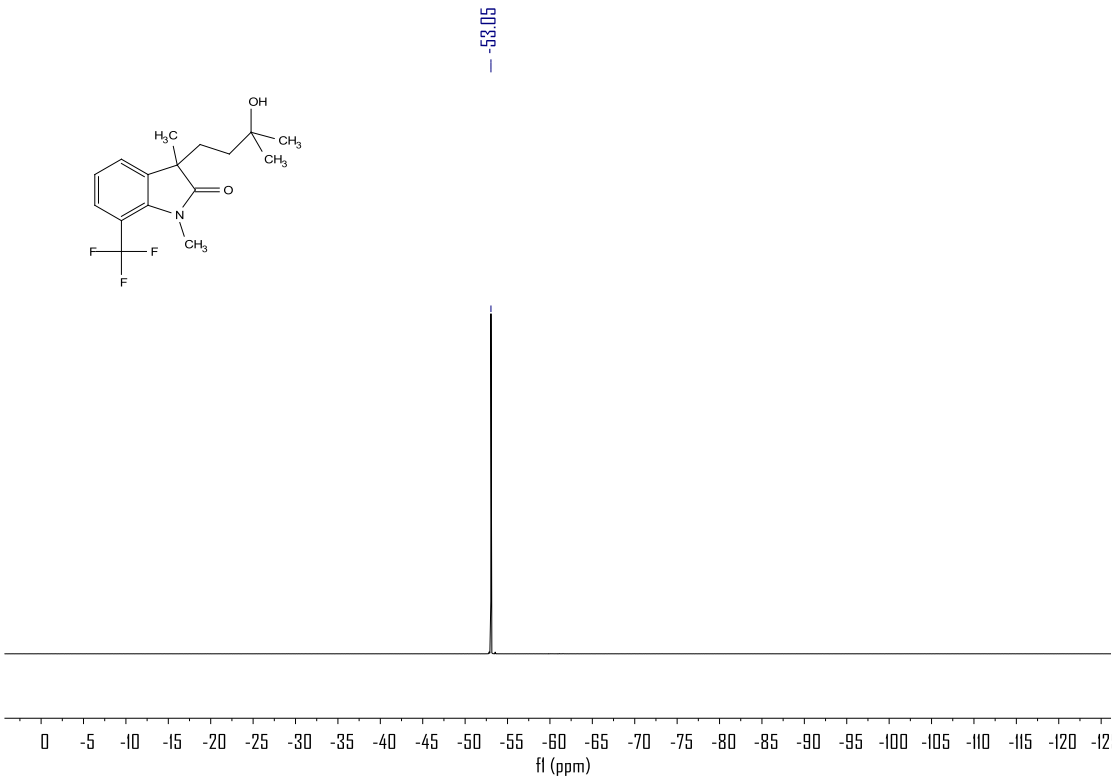


3-(3-hydroxy-3-methylbutyl)-1,3-dimethyl-7-(trifluoromethyl)indolin-2-one

Following the general procedure (**4i**, pale-yellow liquid, 44 mg, 70%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.54 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.33 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 3.40 (d, *J* = 2.5 Hz, 3H), 2.02 (td, *J* = 13.0, 4.6 Hz, 1H), 1.83 (td, *J* = 13.0, 4.0 Hz, 1H), 1.54 (s, 1H), 1.37 (s, 3H), 1.11 (d, *J* = 5.9 Hz, 7H), 0.91 (td, *J* = 13.0, 4.0 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -53.05. **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.43, 141.25, 136.67, 125.92, 125.84 (q, *J* = 6.1 Hz), 123.79 (q, *J* = 271.4 Hz), 122.03, 112.54 (q, *J* = 32.7 Hz), 70.41, 46.56, 37.89, 33.31, 29.42, 29.01, 28.81, 24.47.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}F_3NNaO_2$: 338.1338; found: 338.1346.


7.55
7.55
7.53
7.53
7.34
7.33
7.32
7.32
7.26
7.14
7.12
7.10
3.40
3.40
2.06
2.05
2.03
2.02
2.00
1.98
1.87
1.86
1.84
1.83
1.81
1.80
1.54
1.37
1.14
1.12
1.10
1.07
1.06
0.95
0.94
0.91
0.90
0.88
0.87
OH
H3C
CH3
CH3
O
N
CH3
F
F
F
1.00
1.00
1.00
3.02
1.02
1.00
1.01
3.01
7.02
1.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-53.05
OH
H3C
CH3
CH3
O
N
CH3
F
F
F
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
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-90
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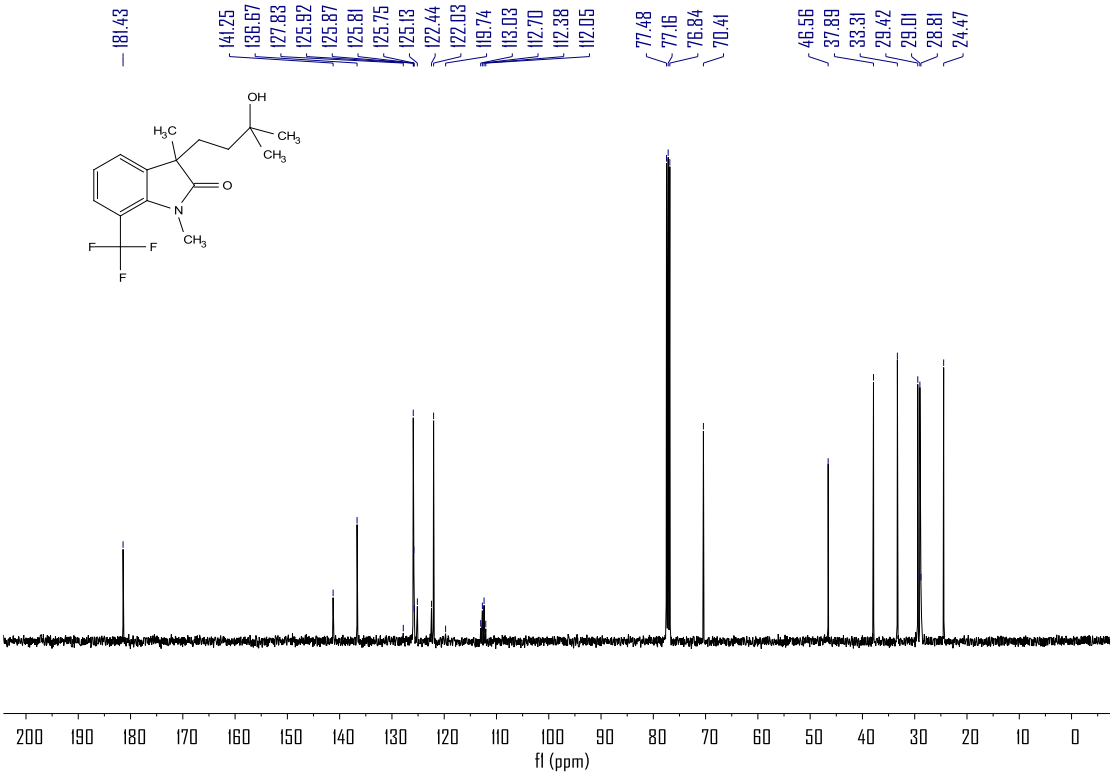
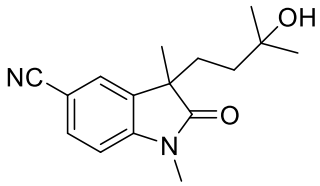
-105
-110
-115
-120
-12
f1 (ppm)

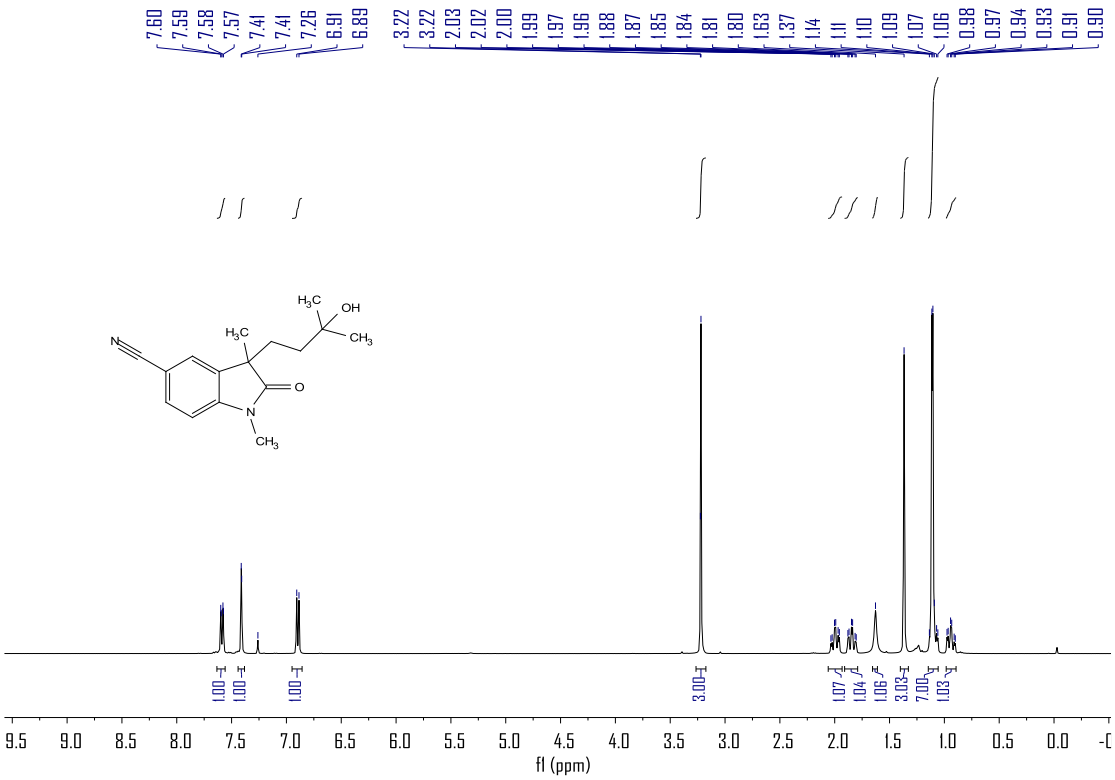


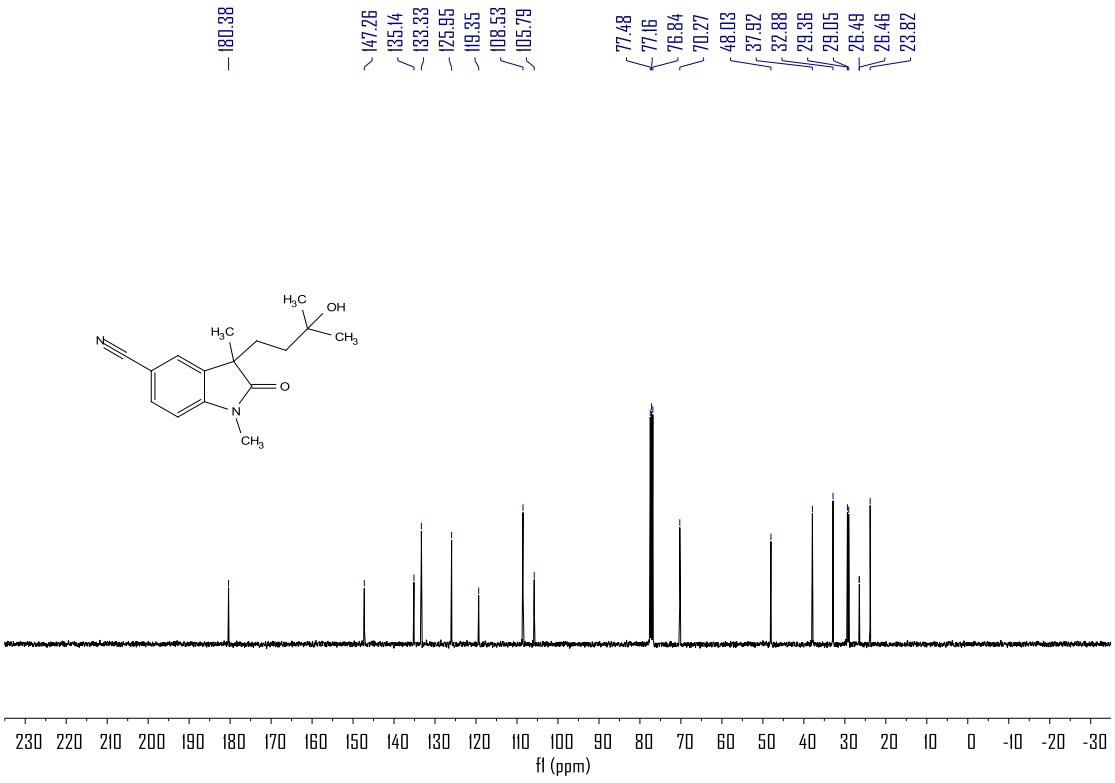


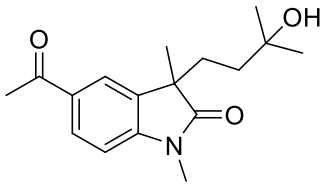
3-(3-hydroxy-3-methylbutyl)-1,3-dimethyl-2-oxoindoline-5-carbonitrile

Following the general procedure (**4j**, pale-yellow liquid, 22 mg, 40%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.59 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.41 (d, *J* = 1.7 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 3.22 (s, 3H), 2.00 (td, *J* = 13.1, 4.5 Hz, 1H), 1.84 (td, *J* = 13.1, 4.1 Hz, 1H), 1.63 (s, 1H), 1.37 (s, 3H), 1.11 (d, *J* = 3.7 Hz, 7H), 0.94 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.38, 147.26, 135.14, 133.33, 125.95, 119.35, 108.53, 105.79, 70.27, 48.03, 37.92, 32.88, 29.36, 29.05, 26.49, 26.46, 23.82.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}N_2NaO_2$: 295.1417; found: 295.1422.


7.60 7.59 7.58 7.57 7.41 7.41 7.26 6.91 6.89
3.22 3.22 2.03 2.02 2.00 1.99 1.97 1.96 1.88 1.87 1.85 1.84 1.81 1.80 1.63 1.37 1.14 1.11 1.10 1.09 1.07 1.06 0.98 0.97 0.94 0.93 0.91 0.90
1.00 1.00 1.00 3.00 1.07 1.04 1.06 3.03 7.00 1.03
fl (ppm)

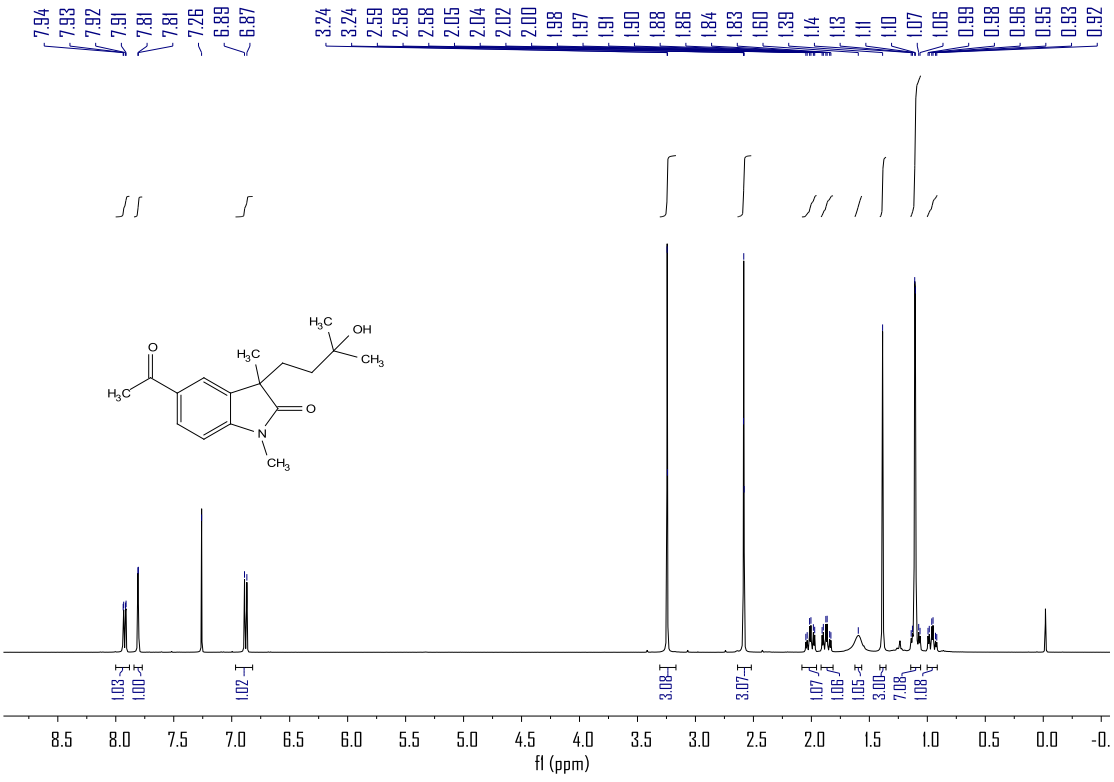

180.38
147.26 135.14 133.33 125.95 119.35 108.53 105.79
77.48 77.16 76.84 70.27 48.03 37.92 32.88 29.36 29.05 28.49 28.46 23.82
fl (ppm)

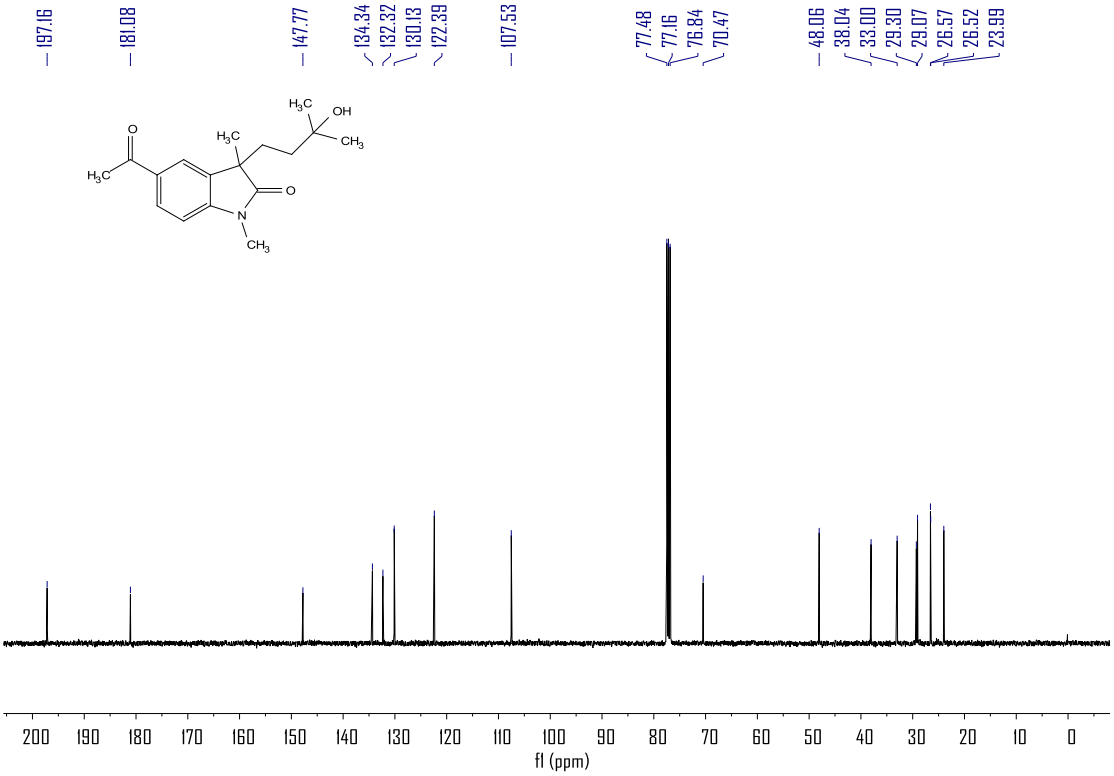


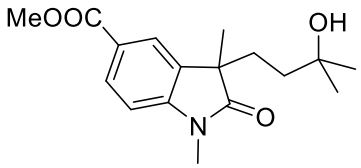
5-acetyl-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4k**, pale-yellow liquid, 33 mg, 58%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.92 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.81 (d, *J* = 1.6 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 3.24 (d, *J* = 1.2 Hz, 3H), 2.58 (d, *J* = 0.9 Hz, 3H), 2.01 (td, *J* = 13.0, 4.5 Hz, 1H), 1.87 (td, *J* = 13.0, 4.3 Hz, 1H), 1.60 (s, 1H), 1.39 (s, 3H), 1.15 – 1.05 (m, 7H), 0.96 (td, *J* = 12.9, 4.3 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 197.16, 181.08, 147.77, 134.34, 132.32, 130.13, 122.39, 107.53, 70.47, 48.06, 38.04, 33.00, 29.30, 29.07, 26.57, 26.52, 23.99.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_3$: 312.1570; found: 312.1576.



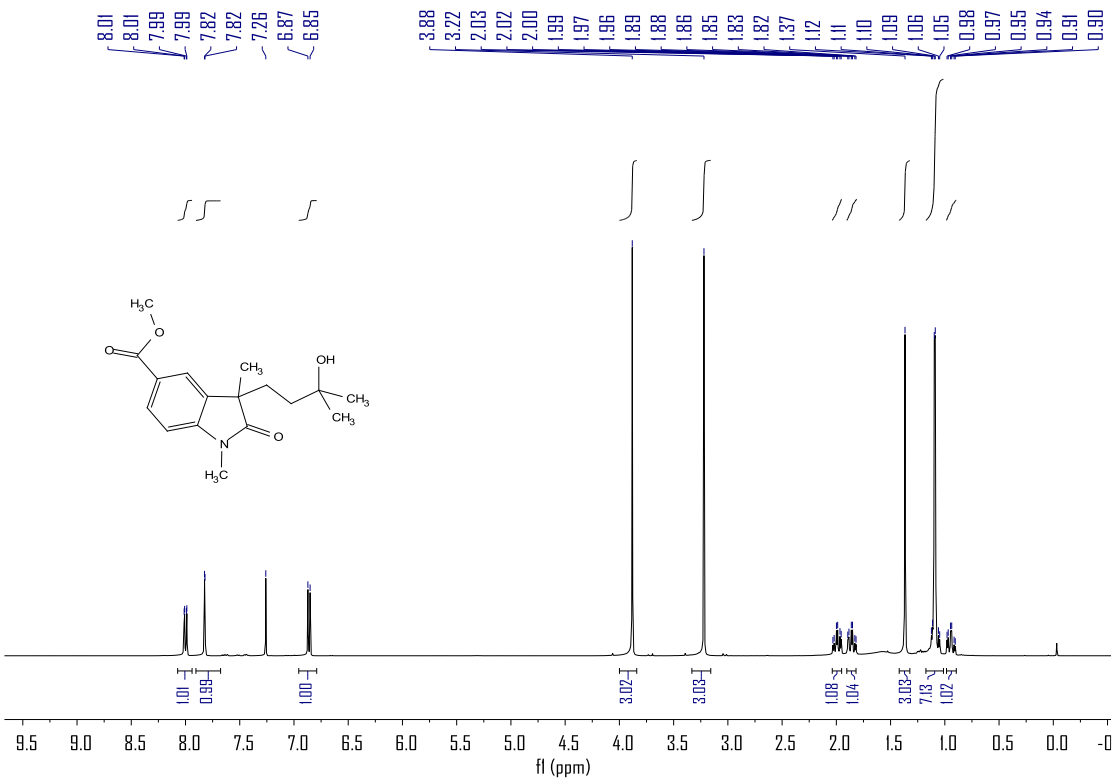


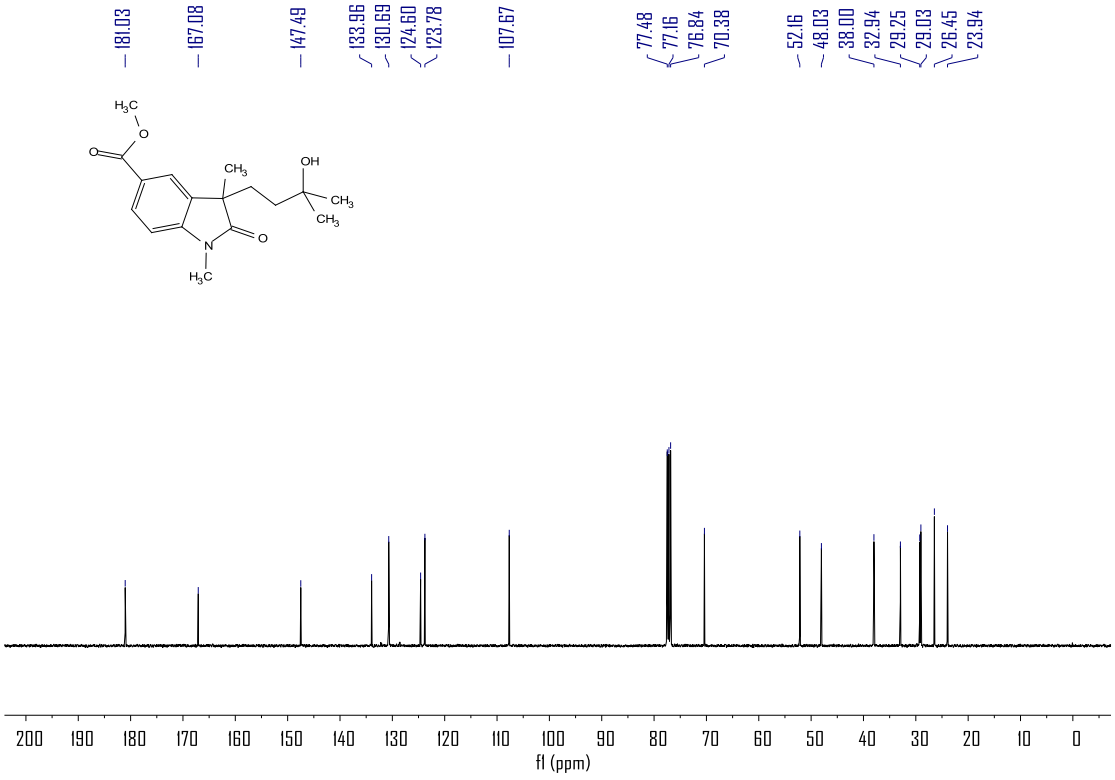


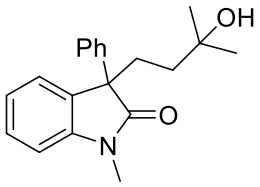
Methyl-3-(3-hydroxy-3-methylbutyl)-1,3-dimethyl-2-oxoindoline-5-carboxylate

Following the general procedure (**4l**, pale-yellow liquid, 37 mg, 61%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.82 (d, *J* = 1.6 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 3.88 (s, 3H), 3.22 (s, 3H), 1.99 (td, *J* = 13.0, 4.5 Hz, 1H), 1.86 (td, *J* = 13.0, 4.3 Hz, 1H), 1.37 (s, 3H), 1.14 – 1.04 (m, 7H), 0.94 (td, *J* = 12.9, 4.3 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.03, 167.08, 147.49, 133.96, 130.69, 124.60, 123.78, 107.67, 70.38, 52.16, 48.03, 38.00, 32.94, 29.25, 29.03, 26.45, 23.94.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_4$: 328.1519; found: 328.1523.


8.01
8.01
7.99
7.99
7.82
7.82
7.26
6.87
6.85
3.88
3.22
2.03
2.02
2.00
1.99
1.97
1.96
1.89
1.88
1.86
1.85
1.83
1.82
1.37
1.12
1.11
1.10
1.09
1.06
1.05
0.98
0.97
0.95
0.94
0.91
0.90
1.01
0.99
1.00
3.02
3.03
1.08
1.04
3.03
7.13
1.02
f1 (ppm)

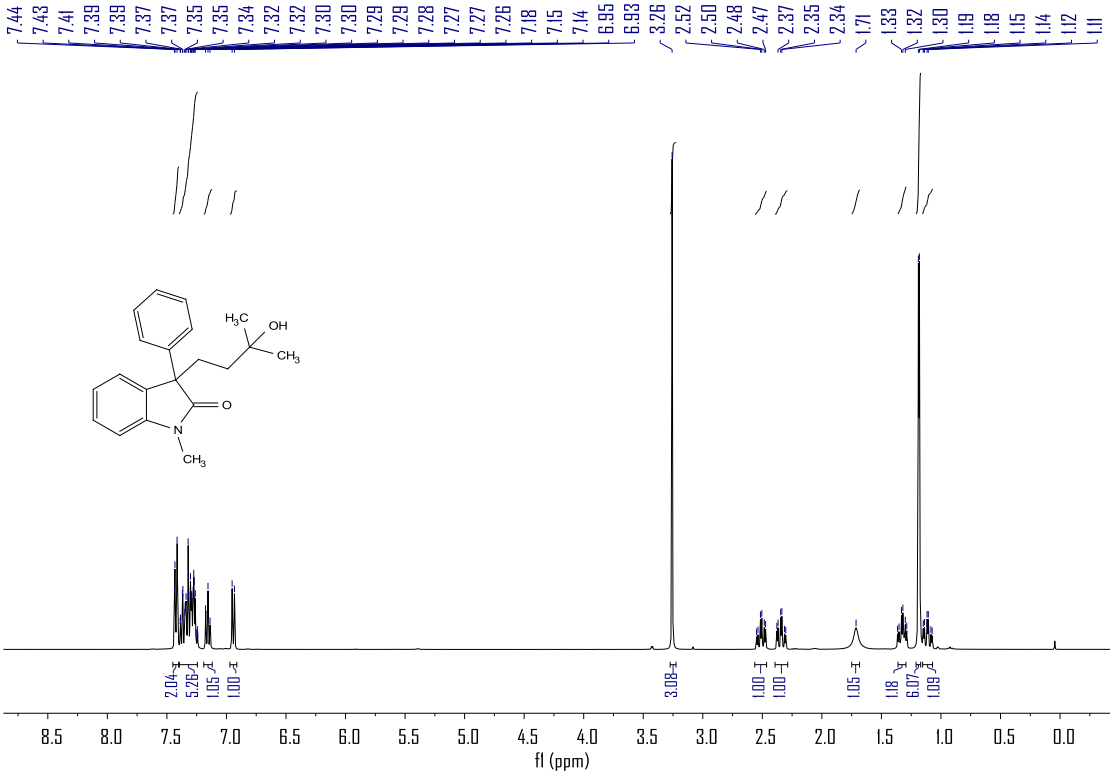

181.03
167.08
147.49
133.96
130.69
124.60
123.78
107.67
77.48
77.16
76.84
70.38
52.16
48.03
38.00
32.94
29.25
29.03
26.45
23.94
f1 (ppm)

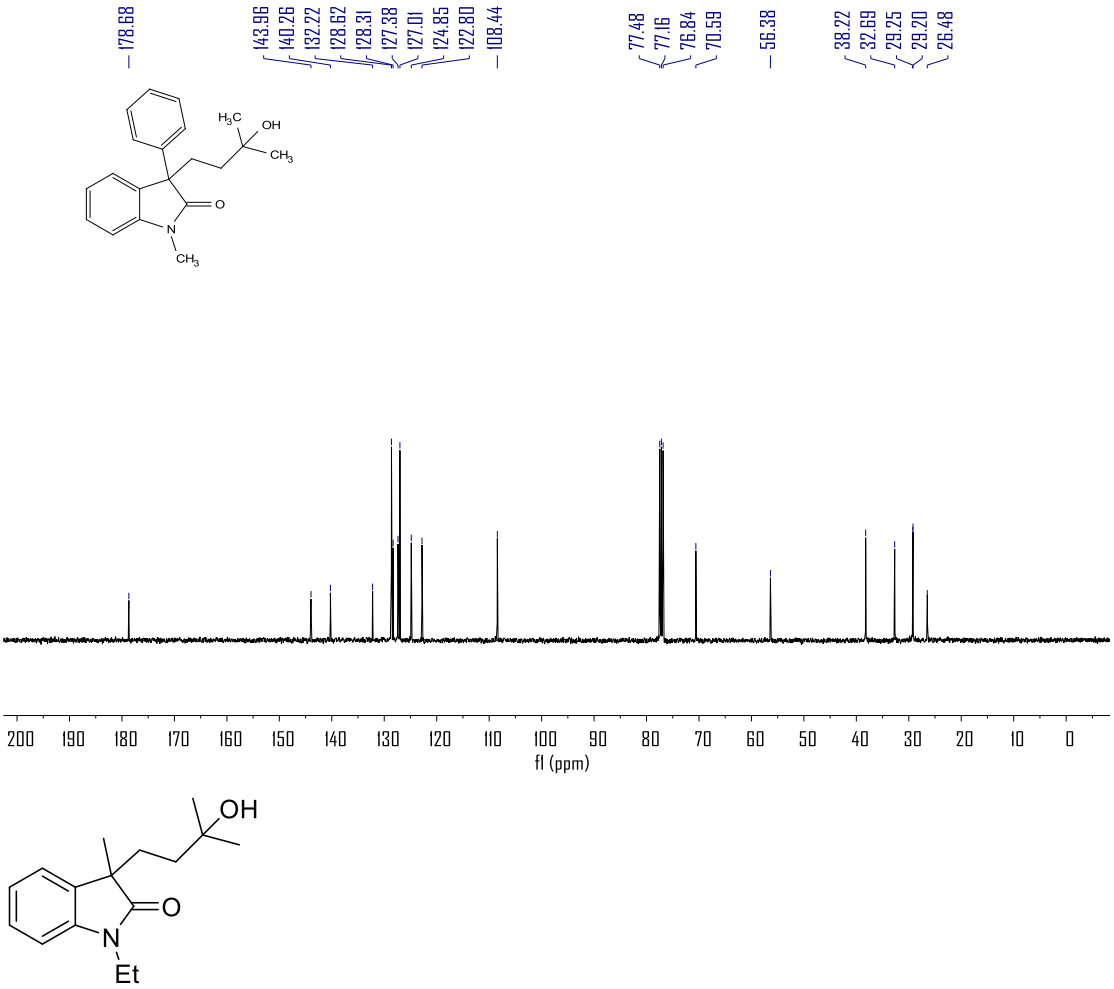


3-(3-hydroxy-3-methylbutyl)-1-methyl-3-phenylindolin-2-one

Following the general procedure (**4m**, pale-yellow liquid, 57 mg, 92%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.46 – 7.40 (m, 2H), 7.39 – 7.24 (m, 5H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 3.26 (s, 3H), 2.51 (td, *J* = 12.8, 4.6 Hz, 1H), 2.34 (td, *J* = 12.9, 3.9 Hz, 1H), 1.71 (s, 1H), 1.33 (td, *J* = 13.0, 4.7 Hz, 1H), 1.19 (d, *J* = 3.2 Hz, 6H), 1.11 (td, *J* = 12.9, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 178.68, 143.96, 140.26, 132.22, 128.62, 128.31, 127.38, 127.01, 124.85, 122.80, 108.44, 70.59, 56.38, 38.22, 32.69, 29.25, 29.20, 26.48.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{23}NNaO_2$: 332.1621; found: 332.1620.

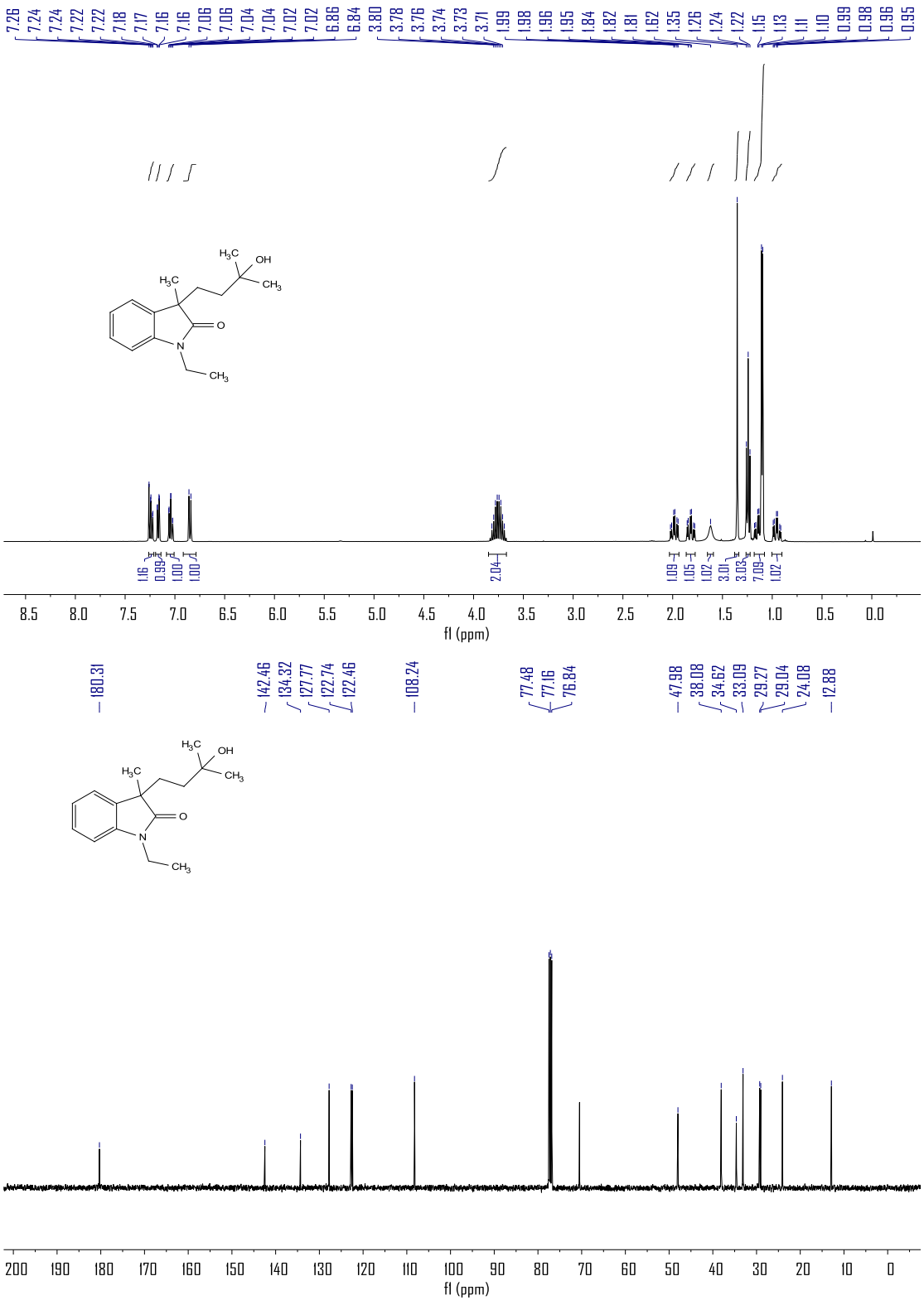


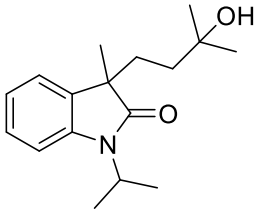


1-ethyl-3-(3-hydroxy-3-methylbutyl)-3-methylindolin-2-one

Following the general procedure (**4n**, pale-yellow liquid, 46 mg, 88%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.22 (m, 1H), 7.17 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 3.82 – 3.68 (m, 2H), 1.98 (td, *J* = 12.9, 4.7 Hz, 1H), 1.82 (td, *J* = 12.9, 4.1 Hz, 1H), 1.62 (s, 1H), 1.35 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.18 – 1.08 (m, 7H), 0.95 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.31, 142.46, 134.32, 127.77, 122.74, 122.46, 108.24, 47.98, 38.08, 34.62, 33.09, 29.27, 29.04, 24.08, 12.88.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}NNaO_2$: 284.1621; found: 284.1628.

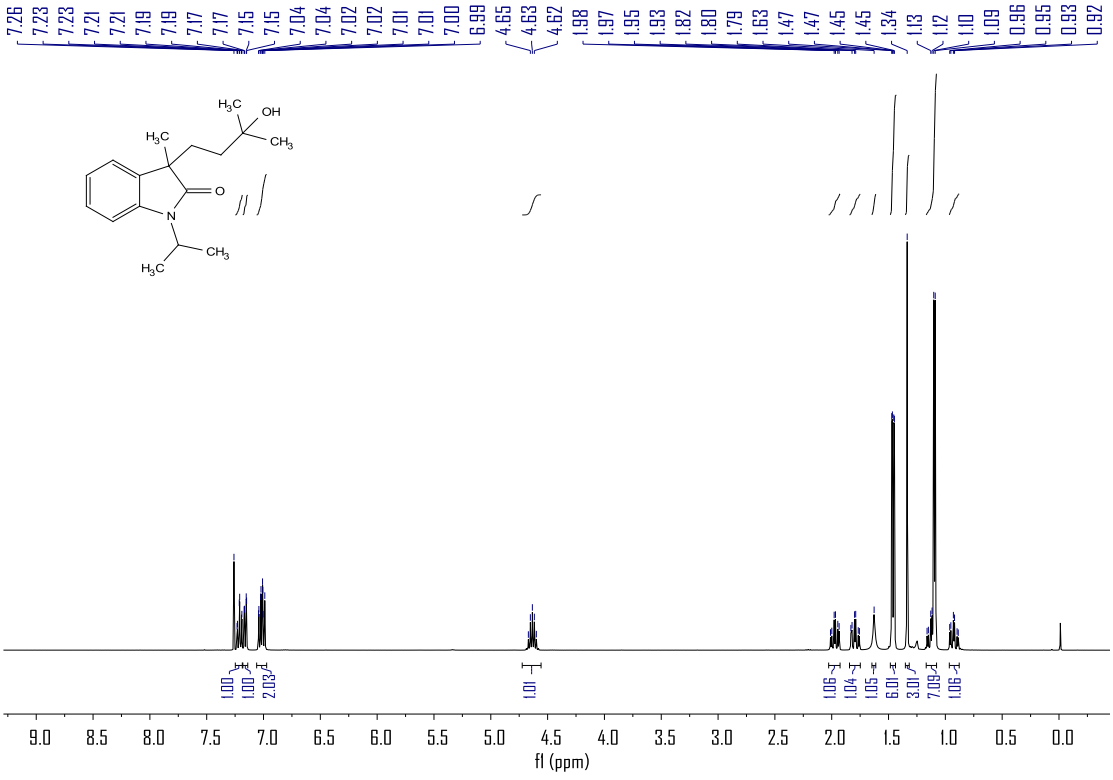

7.26 7.24 7.24 7.22 7.22 7.18 7.17 7.16 7.16 7.06 7.06 7.04 7.04 7.02 7.02 6.86 6.84
3.80 3.78 3.76 3.74 3.73 3.71 1.99 1.98 1.96 1.95 1.84 1.82 1.81 1.62 1.35 1.26 1.24 1.22 1.15 1.13 1.11 1.10 0.99 0.98 0.96 0.95
H3C
OH
CH3
H3C
O
N
CH3
1.16 0.99 1.00 1.00 2.04 1.09 1.05 1.02 3.01 3.03 7.09 1.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
180.31 142.46 134.32 127.77 122.74 122.46 108.24 77.48 77.16 76.84 47.98 38.08 34.62 33.09 29.27 29.04 24.08 12.88
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

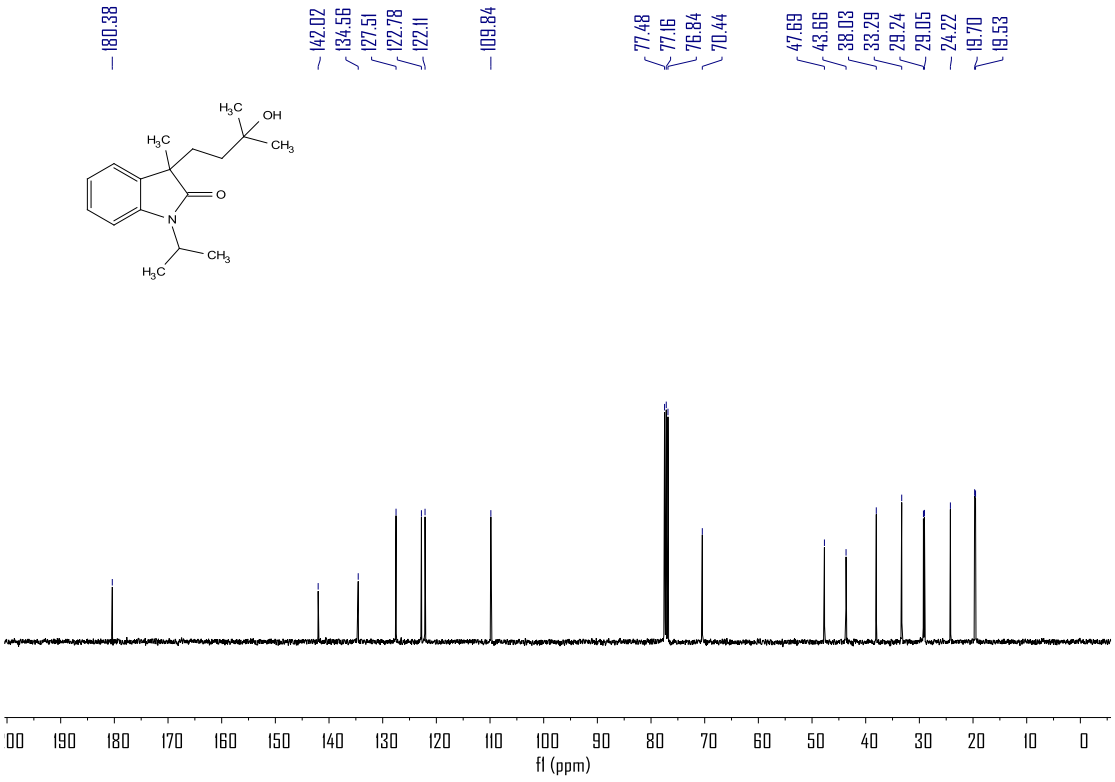


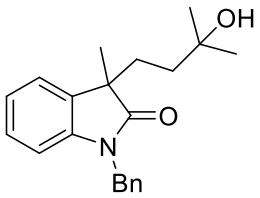
3-(3-hydroxy-3-methylbutyl)-1-isopropyl-3-methylindolin-2-one

Following the general procedure (**4o**, pale-yellow liquid, 46 mg, 83%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.21 (td, *J* = 7.7, 1.4 Hz, 1H), 7.16 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.05 – 6.98 (m, 2H), 4.63 (p, *J* = 7.0 Hz, 1H), 1.97 (td, *J* = 12.9, 4.6 Hz, 1H), 1.79 (td, *J* = 13.0, 4.0 Hz, 1H), 1.63 (s, 1H), 1.46 (dd, *J* = 7.0, 2.3 Hz, 6H), 1.34 (s, 3H), 1.17 – 1.08 (m, 7H), 0.92 (td, *J* = 13.0, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.38, 142.02, 134.56, 127.51, 122.78, 122.11, 109.84, 70.44, 47.69, 43.66, 38.03, 33.29, 29.24, 29.05, 24.22, 19.70, 19.53.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{25}NNaO_2$: 298.1778; found: 298.1781.



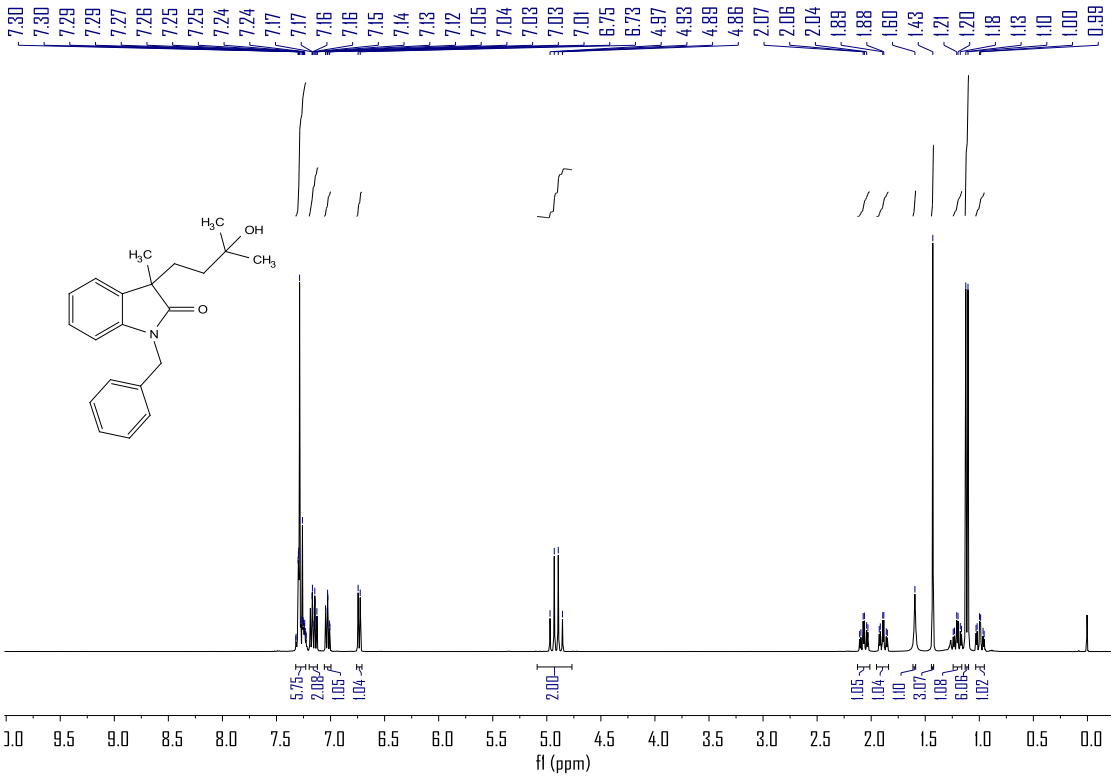


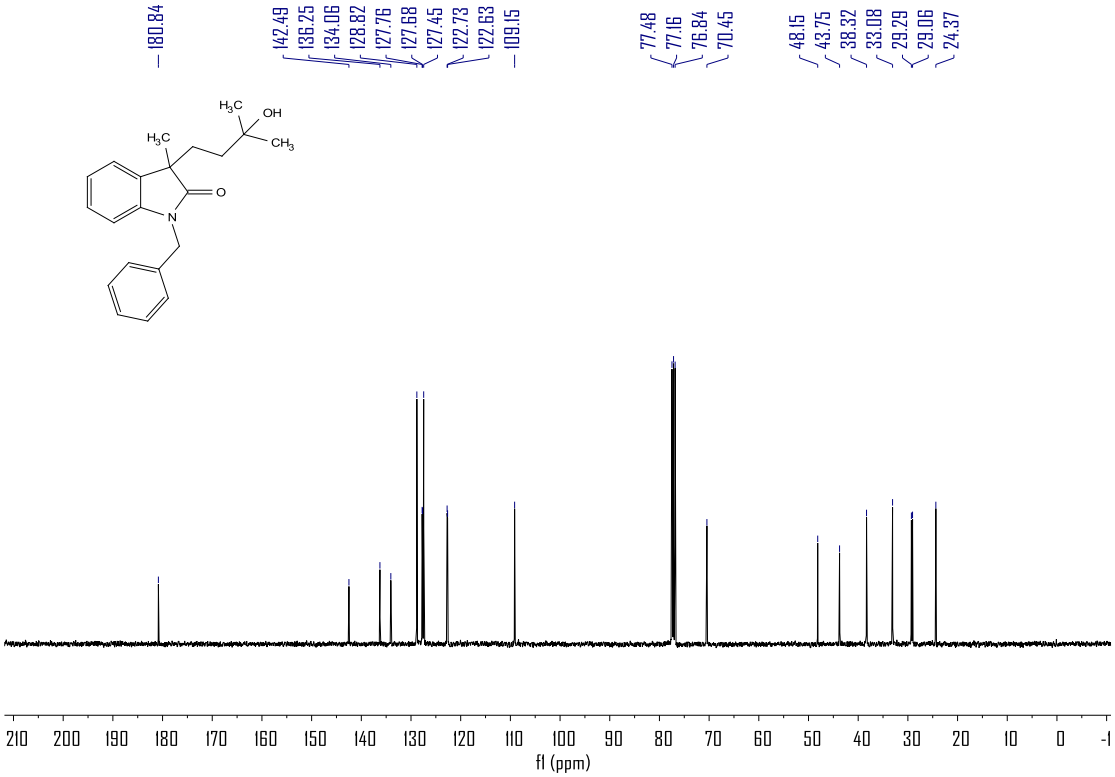


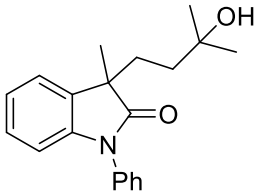
1-benzyl-3-(3-hydroxy-3-methylbutyl)-3-methylindolin-2-one

Following the general procedure (**4p**, pale-yellow liquid, 47 mg, 73%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.22 (m, 5H), 7.20 – 7.12 (m, 2H), 7.03 (td, *J* = 7.5, 1.0 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 4.91 (q, *J* = 15.6 Hz, 2H), 2.07 (td, *J* = 12.9, 4.6 Hz, 1H), 1.89 (td, *J* = 13.0, 4.0 Hz, 1H), 1.60 (s, 1H), 1.43 (s, 3H), 1.20 (td, *J* = 13.0, 4.6 Hz, 1H), 1.11 (d, *J* = 8.1 Hz, 6H), 0.99 (td, *J* = 13.0, 4.0 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.84, 142.49, 136.25, 134.06, 128.82, 127.76, 127.68, 127.45, 122.73, 122.63, 109.15, 70.45, 48.15, 43.75, 38.32, 33.08, 29.29, 29.06, 24.37.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{25}NNaO_2$: 346.1778; found: 346.1783.


7.30 7.30 7.29 7.29 7.27 7.26 7.25 7.25 7.24 7.24 7.17 7.17 7.16 7.16 7.15 7.14 7.13 7.12 7.05 7.04 7.03 7.03 7.01 6.75 6.73 4.97 4.93 4.89 4.86 2.07 2.06 2.04 1.89 1.88 1.60 1.43 1.21 1.20 1.18 1.13 1.10 1.00 0.99
H3C
OH
CH3
O
N
5.75 2.08 1.05 1.04 2.00 1.05 1.04 1.10 3.07 1.08 6.06 1.02
f1 (ppm)

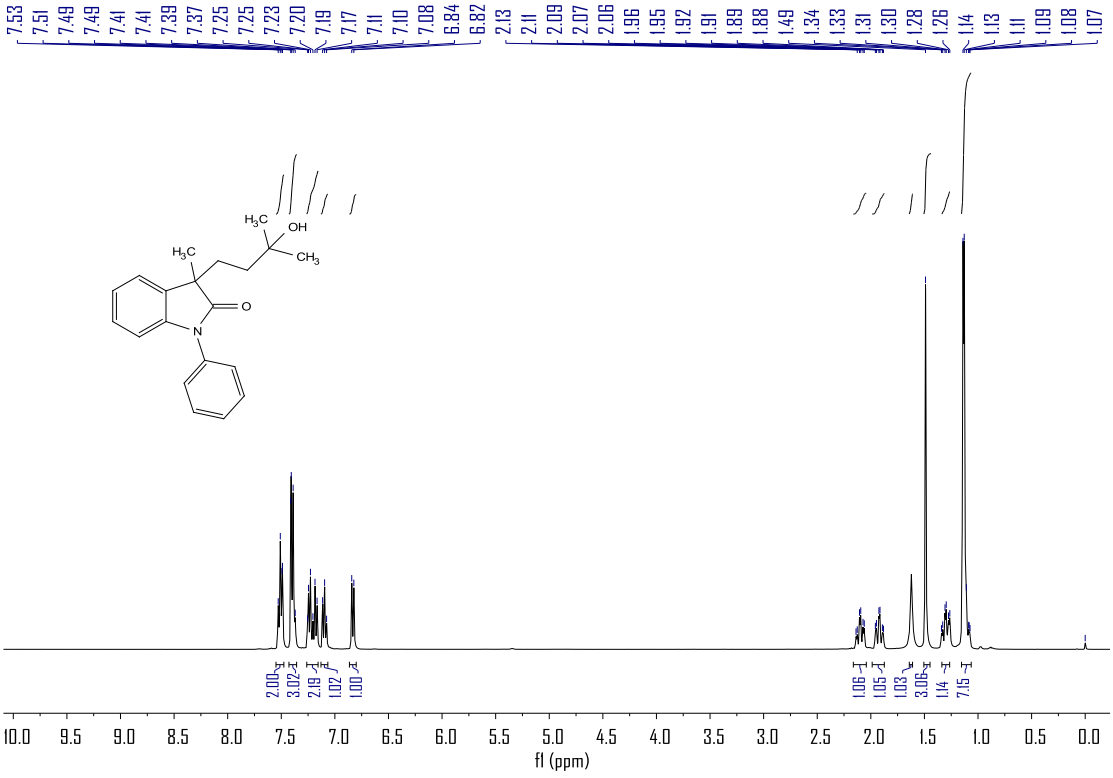

180.84 142.49 136.25 134.06 128.82 127.76 127.68 127.45 122.73 122.63 109.15 77.48 77.16 76.84 70.45 48.15 43.75 38.32 33.08 29.29 29.06 24.37
H3C
OH
CH3
O
N
f1 (ppm)

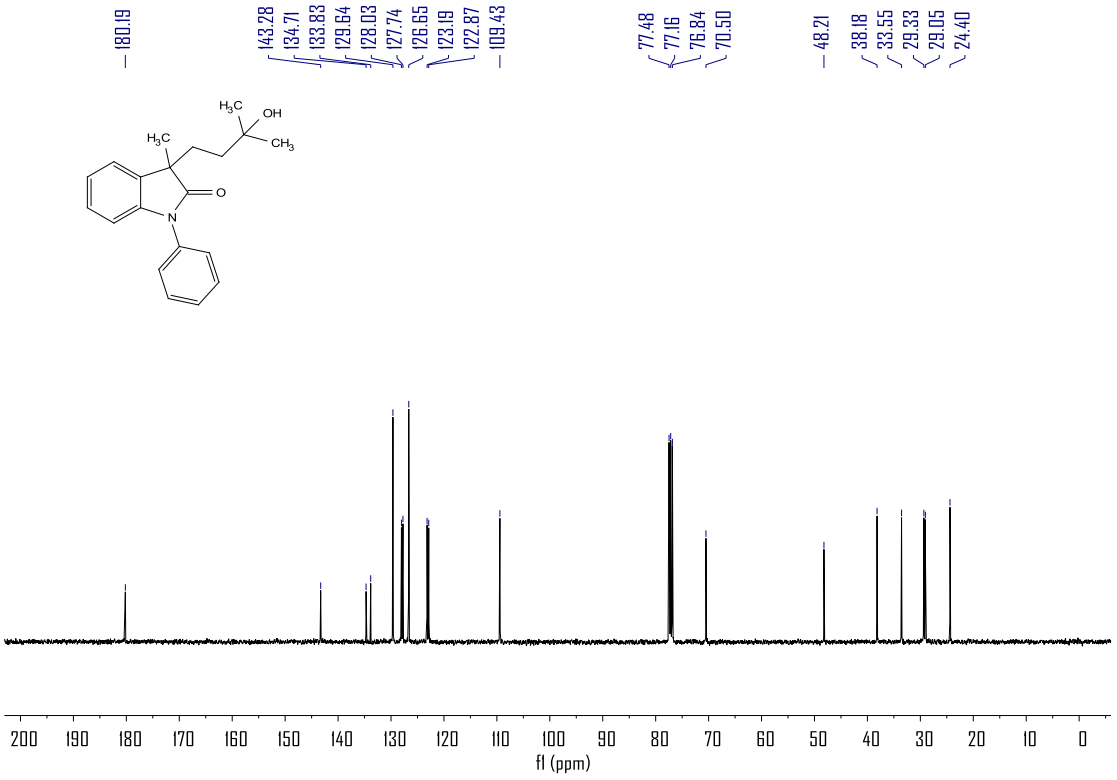


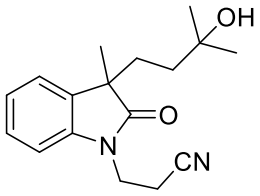
3-(3-hydroxy-3-methylbutyl)-3-methyl-1-phenylindolin-2-one

Following the general procedure (**4q**, pale-yellow liquid, 56 mg, 90%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.55 – 7.47 (m, 2H), 7.42 – 7.36 (m, 3H), 7.26 – 7.16 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 2.10 (td, *J* = 13.1, 4.6 Hz, 1H), 1.92 (td, *J* = 13.1, 4.0 Hz, 1H), 1.62 (s, 1H), 1.49 (s, 3H), 1.30 (td, *J* = 13.3, 4.8 Hz, 1H), 1.13 (d, *J* = 4.6 Hz, 7H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.19, 143.28, 134.71, 133.83, 129.64, 128.03, 127.74, 126.65, 123.19, 122.87, 109.43, 70.50, 48.21, 38.18, 33.55, 29.33, 29.05, 24.40.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{23}NNaO_2$: 332.1621; found: 332.1626.



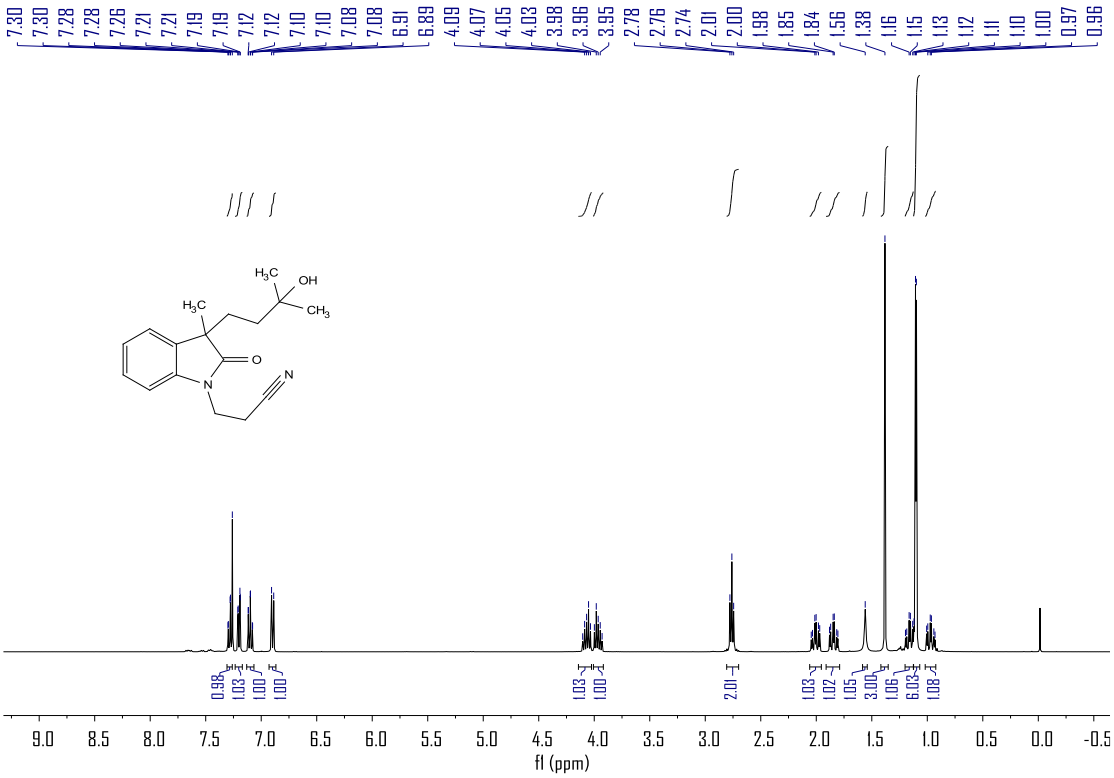


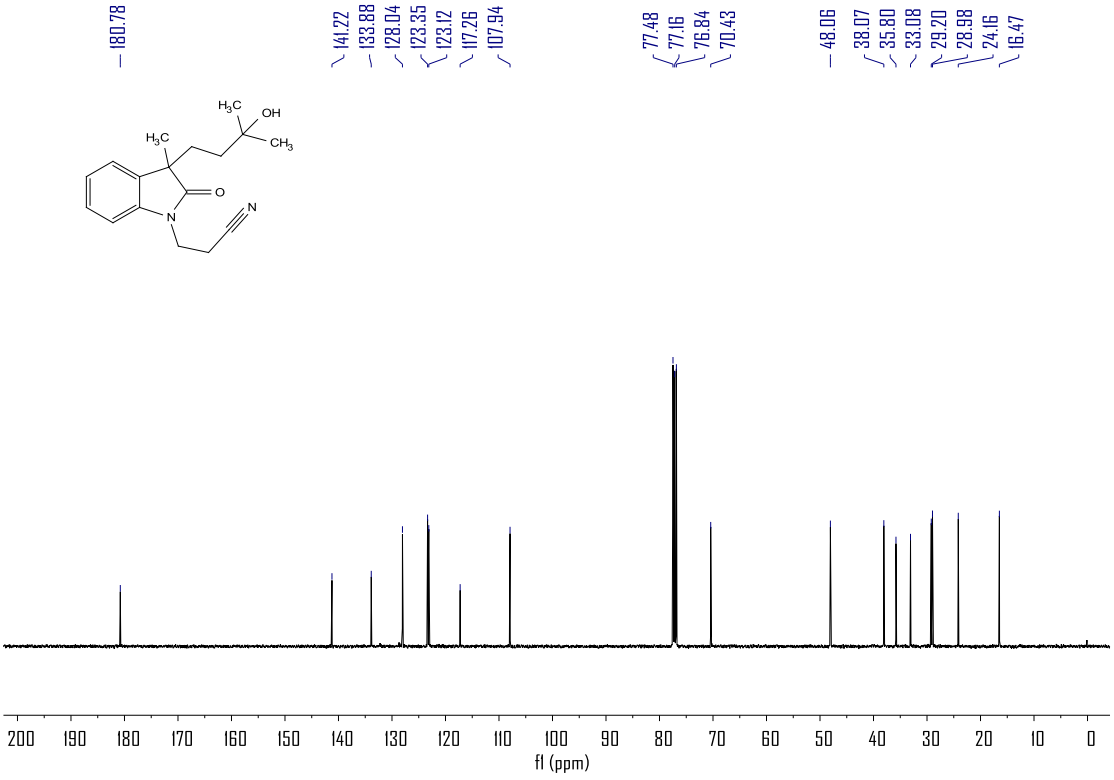


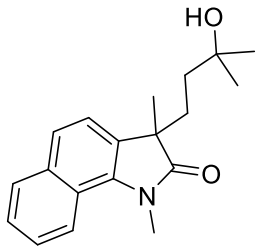
3-(3-(3-hydroxy-3-methylbutyl)-3-methyl-2-oxoindolin-1-yl)propanenitrile

Following the general procedure (**4r**, pale-yellow liquid, 40 mg, 70%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 1H), 7.20 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.10 (td, *J* = 7.5, 0.9 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 4.07 (dt, *J* = 14.0, 6.9 Hz, 1H), 3.96 (dt, *J* = 14.0, 6.8 Hz, 1H), 2.76 (t, *J* = 6.7 Hz, 2H), 2.01 (td, *J* = 12.9, 4.6 Hz, 1H), 1.84 (td, *J* = 13.0, 4.1 Hz, 1H), 1.56 (s, 1H), 1.38 (s, 3H), 1.16 (td, *J* = 13.1, 4.7 Hz, 1H), 1.10 (d, *J* = 3.2 Hz, 6H), 0.97 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.78, 141.22, 133.88, 128.04, 123.35, 123.12, 117.26, 107.94, 70.43, 48.06, 38.07, 35.80, 33.08, 29.20, 28.98, 24.16, 16.47.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{22}N_2NaO_2$: 309.1573; found: 309.1576.


7.30 7.30 7.28 7.28 7.26 7.21 7.21 7.19 7.19 7.12 7.12 7.10 7.10 7.08 7.08 6.91 6.89 4.09 4.07 4.05 4.03 3.98 3.96 3.95 2.78 2.76 2.74 2.01 2.00 1.98 1.85 1.84 1.56 1.38 1.16 1.15 1.13 1.12 1.11 1.10 1.00 0.97 0.96
H3C OH CH3 H3C O N N
0.98 1.03 1.00 1.00 1.03 1.00 2.01 1.03 1.02 1.05 3.00 1.06 6.03 1.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

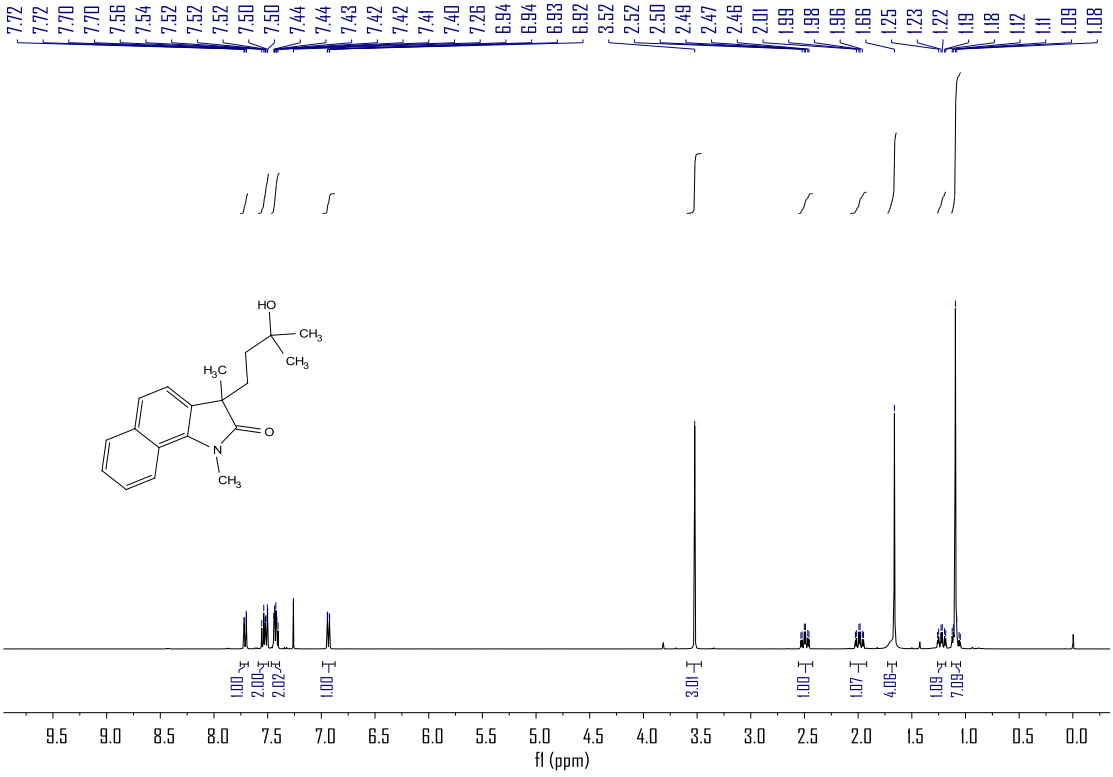

180.78 141.22 133.88 128.04 123.35 123.12 117.26 107.94 77.48 77.16 76.84 70.43 48.06 38.07 35.80 33.08 29.20 28.98 24.16 16.47
H3C OH CH3 H3C O N N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

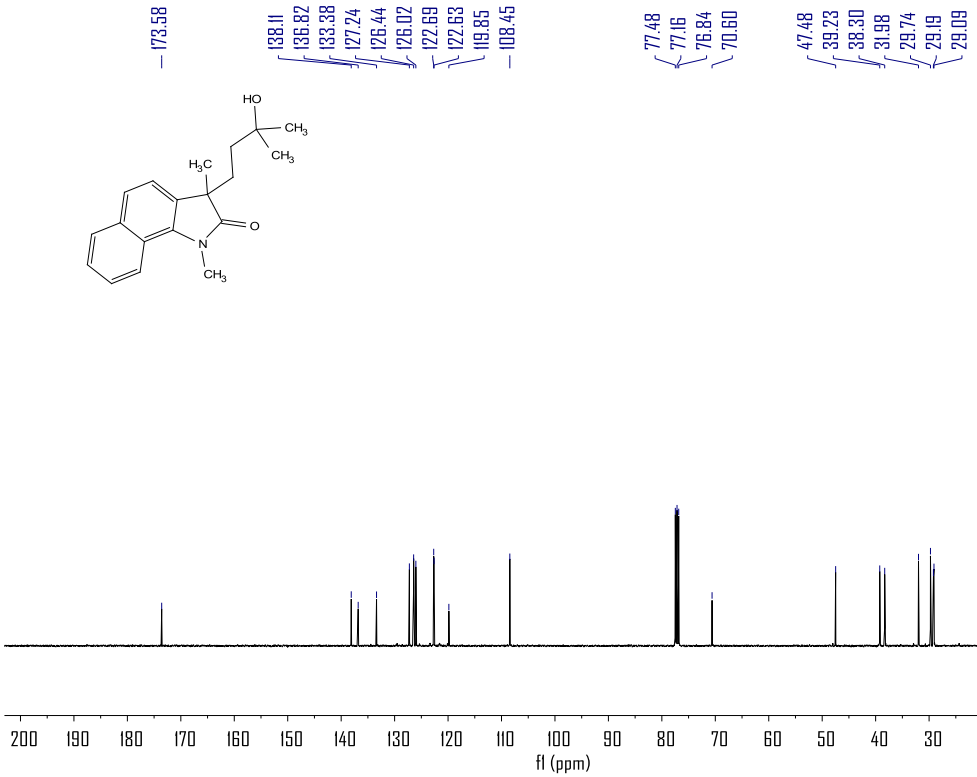


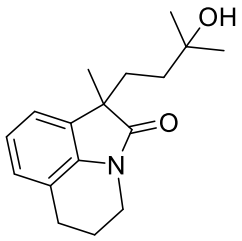
3-(3-hydroxy-3-methylbutyl)-1,3-dimethyl-1,3-dihydro-2H-benzo[g]indol-2-one

Following the general procedure (**4s**, pale-yellow liquid, 35 mg, 59%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.42 (ddd, *J* = 8.1, 4.8, 3.7 Hz, 2H), 6.93 (dd, *J* = 7.6, 0.9 Hz, 1H), 3.52 (s, 3H), 2.50 (td, *J* = 12.8, 4.3 Hz, 1H), 1.99 (td, *J* = 12.9, 4.3 Hz, 1H), 1.66 (s, 3H), 1.22 (td, *J* = 13.0, 4.2 Hz, 1H), 1.09 (s, 7H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 173.58, 138.11, 136.82, 133.38, 127.24, 126.44, 126.02, 122.69, 122.63, 119.85, 108.45, 70.60, 47.48, 39.23, 38.30, 31.98, 29.74, 29.19, 29.09.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{23}NNaO_2$: 320.1621; found: 320.1629.



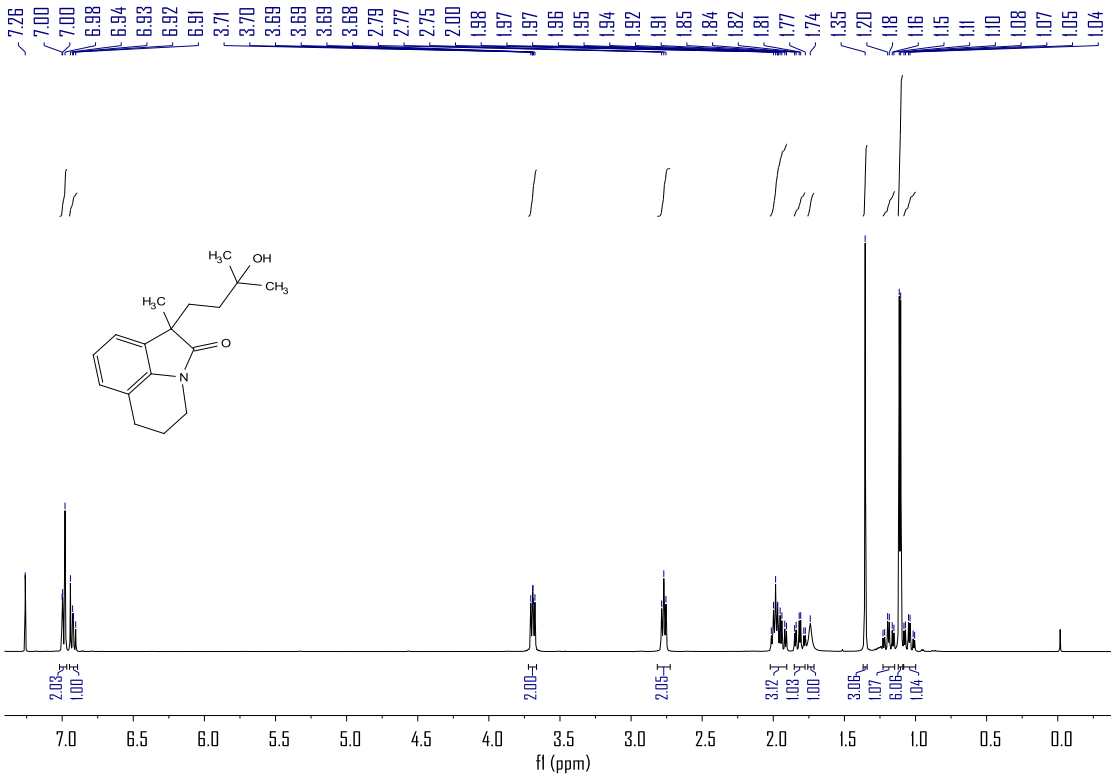


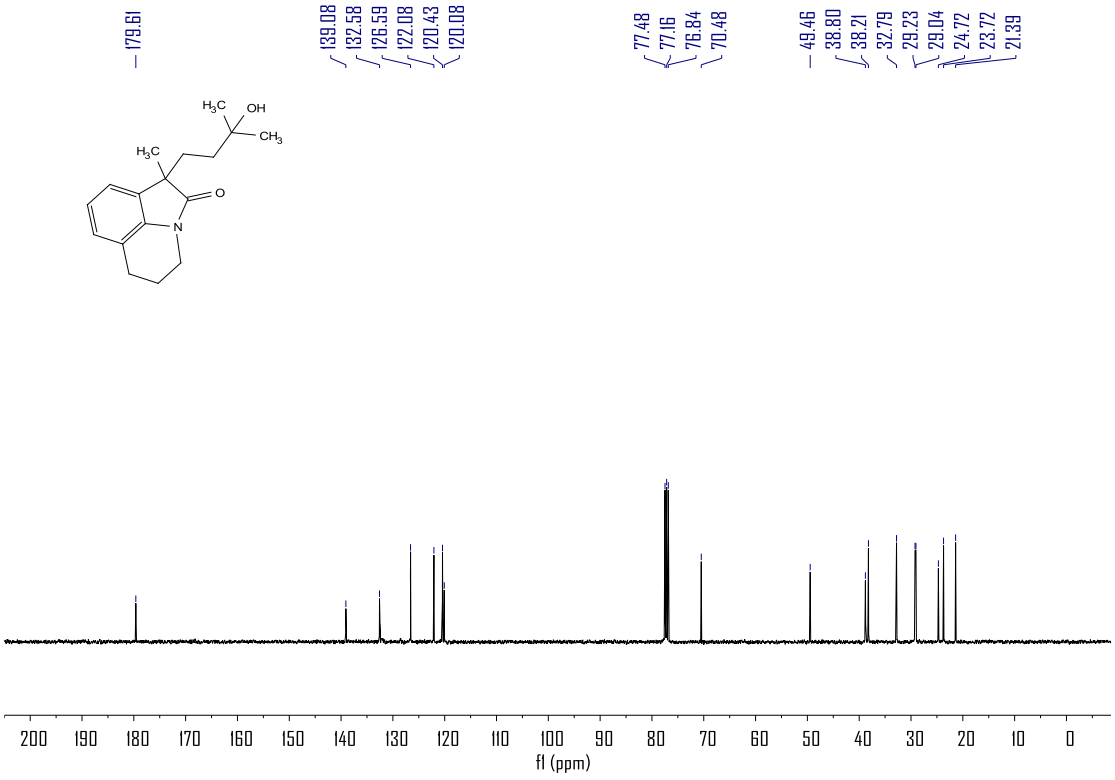


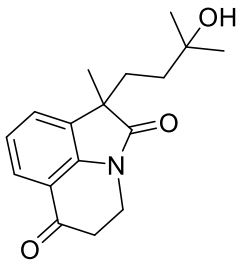
1-(3-hydroxy-3-methylbutyl)-1-methyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2(1H)-one

Following the general procedure (**4t**, pale-yellow liquid, 38 mg, 70%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.99 (d, *J* = 6.6 Hz, 2H), 6.92 (dd, *J* = 8.6, 6.3 Hz, 1H), 3.75 – 3.61 (m, 2H), 2.77 (t, *J* = 6.1 Hz, 2H), 2.02 – 1.90 (m, 3H), 1.85 – 1.78 (m, 1H), 1.74 (s, 1H), 1.35 (s, 3H), 1.19 (td, *J* = 13.0, 4.7 Hz, 1H), 1.11 (d, *J* = 4.0 Hz, 6H), 1.04 (td, *J* = 12.9, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 179.61, 139.08, 132.58, 126.59, 122.08, 120.43, 120.08, 49.46, 38.80, 38.21, 32.79, 29.23, 29.04, 24.72, 23.72, 21.39.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_2$: 296.1621; found: 296.1620.


7.26
7.00
7.00
6.98
6.94
6.93
6.92
6.91
3.71
3.70
3.69
3.69
3.69
3.68
2.79
2.77
2.75
2.00
1.98
1.97
1.97
1.96
1.95
1.94
1.92
1.91
1.85
1.84
1.82
1.81
1.77
1.74
1.35
1.20
1.18
1.16
1.15
1.11
1.10
1.08
1.07
1.05
1.04
H3C
OH
CH3
H3C
O
N
2.03
1.00
2.00
2.05
3.12
1.03
1.00
3.06
1.07
6.06
1.04
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

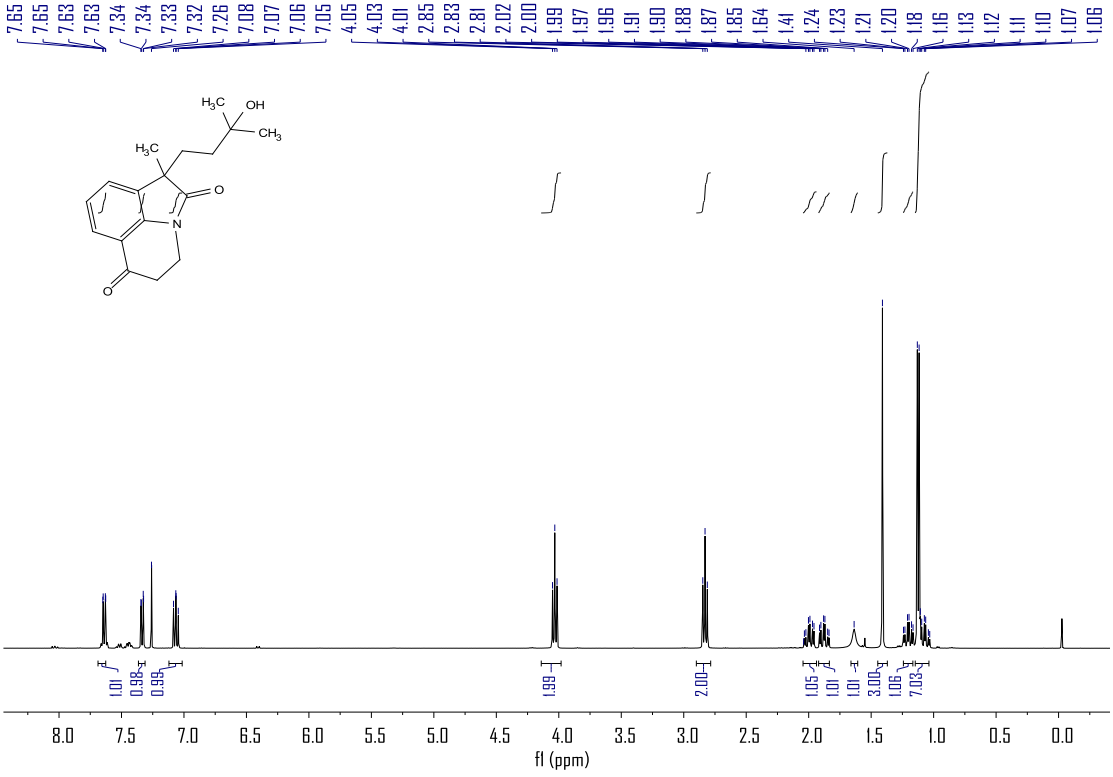

179.61
139.08
132.58
126.59
122.08
120.43
120.08
77.48
77.16
76.84
70.48
49.46
38.80
38.21
32.79
29.23
29.04
24.72
23.72
21.39
H3C
OH
CH3
H3C
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

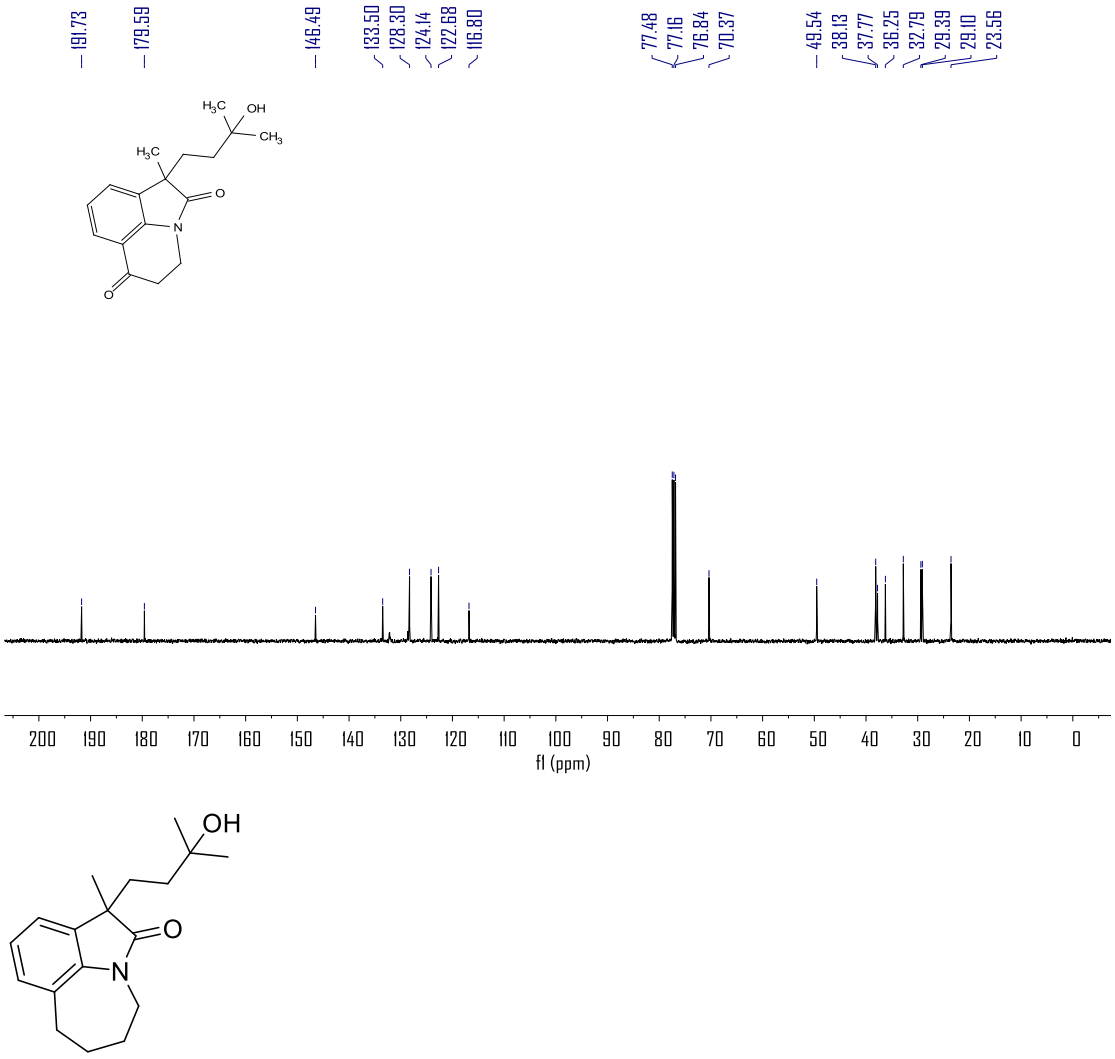


1-(3-hydroxy-3-methylbutyl)-1-methyl-4,5-dihydro-6H-pyrrolo[3,2,1-ij]quinoline-2, 6(1H)-dione

Following the general procedure (**4u**, pale-yellow liquid, 37 mg, 65%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (1:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.64 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.33 (dd, *J* = 7.3, 1.1 Hz, 1H), 7.06 (dd, *J* = 8.0, 7.2 Hz, 1H), 4.03 (t, *J* = 7.2 Hz, 2H), 2.83 (t, *J* = 7.2 Hz, 2H), 2.00 (td, *J* = 13.0, 4.7 Hz, 1H), 1.88 (td, *J* = 13.0, 4.3 Hz, 1H), 1.64 (s, 1H), 1.41 (s, 3H), 1.20 (td, *J* = 12.9, 4.7 Hz, 1H), 1.15 – 1.00 (m, 7H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 191.73, 179.59, 146.49, 133.50, 128.30, 124.14, 122.68, 116.80, 70.37, 49.54, 38.13, 37.77, 36.25, 32.79, 29.39, 29.10, 23.56.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{21}NNaO_3$: 310.1414; found: 310.1416.

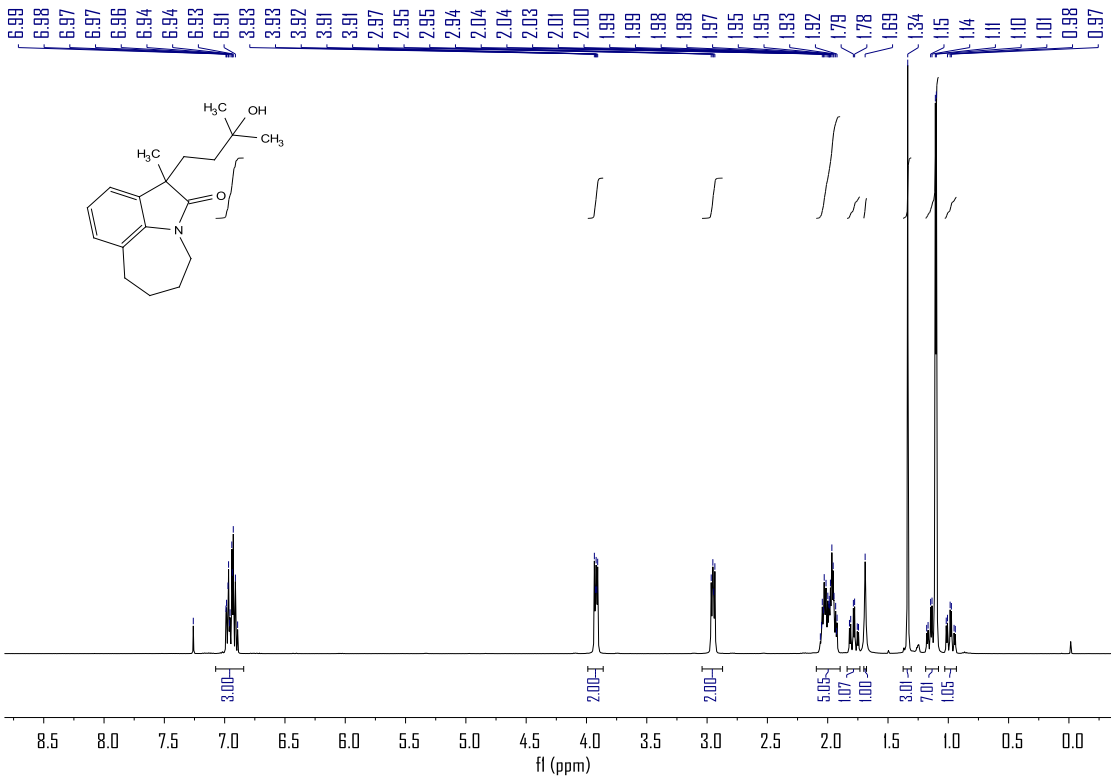


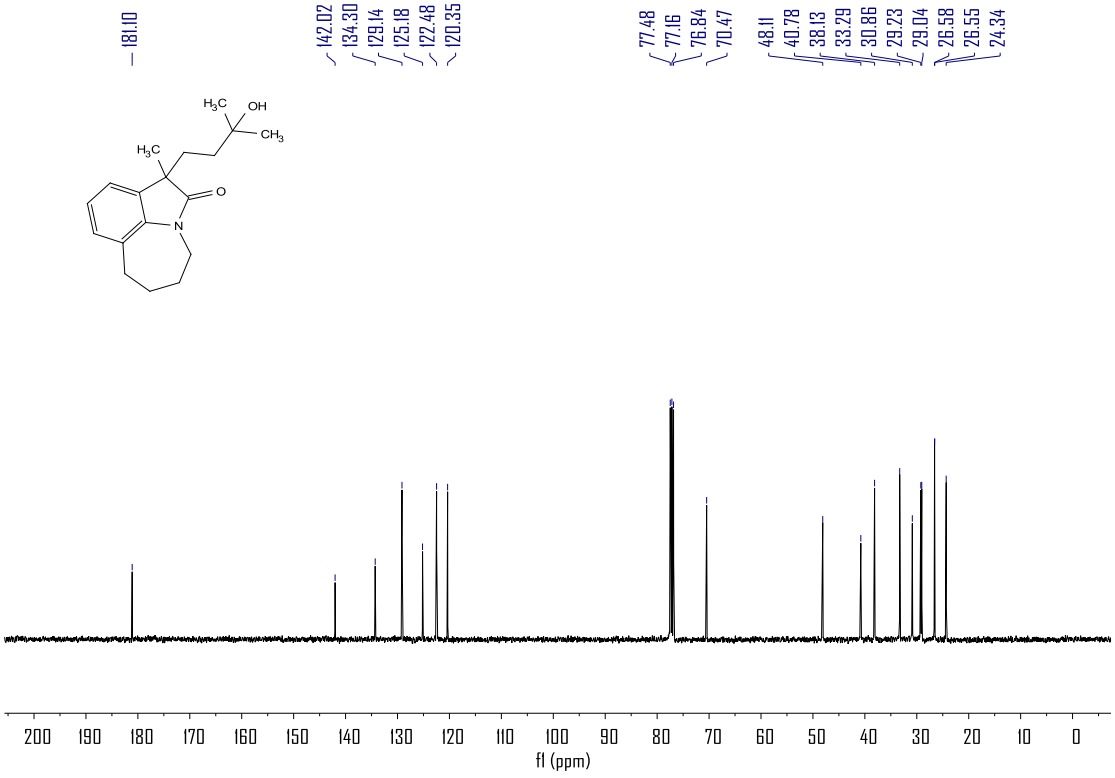


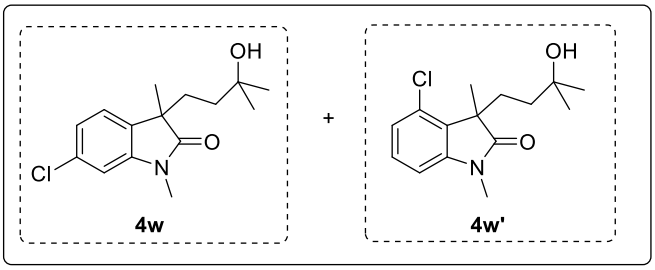
7-(3-hydroxy-3-methylbutyl)-7-methyl-1,2,3,4-tetrahydroazepino[3,2,1-hi]indol-6(7H)-one

Following the general procedure (**4v**, pale-yellow liquid, 39 mg, 68%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.05 – 6.84 (m, 3H), 4.02 – 3.86 (m, 2H), 2.95 (dd, *J* = 7.5, 4.7 Hz, 2H), 2.07 – 1.90 (m, 5H), 1.78 (td, *J* = 13.0, 4.1 Hz, 1H), 1.69 (s, 1H), 1.34 (s, 3H), 1.19 – 1.08 (m, 7H), 0.98 (td, *J* = 13.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.10, 142.02, 134.30, 129.14, 125.18, 122.48, 120.35, 70.47, 48.11, 40.78, 38.13, 33.29, 30.86, 29.23, 29.04, 26.58, 26.55, 24.34.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{25}NNaO_2$: 310.1778; found: 310.1783.


6.99 6.98 6.97 6.97 6.96 6.94 6.94 6.93 6.91 3.93 3.93 3.92 3.91 3.91 2.97 2.95 2.95 2.94 2.04 2.04 2.03 2.01 2.00 1.99 1.99 1.98 1.98 1.97 1.95 1.95 1.93 1.92 1.79 1.78 1.69 1.34 1.15 1.14 1.11 1.10 1.01 0.98 0.97
H3C OH CH3 H3C O N
3.00 2.00 2.00 5.05 1.07 1.00 3.01 7.01 1.05
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


181.10 142.02 134.30 129.14 125.18 122.48 120.35 77.48 77.16 76.84 70.47 48.11 40.78 38.13 33.29 30.86 29.23 29.04 26.58 26.55 24.34
H3C OH CH3 H3C O N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



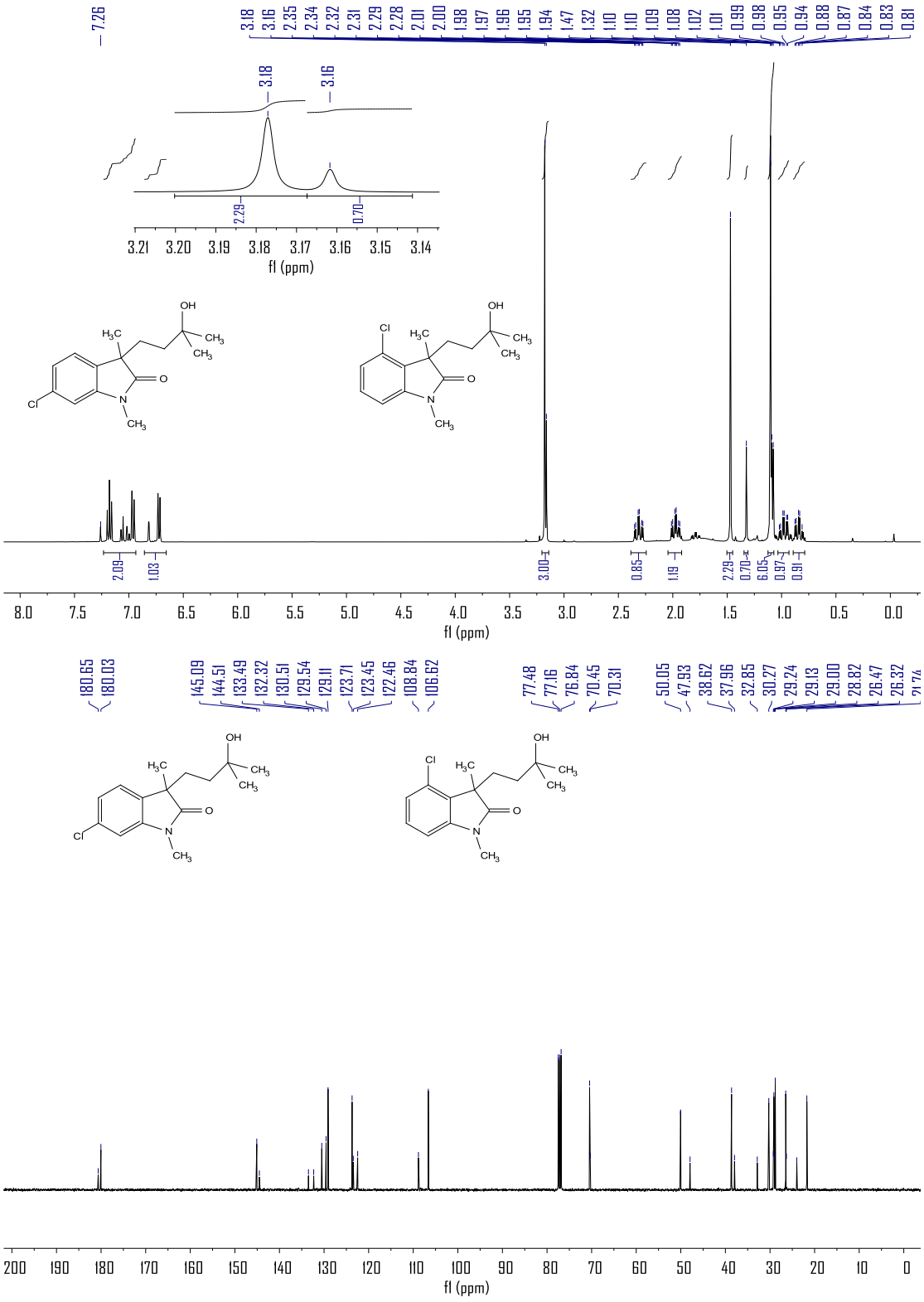
6-chloro-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

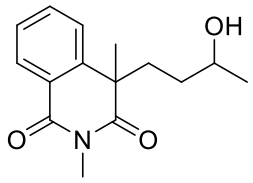
and

4-chloro-3-(3-hydroxy-3-methylbutyl)-1,3-dimethylindolin-2-one

Following the general procedure (**4w:4w' = 3.3:1,** pale-yellow liquid, 49 mg, 88%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 – 6.92 (m, 2H), 6.86 – 6.66 (m, 1H), 3.17 (d, *J* = 6.2 Hz, 3H), 2.31 (td, *J* = 13.2, 4.2 Hz, 1H), 1.97 (td, *J* = 13.0, 4.4 Hz, 1H), 1.47 (s, 2.29H), 1.32 (s, 0.70H), 1.13 – 1.06 (m, 6H), 0.98 (td, *J* = 13.1, 4.4 Hz, 1H), 0.89 – 0.80 (m, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.65, 180.03, 145.09, 144.51, 133.49, 132.32, 130.51, 129.54, 129.11, 123.71, 123.45, 122.46, 108.84, 106.62, 70.45, 70.31, 50.05, 47.93, 38.62, 37.96, 32.85, 30.27, 29.24, 29.13, 29.00, 28.82, 26.47, 26.32, 23.99, 21.74.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClNNaO_2$: 304.1075; found: 304.1078.

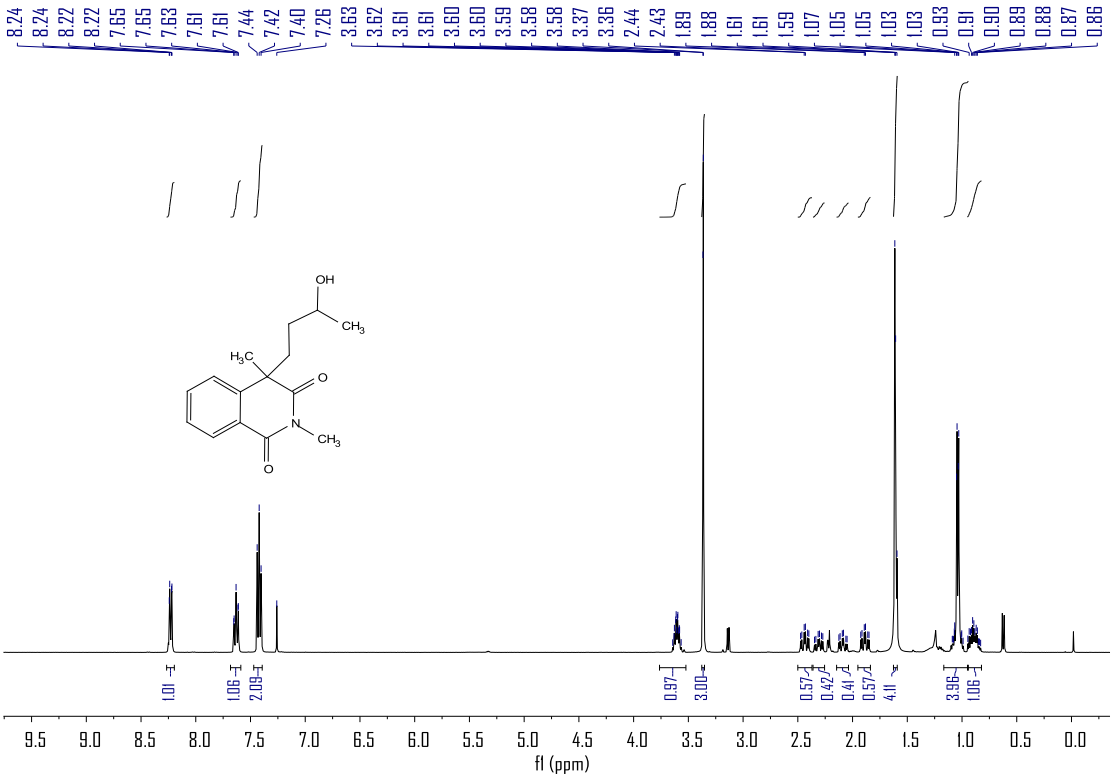

7.26
3.18
3.16
2.35
2.34
2.32
2.31
2.29
2.28
2.01
2.00
1.98
1.97
1.96
1.95
1.94
1.47
1.32
1.10
1.10
1.09
1.08
1.02
1.01
0.99
0.98
0.95
0.94
0.88
0.87
0.84
0.83
0.81
2.29
0.70
f1 (ppm)
OH
Cl
H_3C
CH_3
CH_3
O
N
CH_3
2.09
1.03
3.00
0.85
1.19
2.29
0.70
6.05
0.97
0.91
f1 (ppm)
180.65
180.03
145.09
144.51
133.49
132.32
130.51
129.54
129.11
123.71
123.45
122.46
108.84
106.62
77.48
77.16
76.84
70.45
70.31
50.05
47.93
38.62
37.96
32.85
30.27
29.24
29.13
29.00
28.82
26.47
26.32
f1 (ppm)

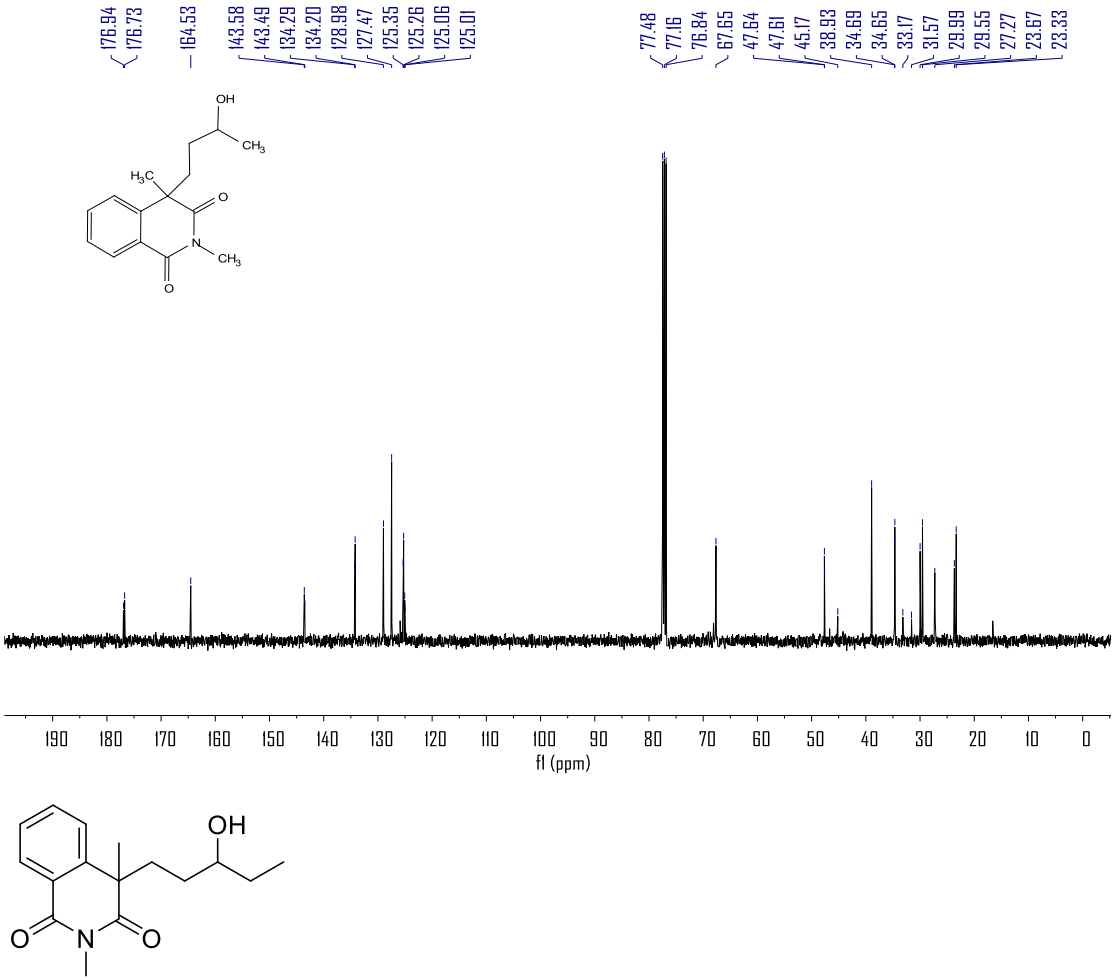


4-(3-hydroxybutyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**5a**, pale-yellow liquid, 42 mg, 81%, *d.r.* = 1.3:1). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.23 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.75 – 7.58 (m, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 3.60 (dtd, *J* = 10.2, 6.5, 5.2 Hz, 1H), 3.36 (d, *J* = 1.2 Hz, 3H), 2.44 (td, *J* = 12.9, 4.5 Hz, 0.57H), 2.36 – 2.28 (m, 0.42H), 2.09 (td, *J* = 12.8, 4.3 Hz, 0.41H), 1.89 (td, *J* = 12.9, 4.5 Hz, 0.57H), 1.63 – 1.58 (m, 4H), 1.10 – 0.98 (m, 4H), 0.95 – 0.83 (m, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.94, 176.73, 164.53, 143.58, 143.49, 134.29, 134.20, 128.98, 127.47, 125.35, 125.26, 125.06, 125.01, 67.65, 47.64, 47.61, 45.17, 38.93, 34.69, 34.65, 33.17, 31.57, 29.99, 29.55, 27.27, 23.67, 23.33.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{19}NNaO_3$: 284.1257; found: 284.1266.

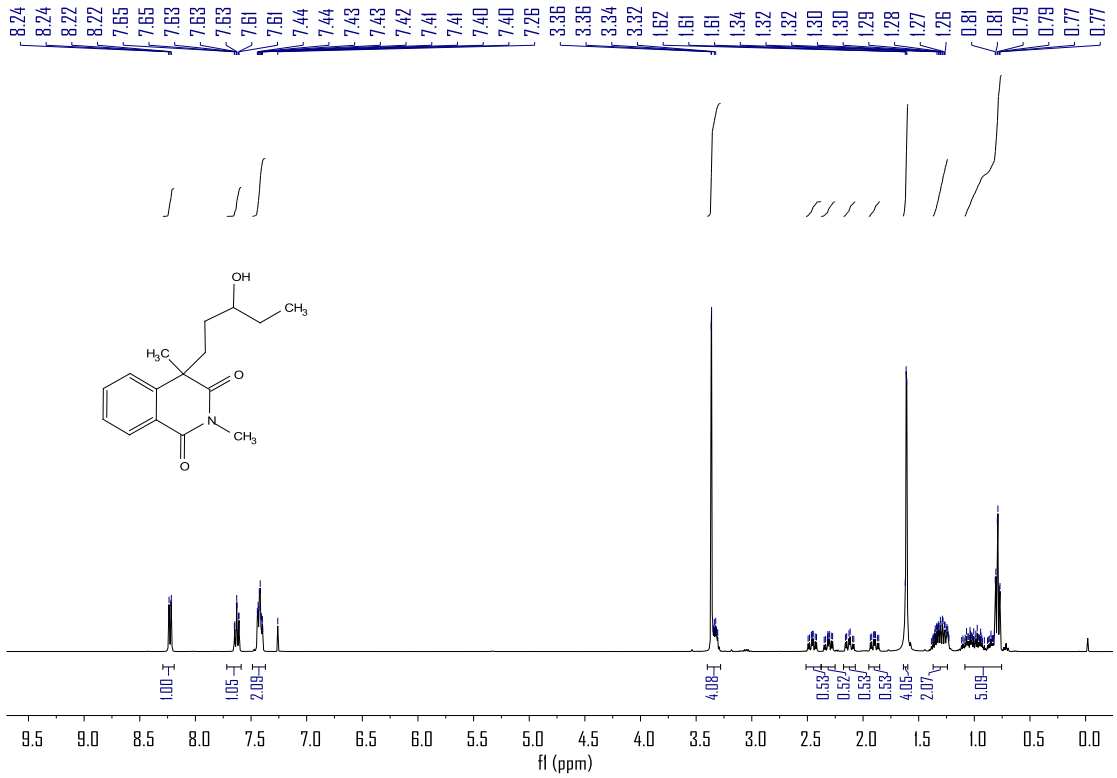


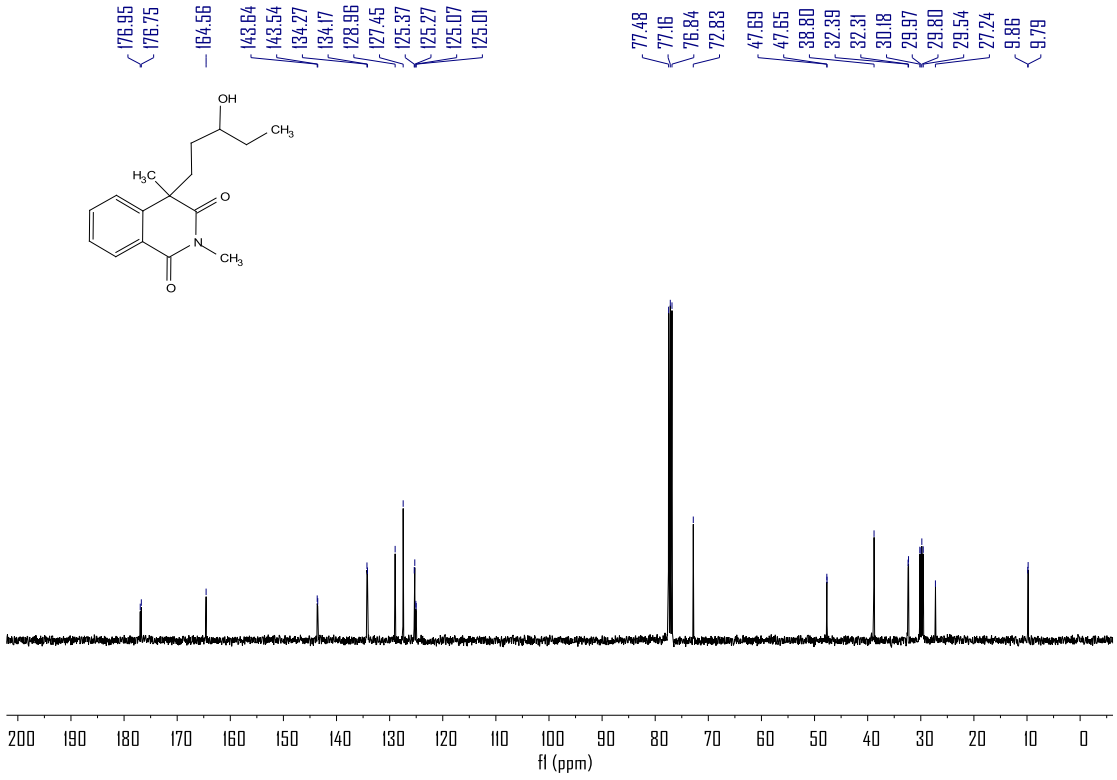


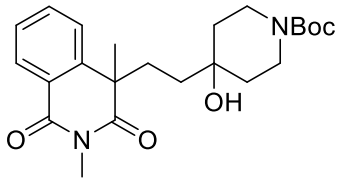
4-(3-hydroxypentyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**5b**, pale-yellow liquid, 48 mg, 88%, *d.r.* = 1.1:1). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.23 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.63 (ddd, *J* = 8.3, 7.3, 1.5 Hz, 1H), 7.42 (ddd, *J* = 7.8, 5.8, 3.1 Hz, 2H), 3.41 – 3.25 (m, 4H), 2.46 (td, *J* = 12.8, 4.8 Hz, 0.5H), 2.33 (dd, *J* = 13.2, 4.9 Hz, 0.5H), 2.12 (td, *J* = 12.9, 4.3 Hz, 0.5H), 1.90 (td, *J* = 12.9, 4.8 Hz, 0.5H), 1.61 (d, *J* = 2.5 Hz, 4H), 1.39 – 1.22 (m, 2H), 1.12 – 0.71 (m, 5H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.95, 176.75, 164.56, 143.64, 143.54, 134.27, 134.17, 128.96, 127.45, 125.37, 125.27, 125.07, 125.01, 72.83, 47.69, 47.65, 38.80, 32.39, 32.31, 30.18, 29.97, 29.80, 29.54, 27.24, 9.86, 9.79.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_3$: 298.1414; found: 298.1421.


8.24 8.24 8.22 8.22 7.65 7.65 7.63 7.63 7.63 7.61 7.61 7.44 7.44 7.43 7.43 7.42 7.41 7.41 7.40 7.40 7.26
3.36 3.36 3.34 3.32 1.62 1.61 1.61 1.34 1.32 1.32 1.30 1.30 1.29 1.28 1.27 1.26 0.81 0.81 0.79 0.79 0.77 0.77
OH
CH3
H3C
O
N
CH3
O
1.00 1.05 2.09 4.08 0.53 0.52 0.53 4.05 2.07 5.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

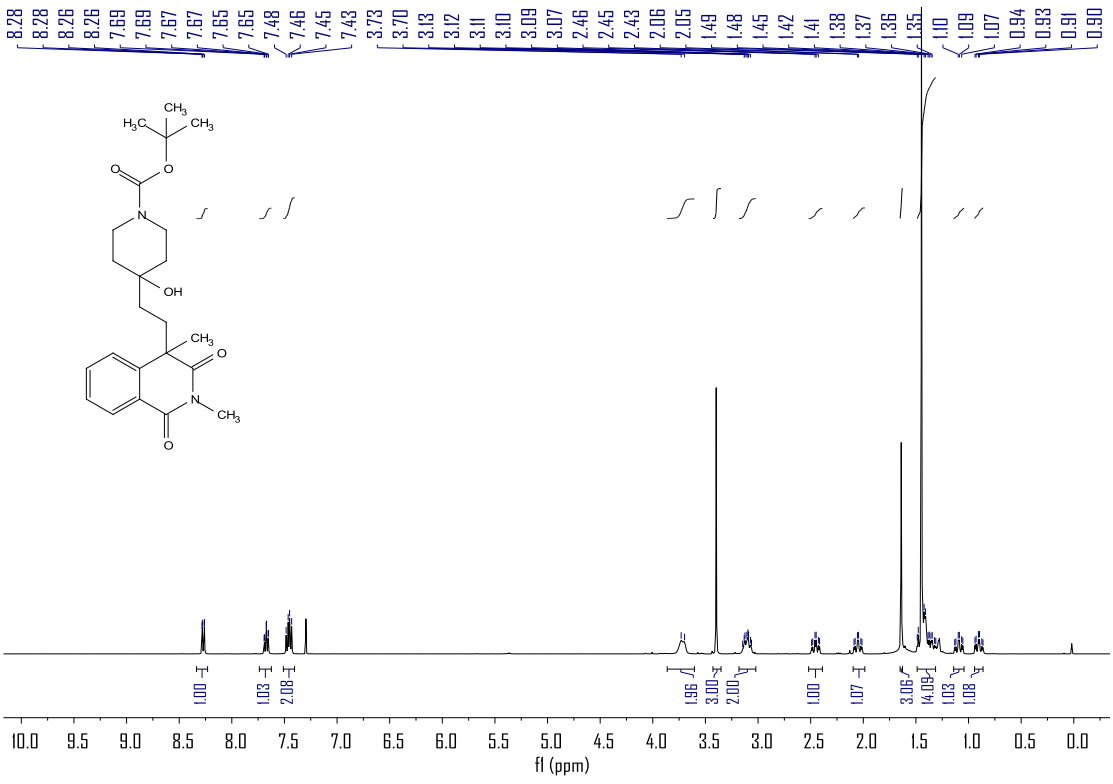

176.95 176.75 164.56 143.64 143.54 134.27 134.17 128.98 127.45 125.37 125.27 125.07 125.01
77.48 77.16 76.84 72.83 47.69 47.65 38.80 32.39 32.31 30.18 29.97 29.80 29.54 27.24 9.86 9.79
OH
CH3
H3C
O
N
CH3
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

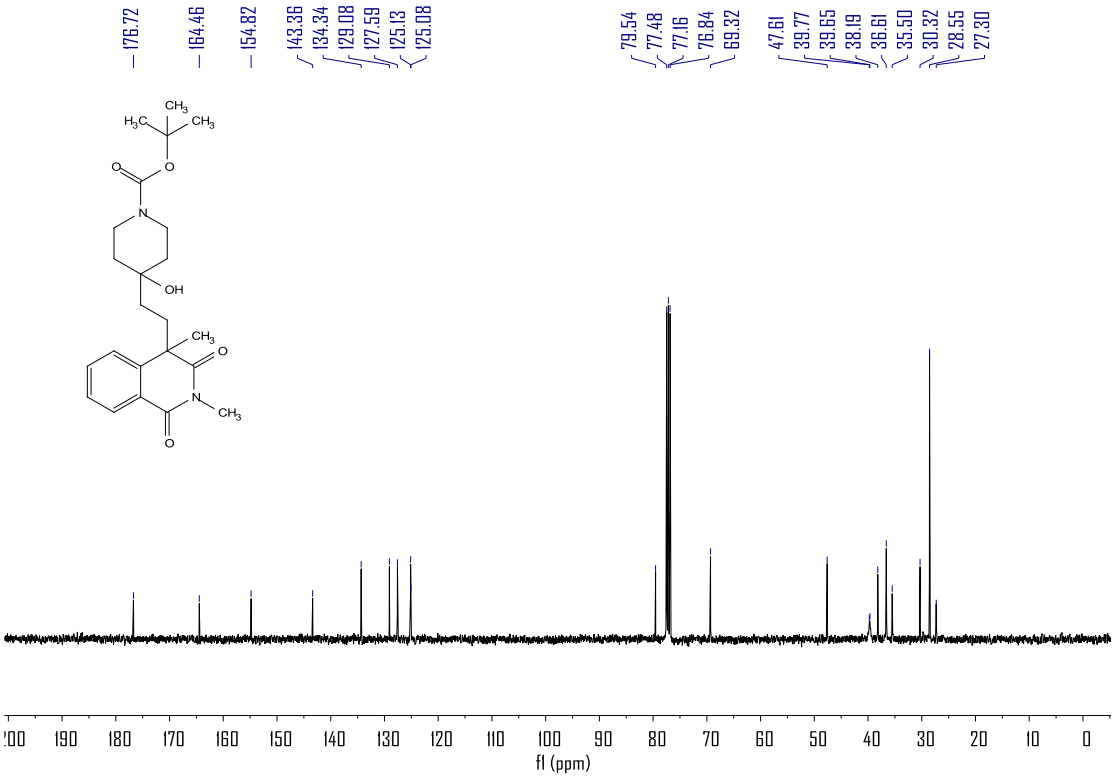


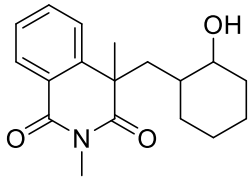
Tert-butyl-4-(2-(2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)ethyl)-4-hydroxypiperidine-1-carboxylate

Following the general procedure (**5c**, pale-yellow liquid, 54 mg, 65%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.27 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.67 (td, *J* = 7.6, 1.5 Hz, 1H), 7.50 – 7.43 (m, 2H), 3.71 (d, *J* = 12.9 Hz, 2H), 3.40 (s, 3H), 3.18 – 3.08 (m, 2H), 2.45 (td, *J* = 12.9, 4.4 Hz, 1H), 2.05 (td, *J* = 13.0, 4.2 Hz, 1H), 1.64 (s, 3H), 1.45 (s, 14H), 1.09 (td, *J* = 13.1, 4.4 Hz, 1H), 0.90 (td, *J* = 13.2, 4.2 Hz, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.72, 164.46, 154.82, 143.36, 134.34, 129.08, 127.59, 125.13, 125.08, 79.54, 69.32, 47.61, 39.77, 39.65, 38.19, 36.61, 35.50, 30.32, 28.55, 27.30.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{32}N_2NaO_5$: 439.2203; found: 439.2207.



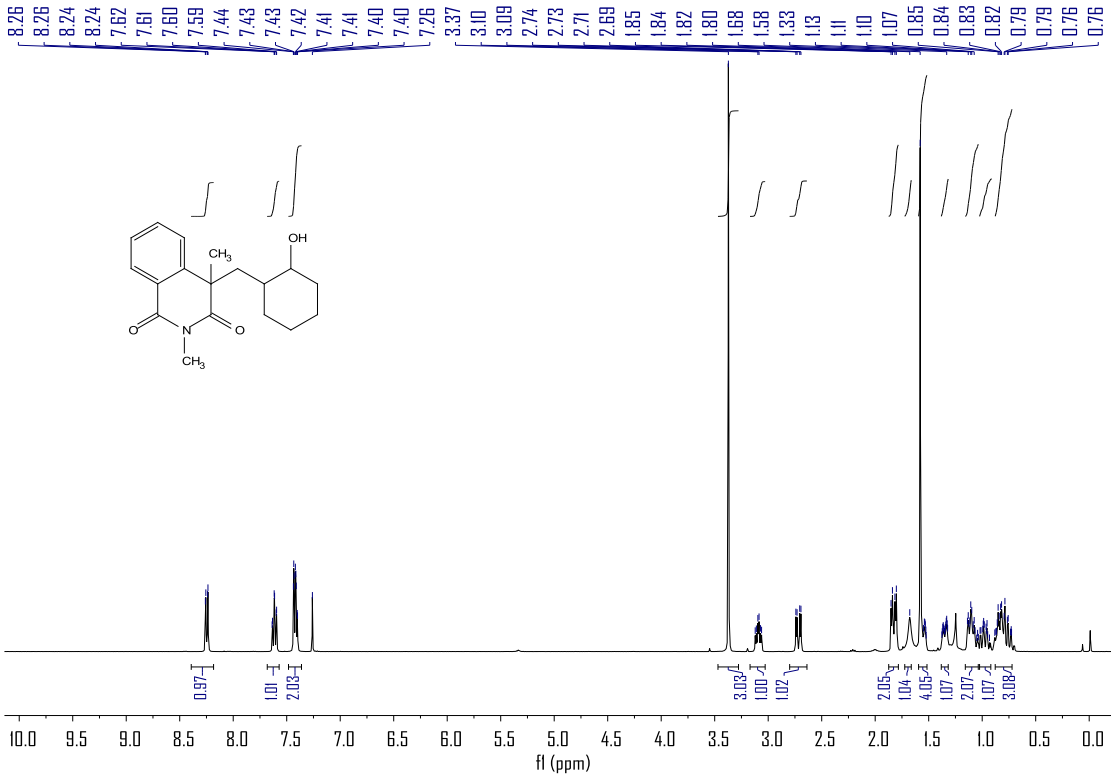


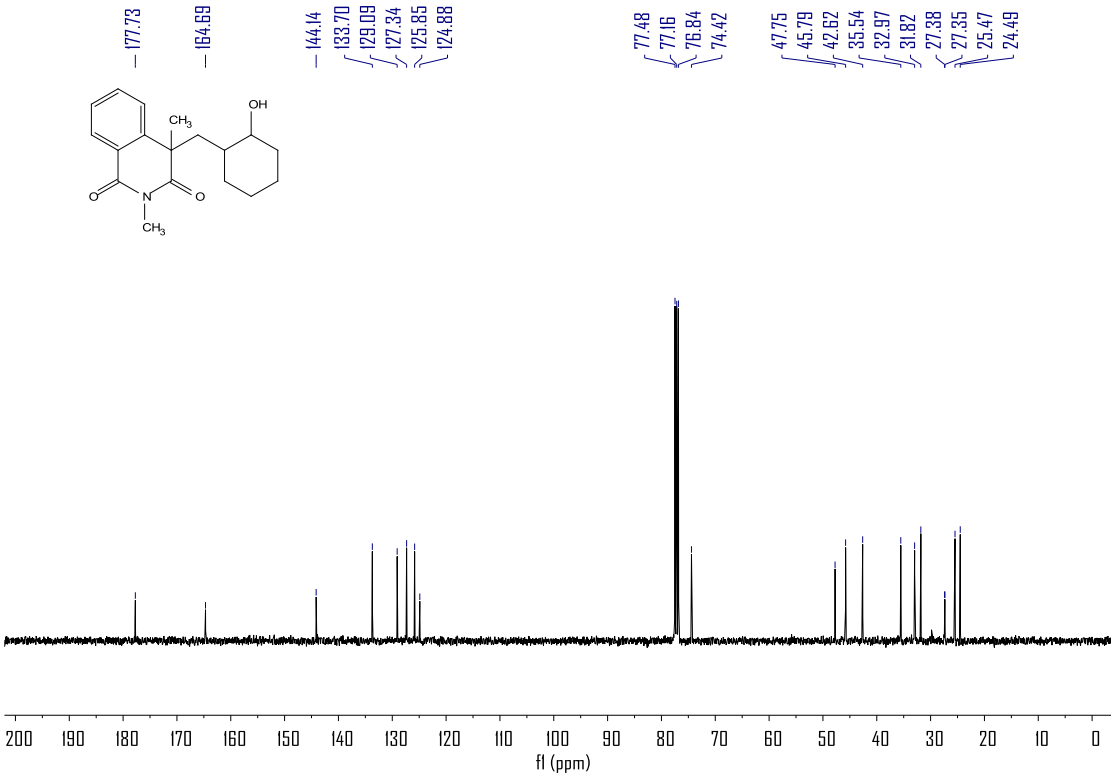


4-((2-hydroxycyclohexyl)methyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**major isomer 1**, **5d**, pale-yellow liquid, 34 mg). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.25 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.62 (td, *J* = 7.6, 1.5 Hz, 1H), 7.42 (ddd, *J* = 8.1, 4.5, 3.1 Hz, 2H), 3.37 (s, 3H), 3.09 (td, *J* = 9.7, 4.3 Hz, 1H), 2.72 (dd, *J* = 14.5, 4.4 Hz, 1H), 1.83 (dd, *J* = 14.6, 5.3 Hz, 2H), 1.68 (s, 1H), 1.59 – 1.52 (m, 4H), 1.39 – 1.32 (m, 1H), 1.15 – 1.04 (m, 2H), 1.02 – 0.93 (m, 1H), 0.89 – 0.71 (m, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 177.73, 164.69, 144.14, 133.70, 129.09, 127.34, 125.85, 124.88, 74.42, 47.75, 45.79, 42.62, 35.54, 32.97, 31.82, 27.38, 27.35, 25.47, 24.49.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_3$: 324.1570; found: 324.1576.


8.26
8.26
8.24
8.24
7.62
7.61
7.60
7.59
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.26
3.37
3.10
3.09
2.74
2.73
2.71
2.69
1.85
1.84
1.82
1.80
1.68
1.58
1.33
1.13
1.11
1.10
1.07
0.85
0.84
0.83
0.82
0.79
0.79
0.76
0.76
OH
CH3
O
N
O
CH3
0.97
1.01
2.03
3.03
1.00
1.02
2.05
1.04
4.05
1.07
2.07
1.07
3.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


177.73
164.69
144.14
133.70
129.09
127.34
125.85
124.88
77.48
77.16
76.84
74.42
47.75
45.79
42.62
35.54
32.97
31.82
27.38
27.35
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CH3
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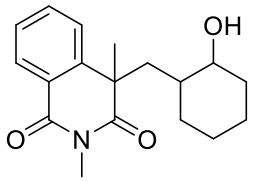
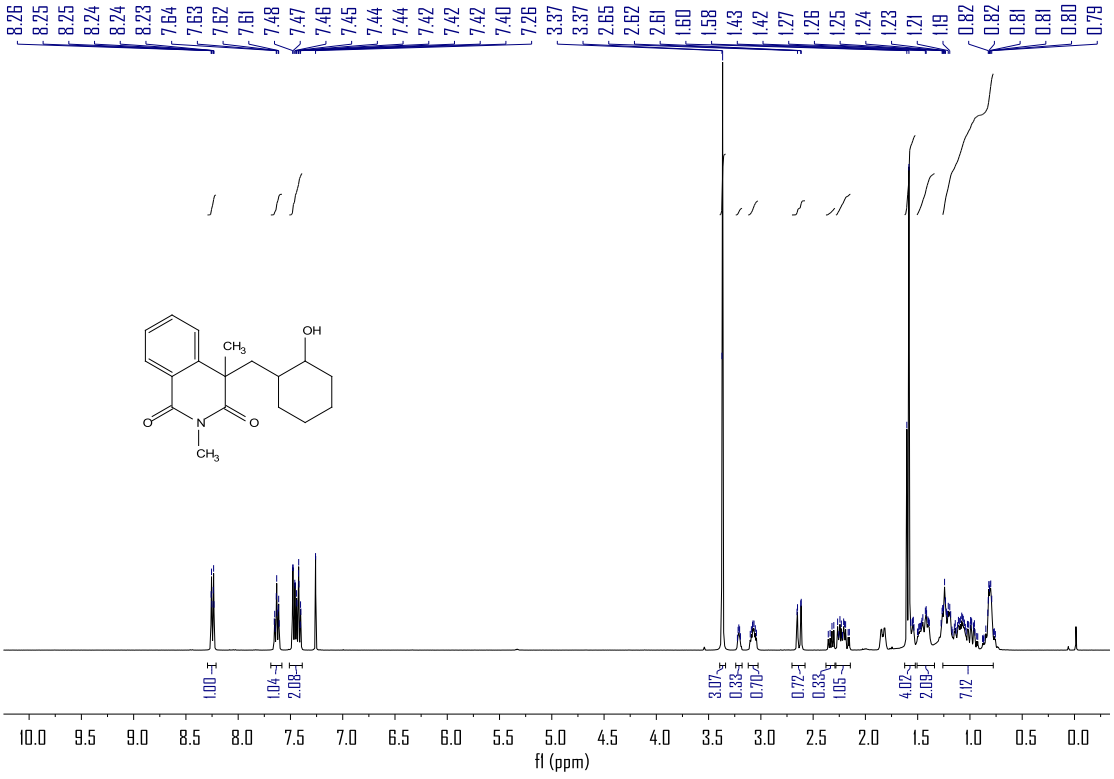
N
O
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

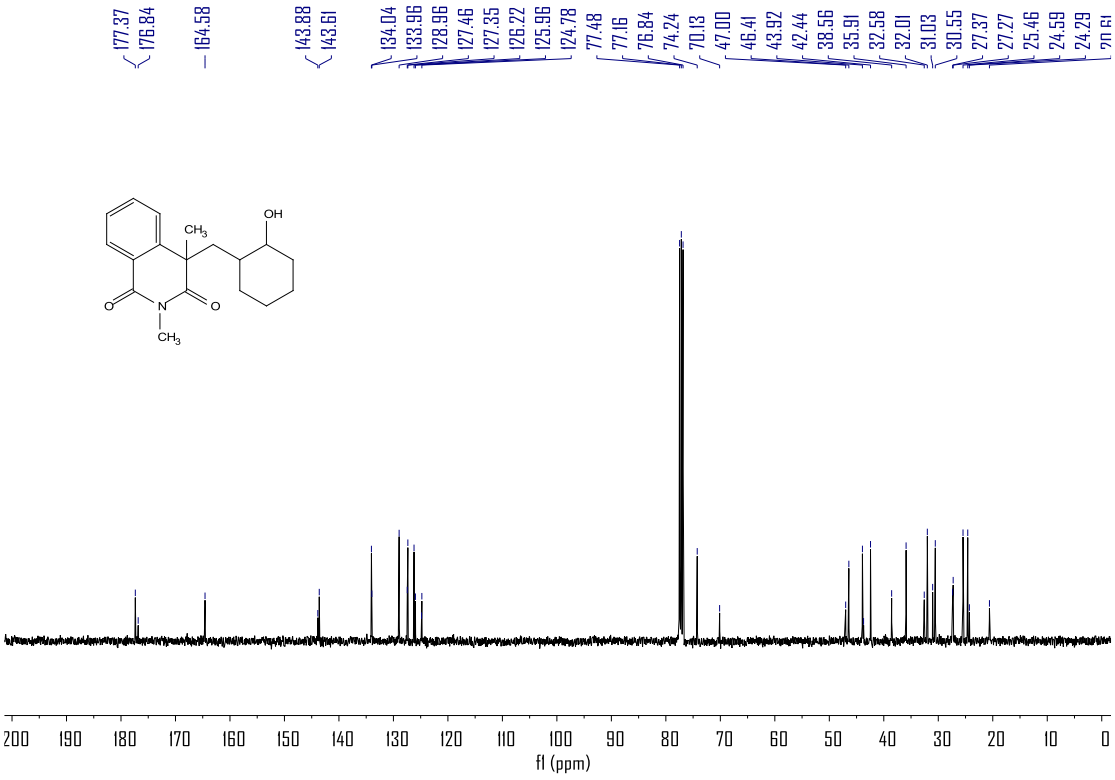


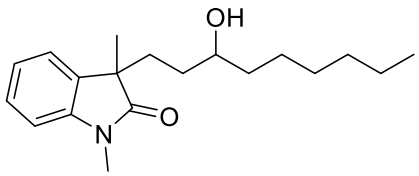
4-((2-hydroxycyclohexyl)methyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**isomer 2:3 = 2.3:1**, **5d**, pale-yellow liquid, 21 mg). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.25 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.63 (tt, *J* = 7.5, 1.7 Hz, 1H), 7.54 – 7.36 (m, 2H), 3.40 – 3.33 (m, 3H), 3.21 (dt, *J* = 6.1, 2.8 Hz, 0.3H), 3.07 (ddd, *J* = 13.1, 9.0, 4.3 Hz, 0.7H), 2.63 (dd, *J* = 14.2, 1.9 Hz, 0.7H), 2.36 – 2.30 (m, 0.3H), 2.28 – 2.14 (m, 1H), 1.62 – 1.53 (m, 4H), 1.51 – 1.38 (m, 2H), 1.26 – 0.77 (m, 7H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 177.37, 176.84, 164.58, 143.88, 143.61, 134.04, 133.96, 128.96, 127.46, 127.35, 126.22, 125.96, 124.84, 124.78, 74.24, 70.13, 47.00, 46.41, 43.92, 43.71, 42.44, 38.56, 35.91, 32.58, 32.01, 31.03, 30.55, 27.37, 27.27, 25.46, 24.59, 24.29, 20.61.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_3$: 324.1570; found: 324.1572.



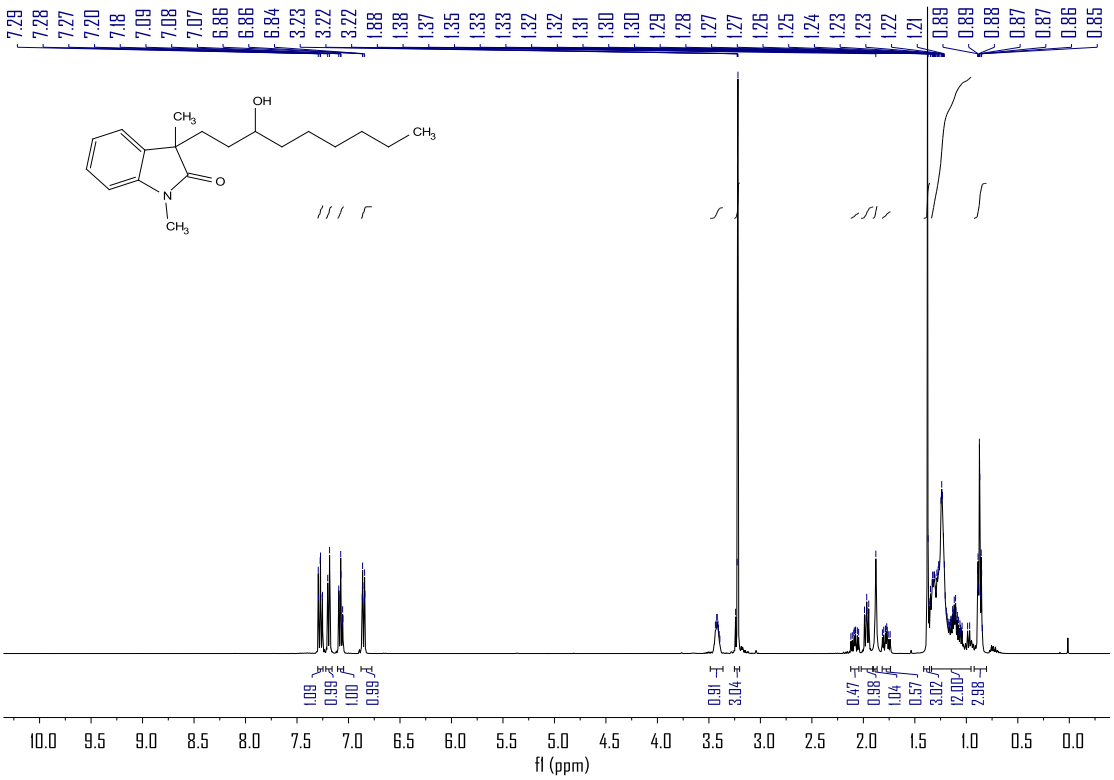


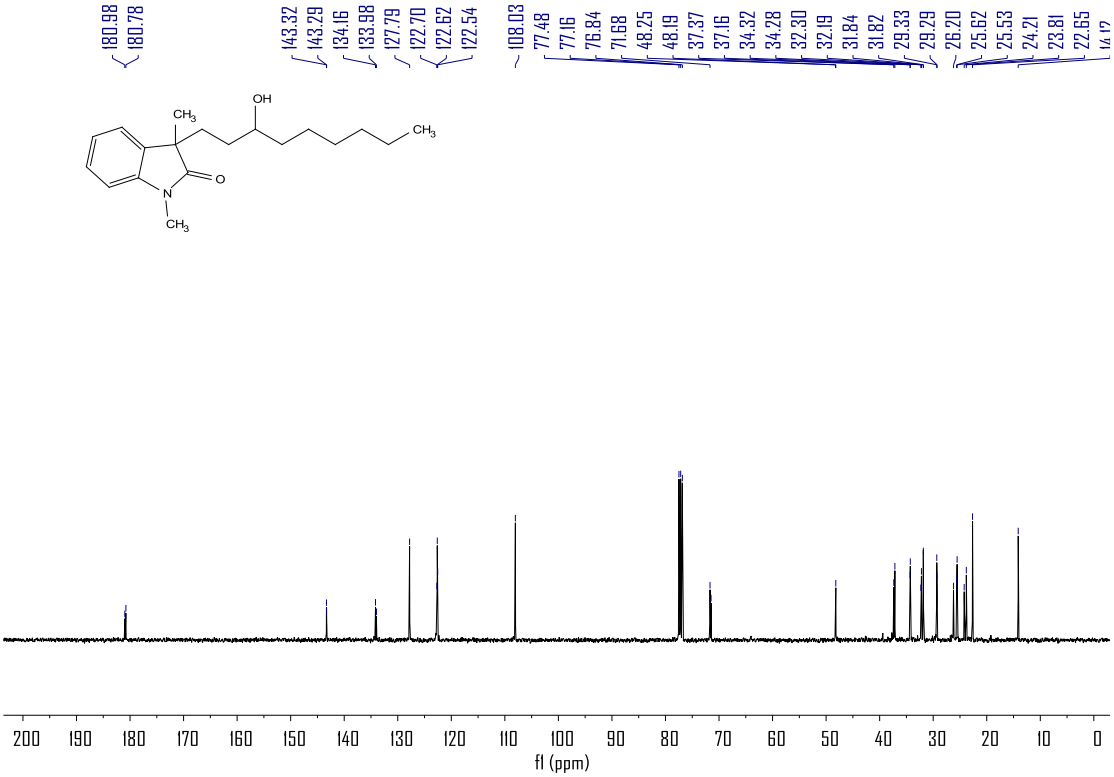


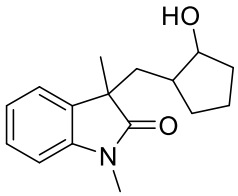
3-(3-hydroxynonyl)-1,3-dimethylindolin-2-one

Following the general procedure (**5e**, pale-yellow liquid, 53 mg, 88%, *d.r.* = 1.2:1). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 (td, *J* = 7.6, 1.2 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.07 (td, *J* = 7.6, 1.0 Hz, 1H), 6.85 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.42 (ddd, *J* = 10.2, 5.3, 2.6 Hz, 1H), 3.22 (d, *J* = 1.4 Hz, 3H), 2.13 – 2.05 (m, 0.45H), 2.00 – 1.94 (m, 1H), 1.88 (s, 1H), 1.78 (ddd, *J* = 13.4, 11.5, 5.2 Hz, 0.55H), 1.38 (s, 1H), 1.35 – 0.96 (m, 12H), 0.90 – 0.84 (m, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 180.98, 180.78, 143.32, 143.29, 134.16, 133.98, 127.79, 122.70, 122.62, 122.54, 108.03, 71.68, 71.49, 48.25, 48.19, 37.37, 37.16, 34.32, 34.28, 32.30, 32.19, 31.84, 31.82, 29.33, 29.29, 26.20, 25.62, 25.53, 24.21, 23.81, 22.65, 14.12.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{29}NNaO_2$: 326.2091; found: 326.2092.


7.29 7.28 7.27 7.20 7.18 7.09 7.08 7.07 6.86 6.86 6.84 3.23 3.22 3.22 1.88 1.38 1.37 1.35 1.33 1.33 1.32 1.32 1.31 1.30 1.30 1.29 1.28 1.27 1.27 1.26 1.25 1.24 1.23 1.23 1.22 1.21 0.89 0.89 0.88 0.87 0.87 0.86 0.85
OH
CH3
CH3
O
N
CH3
1.09 0.99 1.00 0.99 0.91 3.04 0.47 0.98 1.04 0.57 3.02 12.00 2.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

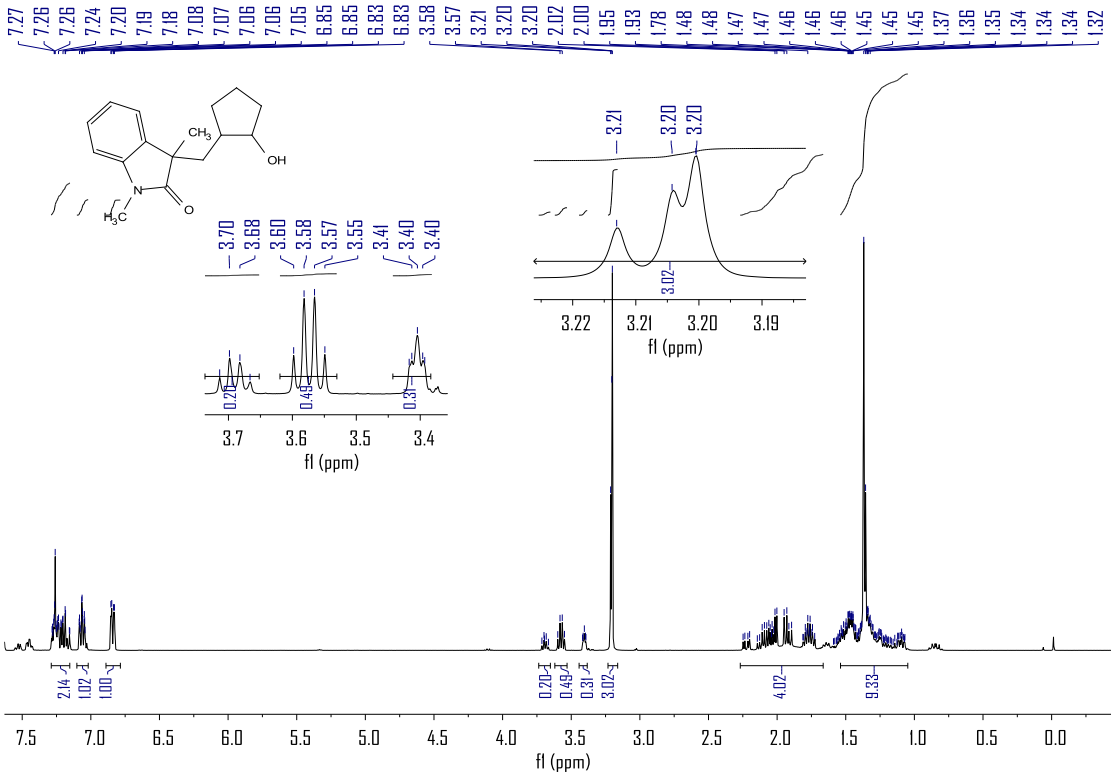

180.98 180.78 143.32 143.29 134.16 133.98 127.79 122.70 122.62 122.54 108.03 77.48 77.16 76.84 71.68 48.25 48.19 37.37 37.16 34.32 34.28 32.30 32.19 31.84 31.82 29.33 29.29 26.20 25.62 25.53 24.21 23.81 22.65 14.17
OH
CH3
CH3
O
N
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

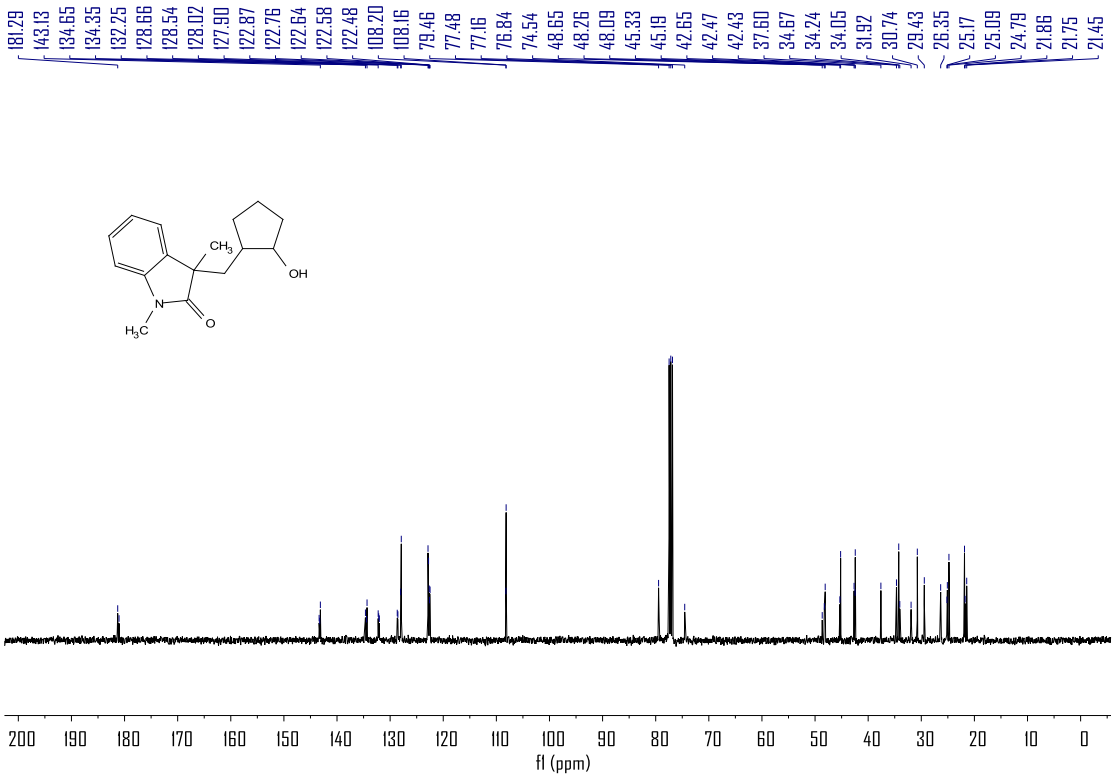


3-((2-hydroxycyclopentyl)methyl)-1,3-dimethylindolin-2-one

Following the general procedure (**isomer 1:2:3 = 1:1.5:2.5**, **5f**, pale-yellow liquid, 44 mg, 85%). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.13 (m, 2H), 7.10 – 7.03 (m, 1H), 6.84 (dd, *J* = 7.8, 2.6 Hz, 1H), 3.73 – 3.66 (m, 0.2H), 3.57 (q, *J* = 6.5 Hz, 0.5H), 3.44 – 3.37 (m, 0.3H), 3.24 – 3.16 (m, 3H), 2.27 – 1.71 (m, 4H), 1.56 – 1.06 (m, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.29, 181.04, 143.37, 143.26, 143.13, 134.65, 134.43, 134.35, 132.25, 132.15, 132.03, 128.66, 128.54, 128.02, 127.90, 122.87, 122.76, 122.64, 122.58, 122.48, 108.20, 108.16, 79.46, 74.54, 48.65, 48.26, 48.09, 45.33, 45.19, 42.65, 42.47, 42.43, 37.60, 34.67, 34.24, 34.05, 31.92, 30.74, 29.43, 26.35, 25.17, 25.09, 24.79, 21.86, 21.75, 21.45.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_2$: 282.1465; found: 282.1470.




181.29
143.13
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134.35
132.25
128.66
128.54
128.02
127.90
122.87
122.76
122.64
122.58
122.48
108.20
108.16
79.46
77.48
77.16
76.84
74.54
48.65
48.26
48.09
45.33
45.19
42.65
42.47
42.43
37.60
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200
190
180
170
160
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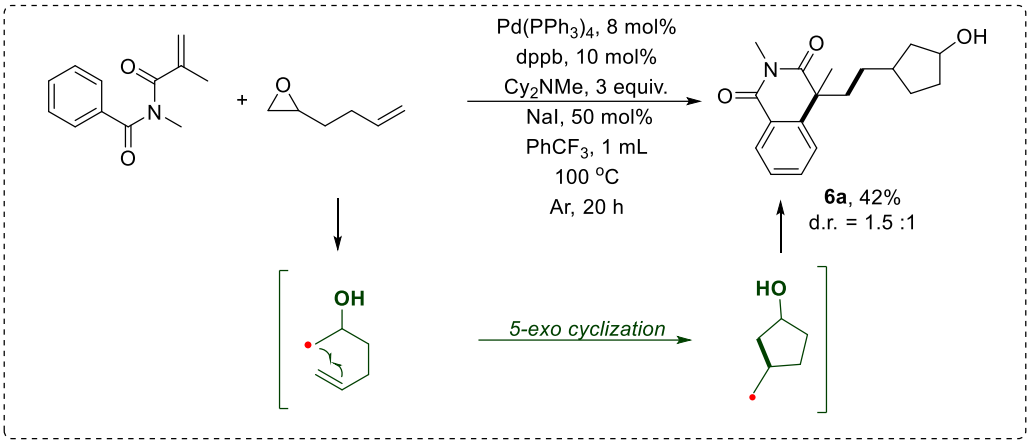
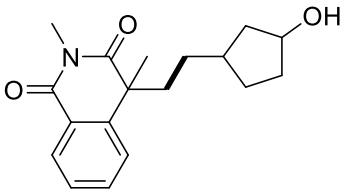
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

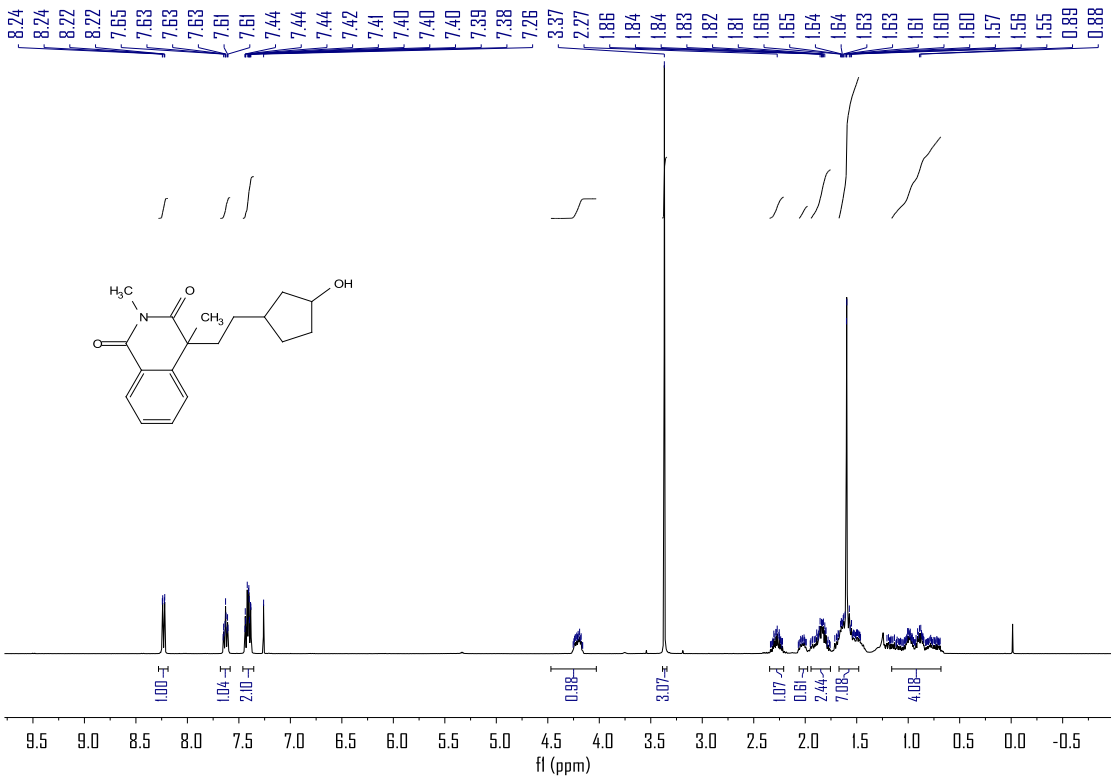


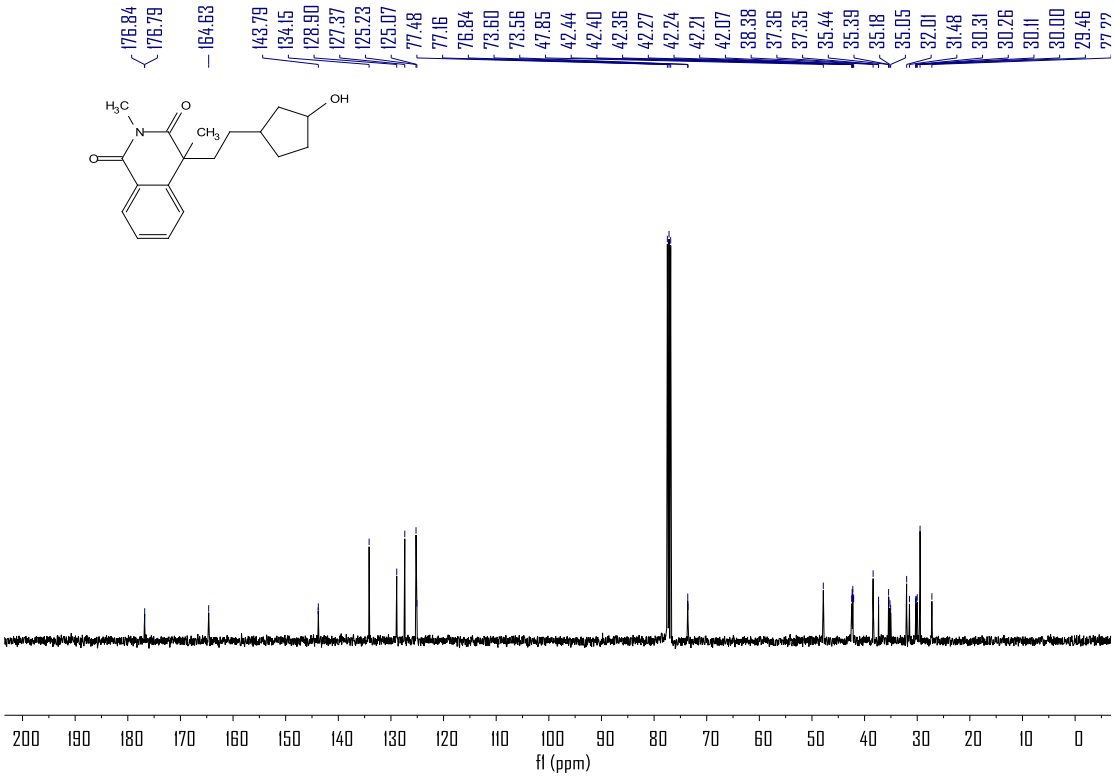


4-(2-(3-hydroxycyclopentyl)ethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione

Following the general procedure (**6a**, pale-yellow liquid, 25 mg, 42%, *d.r.* = 1.5:1). The residue was purified by silica gel-columun chromatography using PE/EtOAc (2:1) as an eluent. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.23 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.63 (tt, *J* = 7.7, 1.7 Hz, 1H), 7.47 – 7.36 (m, 2H), 4.30 – 4.11 (m, 1H), 3.37 (s, 3H), 2.34 – 2.22 (m, 1H), 2.08 – 1.77 (m, 3H), 1.72 – 1.47 (m, 7H), 1.21 – 0.68 (m, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.84, 176.79, 164.63, 143.83, 143.79, 134.15, 128.90, 127.37, 125.23, 125.07, 73.60, 73.56, 47.85, 42.44, 42.40, 42.36, 42.27, 42.24, 42.21, 42.07, 38.38, 37.36, 37.35, 35.44, 35.39, 35.18, 35.05, 32.01, 31.48, 30.31, 30.26, 30.11, 30.00, 29.46, 27.22.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_3$: 324.1570; found: 324.1575.


8.24 8.24 8.22 8.22 7.65 7.63 7.63 7.63 7.61 7.61 7.44 7.44 7.44 7.42 7.41 7.40 7.40 7.40 7.39 7.38 7.26
3.37 2.27 1.86 1.84 1.84 1.83 1.82 1.81 1.66 1.65 1.64 1.64 1.63 1.63 1.61 1.60 1.60 1.57 1.56 1.55 0.89 0.88
1.00 1.04 2.10 0.98 3.07 1.07 0.61 2.44 7.08 4.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


176.84 176.79 164.63 143.79 134.15 128.90 127.37 125.23 125.07 77.48 77.16 76.84 73.60 73.56 47.85 42.44 42.40 42.36 42.27 42.24 42.21 42.07 38.38 37.36 37.35 35.44 35.39 35.18 35.05 32.01 31.48 30.31 30.26 30.11 30.00 29.46
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1a, 0.2 mmol
1.0 equiv.

2a, 0.6 mmol
3.0 equiv.

3a, Trace

[M+H]$^+$
Determined by HRMS
Exact Mass: 230.2115
Found: 230.2110