Enantioselective synthesis of spiro γ-butyrolactones by N-heterocyclic carbene (NHC)-catalyzed formal [3+2] annulation of enals with 3-hydroxy oxindoles

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Supporting Information

1. General Information

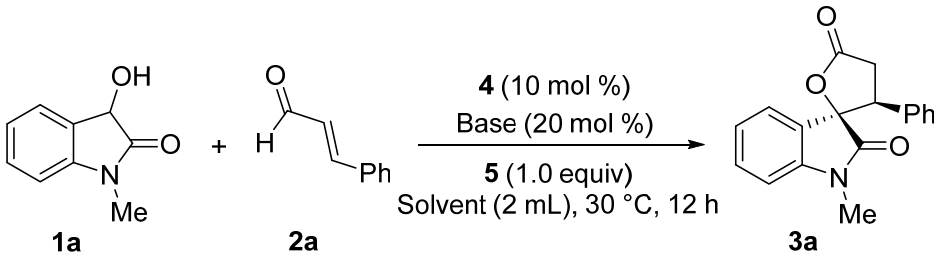
Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. Dry DME was purchased from commercial sources and stored under argon over 4 Å molecular sieves. The α,β-unsaturated aldehydes **2a, 2b, 2h, 2j** were purchased from commercial sources and were used without further purification, and others were synthesized following the literature procedure.[1] The dioxindole derivatives were synthesized by following the literature procedure.[2] The triazolium salt **4** was synthesized following the literature procedure.[3]

Analytical thin layer chromatography was performed on TLC Silica gel 60 F_{254}. Visualization was accomplished with short wave UV light or $KMnO_4$ staining solutions followed by heating. Flash chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with Pet. Ether-EtOAc solvent system.

All compounds were fully characterized. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400, in $CDCl_3$ as solvent. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). *In most of the cases, the two diastereomers are separable. Only in case of **3k, 3l** and **3m** the diastereomers are inseparable.* Infrared spectra were recorded on a Perkin-Elmer 1615 FT Infrared Spectrophotometer Model 60B. The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. HRMS (ESI) data were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. Optical rotation was measured with a JASCO P 2000 digital polarimeter at rt using 50 mm cell of 1 mL capacity. HPLC analysis was performed on Agilent Technologies 1260 Infinity with UV detector, and compound **3h**, **3i** were analyzed on Shimadzu Class-VP V6.12 SP5 with UV detector. X-ray intensity data were collected on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (Mo Kα=0.71073 Å) radiation at ambient temperature.

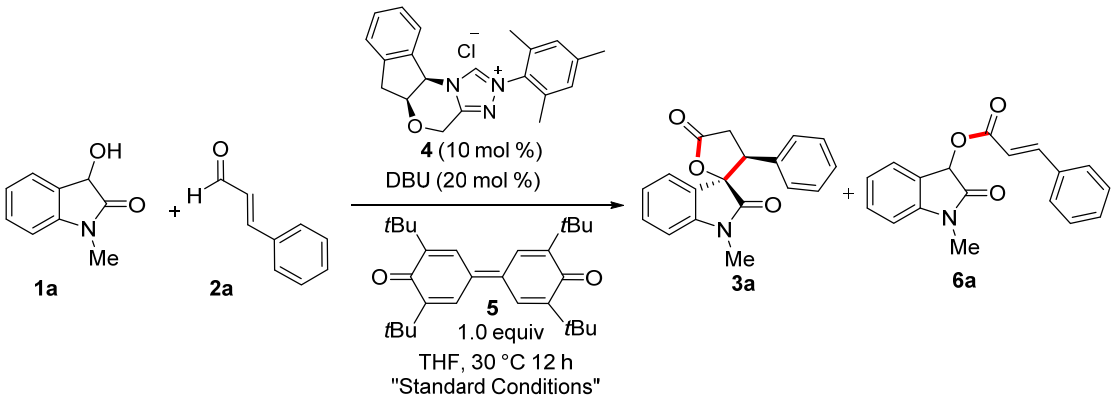
[1] A. A. Wubea, A. Hüfner, C. Thomaschitz, M. Blunder, M. Kollroser, R. Bauer, F. Bucar, *Bioorg. Med. Chem*., 2011, **19**, 567.
[2] B. M. Trost and K. Hirano, *Org. Lett*., 2012, **14**, 2446.
[3] J. R. Struble, and J. W. Bode, *Org. Synth*., 2010, **87**, 362.

2. General Procedure for the Optimization of Reaction Conditions



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1a** (0.25 mmol) and enal **2a** (0.25 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added solvent (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture base (0.05 mmol) was successively added. After 12 h the reaction was quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude products, which was analyzed using ^1H NMR using CH_2Br_2 (18.0 μL, 0.25 mmol) as the internal standard. The enantiomeric excess was determined by HPLC analysis on a chiral column.

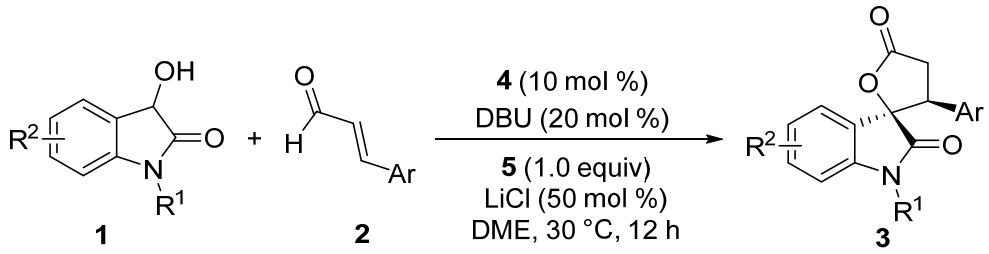
3. Optimization Studies



entry	variation of the standard conditions	yield of **3a** (%)	*d.r* of **3a**[b]	*er* of **3a** (%)[c]	yield of **6a** (%)
1	None	86	4:1	87:13	-
2	Na_2CO_3 instead of DBU	10	>10:1	53:47	74
3	KO*t*-Bu instead of DBU	31	>10:1	53:47	33
4	DABCO instead of DBU	15	>10:1	57:43	57
5	DMAP instead of DBU	25	>10:1	65:35	41
6	TBD instead of DBU	75	6:1	82:18	-
7	toluene instead of THF	68	10:1	60:40	-
8	CH_2Cl_2 instead of THF	89	2:1	88:12	-
9	$CHCl_3$ instead of THF	84	2:1	60:40	-
10	CH_3CN instead of THF	86	3:1	70:30	-
11	1,4-dioxane instead of THF	98	10:1	75:25	-
12	DME instead of THF	84	4:1	89:11	-
13	50 mol % of LiCl in standard condition	81	3:1	95:5	-
14	20 mol % of LiCl in DME	77	3:1	95:5	-
15	***50 mol % of LiCl in DME***	***82(82)***	**4:1**	***95:5***	-
16	1 equiv of LiCl in DME	78	3:1	95:5	-
17	2 equiv of LiCl in DME	91	5:1	94:6	-
18	3 equiv of LiCl in DME	88	5:1	92:8	-
19	4 equiv of LiCl in DME	95	5:1	94:6	-

[a] Standard conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), **4** (10 mol %), DBU (20 mol %), THF (2.0 mL), 30 °C and 12 h. The yields were determined by ^{1}H-NMR analysis of crude products using CH_2Br_2 as the internal standard, isolated yield in parentheses. [b] Determined by ^{1}H-NMR Spectroscopy of crude reaction mixture [c] Determined by HPLC analysis on a chiral column.

4. General Procedure for the Enantioselective Synthesis of Spiro γ-Butyrolactones



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1** (0.25 mmol) and enal **2** (0.25 mmol), and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture DBU (0.008 gm, 7.5 μL, 0.05 mmol) was successively added. After 12 h, when the reaction is complete, the solvent was evaporated and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding functionalized spiro γ-butyrolactone. All the racemic compounds were synthesized using IMes.HCl (10 mol %) and DBU (20 mol %) in THF solvent.

5. X-ray Data of 3n

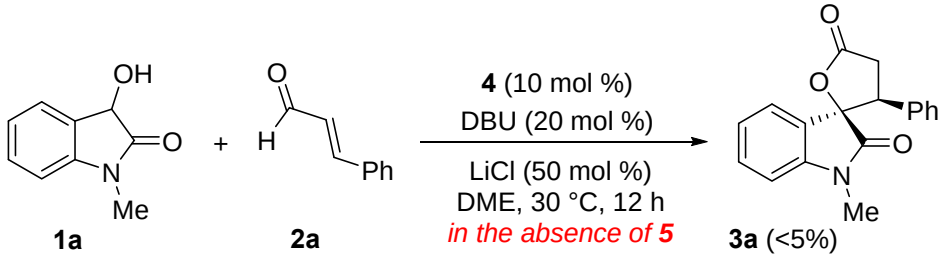
X-ray intensity data measurements of compound **3n** was carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (MoK_α= 0.71073Å) radiation at 100(2) K. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 15 secs keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was monitored by APEX2 program (Bruker, 2006).[4] All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on F^2.[5] All the hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms. An *ORTEP* III[3] view of both compounds were drawn with 50% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii. The absolute configuration of the molecule was found by using Flack parameter refinement.[6] A value of Flack parameter of 0.15(6) established that the configuration of atoms C1 is *R* and C11 is *S*.

Crystal data of **3n** $C_{18}H_{14}ClNO_3$, M = 327.75, colorless plate, 0.43 x 0.31 x 0.20 mm^3, monoclinic, space group $P2_1$, a = 9.020(4) Å, b = 10.237(4) Å, c = 9.318(4) Å, β = 117.399(6)°, V = 764.0(5) $Å^3$, Z = 2, T = 100(2) K, $2\theta_{max}$=50.00°, D_{calc} (g cm^{-3}) = 1.425, $F(000)$ = 340, μ (mm^{-1}) = 0.265, 9508 reflections collected, 2640 unique reflections (R_{int}=0.0883), 2245 observed ($I > 2\sigma(I)$) reflections, multi-scan absorption correction, T_{min} = 0.8947, T_{max} = 9490, 209 refined parameters, number of restraints = 31, S = 1.122, $R1$ = 0.0457, $wR2$ = 0.1121 (all data R = 0.0691, $wR2$ = 0.1350), maximum and minimum residual electron densities; $\Delta\rho_{max}$ = 0.578, $\Delta\rho_{min}$= -0.671 ($eÅ^{-3}$).

[4] Bruker (2006). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
[5] G. M. Sheldrick, *Acta Crystallogr*., 2008, A**64**, 112.
[6] L. J. Farrugia, *J. Appl. Cryst.* 1997, **30**, 565.

6. Mechanistic Experiments

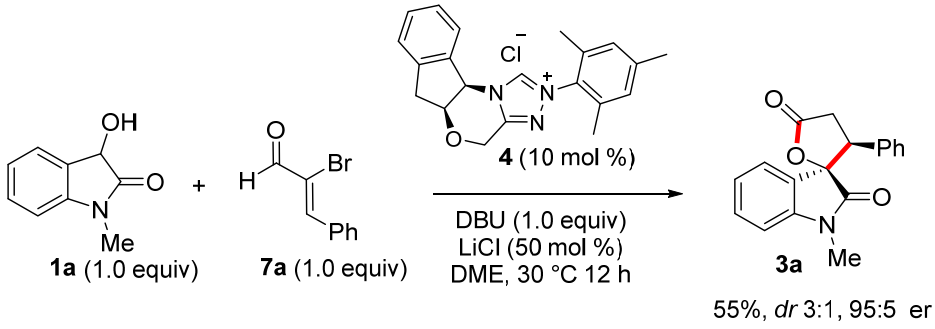
Procedure for the Enantioselective Synthesis of Spiro γ-Butyrolactone in absence of oxidant (Scheme 5, eq 3)



To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and isatin alcohol **1a** (0.25 mmol) and enal **2a** (0.25 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture DBU (0.008 gm, 7.5 µL, 0.05 mmol) was successively added. After 12 h, the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^1H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard. Under these conditions, only traces of product **3a** was observed.

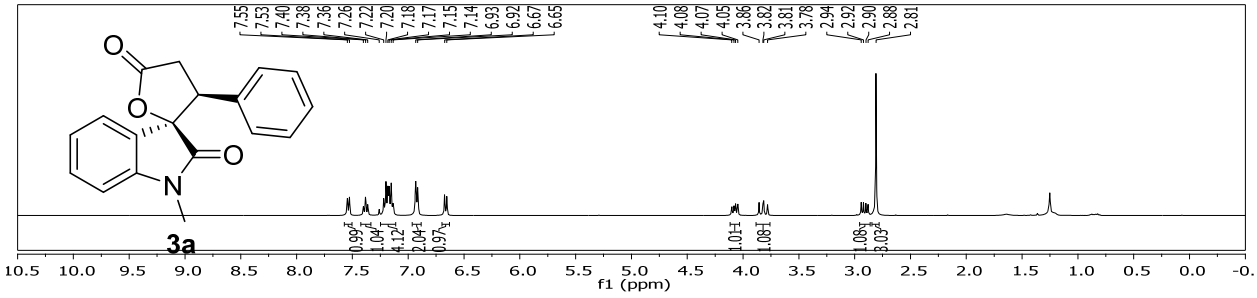
*This experiment indicates the role of oxidant **5** in generating the α,β-unsaturated acyl azolium intermediate. It is noteworthy that under these conditions, the formation of the corresponding N-substituted isatin was also not observed.*

Procedure for the Enantioselective Synthesis of Spiro γ-Butyrolactone by Reactions of Dioxindole with 2-Bromoenal (Scheme 5, eq 4)

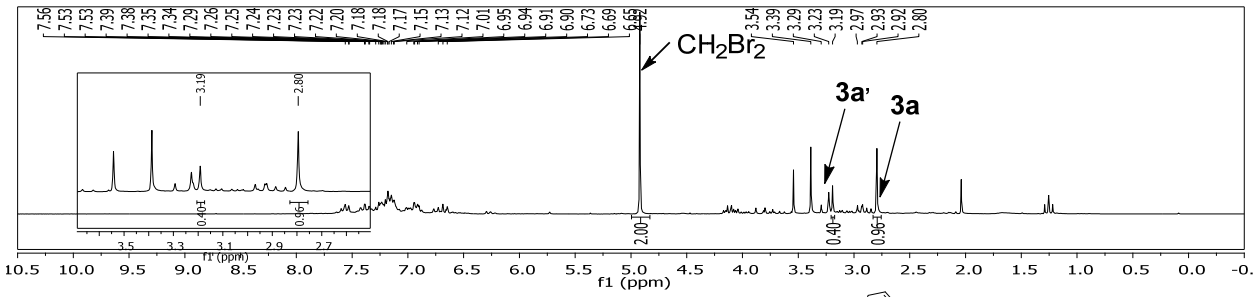


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1a** (0.25 mmol) and 2-bromoenal **7a** (0.25 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture DBU (0.038 gm, 37.0 µL, 0.05 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

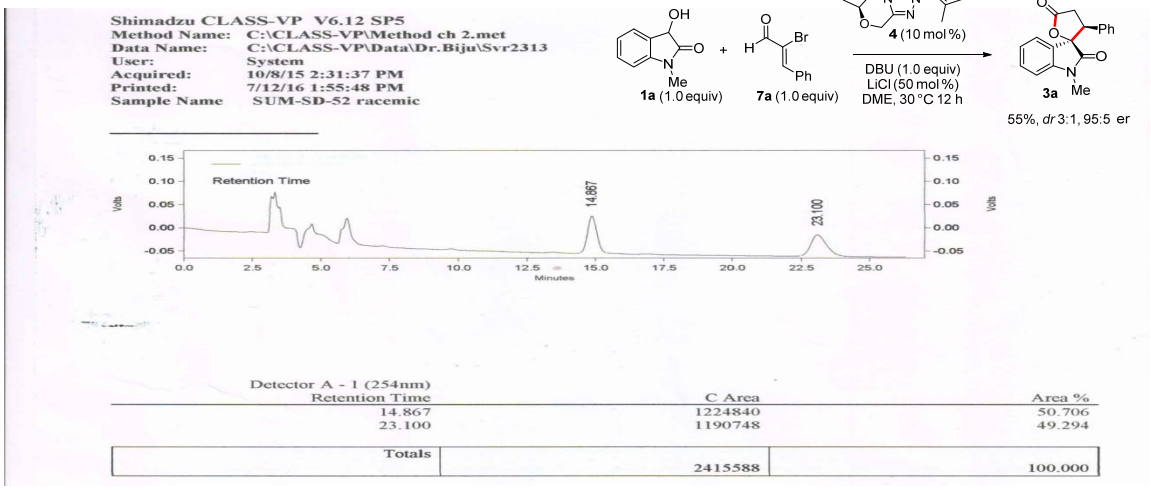
^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)

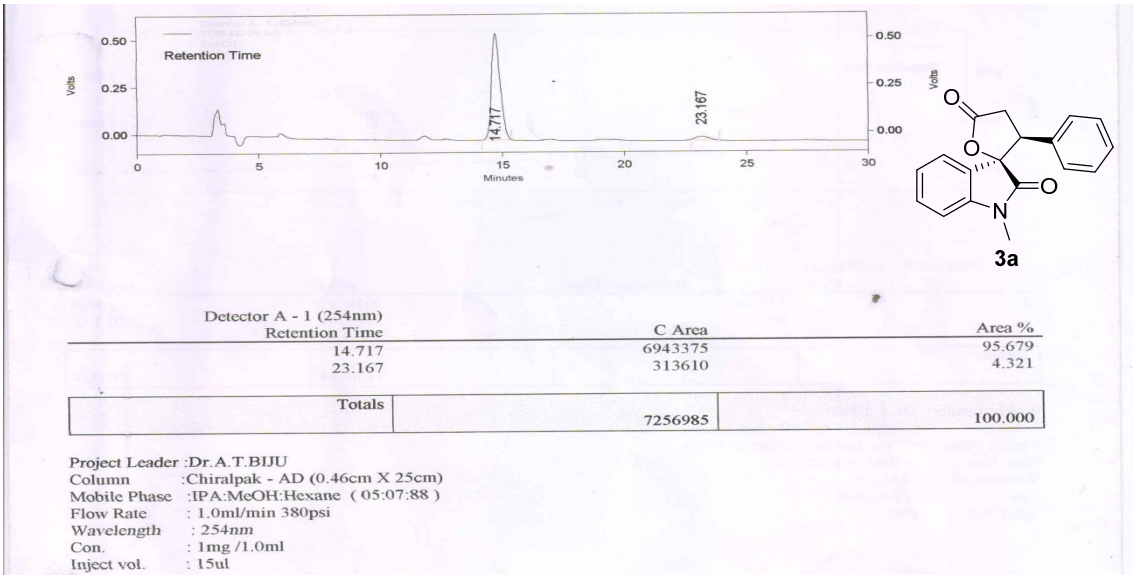


^{1}H-NMR of Crude Reaction Mixture



HPLC data of spiro γ-butyrolactone 3a



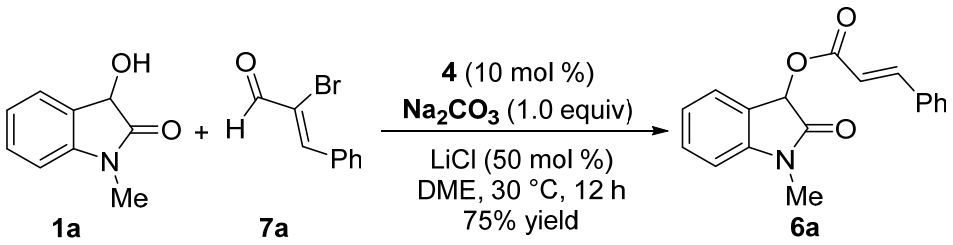


Detector A - 1 (254nm) Retention Time	C Area	Area %
14.717	6943375	95.679
23.167	313610	4.321
Totals	7256985	100.000

Project Leader :Dr.A.T.BIJU
Column :Chiralpak - AD (0.46cm X 25cm)
Mobile Phase :IPA:MeOH:Hexane (05:07:88)
Flow Rate : 1.0ml/min 380psi
Wavelength : 254nm
Con. : 1mg /1.0ml
Inject vol. : 15ul

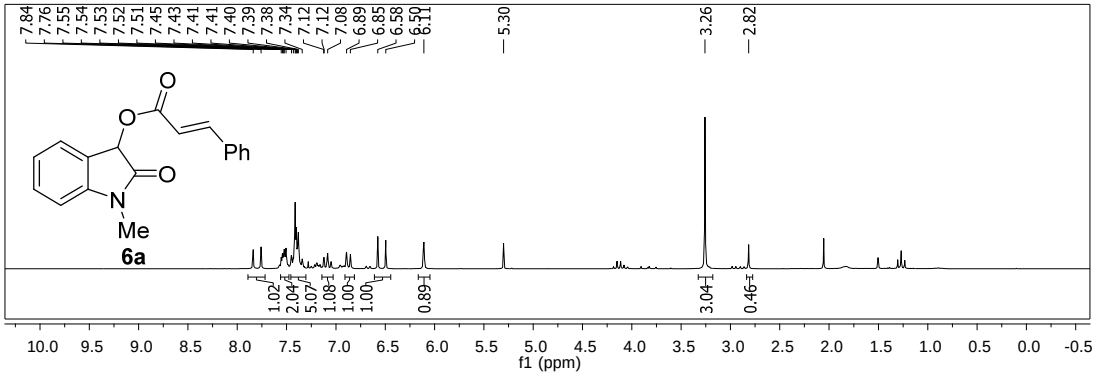
*The formation of **3a** under these conditions clearly indicate the intermediacy of chiral α,β-unsaturated acyl azolium intermediate.*

Procedure for the Reaction of Dioxindole with Bromoenal in Na_2CO_3 as base, leading to α,β-unsaturated ester formation (Scheme 5, eq 5)

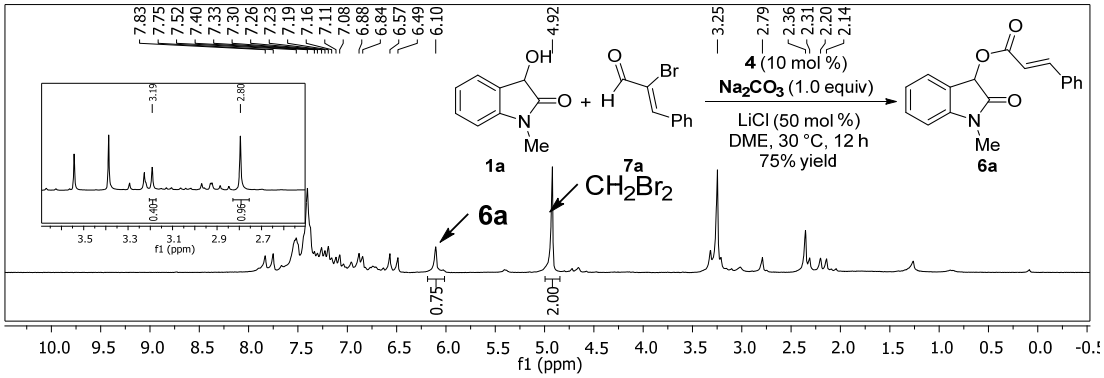


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1a** (0.25 mmol) and 2-bromoenal **7a** (0.25 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture Na_2CO_3 (0.026 gm, 0.25 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^1H NMR using CH_2Br_2 (18.0 μL, 0.25 mmol) as the internal standard.

^{1}H-NMR of 1-methyl-2-oxoindolin-3-yl cinnamate (6a)

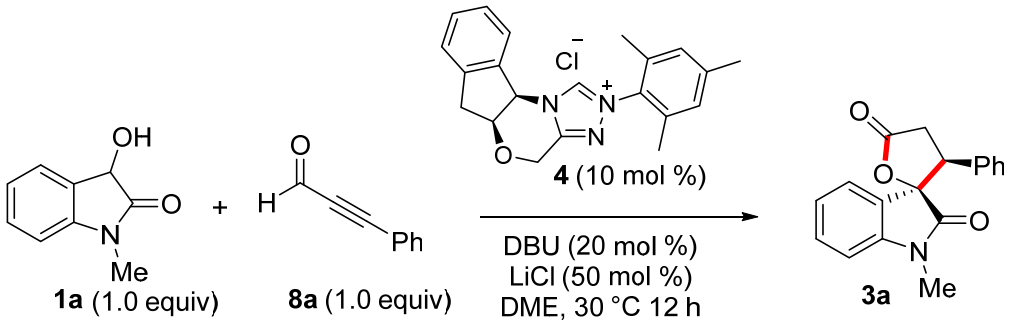


^{1}H-NMR of Crude Reaction Mixture (Scheme 3 eq 4)



It is reasonable to believe that the use of an inorganic base allowed the 1,2-addition of the dioxindole onto the chiral α,β-unsaturated acyl azolium intermediate.

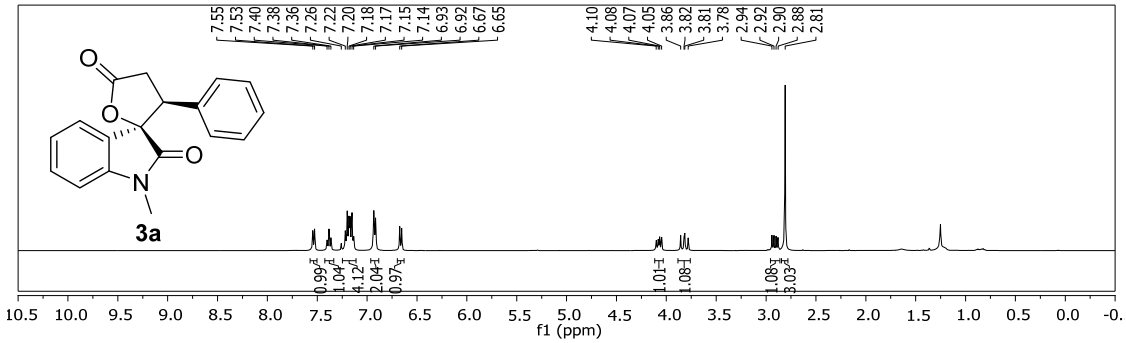
Procedure for the Enantioselective Synthesis of Spiro γ-Butyrolactone by Reactions of Dioxindole with ynal (Scheme 5, eq 6)



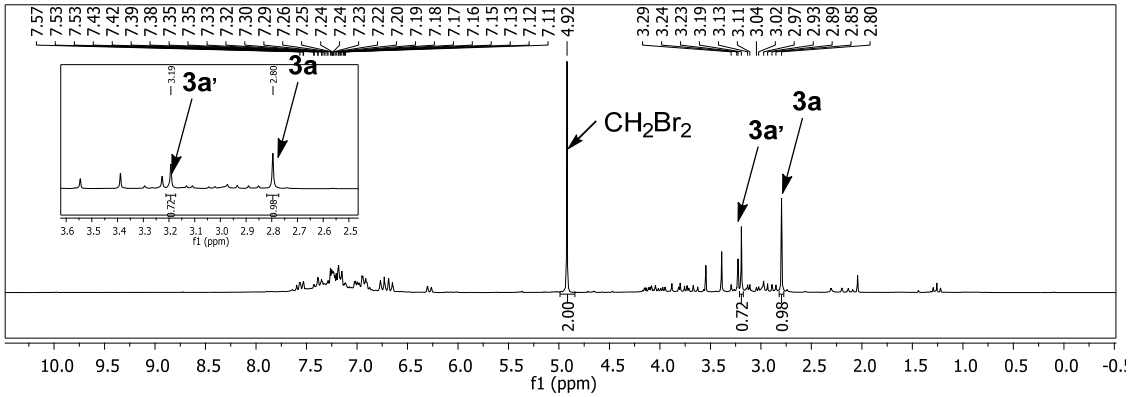
To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1a** (0.25 mmol) and ynal **8a** (0.25 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere.

The resultant reaction mixture was kept stirring at 30 °C. To this mixture DBU (0.008 gm, 7.5 µL, 0.05 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^1H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

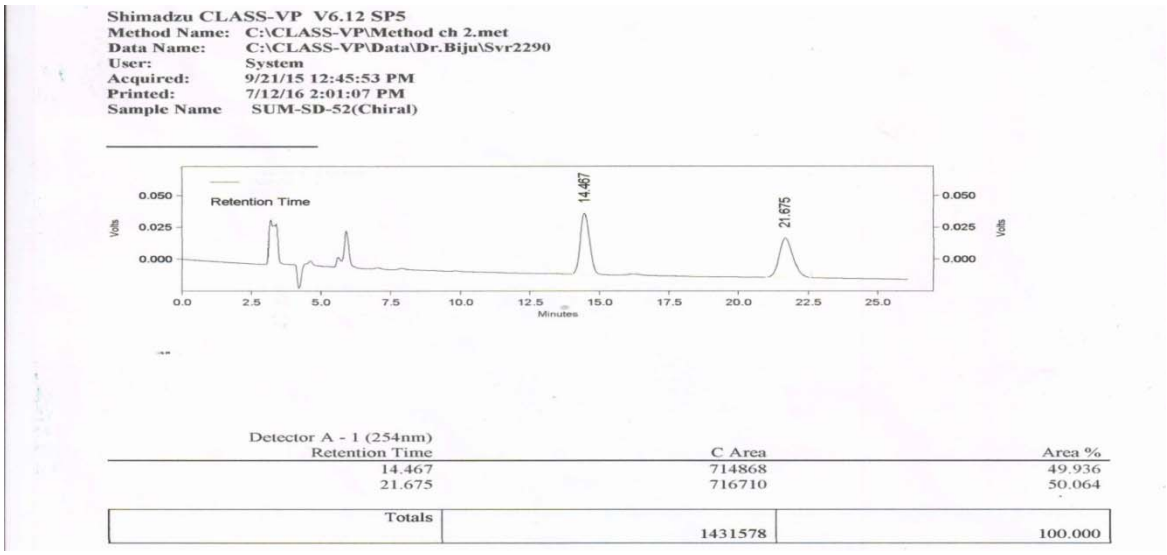
^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)



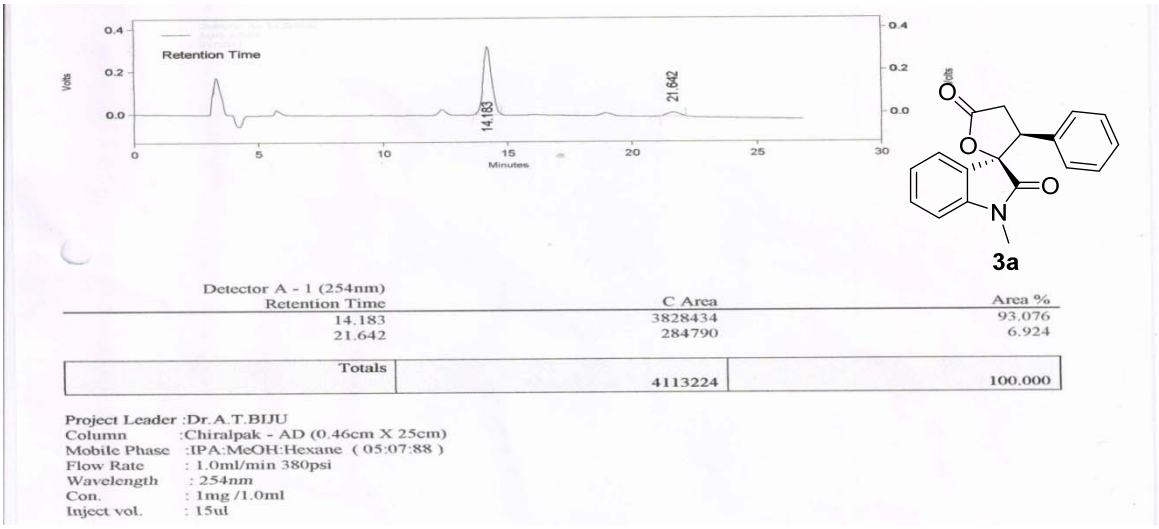
^{1}H-NMR of Crude Reaction Mixture (Scheme 3, eq 5)



HPLC data of spiro γ-butyrolactone 3a



Detector A - 1 (254nm) Retention Time	C Area	Area %
14.467	714868	49.936
21.675	716710	50.064
Totals	1431578	100.000

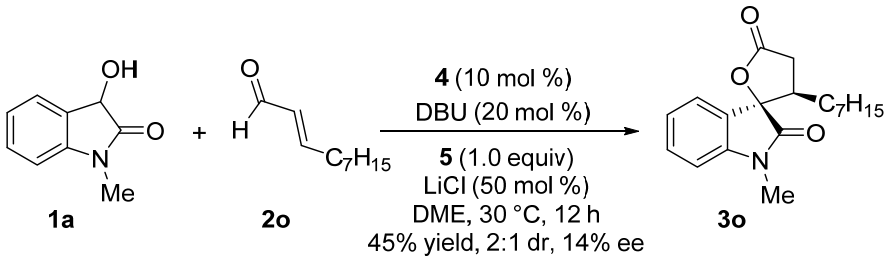


Detector A - 1 (254nm) Retention Time	C Area	Area %
14.183	3828434	93.076
21.642	284790	6.924
Totals	4113224	100.000

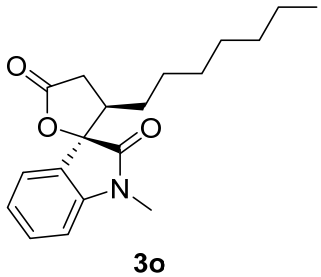
Project Leader :Dr.A.T.BIJU
Column :Chiralpak - AD (0.46cm X 25cm)
Mobile Phase :IPA:MeOH:Hexane (05:07:88)
Flow Rate : 1.0ml/min 380psi
Wavelength : 254nm
Con. : 1mg /1.0ml
Inject vol. : 15ul

*The formation of **3a** under these conditions clearly indicate the intermediacy of chiral α,β-unsaturated acyl azolium intermediate.*

NHC-catalyzed reaction of dioxindole with aliphatic enal (Scheme 6)



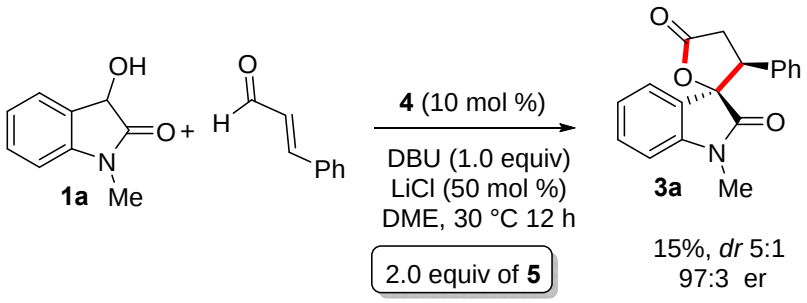
Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and (*E*)-dec-2-enal **2o** (39.0 mg, 46 μL , 0.50 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*R*)-3-heptyl-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **(3o)** as a yellow sticky liquid (35.0 mg, 45% yield, dr 2:1).



***R**f* (Pet. ether /EtOAc = 70/30): 0.66; 57:43 er, **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 11.1 min, Minor: 7.9 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 – 7.30 (m, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 3.16 (s, 3H), 2.95 (m, 1H), 2.74 (m, 2H), 1.50 – 1.30 (m, 1H), 1.30 – 0.95 (m, 12H), 0.81 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.68, 173.3, 144.5, 131.2, 125.4, 124.3,

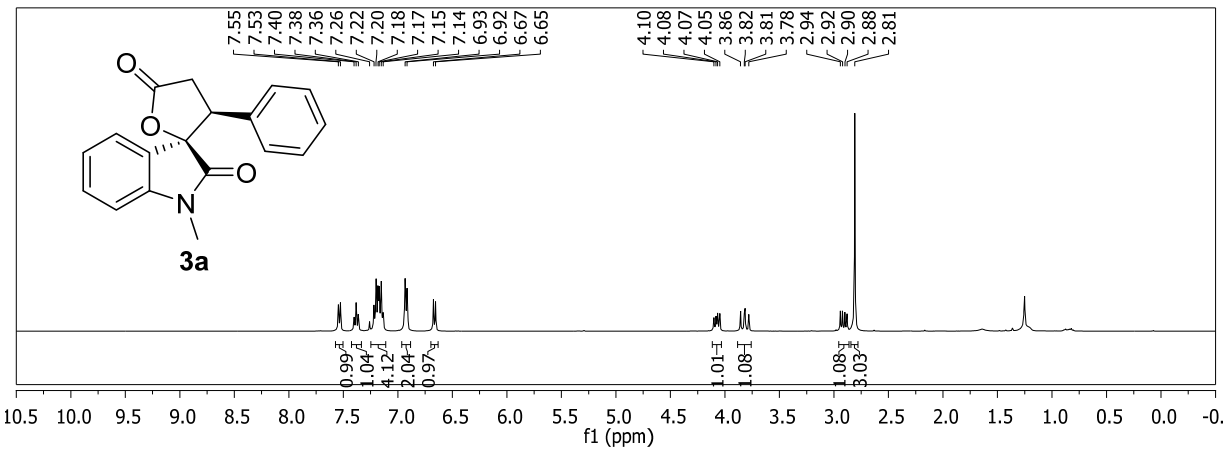
123.6, 108.8, 85.6, 45.5, 33.9, 31.7, 29.3, 29.0, 28.4, 28.0, 26.3, 22.6, 14.1. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{25}NO_3Na$: 338.1727, found: 338.1719. **FTIR (cm^{-1})** 2929, 2861, 2404, 1792, 1726, 1616, 1467, 1422, 1368, 1302, 1216, 1010.

General Procedure for the Reaction with excess oxidant 5 (Scheme 9)

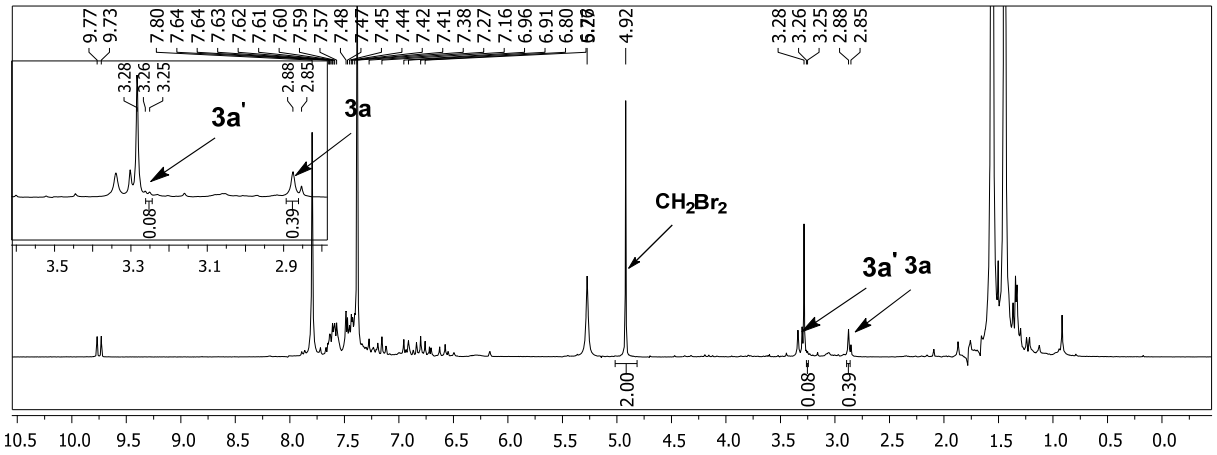


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and isatin alcohol **1a** (0.25 mmol) and oxidant **5** (0.50 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture cinnamaldehyde **2a** (0.25 mmol) and DBU (0.008 gm, 7.5 µL, 0.05 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)

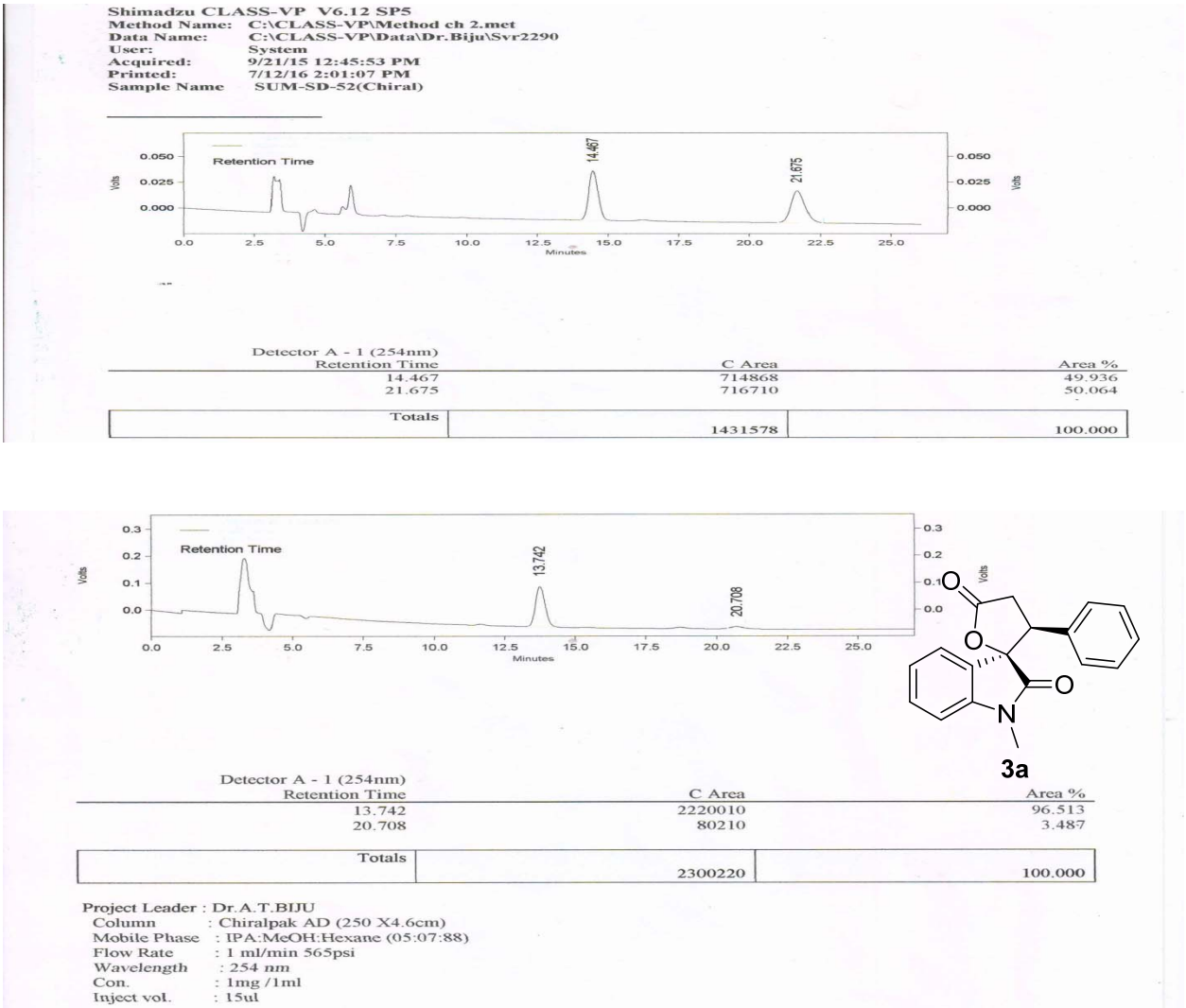


^{1}H-NMR of Crude Reaction Mixture with 2.0 equiv oxidant 5

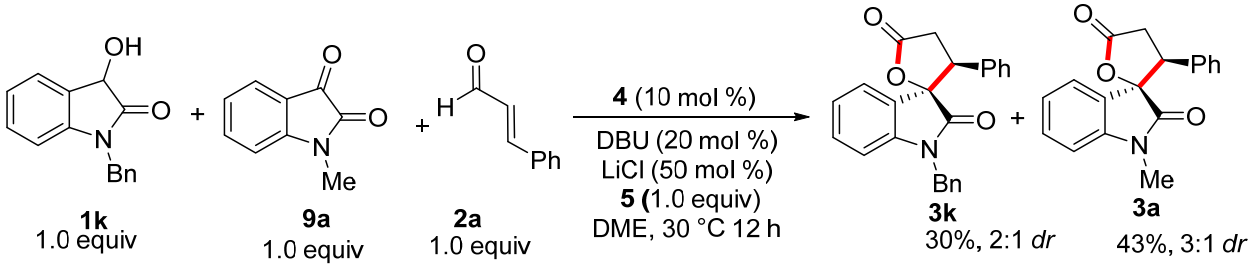


From the above experiments, it is clear that in presence of excess oxidant the reactivity dramatically decreases, which indicates existence of homoenolate reactivity along with α,β-unsaturated acylazolium reactivity.

HPLC data of spiro γ-butyrolactone 3a with 2.0 equiv oxidant loading

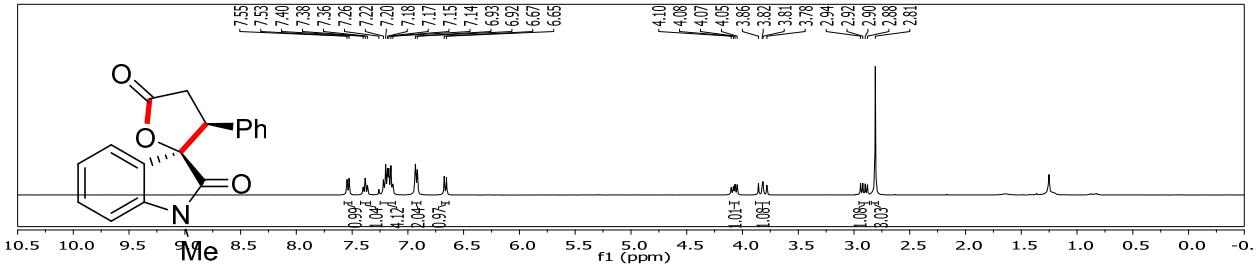


General Procedure for the Competition experiments between Isatin and Dioxindole

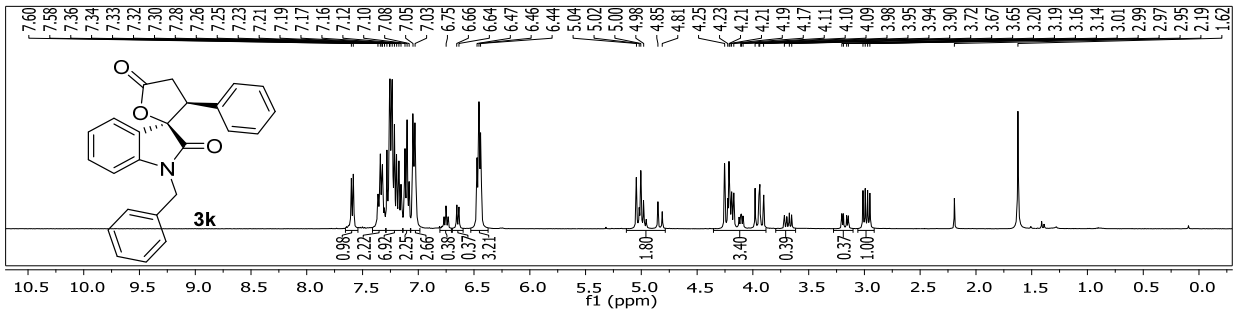


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1k** (0.25 mmol) and Isatin **9a** (0.25 mmol) and LiCl (0.125 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture mixture cinnamaldehyde **2a** (0.25 mmol) and DBU (0.008 gm, 7.5 µL, 0.05 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

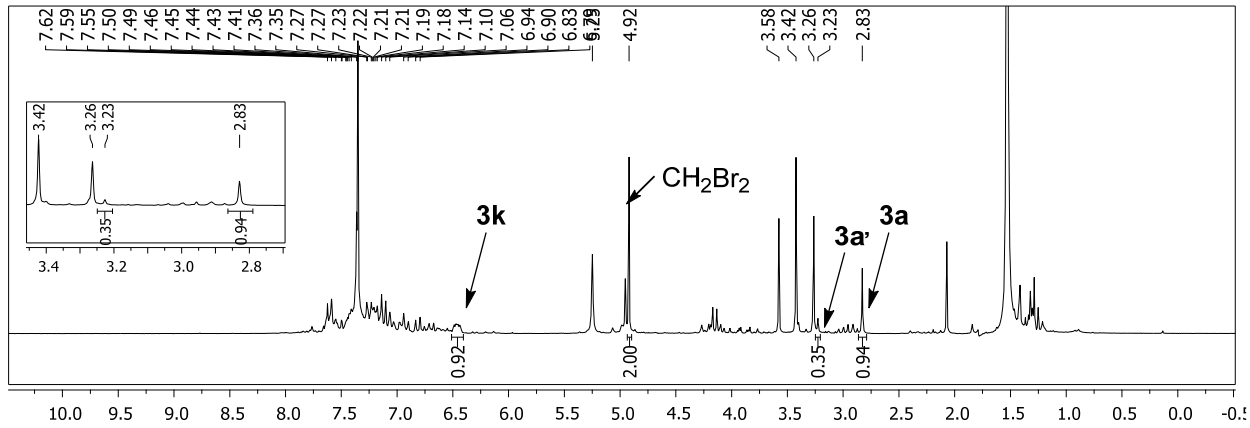
^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)



^{1}H-NMR of (2*R*,3*S*)-1'-benzyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione(3k)

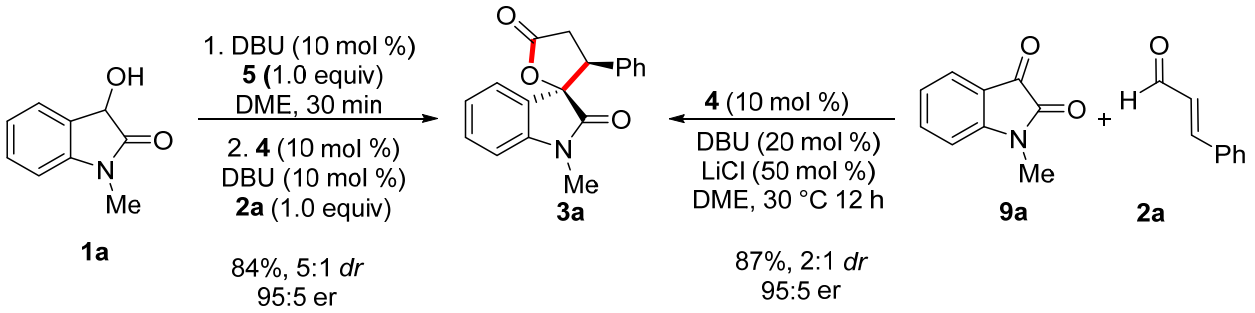


^{1}H-NMR of Crude Reaction Mixture (Scheme 7, eq 6)



This experiment also indicates the compatibility of the [3+2] annulation of α,β-unsaturated acyl azolium with dioxindoles as well as the [3+2] annulation of NHC-bound homoenolate with isatins under the present conditions.

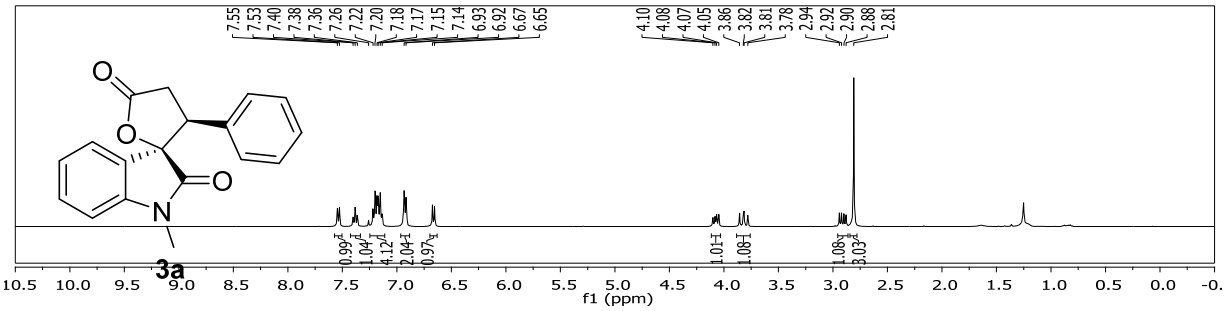
Experiments to isatin formation and Homoenolate Reactivity



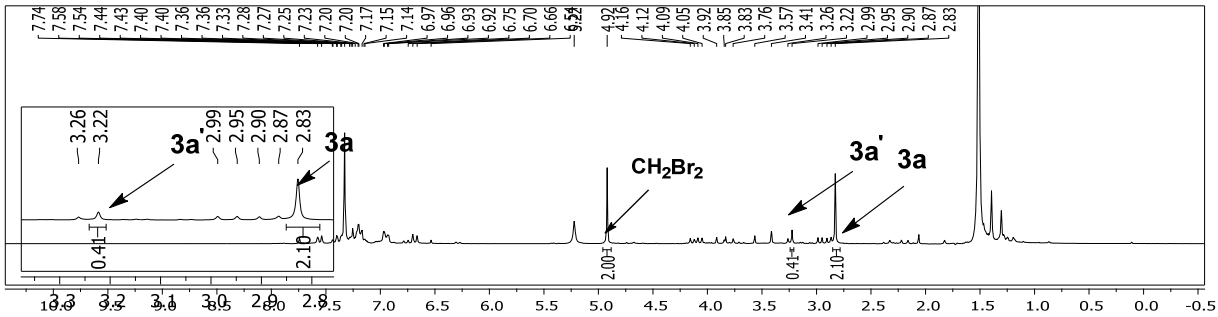
To support homoenolate reactivity, we carried out two parallel experiments. In first experiment, to a flame-dried screw-capped test tube equipped with a magnetic stir bar was added DBU (0.004 gm, 4.0 µL, 0.025 mmol) and isatin alcohol **1a** (0.25 mmol) and oxidant **5** (0.25 mmol) and LiCl (0.125 mmol) in presence of DME (2 mL). The mixture was stirred for 30 min which led to complete conversion of isatin from isatin alchol. To this reaction mixture, triazolium salt **4** (0.009 g, 0.025 mmol), DBU (0.004 gm, 4.0 µL, 0.025 mmol) and cinnamaldehyde **2a** (0.25 mmol) was successfully added. After 12 h, the reaction was quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL), filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude reaction mixture, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard shows spiro lactone in 83% yield and 93% ee.

Similarly in case of second experiments To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and isatin **9a** (0.25 mmol) and LiCl (0.125 mmol). Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture cinnamaldehyde **2a** (0.25 mmol) and DBU (0.008 gm, 7.5 μL, 0.05 mmol) was successively added. After 12 h the reaction was quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude reaction mixture, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 μL, 0.25 mmol) as the internal standard shows spiro lactone in 87% yield and 91% ee.

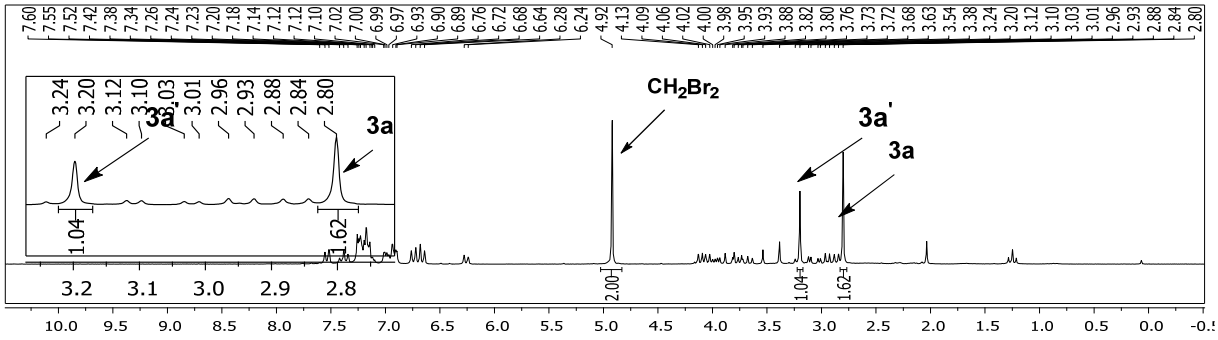
^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)



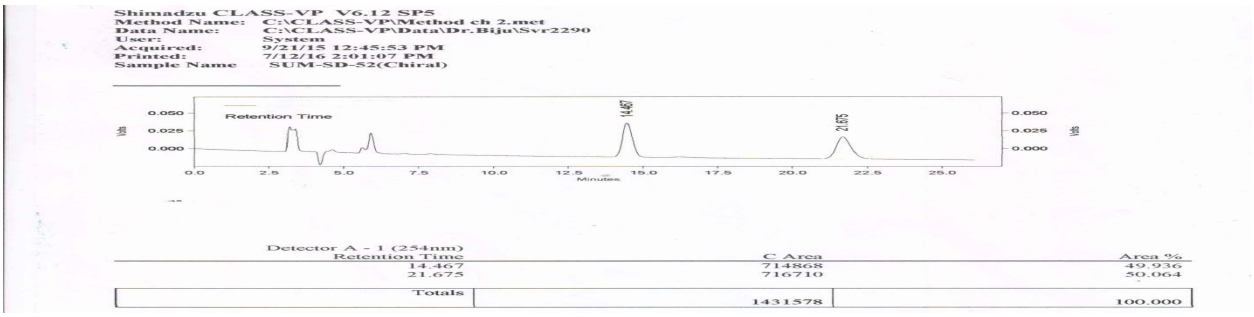
^{1}H-NMR of Crude Reaction Mixture under oxidative condition (Scheme 7 eq 7)



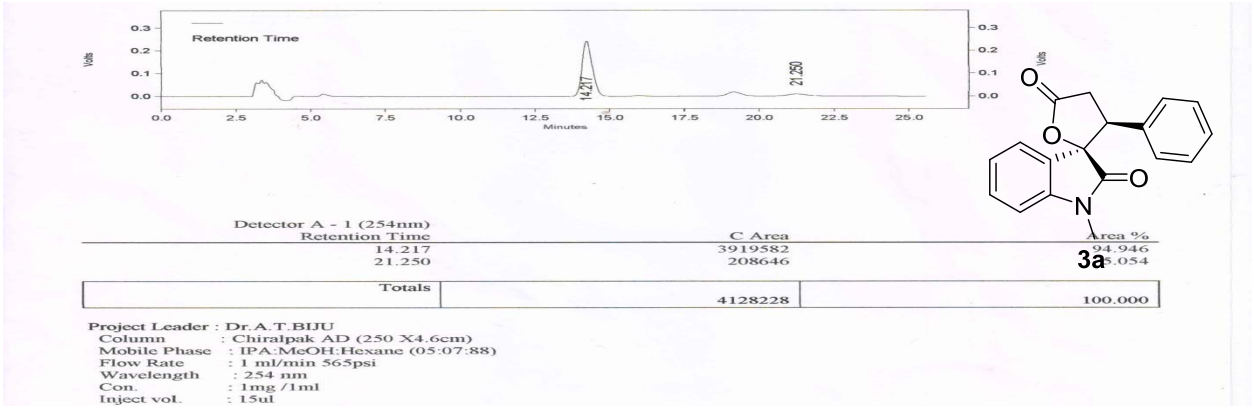
^{1}H-NMR of Crude Reaction Mixture under Homoenolate condition(Scheme 7 eq 7)



HPLC data of spiro γ-butyrolactone 3a under oxidative condition



Detector A - 1 (254nm) Retention Time	C Area	Area %
14.467	714868	49.936
21.675	716710	50.064
Totals	1431578	100.000

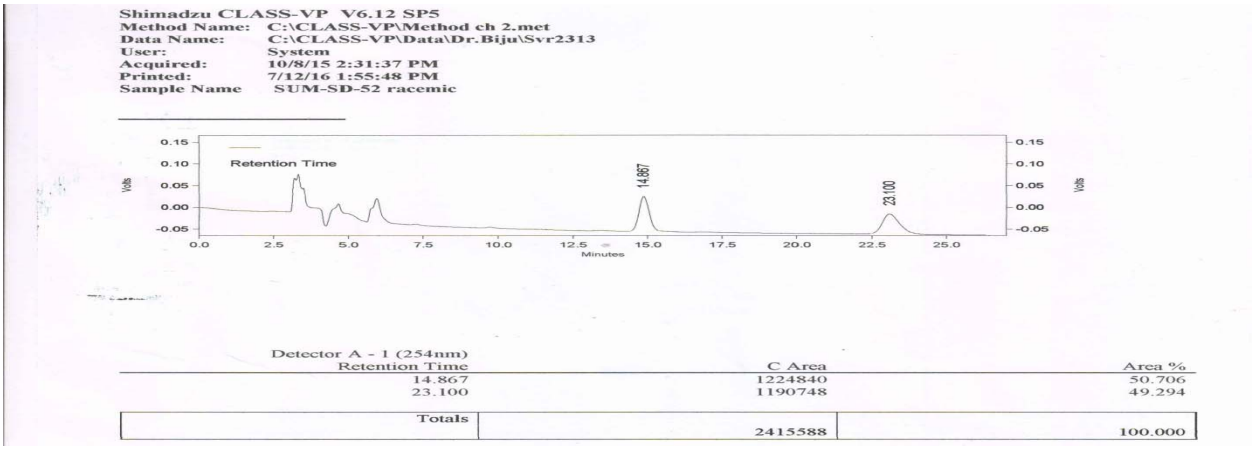


3a

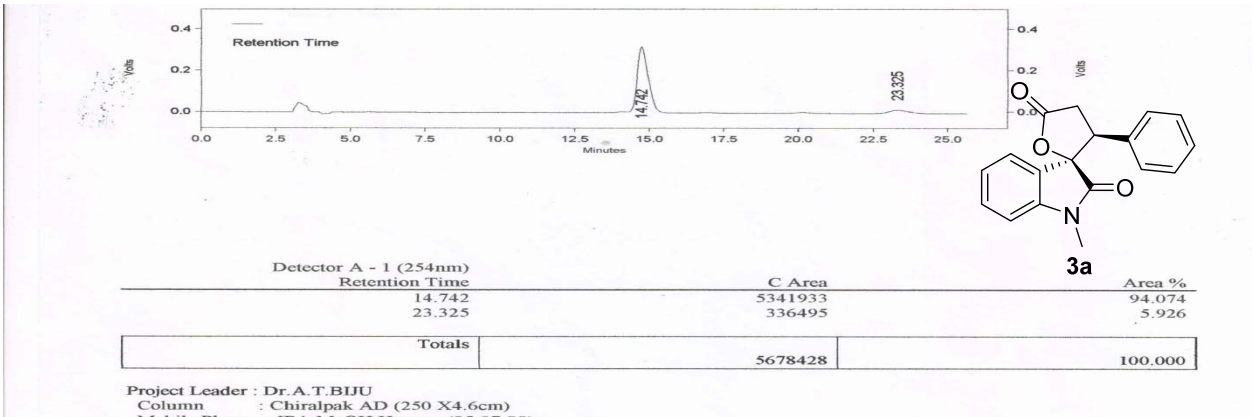
Detector A - 1 (254nm) Retention Time	C Area	Area %
14.217	3919582	94.946
21.250	208646	5.054
Totals	4128228	100.000

Project Leader : Dr.A.T.BIJU
Column : Chiralpak AD (250 X4.6cm)
Mobile Phase : IPA:MeOH:Hexane (05:07:88)
Flow Rate : 1 ml/min 565psi
Wavelength : 254 nm
Con. : 1mg /1ml
Inject vol. : 15ul

HPLC data of spiro γ-butyrolactone 3a under homoenolate condition



Detector A - 1 (254nm) Retention Time	C Area	Area %
14.867	1224840	50.706
23.100	1190748	49.294
Totals	2415588	100.000

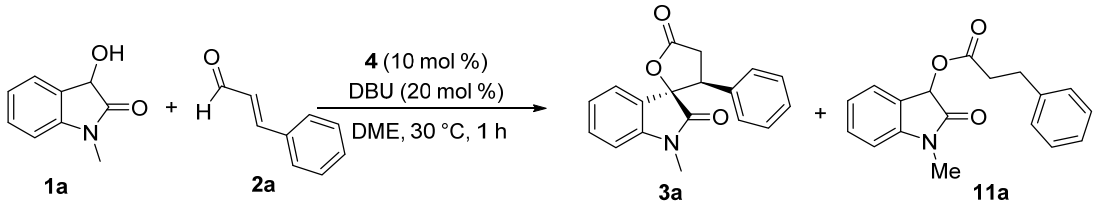


3a

Detector A - 1 (254nm) Retention Time	C Area	Area %
14.742	5341933	94.074
23.325	336495	5.926
Totals	5678428	100.000

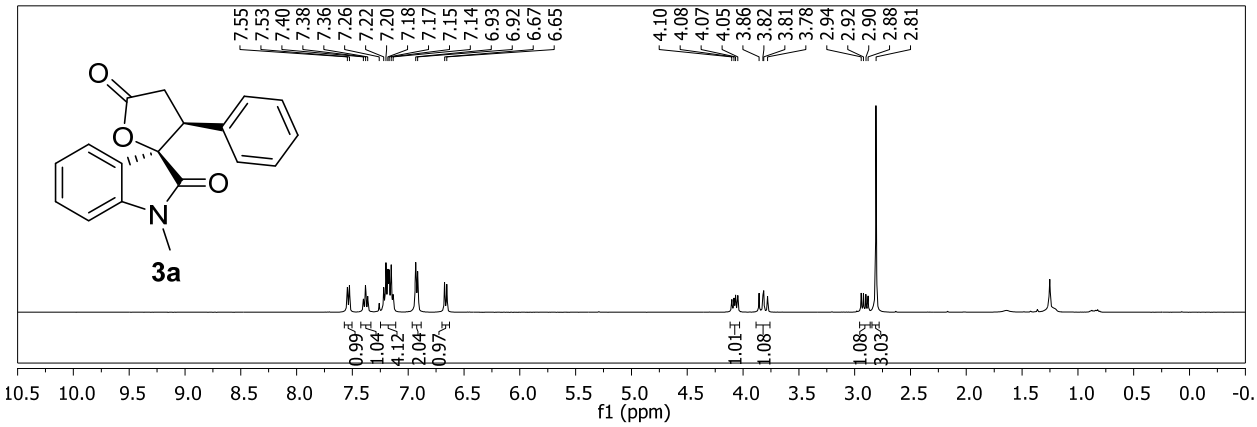
Project Leader : Dr.A.T.BIJU
Column : Chiralpak AD (250 X4.6cm)
Mobile Phase : IPA:MeOH:Hexane (05:07:88)
Flow Rate : 1 ml/min 565psi
Wavelength : 254 nm
Con. : 1mg /1ml
Inject vol. : 15ul

Procedure for the oxidant- free degassed reaction

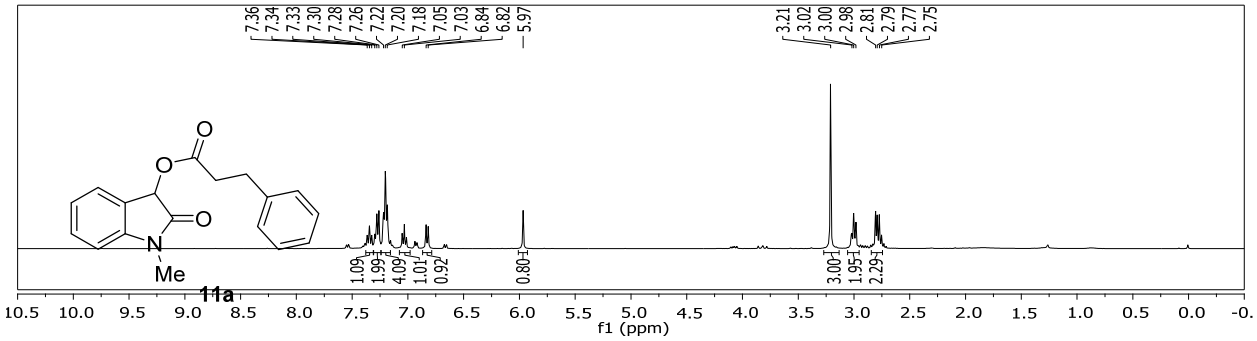


To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt **4** (0.009 g, 0.025 mmol) and dioxindole **1a** (0.25 mmol) and enal **2a** (0.25 mmol) was added. Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added DME (2.0 mL) under argon atmosphere. Then resultant reaction mixture was degassed three times and kept stirring at 30 °C. To this mixture DBU (0.008 gm, 7.5 µL, 0.05 mmol) was successively added. After 12 h the reaction is quenched and the mixture was diluted with CH_2Cl_2 (2.0 mL) and filtered through a short pad of silica gel and eluted with CH_2Cl_2 (10 mL). The solvent was evaporated to obtain the crude product, which was analyzed using ^{1}H NMR using CH_2Br_2 (18.0 µL, 0.25 mmol) as the internal standard.

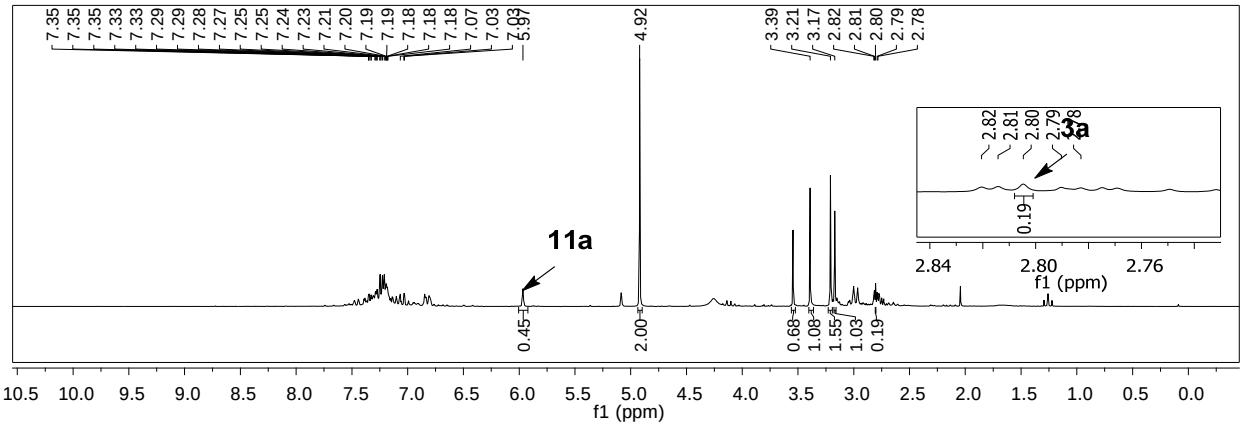
^{1}H-NMR of (2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)



^{1}H-NMR of 1-methyl-2-oxoindolin-3-yl 3-phenylpropanoate (11a)



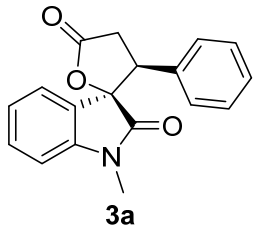
^{1}H-NMR of oxidant free degassed reaction mixture



*Under degassed condition, <10 % formation of annulated product **3a** indicates the involvement of dissolved oxygen in DME under present reaction condition, which is responsible for the oxidation of dioxindole to isatin.*

7. Synthesis and Characterization of spiro γ-butyrolactones

(2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)[7]



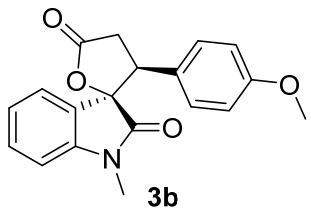
Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *trans* cinnamaldehyde **2a** (33.0 mg, 32 μL, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3a** as a white solid (60.0 mg, 82% yield, *dr* 4:1).

***R**$_f$* (Pet. ether /EtOAc = 70/30): 0.47; 95:5 er, $[\alpha]_D^{25}$ = -51.90 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 11.4 min, Minor: 16.0 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J*= 7.4 Hz, 1H, H_{ar}), 7.38 (t, *J* = 7.8 Hz, 1H, H_{ar}), 7.22-7.14 (m, 4H, H_{ar}), 6.92 (d, *J* = 7.4 Hz, 2H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.07 (dd, *J* = 13.7, 7.9 Hz, 1H), 3.82 (dd, *J* = 16.7, 13.8 Hz, 1H), 2.91 (dd, *J* = 16.8, 7.9 Hz, 1H), 2.82 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.0, 172.7, 144.4, 132.2, 131.4, 128.6, 128.4, 127.7, 124.8, 124.3, 123.6, 108.7, 86.6, 51.1, 32.3, 25.9. **HRMS** calculated $[M+Na]^+$ for $C_{18}H_{15}NO_3Na$:

[7] For the racemic synthesis, see: V. Nair, S. Vellalath, M. Poonoth, R. Mohan and E. Suresh, *Org. Lett.*, 2006, **8**, 507.

316.0944, found: 316.0942. **FTIR (cm^{-1})** 2930, 2940, 1796, 1613, 1482, 1425, 1319, 1287, 1216, 1110, 1036, 769.

(2*R*,3*S*)-3-(4-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3b)[7]



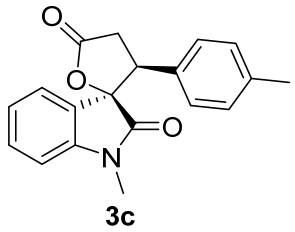
3b

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *(E)*-3-(4-methoxyphenyl)acrylaldehyde **2b** (41.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3b** as a wellow solid (64.0 mg, 78% yield, *dr* 6:1).

***R**$_f$* (Pet. ether /EtOAc = 70/30): 0.32; 90:10 er, $[\alpha]_D^{25}$ = -165.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 15.5 min, Minor: 19.2 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J*= 7.4 Hz, 1H, H_{ar}), 7.39 (t, *J* = 7.8 Hz, 1H, H_{ar}), 7.20 (t, *J* = 15.0 Hz, 1H, H_{ar}), 6.86 (d, *J* = 8.6 Hz, 2H), 6.69 (d, *J* = 7.4 Hz, 3H), 4.05 (dd, *J* = 13.7, 8.0 Hz, 1H), 3.80-3.72 (m, 4H), 2.92-2.84 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.0, 172.8, 159.4, 144.3, 131.3, 128.7, 124.8, 124.2, 123.9, 123.5, 113.8, 108.7, 86.5, 55.2, 50.3, 32.5. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{17}NO_4Na$: 346.1050, found: 346.1051. **FTIR (cm^{-1})** 2952, 1794, 1726, 1615, 1510, 1469, 1369, 1301, 1249, 1215, 1105, 1036.

(2*R*,3*S*)-1'-Methyl-3-(p-tolyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3c)

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *(E)*-3-(p-tolyl)acrylaldehyde **2c** (36.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2R,3*S*)-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3c** as a white solid (63.0 mg, 73% yield, *dr* 2:1).

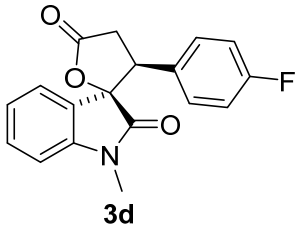


3c

***R**$_f$* (Pet. ether /EtOAc = 70/30): 0.37; 91:9 er, $[\alpha]_D^{25}$ = -82.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 12.2 min, Minor: 17.2 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J*= 7.2 Hz, 1H, H_{ar}), 7.48 (t, *J* = 7.7 Hz, 1H, H_{ar}), 7.30 (t, *J* = 7.5 Hz, 1H, H_{ar}), 7.06 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.15 (dd, *J* = 13.7, 8.0 Hz, 1H), 3.89 (dd, *J* = 16.5, 14.0 Hz, 1H), 3.02-2.94 (m, 4H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.1, 172.8, 144.4, 138.1, 131.3, 129.2, 129.1, 127.5, 124.9, 124.2, 123.6, 108.7, 86.5, 50.7, 34.5, 32.5, 30.4, 26.0, 21.1, 14.3. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{17}NO_3Na$: 330.1101, found: 330.1093. **FTIR (cm^{-1})** 3020, 1794, 1727, 1617, 1515, 1495, 1472, 1423, 1353, 1215, 1165, 1108, 928, 774, 504.

(2*R*,3*S*)-3-(4-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3d)

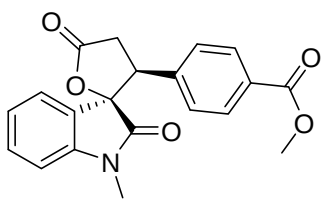


3d

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *(E)*-3-(4-fluorophenyl)acrylaldehyde **2d** (38.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-3-(4-fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3d** as a white solid (56.0 mg, 72% yield, *dr* 4:1).

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.40; 92:8 er, $[\alpha]_D^{25}$ = -90.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 13.4 min, Minor: 24.0 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52 (d, *J* = 7.3 Hz, 1H, H_{ar}), 7.38 (t, *J* = 7.7 Hz, 1H, H_{ar}), 7.19 (t, *J* = 7.5 Hz, 1H, H_{ar}) 6.92-6.81 (m, 4H, H_{ar}), 6.68 (d, *J* = 7.9 Hz, 1H, H_{ar}), 4.05 (dd, J_1 = 8.2 Hz, J_2 = 13.6 Hz, 1H), 3.78-3.70 (m, 1H), 2.90 (dd, J_1 = 8.1 Hz, J_2 = 16.6 Hz, 1H), 2.83 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.6, 172.6, 165.6 (d, *J* = 247.8 Hz), 144.3, 131.5, 129.4 (d, *J* = 8.2 Hz), 127.9 (d, *J* = 2.9 Hz), 124.5, 124.2, 123.7, 115.5 (d, *J* = 21.4 Hz), 108.8, 86.4, 50.3, 32.5, 25.9. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -113.45. **HRMS** calculated $[M+Na]^+$ for $C_{18}H_{14}NO_3FNa$: 334.0850, found: 334.0843. **FTIR (cm^{-1})** 3020, 2400, 2361, 1796, 1727, 1618, 1495, 1472, 1377, 1111. 1005, 771, 669, 495, 417.

Methyl 4-((2*R*,3*R*)-1'-methyl-2',5-dioxo-4,5-dihydro-3*H*-spiro[furan-2,3'-indolin]-3-yl)benzoate (3e)



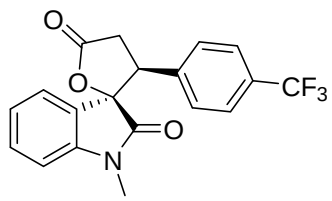
3e

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and methyl (*E*)-4-

(3-oxoprop-1-en-1-yl)benzoate **2e** (48.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded Methyl 4-((2*R*,3*S*)-1'-methyl-2',5-dioxo-4,5-dihydro-3*H*-spiro[furan-2,3'-indolin]-3-yl)benzoate **3e** as a white solid (72.0 mg, 82% yield, *dr* 4:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.34; 96:4 er, $[\alpha]_D^{25}$ = -25.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 30.4 min, Minor: 36.0 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.13 (dd, J_1 = 13.5 Hz ,J_2 = 8.0 Hz, 1H), 3.84 (s, 3H), 3.82 – 3.75 (m, 1H), 2.93 (dd, J_1 = 16.8 Hz , J_2 = 8.0 Hz, 1H), 2.78 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.5, 172.4, 166.6, 144.3, 137.4, 131.6, 130.2, 129.7, 127.8, 124.4, 124.3, 123.8, 108.9, 86.2, 52.3, 50.8, 32.2, 25.9. **HRMS** calculated $[M+Na]^+$ for $C_{20}H_{17}NO_5Na$: 374.0997, found: 374.0999. **FTIR (cm^{-1})** 2966, 2403, 1798, 1724, 1615, 1477, 1431, 1378, 1285, 1216, 1110.

(2*R*,3*S*)-1'-Methyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3f)

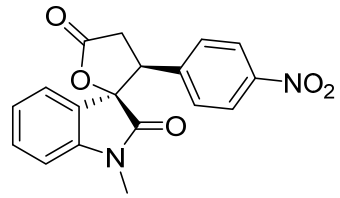


3f

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and (*E*)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde **2f** (50.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*S*,3*R*)-1'-methyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3f** as a yellow solid (75.0 mg, 82% yield, *dr* 4:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.50; 94:6 er, $[\alpha]_D^{25}$ = -80.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 10.0 min, Minor: 14.3 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (d, *J* = 7.4 Hz, 1H), 7.40 (m, 3H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.15 (dd, J_1 = 13.5 Hz , J_2 = 8.0 Hz, 1H), 3.80 (m, 1H), 2.95 (dd, J_1 = 16.8 Hz , J_2 = 8.0 Hz, 1H), 2.82 (s, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.3, 172.4, 144.3, 136.5, 131.7, 128.2, 125.5, 125.5, 124.3, 124.3, 123.9, 109.0, 86.1, 50.5, 32.3, 26.0. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{14}NO_3F_3Na$: 384.0821, found: 384.0818. **FTIR (cm^{-1})** 2405, 1799, 1726, 1616, 1479, 1423, 1367, 1324, 1212, 1172, 1022.

(2*R*,3*S*)-1'-Methyl-3-(4-nitrophenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3g)

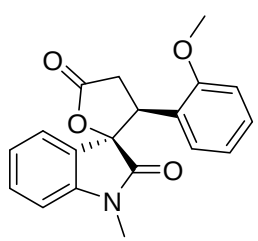


3g

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and (*E*)-3-(4-nitrophenyl)acrylaldehyde **2g** (44.0 mg, 0.25 mmol)with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded methyl (2*S*,3*R*)-1'-Methyl-3-(4-nitrophenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3g** as a white solid (61.0 mg, 72% yield, *dr* 4:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.55; 99:1 er, $[\alpha]_D^{25}$ = -66.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 15.2 min, Minor: 33.6 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.35 (m, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 4.31 (dd, J_1 = 13.4 Hz , J_2 = 8.0 Hz, 1H), 3.94 (m, 1H), 3.11 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H), 2.96 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 173.8, 172.2, 147.9, 144.3, 139.8, 132.0, 128.8, 124.4, 124.0, 124.0, 123.7, 109.1, 85.9, 50.5, 32.3, 26.1. **HRMS** calculated $[M+Na]^+$ for $C_{18}H_{14}N_2O_5Na$: 361.0790, found: 361.0795. **FTIR (cm^{-1})** 2968, 2405, 1800, 1736, 1612, 1525, 1474, 1359, 1216, 1103, 1037.

(2*R*,3*S*)-3-(2-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3h)



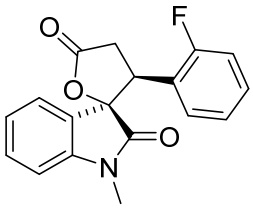
3h

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and (*E*)-3-(2-methoxyphenyl)acrylaldehyde **2h** (40.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-3-(2-methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3h** as a yellow solid (64.0 mg, 79% yield, *dr* 2:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.48; 95:5 er, $[\alpha]_D^{25}$ = -144.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD, 90:5:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 19.4 min, Minor: 22.3 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.8

Hz, 1H), 7.21 – 7.12 (m, 2H), 6.90 (t, J = 7.5 Hz, 1H), 6.63 (dd, J_1 = 7.8 Hz, J_2 = 4.2 Hz, 2H), 4.78 (dd, J_1 = 13.8 Hz, J_2 = 8.3 Hz, 1H), 3.74 (dd, J_1 = 16.8 Hz , J_2 = 4.0 Hz, 1H), 3.27 (s, 3H), 2.93 – 2.76 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.4, 173.2, 157.5, 144.0, 130.7, 129.2, 127.9, 125.1, 122.9, 120.6, 120.5, 110.4, 108.2, 86.5, 54.8, 42.2, 32.8, 25.9. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{17}NO_4Na$: 346.1048, found: 346.1050. **FTIR (cm^{-1})** 2496, 2405, 1792, 1725, 1614, 1481, 1426, 1366, 1296, 1212, 1106, 1388, 1036.

(2*R*,3*S*)-3-(2-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3i)

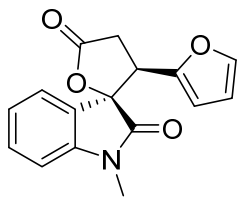


3i

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *(E)*-3-(2-fluorophenyl)acrylaldehyde **2i** (38.0 mg, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-3-(2-fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione as a white solid (69.0 mg, 88% yield, *dr* 4:1).

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.42; 97:3 er, $[\alpha]_D^{25}$ = -82.9 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 90:5:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 16.6 min, Minor: 24.7 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (d, J = 7.4 Hz, 1H, H_{ar}), 7.47 (t, J = 7.5 Hz, 1H, H_{ar}), 7.34 (t, J = 7.6 Hz, 1H, H_{ar}) 7.20-7.14 (m, 2H, H_{ar}), 7.08 (t, J = 7.6 Hz, 1H, H_{ar}), 6.80 (t, J = 9.4 Hz, 1H, H_{ar}), 6.65 (d, J = 7.8 Hz, 1H, H_{ar}) 4.51 (dd, J_1 = 8.3 Hz, J_2 = 13.6 Hz, 1H), 3.80-3.72 (m, 1H), 2.94-2.88 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.6, 172.9, 161.0 (d, J = 248.7 Hz), 144.0, 131.4, 129.9 (d, J = 8.5 Hz), 128.8 (d, J = 2.7 Hz), 124.9, 124.3 (d, J = 3.5 Hz), 124.1, 123.6, 122.7, 119.6 (d, J = 13.3 Hz), 115.5 (d, J = 22.7 Hz), 108.6, 86.1, 42.3, 33.0, 26.0. **HRMS** calculated $[M+Na]^+$ for $C_{18}H_{14}NO_3FNa$: 334.0850, found: 334.0843. **FTIR (cm^{-1})** 3020, 1797, 1727, 1617, 1472, 1215, 1165, 1039, 929, 820, 669, 499.

(2*R*,3*S*)-3-(Furan-2-yl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3j)



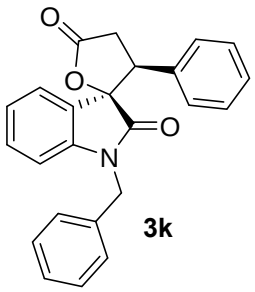
3j

Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and *(E)*-3-(furan-2-yl)acrylaldehyde **2j** (31.0 mg, 0.25 mmol) with triazolium salt **4** (9.2

mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*S*,3*R*)-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3j** as a yellow solid (48.0 mg, 67% yield, *dr* 3:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.39 94:6 er, $[\alpha]_D^{25}$ = -31.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 13.3 min, Minor: 27.8 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 (d, *J* = 7.3 Hz, 1H, H_{ar}), 7.40 (t, *J* = 15.9 Hz, 1H, H_{ar}), 7.19-7.15 (m, 2H, H_{ar}), 6.78 (d, *J* = 7.8 Hz, 1H), 6.21 (d, *J* = 1.7 Hz, 1H), 6.01 (d, *J* = 3.0 Hz, 1H), 4.14 (dd, J_1 = 13.2 Hz, J_2 = 8.4 Hz, 1H), 3.68 (dd, J_1 = 16.9 Hz, J_2 =13.4 Hz, 1H), 3.00-2.94 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.2, 172.5, 147.8, 144.5, 142.6, 131.5, 129.2, 124.8, 124.3, 123.6, 110.6, 108.8, 107.9, 84.7, 44.7, 32.3, 26.2, 18.0. **HRMS** calculated $[M+Na]^+$ for $C_{16}H_{13}NO_4Na$: 306.0737, found: 306.0738. **FTIR (cm^{-1})** 2404, 1799, 1730, 1615, 1480, 1421, 1372, 1214, 1104, 1010, 930.

(2*R*,3*S*)-1'-Benzyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3k)[8]



3k

Following the general procedure, treatment of 1-benzyl-3-hydroxyindolin-2-one **1k** (60.0 mg, 0.25 mmol) and *trans* cinnamaldehyde **2a** (33.0 mg, 32 µL, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-1'-benzyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3k** as a white solid (70.0 mg, 76% yield, *dr* 3:1).

***R**f* (Pet. ether /EtOAc = 70/30): 0.48; 90:10 er, $[\alpha]_D^{25}$ = -41.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 22.6 min, Minor: 25.7 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (d, *J*= 7.4 Hz, 1H, H_{ar}), 7.34-7.29 (m, 2H, H_{ar}), 7.34-7.29 (m, 2H, H_{ar}), 7.26-7.14 (m, 7H, H_{ar}), 7.08 (t, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 7.62 Hz, 2H, H_{ar}), 6.46-6.42(m, 3H), 5.03-4.94 (m, 1H), 4.24-4.15 (m, 1H), 3.92 (dd, J_1 = 16.8 Hz, J_2 =13.8 Hz, 1H), 2.96 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.9, 172.9, 143.8, 134.5, 132.1, 131.4, 129.1, 129.0, 128.8, 128.2, 127.5, 126.5, 124.4, 123.7, 110.1, 86.5, 50.9, 43.8, 32.4, 25.9. Representative Peaks of Minor Isomer: **^{1}H NMR** δ 6.73 (t, *J* = 7.6 Hz), 6.63 (d, *J*= 7.9 Hz), 4.81 (d, *J*= 15.8 Hz), 4.09 (dd, J_1 = 8.6 Hz, J_2 = 5.9

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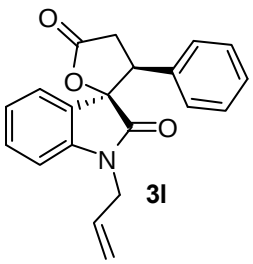
Hz), 3.67 (dd, J_1 = 17.5 Hz, J_2 =8.6 Hz), 3.16 (dd, J_1 = 17.5 Hz, J_2 = 5.9 Hz). **^{13}C NMR** δ 130.86, 128.36, 127.31, 126.10, 124.75, 122.87, 109.74, 48.40, 44.15, 34.17.**HRMS** calculated $[M+Na]^+$ for $C_{24}H_{19}NO_3Na$: 392.1255, found: 392.1257. **FTIR (cm^{-1})**2403, 1784, 1613, 1482, 1425, 1369, 1215, 1037, 924, 769, 671.

(2*R*,3*S*)-1'-Allyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3l)

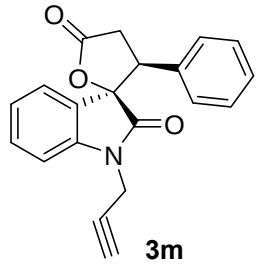


3l

Following the general procedure, treatment of 1-allyl-3-hydroxyindolin-2-one **1l** (47.0 mg, 0.25 mmol) and *trans* cinnamaldehyde **2a** (33.0 mg, 32 μL, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-1'-allyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3l** as a white solid (51.0 mg, 63% yield, *dr* 7:1).

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.55; 93:7 er, $[\alpha]_D^{25}$ = -45.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 13.5 min, Minor: 23.0 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.55 (d, *J* = 7.5 Hz, 1H, H_{ar}), 7.34 (t, *J* = 7.8 Hz, 1H, H_{ar}), 7.24-7.14 (m, 4H, H_{ar}), 6.94 (d, *J* = 7.3 Hz, 2H), 6.63 (d, *J* = 7.9 Hz, 1H), 5.24 – 5.17 (m, 1H), 4.82 (d, *J* = 10.5 Hz, 1H), 4.36 (d, *J* = 17.1 Hz, 1H), 4.29 – 4.19 (m, 1H), 4.10 (dd, J_1 = 13.7 Hz, J_2 =7.9 Hz, 1H), 3.84 (dd, J_1 = 16.7 Hz, J_2 =13.8 Hz, 1H), 3.71 (dd, J_1 = 16.6 Hz, J_2 =5.3 Hz, 1H), 2.92 (dd, J_1 = 16.8 Hz, J_2 =7.9 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.0, 172.4, 156.7, 137.6, 132.2, 128.5, 127.6, 125.9, 115.9, 111.2, 109.3, 86.8, 56.0, 51.1, 32.2, 25.9. **HRMS** calculated $[M+Na]^+$ for $C_{20}H_{17}NO_3Na$: 342.1101, found: 342.1098. **FTIR (cm^{-1})**2403, 1795, 1728, 1614, 1476, 1426, 1372, 1215, 1116, 1040, 926, 767.

(2*R*,3*S*)-3-Phenyl-1'-(prop-2-yn-1-yl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3m)[7]



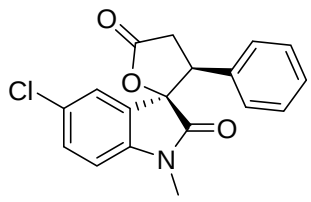
3m

Following the general procedure, treatment of 3-hydroxy-1-(prop-2-yn-1-yl)indolin-2-one **1m** (47.0 mg, 0.25 mmol) and *trans* cinnamaldehyde **2a** (33.0 mg, 32 μL, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME

(2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-3-phenyl-1'-(prop-2-yn-1-yl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3m** as a yellow solid (64.0 mg, 80% yield, *dr* 2:1).

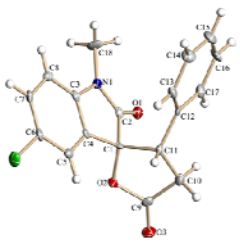
***R**f* (Pet. ether /EtOAc = 70/30): 0.52; 94:6 er, $[\alpha]_D^{25}$ = -38.0 (c=0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 16.3 min, Minor: 42.5 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (d, *J* = 7.5 Hz, 1H, H_{ar}), 7.43 (t, *J* = 7.7 Hz, 1H, H_{ar}), 7.28-7.15 (m, 7H, H_{ar}), 4.19-4.01 (m, 3H), 3.86-3.78(m, 1H), 2.95 (dd, J_1 = 16.77 Hz, J_2 = 7.95 Hz, 1H), 2.01 (bs, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.8, 171.8, 142.5, 136.7, 131.4, 128.7, 128.8, 128.7, 127.6, 126.2, 124.4, 124.0, 109.8, 86.6, 76.1, 72.4, 51.3, 32.1, 29.0. Representative Peaks of Minor Isomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.12 (m, 2H), 6.90 (t, *J* = 8.0 Hz, 9H), 6.78 (t, *J* = 7.6 Hz, 1H), 6.33 (d, *J* = 7.5 Hz, 1H), 4.63 (dd, J_1 = 17.7 Hz, J_2 = 2.3 Hz, 1H), 4.39 (dd, *J* = 17.7 Hz, J_2 = 2.3 Hz, 1H), 3.68 (dd, J_1 = 17.6 Hz, J_2= 8.7 Hz, 1H), 3.12 (dd, J_1 = 17.6 Hz, J_2 = 4.9 Hz, 1H), 2.30 (t, *J* = 2.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ175.9, 173.5, 136.7, 131.9, 130.9, 128.8, 128.4, 128.0, 124.8, 123.2, 109.7, 86.0, 76.1, 73.1, 48.1, 34.0, 29.8. **HRMS** calculated $[M+Na]^+$ for $C_{20}H_{15}NO_3Na$: 340.0942, found: 340.0944. **FTIR (cm^{-1})** 2974, 2403, 1795, 1733, 1614, 1478, 1424, 1369, 1215, 1039, 928.

(2*R*,3*S*)-5'-Chloro-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3n)



3n

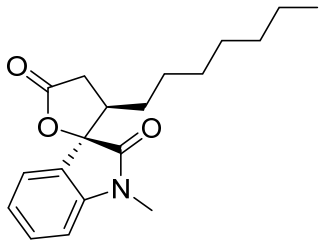
Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1n** (41.0 mg, 0.25 mmol) and *trans* cinnamaldehyde **2a** (33.0 mg, 32 µL, 0.25 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 µL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*S*)-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **3n** as a yellow solid (53.0 mg, 65% yield, *dr* 3:1). CCDC 1487677 (For the further detail about crystal structure please visit www.ccdc.cam.ac.uk/data_request/cif)



***R**f* (Pet. ether /EtOAc = 70/30) 0.48; 91:9 er, $[\alpha]_D^{25}$ = -141.0 (c 0.1, $CHCl_3$). **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 12.3 min, Minor: 20.0 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 1.7 Hz, 1H, H_{ar}), 7.48 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.41-7.28 (m, 3H,

H_{ar}), 7.07 (d, J = 7.1 Hz, 2H), 6.72 (d, J = 7.4 Hz, 1H), 4.16 (dd, J_1 = 13.7 Hz, J_2 = 8.0 Hz, 1H), 3.91 (dd, J_1 = 16.8, J_2 =13.8 Hz, 1H), 3.04 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H), 2.92 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 174.5, 172.4, 143.0, 131.8, 131.4, 129.1, 128.7, 128.6, 127.7, 124.8, 109.8, 86.2, 51.2, 32.1, 30.5, 26.1. **HRMS** calculated $[M+Na]^+$ for $C_{18}H_{14}NO_3ClNa$: 350.0554, found: 350.0554. **FTIR (cm^{-1})** 2972, 2403, 1798, 1728, 1612, 1432, 1216, 1107, 1039, 922.

3 (2*R*,3*R*)-3-Heptyl-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3o)



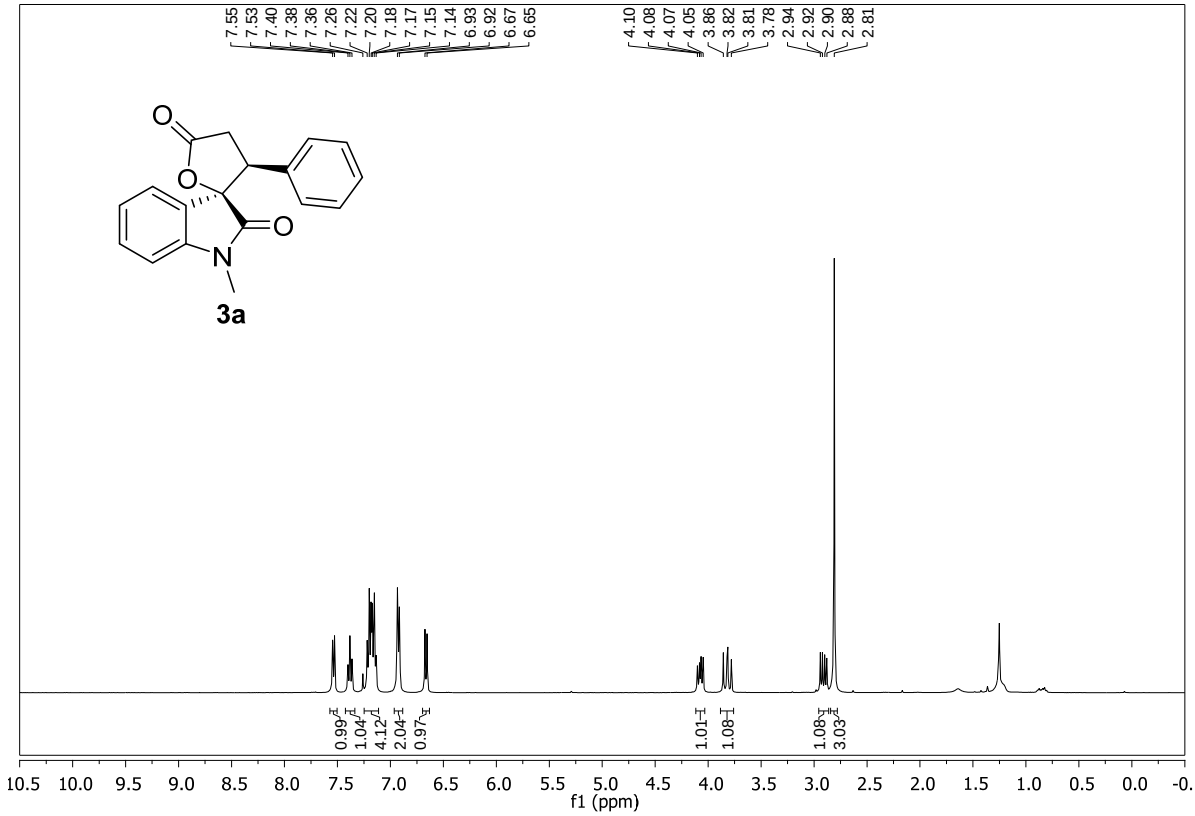
3o

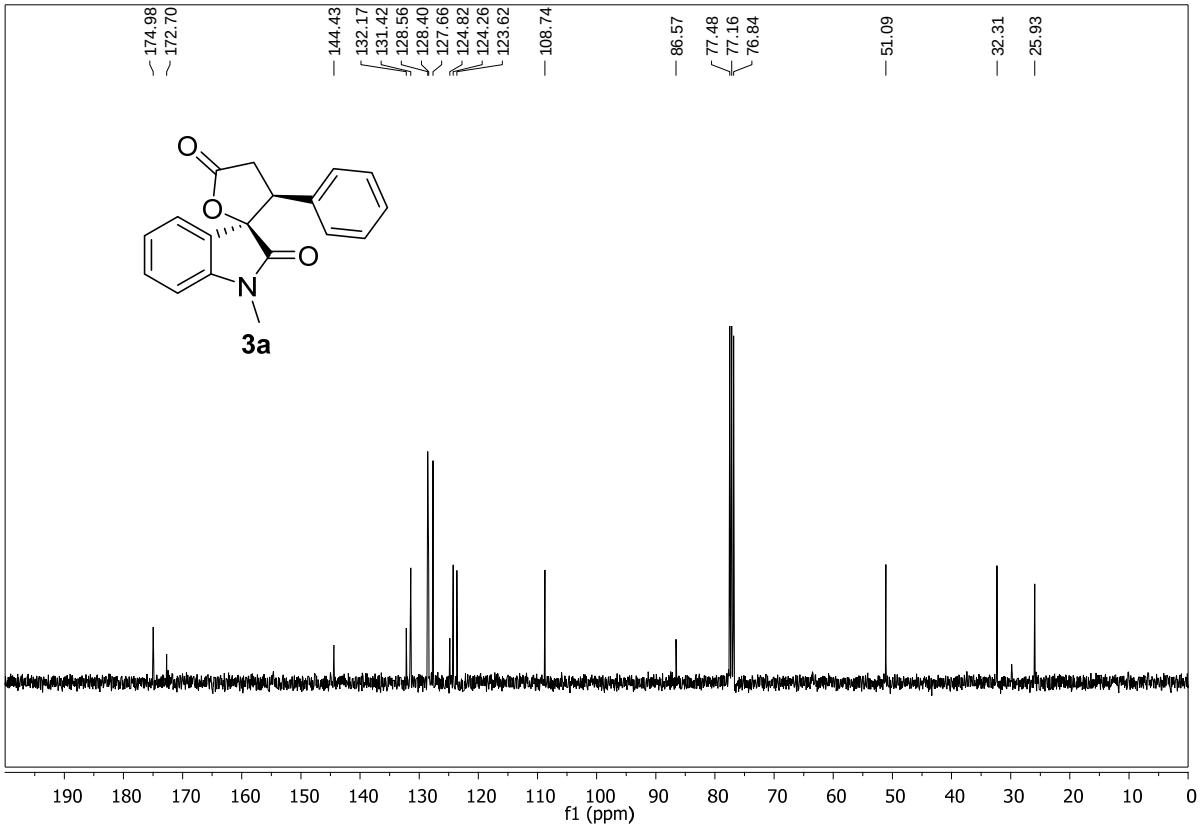
Following the general procedure, treatment of 3-hydroxy-1-methylindolin-2-one **1a** (41.0 mg, 0.25 mmol) and (*E*)-dec-2-enal **2o** (39.0 mg, 46 μL , 0.50 mmol) with triazolium salt **4** (9.2 mg, 0.025 mmol), oxidant **5** (102.0 mg, 0.25 mmol), LiCl (5.2 mg, 0.125 mmol), and DBU (7.6 mg, 7.5 μL, 0.05 mmol) in DME (2.0 mL) at 30 °C for 12 h followed by column chromatography afforded (2*R*,3*R*)-3-heptyl-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione **(3o)** as a yellow sticky liquid (35.0 mg, 45% yield, dr 2:1).

***R*$_f$** (Pet. ether /EtOAc = 70/30): 0.66; 57:43 er, **HPLC** (Chiralpak AD-H, 88:7:5 PE /MeOH/ IPA, 1.0 mL/min.) Major: 11.1 min, Minor: 7.9 min. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42 – 7.30 (m, 2H), 7.11 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 7.8 Hz, 1H), 3.16 (s, 3H), 2.95 (m, 1H), 2.74 (m, 2H), 1.50 – 1.30 (m, 1H), 1.30 – 0.95 (m, 12H), 0.81 (t, J = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.6, 173.3, 144.5, 131.2, 125.4, 124.3, 123.6, 108.8, 85.6, 45.5, 33.6, 31.7, 29.3, 29.0, 28.4, 28.0, 26.3, 22.6, 14.1. **HRMS** calculated $[M+Na]^+$ for $C_{19}H_{25}NO_3Na$: 338.1727, found: 338.1719. **FTIR (cm^{-1})** 2929, 2861, 2404, 1792, 1726, 1616, 1467, 1422, 1368, 1302, 1216, 1010.

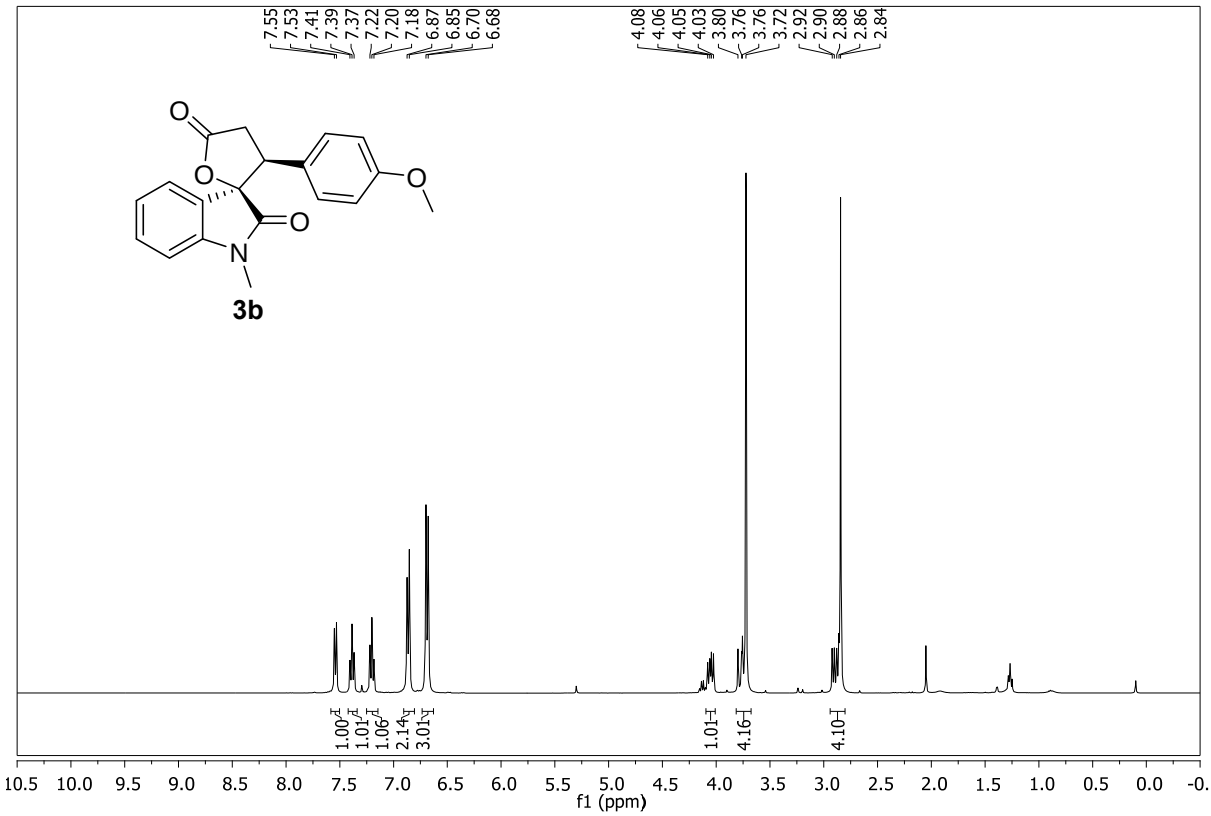
8. ^{1}H and ^{13}C NMR Spectra of spiro γ-butyrolactones

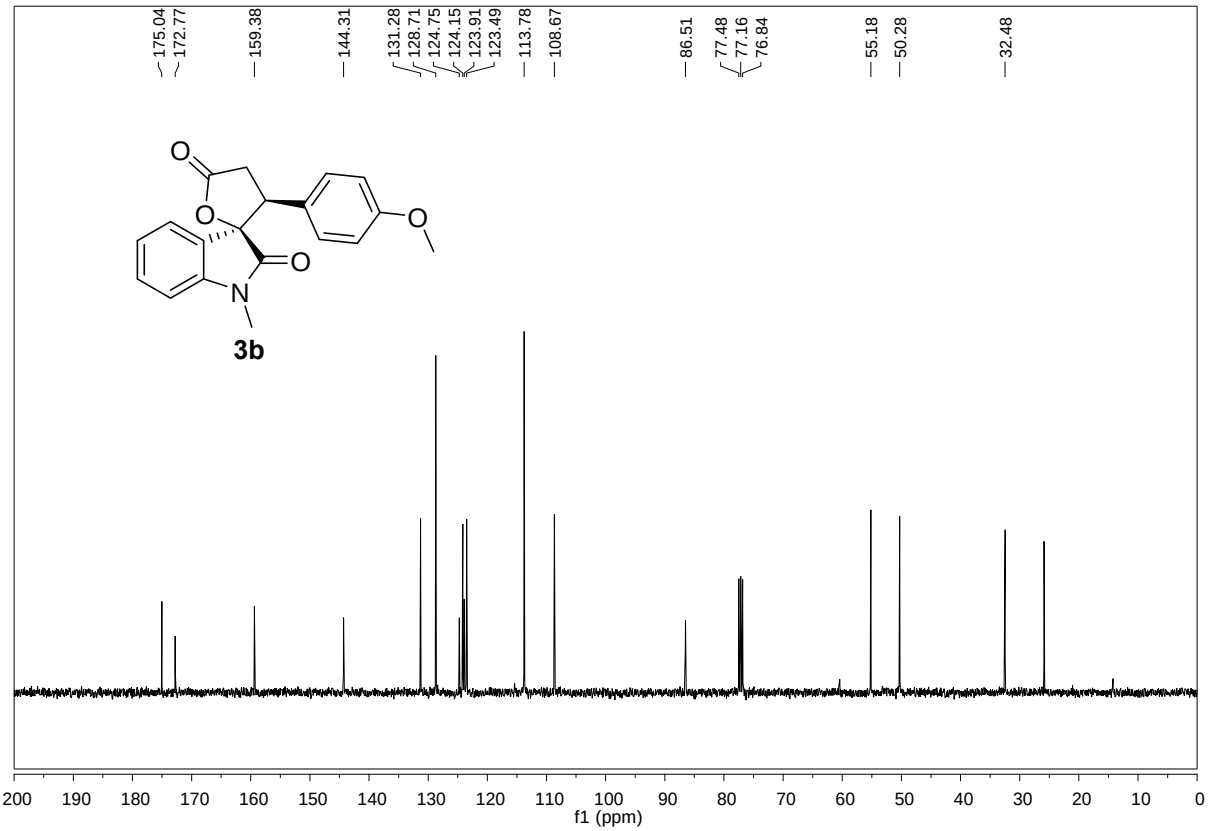
(2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)



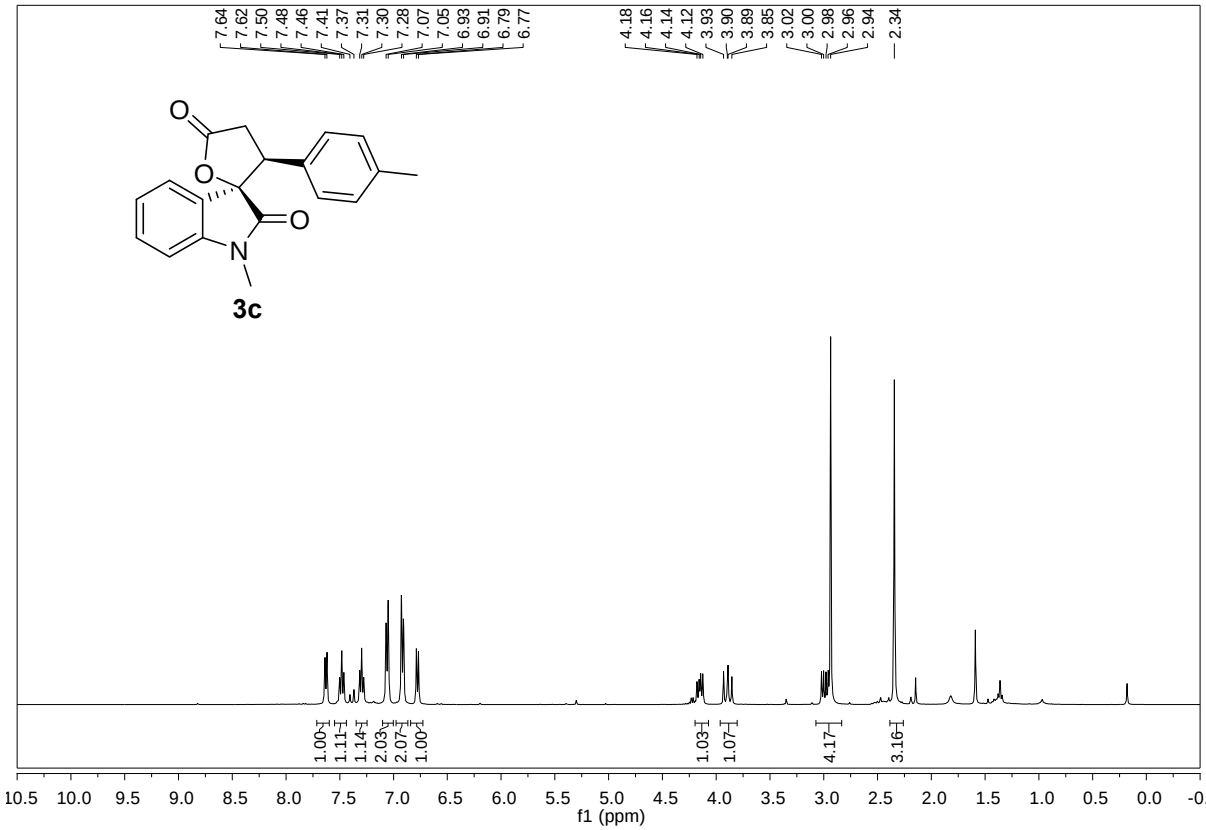


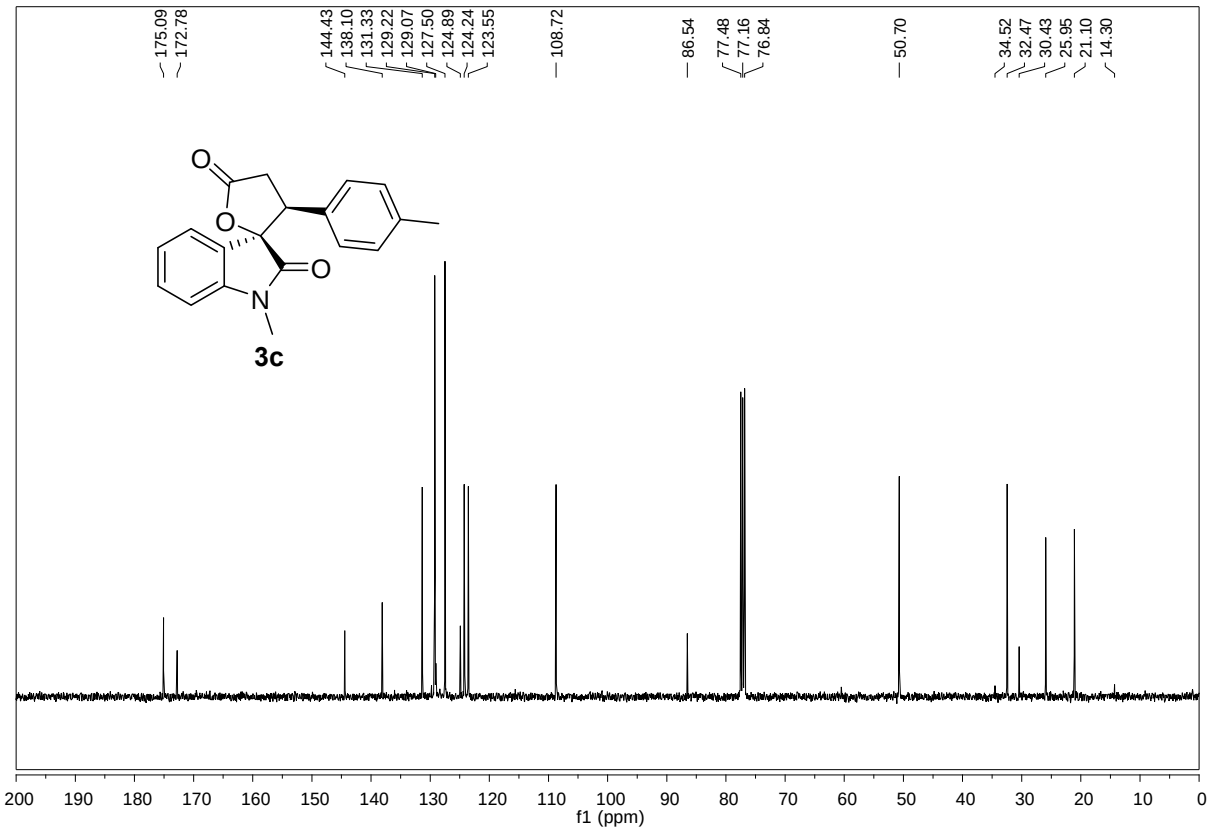
(2*R*,3*S*)-3-(4-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3b)



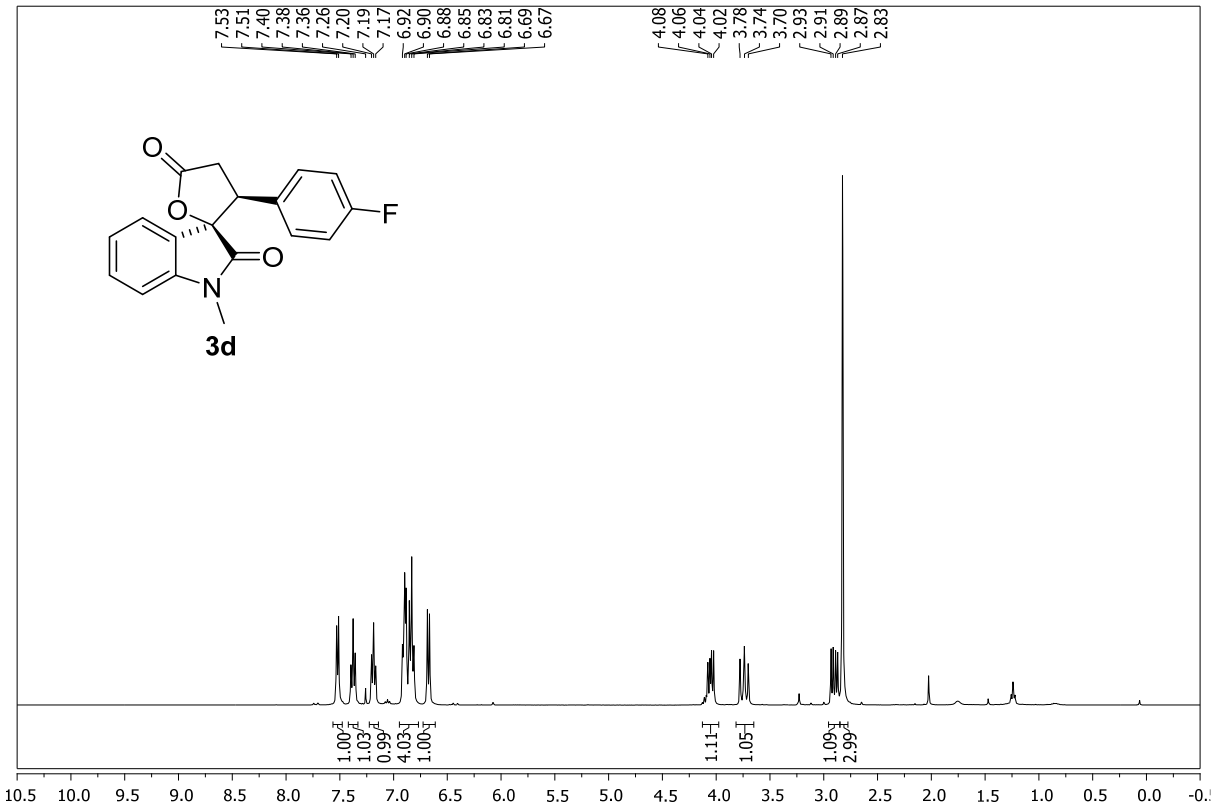


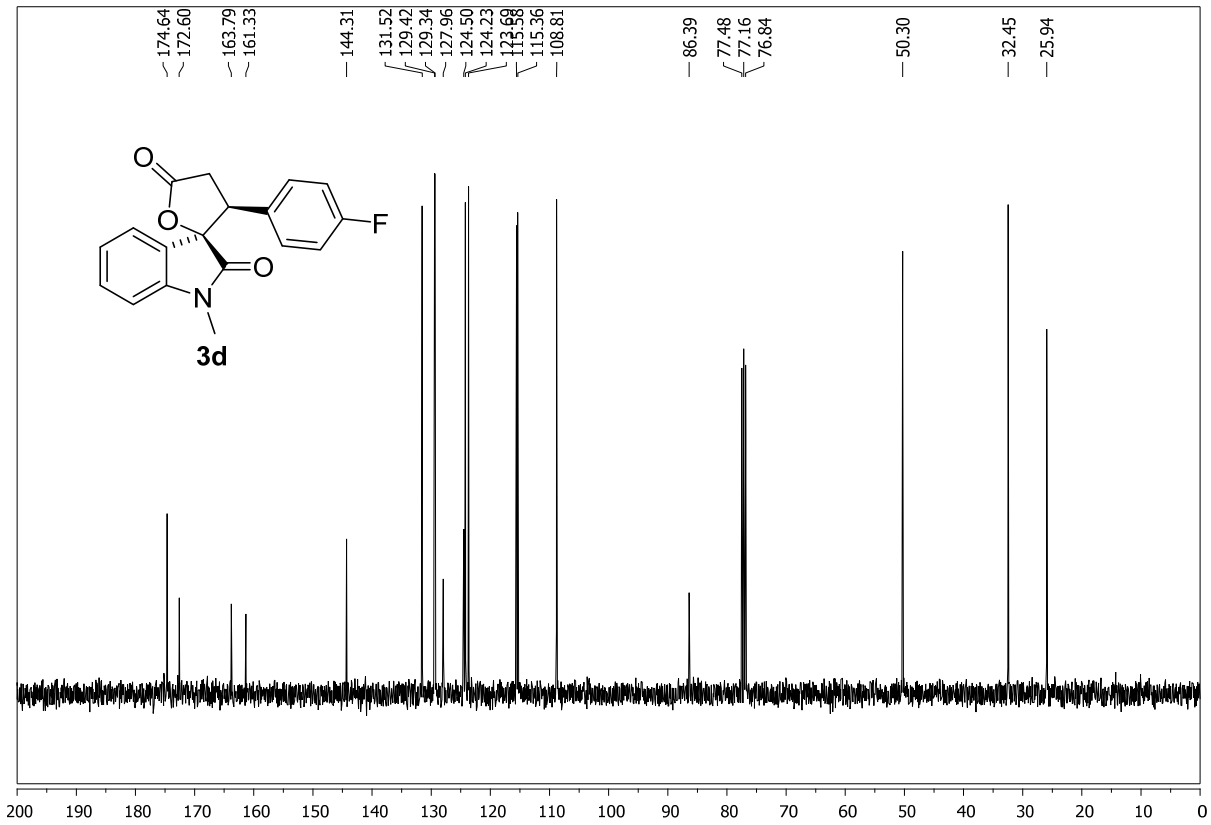
(2*R*,3*S*)-1'-Methyl-3-(p-tolyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3c)



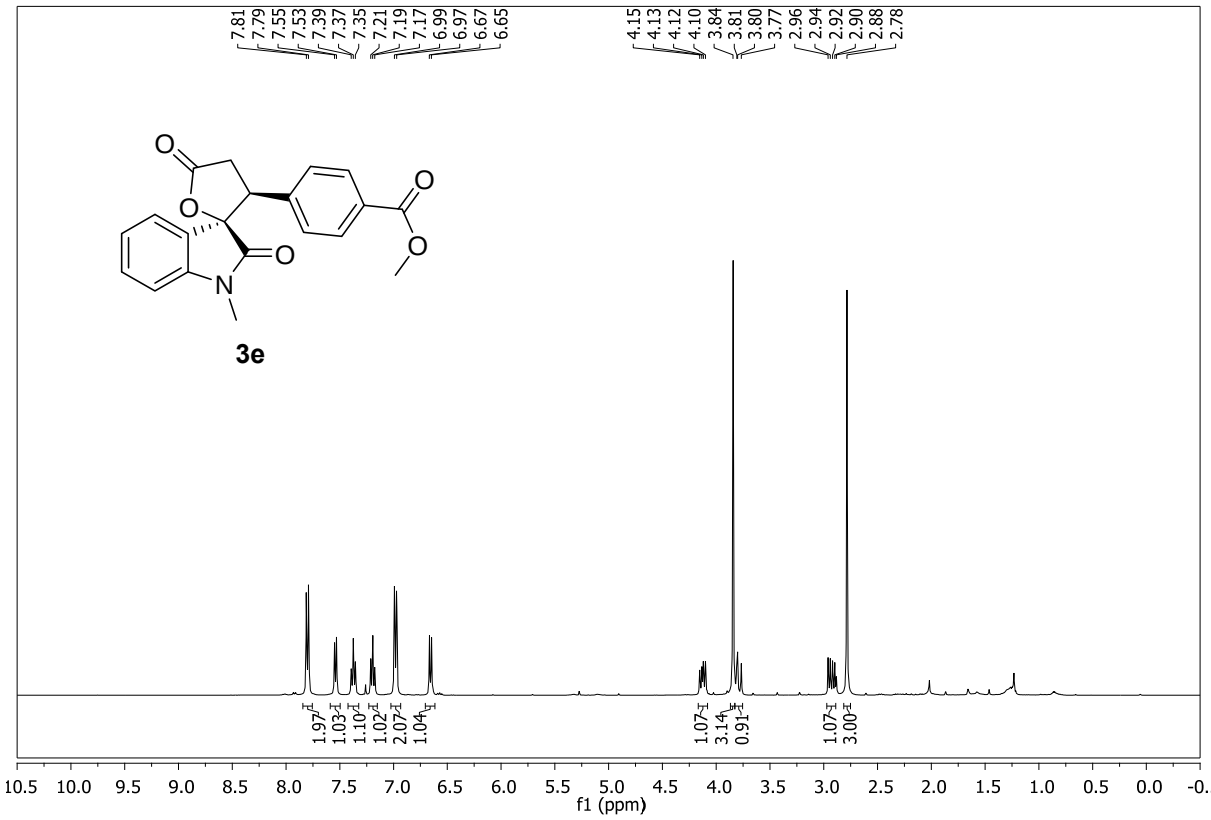


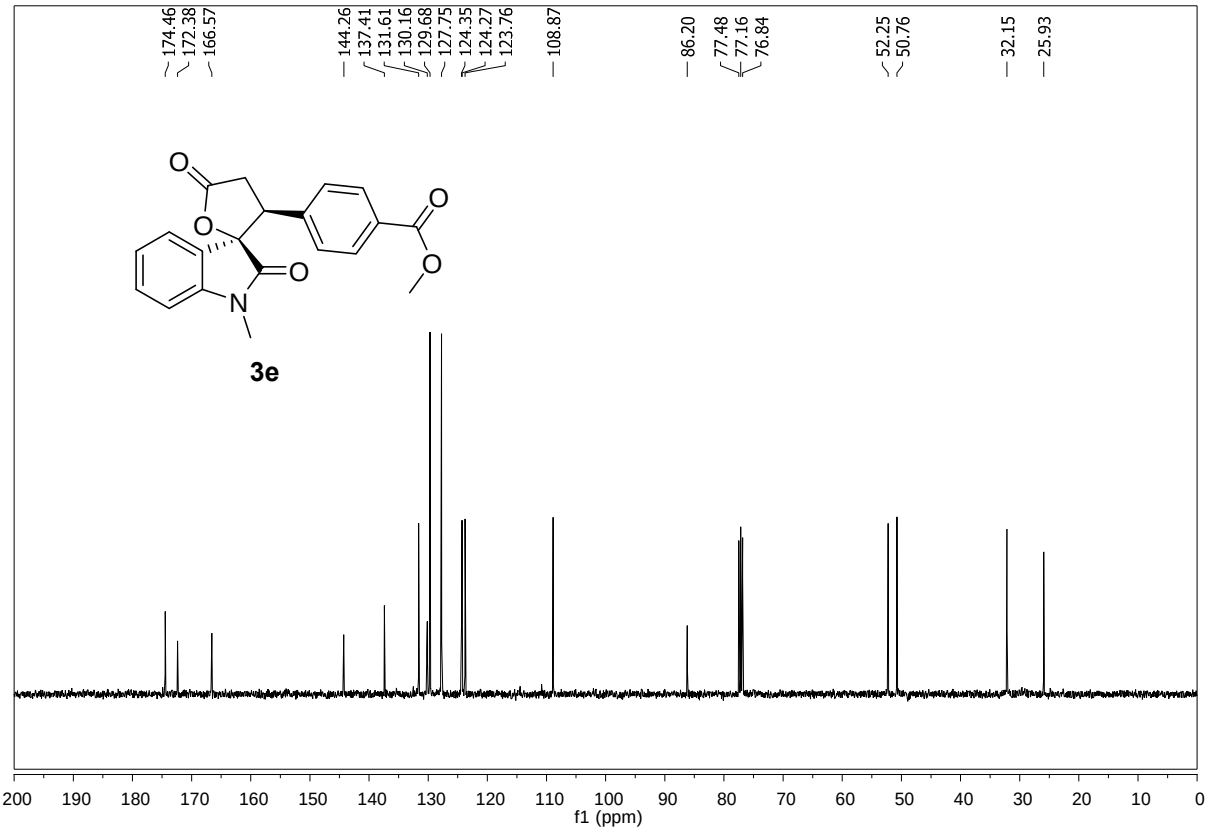
(2*R*,3*S*)-3-(4-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3d)



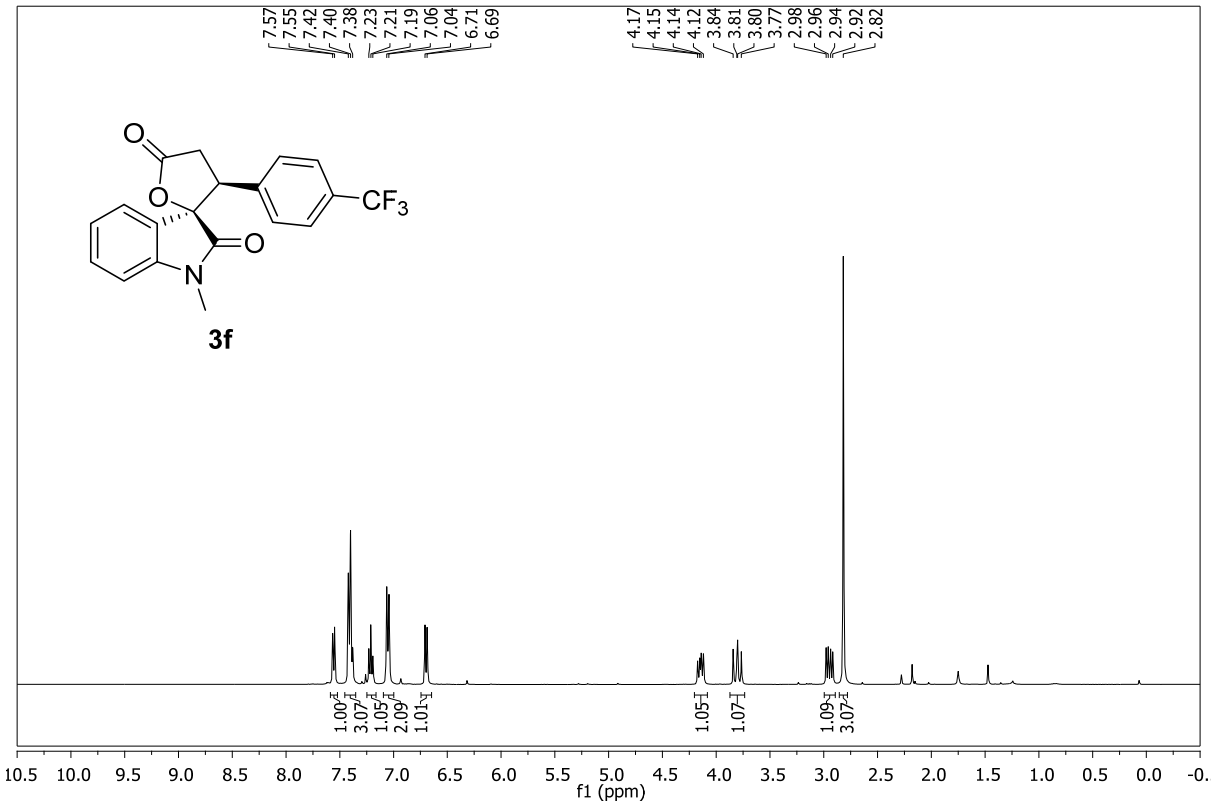


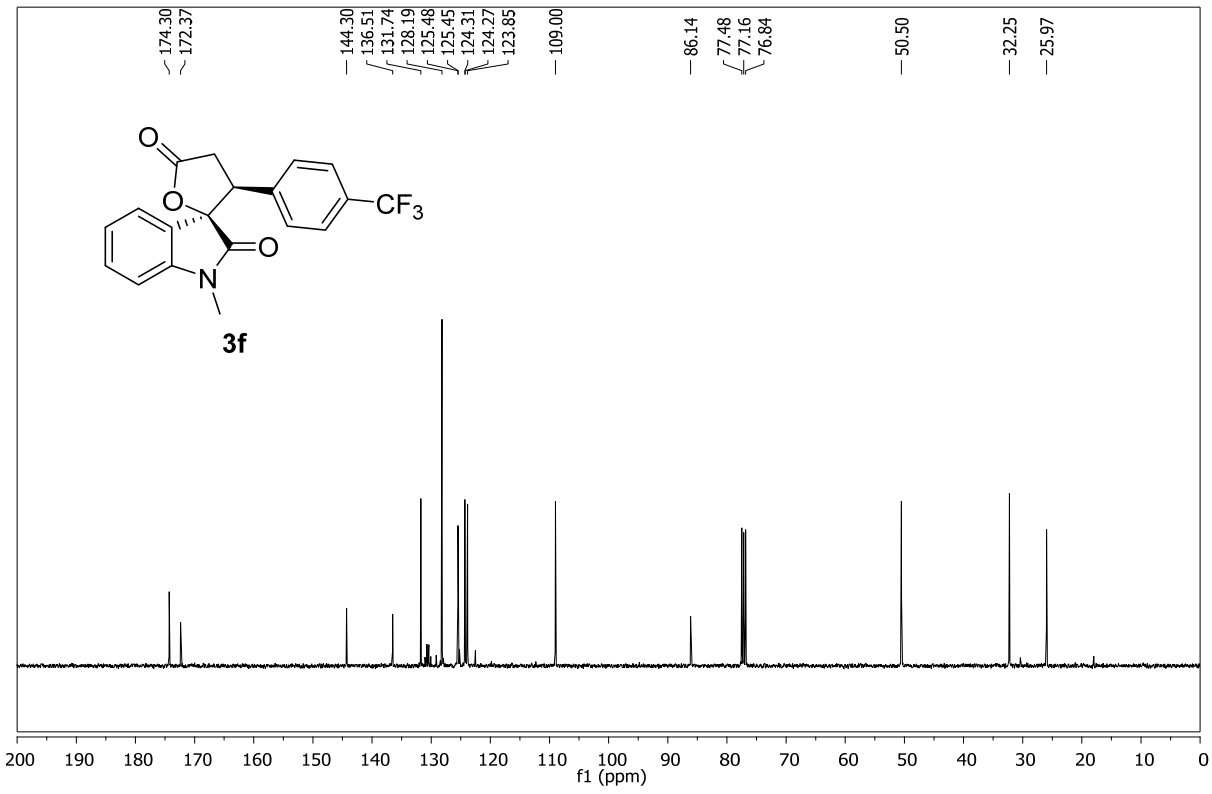
Methyl 4-((2*R*,3*S*)-1'-methyl-2',5-dioxo-4,5-dihydro-3*H*-spiro[furan-2,3'-indolin]-3-yl)benzoate (3e)



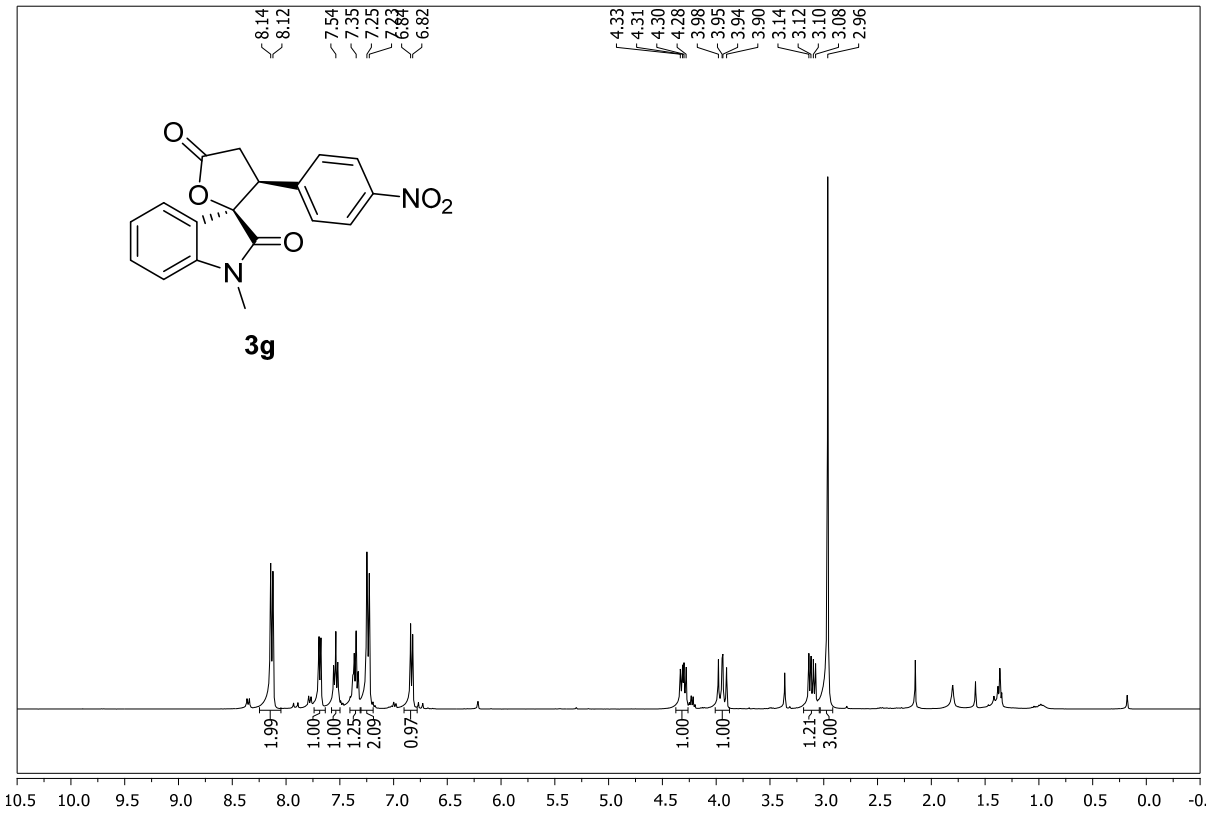


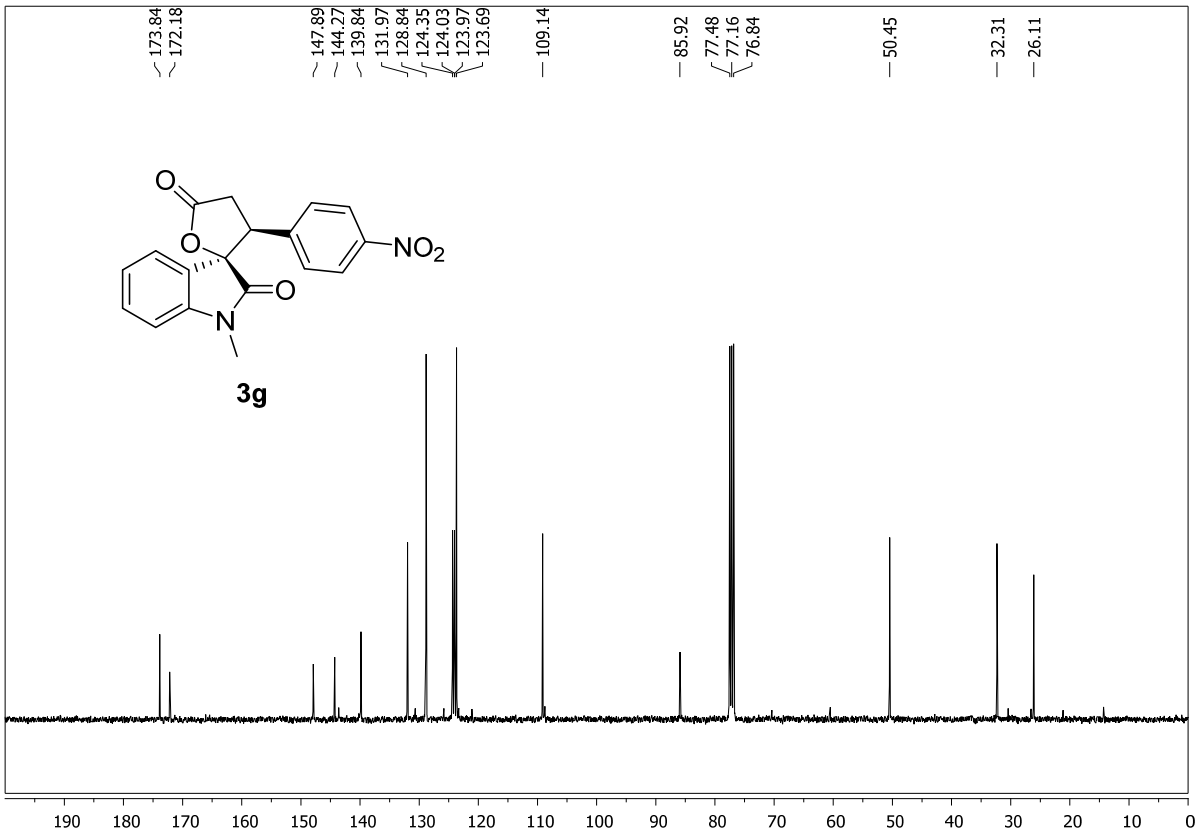
(2*R*,3*S*)-1'-Methyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3f)



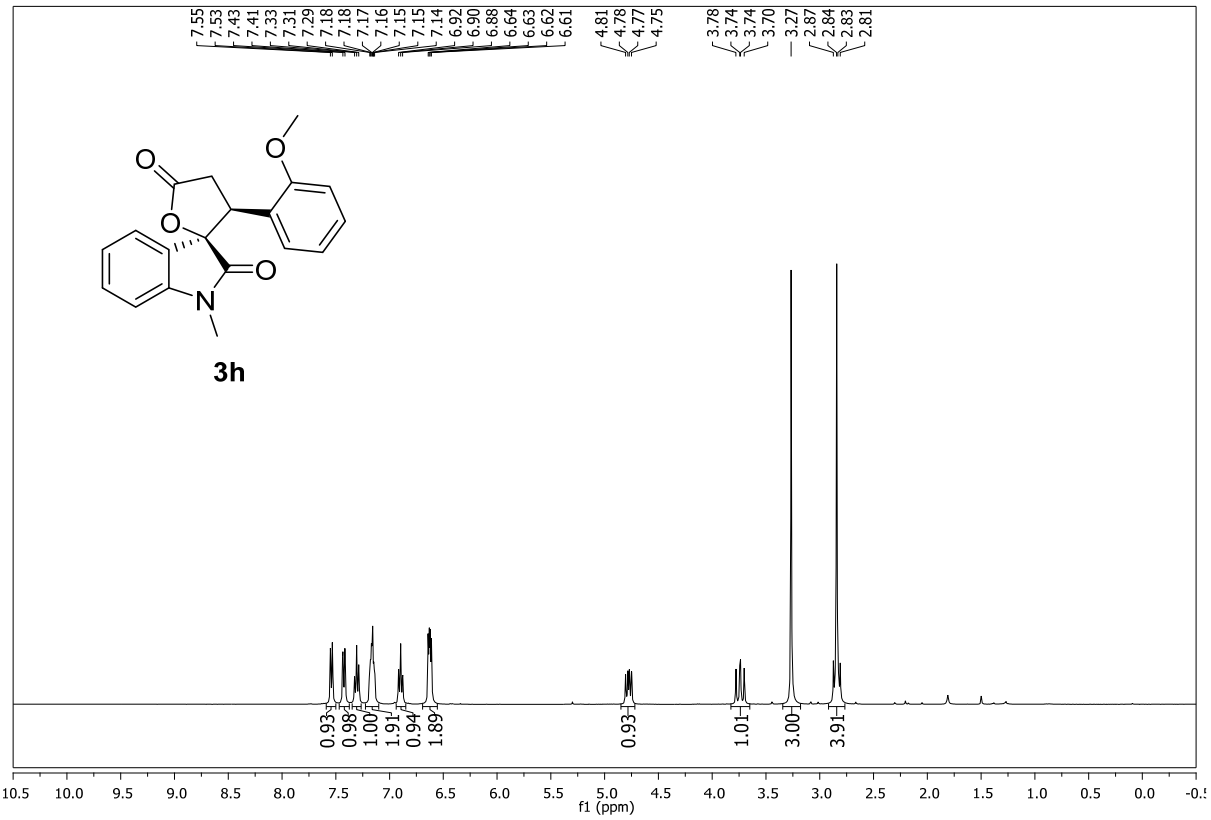


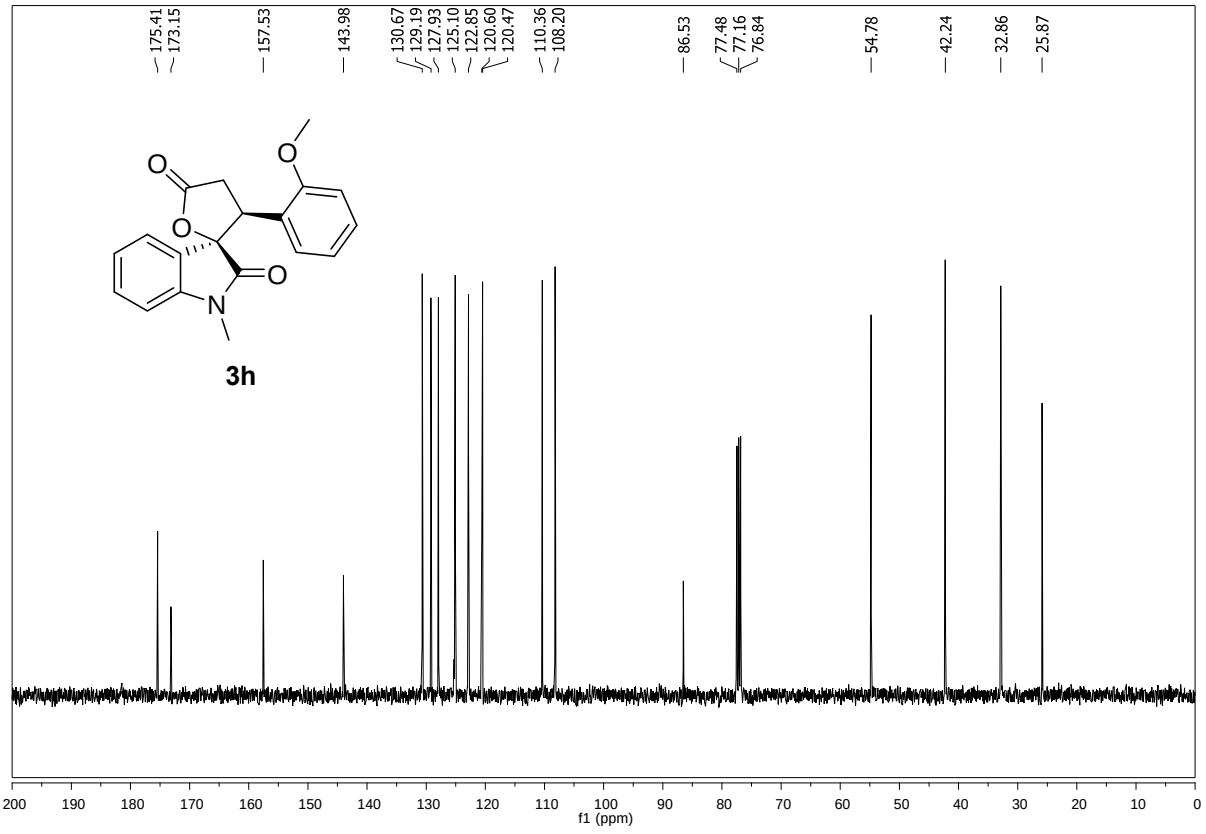
(2*R*,3*S*)-1'-Methyl-3-(4-nitrophenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3g)



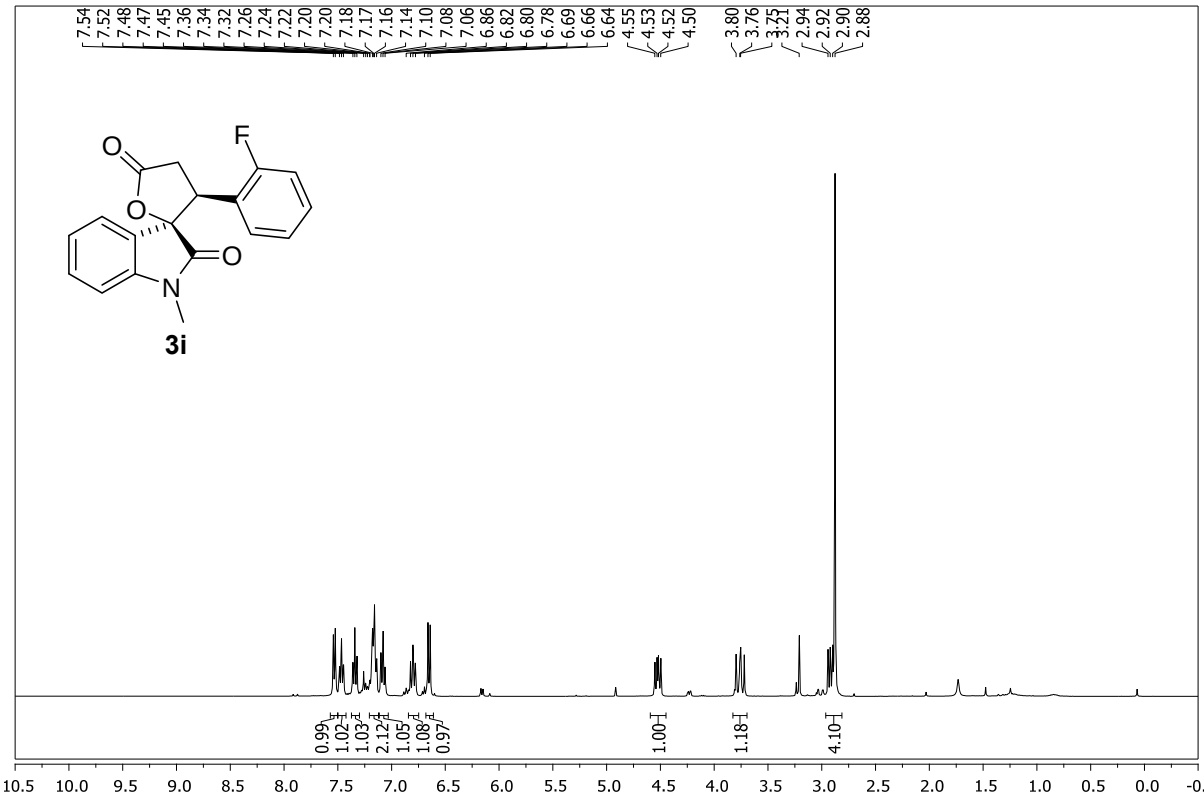


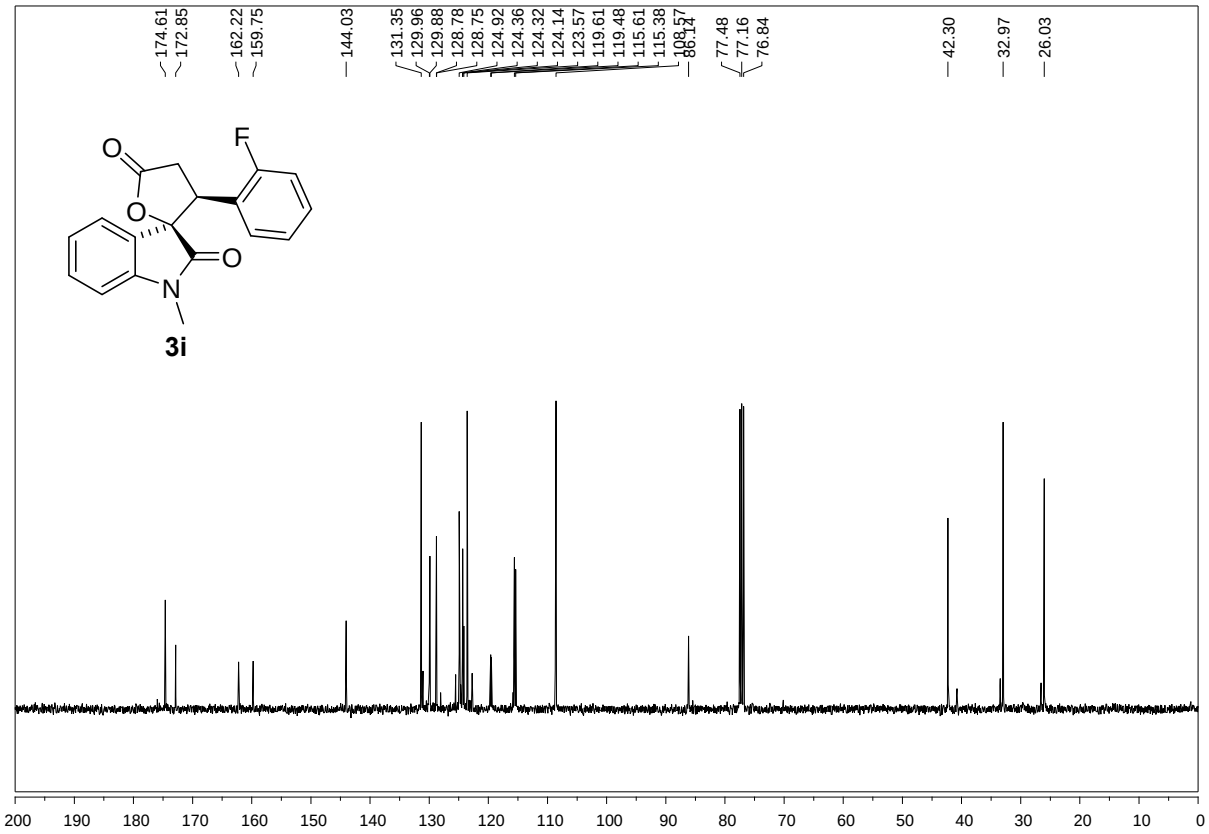
(2*R*,3*S*)-3-(2-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3h)



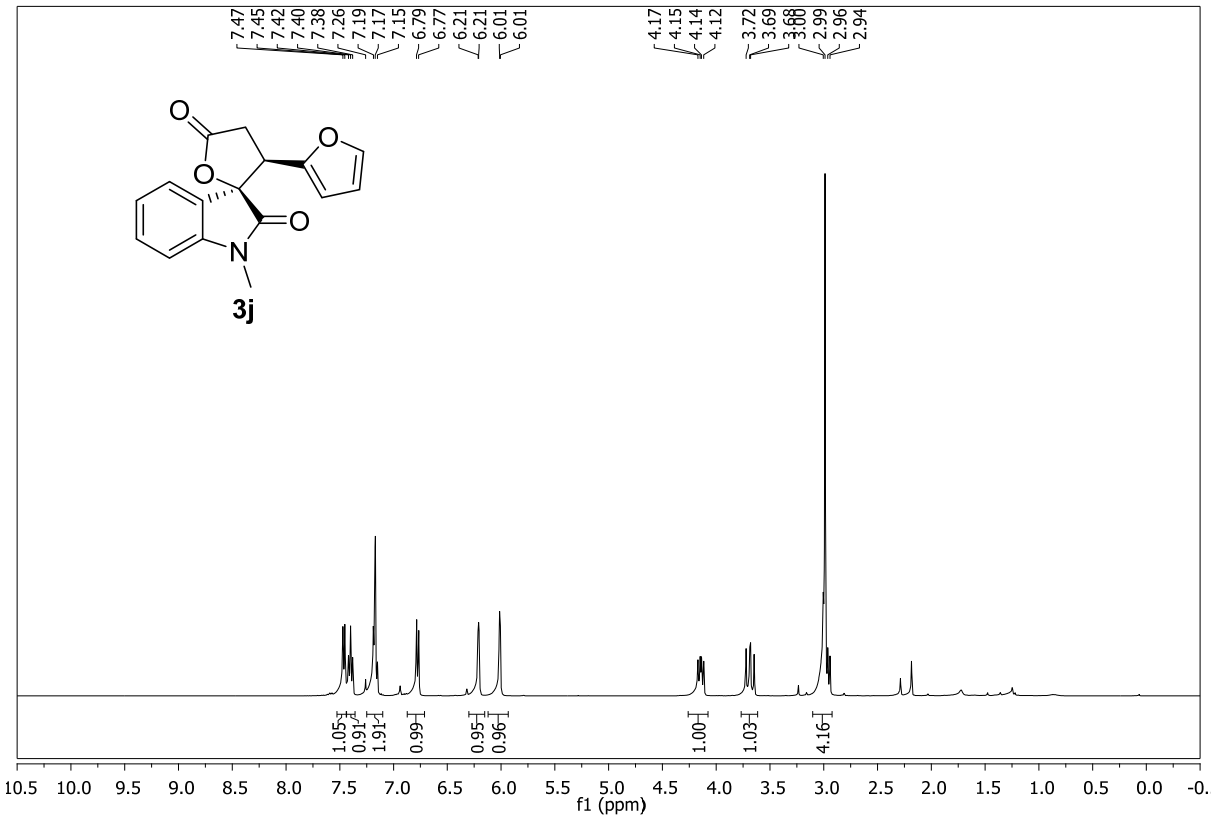


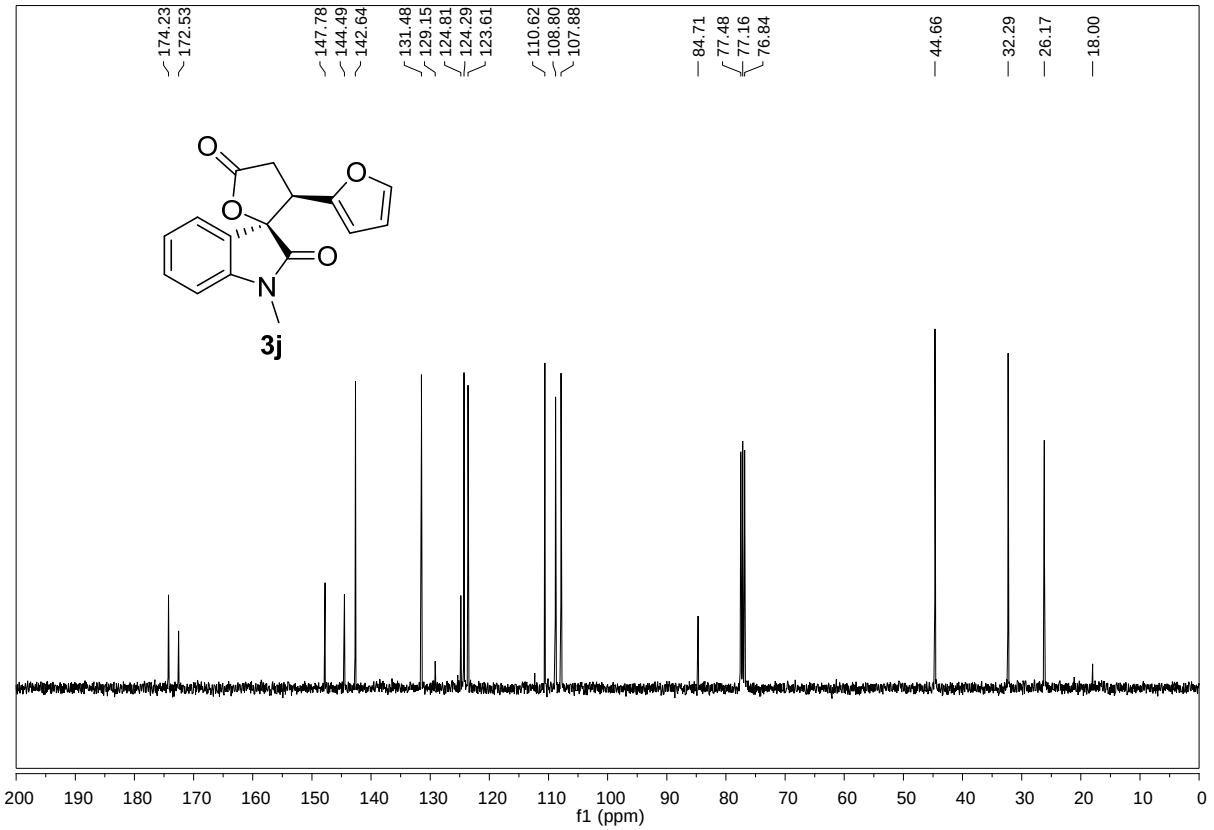
(2*R*,3*S*)-3-(2-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3i)



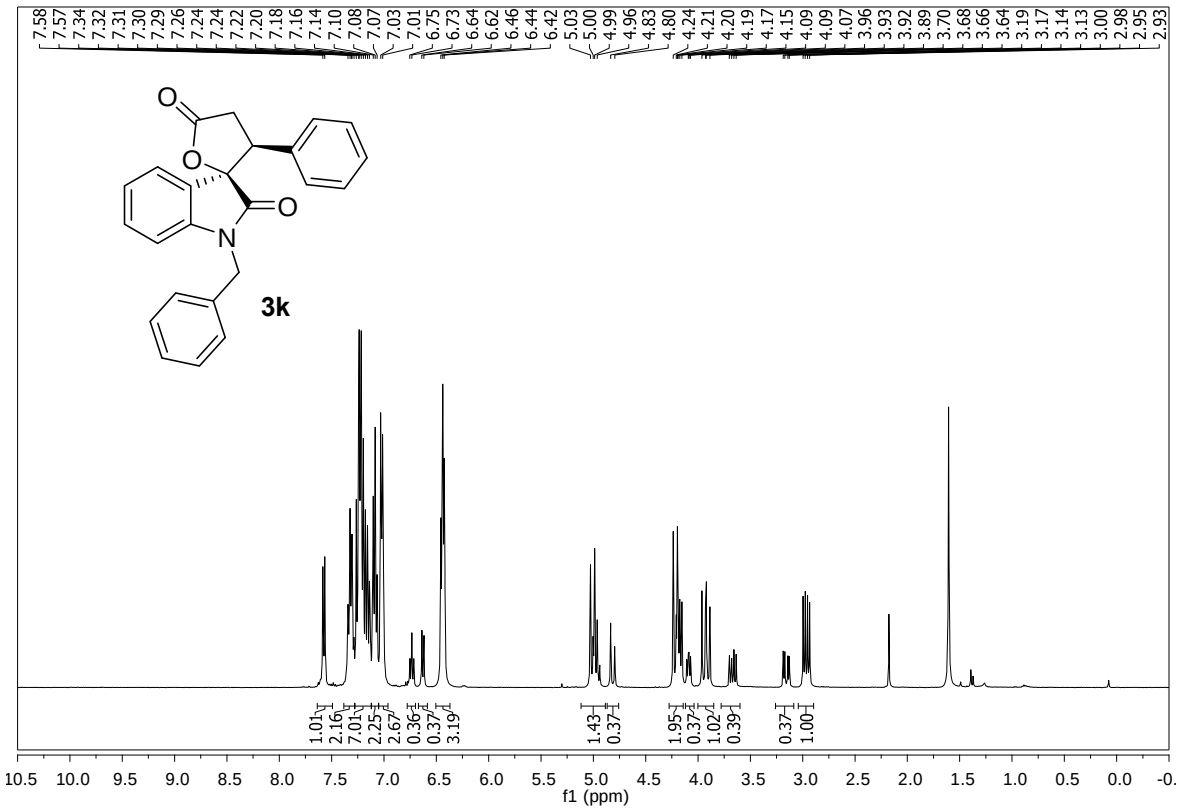


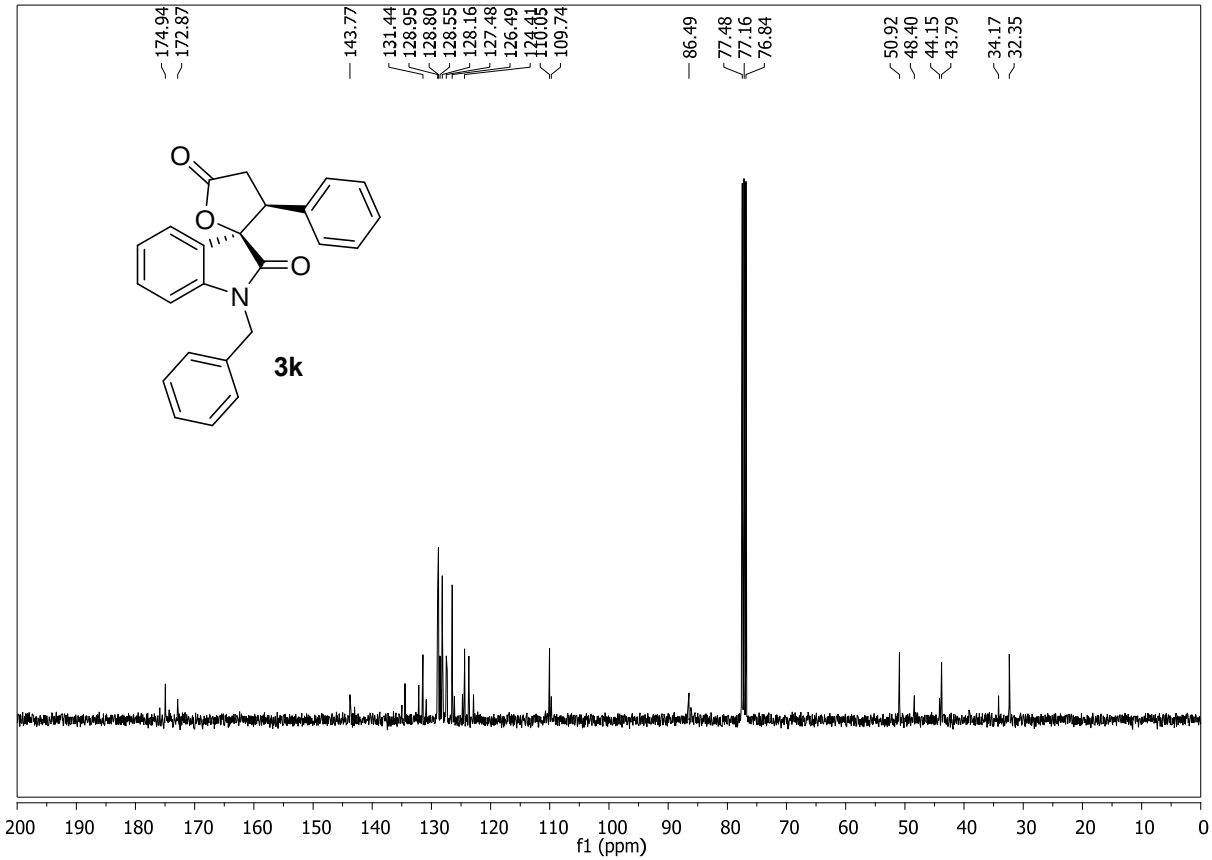
(2*R*,3*S*)-3-(Furan-2-yl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3j)



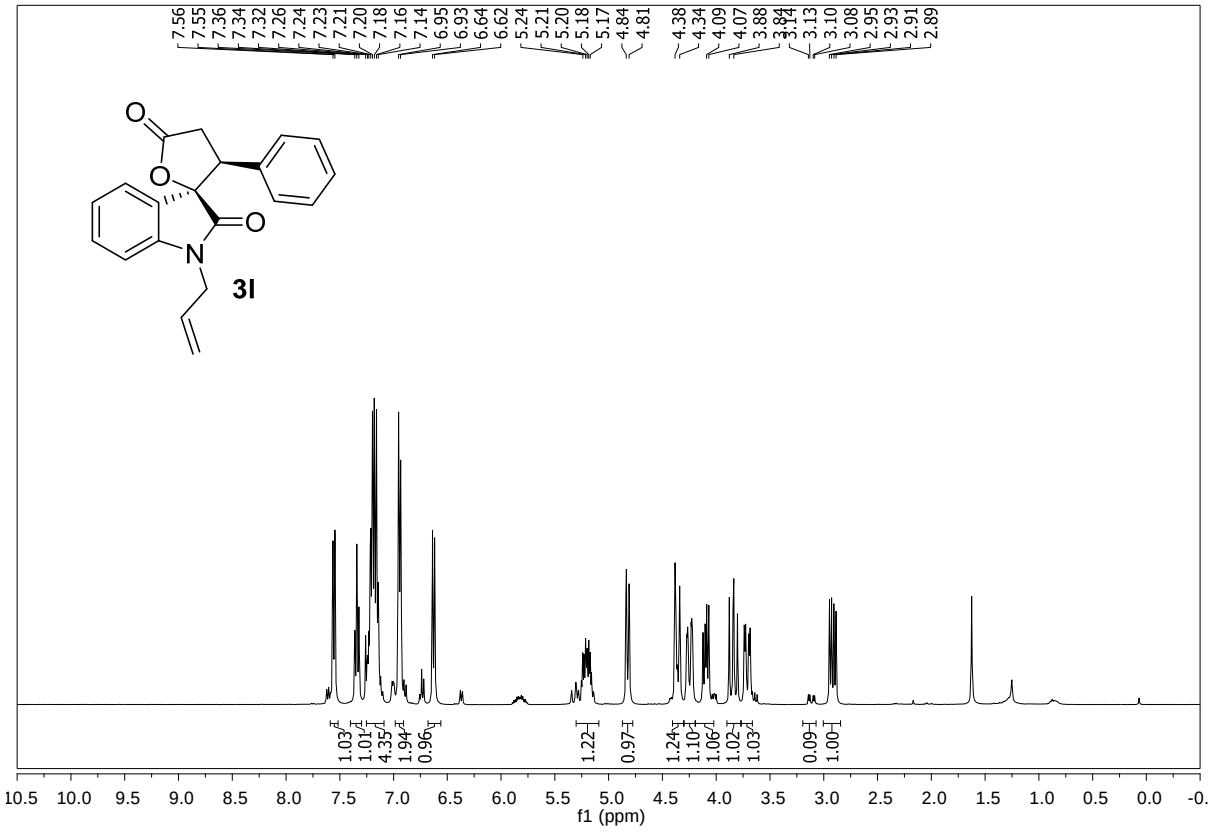


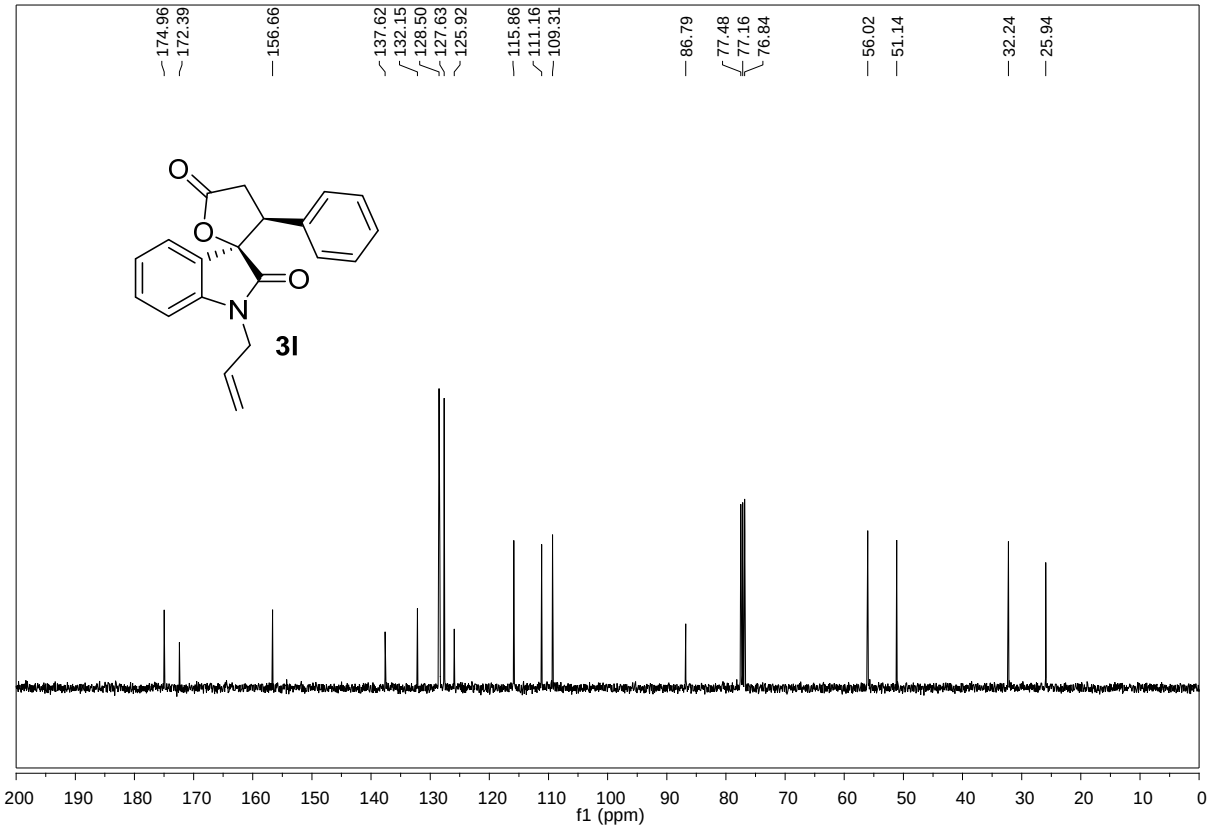
(2*R*,3*S*)-1'-Benzyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3k)



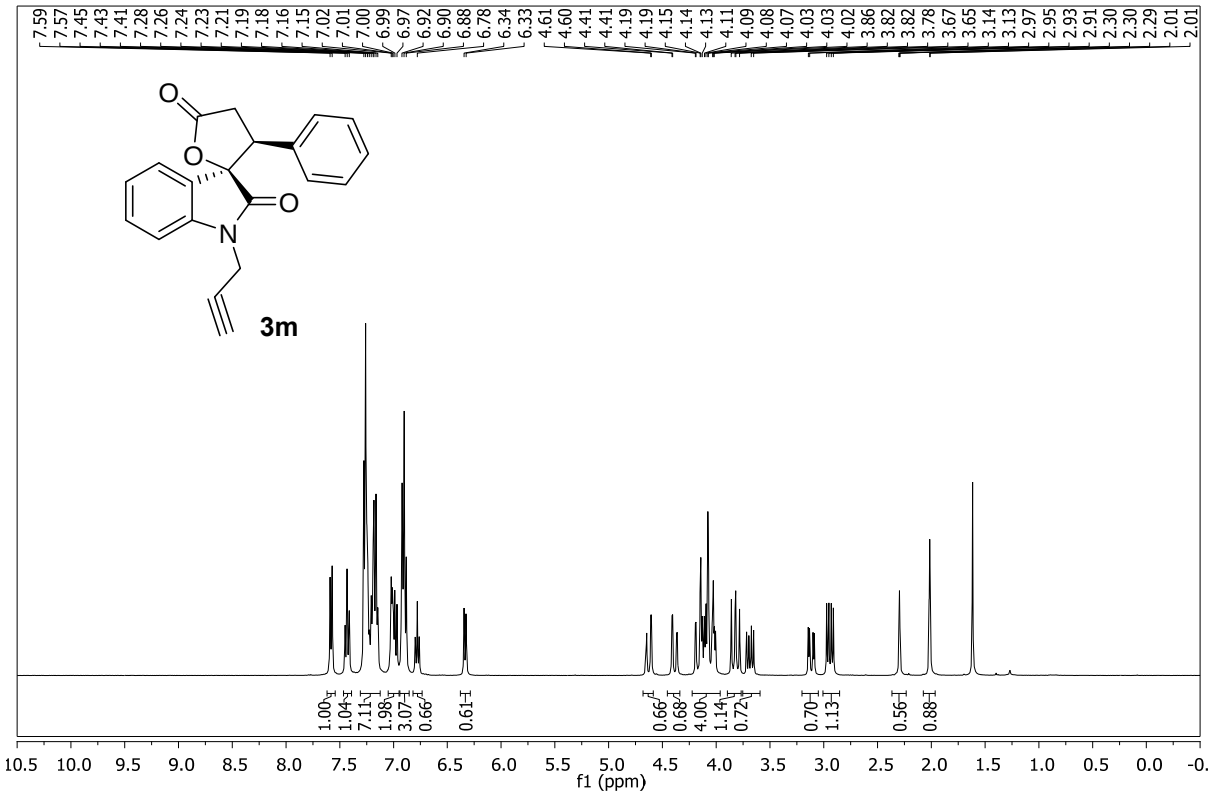


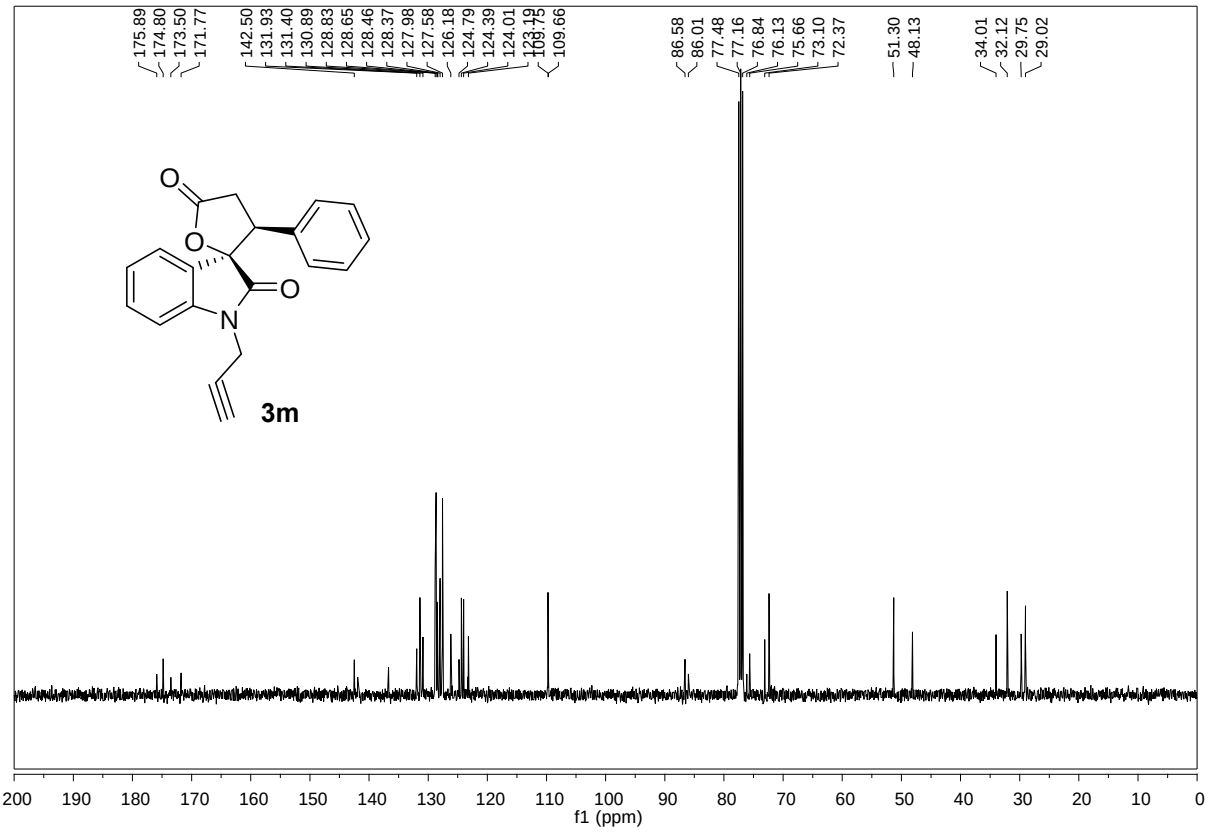
(2*R*,3*S*)-1'-Allyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3l)



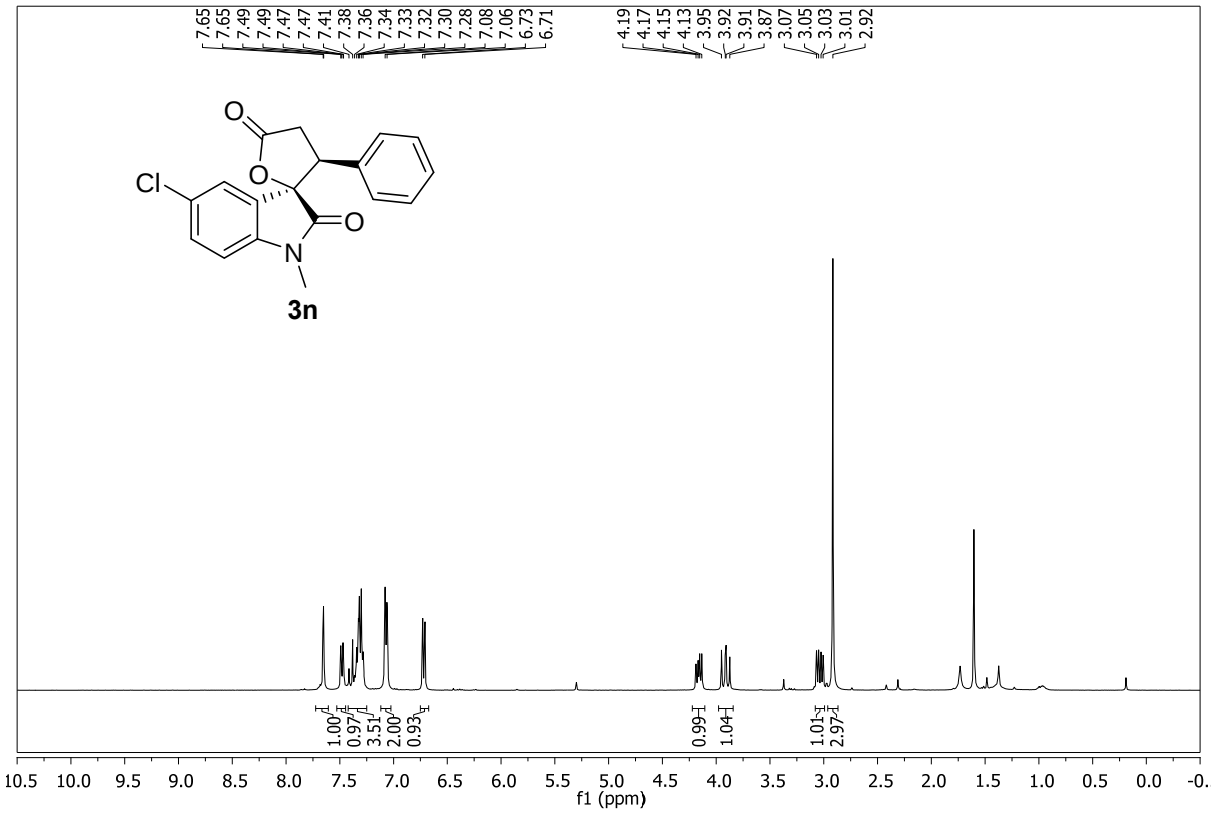


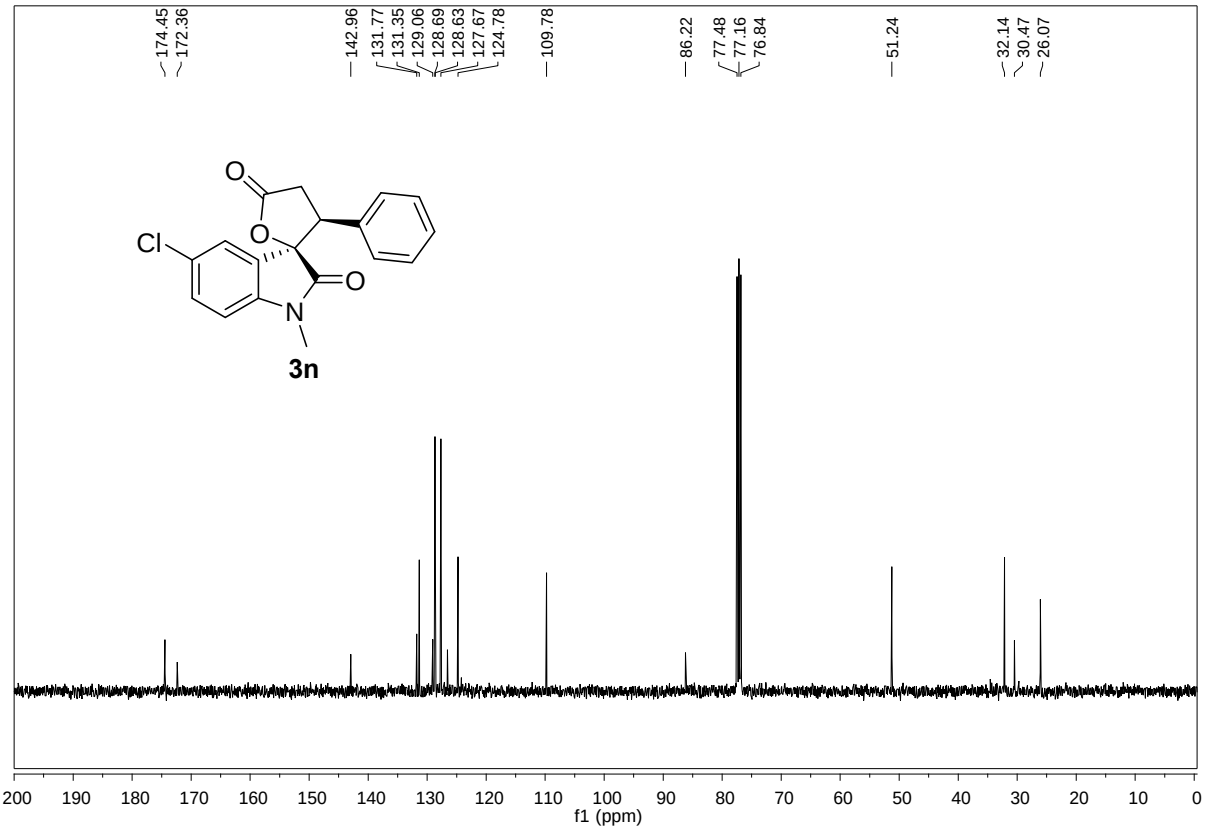
(2*R*,3*S*)-3-Phenyl-1'-(prop-2-yn-1-yl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3m)



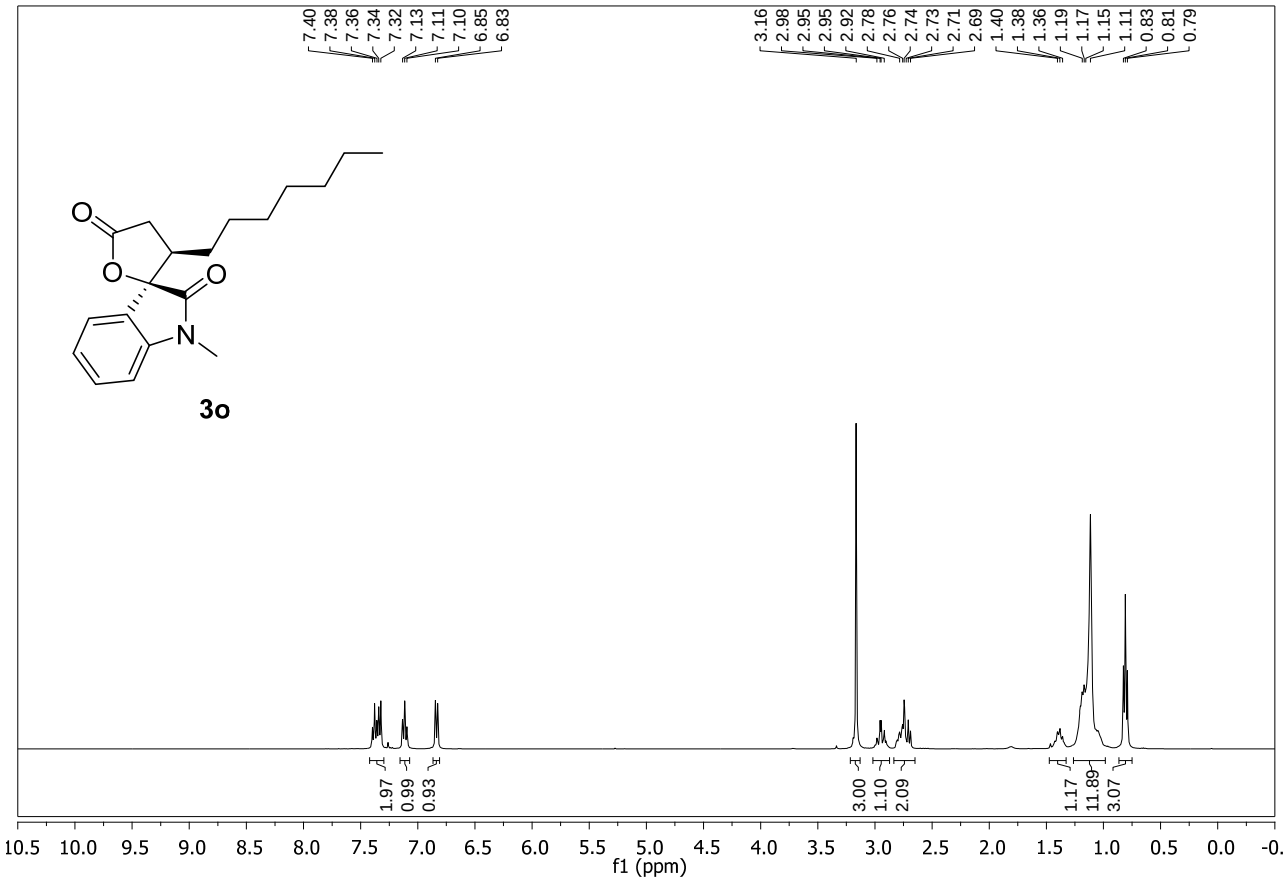


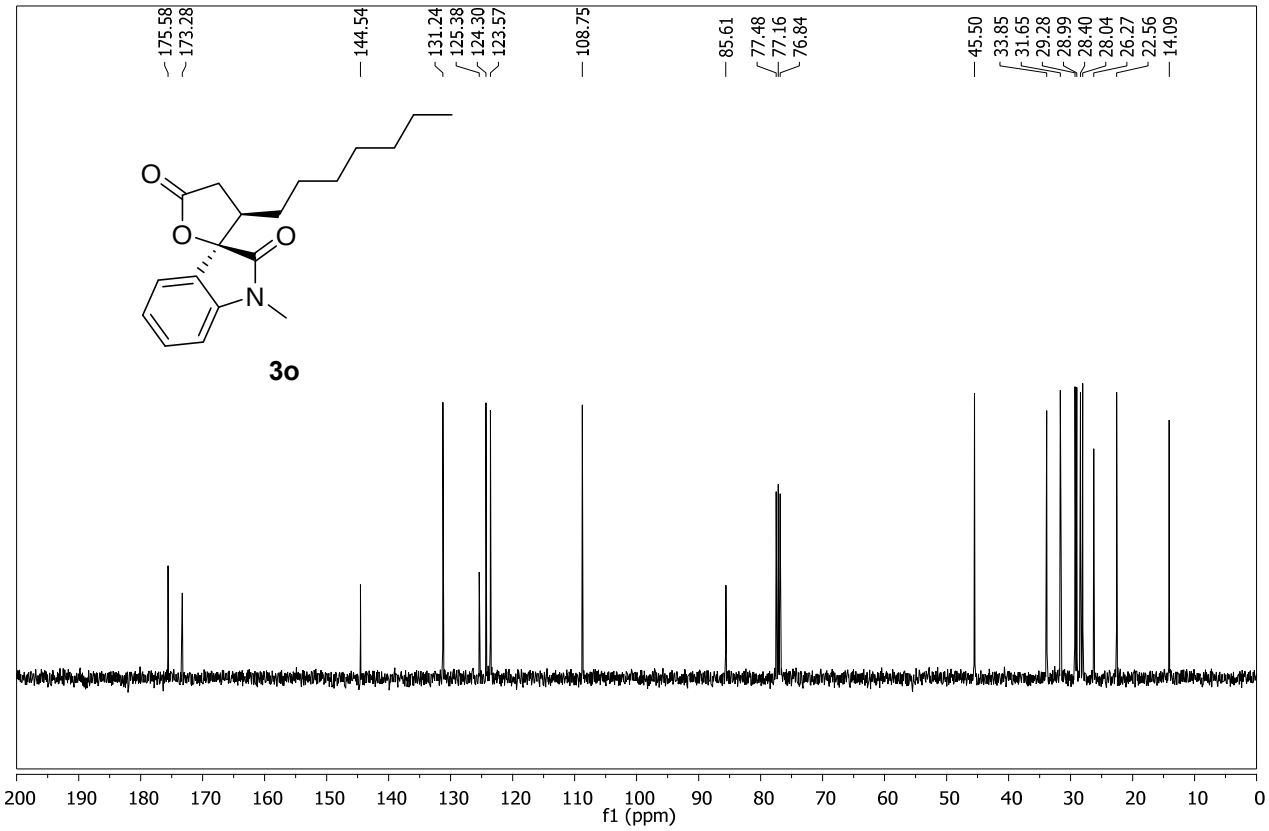
(2*R*,3*S*)-5'-Chloro-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3n)





3 (2*R*,3*R*)-3-Heptyl-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3o)

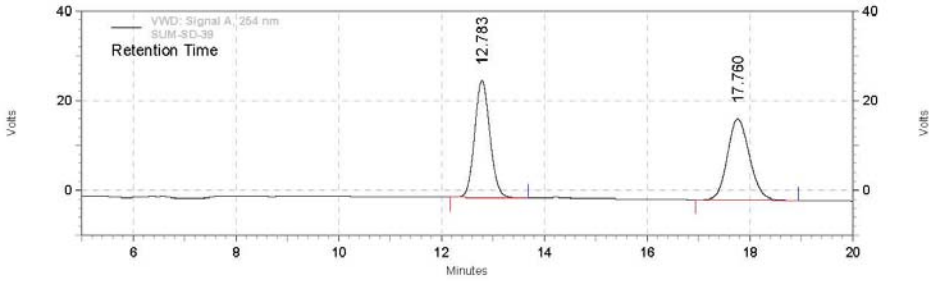




9. HPLC Data of spiro γ-butyrolactones

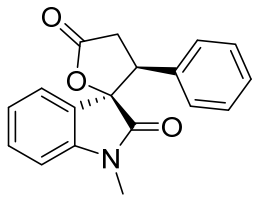
(2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\parent\SUM-SD-39.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 9/8/2015 1:16:57 AM Printed: 7/12/2016 11:03:35 AM

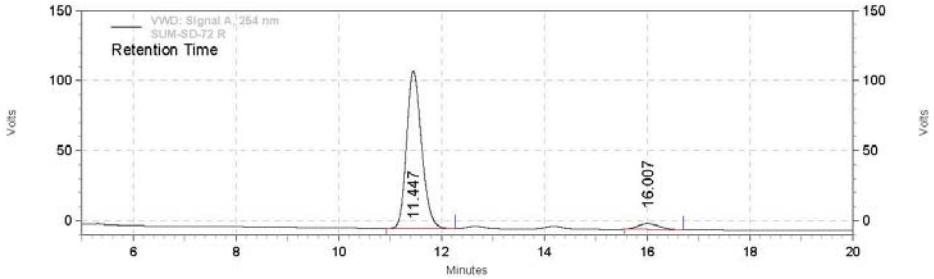


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.783	9029196	49.98
17.760	9037522	50.02
Totals	18066718	100.00



3a



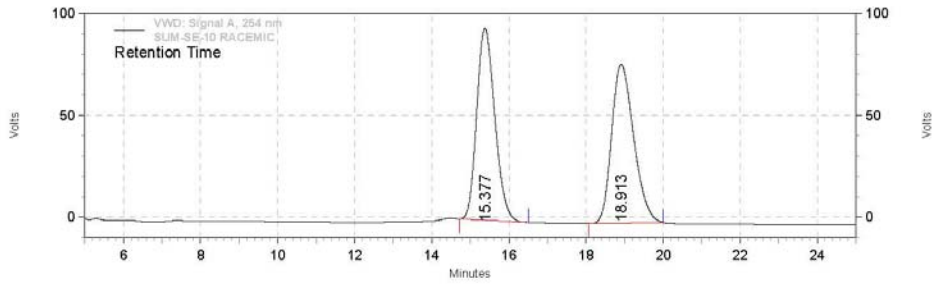
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
11.447	38156779	94.97
16.007	2019334	5.03
Totals	40176113	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

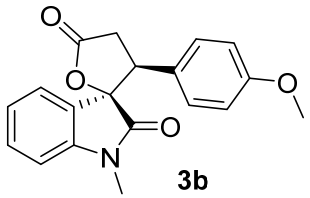
(2*R*,3*S*)-3-(4-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3b)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\4-ome-sum-se-10\SUM-SE-10 RACEMIC.dat
Method: D:\method\10% IPA-PE- C-D 1 port.met
Acquired: 4/20/2016 12:36:37 PM Printed: 7/12/2016 10:22:35 AM

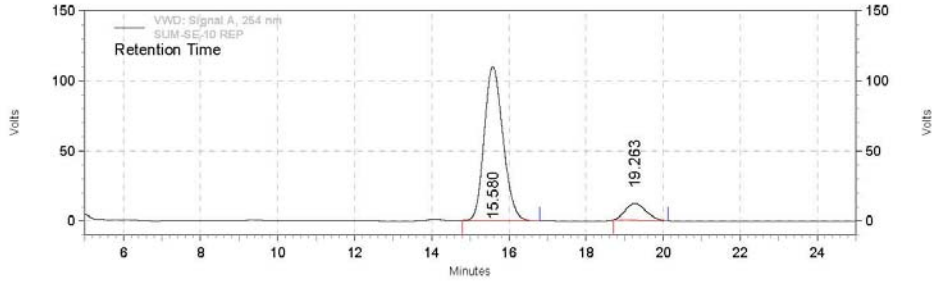


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
15.377	51414329	49.71
18.913	52024537	50.29
Totals	103438866	100.00



3b



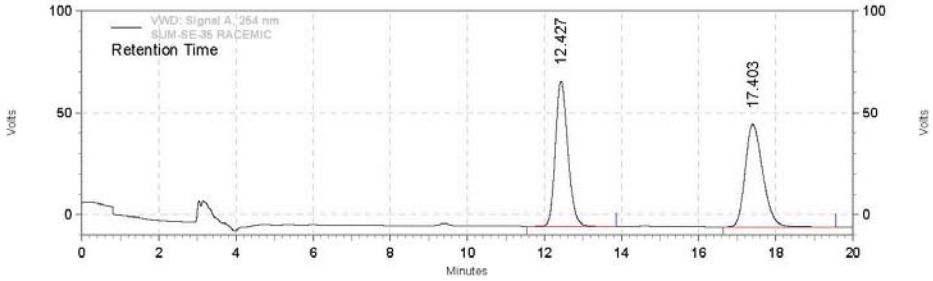
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
15.580	62353751	89.07
19.263	7653599	10.93
Totals	70007350	100.00

Column : Chiralpak AD
Eluent System : 88: 7:5(Pet Ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

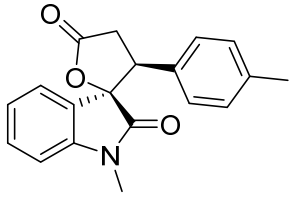
(2*R*,3*S*)-1'-Methyl-3-(p-tolyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3c)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-35 me\SUM-SE-35 RACEMIC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 5/4/2016 3:40:57 PM Printed: 7/12/2016 11:37:06 AM

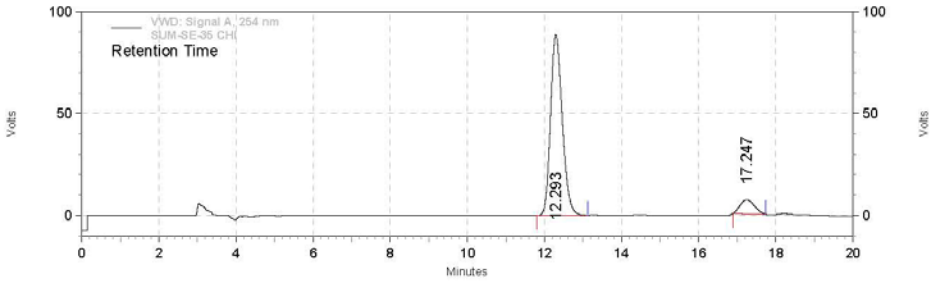


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.427	26764094	49.85
17.403	26922833	50.15
Totals	53686927	100.00



3c



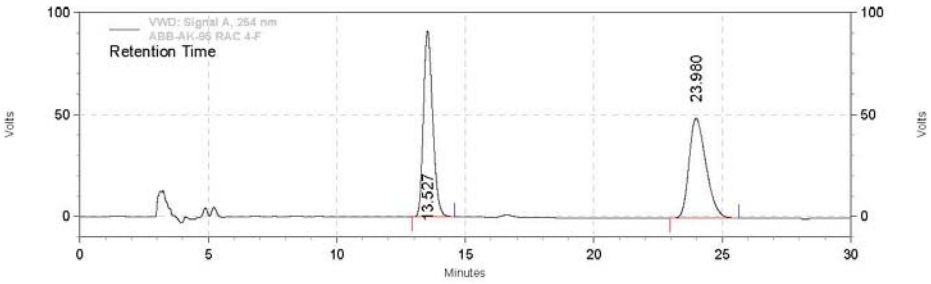
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.293	31347657	91.29
17.247	2989328	8.71
Totals	34336985	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

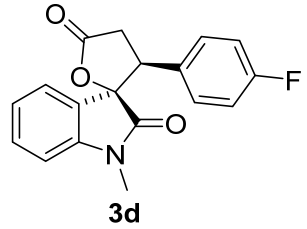
(2*R*,3*S*)-3-(4-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3d)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\4-f enal abb-ak-95\ABB-AK-95 RAC 4-F.dat
Method: D:\method\10% IPA-PE- C-D 1 port.met
Acquired: 4/27/2016 10:56:58 AM Printed: 7/12/2016 10:10:56 AM

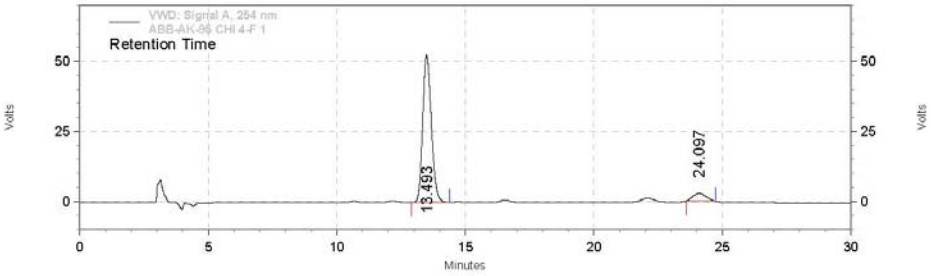


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.527	38500873	50.37
23.980	37936773	49.63
Totals	76437646	100.00



3d



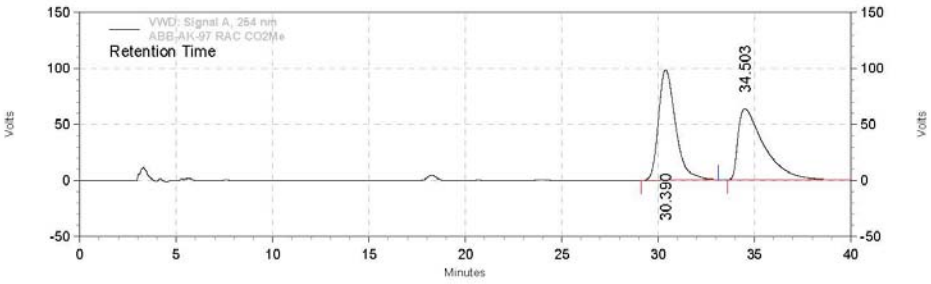
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.493	20561155	92.59
24.097	1645045	7.41
Totals	22206200	100.00

Column : Chiralpak AD
Eluent System : 88: 7:5(Pet Ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

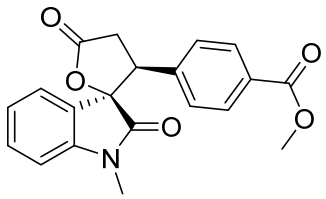
Methyl 4-((2*R*,3*S*)-1'-methyl-2',5-dioxo-4,5-dihydro-3*H*-spiro[furan-2,3'-indolin]-3-yl)benzoate (3e)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\4-co2me abb ak-97\ABB-AK-97 RAC CO2Me.dat
Method: D:\method\10% IPA-PE- C-D 1 port.met
Acquired: 4/29/2016 4:35:05 PM Printed: 7/12/2016 9:59:08 AM

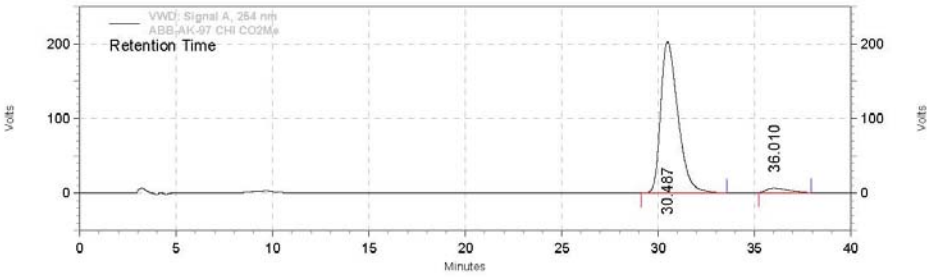


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
30.390	101304668	50.34
34.503	99955890	49.66
Totals	201260558	100.00



3e



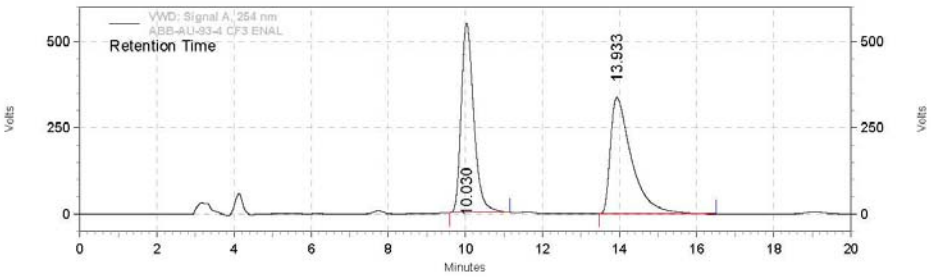
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
30.487	210763918	96.36
36.010	7965598	3.64
Totals	218729516	100.00

Column : Chiralpak AD
Eluent System : 88: 7:5(Pet Ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

(2*R*,3*S*)-1'-Methyl-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3f)

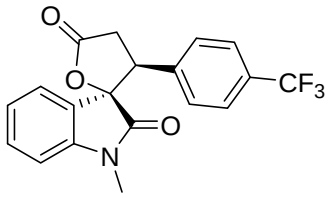
Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\4 cf3 enal-abb-ak-93\ABB-AU-93-4 CF3 ENAL.dat
Method: D:\method\10% IPA-PE- C-D 1 port.met
Acquired: 4/25/2016 12:09:41 AM Printed: 7/11/2016 7:59:08 PM



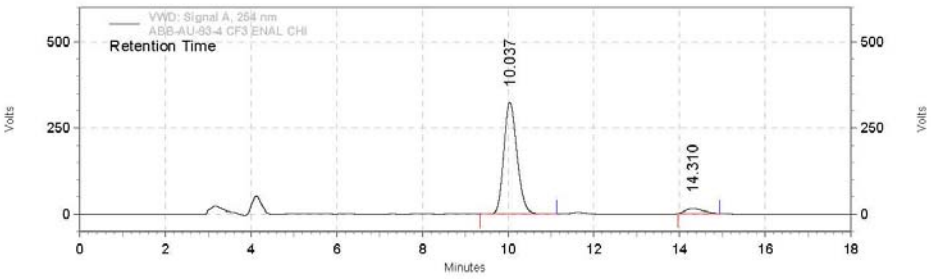
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
10.030	208862565	49.36
13.933	214247312	50.64

Totals		
	423109877	100.00



3f



VWD: Signal A, 254 nm Results

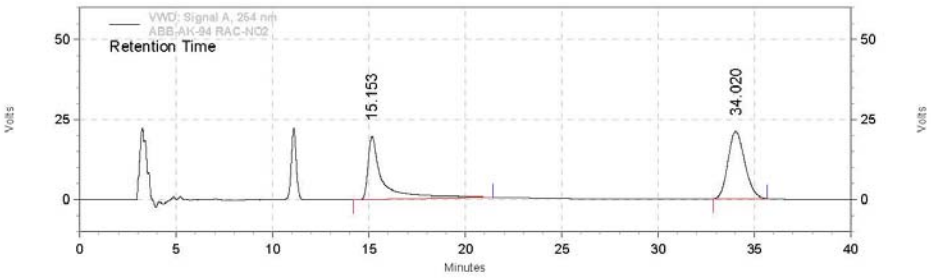
Retention Time	Area	Area %
10.037	116039940	94.15
14.310	7209036	5.85

Totals		
	123248976	100.00

Column : Chiralpak AD
Eluent System : 88: 7:5(Pet Ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

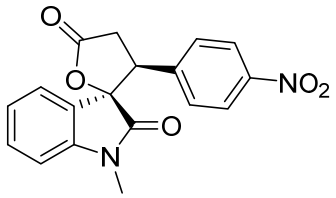
(2*R*,3*S*)-1'-Methyl-3-(4-nitrophenyl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3g)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\4- cf3 enal abb-ak-94\ABB-AK-94 RAC-NO2.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 5/4/2016 8:30:13 PM Printed: 7/11/2016 7:48:39 PM

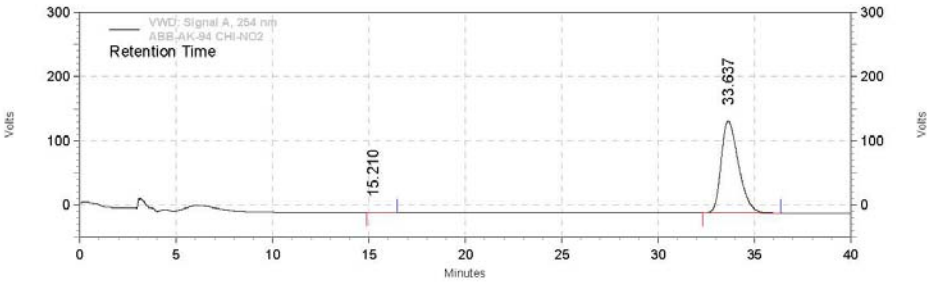


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
15.153	17767445	45.36
34.020	21405039	54.64
Totals	39172484	100.00



3g



VWD: Signal A, 254 nm Results

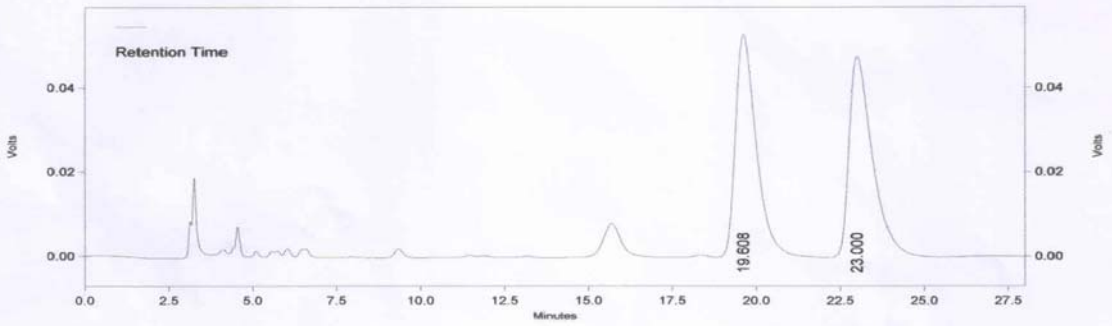
Retention Time	Area	Area %
15.210	111633	0.07
33.637	150765014	99.93
Totals	150876647	100.00

Column : Chiralpak AD
Eluent System : 88: 7:5(Pet Ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

(2*R*,3*S*)-3-(2-Methoxyphenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3h)

Shimadzu CLASS-VP V6.12 SP5 *Area % Report* Page 1 of 1

Sample ID : SVR-SI-119 RAC
Method Name: C:\CLASS-VP\Methods\J impurity.met
Data Name: C:\CLASS-VP\Data\Dr.Biju\SVR 1013
User: System
Acquired: 1/11/17 2:17:05 PM
Printed: 1/11/17 2:45:46 PM

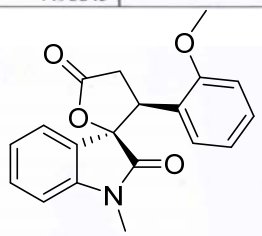


Detector A - 1 (254nm)

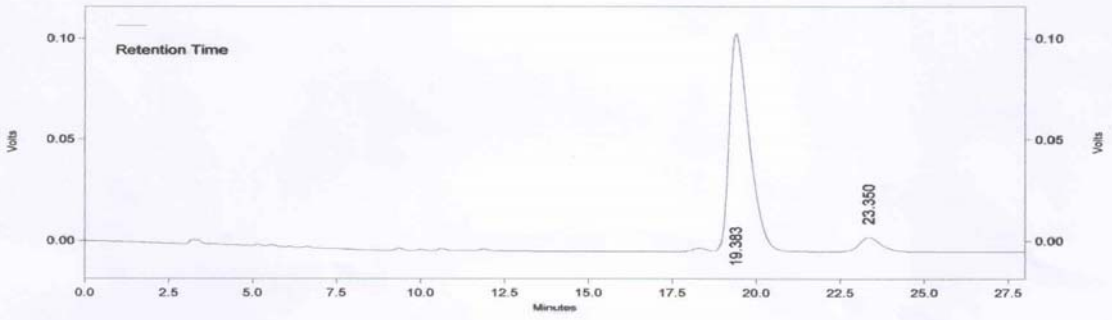
Pk #	Retention Time	Area	Area %
1	19.608	2244987	49.901
2	23.000	2253858	50.099
Totals		4498845	100.000

Shimadzu CLASS-VP V6.12 SP5 *Area % Report* Page 1 of 1

Sample ID : SVR-SI-119 CHI
Method Name: C:\CLASS-VP\Methods\J impurity.met
Data Name: C:\CLASS-VP\Data\Dr.Biju\SVR 1014
User: System
Acquired: 1/11/17 3:32:49 PM
Printed: 1/11/17 4:04:14 PM



3h



Detector A - 1 (254nm)

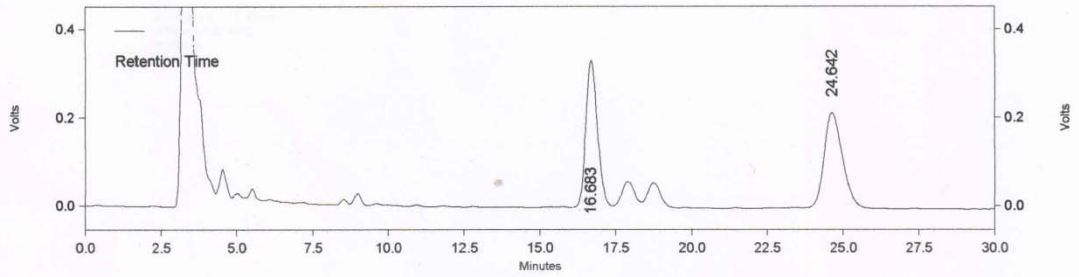
Pk #	Retention Time	Area	Area %
1	19.383	4401840	95.800
2	23.350	192994	4.200
Totals		4594834	100.000

Project Leader :Dr.A.T.BIJU
Column :Chiralcel AD (4.6mm x 250 mm)
Mobile Phase :IPA:Pet ether:MeOH(5:90.5)
Wavelength : 220 nm
Flow : 1 ml/min
Inject vol : 20 ul

(2*R*,3*S*)-3-(2-Fluorophenyl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3i)

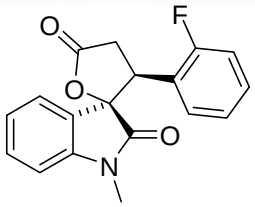
Shimadzu CLASS-VP V6.12 SP5 *Area % Report*
Page 1 of 1 ABB-AK-103 RAC

Method Name: C:\CLASS-VP\Data\Dr. U Das\akm33 chiral
Data Name: C:\CLASS-VP\Data\Dr.Biju\Svr2329
User: System
Acquired: 5/10/16 1:46:42 PM
Printed: 5/10/16 4:01:58 PM

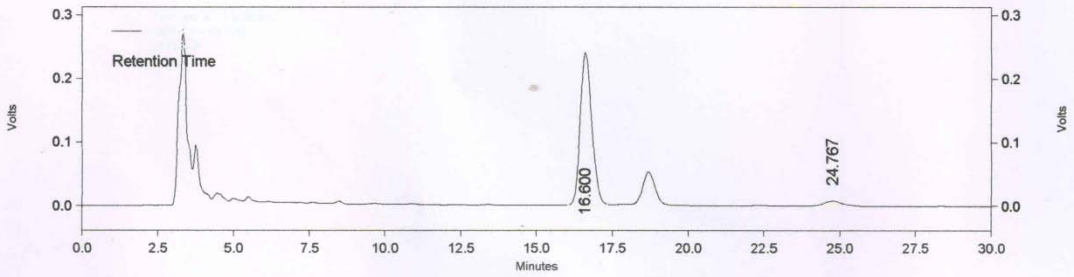


Detector A - 1 (220nm)

Pk #	Retention Time	Area	Area %
1	16.683	4435532	50.855
2	24.642	4286342	49.145
Totals		8721874	100.000



3i



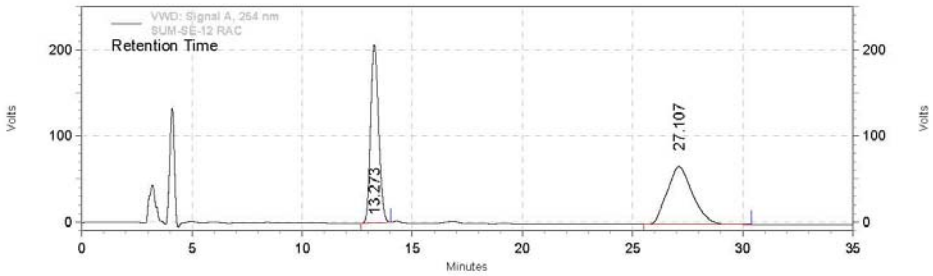
Detector A - 1 (220nm)

Pk #	Retention Time	Area	Area %
1	16.600	6446890	97.391
2	24.767	172698	2.609
Totals		6619588	100.000

Project Leader : Dr.A.T.Biju
Column : Chiralcel AD (250 X4.6cm)
Mobile Phase : IPA:Pet Ether:MEOH (5:90:5)
Flow Rate : 1 ml/min 280psi
Wavelength : 220 nm
Con. : 1 mg /1ml
Inject vol. : 20ul

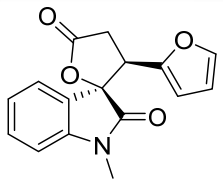
(2*R*,3*S*)-3-(Furan-2-yl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3j)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\furan enal-sum-se-12\SUM-SE-12 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 4/20/2016 12:37:17 PM Printed: 7/12/2016 10:54:03 AM

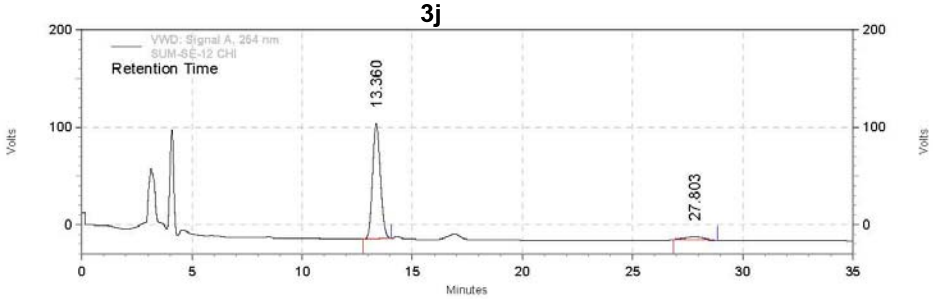


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.273	88487761	49.41
27.107	90617218	50.59
Totals	179104979	100.00



3j



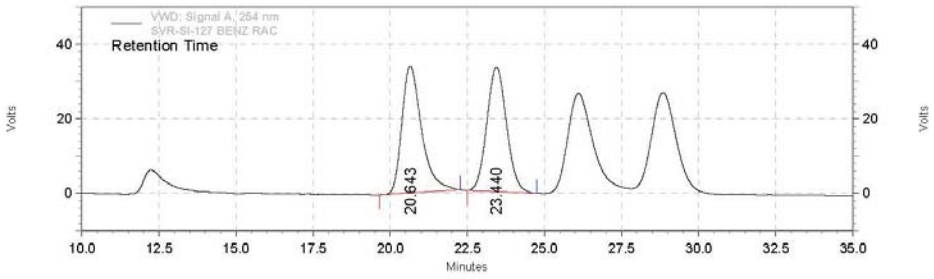
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.360	48793357	94.02
27.803	3106142	5.98
Totals	51899499	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

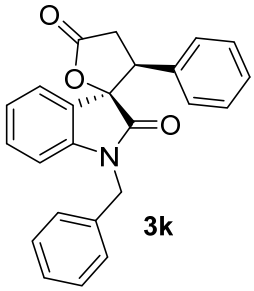
(2*R*,3*S*)-1'-Benzyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3k)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\benz prot-svr si-127\SVR-SI-127 BENZ RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 4/26/2016 1:01:05 PM Printed: 7/12/2016 10:45:00 AM

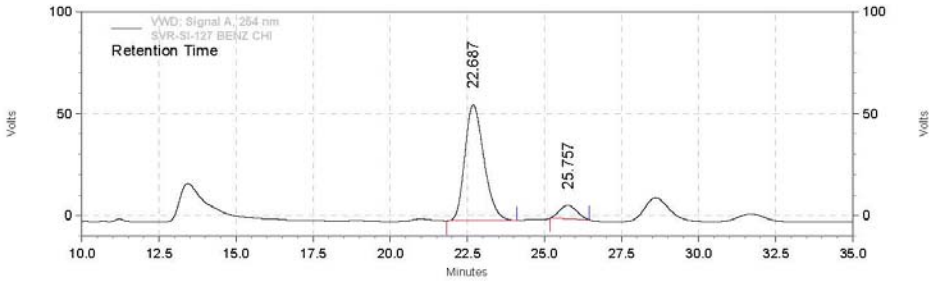


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
20.643	25413284	50.56
23.440	24847823	49.44
Totals	50261107	100.00



3k



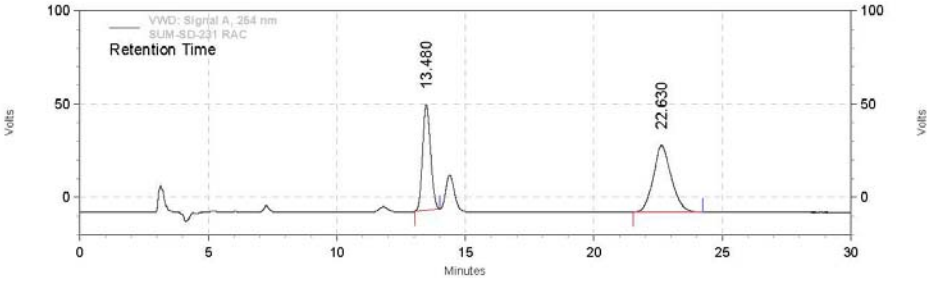
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
22.687	41016498	90.39
25.757	4360718	9.61
Totals	45377216	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

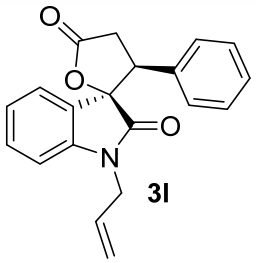
(2*R*,3*S*)-1'-Allyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3l)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-21 allylic protection\SUM-SD-231 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 2/16/2016 12:15:24 PM Printed: 7/12/2016 11:18:40 AM

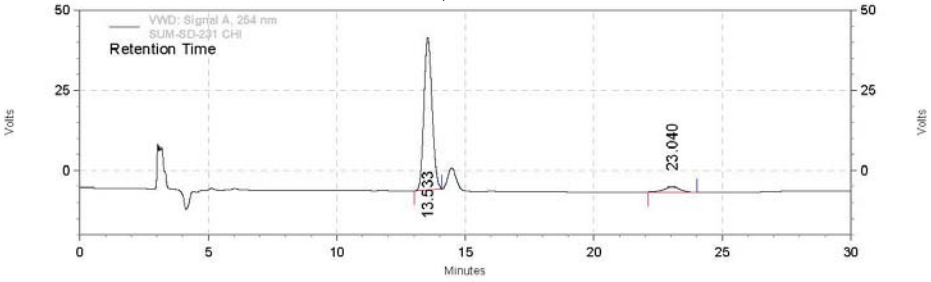


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.480	20587809	41.41
22.630	29126202	58.59
Totals	49714011	100.00



3l



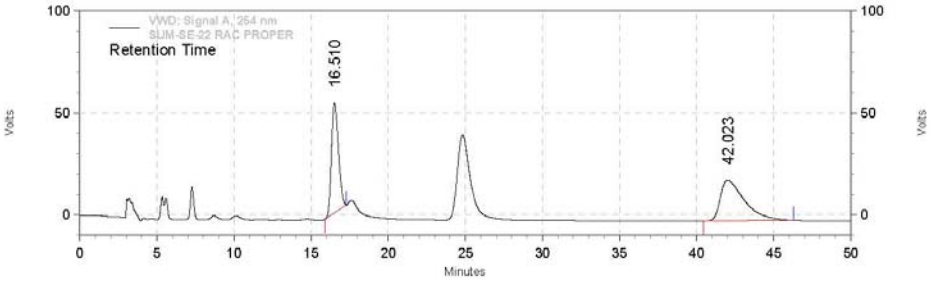
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
13.533	17501994	93.18
23.040	1281494	6.82
Totals	18783488	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

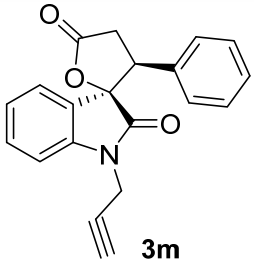
(2*R*,3*S*)-3-Phenyl-1'-(prop-2-yn-1-yl)-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3m)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-22 propergylic\SUM-SE-22 RAC PROPER.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 5/3/2016 11:46:31 AM Printed: 7/12/2016 11:32:19 AM

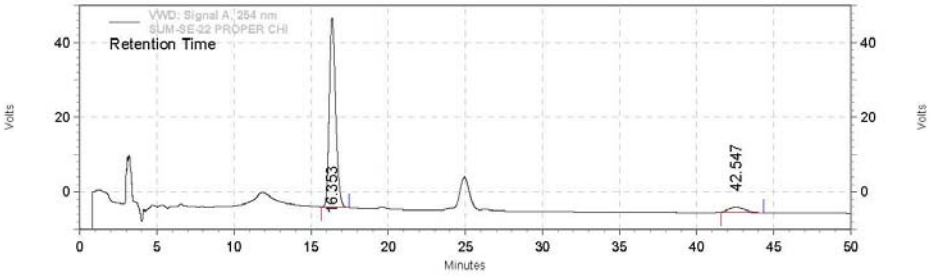


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
16.510	28592735	43.86
42.023	36602580	56.14
Totals	65195315	100.00



3m



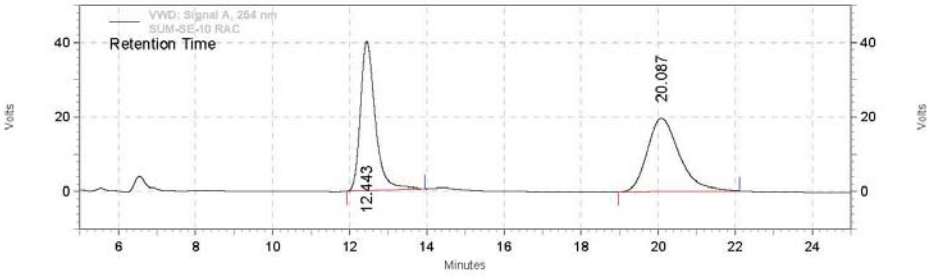
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
16.353	24370973	93.75
42.547	1624128	6.25
Totals	25995101	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

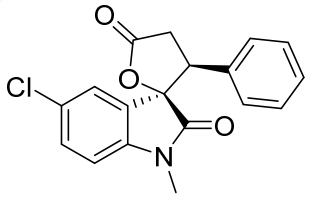
(2*R*,3*S*)-5'-Chloro-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3n)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-18 5 cl isatin\SUM-SE-10 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 4/23/2016 5:55:44 PM Printed: 7/12/2016 11:11:49 AM

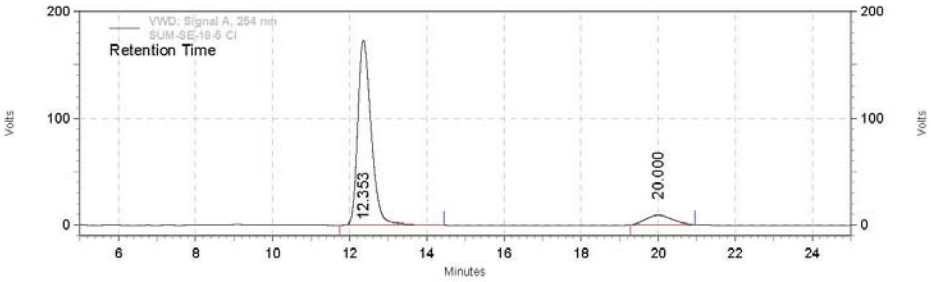


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.443	17889801	48.41
20.087	19064369	51.59
Totals	36954170	100.00



3n



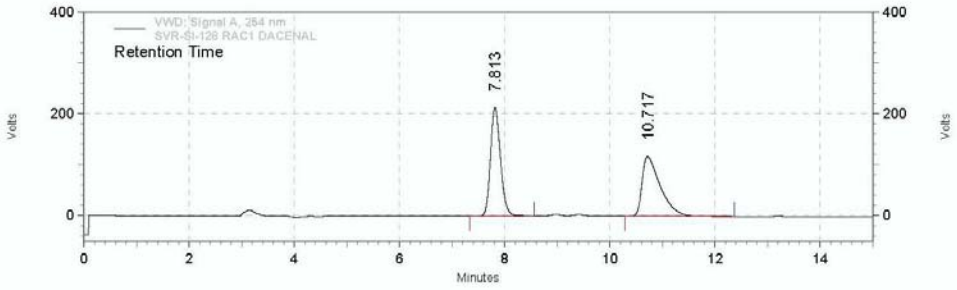
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.353	70260844	90.79
20.000	7128131	9.21
Totals	77388975	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

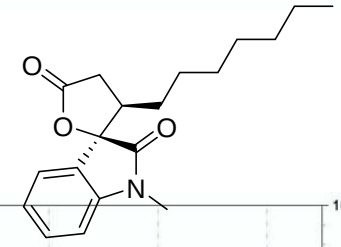
3 (2*R*,3*R*)-3-Heptyl-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3o)

Data File: D:\BIJU\SBM\SVR-SI-128 RAC1 DACENAL.dat
Method: E:\cvr\96comp..met
Acquired: 4/26/2016 11:07:59 PM Printed: 11/28/2016 12:29:50 PM

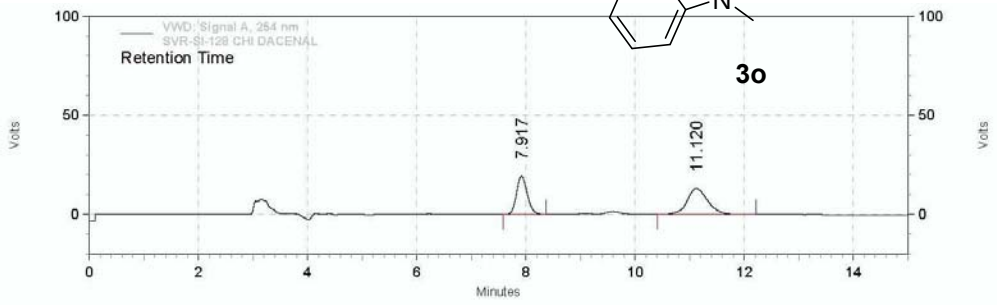


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
7.813	47257655	50.04
10.717	47183542	49.96
Totals	94441197	100.00



3o



VWD: Signal A, 254 nm Results

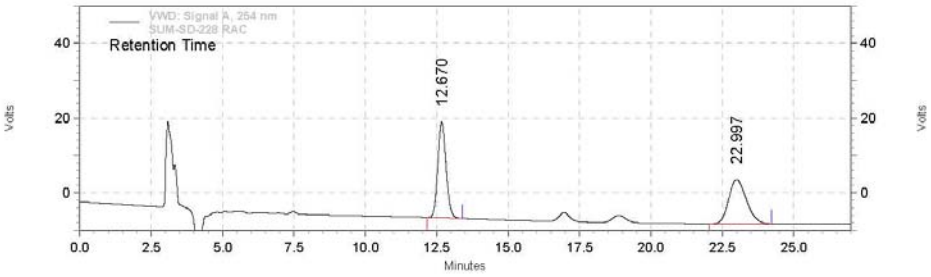
Retention Time	Area	Area %
7.917	4400044	42.98
11.120	5836534	57.02
Totals	10236578	100.00

Column : Chiralcel AD-H
Eluent System : 88:7:5 (PE:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254nm
Sample Conc.: 1 mg/ ml

HPLC data of spiro γ-butyrolactones synthesized in oxidant free condition

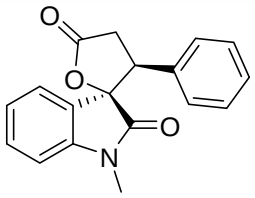
(2*R*,3*S*)-1'-Methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3a)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-45\SUM-SD-228 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 2/21/2016 7:32:18 AM Printed: 7/12/2016 12:03:15 PM

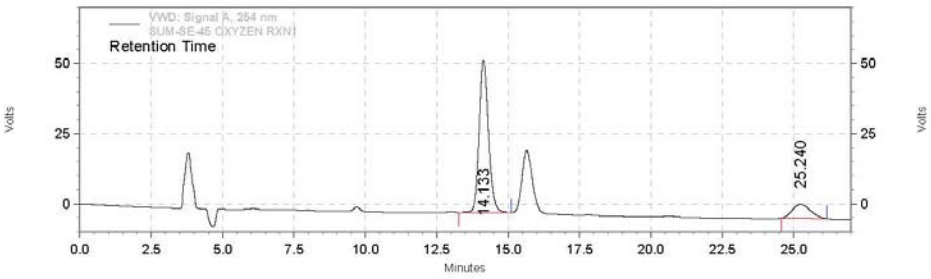


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
12.670	8610446	50.18
22.997	8547599	49.82
Totals	17158045	100.00



3a



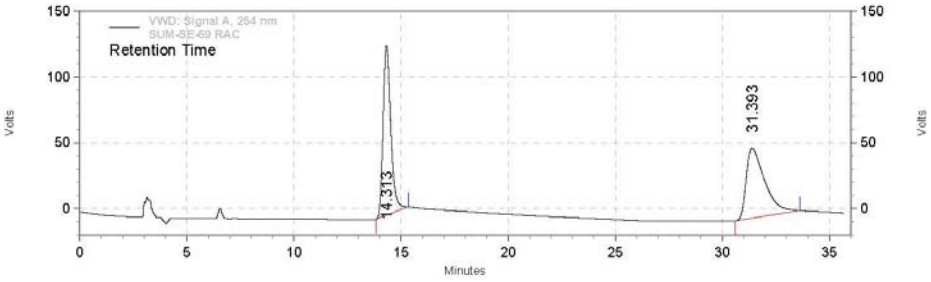
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
14.133	20733660	84.52
25.240	3797961	15.48
Totals	24531621	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

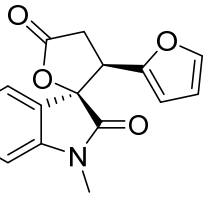
(2*R*,3*S*)-3-(Furan-2-yl)-1'-methyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3j)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-69\SUM-SE-69 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 6/7/2016 8:27:44 PM Printed: 7/12/2016 12:07:22 PM

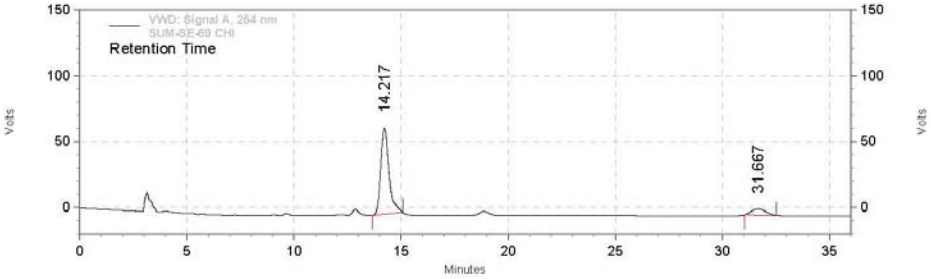


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
14.313	53816572	50.10
31.393	53605548	49.90
Totals	107422120	100.00



3j



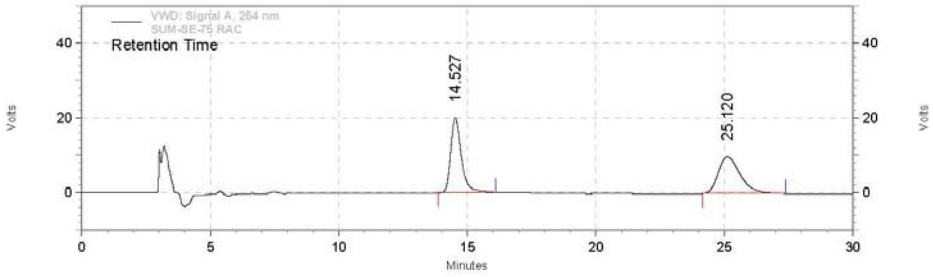
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
14.217	29290347	88.33
31.667	3869140	11.67
Totals	33159487	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml

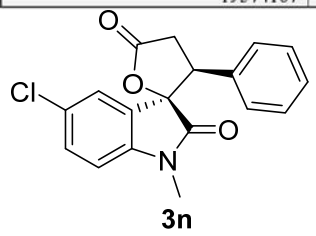
(2*R*,3*S*)-5'-Chloro-1'-methyl-3-phenyl-3,4-dihydro-5*H*-spiro[furan-2,3'-indoline]-2',5-dione (3n)

Data File: D:\BIJU\SBM\ISATIN ALCHOLE FINAL COMPOUND\sum-se-75\SUM-SE-75 RAC.dat
Method: D:\BIJU\Method\5% IPA-7% MeOH-88%PE,254NMrr, 1.0ML-MIN.MET
Acquired: 6/12/2016 12:20:59 PM Printed: 7/12/2016 12:13:22 PM

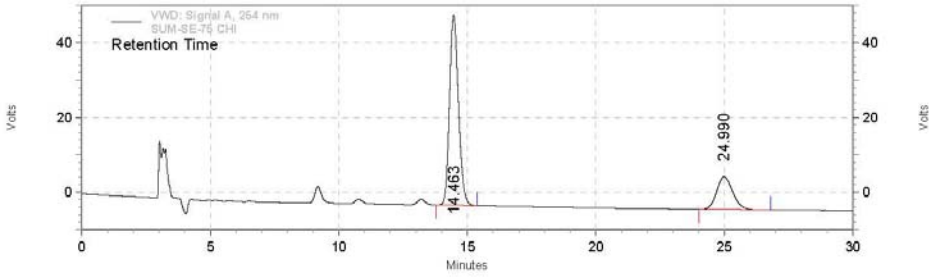


VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
14.527	9761624	49.87
25.120	9812543	50.13
Totals	19574167	100.00



3n



VWD: Signal A, 254 nm Results

Retention Time	Area	Area %
14.463	20702419	76.46
24.990	6373439	23.54
Totals	27075858	100.00

Column : Chiralpak AD
Eluent System : 88:7:5 (Pet ether:MeOH:IPA)
Flow rate: 1.0 ml/min
Injection vol..: 10ul
Wavelength: 254 nm
Sample Conc.: 1 mg/ ml