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Lewis acid-promoted synthesis of 3-tosylisoindolinone from 3-hydroxyisoindolinone: Access to complex furopyrroloisoindoledione

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An efficient methodology has been developed for the synthesis of sulfur-functionalized isoindolone scaffold from hydroxyisoindolinone *via* *N*-acyliminium ion intermediate using TosMIC and Lewis acid in good to excellent yields. The strategy features mild reaction conditions, broad substrate scope and metal-free reaction method. The protocol has been extended for the synthesis of complex furopyrroloisoindoledione derivatives.

Keywords: Lewis acid, hydroxyisoindolinone, furopyrroloisoindoledione, TosMIC, sulfonylation

Sulfone motifs are important functional molecules, due to their numerous chemical and physical applications[1,2]. They are useful building blocks in various transformations such as Julia olefination[3] or the Ramberg-Bäcklund reaction[4,5]. Chemically sulfonyl groups serve as important intermediates for the formation of C–C and C–heteroatom bonds in organic transformations[6-9]. Moreover, the most attractive feature of this motif is that the removal of the sulfonyl group might be possible *via* base-promoted β-elimination reaction[10]. Many sulfone derivatives are useful in medicinal chemistry[11], owing to their biological activity such as antifungal[12], antibacterial[13], antitumor agents[14]. They also act as proton pump inhibitors, antidepressants, and HIV-1 reverse transcriptase inhibitors[15]. Predominant drugs that contain sulfone motif are Apremilast, which is used as a phosphodiesterase 4 (PDE4) inhibitor as a remedy against psoriasis and psoriatic arthritis diseases. On the other hand, Eletriptan is a serotonin 5-HT1 receptor agonist, used to treat acute migraine headaches in adults, while Casodex a non-sterodial anti-androgens are used to cure prostate cancer (Fig. 1) [16].

There are many methods for the synthesis of substituted sulfones in the literature. Jiang's group was the first to report a method for sulfone functionalization catalyzed by $Cu(OAc)_2$ where sodium sulfonate acts as a sulfonating agent[17a]. Fan and Wu group has proposed, a two-step process for the synthesis of sulfones from aryldiazonium tetrafluoroborate, and sulfur dioxide in the presence of suitable base[17b]. Tiwari's group reported a method for the synthesis of biaryl sulfones using aryl halide, TosMIC, and magnetically recovered catalyst Cu^0/Fe_3O_4 with K_2CO_3 as a base[17c]. Reddy's group has discovered a way of synthesizing sulfones by using aryl halides and aryl boronic acid with TosMIC reagent and copper(II) as catalyst and ethanol-ethylene glycol as a solvent[17d]. Recently Zheng's group described a method for the synthesis of $C(sp^3)$-sulfonylation isoindolinones using sulfonic nucleophiles promoted by boron trifluoride etherate[17e]. However, most of the sulfonating reagents are very sensitive to air and moisture. So, chemists constantly contemplate attractive methods for the formation of sulfones.

From the literature it is found that *p*-toluenesulfonylmethyl isocyanide (TosMIC), which is also known as Van Leusen's reagent, holds three functionalized groups–isocyanide, sulfonyl moiety and acidic α-carbon, thereby acting as a versatile reagent in organic synthesis[18]. The chemistry of TosMIC is very well known and also shows competent reactivity in yielding new molecules. Recently, TosMIC was used as a sulfonating agent for the synthesis of different types of vinyl, allyl sulfones[19], and sulfonylation of phenacyl halides[20]. Due to their broad applications, we developed a methodology for the sulfonylation of hydroxyl-isoindolinone using TosMIC and boron trifluoride etherate (Scheme 1).

Results and Discussion

To begin with, 2-benzyl-3-hydroxyisoindolin-1-one (**1a**) and *p*-toluenesulfonylmethyl isocyanide (TosMIC)

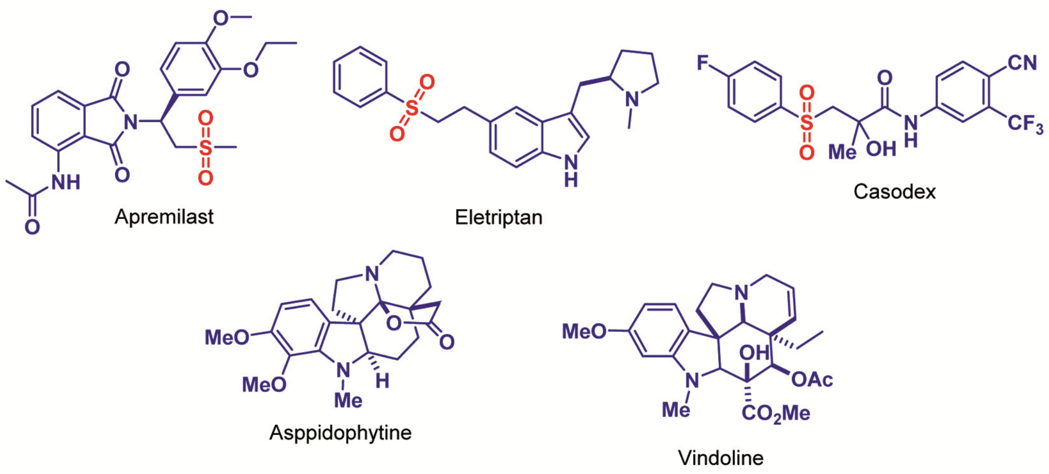
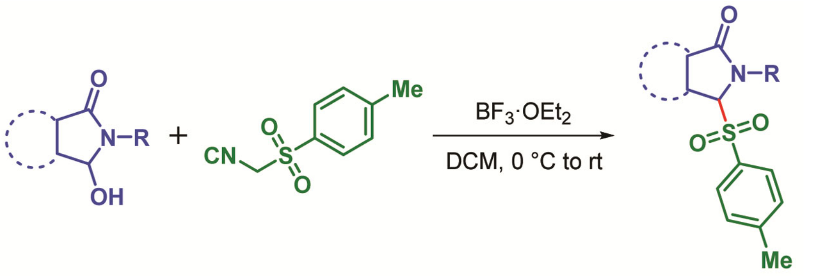


Fig. 1 — Bioactive compounds featuring sulfone moiety and fused pyrrolidine scaffolds



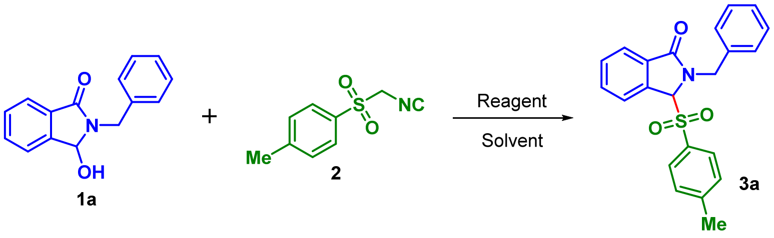
Scheme 1 — Sulfonylation of hydroxyisoindolinone

(**2**) was treated with $BF_3{\cdot}OEt_2$ (1.2 equiv.) in dry DCM at 0°C to RT (Table 1, entry 1). To our delight, a new product **3a** was isolated in 60% yield within 4 h of the reaction. Further screening of the reaction in different solvents like 1,2-dichloroethane (DCE), and acetonitrile with 1.2 equiv. of $BF_3{\cdot}OEt_2$, furnished the desired product in 42 and 51% yields, respectively (Table 1, entries 2 and 3). However, the reaction resulted in a decomposed product with toluene as the solvent (Table 1, entry 4). Other Lewis acids such as $InCl_3$, $FeCl_3$, and $In(OTf)_3$ also produced decomposed products (Table 1, entries 9-11). In contrast, TMSOTf afforded the desired product with a 45% yield (Table 1, entry 7). Furthermore, the reaction was optimized with Brønsted acids as well. Under the influence of p-$TsOH{\cdot}H_2O$ and camphor sulfonic acid (CSA), the reaction remained unresponsive (Table 1, entries 5 and 12). Triflic acid (TfOH) delivered the product with a lower yield of 47% (Table 1, entry 6). Another Brønsted acid, trifluoroacetic acid gave a decomposed product (Table 1, entry 8). Finally, 1.2 equiv. of $BF_3{\cdot}OEt_2$ in dry DCM at 0°C to RT in nitrogen atmosphere are found to be the optimum reaction conditions.

With the optimized condition in hand, the scope of the reaction was investigated with various substitutions in R^1 position (Scheme 2). Introduction of benzyl and substituted benzyl groups in R^1 position afforded the products **3a**, **3b**, and **3c** in 60, 61 and 56% yields, respectively. Aliphatic group (isopropyl) gave the desired product **3d** in 53% yield. Propargyl and phenyl substituted propargyl group furnished their respective products **3e** and **3f** in 49 and 46% yields, respectively. Substitution of R^1 with phenyl group provided the product **3g** in 72% yield. Aromatic groups with electron-donating (p-Me-C_6H_4) and electron-withdrawing groups (p-Cl-C_6H_4 and p-F-C_6H_4) afforded the products **3h**, **3i**, and **3j** in 74, 59 and 69% yields, respectively.

Next, the scope of the reaction was screened with various substituents in R^2 position of the imide. Substitution of R^2 with di-chloro and tetra-chloro groups furnished the product **3k** and **3l** in 59 and 53% yields, respectively. 2,3-Naphthalenedicarboximide gave the product **3m** in 42% yield. Aliphatic imides like succinimide and hexahydro phthalimide provided the product **3n** and **3o** in 41 and 59% yields. Unsaturated imides like maleimide and 5-norbornene-2,3-dicarboximide furnished their respective products

Table 1 — Optimization of the reaction



Entry[a]	Reagent	Equiv.	Solvent	Time (h)	Yield[b] (%)
1	$BF_3 \cdot OEt_2$	1.2	DCM	4.0	60
2	$BF_3 \cdot OEt_2$	1.2	DCE	4.0	42
3	$BF_3 \cdot OEt_2$	1.2	Acetonitrile	4.0	51
4	$BF_3 \cdot OEt_2$	1.2	Toluene	4.0	–[d]
5	*p*-TSA·H_2O	1.2	DCM	12	Nr[c]
6	TfOH	1.2	DCM	4.0	47
7	TMSOTf	1.2	DCM	4.0	45
8	CF_3CO_2H	1.2	DCM	4.0	–[d]
9	$InCl_3$	1.2	DCM	4.0	–[d]
10	$FeCl_3$	1.2	DCM	4.0	–[d]
11	$In(OTf)_3$	1.2	DCM	4.0	–[d]
12	CSA	1.2	DCM	12	Nr[c]

[a] Reaction conditions: All reactions were carried out under nitrogen atmosphere, **1a** (1.0 equiv.) and **2** (1.2 equiv.), solvent (3.0 mL). [b] Isolated yield. [c] No reaction. [d] Complex mixture.

3p and **3q** in 42 and 49% yields, respectively. The strategy was further extended to include unsaturated esters in R^1 position of the substituted imido alcohol. Under the standard reaction conditions, products **3r**, **3s**, and **3t** were obtained in 43-47% yields. The structure of compounds was determined by ^1H, ^{13}C NMR, and mass spectrometry, and finally by X-ray crystallographic analysis of compound **3a** (CCDC: 2430245).

The mechanism of the reaction is delineated in Scheme 3. Under the influence of a Lewis acid, the imido alcohol **1** produced an *N*-acyliminium ion intermediate **A**. Simultaneously, TosMIC transformed to form the intermediate **B**. Subsequent interaction between intermediates **A** and **B** led to the formation of the desired sulfur-functionalized isoindoline derivative **3**.

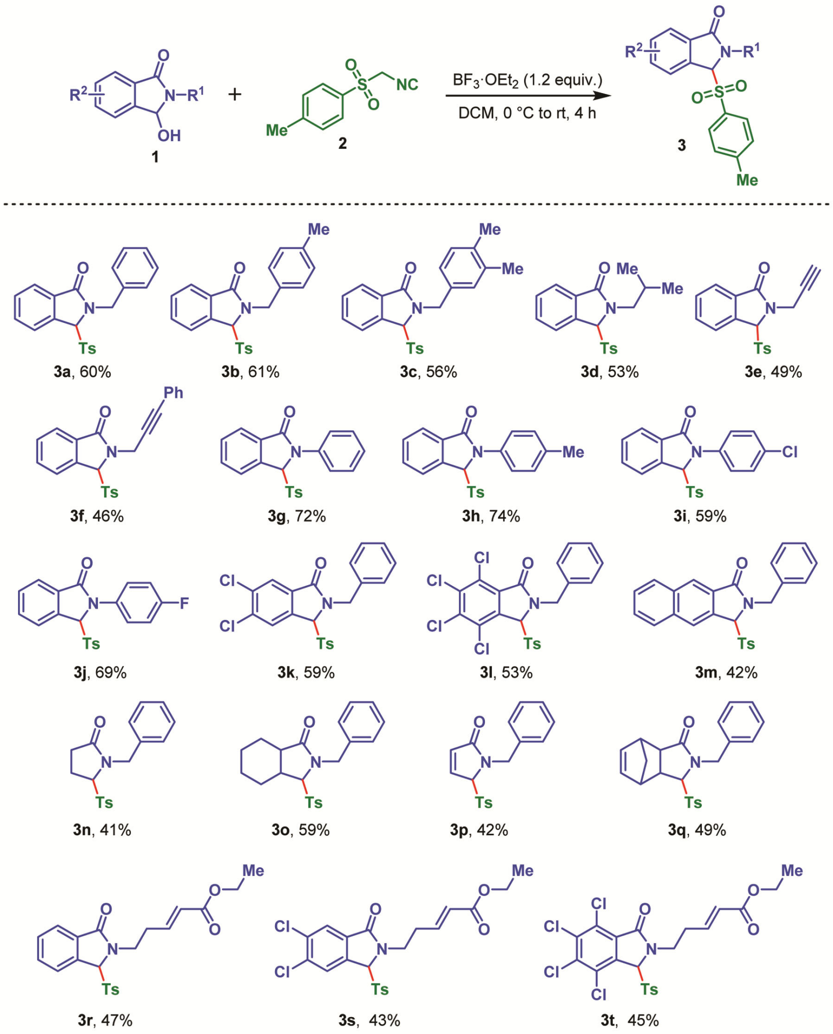
To demonstrate the synthetic utility of the sulfone-derived products **3**, a late-stage modification was carried out with NaH as a base in a mixed solvent (dry THF: dry DMSO = 9:1) at 0°C to RT (Scheme 4). The reaction furnished highly intricated furopyrroloisoindoledione derivatives **4a-4c** in 33-47% yields. These types of alkaloid like compounds with spirocyclic lactone and lactam are of synthetic importance as they are found in many biologically active molecules and natural products[16e,21]. The structure of compound **4** is determined by ^1H, ^{13}C NMR and mass spectrometry, and finally, by X-ray crystallographic analysis of compound **4a** (CCDC: 2430246).

Mechanism for the formation of furo-pyrroloisoindolediones **4** is shown in Scheme 5. Under the influence of a base (NaH), the sulfone substituted imides **3** generates the intermediate **D** *via* an intramolecular Michael addition reaction of the adjacent C-atom of the sulfone group to the unsaturated ester group. Subsequent elimination of sodium tosylsulfinate from intermediate **D** by the concomitant attack through the O-atom of the proximal ester group leads to the formation of intermediate **E**. Finally, acidic hydrolysis of intermediate **E**, followed by a keto-enol tautomerization furnished the desired furo-pyrroloisoindoledione derivative **4**.

Experimental Section

General Information

All the reagents were of reagent grade (AR grade) and were used as purchased without further purification. Silica gel (60-120 mesh size) was used for column chromatography. Reactions were monitored by TLC



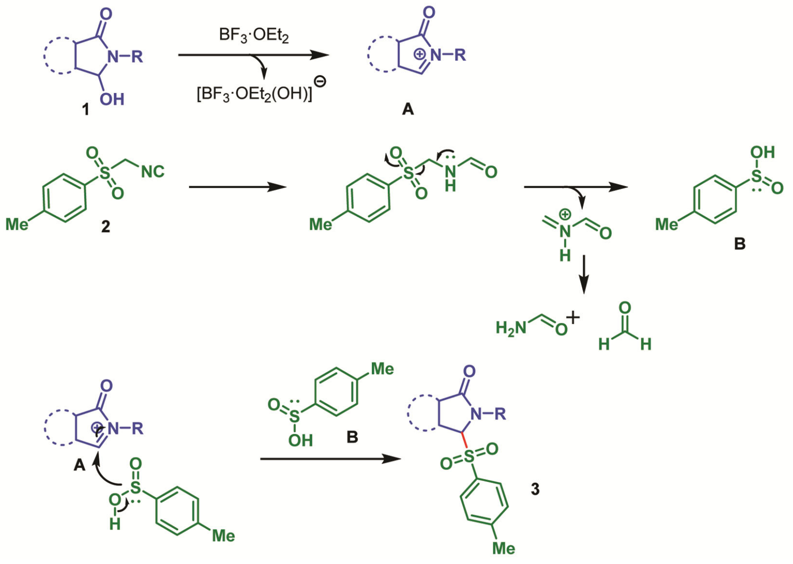
[a]Reaction conditions: All reactions were carried out under nitrogen atmosphere, **1** (1.0 equiv.) and **2** (1.2 equiv.), $BF_3·OEt_2$ (1.2 equiv.), DCM (3.0 mL).

Scheme 2 — Synthesis of 3-tosylisoindolinones

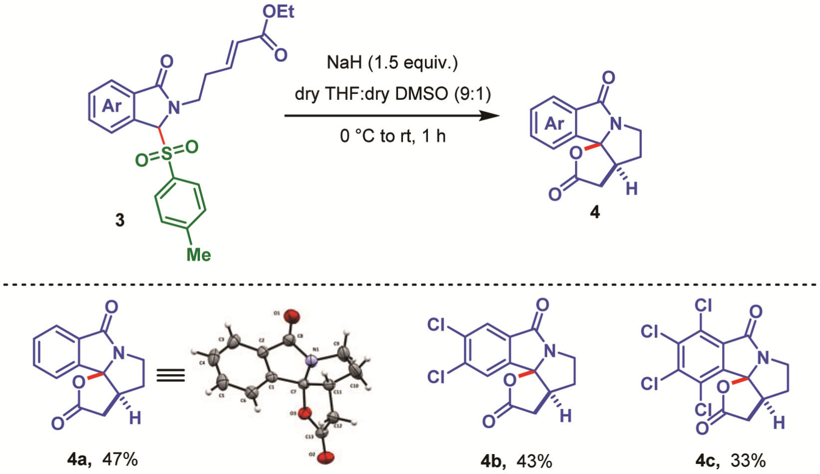
on silica gel GF_{254} (0.25 mm). Melting points were recorded in open capillary tube and are uncorrected. Fourier transform-infrared (FT-IR) spectra were recorded either as neat liquid or KBr pellets. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (600, 500, 400 MHz) or ^{13}C (150, 125, 100 MHz). Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (*J*) are given in Hz. HRMS spectra were recorded using Q-TOF mass spectrometer.

General procedure for synthesis of starting materials 1c, 1l, 1s and 1t

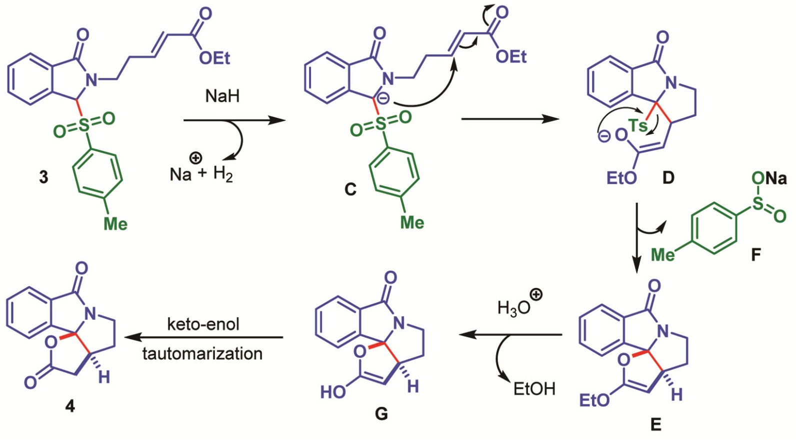
To a stirred solution of *N*-susbtituted imides (2 mmol, 1 equiv.) in MeOH (10 mL), was added $NaBH_4$ (4 mmol, 2 equiv.) at 0°C and the mixture was stirred for half an hour. After completion of the reaction, saturated sodium bicarbonate solution (10 mL) was added and the organic layer was extracted with dichloromethane (2×20 mL). The organic phase was washed with brine, dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the crude product, which was purified by column chromatrography over silica gel using ethyl acetate and hexane as eluent to give the carbinol amides **1.** The starting materials (**1a**, **1n**, **1q**)[22], (**1b**, **1o**)[23], (**1d**, **1m**)[24], (**1e**, **1f**)[25], (**1g**, **1h**, **1i**, **1j**)[26], **1k**[27], **1p**[28] and **1r**[29] were synthesized according to a literature report, and the spectroscopic data of the compound are in good agreement with the literature data.



Scheme 3 — Plausible mechanism for the transformation



Scheme 4 — Post synthetic application



Scheme 5 — Mechanism for the formation of furopyrroloisoindoledione

2-(3,4-Dimethylbenzyl)-3-hydroxyisoindolin-1-one, 1c: Colorless solid. R$_f$ (hexane/EtOAc 7:3) 0.42. m.p.160-162°C. Yield 80 mg, 79%. IR (KBr, neat): 3329, 2921, 1673, 1438, 1053, 747, 698 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.64 (d, *J* = 7.5 Hz, 1 H), 7.56-7.52 (M, 2 H), 7.44 (t, *J* =7.7 Hz, 1 H), 7.07 – 7.02 (M, 3 H), 5.59 (d, *J* = 11.6 Hz, 1 H), 4.79 (d, *J* = 14.5 Hz, 1 H), 4.16 (d, *J* = 14.6 Hz, 1H), 3.59-3.55 (M, 1 H), 2.20 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 167.5, 144.2, 137.2, 136.2, 134.4, 132.5, 131.6, 130.1, 130.0, 129.9, 126.2, 123.6, 81.2, 42.6, 19.9, 19.6; HRMS (ESI): Calcd for $C_{17}H_{18}NO_2$: (M + H)$^+$ 268.1332. Found: 268.1336.

2-Benzyl-4,5,6,7-tetrachloro-3-hydroxyisoindolin- 1-one, 1l:

Colorless solid. R$_f$ (hexane/EtOAc 8:2) 0.43. m.p.236-238°C. Yield 54 mg, 53%. IR (KBr, neat): 3352, 2944, 1706, 1216, 1024, 749, 696 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ 7.35 (t, *J* = 5.4 Hz, 4 H), 7.31-7.247 (M, 1 H), 7.09 (d, *J* = 9.2 Hz, 1 H), 5.73 (d, *J* = 9.1 Hz, 1 H), 4.90 (d, *J* = 15.4 Hz, 1 H), 4.38 (d, *J* = 15.4 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-*d*$_6$): δ 162.2, 143.5, 137.2, 135.8, 134.3, 129.0, 128.8, 128.6, 128.3, 127.8, 79.2, 43.0; HRMS (ESI): Calcd for $C_{15}H_{10}Cl_4NO_2$: (M + H)$^+$ 377.9431. Found: 377.9432.

(*E*)-Ethyl 5-(5,6-dichloro-1-hydroxy-3-oxoisoindolin-2-yl)pent-2-enoate, 1s: Pale yellow solid. R$_f$ (hexane/EtOAc 6:4) 0.57. m.p.136-138°C. Yield 60 mg, 59%. IR (KBr, neat): 3336, 2981, 1692, 1424, 1184, 1057, 768, 682, 627, 428 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.72 (s, 2 H), 6.94-6.87 (M , 1 H), 5.87 (d, *J* = 15.2 Hz, 1 H), 5.76 (s, 1H), 4.16 (q, *J* = 7.2 Hz, 2 H), 3.77 – 3.73 (M, 1 H), 3.62 – 3.59 (M, 1 H), 2.63 (t, *J* = 7.1 Hz, 2 H), 1.29 (t, *J* = 7.2 Hz, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.6, 165.6, 145.1, 143.1, 137.2, 135.1, 131.4, 125.9, 125.3, 123.8, 81.7, 60.8, 38.8, 31.3, 14.4; HRMS (ESI): Calcd for $C_{15}H_{16}Cl_2NO_4$: (M + H)$^+$ 344.0451. Found: 344.0448.

(*E*)-Ethyl 5-(4,5,6,7-tetrachloro-1-hydroxy-3-oxoisoindolin-2-yl)pent-2-enoate, 1t: Pale yellow solid. R$_f$ (hexane/EtOAc 6:4) 0.61. m.p.126-128°C. Yield 50 mg, 34%. IR (KBr, neat): 3356, 2932, 2856, 1732, 1661, 1436, 1326, 1274, 1197, 1095, 907, 847, 742, 428 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.87 – 6.79 (M, 1 H), 5.81 (dt, *J* = 15.7, 1.5 Hz, 1H), 5.74 (d, *J* = 9.4 Hz, 1 H), 4.08 (q, *J* = 7.2 Hz, 2 H), 3.94 (d, *J* = 10.2 Hz, 1 H), 3.78 – 3.72 (M, 1 H), 3.57 – 3.51 (M, 1 H), 2.58 – 2.52 (M, 2 H), 1.20 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.6, 163.3, 144.9, 141.4, 137.6, 136.2, 129.4, 129.1, 127.9, 123.9, 80.3, 60.8, 38.9, 31.1, 14.4; HRMS (ESI): Calcd for $C_{15}H_{14}Cl_4NO_4$: (M + H)$^+$ 413.9642. Found: 413.9634.

General Procedure for the Synthesis of Tosylisoindolone, 3a-t

To a solution of carbinol amides (0.71 mmol, 1 equiv.) and TosMIC (0.85 mmol, 1.2 equiv.) in dichloromethane (5 mL) at 0°C was added boron trifluoride etherate (0.85 mmol, 1.2 equiv.) dropwise under a nitrogen atmosphere. The reaction mixture was brought to RT, and the reaction was stirred for 4 h. After completion of the reaction, the reaction mixture was treated with saturated sodium bicarbonate solution (10 mL). The product was extracted with CH_2Cl_2 (2×15 mL), and the combined organic layer was washed with brine (10 mL). The organic layer was separated and dried over anhydrous Na_2SO_4 and evaporated using a rotary evaporator to obtain the crude product. The crude product was purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford the title compounds **3a-3t**.

2-Benzyl-3-tosylisoindolin-1-one, 3a: White solid; R$_f$ (hexane/EtOAc, 8:2) 0.57. m.p.124 –126°C. Yield 112 mg, 60%. IR (KBr, neat): ν 2924, 1710, 1320, 1032, 704, 574 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.89 (d, *J* = 7.5 Hz, 1 H), 7.61-7.56 (M, 2 H), 7.46 (t, *J* =7.5 Hz, 1 H), 7.37-7.29 (M, 5 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.05 (d, *J* = 8.0 Hz, 2 H), 5.50 (d, *J* = 14.5 Hz, 1 H), 5.37 (s, 1 H), 4.80 (d, *J* = 14.5 Hz, 1 H), 2.30 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.3, 146.0, 136.3, 136.1, 132.5, 132.1, 130.5, 129.6, 129.5, 129.3, 129.2, 128.4, 125.5, 124.1, 77.5, 45.0, 21.9. HRMS (ESI): Calcd for $C_{22}H_{20}NO_3S$: (M + H)$^+$ 378.1158. Found: 378.1148.

2-(4-Methylbenzyl)-3-tosylisoindolin-1-one, 3b: White solid; R$_f$ (hexane/EtOAc, 8:2) 0.56. m.p.160 – 162°C. Yield 94 mg, 61%. IR (KBr, neat): ν 2923, 1710, 1319, 1082, 573 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.88 (d, *J* =7.5 Hz, 1 H), 7.60-7.55 (M, 2 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.25-7.21 (M, 4 H), 7.13 (d, *J* = 7.8 Hz, 2 H), 7.04 (d, *J* = 7.8 Hz, 2 H), 5.46 (d, *J* = 14.5 Hz, 1 H), 5.37 (s, 1 H), 4.74 (d, *J* = 14.5 Hz, 1 H), 2.32 (s, 3 H), 2.30 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.3, 145.9, 138.1, 136.3, 133.1, 132.4, 132.2, 130.4, 129.9, 129.6, 129.5, 129.3, 125.5, 124.1, 77.5, 44.7, 21.9, 21.4. HRMS (ESI): Calcd for $C_{23}H_{22}NO_3S$: $(M + H)^+$ 392.1315. Found: 392.1305.

2-(3,4-Dimethylbenzyl)-3-tosylisoindolin-1-one, 3c: White solid; R_f (hexane/EtOAc, 8:2) 0.58. m.p.173 – 175°C. Yield 85 mg, 56%. IR (KBr, neat): ν 2922, 1710, 1319, 1130, 1082, 574 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* =7.5 Hz, 1 H), 7.59-7.55 (M, 2 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.22 (d, *J* = 7.8 Hz, 2 H), 7.12-7.04 (M, 5 H), 5.44 (d, *J* = 14.3 Hz, 1 H), 5.39 (s, 1 H), 4.70 (d, *J* = 14.3 Hz, 1 H), 2.30 (s, 3 H), 2.22 (s, 6 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.3, 145.9, 137.5, 137.8, 136.4, 133.5, 132.4, 132.2, 130.6, 130.4, 130.3, 129.7, 129.6, 129.5, 126.8, 125.5, 124.1, 77.5, 77.0, 44.7, 21.9, 19.9, 19.7. HRMS (ESI): Calcd for $C_{24}H_{24}NO_3S$: $(M + H)^+$ 406.1471. Found: 406.1467.

2-Isobutyl-3-tosylisoindolin-1-one, 3d: Pale yellow solid; R_f (hexane/EtOAc, 8:2) 0.60. m.p.132–134°C. Yield 88 mg, 53%. IR (KBr, neat): ν 2959, 1702, 1316, 1076, 571 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, *J* =7.5 Hz, 1 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.53 (d, *J* = 7.5 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.16 (d, *J* = 8.2 Hz, 2 H), 7.02 (d, *J* = 8.2 Hz, 2 H), 5.60 (s, 1 H), 3.89 (dd, *J* = 13.8 and 9.5 Hz, 1 H), 3.69 (dd, *J* = 13.8 and 5.8 Hz, 1 H), 2.29 (s, 3 H), 2.20-2.17 (M, 1 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 0.82 (d, *J* = 6.7 Hz, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.5, 145.9, 136.0, 132.4, 132.3, 130.5, 129.53, 129.5, 129.4, 125.5, 123.9, 78.6, 48.7, 27.2, 21.8, 20.6, 19.9. HRMS (ESI): Calcd for $C_{19}H_{22}NO_3S$: $(M + H)^+$ 344.1315. Found: 344.1308.

2-(Prop-2-yn-1-yl)-3-tosylisoindolin-1-one, 3e: White solid; R_f (hexane/EtOAc, 8:2) 0.71. m.p.138 – 140°C. Yield 84 mg, 49%. IR (KBr, neat): ν 2923, 1711, 1318, 1133, 1080, 570 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, *J* =7.7 Hz, 1 H), 7.64 (t, *J* = 7.7 Hz, 1 H), 7.55 (d, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.5 Hz, 1 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 7.03 (d, *J* = 8.1 Hz, 2 H), 5.84 (s, 1 H), 4.99 (dd, *J* = 17.5 and 2.5 Hz, 1 H), 4.48 (dd, *J* = 17.5 and 2.4 Hz, 1 H), 2.33 (t, *J* = 2.5 Hz, 1 H), 2.29 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.9, 146.0, 136.4, 132.9, 131.6, 130.6, 129.6, 129.5, 129.4, 125.4, 124.3, 77.6, 77.5, 73.7, 31.8, 21.8. HRMS (ESI): Calcd for $C_{18}H_{16}NO_3S$: $(M + H)^+$ 326.0845. Found: 326.0836.

2-(3-Phenylprop-2-yn-1-yl)-3-tosylisoindolin-1-one, 3f: White solid; R_f (hexane/EtOAc, 8:2) 0.57. m.p.150 –152°C. Yield 70 mg, 46%. IR (KBr, neat): ν 2923, 1715, 1320, 1135, 1082, 573 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 7.7 and 1.0 Hz, 1 H), 7.64 (dt, *J* = 7.7 and 1.3 Hz, 1 H), 7.56 (d, *J* = 7.7 Hz, 1 H), 7.49-7.42 (M, 3 H), 7.32-7.29 (M, 3 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.03 (d, *J* = 8.0 Hz, 2 H), 5.91 (s, 1 H), 4.99 (d, *J* = 17.5 Hz, 1 H), 4.69 (d, *J* = 17.5 Hz, 1 H), 2.29 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.0, 146.0, 136.5, 132.8, 132.2, 131.8, 130.6, 129.6, 129.58, 129.5, 128.9, 128.5, 125.5, 124.3, 122.4, 85.3, 82.9, 77.7, 32.6, 21.9. HRMS (ESI): Calcd for $C_{24}H_{20}NO_3S$: $(M + H)^+$ 402.1158. Found: 402.1160.

2-Phenyl-3-tosylisoindolin-1-one, 3g: White solid; R_f (hexane/EtOAc, 8:2) 0.76. m.p.174 –176°C. Yield 115 mg, 72%. IR (KBr, neat): ν 2925, 1708, 1321, 1080, 690, 570 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.10 (d, *J* = 7.8 Hz, 1 H), 7.73-7.69 (M, 2 H), 7.57 (t, *J* = 7.8 Hz, 1 H), 7.47-7.40 (M, 4 H), 7.27 (d, *J* = 7.2 Hz, 1 H), 7.17 (d, *J* = 7.9 Hz, 2 H), 7.03 (d, *J* = 7.9 Hz, 2 H), 6.34 (s, 1 H), 2.31 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 146.2, 135.2, 134.8, 133.2, 132.1, 131.9, 131.0, 130.7, 129.7, 129.6, 129.3, 126.0, 125.3, 124.6, 78.7, 21.9. HRMS (ESI): Calcd for $C_{21}H_{18}NO_3S$: $(M + H)^+$ 364.1002. Found: 364.0994.

2-(*p*-Tolyl)-3-tosylisoindolin-1-one, 3h: White solid; R_f (hexane/EtOAc, 8:2) 0.71. m.p.183 –185°C. Yield 92 mg, 74%. IR (KBr, neat): ν 2919, 1706, 1340, 1139, 1082, 572 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, *J* = 7.6 Hz, 1 H), 7.73-7.68 (M, 2 H), 7.56 (t, *J* = 7.6 Hz, 1 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.03 (d, *J* = 8.0 Hz, 2 H), 6.29 (s, 1 H), 2.39 (s, 3 H), 2.32 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 145.9, 136.5, 135.4, 133.7, 132.9, 132.3, 130.8, 130.6, 129.8, 129.7, 129.5, 125.9, 124.4, 124.2, 79.1, 21.9, 21.3. HRMS (ESI): Calcd for $C_{22}H_{20}NO_3S$: $(M + H)^+$ 378.1158. Found: 378.1149.

2-(4-Chlorophenyl)-3-tosylisoindolin-1-one, 3i: White solid; R_f (hexane/EtOAc, 8:2) 0.65. m.p.203 – 205°C. Yield 94 mg, 59%. IR (KBr, neat): ν 2925, 1711, 1495, 1322, 1143, 1082, 571 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, *J* = 7.5 Hz, 1 H), 7.75-7.70 (M, 2 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.42-7.37 (M, 4 H), 7.15 (d, *J* = 8.1 Hz, 2 H), 7.05 (d, *J* = 8.1 Hz, 2 H), 6.29 (s, 1 H), 2.34 (s, 3 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 146.2, 135.2, 134.8, 133.2, 132.1, 131.9, 131.0, 130.7, 129.7, 129.6, 129.3, 125.9, 125.3, 124.6, 78.7, 21.9. HRMS (ESI): Calcd for $C_{21}H_{17}ClNO_3S$: $(M + H)^+$ 398.0612. Found: 398.0603.

2-(4-Fluorophenyl)-3-tosylisoindolin-1-one, 3j:

Yellow solid; R_f (hexane/EtOAc, 7:3) 0.54. m.p.206 –208°C. Yield 106 mg, 69%. IR (KBr, neat): ν 2928, 1710, 1399, 1142, 1081, 705, 577 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.09 (d, J = 7.5 Hz, 1 H), 7.75-7.69 (M, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 7.44-7.41 (M, 2 H), 7.17-7.11 (M, 4 H), 7.05 (d, J = 8.0 Hz, 2 H), 6.27 (s, 1 H), 2.34 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.9, 161.0 (d, J = 245.2 Hz), 146.1, 135.3, 133.1, 132.3, 132.2, 132.0, 131.0, 130.7, 129.6, 129.5, 126.1, 126.0, 125.9, 124.5, 116.1 ((d, J = 22.7 Hz), 79.1, 21.9. ^{19}F NMR (470 MHz, CDCl$_3$/C$_6$F$_6$): δ 46.7. HRMS (ESI): Calcd for $C_{21}H_{17}FNO_3S$: (M + H)$^+$ 382.0908. Found: 382.0894.

2-Benzyl-5,6-dichloro-3-tosylisoindolin-1-one, 3k: White solid; R_f (hexane/EtOAc, 8:2) 0.34. m.p.180 –182°C. Yield 86 mg, 59%. IR (KBr, neat): ν 2924, 1715, 1324, 1079, 704, 550 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.00 (s, 1 H), 7.66 (s, 1 H), 7.34-7.29 (M, 7 H), 7.15 (d, J = 8.0 Hz, 2 H), 5.47 (d, J = 14.5 Hz, 1 H), 5.31 (s, 1 H), 4.74 (d, J = 14.5 Hz, 1 H), 2.36 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 166.3, 146.6, 137.3, 135.7, 135.6, 135.5, 131.7, 129.9, 129.6, 129.4, 129.3, 129.2, 128.6, 127.4, 125.9. HRMS (ESI): Calcd for $C_{22}H_{18}Cl_2NO_3S$: (M + H)$^+$ 446.0379. Found: 446.0366.

2-Benzyl-4,5,6,7-tetrachloro-3-tosylisoindolin-1-one, 3l: White solid; R_f (hexane/EtOAc, 8:2) 0.31. m.p.185 –187°C. Yield 73 mg, 53%. IR (KBr, neat): ν 2926, 1720, 1328, 1079, 704, 577 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.36-7.29 (M, 7 H), 7.20 (d, J = 8.0 Hz, 2 H), 5.46-5.43 (M, 2 H), 4.74 (d, J = 14.7 Hz, 1 H), 2.40 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 163.6, 147.0, 137.8, 136.7, 135.5, 135.1, 130.2, 130.0, 129.9, 129.6, 129.4, 129.3, 129.2, 128.9, 128.7, 77.5, 45.6, 21.9. HRMS (ESI): Calcd $C_{22}H_{16}Cl_4NO_3S$: (M + H)$^+$ 513.9600. Found: 513.9586.

2-Benzyl-3-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindol-1-one, 3m: White solid; R_f (hexane/EtOAc, 8:2) 0.55. m.p.210 –212°C. Yield 61 mg, 42%. IR (KBr, neat): ν 2923, 1708, 1319, 1080, 703, 570 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 8.33 (s, 1 H), 8.11 (s, 1 H), 7.99 (d, J = 8.0 Hz, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.64 (dt, J = 7.0 and 1.5 Hz, 1 H), 7.59 (dt, J = 7.0 and 1.5 Hz, 1 H), 7. 37 (d, J = 8.0 Hz, 2 H), 7.35-7.28 (M, 3 H), 7.22 (d, J = 8.0 Hz, 2 H), 6.97 (d, J = 8.0 Hz, 2 H), 5.58 (d, J = 14.5 Hz, 1 H), 5.51 (s, 1 H), 4.84 (d, J = 14.5 Hz, 1 H), 2.25 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 163.6, 147.0, 137.8, 136.7, 135.5, 135.1, 130.2, 130.0, 129.9, 129.6, 129.4, 129.3, 129.2, 128.9, 128.7, 77.5, 45.6, 21.9. HRMS (ESI): Calcd for $C_{26}H_{22}NO_3S$: (M + H)$^+$ 428.1315. Found: 428.1307.

1-Benzyl-5-tosylpyrrolidin-2-one, 3n: Yellow gum; R_f (hexane/EtOAc, 1:1) 0.40; yield 70 mg, 41%. IR (KBr, neat): ν 2925, 1700, 1292, 1081, 702, 553 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.79 (d, J = 7.9 Hz, 2 H), 7.44 (d, J = 7.9 Hz, 2 H), 7.38-7.29 (M, 3 H), 7.25 (d, J = 7.2 Hz, 2 H), 5.28 (d, J = 14.5 Hz, 1 H), 4.47 (d, J = 8.4 Hz, 1 H), 4.32 (d, J = 14.5 Hz, 1 H), 2.51 (s, 3 H), 2.38-2.34 (M, 1 H), 2.20-2.12 (M, 2 H), 1.71-1.63 (M, 1 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 175.3, 146.4, 135.5, 132.5, 130.6, 129.7, 129.2, 129.0, 128.4, 77.5, 45.6, 28.4, 22.0, 21.5. HRMS (ESI): Calcd for $C_{18}H_{20}NO_3S$: (M + H)$^+$ 330.1158. Found: 330.1161.

2-Benzyl-3-tosyloctahydro-1*H*-isoindol-1-one, 3o: White solid; R_f (hexane/EtOAc, 8:2) 0.55. m.p.119 –121°C. Yield 90 mg, 59%. IR (KBr, neat): ν 2953, 1705, 1667, 1130, 1082, 574 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.77 (d, J = 8.0 Hz, 2 H), 7.40 (d, J = 8.0 Hz, 2 H), 7.34-7.29 (M, 3 H), 7.20-7.18 (M, 2 H), 5.28 (d, J = 14.2 Hz, 1 H), 3.98 (d, J = 14.2 Hz, 1 H), 3.82 (s, 1 H), 2.70-64 (M, 1 H), 2.49 (s, 3 H), 2.12-2.05 (M, 2 H), 1.55-1.47 (M, 3 H), 1.34-1.24 (M, 1 H), 1.08-0.87 (M, 2 H), 0.55-0.44 (M, 1 H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 176.5, 146.2, 135.3, 134.1, 130.7, 129.6, 129.4, 129.1, 128.4, 81.6, 45.9, 38.4, 35.2, 28.6, 23.6, 22.9, 22.7, 22.0. HRMS (ESI): Calcd for $C_{24}H_{26}NO_3S$: (M + H)$^+$ 384.1628. Found: 384.1633.

1-Benzyl-5-tosyl-1,5-dihydro-2H-pyrrol-2-one, 3p: Reddish brown solid; R_f (hexane/EtOAc, 7:3) 0.52. m.p.104 –106°C. Yield 73 mg, 42%. IR (KBr, neat): ν 2925, 1698, 1129, 1080, 572 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.60 (d, J = 8.0 Hz, 2 H), 7.35-7.26 (M, 7 H), 7.04 (d, J = 8.0 Hz, 1 H), 6.08 (d, J = 6.0 Hz, 1 H), 5.28 (d, J = 14.6 Hz, 1 H), 5.04 (s, 1 H), 4.59 (d, J = 14.6 Hz, 1 H), 2.44 (s, 3 H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 170.9, 146.5, 139.8, 136.2, 131.4, 130.0, 129.9, 129.2, 129.0, 128.4, 80.0, 44.8, 22.0. HRMS (ESI): Calcd for $C_{18}H_{18}NO_3S$: (M + H)$^+$ 328.1002. Found: 328.1005.

2-Benzyl-3-tosyl-2,3,3a,4,7,7a-hexahydro-1*H*-4,7-methanoisoindol-1-one, 3q: White solid; R_f

(hexane/EtOAc, 1:1) 0.40. m.p.117 –119°C. Yield 102 mg, 49%. IR (KBr, neat): ν 2925, 1698, 1130, 1082, 701, 573 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.2 Hz, 2 H), 7.39 (d, *J* = 8.2 Hz, 2 H), 7.33-7.29 (M, 5 H), 5.92 (dd, *J* = 5.8 and 3.0 Hz, 1 H), 5.22 (dd, *J* = 5.8 and 3.0 Hz, 1 H), 5.12 (d, *J* = 13.9 Hz, 1 H), 4.31 (d, *J* = 13.9 Hz, 1 H), 3.99 (s, 1 H), 3.12-3.11 (M, 1 H), 2.98-2.97 (M, 1 H), 2.82-2.79 (M, 1 H), 2.47 (s, 3 H), 2.32 (dd, *J* = 8.9 and 4.5 Hz, 1 H), 1.41 (d, *J* = 8.8 Hz, 1 H), 1.19 (d, *J* = 8.8 Hz, 1 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 176.0, 146.1, 137.3, 135.0, 133.0, 131.9, 130.7, 130.4, 129.8, 128.6, 128.4, 79.0, 51.0, 47.4, 46.5, 45.6, 45.5, 38.6, 22.0; HRMS (ESI): Calcd for $C_{23}H_{24}NO_3S$: (M + H)$^{+}$ 394.1471. Found: 394.1475.

Ethyl (*E*)-5-(1-oxo-3-tosylisoindolin-2-yl)pent-2-enoate, 3r: Pale Yellow solid; R$_f$ (hexane/EtOAc, 7:3) 0.56. m.p.149–151°C. Yield 63 mg, 47%. IR (KBr, neat): ν 2922, 1714, 1510, 1141, 1081, 570 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.4 Hz, 1 H), 7.63 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.53 (d, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.5 Hz, 1 H), 7.16 (d, *J* = 8.4 Hz, 2 H), 7.03 (d, *J* = 8.1 Hz, 2 H), 6.96-6.88 (M, 1 H), 5.89 (d, *J* = 15.7 Hz, 1 H), 5.56 (s, 1 H), 4.28-4.21 (M, 1 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 3.99-3.93 (M, 1 H), 2.75-2.58 (M, 2 H), 2.29 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.3, 166.2, 146.1, 144.3, 136.0, 132.5, 132.0, 130.6, 129.6, 129.5, 129.2, 125.5, 124.2, 123.9, 78.4, 60.6, 40.4, 30.7, 21.9, 14.4. HRMS (ESI): Calcd for $C_{22}H_{24}NO_3S$: (M + H)$^{+}$ 414.1370. Found: 414.1360.

(*E*)-Ethyl 5-(5,6-dichloro-1-hydroxy-3-oxo-isoindolin-2-yl) pent-2-enoate, 3s: White solid; R$_f$ (hexane/EtOAc, 6:4) 0.41. m.p.127 –129°C. Yield 62 mg, 43%. IR (KBr, neat): ν 2982, 1714, 1596, 1079, 730, 506 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (s, 1 H), 7.55 (s, 1 H), 7.17 (d, *J* = 8.1 Hz, 2 H), 7.07 (d, *J* = 8.1 Hz, 2 H), 6.84-6.78 (M, 1 H), 5.81 (d, *J* = 15.7 Hz, 1 H), 5.43 (s, 1 H), 4.17 (q, *J* = 7.3 Hz, 1 H), 4.11 (q, *J* = 7.2, 2H), 3.89-3.83 (M, 1 H), 2.65-2.50 (M, 2 H), 2.28 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.2, 166.1, 146.7, 143.8, 137.4, 135.8, 135.1, 131.6, 130.0, 129.6, 129.0, 127.4, 125.7, 124.5, 60.7, 40.7, 30.6, 21.9, 14.4. HRMS (ESI): Calcd for $C_{22}H_{22}Cl_2NO_5S$: (M + H)$^{+}$ 482.0590. Found: 482.0587.

(*E*)-Ethyl 5-(4,5,6,7-tetrachloro-1-oxo-3-tosyl-isoindolin-2-yl) pent-2-enoate, 3t: White solid; R$_f$ (hexane/EtOAc, 6:4) 0.36. m.p.131 –133°C. Yield 61 mg, 45%. IR (KBr, neat): ν 2927, 1716, 1595, 1079, 707, 547 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.27 (M, 2 H), 7.21 (d, *J* = 8.1 Hz, 2 H), 6.89 (dt, *J* = 15.7, 7.1 Hz, 1 H), 5.88 (dt, *J* = 15.7, 1.5 Hz, 1 H), 5.68 (s, 1 H), 4.26 – 4.17 (M, 3 H), 3.94 – 3.87 (M, 1 H), 2.72-2.56 (M, 2 H), 2.41 (s, 3 H), 1.29 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 166.0, 163.7, 147.2, 143.7, 137.8, 136.8, 135.3, 130.1, 130.0, 129.8, 129.6, 129.2, 128.8, 124.5, 60.7, 41.5, 30.5, 21.9, 14.4. HRMS (ESI): Calcd for $C_{22}H_{20}Cl_4NO_5S$: (M + H)$^{+}$ 551.9782. Found: 551.9754.

General Procedure for the Synthesis of tetrahydro-benzopentalenofurandione, 4a-c

To a stirred solution of sodium hydride (0.36 mmol, 1.2 equiv.) in dry tetrahydrofuran (2 mL) at 0°C was added a solution of tosylisoindolone (0.24 mmol, 1 equiv.) in dry tetrahydrofuran (2.5 mL) dropwise under a nitrogen atmosphere. Add dropwise dry DMSO (0.5 mL) to reaction mixture at 0°C . The reaction mixture was brought to RT, and the reaction was stirred for 1 h. After completion of the reaction, the reaction mixture was treated with saturated ammonium chloride solution (10 mL). The product was extracted with EtOAC (2×15 mL), and the combined organic layer was washed with brine (10 mL). The organic layer was separated and dried over anhydrous Na_2SO_4 and evaporated using a rotary evaporator to obtain the crude product. The crude product was purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford the title compounds **4a-4c.**

3,3a,4,5-Tetrahydrofuro[2',3':2,3]pyrrolo[2,1-a]isoindole-2,7-dione, 4a: Pale yellow solid; R$_f$ (hexane/EtOAc, 6:4) 0.81. m.p.170–172°C. Yield 26 mg, 47%. IR (KBr, neat): ν 2924, 1784, 1364, 1017, 695, 544 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.2 Hz, 1 H), 7.64 (td, *J* = 7.4,1.3 Hz, 1 H), 7.58 (td, *J* = 7.5, 1.1 Hz, 1 H), 7.47 (d, *J* = 7.6 Hz, 1 H), 4.11-4.04 (M, 1 H), 3.49-3.42 (M, 1 H), 3.24 (q, *J* = 9.6 Hz, 1 H), 3.11-3.05 (M, 1 H), 2.73 (dd, *J* = 18.3, 2.8 Hz, 1H), 2.53-2.43 (M, 1 H), 2.06-1.99 (M, 1 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 174.2, 169.9, 143.2, 133.6, 132.3, 131.1, 124.4, 122.5, 106.3, 42.1, 40.5, 36.2, 35.9. HRMS (ESI): Calcd for $C_{13}H_{12}NO_3$: (M + H)$^{+}$ 230.0812. Found: 230.0814.

9,10-Dichloro-3,3a,4,5-tetrahydrofuro[2',3':2,3] pyrrolo[2,1-a]isoindole-2,7-dione, 4b: Pale yellow solid; R_f (hexane/EtOAc, 6:4) 0.68. m.p.192–194°C. Yield 27 mg, 43%. IR (KBr, neat): ν 2921, 1787, 1356, 1017, 745, 526 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1 H), 7.60 (s, 1 H), 4.12-4.06 (M, 1 H), 3.49-3.42 (M, 1 H), 3.25 (q, J = 9.7 Hz, 1 H), 3.14-3.09 (M, 1 H), 2.75 (dd, J = 18.3, 2.8 Hz, 1H), 2.54-2.44 (M, 1 H), 2.08-2.03 (M, 1 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.6, 167.5, 142.3, 138.3, 136.3, 132.0, 126.2, 124.9, 105.2, 42.3, 40.5, 36.0, 35.9. HRMS (ESI): Calcd for $C_{13}H_{10}Cl_2NO_3$: $(M + H)^+$ 298.0033. Found: 298.0029.

8,9,10,11-Tetrachloro-3,3a,4,5-tetrahydrofuro [2',3':2,3] pyrrolo[2,1-a]isoindole-2,7-dione, 4c: Pale yellow solid; R_f (hexane/EtOAc, 6:4) 0.71. m.p.242–244°C. Yield 21 mg, 33%. IR (KBr, neat): ν 2925, 1793, 1390, 1056, 940, 750, 553 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 – 4.21 (M, 1 H), 3.44 – 3.32 (M, 3 H), 2.79 – 2.69 (M, 1 H), 2.78 – 2.70 (M, 1 H), 2.06 – 2.00 (M, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.0, 164.3, 140.4, 138.5, 137.4, 130.4, 128.9, 128.1, 103.7, 42.0, 38.8, 36.5, 36.3. HRMS (ESI): Calcd for $C_{13}H_8Cl_4NO_3$: $(M + H)^+$ 367.9224. Found: 367.9206.

Conclusion

In conclusion, this work highlights an efficient methodology for the synthesis of sulfur functionalized isoindolone scaffold utilizing *N*-acyliminium ion intermediate of hydroxyisoindolinone, with TosMIC and Lewis acid. The reaction is compatible with wide range of functional group such as alkyl, aryne, halides and cyclic imides. This methodology has also been extended to synthesize complex furopyrrolo-isoindoledione derivatives. This type of complex molecules might have important biological activities. Further investigation is under consideration.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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