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Synthesis of *N*-protected indolaldehydes using modified Hass procedure

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Abstract—A detailed study on oxidation of *N*-protected bromomethylindoles into the respective aldehydes was carried out. Using a modified Hass procedure, synthesis of aryl-/hetero-aryl aldehydes in particular indolaldehydes is achieved in reasonable yields.

1. Introduction

Oxidation of benzylic bromide into the corresponding aldehydes is one of the most significant transformations in organic synthesis. Plenty of methods have been developed for the conversion of benzyl halides into their corresponding carbonyl compounds. Most commonly used reagents for conversion of benzylic bromides into the corresponding aldehydes are hexamethylene tetramine,[1] dimethyl sulfoxide,[2] $(Bu_4N)_2Cr_2O_7$,[3] pyridine-*N*-oxide,[4] 3,6-bis(triphenylphosphonium)cyclohexene peroxodisulfate (BTPCP),[5] MnO_2,[6] H_2O_2,[7] and $NaIO_4$/DMF.[8] However, all of these reagents have their own limitations and in some cases, the reaction needs to be carried out at elevated temperature. Hydrolysis and succeeding oxidation of benzylic α,α-dihalides[9] and diacetates[10] have been traditionally known for the preparation of aldehydes. The above-mentioned methods, which are routinely employed for the conversion of benzylic halides into the respective aldehydes, are yet to be adopted to the synthesis of indolaldehydes.

Indolaldehydes are crucial intermediates for the synthesis of several indole alkaloids.[11,12,17b] The multi-step syntheses of quino[4,3-*b*]carbazole and quino[3,4-*b*]carbazoles[12] have been achieved using 1-phenylsulfonyl-2-methylindole-3-carboxaldehyde and 1-phenylsulfonyl-3-methylindole-2-carboxaldehyde, respectively. Zhang and Larock reported[13] a versatile synthesis of β- and γ-carbolines starting from the respective indolaldehydes.

Hibino and co-workers[14] recently utilized 2-phenylvinylindole-3-carboxaldehyde as a crucial intermediate for the synthesis of calothrixin. Nagarathnam reported a synthesis of *N*-phenylsulfonylindole-3-carboxaldehyde[15] via hydrolysis of the corresponding dibromomethylindole. Li et al. observed a facile preparation of 1,3-disubstituted indole-2-carboxaldehydes[16] by the reactions of the corresponding dibromomethylindole with DMSO. Moreover, neither the spectral data of the reported indolaldehyde were given nor was the reaction extended to the synthesis of any other indolaldehydes. However, the methodology has been well exploited for the synthesis of several benzaldehydes.

The synthesis of the highly expensive indole-7-carboxaldehyde, which was widely used as a crucial starting material for the synthesis of carbazole alkaloids,[17] was realized through the Bartoli protocol.[18] A simple synthesis of *N*-tosylindole-4-carboxaldehyde[19] was realized through the reactions of the corresponding bromomethylindole with DMSO in the presence of $NaHCO_3$. Suhana and Srinivasan recently observed the synthesis of *N*-protected indolaldehydes through the reactions of bromomethylindole[20] with tetrabutylammonium dichromate. Our recent studies on preparation of indolaldehydes using enamine methodology led us to the synthesis of carbazoles.[21]

Hass and Bender[22] transformed a variety of substituted benzyl halides into the corresponding benzaldehydes using sodium-2-propane nitronate in ethanol as a solvent. In the case of *o*/*p*-nitrobenzylchloride and 2,4-dinitrobenzylchloride, stable C-alkylation products are isolated rather than the expected aldehydes. Later, Hass methodology was extended to the synthesis of several heterocyclic and other carboxaldehydes[23] except for indolaldehydes. We have recently reported our preliminary results on the synthesis of indolaldehydes[24] using a modified Hass procedure.

Keywords: Bromomethylindole; Modified Hass procedure; Indolaldehydes; Aryl-/hetero-aryl aldehydes.
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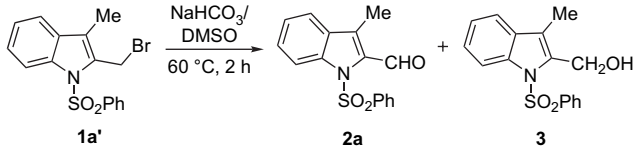
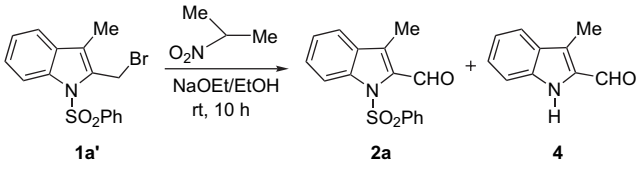
2. Results and discussion

In an ongoing project, we required different types of indolaldehydes as starting materials for the synthesis of indole alkaloids. Since the existing methods for the preparation of indolaldehydes are not scalable to any reasonable extent, a detailed study on smooth transformation of *N*-protected bromomethylindoles into the corresponding aldehydes is undertaken. Initially, the bromo compound **1a′** was reacted with $NaHCO_3$ in dry DMSO at 60 °C (Kornblum reaction)[25] for 2 h. The usual workup followed by column chromatographic purification afforded aldehyde **2a** (35%) and alcohol **3** (30%), Scheme 1.



Scheme 1.

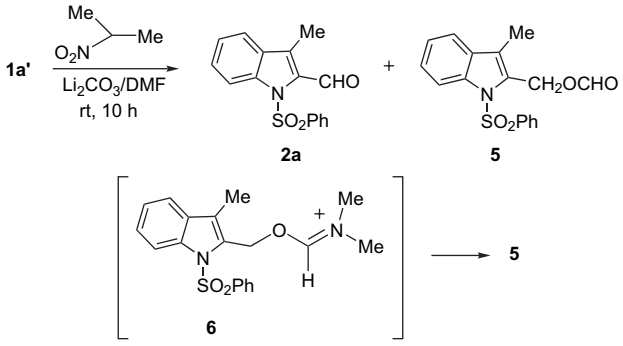
All the conditions tried for the oxidation of bromomethylindole **1a′** using dry DMSO in the presence of $NaHCO_3$ yielded the corresponding indolylmethanol **3** as a side product. Use of Li_2CO_3/K_2CO_3 in place of $NaHCO_3$ also led to the formation of aldehyde and alcohol in almost comparable yields. Further changes in the reaction temperature or prolonging the reaction period was also not useful. Hence, we decided to explore the sodium-2-propane nitronate technique for the oxidation of *N*-phenylsulfonyl-3-methyl-2-bromomethylindole **1a′**. The reaction of the bromo compound **1a′** with sodium-2-propane nitronate in ethanol at room temperature for 10 h led to the formation of a mixture of the *N*-protected and free aldehydes **2a** and **4** in 40 and 25% yields, respectively, Scheme 2.



Scheme 2.

In particular, NaOEt being nucleophilic may cleave the *N*-phenylsulfonyl unit. Hass procedure for the conversion of bromomethylindole into the respective aldehyde is having its own limitations such as longer reaction time, large amount of solvent and cleavage of phenylsulfonyl unit. In order to overcome these problems, we decided to modify the Hass procedure.

Initially, the reaction of bromo compound **1a′** with 2-nitropropane using Li_2CO_3 in DMF at room temperature led to the isolation of formate ester **5** in 56% yield along with minor amount of expected aldehyde **2a**, Scheme 3. The formation of compound **5** can be visualized through the nucleophilic displacement of the bromo compound with DMF to form intermediate **6**. The latter on aqueous workup led to compound **5**. However, the reaction of 2-nitropropane with Li_2CO_3 in DMF at 60 °C for 2 h, followed by addition of bromo compound **1a′** led to the formation of the aldehyde **2a** as major product (40%) along with 10% yield of formate ester **5**.



Scheme 3.

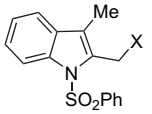
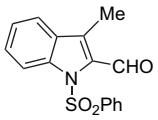
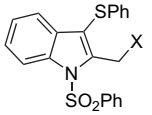
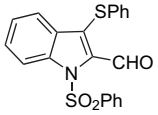
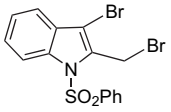
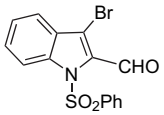
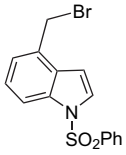
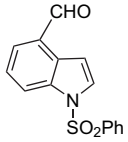
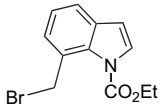
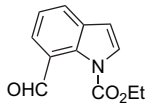
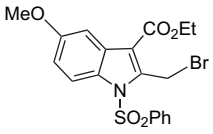
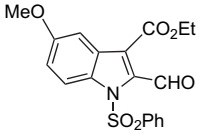
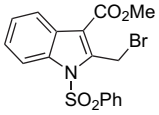
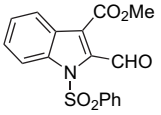
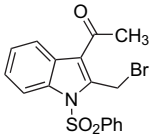
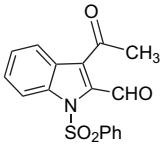
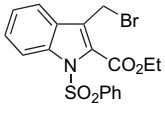
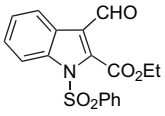
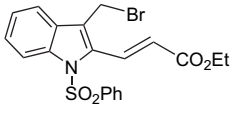
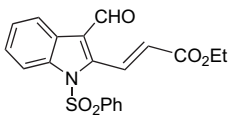
Conditions such as K_2CO_3/DMF, Cs_2CO_3/DMF, and NaOEt/DMF were also explored without any appreciable change in the aldehyde yield. Among the various conditions tried for oxidation of bromomethylindole, NaH/DMF at room temperature was found to be the most efficient.

Thus, using NaH/DMF condition various types of *N*-protected bromomethylindoles **1a′–q** were smoothly converted into the corresponding aldehydes **2a–q**. The conditions followed and the products obtained along with their yields are presented in Table 1.

In most of the cases, *N*-protected aldehydes were obtained in reasonable yields with the exception of bromo compound **1o** wherein the oxidation completely failed (entry 15). The reaction of bromo compounds with 2-nitropropane using NaH/DMF produced the corresponding aldehydes in much better yields than the NaOEt/EtOH condition (entries 2–4, 16, and 18). The oxidation was relatively much faster using the NaH/DMF condition. The *N*-protected chloromethylindoles **1a″** and **1b″** were also smoothly converted into the respective aldehydes **2a** and **2b** in reasonable yields (entries 1 and 2). The *N*-protected indole-7-carboxaldehyde **2e**[17b] was prepared in 61% yield (entry 5). The preparation of *N*-protected aldehydes **2f–i** containing one more carbonyl unit either as ester/ketone was also achieved (entries 6–9). Vinyl ester tethered aldehydes **2j–l** were prepared from the corresponding bromo compounds (entries 10–12). 2-Nitroarylvinyl-indole-3-carboxaldehydes **2m** and **2n** are prepared in good yields (entries 13 and 14). Even though the C-alkylation of 2-nitropropanoate anion is common to benzylic and heterocyclic chloro compounds,[27] we have not observed any alkylation products with *N*-protected bromo-/chloro-methylindoles.

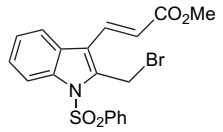
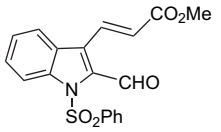
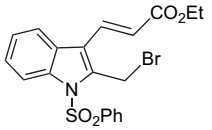
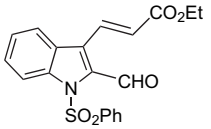
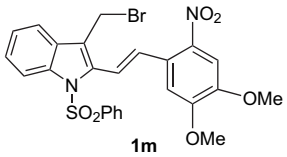
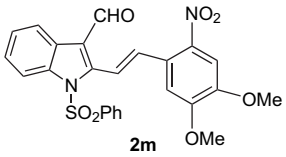
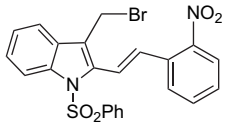
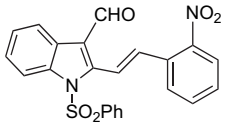
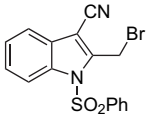
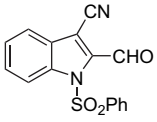
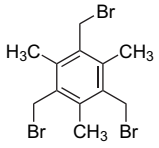
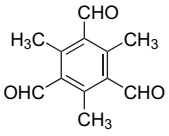
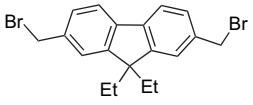
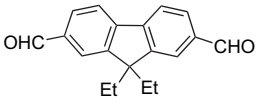
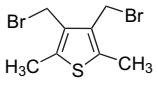
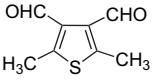
In addition to the indolaldehydes, tribromomethyl mesitylene **1p** could be converted into the respective aldehyde **2p** in relatively better yield (67%) using modified Hass procedure (entry 16). 2,7-Bis(bromomethyl)-9,9-diethyl-9*H*-fluorene **1q** was smoothly converted into the corresponding aldehyde **2q** in 55% yield (entry 17). Finally, 3,4-bis(bromomethyl)-2,5-dimethylthiophene **1r** was converted into 2,5-dimethylthiophene-3,4-dicarboxaldehyde **2r** in relatively better yield using modified Hass procedure (entry 18).

Table 1. Preparation of aryl-/hetero-aryl aldehydes using 2-nitropropane

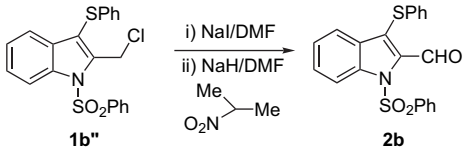
Entry	Bromo/chloro compounds[26]	Conditions	Aldehydes	Yield (%)
1	 **1a'** X = Br **1a"** X = Cl	NaH/DMF, rt, 2 h	 **2a**[11g]	63 58
2	 **1b'** X = Br **1b"** X = Cl	NaOEt/EtOH, rt, 24 h NaH/DMF, rt, 2 h NaH/DMF, rt, 3 h	 **2b**	58 65 57
3	 **1c**	NaOEt/EtOH, rt, 15 h NaH/DMF, rt, 4 h	 **2c**	42 65
4	 **1d**	NaOEt/EtOH, rt, 15 h NaH/DMF, rt, 3 h	 **2d**	55 65
5	 **1e**	NaH/DMF, rt, 0.5 h	 **2e**	61
6	 **1f**	NaH/DMF, rt, 2.5 h	 **2f**	57
7	 **1g**	NaH/DMF, rt, 2 h	 **2g**	63
8	 **1h**	NaH/DMF, rt, 3 h	 **2h**	67
9	 **1i**	NaH/DMF, rt, 3 h	 **2i**	65
10	 **1j**	NaH/DMF, rt, 0.5 h	 **2j**	69

(*continued*)

Table 1. (*continued*)

Entry	Bromo/chloro compounds[26]	Conditions	Aldehydes	Yield (%)
11	 **1k**	NaH/DMF, rt, 0.5 h	 **2k**	68
12	 **1l**	NaH/DMF, rt, 0.5 h	 **2l**	65
13	 **1m**	NaH/DMF, rt, 3 h	 **2m**	65
14	 **1n**	NaH/DMF, rt, 3 h	 **2n**	68
15	 **1o**	NaH/DMF, rt, 15 h	 **2o**	0
16	 **1p**	NaH/DMF, rt, 3 h NaOEt/EtOH, rt, 5 h	 **2p**	67 55
17	 **1q**	NaH/DMF, rt, 4 h	 **2q**	55
18	 **1r**	NaH/DMF, rt, 2.5 h NaOEt/EtOH, rt, 4.5 h	 **2r**	74 65

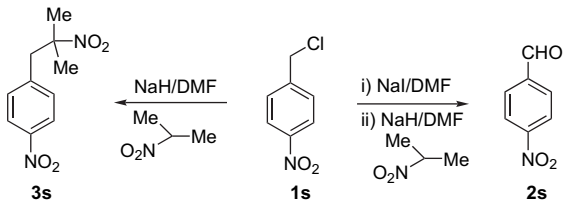
When modified Hass procedure was tried for in situ prepared 1-phenylsulfonyl-3-phenylthio-2-iodomethylindole, the expected aldehyde **2b** was isolated in 69% yield, Scheme 4.



Scheme 4.

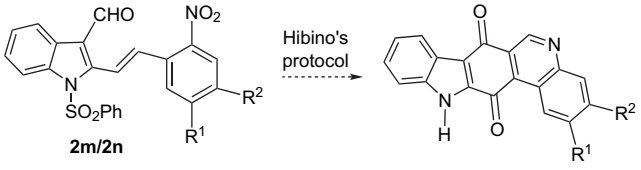
The slight enhancement in the yield of the aldehyde **2b** may be due to the relatively better hard-electrophilic character of the iodo compound.

Reaction of *p*-nitrobenzyl chloride **1q** with sodium salt of 2-nitropropane led to the isolation of stable C-alkylation product.[22,27] We presumed that the conversion of chloride into the corresponding iodide may enhance the feasibility of labile O-alkylation intermediate, which will collapse into the aldehyde. Indeed, when in situ prepared *p*-nitrobenzyl iodide was subjected to modified Hass procedure, *p*-nitrobenzaldehyde was isolated in 62% yield, Scheme 5.



Scheme 5.

Hopefully the aldehydes **2n** and **2m** could be converted into indolo[3,2-*j*]phenanthridine alkaloids and their analog using Hibino's protocol.[14]



3. Summary

After adjudicating various methods for synthesizing indolaldehydes, the modified Hass procedure was found to be the most reliable and better yielding procedure for the smooth transformation of indole methyl halides into their corresponding aldehydes. The existing Hass procedure for the conversion of benzylic halide into the aldehydes has been modified for the benzylic system. Using the modified procedure the synthesis of several aromatic and hetero-aromatic aldehydes was achieved in good yields. For the first time a mild procedure has been developed for the conversion of *N*-protected bromomethylindole into the indolylmethyl formate ester using DMF. Further studies on the synthetic utility of the indolaldehydes will be explored.

4. Experimental

4.1. General

All melting points are uncorrected. IR spectra were recorded on a SHIMADZU FT-IR 8300 instrument. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a JEOL 400, 90 and Bruker 300 MHz spectrometers, respectively. Mass spectra were recorded on a JEOL DX 303 HF spectrometer. Elemental analyses were carried out on a Perkin–Elmer 240 B instrument.

4.2. Representative procedure for the preparation of aldehyde

A suspension of 50% NaH (78 mg, 1.64 mmol) in dry DMF (5 mL) was treated with 2-nitropropane (0.2 mL, 2.19 mmol) at 0 °C. The mixture was stirred for 15 min at the same temperature under a nitrogen atmosphere and was treated dropwise with a solution of bromo compound **1b′** (0.5 g, 1.09 mmol) dissolved in dry DMF (3 mL). After the bromo compound was consumed (monitored by TLC) the reaction mixture was quenched with ice water (10 mL), extracted with $CHCl_3$ (2×10 mL), and dried (Na_2SO_4). Removal of the solvent, followed by column chromatographic purification (silica gel, EtOAc/hexane 1:9) afforded **2b** as a colorless solid.

4.2.1. 3-Methyl-1-(phenylsulfonyl)-1*H*-indole-2-carbaldehyde, 2a. Following the general procedure, compound **2a** was obtained as a colorless solid in 63% yield; mp 210 °C; IR (KBr) ν_{max}: 1672, 1556, 1363, 1176, 1089 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 2.56 (3H, s, CH_3), 7.40–7.58 (2H, m, ArH), 7.63–7.74 (2H, m, ArH), 7.81–7.95 (3H, m, ArH), 8.27 (2H, d, J=7.8 Hz, ArH), 10.65 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 185.0, 137.4, 136.9, 132.3, 130.5, 129.1, 129.0, 128.2, 126.5, 126.1, 121.5, 115.7, 10.4; MS (EI) *m*/*z* (%): 299 (M^+, 35%); found: elemental analysis: C, 64.11; H, 4.45; N, 4.71; S, 10.79%. $C_{16}H_{13}NO_3S$ requires elemental analysis: C, 64.20; H, 4.38; N, 4.68; S, 10.71.

4.2.2. 1-(Phenylsulfonyl)-3-(phenylthio)-1*H*-indole-2-carbaldehyde, 2b. Following the general procedure, compound **2b** was obtained as a colorless solid in 65% yield; mp 112 °C; IR (KBr) ν_{max}: 1654, 1562, 1492, 1373, 1180, 1080 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 6.90 (1H, d, J=7.8 Hz, ArH), 7.00 (1H, m, ArH), 7.10–7.28 (5H, m, ArH), 7.34 (2H, t, J=7.8 Hz, ArH), 7.40 (1H, t, J=3.4 Hz, ArH), 7.47 (1H, t, J=7.3 Hz, ArH), 7.70 (2H, d, J=7.3 Hz, ArH), 8.20 (1H, d, J=8.3 Hz, ArH), 10.48 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 181.9, 134.5, 134.3, 130.4, 129.5, 129.2, 128.2, 127.6, 127.2, 126.9, 126.8, 124.6, 124.5, 123.0, 121.2, 115.7, 114.5; MS (EI) *m*/*z* (%): 393 (M^+, 60%); found: elemental analysis: C, 64.21; H, 4.09; N, 3.50; S, 16.19%. $C_{21}H_{15}NO_3S_2$ requires elemental analysis: C, 64.10; H, 3.84; N, 3.56; S, 16.30.

4.2.3. 3-Bromo-1-(phenylsulfonyl)-1*H*-indole-2-carbaldehyde, 2c. Following the general procedure, compound **2c** was obtained as a colorless solid in 65% yield; mp 142 °C; IR (KBr) ν_{max}: 1685, 1512, 1369, 1257, 1176, 1068 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 7.24–7.41 (2H, m, ArH), 7.48–7.58 (2H, m, ArH), 7.71–7.75 (2H, m, ArH), 7.85 (1H, d, J=7.3 Hz, ArH), 8.17 (2H, d, J=8.3 Hz, ArH), 10.37 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 181.9, 137.0, 134.4, 132.1, 130.0, 129.2, 129.0, 126.8, 125.3, 122.3, 115.5, 111.8; MS (EI) *m*/*z* (%): 365 (M^+, 15%); found: elemental analysis: C, 49.37; H, 2.93; N, 3.76; S, 8.73%. $C_{15}H_{10}BrNO_3S$ requires elemental analysis: C, 49.47; H, 2.77; N, 3.85; S, 8.80.

4.2.4. 1-(Phenylsulfonyl)-1*H*-indole-4-carbaldehyde, 2d. Following the general procedure, compound **2d** was obtained as a colorless solid; mp 102 °C; IR (KBr) ν_{max}: 1693, 1577, 1450, 1377, 1184, 1145 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 7.36–7.43 (4H, m, ArH), 7.48 (1H, t, J=7.32 Hz, ArH), 7.65 (1H, d, J=7.33 Hz, ArH), 7.68 (1H, d, J=3.42 Hz, ArH), 7.79 (2H, t, J=4.39 Hz, ArH), 8.20 (1H, d, J=8.3 Hz, ArH), 10.09 (1H, s, CHO); MS (EI) *m*/*z* (%): 285 (M^+, 54%); found: elemental analysis: C, 63.05; H, 3.69; N, 4.94; S, 11.09%. $C_{15}H_{11}NO_3S$ requires elemental analysis: C, 63.14; H, 3.89; N, 4.91; S, 11.24.

4.2.5. Ethyl 7-formyl-1*H*-indole-1-carboxylate, 2e. Following the general procedure, compound **2e** was obtained

as a colorless solid; mp 54 °C; IR (KBr) ν_{max}: 1739, 1672, 1315, 1041 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 1.41 (3H, t, J=7.3 Hz, $CO_2CH_2CH_3$), 4.44 (2H, q, J=7.3 Hz, $CO_2CH_2CH_3$), 6.66 (1H, d, J=3.9 Hz, *Indole* 3*H*), 7.33 (1H, t, J=7.6 Hz, ArH), 7.64 (1H, d, J=3.9 Hz, *Indole* 2*H*), 7.71–7.74 (2H, m, ArH), 10.54 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 190.8, 151.3, 132.7, 132.0, 127.8, 125.9, 125.5, 125.0, 123.3, 108.5, 64.1, 14.1; MS (EI) *m*/*z* (%): 217 (M^+, 8%); found: elemental analysis: C, 66.48; H, 5.31; N, 6.43%. $C_{12}H_{11}NO_3$ requires elemental analysis: C, 66.35; H, 5.10; N, 6.45.

4.2.6. Ethyl 2-formyl-5-methoxy-1-(phenylsulfonyl)-1*H*-indole-3-carboxylate, 2f. Following the general procedure, compound **2f** was obtained as a white solid; mp 132 °C; IR (KBr) ν_{max}: 1721, 1685, 1609, 1381, 1188, 1054 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 1.30 (3H, t, J=7.4 Hz, $CO_2CH_2CH_3$), 3.76 (3H, s, OCH_3), 4.32 (2H, q, J=7.2 Hz, $CO_2CH_2CH_3$), 7.03 (1H, s, *Indole* 4*H*), 7.41–7.51 (4H, m, ArH), 7.90–7.96 (3H, m, ArH), 10.45 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 184.4, 163.0, 157.4, 139.1, 137.7, 134.4, 131.0, 129.2, 127.3, 126.9, 118.1, 117.6, 115.4, 103.8, 61.5, 55.5, 14.0; MS (EI) *m*/*z* (%): 387 (M^+, 80%); found: elemental analysis: C, 58.76; H, 4.53; N, 3.81; S, 8.16%. $C_{19}H_{17}NO_6S$ requires elemental analysis: C, 58.91; H, 4.42; N, 3.62; S, 8.28.

4.2.7. Methyl 2-formyl-1-(phenylsulfonyl)-1*H*-indole-3-carboxylate, 2g. Following the general procedure, compound **2g** was obtained as a pale yellow solid; mp 134–136 °C; IR (KBr) ν_{max}: 1701, 1662, 1545, 1383, 1185, 1098 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 4.0 (3H, s, CO_2CH_3), 7.41–7.45 (1H, t, J=7.4 Hz, ArH), 7.53–7.59 (2H, t, J=7.4 Hz, ArH), 7.65–7.69 (2H, t, J=8.4 Hz, ArH), 8.09–8.11 (2H, d, J=8.4 Hz, ArH), 8.14–8.16 (1H, d, J=8.0 Hz, ArH), 8.19–8.21 (1H, d, J=8.4 Hz, *Indole* 4*H*), 10.62 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 184.6, 163.3, 139.1, 137.7, 136.3, 134.5, 129.3, 127.8, 127.5, 126.1, 125.0, 123.0, 117.6, 114.4, 52.3; MS (EI) *m*/*z* (%): 343 (M^+, 36%); found: elemental analysis: C, 59.39; H, 3.96; N, 4.00; S, 9.12%. $C_{17}H_{13}NO_5S$ requires elemental analysis: C, 59.47; H, 3.82; N, 4.08; S, 9.34.

4.2.8. 3-Acetyl-1-(phenylsulfonyl)-1*H*-indole-2-carbaldehyde, 2h. Following the general procedure, compound **2h** was obtained as a white solid; mp 113 °C; IR (KBr) ν_{max}: 1685, 1670, 1557, 1450, 1371, 1180, 1108 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 2.55 (3H, s, $COCH_3$), 7.37 (1H, t, J=7.4 Hz, ArH), 7.45–7.49 (2H, t, J=8.4 Hz, ArH), 7.54–7.61 (2H, m, ArH), 7.72–7.74 (1H, d, J=7.9 Hz, *Indole* 7*H*), 7.84–7.86 (2H, d, J=8.0 Hz, ArH), 8.19–8.21 (1H, d, J=8.4 Hz, *Indole* 4*H*), 10.67 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 196.8, 183.8, 136.6, 136.1, 134.8, 134.2, 129.0, 128.8, 128.3, 126.4, 125.6, 124.9, 121.9, 114.3, 30.2; MS (EI) *m*/*z* (%): 327 (M^+, 65%); found: elemental analysis: C, 62.31; H, 4.13; N, 4.32; S, 9.71%. $C_{17}H_{13}NO_4S$ requires elemental analysis: C, 62.37; H, 4.00; N, 4.28; S, 9.80.

4.2.9. Ethyl 3-formyl-1-(phenylsulfonyl)-1*H*-indole-2-carboxylate, 2i. Following the general procedure, compound **2i** was obtained as a pale white solid; mp 176 °C; IR (KBr) ν_{max}: 1726, 1681, 1541, 1373, 1193, 1083 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 1.47 (3H, t, J=7.0 Hz, $CO_2CH_2CH_3$), 4.59 (2H, q, J=7.2 Hz, $CO_2CH_2CH_3$), 7.37 (1H, t, J=7.6 Hz, ArH), 7.45 (1H, t, J=7.5 Hz, ArH), 7.50–7.54 (2H, t, J=8.2 Hz, ArH), 7.61 (1H, t, J=7.8 Hz, ArH), 7.90–8.00 (1H, d, J=7.2 Hz, *Indole* 7*H*), 8.09–8.11 (2H, d, J=7.2 Hz, ArH), 8.27–8.29 (1H, d, J=7.2 Hz, *Indole* 4*H*), 10.16 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 185.1, 160.8, 138.9, 137.2, 135.1, 134.7, 129.4, 127.5, 127.3, 125.6, 125.1, 123.0, 120.9, 113.9, 63.5, 13.9; MS (EI) *m*/*z* (%): 357 (M^+, 86%); found: elemental analysis: C, 60.41; H, 4.29; N, 3.86; S, 9.06%. $C_{18}H_{15}NO_5S$ requires elemental analysis: C, 60.49; H, 4.23; N, 3.92; S, 8.97.

4.2.10. (*E*)-Ethyl 3-(3-formyl-1-(phenylsulfonyl)-1*H*-indol-2-yl)acrylate, 2j. Following the general procedure, compound **2j** was obtained as a white solid; mp 152 °C; IR (KBr) ν_{max}: 1700, 1670, 1370, 1180 cm^{-1}. δ_H (90 MHz, $CDCl_3$): 1.33 (3H, t, J=7.4 Hz, $CO_2CH_2CH_3$), 4.3 (2H, q, J=7.3 Hz, $CO_2CH_2CH_3$), 6.61–8.01 (11H, m, ArH), 9.92 (1H, s, CHO); MS (EI) *m*/*z* (%): 383 (M^+, 57%); found: elemental analysis: C, 62.73; H, 4.18; N, 3.59; S, 8.30%. $C_{20}H_{17}NO_5S$ requires elemental analysis: C, 62.65; H, 4.47; N, 3.65; S, 8.36.

4.2.11. (*E*)-Methyl 3-(2-formyl-1-(phenylsulfonyl)-1*H*-indol-3-yl)acrylate, 2k. Following the general procedure, compound **2k** was obtained as a colorless solid; mp 152 °C; IR (KBr) ν_{max}: 1716, 1668, 1546, 1373, 1176 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 3.79 (3H, s, CO_2CH_3), 6.61 (1H, d, J=16 Hz, *vinyl H*), 7.33–7.40 (2H, m, ArH), 7.51–7.56 (2H, m, ArH), 7.70–7.72 (2H, d, J=8.0 Hz, ArH), 7.80–7.82 (2H, d, J=7.6 Hz, ArH), 8.07 (1H, d, J=16 Hz, *vinyl H*), 8.22–8.24 (1H, d, J=7.6 Hz, *Indole* 4*H*), 10.63 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 184.1, 166.5, 137.4, 136.8, 135.0, 134.2, 129.4, 128.9, 126.9, 126.6, 125.5, 124.8, 122.8, 122.6, 115.61, 51.9; MS (EI) *m*/*z* (%): 369 (M^+, 77%); found: elemental analysis: C, 61.71; H, 4.13; N, 3.72; S, 8.63%. $C_{19}H_{15}NO_5S$ requires elemental analysis: C, 61.78; H, 4.09; N, 3.79; S, 8.68.

4.2.12. (*E*)-Ethyl 3-(2-formyl-1-(phenylsulfonyl)-1*H*-indol-3-yl)acrylate, 2l. Following the general procedure, compound **2l** was obtained as a colorless solid; mp 141 °C; IR (KBr) ν_{max}: 1720, 1668, 1512, 1367, 1174, 1087 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 1.34 (3H, t, J=6.92 Hz, $CO_2CH_2CH_3$), 4.29 (2H, q, J=6.92 Hz, $CO_2CH_2CH_3$), 6.61–6.65 (1H, d, J=16.4 Hz, *vinyl H*), 7.37–7.41 (3H, m, ArH), 7.53–7.59 (2H, m, ArH), 7.73–7.75 (2H, d, J=7.6 Hz, ArH), 7.85–7.87 (1H, d, J=7.8 Hz, *Indole* 7*H*), 8.10–8.14 (1H, d, J=16.4 Hz, *vinyl H*), 8.26–8.28 (1H, d, J=8.4 Hz, *Indole* 4*H*), 10.67 (1H, s, CHO). δ_C (100 MHz, $CDCl_3$): 183.6, 165.6, 136.9, 136.3, 134.2, 134.0, 133.7, 128.9, 128.7, 126.5, 126.1, 125.0, 124.9, 122.0, 115.1, 60.3, 13.7; MS (EI) *m*/*z* (%): 383 (M^+, 65%); found: elemental analysis: C, 62.72; H, 4.35; N, 3.61; S, 8.41%. $C_{20}H_{17}NO_5S$ requires elemental analysis: C, 62.65; H, 4.47; N, 3.65; S, 8.36.

4.2.13. (*E*)-2-(4,5-Dimethoxy-2-nitrostyryl)-1-(phenylsulfonyl)-1*H*-indole-3-carbaldehyde, 2m. Following the general procedure, compound **2m** was obtained as a yellow solid; mp 220 °C; IR (KBr) ν_{max}: 1662, 1517, 1379, 1325, 1272, 1176 cm^{-1}. δ_H (500 MHz, $CDCl_3$): 4.00 (3H, s, OCH_3), 4.09 (3H, s, OCH_3), 7.24 (1H, s, ArH), 7.34 (1H, t, J=7.4 Hz, ArH), 7.39–7.47 (4H, m, ArH), 7.52–7.58 (2H, m, ArH), 7.7 (1H, s, ArH), 7.80–7.82 (2H, d,

J=7.6 Hz, ArH), 8.16–8.18 (1H, d, J=8.4 Hz, ArH), 8.27–8.29 (1H, d, J=7.6 Hz, ArH), 10.12 (1H, s, CHO). δ_C (125 MHz, $CDCl_3$): 187.1, 153.7, 149.6, 147.5, 140.5, 137.4, 137.4, 135.8, 134.8, 129.6, 126.9, 126.8, 126.7, 125.7, 122.5, 121.3, 119.8, 114.3, 110.6, 108.0, 56.7, 56.6; MS (EI) m/z (%): 492 (M^+, 55%); found: elemental analysis: C, 61.04; H, 4.17; N, 5.48; S, 6.57%. $C_{25}H_{20}N_2O_7S$ requires elemental analysis: C, 60.97; H, 4.09; N, 5.69; S, 6.51.

4.2.14. (*E*)-2-(2-Nitrostyryl)-1-(phenylsulfonyl)-1*H*-indole-3-carbaldehyde, 2n. Following the general procedure, compound **2n** was obtained as a yellow solid; mp 182–184 °C; IR (KBr) ν_{max}: 1670, 1555, 1385, 1340, 1220, 1165, 1035 cm^{-1}. δ_H (300 MHz, $CDCl_3$): 7.29–7.40 (5H, m, ArH), 7.47–7.55 (2H, m, ArH), 7.58–7.63 (1H, d, J=16 Hz, *vinyl H*), 7.71 (1H, t, J=7.4 Hz, ArH), 7.75–7.78 (2H, d, J=7.6 Hz, ArH), 7.82–7.85 (1H, d, J=7.2 Hz, ArH), 8.05–8.17 (2H, m, ArH), 8.26–8.28 (1H, d, J=7.4 Hz, ArH), 10.07 (1H, s, CHO). δ_C (75 MHz, $CDCl_3$): 186.9, 147.9, 147.0, 137.5, 136.2, 135.8, 134.7, 134.0, 131.6, 129.9, 129.5, 126.9, 126.8, 126.6, 125.6, 125.1, 122.5, 121.5, 121.0, 114.3; MS (EI) m/z (%): 432 (M^+, 37%); found: elemental analysis: C, 63.57; H, 3.93; N, 6.39; S, 7.57%. $C_{23}H_{16}N_2O_5S$ requires elemental analysis: C, 63.88; H, 3.73; N, 6.48; S, 7.41.

4.2.15. 2,4,6-Trimethylbenzene-1,3,5-tricarbaldehyde, 2p.[28] Following the general procedure, compound **2p** was obtained as a colorless solid; mp 169–170 °C (dec); reported[lit.] mp 171 °C (dec); IR (KBr) ν_{max}: 1685, 1560, 1435, 1050 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 2.64 (9H, s, CH_3), 10.60 (3H, s, CHO). δ_C (100 MHz, $CDCl_3$): 194.1, 143.0, 134.8, 16.1; MS (EI) m/z (%): 204 (M^+, 18%).

4.2.16. 9,9-Diethyl-9*H*-fluorene-2,7-dicarbaldehyde, 2q.[29] Following the general procedure, compound **2q** was obtained as a white solid; mp 140 °C; reported[lit.] mp 140–141 °C; IR (KBr) ν_{max}: 1693, 1604, 1541, 1201 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 0.23 (6H, t, J=7.2 Hz, $CO_2CH_2CH_3$), 2.11 (4H, q, J=7.2 Hz, $CO_2CH_2CH_3$), 7.66–7.90 (6H, m, ArH), 10.54 (2H, s, CHO). δ_C (100 MHz, $CDCl_3$): 192.1, 151.9, 145.9, 136.3, 130.4, 123.1, 121.2, 56.5, 31.8, 8.3; MS (EI) m/z (%): 278 (M^+, 42%).

4.2.17. 2,5-Dimethylthiophene-3,4-dicarbaldehyde, 2r.[30] Following the general procedure, compound **2r** was obtained as a colorless crystalline solid; mp 94 °C; IR (KBr) ν_{max}: 1672, 1521, 1483, 1058 cm^{-1}. δ_H (400 MHz, $CDCl_3$): 2.72 (6H, s, CH_3), 10.33 (2H, s, CHO). δ_C (100 MHz, $CDCl_3$): 186.6, 149.4, 135.0, 14.2; MS (EI) m/z (%): 168 (M^+, 37%).

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