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Synthesis of di-, tri-, and tetra-substituted carbazole analogs involving annulation methodology

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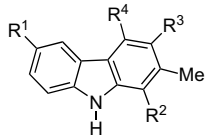
ABSTRACT

Synthesis of substituted carbazole analogs was achieved via Michael addition followed by intramolecular cyclization and subsequent aromatization.

1. Introduction

During the past 50 years the focus on the synthesis of indole derivatives[1] is due to its undisputable importance in nature, where this particular heterocycle is embedded in countless number of natural products and medicinally relevant compounds.[2] Among the indole alkaloids, the carbazole system **1a–e** is the most explored one. Ever since the first isolation of carbazole alkaloid, murraynine,[3] organic chemists have been interested in the synthesis of carbazole and its derivatives[4] due to their promising biological activities. Knölker and Reddy have extensively reviewed[5] the synthesis and biological activities of carbazole alkaloids.



1a R^1 = H, R^2 = Me, R^3 & R^4 = OMe (carbazomycin A)
1b R^1 = H, R^2 = Me, R^3 = OMe, R^4 = OH (carbazomycin B)
1c R^1 = OMe, R^2 = Me, R^3 = OMe, R^4 = OH (carbazomycin C)
1d R^1 = H, R^2 = Ph, R^3 = OMe, R^4 = H (hyellazole)
1e R^1 = H, R^2 = $(CH_2)_4$Me, R^3 = OH, R^4 = NHAc (antiostatin A1)

Several annulation strategies based on the Michael addition followed by intramolecular cyclization have been reported.[6] Over the years, the synthesis of large number of carbazole derivatives has been achieved through Diels–Alder reaction[7] of 2/3-vinylindoles. Similarly, the synthesis of different types of carbazole derivatives has also been realized through Pd-mediated reactions.[8] Jagtap and Mali have reported[9] an annelation of ethyl-*N*-methyl-2-benzylindole-3-carboxylate. Mohanakrishnan and Srinivasan have outlined a simple synthesis of 4-hydroxy carbazoles using 3-carbethoxy-2-indolylmethyl sulfoxide as a bidentate synthon, involving a Michael addition followed by intramolecular cyclization.[10]

Recently, Hauser and co-workers have fully exploited sulfide-, sulfoxide-, and sulfonyl-stabilized carbanions to the synthesis of polycyclic aromatic systems.[11] However, annulation methodologies for carbazoles using 2,3-disubstituted indoles as bidentate synthons have not been thoroughly explored. In further continuation of our studies on carbazole alkaloids,[12] we report here our results on the synthesis of various types of substituted carbazoles via Michael addition promoted annulation strategy.

2. Results and discussion

Required bromomethylindoles **2a–e**[13] were prepared from the corresponding methylindoles via allylic bromination using NBS in CCl_4 at reflux. The bromomethylindoles **2a–e** on treatment with thiophenol using NaH as base in dry THF led to indolylmethyl sulfides **3a–e**.

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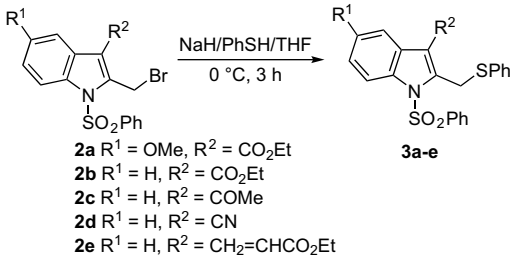
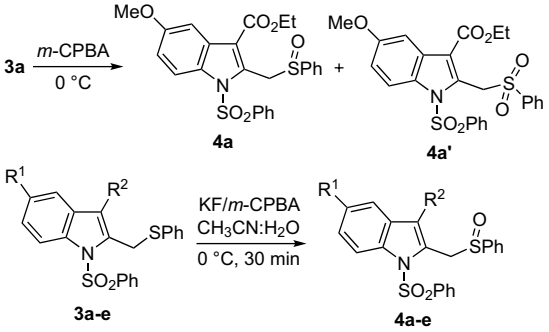


As a representative case, the oxidation of indolylmethyl sulfide **3a** with 1 equiv of *m*-CPBA led to the formation of sulfoxide **4a** (70%) along with corresponding sulfone **5** (15–20%). A slow addition of *m*-CPBA to a solution of sulfide **3a** at 0 °C also led to the formation of sulfone **5** as a minor product. Even with less than 1 equiv of *m*-CPBA, sulfone **5** was always observed in minor amount along with starting material **3a**.

Finally, the required sulfoxides **4a–e** can be smoothly prepared (Scheme 1) using a combination of KF/*m*-CPBA.[14] The interaction of KF/*m*-CPBA in CH_3CN/H_2O at 0 °C for 10 min followed by addition of sulfides **3a–e** led to the isolation of respective sulfoxides **4a–e** in good yields. Further oxidation of sulfoxides **4a–e** into the corresponding sulfones was not observed under this condition, which might be due to the non-nucleophilic character of the fluorine oxide (KOF).[14] The different substituents of the sulfides **3a–e** as well as sulfoxides **4a–e** along with their yields are presented in Table 1.



Scheme 1.

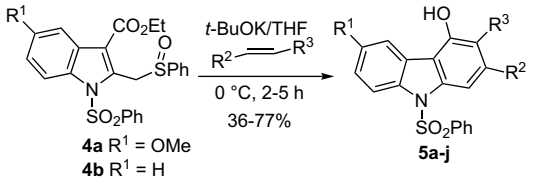
Table 1

Sulfide/sulfoxide	R^1	R^2	Yield (%)
3a/**4a**	OMe	CO_2Et	90/92
3b/**4b**	H	CO_2Et	84/90
3c/**4c**	H	$COCH_3$	86/90
3d/**4d**	H	CN	82/91
3e/**4e**	H	CH_2=$CHCO_2Et$	68/94

Having prepared the required sulfoxides **4a–e**, next the annulation of these sulfoxides using Michael addition as a key step was initiated. The generation of required sulfoxide stabilized carbanion was tried using bases such as K_2CO_3 and NaH. After adjudicating different bases and conditions, finally, the reaction of sulfoxides **4a**/**4b** with various Michael acceptors using *t*-BuOK as a base led to the formation of respective 4-hydroxy carbazoles **5a–j** in 36–77% of yields (Scheme 2, Table 2).

The mechanism of this annulation reaction involves the initial Michael addition of the sulfoxide stabilized carbanion followed by intramolecular cyclization. The resulting intermediate on elimination of PhSOH unit furnished the respective carbazoles **5a–j**.

The annulation of sulfoxides **4a**/**4b** with Michael acceptors such as methyl acrylate, MVK, acrolein, and acrylonitrile was found to proceed in almost comparable yields to afford the corresponding carbazoles **5a–h**. The annulation of sulfoxide **4b** with 2-nitrostyrene was proceeded only in 45% of yield to furnish 3-nitro-2-phenyl-4-hydroxycarbazole **5i**. All attempts to carry out annulation of **4b** with *p*-methoxyphenyl-2-nitrostyrene were found to be unsuccessful; only the starting sulfoxide was recovered unchanged. However using similar condition, the annulation of **4b** with methyl crotonate yielded the respective tri-substituted carbazole **5k** in 36% of yield.

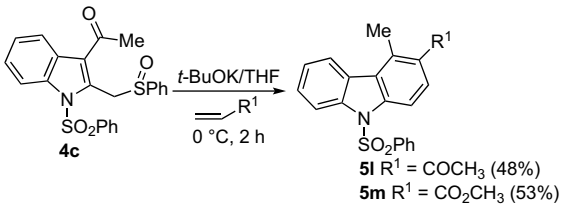


Scheme 2.

Table 2

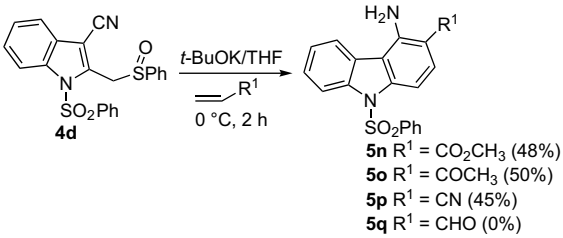
Carbazole	R^1	R^2	R^3	Yield (%)
5a	OMe	H	CO_2Me	70
5b	OMe	H	COMe	77
5c	OMe	H	CHO	68
5d	OMe	H	CN	70
5e	H	H	CO_2Me	70
5f	H	H	COMe	69
5g	H	H	CHO	64
5h	H	H	CN	70
5i	H	Ph	NO_2	45
5j	H	4-OMePh	NO_2	0
5k	H	Me	CO_2Me	36

As expected, the annulation of sulfoxide **4c** could be smoothly carried out with methyl acrylate as well as MVK to afford the expected 4-methylcarbazoles **5l**/**5m** in 53 and 48% yields, respectively (Scheme 3).



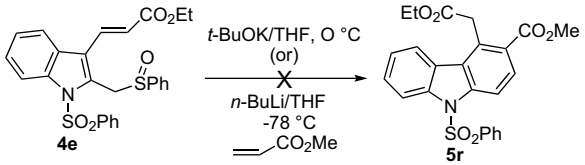
Scheme 3.

The annulation of sulfoxide **4d** with Michael acceptors such as methyl acrylate, MVK, and acrylonitrile afforded respective 4-aminocarbazoles **5n–p** in 45–50% of yields (Scheme 4). Surprisingly, the annulation of sulfoxide **4d** with acrolein didn't afford the expected product **5q**, only an insoluble polymeric material was obtained. Presumably, the formation of polymeric material may be due to the intermolecular self condensation of an aldehyde and amino function of **5q**.



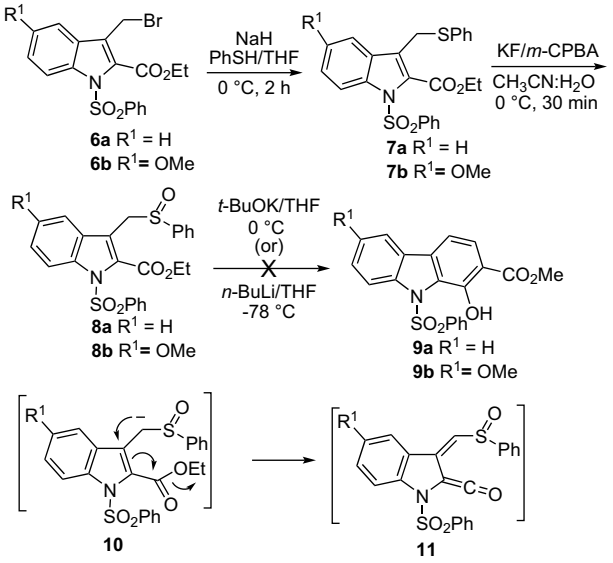
Scheme 4.

Attempted double Michael addition of sulfoxide with methyl acrylate using *t*-BuOK/*n*-BuLi was found to be unsuccessful, only the sulfoxide was recovered unchanged (Scheme 5).



Scheme 5.

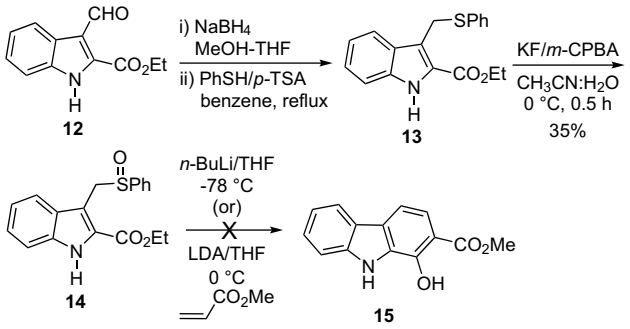
Having succeeded in synthesizing 4-hydroxy carbazoles and 4-aminocarbazoles, next the synthesis of 1-hydroxycarbazoles was planned using isomeric indole-3-methylsulfoxide. Hence, the *N*-phenylsufonyl-3-bromomethylindoles **6a**/**6b** were transformed into the respective sulfides **7a**/**7b**. The usual oxidation of sulfides **7a**/**7b** using KF/*m*-CPBA afforded the required sulfoxides **8a**/**8b**. Surprisingly, the annulation of sulfoxides **8a**/**8b** with methyl acrylate/MVK in the presence of NaH or *t*-BuOK didn't give the expected 1-hydroxycarbazoles **9a**/**9b**. It should be mentioned that the attempted Michael addition of sulfoxides **8a**/**8b** with Michael acceptors even at −78 °C using *n*-BuLi/LDA as base also found to be unsuccessful. In all these conditions, only an insoluble polymeric mixture was obtained. The failure to obtain 1-hydroxycarbazoles **9a**/**9b** may be due to the stabilization of the carbanion, which may lead to the formation of ketene-like intermediate **11** (Scheme 6). Obviously, the ketene intermediate **11** may lead to the formation of glassy polymeric material.



Scheme 6.

Finally, an attempt was made to synthesize 1-hydroxycarbazole involving *N*-free sulfoxide to circumvent the above-mentioned ketene-like intermediate formation. Accordingly, the required sulfoxide **14** was prepared from commercially available ethyl indole-2-carboxylate. Vilsmeier–Haack formylation followed by $NaBH_4$ reduction and subsequent displacement of the benzylic alcohol with thiophenol led to sulfide **13**.

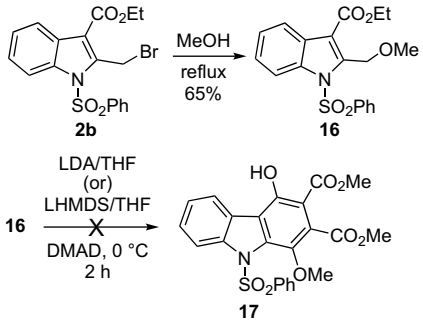
Oxidation of sulfide **13** using KF/*m*-CPBA in CH_3CN/H_2O furnished sulfoxide **14** in 77% of yield. Unfortunately, the Michael addition of sulfoxide **14** with methyl acrylate also led to the formation of polymeric material. Now, it is obvious that the ketene-like intermediate formation was facile even with the sulfoxide stabilized carbanion generated from the *N*-free sulfoxide **14** (Scheme 7). Thus, it may be concluded that the annulation of sulfoxide stabilized carbanion can be successfully performed only at the indole-2-position (Schemes 2–4). All attempts to perform the similar annulation at the indole-3-position were unsuccessful due to the migration of the carbanion to form the corresponding quinodimethane system (Schemes 6 and 7).



Scheme 7.

In addition to the annulation methodology based on sulfoxide stabilized carbanion mentioned above, Katritzky and co-workers reported[15] a facile synthesis of carbazole analogs using carbanion generated from benzotriazolemethylindoles. In these methods, sulfoxide/benzotriazole group was eliminated during aromatization process. Thus, in general most of the annulation reactions were carried out using carbanion stabilized by leaving groups such as PhSO, $PhSO_2$, NO_2, and benzotriazole with vinylic dienophiles. Since, tri- and tetra-substituted carbazoles[16] are most abundant among naturally occurring carbazoles, next the synthesis of these types of carbazoles using carbanion stabilized by electron donating/withdrawing groups such as OMe, Ph/CN, CO_2Me was planned. Of course, in this case the annulation has to be carried out with triple bonded dienophiles rather than olefinic dienophiles.

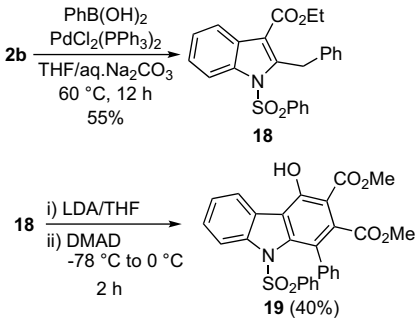
Accordingly, the indolylmethyl ether **16** was prepared from the bromo compound **2b** by refluxing in MeOH for 3 h. However, the expected Michael addition of **16** with DMAD in the presence of bases such as *t*-BuOK or LHMDS was found to be futile, only the starting material was recovered (Scheme 8).



Scheme 8.

Next, a smooth phenylation of bromo compound **2b** was carried out using phenylboronic acid in the presence of $Pd(PPh_3)_2Cl_2$ to afford 2-benzylindole **18** in 55% of yield. When compound **18** was reacted with DMAD using LDA as a base in dry THF furnished the tetra-substituted carbazole **19** in 40% of yield (Scheme 9).

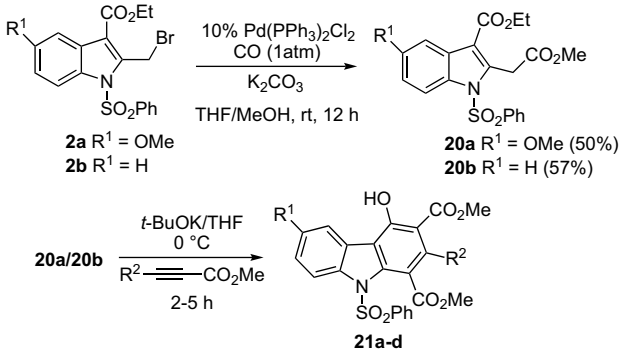
The indolylmethyl acetates **20a**/**20b** were prepared from the corresponding bromo compounds **2a**/**2b** using Stille carbonylation.[17] The indolylmethyl acetates **20a**/**20b** on reaction with DMAD/methyl propiolate using *t*-BuOK in dry THF underwent smooth Michael addition followed by intramolecular cyclization and



Scheme 9.

subsequent aromatization to afford tetra-substituted carbazoles **21a**–**d** in 45–55% yields (Scheme 10, Table 3).

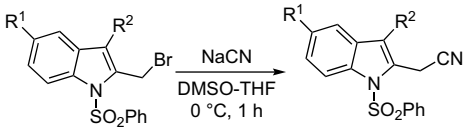
Next, the reaction of bromo compounds **2a**, **2b**, **2c**, and **2e** with NaCN in DMSO/THF at 0 °C for 1 h led to the isolation of respective 2-cyanomethylindoles **22a**–**d** in 42–58% yields (Scheme 11, Table 4).



Scheme 10.

Table 3

Compound	R^1	R^2	Yield (%)
21a	H	H	45
21b	H	CO_2Me	50
21c	OMe	H	52
21d	OMe	CO_2Me	55



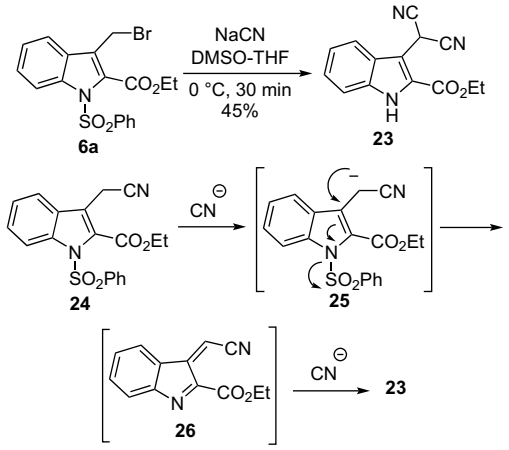
2a R^1 = OMe, R^2 = CO_2Et
2b R^1 =H, R^2 = CO_2Et
2c R^1 = H, R^2 = COMe
2d R^1 = H, R^2 = CH=CHCO_2Et

Scheme 11.

Table 4

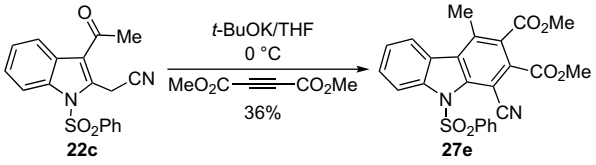
Compound	R^1	R^2	Yield (%)
22a	OMe	CO_2Et	58
22b	H	CO_2Et	53
22c	H	COMe	55
22d	H	CH=$CHCO_2Et$	42

Unfortunately, the interaction of isomeric 3-bromomethylindole **6a** with NaCN in DMSO/THF at 0 °C for 30 min led to the isolation of indolylmalononitrile **23** instead of required 3-cyanomethylindole **24**. The mechanism of formation of **23** could be visualized only through the intermediacy of the elusive 3-cyanomethylindole **24**. Obviously, the cyanide ion behaves as a base to abstract the acidic indole-3-methylene proton, which on cleavage of phenylsulfonyl group followed by nucleophilic addition of cyanide ion led to the formation of **23** (Scheme 12).



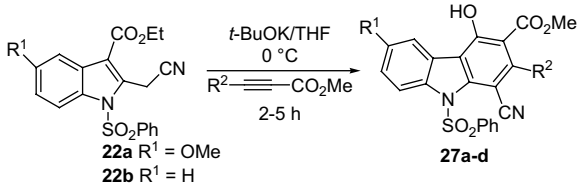
Scheme 12.

As expected, Michael addition of the 2-cyanomethylindoles **22a**/**22b** with methyl propiolate/DMAD in the presence of *t*-BuOK in dry THF gave the respective 1-cyano carbazoles **27a**–**d** in low yields (Scheme 13). The use of LHMDS in place of *t*-BuOK also led to the isolation of these carbazoles only in moderate yields. As expected, when the cyano compound **22c** was reacted with DMAD using *t*-BuOK as a base in dry THF furnished the respective carbazole **27e** of course only in 36% of yield (Table 5).



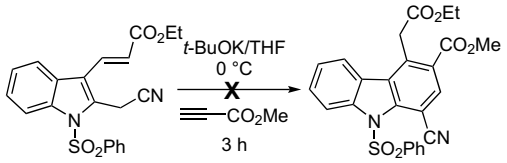
Scheme 13.

Table 5



Compound	R^1	R^2	Yield (%)
27a	H	H	45
27b	H	CO_2Me	32
27c	OMe	H	62
27d	OMe	CO_2Me	40

The attempted double Michael addition of the 2-cyanomethylindole **22d** with methyl propiolate in the presence of *t*-BuOK as a base didn't give the expected carbazole **28**, only the starting material was recovered (Scheme 14).



Scheme 14.

3. Conclusions

In summary, a systematic study on the synthesis of carbazole analogs was carried out using Michael addition promoted annulation methodology as a key step. Thus, using indole-2-methylsulfoxides as bidentate synthons, synthesis of 4-hydroxy, 4-methyl, and 4-aminocarbazole derivatives was successfully achieved in reasonable yields. However, all attempts to prepare the 1-hydroxycarbazoles from the corresponding indole-3-methylsulfoxides were found to be unsuccessful. Similarly, using indole-2-methylacetates/indole-2-methylcyanides, synthesis of tri- as well as tetrasubstituted carbazoles is achieved in moderate yields.

4. Experimental

4.1. General

All melting points are uncorrected. Solvents were purified using standard procedure. Reactions were done under atmosphere of dry nitrogen with magnetic stirring. All chemicals were used as received. Analytical thin layer chromatography (TLC) was performed on silica and components were visualized by observation under iodine or UV-light. Column chromatography was performed using silica gel (60–120 mesh). 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 and Bruker-300 spectrometers. Elemental analyses were performed on either Perkin–Elmer series II 2400 (IIT Madras) elemental analyzer or Euro EA 3000 (CLRI, Chennai). The mass spectra were recorded on a JEOL DX 303 HF mass spectrometer. The bromomethylindoles **2a**–**e** were prepared from the corresponding methyl compounds using published procedure.[12a]

4.2. A representative procedure for the preparation of sulfide 3a from indolyl bromo compound 2a (procedure A)

*4.2.1. Ethyl-1-phenylsulfonyl-5-methoxy-2-phenylthiomethylindole-3-carboxylate (**3a**)*

To a well stirred suspension of NaH (0.24 g, 10 mmol) in dry THF (30 mL) at 0 °C, a solution of thiophenol (1.1 mL, 11 mmol) in dry THF (10 mL) was slowly added under N_2 atmosphere. After 5 min, a solution of bromo compound **2a** (4.50 g, 10 mmol) in THF (20 mL) was added dropwise with vigorous stirring. Then, the reaction mixture was stirred for 2 h and then poured over crushed ice containing concd HCl (5 mL). The precipitated crude sulfide was filtered, washed with water, and dried ($CaCl_2$), which was crystallized from MeOH to give the title compound **3a** (4.40 g, 90%) as a colorless solid; mp 93 °C. [Found: C, 61.9; H, 4.7; N, 3.0; S, 13.6. $C_{25}H_{23}NO_5S_2$ requires C, 62.35; H, 4.81; N, 2.91; S, 13.32%.] R_f (15% EtOAc/hexane) 0.64; ν_{max} (KBr) 1169, 1369, 1710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.00 (1H, d, *J* 9.0 Hz, ArH), 7.93 (2H, d, *J* 8.1 Hz, ArH), 7.57–7.22 (9H, m, ArH), 6.94 (1H, d, *J* 8.7 Hz, ArH), 5.07 (2H, s, CH_2SPh), 4.10 (2H, q, *J* 7.0 Hz, OCH_2), 3.82 (3H, s, OCH_3), 1.27 (3H, t, *J* 7.0 Hz, CH_3); δ_C (75.6 MHz, $CDCl_3$) 164.0, 157.1, 144.2, 134.7, 134.6, 134.2, 133.5, 130.5, 129.3, 128.7, 128.2, 127.8, 126.9, 115.4, 114.6, 113.2, 104.4, 60.5, 55.5, 31.1, 14.1.

*4.2.2. Ethyl-1-phenylsulfonyl-2-phenylthiomethylindole-3-carboxylate (**3b**)*

Yield: 0.9 g (84%); colorless solid; mp 90 °C. [Found: C, 63.5; H, 4.5; N, 3.3; S, 14.4. $C_{24}H_{21}NO_4S_2$ requires C, 63.84; H, 4.69; N, 3.10; S, 14.20%.] R_f (15% EtOAc/hexane) 0.81; ν_{max} (KBr) 1170, 1368, 1708 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.99 (1H, d, *J* 8.4 Hz, ArH), 7.82 (2H, d, *J* 7.5 Hz, ArH), 7.58–7.48 (2H, m, ArH), 7.39 (3H, t, *J* 7.8 Hz, ArH), 7.27–7.20 (6H, m, ArH), 4.31–4.26 (4H, m, CH_2SPh and OCH_2), 1.32 (3H, t, *J* 7.0 Hz, CH_3); δ_C (75.6 MHz, $CDCl_3$) 164.0, 143.8, 138.7, 135.9, 134.5, 134.3, 133.5, 129.3, 128.7, 127.8, 127.0, 125.5, 124.5, 122.2, 114.5, 113.3, 60.6, 31.0, 14.2.

*4.2.3. 1-Phenylsulfonyl-2-phenylthiomethyl-3-acetylindole (**3c**)*

Yield: 0.92 g (86%); colorless solid; mp 116 °C. [Found: C, 65.3; H, 4.5; N, 3.5; S, 15.5. $C_{23}H_{19}NO_3S_2$ requires C, 65.53; H, 4.54; N, 3.32; S, 15.21%.] R_f (15% EtOAc/hexane) 0.5; ν_{max} (KBr) 1170, 1373, 1680 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.13 (1H, d, *J* 8.1 Hz, ArH), 7.97 (2H, t, *J* 7.5 Hz, ArH), 7.71 (1H, d, *J* 7.2 Hz, ArH), 7.56 (1H, t, *J* 7.2 Hz, ArH), 7.44 (2H, t, *J* 7.8 Hz, ArH), 7.34–7.24 (7H, m, ArH), 5.01 (2H, s, CH_2SPh), 2.29 (3H, s, CH_3); δ_C (75.6 MHz, $CDCl_3$) 195.9, 141.7, 138.7, 136.0, 134.3, 133.6, 129.4, 128.9, 127.9, 127.0, 126.5, 125.4, 124.5, 122.5, 122.4, 120.9, 114.9, 31.5, 30.9.

*4.2.4. 1-Phenylsulfonyl-3-cyano-2-phenylthiomethylindole (**3d**)*

Yield: 0.88 g (82%); colorless solid; mp 140 °C. [Found: C, 65.1; H, 4.1; N, 6.5; S, 15.5. $C_{22}H_{16}N_2O_2S_2$ requires C, 65.32; H, 3.99; N, 6.93; S, 15.85%.] R_f (15% EtOAc/hexane) 0.61; ν_{max} (KBr) 1189, 1376, 2221 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.07 (2H, d, *J* 7.2 Hz, ArH), 7.62 (1H, d, *J* 6.9 Hz, ArH), 7.51 (3H, t, *J* 7.8 Hz, ArH), 7.42–7.26 (8H, m, ArH), 4.63 (2H, s, CH_2SPh); δ_C ($CDCl_3$, 75.5 MHz) 145.6, 138.1, 135.6, 134.8, 134.2, 132.9, 130.5, 129.8, 129.5, 129.3, 127.3, 126.6, 126.5, 124.9, 119.7, 114.9, 112.8, 33.2.

*4.2.5. Ethyl-3-[2-(phenylthiomethyl)-1-(phenylsulfonyl)-indol-3-yl]-acrylate (**3e**)*

Yield: 0.72 g (68%); mp 134 °C. [Found: C, 65.1; H, 4.7; N, 3.1; S, 13.8. $C_{26}H_{23}NO_4S_2$ requires C, 65.39; H, 4.85; N, 2.93; S, 13.43%.] R_f (15% EtOAc/hexane) 0.54; ν_{max} (KBr) 1162, 1360, 1690 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.17 (1H, d, *J* 8.1 Hz, ArH), 7.98–7.83 (5H, m, ArH), 7.79 (2H, d, *J* 8.1 Hz, ArH), 7.67–7.53 (3H, m, ArH), 7.47–7.14 (4H, m, ArH), 6.26 (1H, d, *J* 15.9 Hz, HC=CH), 4.61 (2H, s, CH_2SPh), 4.24 (2H, q, *J* 7.2 Hz, OCH_2), 1.29 (3H, t, *J* 7.2 Hz, CH_3); δ_C ($CDCl_3$, 75.5 MHz) 164.4, 138.2, 137.6, 135.7, 135.1, 134.5, 132.5, 128.4, 127.7, 126.2, 125.6, 123.9, 120.2, 119.5, 119.3, 114.7, 60.1, 21.5, 14.2; *m*/*z* (EI) 479 (16, M^++2), 477 (42, M^+).

4.3. A representative procedure for the preparation of sulfoxide 4a from indolyl sulfide 3a (procedure B)

*4.3.1. Ethyl-1-phenysulfonyl-5-methoxy-2-phenylsulfinylmethylindole-3-carboxylate (**4a**)*

To a solution of KF (80 mg, 1.43 mmol) in acetonitrile/water (10 mL, 2 mL), *m*-CPBA (0.25 g, 1.43 mmol) was added and the mixture was stirred at 0 °C for 30 min. To this, sulfide **3a** (0.48 g, 1.00 mmol) was added and the stirring was continued for an additional 30 min. The reaction mixture was then poured into saturated $NaHCO_3$ solution, extracted with EtOAc (2×10 mL), and the combined extract was dried (Na_2SO_4). Removal of solvent followed by crystallization from MeOH afforded sulfoxide **4a** (0.46 g, 92%) as a colorless solid; mp 94 °C. [Found: C, 60.5; H, 4.8; N, 3.0; S, 13.1. $C_{25}H_{23}NO_6S_2$ requires C, 60.35; H, 4.66; N, 2.81; S, 12.89%.] R_f (20% EtOAc/hexane) 0.18; ν_{max} (KBr) 1079,

1181, 1362, 1702 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.99 (1H, d, *J* 9.3 Hz, ArH), 7.81 (2H, d, *J* 7.2 Hz, ArH), 7.61–7.40 (9H, m, ArH), 6.99–6.95 (1H, dd, *J* 2.7 and 9.3, ArH), 5.39 (1H, d, *J* 12.3 Hz, CH_aH_b-SOPh), 5.11 (1H, d, *J* 12.3 Hz, CH_aH_bSOPh), 4.29 (2H, q, *J* 7.2 Hz, OCH_2), 3.83 (3H, s, OCH_3), 1.39 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.6 MHz, $CDCl_3$) 163.9, 157.3, 143.6, 138.1, 136.3, 134.4, 131.3, 130.8, 129.1, 128.9, 128.3, 126.6, 126.4, 124.3, 115.5, 115.3, 104.5, 60.9, 55.5, 55.4, 14.2.

*4.3.2. Ethyl-1-phenylsulfonyl-2-phenylsulfinylmethylindole-3-carboxylate (**4b**)*

Yield: 0.93 g (90%); colorless solid; mp 110 °C. [Found: C, 61.5; H, 4.4; N, 3.2; S, 13.9. $C_{24}H_{21}NO_5S_2$ requires C, 61.65; H, 4.53; N, 3.00; S, 13.72%.] R_f (20% EtOAc/hexane) 0.22; ν_{max} (KBr) 1074, 1180, 1368, 1728 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.07 (2H, d, *J* 6.8 Hz, ArH), 7.86 (2H, d, *J* 8.3 Hz, ArH), 7.62 (2H, d, *J* 7.8 Hz, ArH), 7.58–7.50 (4H, m, ArH), 7.48–7.38 (2H, m, ArH), 7.36–7.30 (2H, m, ArH), 5.43 (1H, d, *J* 12.2 Hz, CH_aH_bSOPh), 5.13 (1H, d, *J* 12.7 Hz, CH_aH_bSOPh), 4.30 (2H, q, *J* 7.2 Hz, OCH_2), 1.40 (3H, t, *J* 7.3 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 163.9, 143.7, 138.1, 136.2, 134.4, 131.3, 129.5, 128.9, 126.8, 125.9, 124.8, 124.3, 122.5, 122.4, 114.6, 114.5 (2C), 60.9, 55.3, 14.2; *m*/*z* (EI) 451 (24, M^+), 311 (24%).

*4.3.3. 1-Phenylsulfonyl-2-phenylsulfinylmethyl-3-acetylindole (**4c**)*

Yield: 0.93 g (90%); colorless solid; mp 130 °C. [Found: C, 63.3; H, 4.1; N, 3.5; S, 14.5. $C_{23}H_{19}NO_4S_2$ requires C, 63.14; H, 4.38; N, 3.20; S, 14.66%.] R_f (20% EtOAc/hexane) 0.16; ν_{max} (KBr) 1080, 1182, 1372, 1676 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.12–8.09 (1H, m, ArH), 7.86 (2H, d, *J* 7.5 Hz, ArH), 7.81–7.78 (1H, m, ArH), 7.69–7.66 (2H, m, ArH), 7.58–7.44 (6H, m, ArH), 7.42–7.32 (2H, m, ArH), 5.27 (1H, d, *J* 12.9 Hz, CH_aH_bSOPh), 5.03 (1H, d, *J* 13.2 Hz, CH_aH_bSOPh), 2.63 (3H, s, CH_3); δ_C (75.6 MHz, $CDCl_3$) 196.4, 143.6, 138.1 136.3, 134.5, 134.0, 131.4 129.6, 129.2, 127.0, 126.8, 126.7, 125.9, 124.8, 124.3, 121.1, 115.0, 55.2, 32.2.

*4.3.4. 1-Phenylsulfonyl-3-cyano-2-phenylsulfinylmethylindole (**4d**)*

Yield: 0.94 g (91%); colorless solid; mp 142 °C. [Found: C, 62.9; H, 4.0; N, 6.5; S, 15.2. $C_{22}H_{16}N_2O_3S_2$ requires C, 62.84; H, 3.84; N 6.66, S, 15.25%.] R_f (20% EtOAc/hexane) 0.18; ν_{max} (KBr) 1083, 1181, 1380, 2221 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.07 (1H, d, *J* 8.0 Hz, ArH), 7.88 (2H, d, *J* 8.0 Hz, ArH), 7.65 (2H, d, *J* 8.4 Hz, ArH), 7.54–7.47 (8H, m, ArH), 7.26 (1H, d, *J* 7.9 Hz, ArH), 4.71 (2H, s, CH_aH_bSOPh); δ_C (100.5 MHz, $CDCl_3$) 143.1, 137.7, 137.5, 135.8, 135.1, 132.0, 129.9, 129.5, 127.2, 126.9, 125.4, 124.2, 120.0, 114.9, 112.8, 99.4, 57.8; *m*/*z* (EI) 405 (9, M−16), 231 (35), 154 (39), 141 (28%).

*4.3.5. Ethyl-3-[2-phenylsulfinylmethyl-1-(phenylsulfonyl)-indol-3-yl]acrylate (**4e**)*

Yield: 0.97 g (94%); colorless solid; mp 118 °C. [Found: C, 63.4; H, 4.9; N, 2.7; S, 12.7. $C_{26}H_{23}NO_5S_2$ requires C, 63.27; H, 4.70; N, 2.84; S, 12.99%.] R_f (20% EtOAc/hexane) 0.16; ν_{max} (KBr) 1040, 1162, 1360, 1690 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.70 (1H, d, *J* 7.8 Hz), 7.49–7.46 (3H, m, ArH), 7.41–7.34 (3H, m, ArH), 7.33–7.29 (6H, m, ArH), 7.19–7.27 (2H, m, ArH), 6.36 (1H, d, *J* 15.9 Hz, CH═CH), 4.70 (1H, d, *J* 3.2 Hz, CH_aH_bSOPh), 4.54 (1H, d, *J* 13.2 Hz, CH_aH_bSOPh), 4.19 (2H, q, *J* 7.2 Hz, OCH_2), 1.27 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.6 MHz, $CDCl_3$) 166.6, 143.3, 138.2, 136.9, 134.4, 133.7, 131.5, 130.9, 129.5, 129.2, 127.1, 126.5, 126.3, 124.8, 124.2, 122.0, 121.0, 120.7, 115.0, 60.6, 56.6, 14.4; *m*/*z* (EI) 477 (46, M^+−16), 336 (27%).

*4.3.6. Ethyl-1-phenylsulfonyl-5-methoxy-2-phenylsulfonyl-me thylindole-3-carboxylate (**4a′**)*

Colorless solid; mp 140–141 °C. [Found: C, 58.6; H, 4.4; N, 2.9; S, 12.2. $C_{25}H_{23}NO_7S_2$ requires C, 58.47; H, 4.51; N, 2.73; S, 12.49.] R_f (20% EtOAc/hexane) 0.40; ν_{max} (KBr) 1700, 1150, 1170, 1200, 1320 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.89–7.85 (1H, d, *J* 9.3 Hz, ArH), 7.78–7.71 (4H, m, ArH), 7.55–7.37 (7H, m, ArH), 6.98–6.94 (1H, dd, *J* 9, 3 Hz, ArH) 5.76 (2H, s, CH_2SO_2Ph), 4.20 (2H, q, *J* 7.2 Hz, OCH_2), 3.76 (3H, s, OCH_3), 1.33 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 163.8, 157.3, 138.9, 137.9, 134.4, 133.8, 133.5, 131.0, 129.4, 128.2, 127.0, 126.6, 117.3, 115.8, 115.7, 115.4, 104.3, 61.0, 55.5, 53.4, 14.2.

4.4. A representative procedure for the preparation of carbazole 5a from the sulfoxide 4a (procedure C)

*4.4.1. Methyl-9-phenylsulfonyl-4-hydroxy-6-methoxycarbazole-3-carboxylate (**5a**)*

To a solution of sulfoxide **4a** (0.5 g, 1.0 mmol) in dry THF (10 mL) under N_2, *t*-BuOK (0.11 g, 1 mmol) in THF (5 mL) was added and stirred at 0 °C for 15 min. To this methyl acrylate (0.10 g, 1.21 mmol) in THF (2 mL) was slowly added. After stirring for 5 h at 0 °C, the reaction mixture was quenched with aq NH_4Cl (5 mL), extracted with $CHCl_3$ (2×20 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from MeOH afforded carbazole **5a** (0.29 g, 70%) as brown solid; mp 160 °C; R_f (15% EtOAc/hexane) 0.65. [Found: C, 61.0; H, 4.3; N, 3.1; S, 8.0. $C_{21}H_{17}NO_6S$ requires: C, 61.30; H, 4.16; N, 3.40; S, 7.79%.] ν_{max} (KBr) 1178, 1368, 1705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 11.61 (1H, s, OH), 8.19 (1H, d, *J* 9.3 Hz, ArH), 7.92–7.77 (5H, m, ArH), 7.49–7.44 (1H, m, ArH), 7.32 (2H, t, *J* 7.8 Hz, ArH), 7.06 (1H, dd, *J* 6.3 and 2.7 Hz, ArH), 3.97 (3H, s, OCH_3), 3.89 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 171.4, 158.4, 157.1, 143.7, 137.7, 133.9, 131.9, 129.1, 128.6, 126.4, 126.2, 115.4, 115.2, 114.5, 114.3, 106.4, 106.2, 55.8, 52.3.

*4.4.2. 6-Methoxy-9-phenylsulfonyl-4-hydroxy-3-acetyl-carbazole (**5b**)*

Yield: 0.18 g (77%); brown solid; mp 190 °C. [Found: C, 63.6; H, 4.5; N, 3.40; S, 8.3. $C_{21}H_{17}NO_5S$ requires C, 63.79; H, 4.33; N, 3.54; S, 8.1%.] R_f (15% EtOAc/hexane) 0.66; ν_{max} (KBr) 1170, 1360, 1650 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 13.33 (1H, s, OH), 8.17 (1H, d, *J* 8.7 Hz, ArH), 7.80–7.78 (5H, m, ArH), 7.47–7.26 (3H, m, ArH), 7.06 (1H, d, *J* 8.7 Hz, ArH), 3.89 (3H, s, OCH_3), 2.67 (3H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 204.1, 159.7, 157.2, 143.9, 137.7, 134.1, 131.8, 129.6, 129.2, 126.4, 126.3, 115.3 (2C), 115.1, 106.2, 106.1, 55.8, 26.8; *m*/*z* (EI) 395 (14, M^+), 394 (55), 254 (100), 77 (43%).

*4.4.3. 6-Methoxy-9-phenylsulfonyl-4-hydroxycarbazole-3-carboxaldehyde (**5c**)*

Yield: 0.16 g (68%); brown solid; mp 196 °C. [Found: C, 62.7; H, 3.8; N, 3.8; S, 8.6. $C_{20}H_{15}NO_5S$ requires C, 62.98; H, 3.96; N, 3.67; S, 8.41%.] R_f (15% EtOAc/hexane) 0.59; ν_{max} (KBr) 1170, 1370, 1640 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 12.04 (1H, s, OH), 9.96 (1H, s, CHO), 8.21 (1H, d, *J* 8.3 Hz, ArH), 8.92 (2H, d, *J* 7.3 Hz, ArH), 7.86–7.68 (2H, m, ArH), 7.45–7.34 (5H, m, ArH), 3.86 (3H, s, OCH_3); δ_C (125 MHz, $CDCl_3$) 189.8, 158.3, 137.8, 137.7, 134.3, 129.7, 128.6, 127.4, 126.8, 126.4, 125.2, 124.4, 123.4, 123.2, 115.4, 114.3, 107.5, 55.8.

*4.4.4. 6-Methoxy-9-phenylsulfonyl-4-hydroxy-3-cyano-carbazole (**5d**)*

Yield: 0.7 g (70%); colorless solid; mp 184 °C. [Found: C, 63.6; H, 3.9; N, 7.6; S, 8.6. $C_{20}H_{15}NO_5S$ requires C, 63.48; H, 3.73; N, 7.40; S, 8.47%.] R_f (15% EtOAc/hexane) 0.50; ν_{max} (KBr) 1172, 1380, 2221 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 12.96 (1H, s, OH), 8.13 (2H, d, *J* 8.4 Hz, ArH), 7.98 (2H, d, *J* 7.4 Hz, ArH), 7.67–7.42 (3H, m, ArH), 7.12–7.36 (3H, m, ArH,) 3.93 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 158.7, 137.7, 137.5, 134.7, 129.7, 128.2, 127.6, 126.8, 126.7, 125.0, 124.8, 123.4, 123.1, 115.5, 114.6, 114.4, 107.5, 55.8.

*4.4.5. Methyl-9-phenylsulfonyl-4-hydroxycarbazole-3-carboxylate (**5e**)*

Yield: 0.28 g (70%); brown solid; mp 152 °C. [Found: C, 62.8; H, 3.8; N, 3.8; S, 8.5. $C_{20}H_{15}NO_5S$ requires C, 62.98; H, 3.96; N, 3.67; S, 8.41%.] R_f (15% EtOAc/hexane) 0.67; ν_{max} (KBr) 1168, 1374, 1705, 3331 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.30 (2H, d, *J* 8.1 Hz, ArH),

7.95–7.82 (4H, m, ArH), 7.48–7.33 (5H, m, ArH), 3.98 (3H, s, CH_3); δ_C ($CDCl_3$, 100.6 MHz) 170.8, 158.4, 143.2, 137.7, 134.1, 129.2, 128.7, 126.9, 126.5, 125.1, 124.5, 123.4, 123.3, 114.7, 114.4, 107.6, 106.2, 52.3; *m*/*z* (EI) 382 (33, M^++1), 381 (54, M^+), 77 (90%).

*4.4.6. 9-Phenylsulfonyl-4-hydroxy-3-acetylcarbazole (**5f**)*

Yield: 0.27 g (69%); colorless solid; mp 178 °C. [Found: C, 65.6; H, 4.30; N, 4.0; S, 8.6. $C_{20}H_{15}NO_4S$ requires C, 65.74; H, 4.14; N, 3.83; S, 8.78%.] R_f (15% EtOAc/hexane) 0.63; ν_{max} (KBr) 1178, 1365, 1692, 3366 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 13.31 (1H, s, OH), 8.31 (2H, t, *J* 8.0 Hz, ArH), 7.89–7.81 (4H, m, ArH), 7.50 (2H, t, *J* 8.0 Hz, ArH), 7.43–7.34 (3H, m, ArH), 2.69 (3H, s, CH_3); δ_C ($CDCl_3$, 100.6 MHz) 204.4, 159.9, 138.1, 137.9, 134.5, 129.9, 129.6, 127.3, 126.8, 125.5, 124.9, 123.7, 115.7, 115.3, 114.6, 106.2, 27.2; *m*/*z* (EI) 367 (37, M^++2), 365 (74, M^+), 166 (49%).

*4.4.7. 9-Phenylsulfonyl-4-hydroxycarbazole-3-carboxaldehyde (**5g**)*

Yield: 0.24 g (64%); colorless solid; mp 154–158 °C. [Found: C, 64.8; H, 4.0; N, 3.7; S, 8.9. $C_{19}H_{13}NO_4S$ requires C, 64.95; H, 3.73; N, 3.99; S, 9.13%.] R_f (15% EtOAc/hexane) 0.64; ν_{max} (KBr) 3330, 1682, 1367, 1172, 3425 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 12.01 (1H, s, OH), 9.95 (1H, s, CHO), 8.31 (1H, t, *J* 8.8 Hz, ArH), 8.10 (1H, d, *J* 8.4 Hz, ArH), 7.87 (2H, d, *J* 7.2 Hz, ArH), 7.64 (1H, d, *J* 8.8 Hz, ArH), 7.52 (2H, t, *J* 8.0 Hz, ArH), 7.41 (4H, quint, *J* 6.8 Hz, ArH); δ_C ($CDCl_3$, 100.6 MHz) 181.1, 159.5, 138.1, 136.6, 134.3, 129.9, 129.8, 127.0, 126.8, 125.9, 124.8, 124.7, 115.7, 115.6, 114.6, 106.3; *m*/*z* (EI) 353 (81, M^++2), 351 (62, M^+), 173 (28%).

*4.4.8. 9-Phenylsulfonyl-4-hydroxy-3-cyanocarbazole (**5h**)*

Yield: 0.26 g (70%); colorless solid; mp 178 °C. [Found: C, 65.4; H, 3.3; N, 8.2; S, 9.0. $C_{19}H_{12}N_2O_3S$ requires C, 65.51; H, 3.47; N, 8.04; S, 9.20%.] R_f (15% EtOAc/hexane) 0.63; ν_{max} (KBr) 1178, 1360, 2221, 3325 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.96 (1H, s, OH), 8.12 (1H, d, *J* 8.2 Hz, ArH), 7.98 (2H, d, *J* 7.2 Hz, ArH), 7.63–7.51 (4H, m, ArH), 7.43–6.98 (4H, m, ArH); δ_C (100.6 MHz, $CDCl_3$) 159.1, 138.1, 137.9, 134.7, 134.5, 129.9, 129.6, 127.7, 126.8, 125.2, 124.9, 123.4, 123.3, 115.7, 115.3, 114.7, 106.9; *m*/*z* (EI) 349 (76, M^++1), 348 (34, M^+), 207 (35%).

*4.4.9. 9-Phenylsulfonyl-4-hydroxy-3-nitro-2-phenylcarbazole (**5i**)*

Yield: 0.21 g (40%); colorless solid; mp 204–206 °C. [Found: C, 65.0; H, 3.5; N, 6.1; S, 7.0. requires $C_{24}H_{16}N_2O_5S$ C, 64.86; H, 3.63; N, 6.30; S, 7.21%.] R_f (15% EtOAc/hexane) 0.60; ν_{max} (KBr) 1178, 1372, 1548, 3325 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 10.98 (1H, s, OH), 8.33–8.31 (2H, m, ArH), 7.89 (1H, s, ArH), 7.88–7.86 (2H, m, ArH), 7.58–7.53 (2H, m, ArH), 7.50–7.46 (4H, m, ArH), 7.42 (2H, t, *J* 7.8 Hz, ArH), 7.37–7.36 (2H, m, ArH); δ_C (125 MHz, $CDCl_3$) 151.8, 141.3, 139.5, 139.0, 138.2, 137.6, 134.7, 130.2, 129.6, 128.8, 128.1, 127.9, 127.8, 126.7, 125.1, 124.6, 123.7, 114.7, 114.6, 110.6; *m*/*z* (EI) 446 (52, M^++2), 444 (25, M^+), 398 (17%).

*4.4.10. Methyl-9-phenylsulfonyl-4-hydroxy-2-methylcarbazole-3-carboxylate (**5k**)*

Yield: 0.15 g (36%); colorless solid; mp 188–190 °C. [Found: C, 65.0; H, 4.4; N, 3.4; S, 7.9. $C_{21}H_{17}NO_5S$ requires C, 63.79; H, 4.33; N, 3.54; S, 8.11%.] R_f (15% EtOAc/hexane) 0.69; ν_{max} (KBr) 1178, 1365, 1704, 3324 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.98 (1H, s, OH), 8.21 (1H, d, *J* 8.1 Hz, ArH), 7.86 (2H, d, *J* 7.1 Hz,), 7.81 (1H, s, ArH), 7.56–7.50 (2H, m, ArH), 7.49 (2H, t, *J* 7.8 Hz,), 7.39–7.27 (2H, m, ArH), 4.00 (3H, s, OCH_3), 2.78 (3H, s, CH_3); δ_C (100.6 MHz, $CDCl_3$) 168.8, 141.3, 139.4, 137.6, 134.5, 128.7, 128.3, 127.7, 127.3, 126.7, 125.5, 124.6, 123.8, 123.7, 117.0, 114.8, 114.5, 53.2, 18.2; *m*/*z* (EI) 396 (22, M^++1), 395 (37, M^+), 254 (17%).

*4.4.11. 9-Phenylsulfonyl-4-methyl-3-acetylcarbazole (**5l**)*

Yield: 0.19 g (48%); brown solid; mp 162–164 °C. [Found: C, 69.1; H, 4.5; N, 3.6; S, 8.7. $C_{21}H_{17}NO_3S$ requires C, 69.40; H, 4.71; N, 3.85; S, 8.82%.] R_f (15% EtOAc/hexane) 0.72; ν_{max} (KBr) 1178, 1365, 1670 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.35 (1H, d, *J* 8.4 Hz, ArH), 8.21 (1H, d, *J* 9.0 Hz, ArH), 8.09 (1H, d, *J* 7.8 Hz, ArH), 7.74 (2H, d, *J* 7.2 Hz, ArH), 7.68 (1H, d, *J* 9.0 Hz, ArH), 7.49–7.29 (5H, m, ArH), 2.83 (3H, s, CH_3), 2.59 (3H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 201.2, 158.7, 147.2, 139.7, 134.9, 129.2, 128.3, 127.6, 127.3, 126.9, 126.5, 124.2, 123.4, 114.9, 111.9, 96.1, 30.5, 17.9.

*4.4.12. Methyl-9-phenylsulfonyl-4-methylcarbazole-3-carboxylate (**5m**)*

Yield: 0.23 g (53%); brown solid; mp 154 °C. [Found: C, 66.3; H, 4.4; N, 3.8; S, 8.2. $C_{21}H_{17}NO_4S$ requires C, 66.47; H, 4.52; N, 3.69; S, 8.45%.] R_f (15% EtOAc/hexane) 0.71; ν_{max} (KBr) 1172, 1368, 1712 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.29 (1H, d, *J* 8.2 Hz, ArH), 7.98 (1H, d, *J* 7.8 Hz, ArH), 7.71 (3H, m, ArH), 7.50–7.37 (6H, m, ArH), 3.97 (s, 3H, OCH_3), 2.78 (s, 3H, CH_3); δ_C (75.5 MHz, $CDCl_3$) 165.6, 147.2, 139.2, 135.3, 134.3, 131.3, 130.9, 128.9, 127.7, 127.3, 127.1, 125.7, 123.4, 117.6, 114.9, 114.7, 99.3, 53.6, 17.4.

*4.4.13. Methyl-9-phenylsulfonyl-4-aminocarbazole-3-carboxylate (**5n**)*

Yield: 0.22 g (48%); brown solid; mp 198 °C. [Found: C, 62.1; H, 4.5; N, 7.5; S, 8.6. $C_{20}H_{16}N_2S$ requires C, 63.14; H, 4.24; N, 7.36; S, 8.43%.] R_f (15% EtOAc/hexane) 0.77; ν_{max} (KBr) 1178, 1368, 1698, 3240 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.98 (1H, d, *J* 8.4 Hz, ArH), 7.88–7.57 (5H, m, ArH), 7.49–7.39 (2H, m, ArH), 7.29 (2H, t, *J* 7.3 Hz, ArH), 7.14 (1H, d, *J* 6.7 Hz, ArH), 4.67 (2H, br s, NH_2), 3.98 (3H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 172.3, 158.4, 157.6, 143.5, 137.8, 137.7, 136.6, 134.3, 130.8, 128.8, 127.7, 126.9, 126.6, 115.7, 115.5, 106.4, 106.3, 55.8.

*4.4.14. 9-Phenylsulfonyl-4-amino-3-acetylcarbazole (**5o**)*

Yield: 0.22 g (50%); brown solid; mp 204 °C. [Found: C, 65.8; H, 4.2; N, 7.4; S, 9.0. $C_{20}H_{16}N_2O_3S$ requires C, 65.92; H, 4.43; N, 7.69; S, 8.80%.] R_f (15% EtOAc/hexane) 0.79; ν_{max} (KBr) IR (KBr) 1164, 1372, 1682, 3248 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.17 (1H, d, *J* 8.7 Hz,), 7.79–7.26 (9H, m, ArH), 7.08 (1H, d, *J* 8.7 Hz, ArH), 3.39 (2H, br s, NH_2), 2.68 (3H, s, CH_3); δ_C (, 75.5 MHz) 203.9, 159.2, 138.1, 137.9, 134.6, 134.5, 129.5, 127.6, 126.4, 125.1, 124.7, 123.7, 121.6, 118.5, 115.7, 112.3, 104.7, 26.9.

*4.4.15. 9-Phenylsulfonyl-4-amino-3-cyanocarbazole (**5p**)*

Yield: 0.18 g (45%); brown solid; mp 232 °C. [Found: C, 65.4; H, 3.6; N, 12.3; S, 9.0. $C_{19}H_{13}N_3O_2S$ requires C, 65.69; H, 3.77; N, 12.10; S, 9.23%.] R_f (15% EtOAc/hexane) 0.73; ν_{max} (KBr) 1176, 1380, 2221, 3235 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.18 (1H, d, *J* 8.2 Hz, ArH), 7.98–7.87 (4H, m, ArH), 7.76–7.45 (4H, m, ArH), 7.32–7.17 (2H, m, ArH), 3.79 (2H, s, NH_2); δ_C (75.5 MHz, $CDCl_3$) 158.7, 137.7, 137.5, 134.7, 129.7, 128.2, 127.6, 126.8, 126.7, 125.0, 124.8, 123.4, 123.1, 115.5, 114.6, 114.4, 107.5.

*4.4.16. Ethyl-1-phenylsulfonyl-3-phenylthiomethylindole-2-carboxylate (**7a**)*

Yield: 0.92 g (84%); colorless solid; mp 90 °C. [Found: C, 64.0; H, 4.9; N, 3.0; S, 14.0. $C_{24}H_{21}NO_4S_2$ requires C, 63.84; H, 4.69; N, 3.10; S, 14.20%.] R_f (15% EtOAc/hexane) 0.83; ν_{max} (KBr) 1182, 1370, 1720 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.94 (1H, d, *J* 8.2 Hz, ArH), 7.81 (2H, d, *J* 6.9 Hz, ArH), 7.52 (2H, d, *J* 7.1 Hz, ArH), 7.48–7.22 (8H, m, ArH), 6.98 (1H, t, *J* 6.9 Hz, ArH), 4.28 (2H, s, CH_2SPh), 4.23 (2H, q, *J* 7.2 Hz, OCH_2), 1.34 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.7, 157.0, 137.2, 137.0, 135.0, 133.7, 132.0, 131.6, 130.1, 129.9, 129.1, 128.9, 127.5, 127.4, 127.2, 127.0, 125.9, 116.6, 116.5, 103.0, 62.4, 29.3, 13.9.

*4.4.17. Ethyl-5-methoxy-1-phenylsulfonyl-3-phenylthiomethyl-indole-2-carboxylate (**7b**)*

Yield: 4.15 g (85%); colorless solid; mp 98 °C. [Found: C, 62.5; H, 5.1; N, 3.1; S, 13.1. $C_{25}H_{23}NO_5S_2$ requires C, 62.35; H, 4.81; N, 2.91; S,

13.32%.] R_f (15% EtOAc/hexane) 0.82; ν_{max} (KBr) 1183, 1370, 1720 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.67 (1H, d, *J* 7.8 Hz, ArH) 7.61 (2H, d, *J* 7.1 Hz, ArH), 7.55–7.49 (3H, m, ArH), 7.38–7.02 (7H, m, ArH), 4.10 (2H, s, CH_2SPh), 4.18 (2H, q, *J* 7.2 Hz, OCH_2), 3.57 (3H, s, OCH_3), 1.26 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.6, 156.9, 137.2, 137.0, 134.9, 133.7, 132.0, 131.6, 130.0, 129.9, 129.1, 128.9, 128.8, 127.5, 127.4, 127.2, 127.0, 125.9, 116.6, 116.5, 103.0, 62.2, 55.6, 29.2, 13.9.

4.4.18. Ethyl-1-phenylsulfonyl-3-phenylsulfinylmethylindole-2-carboxylate (**8a**)

Yield: 0.87 g (85%); colorless solid; mp 118 °C. [Found: C, 61.5; H, 4.4; N, 3.2; S, 13.5. $C_{24}H_{21}NO_5S_2$ requires C, 61.65; H, 4.53; N, 3.00; S, 13.72%.] R_f (15% EtOAc/hexane) 0.23; ν_{max} (KBr) 1082, 1190, 1370, 1720 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.94 (1H, d, *J* 8.3 Hz, ArH), 7.84 (2H, d, *J* 7.5 Hz, ArH), 7.49 (1H, d, *J* 7.4 Hz, ArH), 7.38 (2H, t, *J* 7.8 Hz, ArH), 7.32–7.04 (8H, m, ArH), 4.37–4.01 (4H, m, OCH_2 & CH_aH_bSOPh), 1.28 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.1, 142.8, 137.9, 136.8, 134.0, 131.4, 130.8, 129.0, 128.9, 127.4, 127.2, 124.4, 124.1, 120.7, 117.9, 115.4, 115.3, 62.4, 53.6, 13.9.

4.4.19. Ethyl-5-methoxy-1-phenylsulfonyl-3-phenylsulfinylmethyl-indole-2-carboxylate (**8b**)

Yield: 0.45 g (90%); colorless solid; mp 146 °C. [Found: C, 60.1; H, 4.8; N, 3.0; S, 12.6. $C_{25}H_{23}NO_6S_2$ requires C, 60.35; H, 4.66; N, 2.81; S, 12.89%.] R_f (15% EtOAc/hexane) 0.18; ν_{max} (KBr) 1078, 1187, 1373, 1720 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.91–7.83 (3H, m, ArH), 7.56 (1H, d, *J* 7.5 Hz, ArH), 7.45 (2H, d, *J* 7.2 Hz, ArH), 7.40–7.24 (5H, m, ArH), 6.97 (1H, dd, *J* 2.4, 6.9 Hz, ArH), 6.52 (1H, d, *J* 2.4 Hz,), 4.42–4.23 (4H, m, OCH_2 and CH_aH_bSOPh), 3.69 (3H, s, OCH_3), 1.37 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.1, 157.0, 143.0, 137.5, 133.9, 131.5, 131.4, 131.3, 130.0, 128.9, 127.1, 124.2, 118.2, 116.4, 117.1, 102.1, 62.4, 55.6, 53.7, 13.9.

4.4.20. Ethyl 3-formyl-1H-indole-2-carboxylate (**12**)

Yield: 1 g (87%); colorless solid; mp 182 °C; R_f (15% EtOAc/hexane) 0.38; ν_{max} (KBr) 3235, 1726, 1665 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 10.77 (1H, s, CHO), 9.46 (1H, s, NH), 8.49 (1H, d, 8.1 Hz), 7.49–7.33 (3H, m, ArH), 4.54 (2H, *J* 7.2 Hz, q, OCH_2), 1.48 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 187.9, 160.3, 135.6, 132.3, 125.4, 124.8, 123.0, 122.5, 118.5, 112.6, 61.5, 13.8.

4.4.21. Ethyl 3-((phenylthio)methyl)-1H-indole-2-carboxylate (**13**)

To a stirred solution of aldehydic ester **12** (1 g, 4.60 mmol) in THF/MeOH (10:1) at room temperature, $NaBH_4$ (0.18 g, 4.7 mmol) was added portion wise and stirred for 2 h, then the reaction mixture was quenched with cold dil HCl (2 mL), extracted with EtOAc (10 mL). Then, the solvent was evaporated to afford the crude alcohol (0.9 g), which was used as such for next step. To a solution of crude alcohol (0.9 g, 4.10 mmol), thiophenol (0.56 g, 2.19 mmol), *p*-TSA (0.16 g, 0.36 mmol) was refluxed with toluene (20 mL) for 3 h, then extracted with EtOAc, followed by column chromatographic purification (2% EtOAc/hexane) afforded the required sulfide **13** (0.65 g, 70%); mp 130 °C. [Found: C, 69.6; H, 5.7; N, 4.4; S, 10.1. $C_{18}H_{17}NO_2S$ requires C, 69.43; H, 5.50; N, 4.50; S, 10.30%.] R_f (15% EtOAc/hexane) 0.71; ν_{max} (KBr) 3241, 1726 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.89 (1H, s, NH), 7.68 (1H, d, *J* 8.1 Hz, ArH), 7.38–7.10 (8H, m, ArH), 4.68 (2H, s, CH_2SPh), 4.33 (2H, q, *J* 7.1 Hz, OCH_2), 1.36 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.9, 136.5, 135.8, 131.4, 128.6, 127.4, 126.7, 125.8, 124.1, 120.5, 121.2, 119.2, 111.8, 61.0, 29.5, 14.3.

4.4.22. Ethyl-3-((phenylsulfinyl)methyl)-1H-indole-2-carboxylate (**14**)

Yield: 0.11 g (35%); thick liquid. [Found: C, 65.0; H, 5.0; N, 4.2; S, 9.7. $C_{18}H_{17}NO_3S$ requires C, 66.03; H, 5.23; N, 4.28; S, 9.79%.] R_f (20% EtOAc/hexane) 0.20; ν_{max} (KBr) 3247, 1729, 1172, 1381 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.85 (1H, s, NH), 7.41–7.23 (8H, m, ArH), 7.03 (1H, t, *J* 7.2 Hz, ArH), 4.79 (1H, d, *J* 13.2 Hz, CH_aH_bSOPh), 4.64 (1H, d, *J* 12.1 Hz, CH_aH_bSOPh), 4.32 (2H, q, *J* 7.1 Hz, OCH_2), 1.36 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 161.6, 143.6, 135.7, 131.0, 128.7, 125.8, 125.4, 124.3, 120.9, 120.5, 112.2, 110.8, 61.2, 54.8, 14.3.

4.4.23. Ethyl-2-(methoxymethyl)-1-(phenylsulfonyl)-1H-indole-3-carboxylate (**16**)

The bromo compound **2b** (0.42 g, 1 mmol) was refluxed in MeOH (20 mL) for 3 h. The solvent was evaporated and the crude product was crystallized from MeOH to afford indolyl ether **16** (0.24 g, 65%) as a colorless solid; mp 106 °C. [Found: C, 62.4; H, 5.3; N, 3.9; S, 8.5. $C_{19}H_{19}NO_5S$ requires C, 61.11; H, 5.13; N, 3.75; S, 8.59%.] R_f (20% EtOAc/hexane) 0.72; ν_{max} (KBr) 1182, 1370, 1702 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.19–8.00 (4H, m, ArH), 7.56–7.29 (5H, m, ArH), 5.33 (2H, s, CH_2), 4.43 (2H, q, *J* 6.9 Hz, OCH_2), 3.38 (s, 3H, OCH_2), 1.45 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 164.2 142.4, 138.9, 135.9, 134.0, 129.4, 129.0, 127.2, 126.7, 125.8, 124.4, 122.5, 114.5, 62.8, 60.9, 57.9, 14.4.

4.4.24. Ethyl-1-phenylsulfonyl-2-benzyl-3-carboxylate (**18**)

A mixture of 2-bromomethylindole **2b** (0.3 g, 0.71 mmol), phenylboronic acid (0.1 g, 0.78 mmol), and $Pd(PPh_3)_2Cl_2$ (0.03 g, 0.035 mmol) in THF (20 mL) was stirred well under N_2. To this, aq Na_2CO_3 solution (0.18 g in 5 mL water) was added and the reaction mixture was heated 60 °C for 12 h. The solid was filtered off and the solvent was completely removed under vacuum. Extraction of the crude product with EtOAc (2×10 mL) followed by column chromatography purification (5% EtOAc/hexane) afforded product **18** (0.16 g, 55%) as a colorless solid; mp 138 °C. [Found: C, 68.9; H, 5.2; N, 3.4; S, 7.4. $C_{24}H_{21}NO_4S$ requires C, 68.72; H, 5.05; N, 3.34; S, 7.64%.] R_f (20% EtOAc/hexane) 0.81; ν_{max} (KBr) 1187, 1378, 1705 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.23–8.18 (2H, m, ArH), 7.43 (3H, d, *J* 6.9 Hz, ArH), 7.28–7.19 (7H, m, ArH), 7.40–7.36 (2H, m, ArH), 5.08 (2H, s, CH_2Ph), 4.41 (2H, q, *J* 7.2 Hz, OCH_2), 1.39 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 164.6, 146.3, 138.4, 137.8, 135.9, 133.9, 129.1, 128.6, 127.3, 126.6, 126.2, 125.2, 124.5, 122.1, 114.6, 113.3, 60.6, 31.8, 14.3.

4.4.25. Dimethyl 4-hydroxy-1-phenyl-9-(phenylsulfonyl)-9H-carbazole-2,3-dicarboxylate (**19**)

To a stirred solution of compound **16** (0.2 g, 0.47 mmol) in THF at −78 °C under N_2, 1 M solution of LDA (0.15 g, 1.43 mmol) in dry THF (10 mL) was added slowly and stirred. After 15 min, DMAD (0.11 mL, 0.95 mmol) was added and stirring was continued at the same temperature for 2 h. Then, the reaction mixture was quenched with cold aq NH_4Cl (15 mL) and extracted with EtOAc (2×10 mL). Removal of solvent followed by column chromatographic purification afforded carbazole **19** (0.1 g, 40%) as a colorless solid; mp 222 °C. [Found: C, 65.5; H, 4.32; N, 2.8; S, 6.4. $C_{28}H_{21}NO_7S$ requires C, 65.23; H, 4.11; N, 2.72; S, 6.22%.] R_f (20% EtOAc/hexane) 0.21; ν_{max} (KBr) 1182, 1365, 1715, 3386 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 11.93 (1H, s, OH), 8.28 (1H, d, *J* 7.2 Hz, ArH), 8.13 (1H, d, *J* 8.1 Hz, ArH), 7.49–7.35 (4H, m, ArH), 7.32–7.14 (8H, m, ArH), 3.94 (3H, s, OCH_3), 3.51 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 169.6, 167.4, 157.6, 143.4, 140.9, 137.3, 136.9, 135.9, 133.2, 130.7, 128.6, 127.6, 127.4, 127.2, 126.5, 126.0, 125.5, 123.5, 123.2, 117.9, 105.9, 53.1, 52.0.

4.5. A representative procedure for the preparation of indolylmethyl ester from indolyl bromides (procedure D)

4.5.1. Ethyl 5-methoxy-2-(2-methoxy-2-oxoethyl)-1-phenylsulfonyl-1H-indole-3-carboxylate (**20a**)

To a stirred suspension of bromo compound **2a** (0.5 g, 1.10 mmol), $PdCl_2(PPh_3)_2$ (0.07 g, 0.11 mmol), and K_2CO_3 (0.23 g, 1.6 mmol) in dry THF (5 mL) dry CO gas was purged for 5 min. Then,

dry MeOH (2 mL) was added into the reaction mixture and allowed to stir under CO atmosphere at room temperature for 12 h. The reaction mixture was diluted with water (30 mL) and extracted with EtOAc (2×15 mL). The combined organic layer was dried (Na_2SO_4) and the removal of solvent followed by column chromatographic purification (10% EtOAc/hexane) afforded **20a** (0.24 g, 50%) as a colorless solid; mp 118 °C. [Found: C, 58.6; H, 5.0; N, 3.1; S, 7.1. $C_{21}H_{21}NO_7S$ requires C, 58.46; H, 4.91; N, 3.25; S, 7.43%.] R_f (20% EtOAc/hexane) 0.68; ν_{max} (KBr) 1175, 1375, 1707, 1740 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.93 (1H, d, *J* 6.9 Hz, ArH), 7.87 (2H, d, *J* 5.5 Hz, ArH), 7.55–7.59 (2H, m, ArH), 7.45 (2H, t, *J* 8.0 Hz,), 6.92–6.95 (1H, m, ArH), 4.69 (2H, s, CH_2CO), 4.39 (2H, q, *J* 7.2 Hz, OCH_2), 3.85 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 1.43 (3H, t, *J* 7.1 Hz, CH_3); δ_C (100.6 MHz, $CDCl_3$) 167.4, 165.2, 159.6, 134.2, 129.4, 126.8, 125.8, 124.5, 124.4, 121.7, 119.4, 115.1, 114.5, 104.4, 60.7, 55.6, 52.3, 33.1, 14.3; *m*/*z* (EI) 432 (45, M^++1), 431 (11%, M^+).

*4.5.2. Ethyl 2-(2-methoxy-2-oxoethyl)-1-(phenylsulfonyl)-1H-indole-3-carboxylate (**20b**)*

Yield: 0.25 g (57%); colorless solid; mp 174 °C. [Found: C, 60.0; H, 4.9; N, 3.7; S, 8.2. $C_{20}H_{19}NO_6S$ requires C, 59.84; H, 4.77; N, 3.49; S, 7.99%.] R_f (20% EtOAc/hexane) 0.84; ν_{max} (KBr) 1168, 1370, 1715, 1738 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.27 (1H, d, *J* 8.4 Hz, ArH), 7.95 (1H, d, *J* 7.5 Hz, ArH), 7.84 (2H, d, *J* 7.5 Hz, ArH), 7.55 (1H, t, *J* 7.5 Hz, ArH), 7.44 (2H, t, *J* 7.5 Hz, ArH), 7.24–7.35 (2H, m, ArH), 4.75 (2H, s, CH_2CO), 4.08 (3H, s, OCH_3), 3.58 (2H, q, *J* 7.1 Hz, OCH_2), 1.03 (3H, t, *J* 7.1 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 169.9, 164.5, 140.4, 138.6, 135.7, 134.3, 129.4, 126.9, 126.8, 125.4, 124.5, 122.2, 114.2, 113.7, 60.8, 52.3, 32.9, 14.3.

4.6. A representative procedure for the preparation of carbazole 26a from indolylmethyl acetate 20a (procedure F)

*4.6.1. Dimethyl 4-hydroxy-9-(phenylsulfonyl)-9H-carbazole-1,3-dicarboxylate (**21a**)*

To a stirred suspension of *t*-BuOK (0.13 g, 1.16 mmol) in dry THF (10 mL) at 0 °C, indolylmethyl acetate **20b** (0.40 g, 1.00 mmol) in THF (5 mL) was slowly added. After 5 min, methyl propiolate (0.11 g, 1.30 mmol) was added at the same temperature and stirring was continued for 2 h. Then it was quenched with saturated ammonium chloride solution (10 mL), extracted with EtOAc (2×20 mL), and the extracts were combined and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (5% EtOAc/hexane) afforded **21a** (0.2 g, 45%) as a colorless solid; mp 130 °C. [Found: C, 60.3; H, 3.7; N, 3.3; S, 7.0. $C_{25}H_{21}NO_{10}S$ requires C, 60.13; H, 3.90; N, 3.19; S, 7.30%.] R_f (15% EtOAc/hexane) 0.48; ν_{max} (KBr) 1178, 1365, 1712, 3391 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 12.62 (1H, s, OH), 7.93–7.78 (3H, m, ArH), 7.69 (2H, d, *J* 7.3 Hz, ArH), 7.72 (1H, s, ArH), 7.62 (2H, d, *J* 7.2 Hz, ArH), 7.45–7.21 (2H, m, ArH), 4.05 (3H, s, OCH_3), 4.03 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 163.8, 163.5, 157.2, 148.7, 146.5, 136.7, 134.5, 129.2, 127.1, 126.7, 125.7, 125.5, 124.7, 123.5, 117.4, 115.2, 114.1, 53.4, 53.2; *m*/*z* (EI) 441 (7, M^++2), 439 (26%, M^+).

*4.6.2. Trimethyl 4-hydroxy-9-(phenylsulfonyl)-9H-carbazole-1,2,3-tricarboxylate (**21b**)*

Yield: 0.25 g (50%); colorless solid; mp 128 °C. [Found: C, 57.7; H, 4.0; N, 3.1; S, 6.3. $C_{24}H_{19}NO_9S$ requires C, 57.94; H, 3.85; N, 2.82; S, 6.45%.] R_f (15% EtOAc/hexane) 0.38; ν_{max} (KBr) 1178, 1365, 1704, 3328 cm^{-1}; δ_H (400 MHz, $CDCl_3$), 13.2 (1H, s, OH), 8.18 (2H, d, *J* 8.1 Hz, ArH), 7.68 (2H, t, *J* 7.2 Hz, ArH), 7.51–7.34 (3H, m, ArH), 7.12 (2H, d, *J* 7.1 Hz, ArH), 4.05 (3H, s, OCH_3), 4.03 (3H, s, OCH_3), 4.00 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 163.8, 163.6, 163.3, 148.9, 148.7, 145.2, 136.7, 134.5, 128.9, 128.7, 126.9, 126.6, 125.5, 125.3, 124.7, 123.5, 117.4, 115.2, 114.6, 52.9, 52.5, 52.3; *m*/*z* (EI) 499 (21, M^++2), 497 (35, M^++1), 326 (54%).

*4.6.3. Dimethyl 4-hydroxy-6-methoxy-9-(phenylsulfonyl)-9H-carbazole-1,3-dicarboxylate (**21c**)*

Yield: 0.25 g (52%); colorless solid; mp 168 °C. [Found: C, 58.6; H, 4.3; N, 2.73; S, 7.0. $C_{23}H_{19}NO_8S$ requires C, 58.84; H, 4.08; N, 2.98; S, 6.83%.] R_f (15% EtOAc/hexane) 0.37; ν_{max} (KBr) 1169, 1370, 1705, 3331 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 13.21 (1H, s, OH), 8.16 (2H, d, *J* 8.1 Hz, ArH), 7.77 (1H, s, ArH), 7.98–7.82 (2H, m, ArH), 7.67–7.36 (4H, m, ArH), 4.04 (3H, s, OCH_3), 4.03 (3H, s, OCH_3), 3.91(3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 164.2, 163.8, 157.6, 148.7, 146.5, 137.4, 136.7, 134.5, 128.8, 127.4, 127.1, 126.8, 125.7, 123.6, 118.2, 116.7, 115.2, 114.5, 55.8, 53.4, 53.2; *m*/*z* (EI) 471 (35, M^++2), 469 (17, M^+), 328 (49%).

*4.6.4. Trimethyl 4-hydroxy-6-methoxy-9-(phenylsulfonyl)-9H-carbazole-1,2,3-tricarboxylate (**21d**)*

Yield: 0.28 g (52%); colorless solid; mp 142 °C. [Found: C, 57.2; H, 3.8; N, 2.4; S, 6.2. $C_{25}H_{21}NO_{10}S$ requires C, 56.92; H, 4.01; N, 2.66; S, 6.08%.] R_f (15% EtOAc/hexane) 0.33; ν_{max} (KBr) 1180, 1368, 1709, 3328 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 12.5 (1H, s OH), 8.20 (1H, d, *J* 8.2 Hz, ArH), 7.73 (2H, d, *J* 7.3 Hz, ArH), 7.61 (2H, t, *J* 7.3 Hz, ArH), 7.43–7.11 (3H, m, ArH), 4.05 (3H, s, OCH_3), 4.01 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 3.87 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 163.8, 163.6, 163.3, 157.2, 148.7, 145.2, 136.7, 134.5, 128.9, 128.8, 127.1, 126.6, 125.7, 125.6, 124.7, 123.5, 117.4, 115.2, 113.9, 55.6, 53.1, 52.8, 52.3; *m*/*z* (EI) 529 (11, M^++2), 527 (35, M^+), 356 (18%).

4.7. A representative procedure for the preparation of indolylmethyl cyanide 21a from bromide 2a (procedure E)

*4.7.1. Ethyl 2-(cyanomethyl)-5-methoxy-1-(phenylsulfonyl)-1H-indole-3-carboxylate (**22a**)*

To a stirred suspension of NaCN (60 mg, 1.22 mmol) in DMSO (5 mL) and THF (15 mL) at 0 °C, bromo compound **2a** (0.45 g, 1.0 mmol) was added and stirred at same temperature for 1 h. The reaction mixture was then diluted with water (20 mL). The crude product was extracted with EtOAc (2×15 mL) and washed water (2×20 mL) and dried (Na_2SO_4). Evaporation of solvent, followed by crystallization from EtOH afforded cyano compound **22a** (0.23 g, 58%) as a colorless solid; mp 164 °C. [Found: C, 60.5; H, 4.8; N, 7.2; S, 7.8. $C_{20}H_{18}N_2O_5S$ requires C, 60.29; H, 4.55; N, 7.03; S, 8.05%.] R_f (20% EtOAc/hexane) 0.44; ν_{max} (KBr) 1176, 1382, 1709, 2222 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.49 (3H, t, *J* 7.2 Hz, CH_3), 3.86 (3H, s, OCH_3), 4.47 (2H, q, *J* 7.2 Hz, OCH_2), 4.82 (2H, s, CH_2CN), 7.02 (1H, dd, *J* 2.4, 6.6 Hz, ArH), 7.52–7.47 (2H, m, ArH), 7.64–7.59 (2H, m, ArH), 7.97–7.94 (2H, m, ArH), 8.03 (1H, d, *J* 9.3 Hz, ArH); δ_C (75.5 MHz, $CDCl_3$) 163.7, 157.4, 137.7, 134.9, 134.8, 130.3, 129.6, 127.7, 126.9, 115.8, 115.6, 115.4, 114.3, 104.4, 61.3, 55.6, 16.4, 14.3.

*4.7.2. Ethyl 2-(cyanomethyl)-1-(phenylsulfonyl)-1H-indole-3-carboxylate (**22b**)*

Yield: 0.23 g (53%); brown solid; mp 102 °C. [C, 62.1; H, 4.5; N, 7.5; S, 8.9. $C_{19}H_{16}N_2O_4S$ requires C, 61.94; N, 7.60; S, 8.70H, 4.38%.] R_f (20% EtOAc/hexane) 0.47; ν_{max} (KBr) 1176, 1383, 1709, 2222 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.47 (3H, t, *J* 7.1 Hz, CH_3), 4.47 (2H, q, *J* 7.1 Hz, CH_2), 4.86 (2H, s, CH_2CN), 7.38 (2H, quint, *J* 8.4 Hz, ArH), 7.49 (2H, t, *J* 7.5 Hz, ArH), 7.61 (1H, t, *J* 7.2 Hz, ArH), 7.98 (2H, d, *J* 7.8 Hz, ArH), 8.12 (2H, d, *J* 8.7 Hz, ArH); δ_C (75.5 MHz, $CDCl_3$) 163.8, 137.6, 134.9, 134.8, 130.5, 129.7, 127.1, 126.3, 125.0, 122.5, 115.8, 115.4, 114.4, 61.3, 16.3, 14.3.

*4.7.3. 2-[3-Acetyl-1-(1-phenylsulfonyl)-1H-indol-2yl]acetonitrile (**22c**)*

Yield: 0.24 g (55%); brown solid; mp 150 °C. [Found: C, 64.0; H, 4.3; N, 8.1; S, 9.9. $C_{18}H_{14}N_2O_3S$ requires C, 63.89; H, 4.17; N, 8.28; S, 9.48%.] R_f (20% EtOAc/hexane) 0.42; ν_{max} (KBr) 1172, 1365, 1696, 2221 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.19–8.17 (1H, m, ArH), 7.53–7.39

(4H, m, ArH), 7.65–7.58 (1H, m, ArH), 7.87–7.84 (1H, m, ArH), 8.02–7.97 (2H, m, ArH), 4.75 (2H, s, CH_2CN), 2.73 (3H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 195.5, 137.7, 135.9, 134.9, 133.8, 129.7, 127.1, 126.1, 125.9, 125.0, 121.9, 121.1, 115.9, 114.9, 32.3.

4.7.4. Ethyl 3′-[1-(phenylsulfonyl)-2-cyanomethylindol-3-yl]-acrylate (**22d**)

Yield: 0.18 g (42%); brown solid; mp 210 °C. [Found: C, 64.1; H, 4.8; N, 6.9; S, 8.3. $C_{21}H_{18}N_2O_4S$ requires C, 63.94; H, 4.60; N, 7.10; S, 8.13%.] R_f (20% EtOAc/hexane) 0.35; ν_{max} (KBr) 1164, 1381, 1720, 2245 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.22 (1H, d, *J* 8.2 Hz, ArH) 7.82–7.71 (2H, m, ArH), 7.38–7.10 (7H, m, ArH), 6.57 (1H, d, *J* 15.9 Hz, CH=CH), 4.78 (2H, s, CH_2CN), 4.18 (2H, q, J 7.1 Hz, OCH_2), 1.27 (3H, t, *J* 7.1 Hz, CH_3); *m*/*z* (EI) 394 (5, M^+), 348 (25), 207 (68%).

4.7.5. Methyl 1-cyano-4-hydroxy-9-(phenylsulfonyl)-9H-carbazole-3-carboxylate (**27a**)

Yield: 0.18 g (45%); colorless solid; mp 167 °C. [Found: C, 62.3; H, 3.6; N, 6.6; S, 8.1. $C_{21}H_{14}N_2S$ requires C, 62.06; H, 3.47; N, 6.89; S, 7.89%.] R_f (15% EtOAc/hexane) 0.50; ν_{max} (KBr) 1178, 1365, 2222, 3328 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 12.5 (1H, s, OH), 8.35–8.25 (4H, m, ArH), 7.79 (1H, d, *J* 7.8 Hz, ArH), 7.59–7.55 (2H, m, ArH), 7.49–7.42 (3H, m, ArH), 4.06 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 166.2, 159.8, 141.5, 140.0, 136.7, 136.6, 135.4, 134.4, 131.3, 129.2, 128.7, 127.1, 126.5, 125.3, 123.5, 116.7, 115.1, 114.2, 53.2; *m*/*z* (EI) 406 (56, M^+), 408 (21, M^++2), 380 (39%).

4.7.6. Dimethyl 1-cyano-4-hydroxy-9-(phenylsulfonyl)-9H-carbazole-2,3-dicarboxylate (**27b**)

Yield: 0.16 g (32%); colorless solid; mp 222 °C. [Found: C, 60.4; H, 4.18; N, 5.3; S, 6.28. $C_{25}H_{22}N_2S$ requires C, 60.72; H, 4.48; N, 5.66; S, 6.48%.] R_f (15% EtOAc/hexane) 0.38; ν_{max} (KBr) 1172, 1378, 1712, 2221, 3349 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 12.38 (1H, s, OH), 8.33–8.27 (2H, m, ArH), 7.87 (2H, d, *J* 7.6 Hz, ArH), 7.56 (2H, q, *J* 7.2 Hz, ArH), 7.44 (3H, quint, *J* 7.8 Hz, ArH), 4.04 (3H, s, OCH_3), 4.01 (3H, s, OCH_3); δ_C (75.5 MHz, $CDCl_3$) 168.5, 166.6, 160.9, 142.1, 140.9, 139.5, 137.6, 134.5, 129.3, 128.4, 127.1, 125.5, 123.9, 123.7, 117.8, 115.9, 114.8, 106.0, 91.8, 53.7.

4.7.7. Methyl 1-cyano-4-hydroxy-6-methoxy-9-(phenylsulfonyl)-9H-carbazole-3-carboxylate (**27c**)

Yield: 0.25 g (62%); colorless solid; mp 198 °C. [Found: C, 60.7; H, 3.9; N, 6.2; S, 7.1. $C_{25}H_{21}NO_{10}S$ requires C, 60.54; H, 3.70; N, 6.42; S, 7.35%.] R_f (20% EtOAc/hexane) 0.48; ν_{max} (KBr) 1178, 1365, 1712, 2222, 3328 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 12.38 (1H, s, OH), 7.82 (1H, s, ArH), 7.78–7.71 (2H, m, ArH), 7.57 (3H, d, *J* 7.2 Hz, ArH), 7.48–7.37 (m, 3H, ArH), 4.03 (3H, s, OCH_3), 3.89 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 163.2, 157.2, 148.7, 146.5, 136.9, 136.5, 135.2, 134.7, 132.3, 129.2, 126.8, 126.7, 125.1, 123.7, 122.7, 117.4, 114.9, 114.3, 55.4, 53.2.

4.7.8. Dimethyl 1-cyano-4-hydroxy-6-methoxy-9-(phenylsulfonyl)-9H-carbazole-2,3-dicarboxylate (**27d**)

Yield: 0.19 g (40%); colorless solid; mp 198 °C. [Found: C, 58.5; H, 3.4; N, 5.4; S, 6.3. $C_{24}H_{18}N_2O_8S$ requires C, 58.30; H, 3.67; N, 5.67; S, 6.48%.] R_f (20% EtOAc/hexane) 0.38; ν_{max} (KBr) 1176, 1382, 1709, 2221, 3342 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 12.52 (1H, s, OH), 8.17 (1H, d, *J* 8.8 Hz, ArH), 7.78 (3H, d, *J* 8.0 Hz, ArH), 7.53 (1H, d, *J* 7.2 Hz, ArH), 7.41–7.37 (2H, m, ArH), 7.15 (1H, d, *J* 7.2 Hz, ArH), 4.05 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 3.90 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 168.3, 166.6, 160.9, 157.5, 142.2, 140.9, 139.7, 137.9, 134.8, 129.6, 126.9, 125.6, 123.9, 123.7, 117.8, 115.8, 114.7, 105.9, 55.6, 53.7, 53.6.

4.7.9. Dimethyl 1-cyano-4-methyl-9-(phenylsulfonyl)-9H-carbazole-2,3-dicarboxylate (**27e**)

Yield: 0.16 g (36%); colorless solid; mp 164 °C. [Found: C, 62.5; H, 4.0; N, 6.2; S, 6.7. $C_{24}H_{18}N_2O_6S$ requires C, 62.33; H, 3.92; N, 6.06; S, 6.93%.] R_f (15% EtOAc/hexane) 0.43 ν_{max} (KBr) 1172, 1365, 1706, 2221 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.24 (1H, d, *J* 8.4 Hz, ArH), 7.99 (1H, d, *J* 8.1 Hz, ArH), 7.59–7.56 (3H, m, ArH), 7.51–7.41 (2H, m, ArH), 7.31 (2H, t, *J* 7.8 Hz, ArH), 4.04 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 2.80 (3H, s, CH_3); δ_C (75.5 MHz, $CDCl_3$) 167.1, 165.8, 141.5, 140.0, 136.9, 136.7, 135.3, 134.3, 131.3, 130.9, 129.0, 128.9, 127.0, 126.3, 125.8, 123.4, 117.8, 114.7, 100.1, 53.5, 53.1, 18.3.

4.7.10. Ethyl-3-(dicyanomethyl)-1H-indole-2-carboxylate (**23**)

Yield: 0.13 g (45%); brown solid; mp 164 °C. [Found: C, 66.6; H, 4.6; N, 16.3. $C_{14}H_{11}N_3O_2$ requires C, 66.40; H, 4.38; N, 16.59%.] R_f (20% EtOAc/hexane) 0.60; ν_{max} (KBr) 1687, 2222, 3234 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.13 (1H, s, NH), 7.91 (1H, d, *J* 9.0 Hz, ArH), 7.44–7.26 (3H, m, ArH), 6.35 (1H, s, CHCN), 4.44 (2H, q, *J* 7.2 Hz, OCH_2), 1.41 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75.5 MHz, $CDCl_3$) 159.4, 134.4, 126.0, 123.8, 123.1, 121.6, 118.8, 111.5, 110.5, 105.2, 61.2, 17.7, 13.2.

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