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One-pot synthesis of 2-sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles via cyclization of 1-isothiocyanato-2-[sulfinyl(or sulfonyl)methyl] benzenes with sodium hydride

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ABSTRACT

An efficient one-pot method for the synthesis of 2-sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles from 1-isothiocyanato-2-[sulfinyl(or sulfonyl)methyl]benzenes, derived from *N*-[2-(chloromethyl)phenyl]formamide by an easy four-step sequence, has been developed. The products are formed via cyclization of the precursor isothiocyanates using 2 equiv of sodium hydride followed by S- and/or N-alkylation of the resulting 1-sodio-2-sodiosulfanyl-1*H*-indole intermediates.

1. Introduction

2-Sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles are of potentially biological importance[1] and some of them have been found in nature.[2] However, their general synthesis has been relatively unexplored so far,[3] although quite a number of methods for the preparation of 1*H*-indole derivatives have been reported.[4] 1-Methyl-2-methylsulfanyl-3-methylsulfinyl-1*H*-indole has been prepared by the acid-catalyzed reaction of 1-methyl-1*H*-indole with 4-(methylsulfanyl)morpholine followed by oxidation of the resulting 1-methyl-2,3-bis(methylsulfanyl)-1*H*-indole.[3] In this paper, we wish to describe the results of our investigation, which provide a convenient method to prepare 3-sulfinyl(or sulfonyl)-1*H*-indoles carrying a 2-alkylsulfanyl substituent **7** and those carrying 2-alkylsulfanyl and 1-alkyl substituents **8** and **9** utilizing cyclization of 1-isothiocyanato-2-[sulfinyl(or sulfonyl)methyl]benzenes **5** using 2 equiv of sodium hydride followed by S- and/or N-alkylation of the resulting 1-sodio-2-sodiosulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indole intermediates **6** under mild reaction conditions. In addition, we present an application of this procedure to the synthesis of tricyclic compounds including the 3-sulfinyl(or sulfonyl)-1*H*-indole moiety **10**.

2. Results and discussion

We initiated our investigation by preparing 2-(sulfinyl(or sulfonyl)methyl)phenyl isothiocyanates **5**, the key precursors for our synthesis. The synthesis of these compounds was readily accomplished from *N*-[2-(chloromethyl)phenyl]formamide (**1**) according to the process illustrated in Scheme 1. Substitution of the chloro group with sodium thiolates in DMF provided *N*-[2-(sulfanyl methyl)phenyl]formamides **2** in excellent yields, which were then oxidized with 1 or 2 equiv of sodium metaperiodate in aqueous methanol to furnish *N*-[2-(sulfinyl(or sulfonyl)methyl)phenyl] formamides **3** in good yields. These sulfinyl or sulfonyl formamides **3** were dehydrated with phosphorous oxychloride in the presence of triethylamine in THF to afford 1-isocyano-2-[sulfinyl(or sulfinyl) methyl]benzene **4** in good yields. Finally, these isocyano sulfoxides or sulfones were converted into the corresponding isothiocyanates **5** on treatment with sulfur in the presence of a catalytic amount of selenium and excess triethylamine under Fujiwara's conditions.[5]

First, we tried to prepare 2-methylsulfanyl-3-phenylsulfinyl-1*H*-indole (**7a**) from 1-isothiocyanato-2-[(phenylsulfinyl)methyl]benzene (**5a**) and iodomethane. Thus, compound **5a** was treated with 1 equiv of sodium hydride in THF/DMSO (2:1, v/v) at 0 °C. Vigorous evolution of hydrogen gas revealed the deprotonation from the benzyl hydrogen of **5a**, and TLC analyses on silica gel after 5 min showed complete consumption of the starting materials. However, after addition of iodomethane and the subsequent usual aqueous

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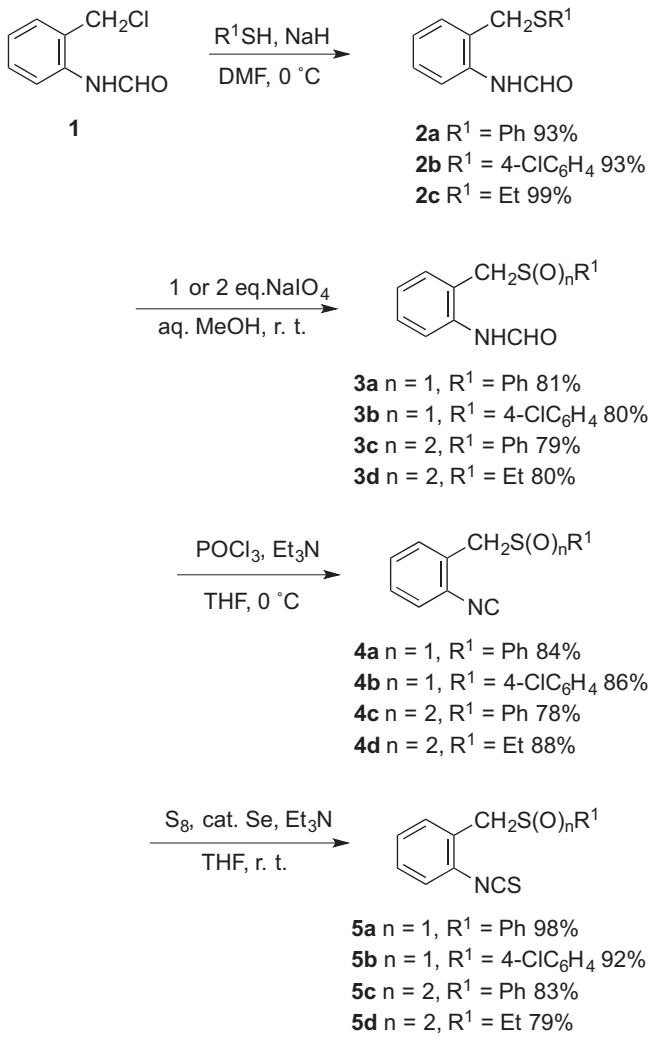
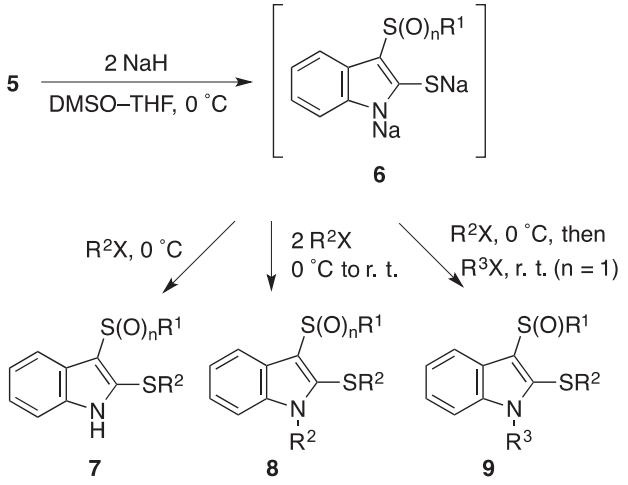


Scheme 1.

workup, a rather complicated mixture, which proved to contain a small amount of **7a** on the basis of its ^{1}H NMR spectrum. So, as shown in Scheme 2, compound **5a** was treated with 2 equiv of sodium hydride to form 3-phenylsulfinyl-1-sodio-2-sodiosulfanyl-1*H*-indole **6a** (n=1, R^1=Ph), then an equivalent of iodomethane was added. The reaction proceeded immediately at 0 °C and the desired product **7a** was obtained in 78% yield. Using four isothiocyanato sulfoxides and sulfones including **5a**, and three haloalkanes including iodomethane, the other five 2-alkylsulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles **7b**–**f** could be obtained under the same reaction conditions in comparable yields to that of **7a**, as summarized in Table 1. The use of DMSO as a co-solvent had a detrimental effect upon the smooth progress of the cyclization forming a pyrrole ring and the subsequent alkylation. The reactions without DMSO both of the cyclization and the alkylation proceeded sluggishly and uncleanly to result in the formation of considerably complex mixtures of products, from which only low yields (<10%) of the desired products contaminated with structurally undefined products were isolated.



Scheme 2.

Table 1
Preparation of 2-sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles **7**

Entry	**5**	R^{2}X	**7**	Yield[a]/%
1	**5a** (n=1, R^1=Ph)	MeI	**7a**	78
2	**5a**	EtI	**7b**	75
3	**5a**	BnBr	**7c**	71
4	**5b** (n=1, R^1=4-ClC$_6$H$_4$)	MeI	**7d**	71
5	**5c** (n=2, R^1=Ph)	MeI	**7e**	73
6	**5d** (n=2, R^1=Et)	EtI	**7f**	83

[a] Isolated yields.

When 2 M amounts of haloalkanes were added after generation of 1-sodio-2-sodiosulfanyl-1*H*-indole intermediates **6**, 1-alkyl-2-alkylsulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles **8** were obtained in good yields in general, as summarized in Table 2. However, after addition of haloalkanes, the reaction temperature was raised to room temperature, because N-alkylation did proceed very sluggishly at 0 °C. It is important to note that only iodomethane was usable in the reactions using **6c** and **6d** (n=2). For example, the reaction of **6d** with 2 equiv of iodoethane resulted in the exclusive formation of only *S*-ethylated product **7f**. This result implies that the reactivity of 2-ethylsulfanyl-3-ethylsulfonyl-1-sodio-1*H*-indole intermediate is not enough efficient to achieve ethylation with iodoethane.

Table 2
Preparation of 1-alkyl-2-sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles **8**

Entry	**5**	R^{2}X	**8**	Yield/%[a]
1	**5a** (n=1, R^1=Ph)	MeI	**8a**	86
2	**5a**	EtI	**8b**	80
3	**5a**	BnBr	**8c**	68
4	**5b** (n=1, R^1=4-ClC$_6$H$_4$)	MeI	**8d**	74
5	**5b**	CH$_2$=CHCH$_2$Br	**8e**	77
6	**5c** (n=2, R^1=Ph)	MeI	**8f**	66
7	**5d** (n=2, R^1=Et)	MeI	**8g**	78

[a] Isolated yields.

Different haloalkanes proved to be usable in S-alkylation and N-alkylation of **6a** and **6b** (n=1). The reaction of these dianionic intermediates with an equivalent each of the first haloalkane followed by second electrophile afforded 1-alkyl-2-alkylsulfanyl-3-sulfinyl-1*H*-indoles **9** in fair yields, as summarized in Table 3. For example, after intermediate **6a** was first treated with iodomethane at 0 °C, (bromomethyl)benzene was added at the same temperature and temperature was raised to room temperature to provide 2-methylsulfanyl-1-phenylmethyl-3-phenylsulfinyl-1*H*-indole (**9a**) (entry 1). The second electrophile was not limited to only haloalkanes, as benzoyl chloride worked equally well. Unfortunately,

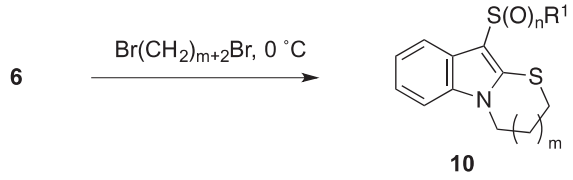
Table 3
Preparation of 1-substituted 2-sulfanyl-3-sulfinyl-1*H*-indoles **9**

Entry	**5**	R^2X	R^3X	**9**	Yield[a]/%
1	**5a** (n=1, R^1=Ph)	MeI	BnBr	**9a**	57
2	**5a**	BnBr	MeI	**9b**	76
3	**5a**	MeI	BzCl	**9c**	57
4	**5b** (n=1, R^1=4-ClC_6H_4)	MeI	BnBr	**9d**	64
5	**5b**	CH_2=$CHCH_2Br$	MeI	**9e**	63

[a] Isolated yields.

however, similar attempts via **6c** and **6d** (n=2) all resulted in failure; the second alkylation at the 1-position did not occur at all.

In order to demonstrate the utility of the present procedure by preparing tricyclic compounds with the 3-sulfinyl(or sulfonyl)-1*H*-indole moiety **10**, 1-sodium-2-sodiosulfanyl-1*H*-indole intermediates **6** were reacted with 1,3-dibromopropane and 1,2-dibromoethane. Not only S-alkylation but also N-alkylation of **6a** and **6b** with these dibromides smoothly occurred at 0 °C to afford the corresponding tricyclic compounds **10a**–**c** as illustrated in Scheme 3. The yields of these products were good as can be seen from Table 4, entries 1–3. The reactions of **6c** and **6d** with 1,3-dibromopropane also proceeded under the same conditions to afford **10d** and **10e**, respectively, but in somewhat lower yields (entries 4 and 5) than those of **10a**–**c**.



Scheme 3.

Table 4
Preparation of tricyclic 1*H*-indole derivatives **10**

Entry	**5**	m	**10**	Yield/%[a]
1	**5a** (n=1, R^1=Ph)	1	**10a**	83
2	**5b** (n=1, R^1=4-ClC_6H_4)	1	**10b**	72
3	**5b**	0	**10c**	75
4	**5c** (n=2, R^1=Ph)	1	**10d**	50
5	**5d** (n=2, R^1=Et)	1	**10e**	64

[a] Isolated yields.

In conclusion, we have demonstrated that 1-isocyanato-2-sulfinyl(or sulfonyl)methylbenzenes can serve as versatile precursors for the preparation of 2-sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles, which are hard to obtain by previous methods. Since the method employs readily available starting materials and is operationally simple, it may be of value in organic synthesis.

3. Experimental

3.1. General

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum65 FTIR spectrophotometer. ^{1}H NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or JEOL LA400FTNMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz or JEOL LA400FTNMR spectrometer operating at 100 MHz. Low-resolution MS spectra (EI, 70 eV) were measured by a JEOL JMS AX505 HA spectrometer. High-resolution MS spectra (DART, positive) were measured by a Thermo Scientific Exactive spectrometer. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

3.2. Starting materials

N-[2-(Chloromethyl)phenyl]formamide (**1**) was prepared accor ding to the reported method.[6] All other chemicals used in this study were commercially available.

*3.2.1. N-[2-(Sulfanylmethyl)phenyl]formamides **2**.* These compounds were prepared by treating **1** with sodium thiolates, generated from thiols and NaH, in DMF at 0 °C.[7]

*3.2.1.1. N-[2-(Phenylsulfanylmethyl)phenyl]formamide (**2a**).* A colorless oil; R_f 0.16 (AcOEt/hexane 1:3); IR (neat) 3275, 1681 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.08 and 4.10 (2s, combined 2H), 7.02–7.31 (m, 9H), 7.82–8.54 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.62, 36.81, 121.84, 124.24, 125.43, 126.08, 127.45, 127.57, 128.59, 128.89, 129.03, 129.06, 130.68, 131.13, 131.25, 131.60, 134.88, 135.32, 159.20, 162.73. Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.76. Found: C, 69.03; H, 5.45; N, 5.71.

*3.2.1.2. N-{2-[(4-Chlorophenyl)sulfanylmethyl]phenyl}formamide (**2b**).* A white solid; mp 92–93 °C (hexane/CH_2Cl_2); IR (KBr) 3292, 1693, 1661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05 and 4.06 (2s, combined 2H), 7.00–7.13 (m, 2H), 7.18–7.32 (m, 6H), 7.83–8.56 (m, 2H). Anal. Calcd for $C_{14}H_{12}ClNOS$: C, 60.54; H, 4.35; N, 5.04. Found: C, 60.31; H, 4.35; N, 4.75.

*3.2.1.3. N-[2-(Ethylsulfanylmethyl)phenyl]formamide (**2c**).* A pale-yellow oil; R_f 0.32 (AcOEt/hexane 1:2); IR (neat) 3307, 1688 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 and 1.24 (2t, J=7.4 Hz each, combined 3H), 2.41 and 2.43 (2q, J=7.4 Hz each, combined 2H), 3.75 and 3.76 (2s, combined 2H), 7.08–7.33 (m, 4H), 8.00–8.69 (m, 2H). Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.50; H, 5.71; N, 7.17. Found: C, 61.49; H, 5.82; N, 7.06.

*3.2.2. N-[2-(Sulfinylmethyl)phenyl]formamides **3a** and **3b**.* These compounds were prepared by treating **2a** and **2b** with an equimolar amount of $NaIO_4$ in aqueous MeOH at room temperature.[8]

*3.2.2.1. N-[2-(Phenylsulfinylmethyl)phenyl]formamide (**3a**).* A pale-yellow oil; R_f 0.40 (1:4 THF/hexane); IR (neat) 3256, 1684, 1020 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 and 3.90 (2d, J=17.5 Hz each, combined 1H), 4.34 and 4.40 (2d, J=17.5 Hz each, combined 1H), 6.58–7.29 (m, 4H), 7.44–7.51 (m, 5H), 7.86–9.81 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.51, 59.07, 120.96, 124.09, 125.29, 125.37, 126.38, 126.45, 129.22, 130.22, 131.51, 131.65, 131.77, 132.27, 133.72, 136.04, 140.61, 145.09, 159.70, 163.11. Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.66; H, 5.08; N, 5.31.

*3.2.2.2. N-{2-[(4-Chlorophenyl)sulfinylmethyl]phenyl}formamide (**3b**).* A reddish-white solid; mp 119–121 °C (hexane/Et_2O); IR (KBr) 3260, 1690, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 and 3.85 (2d, J=13.7 Hz each, combined 1H), 4.40 and 4.42 (2d, J=13.7 Hz, each, combined 1H), 6.56 and 6.67 (2dd, J=7.8, 1.5 Hz each, combined 1H), 6.96 and 7.06 (2ddd, J=7.8, 7.3, 1.5 Hz each, combined 1H), 7.21–7.39 (m, 4H), 7.45 (d, J=8.3 Hz, 2H), 7.86–9.71 (m, 2H). Anal. Calcd for $C_{14}H_{12}ClNO_2S$: C, 57.24; H, 4.12; N, 4.77. Found: C, 57.03; H, 4.16; N, 4.75.

*3.2.3. N-[2-(Sulfonylmethyl)phenyl]formamides **3c** and **3d**.* These compounds were prepared by treating **2a** and **2c** with two equimolar amounts of $NaIO_4$ in aqueous MeOH at room temperature.[8]

*3.2.3.1. N-[2-(Phenylsulfonylmethyl)phenyl]formamide (**3c**).* A white solid; mp 119–121 °C (hexane/Et_2O); IR (KBr) 3333, 1673, 1304 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.38 and 4.40 (2s, combined 2H), 6.67–7.85 (m, 9H), 8.41–8.69 (m, 2H). Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09. Found: C, 60.92; H, 4.52; N, 5.01.

*3.2.3.2. N-[2-(Ethylsulfonylmethyl)phenyl]formamide (**3d**).* A reddish-white solid; mp 91–93 °C (hexane/Et_2O); IR (KBr) 3341, 1692, 1299 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.42 and 1.44 (2t, J=7.8 Hz each, combined 3H), 3.02 and 3.06 (2q, J=7.8 Hz each, combined 2H), 4.315 and 4.324 (2s, combined 2H), 7.23–7.46 (m, 4H), 7.86–8.71 (m, 2H). Anal. Calcd for $C_{10}H_{13}NO_3S$: C, 52.85; H, 5.77; N, 6.16. Found: C, 52.62; H, 5.82; N, 6.02.

*3.2.4. 1-Isocyano-2-(sulfinyl(or sulfonyl)methyl)benzene **4**.* These compounds were prepared by treating **3** with $POCl_3/Et_3N$ in THF at 0 °C.[9]

*3.2.4.1. 1-Isocyano-2-(phenylsulfinylmethyl)benzene (**4a**).* A beige solid; mp 94–96 °C (hexane); IR (KBr) 2124, 1032 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.14 (d, J=12.8 Hz, 1H), 4.24 (d, J=12.8 Hz, 1H), 7.32–7.41 (m, 4H), 7.47–7.52 (m, 5H). Anal. Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80. Found: C, 69.50; H, 4.68; N, 5.51.

*3.2.4.2. 1-[(4-Chlorophenyl)sulfinylmethyl]]-2-isocyanobenzene (**4b**).* A yellow solid; mp 93–94 °C (hexane); IR (KBr) 2121, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (d, J=13.2 Hz, 1H), 4.23 (d, J=13.2 Hz, 1H), 7.34–7.46 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.13, 125.71, 126.09, 126.94, 129.38, 129.47, 129.57, 132.01, 135.16, 137.89, 141.66, 156.61. Anal. Calcd for $C_{14}H_{10}ClNOS$: C, 60.98; H, 3.66; N, 5.08. Found: C, 60.88; H, 3.85; N, 5.08.

*3.2.4.3. 1-Isocyano-2-(phenylsulfonylmethyl)benzene (**4c**).* A pale-orange solid; mp 135–137 °C (hexane); IR (KBr) 2124, 1310 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.51 (s, 2H), 7.27 (d, J=7.8 Hz, 1H), 7.39 (ddd, J=7.8, 7.3, 1.4 Hz, 1H), 7.45 (ddd, J=7.8, 7.3, 1.4 Hz, 1H), 7.51 (dd, J=7.8, 7.3 Hz, 2H), 7.57 (dd, J=7.8, 1.4 Hz, 1H), 7.66 (tt, J=7.3, 1.4 Hz, 1H), 7.70 (dd, J=7.8, 1.4 Hz, 2H). Anal. Calcd for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44. Found: C, 65.24; H, 4.39; N, 5.29.

*3.2.4.4. 1-(Ethylsulfonylmethyl)-2-isocyanobenzene (**4d**).* A reddish-white solid; mp 77–78 °C (hexane/CH_2Cl_2); IR (KBr) 2124, 1316 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, J=7.3 Hz, 3H), 3.00 (q, J=7.3 Hz, 2H), 4.43 (s, 2H), 7.44–7.51 (m, 3H), 7.65 (d, J=8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.27, 54.46, 56.83, 126.47, 127.42, 130.04, 132.08, 132.41, 133.19, 164.42. Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.30; N, 6.69. Found: C, 57.10; H, 5.29; N, 6.68.

*3.2.5. 1-Isothiocyanato-2-(sulfinyl(or sulfinyl)methyl)benzene **5**.* These compounds were prepared by treating **4** with S_8 in the presence of a catalytic amount of Se in THF containing excess Et_3N at room temperature.[5]

*3.2.5.1. 1-Isothiocyanato-2-(phenylsulfinylmethyl)benzene (**5a**).* A pale-orange solid; mp 100–102 °C (hexane/CH_2Cl_2); IR (KBr) 2189, 2133, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, J=13.2 Hz, 1H), 4.15 (d, J=13.2 Hz, 1H), 7.17 (d, J=8.3 Hz, 1H), 7.21–7.26 (m, 2H), 7.31 (ddd, J=8.3, 7.3, 2.9 Hz, 1H), 7.44–7.50 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.25, 124.17, 125.59, 126.98, 127.17, 128.97 (2C), 129.62, 131.57, 132.28 (2C), 142.26. Anal. Calcd for $C_{14}H_{11}NOS_2$: C, 61.51; H, 4.06; N, 5.12. Found: C, 61.36; H, 4.11; N, 5.02.

*3.2.5.2. 1-[(4-Chlorophenyl)sulfinylmethyl]]-2-isothiocyanatobenzene (**5b**).* A yellow solid; mp 64–66 °C (hexane/CH_2Cl_2); IR (KBr) 2188, 2097, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.11 (d, J=12.6 Hz, 1H), 4.13 (d, J=12.6 Hz, 1H), 7.19 (d, J=7.4 Hz, 1H), 7.23 (t, J=7.4 Hz, 1H), 7.26 (d, J=7.4 Hz, 1H), 7.33 (td, J=7.4, 1.7 Hz, 1H), 7.36 (d, J=8.6 Hz, 2H), 7.44 (d, J=8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.16, 125.03, 125.64, 127.11, 127.23, 129.31, 129.83, 131.23, 132.35, 134.07, 137.86, 140.79. Anal. Calcd for $C_{14}H_{10}ClNOS_2$: C, 54.63; H, 3.27; N, 4.55. Found: C, 54.56; H, 3.32; N, 4.41.

*3.2.5.3. 1-Isothiocyanato-2-(phenylsulfonylmethyl)benzene (**5c**).* An orange solid; mp 119–120 °C (hexane/CH_2Cl_2); IR (KBr) 2189, 2116, 1319 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.43 (s, 2H), 7.13 (dd, J=8.0, 1.1 Hz, 1H), 7.28 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.33 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.45 (dd, J=8.0, 1.1 Hz, 1H), 7.50 (t, J=8.0 Hz, 2H), 7.64 (t, J=8.0 Hz, 1H), 7.68 (d, J=8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 58.49, 124.00, 127.33, 127.44, 128.56, 129.05, 130.28 (2C), 132.54, 134.27, 134.78, 138.83. Anal. Calcd for $C_{14}H_{11}NO_2S_2$: C, 58.11; H, 3.83; N, 4.84. Found: C, 58.00; H, 3.84; N, 4.72.

*3.2.5.4. 1-(Ethylsulfonylmethyl)-2-isothiocyanatobenzene (**5d**).* A pale-yellow solid; mp 108–110 °C (hexane/CH_2Cl_2); IR (KBr) 2192, 2134, 1312 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, J=7.3 Hz, 3H), 2.98 (q, J=7.3 Hz, 2H), 4.35 (s, 2H), 7.30–7.43 (m, 3H), 7.53 (dd, J=7.8, 1.5 Hz, 1H). Anal. Calcd for $C_{10}H_{11}NO_2S_2$: C, 49.77; H, 4.59; N, 5.80. Found: C, 49.81; H, 4.38; N, 5.59.

3.3. Typical procedure for the preparation of 2-alkylsulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles 7

*3.3.1. 2-Methylsulfanyl-3-phenylsulfinyl-1H-indole (**7a**).* To a stirred solution of **5a** (0.15 mg, 0.55 mmol) in THF/DMSO (3 mL, 2:1 v/v) at 0 °C was added NaH (60% in mineral oil; 48 mg, 1.2 mmol) in several portions. After 5 min, MeI (78 mg, 0.55 mmol) was added and stirring was continued for an additional 10 min at the same temperature before saturated aqueous NH_4Cl (10 mL) was added. The mixture was extracted with AcOEt (3×10 mL) and the combined extracts were washed with water (4×10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel (AcOEt/hexane 1:1) to give **7a** (0.12 g, 78%); a white solid; mp 101–102 °C (decomp.) (hexane/CH_2Cl_2); IR (KBr) 3152, 983 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 6.92 (dd, J=8.0, 7.4 Hz, 1H), 7.08 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.22 (d, J=8.0 Hz, 1H), 7.29 (d, J=8.0 Hz, 1H), 7.41 (t, J=7.4 Hz, 1H), 7.47 (dd, J=8.0, 7.4 Hz, 2H), 7.71 (d, J=8.0 Hz, 2H), 9.94 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.56, 111.73, 116.51, 118.32, 120.83, 122.77, 123.96, 124.18, 129.04, 129.87, 137.26, 137.93, 144.73; MS m/z 287 (M^+, 14), 239 (100). Anal. Calcd for $C_{15}H_{13}NOS_2$: C, 62.69; H, 4.56; N, 4.87. Found: C, 62.58; H, 4.59; N, 5.50.

*3.3.2. 2-Ethylsulfanyl-3-phenylsulfinyl-1H-indole (**7b**).* A white solid; mp 90–93 °C (decomp.) (hexane/CH_2Cl_2); IR (KBr) 3139, 1007 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.27 (t, J=7.3 Hz, 3H), 3.11–3.16 (m, 2H), 6.90 (dd, J=7.8, 7.3 Hz, 1H), 7.08–7.14 (m, 2H), 7.38 (d, J=8.3 Hz, 1H), 7.44 (t, J=7.3 Hz, 1H), 7.52 (dd, J=7.8, 7.3 Hz, 2H), 7.59 (d, J=7.8 Hz, 2H), 11.08 (br, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.99, 29.34, 111.87, 118.51, 119.06, 120.82, 123.09, 123.82, 124.22, 129.06, 129.89, 135.51, 137.33, 144.77; MS m/z 301 (M^+, 33), 253 (100). Anal. Calcd for $C_{16}H_{15}NOS_2$: C, 63.75; H, 5.02; N, 4.65. Found: C, 63.68; H, 5.08; N, 4.60.

*3.3.3. 2-(Phenylmethyl)sulfanyl-3-phenylsulfinyl-1H-indole (**7c**).* A white solid; mp 94–96 °C (decomp.) (hexane/CH_2Cl_2); IR (KBr)

3141, 1008 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 4.36 (d, J=12.7 Hz, 1H), 4.45 (d, 12.7 Hz, 1H), 6.85 (dd, J=7.8, 7.3 Hz, 1H), 6.99 (d, J=8.3 Hz, 1H), 7.11 (t, J=7.3 Hz, 1H), 7.15–7.18 (m, 2H), 7.27 (s, 5H), 7.38–7.41 (m, 4H), 11.09 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.05, 111.94, 118.66, 119.65, 120.87, 123.33, 123.66, 124.17, 127.50, 128.67, 128.83, 128.94, 129.78, 134.92, 137.40, 137.54, 144.53; MS m/z 363 (M^+, 58), 315 (100). Anal. Calcd for $C_{21}H_{17}NOS_2$: C, 69.39; H, 4.71; N, 3.85. Found: C, 69.24; H, 4.85; N, 3.64.

*3.3.4. 3-[(4-Chlorophenyl)sulfinyl]-2-methylsulfanyl-1H-indole (**7d**).* A yellow solid; mp 124–125 °C (hexane/CH_2Cl_2); IR (KBr) 3141, 1007 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 6.95 (dd, J=8.0, 7.4 Hz, 1H), 7.10 (dd, J=8.0, 7.4 Hz, 1H), 7.22 (d, J=8.0 Hz, 1H), 7.28 (dd, J=8.0 Hz, 1H), 7.44 (d, J=8.6 Hz, 2H), 7.63 (d, J=8.6 Hz, 2H), 9.91 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.82, 109.71, 111.59, 119.05, 121.79, 123.68, 124.29, 126.28, 129.17, 136.18, 137.09, 138.22, 142.30. HRMS calcd for $C_{15}H_{13}ClNOS_2$: M+H, 322.0127. Found: m/z 322.0128. Anal. Calcd for $C_{15}H_{12}ClNOS_2$: C, 55.98; H, 3.76; N, 4.35. Found: C, 55.74; H, 3.87; N, 4.10.

*3.3.5. 2-Methylsulfanyl-3-phenylsulfonyl-1H-indole (**7e**).* An orange solid; mp 172–173 °C (hexane/CH_2Cl_2); IR (KBr) 3318, 1143 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.56 (s, 3H), 7.17 (t, J=7.4 Hz, 1H), 7.22 (t, J=7.4 Hz, 1H), 7.33 (d, J=7.4 Hz, 1H), 7.44 (t, J=7.4 Hz, 2H), 7.49 (t, J=7.4 Hz, 1H), 8.05 (d, J=7.4 Hz, 1H), 8.07 (d, J=7.4 Hz, 2H), 8.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.29, 110.98, 113.48, 119.04, 122.59, 123.29, 125.92, 126.34, 128.90, 132.66, 135.58, 139.39, 143.35. HRMS calcd for $C_{15}H_{14}NO_2S_2$: M+H, 304.0466. Found: m/z 304.0459. Anal. Calcd for $C_{15}H_{13}NO_2S_2$: C, 59.38; H, 4.32; N, 4.62. Found: C, 59.22; H, 4.57; N, 4.40.

*3.3.6. 2-Ethylsulfanyl-3-ethylsulfonyl-1H-indole (**7f**).* A pale-yellow solid; mp 106–107 °C (hexane/CH_2Cl_2); IR (KBr) 3272, 1125 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.25 (t, J=7.4 Hz, 3H), 1.31 (t, J=7.4 Hz, 3H), 3.08 (q, J=7.4 Hz, 2H), 3.30 (q, J=7.4 Hz, 2H), 7.20–7.24 (m, 2H), 7.44 (dd, J=9.2, 2.3 Hz, 1H), 7.99 (dd, J=9.2, 2.8 Hz, 1H), 9.45 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.44, 14.51, 28.96, 51.00, 111.24, 112.20, 119.26, 122.45, 123.56, 126.47, 135.62, 137.48. HRMS calcd for $C_{12}H_{16}NO_2S_2$: M+H, 270.0622. Found: m/z 270.0617. Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 53.50; H, 5.61; N, 5.20. Found: C, 53.33; H, 5.80; N, 5.17.

3.4. Typical procedure for the preparation of 1-alkyl-2-alkyl sulfanyl-3-sulfinyl(or sulfonyl)-1*H*-indoles 8

*3.4.1. 1-Methyl-2-methylsulfanyl-3-phenylsulfinyl-1H-indole (**8a**).* To a stirred solution of **5a** (0.15 mg, 0.55 mmol) in THF/DMSO (3 mL, 2:1 v/v) at 0 °C was added NaH (60% in mineral oil; 48 mg, 1.2 mmol) in several portions. After 5 min, MeI (0.20 g, 1.4 mmol) was added and the temperature was raised to room temperature. Stirring was continued for 1 h before saturated aqueous NH_4Cl (10 mL) was added. The mixture was worked up in a manner similar to that described for **7a**. The residual solid was purified by recrystallization to give **8a** (0.14 g, 86%). A pale-yellow solid; mp 116–118 °C (decomp.) (hexane/CH_2Cl_2); IR (KBr) 1450, 1032 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.51 (s, 3H), 3.91 (s, 3H), 7.02 (t, J=8.0, 7.4 Hz, 1H), 7.24 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.32 (d, J=8.0 Hz, 1H), 7.38–7.42 (m, 2H), 7.45 (dd, J=8.0, 7.4 Hz, 2H), 7.72 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.86, 30.34, 110.26, 120.07, 121.50, 121.78, 123.69, 123.99, 124.77, 128.81, 129.79, 137.73, 138.32, 144.63. HRMS calcd for $C_{16}H_{16}NOS_2$: M+H, 302.0673. Found: m/z 302.0665. Anal. Calcd for $C_{16}H_{15}NOS_2$: C, 63.75; H, 5.02; N, 4.65. Found: C, 63.74; H, 5.09; N, 4.49.

*3.4.2. 1-Ethyl-2-ethylsulfanyl-3-phenylsulfinyl-1H-indole (**8b**).* A pale-yellow solid; mp 97–98 °C (hexane/CH_2Cl_2); IR (KBr) 1436, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J=7.3 Hz, 3H), 1.41 (t, J=7.3 Hz, 3H), 2.97–3.06 (m, 2H), 4.40–4.50 (m, 2H), 6.98 (t, J=7.8 Hz, 1H), 7.21 (td, J=7.8, 1.0 Hz, 1H), 7.32 (d, J=7.8 Hz, 1H), 7.34 (d, J=7.8 Hz, 1H), 7.40 (t, J=7.3 Hz, 1H), 7.45 (dd, J=7.8, 7.3 Hz, 2H), 7.70 (d, J=7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.93, 15.28, 32.76, 38.99, 110.41, 120.17, 121.60, 122.27, 123.82, 123.99, 124.86, 128.80, 129.74, 135.96, 137.23, 144.53; MS m/z 329 (M^+, 67), 281 (100). Anal. Calcd for $C_{18}H_{19}NOS_2$: C, 65.62; H, 5.81; N, 4.25. Found: C, 65.52; H, 5.79; N, 4.23.

*3.4.3. 1-Phenylmethyl-2-(phenylmethyl)sulfanyl-3-phenylsulfinyl-1H-indole (**8c**).* A pale-yellow oil; R_f 0.40 (AcOEt/hexane 1:2); IR (neat) 1444, 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 2H), 5.24 (d, J=16.6 Hz, 1H), 5.33 (d, J=16.6 Hz, 1H), 6.96–7.00 (m, 3H), 7.10–7.16 (m, 4H), 7.21–7.33 (m, 7H), 7.41–7.48 (m, 3H), 7.63 (dd, J=8.3, 2.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.10, 47.15, 111.08, 120.22, 121.90, 123.55, 123.95, 124.29, 124.87 (2C), 126.26, 127.69, 127.79, 128.70, 128.85, 129.01, 129.85, 135.96, 136.42, 136.68, 138.03, 144.31; MS m/z 453 (M^+, 58), 405 (100). Anal. Calcd for $C_{28}H_{23}NOS_2$: C, 74.14; H, 5.11; N, 3.09. Found: C, 73.91; H, 5.15; N, 3.07.

*3.4.4. 3-[(4-Chlorophenyl)sulfinyl]-1-methyl-2-methylsulfanyl-1H-indole (**8d**).* A pale-yellow solid; mp 111–112 °C (hexane/CH_2Cl_2); IR (KBr) 1453, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.52 (s, 3H), 3.92 (s, 3H), 7.05 (dd, J=8.0, 6.9 Hz, 1H), 7.26 (dd, J=8.0, 6.9 Hz, 1H), 7.34 (d, J=8.0 Hz, 1H), 7.39 (d, J=8.0 Hz, 1H), 7.42 (d, J=8.6 Hz, 2H), 7.64 (d, J=8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.91, 30.41, 110.40, 119.90, 121.00, 122.00, 123.54, 124.17, 126.22, 129.08, 136.05, 137.88, 138.27, 143.39. HRMS calcd for $C_{16}H_{15}ClNOS_2$: M+H, 336.0283. Found: m/z 336.0282. Anal. Calcd for $C_{16}H_{14}ClNOS_2$: C, 57.22; H, 4.20; N, 4.17. Found: C, 57.09; H, 4.28; N, 4.17.

*3.4.5. 3-[(4-Chlorophenyl)sulfinyl]-1-(prop-2-enyl)-2-(prop-2-enyl) sulfanyl-1H-indole (**8e**).* A pale-yellow solid; mp 71–72 °C (hexane/CH_2Cl_2); IR (KBr) 1637, 1446, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.53–3.61 (m, 2H), 4.94–5.11 (m, 5H), 5.23 (d, J=10.3 Hz, 1H), 5.83–6.01 (m, 2H), 7.04 (dd, J=8.0, 7.4 Hz, 1H), 7.22 (dd, J=8.0, 7.4 Hz, 1H), 7.30 (d, J=8.0 Hz, 1H), 7.38 (d, J=8.0 Hz, 1H), 7.43 (d, J=8.6 Hz, 2H), 7.65 (d, J=8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.06, 46.36, 111.11, 117.37, 119.40, 120.02, 121.99, 122.92, 123.60, 124.26, 126.29 (2C), 129.08, 132.47, 135.18, 135.99, 137.89, 143.22. HRMS calcd for $C_{20}H_{19}ClNOS_2$: M+H, 388.0596. Found: m/z 388.0597. Anal. Calcd for $C_{20}H_{18}ClNOS_2$: C, 61.92; H, 4.68; N, 3.61. Found: C, 61.82; H, 4.66; N, 3.50.

*3.4.6. 1-Methyl-2-methylsulfanyl-3-phenylsulfonyl-1H-indole (**8f**).* An orange solid; mp 179–180 °C (hexane/CH_2Cl_2); IR (KBr) 1447, 1149 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 3.87 (s, 3H), 7.30–7.36 (m, 3H), 7.42 (t, J=7.4 Hz, 2H), 7.48 (tt, J=7.4, 1.1 Hz, 1H), 8.10 (dd, J=7.4, 1.1 Hz, 2H), 8.36 (dd, J=8.6, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.56, 30.33, 110.29, 119.24, 120.77, 122.79, 124.27, 125.14, 126.82, 128.69, 132.44, 136.84, 136.97, 143.78. HRMS calcd for $C_{16}H_{16}NO_2S_2$: M+H, 318.0622. Found: m/z 318.0635. Anal. Calcd for $C_{16}H_{15}NO_2S_2$: C, 60.54; H, 4.76; N, 4.41. Found: C, 60.26; H, 4.80; N, 4.39.

*3.4.7. 3-Ethylsulfonyl-1-methyl-2-methylsulfanyl-1H-indole (**8g**).* A white solid; mp 82–83 °C (hexane/CH_2Cl_2); IR (KBr) 1451, 1144 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J=7.3 Hz, 3H), 2.52 (s, 3H), 3.35 (q, J=7.3 Hz, 2H), 3.97 (s, 3H), 7.29 (dd, J=8.3, 7.3, 1.0 Hz, 1H), 7.35–7.40 (m, 2H), 8.20 (dd, J=8.3, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.46, 21.14, 30.42, 51.21, 110.27, 116.51, 120.78, 122.73, 124.32, 125.84, 136.79, 136.81. HRMS calcd for $C_{12}H_{16}NO_2S_2$: M+H, 270.0622. Found: m/z 270.0619. Anal. Calcd

for $C_{12}H_{15}NO_2S_2$: C, 53.50; H, 5.61; N, 5.20. Found: C, 53.45; H, 5.77; N, 5.13.

3.5. Typical procedure for the preparation of 1-alkyl-2-alkyl sulfanyl-3-sulfinyl-1*H*-indoles 9

*3.5.1. 2-Methylsulfanyl-1-phenylmethyl-3-phenylsulfinyl-1H-indole (**9a**).* Compound **5a** (0.18 g, 0.66 mmol) was treated with NaH (60% in mineral oil; 58 mg, 1.5 mmol) as described for the preparation of **8a**. After 5 min, MeI (93 mg, 0.66 mmol) was added and the temperature was raised to room temperature. Then, BnBr (0.11 g, 0.66 mmol) was added and stirring was continued for 1 h before the same workup as described for the preparation of **8a**. The crude product was purified by column chromatography on silica gel (AcOEt/hexane 1:1) to give **9a** (0.14 g, 57%). A white solid; mp 122–123 °C (hexane/CH_2Cl_2); IR (KBr) 1445, 1035 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.36 (s, 3H), 5.58 (d, J=16.6 Hz, 1H), 5.67 (d, J=16.6 Hz, 1H), 7.01 (t, J=7.4 Hz, 1H), 7.06 (d, J=7.4 Hz, 2H), 7.16 (dd, J=8.0, 7.4 Hz, 1H), 7.22 (d, J=8.0 Hz, 1H), 7.27–7.31 (m, 3H), 7.40–7.44 (m, 2H), 7.48 (t, J=7.4 Hz, 2H), 7.74 (d, J=7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.35, 47.42, 111.01, 120.17, 121.91, 122.32, 123.94, 124.26, 124.75, 126.17, 127.67, 128.87 (2C), 129.87, 136.61, 137.81, 137.99, 144.50. HRMS calcd for $C_{22}H_{20}NOS_2$: M+H, 378.0986. Found: m/z 378.0981. Anal. Calcd for $C_{22}H_{19}NOS_2$: C, 69.99; H, 5.07; N, 3.71. Found: C, 69.97; H, 5.28; N, 3.70.

*3.5.2. 1-Methyl-2-(phenylmethyl)sulfanyl-3-phenylsulfinyl-1H-indole (**9b**).* A pale-yellow solid; mp 114–115 °C (hexane/CH_2Cl_2); IR (KBr) 1454, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.41 (s, 3H), 4.06 (d, J=12.6 Hz, 1H), 4.16 (d, J=12.6 Hz, 1H), 6.99 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.12 (dd, J=8.0, 1.1 Hz, 2H), 7.18–7.24 (m, 5H), 7.29 (dd, J=8.0, 1.1 Hz, 1H), 7.38–7.45 (m, 3H), 7.64 (dd, J=8.0, 1.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.00, 43.05, 110.34, 120.02, 121.73, 122.68, 123.69, 123.96, 123.83, 124.83, 127.68, 128.66, 128.77, 129.79, 135.71, 136.88, 138.20, 144.39. HRMS calcd for $C_{22}H_{20}NOS_2$: M+H, 378.0986. Found: m/z 377.0975. Anal. Calcd for $C_{22}H_{19}NOS_2$: C, 69.99; H, 5.07; N, 3.71. Found: C, 69.91; H, 5.03; N, 3.43.

*3.5.3. [2-(Methylsulfanyl)-3-(phenylsulfinyl)-1H-indol-1-yl](phenyl) methanone (**9c**).* A yellow viscous oil; R_f 0.80 (THF/hexane 1:1); IR (neat) 1703, 1439, 1042 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.56 (s, 3H), 7.07–7.15 (m, 3H), 7.45 (t, J=7.4 Hz, 1H), 7.51 (dd, J=7.8, 7.4 Hz, 4H), 7.65 (dd, J=7.4, 1.7 Hz, 1H), 7.68 (t, J=7.4 Hz, 1H), 7.73 (d, J=7.8 Hz, 2H), 7.79 (d, J=7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.78, 113.59, 120.37, 123.46, 124.25, 124.64, 125.04, 128.30, 129.00, 129.14, 130.36, 130.42, 133.86, 134.31, 136.88, 137.97, 143.91, 158.91; MS m/z 391 (M^+, 19), 270 (47), 105 (100). Anal. Calcd for $C_{22}H_{17}NO_2S_2$: C, 67.49; H, 4.38; N, 3.58. Found: C, 67.20; H, 4.46; N, 3.38.

*3.5.4. 3-[(4-Chlorophenyl)sulfinyl]-2-methylsulfanyl-1-(phenylmethyl)-1H-indole (**9d**).* A pale-purple solid; mp 118–120 °C (hexane/CH_2Cl_2); IR (KBr) IR 1446, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.35 (s, 3H), 5.58 (d, J=16.6 Hz, 1H), 5.67 (d, J=16.6 Hz, 1H), 7.03–7.06 (m, 3H), 7.17–7.31 (m, 6H), 7.44 (d, J=8.0 Hz, 2H), 7.67 (d, J=8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.39, 47.48, 111.16, 120.00, 121.78, 122.13, 123.78, 124.45, 126.17, 126.20, 127.75, 128.93, 129.17, 136.09, 136.48, 137.94, 138.03, 143.12. HRMS calcd for $C_{22}H_{19}ClNOS_2$: M+H, 412.0596. Found: m/z 412.0598. Anal. Calcd for $C_{22}H_{18}ClNOS_2$: C, 64.14; H, 4.40; N, 3.40. Found: C, 63.87; H, 4.61; N, 3.31.

*3.5.5. 3-[(4-Chlorophenyl)sulfinyl]-1-methyl-2-[(prop-2-enyl)sulfanyl]-1H-indole (**9e**).* A yellow solid; mp 113–115 °C (hexane/CH_2Cl_2); IR (KBr) 1634, 1451, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.53 (dd, J=13.2, 6.9 Hz, 1H), 3.59 (dd, J=13.2, 7.4 Hz, 1H), 3.90 (s, 3H), 5.03 (dd, J=16.6, 1.1 Hz, 1H), 5.06 (d, J=9.7 Hz, 1H), 5.88–5.97 (m, 1H), 7.05 (dd, J=8.0, 7.4 Hz, 1H), 7.26 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.33 (d, J=8.0 Hz, 1H), 7.36 (d, J=8.0 Hz, 1H), 7.42 (d, J=8.6 Hz, 2H), 7.65 (d, J=8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.70, 41.01, 110.45, 119.25, 119.91, 121.95, 122.38, 123.46, 124.17, 126.30, 129.04, 132.49, 135.60, 135.95, 138.40, 143.27. HRMS calcd for $C_{18}H_{17}ClNOS_2$: M+H, 362.0440. Found: m/z 362.0441. Anal. Calcd for $C_{18}H_{16}ClNOS_2$: C, 59.74; H, 4.46; N, 3.87. Found: C, 59.61; H, 4.52; N, 3.80.

3.6. General procedure for the preparation of tricyclic indole derivatives 10

*3.6.1. 10-(Phenylsulfinyl)-3,4-dihydro-2H-[1,3]thiazino[3,2-a]indole (**10a**).* Compound **5a** (0.18 g, 0.64 mmol) was treated with NaH (60% in mineral oil; 52 mg, 1.3 mmol) as described for the preparation of **8a**. After 5 min, $Br(CH_2)_3Br$ (0.13 g, 0.64 mmol) was added and the temperature was raised to room temperature. Stirring was continued for 10 min before the same workup as described for the preparation of **8a**. The residual crude product was purified by recrystallization from hexane/CH_2Cl_2 to give **10a** (0.17 g, 83%). A pale-yellow solid; mp 118–120 °C; IR (KBr) 1434, 1031 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.42–2.48 (m, 2H), 3.13 (t, J=5.7 Hz, 2H), 4.06–4.11 (m, 1H), 4.15–4.20 (m, 1H), 6.99 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.10 (ddd, J=8.0, 7.4, 1.1 Hz, 1H), 7.18 (d, J=8.0 Hz, 1H), 7.28 (d, J=8.0 Hz, 1H), 7.39 (tt, J=7.4, 1.1 Hz, 1H), 7.44 (dd, J=8.0, 7.4 Hz, 2H), 7.70 (dd, J=8.0, 1.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.42, 24.97, 41.98, 108.36, 111.16, 118.41, 121.81, 121.89, 124.30, 124.83, 128.73, 129.67, 136.63, 138.26, 144.26. HRMS calcd for $C_{17}H_{16}NOS_2$: M+H, 314.0673. Found: m/z 314.0673. Anal. Calcd for $C_{17}H_{15}NOS_2$: C, 65.14; H, 4.82; N, 4.47. Found: C, 65.13; H, 5.02; N, 4.42.

*3.6.2. 10-[(4-Chlorophenyl)sulfinyl]-3,4-dihydro-2H-[1,3]thiazino [3,2-a]indole (**10b**).* A yellow solid; mp 134–135 °C (hexane/CH_2Cl_2); IR (KBr) 1433, 1032 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.45–2.48 (m, 2H), 3.14 (t, J=5.7 Hz, 2H), 4.08–4.13 (m, 1H), 4.17–4.22 (m, 1H), 7.03 (dd, J=8.0, 7.4 Hz, 1H), 7.13 (dd, J=8.0, 7.4 Hz, 1H), 7.20 (d, J=8.0 Hz, 1H), 7.27 (d, J=8.0 Hz, 1H), 7.42 (d, J=8.6 Hz, 2H), 7.63 (d, J=8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.38, 24.97, 42.00, 108.49, 110.60, 118.24, 122.00, 122.10, 124.15, 126.30, 128.99, 135.85, 136.92, 138.26, 142.85. HRMS calcd for $C_{17}H_{15}ClNOS_2$: M+H, 348.0283. Found: m/z 348.0280. Anal. Calcd for $C_{17}H_{14}ClNOS_2$: C, 58.69; H, 4.06; N, 4.03. Found: C, 58.70; H, 4.12; N, 3.93.

*3.6.3. 9-[(4-Chlorophenyl)sulfinyl]-2,3-dihydrothiazolo[3,2-a]indole (**10c**).* A white solid; mp 133–134 °C (hexane/CH_2Cl_2); IR (KBr) 1452, 1036 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.79–3.87 (m, 2H), 4.26–4.29 (m, 2H), 7.05 (t, J=7.4 Hz, 1H), 7.11–7.16 (m, 2H), 7.35 (d, J=7.4 Hz, 1H), 7.43 (d, J=8.6 Hz, 2H), 7.64 (d, J=8.6 Hz, 2H): ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.87, 45.51, 107.68, 109.68, 118.48, 121.66, 122.30, 126.31, 129.12, 129.56, 134.61, 136.20, 142.66, 145.93. HRMS calcd for $C_{16}H_{13}ClNOS_2$: M+H, 334.0127. Found: m/z 334.0126. Anal. Calcd for $C_{16}H_{12}ClNOS_2$: C, 57.56; H, 3.62; N, 4.20. Found: C, 57.47; H, 3.35; N, 3.96.

*3.6.4. 10-(Phenylsulfonyl)-3,4-dihydro-2H-[1,3]thiazino[3,2-a]indole (**10d**).* A white solid; mp 218–219 °C (hexane/CH_2Cl_2); IR (KBr) 1426, 1151 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.40–2.45 (m, 2H), 3.08 (t, J=5.7 Hz, 2H), 4.13 (t, J=5.7 Hz, 2H), 7.18–7.25 (m, 3H), 7.43 (dd, J=8.0, 7.4 Hz, 2H), 7.48 (t, J=7.4 Hz, 1H), 8.02 (d, J=8.0 Hz, 1H), 8.06 (d, J=8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.66, 24.63, 42.14, 108.34, 109.33, 118.23, 122.07, 122.64, 124.87, 126.12, 128.78, 132.34, 137.40, 137.54, 143.73. HRMS calcd for $C_{17}H_{16}NO_2S_2$: M+H,

330.0632. Found: *m*/*z* 330.0619. Anal. Calcd for $C_{17}H_{15}NO_2S_2$: C, 61.98; H, 4.59; N, 4.25. Found: C, 61.95; H, 4.73; N, 4.20.

*3.6.5. 10-(Ethylsulfonyl)-3,4-dihydro-2H-[1,3]thiazino[3,2-a]indole (**10e**).* A white solid; mp 144–146 °C (hexane/CH_2Cl_2); IR (KBr) 1432, 1144 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, *J*=7.4 Hz, 3H), 2.43–2.47 (m, 2H), 3.09 (t, *J*=5.7 Hz, 2H), 3.18 (q, *J*=7.4 Hz, 2H), 4.18 (dd, *J*=6.3, 5.7 Hz, 2H), 7.18–7.24 (m, 3H), 7.89 (dd, *J*=6.3, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.53, 22.80, 24.63, 42.21, 50.74, 106.44, 108.34, 118.25, 122.05, 122.58, 125.56, 137.29, 137.82. HRMS calcd for $C_{13}H_{16}NO_2S_2$: M+H, 282.0622. Found: *m*/*z* 282.0619. Anal. Calcd for $C_{13}H_{15}NO_2S_2$: C, 55.49; H, 5.37; N, 4.98. Found: C, 55.49; H, 5.54; N, 4.97.

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