One-Pot Synthesis of 3-Acyl-2-(alkylsulfanyl)indoles and 2-(Alkylsulfanyl)-indole-3-carboxylates from (2-Isocyanophenyl)methyl Ketones or (2-Isocyanophenyl)acetates

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Abstract: An efficient method has been developed for the preparation of 3-acyl-2-(alkylsulfanyl)indoles and ethyl 2-(alkylsulfanyl)indole-3-carboxylates under mild conditions. (2-Isocyanophenyl)methyl ketones and ethyl 2-(2-isocyanophenyl)acetates were converted into the corresponding isothiocyanates by treatment with sulfur in the presence of a catalytic amount of selenium. The isothiocyanates were then treated with two equivalents of sodium hydride to form reactive disodium indol-1-ide-2-thiolate intermediates that were treated with alkyl halides to give the desired indole derivatives in a one-pot process. The method has been applied to the construction of three new indole-fused tricyclic structures by using α,ω-dibromoalkanes.

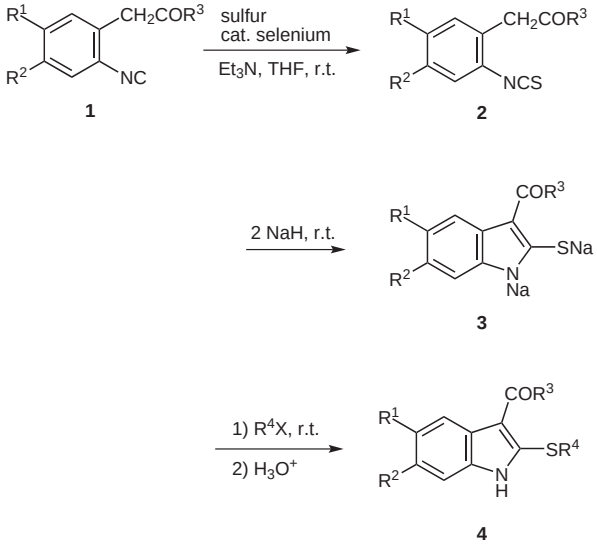
Key words: indoles, isocyanides, isothiocyanates, ring closure, sodium hydride

Because the indole family is one of the most important classes of heterocycles, many chemists have developed new methods for the preparations of indoles.[1] 2-(Lithiomethyl)phenyl isocyanides have been used as intermediates for the syntheses of indole derivatives by reactions with various electrophiles, followed by cyclization.[2,3] (2-Isocyanophenyl)methyl ketones, prepared by treating 2-(lithiomethyl)phenyl isocyanide with carboxylic esters, can be transformed into 3-acylindoles and 2-substituted indoles.[3b] Methyl 2-(2-isocyanophenyl)acetates, which are prepared by treating 2-(lithiomethyl)phenyl isocyanides with chloroformates,[3a] can be transformed into indole-3-carboxylates.[2,4]

In this report, we describe a simple one-pot procedure for the synthesis of 3-acyl-2-(alkylsulfanyl)indoles and ethyl 2-(alkylsulfanyl)indole-3-carboxylates from (2-isocyanophenyl)methyl ketones and ethyl 2-(2-isocyanophenyl)acetates, respectively, through cyclization of the corresponding isothiocyanates using sodium hydride followed by selective S-alkylation of the resulting disodium indol-1-ide-2-thiolates. We also found that the use of α,ω-dibromoalkanes provided a means for the construction of three new indole-containing fused tricyclic structures.

2-(Alkylsulfanyl)indoles are medicinally important heterocyclic compounds.[5] Although several methods for their preparation have recently been reported,[6] these are of limited general applicability. For example, Gonda and coworkers showed that treatment of (2-isothiocyanatobenzyl)(triphenyl)phosphonium bromides or (2-isothiocyanatobenzyl)pyridinium bromides with an appropriate base gave triphenyl(2-thiolatoindol-3-yl)phosphonium[7a] or (2-thiolatoindol-3-yl)pyridinium derivatives, respectively.[7b] These thiolates were subjected to S-alkylation by several alkyl halides.

The 2-(alkylsulfanyl)indole derivatives **4** were synthesized by the process shown in Scheme 1. (2-Isocyanophenyl)methyl ketones or ethyl 2-(2-isocyanophenyl)acetates **1** were converted into the corresponding isothiocyanates **2** by treatment with sulfur in the presence of a catalytic amount of selenium in tetrahydrofuran[8] at room temperature. The isocyanates were then treated with two equivalents of sodium hydride to give the disodium indol-1-ide-2-thiolate intermediates **3**. These reactivate intermediates were allowed to react with an equimolar amount of an alkyl halide, such as methyl iodide, benzyl bromide, or bromoacetonitrile, at the same temperature. S-Alkylation proceeded immediately and highly selectively. The usual aqueous workup and subsequent purification by recrystallization afforded the desired products **4**. The results are summarized in Table 1, which shows that the yields were generally good to excellent.



Scheme 1 Synthesis of 3-acyl-2-(alkylsulfanyl)indoles

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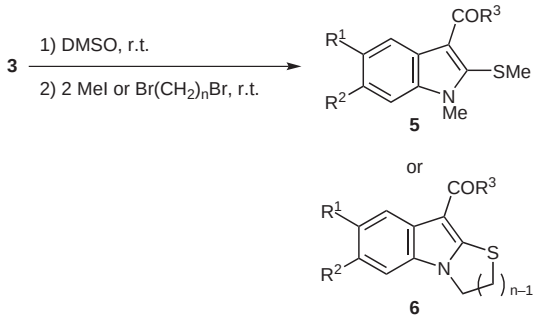
Table 1 Preparation of 3-Acyl-2-(alkylsulfanyl)indoles **4**

Entry	Substrate	R^4X	Product	Yield (%)[a]
1	**1a** (R^1 = R^2 = H; R^3 = Me)	MeI	**4a**	71
2	**1b** (R^1 = R^2 = H; R^3 = Ph)	MeI	**4b**	91
3		BnBr	**4c**	64
4	**1c** (R^1 = Cl; R^2 = H; R^3 = Et)	MeI	**4d**	86
5		$BrCH_2CN$	**4e**	91
6	**1d** (R^1 = OMe; R^2 = H; R^3 = OEt)	MeI	**4f**	88
7	**1e** (R^1 = H; R^2 = Me; R^3 = OEt)	MeI	**4g**	82

[a] Isolated yield.

We next examined the possibility of synthesizing 1-alkyl-2-(alkylsulfanyl)indole derivatives as an application of the present cyclization–alkylation sequence. After the generation of disodium indol-1-ide-2-thiolate intermediates **3**, dimethyl sulfoxide was added, and the mixture was treated with two equivalents of iodomethane. S-Methylation occurred immediately, and N-methylation proceeded slowly but cleanly to give the corresponding 1-methyl-2-(methylsulfanyl)indoles **5** (Scheme 2).



Scheme 2 Preparation of 3-acyl-1-alkyl-2-(alkylsulfanyl)indoles **5** and **6**

Table 2 Preparation of 3-Acyl-1-alkyl-2-(alkylsulfanyl)indoles **5** and **6**

Entry	Substrate	Electrophile	Product	Yield (%)[a]
1	**1b**	2 MeI	**5a**	70
2	**1b**	$Br(CH_2)_3Br$	**6a**	78
3	**1c**	$Br(CH_2)_3Br$	**6b**	75
4	**1d**	2 MeI	**5b**	78
5	**1e**	$Br(CH_2)_2Br$	**6c**	48
6	**1e**	$Br(CH_2)_3Br$	**6d**	79
7	**1e**	$Br(CH_2)_4Br$	**6e**	60

[a] Isolated yield.

The addition of dimethyl sulfoxide was essential for satisfactory N-methylation. Because yields of **5** were relatively good (entries 1 and 4, Table 2), we hypothesized that the use of one equivalent of an α,ω-dihaloalkane in place of the two equivalents of methyl iodide would result in the formation of a tricyclic compound **6** by ring closure between the 1-position of the indole and the sulfur atom at the 2-position. These results are also summarized in Table 2. The reaction of **3** with 1,3-dibromopropane resulted in the formation of six-membered ring to give the corresponding thiazinoindole derivatives **6a**, **6b**, and **6d** (n = 2) in fair-to-good yields (entries 2, 3, and 6). The use of 1,2-dibromoethane gave the corresponding thiazoloindole derivative **6c** (n = 1) in a rather lower yield than those of the thiazinoindole derivatives, probably as a result of ring strain in the five-membered ring (entry 5). A somewhat lower yield of a thiazepinoindole derivative **6e** (n = 3) was obtained by using 1,4-dibromobutane (entry 7); this may be ascribed to the difficulty of forming a seven-membered ring.

We subsequently attempted to prepare a product that was dialkylated on the nitrogen and sulfur atoms with different alkyl groups. Thus, 2-(2-isocyanophenyl)-1-phenylethanone (**1b**) was converted into the corresponding isothiocyanate and treated successively with sodium hydride and iodomethane. Dimethyl sulfoxide was then added, and the mixture was further treated with 2-bromoacetonitrile. Unfortunately, however, no N-cyanomethylation occurred. This was attributed to steric hindrance by the 2-methylsulfanyl group. The range of alkyl halides that can be used in the N,S-dialkylation appears to be limited to iodomethane or α,ω-dihaloalkanes.

In conclusion, (2-isocyanophenyl)methyl ketones and ethyl 2-(2-isocyanophenyl)acetates were used in a one-pot synthesis of 2-(alkylsulfanyl)indoles. Notable advantages of the present synthesis include the simplicity of the procedure, the mild reaction conditions, the ready availability of the starting materials, and the high yields of the products. The procedure has been applied to the synthesis of three new types of indole-fused tricyclic compound.

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer. The ^1H NMR spectra were determined by using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or a JEOL LA400 FT NMR spectrometer operating at 400 MHz. The ^{13}C NMR spectra were determined by using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low- and high-resolution MS spectra (EI, 70 eV) were measured by a JEOL JMS AX505 HA spectrometer. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed on Merck Kieselgel 60 (0.063–0.200 mm). All the organic solvents used in this study were dried over appropriate drying agents and distilled before use. 1-Isocyano-2-methylbenzenes were prepared according to the procedure reported previously by Ito et al.[2] All other chemicals used in this study were commercially available.

(2-Isocyanophenyl)methyl Ketones and Ethyl 2-(2-Isocyanophenyl)acetates 1: General Procedure

These compounds were prepared by treating the corresponding 1-isocyano-2-(lithiomethyl)benzenes, generated from 1-isocyano-2-methylbenzenes and LDA, with ethyl carboxylates or ethyl chloroformate according to the procedure reported by Ito et al.[3] Physical, spectral, and analytical data for new compounds are reported.

1-(5-Chloro-2-isocyanophenyl)butan-2-one (1c)

Colorless needles; yield: 63%; mp 55–57 °C (hexane).

IR (KBr): 2126, 1713 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.3 Hz, 3 H), 2.62 (q, *J* = 7.3 Hz, 2 H), 3.85 (s, 2 H), 7.26 (s, 1 H), 7.29 (d, *J* = 8.2 Hz, 1 H), 7.34 (d, *J* = 8.2 Hz, 1 H).

Anal. Calcd for $C_{11}H_{10}ClNO$: C, 63.62; H, 4.85; N, 6.75. Found: C, 63.52; H, 5.00; N, 6.81.

Ethyl 2-(2-Isocyano-5-methoxyphenyl)acetate (1d)

Pale-yellow liquid; yield: 60%; R_f = 0.20 (Et_2O–hexane, 1:4).

IR (neat): 2118, 1738, 1607 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.3 Hz, 3 H), 3.75 (s, 2 H), 3.82 (s, 3 H), 4.20 (q, *J* = 7.3 Hz, 2 H), 6.81 (dd, *J* = 8.7, 2.8 Hz, 1 H), 6.85 (d, *J* = 2.8 Hz, 1 H), 7.33 (d, *J* = 8.7 Hz, 1 H).

MS (EI, 70 eV): *m/z* (%) = 219 (100) [M^+].

HRMS (EI, 70 eV): *m/z* calcd for $C_{12}H_{13}NO_3$: 219.0895; found: 219.0872.

Ethyl 2-(2-Isocyano-4-methylphenyl)acetate (1e)

Yellow liquid; yield: 57%; R_f = 0.60 (THF–hexane, 1:7).

IR (neat): 2120, 1738, 1618 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.3 Hz, 3 H), 2.35 (s, 3 H), 3.74 (s, 2 H), 4.19 (q, *J* = 7.3 Hz, 2 H), 7.17 (d, *J* = 7.8 Hz, 1 H), 7.21 (s, 1 H), 7.22 (d, *J* = 7.8 Hz, 1 H).

MS (EI, 70 eV): *m/z* (%) = 203 (100) [M^+].

HRMS (EI, 70 eV): *m/z* calcd for $C_{12}H_{13}NO_2$: 203.0946; found: 203.0937.

1-[2-(Methylsulfanyl)-1*H*-indol-3-yl]ethanone (4a); Typical Procedure

A mixture of **1a** (0.18 g, 1.1 mmol), Et_3N (0.28 g, 2.8 mmol), sulfur (43 mg, 1.3 mmol), and selenium (3.0 mg, 33 μmol) in THF (3 mL) was stirred at r.t. After 1.5 h, NaH (60% in oil; 107 mg, 2.7 mmol) was added, and stirring was continued for an additional 30 min at r.t. The resulting mixture was then treated with MeI (0.16 g, 1.1 mmol) and stirred for a further 30 min. Sat. aq NH_4Cl (10 mL) was added and the organic materials were extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried (anhyd Na_2SO_4), and concentrated by evaporation. The residual solid was crystallized (hexane–THF) to give **4a** as a white solid; yield: 0.16 g (71%); mp 170 °C (dec) (hexane–THF).

IR (KBr): 3181, 1601, 1578 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 2.51 (s, 3 H), 2.63 (s, 3 H), 7.15 (td, *J* = 7.3, 2.3 Hz, 1 H), 7.18 (td, *J* = 7.3, 2.3 Hz, 1 H), 7.46 (dd, *J* = 7.3, 2.3 Hz, 1 H), 7.85 (dd, *J* = 7.3, 2.3 Hz, 1 H), 11.75 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 14.33, 30.26, 111.19, 113.63, 119.23, 121.40, 121.52, 126.49, 136.81, 144.83, 191.10.

MS (EI, 70 eV): *m/z* (%) = 205 (100) [M^+].

Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.36; H, 5.61; N, 6.77.

[2-(Methylsulfanyl)-1*H*-indol-3-yl]phenylmethanone (4b)

White solid; mp 159–161 °C (hexane–$CHCl_3$).

IR (KBr): 3233, 1597 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.59 (s, 3 H), 7.05 (t, *J* = 7.8 Hz, 1 H), 7.15 (t, *J* = 7.8 Hz, 1 H), 7.22 (d, *J* = 7.8 Hz, 1 H), 7.35 (d, *J* = 7.8 Hz, 1 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.56 (t, *J* = 7.3 Hz, 1 H), 7.77 (d, *J* = 7.3 Hz, 2 H), 8.77 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.34, 110.61, 110.71, 120.14, 121.74, 122.33, 127.37, 128.25, 128.27, 128.69, 131.32, 131.38, 140.79, 191.54.

MS (EI, 70 eV): *m/z* (%) = 267 (100) [M^+].

Anal. Calcd for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24. Found: C, 71.75; H, 5.05; N, 5.05.

[2-(Phenylmethylsulfanyl)-1*H*-indol-3-yl]phenylmethanone (4c)

Pale-yellow solid; mp 202–204 °C (hexane–$CHCl_3$).

IR (KBr): 3266, 1586 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.19 (s, 2 H), 7.06 (td, *J* = 7.3, 0.9 Hz, 1 H), 7.16 (td, *J* = 7.3, 0.9 Hz, 1 H), 7.21 (d, *J* = 8.2 Hz, 1 H), 7.26–7.33 (m, 6 H), 7.45 (td, *J* = 7.8, 1.4 Hz, 2 H), 7.57 (tt, *J* = 7.8, 1.4 Hz, 1 H), 7.77 (dd, *J* = 7.8, 1.4 Hz, 2 H), 8.33 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 39.26, 110.56, 112.57, 120.74, 121.74, 123.04, 127.12, 127.85, 128.19, 128.70, 128.98, 129.10, 129.19, 131.77, 135.81, 136.90, 140.37, 191.72.

MS (EI, 70 eV): *m/z* (%) = 343 (53) [M^+], 310 (100).

Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 77.74; H, 5.11; N, 3.82.

1-[5-Chloro-2-(methylsulfanyl)-1*H*-indol-3-yl]propan-1-one (4d)

Pale-yellow solid; mp 155–157 °C (hexane–$CHCl_3$).

IR (KBr): 3246, 1601 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 1.11 (t, *J* = 7.3 Hz, 3 H), 2.50 (s, 3 H), 2.91 (q, *J* = 7.3 Hz, 2 H), 7.16 (dd, *J* = 8.7, 1.9 Hz, 1 H), 7.44 (d, *J* = 8.7 Hz, 1 H), 7.84 (d, *J* = 1.9 Hz, 1 H), 11.87 (br, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 8.05, 14.40, 34.58, 112.55, 112.76, 118.66, 121.25, 126.23, 127.48, 135.34, 146.22, 194.06.

Anal. Calcd for $C_{12}H_{12}ClNOS$: C, 56.80; H, 4.77; N, 5.52. Found: C, 56.91; H, 4.61; N, 5.30.

2-[(5-Chloro-3-propanoyl-1*H*-indol-3-yl)sulfanyl]acetonitrile (4e)

Beige solid; mp 165 °C (dec) (hexane–THF).

IR (KBr): 3308, 2251, 1630 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 1.11 (t, *J* = 7.3 Hz, 3 H), 3.01 (q, *J* = 7.3 Hz, 2 H), 4.33 (s, 2 H), 7.23 (dd, *J* = 8.7, 1.9 Hz, 1 H), 7.49 (d, *J* = 8.7 Hz, 1 H), 7.88 (d, *J* = 1.9 Hz, 1 H), 12.37 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 7.92, 17.33, 34.49, 113.09, 114.95, 117.63, 119.13, 122.34, 126.68 (2 C), 135.56, 140.00, 195.01.

Anal. Calcd for $C_{13}H_{11}ClN_2OS$: C, 56.01; H, 3.98; N, 5.52. Found: C, 55.91; H, 4.01; N, 5.50.

Ethyl 5-Methoxy-2-(methylsulfanyl)-1*H*-indole-3-carboxylate (4f)

White solid; mp 154–156 °C (hexane–$CHCl_3$).

IR (KBr) 3277, 1649 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.46 (t, *J* = 7.3 Hz, 3 H), 2.61 (s, 3 H), 3.87 (s, 3 H), 4.22 (q, *J* = 7.3 Hz, 2 H), 6.82 (dd, *J* = 8.7, 2.8

Hz, 1 H), 7.21 (d, *J* = 8.7 Hz, 1 H), 7.57 (d, *J* = 2.8 Hz, 1 H), 8.37 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.60, 14.88, 55.69, 59.85, 102.96, 105.49, 111.01, 111.94, 128.42, 130.79, 142.72, 155.76, 165.36.

MS (EI, 70 eV): *m/z* (%) = 265 (100) [M^+].

Anal. Calcd for $C_{13}H_{15}NO_3S$: C, 58.85; H, 5.70; N, 5.28. Found: C, 58.82; H, 5.70; N, 5.28.

Ethyl 6-Methyl-2-(methylsulfanyl)-1*H*-indole-3-carboxylate (4g)

White solid; mp 125–126 °C (hexane–Et_2O).

IR (KBr): 3331, 1655 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 7.3 Hz, 3 H), 2.44 (s, 3 H), 2.62 (s, 3 H), 4.91 (q, *J* = 7.3 Hz, 2 H), 7.05 (dd, *J* = 8.2, 0.9 Hz, 1 H), 7.12 (d, *J* = 0.9 Hz, 1 H), 7.91 (d, *J* = 8.2 Hz, 1 H), 8.37 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.59, 15.01, 21.56, 59.80, 105.74, 110.37, 120.33, 123.62, 125.16, 132.21, 136.16, 141.70, 165.36.

Anal. Calcd for $C_{13}H_{15}NO_2S$: C, 62.62; H, 6.06; N, 5.62; Found: C, 62.42; H, 6.10; N, 5.72.

1-[1-Methyl-2-(methylsulfanyl)-1*H*-indol-3-yl](phenyl)methanone (5a); Typical Procedure

A mixture of **1b** (0.10 g, 0.45 mmol), Et_3N (0.11 g, 1.1 mmol), sulfur (17 mg, 0.54 mmol), and selenium (1.1 mg, 14 μmol) in THF (3 mL) was stirred at r.t. After 1.5 h, NaH (60% in oil; 43 mg, 1.1 mmol) was added, and the mixture was stirred for an additional 30 min at r.t. DMSO (1.5 mL) and MeI (0.15 g, 1.1 mmol) were added, and the resulting mixture was stirred overnight. Sat. aq NH_4Cl (10 mL) was added and the organic materials were extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried (anhyd Na_2SO_4), and concentrated to give a residue that was purified by preparative TLC (silica gel) to give **5a** as a yellow oil; yield: 89 mg (70%); R_f = 0.27 (benzene).

IR (neat): 1634, 1599 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 3.95 (s, 3 H), 7.14 (ddd, *J* = 8.4, 7.3, 1.1 Hz, 1 H), 7.30 (ddd, *J* = 8.4, 7.3, 1.1 Hz, 1 H), 7.37 (d, *J* = 8.4 Hz, 1 H), 7.45 (t, *J* = 7.3 Hz, 2 H), 7.48 (d, *J* = 8.4 Hz, 1 H), 7.56 (tt, *J* = 7.3, 1.5 Hz, 1 H), 7.82 (dd, *J* = 7.3, 1.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 1.00, 20.21, 30.42, 109.81, 119.55, 121.16, 121.72, 123.43, 127.04, 128.07, 129.52, 131.96, 137.35, 140.46, 192.33.

MS (EI, 70 eV): *m/z* (%) = 281 (100) [M^+].

Anal. Calcd for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98; Found: C, 72.77; H, 5.49; N, 4.91.

Ethyl 5-Methoxy-1-methyl-2-(methylsulfanyl)-1*H*-indole-3-carboxylate (5b)

White solid; mp 82–83 °C (hexane–Et_2O).

IR (KBr): 1686, 1616 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (t, *J* = 7.3 Hz, 3 H), 2.51 (s, 3 H), 3.89 (s, 3 H), 3.90 (s, 3 H), 4.45 (q, *J* = 7.3 Hz, 2 H), 6.96 (dd, *J* = 8.7, 2.3 Hz, 1 H), 7.23 (d, *J* = 8.7 Hz, 1 H), 7.67 (d, *J* = 2.3 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.53, 19.53, 30.56, 55.67, 59.73, 103.26, 109.74, 110.72, 113.81, 127.39, 132.38, 140.14, 155.86, 164.68.

MS (EI, 70 eV): *m/z* (%) = 279 (100) [M^+].

Anal. Calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01; Found: C, 60.09; H, 6.28; N, 4.93.

3,4-Dihydro-2*H*-[1,3]thiazino[3,2-*a*]indol-10-yl)(phenyl)methanone (6a)

Pale-yellow solid; mp 196–197 °C (hexane–CH_2Cl_2).

IR (KBr): 1603 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.51 (quint, *J* = 6.5 Hz, 2 H), 3.12 (t, *J* = 6.5 Hz, 2 H), 4.23 (t, *J* = 6.5 Hz, 2 H), 7.03 (ddd, *J* = 8.2, 7.3, 1.4 Hz, 1 H), 7.07 (d, *J* = 8.2 Hz, 1 H), 7.16 (dd, *J* = 8.2, 7.3, 1.4 Hz, 1 H), 7.26 (d, *J* = 8.2 Hz, 1 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.54 (t, *J* = 7.3 Hz, 1 H), 7.72 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.76, 34.20, 42.07, 108.16, 119.83, 121.51, 121.91, 125.49, 126.12, 128.16, 128.38, 130.85, 138.21, 141.22, 143.17, 190.45.

MS (EI, 70 eV): *m/z* (%) = 293 (100, [M^+]).

Anal. Calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77; Found: C, 73.69; H, 5.28; N, 4.63.

1-(8-Chloro-3,4-dihydro-2*H*-[1,3]thiazino[3,2-*a*]indol-10-yl)propan-1-one (6b)

Pale-yellow solid; mp 135–137 °C (hexane–$CHCl_3$).

IR (KBr): 1622 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.3 Hz, 3 H), 2.45 (quint, *J* = 5.5 Hz, 2 H), 2.96 (q, *J* = 7.3 Hz, 2 H), 3.08 (t, *J* = 5.5 Hz, 2 H), 4.15 (t, *J* = 5.5 Hz, 2 H), 7.16–7.19 (m, 2 H), 7.80 (d, *J* = 1.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.86, 22.54, 24.86, 35.20, 42.09, 109.15, 112.80, 119.15, 121.37, 126.38, 128.20, 136.68, 143.15, 195.12.

MS (EI, 70 eV): *m/z* (%) = 279 (38) [M^+], 250 (100).

Anal. Calcd for $C_{14}H_{14}ClNOS$: C, 60.10; H, 5.04; N, 5.01; Found: C, 60.28; H, 4.93; N, 4.82.

Ethyl 6-Methyl-2,3-dihydro[1,3]thiazolo[3,2-*a*]indole-9-carboxylate (6c)

Beige solid; mp 107–109 °C (hexane–Et_2O).

IR (KBr): 1682 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42 (t, *J* = 7.3 Hz, 3 H), 2.45 (s, 3 H), 3.82 (t, *J* = 7.3 Hz, 2 H), 4.27 (t, *J* = 7.3 Hz, 2 H), 4.37 (q, *J* = 7.3 Hz, 2 H), 6.97 (s, 1 H), 7.02 (d, *J* = 8.2 Hz, 1 H), 7.85 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.62, 21.61, 34.89, 45.49, 59.69, 100.12, 109.41, 120.24, 123.21 (2 C), 128.57, 131.66, 134.78, 164.84.

MS (EI, 70 eV): *m/z* (%) = 261 (100) [M^+].

Anal. Calcd for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.28; H, 5.93; N, 5.32.

Ethyl 7-Methyl-3,4-dihydro-2*H*-[1,3]thiazino[3,2-*a*]indole-10-carboxylate (6d)

Yellow solid; mp 137–139 °C (hexane–CH_2Cl_2).

IR (KBr): 1667 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.3 Hz, 3 H), 2.40 (quint, *J* = 6.0 Hz, 2 H), 2.46 (s, 3 H), 3.07 (t, *J* = 6.0 Hz, 2 H), 4.01 (t, *J* = 6.0 Hz, 2 H), 4.39 (q, *J* = 7.3 Hz, 2 H), 7.00 (s, 1 H), 7.04 (d, *J* = 7.8 Hz, 1 H), 7.87 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.64, 21.68, 23.05, 24.79, 41.89, 59.49, 102.98, 108.09, 119.83, 123.54, 123.92, 131.17, 138.13, 139.47, 165.38.

Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.20; H, 6.50; N, 5.01.

Ethyl 8-Methyl-2,3,4,5-tetrahydro[1,3]thiazepino[3,2-*a*]indole-11-carboxylate (6e)

Pale-yellow solid; mp 133–135 °C (hexane–CH_2Cl_2).

IR (KBr): 1674 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 7.3 Hz, 3 H), 1.86 (quint, *J* = 5.4 Hz, 2 H), 2.14 (quint, *J* = 5.4 Hz, 2 H), 2.49 (s, 3 H), 2.86 (t, *J* = 5.4 Hz, 2 H), 4.39 (t, *J* = 5.4 Hz, 2 H), 4.42 (q, *J* = 7.3 Hz, 2 H), 7.06 (d, *J* = 8.3 Hz, 1 H), 7.12 (s, 1 H), 7.97 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.56, 21.79, 27.67, 30.96, 34.60, 44.75, 59.75, 108.63, 109.17, 121.30, 123.45, 124.12, 132.72, 137.60, 140.99, 165.00.

Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.34; H, 6.83; N, 4.99.

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