Synthesis of 2,*N*,*N*-Trisubstituted 1*H*-Indole-1-carbothioamides from 2-(Acylmethyl)phenyl Isocyanides

by **Kazuhiro Kobayashi***, **Kazuya Yamane**, and **Shuhei Fukamachi**

Division of Applied Chemistry, Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan (phone/fax: +81(857)315263; e-mail: kkoba@chem.tottori-u.ac.jp)

A convenient procedure for the synthesis of 2,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides from 2-(acylmethyl)phenyl isocyanides has been developed. Thus, these isocyanides are converted into (*Z*)-[1-alkyl (or phenyl)-2-(2-isothiocyanatophenyl)ethenyl] 1,1-dimethylethyl carbonates *via* an easy two-step sequence. Treatment with secondary amines gave thiourea intermediates which afforded with CF_3COOH (TFA) the desired products in fair-to-good yields.

Introduction. – Undoubtedly, 1*H*-indole is one of the most important heterocycles. Therefore, a large numbers of synthetic studies on the synthesis of 1*H*-indole derivatives have been reported [1]. However, few general methods have been reported for the synthesis of 1*H*-indole-1-carbothioamide derivatives [2][3], whilst some reports on the biological activity of these 1*H*-indole derivatives have been published [3]. On the other hand, we recently reported a convenient method to prepare 3,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides utilizing the HI-mediated cyclization reaction of the corresponding thiourea intermediates, generated *in situ* from α-substituted 2-isothiocyanatophenyl-β-methoxystyrenes and secondary amines [4]. Now, we would like to disclose a facile method for the synthesis of 2,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides. Our method is based on CF_3COOH (TFA)-mediated cyclization of the thiourea derivatives **4**, derived from (*Z*)-[1-alkyl(or phenyl)-2-(2-isothiocyanatophenyl)ethenyl] 1,1-dimethylethyl carbonates **3** and secondary amines. It should be noted that, after completion of our work, we became aware of the report by *Kaname* and *Sashida*, who described the formation of 2,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides along with 2-imino-4-methylidene-1*H*-1,3-benzothiazines by silver trifluoromethanesulfonate (AgOTf)-promoted cyclization of the *N*-(2-ethynylphenyl)thioureas, derived from 2-ethynylphenyl isothiocyanates and secondary amines [5].

Results and Discussion – The procedure outlined in *Scheme 1* illustrates our synthesis of 2,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides **5** from 2-(acylmethyl)-phenyl isocyanides **1**. Treatment of **1** with di(*tert*-butyl) dicarbonate ($(Boc)_2O$) in pyridine afforded (*Z*)-2-[1-alkyl(or phenyl)-2-(2-isocyanophenyl)ethenyl] 1,1-dimethylethyl carbonates **2**. First, this conversion was conducted at 80° for several hours, and the yields of **2** were low-to-moderate. Subsequently, the reaction proved to proceed smoothly even at room temperature by using a catalytic amount of 4-(dimethylamino)pyridine (DMAP) to provide fair-to-good yields of **2**. The transformation of **2** into

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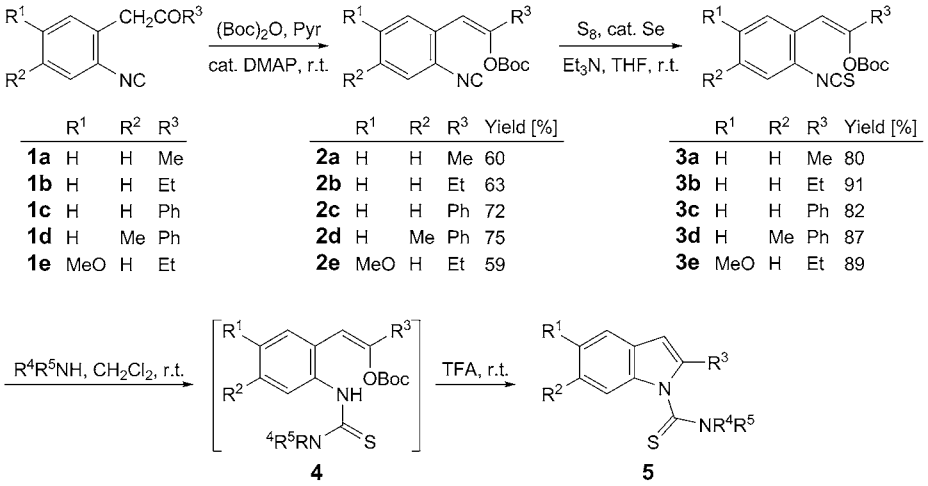
Scheme



	R^1	R^2	R^3
1a	H	H	Me
1b	H	H	Et
1c	H	H	Ph
1d	H	Me	Ph
1e	MeO	H	Et

	R^1	R^2	R^3	Yield [%]
2a	H	H	Me	60
2b	H	H	Et	63
2c	H	H	Ph	72
2d	H	Me	Ph	75
2e	MeO	H	Et	59

	R^1	R^2	R^3	Yield [%]
3a	H	H	Me	80
3b	H	H	Et	91
3c	H	H	Ph	82
3d	H	Me	Ph	87
3e	MeO	H	Et	89

the corresponding isothiocyanates **3** on treatment with S_8 in the presence of a catalytic amount of Se was successfully achieved in good yields according to the procedure of *Fujiwara et al.* [6].

The conversion of carbonates **3** to the desired products **5** could be conducted as a one-pot reaction. Thus, secondary amines were added to the solutions of **3** in CH_2Cl_2 at room temperature, and the attack of the amines on the isothiocyanate C-atom of **3** was complete immediately to give the corresponding thiourea derivatives **4**. After removal of CH_2Cl_2 under reduced pressure, TFA was added. TFA-Mediated cyclization of **4** proceeded smoothly at room temperature to provide **5**. The results compiled in the *Table* indicate that generally good yields of **5** were obtained. However, when the substrate **3** with $R^3 = Ph$ (*i.e.*, **3c** and **3d**) was used, the yields of the products **5g**–**5i** were somewhat lower (*Entries 7–9*) than those of **3** with $R^3 = Me$ or Et.

Table. *Preparation of 2,*N,N-*Trisubstituted 1*H-*Indole-2-carbothioamides* **5**

Entry	**3**	R^4R^5NH	**5**	Yield[a]) [%]
1	**3a** ($R^1 = R^2 = H$, $R^3 = Me$)	Pyrrolidine	**5a**	86
2	**3a**	Morpholine	**5b**	84
3	**3a**	Et_2NH	**5c**	85
4	**3b** ($R^1 = R^2 = H$, $R^3 = Et$)	Piperidine	**5d**	90
5	**3b**	Et_2NH	**5e**	85
6	**3b**	MeNHPh	**5f**	77
7	**3c** ($R^1 = R^2 = H$, $R^3 = Ph$)	Pyrrolidine	**5g**	66
8	**3c**	Piperidine	**5h**	64
9	**3d** ($R^1 = H$, $R^2 = Me$, $R^3 = Ph$)	Pyrrolidine	**5i**	55
10	**3e** ($R^1 = OMe$, $R^2 = H$, $R^3 = Et$)	Pyrrolidine	**5j**	84

[a]) Yields of isolated products.

In conclusion, the developed procedure provides a convenient access to 2,*N*,*N*-trisubstituted 1*H*-indole-1-carbothioamides, which are difficult to prepare by previous methods. Since the method is operationally simple, and the starting materials are readily available, it may be of value in organic synthesis.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E*. M.p.: *Laboratory Devices MEL-TEMP II* melting point apparatus; uncorrected. IR Spectra: *Perkin–Elmer Spectrum65 FTIR* spectrophotometer. ^{1}H-NMR Spectra: in $CDCl_3$ with TMS as an internal reference with *Bruker Biospin AVANCE II 600* spectrometer, at 600 MHz, *JEOL ECP500* FT NMR spectrometer, at 500 MHz, or a *JEOL LA400* FT NMR spectrometer, at 400 MHz. ^{13}C-NMR Spectra: in $CDCl_3$ with TMS as an internal reference with *Bruker Biospin AVANCE II 600*, at 150 MHz, *JEOL ECP500* FT NMR spectrometer, at 125 MHz, or a *JEOL LA400FT* NMR spectrometer, 100 MHz. LR-MS (EI, 70 eV): with *JEOL JMS AX505 HA* spectrometer. HR-MS (DART, pos.-ion mode): *Thermo Scientific Exactive* spectrometer.

2-Methylphenyl isocyanides were prepared as described in [7]. BuLi was supplied by *Asia Lithium Corporation*. All other chemicals used in this study were commercially available.

(2-Isocyanophenyl)methyl ketones **1** were prepared from 2-methylphenyl isocyanides as described in [8]. The physical, spectroscopic, and anal. data for new compounds are given below.

1-(2-Isocyanophenyl)butan-2-one (**1b**). Yield: 0.88 g (51%). Pale-yellow liquid. R_f (AcOEt/hexane 1:5) 0.46. IR (neat): 2121, 1722, 1623. ^{1}H-NMR (400 MHz): 1.12 (*t*, *J* = 7.4, 3 H); 2.60 (*q*, *J* = 7.4, 2 H); 3.88 (*s*, 2 H); 7.26 (*d*, *J* = 7.8, 1 H); 7.31 (*dd*, *J* = 7.8, 6.9, 1 H); 7.36 (*d*, *J* = 7.8, 1 H); 7.39 (*dd*, *J* = 7.8, 6.9, 1 H). HR-MS: 174.0915 ($[M+H]^+$, $C_{11}H_{12}NO^+$; calc. 174.0919).

2-(2-Isocyano-4-methylphenyl)-1-phenylethanone (**1d**). Yield: 0.74 g (63%). Yellow solid. M.p. 108–110° (hexane/Et_2O). IR (KBr): 2127, 1686. ^{1}H-NMR (400 MHz): 2.36 (*s*, 3 H); 4.42 (*s*, 2 H); 7.19 (*s*, 2 H); 7.25 (*s*, 1 H); 7.50 (*dd*, *J* = 7.8, 7.3, 2 H); 7.60 (*t*, *J* = 7.3, 1 H); 8.04 (*d*, *J* = 7.8, 2 H). Anal. calc. for $C_{16}H_{13}NO$ (235.28): C 81.68, H 5.57, N 5.95; found: C 81.50, H 5.59, N 5.91.

1-(2-Isocyano-5-methoxyphenyl)butan-2-one (**1e**). Pale-yellow liquid. R_f (AcOEt/hexane 1:5) 0.41. IR (neat): 2119, 1722, 1606. ^{1}H-NMR (400 MHz): 1.11 (*t*, *J* = 7.4, 3 H); 2.59 (*q*, *J* = 7.4, 2 H); 3.81 (*s*, 3 H); 3.83 (*s*, 2 H); 6.75 (*d*, *J* = 2.9, 1 H); 6.79 (*dd*, *J* = 8.8, 2.9, 1 H); 7.32 (*d*, *J* = 8.8, 1 H). HR-MS: 204.1044 ($[M+H]^+$, $C_{12}H_{14}NO_2^+$; calc. 204.1025).

tert-*Butyl (1Z)-1-(2-Isocyanophenyl)prop-1-en-2-yl Carbonate* (**2a**). *General Procedure.* A soln. of **1a** (0.44 g, 2.8 mmol) and $(Boc)_2O$ (0.60 g, 2.8 mmol) in pyridine (1 ml) containing DMAP (0.10 g, 0.83 mmol) was stirred at r.t. until disappearance of **1a** (TLC (SiO_2; AcOEt/hexane 1:2; *ca.* 15 min)). H_2O (15 ml) was added, and the mixture was extracted with AcOEt (3 × 10 ml). The combined extracts were washed with sat. aq. NH_4Cl (4 × 10 ml) and brine (10 ml), and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was purified by CC (SiO_2) to give **2a** (0.43 g, 60%). Pale-yellow oil. R_f ($CHCl_3$/hexane 1:1) 0.43. IR (neat): 2119, 1756, 1676. ^{1}H-NMR (500 MHz): 1.46 (*s*, 9 H); 2.18 (*d*, *J* = 1.1, 3 H); 6.19 (br. *s*, 1 H); 7.24 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.35 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.36 (*d*, *J* = 8.0, 1 H); 7.69 (*d*, *J* = 8.0, 1 H). Anal. calc. for $C_{15}H_{17}NO_3$ (259.30): C 69.48, H 6.61, N 5.40; found: C 69.40, H 6.65, N 5.47.

tert-*Butyl (1Z)-1-(2-Isocyanophenyl)but-1-en-2-yl Carbonate* (**2b**). Yellow oil. R_f (AcOEt/hexane 1:10) 0.43. IR (neat): 2119, 1757, 1675. ^{1}H-NMR (500 MHz): 1.21 (*t*, *J* = 7.4, 3 H); 1.42 (*s*, 9 H); 2.48 (*q*, *J* = 7.4, 2 H); 6.19 (*s*, 1 H); 7.22 (*t*, *J* = 7.4, 1 H); 7.32–7.37 (*m*, 2 H); 7.68 (*d*, *J* = 7.4, 1 H). Anal. calc. for $C_{16}H_{19}NO_3$ (273.33): C 70.31, H 7.01, N 5.12; found: C 70.36, H 7.07, N 4.95.

tert-*Butyl (Z)-2-(2-Isocyanophenyl)-1-phenylethenyl Carbonate* (**2c**). Pale-yellow solid. M.p. 74–76° (hexane/Et_2O). IR (KBr): 2119, 1762, 1647. ^{1}H-NMR (600 MHz): 1.40 (*s*, 9 H); 6.89 (*s*, 1 H); 7.28 (*td*, *J* = 7.7, 1.4, 1 H); 7.40–7.44 (*m*, 5 H); 7.63 (*dd*, *J* = 7.9, 1.4, 2 H); 7.90 (*d*, *J* = 8.0, 1 H). Anal. calc. for $C_{20}H_{19}NO_3$ (321.37): C 74.75, H 5.96, N 4.36; found: C 74.74, H 5.99, N 4.06.

tert-*Butyl (*Z*)-2-(2-Isocyano-4-methylphenyl)-1-phenylethenyl Carbonate* (**2d**). Pale-yellow solid. M.p. 110–112° (hexane/Et_2O). IR (KBr): 2117, 1762, 1650. ^{1}H-NMR (500 MHz): 1.40 (*s*, 9 H); 2.36 (*s*, 3 H); 6.85 (*s*, 1 H); 7.21–7.23 (*m*, 2 H); 7.37–7.43 (*m*, 3 H); 7.62 (*dd*, *J* = 8.0, 1.7, 2 H); 7.79 (*d*, *J* = 8.6, 1 H). Anal. calc. for $C_{21}H_{21}NO_3$ (335.40): C 75.20, H 6.31, N 4.18; found: C 75.26, H 6.44, N 4.09.

tert-*Butyl (1*Z*)-1-(2-Isocyano-5-methoxyphenyl)but-1-en-2-yl Carbonate* (**2e**). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.56. IR (neat): 2117, 1759, 1674, 1603. ^{1}H-NMR (500 MHz): 1.21 (*t*, *J* = 7.4, 3 H); 1.42 (*s*, 9 H); 2.48 (*qd*, *J* = 7.4, 1.1, 2 H); 3.81 (*s*, 3 H); 6.17 (*s*, 1 H); 6.74 (*dd*, *J* = 8.6, 2.2, 1 H); 7.24 (*d*, *J* = 2.9, 1 H); 7.28 (*d*, *J* = 8.6, 1 H). Anal. calc. for $C_{17}H_{21}NO_4$ (303.35): C 67.31, H 6.98, N 4.62; found: C 67.28, H 7.08, N 4.51.

tert-*Butyl (1*Z*)-1-(2-isothiocyanatophenyl)alk-1-en-2-yl] carbonates* **3** were prepared by treating **2** with S_8 in the presence of Se under conditions reported in [6].

tert-*Butyl (1*Z*)-1-(2-isothiocyanatophenyl)prop-1-en-2-yl carbonate* (**3a**). Pale-yellow oil. R_f (AcOEt/hexane 1:40) 0.29. IR (neat): 2101, 1755, 1678. ^{1}H-NMR (500 MHz): 1.44 (*s*, 9 H); 2.16 (*d*, *J* = 1.1, 3 H); 6.11 (*s*, 1 H); 7.18–7.23 (*m*, 3 H); 7.58 (*dd*, *J* = 8.0, 2.3, 1 H). Anal. calc. for $C_{15}H_{17}NO_3S$ (291.37): C 61.83, H 5.88, N 4.81; found: C 61.82, H 5.93, N 4.73.

tert-*Butyl (1*Z*)-1-(2-Isothiocyanatophenyl)but-1-en-2-yl Carbonate* (**3b**). Pale-yellow oil. R_f (AcOEt/hexane 1:30) 0.34. IR (neat): 2078, 1756, 1674. ^{1}H-NMR (500 MHz): 1.21 (*t*, *J* = 7.4, 3 H); 1.41 (*s*, 9 H); 2.46 (*q*, *J* = 7.4, 2 H); 6.13 (*s*, 1 H); 7.19–7.21 (*m*, 3 H); 7.57 (*dd*, *J* = 8.0, 1.7, 1 H). Anal. calc. for $C_{16}H_{19}NO_3S$ (305.39): C 62.93, H 6.27, N 4.59; found: C 62.80, H 6.36, N 4.59.

tert-*Butyl (*Z*)-2-(2-Isothiocyanatophenyl)-1-phenylethenyl Carbonate* (**3c**). Pale-yellow oil. R_f (THF/hexane 1:4) 0.53. IR (neat): 2081, 1762, 1646. ^{1}H-NMR (600 MHz): 1.39 (*s*, 9 H); 6.83 (*s*, 1 H); 7.25–7.30 (*m*, 3 H); 7.38 (*tt*, *J* = 7.3, 0.9, 1 H); 7.42 (*dd*, *J* = 7.8, 7.3, 2 H); 7.64 (*dd*, *J* = 7.8, 0.9, 2 H); 7.81 (*dd*, *J* = 7.5, 2.0, 1 H). Anal. calc. for $C_{20}H_{19}NO_3S$ (353.43): C 67.97, H 5.42, N 3.96; found: C 67.80, H 5.27, N 3.92.

tert-*Butyl (*Z*)-2-(2-Isothiocyanato-4-methylphenyl)-1-phenylethenyl Carbonate* (**3d**). Pale-yellow solid. M.p. 114–116° (hexane/Et_2O). IR (KBr): 2114, 1755, 1650. ^{1}H-NMR (500 MHz): 1.40 (*s*, 9 H); 2.34 (*s*, 3 H); 6.80 (*s*, 1 H); 7.09 (*d*, *J* = 8.0, 1 H); 7.10 (*s*, 1 H); 7.36 (*t*, *J* = 7.4, 1 H); 7.42 (*t*, *J* = 7.4, 2 H); 7.62 (*d*, *J* = 7.4, 2 H); 7.70 (*d*, *J* = 8.0, 1 H). Anal. calc. for $C_{21}H_{21}NO_3S$ (367.46): C 68.64, H 5.76, N 3.81; found: C 68.46, H 5.83, N 3.70.

tert-*Butyl (1*Z*)-1-(2-Isothiocyanato-5-methoxyphenyl)but-1-en-2-yl Carbonate* (**3e**). Pale-yellow oil. R_f (AcOEt/hexane 1:40) 0.39. IR (neat): 2088, 1756, 1674, 1600. ^{1}H-NMR (400 MHz): 1.21 (*t*, *J* = 7.3, 3 H); 1.42 (*s*, 9 H); 2.46 (*q*, *J* = 7.3, 2 H); 3.79 (*s*, 3 H); 6.10 (*s*, 1 H); 6.73 (*dd*, *J* = 8.8, 2.9, 1 H); 7.13 (*d*, *J* = 8.8, 1 H); 7.16 (*d*, *J* = 2.9, 1 H). Anal. calc. for $C_{17}H_{21}NO_4S$ (335.42): C 60.87, H 6.31, N 4.18; found: C 60.87, H 6.34, N 4.10.

*(2-Methyl-1*H*-indol-1-yl)(pyrrolidin-1-yl)methanethione* (**5a**). *General Procedure.* To a stirred soln. of **3a** (0.27 g, 0.81 mmol) in CH_2Cl_2 (1 ml) at r.t. was added pyrrolidine (58 mg, 0.81 mmol). After confirmation of complete consumption of **3a** (TLC (SiO_2; THF/hexane 1:5; within 5 min)), the solvent was removed under reduced pressure. Then, the residual thiourea precursor was dissolved in TFA (1 ml), and the soln. was stirred at r.t. until TLC analyses (SiO_2; AcOEt/hexane 1:2) indicated that the thiourea precursor had disappeared (*ca.* 10 min). Sat. aq. $NaHCO_3$ (20 ml) was added, and the mixture was extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were washed with sat. aq. $NaHCO_3$ (10 ml) and H_2O (10 ml), and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by prep. TLC (SiO_2) to give **5a** (0.20 g, 86%). Pale-yellow oil. R_f (AcOEt/hexane 1:2) 0.66. IR (neat) 1488, 1451, 1205. ^{1}H-NMR (400 MHz): 1.92–1.98 (*m*, 2 H); 2.10–2.13 (*m*, 2 H); 2.46 (*s*, 3 H); 3.20–3.24 (*m*, 1 H); 3.27–3.31 (*m*, 1 H); 4.00–4.04 (*m*, 2 H); 6.34 (*s*, 1 H); 7.10 (*ddd*, *J* = 8.0, 7.3, 2.3, 1 H); 7.13–7.18 (*m*, 2 H); 7.49 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR (125 MHz): 13.2; 24.8; 25.9; 51.5; 53.5; 103.5; 110.1; 120.0; 120.8; 122.0; 128.5; 134.8 (two overlapped Cs); 178.4. HR-MS: 245.1096 ($[M+H]^+$, $C_{14}H_{17}N_2S^+$; calc. 245.1112). Anal. calc. for $C_{14}H_{16}N_2S$ (244.36): C 68.81, H 6.60, N 11.46; found: C 68.94, H 6.68, N 11.52.

*(2-Methyl-1*H*-indol-1-yl)(morpholin-4-yl)methanethione* (**5b**). Pale-yellow solid. M.p. 66–72° (hexane/Et_2O). IR (KBr): 1483, 1455, 1236. ^{1}H-NMR (500 MHz): 2.46 (*s*, 3 H); 3.27 (br. *s*, 2 H); 3.54–3.58 (*m*, 2 H); 3.94–3.96 (*m*, 2 H); 4.39–4.42 (*m*, 2 H); 6.37 (*s*, 1 H); 7.13 (*ddd*, *J* = 7.4, 6.9, 1.1, 1 H); 7.18 (*ddd*, *J* = 8.0, 6.9, 1.1, 1 H); 7.24 (*d*, *J* = 8.0, 1 H); 7.49 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR (125 MHz): 13.3; 50.5; 50.8; 66.3; 66.6; 104.3; 110.2; 120.1; 121.3; 122.4; 128.5; 135.5; 135.7; 180.9. HR-MS: 261.1066

([$M+H$]$^+$, $C_{14}H_{17}N_2OS^+$; calc. 261.1061). Anal. calc. for $C_{14}H_{16}N_2OS$ (260.35): C 64.58, H 6.19, N 10.76; found: C 64.50, H 6.33, N 10.66.

N,N-*Diethyl-2-methyl-1*H-*indole-1-carbothioamide* (**5c**). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.56. IR (neat): 1501, 1456, 1214. ^{1}H-NMR (500 MHz): 1.08 (*t*, *J* = 7.4, 3 H); 1.51 (*t*, *J* = 7.4, 3 H); 2.46 (*s*, 3 H); 3.22–3.29 (*m*, 1 H); 3.35–3.42 (*m*, 1 H); 4.10–4.17 (*m*, 1 H); 4.23–4.29 (*m*, 1 H); 6.37 (*s*, 1 H); 7.10–7.20 (*m*, 3 H); 7.51 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR (125 MHz): 11.2; 13.0; 13.9; 46.7; 47.5; 103.5; 110.0; 119.9; 120.8; 122.1; 128.5; 135.3; 135.9; 181.0. HR-MS: 247.1263 ([$M+H$]$^+$, $C_{14}H_{19}N_2S^+$; calc. 247.1269). Anal. calc. for $C_{14}H_{18}N_2S$ (246.37): C 68.25, H 7.36, N 11.37; found: C 68.20, H 7.48, N 11.36.

*(2-Ethyl-1*H-*indol-1-yl)(piperidin-1-yl)methanethione* (**5d**). Pale-yellow oil. R_f (AcOEt/hexane 1:10) 0.40. IR (neat): 1489, 1454, 1240. ^{1}H-NMR (500 MHz): 1.33 (*t*, *J* = 7.4, 3 H); 1.43–1.53 (*m*, 2 H); 1.70–1.75 (*m*, 2 H); 1.89–1.91 (*m*, 2 H); 2.73–2.80 (*m*, 1 H); 2.91–2.99 (*m*, 1 H); 2.99–3.27 (*m*, 2 H); 4.29–4.38 (*m*, 2 H); 6.38 (*s*, 1 H); 7.11 (*dd*, *J* = 8.0, 6.9, 1 H); 7.16 (*dd*, *J* = 8.0, 6.9, 1 H); 7.20 (*d*, *J* = 8.0, 1 H); 7.51 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR (125 MHz): 12.7; 20.4; 24.0; 25.3; 26.9; 51.4; 51.6; 101.9; 110.2; 120.0; 120.9; 122.1; 128.3; 135.7; 141.9; 180.1. HR-MS: 273.1415 ([$M+H$]$^+$, $C_{16}H_{21}N_2S^+$; calc. 273.1425). Anal. calc. for $C_{16}H_{20}N_2S$ (272.41): C 70.55, H 7.40, N 10.28; found: C 70.53, H 7.48, N 10.07.

*2,*N,N-*Triethyl-1*H-*indole-1-carbothioamide* (**5e**). Pale-yellow oil. R_f (AcOEt/hexane 1:10) 0.39. IR (neat): 1500, 1455, 1211. ^{1}H-NMR (500 MHz): 1.05 (*t*, *J* = 7.4, 3 H); 1.35 (*t*, *J* = 7.4, 3 H); 1.49 (*t*, *J* = 7.4, 3 H); 2.61–2.69 (*m*, 1 H); 2.91–2.99 (*m*, 1 H); 3.19–3.26 (*m*, 1 H); 3.28–3.35 (*m*, 1 H); 4.10–4.24 (*m*, 2 H); 6.38 (*s*, 1 H); 7.09–7.17 (*m*, 3 H); 7.51 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR (125 MHz): 11.1; 12.3; 13.9; 20.2; 46.7; 47.3; 101.5; 109.9; 120.1; 120.8; 122.1; 128.4; 135.8; 141.6; 181.1. HR-MS. 261.1435 ([$M+H$]$^+$, $C_{15}H_{21}N_2S^+$; calc. 261.1425). Anal. calc. for $C_{15}H_{20}N_2S$ (260.40): C 69.19, H 7.74, N 10.76; found: C 69.12, H 7.89, N 10.61.

2-Ethyl-N-*methyl*-N-*phenyl-1*H-*indole-1-carbothioamide* (**5f**). Pale-yellow solid. M.p. 98–99° (hexane/CH_2Cl_2). IR (KBr): 1492, 1454, 1194. ^{1}H-NMR (500 MHz): 1.28 (*t*, *J* = 7.4, 3 H); 2.59–2.67 (*m*, 1 H); 2.89–2.97 (*m*, 1 H); 3.95 (*s*, 3 H); 6.13 (*s*, 1 H); 6.96–7.34 (*m*, 8 H); 7.46 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR (125 MHz): 12.4; 20.7; 39.3; 102.2; 104.0; 111.0; 119.8; 120.8; 121.9; 123.7; 127.4; 128.4; 128.9; 134.9; 141.7; 179.7. HR-MS: 295.1261 ([$M+H$]$^+$, $C_{18}H_{19}N_2S^+$; calc. 295.1269). Anal. calc. for $C_{18}H_{18}N_2S$ (294.41): C 73.43, H 6.16, N 9.51; found: C 73.44, H 6.37, N 9.40.

*(2-Phenyl-1*H-*indol-1-yl)(pyrrolidin-1-yl)methanethione* (**5g**). Pale-yellow solid. M.p. 172–173° (hexane/CH_2Cl_2). IR (KBr): 1603, 1488, 1450, 1209. ^{1}H-NMR (600 MHz): 1.61–1.77 (*m*, 3 H); 1.94–1.99 (*m*, 1 H); 2.96–2.98 (*m*, 2 H); 3.71–3.76 (*m*, 1 H); 3.92–3.97 (*m*, 1 H); 6.75 (*s*, 1 H); 7.19 (*td*, *J* = 7.9, 0.9, 1 H); 7.27 (*ddd*, *J* = 8.2, 7.9, 0.9, 1 H); 7.35 (*tt*, *J* = 7.4, 1.2, 1 H); 7.40 (*dd*, *J* = 7.8, 7.4, 2 H); 7.61 (*d*, *J* = 7.9, 1 H); 7.69 (*dd*, *J* = 8.2, 0.9, 2 H); 7.75 (*dd*, *J* = 8.2, 0.9, 1 H). ^{13}C-NMR (150 MHz): 24.4; 25.7; 51.6; 53.4; 104.7; 112.0; 120.6; 121.6; 123.3; 127.3; 128.1; 128.7; 128.8; 132.2; 136.6; 138.5; 178.0. HR-MS: 307.1265 ([$M+H$]$^+$, $C_{19}H_{19}N_2S^+$; calc. 307.1269). Anal. calc. for $C_{19}H_{18}N_2S$ (306.42): C 74.47, H 5.92, N 9.14; found: C 74.47, H 5.82, N 9.05.

*(2-Phenyl-1*H-*indol-1-yl)(piperidin-1-yl)methanethione* (**5h**). Colorless crystals. M.p. 106–107° (hexane/Et_2O). IR (KBr): 1604, 1488, 1452, 1247. ^{1}H-NMR (500 MHz): 0.99–1.02 (*m*, 1 H); 1.21–1.27 (*m*, 1 H); 1.40–1.43 (*m*, 1 H); 1.54–1.57 (*m*, 2 H); 1.74–1.80 (*m*, 1 H); 2.77–2.82 (*m*, 1 H); 3.00–3.06 (*m*, 1 H); 3.82–3.87 (*m*, 1 H); 4.29–4.33 (*m*, 1 H); 6.73 (*s*, 1 H); 7.19 (*d*, *J* = 8.0, 7.4, 1 H); 7.26 (*dd*, *J* = 8.0, 7.4, 1 H); 7.35 (*t*, *J* = 7.4, 1 H); 7.42 (*t*, *J* = 7.4, 2 H); 7.60 (*d*, *J* = 8.0, 1 H); 7.68 (*d*, *J* = 7.4, 2 H); 7.75 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR (150 MHz): 23.8; 24.9; 26.1; 51.1; 51.6; 104.6; 112.2; 120.6; 121.6; 123.3; 127.8; 128.1; 128.5; 128.7; 131.9; 137.5; 139.1; 179.9. HR-MS: 321.1414 ([$M+H$]$^+$, $C_{20}H_{21}N_2S^+$; calc. 321.1425). Anal. calc. for $C_{20}H_{20}N_2S$ (320.45): C 74.96, H 6.29, N 8.74; found: C 74.81, H 6.30, N 8.64.

*(6-Methyl-2-phenyl-1*H-*indol-1-yl)(pyrrolidin-1-yl)methanethione* (**5i**). Pale-yellow solid. M.p. 80–84° (hexane/Et_2O). IR (KBr): 1603, 1494, 1447, 1261. ^{1}H-NMR (500 MHz): 1.56–1.75 (*m*, 3 H); 1.95–1.97 (*m*, 1 H); 2.48 (*s*, 3 H); 2.94–2.97 (*m*, 2 H); 3.70–3.75 (*m*, 1 H); 3.92–3.97 (*m*, 1 H); 6.69 (*s*, 1 H); 7.01 (*d*, *J* = 8.0, 1 H); 7.32 (*t*, *J* = 7.4, 1 H); 7.40 (*dd*, *J* = 8.0, 7.4, 2 H); 7.48 (*d*, *J* = 8.0, 1 H); 7.55 (*s*, 1 H); 7.67 (*d*, *J* = 8.0, 2 H). ^{13}C-NMR (150 MHz): 22.0; 24.4; 25.7; 51.5; 53.4; 104.5; 112.0; 120.2; 123.3; 126.6; 127.2; 127.8; 128.6; 132.4; 133.3; 137.0; 137.9; 178.2. HR-MS: 321.1416 ([$M+H$]$^+$, $C_{20}H_{21}N_2S^+$; calc. 321.1425). Anal. calc. for $C_{20}H_{20}N_2S$ (320.45): C 74.96, H 6.29, N 8.74; found: C 74.90, H 6.45, N 8.65.

*(2-Ethyl-5-methoxy-1*H-*indol-1-yl)(pyrrolidin-1-yl)methanethione* (**5j**). Pale-yellow oil. R_f (AcOEt/hexane 1:4) 0.40. IR (neat): 1616, 1476, 1448, 1205. ^{1}H-NMR (500 MHz): 1.30 (*t*, *J* = 7.4, 3 H); 1.91–1.97

(*m*, 2 H); 2.04–2.14 (*m*, 2 H); 2.74–2.81 (*m*, 1 H); 2.90–2.98 (*m*, 1 H); 3.20–3.25 (*m*, 1 H); 3.28–3.24 (*m*, 1 H); 3.83 (*s*, 3 H); 3.96–4.05 (*m*, 2 H); 6.30 (*s*, 1 H); 6.80 (*dd*, $J = 9.2, 2.3$, 1 H); 7.00 (*d*, $J = 2.3$, 1 H); 7.02 (*d*, $J = 9.2$, 1 H). ^{13}C-NMR (100 MHz): 12.7; 20.6; 24.8; 25.9; 51.5; 53.5; 55.9; 101.8; 102.7; 110.7; 111.5; 129.0; 130.0; 142.0; 154.9; 178.7. HR-MS: 289.1373 ($[M+H]^+$, $C_{16}H_{21}N_2OS^+$; calc. 289.1374). Anal. calc. for $C_{16}H_{20}N_2OS$ (288.41): C 66.63, H 6.99, N 9.71; found: C 66.52, H 6.87, N, 9.67.

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