New Entry to Bridged Pentacyclic Indolyltetrahydroisoquinoline Skeleton via Tandem S-Alkylation and Intramolecular C-Alkylation

Firouz Matloubi Moghaddam,* Salman Taheri, Zohreh Mirjafary, Hamdollah Saeidian

Laboratory of Organic Synthesis & Natural Products, Department of Chemistry, Sharif University of Technology, P. O. Box 11155-9516, Tehran, Iran
E-mail: matloubi@sharif.edu

Received 18 August 2009

Abstract: An efficient, single-step synthesis of hitherto unknown indole-annulated pentacyclic indolylhydroisoquinolines via tandem S-alkylation and intramolecular C-alkylation of indolin-2-thiones with *N*-alkylisoquinolinium salts is reported. This new approach provides a powerful entry into polycyclic structures containing nitrogen and sulfur related to alkaloids.

Key words: thiooxindoles, pentacyclic heterocycles, tandem reaction, indolyltetrahydroisoquinoline, isoquinolinium salts

The isoquinoline core is a structural motif common to a large and diverse family of natural products that have shown a remarkable array of biological activities.[1] Among the members of this family, those in which the nitrogen-containing ring is partially hydrogenated, the 1,2,3,4-tetrahydroisoquinolines, constitute a major group in this class of interesting alkaloids (compound **I**).[2] Furthermore, molecules that contain both indole and tetrahydroisoquinoline subunits possess interesting biological activities, and find application in biogenetic type synthesis of missing alkaloids, systems related to naturally occurring alkaloids, such as compound **II** and **III** (Figure 1).[3]

Much effort has been made to discover new reactions to facilitate the construction of heterocycles containing indole and tetrahydroisoquinoline nuclei. A current challenge in organic synthesis involves development of new methodologies that afford complex molecules from relatively simple starting materials via tandem reactions with fewer synthetic steps and mild reaction conditions leading to high yields.[4]

Isoquinolinium salts represent important synthetic building blocks.[5] They are readily generated by alkylation or acylation of isoquinolines and have been used in a number of reactions, for example, with Grignard reagents, cyanide

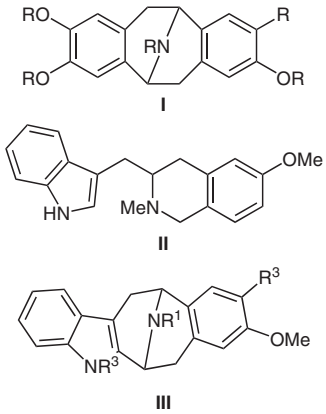
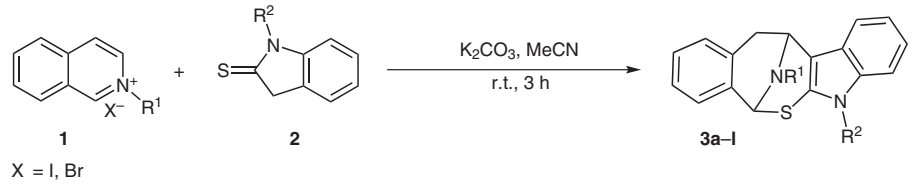


Figure 1

(Reissert reaction),[6] trimethylsilylacetonitrile,[7] allylsilanes silyl enol ethers,[8] diazoesters,[9] and iodolactonization.[10] On the other hand, thioamides have been utilized as synthons in the synthesis of heterocycles.[11] As part of our current research on the development of novel and efficient protocols to heterocyclic systems using thioamides,[12] we now wish to report a hitherto unknown reaction that affords bridged pentacyclic indolyltetrahydroisoquinoline derivatives **3a–l** via tandem reactions of *N*-alkylisoquinolinium salts **1** with indolin-2-thiones **2** (Scheme 1). These compounds may be considered as isoesteric analogues of indolopavine derivatives since they are structurally related to the natural pavine alkaloids.[13]

Initially we set out to investigate solvent and base effects in the reaction of *N*-methylisoquinlinium salts and *N*-ethyl indolin-2-thione as simple model substrates (Table 1). The results showed that a base is required to achieve the desired products and, in the optimized conditions, MeCN



Scheme 1

SYNLETT 2010, No. 1, pp 0123–0127
Advanced online publication: 02.12.2009
DOI: 10.1055/s-0029-1218534; Art ID: D22509ST

and K_2CO_3 were found to be the best solvent and base (Table 1, entry 5).

Table 1 Optimization of Reaction Conditions[a]

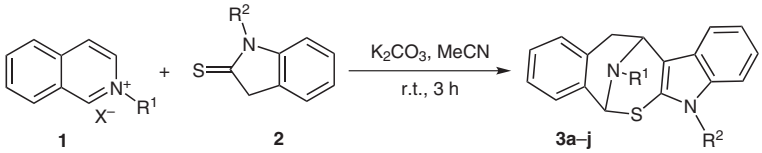
Entry	Base	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	no base	CH_2Cl_2	r.t.	4	n.r.
2	K_2CO_3	CH_2Cl_2	r.t.	4	55
3	K_2CO_3	toluene	r.t.	4	5
4	K_2CO_3	acetone	r.t.	4	40
5	K_2CO_3	MeCN	r.t.	2	86
6	K_2CO_3	MeCN	80	4	80
7	Cs_2CO_3	MeCN	r.t.	4	85
8	Et_3N	MeCN	r.t.	4	30
9	K_2CO_3	H_2O	r.t.	4	30

[a] Reaction conditions: solvent(5 mL), *N*-methyl isoquinolinum salt (1 mmol), K_2CO_3 (1 mmol), and *N*-ethylindolin-2-thione (1 mmol).
[b] Isolated products.

The ^{1}H NMR, ^{13}C NMR, 2DNMR (H-H COSY, HMQC, HMBC) spectra and elemental analysis of the products clearly indicated the formation of **3a–l**. For example, in the ^{1}H NMR spectrum of **3g** the bridgehead H_a hydrogen appears as a singlet at δ = 5.69 ppm, the bridgehead H_b as a doublet (J = 5.0 Hz) at δ = 4.58 ppm, H_c as a doublet (J = 16.0 Hz) at δ = 3.24 ppm, and H_d as a double doublet (J = 16.0, 5.0 Hz) at δ = 3.66 ppm (Figure 2). This can be related to previously reported spectra which were interpreted as representing a system in which the bridgehead hydrogens are coupled appreciably with only one of the two adjacent hydrogens (i.e., H_b coupled with H_d but not with H_c).[14] The ^{1}H-decoupled ^{13}C NMR spectrum of **3g** showed 22 distinct resonances in agreement with the proposed structure. The ^{13}C DEPT experiment showed the presence of a resonance at δ = 36.5 ppm readily recognized as the methylene carbon (C-12), a resonance at δ = 52.6 ppm as the bridgehead carbon (C-13), a resonance at δ = 42.1 ppm as the *N*-methyl carbon, a resonance at δ = 71.3 ppm as the N–CH–S carbon, 12 distinct resonances for the aromatic methine carbons, and 6 other quaternary carbons. Further evidence for the bridged structure is given by the HMBC spectrum in which the key correlations between the methyl proton at δ = 2.69 (NMe) ppm and carbons at δ = 52.6 (C-13) and 71.3 (C-7) ppm indicate that the connection points of the indole ring and the tetrahydroisoquinoline ring are at C-13 and C-7. Some key HMBC correlations are shown in Figure 2.

In view of the success of the above reaction, we explored the scope of this promising reaction by varying the structure of the *N*-alkylisoquinolinium salt **1** and indolin-2-thione **2** components (Table 2). The reaction proceeds very cleanly under mild conditions at room temperature and no side reactions were observed under these conditions.

Table 2 Synthesis of Pentacyclic Indolyltetrahydroisoquinoline Derivatives



1 2 3a–j

Entry	R^1	R^2	Product	Yield (%)[a]
1	Me	Et	**3a**	86
2	Et	H	**3b**	82
3	Bn	H	**3c**	75
4	propargyl	H	**3d**	64
5	Me	H	**3e**	81
6	Me	Me	**3f**	95
7	Me	Ph	**3g**	89
8	propargyl	Ph	**3h**	68
9	Et	Ph	**3i**	90
10	Et	Me	**3j**	91
11	Et	Et	**3k**	86
12	All	Me	**3l**	88

[a] Isolated yield.

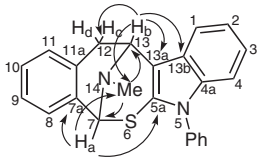
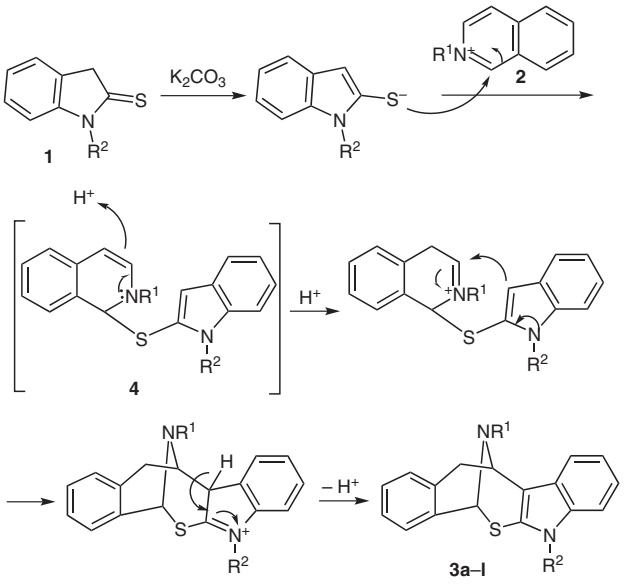


Figure 2 The key HMBC correlations of compound **3g**

In the next stage, we investigated the scope of the reaction with a linear thioamide, 4-(2-phenylethanethioyl)morpholine, as a tertiary thioamide and thioacetamide and thiobenzamide as primary thioamides under the optimized reaction conditions but no reaction was observed, and the initial isoquinolinium salt and thioamide were recovered.

A plausible mechanism for the formation of product is shown in Scheme 2. Indolin-2-thione **1** undergoes S-alkylation with the *N*-alkylisoquinolinium salt **2** affording the intermediate **4**. Subsequent intramolecular nucleophilic cyclization of **4** gives the desired product. All attempts to isolate intermediate **4** failed; although nucleophilic addition of indolic systems to olefins to form a carbon–carbon bond have been widely reported in the literature,[15] but effective alkylation of an indole with an olefin requires strong Lewis acids, an electron-deficient Michael acceptor, or prolonged heating under highly acidic conditions. Interestingly, the present intramolecular alkylation of indole takes place under mild conditions without any catalysts.



Scheme 2

In conclusion, we have reported a novel and highly efficient method for the synthesis of bridged polycyclic indolyltetrahydroisoquinolines. This method offers several advantages, such as high conversions, high selectivity, and experimental simplicity starting from easily accessible starting materials that make it a useful and attractive strategy for the preparation of polycyclic indolyltetrahydroisoquinolines in a single-step operation.

General Procedure for the Synthesis of Polycyclic Indole Derivatives 3a–l

A mixture of an isoquinolinium salt **1** (1 mmol), indoline-2-thione **2** (1 mmol), and K_2CO_3 (0.14 g, 1 mmol) in MeCN (5 mL) was stirred at r.t. for 3 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure, and the residue was separated by flash chromatography on a silica gel column with PE–EtOAc (10:1) as eluent to obtain pure products. The structures of the products were confirmed by the ^{1}H NMR, ^{13}C NMR, 2D NMR (H-H COSY, HMQC, HMBC) spectroscopic and elemental analysis.[16]

Acknowledgment

We would like to acknowledge the Islamic Development Bank (IDB) for financial backing to purchase a 500 MHz NMR spectrometer.

References and Notes

(1) Shamma, M. *Isoquinoline Alkaloids, Chemistry and Pharmacology*; Academic Press: New York, **1972**.
(2) (a) Scott, J. D.; Williams, R. M. *Chem. Rev.* **2002**, *102*, 1669. (b) Arai, T.; Kubo, A. *The Alkaloids*, Vol. 21; Academic: New York, NY, **1983**, 55–100. (c) Varadinova, T. L.; Shishkov, S. A.; Ivanovska, N. D.; Velcheva, M. P.; Danghaaghin, S.; Samadanghiin, Z.; Yansanghiin, Z. *Phytother. Res.* **1996**, *10*, 414. (d) Fujiwara, N.; Ueda, Y.; Ohashi, N. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 743.
(3) (a) Morrison, G. C.; Waite, R. O.; Serafin, F.; Shavel, J. *J. Org. Chem.* **1967**, *32*, 2551. (b) Zinnes, H.; Zuleski, F. R.; Shavel, J. *J. Org. Chem.* **1968**, *33*, 3605.
(4) (a) Yadav, J. S.; Reddy, B. V. S.; Yadav, N. N.; Gupta, M. K. *Tetrahedron Lett.* **2008**, *49*, 2815. (b) Parenty, A. D. C.; Smith, L. V.; Pickering, A. L.; Long, D. L.; Cronin, L. *J. Org. Chem.* **2004**, *69*, 5934. (c) Ho, T. L. *Tandem Organic Reactions*; Wiley and Sons: New York, **1992**. (d) Overman, L. E.; Velthuisen, E. J. *J. Org. Chem.* **2006**, *71*, 1581. (e) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (f) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207.
(5) Scriven, E. F. V. *Pyridines and their Benzo Derivatives:(ii) Reactivity at Ring Atoms,* In *Comprehensive Heterocyclic Chemistry*, Part 2A, Vol. 2; Boulton, A. J.; McKillop, A.; Katritzky, A. R.; Rees, C. W., Eds.; Elsevier Science: Oxford, **1984**, Chap. 2.05.
(6) Bradley, W.; Jeffrey, S. *J. Chem. Soc.* **1954**, 2770.
(7) (a) Diaba, F.; Le Houerou, C.; Grignon-Dubios, M.; Gerval, P. *J. Org. Chem.* **2000**, *65*, 907. (b) Yamaguchi, R.; Hatano, B.; Nakaysau, T.; Kozima, S. *Tetrahedron Lett.* **1997**, *38*, 403.
(8) (a) Akiba, K.; Nishihara, Y.; Wada, M. *Tetrahedron Lett.* **1983**, *24*, 5269. (b) Diaba, F.; Le Houerou, C.; Grignon-Dubois, M.; Rezzonico, B.; Gerval, P. *Eur. J. Org. Chem.* **2000**, 2915. (c) Itoh, T.; Nagata, K.; Miyazaki, M.; Kameoka, K.; Ohsawa, A. *Tetrahedron* **2001**, *57*, 8827. (d) Katritzky, A. R.; Zhang, S.; Kurz, T.; Wang, M. *Org. Lett.* **2001**, *3*, 2807. (e) Comins, D. L.; Sandelier, M. J.; Grillo, T. A. *J. Org. Chem.* **2001**, *66*, 6829.
(9) Yadav, J. S.; Reddy, B. V. S.; Gupta, M. K.; Prabhakar, A.; Jagadeesh, B. *Chem. Commun.* **2004**, 2124.
(10) Ullah, E.; Rotzoll, S.; Schmidt, A.; Michalik, D.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 8997.
(11) Jagodzinski, T. S. *Chem. Rev.* **2003**, *103*, 197.

(12) (a) Moghaddam, F. M.; Saeidian, H.; Mirjafary, Z.; Taheri, S.; Kheirjou, S. *Synlett* **2009**, 1047. (b) Moghaddam, F. M.; Mirjafary, Z.; Saeidian, H.; Javan, M. J. *Synlett* **2008**, 892. (c) Saeidian, H.; Sadeghi, A.; Mirjafary, Z.; Moghaddam, F. M. *Synth. Commun.* **2008**, *38*, 2043. (d) Moghaddam, F. M.; Saeidian, H.; Mirjafary, Z.; Sadeghi, A. *Lett. Org. Chem.* **2007**, *4*, 576. (e) Moghaddam, F. M.; Saeidian, H.; Mirjafary, Z.; Taheri, S. *J. Sulfur Chem.* **2006**, *27*, 545. (f) Moghaddam, F. M.; Zali Boinee, H. *Synlett* **2005**, 1612. (g) Moghaddam, F. M.; Zali Boinee, H. *Tetrahedron* **2004**, *60*, 6085. (h) Moghaddam, F. M.; Zali Boinee, H. *Tetrahedron Lett.* **2003**, *44*, 6253.

(13) Gözler, B. *The Alkaloids: Chemistry and Pharmacology* **1987**, *31*, 317.

(14) (a) Anet, F. A. L. *Can. J. Chem.* **1961**, *89*, 789. (b) Martell, M. J.; Soine, T. O.; Kier, L. B. *J. Am. Chem. Soc.* **1963**, *85*, 1022.

(15) (a) Youn, S. W.; Pastine, S. J.; Sames, D. *Org. Lett.* **2004**, *6*, 581. (b) Liu, C.; Han, X.; Wang, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 3700. (c) Morrison, G. C.; Waite, R. O.; Serafin, F.; Shavel, J. *J. Org. Chem.* **1967**, *32*, 2551. (d) Zhang, Z.; Wang, X.; Widenhoefer, R. A. *Chem. Commun.* **2006**, 3717.

(16) **Spectroscopic Data**

5-Ethyl-14-methyl-5,7,12,13-tetrahydro-7,13-epimino[2]benzothiocino[3,4-*b*]indole (3a)

Pale yellow solid; mp 163–165 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.5 Hz, 1 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.13–7.32 (m, 5 H), 7.05 (d, *J* = 7.5 Hz, 1 H), 5.78 (s, 1 H), 4.53 (d, *J* = 5.5 Hz, 1 H), 4.06 (m, 2 H), 3.61 (dd, *J* = 15.5, 5.5 Hz, 1 H), 3.15 (d, *J* = 15.5 Hz, 1 H), 2.65 (s, 3 H), 1.31 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 136.1 (C), 132.9 (C), 129.6 (CH), 128.0 (C), 127.9 (C), 127.8 (CH), 127.6 (CH) 126.1 (CH), 120.4 (CH), 119.3 (CH), 116.6 (CH), 108.7 (CH), 101.8 (C), 71.7 (CH), 52.6 (CH), 42.0 (CH_3), 38.4 (CH_2), 36.6 (CH_2), 15.4 (CH_3). Anal. Calcd for $C_{20}H_{20}N_2S$: C, 74.96; H, 6.29; N, 8.74. Found: C, 75.01; H, 6.31; N, 8.77.

14-Ethyl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3b)

White solid; mp 107–109 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (br s, NH, 1 H), 7.47 (d, *J* = 7.5 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.25 (d, *J* = 7.5 Hz, 1 H), 7.19 (t, *J* = 8.0 Hz, 1 H), 7.10–7.16 (m, 3 H), 7.03 (d, *J* = 8.0 Hz, 1 H), 5.86 (s, 1 H), 4.60 (d, *J* = 5.0 Hz, 1 H), 3.55 (dd, *J* = 16.0, 5.0 Hz, 1 H), 3.12 (d, *J* = 16.0 Hz, 1 H), 2.88 (m, 1 H), 2.73 (m, 1 H), 1.30 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 5.3 (C), 135.2 (C), 129.6 (CH), 127.9 (CH), 127.6 (CH), 127.4 (C), 126.7 (C), 126.2 (CH), 121.1 (CH), 119.9 (CH), 116.6 (CH), 116.5 (C), 110.5 (CH), 103.1 (C), 70.2 (CH), 50.6 (CH), 47.8 (CH_2), 36.5 (CH_2), 13.1 (CH_3). Anal. Calcd for $C_{19}H_{18}N_2S$: C, 74.47; H, 5.92; N, 9.14. Found: C, 74.92; H, 6.11; N, 9.25.

14-Benzyl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3c)

Yellow solid; mp 88–90 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68 (br s, NH, 1 H), 7.48 (d, *J* = 7.0 Hz, 2 H), 7.44 (d, *J* = 7.5 Hz, 1 H), 7.38 (t, *J* = 8.0 Hz, 2 H), 7.12–7.36 (m, 7 H), 7.04 (d, *J* = 7.5 Hz, 1 H), 5.72 (s, 1 H), 4.58 (d, *J* = 5.5 Hz, 1 H), 4.02 (d, *J* = 13.5 Hz, 1 H), 3.85 (d, *J* = 13.5 Hz, 1 H), 3.59 (dd, *J* = 16.0, 5.5 Hz, 1 H), 3.10 (d, *J* = 16.0 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.0 (C), 137.4 (C), 135.4 (C), 133.3 (C), 129.6 (CH), 129.5 (CH), 128.9 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 127.3 (C), 126.6 (C), 126.1 (CH), 121.2 (CH), 119.9 (CH), 116.7 (CH), 110.5 (CH), 103.1 (C), 70.2 (CH), 58.1 (CH_2), 50.8 (CH), 36.5 (CH_2). Anal. Calcd for $C_{24}H_{20}N_2S$: C, 78.23; H, 5.47. N, 7.60. Found: C, 78.66; H, 5.83; N, 7.63.

14-Prop-2-yn-1-yl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3d)

White solid; mp 131–133 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (s, 1 H, NH), 7.49 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 7.5 Hz, 1 H), 7.12–7.26 (m, 5 H), 7.03 (d, *J* = 7.5 Hz, 1 H), 6.01 (s, 1 H), 4.68 (d, *J* = 5.5 Hz, 1 H), 3.62 (dd, *J* = 16.0, 2.5 Hz, 1 H), 3.61 (dd, *J* = 15.5, 5.5 Hz, 1 H), 3.51 (dd, *J* = 16.0, 2.5 Hz, 1 H), 3.13 (d, *J* = 15.5 Hz, 1 H), 3.39 (t, *J* = 2.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.8 (C), 135.5 (C), 132.9 (C), 129.5 (CH), 128.0 (CH), 127.7 (CH), 127.1 (C), 126.3 (CH), 125.8 (C), 121.4 (CH), 120.1 (CH), 116.7 (CH), 110.6 (CH), 102.7 (C), 79.8 (C), 73.7 (C), 68.3 (CH), 51.0 (CH), 43.2 (CH_2), 36.5 (CH_2). Anal. Calcd for $C_{20}H_{16}N_2S$: C, 75.92; H, 5.10; N, 8.85. Found: C, 75.62; H, 5.23; N, 8.83.

14-Methyl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3e)

Yellow solid; mp 125–127 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (br s, NH, 1 H), 7.49 (d, *J* = 7.5 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.11–7.22 (m, 5 H), 7.04 (d, *J* = 7.5 Hz, 1 H), 5.73 (s, 1 H), 4.49 (d, *J* = 5.0 Hz, 1 H), 3.59 (dd, *J* = 16.0, 5.0 Hz, 1 H), 3.13 (d, *J* = 16.0 Hz, 1 H), 2.67 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.36 (C), 135.42 (C), 132.8 (C), 129.6 (CH), 127.9 (CH), 127.5 (CH), 127.4 (C), 126.2 (CH), 126.1 (C), 121.2 (CH), 119.9 (CH), 116.6 (CH), 110.6 (CH), 102.7 (C), 72.0 (CH), 52.3 (CH), 42.0 (CH_3), 36.5 (CH_2). Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.94; H, 5.52 N, 9.58. Found: C, 74.12; H, 5.71; N, 9.55.

5,14-Dimethyl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3f)

Yellow solid; mp 164–166 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (m, 1 H), 7.37 (d, *J* = 7.5 Hz, 1 H), 7.13–7.28 (m, 5 H), 7.04 (d, *J* = 7.5 Hz, 1 H), 5.78 (s, 1 H), 4.52 (d, *J* = 5.0 Hz, 1 H), 3.60 (dd, *J* = 15.5, 5.5 Hz, 1 H), 3.56 (s, 3 H), 3.15 (d, *J* = 15.5 Hz, 1 H), 2.63 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 137.1 (C), 132.9 (C), 129.5 (CH), 128.9 (C), 127.9 (CH), 127.6 (CH), 126.1 (CH), 119.3 (CH), 116.5 (CH), 108.5 (CH), 101.7 (C), 71.9 (CH), 52.6 (CH), 41.9 (CH_3), 36.6 (CH_2), 29.7 (CH_3). Anal. Calcd for $C_{19}H_{18}N_2S$: C, 74.47; H, 5.92; N, 9.14. Found: C, 74.32; H, 6.11; N, 9.18.

14-Methyl-5-phenyl-5,7,12,13-tetrahydro-7,13-epimino[2]benzothiocino[3,4-*b*]indole (3g)

Yellow solid; mp 170–172 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.0 Hz, 1 H), 7.53 (t, *J* = 7.5 Hz, 1 H), 7.52 (d, *J* = 7.5 Hz, 1 H), 7.43 (m, 3 H), 7.30 (t, *J* = 8.5 Hz, 2 H), 7.23 (t, *J* = 7.5 Hz, 1 H), 7.08–7.18 (m, 4 H), 5.69 (s, 1 H), 4.58 (d, *J* = 5.0 Hz, 1 H), 3.66 (dd, *J* = 16.0, 5.0 Hz, 1 H), 3.24 (d, *J* = 16.0 Hz, 1 H), 2.69 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.45 (C), 137.4 (C), 137.2 (C), 132.7 (C), 129.7 (CH), 129.6 (CH), 129.0 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 126.2 (CH), 121.3 (CH), 120.4 (CH), 116.6 (CH), 109.9 (CH), 103.5 (C), 71.4 (CH), 52.6 (CH), 42.1 (CH_3), 36.5 (CH_2). Anal. Calcd for $C_{22}H_{20}N_2S$: C, 78.23; H, 5.47; N, 7.60. Found: C, 78.37; H, 5.80; N, 7.64.

14-Prop-2-yn-1-yl-5,7,12,13-tetrahydro-7,13-epimino[2]benzothiocino[3,4-*b*]indole (3h)

Yellow solid; mp 183–185 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.0 Hz, 1 H), 7.49–7.56 (m, 4 H), 7.04–7.46 (m, 4 H), 7.10–7.26 (m, 5 H), 5.63 (s, 1 H), 5.41 (d, *J* = 6.0 Hz, 1 H), 3.86 (dd, *J* = 16.0, 6.0 Hz, 1 H), 3.31–3.40 (m, 3 H), 2.38 (t, *J* = 2.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.4 (C), 137.3 (C), 137.1 (C), 133.4 (C), 129.8 (CH), 129.6 (CH), 129.4 (C), 128.1 (C), 127.9 (CH), 127.6 (CH), 127.3 (CH), 125.2 (CH), 121.2 (CH), 120.3 (CH), 116.6

(CH), 109.8 (CH), 103.9 (C), 80.3 (C) 74.6 (C) 69.3 (CH), 50.9 (CH), 47.8 (CH_2), 36.6 (CH_2).

14-Ethyl-5-phenyl-5,7,12,13-tetrahydro-7,13-epimino[2]benzothiocino[3,4-*b*]indole (3i)

Pale yellow solid; mp 178–180 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.30–7.43 (m, 5 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.07–7.18 (m, 4 H), 5.82 (s, 1 H), 4.68 (d, *J* = 5.0 Hz, 1 H), 3.62 (dd, *J* = 15.5, 5.5 Hz, 1 H), 3.22 (d, *J* = 15.5 Hz, 1 H), 2.92 (m, 1 H), 2.78 (m, 1 H), 1.32 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 137.2 (C), 137.1 (C), 133.1 (C), 129.7 (CH), 129.6 (CH), 129.5 (C), 128.1 (C), 127.9 (CH), 127.8 (CH), 127.3 (CH), 126.2 (CH), 121.2 (CH), 120.3 (CH), 116.6 (CH), 109.8 (CH), 103.9 (C), 69.3 (CH), 50.9 (CH), 47.8 (CH_2), 36.6 (CH_2), 13.2 (CH_3).

14-Ethyl-5-methyl-5,7,12,13-tetrahydro-7,13-epimino[2]benzothiocino[3,4-*b*] indole (3j)

Pale yellow solid; mp 167–169 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 7.12–7.27 (m, 5 H), 7.03 (d, *J* = 7.5 Hz, 1 H), 4.63 (d, *J* = 4.5 Hz, 1 H), 3.56 (dd, *J* = 16.0, 4.5 Hz, 1 H), 3.50 (s, 3 H), 3.13 (d, *J* = 16.0 Hz, 1 H), 2.86 (m, 1 H), 2.71 (m, 1 H), 1.30 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 137.0 (C), 133.4 (C), 129.5 (CH), 129.4 (CH), 127.8 (CH), 127.7 (CH), 127.6 (C) 126.1 (CH), 120.4 (CH), 119.3 (CH), 116.4 (CH), 108.5 (CH), 102.1 (C), 70.0 (CH), 50.8 (CH), 47.81 (CH_2), 36.7 (CH_2), 29.7 (CH_3), 13.1 (CH_3). Anal. Calcd for $C_{20}H_{20}N_2S$; C, 74.92; H, 6.29; N, 8.74. Found: C, 75.10; H, 6.48; N, 8.88.

5,14-Diethyl-5,7,12,13-tetrahydro-7,13-epimino[2]-benzothiocino[3,4-*b*]indole (3k)

Pale yellow solid; mp 151–153 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.5 Hz, 1 H), 7.39 (d, *J* = 7.5 Hz, 1 H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.13–7.22 (m, 4 H), 7.05 (d, *J* = 7.5 Hz, 1 H), 4.65 (d, *J* = 5.0 Hz, 1 H), 4.02 (m, 2 H), 3.58 (dd, *J* = 15.5, 5.0 Hz, 1 H), 3.16 (d, *J* = 15.5 Hz, 1 H), 2.89 (m, 1 H), 2.73 (m, 1 H), 1.33 (t, *J* = 7.0 Hz, 3 H), 1.31 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.5 (C), 136.0 (C), 133.4 (C), 129.6 (CH), 128.6 (C), 127.89 (C), 127.83 (CH), 127.74 (CH) 126.1 (CH), 120.4 (CH), 119.27 (CH), 116.59 (CH), 108.6 (CH), 102.2 (C), 69.8 (CH), 50.8 (CH), 47.8 (CH_2), 38.4 (CH_2), 36.7 (CH_2), 15.4 (CH_3), 13.1 (CH_3). Anal. Calcd for $C_{21}H_{22}N_2S$: C, 75.41; H, 6.63; N, 8.38. Found: C, 75.84; H, 6.57; N, 8.29.

14-Allyl-5-methyl-5,7,12,13-tetrahydro-7,13-epimino-[2]benzothiocino[3,4-*b*]indole (3l)

White solid; mp 167–169 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 7.5 Hz, 1 H), 7.29 (d, *J* = 7.5 Hz, 1 H), 7.13–7.23 (m, 4 H), 7.05 (d, *J* = 7.5 Hz, 1 H), 6.05 (m, 1 H), 5.87 (s, 1 H), 5.41 (d, *J* = 17.0 Hz, 1 H), 5.32 (d, *J* = 10.0 Hz, 1 H), 4.64 (d, *J* = 4.5 Hz, 1 H), 3.61 (dd, *J* = 15.5, 4.5 Hz, 1 H), 3.57 (s, 3 H), 3.48 (dd, *J* = 14.0, 6.0 Hz, 1 H), 3.30 (dd, *J* = 14.0, 6.0 Hz, 1 H), 3.15 (d, *J* = 16.0 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.4 (C), 137.1 (C), 134.9 (CH), 133.4 (C), 129.6 (CH), 129.2 (C), 127.9 (CH), 127.7 (CH), 127.5 (C) 126.1 (CH), 120.5 (CH), 119.4 (CH), 119.3 (C), 116.6 (CH), 108.6 (C), 102.16 (CH_2), 69.8 (CH), 56.8 (CH_2), 50.9 (CH), 36.7 (CH_2), 29.8 (CH_3). Anal. Calcd for $C_{21}H_{20}N_2S$: C, 75.87; H, 6.06; N, 8.43. Found: C, 75.92; H, 6.14; N, 8.52.