Tetrahedron 65 (2009) 2178–2183

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A one-pot synthesis and 1,3-dipolar cycloaddition of [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones

Lidia S. Konstantinova, Kirill A. Lysov, Stanislav A. Amelichev, Natalia V. Obruchnikova, Oleg A. Rakitin *

N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospect, 47, 119991 Moscow, Russia

ARTICLE INFO

Article history:
Received 18 November 2008
Received in revised form 23 December 2008
Accepted 15 January 2009
Available online 21 January 2009

Keywords:
Sulfur–nitrogen heterocycles
Fused 3*H*-1,2-dithiole-3-thiones
Cycloaddition
DMAD
1,3-Dipoles

ABSTRACT

Treatment of *N*-substituted 2-methyl-1*H*-indoles **1** with S_2Cl_2 and DABCO in chloroform gave the corresponding [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5** by the addition of triethylamine in high yield. 1,2-Dithiole-3-thiones **5** underwent cycloaddition with one or two DMAD equivalents to afford either 2-(3-thioxo-1,3-dihydro-2*H*-indol-2-ylidene)-1,3-dithioles **10** or fused 4,5-dihydrothiopyrano[3,2-*b*]indoles **9**.

1. Introduction

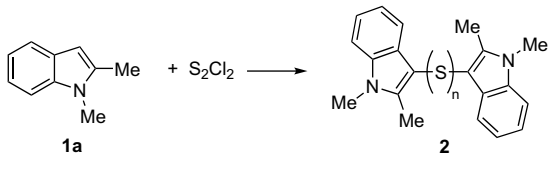
Despite the continuous interest in indoles,[1] only a limited number of polysulfur-containing derivatives of compounds that belong to this class have been reported. One of the examples is 5,10-dihydro-[1,2,3,4]tetrathiocino[5,6-*b*;8,7-*b*]diindole, which is a potent antifungal agent with particularly strong activity against *Botrytis cinerea*.[2] 2-Thioindole derivatives have been demonstrated to be useful intermediates in the synthesis of 2,2′-dithiobisindole tyrosine kinase inhibitors.[3] Indoles fused with sulfur heterocycles have attracted much attention; e.g., 6-chloro-8*H*-thieno[2,3-*b*]indole-2-carboxamide was isolated from the *Streptomyces albogriseolus* culture broth and was shown to have both growth promoting and inhibition activities in rice seedlings.[4] 6-Methylpentathiepino[6,7-*b*]indole have been proposed as a cathode material for storage batteries.[5]

Indoles fused with the 1,2-dithiole-3-thione ring could be of interest as condensed 3*H*-1,2-dithiole-3-thiones, which have a broad spectrum of biological activity and may be useful synthons for many sulfur heterocycles.[6] Few 1,2-dithioloindoles, including non-substituted [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thione[7] and [1,2]dithiolo[3,4-*b*]indole-3(8*H*)-thione[8] and its *N*-methyl derivative,[9] are known, and their syntheses are not of general character and the yields are low. Also the chemistry of dithioloindole thiones has not practically been investigated.

We have recently shown that *N*-isopropyl groups can be converted by S_2Cl_2 into *N*-(1,2-dithiole-3-thiones).[10] Nitrogen heterocycles containing methyl and C–H groups in *ortho*-positions, such as the easily available and even commercial 2- and 3-methylindole, are structurally similar to the isopropyl group and may be considered as potential intermediates in the synthesis of dithioloindole thiones. Fused 1,2-dithole-3-thiones have never been generated from methyl heterocycles bearing C–H groups in *ortho*-positions. In this paper we report a one-pot synthesis of [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones from *N*-substituted 2-methylindoles and their 1,3-dipolar cycloaddition to DMAD.

2. Results and discussion

Treatment of 1,2-dimethylindole **1** with S_2Cl_2 in chloroform for 48 h at room temperature gave a mixture of bis-indoles **2**



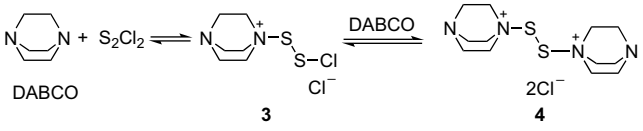
1a **2**

n = 2-4

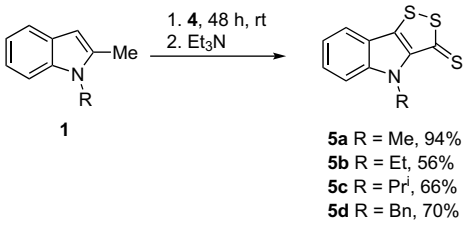
Scheme 1. Reaction of 1,2-dimethylindole with S_2Cl_2.

* Corresponding author. Tel.: +7 499 135 53 27; fax: +7 499 135 53 28.
E-mail address: orakitin@ioc.ac.ru (O.A. Rakitin).

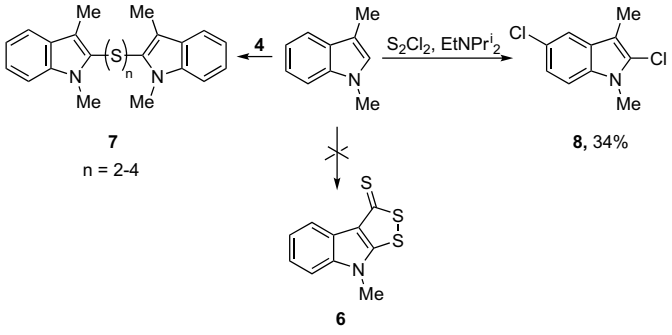
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.01.069



Scheme 2. Complexes **3** and **4**.



Scheme 3. Synthesis of *N*-substituted [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5**.



Scheme 4. Reaction of 1,3-dimethylindole with S_2Cl_2.

connected by two, three, and four sulfur atoms in low yields (NMR and mass spectral data) and the 2-methyl group in indole remains intact under the action of S_2Cl_2 (Scheme 1).

In an attempt to increase the sulfurating ability of S_2Cl_2 we used in this reaction complexes **3** and **4** formed from S_2Cl_2 and 1,4-diazabicyclooctane (DABCO) in ratios 1:1 and 1:2, respectively (Scheme 2).[11] Recently we have shown that these complexes can convert *N*-alkylpyrroles into *N*-alkylpentathiepinopyrroles[11] or bis(dithiolo)pyrroles[12] in high yield.

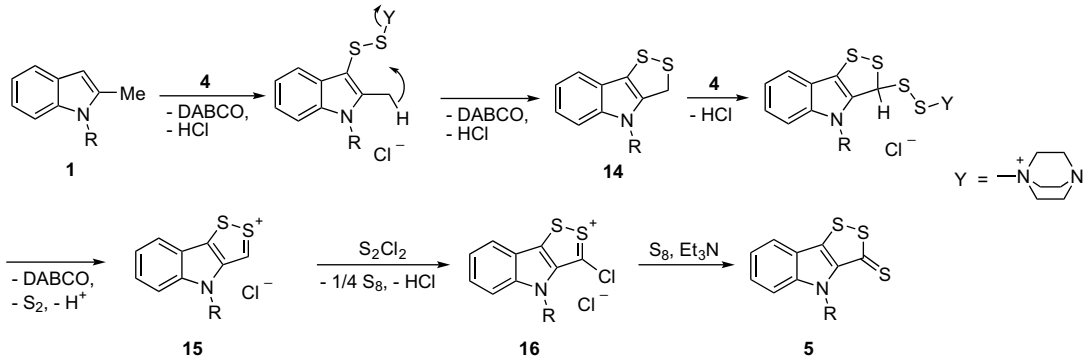
Reaction of 1,2-dimethylindole **1a** with a fivefold excess of complex **3** in chloroform for 48 h at room temperature led after treatment with Et_3N to dithiole thione **5a** in moderate yield (34%). Unsurprisingly, complex **4**, a more selective sulfurating agent, reacted with **1a** in the same conditions more cleanly to afford thione **5a** in high yield (Scheme 3).

Further on, we extended this reaction to other *N*-substituted 2-methylindoles **1**. Fused dithioloindoles **5** were obtained in a reaction with *N*-alkyl- and *N*-benzyl-2-methylindoles **1** in moderate to high yields. *N*-Acetyl- and *N*-benzoyl-2-methylindole did not react with S_2Cl_2 and their complexes **3** and **4** even under forcing conditions (refluxing for 5 h in chloroform); the starting indoles were isolated from the reaction mixtures in high yields. Apparently electron-withdrawing substituents at nitrogen in indole (acetyl or benzoyl groups) suppress the reaction with S_2Cl_2 even under more vigorous conditions.

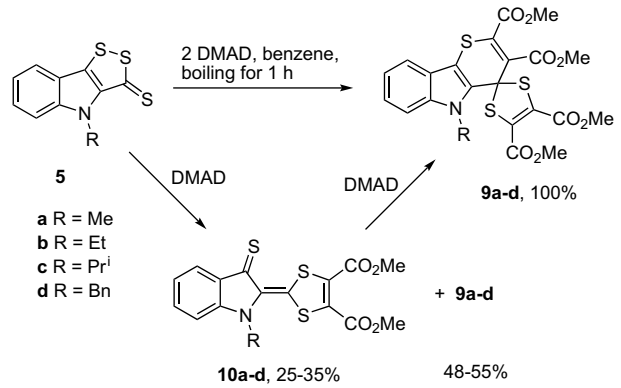
To prepare isomers of indolodithioles **5**—[1,2]dithiolo[3,4-*b*]indole-3(8*H*)-thiones **6**—the reaction of 1,3-dimethylindole with S_2Cl_2 and its complexes with DABCO was investigated in detail. Treatment of 1,3-dimethylindole with complex **4** in chloroform at room temperature for 3 days led to a mixture of polysulfides **7** analogous to **2** prepared from 1,2-dimethylindole and S_2Cl_2. Complex **3** and S_2Cl_2 also did not give dithioloindole **6**. Only traces of 2,5-dichloro-1,3-dimethyl-1*H*-indole **8** were detected in the reaction mixture. A reaction with a more powerful mixture of S_2Cl_2 and *N*-ethyldiisopropylamine[13] in chloroform at 0 °C for 3 days gave this product **8** in moderate yield (Scheme 4). Disulfur dichloride chlorinated both pyrrole and benzene rings in the indole molecules under these conditions but not react with the 3-methyl group.

The 3-methyl group in 1,3-dimethylindole was found to be non-reactive toward S_2Cl_2 and its mixtures in contrast to the 2-methyl group in 1,2-dimethylindole. The ready reactivity of the 2-methyl group can be explained by the low acidity of the 2-methyl hydrogens.[14] The most plausible mechanism for the formation of 1,2-dithole-3-thiones **5** is given in Scheme 5. The key steps are assumed to be similar to those to produce 1,2-dithiole-3-thiones from tertiary *N*-isopropylamines[15] and involve the addition of the S_2Cl_2 molecule with the formation of 1,2-dithiole ring **14** and further oxidation to dithiolium salt **15**, and chlorination to 3-chlorodithiolium salt **16**. Sulfur nucleophiles generated from sulfur and triethylamine are likely to produce thione **5** (Scheme 5).

Depending on the reactivity, fused 1,2-dithiole-3-thiones undergo cycloaddition to one or two molecules of activated acetylenes bearing two electron-withdrawing groups,[16] however, it is hard to predict that. We wished to compare the reactivity of *N*-substituted [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5** and 8-methyl[1,2]dithiolo[3,4-*b*]indole-3(8*H*)-thione **6**.[9] Thione **5a** was the first to be subjected to a reaction with a typical acetylene with two electron-withdrawing groups, i.e., dimethyl acetylenedicarboxylate (DMAD). Thus, the reaction of **5a** (1 equiv) and DMAD (2.4 equiv) in benzene refluxing for 1 h gave product **9a**, a yellow solid, in quantitative yield. The mass spectrometry and microanalysis showed **9a** to be a 1:2 adduct with the composition $C_{22}H_{21}NO_8S_3$. Its ^{13}C and ^1H NMR spectra confirmed the structure. By analogy, reactions of other



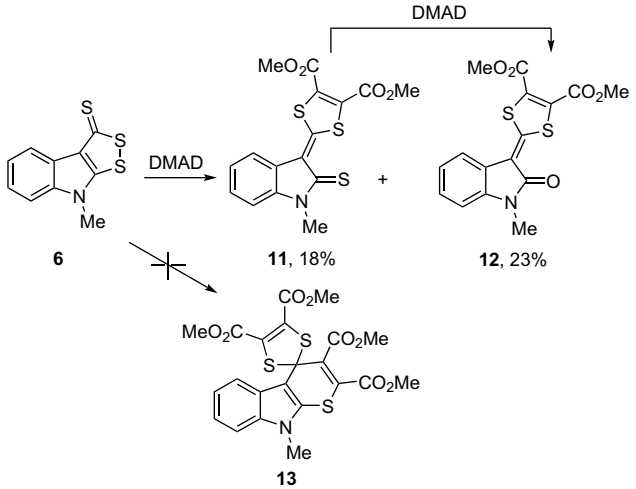
Scheme 5. A plausible mechanism for the formation of [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5**.



Scheme 6. Reaction of 1,2-dithiole-3-thiones **5** with DMAD.

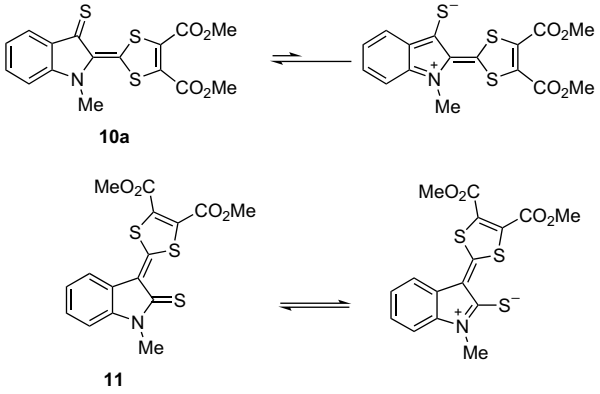
N-substituted [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5** and DMAD in the same ratio and in the same conditions gave, respectively, products **9** in the form of yellow solids, all in practically quantitative yields. It was observed (TLC) that in each reaction a blue spot initially appeared, which then disappeared as the reactants were consumed. We concluded that under thermal conditions the first cycloaddition reaction of **5** with DMAD was more energy demanding than the corresponding reaction of the expected highly reactive 1:1 cycloadduct **10** and DMAD. In search of the intermediate 1:1 adduct **10** we performed a reaction of **5** (1 equiv) and DMAD (1 equiv) in benzene at lower temperature. During 3 days, both at 5 °C and at room temperature, we managed to isolate monoadducts **10** (25–35%) and bisadducts **9** (48–55%) after chromatography (Scheme 6). Monoadducts **10** reacted with 1 equiv of DMAD in benzene refluxing for a few minutes to give **9** in quantitative yield.

Treatment of thione **6** (1 equiv) with a DMAD excess (2.4 equiv) in benzene under reflux (1 h) gave monoadduct **11** (18%)[8] along with ketone **12** (23%) (Scheme 7). No traces of the expected 1:2 adduct **13** were observed. Only product **11** was obtained in high yield (72%) in the reaction of **6** (1 equiv) and DMAD (1.2 equiv) in benzene at room temperature. The generation of ketone **12** in the reactions of 1,2-dithiole-3-thione **6** with DMAD was unexpected, and we investigated this process further. Thione **6** was found to be perfectly stable in benzene solutions under reflux for 10 h, yet the reaction with DMAD (a fivefold excess) in refluxing benzene gave ketone **12** in moderate yield (65%).



Scheme 7. Reaction of 1,2-dithiole-3-thione **6** with DMAD.

Compounds similar to **10** and **11** readily react as heterodienes with activated alkynes to give fused 4*H*-thiopyranes.[16d,e] In our case, only 1,3-dithioles **10** formed 1:2 adducts **9** by treatment with DMAD. On the contrary, adduct **11**, which is a regio isomer of **10a**, did not react with the second DMAD molecule as a dienophile. Apparently, the reason for this is a different reactivity of the two thione groups in **11** and **10a**. The thione group in **11** structurally is a thioamide group neutral to 1,3-dipolar cycloaddition. Also isomers **10a** and **11** have a striking difference in color and electronic spectra: **10a** is crystallized as violet plates with hν 578 nm (lg ε=3.79) and **11** as red prisms (hν 450 nm (lg ε=3.92)). This difference can be explained by an additional opportunity of electronic delocalization for **11** and its low possibility for **10a** due to a loss of the indole ring aromaticity (Scheme 8).



Scheme 8. Resonance structures for **10a** and **11**.

3. Conclusion

The reaction of *N*-substituted 2-methylindoles with S_2Cl_2 provides a new route to [1,2]dithiolo[4,3-*b*]indole-3(4*H*)-thiones **5**, which are of special interest as biologically active compounds. The novelty of the reaction is the formation of condensed 1,2-dithiole-3-thiones from methyl-substituted heterocycles (in our case 2-methylindoles). The described experimental procedures may serve as an efficient basis for a new synthesis of fused 1,2-dithiole-3-thiones from methyl-substituted heterocycles and their further cycloaddition to highly branched sulfur heterocycles.

4. Experimental

4.1. General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Specord M-80 instrument in KBr pellets. ^{1}H NMR spectra were recorded on a Bruker WM 250 spectrometer (250 MHz) and ^{13}C NMR spectra were recorded on a Bruker AM 300 (75.5 MHz) in $CDCl_3$ or pyridine-d_5 solutions with TMS as an internal standard. *J* values are given in hertz. Mass spectra were recorded on a Finnigan MAT INCOS 50 instrument using electron impact ionization. UV spectra were recorded on a Specord UV–VIS. Elemental analyses were performed on Perkin Elmer 2400 Elemental Analyser.

Compounds **1**[17] and **6**[9] were prepared as previously reported.

*4.1.1. General procedure for the preparation of N-substituted [1,2]dithiolo[4,3-b]indole-3(4H)-thiones **5***

Disulfur dichloride (0.4 mL, 5 mmol) was added dropwise at −25 to −35 °C to a stirred solution of DABCO (1.12 g, 10 mmol) in chloroform (25 mL) under argon. The mixture was stirred at room

temperature for 1 h. The corresponding *N*-substituted 2-methyl-1*H*-indole **1** (1 mmol) in chloroform (5 mL) was added and the mixture was stirred at room temperature for 48 h under argon. Then Et_3N (1.4 mL, 10 mmol) was added at 0 °C, the mixture was stirred at room temperature for 2 h, refluxed for 3 h, filtered, and the solvents were evaporated. The residue was separated by column chromatography (Silica gel Merck 60, light petroleum and then light petroleum–CH_2Cl_2 mixtures).

*4.1.1.1. 4-Methyl[1,2]dithiolo[4,3-b]indole-3(4H)-thione (**5a**).* Yield 94%. Orange crystalline solid, mp 165–167 °C; R_f=0.69 (CH_2Cl_2). Anal. Calcd for $C_{10}H_7NS_3$: C, 50.60; H, 2.97; N, 5.90. Found: C, 50.42; H, 2.87; N, 6.02. $C_{10}H_7NS_3$ requires M, 236.9741. Found M^+, 236.9741. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 4.30 (3H, s, CH_3), 7.25 (1H, m, Ar), 7.44 (1H, d, *J* 8.5, Ar), 7.57 (1H, m, Ar), 7.77 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 28.9 (CH_3), 111.5, 121.0, 121.2, and 129.1 (4 CH), 120.4, 141.0, 141.1, and 146.3 (four sp^2 tertiary C), 195.3 (C=S). MS (EI, 70 eV), *m*/*z* (%): 237 (M^+, 100), 204 (48), 191 (40), 145 (36). UV λ_{max} ($CHCl_3$) 256 (lg ε=3.93), 340 (4.14), 381 (3.85), 463 (3.95). IR (KBr): ν=1612, 1436, 1336, 1228, 1132, 1040, 900, 736 cm^{-1}.

*4.1.1.2. 4-Ethyl[1,2]dithiolo[4,3-b]indole-3(4H)-thione (**5b**).* Yield 56%. Orange crystalline solid, mp 90–91 °C; R_f=0.71 (CH_2Cl_2). Anal. Calcd for $C_{11}H_9NS_3$: C, 52.55; H, 3.61; N, 5.57. Found: C, 52.53; H, 3.78; N, 5.58. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.37 (3H, t, *J* 7.2, CH_3), 4.83 (2H, q, *J* 7.2, CH_2), 7.18 (1H, m, Ar), 7.38 (1H, d, *J* 8.5, Ar), 7.50 (1H, m, Ar), 7.70 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 16.0 (CH_3), 37.7 (CH_2), 111.6, 121.1, 121.4, and 129.1 (4CH), 120.7, 140.7, 141.3 and 145.4 (four sp^2 tertiary C), 194.8 (C=S). MS (EI, 70 eV), *m*/*z* (%): 251 (M^+, 100), 236 (75), 223 (42), 218 (20), 191 (39). IR (KBr): ν=1612, 1480, 1340, 1208, 1050, 908, 752 cm^{-1}.

*4.1.1.3. 4-Isopropyl[1,2]dithiolo[4,3-b]indole-3(4H)-thione (**5c**).* Yield 66%. Orange crystalline solid, mp 104–107 °C; R_f=0.73 (CH_2Cl_2). Anal. Calcd for $C_{12}H_{11}NS_3$: C, 54.30; H, 4.18; N, 5.28. Found: C, 54.58; H, 4.34; N, 5.26. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.70 (6H, d, *J* 7.4, CH_3), 4.74 (1H, septet, *J* 7.4, CH), 7.23 (1H, m, Ar), 7.51 (1H, d, *J* 7.4, Ar), 7.71 (1H, m, Ar), 7.78 (1H, d, *J* 8.1, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.3 (CH_3), 44.0 (CH), 114.6, 120.7, 121.6, and 128.6 (4CH), 121.0, 139.8, 142.1, and 144.2 (four sp^2 tertiary C), 195.2 (C=S). MS (EI, 70 eV), *m*/*z* (%): 265 (M^+, 100), 250 (97), 232 (17), 223 (98), 191 (57), 146 (75). IR (KBr): ν=1608, 1464, 1332, 1228, 1140, 1028, 912, 736 cm^{-1}.

*4.1.1.4. 4-Benzyl[1,2]dithiolo[4,3-b]indole-3(4H)-thione (**5d**).* Yield 70%. Orange crystalline solid, mp 120–123 °C; R_f=0.62 (CH_2Cl_2). Anal. Calcd for $C_{16}H_{11}NS_3$: C, 61.31; H, 3.54; N, 4.47. Found: C, 61.56; H, 3.69; N, 4.46. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.20 (2H, s, CH_2), 7.25 (6H, m, Ar), 7.38 (1H, d, *J* 8.5, Ar), 7.47 (1H, m, Ar), 7.80 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 44.2 (CH_2), 112.4, 121.3, 121.4, 127.0, 127.5, 128.7, and 129.2 (7CH), 120.7, 137.2, 140.4, 141.8, and 145.9 (five sp^2 tertiary C), 194.7 (C=S). MS (EI, 70 eV), *m*/*z* (%): 313 (M^+, 17), 280 (13), 264 (7), 249 (6), 191 (15). IR (KBr): ν=1608, 1472, 1436, 1332, 1252, 1060, 880, 744 cm^{-1}.

*4.1.2. 8-Methyl[1,2]dithiolo[3,4-b]indole-3(8H)-thione (**6**)*

Yellow crystalline solid, mp 232–233 °C, lit.[9] mp 234–236 °C; R_f=0.68 (CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.73 (3H, s, CH_3), 7.30 (2H, m, Ar), 7.38 (1H, m, Ar), 8.55 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 32.3 (CH_3), 110.9, 118.0, 122.7, and 124.8 (4CH), 122.1, 127.5, 143.8, and 162.6 (four sp^2 tertiary C), 198.1 (C=S). MS (EI, 70 eV), *m*/*z* (%): 237 (M^+, 100), 204 (62), 191 (24), 172 (17), 160 (37). UV λ_{max} ($CHCl_3$) 288 (lg ε=4.23), 342 (4.05), 398 (3.85). IR (KBr): ν=1584, 1480, 1464, 1312, 1200, 1128, 1076, 980, 744 cm^{-1}.

*4.1.3. 2,5-Dichloro-1,3-dimethyl-1H-indole (**8**)*

Disulfur dichloride (1 mL, 12.5 mmol) was added dropwise at −35 to −25 °C to a stirred solution of anhydrous *N*-ethyldiisopropylamine (1.6 g, 12.5 mmol) in chloroform (100 mL) under argon. The mixture was stirred at this temperature for 1 h. 1,3-Dimethylindole (0.36 g, 2.5 mmol) in chloroform (10 mL) was added, the mixture was stirred for 72 h at 0 °C, filtered, and the solvents were evaporated. The residue was separated by column chromatography (Silica gel Merck 60, light petroleum and then light petroleum–CH_2Cl_2 mixtures), yield 180 mg (34%). Yellow oil, R_f=0.65 (CH_2Cl_2/light petroleum, 1:1). Anal. Calcd for $C_{10}H_9Cl_2N$: C, 56.10; H, 4.24; N, 6.54. Found: C, 56. 01; H, 4.18; N, 6.72. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.29 (3H, s, C–CH_3), 3.63 (3H, s, N–CH_3), 7.12 (1H, d, *J* 10.4, Ar), 7.22 (1H, s, Ar), 7.38 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 8.7 (C–CH_3), 29.8 (N–CH_3), 109.0, 119.2, and 120.1 (3CH), 107.7, 124.1, 125.8, 127.8, and 135.9 (five sp^2 tertiary C). MS (EI, 70 eV), *m*/*z* (%): 213 (M^+, 88), 178 (100), 162 (25), 128 (23).

*4.1.4. General procedure for the reaction of N-substituted dithioloindole thiones **5** and **6** with DMAD*

DMAD (1.2 or 2.4 mmol) was added to a solution of appropriate dithioloindolethione (1 mmol) in benzene (7 mL) at room temperature. The reaction mixture was stirred for 24 h at room temperature or refluxed for 1 h and solvent was evaporated under reduced pressure. The residue was separated by column chromatography (Silica gel Merck 60, light petroleum, then light petroleum–CH_2Cl_2 mixtures, then CH_2Cl_2). Quantity of reagents is given in the text.

*4.1.4.1. Tetramethyl 5′-methyl-5′H-spiro[1,3-dithiole-2,4′-thiopyrano[3,2-b]indole]-2′,3′,4,5-tetracarboxylate (**9a**).* Yield 100%. Yellow crystalline solid, mp 201–203 °C; R_f=0.47 (CH_2Cl_2). Anal. Calcd for $C_{22}H_{19}NO_8S_3$: C, 50.66; H, 3.67; N, 2.69. Found: C, 50.40; H, 3.84; N, 2.68. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.77 (6H, s, CH_3), 3.80 (3H, s, CH_3), 3.87 (3H, s, CH_3), 4.13 (3H, s, N–CH_3), 7.24 (1H, m, Ar), 7.44 (1H, m, Ar), 7.62 (1H, d, *J* 8.1, Ar), 7.74 (1H, d, *J* 8.6, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.2 (N–CH_3), 53.2, 53.3, and 53.8 ($3CH_3$), 65.7 (sp^3 tertiary), 102.1, 122.0, 122.6, 125.2, 128.0, and 139.4 (six sp^2 tertiary C), 110.1, 118.9, and 127.3 (3CH), 160.8, 164.0, and 165.8 (3C=O). MS (EI, 70 eV), *m*/*z* (%): 521 (M^+, 9), 462 (31), 430 (7), 346 (27). UV λ_{max} ($CHCl_3$) 284 (lg ε=4.21), 396 (3.63). IR (KBr): ν=1736 (C=O), 1560, 1432, 1248, 1020, 936, 744 cm^{-1}.

*4.1.4.2. Tetramethyl 5′-ethyl-5′H-spiro[1,3-dithiole-2,4′-thiopyrano[3,2-b]indole]-2′,3′,4,5-tetracarboxylate (**9b**).* Yield 100%. Yellow crystalline solid, mp 205–206 °C; R_f=0.49 (CH_2Cl_2). Anal. Calcd for $C_{23}H_{21}NO_8S_3$: C, 51.58; H, 3.95; N, 2.62. Found: C, 51.73; H, 4.23; N, 2.52. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.61 (3H, t, *J* 7.3, CH_3), 3.83 (6H, s, CH_3), 3.90 (3H, s, CH_3), 3.93 (3H, s, CH_3), 4.78 (2H, q, *J* 7.3, CH_2), 7.24 (1H, m, Ar), 7.46 (3H, m, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 13.8 (CH_2CH_3), 41.0 (CH_2CH_3), 53.2, 53.3, 53.5, and 53.8 ($4CH_3$), 66.1 (sp^3 tertiary), 102.4, 121.8, 123.0, 127.3, 128.4, and 138.4 (six sp^2 tertiary C), 110.8, 119.0, 121.1, and 125.2 (4CH), 160.8, 163.9, and 165.8 (3C=O). MS (EI, 70 eV), *m*/*z* (%): 535 (M^+, 1), 476 (2), 360 (3), 301 (5). IR (KBr): ν=1732 (C=O), 1560, 1428, 1252, 1020, 940, 736 cm^{-1}.

*4.1.4.3. Tetramethyl 5′-isopropyl-5′H-spiro[1,3-dithiole-2,4′-thiopyrano[3,2-b]indole]-2′,3′,4,5-tetracarboxylate (**9c**).* Yield 100%. Yellow crystalline solid, mp 203–206 °C; R_f=0.51 (CH_2Cl_2). Anal. Calcd for $C_{24}H_{23}NO_8S_3$: C, 52.44; H, 4.22; N, 2.55. Found: C, 52.44; H, 4.35; N, 2.56. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.77 (6H, d, *J* 6.6, CH_3), 3.83 (6H, s, 2 CH_3), 3.90 (3H, s, CH_3), 3.92 (3H, s, CH_3), 5.77 (1H, septet, *J* 6.6, CH), 7.20 (1H, m, Ar), 7.33 (1H, m, Ar), 7.50 (1H, d, *J* 8.1, Ar), 7.69 (1H, d, *J* 8.8, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 19.9 ($CH(CH_3)_2$), 49.9 ($CH(CH_3)_2$), 53.2, 53.3, and 53.8 (3 CH_3), 66.3 (sp^3 tertiary), 102.3,

123.9, 121.5, 127.0, 127.4, 128.5, 128.7, and 136.8 (eight sp^2 tertiary C), 113.7, 119.2, 120.6, and 124.6 (4CH), 160.8, 163.9, and 165.8 (3C=O). MS (EI, 70 eV), *m*/*z* (%): 549 (M^+, 1), 490 (3), 416 (3), 374 (64), 301 (72). IR (KBr): ν=1732 (C=O), 1564, 1428, 1244, 1020, 988, 740 cm^{-1}.

*4.1.4.4. Tetramethyl 5′-benzyl-5′H-spiro[1,3-dithiole-2,4′-thiopyrano[3,2-b]indole]-2′,3′,4,5-tetracarboxylate (**9d**).* Yield 100%. Yellow crystalline solid, mp 162–164 °C; R_f=0.41 (CH_2Cl_2). Anal. Calcd for $C_{28}H_{23}NO_8S_3$: C, 56.27; H, 3.88; N, 2.34. Found: C, 56.39; H, 3.80; N, 2.31. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.74 (6H, s, $2CH_3$), 3.90 (3H, s, CH_3), 3.92 (3H, s, CH_3), 6.00 (2H, s, CH_2), 7.02 (2H, m, Ar), 7.23 (6H, m, Ar), 7.56 (1H, d, *J* 7.9, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 49.5 (CH_2), 53.1 and 53.8 ($2CH_3$), 65.9 (sp^3 tertiary), 103.1, 122.5, 125.6, 127.2, 127.4, 128.3, 128.6, and 139.4 (eight sp^2 tertiary C), 111.4, 119.0, 121.4, 122.8, 126.1, 127.0, and 136.6 (7CH), 160.5, 163.8, and 165.7 (3C=O). MS (EI, 70 eV), *m*/*z* (%): 598 (M^+, 2), 538 (9), 504 (7), 478 (7), 422 (100). IR (KBr): ν=1748 (C=O), 1572, 1436, 1236, 1044, 920, 740 cm^{-1}.

*4.1.4.5. Dimethyl 2-(1-methyl-3-thioxo-1,3-dihydro-2H-indol-2-ylidene)-1,3-dithiole-4,5-dicarboxylate (**10a**).* Yield 32%. Violet crystalline solid, mp 219–221 °C; R_f=0.26 (CH_2Cl_2). Anal. Calcd for $C_{16}H_{13}NO_4S_3$: C, 50.64; H, 3.45; N, 3.69. Found: C, 50.52; H, 3.62; N, 3.66. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.93 (6H, s, CH_3), 3.98 (3H, s, N–CH_3), 7.07 (1H, m, Ar), 7.21 (1H, d, *J* 7.8, Ar), 7.56 (1H, m, Ar), 7.98 (1H, d, *J* 7.6, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 34.0 (N–CH_3), 53.8 (CH_3), 110.0, 120.4, 124.5, and 128.0 (4CH), 129.1, 131.8, 133.5, 137.2, 143.8, and 149.1 (six sp^2 tertiary C), 159.3 and 160.6 (2C=O), 182.9 (C=S). MS (EI, 70 eV), *m*/*z* (%): 379 (M^+, 17), 237 (100), 204 (47), 191 (22), 146 (42). UV λ_{max} ($CHCl_3$) 254 (lg ε=4.03), 283 (4.04), 408 (4.22), 578 (3.79). IR (KBr): ν=1740 and 1712 (C=O), 1608, 1584, 1496, 1432, 1260, 1100, 988, 740 cm^{-1}.

*4.1.4.6. Dimethyl 2-(1-ethyl-3-thioxo-1,3-dihydro-2H-indol-2-ylidene)-1,3-dithiole-4,5-dicarboxylate (**10b**).* Yield 35%. Violet crystalline solid, mp 202–204 °C; R_f=0.25 (CH_2Cl_2). Anal. Calcd for $C_{17}H_{15}NO_4S_3$: C, 51.89; H, 3.84; N, 3.56. Found: C, 51.81; H, 3.77; N, 3.69. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.34 (3H, t, *J* 7.3, CH_3), 3.97 (3H, s, CH_3), 3.99 (3H, s, CH_3), 4.35 (2H, q, *J* 7.3, CH_2), 7.05 (1H, m, Ar), 7.20 (1H, d, *J* 8.1, Ar), 7.52 (1H, m, Ar), 7.97 (1H, d, *J* 8.1, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 15.2 (CH_3CH_2), 41.1 (CH_3CH_2), 53.9 (CH_3), 110.1, 120.5, 124.7, and 132.9 (4CH), 129.0, 132.3, 133.9, 136.1, 136.8, and 148.4 (six sp^2 tertiary C), 159.5 and 160.7 (2C=O), 184.1 (C=S). MS (EI, 70 eV), *m*/*z* (%): 393 (M^+, 12), 364 (8), 251 (61), 236 (34), 223 (19), 191 (49), 146 (100). IR (KBr): ν=1748 and 1712 (C=O), 1608, 1584, 1496, 1236, 1092, 992, 744 cm^{-1}.

*4.1.4.7. Dimethyl 2-(1-isopropyl-3-thioxo-1,3-dihydro-2H-indol-2-ylidene)-1,3-dithiole-4,5-dicarboxylate (**10c**).* Yield 31%. Violet crystalline solid, mp 153–156 °C; R_f=0.23 (CH_2Cl_2). Anal. Calcd for $C_{18}H_{17}NO_4S_3$: C, 53.05; H, 4.20; N, 3.44. Found: C, 53.09; H, 4.39; N, 3.44. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.59 (6H, d, *J* 7.4, CH_3), 3.98 (6H, s, CH_3), 4.86 (2H, septet, *J* 7.4, CH), 7.09 (1H, m, Ar), 7.44 (2H, m, Ar), 7.99 (1H, d, *J* 8.1, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.5 ((CH_3)$_2$CH), 50.3 ((CH_3)$_2$CH), 53.8 and 53.9 ($2CH_3$), 114.3, 121.0, 125.0, and 132.0 (4CH), 130.3, 133.8, 134.3, 138.4, 139.1, and 148.9 (six sp^2 tertiary C), 159.6 and 160.5 (2C=O), 185.3 (C=S). MS (EI, 70 eV), *m*/*z* (%): 407 (M^+, 25), 364 (67), 265 (20), 250 (14), 223 (30), 191 (21), 146 (100). IR (KBr): ν=1720 (C=O), 1604, 1588, 1484, 1444, 1256, 1096, 748 cm^{-1}.

*4.1.4.8. Dimethyl 2-(1-benzyl-3-thioxo-1,3-dihydro-2H-indol-2-ylidene)-1,3-dithiole-4,5-dicarboxylate (**10d**).* Yield 25%. Violet crystalline solid, mp 189–193 °C; R_f=0.19 (CH_2Cl_2). Anal. Calcd for $C_{22}H_{17}NO_4S_3$: C, 58.00; H, 3.76; N, 3.07. Found: C, 58.20; H, 3.94; N, 3.06. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.90 (3H, s, CH_3), 3.97 (3H, s, CH_3), 5.55 (2H, s, CH_2), 7.13 (3H, m, Ar), 7.31 (4H, m, Ar), 7.49 (1H, m, Ar), 8.03 (1H, d, *J* 8.1, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 49.6 (CH_2), 53.7 (CH_3), 110.4, 120.8, 124.5, 126.0, 127.7, 129.0, and 132.9 (7CH), 114.1, 131.9, 133.2, 136.4, 136.7, 137.7 and 148.8 (seven sp^2 tertiary C), 159.3 and 160.4 (2C=O), 183.3 (C=S). MS (EI, 70 eV), *m*/*z* (%): 455 (M^+, 10), 364 (85), 313 (4), 297 (5), 280 (5), 146 (42). IR (KBr): ν=1736 and 1724 (C=O), 1608, 1588, 1492, 1436, 1268, 1100, 1024, 736 cm^{-1}.

*4.1.4.9. Dimethyl 2-(1-methyl-2-thioxo-1,2-dihydro-3H-indol-3-ylidene)-1,3-dithiole-4,5-dicarboxylate (**11**).* Yield 16%. Red crystalline solid, mp 242–244 °C, lit.[8] mp 243–244 °C; R_f=0.24 (CH_2Cl_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.77 (3H, s, N–CH_3), 3.99 (3H, s, CH_3), 4.00 (3H, s, CH_3), 7.32 (1H, m, Ar), 7.35 (2H, m, Ar), 7.77 (1H, d, *J* 7.9, Ar). MS (EI, 70 eV), *m*/*z* (%): 379 (M^+, 60), 320 (7), 237 (100), 204 (40), 191 (17), 172 (18), 160 (13), 146 (15). UV λ_{max} ($CHCl_3$) 304 (lg ε=4.27), 310 (4.34), 398 (4.19), 450 (3.92). IR (KBr): ν=1756 and 1728 (C=O), 1576, 1520, 1428, 1356, 1216, 1072, 744 cm^{-1}.

*4.1.4.10. Dimethyl 2-(1-methyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-1,3-dithiole-4,5-dicarboxylate (**12**).* Yield 23%. Yellow crystalline solid, mp 199–203 °C; R_f=0.15 (CH_2Cl_2). Anal. Calcd for $C_{16}H_{13}NO_5S_2$: C, 52.88; H, 3.61; N, 3.85. Found: C, 52.62; H, 3.52; N, 3.98. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.35 (3H, s, N–CH_3), 3.97 (6H, s, CH_3), 6.92 (1H, d, *J* 8.1, Ar), 7.15 (1H, m, Ar), 7.25 (1H, m, Ar), 7.40 (1H, d, *J* 6.6, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 29.7 (N–CH_3), 53.7 (CH_3), 108.0, 121.2, 121.9, and 126.8 (4CH), 114.0, 128.5, 128.9, 137.0, 139.3, and 140.6 (six sp^2 tertiary C), 159.3 and 160.1 (2C=O), 165.5 (C=O). MS (EI, 70 eV), *m*/*z* (%): 363 (M^+, 100), 304 (22), 276 (8), 246 (8), 189 (90), 160 (58), 146 (27). IR (KBr): ν=1716 and 1676 (C=O), 1576, 1468, 1376, 1292, 1036, 736 cm^{-1}.

Acknowledgements

We gratefully acknowledge financial support from the Russian Foundation for Basic Research (grant no. 05-03-32032).

References and notes

1. Bergman, J.; Janosik, T.; Wahlström, N. *Adv. Heterocycl. Chem.* **2001**, *80*, 1–71; Gribble, G. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 2, Chapter 2.04, pp 207–256; d'Ischia, M.; Napolitano, A.; Pezzella, A. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Oxford, 2008; Vol. 3, Chapter 3.04, pp 353–388.
2. Montanari, L.; Pavanetto, F.; Mazza, M. *Farmaco Ed. Sci.* **1981**, *36*, 856–861.
3. Rewcastle, G. W.; Palmer, B. D.; Dobrusin, E. M.; Fry, D. W.; Kraker, A. J.; Denny, W. A. *J. Med. Chem.* **1994**, *37*, 2033–2042; Palmer, B. D.; Rewcastle, G. W.; Thompson, A. M.; Boyd, M.; Showalter, H. D. H.; Sercel, A. D.; Fry, D. W.; Kraker, A. J.; Denny, W. A. *J. Med. Chem.* **1995**, *38*, 58–67.
4. Engquist, R.; Javaid, A.; Bergman, J. *Eur. J. Org. Chem.* **2004**, 2589–2592.
5. Tsutsumi, H.; Higashiyama, H.; Onimura, K.; Oishi, T. *J. Power Sources* **2005**, *146*, 345–348.
6. McKinnon, D. M. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 3; Chapter 3.11, pp 571–604; Marković, R.; Rašović, A. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier: Oxford, 2008; Vol. 4, Chapter 4.11, pp 893–954.
7. Jardine, R. W.; Brown, R. K. T. *Can. J. Chem.* **1965**, *43*, 1293–1297; Tominaga, Y.; Matsuda, Y.; Kobayashi, G. *Yakugaku Zasshi* **1975**, *90*, 980–984.
8. Kobayashi, G.; Furukawa, S.; Matsuda, Y.; Natsuki, R. *Yakugaku Zasshi* **1970**, *90*, 132–138.
9. Rewcastle, G. W.; Denny, W. A. *Heterocycles* **1994**, *37*, 701–708.
10. Konstantinova, L. S.; Rakitin, O. A.; Rees, C. W. *Mendeleev Commun.* **2001**, 165–166.
11. Konstantinova, L. S.; Rakitin, O. A.; Rees, C. W.; Amelichev, S. A. *Mendeleev Commun.* **2004**, 91–92.
12. Amelichev, S. A.; Aysin, R. R.; Konstantinova, L. S.; Obruchnikova, N. V.; Rakitin, O. A.; Rees, C. W. *Org. Lett.* **2005**, *7*, 5725–5727.
13. Amelichev, S. A.; Konstantinova, L. S.; Rakitin, O. A.; Rees, C. W. *Mendeleev Commun.* **2006**, 289–290.

14. Cipiciani, A.; Clementi, S.; Giulietti, G.; Marino, G.; Savelli, G.; Linda, P. *J. Chem. Soc., Perkin Trans. 2* **1982**, 523–530.
15. Rees, C. W.; White, A. J. P.; Williams, D. J.; Rakitin, O. A.; Marcos, C. F.; Polo, C.; Torroba, T. *J. Org. Chem.* **1998**, *63*, 2189–2196.
16. (a) McKinnon, D. M.; Secco, A. S.; Duncan, K. A. *Can. J. Chem.* **1987**, *65*, 1247–1253; (b) Fanghänel, E.; Palmer, T.; Kersten, J.; Ludwigs, R.; von Schnering, H. G. *Synthesis* **1994**, 1067–1071; (c) ShikhalievKh, S.; Medvedeva, S. M.; Ermolova, G. I.; Shatalov, G. V. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1999**, *35*, 587–591; (d) Barriga, S.; Fuertes, P.; Marcos, C. F.; Rakitin, O. A.; Rees, C. W.; Torroba, T. *J. Org. Chem.* **2002**, *67*, 6439–6448; (e) Barriga, S.; Fuertes, P.; Marcos, C. F.; Torroba, T. *J. Org. Chem.* **2004**, *69*, 3672–3682.
17. Seefeld, M. A.; Miller, W. H.; Newlander, K. A.; Burgess, W. J.; DeWolf, W. E., Jr.; Elkins, P. A.; Head, M. S.; Jakas, D. R.; Janson, C. A.; Keller, P. M.; Manley, P. J.; Moore, T. D.; Payne, D. J.; Pearson, S.; Polizzi, B. J.; Qiu, X.; Rittenhouse, S. F.; Uzinskas, I. N.; Wallis, N. G.; Huffman, W. F. *J. Med. Chem.* **2003**, *46*, 1627–1635.