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The formylation of indoles **1** by dithiocarbenium-ions **2** is discussed. The reaction proceeds to thioacetals **4** under mild conditions. Longer reaction times yield bisindolylmonomethylcyanines **5-6**. Generally, the reaction is inhibited by the presence of electron-withdrawing groups at the pyrrol nucleus of indole **1**, e.g. an acetyl group.

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Introduction.

There is considerable interest in "acylated indole compounds" as precursors, since they are versatile in terms of synthesis of diverse indole alkaloids and pharmacologically active compounds [1,2]. Hence, many efforts have been devoted towards the discovery of methods for the introduction of a carbonyl moiety onto the indole nucleus [3]. However, all the established methods give either relatively poor yields or are limited by extreme reaction conditions. There exists therefore an enormous demand to test new acyl-equivalents with high selectivity and which react under mild reaction conditions.

Heteroatom-stabilized carbenium ions are used very commonly as α^1 -synthons in organic chemistry for carbon-carbon bond formation [4]. Particularly, some dithiocarbenium-ions are well-suited as formylequivalents, because the resulting cyclic thioacetal derivatives can be easily hydrolysed to the corresponding aldehydes [5a,b].

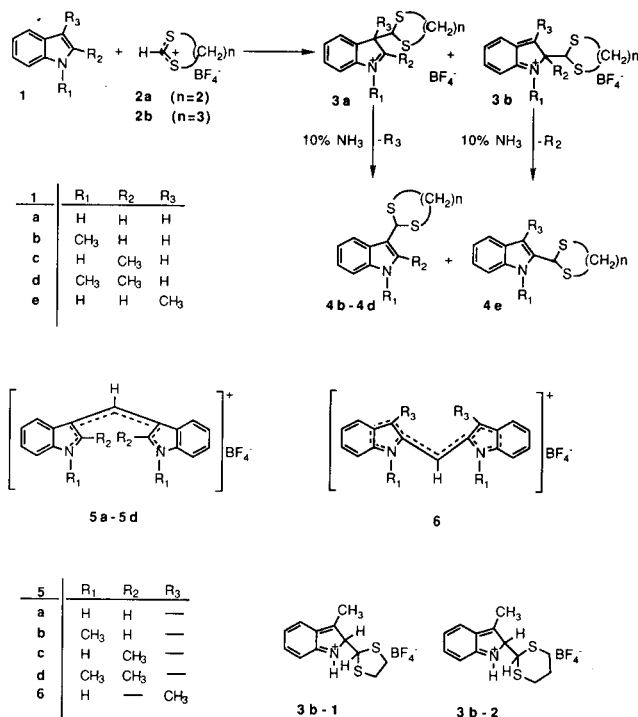
The aim of this report is to investigate the formylation of indoles **1**, by 1,3-dithiolan-2-yl- and 1,3-dithian-2-yl ions as formyl-synthons, respectively. The scope and limitations of this reaction are also established.

Results and Discussion.

Indoles **1** react with 1,3-dithiolan-2-yl-tetrafluoroborate (**2a**) and 1,3-dithian-2-yltetrafluoroborate (**2b**) under very mild conditions (dichloromethane, room temperature). Indolenium ions **3a** and **3b** are assumed to be the intermediates of the reaction sequence [5c]. Subsequent treatment of reaction mixtures (after two hours for indoles **1b-1d**) with 10% ammonia solution gives 3-(1,3-dithiolan-2-yl)- and 3-(1,3-dithian-2-yl)indoles **4b-4d**, respectively (yields 10-30%). Indole **1a** has been thiomethylated using 2-ethoxy-1,3-dithiolan in 64% yield [5a]. However, in contrast to the reported procedure [5a] our method yields only the dye 3,3'-diindolylcarbenium tetrafluoroborate (**5a**). We repeated the reaction several times and each time the pentacyanine dye **5a** was isolated together with some unidentified polymeric materials. Generally, longer reaction times favor the formation of the pentacyanine dyes **5a-5d** in all reactions. The best yield of the pentacyanine

dyes **5** (30-70%) were achieved in runs involving a 2:1 molar ratio of indoles **1** to dithiocations **2**.

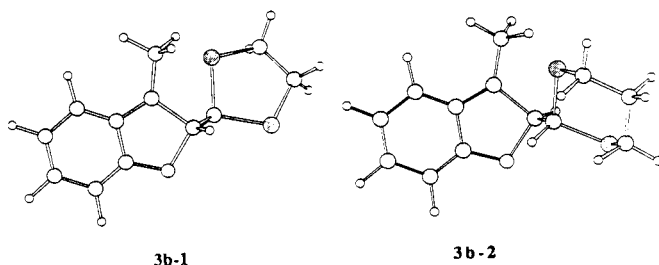
Scheme 1



The formylation process could also be extended to 3-substituted indoles presumably *via* indolenium ion **3b**. For example, 3-methylindole (**1e**) reacts with 1,3-dithian-2-yl ion **2b** giving C-2 thiomethylation within 15 minutes while 1,3-dithiolan-2-yl ion **2a** needs longer reaction times (24 hours). We are somewhat puzzled by the remarkable difference in reaction time for the thiomethylation of 3-substituted indoles, which seems depend on the ring size of the dithiocation ($n = 2$ or $n = 3$). Inspection of models by molecular modeling techniques revealed that this difference in reactivity may result from steric hindrance in the transition state leading to the formation of the indolenium ions **3b**.

In Scheme 2, the computer-generated perspective drawing of the indolenium ions **3b** is depicted. The proximity of the five membered ring **3b-1** ($n = 2$) towards the C-3 methyl group in the transition state (3.402 \AA) as compared to the transition state of the six membered ring **3b-2** (3.384 \AA) could be an explanation for the slower reaction rate. To obtain further insight to structural properties at the molecular level, we have generated the structures of **3b-1** and **3b-2** using the Macromodel^c software V2.0 running on the Evans and Sutherland PS 390/m-VAX II computer of the Biographic Laboratory of the University Kansas [6]. A molecular mechanics optimization using the MM-2 force-field favored **3b-2** by 3.5 Kcal/Mol [7]. Although the influence of the solvent (dichloromethane) has not been evaluated in this study, we feel that the result might at least qualitatively be correct.

Scheme 2



After longer reaction times, as C-3 unsubstituted indoles **1a-1d**, 3-methylindole (**1e**) yields also pentacyanine dye **6**. It is noteworthy to mention that thiomethylation is strongly influenced by the presence of electron-withdrawing groups at the pyrrol nucleus. Particularly, C-3 acetylindole was not formylated by **2**. The present results are generally in good agreement with earlier studies of deactivated indoles [8].

With these experiments, we have demonstrated an example of regioselective thiomethylation of indole derivatives which are certainly capable of initiating further experimental applications for Umpolung [4,8]. Benassar has already used some of 2-(1,3-dithian-2-yl)indole derivatives towards the synthesis of 2-acylindole, which can be used to obtain many indole alkaloids [9]. The structure of product **4** has been unambiguously proved by spectroscopic data and elemental analyses.

EXPERIMENTAL

The melting points were observed on a Büchi apparatus (uncorrected). The ir spectra were measured on a Perkin-Elmer 157 spectrophotometer; the uv spectra were measured on a Perkin-Elmer 330 and Varian DMS 90 spectrophotometers; the ¹H nmr spectra on a Bruker AC 200 spectrometers with TMS as internal standard unless otherwise stated. Likewise the ¹³C nmr spectra were taken on Bruker AC 200 spectrometers. Mass spectra were observed on a LKB 2091 instrument (University of Mainz, FRG).

The elemental analysis were obtained on Carlo Erba Strumentazione Model 1106 apparatus.

General Procedure for the Reaction of 1,3-dithiolan-2-yl and 1,3-dithian-2-yl Tetrafluoroborates **2** with Indoles **1a-1e**.

Ten mmoles of the indoles **1** and 10 mmoles of 1,3-dithiocarbenium-ion **2** were dissolved in dichloromethane (25 ml). After stirring 2 hours for **1b-1d** ($n = 2$ or 3) and 15 minutes for **4e'** ($n = 3$), 24 hours for **4e** ($n = 2$) the reaction mixtures were treated with 10% aqueous ammonia solution and the products were extracted three times with 25 ml portions of dichloromethane. The organic extract was then dried with anhydrous sodium sulfate, and the solid residue was purified by column chromatography on silica gel 60 (Fluka AG), eluting with ethyl acetate/*n*-hexanes.

3-(1-Methyl-1,3-dithian-2-yl)indole (**4b**).

This compound was obtained as a colorless powder, yield 280 mg (11%), mp 127-129°; ir (potassium bromide): ν 3060 (w), 2940 (w), 2900 (m), 1540 (m), 720 (s) cm^{-1} ; ¹H nmr (deuteriochloroform): δ 1.76-2.3 (m, 2, CH₂), 2.6-3.3 (m, 4, 2 x CH₂), 3.7 (s, 3, N-CH₃), 5.6 (s, 1 CH), 7.0-8.0 (m, 5, aromat-H); ¹³C nmr (deuteriochloroform): δ 25.9 (q, CH₃), 32.1 (t, CH₂), 32.2 (t, CH₂-S), 42.9 (d, CH), aromat-C; 110.2, 113.3, 119.3, 120.2, 122.1, 128.3, 134, 136.4; ms: (m/e) 249 (M⁺, 100%), 176 (61%), 175 (99.99%), 174 (99.9%), 170 (50%), 157 (35%), 144 (58%), 131 (21%), 130 (26%), 89 (34%), 77 (12%).

Anal. Calcd. for C₁₁H₁₃NS₂ (249.4): C, 62.60; H, 6.06; N, 5.61. Found: C, 63.02; H, 6.31; N, 5.37.

3-(2-Methyl-1,3-dithiolan-2-yl)indole (**4c**).

This compound was obtained as a colorless powder, yield 918 mg (39%), mp 110-111°; ir (potassium bromide): ν 3390 (s), 3050 (w), 2920 (w), 1460 sh 1420 (m), 770 sh 750 (s) cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.3 (s, 3 CH₃), 3.2-3.8 (m, 4, 2 x CH₂), 6.0 (s, 1 CH), 6.7-8.0 (m, 5, aromat-H + N-H); ¹³C nmr (deuteriochloroform): δ 11.9 (q, CH₃), 40.2 (t, CH₂), 49.4 (d, CH), aromat-C; 106.1, 110.4, 119.2, 119.9, 121.3, 126.6, 133.3, 135.2; ms: (m/e) 235 (M⁺, 99%), 207 (46%), 176 (17%), 175 (75%), 174 (100%), 173 (21%), 142 (95%), 130 (31%), 89 (19%), 77 (9%), 45 (13%).

Anal. Calcd. for C₁₂H₁₃NS₂ (235.4): C, 61.23; H, 5.56; N, 5.95. Found: C, 60.95; H, 5.48; N, 6.20.

3-(2-Methyl-1,3-dithian-2-yl)indole (**4c'**).

This compound was obtained as a colorless powder, yield 346 mg (14%), mp 112-114°; ir (potassium bromide): ν 3600-3300 (m,br), 2920 (w), 1460 (m), 1400 (m), 1080 (m), 720 (m) cm^{-1} ; ¹H nmr (deuteriochloroform): δ 1.7-3.3 (m, 6, 3 x CH₂), 2.5 (s, 3 CH₂), 5.56 (s, 1, CH), 6.7-8.0 (m, 4, aromat-H), 11.0 (s, 1, N-H); ¹³C nmr (deuteriochloroform): δ 11.8 (t, CH₂), 25.1 (q, CH₃), 31.3 (t, CH₂-S), 42.2 (d, CH), aromat-C; 108.3, 110.6, 118.3, 119.2, 120.4, 126.6, 133.2, 135; ms: (m/e) 249 (M⁺, 56.8%), 176 (16%), 175 (100%), 174 (57%), 130 (16%).

Anal. Calcd. for C₁₃H₁₅NS₂ (249.4): C, 62.60; H, 6.06; N, 5.61. Found: C, 63.01; H, 6.39; N, 5.48.

3-(1,2-Dimethyl-1,3-dithiolan-2-yl)indole (**4d**).

This compound was obtained as a colorless powder, yield 823 mg (33%), mp 107-108°; ir (potassium bromide): ν 3040 (w), 2920 (m), 1600 (w), 1450 (m), 1470 (m), 740 (s), cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.43 (s, 3, CH₃), 3.3-3.7 (m, 4, 2 x CH₂), 3.6

(s, 3, *N*-CH₃), 6.13 (s, 1, CH), 7.0-8.0 (m, 4, aromat-H); ¹³C nmr (deuteriochloroform): δ 10.6 (q, CH₃), 30 (q, *N*-CH₃), 40.4 (t, CH₂), 50.3 (d, CH), aromat-C; 109.6, 119, 120.7, 121.3, 127, 135.9, 137.6; ms: (m/e) 249 (M⁺, 59%), 221 (19%), 189 (48%), 188 (100%), 156 (12%), 144 (12.6%), 115 (10%).

Anal. Calcd. for C₁₃H₁₃NS₂ (249.4): C, 62.60; H, 6.06; N, 5.61. Found: C, 62.48; H, 6.26; N, 5.38.

3-(1,2-Dimethyl-1,3-dithian-2-yl)indole (4d')

This compound was obtained as a colorless powder, yield 535 mg (21%), mp 118-122°; ir (potassium bromide): ν 3050 (w), 2900 sh 2940 (w), 1605 (s), 1370 (s), 725 (s) cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.7-2.3 (m, 2, CH₂), 2.46 (s, 3, CH₃), 2.6-3.3 (m, 4, 2 x CH₂), 3.5 (s, 3, *N*-CH₃), 5.5 (s, 1, CH), 6.8-8.0 (m, 4, aromat-H); ¹³C nmr (deuteriochloroform): δ 10.3 (t, CH₂), 25.3 (q, CH₃), 29.2 (q, *N*-CH₃), 31.6 (t, CH₂), 42.6 (d, CH), aromat-C; 108.7, 109, 118.5, 119.4, 120.5, 125.8, 134, 136.4; ms: (m/e) 263 (M⁺, 64%), 189 (100%), 188 (60%), 184 (11%), 171 (10%), 158 (9%), 156 (12%).

Anal. Calcd. for C₁₄H₁₇NS₂ (263.4): C, 64.97; H, 5.45; N, 7.21. Found: C, 65.18; H, 5.85; N, 6.75.

2-(3-Methyl-1,3-dithiolan-2-yl)indole (4e)

This compound was obtained as a colorless powder, yield 1.83 g (78%), mp 98-105°; ir (potassium bromide): ν 3480-3200 (s, br), 3050 (w), 2920 (m), 1620 (m), 1580 (m), 1450 (s), 1440 (s), 1330 (s), 1310 (s), 1260 (s), 1240 (s), 1200 (m), 750 (s), 730 (s), cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.27 (s, 3, CH₃), 3.17-3.6 (m, 4, 2 x CH₂), 5.96 (s, 1, CH), 6.8-7.5 (m, 4 aromat-H), 8.0-8.3 (s, br, 1 *N*-H); ¹³C nmr (deuteriochloroform): δ 8.60 (q, CH₃), 40.7 (t, CH₂), 47.6 (d, CH), aromat-C; 109, 111.8, 119, 119.5, 122.6, 129, 132.7, 137.2; ms: (m/e) 235 (M⁺, 100%), 207 (32%), 175 (89%), 174 (99.9%), 173 (20%), 130 (67%), 105 (15%), 77 (19%).

Anal. Calcd. for C₁₂H₁₃NS₂ (235.4): C, 61.23; H, 5.56; N, 5.96. Found: C, 60.98; H, 5.53; N, 6.23.

2-(3-Methyl-1,3-dithian-2-yl)indole (4e')

This compound was obtained as a colorless powder, yield 698 mg (28%), mp 178-180°; ir (potassium bromide): ν 3400 (s), 3060 (w), 2960-2900 (m), 1460 (m), 1420 (m), 1280 (m), 720 (s) cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.0-2.4 (m, 2, CH₂), 2.3 (s, 3, CH₃), 2.76-3.16 (m, 4, 2 x CH₂), 5.5 (s, 1, CH), 6.8-7.6 (m, 4, aromat-H), 8.0-8.3 (s, br, 1, *N*-H); ¹³C nmr (deuteriochloroform): δ 8.62 (q, CH₃), 24.9 (t, CH₂), 31.1 (t, CH₂), 41.8 (d, CH), aromat-C; 107, 111.3, 118.3, 118.5, 127.7, 131.2, 135.5; ms: (m/e) 249 (M⁺, 65%), 184 (10%), 176 (15%), 175 (100%), 174 (49%), 173 (15%), 144 (12%), 130 (24%).

Anal. Calcd. for C₁₃H₁₃NS₂ (249.4): C, 62.60; H, 6.06; N, 5.56. Found: C, 62.55; H, 5.86; N, 5.47.

General Procedure for the Synthesis of Diindolylcarbenium Tetrafluoroborate 5 and 6.

Twenty mmoles of **1** and 10 mmoles of cation **2** were stirred for 5 hours at room temperature in dichloromethane (25 ml). The precipitates were filtered with suction and washed with dichloromethane until neutral. Then crystalline products were dried under reduced pressure.

3,3'-Diindolylcarbenium Tetrafluoroborate (5a).

This compound was obtained as red-orange crystals, yield 2.49 g (75%), mp 223-225° dec; ir (potassium bromide): ν 3160-3300 (m, br), 1600 sh 1580 (s), 1500 (s), 1410 (s), 1200-1040 (s), 750 (s)

cm⁻¹; uv (methanol): λ max 481 nm (log ε 5.26); ¹H nmr (DMSO-d₆): δ 7.0-8.0 (m, 11, aromat-H, *CH).

Anal. Calcd. for C₁₇H₁₃BF₄N₂ (332.1): C, 61.48; H, 3.94; N, 8.43. Found: C, 61.15; H, 3.86; N, 8.12.

3,3'-Di(1-methylindolyl)carbenium Tetrafluoroborate (5b).

This compound was obtained as red-orange crystals, yield 1.94 g (54%), mp 246-248°, lit 247-249° [10]; ir (potassium bromide): ν 3600-3300 (s), 3120 (w), 3060 (w), 1595 (s), 1440 (s), 1320 (s), 1300 (s), 1040-940 (s), 760 sh 740 (m) cm⁻¹; uv (methanol): λ max 523 nm (log ε 5.96); ¹H nmr (DMSO-d₆): δ 4.05 (s, 3, *N*-CH₃), 7.47-8.18 (m, 10, aromat-H), 9.2 (s, 1, *CH); ¹³C nmr (DMSO-d₆): δ 35.2 (q, CH₃), 146.5 (d, *CH), aromat-C; 113.1, 117.2, 120.3, 125.8, 126.1, 128.1, 138.9, 147.5.

Anal. Calcd. for C₁₉H₁₇BF₄N₂ (360.1): C, 63.36; H, 4.75; N, 7.77. Found: C, 62.96; H, 4.57; N, 7.57.

3,3'-Di(2-methylindolyl)carbenium Tetrafluoroborate (5c).

This compound was obtained as red-orange crystals, yield 2.41 g (67%), mp 237-240°; ir (potassium bromide): ν 3600-2780 (s, br), 1570 (s), 1520 (s), 1330 (s), 1220 (s), 1120-1000 (s, br), 900 (s), 760 (s) cm⁻¹; uv (methanol): λ max 480 nm (log ε 5.67); ¹H nmr (DMSO-d₆): δ 2.93 (s, 6, CH₃), 6.7-7.68 (m, 8, aromat-H), 8.98 (s, 1, *CH), 13.8 (s, 2, 2 x *N*-H); ¹³C nmr (DMSO-d₆): δ 13.3 (q, CH₃), 147.6 (d, *CH), aromat-C; 113.6, 117.6, 123.6, 123.7, 124.0, 125.6, 138.5, 160.7.

Anal. Calcd. for C₁₉H₁₇BF₄N₂ (360.1): C, 63.36; H, 4.75; N, 7.77. Found: C, 63.02; H, 4.60; N, 7.85.

3,3'-Di(1,2-dimethylindolyl)carbenium Tetrafluoroborate (5d).

This compound was obtained as red-orange crystals, yield 970 mg (25%), mp 245-247°, lit 247-249° [10]; ir (potassium bromide): ν 3600-2900 (s), 2950 (w), 1570 (s), 1500 (s), 1240 (s), 1140-1040 (s, br), 900 (s), 820 (s), 770 sh 760 (m) cm⁻¹; uv (methanol): λ max 488 nm (log ε 6.49); ¹H nmr (DMSO-d₆): δ 2.96 (s, 6, 2 x CH₃), 4.01 (s, 6, 2 x *N*-CH₃), 7.0-8.3 (m, 8, aromat-H), 8.92 (s, 1, *CH); ¹³C nmr (DMSO-d₆): δ 12.2 (q, CH₃), 31.8 (q, *N*-CH₃), 146.8 (d, *CH), aromat-C; 112.4, 117.2, 123.1, 124.1, 124.4, 125.5, 140, 160.5.

Anal. Calcd. for C₂₁H₂₁BF₄N₂ (388.2): C, 64.97; H, 5.45; N, 7.21. Found: C, 64.60; H, 5.31; N, 6.85.

2,2'-Di(3-methylindolyl)carbenium Tetrafluoroborate (6).

This compound was obtained as orange powder, yield 1.18 g (33%), mp 248-250° dec, lit 248-250° dec [10]; ir (potassium bromide): ν 3600-3200 (s, br), 3050 (w), 3010 (w), 295 (w), 1470 (w), 1400 (w), 1220 (w), 1070 (w), 900 (m), 820 (m) cm⁻¹; uv (methanol): λ max 542 nm (log ε 4.78). Due to solubility and decomposition problems the nmr spectra could not be achieved.

Anal. Calcd. for C₁₉H₁₇BF₄N₂ (360.1): C, 63.36; H, 4.75; N, 7.77. Found: C, 63.27; H, 5.27; N, 7.40.

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