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## Studies on Fused Indoles. I. Novel Synthesis of 4-Aminomethyltetrahydrothiopyrano[2,3-*b*]indoles through a Thio-Claisen Rearrangement

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Two novel and simple methods for preparing 4-aminomethyl-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indoles are described. Both involve thio-Claisen rearrangements of indol-2-yl propargyl sulfides as a key step which affords thiopyrano[2,3-*b*]indoles in good yields. Elaboration of these compounds led to fused tryptamine analogues which were found to have strong analgesic activity. The mechanism of this novel rearrangement is discussed.

**Keywords**—thiopyrano[2,3-*b*]indole; aryl propargyl sulfide; rigid tryptamine; thio-Claisen rearrangement; analgesic activity

A number of tryptamine derivatives (*e.g.*, serotonin, melatonin, *etc.*) are known to have physiological activity.<sup>1)</sup> From a pharmacological point of view, it seemed interesting to prepare rigid analogues in which an extra ring system is introduced to limit the side-chain flexibility. Therefore, we tried to synthesize thiopyran-fused tryptamines by means of the thio-Claisen rearrangement,<sup>2)</sup> which we have studied extensively.<sup>3)</sup> This report describes the novel synthesis of 4-aminomethyl-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indoles,<sup>4)</sup> which were found to have analgesic activity. Structural modifications and the results of biological evaluation will be reported in the following paper.<sup>5)</sup>

### Synthesis

Chart 1 shows our routes for the preparation of 4-aminomethyltetrahydrothiopyranoindole derivatives (**5**, **8** and **9**). Indol-2-yl propargyl sulfide (**2**) was prepared from indoline-2-thione (**1**) and propargyl bromide in the presence of potassium carbonate in 98% yield. Thermolysis of **2** in refluxing ethanol afforded labile 2,9-dihydrothiopyrano[2,3-*b*]indole (**3**) in quantitative yield after careful work-up. This reaction is considered to involve the thio-Claisen rearrangement and subsequent ring-closure in a similar process to the thermolysis of **6**, which is described later. In practice, **3** prepared *in situ* was treated with aqueous potassium cyanide to give the nitrile **4** in 69% yield from **2**. Reduction of **4** with a mixture of LiAlH<sub>4</sub> and AlCl<sub>3</sub> afforded the desired tryptamine (**5**), in which analgesic activity was originally found, in 72% yield.

The analgesic potency could be enhanced by N<sup>b</sup>-alkylation of **5**, and this finding led us to explore an improved synthetic method suitable for further modifications. We found that the aldehyde **7** could be readily obtained from the thione **1** in only two steps and could serve as a key synthetic intermediate. 4-Hydroxybutyn-2-yl indol-2-yl sulfide (**6**) was prepared quantitatively from **1** and 4-chloro-2-butyn-1-ol. Thermolysis of **6** in pyridine at 100 °C gave the aldehyde **7** in 79% yield. The mechanistic features of this unique transformation will be discussed later.

Treatment of **7** with methylamine in methanol followed by reduction with NaBH<sub>4</sub> in a one-pot procedure gave an *N*-methylaminomethylthiopyranoindole (**8**) in 90% yield. Alternatively, **7** was subjected to reductive amination with dimethylamine and formic acid in

benzene-*N,N*-dimethylformamide (DMF) (a modification of the Leuckart-Wallach reaction<sup>6)</sup>) to afford an *N,N*-dimethylaminomethyl analogue **9** in 88% yield. These methods led to the synthesis of *N*<sup>b</sup>-alkylated analogues in only three steps from the thione **1** and in excellent overall yields (ca. 70%). Their application for further modification will be described in the following paper.<sup>5)</sup>

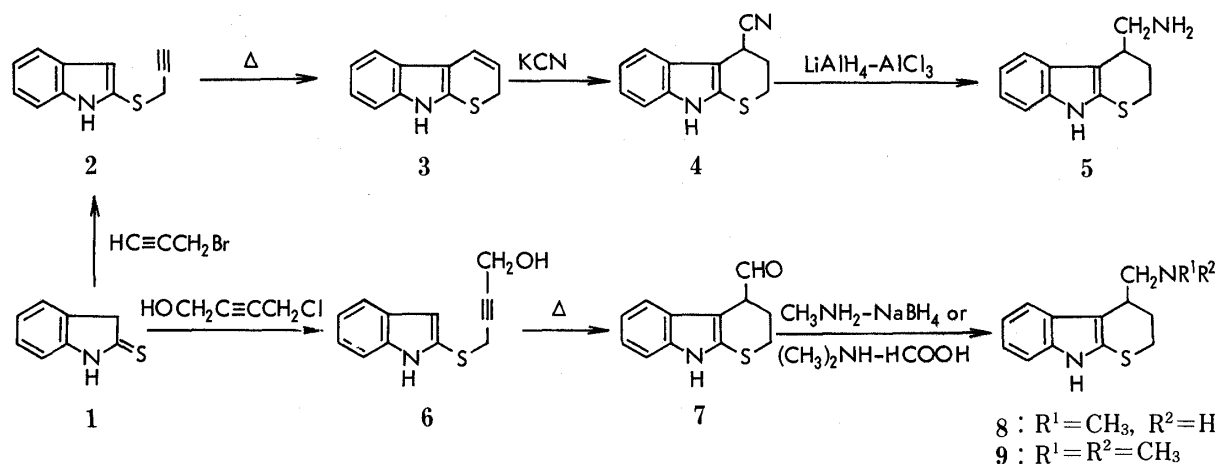


Chart 1

### Mechanism of the Transformation of **6** into **7**

Chart 2 shows a possible pathway for the transformation of **6** into **7**. The sequence for the conversion of **6** into the presumed intermediate **10** is probable, because a similar mechanism was established for the rearrangement of aryl propargyl ethers by Schmid.<sup>7)</sup> However, further conversion of **10** into **7** is unusual in that its allylic alcohol moiety easily

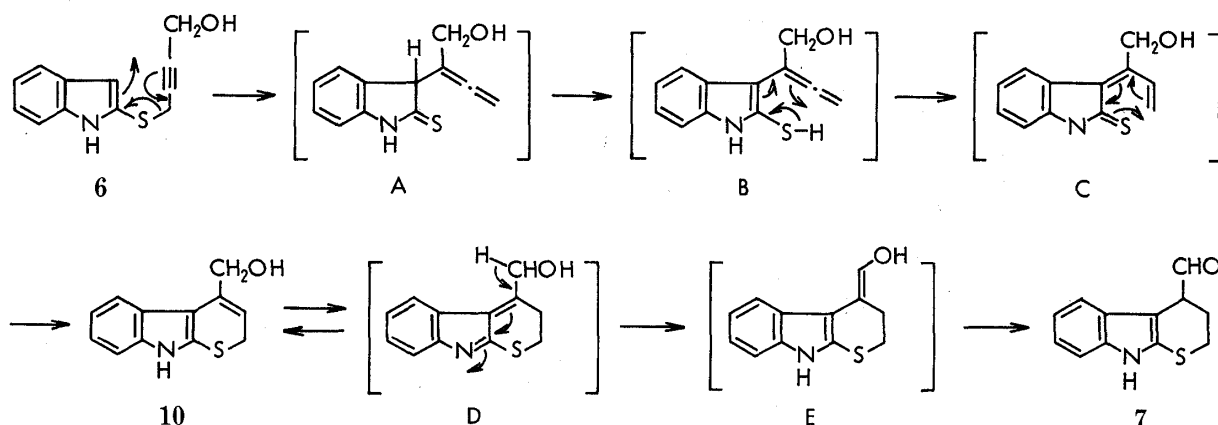


Chart 2

changes into an aldehyde group by thermal isomerization. Therefore, proof was needed that **10** was formed as an intermediate. Since attempted isolation of **10** from the thermal mixture failed, an alternative route was devised as shown in Chart 3. This route is based on the idea that introducing an electron-withdrawing group at the indole nitrogen of **10** may inhibit further thermal conversion.

Reaction of **6** with *tert*-butyldimethylchlorosilane followed by acetylation gave **12**, which was treated with hydrogen fluoride (HF) to afford **13** in good yield. Thermolysis of **13** in toluene-pyridine generated a cyclized product **14** in 88% yield. Careful hydrolysis with NaOCH<sub>3</sub> in methanol gave **10** as an unstable oil, which had a nuclear magnetic resonance

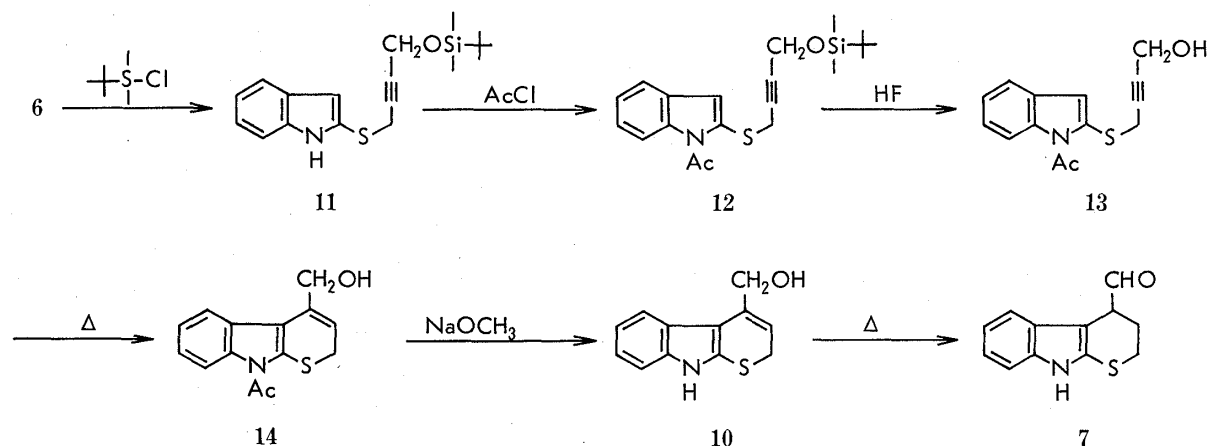


Chart 3

(NMR) spectrum consistent with its expected structure. As anticipated, heating of **10** in pyridine quantitatively yielded the aldehyde **7**. Alternatively, when highly purified<sup>8)</sup> **6** was heated in pyridine-*d*<sub>5</sub> (Py-*d*<sub>5</sub>) and quenched at 50% conversion, transitory formation of **10** was detected in the NMR spectrum of the solution (*ca.* 30% yield based on the signal ratios). These findings indicated the presence of **10** as a real intermediate in the transformation of **6** into **7**.

The conversion of **10** into **7** may be rationalized as follows. Compared to the tautomerism between **10** and **D**, conversion of **D** into **E** seems to be less favorable due to the need for deprotonation from the carbon carrying the hydroxyl group. However, even slight formation of **E** in the tautomerism should lead to complete production of **7** because the final step is essentially irreversible.

### Conclusion

The present studies provide two novel and efficient methods for preparing 4-aminomethyltetrahydrothiopyrano[2,3-*b*]indoles and demonstrate the utility of the thio-Claisen rearrangement of aryl propargyl sulfides in the synthesis of fused heterocycles.

### Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were taken on a Hitachi IR-215 spectrophotometer. NMR spectra were recorded on a Varian T-60 instrument with tetramethylsilane as an internal standard. Mass spectra (MS) were taken on a Hitachi RMU-8GN mass spectrometer.

Unless otherwise noted, reactions were conducted under a nitrogen atmosphere and organic extracts were washed with water and dried over MgSO<sub>4</sub>.

**Indol-2-yl Propargyl Sulfide (2)**—A solution of indoline-2-thione (**1**)<sup>9)</sup> (14.9 g, 0.1 mol) in acetone (300 ml) was treated with K<sub>2</sub>CO<sub>3</sub> (16.5 g, 0.12 mol) and propargyl bromide (14.3 g, 0.12 mol) at room temperature. The mixture was stirred at room temperature for 3 h, then filtered and the filtrate was concentrated. The residue was taken up in H<sub>2</sub>O and extracted with Et<sub>2</sub>O. The extract was washed, dried and concentrated, and the residual oil was chromatographed on silica gel [100 g, benzene-hexane (1 : 1)], giving **2** as a colorless oil (18.3 g, 98%). IR  $\nu_{\max}^{\text{CHCl}_3} \text{ cm}^{-1}$ : 3450, 3300. NMR (CDCl<sub>3</sub>)  $\delta$ : 2.28 (1H, t, *J* = 2.5 Hz), 3.43 (2H, d, *J* = 2.5 Hz), 6.73 (1H, d, *J* = 2 Hz), 6.9–7.7 (4H, m), 8.25 (1H, br, NH). *Anal.* Calcd for C<sub>11</sub>H<sub>9</sub>NS: C, 70.55; H, 4.84; N, 7.48; S, 17.12. Found: C, 70.28; H, 4.89; N, 7.66; S, 17.00.

**2,9-Dihydrothiopyrano[2,3-*b*]indole (3)**—A solution of the sulfide **2** (50 mg) and Et<sub>3</sub>N (1 drop) in EtOH (5 ml) was refluxed for 1.5 h. Evaporation of the solution gave **3** as a pale green solid (*ca.* 50 mg). IR  $\nu_{\max}^{\text{CHCl}_3} \text{ cm}^{-1}$ : 3450. NMR (CDCl<sub>3</sub>)  $\delta$ : 3.60 (2H, dd, *J* = 5, 1.5 Hz), 5.40 (1H, dt, *J* = 10, 5 Hz), 6.78 (1H, td, *J* = 1.5, 10 Hz), 7.0–8.0 (4H, m), 8.35 (1H, br).

**4-Cyano-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indole (4)**—A solution of the sulfide **2** (13.2 g, 0.07 mmol) and Et<sub>3</sub>N (1 ml) in EtOH (300 ml) was refluxed for 1 h, a solution of KCN (25 g, 0.38 mmol) in EtOH (170 ml)–H<sub>2</sub>O (80 ml) was added, and the mixture was refluxed for 2 h, then concentrated, diluted with H<sub>2</sub>O and extracted with Et<sub>2</sub>O. After the extract had been washed, dried and evaporated, the residual oil was chromatographed on silica gel (450 g, benzene) to give **4** as crystals (10.4 g, 69%), mp 125–126 °C (from EtOH–hexane). IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3460, 2230. NMR (CDCl<sub>3</sub>)  $\delta$ : *ca.* 2.5 (2H, m), *ca.* 3.3 (2H, m), 4.15 (1H, t, *J* = 5 Hz), 7.0–7.7 (4H, m), 7.9 (1H, br, NH). *Anal.* Calcd for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>S: C, 67.26; H, 4.70; N, 13.07; S, 14.96. Found: C, 66.97; H, 4.61; N, 12.82; S, 15.07.

**4-Aminomethyl-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indole (5)**—A solution of **4** (12 g, 0.056 mol) in anhydrous Et<sub>2</sub>O (300 ml) was added dropwise to a mixture of AlCl<sub>3</sub> (18.7 g, 0.14 mol) and LiAlH<sub>4</sub> (5.4 g, 0.14 mol) in anhydrous Et<sub>2</sub>O (200 ml) over 45 min at room temperature. The mixture was stirred at room temperature for 2 h, then 20% aq. NaOH (65 ml) was added at ice-bath temperature. The mixture was extracted with Et<sub>2</sub>O and the extract was washed, dried and concentrated. The residual oil was treated with ethanolic oxalic acid to give an oxalate [15 g, mp *ca.* 238 °C (dec.)]. An aqueous suspension of this salt was basified with aq. NaOH and extracted again with Et<sub>2</sub>O. The extract was washed, dried and evaporated, giving an oil (9.4 g), which when crystallized from EtOH–hexane–Et<sub>2</sub>O, afforded **5** (8.8 g, 72%), mp 122–125 °C. IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3450. NMR (CDCl<sub>3</sub>)  $\delta$ : *ca.* 1.3 (2H, br, NH<sub>2</sub>), *ca.* 2.2 (2H, m), *ca.* 3.1 (5H, m), 6.9–7.6 (4H, m), *ca.* 8.5 (1H, br, NH). *Anal.* Calcd for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>S: C, 66.02; H, 6.46; N, 12.83; S, 14.69. Found: C, 66.24; H, 6.51; N, 12.72; S, 14.51.

**4-Hydroxybut-2-ynyl Indol-2-yl Sulfide (6)**—A mixture of indoline-2-thione (**1**) (7.45 g, 0.05 mol), K<sub>2</sub>CO<sub>3</sub> (7.60 g, 1.1 eq) and 4-chloro-2-butyn-1-ol<sup>10</sup> (5.48 g, 1.05 eq) in acetone (75 ml) was stirred at room temperature for 5 h. The mixture was filtered and the filtrate was evaporated completely. The residue was treated with Et<sub>2</sub>NH (10 ml) to decompose the unreacted reagent (room temperature, 1 h). The diethylamine was evaporated off and the residue was dissolved in Et<sub>2</sub>O. The solution was washed (2 N HCl, H<sub>2</sub>O) and dried. Removal of the solvent left **6** as an oil (12 g), which was used without further purification. IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3600, 3450. NMR (CDCl<sub>3</sub>)  $\delta$ : 2.01 (1H, s, OH), 3.57 (2H, t, *J* = 2 Hz), 4.27 (2H, t, *J* = 2 Hz), 6.80 (1H, d, *J* = 2 Hz), 7.0–7.8 (4H, m); (Py-*d*<sub>5</sub>)  $\delta$ : 3.92 (2H, t, *J* = 2 Hz), 4.50 (2H, t, *J* = 2 Hz), *ca.* 4.6 (1H, br, OH), 6.62 (1H, s), 7.0–7.9 (4H, m). If pure **6** was required, the above oil was chromatographed on silica gel with benzene–ethyl acetate (10:1).

**4-Formyl-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indole (7)**—A solution of **6** (12 g) in pyridine (120 ml) was stirred at 100 °C for 2 h. After removal of the solvent, the residue was dissolved in Et<sub>2</sub>O. The solution was washed (2 N HCl, H<sub>2</sub>O) and dried, then evaporation provided an oil (11 g), which was chromatographed on silica gel (55 g, benzene) to give **7** as a colorless oil (8.14 g, 75% from **1**), which solidified on standing in a refrigerator (mp 60–65 °C). IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3450, 1720. NMR (CDCl<sub>3</sub>)  $\delta$ : 1.8–3.2 (4H, m), 3.85 (1H, m), 7.0–7.6 (4H, m), *ca.* 8.1 (1H, br), 9.83 (1H, d, *J* = 2 Hz); (Py-*d*<sub>5</sub>)  $\delta$ : 1.8–3.6 (4H, m), 4.0 (1H, m), 6.4 (1H, br), 7.1–7.9 (4H, m), 10.02 (1H, d, *J* = 2 Hz). *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>NOS: C, 66.33; H, 5.10; N, 6.45; S, 14.76. Found: C, 66.16; H, 5.15; N, 6.20; S, 14.64.

**4-(*N*-Methylaminomethyl)-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indole (8)**—A 30% methanolic solution of CH<sub>3</sub>NH<sub>2</sub> (2.2 ml, *ca.* 1.5 eq) was added to a stirred solution of **7** (2.17 g, 10 mmol) in MeOH (20 ml) at room temperature. After 1 h, NaBH<sub>4</sub> (380 mg, 10 mmol) was added to the mixture at ice-bath temperature and stirring was continued at room temperature for 2 h. The mixture was concentrated and acidified with 2 N HCl, then extracted with CHCl<sub>3</sub> to remove the neutral material (*ca.* 100 mg). The aqueous layer was alkalized again (aq. NaOH) and extracted with CHCl<sub>3</sub>. After the extract had been washed, dried and concentrated, the residue was treated with benzene to give almost pure **8** as a benzene adduct (mp 70–75 °C, 2.21 g, 90%). Recrystallization from benzene gave an analytical sample, mp 78–81 °C. IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3450. NMR (CDCl<sub>3</sub>)  $\delta$ : *ca.* 2.3 (2H, m), 2.50 (3H, s), 2.7–3.5 (5H, m), 7.0–7.7 (5H, m). *Anal.* Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>S (C<sub>6</sub>H<sub>6</sub>)<sub>1/6</sub>: C, 68.53; H, 6.98; N, 11.42; S, 13.07. Found: C, 68.36; H, 6.97; N, 11.38; S, 13.03. This was converted into a hydrochloride by treatment with HCl–Et<sub>2</sub>O, mp 245–250 °C (dec.). *Anal.* Calcd for C<sub>13</sub>H<sub>17</sub>ClN<sub>2</sub>S: C, 58.09; H, 6.37; N, 10.42; S, 11.93. Found: C, 58.27; H, 6.39; N, 10.50; S, 11.90.

**4-(*N,N*-Dimethylaminomethyl)-2,3,4,9-tetrahydrothiopyrano[2,3-*b*]indole (9)**—A 20% methanolic solution of Me<sub>2</sub>NH (5.77 ml, 20 mmol) was mixed with 98% HCOOH (940 mg, 20 mmol) at room temperature. The methanol was removed by distillation at atmospheric pressure and the residue was diluted with benzene (5 ml). To this, a solution of **7** (2.17 g, 10 mmol) in benzene (10 ml) was added dropwise at 60–70 °C, and the mixture was refluxed until evolution of CO<sub>2</sub> gas ceased (within 1 h). During this period DMF (*ca.* 4 ml) was added to dissolve the separating solid (presumably enamine salts). The mixture was taken up in 5% NaOH and extracted with Et<sub>2</sub>O. The extract was washed, dried and concentrated, giving a solid which, when recrystallized from MeOH, afforded pure **9** (2.18 g, 88%), mp 122–124 °C. IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3460. NMR (CDCl<sub>3</sub>)  $\delta$ : 2.33 (6H, s), 1.8–3.6 (7H, m), 6.9–7.6 (4H, m), *ca.* 8.0 (1H, br). *Anal.* Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>S: C, 68.25; H, 7.36; N, 11.37; S, 13.01. Found: C, 68.30; H, 7.43; N, 11.29; S, 13.12.

**4-*tert*-Butyldimethylsilyloxybut-2-ynyl Indol-2-yl Sulfide (11)**—Et<sub>3</sub>N (2.27 g, 1.5 eq), 4-dimethylaminopyridine (183 mg, 0.1 eq), and *tert*-butyldimethylchlorosilane (2.49 g, 1.1 eq) were added to **6** (3.26 g, 15 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (60 ml) at room temperature. After being stirred for 1 h, the mixture was taken up in ice water and extracted with CHCl<sub>3</sub>. The extract was washed (H<sub>2</sub>O, cold 2 N HCl, H<sub>2</sub>O, aq. NaHCO<sub>3</sub>, H<sub>2</sub>O) and dried. Removal of the solvent gave an oil (5 g) which, when chromatographed [silica gel 300 g, petroleum ether–EtOAc (20:1)], gave pure **11** as an oil (3.90 g, 78%). IR  $\nu_{\max}^{\text{CHCl}_3}$  cm<sup>-1</sup>: 3450. NMR (CDCl<sub>3</sub>)  $\delta$ : 0.10 (6H, s), 0.92 (9H, s), 3.53 (2H, t, *J* = 2 Hz), 4.23 (2H, t,

$J=2$  Hz), 6.70 (1H, d,  $J=2$  Hz), 7.0–7.7 (4H, m). MS  $m/z$  (%): 331 (13,  $M^+$ ), 199 (71), 148 (58), 75 (100), 73 (62). High resolution MS  $m/z$ :  $M^+$  Calcd for  $C_{18}H_{25}NOSSi$ : 331.1426. Found: 331.1439.

**1-Acetylidol-2-yl 4-tert-Butyldimethylsilyloxybut-2-ynyl Sulfide (12)**—(*n*-Bu)<sub>4</sub>NHSO<sub>4</sub> (40 mg, 0.01 eq) and NaOH (1 g, powdered) were added to a solution of **11** (3.90 g, 11.78 mmol) in  $CH_2Cl_2$  (30 ml) at ice-bath temperature, then a solution of AcCl (1.38 g, 1.5 eq) in  $CH_2Cl_2$  (10 ml) was added. The mixture was stirred at the same temperature for 50 min, then filtered, and the filtrate was washed ( $H_2O$ , cold  $NaHCO_3$ ,  $H_2O$ ), dried and evaporated. The residue was chromatographed [silica gel, 150 g, petroleum ether–benzene–EtOAc (20:10:1) to provide **12** as an oil (3.87 g, 88%). IR  $\nu_{max}^{CHCl_3} cm^{-1}$ : 1700. NMR ( $CDCl_3$ )  $\delta$ : 0.10 (6H, s), 0.87 (9H, s), 2.84 (3H, s), 3.67 (2H, t,  $J=2$  Hz), 4.31 (2H, t,  $J=2$  Hz), 6.65 (1H, s), 7.1–8.0 (4H, m). MS  $m/z$  (%): 373 (28,  $M^+$ ), 199 (53), 148 (62), 75 (86), 73 (100). High resolution MS  $m/z$ :  $M^+$  Calcd for  $C_{20}H_{27}NOSSi$ : 373.1530. Found: 373.1537.

**1-Acetylidol-2-yl 4-Hydroxybut-2-ynyl Sulfide (13)**—A solution of **12** (1.492 g, 4 mmol) in  $CH_3CN$  (20 ml) was treated with 46% aq. HF (0.53 ml, 3 eq) at ice-bath temperature. After being stirred at the same temperature for 2 h, the mixture was diluted with  $Et_2O$  (150 ml) and washed ( $H_2O$ , cold aq.  $NaHCO_3$ ,  $H_2O$ ). The solution was dried and evaporated, giving a solid which, when washed with benzene, afforded **13**, (1.01 g, 97%), mp 110–112 °C. IR  $\nu_{max}^{CHCl_3} cm^{-1}$ : 3600, ca. 3400, 1700. NMR ( $CDCl_3$ )  $\delta$ : 1.87 (1H, br, OH), 2.83 (3H, s), 3.60 (2H, t,  $J=2$  Hz), 4.20 (2H, t-like), 6.60 (1H, s), 7.0–8.0 (4H, m). Anal. Calcd for  $C_{14}H_{13}NO_2S$ : C, 64.84; H, 5.01; N, 5.40; O, 12.34. Found: C, 64.80; H, 4.99; N, 5.36; O, 12.05.

**9-Acetyl-4-hydroxymethyl-2,9-dihydrothiopyrano[2,3-*b*]indole (14)**—A solution of **13** (777 mg, 3 mmol) in toluene (20 ml)–pyridine (2 ml) was heated at 110 °C for 1 h. The solution was evaporated to give a solid, which was washed with benzene, affording **14** (680 mg, 87%), mp 120–122 °C. IR  $\nu_{max}^{CHCl_3} cm^{-1}$ : 3600, ca. 3400, 1700. NMR ( $CDCl_3$ )  $\delta$ : 1.78 (1H, s, OH), 2.78 (3H, s), 3.73 (2H, d,  $J=5.5$  Hz), 4.60 (2H, br s), 5.64 (1H, tt,  $J=1.5$  Hz, 5.5), 7.0–7.4 (2H, m), 7.6–8.0 (2H, m). Anal. Calcd for  $C_{14}H_{13}NO_2S$ : C, 64.84; H, 5.05; N, 5.40; S, 12.37. Found: C, 64.69; H, 5.20; N, 5.42; S, 12.42.

**4-Hydroxymethyl-2,9-dihydrothiopyrano[2,3-*b*]indole (10)**— $CH_3ONa$  (81 mg, 1.5 eq) was added to a suspension of **14** (259 mg, 1 mmol) in MeOH (4 ml) at –15 °C and the mixture was stirred at –15 °C for 1 h, then diluted with  $Et_2O$ , washed ( $H_2O$ , sat. NaCl) and dried. These operations were carried out at <10 °C. Evaporation of the solution left **10** as an unstable oil (220 mg), which was dissolved in  $Py-d_5$  and kept in a refrigerator. NMR ( $Py-d_5$ )  $\delta$ : 3.60 (2H, d,  $J=6$  Hz), 5.03 (2H, d,  $J=1.5$  Hz), 5.78 (1H, tt,  $J=6, 1.5$  Hz), 6.0 (1H, br, OH), 7.0–7.6 (3H, m), 8.1 (1H, m).

**Thermal Transformation of 10 to 7**—A solution of **10** (ca. 100 mg) in  $Py-d_5$  (1 ml) was heated at 100 °C until complete decomposition of **10** was observed by NMR spectroscopy (ca. 4 h). The solution was evaporated to give almost pure **7**, which was identical with the product obtained above on the basis of comparisons of IR and NMR spectra as well as thin layer chromatography (TLC) behavior.

### References and Notes

- 1) For example, see: R. J. Sundberg, "The Chemistry of Indoles," Academic Press, New York, 1970, pp. 438–439.
- 2) For a review of the thio-Claisen rearrangement, see: L. Morin, J. Leband, D. Paquer, R. Chaussin and D. Barillier, *Phosphor. Sulfur Relat. Elem.*, **7**, 69 (1979).
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- 4) 2,3,4,9-Tetrahydrothiopyrano[2,3-*b*]indole itself has been prepared by oxidative cyclization of 3-indolepropanethiol; T. Hino, H. Miura, T. Nakamura, R. Murata and M. Nakagawa, *Heterocycles*, **3**, 805 (1975); T. Hino, H. Miura, R. Murata and M. Nakagawa, *Chem. Pharm. Bull.*, **26**, 3695 (1978).
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- 6) For application to aliphatic aldehydes, see: P. L. deBenneville and J. M. Macartney, *J. Am. Chem. Soc.*, **72**, 3073 (1950).
- 7) N. Šarčević, J. Zsindely and H. Schmid, *Helv. Chim. Acta*, **56**, 1457 (1973).
- 8) When **6** was used without purification, the conversion of **6** into **7** (more precisely, **10** to **7**) was so facilitated that **10** was hardly detected. Similar rate enhancement was observed when isolated **10** was heated in pyridine containing a small amount of the thione **1**.
- 9) This was prepared from oxindole by thiation with  $P_2S_5$ . The procedure will be described in detail in the following paper.<sup>5)</sup>
- 10) W. J. Bailey and E. Fujiwara, *J. Am. Chem. Soc.*, **77**, 165 (1955).