SHORT STEP SYNTHESIS OF 4-FORMYLINDOLE AND DERIVATIVES FROM 4-OXO-4,5,6,7-TETRAHYODROINDOLE

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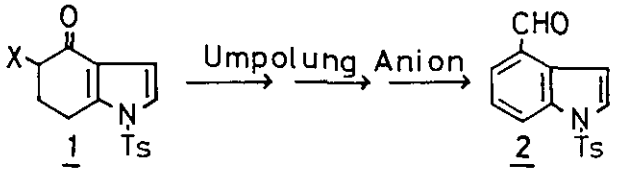
Abstract —— The reaction of 4-oxo-4,5,6,7-tetrahydroindole with umpolung anions provides a new short efficient procedure for the synthesis of 4-formylindole derivatives.

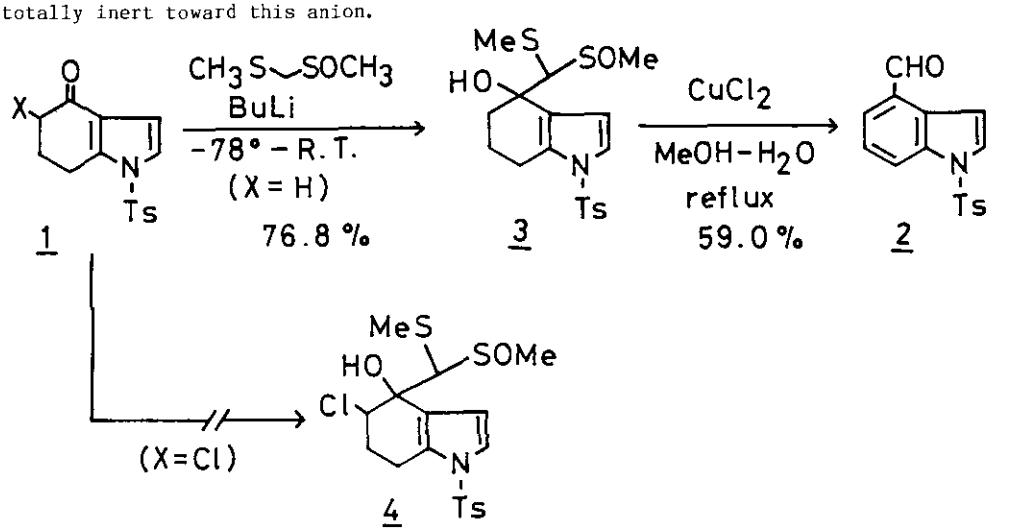
4-Substituted indoles constitute a major section of indole chemistry including ergot alkaloids,[1] and have been drawing much attention of synthetic organic chemists. Most widely employed intermediate for 4-substituted indole synthesis has been 4-formylindole because carbon extention would be easy on aldehyde.[2] Among many attempts of synthesizing 4-formylindole,[2i,3], Kozikowski's method,[3c] which employs Leimgruber-Batcho approach,[4] seems to be the best so far although it is lengthy and fairly expensive in terms of the starting material and reagents.

We have been working on a project to prepare a variety of 4-substituted indoles from versatile intermediate, 4-oxo-4,5,6,7-tetrahydroindole such as 1, with encouraging result.[5] We wish to report here yet another application of our methodology toward 4-substituted indoles from 1. Since compound 1 has a convenient handle (carbonyl group) at 4-position, we figured that reactions of 1 with umpolung anions[6] will provide a convenient way to 4-formylindole derivatives such as 2.

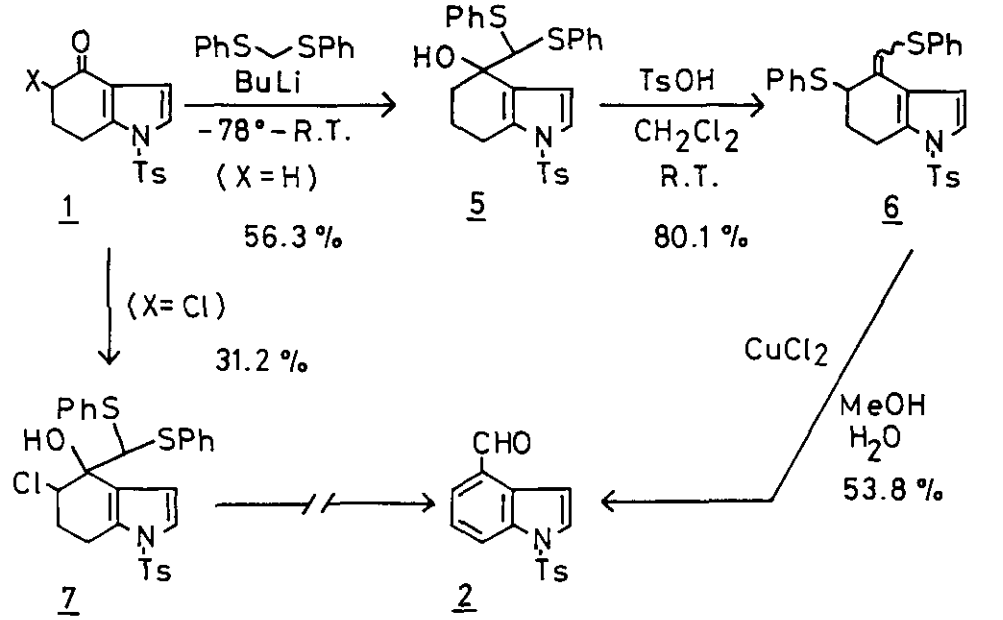


The first umpolung anion source we chose was MMTS (methyl methylthiomethyl sulfoxide). It has been known to produce hydroxyaldehydes with relative ease.[7] The anion of MMTS was generated with butyllithium in tetrahydrofuran at - 78 °C and it reacted with 4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole 1a (X = H) to produce an adduct, 4-hydroxy-4-(1-methylsulfinyl-1-methylthio)methyl-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole 3. The adduct 3 was oxidized and deprotected to 4-formyl-1-(p-toluenesulfonyl)indole 2 by heating with cupric chloride in

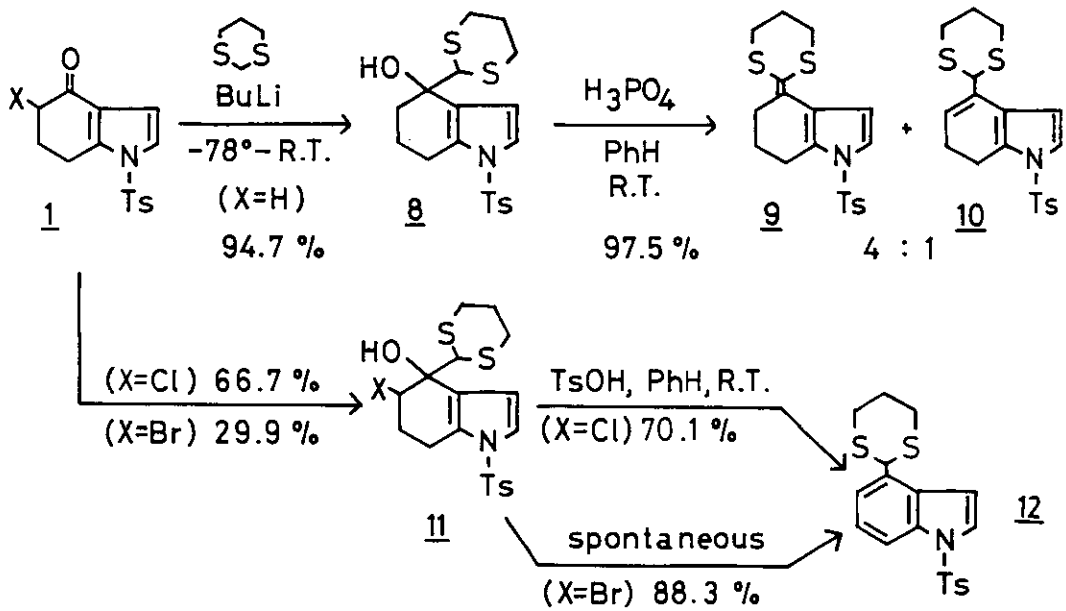
aqueous methanol. 5-Chloro-4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1b) (X = Cl) was totally inert toward this anion.



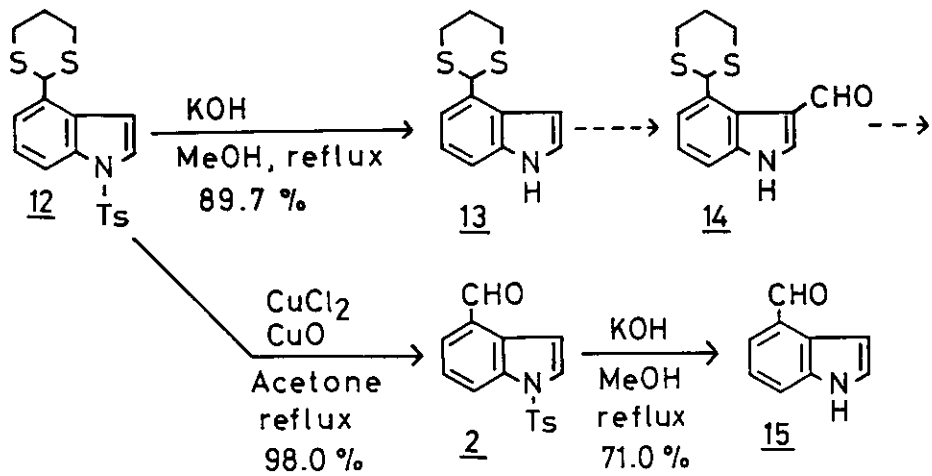
The second anion tried was bis(phenylthio)methyllithium.[8] The anion reacted with 4-oxotetrahydroindole 1a (X = H) to produce an adduct, 4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole 5. The adduct 5 was treated with p-toluenesulfonic acid in dichloromethane to give the dehydrated and rearranged product 6. The compound 6 was oxidized with cupric chloride in aqueous methanol to afford 4-formyl-1-(p-toluenesulfonyl)indole 2. Reaction with 5-chloro-4-oxotetrahydroindole 1b (X = Cl) produced the adduct, 5-chloro-4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole 7. The adduct 12, however, could not be converted to the aldehyde 2.



The third umpolung was the anion of dithiane.[9] The anion generated from dithiane and butyllithium reacted with 4-oxotetrahydroindole 1a (X = H) to produce the adduct, 4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole 8, in a good yield. Although the adduct 8 was converted to a mixture of dehydrated products 9 and 10 (4 : 1), the subsequent oxidation with cupric chloride did not produce any aldehyde 2. The reaction with 5-chloro derivative 1b (X = Cl) and 5-bromo derivative 1c (X = Br) gave the adduct 11b (X = Cl) and 11c (X = Br), respectively. The 5-chloro-adduct 11b (X = Cl) under acidic condition (p-toluenesulfonic acid in benzene) was simultaneously dehydrated and dehydrochlorinated to a protected 4-formylindole derivative 12. The 5-bromo-adduct 11c (X = Br) spontaneously eliminates water and hydrogen bromide upon standing to produce 12.



The protecting group on nitrogen (p-toluenesulfonyl group) was removed from 4-(1,3-dithian-2-yl)-1-(p-toluenesulfonyl)indole 12 by saponification with potassium hydroxide in methanol to give 4-(1,3-dithian-2-yl)indole 13. Once the N-protection is removed, carbon extention reaction such as formylation[10] can be conducted on 3-position for further transformation keeping 4-formyl group protected. The other sequence of deprotection was also tried. First the dithiane moiety of 12 was cleaved (cupric chloride and cupric oxide in acetone[11]) to reveal the aldehyde portion. Thus produced aldehyde 2 was further saponified to 15 with potassium hydroxide in methanol without any complication such as Cannizzaro reaction.



We have established the general method to prepare the versatile intermediate, 4-formylindole and its protected form, from readily available 4-oxo-4,5,6,7-tetrahydroindole using umpolung anions. Further use of this 4-oxo-4,5,6,7-tetrahydroindole is being actively investigated in our laboratories and will be reported in due course.

EXPERIMENTAL

4-Hydroxy-4-(1-methylsulfinyl-1-methylthio)methyl-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (3). To a solution of methyl methylthiomethyl sulfoxide (10.9 g, 88 mmol) in tetrahydrofuran (100 ml) under argon at - 78 °C was added 15 % butyllithium solution in hexane (56.3 ml, 88 mmol). After the mixture was stirred at - 78 °C for 1 h, 4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1a) (15.28 g, 53 mmol) was added. The mixture was stirred at - 78 °C for 2 h and at room temperature for 2 h. The reaction was quenched with saturated aq. NH_4Cl solution and extracted with ethyl acetate. The extract was washed with water and dried over $MgSO_4$. The solution was concentrated to a small volume and 4-hydroxy-4-(1-methylsulfinyl-1-methylthio)methyl-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (3) (16.77 g, 76.8 %) was obtained as a crystaline solid. Mp 96 - 98 °C (colorless needles from ethyl acetate). NMR ($CDCl_3$) δ 1.78 - 3.00 (m, 6H), 2.05 (s, 3H), 2.41 (s, 3H), 2.92 (s, 3H), 3.79 (s, 1H), 5.00 - 5.40 (m, 1H), 6.31 (d, J=3.8 Hz, 1H), 7.13 - 7.43 (m, 3H) and 7.57 - 7.83 (m, 2H) ppm. IR (KBr) 3310, 1600, 1500, 1375 and 1177 cm^{-1}. Mass (m/z, %) 379 (M^+-18-16, 5), 333 (96), 331 (52), 284 (86), 178 (100), 176 (42), 155 (30), 130 (95) and 91 (86).

4-Formyl-1-(p-toluenesulfonyl)indole (2) from 4-Hydroxy-4-(1-methylsulfinyl-1-methylthio)methyl-1-(p-toluenesulfonyl)indole (3). A mixture of 4-hydroxy-4-(1-methylsufinyl-1-methylthio)methyl-1-(p-toluenesulfonyl)indole (3) (1.10 g, 2.7 mmol)and $CuCl_2$ (1.40 g, 10.4 mmol) was heated under

reflux for 1 h. After addition of water (1 ml), the mixture was heated under reflux for 1 h. The mixture was diluted with water and extracted with dichloromethane. The extract was filtered on a celite pad, washed with aq. $NaHCO_3$ solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane to give 4-formyl-1-(p-toluenesulfonyl)indole (2) (470 mg, 59.0 %). Mp 143 - 144 °C (colorless prisms from ether - dichloromethane). NMR ($CDCl_3$) δ 2.30 (s, 3H), 7.19 (broad d, J=8.1 Hz, 2H), 7.30 - 7.54 (m, 2H), 7.60 - 7.85 (m, 4H), 8.26 (broad d, J=8.1 Hz, 1H) and 10.16 (s, 1H) ppm. IR (KBr) 1695, 1370, 1360, 1190, 1160, 1140, 1120, 775, 670, 635 and 565 cm^{-1}. Mass (m/z, %) 299 (M^+, 38), 155 (48), 91 (100), 65 (19).

4-Bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (5). To a solution of bis(phenylthio)methane (1.93g, 8.3 mmol) in tetrahydrofuran (60 ml) at - 78 °C was added butyllithium in hexane (1.50 M, 5.53 ml, 8.3 mmol) and the mixture was stirred at - 78 °C for 1.5 h. The reaction was quenched with saturated aq. NH_4Cl solution and ethyl acetate was added. The organic layer was separated, washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane-1 % triethylamine to give 4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (5) (2.03 g, 56.3 %) (conversion 64.5 %) as viscous oil. NMR ($CDCl_3$) δ 1.57 - 2.10 (m, 4H), 2.32 (s, 3H), 2.46 - 2.90 (m, 2H), 4.63 (s, 1H), 6.21 (d, J=3.2 Hz, 1H), 6.87 - 7.39 (m, 13H) and 7.58 (d, J=8.4 Hz, 2H) ppm. IR (KBr) 3510, 1370, 1180, 1130, 705, 590 and 540 cm^{-1}. Mass (m/z, %) 503 (M^+-H_2O), 394 (98), 284 (32), 239 (38), 206(26), 204 (28), 130 (52), 110 (45), 91 (100) and 77 (31).

5-Phenylthio-4-(phenylthio)methylidene-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (6). To a solution of 4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (5) (2.03 g, 3.89 mmol) in dichloromethane (50 ml) was added p-toluenesulfonic acid hydrate (100 mg) and the mixture was stirred at room temperature overnight. The solution was washed with saturated aq. $NaHCO_3$ solution, saturated aq. NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane-hexane (1:1) to give 5-phenylthio-4-(phenylthio)methylidene-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1:1 E/Z mixture, 1.58 g, 80.8 %) as viscous oil. NMR ($CDCl_3$) δ 1.65 - 2.30 (m, 2H), 2.40 (s, 3H), 2.88 - 3.14 (m, 2H), 4.08 (t, J=3.5 Hz, 1H), 4.65 (t, J=3.0 Hz, 1H), 5.87 (s, 1H), 6.38 (s, 1H), 6.35 (d, J=3.3 Hz, 1H), 6.98 (d, J=3.6 Hz, 1H), 7.05 - 7.63 (m, 12H) and 7.70 (d, J=8.4 Hz, 2H) ppm. IR (KBr) 1375, 1180, 1130, 740 and 675 cm^{-1}. Mass (m/z, %) 503 (M^+, 17), 394 (100), 284 (22), 239 (44), 206 (31), 204 (25), 130 (48), 91 (76) and 77 (27).

4-Formyl-1-(p-toluenesulfonyl)indole (2) from 5-Phenylthio-4-(phenylthio)methylidene-1-(p-

toluenesulfonyl)-4,5,6,7-tetrahydroindole (6). A mixture of 5-phenylthio-4-(phenylthio)methylidene-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (6) (1:1 E/Z, 500 mg, 0.99 mmol), $CuCl_2$ (300 mg, 2.23 mmol), methanol (2 ml), tetrahydrofuran (1 ml) and water (0.5 ml) was stirred at 50 - 60 °C overnight. The mixture was diluted with dichloromethane and filtered. The solution was washed with water, aq. $NaHCO_3$ solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane to give 4-formyl-1-(p-toluenesulfonyl)indole (2) (160 mg, 53.8 %).

5-Chloro-4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (7). To a solution of bis(phenylthio)methane (0.718 g, 3.09 mmol) in tetrahydrofuran (30 ml) at - 20 - -30 °C was added butyllithium in hexane (1.50 M, 2.06 ml, 3.09 mmol) and the mixture was stirred at the same temperature for 1 h. 5-Chloro-4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1b) (1.00 g, 3.09 mmol) was added and the mixture was stirred at - 20 - -30 °C for 2 h and at 0 - 5 °C for 2 h. The reaction was quenched with saturated aq. NH_4Cl solution and ethyl acetate was added. The organic layer was separated, washed with saturated aq. NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silia gel column (activity II) with dichloromethane-5 % hexane to give 5-chloro-4-bis(phenylthio)methyl-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (0.536 g, 31.2 %) (conversion 33.6 %). Mp 135 - 138 °C. NMR ($CDCl_3$) δ 2.03 - 2.68 (m, 2H), 2.40 (s, 3H), 2.68 - 3.30 (m, 3H), 4.97 (dd, J=4.4 Hz, J=9.8 Hz, 1H), 4.98 (s, 1H), 6.68 (d, J=3.5 Hz, 1H), 6.83 - 7.53 (m, 13H) and 7.66 (d, J=8.6 Hz, 2H) ppm. IR (KBr) 3540, 1365, 1185, 1140, 695 and 590 cm^{-1}. Mass (m/z, %) 537 (M^+-H_2O, 2), 501 (4), 428 (47), 329 (100), 393 (79), 394 (38), 324 (76), 284 (100), 232 (72), 218 (96), 204 (91), 155 (100), 110 (100), 109 (100), 91 (100) and 77 (60). Anal. Calcd for $C_{28}H_{26}ClNO_3S_3$: C, 60.47; H, 4.71; N, 2.52; S, 17.30. Found: C, 60.14; H, 4.56; N, 2.45; S, 17.40.

4-(1,3-Dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (8). To a solution of 1,3-dithiane (3.6 g, 30 mmol) in tetrahydrofuran (50 ml) at - 45 °C was added 15 % butyllithium in hexane (19.2 ml, 30 mmol) and the mixture was stirred at - 30 - - 40 °C for 3 h. 4-Oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1a) (7.0 g, 24 mmol) was added and the mixture was stirred at - 30 - - 40 °C for 2.5 h. The reaction was quenched with saturated aq. NH_4Cl and most of tetrahydrofuan was removed. The aqueous residue was extracted with ethyl acetate. The extract was washed with saturated aq. NaCl and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane to give 4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (8). Mp 132 - 133

°C (colorless plates from ethyl acetate). NMR ($CDCl_3$) δ 1.52 - 3.12 (m, 12H), 2.39 (s, 3H), 2.50 (s, 1H), 4.53 (s, 1H), 6.40 (d, J=3.6 Hz, 1H), 7.12 - 7.34 (m, 3H) and 7.50 - 7.72 (m, 2H) ppm. IR (KBr) 3550, 1600 and 1498 cm^{-1}. Mass (m/z, %) 290 (100) and 91 (42). Anal. Calcd for $C_{19}H_{23}NO_3S_3$: C, 55.72; H, 5.66; N, 3.42; S, 23.48. Found: C, 55.98; H, 5.84; N, 3.16; S, 23.56.

4-(1,3-Dithian-2-ylidene)-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (9) and 4-(1,3-Dithian-2-yl)-1-(p-toluenesulfonyl)-6,7-dihydroindole (10). A solution of 4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (8) in benzene (12 ml) was stirred with phosphoric acid (1.2 ml) at room temperature. The mixture was warmed to 80 °C for several minutes and stirred again at room temperature for 1 h. The mixture was poured onto aq. $NaHCO_3$ solution and extracted with ethyl acetate. The extract was washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with ethyl acetate-hexane to give a 79:21 mixture of 4-(1,3-dithia-2-ylidene)1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (9) and 4-(1,3-dithia-2-yl)-1-(p-toluenesulfonyl)-6,7-dihydroindole (10) (1.11 g, 97.5 %).

4-(1,3-Dithian-2-ylidene)-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (9): Mp 171 - 172 °C. NMR ($CDCl_3$) δ 1.60 - 1.94 (m, 2H), 1.94 - 2.27 (m, 2H), 2.38 (s, 3H), 2.45 - 2.66 (m, 2H), 2.66 - 3.12 (m, 6H), 7.10 - 7.34 (m, 4H) and 7.56 - 7.74 (m, 2H). IR (KBr) 1596, 1490 and 1373 cm^{-1}. Mass (m/z, %) 391 (M^+, 42) and 236 (100). Anal. Calcd for $C_{19}H_{21}NO_2S_3$: C, 58.28; H, 5.41; N, 3.58; S, 24.56. Found: C, 58.47; H,5.51; N, 3.63; S, 24.60.

4-(1,3-Dithian-2-yl)-1-(p-toluenesulfonyl)-6,7-dihydroindole (10): Mp 145 - 145.5 °C. NMR ($CDCl_3$) δ 1.40 - 3.20 (m, 10 H), 2.38 (s, 3H), 4.82 (s, 1H), 5.79 (t, J=4.6 Hz, 1H), 6.46 (d, J=3.6 Hz, 1H), 7.06 - 7.34 (m, 3H) and 7.58 - 7.74 (m, 2H) ppm. IR (KBr) 1600 and 1360 cm^{-1}. Mass (m/z, %) 391 (M^+, 100), 330 (34), 284 (34), 162 (40), 130 (60) and 91 (82). Anal. Calcd for $C_{19}H_{21}NO_2S_3$: C, 58.28; H, 5.41; N, 3.58; S, 24.56. Found: C, 58.48; H, 5.57; N, 3.27; S, 24.51.

5-Chloro-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11b). To a solution of 1,3-dithiane (144 mg, 1.2 mmol) in tetrahydrofuran (10 ml) at - 25 °C was added butyllithium in hexane (1.50 M, 0.80 ml, 1.2 mmol) and stirred at - 20 - - 30 °C for 30 min. To the solution at - 30 °C was added 5-chloro-4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (1b) (324mg, 1 mmol) and tetrahydrofuran (5 ml). The mixture was stirred at - 30 - 0 °C for 2 h and at 0 °C for 2 h. The reaction was quenched with saturated aq. NH_4Cl solution and ethyl acetate (50 ml) was added. The organic layer was separated, washed with saturated aq. NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a

silica gel column (activity II) with dichloromethane-hexane to give 5-chloro-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11b) (296 mg, 66.7 %) (conversion 78.4 %). Mp 60 - 65 °C (dec.). NMR ($CDCl_3$) δ 1.94 - 2.51 (m, 4H), 2.53 - 3.04 (m, 6H), 2.39 (s, 3H), 4.54 (s, 2H), 4.77 (dd, J=4.5 Hz, J=7.5 Hz, 1H), 6.76 (d, J=4.0 Hz, 1H), 7.16 - 7.40 (m, 3H) and 7.61 (broad d, J=8.4 Hz, 2H) ppm. IR (KBr) 1370, 1180, 1130, 705, 680 and 585 cm^{-1}. Mass (m/z, %) 389 (M^+-HCl-H_2O, 15), 388 (58), 324 (33), 315 (72), 160 (76), 155 (42), 133 (28), 119 (35), 91 (100) and 89 (27). Anal. Calcd for $C_{19}H_{22}ClNO_3S_3$: C, 51.39; H, 4.99; Cl, 7.98; N, 3.15; S, 21.66. Found: C, 51.34; H, 5.18; Cl, 8.10; N, 2.93; S, 21.51.

4-(1,3-Dithian-2-yl)-1-(p-toluenesulfonyl)indole (12) from 5-Chloro-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11b). A solution of 5-chloro-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (436 mg, 0.98 mmol) and p-toluenesulfonic acid (50 mg, 0.26 mmol) in benzene (20 ml) was heated under reflux for 30 min. The solvent was removed and the residue was chromatographed on a silica gel column to give 4-(1,3-dithian-2-yl)-1-(p-toluenesufonyl)indole (268 mg, 70.1 %). Mp 105 - 106 °C (colorless leaflets from CCl_4). NMR ($CDCl_3$) δ 1.78 - 2.17 (m, 2H), 2.26 (s, 3H), 2.65 - 3.27 (m, 4H), 5.43 (s, 1H), 6.97 (d, J=3.6 Hz, 1H), 7.05 - 7.44 (m, 2H), 7.23 (d, J=8.3 Hz, 1H), 7.56 (d, J=3.6 Hz, 1H), 7.74 (d, J=3.6 Hz, 1H) and 7.83 - 7.98 (m, 1H) ppm. IR (KBr) 1600, 1420, 1375, 1365, 1180, 1130, 780, 680 and 595 cm^{-1}. Mass (m/z, %) 389 (M^+, 70), 315 (85), 160 (100), 159 (35), 155 (33), 133 (31), 91 (75) and 89 (31). Anal. Calcd for $C_{19}H_{19}NO_2S_3$: C, 58.58; H, 4.92; N, 3.60; S, 24.69. Found: C, 58.49; H, 5.09; N, 3.55; S, 24.65.

5-Bromo-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11c). To a solution of 1,3-dithiane (144 mg, 1.2 mmol) in tetrahydrofuran (10 ml) at - 30 °C was added butyllithium in hexane (1.50 M, 0.80 mmol, 1.2 mmol) and the mixture was stirred at - 20 - -30 °C for 1.5 h. 5-Bromo-4-oxo-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11c) (368 mg, 1.0 mmol) was added and the mixture was stirred at - 78 °C - room temperature for 17 h. The reaction was quenched with saturated aq. NH_4Cl solution and dichloromethane (50 ml) was added. The organic layer was separated, washed with water, saturated aq. NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane-ethyl acetate (100:1) to give 5-bromo-4-(1,3-dithian-2-yl)-4-hydroxy-1-(p-toluenesulfonyl)-4,5,6,7-tetrahydroindole (11c) (146 mg, 29.9 %) as viscous oil. NMR ($CDCl_3$) δ 1.61 - 2.17 (m, 2H), 2.23 - 2.50 (m, 2H), 2.39 (s, 3H), 2.56 - 3.17 (m, 6H), 4.53 (s, 1H), 4.98 (dd, J=7.2 Hz, J=4.5 Hz, 1H), 6.75 (d, J=3.6 Hz, 1H), 7.17 (d, J=3.6 Hz, 1H), 7.24 (d, J=8.1 Hz, 2H), 7.59 (d, J=8.1 Hz, 1H) ppm.

4-(1,3-Dithian-2-yl)-1-(p-toluenesulfonyl)indole (12) from 5-Bromo-4-(1,3-dithian-2-yl)-1-(p-toluenesufonyl)-4,5,6,7-tetrahydroindole (11c). 5-Bromo-4-(1,3-dithian-2-yl)-4-hydroxy-4,5,6,7-tetrahydroindole (11c) decomposed spontaneously upon standing and purification of the residue on a silica gel column produced 4-(1,3-dithian-2-yl)-1-(p-toluenesulfonyl)indole (12) (103 mg, 88.3 %).

4-(1,3-Dithian-2-yl)indole (13). A mixture of 4-(1,3-dithian-2-yl)-1-(p-toluenesulfonyl)indole (12) (1.00 g, 2.57 mmol) and NaOH (0.308 g, 7.70 mmol) in methanol (50 ml) was heated under relux overnight. The reaction was quenched with saturated aq. NH_4Cl solution and methanol was removed. The residue was extracted with ethyl acetate (100 ml). The extract was washed with saturated aq. NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane-hexane to give 4-(1,3-dithian-2-yl)indole (12) (0.542 g, 89.7 %). Mp 131.0 - 131.4 °C (colorless leaflets from toluene - hexane). NMR ($CDCl_3$) δ 1.92 - 2.40 (m, 2H), 2.82 - 3.37 (m, 4H), 5.67 (s, 1H), 6.83 - 6.96 (m, 1H), 7.11 - 7.50 (m, 4H) and 8.25 (br s, 1H) ppm. IR (KBr) 3260, 1500, 1415, 1355, 1280, 758 and 502 cm^{-1}. Mass (m/z, %) 235 (M^+, 62) and 161 (100). Anal. Calcd for $C_{12}H_{13}NS_2$: C, 61.24; H, 5.57; N, 5.95; S, 27.25. Found: C, 61.43; H, 5.61; N, 5.93; S, 27.15.

4-Formyl-1-(p-toluenesulfonyl)indole (2) from 4-(1,3-Dithian-2-yl)-1-(p-toluenesulfonyl)indole (12). A mixture of 4-(1,3-dithian-2-yl)-1-(p-toluenesulfonyl)indole (182 mg, 0.47 mmol), CuO (450 mg, 5.6 mmol) and $CuCl_2$ (1.51 g, 11.2 mmol) in acetone (20 ml) was heated under reflux for 1.5 h. Dichloromethane was added and the mixture was filtered on a Celite pad. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane to give 4-formyl-1-(p-toluenesulfonyl)indole (2) (137 mg, 98.0 %).

4-Formylindole (15). A mixture of 4-formyl-1-(p-toluenesulfonyl)indole (2) (0.503 g, 2.19 mmol) and NaOH (0.257 g, 6.42 mmol) in methanol (30 ml) was heated under reflux overnight. The reaction was quenched with saturated aq. NH_4Cl solution and methanol was removed. The residue was extracted with ethyl acetate (40 ml). The extract was washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on a silica gel column with dichloromethane-hexane to give 4-formylindole (15) (0.226 g, 71.0 %). Mp 140 °C (pale yellow plates from ether - dichloromethane). NMR ($CDCl_3$) δ 7.16 - 7.80 (m, 5H), 8.50 (broad s, 1H) and 10.26 (s, 1H) ppm. IR (KBr) 3250, 1672, 1351, 1119, 759 and 698 cm^{-1}. Mass (m/z, %) 145 (M^+, 100), 116 (77) and 89 (37).

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