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SYNTHESIS OF SOME THIOPHENE-FUSED AZEPINO[5,4,3 - *cd*]INDOLES

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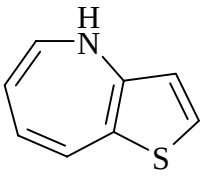
Abstract– Interaction of indolylzinc chloride with 2-chloro-3-nitrothiophene gave 3-(3-nitrothien-2-yl)indole (**7**) which was converted, *via* reduction followed by acylation, into 3-(3-acylaminothien-2-yl)indoles (**9a-c**). Cyclization of **9a-c** induced by phosphorus oxy-chloride under Bischler-Napieralski reaction conditions, took place regioselectively at the indolic C-4 locus to furnish the respective thieno[2',3' : 6,7]azepino[5,4,3-*cd*]indoles (**3a-c**).

INTRODUCTION

Various types of azepine-fused heterocycles, such as thienoazepines [1] and azepinoindoles,[2] have been investigated. Amongst, few recent reports dealt with the synthesis and medicinal activities of compounds having the thieno[3,2-*b*]azepine skeleton (**1**), [3-5] bioisostere of benzo[*b*]azepine. Some derivatives of the latter system are known to display activities such as anticancerigen,[6] calcium antagonists [7] and central nervous system depressors.[8] Different thieno[3,2-*b*]azepines showed vasopressin V1, V2 and oxytocine antagonist activity,[4] as well as affinity towards dopamine D2, serotonin 2 and serotonin 1A receptors.[5] More recently, series of synthetic tricyclic heterocycles structurally based on the thieno[3,2-*b*]azepine skeleton, have revealed interesting biological activity. Examples include substituted pyrazolo[3,4-*d*]-thieno[3,2-*b*]azepines, acting as potent orally active arginine vasopressin (AVP) receptor antagonist, [9] and pyrido[3,2-*d*]thieno[3,2-*b*]azepine derivatives, exhibiting a remarkable selectivity for renal tumor cell lines. [10]

On the other hand, the azepino[5,4,3-*cd*]indole system constitutes the skeleton of the ergot alkaloid claviciptic acid (**2**).[11] Some synthetic analogs of **2** were reported to exhibit potent activity on the central nervous system with potential against migraine attacks,[12] while others were described as dopamine D-1

receptor ligands,[13] useful for treatment of circulatory and digestive tract disorders,[14] as psychotropics, [14] diuretics and smooth muscle relaxants. [15]



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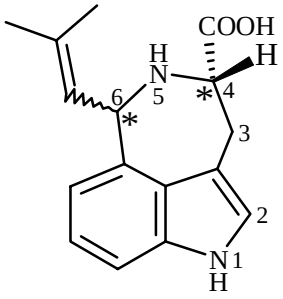

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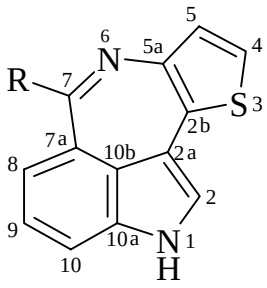

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As part of our work concerning the synthesis of fused heterocycles with potential therapeutic interest, we have described some pyrazoloazepino[5,4,3-*cd*]indoles [16] and pyrazolo-β-carbolines.[17] In continuation, we thought it is worthwhile to prepare the tetracyclic system (**3**) incorporating both thienoazepine (**1**) and azepinoindole (**2**) moieties. Herein, we report on the synthesis of thieno[2',3' : 3,2]azepino[5,4,3-*cd*]-indoles (**3**) as outlined in Scheme 1.

RESULTS AND DISCUSSION

CHEMISTRY

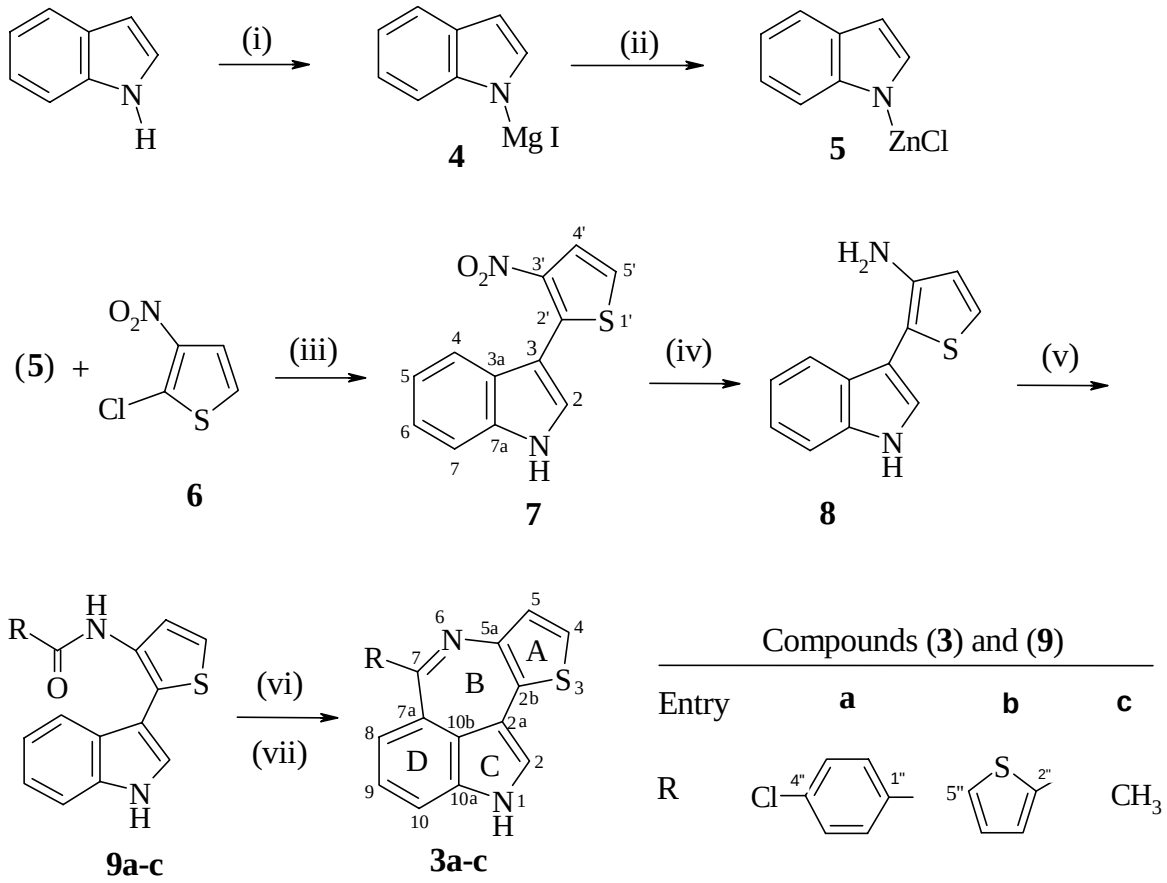
The required 3-(3-nitrothien-2-yl)indole (**7**) is readily prepared *via* coupling of indolylzinc chloride (**5**) with 2-chloro-3-nitrothiophene (**6**) (Scheme 1), following similar procedure previously reported for 3-(4-nitropyrazol-3-yl) indoles[16] and related 3-(heteroaryl)indoles.[18] Reduction of **7,** using tin and hydrochloric acid in the conventional manner, yielded the respective 3-(3-aminothien-2-yl)indole (**8**) characterized as its monohydrochloride salt. Acylation of **8** with the appropriate acyl chloride gave 3-(3-acylamino-thien-2-yl)indoles (**9a-c**) which were cyclized, using phosphorus oxychloride in acetonitrile under reflux, to furnish the desired thieno[2',3' : 6,7]azepino[5,4,3-*cd*]indoles (**3a-c**).

The formation of **3a-c** *via* their precursors (**9a-c**) implies that cyclization under Bischler-Napieralski reaction conditions occurred regioselectively at the indolic C-4 locus instead of the usual C-2 position. In this respect, compounds (**9a-c**) behaved in a similar manner to their 3-(4-aminoacylpyrazol-3-yl)indole analogs which were reported to cyclize into pyrazoloazepino[5,4,3-*cd*]indoles. [16]

SPECTRAL DATA

The new compounds (**7-9** and **3**) were characterized by MS and NMR spectral data, and by elemental

Scheme 1



(i) MeMgI (3.0 *M* in Et_2O)
(ii) $ZnCl_2$ (1.0 *M* in Et_2O)
(iii) Et_2O , 20 ^0C
(iv) Sn , conc. HCl
(v) RCOCl, C_6H_6 , NEt_3 , Δ
(vi) $POCl_3$, MeCN, Δ
(vii) 5 % NaOH

analyses. These data, detailed in the EXPERIMENTAL, are consistent with the assigned structures. Thus, the measured HRMS data for M^+ are in good agreement with the calculated values as suggested by their molecular formulas. DEPT and 2D (COSY, HMQC and HMBC) experiments showed different correlations that helped in the ^1H- and ^{13}C- signal assignments to the various hydrogens and carbons. The indolic H-2 proton`s signal is characterized by a small coupling constant (J_{CH-NH} = 2.0 - 2.5 Hz) for its doublet that collapses to a singlet upon addition of D_2O. This doublet, collapsing to a singlet, prevails in the ^1H NMR spectra of the cyclized products (**3a-c**), indicating that annulation did not occur at the indolic C-2 locus. In addition, long range correlation between H-8 and the azomethine carbon (C-7) in HMBC experiments for **3a-c**, provides supporting evidence that intramolecular cyclization occurred at the indolic C-4 locus. Protons of the methyl group appended at C-7 of **3c**, also displayed long range correlation with C-7a. These and relevant spectral features are in accord with the azepino-indole structure of the cyclized products (**3a-c**).

EXPERIMENTAL

2-Chloro-3-nitrothiophene was purchased from Apollo Scientific Ltd., UK. The acyl chlorides, zinc chloride (1.0 *M* in ether) and methylmagnesium iodide (3.0 *M* in ether) were purchased from Aldrich. Phosphorous oxychloride was purchased from BDH. Melting points (uncorrected) were determined on an electrothermal Mel-Temp. apparatus. ^{1}H- and ^{13}C NMR spectra were measured on a Bruker DPX-300 instrument with TMS as internal reference. Electron-impact MS spectra were obtained using a Finnigan MAT TSQ-70 spectrometer at 70 eV; ion source temperature = 200 ^{0}C. IR spectra were recorded as KBr discs on a Nicolet Impact-400 FT-IR spectrophotometer. Microanalyses were performed at the Microanalytical Laboratory-Inorganic Chemistry Department, Tübingen University, Germany.

3-(3-Nitrothien-2-yl)indole (7)

To a solution of indole (2.0 g; 17 mmol) in dry ether (20 mL), an ethereal solution of methylmagnesium iodide (3.0 *M* in ether, 5 mL) was added, and the mixture was stirred for 30 min at rt. An ethereal solution of $ZnCl_2$ (1.0 *M*, 15 mL) was then added, and the resultant mixture was further stirred at rt for 30 min. Later on, a solution of 2-chloro-3-nitrothiophene (**6**) (1.14 g; 7 mmol) in dry ether (20 mL) was added dropwise to the reaction mixture, and stirring was continued at rt for 6 h. Water (100 mL) was then added to the reaction mixture, the ether layer was separated and the aqueous layer was extracted with ether (3 x 50 mL). The combined ether portions were dried (anhydrous Na_2SO_4), and the solvent was evaporated. The crude product was purified by silica gel TLC chromatography, eluting with CH_2Cl_2, to afford an orange solid. Yield of pure **7** = 1.13 g (66 %), mp 95-96 °C. *Anal.* Calcd for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47; S, 13.13. Found: C, 58.86; H, 3.21; N, 11.42; S, 13.12 . IR (KBr) : *v* 3384, 3129, 3106, 3093, 1608, 1548, 1417, 1316, 1235 cm^{-1} ; MS *m/z* (% rel. int.) : 244 (M^+,100), 227 (6), 214 (8), 196 (5), 187 (40), 171 (50), 160 (13), 132 (14), 117 (20), 99 (15), 89 (13); HRMS : Calcd for $C_{12}H_8N_2O_2S$: 244.030631. Found: 244.029378; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.10 (dd, 1H, *J* = 7.4, 7.6 Hz, H-5), 7.19 (dd, 1H, *J* = 7.4, 7.9 Hz, H-6), 7.40 (d, 1H, *J* = 7.6 Hz, H-4), 7.47 (d, 1H, *J* = 7.9 Hz, H-7), 7.57 (d, 1H, *J* = 5.8 Hz, H-5'), 7.70 (d, 1H, *J* = 5.8 Hz, H-4'), 7.93 (br d, 1H, *J* = 2.2 Hz, H-2), 11.57 (d, 1H, *J* = 2.2 Hz, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 105.6 (C-3), 112.8 (C-7), 119.8 (C-4), 120.9 (C-5), 122.7 (C-6), 124.3 (C-2'), 125.2 (C-3'), 125.9 (C-3a), 128.8 (C-2), 136.7 (C-7a), 140.8 (C-5'), 141.9 (C-4').

3-(3-Aminothien-2-yl)indole (8)

Tin granules (5 g; 4.2 g atom) were added to a solution of 3-(3-nitrothien-2-yl)indole (**7**) (1.27 g; 5.2 mmol) in conc. HCl (35 mL) and 95% ethanol (10 mL).The reaction mixture was refluxed for 2 h. The

resulting solution was cooled, basified with 40 % aqueous NaOH solution, and extracted with CH_2Cl_2 (3 x 100 mL). The combined CH_2Cl_2 extracts were dried (anhydrous Na_2SO_4), and the solvent was evaporated to give a brown solid. Yield of crude product = 0.82g (74 %); A pure sample of **8**, obtained by recrystallization from ether / *n*-hexane, had mp 65-66 ^{0}C. MS *m/z* (% rel. int.) : 214 (M^+,100), 213 (46), 201 (8), 186 (17), 181 (7), 160 (12), 140 (3), 130 (16), 118 (7), 117 (11), 106 (8). Due to the instability of the title amino compound (**8**) as a free base, it was immediately used in the next *N*-acylation step.

Compound (**8**) was characterized as its stable monohydrochloride salt, 3-(3-aminothien-2-yl)indole monohydrochloride, white tiny granules (methanol – ether). Yield = 0.52 g (83 %), mp > 250 ^{0}C. *Anal*. Calcd for $C_{12}H_{11}N_2ClS$: C, 57.48; H, 4.42; N, 11.17; Cl, 14.14 ; S, 12.79. Found : C, 57.21; H, 4.26; N, 11.02; Cl, 14.05 ; S, 12.57. IR (KBr) : *v* 3276, 2981, 2783, 2583, 1607, 1560, 1525, 1429, 1249, 1122 cm^{-1} ; ^{1}H NMR (300 MHz, DMSO-d_6) : δ 7.10 (dd, 1H, *J* = 7.8, 7.5 Hz, H-5), 7.15 (dd, 1H, *J* = 7.8, 7.9 Hz, H-6), 7.25 (d, 1H, *J* = 5.4 Hz, H-5'), 7.45 (d, 1H, *J* = 7.9 Hz, H-7), 7.60 (d, *J* = 5.4 Hz, H-4'), 7.75 (d, 1H, *J* = 7.8 Hz, H-4), 8.05 (d, 1H, *J* = 2.1 Hz, H-2), 10.40 (br s, 3H, -$^+$N*H*$_3$), 11.75 (br s, 1H, N_1-*H*). ^{13}C NMR (75 MHz, DMSO-d_6): δ 105.1 (C-3), 112.6 (C-7), 119.0 (C-4), 120.6 (C-5), 122.7 (C-6), 123.9 (C-2'), 124.5 (C-4'), 124.6 (C-5'), 126.1 (C-2), 126.2 (C-3a), 129.5 (C-3'), 136.7 (C-7a).

3-[3-(4'-Chlorobenzoyl)aminothien-2-yl)]indole (9a)

p-Chlorobenzoyl chloride (0.55 g; 3.2 mmol) was added to a solution of **8** (0.64 g; 3.0 mmol) in dry benzene (30 mL), followed by addition of triethylamine (2 mL; 14.2 mmol). The resulting mixture was refluxed for 4 h. Water was added to the solution, and the resultant mixture was washed with saturated sodium bicarbonate. The aqueous layer was extracted with benzene (2 x 10 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated to give the desired amide as a white solid which was recrystallized from benzene / petroleum ether (bp 40–60 °C). Yield of **9a** = 0.68 g (64 %), mp 204-205 °C (decomp). *Anal*. Calcd for $C_{19}H_{13}N_2OClS$: C, 64.68; H, 3.71; N, 7.94; Cl, 10.05 ; S, 9.09. Found : C, 64.41; H, 3.55; N, 7.68; Cl, 9.92 ; S, 8.83. IR (KBr) : *v* 3407, 3298, 3099, 3058, 1665, 1590, 1538, 1473, 1420, 1269, 1092, 1012 cm^{-1} ; MS *m/z* (% rel. int) : 352 (M^+, 43), 335 (5), 244(3), 213 (100), 212 (38), 185 (7), 160 (4), 139 (41), 111 (21), 89 (6), 78 (17); HRMS : Calcd for $C_{19}H_{13}N_2OClS$: 352.043713. Found: 352.04482; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.03 (dd, 1H, *J* = 7.4, 7.5 Hz, H-6), 7.15 (dd, 1H, *J* = 7.2, 7.5 Hz, H-5), 7.25 (d, 1H, *J* = 5.3 Hz, H-5'), 7.42 (d, 1H, *J* = 7.4 Hz, H-7), 7.45 (d, 1H, *J* = 5.3 Hz, H-4'), 7.55 (d, 2H, *J* = 8.2 Hz, H-3"/H-5"), 7.60 (d, 1H, *J* = 2.4 Hz, H-2), 7.70 (d, 1H, *J* = 7.2 Hz, H-4), 7.92 (d, 2H, *J* = 8.2 Hz, H-2"/H-6"), 9.94 (br s, 1H, -N*H*CO), 11.41 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 107.6 (C–3), 112.4 (C-7), 119.5 (C-4), 120.1 (C-5), 121.9 (C-4'), 122.3 (C-6), 124.9 (C-2), 126.0 (C-3a), 127.8 (C-5'), 128.2 (C-2'), 128.9 (C-3"/C-5"), 130.0 (C-2"/C-6"), 130.7 (C-3'), 133.5 (C-1"), 136.6 (C-7a), 136.8 (C-4"), 165.2 (-*C*ONH).

3-[3-(2'-Thenoyl)aminothien-2-yl]indole (9b)

This compound was prepared from **8** (0.64 g; 3.0 mmol) and 2-thiophenecarbonyl chloride (0.55 g; 3.2 mmol) by following the same procedure and experimental conditions described above for **9a**. The product was recrystallized from benzene / petroleum ether producing white minute prisms. Yield of **9b** = 0.81 g (83 %), mp 130-131°C. *Anal*. Calcd for $C_{17}H_{12}N_2OS_2$: C, 62.94; H, 3.73; N, 8.63; S, 19.77. Found : C, 62.91; H, 3.66; N, 8.48; S, 19.53. IR (KBr) : *v* 3358, 3258, 3098, 1642, 1522, 1480, 1274 cm^{-1} ; MS : *m/z* (% rel. int.): 324 (M^+, 84), 307 (8), 256 (5), 213 (100), 212 (48), 201 (15), 185 (8), 160 (7), 130 (4), 128 (5), 111 (61), 83 (6); HRMS : Calcd for $C_{17}H_{12}N_2OS_2$: 324.039092. Found : 324.041118; ^{1}H NMR (300 MHz, DMSO-d_6) : δ 7.05 (dd, 1H, *J* = 7.6, 7.7 Hz, H-5), 7.08 (dd, 1H, *J* = 7.7, 7.8 Hz, H-6), 7.10 (dd, 1H, *J* = 5.1, 5.2 Hz, H-4", overlapped with H-6 signal), 7.20 (d, 1H, *J* = 5.1 Hz, H-5'), 7.38 (d, 1H, *J* = 7.8 Hz, H-7), 7.40 (d, 1H, *J* = 5.1 Hz, H-5", overlapped with H-7 signal), 7.58 (d, 1H, *J* = 2.5 Hz, H-2), 7.70 (d, 1H, *J* = 7.6 Hz, H-4), 7.80 (d, 1H, *J* = 5.1 Hz, H-4'), 7.85 (dd, 1H, *J* = 5.1, 5.2 Hz, H-4"), 9.95 (s, 1H, -N*H*CO), 11.40 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6) : δ 108.0 (C-3), 112.5 (C-6), 119.5 (C-4), 120.2 (C-5), 122.2 (C-7), 124.8 (C-2), 126.0 (C-3a), 127.8 (C-2'), 127.9 (C-4'), 128.5 (C-4"), 129.5 (C-3"), 130.3 (C-3'), 132.0 (C-5'), 136.5 (C-7a), 140.2 (C-2"), 161.0 (-*C*ONH).

3-[3-(*N*-Acetyl)aminothien-2-yl)]indole (9c)

This compound was prepared from **8** (0.64 g; 3.0 mmol) and acetyl chloride (0.26 g; 3.3 mmol), by following the same procedure and experimental conditions described above for **9a**. The product was recrystallized from benzene / petroleum ether producing white flakes. Yield of **9c** = 0.40 g (52 %), mp 65-66 °C. *Anal*. Calcd for $C_{14}H_{12}N_2OS$: C, 65.60; H, 4.72; N, 10.93; S, 12.51. Found : C, 65.42; H, 4.60; N, 10.73; S, 12.29. IR (KBr) : *v* 3352, 3204, 3112, 3063, 2924, 2858, 1693, 1592, 1487, 1401, 1252, 1091 cm^{-1} ; MS *m/z* (% rel. int.): 256 (M^+,100), 214 (94), 213 (76), 201 (22), 186 (13), 160 (12), 130 (11), 115 (7); HRMS: Calcd for $C_{14}H_{12}N_2OS$: 256.067021. Found : 256.065956; ^{1}H NMR (300 MHz, DMSO-d_6) : δ 2.10 (s, 3H, -CH_3), 7.10-7.20 (m, 3H, H-5, H-6, H-2), 7.29 (d, 1H, *J* = 5.3 Hz, H-5'), 7.45 (d, 1H, *J* = 8.1 Hz, H-7), 7.65 (d, 1H, *J* = 7.9 Hz, H-4), 7.90 (d, 1H, *J* = 5.3 Hz, H-4'), 8.80 (br s, 1H, -CON*H*), 11.40 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 24.1 (-CH_3), 107.5 (C-3), 111.8 (C-7), 119.5 (C-4), 119.8 (C-2'), 120.8 (C-4'), 123.0 (C-5), 123.2 (C-2), 123.4 (C-6), 124.1 (C-5'), 126.2 (C-3a), 132.3 (C-3'), 136.2 (C-7a), 167.6 (-*C*ONH).

7-(4-Chlorophenyl)-1*H*-thieno[2', 3' : 6,7]azepino[5,4,3-*cd*]indole (3a)

To a stirred solution of **9a** (0.74 g; 2.1 mmol) in acetonitrile (30 mL) was added phosphorous oxychloride (12 mL; 128 mmol). The resulting mixture was refluxed for 48 h under continuous stirring.

Excess acetonirile and phosphorous oxychloride were removed under vacuum and the residue was treated with ice-cooled water (100 mL). The cold aqueous solution was basified with 10% NaOH solution, extracted with dichloromethane (3 x 100 mL) and the combined organic extracts were dried (anhydrous $MgSO_4$). Evaporation of the solvent, gave a crude red solid. The product was purified on silica gel TLC plates, eluting with CH_2Cl_2: MeOH (98 : 2, v/v) to afford the title compound in analytically pure form. Yield of pure **3a** = 0.20 g (28 %), mp 240-241 °C. *Anal*. Calcd for $C_{19}H_{11}N_2ClS$: C, 68.16; H, 3.31; N, 8.37 ; Cl, 10.59; S, 9.58. Found: C, 68.03; H, 3.22; N,8.21; Cl,10.46; S, 9.34. IR (KBr) : *v* 3406, 3216, 3114, 3095, 1575, 1487, 1422, 1331, 1264, 1184, 1116 cm^{-1} ; MS *m/z* (% rel. int.) : 334 (M^+,100), 333 (64), 299 (42), 298 (31), 271 (9), 227 (3), 196 (4), 167 (11), 149 (86), 136 (41), 122 (12), 85 (8), 83 (11); HRMS : Calcd for $C_{19}H_{11}N_2ClS$: 334.03315. Found : 334.03374 ; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.15 (d, 1H, *J* = 8.2 Hz, H-8), 6.63 (d, 1H, *J* = 6.2 Hz, H-4), 6.70 (dd, 1H, *J* = 8.2, 8.3 Hz, H-9), 7.00 (d, 1H, *J* = 6.2 Hz, H-5), 7.07 (d, 1H, *J* = 8.3 Hz, H-10), 7.18 (br d, 1H, *J* = 2.0 Hz, H-2), 7.38 (d, 2H, *J* = 8.5 Hz, H-3"/H-5"), 7.45 (d, 2H, *J* = 8.5 Hz, H-2"/H-6"), 11.20 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 113.3 (C-2a), 115.7 (C-10), 117.9 (C-2), 120.5 (C-5), 122.5 (C-8), 123.4 (C-9), 128.2 (C-2"/C-6"), 129.8 (C-2b), 130.1 (C-10b), 130.1 (C-3"/C-5", superimposed over the C-10b signal), 130.8 (C-7a), 133.1 (C-4"), 133.2 (C-4), 138.2 (C-10a), 141.8 (C-1"), 142.9 (C-5a), 163.4 (C-7).

7-(2-Thienyl)-1*H*-thieno[2', 3' : 6,7]azepino[5,4,3-*cd*]indole (3b)

This compound was prepared from **9b** (0.52 g; 1.6 mmol) and phosphorous oxychloride (10 mL; 107 mmol) in acetonitrile (30 mL).This reaction mixture was refluxed for 24 h under continuous stirring, and worked up as described above for **3a**. The product was recrystallized from CH_2Cl_2 / *n*-hexane to afford dark red scales. Yield of pure **3b** = 0.17 g (35 %), mp 187-188 °C. *Anal*. Calcd for $C_{17}H_{10}N_2S_2$: C, 66.64; H, 3.29; N, 9.14; S, 20.93. Found : C, 66.51; H, 3.18; N, 9.06; S, 20.78. IR (KBr) : *v* 3408, 3220, 3072, 3060, 1617, 1547, 1493, 1409, 1321, 1244 cm^{-1} ; MS *m/z* (% rel. int.): 306 (M^+,100), 305 (67), 273 (5), 261 (16), 244 (6), 221 (3), 196 (4), 171 (3), 153 (27), 139 (11), 131 (22), 112 (10); HRMS: Calcd for $C_{17}H_{10}N_2S_2$: 306.028531. Found: 306.027193; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.66 (d, 1H, *J* = 5.2 Hz, H-4), 6.85 (dd, 1H, *J* = 7.4, 8.1 Hz, H-9), 6.95 (d, 1H, *J* = 7.4 Hz, H-8), 7.05 (m, 2H, H-5, H-3'), 7.15 (d, 1H, *J* = 8.1 Hz, H-10), 7.18 (d, 1H, *J* = 2.0 Hz, H-2), 7.42 (dd, 1H, *J* = 5.1, 4.9 Hz, H-4'), 7.60 (d, 1H, *J* = 4.9 Hz, H-5'), 11.20 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 113.2 (C-2a), 115.8 (C-10), 118.2 (C-2), 120.7 (C-5), 121.7 (C-8), 123.3 (C-9), 127.1 (C-5'), 127.7 (C-4'), 128.1 (C-3'), 129.1 (C-2b), 129.8 (C-7a), 130.4 (C-10b), 132.6 (C-4), 138.3 (C-10a), 142.5(C-5a), 146.7 (C-2'), 157.4 (C-7).

7-Methyl-1*H*-thieno[2', 3' : 6,7]azepino[5,4,3-*cd*]indole (3c)

This compound was prepared from **9c** (0.41 g; 1.6 mmol) and phosphorous oxychloride (10 mL; 107 mmol) in acetonitrile (40 mL). The resulting mixture was refluxed for 24 h under continuous stirring, and worked up as described above for **3a**. The product was recrystallized from CH_2Cl_2 / *n*-hexane forming fine red needles . Yield of pure **3c** = 0.13 g (34 %), mp 187-188 °C. *Anal*. Calcd for $C_{14}H_{10}N_2S$: C, 70.56; H, 4.23; N, 11.75; S, 13.45. Found : C, 70.23; H, 4.04; N, 11.52; S, 13.36. IR (KBr) : *v* 3400, 3240, 3096, 3061, 3042, 1583, 1422, 1349, 1265, 1187, 1146 cm^{-1} ; MS *m/z* (% rel. int.) : 238 (M^+,100), 223 (11), 196 (6), 179 (4), 156 (9), 139 (14), 119 (13), 111 (8); HRMS: Calcd for $C_{14}H_{10}N_2S$: 238.056461. Found: 238.057707; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.20 (s, 3H, -CH_3), 6.65 (d, 1H, *J* = 5.2 Hz, H-4), 6.82 (d, 1H, *J* = 7.9 Hz, H-8), 6.85 (d, 1H, *J* = 5.2 Hz, H-5), 7.13 (d, 1H, *J* = 8.2 Hz, H-10), 7.15 (d, 1H, *J* = 2.5 Hz, H-2), 7.90 (dd, 1H, *J* = 7.9, 8.2 Hz, H-9), 11.20 (br s, 1H, N_1-*H*); ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.1 (-CH_3), 113.1 (C-2a), 115.3 (C-10), 117.1 (C-2), 119.9 (C-5), 120.0 (C-8), 123.6 (C-9), 128.7 (C-2b), 129.0 (C-10b), 131.0 (C-7a), 133.1 (C-4), 137.6 (C-10a), 142.7 (C-5a), 161.3 (C-7).

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