Synthesis of New Methylated thieno[2,3-*a*] and [3,2-*b*]carbazoles by Reductive Cyclization of 6-(2'-Nitrophenyl)benzo[*b*]thiophenes Obtained by Palladium-catalyzed Cross-coupling

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The synthesis of new methylated thieno[2,3-*a*] and [3,2-*b*]carbazoles (**5**) (R=H) was achieved by a palladium-catalyzed cross-coupling, intramolecular reductive cyclization sequence of reactions. The cyclization precursors 6-(2'-nitrophenyl)benzo[*b*]thiophenes (**3**) were obtained by Suzuki cross-coupling of 6-boronated methylbenzo[*b*]thiophenes intermediates (**2**) with 2-bromo or iodonitrobenzene. The boronated intermediates (**2**) were prepared *via* bromine-lithium exchange followed by boron transmetalation and coupled *in situ* using $Pd(OAc)_2$ giving thus a "one-pot" three steps reaction from the 6-bromobenzo[*b*]thiophenes (**1**) to the cyclization precursors (**3**). In the reductive cyclization step, *N*-ethylthienocarbazoles (**5**) (R=Et) were also obtained. Several experiments have been made varying the amount of triethylphosphite and the time of reaction, to avoid their formation.

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Thienocarbazoles are considered bioisosteres [1a,b] of the well known anti-tumour pyridocarbazoles [2], ellipticines and olivacines. The presence of the sulphur atom could provide the establishment of additional long distance hydrogen bonds with the DNA chains thus enhancing the biological activity of these intercalating compounds. The importance for biological activity of the presence of methyl groups in key positions of the structure of pyridocarbazoles had been evaluated [3] and led us to the synthesis of different methylated thienocarbazoles.

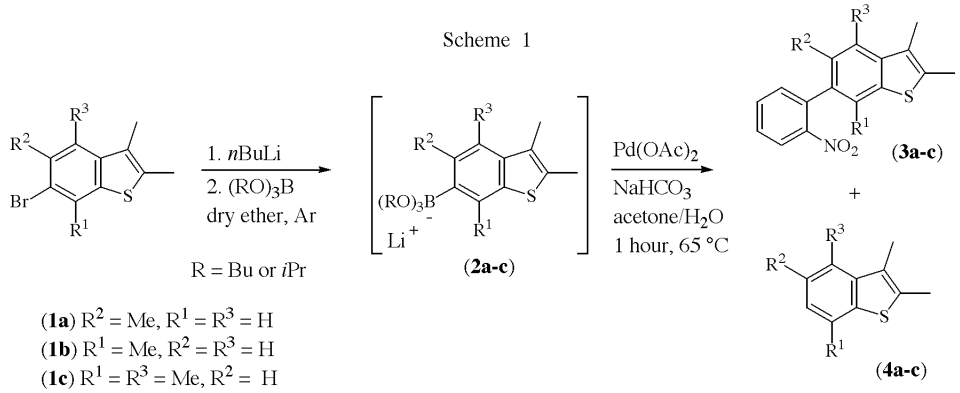
In earlier work [4] we tried to obtain methylated thieno[2,3-*b*]carbazoles by a ring B convergent method of synthesis. Diarylamides were obtained by Goldberg coupling [5] of arylbromides with 6-acetamides of methylated benzo[*b*]thiophenes. After hydrolysis to the corresponding diarylamines, cyclisation using palladium acetate in acidic media [6] only gave a very low yield of the 2,3,10-trimethyl-9*H*-thieno[2,3-*b*]carbazole along with many by-products (may be acetoxylation products) which were not identified.

In this paper we describe the synthesis of new methylated thieno[2,3-*a*] and [3,2-*b*]carbazoles (**5**) by reductive cyclization of 6-(2'-nitrophenyl)benzo[*b*]thiophenes (**3**), which were prepared by Suzuki cross-coupling [7] under phosphine-free and mild conditions [8] in a "one-pot" three steps reaction, starting with 6-bromobenzo[*b*]thiophenes (**1**). Reductive cyclization occurred at 160 °C with triethyl phosphite for 3 or 5 hours depending on the substituents. The corresponding *N*-ethylthienocarbazoles (**5**) (R=Et) were also isolated, sometimes in significant amounts.

Our work is an example of symbiosis of palladium-catalyzed cross-coupling and intramolecular cyclization in order to obtain potentially biological active polycyclic compounds.

Methylated benzo[*b*]thiophenes (**4**) were first prepared from methylthiophenols and 3-bromobutan-2-one [9] and were regioselectively brominated at the 6-position according to literature proceedure [10] to give bromo compounds (**1**). The boron intermediates (**2**) were prepared from the

Scheme 1



(**1a**) R^2 = Me, R^1 = R^3 = H
(**1b**) R^1 = Me, R^2 = R^3 = H
(**1c**) R^1 = R^3 = Me, R^2 = H

6-bromomethylbenzo[*b*]thiophenes (**1**) by bromine-lithium exchange and boron transmetalation using tributyl or triisopropylborates, and were not isolated. The coupling reaction with 2-bromo (or 2-iodo) nitrobenzene was made *in situ* using palladium acetate and sodium hydrogen-carbonate in acetone/water heating for 1 hour at 65 °C (Scheme 1). Methylbenzo[*b*]thiophenes (**4**) were isolated as by-products at the end of the reactional sequence.

The ^{1}H nmr of the crude intermediates (**2**), before adding acetone/water, showed already the presence of the corresponding methylbenzo[*b*]thiophenes (**4**) as by-products, indicating that their isolation at the end of the sequence was not only due to deboronation that normally occurs in the coupling reaction. In order to study the effect of the temperature of the two first steps, halogen-lithium exchange and transmetalation using tributylborate, in the formation of compounds (**4**), several experiments were carried out and the results were compared in terms of coupling product and by-products yields (Table 1). The yields were calculated based in the initial amounts of 6-bromomethylbenzo[*b*]thiophenes (**1**).

conditions, the yield did not increase for (**3a**) (32%) but increased significantly from 30% to 53% for (**3b**). The corresponding methylbenzo[*b*]thiophenes (**4**) were still isolated at the end, (**4a**) in 20% and (**4b**) in 15%.

The advantages of this palladium-catalyzed cross-coupling lie in working under phosphine free conditions, avoiding the isolation of boronic acids and working *in situ* from the 6-bromo derivatives (**1**) with only changing the solvent of the reaction, replacing ether, after vacuum evaporation, by acetone/water. Suzuki couplings are largely unaffected by the presence of water and tolerate a broad range of functionality.

The reductive cyclization of compounds (**3**), using triethyl phosphite [12], afforded the thienocarbazoles (**5**) (R=H) in fair to moderate yields and the corresponding *N*-ethylated compounds (**5**) (R=Et) (Scheme 2 and Table 2).

The presence of methyl groups in ring C together with the formation of *N*-ethyl thienocarbazoles (**5**) (R=Et) may explain partially the low range of yields obtained. The same remarks have been made for the synthesis of methylated carbazoles by Ames *et al*. [13]. For

Table 1

Yields of Coupling Products (**3**) and by-Products (**4**) Changing the Temperatures of Halogen-Lithium Exchange and of Transmetalation steps, using $(BuO)_3B$

SM	Lithiation Temperature (°C)	Transmetalation Temperature (°C)	NO_2-Benzene compound	Coupling product [a] (**3**) (%)	By-product (**4**) (%)
(**1a**)	0	0	2-Br	29	38
	0	-20	2-Br	34	5
	0	-70	2-I	21	26
(**1b**)	0	-20	2-Br	30	10
	0	-70	2-I	17	25
(**1c**)	0	-20	2-Br	51	20
	-20	-20	2-Br	49	__[b]

[a] 3 Mol% of Pd $(OAc)_2$ were used in the coupling reaction; [b] Starting material (**1c**)was recovered in 38%.

From the analysis of Table 1, the best temperature conditions are 0 °C for the halogen-lithium exchange and -20 °C for the transmetalation step. For compound (**3c**) the yield was 49% even performing the halogen-lithium exchange at -20 °C, with the recover of 38% of starting material (**1c**).

The unreacted 2-bromo or iodonitrobenzenes were also isolated in the chromatographic purification, being easier separated from products (**3**) when mixtures of chloroform/petroleum ether were used.

To compare yields, triisopropylborate [11] was used in the transmetalation step, which was performed at -10 °C, in the synthesis of (**3a**) and (**3b**) and in these experiments we followed the suggestion of Wallow and Novak [8] in order to decrease deboronation that occurs in the coupling reaction, using a 10% excess of the boronated compound (**2**) relative to the other coupling component. With these

decreasing the formation of *N*-alkylation products, lower excess of triethyl phosphite and lesser time of reaction were used and the yields for (**5a**) (R=H) and (**5b**) (R=H) were increased. In the case of the synthesis of (**5c**) (R=H) 4 equivalents were needed and 5 hours of reflux to obtain a 36% yield. Following the reaction by tlc it was observed that after 3 hours of reflux using only 2 equivalents of triethyl phosphite a significant amount of starting material remained. Addition of 2 more equivalents and 2 additional hours of reflux increased product (**5c**) formation, which was isolated in 36% yield. No *N*-ethyl compound was isolated in this experiment but another by-product (**5d**) (m/z M^+ 265) was isolated (2%), resulting from loss of the methyl group *ortho* to the C-C bond formed in compound (**3c**) and cyclization at that position.

Scheme 2

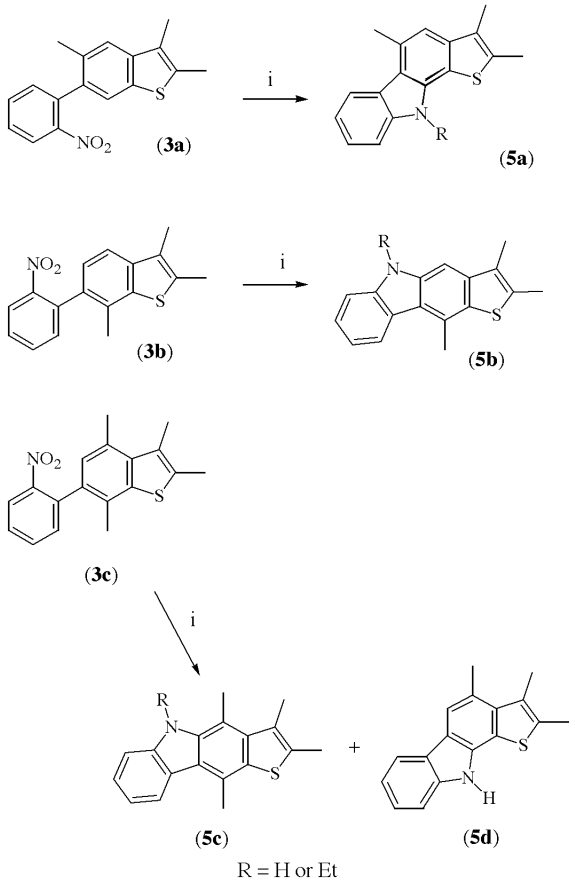


Table 2

Comparative Yields of Compounds (**5**) Changing the Amount of Triethyl Phosphite and the Time of Reaction

SM	Equiv. of $(EtO)_3P$	Reaction time (h)	(**5**)(R=H) (%)	(**5**)(R=Et) (%)	Unreacted (**3**) (%)
(**3a**)	4	4.5	11	6	—
	2	3.5	22	—	11
	2.5	3	53	10	8
(**3b**)	4.5	5	6	17	—
	2	3	22	12	—
	3	4	23	13	6
(**3c**)	4 (2+2)	5	36	—	—
	4	5	42	5	4

When this reaction was repeated beginning with 4 equivalents of triethyl phosphite and heating for 5 hours, by-product (**5c**) (R=Et) was isolated (5%) but the yield for thienocarbazole (**5c**) (R=H) increased to 42%. In this experiment no formation of the by-product (**5d**) was observed.

We have shown that reductive cyclization of nitro derivatives presents a new way to thienocarbazoles synthesis. It has been pointed out that a halogen-lithium exchange reaction followed by boronation and palladium catalyzed coupling could be made in a "one pot" reaction.

EXPERIMENTAL

Melting points were determined in a Gallenkamp apparatus and are uncorrected. The ir spectra were recorded as nujol mulls on a Perkin-Elmer 1600-FTIR spectrophotometer. The uv spectra were recorded in ethanol on a Hitachi U-2000 spectrophotometer. The ^{1}H nmr spectra were measured on a Varian Unity Plus at 300MHz, using the signal of the solvents (chloroform of the deuteriochloroform or dimethylsulfoxide of dimethylsulfoxide-d_6) as internal references. Spin-spin decoupling technique was used. The ^{13}C nmr spectra were measured in the same instrument at 75,4MHz (using DEPT θ 45°). The mass spectra were obtained on a Unicam GC/MS 120 spectrometer by an electronic impact (70eV) direct injection method. Elemental analyses were determined on a LECO CHNS 932 elemental analyser.

Flash chromatography was made on silica gel 230-400 mesh. Petroleum ether refers to the boiling range 40-60 °C.

General Procedures for Bromine-Lithium Exchange, Transmetalation and *in situ* Coupling Reaction.

Procedure A.

To a 0 °C (unless stated otherwise, Table 1) solution of 6-bromo compound (**1**) (6 mmol) in dry ether (30 mL) under Ar, a 1.6 *M* solution of *n*BuLi in hexane (4 mL, 7 mmol) was added dropwise. The solution was stirred for 20 minutes, cooled to -20 °C (unless stated otherwise, Table 1) and tributylborate (2 mL, 7 mmol) was added under Ar. After 10 minutes the mixture was left stirring at room temperature for 2 hours, and the solvent was then removed under vacuum. Acetone (15 mL), water (15 mL), 2-bromo or iodonitrobenzene (6 mmol), $NaHCO_3$ (15 mmol) and $Pd(OAc)_2$ (3 mol%) were added. The mixture was heated at 65 °C for 1 hour and after cooling was extracted with ether (3x50 mL). The organic phase was washed with water, treated with activated carbon, dried ($MgSO_4$), and the solvent removed to give a mixture which was submitted to flash chromatography (ether/petroleum ether) to give coupling products (**3**) and by-products (**4**).

Procedure B.

Same as procedure A with 1.1 equivalents of *n*BuLi at 0 °C and 1.1 equivalent of $(i\text{PrO})_3B$ at -10 °C. In the coupling reaction 0.9 equivalents of 2-bromonitrobenzene was used. Extractions with chloroform gave oily green solids which were submitted to flash chromatography (chloroform/petroleum ether) to give compounds (**3**) and by-products (**4**).

6-(2'-Nitrophenyl)-2,3,5-trimethylbenzo[*b*]thiophene (**3a**).

Compound **3a** was prepared by Procedure A at 0 °C in the two first steps, 2-bromonitrobenzene in the coupling reaction and solvent gradient from petroleum ether to 5% ether/petroleum ether in the flash chromatography. Two products were obtained, the less polar was isolated as a white solid and showed to be

2,3,5-trimethylbenzo[*b*]thiophene (**4a**) (38%), mp 56-58 °C (lit.[9] 56-57 °C), ^{1}H nmr ($CDCl_3$): δ 2.26 (s, 3 H, Me), 2.47 (s, 6 H, 2xMe), 7.10 (dd, 1 H, *J* = 8 and 1.5 Hz, 6-H), 7.49 (broad s, 1 H, 4-H), 7.61 (d, 1 H, *J* = 8 Hz, 7-H), and the second isolated as a yellow solid showed to be compound (**3a**) (29%), mp 140-142 °C; ir: 1608, 1571, 1521, 1459, 1377, 1350, 1299, 1270, 1249, 1148, 1093, 956, 868, 851, 787, 771, 748, 730, 711, 674, 666, 630 cm^{-1}; uv: λ_{max} (EtOH) (ε,dm^3 mol^{-1} cm^{-1}) 275 (sh, 17857), 262 (inf., 20833), 241 (42560) nm; ^{1}H nmr ($CDCl_3$): δ 2.21 (s, 3 H, Me), 2.32 (s, 3 H, Me), 2.50 (s, 3 H, Me), 7.38 (dd, 1 H, *J* = 7.63 and 1.5 Hz, 6'-H), 7.47 (s, 2 H, 4 and 7-H), 7.53 (oct, 1 H, *J* = 7.93, 7.63 and 1.5 Hz, 4'-H), 7.65 (td, 1H, *J* = 7.63 and 1.5 Hz, 5'-H), 8.02 (dd, 1 H, *J* = 7.93 and 1.5 Hz, 3'-H). Irradiation at δ 7.38 changed the octet centred at δ 7.53 into an apparent triplet and the td centred at δ 7.63 into a dd. Irradiation at δ 7.53 changed the dd at δ 8.02 into a *meta* doublet, the td centred at δ 7.63 into a dd and the dd at δ 7.37 into a doublet. Irradiation at δ 7.65 changed the dd at δ 7.38 into a *meta* doublet, the octet centred at δ 7.53 into a broad d and the dd at δ 8.02 into an *ortho* doublet. Irradiation at δ 8.02 turned the octet centred at δ 7.53 into a dd and the td centered at δ 7.63 into an triplet. ^{13}C nmr ($CDCl_3$): δ 11.38 (CH_3), 13.84 (CH_3), 20.23 (CH_3), 121.38, 122.04, 124.07, 126.63 (Cq), 128.33, 131.52 (Cq), 132.46, 132.53, 133.48 (Cq), 134.58(Cq), 135.42 (Cq), 136.70 (Cq), 141.12 (Cq), 149.23 (Cq); ms: *m/z* (%) 297 (M$^+$, 100), 282 (M$^+$-Me, 25), 266 (40), 250 (70), 235 (60), 221 (30), 215 (20), 202 (21), 189 (23), 165 (20).

Anal. Calcd. for $C_{17}H_{15}NO_2S$: C, 68.7; H, 5.1; N, 4.7; S, 10.8. Found C, 68.5; H, 5.2; N, 4.8; S 10.7.

Performing the transmetalation step at -20 °C the yield for (**3a**) increased to 34% and the yield of by-product (**4a**) decreased to 5%, with recovery of some 2-bromonitrobenzene.

Performing the transmetalation step at -70 °C and using 2-iodonitrobenzene in the coupling reaction (**3a**) was obtained in 21% and (**4a**) in 26%.

Following procedure B and using in the flash chromatography mixtures from 20% to 45% $CHCl_3$/petroleum ether, by-product (**4a**) was obtained in 20%, followed by 2-bromonitrobenzene, and (**3a**) was obtained in 32% yield.

6-(2'-Nitrophenyl)-2,3,7-trimethylbenzo[*b*]thiophene (**3b**).

Compound **3b** was prepared by Procedure A. Purification by flash chromatography using solvent gradient from petroleum ether to 15% ether/petroleum ether, gave 2,3,7-trimethylbenzo-[*b*]thiophene (**4b**) (10%) as a white solid, mp 46-48 °C (lit.[9] 51-52 °C), ^{1}H nmr ($CDCl_3$): δ 2.32 (s, 3 H, Me), 2.51 (s, 3 H, Me), 2.52 (s, 3 H, Me), 7.08 (dd, 1 H, *J* = 8 and 1.5 Hz, 6-H), 7.30 (t, 1 H , *J* = 8 Hz, 5-H) 7.45 (d, 1 H, *J* = 8 Hz, 4-H), followed by compound (**3b**) isolated as a yellow solid mp 116-118 °C, contamined with 2-bromonitrobenzene. Crystallization from $CHCl_3$/petroleum ether gave (**3b**) as yellow crystals (30%) mp 127-129 °C; ir: 1607, 1573, 1522, 1460, 1377, 1359, 1298, 1282, 1192, 1160, 1145, 1096, 1001, 853, 819, 810, 784, 758, 749, 731, 716, 666, 638 cm^{-1}; uv: λ_{max} (EtOH) 273(sh, ε 17973), 257 (inf, 19865), 238 (51250), 205 (84628) nm; ^{1}H nmr ($CDCl_3$): δ 2.28 (s, 3H, Me), 2.32 (s, 3H, Me), 2.52 (s, 3H, Me), 7.15 (d, 1H, *J* = 8.24 Hz, 5-H), 7.39 (dd, 1H, *J* = 7.63 and 1.5 Hz, 6'-H), 7.48 (d, 1 H, *J* = 8.24 Hz, 4-H), 7.54 (oct, 1 H, *J* = 7.93, 7.63 and 1.5 Hz, 4'-H), 7.65 (td, 1 H, *J* = 7.63 and 1.2 Hz, 5'-H), 8.00 (dd, 1 H, *J* = 7.93 and 1.2 Hz, 3'-H); ^{13}C nmr: δ 11.49 (CH_3), 13.87 (CH_3), 18.05 (CH_3), 118.66, 123.97, 125.00, 127.84 (Cq), 128.16, 128.94 (Cq), 131.88 (Cq), 132.21, 132.74, 134.27 (Cq), 136.36 (Cq), 138.96 (Cq), 140.67 (Cq), 149.59 (Cq); ms: *m/z* (%) 297 (M$^+$, 80).

Anal. Calcd. for $C_{17}H_{15}NO_2S$: C, 68.7; H, 5.1; N, 4.7; S, 10.8. Found: C, 68.7; H, 5.0; N, 4.7; S, 10.9.

Performing the transmetalation step at -70 °C and using 2-iodonitrobenzene in the coupling reaction, the yield for compound (**4b**) was 25% and (**3b**) was obtained in 17%.

Following procedure B and using in the flash chromatography mixtures from 20% to 45% chloroform/ petroleum ether, by-product (**4b**) was obtained in 15% and the yield for compound (**3b**) increased to 53%.

6-(2'-Nitrophenyl)-2,4,3,7-trimethylbenzo[*b*]thiophene (**3c**).

Compound **3c** was prepared by Procedure A. Purification by flash chromatography using solvent gradient from petroleum ether to 5% ether/petroleum ether, gave a less polar product as a white solid that showed to be 2,3,4,7-tetramethylbenzo[*b*]–thiophene (**4c**) (20%), mp 63-65 °C (lit.[14] 67.5 °C), ^{1}H nmr ($CDCl_3$): δ 2.45 (s, 3 H, Me), 2.48 (s, 3 H, Me), 2.52 (s, 3 H, Me), 2.57 (s, 3 H, Me), 6.93 (dd, 1 H, *J* = 8, 5-H), 7.00 (d, 1 H, *J* = 8 Hz, 6-H), followed by compound (**3c**) as a yellow solid (51%), m.p. 169-171 °C; ir: 1610, 1571, 1523, 1456, 1378, 1352, 1302, 1271, 1183, 1145, 1112, 1091, 1029, 1015, 959, 919, 867, 857, 843, 800, 786, 759, 722, 710, 684, 665, 642, 627 cm^{-1}. uv: λ_{max} (EtOH) 307 (ε, 6526), 296 (sh, 7792), 274 (sh, 12987), 260 (inf. 14610), 238 (35584) nm; ^{1}H nmr ($CDCl_3$): δ 2.33 (s, 3 H, Me), 2.49 (s, 3 H, Me), 2.53 (s, 3 H, Me), 2.73 (s, 3 H, Me), 6.85 (s, 1 H, 5-H), 7.37 (dd, 1 H, *J* = 7.63 and 1.5 Hz, 6'-H), 7.53 (oct, 1 H, *J* =7.93, 7.63 and 1.5Hz, 4'-H), 7.63 (td, 1 H, *J* = 7.63 and 1.5 Hz, 5'-H), 7.98 (dd, 1 H, *J* = 7.93 and 1.5 Hz, 3'-H); ^{13}C nmr ($CDCl_3$): δ 14.16 (CH_3), 15.19 (CH_3), 17.60 (CH_3), 21.31 (CH_3), 123.93, 126.61 (Cq), 127.58, 128.05, 129.31 (Cq), 130.30 (Cq), 131.39 (Cq), 132.17, 132.76, 133.52 (Cq), 136.31 (Cq), 138.81 (Cq), 139.44 (Cq), 149.57 (Cq); ms: *m/z* (%) 311 (M$^+$, 100).

Anal. Calcd. for $C_{18}H_{17}NO_2S$: C, 69.4; H, 5.5; N, 4.5; S 10.3. Found C, 69.3; H, 5.7; N, 4.5; S, 10.1.

Performing the halogen-lithium exchange at -20 °C, starting material (**1c**) was recovered in 38% and (**3c**) was obtained in 49%.

General Procedure for the Reductive Cyclisation.

To compounds (**3**) (0.3 to 1 mmol) triethyl phosphite (2-4 equivalents) was added under Ar. The mixture was heated at 160 °C for 3 to 5 hours (Table 2). The excess triethyl phosphite was removed directly under vacuum or after a work-up with water and extractions with chloroform. The orange oils obtained were submitted to flash chromatography using mixtures of ether/petroleum ether or $CHCl_3$/petroleum ether to give compounds (**5**).

2,3,5-Trimethyl-10*H*-thieno[2,3-*a*]carbazole (**5a**).

Compound (**3a**) (0.3 mmol), triethyl phosphite (0.6 mmol), were heated under reflux for 3.5 hours. Flash chromatography using solvent gradient from petroleum ether to 5% ether/-petroleum ether gave starting material (11%) as less polar product and compound (**5a**) as a white solid (22%) mp 214-216 °C. ir: 3392, 1612, 1553, 1457, 1377, 1353, 1323, 1286, 1245, 1226, 1172, 1152, 1122, 1086, 1036, 878, 839, 772, 745, 733, 666 cm^{-1}; ^{1}H nmr: ($CDCl_3$): δ 2.39 (s, 3 H,

Me), 2.57 (s, 3 H, Me), 2.99 (s, 3 H, Me), 7.25 (s, 1 H, 4-H), 7.30 (spet, 1 H, *J* = 7.93, 7.63 and 1.22 Hz, 7-H), 7.42 (td,1 H, *J* = 7.63 and 1.22 Hz, 8-H), 7.52 (dt, 1 H, *J* = 7.63, 1.22 and 0.92 Hz, 9-H), 8.21 (broad d, 1 H, *J* = 7.93 Hz, 6-H), 8.23 (s, 1H, H/D exchangeable, NH). Irradiation at δ 8.21 changed the sept centred at δ 7.30 into an *o,m* dd, the td centred at δ 7.42 into an *ortho* triplet and the dt centred at 7.52 into an *o,m* dd. ^{13}C nmr ($CDCl_3$): δ 11.87 (CH_3), 13.9 (CH_3), 21.17 (CH_3), 110.63, 114.59, 117.59 (Cq), 118.15 (Cq), 119.77, 122.05, 124.36, 124.78 (Cq), 128.36 (Cq), 129.85 (Cq), 131.83 (Cq), 133.80 (Cq), 138.96 (Cq), 140.24 (Cq).

Anal. Calcd. for $C_{17}H_{15}NS$: C, 76.9; H, 5.7; N, 5.3; S, 12.1. Found: C, 76.7; H, 5.5; N, 5.2; S, 12.0.

From another preparation using compound (**3a**) (0.7 mmol), triethyl phosphite (1.75 mmol), 3 hours of reflux, and using mixtures from 20 to 50% $CHCl_3$/petroleum ether in the chromatographic purification, by-product (**5a**) (R=Et) was isolated (10%) as the less polar product, not in a very pure form, as a pink oily solid, ^{1}H nmr: ($CDCl_3$) excluding signals of impurities: δ 1.52 (t, 3 H, *J* = 7 Hz, NCH_2CH_3), 2.41 (s, 3 H, Me), 2.59 (s, 3 H, Me), 3.00 (s, 3 H, Me), 4.70 (q, 2 H, *J* = 7 Hz, NCH_2CH_3), 7.25-7.34 (m partially obscured by the signal of $CHCl_3$, 2 H , 4 and 7-H), 7.45-7.52 (m, 2 H, 8 and 9-H), 8.26 (d, 1 H, *J* = 8 Hz, 6-H); ms: *m/z* (%) 293 (M^+, 100), 278 (M^+-Me, 30), 265 (20), followed by starting material (**3c**) (8%) and as the most polar product compound (**5a**) (R=H) was isolated in 53% yield.

2,3,10-Trimethyl-5*H*-thieno[3,2-*b*]carbazole (**5b**).

Compound (**3b**) (0.7 mmol), triethyl phosphite (3.15 mmol) were heated for 5 hours. Purification by plc, 30% ether/-petroleum ether, gave the *N*-ethylated product as a green solid, not in a very pure form, **5b** (R=Et) (17%), mp 132-135 °C; ^{1}H nmr ($CDCl_3$) excluding signals of impurities: δ 1.47 (t, 3 H, *J* = 7.2 Hz, NCH_2CH_3), 2.41 (s, 3 H, Me), 2.57 (s, 3 H, Me), 3.06 (s, 3 H, Me), 4.42 (q, 2 H, *J* = 7.2 Hz, NCH_2CH_3), 7.26 (m partially obscured by the signal of $CHCl_3$, 2H, Ar-H), 7.36-7.52 (m, 2H, Ar-H), 8.27 (d, 1 H, *J* = 8 Hz , 9-H), ^{1}H nmr: δ (DMSO-d_6) 1.31 (t, 3 H, *J* = 7.02 Hz, NCH_2CH_3), 2.37 (s, 3 H, Me), 2.51 (s, 3 H, Me), 2.94 (s, 3 H, Me), 4.50 (q, 2 H, *J* = 7.02 Hz, NCH_2CH_3), 7.20 (td, 1 H, *J* = 8.24 and 0.91 Hz, 8H), 7.46 (td, 1 H, , *J* = 7.94 and 0.91 Hz, 7-H), 7.59 (d, 1 H, *J* = 8.24 Hz, 6-H), 7.64 (s, 1 H, 4-H) 8.20 (broad d, 1 H, *J* = 7.94 Hz, 9-H) and the thienocarbazole (**5b**) (R=H) as a white solid (6%) m.p. 212-214 °C; ir: 3392, 3371, 1619, 1606, 1579, 1495, 1456, 1403, 1378, 1354, 1324, 1268, 1223, 1162, 1117, 1095, 1051, 1019, 919, 861, 847, 830, 824, 742, 727, 691, 666, 607 cm^{-1}; ^{1}H nmr (DMSO- d_6): δ 2.32 (s, 3 H, Me), 2.50 (s, 3 H, Me), 2.93 (s, 3 H, Me), 7.16 (td, 1 H, *J* = 7.63 and 1.22 Hz, 8-H), 7.38 (td,1 H, *J* = 7.94 and 1.22 Hz, 7-H), 7.47 (d, 2 H, *J* =7.94 Hz, 4-H and 6-H), 8.17 (broad d, 1H, *J* =7.63 Hz, 9-H), 11.2 (s, 1 H, NH); ^{13}C nmr ($CDCl_3$): δ 11.80 (CH_3), 14.24 (CH_3), 18.79 (CH_3), 99.26, 110.01, 119.16, 120.04 (Cq), 122.44, 123.65 (Cq), 125.19, 125.84 (Cq), 127.14 (Cq), 130.99 (Cq), 133.87 (Cq), 138.83 (Cq), 139.70 (Cq), 140.60 (Cq); ms: *m/z* (%) 265 (M^+, 90) 250 (M^+-Me, 20) 217 (30) 204 (25).

Anal. Calcd. for $C_{17}H_{15}NS$: C, 76.9; H, 5.7; N, 5.3; S, 12.1. Found C, 76.6; H, 6.0; N, 5.4; S 11.8.

From other preparation using compound (**3b**) (0.46 mmol) triethyl phosphite (1.4 mmol) and heating for 4 hours, *N*-ethyl derivative (**5b**) (R=Et) was isolated in 13% yield , and compound (**5b**) (R=H) in 23% yield after flash chromatography (from 20 to 40% $CHCl_3$/petroleum ether).

2,3,4,10-Tetramethyl-5*H*-thieno[3,2-*b*]carbazole (**5c**).

Compound (**3c**) (0.5 mmol) triethyl phosphite (1 mmol +1 mmol after 3 hours of reflux) were heated for 5 hours. Flash chromatography using petroleum ether to 10% ether/petroleum ether gave 2,3,4-trimethyl-10*H*-thieno[2,3-*a*]carbazole (**5d**) (2%) as less polar product, not in a very pure form; ^{1}H nmr ($CDCl_3$) excluding signals of impurities: δ 2.54 (s, 3 H, Me), 2.61 (s, 3 H, Me), 2.91 (s, 3 H, Me), 7.24 (broad t, 1 H, partially obscured by the signal of $CHCl_3$, 7-H), 7.38 (broad t, 1 H, *J* = 8 Hz, 8-H), 7.48 (d, 1 H, *J* =8 Hz, 9-H), 7.72 (s, 1 H, 5-H), 8.03 (d,1 H, *J* = 8 Hz, 6-H), 8.07 (s, 1 H, H/D exchangeable, NH); ms: *m/z* (%) 265 (M^+, 40). Compound (**5c**) (R=H) was isolated in 36% yield as a white solid, m.p. 219-221 °C; ir: 3467, 1602, 1577, 1488, 1456, 1377, 1344, 1324, 1314, 1277, 1252, 1158, 1126, 1111, 1096, 1019, 1005, 918, 863, 846, 773, 748, 738, 688, 666, 601 cm^{-1}. ^{1}H nmr (DMSO-d_6): δ 2.45 (s, 3 H, Me), 2.55 (s, 3 H, Me), 2.88 (s, 3 H, Me), 2.90 (s, 3 H, Me), 7.14 (broad t, 1 H, *J* = 8 Hz, 8-H), 7.37 (broad t, 1 H, *J* = 8 Hz, 7-H), 7.48 (d, 1 H, *J* = 8.2 Hz, 6-H), 8.14 (d, 1 H, *J* = 7.93 Hz, 9-H), 10.97 (s, 1 H, H/D exchangeable, NH). Irradiation at δ 8.14 changed the broad t centred at 7.14 into a broad doublet and the broad t centred at 7.37 into a sharpened triplet. Irradiation at δ 7.48 changed the broad t centred at 7.37 into a dd and the broad t centred at 7.14 into a sharpened triplet. ^{13}C nmr (DMSO-d_6): δ 14.13 (CH_3), 14.27 (CH_3), 15.57 (CH_3), 18.21 (CH_3), 110.43, 110.86 (Cq), 118.28, 118.63 (Cq), 121.71 (Cq) 122.08, 122.68 (Cq), 125.08, 128.62 (Cq), 130.10 (Cq), 132.10 (Cq), 136.49 (Cq), 138.84 (Cq), 141.07 (Cq); ms: *m/z* (%) 279 (M^+, 100) 264 (M^+-Me, 20).

Anal. Calcd. for $C_{18}H_{17}NS$: C, 77.5; H, 6.4; N; 5.3; S, 11.6. Found C, 77.7; H, 6.5; N, 5.2; S, 11.6.

From other preparation using compound (**3c**) (0.7 mmol) triethyl phosphite (2.8 mmol) and 5 hours of reflux, by-product (**5c**) (R=Et) was isolated in 5% yield, ^{1}H nmr ($CDCl_3$): δ 1.41 (t, 3 H, *J* = 7.02 Hz, NCH_2CH_3), 2.52 (s, 3 H, Me), 2.63 (s, 3 H, Me), 2.99 (s, 3 H, Me), 3.12 (s, 3 H, Me), 4.48 (q, 2 H, *J* = 7.02 Hz, NCH_2CH_3), 7.22 (broad t partially obscured by the $CHCl_3$ signal, 1 H, 8-H), 7.44 (m, 2 H, 6 and 7-H), 8.22 (d,1H, *J* = 8 Hz, 9-H), starting material (**3c**) (4%) and thienocarbazole (**5c**) (R=H) in 42% yield.

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