HETEROCYCLES, Vol. 75, No. 12, 2008, pp. 3015 - 3024. © The Japan Institute of Heterocyclic Chemistry
Received, 24th June, 2008, Accepted, 25th July, 2008, Published online, 28th July, 2008. COM-08-11472

NOVEL AND EFFICIENT ACCESS TO THIENO[3,4-*c*]CINNOLINES

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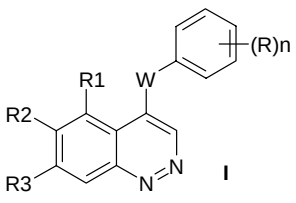
Abstract – New substituted methyl thieno[3,4-*c*]cinnoline-3-carboxylate compounds were synthesized from the corresponding methyl 3-aminothiophene-2-carboxylate precursors by a new route using a modified Sandmeyer reaction. Under proper conditions, Sandmeyer reaction led to the formation of thieno[3,4-*c*] cinnoline compounds by a regioselective intramolecular cyclization, instead of the expected substitution of the amino group by a bromine atom.

INTRODUCTION

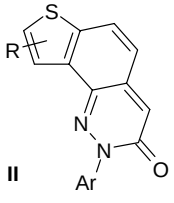
The thienocinnoline system is scarcely described in literature, likewise furocinnoline[1] and other similar cinnoline systems.[2] Thomas *et al.*[3] reported that the cinnoline derivatives of formula **I** posses antiangiogenic properties and they exhibit effects on VEGF, a property which could be useful in the treatment of a number of diseases including cancer and rheumatoid arthritis. Nakao *et al.*[4] have synthesized the thienocinnolines **II** which showed anxiolytic, hypnotic, antiepileptic and nootropic activities, they are potent agonists, partially agonists or inverse agonists of the benzodiazepine receptors (Chart 1).

Chart 1



I

W = O, NH, S, CH_2
n = 1 to 5

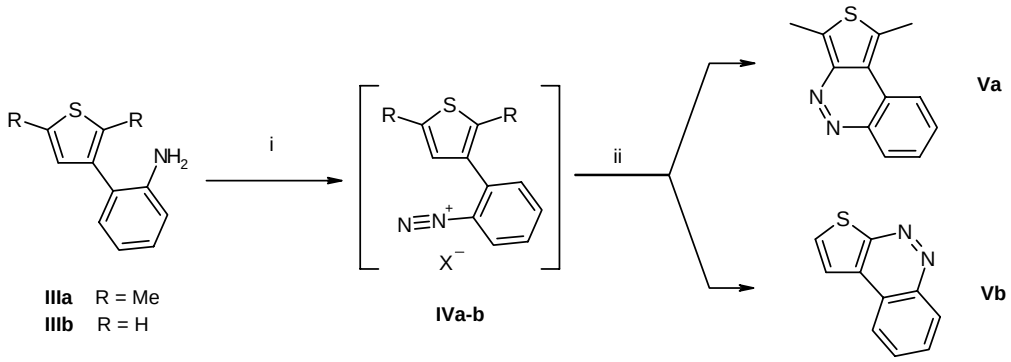


II

R = H, hal, alkyl

Barton[5] described the synthesis of thieno[2,3-*c*]-, thieno[3,2-*c*]- and especially thieno[3,4-*c*]cinnolines from the corresponding 2-aminophenylthiophenes. As depicted in scheme 1, the thieno[2,3-*c*]cinnoline **Vb** was obtained in 69% yield *via* intramolecular electrophilic attack of the diazonium cation at the free α-position of 3-(2-aminophenyl)thiophene **IIIb**. Thieno[3,4-*c*]cinnoline ring system was constructed by the same direct diazotisation procedure through an intramolecular electrophilic attack of the diazonium cation at the less reactive β-position of the thiophene ring. For example, 1,3-dimethylthieno[3,4-*c*]cinnoline **Va** was obtained from 3-(2-aminophenyl)-2,5-dimethylthiophene **IIIa**, in 54% yield.

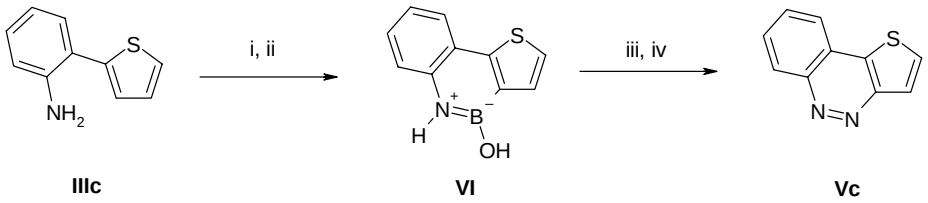
Scheme 1



$NaNO_2$, H_2O, 3N HCl, 1N $EtCO_2H$, 0.15N H_2SO_4, 0-3 °C, 1 h; (ii) NaOAc, H_2O, 0-3 °C, 1 h, then rt, 24 h. **Va** (54%), **Vb** (69%).

The synthesis of thieno[3,2-*c*]cinnoline **Vc** was also described, using 2-aminophenylthiophene **IIIc** as a starting material, *via* an azaborine **VI**[5] in analogy with the synthesis of benzo[*c*]cinnoline described by Dewar and Poesche[6] (Scheme 2).

Scheme 2



IIIc **VI** **Vc**

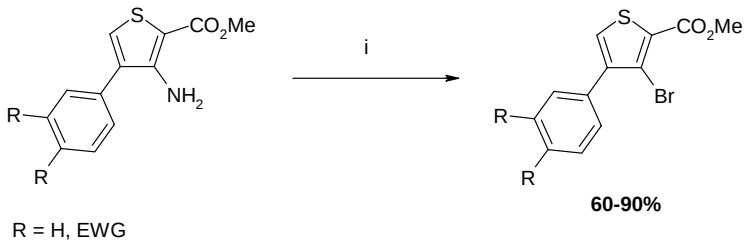
(i) BCl_3, xylene, reflux ; (ii) H_2O; (iii) $NaNO_2$, HCl ; (iv) NaOAc (29-36%).

In this paper, we wish to describe a new efficient methodology for the synthesis of thieno[3,4-*c*] cinnolines, using an alternative approach based on the reactivity of aminothiophenes.[7]

RESULTS AND DISCUSSION

During the synthesis of new methyl-4-aryl-3-bromothiophene-2-carboxylates **4** from the corresponding aminothiophene esters **1** under the classical Sandmeyer reaction conditions, using the procedure described by Corral *et al*.,[8] we have observed that in some cases the yields were rather low and the formed bromothiophenes **4** were accompanied by a non-halogenated by-product. It is worthy to mention that when the aryl group was a simple phenyl or a phenyl group bearing an electron-withdrawing substitutent, the reaction was univocal and led to the expected bromo derivatives in good yields (Scheme 3).

Scheme 3



(i) $NaNO_2$, Cu_2Br_2, HBr 48%, H_2O, 0 °C to 60 °C, 1.5 h.

However, when the phenyl group of the aminoesters **1a-c** bears one or two electron-donating groups, the results obtained were quite different where several by-products including deaminated products, thiophene dimers and poly-halogenated products were formed.

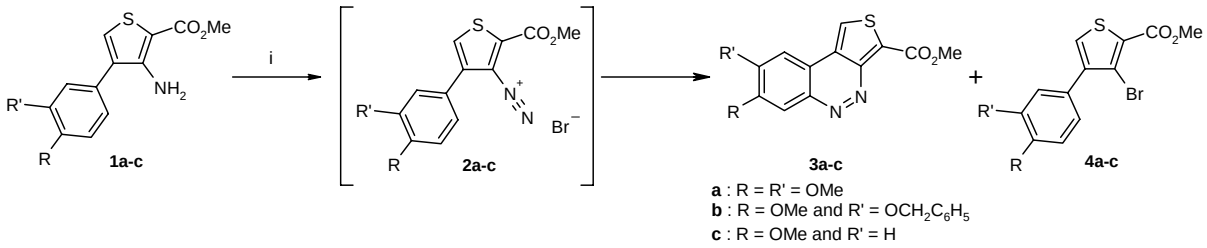
Thus, upon optimizing Sandmeyer reaction conditions by heating the aminoesters **1a-c** in hydrobromic acid with sodium nitrite in the presence of copper(I) bromide (protocol A), a mixture of two products, the bromo derivatives **4a-c** and the thieno[3,4-*c*]cinnolines **3a-c** were obtained. These two products were easily separated by column chromatography, and their structures were confirmed by elemental and spectral analyses. (Scheme 4)

Nevertheless, under the classical Sandmeyer reaction conditions, the above reaction led to the formation of numerous by-products including deaminated products, thiophene dimers and poly-halogenated products.

Unfortunately, this protocol A did not lead to a selective synthesis of either compound **3** or **4**. So, consequently, we tried an other protocol (B) previously described by Doyle who recommended to use *tert*-butyl nitrite and copper(II)bromide to prepare bromo derivatives from the corresponding amino

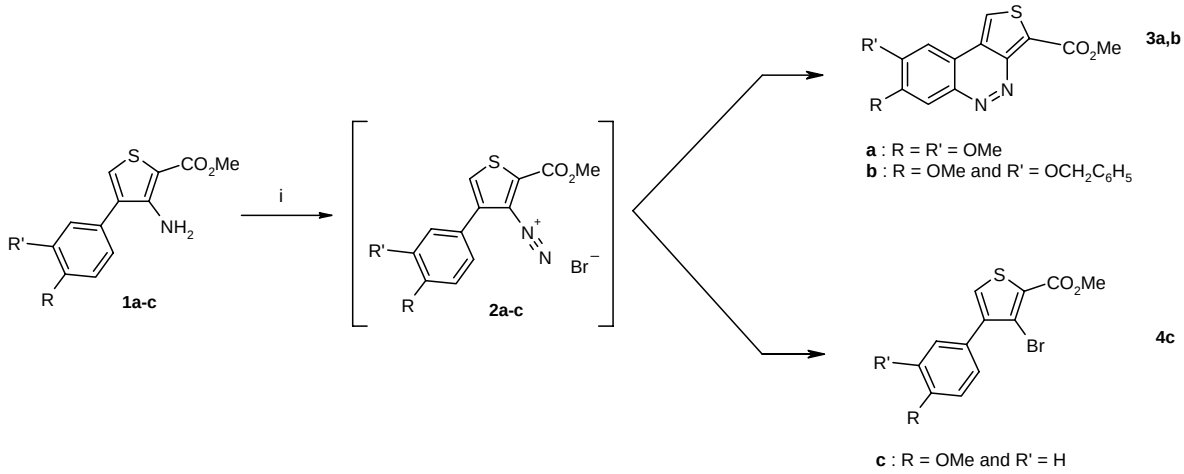
compounds.[9,10] Following this new protocol, treatment of **1a** and **1b** gave only the thieno[3,4-*c*]cinnolines **3a** and **3b** respectively with very high yield (≥ 90%) without any trace of a bromo derivatives. Surprisingly, treatment of **1c** gave exclusively the bromo derivative **4c** in high yield (95%) (Scheme 5).

Scheme 4. Sandmeyer reaction with optimised conditions – Protocol A



$NaNO_2$ (1.0 eq.), HBr 48% / H_2O (2:1), 0 °C, 30 min., then Cu_2Br_2 (1.0 eq.), HBr 48%, 50°C, 1h.
3a/4a (40/60), **3a** (30%); **3b/4b** (40/60), **3b** (30%); **3c/4c** (20/80), **3c** (15%).

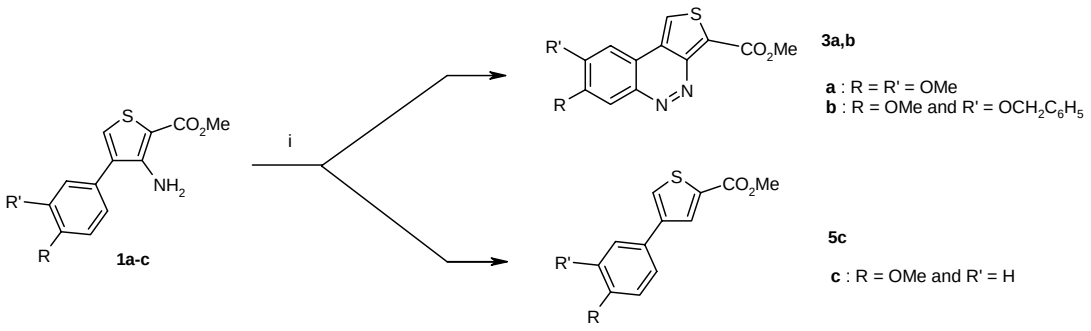
Scheme 5. Sandmeyer reaction with modified conditions – Protocol B



(i) *t*-BuONO (1.5 eq.), $CuBr_2$ (1.2 eq.), MeCN, 60-70 °C, 4 h, then H_2O/HCl 20%, 0 °C-rt.
3a 97%; **3b** 90%; **4c** 95%.

In order to verify that the cupric salt had no influence on the intramolecular cyclization, we repeated this protocol B in the absence of cupric bromide. For **1a** and **1b**, the results were the same as those obtained in the presence of copper bromide and the thieno[3,4-*c*]cinnolines **3a-b** were isolated in a similar yield. However in the case of compound **1c** the diazonium salt did not cyclize and the sole reaction product was found to be the deaminothiophene **5c**[7] (Scheme 6).

Scheme 6. Modified Sandmeyer reaction

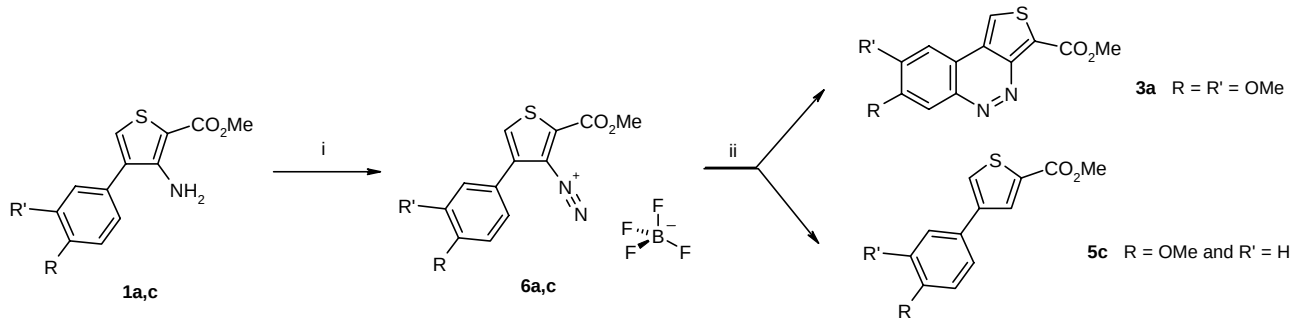


(i) *t*-BuONO (1.5 eq.), MeCN, 60-70 °C, 4 h, then H_2O/HCl 20%, 0 °C-rt.
3a 92%; **3b** 90%; **5c** 95%.

Finally in order to isolate the intermediate diazonium salts we tried another route using tetrafluoroboric acid and sodium nitrite following the procedure described in the literature.[10a,11,12] This protocol allowed us to isolate the two tetrafluoroborate diazonium salts **6a** and **6c** as very stable solids. However, the diazonium salt **6b** could not be isolated even at very low temperature and also we could not check its stability since the thieno[3,4-*c*]cinnoline **3b** was directly formed. When the tetrafluoroborate **6a** was dissolved in MeCN at rt, it led to the formation of the thieno[3,4-*c*]cinnoline **3a**, while **6c** did not cyclize even upon heating at reflux temperature of MeCN, and it gave only the deamino thiophene **5c**[7] (Scheme 7).

In conclusion we have described an efficient method for the synthesis of new thieno[3,4-*c*]cinnolines bearing an ester functionality which could be used to design new compounds of therapeutic importance.

Scheme 7. Synthesis of diazonium tetrafluoroborate salts



(i) $HBF_4.H_2O$ (50%), H_2O, 50 °C, 1 h, then $NaNO_2$ (1.1 eq.), H_2O, –15 °C, 1.5 h, (90%) ; (ii) MeCN, rt to reflux, 1 h. **6a** 93%; **6c** 98%; **3a** 80%; **5c** 85%.

EXPERIMENTAL

Melting points were determined on a Köfler melting point apparatus and are uncorrected. IR spectra were taken with a Perkin Elmer BX FT-IR. HRMS (EI) determinations were made using a spectrometer JEOL JMS GCMate. ESI-MS was performed using a spectrometer LC-MS Waters alliance 2695 (ESI+). ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) were recorded on a JEOL Lambda 400 Spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Thin layer chromatography (TLC) was performed on silica gel 60F-264 (Merck). Elemental analyses were performed at the 'Institut de Recherche en Chimie Organique Fine' (Rouen).

Classical procedure of the Sandmeyer reaction (Protocol A)

Methyl 7-methoxythieno[3,4-*c*]cinnoline-3-carboxylate (3c)

To a stirred solution, cooled to 0 ˚C, of sodium nitrite (0.20 g, 2.99 mmol) in H_2O (4 mL), a solution of methyl 3-amino-4-(4-methoxyphenyl)thiophene-2-carboxylate **1c** (0.80 g, 2.99 mmol) in HBr (48%, 8 mL) was dropwise added. Stirring was continued for 30 min at the same temperature then a solution of Cu_2Br_2 (0.50 g, 2.99 mmol) in HBr was added, followed by heating the reaction mixture at 70 ˚C till the evolution of nitrogen gas ceased, and the completion of the reaction was checked by TLC. After cooling, the reaction mixture was poured onto cold water and the solid precipitate was filtered, washed with water and air dried. Compounds **3c** and **4c** were separated by silica gel column chromatography using AcOEt as an eluent (R_f **3c** = 0.5, R_f **4c** = 0.9). Compound **3c** was crystallized from EtOH to give an orange powder (0.12 g, 15% yield), mp 228 °C. IR (KBr): 3426, 2925, 2248, 1704, 1607-1415, 1274, 1118 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ 8.04 (s, 1H, H_1); 7.64 (s, 1H, H_6); 7.44 (d, $^{3}J_{H8H9}$ = 8.2 Hz, 1H, H_8);7.20 (d, $^{3}J_{H9H8}$ = 8.2 Hz, 1H, H_9); 3.88 (s, 3H, OMe); 3.84 (s, 3H, CO_2OMe). ^{13}C NMR (DMSO-d_6) δ 163.1 (s, 1C, CO); 159.1 (s, 1C, C_7); 155.6 (s, 1C, C_{IV}); 153.2 (s, 1C, C_{IV}); 147.5 (s, 1C, C_3); 145.6 (s, 1C, C_6H); 142.9 (s, 1C, C_8H); 140.6 (s, 1C, C_9H); 130.1 (s, 1C, C_1H); 117.3 (s, 1C, C_{IV}); 115.7 (s, 1C, C_{IV}); 55.1 (s, 1C, Me_{ester}); 54.0 (s, 1C, OMe). MS *m/z* (%): 275 (21) [$M^{+\cdot}$]; 244 (100) [M^{+}-(OMe)]; 216 (42) [M^{+}-(CO_2Me)]; 157 (16). Anal. Calcd for $C_{13}H_{10}N_2O_3S$: C, 56.92; H, 3.67; N, 10.21. Found: C, 56.85; H, 3.48; N, 10.25. Compound **4c** is identical to that obtained following the modified procedure described below.

Methyl 3-bromo-4-(3,4-dimethoxyphenyl)thiophene-2-carboxylate (4a)

This compound was obtained following the same procedure described above for **3c**, using methyl 3-amino-4-(3,4-dimethoxyphenyl)thiophene-2-carboxylate **1a**. Compounds **3a** and **4a** were separated by silica gel column chromatography using AcOEt as eluent (R_f **3a** = 0.5, R_f **4a** = 0.9). Compound **4a** was

crystallized from EtOH as colorless crystals (2.30 g, 38% yield), mp 138 °C. IR (KBr): 2958, 1726, 1610-1421, 1251, 1231, 1074, 785 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.45 (s, 1H, H_5); 7.97 (s, 1H, H_{Ar}); 7.78 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H_{Ar}); 6.96 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H_{Ar}); 3.85 (s, 3H, OMe); 3.83 (s, 3H, OMe); 3.76 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 163.8 (s, 1C, CO); 159.9 (s, 1C, C_{Ar}); 159.7 (s, 1C, C_{IV}); 149.8 (s, 1C, C_3); 147.7 (s, 1C, C_2); 126.9 (s, 1C, CH_{Ar}); 126.6 (s, 1C, CH_{Ar}); 125.4 (s, 1C, C_4); 114.9 (s, 1C, C_5H); 114.5 (s, 1C, CH_{Ar}); 95.8(s, 1C, CH_{Ar}); 55.2 (s, 1C, OMe); 55.1 (s, 1C, OMe); 50.7 (s, 1C, Me). MS *m/z* (%): 356-358 (29) [$M^{+\cdot}$]; 325-327 (100) [M^+-(OMe)]; 297-299 (35) [M^+-(CO_2Me)]; 218 (30) [M^+-(Br, CO_2Me)]; 204 (17). Anal. Calcd for $C_{14}H_{13}BrO_4S$: C, 47.07; H, 3.67. Found: C, 46.85; H, 3.48.
Compound **3a** is idenitical to that obtained following the modified procedure described below.

Methyl 4-[3-(benzyloxy)-4-methoxyphenyl]-3-bromothiophene-2-carboxylate (4b)

This compound was obtained following the same procedure described above for **3c**, using methyl 3-amino-4-(3-benzyloxy-4-methoxyphenyl)thiophene-2-carboxylate **1b**. Compounds **3b** and **4b** were separated by silica gel column chromatography using AcOEt as eluent (R_f **3b** = 0.5, R_f **4b** = 0.9). Compound **4b** was crystallized from EtOH as beige crystals (0.72 g, 36% yield), mp 148 °C. IR (KBr): 3014, 1731, 1603-1420, 1246, 1229, 1074, 765 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.25 (s, 1H, H_5); 8.04 (s, 1H, H_{Ar}); 7.78 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H_{Ar}); 7.55 (d, $^3J_{HoHm}$ = 7.0 Hz, 2H, H_o); 7.50 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H_{Ar}); 7.41 (dd, $^3J_{HmHo}$ = 7.0 Hz, $^3J_{HmHp}$ = 7.6 Hz, 2H, H_m); 7.37 (t, $^3J_{HpHm}$ = 7.6 Hz, 1H, H_p); 5.39 (s, 2H, OCH_2); 4.01 (s, 3H, OMe); 3.89 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 162.8 (s, 1C, CO); 159.9 (s, 1C, C_{Ar}); 159.7 (s, 1C, C_{Ar}); 149.8 (s, 1C, C_3); 147.7 (s, 1C, C_2); 126.9 (s, 1C, CH_{Ar}); 126.6 (s, 1C, CH_{Ar}); 125.4 (s, 1C, C_4); 114.9 (s, 1C, C_5H); 114.5 (s, 1C, CH_{Ar}); 110.3 (s, 2C, CH_o); 110.2 (s, 2C, CH_m); 108.8 (s, 1C, CH_p); 95.8 (s, 1C, CH_{Ar}); 55.9 (s, 1C, CH_2); 55.1 (s, 1C, OMe); 50.7 (s, 1C, Me). MS *m/z* (%): 432-434 (10) [$M^{+\cdot}$]; 401-403 (100) [M^+-(OMe)]; 373-375 (47) [M^+-(CO_2Me)]; 294 (23) [M^+-(Br, CO_2Me)]; 266 (9). Anal. Calcd for $C_{20}H_{17}BrO_4S$: C, 55.44; H, 3.95. Found: C, 55.75; H, 3.68.
Compound **3b** is identical to that obtained following the modified procedure described below.

Modified procedure of the Sandmeyer reaction (Protocol B)

Methyl 7,8-dimethoxythieno[3,4-*c*]cinnoline-3-carboxylate (3a)

To a hot (70°C) stirred solution of anhydrous $CuBr_2$ (0.9 g, 4.09 mmol) and *tert*-butylnitrite (0.7 mL, 5.11 mmol, 90%) in MeCN (20 mL) was added slowly methyl 3-amino-4-(3,4-dimethoxyphenyl) thiophene-2-carboxylate **1a** (1.0 g, 3.41 mmol). The reaction was stirred at this temperature till completion of the reaction (TLC). After cooling to rt the reaction mixture was poured into an aqueous solution of HCl. The

residue obtained after the usual work-up was purified by silica gel column chromatography using AcOEt /MeOH (9:1) as an eluent to give compound **3a** as a bright yellow crystals (1.16 g, 97% yield), mp 236 °C. IR (KBr): 3438, 3180, 1717, 1636-1424, 1315, 1268, 1246, 1072, 1069 cm^{-1}. ^1H NMR (DMSO-d_6) δ 9.16 (s, 1H, H_1); 8.06 (s, 1H, H_6); 8.04 (s, 1H, H_9); 4.06 (s, 3H, OMe); 4.02 (s, 3H, OMe); 3.99 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 163.5; 159.9; 159.2; 155.4; 155.3; 147.5; 145.7; 143.5; 130.0; 126.8; 117.3; 55.2; 54.1; 53.5. LC-MS: tr = 2.88 min. 305 [M^+]. Anal. Calcd for $C_{14}H_{12}N_2O_3S$: C, 55.26; H, 3.97; N, 9.21. Found: C, 54.99; H, 3.72; N, 9.44.

Methyl 8-benzyloxy-7-methoxythieno[3,4-*c*]cinnoline-3-carboxylate (3b)

This compound was obtained following the same procedure described for **3a** using methyl 3-amino-4-(3-benzyloxy-4-methoxyphenyl)thiophene-2-carboxylate **1b**. Bright orange powder (0.93 g, 90% yield), mp 236 °C. IR (KBr): 3090, 2925, 2237, 1704, 1607-1415, 1274, 1259, 1247, 1199, 1190, 1118 cm^{-1}. ^1H NMR (DMSO-d_6) δ 9.11 (s, 1H, H_1); 8.20 (s, 1H, H_6); 8.05 (s, 1H, H_9); 7.57 (d, $^3J_{HoHm}$ = 5.9 Hz, 2H, H_o); 7.44 (dd, $^3J_{HmHo} = {}^3J_{HmHp}$ = 5.9 Hz, 2H, H_m); 7.37 (t, $^3J_{HpHm}$ = 5.9 Hz, 1H, H_p); 5.37 (s, 2H, OCH_2); 4.02 (s, 3H, OMe); 3.99 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 160.8 (s, 1C, CO); 159.7 (s, 1C, C_{IV}); 158.7 (s, 1C, C_{IV}); 155.4 (s, 1C, C_{IV}); 154.3 (s, 1C, C_{IV}); 147.4 (s, 1C, C_{IV}); 145.7 (s, 1C, CH); 144.9 (s, 1C, CH); 129.9 (s, 1C, C_1H); 116.6 (s, 1C, C_{IV}); 114.6 (s, 1C, C_{IV}); 110.3 (s, 2C, CH_o); 110.1 (s, 2C, CH_m); 109.7 (s, 1C, CH_p); 55.6 (s, 1C, CH_2); 55.1 (s, 1C, Me_{ester}); 54.4 (s, 1C, OMe). LC-MS: tr = 10.02 min.; 381 [M^+]. Anal. Calcd for $C_{20}H_{16}N_2O_4S$: C, 63.15; H, 4.24; N, 7.36. Found: C, 62.85; H, 4.48; N, 7.25.

Methyl 3-bromo-4-(4-methoxyphenyl)thiophene-2-carboxylate (4c)

This compound was obtained following the same procedure described for **3a** using methyl 3-amino-4-(4-methoxyphenyl)thiophene-2-carboxylate **1c**

Crystallization from EtOH gave colorless crystals (8.14 g, 95% yield), mp 124 °C. IR (KBr): 3054, 1720, 1602-1418, 1275, 1117 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.06 (s, 1H, H_5); 7.37 (d, $^3J_{HH}$ = 7.8 Hz, 2H, H_{Ar}); 7.01 (d, $^3J_{HH}$ = 7.8 Hz, 2H, H_{Ar}); 3.84 (s, 3H, OMe); 3.79 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 160.6 (s, 1C, CO); 159.2 (s, 1C, C_2); 143.5 (s, 1C, C_{Ar}); 130.5 (s, 2C, CH_{Ar}); 130.0 (s, 1C, C_5H); 127.3 (s, 1C, C_4); 126.7 (s, 1C, C_3); 117.3 (s, 1C, C_{Ar}); 113.8 (s, 2C, CH_{Ar}); 55.2 (s, 1C, Me_{ester}); 52.5 (s, 1C, OMe). MS *m/z* (%): 327-329 (19) [$M^{+\cdot}$]; 296-298 (100) [M^+-(OMe)]; 268-270 (29) [M^+-(CO_2Me)]; 188 (35) [M^+-(Br, CO_2Me)]; 173 (10). Anal. Calcd for $C_{13}H_{11}BrO_3S$: C, 47.72; H, 3.39. Found: C, 47.89; H, 3.51.

Synthesis of diazonium tetrafluoroborate salts

4-(3,4-Dimethoxyphenyl)-2-(methoxycarbonyl)thiophene-3-diazonium tetrafluoroborate (6a)

A solution of methyl 3-amino-4-(3,4-dimethoxyphenyl)thiophene-2-carboxylate **1a** (1.0 g, 3.41 mmol) in an aqueous solution of tetrafluoroboric acid (5 mL, 50%) was stirred at 50 °C during 30 min. Then, the solution was cooled to –15 °C and a solution of sodium nitrite (0.3 g, 3.75 mmol) in H_2O (3 mL) was slowly added during 20 min and the resulting solution was kept at this temperature for 1 h. The reaction mixture was then treated with ether and the diazonium salt precipitate was filtered, washed with ether and air dried to give red powder. (1.25 g, 93% yield), mp 216 °C. IR (KBr): 3093, 2958, 2269, 1702, 1603-1438, 1300, 1249, 1202, 1065, 727 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.45 (s, 1H, H_5); 7.97 (s, 1H, H_{Ar}); 7.78 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{Ar}); 7.20 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{Ar}); 4.01 (s, 3H, OMe); 3.98 (s, 3H, OMe); 3.85 (s, 3H, CO_2Me).

^{13}C NMR (DMSO-d_6) δ 160.8 (s, 1C, CO); 158.9 (s, 1C, C_2); 145.7 (s, 1C, C_{Ar}); 142.6 (s, 1C, C_{Ar}); 130.7 (s, 1C, CH_{Ar}); 130.2 (s, 1C, C_5H); 129.5 (s, 1C, C_3); 127.2 (s, 1C, C_4); 117.1 (s, 1C, C_{Ar}); 113.9 (s, 2C, CH_{Ar}); 55.3 (s, 1C, Me_{ester}); 52.3 (s, 1C, OMe); 52.1 (s, 1C, OMe). LC-MS: tr = 7.78 min.; 306 [M^+].

2-(Methoxycarbonyl)-4-(4-methoxyphenyl)thiophene-3-diazonium tetrafluoroborate (6c)

This compound was obtained following the same procedure described for **6a** using methyl 3-amino-4-(4-methoxyphenyl)thiophene-2-carboxylate **1c**. Red powder (1.3 g, 98% yield), mp 162 °C. IR (KBr): 3412, 3112, 2966, 2248, 1714, 1609-1470, 1438, 1413, 1271, 1256, 1062, 1023 cm^{-1}. ^1H NMR (DMSO-d_6) δ 8.45 (s, 1H, H_5); 7.78 (d, $^3J_{HmHo}$ = 7.8 Hz, 2H, H_{Ar}); 7.19 (d, $^3J_{HoHm}$ = 7.8 Hz, 2H, H_{Ar}); 4.06 (s, 3H, OMe); 3.85 (s, 3H, CO_2Me). ^{13}C NMR (DMSO-d_6) δ 160.8 (s, 1C, CO); 158.9 (s, 1C, C_2); 143.5 (s, 1C, C_{Ar}); 130.7 (s, 2C, CH_{Ar}); 130.2 (s, 1C, C_5H); 129.4 (s, 1C, C_3); 127.3 (s, 1C, C_4); 117.1 (s, 1C, C_{Ar}); 114.0 (s, 2C, CH_{Ar}); 55.3 (s, 1C, Me_{ester}); 52.1 (s, 1C, OMe). LC-MS: tr = 7.73 min.; 276 [M^+].

ACKNOWLEDGMENTS

The authors thank «Les laboratoires Servier» and the « Conseil Régional de Basse-Normandie- France » for their financial support.

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