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Synthesis and Reactivity of Alkyl (4-aminothien-3-yl)carbamates

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***Abstract** : Monocarbamates 2 have been prepared from 3,4-diaminothiophene 1 and were alkylated on the thiophene nucleus using an aldehyde and selenophenol, under acid catalysis. This reaction has allowed the access to 2-alkyl 3,4-diaminothiophenes 9, 3,5-diaminodithieno[3,2-b:2',3'-e]pyridines 10 and 1-alkyl thieno[3,4-d]imidazolones 13.* © 1997 Elsevier Science Ltd.

The chemistry of 3-aminothiophenes and 3,4-diaminothiophenes has been recently reviewed.[1,2] The 3,4-diaminothiophene **1** was originally described as an unstable compound, obtained by reduction of 2,5-dibromo 3,4-dinitrothiophene and used without isolation for some transformations.[3] In fact, the pure diamine **1** is a stable crystalline compound when stored in the refrigerator and is prepared in a fair yield.[4] Its dihydrobromide salt is commercially available.[5] The synthesis of mono- and poly-N-alkylated derivatives of **1** has been studied.[6] Some double electrophilic substitutions on the α and α' positions of the nucleus have also been achieved.[7]

In the course of a work carried out on 3-aminothiophene, we have observed that its important enaminic character is responsible for its acid-catalyzed transformation into bis(thien-3-yl)amine.[7] This property explains also the formation of 2-alkyl-3-aminothiophenes in the reaction of 3-aminothiophenes with a carbonyl compound and selenophenol as a reducing agent, under acid catalysis.[6,8] N-thien-3-yl acetamide and alkyl thien-3-ylcarbamates can be α-alkylated in a same way.[9] The use of α-functionalized aldehydes (or their corresponding acetals) has allowed the α-vinylation of the same substrates.[9]

In this paper, we describe our results concerning the α-alkylation of the diamine **1**, the aminocarbamates **2** and the dicarbamates **3**. The easy access to the monoalkylated products **6** open, now, a way to the synthesis of 2-alkyl 3,4-diaminothiophenes **9** and to the corresponding thienoimidazolones **13** which are attractive intermediates for the synthesis of biotin analogs.

The dicarbamates **3a** (R=Et)[4] and **3b** (R=tBu, COOtBu=Boc)[10] are known compounds. They are easily prepared in yields close to 80 % through the double carbamoylation of the diamine **1**. The reaction was carried out at room temperature in CH_2Cl_2 using two equivalents of ethyl chloroformate and of di-t-butyl dicarbonate respectively. We were surprised to find that the monocarbamate **2a** was the major product when diamine **1** was treated with one equivalent of ethyl chloroformate in the presence of triethylamine. The aminocarbamate **2a** was easily separated from a small amount of dicarbamate **3a** by an acidic aqueous extraction and was isolated in a fair yield (60 %) (Scheme 1). The t-butyl aminocarbamate **2b** was obtained, in the same way, after separation from the mixture **2b/3b/1** (85/10/5) in 55 % yield. The reaction was carried out in a mixture light petroleum/THF allowing dissolution of the diamine **1**. The di-t-butyl dicarbonate was then slowly introduced.

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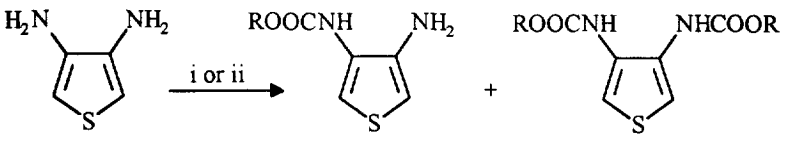
Scheme 1



1 **2** a) R=Et b) R=tBu **3**

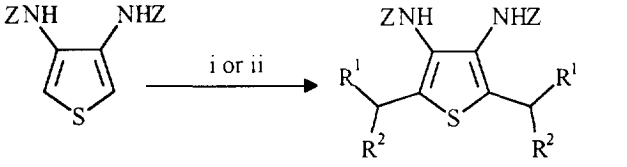
i) ClCOOEt, CH_2Cl_2, Et_3N, RT

ii) Boc_2O, THF, Petroleum ether, RT.

In the course of this study, we have also observed that addition of acid (pTSA, 1 eq.) accelerates the carbamoylation with complete formation of the dicarbamate **3b**. This result could be explained by an activation of the dicarbonate and a more important protonation of the diamine **1** compared to that of the aminocarbamate **2b**.

The synthesis of the monocarbamates **2a** and **2b** in acceptable yields and with simple experimental conditions is a very important result in view of study of the α-alkylation of the thiophene nucleus. The acid-catalyzed reductive alkylation of the diamine **1** was carried out as previously described for 3-aminothiophenes.[8] With an aldehyde or a ketone (2 eq.) and an excess of selenophenol, the 2,5-dialkyl 3,4-diaminothiophenes **4** were formed and isolated in fair to very good yields (Scheme 2, Table 1). The double α-alkylation was achieved at 0°C after 1.5 h of reaction for the aldehydes and 18 h for the ketones. With methyl 5-oxopentanoate[11] (entry 6) and butanone (entry 8), lower yields were observed.

Scheme 2



1 **4** Z=H

3b **5** Z=Boc, R^2 =H

i)R^1COR^2 (2 eq.), PhSeH (5 eq.), CH_2Cl_2, pTSA cat., 0°C.
ii)R^1CHO (10 eq.), PhSeH (8 eq.), CH_2Cl_2, pTSA cat., RT.

The same reaction was carried out on the dicarbamate **3b** and α,α'-dialkylated thiophenes **5** were synthetized in very good yields (Scheme 2, Table 1). The double alkylation, however, needed four days at room temperature in CH_2Cl_2 under acid catalysis. The dicarbamates **5** are crystalline compounds.

Table 1

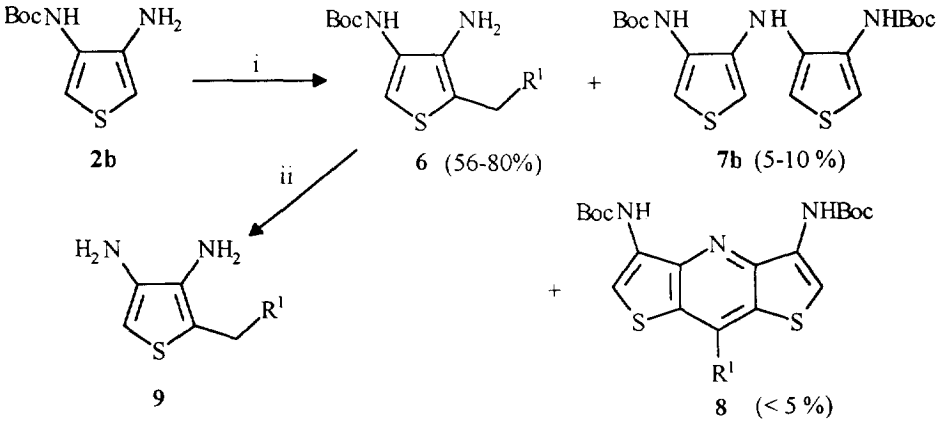
2,5-Dialkyl 3,4-diaminothiophenes **4** and dicarbamates **5**

Entry	N°	R^1	R^2	Yield (%)[a]	Entry	N°	R^1	Yield (%)
1	**4a**	Me	H	70	9	**5a**	Et	70
2	**4b**	Et	H	87	10	**5b**	nPr	75
3	**4c**	nPr	H	90	11	**5c**	iPr	85
4	**4d**	iPr	H	72	12	**5d**	nC_5H_{11}	90
5	**4e**	Ph	H	65	13	**5e**	Ph	75
6	**4f**	$(CH_2)_3COOMe$	H	40				
7	**4g**	Me	Me	80				
8	**4h**	Et	Me	40				

a) Crude products.

The reductive alkylation process was then applied to the aminocarbamate **2b** (Scheme 3). We have observed a good regioselectivity in contrast with the same reaction applied to **2a.** Under the experimental conditions used for the diamine **1**, mono α-alkylated thiophenes **6** were obtained in good yields with aliphatic aldehydes (Table 2, entries 1 to 4). The reaction with benzaldehyde has led to a lower yield (entry 5). Methyl 4-oxobutanoate,[12] methyl 5-oxopentanoate and methyl 6-oxohexanoate[11] have led to the corresponding esters in fair to good yields (entries 6 to 8). In all cases, we cannot avoid the formation of the bis(thien-3-yl)amine **7b** (5-10%) resulting from a fast acid-catalyzed "transamination" of **2b**. This reaction has been already observed for 3-aminothiophene.[7] In each case, the dithienopyridinedicarbamate **8** appeared also in a minor amount (Scheme 3). The cleavage of the carbamate function of compounds **6** was achieved, according to a conventional way, by treatment with an acetic acid solution of hydrobromic acid at room temperature.[13] The 2-alkyl-3,4-diaminothiophenes **9** were isolated in fair to good yields (Scheme 3, Table 2).

Scheme 3



i)R^1CHO (1.2 eq.), PhSeH (2.5 eq.), CH_2Cl_2, pTSA cat., 0°C.
ii)HBr, AcOH, RT ; NaOH, H_2O..

Table 2

t-Butyl (5-alkyl 4-aminothien-3-yl)carbamates **6** and 2-alkyl 3,4-diaminothiophenes **9**

Entry	N°	R^1	Yield (%)	Entry	N°	R^1	Yield (%)
1	**6a**	Et	72	9	**9a**	Et	72
2	**6b**	nPr	80	10	**9b**	nPr	73
3	**6c**	iPr	75	11	**9c**	iPr	80
4	**6d**	nC_5H_{11}	70	12	**9d**	nC_5H_{11}	64
5	**6e**	Ph	57	13	**9e**	Ph	72
6	**6f**	$(CH_2)_2COOMe$	56	14	**9g**	$(CH_2)_3COOMe$	65
7	**6g**	$(CH_2)_3COOMe$	65				
8	**6h**	$(CH_2)_4COOMe$	79				

The formation of dithienopyridines **8** indicates that the reaction of a second molecule of substrate with the first formed cationic intermediate is competitive with the selenophenol reduction of these carbonium ion. The mechanism presented in Scheme 4 is similar to that proposed for the synthesis of 8-alkyldithieno[3,2-b:2',3'-e]pyridines from 3-aminothiophene. We have shown that the oxidation step occurs before the internal "transamination" reaction.[8] When the reaction was performed under argon atmosphere, a complex mixture was obtained. A study is in progress to determine whether the cyclisation can occur when the oxidation step is prevented. The dithienopyridinedicarbamates **8** were then directly prepared, in fair to good yields, from the aminocarbamate **2b** and one-half equivalent of aldehyde at 40°C under acid catalysis without selenophenol (Scheme 4, Table 3).

Scheme 4

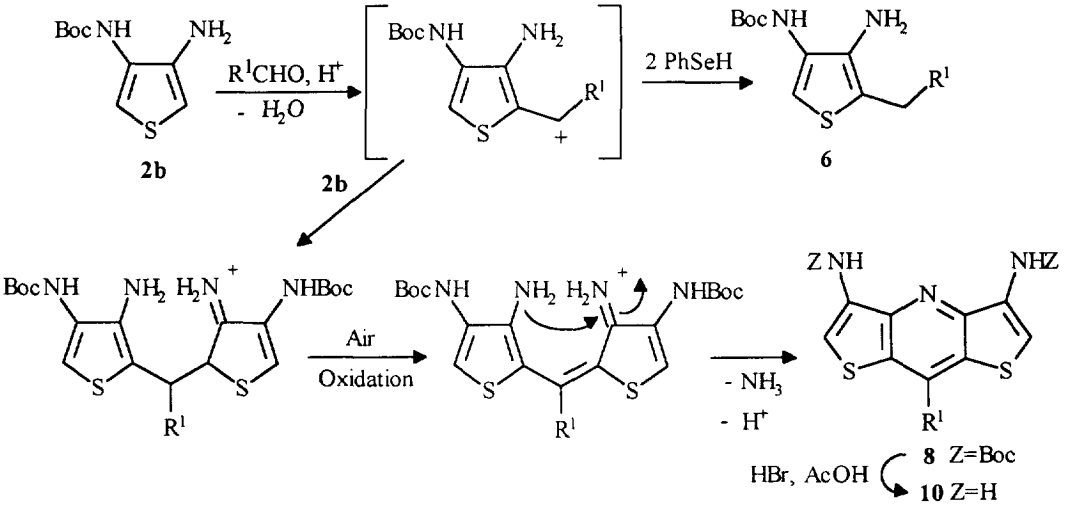


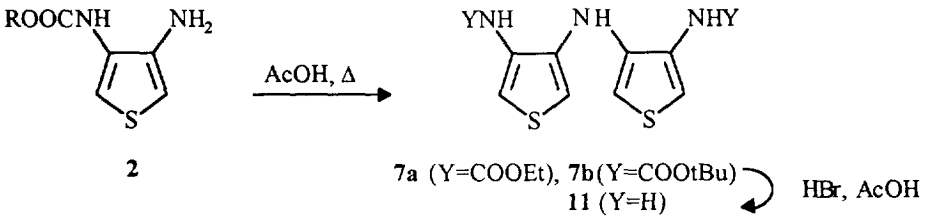
Table 3

Di-t-butyl 8-alkyldithieno[3,2-b:2',3'-e]pyridine-3,5-diyldicarbamates **8** and 8-alkyl 3,5-diamino dithieno[3,2-b:2',3'-e]pyridines **10**.

Entry	N°	R^1	Yield (%)	Entry	N°	R^1	Yield (%)
1	**8a**	Et	75	6	**10a**	Et	78
2	**8b**	nPr	72	7	**10b**	nPr	85
3	**8d**	nC_5H_{11}	50	8	**10e**	Ph	60
4	**8e**	Ph	65				
5	**8i**	$(CH_2)_2Ph$	52				

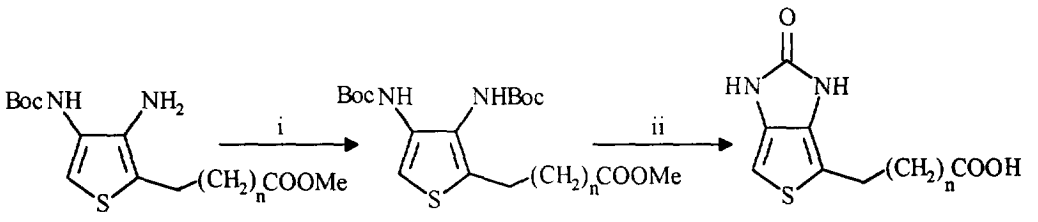
The dicarbamates **8a, b, e** were treated with an acetic acid solution of HBr to liberate the corresponding 8-alkyl 3,5-diamino-dithieno[3,2-b:2',3'-e]pyridines **10** in 60-85 % yields (Table 3). The facile formation of the bis(thien-3-yl)amine **7b** during the mono α-alkylation of **2b** has led us to prepare the secondary amines **7a** and **7b** by heating the corresponding monocarbamates **2a** and **2b** in acetic acid.[7] They were isolated with 95 and 89 % yields respectively. The cleavage of the two carbamoyl groups of **7b** has allowed the synthesis of the triamine **11** with 80 % yield (Scheme 5).

Scheme 5



With a view to proposing a novel procedure for the preparation of biotin derivatives, we have prepared the dicarbamates **12f**, **12g** and **12h**, in nearly quantative yields through carbamoylation of the corresponding aminocarbamates **6** (Scheme 6). According to a known method,[14] these dicarbamates **12** were cyclized into thienoimidazolones **13** bearing an alkyl group $(CH_2)_{n+1}COOH$ with n = 2, 3, 4 (≃ 80 % yield) (Scheme 6).

Scheme 6

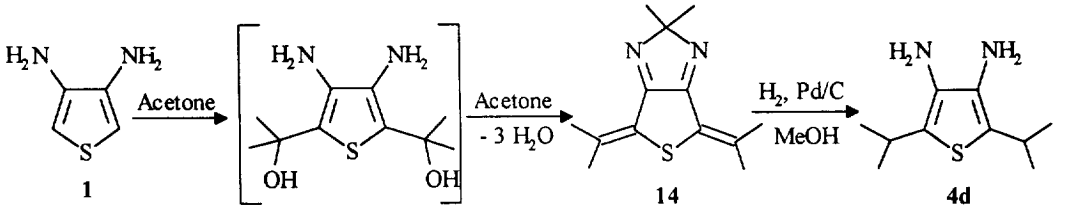


i) $(Boc)_2O$, CH_2Cl_2, RT. ii) KOH, MeOH, Δ

The sequence **1** → **2** → **6** → **12** → **13** furnishes a new general synthetic way to thiophenic precursors of biotin derivatives having a variable chain length. Several routes have been already proposed for the preparation of the thienoimidazolone **13g**.[14-17]

An unexpected formation of the bis-alkylidene thienoimidazole **14** (56 % yield) was observed by simple dissolution of the diamine **1** in acetone (Scheme 7). The formation of this compound could be explained by a double α-alkylation followed by condensation of a third molecule of acetone and loss of water leading to the double conjugated enimine structure **14** which was then hydrogenated. The dealkylation of the amino groups occurs during the reduction and the 3,4-diamino 2,5-diisopropylthiophene **4d** was isolated with 40 % yield.

Scheme 7



EXPERIMENTAL SECTION

All the solvents were distilled before use and light petroleum refers to the fraction with bp 40-60°C. 3,4-Diaminothiophene (m.p.:96°C) was prepared as described.[4] The chromatographic separations were achieved on silicagel 0.060-0.200mm pore diameter ca 4nm available from Acros. ^1H and ^{13}C NMR spectra were recorded on a Brucker AC 200 and the infrared spectra on a Perkin Elmer FTIR spectrophotometer.

3,4-Diaminothiophene 1.[4] M.p.=96°C. NMR ^1H ($CDCl_3$), δ : 6.12 (s, 2H, H_2, H_5), 3.12 (brs, 4H, NH_2). ^{13}C NMR ($CDCl_3$), δ : 135.8 (C_3, C_4), 101.4 (C_2, C_5).

Ethyl (4-aminothien-3-yl)carbamate 2a. To a solution of 3,4-diaminothiophene **1** (0.228g, 2mmol) in CH_2Cl_2 (20ml), ethyl chloroformate (0.217g, 2mmol) dissolved in the same solvent (2ml) was quickly added . An ammonium salt was formed and triethylamine (0.5ml) was then added dropwise. The mixture was stirred for 4 hours and extracted twice with a 1N HCl solution (2x15ml). The aqueous phase was washed with dichloromethane, neutralized with a 4N NaOH solution and extracted with ether (2x20ml). The organic fractions were dried and the solvent was distilled off. The monocarbamate was obtained as an oil. Yield : 64%. ^1H NMR ($CDCl_3$), δ : 7.10 (brs, 1H, NH), 7.00 (d, 1H, H_2, J=3.5Hz), 6.24 (d, 1H, H_5, J=3.5Hz), 4.18 (q, 2H, CH_2, J=7.1Hz), 3.40 (brs, 2H, NH_2), 1.26 (t, 3H, CH_3, J=7.1Hz). ^{13}C NMR ($CDCl_3$), δ : 154.3 (CO), 137.1 (C_4), 127.8 (C_3), 110.6 (C_2), 102.3 (C_5), 61.1 (CH_2), 14.1 (CH_3). Anal. Calc. for $C_7H_{10}N_2O_2S$: C, 45.15 ; H, 5.41 ; N, 15.04. Found : C, 45.19 ; H, 5.40 ; N, 14.95. IR(KBr) : 3326, 3099, 2981, 1719, 1684 cm^{-1}.

t-Butyl (4-aminothien-3-yl)carbamate 2b. Light petroleum (1l) was added to a vigorously stirred THF solution (50ml) of diamine **1** (1.14g, 10mmol). Di-t-butyl dicarbonate (2.185g, 10mmol) in light petroleum (250ml) was introduced dropwise over 2 hours. The stirring was continued for 10 hours and the solvents were distilled off. The solid residue which contains diamine **1** (5%), aminocarbamate **2b** (80%) and dicarbamate **3b** (15%) was dissolved in CH_2Cl_2 and the solution was treated as for the preparation of **2a**. The carbamate **2b**

was dissolved in the minimum amount of chloroform, filtered and precipitated by addition of n-heptane.Yield : 55%. M.p.115°C. ^{1}H NMR ($CDCl_3$), δ : 7.10 (brs, 1H, H_2), 6.50 (brs, 1H, NH), 6.30 (d, 1H, H_5, J=3.5Hz), 3.25 (brs, 2H, NH_2), 1.49 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 153.3 (CO), 136.7 (C_4), 128.9 (C_3), 110.0 (C_2), 103.9 (C_5), 80.6 ($C(CH_3)_3$), 28.2 (CH_3). Anal. Calc. for $C_9H_{14}N_2O_2S$: C, 50.45 ; H, 6.59 ; N, 13.07. Found : C, 50.78 ; H, 6.41 ; N, 12.95. IR (KBr) : 3399, 3362, 3297, 3118, 2977, 1725, 1686, 1154 cm^{-1}.

Diethyl thiophene-3,4-diyldicarbamate 3a. A solution of ethyl chloroformate (0.543g, 5mmol) in CH_2Cl_2 (2ml) was added to the diamine **1** (0.228g, 2mmol) dissolved in the same solvent (15ml). Triethylamine (1ml) was added dropwise at room temperature and the reaction was stirred for 6h. The mixture was washed with a 1N HCl solution (3x10ml) then with water (10ml) and the organic phase was dried and evaporated. The crystalline product was recrystallized in a mixture CH_2Cl_2/light petroleum : 1/2. Yield : 75%. M.p.=110°C. ^{1}H NMR ($CDCl_3$), δ : 7.48 (brs, 2H, NH), 7.14 (brs, 2H, H_2, H_5, H_2), 4.18 (q, 4H, CH_2, J=7.1Hz), 1.25 (t, 6H, CH_3, J=7.1Hz). ^{13}C NMR ($CDCl_3$), δ : 154.6 (CO), 128.3 (C_3, C_4), 111.4 (C_2, C_5), 61.5 (CH_2), 14.2 (CH_3). Anal. Calc. for $C_{10}H_{14}N_2O_4S$: C, 46.50 ; H, 5.46 ; N, 10.85. Found : C, 46.44 ; H, 5.45 ; N, 10.90. IR (KBr) : 3323, 3104, 2976, 1721, 1684 cm^{-1}.

t-Butyl thiophene-3,4-diyldicarbamate 3b. A solution of di-t-butyl dicarbonate (0.874g, 4mmol) in CH_2Cl_2 was added to the diamine **1** (0.228g, 2mmol) dissolved in the same solvent (5ml). The reaction was stirred for 6h at room temperature and evaporated under reduced pressure. The solid dicarbamate **3b** was purified by crystallization in light petroleum. Yield : 81%. M.p.=160°C. ^{1}H NMR ($CDCl_3$), δ : 7.12 (brs, 2H, H_2, H_5), 6.77 (brs, 2H, NH), 1.49 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 153.7 (CO), 128.9 (C_3, C_4), 111.5 (C_2, C_5), 80.9 ($C(CH_3)$), 28.2 (CH_3). Anal. Calc. for $C_{14}H_{22}N_2O_4S$: C, 53.48 ; H, 7.05 ; N, 8.91. Found : C, 53.75 ; H, 7.28 ; N, 9.10. IR (KBr) : 3378, 3158, 2975, 1728, 1679 cm^{-1}.

α-Alkylation of 3,4-diaminothiophene 1 (General procedure). Selenophenol (0.785g, 5mmol) was quickly added to a solution of aldehyde or ketone (2mmol) in CH_2Cl_2 (20ml) containing p-toluenesulfonic acid (40mg) at -20°C. The diamine (0.114g, 1mmol) dissolved in the same solvent (15ml) was then introduced. The reaction was stirred (1.5h for the aldehydes and 18h for the ketones) at 0°C, protected from light. The mixture was then treated with 1N HCl solution (2x15ml). The aqueous phase was washed with ether (5ml), cooled on an ice-bath, neutralized with a 4N NaOH solution and extracted with ether (3x20ml). The organic fractions were washed with water, dried and evaporated. The residue has crystallized for **4e**, **4g** and **4h**. All the diamines **4** were very sensitive to light and heat and cannot be isolated in a pure form. The 3,4-diamino-2,5-dibenzylthiophene **4e** was obtained after silicagel chromatographic purification (elution : CH_2Cl_2). The acidic extraction must be avoided in this case.

3,4-Diamino-2,5-diethylthiophene 4a. Yield : 80%. ^{1}H NMR ($CDCl_3$), δ : 3.26 (brs, 4H, NH_2), 2.55 (q, 4H, CH_2, J=7.3Hz), 1.18 (t, 6H, CH_3, J=7.3Hz). ^{13}C NMR ($CDCl_3$), δ : 131.7 (C_3, C_4), 115.0 (C_2, C_5), 19.8 (CH_2), 14.7 (CH_3).

3,4-Diamino-2,5-di-n-propylthiophene 4b. Yield : 87%. ^{1}H NMR ($CDCl_3$), δ : 3.62 (brs, 4H, NH_2), 2.49 (t, 4H, CH_2, J=7.4Hz), 1.57 (m, 4H, CH_2) 0.94 (t, 6H, CH_3, J=7.4Hz). ^{13}C NMR ($CDCl_3$), δ : 132.2 (C_3, C_4), 114.8 (C_2, C_5), 28.8 (CH_2), 23.8 (CH_2), 13.8 (CH_3).

3,4-Diamino-2,5-di-n-butylthiophene 4c. Yield : 90%.^{1}H NMR ($CDCl_3$), δ : 3.15 (brs, 4H, NH_2), 2.52 (t, 4H, CH_2, J=7.1Hz), 1.54 (m, 4H, CH_2), 1.38 (m, 4H, CH_2), 0.90 (t, 6H, CH_3, J=7.2Hz). ^{13}C NMR ($CDCl_3$), δ : 132.0 (C_3, C_4), 114.9 (C_2, C_5), 32.6 (CH_2), 26.3 (CH_2), 22.3 (CH_2), 13.8 (CH_3).

3,4-Diamino-2,5-diisobutylthiophene 4d. Yield : 72%. ^{1}H NMR ($CDCl_3$), δ : 3.09 (brs, 4H, NH_2), 2.38 (d, 4H , CH_2, J=6.9Hz), 1.81 (m, 2H, CH), 0.92 (d, 12H, CH_3, J=6.8Hz). ^{13}C NMR ($CDCl_3$), δ : 132.5 (C_3, C_4), 114.1 (C_2, C_5), 35.9 (CH_2), 30.0 (CH), 14.7 (CH_3).

3,4-Diamino-2,5-dibenzylthiophene 4e. Yield : 70% . M.p.=90°C. ^{1}H NMR ($CDCl_3$), δ : 7.28-7.18 (m, 10H, Ph), 3.88 (s, 4H, CH_2), 3.39 (brs, 4H, NH_2). ^{13}C NMR ($CDCl_3$), δ : 139.4, 128.5, 128.3, 126.4 (Ph), 130.4 (C_3, C_4), 113.6 (C_2, C_5), 32.8 (CH_2).

Dimethyl (3,4-diaminothiophene-2,5-diyl)dipentanoate 4f. Yield :40 %. ^{1}H NMR ($CDCl_3$), δ : 3.56 (s, 6H, CH_3), 3.34 (brs, 4H, NH_2), 2.45 (t, 4H, CH_2, J=7.0Hz), 2.23 (t, 4H, CH_2, J=6.9Hz), 1.58-1.52 (m, 8H, $(CH_2)_2$). ^{13}C NMR ($CDCl_3$), δ: 173.6 (CO), 132.2 (C_3, C_4), 113.5 (C_2, C_5), 51.1 (CH_3), 33.3 (CH_2), 29.6 (CH_2), 26.0 (CH_2), 24.1 (CH_2).

3,4-Diamino-2,5-diisopropylthiophene 4g. Yield : 79%. M.p.=80°C . ^{1}H NMR ($CDCl_3$), δ : 3.11 (brs, 4H, NH_2), 3.02 (hept., 2H, CH, J=6.8Hz), 1.22 (d, 12H, CH_3, J=6.8Hz). ^{13}C NMR ($CDCl_3$), δ : 130.9 (C_3, C_4), 121.7 (C_2, C_5), 26.7 (CH), 23.3 (CH_3).

3,4-Diamino-2,5-di(1-methylpropyl)thiophene 4h. Yield : 42%. ^{1}H NMR ($CDCl_3$), δ : 3.66 (brs, 4H, NH_2), 2.30 (tq., 2H, CH, J=6.8Hz, J=6.9Hz), 1.53 (q, 4H, CH_2, J= 6.9Hz), 1.18 (d, 6H, CH_3, J=6.8Hz). ^{13}C NMR ($CDCl_3$), δ : 131.2 (C_3, C_4), 121.2 (C_2, C_5), 33.8 (CH), 31.1 (CH_2), 12.1 (CH_3).

α-Alkylation of dicarbamate 3b (General procedure). Selenophenol (3.14g, 8mmol) and the aldehyde (10mmol) were successively added to a solution of dicarbamate **3b** (0.314g, 1mmol) in CH_2Cl_2 (30ml). p-Toluenesulfonic acid (80mg) in suspension in the same solvent was introduced. The reaction was stirred for 4 days at room temperature and washed with a dilute solution of sodium hydroxide. The organic phase was washed with water, dried and evaporated. The oily residue was chromatographied on silicagel (elution light petroleum/ethyl acetate : 80/20). The dialkylated compounds **5** were recrystallized in heptane.

t-Butyl (2,5-di-n-propylthiophene-3,4-diyl)dicarbamate 5a. Yield : 70%. M.p.=138°C. ^{1}H NMR ($CDCl_3$), δ : 6.19 (brs, 2H, NH), 2.60 (t, 4H, CH_2, J=7.6Hz), 1.59 (sext., 4H, CH_2, J=7.6Hz), 1.46 (s, 18H, CH_3), 0.93 (t, 6H, CH_3, J=7.6Hz). ^{13}C NMR ($CDCl_3$), δ : 154.2 (CO), 132.2 (C_3, C_4), 126.6 (C_2, C_5), 79.9 ($C(CH_3)_3$), 29.4 (CH_2), 28.1 (CH_3), 23.5 (CH_2), 13.6 (CH_3). Anal. Calc. for $C_{20}H_{34}N_2O_4S$: C, 60.27 ; H, 8.60 ; N, 7.03. Found : C, 59.92 ; H, 8.42 ; N, 6.87.

t-Butyl (2,5-di-n-butylthiophene-3,4-diyl)dicarbamate 5b. Yield : 75%. M.p.=127°C. ^{1}H NMR ($CDCl_3$), δ : 6.17 (brs, 2H, NH), 2.62 (t, 4H, CH_2, J=7.6Hz), 1.57 (m., 4H, CH_2), 1.46 (s, 18H, CH_3), 1.36 (m, 4H, CH_2), 0.89 (t, 6H, CH_3, J=7.2Hz). ^{13}C NMR ($CDCl_3$), δ : 154.4 (CO), 132.5 (C_3, C_4), 126.6 (C_2, C_5), 80.0 ($C(CH_3)_3$), 30.6 (CH_2), 28.1 (CH_3), 26.6 (CH_2), 22.3 (CH_2), 13.8 (CH_3). Anal. Calc. for $C_{22}H_{38}N_2O_4S$: C, 61.94 ; H, 8.98 ; N, 6.57. Found : C, 61.65 ; H, 8.71 ; N, 6.83. IR (KBr) : 3368, 3259, 3107, 2960, 1708, 1684, 1166 cm^{-1}.

t-Butyl (2,5-diisobutylthiophene-3,4-diyl)dicarbamate 5c. Yield : 72%. M.p.=147°C. ^{1}H NMR ($CDCl_3$), δ : 6.13 (brs, 2H, NH), 2.50 (d, 4H, CH_2, J=7.1Hz), 1.83 (m, 2H, CH), 1.45 (s, 18H, CH_3), 0.89 (d, 12H, CH_3, J=6.6Hz). ^{13}C NMR ($CDCl_3$), δ : 154.1 (CO), 131.7 (C_3, C_4), 127.3 (C_2, C_5), 79.7 ($C(CH_3)_3$), 36.4 (CH_2), 29.6 (CH), 28.0 (CH_3), 22.1 (CH_3). Anal. Calc. for $C_{22}H_{38}N_2O_4S$: C, 61.94; H, 8.98; N, 6.57. Found : C, 62.13; H, 8.66; N, 6.57. IR(KBr) : 3365, 3262, 3109, 2959, 2872, 1709, 1681, 1169 cm^{-1}.

t-Butyl (2,5-di-n-hexylthiophene-3,4-diyl)dicarbamate 5d. Yield : 90%. M.p.=113°C. ^{1}H NMR ($CDCl_3$), δ : 6.23 (brs, 2H, NH), 2.60 (t, 4H, CH_2, J=7.6Hz), 1.54-1.39 (m, 22H, CH_2, CH_3), 1.33-1.26 (m, 12H, $(CH_2)_3$), 0.85 (t, 6H, CH_3, J=6.6Hz). ^{13}C NMR ($CDCl_3$), δ : 154.2 (CO), 132.7 (C_3, C_4), 126.4 (C_2, C_5), 79.9

($C(CH_3)_3$), 31.3 (CH_2), 30.1 (CH_2), 28.6 (CH_2), 28.0 (CH_3), 27.3 (CH_2), 22.3 (CH_2), 13.8 (CH_3). Anal. Calc. for $C_{26}H_{46}N_2O_4S$: C, 64.69; H, 9.61; N, 5.80. Found : C, 65.00; H,9.27 ; N,5.62 .

t-Butyl (2,5-dibenzylthiophene-3,4-diyl)dicarbamate 5e. Yield : 74%. M.p.=140°C. ^1H NMR ($CDCl_3$), δ : 7.30-7.16 (m, 10H, Ph), 6.28(brs, 2H, NH), 3.96 (s, 4H, CH_2), 1.46 (s, 18H, CH_3) . ^{13}C NMR ($CDCl_3$), δ : 154.2 (CO), 131.9 (C_3, C_4), 127.9 (C_2, C_5), 138.9, 128.5, 128.3, 126.3 (C_{Ph}), 80.3 ($C(CH_3)_3$), 33.5 (CH_2), 28.1 (CH_3). Anal. Calc. for $C_{28}H_{34}N_2O_4S$: C, 67.99 ; H, 6.93 ; N, 5.66. Found : C, 68.04; H, 6.89 ; N, 5.49.

α-Alkylation of aminocarbamate 2b (General procedure). To a cooled solution of aldehyde (2.2mmol) and selenophenol (0.785g, 5mmol) in dichloromethane (15ml), a solution of aminocarbamate **2b** (0.428g, 2mmol) in the same solvent (20ml) was quickly added at 0°C. A suspension of p-toluenesulfonic acid (40mg) in CH_2Cl_2 (20ml) was then introduced. The mixture was stirred for 3h at 0°C and the solvent distilled off. The mono α-alkylated thiophenes **6** were obtained as yellow oils purified by silicagel chromatography (elution CH_2Cl_2/ethyl acetate : 95 /5).

t-Butyl (4-amino-5-n-propylthien-3-yl)carbamate 6a. Yield : 72%. ^1H NMR ($CDCl_3$), δ : 6.92 (brs, 1H, H_2), 6.64 (brs, 1H, NH), 3.00 (brs, 2H, NH_2), 2.57 (t, 2H, CH_2, J=7.5Hz), 1.62 (m, 2H, CH_2), 1.48 (s, 9H, CH_3), 0.96 (t, 3H, CH_3, J=7.3Hz). ^{13}C NMR ($CDCl_3$), δ : 153.2 (CO), 132.2 (C_4), 129.0 (C_3), 122.9 (C_5), 104.5 (C_2), 80.0 ($C(CH_3)$), 28.9 (CH_2), 28.0 (CH_3), 23.8 (CH_2), 13.7 (CH_3).Anal. Calc. for $C_{12}H_{20}N_2O_2S$: C, 56.22; H, 7.86; N, 10.93. Found : C, 55.79; H, 7.53; N, 10.56. IR (KBr) : 3330, 2972, 2930, 1723, 1159 cm^{-1}.

t-Butyl (4-amino-5-n-butylthien-3-yl)carbamate 6b. Yield : 80%. ^1H NMR ($CDCl_3$), δ : 6.90 (brs, 1H, H_2), 6.71 (brs, 1H, NH), 3.10 (brs, 2H, NH_2), 2.55 (t, 2H, CH_2, J=7.5Hz), 1.50 (m, 13H, $(CH_2)_2$, CH_3), 0.91 (t, 3H, CH_3, J=7.4Hz). NMR ^{13}C ($CDCl_3$), δ : 153.1 (CO), 132.0 (C_4), 128.9 (C_3), 121.9 (C_5), 104.9 (C_2), 79.9 ($C(CH_3)$), 32.6 (CH_2), 28.1 (CH_3), 26.6 (CH_2), 22.3 (CH_2), 13.8 (CH_3). Anal. Calc. for $C_{13}H_{22}N_2O_2S$: C, 57.75 ; H, 8.20 ; N, 10.36. Found : C, 57.42 ; H, 8.01 ; N, 10.01.

t-Butyl (4-amino-5-isobutylthien-3-yl)carbamate 6c. Yield : 75%. ^1H NMR ($CDCl_3$), δ : 6.94 (brs, 1H, H_2), 6.76 (brs, 1H, NH), 3.00 (brs, 2H, NH_2), 2.44 (d, 2H, CH_2, J=7.1Hz), 1.83 (m, 1H, CH), 1.48 (s, 9H, CH_3), 0.91 (d, 6H, CH_3, J=6.6Hz). ^{13}C NMR ($CDCl_3$), δ : 153.2 (CO), 132.0 (C_4), 128.9 (C_3), 121.7 (C_5), 105.1 (C_2), 79.9 ($C(CH_3)$), 35.9 (CH_2), 29.9 (CH), 28.0 (CH_3), 22.0 (CH_3). Anal. Calc. for $C_{13}H_{22}N_2O_2S$: C, 57.75 ; H, 8.20 ; N, 10.36. Found : C, 57.89 ; H, 8.15 ; N, 10.28

t-Butyl (4-amino-5-hexylthien-3-yl)carbamate 6d. Yield : 70%. ^1H NMR ($CDCl_3$), δ : 6.91 (brs, 1H, H_2), 6.71 (brs, 1H, NH), 2.91 (brs, 2H, NH_2), 2.57 (t, 2H, CH_2, J=7.5Hz), 1.60-1.28 (m, 17H, $(CH_2)_4$, CH_3), 0.86 (t, 3H, CH_3, J=6.5Hz). ^{13}C NMR ($CDCl_3$), δ : 153.2 (CO), 131.4 (C_4), 129.0 (C_3), 122.3 (C_5), 104.8 (C_2), 80.0 ($C(CH_3)$), 31.2 (CH_2), 30.2 (CH_2), 28.6 (CH_2), 28.0 (CH_3), 26.6 (CH_2), 22.3 (CH_2), 13.8 (CH_3). Anal. Calc. for $C_{15}H_{26}N_2O_2S$: C, 60.36 ; H, 8.78 ; N, 9.39. Found : C, 60.92 ; H, 8.56 ; N, 9.67.

t-Butyl (4-amino-5-benzylthien-3-yl) carbamate 6e. Yield : 57%. ^1H NMR ($CDCl_3$), δ : 7.36-7.16 (m, 5H, Ph), 6.99 (brs, 1H, H_2), 6.63 (brs, 1H, NH), 3.95 (s, 2H, CH_2), 2.90 (brs, 2H, NH_2), 1.49 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 153.2 (CO), 138.8, 128.3, 127.9, 126.1 (C_{Ph}), 132.7 (C_4), 128.9 (C_3), 119.4 (C_5), 106.2 (C_2), 80.0 ($C(CH_3)$), 32.6 (CH_2), 28.0 (CH_3). Anal. Calc. for $C_{16}H_{20}N_2O_2S$: C, 63.13 ; H, 6.62 ; N, 9.20. Found : C, 63.45 ; H, 6.53 ; N, 9.37.

Methyl (3-amino-4-t-butoxycarbonylaminothien-2-yl)butanoate 6f. Yield : 56%. ^1H NMR ($CDCl_3$), δ : 6.94 (brs, 1H, H_2), 6.67 (brs, 1H, NH), 3.65 (s, 3H, CH_3), 3.00 (brs, 2H, NH_2), 2.65 (t, 2H, CH_2, J=7.4Hz), 2.33 (t, 2H, CH_2, J=7.0Hz), 1.88 (m, 2H, CH_2), 1.48 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.6 (CO), 153.1 (CO), 132.4 (C_4), 128.9 (C_3), 122.0 (C_5), 105.1 (C_2), 80.2 ($C(CH_3)$), 51.3 (CH_3), 32.4 (CH_2), 28.0 (CH_3),

25.6 (CH_2), 25.3 (CH_2).Anal. Calc. for $C_{14}H_{22}N_2O_4S$: C, 53.48; H, 7.05; N, 8.91. Found : C, 53.56; H, 7.26; N, 9.17.

Methyl (3-amino-4-t-butoxycarbonylaminothien-2-yl)pentanoate 6g. Yield : 65%. ^1H NMR ($CDCl_3$), δ : 6.91 (brs, 1H, H_2), 6.67 (brs, 1H, NH), 3.63 (s, 3H, CH_3), 2.95 (brs, 2H, NH_2), 2.60 (t, 2H, CH_2, J=7.0Hz), 2.31 (t, 2H, CH_2, J=6.9Hz), 1.69-1.56 (m, 4H, $(CH_2)_2$), 1.48 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.8 (CO), 153.1 (CO), 131.7 (C_4), 129.0 (C_3), 121.4 (C_5), 104.9 (C_2), 80.0 ($C(CH_3)$), 51.2 (CH_3), 33.4 (CH_2), 29.6 (CH_2), 28.0 (CH_3), 26.2 (CH_2), 24.1 (CH_2).Anal. Calc. for $C_{15}H_{24}N_2O_4S$: C, 54.86; H, 7.37; N, 8.53. Found : C, 54.61; H, 7.32; N, 8.43.

Methyl (3-amino-4-t-butoxycarbonylaminothien-2-yl)hexanoate 6h. Yield : 79%. ^1H NMR ($CDCl_3$), δ : 6.83 (brs, 1H, H_2), 6.62 (brs, 1H, NH), 3.64 (s, 3H, CH_3), 3.00 (brs, 2H, NH_2), 2.60 (t, 2H, CH_2, J=7.4Hz), 2.15 (t, 2H, CH_2, J=7.3Hz), 1.72-1.27 (m, 15H, $(CH_2)_3$, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.4 (CO), 152.9 (CO), 131.6 (C_4), 128.6 (C_3), 120.5 (C_5), 104.3 (C_2), 79.5 ($C(CH_3)$), 50.8 (CH_3), 33.2 (CH_2), 29.5 (CH_2), 28.0 (CH_3), 27.7 (CH_2), 26.0 (CH_2), 24.0 (CH_2).Anal. Calc. for $C_{16}H_{26}N_2O_4S$: C, 56.11; H, 7.65; N, 8.18. Found : C, 56.03; H, 7.65; N, 8.13. IR(KBr) : 3358, 2976, 2932, 2857, 1732, 1161 cm^{-1}.

Diethyl (amino-3,4-thienylidene)dicarbamate 7a. The aminocarbamate **2a** (2mmol) in acetic acid (5ml) was heated under reflux for 1h. After concentration under reduced pressure, the gummy residue was washed with a 1N HCl solution. The solid was filtered and dissolved in CH_2Cl_2 (20ml). The organic solution was washed with water, dried and evaporated. The aminodicarbamate **7a** was recrystallized in a mixture $CHCl_3$/light petroleum : 1/1. Yield : 95%. M.p.=140°C. ^1H NMR ($CDCl_3$), δ : 7.24 (brs, 2H, H_2, $H_{2'}$), 6.80 (brs, 2H, NH), 6.47 (d, 2H, H_5, $H_{5'}$, J=3.1Hz), 5.80 (brs, 1H, NH), 4.17 (q, 4H, CH_2, J=7.1Hz), 1.25 (t, 6H, CH_3, J=7.1Hz). ^{13}C NMR ($CDCl_3$), δ : 154.3 (CO), 135.7 (C_4, $C_{4'}$), 128.5 (C_3, $C_{3'}$), 110.8 (C_2, $C_{2'}$), 107.8 (C_5, $C_{5'}$), 61.5 (CH_2), 14.3 (CH_3). Anal. Calc. for $C_{14}H_{17}N_3O_4S_2$: C, 47.31; H, 4.82; N, 11.82. Found : C, 46.96; H, 4.91; N, 11.48.

Di-t-butyl (amino-3,4-thienylidene)dicarbamate 7b. This aminodicarbamate was prepared as above. Yield : 89%. M.p.=98°C . ^1H NMR ($CDCl_3$), δ : 7.19 (brs, 2H, H_2, $H_{2'}$), 6.80 (brs, 2H, NH), 6.46 (d, 2H, H_5, $H_{5'}$, J=3.5Hz), 5.70 (brs, 1H, NH), 1.48 (t, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 153.4 (CO), 135.8 (C_4, $C_{4'}$), 128.9 (C_3, $C_{3'}$), 110.3 (C_2, $C_{2'}$, C_5, $C_{5'}$), 80.8 ($C(CH_3)_3$), 28.1 (CH_3). Anal. Calc. for $C_{18}H_{25}N_3O_4S_2$: C, 52.53; H, 6.12; N, 10.21. Found : C, 52.83; H, 6.43; N, 10.46.

Dithienopyridinedicarbamates 8 (General procedure). A cold solution of aldehyde (0.5mmol) in CH_2Cl_2 (15ml) containing p-toluenesulfonic acid (50mg) was added dropwise to the aminocarbamate **2b** in the same solvent (15ml) at 0°C. The reaction was stirred for 2 hours under slight reflux and the solvent was distilled off. The crude product was chromatographied on silicagel (elution CH_2Cl_2/light petroleum : 40/60). The dithienopyridines **8** were isolated as white to pale yellow crystalline solids.

Di-t-butyl (8-ethyldithieno[3,2-b :2',3'-e]pyridine-3,5-diyl)dicarbamate 8a. Yield : 75%. M.p.=213°C. ^1H NMR ($CDCl_3$), δ : 8.02 (brs, 2H, NH), 7.86 (brs, 2H, H_2, H_6), 3.11 (q, 2H, CH_2, J=7.6Hz), 1.47 (s, 18H, CH_3), 1.43 (t, 3H, CH_3, J=7.6Hz). ^{13}C NMR ($CDCl_3$), δ : 152.7 (CO), 146.7 (C_{3a}, C_{4a}), 142.3 (C_8), 129.9 (C_3, C_5), 128.1 (C_{7a}, C_{8a}), 109.6 (C_2, C_6), 80.1 ($C(CH_3)_3$), 27.6 (CH_3), 26.4 (CH_2), 12.1 (CH_3). Anal. Calc. for $C_{21}H_{27}N_3O_4S_2$: C, 56.10; H, 6.05; N, 9.35. Found : C, 55.68; H, 5.97; N, 8.97.

Di-t-butyl (8-n-propyldithieno[3,2-b:2',3'-e]pyridine-3,5-diyl)dicarbamate 8b. Yield : 72%. M.p.=164°C. ^1H NMR ($CDCl_3$), δ : 8.03 (brs, 2H, NH), 7.86 (brs, 2H, H_2, H_6), 3.07 (t, 2H, CH_2, J=7.7Hz), 1.90 (m, 2H, CH_2), 1.46 (s, 18H, CH_3), 1.02 (t, 3H, CH_3, J=7.3Hz). ^{13}C NMR ($CDCl_3$), δ : 152.7 (CO), 146.7 (C_{3a}, C_{4a}), 141.0 (C_8), 129.8 (C_3, C_5), 128.7 (C_{7a}, C_{8a}), 109.7 (C_2, C_6), 80.1 ($C(CH_3)_3$), 35.1 (CH_2), 27.6 (CH_3), 21.2

(CH_2), 14.2 (CH_3). Anal. Calc. for $C_{22}H_{29}N_3O_4S_2$:C, 57.00; H, 6.31; N, 9.06. Found : C, 56.46; H, 6.02; N, 8.64

Di-t-butyl (8-n-pentyldithieno[3,2-b :2',3'-e]pyridine-3,5-diyl)dicarbamate 8d. Yield : 50%. M.p.=67°C. ^{1}H NMR ($CDCl_3$), δ : 8.30 (brs, 2H, NH), 7.86 (brs, 2H, H_2, H_6), 3.06 (t, 2H, CH_2, J=7.8Hz), 1.85 (m, 2H, CH_2), 1.46-1.15 (m, 22H, $(CH_2)_2CH_3$), 0.84 (t, 3H, CH_3, J=6.6Hz). ^{13}C NMR ($CDCl_3$), δ : 152.8 (CO), 146.6 (C_{3a}, C_{4a}), 141.2 (C_8), 129.8 (C_3, C_5), 128.7 (C_{7a}, C_{8a}), 109.7 (C_2, C_6), 80.2 ($C(CH_3)_3$), 33.1 (CH_2), 31.7 (CH_2), 27.7 (CH_3), 27.4 (CH_2), 22.2 (CH_2), 13.7 (CH_3). Anal. Calc. for $C_{24}H_{33}N_3O_4S_2$: C, 58.62; H, 6.71; N, 8.55. Found : C, 58.30; H, 6.46; N, 8.23.

Di-t-butyl (8-phenyldithieno[3,2-b :2',3'-e]pyridine-3,5-diyl)dicarbamate 8e. Yield : 65%. M.p.=225°C. ^{1}H NMR ($CDCl_3$), δ : 8.18 (brs, 2H, NH), 7.92 (brs, 2H, H_2, H_6), 7.87-7.54 (Ph), 3.06 (t, 2H, CH_2, J=7.8Hz), 1.42 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 152.8 (CO), 147.1 (C_{3a}, C_{4a}), 140.3 (C_8), 135.6, 129.9, 129.2, 127.9 (C_{Ph}), 129.6 (C_3, C_5), 128.1 (C_{7a}, C_{8a}), 111.1 (C_2, C_6), 80.5 ($C(CH_3)_3$), 27.9 (CH_3), 26.4 (CH_2), 12.1 (CH_3). Anal. Calc. for $C_{25}H_{27}N_3O_4S_2$: C, 60.34; H, 5.47; N, 8.44. Found : C, 60.05; H, 5.73; N, 8.31. IR(KBr) : 3152, 2987, 1740, 1155 cm^{-1}.

Di-t-butyl [8-(2-phenylethyl)dithieno[3,2-b :2',3'-e]pyridine-3,5-diyl]dicarbamate 8i. Yield : 52%. M.p.=186°C. ^{1}H NMR ($CDCl_3$), δ : 8.18 (brs, 2H, NH), 7.90 (brs, 2H, H_2, H_6), 7.29-7.20 (m, 5H, Ph), 3.42-3.32 (m, 2H, CH_2), 3.15-3.05 (m, 2H, CH_2), 1.49 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 152.7 (CO), 146.6 (C_{3a}, C_{4a}), 140.2 (C_8), 139.8, 128.5, 128.2, 126.4 (C_{Ph}) 129.7 (C_3, C_5), 128.6 (C_{7a}, C_{8a}), 109.6 (C_2, C_6), 80.6 ($C(CH_3)_3$), 35.5 (CH_2), 33.8 (CH_2), 27.9 (CH_3). Anal. Calc. for $C_{27}H_{31}N_3O_4S_2$: C, 61.68; H, 5.94; N, 7.99. Found : C, 61.79; H, 5.87; N, 8.12.

2-Alkyl-3,4-diaminothiophenes 9 (General procedure). The carbamate **6** (1mmol) was introduced in a 20% solution of hydrobromic acid in acetic acid (0.450g, 1mmol). The mixture was stirred for 20 minutes at room temperature and anhydrous ether (20ml) was then added. The reaction was stirred for another 15min. The filtered ammonium salt was washed with ether and dissolved in water (20ml). After neutralisation by a 1N NaOH solution, the oily diamine **9** was extracted with ether (3x10ml) and obtained in a pure form after elimination of the solvent.

3,4-Diamino-2-n-propylthiophene 9a. Yield : 72%. ^{1}H NMR ($CDCl_3$), δ : 5.96 (s, 1H, H_5), 3.08 (brs, 4H, NH_2), 2.53 (t, 2H, CH_2, J=7.5Hz), 1.60 (m, 2H, CH_2) , 0.95 (t, 3H, CH_3, J=7.3Hz). ^{13}C NMR ($CDCl_3$), δ : 137.0 (C_4), 132.4 (C_3), 120.5 (C_2), 96.7 (C_5), 29.0 (CH_2), 23.6 (CH_2), 13.7 (CH_3). Anal. Calc. for $C_7H_{12}N_2S$: C, 53.81; H, 7.74; N, 17.93. Found : C, 53.53; H, 7.52; N, 17.52.

2-n-Butyl-3,4-diaminothiophene 9b. Yield : 73%. NMR ^{1}H ($CDCl_3$), δ : 5.93 (s, 1H, H_5), 3.20 (brs, 4H, NH_2), 2.53 (t, 2H, CH_2, J=7.5Hz), 1.60-1.22 (m, 4H, $(CH_2)_2$) , 0.92 (t, 3H, CH_3, J=7.2Hz). ^{13}C NMR ($CDCl_3$), δ : 137.2 (C_4), 132.1 (C_3), 119.6 (C_2), 96.6 (C_5), 32.5 (CH_2), 28.8 (CH_2), 22.4 (CH_2), 13.9 (CH_3). Anal. Calc. for $C_8H_{14}N_2S$: C, 56.43; H, 8.29; N, 16.45. Found : C, 56.29; H, 7.92; N, 16.82.

3,4-Diamino-2-isobutylthiophene 9c. Yield : 80%. ^{1}H NMR ($CDCl_3$), δ : 5.97 (s, 1H, H_5), 3.14 (brs, 4H, NH_2), 2.42 (d, 2H, CH_2, J=7.0Hz), 1.84 (m, 1H, CH) , 0.93 (d, 6H, CH_3, J=6.6Hz). ^{13}C NMR ($CDCl_3$), δ : 137.2 (C_4), 132.8 (C_3), 118.3 (C_2), 96.9 (C_5), 36.3 (CH_2), 30.1 (CH), 22.3 (CH_3). Anal. Calc. for $C_8H_{14}N_2S$: C, 56.43; H, 8.29; N, 16.45. Found : C, 56.26; H, 8.31; N, 16.24.

3,4-Diamino-2-n-hexylthiophene 9d. Yield : 65%. ^{1}H NMR ($CDCl_3$), δ : 5.94 (s, 1H, H_5), 3.14 (brs, 4H, NH_2), 2.54 (t, 2H, CH_2, J=7.5Hz), 1.61-1.29 (m, 8H, $(CH_2)_4$) , 0.86 (t, 3H, CH_3, J=6.4Hz). ^{13}C NMR ($CDCl_3$), δ : 137.5 (C_4), 132.2 (C_3), 119.8 (C_2), 96.6 (C_5), 31.5 (CH_2), 29.9 (CH_2), 28.8 (CH_2), 27.0 (CH_2),

22.4 (CH_2), 13.9 (CH_3). Anal. Calc. for $C_{10}H_{18}N_2S$: C, 60.56; H, 9.15; N, 14.12. Found : C, 60.03; H, 9.02; N, 14.00.

2-Benzyl-3,4-diaminothiophene 9e. Yield : 72%. ^1H NMR ($CDCl_3$), δ : 7.29-7.19 (m, 5H, Ph), 6.02 (s, 1H, H_5), 3.91 (s, 2H, CH_2), 3.15 (brs, 4H, NH_2). ^{13}C NMR ($CDCl_3$), δ : 137.0 (C_4), 132.1 (C_3), 133.0, 128.4, 128.1, 126.3 (C_{Ph}), 117.3 (C_2), 97.9 (C_5), 33.0 (CH_2). Anal. Calc. for $C_{10}H_{10}N_2S$: C, 64.67; H, 5.92; N, 13.71. Found : C, 64.31; H, 5.86; N, 14.00.

Methyl (3,4-diaminothien-2-yl)pentanoate 9g. Yield : 65%. ^1H NMR ($CDCl_3$), δ : 5.94 (s, 1H, H_5), 3.63 (s, 3H, CH_3), 3.05 (brs, 4H, NH_2), 2.56 (t, 2H, CH_2, J=7.1Hz), 2.31 (t, 2H, CH_2, J=6.8Hz), 1.74-1.59 (m, 4H, $(CH_2)_2$). ^{13}C NMR ($CDCl_3$), δ : 173.9 (CO), 137.1 (C_4), 132.6 (C_3), 116.9 (C_2), 97.0 (C_5), 51.4 (CH_3), 33.6 (CH_2), 29.8 (CH_2), 26.4 (CH_2), 24.4 (CH_2). Anal. Calc. for $C_{10}H_{16}N_2O_2S$: C, 52.61; H, 7.06; N, 12.27. Found : C, 52.31; H, 7.12; N, 12.00.

Diaminodithienopyridines 10. These diamines were synthetized from the corresponding dicarbamates **8** using the experimental procedure described for the preparation of the 2-alkyl-3,4-diaminothiophenes **9**.

3, 5-Diamino-8-ethyl[3,2-b :2',3'-e]pyridine 10a. Yield : 78%. M.p.>230°C. ^1H NMR ($CDCl_3$), δ : 6.50 (s, 2H, H_2, H_6), 4.35 (brs, 4H, NH_2), 3.05 (q, 2H, CH_2, J=7.6Hz), 1.40 (t, 3H, CH_3, J=7.6Hz). ^{13}C NMR ($CDCl_3$), δ : 148.7 (C_{3a}, C_{4a}), 138.8 (C_3, C_5, C_8), 128.7 (C_{7a}, C_{8a}), 100.5 (C_2, C_6), 26.5 (CH_2), 13.2 (CH_3). Anal. Calc. for $C_{11}H_{11}N_3S_2$: C, 52.98; H, 4.45; N, 16.85. Found : C, 52 51; H, 4.33; N, 16.46.

3, 5-Diamino-8-n-propyl[3,2-b :2',3'-e]pyridine 10b. Yield : 85%. M.p.>230°C. ^1H NMR ($CDCl_3$), δ : 6.49 (s, 2H, H_2, H_6), 4.38 (brs, 4H, NH_2), 3.01 (t, 2H, CH_2, J=7.7Hz), 1.88 (m, 2H, CH_2), 1.00 (t, 3H, CH_3, J=7.4Hz). ^{13}C NMR ($CDCl_3$), δ : 148.8 (C_{3a}, C_{4a}), 139.0 (C_3, C_5), 138.2 (C_8), 128.2 (C_{7a}, C_{8a}), 100.3 (C_2, C_6), 34.9 (CH_2), 21.1 (CH_2), 13.5 (CH_3). Anal. Calc. for $C_{12}H_{13}N_3S_2$: C, 54.72; H, 4.98; N, 15.96. Found : C, 54.32; H, 4.85; N, 15.59.

3, 5-Diamino-8-phenyl[3,2-b :2',3'-e]pyridine 10e. Yield : 79%. M.p.>230°C. ^1H NMR ($CDCl_3$), δ : 7.87-7.82 (m, 2H, Ph), 7.59-7.52 (m, 3H, Ph), 6.54 (s, 2H, H_2, H_6), 4.40 (brs, 4H, NH_2). ^{13}C NMR ($DMSOD_6$), δ : 147.6 (C_{3a}, C_{4a}), 139.9 (C_3, C_5), 137.8 (C_8), 136.1, 129.6, 129.2, 127.8 (C_{Ph}), 128.7 (C_{7a}, C_{8a}), 98.6 (C_2, C_6). Anal. Calc. for $C_{15}H_{11}N_3S_2$: C, 60.58; H, 3.73; N, 14.13. Found : C, 60.39; H, 3.78; N, 13.93.

Bis(4-aminothien-3-yl)amine 11. The compound **11** was obtained by HBr/HOAc treatment of the dicarbamate **7b** as described for the synthesis of the 2-alkyl-3,4-diaminothiophenes **9**, and isolated as an oil. Yield : 80%. ^1H NMR ($CDCl_3$), δ : 6.44 (d, 2H, H_2, $H_{2'}$, J=3.4Hz), 6.24 (d, 2H, H_5, $H_{5'}$, J=3.4Hz), 5.45 (brs, 1H, NH), 3.36 (brs, 4H, NH_2). ^{13}C NMR ($CDCl_3$), δ : 137.2 (C_4, $C_{4'}$), 134.8 (C_3, $C_{3'}$), 105.0 (C_2, $C_{2'}$), 102.3 (C_5, $C_{5'}$). Anal. Calc. for $C_8H_9N_3S_2$: C, 45.47; H, 4.29; N, 19.89. Found : C, 45.16; H, 4.17; N, 19.66.

Dicarbamates 12 (General procedure). A solution, containing di-t-butyl dicarbonate (218mg, 1mmol) and the aminocarbamate **6** (1mmol) in dichloromethane (20ml), was stirred for 6h at room temperature. The solvent was evaporated and the oily residue was chromatographied on silicagel. The dicarbamates **12** were obtained in a pure form after elution with a 1/1 mixture of light petroleum/CH_2Cl_2.

Methyl [3,4-bis(methoxycarbonylamino)thien-2-yl]butanoate 12f. Yield : 89%. ^1H NMR ($CDCl_3$), δ : 7.09 (brs, 1H, H_5), 6.83 (brs, 1H, NH), 6.34 (brs, 1H, NH), 3.63 (s, 3H, CH_3), 2.68 (t, 2H, CH_2, J=7.3Hz), 2.28 (t, 2H, CH_2, J=7.1Hz), 1.88 (m, 2H, CH_2), 1.45 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.0 (CO), 154.1, 152.6 (CO), 134.2 (C_3), 131.6 (C_4), 123.6 (C_2), 80.1, 79.7 ($C(CH_3)_3$), 51.0 (CH_3), 32.3 (CH_2), 27.7 (CH_3), 25.9 (CH_2), 25.2 (CH_2). Anal. Calc. for $C_{19}H_{30}N_2O_6S$: C, 55.05; H, 7.30; N, 6.76. Found : C, 54.84; H, 7.53; N, 6.40.

Methyl [3,4-bis(methoxycarbonylamino)thien-2-yl]pentanoate 12g. Yield=92%. ^{1}H NMR ($CDCl_3$), δ : 7.04 (brs, 1H, H_5), 6.83 (brs, 1H, NH), 6.15 (brs, 1H, NH), 3.61 (s, 3H, CH_3), 2.62 (t, 2H, CH_2, J=7.0Hz), 2.27 (t, 2H, CH_2, J=6.9Hz), 1.61-1.52 (m, 4H, $(CH_2)_2$), 1.44 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.7 (CO), 154.4, 153.0 (CO), 135.8 (C_3), 131.7 (C_4), 123.4 (C_2), 80.6 ($C(CH_3)_3$), 51.3 (CH_3), 33.5 (CH_2), 29.6 (CH_2), 28.1, 28.0 (CH_3), 26.9 (CH_2), 24.1 (CH_2). Anal. Calc. for $C_{20}H_{32}N_2O_6S$: C, 56.05; H, 7.52; N, 6.54. Found : C, 55.72; H, 7.41; N, 6.17. IR(KBr) : 3323, 3140, 2977, 2868, 1734, 1716, 1683, 1156 cm^{-1}.

Methyl [3,4-bis(methoxycarbonylamino)thien-2-yl]hexanoate 12h. Yield=97%. ^{1}H NMR ($CDCl_3$), δ : 7.06 (brs, 1H, H_5), 6.83 (brs, 1H, NH), 6.06 (brs, 1H, NH), 3.61 (s, 3H, CH_3), 2.62 (t, 2H, CH_2, J=7.5Hz), 2.26 (t, 2H, CH_2, J=7.3Hz), 1.58-1.30 (m, 24H, $(CH_2)_3$, CH_3). ^{13}C NMR ($CDCl_3$), δ : 173.5 (CO), 154.1, 152.6 (CO), 135.9 (C_3), 131.5 (C_4), 123.0 (C_2), 80.0, 79.6 ($C(CH_3)_3$), 50.9 (CH_3), 33.3 (CH_2), 29.4 (CH_2), 28.0 (CH_2), 27.8, 27.7 (CH_3), 26.6 (CH_2), 24.0 (CH_2). Anal. Calc. for $C_{21}H_{34}N_2O_6S$: C, 56.99; H, 7.74; N, 6.33. Found : C, 56.69; H, 7.64; N, 6.46. IR(KBr) : 3339, 2979, 1808, 1704, 1683, 1157 cm^{-1}.

Thienoimidazolones 13. A solution of dicarbamate **12** (1mmol) in methanol (40ml) containing KOH (4.6g) was heated under reflux for 2 hours. After elimination of the alcohol, the residue was treated with water (20ml) and ethyl acetate (20ml). The mixture was cooled with an ice-bath and neutralized with a 12N HCl solution. The organic phase was separated and the aqueous solution extracted with the same solvent. The organic fractions were washed with water, dried and evaporated. The products were recrystallized in ethanol.

(4,6-Dihydro-5-oxothieno[3,4-d]imidazol-1-yl)butanoic acid 13f. Yield=84%. ^{1}H NMR ($DMSOd_6$), δ : 12.13 (brs, 1H, COOH), 10.23 (brs, 1H, NH), 10.16 (brs, 1H, NH), 6.20 (s, 1H, H_5), 2.65 (t, 2H, CH_2, J=7.4Hz), 2.22 (t, 2H, CH_2, J=6.8Hz), 1.78 (m, 2H, CH_2). ^{13}C NMR ($DMSOd_6$), δ : 174.2 (CO), 160.2 (CO), 131.8 (C_3), 129.2 (C_4), 110.2 (C_2), 90.3 (C_5), 33.0 (CH_2), 26.0 (CH_2), 25.6 (CH_2). Anal. Calc. for $C_9H_{10}N_2O_3S$: C, 47.77; H, 4.46; N, 12.38. Found : C, 47.50; H, 4.12; N, 12.41. IR(KBr) : 3187, 2966, 1717, 1662, 1170 cm^{-1}.

(4,6-Dihydro-5-oxothieno[3,4-d]imidazol-1-yl)pentanoic acid 13g. Yield=85%. ^{1}H NMR ($DMSOd_6$), δ : 10.25 (brs, 1H, NH), 10.16 (brs, 1H, NH), 6.17 (s, 1H, H_5), 2.60 (t, 2H, CH_2, J=6.8Hz), 2.20 (t, 2H, CH_2, J=6.4Hz), 1.53-1.49 (m, 4H, $(CH_2)_2$). ^{13}C NMR ($DMSOd_6$), δ : 174.6 (CO), 160.2 (CO), 131.8 (C_3), 129.2 (C_4), 110.2 (C_2), 90.3 (C_5), 33.0 (CH_2), 26.0 (CH_2), 25.6 (CH_2), 24.1 (CH_2). Anal. Calc. for $C_{10}H_{12}N_2O_3S$: C, 49.99; H, 5.03; N, 11.66. Found : C, 49.91; H, 4.82; N, 11.53. IR(KBr) : 3323, 3140, 2977, 2868, 1734, 1716, 1683, 1156 cm^{-1}.

(4,6-Dihydro-5-oxothieno[3,4-d]imidazol-1-yl)hexanoic acid 13g. Yield=84%. ^{1}H NMR ($DMSOd_6$), δ : 10.25 (brs, 1H, NH), 10.17 (brs, 1H, NH), 8.25 (brs, 1H, COOH), 6.16 (s, 1H, H_5), 2.58 (t, 2H, CH_2, J=7.5Hz), 2.17 (t, 2H, CH_2, J=6.9Hz), 1.52-1.26 (m, 6H, $(CH_2)_3$). ^{13}C NMR ($DMSOd_6$), δ : 175.1 (CO), 160.6 (CO), 131.9 (C_3), 129.2 (C_4), 111.6 (C_2), 90.3 (C_5), 33.9 (CH_2), 30.6 (CH_2), 28.3 (CH_2), 26.4 (CH_2), 24.6 (CH_2). Anal. Calc. for $C_{11}H_{14}N_2O_3S$: C, 51.95; H, 5.15; N, 11.02. Found : C, 52.06; H, 5.14; N, 11.02. IR(KBr) : 3323, 3140, 2977, 2868, 1734, 1716, 1683, 1156 cm^{-1}.

1,3-Dihydro-1,3-bis(isopropylidene)-5,5-dimethylthieno[3,4-d]imidazole 14. The diamine **1** (114mg, 1mmol) was dissolved in acetone (4ml) and stored after filtration for 20h at -20°C. The thienoimidazole **14** has slowly crystallized . Yield=56%. ^{1}H NMR ($CDCl_3$), δ : 2.30 (s, 6H), 1.85 (s, 6H), 1.52 (s, 6H). ^{13}C NMR ($CDCl_3$), δ : 166.2 (CO), 137.2, 116.5, 114.3,24.1, 22.2. Anal. Calc. for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74; N, 11.95. Found : C, 66.30; H, 7.88; N, 12.06. IR(KBr) : 2974, 2927, 1643 cm^{-1}.

Hydrogenation of thienoimidazole 14. Thienoimidazole **14** (0.468g, 2mmol) in ethanol (15ml) was hydrogenated over 10%Pd/C (0.18g) at atmospheric pressure. The reaction was stirred for 4h and the catalyst eliminated by filtration on celite. After evaporation of the solvent, the crude product was dissolved in CH_2Cl_2 (20ml) and treated with 1N HCl solution (2x20ml). The aqueous phase was washed with CH_2Cl_2 (20ml), neutralized with a dilute NaOH solution and extracted with ether (2x30ml). The organic fractions were dried and evaporated providing the 3,4-diamino-2,5-diisopropylthiophene **4d** as white crystals isolated in an analytical pure form. Yield : 40%.

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