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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 3,4diaminothiophene 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.

Scheme 1



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 acidcatalyzed 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 5oxopentanoate¹¹ (entry 6) and butanone (entry 8), lower yields were observed.

Scheme 2



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 CH₂Cl₂ under acid catalysis. The dicarbamates 5 are crystalline compounds.

Entry	N°	R ¹	R ²	Yield (%) ^a	Entry	N°	R ¹	Yield (%)
1	4a	Me	Н	70	9	5a	Et	70
2	4b	Et	Н	87	10	5b	nPr	75
3	4c	nPr	Н	90	11	5c	iPr	85
4	4d	iPr	Н	72	12	5d	nC5H11	90
5	4e	Ph	Н	65	13	5e	Ph	75
6	4f	(CH ₂) ₃ COOMe	Н	40 .				
7	4g	Me	Me	80				
8	4h	Et	Me	40				

 Table 1

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

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-oxohexanoate¹¹ 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 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)R¹CHO (1.2 eq.), PhSeH (2.5 eq.), CH₂Cl₂, pTSA cat., 0°C. ii)HBr, AcOH, RT; NaOH, H₂O..

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Entry	N°	R ¹	Yield (%)	Entry	N°	R ¹	Yield (%)
1	6 a	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 ₅ H ₁₁	70	12	9d	nC ₅ H ₁₁	64
5	6e	Ph	57	13	9e	Ph	72
6	6f	(CH ₂) ₂ COOMe	56	14	9g	(CH ₂) ₃ COOMe	65
7	6g	(CH ₂) ₃ COOMe	65				
8	6h	(CH ₂) ₄ COOMe	79				

 Table 2

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

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

utyl 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.							
	N°	R ¹	Yield (%)	Entry	N°	R ¹	Yield (%)

6

7

8

10a

10Ь

10e

Di-t-bu	tyl 8-alkyldi	thieno[3,2-b di	2',3'-e]pyridine thieno[3,2-b:2',	-3,5-diyldicar ,3'-e]pyridines	bamates 8 a s 10.	and 8-alkyl 3	,5-diamino
Entry	N°	R ¹	Yield (%)	Entry	N°	R1	Yield (%

75

72

50

65

52

Et

nPr

 nC_5H_{11}

Ph

(CH₂)₂Ph

1

2

3

4

5

8a

8b

8d

8e

8i

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).



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 $n = 2, 3, 4 (\simeq 80 \% \text{ yield})$ (Scheme 6).

Scheme 6



78

85

60

Et

nPr

Ph

The sequence $1 \rightarrow 2 \rightarrow 6 \rightarrow 12 \rightarrow 13$ 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.



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 ¹³C 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 (CDCl₃), $\delta : 6.12$ (s, 2H, H₂, H₅), 3.12 (brs, 4H, NH₂). ¹³C NMR (CDCl₃), $\delta : 135.8$ (C₃, C₄), 101.4 (C₂, C₅).

Ethyl (4-aminothien-3-yl)carbamate 2a. To a solution of 3,4-diaminothiophene 1 (0.228g, 2mmol) in CH₂Cl₂ (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 (CDCl₃), δ : 7.10 (brs, 1H, NH), 7.00 (d, 1H, H₂, J=3.5Hz), 6.24 (d, 1H, H₅, J=3.5Hz), 4.18 (q, 2H, CH₂, J=7.1Hz), 3.40 (brs, 2H, NH₂), 1.26 (t, 3H, CH₃, J=7.1Hz). ¹³C NMR (CDCl₃), δ : 154.3 (CO), 137.1 (C₄), 127.8 (C₃), 110.6 (C₂), 102.3 (C₅), 61.1 (CH₂), 14.1 (CH₃). Anal. Calc. for C₇H₁₀N₂O₂S : 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 (11) 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 CH₂Cl₂ 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. ¹H NMR (CDCl₃), δ : 7.10 (brs, 1H, H₂), 6.50 (brs, 1H, NH), 6.30 (d, 1H, H₅, J=3.5Hz), 3.25 (brs, 2H, NH₂), 1.49 (s, 9H, CH₃). ¹³C NMR (CDCl₃), δ : 153.3 (CO), 136.7 (C₄), 128.9 (C₃), 110.0 (C₂), 103.9 (C₅), 80.6 (*C*(CH₃)₃), 28.2 (CH₃). Anal. Calc. for C₉H₁₄N₂O₂S : 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 CH₂Cl₂ (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 CH₂Cl₂/light petroleum : 1/2. Yield : 75%. M.p.=110°C. ¹H NMR (CDCl₃), δ : 7.48 (brs, 2H, NH), 7.14 (brs, 2H, H₂, H₅, H₂), 4.18 (q, 4H, CH₂, J=7.1Hz), 1.25 (t, 6H, CH₃, J=7.1Hz). ¹³C NMR (CDCl₃), δ : 154.6 (CO), 128.3 (C₃, C₄), 111.4 (C₂, C₅), 61.5 (CH₂), 14.2 (CH₃). Anal. Calc. for C₁₀H₁₄N₂O₄S : 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 CH₂Cl₂ 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. ¹H NMR (CDCl₃), δ : 7.12 (brs, 2H, H₂, H₃), 6.77 (brs, 2H, NH), 1.49 (s, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 153.7 (CO), 128.9 (C₃, C₄), 111.5 (C₂, C₅), 80.9 (C(CH₃)), 28.2 (CH₃). Anal. Calc. for C₁₄H₂₂N₂O₄S : 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 CH₂Cl₂ (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-diam no-2,5-dibenzylthiophene 4e was obtained after silicagel chromatographic purification (elution : CH₂Cl₂). The acidic extraction must be avoided in this case.

3,4-Diamino-2,5-diethylthiophene 4a. Yield : 80%. ¹H NMR (CDCl₃), δ : 3.26 (brs, 4H, NH₂), 2.55 (q, 4H, CH₂, J=7.3Hz), 1.18 (t, 6H, CH₃, J=7.3Hz). ¹³C NMR (CDCl₃), δ : 131.7 (C₃, C₄), 115.0 (C₂, C₅), 19.8 (CH₂), 14.7 (CH₃).

3,4-Diamino-2,5-di-n-propylthiophene 4b. Yield : 87%. ¹H NMR (CDCl₃), δ : 3.62 (brs, 4H, NH₂), 2.49 (t, 4H, CH₂, J=7.4Hz), 1.57 (m, 4H, CH₂) 0.94 (t, 6H, CH₃, J=7.4Hz). ¹³C NMR (CDCl₃), δ : 132.2 (C₃, C₄), 114.8 (C₂, C₅), 28.8 (CH₂), 23.8 (CH₂), 13.8 (CH₃).

3,4-Diamino-2,5-di-n-butylthiophene 4c. Yield : 90%.¹H NMR (CDCl₃), δ : 3.15 (brs, 4H, NH₂), 2.52 (t, 4H, CH₂, J=7.1Hz), 1.54 (m, 4H, CH₂), 1.38 (m, 4H, CH₂), 0.90 (t, 6H, CH₃, J=7.2Hz).¹³C NMR (CDCl₃), δ : 132.0 (C₃, C₄), 114.9 (C₂, C₅), 32.6 (CH₂), 26.3 (CH₂), 22.3 (CH₂), 13.8 (CH₃).

3,4-Diamino-2,5-diisobutylthiophene 4d. Yield : 72%. ¹H NMR (CDCl₃), δ : 3.09 (brs, 4H, NH₂), 2.38 (d, 4H, CH₂, J=6.9Hz), 1.81 (m, 2H, CH), 0.92 (d, 12H, CH₃, J=6.8Hz). ¹³C NMR (CDCl₃), δ : 132.5 (C₃, C₄), 114.1 (C₂, C₃), 35.9 (CH₂), 30.0 (CH), 14.7 (CH₃).

3,4-Diamino-2,5-dibenzylthiophene 4e. Yield : 70% . M.p.=90°C. ¹H NMR (CDCl₃), δ : 7.28-7.18 (m, 10H, Ph), 3.88 (s, 4H, CH₂), 3.39 (brs, 4H, NH₂). ¹³C NMR (CDCl₃), δ : 139.4, 128.5, 128.3, 126.4 (Ph), 130.4 (C₃, C₄), 113.6 (C₂, C₅), 32.8 (CH₂).

Dimethyl (3,4-diaminothiophene-2,5-diyl)dipentanoate 4f. Yield :40 %. ¹H NMR (CDCl₃), δ : 3.56 (s, 6H, CH₃), 3.34 (brs, 4H, NH₂), 2.45 (t, 4H, CH₂, J=7.0Hz), 2.23 (t, 4H, CH₂, J=6.9Hz), 1.58-1.52 (m, 8H, (CH₂)₂). ¹³C NMR (CDCl₃), δ : 173.6 (CO), 132.2 (C₃, C₄), 113.5 (C₂, C₅), 51.1 (CH₃), 33.3 (CH₂), 29.6 (CH₂), 26.0 (CH₂), 24.1 (CH₂).

3,4-Diamino-2,5-diisopropylthiophene 4g. Yield : 79%. M.p.=80°C . ¹H NMR (CDCl₃), δ : 3.11 (brs, 4H, NH₂), 3.02 (hept., 2H, CH, J=6.8Hz), 1.22 (d, 12H, CH₃, J=6.8Hz). ¹³C NMR (CDCl₃), δ : 130.9 (C₃, C₄), 121.7 (C₂, C₅), 26.7 (CH), 23.3 (CH₃).

3,4-Diamino-2,5-di(1-methylpropyl)thiophene 4h. Yield : 42%. ¹H NMR (CDCl₃), δ : 3.66 (brs, 4H, NH₂), 2.30 (tq., 2H, CH, J=6.8Hz, J=6.9Hz), 1.53 (q, 4H, CH₂, J= 6.9Hz), 1.18 (d, 6H, CH₃, J=6.8Hz). ¹³C NMR (CDCl₃), δ : 131.2 (C₃, C₄), 121.2 (C₂, C₅), 33.8 (CH), 31.1 (CH₂), 12.1 (CH₃).

 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 CH₂Cl₂ (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. ¹H NMR (CDCl₃), δ : 6.19 (brs, 2H, NH), 2.60 (t, 4H, CH₂, J=7.6Hz), 1.59 (sext., 4H, CH₂, J=7.6Hz), 1.46 (s, 18H, CH₃), 0.93 (t, 6H, CH₃, J=7.6Hz). ¹³C NMR (CDCl₃), δ : 154.2 (CO), 132.2 (C₃, C₄), 126.6 (C₂, C₅), 79.9 (*C*(CH₃)₃), 29.4 (CH₂), 28.1 (CH₃), 23.5 (CH₂), 13.6 (CH₃). Anal. Calc. for C₂₀H₃₄N₂O₄S : 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. ¹H NMR (CDCl₃), δ : 6.17 (brs, 2H, NH), 2.62 (t, 4H, CH₂, J=7.6Hz), 1.57 (m., 4H, CH₂), 1.46 (s, 18H, CH₃), 1.36 (m, 4H, CH₂), 0.89 (t, 6H, CH₃, J=7.2Hz). ¹³C NMR (CDCl₃), δ : 154.4 (CO), 132.5 (C₃, C₄), 126.6 (C₂, C₅), 80.0 (*C*(CH₃)₃), 30.6 (CH₂), 28.1 (CH₃), 26.6 (CH₂), 22.3 (CH₂), 13.8 (CH₃). Anal. Calc. for C₂₂H₃₈N₂O₄S : 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. ¹H NMR (CDCl₃), δ : 6.13 (brs, 2H, NH), 2.50 (d, 4H, CH₂, J=7.1Hz), 1.83 (m, 2H, CH), 1.45 (s, 18H, CH₃), 0.89 (d, 12H, CH₃, J=6.6Hz). ¹³C NMR (CDCl₃), δ : 154.1 (CO), 131.7 (C₃, C₄), 127.3 (C₂, C₅), 79.7 (*C*(CH₃)₃), 36.4 (CH₂), 29.6 (CH), 28.0 (CH₃), 22.1 (CH₃). Anal. Calc. for C₂₂H₃₈N₂O₄S : 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.¹H NMR (CDCl₃), δ : 6.23 (brs, 2H, NH), 2.60 (t, 4H, CH₂, J=7.6Hz), 1.54-1.39 (m, 22H, CH₂, CH₃), 1.33-1.26 (m, 12H, (CH₂)₃), 0.85 (t, 6H, CH₃, J=6.6Hz). ¹³C NMR (CDCl₃), δ : 154.2 (CO), 132.7 (C₃, C₄), 126.4 (C₂, C₃), 79.9

 $(C(CH_3)_3)$, 31.3 (CH₂), 30.1 (CH₂), 28.6 (CH₂), 28.0 (CH₃), 27.3 (CH₂), 22.3 (CH₂), 13.8 (CH₃). Anal. Calc. for C₂₆H₄₆N₂O₄S : 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 (CDCl₃), δ : 7.30-7.16 (m, 10H, Ph), 6.28(brs, 2H, NH), 3.96 (s, 4H, CH₂), 1.46 (s, 18H, CH₃) . ¹³C NMR (CDCl₃), δ : 154.2 (CO), 131.9 (C₃, C₄), 127.9 (C₂, C₃), 138.9, 128.5, 128.3, 126.3 (C_{Ph}), 80.3 (*C*(CH₃)₃), 33.5 (CH₂), 28.1 (CH₃). Anal. Calc. for C₂₈H₃₄N₂O₄S : 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 CH₂Cl₂ (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 CH₂Cl₂/ethyl acetate : 95 /5).

t-Butyl (4-amino-5-n-propylthien-3-yl)carbamate 6a. Yield : 72%. ¹H NMR (CDCl₃), δ : 6.92 (brs, 1H, H₂), 6.64 (brs, 1H, NH), 3.00 (brs, 2H, NH₂), 2.57 (t, 2H, CH₂, J=7.5Hz), 1.62 (m, 2H, CH₂), 1.48 (s, 9H, CH₃), 0.96 (t, 3H, CH₃, J=7.3Hz). ¹³C NMR (CDCl₃), δ : 153.2 (CO), 132.2 (C₄), 129.0 (C₃), 122.9 (C₅), 104.5 (C₂), 80.0 (*C*(CH₃)), 28.9 (CH₂), 28.0 (CH₃), 23.8 (CH₂), 13.7 (CH₃). Anal. Calc. for C₁₂H₂₀N₂O₂S : 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 (CDCl₃), δ : 6.90 (brs, 1H, H₂), 6.71 (brs, 1H, NH), 3.10 (brs, 2H, NH₂), 2.55 (t, 2H, CH₂, J=7.5Hz), 1.50 (m, 13H, (CH₂)₂, CH₃), 0.91 (t, 3H, CH₃, J=7.4Hz). NMR ¹³C (CDCl₃), δ : 153.1 (CO), 132.0 (C₄), 128.9 (C₃), 121.9 (C₅), 104.9 (C₂), 79.9 (*C*(CH₃)), 32.6 (CH₂), 28.1 (CH₃), 26.6 (CH₂), 22.3 (CH₂), 13.8 (CH₃). Anal. Calc. for C₁₃H₂₂N₂O₂S : 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 (CDCl₃), δ : 6.94 (brs, 1H, H₂), 6.76 (brs, 1H, NH), 3.00 (brs, 2H, NH₂), 2.44 (d, 2H, CH₂, J=7.1Hz), 1.83 (m, 1H, CH), 1.48 (s, 9H, CH₃), 0.91 (d, 6H, CH₃, J=6.6Hz). ¹³C NMR (CDCl₃), δ : 153.2 (CO), 132.0 (C₄), 128.9 (C₃), 121.7 (C₅), 105.1 (C₂), 79.9 (*C*(CH₃)), 35.9 (CH₂), 29.9 (CH), 28.0 (CH₃), 22.0 (CH₃). Anal. Calc. for C₁₃H₂₂N₂O₂S : 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 (CDCl₃), δ : 6.91 (brs, 1H, H₂), 6.71 (brs, 1H, NH), 2.91 (brs, 2H, NH₂), 2.57 (t, 2H, CH₂, J=7.5Hz), 1.60-1.28 (m, 17H, (CH₂)₄, CH₃), 0.86 (t, 3H, CH₃, J=6.5Hz). ¹³C NMR (CDCl₃), δ : 153.2 (CO), 131.4 (C₄), 129.0 (C₃), 122.3 (C₃), 104.8 (C₂), 80.0 (*C*(CH₃)), 31.2 (CH₂), 30.2 (CH₂), 28.6 (CH₂), 28.0 (CH₃), 26.6 (CH₂), 22.3 (CH₂), 13.8 (CH₃). Anal. Calc. for C₁₅H₂₆N₂O₂S : 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 (CDCl₃), δ : 7.36-7.16 (m, 5H, Ph), 6.99 (brs, 1H, H₂), 6.63 (brs, 1H, NH), 3.95 (s, 2H, CH₂), 2.90 (brs, 2H, NH₂), 1.49 (s, 9H, CH₃). ¹³C NMR (CDCl₃), δ : 153.2 (CO), 138.8, 128.3, 127.9, 126.1 (C_{Ph}), 132.7 (C₄), 128.9 (C₃), 119.4 (C₅), 106.2 (C₂), 80.0 (*C*(CH₃)), 32.6 (CH₂), 28.0 (CH₃). Anal. Calc. for C₁₆H₂₀N₂O₂S : 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 (CDCl₃), δ : 6.94 (brs, 1H, H₂), 6.67 (brs, 1H, NH), 3.65 (s, 3H, CH₃), 3.00 (brs, 2H, NH₂), 2.65 (t, 2H, CH₂, J=7.4Hz), 2.33 (t, 2H, CH₂, J=7.0Hz), 1.88 (m, 2H, CH₂), 1.48 (s, 9H, CH₃). ¹³C NMR (CDCl₃), δ : 173.6 (CO), 153.1 (CO), 132.4 (C₄), 128.9 (C₃), 122.0 (C₅), 105.1 (C₂), 80.2 (C(CH₃)), 51.3 (CH₃), 32.4 (CH₂), 28.0 (CH₃),

25.6 (CH₂), 25.3 (CH₂). 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 (CDCl₃), δ : 6.91 (brs, 1H, H₂), 6.67 (brs, 1H, NH), 3.63 (s, 3H, CH₃), 2.95 (brs, 2H, NH₂), 2.60 (t, 2H, CH₂, J=7.0Hz), 2.31 (t, 2H, CH₂, J=6.9Hz), 1.69-1.56 (m, 4H, (CH₂)₂), 1.48 (s, 9H, CH₃). ¹³C NMR (CDCl₃), δ : 173.8 (CO), 153.1 (CO), 131.7 (C₄), 129.0 (C₃), 121.4 (C₅), 104.9 (C₂), 80.0 (*C*(CH₃)), 51.2 (CH₃), 33.4 (CH₂), 29.6 (CH₂), 28.0 (CH₃), 26.2 (CH₂), 24.1 (CH₂).Anal. Calc. for C₁₅H₂₄N₂O₄S : 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 (CDCl₃), δ : 6.83 (brs, 1H, H₂), 6.62 (brs, 1H, NH), 3.64 (s, 3H, CH₃), 3.00 (brs, 2H, NH₂), 2.60 (t, 2H, CH₂, J=7.4Hz), 2.15 (t, 2H, CH₂, J=7.3Hz), 1.72-1.27 (m, 15H, (CH₂)₃, CH₃). ¹³C NMR (CDCl₃), δ : 173.4 (CO), 152.9 (CO), 131.6 (C₄), 128.6 (C₃), 120.5 (C₅), 104.3 (C₂), 79.5 (*C*(CH₃)), 50.8 (CH₃), 33.2 (CH₂), 29.5 (CH₂), 28.0 (CH₃), 27.7 (CH₂), 26.0 (CH₂), 24.0 (CH₂).Anal. Calc. for C₁₆H₂₆N₂O₄S : 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 (CDCl₃), δ : 7.24 (brs, 2H, H₂, H₂·), 6.80 (brs, 2H, NH), 6.47 (d, 2H, H₅, H₅·, J=3.1Hz), 5.80 (brs, 1H, NH), 4.17 (q, 4H, CH₂, J=7.1Hz), 1.25 (t, 6H, CH₃, J=7.1Hz). ¹³C NMR (CDCl₃), δ : 154.3 (CO), 135.7 (C₄, C₄·), 128.5 (C₃, C₃·), 110.8 (C₂, C₂·), 107.8 (C₅, C₅·), 61.5 (CH₂), 14.3 (CH₃). 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 (CDCl₃), δ : 7.19 (brs, 2H, H₂, H₂·), 6.80 (brs, 2H, NH), 6.46 (d, 2H, H₅, H₅·, J=3.5Hz), 5.70 (brs, 1H, NH), 1.48 (t, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 153.4 (CO), 135.8 (C₄, C₄·), 128.9 (C₃, C₃·), 110.3 (C₂, C₂·, C₅, C₅·), 80.8 (*C*(CH₃)₃), 28.1 (CH₃). Anal. Calc. for C₁₈H₂₅N₃O₄S₂ : 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 (CDCl₃), δ : 8.02 (brs, 2H, NH), 7.86 (brs, 2H, H₂, H₆), 3.11 (q, 2H, CH₂, J=7.6Hz), 1.47 (s, 18H, CH₃), 1.43 (t, 3H, CH₃, J=7.6Hz). ¹³C NMR (CDCl₃), δ : 152.7 (CO), 146.7 (C_{3a}, C_{4a}), 142.3 (C₈), 129.9 (C₃, C₅), 128.1 (C_{7a}, C_{8a}), 109.6 (C₂, C₆), 80.1 (*C*(CH₃)₃), 27.6 (CH₃), 26.4 (CH₂), 12.1 (CH₃). Anal. Calc. for C₂₁H₂₇N₃O₄S₂ : 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 (CDCl₃), δ : 8.03 (brs, 2H, NH), 7.86 (brs, 2H, H₂, H₆), 3.07 (t, 2H, CH₂, J=7.7Hz), 1.90 (m, 2H, CH₂), 1.46 (s, 18H, CH₃), 1.02 (t, 3H, CH₃, J=7.3Hz). ¹³C NMR (CDCl₃), δ : 152.7 (CO), 146.7 (C_{3a}, C_{4a}), 141.0 (C₈), 129.8 (C₃, C₅), 128.7 (C_{7a}, C_{8a}), 109.7 (C₂, C₆), 80.1 (C(CH₃)₃), 35.1 (CH₂), 27.6 (CH₃), 21.2

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(CH₂), 14.2 (CH₃). 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. ¹H NMR (CDCl₃), δ : 8.30 (brs, 2H, NH), 7.86 (brs, 2H, H₂, H₆), 3.06 (t, 2H, CH₂, J=7.8Hz), 1.85 (m, 2H, CH₂), 1.46-1.15 (m, 22H, (CH₂)₂CH₃), 0.84 (t, 3H, CH₃, J=6.6Hz). ¹³C NMR (CDCl₃), δ : 152.8 (CO), 146.6 (C_{3a}, C₄₄), 141.2 (C₈), 129.8 (C₃, C₅), 128.7 (C_{7a}, C_{8a}), 109.7 (C₂, C₆), 80.2 (C(CH₃)₃), 33.1 (CH₂), 31.7 (CH₂), 27.7 (CH₃), 27.4 (CH₂), 22.2 (CH₂), 13.7 (CH₃). Anal. Calc. for C₂₄H₃₃N₃O₄S₂ : 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. ¹H NMR (CDCl₃), δ : 8.18 (brs, 2H, NH), 7.92 (brs, 2H, H₂, H₆), 7.87-7.54 (Ph), 3.06 (t, 2H, CH₂, J=7.8Hz), 1.42 (s, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 152.8 (CO), 147.1 (C_{3a}, C_{4a}), 140.3 (C₈), 135.6, 129.9, 129.2, 127.9 (C_{Ph}), 129.6 (C₃, C₅), 128.1 (C_{7a}, C_{8a}), 111.1 (C₂, C₆), 80.5 (C(CH₃)₃), 27.9 (CH₃), 26.4 (CH₂), 12.1 (CH₃). Anal. Calc. for C₂₅H₂₇N₃O₄S₂ : 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. ¹H NMR (CDCl₃), δ : 8.18 (brs, 2H, NH), 7.90 (brs, 2H, H₂, H₆), 7.29-7.20 (m, 5H, Ph), 3.42-3.32 (m, 2H, CH₂), 3.15-3.05 (m, 2H, CH₂), 1.49 (s, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 152.7 (CO), 146.6 (C_{3a}, C_{4a}), 140.2 (C₈), 139.8, 128.5, 128.2, 126.4 (C_{Ph}) 129.7 (C₃, C₅), 128.6 (C_{7a}, C_{8a}), 109.6 (C₂, C₆), 80.6 (C(CH₃)₃), 35.5 (CH₂), 33.8 (CH₂), 27.9 (CH₃). Anal. Calc. for C₂₇H₃₁N₃O₄S₂ : 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%. ¹H NMR (CDCl₃), δ : 5.96 (s, 1H, H₅), 3.08 (brs, 4H, NH₂), 2.53 (t, 2H, CH₂, J=7.5Hz), 1.60 (m, 2H, CH₂), 0.95 (t, 3H, CH₃, J=7.3Hz). ¹³C NMR (CDCl₃), δ : 137.0 (C₄), 132.4 (C₃), 120.5 (C₂), 96.7 (C₅), 29.0 (CH₂), 23.6 (CH₂), 13.7 (CH₃). Anal. Calc. for C₇H₁₂N₂S : 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 ¹H (CDCl₃), δ : 5.93 (s, 1H, H₅), 3.20 (brs, 4H, NH₂), 2.53 (t, 2H, CH₂, J=7.5Hz), 1.60-1.22 (m, 4H, (CH₂)₂), 0.92 (t, 3H, CH₃, J=7.2Hz). ¹³C NMR (CDCl₃), δ : 137.2 (C₄), 132.1 (C₃), 119.6 (C₂), 96.6 (C₅), 32.5 (CH₂), 28.8 (CH₂), 22.4 (CH₂), 13.9 (CH₃). Anal. Calc. for C₈H₁₄N₂S : 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%. ¹H NMR (CDCl₃), δ : 5.97 (s, 1H, H₅), 3.14 (brs, 4H, NH₂), 2.42 (d, 2H, CH₂, J=7.0Hz), 1.84 (m, 1H, CH), 0.93 (d, 6H, CH₃, J=6.6Hz). ¹³C NMR (CDCl₃), δ : 137.2 (C₄), 132.8 (C₃), 118.3 (C₂), 96.9 (C₅), 36.3 (CH₂), 30.1 (CH), 22.3 (CH₃). Anal. Calc. for C₈H₁₄N₂S : 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%. ¹H NMR (CDCl₃), δ : 5.94 (s, 1H, H₅), 3.14 (brs, 4H, NH₂), 2.54 (t, 2H, CH₂, J=7.5Hz), 1.61-1.29 (m, 8H, (CH₂)₄), 0.86 (t, 3H, CH₃, J=6.4Hz). ¹³C NMR (CDCl₃), δ : 137.5 (C₄), 132.2 (C₃), 119.8 (C₂), 96.6 (C₅), 31.5 (CH₂), 29.9 (CH₂), 28.8 (CH₂), 27.0 (CH₂),

22.4 (CH₂), 13.9 (CH₃). 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 (CDCl₃), δ : 7.29-7.19 (m, 5H, Ph), 6.02 (s, 1H, H₅), 3.91 (s, 2H, CH₂), 3.15 (brs, 4H, NH₂). ¹³C NMR (CDCl₃), δ : 137.0 (C₄), 132.1 (C₃), 133.0, 128.4, 128.1, 126.3 (C_{Ph}), 117.3 (C₂), 97.9 (C₅), 33.0 (CH₂). Anal. Calc. for C₁₀H₁₀N₂S : 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 (CDCl₃), δ : 5.94 (s, 1H, H₅), 3.63 (s, 3H, CH₃), 3.05 (brs, 4H, NH₂), 2.56 (t, 2H, CH₂, J=7.1Hz), 2.31 (t, 2H, CH₂, J=6.8Hz), 1.74-1.59 (m, 4H, (CH₂)₂). ¹³C NMR (CDCl₃), δ : 173.9 (CO), 137.1 (C₄), 132.6 (C₃), 116.9 (C₂), 97.0 (C₅), 51.4 (CH₃), 33.6 (CH₂), 29.8 (CH₂), 26.4 (CH₂), 24.4 (CH₂). Anal. Calc. for C₁₀H₁₆N₂O₂S : 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 (CDCl₃), δ : 6.50 (s, 2H, H₂, H₆), 4.35 (brs, 4H, NH₂), 3.05 (q, 2H, CH₂, J=7.6Hz), 1.40 (t, 3H, CH₃, J=7.6Hz). ¹³C NMR (CDCl₃), δ : 148.7 (C_{3a}, C_{4a}), 138.8 (C₃, C₅, C₈), 128.7 (C_{7a}, C_{8a}), 100.5 (C₂, C₆), 26.5 (CH₂), 13.2 (CH₃). Anal. Calc. for C₁₁H₁₁N₃S₂ : 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 (CDCl₃), δ : 6.49 (s, 2H, H₂, H₆), 4.38 (brs, 4H, NH₂), 3.01 (t, 2H, CH₂, J=7.7Hz), 1.88 (m, 2H, CH₂), 1.00 (t, 3H, CH₃, J=7.4Hz). ¹³C NMR (CDCl₃), δ : 148.8 (C_{3a}, C_{4a}), 139.0 (C₃, C₅), 138.2 (C₈), 128.2 (C_{7a}, C_{8a}), 100.3 (C₂, C₆), 34.9 (CH₂), 21.1 (CH₂), 13.5 (CH₃). Anal. Calc. for C₁₂H₁₃N₃S₂ : 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 (CDCl₃), δ : 7.87-7.82 (m, 2H, Ph), 7.59-7.52 (m, 3H, Ph), 6.54 (s, 2H, H₂, H₆), 4.40 (brs, 4H, NH₂). ¹³C NMR (DMSOD₆), δ : 147.6 (C_{3a}, C_{4a}), 139.9 (C₃, C₅), 137.8 (C₈), 136.1, 129.6, 129.2, 127.8 (C_{Ph}), 128.7 (C_{7a}, C_{8a}), 98.6 (C₂, C₆). Anal. Calc. for C₁₅H₁₁N₃S₂ : 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 (CDCl₃), δ : 6.44 (d, 2H, H₂, H₂, J=3.4Hz), 6.24 (d, 2H, H₅, H₅, J=3.4Hz), 5.45 (brs, 1H, NH), 3.36 (brs, 4H, NH₂). ¹³C NMR (CDCl₃), δ : 137.2 (C₄, C₄·), 134.8 (C₃, C₃·), 105.0 (C₂, C₂·), 102.3 (C₅, C₅·). Anal. Calc. for C₈H₉N₃S₂ : 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/CH₂Cl₂.

Methyl [3,4-bis(methoxycarbonylamino)thien-2-yl]butanoate 12f. Yield : 89%. ¹H NMR (CDCl₃), δ : 7.09 (brs, 1H, H₅), 6.83 (brs, 1H, NH), 6.34 (brs, 1H, NH), 3.63 (s, 3H, CH₃), 2.68 (t, 2H, CH₂, J=7.3Hz), 2.28 (t, 2H, CH₂, J=7.1Hz), 1.88 (m, 2H, CH₂), 1.45 (s, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 173.0 (CO), 154.1, 152.6 (CO), 134.2 (C₃), 131.6 (C₄), 123.6 (C₂), 80.1, 79.7 (C(CH₃)₃), 51.0 (CH₃), 32.3 (CH₂), 27.7 (CH₃), 25.9 (CH₂), 25.2 (CH₂). Anal. Calc. for C₁₉H₃₀N₂O₆S : 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%. ¹H NMR (CDCl₃), δ : 7.04 (brs, 1H, H₃), 6.83 (brs, 1H, NH), 6.15 (brs, 1H, NH), 3.61 (s, 3H, CH₃), 2.62 (t, 2H, CH₂, J=7.0Hz), 2.27 (t, 2H, CH₂, J=6.9Hz), 1.61-1.52 (m, 4H, (CH₂)₂), 1.44 (s, 18H, CH₃). ¹³C NMR (CDCl₃), δ : 173.7 (CO), 154.4, 153.0 (CO), 135.8 (C₃), 131.7 (C₄), 123.4 (C₂), 80.6 (*C*(CH₃)₃), 51.3 (CH₃), 33.5 (CH₂), 29.6 (CH₂), 28.1, 28.0 (CH₃), 26.9 (CH₂), 24.1 (CH₂). Anal. Calc. for C₂₀H₃₂N₂O₆S : 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%. ¹H NMR (CDCl₃), δ : 7.06 (brs, 1H, H₅), 6.83 (brs, 1H, NH), 6.06 (brs, 1H, NH), 3.61 (s, 3H, CH₃), 2.62 (t, 2H, CH₂, J=7.5Hz), 2.26 (t, 2H, CH₂, J=7.3Hz), 1.58-1.30 (m, 24H, (CH₂)₃, CH₃). ¹³C NMR (CDCl₃), δ : 173.5 (CO), 154.1, 152.6 (CO), 135.9 (C₃), 131.5 (C₄), 123.0 (C₂), 80.0, 79.6 (*C*(CH₃)₃), 50.9 (CH₃), 33.3 (CH₂), 29.4 (CH₂), 28.0 (CH₂), 27.8, 27.7 (CH₃), 26.6 (CH₂), 24.0 (CH₂). Anal. Calc. for C₂₁H₃₄N₂O₆S : 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%. ¹H NMR (DMSOd₆), δ : 12.13 (brs, 1H, COOH), 10.23 (brs, 1H, NH), 10.16 (brs, 1H, NH), 6.20 (s, 1H, H₅), 2.65 (t, 2H, CH₂, J=7.4Hz), 2.22 (t, 2H, CH₂, J=6.8Hz), 1.78 (m, 2H, CH₂). ¹³C NMR (DMSOd₆), δ : 174.2 (CO), 160.2 (CO), 131.8 (C₃), 129.2 (C₄), 110.2 (C₂), 90.3 (C₅), 33.0 (CH₂), 26.0 (CH₂), 25.6 (CH₂). Anal. Calc. for C₉H₁₀N₂O₃S: 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%. ¹H NMR (DMSOd₆), δ : 10.25 (brs, 1H, NH), 10.16 (brs, 1H, NH), 6.17 (s, 1H, H₅), 2.60 (t, 2H, CH₂, J=6.8Hz), 2.20 (t, 2H, CH₂, J=6.4Hz), 1.53-1.49 (m, 4H, (CH₂)₂). ¹³C NMR (DMSOd₆), δ : 174.6 (CO), 160.2 (CO), 131.8 (C₃), 129.2 (C₄), 110.2 (C₂), 90.3 (C₅), 33.0 (CH₂), 26.0 (CH₂), 25.6 (CH₂), 24.1 (CH₂). Anal. Calc. for C₁₀H₁₂N₂O₃S : 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%. ¹H NMR (DMSOd₆), δ : 10.25 (brs, 1H, NH), 10.17 (brs, 1H, NH), 8.25 (brs, 1H, COOH), 6.16 (s, 1H, H₅), 2.58 (t, 2H, CH₂, J=7.5Hz), 2.17 (t, 2H, CH₂, J=6.9Hz), 1.52-1.26 (m, 6H, (CH₂)₃). ¹³C NMR (DMSOd₆), δ : 175.1 (CO), 160.6 (CO), 131.9 (C₃), 129.2 (C₄), 111.6 (C₂), 90.3 (C₅), 33.9 (CH₂), 30.6 (CH₂), 28.3 (CH₂), 26.4 (CH₂), 24.6 (CH₂). Anal. Calc. for C₁₁H₁₄N₂O₃S : 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%. ¹H NMR (CDCl₃), $\delta : 2.30$ (s, 6H), 1.85 (s, 6H), 1.52 (s, 6H). ¹³C NMR (CDCl₃), $\delta : 166.2$ (CO), 137.2, 116.5, 114.3,24.1, 22.2. Anal. Calc. for C₁₃H₁₈N₂S : 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 CH₂Cl₂ (20ml) and treated with 1N HCl solution (2x20ml). The aqueous phase was washed with CH₂Cl₂ (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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