

Electrochemical Oxidation of Methyl (\pm)-4,7-Dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate, a New Type of Dihydropyridine Calcium Blocker

Kyoji UENO* and Tsuneji UMEDA

Shionogi Research Laboratories, Shionogi & Co., Ltd., 5-12-4, Sagisu, Fukushima-ku, Osaka 553, Japan. Received November 11, 1991

Electrochemical oxidation of methyl (\pm)-4,7-dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (**1**), a new dihydropyridine calcium blocker, in both methanol and acetonitrile was investigated by cyclic voltammetry, macroscale controlled potential electrolysis (CPE), *in situ* electron spin resonance (ESR) and ultraviolet-visible spectral studies. CPE of **1** in methanol at the potential of the first anodic peak on cyclic voltammetry gave four final products, the corresponding pyridine (**2**, yield, 73.9%), the 2-methoxy-substituted derivative of **2** (**3**, 11.9%), the 2,2'-dimer (**4**, 7.9%) and the 2,5'-dimer (**5**, 5.8%), while in acetonitrile, CPE of **1** gave **2** (12.2%), **4** (85.3%) and **5** (1.2%). It is suggested that the initial step is a one-electron oxidation of **1** to give the radical cations based on the results of *in situ* ESR. A possible mechanism of the electrode reactions of **1**, which involves one-electron oxidation followed by deprotonation, radical coupling, substitution and further oxidation, is proposed.

Keywords dihydropyridine; dihydrothienopyridine; electrochemical oxidation; cyclic voltammetry; controlled potential electrolysis; electron spin resonance spectrum

Methyl 4,7-dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (**1**, Chart 1) is a new type of dihydropyridine derivative with a fused thiophene nucleus. It possesses potent coronary vasodilator and antihypertensive activities due to a calcium entry-blocking effect.¹⁾ Compound **1** has been subjected to animal experiments as a potential next-generation calcium antagonist in our laboratories.²⁾ Recently, we have reported a sensitive high-performance liquid chromatographic method using an electrochemical detector for the determination of **1** in biological fluid.³⁾

Several studies have been reported on both electrochemical^{4,5)} and enzymatic⁶⁾ oxidation mechanisms of monocyclic 1,4-dihydropyridine derivatives. However, none has been done on those of a dihydropyridine derivative with a fused thiophene nucleus such as **1**, because of its novelty. Understanding the mechanism of the electrochemical oxidation of **1** is essential for optimizing the performance of the electrochemical detector for high-performance liquid chromatography (HPLC), as well as for a deeper insight into enzymatic metabolism. Thus, the mechanism of electrochemical oxidation of **1** seems worthy of further investigation.

This paper reports the results of cyclic voltammetry, controlled potential electrolysis, electron spin resonance (ESR) spectroscopy and ultraviolet-visible (UV-VIS) spectral studies of **1**. The mechanism of the electrochemical oxidation of **1** is discussed.

Results and Discussion

Cyclic Voltammetry Cyclic voltammograms of **1** in methanol and in acetonitrile are shown in Fig. 1. One

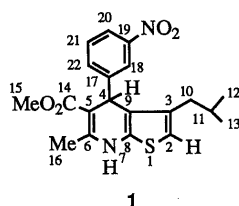


Chart 1. Chemical Structure of **1**

Numbers represent carbon numbers for assignment of the ¹³C-NMR spectra.

anodic peak (I_a) appeared at +0.85 V in methanol (Fig. 1(A)), while two anodic peaks (I_b , I_c) appeared at +0.85 V and +1.08 V in acetonitrile (Fig. 1(B)). The normalized peak current values (i_p/C) for the first anodic peak I_a in methanol, 37.9 $\mu\text{A}/\text{mM}$, was near to that for the anodic peak (1.16 V) of nifedipine⁷⁾ (methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate, molecular weight = 346.34), 36.4 $\mu\text{A}/\text{mM}$. However, the i_p/C value for I_b in acetonitrile, 28.1 $\mu\text{A}/\text{mM}$, was smaller than that for the anodic peak (1.21 V) of nifedipine, 47.1 $\mu\text{A}/\text{mM}$. Since it has been reported that nifedipine undergoes irreversible two-electron oxidation at the peak potential,^{4,7,9)} these results suggest that in the time-scale of the cyclic voltammetry, the electrode process at I_a in methanol involves two-electron oxidation, while that at I_b in acetonitrile involves mainly one-electron oxidation.

Controlled Potential Electrolysis (CPE) CPE of **1** was carried out in methanol and in acetonitrile at +0.85 V with an undivided cell until the value of the current became <0.5% of the initial value. The CPE of **1** in methanol gave four final products, **2**, **3**, **4**, and **5** (Chart 2). In acetonitrile, the CPE of **1** gave three final products, **2**, **4** and **5**. When the electrolysis of **1** in acetonitrile was stopped after 1.5 F/mol of electricity had been passed, another product **6** was isolated, which was found to be a

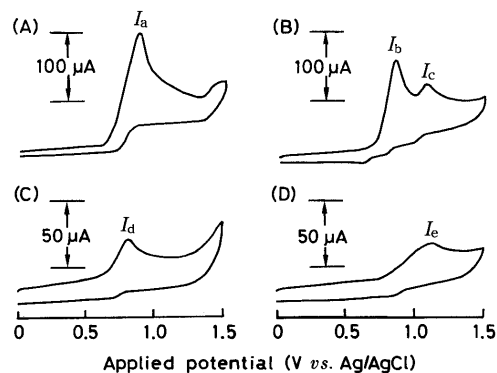


Fig. 1. Cyclic Voltammograms of (A) 5 mM **1** in Methanol, (B) 5 mM **1** in Acetonitrile, (C) 1.3 mM **6** in Methanol and (D) 1.3 mM **6** in Acetonitrile

All solutions contained 50 mM sodium perchlorate as the supporting electrolyte. Scan rate, 0.10 V/s; working electrode, glassy carbon; temperature, 25 °C.

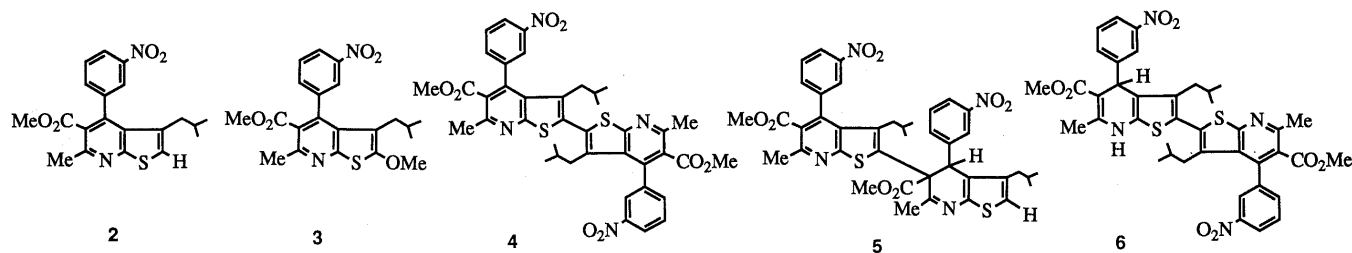


Chart 2. Chemical Structures of Products 2–6 Formed by Controlled Potential Electrolysis in Methanol or in Acetonitrile

TABLE I. Results of Electrolysis of **1**^{a, b}

Solvent ^{c)}	Yield (%) ^{d)}					<i>n</i> value ^{e)}	
	2	3	4	5	Total	Found	Calcd. ^{f)}
Methanol	73.9	11.9	7.9	5.8	99.5	2.34	2.31
Acetonitrile	12.2	nd ^{g)}	85.3	1.2	98.7	2.83	2.83

a) All data are the mean values for three experiments. b) Ca. 2.5 mM **1** was electrolyzed in an undivided cell at room temperature. c) Solvent containing 50 mM sodium perchlorate as a supporting electrolyte. d) Based on substrate. e) Electricity passed per molecule of substrate. f) Based on yield and electricity required for products. g) nd = not detected.

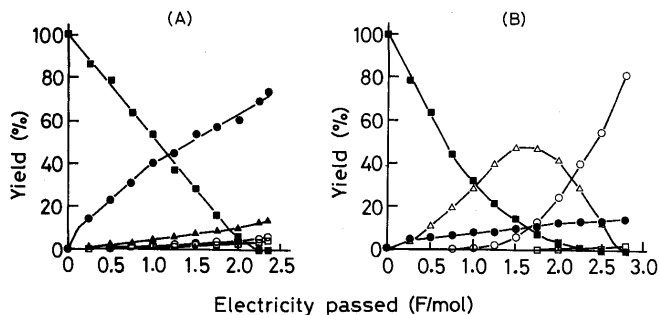


Fig. 2. Change of Product Distribution with Quantity of Electricity Passed in the Controlled Potential Electrolysis of **1** (A) in Methanol and (B) in Acetonitrile

Both solutions contained 50 mM sodium perchlorate. Symbols: ■, **1**; ●, **2**; ▲, **3**; ○, **4**; □, **5**; △, **6**.

2,2'-dimer of **1** and **2** (Chart 2).

The results of the CPE are summarized in Table I. Since the total product yields were about 100%, only small amounts, at most, of other products can be formed by CPE of **1** in methanol or acetonitrile. The final quantity of electricity passed was ca. 2.3 F/mol in methanol and ca. 2.8 F/mol in acetonitrile.

No significant difference was observed between the results of the electrolysis of **1** using a divided cell and those using an undivided cell. Therefore, undivided cells were used in this study.

Change in Amounts of 1 and 2–6 during CPE The change in the product distribution with the quantity of electricity passed during the CPE was determined by HPLC. In methanol, **2**, **3**, **4**, and **5** increased monotonously with an increase in the quantity of electricity passed, with a corresponding decrease of **1** (Fig. 2(A)). However, in acetonitrile, **2** and **6** first increased with an increase in the quantity of electricity passed and with a decrease of **1**, then **4** increased with a decrease of **6**, and finally, **5** appeared as a minor product (Fig. 2(B)).

Electrochemistry of 6 Since **6** was presumed to be an

intermediate, its electrochemistry was studied further. Cyclic voltammograms of **6** in methanol and acetonitrile are included in Fig. 1. In methanol (Fig. 1(C)), one anodic peak (I_d) appeared at +0.82 V, which was 0.03 V less positive than the potential of the anodic peak I_a for **1**, showing that **6** is oxidized slightly more easily than **1**. In acetonitrile (Fig. 1(D)), one anodic peak (I_e) appeared at +1.14 V, which was 0.29 V more positive than the potential of the first anodic peak I_b for **1**, showing that **6** can not be easily oxidized at the potential (+0.85 V) applied for the oxidation of **1**, but **6**, can be finally oxidized after prolonged electrolysis. The second anodic peak of **1** in acetonitrile (I_c) may be due to the oxidation of **6**. Because of these differences of the peak potentials from the applied potentials for the electrolysis of **1**, the formation of **6** is observed clearly in acetonitrile but not in methanol.

CPE of **6** was carried out in both methanol and acetonitrile at +0.85 V, which was the same potential as that for the electrolysis of **1**. Compound **4** was formed quantitatively in both solvents with a coulometric *n*-value of about 2 (2.03 in methanol; 1.94 in acetonitrile).

CPE of an Optical Isomer of 1 Substrate **1** is a racemate of optical isomers which are due to an asymmetric carbon at the 4-position. Of the CPE products, **5** has two asymmetric carbons at the 4'- and 5'-position, and **6** has one at the 4'-position. In order to investigate whether these products retain optical activity, electrolysis of **1-dex** (*dextro*-isomer of **1**, $[\alpha]_D^{20}$ (1%, ethanol) = +279.5 ± 3.2°) was carried out at +0.85 V in both methanol and acetonitrile. Spectral data, except for the optical rotations of **5** and **6** formed by CPE of **1-dex**, agreed with those of the corresponding products formed by CPE of **1**. Thus, products **5** and **6** formed by CPE of **1-dex** had optical activity ($[\alpha]_D^{20}$ (1%, ethanol) = -389.3 ± 4.5° and +347.1 ± 3.9°, respectively), suggesting that racemization did not occur during the formation of **5** and **6** from **1-dex**.

CPE of 2-tert-Butoxycarbonyl Derivative of 1 The carbon atom at the 2-position of **1** takes part in the formation of all CPE products except for **2**. In order to study the effect of a substituent at the 2-position on product formation, CPE of 2-*tert*-butoxycarbonyl derivative of **1** (compound **7**) was carried out in both methanol and acetonitrile at +1.00 and +1.20 V, respectively. These potentials were slightly less positive than the voltammetric peak potentials of **7** (+1.07 and +1.26 V, respectively). A pyridine-type derivative **8**, the 2-*tert*-butoxycarbonyl derivative of **2**, was formed quantitatively with a coulometric *n*-value of about 2 (2.03 in methanol; 1.96 in acetonitrile). These results suggested that the substituted carbon atom at the 2-position of **8** is not likely to take part in the product-forming steps.

In Situ Electrolysis-ESR *In situ* electrolysis of **1** in acetonitrile at -10°C gave an ESR spectrum with the following parameters: $g=2.0066$, $a(4\text{-H})=6.00$, $a(7\text{-N})=3.90$, $a(7\text{-H})=3.90$ and $a(6\text{-CCH}_3)=2.05\text{ G}$ (Fig. 3). Electrolysis in methanol gave no ESR spectrum. In order to gain a better understanding of the spectrum, **1** containing ^2H at the 4-position ($[4\text{-}^2\text{H}]\text{-1}$) was also electrolyzed *in situ*. As shown in Fig. 4, the ESR spectrum of $[4\text{-}^2\text{H}]\text{-1}$ was distinct from that of **1**, although the determination of the hyperfine coupling constants (hfc) of $[4\text{-}^2\text{H}]\text{-1}$ was difficult owing to the poor resolution of the spectrum. The total width of the spectrum of $[4\text{-}^2\text{H}]\text{-1}$, 18.3 G, was close to 18.8 G, which was calculated based on the assumption that the largest hfc (6.00 G) was reduced according to the ratio of atomic hfc $a(^2\text{H})/a(^1\text{H})$, 0.154,⁸⁾ and the other hfc of $[4\text{-}^2\text{H}]\text{-1}$ was not significantly different from those of **1**. Therefore, the largest hfc (6.00 G) of **1** can be ascribed to the hydrogen at the 4-position but not that at the 2-position.

The above results suggest that the radical species observed here is probably the radical cation **9** (Chart 3) generated by initial one-electron transfer from **1**. Although

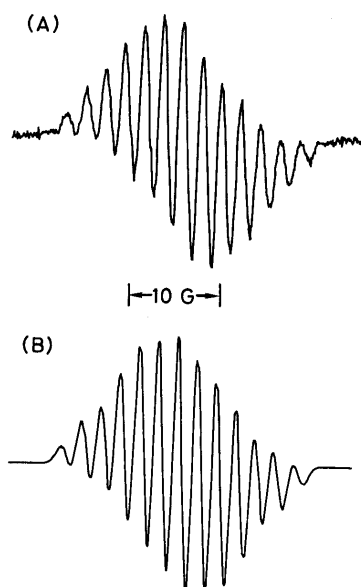


Fig. 3. ESR Spectrum of an *in Situ* Electrolyzed Solution of (A) 10 mM **1** in Deoxygenated Acetonitrile Containing 50 mM Sodium Perchlorate at -10°C and (B) Computer-Simulated Spectrum Using the Coupling Constant Given in the Text and a Linewidth of 1.4 G (Gaussian Lineshape)

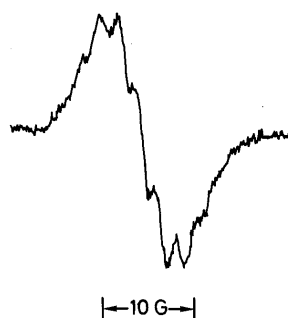


Fig. 4. ESR Spectrum of an *in Situ* Electrolyzed Solution of 10 mM $[4\text{-}^2\text{H}]\text{-1}$ in Deoxygenated Acetonitrile Containing 50 mM Sodium Perchlorate at -10°C

there is low electron spin density at the 2-position, some reactions did occur at the 2-position: 2-methoxy-substitution, 2,2'- and 2,5'-coupling. The reason is not clear, but steric factors probably are involved, *i.e.*, positions other than the 2- and 5-positions are sterically hindered. The resonance structure of the radical cation with an electron localized at the 2-position is possible (Chart 3, Eq. 1), and therefore, at the present stage it is difficult to rule out the possibility that some other radical species gave the ESR spectra.

UV-VIS Spectral Studies In order to obtain further information on the mechanism, the progress of the electrolysis was monitored by recording UV-VIS spectra in the 220–500 nm range at different intervals. The solution of **1** in methanol exhibited two absorption maxima at 249 and 350 nm. When a potential was applied at $+0.85\text{ V vs. Ag}$, the band at λ_{max} (350 nm) decreased and the absorption in the 230–310 nm region increased. The spectrum at the end of the electrolysis was similar to that of **2** and/or **3**. These results agreed with those expected from the HPLC analysis of the sample solution during the electrolysis of **1** in methanol.

In acetonitrile, the solution of **1** also exhibited two absorption maxima at 245 and 344 nm (Fig. 5, curve 1). During the electrolysis, the band at λ_{max} (344 nm) decreased and the absorption in the 230–320 nm region increased, while the absorption in the 410–500 nm region first increased (Fig. 5, curve 2–4) and then decreased (Fig. 5, curves 5 and 6). The spectrum at the end of the electrolysis was similar to that of **4**. Since all of the electrolysis products (**2**–**5**) and the intermediate (**6**) have no absorption in the 410–500 nm region, the increase of absorption followed by a decrease in the longer wavelength region indicated the presence of another intermediate species X with a more extensive π conjugation.

In order to reach a better understanding of the intermediate X, the spectral change of **6** was studied. In acetonitrile, the solution of **6** exhibited two absorption maxima at 249 and 372 nm. During the electrolysis, the band at λ_{max} (372 nm) decreased and the absorption in the 230–340 nm region increased. The spectrum at the end of the electrolysis coincided with that of **4**. Because little spectral change was observed in the 410–500 nm region,

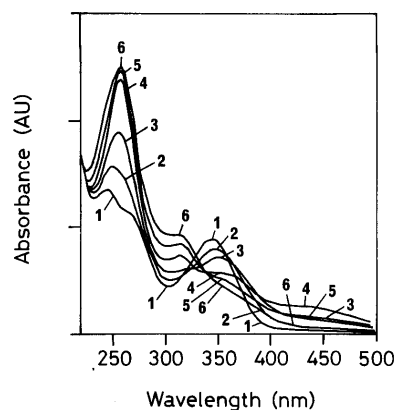


Fig. 5. UV-VIS Spectral Changes of 0.01 mM **1** in Acetonitrile Containing 50 mM Sodium Perchlorate during Electrolysis: before (1) and after Electrolysis for 1, 3, 11, 23, and 120 min (2–6)

Applied potential, $+0.85\text{ V vs. Ag wire}$.

the intermediate X is not produced during the formation process of **4** from **6**.

The change of the spectrum of the intermediate X formed by the electrolysis of **1** in acetonitrile was studied. First, when the absorption at 440 nm reached maximum, the electrolysis was stopped and the spectrum was recorded. Second, after the solution had been left at 25°C with stirring for 60 min, the spectrum was again recorded, but did not differ from the previously recorded spectrum. Since the ESR spectrum of the radical cation **9** was very

weak at 25°C and the lifetime of **9** was not so long, the intermediate X is clearly not the radical cation **9**. Finally, a small amount of methanol (*ca.* 150 μ l) was added to the solution, and a decrease of the absorption in the 410–500 nm region was observed immediately. The spectrum was similar to that of **6**. These results indicate that the intermediate X participates during the formation of **6** from **9**. The intermediate X is presumed to be a symmetrical dimer dication (Chart 3, **16**). The formation of similar dimer dications was observed in the electrolysis of

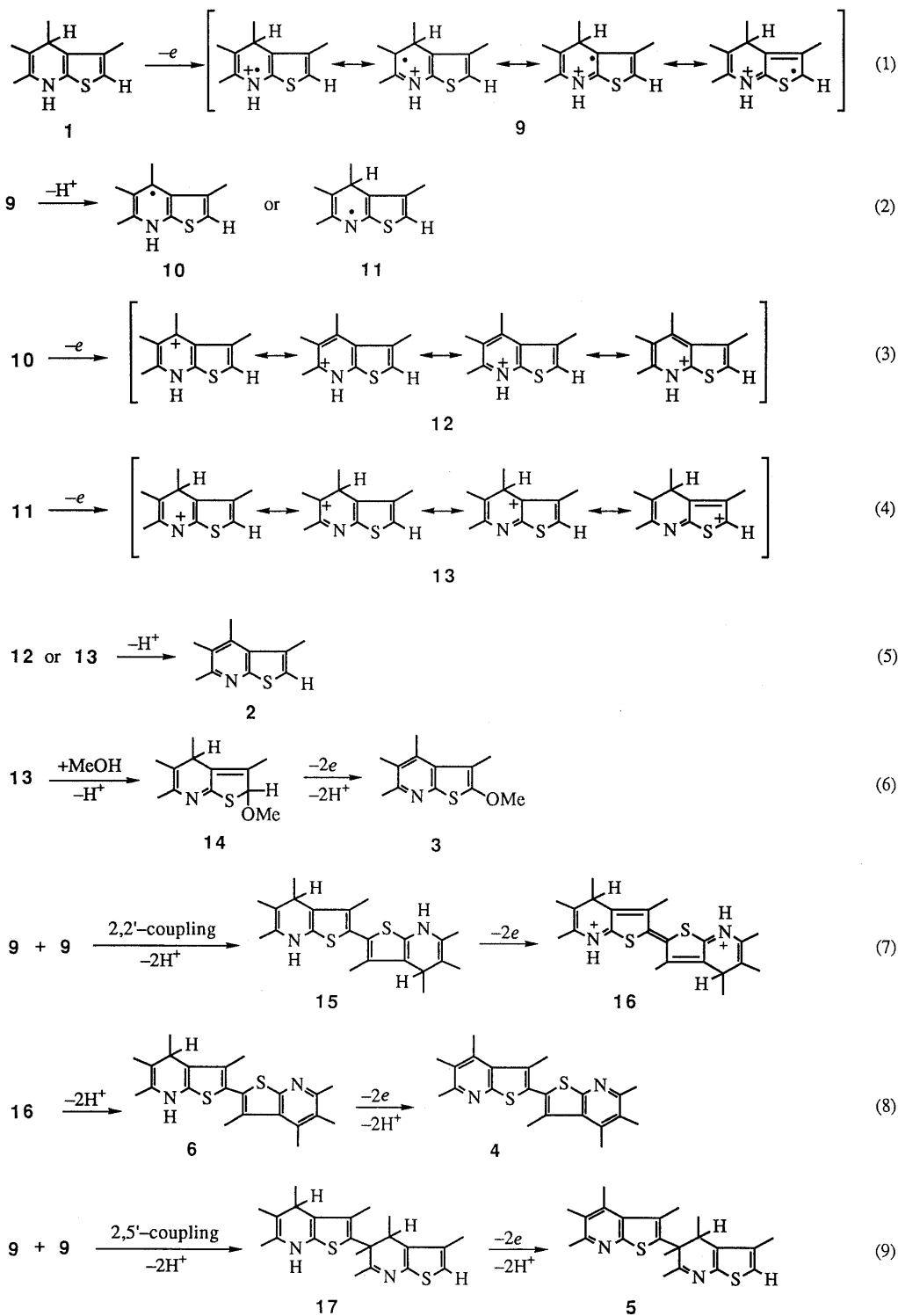


Chart 3. Proposed Mechanism for the Electrochemical Oxidation of **1**

N-allyl[1]benzothieno[3,2-*b*]indole and [1]benzothieno[3,2-*b*]indole.⁹⁾ It is also presumed that the methanol added to the solution participated in the deprotonation from **16** and that **6** is irreversibly formed as a result.

Proposed Mechanism From the results described so far, the following mechanism can be proposed for the electrochemical oxidation of **1** (Chart 3). For simplicity of expression, the substituents having no important role in the mechanism have been omitted.

The initial step in the reaction seems to be a one-electron oxidation of **1** to give a radical cation species **9** (Eq. 1). As shown in Eq. 2, the loss of a proton from **9** will give **10** and/or **11**. One-electron oxidation of **10** will give a cation species **12** (Eq. 3) and that of **11** will give another cation species **13** (Eq. 4). The following loss of a proton from **12** and/or **13** will give **2** (Eq. 5). The process in Eqs. 1–5 is similar to that proposed for the electrochemical oxidation of dihydropyridines to form the corresponding pyridines.^{4a)}

The methoxy-substituted product **3** can be formed in methanol as shown in Eq. 6: a methanol molecule is added to **13** at the 2-position and a proton splits off to form an intermediate **14**, then the methoxy-substituted pyridine derivative **3** is formed by further two-electron, two-proton oxidation.

The 2,2'-dimers **4** and **6** can be formed as follows: as shown in Eq. 7, two radical cations **9** couple with each other and two protons split off to give **15**; further two-electron oxidation generates a dimer dication **16**, which exhibits absorption in the 410–500 nm region (Fig. 5, curves 3–5); the isolated intermediate **6** is formed by subsequent two-proton elimination from **16** and the dihydropyridine moiety in **6** is oxidized to form **4** (Eq. 8). Compound **5** can be formed *via* **17** by a similar process with **4** (Eq. 9).

A proton probably splits off from **9** more easily in methanol than in acetonitrile to give the neutral radicals **10** and/or **11**. The latter radicals will be oxidized more easily than the former radical cation **9** to give immediately the corresponding cations **12** and/or **13**. That is why no ESR spectrum was seen in methanol. Also a proton probably splits off from these cations **12** and/or **13** more easily in methanol to give the pyridine product **2**. Therefore, compound **2** was generated preferentially in methanol (see Table I). In contrast, the dimers were the main products in acetonitrile. Considering with the above discussion, the radical cation coupling process (Eqs. 7 and 9) is more likely to occur than the neutral radical coupling process. In other words, if the dimerization occurred between the neutral radicals the main product in methanol would also be the dimers, because there seems to be no difference in the stability of these radicals between in methanol and in acetonitrile. The result of CPE of *1-dex*, that no racemization is observed in the course of the formation of **5** and **6**, also support the radical cation coupling process.

According to the proposed mechanism, the electricity required per molecule to form **2**, **3**, **4**, **5** and **6** can be calculated as 2, 4, 3, 2 and 2F/mol, respectively. The calculated quantities of electricity needed to obtain the products agree with the measured values (see Table I). These results show that the proposed mechanism is reasonable for the electrochemical oxidation of **1**.

Although the i_p/C value for I_b in acetonitrile was smaller than that for I_a in methanol (Fig. 1), the final quantity of electricity passed for CPE of **1** in acetonitrile was more than that in methanol. The reason is presumed to be that the chemical processes after the initial electron transfer in acetonitrile are slower than those in methanol in the time-scale of the cyclic voltammetry.

Conclusion

Study of the electrochemical oxidation of **1** has led to the proposal of a mechanism that can explain the observed coulometric and spectral behavior as well as the products formed. The primary step in the electrochemical oxidation of **1** is a one-electron oxidation to give a radical cation **9**. Electrolysis of **1** gave four final products: the corresponding pyridine **2**, the 2-methoxy-substituted derivative **3**, the 2,2'-dimer **4** and the 2,5'-dimer **5**.

Experimental

General All melting points are uncorrected. UV-VIS spectra were recorded on a Hitachi U-3200 spectrophotometer. Infrared (IR) spectra were obtained with a JASCO A-702 spectrophotometer. Mass spectra (MS) were recorded on a Hitachi M-68 or M-90 mass spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. Proton nuclear magnetic resonance (¹H-NMR) and carbon-13 nuclear magnetic resonance (¹³C-NMR) spectra were taken with tetramethylsilane as an internal standard on a Varian XL-200 or VXR-200 spectrometer in chloroform-*d*₁ (CDCl₃) or hexadeuterodimethylsulfoxide (DMSO-*d*₆). The chemical shifts and coupling constants (*J*) are given in δ and Hz, respectively, and the abbreviations of signal patterns are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet; br, broad. The carbon numbers for the assignment of ¹³C-NMR spectra were based on those for **1** in Chart 1.

Materials Compounds **1**, *1-dex* (*dextro*-isomer of **1**), [4-²H]-**1** and 7 (*2-tert*-butoxycarbonyl derivative of **1**) were synthesized at the Shionogi Research Laboratories (Osaka, Japan).¹⁾ Nifedipine was purchased and purified according to the literature.^{7b)} Data for **1**, *1-dex*, [4-²H]-**1** and 7 are given below.

RS-(±)-Methyl 4,7-Dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (1**)** Yellow prisms, mp 189–191 °C (from ethanol), $[\alpha]_D^{20}$: $-1.3 \pm 0.4^\circ$ ($c=0.990$, ethanol). *Anal.* Calcd for C₂₀H₂₂N₂O₄S: C, 62.16; H, 5.74; N, 7.25; S, 8.30. Found: C, 62.06; H, 5.77; N, 7.30; S, 8.10. MS *m/z*: 386 (M⁺). IR (KBr): 3320 (NH), 1630 (C=O), 1345 (NO₂) cm⁻¹. UV $\lambda_{\text{max}}^{\text{methanol}}$ nm (ϵ): 350 (9400), 249 (1400). ¹H-NMR (CDCl₃) δ : 0.72 (3H, d, $J=6.5$ Hz, CH-CH₃), 0.88 (3H, d, $J=6.5$ Hz, CH-CH₃), 1.60 (1H, m, CH₂-CH-CH₃), 2.04 (1H, dd, $J=14.4, 6.5$ Hz, CH₂-CH), 2.10 (1H, dd, $J=14.4, 6.5$ Hz, CH₂-CH), 2.40 (3H, s, CH₃), 3.66 (3H, s, OCH₃), 5.26 (1H, s, CH), 6.24 (1H, s, =CH), 6.41 (1H, brs, NH), 7.37 (1H, t, $J=8.0$ Hz, Ar-H), 7.58 (1H, dt, $J=8.0, 2.1$ Hz, Ar-H), 7.98 (1H, dt, $J=8.0, 2.1$ Hz, Ar-H), 8.05 (1H, t, $J=2.1$ Hz, Ar-H). ¹³C-NMR (CDCl₃) δ : 21.07 (q, C(16)), 22.11 (q, C(12)), 22.66 (q, C(13)), 28.19 (d, C(11)), 38.09 (t, C(10)), 40.97 (d, C(4)), 50.88 (q, C(15)), 99.58 (s, C(9)), 109.73 (d, C(2)), 119.69 (s, C(5)), 121.28 (d, C(18)), 123.08 (d, C(20)), 128.77 (d, C(21)), 134.29 (d, C(22)), 136.43 (s, C(17)), 138.81 (s, C(3)), 146.66 (s, C(6)), 148.29 (s, C(19)), 149.58 (s, C(8)), 168.27 (s, C(14)).

S-(+)-Methyl 4,7-Dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (*1-dex*) Yellow plates, mp 175–177 °C (from ethanol), $[\alpha]_D^{20}$: $+279.5 \pm 3.2^\circ$ ($c=1.006$, ethanol). *Anal.* Calcd for C₂₀H₂₂N₂O₄S: C, 62.16; H, 5.74; N, 7.25; S, 8.30. Found: C, 62.11; H, 5.71; N, 7.34; S, 8.41. Other spectral data are essentially the same as for **1**.

RS-(±)-Methyl [4-²H]-4,7-Dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate ([4-²H]-1**)** Yellow prisms, mp 190–192 °C (from ethanol). *Anal.* Calcd for C₂₀H₂₃N₂O₄S: C, 62.00; H, 5.98; N, 7.23; S, 8.28. Found: C, 61.89; H, 5.73; N, 7.07; S, 8.34. MS *m/z*: 387 (M⁺). [4-²H]-**1**/[4-¹H]-**1**=95/5. Other spectral data are essentially the same as for **1**.

RS-(±)-Methyl 2-*tert*-Butoxycarbonyl-4,7-dihydro-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (7**)** Yellow prisms,

mp 208–210 °C (from methanol). *Anal.* Calcd for $C_{22}H_{30}N_2O_6S$: C, 61.71; H, 6.21; N, 5.76; S, 6.59. Found: C, 61.59; H, 6.15; N, 5.69; S, 6.47. MS m/z : 486 (M^+). IR (KBr): 3250 (NH), 1690 (C=O), 1670 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{max}^{methanol}$ nm (ϵ): 370 (16900), 266 (16700), 217 (24100). 1H -NMR ($CDCl_3$) δ : 0.85 (3H, d, $J=6.6$ Hz, CH- CH_3), 0.94 (3H, d, $J=6.6$ Hz, CH- CH_3), 1.82 (1H, m, CH_2 -CH- CH_3), 1.52 (9H, s, C- CH_3), 2.12 (1H, dd, $J=12.9, 7.4$ Hz, CH_2 -CH), 2.41 (3H, s, CH_3), 2.92 (1H, dd, $J=12.9, 7.4$ Hz, CH_2 -CH), 3.69 (3H, s, OCH_3), 5.25 (1H, s, CH), 6.80 (1H, br s, NH), 7.40 (1H, t, $J=8.0$ Hz, Ar-H), 7.58 (1H, dt, $J=8.0, 1.5$ Hz, Ar-H), 7.99 (1H, m, Ar-H), 8.05 (1H, m, Ar-H). ^{13}C -NMR ($CDCl_3$) δ : 20.64 (q, C(16)), 22.24 (q, C(12)), 22.46 (q, C(13)), 28.37 (q, C(25, 26, 27)), 29.59 (d, C(11)), 36.03 (t, C(10)), 40.61 (s, C(4)), 51.10 (q, C(15)), 81.77 (s, C(24)), 100.78 (s, C(9)), 119.21 (s, C(5)), 121.53 (d, C(18)), 121.53 (s, C(2)), 123.20 (d, C(20)), 128.91 (d, C(21)), 134.12 (d, C(22)), 141.78 (s, C(17)), 146.54, 146.94 (s, C(3, 6)), 148.44 (s, C(19)), 149.05 (s, C(8)), 162.62 (s, C(23)), 167.99 (s, C(14)).

Chemicals All solvents were of HPLC grade and all reagents were of analytical grade. Methanol, ethanol and acetonitrile, used for the electrochemical studies, were purchased from Kanto Chemical (Tokyo, Japan) and dried over molecular sieves (3 Å, Merck, Darmstadt, F.R.G.) before use.

Cyclic Voltammetry A Model VMA-010 cyclic voltammetric analyzer (Yanagimoto, Kyoto, Japan) was used for cyclic voltammetric measurements, and a Model WX-1000 x - y recorder (Graphtec, Tokyo, Japan) was used to record cyclic i versus E curves. A glassy carbon disk of 3 mm diameter was used as a working electrode. The surface of the disk was polished to a mirror finish with alumina powder (0.05 μ m) on an acrylic resin plate before use. An Ag/AgCl electrode and a platinum wire were used as a reference and an auxiliary electrode, respectively. These electrodes were purchased from Yanagimoto. Cyclic voltammetry was performed with *ca.* 5 mm compound in methanol or acetonitrile containing 50 mM sodium perchlorate, or in ethanol containing saturated sodium perchlorate. The solution was stored in a 15-ml tube and covered with a PTFE cap through which the three electrodes were inserted. The cyclic voltammograms of the stationary solutions were obtained at 25 °C.

HPLC The HPLC system consisted of a Model L-5000 solvent delivery pump (Yanagimoto) a Model SPD-2A UV detector (Shimadzu). A Model CR-2AX integrator (Shimadzu) was used to calculate peak areas. For HPLC, a Nucleosil 100-Si column (5 μ m, internal diameter, 4.6 mm i.d.; length, 250 mm, Macherey-Nagel, Düren, F.R.G.) was used. Chromatography was performed at room temperature. A mixed solution of *n*-hexane-ethyl acetate (75:25, v/v) was used as the mobile phase at a constant flow rate of 1.0 ml/min. The mobile phase was filtered with a Type FR-20 membrane filter (0.2 μ m, Fuji Photo Film, Tokyo, Japan) and degassed under reduced pressure before use. The wavelength of the ultraviolet (UV) detector was set at 265 nm.

Preparative Thin-Layer Chromatography (PTLC) Normal-phase PTLC was performed on precoated Silica gel 60 F₂₅₄ plates (0.5 mm thick, Merck) with *n*-hexane-ethyl acetate (70:30, v/v) as the developing solvent. Reversed-phase PTLC was performed on precoated RP-18 F₂₅₄ s plates (0.25 mm thick, Merck) with acetonitrile as the developing solvent. Bands were visualized under UV (254 nm) irradiation.

In Situ Electrolysis-ESR The ESR spectrum was recorded on a JEOL JES-RE1X spectrometer with 100 kHz field modulation. The electrolysis cell used for internal generation of the radical cation was a quartz capillary (internal diameter, 1 mm i.d.; length, 100 mm) with a Pyrex reservoir (internal diameter, 30 mm i.d.; length, 25 mm) at the top. The cell was attached to the ESR spectrometer so that the central region of the capillary was located in the center of the ESR cavity. The temperature in the cavity was controlled by cold nitrogen gas. A platinum wire anode (0.3 mm i.d.), which was passed through and connected to a Teflon cap, was inserted into the capillary and a platinum wire cathode (0.3 mm i.d.) was placed in the reservoir. A solution of **1** (*ca.* 10 mM) in acetonitrile containing 50 mM sodium perchlorate in the capillary and the reservoir was deoxygenated in the reservoir by flushing with dry nitrogen gas before measurement. The solution was subjected to constant current electrolysis (20 μ A), which was performed with a Hokuto-Denko HA-151 potentiostat-galvanostat, and the ESR spectrum was monitored. During the electrolysis, nitrogen gas was passed over the solution. The g -value was determined by comparing the spectrum with that of Mn^{2+} ($g=1.981$ and 2.034). Computer simulation of the spectrum was carried out using a FACOM M730/10 computer system.

Spectral Studies The changes in the spectra in the 220–500 nm region during electrochemical oxidation of **1** and **6** were also monitored by using a Hitachi U-3200 spectrophotometer with a Hitachi SDR-10 tem-

perature controller. The reaction cell was a standard spectrophotometric cell of 10 mm light path. Controlled potential electrolysis for these studies was carried out with a Hokuto-Denko HA-151 potentiostat-galvanostat. A Pt gauze (80 mesh, 0.076 mm i.d.), a Pt wire (0.5 mm i.d.) and an Ag wire (0.5 mm i.d.) were used as working, counter and reference electrodes, respectively. The quantity of electricity consumed was measured with a Hokuto-Denko HF-201 coulombmeter. The electrolysis was generally performed with *ca.* 10 or 5 mm substrate in solvent containing 50 mM sodium perchlorate. The solution was stirred during the electrolysis.

Controlled Potential Electrolysis Controlled potential electrolysis was carried out with a Hokuto-Denko HA-151 potentiostat-galvanostat. The anode potential was set against an Ag/AgCl reference electrode through an agar bridge. The current was recorded with a Hitachi 056 y - t recorder and the quantity of electricity consumed was measured with a Hokuto-Denko HF-201 coulombmeter. The electrolysis was generally performed with *ca.* 2.6 mm substrate in 40 ml of solvent containing sodium perchlorate using an undivided cell with a glassy carbon plate electrode (*ca.* 20 cm^2 , GC-30, Tokai Carbon, Tokyo, Japan), a Pt wire (1 mm i.d.) counter electrode and an Ag/AgCl reference electrode.

Isolation and Analysis of Products After the electrolysis, the electrolytic solution was concentrated under reduced pressure below 25 °C. The residue was extracted repeatedly with methylene chloride and the combined extracts were dried over anhydrous sodium sulfate. After concentration, the residue was chromatographed repeatedly on normal- and reversed-phase PTLC until the purity of each product was satisfactory. Data for characterization of the principal products isolated are given below. Carbons were numbered for the assignment of ^{13}C -NMR according to the basic numbering for **1**. The asterisks (*) in the data of 1H - and ^{13}C -NMR for **4**, **5** and **6** indicate signals that were split into two. It seems reasonable to assume that the splitting was caused by the presence of rotational isomers due to the restricted rotation mainly around the C(2)–C(2') bond or the C(2)–C(5') bond, because each pair of split signals was observed as a single signal in the 1H -NMR spectra at 95–120 °C in DMSO- d_6 .

Methyl 3-Isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (2) White prisms, mp 89.5–90.5 °C (from isopropylether). *Anal.* Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29; S, 8.34. Found: C, 62.19; H, 5.25; N, 7.51; S, 8.36. MS m/z : 384 (M^+). IR (KBr): 1720 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{max}^{methanol}$ nm (ϵ): 247 (37200). 1H -NMR ($CDCl_3$) δ : 0.51 (3H, d, $J=6.5$ Hz, CH- CH_3), 0.52 (3H, d, $J=6.5$ Hz, CH- CH_3), 1.25 (1H, m, CH_2 -CH- CH_3), 1.94 (2H, d, $J=6.5$ Hz, CH_2 -CH), 2.69 (3H, s, CH_3), 3.55 (3H, s, OCH_3), 7.14 (1H, s, =CH), 7.64 (1H, t, $J=7.5$ Hz, Ar-H), 7.68 (1H, dt, $J=7.5, 2.0$ Hz, Ar-H), 8.22 (1H, m, Ar-H), 8.32 (1H, dt, $J=7.5, 2.0$ Hz, Ar-H). ^{13}C -NMR ($CDCl_3$) δ : 21.89 (q, C(12)), 22.02 (q, C(13)), 22.87 (q, C(16)), 28.34 (d, C(11)), 40.02 (t, C(10)), 52.29 (q, C(15)), 123.32 (d, C(20)), 124.18 (d, C(2)), 124.27 (d, C(18)), 126.47 (s, C(5)), 126.51 (s, C(9)), 128.85 (d, C(21)), 134.34 (s, C(3)), 135.20 (d, C(22)), 138.01 (s, C(17)), 140.23 (s, C(4)), 147.50 (s, C(19)), 151.27 (s, C(6)), 163.70 (s, C(8)), 168.54 (s, C(14)).

Methyl 3-Isobutyl-2-methoxy-6-methyl-4-(3-nitrophenyl)thieno[2,3-*b*]pyridine-5-carboxylate (3) Pale yellow prisms, mp 98–99 °C (from *n*-hexane). *Anal.* Calcd for $C_{21}H_{22}N_2O_5S$: C, 60.85; H, 5.35; N, 6.76; S, 7.74. Found: C, 61.07; H, 5.40; N, 6.88; S, 7.61. MS m/z : 414 (M^+). IR (KBr): 1725 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{max}^{methanol}$ nm (ϵ): 257 (32100). 1H -NMR ($CDCl_3$) δ : 0.43 (3H, d, $J=6.5$ Hz, CH- CH_3), 0.44 (3H, d, $J=6.5$ Hz, CH- CH_3), 1.66 (1H, m, CH_2 -CH- CH_3), 1.88 (2H, d, $J=6.5$ Hz, CH_2 -CH), 2.62 (3H, s, CH_3), 3.52 (3H, s, OCH_3), 3.99 (3H, s, =CO CH_3), 7.60 (1H, t, $J=7.5$ Hz, Ar-H), 7.65 (1H, dt, $J=7.5, 2.0$ Hz, Ar-H), 8.20 (1H, m, Ar-H), 8.29 (1H, dt, $J=7.5, 2.0$ Hz, Ar-H). ^{13}C -NMR ($CDCl_3$) δ : 21.67 (q, C(12)), 21.88 (q, C(13)), 22.52 (q, C(16)), 29.06 (d, C(11)), 33.70 (t, C(10)), 52.18 (q, C(15)), 61.32 (q, C(23)), 113.01 (s, C(3)), 123.14 (d, C(20)), 124.49 (d, C(18)), 127.23 (s, C(9)), 127.61 (s, C(5)), 128.67 (d, C(21)), 135.44 (d, C(22)), 137.94 (s, C(4)), 138.18 (s, C(17)), 147.36 (s, C(19)), 148.51 (s, C(6)), 155.75 (s, C(8)), 160.08 (s, C(2)), 168.62 (s, C(14)).

Dimethyl 3,3'-Diisobutyl-6,6'-dimethyl-4,4'-di(3-nitrophenyl)[2,2'-bithieno[2,3-*b*]pyridine]-5,5'-dicarboxylate (4) White needles, mp 205–207 °C (from methanol). *Anal.* Calcd for $C_{40}H_{38}N_4O_8S_2$: C, 62.65; H, 4.99; N, 7.31; S, 8.36. Found: C, 62.41; H, 5.10; N, 7.44; S, 8.12. SIMS m/z : 767 ($M^+ + 1$). IR (KBr): 1730 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{max}^{methanol}$ nm (ϵ): 317 (21900), 247 (53700). 1H -NMR ($CDCl_3$) δ : 0.28 (6H, d, $J=6.5$ Hz, CH- CH_3), *0.286/0.287 (6H, d, $J=6.5$ Hz, CH- CH_3), 1.11 (2H, m, CH_2 -CH- CH_3), *1.98/2.00 (4H, dd, $J=15.0, 6.5$ Hz, CH_2 -CH), *2.691/2.693 (6H, s, CH_3), *3.56/3.57 (6H, s, OCH_3), 7.68 (2H, t,

$J=7.5$ Hz, Ar-H), 7.72 (2H, m, Ar-H), 8.23 (2H, m, Ar-H), 8.34 (2H, dt, $J=7.5, 2.0$ Hz, Ar-H). $^{13}\text{C-NMR}$ (CDCl_3) δ : *21.79/21.89 (q, C(12, 12')), *22.12/22.17 (q, C(13, 13')), 22.91 (q, C(16, 16')), 29.36 (d, C(11)), 37.44 (t, C(10)), 52.42 (q, C(15, 15')), 123.49 (d, C(20, 20')), *124.43/124.50 (d, C(18, 18')), *126.91/126.97 (s, C(9, 9')), 127.41 (s, C(5, 5')), *129.05/129.15 (d, C(21, 21')), 132.01 (s, C(2, 2')), *134.05/134.11 (s, C(3, 3')), *135.13/135.27 (d, C(22, 22')), 137.72 (s, C(17, 17')), 140.63 (s, C(4, 4')), 147.56 (s, C(19, 19')), 152.12 (s, C(6, 6')), 168.28 (s, C(8, 8')), 168.37 (s, C(14, 14')).

Dimethyl 4',5'-Dihydro-3,3'-diisobutyl-6,6'-dimethyl-4,4'-di(3-nitrophenyl)[2,5'-bithieno[2,3-b]pyridine]-5,5'-dicarboxylate (5) Pale yellow amorphous powder, mp 123–126°C (from ethanol). *Anal.* Calcd for $\text{C}_{40}\text{H}_{40}\text{N}_4\text{O}_8\text{S}_2$: C, 62.48; H, 5.24; N, 7.29; S, 8.34. Found: C, 62.30; H, 5.21; N, 7.24; S, 8.36. MS m/z : 768 (M^+). IR (KBr): 1735 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{\text{max}}^{\text{methanol}}$ nm (ϵ): 254 (45400). $^1\text{H-NMR}$ (CDCl_3) δ : *0.23/0.25 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.28/0.31 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.59/0.63 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.70/0.72 (3H, d, $J=6.5$ Hz, CH-CH_3), 1.25 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.45 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), *1.97/2.10 (2H, d, $J=7.0$ Hz, $\text{CH}_2\text{-CH}$), 2.08 (2H, m, $\text{CH}_2\text{-CH}$), *2.32/2.40 (3H, s, CH_3), 2.65 (3H, s, CH_3), *3.44/3.49 (3H, s, OCH_3), *3.57/3.58 (3H, s, OCH_3), *4.83/4.88 (1H, s, CH), *6.79/6.80 (1H, s, =CH), 7.33 (1H, m, Ar-H), 7.45 (1H, t, $J=7.5$ Hz, Ar-H), 7.63 (1H, t, $J=7.5$ Hz, Ar-H), 7.67 (1H, m, Ar-H), 7.95 (1H, m, Ar-H), 8.13 (1H, m, Ar-H), 8.20 (1H, m, Ar-H), 8.31 (1H, m, Ar-H). $^{13}\text{C-NMR}$ (CDCl_3) δ : 21.25, *22.11/22.30, *21.70/22.50, 22.42 (q, C(12, 12', 13, 13')), 22.79 (q, C(16)), *26.07/26.78, 27.82 (d, C(11, 11')), *26.07/26.78 (q, C(16')), 37.66, *38.13/38.28 (t, C(10, 10')), *50.49/50.65 (d, C(4')), 52.70, 52.90 (q, C(15, 15')), *58.76/58.82 (s, C(5')), *120.09/120.16 (d, C(2')), *122.41/122.80 (s, C(9')), *122.97/123.12, 123.42 (d, C(18, 18')), *123.97/124.09, *124.48/124.61 (d, C(20, 20')), *126.29/126.64 (s, C(9)), *127.04/127.09 (s, C(5)), 129.04, *129.46/129.55 (d, C(21, 21')), *133.10/133.54 (s, C(3)), *135.08/135.20, *135.24/135.41 (d, C(22, 22')), *137.89/138.05, *138.28/138.32 (s, C(17, 17')), *138.63/138.98 (s, C(2)), 139.85 (s, C(3')), 140.40 (s, C(4)), *147.55/147.55, *148.02/148.08 (s, C(19, 19')), *147.63/148.02 (s, C(6')), *152.17/152.22 (s, C(6)), *160.02/160.58, *160.97/161.21 (s, C(8, 8')), 168.74, *169.85/169.90 (s, C(14, 14')).

Dimethyl 4',7'-Dihydro-3,3'-diisobutyl-6,6'-dimethyl-4,4'-di(3-nitrophenyl)[2,2'-bithieno[2,3-b]pyridine]-5,5'-dicarboxylate (6) Yellow amorphous powder, mp 145–148°C (crude). *Anal.* Calcd for $\text{C}_{40}\text{H}_{40}\text{N}_4\text{O}_8\text{S}_2$: C, 62.48; H, 5.24; N, 7.29; S, 8.34. Found: C, 62.25; H, 5.34; N, 7.14; S, 8.12. MS m/z : 768 (M^+). IR (CHCl_3): 3440 (N-H), 1730 (C=O), 1350 (NO_2) cm^{-1} . UV $\lambda_{\text{max}}^{\text{methanol}}$ nm (ϵ): 372 (15800), 249 (46800). $^1\text{H-NMR}$ (CDCl_3) δ : *0.08/0.09 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.19/0.28 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.61/0.62 (3H, d, $J=6.5$ Hz, CH-CH_3), *0.78/0.79 (3H, d, $J=6.5$ Hz, CH-CH_3), 0.97 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.65 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.80 (2H, m, $\text{CH}_2\text{-CH}$), 1.97 (2H, m, $\text{CH}_2\text{-CH}$), 2.40 (3H, s, CH_3), 2.68 (3H, s, CH_3), *3.54/3.55 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 5.32 (1H, s, CH), 6.44 (1H, br s, NH), 7.38 (1H, m, Ar-H), 7.45 (1H, m, Ar-H), 7.63 (1H, m, Ar-H), 7.67 (1H, m, Ar-H), 8.01 (1H, m, Ar-H), 8.03 (1H, m, Ar-H), 8.20 (1H, m, Ar-H), 8.30 (1H, m, Ar-H). $^{13}\text{C-NMR}$ (CDCl_3) δ : 20.91 (q, C(16')), *21.66/21.78, 22.10, 22.11, 23.00 (q, C(12, 12', 13, 13')), *22.81/22.89 (q, C(16)), *28.57/28.62 (d, C(11')), 29.09 (d, C(11)), 36.92 (t, C(10')), 37.10 (t, C(10)), *40.85/40.91 (d, C(4')), 50.99 (d, C(15')), 52.40 (q, C(15)), 99.97 (s, C(9')), *118.12/118.20 (s, C(2')), 119.95 (s, C(5')), *121.41/121.49, *124.43/124.51 (d, C(18, 18')), 123.38, 123.39 (d, C(20, 20')), *127.18/127.16 (s, C(9)), *127.32/127.46 (s, C(5)), 128.87, 129.01 (d, C(21, 21')), *132.62/132.70 (s, C(2)), *133.55/133.75 (s, C(3)), *134.16/134.25, *135.16/135.29 (d, C(22, 22')), 137.87, *138.47/138.51 (s, C(17, 17')), *138.91/138.99 (s, C(3')), 140.20 (s, C(4)), *146.16/146.21 (s, C(6')), *147.08/147.53, *148.27/148.37 (s, C(19, 19')), *149.12/149.20 (s, C(8')),

151.52 (s, C(6)), 162.71 (s, C(8)), 168.13 (s, C(14')), 168.54 (s, C(14)).

Methyl 2-tert-Butoxycarbonyl-3-isobutyl-6-methyl-4-(3-nitrophenyl)thieno[2,3-b]pyridine-5-carboxylate (8) White plates, mp 122–124°C (from methanol). *Anal.* Calcd for $\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_6\text{S}$: C, 61.97; H, 5.82; N, 5.78; S, 6.62. Found: C, 61.85; H, 5.74; N, 5.75; S, 6.52. MS m/z : 484 (M^+). IR (CHCl_3): 1730 (C=O), 1355 (NO_2) cm^{-1} . UV $\lambda_{\text{max}}^{\text{methanol}}$ nm (ϵ): 303 (13400), 256 (36600), 205 (30600). $^1\text{H-NMR}$ (CDCl_3) δ : 0.44 (3H, d, $J=6.5$ Hz, CH-CH_3), 0.45 (3H, d, $J=6.5$ Hz, CH-CH_3), 1.22 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.59 (9H, s, C-CH_3), 2.58 (2H, d, $J=6.5$ Hz, $\text{CH}_2\text{-CH}$), 2.69 (3H, s, CH_3), 3.54 (3H, s, CH_3), 7.66 (1H, m, Ar-H), 7.69 (1H, m, Ar-H), 8.25 (1H, m, Ar-H), 8.35 (1H, m, Ar-H). $^{13}\text{C-NMR}$ (CDCl_3) δ : 21.46 (q, C(12)), 21.56 (q, C(13)), 23.10 (q, C(16)), 28.15 (q, C(25, 26, 27)), 30.24 (d, C(11)), 35.13 (t, C(10)), 52.37 (q, C(15)), 83.02 (s, C(24)), 123.52 (d, C(20)), 124.26 (d, C(18)), 127.28 (s, C(9)), 127.52 (s, C(5)), 128.97 (d, C(21)), 130.97 (s, C(2)), 135.21 (d, C(22)), 137.49 (s, C(3)), 141.75 (s, C(4)), 142.00 (s, C(17)), 147.53 (s, C(19)), 153.99 (s, C(6)), 162.14 (s, C(8)), 162.49 (s, C(23)), 168.19 (s, C(14)).

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