Synthesis of Dihydrothieno[2,3-*b*]pyridines Based on Titanium(IV) Chloride-Mediated Michael Reactions of 2-Amino-4,5-dihydro-3-thiophenecarbonitriles with α,β-Unsaturated Ketones

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2-Amino-4,5-dihydro-3-thiophenecarbonitriles **1a-c** reacted with α,β-unsaturated ketones (*e.g.* methyl vinyl ketone **2** and benzalacetone **3**) in the presence of titanium(IV) chloride to give the corresponding Michael adducts **4a-c** and **5a-c**. Thermal treatment of compounds **4a-c** and **5a-c** with titanium(IV) chloride caused intramolecular cyclocondensation to yield the corresponding tetrahydrothieno[2,3-*b*]pyridines **6a-c** and **7a-c**. Aromatization of **6a-c** and **7a-c** with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol proceeded smoothly to afford the corresponding dihydrothieno[2,3-*b*]pyridines **8a-c** and **9a-c**.
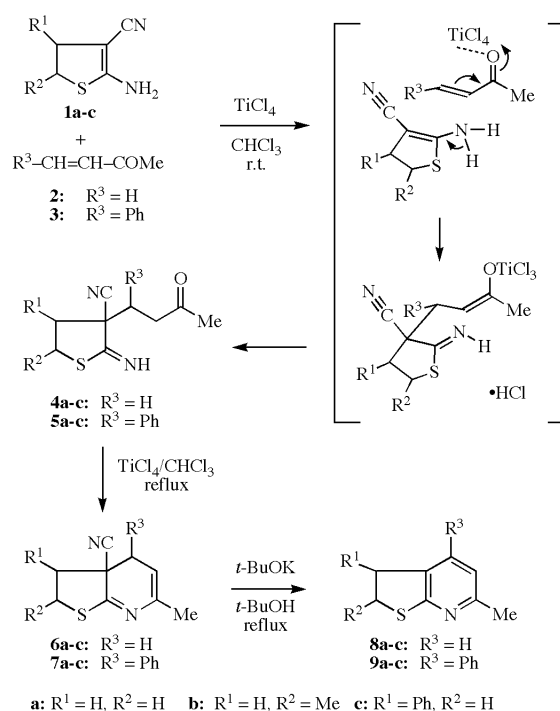
Pyridine derivatives, especially fused pyridines such as quinolines, are important because of their incidence in nature [1], their biological properties [2-6] and their utilities as intermediates for the design of biologically active compounds [7]. Thus, a large number of general methods for the preparation of pyridine derivatives have recently reported [8-15]. For these reasons, we are interested in the development of new methods for the synthesis of pyridine derivatives.

The Michael addition of primary enamines to α,β-unsaturated ketones is an important reaction and this approach has mainly been used for the formation of new carbon-carbon bonds. When α,β-unsaturated ketones are used as electrophiles, conjugate addition of the β-carbon atom of enamines to α,β-unsaturated ketones takes place to produce the initial Michael adducts. Several investigators have reported that primary enaminonitriles react with α,β-unsaturated ketones in the presence of a base to give pyridine derivatives [16-20]. In this context, we have previously described the preparation of Michael adducts from primary enaminonitriles and α,β-unsaturated ketones, and the synthesis of dihydrofuro[2,3-*b*]pyridines [21]. Continuing with our interest in the chemistry of new pyridine derivatives, we report here the results of our investigation, which offer titanium(IV) chloride-mediated Michael reactions of 2-amino-4,5-dihydro-3-thiophenecarbonitriles **1a-c** [22] with α,β-unsaturated ketones and a convenient method for preparing dihydrothieno[2,3-*b*]pyridines.

A base-catalyzed Michael-type reaction of **1a** with benzalacetone **3** according to our previous investigation [21] failed to give the expected Michael adduct **5a** and the reaction was not clean. In order to obtain Michael adduct, we then envisaged that a Lewis acid could act as Michael reaction catalyst. Since there are some disadvantages of base catalysis, *e.g.* incompatibility with base sensitivities or acidic functionalities, ester solvolysis, reverse and other reactions, Lewis acid-catalyzed Michael reactions have

been reported to be efficient under mild conditions [23-29]. Having optimized the Michael reaction parameters, we then examined the reaction with several Lewis acids. Best results were obtained when **1c** was treated with methyl vinyl ketone **2** in the presence of titanium(IV) chloride. Indeed, the Michael addition proceeded smoothly at room temperature giving the corresponding Michael adduct **4c** in 60% yield, and the conjugate addition of the amino group of **1c** to methyl vinyl ketone **2** was not observed (Scheme 1). The use of various other Lewis acids, *e.g.* boron trifluoride diethyl etherate (48%), tin(IV) chloride (28%) and zinc chloride (13%), resulted in lower yield. Thus, we started an investigation of titanium(IV) chloride-mediated Michael-type reaction.

Scheme 1

1a-c
+
R³–CH=CH–COMe
2: R³ = H
3: R³ = Ph

4a-c: R³ = H
5a-c: R³ = Ph

6a-c: R³ = H
7a-c: R³ = Ph

8a-c: R³ = H
9a-c: R³ = Ph

a: R¹ = H, R² = H   **b:** R¹ = H, R² = Me   **c:** R¹ = Ph, R² = H

When a mixture of **1a-c** with methyl vinyl ketone **2** and/or benzalacetone **3** in the presence of titanium(IV) chloride was stirred at room temperature, the expected Michael adducts **4a-c** and **5a-c** were obtained in moderate yield (Table 1). In this case, the reactions of **1b** with methyl vinyl ketone **2** and of **1c** with benzalacetone **3** gave Michael adducts **4b** and **5c** together with tetrahydrothieno[2,3-*b*]pyridines **6b** and **7c** in 11 and 9% yield, respectively (entries 2 and 6). The ir spectra of **4a-c** and **5a-c** display a band near 2230 cm^{-1} due to a non-conjugated cyano group, whereas those of **1a-c** show a conjugated cyano band in the 2160-2170 cm^{-1} region. The ^{1}H nmr spectra of **4a-c** and **5a-c** in DMSO-d$_6$ exhibit a D$_2$O exchangeable signal at δ 5.6-6.0 attributable to the imino proton, whereas those of **1a-c** in deuteriochloroform appear as a D$_2$O exchangeable signal near δ 4.7 assignable to the amino protons. In addition, the ^{1}H nmr spectra of **4a,c** and **5a** show two shinglets near δ 1.3 for the acetyl protons and two shinglets for the imino proton (see experimental section). These observations indicate that **4a,c** and **5a** exist as two diastereomers, which would probably be formed by an effect of the configuration of the imino group, the substituent group at the 3-position and the substituent group at the 4 or 5-position. Elemental analyses and spectral data of **4a-c** and **5a-c** are consistent with the assigned structures. Though the detailed mechanism of the above reaction has not been clarified yet, the formation of Michael adducts **4** and **5** could be explained by the possible mechanism presented in Scheme 1.

chloride in refluxing chloroform for 1 hour caused intramolecular cyclocondensation to afford the corresponding tetrahydrothieno[2,3-*b*]pyridines **6a-c** and **7a-c**. Interestingly, we found the milder condition under which compounds **6a-c** and **7a-c** could be obtained in the presence of titanium(IV) chloride and triethylamine (Table 2). Several investigators have reported an efficient transformation and cyclization by the action of a titanium(IV) chloride-amine combination [32-35]. In our reaction, it seems likely that since the rate of intramolecular cyclocondensation of **4** and **5** could be promoted by using triethylamine as the base at low temperature, **6a-c** and **7a** were obtained in somewhat better yields of 51, 44, 60 and 75%, respectively (entries 2, 4, 6 and 8). Elemental analyses and spectral data of **6a-c** and **7a-c** are consistent with the assigned structures.

On the basis of these results, we examined the direct conversion of **1a** to **6a** in a one-pot process. However, our attempts were unacceptable with respect to yield. A mixture of **1a**, methyl vinyl ketone **2** and titanium(IV) chloride in chloroform stirred at room temperature for 5 hours and then refluxed for 1 hour provided a trace of **6a**, and the reaction was not clean. Although the reason of the low yield is not clear at present, this is probably because the reaction of Michael adduct **4a** with the excess of methyl vinyl ketone **2** would occur.

Table 1

Preparation of Michael Adducts **4** and **5** According to Scheme 1

Entry	**1**	Enone	Product	Yield (%)	Product	Yield (%)
1	**1a**	**2**	**4a**	51	**6a**	0
2	**1b**	**2**	**4b**	41	**6b**	11
3	**1c**	**2**	**4c**	60	**6c**	0
4	**1a**	**3**	**5a**	61	**7a**	0
5	**1b**	**3**	**5b**	50	**7b**	0
6	**1c**	**3**	**5c**	27	**7c**	9

We next investigated the conversion of Michael adducts **4** and **5** into the fused pyridines. The use of sodium methoxide was not successful because of the competitive cleavage of Michael adducts **4a**. This result suggests that when enaminonitriles **1a-c** are used as the substrate, Michael addition reaction does not take place in the presence of a base. It is well known that titanium(IV) chloride has been shown to facilitate the formation of enamines or imines in the reaction of carbonyl compounds with amines [30,31]. Thus, we tested the effectiveness of titanium(IV) chloride for intramolecular cyclocondensation of Michael adducts. Treatment of **4a-c** and **5a-c** with titanium(IV)

Table 2

Intramolecular Cyclization of Michael Adducts **4** and **5** in the Presence of Titanium(IV) Chloride

Entry	Michael adduct	Conditions	Product	Yield (%)
1	**4a**	[a]	**6a**	46
2	**4a**	[b]	**6a**	51
3	**4b**	[a]	**6b**	29
4	**4b**	[b]	**6b**	44
5	**4c**	[a]	**6c**	52
6	**4c**	[b]	**6c**	60
7	**5a**	[a]	**7a**	66
8	**5a**	[b]	**7a**	75
9	**5b**	[a]	**7b**	73
10	**5b**	[b]	**7b**	57
11	**5c**	[a]	**7c**	75
12	**5c**	[b]	**7c**	68

[a] TiCl$_4$ / CHCl$_3$, reflux, 1 hour. [b] TiCl$_4$-Et$_3$N / CHCl$_3$, room temperature, 8 hours.

Finally, we have examined the aromatization of **6** and **7**. Compounds **6a-c** and **7a-c** were allowed to react with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol to give the corresponding dihydrothieno[2,3-*b*]pyridines **8a-c** and **9a-c** in good yields (Table 3). The structural assignments of **8** and **9** were made on the basis of elemental analyses and spectral data.

Table 3

Aromatization of **6** and **7** in the Presence of Potassium *tert*-Butoxide

Entry	Compound	Product	Yield (%)
1	**6a**	**8a**	90
2	**6b**	**8b**	92
3	**6c**	**8c**	93
4	**7a**	**9a**	82
5	**7b**	**9b**	84
6	**7c**	**9c**	90

In conclusion, we have demonstrated that titanium(IV) chloride-mediated Michael reactions of 2-amino-4,5-dihydro-3-thiophenecarbonitriles **1a-c** with α,β-unsaturated ketones provide a novel and efficient method to prepare Michael adducts **4a-c** and **5a-c**. This method is useful because of its efficiency and the ease of operation. Furthermore, fused pyridines can be prepared from Michael adducts in a stepwise fashion. Functionalized pyridines are important synthons in organic synthesis and for the preparation of biologically active compounds with interest in medicinal chemistry.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a JASCO FT/IR-230 spectrometer. The ^{1}H nmr spectra were recorded on a JEOL JNM-A 500 spectrometer (500 MHz). Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. Positive FAB mass spectra were obtained on a JEOL JMS-HX 110 spectrometer. Elemental analyses were performed on a YANACO MT-6 CHN analyzer.

General Procedure for the Preparation of Michael adducts 4a-c and 5a-c.

To an ice-cooled and stirred solution of **1a-c** (10 mmoles) and methyl vinyl ketone **2** (1.40 g, 20 mmoles) or benzalacetone **3** (2.92 g, 20 mmoles) in chloroform (30 ml) was added titanium(IV) chloride (1.90 g, 10 mmoles). After the mixture was stirred at room temperature for 5 hours (in the case of the preparation of **4a-c** and **5a,b**) or overnight (in the case of the preparation of **5c**), anhydrous sodium carbonate (10 g) and a saturated aqueous sodium carbonate solution (5 ml) were successively added to the reaction mixture with stirring and ice-cooling. The solid was removed by filtration and washed with hot chloroform. The combined filtrates were concentrated *in vacuo*. Further processing of the residue is described in the following paragraphs.

(A) The residue was purified by column chromatography on silica gel with methylene chloride-acetone (4:1) as the eluent to give **4a,c** and **5a,b**.

(B) The residue was purified by column chromatography on silica gel with methylene chloride as the eluent to afford **6b** (0.21 g, 11%) and **7c** (0.31 g, 9%). Further the elution with methylene chloride-acetone (4:1) gave of **4b** and **5c**.

Tetrahydro-2-imino-3-(3-oxobutyl)-3-thiophenecarbonitrile (4a).

This compound was obtained as colorless needless (1.00 g, 51%), mp 126-128° (acetone-petroleum ether); ir (potassium

bromide): ν 3171 (NH), 2231 (C≡N), 1631 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.26 (s, 0.75H, COMe), 1.34 (s, 2.25H, COMe), 1.63-2.29 (m, 4H, 4 and 1'-H), 2.49-2.76 (m, 2H, 2'-H), 3.19-3.30 (m, 2H, 5-H), 5.60 (s, 0.75H, NH), 5.72 ppm (s, 0.25H, NH); ms: m/z 197 [M+H]$^+$.

Anal. Calcd. for C$_9$H$_{12}$N$_2$OS: C, 55.08; H, 6.16; N, 14.27. Found: C, 55.10; H, 6.15; N, 14.26.

Tetrahydro-2-imino-5-methyl-3-(3-oxobutyl)-3-thiophenecarbonitrile (4b).

This compound was obtained as colorless needles (0.87 g, 41%), mp 113-115° (acetone-petroleum ether); ir (potassium bromide): ν 3222 (NH), 2232 (C≡N), 1625 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.34 (s, 3H, COMe), 1.62 (d, J = 7.3 Hz, 3H, 5-Me), 1.67-2.28 (m, 3H, 4 and 1'-H), 2.49-2.80 (m, 2H, 4 and 2'-H), 3.24-3.36 (m, 1H, 2'-H), 3.84-3.88 (m, 1H, 5-H), 5.89 ppm (s, 1H, NH); ms: m/z 211 [M+H]$^+$.

Anal. Calcd. for C$_{10}$H$_{14}$N$_2$OS: C, 57.12; H, 6.71; N, 13.32. Found: C, 56.94; H, 6.66; N, 13.38.

Tetrahydro-2-imino-3-(3-oxobutyl)-4-phenyl-3-thiophenecarbonitrile (4c).

This compound was obtained as colorless columns (1.63 g, 60%), mp 174-175° (acetone-petroleum ether); ir (potassium bromide): ν 3192 (NH), 2232 (C≡N), 1634 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.31 (s, 0.9H, COMe), 1.36 (s, 2.1H, COMe), 1.54-1.71 (m, 2H, 1'-H), 1.89-2.08 (m, 2H, 2'-H), 3.40 (dd, J = 5.8, 11 Hz, 1H, 5-H), 3.46-3.54 (m, 1H, 5-H), 3.69-3.74 (m, 1H, 4-H), 5.71 (s, 0.7H, NH), 5.77 (s, 0.3H, NH), 7.37-7.50 ppm (m, 5H, aromatic H); ms: m/z 273 [M+H]$^+$.

Anal. Calcd. for C$_{15}$H$_{16}$N$_2$OS: C, 66.15; H, 5.92; N, 10.29. Found: C, 66.15; H, 5.89; N, 10.25.

Tetrahydro-2-imino-3-(3-oxo-1-phenylbutyl)-3-thiophenecarbonitrile (5a).

This compound was obtained as colorless needles (1.66 g, 61%), mp 179-181° (chloroform-petroleum ether); ir (potassium bromide): ν 3240 (NH), 2232 (C≡N), 1631 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.38 (s, 0.45H, COMe), 1.46 (s, 2.55H, COMe), 1.95-2.00 (m, 1H, 4-H), 2.11-2.35 (m, 3H, 4 and 2'-H), 3.08-3.14 (m, 1H, 1'-H), 3.21-3.33 (m, 2H, 5-H), 5.84 (s, 0.85H, NH), 5.92 (s, 0.15H, NH), 7.33-7.41 ppm (m, 5H, aromatic H); ms: m/z 273 [M+H]$^+$.

Anal. Calcd. for C$_{15}$H$_{16}$N$_2$OS: C, 66.15; H, 5.92; N, 10.29. Found: C, 66.13; H, 5.91; N, 10.27.

Tetrahydro-2-imino-5-methyl-3-(3-oxo-1-phenylbutyl)-3-thiophenecarbonitrile (5b).

This compound was obtained as colorless prisms (1.43 g, 50%), mp 179-180° (acetone-petroleum ether); ir (potassium bromide): ν 3187 (NH), 2242 (C≡N), 1631 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.37 (s, 3H, COMe), 1.51 (d, J = 7 Hz, 3H, 5-Me), 1.94-2.25 (m, 3H, 4 and 2'-H), 2.49-2.72 (m, 1H, 2'-H), 3.20 (dd, J = 2.1, 13.6 Hz, 1H, 1'-H), 3.83-3.86 (m, 1H, 5-H), 5.92 (s, 1H, NH), 7.33-7.41 ppm (m, 5H, aromatic H); ms: m/z 287 [M+H]$^+$.

Anal. Calcd. for C$_{16}$H$_{18}$N$_2$OS: C, 67.10; H, 6.34; N, 9.78. Found: C, 67.14; H, 6.32; N, 9.76.

Tetrahydro-2-imino-3-(3-oxo-1-phenylbutyl)-4-phenyl-3-thiophenecarbonitrile (5c).

This compound was obtained as colorless needles (0.93 g, 27%), mp 201-203° (chloroform-petroleum ether); ir (potassium

bromide): ν 3241 (NH), 2232 (C≡N), 1631 (C=O) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.43 (s, 3H, COMe), 1.83 (dd, J = 2.7, 14.3 Hz, 1H, 2'-H), 2.05-2.11 (m, 1H, 2'-H), 3.26-3.39 (m, 3H, 5 and 1'-H), 3.69 (dd, J = 6.4, 11.6 Hz, 1H, 4-H), 5.90 (s, 1H, NH), 6.88-6.98 (m, 6H, aromatic H), 7.04-7.06 (m, 2H, aromatic H), 7.17-7.18 ppm (m, 2H, aromatic H); ms: m/z 349 [M+H]$^+$.

Anal. Calcd. for C$_{21}$H$_{20}$N$_2$OS: C, 72.38; H, 5.79; N, 8.04. Found: C, 72.39; H, 5.83; N, 7.97.

General Procedure for the Preparation of 6a-c and 7a-c from 4a-c and 5a-c.

(A) To an ice-cooled and stirred solution of **4a-c** and **5a-c** (10 mmoles) in chloroform (30 ml) was added titanium(IV) chloride (1.90 g, 10 mmoles). After the mixture was refluxed for 1 hour, anhydrous sodium carbonate (10 g) and a saturated aqueous sodium carbonate solution (5 ml) were successively added to the reaction mixture with stirring and ice-cooling. The solid was removed by filtration and washed with hot chloroform. The combined filtrates were concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with methylene chloride as the eluent to yield **6a** (0.81 g, 46%), **6b** (0.56 g, 29%), **6c** (1.33 g, 52%), **7a** (1.68 g, 66%), **7b** (1.96 g, 73%) and **7c** (2.48 g, 75%), respectively.

(B) To an ice-cooled and stirred solution of **4a-c** and **5a-c** (10 mmoles) and triethylamine (1.01 g, 10 mmoles) in chloroform (30 ml) was added titanium(IV) chloride (1.90 g, 10 mmoles). After the mixture was stirred at room temperature for 8 hours, anhydrous sodium carbonate (10 g) and a saturated aqueous sodium carbonate solution (5 ml) were successively added to the reaction mixture with stirring and ice-cooling. After work-up as described above, **6a** (0.91 g, 51%), **6b** (0.84 g, 44%), **6c** (1.52 g, 60%), **7a** (1.91 g, 75%), **7b** (1.53 g, 57%) and **7c** (2.24 g, 68%) were obtained.

2,3,3a,4-Tetrahydro-6-methylthieno[2,3-*b*]pyridine-3a-carbonitrile (6a).

This compound was obtained as colorless prisms, mp 105-107° (acetone-petroleum ether); ir (potassium bromide): ν 2227 (C≡N) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.01-2.02 (m, 3H, 6-Me), 2.13-2.26 (m, 2H, 3-H), 2.76 (dd, J = 6.7, 17.1 Hz, 1H, 4-H), 2.91-2.95 (m, 1H, 4-H), 3.23 (dd, J = 6.7, 11.6 Hz, 1H, 2-H), 3.44-3.51 (m, 1H, 2-H), 5.14-5.17 ppm (m, 1H, 5-H); ms: m/z 179 [M+H]$^+$.

Anal. Calcd. for C$_9$H$_{10}$N$_2$S: C, 60.64; H, 5.65; N, 15.72. Found: C, 60.54; H, 5.70; N, 15.61.

2,3,3a,4-Tetrahydro-2,6-dimethylthieno[2,3-*b*]pyridine-3a-carbonitrile (6b).

This compound was obtained as colorless prisms, mp 101-102° (acetone-petroleum ether); ir (potassium bromide): ν 2232 (C≡N) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.74 (d, J = 7.3 Hz, 3H, 2-Me), 2.02-2.03 (m, 3H, 3-H, 6-Me), 2.16-2.21 (m, 1H, 3-H), 2.36 (dd, J = 7.6, 13.4 Hz, 1H, 3-H), 2.67-2.72 (m, 2H, 4-H), 3.87-3.93 (m, 1H, 2-H), 5.17-5.19 ppm (m, 1H, 5-H); ms: m/z 193 [M+H]$^+$.

Anal. Calcd. for C$_{10}$H$_{12}$N$_2$S: C, 62.47; H, 6.29; N, 14.57. Found: C, 62.57; H, 6.34; N, 14.56.

2,3,3a,4-Tetrahydro-6-methyl-3-phenylthieno[2,3-*b*]pyridine-3a-carbonitrile (6c).

This compound was obtained as colorless prisms, mp 122-124° (acetone-petroleum ether); ir (potassium bromide): ν 2232 (C≡N)

cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.00-2.01 (m, 3H, 6-Me), 2.31-2.35 (m, 1H, 4-H), 2.48 (dd, J = 6.7, 17.4 Hz, 1H, 4-H), 3.31 (dd, J = 5.5, 11 Hz, 1H, 2-H), 3.48 (dd, J = 5.5, 12.2 Hz, 1H, 2-H), 3.83 (dd, J = 11, 12.2 Hz, 1H, 3-H), 5.10-5.12 (m, 1H, 5-H), 7.26-7.43 ppm (m, 5H, aromatic H); ms: m/z 255 [M+H]$^+$.

Anal. Calcd. for C$_{15}$H$_{14}$N$_2$S: C, 70.83; H, 5.55; N, 11.01. Found: C, 70.90; H, 5.54; N, 11.00.

2,3,3a,4-Tetrahydro-6-methyl-4-phenylthieno[2,3-*b*]pyridine-3a-carbonitrile (7a).

This compound was obtained as colorless prisms, mp 165-166° (acetone-petroleum ether); ir (potassium bromide): ν 2232 (C≡N) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.09-2.10 (m, 3H, 6-Me), 2.31 (dd, J = 6.7, 12.8 Hz, 1H, 3-H), 2.59 (dd, J = 4.9, 12.8 Hz, 1H, 3-H), 3.21 (dd, J = 6.7, 11.6 Hz, 1H, 2-H), 3.36 (dd, J = 4.9, 11.6 Hz, 1H, 2-H), 3.62-3.63 (m, 1H, 4-H), 5.26-5.27 (m, 1H, 5-H), 7.34-7.41 ppm (m, 5H, aromatic H); ms: m/z 255 [M+H]$^+$.

Anal. Calcd. for C$_{15}$H$_{14}$N$_2$S: C, 70.83; H, 5.55; N, 11.01. Found: C, 70.89; H, 5.61; N, 11.01.

2,3,3a,4-Tetrahydro-2,6-dimethyl-4-phenylthieno[2,3-*b*]pyridine-3a-carbonitrile (7b).

This compound was obtained as colorless prisms, mp 128-130° (acetone-petroleum ether); ir (potassium bromide): ν 2232 (C≡N) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.64 (d, J = 7 Hz, 3H, 2-Me), 2.09-2.10 (m, 3H, 6-Me), 2.31 (dd, J = 0.9, 13.4 Hz, 1H, 3-H), 2.52 (dd, J = 7.6, 13.4 Hz, 1H, 3-H), 3.58-3.59 (m, 1H, 4-H), 3.88-3.91 (m, 1H, 2-H), 5.27-5.28 (m, 1H, 5-H), 7.26-7.39 ppm (m, 5H, aromatic H); ms: m/z 269 [M+H]$^+$.

Anal. Calcd. for C$_{16}$H$_{16}$N$_2$S: C, 71.61; H, 6.01; N, 10.44. Found: C, 71.63; H, 5.99; N, 10.44.

2,3,3a,4-Tetrahydro-6-methyl-3,4-diphenylthieno[2,3-*b*]pyridine-3a-carbonitrile (7c).

This compound was obtained as colorless prisms, mp 189-191° (acetone-petroleum ether); ir (potassium bromide): ν 2224 (C≡N) cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.97-1.98 (m, 3H, 6-Me), 3.28-3.47 (m, 2H, 2-H), 4.03 (dd, J = 7.9, 10.3 Hz, 1H, 3-H), 4.11-4.13 (m, 1H, 4-H), 5.07-5.08 (m, 1H, 5-H), 6.94-7.03 (m, 5H, aromatic H), 7.12-7.17 ppm (m, 5H, aromatic H); ms: m/z 331 [M+H]$^+$.

Anal. Calcd. for C$_{21}$H$_{18}$N$_2$S: C, 76.33; H, 5.49; N, 8.48. Found: C, 76.28; H, 5.59; N, 8.33.

General Procedure for the Preparation of 8a-c and 9a-c from 6a-c and 7a-c.

A solution of **6a-c** and **7a-c** (5 mmoles) and potassium *tert*-butoxide (0.56 g, 5 mmoles) in anhydrous *tert*-butyl alcohol (10 ml) was refluxed for 1 hour. After removal of the solvent *in vacuo*, cold water was added to the residue. The resulting mixture was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with methylene chloride as the eluent to afford **8a-c** and **9a-c**.

2,3-Dihydro-6-methylthieno[2,3-*b*]pyridine (8a).

This compound was obtained as pale yellow oil (0.68 g, 90%); ^{1}H nmr (deuteriochloroform): δ 2.45 (s, 3H, 6-Me), 3.25 (t, J = 7.9 Hz, 2H, 3-H), 3.38 (t, J = 7.9 Hz, 2H, 2-H), 6.74 (d, J = 7.6 Hz, 1H, 5-H), 7.26 ppm (d, J = 7.6 Hz, 1H, 4-H); ms: m/z 152 [M+H]$^+$.

Anal. Calcd. for C_8H_9NS: C, 63.54; H, 6.00; N, 9.26. Found: C, 63.40; H, 6.02; N, 9.38.

2,3-Dihydro-2,6-dimethylthieno[2,3-*b*]pyridine (8b).

This compound was obtained as pale yellow oil (0.76 g, 92%); ^{1}H nmr (deuteriochloroform): δ 1.48 (d, J = 6.7 Hz, 3H, 2-Me), 2.45 (s, 3H, 6-Me), 2.89 (dd, J = 6.7, 15.5 Hz, 1H, 3-H), 3.35 (dd, J = 7.6, 15.5 Hz, 1H, 3-H), 3.97-4.01 (m, 1H, 2-H), 6.73 (d, J = 7.6 Hz, 1H, 5-H), 7.23 ppm (d, J = 7.6 Hz, 1H, 4-H); ms: m/z 166 [M+H][+].

Anal. Calcd. for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48. Found: C, 65.17; H, 6.71; N, 8.72.

2,3-Dihydro-6-methyl-3-phenylthieno[2,3-*b*]pyridine (8c).

This compound was obtained as pale yellow oil (1.06 g, 93%); ^{1}H nmr (deuteriochloroform): δ 2.48 (s, 3H, 6-Me), 3.43 (dd, J = 9.5, 11 Hz, 1H, 2-H), 3.66 (dd, J = 8.5, 11 Hz, 1H, 2-H), 4.63 (dd, J = 8.5, 9.5 Hz, 1H, 3-H), 6.74 (d, J = 7.6 Hz, 1H, 5-H), 6.95 (d, J = 7.6 Hz, 1H, 4-H), 7.25-7.37 ppm (m, 5H, aromatic H); ms: m/z 228 [M+H][+].

Anal. Calcd. for $C_{14}H_{13}NS$: C, 73.97; H, 5.76; N, 6.16. Found: C, 73.97; H, 5.60; N, 6.09.

2,3-Dihydro-6-methyl-4-phenylthieno[2,3-*b*]pyridine (9a).

This compound was obtained as colorless prisms (0.93 g, 82%), mp 114-116° (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 2.50 (s, 3H, 6-Me), 3.29-3.35 (m, 4H, 2 and 3-H), 6.77 (s, 1H, 5-H), 7.35-7.45 ppm (m, 5H, aromatic H); ms: m/z 228 [M+H][+].

Anal. Calcd. for $C_{14}H_{13}NS$: C, 73.97; H, 5.76; N, 6.16. Found: C, 73.87; H, 5.83; N, 6.14.

2,3-Dihydro-2,6-dimethyl-4-phenylthieno[2,3-*b*]pyridine (9b).

This compound was obtained as colorless prisms (1.01 g, 84%), mp 84-86° (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.45 (d, J = 6.7 Hz, 3H, 2-Me), 2.50 (s, 3H, 6-Me), 2.97 (dd, J = 7, 15.5 Hz, 1H, 3-H), 3.41 (dd, J = 7.3, 15.5 Hz, 1H, 3-H), 3.92-3.97 (m, 1H, 2-H), 6.78 (s, 1H, 5-H), 7.35-7.46 ppm (m, 5H, aromatic H); ms: m/z 242 [M+H][+].

Anal. Calcd. for $C_{15}H_{15}NS$: C, 74.65; H, 6.26; N, 5.80. Found: C, 74.62; H, 6.33; N, 5.79.

2,3-Dihydro-6-methyl-3,4-diphenylthieno[2,3-*b*]pyridine (9c).

This compound was obtained as colorless prisms (1.36 g, 90%), mp 98-100° (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 2.54 (s, 3H, 6-Me), 3.19 (dd, J = 3.1, 11.3 Hz, 1H, 2-H), 3.91 (dd, J = 8.5, 11.3 Hz, 1H, 2-H), 4.71 (dd, J = 3.1, 8.5 Hz, 1H, 3-H), 6.73 (s, 1H, 5-H), 6.93-7.00 (m, 4H, aromatic H), 7.11-7.25 ppm (m, 6H, aromatic H); ms: m/z 304 [M+H][+].

Anal. Calcd. for $C_{20}H_{17}NS$: C, 79.17; H, 5.65; N, 4.62. Found: C, 79.22; H, 5.76; N, 4.56.

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