

Synthesis of Dihydrofuro[2,3-*b*]pyridines by the Reaction of 2-Amino-4,5-dihydro-3-furancarbonitriles with α,β -Unsaturated Carbonyl Compounds

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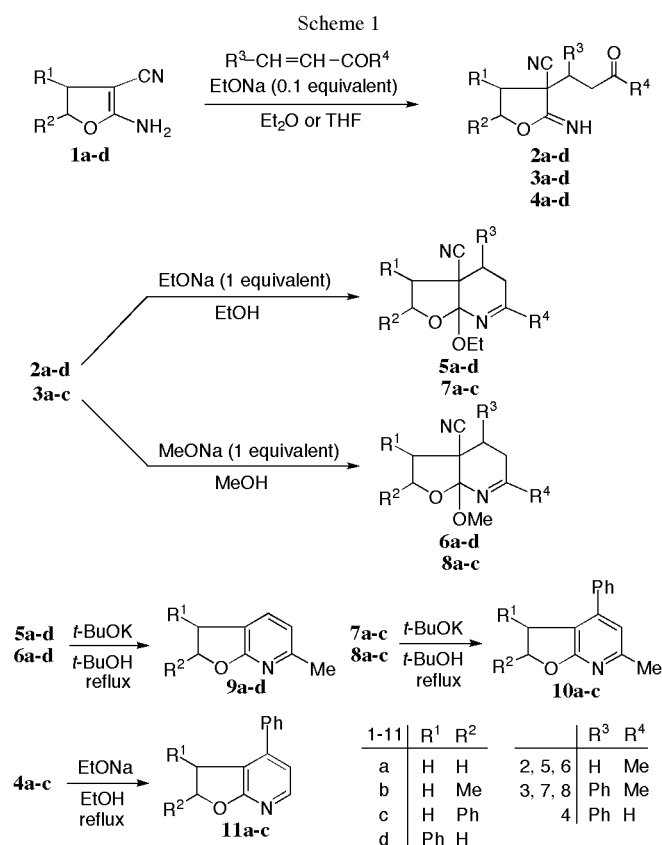
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The reactions of 2-amino-4,5-dihydro-3-furancarbonitriles **1a-d** with α,β -unsaturated carbonyl compounds in the presence of sodium ethoxide (0.1 equivalent) gave the corresponding Michael adducts **2a-d**, **3a-d** and **4a-d**. Compounds **2a-d** and **3a-c** reacted with sodium alkoxide (1 equivalent) to yield the corresponding 7a-alkoxyhexahydrofuro[2,3-*b*]pyridines **5a-d**, **6a-d**, **7a-c** and **8a-c**. Treatment of **5a-d**, **6a-d**, **7a-c** and **8a-c** with potassium *tert*-butoxide produced the corresponding dihydrofuro[2,3-*b*]pyridines **9a-d** and **10a-c**. The reaction of **4a-c** with sodium ethoxide (1 equivalent) afforded the corresponding dihydrofuro[2,3-*b*]pyridines **11a-c**.

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The ir and ^1H nmr spectra of 2-amino-4,5-dihydro-3-furancarbonitriles **1a-d** [1] indicate that **1** exist as the primary enamionitrile forms [2] rather than the imine forms. Therefore, depending on the experimental conditions used, electrophiles are expected to attack at either the enamino nitrogen atom or the β -carbon atom (the 3-position of **1**) in the enamine. In fact, we showed that benzoyl chloride in the presence of sodium hydride attacks the 3-position of **1** to give the intermediate 3-benzoyl-2-imino-3-furancarbonitriles which undergo a ring opening to provide the malononitrile derivatives [3], whereas benzoyl chloride in pyridine attacks the amino group of **1** to yield 2-benzamido-4,5-dihydro-3-furancarbonitriles [1]. When α,β -unsaturated carbonyl compounds are used as electrophiles, conjugate addition of the β -carbon atom of enamines to α,β -unsaturated carbonyl compounds takes place to produce the initial Michael adducts [4,5]. We now report the results of the reactions of **1** with α,β -unsaturated carbonyl compounds in the presence of a base.

When a solution of **1a-d** with methyl vinyl ketone and sodium ethoxide (0.1 equivalent) in diethyl ether or tetrahydrofuran was stirred at room temperature, the expected Michael adducts **2a-d** were obtained. The conjugate addition of the amino group of **1** to methyl vinyl ketone was not observed. The ir spectra of **2a-d** display a band at near 2230 cm^{-1} due to a non-conjugated cyano group, whereas those of **1a-d** show a conjugated cyano band in the $2170\text{--}2190\text{ cm}^{-1}$ region. The ^1H nmr spectra of **2a-d** exhibit a one-proton singlet at near δ 7.30 attributable to an imino group, whereas those of **1a-d** appear as a two-proton singlet at near δ 5 assignable to an amino group. Compounds **1a-d** reacted with benzalacetone and cinnamaldehyde under the same conditions to give the corresponding Michael adducts **3a-d** and **4a-d**. Elemental analyses and spectral data of **2-4** are consistent with the assigned structures.



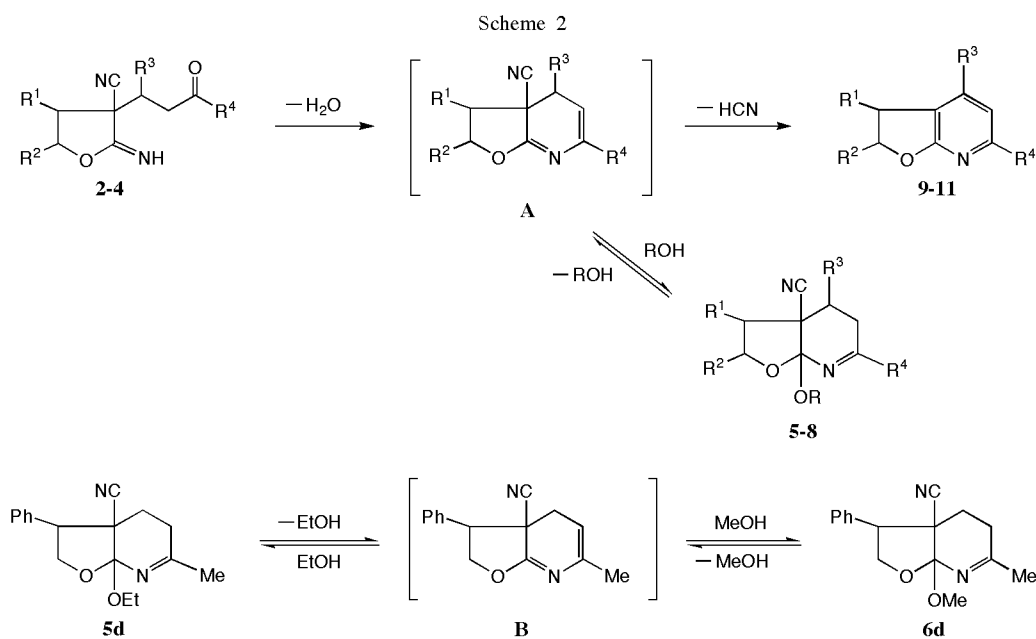
Primary enamines and α,β -unsaturated carbonyl compounds are the components of the Hantzsch pyridine synthesis [6-8]. Several investigators have reported that primary enamionitriles react with α,β -unsaturated carbonyl compounds in the presence of a base to give the pyridines [7, 9-12]. The Hantzsch synthesis is believed to involve the adduct initially formed by a Michael addition of an enamine to an α,β -unsaturated carbonyl compound. Generally, the adduct has not been isolated under the reaction conditions

because of its fast intramolecular cyclization to yield the pyridine derivative. Hence, we investigated the conversion of the Michael adducts **2-4** into the pyridines.

Treatment of **2a-d** or **3a-c** with sodium ethoxide (1 equivalent) in ethanol at room temperature underwent cyclization to give the corresponding 7a-ethoxyhexahydrofuro[2,3-*b*]pyridines **5a-d** or **7a-c**. Similarly, the reaction of **2a-d** or **3a-c** with sodium methoxide afforded the 7a-methoxyhexahydrofuro[2,3-*b*]pyridines **6a-d** or **8a-c**. In contrast, when **3d** was treated with sodium ethoxide or methoxide, a retro-Michael reaction took place to furnish **1d**. The ^1H nmr spectra of **5c**, **6b**, **6c** and **8b** show two triplets at near δ 1.2 for a methyl group of an ethoxy group of **5c**, two doublets at near δ 1.4 for a 2-methyl group of **6b** and **8b**, two singlets at near δ 2.1 for a

cyclization occurred and **4a-d** were recovered unchanged. However, under refluxing ethanol, the reaction of **4a-c** with sodium ethoxide led to the formation of the dihydrofuro[2,3-*b*]pyridines **11a-c**. In this case, ethanol adducts such as **5** and **6** could not be obtained and intramolecular cyclization of **4d** did not proceed.

The formation of **5-8** and **9-11** can be explained in terms of Scheme 2. A Michael addition of **1** to α,β -unsaturated carbonyl compounds gives the adducts **2-4** which undergo intramolecular cyclization and dehydration to form the intermediate dihydropyridines **A**. Elimination of hydrogen cyanide from **A** under basic conditions produces **9-11**. Conjugate addition of ethanol or methanol to **A** results in the formation of **5** and **7** or **6** and **8**. Unfortunately, the key intermediate **A** could not be isolated.



6-methyl group of **5c**, **6b**, **6c** and **8b**, and two singlets at near δ 3.6 for a methyl group of a methoxy group of **6b**, **6c** and **8b**. These observations indicate that **5c**, **6b**, **6c** and **8b** exist as two diastereomers, which would probably be formed by an effect of the configuration of methyl or phenyl group at the 2-position, ethoxy or methoxy group and cyano group. The reaction of **1c** with benzalacetone and sodium ethoxide (1 equivalent) in ethanol gave **7c** in 42% yield. In a similar way, by the reaction of **1c** with benzaldehyde and acetone, **7c** was also obtained in a somewhat lower yield of 25%. The adducts **5a-d**, **6a-d**, **7a-c** and **8a-c** were treated with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol to produce the dihydrofuro[2,3-*b*]pyridines **9a-d** and **10a-c**. On the other hand, when a solution of **4a-d** with sodium ethoxide (1 equivalent) in ethanol was stirred overnight at room temperature, no

Compound **5d** was converted into **6d** by treatment with sodium methoxide in refluxing methanol, and conversely, **6d** was transformed into **5d** by treatment with sodium ethoxide in refluxing ethanol, and **9d** was not obtained. This interconversion probably proceeds through the intermediate **B** (Scheme 2), which would be resistant to elimination of hydrogen cyanide to give **9d** due to the absence of phenyl group at the 4-position. Our results show that sodium ethoxide/ethanol or sodium methoxide/methanol system (milder condition) provides a unique possibility to afford Michael adducts **2-4** and alcohol adducts **5-8**. Aromatization of **5-8** with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol proceeds smoothly to give **9** and **10** in good yields. While, in the case of intramolecular cyclization of **4**, sodium ethoxide in refluxing ethanol system is better than potassium *tert*-butoxide system (stronger condition).

Subsequently, we undertook a one-pot synthesis of **9-11** from **1** and α,β -unsaturated carbonyl compounds. Attempts to prepare **9c** or **10c** from **1c** and methyl vinyl ketone or benzalacetone according to the method of Robinson *et al.* [10] or Shibata *et al.* [12] were unsuccessful; however, a mixture of **1**, benzalacetone or cinnamaldehyde and sodium ethoxide (2 equivalents) in ethanol stirred overnight at room temperature, and then refluxed for 1 hour provided **10a-c** and **11a-c**. In the case of **9a-d**, we carried out elimination of hydrogen cyanide by use of potassium *tert*-butoxide.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a JASCO FT/IR-230 spectrometer. The ^1H nmr spectra were recorded on a HITACHI R-90 H spectrometer (90 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 HERAUS CHNO-RAPID analyzer or YANACO MT-6 CHN analyzer.

General Procedure for the Preparation of Michael adducts **2**, **3** and **4**.

To a solution of sodium (23 mg, 1 mmole) in anhydrous ethanol (2 ml) were added **1a-d** (10 mmoles) and methyl vinyl ketone (0.84 g, 12 mmoles), benzalacetone (1.75 g, 12 mmoles) or cinnamaldehyde (1.58 g, 12 mmoles) and tetrahydrofuran (20 ml, in the case of the preparation of **2a, b**) or diethyl ether (20 ml, **2c, 2d, 3a-d** and **4a-d**) with stirring. The mixture was stirred at room temperature for 5 hours (**2a, b**) or 2 hours (**2c, 2d, 3a-d** and **4a-d**). The reaction mixture was neutralized with acetic acid (60 mg, 1 mmole) with stirring and ice-cooling, and then cold water was added to the resulting mixture. Further processing of the resulting mixture is described in the following paragraphs.

(A) The resulting mixture was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was recrystallized from an appropriate solvent to give **2a, 2b, 2d** and **3b**.

(B) The precipitate was isolated by filtration, washed with water, dried and recrystallized from an appropriate solvent to yield **2c, 3a, 3c, 3d** and **4a-d**.

Tetrahydro-2-imino-3-(3-oxobutyl)-3-furancarboxitrile (**2a**).

This compound was obtained as colorless prisms (1.10 g, 61%), mp 75-77° (acetone-petroleum ether); ir (potassium bromide): ν 3210 (NH), 2240 (C \equiv N), 1705 (C=O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.09-3.12 (m, 6H, 4-H, 1'-H, 2'-H), 2.21 (s, 3H, COCH₃), 4.32 (t, $J = 6.5$ Hz, 2H, 5-H), 7.30 ppm (br s, 1H, NH); ms: m/z 181 [M+H]⁺.

Anal. Calcd. for C₁₉H₁₂N₂O₂: C, 59.99; H, 6.71; N, 15.35. Found: C, 60.05; H, 6.43; N, 15.10.

Tetrahydro-2-imino-5-methyl-3-(3-oxobutyl)-3-furancarboxitrile (**2b**).

This compound was obtained as colorless needles (0.91 g, 47%), mp 102-104° (acetone-petroleum ether); ir (potassium bromide): ν 3245 (NH), 2230 (C \equiv N), 1700 (C=O) cm^{-1} ; ^1H nmr

(deuteriochloroform): δ 1.41 (d, $J = 6$ Hz, 3H, 5-CH₃), 1.80 (dd, $J = 10.5, 13$ Hz, 2H, 1'-H), 2.10-2.37 (m, 2H, 4-H), 2.21 (s, 3H, COCH₃), 2.47-2.81 (m, 2H, 2'-H), 4.43-4.85 (m, 1H, 5-H), 7.24 ppm (br s, 1H, NH); ms: m/z 195 [M+H]⁺.

Anal. Calcd. for C₁₀H₁₄N₂O₂: C, 61.84; H, 7.27; N, 14.42. Found: C, 61.95; H, 7.11; N, 14.53.

Tetrahydro-2-imino-3-(3-oxobutyl)-5-phenyl-3-furancarboxitrile (**2c**).

This compound was obtained as colorless needles (1.72 g, 67%), mp 114-116° (acetone-petroleum ether); ir (potassium bromide): ν 3220 (NH), 2230 (C \equiv N), 1705 (C=O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.05-2.62 (m, 4H, 4-H, 1'-H), 2.20 (s, 3H, COCH₃), 2.73-3.13 (m, 2H, 2'-H), 5.52 (dd, $J = 5.5, 10.5$ Hz, 1H, 5-H), 7.30-7.36 (m, 5H, aromatic H), 7.46 ppm (br s, 1H, NH); ms: m/z 257 [M+H]⁺.

Anal. Calcd. for C₁₅H₁₆N₂O₂: C, 70.29; H, 6.29; N, 10.93. Found: C, 69.98; H, 6.37; N, 10.66.

Tetrahydro-2-imino-3-(3-oxobutyl)-4-phenyl-3-furancarboxitrile (**2d**).

This compound was obtained as colorless needles (2.19 g, 86%), mp 147-148° (chloroform-petroleum ether); ir (potassium bromide): ν 3192 (NH), 2232 (C \equiv N), 1692 (C=O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.09-2.35 (m, 2H, 1'-H), 2.16 (s, 3H, COCH₃), 2.41-3.31 (m, 2H, 2'-H), 3.50 (t, $J = 7$ Hz, 1H, 4-H), 4.49-4.70 (m, 2H, 5-H), 7.29-7.46 ppm (m, 6H, NH, aromatic H); ms: m/z 257 [M+H]⁺.

Anal. Calcd. for C₁₅H₁₆N₂O₂: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.25; H, 6.48; N, 10.70.

Tetrahydro-2-imino-3-(3-oxo-1-phenylbutyl)-3-furancarboxitrile (**3a**).

This compound was obtained as colorless needles (1.24 g, 48%), mp 157-158° (acetone-petroleum ether); ir (potassium bromide): ν 3214 (NH), 2232 (C \equiv N), 1707 (C=O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.65 (s, 3H, COCH₃), 2.06-2.52 (m, 4H, 4-H, 2'-H), 3.16 (t, $J = 8$ Hz, 1H, 1'-H), 4.17-4.47 (m, 2H, 5-H), 7.37 (s, 5H, aromatic H), 7.37 ppm (br s, 1H, NH); ms: m/z 257 [M+H]⁺.

Anal. Calcd. for C₁₅H₁₆N₂O₂: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.26; H, 6.47; N, 10.73.

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

This compound was obtained as colorless needles (1.31 g, 49%), mp 162-164° (acetone-petroleum ether); ir (potassium bromide): ν 3246 (NH), 2232 (C \equiv N), 1702 (C=O) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.46 (d, $J = 6$ Hz, 3H, 5-CH₃), 1.63 (s, 3H, COCH₃), 1.84-2.06 (m, 1H, 4-H), 2.26-2.58 (m, 3H, 4-H, 2'-H), 3.22 (dd, $J = 7.5, 16$ Hz, 1H, 1'-H), 4.55-4.82 (m, 1H, 5-H), 7.35 (s, 5H, aromatic H), 7.35 ppm (br s, 1H, NH); ms: m/z 271 [M+H]⁺.

Anal. Calcd. for C₁₆H₁₈N₂O₂: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.11; H, 6.73; N, 10.32.

Tetrahydro-2-imino-3-(3-oxo-1-phenylbutyl)-5-phenyl-3-furancarboxitrile (**3c**).

This compound was obtained as colorless needles (2.75 g, 83%), mp 184-185° (chloroform-petroleum ether); ir (potassium bromide): ν 3230 (NH), 2240 (C \equiv N), 1705 (C=O) cm^{-1} ; ^1H nmr (DMSO-*d*₆): δ 1.49 (s, 3H, COCH₃), 2.09-2.24 (m, 2H, 4-H),

2.39-2.89 (m, 2H, 2'-H), 3.51 (dd, $J = 4.5$, 11 Hz, 1H, 1'-H), 5.49 (dd, $J = 5$, 10.5 Hz, 1H, 5-H), 5.61 (br s, 1H, NH), 7.31-7.53 ppm (m, 10H, aromatic H); ms: m/z 333 $[M+H]^+$.

Anal. Calcd. for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.70; H, 6.00; N, 8.49.

Tetrahydro-2-imino-3-(3-oxo-1-phenylbutyl)-4-phenyl-3-furancarbonitrile (**3d**).

This compound was obtained as colorless needles (2.29 g, 69%), mp 185-187° (chloroform-petroleum ether); ir (potassium bromide): ν 3221 (NH), 2240 ($C\equiv N$), 1694 ($C=O$) cm^{-1} ; 1H nmr (DMSO- d_6): δ 1.45 (s, 3H, $COCH_3$), 1.81-2.37 (m, 2H, 2'-H), 3.41 (dd, $J = 3.5$, 12 Hz, 1H, 1'-H), 3.92-4.63 (m, 3H, 4-H, 5-H), 5.66 (br s, 1H, NH), 6.98-7.31 ppm (m, 10H, aromatic H); ms: m/z 333 $[M+H]^+$.

Anal. Calcd. for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.70; H, 6.18; N, 8.57.

Tetrahydro-2-imino-3-(3-phenylpropanal-3-yl)-3-furancarbonitrile (**4a**).

This compound was obtained as colorless prisms (1.96 g, 81%), mp 204-205° dec (methanol-petroleum ether); ir (potassium bromide): ν 3220 (NH), 2230 ($C\equiv N$), 1695 ($C=O$) cm^{-1} ; 1H nmr (DMSO- d_6): δ 1.80-2.78 (m, 4H, 4-H, 2'-H), 3.29 (dd, $J = 3$, 12 Hz, 1H, 3'-H), 3.99-4.53 (m, 2H, 5-H), 5.26-5.36 (m, 1H, CHO), 5.87 (d, $J = 4$ Hz, 1H, NH), 7.40 ppm (s, 5H, aromatic H); ms: m/z 243 $[M+H]^+$.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.41; H, 5.89; N, 11.45.

Tetrahydro-2-imino-5-methyl-3-(3-phenylpropanal-3-yl)-3-furancarbonitrile (**4b**).

This compound was obtained as colorless prisms (1.25 g, 49%), mp 186-187° (acetone-petroleum ether); ir (potassium bromide): ν 3180 (NH), 2240 ($C\equiv N$), 1695 ($C=O$) cm^{-1} ; 1H nmr (DMSO- d_6): δ 1.37 (d, $J = 6$ Hz, 3H, 5- CH_3), 1.88-2.38 (m, 4H, 4-H, 2'-H), 3.26 (dd, $J = 3.5$, 12.5 Hz, 1H, 3'-H), 4.35-4.79 (m, 1H, 5-H), 5.03-5.24 (m, 1H, CHO), 5.99 (d, $J = 5$ Hz, 1H, NH), 7.37 ppm (s, 5H, aromatic H); ms: m/z 257 $[M+H]^+$.

Anal. Calcd. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.29; H, 6.37; N, 10.88.

Tetrahydro-2-imino-5-phenyl-3-(3-phenylpropanal-3-yl)-3-furancarbonitrile (**4c**).

This compound was obtained as colorless needles (2.36 g, 74%), mp 196-197° (chloroform-petroleum ether); ir (potassium bromide): ν 3210 (NH), 2240 ($C\equiv N$), 1690 ($C=O$) cm^{-1} ; 1H nmr (DMSO- d_6): δ 1.89-2.73 (m, 4H, 4-H, 2'-H), 3.45 (dd, $J = 3.5$, 12.5 Hz, 1H, 3'-H), 5.13-5.29 (m, 1H, CHO), 5.42-5.82 (m, 1H, 5-H), 6.08 (br s, 1H, NH), 7.23-7.53 ppm (m, 10H, aromatic H); ms: m/z 319 $[M+H]^+$.

Anal. Calcd. for $C_{20}H_{18}N_2O_2 \cdot 0.1H_2O$: C, 75.03; H, 5.73; N, 8.75. Found: C, 74.95; H, 5.75; N, 8.73.

Tetrahydro-2-imino-4-phenyl-3-(3-phenylpropanal-3-yl)-3-furancarbonitrile (**4d**).

This compound was obtained as colorless needles (2.45 g, 77%), mp 200-201° (chloroform-petroleum ether); ir (potassium bromide): ν 3165 (NH), 2230 ($C\equiv N$), 1690 ($C=O$) cm^{-1} ; 1H nmr (DMSO- d_6): δ 1.72-1.92 (m, 1H, 2'-H), 2.45 (dd, $J = 5$, 13 Hz, 1H, 2'-H), 3.44 (dd, $J = 3.5$, 12.5 Hz, 1H, 3'-H),

3.95-4.64 (m, 3H, 4-H, 5-H), 5.20-5.35 (m, 1H, CHO), 5.96 (d, $J = 3$ Hz, 1H, NH), 6.97-7.32 ppm (m, 10H, aromatic H); ms: m/z 319 $[M+H]^+$.

Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.45; H, 5.65; N, 8.86.

General Procedure for the Preparation of **5a-d**, **6a-d**, **7a-c** and **8a-c** from **2a-d** or **3a-c**.

A mixture of **2a-d** or **3a-c** (10 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous ethanol (20 ml) or anhydrous methanol (20 ml) was stirred at room temperature overnight, and then cold water was added to the reaction mixture. 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 give **5a-d**, **6a-d**, **7a-c** and **8a-c**.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-6-methylfuro[2,3-*b*]pyridine-3a-carbonitrile (**5a**).

This compound was obtained as colorless plates (0.79 g, 38%), mp 46-48° (diethyl ether-petroleum ether); ir (potassium bromide): ν 2240 ($C\equiv N$) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.23 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 1.63-2.95 (m, 6H, 3-H, 4-H, 5-H), 2.06 (s, 3H, 6- CH_3), 3.78-4.12 ppm (m, 4H, 2-H, OCH_2CH_3); ms: m/z 209 $[M+H]^+$.

Anal. Calcd. for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45. Found: C, 63.65; H, 7.59; N, 13.23.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-2,6-dimethylfuro[2,3-*b*]pyridine-3a-carbonitrile (**5b**).

This compound was obtained as colorless needles (0.84 g, 38%), mp 54-55° (diethyl ether-petroleum ether); ir (potassium bromide): ν 2242 ($C\equiv N$) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.23 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 1.30 (d, $J = 6.5$ Hz, 3H, 2- CH_3), 1.56-2.48 (m, 5H, 3-H, 4-H, 5-H), 2.07 (s, 3H, 6- CH_3), 2.88 (dd, $J = 8.5$, 12.5 Hz, 1H, 5-H), 3.76-4.48 ppm (m, 3H, 2-H, OCH_2CH_3); ms: m/z 223 $[M+H]^+$.

Anal. Calcd. for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.64; H, 8.16; N, 12.38.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-6-methyl-2-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**5c**).

This compound was obtained as colorless needles (1.50 g, 53%), mp 102-104° (acetone-petroleum ether); ir (potassium bromide): ν 2241 ($C\equiv N$) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.17 and 1.28 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 1.69-2.18 (m, 3H, 3-H, 4-H), 2.09 and 2.11 (s, 3H, 6- CH_3), 2.30-2.64 (m, 2H, 3-H, 5-H), 2.97 and 3.19 (dd, $J = 10$, 12 Hz, dd, $J = 8.5$, 12.5 Hz, 1H, 5-H), 3.78-4.25 (m, 2H, OCH_2CH_3), 5.09-5.32 (m, 1H, 2-H), 7.31-7.36 ppm (m, 5H, aromatic H); ms: m/z 285 $[M+H]^+$.

Anal. Calcd. for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 72.07; H, 7.08; N, 9.94.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-6-methyl-3-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**5d**).

This compound was obtained as colorless needles (1.36 g, 48%), mp 138-140° (acetone-petroleum ether); ir (potassium bromide): ν 2242 ($C\equiv N$) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.34 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 1.70-2.09 (m, 2H, 4-H), 2.09 (s, 3H, 6- CH_3), 2.31-2.50 (m, 2H, 5-H), 3.34 (t, $J = 8.5$ Hz, 1H,

3-H), 3.94-4.44 (m, 4H, 2-H, OCH_2CH_3), 7.31-7.49 ppm (m, 5H, aromatic H); ms: m/z 285 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 72.07; H, 7.05; N, 9.79.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-6-methylfuro[2,3-*b*]pyridine-3a-carbonitrile (**6a**).

This compound was obtained as colorless columns (0.23 g, 12%), mp 62-63° (diethyl ether-petroleum ether); ir (potassium bromide): ν 2240 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.67-2.94 (m, 6H, 3-H, 4-H, 5-H), 2.08 (s, 3H, 6- CH_3), 3.56 (s, 3H, OCH_3), 3.99 ppm (dd, $J = 6.5, 8.5$ Hz, 2H, 2-H); ms: m/z 195 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_2$: C, 61.84; H, 7.27; N, 14.42. Found: C, 62.13; H, 7.18; N, 14.25.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-2,6-dimethylfuro[2,3-*b*]pyridine-3a-carbonitrile (**6b**).

This compound was obtained as colorless prisms (0.25 g, 12%), mp 68-69° (diethyl ether-petroleum ether); ir (potassium bromide): ν 2242 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.31 and 1.37 (t, $J = 6.5$ Hz, 3H, 2- CH_3), 1.58-1.98 (m, 2H, 4-H), 2.06 and 2.08 (s, 3H, 6- CH_3), 2.28-2.49 (m, 3H, 3-H, 5-H), 2.87 (dd, $J = 8.5, 12.5$ Hz, 1H, 5-H), 3.54 and 3.58 (s, 3H, OCH_3), 4.15-4.46 ppm (m, 1H, 2-H); ms: m/z 209 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_2$: C, 63.44; H, 7.74; N, 13.45. Found: C, 63.70; H, 7.96; N, 13.77.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-6-methyl-2-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**6c**).

This compound was obtained as colorless needles (0.68 g, 25%), mp 98-100° (acetone-petroleum ether); ir (potassium bromide): ν 2236 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.90-2.15 (m, 2H, 4-H), 2.10 and 2.13 (s, 3H, 6- CH_3), 2.31-2.65 (m, 3H, 3-H, 5-H), 2.85-3.30 (m, 1H, 5-H), 3.60 and 3.63 (s, 3H, OCH_3), 5.09-5.28 (m, 1H, 2-H), 7.26-7.37 ppm (m, 5H, aromatic H); ms: m/z 271 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.36; H, 6.43; N, 10.54.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-6-methyl-3-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**6d**).

This compound was obtained as colorless needles (0.90 g, 33%), mp 167-169° (acetone-petroleum ether); ir (potassium bromide): ν 2242 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.84-2.17 (m, 2H, 4-H), 2.11 (s, 3H, 6- CH_3), 2.32-2.52 (m, 2H, 5-H), 3.36 (t, $J = 9$ Hz, 1H, 3-H), 3.66 (s, 3H, OCH_3), 4.01 (t, $J = 9$ Hz, 1H, 2-H), 4.35 (t, $J = 9$ Hz, 1H, 2-H), 7.25-7.47 ppm (m, 5H, aromatic H); ms: m/z 271 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.10; H, 6.71; N, 10.39.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-6-methyl-4-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**7a**).

This compound was obtained as colorless prisms (0.54 g, 19%), mp 114-116° (acetone-petroleum ether); ir (potassium bromide): ν 2240 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.25 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 2.12 (s, 3H, 6- CH_3), 2.20-2.94 (m, 5H, 3-H, 4-H, 5-H), 3.93-4.13 (m, 2H, OCH_2CH_3), 7.37 ppm (s, 5H, aromatic H); ms: m/z 285 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.81; H, 7.09; N, 9.87.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-2,6-dimethyl-4-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**7b**).

This compound was obtained as colorless columns (0.53 g, 18%), mp 122-124° (acetone-petroleum ether); ir (potassium bromide): ν 2232 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.25 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 1.37 (d, $J = 6$ Hz, 3H, 2- CH_3), 2.10 (s, 3H, 6- CH_3), 2.22-2.99 (m, 5H, 3-H, 4-H, 5-H), 3.86-4.24 (m, 2H, OCH_2CH_3), 4.34-4.59 (m, 1H, 2-H), 7.39 ppm (s, 5H, aromatic H); ms: m/z 299 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_2$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.47; H, 7.49; N, 9.38.

7a-Ethoxy-2,3,3a,4,5,7a-hexahydro-6-methyl-2,4-diphenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**7c**).

This compound was obtained as colorless prisms (1.55 g, 43%), mp 188-190° (acetone-petroleum ether); ir (potassium bromide): ν 2251 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.17 (t, $J = 7$ Hz, 3H, OCH_2CH_3), 2.15 (s, 3H, 6- CH_3), 2.37-2.89 (m, 4H, 3-H, 4-H, 5-H), 3.07-3.31 (m, 1H, 4-H), 3.71-4.35 (m, 2H, OCH_2CH_3), 5.25-5.44 (m, 1H, 2-H), 7.25-7.50 ppm (m, 10H, aromatic H); ms: m/z 361 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.92; H, 6.63; N, 7.86.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-6-methyl-4-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**8a**).

This compound was obtained as colorless prisms (0.52 g, 19%), mp 153-154° (acetone-petroleum ether); ir (potassium bromide): ν 2241 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.13 (s, 3H, 6- CH_3), 2.13-2.95 (m, 5H, 3-H, 4-H, 5-H), 3.61 (s, 3H, OCH_3), 3.96-4.14 (m, 2H, 2-H), 7.37 ppm (s, 5H, aromatic H); ms: m/z 271 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.12; H, 6.72; N, 10.33.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-2,6-dimethyl-4-phenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**8b**).

This compound was obtained as colorless prisms (0.42 g, 15%), mp 151-153° (acetone-petroleum ether); ir (potassium bromide): ν 2242 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.38 and 1.39 (d, $J = 6.5$ Hz, 3H, 2- CH_3), 2.12 and 2.13 (s, 3H, 6- CH_3), 1.72-3.07 (m, 5H, 3-H, 4-H, 5-H), 3.60 and 3.63 (s, 3H, OCH_3), 4.18-4.60 (m, 1H, 2-H), 7.37 ppm (s, 5H, aromatic H); ms: m/z 285 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.86; H, 7.08; N, 9.87.

2,3,3a,4,5,7a-Hexahydro-7a-methoxy-6-methyl-2,4-diphenylfuro[2,3-*b*]pyridine-3a-carbonitrile (**8c**).

This compound was obtained as colorless prisms (0.48 g, 14%), mp 188-190° (acetone-petroleum ether); ir (potassium bromide): ν 2242 ($\text{C}\equiv\text{N}$) cm^{-1} ; ^1H nmr (deuteriochloroform): δ 2.19 (s, 3H, 6- CH_3), 2.11-3.09 (m, 5H, 3-H, 4-H, 5-H), 3.70 (s, 3H, OCH_3), 5.25 (dd, $J = 5, 8.5$ Hz, 1H, 2-H), 6.97-7.08 (m, 2H, aromatic H), 7.17-7.33 (m, 3H, aromatic H), 7.37 ppm (s, 5H, aromatic H); ms: m/z 347 $[\text{M}+\text{H}]^+$.

Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.29; H, 6.47; N, 8.05.

The Preparation of **7c** from **1c** and Benzalacetone.

A mixture of **1c** (1.86 g, 10 mmoles), benzalacetone (1.75 g, 12 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous ethanol (20 ml) was stirred at room temperature overnight, and then acetic acid (0.60 g, 10 mmoles) was added to the reaction mixture. The solvent was removed *in vacuo*, and then 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 give **7c** (1.50 g, 42%). The melting point and ir spectrum of this compound coincided with those of an authentic sample prepared from **3c** and sodium ethoxide.

The Preparation of **7c** from **1c**, Benzaldehyde and Acetone.

A mixture of **1c** (1.86 g, 10 mmoles), benzaldehyde (1.59 g, 15 mmoles), acetone (1.59 g, 20 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous ethanol (20 ml) was stirred at room temperature overnight. After work-up as described above, compound **7c** (0.89 g, 25%) was obtained. The melting point and ir spectrum of this compound coincided with those of an authentic sample prepared from **3c** and sodium ethoxide.

General Procedure for the Preparation of **9a-d** and **10a-c** from **5a-d**, **6a-d** or **7a-c**, **8a-c**.

A solution of **5a-d**, **6a-d**, **7a-c** or **8a-c** (10 mmoles) and potassium *tert*-butoxide (1.12 g, 10 mmoles) in anhydrous *tert*-butyl alcohol (30 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 yield **9a-d** and **10a-c**.

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

This compound was obtained as colorless plates [from **5a**: 0.88 g (65%), from **6a**: 0.92 g (68%)], mp 41-42° (diethyl ether-petroleum ether); ¹H nmr (deuteriochloroform): δ 2.41 (s, 3H, 6-CH₃), 3.19 (t, J = 8.5 Hz, 2H, 3-H), 4.59 (t, J = 8.5 Hz, 2H, 2-H), 6.62 (d, J = 7 Hz, 1H, 5-H), 7.34 ppm (d, J = 7 Hz, 1H, 4-H); ms: m/z 136 [M+H]⁺.

Anal. Calcd. for C₈H₉NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.02; H, 6.75; N, 10.37.

2,3-Dihydro-2,6-dimethylfuro[2,3-*b*]pyridine (**9b**).

This compound was obtained as pale yellow oil [from **5b**: 1.08 g (72%), from **6b**: 0.93 g (62%)]; ¹H nmr (deuteriochloroform): δ 1.47 (d, J = 6 Hz, 3H, 2-CH₃), 2.41 (s, 3H, 6-CH₃), 2.66 (dd, J = 7, 15.5 Hz, 1H, 3-H), 3.31 (dd, J = 8.5, 15.5 Hz, 1H, 3-H), 4.75-5.13 (m, 1H, 2-H), 6.60 (d, J = 7 Hz, 1H, 5-H), 7.30 ppm (d, J = 7 Hz, 1H, 4-H); ms: m/z 150 [M+H]⁺.

Anal. Calcd. for C₉H₁₁NO: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.19; H, 7.46; N, 9.24.

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

This compound was obtained as colorless prisms [from **5c**: 1.62 g (77%), from **6c**: 1.48 g (70%)], mp 66-67° (diethyl ether-petroleum ether); ¹H nmr (deuteriochloroform): δ 2.46 (s, 3H, 6-CH₃), 3.13 (dd, J = 8, 16 Hz, 1H, 3-H), 3.64 (dd, J = 9.5, 16 Hz, 1H, 3-H), 5.80 (dd, J = 8, 9.5 Hz, 1H, 2-H), 6.66 (d, J = 7 Hz, 1H, 5-H), 7.26-7.43 ppm (m, 6H, 4-H, aromatic H); ms: m/z 212 [M+H]⁺.

Anal. Calcd. for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.52; H, 6.17; N, 6.42.

2,3-Dihydro-6-methyl-3-phenylfuro[2,3-*b*]pyridine (**9d**).

This compound was obtained as colorless prisms [from **5d**: 1.48 g (70%), from **6d**: 1.27 g (60%)], mp 67-68° (diethyl ether-petroleum ether); ¹H nmr (deuteriochloroform): δ 2.46 (s, 3H, 6-CH₃), 4.35-4.73 (m, 2H, 2-H), 4.94 (dd, J = 7, 8.5 Hz, 1H, 3-H), 6.66 (d, J = 7 Hz, 1H, 5-H), 7.14-7.36 ppm (m, 6H, 4-H, aromatic H); ms: m/z 212 [M+H]⁺.

Anal. Calcd. for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.49; H, 6.30; N, 6.71.

2,3-Dihydro-6-methyl-4-phenylfuro[2,3-*b*]pyridine (**10a**).

This compound was obtained as colorless needles [from **7a**: 1.89 g (90%), from **8a**: 1.71 g (80%)], mp 105-106° (acetone-petroleum ether); ¹H nmr (deuteriochloroform): δ 2.47 (s, 3H, 6-CH₃), 3.30 (t, J = 8.5 Hz, 2H, 3-H), 4.60 (t, J = 8.5 Hz, 2H, 2-H), 6.75 (s, 1H, 5-H), 7.45 ppm (s, 5H, aromatic H); ms: m/z 212 [M+H]⁺.

Anal. Calcd. for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.69; H, 6.18; N, 6.58.

2,3-Dihydro-2,6-dimethyl-4-phenylfuro[2,3-*b*]pyridine (**10b**).

This compound was obtained as colorless needles [from **7b**: 2.08 g (92%), from **8b**: 1.83 g (81%)], mp 115-117° (acetone-petroleum ether); ¹H nmr (deuteriochloroform): δ 1.48 (d, J = 6 Hz, 3H, 2-CH₃), 2.47 (s, 3H, 6-CH₃), 2.88 (dd, J = 7, 16 Hz, 1H, 3-H), 3.44 (dd, J = 9.5, 16 Hz, 1H, 3-H), 4.77-5.17 (m, 1H, 2-H), 6.74 (s, 1H, 5-H), 7.44 ppm (s, 5H, aromatic H); ms: m/z 226 [M+H]⁺.

Anal. Calcd. for C₁₅H₁₅NO: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.07; H, 6.72; N, 6.25.

2,3-Dihydro-6-methyl-2,4-diphenylfuro[2,3-*b*]pyridine (**10c**).

This compound was obtained as colorless needles [from **7c**: 2.62 g (91%), from **8c**: 2.61 g (91%)], mp 119-121° (acetone-petroleum ether); ¹H nmr (deuteriochloroform): δ 2.51 (s, 3H, 6-CH₃), 3.27 (dd, J = 8, 16 Hz, 1H, 3-H), 3.76 (dd, J = 9.5, 16 Hz, 1H, 3-H), 5.82 (dd, J = 8, 9.5 Hz, 1H, 2-H), 6.80 (s, 1H, 5-H), 7.25-7.51 ppm (m, 10H, aromatic H); ms: m/z 288 [M+H]⁺.

Anal. Calcd. for C₂₀H₁₇NO: C, 83.59; H, 5.96; N, 4.87. Found: C, 83.47; H, 5.96; N, 4.90.

General Procedure for the Preparation of **11a-c** from **4a-c** and Sodium Ethoxide.

A mixture of **4a-c** (10 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous ethanol (30 ml) was refluxed for 2 hours. 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 give **11a-c**.

2,3-Dihydro-4-phenylfuro[2,3-*b*]pyridine (**11a**).

This compound was obtained as colorless columns (1.16 g, 59%), mp 77-78° (diethyl ether-petroleum ether); ¹H nmr (deuteriochloroform): δ 3.36 (t, J = 8.5 Hz, 2H, 3-H), 4.62 (t, J = 8.5 Hz, 2H, 2-H), 6.88 (d, J = 5.5 Hz, 1H, 5-H), 7.47 (s, 5H, aromatic H), 8.05 ppm (d, J = 5.5 Hz, 1H, 6-H); ms: m/z 198 [M+H]⁺.

Anal. Calcd. for C₁₃H₁₁NO: C, 79.17; H, 5.62; N, 7.10. Found: C, 79.16; H, 5.73; N, 7.12.

2,3-Dihydro-2-methyl-4-phenylfuro[2,3-*b*]pyridine (**11b**).

This compound was obtained as colorless needles (0.97 g, 46%), mp 55-56° (diethyl ether-petroleum ether); ¹H nmr (deuteriochloroform): δ 1.50 (d, J = 6 Hz, 3H, 2-CH₃), 2.94 (dd, J = 7.5, 16.5 Hz, 1H, 3-H), 3.48 (dd, J = 8, 16.5 Hz, 1H, 3-H), 4.77-5.16 (m, 1H, 2-H), 6.87 (d, J = 5.5 Hz, 1H, 5-H), 7.46 (s, 5H, aromatic H), 8.04 ppm (d, J = 5.5 Hz, 1H, 6-H); ms: m/z 212 [M+H]⁺.

Anal. Calcd. for C₁₄H₁₃NO: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.59; H, 6.26; N, 6.65.

2,3-Dihydro-2,4-diphenylfuro[2,3-*b*]pyridine (**11c**).

This compound was obtained as colorless needles (0.77 g, 28%), mp 120-122° (acetone-petroleum ether); ¹H nmr (deuteriochloroform): δ 3.33 (dd, J = 8, 16.5 Hz, 1H, 3-H), 3.82 (dd, J = 9.5, 16.5 Hz, 1H, 3-H), 5.83 (dd, J = 8, 9.5 Hz, 1H, 2-H), 6.94 (d, J = 5.5 Hz, 1H, 5-H), 7.25-7.53 (m, 10H, aromatic H), 8.12 ppm (d, J = 5.5 Hz, 1H, 6-H); ms: m/z 274 [M+H]⁺.

Anal. Calcd. for C₁₉H₁₅NO: C, 83.49; H, 5.53; N, 5.12. Found: C, 83.47; H, 5.67; N, 5.11.

The Preparation of **6d** from **5d** and Sodium Methoxide.

A mixture of **5d** (1.42 g, 5 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous methanol (50 ml) was refluxed for 3 hours. 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 **6d** (0.84 g, 62%). The melting point and ir spectrum of this compound coincided with those of an authentic sample prepared from **2d** and sodium methoxide.

The Preparation of **5d** from **6d** and Sodium Ethoxide.

A mixture of **6d** (1.35 g, 5 mmoles) in a solution of sodium (0.23 g, 10 mmoles) in anhydrous ethanol (50 ml) was refluxed for 3 hours. After work-up as described above, compound **5d** (0.31 g, 22%) was obtained. The melting point and ir spectrum of this compound coincided with those of an authentic sample prepared from **2d** and sodium ethoxide.

General Procedure for the Preparation of **10a-c** and **11a-c** from **1a-c** and Benzalacetone or Cinnamaldehyde.

A mixture of **1a-c** (10 mmoles) and benzalacetone (1.75 g, 12 mmoles) or cinnamaldehyde (1.58 g, 12 mmoles) in a solution of sodium (0.46 g, 20 mmoles) in anhydrous ethanol (30 ml) was stirred at room temperature overnight, and then refluxed for 1 hours. 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 **10a** (0.97 g, 46%), **10b** (0.99 g, 44%), **10c** (1.29 g, 45%), **11a** (0.86 g, 44%), **11b** (0.79 g, 37%) and **11c** (0.83 g, 30%), respectively.

General Procedure for the Preparation of **9a-d** from **1a-d** and Methyl Vinyl Ketone.

A mixture of **1a-d** (10 mmoles) and methyl vinyl ketone (0.84 g, 12 mmoles) in a solution of sodium (0.46 g, 20 mmoles) in anhydrous ethanol (30 ml) was stirred at room temperature overnight. 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*. After potassium *tert*-butoxide (2.24 g, 20 mmoles) was added to the residue in anhydrous *tert*-butyl alcohol (30 ml), the mixture 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 yield **9a** (0.58 g, 43%), **9b** (0.82 g, 55%), **9c** (1.01 g, 48%) and **9d** (0.96 g, 45%), respectively.

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