Ultrasound Assisted Pictet–Spengler Synthesis of Tetrahydro-β-Carboline Derivatives

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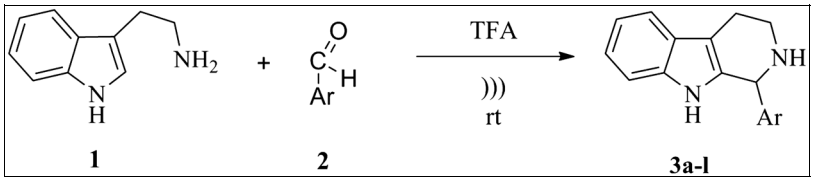

The synthesis of twelve tetrahydro-β-carboline derivatives **3a–3l** prepared via the Pictet–Spengler reaction is described. The reaction of tryptamine and a variety of arylaldehydes were carried out under ultrasonic irradiation and trifluoracetic acid catalysis at room temperature. These tetrahydro-β-carbolines have been synthesized in higher yields and shorter reaction times compared to the conventional method. Moreover, the reaction proceeded successfully even employing arylaldehydes with electron-donating or electron-attracting substituents which did not react under conventional method.

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The β-carboline core is the common nucleus of many synthetic indole alkaloids as well as those extracted from natural sources associated with a broad spectrum of biochemical and pharmacological properties [1–6].

β-Carbolines possess planar aromatic tricyclic structures, and many derivatives are widely distributed in nature: in plants, marine life, human tissues, and body fluids. Several β-carboline compounds have antitumor and anti-cancer properties. Moreover, their multiple physiological effects, such as the inhibition of cyclin-dependent kinase (CDK), IkappaB kinase (IKK), and topoisomerase I lead to an increasing interest in this class of structure for clinical purposes. A series of 3-amino- or 3-benzylamino-β-carboline derivatives was recently synthesized, and their antitumor activities for Hela S-3 and Sarcoma 180 cell lines were evaluated [7]. 3-Benzylamino-β-carboline derivatives induce apoptosis through G2/M arrest in human carcinoma cells HeLa S-3 [8]. Mechanistic studies indicate that β-carboline derivatives inhibit DNA topoisomerases and interfere with DNA synthesis. They interact with DNA via both groove binding and intercalative modes and cause major DNA structural changes [9]. In this sense, β-carboline derivatives were tested as novel photosensitizers [10], and their solid-state photoluminescent properties were also discussed [11].

Many alkaloids have been reported to be active against leishmaniasis. The β-carboline alkaloid harmaline isolated from *Peganum harmala* (Syrian Rue) has exhibited a strong amastigote specific activity with an IC_{50} of 1.16 μM. The metabolite harmine occurring in same plant has also shown significant activity *in vivo*. The pyrimidine-β-carboline alkaloid annomontine, isolated from *Annona foetida*, has been reported to show antileishmanial activity (IC_{50} 34.8 μM) against *Leishmania braziliensis* (Fig. 1). Moreover, several synthetically modified β-carboline derivatives have also been studied against leishmaniasis [12,13]. The interactions between β-carboline alkaloids and bovine serum albumin (BSA) were analyzed recently [14] as well as the wild type B-Raf kinase inhibitory activity of 1-carboxamide and 6-sulfonamide-substituted β-carboline derivatives [15] and the antioxidant activity of 1-aryl-tetrahydro-β-carboline derivatives [16].

The extensive biological activity of this class of molecules has naturally attracted much attention from the synthetic community. Traditional methods toward β-carbolines involve Pictet–Spengler [17] or Bischler–Napieralski condensations of tryptamine or tryptophan (Scheme 1), followed by aromatization. More recent approaches have involved palladium-catalyzed cross-coupling methodologies [18].

In this regard the use of ultrasound (US) in chemistry (sonochemistry) offers the synthetic chemist a method of chemical activation which has broad applications and uses equipment which is relatively inexpensive. The driving force for sonochemistry is cavitation, and so a general requirement is that at least one of the phases of the reaction mixture should be a liquid. The ever expanding number of applications of sonochemistry in synthesis has made the subject attractive to many experimentalists and interest has spread beyond academic laboratories into industry and chemical engineering [19].

Recently, US has been utilized to accelerate a wide number of synthetically useful organic reactions. In addition to the field of organic chemistry, sonochemistry has also been used in the preparation of micro and

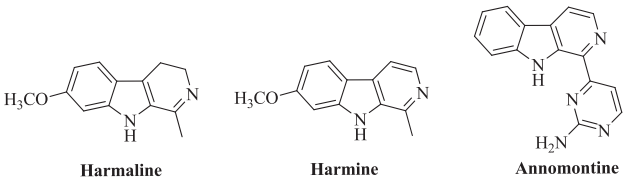


Figure 1. Natural β-carboline alkaloids.

nanomaterials and also has many therapeutic and diagnostic applications [20].

The Pictet–Spengler synthesis of tetrahydro-β-carbolines at room temperature, in methylene chloride and trifluoracetic acid (TFA) as catalyst has been reported by Buthani *et al*. [12]. In this work we present the preparation of 1-aryl-tetrahydro-β-carbolines under US-assisted methodology in order to remark its advantages [21]. Our interest in this target heterocycle is stimulated by their close structural relationship to molecules with antileishmanial and antitubercular activities [22,23].

Herein, the synthesis of 12 tetrahydro-β-carboline derivatives (**3a–3l**) prepared via the Pictet–Spengler reaction and a sonochemical method is described (Table 1). The reaction of tryptamine (**1**) and a variety of arylaldehydes (**2**) was carried out under ultrasonic irradiation in methylene chloride and TFA catalysis at room temperature in good to excellent yields (Scheme 2). The reactions proceed to completion between 1 and 2 h; meanwhile, when they were performed under conventional method the reaction times extended to 24–48 h, and the yields were lower or similar, and no reaction took place with some arylaldehydes. Moreover the US-assisted synthesis succeeded when the conventional method failed. Arylaldehydes having either electron-withdrawing or -donating groups underwent Pictet–Spengler reaction with **1** to furnish **3a–l**. This is unlike the traditional Pictet–Spengler protocol involving aprotic solvents wherein aldehydes bearing electron-donating substituents failed to undergo cyclization and furnished imines as the only product. This was attributed to the decrease in the reactivity of the iminium ion intermediate derived from aldehydes bearing the electron-donating group, which in turn prevented the formation of tetrahydro-β-carbolines [23]. The use of TFA proved to be more efficient than the hydrochloric acid catalysis under both experimental conditions and the reactions did not take place without catalysis [23–25]. The ^{1}H NMR, ^{13}C NMR spectra, and HSQC data unequivocally proved the 1-aryl-tetrahydro-β-carboline structures.

In conclusion, we worked out a novel synthesis of 12 1-aryl-tetrahydro-β-carboline derivatives under ultrasonic irradiation. We described a mild, convenient, and simple procedure for the condensation of tryptamine and a substituted arylaldehyde, and the method can be extended to aliphatic aldehydes. This series could be obtained in good yields and short times in a one-pot US-assisted Pictet–Spengler reaction from affordable starting materials and under TFA catalysis. These advantages are noteworthy when the synthesis is focused on designing potential pharmacological compounds such as 1-substituted tetrahydro-β-carbolines as well as 1-substituted-β-carbolines.

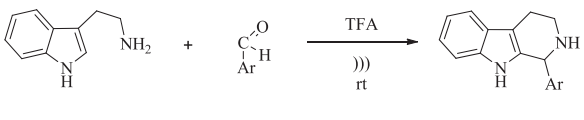
Table 1

Synthesized tetrahydro-β-carbolines: advantages of sonochemical method over conventional method.

		Conventional method		Ultrasound irradiation	
Compound	Ar	Time (h)	Yield (%)	Time (h)	Yield (%)
3a	C_6H_5	24	25	2	66
3b	2-$NO_2C_6H_4$	48	70	1	71
3c	4-$NO_2C_6H_4$	24	50	1	82
3d	2-ClC_6H_4	48	nr	1	87
3e	4-ClC_6H_4	24	51	2	85
3f	4-$CF_3C_6H_4$	48	nr	2	72
3g	3-OCH_3-4-OHC_6H_3	12	51	2	64
3h	3,4-*di*-$OCH_3C_6H_3$	48	nr	1	54
3i	3,5-*di*-$OCH_3C_6H_3$	48	nr	1	63
3j	3,4,5-*tri*-$OCH_3C_6H_2$	24	33	1	43
3k	3,5-*di*-OCH_3-4-BrC_6H_3	24	53	2	62
3l	6-OCH_3-2-Naph.	48	12	2	79

nr: no reaction

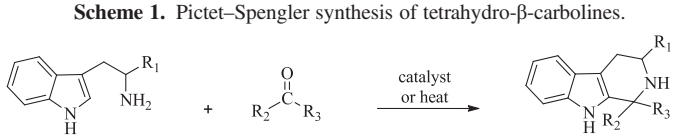
Scheme 2. Synthesis of 1-aryl- tetrahydro-β-carbolines **3a–l** by US-assisted method.



1 **2** **3a-l**

Ar:
a C_6H_5 **g** 3-OCH_3-4-OHC_6H_3
b 2-$NO_2C_6H_4$ **h** 3,4-*di*-$OCH_3C_6H_3$
c 4-$NO_2C_6H_4$ **i** 3,5-*di*-$OCH_3C_6H_3$
d 2-ClC_6H_4 **j** 3,4,5-*tri*-$OCH_3C_6H_2$
e 4-ClC_6H_4 **k** 4-Br-3,5-*di*-$OCH_3C_6H_2$
f 4-$CF_3C_6H_4$ **l** 6-OCH_3-2-Naph

Scheme 1. Pictet–Spengler synthesis of tetrahydro-β-carbolines.



Tryptophan, R_1= COOH
Tryptamine, R_1= H

1,2,3,4-tetrahydro-β-carboline

EXPERIMENTAL

Melting points were determined in a capillary Electrothermal 9100 SERIES-Digital apparatus and are uncorrected. ^{1}H and ^{13}C-NMR spectra were recorded at room temperature using a Bruker 300-MHz spectrometer and DMSO-d_6 as solvent. The operating frequencies for protons and carbons were 300.13 and 75.46 MHz, respectively. The chemical shifts (δ) were given in ppm. IR spectra were recorded on an FT Perkin Elmer Spectrum One from KBr discs. Mass spectra were measured on MS/DSQ II. Elemental analysis (C, H, and N) were performed on an Exeter CE 440, and the results were within ±0.4% of the calculated values. Analytical TLCs were performed on DC-Alufolien Kieselgel 60F_{254} Merck. The ultrasonic irradiation was performed by using an Arcano ultrasonic cleaner bath, with digital timer and heater switch, 70 W, 2.0 L, and 40 KHz.

General procedure for the synthesis of compounds 3a–3l. A mixture of 1.00 mmol (0.16 g) of tryptamine, 1.5 mmol of a variety of arylaldehydes, 0.15 mL TFA, and 10 mL of CH_2Cl_2 was subjected to ultrasonic irradiation or conventional method, at room temperature. The reaction was monitored by TLC (CH_2Cl_2: CH_3OH, 4:1).

(±) 2,3,4,9-Tetrahydro-1-phenyl-1H-pyrido[3,4-b]-indole 3a. The product was triturated with benzene at rt, white powder, mp 160–162°C according to lit 160–161°C [26].

^{1}H-NMR: δ 3.05–3.10 (2H, m, 4-CH_2), 3.46–3.51 (2H, m, 3-CH_2), 6.07 (1H, s, CH), 7.11 (1H, t, Het-H, *J* = 7.6 Hz), 7.15 (1H, t, Het-H, *J* = 7.8 Hz), 7.27–7.44 (7H, m, Ph-H and H-Het), 9.70 (1H, s, NH), 10.8 (1H, s, NH). ^{13}C-NMR: δ 22.6, 58.1, 107.2, 111.0, 118.4, 119.5, 121.7, 127.4, 128.3, 128.7, 129.2, 134.7, 136.5, 142.3. IR (cm^{-1}): υ 3401, 2930, 2857, 1597, 770. Anal. Calcd. for $C_{17}H_{16}N_2$: C, 82.22; H, 6.49; N, 11.28. Found: C, 81.92; H, 6.17; N, 11.16.

(±) 2,3,4,9-Tetrahydro-1-(2-nitrophenyl)-1H-pyrido[3,4-b]-indole 3b. The product was crystallized from benzene, yellow powder, mp 212–215°C.

^{1}H-NMR: δ 3.02–3.08 (2H, m, 4-CH_2), 3.13–3.19 (1H, m, 3-H), 3.56–3.60 (1H, m, 3′-H), 6.45 (1H, s, CH), 7.05–7.17 (2H, m, Ph-H), 7.23–7.26 (1H, m, Het-H), 7.34 (1H, d, *J* = 7.9 Hz, Het-H), 7.58 (1H, d, *J* = 7.6 Hz, Het-H), 7.77- 7.80 (2H, m, Ph-H), 8.32- 8.35 (1H, m, Het-H), 9.44 (1H, s, NH), 10.20 (1H, s, NH). ^{13}C-NMR: δ 11.8, 50.8, 108.8, 112.2, 118.9, 119.7, 122.8, 125.9, 126.0, 127.6, 129.9, 131.8, 132.9, 135.0, 136.9, 149.2. MS (*m/z*): 293 (M^+, 100), 247 ([$M^+ - NO_2$], 22), 171 ([$M^+ - C_6H_4NO_2$], 60), 69 (C_4H_7N, 81). Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.60; H, 5.15; N, 14.30. Found: C, 70.20; H, 5.47; N, 13.8.

(±) 2,3,4,9-Tetrahydro-1-(4-nitrophenyl)-1H-pyrido[3,4-b]-indole 3c. The product was triturated with hot CH_2Cl_2, yellow powder, mp 194–196°C.

^{1}H-NMR: δ 3.06–3.10 (2H, m, 4-CH_2), 3.45–3.49 (2H, m, 3-CH_2), 6.14 (1H, s, CH), 7.06 (1H, t, *J* = 7.3 Hz, Het-H), 7.13 (1H, t, *J* = 7.3 Hz, Het-H), 7.29 (1H, d, *J* = 8.1 Hz, Het-H), 7.55 (1H, d, *J* = 8.1 Hz, Het-H), 7.67 (2H, d, *J* = 8.8 Hz, Ph-H), 8.34 (2H, d, *J* = 8.8 Hz, Ph-H), 9.79 (1H, s, NH), 10.95 (1H, s, NH). ^{13}C-NMR: δ 18.1, 54.6, 107.7, 111.6, 118.3, 119.2, 122.2, 123.8, 125.6, 127.5, 131.6, 136.6, 141.5, 148.3. IR (cm^{-1}): υ 3394, 2495, 1666, 1514, 1353, 1178, 842. Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.60; H, 5.15; N, 14.30. Found: C, 69.30; H, 5.35; N, 14.10.

(±) 1-(2-Chlorophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indole 3d. The product was crystallized from cyclohexane, white powder mp 206–209°C.

^{1}H-NMR: δ 2.93–3.10 (2H, m, 4-CH_2), 3.27–3.47 (2H, m, 3-CH_2), 6.09 (1H, s, CH), 7.02–7.14 (3H, m, Ph-H), 7.28 (1H, d, *J* = 7.8 Hz, Het-H), 7.37 (1H, t, *J* = 7.3 Hz, Het-H), 7.47–7.55 (2H, m, Het-H y Ph-H), 7.66 (1H, d, *J* = 7.8 Hz, Het-H), 9.35 (1H, s, NH), 10.91 (1H, s, NH). ^{13}C-NMR: δ 19.4, 52.9, 108.6, 111.9, 118.6, 119.5, 122.4, 126.2, 127.7, 128.1, 129.1, 130.4, 131.6, 131.8, 134.1, 134.5, 136.9. Anal. Calcd. for $C_{17}H_{15}ClN_2$: C, 72.21; H, 5.35; N, 9.91. Found: C, 71.80; H, 5.54; N, 10.11.

(±) 1-(4-Chlorophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indole 3e. The product was triturated with CH_2Cl_2 at rt, yellow powder, mp 220–222°C.

^{1}H-NMR: δ 3.00–3.16 (2H, m, 4-CH_2), 3.44–3.50 (2H, m, 3-CH_2), 6.00 (1H, s, CH), 7.07 (1H, t, *J* = 7.8 Hz, Het-H), 7.14 (1H, t, *J* = 7.8 Hz, Het-H), 7.31 (1H, d, *J* = 8.0 Hz, Het-H), 7.40 (2H, d, *J* = 8.7 Hz, Ph-H), 7.56 (1H, d, *J* = 7.8 Hz, Het-H), 7.59 (2H, d, *J* = 8.5 Hz, Ph-H), 9.20 (1H, s, NH), 10.90 (1H, s, NH). ^{13}C-NMR: δ 18.6, 55.3, 197.9, 112.0, 118.7, 119.6, 122.6, 126.1, 128.5, 129.4, 132.3, 134.0, 135.1, 137.0. Anal. Calcd. for $C_{17}H_{15}ClN_2$: C, 72.21; H, 5.35; N, 9.91. Found: C, 72.50; H, 5.21; N, 9.76.

(±) 1-(4-(Trifluorometyl)phenyl)-2,3,4,9-tetrahydro-1H-pyrido [3,4-b]-indole 3f. The product was triturated with hot CH_2Cl_2, white powder, mp 243–245°C.

^{1}H-NMR: δ 3.04–3.08 (2H, m, 4-CH_2), 3.36–3.51 (2H, m, 3-CH_2), 6.10 (1H, s, CH), 7.06 (1H, t, *J* = 7.0 Hz, Het-H), 7.14 (1H, t, *J* = 6.9 Hz, Het-H), 7.30 (1H, d, *J* = 8.0 Hz, Het-H), 7.56 (1H, d, *J* = 7.6 Hz, Het-H), 7.62 (2H, d, *J* = 8.0 Hz, Ph-H), 8.00 (2H, d, *J* = 7.9 Hz, Ph-H), 9.70 (1H, s, NH), 10.90 (1H, s, NH). ^{13}C-NMR: δ 18.6, 55.4, 108.1, 112.0, 118.8, 119.7, 122.7, 126.1, 126.3, 128.2, 130.4, 130.8, 131.4, 137.0, 139.6. Anal. Calcd. for $C_{18}H_{15}F_3N_2$: C, 68.35; H, 4.78; N, 8.86. Found: C, 68.13; H, 4.89; N, 8.97.

(±)1-(4-Hydroxy-2-methoxyphenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indole 3g. The product was triturated with hot CH_2Cl_2, white powder, mp 217–219°C.

^{1}H-NMR: δ 2.97–3.13 (2H, m, 4-CH_2), 3.46–3.48 (2H, m, 3-CH_2), 3.74 (3H, s, OCH_3), 5.84 (1H, s, CH), 6.70 (1H, d, *J* = 8.1 Hz, Ph-H), 6.85 (1H, d, *J* = 8.3 Hz, Ph-H), 7.01–7.14 (3H, m, 2 Het-H y Ph-H), 7.30 (1H, d, *J* = 8.0 Hz, Het-H), 7.52 (1H, d, *J* = 7.6 Hz, Het-H), 9.48 (1H, s, NH), 9.77 (1H, s, OH), 9.82 (1H, s, NH). ^{13}C-NMR: δ 18.6, 56.1, 56.2, 107.6, 112.0, 114.2, 115.9, 118.6, 119.5, 122.4, 123.1, 125.5, 126.1, 129.2, 136.9, 148.2, 148.5. MS (*m/z*): 293 (M^+, 28), 294 ([M^++1], 40), 171 ([M^++1- $C_7H_7O_2$], 13), 69 (C_4H_7N, 100). Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 70.45; H, 6.17; N, 9.50. Found: C, 70.40; H, 6.36; N, 9.02.

(±) 2,3,4,9-Tetrahydro-1-(3,4-dimethoxyphenyl)-1H-pyrido [3,4-b]-indole 3h. The product was triturated with hot CH_2Cl_2, white powder, mp 238–239°C.

^{1}H-NMR: δ 3.03–3.10 (2H, m, 4-CH_2), 3.10–3.45 (2H, m, 3-CH_2), 3.74 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 5.89 (1H, s, CH), 6.82 (1H, d, *J* = 8.3 Hz, Ph-H), 7.03–7.15 (4H, m, Ph-H y Het-H), 7.30 (1H, d, *J* = 7.9 Hz, Het-H), 7.53 (1H, d, *J* = 7.7 Hz, Het-H), 9.21 (1H, s, NH), 9.83 (1H, s, NH). ^{13}C-NMR: δ 18.6, 56.1, 99.1, 107.6, 112.0, 112.2, 113.7, 118.7, 119.5, 122.5, 122.9, 126.1, 127.0, 129.1, 136.9, 149.3, 150.4. MS (*m/z*): 308 (M^+, 100), 248 ([M^+- 2(CH_3)], 46), 171 ([M^+- $C_8H_9O_2$], 38), 69 (C_4H_7N, 55). Anal. Calcd. for $C_{19}H_{20}N_2O_2$: C, 74.20; H, 6.51; N, 9.08. Found: C, 73.81; H, 6.04; N, 8.94.

(±) 2,3,4,9-Tetrahydro-1-(3,5-dimethoxyphenyl)- 1H-pyrido [3,4-b]-indole 3i. The product was triturated with hot CH_2Cl_2, white powder, mp 208–209°C.

^{1}H-NMR: δ 2.97–3.15 (2H, m, 4-CH_2), 3.38–3.53 (2H, m, 3-CH_2), 3.75 (6H, s, OCH_3), 5.88 (1H, s, CH), 6.56 (2H, s, Ph-H), 6.65 (1H, s, Ph-H), 7.05 (1H, t, J = 6.9 Hz, Het-H), 7.13 (1H, t, J = 6.0 Hz, Het-H), 7.31 (1H, d, J = 8.0 Hz, Het-H), 7.53 (1H, d, J = 7.7 Hz, Het-H), 9.31 (1H, s, NH), 9.92 (1H, s, NH). ^{13}C-NMR: δ 19.3, 46.2, 55.9, 56.2, 101.5, 107.6, 108.3, 112.0, 118.7, 119.5, 122.5, 126.1, 128.7, 136.9, 137.1, 159.2, 161.2. Anal. Calcd. for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 73.65; H, 6.69; N, 9.28.

(±) 2,3,4,9-Tetrahydro-1-(3,4,5-trimethoxyphenyl)-1H-pyrido [3,4-b]-indole 3j. The product was triturated with hot CH_2Cl_2, white powder, mp 227–230°C.

^{1}H-NMR: δ 2.98–3.04 (1H, m, 4-H), 3.11–3.17 (1H, m, 4′-H), 3.44–3.46 (1H, m, 3-H), 3.58–3.60 (1H, m, 3′-H), 3.70 (3H, s, OCH_3), 3.74 (6H, s, OCH_3), 5.89 (1H, s, CH), 6.75 (2H, s, Ph-H), 7.06 (1H, t, J = 7.7 Hz, Het-H), 7.11 (1H, t, J = 7.1 Hz, Het-H), 7.32 (1H, d, J = 8.0 Hz, Ph-H), 7.54 (1H, d, J = 7.6 Hz, Het-H), 9.46 (1H, s, NH), 9.87 (1H, s, NH). ^{13}C-NMR: δ 18.7, 23.4, 56.5, 56.7, 60.5, 107.6, 107.7, 112.1, 118.7, 119.5, 122.5, 126.2, 128.9, 130.4, 137.0, 139.0, 153.5. Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 14.18. Found: C, 71.30; H, 6.41; N, 13.97.

(±) 1-(4-Bromo-3,5-dimethoxyphenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indole 3k. The product was triturated with hot CH_2Cl_2, yellow powder, mp 166–169°C.

^{1}H-RMN: δ 3.05–3.18 (2H, m, 4-CH_2), 3.61–3.65 (2H, m, 3-CH_2), 3.80 (6H, s, OCH_3), 5.95 (1H, s, CH), 6.83 (2H, s, Ph-H), 7.05 (1H, t, J = 6.9 Hz, Het-H), 7.13 (1H, t, J = 7.0 Hz, Het-H), 7.30 (1H, d, J = 7.9 Hz, Het-H), 7.53 (1H, d, J = 7.7 Hz, Het-H), 9.51 (1H, s, NH), 10.11 (1H, s, NH). ^{13}C-RMN: δ 18.6, 41.6, 57.0, 101.7, 106.8, 107.7, 112.1, 118.8, 119.6, 122.6, 126.1, 128.6, 135.8, 137.1, 157.2. Anal. Calcd. for $C_{19}H_{19}BrN_2O_2$: C, 58.93; H, 4.95; N, 7.23. Found: C, 59.19; H, 4.80; N, 7.16.

(±) 2,3,4,9-Tetrahydro-1-(2-methoxynaphthalen-6-yl)-1H-pyrido [3,4-b]-indole 3l. The product was triturated with hot CH_2Cl_2, white powder, mp 234–236°C.

^{1}H-RMN: δ 3.02–3.16 (2H, m, 4-CH_2), 3.51–3.52 (2H, m, 3-CH_2), 3.90 (3H, s, OCH_3), 6.09 (1H, s, CH), 7.07–7.13 (2H, m, Het-H), 7.23 (1H, dd, J = 2.5 y 8.9 Hz, Naft-H), 7.28 (1H, d, J = 7.8 Hz, Het-H), 7.40 (1H, d, J = 2.1 Hz, Naft-H), 7.45 (1H, d, J = 8.5 Hz, Naft-H), 7.56 (1H, d, J = 7.5 Hz, Het-H), 7.88–7.95 (3H, m, Naft-H), 9.36 (1H, s, NH), 9.98 (1H, s, NH). ^{13}C-RMN: δ 55.8, 56.4, 106.3, 107.9, 112.1, 118.7, 119.6, 119.9, 122.5, 126.2, 127.6, 127.9, 128.4, 129.0, 129.9, 130.0, 135.4, 137.1, 158.6. Anal. Calcd. for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.83; H, 5.93; N, 8.29.

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