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A SIMPLE METHOD FOR THE SYNTHESIS OF 1-SUBSTITUTED β-CARBOLINE DERIVATIVES FROM TRYPTAMINE AND CARBOXYLIC ACIDS IN POLYPHOSPHORIC ACID

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Abstract – A number of 1-substituted 3,4-dihydro-9*H*-β-carboline derivatives (**4**) with high purity and yields have been synthesized by treating of tryptamine (**1**) with carboxylic acids (**2**) in polyphosphoric acid. 3,4-Dihydro-9*H*-β-carbolines (**4**) were successfully transformed to 1,2,3,4-tetrahydro-9*H*-β-carbolines (**5**) and 9*H*-β-carbolines (**6**).

INTRODUCTION

The use of chemotherapeutic agents in cancer has advanced from the treatment of late diseases to the early use of effective agents in patients with relatively small tumors. Among the various chemotherapeutic agents, 1-substituted β-carboline derivatives have attracted the attention of organic chemists because of their biological[1] and potential antitumor activity.[2] New β-carbolines are continually being isolated from natural sources,[3] like Eudistoma alkaloids and bengacarbolines,[4] and these compounds subsequently become targets for total synthesis.[5] Recently, endogenously formed β-carbolines, "mammalian alkaloids", have come under increasing scrutiny in connection with Parkinson's disease.[6] In addition, the antiviral eudistomines C, H, I, V and E exhibit potent inhibitory activity toward DNA viruses *HSV*-1, *HSV*-2, the *Vaccinia* virus and RNA viruses.[7] Recently, the novel structures of manzamines, like A-D and H, possess potent antitumor,[8] antibacterial, antifungal, anti-HIV[9] and cytotoxic activity.[10]

However, the synthesis of these compounds involves problems. The Pictet-Spengler reaction is the most commonly employed synthethic route towards β-carbolines, but in this method, the reaction products are

the tetrahydro-β-carboline, which requires subsequent oxidation. The Bischler-Napieralski reaction is not satisfactorily efficient and may afford products of insufficient purity,[11] yields[12] or lead to negative results,[13] particularly in the case of dihydro-β-carbolines containing 1-heterocycling[12] and 5- or 7-methoxy substituent. The applicability of other synthetic methods such as cyclization of 2-acyltryptamine[14] or dehydrogenation of appropriate 1,2,3,4-tetrahydro-9*H*-β-carboline derivatives[11,15] also is very limited. As a result of microwave assisted Bischler-Napieralski reaction, 1-substituted β-carbolines are obtained from the corresponding tryptamine derivatives with higher yields.[16]

RESULTS AND DISCUSSION

Since the interest for the preparation of functionalized 3,4-dihydro-9*H*- and 1,2,3,4-tetrahydro-9*H*-β-carbolines keeps growing, we considered of the possibility of cyclizing of tryptamine (**1**) with various carboxylic acids (**2**). As cyclization agent we used polyphosphoric acid (PPA), which is a permanent interest in synthetic applications for us.[17]

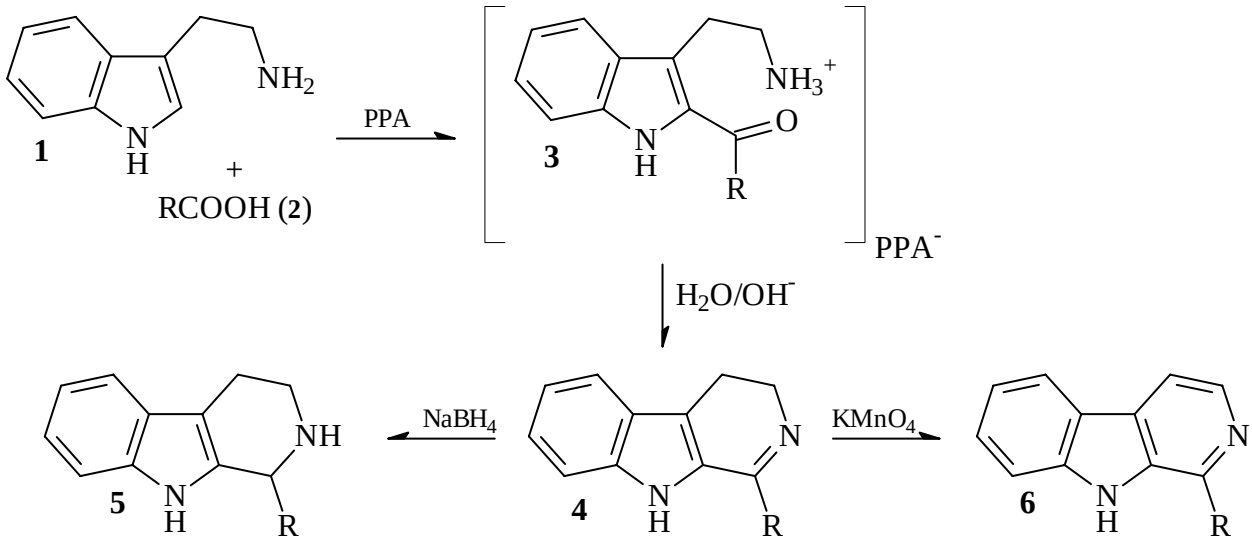
In our previous report[17] the reaction of equimolar amounts of 2-phenylethylamines with carboxylic acids in PPA afforded very conveniently the corresponding 3,4-dihydroisoquinolines in very good yields and purity. The successful application of this way to the synthesis of 3,4-dihydroisoquinolines indicated to enlarge applications opportunities. In this paper, we continue our research with the application of this reaction with other primary amines. There are number of publications regarding the synthesis of 1-substituted 3,4-dihydro-9*H*-β-carboline derivatives. So far there are no reports for condensation of tryptamine with carboxylic acids in PPA for the preparation of β-carboline derivatives. We applied this approach for the synthesis of 1-methyl- and 1-phenyl-3,4-dihydro-9*H*-β-carbolines at first.

When the dichloromethane solution of tryptamine (**1**) and acetic or benzoic acid was mixed in PPA at 80°C for 2 h, the 1-substituted 3,4-dihydro-9*H*-β-carbolines were obtained with low purity and yield. The same products with higher yields and purity, were also obtained, when the mixture was permanently stirred at room temperature or at 50°C for 2 h. These results prompted us to continue our researches with other alkyl- and arylcarboxylic acids.

We assumed that the reaction first formed ammonium salt and then the acylation occurred on the 2-position in the indole ring. This afforded the intermediate (**3**), which spontaneously cyclizing to **4** at the reaction condition (Scheme 1).

This convenient route to preparation of 3,4-dihydro-9*H*-β-carbolines showed to enlarge applications possibility. The newly synthesized 3,4-dihydro-9*H*-β-carbolines (**4**) easily were transformed to 1,2,3,4-tetrahydro-9*H*-β-carbolines or to 9*H*-β-carbolines, which are known as alkaloids (harman, tetrahydroharman, etc.).[1] First we hydrogenated the obtained 1-methyl-3,4-dihydro-9*H*-β-carboline (**4a**)

with $NaBH_4$ in methanol. We investigated that reduction afforded the 1-methyl-1,2,3,4-tetrahydro-9*H*-β-carboline (**5a**). By analogy we obtained the corresponding 1,2,3,4-tetrahydro-9*H*-β-carbolines (**5b-i**) in very good yields (88-92 %) and purity.



Scheme 1

Table 1

Entry	R	Yield, [%]	Entry	R	Yield, [%]
4a	CH_3	77	**5c**	$CH_2CH(CH_3)_2$	92
4b	C_2H_5	60	**5d**	C_6H_5	90
4c	C_3H_7	65	**5e**	4-Cl-C_6H_4	88
4d	C_6H_5	55	**5f**	3,4-$(MeO)_2$-C_6H_3	92
4e	4-Cl-C_6H_4	77	**5g**	3,4,5-$(MeO)_3$-C_6H_2	90
4f	2,4-Cl_2-C_6H_3	70	**5h**	$C_6H_5CH_2$	88
4g	3,4-$(MeO)_2$-C_6H_3	70	**5i**	2-naphthyl	90
4h	3,4,5-$(MeO)_3$-C_6H_2	67	**6a**	CH_3	92
4i	2-naphthyl	70	**6b**	C_2H_5	90
5a	CH_3	90	**6c**	C_3H_7	90
5b	C_2H_5	89	**6d**	C_6H_5	92

Finally the fully aromatic 9*H*-β-carbolines (**6**) were prepared. It is well known that fully aromatic β-carbolines are more potent *in vitro*, than their corresponding tetrahydro-β-carboline derivatives. A number of authors tried to oxidize 3,4-dihydro-9*H*-β-carbolines (some of them were unsuccessful) for preparation of fully aromatic products.[1] S. Misztal *et al.*[12] unsuccessfully overoxidized these derivatives to fully aromatic byproducts by solid potassium permanganate in tetrahydrofuran at 0°C. B. Love and P. Raje also tried to converse tetrahydro-β-carbolines to the aromatic system.[2] They initiated this reaction by treatment with *p*-toluensulfonic acid in toluene, butyllithium in THF or KOH in DMSO and oxidize dihydro-β-carbolines in moderate yields. We also used potassium permanganate. It is known that 3,4-

dihydro-9*H*-β-carbolines are stable to oxidizing agents under nonacidic conditions and the oxidation of 1-methyl-1,2,3,4-tetrahydro-9*H*-β-carboline (**5a**) with $KMnO_4$ in acetone afforded 1-methyl-3,4-dihydro-9*H*-β-carboline, while the oxidation of 1-phenyl-1,2,3,4-tetrahydro-9*H*-β-carboline (**5e**) in tetrahydrofuran led to a mixture of 1-phenyl-9*H*-β-carboline and 1-phenyl-3,4-dihydro-9*H*-β-carboline (**4e**).[11] We carried out the oxidation of the obtained 1-phenyl-3,4-dihydro-9*H*-β-carboline (**4e**) with $KMnO_4$ in acetone by stirring overnight at room temperature and found that the corresponding 1-phenyl-9*H*-β-carboline could be obtained in good yield (92 %). By analogy we obtained 1-methyl-, 1-ethyl- and 1-propyl-9*H*-β-carbolines (**6a-d**) in high purity and good yields. The synthesized 9*H*-β-carbolines are compounds with known antitumor and anti-HIV activity.[7,10] The compounds were successfully oxidized to their aromatic derivatives, but we investigated that 9*H*-β-carbolines were obtained more difficult than isoquinolines in the same reaction conditions.

In conclusion, we report for the first time the application of this method for the preparation of 1-substituted β-carboline derivatives. This represents a convenient route to obtain some biologically important antitumor and anti-HIV active β-carboline alkaloids. The synthesized compounds were used for the synthesis of fully aromatic 9*H*-β-carbolines with known *in vitro* neurochemical and pharmacological activity.[19,20]

EXPERIMENTAL

Melting points were determined on a Boetius hostage apparatus and were uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were measured in Bruker-250 devise by using $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts (δ, ppm) were referenced to the chemical shifts of either TMS (δ=0.00ppm) as an internal standard and coupling constants are indicated in Hz. Unless otherwise noted, all the NMR spectra were taken at room temperature (ac. 295 K). MS spectra were recorded on a JEOL JMS-D300 spectrometer (70 eV). All new compounds had correct parent ion peaks by MS spectrometry.

Polyphosphoric acid was obtained from 85% phosphoric acid and P_2O_5 (1:1 w/w).

1-Substituted 3,4-dihydro-9*H*-β-carbolines (4a-i); **Typical procedure**: Tryptamine (0.320 g, 2 mmol) and the corresponding carboxylic acid (3 mmol) were dissolved in CH_2Cl_2 (3-5 mL) in an open flask and polyphosphoric acid (10 g) was added. The mixture was stirred on a mechanical stirrer carefully at rt or 50°C for 2-3 h, then poured on crushed ice. The solution was carefully alkalized with 25% ammonia, then extracted with CH_2Cl_2 (3x20 mL) and combined extracts were dried (Na_2SO_4) and filtrated on short column with basic Al_2O_3. The products, after evaporation of the solvent, were purified by recrystallization from ether.

1-Methyl-3,4-dihydro-9*H*-β-carboline (harmalan) (4a): yellow solid, mp 178-180°C (lit.,[21] mp 182-

183). ^{1}H-NMR ($CDCl_3$): 2.38 (3H, s, CH_3), 2.87 (2H, t, CH_2, J=8.0 Hz), 3.87 (2H, t, CH_2N, J=8.0 Hz), 7.15-7.73 (4H, m, Ar), 8.56 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 158.3, 137.1, 129.3, 125.5, 124.3, 120.1, 120.0, 116.3, 112.1, 38.0, 21.8, 19.4. MS m/z 184 (M^+). Anal. Calcd for $C_{12}H_{12}N_2$: C 78.23, H 6.57, N 15.20. Found: C 78.36, H 6.70, N 15.26.

1-Ethyl-3,4-dihydro-9*H*-β-carboline (4b): yellow solid, mp 165-167°C (lit.,[21] mp 164-166). ^{1}H-NMR (DMSO-d_6, 323K): 1.15 (3H, t, CH_3, J=7.3 Hz), 2.67 (2H, q, CH_2, J=7.3 Hz), 2.74 (2H, t, H-4, J=8.1 Hz), 3.72 (2H, t, H-3, J=8.1 Hz), 3.87 (2H, t, CH_2N, J=7.5 Hz), 7.04-7.54 (4H, m, Ar), 11.26 (1H, br s, NH-9). ^{13}C-NMR (DMSO-d_6): 160.8, 136.4, 128.7, 125.0, 123.3, 119.4, 119.3, 114.1, 112.3, 47.6, 27.7, 18.9, 10.5. MS m/z: 198 (M^+). Anal. Calcd for $C_{13}H_{14}N_2$: C 78.75, H 7.12, N 14.13. Found: C 78.83, H 7.20, N 14.28.

1-Propyl-3,4-dihydro-9*H*-β-carboline (4c): yellow solid, mp 161-162°C (lit.,[22] mp 162-165). ^{1}H-NMR ($CDCl_3$): 1.00 (3H, t, CH_3, J=7.4 Hz), 1.76 (m, 2H), 2.66 (2H, t, CH_2, J=7.6 Hz), 2.86 (2H, t, H-4, J=8.3 Hz), 3.88 (2H, t, H-3, J=8.2 Hz), 6.97-7.60 (4H, m, Ar), 8.88 (1H, br s, NH-9). ^{13}C-NMR ($CDCl_3$): 161.0, 136.7, 128.8, 125.7, 124.4, 120.3, 120.0, 116.8, 111.9, 48.2, 37.5, 20.2, 19.3, 13.9. MS m/z: 212 (M^+). Anal. Calcd for $C_{14}H_{16}N_2$: C 79.24, H 7.60, N 13.20. Found: C 79.30, H 7.68, N 13.27.

1-Phenyl-3,4-dihydro-9*H*-β-carboline (4d): yellow solid, mp 230-232°C (lit.,[12] mp 232-234°C). ^{1}H-NMR ($CDCl_3$): 3.04 (2H, t, H-4, J=8.0 Hz), 4.13 (2H, t, H-3, J=8.0 Hz), 7.23-7.89 (9H, m, Ar), 8.25 (1H, br s, NH-9). ^{13}C-NMR ($CDCl_3$): 159.5, 137.1, 136.7, 130.1, 127.8, 124.7, 120.4, 118.1, 112.0, 48.4, 19.2. MS m/z: 246 (M^+). Anal. Calcd for $C_{17}H_{14}N_2$: C 82.82, H 5.68, N 11.37. Found: C 82.90, H 5.75, N 11.45.

1-(4′-Chlorophenyl)-3,4-dihydro-9*H*-β-carboline (4e): white solid, mp 102-103°C (lit.,[10] mp 102-104°C). ^{1}H-NMR ($CDCl_3$): 2.99 (2H, t, H-4, J=8.3 Hz), 4.06 (2H, t, H-3, J=8.3 Hz), 7.20-7.67 (4H, m, Ar), 8.04 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 159.9, 136.2, 126.9, 122.4, 120.8, 118.1, 111.1, 41.2, 39.9, 27.1, 25.7. MS m/z: 280 (M^+). Anal. Calcd for $C_{17}H_{13}N_2Cl$: C 72.66, H 4.63, N 9.97. Found: C 72.76, H 4.70, N 10.05.

1-(2′,4′-Dichlorophenyl)-3,4-dihydro-9*H*-β-carboline (4f): yellow solid, mp 193-195°C. ^{1}H-NMR ($CDCl_3$): 3.02 (2H, t, H-4, J=8.5 Hz), 4.08 (2H, t, H-3, J=8.5 Hz), 7.17-7.66 (7H, m, Ar), 8.28 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 157.8, 137.0, 136.0, 131.3, 127.8, 125.3, 120.5, 117.5, 112.0, 48.8, 19.2. MS m/z: 315 (M^+). Anal. Calcd for $C_{17}H_{12}N_2Cl_2$: C 64.72, H 3.81, N 8.88. Found: C 64.79, H 3.90, N 8.98.

1-(3′,4′-Dimethoxyphenyl)-3,4-dihydro-9*H*-β-carboline (4g): yellow solid, mp 285-288°C (lit.,[10] mp 288-290°C). ^{1}H-NMR ($CDCl_3$): 2.95 (2H, t, H-4, J=8.0 Hz), 3.88 (6H, s, OMe), 4.03 (2H, t, H-3, J=8.0 Hz), 7.20-7.66 (7H, m, Ar), 8.90 (1H, br s, NH-9). ^{13}C-NMR ($CDCl_3$): 158.9, 136.7, 129.8, 127.7, 124.6, 120.4, 118.2, 112.1, 48.3, 19.2. MS m/z: 306 (M^+). Anal. Calcd for $C_{19}H_{18}N_2O_2$: C 74.41, H 5.87, N 9.14. Found: C 74.49, H 5.95, N 9.21.

1-(3′,4′,5′-Trimethoxylphenyl)-3,4-dihydro-9*H*-β-carboline (4h): yellow solid, mp 250-252°C (lit.,[10] mp 251°C). ^{1}H-NMR ($CDCl_3$): 2.96 (2H, t, H-4, J=7.5 Hz), 3.85 (9H, s, OMe), 4.01 (2H, t, H-3, J=7.5 Hz), 7.21-7.68 (6H, m, Ar), 9.12 (1H, br s, NH-9). ^{13}C-NMR($CDCl_3$): 159.4, 153.0, 139.0, 136.7, 133.2, 127.9, 125.4, 120.2, 119.9, 117.9, 112.1, 105.0, 48.8, 19.2. MS m/z: 336 (M^+). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C 71.35, H 5.95, N 8.32. Found: C 71.43, H 6.01, N 8.40.

1-(2′-Naphthyl)-3,4-dihydro-9*H*-β-carboline (4i): white solid**,** mp 145-150°C. ^{1}H-NMR($CDCl_3$): 2.95 (2H, t, H-4, J=8.0 Hz), 4.01 (2H, t, H-3, J=8.0 Hz), 7.18-7.65 (11H, m, Ar), 8.76 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 159.5, 136.7, 134.4, 127.8, 126.5, 120.3, 118.1, 112.1, 48.5, 19.2. MS m/z: 296 (M^+). Anal. Calcd for $C_{21}H_{16}N_2$: C 85.03, H 5.40, N 9.45. Found: C 85.13, H 5.48, N 9.54.

1-Substituted 1,2,3,4-tetrahydro-9*H*-β-carboline (5a-i); **Typical procedure:** To solution of 1 mmol of the corresponding 3,4-dihydro-9*H*-β-carboline (**4**) in 15 mL of methanol, $NaBH_4$ (2 mmol, 0,1 g) was added portionwise. The solution was stirred 30 min at rt, than the solvent was removed under vacuum. Water (30 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (3x20 mL), then the combined extracts were dried (Na_2SO_4) and filtered on short column with basic Al_2O_3. The products, after evaporation of the solvent, were purified by recrystallization from n-hexane or ether.

1-Methyl-1,2,3,4-tetrahydro-9*H*-β-carboline (tetrahydroharman) (5a): semi-solid.[23] ^{1}H-NMR ($CDCl_3$): 1.46 (d, 3H, J=6.8 Hz), 1.58 (s,1H, NH), 2.72 (m, 1H, H-4), 3.06 (m, 1H, H-3), 4.20 (q, 1H, H-1, J=6.8 Hz), 7.1-7.48 (m, 4H, Ar), 7.75 (1H, s, NH). MS m/z: 187 (M^+H^+). Anal. Calcd for $C_{12}H_{14}N_2$: C 77.32, H 7.52, N 15.03. Found: C 77.40, H 7.60, N 15.10.

1-Ethyl-1,2,3,4-tetrahydro-9*H*-β-carboline (5b): yellow solid, mp 223-225°C (lit.,[20] mp 225-228°C). ^{1}H-NMR (DMSO-d_6,323K): 1.08 (t, 3H, $CH_2C\underline{H}_3$, J=7.6 Hz), 1.93, 2.20 (each 1H, m, $C\underline{H}_2CH_3$), 2.96 (m, 2H, H-4), 3.35, 3.58 (each 1H, m, H-3), 4.58 (1H, br s, H-1), 7.02-7.45 (m, 4H, Ar), 9.12 (1H, s, NH). MS m/z: 201 (M^+H^+). Anal. Calcd for $C_{13}H_{16}N_2$: C 77.89, H 7.99, N 13.98. Found: C 77.98, H 8.08, N 14.04.

1-i-Buthyl-1,2,3,4-tetrahydro-9*H*-β-carboline (5c): oil.[23] ^{1}H-NMR ($CDCl_3$): 1.00 (6H, d, 2xCH_3, J=6.3 Hz), 1.63 (1H, m), 1.82 (1H, s, NH), 1.98 (2H, m), 2.80 (2H, t, CH_2, J=5.8 Hz), 3.18 (2H, t, CH_2, J=5.8 Hz), 4.12 (1H, dd, J=5.6, 13.8 Hz), 7.49-7.14 (m, 4H, Ar), 7.78 (1H, s, NH). MS m/z: 229 (M^+H^+). Anal. Calcd for $C_{15}H_{20}N_2$: C 78.83, H 8.76, N 12.26. Found: C 78.92, H 8.83, N 12.34.

1-Phenyl-1,2,3,4-tetrahydro-9*H*-β-carboline (5d): white solid, mp 257-258°C (lit.,[24] mp 258-259°C). ^{1}H-NMR ($CDCl_3$): 2.50-3.30 (m, 4H, 2xCH_2), 5.22 (s, 1H, CH), 7.00-7.70 (m, 9H, Ar), 10.40 (1H, br s, NH). ^{13}C-NMR ($CDCl_3$): 141.72, 135.86, 134.33, 128.63, 128.46, 128.05, 127.23, 121.53, 119.18, 118.07, 110.79, 109.97, 57.89, 42.51, 22.43. MS m/z: 249 (M^+H^+). Anal. Calcd for $C_{17}H_{16}N_2$: C 82.15, H 6.44, N 11.28. Found: C 82.27, H 6.52, N 11.34.

1-(4′-Chlorophenyl)-1,2,3,4-tetrahydro-9*H*-β-carboline (5e): white solid plates, mp 162-163°C (lit.,[10]

mp 165°C). ^{1}H-NMR ($CDCl_3$): 2.85 (2H, m, H-4), 3.11 (1H, m, H-3), 5.09 (1H, s, H-1), 7.17-7.57 (4H, m, Ar), 7.87 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 140.3, 135.9, 133.9, 133.7, 129.8, 128.9, 127.2, 121.8, 119.4, 118.2, 110.8, 110.2, 57.1, 42.4, 22.3. MS m/z: 282 (M^+). Anal. Calcd for $C_{17}H_{15}N_2Cl$: C 72.14, H 5.30, N 9.90. Found: C 72.21, H 5.40, N 9.97.

1-(3′,4′-Dimethoxylphenyl)-1,2,3,4-tetrahydro-9*H*-β-carboline (5f): pale yellow solid, mp 302-305°C (lit.,[20] mp>300°C). ^{1}H-NMR ($CDCl_3$): 2.89 (2H, m, H-4), 3.10 (1H, m, H-3), 3.70 (3H, s, OMe), 3.84 (3H, s, OMe), 5.04 (1H, s, H-1), 7.12-7.56 (4H, m, Ar), 8.32 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 149.0, 148.6, 135.8, 134.5, 134.2, 127.2, 121.4, 120.5, 119.0, 118.0, 111.2, 110.8, 109.7, 57.9, 55.7, 55.6, 42.9, 22.3. MS m/z: 308 (M^+). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C 73.99, H 6.49, N 9.09. Found: C 74.08, H 6.54, N 9.18.

1-(3′,4′,5′-Trimethoxylphenyl)-1,2,3,4-tetrahydro-9*H*-β-carboline (5g): pale yellow solid, mp 160-160.5°C. ^{1}H-NMR ($CDCl_3$): 3.29 (2H, m, H-4), 3.59 (1H, m, H-3), 3.71 (9H, s, OMe), 5.85 (1H, s, H-1), 7.11-7.55 (4H, m, Ar), 8.30 (1H, s, NH-9). ^{13}C-NMR ($CDCl_3$): 153.8, 153.4, 136.2, 133.3, 128.6, 126.7, 122.4, 119.7, 118.4, 111.1, 109.4, 60.7, 56.1, 51.5, 41.7. MS m/z: 338 (M^+). Anal. Calcd for $C_{20}H_{22}N_2O_3$: C 70.97, H 6.51, N 8.28. Found: C 71.06, H 6.60, N 8.38.

1-Benzyl-1,2,3,4-tetrahydro-9*H*-β-carboline (5h): yellow oil.[25] ^{1}H-NMR ($CDCl_3$): 1.80 (1H, br s, NH), 2.50-3.50 (m, 4H, 2xCH_2), 3.01 (d, 2H, CH_2Ar, J=7.0 Hz), 4.33 (t, 1H, H-1, J=7.0 Hz), 7.73-6.94 (m, 10H, Ar and NH-9). ^{13}C-NMR ($CDCl_3$): 138.1, 135.56, 135.5, 129.3, 128.8, 127.2, 126.88, 121.5, 119.28, 118.08, 110.7, 109.28, 53.98, 42.8, 41.64, 22.6. MS m/z: 262 (M^+). Anal. Calcd for $C_{18}H_{18}N_2$: C 82.33, H 6.86, N 10.67. Found: C 82.42, H 6.93, N 10.73.

1-(2′-Naphtyl)-1,2,3,4-tetrahydro-9*H*-β-carboline (5i): yellow solid, mp 183-185°C (lit.,[1] mp 184-185°C). ^{1}H-NMR ($CDCl_3$): 2,37 (1H, s, NH), 2.87-2.97 (m, 2H, H-4), 3.10-3.18 (m, 1H, H-3), 3.33-3.42 (m, 1H, H-3), 5.28 (s, 1H, H-1), 7.13-7.17 (m, 3H, Ar), 7.47-7.51 (m, 4H, Ar), 7.71-8.06 (m, 5H, Ar and NH-9). ^{13}C-NMR ($CDCl_3$): 139.0, 135.96, 134.3, 128.7, 127.9, 127.3, 126.3, 121.7, 119.4, 118.2, 110.9, 110.2, 58.1, 42.8, 22.4. MS m/z: 298 (M^+). Anal. Calcd for $C_{21}H_{18}N_2$: C 84.46, H 6.03, N 9.38. Found: C 84.54, H 6.09, N 9.46.

1-Substituted 9*H*-β-carbolines (6a-d). **Typical procedure:** To the stirred solution of 1 mmol of corresponding 3,4-dihydro-9*H*-β-carboline (**4**) in 20 mL of acetone at rt $KMnO_4$ (0.316 g, 2 mmol) was added portionwise. The colour of the reaction mixture gradually turned from violet to brown from the formed MnO_2. Saturated aqueous sodium metabisulfite solution (50 mL) was added carefully. The resulting mixture was alkalized with 25% ammonia and the solution was extracted with CH_2Cl_2 (3x20 mL). The combined extracts were dried (Na_2SO_4), the solvent evaporated and the products purified by recrystallization from ether.

1-Methyl-9*H*-β-carboline (6a): colorless needles, mp 202-202.5°C (lit.,[20] mp 202°C). ^{1}H-NMR (DMSO-

d_6, 323 K): 2.76 (s, 3H, CH_3), 7.23-7.92 (m, 4H), 8.19 (1H, d, H-5, J=8.2 Hz), 8.20 (1H, d, H-3, J=5.3 Hz), 11.53 (1H, br s, NH). MS m/z: 182 (M^+). Anal. Calcd for $C_{12}H_{10}N_2$: C 79.10, H 5.53, N 15.37. Found: C 79.30, H 5.89, N 15.66.

1-Ethyl-9*H*-β-carboline (6b): colorless needles, mp 193-195°C (lit.,[20] mp 195-197°C). ^{1}H-NMR (DMSO-d_6, 323 K): 1.42 (3H, t, $CH_2C\underline{H}_3$, J=7.7 Hz), 3.19 (2H, q, $C\underline{H}_2CH_3$, J=7.7 Hz), 7.24-7.91 (m, 4H, Ar), 8.18 (1H, d, H-5, J=8.1 Hz), 8.29 (1H, d, H-3, J=5.5 Hz), 11.53 (1H, br s, NH). MS m/z: 196 (M^+). Anal. Calcd for $C_{13}H_{12}N_2$: C 79.49, H 6.11, N 14.27. Found: C 79.60, H 6.20, N 14.40.

1-Propyl-9*H*-β-carboline (6c): colorless needles, mp 217-219°C (lit.,[20] mp 218-220°C). ^{1}H-NMR (DMSO-d_6, 323 K): 1.00 (3H, t, $CH_2CH_2C\underline{H}_3$, J=7.3 Hz), 1.86 (2H, m, $CH_2C\underline{H}_2CH_3$), 3.08 (m, 2H, $C\underline{H}_2CH_2CH_3$), 7.22-7.89 (m, 4H), 8.17 (1H, d, H-5, J=8.1 Hz), 8.25 (1H, d, H-3, J=5.1 Hz), 11.43 (1H, br s, NH). MS m/z: 210 (M^+). Anal. Calcd for $C_{14}H_{14}N_2$: C 79.97, H 6.71, N 13.32. Found: C 79.90, H 6.84, N 13.11.

1-Phenyl-9*H*-β-carboline (6d): yellow powder, mp 241-242°C (lit.,[2] mp 240-243°C). ^{1}H-NMR ($CDCl_3$): 7.25 (t, 1H, J=5.3 Hz), 7.4-8.5 (m, 9H, Ar), 11.07 (1H, s, NH). ^{13}C-NMR ($CDCl_3$): 111.4, 112.6, 118.5, 120.25, 120.3, 127.1, 127.4, 127.6, 127.8, 128.6, 132.6, 137.5, 137.8, 140.4, 141.8. MS m/z: 244 (M^+). Anal. Calcd for $C_{17}H_{12}N_2$: C 83.51, H 4.91, N 11.46. Found: C 83.60, H 4.99, N 11.55.

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