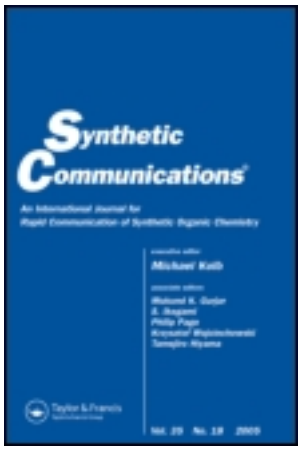

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Microwave Assisted Pictet–Spengler and Bischler–Napieralski Reactions

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ABSTRACT

Pictet–Spengler and Bischler–Napieralski reaction products have been prepared–using microwave irradiation on silicagel support under solvent free condition. Microwave assisted reactions have resulted in better yields of the desired products than prepared under conventional conditions.

Key Words: Microwave; Indole; Isoquinoline; β-carboline; Pictet–Spengler; Bischler–Napieralski.

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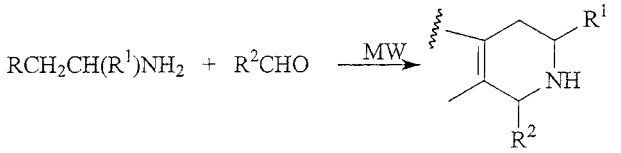
Pictet–Spengler,[1] Bischler–Napieralski[2] are the two most widely used reactions in the synthesis of β-carboline and isoquinoline backbones of the indole and isoquinoline alkaloids respectively. The reactions are well known but it has been observed that sometimes these reactions become hazardous resulting in poor yields of the products. In order to overcome this problem it was decided to study the above reactions using microwave irradiation under solvent free condition.

Microwave heating has been employed as a frequent resource for improvement of classical reactions. The use of such non-conventional reaction conditions reveals several features like a short reaction time compared to conventional eating, ease of isolation of the products after easy work-up and better selectivity.[3] It has also been observed that sometimes the intermediate tetrahydro or dihydro products undergo dehydrogenation resulting in isoquinolines or β-carbolines.

Microwave assisted Pictet–Spengler reaction of tryptamine (**1**) with *Para*-nitrobenzaldehyde (**2**) afforded the expected tetrahydro (**3**) and the dihydro-β-carbolines (**3a**) whereas *ortho*-nitrobenzaldehyde (**4**) with tryptamine (**1**) yielded not only the tetrahydro (**5**) and the dihydro β-carbolines (**5a**) but also the fully aromatized product 1-(2-nitrophenyl)-β-carboline (**5b**) (Sch. 1). Similar irradiation of *meta*-Nitro-benzaldehyde (**6**) with **1** gave only the tetrahydro-β-carboline product (**7**) (Table 1). On the other hand, *para*-fluorobenzaldehyde (**8**) with tryptamine (**1**) afforded both the tetrahydro (**9**) and the dihydro-β-carbolines (**9a**).

The microwave assisted Pictet–Spengler reaction has also been performed with chiral substrates. Thus, tryptamine (**1**) with the sugar derivative **10**[4] under microwave irradiation gave the chiral β-carboline compounds (**11**)[5] and (**11a**) respectively (Table 1a). Expectedly L and D tryptophan methyl esters (**12**) and (**14**) under the same irradiation condition gave the corresponding carbomethoxy substituted chiral β-carbolines **13** and **15** respectively. On the other hand, β-phenylethyl-amine (**16**) with the same sugar derivative, di-(**1**,**2**)-*O*-cyclo

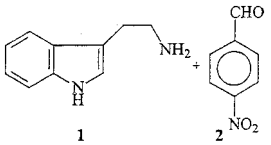
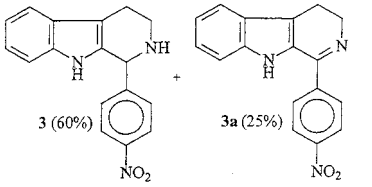
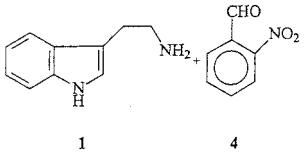
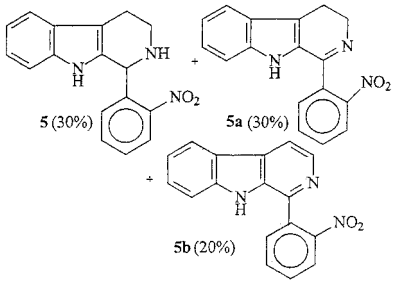
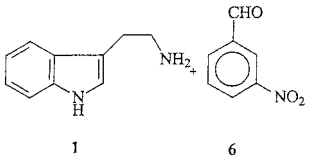
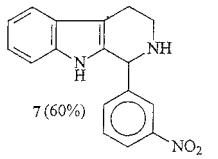
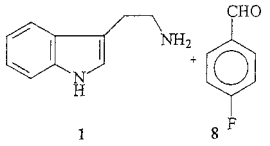
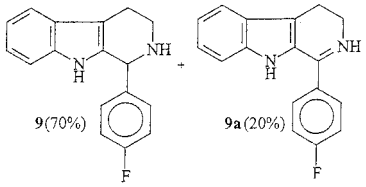


R = Indolyl or Isoquinolinyl; R^1 = H or COOMe

R^2 = H or CH_3 or furanose derivatives or benzene derivatives

Scheme 1.

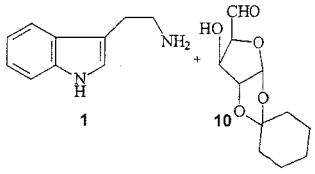
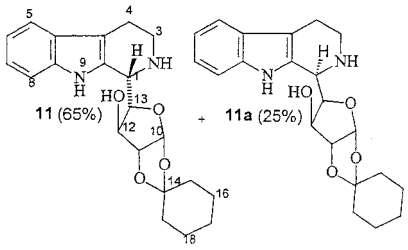
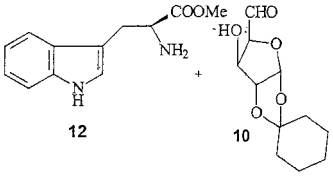
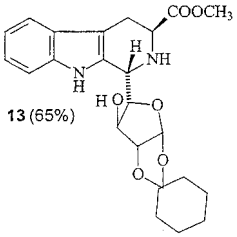
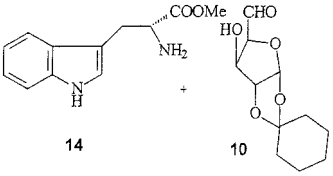
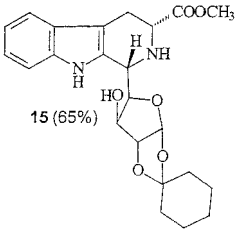
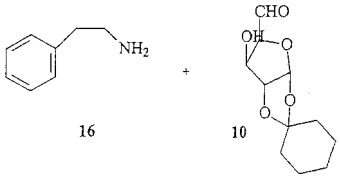
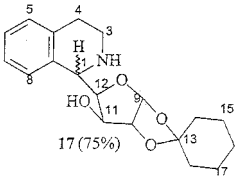
Table 1. Pictet–Spengler reaction products.

Entry	Substrate	Products (yield)
1		
2		
3		
4		

hexylidene-α-D-xylo-pentodialdofuranose-5-hydrate)-5,5′:3′,5-dianhydride (**10**) gave an inseparable diastereomeric mixture (1:1) of the chiral isoquinolines **17**.

Microwave assisted Bischler–Napieralski reaction of *N*-formyltryptamine (**18**) and *N*-acetyltryptamine (**20**) gave the expected dihydro-β-carboline (**19**) and 1 methyl-3,4-dihydro-β-carboline (**21**) respectively in very good yield (Table 2). Interestingly, *N*-formyltryptophan methyl ester (**22**) under similar condition afforded apart from the expected 3-carbomethoxy-β-carboline (**23**), also a dimeric β-carboline **23a**. The dimmer **23a** could not be obtained under classical reaction condition.

Table 1a. Chiral reaction products.

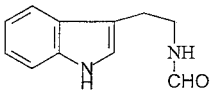
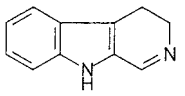
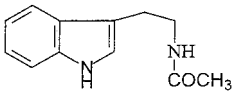
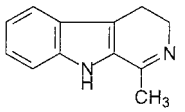
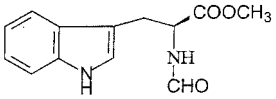
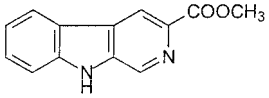
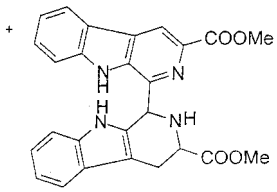
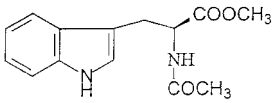
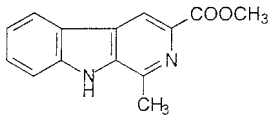
Entry	Substrate	Products (yield)
1		
2		
3		
4		

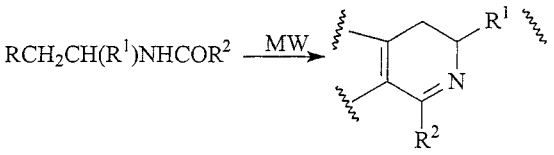
N-acetyltryptophan methyl ester (**24**) under microwave irradiation gave only 1-methyl-3-carbomethoxy-β-carboline (**25**) (Sch. 2).

All the compounds have been characterized using physical data mainly NMR and compared with those prepared by classical methods.

In conclusion, the method described above could be used to synthesize in a convenient manner both isoquinoline and β-carboline derivatives as an alternate to the classical methods employed.

Table 2. Bischler–Napieralski reaction products.

Entry	Substrate	Products (yield)
1	 **18**	 **19** (75%)
2	 **20**	 **21** (70%)
3	 **22**	 **23** (60%)
		 **23a** (30%)
4	 **24**	 **25**(60%)



R = Indolyl or Isoquinolinyl; R^1 = H or COOMe
R^2 = H or CH_3 or furanose derivatives or benzene derivatives

Scheme 2.

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EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Infra red spectra were recorded in FT/IR 410 JASCO spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured in a 300 MHz BRUKER 300 DPX spectrometer using TMS as internal standard. The mass spectra were run on a JEOL AX–500 spectrometer at 70 eV. Optical rotations were. recorded at 25°C in P–1020 JASCO polarimeter. Petroleum ether refers to the fraction boiling in the range 60–80°C. Solvents like petroleum ether, chloroform, methanol, ether, THF, DMF, and DMSO were purified and dried before use. Column chromatography was carried out on silica gel of 60–120 mesh. TLC was done on standard Merck TLC aluminium sheets. Unless otherwise mentioned the compounds have been crystallized from either petroleum ether–$CHCl_3$ mixture or MeOH.

Typical procedure for Pictet–Spengler condensation. Ten gram silica-gel (60–120 mesh) was initially activated irradiating in a microwave (Domestic oven; AEG, Micromat) oven for 5 min. at 850 W. A mixture of 1 mmol of the amine and 1 mmol of the aldehyde in 1 mL of glacial HOAc was adsorbed over activated silica gel. It was then irradiated at 600 W initially for 5 min, then for another 5 min, and finally for 2 more min. i.e., for a total of 12 min. The reaction was monitored at the end of each irradiation. The silica gel was then soaked in a mixture of $CHCl_3$ and MeOH (7:3) and filtered. Filtrate was concentrated, diluted with water, neutralized with $NaHCO_3$ and extracted with $CHCl_3$. The extract was concentrated and the residue chromatographed over silica gel to yield the products.

1-(4-Nitrophenyl)-1,2,3,4-tetrahydro-β-carboline (3). M.p. 168–170°C; IR (KBr): 3408, 3229, 1514, 1348. ^{1}H NMR (DMSO-d_6): δ 2.72–2.98 (m, 2H), 3.18 (m, 1H), 3.28 (m, 1H), 5.27 (s, 1H), 7.00–7.20 (m, 2H), 7.22–7.27 (m, 1H), 7.51 (d, $J = 8.4$ Hz, 2H), 7.56 (brd, 1H), 8.19 (d, $J = 8.4$ Hz, 2H), 11.02 (s, NH). m/z: 293 (M^+, 100), 264 (35), 218 (30), 171 (35). Anal. calcd. for $C_{17}N_3O_2H_{15}$: C, 69.68; H, 5.16; N, 14.34. Found: C, 69.58; H, 5.09; N, 14.47.

1-(4-Nitrophenyl)-3,4-dihydro-β-carboline (3a). M.p. 220–222°C. IR (KBr): 3393, 1513, 1350. ^{1}H NMR (DMSO-d_6): δ 2.90 (t, 2H), 3.96 (t, 2H), 7.09 (t, 1H), 7.23 (t, 1H), 7.42 (d, $J = 7.5$ Hz, 1H), 7.64 (d, $J = 7.2$ Hz, 1H), 8.01 (d, $J = 6.9$ Hz, 2H), 8.38 (t, 2H), 11.21 (s, NH). m/z: 291 (M^+, 100), 244 (30), 143 (20). Anal. calcd. for $C_{17}N_3O_2H_{13}$: C, 70.16; H, 4.50; N, 14.44. Found: C, 69.98; H, 4.39; N, 14.58.

1-(2-Nitrophenyl)-1,2,3,4-tetrahydro-β-carboline (5). M.p. 238–240°C. IR (KBr): 3311, 1617, 1539, 1369. ^{1}H NMR (DMSO-d_6): δ 2.95–3.50

(m, 3H), 3.55 (m, 1H), 6.42 (s, 1H), 7.07 (t, 1H), 7.15 (t, 1H), 7.28 (m, 1H), 7.34 (d, $J = 7.8$ Hz, 1H), 7.57 (d, $J = 2.5$ Hz, 1H), 7.70–7.90 (m, 2 H), 8.31 (m, 1H), 10.72 (s, NH). *m*/*z*: 293 (M^+, 40), 276 (80), 259 (100), 246 (50), 171 (20). Anal. calcd. for $C_{17}N_3O_2H_{I5}$: C, 69.68; H, 5.16; N, 14.34. Found: C, 69.60; H, 5.07; N, 14.43.

1-(2-Nitrophenyl)-3,4-dihydro-β-carboline (5a). M.p. 268–270°C. IR (KBr): 3150, 1612, 1540, 1373. ^{1}H NMR (DMSO-d_6): δ 3.34 (t, 2H), 4.60 (t, 2H), 7.08 (t, 1H), 7.17 (t, 1H), 7.22 (t, 1H), 7.30 (t, 1H), 7.46 (d, $J = 7.8$ Hz, 1H), 7.56 (brd, 2H), 8.27 (d, $J = 6.6$ Hz, 1H), 11.7 (s, NH). *m*/*z*: 291 (M^+ 100), 171 (20), 117 (10). Anal. calcd. for $C_{17}N_3O_2H_{13}$: C, 70.16; H, 4.50; N, 14.44. Found. C, 70.02; H, 4.41; N, 14.58.

1-(2-Nitrophenyl)-β-carboline (5b). M.p. 275–277°C. IR (KBr): 3231, 1530, 1345. ^{1}H NMR (DMSO-d_6): δ 7.31 (t, 1H), 7.38 (t, 1H), 7.50 (t, 1H), 7.58 (t, 1H), 7.66 (d, $J = 6.9$ Hz, 1H), 7.81 (d, $J = 6.9$ Hz, 1H), 7.93 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 7.8$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H), 8.69 (d, $J = 6.9$ Hz, 1H), 9.10 (s, NH). *m*/*z*: 289 (M^+, 40), 171 (25), 117 (20), 94 (100). Anal. calcd. for $C_{I7}N_3O_2H_{11}$: C, 70.65; H, 3.84; N, 14.54. Found: C, 70.56; H, 3.78; N, 14.65.

1-(3-Nitrophenyl)-1,2,3,4-tetrahydro-β-carboline (7). M.p. 142–144°C. IR (KBr): 3310, 1526, 1348. ^{1}H NMR (DMSO-d_6): δ 2.72 (m, 2H), 3.02 (m, 2H), 5.26 (s, 1H), 6.90–7.10 (m, 2H), 7.23 (d, $J = 7.5$ Hz, 1H), 7.43 (d, $J = 7.5$ Hz, 1H), 7.61 (t, $J = 7.5$ Hz, 1H), 7.73 (d, $J = 7.5$ Hz, 1H), 8.03 (s, 1H), 8.13 (d, $J = 7.8$ Hz, 1H), 10.51 (s, NH); *m*/*z*: 293 (M^+, 100), 246 (30), 216 (70), 171 (70), 115 (15). Anal. calcd. for $C_{17}N_3O_2H_{15}$: C, 69.68; H. 5.16; N, 14.34. Found: C, 69.59; H, 5.11; N, 14.40.

1-(4-Flurophenyl)-1,2,3,4-tetrahydro-β-carboline (9). M.p. 138–140°C. IR (KBr): 3150, 1506, 1223, 746. ^{1}H NMR ($CDC1_3$): δ 2.70–3.00 (m, 2H), 3.01–3.25 (m, 1H), 3.26–3.40 (m, 1H), 5.15 (s, 1H), 7.03 (m, 2H), 7.13 (m, 2H), 7.20–7.34 (m, 4H), 7.40 (brs, NH). 7.54 (m, 1H). *m*/*z*: 266 (M^+, 100), 237 (60). 171 (30). Anal. calcd. for $C_{17}N_2FH_{15}$: C, 76.76; H, 5.68; N, 10.53. Found: C, 76.68; H, 5.60; N, 10.62.

1-(4-Flurophenyl)-3,4-dihydro-β-carboline (9a). M.p. 244–246°C. IR (KBr): 3373, 1537, 1339. ^{1}H NMR (DMSO-d_6): δ 2.89 (t, 2H), 3.89 (t, 2H), 7.08 (t, 1H), 7.22 (t, 1H), 7.30–7.50 (m, 3H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.77–7.88 (m, 2H), 12.11 (s, NH). *m*/*z*: 264 (M^+, 100), 235 (30), 144 (20), 116 (15). Anal. calcd. for $C_{17}N_2FH_{13}$: C, 77.34; H, 4.96; N, 10.61. Found: C, 77.27; H, 4.89; N, 10.56.

10,11-*O*-Cyclohexylidene-12-β-hydroxy-13β-(1-tetrahydro-β-carbolinyl)tet rahydro-furan (11). M.p. 200–202°C. $[\alpha]_D = -54.0°$ ($c = 0.48$, $CHC1_3$). IR (KBr): 3454, 3088, 1034, 735. ^{1}H NMR ($CDCl_3$): δ

1.40–1.90 (brs, 10H), 2.64–2.84 (m, 2H), 2.90–3.20 (m, 2H), 3.30–3.60 (m, 2H, OH, NH), 4.24 (m, 1H), 4.40–4.60 (m, 3H), 6.04 (d, $J = 5.1$ Hz, 1H), 7.04–7.60 (m, 4H), 8.44 (brs, NH). ^{13}C NMR ($CDCl_3$): δ 21.89 (t, C-4), 23.4 (t, C-18), 23.76 (t, C-16), 24.75 (t, C-17), 35.23 (t, C-19), 36.22 (t, C-15), 42.71 (t, C-3), 52.78 (d, C-1), 75.42 (d, C-12), 81.33 (d, C-13), 85.07 (d, C-11), 104.78 (d, C-10), 109.35 (s, C-14), 110.93 (d, C-8), 112.45 (s, C-4a), 118.01 (d, C-15), 119.18 (d, C-6), 121.63 (d, C-7), 126.90 (s, C-4b), 131.17 (s, C-9a), 136.08 (s, C-8a). *m*/*z*: 370 (M^+, 90), 327 (25),271 (20), 255 (28), 237 (22), 213 (50), 199 (30), 184 (84), 172 (98), 171 (100); Anal. calcd. for $C_{21}N_2O_4H_{26}$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.97; H, 7.14; N, 7.63.

Diastereomer of 11 (11a). M.p. 235–237°C. $[\alpha]_D = -19.70^\circ$ ($c = 0.58$, $CHC1_3$); 1R (KBr): 3454, 2936, 1448, 1120, 1016. ^{1}H NMR ($CDCl_3$): δ 1.30–1.90 (m, 10H), 2.60–2.90 (m, 2H), 3.01–3.40.(m, 2H), 4.36–4.39 (m, 2H, OH, NH), 4.45–4.55 (m, 2H), 5.98 (d, $J = 3.3$ Hz, 1H), 7.04–7.20 (m, 3H), 7.47 (d, $J = 7.2$ Hz, 1H), 8.20 (s, NH). ^{13}C NMR ($CDCl_3$): δ 22.37 (t, C-4), 23.95 (t, C-18), 24.33 (t, C-16), 25.28 (t, C-17), 35.96 (t, C-19), 37.05 (t, C-15), 41.91 (t, C-3), 52.71 (d, C1), 77.83 (d, C-12), 79.30 (d, C-13), 85.57 (d, C-11), 105 (d, C-10), 110.64 (s, C-4a), 111.40 (d, C-8), 112.78 (s, C-14), 118.51 (d, C-5), 119.84 (d, C-6), 122.36 (d, C-7), 127.78 (s, C-4b), 131.80 (s, C-9a), 136.31 (s, C-8a). *m*/*z*: 370 (M^+, 90), 327 (25),271 (20), 255 (28), 237 (22), 213 (50), 199 (30), 184 (84), 172 (98), 171 (100). Anal. calcd. for $C_{21}N_2O_4H_{26}$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.94; H, 7.11; N, 7.66.

10,11-*O*-Cyclohexylidene-12-β-hydroxy-13β-(1-tetrahydro-3β-carbomethoxy-β-carbolinyl)tetrahydrofuran (13). M.p. 194–196°C. $[\alpha]_D = -77.6^\circ$ ($c = 0.39$, $CHCl_3$). IR (KBr): 3446, 3378, 1742, 1654, 753. ^{1}H NMR ($CDCl_3$): δ 1.25–1.75 (m, 11H), 2.88 (dd, $J = 11{:}9$ Hz, 2.4 Hz, 1H), 3.19 (dd, $J = 14.4$ Hz, 2.5 Hz, 1H), 3.77 (dd, $J = 11.2$ Hz, 4.1 Hz, 1H), 3.83 (s, 3H), 4.33 (d, $J = 2.8$ Hz, 1H), 4.37 (dd, $J = 2.8$ Hz, 6.7 Hz, 1H), 4.55 (d, $J = 3.6$ Hz, 1H), 4.64 (d, $J = 6.7$ Hz, 1H), 4.90 (brs, NH), 6.11 (d, $J = 5.0$ Hz, 1H), 7.09 (t, $J = 7.0$ Hz, 1H), 7.19 (t, $J = 7.0$ Hz, 1H), 7.50 (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 1H), 8.51 (brs, NH). ^{13}C NMR ($CDCl_3$): δ 23.57 (C-18), 23.88 (C-16), 24.84 (C-17), 25.39 (C-4), 35.56 (C-19), 36.44 (C-15), 52.37 (C-1), 55.88 (C-3), 75.34 (C-12), 81.76 (C-13), 84.92 (C-11), 104.97 (C-10), 108.26 (C-14), 111.19 (C-8), 112.68 (C-4a), 118.10 (C-5), 119.60 (C-6), 122.10 (C-7), 126.69 (C-4b), 131.67 (C-9a), 136.28 (C-8a), 172.87 (C-20). *m*/*z*: 428 (M^+, 16), 427 (61), 369 (26), 271 (28), 241 (34), 230 (100), 211 (21), 183 (70), 170 (92), 169 (100); Anal calcd. for $C_{23}N_2O_6H_{28}$: C, 64.47; H, 6.59; N, 6.54. Found: C, 64.61; H, 6.50; N, 6.60.

10,11-*O*-Cyclohexylidene-12-β-hydroxy-13β-(1-tetrahydro-3α-carbomethoxy β-carbolinyl) tetrahydrofuran (15). M.p. 175–177°C. $[\alpha]_D = -60.17^\circ$ ($c = 0.339$, $CHCl_3$); IR (KBr): 3364, 1740, 1654, 747. ^{1}H NMR (DMSO-d_6): δ 1.25–1.90 (m, 11H), 3.00–3.19 (m, 2 H), 3.69 (s, 3 H), 3.98 (t, $J = 5.1$ Hz, 1H), 4.29 (d, $J = 3.0$ Hz, 1H), 4.36 (dd, $J =$ 2.7, 13.8 Hz, 1H), 4.53 (d, $J = 3.6$ Hz, 1H), 4.79 (d, $J = 6.6$ Hz, 1H), 6.08 (d, $J = 3.3$ Hz, 1H), 7.10 (t, $J = 6.3$ Hz, 1H), 7.13 (t, $J = 7.50$ Hz, 1H), 7.34 (d, $J = 7.5$ Hz, 1H), 7.50 (d, $J = 7.5$ Hz, 1H), 8.29 (s, NH). ^{13}C NMR (DMSO-d_6): δ 24.83 (C-4), 23.61 (C-18), 23.68 (C-16), 23.89 (C-17), 36.04 (C-19), 36.79 (C-15), 55.64 (C-3), 51.78 (C-1), 78.50 (C-12), 81.83 (C-13), 83.62 (C-11), 105.63 (C-10), 105.42 (C-14), 111.13 (C-8), 113.08 (C-4a), 118.16 (C-5), 119.19 (C-6), 120.02 (C-7), 126.76 (C-4b), 131.70 (C-9a), 136.35 (C-8a), 172.37 (C-20). m/z: 428 (M^+, 17), 427 (59), 369 (26), 271 (48), 241 (30), 230 (100), 211(20), 183 (62), 170 (90), 169 (100). Anal. calcd. for $C_{23}N_2O_6H_{28}$: C, 64.47; H, 6.59; N, 6.54. Found: C, 64.65; H, 6.52; N, 6.63.

9,10-*O*-Cyclohexylidene-11-β-hydroxy-12β-(1,2,3,4-tetrahydroisoquinolinyl) tetra-hydrofuran (17). IR (KBr): 3328, 1495, 1102. ^{1}H NMR ($CDC1_3$): δ 1.35–2.50 (m, 20H), 2.64–2.90 (m, 8H), 3.10–3.35 (m, 2H), 3.89 (brs, 2H), 4.24 (brd, 1H), 4.30 (brd, 2H), 4.58 (d, $J = 3.6$ Hz, 1H), 5.75 (d, $J = 4.8$ Hz, 1H), 5.97 (d, $J = 3.6$ Hz, IH), 7.00–7.40 (m, 8H). ^{13}C NMR ($CDC1_3$): δ 23.39, 23.49, 23.59, 23.74, 23.90, 24.90, 35.65, 36.07, 36.21, 36.47, 36.75, 36.96 (C-4, C-14, C-15, C-16, C-17, C-18), 46.66, 46.93 (C-3), 56.56 (C-1), 72.41, 77.90 (C-11), 79.05, 83.53 (C-12), 89.25, 89.69 (C-10), 104.11, 104.42 (C-9), 112.18, 113.24 (C-13), 125.95, 126.45, 128.27, 128.45, 128.50, 128.51, 128.55, 128.62, 128.63, 128.64 (C-4a, C-5, C-6, C-7, C-8), 139.65, 140.30 (C-8a). m/z: 331 (M^+, 20), 284 (90), 240 (20), 174 (50), 132 (30), 86 (100).

Typical Procedure for Bischler–Napieralski Condensation. Ten gram silicagel (60–120 mesh) was initially activated by irradiating in a microwave (Domestic oven: AEG, Micromat) oven for 5 min. at 850 W. A mixture of 1 mmol of the amide and 0.5 mL of $POC1_3$ was adsorbed over activated silica gel. It was then irradiated at 600 W initially for 5 min, then for another 2 min and finally for 2 more min. i.e., for a total of 9 min. The reaction was monitored at the end of each irradiation. The silica gel was then processed as has been described for Pictet–Spengler condensation and the products purified by column chromatography over silica gel.

3,4-dihydro-β-carboline (19). M.p. 86°C and then at 175–177°C (Lit.[6] m.p. 87°C and then at 175–176°C) crystallized from ether.

1-methyl 3,4-dihydro-β-carboline (21). M.p. 236–238°C (Lit.[7] 235–237°C).

3-carbomethoxy β-carboline (23). M.p. 242–244°C. IR (KBr): 3263, 1725, 1434, 1247. ^{1}H NMR ($CDC1_3$): δ 4.07 (s, 3H), 7.38 (m, 1H),

7.45–7.65 (m, 2H), 8.22 (d, $J = 8.1$ Hz, 1H), 8.90 (s, 1H), 8.95 (brs, 1H), 9.03 (s, 1H). m/z: 226 (M^+, 100). 195 (30), 171 (40), 140 (100). Anal. calcd. for $C_{13}N_2O_2H_{10}$: C, 69.08; H, 4.46; N, 12.40. Found: C, 69.12; H, 4.38; N, 12.58.

1-(3-carbomethoxy-1,2,3,4-tetrahydro-β-carbolinyl)-3-carbomethoxy-β-carboline (23a). M.p. 208–210°C. IR (KBr): 3349, 3293, 1739, 1673, 1223. ^{1}H NMR ($CDC1_3$): δ 2.85 (m, 1H), 4.65 (m, 2H), 3.84 (s, 3H), 4.05 (s, 3H), 6.04 (s, 1H), 6.72–7.50 (m, 6H), 7.52–7.82 (m, 2H), 8.78 (s, 1H), 9.50 (s, NH), 10.93 (s, 1H). m/z: 454 (M^+,100), 395 (24), 366 (36), 333 (37), 307 (40), 229 (30), 169 (65).

1-methyl,3-carbomethoxy-β-carboline (25). M.p. 168–170°C. IR (KBr): 3331, 1717, 1352, 1256. ^{1}H NMR ($CDCl_3$): δ 2.89 (s, 3H), 4.05 (s, 3H), 7.37 (m, 1H), 7.45–7.65 (m, 2H), 8.18 (d, $J = 7.8$ Hz, 1H), 8.68 (brs, 1H), 8.79 (s, NH). m/z: 240 (M^+, 100), 181 (85), 170 (90). Anal. calcd. for $C_{14}N_2O_2H_{12}$: C, 70.06; H, 5.04; N, 11.67. Found: C, 69.89; H, 5.15; N, 11.54.

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