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SYNTHESIS OF 1-ALKYLTETRAHYDROISOQUINOLINES

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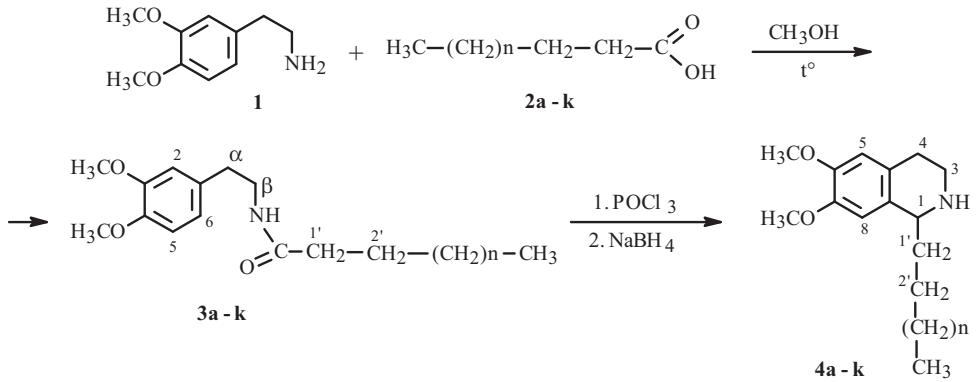
1-Alkyltetrahydroisoquinolines were prepared by a Bischler–Napieralski reaction starting from homoveratrylamine and monobasic acids. Their structures were confirmed by IR and NMR spectral data.

Keywords: Bischler–Napieralski reaction, 1-alkyltetrahydroisoquinolines, monobasic acids, homoveratrylamine.

Natural isoquinolines and their numerous derivatives exhibit high activity and are incorporated into many drugs [1, 2]. Derivatives of 3,4-dihydroisoquinoline garner the greatest number of publications on preparation methods, chemical transformations, and pharmacological activity of simple isoquinolines [3–5].

Compounds combining rather long hydrocarbon chains with a cyclic tetrahydroisoquinoline moiety are of special interest from a pharmacological viewpoint.

A simple synthetic scheme was used to synthesize the target products. This involved preparation of amides from homoveratrylamine (**1**) and available fatty acids **2a**–**k** (7:0, 9:0, 10:0, 12:0, 14:0, 16:0, 17:0, 18:0, 22:0, *cis*-18:1n9, *trans*-18:1n9) with subsequent the Bischler–Napieralski cyclization and reduction of the 3,4-dihydroisoquinolines to tetrahydroisoquinolines **4a**–**k**.



a: n = 3; **b:** = 5; **c:** n= 6; **d:** n = 8; **e:** n = 10; **f:** n = 12; **g:** n = 13; **h:** n = 14
i: n = 18; **j:** n = 14, Δ^9 *cis;* **k:** n = 14, Δ^9 *trans*

Use in the first step of a previously prepared salt rather than a mixture of compounds enabled amides **3** to be obtained in high yields. IR spectra of amides **3a**–**k** contained strong bands at 1638–1645 and 3010–3018 cm^{-1} that corresponded to stretching vibrations of CO and NH groups. PMR spectra of **3a**–**k** showed resonances for protons of all structural fragments. A feature of the PMR spectra was the fact that the 2-, 5-, and 6-protons of the aromatic ring formed a strongly coupled ABC-system. Therefore, for example, proton H-5 in **3a**–**k** appeared as a doublet at δ 6.74 ppm with SSCC J = 8 Hz with additional splitting because of the overlap of the H-2 and H-6 resonances. This was a second-order artifact. The nature of the spectrum changed slightly upon heating to 50°C. The H-2 and H-6 resonances shifted whereas the H-5 resonance became almost a regular doublet at 6.74 ppm with SSCC J = 8.6 Hz. Therefore, we present only chemical shifts for aromatic protons of all amides **3a**–**k** without indicating the resonance shape and SSCC.

The cyclization rate of amides **3a**–**k** and high yields of isoquinolines **4a**–**k** were practically independent of the alkyl chain length. Only the reactions with oleic (*cis*-18:1, **2j**) and elaidic (*trans*-18:1, **2k**) acids gave very low product yields.

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The structures of the synthesized compounds were confirmed by IR and PMR spectral data. IR spectra of **4a**–**k** lacked bands for amide carbonyl. PMR spectra exhibited a resonance for the H-1 proton at 4.35 ppm as a triplet with J = 6–7 Hz. The nature of the resonances for aromatic H-5 and H-8 protons also changed. They appeared as singlets.

The facts that the melting points of the amides increased upon lengthening the chain whereas the melting points of the tetrahydroisoquinoline hydrochlorides decreased and that the hydrochlorides of **4a**–**k** dissolved readily in $CHCl_3$ and poorly in H_2O deserve attention.

EXPERIMENTAL

IR spectra were recorded in KBr pellets on an FTIR system 2000 instrument (PerkinElmer). PMR spectra were taken in $CDCl_3$ with HMDS internal standard on a Unity-400+ spectrometer (400 MHz, Varian). R_f values were determined on LS 5/40 silica gel (Czech Rep.) using $CHCl_3$:MeOH (15:1, system 1; 10:1, system 2; 6:1, system 3; 4:1, system 4). Melting points of all synthesized compounds were determined on a Boetius microstage.

General Method for Preparing Amides 3a–k. A mixture of homoveratrylamine (0.012 mol, using an excess of amine) and monobasic acid (0.01 mol) in MeOH (5 mL) underwent spontaneous heating. The mixture was heated on an oil bath for 2 h at 178°C, treated with $CHCl_3$ (100 mL), and washed with HCl solution (3%), NaOH solution (2%), and H_2O until neutral. The $CHCl_3$ was evaporated. The residue was crystallized from Me_2CO or hexane. The resulting crystals were filtered off.

***N*-(3,4-Dimethoxy-β-phenylethyl)heptanamide (3a).** $C_{17}H_{27}NO_3$. Prepared from homoveratrylamine (1.84 g, 0.01 mol) and heptanoic acid (7:0, 1.32 g, 0.01 mol). Yield 84% (2.47 g), mp 55–57°C (hexane), R_f 0.54 (system 1).

IR spectrum (ν, cm^{-1}): 3310 (NH), 2933 (Ar-CH), 1645 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.3, CH_3), 1.21 (6H, br. s, $3CH_2$), 1.52 (2H, m, H-2′), 2.05 (2H, t, J = 7.3, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.795 (3H, s, OCH_3), 3.801 (3H, s, OCH_3), 5.45 (1H, m, NH), 6.65 (1H, H-2), 6.67 (1H, H-6), 6.74 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)nonanamide (3b).** $C_{19}H_{31}NO_3$. Prepared from homoveratrylamine (2 g, 0.011 mol) and nonanoic acid (9:0, 1.32 g, 0.008 mol). Yield 92% (2.47 g), mp 69–71°C (hexane), R_f 0.6 (system 1).

IR spectrum (ν, cm^{-1}): 3310 (NH), 2925 (Ar-CH), 1639 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.5, CH_3), 1.20 (10H, br. s, $5CH_2$), 1.52 (2H, m, H-2′), 2.05 (2H, t, J = 7.5, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.799 (3H, s, OCH_3), 3.805 (3H, s, OCH_3), 5.37 (1H, m, NH), 6.68 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)decanamide (3c).** $C_{20}H_{33}NO_3$. Prepared from homoveratrylamine (0.28 g, 1.5 mmol) and decanoic acid (10:0, 0.27 g, 1.5 mmol). Yield 83% (0.44 g), mp 81–82°C (Me_2CO), R_f 0.8 (system 1).

IR spectrum (ν, cm^{-1}): 3318 (NH), 2923 (Ar-CH), 1638 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Гц): 0.81 (3H, t, J = 7.7, CH_3), 1.19 (12H, br. s, $6CH_2$), 1.53 (2H, m, H-2′), 2.05 (2H, t, J = 7.7, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.36 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)dodecanamide (3d).** $C_{22}H_{37}NO_3$. Prepared from homoveratrylamine (0.2 g, 1.1 mmol) and dodecanoic acid (12:0, 0.18 g, 0.9 mmol). Yield 88% (0.29 g), mp 88–90°C (Me_2CO), R_f 0.88 (system 1).

IR spectrum (ν, cm^{-1}): 3318 (NH), 2917 (Ar-CH), 1638 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.7, CH_3), 1.18 (16H, br. s, $8CH_2$), 1.51 (2H, m, H-2′), 2.05 (2H, t, J = 7.7, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.33 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)tetradecanamide (3e).** $C_{24}H_{41}NO_3$. Prepared from homoveratrylamine (0.16 g, 0.9 mmol) and tetradecanoic acid (14:0, 0.14 g, 0.6 mmol). Yield 71% (0.17 g), mp 94–95°C (Me_2CO), R_f 0.9 (system 1).

IR spectrum (ν, cm^{-1}): 3318 (NH), 2917 (Ar-CH), 1638 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.5, CH_3), 1.18 (20H, br. s, $10CH_2$), 1.5 (2H, m, H-2′), 2.05 (2H, t, J = 7.5, H-1′), 2.70 (2H, t, J = 7, Hα), 3.44 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.32 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)hexadecanamide (3f).** $C_{26}H_{45}NO_3$. Prepared from homoveratrylamine (0.6 g, 3.3 mmol) and hexadecanoic acid (16:0, 0.75 g, 3 mmol). Yield 84.5% (1.04 g), mp 102–103°C (Me_2CO), R_f 0.9 (system 2).

IR spectrum (ν, cm^{-1}): 3318 (NH), 2917 (Ar-CH), 1638 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.7, CH_3), 1.18 (24H, br. s, $12CH_2$), 1.53 (2H, m, H-2′), 2.05 (2H, t, J = 7.7, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.35 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)heptadecanamide (3g).** $C_{27}H_{47}NO_3$. Prepared from homoveratrylamine (1.4 g, 7.7 mmol) and heptadecanoic acid (17:0, 2 g, 7.4 mmol). Yield 82% (2.62 g), mp 99–101°C (Me_2CO), R_f 0.8 (system 2).

IR spectrum (ν, cm^{-1}): 3312 (NH), 2920 (Ar-CH), 1639 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.2, CH_3), 1.18 (26H, br. s, $13CH_2$), 1.52 (2H, m, H-2′), 2.05 (2H, t, J = 7.2, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.32 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)octadecanamide (3h).** $C_{28}H_{49}NO_3$. Prepared from homoveratrylamine (0.4 g, 2.2 mmol) and octadecanoic acid (18:0, 0.61 g, 2 mmol). Yield 82% (0.79 g), mp 103–104°C (Me_2CO), R_f 0.88 (system 2).

IR spectrum (ν, cm^{-1}): 3309 (NH), 2920 (Ar-CH), 1639 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.7, CH_3), 1.18 (28H, br. s, $14CH_2$), 1.55 (2H, m, H-2′), 2.05 (2H, t, J = 7.7, H-1′), 2.70 (2H, t, J = 6.8, Hα), 3.43 (2H, q, J = 6.1, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.35 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)docosanamide (3i).** $C_{32}H_{53}NO_3$. Prepared from homoveratrylamine (0.5 g, 2.8 mmol) and docosanoic acid (22:0, 0.84 g, 2.6 mmol). Yield 83% (1.03 g), mp 105–107°C (Me_2CO), R_f 0.9 (system 2).

IR spectrum (ν, cm^{-1}): 3313 (NH), 2920 (Ar-CH), 1639 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.7, CH_3), 1.18 (36H, br. s, $18CH_2$), 1.52 (2H, m, H-2′), 2.05 (2H, t, J = 7.7, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.35 (1H, m, NH), 6.65 (1H, H-2), 6.70 (1H, H-6), 6.76 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)octadecen-9-amide (*cis*) (3j).** $C_{28}H_{47}NO_3$. Prepared from homoveratrylamine (1 g, 5.5 mmol) and oleic acid (18:1n9, 1.5 g, 5.3 mmol). Yield 63% (1.5 g), mp 105–107°C (Me_2CO), R_f 0.83 (system 2).

IR spectrum (ν, cm^{-1}): 3317 (NH), 2920 (Ar-CH), 1639 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.82 (3H, t, J = 7, CH_3), 1.20 (22H, br. s, $11CH_2$), 1.52 (3H, m, H-7′, 10′), 1.98 (1H), 2.04 (2H, t, J = 7.6, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.79 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 5.28 (2H, m, CH=CH); 6.66 (1H, H-2), 6.67 (1H, H-6), 6.75 (1H, H-5).

***N*-(3,4-Dimethoxy-β-phenylethyl)octadecen-9-amide (*trans*) (3k).** $C_{28}H_{47}NO_3$. Prepared from homoveratrylamine (0.2 g, 1.1 mmol) and elaidic acid (18:1n9, 0.27 g, 1 mmol). Yield 70% (0.3 g), mp 105–107°C (Me_2CO), R_f 0.73 (system 2).

IR spectrum (ν, cm^{-1}): 3318 (NH), 2920 (Ar-CH), 1638 (N-C=O). ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7, CH_3), 1.20 (20H, br. s, $10CH_2$), 1.50 (2H, m, H-2′), 1.88 (2H, t, J = 7.2, H-7, 10), 2.05 (2H, t, J = 7, H-1′), 2.70 (2H, t, J = 7, Hα), 3.43 (2H, q, J = 7, Hβ), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.31 (2H, m, CH), 6.65 (1H, H-2), 6.67 (1H, H-6), 6.75 (1H, H-5).

General Method for Preparing Tetrahydroisoquinolines 4a–k. A mixture of amide of monobasic acid (6 mmol), anhydrous benzene (30 mL), and $POCl_3$ (12 mmol) was refluxed for 1 h. The course of the reaction was monitored by TLC. The benzene and $POCl_3$ were distilled off. The residue was dissolved in MeOH (30 mL) and treated in portions at 0–5°C with $NaBH_4$ (0.02 mol). The MeOH was distilled off. The residue was dissolved in H_2O and extracted with $CHCl_3$. The $CHCl_3$ was removed. Isoquinolines **4a**–**k** were crystallized from Me_2CO.

1-Hexyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4a). $C_{17}H_{27}NO_2$. Prepared from amide **3a** (1 g, 3.4 mmol) and $POCl_3$ (0.7 mL). Yield 74% (0.7 g), mp of hydrochloride 188–191°C (Me_2CO), R_f 0.6 (system 4).

IR spectrum (ν, cm^{-1}): 3450, 2930, 1611, 1519, 1450, 1264. ^1H NMR spectrum (400 MHz, CD_3OD, δ, ppm, J/Hz): 0.86 (3H, m, J = 6, CH_3), 1.30 (6H, d, J = 6, $3CH_2$), 1.38 and 1.44 (each 1H, m, CH_2), 1.84 and 2.05 (each 1H, m, H-1′), 2.96 (2H, m, H-4), 3.47 (2H, q, J = 6, H-3), 3.76 (6H, s, $2OCH_3$), 4,40 (1H, m, H-1), 6.74 (2H, s, H-5, 8).

1-Octyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4b). $C_{19}H_{31}NO_2$. Prepared from amide **3b** (1.3 g, 4 mmol) and $POCl_3$ (0.8 mL). Yield 71% (0.87 g), mp of hydrochloride 177–180°C (Me_2CO), R_f 0.6 (system 4).

IR spectrum (ν, cm^{-1}): 3611, 2928, 1611, 1519, 1460, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, m, J = 7.0, CH_3), 1.20 (10H, br. s, $5CH_2$), 1.57 (2H, q, J = 7.4, H-1′, 2′), 2.98 and 3.09 (each 1H, t, J = 6, H-4), 3.26 and 3.50 (each 1H, q, J = 6.4, H-3), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6.6, H-1), 6.50 (1H, s, H-8), 6.53 (1H, s, H-5).

1-Nonyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4c). $C_{20}H_{33}NO_2$. Prepared from amide **3c** (0.26 g, 0.8 mmol) and $POCl_3$ (0.25 mL). Yield 80% (0.2 g), mp of hydrochloride 173–176°C (Me_2CO), R_f 0.55 (system 3).

IR spectrum (ν, cm^{-1}): 3749, 2926, 1611, 1519, 1449, 1265. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7.0, CH_3), 1.20 (12H, br. s, $6CH_2$), 1.57 (4H, q, J = 8, H-1′, 2′), 2.99–3.10 (each 1H, t, J = 6, H-4), 3.26 (1H, q, J = 6, H-3a), 3.50 (1H, q, J = 6, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6, H-1), 6.50 (1H, s, H-8), 6.53 (1H, s, H-5).

1-Undecyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4d). $C_{22}H_{37}NO_2$. Prepared from amide **3d** (0.14 g, 0.4 mmol) and $POCl_3$ (0.10 mL). Yield 77% (0.1 g), mp of hydrochloride 165–168°C (Me_2CO), R_f 0.62 (system 3).

IR spectrum (ν, cm^{-1}): 3450, 2925, 1612, 1519, 1460, 1263. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7, CH_3), 1.19 (16H, br. s, $8CH_2$), 1.56 (4H, q, J = 7.4, H-1′, 2′), 2.98 and 3.10 (each 1H, t, J = 6, H-4), 3.26 (1H, q, J = 6, H-3a), 3.50 (1H, q, J = 6, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6, H-1), 6.50 (1H, s, H-85), 6.53 (1H, s, H-5).

1-Tridecyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4e). $C_{24}H_{41}NO_2$. Prepared from amide **3e** (0.15 g, 0.4 mmol) and $POCl_3$ (0.10 mL). Yield 71% (0.1 g), mp of hydrochloride 155–158°C (Me_2CO), R_f 0.44 (system 3).

IR spectrum (ν, cm^{-1}): 3608, 2923, 1612, 1519, 1460, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7, CH_3), 1.19 (20H, br. s, $10CH_2$), 1.57 (4H, q, J = 7.4, H-1′, 2′), 2.98 and 3.09 (each 1H, t, J = 6.4, H-4), 3.26 (1H, q, J = 6.6, H-3a), 3.50 (1H, q, J = 6.6, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6, H-1), 6.50 (1H, s, H-8), 6.53 (1H, s, H-5).

1-Pentadecyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4f). $C_{26}H_{45}NO_2$. Prepared from amide **3f** (0.9 g, 0.002 mol) and $POCl_3$ (0.4 mL). Yield 88% (0.76 g), mp of hydrochloride 155–158°C (Me_2CO), R_f 0.62 (system 4).

IR spectrum (ν, cm^{-1}): 3608, 2921, 1612, 1519, 1469, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.80 (3H, t, J = 7.0, CH_3), 1.16 (26H, br. s, $13CH_2$), 1.57 (2H, m, H-2′), 2.34 (1H, m, H-4a), 2.58 (2H, br. s, H-1′), 2.77 (1H, m, H-4b), 3.04 (1H, m, H-3a), 3.48 (1H, q, J = 6.6, H-3b), 3.73 (6H, s, $2OCH_3$), 4.35 (1H, q, J = 5.6, H-1), 6.43 (1H, s, H-8), 6.47 (1H, s, H-5).

1-Hexadecyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4g). $C_{27}H_{47}NO_2$. Prepared from amide **3g** (1 g, 2.3 mmol) and $POCl_3$ (0.5 mL). Yield 90% (0.86 g), mp of hydrochloride 154–156°C (Me_2CO), R_f 0.42 (system 3).

IR spectrum (ν, cm^{-1}): 3607, 2923, 1611, 1519, 1462, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 6.7, CH_3), 1.19 (26H, br. s, $13CH_2$), 1.44 (2H, q, J = 8, H-2′), 1.92 (2H, q, J = 8.5, H-1′), 2.65 and 2.73 (each 1H, t, J = 6.4, H-4), 2.95 (1H, q, J = 6, H-3a), 3.21 (1H, q, J = 6, H-3b), 3.78 (6H, s, OCH_3), 3.92 (1H, q, J = 6, H-1), 6.50 (1H, s, H-8), 6.54 (1H, s, H-5).

1-Heptadecyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4h). $C_{28}H_{49}NO_2$. Prepared from amide **3h** (0.75 g, 1.7 mmol) and $POCl_3$ (0.4 mL). Yield 70% (0.5 g), mp of hydrochloride 143–146°C (Me_2CO), R_f 0.57 (system 3).

IR spectrum (ν, cm^{-1}): 3450, 2920, 1612, 1519, 1470, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7, CH_3), 1.18 (30H, br. s, $15CH_2$), 1.57 (4H, q, J = 7.5, H-1′, 2′), 2.99 (1H, t, J = 6.17, H-4a), 3.10 (1H, t, J = 6.17, H-4b), 3.33 (1H, q, J = 6, 12.5, H-3a), 3.50 (1H, q, J = 6, 12.5, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6.4, H-1), 6.50 (1H, s, H-8), 6.53 (1H, s, H-5).

1-Heneicosyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4i). $C_{32}H_{57}NO_2$. Prepared from amide **3i** (0.9 g, 1.8 mmol) and $POCl_3$ (0.4 mL). Yield 92% (0.8 g), mp of hydrochloride 143–146°C (Me_2CO), R_f 0.57 (system 3).

IR spectrum (ν, cm^{-1}): 3342, 2916, 1610, 1518, 1451, 1257. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 6.7, CH_3), 1.19 (38H, br. s, $19CH_2$), 1.57 (4H, m, H-1′, 2′), 2.60 and 2.65 (each 1H, t, J = 6, H-4), 2.90 (1H, q, J = 6, H-3a), 3.15 (1H, q, J = 7.6, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.82 (1H, m, H-1), 6.50 (1H, s, H-8), 6.55 (1H, s, H-5).

1-(Heptadecen-8-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (*cis*) (4j). $C_{28}H_{47}NO_2$. Prepared from amide **3j** (0.5 g, 1.1 mmol) and $POCl_3$ (0.25 mL). Yield 62% (0.3 g), mp of hydrochloride 146–149°C (Me_2CO), R_f 0.4 (system 3).

IR spectrum (ν, cm^{-1}): 3424, 2922, 1612, 1519, 1460, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.80 (3H, t, J = 7, CH_3), 1.18 (24H, br. s, $12CH_2$), 1.57 (2H, q, J = 6.8, H-1′), 1.99 (2H, q, J = 7, H-7′), 2.99 (1H, t, J = 6.5, H-4a), 3.09 (1H, t, J = 6.5, H-4b), 3.26 (1H, q, J = 6.4, H-3a), 3.50 (1H, q, J = 6.4, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.35 (1H, t, J = 6, CH-1), 5.23 (1H, m, CH=CH), 6.49 (1H, s, H-8), 6.52 (1H, s, H-5).

1-(Heptadecen-8-yl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (*trans*) (4k). $C_{28}H_{47}NO_2$. Prepared from amide **3k** (0.15 g, 0.34 mmol) and $POCl_3$ (0.1 mL). Yield 71% (0.1 g), mp of hydrochloride 148–151°C (Me_2CO), R_f 0.4 (system 3).

IR spectrum (ν, cm^{-1}): 3424, 2922, 1611, 1519, 1469, 1264. ^1H NMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81 (3H, t, J = 7, CH_3), 1.19 (22H, br. s, 11CH_2), 1.57 (2H, q, J = 7.4, H-1′), 1.90 (2H, q, J = 7, H-7′), 2.04 (2H, t, J = 7, H-10′), 2.99 (1H, t, J = 6, H-4a), 3.12 (1H, t, J = 6, H-4b), 3.26 (1H, q, J = 6.6, H-3a), 3.50 (1H, q, J = 6.6, H-3b), 3.78 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.34 (1H, t, J = 6.4, H-1), 5.33 (2H, q, J = 2, CH=CH), 6.50 (1H, s, H-8), 6.53 (1H, s, H-5).

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