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# Photochemically induced cyclization of *N*-[2-(*o*-styryl)phenylethyl]acetamides and 5-styryl-1-methyl-1,2,3,4-tetrahydroisoquinolines: new total syntheses of 1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinolines

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**Abstract**—Two new total syntheses of 1-methyl-1,2,3,4-dihydronaphtho[1,2-*f*]isoquinolines are based on the construction of their phenanthrene ring system by photochemically induced cyclization of *N*-{2-[(*E*)-2-phenyl-1-ethenyl]phenylethyl}acetamides or 1-methyl-5-[(*E*)-2-phenyl-1-ethenyl]-1,2,3,4-tetrahydroisoquinolines. 

Our previous paper[1] reported the first total syntheses of naphtho[2,1-*f*]isoquinolines (**1**), a class of isoquinolines that received negligible attention until the recent isolation of litebamine[2] and annoretine,[3] and two subsequent partial syntheses of litebamine[4,5] from its probable biogenetic precusor,[4] the aporphine boldine.

Here, we describe two additional total syntheses of naphthoisoquinolines **1**. Like those described in Ref. 1, they are both based on a sequential construction of rings C and A, but start from styrylphenylethylacetamides **3**, these latter include a stilbene-like system allowing construction of the phenanthrene ring system of acetamides **2** transformation of which into the target compounds **1** is described in Ref. 1. Alternatively, ring A can be constructed first, giving 5-styrylisoquinolines **4**,[5] that can be transformed into naphthoisoquinolines **1** by electrocyclic cyclization (Scheme 1).

We first studied the preparation of starting *o*-styrylphenylethylacetamide **3a** by Heck[6] coupling of an appropriate halobenzene to styrene (Scheme 2). When a deoxygenated solution of phenylethylacetamide **6a**,[7] styrene (**5a**), triethylamine and palladium acetate was heated at 135°C in a sealed tube for 3 days, the desired unsubstituted *o*-styrylphenylethylacetamide **3a** was obtained in 81% yield. Its mass spectrum confirmed the expected molecular weight ($m/z$=265) and its $^1$H NMR spectrum the *E* configuration of the stilbene double bond showing two doublets at 7.03 (1H, $J$=16.1 Hz) and 7.27 ppm (1H, $J$=16.1 Hz).

We next studied the preparation of dimethoxystyrylphenylethylacetamide **3b** by this route. Since Heck coupling between **6b**[8] and styrene in the above conditions furnished **3b** in only 25% yield, we explored a longer but, as it turned out, more efficient route based on the opening of benzylideneisoquinolines **10** to *o*-phenylacetylphenylethylacetamides **11**[9] (Scheme 2). Reaction between homoveratrylamine (**6c**) and phenylacetyl chloride (**7a**) gave phenylacetylphenylethylamine **8a**, which was cyclized to benzyldihydroisoquinoline **9a** under typical Bichler–Napieralski conditions.[10] Treatment of this isoquinoline with $Ac_2O$ gave *N*-acetyl-1-benzylideneisoquinoline **10a**, which upon treatment with 10% aqueous HCl solution opened to the desired phenylacetylphenylacetamide **11a**.[9] Reduction of this latter with $NaBH_4$ gave its hydroxy derivative **12a**, which was directly dehydrated to styrylphenylethylacetamide **3b**. The overall yield for this indirect route to **3b** was 70%.

Finally, tetramethoxystyrylphenylethylacetamide **3c** was prepared by the above both routes. Heck coupling of *o*-bromohomoveratrylamine (**6b**) with dimethoxystyrene **5b**[11] afforded **3c** in 47% yield. The indirect route from previously prepared *o*-acetylphenylethylacetamide **11b**[1] via hydroxyacetamide **12b** gave a yield of 75%.

*Keywords*: alkaloids; biaryls; isoquinolines; electrocyclic reactions; photochemistry.

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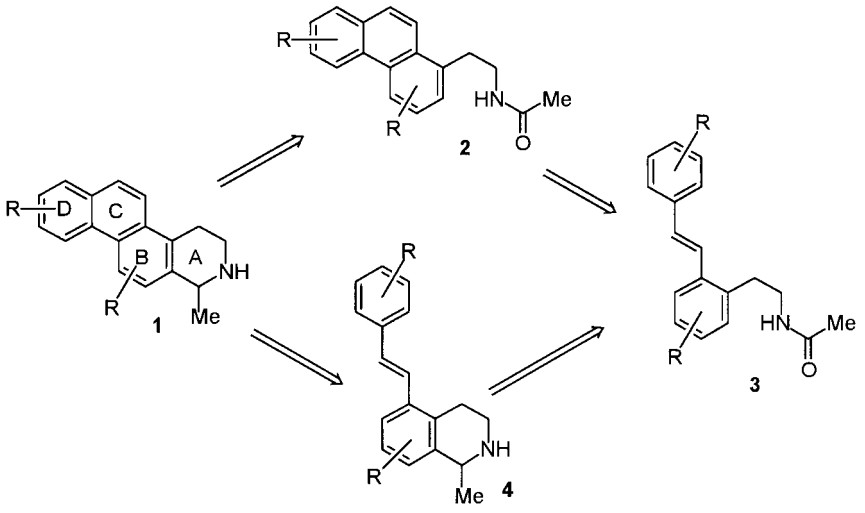
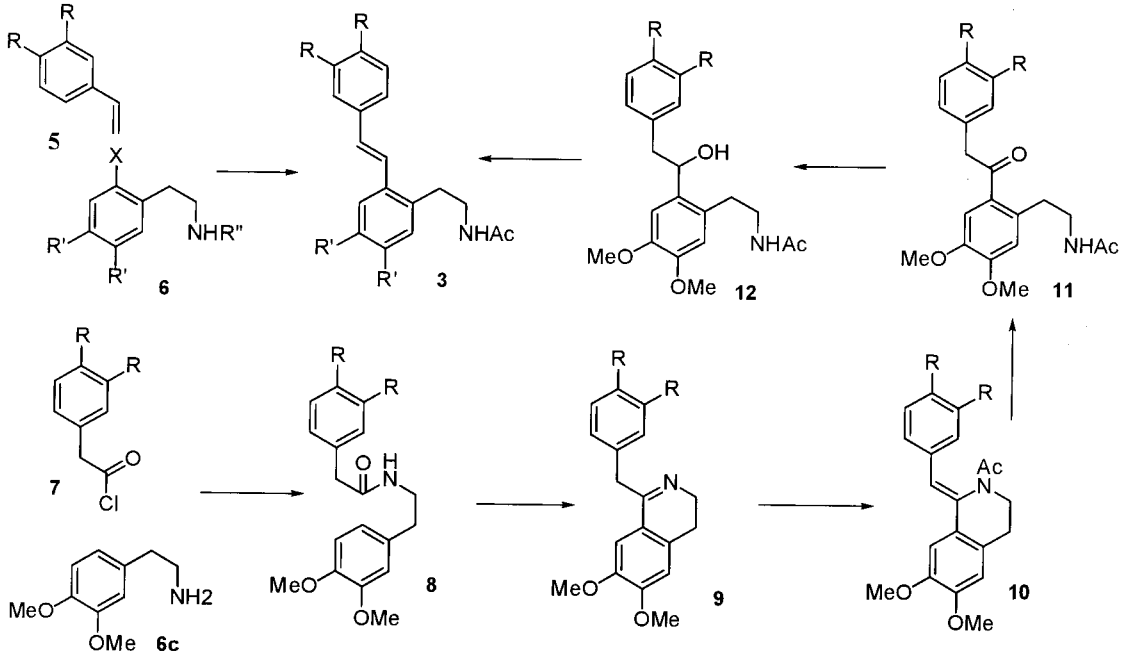


**Scheme 1.**

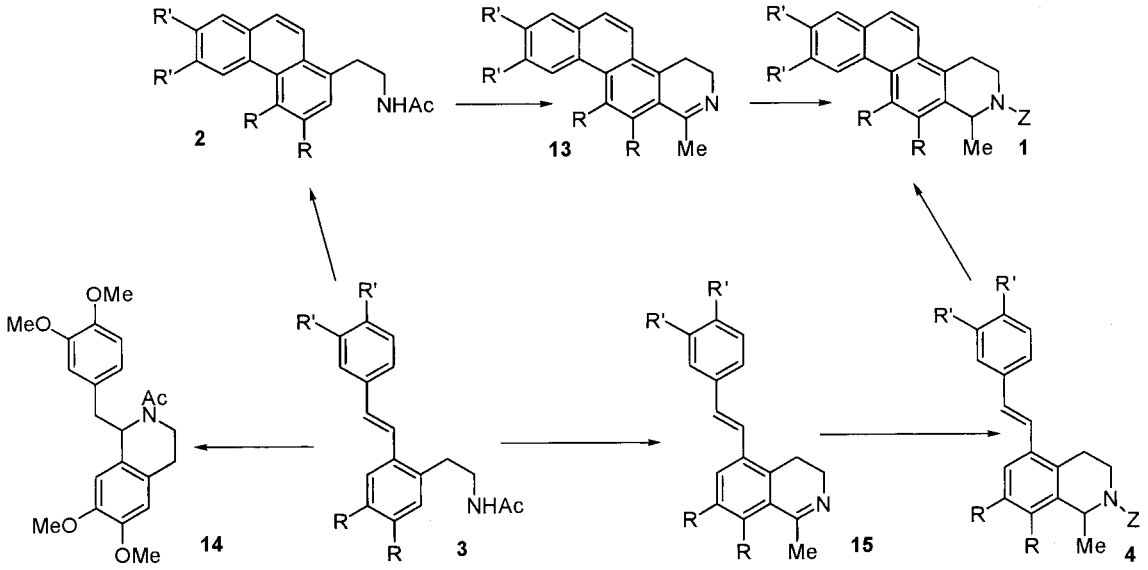
To sum up, the results of this part of the study suggest that influence of the substituents present on starting materials **5** and **6** is such that Heck coupling is efficient for the preparation of the unsubstituted styrylphenylethylacetamide **3a**, but the alternative sequence from 1-benzylisoquinolines **9** is more efficient for methoxy-substituted compounds **3**.

We next studied the photochemically induced electrocyclic cyclization[12] of styrylphenylethylacetamides **3**. Irradiation of **3a** with a 450 W Hanovia medium-pressure lamp equipped with a Pyrex filter gave a 70% yield of the expected phenanthrylacetamide **2a**, as deduced from spectroscopic and analytical data. $^1$H NMR spectrum of this product showed signals for a total of nine aromatic protons, including a multiplet at 8.58–8.67 ppm corresponding to the deshielded protons on C(4) and C(5). Treatment of **2a** with $POCl_3$ under Bichler–Napieralki conditions afforded a 73% yield of naphthodihydroisoquinoline **13a**, which was reduced with $NaBH_4$ to the desired naphthoisoquinoline **1a** in 93% yield (Scheme 3).

Photolysis of dimethoxystyrylacetamide **3b** under the above conditions gave a 30% yield of phenanthreneacetamide **2b**, which in the previous work[1] had been converted into tetrahydronaphthoisoquinoline **1b** via dihydronaphthoisoquinoline **13b** by successive treatment with $POCl_3$ and $NaBH_4$. Similar photolysis of tetramethoxystyrylacetamide **3c** gave the corresponding naphthoisoquinoline **2c** in only 6% yield, the main product being *N*-acetyltetrahydroisoquinoline **14**, which was probably formed by a radical process involving photochemically induced attack[13] on the stilbene double bond by nitrogen. Following the same procedure as for the preparation of **2a** and **2b**, **3c** was easily converted into naphthoisoquinoline **1c** via its dihydroderivative **13c**.



**Scheme 2. 3**: (**a**) R=R′=H; (**b**) R=H, R′=OMe; (**c**) R=R′=OMe. **5**: (**a**) R=H; (**b**) R=OMe. **6**: (**a**) R′=H, R″=Ac, X=Br; (**b**) R′=OMe, R″=Ac, X=Br; (**c**) R′=OMe, R″=X=H. **7–12**: (**a**) R=H; (**b**) R=OMe.




**Scheme 3.** **1**,**4**: (**a**) R=R′=Z=H; (**b**) R=OMe, R′=Z=H; (**c**) R=OMe, R′=H, Z=$CO_2Et$; (**d**) R=R′=OMe, Z=H; (**e**) R=R′=OMe, Z=$CO_2Et$. **2**,**3**,**13**,**15**: (**a**) R=R′=H; (**b**) R=OMe, R′=H; (**c**) R=R′=OMe.

The foregoing results suggest that the stilbene chromophore of compounds **3** is altered by electron donating groups in a way that disfavours the desired electrocyclization. This led us to explore the alternative route from **3** to **1** via 5-styryl-isoquinolines **4** (Scheme 1). Treatment of unsubstituted styrylphenylethylamide **3a** with $POCl_3$ gave the corresponding 5-styryldihydroisoquinoline **15a** in a low yield (15%), that we attribute to the absence of activating substituents on the aromatic ring. We desisted from pursuing this route to **1a** any further. However, the same conditions efficiently transformed **3b** and **3c** into the substituted styrylisoquinolines **15b** and **15c** in 84% and 96% yield, respectively. Compounds **15b** and **15c** were then efficiently reduced with $NaBH_4$ to the corresponding tetrahydroisoquinolines **4b** and **4d**, respectively.

We next studied the photolysis of 5-styrylisoquinolines **4**. Irradiation of dimethoxystyrylisoquinoline **4b** in the same conditions as for **2b** led to a complex reaction mixture. This is attributed to the unshared electron pair on the nitrogen[13] because protection of the nitrogen atom as the uretane (Z=$CO_2Et$) by treatment with ethyl chloroformiate allowed the resulting compound **4c** to be cyclized to the expected naphthoisoquinoline **1c** in 60% yield (established from analytical and spectroscopic data). $^1H$ NMR spectrum of **1c** is very complex in the aliphatic region and shows signals for a total of six aromatic protons, the signal at 9.63 ppm corresponding to the deshielded proton on C(10). Similarly, tetramethoxystyrylisoquinoline **4d** was reacted with ethyl chloroformiate to give **4e**, which upon irradiation with UV light as above afforded a 20% yield of the desired *N*-carbethoxyisoquinoline **1e**. Final basic hydrolysis of **1c** and **1e** gave products identical to the naphthoisoquinolines **1b** and **1d** that were obtained[1] in our earlier work.

To sum up, we have developed two alternative photochemical routes for the transformation of *o*-styryl-phenylethylacetamides **3** into naphthoisoquinolines **1** via the corresponding phenanthrenylethylacetamides **2** or via the 5-styrylisoquinolines **4**. In both routes, the yield of the photocyclization step is highly influenced by the presence of electron-donating substituents on the aromatic rings; for substituted naphthoisoquinolines, the route via 5-styrylisoquinolines gives best results, because interaction between its N atom and the stilbene-like system under irradiation is prevented.

These photochemical approaches to naphthoisoquinolines **1** are simpler but not always as efficient as the free radical route described in our previous work.[1] On the whole, the radical approach seems to be preferable for the preparation of substituted naphthoisoquinolines.

Finally, we note the contribution of this study to the chemistry of 5-styrylisoquinolines, which have hitherto received virtually no attention.[5]

## 1. Experimental

### 1.1. General

Melting points were determined in a Kofler Thermogerate apparatus and are uncorrected. Infrared spectra were recorded on a MIDAC FTIR spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Bruker WM-250 apparatus, using deuteriochloroform solutions containing tetramethylsilane as internal standard. Mass spectra were obtained on a Kratos MS 50 TC mass spectrometer. Thin layer chromatography (TLC) was performed using Merck GF-254 type 60 silica gel and dichloromethane/methanol mixtures as eluant; the TLC spots were visualized with ultraviolet light or iodine vapour. Column chromatography was carried out using Merck type 9385 silica gel. Compounds **9a** and **b** were prepared as per Ref. 10. Solvents were purified as per Ref. 14. Solutions of extracts in organic solvents were dried with anhydrous sodium sulphate.

**1.1.1. *N*-{2-[(*E*)-2-Phenyl-1-ethenyl]phenylethyl}acetamide (3a).** A deoxygenated mixture of 2-bromophenylethylacetamide (0.3 g, 1.2 mmol), styrene (0.16 mL, 1.37 mmol), palladium acetate (15 mg, 0.05 equiv.), triphenylphosphine (32 mg, 0.1 equiv.) and triethylamine (0.34 mL, 2.46 mmol) in dry acetonitrile (10 mL) was heated in a sealed tube at 130°C for 3 days. The suspension was then filtered through celite, the filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (eluant: 3:1 hexane/ethyl acetate), giving compound **3a** (0.26 mg, 81% yield). Mp 132–134°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl); 3280 (NH), 1645 (C═O). $^1H$ NMR ($\delta$, ppm): 1.88 (s, 3H, $-CH_3$), 2.97–3.01 (m, 2H, $-CH_2-$), 3.35–3.58 (m, 2H, $-CH_2-$), 5.82 (bs, 1H, –NH), 7.03 (d, $J$=16.1 Hz, 1H, –C═CH–), 7.16–7.68 (m, 9H, 9×Ar-H), 7.27 (d, $J$=16.1 Hz, 1H, –CH═C–). MS (*m*/*z*, %): 265 ($M^+$, 18), 206 (100), 91 (83). Anal. calcd for $C_{18}H_{19}NO_3$, C 81.47, H 7.22, N 5.28; found, C 81.12, H 7.36, N 5.40.

**1.1.2. *N*-{4,5-Dimethoxy-2-[(*E*)-2-phenyl-1-ethenyl]phenylethyl}acetamide (3b).** *Procedure a*. Compound **3b** was prepared in 25% yield from 2-bromo-4,5-dimethoxyphenylethylacetamide (0.15 g, 0.49 mmol) and styrene (0.063 mL, 0.54 mmol) following the same procedure as for compound **3a**. Mp 154–156°C (methanol). IR ($\nu$, $cm^{-1}$, KBr): 3239 (–NH), 1648 (C═O). $^1H$ NMR ($\delta$, ppm): 1.88 (s, 3H, $-CH_3$), 2.93–2.97 (m, 2H $-CH_2-$), 3.45–3.49 (m, 2H, $-CH_2-$), 3.90 (s, 3H, $-OCH_3$), 3.95 (s, 3H, $-OCH_3$), 5.53 (bs, 1H, –NH), 6.68 (s, 1H, Ar-H), 6.92 (d, $J$=16.0 Hz, 1H, –C═CH–), 7.15 (s, 1H, Ar-H), 7.23–7.56 (m, 6H, 5×Ar-H and –CH═C–) MS (*m*/*z*, %): 326 [$(M+1)^+$, 19], 325 ($M^+$, 82), 267 (21), 266 (100), 265 (9), 253 (27), 251 (18), 235 (38), 234 (68), 223 (10), 222 (35), 192 (66), 175 (45), 165 (18). Anal. calcd for $C_{20}H_{23}NO_3$, C 73.82, H 7.12, N 4.30; found, C 73.73, H 7.11, N 4.40.

*Procedure b*. A solution of hydroxyamide **12a** (1 g, 2.91 mmol) and 10% aqueous hydrogen chloride solution (7 mL) in dioxan (20 mL) was refluxed for 45 min. The dioxan was evaporated in vacuo and the aqueous residue was diluted in water (20 mL) and extracted with chloroform (3×15 mL). The pooled organic layers were dried, filtered and concentrated in vacuo, and the residue was purified by flash column chromatography (eluant: 7:1 ethylacetate/hexane), giving compound **3b** as a white solid (0.89 g, 95% yield).

**1.1.3. *N*-[4,5-Dimethoxy-2-(2-phenylacetyl)phenylethyl]-acetamide (11a).** Ten percent aqueous hydrochloric acid solution (25 mL) was added to a solution of acetamide **10a** (1 g, 3.0 mmol) in methanol (12.5 mL) and the mixture was refluxed for 5 h. The methanol was evaporated in vacuo and the resulting suspension was basified with saturated aqueous potassium carbonate solution and extracted with chloroform (3×25 mL). The pooled organic layers were dried, filtered and concentrated in vacuo, giving amide **11a** (1 g, 96% yield) as a white solid. Mp 118–120°C (ethyl acetate). IR ($\nu$, $cm^{-1}$, NaCl): 3485 (–NH), 1667 (C═O) 1640 (C═O). $^1H$ NMR ($\delta$, ppm): 1.89 (s, 3H, $-CH_3$), 2.90–2.98 (m, 2H, $-CH_2-$), 3.41–3.52 (m, 2H, $-CH_2-$), 3.89 (s, 3H, $-OCH_3$), 3.91 (s, 3H, $-OCH_3$), 4.22 (s, 2H, $-CH_2-$), 6.56 (bs, 1H, –NH), 6.77 (s, 1H, Ar-H), 7.22–7.38 (m, 5H, 5×Ar-H), 7.27 (s, 1H, Ar-H). MS (*m*/*z*, %): 341 ($M^+$, 3), 323 (6), 281 (43), 280 (100), 250 (33), 208 (53), 191 (22), 167 (21), 149 (61), 91 (22), 58 (38). Anal. calcd for $C_{22}H_{27}NO_6$, C 65.82, H 6.78, N 3.49; found, C 65.97, H 6.92, N 3.61.

**1.1.4. *N*-[2-(1-Hydroxy-2-phenyl-1-hydroxyethyl)-4,5-dimethoxyphenylethyl]acetamide (12a).** Small portions of sodium borohydride (250 mg) were added over 3 h to a solution of acetamide **11a** (1 g, 2.93 mmol) in THF (40 mL) and after stirring at room temperature for 30 min, the reaction mixture was poured into water (30 mL) and acidified to pH 3 with 20% aqueous hydrogen chloride solution. The methanol was evaporated in vacuo and the residue was extracted with dichloromethane (3×40 mL), and the pooled organic layers were washed with water (60 mL), dried, filtered and concentrated in vacuo, giving compound **12a** (1 g, 100% yield), which was used without further purification.

**1.1.5. *N*-{2-[(*E*)-2-(3,4-Dimethoxyphenyl)-1-ethenyl]-4,5-dimethoxyphenylethyl}acetamide (3c).** *Procedure a*. Following the same procedure as for the preparation of compound **3a**, compound **3c** was obtained in 47% yield from 2-bromo-4,5-dimethoxyphenylethylacetamide (0.15 g, 0.49 mmol) and 3,4-dimethoxystyrene (0.17 g, 1.04 mmol). Mp 168–170°C (ethyl acetate/ethyl ether). IR ($\nu$, $cm^{-1}$, KBr): 1654 (C═O). $^1H$ NMR ($\delta$, ppm): 1.87 (s, 3H, $-CH_3$), 2.93–2.98 (m, 2H, $-CH_2-$), 3.40–3.48 (m, 2H, $-CH_2-$), 3.89 (s, 3H, $-OCH_3$), 3.90 (s, 3H, $-OCH_3$), 3.95 (s, 3H, $-OCH_3$), 4.00 (s, 3H, $-OCH_3$), 5.57 (bs, 1H, –NH), 6.66 (s, 1H, Ar-H), 6.77 (d, $J$=15.9 Hz, 1H, –C═CH–), 6.84 (s, 1H, Ar-H), 7.04–7.23 (m, 3H, 3×Ar-H), 7.26 (d, $J$=15.9 Hz, 1H, –C═CH–). MS (*m*/*z*, %): 386 [$(M+1)^+$, 26], 385 ($M^+$, 100), 326 (22), 282 (21), 234 (17), 151 (79). Anal. calcd for $C_{22}H_{27}NO_5$, C 68.63, H 7.30, N 3.42; found, C 68.55, H 7.06, N 3.63.

*Procedure b*. Compound **3c** was prepared in 91% yield from compound **12b** (1.15 g, 2.85 mmol) following the same procedure as for compound **3b** (procedure b).

**1.1.6. *N*-{2-[2-(3,4-Dimethoxyphenyl)-1-hydroxyethyl]-4,5-dimethoxyphenyl}acetamide (12b).** Compound **12b** was prepared in quantitative yield from compound **11b** (1.16 g, 2.90 mmol) following the same procedure as for compound **12a** and was used without further purification.

**1.1.7. *N*-[2-(1-Phenanthryl)ethyl]acetamide (2a).** Air was bubbled for 10 min through a stirred solution of compound **3a** (88 mg, 0.33 mmol) in ethyl ether (180 mL) and dichloromethane (5 mL). A catalytic amount of iodine (12 mg, 0.03 mmoles) was added and the new mixture was then irradiated for 2 h in a photochemical reactor equipped with a Pyrex condenser and a Hanovia 450 W medium pressure Hg vapour lamp. After addition of saturated sodium thiosulphate (100 mL), and extraction of the resulting mixture with dichloromethane (3×50 mL), the pooled organic layers were dried, filtered and concentrated in vacuo, giving a residue that upon purification by preparative TLC (eluant: 3:1 ethyl acetate/hexane) afforded phenanthrene **2a** (57 mg, 65% yield). Mp 140–142°C

(methanol). IR ($\nu$, $cm^{-1}$, NaCl): 3277 (–NH), 1647 (C═O). $^1H$ NMR ($\delta$, ppm): 1.92 (s, 3H, $-CH_3$), 3.30–3.35 (m, 2H, $-CH_2-$), 3.58–3.66 (n, 2H, $-CH_2-$), 5.70 (bs, 1H, –NH), 7.43 (s, 1H, Ar-H), 7.55–7.67 (m, 3H, 3×Ar-H), 7.79 (d, $J$=9.2 Hz, 1H, 2×Ar-H), 7.89 (s, 1H, Ar-H), 8.03 (d, $J$=9.2 Hz, 1H, 2×Ar-H), 8.58–8.67 (m, 2H, 2×Ar-H). MS (*m/z*, %): 264 [$(M+1)^+$, 2], 263 ($M^+$, 13), 204 (100), 203 (27), 191 (34), 190 (12), 189 (21). Anal. calcd for $C_{18}H_{17}NO$, C 82.10, H 6.51, N 5.32; found, C 81.75, H 4.96, N 5.60.

**1.1.8. 1-Methyl-3,4-dihydronaphtho[2,1-*f*]isoquinoline (13a).** $POCl_3$ (0.089 mL, 0.95 mmol) was added dropwise over 5 min to a solution of compound **2a** (200 mg, 0.38 mmol) in dry acetonitrile (16 mL) and the mixture was refluxed for 18 h under a calcium chloride tube and then concentrated in vacuo. The residue was dissolved in dichloromethane (40 mL), and this solution was washed with 10% aqueous NaOH solution (2×30 mL) and water (30 mL), dried, filtered and concentrated, giving dihydroisoquinoline **13a** (68 mg, 73% yield). Mp 200–204°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 2351 (–CH), 1625 (C═N). $^1H$ NMR ($\delta$, ppm): 2.52 (s, 3H, $-CH_3$), 3.07–3.13 (m, 2H, $-CH_2-$), 3.78–3.86 (m, 2H, $-CH_2-$), 7.60–7.69 (m, 6H, 6×Ar-H), 8.59–8.70 (m, 2H, 2×Ar-H). MS (*m/z*, %): 246 [$(M+1)^+$, 13], 245 ($M^+$, 74), 244 (100). High resolution MS calcd for $C_{19}H_{15}N$, 245.1204; found, 245.1211.

**1.1.9. 1-Methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinoline (1a).** Following the same procedure as for reduction of **12a**, treatment of compound **13a** (60 mg, 0.24 mmol) with $NaBH_4$ (360 mg) gave naphthoisoquinoline **1a** (56 mg, 93% yield). Mp 143–145°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 3261 (–NH). $^1H$ NMR ($\delta$, ppm): 1.56–1.58 (m, 3H, $-CH_3$), 1.89 (bs, 1H, –NH), 3.18–3.24 and 3.46 (2×m-3H, 2×$-CH_2-$), 4.33 (m, 1H, –CH–), 7.47 (d, $J$=8.7 Hz, 1H, Ar-H), 7.55–7.69 (m, 2H, 2×Ar-H), 7.79 (m, 1H, Ar-H), 7.88 (m, 1H, Ar-H), 7.93 (d, $J$=8.9 Hz, 1H, Ar-H), 8.54 (m, 1H, Ar-H), 8.69 (m, 1H, Ar-H). MS (*m/z*, %): 247 ($M^+$, 7), 246 (8), 232 (100). Anal. calcd for $C_{20}H_{21}NO_5$, C 67.61, H 5.92, N 3.94; found, C 67.21, H 6.09, N 3.61.

**1.1.10. *N*-[2-(3-4-Dimethoxy-1-phenanthryl)ethyl]acetamide (2b).** Irradiation of *o*-styrylphenylethylacetamide **3b** (100 mg, 0.31 mmol) under the same conditions as for cyclization of **3a** afforded a 30% yield of the corresponding phenanthrylethylacetamide **2b**, which was identified by comparison with an authentic sample.

**1.1.11. 11,12-Dimethoxy-1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinoline (1b).** A mixture of potassium hydroxide (2 g) and absolute ethanol (10 mL) was refluxed under argon until total dissolution. This solution was added under an argon atmosphere to 100 mg (0.323 mmol) of *N*-ethoxycarbonylnaphthoisoquinoline **4c** and the mixture was refluxed for 15 h. Then a solution of citric acid (2 g) in water (15 mL) was added dropwise and the mixture was stirred at room temperature for 15 min. The ethanol was evaporated and the residue was extracted with dichloromethane (3×25 mL). The pooled organic layers were washed with water, dried and concentrated in vacuo, providing 75 mg (75% yield) of naphthoisoquinoline **1b**, which was identified by direct comparison with an authentic sample.

**1.1.12. *N*-[2-(3,4,6,7-Tetramethoxy-1-phenanthryl)ethyl]-acetamide (2c).** Starting from **3c** (125 mg, 0.33 mmol), the photochemical procedure applied to cyclization of **3a** gave a 6% yield of compound **2c**, identified by comparison with an authentic sample.

**1.1.13. 8,9,11,12-Tetramethoxy-1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinoline (1d).** Hydrolysis of urethane **1e** (100 mg, 0.26 mmol) under the conditions described above for transformation of **1c** afforded a 70% yield of compound **1d**, which was identified by direct comparison with an authentic sample.

**1.1.14. 1-Methyl-5[(*E*)-2-phenyl-1-ethenyl]3,4-dihydroisoquinoline (15a).** Compound **3a** (90 mg, 0.34 mmol) was transformed into a yellow oil identified as imine **15a** (14 mg, 19% yield) following the procedure used to obtain **13a**. IR ($\nu$, $cm^{-1}$, NaCl): 1634 (C═O). $^1H$ NMR ($\delta$, ppm): 2.42 (s, 3H, $-CH_3$), 2.79–2.89 (m, 2H, $-CH_2-$), 3.61–3.78 (m, 2H, $-CH_2-$), 7.01 (d, $J$=16.1 Hz, 1H, –CH═C–), 7.27–7.70 (m, 8H, 8×Ar-H), 7.34 (d, $J$=16.1 Hz, 1H, –C═CH–). MS (*m/z*, %): 248 [$(M+1)^+$, 19], 247 ($M^+$, 100), 246 (85) High resolution MS calcd for $C_{18}H_{17}N$, 247.1361; found, 247.1357.

**1.1.15. 7,8-Dimethoxy-1-methyl-5-[(*E*)-2-phenyl-1-ethenyl]-3,4-dihydroisoquinoline (15b).** Compound **15b** was prepared in 54% yield as a yellow oil from compound **3b** (100 mg, 0.31 mmol) following the same procedure as for the preparation of compound **13a**. IR ($\nu$, $cm^{-1}$, NaCl): 1610 (C═N). $^1H$ NMR ($\delta$, ppm): 2.52 (s, 3H, $-CH_3$), 2.64–2.69 (m, 2H, $-CH_2-$), 3.49–3.55 (m, 2H, $-CH_2-$), 3.88 (s, 3H, $-OCH_3$), 3.95 (s, 3H, $-OCH_3$), 6.91 (d, $J$=16.1 Hz, 1H, –CH═C–), 7.21–7.53 (m, 6H, 6×Ar-H), 7.37 (d, $J$=16.1 Hz, 1H, –C═CH–). MS (*m/z*, %): 308 [$(M+1)^+$, 23], 307 ($M^+$, 100), 306 (18), 293 (8), 292 (39), 276 (8), 248 (8), 216 (9), 202 (7). High resolution MS calcd for $C_{20}H_{21}NO_2$, 307.1572; found, 307.1569.

**1.1.16. 7,8-Dimethoxy-1-methyl-5-[(*E*)-2-phenyl-1-ethenyl]-1,2,3,4-tetrahydroisoquinoline (4b).** Compound **4b** was prepared in 99% yield from dihydroisoquinoline **15b** (185 mg, 0.6 mmol) following the same procedure as for the reduction of compound **13a**. Mp 112–114°C (methanol). $^1H$ NMR ($\delta$, ppm): 1.48 (m, 3H, $-CH_3$), 2.73–2.78 (m, 2H, $-CH_2-$), 3.11–3.84 (m, 2H, $-CH_2-$), 3.89 (s, 3H, $-OCH_3$), 3.91 (s, 3H, $-OCH_3$), 4.36 (q, $J$=6.7 Hz, 1H, –CH–), 5.90 (bs, 1H, –NH), 6.90 (d, $J$=16.0 Hz, 1H, –CH═C–), 7.07 (s, 1H, Ar-H), 7.27 (d, $J$=16.0 Hz, H, –C═CH–), 7.29–7.53 (m, 5H, 5×Ar-H). MS (*m/z*, %): 308 ($M^+$, 0.7), 293 (35), 149 (100). Anal. calcd for $C_{20}H_{23}NO_2$, C 77.64, H 7.49, N 4.53; found, C 77.89, H 7.18, N 4.26.

**1.1.17. *N*-Carbethoxy-7,8-dimethoxy-1-methyl-5-[(*E*)-2-phenyl-1-ethenyl]-1,2,3,4-tetrahydroisoquinoline (4c).** Ethyl chlorformate (0.24 mL, 2.44 mmol) was added to a solution of crude amine **4b** (150 mg, 0.28 mmol) and triethylamine (0.32 mL) in chloroform (20 mL), and after stirring at room temperature for 45 min, the reaction mixture was concentrated in vacuo and the residue was

dissolved in dichloromethane (100 mL). The solution was washed with 10% aqueous hydrochloric acid solution (3×50 mL) and water (50 mL), dried, filtered and concentrated in vacuo, giving a residue that purified by preparative TLC (eluant: 1:4 ethyl acetate/hexane) afforded urethane **4c** (150 mg, 81%). Mp 140–142°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 1690 (C═O). $^1H$ NMR ($\delta$, ppm): 1.30 (t, $J$=7.0 Hz, 3H, $-CH_3$), 1.47–1.48 (m, 3H, $-CH_3$), 2.74–4.19 (m, 6H, 3×$-CH_2-$), 3.93 (s, 6H, 2×$-OCH_3$), 5.43 (m, 1H, –CH–), 6.92 (d, $J$=16.0 Hz, 1H, –CH═C–), 7.08 (8s, 1H, Ar-H), 7.27 (d, $J$=16.0 Hz, 1H, –C═CH–), 7.16–7.54 (m, 5H, 5×Ar-H). MS ($m/z$, %): 381 ($M^+$, 31), 368 (16), 367 (26), 366 (100), 338 (24). Anal. calcd for $C_{23}H_{27}NO_4$, C 72.42, H 7.13, N 3.67; found, C 72.81, H 6.98, N 3.47.

**1.1.18. *N*-Carbethoxy-11,12-dimethoxy-1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinoline (1c).** Photolysis of compound **4c** (75 mg, 0.2 mmol) in the conditions used to obtain **2a** afforded phenanthrene **1c** as yellow oil (37 mg, 50% yield). Mp 189–191°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 1694 (C═O). $^1H$ NMR ($\delta$, ppm): 1.33 (t, $J$=6.8 Hz, 3H, $-CH_3$), 1.55–1.59 (m, 3H, $-CH_3$), 3.19–3.24 (m, 2H, $-CH_2$ ), 3.39–3.49 (m, 4H, 2×$-CH_2-$), 3.94 (s, 3H, $-OCH_3$), 4.11 and 4.13 (2×s, 3H, $-OCH_3$), 5.57 (m, 1H, –CH–), 7.57–7.71 (m, 3H, 3×Ar-H), 7.82–7.88 (m, 2H, 2×Ar-H), 9.63 (8m, 1H, Ar-H). MS ($m/z$, %): 380 [$(M+1)^+$, 10], 379 ($M^+$, 35), 365 (27), 364 (100). Anal. calcd for $C_{23}H_{25}NO_4$, C 72.80, H 6.64, N 3.69; found, C 73.08, H 6.69, N 3.82.

**1.1.19. 7,8-Dimethoxy-1-methyl-5-[(*E*)-2-(3,4-dimethoxyphenyl)-1-ethenyl]-3,4-dihydroisoquinoline (15c).** Applied to compound **3c** (125 mg, 0.33 mmol), the procedure for the preparation of **13a**, gave a 96% yield of a yellow oil identified as compound **15c**. IR ($\nu$, $cm^{-1}$, NaCl): 2940 (–CH), 1587 (C═N). $^1H$ NMR ($\delta$, ppm): 2.48 (s, 3H, $-CH_3$), 2.61–2.67 (m, 2H, $-CH_2-$), 3.47–3.52 (m, 2H, $-CH_2-$), 3.85 (s, 3H, $-OCH_3$), 3.88 (s, 3H, $-OCH_3$), 3.92 (6H, 2×$OCH_3$), 6.84 (d, $J$=16.0 Hz, 1H, –CH═C–), 6.81–7.17 (m, 4H, 4×Ar-H), 7.06 (d, $J$=16.0 Hz, 1H, –C═CH–). MS ($m/z$, %): 369 [$(M+2)^+$, 5], 368 [$(M+1)^+$, 26], 367 ($M^+$, 100), 366 (15), 352 (24), 336 (7). High resolution MS clacd for $C_{22}H_{25}NO_4$, 367.1784; found, 367.1778.

**1.1.20. 7,8-Dimethoxy-1-methyl-5-[(*E*)-2-(3,4-dimethoxyphenyl)-1-ethenyl]-1,2,3,4-tetrahydroisoquinoline (4d).** Compound **4d** was prepared in quantitative yield from dihydroisoquinoline **15c** following the same procedure as for the reduction of compound **13a**. Mp 133–135°C (methanol). $^1H$ NMR ($\delta$, ppm): 1.48–1.59 (m, 3H, $-CH_3$), 3.07–3.55 (m, 4H, 2×$-CH_2-$), 3.88 (s, 9H, 3×$-OCH_3$), 3.91 (s, 3H, $-OCH_3$), 4.83–4.87 (m, 1H, –CH–), 6.77–6.96 (m, 2H, 2×Ar-H), 6.98–7.05 (m, 4H, 2×Ar-H and 2×–CH═C–), 9.94 (bs, 1H, –NH). MS ($m/z$, %): 370 [$(M+2)^+$, 5], 368 ($M^+$, 2), 356 (5), 355 (24), 354 (100), 339 (5), 338 (7), 177 (6). Anal. calcd for $C_{22}H_{27}NO_4$, C 71.52, H 7.37, N 3.79; found, C 7.17, H 7.51, N 4.02.

**1.1.21. *N*-Carbethoxy-7,8-dimethoxy-1-methyl-5-[(*E*)-2-(3,4-dimethoxyphenyl)-1-ethenyl]-1,2,3,4-tetrahydroisoquinoline (4e).** Compound **4e** was prepared in 65% yield from compound **4d** (225 mg, 0.61 mmol) following the procedure used to obtain compound **4c**. Mp 165–167°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 2945 (–CH), 1690 (C═O). $^1H$ NMR ($\delta$, ppm): 1.26 (m, 3H, $-CH_3$), 1.43 (m, 3H, $-CH_3$), 2.83 (m, 2H, $-CH_2-$), 3.32–3.38 (m, 1H, $-CH_2-$), 3.89–3.93 (m, 12H, 4×$-OCH_3$), 4.00–4.21 (m, 3H, 2×$-CH_2-$), 5.34–5.50 (8m, 1H, –CH–), 6.83–7.10 (m, 6H, 4×Ar-H and 2×–CH═C–). MS ($m/z$, %): 443 [$(M+2)^+$, 4], 442 [$(M+1)^+$, 15], 441 ($M^+$, 53), 429 (3), 428 (14), 427 (27), 426 (100). Anal. calcd for $C_{25}H_{31}NO_6$, C 68.01, H 7.08, N 3.17; found, C 67.73, H 6.87, N 3.43.

**1.1.22. *N*-Carbethoxy-8,9,11,12-tetramethoxy-1-methyl-1,2,3,4-tetrahydronaphtho[2,1-*f*]isoquinoline (1e).** Irradiation of compound **4e** (110 mg, 0.24 mmol) as for cyclization of compound **3a** gave a 15% yield of compound **1e**. Mp 212–214°C (methanol). IR ($\nu$, $cm^{-1}$, NaCl): 1649 (C═O). $^1H$ NMR ($\delta$, ppm): 1.26–1.46 (m, 3H, $-CH_3$), 1.54–1.61 (m, 3H, $-CH_3$), 3.20–4.20 (m, 6H, 3×$-CH_2-$), 3.95 (s, 3H, $-OCH_3$), 4.06 (s, 3H, $OCH_3$), 4.11 (s, 6H, 2×$-OCH_3$), 5.56 (m, 1H, –CH), 7.23 (s, 1H, Ar-H), 7.46–7.94 (m, 2H, 2×Ar-H), 9.20 (s, 1H, Ar-H). MS ($m/z$, %): 440 [$(M+1)^+$, 13], 439 ($M^+$, 47), 425 (27), 424 (100), 397 (4), 396 (18), 351 (5). Anal. calcd for $C_{25}H_{29}NO_6$, C 68.32, H 6.65, N 3.19; found, C 68.73, H 6.49, N 3.01.

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