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Tetrahedron 62 (2006) 5725–5735
Tetrahedron

1,7-Electrocyclization reactions of stabilized α,β:γ,δ-unsaturated azomethine ylides

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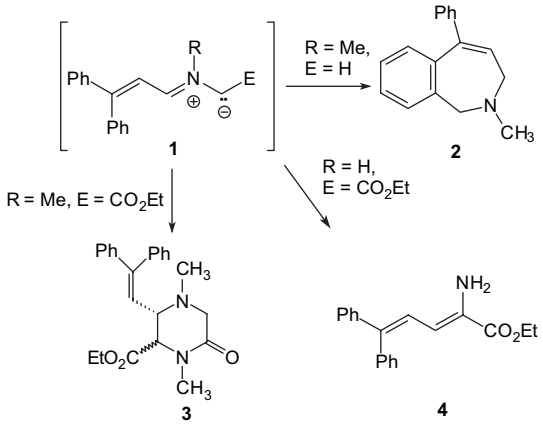
Received 24 January 2006; revised 28 February 2006; accepted 23 March 2006
Available online 2 May 2006

Abstract—Stabilized α,β:γ,δ-unsaturated azomethine ylides were generated by the deprotonation of isoquinolinium salts. 1,7-Electrocyclization of these dipoles, followed by a 1,5-hydrogen shift, gives tetrahydro[5,6]azepino[2,1-*a*]isoquinolines.

1. Introduction

For many years 1,3-dipoles have been used extensively in the construction of five-membered heterocyclic rings via their cycloadditions with suitable dipolarophiles[1] and by the 1,5-electrocyclization reactions of α,β-unsaturated 1,3-dipoles.[2] More recently, the electrocyclization of diene-conjugated 1,3-dipolar intermediates has provided a powerful general synthetic route to seven-membered heterocyclic ring systems.[3] We have been concerned for some years with synthetic and mechanistic aspects of these reactions and, in particular, with the cyclizations of azomethine ylides to give azepines.[4] During these studies we have found significant differences between the reactivity of α,β:γ,δ-unsaturated, non-stabilized **1** (E=H) and α,β:γ,δ-unsaturated, ester-stabilized azomethine ylides **1** (E=CO_2Et). The former dipoles react via a 1,7-electrocyclization,[5] followed by a [1,5]-hydrogen shift to give dihydroazepines **2**, while the latter give other products (**3** or **4**) via novel rearrangements (Scheme 1).[6,7]

We recently published the first examples of the 1,7-electrocyclizations of an azomethine ylide onto a nitro group, producing indazole-*N*-oxides after the ring contraction of the unstable oxadiazepine intermediates.[8] As a continuation of these studies we have now examined the reactivity of some α,β:γ,δ-unsaturated, ester-stabilized azomethine ylides generated by the deprotonation of iminium salts derived from 3,4-dihydroisoquinolines.[9]



Scheme 1.

2. Results and discussion

The synthesis of the dipole precursors was carried out according to the Bischler–Napieralski procedure[10] by cyclization of amides **6a**–**b** in the presence of $POCl_3$ and resulted in the formation of 3,4-dihydroisoquinolines **7a**–**b**. Subsequent reaction with different bromoalkyl derivatives, in anhydrous ether, gave the quaternary salts **8** (Scheme 2, Table 1).

Reacting the isoquinolinium salts **8a**–**j** with triethylamine, at ambient temperature in dry methanol, leads to the formation of 8-substituted-2,3-dimethoxy-13-phenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinolines **11a**–**j** via

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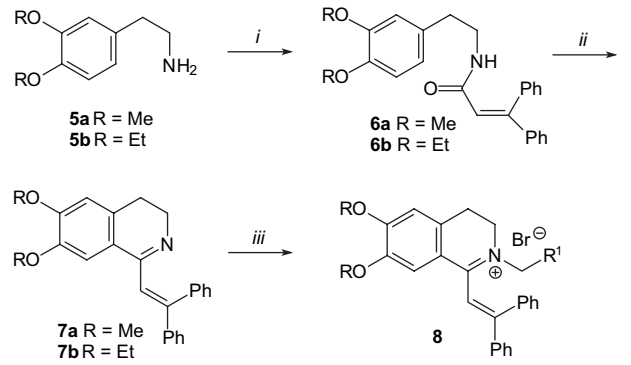
doi:10.1016/j.tet.2006.03.088

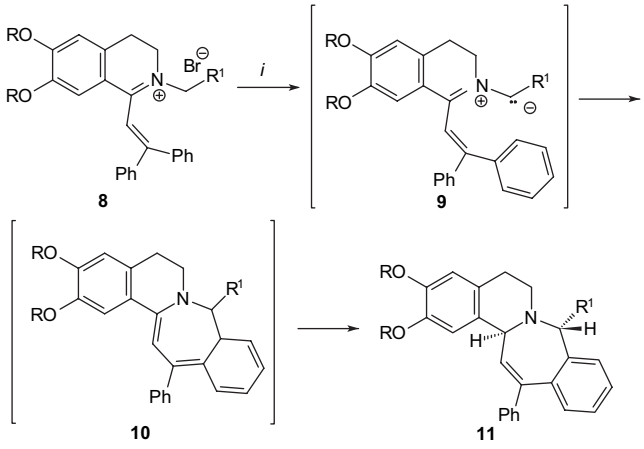


Scheme 2. Reagents and conditions: (i) $Ph_2C{=}CHCOCl$, NaOH, Et_2O, H_2O, rt; (ii) $POCl_3$, toluene, reflux and (iii) R^1CH_2Br, Et_2O, rt.

Table 1

Entry	R	R^1	Product	Yield (%)	Product	Yield (%)
1	Me	$-CO_2Me$	**8a**	100	**11a**	83
2	Et	$-CO_2Me$	**8b**	100	**11b**	86
3	Me	Ph–	**8c**	98	**11c**	77
4	Et	Ph–	**8d**	96	**11d**	82
5	Me	$CH_2{=}CH$–	**8e**	95	**11e**	53
6	Et	$CH_2{=}CH$–	**8f**	97	**11f**	50
7	Me	PhCO–	**8g**	100	**11g**	81
8	Et	PhCO–	**8h**	100	**11h**	80
9	Me	3-MeOPhCO–	**8i**	100	**11i**	85
10	Me	2-CNPh–	**8j**	99	**11j**	73

azomethine ylide intermediates **9a–j**. The benzazepinoisoquinolines could be isolated in moderate to good yields by simple filtration. In this reaction the azomethine ylides are produced by dehydrohalogenation of the isoquinolinium salts,[11] which leads, via a 1,7-electrocyclization to the azepines **10**, and finally, by a [1,5]-hydrogen shift, to the products **11a–j** (Scheme 3, Table 1). The relative stereochemistry of the tetracycles **11a–j** was deduced by NOE studies.

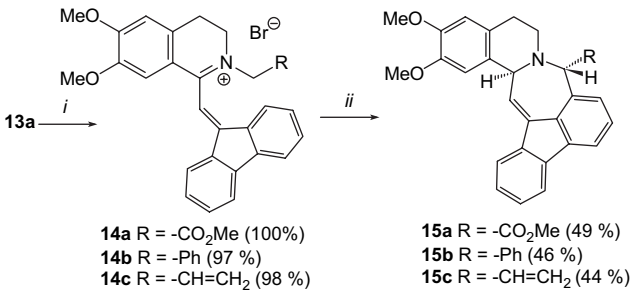


Scheme 3. Reagents and conditions: (i) Et_3N, MeOH, rt.

We next studied the influence of steric restrictions on the ethenyl side chain on the course of 1,7-electrocyclization reaction. The synthesis of the requisite precursors commenced with the conversion of the amides **12**, derived by coupling 2-(3,4-dimethoxyphenyl)ethylamine **5a** with fluorenylidene[12] and naphthoic acid chlorides, to the dihydroisoquinolines **13**.

The cyclized products **13a–b** were obtained in isolated yields greater than 70%, thus showing that the replacement of the side-chains had no affect on the outcome of the cyclization reaction (Scheme 4).

The alkylation of **13a** with three bromoalkyl derivatives, in anhydrous ether, gave the quaternary salts **14a–c**, the reaction of which, with triethylamine at room temperature in methanol, provided the expected hexacyclic products **15a–c**. These novel compounds were isolated in acceptable yields after column chromatography (Scheme 5).

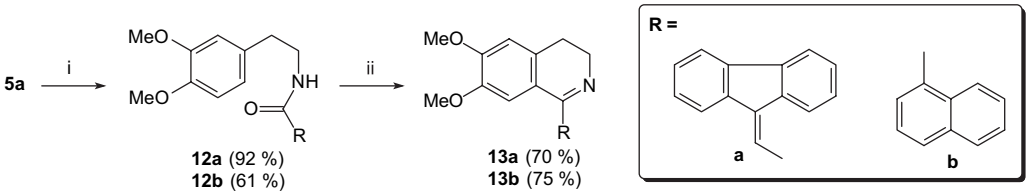


Scheme 5. Reagents and conditions: (i) R^1CH_2Br, Et_2O, rt; (ii) Et_3N, MeOH, rt.

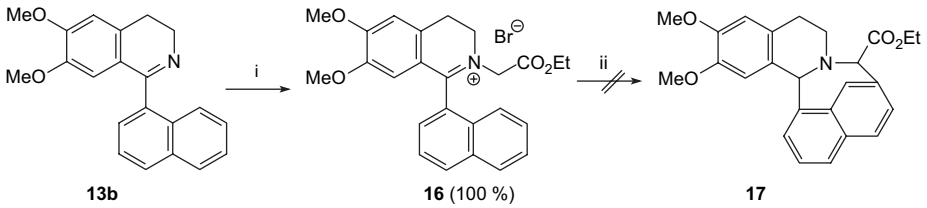
The reaction of quaternary salt **16**, prepared from isoquinoline **13b** and ethyl bromoacetate, with triethylamine or with other bases such as DBU, DABCO, or $KOBu^t$ and in different solvents, did not give the expected cyclized product—only the dihydroisoquinoline **13b** was isolated from the complex reaction mixture formed (Scheme 6).

These experiments show the scope and limitations of our strategy for the construction of the azepine ring system via the 1,7-electrocyclization of these azomethine ylides. The reactions with the diphenylethenyl side chains proceeded in good to excellent yield, depending upon the electron-withdrawing ability of the substituent on the azomethine ylide. The steric restrictions caused by the additional bond between the two phenyl groups in the dipoles derived from **14a–c** resulted in significant decrease in the yields of the electrocyclization products **15a–c** and the rigid nature of the naphthalene side chain makes the reaction of **16** impossible.

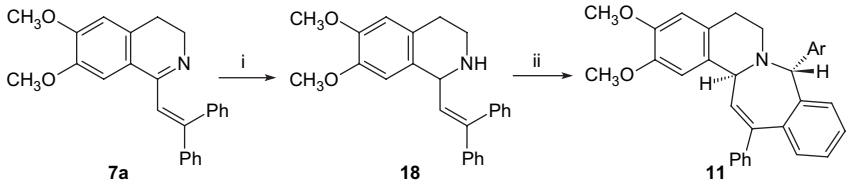
In order to extend the scope of this reaction we have used a different method for the generation of α,β:γ,δ-unsaturated



Scheme 4. Reagents and conditions: (i) RCOCl, NaOH, Et_2O, H_2O, rt and (ii) $POCl_3$, toluene, reflux.



Scheme 6. Reagents and conditions: (i) EtO_2CCH_2Br, Et_2O, rt and (ii) Et_3N, MeOH, rt.



Scheme 7. Reagents and conditions: (i) $NaBH_4$, EtOH and (ii) ArCHO, xylene, reflux.

azomethine ylides **9** where R^1 is derived from an aromatic aldehyde. This method was efficiently used by Grigg and co-workers in the synthesis of a pyrrolo[2,1-*a*]isoquinoline via a 1,5-electrocyclization.[13] The reduction of **7a** with sodium borohydride gave the tetrahydroisoquinoline **18**, which on refluxing with xylene, reacted slowly with various aromatic aldehydes furnishing tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinolines **11c**, **11k**, **11l** and **11m** in low yield (Scheme 7, Table 2).

Table 2

Entry	Ar	Reaction time (h)	Product	Yield (%)
1	Ph–	16	**11c**	24
2	4-ClPh–	12	**11k**	32
3	4-MeO–Ph–	30	**11l**	26
4	3,4-MeO–Ph–	48	**11m**	11

We have thus successfully developed a mild and efficient protocol for the convenient synthesis of tetrahydrobenz[5,6]-azepino[2,1-*a*]isoquinolines from stabilized azomethine ylides. The mechanistic course of the reaction suggests the involvment of an 8π-electrocyclization process, followed by a sigmatropic 1,5-hydrogen shift. This methodology may find application in the synthesis of the pharmacologically interesting homoprotoberberine derivatives.[14]

3. Experimental

3.1. General

Melting points were determined on a Gallenkamp apparatus and are uncorrected. Column chromatography was performed using Merck Kieselgel 60, 70–230 mesh, TLC on aluminium sheets coated with Kieselgel 60 F_{254}. Plates were stained with anisaldehyde solution (100 ml glacial acetic acid, 2 ml concd sulfuric acid and 1 ml anisaldehyde) and heated at ca. 150 °C. IR spectra were obtained on a Bruker VECTOR 22 FTIR instrument. NMR spectra were obtained on Varian INOVA 500, Bruker DRX-500 and Bruker 250 instruments. Chemical shifts are given relative to δ_{TMS}. All solvents were purified according to standard procedures.

3.1.1. *N*-[2-(3′,4′-Dimethoxyphenyl)ethyl]-3,3-diphenyl-2-propenamide (6a). 2-(3,4-Dimethoxy-phenyl)ethyl amine **5a** (7.27 g, 40 mmol) was dissolved in ether (40 ml) and 10% aqueous sodium hydroxide (1.6 g, 40 mmol in 15 ml water) was added at 0 °C. A solution of β-phenylcinnamoyl chloride (9.97 g, 40 mmol) in ether (30 ml) was added dropwise. After 4 h stirring at room temperature the precipitated product was filtered off and washed with water then ether and dried in air to give the product as a white powder (10.70 g, 69%), mp 162–163 °C; [Found: C, 77.7; H, 6.5; N, 3.5. $C_{25}H_{25}NO_3$ requires C, 77.5; H, 6.5; N, 3.6%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.35–7.21 (m, 10H, Ar–H), 6.73 (d, 1H, *J*=8.0 Hz, H-5′), 6.57 (s, 1H, H-2′), 6.51 (d, 1H, *J*=8.0 Hz, H-6′), 6.35 (s, 1H, H-2), 5.35 (br s, 1H, NH), 3.85 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.33 (t, 2H, *J*=7.2 Hz, CH_2), 2.48 (t, 2H, *J*=7.2 Hz, NCH_2); ^{13}C NMR (63 MHz, $CDCl_3$): 166.7 (quat.), 149.4 (quat.), 148.8 (quat.), 147.5 (quat.), 140.6 (quat.), 138.3 (quat.), 131.1 (quat.), 129.3 (2×CH), 128.8 (CH), 128.4 (2×CH), 128.35 (CH), 128.3 (2×CH), 127.8 (2×CH), 122.5 (CH), 120.4 (CH), 111.6 (CH), 111.2 (CH), 55.8 (CH_3), 55.7 (CH_3), 40.4 (CH_2), 34.6 (CH_2); IR (KBr, cm^{-1}): 3286, 3057, 2962, 2925, 2835, 1639, 1614, 1547, 1518, 1464, 1442, 1417, 1386, 1356, 1287, 1270, 1225, 1160, 1151, 1137, 1028.

3.1.2. *N*-[2-(3′,4′-Diethoxyphenyl)ethyl]-3,3-diphenyl-2-propenamide (6b). Compound **6b** was prepared, in a manner analogous to that for **6a**, from amine **5b** (8.4 g, 40 mmol) and was isolated as a white powder (11.2 g, 67.5%), mp 158–159 °C; [Found: C, 77.9; H, 6.8; N, 3.5. $C_{27}H_{29}NO_3$ requires C, 78.0; H, 7.0; N, 3.4%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.35–7.18 (m, 10H, Ar–H), 6.74 (d, 1H, *J*=8.1 Hz, H-5′), 6.58 (d, 1H, *J*=1.7 Hz, H-2′), 6.45 (dd, 1H, *J*=8.1 and 1.7 Hz, H-6′), 6.35 (s, 1H, H-2), 5.40 (br s, 1H, NH), 4.08–3.98 (m, 4H, OCH_2), 3.33 (t, 2H, *J*=7.2 Hz, CH_2), 2.48 (t, 2H, *J*=7.2 Hz, NCH_2), 1.42 (t, 6H, *J*=7.0 Hz, 2×CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 166.2 (quat.), 149.4 (quat.), 148.5 (quat.), 147.0 (quat.), 140.6 (quat.), 138.2 (quat.), 132.2 (quat.), 131.1 (CH), 129.1 (2×CH), 128.6 (CH), 128.3 (2×CH), 128.1 (2×CH), 127.7 (2×CH), 122.3 (CH), 120.5 (CH), 113.7 (CH), 113.4 (CH), 64.4 (CH_2), 64.2 (CH_2), 40.3 (CH_2), 34.5 (CH_2), 14.7 (2×CH_3); IR (KBr, cm^{-1}): 3281, 3107,

2955, 2845, 1638, 1612, 1539, 1520, 1441, 1386, 1301, 1282, 1271, 1150, 1132, 1022.

3.1.3. 6,7-Dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinoline (7a). *N*-[2-(3,4-Dimethoxyphenyl)-ethyl]-3,3-diphenyl-2-propenamide **6a** (7.0 g, 18 mmol) was dissolved in dry benzene (30 ml) and freshly distilled phosphorus oxychloride (3.67 g, 24 mmol) was added dropwise to the well-stirred mixture at 0 °C. The reaction mixture was then refluxed and stirred for 4 h, followed by cooling to room temperature. Then benzene was decanted and the semi-solid residue was stirred overnight with an excess of 10% aqueous sodium hydroxide solution. The aqueous phase was extracted with ethyl acetate (3×25 ml) and the combined organic extracts were washed with brine (25 ml), then dried ($MgSO_4$) and the solvent evaporated in vacuo to yield the title product as a yellow solid (4.92 g, 74%), mp 171 °C (lit.[10a] 168–170 °C); ^{1}H NMR (250 MHz, DMSO-d_6): 7.40–7.30 (m, 6H, Ar–H), 7.10 (m, 4H, Ar–H), 6.85 (s, 1H, H-8), 6.79 (s, 1H, H-5), 6.57 (s, 1H, CH═), 3.82 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.59 (t, 2H, *J*=7.5 Hz, H-4), 2.55 (t, 2H, *J*=7.5 Hz, H-3); ^{13}C NMR (63 MHz, DMSO-d_6): 164.2 (quat.), 150.1 (quat.), 148.0 (quat.), 146.5 (quat.), 141.7 (quat.), 139.2 (quat.), 130.7 (quat.), 129.5 (2×CH), 128.0 (2×CH), 127.7 (CH), 127.2 (4×CH), 125.5 (2×CH), 121.2 (quat.), 109.6 (CH), 109.4 (CH), 55.5 (CH_3), 55.3 (CH_3), 46.7 (CH_2), 25.0 (CH_2); IR (KBr, cm^{-1}): 2995, 2952, 2937, 2904, 2825, 1616, 1595, 1563, 1509, 1490, 1461, 1404, 1361, 1346, 1331, 1317, 1287, 1271, 1232, 1142, 1075, 1026; (HRMS Found: *m*/*z* 369.1711. $C_{25}H_{23}NO_2$ requires *m*/*z* 369.1729).

3.1.4. 6,7-Diethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinoline (7b). Compound **7b** was prepared, in a manner analogous to that for **7a**, from **6b** (9.95 g, 24 mmol) and was isolated as a yellow semi-solid material (6.50 g, 69%); ^{1}H NMR (250 MHz, $CDCl_3$): 7.41–7.12 (m, 11H, Ar–H), 6.85 (s, 1H, H-5), 6.62 (s, 1H, CH═), 4.19 (q, 2H, *J*=7.0 Hz, OCH_2), 3.81 (m, 4H, H-4 and OCH_2), 2.89 (br s, 2H, H-3), 1.45 (t, 3H, *J*=7.0 Hz, CH_3), 1.28 (t, 3H, *J*=7.0 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 164.2 (quat.), 150.3 (quat.), 147.7 (quat.), 146.3 (quat.), 142.0 (quat.), 139.4 (quat.), 130.95 (quat.), 129.6 (2×CH), 128.1 (2×CH), 127.9 (3×CH), 127.8 (CH), 127.3 (2×CH), 125.9 (CH), 121.6 (quat.), 112.3 (CH), 111.2 (CH), 64.6 (CH_2), 63.95 (CH_2), 47.0 (CH_2), 25.2 (CH_2), 14.5 (CH_3), 14.4 (CH_3); IR (KBr, cm^{-1}): 2955, 2947, 2911, 1612, 1599, 1567, 1514, 1488, 1462, 1404, 1388, 1342, 1337, 1319, 1277, 1233, 1200, 1144, 1075, 1033; (HRMS Found: *m*/*z* 397.2055. $C_{27}H_{27}NO_2$ requires *m*/*z* 397.2041).

3.1.5. 6,7-Dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-2-methoxycarbonylmethyl-3,4-dihydroisoquinolinium bromide (8a). Compound **8a** 6,7-dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinoline (0.5 g, 1.35 mmol) was dissolved in dry diethyl ether (30 ml) and methyl bromoacetate (0.56 ml, 0.82 g, 6 mmol) was added. The reaction mixture was stirred at room temperature overnight. The yellow precipitate was filtered off, washed with diethyl ether and dried in vacuo to give a yellow powder (0.70 g, 100%), mp 260–262 °C; [Found: C, 64.5; H, 5.6; N, 2.7. $C_{28}H_{28}NO_4Br$ requires C, 64.5; H, 5.4; N, 2.7%]; ^{1}H NMR (250 MHz, DMSO-d_6): 7.52 (m, 5H, Ph–H), 7.32 (m, 6H, Ph–H and CH═), 7.00 (s, 1H, H-5), 6.91 (s, 1H, H-8), 5.58 (d, 1H, *J*=17.4 Hz, *N*CH_2), 5.17 (d, 1H, *J*=17.4 Hz, *N*CH_2), 3.79 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3), 3.55 (m, 2H, H-4), 3.26 (m, 2H, H-3); ^{13}C NMR (63 MHz, DMSO-d_6): 172.1 (quat.), 166.6 (quat.), 158.2 (quat.), 155.7 (quat.), 147.0 (quat.), 139.2 (quat.), 137.6 (quat.), 134.5 (quat.), 130.4 (CH), 130.0 (2×CH), 129.9 (CH), 129.4 (2×CH), 128.7 (2×CH), 128.3 (2×CH), 117.6 (quat.), 117.1 (CH), 114.5 (CH), 110.9 (CH), 57.6 (CH_2), 56.5 (CH_3), 55.5 (CH_3), 53.1 (CH_3), 50.8 (CH_2), 27.0 (CH_2); IR (KBr, cm^{-1}): 3001, 2950, 2922, 2861, 2832, 1747, 1606, 1550, 1520, 1464, 1387, 1338, 1294, 1270, 1218, 1014.

3.1.6. 6,7-Diethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-2-methoxycarbonylmethyl-3,4-dihydroisoquinolinium bromide (8b). Compound **8b** was prepared analogously to **8a** from **7b** (0.5 g, 1.25 mmol) and was isolated as a yellow powder (0.68 g, 100%), mp 266–267 °C; [Found: C, 65.9; H, 5.7; N, 2.7. $C_{30}H_{32}NO_4Br$ requires C, 65.6; H, 5.9; N, 2.6%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.50–7.43 (m, 5H, Ar–H), 7.18 (m, 6H, Ph–H and CH═), 6.97 (s, 1H, H-5), 6.72 (s, 1H, H-8), 5.73 (d, 1H, *J*=17.9 Hz, *N*CH_2), 5.22 (d, 1H, *J*=17.9 Hz, *N*CH_2), 4.34–4.17 (4H, m, 2×OCH_2), 3.80 (s, 3H, OCH_3), 3.51 (2H, m, H-4), 3.22 (2H, m, H-3), 1.42 (3H, t, *J*=6.9 Hz, CH_3), 1.27 (3H, t, *J*=6.9 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 172.7 (quat.), 166.9 (quat.), 159.3 (quat.), 156.6 (quat.), 147.3 (quat.), 138.9 (quat.), 137.2 (quat.), 130.9 (CH), 130.4 (CH), 130.2 (2×CH), 129.4 (2×CH), 129.0 (2×CH), 128.7 (2×CH), 117.8 (quat.), 116.5 (CH), 115.7 (CH), 111.4 (CH), 65.3 (CH_2), 65.0 (CH_2), 58.7 (CH_2), 53.3 (*O*CH_3), 51.7 (CH_2), 26.2 (CH_2), 14.7 (CH_3), 14.4 (CH_3); IR (KBr, cm^{-1}): 3406, 2979, 2934, 1753, 1604, 1550, 1519, 1475, 1444, 1387, 1334, 1292, 1270, 1215, 1180, 1031.

3.1.7. 2-Benzyl-6,7-dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinolinium bromide (8c). Compound **8c** was prepared analogously to **8a** from **7a** (0.5 g, 1.35 mmol), benzyl bromide (0.36 ml, 0.50 g, 3 mmol) and was isolated as a yellow powder (0.72 g, 98%), mp 241–242 °C; [Found: C, 71.2; H, 5.7; N, 2.7. $C_{32}H_{30}NO_2Br$ requires C, 71.2; H, 5.6; N, 2.6%]; ^{1}H NMR (250 MHz, DMSO-d_6): 7.52–7.31 (m, 11H, Ph–H), 7.20 (m, 4H, Ph–H), 7.08 (s, 1H, CH═), 7.00 (s, 1H, H-5), 6.92 (s, 1H, H-8), 5.53 (br s, 2H, NCH_2), 3.78 (s, 3H, *O*Me), 3.70 (m, 2H, H-4), 3.63 (s, 3H, OMe), 3.02 (m, 2H, H-3); ^{13}C NMR (63 MHz, DMSO-d_6): 170.7 (quat.), 156.0 (quat.), 155.5 (quat.), 147.0 (quat.), 139.2 (quat.), 137.5 (quat.), 133.8 (quat.), 132.5 (quat.), 130.1 (CH), 129.6 (CH), 129.4 (2×CH), 129.0 (7×CH), 128.75 (2×CH), 128.3 (2×CH), 117.9 (quat.), 117.8 (CH), 114.4 (CH), 110.8 (CH), 59.8 (CH_2), 56.3 (CH_3), 55.6 (CH_3), 49.8 (CH_2), 24.9 (CH_2); IR (KBr, cm^{-1}): 2952, 2949, 2934, 2901, 2867, 1606, 1550, 1520, 1455, 1384, 1337, 1291, 1215, 1171, 1001.

3.1.8. 2-Benzyl-6,7-diethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinolinium bromide (8d). Compound **8d** was prepared analogously to **8c** from **7b** (0.5 g, 1.25 mmol) and was isolated as a yellow powder (0.69 g, 96%), mp 272 °C; [Found: C, 71.9; H, 6.1; N, 2.7. $C_{34}H_{34}NO_2Br$ requires C, 71.9; H, 6.0; N, 2.5%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.60 (m, 4H, Ar–H), 7.38 (m, 6H,

Ar–H), 7.12–7.08 (m, 7H, Ar–H and H-5 and CH═), 6.74 (s, 1H, H-8), 5.75 (d, 1H, J=15 Hz, NCH_2), 5.49 (d, 1H, J=15 Hz, NCH_2), 4.12 (q, 2H, J=7 Hz, OCH_2), 3.95 (q, 2H, J=7 Hz, OCH_2), 3.50 (m, 2H, H-4), 3.00 (m, 2H, H-3), 1.42 (t, 3H, J=7 Hz, CH_3), 1.36 (t, 3H, J=7 Hz, CH_3); ^{13}C NMR (63 MHz, DMSO-d_6): 170.8 (quat.), 155.6 (quat.), 155.2 (quat.), 146.3 (quat.), 139.2 (quat.), 139.1 (quat.), 137.4 (quat.), 133.8 (quat.), 132.4 (CH), 130.0 (CH), 129.5 (CH), 129.4 (2×CH), 128.9 (6×CH), 128.7 (2×CH), 128.3 (2×CH), 118.0 (CH), 117.9 (CH), 116.0 (quat.), 111.5 (CH), 64.6 (CH_2), 64.1 (CH_2), 59.7 (CH_2), 49.7 (CH_2), 24.9 (CH_2), 14.5 (CH_3), 14.3 (CH_3); IR (KBr, cm^{-1}): 2954, 2945, 2933, 2869, 1603, 1551, 1522, 1458, 1384, 1292, 1225, 1141, 1011.

3.1.9. 2-Allyl-6,7-dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinolinium bromide (8e). 6,7-Dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl]-3,4-dihydroisoquinoline (0.5 g, 1.35 mmol) was dissolved in allyl bromide (8 ml). The resulting solution was heated for 24 h under reflux, under an argon atmosphere. The excess allyl bromide was removed in vacuo and the residue was triturated with dry diethyl ether. The yellow precipitate was filtered off, washed with diethyl ether and dried in vacuo. The product is a yellow powder (0.63 g, 95%), mp 233–234 °C; [Found: C, 68.8; H, 6.1; N, 2.7. $C_{28}H_{28}NO_2Br$ requires C, 68.7; H, 5.8; N, 2.9%]; ^{1}H NMR (250 MHz, DMSO-d_6): 7.46–7.25 (m, 10H, Ar–H), 7.17 (s, 2H, H-5 and H-8), 7.15 (s, 1H, CH═), 5.99 (d, 1H, J=8.1 Hz, allyl–H), 5.80 (m, 1H, allyl–H), 5.45 (m, 1H, allyl–H), 4.76 (d, 1H, J=18.8 Hz, NCH_2), 4.39 (d, 1H, J=18.8 Hz, NCH_2), 3.93 (s, 3H, OMe), 3.90 (s, 3H, OMe), 3.62 (m, 2H, H-4), 3.21 (m, 2H, H-3); ^{13}C NMR (63 MHz, DMSO-d_6): 175.6 (quat.), 157.0 (quat.), 148.2 (quat.), 144.8 (quat.), 141.2 (quat.), 139.2 (quat.), 133.5 (quat.), 130.2 (CH), 128.8 (CH), 128.5 (2×CH), 128.3 (3×CH), 127.1 (2×CH), 126.7 (2×CH), 124.6 (CH_2), 114.9 (quat.), 115.8 (CH), 113.5 (CH), 111.7 (CH), 56.6 (CH_3), 56.4 (CH_3), 44.5 (CH_2), 43.2 (CH_2), 25.2 (CH_2); IR (KBr, cm^{-1}): 3005, 2952, 2934, 2867, 1627, 1602, 1559, 1526, 1466, 1423, 1398, 1342, 1298, 1278, 1218, 1167, 1006.

3.1.10. 2-Allyl-6,7-diethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinolinium bromide (8f). Compound **8f** was prepared analogously to **8e** from **7b** (0.5 g, 1.25 mmol) and was isolated as a yellow powder (0.62 g, 97%), mp 274–278 °C; [Found: C, 69.6; H, 6.2; N, 2.7. $C_{30}H_{32}NO_2Br$ requires C, 69.6; H, 6.2; N, 2.7%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.47 (m, 6H, Ar–H), 7.26 (m, 4H, Ar–H), 7.02 (s, 1H, CH═), 6.98 (s, 1H, H-5), 6.73 (s, 1H, H-8), 5.73 (m, 1H, allyl–H), 5.45 (m, 2H, allyl–H), 5.13 (d, 1H, J=19 Hz, NCH_2), 4.90 (d, 1H, J=19 Hz, NCH_2), 4.35–4.15 (m, 4H, 2×OCH_2CH_3), 3.54 (m, 2H, H-4), 3.29 (m, 2H, H-3), 1.48 (t, 3H, J=6.9 Hz, CH_3), 1.23 (t, 3H, J=6.9 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 170.8 (quat.), 157.4 (quat.), 156.3 (quat.), 147.4 (quat.), 138.9 (quat.), 137.3 (quat.), 134.2 (quat.), 130.6 (CH), 130.2 (CH), 129.8 (2×CH), 129.2 (2×CH), 128.9 (2×CH), 128.8 (2×CH), 128.3 (CH), 122.6 (CH_2), 118.1 (quat.), 116.4 (CH), 116.1 (CH), 111.6 (CH), 65.3 (CH_2), 65.1 (CH_2), 60.1 (CH_2), 49.0 (CH_2), 26.1 (CH_2), 14.7 (CH_3), 14.4 (CH_3); IR (KBr, cm^{-1}): 2966, 2944, 2934, 2868, 1628, 1603, 1561, 1522, 1454, 1399, 1345, 1278, 1222, 1169, 1122, 1008.

3.1.11. 6,7-Dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-2-(2-oxo-2-phenylethyl)-3,4-dihydroisoquinolinium bromide (8g). Compound **8g** was prepared analogously to **8a** from **7a** (0.5 g, 1.35 mmol) and phenacyl bromide (0.60 g, 3 mmol) and was isolated as a yellow powder (0.77 g, 100%), mp 263–264 °C; [Found: C, 70.1; H, 5.2; N, 2.7. $C_{33}H_{30}NO_3Br$ requires C, 69.8; H, 5.3; N, 2.5%]; ^{1}H NMR (500 MHz, $CDCl_3$): 7.98 (d, 2H, J=7.4 Hz, Ph–H), 7.89 (d, 2H, J=7.5 Hz, Ph–H), 7.40 (m, 4H, Ph–H), 7.23 (m, 3H, Ph–H), 7.18 (s, 1H, H-8), 7.01 (d, 2H, J=7.4 Hz, Ph–H), 7.00 (s, 1H, H-5), 6.90 (s, 1H, CH═), 6.89 (d, 2H, J=7.5 Hz, Ph–H), 5.80 (m, 1H, H-4), 4.66 (d, 1H, J=18.4 Hz, NCH_2), 4.04 (s, 3H, OMe), 3.98 (s, 3H, OMe), 3.80 (d, 1H, J=18.4 Hz, NCH_2), 3.73 (m, 1H, H-4), 3.47 (m, 1H, H-3), 3.20 (m, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): 193.1 (quat.), 177.9 (quat.), 157.2 (quat.), 148.1 (quat.), 144.0 (quat.), 136.8 (quat.), 135.2 (quat.), 134.6 (quat.), 133.2 (quat.), 128.4 (2×CH), 128.3 (5×CH), 127.6 (2×CH), 127.3 (2×CH), 127.1 (CH), 126.9 (CH), 126.6 (2×CH), 121.9 (CH), 120.0 (quat.), 114.3 (CH), 112.9 (CH), 110.8 (CH), 56.2 (CH_3), 56.1 (CH_3), 44.4 (CH_2), 44.1 (CH_2), 25.1 (CH_2); IR (KBr, cm^{-1}): 3422, 3011, 2950, 1684, 1625, 1603, 1559, 1527, 1448, 1426, 1402, 1343, 1299, 1169, 1011.

3.1.12. 6,7-Diethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-2-(2-oxo-2-phenylethyl)-3,4-dihydroisoquinoliniumbromide (8h). Compound **8h** was prepared analogously to **8a** from **7b** phenacyl bromide (0.60 g, 3 mmol) and was isolated as a yellow powder (0.75 g, 100%); mp 260–261 °C; [Found: C, 70.5; H, 6.1; N, 2.3. $C_{35}H_{34}NO_3Br$ requires C, 70.6; H, 5.8; N, 2.3%]; ^{1}H NMR (500 MHz, $CDCl_3$): 8.07 (m, 1H, Ph–H), 7.98 (d, 2H, J=7.8 Hz, Ph–H), 7.86 (d, 2H, J=8.1 Hz, Ph–H), 7.40 (m, 3H, Ph–H), 7.24 (m, 3H, Ph–H and H-8), 7.14 (m, 2H, Ph–H), 7.00 (m, 2H, Ph–H and H-5), 6.92 (s, 1H, CH═), 6.90 (m, 2H, Ph–H), 5.77 (m, 1H, H-4), 4.63 (d, 1H, J=17.1 Hz, NCH_2), 4.25 (q, 2H, J=7.0 Hz, OCH_2), 4.15 (q, 2H, J=7.0 Hz, OCH_2), 3.72 (d, 1H, J=17.1 Hz, NCH_2), 3.70 (m, 1H, H-4), 3.49 (m, 1H, H-4), 3.17 (m, 2H, H-3), 1.51 (t, 3H, J=7.0 Hz, CH_3), 1.49 (t, 3H, J=7.0 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): 194.5 (quat.), 177.1 (quat.), 158.0 (quat.), 148.3 (quat.), 144.2 (quat.), 137.3 (quat.), 135.7 (quat.), 134.4 (quat.), 133.8 (quat.), 129.6 (2×CH), 129.3 (2×CH), 128.7 (2×CH), 128.3 (2×CH), 128.0 (2×CH), 127.8 (CH), 127.6 (3×CH), 127.5 (CH), 114.7 (CH), 114.0 (quat.), 112.1 (CH), 112.0 (CH), 65.5 (2×CH_2), 45.7 (CH_2), 44.7 (CH_2), 26.2 (CH_2), 14.6 (CH_3), 14.3 (CH_3); IR (KBr, cm^{-1}): 3031, 2969, 2943, 1670, 1629, 1599, 1587, 1557, 1527, 1464, 1456, 1446, 1426, 1399, 1340, 1298, 1228, 1169, 1093, 1010.

3.1.13. 6,7-Dimethoxy-1-(2′,2′-diphenyl-1′-ethenyl)-2-[2-(4-methoxyphenyl)-2-oxoethyl]-3,4-dihydroisoquinolinium bromide (8i). Compound **8i** was prepared analogously to **8a** from **7a** (0.5 g, 1.35 mmol) and 2′-bromo-4-methoxyacetophenone (0.69 g, 3 mmol) and was isolated as a yellow powder (0.77 g, 100%), mp 272 °C; [Found: C, 68.3; H, 5.2; N, 2.3. $C_{34}H_{34}NO_4Br$ requires C, 68.2; H, 5.4; N, 2.3%]; ^{1}H NMR (500 MHz, $CDCl_3$): 7.88 (d, 2H, J=8.3 Hz, Ar–2′ and 6′H), 7.41 (m, 4H, Ph–H), 7.30 (m, 6H, Ph–H), 7.06 (s, 1H, H-8), 6.94 (s, 1H, H-5 and CH═), 6.58 (d, 2H, J=8.3 Hz, Ar–3′ and 5′H), 5.63 (m, 1H, H-4), 4.81 (d, 1H, J=19.0 Hz, NCH_2), 4.68 (d, 1H, J=19.0 Hz, NCH_2), 4.03

(s, 3H, OMe), 3.98 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.70 (m, 1H, H-4), 3.55 (m, 1H, H-3), 3.22 (m, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): 191.8 (quat.), 177.3 (quat.), 164.3 (quat.), 157.7 (quat.), 148.8 (quat.), 144.4 (quat.), 137.6 (quat.), 135.9 (quat.), 134.3 (quat.), 129.2 (2×CH), 128.8 (2×CH), 128.7 (2×CH), 128.6 (quat.), 128.5 (CH), 127.9 (2×CH), 127.6 (2×CH), 127.4 (CH), 115.1 (quat.), 114.3 (quat.), 113.6 (2×CH), 112.1 (CH), 111.3 (CH), 56.9 (CH_3), 56.7 (CH_3), 55.8 (CH_3), 45.5 (CH_2), 45.1 (CH_2), 26.0 (CH_2); IR (KBr, cm^{-1}): 2936, 2838, 1675, 1600, 1559, 1526, 1513, 1457, 1424, 1401, 1341, 1297, 1244, 1169, 1045.

3.1.14. 2-(2-Cyanobenzyl)-1-(2′,2′-diphenyl-1′-ethenyl)-6,7-dimethoy-3,4-dihydroisoquinolinium bromide (8j). Compound **8j** was prepared analogously to **8a** from **7a** (0.5 g, 1.35 mmol) and 2-bromomethyl-benzonitrile (0.39 g, 2 mmol) and was isolated as a yellow powder (0.76 g, 99%), mp 192–193 °C; [Found: C, 70.2; H, 5.2; N, 4.8. $C_{33}H_{29}N_2O_2Br$ requires C, 70.2; H, 5.2; N, 5.0%]; ^{1}H NMR (500 MHz, $CDCl_3$): 8.24 (d, 1H, J=7.8 Hz, Ar–3′H), 7.76 (d, 1H, J=7.8 Hz, Ar–6′H), 7.72 (t, 1H, J=7.8 Hz, Ar–5′H), 7.59–7.44 (m, 5H, Ph–H and Ar–4′H), 7.40 (d, 2H, J=7.5 Hz, Ph–H), 7.35 (m, 2H, Ph–H and H-8), 7.26 (t, 1H, J=7.5 Hz, Ph–H), 7.19 (d, 2H, J=7.5 Hz, Ph–H), 7.07 (s, 1H, H-5), 6.79 (s, 1H, CH═), 6.21 (d, 1H, J= 15.1 Hz, NCH_2), 5.72 (d, 1H, J=15.1 Hz, NCH_2), 3.91 (s, 3H, OMe), 3.73 (s, 3H, OMe), 3.55 (m, 1H, H-4), 3.47 (m, 1H, H-4), 2.98 (m, 1H, H-3), 2.78 (m, 1H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): 171.9 (quat.), 158.4 (quat.), 156.3 (quat.), 147.5 (quat.), 138.5 (quat.), 136.7 (quat.), 135.0 (quat.), 134.3 (quat.), 134.0 (CH), 133.3 (CH), 133.2 (CH), 130.4 (CH), 130.0 (CH), 129.9 (CH), 129.6 (2×CH), 128.8 (2×CH), 128.65 (2×CH), 128.6 (2×CH), 118.1 (quat.), 117.3 (CH), 116.7 (quat.), 113.9 (CH), 111.6 (CH), 110.3 (CH), 58.0 (CH_2), 56.5 (CH_3), 55.7 (CH_3), 48.8 (CH_2), 25.8 (CH_2); IR (KBr, cm^{-1}): 2937, 2889, 2224, 1604, 1545, 1521, 1447, 1386, 1338, 1292, 1272, 1216, 1172, 1002.

3.2. 1,7-Electrocyclizations—method A

The corresponding 1-(2′,2′-diphenyl-1′-ethenyl)-3,4-dihydroisoquinolinium bromide (0.75 mmol) was dissolved in dry methanol (10 ml) and triethylamine (0.11 ml, 1.5 mmol) was added. The reaction mixture was stirred for 24 h at room temperature under an argon atmosphere. The precipitated products were filtered off, washed with ethanol and dried in air.

3.2.1. Methyl 2,3-dimethoxy-13-phenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline-8-carboxylate (11a). White powder (0.27 g, 83%), mp 148–149 °C; [Found: C, 76.0; H, 6.2; N, 2.9. $C_{28}H_{27}NO_4$ requires C, 76.2; H, 6.2; N, 3.1%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.63 (m, 2H, Ar–H), 7.40 (m, 2H, Ar–H), 7.26 (m, 6H, Ar–H), 7.11 (s, 1H, H-1), 6.64 (s, 1H, H-14), 5.52 (s, 1H, H-14*a*), 4.82 (s, 1H, H-8), 3.89 (s, 6H, 2×OCH_3), 3.34 (s, 3H, CO_2CH_3), 3.31 (m, 2H, H-6), 2.18 (m, 2H, H-5); ^{13}C NMR (63 MHz, $CDCl_3$): 170.7 (quat.), 149.3 (quat.), 147.4 (quat.), 146.2 (quat.), 144.5 (quat.), 143.8 (quat.), 128.6 (quat.) 128.5 (CH, C-9), 128.2 (2×CH), 127.9 (CH, C-11), 127.8 (CH), 127.5 (2×CH), 126.5 (CH, C-10), 126.0 (CH, C-12), 121.1 (quat.), 119.5 (quat.), 110.4 (CH), 107.2 (CH), 102.1 (CH), 76.5 (CH, C-14*a*), 62.1 (CH), 55.8 (CH_3), 55.7 (CH_3), 51.3 (CH_3), 46.5 (CH_2), 29.0 (CH_2); IR (KBr, cm^{-1}): 2985, 2956, 2834, 1723, 1513, 1464, 1450, 1355, 1342, 1275, 1234, 1212, 1177, 1149, 1025.

3.2.2. Methyl 2,3-diethoxy-13-phenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline-8-carboxylate (11b). White powder (0.30 g, 86%), mp 157–159 °C; [Found: C, 76.7; H, 6.5; N, 2.9. $C_{30}H_{31}NO_4$ requires C, 76.7; H, 6.6; N, 3.0%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.60 (m, 2H, Ar–H), 7.37 (m, 2H, Ar–H), 7.27–7.11 (m, 7H, Ar–H), 6.63 (s, 1H, H-14), 5.46 (s, 1H, H-14*a*), 4.79 (s, 1H, H-8), 4.07 (m, 4H, 2×OCH_2), 3.31 (s, 3H, CO_2CH_3), 3.27 (m, 2H, CH_2-6), 2.78 (m, 2H, CH_2-5), 1.44 (t, 3H, J=7.1 Hz, CH_3), 1.42 (t, 3H, J=7.1 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 170.8 (quat.), 149.3 (quat.), 147.1 (quat.), 146.4 (quat.), 144.7 (quat.), 143.9 (quat.), 128.6 (CH), 128.2 (2×CH), 127.8 (CH), 127.6 (2×CH), 127.5 (CH), 127.1 (quat.), 126.5 (CH), 126.1 (CH), 121.3 (quat.), 119.6 (quat.), 112.3 (CH), 109.7 (CH), 102.0 (CH), 76.6 (CH), 64.6 (CH_2), 64.3 (CH_2), 62.2 (CH), 51.4 (CH_3), 46.6 (CH_2), 29.0 (CH_2), 14.8 (CH_3), 14.7 (CH_3); IR (KBr, cm^{-1}): 3053, 3030, 2980, 2932, 2879, 2815, 1749, 1731, 1608, 1509, 1444, 1392, 1333, 1275, 1235, 1208, 1177, 1153, 1108, 1041.

3.2.3. 2,3-Dimethoxy-8,13-diphenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11c). White powder (0.26 g, 77%), mp 140 °C; [Found: C, 83.7; H, 6.2; N, 3.0. $C_{32}H_{29}NO_2$ requires C, 83.6; H, 6.4; N, 3.0%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.53 (m, 2H, Ar–H), 7.33 (m, 2H, Ar–H), 7.20 (m, 2H, Ar–H), 7.02 (m, 7H, Ar–H), 6.87 (m, 3H, Ar–H), 6.63 (s, 1H, H-14), 5.50 (s, 1H, H-14*a*), 5.17 (s, 1H, H-8), 3.89 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.08 (m, 1H, CH_2-6), 3.02 (m, 1H, CH_2-6), 2.70 (m, 2H, CH_2-5); ^{13}C NMR (63 MHz, $CDCl_3$): 147.6 (quat.), 147.4 (quat.), 145.5 (quat.), 143.6 (quat.), 138.4 (quat.), 129.9 (2×CH), 129.2 (quat.), 129.1 (CH), 128.1 (2×CH), 127.9 (3×CH), 127.7 (quat.), 127.4 (quat.), 127.0 (CH), 126.9 (3×CH), 125.7 (2×CH), 120.1 (quat.), 110.7 (CH), 107.2 (CH), 103.2 (CH), 77.8 (CH), 63.2 (CH), 55.9 (2×CH_3), 45.6 (CH_2), 29.4 (CH_2); IR (KBr, cm^{-1}): 2945, 2922, 2830, 1608, 1500, 1462, 1337, 1270, 1231, 1212, 1174, 1148, 1020.

3.2.4. 2,3-Diethoxy-8,13-diphenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11d). White powder (0.30 g, 82%), mp 142–143 °C; [Found: C, 83.8; H, 7.0; N, 2.9. $C_{34}H_{33}NO_2$ requires C, 83.7; H, 6.8; N, 2.9%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.58 (m, 2H, Ar–H), 7.37 (m, 2H, Ar–H), 7.27 (m, 2H, Ar–H), 7.12–7.01 (m, 10H, Ar–H), 6.69 (s, 1H, H-14), 5.52 (s, 1H, H-14*a*), 5.22 (s, 1H, H-8), 4.13 (m, 4H, OCH_2), 3.17 (m, 1H, CH_2-6), 2.96 (m, 1H, CH_2-6), 2.74 (m, 2H, CH_2-5), 1.51 (t, 3H, J=7.1 Hz, CH_3), 1.49 (t, 3H, J=7.1 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 149.0 (quat.), 147.2 (quat.), 145.0 (quat.), 144.4 (quat.), 143.5 (quat.), 129.8 (2×CH), 129.0 (2×CH), 127.9 (2×CH), 127.75 (2×CH), 127.7 (quat.), 127.6 (quat.), 127.4 (quat.), 127.2 (2×CH), 126.8 (CH), 125.5 (3×CH), 119.9 (quat.), 112.3 (CH), 109.4 (CH), 102.8 (CH), 77.7 (CH, C-8), 64.5 (CH_2), 64.2 (CH_2), 63.0 (CH), 45.4 (CH_2), 29.2 (CH_2), 14.6 (CH_3), 14.5 (CH_3); IR (KBr, cm^{-1}): 2963, 2955, 2932, 2811, 1609, 1508, 1488, 1463, 1338, 1270, 1233, 1210, 1179, 1166, 1141, 1011.

3.2.5. 8-Ethenyl-2,3-dimethoxy-13-phenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11e). White powder (0.16 g, 53%), mp 133 °C; [Found: C, 82.4; H, 6.5; N, 3.0. $C_{28}H_{27}NO_2$ requires C, 82.1; H, 6.6; N, 3.4%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.44 (m, 2H, Ar–H), 7.33 (m, 2H, Ar–H), 7.25–7.11 (m, 7H, Ar–H), 6.64 (s, 1H, H-14), 5.67 (s, 1H, H-14*a*), 5.46–5.33 (m, 3H, vinyl–H and H-8), 5.23 (dd, 1H, *J*=2.8 and 8.6 Hz, vinyl–H), 3.88 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.20 (m, 1H, CH_2-6), 3.05 (m, 1H, CH_2-6), 2.71 (m, 2H, CH_2-5); ^{13}C NMR (63 MHz, $CDCl_3$): 149.3 (quat.), 149.2 (quat.), 145.9 (quat.), 144.6 (quat.), 136.5 (quat.), 129.7 (quat.), 129.2 (2×CH), 128.3 (CH), 128.2 (CH), 128.0 (quat.), 127.6 (CH), 127.5 (CH), 127.45 (CH), 126.2 (2×CH), 126.1 (CH_2), 126.0 (CH), 119.9 (quat.), 112.5 (CH), 109.8 (CH), 103.7 (CH), 78.5 (CH), 60.9 (CH), 55.95 (CH_3), 55.9 (CH_3), 45.2 (CH_2), 29.4 (CH_2); IR (KBr, cm^{-1}): 3052, 3011, 2980, 2921, 2811, 1611, 1514, 1478, 1437, 1417, 1389, 1333, 1234, 1184, 1177, 1155, 1111, 1021.

3.2.6. 2,3-Diethoxy-13-phenyl-8-vinyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11f). White powder (0.16 g, 50%), mp 139–140 °C; [Found: C, 82.3; H, 6.9; N, 3.0. $C_{30}H_{31}NO_2$ requires C, 82.3; H, 7.1; N, 3.2%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.44 (m, 2H, Ar–H), 7.33 (m, 2H, Ar–H), 7.25–7.11 (m, 7H, Ar–H), 6.64 (s, 1H, H-14), 5.67 (s, 1H, H-14*a*), 5.46–5.33 (m, 3H, vinyl and H-8), 5.23 (dd, 1H, *J*=2.8 and 8.6 Hz, vinyl–H), 4.09 (m, 4H, OCH_2), 3.18 (m, 1H, CH_2-6), 3.08 (m, 1H, CH_2-6), 2.76–2.55 (m, 2H, CH_2-5), 1.45 (t, 6H, *J*=6.9 Hz, 2×CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 149.3 (quat.), 149.2 (quat.), 145.8 (quat.), 144.6 (quat.), 136.8 (quat.), 129.7 (quat.), 129.2 (2×CH), 128.3 (CH), 128.1 (CH), 128.0 (quat.), 127.6 (2×CH), 127.5 (CH), 126.2 (2×CH), 126.15 (CH_2), 126.1 (CH), 120.0 (quat.), 112.5 (CH), 109.6 (CH), 103.4 (CH, C-1), 78.3 (CH, C-8), 64.8 (OCH_2), 64.4 (OCH_2), 61.1 (CH), 45.1 (CH_2-6), 29.4 (CH_2-5), 14.9 (CH_3), 14.8 (CH_3); IR (KBr, cm^{-1}): 3077, 2978, 2917, 2879, 2807, 1608, 1511, 1474, 1438, 1416, 1388, 1334, 1273, 1233, 1208, 1184, 1150, 1110, 1088, 1037.

3.2.7. 2,3-Dimethoxy-13-phenyl-8-benzoyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11g). White powder (0.31 g, 81%), mp 164–165 °C; [Found: C, 81.3; H, 6.0; N, 3.0. $C_{33}H_{29}NO_3$ requires C, 81.3; H, 6.0; N, 2.9%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.98 (d, 2H, *J*=7.7 Hz, Ph–2′ and 6′H), 7.65 (d, 2H, *J*=7.4 Hz, Ph–2′ and 6′H), 7.37–7.24 (m, 3H), 7.15–6.70 (m, 9H), 6.67 (s, 1H, H-14), 5.50 (s, 1H, H-14*a*), 5.32 (s, 1H, H-8), 4.01 (s, 3H, OMe), 3.90 (s, 3H, OMe), 3.15 (m, 1H, CH_2-6), 3.05 (m, 1H, CH_2-6), 2.72 (m, 2H, CH_2-5); ^{13}C NMR (63 MHz, $CDCl_3$): 199.8 (quat.), 148.6 (quat.), 148.3 (quat.), 147.4 (quat.), 144.1 (quat.), 139.9 (quat.), 132.0 (quat.), 130.0 (quat.), 128.8 (CH), 128.6 (2×CH), 128.4 (CH), 128.0 (2×CH), 127.8 (CH), 127.3 (2×CH), 127.2 (CH), 127.1 (2×CH), 126.9 (CH), 126.3 (CH), 125.4 (quat.), 119.3 (quat.), 111.9 (CH), 109.3 (CH), 101.6 (CH), 80.5 (CH), 56.3 (CH_3), 56.2 (CH_3), 62.5 (CH), 46.1 (CH_2), 28.8 (CH_2); IR (KBr, cm^{-1}): 2967, 2954, 2887, 1692, 1625, 1606, 1560, 1525, 1448, 1428, 1404, 1349, 1278, 1230, 1170, 1024, 1001.

3.2.8. 2,3-Diethoxy-13-phenyl-8-benzoyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11h). White powder (0.31 g, 80%); mp 167 °C; [Found: C, 81.5; H, 6.4; N, 2.7. $C_{30}H_{31}NO_2$ requires C, 81.5; H, 6.4; N, 2.7%]; ^{1}H NMR (250 MHz, $CDCl_3$): 7.95 (d, 2H, *J*=7.7 Hz, Ar–2′ and 6′H), 7.63 (d, 2H, *J*=7.4 Hz, Ph–2′ and 6′H), 7.37–7.21 (m, 3H), 7.17–6.99 (m, 6H), 6.66 (m, 3H), 6.64 (s, 1H, H-14), 5.51 (s, 1H, H-14*a*), 5.35 (s, 1H, H-8), 4.24–4.07 (m, 4H, OCH_2), 3.12 (m, 1H, CH_2-6), 3.01 (m, 1H, CH_2-6), 2.84 (m, 1H, CH_2-5), 2.73 (m, 1H, CH_2-5), 1.50 (t, 3H, *J*=7.1 Hz, CH_3), 1.47 (t, 3H, *J*=7.1 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$): 200.0 (quat.), 149.1 (quat.), 148.0 (quat.), 147.0 (quat.), 144.1 (quat.), 144.0 (quat.), 129.9 (CH), 128.9 (CH), 128.6 (2×CH), 128.5 (CH), 127.9 (2×CH), 127.7 (CH), 127.3 (2×CH), 127.2 (quat.), 127.1 (2×CH), 127.0 (CH), 126.1 (CH), 125.9 (quat.), 125.5 (quat.), 119.4 (quat.), 111.8 (CH), 109.5 (CH), 101.6 (CH), 80.5 (CH), 64.5 (CH_2), 64.1 (CH_2), 62.5 (CH), 46.1 (CH_2), 28.8 (CH_2), 14.5 (CH_3), 14.4 (CH_3); IR (KBr, cm^{-1}): 2957, 2954, 2899, 2834, 1691, 1626, 1606, 1562, 1524, 1444, 1400, 1279, 1233, 1144, 1102, 1024, 1011.

3.2.9. 2,3-Dimethoxy-13-phenyl-8-(4′-methoxybenzoyl)-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11i). White powder (0.33 g, 85%), mp 179–180 °C; [Found: C, 78.9; H, 6.0; N, 2.9. $C_{34}H_{31}NO_4$ requires C, 78.9; H, 6.0; N, 2.7%]; ^{1}H NMR (500 MHz, $CDCl_3$): 7.85 (d, 2H, *J*=7.5 Hz, Ar–2′ and 6′H), 7.67 (d, 2H, *J*=6.7 Hz, Ph–2′ and 6′H), 7.35 (m, 2H, H-10 and H-12), 7.17 (m, 4H, Ph–3′, 4′ and 5′H, H-9), 6.96–6.88 (m, 3H, H-1, H-4 and H-8), 6.63 (s, 1H, H-14), 6.57 (d, 2H, *J*=7.5 Hz, Ar–3′ and 5′H), 5.55 (s, 1H, H-14*a*), 5.29 (s, 1H, H-8), 3.91 (s, 3H, OMe), 3.88 (s, 3H, OMe), 3.74 (s, 3H, OMe), 3.04 (m, 2H, CH_2-6), 2.81 (m, 1H, CH_2-5), 2.70 (m, 1H, CH_2-5); ^{13}C NMR (125 MHz, $CDCl_3$): 198.4 (quat.), 162.7 (quat.), 149.5 (quat.), 147.7 (quat.), 147.3 (quat.), 144.3 (quat.), 144.0 (quat.), 131.5 (2×CH), 130.2 (quat.), 129.5 (2×CH), 128.2 (CH), 127.7 (CH), 127.4 (2×CH), 127.2 (quat.), 126.4 (CH), 125.9 (quat.), 125.85 (CH), 125.8 (CH), 119.8 (quat.), 112.4 (2×CH), 110.7 (CH), 107.5 (CH), 102.3 (CH), 81.2 (CH), 62.8 (CH), 55.9 (CH_3), 55.8 (CH_3), 55.1 (CH_3), 46.5 (CH_2), 29.1 (CH_2); IR (KBr, cm^{-1}): 3057, 3005, 2965, 2838, 1648, 1593, 1510, 1490, 1457, 1447, 1314, 1300, 1276, 1260, 1235, 1210, 1170, 1020.

3.2.10. 2,3-Dimethoxy-8-(2-cyanophenyl)-13-phenyl-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11j). White powder (0.26 g, 73%), mp 155 °C; [Found: C, 82.0; H, 5.9; N, 5.7. $C_{33}H_{28}N_2O_2$ requires C, 81.8; H, 5.8; N, 5.8%]; ^{1}H NMR (500 MHz, $CDCl_3$): 7.57 (d, 2H, *J*=7.5 Hz, Ph–2′ and 6′H), 7.48 (dd, 1H, *J*=2.1 and 7.2 Hz, Ar–6′H), 7.37 (t, 1H, *J*=7.5 Hz, Ph–4′H), 7.35 (d, 2H, *J*=7.5 Hz, Ph–3′ and 5′H), 7.23 (d, 1H, *J*=7.2 Hz, Ar–3′H), 7.19 (m, 2H, H-10 and H-11), 7.13 (dt, 1H, *J*=2.1 and 7.2 Hz, Ar–5′H), 7.03 (m, 4H, H-1, H-4, H-12 and Ar–4′H), 6.98 (d, 1H, *J*=7.8 Hz, H-9), 6.67 (s, 1H, H-14), 5.80 (s, 1H, H-14*a*), 5.47 (s, 1H, H-8), 3.93 (s, 3H, OMe), 3.90 (s, 3H, OMe), 2.94 (m, 2H, CH_2-6), 2.88 (m, 2H, CH_2-5); ^{13}C NMR (125 MHz, $CDCl_3$): 149.4 (quat.), 147.6 (quat.), 147.0 (quat.), 144.0 (quat.), 143.2 (quat.), 142.9 (quat.), 132.1 (CH), 131.4 (CH), 130.3 (CH), 129.9 (CH), 128.1 (CH), 128.0 (2×CH), 127.5 (2×CH), 127.4 (quat.), 127.1 (2×CH), 126.0 (CH), 125.9 (CH), 125.8 (quat.), 119.8 (quat.), 118.3 (quat.), 112.9 (quat.), 110.6 (CH), 107.3 (CH), 101.3 (CH), 75.0 (CH), 64.3 (CH), 55.8

(CH_3), 55.7 (CH_3), 44.6 (CH_2), 29.4 (CH_2); IR (KBr, cm^{-1}): 3058, 2934, 2223, 1700, 1603, 1493, 1450, 1432, 1338, 1275, 1167, 1090, 1002.

3.2.11. *N*-1-(3′,4′-Dimethoxyphenethyl)-2-(9*H*-9-fluorenylidenyl)acetamide (12a). 2-(3′,4′-Dimethoxyphenyl)-ethylamine (4.54 g, 25 mmol) was dissolved in dry dichloromethane (30 ml) and triethylamine (3.6 ml, 2.5 g, 25 mmol) was added at 0 °C. Fluorylidenylcarboxylic acid chloride (6.02 g, 25 mmol), dissolved in dry dichloromethane (50 ml), was added dropwise. The reaction mixture was stirred at room temperature for 3 h and water was added (50 ml). The organic layer was washed with brine (25 ml), then dried ($MgSO_4$) and evaporated in vacuo to yield the title product as a white solid (8.87 g, 92%), mp 154–155 °C; [Found: C, 78.0; H, 5.9; N, 3.6. $C_{25}H_{23}NO_3$ requires C, 77.9; H, 6.0; N, 3.6%]; ^{1}H NMR (500 MHz, DMSO-d_6): 8.68 (d, 1H, *J*=7.6 Hz, Flu–H), 8.58 (t, 1H, *J*=5.5 Hz, NH), 7.83 (m, 2H, Flu–H), 7.77 (d, 1H, *J*=7.6 Hz, Flu–H), 7.43 (t, 2H, *J*=7.6 Hz, Flu–H), 7.34 (t, 1H, *J*=7.6 Hz, Flu–H), 7.30 (t, 1H, *J*=7.6 Hz, Flu–H), 7.08 (s, 1H, CH═), 6.80 (m, 2H, Ar–2′ and 5′H), 6.78 (dd, 1H, *J*=1.8 and 8 Hz, Ar–6′H), 3.72 (s, 3H, OMe), 3.71 (s, 3H, OMe), 3.51 (m, 2H, H-1), 2.80 (t, 2H, *J*=7.2 Hz, H-2); ^{13}C NMR (125 MHz, DMSO-d_6): 165.5 (quat.), 148.8 (quat.), 147.4 (quat.), 141.3 (quat.), 139.6 (quat.), 138.7 (quat.), 135.1 (quat.), 131.9 (CH), 130.1 (quat.), 129.9 (CH), 128.1 (CH), 127.7 (3×CH), 121.1 (CH), 120.6 (CH), 120.5 (CH), 120.2 (CH), 120.0 (quat.), 112.7 (CH), 112.1 (CH), 55.7 (CH_3), 55.5 (CH_3), 40.7 (CH_2), 34.7 (CH_2); IR (KBr, cm^{-1}): 3311, 2935, 2841, 1625, 1605, 1516, 1451, 1443, 1301, 1290, 1262, 1236, 1190, 1157, 1141, 1027.

3.2.12. 1-(3′,4′-Dimethoxyphenethyl)-1-naphthamide (12b). Compound **12b** was prepared analogously to **6a** from naphthoic-1-carboxylic acid (9.53 g, 50 mmol) and was isolated as a white powder (10.2 g, 61%), mp 137–139 °C; [Found: C, 75.0; H, 6.3; N, 4.1. $C_{21}H_{21}NO_3$ requires C, 75.2; H, 6.3; N, 4.2%]; ^{1}H NMR (500 MHz, DMSO-d_6): 8.56 (t, 1H, *J*=5.5 Hz, NH), 8.04 (d, 1H, *J*=8.9 Hz, Naph–4′H), 7.98 (t, 1H, *J*=8.9 Hz, Naph–6′H), 7.95 (d, 1H, *J*=8.9 Hz, Naph–8′H), 7.56–7.46 (m, 4H, Naph–2′, 3′, 5′, and 7′H), 6.89 (m, 2H, Ar–2′ and 5′H), 6.80 (dd, 1H, *J*=2.0 and 8.1 Hz, Ar–6′H), 3.73 (s, 3H, OMe), 3.71 (s, 3H, OMe), 3.57 (m, 2H, CH_2), 2.85 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): 168.6 (quat.), 148.8 (quat.), 147.5 (quat.), 135.4 (quat.), 133.3 (quat.), 132.1 (quat.), 129.9 (CH), 129.7 (CH), 128.3 (CH), 126.7 (CH), 126.5 (quat.), 126.3 (CH), 125.6 (CH), 125.0 (CH), 120.8 (CH), 112.9 (CH), 112.1 (CH), 55.7 (CH_3), 55.5 (CH_3), 40.9 (CH_2), 34.8 (CH_2); IR (KBr, cm^{-1}): 3335, 3001, 2956, 2938, 2914, 2835, 1633, 1619, 1592, 1538, 1518, 1461, 1329, 1291, 1265, 1201, 1161, 1025.

3.2.13. 6,7-Dimethoxy-1-(9*H*-9-fluorenylidenmethyl)-3,4-dihydroisoquinoline (13a). *N*-1-(3′,4′-Dimethoxyphenethyl)-2-(9*H*-9-fluorenyliden)acetamide (8.0 g, 20.8 mmol) was dissolved in dry toluene (50 ml) and freshly distilled phosphorus oxychloride (3.15 g, 21 mmol) was added dropwise to the well-stirred mixture at 0 °C. The reaction mixture was stirred at reflux for 6 h, cooled to 5–10 °C and then the mixture was stirred with an excess of 10% aqueous sodium hydroxide solution. The aqueous phase was washed with ethyl acetate (3×30 ml) and the combined organic extracts were washed with brine (30 ml), then dried ($MgSO_4$) and evaporated in vacuo to give the title product as a yellow solid (5.34 g, 70%), mp 118–119 °C; [Found: C, 82.0; H, 5.9; N, 4.0. $C_{25}H_{21}NO_2$ requires C, 81.7; H, 5.8; N, 3.8%]; ^{1}H NMR (500 MHz, $CDCl_3$): 7.78 (d, 1H, *J*=7.4 Hz, Flu–H), 7.67 (d, 1H, *J*=7.4 Hz, Flu–H), 7.64 (d, 1H, *J*=7.4 Hz, Flu–H), 7.55 (d, 1H, *J*=7.4 Hz, Flu–H), 7.38 (t, 1H, *J*=7.4 Hz, Flu–H), 7.32 (s, 1H, H-8), 7.31 (t, 1H, *J*=7.4 Hz, Flu–H), 7.28 (t, 1H, *J*=7.4 Hz, Flu–H), 7.06 (t, 1H, *J*=7.4 Hz, Flu–H), 6.96 (s, 1H, H-5), 6.77 (s, 1H, CH═), 3.96 (t, 2H, *J*=7.7 Hz, H-4), 3.92 (s, 3H, *O*Me), 3.63 (s, 3H, *O*Me), 2.82 (t, 2H, *J*=7.7 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): 163.7 (quat.), 151.3 (quat.), 147.6 (quat.), 141.3 (quat.), 140.4 (quat.), 139.8 (quat.), 138.8 (quat.), 136.0 (quat.), 131.0 (quat.), 128.9 (CH), 128.8 (CH), 127.0 (CH), 126 5 (quat.), 126.9 (CH), 125.7 (CH), 122.7 (CH), 121.6 (quat.), 120.6 (CH), 119.5 (CH), 119.4 (CH), 110.4 (CH), 109.9 (CH), 56.1 (CH_3), 55.9 (CH_3), 47.4 (CH_2), 25.5 (CH_2); IR (KBr, cm^{-1}): 3426, 3001, 2933, 2830, 1714, 1603, 1562, 1512, 1463, 1450, 1357, 1317, 1277, 1207, 1151, 1140, 1024.

3.2.14. 6,7-Dimethoxy-1-(1-naphthyl)-3,4-dihydroisoquinoline (13b). 1-(3′,4′-Dimethoxyphenethyl)-1-naphthamide (10.0 g, 29.8 mmol) was dissolved in dry toluene (50 ml) and freshly distilled phosphorus oxychloride (9.12 g, 60 mmol) was added dropwise to the well-stirred mixture at 0 °C. The reaction mixture was stirred at reflux for 6 h, cooled to 5–10 °C and then the mixture was stirred with an excess of 10% aqueous sodium hydroxide solution. The aqueous phase was washed with ethyl acetate (3×30 ml) and the combined organic extracts were washed with brine (30 ml), then dried ($MgSO_4$) and evaporated in vacuo to yield the title product as a yellow solid (7.09 g, 75%), mp 105–107 °C; [Found: C, 79.2; H, 5.9; N, 4.2. $C_{21}H_{19}NO_2$ requires C, 79.5; H, 6.0; N, 4.4%]; ^{1}H NMR (500 MHz, DMSO-d_6): 8.00 (d, 1H, *J*=8.3 Hz, Naph–4′H), 7.98 (d, 1H, *J*=8.3 Hz, Naph–8′H), 7.73 (dd, 1H, *J*=1 and 8.3 Hz, Naph–5′H), 7.59 (t, 1H, *J*=8.3 Hz, Naph–6′H), 7.51 (m, 2H, Naph–7′ and 2′H), 7.42 (dt, 1H, *J*=1 and 8.3 Hz, Naph–3′H), 7.02 (s, 1H, H-8), 6.26 (s, 1H, H-5), 3.86 (m, 2H, H-3), 3.85 (s, 3H, *O*Me), 3.29 (s, 3H, *O*Me), 2.84 (m, 1H, H-4); ^{13}C NMR (125 MHz, DMSO-d_6): 165.6 (quat.), 151.3 (quat.), 147.1 (quat.), 137.1 (quat.), 133.3 (quat.), 131.4 (quat.), 131.2 (CH), 128.7 (CH), 128.4 (quat.), 126.5 (CH), 126.3 (CH), 126.1 (CH), 125.7 (quat.), 125.4 (CH), 122.5 (CH), 111.25 (CH), 111.2 (CH), 55.8 (CH_3), 55.7 (CH_3), 47.5 (CH_2), 25.3 (CH_2); IR (KBr, cm^{-1}): 3013, 2933, 2896, 2830, 1604, 1564, 1510, 1464, 1456, 1432, 1353, 1318, 1277, 1262, 1236, 1213, 1197, 1163, 1131, 1057, 1040, 1017.

3.2.15. 6,7-Dimethoxy-1-(9*H*-9-fluorenylidenylmethyl)-2-methoxycarbonylmethyl-3,4-dihydroisoquinolinium bromide (14a). Compound **14a** was prepared analogously to **8a** from **13a** (0.5 g, 1.36 mmol) and was isolated as a yellow powder (0.71 g, 100%), mp 222–223 °C; [Found: C, 64.6; H, 5.0; N, 2.7. $C_{28}H_{26}NO_4Br$ requires C, 64.6; H, 5.0; N, 2.7%]; ^{1}H NMR (500 MHz, $CDCl_3$): 8.12 (d, 1H, *J*=7.5 Hz, Flu–H), 7.62 (m, 3H, Flu–H), 7.46 (t, 1H, *J*=7.5 Hz, Flu–H), 7.39 (d, 1H, *J*=7.5 Hz, Flu–H), 7.28 (m, 1H, Flu–H), 7.10 (s, 1H, H-8), 7.07 (s, 1H, H-5), 7.02 (s, 1H, CH═), 6.86 (d, 1H, *J*=7.5 Hz, Flu–H), 5.64 (d, 1H *J*=17 Hz, NCH_2), 5.13 (d,

1H, J=17 Hz, NCH_2), 3.84 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.72 (m, 2H, H-3), 3.59 (s, 3H, OMe), 3.28 (m, 2H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$): 179.0 (quat.), 166.1 (quat.), 158.1 (quat.), 149.0 (quat.), 145.0 (quat.), 144.6 (quat.), 142.3 (quat.), 140.6 (quat.), 140.1 (quat.), 134.4 (CH), 134.3 (quat.), 129.5 (CH), 129.3 (CH), 129.1 (CH), 128.4 (quat.), 127.5 (CH), 126.4 (CH), 123.0 (CH), 120.2 (CH), 119.7 (CH), 118.6 (quat.), 112.5 (CH), 111.5 (CH), 57.0 (CH_3), 56.4 (CH_3), 55.4 (CH_2), 52.2 (CH_3), 45.9 (CH_2), 26.7 (CH_2); IR (KBr, cm^{-1}): 3425, 2938, 2831, 1744, 1609, 1513, 1465, 1449, 1436, 1426, 1390, 1340, 1276, 1235, 1224, 1210, 1180, 1165, 1148, 1115, 1085, 1022.

3.2.16. 2-Benzyl-6,7-dimethoxy-1-(9*H*-9-fluorenylidenylmethyl)-3,4-dihydroisoquinolinium bromide (14b). Compound **14b** was prepared analogously to **8a** from **13a** (0.5 g; 1.36 mmol) and benzyl bromide (0.36 ml, 0.50 g, 3 mmol) and was isolated as a yellow powder (0.71 g, 97%), mp 239–241 °C; [Found: C, 71.3; H, 5.2; N, 2.6. $C_{32}H_{28}NO_2Br$ requires C, 71.4; H, 5.2; N, 2.6%]; ^1H NMR (500 MHz, $CDCl_3$): 8.12 (d, 1H, J=7.5 Hz, Flu–H), 7.71 (m, 3H, Flu–H), 7.52 (m, 2H, Ph–H), 7.44 (m, 3H, Ar–H and Flu–H), 7.30 (m, 2H, Ar–H), 7.22 (d, 1H, J=7.5 Hz, Flu–H), 7.05 (s, 2H, H-8 and H-5), 6.85 (d, 1H, J=7.5 Hz, Flu–H), 6.51 (s, 1H, CH═), 5.64 (d, 1H, J=17.7 Hz, NCH_2), 5.10 (d, 1H, J=17.7 Hz, NCH_2), 4.04 (s, 3H, *O*Me), 3.84 (s, 3H, *O*Me), 3.58 (m, 2H, H-4), 3.48 (m, 2H, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): 171.6 (quat.), 157.6 (quat.), 148.9 (quat.), 146.2 (quat.), 142.8 (quat.), 140.4 (quat.), 136.7 (quat.), 134.1 (quat.), 133.5 (quat.), 131.3 (CH), 129.5 (2×CH), 129.4 (CH), 129.2 (2×CH), 129.0 (CH), 128.5 (CH), 128.3 (quat.), 127.9 (CH), 125.5 (CH), 123.3 (CH), 120.8 (CH), 120.3 (CH), 118.7 (quat.), 115.2 (CH), 114.0 (CH), 111.5 (CH), 62.0 (CH_2), 57.2 (CH_3), 56.4 (CH_3), 49.7 (CH_2), 26.4 (CH_2); IR (KBr, cm^{-1}): 2955, 2938, 1602, 1551, 1496, 1451, 1386, 1338, 1293, 1271, 1219, 1170, 1004.

3.2.17. 2-Allyl-6,7-dimethoxy-1-(9*H*-9-fluorenylidenmethyl)-3,4-dihydroisoquinolinium bromide (14c). Compound **14c** was prepared analogously to **8e** from **13a** (0.5 g, 1.36 mmol) and was isolated as a yellow powder (0.65 g, 98%), mp 233 °C; [Found: C, 69.0; H, 5.2; N, 2.7. $C_{28}H_{26}NO_2Br$ requires C, 68.9; H, 5.4; N, 2.9%]; ^1H NMR (500 MHz, $CDCl_3$): 7.72 (d, 1H, J=7.8 Hz, Flu–H), 7.67 (m, 1H, Flu–H), 7.41 (m, 3H, Flu–H), 7.25 (t, 1H, J=7.5 Hz, Flu–H), 7.17 (m, 2H, Flu–H), 7.07 (s, 2H, H-5 and H-8), 7.00 (s, 1H, CH═), 6.05 (d, 1H, J=9.5 Hz, allyl), 5.47 (m, 1H, allyl), 5.24 (d, 1H, J=18 Hz, NCH_2), 5.13 (m, 1H, allyl), 4.85 (d, 1H, J=18 Hz, NCH_2), 4.02 (s, 3H, OMe), 3.91 (m, 1H, H-3), 3.85 (s, 3H, OMe), 3.70 (m, 2H, H-3 and H-4), 3.33 (m, 1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$): 177.4 (quat.), 157.6 (quat.), 148.9 (quat.), 145.3 (quat.), 143.9 (quat.), 140.8 (quat.), 140.4 (quat.), 133.6 (quat.), 129.1 (CH), 128.9 (CH), 128.8 (CH), 128.3 (CH), 127.6 (CH), 127.4 (CH), 126.4 (CH_2), 125.7 (quat.), 123.0 (CH), 125.3 (CH_2), 120.8 (CH), 119.8 (CH), 116.2 (quat.), 112.4 (CH), 111.6 (CH), 80.5 (CH), 56.9 (CH_3), 56.3 (CH_3), 44.3 (CH_2), 26.4 (CH_2); IR (KBr, cm^{-1}): 2937, 1603, 1554, 1521, 1450, 1387, 1338, 1291, 1271, 1219, 1171, 1004.

3.2.18. 6,7-Dimethoxy-1-(1-naphthyl)-2-ethoxycarbonylmethyl-3,4-dihydroisoquinolinium bromide (16). Compound **16** was prepared analogously to **8a** from **13b** (0.5 g, 1.57 mmol) and was isolated as a yellow powder (0.73 g, 100%); mp 211–212 °C; [Found: C, 61.3; H, 5.2; N, 2.9. $C_{24}H_{24}NO_4Br$ requires C, 61.3; H, 5.1; N, 3.0%]; ^1H NMR (500 MHz, DMSO-d_6): 8.33 (d, 1H, J=8.0 Hz, Naph–4′H), 8.15 (d, 1H, J=8.0 Hz, Naph–8′H), 7.83 (dd, 1H, J=1.5 and 8.0 Hz, Naph–5′H), 7.80 (t, 1H, J=8.0 Hz, Naph–6′H), 7.65 (dt, 1H, J=1.5 and 8 Hz, Naph–7′H), 7.58 (dt, 1H, J=1.5 and 8.0 Hz, Naph–3′H), 7.53 (d, 1H, J=8.0 Hz, Naph–2′H), 7.47 (s, 1H, H-5), 6.17 (s, 1H, H-8), 4.80 (d, 1H, J=17.1 Hz, NCH_2), 4.64 (d, 1H, J=17.1 Hz, NCH_2), 4.59 (m, 1H, H-4), 4.48 (m, 1H, H-4), 4.03 (q, 2H, J=7.1 Hz, OCH_2), 3.98 (s, 3H, OMe), 3.61 (m, 1H, H-3), 3.50 (m, 1H, H-3), 3.21 (s, 3H, *O*Me), 1.03 (t, 3H, J=7.1 Hz, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): 174.6 (quat.), 165.8 (quat.), 157.8 (quat.), 148.0 (quat.), 135.8 (quat.), 133.0 (quat.), 132.5 (quat.), 129.1 (CH), 128.9 (CH), 128.5 (quat.), 127.6 (CH), 127.3 (CH), 126.2 (CH), 125.6 (quat.), 124.3 (CH), 119.4 (CH), 114.7 (CH), 112.1 (CH), 62.3 (CH_2), 58.4 (CH_2), 57.1 (CH_3), 55.7 (CH_3), 51.7 (CH_2), 25.2 (CH_2), 13.8 (CH_3); IR (KBr, cm^{-1}): 3020, 3002, 2985, 1747, 1602, 1551, 1520, 1506, 1473, 1403, 1376, 1342, 1292, 1276, 1224, 1178, 1120, 1007.

3.3. 1,7-Electrocyclizations—method B

The corresponding 6,7-dimethoxy-1-(9*H*-9-fluorenylidenemethyl)-3,4-dihydroisoquinolinium bromide (0.75 mmol) was dissolved in dry methanol (10 ml) and triethylamine (0.11 ml, 1.5 mmol) was added. The reaction mixture was stirred for 24 h at room temperature under an argon atmosphere. The solvent was removed in vacuo, the residue was dissolved in dichloromethane (15 ml) and washed with water (2×10 ml) and brine (10 ml). The organic layer was dried over magnesium sulfate and evaporated in vacuo. The residue was further purified by column chromatography on silica gel, eluting with hexane–acetone (3:1).

3.3.1. Methyl 14,15-dimethoxy-1,2,4,12*a*-tetrahydrofluoreno[9′,1′:4,5,6]azepino[2,1-*a*]isoquinoline-4-carboxylate (15a). Pale yellow oil, (0.16 g, 49%); ^1H NMR (500 MHz, $CDCl_3$): 7.70 (m, 2H, H-5 and H-11), 7.56 (m, 2H, H-7 and H-8), 7.37 (m, 2H, H-6 and H-16), 7.31 (dt, 1H, J=1.0 and 7.5 Hz, H-10), 7.21 (dt, 1H, J=1.0 and 7.5 Hz, H-9), 6.98 (s, 1H, H-13), 6.69 (s, 1H, H-12), 5.00 (s, 1H, H-4), 4.42 (s, 1H, H-12*a*), 3.89 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.47 (m, 2H, H-1), 3.05 (s, 3H, OMe), 2.84 (m, 2H, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): 169.8 (quat.), 150.4 (quat.), 149.7 (quat.), 148.0 (quat.), 147.8 (quat.), 147.0 (quat.), 141.0 (quat.), 139.7 (quat.), 129.1 (quat.), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.4 (CH), 127.2 (quat.), 125.6 (CH), 124.3 (CH), 120.0 (quat.), 119.7 (CH), 110.8 (CH), 107.5 (CH), 99.0 (CH), 77.3 (CH), 56.0 (CH_3), 55.85 (CH_3), 53.9 (CH), 51.3 (CH_3), 47.8 (CH_2), 29.3 (CH_2); IR (neat, cm^{-1}): 2938, 2831, 1744, 1629, 1513, 1465, 1449, 1436, 1426, 1276, 1235, 1224, 1210, 1180, 1165, 1148, 1115, 1085, 1022; (HRMS Found: *m/z* 439.1747. $C_{28}H_{25}NO_4$ *m/z* 439.1783).

3.3.2. 14,15-Dimethoxy-4-phenyl-1,2,4,12*a*-tetrahydrofluoreno[9′,1′:4,5,6]azepino[2,1-*a*]isoquinoline (15b). Pale yellow oil, (0.16 g, 46%); ^1H NMR (500 MHz, $CDCl_3$): 7.82 (m, 2H, H-5 and H-11), 7.61 (m, 2H, H-7 and H-8), 7.40 (m, 5H, Ph–H and H-6, H-16), 7.21 (m, 2H, H-9

and H-10), 7.08 (m, 2H, Ph–H), 6.76 (s, 1H, H-13), 6.73 (s, 1H, H-12), 5.21 (s, 1H, H-12*a*), 4.84 (s, 1H, H-4), 3.92 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.32 (m, 2H, H-1), 2.82 (m, 2H, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): 149.9 (quat.), 148.2 (quat.), 147.7 (quat.), 147.1 (quat.), 146.2 (quat.), 142.3 (quat.), 140.0 (quat.), 133.4 (quat.), 129.7 (2×CH), 129.4 (quat.), 128.9 (2×CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.3 (quat.), 125.9 (CH), 124.8 (CH), 121.1 (CH), 119.9 (quat.), 111.0 (CH), 108.0 (CH), 101.8 (quat.), 80.2 (CH), 55.9 (CH_3), 55.85 (CH_3), 55.8 (CH), 45.9 (CH_2), 29.2 (CH_2); IR (neat, cm^{-1}): 2932, 2835, 1607, 1513, 1502, 1494, 1464, 1390, 1345, 1267, 1211, 1148, 1025; (HRMS Found: *m/z* 457.2040. $C_{32}H_{27}NO_2$ requires *m/z* 457.2042).

3.3.3. 14,15-Dimethoxy-4-ethenyl-1,2,4,12*a*-tetrahydrofluoreno[9′,1′:4,5,6]azepino[2,1-*a*]isoquinoline (15c). Pale yellow oil, (0.13 g, 44%); ^{1}H NMR (500 MHz, $CDCl_3$): 7.72 (m, 2H, H-5 and H-11), 7.41 (m, 3H, H-6, H-7 and H-8), 7.27 (s, 1H, H-16), 7.22 (m, 2H, H-9 and H-10), 7.09 (s, 2H, H-12 and H-13), 6.03 (d, 1H, *J*=9.3 Hz, H-4), 5.47 (m, 1H, vinyl–CH), 5.17 (d, 1H, *J*=18 Hz, vinyl–CH_2), 5.11 (s, 1H, H-12*a*), 4.85 (d, 1H, *J*=18 Hz, vinyl–CH_2), 4.32 (m, 1H, H-1), 4.02 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.68 (m, 2H, H-1 and H-2), 3.36 (m, 1H, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): 150.1 (quat.), 147.9 (quat.), 147.7 (quat.), 147.5 (quat.), 147.1 (quat.), 143.1 (quat.), 139.5 (quat.), 129.7 (quat.), 128.6 (CH), 127.7 (CH), 127.6 (2×CH), 127.3 (CH), 127.2 (quat.), 126.3 (CH_2), 126.1 (CH), 124.9 (CH), 121.4 (CH), 119.8 (quat.), 110.7 (CH), 107.9 (CH), 102.1 (CH), 79.2 (CH), 59.9 (CH), 55.8 (CH_3), 55.7 (CH_3), 46.0 (CH_2), 29.2 (CH_2); IR (neat, cm^{-1}): 3387, 2937, 1711, 1604, 1559, 1524, 1450, 1421, 1397, 1337, 1291, 1220, 1164, 1083, 1006; (HRMS Found: *m/z* 407.1907. $C_{28}H_{25}NO_2$ requires *m/z* 407.1885).

3.3.4. 1-(2,2-Diphenylethenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (16). 6,7-Dimethoxy-1-(2′,2′-diphenyl-1-ethenyl]-3,4-dihydroisoquinoline (3.73 g, 10 mmol) was dissolved in ethanol (50 ml) and sodium borohydride (1.89 g, 50 mmol) was added in small portions. The mixture was refluxed for 1 h, then the solvent was removed in vacuo. The residue was dissolved in dichloromethane (100 ml) and washed with water (2×50 ml) and brine (30 ml). The organic layer was dried over magnesium sulfate and evaporated in vacuo to give a white semi-solid product (3.71 g, 100%). ^{1}H NMR (500 MHz, $CDCl_3$): 7.41–7.23 (m, 10H, Ph), 6.63 (s, 1H, H-5), 6.58 (s, 1H, H-8), 6.20 (d, 1H, *J*=9.6 Hz, CH═), 4.58 (d, 1H, *J*=9.6 Hz, H-1), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.27 (m, 1H, H_2-4), 2.90 (m, 1H, H_2-4), 2.63 (m, 2H, H_2-3); ^{13}C NMR (125 MHz, $CDCl_3$): 147.7 (quat.), 147.3 (quat.), 143.6 (quat.), 141.9 (quat.), 139.6 (quat.), 130.7 (quat.), 129.7 (2×CH), 129.6 (quat.), 128.6 (2×CH), 128.3 (2×CH), 127.6 (CH), 127.5 (3×CH), 126.9 (CH), 111.9 (CH), 110.4 (CH), 56.0 (CH_3), 55.9 (CH_3), 55.5 (CH), 42.4 (CH_2), 29.2 (CH_2); IR (KBr, cm^{-1}): 3047, 3023, 3000, 2958, 2921, 2826, 1599, 1575, 1509, 1466, 1446, 1427, 1369, 1329, 1281, 1265, 1218, 1126, 1033; (HRMS: Found: *m/z* 371.1872. $C_{25}H_{25}NO_2$ requires *m/z* 371.1885).

3.4. 1,7-Electrocyclization—method C

1-(2,2-Diphenylethenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (0.37 g, 1 mmol) and the corresponding aldehyde (1.1 mmol) were dissolved in dry xylene (15 ml), the reaction mixture was refluxed for 11–32 h and the water formed was removed with the aid of a Dean–Stark trap. After cooling, the solvent was removed in vacuo and the resulting residue purified by column chromatography on silica, eluting with hexane–acetone (90:10 to 50:50).

3.4.1. 2,3-Dimethoxy-13-phenyl-8-(4-chlorophenyl)-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11k). Pale yellow oil (0.16 g, 32%); ^{1}H NMR (500 MHz, $CDCl_3$): 7.50 (d, 2H, *J*=7.5 Hz, Ar–H, H-2′ and 6′), 7.37–7.22 (m, 5H, Ar–H), 7.18 (s, 1H, H-1), 7.01 (d, 2H, *J*=7.5 Hz, Ar–3′ and 5′H), 6.96 (m, 2H, Ar–H), 6.85 (m, 2H, Ar–H), 6.65 (s, 1H, H-14), 5.49 (s, 1H, H-14*a*), 5.14 (s, 1H, H-8), 3.91 (s, 3H, OMe), 3.89 (s, 3H, OMe), 3.85 (m, 2H, H_2-6), 3.07 (m, 1H, H_2-5), 2.89 (m, 1H, H_2-5); ^{13}C NMR (125 MHz, $CDCl_3$): 152.7 (quat.), 150.2 (quat.), 147.9 (quat.), 144.2 (quat.), 141.2 (quat.), 140.1 (quat.), 137.8 (quat.), 136.6 (quat.), 129.5 (quat.), 129.2 (2×CH), 128.5 (CH), 128.2 (2×CH), 130.2 (2×CH), 128.5 (2×CH), 128.45 (2×CH), 128.2 (CH), 128.0 (2×CH), 120.3 (quat.), 111.0 (CH), 110.1 (CH), 104.7 (CH), 77.4 (CH), 56.2 (CH_3), 56.1 (CH_3), 45.0 (CH_2), 30.0 (CH_2); IR (KBr, cm^{-1}): 2940, 2921, 2910, 2845, 1611, 1501, 1460, 1337, 1319, 1296, 1271, 1212, 1177, 1149, 1111, 1029; (HRMS Found: *m/z* 493.1803. $C_{32}H_{28}NO_2Cl$ requires *m/z* 493.1809).

3.4.2. 2,3-Dimethoxy-13-phenyl-8-(4-methoxyphenyl)-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11l). Pale yellow oil (0.13 g, 26%); ^{1}H NMR (500 MHz, $CDCl_3$): 7.53 (d, 2H, *J*=7.5 Hz, Ar^8-2′ and 6′H), 7.34–7.15 (m, 7H, Ar–H), 7.01 (m, 3H, Ar–H), 6.90 (m, 3H, Ar–H), 6.66 (s, 1H, H-14), 5.54 (s, 1H, H-14*a*), 5.12 (s, 1H, H-8), 3.89 (s, 3H, OMe), 3.87 (s, 3H, OMe), 3.77 (m, 2H, H_2-6), 3.00 (m, 1H, H_2-5), 2.74 (m, 1H, H_2-5); ^{13}C NMR (125 MHz, $CDCl_3$): 162.8 (quat.), 149.6 (quat.), 147.3 (quat.), 144.8 (quat.), 142.5 (quat.), 141.1 (quat.), 137.6 (quat.), 133.2 (2×CH), 129.0 (2×CH), 128.2 (quat.), 128.1 (2×CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 127.3 (CH), 126.3 (CH), 126.1 (quat.), 120.0 (quat.), 112.7 (2×CH), 110.8 (CH), 109.9 (CH), 103.0 (CH), 77.6 (CH), 56.0 (CH_3), 55.8 (CH_3), 45.3 (CH_2), 29.6 (CH_2); IR (KBr, cm^{-1}): 2963, 2836, 1604, 1559, 1513, 1464, 1399, 1258, 1168, 1113, 1028; (HRMS Found: *m/z* 489.2324. $C_{33}H_{31}NO_3$ requires *m/z* 489.2303).

3.4.3. 2,3-Dimethoxy-13-phenyl-8-(3,4-methoxyphenyl)-5,6,8,14*a*-tetrahydrobenz[5,6]azepino[2,1-*a*]isoquinoline (11m). Pale yellow oil, 0.06 g (11%); ^{1}H NMR (500 MHz, $CDCl_3$): 7.52 (m, 2H, Ar–H), 7.33 (m, 2H, Ar–H), 7.24 (m, 3H, Ar–H), 7.06 (m, 4H, Ar–H), 6.88 (m, 3H, Ar–H), 6.66 (s, 1H, H-14), 6.14 (s, 1H, H-14*a*), 5.47 (s, 1H, H-8), 3.93 (s, 3H, OMe), 3.90 (s, 3H, OMe), 3.81 (s, 6H, 2×OMe), 3.39 (m, 2H, H_2-6), 3.05 (m, 1H, H_2-5), 2.63 (m, 1H, H_2-5); ^{13}C NMR (125 MHz, $CDCl_3$): 149.2 (quat.), 149.1 (quat.), 148.8 (quat.), 147.1 (quat.), 144.9 (quat.), 143.9 (quat.), 143.0 (quat.), 137.2 (quat.), 129.1 (quat.), 128.8 (2×CH), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.8 (2×CH), 127.5 (2×CH), 127.25 (CH), 127.2 (quat.), 120.0 (quat.), 119.3 (CH), 112.7 (CH), 112.0 (CH), 110.8 (CH), 109.9 (CH), 102.9 (CH), 77.5 (CH), 56.0 (CH_3), 55.9 (2×CH_3), 55.8 (CH_3), 45.4 (CH_2), 29.6 (CH_2); IR (KBr,

cm^{-1}): 2937, 2836, 1603, 1514, 1495, 1464, 1399, 1268, 1147, 1025; (HRMS Found: *m/z* 519.2398. $C_{34}H_{33}NO_4$ requires *m/z* 519.2409).

Acknowledgements

This work was financially supported by the National Fund for Science and Research, Hungary (OTKA Project No. T 046196). N.M. thanks the Hungarian Academy of Sciences for a Bolyai J. fellowship. A grant from the József Varga Foundation provided to J.T. is gratefully appreciated.

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