11. Cyclization Studies with *N-Mannich* Bases of 2-Substituted Indoles

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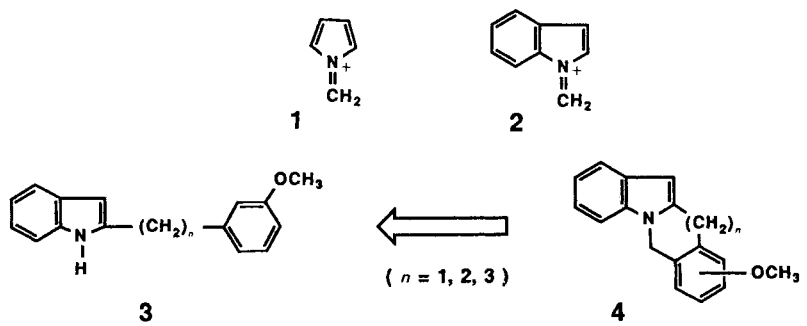
The synthesis of the indoles **7**, **15**, **16** with a 3-methoxyphenyl group, attached *via* an α-side chain of 1, 2, or 3 CH_2 units, is reported. These compounds, after appropriate protection at C(3), were transformed into the *N*-[(dimethylamino)methyl]indoles **22**, **23**, and **24**, respectively. When treated with AcCl, these *N-Mannich* bases gave, in two cases, stable *N*-(chloromethyl)indoles **25** and **26**. In the presence of $SnCl_4$, ring closure occurred *via* electrophilic attack of 1-methylideneindolium ions on the methoxyphenyl group. Formation of seven-membered rings (→**27**, **28**) and eight-membered rings (→**29**) was found to be a favorable process. Cyclization to six-membered rings did not occur within this series.

Previous studies in our laboratory have revealed that *N-Mannich* bases of pyrrole and indole are suitable precursors for the 5-azoniafulvene ion **1** and its benzo-annellated analogue **2**, respectively [1] *(Scheme 1)*. These interesting iminium-type ions combine structural and functional features with promising synthetic potential. For example,

Scheme 1

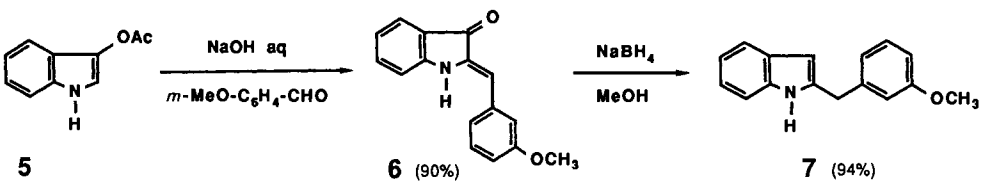


we demonstrated recently, that ions **1** and **2** can undergo formal [$6\pi + 4\pi$] cycloadditions when allowed to react with selected 1,3-dipolar compounds [2]. The present communication deals with the question, whether the reactivity of ion **2** towards electron-rich π systems can be exploited intramolecularly for the preparation of novel [*a*]-annellated indoles. For this purpose, we have synthesized the homologous series of type **3**, having a π nucleophile attached *via* a side chain of variable length ($n = 1, 2$, or 3). The anisyl group was chosen as nucleophile on account of its established reactivity towards iminium ions, and because of its suitability for subsequent reductive transformation. These compounds, after appropriate protection of the free indolic C(3) position, were transformed into *N-Mannich* bases and examined under various cyclization conditions. The expected

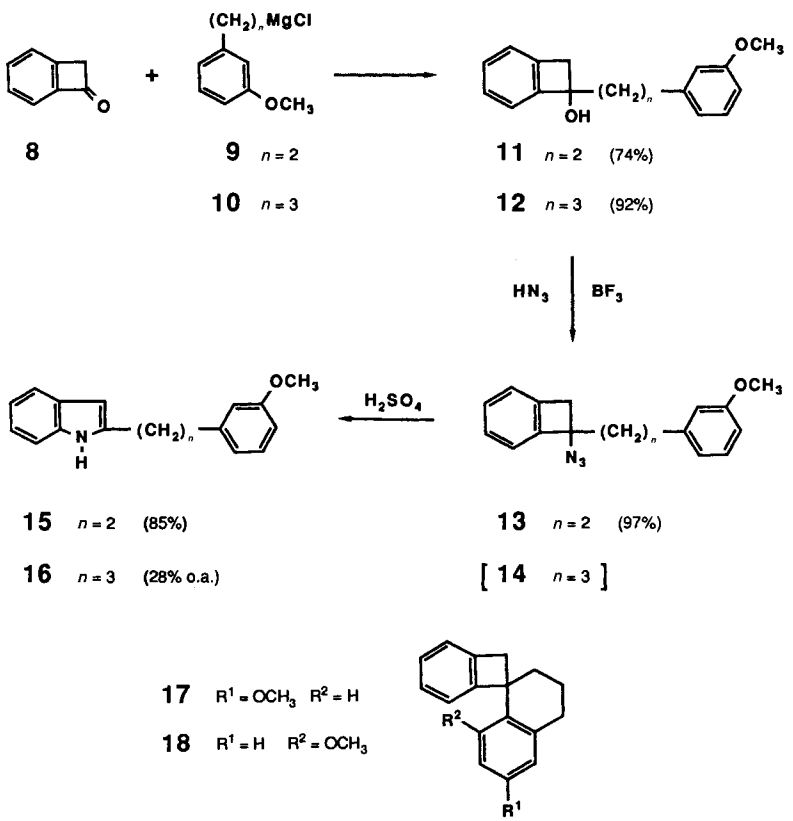
[*a*]-annellated indoles **4** belong to a class of heterocyclic compounds which has only found occasional attention in the past [3] [4].

Syntheses of the 2-Substituted Indoles. – To obtain compound **7**, *i.e.* the first member of the homologous series, we have modified a known preparation of 2-benzylindole [5]. This modification, outlined in *Scheme 2*, consists in using the commercially available 3-acetoxyindole (**5**) as starting material, instead of its *N*-acetyl analogue. Basic cleavage, under rigorous exclusion of air, and condensation with 3-methoxybenzaldehyde gave the derivative **6**. We tentatively assign the (*Z*)-configuration to this product. Its reduction with $NaBH_4$ in MeOH gave the desired indole **7** in 86.5% overall yield.

Scheme 2



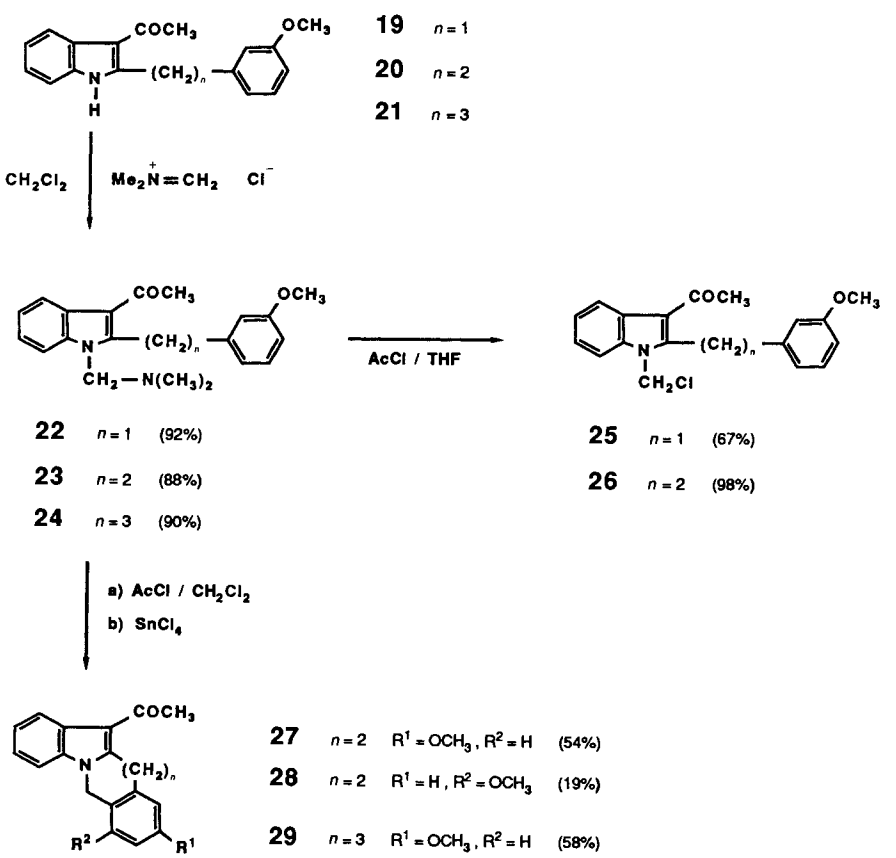
Scheme 3



Unfortunately, this condensation method is limited to aldehydes lacking an α-H-atom. For the preparation of the higher homologues, we, therefore, had to consider alternative methods [6] [7]. Preference was given to an elegant indole synthesis reported by *Adam et al.* [7]. As shown in *Scheme 3*, it consists of the addition of appropriate *Grignard* compounds to the readily available cyclobutabenzenone **8** [8]. The ensuing tertiary alcohols **11** and **12** were converted into azides by reaction with HN_3 in presence of BF_3 and then expanded in a *Schmidt*-type reaction to afford the desired indoles **15** and **16**, respectively. These transformations can be run in a one-pot procedure without isolation of the azides. In our hands, this method gave very satisfactory results for the compound with the shorter side chain, *i.e.* **11**→**15**. However, for the next higher member of the series, spirocyclization occurred, giving **17** and **18** in competition with azide formation. A high concentration (1M) of HN_3 was necessary to obtain the desired indole **16** by this one-pot procedure in modest 28% yield.

Aminomethylation of 2-Substituted Indoles. – The parent indole is known to give a *Mannich* base at the N-atom when allowed to react with Me_2NH and aqueous H_2CO in

Scheme 4



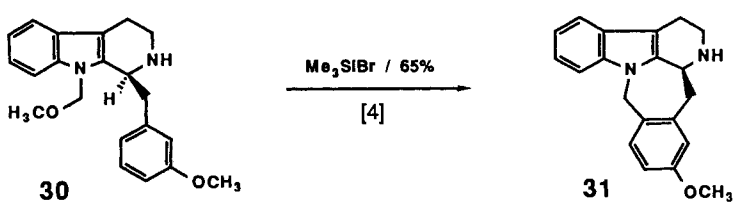
absence of an acid [9]. Our 2-substituted indoles, however, reacted in a sluggish and unspecific way under these conditions. When using *N,N*-dimethylmethylideneiminium chloride [10] in CH_2Cl_2, we obtained predominantly (> 90%) substitution at C(3). To direct the aminomethylation onto the N-atom, indoles **7**, **15**, and **16** were first *C*-acylated and then treated with the *Eschenmoser* salt to give compounds **22**, **23**, and **24** *(Scheme 4)*.

***N*-(Chloromethyl)indoles and the Cyclization Reaction.** – *N-Mannich* bases of indoles often behave like aminals and can be cleaved by acyl chlorides [1] [11]. The ensuing iminium ions normally undergo fast reaction with π nucleophiles or other suitable substrates. When we allowed compounds **22** and **23** to react with AcCl in THF, we obtained, to our surprise, the stable *N*-(chloromethyl) compounds **25** and **26**. These N,Cl-heterogeminals are, to our knowledge, unprecedented in pyrrole and indole chemistry (*cf.* [12]). They, undoubtedly, owe their stability to steric protection. This, at least, is suggested by the failure of obtaining corresponding stable *N*-(chloromethyl)indoles from the next higher member of the series, *i.e.* **24**, or from other *N*-[(dimethylamino)-methyl]indoles that lack the bulky ligand at C(2).

When we ran the acylation reaction of the *N-Mannich* bases **23** and **24** in presence of $SnCl_4$, cyclization occurred with formation of seven-membered and eight-membered rings, respectively. Compound **23** gave the cyclization products resulting from both the *para*-substitution (→**27**; 54%) and the *ortho*-attack (→**28**; 19%). A nearly identical product ratio and yield (**27**, 57%; **28**, 21%) was obtained, when the chloride **26** was allowed to react directly with the *Lewis* acid. Starting from the *Mannich* base **24**, which has the most flexible side chain, we isolated the crystalline cyclization product **29** (58%). No *ortho*-substitution was observed in this case. In contrast to the *N-Mannich* bases **23** and **24**, the first member of the homologous series, *i.e.* compound **22**, did not cyclize under the acylation conditions in presence of $SnCl_4$, nor did the corresponding *N*-(chloromethyl)indole **25** undergo ring closure when treated with the *Lewis* acid.

Discussion. – Cyclization reactions involving iminium ions are very common and are found amongst the eldest methods of heterocyclic synthesis. The present ring-closure reactions, however, present the first examples where the iminium N-atom is embedded rigidly in an indole skeleton. When this study was completed, *Meyers et al.* [4], reporting on their yohimbone synthesis, mentioned the fortuitous observation of a ring closure that is clearly related to our work. When deprotection of the *N*-(methoxymethyl)-β-carboline **30** was attempted by these authors, cyclization was observed giving the seven-membered ring of compound **31** *(Scheme 5)*. This process, undoubtedly, follows the same mechanistic scheme as the cyclization **23**→**27**. Obviously, formation of seven- or eight-membered

Scheme 5



rings, and presumably that of even larger cycles, can occur easily within the present system. However, from the failure of compounds **22** and **25** to undergo ring closure, when suitably treated, it is obvious that the iminium ion cannot cyclize *via* a six-membered transition state.

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Experimental Part

General. GC: *Perkin-Elmer-900;* glass columns. IR spectra [cm^{-1}]: *Polaris-Mattson* FT-IR spectrometer. NMR spectra: *Bruker WM-360* (8.46 Tesla) or *Varian XL-200* (4.7 Tesla); chemical shifts in δ[ppm] relative to internal TMS; apparent scalar coupling constants J in Hz; multiplicities for ^{13}C under off-resonance decoupling or according to attached proton test (APT). MS: (*m/z* (rel. %)): *Finnigan-4023* with INCOS data system; electron impact, 70 eV. FC = flash chromatography.

*2,3-Dihydro-2-(3-methoxybenzylidene)-1*H*-indol-3-one* (**6**). *Indol-3-yl acetate* (**5**; 3.0 g, 17.1 mmol) was added to 1.5M aq. NaOH (94 ml, 141 mmol) which was previously deoxygenated with Ar. The mixture was heated for 5 min to 100° to give a yellowish green soln. After cooling to 0–5°, a soln. of *m*-methoxybenzaldehyde (2.33 g, 17.1 mmol) in MeOH (2.5 ml) was added. After 24 h at r.t., orange crystalline **6** had precipitated. It was filtered, washed with H_2O, and dried *in vacuo:* 3.84 g (90%) of **6** as orange crystals. M.p. 168°. IR ($CDCl_3$): 3690*m*, 3610*m*, 2950*w*, 1695*m*, 1635*s*, 1615*s*, 1600*s*, 1485*s*, 1470*m*, 1260*m*, 1135*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 3.88 (*s*, CH_3O); 6.82–7.7 (*m*, 10 H). ^{13}C-NMR ((D$_6$)DMSO, 50 MHz): 55.07 (CH_3); 109.6 (CH); 112.6 (CH); 114.0 (CH); 115.2 (CH); 119.7 (CH); 119.9 (C); 122.2 (CH); 124.0 (CH); 129.8 (CH); 134.5 (C); 135.4 (C); 136.3 (CH); 154.2 (C); 159.5 (C); 186.3 (CO). MS: 251 (61, $C_{16}H_{13}NO_2$), 250 (36), 236 (28), 220 (70), 180 (36), 152 (30), 89 (47), 77 (100), 76 (93), 63 (42).

*2-(3-Methoxybenzyl)-1*H*-indole* (**7**; *cf.* [5]). $NaBH_4$ (30.7 g, 811 mmol) was added in small portions, with stirring, to a soln. of **6** (3.84 g, 15.3 mmol) in 300 ml of MeOH. The mixture was allowed to react over night, poured into hot H_2O (900 ml), and acidified (pH 3) with 2N HCl. After cooling, the product was extracted with Et_2O, washed with sat. $NaHCO_3$ and brine, and dried ($MgSO_4$). Removal of the solvent gave **7** (3.41 g, 94%) as yellowish crystals. M.p. 81–83°. IR ($CDCl_3$): 3470*m*, 2960*w*, 1605*m*, 1590*m*, 1490*s*, 1460*s*, 1290*m*, 1260*s*, 1050*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 3.80 (*s*, CH_3O); 4.12 (*s*, 2 H); 6.37 (*s*, 1 H); 6.8–6.9 (*m*, 3 H); 7.1–7.6 (*m*, 5 H); 7.8 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50 MHz): 34.76 (CH_2); 55.28 (CH_3); 101.1 (CH); 110.6 (CH); 112.1 (CH); 114.7 (CH); 119.8 (CH); 120.1 (CH); 121.3 (CH); 121.4 (CH); 128.8 (C); 129.8 (CH); 136.3 (C); 137.7 (C); 140.2 (C); 160.0 (C). MS: 237 (100, $C_{16}H_{15}NO$), 236 (36), 130 (74). Anal. calc. for C 80.98, H 6.37, N 5.90; found: C 80.90, H 6.43, N 5.78.

1,2-Dihydro-1-[2-(3-methoxyphenyl)ethyl]cyclobutabenzen-1-ol (**11**). A soln. of **8** (7.6 g, 64 mmol) in dry Et_2O (50 ml) was added at 0° to a *Grignard* reagent prepared from 2-(3-methoxyphenyl)ethyl chloride (11 g, 64.5 mmol) in Et_2O (100 ml) and Mg turnings (1.55 g, 64.5 mmol). Hydrolysis (sat. NH_4Cl) and standard workup gave crude material (15 g) which was purified by FC (silica gel 40–63 μm, hexane/AcOEt 9:1) to give **11** (12.1 g, 74%) as a colourless oil. IR ($CDCl_3$): 3600*m*, 3460*m* (br.), 3080*w*, 2960*s*, 2735*s*, 1605*s*, 1590*s*, 1490*s*, 1469*s*, 1440*m*, 1380*s*, 1260*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.2 (*m*, 2 H); 2.4 (br. OH); 2.9 (*m*, 2 H); 3.25 (*AB*, J = 14); 3.8 (*s*, CH_3O); 6.7–6.9 (*m*, 3 arom. H); 7.1–7.4 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 31.47 (CH_2); 40.91 (CH_2); 46.87 (CH_2); 55.13 (CH_3); 80.52 (C); 111.27 (CH); 114.1 (CH); 120.9 (CH); 121.17 (CH); 124.0 (CH); 127.2 (CH); 129.4 (2 CH); 141.5 (C); 143.9 (C); 150.2 (C); 159.6 (C). MS: 254 (11, $C_{17}H_{18}O_2$), 236 (13), 141 (43), 135 (86), 121 (37), 119 (100), 105 (10), 91 (43), 77 (16), 65 (10).

1,2-Dihydro-1-[3-(3-methoxyphenyl)propyl]cyclobutabenzen-1-ol (**12**). Compound **12** was prepared by the same procedure as described above for **11**, with the *Grignard* reagent obtained from 3-(3-methoxyphenyl)propyl chloride, however. Yield 92%. **12**: colourless oil. IR ($CDCl_3$): 3600*m*, 3460 (br.), 3080*m*, 2950*s*, 2840*s*, 1605*s*, 1590*s*, 1490*s*, 1460*s*, 1440*m*, 1260*s*, 1155*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 1.8–2.0 (*m*, 4 H); 2.4 (br., OH); 2.6–2.7 (*m*, 2 H); 3.1–3.4 (*AB*, J = 14, CH_2–C(1)); 3.8 (*s*, CH_3O); 6.7–6.9 (*m*, 3 arom. H); 7.1–7.4 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 26.64 (CH_2); 36.13 (CH_2); 38.65 (CH_2); 46.83 (CH_2); 55.11 (CH_3); 80.72 (C); 110.0 (CH); 114.2 (CH); 120.9 (CH); 121.1 (CH); 124.0 (CH); 127.1 (CH); 129.2 (2 CH); 141.5 (C); 144.0 (C); 150.2 (C); 159.5 (C). MS: 268 (4, $C_{18}H_{20}O_2$), 250 (10), 219 (11), 134 (100), 129 (22), 119 (41), 91 (36), 77 (10), 65 (11).

1-Azido-1,2-dihydro-1-[2-(3-methoxyphenyl)ethyl]cyclobutabenzene (**13**). A soln. of HN_3 (58 ml, 0.25M) [7b] in dry benzene was added slowly at 5° under N_2 to a soln. of **11** (2.16 g, 8.52 mmol) in 45 ml of benzene. After dropwise addition of $BF_3 \cdot Et_2O$ (1.82 ml, 14.5 mmol), the mixture was kept at 5° for another 20 min and then made alcaline by addition of aq. NH_3 (2M). The product was extracted into Et_2O, washed with sat. brine, and dried ($MgSO_4$). Removal of Et_2O gave crude **13** as a rose-coloured liquid (2.3 g, 97%). This material was used without further purification. IR ($CDCl_3$): 3100*m*, 3040*s*, 2940*m*, 2100*s*, 1605*s*, 1590*s*, 1490*s*, 1480*s*, 1460*s*, 1260*s*, 1155*s*, 1040*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.30 (*m*, 2 H); 2.95 (*m*, 2 H); 3.45 (*AB*, J = 14, CH_2–C(1)); 3.8 (*s*, CH_3O); 6.6–6.9 (*m*, 3 arom. H); 7.2–7.5 (*m*, 5 arom. H). MS: 279 (< 1, $C_{17}H_{17}N_3O$), 251 (25, $M^+ - N_2$), 250 (42), 236 (15), 144 (14), 135 (57), 130 (100), 117 (49), 105 (33), 91 (37), 77 (35).

*2-[2-(3-Methoxyphenyl)ethyl-1*H*-indole* (**15**). H_2SO_4 (96%; 5 ml, 51 mmol) was added dropwise at −5° to a stirred soln. of **13** (2.5 g, 8.5 mmol) in $CHCl_3$ (50 ml). The mixture was kept at 0°, until gas ceased from evolving (*ca.* 40 min). Then, it was poured on a mixture of ice and 2M aq. NH_3. The crude product was extracted from the re-acidified mixture (pH 5) into $CHCl_3$, washed with sat. brine, and dried ($MgSO_4$). FC (silica gel 40–63 μm, hexane/AcOEt 3:1) gave colourless crystalline **15**, (1.91 g, 89.5%). IR ($CDCl_3$): 3480*s*, 3060*m*, 2950*w*, 1605*s*, 1590*s*, 1495*s*, 1460*s*, 1290*s*, 1260*s*, 1155*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 3.0–3.15 (*m*, 4 H); 3.8 (*s*, CH_3O); 6.35 (*s*, 1 H); 6.8–6.9 (*m*, 3 arom. H); 7.1–7.3 (*m*, 4 arom. H); 7.6 (br. *d*, J = 8, 1 arom. H); 7.8 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50 MHz): 29.94 (CH_2); 35.62 (CH_2); 55.13 (CH_3); 99.75 (CH); 110.3 (CH); 111.6 (CH); 114.1 (CH); 119.6 (CH); 119.8 (CH); 120.7 (CH); 121.1 (CH); 128.6 (C); 129.5 (CH); 135.7 (C); 139.0 (C); 142.8 (C); 159.7 (C). MS: 251 (23, $C_{17}H_{17}NO$), 237 (34), 218 (17), 204 (23), 143 (15), 130 (100), 77 (7).

*2-[3-(3-Methoxyphenyl)propyl]-1*H*-indole* (**16**), *1′,2′,3′,4′-Tetrahydro-6′-methoxyspiro[cyclobutabenzene-1,1′-naphthalene]* (**17**), *and 1′,2′,3′,4′-Tetrahydro-8′-methoxyspiro[cyclobutabenzene-1,1′-naphthalene]* (**18**). $BF_3 \cdot Et_2O$ (1.82 ml, 14.5 mmol) was added dropwise at 5° to a soln. of **12** (2.29 g, 8.54 mmol) in 1M HN_3 in benzene (14.5 ml, 14.5 mmol). The mixture was allowed to stir for 25 min at 5°. Then, it was poured on a mixture of ice and 2M aq. NH_3. The products were extracted from the re-acidified mixture (pH 5) into Et_2O, washed with sat. brine, dried ($MgSO_4$), and finally isolated by FC (silica gel 40–63 μm, hexane/AcOEt 5:1). They were eluted in the following order **18** (555 mg, 26%), **17** (726 mg, 34%), and **16** (635 mg, 28%).

Data for **16**: colourless oil. IR ($CDCl_3$): 3480*s*, 3060*w*, 2940*m*, 1600*s*, 1585*s*, 1490*m*, 1455*s*, 1285*s*, 1260*s*, 1150*s*, 1040*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.1 (*m*, 2 H); 2.7 (*m*, 2 H); 2.8 (*m*, 2 H); 3.8 (*s*, CH_3O); 6.3 (*s*, 1 H); 6.8–6.9 (*m*, 3 arom. H); 7.1–7.35 (*m*, 4 arom. H); 7.6 (br. *d*, J = 7, 1 arom. H); 7.9 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50 MHz): 27.63 (CH_2); 30.53 (CH_2); 33.32 (CH_2); 55.17 (CH_3); 99.71 (CH); 110.35 (CH); 111.18 (CH); 114.37 (CH); 119.62 (CH); 119.78 (CH); 120.95 (CH); 121.04 (CH); 128.83 (C); 129.4 (CH); 135.86 (C); 139.36 (C); 143.47 (C); 159.7 (C). MS: 265 (96, $C_{18}H_{19}NO$), 204 (5), 144 (9), 132 (13), 131 (100), 130 (83), 122 (9), 103 (10).

Data for **17**: colourless oil. IR ($CDCl_3$): 3080*w*, 2940*s*, 2840*m*, 1610*s*, 1500*s*, 1460*m*, 1280*m*, 1260*s*, 1245*s*, 1040*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 1.8–2.2 (*m*, 4 H); 1.9 (*m*, 2 H); 3.2 (apparent *s*, 2 H) (in (D_6)benzene this signal splitts into an *AB* pattern, J = 13); 3.8 (*s*, CH_3O); 6.6–6.9 (*m*, 3 arom. H); 7.0–7.3 (*m*, 4 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 21.51 (CH_2); 30.48 (CH_2); 35.76 (CH_2); 48.62 (CH_2); 50.89 (C); 55.17 (CH_3); 112.43 (CH); 113.16 (CH); 120.88 (CH); 123.69 (CH); 127.26 (CH); 127.40 (CH); 127.84 (CH); 133.52 (C); 137.92 (C); 143.10 (C); 153.65 (C); 157.84 (C). MS: 250 (3, $C_{18}H_{18}O$), 249 (4), 166 (30), 165 (54), 163 (41), 149 (27), 138 (21), 118 (100).

Data for **18**: colourless oil. IR ($CDCl_3$): 3070*w*, 2930*s*, 2840*w*, 1600*w*, 1580*m*, 1470*s*, 1460*s*, 1440*m*, 1260*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 1.8–2.2 (*m*, 4 H); 2.85–2.95 (*m*, 2 H); 3.05 (*AB*, J = 13, 1 H); 3.3 (*s*, CH_3O); 3.65 (*AB*, J = 13, 1 H); 6.6 (*d*, J = 8, 1 arom. H); 6.8 (*dd*, J = 8, 1, 1 arom. H); 6.95 (*m*, 1 arom. H); 7.1–7.4 (*m*, 4 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 21.56 (CH_2); 31.17 (CH_2); 39.05 (CH_2); 45.76 (CH_2); 49.11 (C); 55.49 (CH_3); 109.49 (CH); 119.30 (CH); 121.90 (CH); 122.74 (CH); 126.03 (CH); 126.22 (CH); 126.78 (CH); 128.73 (C); 139.68 (C); 143.35 (C); 155.98 (C); 159.43 (C). MS: 250 (10, $C_{18}H_{18}O$), 235 (11), 219 (100), 202 (12), 191 (52), 178 (25), 165 (12), 115 (17), 91 (16).

The acylation of **7**, **15**, and **16**, to give the indoles **19** (colourless oil, 72%), **20** (colourless crystalls, m.p. 122°, 78%), and **21** (colourless crystalls, m.p. 130°, 70%) was performed according to [13].

*1-[(Dimethylamino)methyl]-2-(3-methoxybenzyl)-1*H*-indol-3-yl Methyl Ketone* (**22**). A soln. of **19** (380 mg, 1.36 mmol) in 6 ml of CH_2Cl_2 was combined at r.t. under N_2 with *N,N*-dimethylmethylideneiminium chloride (543 mg, 5.45 mmol) and stirred for 1 h. 2,6-Dimethylpyridine (145 mg, 1.36 mmol) was added, and stirring was continued for 4 h. After treatment with 20 ml of H_2O, the product was extracted into AcOEt, washed with sat. brine, and dried ($MgSO_4$). Removal of the solvent gave **22** (420 mg, 92%) as a colourless liquid which was used without further purification. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.25 (*s*, 2 Me_2N); 2.70 (*s*, Ac); 3.75 (*s*, CH_3O); 4.50 (*s*, 2 H); 4.81 (*s*, NCH_2N); 6.7–9.1 (*m*, 8 arom. H). MS: 336 (2, $C_{21}H_{22}N_2O_2$), 291 (6), 279 (24), 264 (20), 220 (17), 204 (19), 58 (100).

1-[(Dimethylamino)methyl]-2-[2-(3-methoxyphenyl)ethyl]-1H-indol-3-yl Methyl Ketone (**23**) was prepared, in 88% yield, as described above for **22**. Compound **23**: colourless oil. IR ($CDCl_3$): 3060*w*, 2960*m*, 2880*w*, 2780*w*, 1650*s*, 1605*m*, 1590*m*, 1510*s*, 1490*m*, 1465*s*, 1440*s*, 1380*m*, 1270*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.2 (*s*, 2 Me_2N); 2.7 (*s*, Ac); 2.9–3.5 (*m*, CH_2CH_2); 3.7 (*s*, CH_3O); 4.45 (*s*, NCH_2N); 6.7–8.0 (*m*, 8 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 29.06 (CH_2); 31.85 (CH_3); 35.61 (CH_2); 42.72 (Me_2N); 55.13 (CH_3); 65.43 (CH_2); 110.6 (CH); 111.9 (CH); 113.9 (CH); 114.2 (C); 120.6 (CH); 121.0 (CH); 122.0 (CH); 122.2 (CH); 126.2 (C); 129.5 (CH); 136.8 (C); 143.25 (C); 149.3 (C); 159.7 (C); 194.5 (CO). MS: 350 (19, $C_{22}H_{26}N_2O_2$), 305 (17), 293 (31), 278 (12), 250 (13), 172 (100), 144 (14), 129 (13), 58 (22).

1-[(Dimethylamino)methyl]-2-[3-(3-methoxyphenyl)propyl]-1H-indol-3-yl Methyl Ketone (**24**) was prepared, in 90% yield, as described above for **22**. Compound **24**: colourless oil. IR ($CDCl_3$): 2950*s*, 2840*m*, 2780*m*, 1650*s*, 1605*m*, 1520*s*, 1470*s*, 1440*s*, 1430*s*, 1380*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.0 (*m*, 2 H); 2.2 (*s*, 6 H); 2.7 (*s*, 3 H); 2.8 (*t*, J = 7, 2 H); 3.2–3.3 (*m*, 2 H); 3.8 (*s*, CH_3O); 4.45 (*s*, NCH_2N); 6.7–8.0 (*m*, 8 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 25.55 (CH_2); 30.72 (CH_2); 31.75 (CH_3); 36.01 (CH_2); 42.63 (Me_2N); 55.17 (CH_3); 65.46 (CH_2); 110.6 (CH); 111.3 (CH); 114.3 (C); 114.4 (CH); 120.6 (CH); 121.1 (CH); 122.0 (CH); 122.1 (CH); 126.3 (C); 129.4 (CH); 136.8 (C); 143.5 (C); 149.8 (C); 159.7 (C); 194.6 (CO).

1-(Chloromethyl)-2-(3-methoxybenzyl)-1H-indol-3-yl Methyl Ketone (**25**). A soln. of **22** (383 mg, 1.14 mmol) and 2,6-dimethylpyridine (246 mg, 2.30 mmol) in dry THF (10 ml) was slowly combined at r.t. under N_2 with a soln. of AcCl (371 mg, 4.50 mmol) in the same solvent (2 ml). After 4 h, the mixture was diluted with Et_2O (50 ml), hydrolysed with 2N Na_2CO_3 soln., washed with brine, and dried ($MgSO_4$). Removal of the solvent left a colourless oil. **25**: yield 220 mg (67%). IR ($CDCl_3$): 2965*w*, 1655*s*, 1610*m*, 1600*m*, 1590*m*, 1530*s*, 1490*m*, 1465*s*, 1410*s*, 1285*s*, 1260*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.74 (*s*, $COCH_3$); 3.77 (*s*, OCH_3); 4.75 (*s*, 2 H); 5.83 (*s*, CH_2Cl); 6.7–6.8 (*m*, 3 arom. H); 7.2–7.5 (*m*, 4 arom. H); 8.06 (*m*, 1 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 31.04 (CH_2); 31.80 (CH_3); 51.55 (CH_2); 55.22 (CH_3); 109.9 (CH); 111.9 (CH); 114.1 (CH); 117.9 (C); 120.4 (CH); 121.5 (CH); 123.3 (CH); 123.6 (CH); 126.7 (C); 129.9 (CH); 135.6 (C); 138.5 (C); 144.2 (C); 160.1 (C); 194.9 (CO). MS: 329/327 (35/100, $C_{19}H_{18}NO_2Cl$), 292 (57), 276 (57), 248 (40), 206 (66), 121 (66). HR-MS: $C_{19}H_{18}{}^{37}ClNO_2$: calc.: 329.0996, found: 329.1010; $C_{19}H_{18}{}^{35}ClNO_2$: calc.: 327.1026, found: 327.1012.

1-(Chloromethyl)-2-[2-(3-methoxyphenyl)ethyl]-1H-indol-3-yl Methyl Ketone (**26**) was prepared, in 98% yield, as described above for **25**. Compound **26**: colourless solid. M.p. 104–105°. IR ($CDCl_3$): 2960*m*, 2940*m*, 1655*s*, 1605*m*, 1520*s*, 1465*s*, 1440*m*, 1410*m*, 1160*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.7 (*s*, Ac); 3.05 (*t*, J = 7, 2 H); 3.50 (*t*, J = 7, 2 H); 3.70 (*s*, CH_3O); 5.6 (*s*, CH_2Cl); 6.7–8.0 (*m*, 8 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 28.20 (CH_2); 31.85 (CH_3); 35.47 (CH_2); 50.92 (CH_2); 55.13 (CH_3); 110.1 (CH); 112.1 (CH); 114.0 (CH); 116.3 (C); 120.9 (CH); 121.0 (CH); 123.2 (CH); 123.3 (CH); 126.6 (C); 129.7 (CH); 135.3 (C); 142.4 (C); 147.1 (C); 159.8 (C); 194.7 (CO). MS: 343/341 (2/7, $C_{20}H_{20}ClNO_2$), 305 (12), 290 (13), 262 (20), 220 (36), 202 (17), 184 (49), 172 (86), 144 (20), 129 (23), 121 (32), 97 (38), 83 (45), 69 (76), 55 (100).

9-Methoxy-11,12-dihydro-1H-indolo[1,2-a][2]benzazepin-13-yl Methyl Ketone (**27**) *and 7-Methoxy-11,12-dihydro-1H-indolo[1,2-a][2]benzazepin-13-yl Methyl Ketone* (**28**). A soln. of **23** (402 mg, 1.15 mmol) and 2,6-dimethylpyridine (246 mg, 2.30 mmol) in dry THF (10 ml) was slowly combined at r.t. under N_2 with a soln. of AcCl (371 mg, 4.50 mmol) in THF (2 ml). After 2 h, a soln. of $SnCl_4$ in CH_2Cl_2 (1.1M, 7.5 ml) was added dropwise with stirring. After another 4 h, the mixture was hydrolysed with 2N Na_2CO_3 soln., extracted with CH_2Cl_2, washed with brine, and dried ($MgSO_4$). Medium-pressure chromatography (silica gel, 40–63 μm, hexane/AcOEt 2:1) gave **27** (190 mg, 54%) and **28** (67 mg, 19%). Compound **28** was eluted first.

Data for **27**: colourless crystals. M.p. 144–146°. IR ($CDCl_3$): 3010*w*, 2940*w*, 1640*s*, 1505*s*, 1465*s*, 1450*m*, 1430*m*, 1350*m*, 1260*m*, 1220*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.70 (*s*, Ac); 3.25 (*m*, 2 H); 3.70 (*m*, 2 H); 3.76 (*s*, CH_3O); 5.30 (*s*, NCH_2); 6.58 (*dd*, J = 8, 2.9, 1 arom. H); 6.75 (*d*, J = 2.9, 1 arom. H); 7.2–8.0 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 26.68 (CH_2); 30.76 (CH_2); 31.80 (CH_3); 46.61 (CH_2); 55.29 (CH_3); 109.3 (CH); 111.4 (CH); 113.7 (C); 115.4 (CH); 120.7 (CH); 121.8 (CH); 121.9 (CH); 126.1 (C); 126.2 (C); 130.0 (CH); 135.8 (C); 141.6 (C); 147.8 (C); 159.7 (C); 194.6 (CO). HR-MS: 305.14186 ($C_{20}H_{19}NO_2$, calc. 305.14216).

Data for **28**: colourless oil. IR ($CDCl_3$): 2990*w*, 2910*w*, 1640*s*, 1465*s*, 1430*m*, 1265*s*, 1220*m*, 1095*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.65 (*s*, Ac); 3.30 (*m*, 2 H); 3.75 (*m*, 2 H); 3.90 (*s*, CH_3O); 5.60 (*s*, NCH_2); 6.75 (*d*, J = 8, 1 arom. H); 6.85 (*d*, J = 7, 1 arom. H); 7.1–8.0 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 27.48 (CH_2); 30.28 (CH_2); 31.81 (CH_3); 37.85 (CH_2); 55.92 (CH_3); 108.7 (CH); 109.8 (CH); 113.8 (C); 120.5 (CH); 121.7 (CH); 121.8 (CH); 121.9 (CH); 123.1 (C); 125.9 (C); 129.1 (CH); 136.3 (C); 142.2 (C); 148.1 (C); 156.1 (C); 194.5 (CO). MS: 305 (23, $C_{20}H_{19}NO_2$), 290 (29), 262 (12), 247 (10), 217 (13), 191 (19), 172 (32), 149 (34), 128 (19), 115 (19), 71 (34), 57 (100).

3-Methoxy-5,6,7,14-tetrahydroindolo[1,2-a][2]benzazocin-8-yl Methyl Ketone (**29**) was prepared, in 58% yield, from **24** as described above for **27** and **28**. Compound **29**: yellowish crystals. M.p. 175–176°. IR ($CDCl_3$):

2940*w*, 1640*s*, 1610*m*, 1515*s*, 1465*m*, 1445*m*, 1430*s*, 1270*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz, −50°; strong dynamic line broadening occurs at r.t.): 1.54 (*m*, 1 H); 2.49 (*m*, 1 H); 2.68 (*s*, Ac); 2.81 (*m*, 1 H); 3.01 (*m*, 1 H); 3.18 (*m*, 1 H); 3.70 (*s*, CH_3O); 4.52 (*m*; 1 H); 5.24 (narrow *AB*, $J = 15$, NCH_2); 6.60 (*dd*, $J = 8.5, 2.8$, 1 H); 6.65 (*d*, $J = 2.8$, 1 H); 7.2–7.9 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 50 MHz, r.t.): 27.08 (CH_2); 28.82 (CH_2); 31.84 (CH_3); 37.51 (CH_2); 44.85 (CH_2); 55.16 (CH_3); 110.2 (CH); 111.4 (CH); 114.0 (C); 116.7 (CH); 121.1 (CH); 121.8 (CH); 122.0 (CH); 126.8 (C); 128.4 (C); 131.0 (CH); 135.2 (C); 142.8 (C); 148.7 (C); 159.6 (C); 194.8 (CO). MS: 319 (91, $C_{21}H_{21}NO_2$), 304 (61), 276 (48), 184 (45), 159 (51), 147 (90), 134 (100), 115 (60), 103 (31), 91 (87), 77 (34).

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