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Angularly Substituted Octahydroindoles, Decahydroquinolines, Octahydropyrindines, and Octahydrocyclopenta[b]pyrroles by *Bruylants* Reaction

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Summary. The easily available cycloalkanoyl acetic- and propionic acid esters are transformed to the corresponding amines by standard procedures. These in turn provided an efficient access to cyclic α-aminonitriles, which were reacted with a series of *Grignard* reagents yielding stereoselectively the *cis*-configured title compounds; the scope and limitation of this route were investigated. The stereochemical assignment was achieved by X-ray crystallography and NMR spectroscopy.

Keywords. Intramolecular *Strecker* reaction; X-Ray structure determination; Angularly substituted *N*-heterocycles.

Introduction

The phenyl cyclohexyl-amine-fragment forms part of several remarkable substances possessing highly potent activity on central nervous system. Perhaps the best known example is phencyclidine (*PCP*), which has been developed in the 1950s as an intravenous anaesthetic but, due to the serious side effects, its use was stopped, but until today it is abused as a dangerous psychotomimetikum [1, 2] (Fig. 1, **I**).

The search for *PCP* replacements soon after led to the structural analogue ketamine **II** which proved to be a strong analgesic and, because of its rapid anaesthetic onset after injection, it has found increased use in the induction of anesthesia and in the emergency surgery. But hallucinatory side effects particularly occurring in the post-narcotic stage have been also reported [3, 4]. Furthermore, a series of

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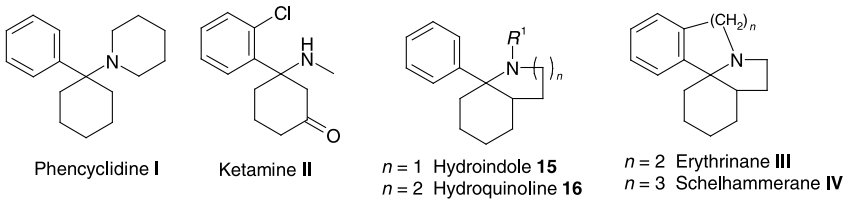


Fig. 1. Compounds with an integrated phenylcyclohexylamine framework

more complex structures obviously connected to the search for *PCP* analogues contain a rigid aryl cyclohexylamine framework, *e.g*. the angularly arylated hydroindoles and -quinolines **15** and **16** (Fig. 1, $R^1 = H$), which are claimed to exhibit also CNS depressant properties similar to those attributed to *PCP*. Unfortunately, detailed pharmacological data are not available hitherto [5].

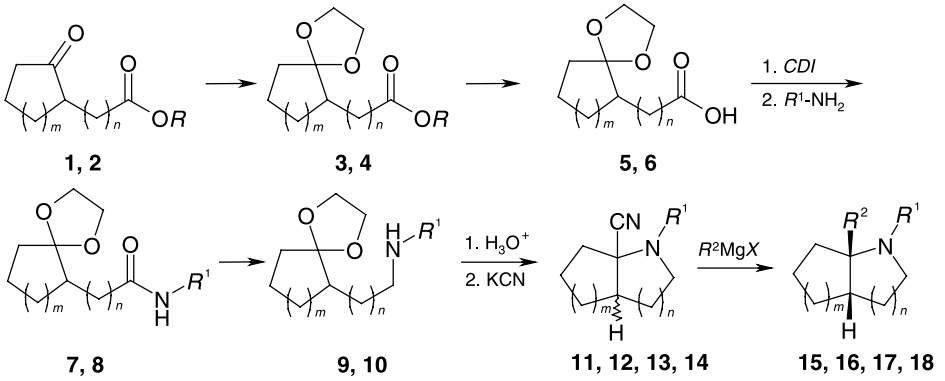
The title compounds attracted our interest not only because of their biological activities mentioned; they also suggest to be appropriate precursors for the construction of the frameworks of the erythrina and schelhammerane alkaloids (Fig. 1, **III**, **IV**) since they differ from title compound **15** only by the C_2- or C_3-bridge connecting the nitrogen- and the carbon atom C-12 of the aryl moiety. Thus in connection with our investigations relating to the intramolecular alkylation of aromatic compounds, we wish to report in this paper a general stereoselective approach to the title compounds **15**–**18** as well as to check its scope and limitations.

Results and Discussion

The first synthesis of the compounds like **15** and **16** (Fig. 1, $R^1 = H$) – being the only one to our knowledge – was based on partially hydrogenated indoles and quinolines, each involving an intact bridgehead imino moiety. The angular substituents were introduced by addition of aryllithium compounds or in a two step route by formation of the α-aminocarbonitriles followed by replacement of the nitrile group by the corresponding *Grignard* reagents known as *Bruylants* reaction [6]. Unfortunately, the total yields of the compounds reported were unsatisfactory or given not at all. Furthermore, no information concerning the stereochemistry of the bicyclic frameworks had been reported [5]. This gave rise to a more detailed investigation in this field described in the present work.

Following the *Bruylants* strategy mentioned above, at first we focused our interest on the preparation of the bicyclic α-aminonitriles **11**–**14**, which could be prepared in excellent yields by intramolecular *Strecker* reaction using the O-protected aminoketones **9** and **10** to afford the perhydrogenated indole-, quinoline-, pyrindine-, and cyclopenta[b]pyrrole-carbonitriles **11**, **12a**, **13**, and **14**. Compound **12b** was prepared starting from nitrile **19b** *via* the amine **9g**, whereas **9f** failed to give the corresponding aminonitrile (Scheme 3, A). The educts **9** and **10** in turn were easily available starting from the known cycloalkanone acid esters **1** and **2** [7–9] and further transformation by standard procedures *via* **3** → **8** (see Schemes 1 and 2).

Concerning the stereochemistry, **12a**, **12b**, and **14** only showed a single set of lines in the NMR spectra indicating a stereoselective formation of the possible



	m	*n*	*R*
1a, 3a, 5a	2	1	*Et*
1b, 3b, 5b	2	2	*Me*
2a, 4a, 6a	1	2	*Me*
2b, 4b, 6b	1	1	*Me*

	m	*n*	R^1	*trans**	*cis**
11a	2	1	*Bn*	47.30	42.42
11b	2	1	*Me*	48.39	43.23
11c	2	1	*PhEt*	49.64/ 48.85	45.09/ 44.46
11d	2	1	*i-Pr*	49.27	44.23
12a	2	2	*Bn*	44.94	-
12b	2	2	H	44.35	-
13	1	2	*Bn*	48.84	45.64
14	1	1	*Bn*	-	50.94

* ^{13}C δ-values of C-3a or C-4a/ppm

	m	*n*	R^1
7a, 9a	2	1	*Bn*
7b, 9b	2	1	*Me*
7c, 9c	2	1	*PhEt*
7d, 9d	2	1	*i-Pr*
7e, 9e	2	2	*Bn*
9f	2	1	H
9g	2	2	H
8a, 10a	1	2	*Bn*
8b, 10b	1	1	*Bn*

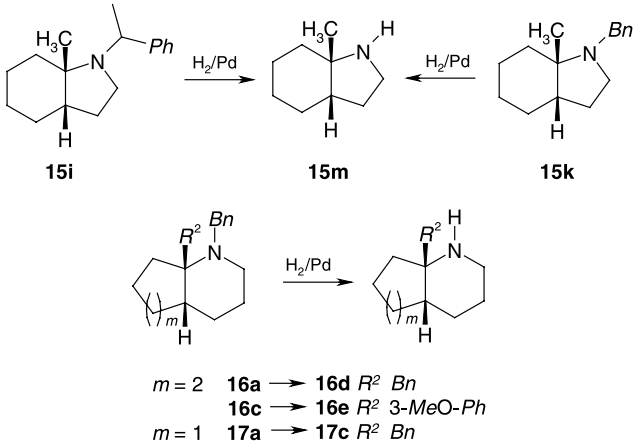
	m	*n*	R^1	R^2	yield/%	^{13}C δ/ppm
15a	2	1	*Bn*	C_6H_5	25	46.67
15b	2	1	*Bn*	3-*Me*OC_6H_4	17	46.69
15c	2	1	*Bn*	4-*Me*OC_6H_4	17	46.41
15d	2	1	*Bn*	3,4-(*Me*O)$_2C_6H_3$	12	46.57
15e	2	1	*Bn*	3,4-(OCH_2O)C_6H_3	14	46.61
15f	2	1	*Me*	C_6H_5	34	45.58
15g	2	1	*PhEt*	*Bn*	63	39.2/38.8
15h	2	1	*i-Pr*	*Bn*	72	38.42
15i	2	1	*PhEt*	*Me*	38	45.1/44.5
15k	2	1	*Bn*	*Me*	80	44.18
15l	2	1	*Bn*	*Bn*	83	38.48
16a	2	2	*Bn*	*Bn*	76*	36.35**
16b	2	2	*Bn*	C_6H_5	17	42.19
16c	2	2	*Bn*	3-*Me*OC_6H_4	11	42.22
17a	1	2	*Bn*	Bn	78	39.23
17b	1	2	*Bn*	3-*Me*OC_6H_4	0.2	47.16
18	1	1	*Bn*	3-*Me*OC_6H_4	78	51.91

* +6% *trans*-product; ***trans*: 46.32 ppm

Bn = benzyl; *PhEt* = 1-phenylethyl

Scheme 1

cis- or *trans*-fused heterocycles, whereas the produtcs **11a**–**11d** and **13** were found to be diastereomeric mixtures unseparable by TLC. Due to an additional chirality center located at the N-substituent compound **11c** exhibited four sets of signals in the ^{13}C NMR spectrum. The ratios of the diastereomers were determined using the integrals of the ^{1}H NMR absorptions originating from the corresponding *N*-methyl- or benzyl groups.

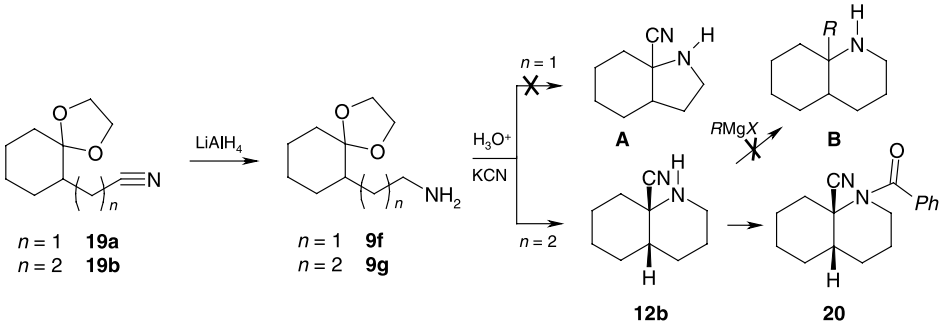


Scheme 2

The configuration of compounds **12a** and **12b** as well as **14** could be assigned comparing appropriate NMR data, namely the $^{13}C\delta$-values of the tertiary bridgehead atom, with those of known closely related compounds. Thus, the carbon atoms concerned resonates in *trans*-decaline-4a-carbonitrile [10] or in a more complex structure containing the *trans* configured unit of **12** [11] at $\delta = 44.8$ and 44.5 ppm. These results matched very well with those observed for **12a** and **12b** ($\delta = 44.94$ and 44.35 ppm, Scheme 1) indicating the *trans*-configuration of the products.

Angularly substituted carbonitriles of type **14** obviously have not yet been reported until now. NMR Data published concerning the stereochemistry exclusively refer to *cis*-configured bicyclo[3.3.0]octanes, corresponding values for *trans*-fused compounds are lacking [12]. Therefore the assignment of **14** was based on the downfield shift of about 6–8 ppm induced by angular substituents, *e.g.* methyl or carboxyl, on the neighbouring bridgehead carbon atom of the *cis*-fused parent bicyclooctane ($\delta_{C\text{-ang}} = 43.2$ ppm *vs.* $\delta_{C\text{-6a}} = 50.9$ or 49.8 ppm) [12]. In addition, the C-3a atom of a more complex structure containing the *cis*-fused cyclopentapyrrole framework resonates at $\delta = 50.4$ ppm [13]. The value $\delta_{C\text{-3a}} = 50.94$ ppm found for **14** is in line with the reported ones proving the *cis*-fused framework of the product.

In the same manner the configurations of compounds **11** and **13** could be assigned, since both stereomers were available. In the perhydroindoles **11** the inversion from the *trans*- to the *cis*-fused ring system caused an upfield shift of about 5 ppm at carbon atom C-3a comparable with those observed at C-4a in *N*-methyldecahydroquinolines [14–17]. On the other hand the corresponding bridgehead carbon atom C-4a of the pyrindine derivative **13** exhibited a somewhat smaller difference ($\Delta\delta = 3.2$ ppm, Scheme 1). In this connection it should be noted, that the oily product **13** solidified after some time. The NMR spectrum of the crystals measured immediately after their dissolution indicated only the *trans*-stereomer, after about 3 hours a 1:1-mixture of both stereomers could be observed, and after several further hours, a stable 2:1-equilibrium was reached revealing the *cis*-configured compound as the main stereomer. Compounds **11** gave the same *cis*/*trans* ratios.



Scheme 3

In the final step the nitriles **11**–**14** were reacted with a number of *Grignard* reagents according to *Bruylants* giving the new title compounds **15**–**18** (Scheme 1). Using aryl *Grignard* reagents the yields of the products **15a**–**15f** and **16b** and **16c** were low (11–34%) with the exception of **18** and **17b**, which were formed with 78% or only in traces (0.2%). Reacting the secondary base **12b** with *Grignard* reagents no products were observed (Scheme 3, B). Changing the experimental procedure, *e.g.* inverse order of addition of the reagents, variation of the temperature and the reaction time as well as the halogen of the *Grignard* reagent did not improve the result. Byproducts, *e.g.* enamines and their hydrolysis products which were reported to be formed during the *Bruylants* reaction [18], or arylketones formed by addition to the nitrile function were not observed. The ketone **21**, however, could be obtained when the educt **11a** was reacted with phenyl lithium (Scheme 4).

The low yields obtained suggested, that the reaction rate depended on the steric bulk of both the *Grignard* reagent and the *N*-substituent of the educts. Indeed support of this assumption was best seen by reacting phenyl magnesium bromide with *N*-benzylated and *N*-methylated educts **11a** and **11b** yielding 25 and 34% of **15a** and **15f**, whereas bulky N-substituents, *e.g.* 1-phenylethyl or isopropyl in the educts **11c** and **11d**, were found to inhibit the desired conversion completely. In contrast, replacement of aryl *Grignard* reagents by those possessing a smaller steric demand at the reaction center provided high yields of the products. Thus, reacting the educts **11a** and **11b** with benzyl- and methyl *Grignard* reagents, **15k**, **15l**, **16a**, and **17a** were obtained in 76–83% yields. Even the same was true for the educts **11c** and **11d** giving also moderate to satisfactory yields of products **15g**, **15h**, and **15i** (Scheme 1).

NMR Spectroscopy of the target compounds **15**–**18** indicated them all to be single diastereomers independent of the stereochemical property and purity of the educts **11**–**14** signifying that the *Bruylants* reaction had diastereoselectively occured. Since an unequivocal stereochemical assignment of the octahydroindoles **15** failed by NMR, an X-ray diffraction analysis of compound **15a** was performed showing a *cis*-fused hydroindole framework and the aryl group axially attached to the carbocyclus (Fig. 2). The true configuration of **15a** now also enabled the stereochemical assignment of the analogous compounds **15b**–**15f** including the N-regioisomer pyrindine **17b**, using the same reasoning described above for the

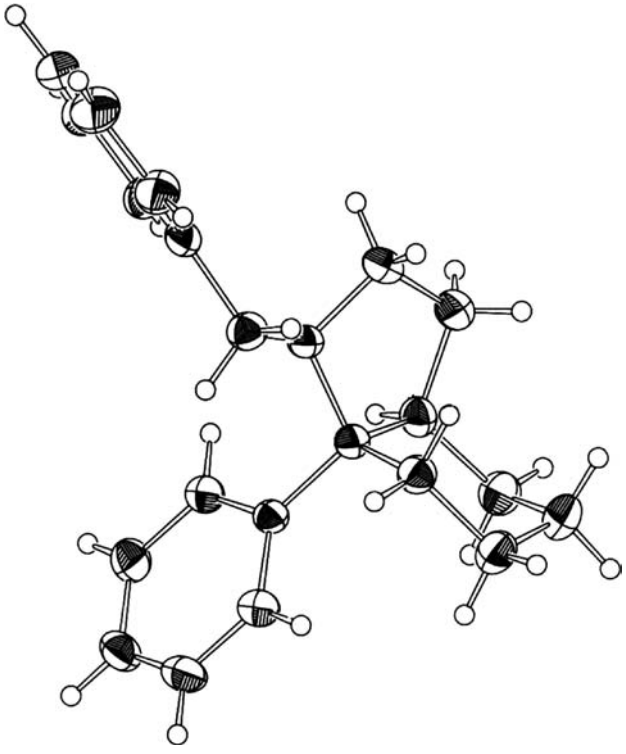
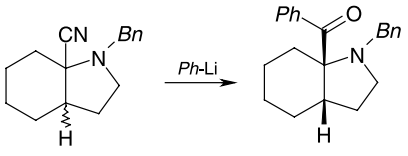


Fig. 2. Crystal structure of **15a**

educts **11**–**14**. Thus, the $^{13}C\delta$ values of the bridgehead carbon atom C-3a of the products **15b**–**15f** as well as of C-4a of **17b** were found to be in good accordance with that available from **15a** ($\delta = 45.58$–47.16 *vs.* 46.67 ppm, Scheme 1 and Exp.) indicating also the *cis*-configuration of the compounds concerned.

The *cis*-configuration of the angular methyl derivatives **15i** and **15k** was proved by comparison with a known compound. Their hydrogenolysis afforded the same deprotected amine **15m** (Scheme 4), exhibiting $^{1}H\delta$-values, which were completely in line with those of the identical *cis*-configured product reported in Ref. [21]. In addition, the $^{13}C\delta$ values of the bridgehead carbon atom C-3a of **15i**, **15k**, and **15m** now were available resonating between $\delta = 44.18$ and 45.06 ppm (Scheme 1 and Exp.).

In a similar manner the configurations of the quinoline derivatives **16b** and **16c** were established by way of debenzylated product **16e** (Scheme 2). The NMR data



11a **21**

Scheme 4

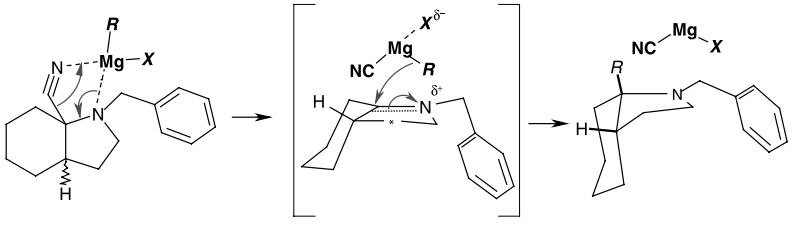
found, namely the δ-value of the carbon atom C-4a were in line with those reported for the known *cis*-8a-phenyldecahydroquinoline [19] ($\delta_{\text{C-4a}} = 35.90$ *vs.* 35.70 ppm). In contrast, the corresponding absorptions of the *N*-benzylated compounds **16b** and **16c** were found at lower field ($\delta_{\text{C-4a}} = 42.19$ and 42.22 ppm, Scheme 1).

The *cis*-configuration of the angularly substituted benzyl-indoles **15g**, **15i**, and **15l**, as well as **16a**, and **17a** was assigned by a significant *NOE* between the bridgehead methin proton and one of the protons of the angular benzyl group attached either to the methylene group or to the ortho position of the aryl moiety. In the case of **16a** and **17a** the hydrochlorides of the *N*-deprotected compounds **16d** and **17c** were prepared providing more distinct results than the educts (Scheme 2). In addition it should be noted that a small amount of the *trans*-configured stereomer **16b** could be separated (Exp.). For comparison purposes the corresponding $^{13}C\delta$ values of the bridgehead methin carbon atom now available are also presented in Scheme 1.

The assignment of the stereochemistry of the cyclopentanopyrrole **18** by *NOE* failed because of unseparable superimpositions of the peaks of the methin proton. But due to the similar absorption of C-3a in **14** as well as to that of the reference compound mentioned above [11] the *cis*-configuration could be assumed.

The highly stereoselective course of the syntheses of the target compounds may be explained on the basis of the reported mechanism of the *Bruylants* reaction [20]. In the first step the *Grignard* reagent coordinates with the nitrogen atoms of the α-aminonitrile as shown in Scheme 5 (**V**) followed by the formation of an intermediate iminium salt with a preferred puckered ringfusion. The subsequent nucleophilic attack of the *Grignard* reagent is favored from the *re*-face of the carbon-nitrogen double bond (**VI** $\rightarrow$ **VII**). Finally it should be noted that the presence of the cyanide group in the intermediate seems to play an important role concerning the stereoselective course of the reaction, since the preparation of **15k** gave a stereomeric mixture when the corresponding pure *N*-benzylhexahydroindolium bromide was used as educt [21].

In conclusion, we have established a general, stereoselective route to the title compounds. The dominant features consist of the initial intramolecular *Strecker* reaction followed by the *Bruylants* reaction. We are currently investigating this pathway in further detail and applying the procedure to natural product and drug synthesis.



V **VI** **VII**

Scheme 5

Experimental

Melting points are measured with a Reichert hot-stage microscope and are uncorrected. IR: Perkin Elmer FT-IR Paragon 1000 and Jasco FT-IR 410. NMR: Jeol GSX 400 and Jeol GSX 500 (^{1}H: 400 and 500 MHz, ^{13}C: 100 and 125 MHz, $CDCl_3$, *TMS* as internal reference), $t = 25°C$ (unless otherwise stated); MS (70 eV): Hewlett Packard MS-Engine. Elemental analyses: Heraeus CHN-Rapid and Elementar Vario EL; the results are in good agreement with the calculated values. Thin layer chromatography (TLC): aluminum sheets Kieselgel 60 F_{254} (Merck) and aluminum sheets Aluminiumoxid F_{254} (Fluka), each thickness of layer 0.2 mm. Flash chromatography (FC): ICN-Sili Tech 32–63, 60 A and Aluminiumoxid Typ 507 C neutral 0.05–0.15 mm. (Oxocycloalkyl)alkanoic acid ethyl esters **1** and **2** were prepared according to literature: **1a**/Ref. [7], **2b**/Ref. [8], **1b** and **2a**/Ref. [9].

*Improved General Procedure for the Synthesis of Dioxolanes **3** and **4** According to Ref. [22]*

A solution of the corresponding cycloalkanone **1** or **2**, ethane-1,2-diol, and pyridinium tosylate (*PPTS*) in 300 cm^3 of benzene was refluxed with water separation by a *Dean-Stark* trap until the reaction was completed (about 5 h; IR monitoring). After evaporating the solvent *in vacuo* the residue was dissolved in 150 cm^3 of Et_2O and the solution was consecutively washed with 4×100 cm^3 of H_2O, 100 cm^3 of saturated $NaHCO_3$ solution, 100 cm^3 of brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure to give sufficiently pure products for the next step.

(1,4-Dioxaspiro[4.5]dec-6-yl)acetic acid ethyl ester (**3a**)

1a 54.5 g (296 mmol), ethane-1,2-diol 91.8 g (1.48 mol), *PPTS* 22.3 g (89.2 mmol); yield 66.8 g (99%) colourless oil, bp 96°C/19 Pa (Ref. [23] 106–109°C/66 Pa); TLC (CH_2Cl_2): $R_f = 0.40$; IR (film): $\bar{\nu} = 1736$ (CO_2R) cm^{-1}; MS (CI): m/z (%) = 229 ($M^{+\bullet}$+1, 10), 183 ($M^{+\bullet}$–C_2H_5O, 100), 155 (14), 99 (5); ^{1}H NMR: $\delta = 4.05$ (dq, $J = 7.1$, 1.8 Hz, CO_2CH_2), 3.90–3.81 (m, OCH_2CH_2O), 2.47 (dd, $J = 14.9$, 5.6 Hz, 1H, CH_2CO_2), 2.19–2.10 (m, CH), 1.99 (dd, $J = 14.9$, 7.9 Hz, 1H, CH_2CO_2), 1.74–1.68 and 1.61–1.52 (2m, each 2H), 1.47–1.35 (m, 1H), 1.35–1.21 (m, 3H), 1.18 (t, $J = 7.1$ Hz, CH_3) ppm.

3-(1,4-Dioxaspiro[4.5]dec-6-yl)propionic acid methyl ester (**3b**)

1b 50.0 g (272 mmol), ethane-1,2-diol 84.2 g (1.36 mol), *PPTS* 20.4 g (81.6 mmol); yield 60.1 g (97%) colourless oil, bp 101–108°C/57 Pa (Ref. [24] 110–130°C/66 Pa); IR (film): $\bar{\nu} = 1739$ (CO_2R) cm^{-1}; MS (EI): m/z (%) = 228 ($M^{+\bullet}$, 10), 183 (32), 155 (9), 113 (25), 99 (100), 55 (28); ^{1}H NMR data are in line with those published in Ref. [25]; ^{13}C NMR: $\delta = 174.23$, 110.35, 64.51, 64.35, 51.20, 43.80, 34.37, 33.98, 28.29, 24.29, 23.63, 23.52 ppm.

3-(1,4-Dioxaspiro[4.4]non-6-yl)propionic acid methyl ester (**4a**)

2a 52.0 g (306 mmol), ethane-1,2-diol 94.8 g (1.53 mol), *PPTS* 25.5 g (102 mmol); yield 64.83 (99%) colourless oil; TLC (CH_2Cl_2): $R_f = 0.40$; IR (film): $\bar{\nu} = 1738$ (CO_2R) cm^{-1}; MS (EI): m/z (%) = 214 ($M^{+\bullet}$, 15), 183 (10), 141 (17), 125 (11), 99 (100); ^{1}H NMR data are in line with those published in Ref. [26]; ^{13}C NMR: $\delta = 174.24$, 117.95, 64.58, 64.42, 51.46, 45.45, 35.71, 32.82, 29.31, 24.38, 20.63 ppm.

(1,4-Dioxaspiro[4.4]non-6-yl)acetic acid methyl ester (**4b**)

2b 43.5 g (278 mmol), ethane-1,2-diol 86.4 g (1.39 mol), *PPTS* 20.9 g (83.6 mmol); yield 66.8 g (99%) colourless oil, bp 68°C/5.7 Pa; TLC (CH_2Cl_2:*Me*OH = 10:1): $R_f = 0.62$; IR (film): $\bar{\nu} = 1737$

(CO_2R) cm^{-1}; MS (CI): m/z (%) = 169 ($M^{+\bullet}-CH_3O$, 100), 125 (59), 99 (20); ^1H NMR: $\delta = 3.94–3.83$ (m, OCH_2CH_2O), 3.66 (s, OCH_3), 2.48 (dd, $J = 14.8$, 5.9 Hz, 1H, CH_2CO_2), 2.47–2.37 (m, CH), 2.23 (dd, $J = 14.8$, 8.1 Hz, 1H, CH_2CO_2), 2.00 (ddt, $J = 12.6$, 7.8, 4.5 Hz, 1H), 1.80–1.74 (m, 2H), 1.74–1.61 (m, 2H), 1.45–1.35 (m, 1H) ppm; ^{13}C NMR: $\delta = 173.71$, 117.68, 64.67 (2C), 51.44, 42.60, 35.12, 34.32, 29.44, 20.51 ppm.

General Procedure for the Synthesis of (Dioxaspiroalkyl)alkanoic acids ***5*** *and* ***6*** *According to Ref. [27]*

The mixture of the corresponding ester **3** or **4**, KOH/H_2O, and *Et*OH was refluxed for 2 h. After addition of 6 *N* H_2SO_4 with ice-cooling the solution was saturated with NaCl and extracted with $3\times100\,cm^3$ of Et_2O. The combined organic extracts were washed with 100 cm^3 of brine and dried (Na_2SO_4). After removing the solvent *in vacuo*, the remaining colourless or light yellow oils were used for the next step without further purification.

(1,4-Dioxaspiro[4.5]dec-6-yl)acetic acid (**5a**)

3a 58.8 g (257 mmol), KOH 23.2 g (407 mmol)/H_2O 60 cm^3, *Et*OH 60 cm^3, 6 *N* H_2SO_4 54.8 cm^3; yield 49.86 g (97%), bp 128–131°C/7.8 Pa (Ref. [27] 123°C/2.7 Pa), the product crystallized when it was stored in the refrigerator, mp 54°C (Ref. [23] 54–56°C); IR (film): $\bar{\nu} = 3650–2360$ (OH), 1704 (C=O) cm^{-1}; MS (CI): m/z (%) = 201 ($M^{+\bullet}+1$, 100), 183 (29), 139 (23); ^1H NMR: $\delta = 9.81$ (broad s, CO_2H), 3.92–3.83 (m, OCH_2CH_2O), 2.53 and 2.05 (2dd, $J = 15.2$, 5.8 and 15.2, 7.4 Hz, each 1H, CH_2CO_2), 2.19–2.11 (m, CH), 1.76–1.70 and 1.62–1.55 (2m, each 2H), 1.47–1.18 (m, 4H) ppm; ^{13}C NMR: $\delta = 179.57$, 109.84, 64.68, 64.49, 41.53, 34.36, 34.25, 30.07, 24.60, 23.64 ppm.

3-(1,4-Dioxaspiro[4.5]dec-6-yl)propionic acid (**5b**)

3b 42.1 g (184 mmol), KOH 16.6 g (296 mmol)/H_2O 70 cm^3, *Et*OH 70 cm^3, 6 *N* H_2SO_4 39.2 cm^3; yield 37.43 g (97%); IR (film): $\bar{\nu} = 3650–2355$ (OH), 1710 (C=O) cm^{-1}; MS (CI): m/z (%) = 215 ($M^{+\bullet}+1$, 100), 197 (51), 153 (58); ^1H NMR data were in line with those published in Ref. [24].

3-(1,4-Dioxaspiro[4.4]non-6-yl)propionic acid (**6a**, $C_{10}H_{16}O_4$)

4a 39.0 g (182 mmol), KOH 16.6 g (296 mmol)/H_2O 70 cm^3, *Et*OH 70 cm^3, 6 *N* H_2SO_4 38.8 cm^3; yield 33.12 g (91%, purification of the crude product failed); TLC (CH_2Cl_2:*Me*OH = 10:0.2): $R_f = 0.42$; IR (film): $\bar{\nu} = 3650–2250$ (OH), 1710 (C=O) cm^{-1}; MS (CI): m/z (%) = 201 ($M^{+\bullet}+1$, 96), 183 (90), 139 (100); ^1H NMR: $\delta = 10.41$ (broad s, CO_2H), 4.98–3.83 (m, OCH_2CH_2O), 2.42–2.32 (m, 2H), 1.80–1.52 (m, 8H), 1.40–1.29 (m, 1H) ppm; ^{13}C NMR: $\delta = 179.91$, 117.97, 64.53, 64.40, 45.25, 35.69, 32.70, 29.29, 24.04, 20.61 ppm.

(1,4-Dioxaspiro[4.4]non-6-yl)acetic acid (**6b**, $C_9H_{14}O_4$)

4b 18.21 g (91.1 mmol), KOH 8.21 g (144 mmol)/H_2O 45 cm^3, *Et*OH 45 cm^3, 6 *N* H_2SO_4 19.4 cm^3; yield 15.17 g (90%, purification of the crude product failed); IR (film): $\bar{\nu} = 3650–2360$ (OH), 1708 (C=O) cm^{-1}; MS (CI): m/z (%) = 188 ($M^{+\bullet}+1$, 2), 183 (67), 139 (100); ^1H NMR: $\delta = 3.97–3.85$ (m, OCH_2CH_2O), 2.53 and 2.28 (2dd, $J = 15.5$, 5.8 and 15.5, 8.2 Hz, each 1H, CH_2CO_2), 2.48–2.35 (m, CH), 2.09–1.97 (m, 1H), 1.82–1.73 and 1.73–1.61 (2m, each 2H), 1.47–1.37 (m, 1H) ppm.

General Procedure for the Synthesis of Amides ***7*** *and* ***8***

A mixture of the acid **5** or **6** and *N,N′*-carbonyldiimidazole (*CDI*) in anhydrous *THF* was stirred until generation of CO_2 was completed (ca. 30 min). Then the amine was added and the solution was refluxed for 8 h. After evaporating the solvent *in vacuo* the residue was dissolved in 200 cm^3 of CH_2Cl_2 and the solution was consecutively washed with 3×100 cm^3 of H_2O, 100 cm^3 of 1 *N* HCl and 2×250 cm^3 of saturated Na_2CO_3 solution. After drying with Na_2SO_4 and removing the solvent *in vacuo* the residue was crystallized from Et_2O and finally washed with a small volume of ice-cold Et_2O. If the product did not crystallize or further product could not be obtained from the mother liquor, the solvent was evaporated under reduced pressure and the residue purified by FC (eluents are the same as described under TLC).

N-Benzyl-2-(1,4-dioxaspiro[4.5]dec-6-yl)acetamide (**7a**, $C_{17}H_{23}NO_3$)

5a 32.8 g (164 mmol), *CDI* 26.0 g (160 mmol), benzylamine 22.8 g (328 mmol), *THF* 350 cm^3; yield 38.4 g (81%) colourless crystals, mp 110°C; TLC (CH_2Cl_2:*Me*OH = 10:0.3): $R_f = 0.36$; IR (KBr): $\bar{\nu} = 3343$ (NH), 1639, 1570, and 1496 (CONH) cm^{-1}; MS (EI): m/z (%) = 289 ($M^{+\bullet}$, 14), 244 (18), 155 (37), 106 (22), 99 (100), 91 (54), 55 (37); ^{1}H NMR: $\delta = 7.35$–7.24 (m, 5arom H), 6.14 (broad s, NH), 4.42 (d, $J = 5.6$ Hz, benzyl–CH_2), 3.98–3.80 (m, OCH_2CH_2O), 2.55 and 1.95 (2dd, $J = 14.5$, 4.8 and 14.5, 7.9 Hz, each 1H, CH_2CON), 2.25–2.17 (m, CH), 1.85–1.75 and 1.68–1.58 (2m, each 2H), 1.52–1.23 (m, 4H) ppm.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)-N-methylacetamide (**7b**, $C_{11}H_{19}NO_3$)

5a 4.53 g (22.7 mmol), *CDI* 3.60 g (22.2 mmol)/*THF* 70 cm^3. The solution was cooled to −20°C and added to a solution of 7 cm^3 of methylamine in 30 cm^3 of *THF* at −40°C under stirring. After removing the cooling bath, the mixture was stirred for 1 h at ambient temperature, then for 8 h at 45°C. Further work up was accomplished following the general procedure. Yield 2.65 g (55%) colourless crystals, mp 103°C (Et_2O); TLC (CH_2Cl_2:*Me*OH = 10:0.8): $R_f = 0.47$; IR (KBr): $\bar{\nu} = 3260$, 3089 (NH), 1636, 1574 (amide I/II) cm^{-1}; MS (EI): m/z (%) = 213 ($M^{+\bullet}$, 9), 155 (28), 141 (12), 99 (100), 55 (28); ^{1}H NMR: $\delta = 5.92$ (br s, NH), 4.01–3.87 (m, OCH_2CH_2O), 2.79 (m, NCH_3), 2.52 and 1.91 (2dd, each $J = 14.4$, 4.7 Hz, each 1H), 2.21–2.13 (m, 1H), 1.82–1.76 and 1.69–1.57 (2m, each 2H), 1.53–1.41 (m, 1H), 1.41–1.23 (m, 3H) ppm; ^{13}C NMR: $\delta = 173.57$ (C=O), 110.17, 64.59, 64.55, 41.81, 36.52, 34.30, 30.16, 26.28, 24.54, 23.74 ppm.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)-N-(1-phenylethyl)acetamide
(**7c**, $C_{18}H_{25}NO_3$, *diastereomeric mixture*)

5a 4.89 g (24.5 mmol), CDI 3.88 g (24.0 mmol), (±)-1-phenylethylamine 3.85 g (31.8 mmol), *THF* 100 cm^3; yield 5.47 g (74%) colourless crystals, mp 110°C (Et_2O); TLC (CH_2Cl_2:*Me*OH = 10:0.2): $R_f = 0.31/0.29$; IR (KBr): $\bar{\nu} = 3326$ (NH), 1632, 1553 (amide I/II) cm^{-1}; MS (EI): m/z (%) = 303 ($M^{+\bullet}$, 27), 258 (22), 155 (46), 120 (31), 105 (63), 99 (100); ^{1}H NMR: $\delta = 7.36$–7.29 (m, 4arom H), 7.27–7.22 (m, 1arom H), 6.10–6.08 (br m, NH), 5.13 (m, 1H), 3.99–3.77 (m, OCH_2CH_2O), 2.55–2.48, 2.22–2.13 and 1.95–1.88 (3m, each 1H), 1.81–1.72 and 1.67–1.54 (2m, each 2H), 1.49–1.16 (m, 4H), 1.47 (d, $J = 7.0$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 171.79$, 171.72, 143.49, 143.47, 128.54, 127.16, 126.17, 110.16, 110.12, 64.54, 64.53, 64.44, 64.39, 48.54, 48.51, 41.76, 41.68, 36.85, 36.23, 34.26, 30.63, 30.14, 24.49, 23.68, 21.81, 21.75 ppm.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)-N-isopropylacetamide (**7d**, $C_{13}H_{23}NO_3$)

5a 8.20 g (41.0 mmol), *CDI* 6.51 g (40.2 mmol), isopropylamine 4.6 cm^3 (53.8 mmol), *THF* 100 cm^3; yield 7.41 g (75%) colourless crystals, mp 101°C (Et_2O); TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.3:0.05): $R_f = 0.78$; IR (KBr): $\bar{\nu} = 3325$ (NH), 1634, 1573 (amide I/II) cm^{-1}; MS (EI): m/z (%) = 241 ($M^{+\bullet}$, 3), 258 (22), 155 (38), 99 (100), 55 (45); ^{1}H NMR: $\delta = 5.57$ (br s, NH),

4.06–3.96 (m, $J = 6.7$, 1.4, 1H), 3.95–3.81 (m, OCH_2CH_2O), 2.42 and 1.80 (2dd, $J = 14.3$, 5.0 and 14.3, 8.3 Hz, each 1H), 2.14–2.06 (m, 1H), 1.76–1.68 and 1.62–1.52 (2m, each 2H), 1.47–1.18 (m, 4H), 1.08 (d, $J = 6.7$ Hz, $2CH_3$) ppm; ^{13}C NMR: $\delta = 171.69$ (C=O), 110.02, 64.46, 64.37, 41.64, 40.96, 36.66, 34.20, 29.88, 24.34, 23.59, 22.71, 22.66 ppm.

N-Benzyl-3-(1,4-dioxaspiro[4.5]dec-6-yl)propionamide (**7e**, $C_{18}H_{25}NO_3$)

5b 28.1 g (132 mmol), *CDI* 20.9 g (129 mmol), benzylamine 18.4 g (172 mmol), *THF* 300 cm^3; yield 28.84 g (72%) colourless crystals, mp 75°C; TLC (CH_2Cl_2:*Me*OH = 10:0.2): $R_f = 0.46$; IR (KBr): $\bar{\nu} = 3305$ (NH), 1637 and 1538 (CONH) cm^{-1}; MS (EI): m/z (%) = 303 ($M^{+\bullet}$, 25), 258 (26), 169 (11), 155 (27), 106 (32), 99 (100), 91 (63), 55 (49); ^1H NMR: $\delta = 7.35$–7.24 (m, 5arom H), 6.08 (broad s, NH), 4.43 (d, $J = 5.7$ Hz, benzyl–CH_2), 3.95–3.84 (m, OCH_2CH_2O), 2.33 and 2.18 (2ddd, $J = 14.8$, 9.0, 6.3 and 14.8, 8.8, 6.9 Hz, each 1H, CH_2CON), 1.94 (dddd, $J = 13.6$, 9.0, 6.9, 4.1 Hz, 1H, CH_2–C–CON), 1.78–1.71 (m, 2H), 1.66–1.53 (m, 3H), 1.51–1.39 (m, 2H), 1.35–1.15 (m, 3H) ppm; ^{13}C NMR: $\delta = 173.13$, 138.60, 128.65 (2C), 127.88 (2C), 127.41, 110.78, 64.68, 64.45, 43.98, 43.58, 35.02, 34.46, 29.56, 24.68, 24.51, 23.72 ppm.

N-Benzyl-3-(1,4-dioxaspiro[4.4]non-6-yl)propionamide (**8a**, $C_{17}H_{23}NO_3$)

6a 29.0 g (145 mmol), *CDI* 23.0 g (142 mmol), benzylamine 20.2 g (189 mmol), *THF* 330 cm^3; yield 29.8 g (71%) light yellow oil, bp 173–174°C/3 Pa (the crude product contained some impurities, which could not be removed by FC and attempted crystallization); TLC (CH_2Cl_2:*Me*OH = 10:0.2): $R_f = 0.38$; IR (film): $\bar{\nu} = 3290$ (NH), 1644 and 1546 (CONH) cm^{-1}; MS (EI): m/z (%) = 289 ($M^{+\bullet}$, 9), 244 (21), 155 (9), 141 (20), 106 (27), 99 (100), 91 (52); ^1H NMR: $\delta = 7.35$–7.24 (m, 5arom H), 5.93 (broad s, NH), 4.44 (d, $J = 5.6$ Hz, benzyl–CH_2), 3.92–3.83 (m, OCH_2–CH_2O), 2.31–2.18 (m, CH_2CON), 1.98–1.82 and 1.76–1.72 (2m, each 3H), 1.71–1.54 (m, 2H), 1.38–1.30 (m, 1H) ppm.

N-Benzyl-2-(1,4-dioxaspiro[4.4]non-6-yl)acetamide (**8b**, $C_{16}H_{21}NO_3$)

6b 14.18 g (76.2 mmol), *CDI* 12.09 g (74.7 mmol), benzylamine 10.61 g (99.1 mmol), *THF* 300 cm^3; yield 8.34 g (40%) colourless crystals, mp 92°C; TLC (CH_2Cl_2:*Me*OH = 10:0.2): $R_f = 0.54$; IR (KBr): $\bar{\nu} = 3266$ (NH), 1643 and 1561 (CONH) cm^{-1}; MS (EI): m/z (%) = 275 ($M^{+\bullet}$, 10), 203 (30), 141 (27), 106 (27), 99 (100), 91 (74), 55 (32); ^1H NMR: $\delta = 7.34$–7.23 (m, 5arom H), 6.41 (broad s, NH), 4.44 and 4.38 (2dd, $J = 14.7$, 5.8 and 14.7, 5.7 Hz, each 1H, benzyl–CH_2), 3.86–3.70 (m, OCH_2CH_2O), 2.50–2.41 (m, 2H), 2.24–2.13 and 2.02–1.93 (2m, each 1H), 1.81–1.72 and 1.72–1.57 (2m, each 2H), 1.45–1.32 (m, 1H) ppm; ^{13}C NMR: $\delta = 172.38$, 138.63, 128.63 (2C), 127.82 (2C), 127.38, 117.62, 64.60, 64.25, 43.58, 42.65, 36.65, 35.43, 30.02, 20.73 ppm.

*General Procedure for the Synthesis of Amines **9** and **10***

To a solution of the amide **7** or **8** in anhydrous *THF* was added $LiAlH_4$ during 20 min under stirring, ice cooling, and N_2. The mixture was allowed to warm up to ambient temperature, heated under reflux for 16 h, diluted with 100 cm^3 of Et_2O, and then cautiously(!) poured into a mixture of 2 *N* NaOH and Et_2O (each 150 cm^3) under stirring, cooling, and N_2. After separating the organic layer the aqueous layer was extracted with 3×150 cm^3 of Et_2O. The combined ether extracts were washed with 150 cm^3 of saturated Na_2CO_3 solution, dried (Na_2SO_4), and evaporated *in vacuo*. The crude products were used for the next step without further purification, or, if necessary, were purified by FC (eluents are the same as described under TLC).

Benzyl[2-(1,4-dioxaspiro[4.5]dec-6-yl)ethyl]amine (**9a**)

7a 12.47 g (43.1 mmol), $LiAlH_4$ 3.28 g (86.3 mmol), *THF* 250 cm^3; yield 12.2 g (99%, Ref. [25] 88%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.2:0.1): $R_f = 0.23$; IR (film): $\bar{\nu} = 3313$ (NH)

cm^{-1}; MS (EI): m/z (%) = 275 ($M^{+\bullet}$, 2), 230 (33), 120 (66), 91 (100), 55 (19); ^1H NMR data are in line with those published in Ref. [25]; ^{13}C NMR: δ = 139.56, 127.49 (2C), 127.29 (2C), 125.99, 109.79, 63.83, 63.65, 53.03, 46.81, 41.66, 33.70, 28.62, 27.86, 23.55, 22.82 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl]methylamine (**9b**, $C_{11}H_{21}NO_2$)

7b 1.73 g (8.1 mmol), $LiAlH_4$ 616 mg (16.2 mmol), *THF* 50 cm^3; yield 1.56 g (97%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.5:0.1): R_f = 0.30; IR (film): $\bar{\nu}$ = 3312 (NH) cm^{-1}; MS: a. (CI): m/z (%) = 200 ($M^{+\bullet}$+1, 100), b. (EI): m/z (%) = 199 ($M^{+\bullet}$, 5), 156 (91), 99 (75), 55 (100); ^1H NMR: δ = 3.99–3.90 (m, OCH_2–CH_2O), 2.63 and 2.54 (2ddd, J = 11.3, 9.5, 5.3 and 11.3, 9.9, 6.8 Hz, each 1H, N–CH_2), 2.43 (s, N–CH_3), 1.73–1.67 and 1.67–1.59 (2m, each 3H), 1.53–1.42 (m, 1H), 1.40–1.20 (m, 4H) ppm; ^{13}C NMR: δ = 110.74, 64.80, 64.65, 50.61, 42.80, 36.57, 34.69, 29.62, 28.78, 24.54, 23.84 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl](1-phenylethyl)amine (**9c**, $C_{18}H_{27}NO_2$, *diastereomeric mixture*)

7c 4.19 g (13.8 mmol), $LiAlH_4$ 1.05 g (27.6 mmol), *THF* 100 cm^3; yield 3.67 g (92%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.5:0.1): R_f = 0.34; IR (film): $\bar{\nu}$ = 3322 (NH) cm^{-1}; MS: a. (CI): m/z (%) = 290 ($M^{+\bullet}$+1, 100), b. (EI): m/z (%) = 289 ($M^{+\bullet}$, 2), 274 (25), 105 (100); ^1H NMR: δ = 7.34–7.28 (m, 4arom H), 7.25–7.19 (m, 1arom H), 3.97–3.83 (m, OCH_2CH_2O), 3.75 (q, J = 6.5 Hz, 1H), 2.58–2.31 (m, 2H), 1.82–1.53 (m, 6H), 1.52–1.38 (m, 1H), 1.38–1.11 (m, 4H), 1.34 (d, J = 6.5 Hz, CH_3) ppm; ^{13}C NMR: δ = 145.98, 128.35, 126.76, 126.74, 126.56, 110.70, 64.79, 64.75, 64.61, 64.58, 58.40, 46.13, 46.08, 42.80, 42.61, 34.77, 34.70, 29.68, 29.43, 29.32, 29.01, 24.56, 24.53, 24.47, 24.30, 23.81 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl]isopropylamine (**9d**, $C_{13}H_{25}NO_2$)

7d 6.34 g (26.3 mmol), $LiAlH_4$ 2.00 g (52.6 mmol), *THF* 150 cm^3; yield 5.43 g (91%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.3:0.05): R_f = 0.59; IR (film): $\bar{\nu}$ = 3157 (NH) cm^{-1}; MS: a. (CI): m/z (%) = 228 ($M^{+\bullet}$+1, 100), b. (EI): m/z (%) = 227 ($M^{+\bullet}$, 1), 212 (11), 184 (14), 125 (15), 99 (16), 72 (100), 55 (29); ^1H NMR: δ = 3.99–3.91 (m, OCH_2CH_2O), 2.79 (sept, J = 6.2 Hz, N–CH), 2.66 (dt, J = 10.9, 5.4 Hz, 1H), 1.82–1.73 and 1.67–1.57 (2m, each 3H), 1.54–1.42 (m, 1H), 1.39–1.17 (m, 4H), 1.05 and 1.04 (2d, each J = 6.2 Hz, $2CH_3$) ppm; ^{13}C NMR: δ = 110.61, 64.70, 64.52, 48.64, 45.98, 42.80, 34.58, 29.51, 29.16, 24.41, 23.66, 22.91, 22.82 ppm.

Benzyl[3-(1,4-dioxaspiro[4.5]dec-6-yl)propyl]amine (**9e**, $C_{18}H_{27}NO_2$)

7e 9.97 g (32.9 mmol), $LiAlH_4$ 2.49 g (66.0 mmol), *THF* 200 cm^3; yield 9.3 g (98%) colourless oil; TLC (CH_2Cl_2:*Me*OH = 10:0.3): R_f = 0.21; IR (film): $\bar{\nu}$ = 3313 (NH) cm^{-1}; MS: a. (CI): m/z (%) = 290 ($M^{+\bullet}$+1, 100), b. (EI): m/z (%) = 244 (62), 120 (48), 99 (11), 91 (100), 55 (16); ^1H NMR: δ = 7.32–7.30 (m, 4arom H), 7.27–7.21 (m, 1arom H), 3.98–3.87 (m, OCH_2CH_2O), 3.78 (s, benzyl–CH_2), 2.67–2.56 and 1.84–1.71 (2m, each 2H), 1.67–1.38 (m, 8H), 1.38–1.27 (m, 1H), 1.27–1.16 (m, 2H), 1.15–1.07 (m, 1H) ppm; ^{13}C NMR: δ = 140.61, 128.35 (2C), 128.12 (2C), 126.84, 110.87, 64.74, 64.63, 54.06, 49.83, 44.50, 34.61, 29.08, 28.05, 25.74, 24.48, 23.89 ppm.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethylamine (**9f**)

19a [28] 5.04 g (27.8 mmol), $LiAlH_4$ 2.00 g (52.6 mmol), *THF* 100 cm^3; refluxing time 4 h; yield 4.73 g (92%, Ref. [28] 78%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.8:0.1): R_f = 0.28; IR (film): $\bar{\nu}$ = 3364 (NH) cm^{-1}; MS (CI): m/z (%) = 186 ($M^{+\bullet}$+1, 100); 169 (25);

^{1}H NMR: $\delta = 4.05$–3.89 (m, OCH_2CH_2O), 2.77 and 2.64 (2ddd, $J = 15.0$, 9.3, 5.3 and 15.0, 8.6, 6.9 Hz, each 1H, N–CH_2), 1.79–1.51 (m, 6H), 1.30–1.11 (m, 7H) ppm.

3-(1,4-Dioxaspiro[4.5]dec-6-yl)propylamine (**9g**)

19b [13] 13.5 g (69.2 mmol), $LiAlH_4$ 4.00 g (105.3 mmol), *THF* 250 cm^3; refluxing time 4 h; yield 13.6 g (99%, Ref. [13] 74%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.5:0.1): $R_f = 0.21$; IR (film): $\bar{\nu} = 3370$ (NH) cm^{-1}; MS (CI): m/z (%) = 200 ($M^{+\bullet}$+1, 100); 199 ($M^{+\bullet}$, 58); ^{1}H NMR: $\delta = 4.00$–3.88 (m, OCH_2–CH_2O), 2.71–2.63 and 1.88–1.70 (2m, each 2H), 1.67–1.41 (m, 9H), 1.40–1.16 (m, 3H), 1.15–1.04 (m, 1H) ppm; ^{13}C NMR: $\delta = 110.87$, 64.76, 64.65, 44.47, 42.55, 34.61, 31.83, 29.10, 25.27, 24.51, 23.87 ppm.

Benzyl[3-(1,4-dioxaspiro[4.4]non-6-yl)propyl]amine (**10a**, $C_{17}H_{25}NO_2$)

8a 15.05 g (52.1 mmol), $LiAlH_4$ 3.96 g (104.2 mmol), *THF* 250 cm^3; yield 13.5 g (94%) colourless oil; TLC (CH_2Cl_2:*Me*OH = 10:0.4): $R_f = 0.18$; IR (film): $\bar{\nu} = 3313$ (NH) cm^{-1}; MS: a. (CI): m/z (%) = 276 ($M^{+\bullet}$+1, 100), b. (EI): m/z (%) = 230 (59), 120 (43), 106 (6), 91 (100); ^{1}H NMR: $\delta = 7.34$–7.29 (m, 4arom H), 7.27–7.21 (m, 1arom H), 3.94–3.82 (m, OCH_2CH_2O), 3.79 (s, 2H), 2.69–2.58 (m, 2H), 2.10 (br s, NH), 1.95–1.83 (m, 2H), 1.79–1.43 (m, 7H), 1.37–1.16 (m, 2H) ppm; ^{13}C NMR: $\delta = 140.55$, 128.33 (2C), 128.10 (2C), 126.81, 118.17, 64.55, 64.40, 54.09, 49.80, 46.06, 35.69, 29.46, 28.80, 26.64, 20.63 ppm.

Benzyl[2-(1,4-dioxaspiro[4.4]non-6-yl)ethyl]amine (**10b**, $C_{16}H_{23}NO_2$)

8b 6.11 g (22.2 mmol), $LiAlH_4$ 1.69 g (44.8 mmol), *THF* 120 cm^3; yield 5.79 g (98%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 10:0.3:0.1): $R_f = 0.35$; IR (film): $\bar{\nu} = 3313$ (NH) cm^{-1}; MS (EI): m/z (%) = 262 ($M^{+\bullet}$+1, 2), 216 (21), 120 (57), 99 (15), 91 (100), 55 (16); ^{1}H NMR: $\delta = 7.30$ (m, 4arom H), 7.26–7.20 (m, 1arom H), 3.92–3.81 (m, OCH_2CH_2O), 3.80 and 3.77 (2d, each $J = 13.1$ Hz, each 1H, N-benzyl–CH_2), 2.68 and 2.61 (2ddd, $J = 11.3$, 9.2, 3.6 and 11.3, 9.00, 6.4 Hz, each 1H), 2.00–1.91 (m, 1H), 1.87 (ddt, $J = 12.1$, 7.9, 3.7 Hz, 1H), 1.78–1.55 (m, 5H), 1.45 (ddt, $J = 13.1$, 9.0, 5.6 Hz, 1H), 1.42–1.28 (m, 2H) ppm; ^{13}C NMR: $\delta = 140.66$, 128.33 (2C), 128.09 (2C), 126.80, 118.20, 64.54, 64.45, 54.04, 48.22, 44.11, 35.69, 29.65, 29.46, 20.71 ppm.

General Procedure for the Synthesis of Bicyclic α-Aminonitriles ***11–14***

The amine **9** or **10** was dissolved in 2 *N* HCl and H_2O, if necessary under warming up to 40–50°C. After the mixture was stirred for 1.5 h at ambient temperature, an aqueous solution of KCN was dropwise added over a period of 20 min under vigorous stirring. Thereafter the reaction mixture exhibited a *pH* of 7–8; deviations of this value were corrected by addition of a small amount of 2 *N* HCl or KCN. Stirring of the mixture was continued for 1 h. The oily product separated was dissolved in 100 cm^3 of Et_2O. The aqueous layer was rendered alkaline by saturated Na_2CO_3 solution and extracted with 3×100 cm^3 of Et_2O. The combined organic layers were washed with 200 cm^3 of brine, dried (Na_2SO_4), and evaporated *in vacuo*. The crude products were used for the next step without further purification. Attempted purification by FC caused decomposition and remarkable loss of the products.

cis/trans-1-Benzyloctahydroindole-7a-carbonitrile (**11a**, $C_{16}H_{20}N_2$, *diastereomeric mixture*)

9a 10.31 g (37.5 mmol), 2 *N* HCl 37.5 cm^3 (75.0 mmol), H_2O 300 cm^3, KCN 4.88 g (75.0 mmol)/H_2O 10 cm^3; yield 8.84 g (98%) light yellow oil; TLC (Al_2O_3, *n*-hexane:Et_2O = 8:2): $R_f = 0.58$; IR (film): $\bar{\nu} = 2214$ (CN) cm^{-1}; MS (EI): m/z (%) = 240 ($M^{+\bullet}$, 11), 213 (32), 184 (23), 149 (16), 91 (100); ^{1}H NMR: $\delta = 7.35$–7.22 (m, 5arom H), 4.03 and 3.42 (2d, each $J = 12.8$ Hz, each 0.3H), 4.00 and 3.36

(2d, each $J = 13.3$ Hz, each 0.7H), 3.08–2.99 and 2.46–2.38 (2m, each 1H), 2.34–2.28 (m, 0.7H), 2.23–2.09 (m, 1.7H), 1.91–1.76 (m, 2.2H), 1.74–1.55 (m, 2H), 1.55–1.36 (m, 3.4H), 1.36–1.21 (m, 1H) ppm; ^{13}C NMR: $\delta = 138.83$, 137.67, 127.75, 127.48, 127.43, 127.41, 126.26, 126.17, 119.64, 117.23, 68.07, 63.53, 53.81, 53.14, 49.23, 48.73, 47.30, 42.42, 32.92, 29.14, 27.72, 26.60, 26.35, 25.37, 24.24, 23.42, 21.42, 18.54 ppm.

cis/trans-1-Methyloctahydroindole-7a-carbonitrile (**11b**, $C_{10}H_{16}N_2$, *diastereomeric mixture*)

9b 1.39 g (7.0 mmol), 2 *N* HCl 7.0 cm^3 (14.0 mmol), H_2O 50 cm^3, KCN 910 mg (14.0 mmol)/H_2O 5 cm^3; yield 1.06 g (92%) light yellow oil; IR (film): $\bar{\nu} = 2214$ (CN) cm^{-1}; MS (EI): m/z (%) = 137 ($M^{+\bullet}$–HCN, 71), 109 (100); ^{1}H NMR: $\delta = 3.22$–3.15 (m, 0.33H), 3.18 (dt, $J = 9.5$, 5.3 Hz, 0.66H), 2.52 and 2.45 (2ddd, $J = 11.0$, 9.5, 5.1 and 10.8, 10.0, 4.1 Hz, 0.66 and 0.33H), 2.37 and 2.31 (2s, 1 and 2H, N–CH_3), 2.30–2.22 (m, 0.66H), 2.21–2.01 (m, 1.66H), 1.97–1.80 (m, 1.33H), 1.80–1.53 and 1.53–1.31 (2m, each 3H), 1.31–1.18 (m, 1.33H) ppm; ^{13}C NMR: $\delta = 120.00$, 117.44, 69.61, 65.25, 52.05, 52.91, 48.39, 43.23, 35.81, 35.38, 33.23, 29.64, 29.00, 27.60, 27.43, 26.43, 25.10, 24.26, 22.36, 19.31 ppm.

1-(1-Phenylethyl)octahydroindole-7a-carbonitrile (**11c**, $C_{17}H_{22}N_2$, *mixture of 4 diastereomers*)

9c 3.53 g (12.2 mmol), 2 *N* HCl 12.2 cm^3 (24.4 mmol), H_2O 100 cm^3, KCN 1.59 g (24.4 mmol)/H_2O 10 cm^3; yield 3.01 g (97%) pale yellow oil; TLC (*n*-hexane:$Et_2O = 8{:}2$): $R_f = 0.59$; IR (film): $\bar{\nu} = 2214$ (CN) cm^{-1}; MS: a. (CI): m/z (%) = 228 ($M^{+\bullet}$+1–HCN, 100), 124 (13), 105 (11), b. (EI): m/z (%) = 227 ($M^{+\bullet}$–HCN, 11), 105 (100); ^{1}H NMR: $\delta = 7.38$–7.19 (m, 5arom H), 4.02 and 3.93 (2q, $J = 6.8$ Hz, 0.38 and 0.13H), 3.82–3.74 (m, 0.5H), 3.33 (ddd, $J = 9.9$, 9.1, 6.0 Hz, 0.38H), 3.00–2.93 (m, 0.5H), 2.88 (m, 0.38H), 2.83–2.80 (m, 0.13H), 2.75–2.63 (m, 0.5H), 2.57–2.50 (m, 0.13H), 2.38–2.23 (m, 0.75H), 2.12–2.02 (m, 0.38H), 2.00–1.20 (m, 8.75H), 1.51, 1.46, 1.44, and 1.42 (4d, each $J = 6.8$ Hz, 1.13, 0.38, 0.38, and 1.13H, CH_3), 1.08 (tq, $J = 13.3$, 4.3 Hz, 0.38H), 0.93 and 0.83 (2dt, $J = 12.9$, 3.5 and 12.9, 4.0 Hz, each 0.38H) ppm.

cis/trans-1-Isopropyloctahydroindole-7a-carbonitrile (**11d**, $C_{12}H_{20}N_2$, *diastereomeric mixture*)

9d 1.48 g (6.52 mmol), 2 *N* HCl 6.5 cm^3 (13.0 mmol), H_2O 80 cm^3, KCN 845 mg (13.0 mmol)/H_2O 5 cm^3; yield 1.2 g (96%) light yellow oil; IR (film): $\bar{\nu} = 2212$ (CN) cm^{-1}; MS (EI): m/z (%) = 165 ($M^{+\bullet}$–HCN, 55), 150 (100), 122 (65); ^{1}H NMR: $\delta = 3.18$–3.07 (m, 0.33H), 3.17 and 3.08 (2sept, $J = 6.7$ and 6.5 Hz, 0.66 and 0.33H, N–CH), 3.02–2.90 (m, 1.33H), 2.73 (ddd, $J = 10.9$, 9.7, 3.2 Hz, 0.33H), 2.35 (dt, $J = 12.5$, 3.2 Hz, 0.33H), 2.27–2.20, 2.13–2.01, and 1.93–1.67 (3m, 0.66, 1.33, and 2.33H) ppm; ^{13}C NMR: $\delta = 123.81$, 119.72, 66.76, 61.55, 49.67, 49.27, 45.88, 45.55, 44.23, 41.32, 35.64, 30.11, 27.71, 27.21, 27.17, 26.41, 25.15, 23.72, 23.56, 23.09, 22.49, 19.61, 19.26, 16.25 ppm.

trans-1-Benzyloctahydroquinoline-8a-carbonitrile (**12a**, $C_{17}H_{22}N_2$)

9e 10.23 g (35.4 mmol), 2 *N* HCl 35.4 cm^3 (70.8 mmol), H_2O 300 cm^3, KCN 4.60 g (70.8 mmol)/H_2O 10 cm^3; yield 8.86 g (99%) light yellow oil; TLC (Al_2O_3, *n*-hexane:$Et_2O = 8{:}2$): $R_f = 0.60$; IR (film): $\bar{\nu} = 2215$ (CN) cm^{-1}; MS (EI): m/z (%) = 254 ($M^{+\bullet}$, 3), 227 (100), 226 (61), 198 (36), 136 (10), 91 (90); ^{1}H NMR: $\delta = 7.34$–7.28 (m, 4arom H), 7.27–7.21 (m, 1H), 4.18 and 3.11 (2d, each $J = 13.9$ Hz, each 1H, benzyl–CH_2), 2.80–2.74 (m, among others $J = 12.2$ Hz, 1H), 2.40 (br dt, $J = 13.1$, 3.0 Hz, 1H), 2.34 (dt, $J = 12.2$, 3.2 Hz, 1H), 1.88–1.81, 1.79–1.72, and 1.74–1.63 (3m, each 1H), 1.63–1.34 (m, 8H), 1.36–1.22 (m, 1H) ppm; ^{13}C NMR: $\delta = 139.43$, 128.42 (2C), 128.39 (2C), 126.92, 117.97, 65.98, 54.73, 50.08, 44.94, 34.82, 30.38, 29.23, 25.28, 25.11, 23.52 ppm.

trans-Octahydroquinoline-8a-carbonitrile (**12b**, $C_{10}H_{16}N_2$)

22 2.80 g (14.1 mmol), 2 *N* HCl 14.0 cm^3 (28.0 mmol), H_2O 300 cm^3, KCN 1.83 mg (28.2 mmol)/H_2O 20 cm^3. After stirring for 1 h the reaction mixture was decanted from lumpy precipitate possibly separated and rendered alkaline with Na_2CO_3. Further workup was accomplished following the general procedure. Yield 1.69 g (73%) light yellow oil; IR (film): $\bar{\nu} = 3322$ (NH), 2216 (CN) cm^{-1}; MS (EI): m/z (%) = 137 ($M^{+\bullet}$–HCN, 100); ^{1}H NMR: $\delta = 3.10$–2.97 and 1.94–1.87 (2m, 2 and 1H), 1.83–1.66 (m, 5H), 1.64–1.48 and 1.45–1.25 (2m, each 4H) ppm; ^{13}C NMR: $\delta = 120.81$, 61.18, 44.35, 43.65, 37.39, 29.75, 28.83, 25.53, 25.45, 23.00 ppm.

cis/trans-1-Benzyloctahydro-1-pyrindine-7a-carbonitrile
(**13**, $C_{16}H_{20}N_2$, *diastereomeric mixture*)

10a 9.40 g (34.2 mmol), 2 *N* HCl 34.2 cm^3 (68.4 mmol), H_2O 400 cm^3, KCN 4.45 g (68.4 mmol)/H_2O 10 cm^3; yield 8.02 g (98%) light yellow oil, which crystallized during several hours, mp 77°C (after washing with a small volume of ice cold Et_2O); TLC (Al_2O_3, *n*-hexane:Et_2O = 8:1): $R_f = 0.52$; IR (film): $\bar{\nu} = 2217$ (CN) cm^{-1}; MS (EI): m/z (%) = 239 ($M^{+\bullet}$–1, 5), 213 (20), 212 (26), 91 (100); ^{1}H NMR: $\delta = 7.35$–7.22 (m, 5arom H), 4.00 and 3.16 (2d, each $J = 14.4$ Hz, each 0.66H), 3.95 and 3.30 (2d, each $J = 13.3$ Hz, each 0.33H), 2.76–2.72 (m, 0.33H), 2.71–2.66 (m, 0.66H), 2.40–2.37 (m, 1.66H), 2.25–2.16 (m, 1H), 2.04–1.93 (m, 2H), 1.74–1.63 (m, 6H), 1.48–1.37 (m, 1.33H) ppm; ^{13}C NMR: $\delta = 139.05$, 138.36, 18.70, 128.36, 128.30, 128.13, 127.14, 126.98, 119.52, 118.44, 70.38, 64.56, 58.02, 56.18, 49.18, 48.94, 48.84, 45.64, 37.16, 36.14, 27.42, 26.36, 26.26, 25.32, 22.99, 21.78, 20.41, 19.07 ppm.

cis-1-Benzylhexahydrocyclopenta[b]pyrrole-6a-carbonitrile (**14**, $C_{15}H_{18}N_2$)

10b 4.23 g (26.3 mmol), 2 *N* HCl 26.3 cm^3 (52.6 mmol), H_2O 220 cm^3, KCN 3.42 g (52.6 mmol)/H_2O 10 cm^3; yield 5.71 g (98%) light yellow oil; TLC (Al_2O_3, *n*-hexane:Et_2O = 8:1): $R_f = 0.46$; IR (film): $\bar{\nu} = 2217$ (CN) cm^{-1}; MS (EI): m/z (%) = 226 ($M^{+\bullet}$, 12), 225 ($M^{+\bullet}$–1, 23), 91 (100), 84 (23), 57 (27); ^{1}H NMR: $\delta = 7.33$–7.30 (m, 4arom H), 7.29–7.23 (m, 1arom H), 3.95 and 3.54 (2d, each $J = 13.4$ Hz, each 1H, N-benzyl–CH_2), 3.03–2.92 (m, 1H), 2.87 (m, 1H), 2.36 (ddd, $J = 11.0$, 9.6, 6.1 Hz, 1H), 2.08 (br ddd, $J = 12.3$, 9.6, 5.9 Hz, 1H), 2.05–1.98 (m, 1H), 1.94–1.80 and 1.80–1.69 (2m, each 2H), 1.59–1.50 (m, 1H), 1.38 (ddt, $J = 12.3$, 11.0, 7.3 Hz, 1H) ppm; ^{13}C NMR: $\delta = 138.80$, 128.44 (2C), 128.33 (2C), 127.14, 120.73, 69.68, 55.04, 52.51, 50.94, 37.70, 33.72, 31.15, 24.86 ppm.

*Angularly Substituted Compounds **15–18***

*A. General Procedure for the Synthesis of 7a-Methyl- and 7a-Aryl-derivatives **15a–15f, 15i, 15k, 16b, 16c, 17b,** and **18***

The *Grignard* reagent was prepared from Mg and the corresponding halogenide in anhydrous *THF* and the reaction was completed by heating the mixture to reflux (temperature of the oil bath 70°C). A solution of the aminonitrile **11–14** in toluene was slowly added over a period of 45 min under vigorous stirring and N_2. After the addition was complete the temperature of the heating bath was raised to 130°C and the mixture was stirred for additional 16 h, then quenched with 50 cm^3 of saturated NH_4Cl solution under ice cooling and diluted with 300 cm^3 of Et_2O and 200 cm^3 of 1 *N* HCl. The aqueous layer was separated and the organic phase was extracted with 3×100 cm^3 of 0.5 *N* HCl. The combined aqueous layers were rendered alkaline with saturated Na_2CO_3 solution and extracted with 3×200 cm^3 of Et_2O. After drying the ether extracts with Na_2SO_4 and removing the solvent *in vacuo* the crude product was purified by FC (neutral Al_2O_3; for eluent see TLC).

cis-1-Benzyl-7a-phenyloctahydroindole (**15a**, $C_{21}H_{25}N$)

Mg 1.20 g (50.0 mmol)/*THF* 5 cm^3, bromobenzene 7.85 g (50.0 mmol)/*THF* 30 cm^3, **11a** 3.0 g (12.5 mmol)/toluene 50 cm^3; yield 909 mg (25%) colorless crystals, mp 73°C (MeOH); TLC (Al_2O_3, *n*-hexane:Et_2O = 8:1): $R_f = 0.78$; MS (EI): m/z (%) = 291 ($M^{+\bullet}$, 36), 248 (100), 214 (15), 91 (77); ^{1}H NMR: $\delta = 7.70–7.67$ (dd, $J = 8.5$, 1.2 Hz, 2arom H), 7.37–7.32 (m, 2arom H), 7.25–7.13 (m, 6arom H), 3.45 and 3.14 (2d, each $J = 13.0$ Hz, each 1H, benzyl–CH_2), 3.02 (dt, $J = 9.1$, 5.2 Hz, 1H), 2.57–2.48 (m, 2H), 2.14–2.08 (m, 1H), 1.95–1.78 (m, 3H), 1.65 (m, 1H), 1.63–1.41 (m, 4H), 1.35–1.25 (m, 1H) ppm; ^{13}C NMR: $\delta = 145.61$, 140.99, 128.42 (2C), 128.39 (2C), 128.11 (2C), 127.87 (2C), 126.52, 126.49, 66.49, 52.67, 48.87, 46.67, 25.93, 23.50, 23.74, 22.87, 20.26 ppm.

Table 1. Crystallographic data of **15a**[a]

Formula	$C_{21}H_{25}N$
Formula weight	291.44
Temperature/K	294
Color, shape	Colourless rods
Crystal dimensions/mm	0.27×0.33×0.47
Crystal system	triclinic
Space group	*P1*
Cell dimensions:	
a/Å	7.847(2)
b/Å	9.7580(10)
c/Å	11.646(4)
α/°	73.73(2)
β/°	83.28(2)
γ/°	77.147(13)
V/Å^3	833.2(3)
Radiaton	MoK_α ($\lambda = 0.71073$ Å)
Θ_{min}–Θ_{max}/°	2.48–23.97
Z	2
F(000)	316
μ/mm^{-1}	0.066
Density/g cm^{-3}	1.167
Reflections collected	5656
Independent reflections	2601 ($R_i = 0.0341$)
Observed reflections	2107 ($I > 2\sigma(I)$)
No. of parameters refined	199/0
R-values	
$R1$ ($2\sigma(I)$/all data)	0.0414/0.0528
$wR2$ ($2\sigma(I)$/all data)	0.1054/0.1143
Goodness of Fit	1.111
Residual electron density (e/Å^3)	0.141/−0.144
System used	SHELXS-86/SHELXL-93 [29]

[a] Further details of the crystal structure determination are available from Cambridge Crystallographic Data Center, 12 Union Road, GB Cambridge CB21EZ quoting the deposition number CCDC 169365 and the complete literature source (E-mail: deposit@ccdc.cam.ac.uk)

cis-1-Benzyl-7a-(3-methoxyphenyl)octahydroindole (**15b**, $C_{22}H_{27}NO$)

Mg 2.78 g (116.0 mmol)/*THF* 10 cm^3, 3-bromoanisol 21.69 g (116.0 mmol)/*THF* 70 cm^3, **11a** 6.96 g (29.0 mmol)/toluene 50 cm^3; yield 1.56 g (17%) colourless oil; TLC (Al_2O_3, *n*-hexane:Et_2O = 9:1): R_f = 0.51; MS (EI): m/z (%) = 321 ($M^{+\bullet}$, 38), 278 (100), 214 (17); ^{1}H NMR: δ = 7.28–7.15 (m, 8arom H), 6.79–6.73 (m, 1arom H), 3.83 (s, OCH_3), 3.48 and 3.15 (2d, each J = 13.1 Hz, each 1H, benzyl–CH_2), 3.02 (dt, J = 9.2, 5.1 Hz, 1H), 2.55–2.47 (m, 2H), 2.10–2.05 (m, 1H), 1.95–1.78 (m, 3H), 1.72–1.56 (m, 2H), 1.56–1.43 (m, 3H), 1.37–1.25 (m, 1H) ppm; ^{13}C NMR: δ = 159.48, 147.71, 140.99, 128.61, 128.38 (2C), 128.10 (2C), 126.50, 120.93, 114.52, 111.55, 66.53, 55.24, 52.64, 48.80, 46.69, 25.91, 25.50, 23.75, 23.08, 20.27 ppm.

cis-1-Benzyl-7a-(4-methoxyphenyl)octahydroindole (**15c**, $C_{22}H_{27}NO$)

Mg 0.53 g (21.8 mmol)/*THF* 5 cm^3, 4-bromoanisol 4.10 g (21.8 mmol)/*THF* 20 cm^3, **11a** 1.31 g (5.45 mmol)/toluene 20 cm^3; yield 1.56 g (17%) colorless oil; TLC (Al_2O_3, *n*-hexane:Et_2O = 9:1): R_f = 0.51; MS (EI): m/z (%) = 321 ($M^{+\bullet}$, 29), 278 (100), 214 (7); ^{1}H NMR: δ = 7.59 (m, 2arom H), 7.25–7.13 (m, 5arom H), 6.89 (br t, J = 9.0 Hz, 2arom H), 3.81 (s, OCH_3), 3.45 and 3.10 (2d, each J = 13.0 Hz, each 1H, benzyl–CH_2), 3.00 (dt, J = 9.3, 5.4 Hz, 1H), 2.54–2.45 (m, 2H), 2.09–2.03 (m, 1H), 1.93–1.77 (m, 3H), 1.67–1.42 (m, 5H), 1.35–1.25 (m, 1H) ppm; ^{13}C NMR: δ = 158.17, 141.06, 137.29, 129.48 (2C), 128.43 (2C), 128.11 (2C), 126.49, 113.15 (2C), 66.06, 55.23, 52.58, 48.74, 46.41, 25.74, 25.42, 23.76, 22.74, 20.27 ppm.

cis-1-Benzyl-7a-(3,4-dimethoxyphenyl)octahydroindole (**15d**, $C_{23}H_{29}NO_2$)

Mg 2.88 g (120.0 mmol)/*THF* 10 cm^3, 4-bromo-1,2-dimethoxybenzene 25.04 g (120.0 mmol)/*THF* 80 cm^3, **11a** 7.23 g (30.0 mmol)/toluene 50 cm^3; yield 1.26 g (12%) colourless oil; TLC (Al_2O_3, *n*-hexane:Et_2O = 7:3): R_f = 0.38; MS (EI): m/z (%) = 351 ($M^{+\bullet}$, 25), 308 (100), 214 (11), 91 (65); ^{1}H NMR: δ = 7.33 (d, J = 2.1 Hz, 1arom H), 7.25–7.15 (m, 5arom H), 7.14 (dd, J = 8.4, 2.1 Hz, 1arom H), 6.82 (d, J = 8.4 Hz, 1arom H), 3.93 and 3.88 (2s, $2OCH_3$), 3.47 and 3.10 (2d, each J = 13.1 Hz, each 1H, benzyl–CH_2), 3.04 (dt, J = 8.9, 5.2 Hz, 1H), 2.53–2.43 (m, 2H), 2.09–2.03 (m, 1H), 1.93–1.80 (m, 3H), 1.68–1.44 (m, 5H), 1.37–1.25 (m, 1H) ppm; ^{13}C NMR: δ = 148.64, 147.63, 140.82, 138.07, 128.24 (2C), 127.94 (2C), 126.36, 120.61, 111.65, 109.85, 66.29, 55.93, 55.77, 52.50, 48.65, 46.57, 25.71, 25.39, 23.86, 22.93, 20.17 ppm.

cis-1-Benzyl-7a-(3,4-methylenedioxyphenyl)octahydroindole (**15e**, $C_{22}H_{25}NO_2$)

Mg 2.88 g (120.0 mmol)/*THF* 10 cm^3, 4-bromo-1,2-methylenedioxybenzene 24.87 g (120.0 mmol)/*THF* 80 cm^3, **11a** 7.23 g (30.0 mmol)/toluene 50 cm^3; yield 1.43 g (14%) colourless crystals, mp 96°C (*Me*OH); TLC (Al_2O_3, *n*-hexane:Et_2O = 9:1): R_f = 0.49; MS (EI): m/z (%) = 335 ($M^{+\bullet}$, 30), 292 (100), 214 (10), 91 (80); ^{1}H NMR: δ = 7.26–7.14 (m, 6arom H), 7.09 (dd, J = 8.3, 2.0 Hz, 1arom H), 6.76 (d, J = 8.3 Hz, 1H), 5.95 and 5.94 (2d, each J = 2.0 Hz, each 1H, OCH_2O), 3.47 and 3.11 (2d, each J = 13.4 Hz, each 1H, benzyl–CH_2), 3.00 (dt, J = 9.3, 5.2 Hz, 1H), 2.50–2.41 (m, 2H), 2.05–1.98 (m, 1H), 1.93–1.77 (m, 3H), 1.66–1.42 (m, 5H), 1.36–1.25 (m, 1H) ppm; ^{13}C NMR: δ = 147.57, 145.96, 140.78, 139.55, 128.28 (2C), 128.02 (2C), 126.42, 121.50, 108.81, 107.08, 100.80, 66.39, 52.47, 48.66, 46.61, 25.67, 25.36, 23.70, 23.09, 20.16 ppm.

cis-1-Methyl-7a-phenyloctahydroindole (**15f**)

Mg 339 mg (16.4 mmol)/*THF* 3 cm^3, bromobenzene 2.61 g (16.6 mmol)/*THF* 10 cm^3, **11b** 682 mg (4.16 mmol)/toluene 20 cm^3; yield 306 mg (34%) colorless powder, mp 189°C (Ref. [5] oil, bp 115–120°C/15.6 Pa); TLC (Al_2O_3, *n*-hexane:Et_2O = 10:1): R_f = 0.66; MS (EI): m/z (%) = 215 ($M^{+\bullet}$, 22),

172 (100), 138 (20); ^{1}H NMR: $\delta = 7.55–7.52$ and 7.35–7.31 (2m, each 2arom H), 7.22 (tt, $J = 7.2$, 1.5 Hz, 1arom H), 3.21 (dt, $J = 9.5$, 4.4 Hz, 1H), 2.68–2.57 and 2.10–1.94 (2m, each 2H), 1.98 (s, N–CH_3), 1.90–1.80 and 1.77–1.71 (2m, each 1H), 1.55–1.25 (m, 6H) ppm; ^{13}C NMR: $\delta = 127.90$ (2C), 127.87 (2C), 126.42, 51.66, 45.58, 33.90, 25.88, 25.46, 23.28, 21.63, 20.44 ppm.

cis-(1RS)-7a-Methyl-1-(1-phenylethyl)octahydroindole
(**15i**, $C_{17}H_{25}N$, *diastereomeric mixture*)

Preparation according to **15k**: **11c** 330 mg (1.3 mmol)/*THF* 5 cm^3, 3 *M* CH_3MgBr in Et_2O 2 cm^3 (6 mmol). The mixture was separated by FC (silica gel, *Et*OAc:*Me*OH:NH_3 (25%) = 10:0.7:0.2) giving the diastereomers *cis*-A and *cis*-B.

Diastereomer cis-A. Yield 120 mg (38%) colourless oil; TLC (*Et*OAc:*Me*OH:NH_3 (25%) = 10:0.2:0.1): $R_f = 0.56$; MS (CI): m/z (%) = 244 ($M^{+\bullet}$+1, 100); ^{1}H NMR: $\delta = 7.35$ (br d, $J = 7.2$ Hz, 2arom H), 7.27 (br t, $J = 7.2$ Hz, 2arom H), 7.17 (tt, $J = 7.2$, 1.6 Hz, 1arom H), 3.92 (q, $J = 6.9$ Hz, N–CH), 2.84 and 2.69 (2dt, $J = 9.5$, 4.6 and 9.5, 5.4 Hz, each 1H), 1.85 and 1.68 (2m, 2 and 6H), 1.39 (d, $J = 6.9$ Hz, CH_3–C–Ph), 1.31–1.20 and 1.20–1.12 (each m, 2 and 1H), 1.15 (s, CH_3) ppm; ^{13}C NMR: $\delta = 146.69$, 127.99 (2C), 127.52 (2C), 126.21, 61.52, 55.67, 45.12, 45.06, 31.11, 27.83, 26.46, 24.59, 23.04, 22.19, 21.38 ppm.

Diastereomer cis-B. Yield 98 mg (31%) colourless oil; TLC: $R_f = 0.27$; MS (EI): m/z (%) = 243 ($M^{+\bullet}$, 8), 105 (43), 57 (100); ^{1}H NMR: $\delta = 7.37$ (br d, $J = 7.2$ Hz, 2arom H), 7.27 (br t, $J = 7.2$ Hz, 2arom H), 7.21–7.16 (m, 1arom H), 3.88 (q, $J = 6.7$ Hz, N–CH), 3.00–2.91 and 2.83–2.76 (2m, each 1H), 1.85–1.71, 1.64–1.48, and 1.43–1.30 (3m, 2, 5 and 3H), 1.39 (d, $J = 6.7$ Hz, CH_3–C-Ph), 1.22–1.11 (m, 1H), 0.77 (s, CH_3) ppm; ^{13}C NMR: $\delta = 147.32$, 127.91 (2C), 127.49 (2C), 126.25, 61.45, 55.77, 45.35, 44.48, 29.22, 26.12, 25.02, 24.28, 22.60, 21.63, 21.45 ppm.

cis-1-Benzyl-7a-methyloctahydroindole (**15k**)

To a solution of 230 mg (0.96 mmol) of **11a** in 5 cm^3 of anhydrous *THF* was added 2 cm^3 (6 mmol) of 3 *M* CH_3MgBr (Et_2O) under N_2 and stirring. After stirring 8 h at ambient temperature the reaction was quenched under ice cooling with 5 cm^3 of saturated NH_4Cl solution, diluted with 15 cm^3 of Et_2O, and extracted with 3×10 cm^3 of 0.5 *N* HCl. The combined aqueous layers were rendered alkaline with saturated Na_2CO_3 solution and extracted with 3×20 cm^3 of Et_2O. The combined ether layers were dried with Na_2SO_4 and evaporated *in vacuo*. The residue was purified by FC (silica gel, for eluent see TLC). Yield 176 mg (80%, Ref. [21] 66%, diastereomeric mixture), colourless oil; TLC (CH_2Cl_2:*Me*OH = 10:0.3): $R_f = 0.33$; MS (EI): m/z (%) = 229 ($M^{+\bullet}$, 17), 214 (26), 186 (54), 91 (100); ^{1}H NMR: $\delta = 7.28–7.25$ and 7.23–7.19 (2m, each 2arom H), 7.12 (tt, $J = 7.1$, 1.7 Hz, 1arom H), 3.54 and 3.39 (2d, each $J = 13.3$ Hz, each 1H, benzyl–CH_2), 2.60–2.51 and 1.79–1.69 (2m, each 2H), 1.62–1.32 (m, 6H), 1.32–1.15 (m, 3H), 1.01 (s, CH_3) ppm; ^{13}C NMR: $\delta = 141.23$, 128.43 (2C), 128.09 (2C), 126.39, 60.81, 52.63, 49.30, 44.18, 29.19, 27.57, 26.24, 22.91, 22.30, 2.00 ppm.

cis-1-Benzyl-8a-phenyldecahydroquinoline (**16b**, $C_{22}H_{27}N$)

Mg 211 mg (8.8 mmol)/*THF* 2 cm^3, bromobenzene 1.38 g (8.8 mmol)/*THF* 10 cm^3, **12a** 560 mg (2.2 mmol)/toluene 5 cm^3; yield 114 mg (17%) colourless oil; TLC (Al_2O_3, *n*-hexane: Et_2O = 9:1): $R_f = 0.71$; MS (EI): m/z (%) = 305 ($M^{+\bullet}$, 26), 262 (100), 228 (18), 91 (62); ^{1}H NMR (45°C): $\delta = 7.72$ (d, $J = 7.5$ Hz, 2arom H), 7.32 (br t, $J = 7.5$ Hz, 2arom H), 7.20–7.14 and 7.13–7.06 (2m, each 3arom H), 3.45 and 2.98 (2d, each $J = 13.6$ Hz, 2H, benzyl–CH_2), 2.59 (br dt, $J = 11.9$, 2.8 Hz, 1H), 2.42–2.35 (m, among others $J = 11.9$ Hz, 1H), 2.33–2.26 (m, among others $J = 3.2$ Hz, 1H), 2.16 (ddd, $J = 14.0$, 12.5, 5.8 Hz, 1H), 2.06–1.99 (m, among others $J = 14.0$ Hz, 1H), 1.92–1.71 (m, 3H), 1.70–1.61, 1.59–1.45, and 1.37–1.26 (3m, each 2H), 1.18 (tt, $J = 12.5$, 4.0 Hz, 1H) ppm; ^{13}C NMR (45°C):

$\delta = 146.80$, 141.67, 128.82 (2C), 128.16 (2C), 127.83 (2C), 127.59 (2C), 126.24, 126.21, 62.85, 54.08, 45.79, 42.19, 28.99, 26.70, 26.09, 23.81, 20.21, 19.88 (br) ppm.

cis-1-Benzyl-8a-(3-methoxyphenyl)decahydroquinoline (**16c**, $C_{23}H_{29}NO$)

Mg 2.30 g (96.0 mmol)/*THF* 10 cm^3, 3-bromoanisol 17.95 g (96.0 mmol)/*THF* 60 cm^3, **12a** 6.10 g (24.0 mmol)/toluene 50 cm^3; yield 884 mg (11%) colourless oil; TLC (Al_2O_3, *n*-hexane:$Et_2O = 9.5{:}0.5$): $R_f = 0.65$; MS (EI): m/z (%) = 335 ($M^{+\bullet}$, 30), 292 (100), 244 (3), 228 (23), 201 (11), 91 (56); ^{1}H NMR (45°C): $\delta = 7.35$–7.27 (m, 2arom H), 7.23 (br t, $J = 7.8$ Hz, 1arom H), 7.20–7.13 and 7.12–7.07 (2m, 2 and 3arom H), 6.76 (br dd, $J = 7.8$, 2.0 Hz, 1arom H), 3.81 (s, OCH_3), 3.48 and 3.00 (2dd, each $J = 13.7$ Hz, each 1H, benzyl–CH_2), 2.64–2.56, 2.42–2.33, 2.29–2.21, 2.20–2.08, and 2.03–1.93 (5m, each 1H), 1.91–1.72 (m, 3H), 1.70–1.60 and 1.59–1.43 (2m, each 2H), 1.38–1.33 (m, 3H) ppm; ^{13}C NMR (45°C): $\delta = 159.32$, 148.78, 141.69, 128.32, 128.14 (2C), 127.86 (2C), 126.20, 121.49, 115.50, 111.17, 62.92, 55.23, 54.11, 45.75, 42.22, 28.96, 26.65, 26.04, 23.78, 20.18 (2C) ppm.

cis-1-Benzyl-7a-(3-methoxyphenyl)octahydro[1]pyrindine (**17b**, $C_{22}H_{27}NO$)

Mg 3.20 g (133.2 mmol)/*THF* 10 cm^3, 3-bromoanisol 24.91 g (133.2 mmol)/*THF* 60 cm^3, **13** 8.00 g (33.3 mmol)/toluene 50 cm^3; yield 21 mg (0.2%) colourless oil; TLC (Al_2O_3, *n*-hexane:$Et_2O = 9{:}1$): $R_f = 0.66$; MS (EI): m/z (%) = 321 ($M^{+\bullet}$, 34), 292 (100), 278 (10), 214 (13), 201 (11), 91 (62); ^{1}H NMR: $\delta = 7.34$ (br t, $J = 2.0$ Hz, 1arom H), 7.28–7.20 (br m, 6arom H), 7.19–7.13 (m, 1arom H), 6.74 (ddd, $J = 7.7$, 2.5, 1.3 Hz, 1arom H), 3.82 (s, OCH_3), 3.51 and 2.95 (2d, each $J = 13.7$ Hz, each 1H, benzyl–CH_2), 2.69 (ddt, $J = 11.0$, 3.4, 1.5 Hz, 1H), 2.31–2.21 (m, 2H), 2.01–1.86 (m, 4H), 1.66–1.55 (m, 3H), 1.45–1.36 (m, 1H), 1.35–1.15 (m, 2H) ppm; ^{13}C NMR: $\delta = 159.24$, 150.84, 140.92, 128.33, 128.22 (2C), 127.92 (2C), 126.31, 119.91, 113.50, 111.31, 72.48, 56.60, 55.16, 47.16, 45.82, 28.26, 28.22, 25.03, 21.24, 20.68 ppm. Hydrochlorid (**17b**-HCl): colourless, amorphous solid, mp 254°C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 11.03$ (br s, N^+H), 7.37–7.28 (m, 8arom H), 6.97 (dd, $J = 8.3$, 2.0 Hz, 1arom H), 4.17 (d, $J = 12.9$ Hz, 1H), 4.03 (br s, OCH_3), 3.65–3.58 and 3.48–3.41 (2m, each 1H), 2.99–2.87 (m, 2H), 2.78 (dt, $J = 12.4$, 5.5 Hz, 1H), 2.52–2.44, 2.28, and 2.06–1.93, (3m, each 1H), 1.86–1.76 and 1.46–1.21 (2m, each 3H) ppm.

cis-1-Benzyl-6a-(3-methoxyphenyl)octahydrocyclopenta[b]pyrrole (**18**, $C_{21}H_{25}NO$)

Mg 1.41 g (58.9 mmol)/*THF* 10 cm^3, 3-bromoanisol 11.02 g (58.92 mmol)/*THF* 30 cm^3, **14** 3.33 g (14.73 mmol)/toluene 35 cm^3; yield 3.53 g (78%) colourless oil; TLC (Al_2O_3, *n*-hexane:$Et_2O = 9.5{:}0.5$): $R_f = 0.61$; MS (EI): m/z (%) = 307 ($M^{+\bullet}$, 33), 278 (100), 264 (20), 91 (60); ^{1}H NMR: $\delta = 7.30$–7.22 (m, 5arom H), 7.21–7.15 (m, 1arom H), 7.15 (br t, $J = 2.1$ Hz, 1arom H), 7.09 (br dt, $J = 7.7$, 0.7 Hz, 1arom H), 6.76 (br dd, $J = 8.1$, 2.6 Hz, 1arom H), 3.80 (s, OCH_3), 3.44 and 3.23 (2d, each $J = 13.7$ Hz, each 1H, benzyl–CH_2), 2.73 (ddd, $J = 9.0$, 7.1, 4.4 Hz, 1H), 2.62–2.54 and 2.15–2.04 (2m, each 2H), 2.00–1.90 (m, 3H), 1.79–1.68 (m, 1H), 1.46–1.36 (m, 2H) ppm; ^{13}C NMR: $\delta = 159.34$, 149.36, 140.95, 128.66, 128.27 (2C), 128.02 (2C), 126.41, 119.48, 113.23, 111.00, 77.58, 55.14, 53.64, 51.91, 49.79, 34.52, 33.21, 31.84, 26.21 ppm.

B. General Procedure for the Synthesis of 7a-Benzyl-derivatives ***15g***, ***15h***, ***15l***, ***16a***, *and* ***17a***

The *Grignard* reagent was prepared from Mg and benzylbromide in anhydrous *THF* and the reaction was completed by heating the mixture to reflux (temperature of the oil bath 70°C). A solution of the

corresponding aminonitrile **11**–**14** in *THF* was slowly added over a period of 45 min at 70°C under vigorous stirring and N_2. After the addition was complete the mixture was stirred for an additional 16 h at the same temperature, then quenched with 5 cm^3 of saturated NH_4Cl solution under ice cooling and diluted with 30 cm^3 of Et_2O and 20 cm^3 of 1 *N* HCl. The aqueous layer was separated and the organic phase was extracted with 3×15 cm^3 0.5 *N* HCl. The combined aqueous layers were rendered alkaline with saturated Na_2CO_3 solution and extracted with 3×25 cm^3 of Et_2O. After drying the ether extracts with Na_2SO_4 and removing the solvent *in vacuo* the crude product was crystallized from *Me*OH. The solid was collected by filtration, washed with a small volume of ice cold *Me*OH, and dried *in vacuo*. If the crystallization failed to occur or the concentrated mother liquor afforded no further product, the solvent was removed *in vacuo* and the residue purified by FC (for eluents see the corresponding TLC).

cis-(1RS)-7a-Benzyl-1-(1-phenylethyl)octahydroindole (**15g**, $C_{23}H_{29}N$, *diastereomeric mixture*)

Mg 567.0 mg (23.6 mmol)/*THF* 3 cm^3, benzylbromide 4.04 g (23.6 mmol)/*THF* 10 cm^3, **11c** 1.50 g (5.9 mmol)/*THF* 5 cm^3. The residue of the ether extracts was purified by FC (Al_2O_3, *n*-hexane:Et_2O = 9.5:0.5). Yield 1.19 g (63%) colourless oil; TLC (Al_2O_3, eluent see FC): R_f = 0.79. Partial separation of the diastereomers by FC (eluent see TLC, below).

Diastereomer A. Yield 72 mg; TLC (Al_2O_3, *n*-hexane:Et_2O = 10:0.1): R_f = 0.53; MS (CI): *m*/*z* (%) = 320 ($M^{+\bullet}$+1, 63), 228 (100); ^{1}H NMR: δ = 7.41–7.37 and 7.34–7.28 (2m, each 2arom H), 7.24–7.15 and 7.09–7.05 (2m, 4 and 2arom H), 4.21 (q, *J* = 6.7 Hz, 1H), 3.10 and 2.82 (2dt, *J* = 9.5, 5.6 and 9.5, 4.5 Hz, each 1H), 2.64 and 2.58 (2d, each *J* = 13.8 Hz, each 1H, benzyl–CH_2), 1.93–1.83, 1.83–1.75, and 1.74–1.63 (3m, 2, 1, and 1H), 1.60–1.36 (m, 6H), 1.49 (d, *J* = 6.7 Hz, CH_3), 1.21–1.11 (m, 1H) ppm.

Diastereomer B. Yield 53 mg; TLC: R_f = 0.46; MS: same fragmentation and intensities as given for A; ^{1}H-NMR: δ = 7.41–7.14 (m, 10arom H), 4.22 (q, *J* = 6.9 Hz, 1H), 3.11–3.01 (m, 2H), 2.88 and 2.61 (2d, each *J* = 13.2 Hz, each 1H, benzyl–CH_2), 2.09–1.96 and 1.85–1.75 (2m, each 1H), 1.51–1.24 (m, 7H), 1.48 (d, *J* = 6.9 Hz, CH_3), 1.16–1.06 and 0.97–0.79 (2m, each 1H) ppm.

cis-7a-Benzyl-1-isopropyloctahydroindole (**15h**, $C_{18}H_{27}N$)

Mg 288.0 mg (12.0 mmol)/*THF* 3 cm^3, benzylbromide 2.05 g (12.0 mmol)/*THF* 10 cm^3, **11d** 576 mg (3.0 mmol)/*THF* 5 cm^3. Yield 555 mg (72%) colourless crystals; TLC (*n*-hexane:Et_2O = 10:1): R_f = 0.66; MS (CI): *m*/*z* (%) = 258 ($M^{+\bullet}$+1, 58), 166 (100); ^{1}H NMR: δ = 7.26–7.21 and 7.19–7.14 (2m, 2 and 3arom H), 3.30 (sept, *J* = 6.6 Hz, 1H), 2.92–2.89 and 2.89–2.83 (2m, each 1H), 2.74 and 2.58 (2d, each *J* = 13.5 Hz, each 1H, benzyl–CH_2), 1.85–1.76 and 1.75–1.68 (2m, each 1H), 1.59 (ddd, *J* = 13.0, 8.3, 3.5 Hz, 1H), 1.54–1.24 and 1.16–1.05 (2m, 7 and 1H), 1.10 and 1.06 (2d, each *J* = 6.6 Hz, $2CH_3$) ppm.

cis-1,7a-Dibenzyloctahydroindole (**15l**, $C_{22}H_{27}N$)

Mg 96.0 mg (4.0 mmol)/*THF* 3 cm^3, benzylbromide 684 mg (4.0 mmol)/*THF* 10 cm^3, **11a** 240 mg (1.0 mmol)/*THF* 5 cm^3. Yield 253 mg (83%) colourless crystals, mp 74°C; TLC (Al_2O_3, *n*-hexane): R_f = 0.20; MS (CI): *m*/*z* (%) = 306 ($M^{+\bullet}$+1, 66), 214 (100), 91 (9); ^{1}H NMR: δ = 7.39–7.34 and 7.33–7.18 (2m, 2 and 8arom H), 3.84 and 3.64 (2d, each *J* = 13.8 Hz, each 1H, N-benzyl–CH_2), 2.79 and 2.73 (2d, *J* = 13.9 Hz, each 1H, benzyl–CH_2), 2.67 and 2.61 (2dt, *J* = 9.8, 4.8 and 9.8, 5.2 Hz, each 1H), 1.95–1.74, 1.74–1.33, and 1.29–1.18 (3m, 2, 8, and 1H) ppm; ^{13}C NMR: δ = 140.82, 139.10,

130.86 (2C), 128.16 (2C), 128.09 (2C), 127.62 (2C), 126.35, 125.78, 64.25, 51.94, 49.00, 38.48, 38.42, 27.71, 27.53, 26.18, 22.72, 22.15 ppm.

cis- and trans-1,8a-Dibenzyldecahydroquinoline (**16a**, $C_{23}H_{29}N$)

Mg 151.0 mg (6.3 mmol)/*THF* 3 cm^3, benzylbromide 1.08 g (6.3 mmol)/*THF* 10 cm^3, **12a** 400 mg (1.6 mmol)/*THF* 10 cm^3. The mother liquor was evaporated and the *trans* stereomer was separated from the residue by FC.

cis-**16a**. Yield 382 mg (76%) colourless crystals, mp 99°C; TLC (CH_2Cl_2:*Me*OH = 10:0.5): $R_f = 0.73$; MS (CI): m/z (%) = 320 ($M^{+\bullet}$+1, 45), 228 (100), 91 (17); ^{1}H NMR: $\delta = 7.40$ (br d, $J = 7.4$ Hz, 2arom H), 7.29 (br t, $J = 7.4$ Hz, 2arom H), 7.27–7.16 (m, 6arom H), 4.08 and 3.20 (2d, each $J = 14.1$ Hz, each 1H, N-benzyl–CH_2), 3.40 and 2.55 (2d, each $J = 13.3$ Hz, each 1H, benzyl–CH_2), 2.65 (dt, $J = 12.2$, 3.4 Hz, 1H), 2.62–2.56 (m, 1H), 2.28–2.08 and 2.00–1.94 (2m, 2 and 1H), 1.89–1.78, 1.73–1.63, and 1.58–1.51 (3m, 1, 2, and 1H), 1.41–1.33, 1.33–1.21, and 1.20–1.00 (3m, each 2H) ppm; ^{13}C NMR: $\delta = 141.76$, 139.98, 130.83 (2C), 128.20 (2C), 128.10 (2C), 127.79 (2C), 126.30, 125.67, 59.16, 52.22, 46.12, 36.35, 35.30, 33.24 (br), 27.41, 26.66, 26.55 (br), 21.40 (br), 21.11 ppm.

trans-**16a**. Yield 30 mg (6%) colourless crystals, mp 86°C; TLC (CH_2Cl_2:*Me*OH = 10:0.5): $R_f = 0.46$; MS (CI): m/z (%) = 320 ($M^{+\bullet}$+1, 100), 228 (72); ^{1}H NMR: $\delta = 7.37$–7.08 (m, 10arom H), 3.55 and 2.91 (2d, each $J = 15.4$ Hz, each 1H, N-benzyl–CH_2), 3.35 and 2.79 (2d, each $J = 13.9$ Hz, each 1H, benzyl–CH_2), 3.19 (br t, $J = 10.8$ Hz, 1H), 2.59–2.52 and 2.24–2.15 (2m, each 1H), 1.86–1.53 and 1.53–1.12 (2m, 7 and 5H) ppm; ^{13}C NMR: $\delta = 142.21$, 139.30, 130.11 (2C), 127.10 (2C), 126.82 (2C), 126.40 (2C), 124.87 (2C), 59.05, 51.57, 46.32, 45.45, 32.32, 28.99, 28.51, 26.50, 25.51, 24.58, 22.23 ppm.

cis-1,7a-Dibenzyloctahydro-1-pyrindine (**17a**, $C_{22}H_{27}N$)

Mg 266.0 mg (11.1 mmol)/*THF* 3 cm^3, benzylbromide 1.90 g (11.1 mmol)/*THF* 10 cm^3, **13** 665 mg (2.8 mmol)/*THF* 10 cm^3. Yield 684 mg (78%) colourless crystals, mp 119°C; TLC (*n*-hexane:Et_2O = 10:0.5): $R_f = 0.90$; MS (CI): m/z (%) = 306 ($M^{+\bullet}$+1, 100), 214 (15); ^{1}H NMR: $\delta = 7.37$–7.17 (m, 10arom H), 4.06 and 3.24 (2d, each $J = 14.6$ Hz, each 1H, N-benzyl–CH_2), 3.14 and 2.73 (2d, each, $J = 13.2$ Hz, C-benzyl–CH_2), 2.58–2.46 (m, 2H), 1.99–1.67 and 1.59–1.32 (2m, 6 and 5H) ppm; ^{13}C NMR: $\delta = 141.79$, 139.82, 130.72 (2C), 128.10 (2C), 128.00 (2C), 127.81 (2C), 126.30, 125.60, 66.76, 54.08, 46.09, 39.23, 33.48, 33.04, 26.92, 23.26, 21.24, 20.79 ppm.

Hydrogenolyses

The mixture of the benzylamine **15**–**17** (1 molequiv.), *Me*OH, 2 *N* HCl (1 molequiv.), and 10% Pd–C was hydrogenated for 3 h at 50°C and 6.5×10^6 Pa initial pressure of H_2. After centrifuging off the catalyst and washing with 30 cm^3 of *Me*OH the solvent was evaporated *in vacuo*. The residue was dissolved in 10 cm^3 of Et_2O and extracted with 1 *N* HCl (3×10 cm^3). The combined aqueous layers were rendered alkaline with 32% NaOH solution and extracted with Et_2O (3×10 cm^3). After drying the combined ether extracts (Na_2SO_4) the solvent was removed *in vacuo*. If necessary, the products were purified by FC (eluents were the same as used in TLC).

cis-7a-Methyloctahydroindole (**15m**)

15i or **15k** 58 or 61 mg (0.25 mmol), 2 *N* HCl 0.15 cm^3 (0.3 mmol), Pd–C 7 mg, *Me*OH 5 cm^3; yield 30 mg (86%) slight yellowish oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 100:7:1): $R_f = 0.34$; MS (EI): m/z (%) = 139 ($M^{+\bullet}$, 17), 124 (38), 96 (100); ^{1}H NMR data are completely in line with those published in Ref. [21]; ^{13}C NMR: $\delta = 59.71$, 44.38, 42.72, 33.69, 29.99, 26.73, 26.19, 22.92, 22.04 ppm.

cis-8a-Benzyldecahydroquinoliniumchlorid (**16d**-HCl, $C_{16}H_{24}ClN$)

16a 100 mg (0.31 mmol), 2 *N* HCl 0.15 cm^3 (0.3 mmol), Pd–C 10 mg, *Me*OH 5 cm^3; the residue was dissolved in 5 cm^3 of Et_2O and ether saturated with HCl. After removing the solvent the residue was crystallized from *Et*OA*c*. Yield 75 mg (91%) colourless crystals, mp 231°C (*Et*OA*c*); TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 100:9:0.5): $R_f = 0.39$; MS (CI): m/z (%) = 230 (100), 138 (63); ^{1}H NMR (50°C): $\delta = 9.37$ and 8.65 (2br s, each 1H, N^+H_2), 7.36–7.25 (m, 5arom H), 3.54 and 3.13 (2br d, each $J = 13.2$ Hz, each 1H, benzyl–CH_2), 3.46–3.31 (m, 2H), 2.21–1.90, 1.86–1.68, 1.65–1.48, and 1.15–1.03 (4m, 5, 3, 4, and 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 135.00$, 131.11 and 128.52 (each 2C), 127.26, 60.35, 39.96, 39.82, 34.16, 31.50 (br), 26.29, 24.21, 23.82 (br), 20.63, 18.08 (br) ppm.

cis-8a-(3-Methoxyphenyl)-decahydroquinoline (**16e**, $C_{16}H_{23}NO$)

16c 533 mg (1.59 mmol), 2 *N* HCl 0.8 cm^3, Pd–C 65 mg, *Me*OH 8 cm^3; yield 372 mg (95%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 100:5:1): $R_f = 0.21$; MS (EI): m/z (%) = 245 ($M^{+\bullet}$, 24), 202 (100); ^{1}H NMR (45°C): $\delta = 7.26$ (t, $J = 8.0$ Hz, 1arom H), 7.10–7.05 (m, 2H), 6.77–6.73 (ddd, $J = 8.0$, 2.6, 0.9 Hz, 1arom H), 3.81 (s, OCH_3), 2.85–2.79 (m, 1H), 2.74–2.66, 2.45–2.31, 2.07–1.97, 1.82–1.25, and 1.20–1.11 (5m, 1, 1, 1, 11, and 1H) ppm; ^{13}C NMR (40°C): $\delta = 160.13$, 150.23, 129.34, 118.42, 112.62, 110.66, 58.39, 55.26, 43.09 (br), 42.17, 35.90, 27.27, 26.74, 25.98, 22.48, 21.31 ppm.

cis-7a-Benzyloctahydro-1-pyrindine (**17c**, $C_{15}H_{21}N$)

17a 90 mg (0.3 mmol), 2 *N* HCl 0.15 cm^3 (0.3 mmol), Pd–C 9 mg, *Me*OH 5 cm^3; yield 58 mg (91%) colourless oil; TLC (CH_2Cl_2:*Me*OH:NH_3 (25%) = 100:9:0.5): $R_f = 0.39$; MS (CI): m/z (%) = 216 ($M^{+\bullet}$+1, 100), 124 (48); ^{1}H NMR: $\delta = 7.31$–7.27, 7.24–7.20, and 7.19–7.17 (3m, 2, 1, and 2arom H), 3.19 and 2.56 (2d, each $J = 13.3$ Hz, each 1H, benzyl–CH_2), 2.97 (ddd, $J = 12.1$, 10.6, 3.0 Hz, 1H), 2.85–2.81 (m, 1H), 2.55 (br s, NH), 1.90–1.68, 1.67–1.53, and 1.44–1.37 (3m, 6, 3, and 2H) ppm; ^{13}C NMR: $\delta = 138.59$, 130.04, 128.05, 126.06, 66.81, 41.76, 41.04, 40.68, 37.40, 27.92, 23.63, 21.10, 20.46 ppm; **17c**-HCl: mp 185.5°C (*Et*OA*c*/Et_2O).

trans-1-Benzoyloctahydroquinoline-8a-carbonitrile (**20**, $C_{17}H_{20}N_2O$)

To a solution of 200 mg of **12b** (1.23 mmol) and 130 mg of Et_3N (1.29 mmol) in 5 cm^3 of $CHCl_3$ was added a solution of 172 mg of benzoylchloride (1.23 mmol) in 2 cm^3 of $CHCl_3$ and the mixture was heated under reflux for 1.5 h. The cold solution was diluted with 10 cm^3 of $CHCl_3$ and consecutively washed with 2×10 cm^3 of H_2O and 10 cm^3 of saturated NH_4Cl solution. The organic layer was dried (Na_2SO_4) and evaporated. The residue first was purified by FC (silica gel, CH_2Cl_2), then recrystallized from *n*-hexane. Yield 116 mg (35%) colourless crystals, mp 142°C; TLC (CH_2Cl_2): $R_f = 0.38$; IR (KBr): $\bar{\nu} = 2229$ (CN), 1661 and 1636 (C=O) cm^{-1}; MS (CI): m/z (%) = 269 ($M^{+\bullet}$+1, 100), 242 (56), 105 (10); ^{1}H NMR: $\delta = 7.61$–7.56, 7.53–7.44, and 7.43–7.38 (3m, 2, 1, and 2arom H), 3.66–3.58, 3.39–3.32, and 3.31–3.23 (3m, each 1H), 1.92–1.65, 1.64–1.43, and 1.41–1.28 (3m, 8, 3, and 1H) ppm; ^{13}C-NMR: $\delta = 174.19$, 136.05, 131.14, 128.56, 128.27, 118.13, 60.42, 47.06, 42.88, 35.59, 30.27, 26.81, 25.16, 23.56. 23.32 ppm.

cis-(1-Benzyloctahydroindol-7a-yl)phenylmethanone (**21**, $C_{22}H_{25}NO$)

To a solution of 560 mg (2.3 mmol) of **11a** in 5 cm^3 of cyclohexane:Et_2O (7:3) was added 5 cm^3 of 1.8 *M* phenyllithium (9.0 mmol) in the same solvent. After stirring for 16 h at ambient temperature the mixture was quenched with 3 cm^3 of saturated NH_4Cl solution and diluted with 20 cm^3 of 0.5 *N* HCl. The aqueous layer was washed with 2×10 cm^3 of Et_2O, rendered alkaline with saturated Na_2CO_3 solution and extracted with 3×30 cm^3 of Et_2O. The ether extracts were dried (Na_2SO_4) and evaporated

in vacuo. The residue was purified by FC (silica gel, *n*-hexane:$Et_2O = 9{:}1$) giving a colourless oil, which was crystallized from hot *Me*OH. The colourless solid was collected by filtration, washed with a small volume of ice cold *Me*OH, and dried *in vacuo*. Yield 128 mg (17%), mp 100°C (*Me*OH); TLC (for eluent see FC): $R_f = 0.77$; IR (KBr): $\bar{\nu} = 1673$ (C=O) cm^{-1}; MS (CI): m/z (%) = 320 ($M^{+\bullet}$+1, 100), 214 (41); ^{1}H NMR: $\delta = 8.34$–8.31 (m, 2arom H), 7.50 (tt, $J = 7.4$, 1.3 Hz, 1arom H), 7.42–7.37 and 7.36–7.15 (2m, 2 and 5arom H), 3.79 and 3.43 (2d, each $J = 12.9$ Hz, each 1H, benzyl–CH_2), 3.12 (ddd, $J = 9.6$, 7.8, 7.0 Hz, 1H), 3.00–2.91 (m, 1H), 2.61 (dt, $J = 9.6$, 8.1 Hz, 1H), 2.36–2.30 (m, 1H), 1.89 (m, 2H), 1.80–1.71 and 1.60–1.28 (2m, 1 and 6H) ppm; ^{13}C NMR: $\delta = 204.85$, 139.63, 137.39, 131.60, 129.72 (2C), 128.82 (2C), 128.10 (2C), 127.80 (2C), 126.71, 73.84, 54.14, 49.85, 42.57, 26.54, 25.97, 22.98, 22.73, 20.35 ppm.

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