Monatshefte für Chemie 135, 1143–1155 (2004)
DOI 10.1007/s00706-004-0184-8

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

An Improved Stereocontrolled Route to *cis*-Erythrinanes by Combined Intramolecular *Strecker* and *Bruylants* Reaction

Eberhard Reimann* and **Christian Ettmayr**[a]

Department Pharmazie – Zentrum für Pharmaforschung, Ludwig-Maximilians-Universität München, D-81377 München, Germany

Received February 2, 2004; accepted February 4, 2004
Published online June 24, 2004

Summary. Condensation of (2-iodophenyl)ethylamines with cyclohexanoylacetaldehyde provided the corresponding aldimines which were reduced yielding secondary phenethylcyclohexanoylethylamines. These in turn were appropriate intermediates to prepare several erythrinanes by a sequential intramolecular *Strecker* and intramolecular *Bruylants* reaction. In contrast, the C-ring homologue schelhammeranes were not available on this route.

Keywords. Alkaloids; Spiro compounds; Diastereoselective cyclizations; Iodine-magnesium exchange reaction.

Introduction

Very recently we reported a new stereoselective approach to erythrinanes and several homologue ring systems. As educts different angularly arylated N-heterocycles were used, which in turn could be obtained in two steps from certain aminoalkyl cycloalkanones by intramolecular *Strecker* reaction followed by an intermolecular *Bruylants* reaction. The last step generating the C-ring framework was accomplished by *Friedel-Crafts* acylation [1].

A real drawback of this route was seen in the low yields of the *Bruylants* reaction. On the other hand the success of the synthesis depended on the intramolecular acylation of the aromatic subunit; thus dihydroxylated derivatives corresponding to the substitution pattern of the natural occurring erythrinanes as well as the parent compound lacking any phenolic group were not accessible.

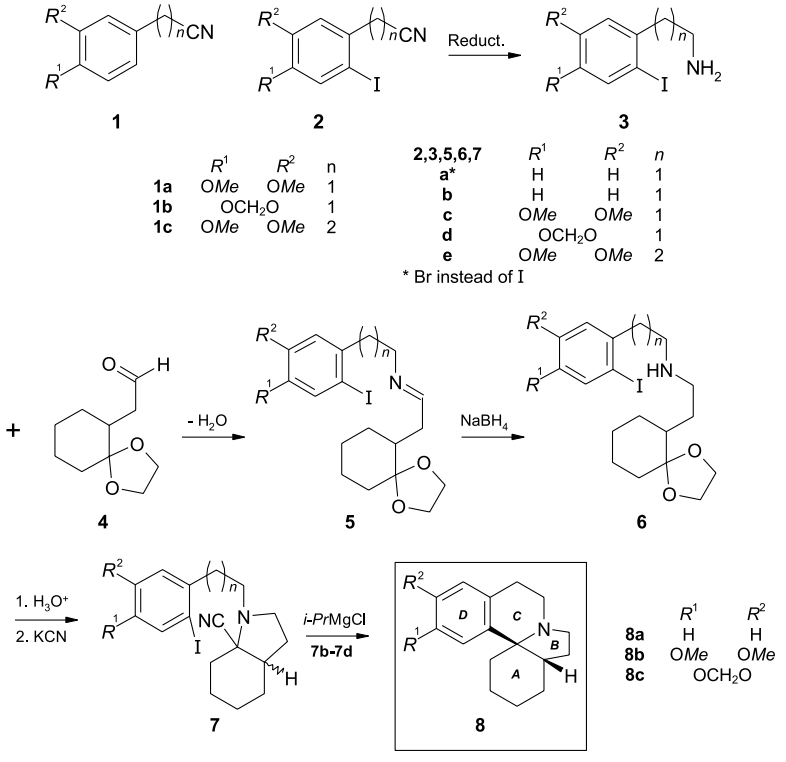
To overcome these limitations an alternative strategy appeared very promising to generate the C-ring. Thus, apart from the *Strecker* reaction the *Bruylants* reac-

* Corresponding author. E-mail: ebrei@cup.uni-muenchen.de
[a] Part of PhD thesis, LMU München, D

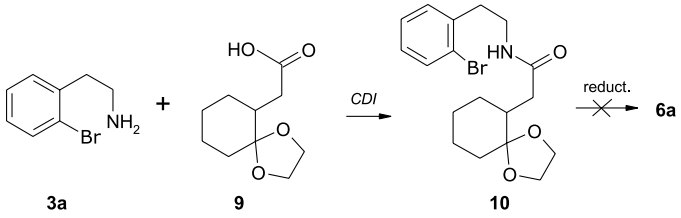
tion was also intended to be carried out intramolecularly. This required the cyclohexanoylphenethylamines **6** as the key intermediates which should avoid not only the separate introduction of the N-9/C-12-bridge but also the crucial *Friedel-Crafts* acylation. Furthermore an intramolecular *Bruylants* reaction was expected to provide higher yields than those obtained in our preceding investigations [2]. In this paper, we would like to report the outcome of this strategy.

Results and Discussion

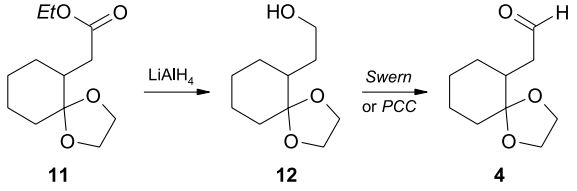
The synthetic pathway is outlined in Scheme 1. First our attention was turned to the required key intermediates, the cyclohexanoylphenethylamines **6**. We anticipated that they might be obtained by acylation of the halogenated phenethylamines **3** with the protected cyclohexanoylacetic acid **9** [2] followed by reduction of the amide **10** formed (Scheme 2). However, the latter defied all our attempts to react with *e.g.* lithium aluminum hydride, diisobutylaluminum hydride or borane, giving exclusively heterogeneous mixtures in which the desired product could not be detected. Therefore the carboxylic acid **9** was replaced by the corresponding aldehyde **4** giving the *Schiff* bases **5**. As indicated by IR- and ^{1}H NMR monitoring the condensation quantitatively occurred. TLC monitoring failed due to the decomposition of the product on silicagel. In contrast to the amides of the type **10**, the imines **5** were smoothly reduced with $NaBH_4$ affording the secondary amines **6** in satisfactory yields (60–67%; Scheme 1). Only in the case of **5d** the yield was



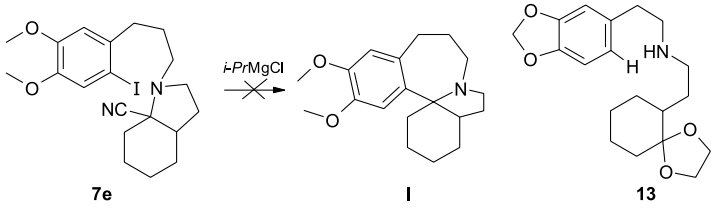
Scheme 1



Scheme 2



Scheme 3



Scheme 4

somewhat lower (49%) due to the additional formation of a small amount (13%) of the dehalogenated amine **13** (Scheme 4 and Exp.)

The required starting cyclohexanoyl derivatives **4**, **9** [2] and **11** [2], as well as the halogenated phenethylamines **3** were easily available. Thus the latter were prepared by reduction of the phenylacetonitriles **2** providing the corresponding known products **3a**–**3d**. To our knowledge no preparation of **3e** has yet been reported. The iodophenylacetonitriles **2c**–**2e** in turn were obtained from the known educts **1a**–**1c** (Scheme 1 and Exp.). Finally, the hithertoo unkwown cyclohexanoylacetaldehyde **4** was synthesized in excellent yields by $LiAlH_4$ reduction of the ester **11** affording the carbinol **12** followed by *Swern* or *PCC* oxidation according to Scheme 3. Attemps to reduce the carboxylic acid **9** or its azolid straight forward to the aldehyde **4** failed.

With the compounds **6** in hand, first the intramolecular *Strecker* reaction was investigated which was expected to provide the N-substituted octahydroindoles of the type **7**. Utilizing a similar procedure previously published [2] the amines **6** readily cyclized giving the α-aminonitriles **7** in nearly quantitative yields. The ^{13}C NMR spectra of the products showed mixtures of diastereomers to be present in ratios from 2:1 to 3:1 (Exp.), but an assignment of the respective configuration failed.

In the final step the cyclization of the α-aminonitriles **7** by the *Bruylants* reaction was studied using similar conditions as previously reported [2]. Thus, in an

initially model reaction the bromo-compound **7a** was treated with magnesium to generate the *Grignard* reagent, which in turn should start the following *Bruylants* reaction. However, the desired cyclization did not occur. Only the educt and a substantial amount of the dehalogenated educt indicating that the *Grignard* reagent was really formed, could be detected by NMR and mass spectroscopy. Furthermore, an unidentified compound lacking the cyano-group was isolated.

Because of these complex reaction mixtures obtained, a more efficient and clean generation of the required *Grignard* reagents was desirable. The iodine-magnesium exchange reaction [3] using *i*-propylmagnesiumhalogenide appeared to be very promising for this purpose, since it occurs at low temperature and tolerates a number of magnesium sensitive functional groups, including the cyano group, even attached in the same molecule as in the present compounds **7b**–**7e**. The following *Bruylants* reaction then should be initiated by elevating the temperature of the reaction mixture. According to this strategy we reacted the iodinated compounds **7b**–**7e** with a small excess of *i*-propylmagnesiumchloride in *THF* at -50°C, then the reaction mixture was slowly warmed up to ambient temperature and finally to 60°C. Thus the *cis*-erythrinanes **8a**–**8c** were stereoselectively obtained with surprisingly good yields (71–78%) in contrast to those (11–34%) obtained from the intermolecular reaction of α-aminonitriles with conventionally generated aryl *Grignard* reagents [2]. To our knowledge this cyclization represents the first example of a *Bruylants* reaction which has been carried out intramolecularly.

The *cis*-configuration of the title compounds was proved by NMR spectroscopy. Thus in the case of the dimethoxy derivative **8b** the ^{1}H and ^{13}C spectra were completely in line with those published [4, 5]. Furthermore the spectra of the parent compound **8a** and of the methylenedioxy derivative **8c** lacking until now were – except for the data of the aromatic subunit – in good accordance with that of the *cis*-15-monomethoxyerythrinane [1]. Additionally their *cis*-configuration was confirmed by a positive N*O*E between 6-H and 14-H [1].

Unfortunately, the corresponding α-aminonitrile **7e** did not provide the expected schelhammerane I. This was not surprising because it is well known, that the construction of the C-homoerythrinane framework is far more difficult than that of the erythrinane, that is, methods developed for the synthesis of erythrinanes are not automatically transferable to schelhammerane synthesis. This substantial difference concerning the synthesis of both ring systems is attributed to the skewed nature of the sevenmembered ring [6]. In this connection MMX force field calculations [7] are of interest revealing the parent *cis*-erythrinane to be essentially more stable than the corresponding homologue schelhammerane. Assuming the chair form of the benzocycloheptene core [8] the strain energy difference was found to be $\Delta SE = 41.5$ kJ.

In conclusion, we established a new stereoselective approach to aromatic *cis*-erythrinanes by a two fold intramolecular *Strecker* and *Bruylants* reaction. This route involving readily available starting materials and providing a satisfactory overall yield offered the possibility to prepare the parent framework as well as the dihydroxylated derivatives both not obtainable otherwise [1]. In contrast the aminonitrile **7e** failed to give the *Bruylants* reaction forming the homologue schelhammerane. Further investigations in this field are currently in progress.

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); 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): Al sheets Kieselgel 60 F_{254} (Merck) and Al 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. **3b** is reported in Ref. [9], but preparation and analytical data are lacking (see below). **1a**, **1b**, and **2a** are commercial products; **2b** and **1c** were prepared according to Refs. [10] and [11].

*General Procedure for the Synthesis of 2-(2-Iodophenyl)acetonitriles **2c–2e***

To a solution of the phenylacetonitrile **1** (1 molequiv.) in anhydrous CH_2Cl_2 was added F_3CCO_2Ag and I_2 (1.1 molequiv. each) at −5°C and the mixture was stirred for 6 min. The end of the reaction was indicated by a light red colour of the mixture. The yellow solid formed was filtered off and washed with 50 cm^3 of CH_2Cl_2. The fitrate was consecutively washed with 3 × 100 cm^3 of saturated $Na_2S_2O_3$ and 150 cm^3 of brine, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was crystallized from CH_3OH. The crystals were filtered off, washed with a small amount of ice-cold CH_3OH and dried *in vacuo*. When the crystallization failed or no further product could be obtained from the mother liquor, the solvent was removed *in vacuo* and the residue was purified by FC (eluents see TLC).

2-(2-Iodo-4,5-dimethoxyphenyl)acetonitrile (**2c**)

1a 8.05 g (45.5 mmol), F_3CCO_2Ag 11.04 g (50.0 mmol), I_2 12.7 g (50 mmol), CH_2Cl_2 100 cm^3; yield: 12.80 g (93%; Ref. [12]: 41%) colourless crystals; mp 118°C (Ref. [12]: 116–117°C); TLC (CH_2Cl_2): $R_f = 0.52$; MS (CI): m/z (%) = 304 ($M^{+\bullet} + 1$, 100), 277 (97), 244 (61), 177 (20); ^{1}H NMR data were in line with those reported in Ref. [12].

2-(2-Iodo-3,4-methylenedioxyphenyl)acetonitrile (**2d**, $C_9H_6INO_2$)

1b 5.33 g (33.1 mmol), F_3CCO_2Ag 8.04 g (36.4 mmol), I_2 9.25 g (36.4 mmol), CH_2Cl_2 75 cm^3; yield: 7.68 g (81%) colourless crystals; mp 84°C (CH_3OH); TLC (CH_2Cl_2): $R_f = 0.75$; MS (CI): m/z (%) = 288 ($M^{+\bullet} + 1$, 100), 261 (75), 161 (8); IR (KBr): $\bar{\nu} = 2251$ (CN) cm^{-1}; ^{1}H NMR: $\delta = 7.27$ and 7.02 (2s, 2 arom H), 6.02 and 3.74 (2s, OCH_2O and CH_2CN) ppm; ^{13}C NMR: $\delta = 149.07$, 148.51, 126.14, 118.78, 117.26, 109.15, 102.08, 87.08, 29.65 ppm.

3-(2-Iodo-4,5-dimethoxyphenyl)propionitrile (**2e**, $C_{11}H_{12}INO_2$)

1c 4.50 g (23.6 mmol), F_3CCO_2Ag 5.72 g (25.9 mmol), I_2 6.58 g (25.9 mmol), CH_2Cl_2 75 cm^3; yield: 6.08 g (81%) colourless crystals; mp 77°C (Et_2O); TLC (*Et*OA*c*:*n*-hexane = 1:1): $R_f = 0.68$; MS (EI): m/z (%) = 317 ($M^{+\bullet}$, 38), 277 (100), 234 (3), 150 (10); IR (KBr): $\bar{\nu} = 2245$ (CN) cm^{-1}; ^{1}H NMR: $\delta = 7.23$ and 6.83 (2s, 2 arom H), 3.87 and 3.86 (2s, $2OCH_3$), 3.01 and 2.63 (2t, each $J = 7.3$ Hz, benzyl-CH_2 and CH_2CN) ppm; ^{13}C NMR: $\delta = 149.58$, 148.80, 132.86, 121.83, 118.82, 112.67, 87.39, 56.20, 56.04, 36.18, 18.19 ppm.

2-(2-Bromophenyl)ethylamine (**3a**)

Preparation according to Ref. [13] from **2a** 4.40 g (22.45 mmol)/Et_2O 20 cm^3, anhydrous $AlCl_3$ 3.60 (27.0 mmol), $LiAlH_4$ 1.33 g (27.0 mmol), Et_2O 110 cm^3; purification by FC (CH_2Cl_2:CH_3OH:25%

$NH_3 = 100:5:1$) instead of destillation; yield: 3.83 g (85%) colourless oil; TLC (eluent see FC): $R_f = 0.25$; ^1H and ^{13}C NMR were in line with those reported [13].

*General Procedure for the Synthesis of (2-Iodophenyl)ethylamines **3b–3e***

To a solution of the nitrile **2** in anhydrous *THF* was added dropwise 1 *M* borane complex in the same solvent (=BH_3-*THF*). After refluxing for 16 h the mixture was cautiously diluted with CH_3OH under N_2 and ice cooling until no more foam was formed. The solvents were evaporated *in vacuo* and after dissolving the residue in 15 cm^3 of CH_3OH evaporation was repeated. Now the residue was dissolved in 30 cm^3 of 0.5 *N* HCl and the solution was refluxed for 1 h. After washing with 3×30 cm^3 of Et_2O the mixture was rendered alkaline by 32% NaOH and extracted with 3×50 cm^3 of Et_2O. The combined ether extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The products thus obtained were purified by FC (eluents see TLC).

2-(2-Iodophenyl)ethylamine (**3b**)

2b 2.00 g (8.2 mmol), BH_3-*THF* 20 cm^3 (20 mmol), *THF* 10 cm^3; yield: 1.66 g (82%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% $NH_3 = 100:5:1$): $R_f = 0.27$; MS (EI): m/z (%) = 246 ($M^{+\bullet} - 1$, 100), 231 (15), 217 (46), 104 (23), 91 (30), 90 (32); ^1H NMR: $\delta = 7.82$ (dd, $J = 7.7/1.0$ Hz, arom H), 7.28 (dt, $J = 7.5/1.0$ Hz, arom H), 7.22 (d, $J = 7.5/1.6$ Hz, arom H), 6.90 (dt, $J = 7.7/1.6$ Hz, arom H), 2.98–2.91 (t, $J = 7.2$ Hz, benzyl–CH_2), 2.91–2.84 (t, $J = 7.2$ Hz, N–CH_2) ppm; ^{13}C NMR: $\delta = 142.37$, 139.56, 129.82, 128.29, 128.04, 100.82, 44.74, 42.35 ppm. **3b**-HCl: see Ref. [14].

2-(2-Iodo-4,5-dimethoxyphenyl)ethylamine (**3c**)

2c 5.00 g (16.5 mmol), BH_3-*THF* 40 cm^3 (40 mmol), *THF* 25 cm^3; yield: 4.05 g (80%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% $NH_3 = 100:8:0.5$): $R_f = 0.14$; MS (CI): m/z (%) = 308 ($M^{+\bullet} + 1$, 100), 278 (13), 180 (67), 164 (53), 152 (45); ^1H NMR: $\delta = 7.22$ and 6.75 (2s, 2 arom H), 3.86 and 3.85 (2s, 2OCH_3), 2.93 and 2.82 (2t, each $J = 7.0$ Hz, benzyl–CH_2 and N–CH_2), 1.40 (br s, NH_2) ppm. Analytical data are reported only for the hydrochloride and for the *N*-acetylderivatives (see Refs. [12, 15]).

2-(2-Iodo-3,4-methylenedioxyphenyl)ethylamine (**3d**)

2d 7.00 g (24.4 mmol), BH_3-*THF* 70 cm^3 (70 mmol), *THF* 50 cm^3; yield: 5.86 g (83%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% $NH_3 = 100:8:0.5$): $R_f = 0.22$; MS (CI): m/z (%) = 292 ($M^{+\bullet} + 1$, 100), 275 (21), 164 (35), 148 (40); ^1H and ^{13}C NMR data were in line with those published in Ref. [16].

2-(2-Iodo-4,5-dimethoxyphenyl)propylamine (**3e**, $C_6H_{11}INO_2$)

2e 3.50 g (11.0 mmol), BH_3-*THF* 35 cm^3 (35 mmol), *THF* 20 cm^3; yield: 3.18 g (90%) colourless amorphous solid; TLC (CH_2Cl_2:CH_3OH:25% $NH_3 = 100:10:1$): $R_f = 0.25$; MS (CI): m/z (%) = 322 ($M^{+\bullet} + 1$, 87), 195 (100), 194 (70), 178 (32), 166 (10); ^1H NMR: $\delta = 7.20$ and 6.74 (2s, 2 arom H), 3.85 and 3.84 (2s, 2OCH_3), 2.22 (t, $J = 7.0$ Hz, benzyl–CH_2), 2.71–2.68 (m, N–CH_2), 1.77–1.69 (m, 4H, CCH_2C and NH_2) ppm; ^{13}C NMR: $\delta = 149.35$, 147.75, 137.08, 121.63, 112.13, 87.89, 56.15, 55.93, 41.64, 37.78, 34.43 ppm.

N-[2-(2-Bromophenyl)ethyl]-2-(1,4-dioxaspiro[4.5]dec-6-yl)acetamide (**10**, $C_{18}H_{24}BrNO_3$)

Preparation according to the general procedure reported in Ref. [2] from (1,4-dioxaspiro[4.5]dec-6-yl)acetic acid [2] 1.00 g (5.00 mmol), CDI 794 mg (4.90 mmol), **3a** 1.01 g (5.05 mmol), *THF* 20 cm^3.

After refluxing the mixture for 8 h the solvent was removed *in vacuo* and the residue was dissolved in 25 cm^3 of CH_2Cl_2. The solution was consecutively washed with 3×15 cm^3 of H_2O, 15 cm^3 of 1 *N* HCl, and 2×25 cm^3 of saturated Na_2CO_3 solution, dried (Na_2SO_4), and evaporated *in vacuo*. Further purification was performed as reported. Yield: 1.12 g (58%) colourless crystals; mp 90°C (*Et*$_2$O); TLC (CH_2Cl_2:CH_3OH = 100:5): $R_f = 0.51$; MS (CI): m/z (%) = 384 ($M^{+\bullet} + 1$, 97), 382 ($M^{+\bullet} + 1$, 100), 212 (5), 183 (15); IR (film): $\bar{\nu} = 3289$ (NH), 1642 (amide I), 1551 (amide II) cm^{-1}; ^{1}H NMR: $\delta = 7.53$ (br d, $J = 7.9$ Hz, arom H), 7.26–7.22 (m, 2 arom H), 7.09 (ddd, $J = 7.9/5.6/3.5$ Hz, arom H), 5.81 (br s, NH), 3.97–3.79 (m, OCH_2–CH_2O), 3.53 (ddd, $J = 13.0/7.0/4.2$ Hz, NCH_2), 2.97 (t, $J = 7.0$ Hz, benzyl-CH_2), 2.49 and 1.87 (2dd, $J = 14.5/4.8$ Hz and 14.5/8.4 Hz, 2H, CH_2CON), 2.17–2.10 (m, CH), 1.81–1.73 and 1.67–1.56 (2m, each 2H), 1.52–1.40 (m, 1H), 1.38–1.24 (m, 3H) ppm; ^{13}C NMR: $\delta = 172.85$, 138.44, 132.89, 130.98, 128.17, 127.55, 124.62, 110.11, 64.55, 64.47, 41.72, 39.14, 36.69, 35.80, 34.26, 30.15, 24.52, 23.71 ppm.

2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethanol (**12**), *Modified Procedure According to Ref.* [17]

To a solution of 9.12 g (40 mmol) of the cyclohexanone ester **11** [2] in 100 cm^3 of anhydrous *Et*$_2$O was portionwise added 3.04 g (80 mmol) of $LiAlH_4$ under N_2, ice cooling, and stirring. After removing of the ice bath the mixture was allowed to return to ambient temperature followed by refluxing for 30 min. The reaction was quenched by cautiously pouring the ice-cold mixture into 2 *N* NaOH and *Et*$_2$O (100 cm^3 in each case) under N_2, ice cooling, and stirring. The organic phase was separated and the aqueous layer was extracted with 3×100 cm^3 of *Et*$_2$O. The combined organic layers were washed with 250 cm^3 of brine, dried (Na_2SO_4), and evaporated *in vacuo*. The remaining product was used for the next step without further purification. Yield: 7.16 g (96%) colourless oil; MS (EI): m/z (%) = 186 ($M^{+\bullet}$, 5), 155 (35), 125 (12), 99 (100), 55 (62); IR and ^{1}H NMR data were in line with those reported [17, 18]; ^{13}C NMR: $\delta = 110.58$, 64.60, 64.33, 61.56, 41.86, 34.72, 32.24, 30.46, 24.55, 23.68 ppm.

(1,4-Dioxa-spiro[4.5]dec-6-yl)acetaldehyde (**4**, $C_{10}H_{16}O_3$)

Method A (*Swern* oxidation): To a solution of 2.16 cm^3 (23.8 mmol) of oxalyl chloride in 40 cm^3 of anhydrous CH_2Cl_2 was slowly added a solution of 3.7 cm^3 (47.5 mmol) of *DMSO* in 10 cm^3 of the same solvent at −70°C under N_2. After stirring for 30 min first a solution of 4.00 g (21.5 mmol) of the alcohol **12** in 20 cm^3 of CH_2Cl_2 then, after stirring for further 30 min, 15.2 cm^3 (~109 mmol) of triethyl amine were added dropwise. After warming up to ambient temperature the mixture was diluted with 70 cm^3 of H_2O, the organic phase was separated, and the aqueous layer was extracted with 2×50 cm^3 of CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with saturated Na_2CO_3 solution, dried (Na_2SO_4), and evaporated *in vacuo*. Yield: 3.76 g (95%) colourless oil.

Method B (oxidation with pyridinium chlorochromate (*PPC*)): To a suspension of 2.68 g (12.4 mmol) of *PPC* and 203 mg (2.48 mmol) of sodium acetate in 15 cm^3 of anhydrous CH_2Cl_2 was rapidly added a solution of 1.54 g (8.28 mmol) of **12** in 5 cm^3 of the same solvent. After stirring for 2 h at ambient temperature the mixture was diluted with 60 cm^3 of *Et*$_2$O. The organic layer was decanted and the black residue washed with 3×30 cm^3 of *Et*$_2$O. The combined organic phases were rapidly filtered by a short column (SiO_2, $h \times d = 3 \times 7$ cm), and the eluat was evaporated *in vacuo*. Yield: 1.37 g (90%) colourless oil; IR (film): $\bar{\nu} = 1720$ (C=O) cm^{-1}; MS (CI): m/z (%) = 185 ($M^{+\bullet} + 1$, 22), 183 (63), 155 (21), 139 (100), 125 (42), 99 (28); ^{1}H NMR: $\delta = 9.67$ (dd, $J =$ 3.7/1.7 Hz, CHO), 4.00–3.87 and 3.84–3.75 (2m, OCH_2CH_2O), 2.50 and 2.14 (2ddd, $J =$ 15.9/7.7/3.7 and 15.9/5.5/1.7 Hz, 2H, CH_2CO), 2.31 (dddd, $J = 11.6/7.7/5.5/1.7$ Hz, CH), 1.84–1.64 and 1.55–1.25 (2m, each 4H) ppm; ^{13}C NMR: $\delta = 201.85$, 109.71, 64.74, 64.11, 44.40, 40.47, 34.55, 30.49, 24.89, 23.68 ppm.

General Procedure for the Synthesis of Imines **5**

A mixture of the aldehyde **4** and the primary amine **3** (each 1 molequiv.) in anhydrous toluene was refluxed with water separation by a *Dean-Stark* trap until the reaction was completed (about 2 h, IR monitoring). Evaporation of the solvent *in vacuo* afforded yellow oils in nearly quantitative yields.

[2-(2-Bromophenyl)ethyl][2-(1,4-dioxaspiro[4.5]dec-6-yl)ethylidene]amine
(**5a**, $C_{18}H_{24}BrNO_2$)

4 877 mg (4.77 mmol), **3a** 954 mg (4.77 mmol), toluene 60 cm^3; yield: 1.73 g (99%); IR (film): $\bar{\nu} = 1667$ (N=C) cm^{-1}; MS (CI): m/z (%) = 368 ($M^{+\bullet} + 1$, 87), 366 ($M^{+\bullet} + 1$, 100), 286 (7), 227 (14), 225 (14), 196 (27), 146 (22), 99 (14); ^{1}H NMR: $\delta = 7.57–7.53$ (m, N=CH), 7.53–7.50 (m, 1 arom H), 7.24–7.16 and 7.07–7.01 (2m, 2 + 1 arom H), 3.96–3.82 (m, OCH_2CH_2O), 3.60 (dt, $J = 7.5/0.8$ Hz, NCH_2), 3.02 (t, $J = 7.5$ Hz, benzyl–CH_2), 2.47 (ddt, $J = 14.7/4.9/1.0$ Hz, 1H, N=C–CH_2), 2.04 (ddd, $J = 14.7/8.1/5.8$ Hz, 1H, N=CH–CH_2), 1.92–1.84 (m, CH), 1,77 (ddt, $J = 12.8/3.8/1.3$ Hz, 1H), 1.68–1.57 (m, 3H), 1.54–1.41 (m, 1H), 1.41–1.15 (m, 3H) ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethylidene][2-(2-iodophenyl)ethyl]amine
(**5b**, $C_{18}H_{24}INO_2$)

4 1.00 g (5.43 mmol), **3b** 1.34 g (5.43 mmol), toluene 60 cm^3; yield: 2.20 g (98%); IR (film): $\bar{\nu} = 1667$ (N=C) cm^{-1}; MS (CI): m/z (%) = 414 ($M^{+\bullet} + 1$, 100), 273 (8), 198 (14), 146 (7); MS (EI): m/z (%) = 286 ($M^{+\bullet} - I$, 22), 272 (42), 224 (23), 196 (62), 146 (72), 124 (33), 104 (37), 99 (24), 56 (100), 55 (52); ^{1}H NMR (500 MHz): $\delta = 7.80$ (dd, $J = 7.8/1.2$ Hz, 1 arom H), 7.57 (br t, $J = 5.1$ Hz, N=CH), 7.25 (dt, J = 7.5/1.2 Hz, 1 arom H), 7.20 (dd, $J = 7.5/1.8$ Hz, 1 arom H), 6.88 (dt, $J = 7.8/1.8$ Hz, 1 arom H), 3.95–3.88 and 3.87–3.84 (2m, 3 + 1H, OCH_2CH_2O), 3.59 (br t, $J = 7.5$ Hz, NCH_2), 3.01 (dt, $J = 7.5/1.8$ Hz, benzyl–CH_2), 2.49 (dt, $J = 14.7/4.9$ Hz, 1H, N = C–CH_2), 2.10–2.02 (ddd, $J = 14.5/8.3/5.8$ Hz, 1H, N = C–CH_2), 1.93–1.86 (m, CH), 1.80–1.74 (ddt, $J = 13.0/3.7/1.1$ Hz, 1H), 1.66–1.59 and 1.53–1.43 (2m, 3 + 1H), 1.39–1.28 and 1.27–1.17 (2m, 2 + 1H) ppm; ^{13}C NMR (100 MHz): $\delta = 166.05$, 142.48, 139.43, 130.39, 128.14, 127.92, 110.16, 100.69, 64.83, 64.49, 60.83, 42.38, 42.00, 35.63, 34.87, 29.87, 24.68, 23.80 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethylidene][2-(2-iodo-4,5-dimethoxyphenyl)ethyl]amine
(**5c**, $C_{20}H_{28}INO_4$)

4 887 mg (4.82 mmol), **3c** 1.48 g (4.82 mmol), toluene 60 cm^3; yield: 2.23 g (98%); IR (film): $\bar{\nu} = 1666$ (N=C) cm^{-1}; MS (CI): m/z (%) = 474 ($M^{+\bullet} + 1$, 100), 346 (56), 196 (42), 125 (13), 99 (16); ^{1}H NMR (500 MHz): $\delta = 7.54$ (br t, $J = 5.1$ Hz, N=CH), 7.20 and 6.72 (2s, 2 arom H), 3.98–3.84 (m, OCH_2CH_2O), 3.84 and 3.83 (2s, $2OCH_3$), 3.57 (br t, $J = 7.3$ Hz, N–CH_2), 2.95 (dt, $J = 7.3/1.6$ Hz, benzyl–CH_2), 2.48 (dt, $J = 14.7/4.9$ Hz, 1H, N=C–CH_2), 2.09–2.00 (ddd, $J = 14.5/8.2/5.9$ Hz, 1H, N=C–CH_2), 1.92–1.83 (m, CH), 1.80–1.73 (ddt, $J = 12.8/3.8/1.4$ Hz, 1H), 1.67–1.56 and 1.53–1.40 (2m, 3 + 1H), 1.39–1.28 and 1.28–1.15 (2m, 2 + 1H) ppm; ^{13}C NMR (100 MHz): $\delta = 166.12$, 149.06, 147.91, 134.86, 121.55, 113.29, 110.11, 88.02, 64.82, 64.38, 61.39, 56.09, 55.85, 42.41, 41.50, 35.61, 34.86, 29.89, 24.66, 23.77 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethylidene][2-(2-iodo-4,5-methylenedioxyphenyl) ethyl]amine (**5d**, $C_{19}H_{24}INO_4$)

4 632 mg (3.44 mmol), **3d** 1.00 g (3.44 mmol), toluene 50 cm^3; yield: 1.54 g (98%); IR (film): $\bar{\nu} = 1666$ (N=C) cm^{-1}; MS (CI): m/z (%) = 458 ($M^{+\bullet} + 1$, 100), 330 (72), 196 (42), 125 (60), 99 (16); ^{1}H NMR

(500 MHz): $\delta = 7.59–7.57$ (m, N=CH), 7.22 and 6.73 (2s, 2H), 5.93 and 5.92 (2d, each $J = 1.4$ Hz, OCH_2O), 3.98–3.88 and 3.88–3.85 (2m, 3 + 1H, OCH_2CH_2O), 3.53 (br t, $J = 7.4$ Hz, N–CH_2), 2.93 (dt, $J = 7.4/1.5$ Hz, benzyl–CH_2), 2.49 (dt, $J = 14.8/4.9$ Hz, 1H, N=C–CH_2), 2.10–2.04 (ddd, $J = 14.7/8.1/5.9$ Hz, 1H, N=C–CH_2), 1.94–1.88 (m, CH), 1.90 (ddt, $J = 13.1/3.8/1.4$ Hz, 1H), 1.67–1.59 and 1.53–1.43 (2m, 3 + 1H), 1.40–1.28 and 1.28–1.19 (2m, 2 + 1H) ppm; ^{13}C NMR (100 MHz): $\delta = 166.10$, 148.27, 146.98, 135.77, 118.51, 110.21, 110.17, 101.46, 87.94, 64.84, 64.51, 61.04, 42.42, 41.88, 35.64, 34.86, 29.89, 24.67, 23.83 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethylidene][3-(2-iodo-4,5-dimethoxyphenyl) propyl]amine (**5e**, $C_{21}H_{30}INO_4$)

4 950 mg (5.16 mmol), **3e** 1.66 g (5.16 mmol), toluene 60 cm^3; yield: 2.44 g (97%); IR (film): $\bar{\nu} = 1666$ (N=C) cm^{-1}; MS (CI): m/z (%) = 488 ($M^{+\bullet} + 1$, 100), 360 (32), 322 (20), 125 (20); ^{1}H NMR (400 MHz): $\delta = 7.71–7.68$ (m, N=CH), 7.20 and 6.74 (2s, 2 arom H), 3.96–3.88 (m, OCH_2CH_2O), 3.86 and 3.84 (2s, $2OCH_3$), 3.43 (t, $J = 6.8$ Hz, N–CH_2), 2.67–2.63 (m, benzyl–CH_2), 2.54 (tt, $J = 14.6/5.0$ Hz, 1H, N=C–CH_2), 2.11 (ddd, $J = 14.6/8.2/5.7$ Hz, 1H, N=C–CH_2), 2.00–1.93 (m, CH), 1.92–1.83 and 1.83–1.58 (2m, 2 + 4H), 1.55–1.43 and 1.43–1.19 (2m, 1 + 3H) ppm; ^{13}C NMR (100 MHz): $\delta = 165.42$, 149.34, 147.74, 137.22, 121.69, 112.18, 110.23, 87.95, 64.85, 64.54, 60.61, 56.16, 55.91, 42.47, 38.14, 35.69, 34.89, 31.58, 30.02, 24.75, 23.81 ppm.

General Procedure for the Synthesis of Secondary Amines **6**

The crude imine **5** (see above) was dissolved in CH_3OH and $NaBH_4$ was added under ice cooling. After refluxing the mixture for 2 h the solvent was removed *in vacuo*. The residue was diluted with 50 cm^3 of H_2O and extracted with 3×50 cm^3 of Et_2O. The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by FC (eluents were the same as used for TLC).

[2-(2-Bromophenyl)ethyl][2-(1,4-dioxaspiro[4.5]dec-6-yl)ethyl]amine (**6a**, $C_{18}H_{26}BrNO_2$)

5a 1.73 g (4.72 mmol), $NaBH_4$ 538 mg (14.2 mmol), CH_3OH 70 cm^3; yield: 1.14 g (65%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:5:0.5): $R_f = 0.28$; IR (film): $\bar{\nu} = 3321$ (NH) cm^{-1}; MS (CI): m/z (%) = 370 ($M^{+\bullet} + 1$, 100, ^{81}Br), 368 ($M^{+\bullet} + 1$, 100, ^{79}Br), 198 (79), 138 (17); ^{1}H NMR (400 MHz): $\delta = 7.53$ (br d, $J = 7.8$ Hz, arom H), 7.26–7.22 (m, 2 arom H), 7.06 (ddd, $J = 7.8/6.0/3.1$ Hz, arom H), 3.98–3.89 (m, OCH_2CH_2O), 2.97–2.92 (m, benzyl–CH_2), 2.90–2.85 (m, aryl–C–CH_2N), 2.72 (ddd, $J = 11.3/9.9/5.3$ Hz, 1H, CH_2N), 2.61 (ddd, $J = 11.3/9.4/6.4$ Hz, 1H, CH_2N), 1.83–1.73 and 1.66–1.57 (2m, each 3H), 1.55–1.40 and 1.40–1.17 (2m, 2 + 4H) ppm; ^{13}C NMR (100 MHz): $\delta = 139.52$, 132.84, 130.70, 127.76, 127.37, 124.58, 110.66, 64.72, 64.55, 49.48, 48.24, 42.65, 36.72, 34.57, 29.61, 28.98, 24.45, 23.77 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl][2-(2-iodophenyl)ethyl]amine (**6b**, $C_{18}H_{26}INO_2$)

5b 2.20 g (5.32 mmol), $NaBH_4$ 606 mg (16.0 mmol), CH_3OH 70 cm^3; yield: 1.48 g (66%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:4:0.5): $R_f = 0.41$; IR (film): $\bar{\nu} = 3321$ (NH) cm^{-1}; MS (CI): m/z (%) = 416 ($M^{+\bullet} + 1$, 100), 288 (4), 198 (77); ^{1}H NMR (500 MHz): $\delta = 7.81$ (dd, $J = 7.7/1.2$ Hz, arom H), 7.27 (dt, $J = 7.6/1.2$ Hz, arom H), 7.23 (dd, $J = 7.6/1.9$ Hz, arom H), 6.89 (dt, $J = 7.7/1.9$ Hz, arom H), 3.98–3.88 (m, OCH_2CH_2O), 2.94–2.89 and 2.87–2.83 (2m, benzyl–CH_2 and aryl–C–CH_2N), 2.72 (ddd, $J = 11.3/9.9/5.3$ Hz, 1H, CH_2N), 2.62 (ddd, $J = 11.3/9.4/6.4$ Hz, 1H, CH_2N), 1.83–1.72 and 1.66–1.57 (2m, each 3H), 1.53–1.43 and 1.38–1.18 (2m, 1 + 5H) ppm; ^{13}C NMR (100 MHz): $\delta = 142.80$, 139.54, 129.77, 128.31, 127.95, 110.66, 100.67, 64.76, 64.60, 49.78, 48.30, 42.67, 41.26, 34.61, 29.62, 28.99, 24.48, 23.80 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl][2-(2-iodo-4,5-dimethoxyphenyl)ethyl]amine (**6c**, $C_{20}H_{30}INO_4$)

5c 2.23 g (4.71 mmol), $NaBH_4$ 537 mg (14.1 mmol), CH_3OH 70 cm^3; yield: 1.53 g (67%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:5:0.5): R_f = 0.28; IR (film): $\bar{\nu}$ = 3316 (NH) cm^{-1}; MS (CI): m/z (%) = 476 ($M^{+\bullet}$ + 1, 64), 348 (7), 277 (5), 198 (100); ^{1}H NMR (500 MHz): δ = 7.21 and 6.77 (2s, 2 arom H), 3.99–3.88 (m, OCH_2CH_2O), 3.85 and 3.84 (2s, $2OCH_3$), 2.89–2.79 (m, 4H), 2.73 (ddd, J = 11.3/9.8/5.3 Hz, 1H, CH_2N), 2.62 (ddd, J = 11.3/9.3/6.4 Hz, 1H, CH_2N), 1.84–1.72 and 1.68–1.56 (2m, 3 + 4H), 1.54–1.41 and 1.38–1.16 (2m, 1 + 4H) ppm; ^{13}C NMR (100 MHz): δ = 149.32, 147.97, 135.18, 121.75, 112.62, 110.66, 88.05, 64.76, 64.60, 56.16, 55.94, 49.99, 48.35, 42.68, 40.79, 34.59, 29.67, 28.99, 24.49, 23.80 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl][2-(2-iodo-4,5-methylenedioxyphenyl)ethyl]amine (**6d**, $C_{19}H_{26}INO_4$) *and [2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl][2-(3,4-methylenedioxyphenyl)ethyl]amine* (**13**, $C_{19}H_{27}NO_4$)

5d 1.54 g (3.37 mmol), $NaBH_4$ 384 mg (10.1 mmol), CH_3OH 60 cm^3. 1. Fraction **6d**: yield: 782 mg (49%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:8:0.5): R_f = 0.38; IR (film): $\bar{\nu}$ = 3315 (NH) cm^{-1}; MS (CI): m/z (%) = 460 ($M^{+\bullet}$ + 1, 38), 332 (11), 261 (2), 198 (100); ^{1}H NMR (400 MHz): δ = 7.23 and 6.77 (2s, 2H), 5.94 (s, 2H), 3.99–3.91 (m, OCH_2CH_2O), 2.88–2.77 (m, 4H), 2.73 (ddd, J = 11.5/9.9/5.3 Hz, 1H, CH_2N), 2.62 (ddd, J = 11.5/9.6/6.6 Hz, 1H, CH_2N), 1.85–1.72 and 1.67–1.58 (2m, 4 + 3H), 1.54–1.40 and 1.39–1.18 (2m, 1 + 4H) ppm; ^{13}C NMR (100 MHz): δ = 148.45, 146.92, 135.85, 118.63, 110.65, 109.64, 101.52, 87.86, 64.77, 64.60, 49.82, 48.26, 42.68, 40.87, 34.59, 29.68, 28.84, 24.50, 23.79 ppm.

2. Fraction **13**: yield: 152 mg (13%); TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:8:0.5): R_f = 0.32; IR (film): $\bar{\nu}$ = 3316 (NH) cm^{-1}; MS (CI): m/z (%) = 344 ($M^{+\bullet}$ + 1, 100), 198 (44); MS (EI): m/z (%) = 198 (100), 138 (97), 125 (12), 99 (7), 55 (41); ^{1}H NMR (400 MHz): δ = 6.74 (dd, J = 7.9/0.9 Hz, 1H), 6.71 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H), 5.92 (d, J = 1.3 Hz, OCH_2O), 3.98–3.87 (m, OCH_2CH_2O), 2.90–2.79 (m, aryl–C–CH_2N), 2.78–2.72 (m, benzyl–CH_2), 2.73–2.65 (m, 1H, CH_2N), 2.63–2.55 (ddd, J = 11.2/9.4/6.3 Hz, 1H, CH_2N), 2.24 (br s, NH), 1.84–1.70 and 1.66–1.54 (2m, each 3H), 1.53–1.41 and 1.38–1.16 (2m, 1 + 4H) ppm; ^{13}C NMR (100 MHz): δ = 147.66, 145.90, 133.64, 121.55, 110.61, 109.06, 108.24, 100.80, 64.75, 64.57, 51.18, 48.27, 42.68, 35.77, 34.57, 29.66, 28.67, 24,49, 23.77 ppm.

[2-(1,4-Dioxaspiro[4.5]dec-6-yl)ethyl][3-(2-iodo-4,5-dimethoxyphenyl)propyl]amine (**6e**, $C_{21}H_{32}INO_4$)

5e 2.44 g (5.01 mmol), $NaBH_4$ 570 mg (15.0 mmol), CH_3OH 70 cm^3; yield: 1.38 g (55%) colourless oil; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:5:0.5): R_f = 0.37; IR (film): $\bar{\nu}$ = 3317 (NH) cm^{-1}; MS (CI): m/z (%) = 490 ($M^{+\bullet}$ + 1, 100), 362 (56), 198 (20); ^{1}H NMR (400 MHz): δ = 7.20 and 6.74 (2s, 2H), 4.00–3.91 (m, OCH_2-CH_2O), 3.85 and 3.84 (2s, $2OCH_3$), 2.74–2.65 (m, 5H), 2.59 (ddd, J = 11.2/9.4/6.5 Hz, 1H), 1.85–1.72 and 1.67–1.42 (2m, each 5H), 1.39–1.19 (m, 4H) ppm; ^{13}C NMR (100 MHz): δ = 149.32, 147.73, 137.24, 121.81, 112.10, 110.68, 87.90, 64.78, 64.63, 56.15, 55.91, 49.37, 48.51, 42.75, 38.20, 34.65, 30.96, 29.67, 29.02, 24.54, 23.81 ppm.

*General Procedure for the Synthesis of α-Aminonitriles **7** by Intramolecular Strecker Reaction*

The solution of amine 6 (1 molequiv.) in H_2O and 2 *N* HCl (2 molequiv.) was stirred at 60°C (bath temperature) for 1.5 h. After cooling the mixture to ambient temperature, an aqueous solution of KCN (2 molequiv.) 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 0.5 *N* HCl or KCN. Stirring of the mixture was continued for 1 h. The oily product separated was dissolved in 30 cm^3 of Et_2O. The aqueous layer was rendered alkaline by saturated Na_2CO_3 solution and extracted with $3 \times 30\,cm^3$ of Et_2O. The combined organic layers were washed with 20 cm^3 of brine, dried (Na_2SO_4), and evaporated *in vacuo*. The crude products were found to be remarkably pure and were used for the next step. Attempted further purification by FC failed because of the rapidly occurring decompostion of the products.

1-[2-(2-Bromophenyl)ethyl]octahydroindole-7a-carbonitrile (2:1 mixture of diastereomers) (**7a**, $C_{17}H_{21}BrN_2$)

6a 468 mg (1.27 mmol), 40 cm^3 H_2O, 2 *N* HCl 1.27 cm^3 (2.54 mmol), KCN 165 mg (2.54 mmol)/3 cm^3 H_2O; yield: 409 mg (97%) light yellow oil; TLC (Al_2O_3; *n*-hexane:Et_2O = 9:1): $R_f = 0.54$; IR (film): $\bar{\nu} = 2214$ (C≡N) cm^{-1}; MS (CI): m/z (%) = 308 ($M^{+\bullet} + 1 -$ HCN, 91; ^{81}Br), 306 ($M^{+\bullet} + 1 -$ HCN, 100; ^{79}Br), 226 (8), 136 (61); ^{1}H NMR (400 MHz): $\delta = 7.52$ (m, arom H), 7.24–7.20 (m, 2 arom H), 7.09–7.03 (m, arom H), 3.51–3.35, 3.08–2.84, and 2.63–2.51 (3m, 1 + 3 + 2H), 2.24–2.12 (m, 1.66H), 1.98 (dt, $J = 14.5/3.3$ Hz, 0.66H), 1.96–1.90 (m, 0.33H), 1.88–1.76 (m, 1H), 1.74–1.59, 1.59–1.42, 1.35–1.10, and 1.06–0.94 (4m, 1.66 + 2.33 + 2.66 + 0.66H) ppm; ^{13}C NMR (100 MHz): $\delta = 139.60$, 139.29, 132.78, 130.96, 130.69, 127.88, 127.33, 127.23, 124.50, 124.42, 120.72, 118.14, 69.08, 64.49, 50.39, 50.10, 49.92, 49.75, 48.10, 43.38, 35.46, 35.41, 33.64, 30.19, 28.36, 27.83, 27.25, 26.57, 25.20, 24.29, 22.29, 18.90 pmm.

1-[2-(2-Iodophenyl)ethyl]octahydroindole-7a-carbonitrile (7:3 mixture of diastereomers) (**7b**, $C_{17}H_{21}IN_2$)

6b 585 mg (1.41 mmol), 50 cm^3 H_2O, 2 *N* HCl 1.40 cm^3 (2.80 mmol), KCN 184 mg (2.80 mmol)/5 cm^3 H_2O; yield: 519 mg (97%) light yellow oil; TLC (Al_2O_3; *n*-hexane:Et_2O = 9:1): $R_f = 0.61$; IR (film): $\bar{\nu} = 2213$ (C≡N) cm^{-1}; MS (CI): m/z (%) = 354 ($M^{+\bullet} + 1 -$ HCN, 100), 226 (8), 163 (17), 136 (37); ^{1}H NMR (400 MHz): $\delta = 7.80$ (dd, $J = 7.9/0.8$ Hz, arom H), 7.29–7.20 and 6.92–6.86 (2m, 2 + 1 arom H), 3.47–3.34, 3.05–2.80, 2.64–2.55, and 2.55–2.47 (4m, 1 + 3 + 1 + 1H), 2.24–2.11 (m, 1.7H), 2.00 (dt, $J = 14.4/3.3$ Hz, 0.7H), 1.97–1.89 and 1.87–1.75 (2m, 0.3 + 0.9H), 1.75–1.58 (m, 4H), 1.38–1.11 and 1.11–0.97 (2m, 2.7 + 0.7H) ppm; ^{13}C NMR (100 MHz): $\delta = 142.83$, 142.56, 139.47, 130.05, 129.78, 128.26, 128.14, 128.04, 128.03, 120.73, 118.15, 100.60, 100.43, 69.03, 64.49, 50.69, 50.20, 50.13, 49.79, 48.07, 43.33, 39.90, 39.87, 33.62, 30.16, 28.37, 27.83, 27.25, 26.57, 25.19, 24.29, 22.29, 18.96 ppm.

1-[2-(2-Iodo-4,5-dimethoxyphenyl)ethyl]octahydroindole-7a-carbonitrile (7:3 mixture of diastereomers) (**7c**, $C_{19}H_{25}IN_2O_2$)

6c 573 mg (1.21 mmol), 50 cm^3 H_2O, 2 *N* HCl 1.20 cm^3 (2.40 mmol), KCN 156 mg (2.40 mmol)/5 cm^3 H_2O; yield: 527 mg (99%) light yellow oil; TLC (Al_2O_3; *n*-hexane:Et_2O = 9:1): $R_f = 0.61$; IR (film): $\bar{\nu} = 2253$, 2213 (C≡N) cm^{-1}; MS (CI): m/z (%) = 414 ($M^{+\bullet} + 1 -$ HCN, 100), 286 (31), 164 (6), 136 (63); ^{1}H NMR (400 MHz): $\delta = 7.27$ (s, arom H), 6.75 and 6.74 (2s, 0.3 + 0.7 arom H), 3.85 and 3.84 (2s, 2OCH_3), 3.45–3.35, 3.03–2.75, 2.66–2.56, and 2.56–2.46 (4m, 1 + 3 + 1 + 1H), 2.27–2.12 (m, 1.7H), 2.03 (dt, $J = 14.8/3.3$ Hz, 0.7H), 1.99–1.91 and 1.89–1.78 (2m, 0.3 + 0.9H), 1.77–1.63, 1.53–1.43, and 1.41–1.12 (3m, 1 + 3 + 3.4H) ppm; ^{13}C NMR (100 MHz): $\delta = 149.23$, 148.03, 135.30, 134.99, 121.69, 120.77, 118.15, 112.75, 112,51, 88.18, 88.10, 69.11, 64.52, 56.18, 55.97, 50.90, 50.48, 50.13, 49.85, 48.13, 43.30, 39.61, 39.54, 33.67, 30.13, 28.39, 27.84, 27.26, 26.57, 25.20, 24.25, 22.23, 19.09 ppm.

1-[2-(2-Iodo-4,5-methylenedioxyphenyl)ethyl]octahydroindole-7a-carbonitrile (3:1 mixture of diastereomers) (**7d**, $C_{18}H_{21}IN_2O_2$)

6d 339 mg (0.74 mmol), 25 cm^3 H_2O, 2 *N* HCl 0.74 cm^3 (1.48 mmol), KCN 96 mg (1.48 mmol)/3 cm^3 H_2O; yield: 308 mg (98%) light yellow oil; TLC (Al_2O_3; *n*-hexane:Et_2O = 9:1): $R_f = 0.61$; IR (film): $\bar{\nu} = 2251$, 2214 (C≡N) cm^{-1}; MS (CI): m/z (%) = 398 ($M^{+\bullet} + 1 -$ HCN, 98), 271 (29), 270 (28), 163 (14), 136 (100); ^{1}H NMR (500 MHz): $\delta = 7.22$ (s, arom H), 6.76 and 6.75 (2s, 0.25 + 0.75 arom H), 5.95–5.94 (d, $J = 1.4$ Hz, OCH_2O), 3.44–3.34, 3.00–2.81, and 2.81–2.73 (3m, 1 + 2 + 1H), 2.64–2.51 and 2.51–2.43 (2m, 1 + 1H), 2.26–2.12 (m, 1.75H), 2.03 (dt, $J = 14.5/3.5$ Hz, 0.75H), 1.99–1.89 and 1.89–1.77 (2m, 0.25 + 0.75H), 1.77–1.63 and 1.42–1.11 (2m, 4 + 3.5H) ppm; ^{13}C NMR (125 MHz): $\delta = 148.34$, 146.87, 136.06, 135.77, 120.68, 118.51, 118.10, 109.71, 109.53, 101.46, 87.82, 87.69, 69.02, 64.49, 50.78, 50.37, 50.10, 49.78, 48.02, 43.28, 39.80, 39.67, 33.60, 30.13, 28.36, 27.79, 27.22, 26.53, 25.15, 24.26, 22.27, 19.05 ppm.

1-[3-(2-Iodo-4,5-dimethoxyphenyl)propyl]octahydroindole-7a-carbonitrile (7:3 mixture of diastereomers) (**7e**, $C_{20}H_{27}IN_2O_2$)

6e 713 mg (1.31 mmol), 50 cm^3 H_2O, 2 *N* HCl 1.40 cm^3 (2.60 mmol), KCN 169 mg (2.60 mmol)/5 cm^3 H_2O; yield: 554 mg (93%) light yellow oil; TLC (Al_2O_3; *n*-hexane:Et_2O = 9:1): $R_f = 0.61$; IR (film): $\bar{\nu} = 2213$ (C≡N) cm^{-1}; MS (CI): m/z (%) = 428 ($M^{+\bullet} + 1 -$ HCN, 100), 300 (22), 137 (26), 136 (24); ^{1}H NMR (400 MHz): $\delta = 7.21$, 7.20, 6.73, and 6.72 (4s, 0.7 + 0.3 + 0.3 + 0.7 arom H), 3.86, 3.85, and 3.84 (3s, 2.1 + 0.9 + 3H, $2OCH_3$), 3.39 and 3.32 (2dt, $J = 9.2/6.1$ and $9.3/6.3$ Hz, 0.7 + 0.3H), 2.86–2.70, 2.66–2.54, and 2.54–2.38 (3m, 2 + 1 + 2H), 2.31–2.24, 2.21–2.07, and 1.97–1.88 (3m, 0.7 + 1.7 + 0.3H), 1.88–1.71 and 1.71–1.56 (2m, 3.9 + 2H), 1.56–1.39 and 1.38–1.20 (2m, 3.1 + 1.3H) ppm; ^{13}C NMR (100 MHz): $\delta = 149.38$, 149.30, 147.76, 137.29, 137.10, 121.69, 120.70, 118.13, 112.15, 111.98, 87.93, 69.19, 64.65, 56.16, 55.95, 49.84, 49.77, 49.43, 49.34, 48.13, 43.45, 38.57, 38.29, 33.73, 30.02, 29.53, 29.19, 28.53, 27.63, 27.29, 26.43, 25.27, 24.34, 22.37, 19.45 ppm.

*General Procedure for the Synthesis of cis-Erythrinanes **8** by Intramolecular Brylants Reaction*

To a solution of aminonitrile **7** (1 molequiv.) in dry *THF* was added a solution of 2 *M i-Pr*MgCl (1.05 molequiv.) in the same solvent at −50°C under N_2. After stirring at −50°C for an additional hour the mixture was slowly warmed up to ambient temperature during 3–4 h and then refluxed under N_2 at 60°C for 3 h. The cold mixture was poured into 30 cm^3 of H_2O, rendered alkaline with an aqueous solution of Na_2CO_3 and extracted with 3 × 30 cm^3 of Et_2O. The combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by FC (eluents were the same as used for TLC).

cis-Erythrinane (**8a**)

7b 204 mg (0.54 mmol), 2 *M i-Pr*MgCl 0.28 cm^3 (0.56 mmol), *THF* 5 cm^3; yield: 91 mg (75%) light yellow oil [19]; TLC (CH_2Cl_2:CH_3OH = 100:7): $R_f = 0.47$; MS (EI): m/z (%) = 227 ($M^{+\bullet}$, 23), 184 (100), 170 (31); ^{1}H NMR (400 MHz): $\delta = 7.24$ (dd, $J = 7.9/1.2$ Hz, 14-H), 7.16–7.12 (m, 15-H), 7.06 (dt, $J = 7.4/1.2$ Hz, 16-H), 7.01 (m, 17-H), 3.27–3.03 (m, 4H), 2.86 (dt, $J = 10.2/3.1$ Hz, 1H), 2.44–2.34 (m, 1H), 2.34–2.27 (m, CH), 1.98–1.96 (m, 1H), 1.78–1.64 and 1.62–1.41 (2m, 2 + 5H), 1.41–1.35 (dt, $J = 12.0/3.4$ Hz, 1H), 1.31–1.23 (m, 1H) ppm; ^{13}C NMR (100 MHz): $\delta = 144.47$, 134.96, 128.89, 125.89, 125.50, 125.37, 64.54, 46.46, 43.59, 40.45, 35.90, 28.99, 28.69, 24.97, 21.93, 21.42 ppm.

15,16-Dimethoxy-cis-erythrinane (**8b**)

7c 215 mg (0.49 mmol), 2 *M i-Pr*MgCl 0.26 cm^3 (0.52 mmol), *THF* 5 cm^3; yield: 109 mg (78%) light yellow oil [28]; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:5:0.5): $R_f = 0.36$; MS (EI): m/z (%) = 287 ($M^{+\bullet}$, 24), 244 (100), 230 (24); ^1H and ^{13}C NMR data were in line with those published in Refs. [4] and [5].

15,16-Methylenedioxy-cis-erythrinane (**8c**)

7d 200 mg (0.47 mmol), 2 *M i-Pr*MgCl 0.25 cm^3 (0.50 mmol), *THF* 5 cm^3; yield: 91 mg (71%) light yellow oil [20]; TLC (CH_2Cl_2:CH_3OH:25% NH_3 = 100:5:0.5): $R_f = 0.34$; MS (EI): m/z (%) = 271 ($M^{+\bullet}$, 22), 228 (100), 214 (25); ^1H NMR (500 MHz): $\delta = 6.71$ (s, 14-H), 6.48 (s, 17-H), 5.88 and 5.87 (2d, each $J = 1.3$ Hz, OCH_2O), 3.22–3.13 and 3.12–3.02 (2m, each 2H), 2.84 (dt, $J = 10.3/2.8$ Hz, 1H), 2.30 (m, 1H), 2.25–2.18 (dt, $J = 11.0/6.1$ Hz, CH), 1.96–1.89 (m, 1H), 1.77–1.71 (dt, $J = 12.7/3.7$ Hz, 1H), 1.70–1.63 and 1.63–1.42 (2m, 1 + 5H), 1.40–1.32 (tt, $J = 12.6/3.7$ Hz, 1H), 1.32–1.24 (m, 1H) ppm (see also Ref. [4]; ^{13}C NMR (125 MHz): $\delta = 145.83$, 145.34, 137.02, 127.73, 108.19, 105.74, 100.48, 65.05, 46.21, 43.67, 40.28, 35.73, 28.85, 28.45, 25.00, 21.93, 21.39 ppm.

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