

**NOVEL COMPLEX *N*-HETEROCYCLES VIA INTRA-MOLECULAR 1,5-ELECTROCYCLIZATIONS:
1,2,4,4a,5,5a,10-OCTAHYDROPYRIDO[4'',3'':2',3']-CYCLOBUTA[1',2':4,5]PYRROLO[2,3-*b*]PYRIDINES**

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Abstract- The synthesis of 2-amino-3-isopropenylpyridine (**5**) and 2-amino-5-chloro-3-isopropenylpyridine (**6**) and their toluenesulfonic acid catalyzed reactions in refluxing toluene with some 1-substituted piperidin-4-ones are described. The toluenesulfonic acid catalyzed reaction of the pyridine derivatives (**5**) and (**6**) with 1-benzyl-, 1-benzoyl- and 1-methylpiperidin-4-one lead to novel pyrrolo[2,3-*b*]-pyridines (**7-12**) in good to excellent yields in diastereoisomeric pure form (Scheme 2, Table 1). An intramolecular 1,5-electrocyclization of the dipolar reactive intermediate (**13**) as a key step (Scheme 3) is proposed for the formation of the compounds (**7-12**).

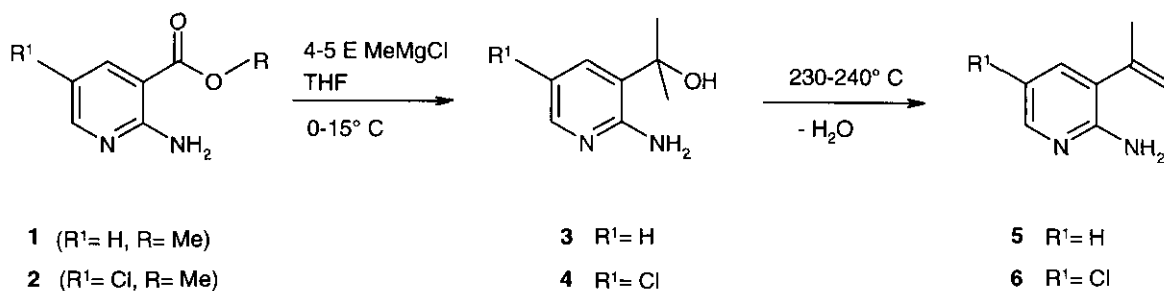
During the last years, acid catalyzed reactions of 2-vinylaniline derivatives with aldehydes and ketones were carefully studied in our laboratories.¹ Our earlier results in this field impressively showed that these reactions could be very useful for the synthesis of heterocycles such as quinoline¹⁻³ and cyclobut[1,2-*b*]indole derivatives.^{4,5} The selectivity of these reactions turned out to be strongly dependent on the structure of the chosen 2-vinylanilines and ketones.¹⁻⁵ As we have shown earlier, in some cases good selectivities and yields could be achieved. But our knowledge on the selectivity of these reactions is still not satisfactory. Recently, we reported on the results of the toluenesulfonic acid catalyzed reaction of 2-vinylanilines with 1-benzyl- and 1-methyl-4-piperidin-4-one. In this case, the outcome of the reaction turned out to be independent of the 2-vinylaniline derivative used, and cyclobut[1,2-*b*]indoles were obtained as sole products in preparatively useful yields.⁴ Due to this observed selectivity, we thought that

the use of 2-amino-3-vinylpyridine derivatives instead of 2-vinylanilines in the acid catalyzed reactions with piperidin-4-ones might give selective reactions too, and might lead to interesting new heterocycles. In this paper, we report on the first synthesis of some new 2-amino-3-isopropenylpyridines and their acid catalyzed reaction with 1-substituted piperidin-4-ones, which delivered new 'alkaloid-type' heterocycles.

RESULTS AND DISCUSSION

As the first two simpler candidates of pyridines, we chose 2-amino-3-isopropenylpyridine (**5**) and 2-amino-5-chloro-3-isopropenylpyridine (**6**), which were both unknown in the literature. In our simple and efficient approach to **5** and **6** (see Scheme 1), we started from the known or even commercially available ($R^1=H$, $R=Me$) 2-aminopyridine-3-carboxylic acid esters (**1**) and (**2**),⁷ which after Grignard reaction with 4 to 5 equivalents of $MeMgCl$ in THF gave the 2-(2-aminopyridin-3-yl)propan-2-ols (**3**) and (**4**) in very good yields (85-95%). The use of acid ($p-TsOH$, H_2SO_4 etc.) as a catalyst in the remaining elimination step under our standard conditions (refluxing toluene, water separator) only gave starting material and a small amount of unidentified products. In our hands, heating of the pure alcohols to 230-240° C and directly distilling off the reaction water from the reaction flask turned out to be the method of choice and delivered the aminoisopropenylpyridines (**5**) and (**6**) in excellent yields (90-95%).

Scheme 1



With the two pyridine model-compounds (**5**) and (**6**) in hand, we were able to study the toluenesulfonic acid catalyzed reaction of these intermediates with 1-benzyl-, 1-benzoyl-, and 1-methylpiperidin-4-ones. With satisfaction, in all cases, we observed a clean and diastereoselective reaction, which led in good to excellent yields to octahydropyrido[4''',3''':2',3']cyclobuta[1',2':4,5]pyrrolo[2,3-*b*]pyridine derivatives (**7-12**) (Scheme 2, Table 1).

Scheme 2

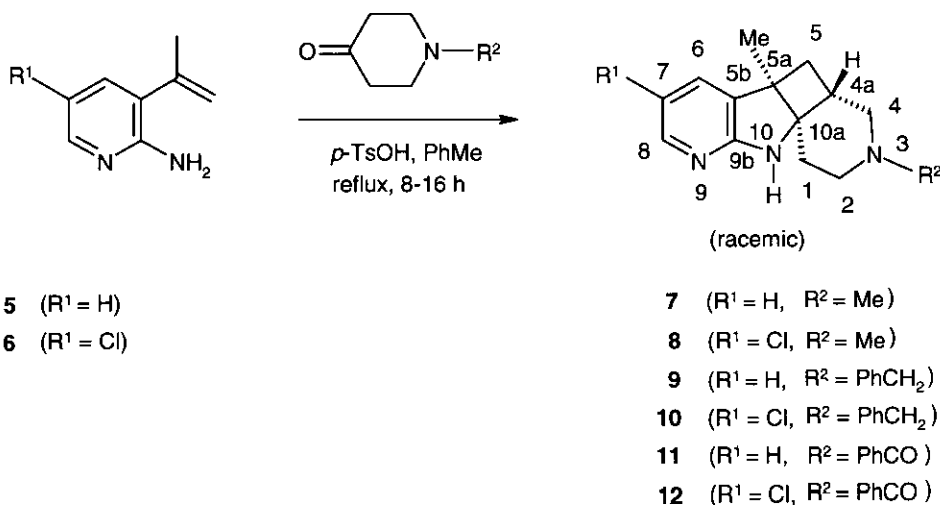


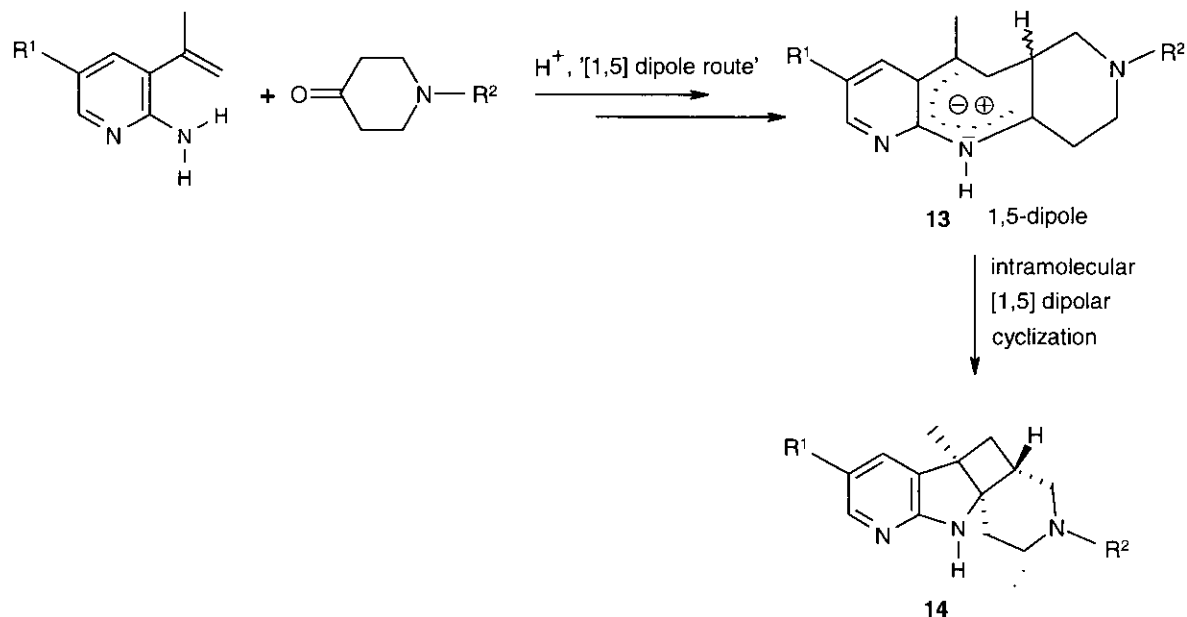
Table 1 *p*-TsOH Catalyzed Reactions of 2-Amino-3-isopropenylpyridines with 1-Substituted Piperidin-4-ones^a

R ¹	R ²	Reaction time [h]	Product	Yield [%]
H	Me	16	7	70
Cl	Me	16	8	92
H	PhCH ₂	12	9	80
Cl	PhCH ₂	12	10	82
H	PhCO	8	11	80
Cl	PhCO	10	12	74

^a The reaction conditions are not optimized. In all cases *p*-TsOH was used as the catalyst and the reaction carried out in refluxing toluene

As Table 1 shows, the yields for these one-pot-reactions are astonishing. In addition, NMR-spectroscopic investigations clearly show, that the racemic heterocycles are only consisting of a single diastereoisomer. In all cases, no other diastereoisomers are obtained. Looking at the relative stereochemistry of the compounds (7-12), we found out, that it is the same as the one of the cyclobut[1,2-*b*]indoles, obtained in the acid catalyzed reaction of 2-vinylanilines with *N*-substituted piperidin-4-ones.⁵ The fact, that the acid catalyzed reactions of 2-vinylanilines and 2-amino-3-vinylpyridine derivatives with *N*-substituted piperidin-4-ones only gave products arising from the '1,5-dipole-route' (Scheme 3)⁸ and these products show the same relative stereochemistry, is a clear proof for the mechanism in these two reactions to be the same.

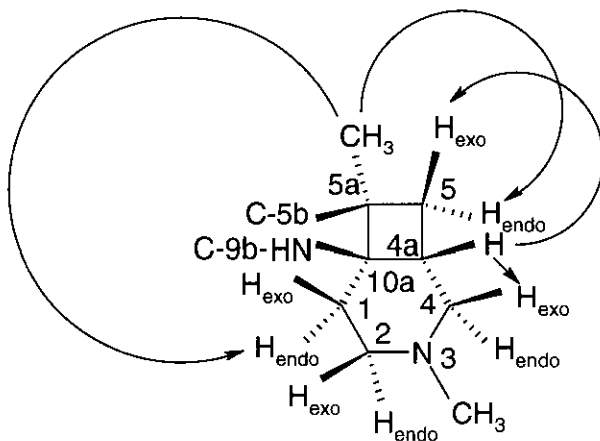
Scheme 3



SPECTROSCOPIC PART

The assignment of the ^1H - and ^{13}C -NMR signals were confirmed by 2D NMR (COSY, HSQC⁹). The whole set of H-H coupling constants was only determined for compound (7) and is given in the experimental part. For the compounds (11) and (12) good NMR-spectra are only obtained in CD_3OD . In this solvent assignments of the signals for the major rotamer¹⁰ could be made (see experimental part). The stereochemistry of the compounds (7-12) was assigned on the basis of 1D ^1H -NOE difference spectroscopy. As an example, the crucial NOE's for compound (7) (solution in benzene- d_6) are shown in Figure 1.

Figure 1



The observed NOE's clearly indicate the cis-configuration as well as for the azaindoline- as the piperidine ring and therefore both ring systems are on different sites of the cyclobutane ring.

The proof for the compounds (7-12) being racemic, was given by ^1H -NMR spectroscopy and will be discussed only for compound (8). The ^1H -NMR spectra of this compound in CDCl_3 in the presence of (+)- (S)-2,2,2-trifluoro-1-anthra-9-yl)ethanol ((+)-TAE¹¹) shows as well as for Me-C-5a as for Me-N(3) two separated singlets (Me-signals of the diastereoisomeric solvate complexes (+)-TAE/(+)-8 and (+)-TAE/(-)-8) with an integration ratio 1:1 (δ 0.96, 1.08, 2.01, 2.03 ppm). This experiment clearly shows, the compound (8) to be racemic and is in accordance with the proposed mechanism (Scheme 3),⁸ in which asymmetric induction is impossible.

CONCLUSION

We have shown that the *p*-TsOH-catalyzed reactions of some 2-amino-3-vinylpyridines with 1-substituted piperidin-4-ones are comparable to the reactions of 2-vinylanilines with piperidin-4-ones in respect to selectivity ('1,5-dipole-route') and yields.⁵ These results for the first time show, that 2-vinylaniline derivatives can be substituted by suitable aminovinyl-heterocycles in their acid catalyzed reactions with ketones such as piperidine-4-ones. We therefore think that this finding might lead to a new methodology for the synthesis of many new complex heterocycles, by using diverse 1,2-aminovinyl-substituted heterocycles in the acid catalyzed reaction with 1-substituted piperidin-4-ones. The use of other ketones in these reactions might also lead to interesting results and will be an additional topic for us in the near future.

EXPERIMENTAL SECTION

General. Melting points were measured on a Büchi B-510 apparatus and are uncorrected. ¹H-NMR spectra were taken on a 500 MHz-Varian Unity 500 spectrometer. ¹³C-NMR spectra were recorded on a 125 MHz-Varian Unity 500 instrument. Chemical shifts are reported in ppm referenced to TMS (¹H-NMR) and CDCl₃, CD₃OD or benzene-d₆ (¹³C-NMR). IR spectra were recorded by using a Bruker IFS 48 spectrophotometer. MS were obtained on a Finnigan MAT 212/SS spectrometer. TLC was performed on Merck silica gel 60F-254.

Standard Procedure for the Synthesis of Compounds (3) and (4). A mixture of 25 mmol of a 2-amino-3-pyridinecarboxylic acid methyl(ethyl) ester was dissolved in 100 mL of absolute THF. Then 125 mmol of a *ca.* 3 molar solution of MeMgCl in THF were added dropwise under stirring over a period of 30 min in such a manner, that the internal temperature remains constant at *ca.* 10° C. The reaction mixture was stirred for 3 h at 20° C and then cooled again and saturated aqueous NH₄Cl solution was added in such a manner that the temperature remains constant between 10-15° C. After completion of the hydrolysis additional water was added to get a clear solution. The mixture was extracted three times with *tert.*-butyl methyl ether (TBME) and the combined organic phase washed two times with brine. After drying the TBME phase over sodium sulfate and evaporation of the solvent in a water-jet-vacuum, the crude alcohol was obtained, which was normally pure enough for the use in the elimination step.

Standard Procedure for the Synthesis of Compounds (5) and (6). In a small distillation apparatus one of the amino alcohols (3) or (4) was heated at an oil bath temperature of 230-240° C. Soon water distills

off and the alcohol was heated for *ca.* 1 h at this external temperature. After cooling, the residue was purified by flash chromatography on silica gel (eluent: THF/hexane 1:1).

Standard Procedure for the Synthesis of Compounds (7-12). A mixture of a 2-amino-3-isopropenylpyridine derivative (10 mmol), *N*-substituted piperidin-4-one (15-20 mmol), TsOH (Merck, 0.1 g) and abs. toluene (25 mL) was heated under reflux (Dean-Stark-trap) for 8-16 h (see Table 1). The mixture was evaporated and the residue purified by flash chromatography (FC, SiO₂, THF/hexane 2:1-1:1 or THF pure and then ETOH/THF 1:1). In some cases, chromatography as well as recrystallization was used to obtain analytical pure samples.

2-(2-Aminopyridin-3-yl)propan-2-ol (3). Purified by FC (THF/hexane 2:1): mp 72-74° C.

IR (KBr, cm⁻¹) 3468, 3432, 3335, 3222, 2977, 1616, 1575, 1455, 1431, 1151, 774; ¹H-NMR (CDCl₃) δ 1.54 (s, 3H, Me), 5.54 (br s, 3H, OH and NH₂), 6.45 (dd, *J* = 7.6, 5.0 Hz, 1H, H-5), 7.23 (dd, *J* = 7.6, 1.7 Hz, 1H, H-4), 7.63 (dd, *J* = 5.0, 1.7 Hz, 1H, H-6); ¹³C-NMR (CDCl₃) δ 28.8 (Me), 71.8 (C_q-OH), 112.9 (C-5), 126.0 (C-3), 133.3 (C-4), 145.5 (C-6), 156.9 (C-2); EI-MS, *m/z* (rel. inten.) 152 (M⁺, 24), 137 (41), 133 (12), 119 (28), 93 (13), 42 (100). Anal. Calcd for C₈H₁₂N₂O: C, 63.13; H, 7.95; N, 18.41. Found: C, 62.99; H, 7.99; N, 18.28.

2-(2-Amino-5-chloropyridin-3-yl)propan-2-ol (4). Purified by FC (THF/hexane 2:1): mp 112-113° C.

IR (KBr, cm⁻¹) 3464, 3436, 3329, 2978, 1616, 1456, 1437, 1156, 958; ¹H-NMR (CDCl₃) δ 1.59 (s, 3H, Me), 4.00 (s, 1H, OH), 5.61 (s, 1H, NH₂), 7.24 (d, *J* = 2.2 Hz, 1H, H-4), 7.72 (d, *J* = 2.2 Hz, 1H, H-6); ¹³C-NMR (CDCl₃) δ 28.8 (Me), 72.8 (C_q-OH), 119.8 (C-5), 126.9 (C-3), 133.5 (C-4), 144.1 (C-6), 155.4 (C-2); EI-MS, *m/z* (rel. inten.) 188 (M⁺(³⁷Cl), 14), 186 (M⁺(³⁵Cl), 38), 173 (20), 171 (50), 167 (28), 155 (20), 153 (50), 43 (100). Anal. Calcd for C₈H₁₁N₂OCl: C, 51.48, H, 5.94; N, 15.01; Cl, 19.00. Found: C, 51.60, H, 5.85; N, 14.93; Cl, 18.84.

2-Amino-3-isopropenylpyridine (5). Purified by FC (THF/hexane 1:1): yellow liquid. IR (KBr, cm⁻¹)

3477, 3390, 3302, 3169, 1626, 1603, 1446, 1246, 907, 771; ¹H-NMR (CDCl₃) δ 2.00 (m, 3H, Me), 4.85 (s, 2H, NH₂), 5.08 (m, 1H, olefinic H), 5.24 (m, 1H, olefinic H), 6.56 (dd, *J* = 7.3, 5.0 Hz, 1H, H-5), 7.20 (dd, *J* = 7.3, 2.0 Hz, 1H, H-4), 7.91 (dd, *J* = 5.0, 1.9 Hz, 1H, H-6); ¹³C-NMR (CDCl₃) δ 23.1 (Me), 113.6 (C-5), 115.8 (olefinic CH₂), 123.1 (C-3), 135.5 (C-4), 142.0 (olefinic C_q), 146.4 (C-6), 155.3 (C-2); EI-MS, *m/z* (rel. inten.) 134 (M⁺, 94), 133 (M⁺-1, 100), 119 (66), 92 (30), 65 (30). Anal. Calcd for C₈H₁₀N₂: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.41; H, 7.61, N, 20.72.

2-Amino-5-chloro-3-isopropenylpyridine (6). Purified by FC (THF/hexane 1:1): mp 40-41° C.

IR (KBr, cm^{-1}) 3462, 3288, 3151, 1626, 1560, 1456, 1248, 911, 900; $^1\text{H-NMR}$ (CDCl_3) δ 2.05 (m, 3H, Me), 4.69 (s, 2H, NH_2), 5.16 (m, 1H, olefinic H), 5.33 (m, 1H, olefinic H), 7.24 (d, $J = 2.5$ Hz, 1H, H-4), 7.93 (d, $J = 2.5$ Hz, 1H, H-6); $^{13}\text{C-NMR}$ (CDCl_3) δ 22.7 (Me), 116.7 (olefinic CH_2), 119.9 (C-5), 123.9 (C-3), 135.0 (C-4), 140.8 (olefinic C_q), 144.3 (C-6), 153.9 (C-2); EI-MS, m/z (rel. inten.) 170 (M^+ (^{37}Cl), 40), 169 ($\text{M}^+ - 1$ (^{37}Cl), 42), 168 (M^+ (^{35}Cl), 100), 167 ($\text{M}^+ - 1$ (^{35}Cl), 82), 155 (26), 153 (66), 132 (28), 131 (38), 118 (28), 117 (32). Anal. Calcd for $\text{C}_8\text{H}_9\text{N}_2\text{Cl}$: C, 56.98; H, 5.38; N, 16.61; Cl, 21.02. Found: C, 56.85; H, 5.30; N, 16.78; Cl, 21.07.

(±)-(4a RS, 5a RS, 10a RS)-3,5a-Dimethyl-1,2,4,4a,5,5a,10-octahydropyrido[4'',3'':2',3']cyclobuta[1',2':4,5]pyrrolo[2,3-b]pyridine (7). Purified by FC (THF then ETOH/THF 1:1) and recrystallization from cold hexane: mp 122-123° C; IR (KBr, cm^{-1}) 3187, 3068, 2962, 2925, 2793, 1609, 1584, 1476, 1462, 1429, 1252, 1102, 766; $^1\text{H-NMR}$ (benzene- d_6) δ 1.03 (s, 3H, C-5a-Me), 1.49 (m, $J = 14.6, 4.2, 0.5$ Hz, 1H, H-1 exo), 1.73 (m, $J = 11.4, 10.8, 3.9$ Hz, 1H, H-2 exo), 1.90 (m, $J = 12.0, 6.6$, 1H, H-4 exo), 1.92 (m, $J = 10.8, 9.0$ Hz, 1H, H-5 endo), 1.97 (m, $J = 10.8, 8.7$ Hz, 1H, H-5 exo), 2.09 (m, $J = 14.6, 10.8, 5.2$ Hz, 1H, H-1 endo), 2.13 (m, $J = 12.0, 2.8, 1.7$ Hz, 1H, H-4 endo), 2.21 (m, $J = 9.0, 8.7, 6.6, 2.8$ Hz, 1H, H-4a), 2.30 (m, $J = 11.4, 5.2, 4.2, 1.7$ Hz, 1H, H-2 endo), 5.83 (s, 1H, NH), 6.38 (dd, $J = 7.1, 5.0$ Hz, 1H, H-7), 6.89 (dd, $J = 7.0, 1.8$ Hz, 1H, H-6), 8.08 (dd, $J = 5.0, 1.8$ Hz, 1H, H-8); $^{13}\text{C-NMR}$ (benzene- d_6) δ 20.6 (C-5a-Me), 29.0 ($J = 125$ Hz, C-1), 36.6 ($J = 136$ Hz, C-5), 39.5 ($J = 134$ Hz, C-4a), 46.7 (N-Me), 47.8 (C-5a), 52.9 (C-2), 57.6 (C-4), 61.8 (C-10a), 113.5 (C-7), 130.8 (C-6), 131.0 (C-5b), 146.1 (C-8), 163.6 (C-9a); EI-MS, m/z (rel. inten.) 229 (M^+ , 33), 145 (10), 84 (100), 40 (70). Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{N}_3$: C, 73.33; H, 8.35; N, 18.32. Found: C, 73.21; H, 8.41; N, 18.26.

(±)-(4a RS, 5a RS, 10a RS)-7-Chloro-3,5a-dimethyl-1,2,4,4a,5,5a,10-octahydropyrido[4'',3'':2',3']cyclobuta[1',2':4,5]pyrrolo[2,3-b]pyridine (8). Purified by FC (THF then EtOH/THF 1:1) and recrystallization from cold TBME/hexane 1:2: mp 139-140° C. IR (KBr, cm^{-1}) 3122, 3051, 2961, 2926, 2792, 1603, 1571, 1462, 1404, 1252, 1166, 896; $^1\text{H-NMR}$ (CDCl_3) δ 1.22 (s, 3H, C-5a-Me), 1.71 (m, 1H, H-1), 1.96 (m, 1H, H-5), 2.08-2.32 (m, 4H, H-1, H-2, H-3 and H-5), 2.42 (m, 2H, H-4 and H-4a), 2.57 (m, H-2), 6.16 (s, 1H, NH), 7.06 (d, $J = 2.1$ Hz, 1H, H-6), 7.69 (d, $J = 2.1$ Hz, 1H, H-8); $^{13}\text{C-NMR}$ (CDCl_3) δ 20.4 (C-5a-Me), 28.7 (C-1), 36.5 (C-5), 39.6 (C-4a), 46.6 (N-Me), 47.8 (C-5a), 52.7 (C-2), 57.4 (C-4), 62.7 (C-10a), 120.1 (C-7), 131.0 (C-6), 132.8 (C-5b), 143.9 (C-8), 162.1 (C-9b); EI-MS, m/z (rel. inten) 265 (M^+ (^{37}Cl), 13), 263 (M^+ (^{35}Cl), 40), 220 (20), 205 (24), 96(16), 85 (22), 84 (100). Anal. Calcd for

C₁₄H₁₈N₃Cl: C, 63.75; H, 6.88; N, 15.93; Cl, 13.44. Found: C, 63.60; H, 6.95; N, 15.88; Cl, 13.31.

(±)-(4a *RS*, 5a *RS*, 10a *RS*)-3-Benzyl-5a-methyl-1,2,4,4a,5,5a,10-octahydropyrido[4'':3'':2',3']-cyclobuta[1',2':4,5]pyrrolo[2,3-*b*]pyridine (9). Purified by FC (THF/hexane 1:1) and recrystallization from cold hexane: mp 109-110° C; IR (KBr, cm⁻¹) 3146, 3080, 3053, 2951, 2922, 2791, 2751, 1610, 1588, 1481, 1440, 1422, 1359, 1258, 1107, 771, 732; ¹H-NMR (CDCl₃) δ 1.33 (s, 3H, C-5a-Me), 1.74 (m, 1H, H-1), 2.05 (m, 1H, H-5), 2.18 (m, 1H, H-5), 2.26 (m, 2H, H-1 and H-2), 2.46 (m, 3H, H-4 and H-4a), 2.69 (m, 1H, H-2), 3.54 (m, AB-system (*J* = 13.3 Hz), 2H, CH₂-phenyl), 5.54 (s, 1H, NH), 6.52 (dd, *J* = 7.1, 5.1 Hz, 1H, H-7), 7.21 (dd, *J* = 7.1, 1.7 Hz, 1H, H-6), 7.26 (m, 1H, arom. H), 7.30-7.40 (m, 4H, arom. H), 7.84 (dd, *J* = 5.1, 1.7 Hz, 1H, H-8); ¹³C-NMR (CDCl₃) δ 20.7 (C-5a-Me), 29.0 (C-1), 36.8 (C-5), 39.9 (C-4a), 47.8 (C-5a), 50.7 (C-2), 55.4 (C-4), 62.5 (C-10a), 63.1 (CH₂-phenyl), 113.4 (C-7), 126.6 (2C para (Bn)), 128.2 (2C meta (Bn)), 128.8 (2C ortho (Bn)), 130.6 (C-6), 131.2 (C-5b), 138.8 (C ipso (Bn)), 146.1 (C-8), 163.7 (C-9b); EI-MS, *m/z* (rel. inten.) 305 (M⁺, 33), 161 (13), 160 (62), 91 (100). Anal. Calcd for C₂₃H₂₃N₃: C, 78.65; H, 7.59; N, 13.76. Found: C, 78.48; H, 7.52; N, 13.88.

(±)-(4a *RS*, 5a *RS*, 10a *RS*)-3-Benzyl-7-chloro-5a-methyl-1,2,4,4a,5,5a,10-octahydropyrido[4'':3'':2',3']cyclobuta[1',2':4,5]pyrrolo[2,3-*b*]pyridine (10). Purified by FC (THF/hexane 1:2) and recrystallization from TBME/hexane 1:2: mp 108-110° C; IR (KBr, cm⁻¹) 3190, 3030, 2957, 2925, 2804, 2759, 1607, 1575, 1475, 1453, 1359, 1255, 1109, 741, 699; ¹H-NMR (CDCl₃) δ 1.33 (s, 3H, C-5a-Me), 1.74 (m, 1H, H-1), 2.06 (m, 1H, H-5), 2.19 (m, 1H, H-5), 2.27 (m, 2H, H-1 and H-2), 2.43-2.53 (m, 2H, H-4 and H-4a), 2.70 (m, 1H, H-2), 3.55 (m, AB-system (*J* = 13.3 Hz), 2H, CH₂-phenyl), 5.95 (s, 1H, NH), 7.15 (d, *J* = 2.1 Hz, 1H, H-6), 7.27 (m, 1H, arom. H), 7.32-7.40 (m, 4H, arom. H), 7.78 (d, *J* = 2.1 Hz, 1H, H-8); ¹³C-NMR (CDCl₃) δ 20.5 (C-5a-Me), 28.9 (C-1), 36.8 (C-5), 40.1 (C-4a), 47.9 (C-5a), 50.5 (C-2), 55.3 (C-4), 63.0 (CH₂-phenyl), 63.5 (C-10a), 120.2 (C-7), 126.9 (C para (Bn)), 128.2 (2C meta (Bn)), 128.8 (2C ortho (Bn)), 131.0 (C-6), 138.8 (C ipso (Bn)), 144.0 (C-8), 162.1 (C-9b), EI-MS, *m/z* (rel. inten.) 341 (M⁺(³⁷Cl), 5), 339 (M⁺(³⁵Cl), 9), 161 (16), 160 (62), 91 (100). Anal. Calcd for C₂₀H₂₂N₃Cl: C, 70.68; H, 6.52; N, 12.36; Cl, 10.43. Found: C, 70.75; H, 6.59; N, 12.29; Cl, 10.32.

(±)-(4a *RS*, 5a *RS*, 10a *RS*)-3-Benzoyl-5a-methyl-1,2,4,4a,5a,10-octahydropyrido[4'':3'':2',3']-cyclobuta[1',2':4,5]pyrrolo[2,3-*b*]pyridine (11). Purified by FC (THF/hexane 1:1) and recrystallization

from THF: mp 168-169° C; IR (KBr, cm^{-1}) 3277, 3056, 2923, 2853, 1596, 1570, 1474, 1427, 1271, 1131, 773, 719; $^1\text{H-NMR}$ (CD_3OD) δ (major rotamer) 1.37 (s, 3H, C-5a-Me), 1.94 (m, 1H, H-5), 2.09 (m, 1H, H-1), 2.22 (m, 1H, H-5), 2.37 (m, 1H, H-1), 2.49 (m, 1H, H-4a), 3.35 (m, 1H, H-4), 3.68-3.80 (m, 2H, H-2 and H-4), 3.97 (m, 1H, H-2), 6.58 (dd, $J = 7.1, 5.2$ Hz, 1H, H-7), 7.34 (dd, $J = 7.1, 1.7$ Hz, 1H, H-6), 7.38-7.50 (m, 6H, arom. H), 7.72 (dd, $J = 5.2, 1.7$ Hz, 1H, H-8); $^{13}\text{C-NMR}$ (CD_3OD) δ (major rotamer) 21.4 (C-5a-Me), 25.4 (C-1), 36.7 (C-5), 40.0 (C-2), 40.5 (C-4a), 47.1 (C-4), 47.9 (C-5a), 63.0 (C-10a), 113.9 (C-9), 126.9 (2C ortho (benzoyl)), 128.4 (2C meta (benzoyl)), 129.6 (C para (benzoyl)), 130.9 (C-6), 131.4 (C-5b), 136.3 (C ipso (benzoyl)), 146.5 (C-8), 162.9 (C-9b), 171.4 (Carbonyl-C); EI-MS, m/z (rel. inten.) 319 (M^+ , 44), 185 (10), 158 (64), 145 (30), 105 (100). Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{Cl}$: C, 75.21; H, 6.63; N, 13.16. Found: C, 74.92; H, 6.58; N, 13.27.

(\pm)-(4a RS, 5a RS, 10a RS)-3-Benzoyl-7-chloro-5a-methyl-1,2,4,4a,5a,10-octahydropyrido-[4'',3'': 2',3']cyclobuta[1',2': 4,5]pyrrolo[2,3-*b*]pyridine (12). Purified by FC (THF/hexane 2:1) and recrystallization from cold TBME/hexane 1:1: mp 152-153° C; IR (KBr, cm^{-1}) 3269, 3050, 2951, 2858, 1606, 1573, 1461, 1425, 1283, 1072, 725, 711; $^1\text{H-NMR}$ (CD_3OD) δ (major rotamer) 1.36 (s, 3H, C-5a-Me), 1.94 (m, 1H, H-5), 2.08 (m, 1H, H-1), 2.25 (m, 1H, H-5), 2.38 (m, 1H, H-1), 2.51 (m, 1H, H-4a), 3.35 (m, 1H, H-4), 3.67-3.82 (m, 2H, H-2 and H-4), 3.95 (m, 1H, H-2), 7.32 (d, $J = 2.3$ Hz, 1H, H-6), 7.37-7.50 (m, 6H, arom. H), 7.69 (d, $J = 2.3$ Hz, 1H, H-8); $^{13}\text{C-NMR}$ (CD_3OD) δ (major rotamer) 21.1 (C-5a-Me), 25.2 (C-1), 36.4 (C-5), 39.9 (C-2), 40.6 (C-4a), 46.9 (C-4), 48.0 (C-5a), 63.8 (C-10a), 120.8 (C-7), 126.9 (2C ortho (benzoyl)), 128.4 (2C meta (benzoyl)), 129.6 (C para (benzoyl)), 131.2 (C-6), 133.1 (C-5b), 136.1 (C ipso (benzoyl)), 144.5 (C-8), 161.3 (C-9b), 171.4 (Carbonyl-C); EI-MS, m/z (rel. inten.) 355 (M^+ (^{37}Cl), 4), 353 (M^+ (^{35}Cl), 8), 192 (54), 105 (100). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{OCl}$: C, 67.89, H, 5.70; N, 11.88; Cl, 10.02. Found: C, 67.99; H, 5.81; Cl, N, 11.79; Cl, 9.95

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