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Fischer indolization of octahydroindol-6-one derivatives revisited: diastereoisomerization and racemization processes

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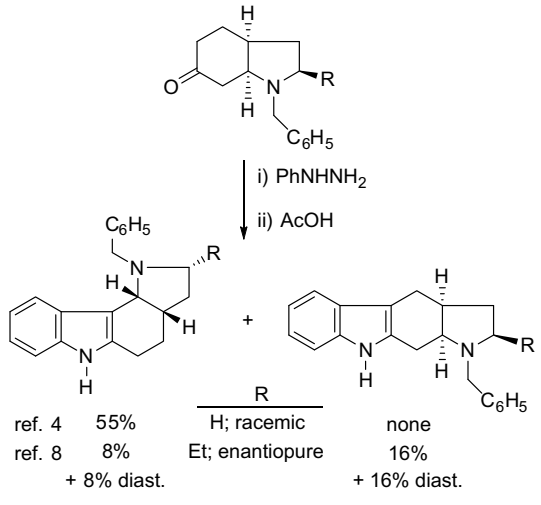
ABSTRACT

Fischer indolization of enantiopure 2-methoxycarbonyl-*cis*-octahydroindol-6-ones using AcOH as a catalyst induces racemization of the octahydropyrrolocarbazoles obtained. Conversely, when using TsOH, the α-amino ester moiety preserves its configuration, although the other stereogenic centers show a partial or total stereolability according to the constitutional framework.

1. Introduction

The Fischer indolization of β-amino ketones has been reported in the field of indole alkaloid synthesis, either as a crucial step in total syntheses (e.g., aspidopermidine[1] and ibogamine[2]) or in synthetic approaches to dasycarpidan,[3] ibophyllidine,[4] *strychnos*,[5] or aspidospermane alkaloids.[6] A drawback of this annulation process can be the regioselectivity of the reaction.[7] Another, less reported, problem is the loss of the absolute stereochemistry in the resulting indole compounds, when enantiopure β-amino ketones are used.



Scheme 1. Previous results in the Fischer indolization of *cis*-octahydroindol-6-ones.

Our group has previously studied the Fischer indolization of *cis*-octahydroindol-6-ones to achieve a synthetic entry to pyrrolocarbazoles as precursors to ibophyllidine alkaloids.[4,8] In the unsubstituted racemic series (R = H, Scheme 1), the process was regioselective, leading to a octahydropyrrolo[3,2-*c*]carbazole as the only compound.[7] Conversely, using an enantiopure 2-ethyl substituted derivative resulted in the formation of both the linear and angular isomers and, interestingly, diastereoisomerization processes were observed when acetic acid was used to promote the indolization[8] (Scheme 1).

There are two reasons why we decided to revisit this process and to study, in the work reported here, the Fischer indolization of the *exo*- and *endo*-isomers of enantiopure methyl 6-oxo-octahydroindole-2-carboxylate **1** and **2**: (i) to evaluate the influence of a sterically less demanding substituent at C(2) on the regioselectivity by replacing the ethyl group with a methoxycarbonyl group; (ii) to gain insight into the stereolability of pyrrolocarbazoles obtained from β-amino ketones.

2. Results and discussion

Enantiopure octahydroindolones **1** and **2** were synthesized from *O*-methyltyrosine in three steps according to our described procedure.[9] The Fischer indolization of the phenylhydrazone of ketone (−)-**1** in acetic acid gave a complex mixture of pyrrolocarbazoles **3**–**8** in 60% overall yield (Scheme 2), which was characterized after careful purification of the reaction mixture. Firstly, three compounds with an *exo*-relationship between the ester at C-2 and the tetracyclic skeleton were eluted: the linear *trans*-isomer **3**, the linear *cis*-isomer **4**, and the angular pyrrolocarbazole **5**. Three other pyrrolocarbazoles were then isolated, this time with an *endo*-relationship: the linear *cis*-isomer **6**, the *trans*-linear isomer **7**, and the angular pyrrolocarbazole **8**. The ratio of the *exo*/*endo* isomers was 1:3, with the linear pyrrolocarbazole **7** (22%) and the angular pyrrolocarbazole **8** (14%) being the main compounds of

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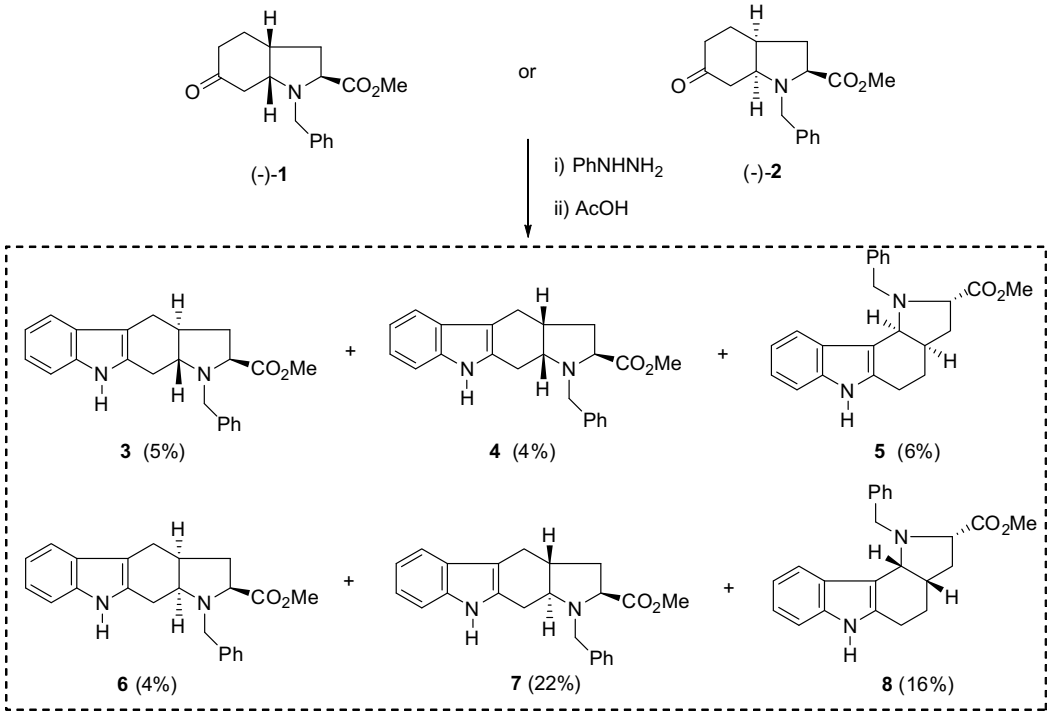


Scheme 2. Racemization in the Fischer indole synthesis (the depicted compounds **3**–**8** are racemic).

the indolization process. The same result was obtained starting from the phenylhydrazone of ketone (−)-**2**. It is noteworthy that the compounds isolated were racemic (see Section 4), in spite of the enantiopure character of the starting amino ketones **1** or **2**. Thus, acetic acid not only promoted the expected equilibration of the ring-fused system but also two previously unreported processes: the racemization of the stereogenic methine carbon of the α-amino ester unit and the formation of *trans*-pyrrolocarbazole derivatives. Indeed, although the methoxycarbonyl group at C-2 induces a slightly better regioselectivity in the indolization process of octahydroindol-6-ones than that observed in the 2-ethyl derivative (at 2:3 instead of the 1:2 ratio), the stereolability of the intermediates under these reaction conditions does not permit the synthesis of enantiopure pyrrolocarbazoles.[10–12] Although it is well known that *N*-benzylidene-protected amino acid derivatives are liable to be racemized due to the high acidity of the α-proton of the ester,[13] it is notable that we were unable to find a precedent for the epimerization of *N*-alkylproline derivatives.[14,15]

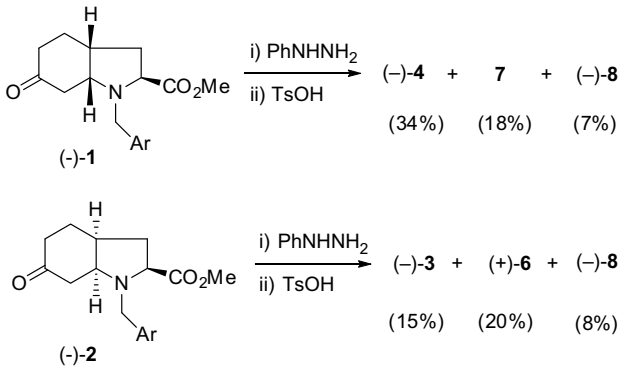
At this point, we evaluated the stereochemical behavior of the starting α-amino ketones **1** and **2** in acetic acid at 80 °C for 3 h (the same reaction conditions as used for the indolization). A total loss of the stereochemistry of the amino ester unit was once again observed, but in these compounds, the racemization was only partial (Table 1), indicating that it is more difficult to change the configuration at the carbon-fused atoms in β-amino ketones than in their corresponding phenylhydrazones or pyrrolocarbazole derivatives.

After these results (generation of twelve compounds, six racemic pairs, from a unique compound, **1** or **2**), we decided to examine the Fischer indolization using TsOH as the acid catalyst. Initially, we checked the stereochemical behavior of ketones **1** and **2** in the presence of TsOH. β-Amino ketone **1** suffered from a partial transformation to **2**, but in this case the (*S*)-configuration at C-2 of both ketones remained stable (Table 1). As expected, in the light of our previous studies of the equilibration of both compounds,[9] β-amino ketone **2** was more stable than **1** under these reaction conditions. When the phenylhydazone of *exo*-ketone **1** was heated in an ethanol solution containing TsOH, a Fischer indolization took place to give a mixture of three compounds **4**, **7**, and **8** (Scheme 3). We assumed that these compounds were enantiopure, since the stereogenic center of the α-amino ester moiety is stereostable under these reaction conditions, maintaining the (*S*)-configuration,

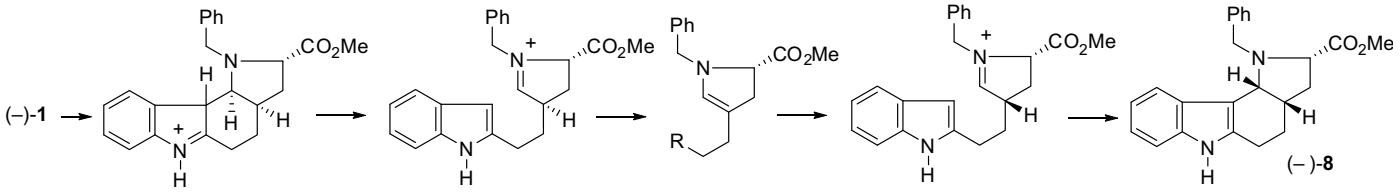
Table 1
Isomerization of octahydroindoles **1** and **2**[a]

	Reaction conditions[b]	Enantiomeric excess[c]	Ratio
(−)-**1**	AcOH neat, 90 °C, 3 h	(+)-**1**, 50% ee; (−)-**2**, 87% ee	1:1
(−)-**2**	AcOH neat, 90 °C, 3 h	(+)-**2**, 52% ee; (−)-**1**, 64% ee	1:1
(−)-**1**	TsOH·H_2O (1 equiv), benzene, 80 °C, 4 h	(−)-**1**, >99% ee; (−)-**2**, >99%	1.2:1
(−)-**2**	TsOH·H_2O (1 equiv), benzene, 80 °C, 4 h	(−)-**2**, >99% ee; (−)-**1**	7:1
(−)-**1**	5 M HCl in MeOH, 65 °C, overnight	(−)-**2**, >99% ee; (−)-**1**	7:1 Ref. 9

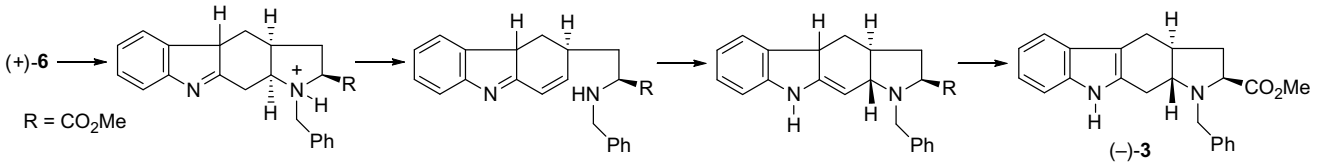
[a] The reactions were performed on a 0.2 mmol scale.
[b] Compounds isolated after column chromatography.
[c] Determined by comparison of the optical rotation with the literature value.[9]



Scheme 3. Fischer indolization of **1** and **2** using TsOH as promoter.



Scheme 4. Diastereoisomerization of pyrrolo[3,2-*c*]carbazole **5**.



Scheme 5. Epimerization of pyrrolo[2,3-*b*]carbazole **4**.

according to the results reported in Table 1. Interestingly, an epimerization occurred at C-10a, the *trans* pyrrolocarbazole **7** being isolated. The formation of indole **8** would have required a double configurational change. A similar result was observed with *endo*-ketone **2**, which produced a mixture of *trans*- and *cis*-linear pyrrolocarbazoles **3** and **6**, respectively, and again the angular pyrrolocarbazole **8** (Scheme 3). Thus, although enantiopure compounds were isolated using TsOH as the catalyst, the regioselectivity (5:1 from **1** and 2:1 from **2**) once again favored the linear pyrrolocarbazoles over the angular fused compound **8**.

The epimerization of stereogenic centers linked to the indole nucleus at either the α- or β-carbon, when bonded to a nitrogen atom, has been reported with particularly exhaustive studies on indoloquinolizidines.[16,17] This stereolability has also been described in compounds bearing units of 3-(α-aminomethyl)indole.[18] A plausible mechanism for the diastereosiomerization, leading to pyrrolocarbazole (−)-**8** from (−)-**1**, is depicted in Scheme 4. It involves a Grob-type fragmentation of the protonated indole **5** (a retro Pictet-Spengler process), followed by an epimerization at the β-amino carbon through a tautomeric equilibrium of the initially formed iminium salt and a later reprotonation. The same tandem ring-opening/ring-closure mechanism could operate in the racemization processes using AcOH as reported above (Scheme 2).

More interesting was the epimerization in linear pyrrolocarbazole derivatives to give the previously unreported *trans*-octahydropyrrolo[2,3-*b*]carbazole compounds. A possible pathway, in which the protonated indole undergoes a retro-imino aza-Michael process followed by an intramolecular conjugate addition of the resulting secondary amine upon the vinylindole system, as depicted in Scheme 5, could be considered.

The constitutional and strereochemical arrangement of *cis*-**4** and **6** and *trans*-linear **3** and **7** isomers, and *cis*-angular isomers **5** and **8** were assigned by ^{1}H and ^{13}C NMR spectroscopic analyses aided by COSY and HSQC experiments (Fig. 1 and Table 2). The differentiation between linear and angular isomers was made on the basis that H-10c of the angular isomers **5** and **8**, which corresponds to H-10a of **4**-**7**, appeared downfield at δ 4.63 and 3.99 relative to H-10a of the linear isomers (δ 3.20–3.55). For the *cis*-derivatives, the chemical shifts of the methine protons H-3a and H-10a (for **4** and **6**) or H-10c (for **5** and **8**) are more deshielded in the *exo*- than in the *endo*-compounds due to the *syn*-relationship of the methoxycarbonyl group with both protons.[19] In the ^{13}C NMR spectra, the chemical shift of the benzylic methylene carbon of *endo* ($\delta \sim 58$–59) and *exo* isomers ($\delta \sim 52$–53) was also characteristic.

In the linear compounds, the *cis*-isomers **4** and **6** were distinguished from *trans*-isomers **3** and **7** on the basis of the chemical shifts and multiplicity of the ring junction proton H-10a. The H-10a of **3** and **7** appeared upfield at δ 3.38 (td, J = 10, 5 Hz) and δ 2.74, respectively, relative to that of **4** and **6** (δ 3.60 and 3.22). In the ^{13}C NMR spectra, ring junction carbons C-3a (δ 34.3 and 35.9) and C-10a (δ 58.8 and 61.8) of *cis* isomers **4** and **6** appeared upfield relative to C-3a (δ 42.6 and 41.4) and C-10a (δ 64.1 and 65.6) of *trans* isomers **3** and **7**.

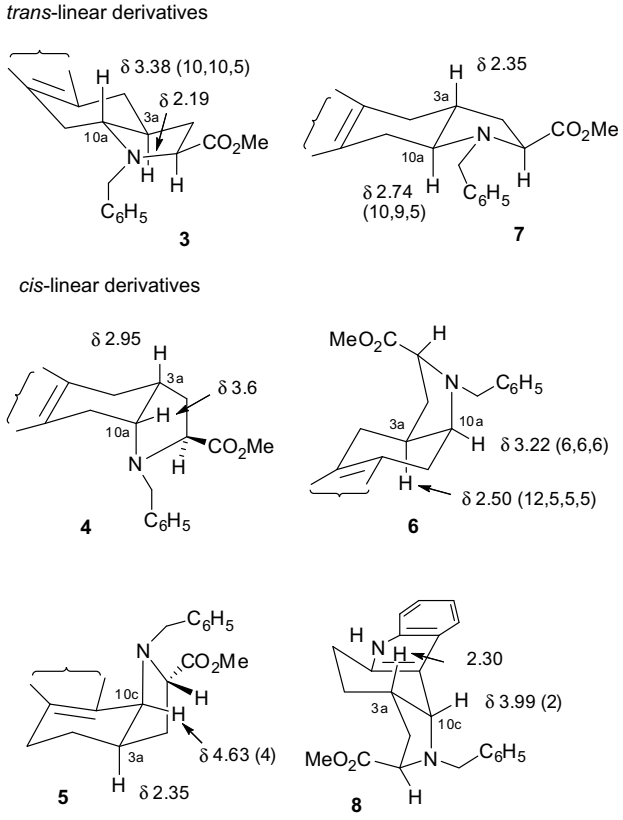


Figure 1. Preferred conformations of compounds **3**–**8**.

Table 2
^{13}C NMR data of pyrrolocarbazoles **3**–**8**

Carbon	**3** (*exo*/*trans*)	**4** (*exo*/*cis*)	**6** (*endo*/*cis*)	**7** (*endo*/*trans*)	Carbon	**5** (*exo*)	**8** (*endo*)
C-2	62.5	62.6	65.1	65.6	C-2	59.9	66.0
C-3	34.2	35.9	35.1	33.7	C-3	34.2	34.6
C-3a	42.6	34.3	35.9	41.4	C-3a	37.1	37.2
C-4	25.9	22.0	23.1	25.9	C-4	27.6	26.3
C-4a	110.5	107.9	108.1	110.3	C-10b	109.6	109.7
C-4b	127.2	127.0	127.0	127.0	C-10a	128.1	128.2
C-5	117.8	117.7	117.7	117.8	C-10	118.5	118.4
C-6	119.3	119.2	119.0	119.2	C-9	119.6	119.5
C-7	121.2	121.1	120.9	121.1	C-8	121.1	121.0
C-8	110.8	110.5	110.4	110.5	C-7	110.5	110.5
C-8a	136.5	136.2	136.1	136.4	C-6a	136.5	136.5
C-9a	133.0	131.6	131.8	132.9	C-5a	135.9	135.9
C-10	30.2	22.2	26.1	30.0	C-5	23.0	23.0
C-10a	64.1	58.8	61.8	67.3	C-10c	56.8	61.8
NCH_2	51.8	53.6	58.0	57.7	NCH_2	52.8	59.6
CO_2Me	175.1	175.0	175.0	175.0	CO_2Me	175.5	175.4
CH_3	51.2	51.6	51.8	51.8	CH_3	51.0	51.1

The numbering of angular derivatives **5** and **8** has been arranged for an easier comparison of their data with those of the other pyrrolocarbazoles.

3. Conclusion

In conclusion, the α-carbon of the amino ester in polycyclic proline analogues **1**–**8** reported here has shown its stereolability in an acetic medium at 80–90 °C. Moreover, attention should be paid to the possibility of epimerization (or racemization) in pyrrolo[3,2-*c*]- and pyrrolo[2,3-*b*]carbazoles working, in either acetic or *p*-toluenesulfonic acid, since these compounds are prone to suffering retro-Pictet Spengler and fragmentation processes, which promotes the loss of their stereochemical integrity.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded in a $CDCl_3$ solution at 400 MHz, and 75 or 100 MHz, respectively. In addition, chemical shifts are reported as δ values (ppm) relative to internal Me_4Si. Infrared spectra were recorded on a Nicolet 205 FT-IR spectrophotometer. HRMS were determined on an Autospec-VG apparatus. Optical rotations were taken on a Perkin–Elmer 241 polarimeter with a 1 ml (L = 1 dm) cell. TLC was performed on SiO_2 (silica gel 60 F254, Merck). The spots were located by UV light and a 1% $KMnO_4$ solution. Column chromatography was carried out on SiO_2 (silica gel 60, SDS, 230–400 mesh). All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions. As a chiral starting material L-tyrosine was used.

4.2. Fischer indolization of 1 and 2

4.2.1. Fischer indolization of *exo* ketone 1 using AcOH

To a solution of ketone **1** (200 mg, 0.69 mmol) in EtOH (5 mL) were added phenylhydrazine (103 mg, 0.7 mmol) and Na_2CO_3 (81 mg, 0.75 mmol). The mixture was heated at reflux for 2 h (until disappearance of ketone carbonyl absorption in IR spectum), filtered, and concentrated: ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 23.1 (CH_2), 25.0 (CH_2), 33.9 (CH_2), 35.1 (CH_2), 35.2 (CH), 50.9 (CH_3), 52.5 (CH_2), 59.7 (CH), 62.0 (CH), 112.9 (CH), 119.5 (CH), 126.8 (CH), 128.1 (CH), 128.7 (CH), 129.0 (CH), 139.3 (C), 145.8 (C), 148.0 (C), 174.5 (C). The residue was dissolved in glacial AcOH (8 mL), and the solution was heated at 90 °C for 2 h. The reaction mixture was concentrated and the residue was partitioned between CH_2Cl_2 and saturated Na_2CO_3 solution. After additional extractions of the aqueous phase, the dried organic extracts were concentrated and purified by chromatography (hexane/EtOAc 1:4 increasing to 1:1) to give, in order of elution the *exo*-isomers **3** (12 mg, 5%), **4** (10 mg, 4%), and **5** (16 mg, 6%) and the *endo* isomers **6** (10 mg, 4%), **7** (54 mg, 22%), and **8** (40 mg, 16%). Overall yield was 57%. Compound **7**: $[\alpha]_D^{22} = 0$ (c 1, $CHCl_3$); Compound **8**: $[\alpha]_D^{22} = 0$ (c 1, $CHCl_3$). For analytical data see below. An analogous result was found using the *endo* (−)-ketone **2**.

4.2.2. Fischer indolization of exo ketone 1 using TsOH

To a solution of ketone **1** (97 mg, 0.34 mmol) in EtOH (4 mL) were added phenylhydrazine (50 mg, 0.34 mmol) and Na_2CO_3 (39 mg, 0.37 mmol). The mixture was heated at reflux for 3 h (until the disappearance of the ketone carbonyl absorption in the IR spectrum), filtered, and concentrated. $TsOH{\cdot}H_2O$ (129 mg, 0.68 mmol) was added to a solution of the crude hydrazone in EtOH (3.5 mL). The reaction mixture was heated at reflux temperature for 3 h, quenched with Et_2O (8 mL) and saturated $NaHCO_3$ solution (8 mL). The aqueous phase was extracted with Et_2O, and the combined organic extracts were washed with brine, dried, concentrated, and the residue was purified by chromatography. On elution with hexane/EtOAc (1:1) were successively isolated (−)-**4** (39 mg, 34%), **7** (21 mg, 18%), and (−) **8** (8 mg, 7%). Overall yield was 59%.

4.2.3. Fischer indolization of endo ketone 2 using TsOH

Operating as above, using ketone **1** (130 mg, 0.45 mmol), the reaction mixture resulting from the indolization process was purified by chromatography. On elution with hexane/EtOAc (4:1) (−)-**3** (21 mg, 12%), (+)-**6** (28 mg, 16%), and (−)-**8** (26 mg, 15%) were isolated successively. Overall yield: 43%.

4.3. Analytical data for pyrrolocarbazole 3–8

4.3.1. (2*S*,3a*S*,10a*R*)-1-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,9,10,10a-octahydropyrrolo[2,3-*b*]carbazole 3

$[\alpha]_D^{22} = -102$ (c 1.25, $CHCl_3$); ^1H NMR (gCOSY, 400 MHz) 1.72 (ddd, J = 12.8, 10.4, 5.6 Hz, H-3), 2.19 (m, H-3a), 2.45–2.57 (m, H-3, H-4, H-10), 2.97 (dd, J = 13.6, 4.8 Hz, H-10eq), 3.02 (dd, J = 14, 5.2 Hz, H-4eq), 3.38 (td, J = 10, 5 Hz, H-10a), 3.63 (s, 3H, OMe), 3.85 and 4.05 (2d, J = 13.6, 1H each, NCH_2Ar), 3.93 (dd, J = 8.8, 6 Hz, H-2), 7.04 and 7.07 (2t, J = 7.5 Hz each, H-7 and H-6), 7.20–7.30 (m, 6H, ArH), 7.40 (d, J = 7.5 Hz, 1H, H-5), 7.75 (br s, 1H,

NH); ^{13}C NMR (HSQC), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1918.

4.3.2. (2*S*,3a*R*,10a*R*)-1-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,9,10,10a-octahydropyrrolo[2,3-*b*]carbazole 4

$[\alpha]_D^{22} = -129.3$ (*c* 2.14, $CHCl_3$); ^{1}H NMR (gCOSY, 400 MHz) 1.95–2-05 (m, 2H, H-3), 2.60–2.80 (m, 4H, H-4 and H-10), 2.95 (m, H-3a), 3.55 (dd, *J* = 9.0, 1.2 Hz, H-2), 3.60 (masked, 1H, H-10a) 3.61 (s, 3H, OCH_3), 3.87 and 3.96 (2d, *J* = 13 Hz, 1H each, NCH_2Ar), 7.00–7.05 (m, 2H, ArH), 7.20–7.30 (m, 6H, ArH), 7.40 (d, *J* = 7.5 Hz, H-5), 7.60 (s, 1H, NH); ^{13}C NMR (100 MHz, gHSQC), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1915.

4.3.3. *rac*-(2*S*,3a*R*,10c*S*)-1-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,5,6,10c-octahydropyrrolo[3,2-*c*]carbazole 5

^{1}H NMR (400 MHz, $CDCl_3$) 1.60 (m, 1H, H-4), 1.95 (m, 1H, H-3), 2.15 (m, 1H, H-3 and H-4), 2.35 (m, 1H, H-3a), 2.80 (m, 2H, H-5), 3.60 (masked, H-2), 3.63 (s, 3H, OMe), 3.92 and 4.23 (2d, *J* = 13 Hz, 1H each, NCH_2Ar), 4.63 (d, *J* = 4 Hz, H-10c), 7.05–7.30 (m, 8H, ArH), 7.65 (d, *J* = 7.5 Hz, 1H, H-10), 7.95 (br s, 1H, NH); ^{13}C NMR (HSQC, 75 MHz, $CDCl_3$), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1913.

4.3.4. (2*S*,3a*S*,10a*S*)-1-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,9,10,10a-octahydropyrrolo[2,3-*b*]carbazole 6

$[\alpha]_D^{22} = +3$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (gCOSY, 400 MHz) 1.93 (dt, *J* = 12.4, 7.2 Hz, H-3), 2.30 (ddd, *J* = 12.4, 8.8, 7.2 Hz, 1H), 2.50 (dq, *J* = 12, 5,4 Hz, H-3a), 2.75-2.94 (m, 4H, H-4 and H-10), 3.22 (q, *J* = 6 Hz, H-10a), 3.54 (dd, *J* = 8.8, 7.2 Hz, H-2), 3.56 (s, 3H, OCH_3), 3.92 (s, 2H, NCH_2Ar), 7.00–7.05 (m, 2H, ArH), 7.20–7.30 (m, 6H, ArH), 7.40 (d, *J* = 7.5 Hz, H-5), 7.60 (br s, 1H, NH); ^{13}C NMR (100 MHz, gHSQC), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1918.

4.3.5. (2*S*,3a*R*,10a*S*)-1-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,9,10,10a-octahydropyrrolo[2,3-*b*]carbazole 7

^{1}H NMR (COSY, 500 MHz, $CDCl_3$) 1.89 (dt, *J* = 12, 11 Hz, 1H, H-3), 2.24 (ddd, *J* = 12, 7.5, 3.5 Hz, 1H, H-3), 2.33–2.38 (m, 1H, H-3a), 2.36 (dd, *J* = 10, 1.5 Hz, 1H, H-4), 2.61 (dd, *J* = 14.5, 9.5 Hz, 1H, H-10), 2.74 (ddd, *J* = 10, 9, 5 Hz, 1H, H-10a), 2.80 (dd, *J* = 15, 5 Hz, 1H, H-10), 2.99 (ddd, *J* = 10, 9, 1.5 Hz, 1H, H-4), 3.57 (s, 3H, OMe), 3.57 (dd, *J* = 11, 3.5 Hz, 1H, H-2), 3.89 and 3.94 (2d, *J* = 13.5 Hz, 1H each, NCH_2Ar), 7.04 (t, *J* = 7.5 Hz, 1H, H-7), 7.09 (t, *J* = 7.5 Hz, 1H, H-6), 7.21–7.33 (m, 6H, ArH), 7.41 (d, *J* = 7.5 Hz, H-5), 7.65 (br s, 1H, NH); ^{13}C NMR (HSQC, 75 MHz, $CDCl_3$), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1913.

4.3.6. (2*S*,3a*S*,10c*R*)-Benzyl-2-methoxycarbonyl-1,2,3,3a,4,5,6,10c-octahydropyrrolo[3,2-*c*]carbazole 8

$[\alpha]_D^{22} = -13$ (*c* 1.4, $CHCl_3$); IR (film) 3340, 1739; ^{1}H NMR (COSY, 500 MHz, $CDCl_3$) 1.69–1.75 (m, 2H, H-3 and H-4), 2.26–2.32 (m, 1H, H-3a), 2.42–2.52 (m, 1H, H-3), 2.52–2,59 (m, 1H, H-4), 2.70 (dd, *J* = 16, 11, 5.5 Hz, 1H. H-5), 2.77 (ddd, *J* = 16.5, 6, 3 Hz, H-5), 3.10 (s, 3H, OMe), 3.43 (dd, *J* = 7, 3.5 Hz, 1H, H-2), 3.61 (d, *J* = 12 Hz, 1H, NCH_2Ar), 3.99 (d, *J* = 2 Hz, 1H, H-10c), 4.59 (d, *J* = 12 Hz, 1H, NCH_2Ar), 7.04 (t, *J* = 8 Hz, 1H, H-8), 7.08 (t, *J* = 8 Hz, 1H, H-9), 7.15–7.30 (m, 6H, ArH), 7.61 (d, *J* = 7.5 Hz, 1H, H-10), 8.1 (br s, 1H, NH); ^{13}C NMR (HMQC, 75 MHz, $CDCl_3$), see Table 2. HRMS (ESI-TOF) calcd for $C_{23}H_{25}N_2O_2$: 361.1910 (M^++1), found 361.1912.

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