118. Synthesis of (−)-Hobartine and Related Indole Alkaloids[1])

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Summary

An improved method for obtaining optically pure (*S*)-(1-*p*-menthen-8-yl)amine (**12**) has led to expedient syntheses of two hypothetical biogenetic intermediates on the way to aristoteline (**7**), namely (*S*)-*N*-(1-*p*-menthen-8-yl)-2-(3-indolyl)ethylamine (**3**) and (*S*)-*N*-(1-*p*-menthen-8-yl)-2-(3-indolyl)ethylideneamine (**4**). The latter has been transformed into (−)-hobartine (**6**) in 64% yield *via* a stereoselective biomimetic cyclization by treatment with HCOOH. This unambiguous synthesis establishes the hitherto unknown absolute configuration of (−)-hobartine (**6**). Several model cyclization reactions of *N*-substituted α-(terpen-8-yl)imine derivatives yielding unsaturated 3-azabicyclo-[3.3.1]nonane compounds are described.

Aristoteline (**7**) was isolated in 1975 by *Bick et al.* [1] from the New Zealand plant *Aristotelia serrata* as the first member of a novel group of indole alkaloids. The same authors determined its pentacyclic structure by X-ray crystallography. Subsequently, this natural product was detected in other plants [2] [3] together with several related alkaloids[2]), of which two, the tetracyclic compounds makomakine (**5**) and hobartine (**6**) *(Scheme 1)*, are on the same oxidation level as aristoteline (**7**).

The outstanding feature of this alkaloid family is that most of its members embody an intact monoterpene unit, whereas the vast majority of the known mevalonoid indole alkaloids originate from secologanin which arises from an oxidative cleavage of a preformed cyclopentane monoterpene. (*cf. e.g.* [14] and ref. therein). A plausible pathway to the aristoteline family has been proposed by *Bick et al.* [15] and, in a slightly modified version, by *Hesse et al.* [3]. Their proposal which is relevant to the present discussion is shown in *Scheme 1:*

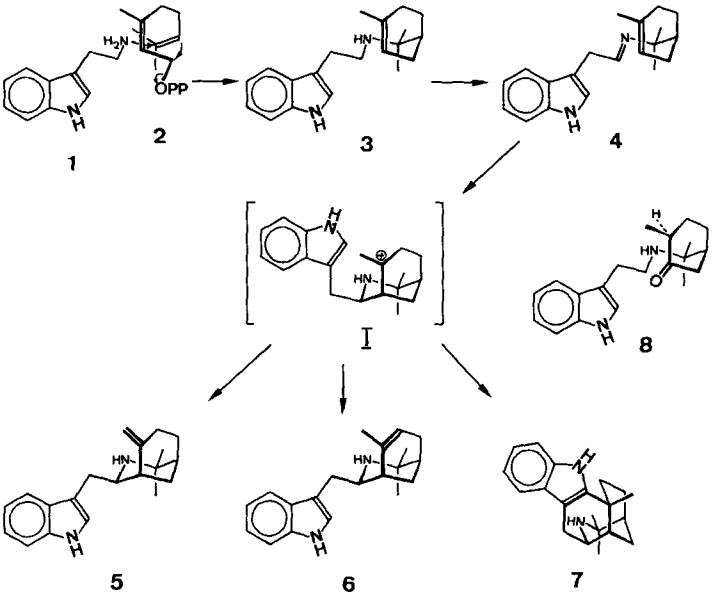
According to *Scheme 1* cyclization of nerylpyrophosphate (**2**) in the presence of tryptamine (**1**) leads to **3** as the first biogenetic intermediate containing all C-atoms of the aristoteline-type alkaloids. To date, this compound has not been detected in natural sources, but an oxidized version of its skeleton is present in frutico-

[1]) Presented in part at the 'Herbstversammlung der Schweizerischen Chemischen Gesellschaft', October 14, 1983 in Bern.

[2]) Aristotelone [2]; tasmanine [3]; makomakine [4]; makonine [4]; hobartine [5]; sorelline [5]; aristotelinine [6]; aristone [7] [8]; aristotelinone [7]; fruticosonine [9]; peduncularine [10]; aristoserratine [11]; aristomakine [12]; serratoline [13]; serratenone [13].

sonine (**8**) *(Scheme 1)* which was isolated from *Aristotelia fruticosa* by *Bick et al.* [9]. The next biogenetic step is thought to involve dehydrogenation of **3** to the aldimine **4**, which upon acid-catalyzed cyclization yields the ionic intermediate **I**. This species can either generate makomakine (**5**) and hobartine (**6**) by proton loss, or alternatively, undergo a further ring closure involving the indole moiety to give aristoteline (**7**), possibly *via* a 3,3-disubstituted spiroindolenine derivative [3].

Scheme 1



The novel structures of **5** and **6** and the very low concentration in natural sources (*ca.* 10^{-5}% of the dried plant extracts) raised our interest in a total synthesis of these compounds[3]). Our plan involved the incorporation of a N-atom into a cyclic monoterpene unit followed by condensation with a suitable 3-substituted indole derivative.

The obvious N-containing monoterpene building block for the planned synthesis is represented by (*S*)-(1-*p*-menthen-8-yl)amine (**12**)[4]) *(Scheme 2)*.

Conversion of optically pure (*S*)-α-terpineol (**9**) (readily available in more than 98% e.e. [20]) into the dibromide **10** [21] was followed by treatment with HN_3/BF_3 to yield **11** and the latter was reduced as a crude product with $LiAlH_4$ to give **12** (71% yield overall). This reduction step restores the original double bond [22], protection of

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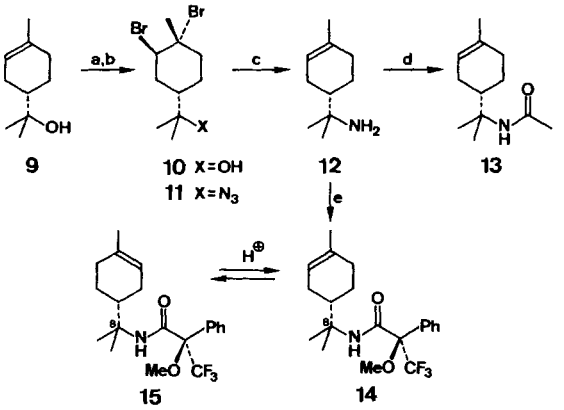
[3]) Recently *Lévy et al.* [16] and *Stevens et al.* [17] have published independent syntheses of (+)-makomakine (**5**) and (+)-aristoteline (**7**) starting from (−)-β-pinene, and of racemic hobartine (**6**) from α-pinene, with overall yields ranging from 10 to 20%. Both approaches were based on *Khuong-Huu*'s Hg^{2+}-catalyzed version of the *Ritter* reaction [18].

[4]) This compound has been prepared previously in unspecified optical and chemical yield *via* a similar route by *Khuong-Huu et al.* [19] using α-pinene as starting material. In our laboratory all batches of **12** prepared according to their procedure were contaminated with *ca.* 25% of isomeric amines which were difficult to remove.

Scheme 2



Reagents: a) Br_2, Et_2O; b) HN_3, $BF_3 \cdot Et_2O$, benzene; c) $LiAlH_4$; d) Ac_2O, Et_3N; e) (*R*)-MTPA · Cl, pyridine.

which is essential for the success of this reaction sequence because direct treatment of **9** with HN_3/BF_3 results in extensive racemization.

The enantiomeric purity of **12** was determined by ^{1}H-NMR spectroscopy (300 MHz, C_6D_6) of the mixture of diastereomeric amides **14** and **15**, which resulted from the reaction of crude **12** with *Mosher*'s reagent [23] ((*R*)-α-methoxy-α-trifluoromethylphenylacetic acid chloride = MTPA · Cl). Comparison of the data shown in *Table 1* with the ^{1}H-NMR spectrum of an equimolar mixture of **14** and **15** generated from the original sample by treatment with mesitylenesulfonic acid, indicated an optical purity of 86 ± 6% for **12**. Confirming this result, an e.e. value of 87% was obtained by comparing the optical rotations of crude and optically pure **12** (the latter was prepared by repeated crystallization of the (2*R*,3*R*)-tartaric-acid salt of crude **12**).

Table 1. *Selected ^{1}H-NMR Chemical Shifts*[a]) *of the (R)-MTPA Amides* **14** *and* **15**

Component	Rel. amount	$(CH_3)_2$–C(8)	Integral[b])	CH_3O	Integral[b])
14	93 ± 3%	1.18 (*s*)	2.73 H	3.16 (*q*, *J* = 1.6)[c])	2.85 H
		1.19 (*s*)	2.79 H		
15	7 ± 3%	1.09 (*s*)	0.15 H	3.20 (*q*, *J* = 1.6)[c])	0.15 H
		1.22 (*s*)	0.30 H		

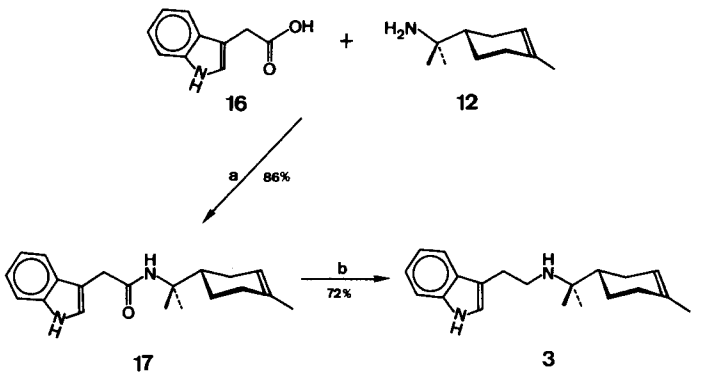
[a]) Recorded in C_6D_6 (300 MHz).

[b]) Relative number of protons, related to the sum of integrals of the CH_3O-groups of **14** and **15** (arbitrarily set equal 3.00).

[c]) These splittings are ascribed to a $^5J(^1H,^{19}F)$ long-range coupling. Similar values have been observed in *o*-fluoroanisole derivatives [24].

With this expedient method at hand for obtaining optically pure **12**, the first intermediate **3** could be prepared as shown in *Scheme 3*. Condensation of **12** with (3-indolyl)acetic acid (**16**) according to *Mukaiyama et al.* [25] furnished **17** in good yield. Subsequent reduction of **17** with $LiAlH_4$ led to the desired intermediate **3**, which is a stable crystalline compound.

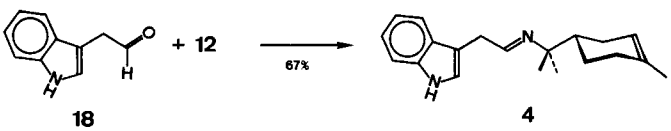
Scheme 3



Reagents: a) 2-Chloro-1-methylpyridinium iodide, Et_3N, CH_2Cl_2; b) $LiAlH_4$.

For the synthesis of the next intermediate **4**, sizeable amounts of (3-indolyl)acetaldehyde (**18**) *(Scheme 4)* were needed. The difficulties encountered in obtaining reproducible and acceptable yields of **18** when using known procedures [26] [27] led us to develop a new route to **18**: reduction of commercially available (3-indolyl)acetonitrile with diisobutylaluminum hydride (DIBAH) (for a review see [28]) routinely furnished **18** (isolated as the bisulfite adduct [26]) in 55–65% yield[5]). Imine **4** was readily prepared by mixing roughly equimolar benzene solutions of **12** and **18**, whereupon **4** crystallized in 50–60% yield [30].

Scheme 4



Whereas **4** is perfectly stable in the crystalline state (no signs of decomposition after several years at −20°), freshly prepared solutions in $CHCl_3$ decompose rapidly, preventing full characterization. Nonetheless, sufficient evidence to support structure **4** could be obtained. The presence of the aldimine moiety is supported by an IR absorption at 1660 cm^{-1} and the appearance of a well-separated ^{1}H-NMR signal at 7.68 ppm, which appears as a triplet (J = 5.1 Hz) as a consequence of a coupling with the benzylic CH_2-group (δ = 3.72 ppm). The (*E*)-configuration of **4** is favored on the basis of studies by *Karabatsos et al.* [31].

Since **4** is regarded as the immediate precursor of the pivotal cationic species **I** *(Scheme 1)*, the possibility of a biomimetic *in vitro* cyclization of **4** was examined[6]).

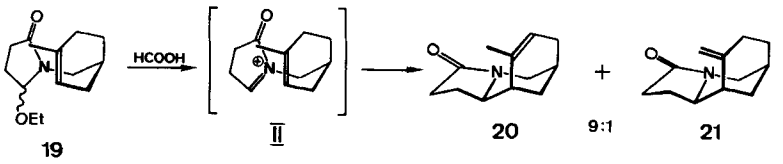
[5]) In a preliminary communication lacking experimental details *Kametani et al.* [29] recently described a similar preparation of **18** (DIBAH reduction of (3-indolyl)acetic acid).

[6]) The feasibility of such an approach to aristoteline-type alkaloids was also discussed by *Hesse et al.* ([3], *Footnote 5*), but no report of a successful experimental realization of their scheme has been forthcoming so far.

Many attempts to induce this reaction with a variety of *Lewis* and *Brönsted* acids led to intractable mixtures containing little, if any, **5**, **6** or **7**, and for this reason different approaches to the synthesis of aristoteline-type alkaloids were investigated.

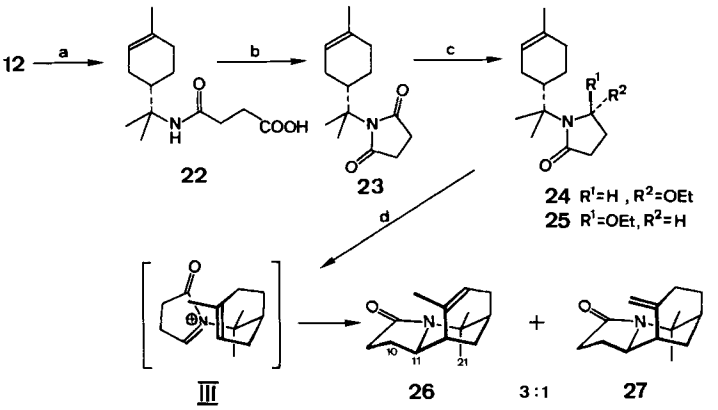
An efficient route to the 3-azabicyclo[3.3.1]nonane skeleton has been described by *Speckamp et al.* [32], who have reported that the ethoxylactam **19** *(Scheme 5)* cyclizes smoothly upon treatment with HCOOH to give a 9:1 mixture of **20** and **21**.

Scheme 5



The outcome of this reaction prompted us to attempt a similar cyclization[7]). When the ethoxylactam mixture **24/25** (readily prepared from **12** *via* **22** and **23**, *Scheme 6*) was subjected to the *Speckamp* conditions (HCOOH, 16 h, r.t.) a 3:1 mixture of **26** and **27** was formed, which could be separated by column chromatography.

Scheme 6



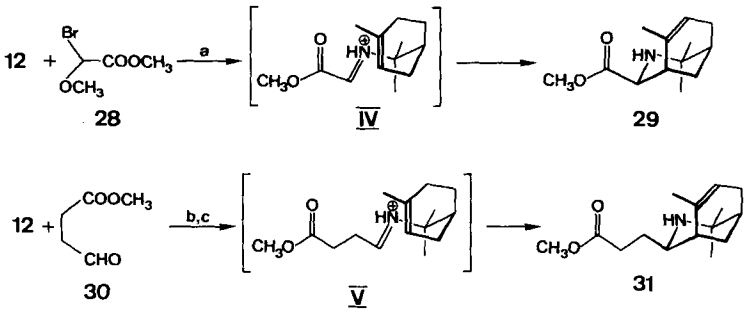
Reagents: a) Succinic anhydride; b) NaOAc, Ac_2O, 100°, 4 h; c) $NaBH_4$, EtOH, H^+; d) HCOOH, 16 h, r.t.

The configuration of **26** and **27** could not be determined unambiguously, but an evaluation of the NMR data collected for these and other cyclization products, presented in the *Appendix* (*Table 2* and *3*), clearly indicates that all of them have the same configuration (*endo*) at C(11). Various authors have concluded that *endo*-configurated products are formed invariably in this type of cyclization [32] [33] and in one case a definite proof has been provided by X-ray crystallography ([32], 'Note added in proof'). The exclusive formation of products with *endo*-configuration in all cases reported so far, has been explained by invoking a chair transition state between an (*E*)-iminium ion (such as **II** and **III**) and the reaction products [32] [33]. In our case, the preference to adopt a chair transition state is expected to be even more pronounced because the (potential) products of a boat transition state would suffer from a 1,3-diaxial interaction between $H_3C(21)$ and $H_2C(10)$.

[7]) The *N*-acyliminium ion approach to the construction of annelated *N*-heterocycles has become increasingly popular, *cf. e.g.* [33]. A cyclization reaction involving *N*-acylamino radicals has been investigated by *Hart & Yeun-Min* [34].

Further exploitation of **26** and **27** as intermediates for a synthesis of **6** and **5**, respectively, had to be discontinued when it was found that they resisted attempted hydrolysis even under drastic conditions and failed to undergo reduction to the corresponding amino aldehydes. For this reason an approach leading directly to *bicyclic secondary amines* had to be developed. Accordingly, the cyclization of aldimines derived from **12** and acyclic aldehydes or their equivalents was investigated next. In this context, it was found, that the reaction of methyl 2-bromo-2-methoxyacetate (**28**) [35] with **12** in toluene led to a crystalline precipitate of the hydrobromide of **29** in 30% yield (not optimized) *(Scheme 7)*. In this case the configuration of the cyclization product **29** could be assigned unambiguously by ^{1}H-NMR spectroscopy: the pronounced shielding of the olefinic CH_3-group *(cf. Table 2)* must originate from the methoxycarbonyl group, thus the two substituents have to be located *syn* to each other. This reaction presumably proceeds *via* the *C*-acyliminium ion **IV**[8]).

Scheme 7



Reagents: a) toluene, r.t.; b) benzene, r.t.; c) HCOOH.

Similarly, the reactivity of an aldiminium ion with two alkyl substituents was examined[9]). HCOOH-treatment of the crude condensation product from **12** and methyl (3-formyl)propionate (**30**) [38] resulted in the formation of a single product (**31**, *Scheme 7*) in 60% yield.

Encouraged by these results, we returned to the imine **4** and subjected it to the same reaction conditions *(Scheme 8)*. We found that treatment of **4** with HCOOH led to (−)-hobartine (**6**) in 64% yield as the only detectable reaction product.

Whereas most of the properties of synthetic **6** (m.p., IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrum) agree within experimental error with the reported data of natural (−)-hobartine (**6**) [5], the optical rotation of our preparation is somewhat higher than the value determined by *Hesse et al.* [5].

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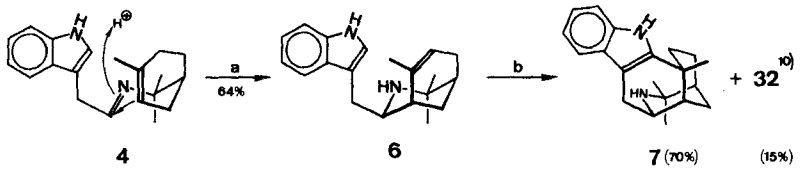
[8]) We are not aware of other reports concerning the cyclization of *C*-acyliminium ions. The outcome of the sequence **12** + **28**→**29** suggests that it might represent a useful general approach to the synthesis of γ-functionalized cyclic α-amino acids.

[9]) For a review of various aspects of iminium salts see [36]. Leading references to older literature concerning the cyclization of iminium ions can be found in a recent paper by *Demailly & Solladie* [37].

Scheme 8



Reagents: a) HCOOH, 16 h, r.t.; b) 20% HCl, 8 h reflux.

The unambiguous transformation of (*S*)-α-terpineol (**9**) into (−)-hobartine (**6**) in 5 steps with an overall yield of *ca.* 30% defines the hitherto unknown absolute configuration of **6** as shown in *Scheme 8*. As a confirmation, synthetic (−)-hobartine was transformed into (+)-aristoteline (**7**) according to *Lévy et al.* [16].

We thank Prof. Dr. *D. Arigoni* for his support of this work.

Appendix. – Tabular survey and interpretation of some NMR data of the cyclization products **6**, **26**, **29** and **31** (*cf. Table 2* and *3*).

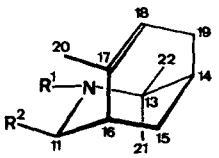


Figure. *The biogenetic numbering of hobartine* (**6**) [5]. (For convenience this numbering has been adopted for all compounds listed in *Table 2* and *3*.)

Experimental Part

General. See [39]. Optical rotations were measured on a *Perkin-Elmer-141* polarimeter. $CHCl_3$ used for IR and optical rotations was purified by passage through basic alumina *(Woelm B, activity I)* immediately before use.

Purification of α-Terpineol (**9**), [20]. Commercially available α-terpineol (*Merck, 'α-Terpineol zur Synthese'*, m.p. 34–37°, $[\alpha]_D^{25} = -68°$ (c = 19.5, EtOH)) was recrystallized 3 times from petroleum ether (b.p. 50–70°) and then showed $[\alpha]_D^{25} = -98.4°$ (c = 18.5, EtOH) indicating 98% e.e.

(S)-(1-p-Menthen-8-yl)amine (**12**). To a solution of 6.17 g (40 mmol) of (*S*)-α-terpineol (**9**), purified as described above, in 50 ml of dry Et_2O which was kept at −70° were rapidly added 6.4 g (40 mmol) Br_2 *(Fluka, puriss.)*. After removal of the solvent (RV, r.t.) the crystalline residue was dried (h.v., 6 h, r.t.). The resulting material was dissolved in 20 ml of dry benzene and added to a benzene solution containing 120 mmol HN_3 [40] at r.t. Next were added 7.5 ml (60 mmol) of freshly distilled $BF_3 \cdot Et_2O$ *(Fluka, pract.)*. After 2 h at r.t. the mixture was poured into crushed ice and washed 3 times with aq. 1N Na_2CO_3. The benzene layer was dried ($MgSO_4$) and evaporated to *ca.* 10 ml (RV, r.t.). The resulting solution was added within 2 h to a suspension of 6.08 g (160 mmol) $LiAlH_4$ in 200 ml Et_2O at reflux under N_2. After 16 h at reflux the mixture was cooled to 0° and excess reagent was destroyed by dropwise addition of H_2O. The filtered solution was extracted with 4 portions of 1N H_2SO_4 which were adjusted immediately to pH 14 (20% NaOH) and extracted with Et_2O (4 × 100 ml). The combined org. layers were dried (K_2CO_3) and evaporated. The crude product was distilled (80–90°/12 Torr) to yield 4.35 g (2.83 mmol; 71%) of **12** as a colorless oil. $[\alpha]_D^{25} = -92°$ (c = 2.05, EtOH), indicating 87% e.e. *(vide infra)*. IR (neat): 3400–3100 br. *m*, 3005*m*, 2957*s*, 2920*s*, 1380*m*, 1362*m*. ^{1}H-NMR

[10]) The structure and the properties of this side product will be discussed in a forthcoming communication.

Table 2. *Selected ^{1}H-NMR Data* ($CDCl_3$, 300 MHz) *of the Cyclization Products*[a])

Compound	R^1	R^2	H–C(11)	H–C(14)	H_R–C(15)	H–C(18)	H_S–C(19)	CH_3–C(20)	$(CH_3)_2$–C(13)
6	H	CH_2–(3-ind.)	3.49 (*ddd*) (J = 8/6/2)	1.44 (*m*)	1.61 (*dt*) (J = 12/3)	5.62 (*m*)	2.28 (*m*)	1.81 (*m*)	1.16 (*s*); 1.09 (*s*)
26		–CO–CH_2–CH_2–	3.68 (*ddd*) (J = 9/6/3)	1.46 (*m*)	1.70 (*dt*) (J = 13/3)	5.48 (*m*)	2.41 (*m*)	1.74 (*m*)	1.72 (*s*); 1.30 (*s*)
29	H	COOMe	3.83 (*d*) (J = 3)	1.46 (*m*)	1.67 (*dt*) (J = 13/3)	5.61 (*m*)	2.20 (*m*)	1.48 (*m*)	1.19 (*s*); 1.15 (*s*)
[b])	H	CH_2OH	3.49 (*m*)	1.48 (*m*)	1.62 (*dt*) (J = 12/3)	5.57 (*m*)	2.21 (*m*)	1.61 (*m*)	1.19 (*s*); 1.08 (*s*)
31	H	$(CH_2)_2$COOMe	2.87 (*ddd*) (J = 9/5/3)	1.45 (*m*)	1.60 (*dt*) (J = 12/3)	5.57 (*m*)	2.22 (*m*)	1.70 (*m*)	1.14 (*s*); 1.04 (*s*)

[a]) Coupling constants rounded to nearest integer. For more precise values see *Exper. Part.*

[b]) This compound was prepared from **29** by reduction with $LiAlH_4$ (not included in *Exper. Part*).

Table 3. *Selected ^{13}C-NMR Data* ($CDCl_3$, 25 MHz) *of the Cyclization Products*

Compound	R^1	R^2	C(11)	C(13)	C(14)	C(15)*	C(16)	C(17)	C(18)	C(19)*	C(20)	C(21)	C(22)
6	H	CH_2–(3-ind.)	54.6	53.8	35.1	29.2	38.2	133.5	124.9	27.9	25.7[a])	25.7[a])	29.9[a])
26		–CO–CH_2–CH_2–	60.5	56.8	32.3	27.8	38.0	131.8	124.3	23.2	25.5	23.7	27.5
29	H	$COOCH_3$	56.4	52.7	33.6	28.3	37.5	131.1	125.1	27.1	22.8	25.2	29.3
[b])	H	CH_2OH	57.4	53.4	35.0	28.9	36.6	133.0	124.5	27.6	24.5	25.5	29.7
31	H	$(CH_2)_2COOCH_3$	54.7	53.2	34.6	29.1	38.5	132.9	124.6	27.6	25.1	25.6	29.8

*) Assignments may be interchanged throughout the *Table.*

[a]) These assignments differ from the ones proposed by *Hesse et al.* [5]. In our opinion a better agreement with the corresponding values of the other cyclization products results by putting them in the sequence shown. Since no selective heteronuclear decoupling experiments have been carried out the assignments of the CH_3-signals remain tentative, however.

[b]) This compound was prepared from **29** by reduction with $LiAlH_4$ (not included in the *Exper. Part*).

(300 MHz): 5.38 (*m*, 1H); 1.65 (*m*, 3H); 1.17 (br. *s*, 2H); 1.06 (*s*, 3H); 1.05 (*s*, 3H). ^{13}C-NMR (25 MHz); 133.4 (*s*); 121.0 (*d*); 50.9 (*s*); 45.4 (*d*); 31.4 (*t*); 28.6 (*q*); 27.7 (*q*); 26.9 (*t*); 24.1 (*t*); 23.3 (*q*). MS: 153 (1, M^+), 138 (5), 136 (9), 121 (10), 93 (8), 70 (13), 58 (100). Anal. calc. for $C_{10}H_{19}N$ (153.27): C 78.37, H 12.50, N 9.14; found: C 78.16, H 12.38, N 9.12.

(R)-MTPA Amides **14** *and* **15**. To a solution of 76 mg (0.5 mmol) **12** and 1.5 ml dry pyridine in 1.5 ml dry CCl_4 were added 0.13 ml of freshly prepared (*R*)-MTPA chloride [23]. After 16 h at r.t. the mixture was treated with 0.1 ml 3-(dimethylamino)-1-propylamine *(Fluka, purum)* and worked up 15 min later with CH_2Cl_2/1N H_2SO_4. The org. layer was dried (Na_2SO_4) and evaporated to give 180 mg of crude material which was purified by chromatography (benzene)[11]: oily product. ^{1}H-NMR (300 MHz, C_6D_6): 7.73 (br. *d*, *J* = 7, 2H); 7.2–7.0 (*m*, 3H); 6.32 (br. *s*, *ca.* 0.95H); 6.30 (br. *s*, *ca.* 0.05H)*; 5.27 (*m*, 1H); 3.20 (*q*, *J* = 1.6, 0.15H)*; 3.16 (*q*, *J* = 1.6, 2.85H); 2.0 (*m*, 1H); 1.9–1.7 (*m*, 2H); 1.57 (br. *s*, 3H); 1.22 (*s*, 0.3H)*; 1.19 (*s*, 2.79H); 1.18 (*s*, 2.73H); 1.09 (*s*, 0.15H)*. (*: signals ascribed to the minor stereoisomer **15**).

Equilibration of (R)-MTPA Amides **14** *and* **15**. 22 mg of the 93:7 mixture of **14** and **15** analyzed above and 5 mg of mesitylenesulfonic acid dihydrate *(Fluka, puriss.)* were heated at reflux in 10 ml CCl_4 for 6 h. The resulting solution was washed once with aq. $KHCO_3$, dried (Na_2SO_4) and evaporated to give 20 mg of an oil which showed a single spot on TLC (benzene). A ^{1}H-NMR spectrum (300 MHz, C_6D_6) demonstrated that equal amounts of **14** and **15** were present.

Upgrading of the Optical Purity of **12**. A mixture of 3.7 g (24 mmol) crude **12** and 3.7 g (24.6 mmol) of L(+)-tartaric acid *(Fluka, puriss.)* was dissolved in 30 ml of hot CH_3OH and let stand at r.t. for 3 days. The crystals formed were collected (5.19 g, m.p. 173–175°; $[\alpha]_D^{25} = -99°$ (*c* = 1.7, EtOH) for regenerated **12**). The evaporated mother liquor became solid after 2 h at HV/r.t.: 2.0 g; m.p. 160–167°; $[\alpha]_D^{25} = -62°$ (*c* = 1.4, EtOH) for regenerated **12**. A second recrystallization of the material with m.p. 173–175° gave 2.4 g, m.p. 174–175°; $[\alpha]_D^{25} = -106°$ (*c* = 2.1, EtOH) and a mother liquor with m.p. 170–173°; $[\alpha]_D^{25} = -91°$ (*c* = 1.1, EtOH). Further recrystallizations did not raise the m.p. of the salt, nor increase the value of the optical rotation of regenerated **12**. To regenerate **12** from its tartaric acid salt the latter was dissolved in 10% NaOH and extracted 3 times with Et_2O. The combined extracts were dried (K_2CO_3), evaporated and distilled (90°/15 Torr).

(S)-N-(1-p-Menthen-8-yl)acetamide (**13**). A mixture of 153 mg (1 mmol) of optically pure **12**, 0.7 ml Ac_2O and 0.7 ml Et_3N in 5 ml benzene was kept at r.t. for 6 h. Workup with aq. phosphate buffer (pH 4) and Et_2O resulted in 176 mg (0.9 mmol, 90% yield) of crystalline **13**. An analytical sample was prepared by 2 crystallizations from $CHCl_3$/hexane. M.p. 119–120° ([16]: 111°)[12]) $[\alpha]_D^{25} = -62°$ (*c* = 0.94, $CHCl_3$). IR (KBr): 3085*m*, 1640*s*, 1566*s*, 1383*m*, 1377*m*, 1361*m*. ^{1}H-NMR (100 MHz): 5.32 (br. *m*, 2H)[13]); 1.88 (*s*, 3H); 1.62 (br. *s*, 3H); 1.28 (*s*, 3H); 1.26 (*s*, 3H). ^{13}C-NMR (25 MHz): 169.7 (*s*); 133.6 (*s*); 120.7 (*d*); 56.1 (*s*); 40.6 (*d*); 31.2 (*t*); 26.6 (*t*); 24.2 (2*q*); 24.0 (*q*); 23.8 (*t*); 23.2 (*q*). MS: 195 (10, M^+), 136 (58), 121 (49), 100 (34), 93 (32), 58 (100). Anal. calc. for $C_{12}H_{21}NO$ (195.30): C 73.80, H 10.84, N 7.17; found: C 73.87, H 10.80, N 7.13.

(S)-N-(1-p-Menthen-8-yl)(3-indolyl)acetamide (**17**). (Method: [25]). (3-Indolyl)acetic acid (642 mg, 3.66 mmol) *(Fluka, purum)*, 561 mg (3.66 mmol) optically pure **12** and 916 mg Et_3N were dissolved in 40 ml of dry CH_2Cl_2. After addition of 1.13 g (4.42 mmol) 2-chloro-1-methylpyridinium iodide *(Fluka, purum)* the mixture was refluxed for 2 h under N_2. Then the cold mixture was diluted with CH_2Cl_2 and washed successively with aq. phosphate buffer (pH 4), aq. $NaHCO_3$ and brine. The org. layer was dried ($MgSO_4$), filtered and evaporated to give 1.40 g of crude product. Chromatography (Et_2O) furnished 976 mg (3.14 mmol, 86% yield) of **17** as a white solid which was recrystallized twice (Et_2O/MeOH) and sublimed (130°/0.005 Torr). M.p. 135–136°. $[\alpha]_D^{25} = -36°$ (*c* = 1.65, $CHCl_3$). UV (EtOH): max. 222 (4.51), 283 (3.81), 292 (3.74); sh 276 (3.77). IR (KBr): 1640*s*, 1550*s*, 1459*m*, 1363*m*, 1341*m*, 1224*m*, 743*s*. ^{1}H-NMR (300 MHz): 8.55 (br. *s*, 1H); 7.56 (*d*, *J* = 7.8, 1H); 7.39 (*d*, *J* = 8, 1H); 7.25–7.10 (*m*, 3H); 5.49 (br. *s*, 1H); 5.23 (*m*, 1H); 3.66 (*d*, *J* = 0.7, 2H); 2.0–1.7 (*m*, 4H); 1.57 (br. *s*, 3H); 1.54–1.40 (*m*, 2H); 1.19 (*s*, 6H); 0.98 (*m*, 1H). ^{13}C-NMR (75 MHz): 170.9 (*s*); 136.5 (*s*); 133.9 (*s*); 126.9 (*s*); 123.5 (*d*); 122.5 (*d*); 120.4 (*d*); 119.9 (*d*); 118.7 (*d*); 111.5 (*d*); 109.5 (*s*); 56.0 (*s*); 41.4 (*d*); 34.8 (*t*); 31.0 (*t*); 26.4 (*t*); 23.9 (2*q*); 23.6 (*t*); 23.2 (*q*). MS: 310 (11, M^+), 175 (16), 174 (12), 136 (18), 131 (34), 130 (100), 121 (12), 58 (21). Anal. calc. for $C_{20}H_{26}N_2O$ (310.44): C 77.38, H 8.44, N 9.03; found: C 77.20, H 8.29, N 8.96.

(S)-N-(1-p-Menthen-8-yl)-2-(3-indolyl)ethylamine (**3**). To a solution of **17** (750 mg, 2.41 mmol) in 50 ml of dry Et_2O were added 500 mg (13.17 mmol) $LiAlH_4$. This mixture was heated at reflux under N_2 for 16 h and

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[11]) An analoguous purification of an equimolar mixture of **14** and **15** had been shown previously not to lead to an enrichment of either diastereomer.

[12]) The discrepancy of the melting points can be explained by assuming that *Khuong-Huu et al.* had a partially racemic sample of **13** in their hands.

[13]) In CCl_4 this signal is resolved into a broad *s* at 6.19 ppm (N*H*) and a *m* at 5.26 ppm (*H*–C(2)).

decomposed by dropwise addition of H_2O at 0°. The resulting suspension was dried (K_2CO_3), filtered and evaporated to yield 520 mg (1.75 mmol, 72%) of a yellow solid. Recrystallization (Et_2O/petroleum ether) furnished a colorless analytical sample of **3**. M.p. 137–138°. $[\alpha]_D^{25} = -34°$ ($c = 1.92$, $CHCl_3$). UV (EtOH): max. 224 (4.51), 284 (3.77), 293 (3.71); sh 276 (3.73). IR ($CHCl_3$): 3480*s*, 1620*w*, 1453*s*, 1415*m*, 1383*m*, 1360*m*, 1335*m*, 1258*m*, 1089*s*, 1009*m*, 912*w*. ^{1}H-NMR (300 MHz): 8.15 (br. *s*, 1H); 7.61 (*ddd*, $J = 7.8$, 1.2 and 1,1H); 7.33 (*ddd*, $J = 7.9$, 1.2 and 1,1H); 7.17 (*ddd*, $J = 7.9$, 7.1 and 1.2, 1H); 7.09 (*ddd*, $J = 7.8$, 7.1 and 1.2, 1H); 7.02 (br. *d*, $J = 2.3$, 1H); 5.32 (*m*, 1H); 3.0–2.85 (*m*, 4H); 1.9–1.65 (*m*, 4H); 1.60 (*s*, 3H); 1.55–1.1 (*m*, 6H); 0.98 (*s*, 6H). ^{13}C-NMR (25 MHz): 136.6 (*s*); 133.9 (*s*); 126.5 (*s*); 122.0 (2*d*); 121.1 (*d*); 119.3 (*d*); 119.0 (*d*); 114.4 (*s*); 111.1 (*d*); 54.3 (*s*); 41.7 (*t*); 41.1 (*d*); 31.3 (*t*); 26.7 (2*t*); 24.3 (2*q*); 23.9 (*t*); 23.3 (*q*). MS: 296 (4, M^+), 201 (60), 166 (72), 144 (100), 137 (44), 131 (34), 130 (57), 117 (11), 81 (94), 30 (72). Anal. calc. for $C_{20}H_{28}N_2$ (296.45): C 81.03, H 9.52, N 9.45; found: C 81.15, H 9.58, N 9.44.

(3-Indolyl)acetaldehyde (**18**). (For other methods of preparation see [26] [27] [29].) A solution of 1.56 g (10 mmol) (3-indolyl)acetonitrile *(Fluka, purum)* in 20 ml of dry benzene was cooled to 0° and treated with 1.1 eq. of a 1.2N toluene solution of diisobutylaluminum hydride *(Schering, DIBAH 20 T)*. After 1 h at 0° the mixture was added dropwise to 100 ml of a vigorously stirred sat. aq. solution of L(+)-tartaric acid. The heterogeneous mixture was extracted with Et_2O (4 × 150 ml). The combined org. layers were dried (Na_2SO_4), treated with decolorizing carbon, filtered through *Celite* and evaporated (RV, r.t.). The oily residue was added to 15 ml of a cold sat. aq. $NaHSO_3$-solution and stirred at 0° for 1 h. The crystalline precipitate was filtered off, washed successively with 95% EtOH, EtOH/Et_2O 1:1 and Et_2O and dried (h.v., 16 h, r.t.). Yield: 1.74 g (6.6 mmol; 66%) of the bisulfite addition product of **18**. Aldehyde **18** was regenerated immediately before use according to *Gray* [26].

(S,E)-N-(1-p-Menthen-8-yl)-2-(3-indolyl)ethylideneamine (**4**) [30]. A solution of 195 mg (1.22 mmol) **18** in 1 ml of dry benzene was combined with 153 mg (1 mmol) optically pure **12** dissolved in 0.5 ml of cold benzene. After 5 min at 5° an oily precipitate began to settle which crystallized when scratched with a glass rod. After 2 h at 5° the orange mother liquor was removed and the crystals were washed (2 × 0.5 ml of cold benzene) and dried (h.v., 16 h, r.t.). Yield: 196 mg (0.67 mmol; 67%) of almost colorless crystals which showed no sign of decomposition when kept for 3 years at −20° under N_2[14]). M.p. 138–139° (dec.). $[\alpha]_D^{25} = -63°$ ($c = 0.4$, $CHCl_3$). IR ($CHCl_3$): 3485*s*, 2960*s*, 2922*s*, 1660*m*, 1450*m*, 1411*m*, 1379*m*, 1361*m*, 1331*m*. ^{1}H-NMR (300 MHz): 8.17 (br. *s*, 1H); 7.68 (*t*, $J = 5.1$, 1H); 7.62 (*dd*, $J = 7.8$ and 1.2, 1H); 7.4–7.05 (*m*, 4H); 5.37 (*m*, 1H); 3.73 (*dd*, $J = 5.1$ and 0.9, 2H); 1.64 (br. *s*, 3H); 1.11 (*s*, 3H); 1.10 (*s*, 3H). MS: 294 (2, M^+), 199 (1), 164 (6), 138 (6), 136 (12), 130 (3), 121 (13), 93 (12), 70 (14), 58 (100).

(−)-Hobartine (= *(−)-4-(Indol-3-ylmethyl)-2,2,6-trimethyl-3-azabicyclo[3.3.1]non-6-ene*, **6**). Imine **4** (191 mg. 0.65 mmol) was dissolved in 5 ml HCOOH (*Fluka, puriss.*; freshly distilled from anh. $CuSO_4$ at 80 Torr) and was allowed to stand at r.t. for 16 h. The mixture was poured onto crushed ice and was distributed between $CHCl_3$ and 0.2N H_2SO_4. The combined aq. extracts were adjusted to pH 11 (10% aq. NH_3) and extracted with $CHCl_3$ (4 × 100 ml). The org. layers were dried (K_2CO_3), evaporated and passed through 4 g of basic alumina *(Woelm B, activity III)* using CH_2Cl_2. Yield 122 mg (0.42 mmol; 64%) of crystalline **6** which was more than 90% pure (^{1}H-NMR). An analytical sample was prepared by recrystallization (CH_2Cl_2/hexane). M.p. 151° ([5]: 149–150.5°). $[\alpha]_D^{25} = -28°$ ($c = 1.2$, $CHCl_3$) ([5]: $-20 \pm 3°$ ($c = 1.66$, $CHCl_3$)). The IR, ^{1}H-NMR (300 MHz), ^{13}C-NMR (75 MHz) and mass spectrum agreed within experimental error with the published values of natural (−)-hobartine (**6**) [5].

(+)-Aristoteline (= *(+)-2,3,4,4a,5,6,11,11a-Octahydro-2,2,5-trimethyl-3,5-ethano-1H-pyrido[3,2-b]carbazole*, **7**). Synthetic (−)-hobartine (**6**) (40 mg, 0.14 mmol) was dissolved in 15 ml 20% aq. HCl and heated at reflux under N_2 for 8 h [16]. The cold mixture was put into an ice bath and treated with 30% NaOH until pH 10 was reached. Threefold extraction with $CHCl_3$, drying of the org. layers (K_2CO_3) and evaporation resulted in 40 mg of a brownish oil. Chromatography ($CHCl_3$/MeOH/conc. aq. NH_3 92:2:5, lower phase) gave 6 mg (0.02 mmol; 14% yield) of an oily unpolar component and 33 mg of crude **7** which was purified further by recrystallization (MeOH/Et_2O/hexane): 28 mg (0.09 mmol; 70% yield) of (+)-aristoteline (**7**). M.p. 161–162°, sintering at 82–84° ([3]: 160–162.5°). $[\alpha]_D^{25} = +19°$ ($c = 0.7$, $CHCl_3$) ([3]: $[\alpha]_D^{25} = +23 \pm 4°$ ($c = 1.84$, $CHCl_3$)). The IR, ^{1}H-NMR (300 MHz) and mass spectrum were in agreement with the reported values of natural (+)-aristoteline (**7**) [3].

(S)-N-(1-p-Menthen-8-yl)succinamic Acid (**22**). Optically pure **12** (3.3 g, 21.5 mmol) was dissolved in 15 ml of freshly distilled dioxane and combined with a solution of 2.2 g (22 mmol) succinic anhydride *(Fluka, puriss.)* and 2.2 g (21.8 mmol) Et_3N in 5 ml dioxane. The resulting mixture was kept at r.t. for 20 min and then

[14]) The marked instability of **4** in solution prevented a full characterization of this compound.

at 75° for 90 min. The cold reaction mixture was acidified to pH 2 (2N HCl) and extracted with 3 portions of $CHCl_3$. The combined org. extracts were dried ($MgSO_4$), filtered and evaporated to give 5.97 g of a brown foam. Crystallization (Et_2O/CH_2Cl_2/hexane) resulted in 4.06 g (16 mmol; 74% yield) of **22**, m.p. 130–132°. An analytical sample was prepared by recrystallization from hot 1,2-dichloroethane followed by sublimation (120°/0.03 Torr). M.p. 134–135°. $[\alpha]_D^{25} = -50°$ ($c = 0.98$, $CHCl_3$). IR (KBr): 3360*s*, 1718*s*, 1704*s*, 1634*s*, 1548*s*, 1411*m*, 1403*m*, 1171*s*. ^{1}H-NMR (100 MHz): 10.7 (br. *s*, 1H); 5.75 (br. *s*, 1H); 5.32 (*m*, 1H); 2.75–2.30 (*m*, *AA'BB'*-system, 4H); 1.62 (*s*, 3H); 1.28 (*s*, 3H); 1.25 (*s*, 3H). ^{13}C-NMR (25 MHz): 174.6 (*s*); 171.3 (*s*); 133.5 (*s*); 120.7 (*d*); 55.9 (*s*); 40.6 (*d*); 31.6 (*t*); 31.1 (*t*); 29.9 (*t*); 26.4 (*t*); 24.0 (*t*); 24.0 (*q*); 23.8 (*q*); 23.3 (*q*). MS: 253 (6, M^+), 159 (13), 158 (21), 136 (43), 121 (37), 118 (10), 93 (24), 58 (100). Anal. calc. for $C_{14}H_{23}NO_3$ (253.34): C 66.37, H 9.15, N 5.53; found: C 66.51, H 9.15, N 5.48.

(S)-N-(1-p-Menthen-8-yl)succinimide (**23**). A mixture of **22** (6.33 g, 25 mmol) and 6.15 g (75 mmol) of anh. NaOAc *(Fluka, puriss.)* in 40 ml Ac_2O *(Fluka, puriss.)* was kept at 100° for 4 h under N_2. The cold mixture was diluted with 150 ml toluene, filtered and evaporated. The residue was taken up in 200 ml $CHCl_3$, washed twice with aq. 2N K_2CO_3, dried ($MgSO_4$) and evaporated to yield 6.1 g of a brown oil. Chromatography (benzene/AcOEt 6:1) gave 5.11 g (21.7 mmol; 86%) of pure **23** as a colorless oil. An analytical sample was prepared by distilling some of this material (120°/0.02 Torr). $[\alpha]_D^{25} = -45°$ ($c = 1.04$, EtOH). IR (CCl_4): 1710*s*, 1439*w*, 1397*w*, 1371*w*, 1340*m*, 1252*m*, 1197*m*, 1136*m*. ^{1}H-NMR (300 MHz): 5.32 (*m*, 1H); 2.59 (*s*, 4H); 1.62 (br. *s*, 3H); 1.61 (*s*, 3H); 1.57 (*s*, 3H). ^{13}C-NMR (25 MHz): 178.7 (2*s*); 133.9 (*s*); 120.3 (*d*); 64.8 (*s*); 39.9 (*d*); 31.1 (*t*); 28.6 (2*t*); 26.7 (*t*); 24.4 (*t*); 24.2 (*q*); 23.6 (*q*); 23.2 (*q*). MS: 235 (2, M^+), 140 (25), 136 (100), 121 (64), 93 (43). Anal. calc. for $C_{14}H_{21}NO_2$ (235.32): C 71.46, H 8.99, N 5.95; found: C 71.41, H 8.83, N 5.91.

Cyclization of the Ethoxylactam Mixture **24**/**25**. Method: [32]. To a cold solution of **23** (405 mg, 1.7 mmol) in 40 ml EtOH were added 151 mg (4 mmol) $NaBH_4$ *(Fluka, purum)*. The mixture was stirred at 0° for 6 h. During this time every 15 min 3 drops of 2N HCl(g) in EtOH were added. Then the pH was adjusted to 3 by addition of 2N HCl(g) in EtOH and kept at r.t. for 2 h. Workup with aq. K_2CO_3 and $CHCl_3$ gave 460 mg of a 1:1 mixture of **24** and **25** as a brown foam which was dissolved in 15 ml HCOOH *(Fluka, puriss.)* and kept at r.t. for 16 h. The mixture was diluted with 100 ml toluene and evaporated. The residue was taken up in $CHCl_3$ and washed with aq. 1N $KHCO_3$, dried ($MgSO_4$) and evaporated. Chromatography (benzene/AcOEt 7:3) gave 142 mg (0.65 mmol; 38% yield) of a 3:1 mixture of **26** and **27** (^{1}H-NMR evidence). A second chromatography (Et_2O) led to a partial separation of the two isomers which were characterized as follows: Minor, less polar isomer *(1S,7R,8S)-2,2-dimethyl-9-methylidene-3-azatricyclo[6.3.1.0^{3,7}]dodecan-4-one* (**27**): oil. $[\alpha]_D^{25} = +105°$ ($c = 0.5$, EtOH). IR (CCl_4): 3065*w*, 1692*s*, 1643*w*, 1384*m*, 1282*m*, 892*m*. ^{1}H-NMR (300 MHz): 4.80 (*t*, $J = 2.3$, 1H); 4.64 (*t*, $J = 2.3$, 1H); 3.67 (*ddd*, $J = 10.4$, 6.2 and 3.4, 1H); 1.77 (*s*, 3H); 1.32 (*s*, 3H). ^{13}C-NMR (25 MHz): 175.7 (*s*); 147.9 (*s*); 110.6 (*t*); 59.4 (*d*); 56.8 (*s*); 42.2 (*d*); 39.1 (*d*); 32.0 (*t*); 31.9 (*t*); 29.8 (*t*); 29.1 (*t*); 26.6 (*q*); 23.9 (*q*); 22.5 (*t*). MS: 219 (15, M^+), 204 (87), 136 (22), 126 (34), 93 (100), 84 (61). Anal. calc. for $C_{14}H_{21}NO$ (219.33): C 76.66, H 9.65, N 6.39; found: C 76.61, H 9.76, N 6.32.

Major, more polar isomer *(1S,7R,8S)-2,2,9-trimethyl-3-azatricyclo[6.3.1.0^{3,7}]dodec-9-en-4-one* (**26**): m.p. 67–68°. $[\alpha]_D^{25} = -69°$ ($c = 0.95$, EtOH). IR (CCl_4): 1697*s*, 1388*m*, 1305*m*, 1278*m*, 1170*m*. ^{1}H-NMR (300 MHz): 5.48 (*m*, 1H); 3.68 (*ddd*, $J = 9.4$, 6.0 and 3.3, 1H); 2.20 (*ddd*, $J = 16.5$, 9.5 and 3.1, 1H); 1.87 (*dddd*, $J = 12.0$, 8.1, 6.0 and 3.1, 1H); 1.74 (*ddd*, $J = 2.4$, 1.8 and 1.8, 3H); 1.72 (*s*, 3H); 1.30 (*s*, 3H). ^{13}C-NMR (25 MHz): 176.5 (*s*); 131.8 (*s*); 124.3 (*d*); 60.5 (*d*); 56.8 (*s*); 38.0 (*d*); 37.5 (*d*); 32.3 (*t*); 27.8 (*t*); 27.5 (*q*); 27.5 (*t*); 25.3 (*q*); 23.7 (*q*); 23.2 (*t*). MS: 219 (40, M^+), 204 (30), 136 (8), 126 (28), 121 (14), 93 (100), 84 (46). Anal. calc. for $C_{14}H_{21}NO$ (219.33): C 76.66, H 9.65, N 6.39; found: C 76.65, H 9.66, N 6.30.

Methyl (1S,4S,5S)-(2,2,6-Trimethyl-3-azabicyclo[3.3.1]non-6-en-4-carboxylate (**29**). To a solution of 1.53 g (10 mmol) **12** in 30 ml of dry toluene were added 1.83 g (10 mmol) of freshly distilled **28** (prepared according to [35]). The mixture, from which crystals began to seperate after *ca.* 30 min, was kept at r.t. for 20 h. The colorless crystals (920 mg, 3.03 mmol; 30% yield) were collected, dissolved in 10 ml 2N NaOH and extracted with $CHCl_3$ to give 670 mg (3 mmol) of **29**. Oil. IR (CCl_4): 3325*w*, 1745*s*, 1432*m*, 1340*m*, 1200*s*, 1173*s*. ^{1}H-NMR (300 MHz): 5.61 (*m*, 1H); 3.83 (*d*, $J = 2.7$, 1H); 3.68 (*s*, 3H); 2.46 (br. *q*, $J =$ *ca.* 2.9, 1H); 2.16 (*dddd*, $J = 12.6$, 3.1, 3.1 and 1.3, 1H); 1.67 (*ddd*, $J = 12.6$, 3.3 and 3.3, 1H); 1.48 (*m*, 3H); 1.19 (*s*, 3H); 1.15 (*s*, 3H). ^{13}C-NMR (25 MHz): 173.1 (*s*); 131.1 (*s*); 125.1 (*d*); 56.4 (*d*); 52.7 (*s*); 51.3 (*q*); 37.5 (*d*); 33.6 (*d*); 29.3 (*q*); 28.3 (*t*); 27.1 (*t*); 25.2 (*q*); 22.8 (*q*). MS: 223 (32, M^+), 208 (54), 164 (92), 130 (27), 129 (41), 128 (68), 107 (21), 105 (21), 97 (30), 93 (100). Anal. calc. for $C_{13}H_{21}NO_2$ (223.32): C 69.92, H 9.48, N 6.27; found: C 69.74, H 9.60, N 6.30.

Methyl (1S,4R,5S)-3-(2,2,6-Trimethyl-3-azabicyclo[3.3.1]non-6-en-4-yl)propionate (**31**). To a solution of 85 mg (0.73 mmol) of freshly distilled **30** [38] in 3 ml benzene were added 111 mg (0.73 mmol) of optically pure **12**. After 2 h at r.t. the turbid mixture was diluted with 10 ml benzene and dried (Na_2SO_4, 30 min r.t.), filtered

and evaporated. The crude imine was dissolved in 3 ml HCOOH (*Fluka, puriss.*; distilled from anh. $CuSO_4$ at 80 Torr) and kept at r.t. for 16 h. The solvent was evaporated and the residue was taken up in 1N H_2SO_4 and extracted once with $CHCl_3$. The aq. phase was adjusted to pH 11 and extracted with $CHCl_3$ (2×) and Et_2O (2×). The combined org. layers were dried (K_2CO_3) and evaporated. The resulting oil was passed through 2 g of silica (Et_2O) and distilled at 70°/0.005 Torr to give 110 mg (0.44 mmol; 60% yield) of pure **31**. Oil. $[\alpha]_D^{25} = -47°$ ($c = 1.33$, $CHCl_3$). IR (CCl_4): 1736*s*, 1434*m*, 1380*m*, 1361*m*, 1237*s*, 1084*m*. ^{1}H-NMR (300 MHz): 5.57 (*m*, 1H); 3.65 (*s*, 3H); 2.87 (*ddd*, $J = 9.1$, 5 and 2.5, 1H); 2.43 (*m*, 2H); 1.70 (*m*, 3H); 1.60 (*ddd*, $J = 12.4$, 3.2 and 3.2, 1H); 1.14 (*s*, 3H); 1.04 (*s*, 3H). ^{13}C-NMR (25 MHz): 174.2 (*s*); 132.9 (*s*); 124.6 (*d*); 54.7 (*d*); 53.2 (*s*); 51.2 (*q*); 38.5 (*d*); 34.6 (*d*); 31.8 (*t*); 30.7 (*t*); 29.8 (*q*); 29.1 (*t*); 27.6 (*t*); 25.6 (*q*); 25.1 (*q*). MS: 251 (17, M^+), 236 (40), 164 (23), 158 (26), 157 (16), 156 (38), 121 (15), 116 (15), 93 (100), 84 (61). Anal. calc. for $C_{15}H_{25}NO_2$ (251.37): C 71.67, H 10.02, N 5.57; found: C 71.48, H 10.17, N 5.84.

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