183. Synthesis of *Aristotelia*-Type Alkaloids

Part XIII[1])

Total Syntheses of (+)-Makonine, (+)-Aristotelinone, and (+)-11,12-Didehydroaristoteline

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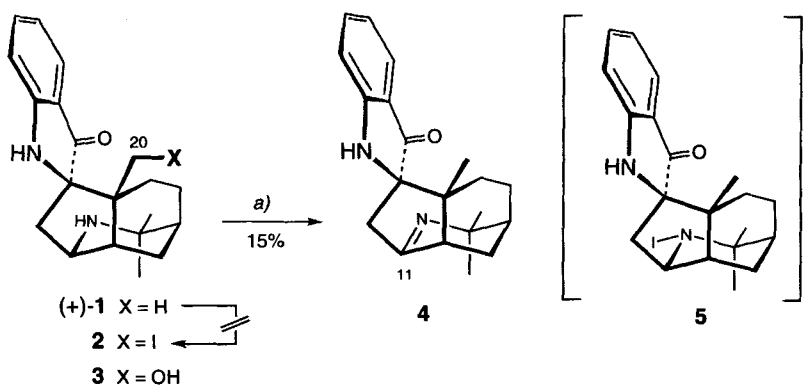
The oxidative transformation of synthetic (+)-aristoteline ((+)-**6**) into other metabolites which had been isolated from *Aristotelia* species was investigated. Thus, treatment of (+)-**6** with I_2 as the single oxidant furnished the naturally occurring indole alkaloids (+)-makonine ((+)-**9**), (+)-aristotelinone ((+)-**11**), or (+)-11,12-didehydroaristoteline ((+)-**7**) in good yields, the selectivity of the oxidation process depending on the chosen reaction conditions.

1. Introduction. – Some time ago, we tried to functionalize the angular Me group (C(20)) of synthetic (+)-aristotelone ((+)-**1**; *Scheme 1*) [2] [3] with the aim to get access to the *Aristotelia* alkaloid aristolarine (**3**) [4]. When *Barton*'s protocol [5] was applied to (+)-**1**, the only isolable product besides starting material was not the anticipated 20-iodoaristotelone (**2**), but the didehydro compound **4** which was isolated in 15% yield [2]. Presumably, this material was formed *via* the *N*-iodo intermediate **5**.

Scheme 1



a) $(PhCOO)_2$, 0.2 equiv. of I_2, 0.2 equiv. of AIBN, $CHCl_3$, *hv* (366 nm).

[1]) Part XII, see [1].

Subsequent experiments showed that radical initiators and UV light are not necessary to induce this type of dehydrogenation, but that I_2 alone is a very effective oxidant for that purpose [6][2]). Since several *Aristotelia* alkaloids are known which are oxidized at position 11 and/or 10 (for reviews, see [8]), the behavior of synthetic[3]) (+)-aristoteline ((+)-**6**; *Scheme 2*) under the above conditions was investigated[4]).

2. Results and Discussion. – When (+)-aristoteline ((+)-**6**) was oxidized with 5 equiv. of I_2 in THF, the corresponding 11,12-didehydro compound (+)-**7** was formed in 74% yield. A natural product with this structure had been isolated before from *Aristotelia australasica* and correlated chemically with aristoteline (**6**) [12], but the small amount of **6** obtained did not allow a determination of its optical rotation. For this reason, the absolute configuration of natural (+)-**7** has remained unknown up to now. Since the $[\alpha]_D$ values of synthetic and natural (+)-**7** [12] agree within experimental error, the absolute configuration of this alkaloid must be as shown in *Scheme 2*.

When the same starting material ((+)-**6**) was oxidized with I_2 in the presence of Et_3N, the major product, formed in 70% isolated yield, turned out to be identical with (+)-makonine ((+)-**9**). This alkaloid was isolated by *Bick* and *Hai* from *Aristotelia serrata* W.R.B. OLIVER and its structure deduced by spectroscopic means. The same authors corroborated their proposal and determined the absolute configuration of this metabolite through oxidation of natural aristotelinone ((+)-**11**) to makonine ((+)-**9**) with $Hg(OAc)_2$ in 25% yield [13].

Yet another product was obtained when (+)-**6** was oxidized with I_2 in the presence of aqueous base, namely the allylic alcohol (+)-**8**, a likely precursor of makonine ((+)-**9**). Neither (+)-**8** nor the corresponding dihydro product (−)-**10**[5]) have been isolated from natural sources up to now; however, the latter could now be taken advantage of as a convenient precursor in the first synthesis of the alkaloid (+)-aristotelinone ((+)-**11**).

Aristotelinone ((+)-**11**) occurs in ppm-quantities in *Aristotelia serrata* W.R.B. OLIVER [15] and in *A. australasica* [16]. The derived aristotelin-10-one structure was established at the same time by reduction with $LiAlH_4$ to (+)-**6** in 19% yield. The major product in this reaction was reported to be (−)-**10** (39%), and (+)-**12** was formed in 9% yield [15b]. Whereas the latter structure assignment is undoubtedly correct, the data reported for the major product is clearly different from our and *Heathcock*'s values and is not compatible with the proposed structure **10**. Therefore, we repeated this reaction using synthetic aristotelinone ((+)-**11**) with the result shown in *Scheme 2*. In our hands, the major product, formed in 62% yield, was aristoteline ((+)-**6**), and (+)-**12** was isolated in similar amounts as reported before. A third component, shown to be (−)-serratoline ((−)-**13**) through comparison with an authentic sample [3], has spectroscopic parameters that closely match the ones reported by *Hai* [15b] for his major product which he believed to be **10**. There is little doubt that he had actually also isolated (−)-serratoline which is known to be transformed slowly into aristoteline ((+)-**6**) on treatment with $LiAlH_4$ [15a] [17].

The (reproducible!) formation of the 3-hydroxyindolenine derivative serratoline ((−)-**13**) from the 3-acylindole precursor (+)-**11** in the presence of $LiAlH_4$ seems to be unprecedented, though this reagent is known to give rise to rearrangements under certain circumstances (for reviews, see [18]). A tentative explanation for the formation

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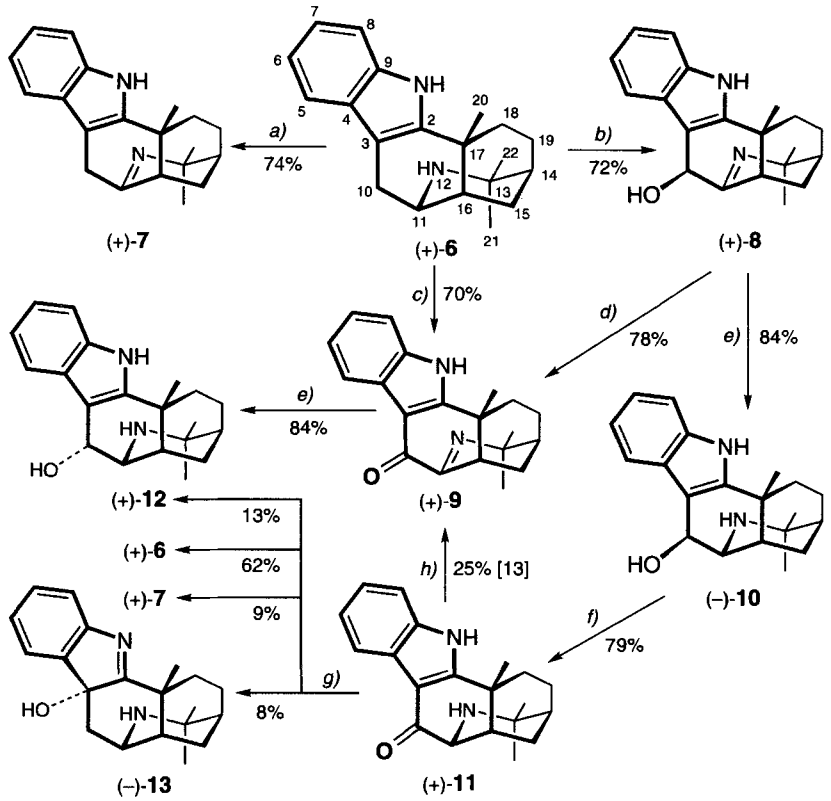
[2]) Seemingly, I_2 was not used before to oxidize secondary amines to the corresponding imines. However, tertiary amines of the ibogamine type were transformed into lactams under similar conditions [7].

[3]) Optically pure (+)-**6** was prepared either by our own method [9] or by applying a modified procedure of *Steven*'s and *Kenney*'s protocol [10]. For other syntheses, see [11].

[4]) Analogous oxidative transformations of tetracyclic representatives like hobartine and makomakine will be discussed in a forthcoming paper in this journal.

[5]) This compound was isolated before in small amounts by *Stoermer* and *Heathcock* when they oxidized (+)-**6** with O_2/Pt [14]. We would like to thank these authors for providing us with copies of their IR and NMR spectra which allowed an unambiguous verification of the identity of the two samples.

Scheme 2



a) 5 equiv. of I_2, THF, 5 min, 25°. *b*) 5 equiv. of I_2, THF/1M aq. $NaHCO_3$, 5 min, 25°. *c*) 1. 5 equiv. of I_2, THF, 3 min, 25°; 2. Et_3N, 10 min, 25°. *d*) 5 equiv. of I_2, THF, 20 min, 25°. *e*) $NaBH_4$, dioxane/H_2O. *f*) MnO_2, $CHCl_3$, 8 h, 25°. *g*) $LiAlH_4$, THF, 5 h, reflux. *h*) $Hg(OAc)_2$ [13].

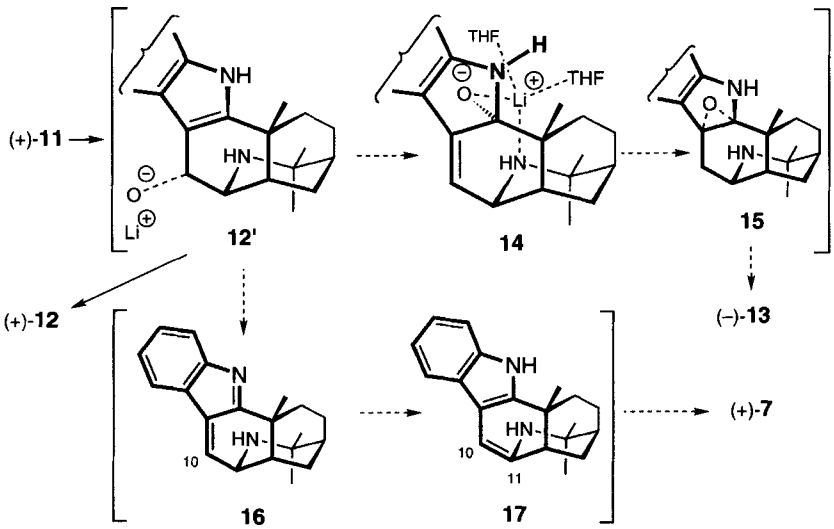
of (−)-**13** is presented in *Scheme 3*. Part of the expected primary reduction product **12′** could undergo an allylic rearrangement to **14**, which probably resists further reduction. During the workup procedure, (−)-**13** might be formed from **14** *via* the 1*H*-indole 2,3-epoxide intermediate **15**[6]). The formation of small amounts of (+)-**7** can be explained by invoking an elimination, followed by an imine-enamine tautomerization sequence *via* **16** and **17**.

There is some ambiguity about the mechanism by which aristoteline ((+)-**6**) is oxidized to the compounds (+)-**7**, (+)-**8**, or (+)-**9**, because either of the two most nucleophilic sites of the substrate, N(12) or C(3), could react with an electrophilic iodine species to yield **19** or **21**, respectively (*Scheme 4*). Within the *Aristotelia* alkaloid family, there is precedent for both modes of preferential attack: 3-chloroperbenzoic acid in the absence of an additional strong acid[7]) was shown to attack the piperidine N-atom of (+)-**6** to furnish the hydroxylamine derivative (+)-**18** in 78% yield; on the other hand, dibenzoyl

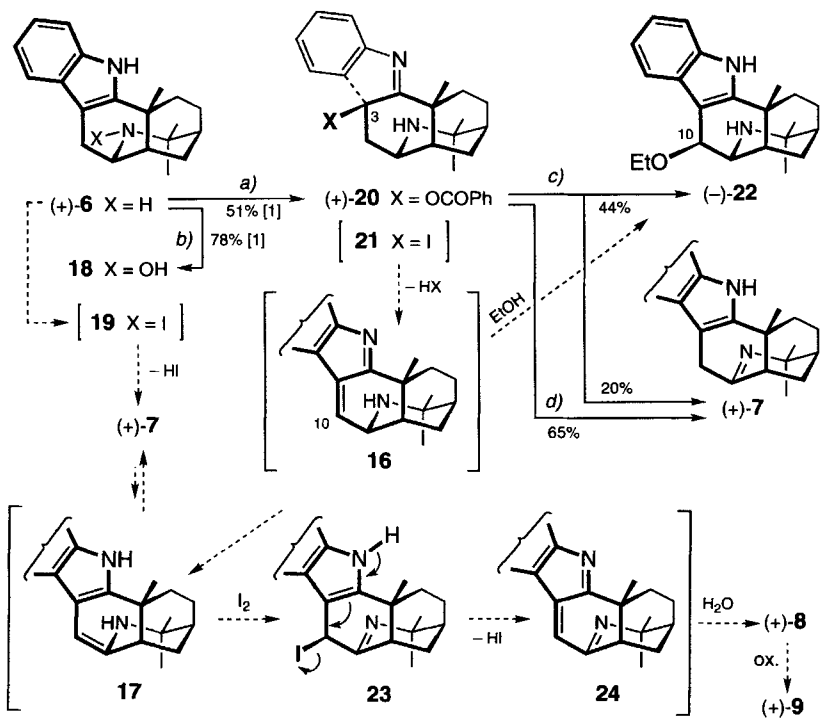
[6]) Derivatives of 1*H*-indole 2,3-epoxide were isolated and characterized recently (see, *e.g.*, [19] and refs. cit. therein).

[7]) In the presence of at least 1 equiv. of CF_3COOH, the same reagent reacted exclusively at position 3 to give serratoline ((−)-**13**) in excellent yield and diastereoselectivity [1] [3].

Scheme 3



Scheme 4



a) $(PhCOO)_2$, $CHCl_3$, 90 min, 25°. *b*) 3-$ClC_6H_4CO_3H$, petroleum ether, 10 min, reflux. *c*) $(H_3PO_4)_n$, EtOH, 26 h, 25°. *d*) $(H_3PO_4)_n$, EtOH, 44 h, 100°.

peroxide reacted with the same substrate at position 3 from the less hindered convex face to give *O*-benzoyl-3-episerratoline ((+)-**20**) [1]. On treatment with anhydrous polyphosphoric acid in EtOH, this rather labile compound was transformed into a mixture 10β-ethoxyaristoteline ((−)-**22**) and 11,12-didehydroaristoteline ((+)-**17**) [2]. Our tenta-

Table 1. *^{1}H-NMR Chemical Shift Values* [ppm] *of Compounds* **6**–**12** *and* **22** ($CDCl_3$, δ rel. to $SiMe_4$)

	6	**7**	**8**	**9**[a])	**10**	**11**[a])	**12**	**22**
H–C(5)	7.45	7.45	7.73	8.18	7.64	8.12	7.84	7.56
H–C(6)	7.05	7.08	7.14	7.19	7.10	7.20	7.08	7.08
H–C(7)	7.11	7.13	7.16	7.22	7.15	7.20	7.13	7.12
H–C(8)	7.29	7.30	7.32	7.37	7.32	7.40	7.29	7.29
H_β–C(10)	3.07	3.71	–	–	–	–	5.22	–
H_α–C(10)	2.63	3.42	5.43	–	4.67	–	–	4.32
H–C(11)	3.62	–	–	–	3.54	3.66	3.60	3.56
H–C(14)	1.40	1.73	1.76	1.78	1.43	1.50	1.46	1.43
H_α–C(15)	2.06	2.02	1.98	1.93	2.04	2.03	2.03	2.06
H_β–C(15)	1.97	1.93	1.98	1.93	1.97	1.98	1.94	1.96
H–C(16)	1.70	2.46	2.99	2.69	1.98	2.07	1.73	2.01
H_β–C(18)	1.61	1.61	1.53	1.64	1.54	1.61	1.63	1.56
H_α–C(18)	2.62	1.62	1.50	1.64	2.32	2.68	2.36	2.17
H_β–C(19)	1.67	1.75	1.68	1.68	1.65	1.76	1.69	1.65
H_α–C(19)	1.92	1.81	1.82	1.80	1.88	2.01	1.92	1.87
Me(20)	1.46	1.53	1.57	1.61	1.48	1.60	1.43	1.47
Me(21)	1.29	1.29	1.23	1.27	1.30	1.10	1.27	1.31
Me(22)	0.97	1.25	1.32	1.32	1.04	1.32	1.09	1.04

[a]) $CDCl_3/CD_3OD$ (see *Exper. Part*).

Table 2. *^{13}C-NMR Chemical Shift Values* [ppm] *of Compounds* **6**–**12** *and* **22** ($CDCl_3$, δ rel. to $SiMe_4$)

	6	**7**	**8**[a])	**9**[a])	**10**[a])	**11**[a])	**12**	**22**
C(2)	142.6	142.6	145.8	160.5	145.8	162.8	143.8	145.6
C(3)	104.4	106.7	107.8	112.1	106.1	109.0	108.2	106.0
C(4)	128.2	127.4	126.4	124.8	127.4	126.0	127.3	128.3
C(5)	118.2	118.3	117.8	121.7	118.2	121.7	120.1	118.6[b])
C(6)	119.1	119.6	119.3	123.6	119.6	123.5[b])	119.6	119.7[b])
C(7)	121.0	121.5	121.2	122.8	121.5	122.7[b])	121.4	121.4
C(8)	110.5	110.7	110.9	111.7	110.9	112.0	110.6	110.6
C(9)	136.1	135.9	136.4	136.6	136.6	137.6	136.2	136.3
C(10)	28.6	35.9	68.7	185.9	66.7	195.6	68.0	75.2
C(11)	50.4	168.5	173.2	169.7	58.4	60.9	54.6	55.5
C(13)	53.3	57.4	57.2	58.4	53.1	53.3	53.1	53.1
C(14)	35.6	35.7	35.7	35.9	36.0	36.8	36.2	35.7
C(15)	27.9	21.8	21.0	21.4	27.2	26.0	28.0	27.3
C(16)	39.3	41.8	36.9	45.3	34.8	41.2	39.5	36.1
C(17)	33.2	38.8	39.3	40.1	33.3	35.4	33.1	33.3
C(18)	36.0	34.9	33.7	33.1	36.0	34.3	36.0	35.8
C(19)	25.5	25.1	24.5	24.2	25.2	24.9	25.6	25.3
C(20)	25.2	20.8	19.8	19.3	24.8	22.8	25.4	24.8
C(21)	27.6	27.5	26.4	27.1	27.1	27.3	27.2	27.7
C(22)	29.1	30.7	30.0	29.8	28.6	29.3	29.1	29.0

[a]) $CDCl_3/CD_3OD$ (see *Exper. Part*). [b]) Assignments may be interchanged.

tive explanation for the formation of these rather unexpected products again involves the elusive unsaturated intermediates **16** and **17**. An acid-catalyzed vinylogous addition of EtOH to the conjugated imine function of **16** would lead to (−)-**22**. As an alternative, **16** could tautomerize to (+)-**7** *via* the enamine intermediate **17**. At present, our experiments allow no definite conclusion as to which pathway is followed during the oxidation of (+)-**6** with I_2, but in any case, **17** seems to be the prime candidate for further oxidation to (+)-**8**, presumably *via* **23** and **24**.

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Experimental Part

General. Reagents and solvents: purchased from *Fluka AG* in the highest obtainable purity, unless stated otherwise. $CHCl_3$ and $CDCl_3$ were passed through basic alumina (*Woelm*, act. I) immediately before use. M.p. (not corrected): *Tottoli* apparatus; sealed evacuated capillaries. Optical rotations: *Perkin-Elmer 241* at 25° and 589 nm (Na_D). UV/VIS Spectra (λ_{max} [nm], log ε [dm^3/mol·cm]): *Kontron Uvikon 869*. IR Spectra: ($\tilde{\nu}_{max}$ [cm^{-1}]): *Perkin-Elmer-PE-781* spectrometer. ^{1}H-NMR Spectra: δ in ppm rel. to internal $SiMe_4$ (≡ 0 ppm), *J* in Hz; 400 MHz, *Bruker AMX 400*; 500 MHz, *Bruker AMX 500*. ^{13}C-NMR Spectra: multiplicities from DEPT experiments; 100 MHz, *Bruker AMX 400*; 125 MHz, *Bruker AMX 500*. NOE: *Bruker WM 300* (300 MHz, $CDCl_3$); irradiated proton → affected signal(s). HETCOR: *Varian Gemini 300* (300 MHz, $CDCl_3$); cross-peaks, $\delta(^{13}C)/\delta(^1H)$. Mass spectra (*m/z* [amu] (% base peak)): *Hitachi-Perkin-Elmer, VG TRIBRID*; EI, 70 eV, unless stated otherwise; FAB, 3-nitrobenzyl alcohol matrix.

(+)-11,12-Didehydroaristoteline (= *(3S,4aS,5R)-2,3,4,4a,5,11-Hexahydro-2,2,5-trimethyl-3,5-ethano-6H-pyrido[3,2-b]carbazole*; (+)-**7**). To a soln. of 50 mg (0.17 mmol) of synthetic (+)-aristoteline ((+)-**6**) in 3.5 ml of THF were added 50 mg (0.36 mmol) of K_2CO_3 and 230 mg (0.85 mmol) of I_2 at r.t. under Ar. After stirring for 5 min, a mixture of 20 ml of $CHCl_3$, 4 ml of H_2O, and 1M aq. $Na_2S_2O_3$ was added. Workup with $CHCl_3$ furnished a yellow crude material which was chromatographed (silica gel, $CHCl_3$/THF/Et_3N 100:10:5): 37 mg (74%) of (+)-**7**. White foam. M.p. 128–134° (MeOH; [12]: amorphous). $[\alpha]_D$ = +265 (*c* = 1.2, $CHCl_3$; [12]: +272 (*c* = 0.8, $CHCl_3$)). UV (EtOH): 290 (4.14), 281 (4.20), 275 (4.82), 233 (4.82). IR ($CHCl_3$): 3476, 2934, 1660, 1462, 1302. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.83 (br. *s*, 1 H); 7.45 (*dddd*, *J* = 7.6, 1.3, 0.8, 0.6, 1 H); 7.30 (*ddd*, *J* = 7.6, 1.3, 0.6, 1 H); 7.13 (*td*, *J* = 7.5, 1.3, 1 H); 7.08 (*td*, *J* = 7.6, 1.2, 1 H); 3.71 (*d*, *J* = 15.3, 1 H); 3.42 (*d*, *J* = 15.3, 1 H); 2.46 (*m*, 1 H); 2.02 (*dq*, *J* = 13.3, 3.1, 1 H); 1.93 (*ddd*, *J* = 13.4, 3.2, 2.1, 1 H); 1.86–1.71 (*m*, 3 H); 1.71–1.58 (*m*, 2 H); 1.53 (*s*, 3 H); 1.29 (*s*, 3 H); 1.25 (*s*, 3 H); max. deviation from natural (+)-**7** [12]: ±0.05 ppm. ^{13}C-NMR (125 MHz, $CDCl_3$): 168.5 (*s*); 142.6 (*s*); 135.9 (*s*); 127.4 (*s*); 121.5 (*d*); 119.6 (*d*); 118.3 (*d*); 110.7 (*d*); 106.7 (*s*); 57.4 (*s*); 41.8 (*d*); 38.8 (*s*); 35.9 (*t*); 35.7 (*d*); 34.9 (*t*); 30.7 (*q*); 27.5 (*q*); 25.1 (*t*); 21.8 (*t*); 20.8 (*q*); max. deviation from natural (+)-**7** [12]: ±0.3 ppm, apart from C(11) (168.5 *vs.* 173.8 [12]); this might be due to traces of HCl in the solvent employed in the previous work. HETCOR: 121.5/7.13; 119.6/7.08; 118.3/7.45; 110.7/7.30; 41.8/2.46; 35.9/3.71, 3.42; 35.7/1.73; 34.9/1.62, 1.61; 30.7/1.25; 27.5/1.29; 25.1/1.81, 1.75; 21.8/2.02, 1.93; 20.8/1.53. EI-MS: 292 (72, M^+), 290 (11), 238 (21), 237 (98), 235 (15), 183 (16), 181 (30), 180 (16), 111 (16), 86 (63), 84 (100).

(+)-11,12-Didehydroaristotelin-10β-ol (= *(3S,4aS,5R,11S)-2,3,4,4a,5,11-Hexahydro-2,2,5-trimethyl-3,5-ethano-6H-pyrido[3,2-b]carbazol-11-ol*; (+)-**8**). To a soln. of 150 mg (0.51 mmol) of synthetic (+)-**6** in 7.5 ml of THF were added 6 ml of 1M aq. $NaHCO_3$ and 677 mg (2.67 mmol) of I_2 at r.t. under Ar. After stirring for 5 min, a mixture of 20 ml of $CHCl_3$, 4 ml of H_2O, and 1M aq. $Na_2S_2O_3$ was added. Workup with $CHCl_3$ furnished a yellow crude material which was chromatographed (silica gel, $CHCl_3$/THF/Et_3N 100:30:5): 112 mg (72%) of (+)-**8**. White foam. M.p. 154–162° (MeOH). $[\alpha]_D$ = +232 (*c* = 0.9, $CHCl_3$). UV (EtOH): 289 (3.63), 267 (3.74), 219 (4.40). IR ($CHCl_3$): 3470, 1661, 1462, 1301, 1260, 906. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.94 (br. *s*, 1 H); 7.73 (*dm*, *J* = 7.5, 1 H); 7.32 (*dm*, *J* = 7.5, 1 H); 7.16 (*td*, *J* = 7.5, 1.5, 1 H); 7.14 (*td*, *J* = 7.5, 1.2, 1 H); 5.43 (*s*, 1 H); 2.99 (*s*, 1 H); 1.98 (*m*, 2 H); 1.82 (*m*, 1 H); 1.76 (*m*, 1 H); 1.68 (*tdd*, *J* = 13.6, 5.0, 3.5, 1 H); 1.57 (*s*, 3 H); 1.54–1.50 (*m*, 2 H); 1.32 (*s*, 3 H); 1.23 (*s*, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$ + CD_3OD): 173.2 (*s*); 145.8 (*s*); 136.4 (*s*); 126.4 (*s*); 121.2 (*d*); 119.3 (*d*); 117.8 (*d*); 110.9 (*d*); 107.8 (*s*); 68.7 (*d*); 57.2 (*s*); 39.3 (*s*); 36.9 (*d*); 35.7 (*d*); 33.7 (*t*); 30.0 (*q*); 26.4 (*q*); 24.5 (*t*); 21.0 (*t*); 19.8 (*q*). HETCOR: 121.2/7.16; 119.3/7.14; 117.8/7.73; 110.9/7.32; 68.7/5.43; 36.9/2.99; 35.7/1.76; 33.7/1.53, 1.50; 30.0/1.32; 26.4/1.23; 24.5/1.82, 1.68; 21.0/1.98 (2 H); 19.8/1.57. EI-MS: 308 (3, M^+), 291 (23), 290 (95), 275 (15), 236 (38), 235 (100), 85 (43), 83 (67).

(+)-Makonine (= *(3S,4aS,5R)-2,3,4,4a,5,11-Hexahydro-2,2,5-trimethyl-3,5-ethano-6H-pyrido[3,2-b]carbazol-11-one*; (+)-**9**). To a soln. of 50 mg (0.17 mmol) of synthetic (+)-**6** in 2.5 ml of THF were added 50 mg (0.36 mmol) of K_2CO_3 and 230 mg (0.91 mmol) of I_2 at r.t. under Ar. After stirring for 3 min, there were added 0.1 ml of Et_3N, and stirring was continued for additional 10 min. Then a mixture of 20 ml of $CHCl_3$, 4 ml of H_2O, and 1M aq. $Na_2S_2O_3$ was added. Workup with $CHCl_3$ furnished a yellow crude material which was chromatographed (silica gel, $CHCl_3$/THF/Et_3N 100:10:5) to give 35 mg (70%) of (+)-**9**. White foam. M.p. 300–305° (MeOH; [13]: 310–312°). $[\alpha]_D$ = +428 (*c* = 1.2, MeOH/$CHCl_3$ 1:1; [13]: +431 (*c* = 0.9, MeOH/$CHCl_3$)). UV (EtOH): 315 (3.94), 270 (4.05), 255 (4.05), 211 (4.50). IR (KBr): 1661, 1618, 1558, 1458, 743. ^{1}H-NMR (400 MHz, $CDCl_3$ + 2 drops of CD_3OD): 8.18 (*m*, 1 H); 7.37 (*m*, 1 H); 7.22 (*td*, *J* = 7.2, 1.6, 1 H); 7.19 (*td*, *J* = 7.2, 1.7, 1 H); 2.69 (*m*, 1 H); 1.93 (*m*, 2 H); 1.85–1.61 (*m*, 5 H); 1.61 (*s*, 3 H); 1.32 (*s*, 3 H); 1.27 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$ + CD_3OD): 185.9 (*s*); 169.7 (*s*); 160.5 (*s*); 136.6 (*s*); 124.8 (*s*); 123.6 (*d*); 122.8 (*d*); 121.7 (*d*); 112.1 (*s*); 111.7 (*d*); 58.4 (*s*); 45.3 (*d*); 40.1 (*s*); 35.9 (*d*); 33.1 (*t*); 29.8 (*q*); 27.1 (*q*); 24.2 (*t*); 21.4 (*t*); 19.3 (*q*). HETCOR: 123.6/7.19; 122.8/7.22; 121.7/8.18; 111.7/7.37; 45.3/2.69; 35.9/1.78; 33.1/1.64 (2 H); 29.8/1.32; 27.1/1.27; 24.2/1.80, 1.68; 21.4/1.93 (2 H); 19.3/1.61. EI-MS: 306 (8, M^+), 251 (32), 236 (32), 235 (16), 209 (19), 167 (57), 154 (40), 41 (100).

(−)-Aristotelin-10β-ol (= *(3S,4aS,5R,11S,11aS)-2,3,4,4a,5,6,11,11a-Octahydro-2,2,5-trimethyl-3,5-ethano-1H-pyrido[3,2-b]carbazol-11-ol*; (−)-**10**). To a soln. of 91 mg (0.31 mmol) of (+)-**8** in 6.6 ml of dioxane was added a soln. of 16 mg (0.42 mmol) of $NaBH_4$ in 1.65 ml of H_2O at r.t. under Ar. After stirring for 45 min, 0.5 ml of 1M HCl was added. When the gas evolution had stopped, the mixture was rendered basic by addition of conc. aq. NH_3 soln. Workup with $CHCl_3$ furnished a colorless crude material which was chromatographed (silica gel, $CHCl_3$/THF/Et_3N 100:30:5): 76 mg (84%) of (−)-**10**. White foam. M.p. 188–203°. $[\alpha]_D$ = −22 (*c* = 0.8, MeOH/$CHCl_3$ 1:1). UV (EtOH): 288 (3.64), 277 (3.72), 250 (3.41), 222 (4.42). IR (KBr): 3520, 3260, 1466. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.92 (br. *s*, 1 H); 7.64 (*dm*, *J* = 7.8, 1 H); 7.32 (*dm*, *J* = 7.8, 1 H); 7.15 (*ddd*, *J* = 7.8, 7.2, 1.4, 1 H); 7.10 (*ddd*, *J* = 7.8, 7.2, 1.1, 1 H); 4.67 (*d*, *J* = 1.6, 1 H); 3.54 (*t*, *J* = 2.0, 1 H); 2.32 (*td*, *J* = 13.7, 5.9, 1 H); 2.04 (*dq*, *J* = 14.5, 3.3, 1 H); 1.98 (*m*, 1 H); 1.97 (*dt*, *J* = 14.5, 3.2, 1 H); 1.88 (*m*, 1 H); 1.65 (*tdd*, *J* = 14.0, 5.6, 3.7, 1 H); 1.54 (br. *dd*, *J* = 13.2, 5.5, 1 H); 1.48 (*s*, 3 H); 1.43 (*quint.*, *J* = 3.1, 1 H); 1.30 (*s*, 3 H); 1.04 (*s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$/CD_3OD): 145.8 (*s*); 136.6 (*s*); 127.4 (*s*); 121.5 (*d*); 119.6 (*d*); 118.2 (*d*); 110.9 (*d*); 106.1 (*s*); 66.7 (*d*); 58.4 (*d*); 53.1 (*s*); 35.98 (*d*); 35.96 (*t*); 34.8 (*d*); 33.3 (*s*); 28.6 (*q*); 27.2 (*t*); 27.1 (*q*); 25.2 (*t*); 24.8 (*q*). HETCOR: 121.5/7.15; 119.6/7.10; 118.2/7.64; 110.9/7.32; 66.7/4.67; 58.4/3.54; 36.0/2.32, 1.54, 1.43; 34.8/1.98; 28.6/1.04; 27.2/2.04, 1.97; 27.1/1.30; 25.2/1.88, 1.65; 24.8/1.48. EI-MS: 310 (0.4, M^+), 292 (93), 277 (41), 237 (100), 235 (79), 220 (28), 194 (23), 193 (32), 181 (57), 180 (27).

(+)-Aristotelinone (= *(3S,4aS,5R,11aS)-2,3,4,4a,5,6,11,11a-Octahydro-2,2,5-trimethyl-3,5-ethano-1H-pyrido[3,2-b]carbazol-11-one*; (+)-**11**). To a soln. of 43.5 mg (0.14 mmol) of (−)-**10** in 11 ml of $CHCl_3$ were added 255 mg of MnO_2 (*Merck*) at r.t. under Ar. After stirring for 8 h, the mixture was filtered through *Celite*® and evaporated. The crude product was crystallized from $CHCl_3$ to give 35 mg (79%) of pure (+)-**11**. M.p. 169–177°. $[\alpha]_D$ = +117 (*c* = 1.1, $CHCl_3$). UV (EtOH): 302 (4.53), 266 (4.60), 245 (4.73). IR (KBr): 3244, 1616, 1584, 1466, 1254, 1168, 1104, 749. ^{1}H-NMR (500 MHz, $CDCl_3$/CD_3OD 1:1): 8.12 (*m*, 1 H); 7.40 (*m*, 1 H); 7.20 (*m*, 2 H); 3.66 (*d*, *J* = 3.2, 1 H); 2.68 (*td*, *J* = 13.7, 5.5, 1 H); 2.10–1.95 (*m*, 4 H); 1.76 (*tdd*, *J* = 14.1, 5.5, 3.8, 1 H); 1.61 (*m*, 1 H); 1.60 (*s*, 3 H); 1.50 (*quint.*, *J* = 3.1, 1 H); 1.32 (*s*, 3 H); 1.10 (*s*, 3 H); max. deviation from natural (+)-**11** [15b]: ±0.05 ppm. ^{13}C-NMR (125 MHz, $CDCl_3$/CD_3OD 1:1): 195.6 (*s*); 162.8 (*s*); 137.6 (*s*); 126.0 (*s*); 123.5 (*d*); 122.7 (*d*); 121.7 (*d*); 112.0 (*s*); 109.0 (*s*); 60.9 (*d*); 53.3 (*s*); 41.2 (*d*); 36.8 (*d*); 35.4 (*s*); 34.3 (*t*); 29.3 (*q*); 27.3 (*q*); 26.0 (*t*); 24.9 (*t*); 22.8 (*q*); max. deviation from natural (+)-**11** [15b]: ±1.4 ppm (±0.2 ppm in the aliphatic region). HETCOR: 123.5/7.20; 122.7/7.20; 121.7/8.12; 112.0/7.40; 60.9/3.66; 41.2/2.07; 36.8/1.50; 34.3/2.68, 1.61; 29.3/1.32; 27.3/1.10; 26.0/2.03, 1.98; 24.9/2.01, 1.76; 22.8/1.60. EI-MS: 308 (7, M^+), 293 (100), 251 (7), 196 (11), 184 (30), 168 (33), 167 (36), 154 (22).

Reduction of (+)-11 with $LiAlH_4$ (Method: [15b]). To a suspension of 18.3 mg (0.48 mmol) of $LiAlH_4$ in 15 ml of THF was added a soln. of 49.3 mg (0.16 mmol) of (+)-**11** in 8 ml of THF. After 5 h reflux, the mixture was cooled to 0°, 0.5 ml of H_2O were added, followed by 1 g of anh. Na_2SO_4 after 5 min. Filtration and workup of the filtrate with $CHCl_3$/aq. Na_2CO_3 soln. furnished 54.6 mg of a mixture which was chromatographed (silica gel, $CHCl_3$/MeOH 9:1): 29.3 mg (62%) of (+)-**6**, 6.3 mg (12.7%) of (+)-**12**, and 11.2 mg of a mixture. The latter was chromatographed again (silica gel, $CHCl_3$/MeOH 19:1): 4.2 mg (8.9%) of (+)-**7** and 4.1 mg (8.3%) of (−)-**13**.

(+)-Aristotelin-10α-ol (= *(3S,4aS,5R,11R,11aS)-2,3,4,4a,5,6,11,11a-Octahydro-2,2,5-trimethyl-3,5-ethano-1H-pyrido[3,2-b]carbazol-11-ol*; (+)-**12**): M.p. 184–192° (MeOH; [15b]: 203–204°). $[\alpha]_D$ = +52 (*c* = 1.2, $CHCl_3$; [15b]: not determined). UV (EtOH): 288 (3.37), 280 (3.44), 225 (4.14). IR ($CHCl_3$): 3580, 3470, 1462, 1383, 1292, 1056, 1010, 999. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85 (br. *s*, 1 H); 7.84 (*dm*, *J* = 7.5, 1 H); 7.29 (*dm*, *J* = 7.4, 1 H); 7.13 (*td*, *J* = 7.4, 1.4, 1 H); 7.08 (*td*, *J* = 7.3, 1.3, 1 H); 5.22 (*d*, *J* = 5.7, 1 H); 3.60 (*dd*, *J* = 5.7, 2.2, 1 H); 2.36 (*m*, 1 H); 2.03 (*dq*, *J* = 13.6, 3.0, 1 H); 1.94 (*dt*, *J* = 13.6, 3.1, 1 H); 1.92 (*m*, 1 H); 1.73 (*m*, 1 H); 1.70–1.58 (*m*, 2 H); 1.46

(*m*, 1 H); 1.43 (*s*, 3 H); 1.27 (*s*, 3 H); 1.09 (*s*, 3 H); max. deviation from (+)-**12**, derived from natural (+)-**11** [15b]: ±0.05 ppm. ^{13}C-NMR (100 MHz, $CDCl_3$): 143.8 (*s*); 136.2 (*s*); 127.3 (*s*); 121.4 (*d*); 120.1 (*d*); 119.6 (*d*); 110.6 (*d*); 108.2 (*s*); 68.0 (*d*); 54.6 (*d*); 53.1 (*s*); 39.5 (*d*); 36.2 (*d*); 36.0 (*t*); 33.1 (*s*); 29.1 (*q*); 28.0 (*t*); 27.2 (*q*); 25.6 (*t*); 25.4 (*q*). HETCOR: 121.4/7.13; 120.1/7.84; 119.6/7.08; 110.6/7.29; 68.0/5.22; 54.6/3.60; 39.5/1.73; 36.2/1.46; 36.0/2.36, 1.63; 29.1/1.09; 28.0/2.03, 1.94; 27.2/1.27; 25.6/1.92, 1.69; 25.4/1.43. EI-MS: 310 (0.6, M^+), 277 (18), 237 (17), 220 (22), 204 (24), 194 (45), 193 (33), 182 (33), 181 (80), 180 (100), 168 (44), 167 (71), 58 (61).

(−)-10β-Ethoxyaristoteline (= *(3S,4aS,5R,11S,11aS)-11-Ethoxy-2,3,4,4a,5,6,11,11a-octahydro-2,2,5-trimethyl-3,5-ethano-1H-pyrido[3,2-b]carbazole*; (−)-**22**). To a soln. of 123 mg (0.3 mmol) of (+)-**20** [1] in 10 ml of EtOH was added a soln. of 4.5 g of polyphosphoric acid in 20 ml of EtOH. After stirring for 153 h at r.t. under Ar, the mixture was poured onto 80 g of crushed ice and rendered basic through addition of 8 ml of conc. aq. NH_3 soln. Workup with $CHCl_3$ furnished 116.4 mg of a yellow foam which was chromatographed (silica gel, benzene/Et_2O/Et_2NH 25:4:1): 21 mg (24%) of (+)-**7** and 45 mg (44%) of (−)-**22**. M.p. 158° ($CHCl_3$). $[\alpha]_D = -26$ (*c* = 0.6, $CHCl_3$). IR ($CHCl_3$): 3325, 1462, 1443, 1384, 1296, 1132, 1109, 1069, 1009. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.86 (br. *s*, 1 H); 7.56 (*dm*, *J* = 7.6, 1 H); 7.29 (*dm*, *J* = 7.6, 1 H); 7.12 (*ddd*, *J* = 7.6, 7.1, 1.4, 1 H); 7.08 (*ddd*, *J* = 7.5, 7.1, 1.2, 1 H); 4.32 (*d*, *J* = 1.4, 1 H); 3.80 (*dq*, *J* = 9.1, 7.0, 1 H); 3.74 (*dq*, *J* = 9.1, 7.0, 1 H); 3.56 (*dd*, *J* = 2.6, 1.4, 1 H); 2.17 (*td*, *J* = 13.8, 5.9, 1 H); 2.06 (*dq*, *J* = 13.2, 3.0, 1 H); 2.01 (*m*, 1 H); 1.96 (*dt*, *J* = 13.2, 3.1, 1 H); 1.87 (*m*, 1 H); 1.65 (*tdd*, *J* = 14.0, 5.8, 3.7, 1 H); 1.56 (br. *dd*, *J* = 13.5, 5.6, 1 H); 1.47 (*s*, 3 H); 1.43 (*m*, 1 H); 1.31 (*s*, 3 H); 1.26 (*t*, *J* = 7.0, 3 H); 1.04 (*s*, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 145.6 (*s*); 136.3 (*s*); 128.3 (*s*); 121.4 (*d*); 119.7 (*d*); 118.6 (*d*); 110.6 (*d*); 106.0 (*s*); 75.2 (*d*); 64.6 (*t*); 55.5 (*d*); 53.1 (*s*); 36.1 (*d*); 35.8 (*t*); 35.7 (*d*); 33.3 (*s*); 29.0 (*q*); 27.7 (*q*); 27.3 (*t*); 25.3 (*t*); 24.8 (*q*); 15.9 (*q*). EI-MS: 338 (3, M^+), 294 (9), 293 (25), 292 (88), 277 (73), 237 (93), 235 (100), 220 (47), 181 (76), 180 (40).

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