Tetrahedron: Asymmetry Vol. 3, No. 11, pp. 1411-1420, 1992
Printed in Great Britain

0957-4166/92 $5.00+.00
Pergamon Press Ltd

Synthesis of *Aristotelia*-Type Alkaloids. Part XI [1]. Total Syntheses of (+)-Sorelline and (+)-Aristolasene

Markus Dobler, René Beerli, Walter K. Weissmahr, and Hans-Jürg Borschberg*

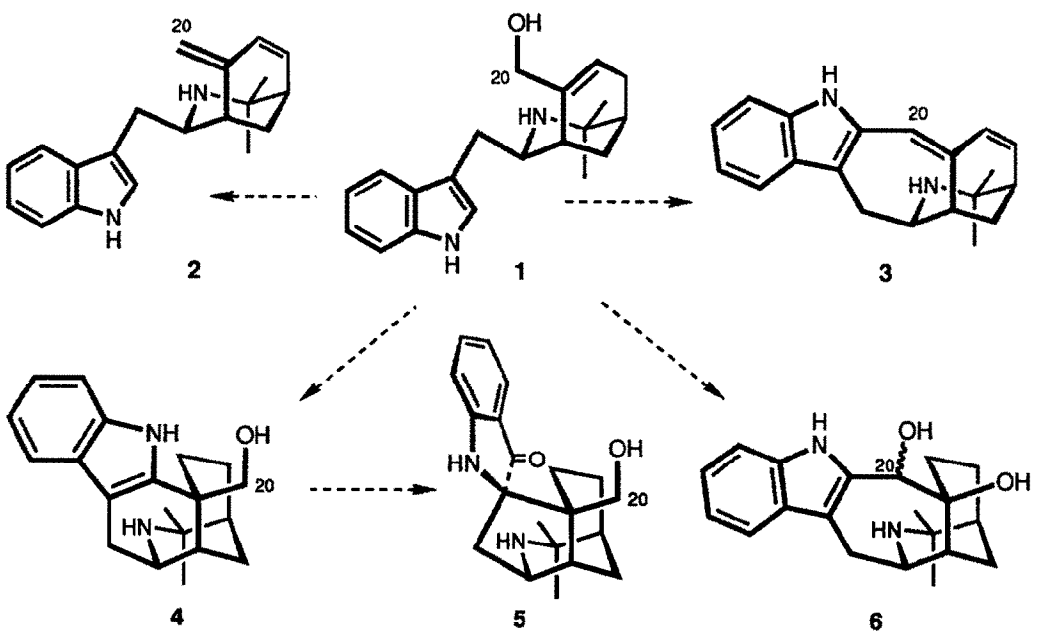
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule,
ETH Zentrum, Universitätstrasse 16, CH - 8092 Zürich, Switzerland

(*Received* 21 *September* 1992)

Abstract: Optically pure samples of the rare *Aristotelia* alkaloids (+)-sorelline (**2**) and (+)-aristolasene (**3**) have been synthesized for the first time. Since natural *(S)*-perilla alcohol served as one of the starting building blocks, these syntheses delineate the previously unknown absolute configurations of these metabolites as shown in the schemes. In connection with this work we also prepared (-)-20-hydroxyhobartine (**1**), which, however, turned out to be different from a natural product that had been assigned this structure six years ago.

There are several biogenetically interrelated members of the *Aristotelia* alkaloid family [2] that are functionalized at C(20),[3] such as 20-hydroxyhobartine (**1**),[4] sorelline (**2**),[5] aristolasene (**3**),[6] aristocarbinol (**4**),[7] aristolarine (**5**),[8] and aristolasol (**6**) [6] (see *Scheme 1*). Since no synthetic approach to these metabolites has been reported up to now,[9] and since they occur in such small amounts in natural sources that their potential pharmacological properties could not be evaluated, we decided to elaborate a feasible route to these scarce indole alkaloids.

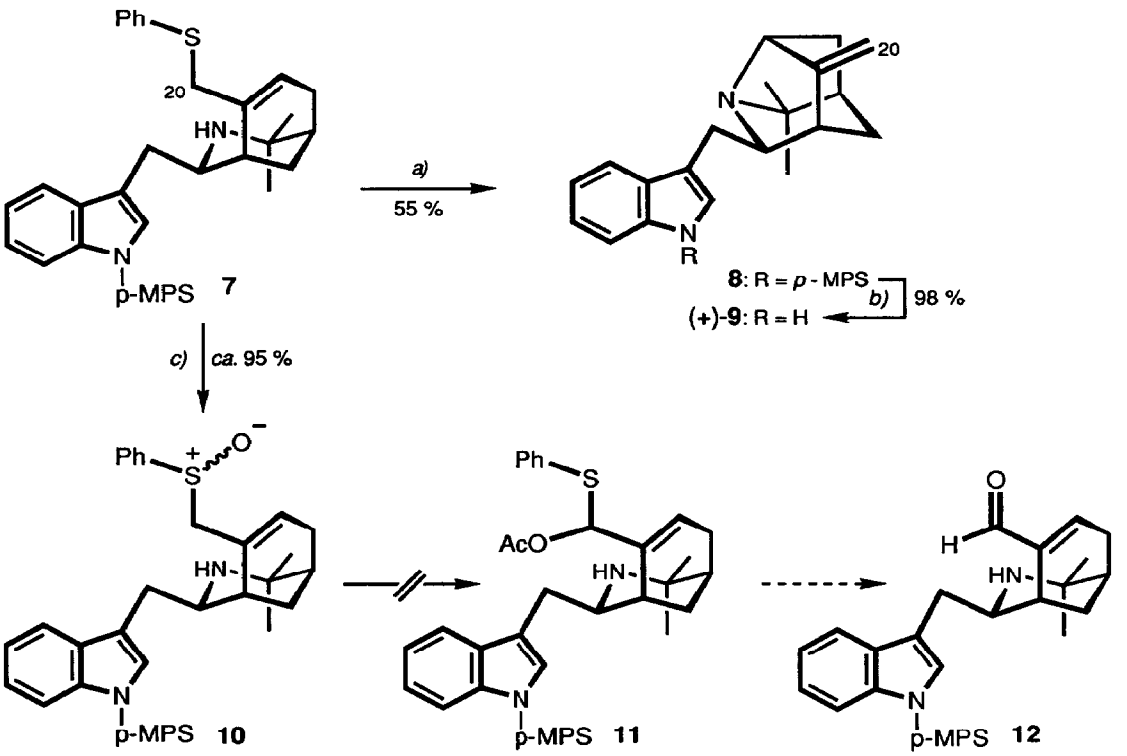
Scheme 1



Recently, we disclosed an efficient synthesis of the unique indole alkaloid (+)-aristofruticosine ((+)-**9**), which was assembled from *(S)*-perilla alcohol and *N*-protected 1*H*-indole-3-acetaldehyde in 7 steps with an overall yield of 15 %.[10] Thiophenyl ether **7** *(Scheme 2)* was the key intermediate in that synthesis, and we felt that this readily available compound should prove useful for providing access to some of the rare alkaloids shown in *Scheme 1*. For this purpose it was necessary to convert the thiophenyl substituent into an oxygen functional group. Since the *Pummerer* reaction [11] represents the method of choice for the required transformation, compound **7** was oxidized with $NaIO_4$ in MeOH / THF [12] to give the corresponding sulfoxide **10** (70:30-mixture of two diastereoisomers) in nearly quantitative yield.

Scheme 2

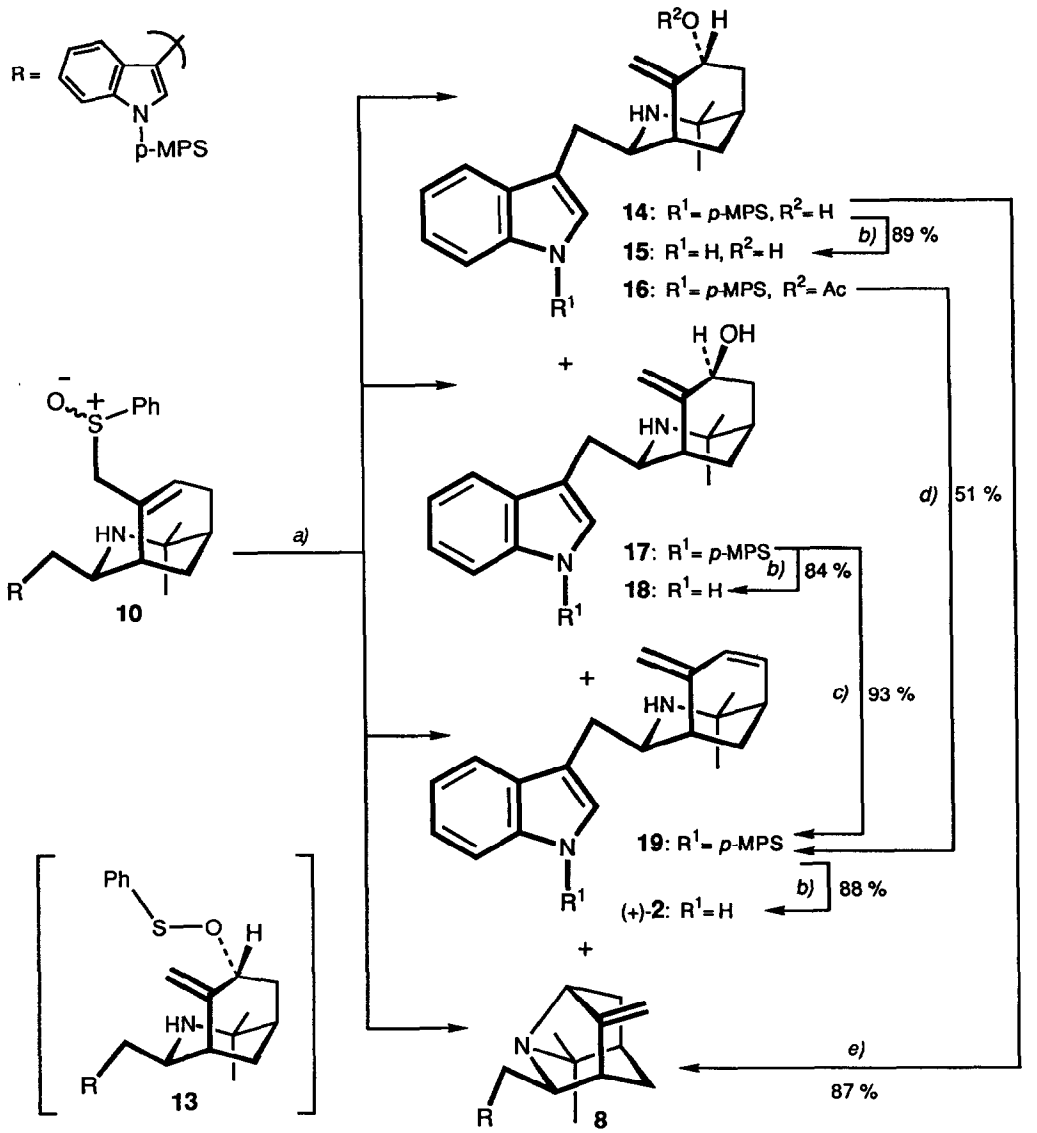
p-MPS = *p*-methoxyphenylsulfonyl



Reagents: *a) 2,6-Difluorobenzylbromide / 1,2,2,6,6-pentamethylpiperidine / $AgBF_4$ / DMF, 7 d at 25 °;* [10] *b) Na/Hg in MeOH, 90 min. at 25 °; c) $NaIO_4$ in THF/MeOH, 48 h at 25 °.*

However, all attempts to convert **10** into aldehyde **12** through a *Pummerer* reaction failed. In most cases the major product was indole-protected 18-*endo*-hydroxymakomakine (**14**) *(Scheme 3)* or the corresponding *O*-acetate **16**, depending on the reaction conditions (see *Table 1*). Obviously, the desired transformation can not compete with the alternative allylsulfoxide *[2,3]*-sigmatropic rearrangement.[13] The fact that in the absence of external thiophiles only the *endo*-products **14** and **16** are formed has been interpreted as follows:[14] at elevated temperatures an equilibrium among **10**, the sulfenic acid ester **13** and the corresponding *exo*-isomer is set up. In the case of **13** the piperidine *N* atom acts as an internal thiophile,[15] and since the formation of the resulting sulfenic acid amide is probably an irreversible process, **13** is constantly removed from the equilibrium mixture. In the presence of a good external thiophile, such as a trialkyl phosphite, both epimeric sulfenic acid esters are cleaved (presumably under kinetic control) and give rise to the observed mixture of **14** and **17** (*Table 1*, run 6).

Scheme 3



Reagents: a) see Table 1; *b) NaHg in MeOH, 90 min. at 25°; c) $BF_3 \cdot Et_2O$ in CH_2Cl_2; d) p-TsOH, $(CH_2Cl)_2$, 14 h 70°; e) MesCl, Et_3N, CH_2Cl_2, 24 h 25°.*

Both 18-hydroxymakomakine derivatives **14** and **17** were deprotected to give the alkaloids **15** and **18**, respectively, which have not been detected yet in natural sources. On the other hand, treatment of **16** with *p*-TsOH in boiling 1,2-dichloroethane, or of **17** with $BF_3 \cdot Et_2O$ in CH_2Cl_2 furnished indole-protected sorelline (**19**) in decent yield. Attempts to convert the readily available allylic alcohol **14** into **19** met with little success, but it was found that treatment of **14** with mesyl chloride and Et_3N furnished indole-protected aristofruticosine (**8**) in excellent yield. This intramolecular SN reaction, which formally proceeds with retention of configuration at C(18), is probably the result of a double inversion, involving the 18-*exo*-chloride as the second intermediate.

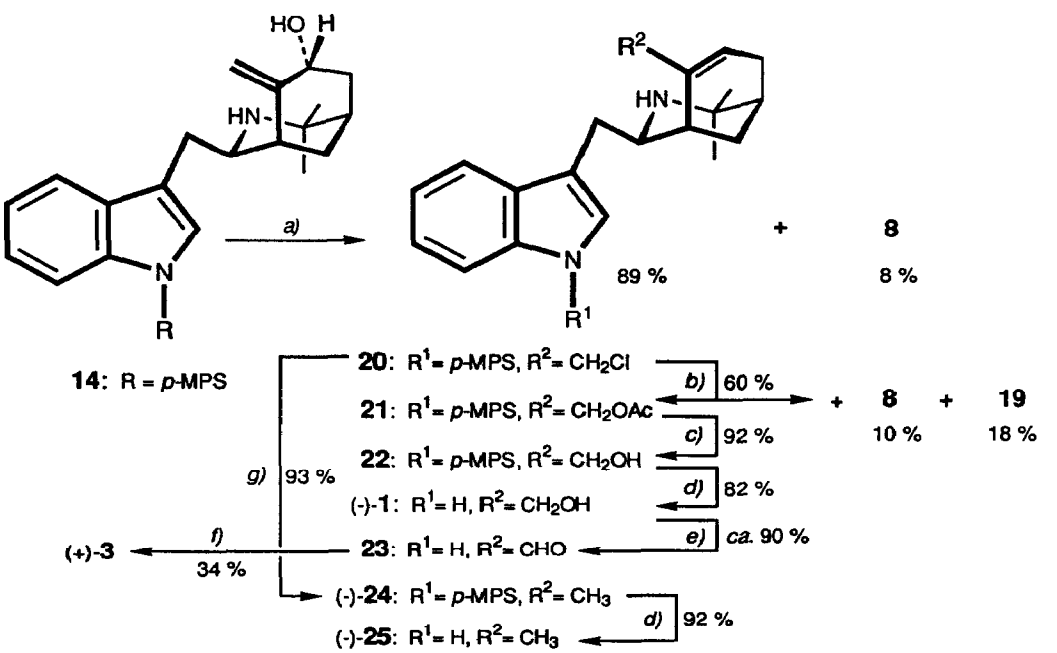
The free plant metabolite (+)-**2** was prepared in 88 % yield from **19** by treatment of with Na / Hg in MeOH. Since the spectral properties and the optical rotation of our preparation coincide within experimental limits with the data reported for the natural product,[5] the previously unknown absolute configuration of (+)-sorelline (**2**) is established as shown in *Scheme 1*.

Table 1. Product Compositions Resulting from Thermal Treatments of Sulfoxide **10**.

Run	Method	Conditions	**10**	**14**	**16**	**17**	**19**	**8**
1	[16]	1eq. P_4O_{10}, 5 eq. $(Me_3Si)_2O$ CH_2Cl-CH_2Cl, 120 h at 80°	25 %	51 %	/	/	18 %	< 5 %
2		Toluene, 20 h at 100°	10 %	41 %	/	/	24 %	/
3		CH_3CN, 75 h at 50°	55 %	42 %	/	/	/	/
4	[17]	1 eq. NH_4Cl, CH_3CN, 5 h at 50°	36 % *	43 %	/	/	/	/
5	[18]	1 eq. piperidine, EtOH, 24 h 70°	5 %	87 %	/	/	/	/
6	[15]	1 eq. $P(OMe)_3$, toluene, 16 h at 110°	/	28 %	/	21 %	2 %	13 %
7		AcOH/Ac_2O, 2h at 80°	/	/	80 %	/	/	/

* According to the ^{1}H-NMR spectrum of the crude reaction mixture, only the minor diastereoisomer of the starting material **10** was left.[19]

Scheme 4



Reagents: *a) $SOCl_2$, CF_3COOH, CH_2Cl_2, 16 h 0°; b) KOAc, dicyclohexyl-18-crown-6, CH_3CN, 6 d at 25°; c) KOH, EtOH, 24 h at 25°; d) Na/Hg, MeOH, 90 min. at 25°; e) DCC, DMSO, H_3PO_4; f) p-TsOH, MeOH, $HC(OMe)_3$; g) $LiBHEt_3$, THF, 40 h at 25°.*

While it was not possible to introduce an oxygen substituent at C(20) by way of a *Pummerer* reaction [20] or an alternative procedure, [21] it was discovered that treatment of the readily available allylic alcohol **14** with thionyl chloride gave the rearranged allyl chloride **20** *(Scheme 4)* in high yield. In addition, small amounts of **8** were formed. The required transformation of indole-protected 20-chlorohobartine (**20**) into (-)-20-hydroxy-hobartine ((-)-**1**) was straightforward and proceeded with an overall yield of *ca.* 45 %. Structure **1** has been proposed by *Quirion* for an alkaloid he had isolated from *Aristotelia australasica*.[4] Surprisingly, the physical data (m.p., $[\alpha]_D$, ^{1}H-NMR spectrum,[22] and MS) of our synthetic material is decidedly different from the reported values for the natural product.[23] At present, the reasons for the observed discrepancies are not obvious, but the following arguments convinced us that our preparation indeed possesses structure (-)-**1**: there is a near coincidence of the ^{1}H-NMR chemical shift values of (-)-**1** and of the metabolite (-)-hobartine ((-)-**25**) [24] in the region which is expected not to be influenced much by the presence of a OH-group at C(20), namely around the gem. dimethyl group, C(14) and C(15). This is not the case for natural "20-hydroxyhobartine" (see *Table 3).* To corroborate the claim that our preparation unequivocally possesses the constitutional formula **1**, its precursor **20** was correlated chemically with (-)-hobartine ((-)-**25**) *via* the protected intermediate **24** [25] (see *Scheme 4).*

Notwithstanding a future issue of this disagreement, we oxidized synthetic (+)-**1** with DCC/DMSO [26] to the corresponding aldehyde **23**, which was transformed into (+)-aristolasene ((+)-**3**) in a single operation. While this acid-catalyzed cyclization looked quite clean on TLC, and though a ^{1}H-NMR spectrum of the crude reaction mixture indicated a *ca.* 80 % yield of (+)-**3**, the subsequent purification steps caused serious losses of product. The spectral data of our preparation agrees within experimental limits with the reported values of natural (+)-aristolasene.[6] Since the optical rotations of the two specimen are of the same sign and order of magnitude ($[\alpha]_D$= + 475 (c=0.28, $CHCl_3$) *vs.* + 493 (c=0.3, $CHCl_3$) [4]), the previously unknown absolute configuration of (+)-**3** is defined as shown in *Scheme 1.*

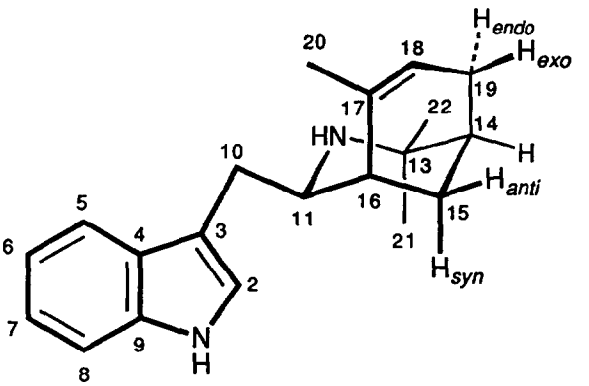


Figure. Biogenetic Numbering of the Hobartine Skeleton. [3]

Acknowledgments: The authors would like to thank the *Swiss National Science Foundation* (project No. 20-28267.90) and the *Stipendienfonds zur Unterstützung von Doktoranden auf dem Gebiete der Chemie* for financial support.

Table 2. ^{13}C-NMR values (100 MHz, $CDCl_3$, ppm from TMS); for numbering system, see Figure.

Nr. \ Cpd.	**1** a)	**1** b)	**25** a)	**2** a)	**3** c)	**9** a)	**15**	**18**
2	122.2	122.4	122.3	122.4	143.5	122.0	122.9	122.4
3	113.4	112.3	113.5	113.6	115.6	113.5	112.3	113.5
4	127.6	127.5	127.6	127.8	128.2	127.8	127.5	127.8
5	119.0	118.6	118.9	119.2	117.9	119.2	119.0	119.2
6	119.3	118.9	118.9	119.1	119.6	119.1	119.3	119.2
7	122.0	121.6	121.6	121.9	122.0	121.8	122.0	121.9
8	111.1	111.2	111.0	111.0	110.8	111.0	111.3	111.0
9	136.4	136.6	136.3	136.4	136.1	136.2	136.6	136.5
10	31.5	30.8	31.7	30.3	27.6	30.8	30.8	31.3
11	54.4	54.4	54.6	53.9	64.3	62.3	53.0	53.4
13	53.7	53.8	54.2	53.3	52.4	65.9	52.3	52.6
14	35.5	35.6	35.1	39.0	39.8	42.9	37.3	39.4
15	29.4	29.1	29.3	29.5	30.4	33.8	32.7	33.1
16	33.8	35.6	38.3	38.7	37.1	44.8	45.4	45.3
17	137.7	137.2	135.5	142.8	134.7	158.7	149.6	153.1
18	126.9	126.3	124.7	131.9	131.6	64.8	69.2	69.0
19	27.8	27.6	27.9	132.7	134.1	43.0	36.1	39,8
20	67.8	66.8	25.7	114.7	116.2	99.0	114.6	106.9
21	25.9	26.5	25.9	24.9	25.8	24.0	26.0	26.4
22	30.0	29.4	30.0	29.7	30.5	30.8	29.4	29.8

a) Assignments corroborated through HETCOR. b) Data of natural "20-hydroxyhobartine".[4] c) Tentative assignments.

Table 3. ^1H-NMR chemical shift values (400 MHz, $CDCl_3$, ppm from TMS).

Nr. \ Cpd.	**1**	**1** a)	**25**	**2**	**3**	**9**	**15**	**18**
2	7.09	7.03	7.09	7.04	-	6.94	7.01	6.99
5	7.62	7.58	7.64	7.64	7.54	7.61	7.61	7.62
6	7.11	7.03	7.11	7.10	7.10	7.10	7.11	7.10
7	7.19	7.12	7.18	7.18	7.14	7.17	7.20	7.19
8	7.34	7.33	7.35	7.33	7.31	7.34	7.38	7.36
10	2.76	2.53	2.82	2.83	3.48	2.81	2.89	2.75
10'	2.67	2.53	2.69	2.72	1.95	2.66	2.77	2.56
11	3.51	3.33	3.49	3.48	3.93	3.75	3.40	3.40
14	1.53	1.31	1.46	2.01	1.32	1.85	1.55	1.60
15_{anti}	1.60	1.34	1.62	1.77	1.78	1.47	1.60	1.58
15_{syn}	2.15	1.85	2.08	2.04	2.00	1.96	2.17	2.07
16	2.42	2.11	2.17	2.38	2.46	2.25	2.53	2.51
18_{endo}	5.95	5.85	5.63	6.35	6.57	-	-	5.30
18_{exo}	-	-	-	-	-	3.91	4.09	-
19_{endo}	2.39	2.14	2.28	5.94	6.10	2.52	2.23	2.41
19_{exo}	2.15	1.91	2.08	-	-	1.71	1.74	1.26
20	4.15	3.90	1.81	5.08	6.39	4.82	5.12	5.11
20'	4.09	3.90	-	4.75	-	4.72	4.89	4.81
21	1.17	0.97	1.16	1.28	1.32	1.14	1.15	1.10
22	1.10	0.87	1.09	1.01	1.10	1.43	1.18	1.10

a) Data of natural "20-hydroxyhobartine".[4]

Experimental Section

General. All solvents employed as reaction media were reagent grade *(Fluka, puriss.)* and were further purified and dried as follows: CH_2Cl_2 and $CHCl_3$, filtered through Al_2O_3 *(Woelm,* basic act. I); THF was freshly distilled from K under Ar; benzene, toluene and pyridine were freshly distilled from $LiAlH_4$; DMF and DMSO were freshly distilled from CaH_2 under slightly reduced pressure. M.p. (not corrected): *Tottoli* apparatus, sealed evacuated capillaries, unless mentioned otherwise. Optical rotations: *Perkin-Elmer 241.* UV spectra: *Uvikon 860.* IR spectra: *Perkin-Elmer 781.* ^{1}H-NMR spectra (δ [ppm] from TMS, appearant coupling constants *J* [Hz]): *Bruker AMX 400* (400 MHz). ^{13}C NMR spectra (δ [ppm] from TMS, multiplicities as determined from DEPT spectra): *Bruker AMX 400* (100 MHz). ^{1}H / ^{13}C-COSY (HETCOR) spectra were recorded on a *Varian Gemini* (200/50 MHz). Mass spectra (m/z [amu] (% base peak)): *VG TRIBID* (EI, 70 eV) or GC-MS: *HP 5890 series II* GC with *HP 5971A* MS, EI (70 eV) T= 190°; column: *Supelco SPB-5*, fused silica, 30 m, Ø 0.25 mm, film thickness 0.25 μm; mode: 25-90°: 70°/min., 90-300°: 10°/min., hold at 300°: 30 min.

General Procedure for the Removal of the Indole Protecting Group [27]. To a solution of the protected alkaloid in MeOH (80 ml per mmol) were added 2 eq. of NaH_2PO_4 *(Fluka, purum)* and 16 eq. of 6% sodium amalgam. After stirring for 4 h at 25°, the mixture was decanted from the mercury and evaporated. The residue was worked up with $CHCl_3$ / aq. $NaHCO_3$ and the resulting org. phase dried over K_2CO_3. The crude material was chromatographed (benzene/Et_2O/Et_2NH 8:4:1).

20-Phenylsulfinyl-(*N*(1)-*p*-methoxyphenylsulfonyl)hobartine (10). To a solution of 739.6 mg (1.29 mmol) of **7** in 50 ml of THF/MeOH 1:1 was added a solution of 321 mg $NaIO_4$ *(Fluka, purum)* in 25 ml of H_2O at 25°C. After stirring for 48 h, the suspension was filtered and the filtrate evaporated. The residue was worked up with $CHCl_3$ and H_2O, and the combined organic layers dried over K_2CO_3 and evaporated to yield 732.4 mg (96 %) of **10** (yellow-white crystals, 70:30-mixture of two diastereoisomers).

M.p.: 123-124°

IR (KBr): 1594, 1497, 1444, 1369, 1265, 1167, 748, 665, 580, 546.

^{1}H-NMR: 8.06(*dt, J*=8.3, 0.8, 0.7H); 8.00(*dt, J*=8.3, 0.8, 0.3H); 7.82(*dm, J*=9.1, 1.4H); 7.80(*dm, J*=9.1, 0.6H); 7.47(br.*s*, 0.7H); 7.45-7.2(*m*, 6.3H); 6.86(*dm, J*=9.1, 0.6H); 6.75(*dm, J*=9.1, 1.4H); 6.69(*ddm, J*=8.1, 1.1, 0.7H); 5.96(br.*t*, *J*=3.4, 0.7H); 5.73(br.*t*, *J*=3.4, 0.3H); 3.73(*s*, 0.9H); 3.62(*s*, 2.1H); 3.56(*ddd, J*=9.0, 6.1, 2.5, 0.7H); 3.49(br.*d*, *J*=12.6, 0.3H); 3.35(br.*d, J*=12.6, 0.3H); 3.33(*ddd, J=ca.*8, *ca.*7, 2.1, 0.3H); 3.27(*d, J*=12.5, 0.7H); 2.96(br.*d*, *J*=12.5, 0.7H); 2.64-1.9(*m*, 6H); 1.70(*dt, J*=12.8, 3.2, 0.7H); 1.57(*m*, 0.7H); 1.50(*dt, J*=12.4, 3.2, 0.3H); 1.46(*m*, 0.3H); 1.25(*s*, 2.1H); 1.16(*s*, 3H); 1.05(*s*, 0.9H).

MS (FAB): 589(100, M^++1), 481(18), 464(15), 463(34), 307(19), 293(15), 288(18), 164(63), 155(29), 154(86),138(36), 137(57), 136(72), 107(36), 89(30), 77(37).

(+)-18-*endo*-Hydroxymakomakine ((+)-15). A solution of 748 mg (1.27 mmol) of **10** and 0.2 ml (1.9 mmol) of piperidine *(Merck, p.a.)* in 150 ml of EtOH was heated under Ar at 70° for 24 h. After removal of the solvent under reduced pressure, the residue was chromatographed ($CHCl_3$/Et_2O/Et_2NH 40:1:2) to yield 527.5 mg (86.5 %) of **14** (pale brown crystals, m.p. 226-227°) and 37.4 mg (5 %) of starting material **10**. A 83.7 mg sample of **14** was deprotected using the *General Procedure* to give 48.3 mg (89 %) of (+)-**15**.

M.p.: 174-175° (Et_2O).

$[\alpha]_D$: + 91.5 (c=0.82, $CHCl_3$).

UV (EtOH): 290 (3.65), 282 (3.71), 222 (4.51).

IR (KBr): 1640, 1619, 1458, 1422, 1386, 1360, 1341, 1111, 1069, 1035, 971, 910, 743.

^{1}H-NMR: 7.61(*dm, J*=8.0, 1H); 7.38(*ddd, J*=8.1, 1.0, 0.7, 1H); 7.20(*ddd, J*=8.1, 7.1, 1.1, 1H); 7.11(*ddd, J*=8.0, 7.1,1.0, 1H); 7.01(*d, J*=2.3, 1H); 5.12(*d, J*=2.2, 1H); 4.89(*d, J*=2.2, 1H); 4.09 (*m*, 1H); 3.40(*ddd, J*=9.4, 4.8, 2.7, 1H); 2.89(*ddd J*=14.5, 4.8, 0.8, 1H); 2.77(*dd, J*=14.5, 9.4, 1H); 2.53(*m*, 1H); 2.23(*dm, J*=14.3, 1H); 2.17(*dq, J*=12.8, 3.1, 1H); 1.74(*dt, J*=14.9, 3.1, 1 H); 1.60(*dt, J*=12.8, 3.1, 1H); 1.55(*m*, 1H); 1.18(*s*, 3H); 1.15(*s*, 3H).

^{13}C-NMR: 149.6*(s)*, 136.6*(s)*, 127.5*(s)*, 122.9*(d)*, 122.0*(d)*, 119.3*(d)*, 119.0*(d)*, 114.6*(t)*, 112.3*(s)*, 111.3*(d)*, 69.2*(d)*, 53.0*(d)*, 52.3*(s)*, 45.4*(d)*, 37.3*(d)*, 36.1*(t)*, 32.7*(t)*, 30.8*(t)*, 29.4*(q)*, 26.0*(q)*.

GC/MS: 310(4, M^+), 295(3), 292(2), 199(5), 181(13), 180(100), 159(13), 130(28), 117(6), 58(7).

(+)-18-*exo*-Hydroxymakomakine ((+)-18). A solution of 183.2 mg (0.311 mmol) of **10** and 150 μl (1.25 mmol) of trimethylphosphite *(Fluka, pract.)* in 4 ml of toluene was heated in a sealed glass tube (110°) for 18 h. After removal of the solvent under reduced pressure, the residue was chromatographed on silica (hexane/benzene/Et_2O/Et_2NH 18:8:4:1) to furnish

42.3 mg (28.3 %) of **14**, 30.9 mg (20.7 %) of **17**, 18.5 mg (12.7 %) of **8**,[10] and 18.6 mg (10.4 %) of starting material **10**. A sample of **17** (30.4 mg, 0.063 mmol) was deprotected using the *General Procedure* to give 19.6 mg (84.5 %) of (+)-**18**.

M.p.: 58-61° ($CHCl_3$).

$[\alpha]_D$: + 84 (c=0.35, $CHCl_3$).

UV (EtOH): 290 (3.56), 282 (3.62), 223 (4.32).

IR ($CHCl_3$): 3582, 3480, 1453, 1430, 1416, 1380, 1337, 1254, 1089, 1066, 1023, 1009, 906.

^{1}H-NMR: 7.62(*dd*, *J*=7.9, 1.0, 1H); 7.36(*dm*, *J*=8.1, 1H); 7.19(*ddd*, *J*=8.1, 7.1, 1.0, 1H); 7.10(*ddd*, *J*=7.9, 7.1, 1.0, 1H); 6.99(*d*, *J*=2.2, 1H); 5.30(*ddt*, *J*=11.2, 6.7, 2.2, 1H); 5.11(*t*, *J*=2.2, 1H); 4.81(*t*, *J*=2.2, 1H); 3.40(*ddd*, *J*=8.5, 5.3, 2.6, 1H); 2.75(*ddd J*=14.3, 5.3, 0.8, 1H); 2.56(*ddd*, *J*=14.3, 8.5, 0.6, 1H); 2.51(*m*, 1H); 2.41(*ddt*, *J*=14.8, 6.7, 2.5, 1H); 2.07(*dm*, *J*=12.5, 1H); 1.60(*m*, 1H); 1.58(*dt*, *J*=12.5, 3.3, 1 H); 1.26(*ddd*, *J*=12.8, 11.2, 4.0, 1H); 1.103(*s*, 3H); 1.099(*s*, 3H).

^{13}C-NMR: 153.1(*s*), 136.5(*s*), 127.8(*s*), 124.3(*d*), 122.4(*d*), 121.9(*d*), 119.2(2*d*), 113.5(*s*), 111.0(*d*), 106.9(*t*), 69.0(*d*), 53.4(*d*), 52.6(*s*), 45.3(*d*), 39.8(*t*), 39.4(*d*), 33.1(*t*), 31.3(*t*), 29.8(*q*), 26.4(*q*).

GC/MS: 310(30, M^+), 295(2), 292(6), 184(5), 181(14), 180(100), 162 (8), 159(20), 143(11), 131(14), 130(73), 117(12), 77(11), 58(29), 41(11), 30(17).

(+)-Sorelline ((+)-2):

Method A: To a solution of 18 mg (0.034 mmol) of **16** in 5 ml of 1,2-dichloroethane were added 3.7 mg *p*-TsOH (*Fluka, puriss.*). The mixture was stirred under Ar at 70° for 14 h. Workup with CH_2Cl_2 gave 16 mg of a mixture that was chromatographed to give 8.2 mg (51 %) of **19** and 4 mg of a 2:1-mixture of two unknown compounds which are presently under investigation.

Method B: To a solution of 11.2 mg (mmol) of **17** in 2 ml of dry tuluene were added 8.8 µl of freshly distilled $BF_3{\cdot}Et_2O$ (*Fluka, purum*). After stirring at 25° for 3 h, the mixture was worked up with 10 % aq. NH_3 solution and Et_2O to to yield 10.0 mg (93 %) of a yellow oil which according to ^{1}H-NMR spectroscopy consisted of pure **19**.

A sample of **19** (83.7 mg, 0.181 mmol) was deprotected according to the *General Procedure* to give 47.2 mg (89.2 %) of (+)-sorelline ((+)-2).

M.p.: 165-167° ($CHCl_3$) [Lit.: 165-168° (Et_2O) [5]].

$[\alpha]_D$: + 158.3 (c=0.97, $CHCl_3$) [Lit.: + 157 (c=1.07, $CHCl_3$) [5]].

UV (EtOH): 290 (3.76), 282 (3.81), 223 (4.72) [Lit.: 291 (3.80), 282 (3.85), 224 (4.72) [5]].

IR ($CHCl_3$): 3480, 3005, 1595, 1456, 1418, 1381, 1090, 1011, 892.

^{1}H-NMR: 7.64(*dm*, *J*=8, 1H); 7.33(*dm*, *J*=8, 1H); 7.18(*ddd*, *J*=8, 7.1, 1.2, 1H); 7.10(*ddd*, *J*=8, 7.1, 1.1, 1H); 7.04(*m*, 1H); 6.35(*d*, *J*=9.6, 1H); 5.94(br.*dd*, *J*=9.6, 6.6, 1H); 5.08(*d*, *J*=2.0, 1H); 4.75(*dd*, *J*=2.0, 1.5, 1H); 3.48 (*ddd*, *J*=7.7, 6.3, 2.7, 1H); 2.83(*ddd*, *J*=14.6, 7.7, 0.6, 1H); 2.72(*ddd*, *J*=14.6, 6.3, 1.0, 1H); 2.38(*m*, 1H); 2.08-1.98(*m*, 2H); 1.77(*dt*, *J*=12.5, 3.3, 1H); 1.28(*s*, 3H); 1.01(*s*, 3H).
(Max. deviation from reported values for natural (+)-2 [5]: + 0.07 ppm).

^{13}C-NMR: 142.8(*s*), 136.4(*s*), 132.7(*d*), 131.9(*d*), 127.8(*s*), 122.4(*d*), 121.9(*d*), 119.2(*d*), 119.1(*d*), 114.7(*t*), 113.6(*s*), 111.0(*d*), 53.9(*d*), 53.3(*s*), 39.0(*d*), 38.7(*d*), 30.3(*t*), 29.7(*q*), 29.5(*t*), 24.9(*q*).
(Max. deviation from reported values for natural (+)-2 [5]: ± 0.4 ppm [28]).

MS: 292(6, M^+), 199(17), 162(18), 162(100), 159 (50), 130(40), 117(16), 105(15), 91(27), 77(11).

(*N* (1)-*p*-Methoxyphenylsulfonyl)aristofruticosine (8): A solution of 22.6 mg (0.047 mmol) of **14** and 16 µl (0.116 mmol) of Et_3N (*Fluka, purum*; dist. from CaH_2) in 5 ml of CH_2Cl_2 was cooled to 0°. After adding 9 µl (0.116 mmol) of methanesulfonyl chloride (*Fluka, puriss.*) under Ar, the mixture was stirred at 0° for 2 h and at 25° for 24 h. The mixture was worked up with CH_2Cl_2/sat. aq. $NaHCO_3$ to give 23.2 mg of crude material. Chromatography (benzene/Et_2O/Et_2NH 8:4:1) furnished 19 mg (87 %) of pure **8**, which was identical with a sample that had been prepared before *via* a different route. [10]

(-)-20-Hydroxyhobartine ((-)-1): To a solution of 50 mg (0.104 mmol) of **14** in 20 ml of CH_2Cl_2 were added 11.5 µl (0.15 mmol) of CF_3COOH (*Fluka, purum*) and the stirred mixure cooled to -20°. After addition of 11.5 µl (0.15 mmol) of freshly dist. $SOCl_2$, the mixture was allowed to reach room temperature and was stirred under Ar for 15 h. Workup with $CHCl_3$/sat. aq. $NaHCO_3$, followed by chromatography (EtOAc), furnished 46.4 mg (89.4 %) of **20** (white crystalline foam, m.p. 54-55°) and 3.8 mg (8 %) of **8**.

A solution of 81 mg (0.163 mmol) of **20** and 9.3 µl (1.63 mmol) of AcOH (*Fluka, puriss.*) in 10 ml of MeCN was stirred under Ar at 25° for 5 min. Then were added 29.4 mg (0.5 mmol) of KOAc (*Fluka, purum*, dehydrated) and 6 mg of dicyclohexyl-18-crown-6 (*Fluka, purum*). The resulting turbid mixture was stirred under Ar at 40° for 13 h. The solvent was evaporated and the residue chromatographed (EtOAc) to yield 58.1 mg (68.1 %) of **21** (oil), 11.2 mg (14.8 %) of **8** and 3.4 mg (4.5 %) of **19**.

To a solution of 55 mg (0.12 mmol) of **21** in 5 ml of EtOH were added 250 µl of 0.5 M KOH in EtOH at 0°. The mixture was stirred under Ar for 20 h at 25°, then was added 1 ml of sat. aq. NH_4Cl. Most of the solvent was removed under reduced pressure and the residue worked up with CH_2Cl_2. The resulting buff foam was purified by chomatography (benzene/Et_2O/Et_2NH 8:4:1) to give 46.6 mg (92.2 %) of white crystalline **22** (m.p. 80-82°). A sample of this material (35.6 mg, 0.074 mmol) was deprotected according to the *General Procedure* to give 18.9 mg (82.4 %) of (-)-1.

M.p.: 99-100° ($CHCl_3$, colorless crystals) [Lit.: amorphous, no m.p. recorded[4]].

$[\alpha]_D$: - 16 (c=0.242, $CHCl_3$) [Lit.: +113 (c=0.38, $CHCl_3$) [4]].

UV (EtOH): 290 (3.58), 282 (3.66), 222 (4.46) [Lit.: 290 (3.56), 282 (3.63), 220 (4.18) [4]].

IR ($CHCl_3$): 3455, 1621, 1445, 1381, 1370, 1335, 1148, 1091.

^{1}H-NMR: 8.04(br.*s*, 1H); 7.62(*dm*, *J*=8.0, 1H); 7.34(*dm*, *J*=8.0, 1H); 7.19(*ddd*, *J*=8.0, 7.1, 1.2, 1H); 7.11(*ddd*, *J*=8.0, 7.1, 1.0, 1H); 7.09(br.*s*, 1H); 5.95(*m*, 1H); 4.15(*dm*, *J*=13.0, 1H); 4.09(*dm*, *J*=13.0, 1H); 3.51(*ddd*, *J*=7.8, 6.7, 2.4, 1H); 2.76(*ddd*, *J*=14.5, 7.7, 0.5, 1H); 2.67(*ddd*, *J*=14.5, 6.7, 0.7, 1H); 2.40(*m*, 2H); 2.13(*m*, 2H); 1.60(*dt*, *J*=12.6, 3.2, 1H); 1.52(*m*, 1H); 1.48(br.*s*, 2H); 1.17(*s*, 3H); 1.10(*s*, 3H).

[Lit.: 7.58(*d*, *J*=7.5, 1H); 7.33(*d*, *J*=7.5, 1H); 7.12(*t*, *J*=7.5, 1H); 7.03(*t*, *J*=7.5, 1H); 7.03(*s*, 1H); 5.85(*t*, *J*=3.5, 1H); 3.90(*AB*, *J*=14.2, 2H); 3.33(*dt*, *J*=7.5, 2.5, 1H); 3.00(br.*s*, 2H); 2.53(*d*, *J*=7.5, 2H); 2.14(*ddd*, *J*=16.3, 3.5, 1.5, 1H); 2.11(*ddd*, *J*=3.3, 3.0, 2.5, 1H); 1.91(*ddd*, *J*=16, 3.5, 3, 1H); 1.85(*ddd*, *J*=13, 3.5, 3, 1H); 1.34(*qd*, *J*=3.0, 1.5, 1H); 0.97(*s*, 3H); 0.87(*s*, 3H) [4]].

^{13}C-NMR: 137.7(*s*), 136.4(*s*), 127.6(*s*), 126.9(*d*), 122.2(*d*), 122.0(*d*), 119.3(*d*), 119.0(*d*), 113.4(*s*), 111.1(*d*), 67.8(*t*), 54.4(*d*), 53.7(*s*), 35.5(*d*), 33.8(*d*), 31.5(*t*), 30.0(*q*), 29.4(*t*), 27.8(*t*), 25.9(*q*).

[Lit.: 137.2(*s*), 136.6(*s*), 127.5(*s*), 126.3(*d*), 122.4(*d*), 121.6(*d*), 118.9(*d*), 118.6(*d*), 112.3(*s*), 111.2(*d*), 66.8(*t*), 54.4(*d*), 53.8(*s*), 35.6(*d*), 35.5(*d*), 30.8(*t*), 29.4(*q*), 29.1(*t*), 27.6(*t*), 25.5(*q*) [4]].

MS: 295(1.5, M^+-15), 194(0.6), 181(12), 180(100), 159(6), 158(3), 131(6), 130(33), 79(7), 77(6).
[Lit.: 310(61, M^+), 295(71), 294(78), 279(100), 237(39), 222(36), 193(19), 182(34), 174(31), 164(64) [4]].

(+)-Aristolasene ((+)-3): To a solution of 44 mg (0.143 mmol) of (-)-1 in 8ml of DMSO (*Fluka, puriss.*, stored over 3 Å mol. sieves) were added 30 mg orthophosphoric acid (*Fluka, puriss.*) and 65 mg of dicyclohexylcarbodiimid (*Fluka, puriss.*). After stirring for 2 h at 25° the mixture was worked up with $CHCl_3$/sat. aq. $NaHCO_3$. According to ^{1}H-NMR spectroscopy the crude product consisted of at least 90 % pure aldehyde **23**. All attempts to prepare an analytically pure sample led to severe decomposition of this labile intermediate.

To a solution of 11 mg (0.036 mmol) of crude **23** in 10 ml of degassed MeOH were added 5 mg of *p*-TosOH (*Fluka, puriss.*) and 5 ml of trimethyl orthoformate (*Fluka, purum*). The mixture was kept under Ar for 72 h at 25°. The crude product left after evaporation of the solvent consisted of at least 80 % pure aristolasene (^{1}H-NMR evidence) and was chromatographed (benzene/Et_2O/Et_2NH 8:4:1) to give 3.7 mg (33.6 %) of the rather unstable alkaloid (+)-3 (yellow, strongly fluorescent oil).

$[\alpha]_D$: + 475 (c=0.28, $CHCl_3$) [Lit.: + 493 (c=0.3, $CHCl_3$) [4]].

UV (EtOH): 330 (3.91), 262 (3.93), 214 (4.13) [Lit.:330 (3.89), 262 (3.90), 215 (4.13) [4]].

IR ($CHCl_3$): 3470, 1455, 1380, 1366, 1343, 1310, 1291, 1170, 1157, 1096 [Lit.: 3400, 1460 (film) [4]].

^{1}H-NMR: 7.94(br.*s*, 1H); 7.54(*dm*, *J*=7.8, 1H); 7.31(*dm*, *J*=7.7, 1H); 7.14(*ddd*, *J*=7.7, 7.1, 1.3, 1H); 7.10(*ddd*, *J*=7.8, 7.1, 1.3, 1H); 6.57(*d*, *J*=9.5, 1H); 6.39(*s*, 1H); 6.10(br.*dd*, *J*=9.5, 6.8, 1H); 3.93 (*td*, *J*=8.7, 3.0, 1H); 3.48(*dd*, *J*=15.4, 9.0, 1H); 2.46(*m*, 1H); 2.14(*dt*, *J*=6.8, 3.0,1H); 2.00(*dm*, *J*=12.6, 1H); 1.95(*ddm*, *J*=15.4, 8.4, 1H); 1.78 (*dt*, *J*=12.6, 3.6, 1H); 1.32(*s*, 3H); 1.10(*s*, 3H).
(Max. deviation from reported values for natural (+)-3 [4]: ± 0.03 ppm).

^{13}C-NMR: 143.5(*s*), 136.1(*s*), 134.7(*s*), 134.1(*d*), 131.6(*d*), 128.2(*s*), 122.0(*d*), 119.6(*d*), 117.9(*d*), 116.2(*d*), 115.6(*s*), 110.8(*d*), 64.3(*d*), 52.4(*s*), 39.8(*d*), 37.1(*d*), 30.5(*q*), 30.4(*t*), 27.6(*t*), 25.8(*q*).

MS: 290(60, M^+), 233(33), 232(69), 221(18), 218(100), 217(52), 207(22), 206(16), 205(20), 204(19), 167(11), 58(23), 42(28).

Chemical correlation of compound **20** with **(-)-Hobartine ((-)-25)**: To a solution of 3 mg (0.006 mmol) of **20** in 2.5 ml of THF were added 12 µl of 0.3 M $LiBHEt_3$ in THF (*Aldrich*). After stirring for 40 h at 25° the mixture was worked up with CH_2Cl_2. The crude product was purified through prep. TLC ($CHCl_3$/EtOH 9:1) to give 2.6 mg (93.5 %) of **24**.[25] Standard deprotection of this material furnished 1.4 mg (92 %) of a compound that was identical with synthetic (-)-hobartine ((-)-25). [24b]

References and Notes

1. For Part X, see: Güller, R.; Borschberg, H.-J. *Tetrahedron Asymmetry* **1992**, *3*, 1197.
2. For a review, see: Bick, I.R.C.; Hai, M.A. In *The Alkaloids*, Brossi, A.; Ed.; Academic Press: New York, 1985; Vol.XXIV, Chapt. 3.
3. Biogenetic numbering, as proposed by *Bick* and *Hesse* and coworkers: Kyburz, R.; Schöpp, E.; Bick, I.R.C.; Hesse, M. *Helv. Chim. Acta* **1981**, *64*, 2555.
4. Quirion, J.C., PhD Thesis, Université de Paris-Sud, Centre d'Orsay, **1986**.
5. Kyburz, R.; Schöpp, E.; Bick, I.R.C.; Hesse, M. *Helv. Chim. Acta* **1979**, *62*, 2539.
6. Quirion, J.C.; Kan-Fan, C.; Bick, I.R.C.; Husson, H.-P. *Phytochemistry* **1988**, *27*, 3337.
7. Kan-Fan, C.; Quirion, J.-C.; Bick, I.R.C.; Husson, H.-P. *Tetrahedron* **1988**, *44*, 1651.
8. Kyburz, R.; Schöpp, E.; Hesse, M. *Helv. Chim. Acta* **1984**, *67*, 804.
9. Racemic sorelline ((±)-**2**) has been obtained before: Burkard, S.; Borschberg, H.-J. *Helv. Chim. Acta* **1991**, *74*, 275.
10. Beerli, R.; Borschberg, H.-J. *Helv. Chim. Acta* **1991**, *74*, 110.
11. For reviews, see: a) Russell, G.A.; Mikol, G.J. In *Mechanisms of Molecular Migrations*; Thyagarajan, B.S., Ed.; Wiley Interscience: New York, 1968; Vol. 1; b) Warren, S. *Chem. Ind. (London)* **1980**, 824; c) Oae, S. *Top. Org. Sulphur Chem.* **1978**, 289.
12. a) Leonhard, N.J.; Johnson, C.R. *J. Org. Chem.* **1962**, *27*, 282;
b) Johnson, C.R.; Keiser, J.E. *Org. Synth.* **1966**, *46*, 78.
13. For reviews, see: a) Hoffmann, R.W. *Angew. Chem.* **1979**, *91*, 625. b) Evans, D.A.; Andrews, G.C. *Acc. Chem. Res.* **1974**, *7*, 147; c) Hoffmann, R.W. In *Organic Sulfur Chemistry*, Freidlina, R.K.; Skorova, A.E., Eds.; Pergamon Press: Oxford, 1981; p. 69-80.
14. Borschberg, H.-J. *Chimia* **1991**, *45*, 329.
15. Evans, D.A.; Andrews, G.C. *J. Am. Chem. Soc.* **1972**, *94*, 3672.
16. Kakimoto, M.; Imai, Y. *Chem. Lett.* **1984**, 1831.
17. Hoffmann, R.W. *Chem. Ber.* **1980**, *113*, 819.
18. Remiszewski, S.W.; Whittle, R.; Weinreb, S.M. *J. Org. Chem.* **1984**, *49*, 3243.
19. This finding allows a tentative assignment of the absolute configurations at the sulfur atoms of the two sulfoxides: the transition state in the allylsulfoxide rearrangement involving the major, more reactive isomer is obviously sterically less crowded, and an examination of molecular models shows that this is to be expected for the *(S)*-isomer.
20. For successful *Pummerer* reactions involving 2,4-dienyl-thiophenyl ethers, see *e.g.* Corey, E.J.; Hoover, D.J. *Tetrahedron Lett.* **1982**, 3463, and: Schreiber, S.L.; Satake, K. *J. Am. Chem. Soc.* **1984**, *106*, 4186.
21. Bakuzis, P.; Campos, O.O.S.; Bakuzis, M.L.F. *J. Org. Chem.* **1976**, *41*, 3261.
22. To exclude the possibility that different degrees of inadvertent protonation had caused the observed differences, ^{1}H-NMR spectra in the presence of deliberately added acid or base were also recorded. However, under no circumstances the reported spectrum of the natural product could be reproduced.
23. Unfortunately, the only available sample of natural "20-hydroxyhobartine" has decomposed in the meantime (*J.C. Quirion*, CNRS, Gif sur Yvette, France; personal communication).
24. a) Ref. [5]; b) Darbre, T.; Nussbaumer, C.; Borschberg, H.-J. *Helv. Chim. Acta* **1984**, *67*, 1040; c) Gribble, G.W.; Barden, T.C. *J. Org. Chem.* **1985**, *50*, 5900.
25. This compound has been prepared before *via* a different route (acid-catalyzed cyclization of the imine formed by condensation of (*N-p*-MPS)-3-indolylacetaldehyde with *(S)*-α-terpinylamine): Anderson, J.; Diploma Thesis, ETH Zürich (1987).
26. Albright, J.D.; Goldman, L. *J. Org. Chem.* **1965**, *30*, 1107.
27. Trost, B.M.; Arndt, H.C.; Stege, P.E.; Verhoeven, T.R. *Tetrahedron Lett.* **1976**, 3477.
28. In ref.[5] the multiplicities of the signals at 112.9 and 110.9 ppm have been interchanged inadvertently (*M. Hesse*, Universität Zürich, Switzerland; personal communication).