Enantioselective Synthesis of (−)-(19*R*)-Ibogamin-19-ol

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The first total synthesis of the natural product (−)-(19*R*)-ibogamin-19-ol ((−)-**1**) is reported (biogenetic atom numbering). Starting with L-glutamic acid from the chiral pool and (2*S*)-but-3-en-2-ol, the crucial aliphatic isoquinuclidine (=2-azabicyclo[2.2.2]octane) core containing the entire configurational information of the final target was prepared in 15 steps (overall yield: 15%). The two key steps involved a highly effective, self-immolating chirality transfer in an *Ireland–Claisen* rearrangement and an intramolecular nitrone-olefin 1,3-dipolar cycloaddition reaction (*Scheme 3*). Onto this aliphatic core was grafted the aromatic moiety in the form of N(1)-protected 1*H*-indole-3-acetic acid by application of the dicyclohexylcarbodiimide (DCC) method (*Scheme 4*). Four additional steps were required to adjust the substitution pattern at C(16) and to deprotect the indole subunit for the closure of the crucial 7-membered ring present in the targeted alkaloid family (*Schemes 4* and *5*). The spectral and chiroptical properties of the final product (−)-**1** matched the ones reported for the naturally occurring alkaloid, which had been isolated from *Tabernaemonatana quadrangularis* in 1980. The overall yield of the entire synthesis involving a linear string of 20 steps amounted to 1.9% (average yield per step: 82%).

1. Introduction. – The *Iboga*-alkaloid family presently comprises more than 80 structurally closely related members (for reviews, see [1]). These monoterpene indole alkaloids occur in tropical shrubs, being represented by *ca.* 120 species that form part of the botanical tribe *Tabernaemontanae* (family *Apocynaceae*). The few *Iboga* alkaloids that have been investigated pharmacologically so far all show very interesting profiles [2]. Especially noteworthy are the beneficial effects of orally administered ibogaine, its catabolite noribogaine, and of 18-methoxycoronaridine in the curing of drug addicts. As a consequence, in 2001, the entire volume of the well-renowned series 'The Alkaloids' was dedicated to the diverse biological activities and medical implications of these three compounds [3].

A sizable sub-group of the *Iboga* alkaloids is endowed with an OH group at C(19) as shown in **A**[2]), and representatives with either relative configuration at this centre are known (for an incomplete listing, see **1**–**13** in *Table 1* and **14**–**21** in *Scheme 1*). To the best of our knowledge, none of these scarce natural products has been prepared by total synthesis up to now. As our recently disclosed concept towards the synthesis of the *Iboga* alkaloids appeared made-to-measure to prepare such compounds, we addressed this issue and wish to report the synthesis of (19*R*)-ibogamin-19-ol ((−)-**1**) to illustrate the inherent power of the underlying strategy. This alkaloid was first iso-

[1]) Taken from the forthcoming Ph.D. thesis of *S. H.*

[2]) Biogenetic atom numbering, *cf. Footnote 3*; for systematic names, see *Exper. Part.*

Table 1. Iboga *Alkaloids of the General Formula* **A**)[2]) *Endowed with an OH-Group at C(19)*. See *Scheme 1*.

	No.	R^1	R^2	R^3	X	Y	Ref.
(19*R*)-Ibogamin-19-ol	(−)-**1**	H	Me	H	H	H	[4][a])
(19*S*)-Ibogamin-19-ol	(−)-**2**	Me	H	H	H	H	[5][a])
Iboxygaine	(−)-**3**	Me	H	H	H	OMe	[5b][6]
Heyneanine[b])	(−)-**4**	Me	H	COOMe	H	H	[5b][6d][7][a])
19-Epiheyneanine (=19-isoheyneanine)	(−)-**5**	H	Me	COOMe	H	H	[5a][7b,g,k,o][8][a])
Voacristine (=voacangarine)	(−)-**6**	Me	H	COOMe	OMe	H	[5b][6c,f,g][7b,d,k–o][9]
19-Epivoacangarine	(−)-**7**	H	Me	COOMe	OMe	H	[6c][9a][7o][10]
10-Hydroxyheyneanine	**8**	Me	H	COOMe	H	OH	[6f][9b]
11-Hydroxyheyneanine	(−)-**9**	Me	H	COOMe	OH	H	[7q]
Isovoacristine	**10**	Me	H	COOMe	H	OMe	[5a][6d,e][7o][11]
19-Epiisovoacristine	(−)-**11**	H	Me	COOMe	H	OMe	[5a]
(19*R*)-19-Hydroxyconopharyngine[c])	**12**	H	Me	COOMe	OMe	OMe	[10b][12]
(19*R*)-18,19-Dihydroxycoronaridine	(−)-**13**	H	CH_2OH	COOMe	H	H	[7k]

[a]) There is an ambiguity in [5a] in as much as the claimed isolated compounds were named heyneanine (**4**) and 19-epiheyneanine (**5**), implying R^3 = COOMe. On the other hand, their structures were represented in the form of the 16-nor compounds **1** and **2** (R^3 = H), respectively. We have been informed recently that these drawings are erroneous and that in fact R^3 = COOMe (private communication from Dr. *D. G. I. Kingston*, Virginia Polytechnic Institute and State University, USA). [b]) Racemic heyneanine ((±)-**4**) was isolated from *Tabernaemontana divaricata* [7e]. [c]) Originally named '20-hydroxyconopharyngine' [17h][5a].

lated from natural sources in 1980 as a minor component from *Tabernaemonatana quadrangularis* by *Achenbach* and *Raffelsberger* [4][3]) who deduced its structure by spectroscopic means. Actually, it had already been prepared 5 years before by chemical degradation of natural 19-epiheyneanine ((−)-**5**) [7b]. Oxidation of **1**, be it enzymatically controlled or occurring through a spontaneous process, leads to the 7α-hydroxyindolenine derivative **20**, which undergoes a ring contraction under very mild conditions to furnish the yellow, strongly fluorescent pseudoindoxyl **21**. The latter compound was detected in *T. quadrangularis*, where it accounts for 0.07% of the total alkaloid content [4].

2. Results and Discussion. – The chosen retrosynthetic plan is shown in *Scheme 2* and involves closure of the 7-membered ring of the chosen target (−)-**1** at a late stage of the synthesis. Immediately before this event, the required intermediate **22** should be prepared by linking the two building blocks **23** and **24**. The preparation of the aliphatic isoquinuclidine (=2-azabicyclo[2.2.2]octane) core (+)-**24** was described recently and involved isoxazole **25** as the key intermediate, which was prepared through an intramolecular nitrone–olefin [2+3] cycloaddition reaction of **26** [14]. The latter was prepared from the two chiral building blocks L-glutamic acid ((*S*)-**28**) and (+)-(2*S*)-but-3-en-2-ol ((*S*)-**27**) (for earlier attempts along similar lines, see [15]).

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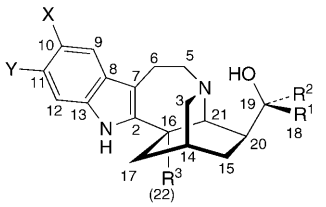
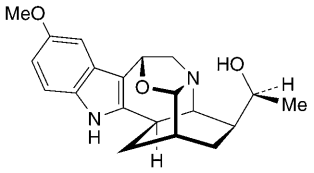
[3]) Due to their utilization of a different numbering system, the IUPAC and *Chem. Abstr.* numbering, these authors named their compound '(20*R*)-20-hydroxyibogamine'. We prefer the biogenetic nomenclature introduced by *Le Men* and *Taylor* [13], as shown in *Scheme 1*, which is used by the majority of the specialists and reviewers in this field.

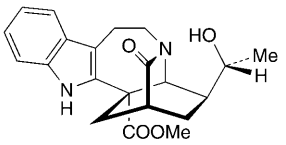
Scheme 1[2])



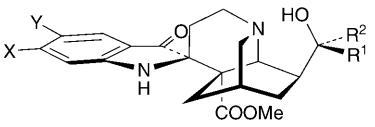
A [a])



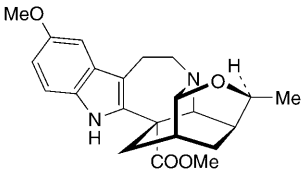
(–)-**14** 3,6-Epoxyiboxygaine [6f]



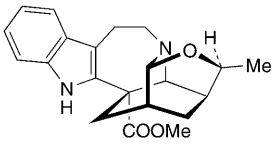
(–)-**15** 3-Oxo-19-epiheyneanine [13]



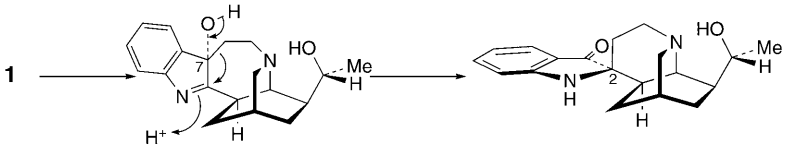
(±)-**18** X = OMe, Y = R^1 = H, R^2 = Me Ervatine [7n]
(+)-**19** X = R^2 = H, Y = OMe, R^1 = Me Voacristine pseudoindoxyl [6c]



(–)-**16** Heyneatine [7d]



(–)-**17** (19*R*)-3,19-Epoxycoronaridine [8c]

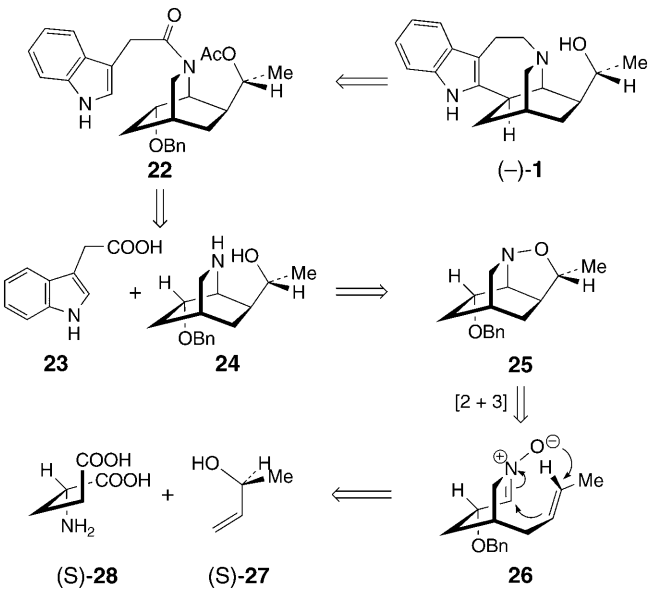


20 **21**

[a]) See *Table 1* for R^1,R^2,R^3, X, and Y.

The above plan was adhered to as shown in *Schemes 3–5*. The yields in some of the early steps could meanwhile be improved considerably (see Exper. Part), and the allylic alcohol (*S*)-**27** (85% ee), which was required for the esterification of **31** (obtained from (+)-**29** *via* (+)-**30**) and synthesized before according to *Balmer et al.* [16], was now prepared with ≥98% ee by catalytic reduction of the commercially available (*S*)-but-3-yn-2-ol (**32**) with *Lindlar*'s catalyst (for a closely related precedent, see [17]). As shown previously, the crucial chirality transfer in the *Ireland–Claisen* rearrangement of the silyl ketene acetal derived from ester (–)-**33** was very high. The observed ratio of 96:4 of the final cycloaddition products (+)-**25** and (–)-**37** points to a de of 92%, and this value very likely holds for all intermediates (–)-**34**/**35** and **26**/**36**, where the predominant diastereoisomers are all endowed with the *ul* (2*S*,4*R*)-configuration. The reductive cleavage of the N–O-bond of (+)-**25** with Zn/AcOH proceeded in virtually quantitative yield to furnish the required amino alcohol (+)-**24**.

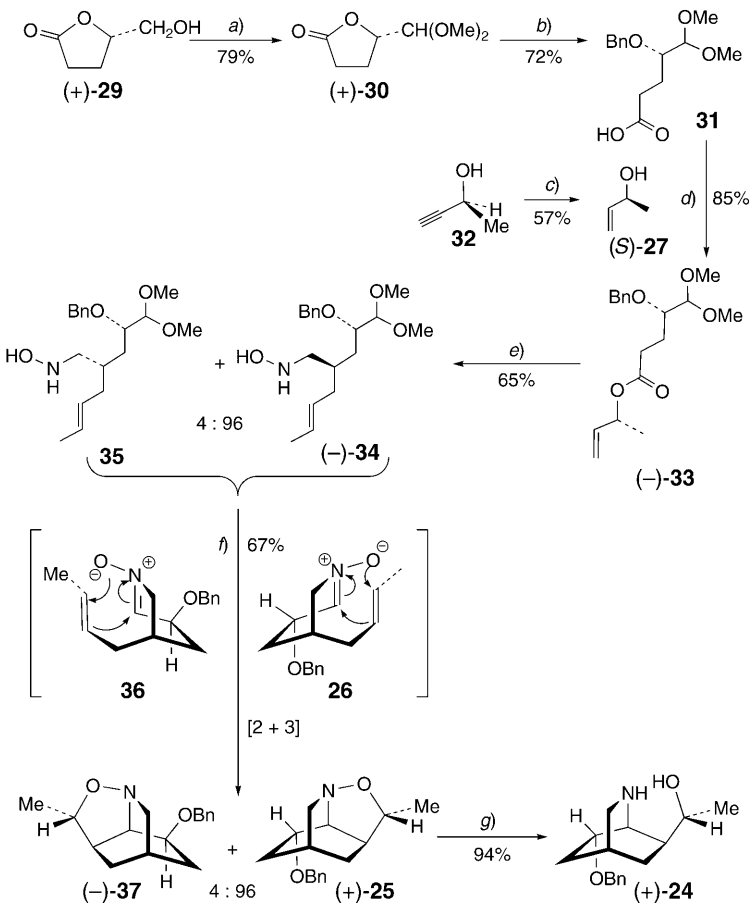
Scheme 2



The new steps in the present synthesis are shown in *Schemes 4* and *5*. The amino alcohol (+)-**24** was transformed into amide (+)-**39** with 1-[(4-methoxyphenyl)sulfonyl]-1*H*-indole-3-acetic acid (**38**) in the presence of dicyclohexylcarbodiimide (DCC) as coupling agent [18], followed by *O*-acetylation. The resulting amide (+)-**39**, obtained in 82% yield, and the following compounds containing the same amide group all turned out to be mixtures of two rotamers according to their NMR spectra. In the case of (+)-**39**, two identically structured sets of signals in the ratio 5 : 3 could be discerned in the ^{1}H-NMR spectrum of the purified product. The most significant differences between the two isomers reside in the bridgehead next to the carboxamide N-atom. In the major rotamer **39A**, C(21) showed up at δ(C) 43.1, shielded by almost 6 ppm compared to the corresponding signal in the minor component. We assume that this shielding is caused by a *syn*-γ effect exerted by the *cis*-positioned CH_2(6) group present in rotamer **39A** (*Scheme 4*). On the other hand, *H*–C(21) of the minor isomer **39B** is shielded by 1.1 ppm as compared to the major **39A**, because it clearly lies in the shielding zone of the carbonyl group [19]. To confirm that we really dealt with rotamers, a sample of (+)-**39** was reduced with $LiAlH_4$ in THF to furnish amino alcohol (+)-**40** as the only product, showing straight sets of ^{1}H- and ^{13}C-NMR signals. The rotamer composition and relevant chemical shifts of the related amides **41**–**44** are summarized in *Table 2*.

Amide (+)-**39** was hydrogenolytically debenzylated to furnish (+)-**41** in almost quantitative yield. *Swern* oxidation of the resulting secondary alcohol gave ketone (+)-**42**, which was transformed into the corresponding dimethyl acetal (+)-**43**. After reductive removal of the indole-protecting group to give (–)-**44**, the stage was set for the crucial formation of the 7-membered ring (*Scheme 5*). To this end, we at first followed the protocol devised by *Imanishi et al.* in the 19-deoxy series, which consists in

Scheme 3

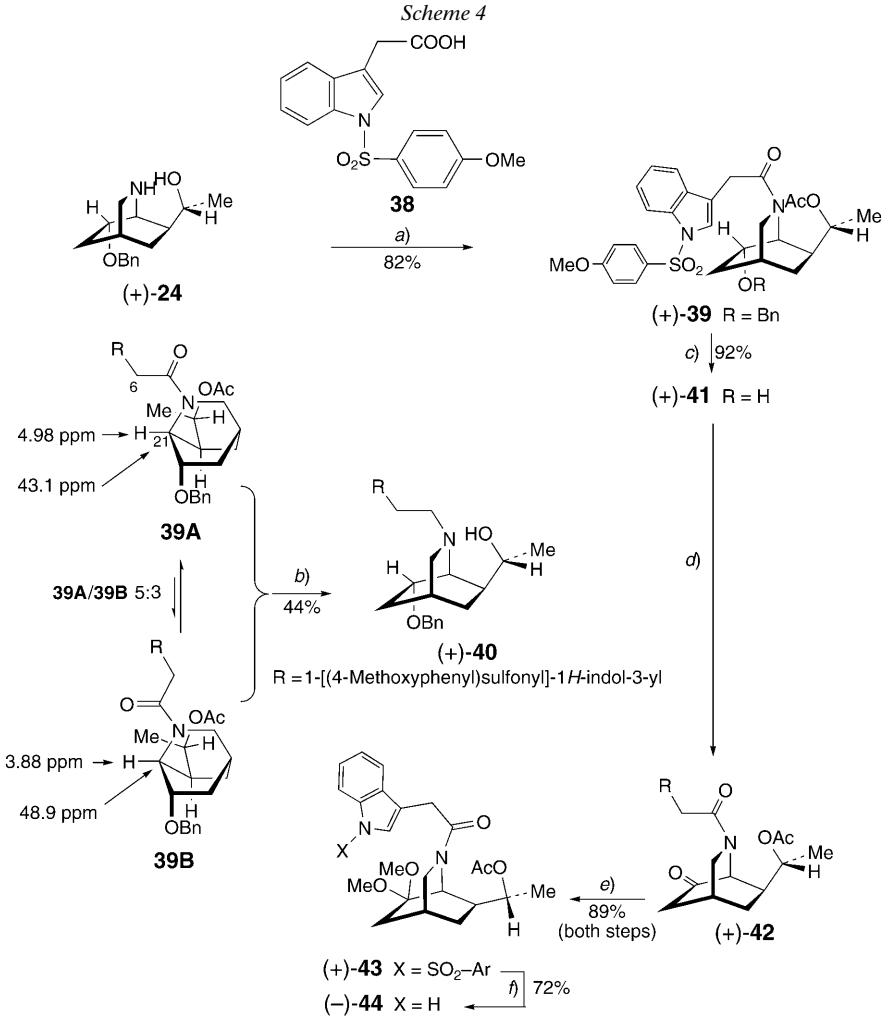


a) 1. DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; 2. $HC(OMe)_3$, MeOH, pyridine·TsOH, 5 d at 23°. *b*) 1. NaH, H_2O, [15]crown-5, benzene; 2. $PhCH_2Cl$, 24 h reflux. *c*) H_2, *Lindlar*'s catalyst; bis(2-hydroxyethyl) ether, 13 d at 23°. *d*) (2*S*)-But-3-en-2-ol, diisopropyl diazenedicarboxylate (DIAD), PPh_3, THF, 3 Å molecular sieves, 2 h at 23°. *e*) 1. Lithium diisopropylamide (LDA), THF, hexamethylphosphoric triamide (HMPT), ^{t}BuMe$_2$SiCl, 5 h reflux; 2. $LiAlH_4$, THF, 16 h at 23°; 3. DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; 4. NH_2OH•HCl, MeOH, pyridine, 1 h at 23°; 5. $NaBH_3CN$, AcOH/THF, 2.5 h at −10°. *f*) 1.5M H_2SO_4, 8 h at 47°. *g*) Zn, AcOH/MeOH, 2 h at 23°.

Table 2. *(*E*)/(Z)-Rotamer Composition of the Carboxamides* **39**–**44***, and Relevant Chemical Shifts*

	(+)-**39**		(+)-**41**		(+)-**42**		(+)-**43**		(−)-**44**	
	(*E*)	(*Z*)	(*E*)	(*Z*)	(*E*)	(*Z*)	(*E*)	(*Z*)	(*E*)	(*Z*)
Composition [%]	62	38	71	29	66	34	86	14	88	12
C(21) [ppm]	43.1	48.9	46.7	52.1	53.3	58.3	46.0	51.5	45.8	51.4
H–C(21) [ppm]	4.95	3.88	4.68	3.82	5.05	4.31	4.88	4.12	4.89	4.17

Scheme 4

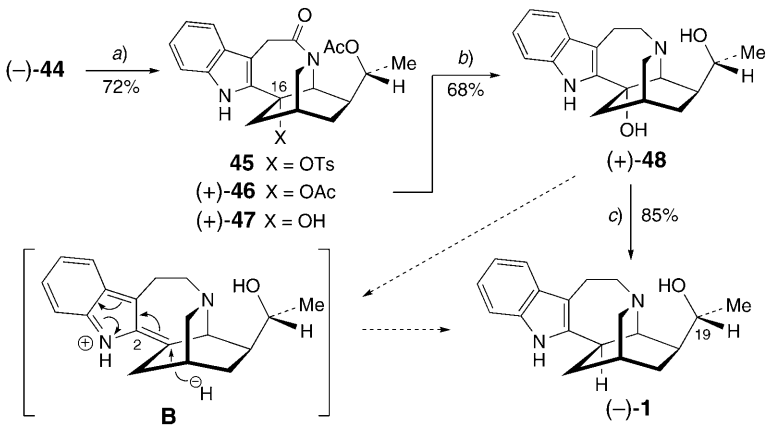


a) 1. DCC, CH_2Cl_2, 4 h at 0°; 2. 2M KOH in MeOH, 2 h at 23°; 3. Ac_2O, pyridine, *N*,*N*-dimethylpyridin-4-amine (DMAP; cat.), CH_2Cl_2, 4 h at 23°. *b*) $LiAlH_4$, THF, 16 h at 23°. *c*) H_2, Pd/C, EtOH/AcOH, 3 d at 23°. *d*) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2. *e*) $HC(OMe)_3$, MeOH, TsOH (cat.), 6.5 h at 23°. *f*) Na/Hg, KH_2PO_4, THF/MeOH, 5 h at −20°.

the treatment of a C(16) dimethyl acetal with TsOH in boiling benzene [20]. In the case of our intermediate (−)-**44**, however, this procedure turned out to be rather unreliable, giving erratic and low yields of the cyclized tosylate **45**. After many frustrating experiments, the method of choice finally turned out to consist in treating (−)-**44** with acetyl chloride in strictly anhydrous glacial acetic acid[4]). This procedure led to rapid consump-

[4]) Traces of H_2O lead to irreversible formation of the corresponding ketone, which was completely inert toward cyclization to (+)-**47** (*Scheme 5*) in the presence of a wide variety of *Lewis* or *Brønsted* acids.

Scheme 5



a) AcCl, MeOH (cat.), AcOH, 2 h at 45°. *b*) 1. $LiAlH_4$ (10 equiv.), THF , 2.5 h 23°; 2. $BF_3 \cdot Et_2O$ (2 equiv.), 3 h at 0–23°. *c*) $LiAlH_4/AlCl_3$ 1:1, THF, 24 h at 23°.

tion of the starting material to furnish diacetate (+)-**46** in 72% yield. The acetyloxy group at C(16) is very prone to hydrolysis, and unless special precautions were taken during the workup, variable amounts of the corresponding alcohol (+)-**47** turned up in the crude reaction mixtures.

The final reductive transformation of (+)-**46** into the target molecule (–)-**1** also turned out to be a rather delicate operation. Successful simultaneous reductions of the 'lactam' moiety[5]) and of the O-functional group at C(16) were reported before [20] but the recommended procedure furnished at best decent yields of (–)-**1**. In our hands, the most reliable method consisted in a two-step approach, involving at first the reduction of the brigded lactam unit and of the two acetoxy groups with $LiAlH_4/BF_3$ to furnish diol (+)-**48** in 68% yield. The subsequent reductive substitution of OH–C(16) by a H-atom was effected by $LiAlH_4/AlCl_3$ and probably resulted from an elimination leading to the strained[6]) iminium ion **B**, which is reduced by an ε-attack of a hydride ion at C(16). The resulting compound (–)-**1** crystallized from Et_2O/pentane to furnish colorless needles with a m.p. and optical rotation somewhat higher than the reported ones for samples isolated from natural sources [4][7b] (see *Exper. Part*). The overall yield of the entire synthesis involving 20 steps amounted to 1.9% (average yield per step: 82%).

In earlier investigations, the relative configuration at C(19) of naturally occurring *Iboga* alkaloids was deduced from the typical ^{13}C-NMR chemical shifts of C(15) and C(21). These correlations, first pointed out by *Wenkert et al.* [7c], originate from the restricted conformational freedom of the 1-hydroxyethyl side chain, which is due to

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[5]) Steric inhibition of the usual lactam resonance in this bridged system should lead to an enhanced electrophilicity of the carboxy C-atom, which might thus be comparable to, or even slightly higher than the one of a thioester.

[6]) As the *trans*-positioned part at the ΔC(2)=C(16) bond is confined to a 9-membered ring, the inherent strain in intermediate **B** is expected to be substantial but acceptable.

a strong intramolecular H-bridge (see *Figure* and also *Table 3*). This contention has now been corroborated independently by starting with two optically pure chiral building blocks of established absolute configuration, as well as through an X-ray structure elucidation of compound (−)-**37** [14], which has been correlated chemically with the crucial intermediate (+)-**25** [15b].

Table 3. *^{13}C-NMR Chemical Shifts of (−)-**1**, (−)-**2**, (−)-**4**, (−)-**5**, and (+)-**46**–**48** in $CDCl_3$. δ* in ppm.

	(−)-**1**[a])[b])	(−)-**2** [5a][b])	(−)-**4** [7c]	(−)-**5** [7c]	(+)-**46**[a])	(+)-**47**[a])	(+)-**48**[a])
C(2)	140.9	140.7	136.5	135.9	136.0	138.0	142.0
C(3)	49.1	49.3	52.1	52.0	47.9	47.6	48.2
C(5)	52.8	52.9	51.1	50.9	169.9	169.8	52.5
C(6)	20.2	20.2	21.3	21.6	32.9	32.6	20.8
C(7)	108.6	108.4	110.7	109.6	105.6	104.3	106.2
C(8)	129.5	129.5	129.5	128.4	126.8	126.9	128.8
C(9)	118.0	118.0	119.3	118.3	118.8	119.1	118.6
C(10)	119.3	119.2	119.3	120.3	120.0	120.4	119.3
C(11)	121.3	121.3	123.2	122.1	122.8	123.3	122.0
C(12)	110.2	110.2	111.4	110.4	111.0	111.0	110.7
C(13)	134.8	134.8	136.3	135.6	134.9	135.6	134.2
C(14)	26.1	25.9	26.7	26.0	27.7	28.5	27.1
C(15)	29.1	23.0	22.9	28.6	26.7	25.7	28.4
C(16)	40.1	40.2	56.8	54.1	78.7	66.0	73.0
C(17)	34.2	34.3	36.8	36.5	38.5	44.2	42.6
C(18)	22.8	20.1	20.2	22.1	21.1	21.2	22.3
C(19)	71.6	71.5	72.3	70.7	71.7	72.0	70.8
C(20)	42.5	42.2	39.5	40.2	36.1	37.6	36.3
C(21)	54.7	60.9	59.7	54.7	50.8	53.7	60.7

[a]) This work. [b]) Assignments corroborated by means of a HSQC spectrum.

3. Conclusion. – The described new route from an appropriately functionalized, optically pure isoquinuclidine building block led to (19*R*)-ibogamin-19-ol ((−)-**1**), which thus was synthesized for the first time. Starting from isoquinuclidine (+)-**24**, the *iboga* alkaloid (−)-**1** was synthesized in 9 steps with 20% overall yield (average yield: 84% per step). The chosen flexible approach should eventually pave the way to numerous representatives of the *Iboga* alkaloid family with varying substitution patterns in the aromatic part, and in both antipodal forms, if desired.

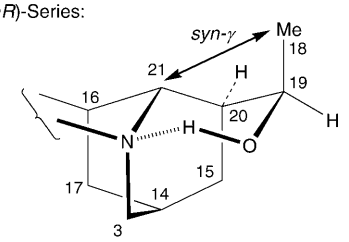
We express our gratitude towards the *Swiss National Science Foundation* for generous grants for this project (No. 2-77054-01, followed by No. 2-77365-03). We also wish to thank our chemical technician apprentice, Mrs. *Angela Brändli*, for her skilful and most valuable experimental contributions to the presented project.

Experimental Part

General. See [14] and [15]. Solvent for all NMR spectra: $CDCl_3$.

(2S)-But-3-en-2-ol ((+)-**27**). New method: In a *Schlenk* flask (with balloon) was placed (2*S*)-but-3-yn-2-ol (15.875 g, 220 mmol; *Aldrich*; 97%) in diethylene glycol (4 ml; *Fluka, puriss.*). After addition

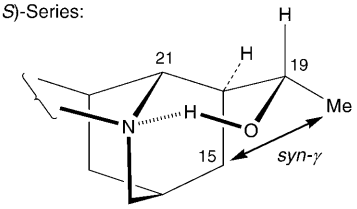
(19*R*)-Series:



	C(15)	C(21)	Ref.
(–)-**1**	29.1	54.7	[a]
(–)-**5**	28.6	54.7	[7c]
(–)-**11**	28.6	54.4	[5a]
(–)-**15**	28.0	53.1	[7h]
Average	*28.6 ± 0.5*	*54.2 ± 0.8*	

[a]) This work.

(19*S*)-Series:



	C(15)	C(21)	Ref.
(–)-**2**	23.0	60.9	[5a]
(–)-**4**	22.9	59.7	[7c]
(–)-**6**	23.7	60.5	[7d]
(–)-**9**	22.8	59.7	[7g]
Average	*23.1 ± 0.4*	*60.2 ± 0.6*	

Figure. *Differentiation between the (19*R*)- and (19*S*)-ibogamine derivatives by means of ^{13}C-NMR spectroscopy according to* Wenkert *and co-workers* [7c]

of (1.50 g; *Lindlar*'s catalyst *Lancaster*), the resulting mixture was purged 3 times with Ar and H_2 in turn. Finally an atmosphere of H_2 at 1 bar was established, and the mixture stirred vigorously for 13 d. The reduction was monitored by ^{1}H-NMR. The product was isolated in pure form by distillation under atmospheric pressure: 7.864 g (50% of (+)-**27**). Colorless liquid. B.p. 90–95°/760 Torr. Analysis of the corresponding *Mosher* ester [21] revealed an ee value >95% (^{1}H- and ^{19}F-NMR).

*(4*S*)-4-(Dimethoxymethyl)butano-4-lactone* ((+)-**30**). Improved method: To a soln. of oxalyl chloride (6.9 ml, 77.4 mmol; *Fluka, purum*) in dry CH_2Cl_2 (100 ml) was added at −78° under Ar a soln. of DMSO (11.0 ml, 155 mmol; *Fluka, puriss.*) in CH_2Cl_2 (70 ml). After stirring for 30 min at −78°, a soln. of alcohol (+)-**29** [14] (6.90 g, 59.5 mmol) in CH_2Cl_2 (70 ml) was added dropwise, and stirring of the resulting white suspension was continued for another 45 min at −78°. Then, Et_3N (22 ml, 167 mmol; *Fluka, puriss.*, dist. from CaH_2) was added, and the cooling bath was removed. At 0°, MeOH (40 ml; dist. from Mg), trimethyl orthoformate (40 ml; *Fluka, puriss.*), and pyridinium *p*-toluenesulfonate (14.1 g, 59.5 mmol; *Fluka, puriss.*) were added. The brownish homogeneous mixture was stirred at 23° for 120 h and washed once with aq. 1M phosphate buffer (400 ml; pH 3, readjusted to this value with conc. HCl soln. during the extraction procedure), sat. aq. $CuSO_4$ soln. (400 ml), and once with sat. aq. NaCl soln. (400 ml). The aq. phases were extracted twice with CH_2Cl_2 (2×400 ml) and the combined org. extracts dried ($MgSO_4$) and evaporated at normal pressure, by using a *Vigreux* column. The crude product was subjected to CC (silica gel 230 g), pentane/^{t}BuOMe 1:2 → pure ^{t}BuOMe): 6.97 g (73%) of pure (+)-**30** as a colorless oil (to obtain this yield it is mandatory to evaporate the relevant fractions at normal pressure (*Vigreux* column)). For the spectroscopic characterization of (+)-**30**, see [14].

*(4*S*)-4-(Benzyloxy)-5,5-dimethoxypentanoic Acid* ((−)-**31**). To a soln. of (+)-**30** (6.932 g, 43.3 mmol) in benzene (170 ml; *Fluka, puriss.*) under Ar at 23°, 87% NaH/oil (8.422 g, 260 mmol; prepared from *Fluka, pract.*, 55–60% NaH/oil by washing 4 times with hexane) and [15]crown-5 (0.86 ml, 4.35 mmol; *Fluka, purum*) were added. After careful addition of H_2O (1.6 ml, 88.8 mmol), the resulting grey suspension was refluxed for 16 h. After cooling to 23°, benzyl chloride (10 ml, 86.8 mmol; *Fluka, purum*) was added, and refluxing was continued for another 24 h. The mixture was cooled to 0° and poured carefully onto cold (0°) aq. 1M phosphate buffer (300 ml; pH 3), The aq. phase was acidified to pH 3–4 by adding

conc. HCl soln. (18 ml) and extracted *t*BuOMe with (2×300 ml). The combined org. extract was dried ($MgSO_4$) and evaporated and the residue subjected to CC (silica gel 150 g), cyclohexane/AcOEt 8:1 → pure AcOEt): 8.528 g (73%) of (−)-**31**. Slightly yellow oil. $[\alpha]_D = -32.8$ ($c = 0.8$, $CHCl_3$). IR ($CHCl_3$): 3515, 3500–2500 (br.), 3006, 2936, 2836, 1710, 1454, 1415, 1280, 1082, 1028, 957. ^{1}H-NMR (300): 7.35–7.23 (*m*, 5 H); 4.73 (*d*, *J* = 11.2, 1 H); 4.54 (*d*, *J* = 11.5, 1 H); 4.24 (*d*, *J* = 5.9, 1 H); 3.48 (*ddd*, *J* = 8.7, 5.9, 3.7, 1 H); 3.44 (*s*, 3 H); 3.40 (*s*, 3 H); 2.43 (*m*, 2 H); 1.97 (*m*, 1 H); 1.78 (*m*, 1 H). ^{13}C-NMR (75 MHz): 179.9 (*s*); 138.5 (*s*); 128.6 (2*d*); 128.2 (2*d*); 127.9 (*d*); 107.1 (*d*); 78.2 (*d*); 73.3 (*t*); 56.0 (*q*); 55.3 (*q*); 30.0 (*t*); 25.4 (*t*). EI-HR-MS: 237.1128 (0.3, $[M-OMe]^+$, $C_{13}H_{17}O_4^+$; calc. 237.1127), 130.0647 (12, $C_6H_{10}O_3^+$; calc. 130.0630), 91.0571 (85, $C_7H_7^+$; calc. 91.0548), 75.0455 (100, $C_3H_7O_2^+$; calc. 75.0416), 65.0402 (11, $C_5H_5^+$; calc. 65.0341), 47.0497 (14, $C_2H_7O^+$; calc. 47.0497).

(*1*R*)-1-Methylprop-2-enyl (4*S*)-4-(Benzyloxy)-5,5-dimethoxypentanoate* ((−)-**33**). Modified procedure: To a soln. of (−)-**31** (19.904 g, 74.2 mmol), (+)-**27** (6.419 g, 89 mmol), and Ph_3P (29.48 g, 111 mmol; *Acros*, 98%) in THF (240 ml), 3 Å molecular sieves (12 g) and slowly DIAD (= diisopropyl diazenedicarboxylate = diisopropyl azodicarboxylate; 23 ml, 113 mmol; *Lancaster*, 95%) were added. After stirring at 23° for 2 h, the mixture was filtered and the filtrate evaporated. The residue was poured onto aq. 1M HCl (500 ml), the mixture extracted with CH_2Cl_2 (3×500 ml), and the combined org. phase dried ($MgSO_4$) and evaporated. The crude residue was dissolved in *t*BuOMe (400 ml) and kept in a freezer (−20°) for 16 h after inocculation with a triphenylphosphine oxide seeding crystal. The precipitate was removed by filtration and the filtrate evaporated. FC (silica gel, 600 g), cyclohexane/AcOEt 8:1 → 4:1) furnished 19.031 g (80%) of (−)-**33**. Yellowish oil. For anal. data, see [14].

*1-[(4-Methoxyphenyl)sulfonyl]-1*H*-3-indole-3-acetic Acid* (**38**). To a soln. of 1*H*-indole-3-acetic acid (5.00 g, 28.0 mmol; *Lancaster*, 98%) in dry THF (200 ml) was added 1M BuLi in hexane (35 ml, 56 mmol; *Fluka*) at −78° under Ar. After stirring for 1 h at −78°, a soln. of 4-methoxybenzenesulfonyl chloride (5.898 g, 28.0 mmol; *Fluka*, 98%) in THF (100 ml) was added. The cooling bath was removed und stirring continued for 16 h at 23°. The resulting brown suspension was poured onto cold (0°) aq. 1M HCl (250 ml) and extracted with *t*BuOMe (3×250 ml). The combined org. extracts were dried ($MgSO_4$) and evaporated, and the residue triturated with *t*BuOMe (50 ml), filtered, washed with a little *t*BuOMe, and dried at 23°/0.01 Torr: 9.358 g (93%) of pure **38**. Brownish powder. M.p. 137–141°. IR ($CHCl_3$): 3510, 3400–2600 (br.), 2974, 2843, 1715, 1596, 1579, 1498, 1449, 1416, 1374, 1310, 1285, 1187, 1121, 1099, 1029, 979, 939, 833, 630. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.98 (*dm*, *J* = 8.4, 1 H); 7.81 (*dm*, *J* = 9.0, 2 H); 7.58 (*s*, 1 H); 7.49 (*dt*, *J* = 7.8, 0.6, 1 H); 7.32 (*td*, *J* = *ca.* 7.5, 1.3, 1 H); 7.24 (*td*, *J* = *ca.* 7.5, 1.3, 1 H); 6.85 (*dm*, *J* = 9.0, 2 H); 3.75 (*s*, 3 H); 3.73 (*s*, 2 H). ^{13}C-NMR (75 MHz): 176.5 (*s*); 163.6 (*s*); 134.8 (*s*); 130.2 (*s*); 129.5 (*s*); 129.0 (2*d*); 124.9 (*d*); 124.8 (*d*); 123.2 (*d*); 119.4 (*d*); 114.4 (2*d*); 114.1 (*s*); 113.6 (*d*); 55.7 (*q*); 30.8 (*t*). EI-HR-MS: 345.0666 (69, M^+, $C_{17}H_{15}NO_5S^+$; calc. 345.0671), 300.0681 (13, $C_{16}H_{14}NO_3S^+$; calc. 300.0694), 172.0157 (10), 171.0115 (100, $C_7H_7O_3S^+$; calc. 171.0116), 132.0459 (24), 130.0663 (42, $C_9H_8N^+$; calc. 130.0657), 129.0585 (26), 123.0451 (19), 107.0504 (45, $C_7H_7O^+$; calc. 107.0497), 103.0537 (10), 102.0475 (11), 92.0267 (17), 77.0386 (37).

*(α*R*,1*S*,6*S*,7*S*)-7-(Benzyloxy)-2-{[1(4-methoxyphenyl)sulfonyl]-1*H*-indol-3-yl}acetyl]-2-azabicyclo-[2.2.2]octane-6-methanol Acetate* ((+)-**39**). To a soln. of (+)-**24**[7]) (100 mg, 0.383 mmol) and **38** (529 mg, 1.53 mmol) in CH_2Cl_2 (4 ml) under Ar was added DCC (316 mg, 1.53 mmol; *Fluka, purum*) at 0°. After stirring the mixture at 0° to 23° for 4 h, the precipitated dicyclohexylurea was removed by filtration and the filtrate evaporated. The residue was treated with 3M KOH in MeOH (3 ml) for 2 h at 23°[8]). The mixture was distributed between *t*BuOMe and aq. 2M NaOH soln. The combined org. layers were dried ($MgSO_4$) and evaporated. To a soln. of the resulting residue in CH_2Cl_2 (4 ml) were added under Ar at 23° Ac_2O (72 µl, 0.762 mmol; *Fluka, puriss*), pyridine (62 µl, 0.77 mmol, dist. over CaH_2), and DMAP (5 mg, 38 mmol; *Fluka, purum*). After stirring the mixture for 16 h at 23°, CH_2Cl_2 (20 ml) was added, and the resulting soln. was washed with aq. 1M HCl (20 ml) and sat. aq. $NaHCO_3$ soln. The aq. extracts were re-extracted twice with CH_2Cl_2 (2×20 ml). The combined org. phase was dried ($MgSO_4$) and evapo-

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[7]) Prepared as described before [15], but with material of 96% de ($[\alpha]_D = +59.2$ ($c = 0.9$, $CHCl_3$).

[8]) This step served to saponify the *N*,*O*-diacylated by-product to give the *N*-acylated hydroxyethyl derivative as the single intermediate.

rated and the crude material subjected to FC (silica gel, 6 g), pentane/^{t}BuOMe 1:1 → pure ^{t}BuOMe: 197 mg (82%) of (+)-**39**. White foam. $[\alpha]_D = +31.0$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3006, 2935, 2867, 1727, 1642, 1596, 1579, 1522, 1498, 1448, 1370, 1304, 1167, 1120, 1098, 1028, 974, 953, 834. ^{1}H-NMR (500 MHz; rotamer mixture 5:3): major component: 7.98 (*dt*, *J* = 8.3, 0.9, 1 H); 7.85 (*dm*, *J* = 9.1, 2 H); 7.54 (*s*, 1 H); 7.51 (*ddd*, *J* = 7.8, 1.2, 0.8, 1 H); 7.4–7.2 (*m*, 7 H); 6.85 (*dm*, *J* = 9.2, 2 H); 4.95 (*dm*, *J* = 3.8, 1.8, 1 H); 4.62 (*dq*, *J* = 10.2, 6.2, 1 H); 4.60 (*d*, *J* = 11.6, 1 H); 4.50 (*d*, *J* = 11.6, 1 H); 3.78 (*s*, 3 H); 3.73 (*dt*, *J* = 9.6, 3.9, 1 H); 3.63 (*dd*, *J* = 15.9, 1.0, 1 H); 3.57 (*dd*, *J* = 15.9, 1.3, 1 H); 3.33 (*m*, 1 H); 3.28–3.22 (*m*, 1 H); 2.38 (*tdd*, *J* = 10.5, 5.6, 1.9, 1 H); 2.06 (*s*, 3 H); 1.99 (*m*, 1 H); 1.97–1.83 (*m*, 2 H); 1.54 (*ddt*, *J* = 14.0, *ca.* 4, *ca.* 2, 1 H); 1.22 (*d*, *J* = 6.1, 3 H); 1.11–1.04 (*m*, 1 H); minor component: 8.00 (*dt*, *J* = 8.3, 0.8, 1 H); 7.81 (*dm*, *J* = 9.1, 2 H); 7.48 (*dt*, *J* = 7.9, *ca.* 1, 1 H); 7.47 (*s*, 1 H); 7.4–7.2 (*m*, 7 H); 6.83 (*dm*, *J* = 9.4, 2 H); 4.76 (*dq*, *J* = 9.3, 6.1, 1 H); 3.93 (*d*, *J* = 11.7, 1 H); 3.88 (*dd*, *J* = 3.4, 1.3, 1 H); 3.77 (*m*, 2 H); 3.75 (*s*, 3 H); 3.66 (br. *d*, *J* = 15.7, 1 H); 3.53 (*dd*, *J* = 15.7, 1.6, 1 H); 3.33 (*m*, 1 H); 3.28–3.22 (*m*, 1 H); 2.32 (*m*, 1 H); 2.09 (*s*, 3 H); 2.06 (*m*, 1 H); 1.97–1.83 (*m*, 2 H); 1.47 (*ddt*, *J* = 14.0, 4.7, 2.4, 1 H); 1.24 (*d*, *J* = 6.1, 3 H); 1.11–1.04 (*m*, 1 H). ^{13}C-NMR (125 MHz; rotamer mixture 5:3): major component: 170.8 (*s*); 169.5 (*s*); 163.7 (*s*); 138.1 (*s*); 135.1 (*s*); 130.6 (*s*); 129.9 (*s*); 129.2 (2*d*); 128.5 (2*d*); 127.8 (2*d*); 127.7 (*d*); 124.7 (*d*); 124.2 (*d*); 123.1 (*d*); 119.7 (*d*); 115.7 (*s*); 114.4 (2*d*); 113.6 (*d*); 73.6 (*d*); 71.2 (*d*); 70.7 (*t*); 55.6 (*q*); 49.6 (*t*); 43.1 (*d*); 35.5 (*d*); 32.9 (*t*); 30.5 (*t*); 28.4 (*t*); 27.0 (*d*); 21.4 (*q*); 17.7 (*q*); minor component: 170.5 (*s*); 169.6 (*s*); 163.8 (*s*); 137.9 (*s*); 135.0 (*s*); 130.3 (*s*); 129.6 (*s*); 129.1 (2*d*); 128.3 (2*d*); 127.6 (*d*); 127.3 (2*d*); 125.1 (*d*); 124.0 (*d*); 123.3 (*d*); 119.3 (*d*); 115.9 (*s*); 114.5 (2*d*); 113.8 (*d*); 74.9 (*d*); 72.0 (*d*); 70.5 (*t*); 55.6 (*q*); 48.9 (*d*); 48.5 (*t*); 35.7 (*d*); 32.4 (*t*); 30.6 (*t*); 28.6 (*t*); 25.9 (*d*); 21.7 (*q*); 17.6 (*q*). EI-HR-MS: 630.2410 (36, M^+, $C_{35}H_{38}N_2O_7S^+$; calc. 630.2400), 479.1617 (57, $C_{26}H_{27}N_2O_5S^+$; calc. 479.1641), 460.2285 (28, $C_{28}H_{32}N_2O_4^+$; calc. 460.2362), 459.2214 (19), 437.1510 (14), 399.2064 (20), 353.1851 (21), 300.0686 (21, $C_{16}H_{14}NO_3S^+$; calc. 300.0694), 171.0106 (49, $C_7H_7SO_3^+$; calc. 171.0116), 152.1082 (76, $C_9H_{14}NO^+$; calc. 152.1075), 130.0665 (26, $C_9H_8N^+$; calc. 130.0657), 129.0586 (21), 107.0511 (26, $C_7H_7O^+$; calc. 107.0497), 91.0558 (100, $C_7H_7^+$; calc. 91.05477), 43.0124 (11).

*(*α*R,1S,6S,7S)-7-(Benzyloxy)-2-{2-{1-[(4-methoxyphenyl)sulfonyl]-1*H*-indo-3-yl}ethyl}-2-azabicyclo[2.2.2]octane-6-methanol* ((+)-**40**). To a soln. of (+)-**39** (155 mg, 0.246 mmol) in THF (5 ml) was added $LiAlH_4$ (47 mg, 1.24 mmol; *Fluka, puriss.*) at 23° under Ar. The grey suspension was stirred for 16 h at 23° and then poured carefully onto cold aq. 2M NaOH (15 ml). The mixture was extracted with ^{t}BuOMe (3×15 ml), the combined extract dried ($MgSO_4$) and evaporated, the crude product subjected to FC (silica gel (6 g), cyclohexane/AcOEt 4:1 → cyclohexane/AcOEt/Et_2NH 12:6:1): 62 mg (44%) of pure (+)-**40** (single product formed). Yellow oil. $[\alpha]_D + 46.8$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3400–2800, 3005, 2937, 2864, 1655, 1596, 1579, 1498, 1449, 1416, 1367, 1310, 1264, 1167, 1124, 1091, 1069, 1028, 976, 909, 878, 833, 629. ^{1}H-NMR (400 MHz): 7.96 (*dt*, *J* = 8.2, 0.9, 1 H); 7.82 (*dm*, *J* = 9.2, 2 H); 7.45 (*ddd*, *J* = 7.8, 1.2, *ca.* 0.6, 1 H); 7.36–7.26 (*m*, 7 H); 7.23 (*ddd*, *J* = 8.3, 7.3, 1.1, 1 H); 6.87 (*dm*, *J* = 9.1, 2 H); 4.52 (*d*, *J* = 12.0, 1 H); 4.47 (*d*, *J* = 11.9, 1 H); 3.91–3.83 (*m*, 2 H); 3.78 (*s*, 3 H); 3.18–3.15 (*m*, 2 H); 2.96–2.75 (*m*, 4 H); 2.23 (br. *d*, *J* = 9.5, 1 H); 2.07 (*tdd*, *J* = *ca.* 13.5, 4.4, 2.4, 1 H); 2.00 (*dddd*, *J* = 10.6, *ca.* 7.5, 1.9, *ca.* 1, 1 H); 1.90 (*m*, 1 H); 1.77 (*tdd*, *J* = 12.8, 3.9, 1.9, 1 H); 1.69 (*ddt*, *J* = 12.7, 7.7, 2.3, 1 H); 1.47 (*ddt*, *J* = 13.4, 5.6, 2.1, 1 H); 1.23 (*d*, *J* = 6.4, 3 H); the OH signal could not be localized with certainty. ^{13}C-NMR (100 MHz): 163.7 (*s*); 138.5 (*s*); 135.2 (*s*); 130.8 (*s*); 129.9 (*s*); 129.1 (2*d*); 128.5 (2*d*); 127.7 (*d*); 127.6 (2*d*); 124.7 (*d*); 123.0 (2*d*); 120.3 (*s*); 119.3 (*d*); 114.4 (2*d*); 113.7 (*d*); 71.3 (*d*); 70.6 (*t*); 70.0 (*d*); 55.6 (*q*); 55.4 (*t*); 55.3 (*t*); 53.7 (*d*); 35.2 (*d*); 34.0 (*t*); 29.1 (*t*); 27.1 (*d*); 24.3 (*t*); 22.5 (*q*). EI-HR-MS: 574.2499 (2, M^+, $C_{33}H_{38}N_2O_5S^+$; calc. 574.2499), 483.1987 (8, $C_{26}H_{31}N_2O_5S^+$; calc. 483.1954), 439.1740 (7, $C_{24}H_{27}N_2O_4S^+$; calc. 439.1692), 275.1880 (51, $C_{17}H_{25}NO_2^+$; calc. 275.1885), 274.1971 (66), 274.1620 (59), 171.0181 (29), 168.1447 (11), 167.1327 (12), 166.1293 (100, $C_{10}H_{16}NO^+$; calc. 166.1293), 144.0874 (12), 138.0982 (65), 107.0563 (17), 91.0593 (74), 77.0426 (13).

*(*α*R,1S,6S,7S)-7-Hydroxy-2-{{1-[(4-methoxyphenyl)sulfonyl]-1*H*-indol-3-yl}acetyl}-2-azabicyclo[2.2.2]octane-6-methanol* α*-Acetate* ((+)-**41**). In a *Schlenk* flask (with balloon), were placed (+)-**39** (1.018 g, 1.61 mmol) and 10% Pd/C (250 mg; *Fluka*) in EtOH (7 ml; Merck, >99%) and AcOH (7 ml; *Scharlau*, 100%). The resulting mixture was purged 3 times with Ar and H_2 in turn. Finally, an atmosphere of H_2 at 1 bar was established and the mixture stirred vigorously for 68 h with refilling the balloon once a day with H_2. The crude product was subjected to FC (silica gel (16 g), cyclohexane/AcOEt 1:1 →

pure AcOEt): 801 mg (92%) of (+)-**41**. White foam. $[\alpha]_D = +11.2$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3604, 3420 (br.), 3006, 2946, 2870, 1725, 1640, 1596, 1579, 1498, 1448, 1374, 1303, 1132, 1120, 1098, 1046, 1030, 973. ^{1}H-NMR (500 MHz; rotamer mixture 5:2): major component: 7.97 (*dm*, *J* = 8.3, 1 H); 7.84 (*dm*, *J* = 9.1, 2 H); 7.52 (*s*, 1 H); 7.49 (*dt*, *J* = 8.2, *ca.* 0.8, 1 H); 7.31 (*ddd*, *J* = 8.3, 7.3, 1.2, 1 H); 7.23 (*ddd*, *J* = 7.9, 7.3, 1.0, 1 H); 6.85 (*dm*, *J* = 9.1, 2 H); 4.68 (*dd*, *J* = 3.8, 1.8, 1 H); 4.61 (*dq*, *J* = 10.4, 6.1, 1 H); 3.98 (*dt*, *J* = *ca.* 9.5, *ca.* 4.5, 1 H); 3.77 (*s*, 3 H); 3.64 (*dd*, *J* = 15.9, 1.1, 1 H); 3.56 (*dd*, *J* = 15.9, 1.4, 1 H); 3.37 (*dm*, *J* = 10.1, 1 H); 3.21 (*dm*, *J* = 10.1, 1 H); 2.53 (br. *s*, 1 H); 2.42 (*tdd*, *J* = 10.6, 5.6, 1.8, 1 H); 2.071 (*s*, 3 H); 1.97 (*m*, 1 H); 1.87 (*dt*, *J* = 13.6, 2.7, 1 H); 1.85 (*dt*, *J* = 13.6, *ca.* 3, 1 H); 1.39 (*ddt*, *J* = 13.9, 4.4, 2.2, 1 H); 1.22 (*d*, *J* = 6.1, 3 H); 1.03 (*ddt*, *J* = 13.5, 5.5, 2.7, 1 H); minor component: 7.97 (*dm*, *J* = 8.3, 1 H); 7.82 (*dm*, *J* = 8.9, 2 H); 7.51 (*dt*, *J* = 8.3, *ca.* 0.8, 1 H); 7.46 (*s*, 1 H); 7.32 (*ddd*, *J* = 8.3, 7.2, 1.1, 1 H); 7.24 (*ddd*, *J* = 7.9, 7.3, 1.0, 1 H); 6.87 (*dm*, *J* = 9.1, 2 H); 4.74 (*dq*, *J* = 9.6, 6.1, 1 H); 3.82 (*dd*, *J* = 3.4, 1.5, 1 H); 3.78 (*s*, 3 H); 3.68 (*m*, 1 H); 3.68 (br. *d*, *J* = 15.9, 1 H); 3.54 (*dd*, *J* = 15.7, 1.4, 1 H); 3.37 (*dm*, *J* = 10.1, 1 H); 3.21 (*dm*, *J* = 10.1, 1 H); 2.39 (*m*, 1 H); 2.065 (*s*, 3 H); 2.05 (*m*, 1 H); 1.96 (*m*, 1 H); 1.93 (*dt*, *J* = 9.6, *ca.* 3.5, 1 H); 1.79 (br. *s*, 1 H); 1.34 (*dm*, *J* = *ca.* 13.5, 1 H); 1.26 (*d*, *J* = 6.1, 3 H); 1.08 (*ddt*, *J* = 13.3, 7.1, *ca.* 2.5, 1 H). ^{13}C-NMR (125 MHz; rotamer mixture 5:2): major component: 170.8 (*s*); 169.7 (*s*); 163.7 (*s*); 135.0 (*s*); 130.6 (*s*); 129.8 (*s*); 129.2 (2*d*); 124.8 (*d*); 124.2 (*d*); 123.1 (*d*); 119.6 (*d*); 115.6 (*s*); 114.4 (2*d*); 113.6 (*d*); 71.2 (*d*); 66.5 (*d*); 55.6 (*q*); 49.2 (*t*); 46.7 (*d*); 35.1 (*d*); 34.1 (*t*); 30.5 (*t*); 28.7 (*t*); 27.1 (*d*); 21.4 (*q*); 17.7 (*q*); minor component: 170.4 (*s*); 169.3 (*s*); 163.8 (*s*); 135.0 (*s*); 130.4 (*s*); 129.7 (*s*); 129.1 (2*d*); 124.9 (*d*); 124.0 (*d*); 123.3 (*d*); 119.6 (*d*); 116.1 (*s*); 114.5 (2*d*); 113.6 (*d*); 72.0 (*d*); 67.5 (*d*); 55.7 (*q*); 52.1 (*d*); 48.1 (*t*); 35.3 (*d*); 34.4 (*t*); 30.4 (*t*); 28.8 (*t*); 26.1 (*d*); 21.6 (*q*); 17.6 (*q*). EI-HR-MS: 540.1931 (47, M^+, $C_{28}H_{32}N_2O_7S^+$; calc. 540.1931), 481.1796 (10), 370.1859 (13), 369.1827 (46, $C_{21}H_{25}N_2O_4^+$; calc. 369.1814), 327.0577 (11), 309.1607 (31, $C_{19}H_{21}N_2O_2^+$; calc. 309.1603), 301.0743 (14), 300.0704 (52, $C_{16}H_{14}NO_3S^+$; calc. 300.0694), 198.1141 (76, $C_{10}H_{16}NO_3^+$; calc. 198.1130), 180.1023 (19), 172.0156 (10), 171.0124 (100, $C_7H_7SO_3^+$; calc. 171.0116), 156.0433 (11), 154.1238 (79, $C_9H_{16}NO^+$; calc. 154.1232), 153.1145 (11), 152.1077 (32, $C_9H_{14}NO^+$; calc. 152.1075), 130.0656 (50, $C_9H_8N^+$; calc. 130.0657), 129.0582 (38), 123.045 (15), 108.0733 (20), 107.0516 (48, $C_7H_7O^+$; calc. 107.0497), 92.0296 (15), 81.0717 (11), 77.0423 (29), 69.0694 (10), 67.0545 (12), 57.07 (11), 55.0541 (17), 43.0425 (10), 43.0065 (54), 41.0233 (13).

*(1*S*,7*S*)-7-[(1*R*)-1-(Acetyloxy)ethyl]-2-{[1-[(4-methoxyphenyl)sulfonyl]-1*H*-indol-3-yl]acetyl}-2-aza-bicyclo[2.2.2]octan-6-one* ((+)-**42**). To a soln. of oxalyl chloride (160 µl, 1.86 mmol; *Fluka*, *purum*) in CH_2Cl_2 (7 ml; dist. from P_2O_5) at $-78°$ under Ar was added *via* syringe a soln. of (280 µl, 3.94 mmol; *Fluka*, *puriss.*) in CH_2Cl_2 (9 ml), and the mixture was stirred at $-78°$ for 30 min. Then was added a soln. of (+)-**41** (815 mg, 1.51 mmol) in CH_2Cl_2 (14 ml) and stirring was continued for 60 min at $-78°$. After addition of Et_3N (1.1 ml, 7.89 mmol; dist. from CaH_2), the mixture was allowed to reach 23° and then poured onto aq. 1M HCl (30 ml). The aq. phase was extracted with CH_2Cl_2 (2×30 ml) and the combined org. layer dried ($MgSO_4$) and evaporated. The crude product (815 mg) was employed as such for the next step. An anal. sample was prepared by FC (silica gel, cyclohexane/AcOEt 2:1). Colorless foam. $[\alpha]_D = +10.1$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3006, 2946, 2876, 2843, 1736, 1653, 1596, 1579, 1498, 1448, 1415, 1374, 1304, 1263, 1168, 1132, 1121, 1099, 1068, 1030, 973, 834. ^{1}H-NMR (500 MHz; rotamer mixture 2:1): major component: 7.98 (*dt*, *J* = 8.3, 0.8, 1 H); 7.85 (*dm*, *J* = 9.1, 2 H); 7.55 (*s*, 1 H); 7.49 (*dm*, *J* ≈ 8.0, 1 H); 7.31 (*ddd*, *J* = 8.3, 7.2, 1.2, 1 H); 7.24 (*ddd*, *J* = *ca.* 8, *ca.* 7, 1.0, 1 H); 6.87 (*dm*, *J* = 9.1, 2 H); 5.05 (*d*, *J* = 2.0, 1 H); 4.70 (*dq*, *J* = 10.1, 6.1, 1 H); 3.78 (*s*, 3 H); 3.66 (*dd*, *J* = 16.1, 1.1, 1 H); 3.62 (*dd*, *J* = 16.1, 1.2, 1 H); 3.55 (*m*, 1 H); 3.48 (*dt*, *J* = 10.1, 2.6, 1 H); 2.43 (*m*, 1 H); 2.41 (*m*, 1 H); 2.27 (*dm*, *J* ≈ 19, 1 H); 2.23–2.14 (*m*, 1 H); 2.05 (*s*, 3 H); 1.89 (*ddt*, *J* = *ca.* 13.5, 11.2, *ca.* 2.5, 1 H); 1.28–1.23 (*m*, 1 H); 1.25 (*d*, *J* = 6.2, 3 H); minor component: 7.92 (*dm*, *J* = 8.3, 1 H); 7.86 (*dm*, *J* = 9.1, 2 H); 7.50 (*s*, 1 H); 7.45 (*dm*, *J* = 7.6, 1 H); 7.29 (*ddd*, *J* = 8.3, 7.3, 1.2, 1 H); 7.22 (*ddd*, *J* = *ca.* 8, *ca.* 7, 1.0, 1 H); 6.88 (*dm*, *J* = 9.1, 2 H); 4.82 (*dq*, *J* = 9.4, 6.1, 1 H); 4.31 (*d*, *J* = 1.7, 1 H); 3.78 (*s*, 3 H); 3.66 (*dd*, *J* = 16.1, 1.1, 1 H); 3.62 (*dd*, *J* = 16.1, 1.2, 1 H); 3.55 (*m*, 1 H); 3.44 (*dt*, *J* = 12.4, 2.2, 1 H); 2.51 (*quint.*, *J* = 2.8, 1 H); 2.45 (*m*, 1 H); 2.35 (*dt*, *J* = *ca.* 19, 2.6, 1 H); 2.23–2.14 (*m*, 1 H); 2.03 (*s*, 3 H); 1.95 (*ddt*, *J* = 13.9, 11.1, 3.0, 1 H); 1.34 (*ddt*, *J* = 13.9, 5.7, 2.8, 1 H); 1.29 (*d*, *J* = 6.1, 3 H). ^{13}C-NMR (125 MHz; rotamer mixture 2:1): major component: 206.0 (*s*); 170.6 (*s*); 169.5 (*s*); 163.7 (*s*); 135.0 (*s*); 130.5 (*s*); 129.8 (*s*); 129.2 (2*d*); 124.8 (*d*); 124.4 (*d*); 123.2 (*d*); 119.6 (*d*); 115.0 (*s*); 114.5 (2*d*); 113.6 (*d*); 69.8 (*d*); 55.6 (*q*); 53.3 (*d*); 49.6 (*t*); 42.3 (*t*); 40.9 (*d*); 30.7 (*t*); 28.6 (*d*); 27.6 (*t*); 21.3 (*q*); 17.9 (*q*); minor component: 204.9 (*s*);

170.1 (*s*); 169.5 (*s*); 163.7 (*s*); 134.9 (*s*); 130.5 (*s*); 129.3 (*s*, 2*d*); 124.72 (*d*); 124.70 (*d*); 123.2 (*d*); 119.5 (*d*); 114.8 (*s*); 114.5 (2*d*); 113.5 (*d*); 70.7 (*d*); 58.3 (*d*); 55.6 (*q*); 48.6 (*t*); 41.6 (*t*); 40.7 (*d*); 29.5 (*t*); 27.6 (*t*); 27.5 (*d*); 21.3 (*q*); 17.8 (*q*). EI-HR-MS: 538.1776 (59, M^+, $C_{28}H_{30}N_2O_7S^+$; calc. 538.1774), 451.1654 (11), 367.1669 (13), 339.1737 (18), 301.0748 (17), 300.0703 (74, $C_{16}H_{14}NO_3S^+$; calc. 300.0694), 279.1511 (15), 172.0154 (11), 171.0109 (100, $C_7H_7SO_3^+$; calc. 171.0116), 168.1029 (57), 156.0452 (10), 152.1080 (16), 130.0660 (34), 129.0577 (28), 124.1135 (52), 123.1050 (18), 123.0458 (14), 107.0502 (43), 92.0289 (14), 77.0411 (24), 68.9952 (18), 43.0060 (44).

*(*αR,*1*S,*7*S*)-7,7-Dimethoxy-2-{{1-[(4-methoxyphenyl)sulfonyl]-1*H*-indol-3-yl}acetyl}-2-azabicyclo-[2.2.2]octane-6-methanol Acetate* ((+)-**43**). To a soln. of crude (+)-**42** (815 mg, 1.51 mmol) in a mixture of MeOH (6 ml; dried over Mg) and trimethyl orthoformate (6 ml; *Fluka*, *puriss.*) was added *p*-toluenesulfonic acid monohydrate (29 mg, 151 μmol; *Fluka*, *puriss.*) under Ar and stirred at 23° for 6.5 h. The mixture was poured onto sat. aq. $NaHCO_3$ soln. (50 ml) and extracted with CH_2Cl_2 (3×50 ml), the combined org. layer dried ($MgSO_4$) and evaporated, and the crude product subjected to FC (silica gel (30 g), cyclohexane/AcOEt, 1:1 → pure AcOEt): 784 mg (89% over 2 steps of (+)-**43**). Colorless foam. $[\alpha]_D = +13.0$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 3006, 2944, 1728, 1643, 1596, 1579, 1498, 1448, 1368, 1303, 1121, 1098, 1054. ^{1}H-NMR (400 MHz; rotamer mixture 6:1): major component: 7.96 (*dm*, $J = 8.2$, 1 H); 7.84 (*dm*, $J = 9.1$, 2 H); 7.56 (*s*, 1 H); 7.48 (*dm*, $J = \sim 7.1$, 1 H); 7.30 (*ddd*, $J = 8.3$, 7.3, 1.3, 1 H); 7.23 (*ddd*, $J =$ *ca.* 8, *ca.* 7, 1.1, 1 H); 6.85 (*dm*, $J = 9.1$, 2 H); 4.88 (*d*, $J = 1.6$, 1 H); 4.52 (*dq*, $J = 10.4$, 1 H); 3.77 (*s*, 3 H); 3.65 (*dd*, $J = 15.7$, 1.2, 1 H); 3.55 (*dd*, $J = 15.8$, 1.4, 1 H); 3.31 (br. *dt*, $J \approx 9.8$, 2, 1 H); 3.27 (*dt*, $J =$ *ca.* 9.8, 2.2, 1 H); 3.25 (*s*, 3 H); 3.20 (*s*, 3 H); 2.24 (*ddt*, $J = 10.6$, 5.8, 1.7, 1 H); 2.09 (*s*, 3 H); 2.06 (*m*, 1 H); 1.79–1.74 (*m*, 2 H); 1.66 (br. *dt*, $J = 13.8$, *ca.* 3, 1 H); 1.23 (*d*, $J = 6.1$, 3 H); 1.01 (*ddt*, $J = 13.4$, 5.8, 2.9, 1 H). ^{13}C-NMR (100 MHz; rotamer mixture 6:1): major component: 170.9 (*s*); 169.6 (*s*); 163.7 (*s*); 135.1 (*s*); 130.7 (*s*); 129.9 (*s*); 129.2 (2*d*); 124.7 (*d*); 124.1 (*d*); 123.1 (*d*); 119.6 (*d*); 115.8 (*s*); 114.4 (2*d*); 113.6 (*d*); 101.7 (*s*); 71.2 (*d*); 55.6 (*q*); 49.1 (*t*); 48.9 (*q*); 48.2 (*q*); 46.0 (*d*); 37.9 (*d*); 36.8 (*t*); 30.7 (*t*); 28.1 (*t*); 27.5 (*d*); 21.4 (*q*); 17.8 (*q*). EI-MS: 584 (3, M^+), 301 (16), 210 (10), 192 (16), 182 (28), 171 (31), 166 (11), 151 (14), 136 (16), 135 (12), 132 (13), 131 (39), 130 (100), 129 (25), 128 (41), 127 (12), 126 (17), 125 (13), 123 (25), 117 (13), 112 (12), 111 (18), 110 (62), 109 (26), 105 (13), 103 (22), 102 (18), 97 (13), 95 (16), 92 (10), 91 (16), 80 (20), 79 (23), 78 (11), 77 (37), 75 (11), 74 (11), 68 (14), 65 (17), 64 (21), 63 (36), 62 (14). EI-HR-MS: 584.2187 (3, M^+, $C_{30}H_{36}N_2O_8S^+$; calc. 584.2192).

(*α*R,*1*S,*7*S*)-2-(1*H*-Indol-3-yl-acetyl)-7,7-dimethoxy-2-azabicyclo[2.2.2]octene-6-methanol Acetate* ((−)-**44**). To a soln. of (+)-**43** (784 mg, 1.34 mmol) in THF (20 ml; dist. over K/benzophenone) and MeOH (10 ml; dried over Mg) was added KH_2PO_4 (547 mg, 4.02 mmol, 3 equiv.; *Fluka, puriss.*) at −20° under Ar. After addition of sodium amalgam (7.707 g, 20.1 mmol; 6% Na) [22], stirring was continued for 5 h at −20°. The solvent was decanted from the mercury and poured onto sat. aq. $NaHCO_3$ soln. (50 ml) and extracted with ^{t}BuOMe (3×50 ml). The combined org. phase was dried ($MgSO_4$) and evaporated and the crude product subjected to FC, (silica gel (35 g), cyclohexane/AcOEt 1:2 → pure AcOEt): 399 mg (72 %) of (−)-**44**. Slightly rose foam. $[\alpha]_D = -25.4$ ($c = 0.5$, $CHCl_3$). IR ($CHCl_3$): 3480, 3005, 2944, 2870, 2836, 1725, 1638, 1457, 1418, 1370, 1356, 1320, 1138, 1121, 1078, 1054, 954. ^{1}H-NMR (400 MHz; rotamers mixture 7:1): major component: 8.26 (br. *s*, 1 H); 7.55 (*ddd, J* = 7.8, 1.2, 0.6, 1 H); 7.34 (*dt, J* = 8.0, 0.9, 1 H); 7.21 (*m*, 1 H); 7.17 (*ddd*, $J = 8.2$, 7.1, 1.2, 1 H); 7.12 (*ddd*, $J = 7.9$, 7.1, 1.1, 1 H); 4.89 (*d*, $J = 1.5$, 1 H); 4.50 (*dq*, $J = 10.5$, 6.1, 1 H); 3.72 (*dd*, $J = 15.2$, 1.0, 1 H); 3.68 (*dd*, $J = 15.2$, 1.2, 1 H); 3.38 (*dt*, $J = 10.0$, 2.3, 1 H); 3.27 (*dt*, $J = 10.0$, *ca.* 2.5, 1 H); 3.24 (*s*, 3 H); 3.18 (*s*, 3 H); 2.22 (*ddd*, $J = 10.6$, 6.1, 1.6, 1 H); 2.11 (*s*, 3 H); 2.02 (*m*, 1 H); 1.76 (*dt*, $J = 13.7$, 2.2, 1 H); 1.70 (*m*, 1 H); 1.64 (*dt*, $J = 13.7$, *ca.* 3.0, 1 H); 1.20 (*d*, $J = 6.1$, 3 H); 0.93 (*ddt*, $J = 10.9$, *ca.* 5.5, 2.5, 1 H). ^{13}C-NMR (100 MHz; rotamer mixture 7:1): major component: 171.3 (*s*); 171.1 (*s*); 136.1 (*s*); 127.4 (*s*); 122.9 (*d*); 121.9 (*d*); 119.3 (*d*); 118.4 (*d*); 111.2 (*d*); 109.0 (*s*); 101.8 (*s*); 71.4 (*d*); 49.0 (*q*); 48.9 (*t*); 48.1 (*q*); 45.8 (*d*); 38.1 (*d*); 36.9 (*t*); 30.6 (*t*); 28.2 (*t*); 27.5 (*d*); 21.5 (*q*); 17.8 (*q*). EI-HR-MS: 414.2148 (21, M^+, $C_{23}H_{30}N_2O_5^+$; calc. 414.2148), 382.1882 (30, $C_{22}H_{26}N_2O_4^+$; calc. 382.1893), 226.1420 (28, $C_{12}H_{20}NO_3^+$; calc. 226.1443), 207.0882 (13, $C_{11}H_{12}NO_3^+$; calc. 207.0895), 182.1168 (57, $C_{10}H_{16}NO_2^+$; calc. 182.1181), 157.0520 (30, $C_{10}H_7NO^+$; calc. 157.0520), 131.0696 (18), 130.0643 (100, $C_9H_8N^+$; calc. 130.0657), 110.0590 (10), 43.0102 (15).

*(19*R*)-16,19-Bis(acetyloxy)ibogamin-5-one*[2]) (=*(20*R*)-18,20-Bis(acetyloxy)ibogamin-7-one*[3]); (+)-**46**). Into a flame-dried flask, kept in an ice bath and containing (−)-**44** (453 mg, 1.09 mmol), AcOH

(*ca.* 12 ml) was distilled from anhy. $CuSO_4$. To the resulting soln. were added under Ar AcCl (390 µl, 5.49 mmol; *Fluka, puriss.*) and MeOH (4.4 µl, 109 µmol; *Fluka, puriss.*), and the resulting mixture was stirred for 2 h at 45° (bath temp.). After cooling in an ice bath, the reaction was quenched by adding Et_3N (910 µl, 6.53 mmol; *Fluka,* dist. over CaH_2). The solvent was evaporated and the residue dissolved in ^{t}BuOMe (20 ml) and washed with sat. aq. $NaHCO_3$ soln. (20 ml). The combined org. layer was dried ($MgSO_4$) and evaporated and the crude product subjected to FC (silica gel (10 g), cyclohexane/AcOEt 1:1 → pure AcOEt); 322 mg (72%) of (+)-**46**. Brownish foam. $[\alpha]_D = +73.6$ ($c = 0.6$, $CHCl_3$). IR ($CHCl_3$): 3464, 3408, 3006, 2941, 2885, 2462, 1733, 1655, 1483, 1459, 1441, 1412, 1370, 1343, 1316, 1248, 1153, 1130, 1109, 1079, 1055, 1036, 1011, 990, 950, 903, 854, 855. ^{1}H-NMR (400 MHz): 8.88 (br. *s*, 1 H); 7.52 (br. *d*, $J = 7.9$, 1 H); 7.28 (*dm*, $J = 8.0$, 1 H); 7.16 (*ddd*, $J = 8.2$, 7.0, 1.3, 1 H); 7.10 (*ddd*, $J = 8.0$, 7.1, 1.1, 1 H); 5.04 (*d*, $J = 2.9$, 1 H); 4.82 (*dq*, $J = 12.1$, 6.0, 1 H); 3.97 (*d*, $J = 15.2$, 1 H); 3.73 (*d*, $J = 15.4$, 1 H); 3.54 (br. *dt*, $J = 11.9$, 3.3, 1 H); 3.13 (br. *d*, $J = 11.9$, 1 H); 2.44 (*ddd*, $J = 15.3$, 3.6, 1.6, 1 H); 2.40 (*tt*, $J = 10.9$, 2.9, 1 H); 2.20 (*m*, 1 H); 2.12 (*s*, 3 H); 2.08 (*s*, 3 H); 2.08 (*m*, 1 H); 1.90 (*ddt*, $J = 13.8$, 11.4, *ca.* 2.6, 1 H); 1.42 (*dq*, $J = 13.6$, *ca.* 3.5, 1 H); 1.36 (*d*, $J = 6.1$, 3 H). ^{13}C-NMR (100 MHz; see *Table 3*): 176.0 (*s*); 170.9 (*s*); 169.9 (*s*); 136.0 (*s*); 134.9 (*s*); 126.8 (*s*); 122.8 (*d*); 120.0 (*d*); 118.8 (*d*); 111.0 (*d*); 105.6 (*s*); 78.7 (*s*); 71.7 (*d*); 50.8 (*d*); 47.9 (*t*); 38.5 (*t*); 36.1 (*d*); 32.9 (*t*); 27.7 (*d*); 26.7 (*t*); 22.0 (*q*); 21.1 (*q*); 17.9 (*q*). EI-HR-MS: 410.1832 (34, M^+, $C_{23}H_{26}N_2O_5^+$; calc. 410.1842), 351.1661 (28), 350.1605 (79, $C_{21}H_{22}N_2O_3^+$; calc. 350.1630), 308.1489 (10), 307.1419 (16), 291.1452 (47), 290.1403 (99, $C_{19}H_{18}N_2O^+$; calc. 290.1416), 235.1278 (15), 234.1258 (63), 233.1175 (27), 224.0879 (11), 223.0841 (59), 222.0750 (38), 221.0694 (65, $C_{11}H_{11}NO_4^+$; calc. 221.0688), 207.0965 (24), 206.0953 (66, $C_{12}H_{14}O_3^+$; calc. 206.0943), 205.0854 (15), 204.0789 (15), 195.0916 (20), 193.0816 (12), 180.0810 (12), 167.0723 (13), 130.0651 (26), 128.0511 (10), 108.0809 (12), 80.0490 (10), 60.0189 (13), 56.0479 (13), 44.9946 (11), 43.0151 (100), 41.0360 (10), 15.0174 (11).

*(19*R*)-Ibogamine-16,19-diol*[2]) (=*(20*R*)-Ibogamine-18,20-diol*[3]); (+)-**48**). To a soln. of (+)-**46** (149 mg, 363 µmol) in THF (9 ml, dist. over K/benzophenone) was added under Ar at 23° $LiAlH_4$ (138 mg, 3.63 mmol; *Fluka, purum*). The resulting grey suspension was stirred for 150 min. Then $BF_3 \cdot Et_2O$ (91 µl, 725 µmol; *Fluka, purum*) was added at 0°, and stirring was continued for 3 h at 0° to 23°. The mixture was transferred into a small separatory funnel containing a cold soln. of triethanolamine (=2,2′2″-nitrilotris[ethanol]; 1 ml) in 1M aq. HCl (15 ml). After vigorous agitation, the mixture was rendered basic by addition of 2M aq. NaOH and extracted with ^{t}BuOMe 3×25 ml). The combined org. extract was dried (Na_2SO_4) and evaporated and the crude material subjected to FC (silica gel (3 g), cyclohexane/AcOEt/Et_2NH 10:10:1 → AcOEt/Et_2NH 20:1): 76.7 mg (85%) of (+)-**48**. $[\alpha]_D = +9.7$ ($c = 0.3$, $CHCl_3$). IR ($CHCl_3$): 3568, 3500–3000 (br.), 3466, 3061, 3005, 2933, 2862, 1597, 1486, 1462, 1437, 1374, 1344, 1310, 1248, 1160, 1119, 1080, 1052, 1024, 946, 891, 873, 832. ^{1}H-NMR (400 MHz): 8.62 (br. *s*, 1 H); 7.43 (*d*, $J = 7.7$, 1 H); 7.31 (*d*, $J = 8.0$, 1 H); 7.17 (*td*, $J = 7.6$, 1.2, 1 H); 7.09 (*td*, $J = 8.0$, 1.0, 1 H); 3.98 (*qd*, $J = 6.4$, 4.1, 1 H); 3.33 (br. *s*, 1 H); 3.31 (*m*, 1 H); 3.22 (br. *d*, $J = 11.6$, 1 H); 3.16 (*d*, $J = 12.1$, 1 H); 3.00 (*dt*, $J = 9.5$, 2.7, 1 H); 2.80 (*d*, $J = 9.6$, 1 H); 2.74 (*dm*, $J \approx 13$, 1 H); 2.26 (*m*, 1 H); 2.03 (*m*, 1 H); 1.99 (*dt*, $J = 13.7$, 2.5, 1 H); 1.86 (*dm*, $J = 13.5$, 1 H); 1.84 (*m*, 1 H); 1.71 (*ddt*, $J = 13.1$, 6.8, *ca.* 2, 1 H); 1.27 (*d*, $J = 6.4$, 3 H); the two OH signals could not be localized with certainty. ^{13}C-NMR (100 MHz; see *Table 3*): 142.0 (*s*); 134.2 (*s*); 128.8 (*s*); 122.0 (*d*); 119.3 (*d*); 118.6 (*d*); 110.7 (*d*); 106.2 (*s*); 73.0 (*s*); 70.8 (*d*); 60.7 (*d*); 52.5 (*t*); 48.2 (*t*); 42.6 (*t*); 36.3 (*d*); 28.4 (*t*); 27.1 (*d*); 22.3 (*q*); 20.8 (*t*). EI-HR-MS: 312.1831 (26, M^+, $C_{19}H_{24}N_2O_2^+$; calc. 312.1838), 294.1712 (13, $C_{19}H_{22}N_2O^+$; calc. 294.1732), 250.1453 (11), 221.1145 (16), 220.1113 (26, $C_{16}H_{14}N^+$; calc. 220.1116), 209.1098 (36, $C_{14}H_{13}N_2^+$; calc. 209.1079), 208.1096 (10), 207.0999 (23), 206.0965 (13), 161.0888 (10), 144.0842 (18), 143.0768 (19, $C_{10}H_9N^+$; calc. 143.0735), 140.1109 (12), 130.0695 (43, $C_9H_8N^+$; calc. 130.0657), 94.0687 (10), 86.0998 (14), 73.0320 (10), 70.0472 (18), 61.0291 (22), 45.0313 (31), 43.0160 (100, $C_2H_3O^+$; calc. 43.0184), 42.0233 (13), 41.0354 (14), 29.0386 (23).

*(19*R*)-Ibogamin-19-ol*[2]) (=*(20*R*)-Ibogamin-20-ol*[3]); (−)-**1**). To a suspension of $LiAlH_4$ (40 mg, 1.06 mmol; *Fluka, purum*) in Et_2O (4 ml; *Fluka, puriss.*) was added under Ar at 0° $AlCl_3$ (141 mg, 1.06 mmol; *Fluka, purum*) in small portions, and stirring was continued for 5 min. Then a soln. of (+)-**48** (66.0 mg, 211 µmol) in Et_2O (1 ml) was added. The mixture was warmed to 23° and stirred for 24 h. The mixture was quenched by adding AcOEt (1.5 ml) at 0° and stirring for 5 min. The mixture was transferred into a small separatory funnel containing a cold soln. of 'triethanolamine' (1 ml) in 1M aq. HCl (10

ml). After vigorous agitation, the mixture was rendered basic by addition of 2M aq. NaOH and extracted with ^{t}BuOMe (3×15 ml). The combined org. extract was dried (Na_2SO_4) and evaporated. The crude material was subjected to FC (silica gel (3 g), cyclohexane/AcOEt/Et_2NH 12:6:1 → 10:10:1): 56.4 mg (85%) of (−)-**1**. The brownish foam crystallized when an Et_2O soln. was triturated with pentane at 23°. M.p. 174.3–175.3°. ([4]: 172–174°; [7b]: 168–173°). $[\alpha]_D = -38.4$ ($c = 0.6$, $CHCl_3$) ([4]: $[\alpha]_D = -28$ ($c = 1.0$, $CHCl_3$); [7b]: $[\alpha]_D = -29$ (c unknown, $CHCl_3$)). IR ($CHCl_3$): 3468, 3196 (br.), 2968, 2935, 2865, 1621, 1486, 1462, 1374, 1330, 1281, 1259, 1156, 1094, 1066, 1020, 909, 885. ^{1}H-NMR (500 MHz): 7.84 (br. *s*, 1 H); 7.47 (*ddd*, *J* = 7.7, 1.4, *ca.* 0.6, 1 H); 7.37 (*ddd*, *J* = 7.7, *ca.* 1.3, *ca.* 0.7, 1 H); 7.13 (*ddd*, *J* = 7.7, 7.1, 1.4, 1 H); 7.09 (*ddd*, *J* = 7.7, 7.1, 1.3, 1 H); 3.90 (*qd*, *J* = 6.5, 2.5, 1 H); 3.39 (*t*, *J* = 1.7, 1 H); 3.33 (*m*, 1 H); 3.29 (*m*, 1 H); 3.19 (*m*, 1 H); 3.07 (*m*, 2 H); 2.93 (*ddd*, *J* = 11.8, 3.9, 2.0, 1 H); 2.76 (*m*, 1 H); 2.09 (*tm*, *J* = 12.5, 1 H); 2.00 (*m*, 1 H); 1.94 (*ddt*, *J* = 13.1, 6.6, 2.6, 1 H); 1.86 (*dddd*, *J* = 13.1, 11.0, *ca.* 4, *ca.* 1.5, 1 H); 1.68 (*dq*, *J* = 13.2, 3.4, 1 H); 1.62 (*dddd*, *J* = 10.8, 6.6, 2.5, 1.6, 1 H); 1.28 (*d*, *J* = 6.5, 3 H); [29]: 7.90 (br. *s*, 1 H); 7.52–6.98 (*m*, 4 H); 3.93 (*qd*, *J* = 7, 2, 1 H); 3.45–2.7 (*m*, ca. 8 H); 2.25–1.55 (*m*, ca. 7 H); 1.34 (*d*, *J* = 7, 3 H). ^{13}C-NMR (125 MHz; see *Table 3*): 140.9 (*s*); 134.8 (*s*); 129.5 (*s*); 121.3 (*d*); 119.3 (*d*); 118.0 (*d*); 110.2 (*d*); 108.6 (*s*); 71.6 (*d*); 54.7 (*d*); 52.8 (*t*); 49.1 (*t*); 42.5 (*d*); 40.1 (*d*); 34.2 (*t*); 29.1 (*t*); 26.1 (*d*); 22.8 (*q*); 20.2 (*t*). HSQC (125×500 MHz): 121.3/7.13; 119.3/7.09; 118.0/7.47; 110.2/7.37; 71.6/3.90; 54.7/3.39; 52.8/(3.29, 3.19); 49.1/3.07; 42.5/1.62; 40.1/2.93; 34.2/2.09, 1.68; 29.1/1.94, 1.86; 26.1/2.00; 22.8/1.28; 20.2/3.33, 2.76. Diff.-NOE (500 MHz): irrad. at 7.47 (H−C(9), strong NOEs at 7.13 (H−C(10)) and 2.76 (H_{eq}−C(6)); irrad. at 3.07 (CH_2(3)), strong NOEs at 3.29 (H_{eq}−C(5)), 2.00 (H−C(14)), 1.94 (H_{exo}−C(15)), 1.68 (H_{exo}−C(17)); irrad. at 1.68 (H_{exo}−C(17)), strong signals at 3.07 ($H_{pro\text{-}S}$−C(3)), 2.09 (H_{endo}−C(17)), and 2.00 (H−C(14)). EI-HR-MS: 296.1886 (100, M^+, $C_{19}H_{24}N_2O^+$; calc. 296.1889), 295.1798 (11), 282.1715 (11), 281.1661 (71, $C_{18}H_{21}N_2O^+$; calc. 281.1654), 279.1851 (32), 278.1800 (47, $C_{19}H_{22}N^+$; calc. 278.1783), 252.1647 (12), 251.1559 (13), 212.1661 (13), 195.1052 (31, $C_{14}H_{13}N^+$; calc. 195.1048), 184.1329 (17), 180.0805 (11), 170.0953 (10), 169.0881 (13), 168.0814 (17), 167.0732 (21), 166.1244 (26), 165.1169 (18), 156.0833 (29), 154.0679 (12), 152.1092 (50, $C_9H_{14}NO^+$; 152.1075), 151.1024 (31), 150.0945 (18), 144.0833 (14), 143.0740 (12), 140.1096 (12), 138.0934 (21), 134.0991 (10), 130.0660 (15), 129.0709 (13), 122.0975 (14), 118.9920 (22), 108.0817 (13), 94.0683 (15).

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