120. A Reinvestigation of the Oxidative Rearrangement of Yohimbane-Type Alkaloids

Part A

Formation of Pseudoindoxyl (= 1,2-Dihydro-3*H*-indol-3-one) Derivatives

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Contrary to earlier reports, the base-induced rearrangement of the 7-hydroxy-7*H*-indolenines derived from ajmalicine (**1**), yohimbine (**5**), corynanthine (**6**), methyl reserpate (**16**), and methyl isoreserpate (**17**) in each case furnished not just one, but two epimeric spiro-pseudoindoxyl derivatives which have opposite configuration at the spiro centre C(2). In all cases, the major component was shown by NOE experiments to be the *A*-type isomer (carbonyl group located below the plane defined by rings C and D). The thermodynamically less stable *B*-type pseudoindoxyl epimers **4**, **10**, **12**, and **22** were isolated and characterized for the first time.

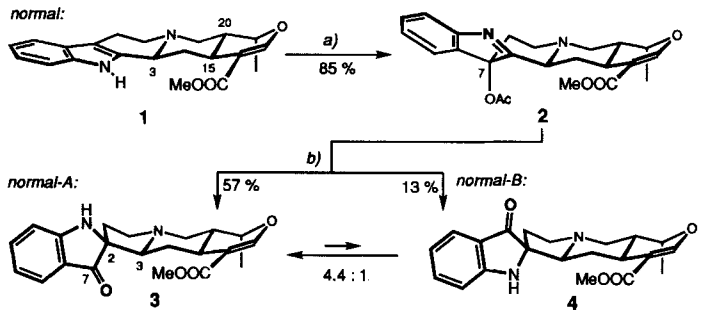
1. Introduction. – Within the *Aristotelia* alkaloid family, the formation of pseudoindoxyls (= 1,2-dihydro-3*H*-indol-3-ones) and oxindoles (= 1,3-dihydro-2*H*-indol-2-ones) from the corresponding 3*H*-indol-3-ol precursors was shown recently to proceed under strict kinetic control [1]. This is not the case within alkaloid families that contain a tetrahydro-β-carboline ring system, such as the yohimbane and heteroyohimbane alkaloids, because subsequent equilibration at the spiro centre and/or C(3) usually takes place. Early claims that certain oxindole alkaloids endowed with this skeleton are equilibrated upon treatment with AcOH or Ac_2O [2] were confirmed by a Canadian team who demonstrated that such oxindoles are isomerized under very mild conditions and that they differ in their relative configuration at the spiro centre [3]. These findings were rationalized by *Wenkert et al.* [4] who postulated a *retro-Mannich* cleavage of the C(3)–C(7) bond, followed by rotation of the oxindole side chain and a *Mannich* ring re-closure (for reviews, see [5]).

Curiously, the above type of isomerization seemingly has never been observed in the case of the related pseudoindoxyls: no matter whether compounds endowed with this functional unit were isolated from plant material or prepared by partial synthesis from their indole precursors, in each case, only a single spiro epimer was isolated[1]). However, inspection of *Dreiding* models or even just a glance at the perspective drawings of

[1]) In a preliminary communication, *Finch et al.* [6] mentioned that, on treatment with hot AcOH, yohimbine pseudoindoxyl was transformed to the extent of *ca.* 10% into an isomeric pseudoindoxyl which was 'instantly reconverted to the starting material in the presence of base'. However, this compound was not characterized and was not mentioned anymore in the full paper of these authors [7].

compounds **3** and **4** (*Scheme 1*) suggest that these pseudoindoxyl epimers should be of comparable thermodynamic stability. In addition, in no case was the relative configuration at C(2) of the single isolated isomer determined with certainty. Therefore, these questions have been addressed in the present reinvestigation, and the results are discussed below.

Scheme 1



a) $Pb(OAc)_4$, CH_2Cl_2, 30 min, 25°. *b*) NaOMe, MeOH, 40 min, reflux.

2. Results and Discussion. – At first, the oxidative rearrangement of ajmalicine (**1**) was investigated, which has a skeleton of the *normal* type[2]). Treatment with lead tetraacetate according to *Taylor* and coworkers [7] furnished the 7α-acetoxyindole derivative **2** in 85% yield. The configuration at C(7) was inferred by the earlier workers to be 7α in analogy to the corresponding yohimbine derivative **7** (*Scheme 2*), the structure of which was determined by X-ray crystallography [7]. The NMR data now obtained for **2** (see *Tables 1* and *2*) is fully consistent with the original proposal in showing that ring C adopts a chair conformation and *H*–C(3) an axial position relative to ring D.

Contrary to an earlier claim [7], treatment of **2** with NaOMe in MeOH furnished not a single pseudoindoxyl, but a 4.4:1 mixture of two compounds in a combined yield of 70%. These were readily separated by chromatography on silica gel, and the major component was shown to be identical with the pseudoindoxyl derivative that had been isolated previously. The original, rather tentative structure proposal **3** was now unambiguously shown to be correct by means of a NOE difference experiment, shown in the *Figure*, which clearly demonstrates that this compound belongs to the *normal-A* series (H_{ax}–C(14) *cis* to *H*–N(1)).

The minor component showed very similar NMR spectroscopic data (see *Tables 1* and *2*) that can only be reconciled with isomerism at C(2)[3]). The resulting structure **4**

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[2]) The standard nomenclature for the description of the relative configuration of yohimbane-type alkaloids was followed [3]; *normal*: rings D and E *trans*-fused (*i.e.* 20β) and *H*–C(3) on α-face; *pseudo*: D/E *trans* (*i.e.* 20β), *H*–C(3) on β-face; *allo*: D/E *cis* (*i.e.* 20α), *H*–C(3), *H*–C(15), and *H*–C(20) all on α-face; *epiallo*: D/E *cis* (*i.e.* 20α), *H*–C(3) on β-face. Following a convention introduced by *Taylor* and coworkers [6] [7], the relative configuration at the spiro centre C(2) is designated as *A* (carbonyl group below the plane defined by rings C and D) or *B* (carbonyl group above this plane).

[3]) The only other possibilities (type *pseudo-A* or *-B*) are ruled out by the ^{13}C-NMR chemical-shift values of C(3), C(5), C(15), and C(21) [8] (see, *e.g.*, *Table 2*, **5** *vs.* **6**, **7** *vs.* **9** and **18** *vs.* **20**).

Table 1. *^{1}H-NMR Chemical-Shift Values* δ [ppm]. In $CDCl_3$.

Type	*normal*												*pseudo*		*allo*				*epiallo*	
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**17**	**20**	**21**	**22**	**16**[c])	**18**
H–N(1)	7.97	–	5.01	4.69	7.77	8.56	–	–	5.18	4.60	5.42	4.74	8.11	–	7.81	–	5.23	4.59	7.58	–
H–C(3)	3.39	3.05	2.44	2.31	3.32	3.29	2.95	2.91	2.35	2.20	2.34	2.25	4.46	4.02	3.08	2.74	2.19	2.00	4.42	3.96
H_α–C(5)	2.68	2.71	2.43	2.42	2.61	2.59	2.65	2.61	2.40	2.36	2.32	2.38	3.28	2.75	2.50	2.51	2.28	2.20	3.17	2.64
H_β–C(5)	3.10	2.75	3.22	3.27	3.07	3.07	2.75	2.75	3.20	3.33	3.23	3.26	2.54	3.37	2.90	2.65	3.13	3.17	3.17	3.31
H_α–C(6)	2.75	2.74	2.37	2.40	2.71	2.72	2.68	2.69	2.32	2.38	2.32	2.40	2.60	2.55	2.88	2.66	1.87	1.80	2.94	2.55
H_β–C(6)	3.00	1.48	1.92	1.88	2.98	2.99	1.47	1.49	1.90	1.87	1.94	1.89	3.02	1.81	1.71	1.45	2.28	2.41	2.50	1.80
H–C(9)	7.46	7.41	7.58	7.57	7.46	7.47	7.38	7.40	7.56	7.54	7.55	7.59	7.47	7.37	7.32	7.28	7.45	7.52	7.32	7.26
H–C(10)	7.07	7.20	6.77	6.78	7.07	7.08	7.20	7.19	6.77	6.78	6.76	6.81	7.09	7.19	6.75	6.73	6.34	6.39	6.77	6.71
H–C(11)	7.13	7.37	7.41	7.40	7.12	7.16	7.37	7.37	7.43	7.40	7.42	7.41	7.15	7.38	–[b])	–[b])	–[b])	–[b])	–[b])	–[b])
H–C(12)	7.29	7.62	6.78	6.78	7.29	7.35	7.61	7.60	6.83	6.79	6.81	6.81	7.40	7.68	6.81	7.23	6.24	6.20	6.84	7.18
H_{ax}–C(14)	1.31	1.77	1.01	1.08	1.36	1.44	1.82	1.44	1.09	1.17	1.36	1.62	1.66	1.61	1.76	2.20	1.54	1.63	2.23	2.00
H_{eq}–C(14)	3.20	3.08	2.31	2.37	1.99	1.81	2.05	2.02	1.12	1.17	1.14	1.24	2.23	2.20	2.61	1.81	1.00	1.01	1.75	2.01
H–C(15)	2.43	2.33	2.18	2.10	2.02	1.91	1.94	1.88	1.75	1.68	1.72	1.63	1.61	2.65	2.23	2.20	2.04	1.93	1.97	2.95
H–C(16)	–	–	–	–	2.34	2.67	2.37	2.80	2.19	2.23	2.59	2.60	2.28	2.18	2.63	2.59	2.57	2.54	2.52	2.60
H–C(17)	7.53	7.47	7.42	7.41	4.22	4.18	4.19	4.23	4.12	4.11	4.17	4.15	4.19	4.18	3.41	3.64	3.46	3.43	3.52	3.54
H_{ax}–C(18)	–	–	–	–	1.56	2.10	1.50	2.01	1.45	1.45	2.00	2.05	1.54	1.45	3.58	3.50	3.58	3.50	3.55	3.56
H_{eq}–C(18)	–	–	–	–	1.97	1.74	1.96	1.72	1.92	1.92	1.72	1.68	1.84	1.94	–	–	–	–	–	–
H_{ax}–C(19)	–[a])	–[a])	–[a])	–[a])	1.56	1.39	1.50	1.39	1.55	1.45	1.36	1.31	1.25	1.52	2.19	2.11	2.10	2.13	2.25	2.18
H_{eq}–C(19)	4.42	4.36	4.36	4.35	1.42	1.45	1.39	1.43	1.38	1.36	1.42	1.43	1.30	1.25	1.73	1.69	1.73	1.77	2.20	1.65
H–C(20)	2.14	2.02	1.90	2.05	1.55	2.04	1.46	2.15	1.29	1.45	1.95	2.02	1.41	1.35	1.88	1.89	1.83	1.80	1.75	1.83
H_{ax}–C(21)	2.24	2.19	1.93	1.81	2.23	2.10	2.18	2.05	1.92	1.80	1.79	1.73	2.55	2.25	2.55	2.50	2.27	2.13	2.45	2.18
H_{eq}–C(21)	2.96	2.93	3.05	3.13	2.94	2.93	2.92	2.95	3.03	3.10	3.07	3.14	3.26	2.25	2.77	2.82	2.94	3.03	3.02	2.68
COOMe	3.73	3.71	3.56	3.57	3.81	3.59	3.76	3.69	3.52	3.52	3.58	3.60	3.79	3.77	3.78	3.75	3.59	3.56	3.80	3.80
AcO	–	2.07	–	–	–	–	2.05	2.04	–	–	–	–	–	2.03	–	2.04	–	–	–	2.02
MeO–C(17)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3.54	3.61	3.56	3.54	3.58	3.60

[a]) Me_{ax}–C(19) at δ 1.18 (**1**), 1.16 (**2**), 1.12 (**3**), and 1.10 (**4**).

[b]) MeO–C(11) at δ 3.82 (**17**), 3.84 (**20**), 3.85 (**21**), 3.83 (**22**), 3.83 (**16**), and 3.83 (**18**).

[c]) Values taken from [25].

Table 2. *^{13}C-NMR Chemical-Shift Values* δ [ppm]. In $CDCl_3$.

Type	*normal*													*pseudo*		*epiallo*		*allo*			
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**24**[a])	**13**	**14**	**16**	**18**	**17**	**20**	**21**	**22**
C(2)	134.4	179.2	74.1	72.7	134.5	134.5	179.7	179.7	74.4	73.2	74.4	73.4	73.3	123.3	177.2	130.7	178.8	133.2	180.8	75.2	73.2
C(3)	60.1	60.5	71.5	72.9	59.9	60.6	60.4	61.3	71.4	72.9	72.4	73.6	71.2	54.3	54.6	53.7	54.5	60.0	60.8	71.2	73.4
C(5)	53.3	50.0	52.6	53.1	52.9	52.9	49.9	49.9	52.7	53.3	52.9	53.0	52.8	51.0	48.8	51.2	48.9	53.1	50.0	52.9	53.6
C(6)	21.8	36.0	35.9	35.5	21.8	21.5	36.2	35.7	35.3	35.2	35.1	35.1	34.4[b])	16.9	35.9	16.7	36.3	21.8	35.9	35.9	35.2
C(7)	106.7	84.9	202.1	203.1	108.3	107.6	84.8	84.8	202.1	203.0	202.3	202.4	202.1	107.2	86.3	108.0	86.1	108.2	84.6	199.7	200.5
C(8)	127.3	137.1	120.5	120.5	127.4	127.3	137.2	137.1	120.4	120.5	120.2	120.6	119.6	127.5	137.0	122.2	129.1	121.8	129.0	113.7	114.1
C(9)	118.1	122.3	124.7	124.7	118.1	118.1	122.0	122.2	124.6	124.6	124.5	124.7	124.5	117.9	122.0	118.5	122.7	118.6	122.8	126.0	126.4
C(10)	119.4	126.1	118.5	118.9	119.4	119.2	126.1	126.1	118.3	118.8	118.2	118.9	118.2	119.2	125.8	109.0	111.6	108.7	111.9	108.6	108.3
C(11)	121.4	129.9	137.3	137.0	121.4	121.2	129.8	129.9	137.2	136.9	137.3	136.9	137.5	121.4	129.7	156.1[c])	161.3[c])	156.0[c])	161.4[c])	168.0[c])	167.5[c])
C(12)	110.8	121.6	111.7	111.9	110.7	110.9	121.5	121.5	111.8	111.8	111.6	111.7	111.8	111.4	121.9	95.2	107.3	95.1	107.3	94.0	94.4
C(13)	136.0	154.1	160.5	160.4	136.0	136.1	153.9	154.1	160.5	160.3	160.7	160.2	160.7	136.1	154.3	136.4	155.9	136.8	155.7	162.7	162.3
C(14)	32.9	30.3	27.8	28.0	34.4	33.5	31.0	30.3	28.8	29.4	27.9	28.8	28.3[b])	32.1	30.0	24.3	22.3	27.9	23.9	21.9	22.5
C(15)	30.7	30.0	29.8	30.7	36.7	36.9	36.2	36.3	35.8	36.8	35.7	36.8	41.0	31.3	31.7	32.8	31.9	37.8	37.6	37.1	38.3
C(16)	107.9	107.6	107.4	107.0	52.4	51.3	52.0	51.0	52.5	52.2	51.3	51.3	57.6	52.1	52.7	51.4	51.6	51.8	52.0	51.3	51.8
C(17)	154.7	153.7	153.9	153.9	67.0	66.8	66.7	67.8	66.5	66.7	67.5	67.5	71.7	67.2	66.6	81.4	81.5	81.5	81.1	81.3	81.1
C(18)	15.0	14.8	14.8	14.8	31.5	28.5	31.1	28.5	31.3	31.2	28.7	28.8	34.0	31.6	31.1	75.2	75.2	75.2	75.4	74.9	75.7
C(19)	73.8	73.3	73.9	73.7	23.3	23.8	23.1	23.6	23.4	23.4	23.7	23.7	27.8	23.1	23.4	32.3	32.0	33.1	32.6	32.9	33.4
C(20)	41.0	40.9	40.9	40.3	40.8	34.8	40.4	34.4	40.5	39.6	34.2	33.4	39.2	39.9	41.6	34.5	35.0	35.3	35.1	34.8	34.9
C(21)	56.9	57.0	54.2	54.3	61.4	62.1	61.5	62.6	58.6	58.7	59.5	59.3	58.2	51.0	51.9	49.3	50.2	59.9	60.2	57.4	57.6
C(22)	167.5	167.3	167.1	167.1	175.6	172.9	175.8	172.4	175.4	175.9	172.5	172.3	174.0	175.4	176.3	173.4	172.8	173.0	172.3	172.3	172.5
COO*Me*	51.0	51.1	50.8	50.8	52.0	51.5	52.0	51.5	51.7	51.5	51.2	51.3	51.7	51.9	51.9	51.8	51.8	51.8	51.8	51.8	51.5
Me*C*OO	–	168.6	–	–	–	–	168.7	168.7	–	–	–	–	–	–	168.9	–	168.9	–	168.9	–	–
*Me*COO	–	21.0	–	–	–	–	21.0	21.0	–	–	–	–	–	–	21.0	–	21.1	–	21.1	–	–
MeO–C(17)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	61.0	61.1	61.1	61.2	61.1	61.1

[a]) Values taken from [15].

[b]) To obtain a better correlation with the values of compounds **9**–**12**, the original assignments were interchanged for *Table 2*.

[c]) *Me*O–C(11) at δ 55.8 (**16**), 55.6 (**18**), 55.7 (**17**), 55.6 (**20**), 55.6 (**21**), and 55.6 (**22**).

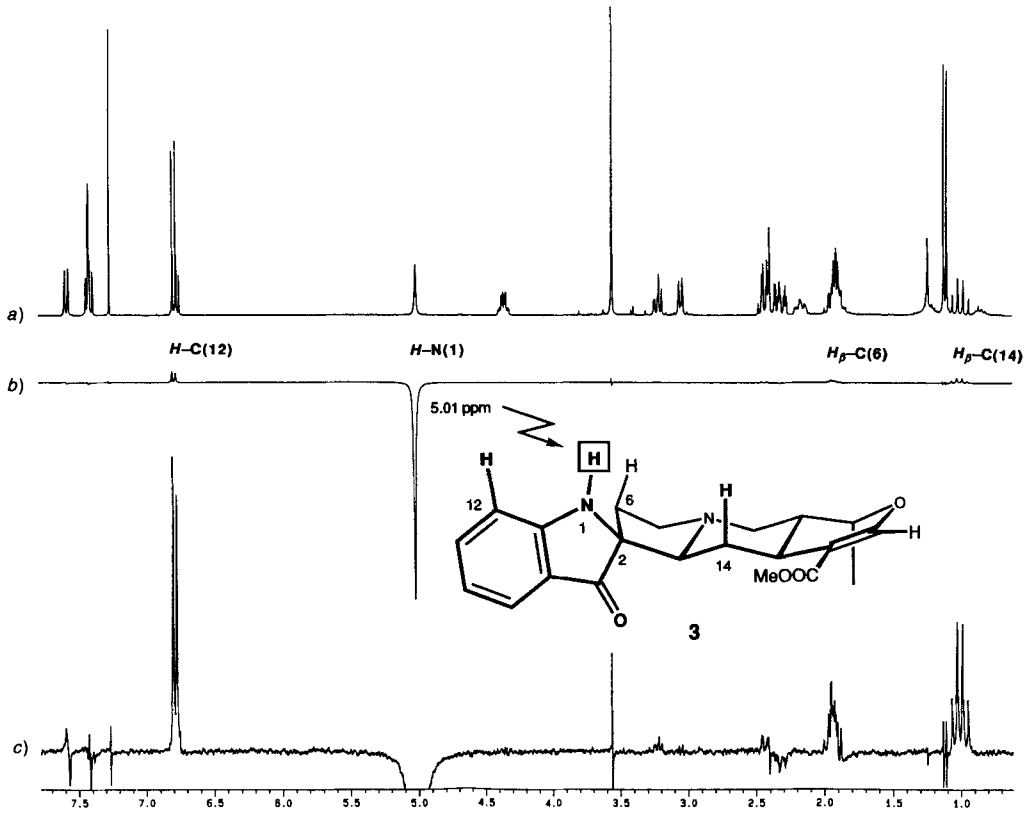


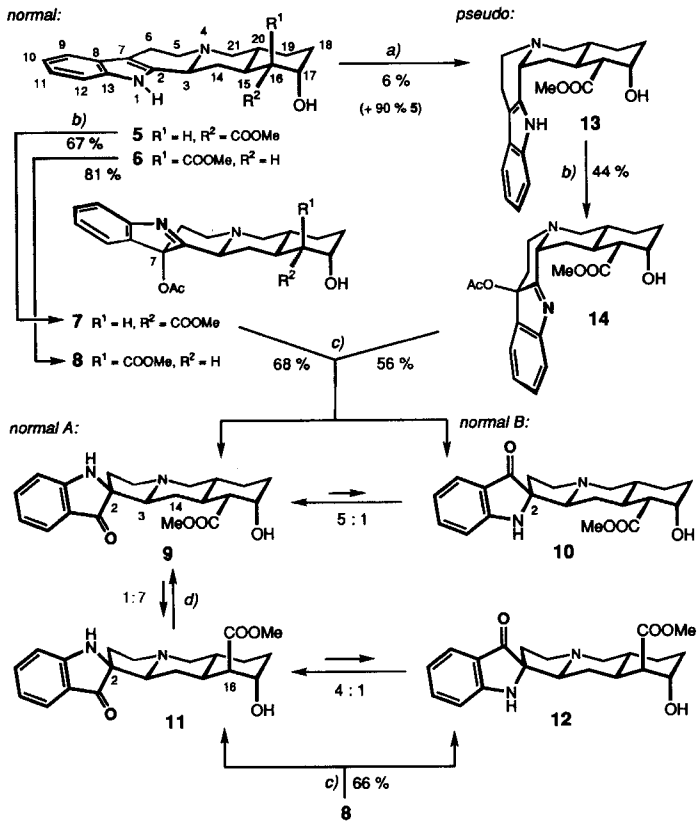
Figure. a) *Standard ^{1}H-NMR spectrum of* **3** (300 MHz, $CDCl_3$), b) *NOE difference spectrum obtained upon irradiating* H–*N(1) at 5.01 ppm, and* c) *as* b) *with enhanced sensitivity*

represents the first pseudoindoxyl derivative of type *B* within the tetrahydro-β-carboline alkaloids. Since ajmalicine pseudoindoxyl A (**3**) undoubtedly represents the primary rearrangement product, the formation of considerable amounts of **4** is indicative of an equilibrium being set up under the employed reaction conditions. We verified this contention experimentally by showing that either of the pure isomers **3** and **4** give rise to the same 4.4:1 mixture under the reaction conditions employed to prepare these compounds from **2**.

To check the generality of the above findings, we then investigated the behavior of yohimbine (**5**; *Scheme 2*) under similar conditions. While the oxidation with $Pb(OAc)_4$ was uneventful and in accordance with earlier work [7], treatment of the resulting 7α-acetoxy-7*H*-yohimbine (**7**) again resulted in formation of two epimeric pseudoindoxyls, this time in a ratio of 5:1. As in the case discussed above, the major, more polar component is identical with the product isolated before [7], and now unambiguously shown by NOE experiments to be yohimbine pseudoindoxyl A (**9**)[4]). The spectral data of

[4]) The same configuration was tentatively assigned by *Taylor* and coworkers [6] [7] to this product on the basis that the corresponding N^1-methyl derivative was a slightly weaker base (pK_a' 5.30) than **9** (pK_a' 5.76).

Scheme 2



a) 1. $Hg(OAc)_2$, AcOH, 2 h, 60°; 2. Zn, HCl, 30 min, 0°. *b*) $Pb(OAc)_4$, CH_2Cl_2, 15 min, 25°. *c*) 0.1N NaOMe, MeOH, 90 min, reflux. *d*) 0.5N NaOMe, MeOH, reflux (see *Table 1*).

the minor component is fully consistent with what one would expect for the missing *B*-type pseudoindoxyl **10**.

During equilibration experiments of **9** and **10** with NaOMe in hot MeOH, the appearance of a third isomeric component (*ca.* 5% yield) was noted after prolonged reaction times. Its UV and IR data are only compatible with a pseudoindoxyl chromophore. In the ^{1}H-NMR spectrum, H–C(16) appears as narrow *m* ($w_{1/2}$ = 10 Hz) at 2.59 ppm. The conclusion that the COOMe group is now in an axial position is supported by the ^{13}C-NMR spectrum (shielding of C(20) by 6.3 ppm and of C(18) by 2.5 ppm as compared to **9**, in accordance with precedent cases, *cf.* [8] and [9]). The resulting structure proposal **11** represents the pseudoindoxyl-*A* derivative of the parent indole alkaloid corynanthine (**6**), a strong α_1-adrenoceptor antagonist [10].

Since the amount of the putative type-*B* isomer **12** in the equilibrium mixture of the four isomers **9**–**12** was expected to be very low (*ca.* 1–2% by extrapolation of the established equilibria **9** ⇄ **11** and **9** ⇄ **10**), an attempt was made to prepare **11** and **12** directly from corynanthine (**6**). Gratifyingly, sufficiently mild conditions could be found

Table 3. *Base-Catalyzed Equilibration of Pseudoindoxyls* **9**–**12**, *Starting from* **11**[a])

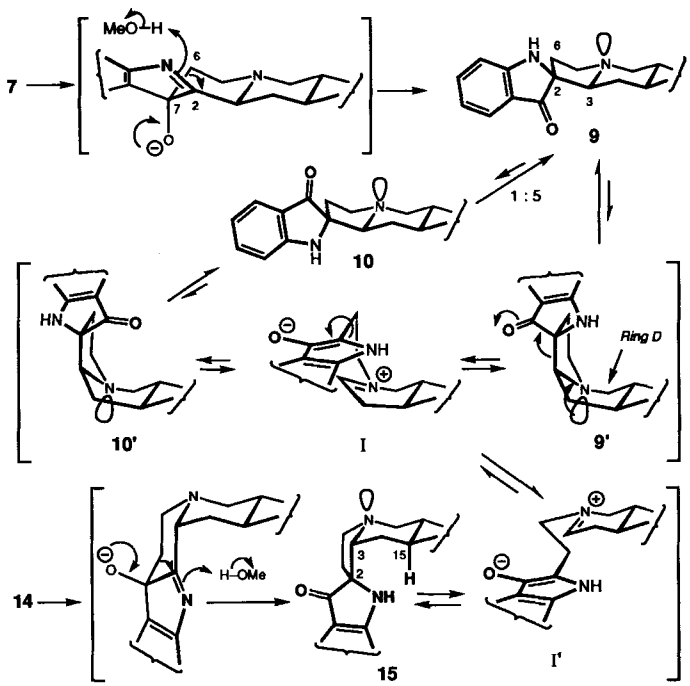
Time [h][b])	% **11**	% **12**	% **9**	% **10**	**9**/**10**
0	100	0	0	0	–
2.5	38	8	45	9	5:1
5	22	< 2	65	13	5:1
6	17	< 2	69	14	4.9:1

[a]) Conditions: 0.5M NaOMe in MeOH at 64°.
[b]) After the indicated time lapse, a sample was worked up and analyzed by ^{1}H-NMR spectroscopy (MeO-signal area) without purification.

that converted the corresponding 7α-acetate **8** into a readily separated 5:1 mixture of the hitherto unknown pseudoindoxyl derivatives **11** and **12** without concomitant isomerization at C(16). However, treatment of **11** with a stronger base slowly led to an equilibrium mixture in which the four isomers **9**–**12** were present in the expected proportions (see *Table 3*).

In accordance with earlier work [7], the isomeric 7β-acetoxy-7*H*-pseudoyohimbine (**14**; prepared from **5** *via* pseudoyohimbine (**13**)) underwent concomitant epimerization at C(3) upon treatment with base, giving again a 5:1 mixture of *normal-A* (**9**) and *normal-B* (**10**) pseudoindoxyls. Conceivably, this epimerization follows a mechanistic course analogous to the one that was postulated for the equilibration of the corresponding oxindoles [4]. As shown in *Scheme 3*, the base-catalyzed rearrangement of the 7α-

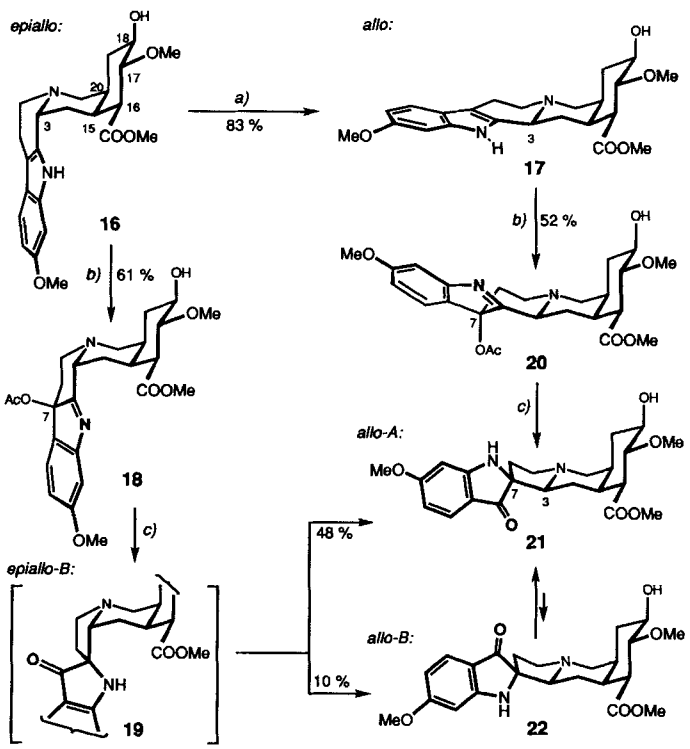
Scheme 3



acetates, such as **7**, leads directly to the more stable *A*-type pseudoindoxyls, *e.g.* **9**. On the other hand, a kinetically controlled rearrangement of 7*β*-acetate **14** leads to the unstable[5]) *pseudo-B* derivative **15**. This intermediate fulfils the stereoelectronic requirements for a *retro-Mannich* reaction (lone pair at N(4) antiperiplanar to the C(2)–C(3) bond to be cleaved; for a discussion and leading ref., see [12]). In the most stable conformation within the *normal* series (**9**), the pertinent orbitals are aligned synclinal to each other, and for a stereoelectronically supported cleavage, ring D first has to switch into a boat-like conformation (**9′**). The resulting intermediate **I** can either revert to **9** *via* **9′** or cyclize *via* **10′** to the chair conformer **10** of the *B*-type pseudoindoxyl.

We then turned our attention to the conformationally more flexible systems of the *epiallo*- and the *allo*-type (for a discussion, see [13]), namely to the readily available methyl reserpate (**16**) and methyl isoreserpate [14] (**17**; *Scheme 4*). The 7*β*-acetate **18** was described earlier to rearrange to methyl isoreserpate pseudoindoxyl A (**21**) upon treatment with NaOMe in MeOH [7]. When repeating this experiment, we obtained a 5:1 mixture of the two epimers **21** and **22**. Again these structures were deduced by NMR

Scheme 4



a) TsOH, collidine, 4 h, reflux. *b*) $Pb(OAc)_4$, CH_2Cl_2, 30 min, 25°. *c*) 0.2N NaOMe, MeOH, 3 h, reflux.

[5]) The parent system *cis*-quinolizine was shown to be destabilized by 2.6 kcal/mol compared to its *trans*-counterpart [11]. In the case at hand, the difference in stability between **15** and **10** (or **9**) should be even greater due to an additional unfavorable steric interaction between *H*–N(1) and *H*–C(15) in **15**.

spectroscopy and NOE experiments. Obviously, the situation in the *epiallo*-series is similar to the one discussed before in the *pseudo*-case (see *Scheme 3*) in that the first intermediate **19** epimerizes very rapidly to a mixture of the *allo* derivatives **21** and **22**. Seemingly, at least part of the strain present in **19** manifests itself in the preceding transition state, since **18** is known to react at a much slower rate then **20** [7].

3. Conclusions. – As expected, there are only small differences between the spectroscopic data of the isomeric pairs of pseudoindoxyls (see *Tables 1* and *2* and *Exper. Part*). However, some recurring deviations seem to be characteristic (see *Table 4*) and may be of help in assigning the relative configuration at the spiro centre in those cases where only one epimer was isolated, at least in the *normal* and in the *allo* series. The most significant difference lies in the values for the optical rotation: in all cases, the $[\alpha]_D$ of the *A*-type isomer is more negative than the optical rotation of the parent indole alkaloid, whereas the *B*-type epimers invariably show a more positive value.

Table 4. *Comparison of Some Characteristic Data of Pseudoindoxyl Epimers*

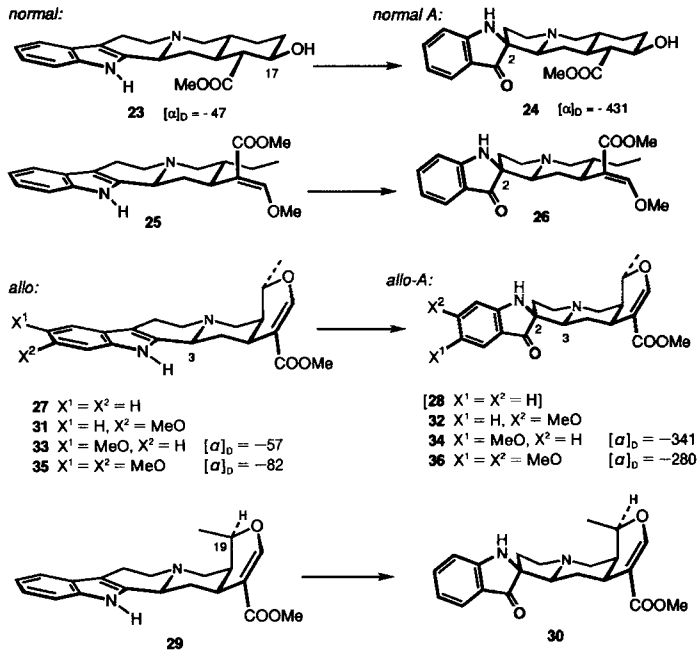
	3	**4**	*Δ*	**9**	**10**	*Δ*	**11**	**12**	*Δ*	**21**	**22**	*Δ*
^{13}C-NMR (δ [ppm])												
C(2)	74.1	72.7	*1.4*	74.4	73.2	*1.2*	74.4	73.4	*1.0*	75.2	73.2	*2.0*
C(3)	71.5	72.9	*−1.4*	71.4	72.9	*−1.5*	72.4	73.6	*−1.2*	71.2	73.4	*−2.2*
Δ(C(2)–C(3))	*2.6*	*−0.2*		*3.0*	*0.3*		*2.0*	*−0.2*		*4.0*	*−0.2*	
C(7)	202.1	203.1	*−1.0*	202.1	203.0	*−0.9*	202.3	202.4	*−0.1*	199.7	200.5	*−0.8*
^{1}H-NMR (δ [ppm])												
H_{ax}–C(14)	1.01	1.08	*−0.07*	1.09	1.17	*−0.08*	1.36	1.62	*−0.26*	1.54	1.63	*−0.09*
H_{ax}–C(21)	1.93	1.81	*0.12*	1.92	1.80	*0.12*	1.79	1.73	*0.06*	2.27	2.13	*0.14*
H_{eq}–C(21)	3.05	3.13	*−0.08*	3.03	3.10	*−0.07*	3.07	3.14	*−0.07*	2.94	3.03	*−0.09*
H–N(1)	5.01	4.69	*0.32*	5.18	4.60	*0.58*	5.42	4.74	*0.68*	5.23	4.59	*0.64*
$[\alpha]_D$ ($CHCl_3$)												
	−203	+38	*−241*	−171	+83	*−254*	−159	+38	*−197*	−126	−29	*−97*
standard[a])	−66			+10			−101			−51		
Δ[b])	*−137*	*+104*		*−181*	*+73*		*− 58*	*+139*		*− 75*	*+22*	

[a]) Optical rotation of the corresponding parent indole alkaloid **1**, **5**, **6**, and **17**, resp.

[b]) Difference between the rotations of the pseudoindoxyl in question and the corresponding parent alkaloid.

With the aid of the above correlations, an attempt is made to delineate the relative configuration at C(2) of some yohimbane and corynantheane pseudoindoxyl derivatives that were isolated by others from various plants. A pseudoindoxyl **24** of *β*-yohimbine (*Scheme 5*) was isolated from *Aspidosperma oblungum* (A. DC.) PICHON [15] and from *Ervatamia hirta* (HOOK. f.) KING and GAMBLE [16] and prepared by partial synthesis from *β*-yohimbine [15] (**23**). The data reported for **24** provides strong evidence that this natural product belongs to the *normal-A* series: its optical rotation is much more negative than the one of **23**, in the ^{13}C-NMR data set, which is included in *Table 2*, the δ values of C(2) and C(3) differ by 2.1 ppm [15], and *H*–N(1) absorbs at 5.15 ppm in the ^{1}H-NMR spectrum [16]. Dihydrocorynantheine pseudoindoxyl A (**26**), another metabolite endowed with the *normal* sekeleton, was isolated from *Uncaria attenuata* and prepared through partial synthesis from **25** [16] (*Scheme 5*). Unfortunately, no optical rotation nor

Scheme 5

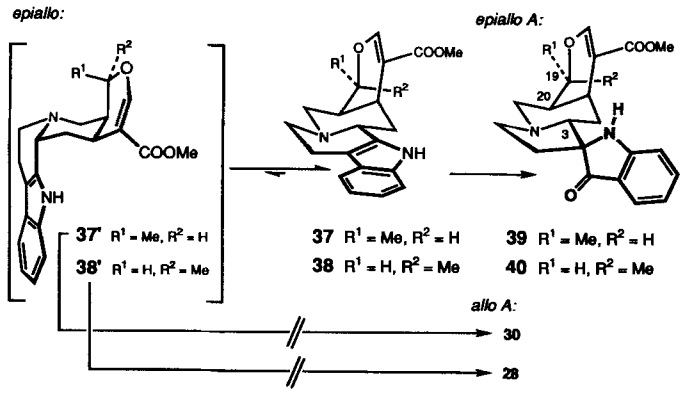


relevant spectroscopic parameters were reported for **26**, and the *A*-type structure proposed by *Phillipson* and *Hemingway* [17], though probably correct, must be regarded as tentative.

Some pseudoindoxyl alkaloids belonging to the *allo* series were also isolated from natural sources. While the derivative **28** of tetrahydroalstonine (**27**) remains to be detected, the corresponding 19-epi compound rauniticine pseudoindoxyl (**30**) was isolated from *Uncaria elliptica* [18] (parent **29**). Again, no significant parameters were revealed that would allow an assignment of the configuration at C(2). In the case of tetraphylline pseudoindoxyl (**32**), isolated from *Neissosperma glomerata* [19] (parent **31**), the indicated chemical shift of *H*–N(1) (5.08 ppm) would point to type *A*. In the case of the isomeric compound aricine pseudoindoxyl (**34**), which was isolated from *E. hirta* [15], the measured optical rotation ($[\alpha]_D = -341$ *vs.* −57 for the parent alkaloid **33**) suggests that it belongs to the *A*-series as well. Isoreserpiline pseudoindoxyl (**36**) seems to represent the most widespread heteroyohimbane derivative within this specialized class of indole alkaloids, since it was isolated from *Rauwolfia vomitoria* AFZEL [6] [20], *Aspidosperma discolor* A. DC. [21], *Rauwolfia volkensii* STAPF. [22], and *Ochrosia moorei* [23]. A partial synthesis from isoreserpiline (**35**; 25% yield over two steps) defined the configuration at all positions, except the spiro centre [6] which was believed to be *A* on the basis of pK_a arguments derived from model compounds[4]). Again, the observed optical rotation for **36** *vs.* **35** is in accordance with the original proposal.

The pseudoindoxyl derivatives **39** and **40** (*Scheme 6*) which are derived from isorauniticine (**37**) and akuammigine (**38**), respectively, are the first and so far only representatives endowed with an *epiallo*-skeleton. They were isolated from *Uncaria elliptica* and

Scheme 6



synthesized from their respective indole precursors [24]. In contrast to **19** (*Scheme 4*), the *epiallo*-pseudoindoxyl of methyl reserpate (**16**), **39** and **40** are not transformed into the corresponding *allo*-compounds, such as **28** and **30**. This different behavior is most probably caused by the different ground-state conformations in the two series: it is known that isorauniticine and akuammigine do not adopt the reserpate-like conformations **37'** and **38'**, but **37** and **38** instead (see [13] and ref. cit. therein), and this seems to hold for the pseudoindoxyls **39** and **40** as well[6]).

Experimental Part

General. $CHCl_3$ and $CDCl_3$ were passed through basic alumina (*Woelm*, act. I) immediately before use. Lead tetraacetate was from *Fluka* (*purum*), recrystallized from AcOH, and dried 24 h at 25°/0.001 Torr. 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], $\log \varepsilon$ [dm^3/mol·cm]): *Kontron Uvikon 869*. IR: *Perkin-Elmer-PE-781* spectrometer; $\tilde{\nu}_{max}$ in cm^{-1}. ^{1}H-NMR: 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: 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, $CDCl_3$); indication of cross-peaks as δ (^{13}C)/δ ('s) (^{1}H). Mass spectra (*m/z* [amu] (% base peak)): *Hitachi-Perkin-Elmer, VG TRIBID*; EI at 70 eV, unless stated otherwise; for FAB; 3-nitrobenzyl alcohol as matrix.

(+)-7α-Acetoxy-7 H-*ajmalicine* (= *Methyl 7α-Acetoxy-16,17-didehydro-19α-methyl-7* H-*18-oxayohimban-16-carboxylate*; (+)-**2**) [7]. To a soln. of ajmalicine (**1**; *Fluka, purum*; 201.3 mg, 0.57 mmol) in CH_2Cl_2 (10 ml) was added PB $(OAc)_4$ (271.2 mg, 0.62 mmol) at r.t. under Ar. After stirring for 30 min, the mixture was filtered through *Celite*® and evaporated. The crude material (^{1}H-NMR: almost pure **2**) was chromatographed (silica gel, cyclohexane/THF/Et_3N 100:40:15): 198.4 mg (85%) of (+)-**2**. White foam. M.p. 184–188° (MeOH; [7]: 198–199°). $[\alpha]_D$ = +218 (*c* = 1.2, $CHCl_3$; [7]: $[\alpha]_D$ = +256). UV (EtOH): 261 (3.73), 238 (4.05), 225 (4.34), 219 (4.39). IR ($CHCl_3$): 2980, 2950, 2815, 2760, 1749, 1702, 1620, 1598, 1437, 1300, 1102, 1091, 1019. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.62 (*ddd*, *J* = 7.7, 1.0, 0.6, 1 H); 7.47 (*d*, *J* = 1.8, 1 H); 7.41 (*ddd*, *J* = 7.4, 1.3, 0.6, 1 H); 7.37 (*td*, *J* = 7.6, 1.3, 1 H); 7.20 (*td*, *J* = 7.5, 1.0, 1 H); 4.36 (*qd*, *J* = 6.6, 4.0, 1 H); 3.71 (*s*, 3 H); 3.08 (*dt*, *J* = 13.2, 2.6, 1 H); 3.05 (*dd*, *J* = 13.2, 2.6, 1 H); 2.93 (*dd*, *J* = 10.5, 2.8, 1 H); 2.73 (*m*, 3 H); 2.33 (*tdd*, *J* = 11.3, 3.2, 1.8, 1 H); 2.19 (*t*,

[6]) *Phillipson* and *Supavita* reported a coupling constant of 4 Hz between *H*–C(19) and *H*–C(20) for akuammigine pseudoindoxyl (**40**) [24]. This value is consistent with the conformation shown in *Scheme 6* and rules out the alternative methyl-reserpate type, like **38'**, for which a higher value would be expected (*trans*-diaxial alignment of the two H-atoms in question) [13].

J = 11.0, 1 H); 2.07 (*s*, 3 H); 2.02 (*tdd*, J = 11.2, 3.8, 3.0, 1 H); 1.77 (*td*, J = 12.3, 10.2, 1 H); 1.48 (*ddd*, J = 14.7, 12.0, 5.2, 1 H); 1.16 (*d*, J = 6.6, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 179.2 (*s*); 168.6 (*s*); 167.3 (*s*); 154.1 (*s*); 153.7 (*d*); 137.1 (*s*); 129.9 (*d*); 126.1 (*d*); 122.3 (*d*); 121.6 (*d*); 107.6 (*s*); 84.9 (*s*); 73.3 (*d*); 60.5 (*d*); 56.9 (*t*); 51.0 (*q*); 50.0 (*t*); 40.9 (*d*); 35.9 (*t*); 30.3 (*t*); 30.0 (*d*); 21.0 (*q*); 14.8 (*q*). HETCOR: 153.7/7.47; 129.9/7.37; 126.1/7.20; 122.3/7.41; 121.6/7.62; 73.3/4.36; 60.5/3.05; 56.9/2.93, 2.19; 51.0/3.71; 50.0/2.75, 2.71; 40.9/2.02; 35.9/2.74, 1.48; 30.3/3.08, 1.77; 30.0/2.33; 21.0/2.07; 14.8/1.16. MS: 410 (3, M^+), 379 (55), 350 (100), 209 (12), 184 (12), 169 (14), 156 (19), 130 (13), 115 (10), 77 (14), 55 (27), 43 (25), 42 (24), 41 (11).

*Base Treatment of (+)-***2** [7]. To a soln. of Na (145 mg, 6.3 mmol) in MeOH (30 ml) was added (+)-**2** (499 mg, 1.22 mmol). The resulting pale yellow soln. was refluxed for 40 min under Ar. The cold deep yellow mixture was poured onto H_2O (20 ml) and extracted 3 times with $CHCl_3$ (80 ml). The combined org. extract was dried (K_2CO_3) and evaporated: 678 mg of a brown foam. The foam was chromatographed (silica gel, $CHCl_3/Et_2O/Et_2NH$ [7]) 100:40:15): 256.2 mg (57%) of the more polar (−)-**3** and 55 mg (13%) of the less polar (+)-**4**.

Ajmalicine Pseudoindoxyl A ((−)-**3**): Yellow, strongly fluorescent crystals. M.p. 210–213° (MeOH; [7]: 223–225°). $[\alpha]_D$ = −183 (c = 0.8, $CHCl_3$; [7]: $[\alpha]_D$ = −203). UV (EtOH): 400 (3.35), 234 (4.30). IR ($CHCl_3$): 3440, 2930, 2810, 1700, 1616, 1486, 1323, 1300, 1187, 1107, 1092. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.58 (*dm*, J = 7.8, 1 H); 7.42 (*d*, J = 1.9, 1 H); 7.41 (*ddd*, J = 7.8, 7.1, 1.4, 1 H); 6.78 (*m*, 2 H); 5.01 (br. *s*, 1 H); 4.36 (*qd*, J = 6.6, 3.5, 1 H); 3.56 (*s*, 3 H); 3.22 (*td*, J = 8.5, 2.2, 1 H); 3.05 (*m*, 1 H); 2.44 (*dd*, J = 11.2, 2.6, 1 H); 2.44 (*ddd*, J = 9.5, 8.5, 7.0, 1 H); 2.36 (*ddd*, J = 14.0, 8.5, 2.5, 1 H); 2.31 (*dt*, J = 12.5, 3.1, 1 H); 2.18 (*m*, 1 H); 1.94–1.88 (*m*, 3 H); 1.12 (*d*, J = 6.6, 3 H); 1.01 (*dt*, J = 12.4, 11.3, 1 H). NOE: irrad. at 5.01 (H–N(1)) → 6.78 (H–C(12)), 1.92 (H_β–C(6)), 1.01 (H_β–C(14)); irrad. at 1.01 (H_β–C(14))→5.01 (H–N(1)), 2.31 (H_α–C(14)). ^{13}C-NMR (100 MHz, $CDCl_3$): 202.1 (*s*); 167.1 (*s*); 160.5 (*s*); 153.9 (*d*); 137.3 (*d*); 124.7 (*d*); 120.5 (*s*); 118.5 (*d*); 111.7 (*d*); 107.4 (*s*); 74.1 (*s*); 73.9 (*d*); 71.5 (*d*); 54.2 (*t*); 52.5 (*t*); 50.8 (*q*); 40.9 (*d*); 35.9 (*t*); 29.8 (*d*); 27.8 (*t*); 14.8 (*q*). HETCOR: 153.9/7.42; 137.3/7.41; 124.7/7.58; 118.5/6.78; 111.7/6.78; 73.9/4.36; 71.5/2.44; 54.2/3.05, 1.93; 52.5/3.22, 2.44; 50.8/3.56; 40.9/1.90; 35.9/2.37, 1.92; 29.8/2.18; 27.8/2.31, 1.01; 14.8/1.12. MS: 368 (100, M^+), 351 (10), 337 (8), 223 (13), 222 (29).

Ajmalicine Pseudoindoxyl B ((+)-**4**): Yellow, strongly fluorescent crystals. M.p. 183–187° (MeOH). $[\alpha]_D$ = +38 (c = 1.0, $CHCl_3$). UV (EtOH): 400 (3.45), 234 (4.45). IR ($CHCl_3$): 3440, 2980, 2800, 1695, 1617, 1299, 1185, 1100. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.57 (*dm*, J = 7.8, 1 H); 7.41 (*d*, J = 1.6, 1 H); 7.40 (*ddd*, J = 7.8, 7.1, 1.3, 1 H); 6.78 (*m*, 2 H); 4.69 (br. *s*, 1 H); 4.35 (*qd*, J = 6.6, 3.6, 1 H); 3.57 (*s*, 3 H); 3.27 (*m*, 1 H); 3.13 (*dd*, J = 10.1, 2.7, 1 H); 2.43–2.35 (*m*, 3 H); 2.31 (*dd*, J = 11.2, 2.6, 1 H); 2.1–2.0 (*m*, 2 H); 1.88 (*m*, 1 H); 1.81 (*t*, J = 10.4, 1 H); 1.10 (*d*, J = 6.6, 3 H); 1.08 (*dt*, J = 12.4, 11.3, 1 H). ^{1}H-NMR (100 MHz, $CDCl_3$): 203.1 (*s*); 167.1 (*s*); 160.4 (*s*); 153.9 (*d*); 137.0 (*d*); 124.7 (*d*); 120.5 (*s*); 118.9 (*d*); 111.9 (*d*); 107.0 (*s*); 73.7 (*d*); 72.9 (*d*); 72.7 (*s*); 54.3 (*t*); 53.1 (*t*); 50.8 (*q*); 40.3 (*d*); 35.5 (*t*); 30.7 (*d*); 28.0 (*t*); 14.8 (*q*). MS: 368 (40, M^+), 351 (4), 337 (4), 223 (46), 222 (100).

*(+)-7α-Acetoxy-7*H*-yohimbine* (= *Methyl 7α-Acetoxy-17α-hydroxy-7*H*-yohimbane-16α-carboxylate*; (+)-**7**) [7]. As described for (+)-**2**, with yohimbine (**5**; *Fluka, purum*; 196.6 mg, 0.555 mmol), CH_2Cl_2 (15 ml), and $Pb(OAc)_4$ (258.8 mg, 0.59 mmol; 15 min): 154.3 mg (67%) of (+)-**7**. White foam. M.p. 121–122° (MeOH; [7]: 123–124°). $[\alpha]_D$ = +174 (c = 1.1, $CHCl_3$; [7]: $[\alpha]_D$ = +198). UV (EtOH): 261 (3.63), 219 (4.29). IR ($CHCl_3$): 2930, 2815, 2750, 1748, 1710, 1597, 1437, 1369, 1149, 1078, 1020. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.61 (*ddd*, J = 7.5, 1.3, 1.0, 1 H); 7.38 (*dm*, J = 7.3, 1 H); 7.37 (*td*, J = 7.5, 1.3, 1 H); 7.20 (*ddd*, J = 7.5, 7.3, 1.0, 1 H); 4.19 (*m*, 1 H); 3.76 (*s*, 3 H); 2.95 (*dd*, J = 10.9, 2.6, 1 H); 2.92 (*dd*, J = 11.1, 3.5, 1 H); 2.80–2.60 (*m*, 3 H); 2.37 (*dd*, J = 11.3, 2.1, 1 H); 2.18 (*t*, J = 10.8, 1 H); 2.05 (*s*, 3 H); 2.05 (*dt*, J = 12.6, 2.7, 1 H); 2.00–1.86 (*m*, 2 H); 1.82 (*dt*, J = 12.6, 11.5, 1 H); 1.62–1.33 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 179.7 (*s*); 175.8 (*s*); 168.7 (*s*); 153.9 (*s*); 137.2 (*s*); 129.8 (*d*); 126.1 (*d*); 122.0 (*d*); 121.5 (*d*); 84.8 (*s*); 66.7 (*d*); 61.5 (*t*); 60.4 (*d*); 52.0 (*d*); 52.0 (*q*); 49.9 (*t*); 40.4 (*d*); 36.2 (*d*); 36.2 (*t*); 31.1 (*t*); 31.0 (*t*); 23.1 (*t*); 21.0 (*q*). HETCOR: 129.8/7.37; 126.1/7.20; 122.0/7.38; 121.5/7.61; 66.7/4.19; 61.5/2.92, 2.18; 60.4/2.95; 52.0/2.37; 52.0/3.76; 49.9/2.75, 2.65; 40.4/1.46; 36.2/2.68, 1.47; 36.2/1.94; 31.1/1.96, 1.50; 31.0/2.05, 1.82; 23.1/1.50, 1.39; 21.0/2.05. FAB-MS: 413 (97, $[M + 1]^+$), 353 (59), 352 (73), 307 (49), 137 (100), 107 (39), 89 (33), 77 (35).

*Base Treatment of (+)-***7** [7]. As described for (−)-**3**/(+)-**4**, with Na (140 mg, 6.1 mmol), MeOH (30 ml), and (+)-**7** (620.5 mg, 1.50 mmol; 90 min; → 730.4 mg of crude brown foam): 300.1 mg (54%) of the more polar (−)-**9** and 81.3 mg (15%) of the less polar (+)-**10**.

Yohimbine Pseudoindoxyl A ((−)-**9**): M.p. 219–220° (dec., MeOH; [7]: 218°). $[\alpha]_D$ = −177 (c = 1.0, $CHCl_3$; [7]: $[\alpha]_D$ = −192). UV (EtOH): 401 (3.53), 234 (4.32). IR ($CHCl_3$): 3440, 2930, 2810, 1700, 1619, 1486, 1466, 1323, 1100, 1008. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.56 (*dm*, J = 7.8, 1 H); 7.43 (*ddd*, J = 8.3, 7.0, 1.3, 1 H); 6.83 (*dt*, J = 8.3, 0.7, 1 H); 6.77 (*ddd*, J = 7.8, 7.0, 0.7, 1 H); 5.18 (br. *s*, 1 H); 4.12 (*m*, 1 H); 3.52 (*s*, 3 H); 3.20 (*td*, J = 8.3,

[7]) With Et_3N instead of Et_2NH, the two epimers could also be separated, but during evaporation of the solvent, some 20% of the *B*-isomer (+)-**4** isomerized back to (−)-**3**.

2.2, 1 H); 3.03 (*dd*, *J* = 11.0, 3.7, 1 H); 2.44–2.32 (*m*, 3 H); 2.18 (*dd*, *J* = 11.6, 2.1, 1 H); 1.96–1.88 (*m*, 3 H); 1.75 (*qd*, *J* = 11.2, 4.0, 1 H); 1.55 (*qd*, *J* = 13.5, 3.3, 1 H); 1.45 (*m*, 1 H); 1.38 (*m*, 1 H); 1.29 (*m*, 1 H); 1.15–1.05 (*m*, 2 H). NOE: irrad. at 5.18 (H–N(1)) → 6.83 (H–C(12)), 1.92 (H_β–C(6)), 1.12 (H_β–C(14)). ^{13}C-NMR (100 MHz, $CDCl_3$): 202.1 (*s*); 175.4 (*s*); 160.5 (*s*); 137.2 (*d*); 124.6 (*d*); 120.4 (*s*); 118.3 (*d*); 111.8 (*d*); 74.4 (*s*); 71.4 (*d*); 66.5 (*d*); 58.6 (*t*); 52.7 (*t*); 52.5 (*d*); 51.7 (*q*); 40.5 (*d*); 35.8 (*d*); 35.3 (*t*); 31.3 (*t*); 28.8 (*t*); 23.4 (*t*). HETCOR: 137.2/7.43; 124.6/7.56; 118.3/6.77; 111.8/6.83; 71.4/2.35; 66.5/4.12; 58.6/3.03, 1.92; 52.7/3.20, 2.40; 52.5/2.19; 51.7/3.52; 40.5/1.29; 35.8/1.75; 35.3/2.32, 1.90; 31.3/1.92, 1.45; 28.8/1.12, 1.09; 23.4/1.55, 1.38. FAB-MS: 371 (100, $[M + 1]^+$), 370 (54), 369 (35), 224 (27).

Yohimbine Pseudoindoxyl B ((+)-**10**): M.p. 193° (MeOH). $[\alpha]_D$ = +83 (*c* = 1.1, $CHCl_3$). UV (EtOH): 399 (3.38), 254 (3.76), 230 (4.27). IR ($CHCl_3$): 3440, 2935, 2800, 1706, 1620, 1486, 1469, 1438, 1322, 1170. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.54 (*dm*, *J* = 7.8, 1 H); 7.40 (*ddd*, *J* = 8.0, 7.1, 1.3, 1 H); 6.79 (*dm*, *J* = 8.0, 1 H); 6.78 (*m*, 1 H); 4.60 (br. *s*, 1 H); 4.11 (*m*, 1 H); 3.52 (*s*, 3 H); 3.33 (*m*, 1 H); 3.10 (*dd*, *J* = 10.9, 3.2, 1 H); 2.45–2.30 (*m*, 2 H); 2.23 (*dd*, *J* = 11.5, 2.1, 1 H); 2.20 (br. *dd*, *J* = 8.0, 5.6, 1 H); 1.96–1.82 (*m*, 2 H); 1.80 (*t*, *J* = 10.5, 1 H); 1.68 (*m*, 1 H); 1.50–1.35 (*m*, 4 H); 1.17 (*m*, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 203.0 (*s*); 175.9 (*s*); 160.3 (*s*); 136.9 (*d*); 124.6 (*d*); 120.5 (*s*); 118.8 (*d*); 111.8 (*d*), 73.2 (*s*); 72.9 (*d*); 66.7 (*d*); 58.7 (*t*); 53.3 (*t*), 52.2 (*d*); 51.5 (*q*); 39.6 (*d*); 36.8 (*d*); 35.2 (*t*); 31.2 (*t*); 29.4 (*t*); 23.4 (*t*). HETCOR: 136.9/7.40; 124.6/7.54; 118.8/6.78; 111.8/6.79; 79.2/2.20; 66.7/4.11; 58.7/3.10, 1.80; 53.3/3.33, 2.36; 52.2/2.22; 51.5/3.52; 39.6/1.45; 36.8/1.68; 35.2/2.38, 1.87; 31.2/1.92, 1.45; 29.4/1.17; 23.4/1.45, 1.36. MS: 370 (17, M^+), 225 (38), 224 (100), 130 (11).

*(+)-7α-Acetoxy-7*H*-corynanthine* (= *Methyl 7α-Acetoxy-17α-hydroxy-7*H*-yohimbane-16β-carboxylate*; (+)-**8**). As described for (+)-**2**, with corynanthine (**6**, 300.8 mg, 0.85 mmol; prepared from the commercially available hydrochloride (*Aldrich*)), CH_2Cl_2 (25 ml), and $Pb(OAc)_4$ (361.8 mg, 0.82 mmol; 40 min). Chromatography (silica gel, $CHCl_3$/EtOH 5:1) gave 279.8 mg (81%) of crystalline (+)-**8**. M.p. 128–129° (MeOH). $[\alpha]_D$ = +113 (*c* = 0.8, $CHCl_3$). UV (EtOH): 264 (3.59), 219 (4.28). IR ($CHCl_3$): 3615, 2930, 2860, 2815, 2750, 1740, 1596, 1434, 1368, 1162, 1119, 1076, 1015, 1010, 952. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.60 (*dt*, *J* = 7.6, 0.8, 1 H); 7.40 (*ddd*, *J* = 7.3, 1.3, 0.6, 1 H); 7.37 (*td*, *J* = 7.7, 1.3, 1 H); 7.19 (*td*, *J* = 7.4, 1.0, 1 H); 4.23 (*q*, *J* = 2.7, 1 H); 3.69 (*s*, 3 H); 2.95 (*dd*, *J* = 10.9, 3.8, 1 H); 2.91 (*dd*, *J* = 10.1, 3.3, 1 H); 2.80 (*m*, 1 H); 2.75 (*ddd*, *J* = 11.6, 4.1, 2.3, 1 H); 2.69 (*dt*, *J* = 14.2, 2.2, 1 H); 2.61 (*ddd*, *J* = 12.7, 11.6, 2.2, 1 H); 2.14 (*m*, 1 H); 2.10–1.95 (*m*, 6 H, incl. 2.04 (*s*, 3 H)); 1.87 (*tt*, *J* = 11.7, 4.2, 1 H); 1.71 (*dm*, *J* = 14.1, 1 H); 1.49 (*ddd*, *J* = 14.2, 12.7, 4.3, 1 H); 1.45–1.35 (*m*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 179.7 (*s*); 172.4 (*s*); 168.7 (*s*); 154.1 (*s*); 137.1 (*s*); 129.9 (*d*); 126.1 (*d*); 122.2 (*d*); 121.5 (*d*); 84.8 (*s*); 67.8 (*d*); 62.6 (*t*); 61.3 (*d*); 51.5 (*q*); 51.0 (*d*); 49.9 (*t*); 36.3 (*d*); 35.7 (*t*); 34.4 (*d*); 30.3 (*t*); 28.5 (*t*); 23.6 (*t*); 21.0 (*q*). HETCOR: 129.9/7.37; 126.1/7.19; 122.2/7.40; 121.5/7.60; 67.8/4.23; 62.6/2.95, 2.02; 61.3/2.91; 51.5/3.69; 51.0/2.80; 49.9/2.75, 2.61; 36.3/1.87; 35.7/2.69, 1.49; 34.4/2.14; 30.3/2.0, 1.42; 28.5/2.0, 1.87; 23.6/2× *ca.* 1.4; 21.0/2.04. MS: 412 (0.5, M^+), 381 (2), 352 (100), 293 (13), 277 (12), 221 (14), 205 (20).

*Base Treatment of (+)-***8**. A soln. of (+)-**8** (203.7 mg, 0.50 mmol) in 0.2M NaOMe/MeOH (12 ml) was refluxed for 30 min. Workup with ice and $CHCl_3$ furnished a brown foam (168.5 mg) which was chromatographed (silica gel, $CHCl_3$/EtOH 5:1): 19 mg (10%) of the more polar (+)-**12** and 102.8 mg (56%) of the less polar (−)-**11**.

Corynanthine Pseudoindoxyl A ((−)-**11**): M.p. 190° (dec., MeOH). $[\alpha]_D$ = −159 (*c* = 0.5, $CHCl_3$). UV (EtOH): 400 (3.32), 234 (4.13). IR ($CHCl_3$): 3610, 3435, 2930, 2805, 1728, 1695, 1619, 1486, 1467, 1323, 1163. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.55 (*dm*, *J* = 7.8, 1 H); 7.42 (*ddd*, *J* = 8.3, 7.0, 1.3, 1 H); 6.81 (*dt*, *J* = 8.3, 0.8, 1 H); 6.76 (*ddd*, *J* = 7.8, 7.0, 0.8, 1 H); 5.42 (br. *s*, 1 H); 4.17 (*q*, *J* = 2.7, 1 H); 3.58 (*s*, 3 H); 3.23 (*m*, 1 H); 3.07 (*dd*, *J* = 10.7, 3.9, 1 H); 2.59 (*m*, 1 H); 2.40–2.31 (*m*, 3 H); 2.00–1.88 (*m*, 3 H); 1.79 (*t*, *J* = 10.8, 1 H); 1.75–1.65 (*m*, 2 H); 1.45–1.30 (*m*, 3 H); 1.14 (*dt*, *J* = 12.5, 3.1, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 202.3 (*s*); 172.5 (*s*); 160.7 (*s*); 137.3 (*d*); 124.5 (*d*); 120.2 (*s*); 118.2 (*d*); 111.6 (*d*); 74.4 (*s*); 72.4 (*d*); 67.5 (*d*); 59.5 (*t*); 52.9 (*t*); 51.3 (*d*); 51.2 (*q*); 35.7 (*d*); 35.1 (*t*); 34.2 (*d*); 28.7 (*t*); 27.9 (*t*); 23.7 (*t*). HETCOR: 137.3/7.42; 124.5/7.55; 118.2/6.76; 111.6/6.81; 72.4/2.34; 67.5/4.17; 59.5/3.07, 1.79; 52.9/3.23, 2.32; 51.3/2.59; 51.2/3.58; 35.7/1.72; 35.1/2.32, 1.94; 34.2/1.95; 28.7/2.00, 1.72; 27.9/1.36, 1.14; 23.7/1.42, 1.36. MS: 370 (26, M^+), 225 (45), 224 (100).

Corynanthine Pseudoindoxyl B ((+)-**12**): M.p. 178–182 (MeOH). $[\alpha]_D$ = +38 (*c* = 0.8, $CHCl_3$). UV (EtOH): 399 (3.40), 247 (3.78), 233 (4.25). IR ($CHCl_3$): 3610, 3435, 2930, 2855, 2790, 1728, 1697, 1619, 1483, 1468, 1319, 1163, 1150, 1100. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.59 (*dm*, *J* = 7.6, 1 H); 7.41 (*ddd*, *J* = 8.2, 7.1, 1.3, 1 H); 6.81 (*m*, 2 H); 4.74 (br. *s*, 1 H); 4.15 (*q*, *J* = 2.6, 1 H); 3.60 (*s*, 3 H); 3.26 (*m*, 1 H); 3.14 (*dd*, *J* = 11.0, 4.0, 1 H); 2.60 (*m*, 1 H); 2.45–2.35 (*m*, 2 H); 2.25 (*m*, 1 H); 2.10–1.95 (*m*, 2 H); 1.89 (*m*, 1 H); 1.75–1.55 (*m*, 3 H); 1.45–1.20 (*m*, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 202.4 (*s*); 172.3 (*s*); 160.2 (*s*); 136.9 (*d*); 124.7 (*d*); 120.6 (*s*); 118.9 (*d*); 111.7 (*d*); 73.6 (*s*); 73.4 (*d*); 67.5 (*d*); 59.3 (*t*); 53.0 (*t*); 51.35 (*q*); 51.28 (*d*); 36.8 (*d*); 35.1 (*t*); 33.4 (*d*); 28.8 (2x*t*); 23.7 (*t*). HETCOR: 136.9/7.41; 124.7/7.59; 118.9/6.81; 111.7/6.81; 73.4/2.25; 67.5/4.15; 59.3/3.14, 1.62; 53.0/3.26, 2.38; 51.35/3.60; 51.28/2.60; 36.8/1.63; 35.1/2.40, 1.89; 33.4/2.05; 28.8/2.02, 1.71 + 1.68, 1.24; 23.7/1.43, 1.31. MS: 370 (22, M^+), 225 (35), 224 (100).

*(−)-7β-Acetoxy-7*H*-pseudoyohimbine* (= *Methyl 7β-Acetoxy-17α-hydroxy-7*H*-3β-yohimbane-16α-carboxylate*; (−)-**14**). As described for (+)-**2**, with pseudoyohimbine (**13**; 44.6 mg, 0.126 mmol; prepared from **5** according to [26]), CH_2Cl_2 (12 ml), and $Pb(OAc)_4$ (67.2 mg, 0.15 mmol; 85 min). The crude material (79.4 mg) was chromatographed (silica gel, benzene/Et_2O/MeOH 7:2:1): 22.6 mg (44%) of (−)-**14**. Buff crystals. M.p. 191–192° (MeOH). $[\alpha]_D = -135$ ($c = 1.0$, $CHCl_3$). UV (EtOH): 289 (3.56), 252 (3.70), 219 (4.23). IR ($CHCl_3$): 2930, 2860, 1745, 1712, 1590, 1438, 1369, 1238, 1170, 1017. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (*dm*, $J = 7.6$, 1 H); 7.40–7.32 (*m*, 2 H); 7.19 (*td*, $J = 7.4, 0.9$, 1 H); 4.18 (*m*, 1 H); 4.02 (*dd*, $J = 5.8, 1.4$, 1 H); 3.77 (*s*, 3 H); 3.37 (*td*, $J = 13.4, 2.4$, 1 H); 2.75 (*ddd*, $J = 14.3, 4.1, 1.5$, 1 H); 2.65 (*qd*, $J = 11.4, 3.9$, 1 H); 2.55 (*dt*, $J = 14.5, 2.0$, 1 H); 2.28–2.15 (*m*, 4 H); 2.03 (*s*, 3 H); 1.94 (*m*, 1 H); 1.81 (*td*, $J = 14.5, 4.2$, 1 H); 1.61 (*td*, $J = 12.3, 5.9$, 1 H); 1.55–1.40 (*m*, 2 H); 1.35 (*m*, 1 H); 1.25 (*m*, 1 H). NOE: irrad. at 4.02 (H–C(3)) → 3.37 (H_β–C(5)), 2.03 (AcO), 2.20 (H_α–C(14)), 1.61 (H_β–C(14)); irrad. at 2.03 (AcO) → 4.02 (H–C(3)), 3.37 (H_β–C(5)). ^{13}C-NMR (100 MHz, $CDCl_3$): 177.2 (*s*); 176.3 (*s*); 168.9 (*s*); 154.3 (*s*); 137.0 (*s*); 129.7 (*d*); 125.8 (*d*); 122.0 (*d*); 121.9 (*d*); 86.3 (*s*); 66.6 (*d*); 54.6 (*d*); 52.7 (*d*); 51.9 (*q*); 51.9 (*t*); 48.8 (*t*); 41.6 (*d*); 35.9 (*t*); 31.7 (*d*); 31.1 (*t*); 30.0 (*t*); 23.4 (*t*); 21.0 (*q*). HETCOR: 129.7/7.38; 125.8/7.19; 122.0/7.37; 121.9/7.68; 66.6/4.18; 54.6/4.02; 52.7/2.18; 51.9/3.77; 51.9/2.26, 2.25; 48.8/3.37, 2.75; 41.6/1.35; 35.9/2.55, 1.81; 31.7/2.65; 31.1/1.94, 1.45; 30.0/2.20, 1.61; 23.4/1.52, 1.25; 21.0/2.03. FAB-MS: 413 (100, $[M + 1]^+$), 353 (51), 352 (70).

*Base Treatment of (−)-***14**. As described for (+)-**12**/(−)-**11**, with (−)-**14** (83 mg, 0.20 mmol) and 0.2M NaOMe/MeOH (25 ml; 2 h). The brown foam (68.7 mg) was chromatographed (silica gel, $CHCl_3/Et_2O/Et_2NH$ 100:40:15): 43.2 mg (58%) of (−)-**9** and 8.9 mg (12%) of (+)-**10** (see above).

*Methyl 7β-Acetoxy-7*H*-reserpate* (= *Methyl 7β-Acetoxy-18β-hydroxy-11,17α-dimethoxy-7*H*-3β,20α-yohimbane-16β-carboxylate*; (−)-**18**). As described for (+)-**2**, with methyl reserpate [14] (**16**; 625.8 mg, 1.51 mmol; prepared from commercially available reserpine (*Aldrich*)), CH_2Cl_2 (35 ml), and $Pb(OAc)_4$ (770 mg, 1.76 mmol; 40 min). The crude material (1124 mg) was chromatographed (silica gel, $CHCl_3/Et_3O/Et_3N$ 10:5:1): 431.8 mg (61%) of slightly yellow amorphous (−)-**18**. M.p. 146–147° (sintering). $[\alpha]_D = -175$ ($c = 0.9$, $CHCl_3$). UV (EtOH): 285 (3.47), 231 (4.27). IR ($CHCl_3$): 3640, 3600, 2950, 2815, 1735, 1590, 1480, 1368, 1278, 1125, 1025. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.26 (*d*, $J = 8.1$, 1 H); 7.18 (*d*, $J = 2.3$, 1 H); 6.71 (*dd*, $J = 8.1, 2.3$, 1 H); 3.96 (*t*, $J = 3.2$, 1 H); 3.83 (*s*, 3 H); 3.80 (*s*, 3 H); 3.60 (*s*, 3 H); 3.59–3.52 (*m*, 2 H); 3.31 (*ddd*, $J = 14.2, 13.5, 2.2$, 1 H); 2.95 (*m*, 1 H); 2.68 (*dd*, $J = 11.5, 3.3$, 1 H); 2.64 (*ddd*, $J = 14.3, 4.2, 1.5$, 1 H); 2.60 (*dd*, $J = 10.6, 4.9$, 1 H); 2.55 (*dt*, $J = 14.5$, *ca.* 2, 1 H); 2.21–2.13 (*m*, 2 H); 2.02 (*s*, 3 H); 2.02–1.96 (*m*, 2 H); 1.85–1.75 (*m*, 2 H); 1.65 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 178.8 (*s*); 172.8 (*s*); 168.9 (*s*); 161.3 (*s*); 155.9 (*s*); 129.1 (*s*); 122.7 (*d*); 111.6 (*d*); 107.3 (*d*); 86.1 (*s*); 81.5 (*d*); 75.2 (*d*); 61.1 (*q*); 55.6 (*q*); 54.5 (*d*); 51.8 (*q*); 51.6 (*d*); 50.2 (*t*); 48.9 (*t*); 36.3 (*t*); 35.0 (*d*); 32.0 (*t*); 31.9 (*d*); 22.3 (*t*); 21.1 (*q*). HETCOR: 122.7/7.26; 111.6/6.71; 107.3/7.18; 81.5/3.54; 75.2/3.56; 61.1/3.60; 55.6/3.83; 54.5/3.96; 51.8/3.80; 51.6/2.60; 50.2/2.68, 2.18; 48.9/3.31, 2.64; 36.3/2.55, 1.80; 35.0/1.83; 32.0/2.18, 1.65; 31.9/2.95; 22.3/2.01, 2.00; 21.1/2.02. MS: 472 (0.3, M^+), 441 (1), 430 (1), 412 (100), 251 (40), 205 (45).

*Methyl 7α-Acetoxy-7*H*-3-isoreserpate* (= *Methyl 7α-Acetoxy-18β-hydroxy-11,17α-dimethoxy-7*H*-20α-yohimbane-16β-carboxylate*; (+)-**20**) [7]. As described for (+)-**2**, with methyl isoreserpate (**17**; 684.3 mg, 1.65 mmol; prepared in 86% yield from methyl reserpate (**16**) according to [14]), CH_2Cl_2 (35 ml), and $Pb(OAc)_4$ (880 mg, 2.01 mmol; 30 min). The crude material (1008 mg) was chromatographed (silica gel, $CHCl_3/Et_2O/Et_3N$ 10:5:1): 375.4 mg (52%) of slightly yellow amorphous (+)-**20**. M.p. 134–140° (sintering). $[\alpha]_D = +102$ ($c = 1.1$, $CHCl_3$). UV (EtOH): 288 (3.13), 231 (4.06). IR ($CHCl_3$): 3600, 2950, 2810, 2755, 1738, 1599, 1481, 1368, 1278, 1145, 1025. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.28 (*d*, $J = 8.2$, 1 H); 7.23 (*d*, $J = 2.3$, 1 H); 6.73 (*dd*, $J = 8.2, 2.3$, 1 H); 3.84 (*s*, 3 H); 3.75 (*s*, 3 H); 3.64 (*dd*, $J = 10.8, 9.0$, 1 H); 3.61 (*s*, 3 H); 3.50 (*m*, 1 H); 2.82 (*dd*, $J = 11.4, 1.8$, 1 H); 2.74 (*dm*, $J = 11.5$, 1 H); 2.68–2.62 (*m*, 2 H); 2.59 (*dd*, $J = 10.9, 3.8$, 1 H); 2.54–2.47 (*m*, 2 H); 2.22–2.08 (*m*, 3 H); 2.04 (*s*, 3 H); 1.89 (*m*, 1 H); 1.81 (*m*, 1 H); 1.69 (*dt*, $J = 13.0, 4.1$, 1 H); 1.45 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 180.8 (*s*); 172.3 (*s*); 168.9 (*s*); 161.4 (*s*); 155.7 (*s*); 129.0 (*s*); 122.8 (*d*); 111.9 (*d*); 107.3 (*d*); 84.6 (*s*); 81.1 (*d*); 75.4 (*d*); 61.2 (*q*); 60.8 (*d*); 60.2 (*t*); 55.6 (*q*); 52.0 (*d*); 51.8 (*q*); 50.0 (*t*); 37.6 (*d*); 35.9 (*t*); 35.1 (*d*); 32.6 (*t*); 23.9 (*t*); 21.1 (*q*). HETCOR: 122.8/7.28; 111.9/6.73; 107.3/7.23; 81.1/3.64; 75.4/3.50; 61.2/3.61; 60.8/2.74; 60.2/2.82, 2.50; 55.6/3.84; 52.0/2.59; 51.8/3.75; 50.0/2.65, 2.51; 37.6/2.20; 35.9/2.66, 1.45; 35.1/1.89; 32.6/2.11, 1.69; 23.9/2.20, 1.81; 21.1/2.04. EI-MS: 472 (0.3, M^+), 441 (1.5), 430 (1), 412 (100), 251 (20), 199 (20).

*Base Treatment of (+)-***20** [7]. As described for (−)-**3**/(+)-**4**, with Na (128 mg, 5.6 mmol), MeOH (25 ml), and (+)-**20** (427.3 mg, 0.90 mmol; 3 h). Workup with H_2O (15 ml) and $CHCl_3$ (60 ml). The brown foam (323.8 mg) was chromatographed (silica gel, $CHCl_3/Et_2O/Et_2NH$ 10:5:1): 204.1 mg (48%) of the more polar (−)-**21** and 39 mg (10%) of the less polar (+)-**22**.

Methyl Isoreserpate Pseudoindoxyl A (**21**): M.p. 160–165° (MeOH). $[\alpha]_D = -126$ ($c = 0.9$, $CHCl_3$; [7]: $[\alpha]_D = -93$). UV (EtOH): 381 (3.55), 282 (3.94), 248 (4.20), 227 (4.15). IR ($CHCl_3$): 3600, 3440, 2945, 2800, 2735, 1731, 1675, 1620, 1456, 1302, 1167, 1100. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.45 (*d*, $J = 8.6$, 1 H); 6.34 (*dd*, $J = 8.6, 2.1$, 1 H); 6.24 (*d*, $J = 2.1$, 1 H); 5.23 (br. *s*, 1 H); 3.85 (*s*, 3 H); 3.59 (*s*, 3 H); 3.58 (*td*, $J = 9.2, 5.0$, 1 H); 3.56 (*s*, 3 H); 3.46

(*dd*, *J* = 11.0, 9.1, 1 H); 3.13 (*m*, 1 H); 2.94 (*dd*, *J* = 11.2, 1.7, 1 H); 2.57 (*dd*, *J* = 11.0, 4.7, 1 H); 2.32–2.24 (*m*, 3 H); 2.19 (*dd*, *J* = 11.1, 2.8, 1 H); 2.10 (*q*, *J* = 12.5, 1 H); 2.04 (*m*, 1 H); 1.88–1.80 (*m*, 2 H); 1.73 (*dt*, *J* = 12.9, 3.9, 1 H); 1.54 (*td*, *J* = 13.0, 11.5, 1 H); 1.00 (*dt*, *J* = 13.2, 3.3, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 199.7 (*s*); 172.3 (*s*); 168.0 (*s*); 162.7 (*s*); 125.9 (*d*); 113.7 (*s*); 108.6 (*d*); 94.0 (*d*); 81.3 (*d*); 75.2 (*s*); 74.9 (*d*); 71.2 (*d*); 61.1 (*q*); 57.4 (*t*); 55.6 (*q*); 52.9 (*t*); 51.8 (*q*); 51.3 (*d*); 37.1 (*d*); 35.9 (*t*); 34.8 (*d*); 32.9 (*t*); 21.9 (*t*). HETCOR: 125.9/7.45; 108.6/6.34; 94.0/6.24; 81.3/3.46; 74.9/3.58; 71.2/2.19; 61.1/3.56; 57.4/2.94, 2.27; 55.6/3.85; 52.9/3.13, 2.28; 51.8/3.59; 51.3/2.57; 37.1/2.04; 35.9/2.28, 1.87; 34.8/1.83; 32.9/2.10, 1.73; 21.9/1.54, 1.00. EI-MS: 430 (17, M^+), 255 (22), 254 (100), 176 (17), 150 (11), 94 (16).

Methyl Isoreserpate Pseudoindoxyl B (**22**): M.p. 151–154° (MeOH). $[\alpha]_D = +35$ ($c = 0.7$, $CHCl_3$). UV (EtOH): 380 (3.58), 280 (4.00), 249 (4.26), 228 (4.20). IR ($CHCl_3$): 3590, 3430, 2945, 2790, 2735, 1730, 1709, 1685, 1610, 1456, 1291, 1164, 1098. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.52 (*d*, *J* = 8.6, 1 H); 6.39 (*dd*, *J* = 8.6, 2.1, 1 H); 6.20 (*d*, *J* = 2.1, 1 H); 4.59 (br. *s*, 1 H); 3.83 (*s*, 3 H); 3.56 (*s*, 3 H); 3.54 (*s*, 3 H); 3.50 (*m*, 1 H); 3.43 (*dd*, *J* = 10.9, 9.3, 1 H); 3.17 (*tm*, *J* = 8.2, 2 H); 3.03 (*dd*, *J* = 10.9, 1.6, 1 H); 2.54 (*dd*, *J* = 10.9, 4.7, 1 H); 2.41 (*ddd*, *J* = 13.5, 10.5, 8.0, 1 H); 2.25–2.09 (*m*, 3 H); 2.00 (br. *dd*, *J* = 11.2, 2.5, 1 H); 1.93 (*dq*, *J* = 13.0, 4.0, 1 H); 1.82–1.74 (*m*, 3 H); 1.63 (*q*, *J* = 13.0, 1 H); 1.01 (*dt*, *J* = 13.0, 3.0, 1 H). NOE: irrad. at 4.59 (H–N(1)) → 6.20 (H–C(12)), 2.00 (H–C(3)), 1.80 (H_π–C(6)), weak signal at 1.01 (H_α–C(14)). ^{13}C-NMR (100 MHz, $CDCl_3$): 200.5 (*s*); 172.5 (*s*); 167.5 (*s*); 162.3 (*s*); 126.4 (*d*); 114.1 (*s*); 108.3 (*d*); 94.4 (*d*); 81.1 (*d*); 75.7 (*d*); 73.4 (*d*); 73.2 (*s*); 61.1 (*q*); 57.6 (*t*); 55.6 (*q*); 53.6 (*t*); 51.8 (*d*); 51.5 (*q*); 38.3 (*d*); 35.2 (*t*); 34.9 (*d*); 33.4 (*t*); 22.5 (*t*). MS: 430 (9, M^+), 255 (11), 254 (61), 240 (12), 176 (100).

*Base Treatment of (–)-***18** [7]. As described for (+)-**12**/(–)-**11**, with (–)-**18** (375.4 mg, 0.79 mmol) and 0.2M NaOMe in MeOH (25 ml; 85 min). The brown foam (308 mg) was chromatographed (silica gel, $CHCl_3$/EtOH 10:1): 40.8 mg (12%) of (–)-**22** and 173.2 mg (51%) of (+)-**21**.

REFERENCES

[1] R. Güller, H.-J. Borschberg, *Helv. Chim. Acta* **1993,** *76,* 1847.

[2] a) H. Kondo, T. Fukuda, M. Tomita, *J. Pharm. Soc. Japan* **1928,** *48*, 54; b) T. Nozoye, *Pharm. Bull. (Japan)* **1958,** *6,* 300.

[3] J. C. Seaton, M. D. Nair, O. E. Edwards, L. Marion, *Can. J. Chem.* **1960,** *38,* 1035.

[4] E. Wenkert, J. H. Udelhofen, N. K. Bhattacharyya, *J. Am. Chem. Soc.* **1959,** *81,* 3763.

[5] a) J. S. Bindra, 'Oxindole Alkaloids', in 'The Alkaloids', Ed. R. H. F. Manske, Academic Press, New York, 1973, Vol. XIV, pp. 83–121; b) R. T. Brown, in 'The Monoterpenoid Indole Alkaloids', Ed. J. E. Saxton, John Wiley & Sons, New York, 1983, Chapt. III, pp. 85–96; c) J. E. Saxton, 'Alkaloids of *Mitragyna* and *Ourouparia* Species', in 'The Alkaloids', Ed. R. H. F. Manske, Academic Press, New York, 1965, Vol. VIII, pp. 59–91; d) J. E. Saxton, *ibid.*, 1968 Vol. X, pp. 521–548.

[6] N. Finch, W. I. Taylor, P. R. Ulshafer, *Experientia* **1963,** *19,* 296.

[7] N. Finch, C. W. Gemenden, I. H.-C. Hsu, A. Kerr, G. A. Sim, W. I. Taylor, *J. Am. Chem. Soc.* **1965,** *87,* 2229.

[8] E. Wenkert, C.-J. Chang, H. P. S. Chawla, D. W. Cochran, E. W. Hagaman, J. C. King, K. Orito, *J. Am. Chem. Soc.* **1976,** *98,* 3645.

[9] R. H. Levin, J.-Y. Lallemand, J. D. Roberts, *J. Org. Chem.* **1973,** *38,* 1983.

[10] I. W. Southon, J. Buckingham, 'Dictionary of Alkaloids', Chapman and Hall, London–New Work, 1989, p. 251.

[11] H. S. Aaron, C. P. Ferguson, *Tetrahedron Lett.* **1968,** 6191.

[12] P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry', Pergamon Press, Oxford, 1983, Chapt. 6.

[13] M. Lounasmaa, S.-K. Kan, *Tetrahedron* **1980,** *36,* 1607.

[14] H. B. MacPhillamy, C. F. Hübner, E. Schlittler, A. F. St. André, P. R. Ulshafer, *J. Am. Chem. Soc.* **1955,** *77,* 4335.

[15] G. M. T. Robert, A. Ahond, C. Poupat, P. Potier, H. Jacquemin, S. K. Kan, *J. Nat. Prod.* **1983,** *46,* 708.

[16] P. Clivio, B. Richard, J.-R. Deverre, T. Sévenet, M. Zeches, L. Le Men-Olivier, *Phytochemistry* **1991,** *30,* 3785.

[17] J. D. Phillipson, S. R. Hemingway, *Phytochemistry* **1975,** *14,* 1855.

[18] J. D. Phillipson, N. Supavita, *Phytochemistry* **1983,** *22,* 1809.

[19] E. Seguin, F. Hotellier, M. Koch, T. Sévenet, *J. Nat. Prod.* **1984,** *47,* 687.

[20] a) M. M. Iwu, W. E. Court, *Planta Med.* **1977,** *32,* 88; b) N. N. Sabri, W. E. Court, *Phytochemistry* **1978,** *17,* 2023; c) W. E. Court, M. M. Iwu, *J. Chromatogr.* **1980,** *187,* 19.

[21] N. Dastoor, H. Schmid, *Experientia* **1963,** *19,* 297.

[22] B. A. Akinloye, W. E. Court, *J. Ethnopharmacol.* **1981,** 99.

[23] A. Ahond, H. Fernandez, M. Julia-Moore, C. Poupat, V. Sanchez, P. Potier, *J. Nat. Prod.* **1981,** *44,* 193.

[24] J. D. Phillipson, N. Supavita, *Phytochemistry* **1983,** *22,* 1809.

[25] M. Lounasmaa, A. Tolvanen, S.-K. Kan, *Heterocycles* **1985,** *23,* 371.

[26] W. O. Godfredsen, S. Vangedal, *Acta Chem. Scand.* **1956,** *10,* 1414.