Buxus alkaloids
XX.* Alkaloids of *Buxus arborescens* MILL.

P. MOKRÝ and Z. VOTICKÝ

Institute of Chemistry, Centre for Chemical Research, Slovak Academy of Sciences, CS-842 38 Bratislava

Received 25 October 1982

Twelve steroid alkaloids were isolated from the leaves of *Buxus arborescens* MILL. Cyclobuxine-D, cyclovirobuxine-D, cycloprotobuxine-A, cycloprotobuxine-C, cycloprotobuxine-D, buxamine-A, buxamine-E, buxaminol-E, buxtauine-M, and buxpsiine-K have already been reported in other species of the Buxus family, the two new alkaloids, the structures of which were adduced from spectral data, and for the first one also corroborated by correlation, were denominated *O*-tigloylcyclovirobuxeine-A and buxbarbarine-K.

Из листьев *Buxus arborescens* MILL. было выделено двенадцать стероидных алкалоидов: циклобуксин-D, цикловиробуксин-D, циклопротобуксин-A, циклопротобуксин-C, циклопротобуксин-D, буксамин-A, буксамин-E, буксаминол-E, букстауин-M и букспсиин-K были уже раннее выделены из других видов рода Buxus L.; новый алкалоид, структура которого была установлена спектральными методами и подтверждена корреляцией, был назван *O*-тиглоилцикловиробуксеин-A. Другой новый алкалоид, состав которого был предложен на основе спектральных данных, был назван буксбарбарин-K.

The curative effect of compounds present in box trees was known in ancient times and the extract of those plants was used to cure various diseases. The number of alkaloids having been isolated from various species and varieties exceeded one hundred [1—3], some of them being, however, artifacts [4, 5]. This paper is a continuation of a systematic chemical investigation of Buxus alkaloids; those present in *Buxus arborescens* MILL. have not been studied as yet.

The chloroform solution of the mixture of bases, obtained from the ground dried leaves in a routine way [6], was separated into portions extractable with McIlvain

* For Part XIX see *Collect. Czech. Chem. Commun. 46*, 1425 (1981).

buffer solutions of pH 6.5, 6.0, 5.0, 4.0, and 3.0. The individual alkaloids were prepared from them by the procedure already described [6].

The pH 6.5 portion afforded a crystalline compound the molecular radical ion peak of which appeared at *m/z* 414.3966 (for $C_{28}H_{50}N_2$ calculated $M_r = 414.3974$), the peaks of other fragment ions indicated dimethylamino groups at C-20 and C-3 [7]. The infrared spectrum displayed vibration bands of a dimethylamino grouping, a methylene in the cyclopropane ring, and a geminal dimethyl group. These data together with optical rotation, melting point, R_f data [5], and a mixed melting point with the specimen without depression characterized this alkaloid as cycloprotobuxine-A.

Another compound of this portion revealed vibration bands in the i.r. spectrum attributable to a secondary amino group, a methylene in the cyclopropane ring, and a hydroxyl group. The peak of molecular radical ion occurred at *m/z* 386.3305 (for $C_{25}H_{42}N_2O$ calculated $M_r = 386.3297$), peaks of fragment ions indicated the presence of methylamino groups at C-20 and C-3. The lowered intensity of the fragmentation series associated with the methylamino group at C-3 at *m/z* 70 and 57 evidenced the exocyclic methylene group at C-4 [7]. These data and the physicochemical constants determined were in line with those reported [8] for cyclobuxine-D.

The third compound isolated from this portion was identified on the basis of spectral findings proving the presence of a secondary amine, a geminal dimethyl group, a methylene in the cyclopropane ring, a hydroxyl group, methylamino groups at C-20 and C-3, a peak of molecular radical ion at *m/z* 402.3618 (for $C_{26}H_{46}N_2O$ calculated $M_r = 402.3609$), as well as on the basis of physicochemical constants as being cyclovirobuxine-D [9].

Five bases were isolated from the pH 6.0 portion: two of them had identical characteristic data with those already obtained from the pH 6.5 portion (cycloprotobuxine-A and cyclobuxine-D). The third one had i.r. vibration bands indicative of an amino group, a dimethylamino group and a methylene in the cyclopropane ring, peaks of the mass spectrum showed a dimethylamino group at C-20 and a methylamino group at C-3 and the $M^{+\cdot}$ peak at *m/z* 400.3825 (for $C_{27}H_{48}N_2$ calculated $M_r = 400.3817$). Considering this spectral evidence, the data of optical rotation and the mixed melting point with the specimen with no depression, this alkaloid is identical with cycloprotobuxine-C [9].

Elemental analysis of the next compound showed its composition $C_{26}H_{46}N_2$ (*w*(calculated): 80.76 % C, 11.99 % H, 7.25 % N; *w*(found): 80.79 % C, 12.15 % H, 7.06 % N). The bands in the i.r. spectrum were attributed to a secondary amino group, methylene in the cyclopropane ring, a geminal dimethyl group; the mass spectrum had peaks diagnostic of methylamino groups at C-20 and C-3 in addition to the peak at *m/z* 386 ($M^{+\cdot}$). These data agreed when compared with those reported for cycloprotobuxine-D [10] and since the mixed melting

point with the specimen was undepressed, both compounds have to be equal.

The principal alkaloid of this portion was an amorphous base with the peak of molecular radical ion at *m/z* 400.3462 (for $C_{26}H_{44}N_2O$ calculated $M_r = 400.3453$) and other peaks at $M-15$ and $M-43$ indicative of a primary amino group at C-20; the fragmentation pattern *m/z* 84, 71, 58 characterized the dimethylamino grouping at C-3. The u.v. spectrum displayed bands of a conjugated heteroannular diene [11], the i.r. spectrum was in line with requirements for the hydroxyl group, a double bond, amino, dimethylamino, and methyl groups. These data were identical with those reported for buxaminol-E [6]. The base was converted into its crystalline *N*-isopropylidenebuxaminol-E [12], the mixed melting point of which with the specimen was without depression.

The crystalline compound of the pH 5.0 portion absorbed in the u.v. spectral region typical of a heteroannular diene, and the i.r. absorption bands were associated with the presence of a dimethylamino group, a double bond, and a geminal dimethyl group. These data, the M_r 412.3825 (for $C_{28}H_{48}N_2$ calculated $M_r = 412.3817$) and the fragmentation series revealing the dimethylamino groups at C-20 and C-3 in conjunction with further constants entitled us to assign the structure of buxamine-A [13] to this base.

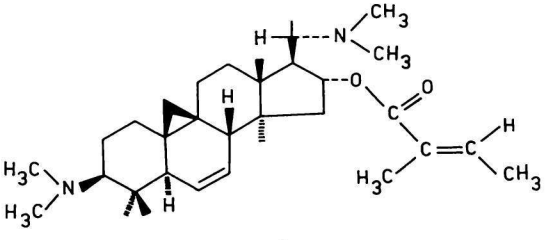
Another amorphous alkaloid of this portion had the u.v. absorption bands diagnostic of a conjugated heteroannular diene; its i.r. spectrum showed vibrations of an amino group and a double bond. The peak of molecular radical ion at *m/z* 384.3496 (for $C_{26}H_{44}N_2$ calculated $M_r = 384.3504$) and species at $M-15$ and $M-43$ (a primary amino group at C-20), and at *m/z* 84, 71, and 58 (a dimethylamino group at C-3) are identical with those reported [14] for buxamine-E. To prove this assignment a crystalline acetyl derivative was prepared; also its physicochemical constants were in accordance with the published [15] data.

The crystalline alkaloid of molecular formula $C_{24}H_{37}NO_2$ (M_r(calculated) = = 371.2824; *m/z*(found) = 371.2833) had, according to the mass spectral data a carbonyl group at C-20 and a methylamino group at C-3 in the neighbourhood of the C-4 exomethylene (a fragmentation series of lowered intensity at *m/z* 70 and 57). The R_f values, optical rotation, and the mixed melting point with buxtauine-M [9] without depression proved both bases to be identical.

The spectral data of the last two compounds of the pH 5.0 portion agreed with those of cycloprotobuxine-C and buxaminol-E isolated from the preceding pH 6.0 portion.

The mass spectrum of the alkaloid from the pH 4.0 portion displayed the peak of molecular radical ion at *m/z* 510.4188 (for $C_{33}H_{54}N_2O_2$ calculated $M_r = 510.4184$) and further peaks $M-15$, $M-43$, $M-71$, $M-83$ and at *m/z* 84, 72, 71, 58, and 43. Species at *m/z* $M-15$ and 72 were ascribed to the fragmentation of the dimethylamino group at C-20, those at *m/z* 84, 71, and 58 to the dimethylamino group at C-3. The peak at *m/z* $M-83$ originated from the residue of the molecule

after cleavage of the C_5H_7O radical. The absorption band in the u.v. region at $\lambda = 203$ nm ($\log\{\varepsilon\} = 4.01$) might be due to an isolated double bond, those at $\lambda = 221$ and 283 nm ($\log\{\varepsilon\} = 3.95$ and 3.19) to a conjugated diene. The i.r. spectrum provided evidence for the presence of an ester and dimethylamino groups, and a methylene in the cyclopropane ring. The ^{1}H-n.m.r. spectrum contained proton signals of the methylene group in a cyclopropane ring at $\delta_r = -0.17$ ppm (1 H) and -0.21 ppm (1 H, dd, $J = 4$ Hz). Four singlets (3 H each) at δ_r/ppm 0.80, 0.96, 1.01, and 1.06 were ascribed to two methyl groups at the tertiary carbon C-4 and two at C-13 and C-14. The doublet of the secondary methyl group at C-21 appeared at $\delta_r = 0.86$ ppm (3 H, $J = 11$ Hz), the intense proton signals of the dimethylamino group at C-20 resonated at 2.11 ppm (6 H), those at C-3 at 2.31 ppm (6 H). Resonance of the proton at C-16 through which the acid residue is attached to the steroid skeleton was found at 5.16 ppm (1 H, m). Signals of olefinic protons at 5.54 ppm (2 H) belong to hydrogens at the double bond of the pregnane backbone. The downfield-shifted signal of the methyl group at the double bond of the side chain of the acid residue at 1.79 ppm (3 H) was attributed to that closer to the carbonyl group because of the anisotropic effect evoked by its negative mesomeric effect. The second methyl group resonated at 1.72 ppm (3 H). The proton at the double bond in the proximity of the methyl group in a *cis* arrangement [16] was seen at 6.76 ppm (1 H) as a doublet; in a *trans* arrangement this value should be upfield-shifted to 5.98 ppm [17]. These data identify the species at $M-83$ (C_5H_7O) as a residue of the *(E)*-2-methyl--2-butenoic (tiglic) acid. The presented arguments entitled us to propose structure *I* for this base and the suffix-A according to the Kyoto convention [18, 19] to the semisystematic name *O*-tigloylcyclovirobuxeine. Spectral data and other



I

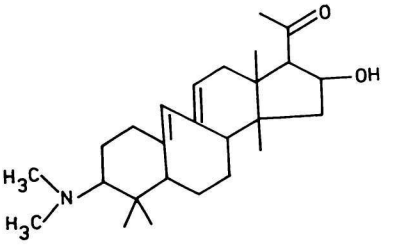
physicochemical constants of the product of hydrolysis of *I* were in line with those reported [20] for cyclovirobuxeine-A.

Further alkaloids isolated from this portion were identified as buxtauine-M and buxaminol-F also isolated from the preceding pH extracts.

The portion of pH 3.0 contained an additional amount of *O*-tigloylcyclovirobuxeine-A and a base the u.v. spectrum of which was characteristic of a conjugated heteroannular diene and an α,β-unsaturated carbonyl. The vibra-

tional bands in its i.r. spectrum were attributed to a dimethylamino group, a geminal dimethyl group, and an α,β-unsaturated ketone. The mass spectrum corroborated the presence of a dimethylamino group at C-3 and a carbonyl group at C-20; the peak of molecular radical ion at *m/z* 381.3027 fits the molecular formula $C_{26}H_{39}NO$ (calculated $M_r = 381.3031$) and consequently, the alkaloid buxpsiine-K [21].

The last base separated from this portion had, according to high resolution measurement, molecular formula $C_{26}H_{41}NO_2$ (M_r(calculated) = 399.3137; *m/z* (found) = 399.3142). The peak at $M-43$ and that at *m/z* 43 indicated the carbonyl group at C-20, whilst the fragmentation pattern *m/z* 84, 71, and 58 proved the dimethylamino substitution at C-3, and, since no lowering of intensity was observed, no exomethylene should be attached to C-4. The absorption bands in the u.v. region were due to a carbonyl group and a conjugated heteroannular diene, those in the i.r. spectrum to hydroxyl, methyl, and dimethyl groups, and a double bond. The afore-mentioned data were not consistent with any Buxus alkaloid so far isolated, and therefore, a tentative structure *II* was proposed to this



II

base denominated buxbarbarine-K. Because of a lack of material this assignment could not be verified.

A survey of alkaloids isolated from the leaves of *Buxus arborescens* MILL. is presented in Table 1.

Experimental

Melting points were determined on a Kofler micro hot-stage, optical rotation was measured with a Perkin—Elmer, model 141, polarimeter in chloroform, unless stated otherwise. The i.r. spectra in KBr were recorded with a Perkin—Elmer, model 457, the u.v. spectra of methanolic solutions with a Beckman DB-GT spectrophotometers. The mass spectra were taken with an AEI-MS 902 (high resolution measurements) and Jeol MS 100 D apparatuses. The ^{1}H-n.m.r. spectrum in deuteriochloroform containing tetramethylsilane was recorded with a Jeol FT FX-100 spectrometer operating at 100 MHz.

Table 1

Alkaloids isolated from portions of various pH

pH of the portion	Total amount of alkaloids		Alkaloid	Separated *m*/mg[b]
	m/g	Yield/%[a]		
6.5	28	18.3	Cycloprotobuxine-A	22.1
			Cyclobuxine-D	48.2
			Cyclovirobuxine-D	31.5
6.0	33	21.6	Cycloprotobuxine-A	11.9
			Cyclobuxine-D	111.1
			Cycloprotobuxine-C	15.1
			Cycloprotobuxine-D	23.5
			Buxaminol-E	331.0
5.0	32	21.0	Buxamine-A	25.7
			Buxamine-E	21.1
			Buxtauine-M	38.4
			Cycloprotobuxine-C	10.5
			Buxaminol-E	23.4
4.0	34	22.2	*O*-Tigloylcyclovirobuxeine-A	76.0
			Buxtauine-M	19.9
			Buxaminol-E	18.4
3.0	3	1.9	*O*-Tigloylcyclovirobuxeine-A	8.3
			Buxpsiine-K	15.5
			Buxbarbarine-K	5.3
$CHCl_3$ residue	21	13.7		

a) refers to the mixture of alkaloids (153 g); *b*) 2.5 g were taken for work-up from each pH portion with the exception of the pH 4.0 one, from which 20 g were worked up.

Thin-layer chromatographic plates coated with alumina Woelm neutral were dried at an ambient temperature for 24 h; solvent systems: chloroform—benzene—ethanol at volume ratios 7:5.5:0.5 (S_1), 7:5:1 (S_2), 7:4:2 (S_3).

Extraction of the drug and isolation of alkaloids

The dried and ground leaves of *Buxus arborescens* MILL. (15.5 kg) collected in August 1978 in the Arboretum of the Slovak Academy of Sciences at Mlyňany were macerated with stirring with the mixture methanol—water—acetic acid (28.5:28.5:3) and then five times with another mass ratio (19.9:19.9:0.2) of the same substances. The combined extracts

(300 dm^3) were concentrated under diminished pressure to 10 dm^3. Saccharides were removed from this solution by addition of a 5-fold excess of ethanol under stirring as a yellow precipitate, the filtrate was concentrated to the original volume and alkalinized with concentrated ammonium hydroxide solution. The mixture of alkaloids extracted with chloroform till the negative reaction of the aqueous layer with Mayer reagent (153 g) was worked up in usual manner to furnish the pH portions, which were chromatographed on an alumina Reanal neutral (Hungary, activity grade IV, a 45-fold excess) and eluted by benzene and benzene—ethanol in various ratios.

Characteristics of alkaloids isolated

Cycloprotobuxine-A: m.p. = 203—205 °C (ethanol), $[\alpha] = +79°$ ($\varrho = 1.0\,\%$), $R_f = 0.82$ (S_1). Ref. [5] gives m.p. = 206—207 °C, $[\alpha] = +76°$. Mass spectrum (*m/z*): 414 ($M^{+\cdot}$), 399, 370, 343, 84, 72, 71, 58. IR spectrum ($\tilde{\nu}/cm^{-1}$): 2779 ($(CH_3)_2N$), 1449 (—CH_2—), 1368 ($(CH_3)_2$ =).

Cyclobuxine-D: m.p. = 234—236 °C (benzene—ethanol, $\varphi = 9:1$), $[\alpha] = +99°$ ($\varrho = 0.85\,\%$), $R_f = 0.32$ (S_2). Ref. [8] gives m.p. = 237 °C, $[\alpha] = +96°$. Mass spectrum (*m/z*): 386 (M^+), 371, 356, 328, 70, 58, 57, 44. IR spectrum ($\tilde{\nu}/cm^{-1}$): 3300 (NH), 1442 (—CH_2—), 1035 (OH).

Cyclovirobuxine-D: m.p. = 207—211 °C (ethanol), $[\alpha] = +27°$ ($\varrho = 0.9\,\%$, ethanol), $R_f = 0.25$ (S_2). Ref. [9] gives m.p. = 205—210 °C, $[\alpha] = +25°$ (ethanol). IR spectrum ($\tilde{\nu}/cm^{-1}$): 3308 (NH), 1371 ($(CH_3)_2$ =), 1448 (—CH_2—), 1027 (OH). Mass spectrum (*m/z*): 402 (M^+), 387, 372, 344, 70, 58, 57.

Cycloprotobuxine-C: m.p. = 191—194 °C (ether—benzene, $\varphi = 9:1$), $[\alpha] = +44°$ ($\varrho = 0.9\,\%$, ethanol), $R_f = 0.76$ (S_1). Ref. [9] gives m.p. = 195 °C, $[\alpha] = +40°$ (ethanol). IR spectrum ($\tilde{\nu}/cm^{-1}$): 3375 ($NHCH_3$), 2767 ($(CH_3)_2N$), 1441 (—CH_2—). Mass spectrum (*m/z*): 400 (M^+), 385, 356, 329, 84, 72, 70, 57, 44.

Cycloprotobuxine-D: m.p. = 135—138 °C (ether), $[\alpha] = +110°$ ($\varrho = 1.0\,\%$), $R_f = 0.38$ (S_2). Ref. [10] gives m.p. = 140—142 °C, $[\alpha] = +112°$. IR spectrum ($\tilde{\nu}/cm^{-1}$): 3366 (NH), 1450 (—CH_2—), 1373 ($(CH_3)_2$ =). Mass spectrum (*m/z*): 386 (M^+), 371, 356, 340, 328, 70, 58, 57.

Buxaminol-E: amorphous, $[\alpha] = +41°$ ($\varrho = 0.8\,\%$), $R_f = 0.15$ (S_3). Ref. [6] gives $[\alpha] = +38°$. UV spectrum (λ_{max}/nm (log {ε})): 245 (4.49), 254 (4.28), 287 (2.58). IR spectrum ($\tilde{\nu}/cm^{-1}$): 3390 (OH), 1605 (double bond), 1578 (NH_2), 2710 ($(CH_3)_2N$). *N-Isopropylidenebuxaminol-E:* buxaminol-E (20 mg) was dissolved in acetone (4 cm^3), gently heated and left to crystallize. Yield 12.5 mg, m.p. = 201—202 °C, $[\alpha] = +81°$ ($\varrho = 0.8\,\%$), $R_f = 0.45$ (S_2). Ref. [12] gives m.p. = 205 °C, $[\alpha] = +84°$. Mass spectrum (*m/z*): 440 (M^+). IR spectrum ($\tilde{\nu}/cm^{-1}$): 3385 (OH), 1604 (double bond), 1663 (C=N).

Buxamine-A: m.p. = 131—133 °C (acetone), $[\alpha] = +36°$ ($\varrho = 1.1\,\%$), $R_f = 0.91$ (S_1). Ref. [13] gives m.p. = 134 °C, $[\alpha] = +40°$. UV spectrum (λ_{max}/nm (log {ε})): 238 (3.45), 245 (3.65), 251 (3.41). IR spectrum ($\tilde{\nu}/cm^{-1}$): 2703 ($(CH_3)_2N$), 1615 (double bond), 1364 ($(CH_3)_2$ =). Mass spectrum (*m/z*): 412 (M^+), 397, 84, 72, 71, 58.

Buxamine-E: amorphous, $[\alpha] = +35°$ ($\varrho = 0.9\,\%$), $R_f = 0.35$ (S_2). Ref. [14] gives $[\alpha] = +32°$. UV spectrum (λ_{max}/nm (log {ε})): 230 (3.91), 245 (4.08), 256 (3.83). IR

spectrum ($\tilde{\nu}$/cm^{-1}): 3391 (NH_2), 2753 ($(CH_3)_2N$), 1608 (double bond). *N-Acetylbuxamine-E:* buxamine-E (10 mg) dissolved in pyridine (1 cm^3) and acetic anhydride (1 cm^3) was left to stand at room temperature for 48 h. The acetylation mixture was removed at reduced pressure and the solid residue was crystallized from acetone. Yield 6.8 mg, m.p. = 202—204 °C, $[\alpha] = +8°$ ($\varrho = 0.4$ %), $R_f = 0.76$ (S_1). Ref. [15] gives m.p. = 210 °C, $[\alpha] = +5°$. Mass spectrum (*m/z*): 426 (M^+). IR spectrum ($\tilde{\nu}$/cm^{-1}): 2758 ($(CH_3)_2N$), 1620 (N—CO), 1606 (double bond).

Buxtauine-M: m.p. = 171—176 °C (ether—benzene; $\varphi = 1:1$), $[\alpha] = +160°$ ($\varrho = 1.0$ %), $R_f = 0.83$ (S_2). Ref. [9] gives m.p. = 182 °C, $[\alpha] = +154°$ IR spectrum ($\tilde{\nu}$/cm^{-1}): 1454 (—CH_2—), 1691 (C=O), 3560 and 1035 (OH), 3301 (NH). Mass spectrum (*m/z*): 371 (M^+), 356, 353, 338, 328, 310, 70, 57, 44.

O-Tigloylcyclovirobuxeine-A (I): m.p. = 191 °C (dichloromethane), $[\alpha] = -123°$ ($\varrho = 0.53$ %), $R_f = 0.96$ (S_1). IR spectrum ($\tilde{\nu}$/cm^{-1}): 1710 (C=O), 1276 (C—O_{ester}), 2779 ($(CH_3)_2N$), 1605 (conjugated diene), 1442 (—CH_2—), 1376 ($(CH_3)_2$=).

Cyclovirobuxeine-A from O-tigloylcyclovirobuxeine-A: A solution of *I* (20 mg) dissolved in 5% methanolic KOH (5 cm^3) was heated under reflux at a steam bath for 1 h. The cooled solution was concentrated under diminished pressure, the residue was dissolved in water (10 cm^3) and extracted with chloroform. The organic layer was dried, concentrated *in vacuo* and crystallized from acetone. Yield 5.4 mg (27 %), m.p. = 221 °C (acetone), $[\alpha] = -83°$ ($\varrho = 0.27$ %). Ref. [20] gives m.p. = 220 °C, $[\alpha] = -87°$ IR spectrum ($\tilde{\nu}$/cm^{-1}): 1022 and 3391 (OH), 2783 ($(CH_3)_2N$), 1445 (—CH_2—). Mass spectrum (*m/z*): 428 (M^+), 413, 384, 84, 72, 71, 58, 44. Mixed melting point with cyclovirobuxeine-A was undepressed.

Buxpsiine-K: m.p. = 181 °C (acetone), $[\alpha] = +115°$ ($\varrho = 0.71$ %), $R_f = 0.85$ (S_1)). Ref. [21] gives m.p. = 180—183 °C, $[\alpha] = +118°$ UV spectrum (λ_{max}/nm (log {ε})): 238 (4.71), 247 (4.60), 257 (4.41). IR spectrum ($\tilde{\nu}$/cm^{-1}): 2771 ($(CH_3)_2N$), 1671, and 1599 (α,β-unsaturated ketone), 1376 ($(CH_3)_2$=). Mass spectrum (*m/z*): 381 (M^+), 366, 338, 84, 71, 58, 43.

Buxbarbarine-K (II): amorphous, $R_f = 0.55$ (S_3). UV spectrum (λ_{max}/nm (log {ε})): 206 (3.67), 246 (3.83), 255 (3.71), 279 (3.11). IR spectrum ($\tilde{\nu}$/cm^{-1}): 3553 and 1022 (OH), 2960 and 2875 (methyl groups), 2753 ($(CH_3)_2N$), 1676 (C=O), 1604 (double bond), 1377 ($(CH_3)_2$=).

Acknowledgements. Our thanks are due to Dr. L. Dolejš (Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague) for high resolution measurements of mass spectra and to colleagues of our Institute for recording the other spectra.

References

1. Brown, K. S., Jr., in *Chemistry of the Alkaloids.* (Peletier, S. W., Editor.) Vol. *IX*, p. 375. Academic Press, New York, 1967.
2. Tomko, J. and Votický, Z., in *The Alkaloids.* (Manske, R. H. F., Editor.) Vol. *XIV*, p. 1. Academic Press, New York, 1973.

3. Khuong-Huu-Lainé, F. and Goutarel, R., in *The Alkaloids.* (Saxton, J. E., Editor.) Vol. 7, p. 268. The Chemical Society, London, 1977.
4. Votický, Z. and Paulík, V., *Chem. Zvesti 26*, 376 (1972).
5. Nakano, T., Terao, S., and Saeki, Y., *J. Chem. Soc. C1966*, 1412.
6. Bauerová, O. and Votický, Z., *Pharmazie 28*, 212 (1973).
7. Dolejš, L., Hanuš, V., Votický, Z., and Tomko, J., *Collect. Czech. Chem. Commun. 30*, 2869 (1965).
8. Khodzhaev, B. U., Shakirov, R., and Yunusov, S. Yu., *Khim. Prir. Soedin. 1980*, 130.
9. Vassová, A., Tomko, J., Votický, Z., and Beal, J. L., *Pharmazie 25*, 363 (1970).
10. Kupchan, S. M. and Kurosawa, E., *J. Org. Chem. 30*, 2046 (1965).
11. Nakano, T. and Terao, S., *Tetrahedron Lett. 1964*, 1035.
12. Khuong-Huu, F., Herlem-Gaulier, D., Khuong-Huu, Q., Stanislas, E., and Goutarel, R., *Tetrahedron 22*, 3321 (1966).
13. Khuong-Huu, F., Paris, R., Razafindrambao, R., Cave, A., and Goutarel, R., *C. R. Acad. Sci., Ser. C 1971*, 558.
14. Stauffacher, D., *Helv. Chim. Acta 47*, 928 (1964).
15. Nakano, T. and Hasegawa, M., *J. Chem. Soc. C1965*, 6688.
16. Kupchan, S. M., Kennedy, R. M., Schleigh, W. R., and Ohta, G., *Tetrahedron 23*, 4563 (1967).
17. Herz, W. and Lakshmikantham, M. V., *Tetrahedron 21*, 1711 (1965).
18. Brown, K. S., Jr. and Kupchan, S. M., *Tetrahedron Lett. 1964*, 2895.
19. Calame, J. P., *PhD. Thesis.* Technical University, Zurich, 1965.
20. Khuong-Huu-Lainé, F., Magdeleine, M. J., Bisset, N. G., and Goutarel, R., *Bull. Soc. Chim. Fr. 1966*, 758.
21. Kurakina, I. O., Proskurnina, N. F., and Shtepanyants, A. U., *Khim. Prir. Soedin. 1969*, 406.

Translated by Z. Votický