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Quantitative determination of conformational equilibrium in quinolizidine-piperidine alkaloids. Part 2: Synthesis and conformational study of *N*-methylalbine☆

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Respectfully dedicated to Professor Maciej Wiewiorówski on the occasion of his 85th birthday

Abstract—*N*-methylalbine (**5**) was synthesized for the first time. The structure is other than the one bearing hitherto its name. The fraction of the conformer with the boat ring C in the conformational equilibrium in **5** in benzene solution was determined to be ca. 22% using coupling constant $J_{9-11\beta}$. The reason of the occurrence of a significant amount of the boat conformer is, similarly to *N*-methylangustifoline (**2**), the interaction of an axial allyl group with the bridge H8α hydrogen atom. The smaller fraction of the boat conformation in **5** than in **2** is caused by the repulsion of one of the H14 hydrogen atoms of the allyl group with the axial H5α proton in the boat conformer of **5**.

1. Introduction

The conformational equilibrium is well documented in many bis-quinolizidine alkaloids with a sparteine (**1**) skeleton[2] and has also been proved for the related 3,7-diaza-bicyclo[3.3.1]nonane (bispidine) system.[3] The main reasons for a shift of the equilibrium in four-ring compounds with a sparteine skeleton towards a greater participation of the boat form (**1A** in **1**) are:

interaction related to skeleton strain, especially in rings B and C and
van der Waals repulsion of pairs of hydrogen atoms situated in the *cis*-quinolizidine moiety (rings C and D): H8α–H12β, H12β–H17β and H14β–H17β in the all-chair conformation Figure 1.

In the alkaloids which, like **1**, have diamine nature a third important factor is the repulsion of trialkylamine dipoles often referred to as repulsion of lone electron pairs.

In most tricyclic quinolizidine-piperidine alkaloids, the van der Waals repulsion of the above mentioned hydrogen atom pairs is lacking and the strain of the skeleton could be diminished by a simple flattening of the B and C rings (a flattening of ring C in **1** would cause a greater strain in rings C/D). Therefore, it was difficult to find any example of such equilibrium in quinolizidine-piperidine alkaloids.

A few years ago we published the first such case.[1] In *N*-methylangustifoline (**2**) we found ca. 34% of the boat form. The main reason for the equilibrium shift is the interaction of one of hydrogen atoms at C14 in the axial allyl group in position 11 with H8α, an analogy to H8α–H12β repulsion in **1**. We could not support our result of the conformational equilibrium in tricyclic alkaloids with any other example. We failed to prove it in angustifoline (**3**) itself because of the impossibility of measuring the coupling

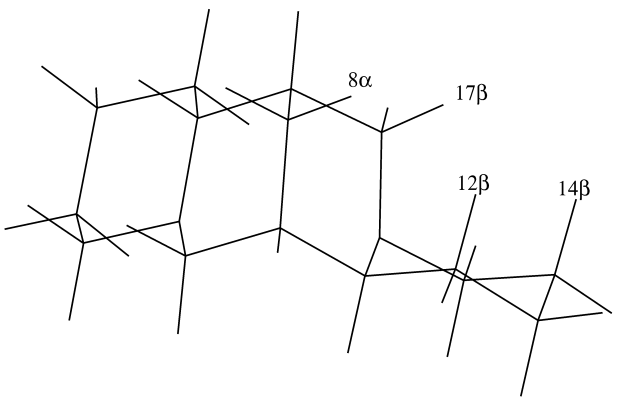

Figure 1. Hydrogen atoms involved in repulsion in the all-chair conformation of sparteine (**1**).

☆ Part 1: Ref. 1.

Keywords: lupin alkaloids; NMR; *seco*(11,12)-12,13-didehydromultiflorine; tetrahydrorhombifoline; *N*-methylangustifoline.

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Table 1. ^{13}C chemical shifts of some three-ring alkaloids (ppm from TMS)

C atom	**8** C_6D_6	**5** C_6D_6	**4**[a] $CDCl_3$	**2**[b] C_6D_6	**3**[b] C_6D_6	**9**[b] C_6D_6
2	152.34	152.91	154.7	168.48	169.44	167.78
3	98.10	98.73	100.0	33.34	34.05	33.53
4	190.91	191.07	192.7	20.26	21.07	20.45
5	41.02	40.81	40.0	28.02	28.63	28.23
6	58.36	59.46	60.5 (59.8?)[c]	59.42	60.61	58.56
7	32.23	33.64	28.1	33.90	33.72	34.31
8	31.59	24.92	26.3	27.22	28.82	33.83
9	29.26	28.83	34.1	30.94	32.13	29.62
10	55.34	56.33	57.0	47.48	48.65	46.33
11	58.81	54.24	46.2	64.03	57.84	59.19
13	53.45	57.83	51.9 (51.2?)[c]	50.81	42.55	54.38
(14)	58.15					58.70
Allyl	(C15) 31.53	(C14) 27.44	36.9 (36.2?)[c]	30.16	38.43	31.88
Vinyl	(C16) 137.09	(C15) 136.48	134.9	(C15) 136.34	(C15) 137.53	137.42
Vinyl	(C17) 115.51	(C16) 116.44	116.8	(C16) 116.34	(C16) 116.61	115.44
N-methyl		42.34		42.46		

[a] Ref. 16.
[b] Ref. 1.
[c] In parenthesis: chemical shifts for the respective carbon atoms in the possible minor conformer according to Ref. 16 (assignment perhaps uncertain).

constant $J_{7-13\beta}$, although there were some arguments showing the participation of a minor conformer.[1]

Recently, we have isolated albine (**4**), a three-ring alkaloid containing a γ-oxo-α,β-enamine system in ring A and an allyl chain at ring C, from *Lupinus albus* var. Satmarean. **4** was isolated for the first time from *L. albus* seeds in early sixties and its properties were described, including IR and UV spectra, however a wrong formula was postulated at first.[4,5] X-Ray analyses of its perchlorate revealed unexpectedly that the allyl group was attached to C13 atom and not to C11 as was formerly supposed.[6,7] We have succeeded in obtaining albine although for many years our attempts to isolate **4** from various new cultivars of *L. albus* failed, probably due to elimination or substantial reduction of the amount of this alkaloid in the course of the breeding process. We have not obtained NMR spectra of **4** suitable for interpretation as there were always some additional signals not attributed to impurities. To make sure if the additional signals were just the split signals of **4**, we have decided to take the NMR spectra of methylated derivative of **4**. The study of *N*-methylalbine (**5**) was expected to help to clarify the errors in the long story of investigations of the compound hitherto bearing this name.

In 1961 a new alkaloid was isolated from *Lupinus albus* L. and its structure (**6**) was published according to its elemental analysis, IR and UV spectra as well as the IR spectra and physico-chemical properties of its total reduction product **7** then thought to have the structure **7a**.[8,9] The properties of **7** were the same as those of a total reduction product of a compound which was reckoned to be *N*-methylangustifoline (**2**). The original alkaloid was called *N*-methylalbine because it was believed to be a methyl derivative of albine.

Our ^{13}C NMR investigations of the alleged *N*-methylalbine demonstrated that its spectrum was not in accordance with any of the formerly proposed structures and we postulated formula **8** as the correct one and the name *seco*(11,12)-12,13-didehydromultiflorine.[10] The structure was corroborated by our ^{1}H NMR[11] of **8** and X-ray crystallography of its perchlorate.[12]

The aim of the paper was to test the conformational equilibrium in **5** by the ^{13}C and ^{1}H NMR method. Moreover, we wish to present for the first time the correct structure and stereochemistry of *N*-methylalbine, to finally eliminate the structure **6** still included in the Beilstein database.[13]

2. Results and discussion

The ^{13}C and ^{1}H chemical shifts of *N*-methylalbine (**5**) and some related compounds are presented in Tables 1 and 2. As the spectra of all other compounds were recorded in C_6D_6 (lupin alkaloids are not decomposed in benzene as easily as in most other solvents) we decided to perform a new series of the spectra of *seco*(11,12)-12,13-didehydromultiflorine (**8**) also in C_6D_6. The ^{13}C signals in **5** were assigned tentatively by a comparison with spectra of similar compounds and verified by HMQC spectra. The ^{1}H signals were assigned using HMQC and $^{1}H,^{1}H$ COSY spectra, the axial and equatorial protons were mainly discerned by means of the NOESY spectrum.

It is known that *seco*(11,12)-12,13-didehydromultiflorine (**8**) adopts a conformation with chair conformation for rings B and C in solution.[10,14] On the other hand, the *N*-methyl group combined with an axial allyl substituent at C13 in *N*-methylangustifoline (**2**) shifts the conformational equilibrium towards the ca. 34% fraction of the conformation with a boat ring C.[1] There are the same substituents in *N*-methylalbine (**5**), the only difference is in the position of the allyl group but the steric implications of the groups in **5** are very similar to those in **2**. Thus it is interesting whether also in **5** we will be able to detect the conformational equilibrium or not.

The ^{13}C signals in **5** attributed to the ring A carbon atoms have chemical shifts very similar to those of ring A carbon atoms in **8**. The only slight difference is in the chemical shifts of the carbon atom C6 (1.1 ppm) which can be attributed to the γ-anti effect of the axial substituent at C13 in **5**. This is a strong argument for a similarity in the ring A structure of the two compounds. The chemical shift of the

Table 2. [1]H Chemical shifts of some three-ring alkaloids (ppm)

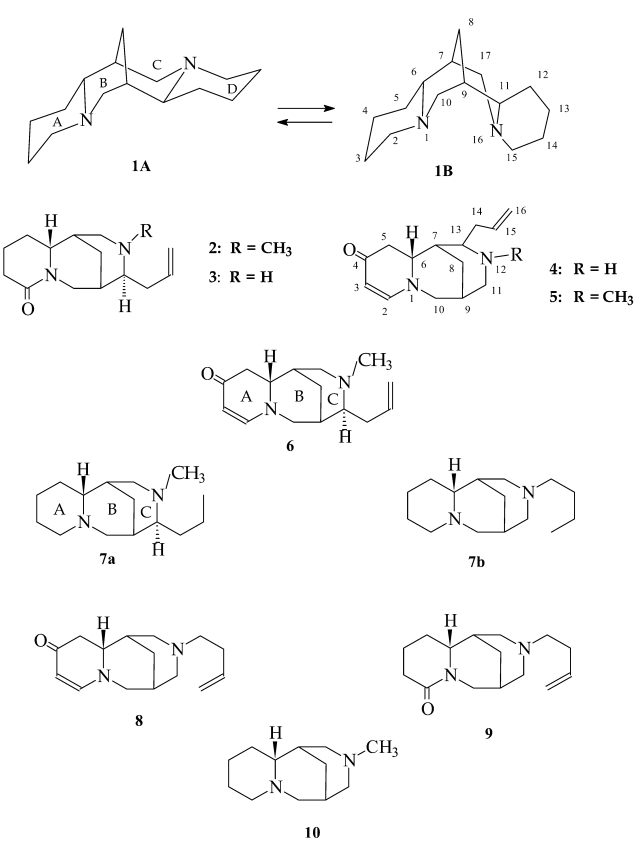
H atom	**8** (C_6D_6)	**5** (C_6D_6)	**2**[a] (C_6D_6)	**3**[b] (C_6D_6)	**9**[b] (C_6D_6)	**10**[c] ($CDCl_3$)
2	6.18	6.15				
3α	5.19	5.19	2.12	2.10	2.19	1.64
3β			2.40	2.40	2.44	1.45
4α			1.35	1.25	1.37	1.70
4β			1.19	1.24	1.22	1.23
5α	2.67	2.62	1.22	1.06	1.37	1.53
5β	2.04	2.05	1.16	1.09	1.15	1.27
6	3.03	3.00	2.82	2.84	2.90	1.86
7	1.00	1.21	1.12	0.84	1.00	1.45
8α[d]	1.17	1.49	1.71	1.72	1.31	1.47
8β	1.00	0.74	1.01	1.35	1.23	1.46
9	1.16	1.17	1.62	1.29	1.41	1.77
10α	2.64	2.61	4.89	4.83	4.95	2.84
10β	2.55	2.49	2.55	2.57	2.57	2.09
11α	2.49	2.10	2.52	2.76	2.74	2.92
11β	1.82	2.36			1.85	2.10
13α	2.63	2.59	2.23	~2.70	2.79	2.95
13β	1.53		2.34	~2.70	1.67	1.93
14A	~2.06				2.08	
14B	~1.97				2.00	
Allyl	(15)~1.98	(14A) 2.05	(14A) ~2.10	(14A)~2.30	(15) 2.10	
	(15)~1.98	(14B) 1.85	(14B) 1.97	(14B) 2.01	(15) 2.10	
Vinyl	(16) 5.70	(15) 5.40	(15) 5.57	(15) 5.73	(16) 5.86	
	(17t) 4.98	(16t) 4.91	(16t) 5.04	(16t) 5.08	(17t) 5.06	
	(17c) 4.97	(16c) 4.95	(16c) 4.98	(16c) 5.01	(17c) 5.05	
N-Me		1.95	2.04			2.09

[a] Ref. 1.
[b] Ref. 11.
[c] Ref. 15.
[d] Equatorial in ring B.

N-methyl carbon is almost the same as that of the respective atom in *N*-methylangustifoline (**2**). Chemical shifts of C9 are also very similar in **5** and **8**. The chemical shift of C7 in **5** with respect to that of **8** is easily understood taking into consideration the β-effect of the substituent at C13 in **5**.

The most interesting resonance is the signal for C8 in *N*-methylalbine (**5**). It occurs at 24.92 ppm while the corresponding signal in *seco*(11,12)-12,13-didehydromultiflorine (**8**) is at 31.59 ppm and in tetrahydrorhombifoline (**9**) which has the same conformation as **8**[1] and in all-chair 11-methyl-7,11-diazatricyclo[7.3.1.$0^{2,7}$]tridecane (**10**)[15] even occurs at 33.8 ppm. Such a great difference (6.67 ppm between the values in **5** and **8**) is mostly caused by the γ-*gauche* effect from the axial allyl substituent at C13 in **5**, but it seems too great to be exclusively due to this effect. It is possible that there is an effect of change of conformation on C8. Comparing the spectra of the series of compounds described in Table 1 we can see that the lactam group has a very small effect on the signal of C8 while the γ-oxo-α,β-enamine system shifts the signal by about 2 ppm upfield. Also the *N*-methyl group seems to shift the C8 signal upfield: the difference between the chemical shifts of the corresponding atoms in **5** and **4**[16] as well as in **3** and **2**[1] is −1.3 and −1.6, respectively.

The chemical shift of C11 in *N*-methylalbine (**5**) is also interesting. The difference between its value and that of the chemical shift of the respective carbon in **8** is about −4.6 ppm. This can be explained by a γ-*gauche* effect in the chair conformation of ring C. The effect of the *N*-butenyl chain compared with that of *N*-methyl group must also be taken into account. In model compounds **9**[1] and **10**[15] this effect in $CDCl_3$ amounts to ca. 1.1 ppm. This means that the total effect of the axial allyl group at C13 and other possible effects, reaches ca. −5.7 ppm. The difference with respect to the expected ca. −5 ppm is rather small and not certain,



but it is probable that this is due to a contribution of a boat conformation of ring C in which the γ-*gauche* effect of the allyl group on C11 is not possible.

Protons attached to carbon atoms of ring A in *N*-methylalbine (**5**) give rise to NMR signals whose chemical shifts are almost the same as those of respective protons in *seco*(11,12)-12,13-didehydromultiflorine (**8**) (Table 2) corroborating the similarity of their structure. It was difficult to assign the signals to the protons attached to C10 and C11 atoms, they were discerned by NOESY spectra. The signal at 2.49 ppm must originate from the axial H10β proton because it is coupled with H8β (axial in ring B) and H6. The signal at 2.36 ppm has cross-peaks with the proton at C8 which is equatorial in ring B (H8α) and with one of the protons at allyl C14 (which should be called *syn*), therefore it must be that of axial H11β. Consequently, the signals at 2.61 and 2.10 ppm must derive from equatorial H10α and H11α, respectively. The differences in chemical shifts of H7, H8α and H8β in *N*-methylalbine compared to **8** are easily understood by the effect of an axial allyl group at C13, the other protons of ring B have similar chemical shifts in both compounds. Also the rest of the C ring protons are influenced by the allyl group. The chemical shift of the *N*-methyl protons is similar to that observed for *N*-methylangustifoline.

The chemical shift of H8β (0.74 ppm) as well as the difference in chemical shifts of H8α and H8β indicate the participation of a boat conformation.[1,17] Another important argument is the value of the coupling constant $J_{9-11\beta}$= 4.1 Hz (Table 3). It is not as high as that of $J_{7-13\beta}$=5.1 Hz in *N*-methylangustifoline (**2**), but significantly higher than the lowest possible value for this class of compound: 2.3 Hz for **8**. Using the same procedure as for **2**,[1] we can calculate that the fraction of the boat conformer amounts to ca. 22% in the conformational equilibrium for **5**. Now we can maintain that the low value of the ^{13}C chemical shift of C8 in **5** is partly also due to the effect of the boat conformation participating in the equilibrium.

It is difficult to support our experimental results by the results of the computational methods.[18] The semi-empirical method which we used, PM3, does not give the exact geometry of quinolizidine compounds, but as far as the conformational equilibrium is concerned, it indicates ca. 15.9% of the minor boat conformer in **5**. Mechanical mechanics (MM) version amber gives totally absurd values for the conformational equilibrium (e.g. according to MM sparteine should be almost only in the all-chair conformation, whereas in reality it occurs almost exclusively in the boat conformation) but the geometry calculated by this method seems to be quite well reproduced. Unfortunately, the Haasnoot–de Leeuw–Altona equation[19] underestimates the high values of coupling constants and overestimates the low ones in quinolizidine alkaloids. Therefore we cannot use the $J_{9-11\beta}$ calculated from MM and the Haasnoot equation to check our ^1H NMR result.

Table 3. $^1H-^1H$ coupling constants of some three-ring alkaloids (Hz)

Coupling constant	**8**[a] ($CDCl_3$)	**5** (C_6D_6)	**2**[b] ($CDCl_3$)	**3**[a] ($CDCl_3$)	**9**[b] ($CDCl_3$)
5α–6	16.5	15.5	~10	10.7	10.3
5β–6	4.5	4.1	5.3	5.0	4.3
6–7	3.0	3.8	2.5	2.6	3.0
7–8α[c]	3.7	3.8	3.7	5.9	3.4
7–8β	3.5	~3	3.0	1.9	4.8? 2.7?[d]
8α[c]–9	3.7	3.8	3.7	3.5	3.4
8β–9	5	~3	3.0	3.5	4.8? 2.7?[d]
9–10α	2.1	–[e]	2.1	2.3	2.2
9–10β	3.2	3.8	3.6	3.5	3.5
9–11α	2.5	2.1	2.3	<1.4	2.6
9–11β	2.5	4.1	–	–	2.4
7–13α	–[e]	–[e]	3.0	–[e]	3.2
7–13β	2.3	–	5.1	–[e]	2.4

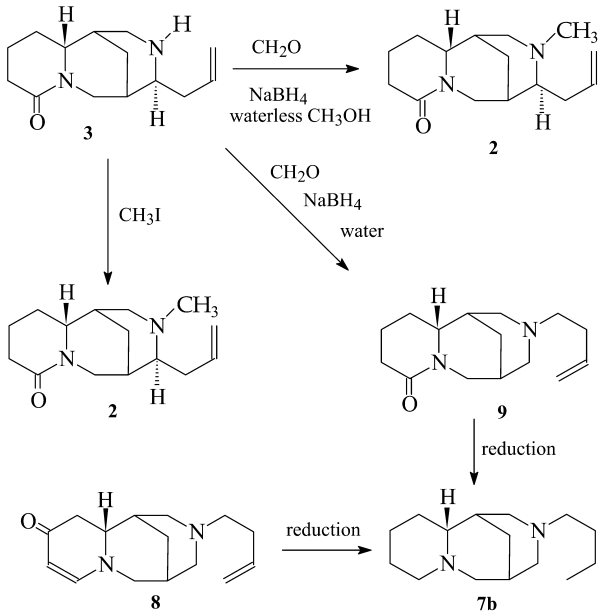
[a] Ref. 11.
[b] Ref. 1.
[c] Equatorial in ring B.
[d] In benzene, one of the two possibilities.
[e] Not found.

The reason for a significant participation of the boat conformer in the equilibrium in **5** is the same as in **2**, that is the destabilization of the chair conformer by the repulsion of the *syn* allyl H14B hydrogen atom with H8α. The contribution of the boat conformer is lower in **5** than in **2** and this could be explained by a higher enthalpy of the boat conformer of *N*-methylabine (**5**) than that of *N*-methylangustifoline (**2**) due to the repulsion of one of the allyl hydrogen atoms at C14 with the axial H5α hydrogen atom in the boat conformation. Analogous repulsion does not occur in the boat conformation of **2**.

A question arises as to why Mocydlarz and Wiewiórowski claimed that the alleged *N*-methylalbine and *N*-methylangustifoline gave the same total reduction product **7**.

Mocydlarz and Wiewiórowski tried to methylate angustifoline (**3**) probably by means of formaldehyde and $NaBH_4$. Wiewiórowska demonstrated that such a methylation leads to a rearrangement and gives as a result tetrahydrorhombifoline (**9**) instead of *N*-methylangustifoline (**2**) if even traces of water are present.[20] When reducing **9**, the same product **7b** was obtained as when reducing *seco*(11,12)-12,13-didehydromultiflorine (**8**) (Scheme 1).

Another question is the impossibility of recording a good NMR spectrum of albine **4**. Mohamed et al. published a double set of carbon signals of **4**.[16] They postulate the presence of two conformers of **4** in equilibrium: one with an axial position for the N–H bond and an intramolecular hydrogen bond and the other without an intramolecular hydrogen bond and with the N–H bond oriented equatorial. It corresponds with the Mocydlarz and Wiewiórowski's observation of the presence of a band at 1720 cm^{-1} in the IR spectrum of **4**.[4,5] The intensity of the band is high in nonpolar solvent (CCl_4), lower in $CDCl_3$ and the lowest in pure liquid. The lack of the Bohlmann band in CCl_4 solution suggests an axial location for the N12–H bond which can participate in an intramolecular hydrogen bond and thus hinder the delocalization of electrons of enaminon system and create a form with the carbonyl bond not taking part in the π–π–p electron conjugation. One of the consequences of a participation of such a form in the population of molecules of **4** can be the presence of a signal at 207.9 ppm in Mohamed's ^{13}C NMR spectrum of **4**[16] almost typical of ketone. The double signals of C11, C13, C14, C15, and C16



Scheme 1.

can be attributed to the two conformers: one with the axial and the second with the equatorial N–H bond. In the IR spectrum of perchlorate of **4** there are only two bands in the region 1590–1650 cm^{-1}, the authors[5] postulate the existence of intermolecular hydrogen bonds involving both protons at N12: the axial one with the ClO_4^- anion and the equatorial one with the carbonyl oxygen atom of the neighbour cation of **4** and as a consequence no conformational equilibrium occurs.

3. Conclusion

The real *N*-methylalbine (**5**) was obtained in conditions which excluded rearrangement. Its properties are distinctly different than those of alleged *N*-methylalbine published by Wolińska-Mocydlarz and Wiewiórowski in the sixties. The ^{13}C and ^{1}H NMR spectra corroborate its structure. The chemical shifts of C8, H8β and C11, a significant difference between chemical shifts of H8α and H8β and most of all the coupling constant $J_{9-11\beta}$=4.1 Hz testify to the existence of a conformational equilibrium of two forms of **5**: with a chair and with a boat ring C. The fraction of the boat conformation can be calculated as equal to ca. 22%, which is qualitatively corroborated by semi-empirical calculation. The reason for such a value could be the repulsion of one of the allyl hydrogen atoms at C14 with H8α in the chair conformation (similar as in **2**) and with H5α in the boat conformation (which does not occur in **2** and explains the lower contribution of the boat conformer in equilibrium for **5** than for **2**).

The possible explanation of the former scientists having assigned to *seco*(11,12)-12,13-didehydromultiflorine (**8**) the structure **6** could be a rearrangement of the methylation product of angustifoline **3** giving as a result tetrahydrorhombifoline (**9**) the reduction of which leads to the same product **7b** as the reduction of **8**. The doubling of some ^{13}C NMR signals in **4**[16] may be a result of the coexistence of two conformers differing in the orientation of N12–H bond and full π–π–p electron conjugation in the *exo*-conformer while in the *endo*-conformer a non-conjugated ketone carbonyl group occurs.

4. Experimental materials and methods

IR spectra were recorded with a FTIR Bruker 113v spectrophotometer. EIMS spectra were performed with an AMD 402 spectrometer (ionizing voltage 66 eV, accelerating voltage 8 kV, temp. 200°C). ^{13}C NMR spectra were obtained on a Varian 300 Mercury spectrometer at 75.462 MHz (number of transients 10000, acquisition time 1.5 s, spectral width 13718 Hz, number of points 27372, digital resolution 0.50 Hz. ^{1}H NMR spectra: number of transients 64, acquisition time 3.0 s, the 90° pulse width 8 μs, the 45° pulse width 4 μs, spectral width 9000 Hz, number of points 54016, digital resolution 0.167 Hz per point). The ^{1}H and all 2D NMR (^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY, 2D-*J*-resolved, HMQC, and HMBC) spectra were recorded with a Bruker Avance 600 spectrometer equipped with a 5 mm TBI ^{1}H inverse probe head, operating at 600.13 MHz using standard Bruker programs. The concentrations were ca. 0.05 M. Apodization:[21]

Lorentzian/Gaussian, LB-1.5, GB 0.2.

TLC was performed on silica gel pre-coated plates (Merck). System 1: acetone–methanol–methanol saturated with NH_3 20:1:1, system 2: CH_2C1_2–methanol–methanol saturated with NH_3 18:2:1, system 3: $CHC1_3$–C_2H_5OH 3:2.

4.1. Plant material

L. albus var. Satmarean is a primitive line descending from Portuguese wild lupins. A voucher specimen is deposited in the Home Lupin Genes Bank, Wiatrowo near Wągrowiec, Poland, No Wt 95098.

4.2. Extraction of albine (4)

The procedure is an adaptation of the method described previously.[22] White Lupin var. Satmarean seeds (2.00 kg) were ground and the flour was defatted in an extractor by means of CH_2Cl_2. After drying, it was mixed with 3.00 dm^3 of 30% aqueous KOH and allowed to stand overnight. The obtained substance was then mixed with ca. 1.8 kg of diatomaceous earth and the alkaloids were extracted by means of 6.00 dm^3 of CH_2C1_2. After about 25 h extraction and solvent evaporation, ca. 60 g of crude alkaloid mixture was obtained. This amount was dissolved in CH_2C1_2, mixed with purified sea sand and the solvent was allowed to evaporate, then the alkaloids were extracted in a Soxhlet extractor by means of petroleum ether, ethyl ether and CH_2C1_2 giving fractions 18.9, 23.9 and 12.3 g, respectively (total 55.1 g of preliminary purified alkaloids). Each fraction was mixed again with sand in the same way and re-extracted with the three solvents in the Soxhlet once again. All fractions were chromatographically checked, those containing albine were submitted to a series of chromatographic separations on $A_{12}O_3$ (activity grade 2) with petroleum ether, ethyl ether, CH_2C1_2, $CHCl_3$ and CH_3OH. The fractions which contained mainly lupanine

were neutralized with $HClO_4$, the precipitated lupanine perchlorate was separated and the mother liquor was converted to a mixture of free bases of alkaloids and submitted to column chromatography once again. Six fractions enriched with albine obtained by separation in the Soxhlet extractor or chromatographic column were combined (total 6.735 g). TLC revealed mainly 13α-hydroxylupanine and small amounts of lupanine, multiflorine, 13α-hydroxymultiflorine, albine, and an unidentified alkaloid. The mixture was re-chromatographed on Al_2O_3 (1:50). About 3.0 g of 13α-hydroxylupanine were isolated, the rest was re-chromatographed once again on Al_2O_3 (1:100). From the CH_2Cl_2 fraction, 0.54 g of mixture of 13α-hydroxylupanine and multiflorine enriched with albine were obtained. This mixture was several times separated on a short column (silica gel, 1:200, $CHCl_3$–C_2H_5OH 3:2) giving in result a yellow precipitate (0.100 g). The precipitate was converted to perchlorate and a yellow mud (0.110 g) was precipitated, giving 0.070 g (0.09% of the total preliminary purified alkaloids) of chromatographically pure white powder, mp 255–260°C, after a series of recrystallizations from methanol. The perchlorate was converted to the free base of albine, colorless oil, IR like Ref. 4, MS: *m/z* 232 (20, parent ion), 191 (100), 149 (48), 122 (34), 120 (22), 112 (31), 110 (66), 96 (30), 80 (25), 55 (21), 41 (50)—similar to that of Ref. 16.

4.3. *N*-Methylalbine

35 mg of albine was dissolved in 3.0 ml of anhydrous acetone. 0.01 ml of CH_3I was added and the whole was magnetically stirred under reflux. According to a TLC analysis, the reaction seemed to be finished after 75 min. Acetone was evaporated and the residue was dissolved in a small portion of water, strongly alkalized by means of NaOH and mixed with ca. 2 g of diatomaceous earth. The obtained mass was placed to a column with a small amount of alkaline diatomaceous earth and the alkaloids were eluted by means of hexane (ca. 100 ml) and subsequently by CH_2C1_2 (ca. 30 ml) to negative Dragendorff test.[23] From the hexane and CH_2C1_2 fractions, 35 and 9 mg, respectively, of alkaloids were obtained but the TLC analysis revealed that the hexane fraction contained quite a lot of the substrate. After double chromatography on Al_2O_3 (1:20) from fractions of ethyl ether and CH_2C1_2 21 mg of pure *N*-methylalbine were obtained. EIMS: *m/z* 246 (2%, parent ion), 205 (100), 110 (77), 94 (43), 82 (9), 58 (8). HRMS-parent ion 246.17253 (calcd for $C_{15}H_{22}N_2O$: 246.17322). Anal. calcd (%) for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 72.99; H, 9.13; N, 11.28.

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