

STRUCTURE OF THE ALKALOID KALIDINE

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The spatial structure of the alkaloid kalidine obtained from the epigeal part of *Kalidium gracile* Fenzl. has been determined by IR and NMR spectroscopy and x-ray structural analysis. It has been established that it is the chloride of the trimethyl derivative of glycineamide.

Continuing a study of the alkaloid composition of plants growing in Mongolia [1], we have investigated the epigeal part of *Kalidium gracile* Fenzl. (family Chenopodiaceae) collected in the South Gobi aimak of the Mongolian People's Republic in the flowering stage.

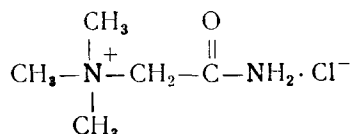
The comminuted epigeal part was extracted with ethanol. Acidification of the extract with hydrochloric acid yielded a crystalline substance with mp 238-239°C (acetone-water) giving a positive reaction for alkaloids with tungstosilicic acid and the Dragendorff reagent. The substance contained a chloride ion, the presence of which was detected by the Beilstein test and by a qualitative reaction with aqueous silver nitrate solution. The alkaloid is new and we have called it kalidine.

The IR spectrum of kalidine had the band of the stretching vibrations of a carbonyl group at 1730 cm⁻¹. The PMR spectrum showed only two signals, in the form of broadened singlets at 3.68 and 4.57 ppm, the ratio of the intensities of which was approximately 4.4:1. According to the values of their chemical shifts, these signals can be assigned to the protons of $\overset{+}{N}-CH_3$ and $\overset{+}{N}-CH_2-C=O$ groups, respectively [2]. Their singlet nature indicates the absence of spin-spin coupling of the protons of the methyl and methylene groups, i.e., these protons do not interact vicinally. It follows from the ratio of the intensities of the signals of the protons of the methyl and methylene groups that they are present in the molecule in a ratio of 3:1.

Thus, the facts given above make it possible to assume the presence in kalidine of the $(CH_3)_3\overset{+}{N}-CH_2-C=O$ structural element.

In the ¹³C NMR spectrum obtained under the conditions of complete and incomplete decoupling of C-H interactions, three signals appeared at (ppm): 54.00 (quartet), 63.77 (triplet), and 166.77 (singlet). From the values of the chemical shifts, the strong-field quartet can be assigned to the carbon atoms of $(CH_3)_3\overset{+}{N}$ -, the triplet signal at 63.77 ppm to the carbon atom of the methylene group of $\overset{+}{N}-CH_2-C=O$, and the weak-field singlet signal to the carbon of a carbonyl group. The position of the singlet signal (166.77 ppm) shows that the carbonyl group is most probably linked to a heteroatom.

The composition of kalidine could not be established by elemental analysis and from its mass spectrum. Therefore, in order to establish the structure completely and reliably we performed an x-ray structural investigation. The x-ray structural analysis permitted the following structure to be established for kalidine:



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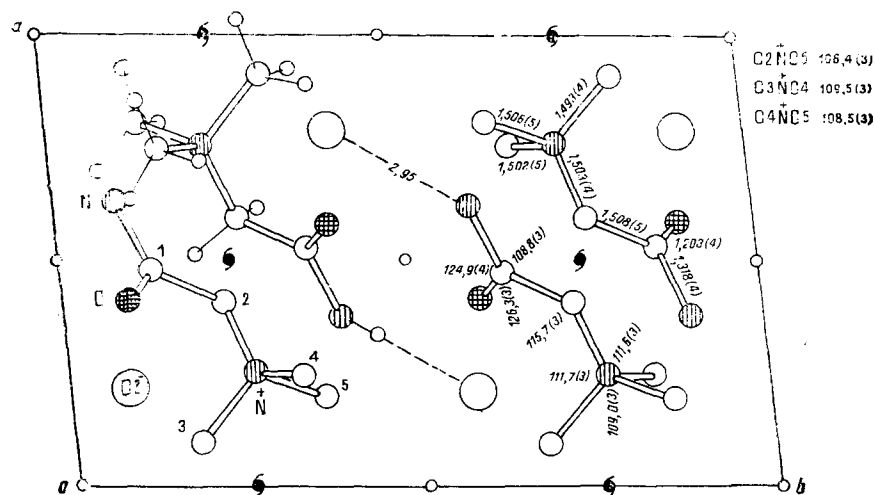


Fig. 1. Crystal and molecular structure of kalidine (for clarity the H atoms found experimentally are shown in only one molecule).

TABLE 1. Coordinates of Atoms ($\times 10^4$, for H atoms $\times 10^3$) in the Structure of Kalidine

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C	2146 (1)	923 (1)	7581 (1)	H (N)	337	-55	653
N	6238 (4)	-982 (2)	3901 (3)	H21	496	-299	579
N	2375 (4)	2684 (3)	3726 (3)	H22	611	-270	471
O	4298 (4)	1901 (3)	2096 (3)	H31	917	-134	529
C1	4813 (5)	1345 (3)	3261 (5)	H32	892	-111	708
C2	4124 (5)	2268 (3)	4212 (4)	H33	1032	-274	647
C3	851 (5)	1719 (4)	3727 (5)	H41	622	-387	781
C4	2544 (5)	3230 (4)	2227 (4)	H42	731	-258	849
C5	1964 (6)	3598 (4)	4817 (5)	H43	859	-371	804
				H51	802	-323	417
				H52	694	-427	528
				H53	925	-375	531

Thus, an NH_2 group is attached to the fragment found earlier, and the chloride anion is present in the immediate vicinity of the amide group, forming a hydrogen bond with one of the hydrogen atoms of this group. This bond is also, apparently, responsible for the high value of the frequency of the absorption of the amide carbonyl in the IR spectrum of kalidine (1730 cm^{-1}). When the chloride anion was replaced by a hydroxide anion by the reaction of kalidine with freshly prepared silver oxide, the amide carbonyl appeared in the IR spectrum of the tertiary base at 1640 cm^{-1} .

Figure 1 shows the crystal and molecular structure of kalidine in projection on the (001) plane. It also gives the bond lengths and valence angles. The geometric parameters found by x-ray structural analysis agree well with literature [3] and standard [4] figures, i.e., the lengths of the bonds $\text{C}_{\text{sp}^3}-\text{N}$ (averaging 1.501 \AA) and $\text{C}_{\text{sp}^2}-\text{N}$ in the amide moiety (1.318 \AA), and $\text{C}=\text{O}$ (1.203 \AA) are the usual ones. An analysis of the crystal structure of kalidine shows that the Cl^- anion is close to the amide moiety of the cation ($\text{N} \cdots \text{Cl}$ distance 2.95 \AA), forming a hydrogen bond of the $\text{N-H} \cdots \text{Cl}$ type.

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrophotometer using tablets with KBr, PMR spectra on a JNM-C-60 HL spectrometer with a working frequency of 60 MHz in D_2O with HMDS as external standard (0), and ^{13}C NMR spectra on a Varian XR-100-15 Fourier spectrometer at a frequency of 25.16 MHz in D_2O under conditions of complete and incomplete decoupling of C-H interactions. The chemical shifts of the carbon atoms were calculated relative to the signals of the carbon atoms of the methyl radical of acetone as internal standard, which is 30.4 ppm , $\delta_{\text{TMS}} = \delta(\text{CH}_3)_2\text{CO} + 30.4 \text{ ppm}$.

Isolation of Kalidine. The raw material (17 kg) was extracted with ethanol. The concentrated ethanolic extract was diluted with water (1:1) and was extracted successively with hexane (20 g [sic]), chloroform, (103 g [sic]), ethyl acetate (40 g [sic]), and butanol (140 g [sic]). The aqueous alcoholic mother liquor was concentrated. Methanol was added to 1/4 of the concentrated mother liquor and the mixture was filtered and was acidified with an acetone solution of hydrochloric acid. The precipitate formed (126.7 g) was separated off and crystallized from water, from aqueous alcohol, and from a mixture of acetone and water (1:2); mp 238-239°C. Found, %: C 39.66; H 8.32; $C_5H_{13}N_2OC$. Calculated, %: C 39.34; H 8.52.

Preparation of the Quaternary Base. With shaking, freshly prepared silver oxide was added in portions to a solution of kalidine (0.28 g) in water (3 ml). The precipitate of silver chloride that deposited was separated off. When dimethyl sulfoxide was added to the filtrate, a precipitate of the quaternary base (0.05 g) deposited. PMR spectrum (δ , ppm): 3.90 (singlet, 9 H, $(CH_3)_3N^+$); 4.30 (singlet, 2H, $-N^+-CH_2-C=O$).

X-Ray Structural Analysis. Crystals of kalidine were grown from a solution in aqueous ethanol. The spectral group and the parameters of the elementary cell were determined from precession photographs and were refined on a Syntex P2₁ diffractometer using $CuK\alpha$ radiation: $a = 7.425(4)$, $b = 11.554(5)$, $c = 9.097(4)$ Å, $\gamma = 96.67(4)^\circ$, space group P2₁/b, $z = 4$. The complete set of experimental figures was obtained on the diffractometer mentioned (B. T. Ibragimov, Institute of Bioorganic Chemistry of the Uzbek SSR Academy of Sciences took part in the experiment). The calculations made use of 918 reflections with intensities exceeding 2σ . The structure was interpreted by the direct method using the Rentgen-75 group of programs in the automatic regime and was refined by the method of least squares in the anisotropic approximation to $R = 0.066$. The coordinates of the basis atoms, including H atoms found from a difference electron density synthesis are given in Table 1.

CONCLUSION

The spatial structure of the new alkaloid kalidine, which is the chloride of the trimethyl derivative of glycineamide has been established.

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