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ALKALOIDS OF *Aconitum kirinense*. STRUCTURE OF AKIRAMIDINE

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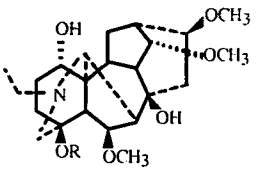
A new alkaloid called akiramidine is isolated from the aerial part of Aconitum kirinense. *The structure 6β,14α,16β-trimethoxy-1α,4β,8β-trihydroxy-N-ethylaconitane is proposed based on spectral data and confirmed by chemical transformation from akiramine.*

Active alkaloids of *Aconitum* sp. have come under intense scientific scrutiny. The medicinal plant *Aconitum kirinense* Nakai is native to Russia, China, and Japan [1]. It is used in Chinese folk medicine to treat rheumatic fever, rheumatoid arthritis, neuralgia, endemic deformative osteoarthrosis, atetoid spasms, and chest and stomach pain caused by hypothermia [2]. Nine C-20 diterpene alkaloids have been isolated from the plant growing in northeastern provinces of China [3, 4].

The alkaloid composition of *A. kirinense* from Primorskii Krai of Russia that was studied by us differed substantially from that of the plant grown in China. The alkaloids consist quantitatively of the new bisnorditerpene alkaloids with the lycoctonine skeleton, the C framework of which consists of 18 atoms [5]. The different alkaloid compositions obviously explain the different ethnopharmacologies of the plants used in Chinese and Russian Far-East folk medicine [6].

Our investigations of the alkaloids of this plant isolated a new base that we called akiramidine (**1**).



1: R=H
2: R=$COCH_3$

Akiramidine (**1**) is an amorphous base of empirical formula $C_{23}H_{37}NO_6$. The IR spectrum of **1** indicates the presence of hydroxyls and ethers. According to the PMR spectrum, **1** contains an N-ethyl and three methoxy groups. Electron-impact mass spectrometry of **1** reveals that akiramidine has the lycoctonine skeleton. The base peak in the mass spectrum of **1** is [M - 17], which forms via loss of a hydroxy radical from C-1. The molecular peak (M^+ 423, 9%) and [M^+ - 15] (*m/z* 408, 22%), which results from loss of a methyl radical from the N-ethyl group, are also present.

The PMR spectra of **1** and akiramine (**2**) (Table 1), which was previously isolated from this plant [5], are very similar, indicating that the structures are similar. A one-proton triplet at 3.56 ppm (J = 5 Hz) is consistent with the presence of an α-methoxy group on C-14 and the lack of substituents on C-9 and C-13. A one-proton triplet at 3.71 ppm (J = 2.5 Hz) suggests that C-1 has an α-hydroxyl. A one-proton doublet at 4.06 ppm (J = 7 Hz) indicates that C-6 has a β-methoxy group. Keeping in mind the functional composition of akiramidine and the lack of an acetoxy group in it, the alkaloid can be formulated as an aminoalcohol of akiramine. Alkaline hydrolysis of akiramine produces an aminoalcohol that is identical to akiramidine. Therefore, akiramidine has the structure **1**.

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TABLE 1. PMR Data for Akiramidine (**1**) and Akiramine (**2**)

Compound	Chemical shift, δ, ppm: SSCC, J, Hz					
	$N\text{-}CH_2CH_3$	$OCOCH_3$	OCH_3	H-1β	H-6α	H-14β
1	1.07, 3H, t, J = 7		3.32, 3.30 3.36, each 3H, s	3.71, t, J = 2.5	4.06, d, J = 7	3.56, t, J = 5
2	1.06, 3H t, J = 7	1.97, 3H, s	3.28, 3.29 3.35, each 3H, s	3.72, t, J = 2.5	4.02, d, J = 7	3.55, t, J = 5

EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer 2000 Fourier-spectrometer in KBr pellets. PMR spectra were obtained on a Tesla BS-567 (100 MHz) spectrometer with HMDS internal standard in $CDCl_3$. Mass spectra were measured on a MX-1310 spectrometer equipped with a direct probe for introducing samples into the ion source.

Silica gel (LS, Czech Republic) was used for chromatography. TLC on silica gel used the solvent systems $CHCl_3$—CH_3OH, 10:1 (1) and benzene—CH_3OH, 4:1 (2); on aluminum oxide, $CHCl_3$—CH_3OH, 100:1.

Isolation of Akiramidine (1). Further chromatography of the hexane mother liquors of *Aconitum kirinense* [5] with elution by solvents mixture benzene—CH_3OH (20:1) yielded akiramidine (0.04 g). IR spectrum (ν, cm^{-1}): 3423, 2932, 2364, 2458, 1398, 1303, 1226, 1089, 1004, 977, 880, 592. Mass spectrum, *m/z* (%): M^+ 423 (9), 408 (22), 406 (100), 390 (9), 388 (5): PMR spectra are listed in Table 1.

Alkaline Hydrolysis of Akiramine (2). A solution of akiramine (0.03 g) in CH_3OH (3 ml) was treated with KOH (0.15 g) and refluxed for 2 h. The solid remaining after the CH_3OH was removed was dissolved in water (10 ml) and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4. The $CHCl_3$ was removed. The product was purified on a silica-gel column with elution by $CHCl_3$—CH_3OH (10:1). The resulting powdered aminoalcohol (0.017 g) was identified as akirimidine by TLC and IR and PMR spectra.

REFERENCES

1. *Flora of the USSR*, Academy of Sciences of the USSR, Moscow (1937), Vol. 7. p. 205.
2. *The Editorial Board of Zhong Guo Ben Cao Tu Lu*, Zhong Guo Ben Cao Tu Lu, People's Health Press, Beijing (1989), p. 46.
3. Feng Feng and J.-H. Liu, *J. China Pharm. Univ.*, **27**, No. 2, 74 (1996).
4. Feng Feng and Y.-H. Liu, Proceeding of UNESCO Regional Symposium on Drug Development from Medicinal Plants, Hanghou, China (1996), p. 357.
5. U. T. Teshebaeva, M. N. Sultankhodzhaev, and A. A. Nishanov, *Khim. Prir. Soedin.*, 498 (1999).
6. M. N. Sultankhodzhaev, A. A. Nishanov, Z. S. Boronova, U. T. Teshebaeva, and V. G. Kondrat'ev, in: Materials of the International Conference Dedicated to the Memory of V. G. Minaeva, Novosibirsk (1998), p. 61.