Crystal structure of lappaconitine-ium nitrate monohydrate, $C_{32}H_{47}N_3O_{12}$

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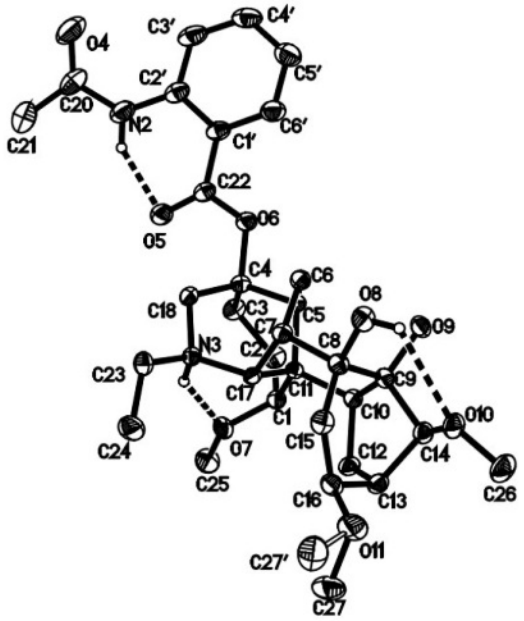

Abstract

$C_{32}H_{47}N_3O_{12}$, monoclinic, $P2_1$ (no. 4), a = 10.5829(4) Å, b = 12.4835(5) Å, c = 12.3115(5) Å, β = 91.699(2)°, V = 1625.8 Å^3, Z = 2, $R_{gt}(F)$ = 0.0415, $wR_{ref}(F^2)$ = 0.1016, T = 294 K.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.18×0.24×0.26 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.04 cm^{-1}
Diffractometer, scan mode:	CCD area detector, φ and ω
$2\theta_{max}$:	54.86°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	10077, 3828
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3040
$N(param)_{refined}$:	456
Programs:	CrysAlis PRO [6], SHELX [7], DIAMOND [8]

Source of material

The synthesis of lappaconitine-ium nitrate was carried out by adding 1 mmol lappaconitine and 1 mmol nitric acid into 20 ml ethanol, followed by stirring at 348K for 24h. After evaporation of the solution by decompression, acetone was added to the reaction mixture. At last, acetone was vaporized and colourless crystals of $C_{32}H_{47}N_3O_{12}$ were obtained.

Experimental details

Because of a disorder of the molecule, C27 has two possible positions with an occupancy of 0.5/0.5. And some disorder of other groups in the molecule caused larger than usual U_{eq} values for the specified element type and some hydrogen atoms in the non-solvent part of the structure.

Discussion

Lappaconitine, isolated originally first by Rosendahl [1], is an important alkaloid of the aconite family [2]. The biological activity is closely related to the structure, and lappaconitine and its salts exhibited a wide rang of biological activities [3]. In particular, their analgesic ability is excellent. The structures of lappaconitine derivatives have revealed many interesting structural phenomena, including intramolecular hydrogen bonds and chirality. Marion and co-workers investigated the structure of lappaconitine since 1963. But certain unusual results have precluded a complete elucidation of the structure through IR, MS and NMR [4, 5]. Lappaconitine is almost insoluble in water, so it reacts slowly as an analgesic medicine. In order to overcome the dissolubility and investigate the structure of lappaconitine derivatives, the lappaconitine was extracted from the root of *Aconitum sinomontanum Nakai* which is own in Gansu province China and the title compound was synthesized. The title compound can be dissolved in water easily. A water molecule and the nitrate counter anion is part of the structure. A proton is found at the atom N3. Both N–H atoms participate in the formation of intramolecular hydrogen bonds (N2–H2N···O5, N3–H3N···O7), which form two six-members rings including the atoms C2', C1', C22 and the atoms C17, C11, C1. Another six-member ring was shaped through O8–H8···O10 intramolecular hydrogen bond with atoms C8, C9 and C14. Though intramolecular hydrogen bonds the molecule structure gets stabilized. In the structure, there are four six-member rings, denoted A, B, D and E, and two five-member rings, denoted C and F. Ring A (C1, C2, C3, C4, C5, C11) posess a boat conformation stabilized by a hydrogen bond, ring B (C7, C8, C9, C10, C11, C17) adopts a chair form, ring C (C9, C10, C11, C12,C13, C14) is an envelope form with atom C13 at the flap, ring D (C8, C9, C14, C13, C16, C15) is a boat form, ring E (C4, C5, C11, C17, N2, C18) comes into being a chair form and ring F (C5, C6, C7, C17, C11) forms an envelope form with atom C17 as the flap. Because the title compound is a chiral molecule, in order to obtain its absolute configuration, we used lappaconitine hydrobromide as a chiral reference molecule of known absolute configuration. On this basis, the absolute configuration of lappaconitine nitrate was assigned as 1*S*, 4*S*, 5*S*, 7*S*, 8*S*, 9*S*, 10*S*, 11*S*, 13*R*, 14*S*, 16*S*, 17*R*. The nitrate counter anion an the water molecule participate in intermolecular hydrogen bonds (O12–H12D···O3, N3–H3N···O2, N3–H3N···O1, O9–H9···O12). Through the four intermolecular hydrogen bonds, the molecules connect one by one along the *c* axis.

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Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	Occ.	*x*	*y*	*z*	U_{iso}
H(1)	2*a*		1.0017	0.1866	0.3453	0.039
H(2A)	2*a*		1.1739	0.1588	0.2334	0.050
H(2B)	2*a*		1.2062	0.2444	0.3232	0.050
H(3A)	2*a*		1.1575	0.2853	0.1006	0.048
H(3B)	2*a*		1.2807	0.3157	0.1676	0.048
H(5)	2*a*		1.1583	0.4239	0.3618	0.038
H(6A)	2*a*		1.0507	0.5944	0.2678	0.044
H(6B)	2*a*		1.0484	0.5747	0.3943	0.044
H(7)	2*a*		0.8397	0.5758	0.2682	0.039
H(10)	2*a*		1.0136	0.3097	0.4842	0.036
H(12A)	2*a*		0.7943	0.2394	0.3856	0.044
H(12B)	2*a*		0.8583	0.1957	0.4939	0.044
H(13)	2*a*		0.6851	0.2677	0.5694	0.047
H(14)	2*a*		0.8655	0.3502	0.6417	0.045
H(15A)	2*a*		0.6386	0.5427	0.4703	0.051
H(15B)	2*a*		0.6491	0.5092	0.3489	0.051
H(16)	2*a*		0.6198	0.3401	0.3824	0.051
H(17)	2*a*		0.7924	0.3767	0.2751	0.033
H(18A)	2*a*		1.0209	0.5347	0.1112	0.039
H(18B)	2*a*		1.0475	0.4339	0.0395	0.039
H(21A)	2*a*		1.4407	0.5631	–0.3505	0.115
H(21B)	2*a*		1.3057	0.5866	–0.3071	0.115
H(21C)	2*a*		1.3816	0.4863	–0.2651	0.115
H(23A)	2*a*		0.7802	0.5318	0.0963	0.047
H(23B)	2*a*		0.8252	0.4651	–0.0032	0.047

Table 2. continued.

Atom	Site	Occ.	*x*	*y*	*z*	U_{iso}
H(24A)	2*a*		0.6377	0.4045	0.1403	0.090
H(24B)	2*a*		0.6951	0.3219	0.0596	0.090
H(24C)	2*a*		0.6200	0.4214	0.0146	0.090
H(25A)	2*a*		0.9371	0.0530	0.2235	0.084
H(25B)	2*a*		1.0272	0.0886	0.1314	0.084
H(25C)	2*a*		0.8808	0.0831	0.1083	0.084
H(26A)	2*a*		0.7649	0.4063	0.7918	0.091
H(26B)	2*a*		0.6355	0.3874	0.7293	0.091
H(26C)	2*a*		0.6644	0.4985	0.7842	0.091
H(27A)	2*a*	0.5	0.3537	0.3219	0.5193	0.130
H(27B)	2*a*	0.5	0.4634	0.2409	0.4981	0.130
H(27C)	2*a*	0.5	0.4083	0.3117	0.4028	0.130
H(27D)	2*a*	0.5	0.3462	0.4086	0.4986	0.131
H(27E)	2*a*	0.5	0.4017	0.3441	0.4018	0.131
H(27F)	2*a*	0.5	0.4203	0.4685	0.4085	0.131
H(3')	2*a*		1.6044	0.7238	–0.0432	0.076
H(4')	2*a*		1.6671	0.7857	0.1252	0.076
H(5')	2*a*		1.5638	0.7324	0.2785	0.074
H(6')	2*a*		1.3953	0.6155	0.2614	0.064
H(12C)	2*a*		0.165(5)	0.271(5)	0.628(4)	0.11(2)
H(12D)	2*a*		0.135(5)	0.336(5)	0.726(4)	0.10(2)
H(2N)	2*a*		1.379(4)	0.529(4)	–0.091(3)	0.07(1)
H(3N)	2*a*		0.900(3)	0.344(2)	0.127(2)	0.018(7)
H(8)	2*a*		0.8255	0.6288	0.5324	0.067
H(9)	2*a*		1.0509	0.4557	0.5855	0.060

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	Occ.	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2*a*		1.0166(3)	0.2367(2)	0.2857(2)	0.038(2)	0.026(1)	0.033(1)	0.002(1)	0.001(1)	0.000(1)
C(2)	2*a*		1.1549(3)	0.2306(3)	0.2582(3)	0.042(2)	0.034(2)	0.049(2)	0.010(1)	0.003(1)	0.001(1)
C(3)	2*a*		1.1894(3)	0.3108(2)	0.1707(3)	0.037(2)	0.040(2)	0.044(2)	0.007(1)	0.011(1)	0.001(1)
C(4)	2*a*		1.1345(3)	0.4235(2)	0.1922(2)	0.030(2)	0.032(1)	0.036(1)	–0.002(1)	0.004(1)	0.000(1)
C(5)	2*a*		1.0888(3)	0.4347(2)	0.3086(2)	0.031(2)	0.033(2)	0.031(1)	–0.005(1)	0.003(1)	0.000(1)
C(6)	2*a*		1.0255(3)	0.5447(2)	0.3237(2)	0.045(2)	0.031(2)	0.034(2)	–0.005(1)	0.004(1)	–0.004(1)
C(7)	2*a*		0.8824(3)	0.5223(2)	0.3145(2)	0.039(2)	0.026(1)	0.034(1)	0.001(1)	0.002(1)	–0.000(1)
C(8)	2*a*		0.8241(3)	0.5190(2)	0.4276(2)	0.040(2)	0.028(1)	0.035(1)	0.001(1)	0.004(1)	–0.006(1)
C(9)	2*a*		0.8994(3)	0.4407(2)	0.5047(2)	0.036(2)	0.034(2)	0.031(1)	–0.003(1)	0.000(1)	–0.003(1)
C(10)	2*a*		0.9409(3)	0.3395(2)	0.4433(2)	0.032(2)	0.027(1)	0.031(1)	0.001(1)	0.002(1)	–0.001(1)
C(11)	2*a*		0.9814(3)	0.3518(2)	0.3244(2)	0.030(2)	0.025(1)	0.029(1)	–0.002(1)	–0.000(1)	–0.001(1)
C(12)	2*a*		0.8295(3)	0.2598(2)	0.4563(2)	0.045(2)	0.028(1)	0.039(2)	–0.004(1)	0.006(1)	0.002(1)
C(13)	2*a*		0.7293(3)	0.3182(2)	0.5228(2)	0.044(2)	0.039(2)	0.035(2)	–0.006(1)	0.010(1)	–0.000(1)
C(14)	2*a*		0.8137(3)	0.3931(2)	0.5907(2)	0.043(2)	0.038(2)	0.033(1)	–0.000(1)	0.004(1)	–0.002(1)
C(15)	2*a*		0.6800(3)	0.4932(3)	0.4220(3)	0.040(2)	0.045(2)	0.042(2)	0.006(2)	0.005(1)	–0.001(1)
C(16)	2*a*		0.6349(3)	0.3803(3)	0.4499(3)	0.035(2)	0.053(2)	0.041(2)	–0.007(2)	0.006(1)	–0.012(1)
C(17)	2*a*		0.8742(3)	0.4103(2)	0.2617(2)	0.033(2)	0.025(1)	0.026(1)	–0.002(1)	0.006(1)	–0.001(1)
C(18)	2*a*		1.0271(3)	0.4572(2)	0.1120(2)	0.035(2)	0.033(1)	0.029(1)	–0.001(1)	0.004(1)	0.003(1)
C(20)	2*a*		1.4457(4)	0.6250(4)	–0.1984(3)	0.068(3)	0.062(2)	0.059(2)	0.011(2)	0.025(2)	0.017(2)
C(21)	2*a*		1.3883(5)	0.5594(4)	–0.2883(3)	0.087(3)	0.087(3)	0.056(2)	0.013(3)	0.006(2)	0.012(2)
C(22)	2*a*		1.2952(3)	0.5150(3)	0.0914(2)	0.035(2)	0.038(2)	0.042(2)	0.001(1)	0.008(1)	0.005(1)
C(23)	2*a*		0.7969(3)	0.4598(3)	0.0708(2)	0.039(2)	0.044(2)	0.034(1)	0.006(1)	–0.005(1)	0.002(1)
C(24)	2*a*		0.6766(3)	0.3962(3)	0.0714(3)	0.041(2)	0.069(2)	0.069(2)	–0.006(2)	–0.012(2)	0.010(2)
C(25)	2*a*		0.9457(4)	0.0993(3)	0.1619(3)	0.082(3)	0.032(2)	0.054(2)	–0.002(2)	0.003(2)	–0.014(2)
C(26)	2*a*		0.7004(4)	0.4390(3)	0.7465(3)	0.064(2)	0.073(3)	0.047(2)	0.001(2)	0.025(2)	–0.003(2)
C(27)	2*a*	0.5	0.4288(9)	0.310(1)	0.4792(9)	0.061(6)	0.121(9)	0.079(6)	–0.045(7)	0.017(5)	–0.019(6)
C(27')	2*a*	0.5	0.4152(8)	0.404(1)	0.4501(8)	0.033(5)	0.16(1)	0.068(5)	–0.003(6)	0.005(4)	0.003(7)
C(1')	2*a*		1.3988(3)	0.5950(2)	0.0993(3)	0.031(2)	0.038(2)	0.054(2)	0.001(1)	0.006(1)	0.009(1)
C(2')	2*a*		1.4624(3)	0.6272(3)	0.0054(3)	0.038(2)	0.046(2)	0.056(2)	0.001(2)	0.008(2)	0.013(2)
C(3')	2*a*		1.5625(4)	0.7005(3)	0.0178(4)	0.043(2)	0.065(3)	0.081(3)	–0.011(2)	0.014(2)	0.022(2)
C(4')	2*a*		1.5996(4)	0.7382(3)	0.1188(4)	0.043(2)	0.056(2)	0.092(3)	–0.014(2)	–0.005(2)	0.016(2)
C(5')	2*a*		1.5382(4)	0.7067(3)	0.2105(4)	0.054(2)	0.058(2)	0.072(3)	–0.009(2)	–0.008(2)	–0.001(2)
C(6')	2*a*		1.4379(3)	0.6361(3)	0.1997(3)	0.045(2)	0.055(2)	0.060(2)	–0.010(2)	0.004(2)	0.005(2)
N(1)	2*a*		–0.0038(3)	0.2720(2)	0.8921(2)	0.070(2)	0.038(2)	0.042(2)	0.002(2)	0.002(1)	–0.008(1)
N(2)	2*a*		1.4245(3)	0.5858(3)	–0.0966(3)	0.057(2)	0.061(2)	0.054(2)	–0.008(2)	0.013(2)	0.013(2)
N(3)	2*a*		0.9007(2)	0.4106(2)	0.1412(2)	0.036(1)	0.024(1)	0.030(1)	0.002(1)	0.0002(9)	0.0010(9)
O(1)	2*a*		0.0822(3)	0.2099(3)	0.8746(3)	0.077(2)	0.058(2)	0.152(3)	0.014(2)	0.009(2)	–0.029(2)
O(2)	2*a*		–0.0866(4)	0.2472(3)	0.9547(3)	0.116(3)	0.089(2)	0.073(2)	–0.006(2)	0.038(2)	0.003(2)
O(3)	2*a*		–0.0059(4)	0.3605(3)	0.8499(3)	0.151(3)	0.052(2)	0.082(2)	0.007(2)	0.010(2)	0.022(2)
O(4)	2*a*		1.5059(4)	0.7069(3)	–0.2137(3)	0.118(3)	0.084(2)	0.070(2)	–0.014(2)	0.028(2)	0.025(2)

Table 3. continued.

Atom	Site	Occ.	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(5)	2*a*		1.2663(2)	0.4631(2)	0.0113(2)	0.053(1)	0.054(1)	0.043(1)	–0.010(1)	0.012(1)	–0.004(1)
O(6)	2*a*		1.2343(2)	0.5047(2)	0.1851(2)	0.035(1)	0.044(1)	0.039(1)	–0.007(1)	0.0076(9)	–0.0006(9)
O(7)	2*a*		0.9338(2)	0.2085(2)	0.1956(2)	0.053(1)	0.028(1)	0.038(1)	0.001(1)	–0.0052(9)	–0.0072(8)
O(8)	2*a*		0.8362(2)	0.6276(2)	0.4667(2)	0.060(2)	0.033(1)	0.041(1)	0.005(1)	0.009(1)	–0.0099(9)
O(9)	2*a*		1.0031(2)	0.4980(2)	0.5541(2)	0.044(1)	0.039(1)	0.038(1)	–0.004(1)	–0.0048(9)	–0.0055(9)
O(10)	2*a*		0.7541(2)	0.4758(2)	0.6491(2)	0.054(1)	0.050(1)	0.035(1)	0.001(1)	0.013(1)	–0.0079(9)
O(11)	2*a*		0.5184(2)	0.3901(2)	0.5049(2)	0.036(1)	0.089(2)	0.071(2)	–0.007(1)	0.015(1)	–0.017(2)
O(12)	2*a*		0.1587(3)	0.3383(3)	0.6619(3)	0.073(2)	0.076(2)	0.061(2)	–0.002(2)	–0.002(2)	0.014(2)

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