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The Absolute Configuration of Tsukushinamine-A.1,2) A New Cage-Type Lupin Alkaloid from *Sophora franchetiana*

The absolute configuration of tsukushinamine-A, a novel cage-type lupin alkaloid, was determined by the X-ray analysis as 2 (6*R*, 7*R*, 9*S*, 14*R*).

Keywords——*Sophora franchetiana*; Leguminosae; tsukushinamine-A; alkaloid; cage-type lupin alkaloid; lupin alkaloid; X-ray analysis; absolute configuration; biosynthesis; baptifoline

As a result of screening plants belonging to the Leguminosae for lupin alkaloid,3–6) a novel cage-type lupin alkaloid, tsukushinamine (tsukushinamine-A),1) was isolated from the fresh epigeal parts of *Sophora franchetiana* as a colourless oil, $[\alpha]_D^{25}$ $-72.3°$ ($c=0.56$, EtOH), HBr-salt mp 260° (MeOH–acetone), together with (—)-cytisine, (—)-N-formylcytisine, (—)-rhombifoline, (—)-anagyrine, (—)-baptifoline and (±)-ammodendrine. Its structure has been proposed to be shown as **1** from spectroscopic data.7)

With regard to the final structure determination and the absolute configuration of tsukushinamine-A, we further wish to report that tsukushinamine-A can be drawn as **2** (6*R*, 7*R*, 9*S*, 14*R*) by the X-ray analysis.

Crystals of tsukushinamine-A hydrobromide suitable for an X-ray analysis were grown by the slow evaporation of a methanol/acetone solution. These crystals belonged to the

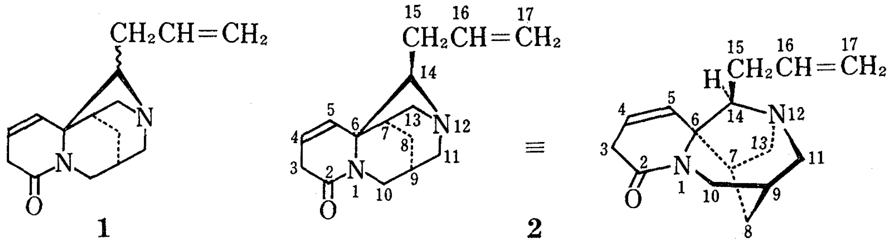

Chart 1

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1) The name of tsukushinamine was altered into tsukushinamine-A as a result of the presence of isomers B and C, and the numbering system of tsukushinamine-skeleton was also changed as **2**.
2) A part of this work was presented at the 22th Symposium on the Chemistry of Natural Products of Japan, Fukuoka, October 26, 1979, "Symposium Papers" p. 525.
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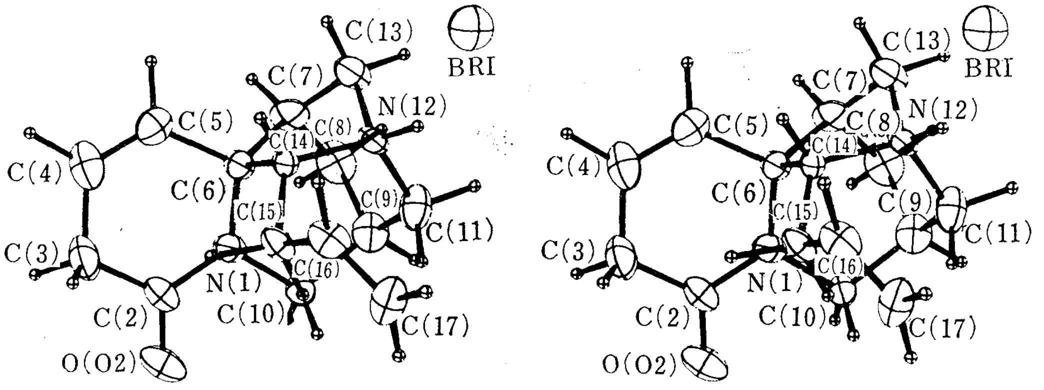

Fig. 1. A Stereoscopic View of the Tsukushinamine-A(**2**) Hydrobromide

orthorhombic space group $P2_12_12_1$ with the following unit cell dimensions: a=11.700(1), b=7.3809(9), and c=16.423(3) Å. A one Angstrom data set (maximum $\sin\theta/\lambda=0.5$) was collected at room temperature on a Syntex $P\bar{1}$ diffractometer using Cu–Kα radiation (λ=1.5418 Å). A trial structure was obtained using convention Patterson and Fourier techniques. This trial structure was verified as correct by full-matrix, least-squares refinement. The later stages of refinement included a full-matrix treatment of scale factor, secondary extinction factor, all non-hydrogen atom coordinates (Table I) and anisotropic temperature factors (Table II) in one matrix. Hydrogen atoms were included in the structure factor calculation of these later stages of refinement, but the hydrogen parameters (Table III) were not refined. The final R-index ($R=\sum||Fo|-|Fc||/\sum|Fo|$) was 0.034. A final difference Fourier revealed no missing or misplaced electron density. The absolute configuration of the molecule was

TABLE I. Non-hydrogen Atom Coordinates and Their Standard Deviations[a)]

	x/a	y/b	z/c
BR-(1)	28(1)	−7252 (1)	5566(0)
N (1)	8293(4)	−3588 (7)	2872(3)
C (2)	8302(5)	−4637 (9)	2203(4)
C (3)	8224(6)	−3755(10)	1380(4)
C (4)	8407(6)	−1758(10)	1393(4)
C (5)	8351(5)	−820 (9)	2068(4)
C (6)	8079(5)	−1626 (8)	2886(4)
C (7)	8801(5)	−659 (9)	3563(4)
C (8)	9252(5)	−1983(10)	4190(4)
C (9)	8285(5)	−3281 (9)	4373(3)
C (10)	8235(5)	−4575 (8)	3665(4)
C (11)	7154(5)	−2311 (9)	4569(3)
N (12)	6915(4)	−724 (7)	4006(3)
C (13)	7913(5)	525(10)	3990(4)
C (14)	6828(4)	−1224 (8)	3114(3)
C (15)	5949(4)	−2621 (9)	2903(3)
C (16)	4750(5)	−2113 (8)	3116(4)
C (17)	4033(5)	−3120(10)	3527(4)
O (02)	8370(4)	−6311 (7)	2264(3)

a) The values have been multipled by 10^4.

established at the 99.5% confidence level by the method of Ibers and Hamilton.[8,9] A stereoplot of the molecule is given in **2** (Fig. 1).[10] Table IV and V contained the bond distances and bond angles.

Table II. Non-hydrogen Anisotropic Temperature Factors and Their Standard Deviations[a]

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
BR-	671 (6)	636 (6)	467 (5)	−247 (5)	79 (3)	−89 (3)
1	388 (28)	326 (29)	416 (29)	48 (25)	42 (25)	−4 (28)
2	368 (37)	421 (46)	628 (48)	−4 (32)	10 (35)	−139 (40)
3	560 (42)	742 (55)	421 (39)	115 (41)	22 (34)	−139 (41)
4	551 (40)	688 (47)	401 (39)	56 (39)	−43 (35)	79 (41)
5	497 (37)	467 (39)	454 (37)	−8 (33)	64 (34)	79 (38)
6	444 (35)	360 (38)	432 (35)	73 (31)	60 (31)	21 (33)
7	405 (34)	470 (37)	529 (38)	−55 (32)	−18 (31)	−32 (36)
8	428 (33)	640 (43)	463 (36)	42 (35)	−102 (29)	−46 (37)
9	558 (39)	570 (39)	367 (33)	93 (27)	−55 (31)	95 (35)
10	491 (37)	408 (36)	530 (38)	79 (34)	33 (34)	121 (36)
11	494 (34)	578 (42)	360 (31)	37 (34)	7 (26)	37 (34)
12	387 (27)	389 (28)	359 (26)	20 (26)	44 (22)	−68 (25)
13	522 (38)	496 (41)	548 (41)	22 (36)	−112 (34)	−145 (37)
14	422 (33)	350 (32)	297 (30)	23 (29)	−7 (26)	21 (29)
15	437 (32)	431 (35)	330 (30)	23 (32)	1 (26)	−42 (33)
16	439 (35)	433 (35)	470 (35)	18 (33)	−156 (31)	57 (31)
17	465 (37)	600 (43)	493 (37)	−40 (36)	−1 (32)	−39 (38)
02	671 (31)	431 (33)	811 (37)	63 (26)	19 (27)	−196 (29)

a) The values have been multipled by 10^4.

Table III. Hydrogen Coordinates[a]

	x/a	y/b	z/c
H (C 3)	7374	−4007	1132
H (C 3)	8851	−4351	982
H (C 4)	8595	−1044	830
H (C 5)	8527	606	2012
H (C 7)	9549	4	3314
H (C 8)	9493	−1240	4739
H (C 8)	9984	−2684	3958
H (C 9)	8457	−4047	4929
H (C10)	8929	−5533	3701
H (C10)	7427	−5324	3694
H (C11)	7197	−1794	5187
H (C11)	6466	−3251	4514
H (N12)	6129	−162	4241
H (C13)	7705	1737	3656
H (C13)	8149	891	4609
H (C14)	6478	−138	2736
H (C15)	6173	−3872	3214
H (C15)	5991	−2881	2245
H (C16)	4423	−813	2917
H (C17)	3177	−2644	3665
H (C17)	4300	−4439	3747

a) The values have been multipled by 10^4. Temperature factors were fixed at 3.10 Å^2.

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8) J. Ibers and W.C. Hamilton, *Acta Crystallogr.*, **17**, 781 (1964).

9) W.C. Hamilton, *Acta Crystallogr.*, **18**, 502 (1965).

10) Full crystallographic details and parameters can be obtained from one (J.B.) of the authors.

Table IV. Bond Distances (Å) for Tsukushinamine-A·HBr

N (1)-C (2)	1.343 (8)	C (7)-C (13)	1.528(9)
N (1)-C (6)	1.470 (8)	C (8)-C (9)	1.514(9)
N (1)-C (10)	1.494 (8)	C (9)-C (10)	1.507(9)
C (2)-C (3)	1.504 (9)	C (9)-C (11)	1.538(8)
C (2)-O	1.242 (9)	N (12)-C (11)	1.518(8)
C (3)-C (4)	1.490 (11)	N (12)-C (14)	1.513(7)
C (4)-C (5)	1.309 (9)	C (13)-N (12)	1.488(8)
C (5)-C (6)	1.503 (9)	C (14)-C (15)	1.497(8)
C (6)-C (7)	1.569 (8)	C (15)-C (16)	1.494(8)
C (6)-C (14)	1.540 (7)	C (16)-C (17)	1.308(8)
C (7)-C (8)	1.515 (9)		

Table V. Bond Angles (°) for Tsukushinamine-A·HBr

C (6)-N (1)-C (2)	125.6(5)	C (14)-C (6)-N (1)	110.9(5)	C (9)-C (10)-N (1)	111.2(5)
C (10)-N (1)-C (2)	115.6(5)	C (7)-C (6)-C (5)	109.8(5)	N (12)-C (11)-C (9)	113.0(4)
C (10)-N (1)-C (6)	117.3(5)	C (14)-C (6)-C (5)	110.1(5)	C (11)-N (12)-C (13)	110.1(4)
C (3)-C (2)-N (1)	119.0(6)	C (14)-C (6)-C (7)	104.6(5)	C (14)-N (12)-C (13)	100.8(4)
O -C (2)-N (1)	120.6(6)	C (8)-C (7)-C (6)	112.1(5)	C (14)-N (12)-C (11)	114.4(4)
O -C (2)-C (3)	120.4(6)	C (13)-C (7)-C (6)	102.6(4)	N (12)-C (13)-C (7)	100.8(5)
C (4)-C (3)-C (2)	114.0(6)	C (13)-C (7)-C (8)	107.1(5)	N (12)-C (14)-C (6)	102.7(4)
C (5)-C (4)-C (3)	121.9(6)	C (9)-C (8)-C (7)	106.5(4)	C (15)-C (14)-C (6)	117.6(5)
C (6)-C (5)-C (4)	123.9(6)	C (10)-C (9)-C (8)	106.0(5)	C (15)-C (14)-N (12)	116.0(4)
C (5)-C (6)-N (1)	109.9(5)	C (11)-C (9)-C (8)	113.0(5)	C (16)-C (15)-C (14)	114.7(5)
C (7)-C (6)-N (1)	111.6(5)	C (11)-C (9)-C (10)	115.0(5)	C (17)-C (16)-C (15)	125.4(6)

Thus, the further identity of the structure and the absolute configuration of tsukushinamine-A as **2** (6*R*, 7*R*, 9*S*, 14*R*) was confirmed by the X-ray analysis.

The absolute configurations at positions 7 and 9 of tsukushinamine-A are the same as those of (—)-cytisine (7*R*, 9*S*),[11,12] (—)-baptifoline (7*R*, 9*R*)[12] and (—)-rhombifoline (7*R*, 9*S*),[11,12] coexisted in the same plant. From these stereochemical point of view among the lupin alkaloids, it can therefore be presumed that **2** is a metabolite of the anagyrine-type alkaloids, such as (—)-baptifoline and (—)-rhombifoline.[2,13]

2 has also been found in the roots in a yield of 0.013%/fresh weight.

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13) The biosynthetic mechanism of tsukushinamine-A will be discussed in a subsequent paper.

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