CONCLUSION

A new synthesis of O-methyldauricine has been effected through an intermediate bisthio-amide obtained by the Wilgerodt–Kindler reaction from 5-acetyl-2-methoxyphenyl 4'-acetylphenyl ether and homoveratrylamine. Subsequent Bischler–Napieralski cyclization, methylation, and reduction yielded racemic O-methyldauricine.

LITERATURE CITED

1. R. Tschesche, R. Geipel, and H.-W. Fehlhaber, Phytochemistry, 9, 1683 (1970).
2. M. Tomita, Y. Okamot, N. Nagai, K. Kitayama, and H. Yanasawa, Yakugaku Zasshi, 90, 1178 (1970).
3. S. R. Johns, J. A. Lamberton, C. S. Li, and A. A. Sioumis, Aust. J. Chem., 23, 363 (1970).
4. S. M. Kupchan and H. W. Altland, J. Med. Chem., 16, 913 (1973).
5. H. Kondo, Z. Narita, and S. Uyeo, Chem. Ber. 68, 519 (1935).
6. T. Kametani and K. Fukumoto, Tetrahedron Lett., 2771 (1964).
7. I. N. Gorbacheva, G. V. Bushbek, L. P. Varnakova, L. M. Shulov, and N. A. Preobrazhenskii, Zh. Obshch. Khim., 27, 2297 (1957).
8. O. N. Tolkachev, E. P. Nakova, A. I. Bukolova, G. I. Aranovich, and R. P. Evstigneeva, Zh. Obshch. Khim., 44, 410 (1974).
9. F. D. Popp, H. W. Gibson, and A. C. Noble, J. Org. Chem., 31, 2296 (1966).
10. H. W. Gibson, F. D. Popp, and A. C. Noble, J. Heterocyl. Chem., 3, 99 (1966).
11. M. Tomita, K. Ito, and H. Yamaguchi, Chem. Pharm. Bull., 3, 449 (1955).
12. K. Fujitani, Y. Aoyagi, and Y. Masaki, Yakugaku Zasshi, 84, 1234 (1964); 86, 654 (1966).
13. E. P. Nakova, O. N. Tolkachev, and R. P. Evstigneeva, Second Symposium with International Participation on Structure and Reactivity of Organic Compounds. Manuscripts of Contributed Papers, September 23–October 2, 1978, Slanchev Bryag, Burgas, Bulgaria (1978), p. 45.
14. O. N. Tolkachev, E. P. Nakova, and R. P. Evstigneeva, 11th IUPAC International Symposium on Chemistry of Natural Compounds, September 17–23, 1978, Golden Sands, Bulgaria, Symposium Papers, 3, 47 (1978).
15. E. P. Nakova, O. N. Tolkachev, and R. P. Evstigneeva, USSR Authors' Certificate No. 550,386, November 22, 1976; Byull. Izobret., No. 10, March 15, 1977.
16. E. P. Nakova, O. N. Tolkachev, and R. P. Evstigneeva, USSR Authors' Certificate No. 554,674, December 21, 1976.

STRUCTURE OF ISOSOPHORIDINE

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A complete x-ray study of the structure of a stereoisomer of the alkaloid matrine — isosophoridine — has been made. Rings A and B have the cis type of linkage. Rings A, B, and C have the chair form and D the half-chair form.

For a definitive answer to the question of the configurational ambiguity of the structure of isosophoridine, we have made an x-ray structural study of it. Preliminary results have been reported previously [1]. In the present paper the geometry of the isosophoridine molecule is discussed in more detail.
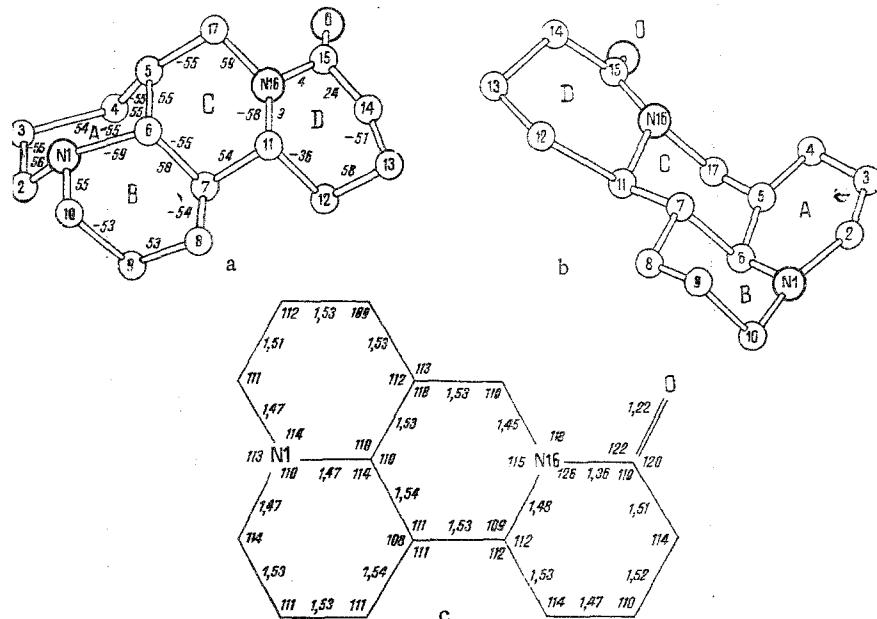
Fig. 1. Isosophoridine molecule: a) conformation in the
crystal (the values of the torsional angles are given);
b) conformation in the matrine "arrangement;" c) bond
lengths and sizes of the valence angles.

In the isosophoridine molecule (Fig. 1, a), the C(2) atom of ring A with the $^2C_5$-chair
conformation occupies at the N(1) atom the axial position with respect to ring B, which has
the $^7C_{10}$-chair conformation. The C(5) atom of ring A is an equatorial substituent at the
C(6) atom of ring B. Ring A is linked to ring C, which has the $^6C_{16}$-chair form, in the cis
manner. The cis linkage is effected by equatorial (C(17) atom) and axial (C(7) atom) bonds
with respect to ring A. The trans linkage of ring B and C takes place through equatorial
bonds. Ring D, in the form of a $^{12}H_{13}$-half-chair is linked to ring C in the trans manner.

In Fig. 1b, the projection of the isosophoridine molecule is shown; this resembles
the mutual positions of rings A, B, and C in matrine if we exclude ring D from consideration
and in place of rings A/B of matrine consider rings B/C of isosophoridine. The position of
ring C in matrine is "occupied" by ring A in isosophoridine. With such a way of considering
the situation, the isosophoridine molecule proves to be similar to the matrine molecule in
the relative arrangement of the rings, which permits the structures of these molecules to be
compared on the basis of the structure of matrine, which is well known to us [2].

Below we give the lengths of the intramolecular nonvalent contacts in the isosophoridine
molecule that are shortened in comparison with the normal values and the designations of
these contacts by analogy with the matrine molecule (in the matrine "arrangement"), and also
the normal values of the lengths of the contacts according to the literature [3, 4].

Contact	The same contact only matrine "arrangement"	Length of the contact, Å	Normal value, Å
C(2)...C(7)	C(11)...N( )	3.12	3,42
C(2)...C(9)	C(11)...C(9)	3.13	3,42
C(4)...N(16)	C(17)...C(3)	3,08	3.20
C(4)...C(7)	C(17)...N(1)	3.14	3.42

Let us follow how the values of the lengths of the nonbound contacts and the geometric
parameters given in Fig. 1 were established for the isosophoroidine molecules. For this pur-
pose let us consider separately the left (the C(14) atom and rings C and D) and the right
(the C(2) atom and ring B) parts of the molecule located, respectively, to the left and to the
right of the plane of the C(3), C(6), and C(7) atoms.

In the left part, the C(4) atom forms shortened contacts with the C(7) and N(16) atoms
having lengths of 3.14 and 3.08 Å. The first contact is greatly shortened, while the length
of the second contact is close to normal. Consequently, the interaction of the C(4) and C(7)
atoms leads to some increase in the C(4)C(5)C(6) angle (112°) and the interaction of the C(4)

TABLE 1. Coefficients of the Equations of the Planes and the Deviations of the Atoms δ from These Planes in the Isosophoridine Structure

Plane	Atom	Coeffs. of the eqns. of the plane A	B	C	D	δ, Å
I (ring A)	N(1)					—0.001
	C(3)					0.001
	C(4)	7.80	—5.26	4.39	2.98	—0.001
	C(6)					0.001
	C(2)*					—0.640
	C(5)*					0.656
II (ring B)	N(1)					—0.017
	C(6)					0.018
	C(8)	7.62	—5.87	3.85	2.05	—0.017
	C(9)					0.017
	C(7)*					—0.698
	C(10)*					0.622
III (ring C)	C(7)					0.003
	C(11)					—0.003
	C(17)	9.09	2.41	3.43	4.67	0.003
	C(5)					—0.003
	C(6)*					0.671
	N(16)*					—0.633
IV (ring D)	C(11)					0.007
	N(16)					—0.006
	C(15)	9.47	2.05	1.31	4.30	0.014
	C(14)					—0.015
	C(12)*					—0.155
	C(13)*					0.516

*Atoms not included in the calculations of the equations of the planes.

TABLE 2. Coordinates and Parameters of the Anisotropic Thermal Vibrations of the Nonhydrogen Atoms in the Isosophoridine Structure (all values multiplied by 10^4; the standard deviations are given in parentheses)

Atom	x/a	y/b	z/c	B(11)	B(22)	B(33)	B(12)	B(23)	B(13)
N(1)	2014(4)	49(3)	3237(3)	116(5)	81(3)	50(2)	13(7)	6(5)	—8(6)
C(2)	533(5)	3?2(4)	3173(4)	98(5)	105(5)	71(3)	—17(9)	2(7)	9(7)
C(3)	182(5)	1462(5)	3813(4)	118(6)	102(5)	69(3)	21(10)	8(7)	26(8)
C(4)	1073(5)	2572(4)	3504(3)	126(6)	91(4)	55(3)	20(9)	—4(6)	19(7)
C(5)	2593(5)	2215(4)	3571(3)	126(6)	9(4)	42(3)	—22(9)	—6(6)	—5(7)
C(6)	2921(5)	1068(4)	2927(3)	101(5)	88(4)	43(3)	13(9)	4(5)	—5(6)
C(7)	2867(5)	1363(4)	1748(3)	112(5)	78(4)	42(2)	6(8)	—5(5)	—2(6)
C(8)	3279(5)	185(4)	1155(3)	144(6)	91(4)	58(3)	17(10)	—25(6)	15(8)
C(9)	2391(6)	—918(4)	1486(4)	164(7)	91(5)	59(3)	14(1)	—25(6)	15(8)
C(10)	2394(5)	—1078(4)	2666(4)	142(7)	78(4)	65(3)	16(10)	3(6)	—9(8)
C(11)	3821(5)	2433(4)	1474(3)	141(6)	95(5)	52(3)	—28(10)	11(6)	24(8)
C(12)	3739(8)	27 9(6)	318(4)	292(13)	123(6)	50(4)	—43(16)	7(9)	74(12)
C(13)	4210(8)	4018(7)	71(5)	274(13)	171(9)	80(5)	20(20)	46(12)	89(13)
C(14)	3372(8)	4457(5)	681(4)	211(10)	105(6)	72(4)	52(14)	35(8)	35(11)
C(15)	3293(8)	4685(4)	1830(4)	108(5)	107(5)	73(4)	—1(10)	16(8)	5(8)
N(16)	3476(4)	3498(3)	2144(3)	135(5)	83(3)	52(2)	—23(8)	6(5)	11(6)
C(17)	3569(6)	3266(5)	3259(4)	166(8)	56(5)	60(3)	—52(11)	13(7)	—20(9)
O	3070(4)	5523(3)	2444(3)	202(6)	92(3)	94.3	25(8)	—11(5)	—1(8)

and N(16) atoms is not reflected in the values of the valence angles. In the right part of the molecule, the C(2) atom is close to the C(7) and C(9) atoms (see above).

The lengths of the bonds of the nitrogen atom N(1)–C(2) (1.47 Å) and N(1)–C(6) (1.47 Å) are smaller than the lengths of the corresponding bonds in the left part, C(4)–C(5) (1.53 Å).

A comparison of the lengths of the N(1)–C(10) and N(1)–C(2) bonds with the lengths of the corresponding bonds C(5)–C(17) and C(4)–C(5) shows an appreciable decrease of the non-valent distance C(2)...C(9) as compared with the C(4)...N(16) distance, as well. As a result of this pronounced shortening of the length of the nonbond C(2)...C(7) contact, the contacting atoms are repelled by one another, with increases in the C(2)N(1)C(6) and N(1)C(6)C(7) valence angles to 114°. The tendency of the C(2) and C(9) atoms to move away from one another likewise leads to an increase in the C(2)N(1)C(10) and N(1)C(10)C(9) angles, also to 114°.

TABLE 3. Coordinates and Isotropic Thermal Parameters of the Hydrogen Atoms in the Isosophoridine Structure (values of coordinates multiplied by 10^3)

Atom	x/a	y/b	z/c	B_j	Atom	x/a	y/b	z/c	B_j
$H_2(1)$	270	52	235	4,36	$H_{10}(1)$	166	—183	288	4,54
$H_2(2)$	—6	—47	344	4 36	$H_{10}(2)$	343	137	292	4,54
$H_3(1)$	—93	169	373	4,61	H_{11}	491	219	165	4,46
$H_3(2)$	33	125	466	4,61					
$H_4(1)$	81	283	271	4,16	$H_{12}(1)$	434	210	—18	6,49
$H_4(2)$	83	335	403	4,16	$H_{12}(2)$	265	271	3	6,49
H_5	285	206	442	3,70	$H_{13}(1)$	532	410	32	8,65
H_6	400	73	315	3,53	$H_{13}(2)$	419	421	—80	8,65
H_7	181	162	151	3,58	$H_{14}(1)$	383	586	52	5,86
$H_8(1)$	319	33	28	4,43	$H_{14}(2)$	234	492	31	5,86
$H_8(2)$	438	—4	129	4,43					
$H_9(1)$	132	—73	119	4,58	$H_{17}(1)$	343	409	373	5 50
$H_9(2)$	275	—175	108	4,58	$H_{17}(2)$	466	296	348	5,50

Thus, the deviations of the torsional angles from the ideal values of $\pm60°$ in rings A and B must be practically identical. Ring C must be the least deformed, as is confirmed by the values given in Fig. 1a. The deviations of the "angular" atoms from the plane of the "basis" atoms in the chairs, which are different from one another, are less than the ideal value of ±0.73 Å [5]. The minimum departure of the C(10) atom has a value of 0.62 Å (Table 1). The C(12) and C(13) atoms of ring D depart by 0.15 and 0.52 Å from the plane of the "lactam fragment" C(11)N(16)C(15)C(14).

The length of the bonds between the tetrahedral carbon atoms are close to the usual values, with the exception of C(12)-C(13) distance (Fig. 1c), which is shorter at 1.47 Å. The mean value for all these bonds is 1.53 Å and is the same in all the compounds of the matrine series that have been studied [6-8]. All the N(1)-C bonds have the same length of 1.47 Å, while the lengths of the N(16)-C(17) and N(16)-C(11) bonds differ somewhat from one another (1.45 and 1.48 Å). The N(16)-C(15) bond is shortened to 1.36 Å, and the length of the C(15)-O double bond (1.22 Å) is the same in all the stereoisomers that we have investigated.

The majority of the valence angles at the tetrahedral carbon atoms are close to the normal values, but a considerable number of angles have increased values (Fig. 1c). The reason for the increase in the size of these angles has been given above. The distribution of the valence angles at C(15) and N(16) in isosophoridine is close to their distribution in matrine [2].

A comparative consideration of the molecule given in the matrine "arrangement" permits the degree of its relative strain to be judged. The numbers and lengths of the shortened intramolecular nonvalent contacts, and also the numbers and values of the increased valence angles in isosophoridine and matrine show that the strains in these two compounds are of the same order.

Packing is characterized by the absence of shortened contacts. The crystal structure is a typical "island" structure.

EXPERIMENTAL

Single crystals of isosophoridine were obtained by crystallization from petroleum ether. They were unstable in the air. To determine the parameters of the elementary cell in a precesion camera and for their subsequent investigation in a diffractometer, single crystals were sealed into thin-walled quartz capillaries.

The crystallographic parameters of isosophoridine are as follows: $a = 9.696(1)$, $b = 10.844(2)$, $c = 12.837(2)$ Å; $\rho_{calc} = 1.22$ g/cm^3; $z = 4$; space group $P2_12_12_1$.

The intensities of 1392 reflections were measured on a Syntex P2$_1$ automatic diffractometer by the $\vartheta/2\vartheta$-scanning method (Cu K_α radiation, graphite monochromator). After preliminary treatment, 1141 reflections with $I \geqslant 2\sigma$ were included in the calculations.

We found a model of the structure by the direct method using the programmes of the Rentgen-75 group [9]. The calculation of 1024 phase variants was made in the automatic regime. The computer left the seven best sets of phases for calculating the E-syntheses.

The third variant, with an R factor of 0.20, permitted the localization of 17 nonhydrogen atoms of the structure. The coordinates of the missing atom were determined from an electron density (ED) synthesis. The next two ED syntheses were calculated to define the structure. Further refinement was carried out by means of the programmes of the Kristall complex [10] using the method of least squares (MLS) in the isotropic (R = 0.13) and the anisotropic (R = 0.10) approximations. The position and isotropic thermal parameters of the hydrogen atoms located provisionally from stereochemical considerations were refined. As the initial values of B_j for the hydrogen atoms we took the individual isotropic temperature factors of the carbon atoms connected to them. Then the refinement of the nonhydrogen atoms of the structure was continued in the anisotropic approximation. The final value of the R factor was 0.065. The coordinates and anisotropic temperature factors for the nonhydrogen atoms of the structure are given in Table 2, and the coordinates and isotropic temperature factors of the hydrogen atoms in Table 3.

CONCLUSION

A complete x-ray structural study of isosophoridine has been made. In this stereoisomer of matrine, rings A and B are linked in the cis manner. Rings A, B, and C have the chair form and ring D the half-chair form.

LITERATURE CITED

1. B. T. Ibragimov, S. A. Talipov, G. N. Tishchenko, Yu. K. Kushmuradov, and T. F. Aripov, Khim. Prir. Soedin., 586 (1979).
2. B. T. Ibragimov, S. A. Talipov, G. N. Tishchenko, Yu. K. Kushmuradov, and T. F. Aripov, Kristallografiya, 23, 1189 (1978).
3. Yu. V. Zefirov and P. M. Zorkii, Zh. Strukt. Khim., 15, 119 (1974).
4. Yu. V. Zefirov and P. M. Zorkii, Zh. Strukt. Khim., 17, 994 (1976).
5. G. I. Birnbaum, Acta Crystallogr., B26, 755 (1970).
6. B. T. Ibragimov, G. N. Tishchenko, Yu. K. Kushmuradov, T. F. Aripov, and A. S. Sadykov, Khim. Prir. Soedin., 355 (1979).
7. B. T. Ibragimov, G. N. Tishchenko, Yu. K. Kushmuradov, T. F. Aripov, and A. S. Sadykov, Khim. Prir. Soedin., 416 (1979).
8. B. T. Ibragimov, S. A. Talipov, G. N. Tishchenko, Yu. K. Kushmuradov, and T. F. Aripov, Kristallografiya, 24, 45 (1979).
9. V. I. Andrianov, Z. Sh. Safina, and B. L. Tarnopol'skii, Zh. Strukt. Khim., 15, 911 (1974).
10. L. A. Muradyan and V. I. Simonov, Kristallografiya, 18, 75 (1974).