CRYSTAL AND MOLECULAR STRUCTURE OF CARYOPHYLLENE α-OXIDE

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An x-ray study (λMo K_α, $2\theta/\omega$ scanning for $2\theta < 30°$, MLS in the anisotropic approximation) has been made of caryophyllene α-oxide (I) at −(98–100)°C (1182 reflections, R = 0.051); crystals of the orthorhombic system, a = 8.975, b = 10.160, c = 14.882 Å, z = 4, space group $P2_12_12_1$, mp 62–63°C. The crystalline and molecular structures of caryophyllene α-oxide (I) have been studied and the configuration of the oxide ring has been confirmed.

At the present time, two monoepoxides of caryophyllene are known — caryophyllene α-oxide (I), with mp 63–64°C, and caryophyllene β-oxide (II). They are both formed when caryophyllene is treated with peracids [1, 2]. Compound (I) was readily separated by crystallization and for a long time was considered the only caryophyllene monoepoxide [2, 3]; it is known in the literature as caryophyllene oxide.

Caryophyllene α-oxide is present in a number of essential oils [4] and was first isolated from oil of cloves (*Eugenia caryophyllata*) [5]. The configuration of the oxide ring was established on the basis of a study of the tricyclic products of the acid-catalyzed cyclization of this compound [6]. The α-oxide (I) has repeatedly been used in syntheses of new compounds [1, 4, 7, 8], and recently the possibility of obtaining perfume materials from it has again attracted attention [9]. In order to confirm the configuration of the

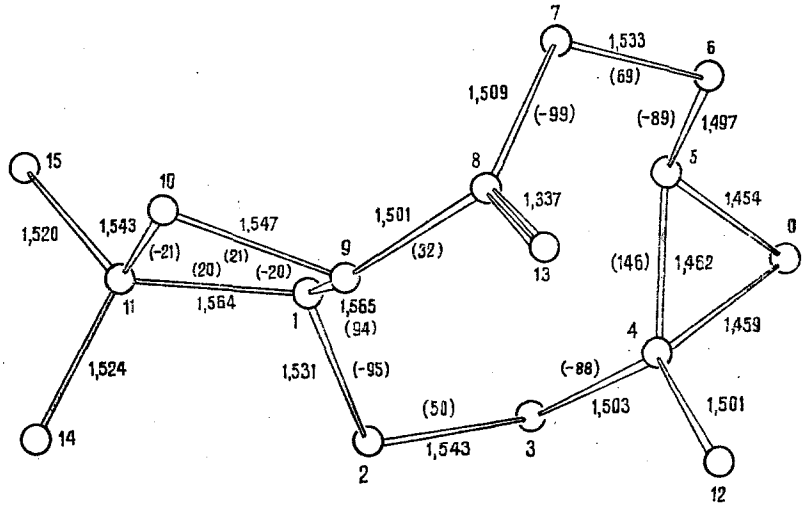

Fig. 1. Structure of the caryophyllene α-oxide molecule in the crystal. The probable error in the bond lengths given is 0.005 Å. The values of some torsion angles are given in parentheses.

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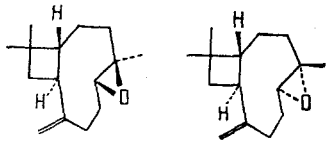
TABLE 1. Valence Angles (degrees) of the Caryophyllene α-Oxide Molecule

Angle	Value	Angle	Value
$C_2C_1C_9$	120,6 (3)	$C_6C_7C_8$	113,2 (3)
$C_2C_1C_{11}$	119,0 (3)	$C_7C_8C_9$	121,7 (3)
$C_9C_1C_{11}$	88,3 (2)	$C_7C_8C_{13}$	119,2 (3)
$C_1C_2C_3$	114,8 (3)	$C_9C_8C_{13}$	119,0 (3)
$C_2C_3C_4$	112,2 (3)	$C_1C_9C_8$	125,6 (3)
$C_3C_4C_5$	115 4 (3)	$C_1C_9C_{10}$	86,7 (2)
$C_3C_4C_{12}$	116,4 (3)	$C_8C_9C_{10}$	117,3 (3)
C_3C_4O	115,0 (3)	$C_9C_{10}C_{11}$	89,8 (3)
$C_5C_4C_{12}$	123,7 (3)	$C_1C_{11}C_{10}$	87,2 (3)
C_5C_4O	59,7 (2)	$C_1C_{11}C_{14}$	113,9 (3)
$C_{12}C_4O$	113,3 (3)	$C_1C_{11}C_{15}$	115,4 (3)
$C_4C_5C_6$	125,3 (3)	$C_{10}C_{11}C_{14}$	111,9 (3)
C_4C_5O	60,0 (2)	$C_{10}C_{11}C_{15}$	116,2 (3)
C_6C_5O	120,6 (3)	$C_{14}C_{11}C_{15}$	110,5 (3)
$C_5C_6C_7$	108,9 (3)	C_4OC_5	60,3 (2)

TABLE 2. Coordinates of the Atoms ($\times10^4$, $\times10^3$ for H) of the Caryophyllene α-Oxide Molecule

Atom	x	y	z	Atom	x	y	z
C_1	2636 (4)	0134 (3)	3978 (2)	$2H_3$	106 (3)	—077 (3)	554 (2)
C_2	1303 (4)	0630 (4)	4525 (2)	H_5	199 (3)	—256 (3)	475 (2)
C_3	0414 (4)	—0455 (4)	5013 (2)	$1H_6$	059 (3)	—354 (3)	315 (2)
C_4	0017 (4)	—1576 (4)	4398 (2)	$2H_6$	180 (3)	—428 (3)	369 (2)
C_5	1127 (4)	—2626 (4)	4338 (2)	$1H_7$	356 (3)	—257 (3)	333 (2)
C_6	1450 (4)	—3425 (3)	3515 (3)	$2H_7$	303 (3)	—329 (3)	252 (2)
C_7	2664 (4)	—2734 (4)	2965 (2)	H_9	171 (3)	048 (2)	268 (2)
C_8	2140 (4)	—1469 (3)	2539 (2)	$1H_{10}$	481 (3)	—031 (3)	289 (2)
C_9	2476 (4)	—0153 (3)	2950 (2)	$2H_{10}$	421 (3)	094 (3)	232 (2)
C_{10}	4079 (4)	0384 (4)	2844 (2)	$1H_{12}$	—074 (3)	—063 (3)	324 (2)
C_{11}	3924 (4)	1114 (3)	3748 (2)	$2H_{12}$	—202 (3)	—101 (3)	398 (2)
C_{12}	—1100 (4)	—1284 (4)	3675 (3)	$3H_{12}$	—132 (3)	—204 (3)	333 (2)
C_{13}	1125 (4)	—1515 (4)	1751 (3)	$1H_{13}$	098 (3)	—070 (3)	148 (2)
C_{14}	3410 (5)	2532 (4)	3621 (3)	$2H_{13}$	126 (3)	—238 (2)	143 (2)
C_{15}	5266 (4)	1060 (4)	4370 (2)	$1H_{14}$	251 (3)	262 (3)	325 (2)
O	—0238 (3)	—2834 (2)	4845 (2)	$2H_{14}$	429 (3)	302 (3)	338 (2)
H_1	310 (3)	—058 (3)	429 (2)	$3H_{14}$	322 (3)	287 (3)	424 (2)
$1H_2$	065 (3)	106 (3)	415 (2)	$1H_{15}$	615 (3)	158 (3)	412 (2)
$2H_2$	163 (3)	125 (3)	494 (2)	$2H_{15}$	557 (3)	015 (3)	451 (2)
$1H_3$	—057 (3)	—009 (3)	525 (2)	$3H_{15}$	499 (3)	145 (3)	496 (2)

oxide ring by a direct physical method and to elucidate the structural features of the molecule, we undertook an x-ray structural analysis of a crystal of caryophyllene α-oxide.



I II

The structure of the caryophyllene α-oxide molecule, the bond lengths, and some torsion angles are given in Fig. 1. The values of the valence angles are given in Table 1.

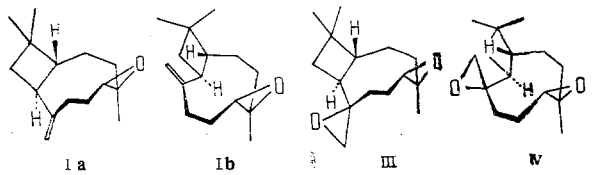
The geometry of the cyclobutane moiety (mean length of a C—C bond 1.555 Å, mean valence angle 88.0°, angle of folding of the ring 33.8°) corresponds to literature figures for the trans linkage of the rings [10,11]. The lengths of the C—O and C—C bonds in the oxide ring (1.456 Å and 1.462 Å, respectively) are close to figures given in the literature [12].

The strain of the molecule of the α-oxide (I) appears appreciably in a decrease of the C_3—C_4—C_5—C_6 torsion angle to 146° as compared with the usual value of 155° [12]. We may

note that in the molecule of buddledin bromohydrin the corresponding C=C angle is decreased from 180° to 160° [11]. On using the analogy in the stereochemical respect between an oxide ring and a double bond, the conformation of the nine-membered ring of caryophyllene α-oxide (I) can be compared with the conformation of the similar fragment of the buddledin bromohydrin molecule [11]. The comparison shows that the conformations of these rings are different: the conformation of the molecule of the (I) in the crystal is close to the αα conformation of caryophyllene [13], and that of the buddledin bromohydrin molecule to the ββ conformation. We may note that the conformation of caryophyllene α-oxide that we have found does not correspond to the most stable, βα, conformation of caryophyllene [13].

In the crystal, the molecules of (I) are separated by the normal contacts [14].

The results that we have obtained, confirm the configuration of the oxide ring in the molecule established previously by ordinary chemical methods. Caryophyllene α-oxide crystallizes only in the conformation (Ia), but in solution this conformation probably exists in equilibrium with conformation (Ib). This conclusion can be drawn both from a consideration of a Dreiding model of the α-oxide itself and also from the results of the epoxidation of this compound at the second double bond. In this reaction, two diepoxides are formed: the main product (III) can be obtained from the conformation (Ia), and the minor product (IV), the proportion of which is 20–35%, from conformation (Ib) [8].



Ia Ib III IV

EXPERIMENTAL

Caryophyllene α-oxide (I) was obtained by Treibs' method [1], with mp 62–63°C. The x-ray structural experiment was performed on a Syntex $P2_1$ diffractometer in molybdenum radiation with a graphite monochromator, using a single crystal with dimensions of 0.3 × 0.5 × 0.8 mm. In view of the low melting point of the crystals, the experiment was carried out at −(98–100)°C. Crystals of the orthorhombic system with a = 8.975(2), b = 10.160(2), c = 14.882(4) Å, z = 4, space group $P2_12_12_1$. By the standard $2\theta/\omega$ scanning method (with the unobserved reflections being discarded), 1263 independent reflections in the region $2\theta \leq 55°$ were measured, of which 1182 had $I > 2\delta$ and were used in the calculations. No corrections were made for absorption. The structure was readily deciphered by the direct method using the MULTAN–XTL program. The positions of the hydrogen atoms were found from a difference synthesis. The final refinement of the structure was carried out by the method of least squares in the full-matrix anisotropic (isotropic for H) approximation to R = 0.051 and R_ω = 0.047, where $\omega^{-1} = \sigma_F^2 + (0.007F)^2$. The coordinates of the atoms of the caryophyllene α-oxide molecule obtained are given in Table 2.

SUMMARY

The crystal and molecular structures of caryophyllene α-oxide have been studied, and the configuration of the oxide ring has been confirmed.

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TRITERPENE SAPONINS FROM *Thalictrum minus*.

II. STRUCTURE OF AN ARTEFACT

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The acid hydrolysis of the predominating saponins isolated from *Thalictrum minus* L. has led to the formation of a triterpenoid (I), which is an artefact of the native genin. The structure of (I) has been established as 22,25-epoxylanost-9(11)-ene-3β,16β,29-triol.

The genus *Thalictrum* (family Ranunculaceae) is represented by 85 species, but only two are used in medicinal practice: *Thalictrum minus* L. and *T. foetidum* L. [1].

We have previously reported the isolation from low meadowrue (*T. minus*) of two saponins, A and B, the acid hydrolysis of which led to a triterpenoid (I) and oleanolic acid, respectively [2, 3].

In the present paper we consider the establishment of the structure of the triterpenoid (I), which, as has been found, is an artefact of the native genin of saponin A. This follows from a comparison of the signals in the strong-field region of the PMR spectra of triterpenoid (I) and saponin A.

The PMR spectrum of (I) contains the signals of seven methyl groups one of which (δ = 0.83 ppm) is split into a doublet (J = 8 Hz). These facts, in combination with the molecular formula $C_{30}H_{50}O_4$ (elementary analysis and mass spectrometry), and also with the presence in the mass spectrum of strong ions with m/z 126 ($C_8H_{14}O$) and 99 (126 − C_2H_3) permitted the compound under investigation to be assigned to the tetracyclic triterpenoids with a tetrahydrofuran ring in the side chain [4].

The results of spectroscopy in the IR (812, 837 cm^{-1}) and the UV (λ_{max} 204 nm) and of PMR spectroscopy (one-proton doublet at δ = 5.15 ppm, J = 4.5 Hz) indicate the presence in compound of (I) of an isolated trisubstituted double bond. The mass-spectral fragmentation shows that this bond is present in the cyclic system and not in the side chain (scheme).

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