CRYSTAL AND MOLECULAR STRUCTURE OF MUUROLENE AND CADINENE DIHYDROCHLORIDES

Yu. Gatilov, S. A. Oadchii,
and Zh. V. Dubovenko

UDC 539.26:547.913.2

An x-ray structural investigation (λ Mo $K_{\alpha}2\theta/\omega$ scanning for $2\theta < 50°$, MLS in the anisotropic approximation) has been performed of cadinene dihydrochloride (I) (1213 reflections, R = 0.053) and muurolene dihydrochloride (II) 1643 reflections, R = 0.087). The crystals of (I) belong to the rhombic system with a = 6.053(2), b = 14.622(5), c = 17.926(7) A, Z = 4, sp. gr. $P2_12_12_1$, mp 117°C. The crystals of (II) belong to the monoclinic system, with a = 9.842(4), b = 11.627(6), c = 13.677(9) Å, β = 95.10(4)°, Z = 4, sp. gr. $P2_1$, mp 86°C. The six-membered rings of the molecules (I) and (II) have the chair conformation with equatorial alkyl groups. The chlorine atoms have the axial arrangement. The molecule of (I) has the 3α,9α-dichlorocadinane structure, and that of (II) the 3β,9α-dichloromuurolane structure. The increased mean length of the C—Cl bonds of 1.844 Å in the molecule of (I) and 1.879 Å in the molecule of (II) must be mentioned.

Sesquiterpene compounds of the four stereochemical groups of cadinane, muurolane, amorphane, and bulgarane are widely distributed in nature. The spectral characteristics of these compounds are very close, and the assignment of a particular sesquiterpenoid to a definite stereochemical group has been made on the basis of the formation of crystalline dihydrochlorides or dihydrobromides.

Dihydrobromides with mp 124-125°C or dihydrochlorides with mp 117-118 C are obtained from cadinenes and cadinols [1], and a dihydrobromide with mp 116-117°C and a dihydrochloride with mp 85°C from ε-bulgarene [2]. With HCl, sesquiterpenoids of the muurolane type also form cadinene dihydrochloride (I) (mp 117-118°C) and muurolene dihydrochloride (II) (mp 84-86°C) with a predominance of the latter [3], from ε-muurolene in a ratio of 1:3, from α-muurolene 1:7, and from γ-muurolene 1:20. A mixture of these two dihydrochlorides (I and II) is also obtained from δ-cadinol [4] and T-muurolol [5]. Compounds of the amorphane type are distinguished form compounds stereoisomeric with them of the other three groups by the fact that they do not give crystalline derivatives when HCl is passed through their solutions in absolute diethyl ether [6].

The structure of cadinene dihydrobromide was the first to be studied by the method of x-ray structural analysis (XSA) [7]. Later, Mani [8] investigated the crystal and molecular structure of racemic cadinene dihydrochloride. The addition of HBr to ε-bulgarene takes place in a more complex fashion, and, as has been shown by the XSA method [9], one bromine atom is present in an angular position. The structure of muurolene dihydrochloride has not been investigated by this method while the molecular structures of a number of sesquiterpenoids of the muurolene type have been studied [10] and configurations of the main asymmetric centers at C_5, C_6, and C_{10} have been confirmed.

Since both muurolene dihydrochloride and cadinene dihydrochloride are obtained from muurolenes and muurolols, it was assumed that epimerization partially affects the angular C_{10} atom. In muurolene dihydrochloride itself, the configurations at C_5, C_6, and C_{10} remain the same as in the compounds from which it is obtained. This has been shown by the synthesis of ε-muurolene from muurolene dihydrochloride [11].

The present paper gives the results of an x-ray structural investigation of the optically active cadinene and muurolene dihydrochlorides obtained from (—)α-muurolene. We also

---

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 52-57, January-February, 1981. Original article submitted July 17, 1980.

TABLE 1. Bond Lengths (Å) and Valence Angles (deg) of the Cadinene Dihydrochloride (I) and Muurolene Dihydrochloride (II) Molecules*

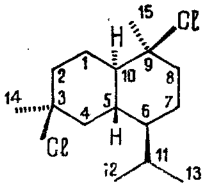
Parameter	Value			Parameter	Value		
	I	IIa	IIb		I	IIa	IIb
$C_1—C_2$	1,51	1,53	1,48	C_4C_3Cl	106,5	108	108
$C_1—C_{10}$	1,53	1,50	1,52	$C_{14}C_3Cl$	105,8	104	107
$C_2—C_3$	1,50	1,48	1,55	$C_3C_4C_5$	116,8	120	119
$C_3—C_4$	1,51	1,49	1,52	$C_4C_5C_6$	112,5	115	116
$C_3—C_{14}$	1,51	1,50	1,47	$C_4C_5C_{10}$	110,7	109	110
$C_3—Cl$	1,844	1,88	1,88	$C_6C_5C_{10}$	113,1	113	113
$C_4—C_5$	1,52	1,51	1,50	$C_5C_6C_7$	109,7	109	110
$C_5—C_6$	1,53	1,55	1,52	$C_5C_6C_{11}$	115,2	113	115
$C_5—C_{10}$	1,52	1,52	1,57	$C_7C_6C_{11}$	113,0	111	113
$C_6—C_7$	1,50	1,54	1,51	$C_6C_7C_8$	114,5	111	112
$C_6—C_{11}$	1,51	1,53	1,54	$C_7C_8C_9$	114,2	113	115
$C_7—C_8$	1,51	1,53	1,52	$C_8C_9C_{10}$	111,1	110	111
$C_8—C_9$	1,51	1,52	1,56	$C_8C_9C_{15}$	111,4	111	112
$C_9—C_{10}$	1,52	1,53	1,52	C_8C_9Cl	105,8	106	104
$C_9—C_{15}$	1,52	1,54	1,53	$C_{10}C_9C_{15}$	114,3	115	116
$C_9—Cl$	1,845	1,85	1,87	$C_{10}C_9Cl$	108,5	107	106
$C_{11}—C_{12}$	1,54	1,49	1,51	$C_{15}C_9Cl$	105,1	107	106
$C_{11}—C_{13}$	1,54	1,57	1,52	$C_1C_{10}C_5$	112,6	113	111
$C_2C_1C_{10}$	112,3	110	109	$C_1C_{10}C_9$	113,4	111	112
$C_1C_2C_3$	115,0	115	117	$C_5C_{10}C_9$	113,9	114	114
$C_2C_3C_4$	110,5	113	110	$C_6C_{11}C_{12}$	113,5	115	113
$C_2C_3C_{14}$	112,5	112	113	$C_6C_{11}C_{13}$	113,1	112	111
C_2C_3Cl	107,5	10[illegible]	104	$C_{12}C_{11}C_{13}$	108,5	111	107
$C_4C_3C_{14}$	113,5	114	113				

---

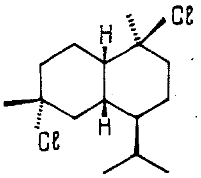
*Standard deviations for the bond lengths are about 0.01 and 0.02 Å, and for the angles 0.5 and 1.0°, respectively, for (I) and (II).

studied cadinene dihydrochloride again, since in his work Mani [8] used the synthetic racemic dihydrochloride; the values of the valence angles given in his paper of 95° for $Cl—C_9—C_{10}$, 101° for $C_7—C_8—C_9$, 103.5° for $C_6—C_5—C_{10}$, and 119.3° for $C_8—C_9—C_{10}$ greatly differed from the usual ones, and some intermolecular contacts are very short, for example, the $C_1 \ldots C_8'$ and $C_1 \ldots C_1'$ distances are, respectively, 2.94 and 2.98 Å (Mani's symbols).

The results that we have obtained show that cadinene hydrochloride has the structure (I) and muurolene dihydrochloride (II) (Fig. 1).



I



II

The lengths of the bonds and the valence angles are given in Table 1. As can be seen from Fig. 1 and Table 1, our results agree with those of Mani [8] for cadinene dihydrochloride, with the exception of the valence angles, as was discussed above. The two crystallographically independent molecules of muurolene dihydrochloride have similar spatial structures. For both dihydrochlorides the six-membered rings have the chair form with equatorial alkyl groups. The arrangement of the chlorine atoms is diaxial, while in cadinene dihydrochloride they are located on the same side of the rings, and in muurolene dihydrochloride on different sides. Both configurations at the C_5, C_6, and C_9 atoms are the same in the two compounds.

The structures of muurolene and cadinene also have other common features. The C—Cl bond is lengthened to 1.84 Å in cadinene hydrochloride and to 1.85-1.88 Å in muurolene dihydrochloride as compared with the mean value of 1.767 Å adopted for chloroparaffins [12]. A similar lengthening of the C—Cl bond to 1.86 Å has been reported for the isoclovene dihydrochloride molecule [13], A theoretical calculation by the MINDO/3 method with full optimi-

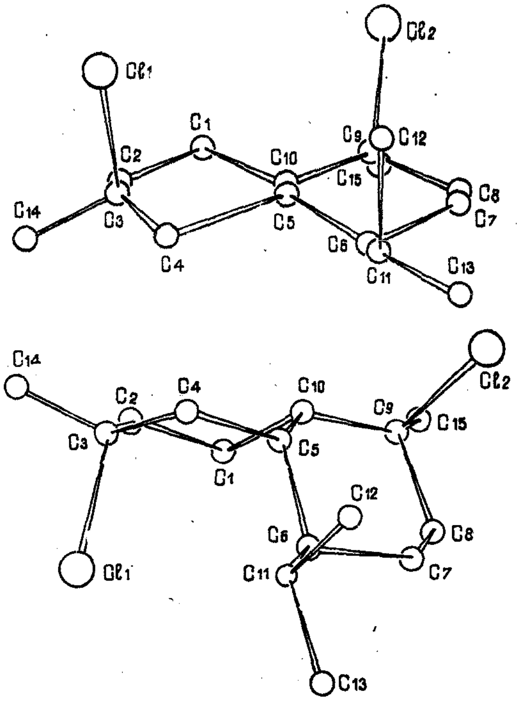


Fig. 1. Molecular structures of cadinene dihydrochloride (top) and muurolene dihydrochloride (bottom).

zation of the geometry of the molecule of exo-2- and endo-2-chloro-2-methylnorbornane also gave 1.84 Å for the C–Cl bond [14]. A value of 1.79 Å is given for the C–Cl bond by Mani [8]. The flattening of the chair shape, particularly of the fragments containing the tetrasubstituted carbon atoms, must be mentioned, this apparently being connected with the axial arrangement of the chlorine atoms. In muurolene dihydrochloride there is an additional 1,3-diaxial $Cl_1 \ldots C_6$ interaction with a mean distance of 3.36 A, as a result of which the C_3–C_4–C_5 valence angle is increased still further to 119-120°C.

The intermolecular contacts are normal in all cases.

EXPERIMENTAL

Cadinene and muurolene dihydrochlorides were obtained from α-muurolene with $[\alpha]_D^{20}$ −75° (without a solvent) by Westfelt's method [3] and were separated by crystallization.

The x-ray structural experiment was performed on a Syntex $P2_1$ diffractometer using molybdenum radiation with a graphite monochromator. The crystals of cadinene dihydrochloride are rhombic, with a = 6.052(2), b = 14.622(5), c = 1.7926(7) Å, Z = 4, sp. gr. $P2_12_12_1$, mp 117°, $[\alpha]_D^{20}$ −34.9° (c 1.60, $CHCl_3$). Intensities of the reflections were measured with a crystal having dimensions of 1 × 0.3 × 0.25 mm^3 by the $2\theta/2\omega$ scanning method in the interval up to $2\theta = 50°$. In the calculations 1213 independent reflections with $I > 2\sigma$ without taking absorption into account were used. The structure was easily found by the direct method using the MULTAN-XTL program. The final refinement was carried out in the full-matrix anisotropic approximation with no refinement of the isotropic temperature factors of the hydrogen atoms. Finally, R = 0.053 and $R_w = 0.042$, where $w^{-1} = \sigma_F^2 + (0.005\ F)^2$.

The crystals of muurolene dihydrochloride were monoclinic, with a = 9.842(4), b = 11.627(6), c = 13.677(9) Å, β = 95.10 (4)°, Z = 4, sp. gr. $P2_1$, mp 86°C, $[\alpha]_D^{20}$ −13.1° (c 1.0, $CHCl_3$). To measure the intensities of the Friedel pairs of reflections by the $2\theta/\omega$ scanning method in the $2\theta < 50°$ region, a crystal was selected with dimensions of 0.3 × 0.4 × 0.7 mm^3. In the calculations 1643 independent averaged reflections $I > 1.5\sigma$ were used. No corrections for absorption were made. The structure was deciphered by the direct method using the MULTAN-XTL program. The positions of the chlorine atoms were obtained from the E synthesis of the best variant of the phases with respect to NQEST [15] (NQEST = −0.214). The coordinates of the other nonhydrogen atoms were found from F-syntheses. The refinement of the structure

TABLE 2. Coordinates (× 10^4) of the Atoms of the Cadinene Dihydrochloride Molecule (first column) and of the Two Molecules of Muurolene Dihydrochloride (second and third columns)

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
Cl_1	−1163 (2)	0990 (1)	1171 (1)	C_8	0214 (16)	6341 (12)	3856 (13)
	3695 (3)	3794 (3)	3551 (2)		3449 (10)	4170 (6)	2436 (5)
	0076 (3)	3838 (3)	1088 (2)		7585 (15)	1347 (13)	2528 (12)
Cl_2	−0363 (2)	4158 (1)	1671 (1)	C_9	1697 (12)	6715 (10)	3850 (9)
	6546 (3)	−0712 (3)	1930 (2)		2633 (8)	3927 (4)	1664 (4)
	1135 (3)	8852 (3)	3110 (2)		6773 (12)	0365 (9)	2933 (8)
C_1	2152 (10)	2623 (5)	0734 (4)	C_{10}	2035 (14)	7457 (10)	2940 (10)
	5403 (13)	1434 (11)	4091 (9)		2990 (9)	2915 (5)	1501 (4)
	2223 (13)	5972 (10)	1599 (11)		5352 (11)	0778 (10)	3137 (8)
C_2	2630 (11)	1634 (5)	0570 (4)	C_{11}	1375 (11)	6943 (9)	1985 (9)
	3953 (18)	1688 (14)	4351 (11)		2401 (12)	1918 (5)	3523 (4)
	1640 (19)	5652 (13)	0597 (13)		4710 (12)	3062 (12)	1027 (11)
C_3	1885 (8)	0975 (4)	1157 (3)	C_{12}	−1760 (11)	5253 (10)	2948 (9)
	3063 (13)	2258 (10)	3561 (10)		−0116 (14)	1902 (6)	3652 (5)
	0113 (15)	5298 (9)	0477 10)		4339 (16)	2326 (12)	0151 (10)
C_4	2633 (10)	1288 (4)	1922 (3)	C_{13}	−1828 (17)	4469 (11)	3833 (12)
	3202 (14)	1755 (12)	2572 (10)		3528 (15)	2151 (8)	4267 (5)
	−0725 (15)	6121 (11)	1048 (9)		5511 (20)	4174 (14)	0741 (10)
C_5	2191 (9)	2282 (4)	2121 (4)	C_{14}	−2839 (15)	6168 (12)	3015 (12)
	4600 (11)	1422 (9)	2285 (7)		2523 (14)	0003 (5)	0983 (5)
	−0145 (11)	6543 (9)	2039 (8)		1619 (20)	2378 (15)	3817(15)
C_6	3108 (10)	2538 (5)	2889 (4)	C_{15}	−0432 (17)	5151 (14)	−0554 (10)
	5444 (13)	2428 (10)	1904 (9)		3584 (13)	4567 (5)	1076 (5)
	−0312 (11)	5749 (11)	2908 (8)		7590 (14)	−0233 (14)	3811 (13)
C_7	2671 (12)	3530 (5)	3042 (4)		3551 (12)	7749 (13)	2965 (13)
	6832 (13)	1961 (10)	1647 (9)				

was carried out separately for the two independent molecules in the full-matrix anisotropic approximation (B_{iso} of the hydrogen atoms was not refined) to R = 0.087 and R_w = 0.063, where $w^{-1} = \sigma_F^2 + (0.015F)^2$.

The coordinates of the nonhydrogen atoms of the molecules of cadinene and muurolene dihydrochlorides are given in Table 2.

SUMMARY

The structures of muurolene and cadinene dihydrochlorides have been studied by the method of x-ray structural analysis.

LITERATURE CITED

1. M. Goryaev and I. Pliva, Methods of Investigating Essential Oils [in Russian], Alma-Ata (1962), p. 258.366.
2. R. Vlahov, M. Holub, and V. Herout, Collec. Czech. Chem. Commun., 32, 822 (1967).
3. Z. Westfelt, Acta Chem. Scand., 20, 2852 (1966).
4. Z. Westfelt, Acta Chem. Scand., 20, 2893 (1966).
5. V. S. Cheng, Y. H. Kuo, and Y. T. Lin, Chem. Commun., 12, 565 (1967).
6. O. Motl, M. Romanuk, and V. Herout, Collect. Czech. Chem. Commun., 31, 2025 (1966).
7. F. Hanic, Chem. Listy, 52, 165 (1958).
8. N. V. Mani, Z. Kristalogr., 118, 103 (1963).
9. A. Linek, R. Vlahov, M. Holub, and V. Herout, Tetrahedron Lett., 23 (1968).
10. Yu. V. Gatilov, Zh. V. Dubovenko, and V. A. Khan, Zh. Strukt. Khim., 20, 509 (1979); Yu. V. Gatilov and Zh. V. Dubovenko, Zh. Strukt. Khim., 20, 319 (1979); Yu. V. Gatilov, V. A. Khan, Zh. V. Dubovenko, Khim. Prir. Soedin., 158 (1979).
11. Z. Westfelt, Acta Scand., 18, 572 (1964).
12. A. J. Gordon and R. A. Ford, The Chemist's Companion, Wiley-Interscience, New York (1962).
13. J. S. Clunie and J. M. Robertson, J. Chem. Soc., 4382 (1961).
14. W. L. Jorgensen and J. E. Munroe, J. Am. Chem. Soc., 100, 1511 (1978).
15. G. T. De Titta, J. W. Edmonds, D. A. Langs, and H. Hauptman, Acta Crystallogr., A31, 472 (1975).