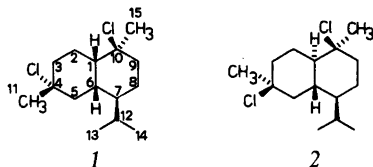


The Structure of Muurolene Dihydrochloride and its Transformation to Cadinene Dihydrochloride

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Muurolene dihydrochloride (*1*) is a useful and characteristic derivative for the identification and characterization of sesquiterpenes of the muurolene type.^{1,2} It shall be noted that the muurolene dihydrochloride (*1*) is formed together with cadinene dihydrochloride (*2*)^{3,4} in the hydrochlorination reaction of a muurolene derivative.^{1,2} There are also indications for a conversion of *1* to *2* under the conditions used for the reaction.



The structure of cadinene dihydrochloride (*2*) was settled already in 1958.^{3,4} The structure of muurolene dihydrochloride (*1*) has still not been

determined although the *cis*-ring junction of the decalin system follows from a chemical transformation of *1* to ϵ -muurolene of a known configuration.⁵ In this communication we report a structure determination of muurolene dihydrochloride (*1*) by X-ray diffraction methods.* We also report that muurolene dihydrochloride (*1*) almost quantitatively is converted to cadinene dihydrochloride (*2*) by treatment with hydrogen chloride in ethanol.

Muurolene dihydrochloride (*1*) crystallizes in space group $P2_1$ with two molecules in the asymmetric unit. The cell dimensions are $a = 13.699(5)$, $b = 11.633(4)$, $c = 9.855(2)$ Å and $\beta = 95.08(4)^\circ$. Intensity data were recorded on a Philips 1100 computer-controlled diffractometer with Cu-radiation. Out of the 3220 reflexions collected ($\theta \leq 65^\circ$), 2107 were considered to be significant $I_{\text{net}} \leq 3\sigma(I_{\text{net}})$ and were used in the subsequent refinements. Correction for intensity loss due to deterioration was made as a linear function of time. The structure was solved by a combination of the heavy atom technique and direct methods.⁶ It was refined to an R value of 0.135 using the block-diagonal least-squares method with unitary weights. No hydrogens have been included in the calculations. The final parameters for the non-hydrogen atoms are listed in Table 1.

The rather low accuracy in the crystal structure determination is partly due to deterioration and to difficulties in finding crystals suitable for the investigation. The diffraction peaks of the crystal

*The structure *1* of muurolene dihydrochloride was recently reported by Dr. V. A. Barkhash (Institute of Organic Chemistry, Siberian Division of the Academy of Sciences, Novosibirsk 90, USSR) in a lecture of the 9th Conference on Isoprenoids, Prague, September 1981. [cf. Gatilov, Yu. V., Osadchii, S. A. and Dubovenko, Zh. V. *Khim. Prir. Soedin.* (1981) 52; *Chem. Abstr.* 95 (1981) 98046].

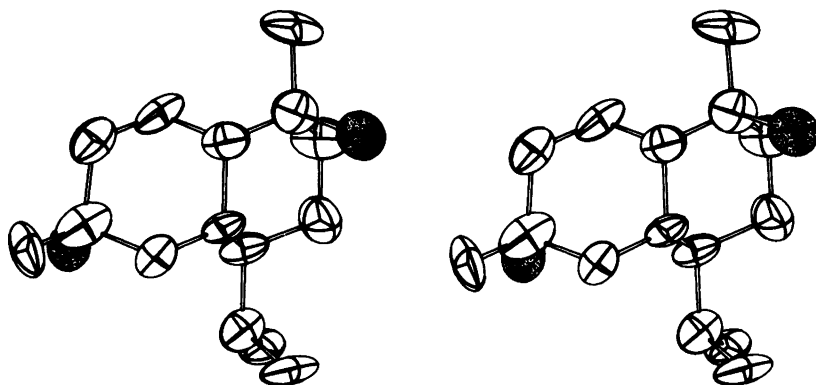


Fig. 1. An ORTEP drawing of one of the independent molecules. The chlorine atoms are shaded.

Table 1. Positional and thermal parameters for the non-hydrogen atoms in the two molecules. Values are $\times 10^3$ for the coordinates and $\times 10^2$ for the U 's. E.s.d.'s are given within parentheses. The U -values refer to the temperature factor expression $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{23}klb^*c^* + 2U_{13}hla^*c^* + 2U_{12}kha^*b^*)]$.

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	317(2)	215(3)	1036(4)	4(2)	5(2)	5(2)	0(2)	0(2)	0(2)
C2	410(3)	148(4)	1043(4)	8(3)	5(3)	8(3)	0(3)	1(2)	0(2)
C3	440(3)	128(4)	889(4)	12(3)	6(4)	7(3)	-3(3)	2(3)	0(3)
C4	353(3)	62(4)	807(4)	10(3)	6(3)	5(3)	0(3)	1(3)	-4(3)
C5	253(2)	116(4)	815(4)	2(2)	11(4)	6(2)	-1(3)	0(2)	1(2)
C6	224(3)	151(3)	964(4)	5(2)	5(2)	7(2)	0(2)	2(2)	2(2)
C7	190(3)	43(3)	1044(4)	9(3)	3(2)	8(3)	0(2)	4(3)	1(2)
C8	162(4)	98(5)	1189(4)	11(4)	11(5)	6(3)	-1(3)	5(3)	0(4)
C9	258(4)	154(4)	1265(4)	12(4)	7(3)	4(2)	1(2)	2(3)	-1(3)
C10	298(3)	258(3)	1188(4)	8(3)	3(2)	9(3)	-1(2)	3(3)	2(3)
C12	100(3)	-14(4)	968(4)	6(2)	8(3)	9(3)	-2(3)	1(2)	-6(2)
C14	76(4)	-122(5)	1052(5)	5(4)	14(5)	11(4)	-3(4)	-1(3)	-3(4)
C13	12(3)	58(5)	936(5)	3(3)	8(4)	19(6)	2(4)	-2(3)	0(3)
C11	380(4)	47(4)	652(4)	13(5)	8(3)	6(3)	1(3)	2(3)	-3(4)
C15	383(4)	308(4)	1258(4)	13(4)	7(3)	6(3)	-5(3)	-1(3)	-2(3)
Cl1	355(1)	-89(1)	871(2)	11(1)	7(1)	10(1)	-3(1)	3(1)	0(1)
Cl2	194(1)	362(1)	1156(1)	8(1)	6(1)	11(1)	-1(1)	1(1)	2(1)
C'1	198(2)	592(3)	641(3)	5(2)	12(3)	5(2)	1(2)	0(2)	-1(2)
C'2	158(3)	694(3)	719(3)	10(3)	9(3)	5(2)	-2(2)	4(2)	-1(2)
C'3	55(2)	728(3)	664(3)	7(2)	8(3)	8(3)	0(2)	3(2)	-1(2)
C'4	42(3)	769(3)	505(4)	11(3)	6(2)	8(3)	-2(2)	4(2)	-4(2)
C'5	100(2)	679(3)	424(3)	4(2)	6(2)	6(2)	-2(2)	1(2)	-2(2)
C'6	200(2)	638(3)	481(3)	6(2)	7(2)	3(2)	-2(2)	1(2)	-1(2)
C'7	290(2)	720(3)	470(3)	6(2)	7(2)	4(2)	0(2)	2(2)	-3(2)
C'8	393(2)	660(4)	522(3)	6(2)	10(3)	9(2)	1(3)	0(2)	1(3)
C'9	384(2)	621(3)	674(3)	7(2)	12(4)	7(2)	1(2)	-1(2)	-5(2)
C'10	296(3)	544(3)	696(4)	11(3)	5(2)	6(3)	2(2)	0(2)	1(2)
C'12	297(2)	232(3)	321(3)	9(2)	5(2)	7(2)	-1(2)	3(2)	-1(2)
C'14	384(2)	153(3)	318(3)	8(2)	6(2)	6(2)	1(2)	3(2)	-1(2)
C'13	301(3)	330(3)	214(3)	14(4)	9(3)	3(2)	0(2)	3(3)	-3(3)
C'11	57(2)	783(3)	451(4)	4(2)	10(3)	13(4)	2(3)	0(2)	2(2)
C'15	296(4)	481(3)	857(3)	24(5)	3(2)	5(2)	1(2)	1(3)	1(3)
Cl'1	109(1)	907(1)	505(1)	10(1)	7(1)	9(1)	1(1)	3(1)	2(1)
Cl'2	311(1)	408(-)	613(1)	13(1)	5(1)	9(1)	0(1)	1(1)	1(1)

used showed a small splitting; however, intensities were measured as sums of the two components.

A stereoscopic view⁷ of one of the molecules in the asymmetric unit is shown in Fig. 1. The bond lengths and angles of the two independent molecules appear to be normal, within the rather low accuracy. The two molecules in the asymmetric unit are similar within estimated standard deviations.

It is interesting to note the strong steric interaction between the axially oriented chlorine atom on C(4) and the carbon atom C(7). It is therefore not surprising to find that muurolene dihydrochloride (1) is not stable upon treatment with hydrogen chloride in ethanol and that it is

transformed into the more stable cadinene dihydrochloride (2). This transformation involves inversions at C(1) and C(4).

The transformation may proceed *via* a nucleophilic S_N2 replacement or a dehydrochlorination/hydrochlorination reaction leading to an inversion at C(4) and a dehydrochlorination-hydrochlorination involving the C(1)-C(10) positions to invert the C(1)-position.

Conversion of muurolene dihydrochloride (1) to cadinene dihydrochloride (2). Muurolene dihydrochloride (0.8 g; m.p. 84-86 °C; $[\alpha]_D^{22} - 13.9^\circ$, c in CHCl_3 1.5)² was dissolved in ethyl alcohol (99.5%, 2 ml). To this solution hydrochloric acid (6N, 3 drops)

was added and the mixture was warmed on a water bath (80 °C) for 5 min. The excess ethyl alcohol was then removed by applying reduced pressure. The concentrated solution was cooled thoroughly to obtain a white solid. This solid was filtered and recrystallized from light petroleum (b.p. 40–60 °C). The yield of colourless needles of cadinene dihydrochloride (2) was almost quantitative: m.p. 117–119 °C; $[\alpha]_D^{22} -36^\circ$ (c in CHCl_3 2.0).

1. Aschan, O. *Naphtenverbindungen, Terpene und Camperarten*, Walter de Gruyter & Co., Berlin, Leipzig 1929, p. 248.
2. Westfelt, L. *Acta Chem. Scand.* 20 (1966) 2852.
3. Hanic, F. *Chem. Listy* 52 (1958) 165.
4. Sýkora, Y., Herout, V. and Šorm, F. *Collect. Czech. Chem. Commun.* 23 (1958) 2181.
5. Westfelt, L. *Acta Chem. Scand.* 18 (1964) 572.
6. Sheldrick, G. M. *Shelx. A Program for Crystal Structure Determination*, Cambridge Univ. Press, London 1976.
7. Johnson, C. K. *Ortep*, Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge 1965.

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