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Studies on the Chlorinated α-Santonins. II. The Crystal and Molecular Structure of 14-Chlorosantonin

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The crystal structure of monochlorosantonin, $C_{15}H_{17}ClO_3$ has been determined in order to elucidate the molecular structure. The crystals are orthorhombic with space group $P2_12_12_1$ and the unit-cell dimensions are $a=11.180$ Å, $b=13.894$ Å, $c=9.211$ Å, $Z=4$. The crystal structure was solved by the heavy-atom method and the atomic parameters were refined to a final R value of 0.076 for 842 reflexions. From the analytical data the compound was confirmed to be 14-chlorosantonin (I).

Keywords——α-santonin; 2-chlorosantonin; 14-chlorosantonin; X-ray analysis; conformation; heavy-atom method

The authors have been studying the chlorination of santonin derivatives.[2] During the study, monochlorosantonin (I) was separated from a reaction mixture of hydrogen chloride gas and santonin α-epoxide in methanol. It was different from the known compound, 2-chlorosantonin (II).[3] We already reported the results of the mass spectra of the two monochlorosantonins (I and II).[4] It was expected by the mass spectra that the chlorine atom of monochlorosantonin (I) was bonded with the 14-carbon atom. However, the position of the chlorine atom is not yet decisive and should be confirmed in order to study the unusual reaction. Therefore, an X-ray analysis of monochlorosantonin (I) was undertaken to elucidate the position of the chlorine atom and to determine the conformation of the compound.

Table I. Final Atomic Parameters (×10⁴)

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	5317 (5)	5645 (3)	6706 (4)	204 (6)	96(3)	121 (4)	−29 (4)	28 (5)	9 (3)
C (1)	7036(12)	7322 (9)	2076(13)	69(13)	71(9)	133(19)	−9 (9)	12(12)	−6(10)
C (2)	7818(13)	7053(10)	3100(15)	71(13)	81(9)	159(20)	−8 (9)	13(14)	−30(11)
C (3)	7521(12)	6304 (9)	4141(13)	60(12)	62(8)	137(17)	6 (8)	−19(12)	−28 (9)
C (4)	6318(11)	5821 (8)	4039(11)	59(12)	51(7)	103(14)	−1 (7)	−17(11)	−12 (8)
C (5)	5565(10)	6073 (7)	2960(10)	57(11)	41(6)	79(12)	1 (7)	9 (9)	−15 (7)
C (6)	4282(11)	5752 (7)	2712(11)	60(12)	39(6)	109(14)	−8 (7)	2(10)	−1 (8)
C (7)	3408(11)	6567 (8)	3047(11)	62(11)	48(6)	92(14)	1 (7)	−1(11)	−1 (8)
C (8)	3591(12)	7390 (8)	1934(13)	81(13)	50(7)	142(17)	0 (8)	−15(13)	33 (9)
C (9)	4891(12)	7713 (8)	2055(13)	78(13)	50(7)	133(17)	−12 (8)	−3(12)	27 (9)
C (10)	5823(11)	6893 (7)	1849(11)	61(10)	42(6)	85(13)	−14 (7)	1(11)	4 (7)
C (11)	2258(11)	6018 (8)	3125(12)	69(12)	50(7)	107(15)	−1 (8)	−10(11)	−6 (8)
C (12)	2684(11)	5085 (8)	3841(11)	64(11)	47(6)	105(14)	−12 (7)	−2(11)	−4 (8)
C (13)	5805(14)	6478(10)	285(11)	106(16)	89(9)	66(13)	−18(11)	18(12)	−9 (9)
C (14)	6053(14)	5067(10)	5143(13)	97(15)	64(8)	142(17)	9(10)	−11(14)	12(10)
O (1)	8209(10)	6096 (7)	5115(10)	85(11)	103(7)	187(14)	2 (8)	−47(10)	5 (8)
O (2)	3875 (7)	4968 (5)	3640 (7)	68 (7)	40(4)	113 (9)	−10 (5)	−5 (7)	11 (5)
O (3)	2122 (9)	4496 (6)	4516 (8)	90(10)	72(6)	133(12)	−20 (7)	30(8)	4 (7)

(Temperature factors are expressed as
$T=\exp\{-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{22}kl)\}$.
The e.s.d.'s given in the parentheses denote the least significant digits).

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TABLE II. Final Observed and Calculated Structure Factors, F_o and F_c

H	FO	FC
K,L=	2	0
0	48	60
K,L=	4	0
0	3	2
K,L=	6	0
0	25	27
K,L=	8	0
0	11	14
K,L=	10	0
0	9	8
K,L=	12	0
0	16	16
K,L=	14	0
0	11	11
K,L=	1	1
0	34	39
1	36	41
2	38	37
3	40	39
4	25	23
5	39	37
6	9	9
7	17	18
8	9	9
9	14	16
10	5	6
11	4	4
K,L=	2	1
0	89	86
1	60	62
2	50	49
3	43	39
4	28	26
5	36	31
6	32	32
7	14	15
8	5	5
9	6	8
11	5	4
K,L=	3	1
1	74	69
2	41	41
3	23	22
4	42	40
5	43	41
6	11	12
7	7	8
8	13	12
9	14	15
10	6	7
12	3	3
K,L=	4	1
0	51	57
1	47	47
2	15	12
3	31	28
4	6	9
5	11	9
6	9	9
7	8	9
8	5	6
9	19	20
10	12	13
11	3	4
12	4	4
K,L=	5	1
0	19	15
1	10	8
2	51	48
3	38	38
4	23	21
5	31	29
6	8	7
7	3	5
8	6	8
9	7	10
10	12	11
11	5	6
K,L=	6	1
0	30	27
1	11	9
2	30	30
3	11	11
4	17	15
5	4	4
6	5	5
8	4	4
9	6	5
10	8	8
11	7	7
K,L=	7	1
0	22	22
1	7	10
2	15	17
3	22	20
4	20	19
6	8	10
7	11	12
8	8	8
9	7	8
10	3	4
11	4	2
K,L=	8	1
0	16	15
1	24	26
2	12	15
3	8	11
4	7	9
5	17	17
6	15	16
7	3	4
8	8	8
9	7	6
K,L=	9	1
0	7	9
1	7	8
2	7	7
3	6	6
4	9	9
5	15	16
6	20	20
7	7	6
8	9	10
9	9	10
10	5	4
K,L=	10	1
0	4	4
1	15	14
2	11	11
3	9	9
4	13	14
5	10	12
6	4	4
8	4	3
K,L=	11	1
0	6	4
1	12	13
2	9	11
3	19	21
4	5	6
5	7	7
6	6	4
7	6	6
K,L=	12	1
0	9	10
1	9	9
2	9	10
3	14	13
4	13	13
5	7	6
6	4	5
K,L=	13	1
1	9	10
2	13	13
3	13	13
4	6	7
K,L=	14	1
0	7	6
1	3	5
2	6	5
3	7	8
4	4	3
5	6	5
K,L=	15	1
0	4	4
1	5	4
2	4	5
3	5	4
K,L=	0	2
0	58	63
K,L=	1	2
0	69	70
1	61	54
2	73	76
3	16	15
4	18	21
5	23	24
6	31	31
7	12	13
8	19	18
9	13	13
10	6	4
11	5	5
12	6	5
K,L=	2	2
0	70	64
1	65	67
2	45	44
3	2	2
4	8	10
5	19	20
6	21	23
7	7	7
8	5	6
9	22	21
10	11	10
11	7	7
K,L=	3	2
0	13	1
1	10	16
2	21	19
3	48	45
4	23	23
5	4	3
6	26	27
7	10	11
8	9	9
10	11	12
11	8	6
K,L=	4	2
0	29	26
1	39	35
2	13	15
3	39	39
4	11	12
5	15	14
6	16	16
7	12	13
8	8	8
9	8	8
10	4	5
11	2	2
K,L=	5	2
0	10	9
1	41	39
2	9	10
3	33	33
4	13	11
5	14	16
6	16	16
7	9	9
8	8	7
9	10	10
10	7	7
K,L=	6	2
0	42	40
1	29	26
2	31	32
3	35	32
4	10	11
5	27	27
6	23	23
7	16	18
8	6	6
9	7	6
10	5	5
K,L=	7	2
0	36	38
1	26	27
2	8	8
3	12	10
4	10	10
5	18	19
6	8	9
7	6	5
8	9	8
10	3	3
K,L=	8	2
0	16	16
1	10	12
2	18	17
3	5	6
4	4	6
5	15	16
6	8	9
7	15	16
8	4	4
9	5	5
K,L=	9	2
0	25	24
1	10	10
2	14	14
3	9	8
4	11	12
5	14	11
6	12	11
7	9	8
8	6	6
K,L=	10	2
1	12	13
2	6	5
3	11	11
4	11	12
6	13	12
7	11	11
8	4	3
K,L=	11	2
0	11	11
1	10	10
2	11	12
3	10	10
4	8	7
7	4	3
8	3	3
K,L=	12	2
0	7	7
1	8	8
2	3	4
3	5	5
5	4	4
6	9	9
7	4	5
K,L=	13	2
0	7	7
1	6	7
3	12	13
4	8	8
K,L=	14	2
1	5	4
2	5	6
3	9	9
4	4	4
K,L=	15	2
2	10	10
K,L=	1	3
0	25	20
1	74	72
2	20	21
3	5	8
4	14	17
5	15	16
6	14	13
7	3	3
9	10	11
10	7	6
11	7	6
K,L=	2	3
0	4	5
1	34	38
2	12	14
3	33	33
4	14	10
5	21	22
6	28	29
7	13	13
8	22	22
9	10	10
10	7	7
K,L=	3	3
0	91	90
1	41	40
2	44	44
3	9	10
4	25	24
5	9	11
6	15	17
7	15	15
8	4	3
9	17	15
10	6	6
11	6	6
K,L=	4	3
0	15	14
1	9	11
2	40	41
3	43	41
4	12	11
5	14	15
6	12	12
7	11	12
8	20	20
9	5	5
10	4	4
11	5	4
K,L=	5	3
0	4	5
1	32	32
2	33	27
3	18	19
4	23	24
5	6	6
6	7	7
7	6	7
8	7	8
9	8	9
11	6	5
K,L=	6	3
0	19	19
1	15	13
2	46	44
3	10	8
5	7	7
6	11	9
7	13	14
8	4	5
9	6	6
10	8	7
11	3	2
K,L=	7	3
0	18	18
1	10	11
2	17	16
3	29	30
4	5	4
5	7	7
6	16	16
7	13	12
8	7	7
9	7	8
K,L=	8	3
0	7	7
2	6	5
4	9	10
5	9	8
6	12	13
7	9	9
9	7	6
10	6	7
K,L=	9	3
0	11	12
1	6	6
2	17	18
3	8	6
4	6	7
5	8	8
6	9	9
8	8	6
K,L=	10	3
1	5	5
2	10	11
3	17	16
4	16	17
5	7	7
6	8	9
7	5	7
8	5	5
K,L=	11	3
0	11	12
1	9	9
2	11	12
3	10	9
4	5	4
5	3	3
7	4	4
8	5	5
K,L=	12	3
0	4	3
1	5	5
2	10	9
4	3	3
6	3	4
K,L=	13	3
0	7	7
1	8	9
2	7	6
3	5	4
4	6	6
5	6	6
K,L=	14	3
1	3	3
2	6	6
K,L=	0	4
0	4	3
K,L=	1	4
0	21	21
1	37	35
2	15	17
3	13	11
4	18	19
5	24	25
6	7	7
7	13	13
8	11	10
9	16	15
K,L=	2	4
0	29	30
1	6	3
2	23	20
3	21	21
4	6	7
5	19	17
6	3	5
7	13	14
8	13	14
9	15	14
11	3	2
K,L=	3	4
0	24	24
1	7	11
2	22	23
3	10	9
4	17	18
5	14	14
6	11	11
7	17	16
8	8	8
9	8	7
K,L=	4	4
0	16	16
1	25	22
2	7	6
3	18	19
4	25	25
5	7	5
6	8	7
7	10	10
8	16	16
9	11	11
11	3	3
K,L=	5	4
1	49	47
2	9	10
3	13	14
4	16	14
5	16	17
6	13	13
7	19	18
8	15	14
K,L=	7	4
0	28	26
K,L=	5	4
9	6	6
K,L=	6	4
0	19	19
1	10	9
2	16	16
3	14	14
4	19	21
5	12	12
6	18	17
8	4	2
K,L=	7	4
1	19	21
2	14	13
3	26	26
4	12	12
5	8	8
6	8	7
7	16	16
8	3	4
9	4	4
K,L=	8	4
1	9	9
2	9	9
3	32	32
5	4	4
6	12	12
7	9	8
8	8	8
9	4	4
K,L=	9	4
0	23	21
1	20	21
2	12	12
3	4	6
4	12	11
5	5	5
6	4	4
9	3	3
K,L=	10	4
0	5	4
1	3	3
2	14	14
4	8	9
7	9	9
8	4	4
K,L=	11	4
0	10	9
1	9	8
2	10	10
3	10	8
4	4	4
5	3	3
6	3	3
7	6	6
K,L=	12	4
0	5	5
1	6	5
2	5	5
3	5	6
6	6	6
K,L=	13	4
1	5	5
3	5	4
4	4	3
K,L=	14	4
0	6	5
2	4	4
K,L=	1	5
0	10	9
1	17	19
2	24	23
3	25	26
4	8	8
5	8	8
6	11	11
8	11	12
9	10	10
10	9	10
K,L=	2	5
0	12	12
1	11	11
2	34	34
3	25	23
4	5	4
5	3	2
6	12	13
7	14	14
8	14	14
9	10	10
10	5	6
K,L=	3	5
0	44	46
1	17	14
2	22	21
3	5	4
4	8	9
5	12	14
6	7	8
7	10	12
8	13	14
9	7	5
10	5	5
10	5	5
K,L=	4	5
0	17	18
1	20	19
2	40	41
3	15	15
4	3	3
5	12	14
6	19	19
7	12	12
8	5	4
9	7	7
K,L=	5	5
1	16	14
2	15	16
3	12	12
4	6	6
5	6	5
6	17	17
7	17	16
8	4	5
10	4	3
K,L=	6	5
1	23	23
2	12	13
3	12	13
4	10	9
5	4	6
6	8	7
7	9	7
8	8	9
9	7	8
K,L=	7	5
1	8	7
2	5	6
3	21	22
4	7	5
5	6	4
6	14	12
7	8	6
8	8	9
K,L=	8	5
1	15	15
2	12	13
3	6	7
4	5	4
5	4	4
6	3	5
7	9	9
8	7	7
K,L=	9	5
0	15	14
1	8	7
3	14	14
4	12	12
5	8	9
6	7	8
K,L=	10	5
0	5	6
1	11	11
2	10	8
3	9	8
5	11	11
6	4	4
K,L=	11	5
1	6	5
2	5	6
4	4	3
6	5	5
K,L=	12	5
0	7	8
2	4	4
5	4	2
K,L=	13	5
1	5	5
3	4	5
K,L=	0	6
0	42	40
K,L=	1	6
0	10	7
1	11	12
3	19	18
4	21	22
5	11	12
6	11	11
7	13	12
8	10	9
9	9	8
10	6	6
K,L=	2	6
0	8	7
1	15	15
2	24	22
3	20	19
4	6	6
5	4	3
6	4	5
7	6	6
9	3	3
K,L=	3	6
0	10	10
1	17	16
2	6	6
3	8	8
4	12	13
5	12	12
6	15	15
7	6	7
8	8	7
9	5	6
K,L=	4	6
0	5	5
1	20	18
3	19	21
4	8	8
5	10	12
6	7	7
7	8	7
8	9	9
9	7	6
K,L=	5	6
0	19	19
1	10	9
2	8	8
3	10	9
4	4	6
5	6	6
6	17	18
7	15	14
8	4	5
K,L=	6	6
1	13	13
2	8	9
3	8	9
4	17	18
5	6	5
6	16	16
7	5	6
8	6	6
K,L=	7	6
0	14	17
1	5	3
2	10	9
3	9	9
4	5	6
5	13	15
6	11	11
7	10	10
8	5	6
K,L=	8	6
0	5	5
1	11	11
2	9	8
3	13	12
4	13	14
5	6	4
6	3	3
7	3	3
K,L=	9	6
0	6	6
1	5	4
2	12	11
3	4	5
4	8	8
5	7	7
6	4	4
K,L=	10	6
1	8	9
2	9	8
3	6	6
4	3	4
5	7	7
6	4	4
K,L=	11	6
0	7	7
K,L=	12	6
1	4	4
2	3	4
K,L=	1	7
1	1	4
3	5	6
4	8	8
5	5	6
6	12	11
7	5	5
8	12	14
9	14	15
K,L=	2	7
0	9	8
1	26	27
2	8	8
3	2	3
4	11	12
5	7	7
6	5	5
7	5	5
8	9	9
9	4	4
K,L=	3	7
0	13	12
1	17	17
2	4	4
3	4	4
4	16	16
5	4	5
6	7	8
7	6	5
K,L=	4	7
0	34	34
1	6	6
2	10	9
3	7	6
5	5	6
6	8	8
7	7	7
8	4	3
K,L=	5	7
0	17	17
1	13	12
3	21	22
4	9	9
5	9	8
6	8	7
7	6	7
8	3	3
K,L=	6	7
0	11	10
1	12	13
2	7	6
3	7	8
4	5	6
5	10	9
K,L=	7	7
1	10	11
2	4	5
3	7	5
4	4	5
5	10	10
6	9	8
7	5	5
K,L=	8	7
1	10	10
2	10	11
3	6	6
4	6	7
5	6	7
6	6	5
K,L=	9	7
2	4	3
3	9	9
5	6	6
K,L=	10	7
2	6	6
3	8	7
K,L=	0	8
0	23	21
K,L=	1	8
0	25	25
1	9	8
2	13	12
3	12	12
4	9	8
5	13	14
6	6	6
7	4	3
K,L=	2	8
0	11	13
1	15	14
2	7	9
3	4	3
4	10	12
K,L=	3	8
0	6	9
1	22	21
2	8	8
3	7	7
4	7	7
5	3	4
6	6	7
K,L=	4	8
0	7	7
1	5	6
2	6	4
3	9	8
5	9	10
6	8	8
7	2	2
K,L=	5	8
0	13	11
1	10	10
2	4	3
3	9	9
4	3	5
K,L=	6	8
0	16	16
4	6	7
5	3	3
K,L=	7	8
0	4	3
2	12	12
3	7	7
4	5	6
5	3	4
K,L=	8	8
0	9	10
2	3	3
3	6	5
K,L=	9	8
1	6	5
2	7	8
3	3	4
K,L=	1	9
3	9	10
4	8	8
5	6	6
6	5	6
K,L=	2	9
0	12	12
1	8	7
2	10	10
3	3	3
4	4	4
5	5	5
K,L=	3	9
2	10	11
3	6	7
4	6	5
5	4	4
K,L=	4	9
1	4	3
3	6	5
5	8	9
K,L=	5	9
0	6	6
2	8	8
4	5	4
K,L=	6	9
1	7	8
2	4	4
K,L=	7	9
2	5	5
K,L=	0	10
0	14	14
K,L=	1	10
0	8	8
1	5	5
2	8	8
3	4	5
K,L=	2	10
0	9	9
1	3	3
K,L=	3	10
0	8	8
1	8	7
2	5	5

Experimental

Preparation of 14-Chlorosantonin (I)——Santonin α-epoxide[5] (III) (500 mg) was dissolved into 100 ml of MeOH saturated with dry HCl gas. After 10 min, a great part of the reaction mixture was evaporated under reduced pressure, to which 100 ml of H_2O was added. The deposit was collected, washed with H_2O and dried. The residue was chromatographed over silica gel. Elution with $CHCl_3$–MeOH gave 50 mg of I, which was recrystallized from MeOH, colorless prisms, mp 173—174°. *Anal.* Calcd. for $C_{15}H_{17}ClO_3$: C, 64.17; H, 6.10; Cl, 12.63. Found: C, 64.24; H, 6.19; Cl, 12.53. IR ν_{max}^{KBr} cm^{-1}: 1786, 1664, 1640, 1618. UV λ_{max}^{EtOH} nm (log ε): 242 (4.03). NMR ($CDCl_3$) δ: 1.22 (3H, doublet, J=6.2 Hz, 11-Me), 1.34 (3H, singlet, 10-Me), 4.74 (2H, singlet, CH_2Cl), 4.80 (1H, doublet, J=10.0 Hz, 6-H), 6.23 (1H, doublet, J=10.3 Hz, 2-H), 6.70 (1H, doublet, J=10.3 Hz, 1-H). Mass Spectrum *m/e*: 280 (M^+).[4]

Crystal Data——The crystal was orthorhombic, space group $P2_12_12_1$, with four molecules in a unit cell of dimensions a=11.180 Å, b=3.894 Å, c=9.211 Å, V_0=1430.8 Å^3, $D_{calc.}$=1.274 g/cm^3. The reflexion data were collected on a Rigaku four-circle diffractometer using graphite monochromated Cu Kα radiation. Intensities of reflexions with 2θ values up to 120° were collected by the θ-2θ scan method with a 2θ scan rate of 2° min^{-1}. The background was measured at each end of the scan range for 10 sec. Those reflexions having an intensity exceeding 2 times of the corresponding standard deviations were collected. 842 reflexions out of 951 reflexions were used as data, and corrected for Lorentz and polarization factor but not for absorption and extinction factors. The atomic scattering factors used in the calculations were taken from "International Tables for X-ray Crystallography."[6]

Determination of the Structure——The position of the chlorine atom was derived from the three Patterson-Harker sections at u=0.5, v=0.5, and w=0.5, respectively. The whole structure was revealed after calculating several successive Fourier and Difference Fourier maps. Refinement of the positional parameters of the 19 atoms including chlorine atom was carried out by the block-diagonal matrix least-squares method using the isotropic temperature factors, and gave an R value of 0.145. The oxygen atoms were identified with the help of structural considerations. Five cycles of refinement by the block-diagonal least-squares method with anisotropic temperature factors for all the atoms gave the final R value of 0.076 for 842 reflexions. The final atomic parameters are presented in Table I along with their standard deviations. The observed and calculated structure factors are listed in Table II.

Results and Discussion

The above study on the structure reveals that the chlorine atom is bonded with 14-carbon atom as expected from the results of the mass analysis.[4] The chlorine atom is situated below the molecular plane, which is the opposite side of the angular methyl group. Important dihedral angles are shown in Table III, in which it is shown that the C(4)–C(14)–Cl triangular plane is almost at a right angle to the molecular plane (Dihedral angles C(3)–C(4)–C(14)-Cl and C(5)–C(4)–C(14)-Cl are 90.9 and −90.4 degrees, respectively). The bond lengths and numbering are shown in Fig. 1, and their standard deviations are between 0.013 and 0.020 Å. The bond angles are shown in Table IV. The bond lengths and angles are almost the same as obtained from the X-ray analysis of 2-bromo-α-santonin.[7] The projection of the crystal

TABLE III. Torsional Angles (°)

C(10)-C(1)-C(2)-C(3)	−1.6	C(8)-C(9)-C(10)-C(5)	−55.9
C(1)-C(2)-C(3)-C(4)	0.9	C(9)-C(10)-C(5)-C(6)	56.7
C(2)-C(3)-C(4)-C(5)	2.0	C(6)-O(2)-C(12)-C(11)	−4.2
C(3)-C(4)-C(5)-C(10)	−4.2	O(2)-C(12)-C(11)-C(7)	−21.9
C(4)-C(5)-C(10)-C(1)	3.3	C(12)-C(11)-C(7)-C(6)	36.8
C(5)-C(10)-C(1)-C(2)	−0.3	C(11)-C(7)-C(6)-O(2)	−41.1
C(10)-C(5)-C(6)-C(7)	−63.8	C(7)-C(6)-O(2)-C(12)	28.4
C(5)-C(6)-C(7)-C(8)	66.0	C(3)-C(4)-C(14)-Cl	90.9
C(6)-C(7)-C(8)-C(9)	−58.3	C(5)-C(4)-C(14)-Cl	−90.4
C(7)-C(8)-C(9)-C(10)	55.4		

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5) J.B. Hendrickson and T.L. Bogard, *J. Chem. Soc.*, **1962**, 1678.
6) C.H. MacGillavry and G.D. Rieck, "International Tables for X-ray Crystallography," Vol. III, Kynoch Press, Birmingham, 1968, p. 201.
7) J.D.M. Asher and G.A. Sim, *Proc. Chem. Soc.*, **1962**, 335; *J. Chem. Soc.*, **1965**, 6041.

structure viewed along the *c* axis is shown in Fig. 2. All intermolecular contacts are more than 3.4 Å.

The NMR spectrum of 14-chlorosantonin (I) also supports the structure obtained from the X-ray analysis. The peak at δ 1.33, corresponding to three protons, is the signal for the methyl group attached to C(4) of α-santonin.[5] In the case of 14-chlorosantonin (I), this

Table IV. Bond Angles (°) (Estimated Standard Deviations in Parentheses)

C(1)-C(10)-C(9)	107.4 (9)	C(7)-C(6)-O(2)	103.7 (8)
C(1)-C(10)-C(5)	111.6 (9)	C(5)-C(6)-C(7)	110.9 (9)
C(1)-C(10)-C(13)	106.9 (9)	C(9)-C(8)-C(7)	107.1 (10)
C(2)-C(1)-C(10)	125.4 (12)	C(9)-C(10)-C(13)	112.1 (9)
C(2)-C(3)-O(1)	121.0 (12)	C(10)-C(5)-C(6)	106.9 (8)
C(3)-C(2)-C(1)	121.0 (12)	C(10)-C(5)-C(4)	123.9 (9)
C(4)-C(3)-C(2)	118.8 (11)	C(10)-C(9)-C(8)	114.5 (10)
C(4)-C(3)-O(1)	120.1 (11)	C(11)-C(12)-O(3)	129.5 (11)
C(5)-C(4)-C(3)	119.2 (10)	C(11)-C(12)-O(2)	110.4 (9)
C(5)-C(10)-C(13)	109.6 (9)	C(11)-C(7)-C(8)	121.4 (10)
C(5)-C(10)-C(9)	109.3 (9)	C(12)-C(11)-C(15)	111.9 (10)
C(5)-C(6)-O(2)	115.2 (9)	C(12)-O(2)-C(6)	107.3 (8)
C(6)-C(7)-C(11)	100.5 (9)	C(14)-C(4)-C(5)	124.1 (11)
C(6)-C(7)-C(8)	109.2 (9)	C(14)-C(4)-C(3)	116.7 (10)
C(6)-C(5)-C(4)	128.6 (10)	O(3)-C(12)-O(2)	120.1 (10)
C(7)-C(11)-C(12)	100.6 (9)	Cl-C(14)-C(4)	108.4 (9)
C(7)-C(11)-C(15)	117.0 (10)		

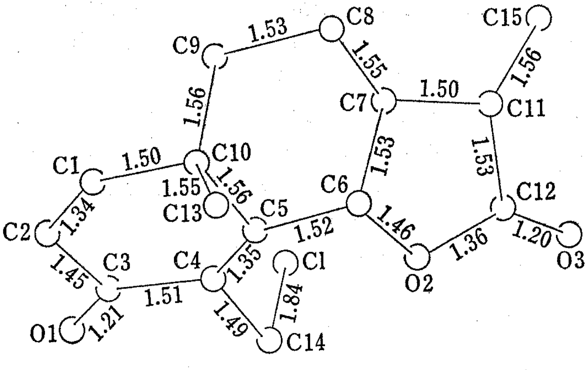


Fig. 1. Numbering and Bond Lengths (Å)

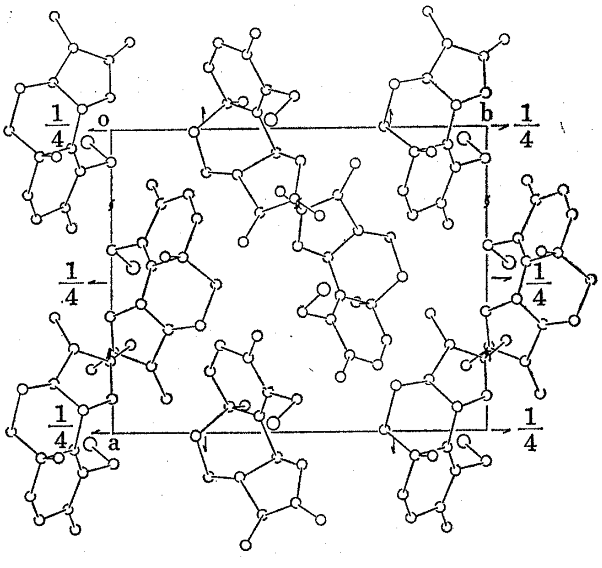
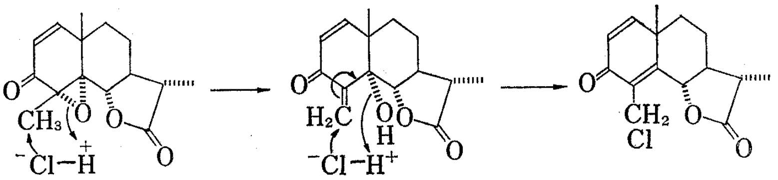


Fig. 2. Projection of the Crystal Structure Along *c* Axis



III IV I

Chart 1

peak appears at δ 4.74 ppm. This shift to a lower field is most probably caused by the substitution of a chlorine atom on the methyl group attached to C(4) of α-santonin.

A possible reaction mechanism from santonin α-epoxide (III) to 14-chlorosantonin (I) is shown in Chart 1. The reaction is thought to proceed by the attack of hydrogen chloride on the epoxide (III) to form an intermediate ion (IV), which will be rearraged by the *SN*2′ reaction with hydrogen chloride to form 14-chlorosantonin (I).

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