Vol. XXIX No. 1 SCIENTIA SINICA (Series B) January 1986

MOLECULAR STRUCTURE AND ABSOLUTE CONFIGURATION OF SUBEROGORGIN

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Received July 12, 1984; revised January 10, 1985.

ABSTRACT

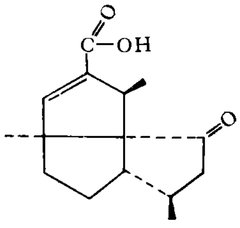
In the present paper it is reported that the molecular structure and absolute configuration of poisonous suberogorgin are determined by using X-ray diffraction method. The crystal of suberogorgin belongs to orthogonal system with space group D_2^4-$P2_12_12_1$. The crystallographic parameters are: $a = 16.135\text{Å}$, $b = 13.189\text{Å}$, $c = 12.901\text{Å}$, $Z = 8$. The initial model of the crystal structure was solved by the direct method. The refinement of the structure parameters was carried out by using the least square method and led to a final R-factor of 0.056. In accordance with the molecular structure of suberogorgin mentioned above, the solvent effect of NMR has been further discussed and the relationship between the molecular structure of suberogorgin and its toxicity has also been preliminarily investigated.

In the investigation of the chemical constituents of Chinese gorgonias by using chromatography, suberogorgin, a novel sesquiterpene, was isolated from the crude CH_3OH extract of *Subcrogorgia sp.* collected from the South China Sea. It was only 0.1 per cent of dry weight of *Subcrogorgia sp.* According to the spectral data and chemical conversions, the chemical structure of this marine natural product has been determined[1].

Suberogorgin is intensely toxic with a median dose of $LD_{50} = 22.8 \pm 1.8$mg/kg for mice and is probably the perfect chemical self-protective means of the gorgonias. Suberogorgin possesses the novel skeleton of tricycloundecane terpene which is the first example of the marine natural product possessing this unique cyclic system. In the present paper it is first reported that the skeleton of a novel sesquiterpene is demonstrated by using X-ray diffraction method and the molecular structure and absolute configuration of suberogorgin are determined (Fig. 1). This is very significant for terpene chemistry. The distinct structure of a natural product like suberogorgin was very rare and never discovered until this hydrocarbon of tricyclo-undecane system was gained from the complicated extract of *Silphium sp.* in 1980, which chemical structure was determined by NMR method[2].

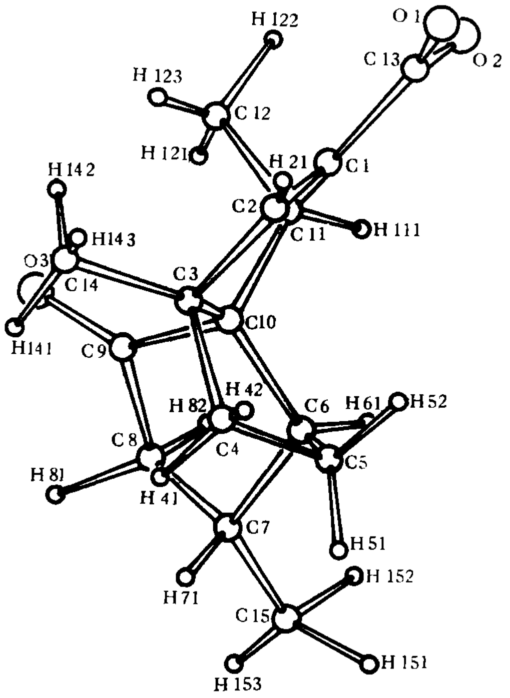
I. EXPERIMENTAL

The molecular formula of suberogorgin is $C_{15}H_{20}O_3$, melting at 200—202°C and *M. W.* 248.32 daltons[1]. X-ray crystallographic analysis of suberogorgin crys-



(a)

Fig. 1(a). The chemical structure of suberogorgin.



(b)

Fig. 1(b). The molecular structure and absolute configuration of suberogorgin.

tals was performed by using Weissenberg's method. The crystal belongs to orthogonal system with *Laue* group mmm. The space group D_2^4-p$2_12_12_1$ of the crystal was uniquely determined since there were systematic absences for the reflections $\{h00\}$ with $h = 2n + 1$, $\{0k0\}$ with $k = 2n + 1$ and $\{00l\}$ with $l = 2n + 1$. The refined unit cell dimensions were measured on a Philips PW-1100 four-circle diffractometer as follows: $a = 16.135$Å, $b = 13.189$Å, $c = 12.901$Å and $V = 2745$Å^3. The number of suberogorgin molecules per unit cell is $Z = 8$ and each asymmetric unit contains two molecules. Calculated density of the crystal is $D_c = 1.20\text{g} \cdot \text{cm}^{-3}$.

X-ray diffraction intensities with indices hkl and $\bar{h}\bar{k}\bar{l}$ were sequentially measured on the diffractometer by means of CuKα (λ=1.5418Å) radiation, l being the slowest moving index. Intensities were corrected by Lorentz and polarization factor, but not by absorption and radiation factors. In the structure solution and initial refinement 2696 independent reflections with $I_0 > 3\sigma(I_0)$ of indices hkl were used. In the final refinement 2542 independent reflections with $\bar{F}_0 > 3\sigma(\bar{F}_0)$ of indices hkl and $\bar{h}\bar{k}\bar{l}$ were used.

II. Structure Solution and Refinement

The initial model of the crystal structure was solved by using direct method and Fourier synthesis with $R = 0.26$. The coordinates of all hydrogen atoms except the ones in the carboxyl groups were determined by stereochemical calculation and demonstrated by a difference Fourier synthesis. The refinement of the structure

Table 1

The Atomic Positional and Thermal Parameters of All Non-Hydrogen Atoms in Asymmetric Unit

	Atom	$\times 10^{-4}$			$\times 10^{-5}$					
		x	y	z	B11	B22	B33	B12	B13	B23
Molecule I	O1	3111	582	3695	345	547	518	183	136	−106
	O2	3169	732	1974	399	830	553	573	111	323
	O3	5304	−2850	1322	718	530	872	214	222	−227
	C1	4128	−344	2771	269	428	434	190	15	−44
	C2	4495	−758	3589	415	673	441	427	27	−70
	C3	5209	−1461	3297	432	806	370	655	60	175
	C4	6014	−1089	3808	575	1632	526	1076	−362	−528
	C5	6246	−145	3239	403	1230	1124	319	−402	−1233
	C6	6056	−403	2093	287	548	770	179	−181	−203
	C7	6783	−941	1559	309	715	707	290	−33	189
	C8	6347	−1658	788	414	862	501	360	110	−115
	C9	5614	−2017	1401	427	449	528	265	−26	−45
	C10	5327	−1184	2114	308	439	384	270	−18	−9
	C11	4485	−708	1750	271	457	391	143	−61	−62
	C12	3879	−1428	1219	391	616	617	−48	−149	−264
	C13	3435	361	2820	253	408	535	37	27	−6
	C14	4980	−2549	3553	950	855	745	936	603	790
	C15	7415	−225	1075	384	1077	1230	150	29	691
Molecule II	O1	3109	−1937	8645	347	586	541	217	123	−163
	O2	3173	−1748	6924	417	891	592	614	120	339
	O3	5190	−5358	6168	629	532	932	−25	210	−466
	C1	4128	−2854	7700	249	378	453	116	63	−61
	C2	4495	−3289	8502	330	532	426	195	133	−2
	C3	5190	−4004	8185	334	491	383	300	63	196
	C4	6007	−3667	8703	400	888	448	380	−177	−87
	C5	6265	−2720	8126	348	772	677	20	−185	−496
	C6	6057	−2976	6984	252	419	522	67	−31	−44
	C7	6768	−3542	6447	262	617	560	178	59	110
	C8	6318	−4266	5692	367	726	456	202	82	−190
	C9	5554	−4564	6275	362	429	545	109	−54	−112
	C10	5306	−3716	7002	257	377	360	114	5	−30
	C11	4478	−3188	6665	234	454	401	86	−57	−59
	C12	3849	−3849	6083	346	775	662	−55	−204	−415
	C13	3434	−2143	7782	243	444	538	98	18	31
	C14	4949	−5089	8425	581	594	703	325	284	470
	C15	7394	−2850	5925	353	986	973	−55	249	289

parameters was carried out by using the least square method and led to a final R-factor value of 0.056 for 2542 independent reflections with $\bar{F}_0 > 3\sigma(\bar{F}_0)$ and positional parameters and anisotropic thermal parameters of all non-hydrogen atoms

Table 2

The Atomic Positional and Thermal Parameters of Thirty-eight Hydrogen Atoms in Asymmetric Unit

	Atom	$x \times 10^{-4}$	$y \times 10^{-4}$	$z \times 10^{-4}$	Biso(Å^2)
Molecule I	H21	4276	−632	4334	4.65
	H41	6448	−1595	3704	8.64
	H42	5821	−833	4600	7.86
	H51	6859	59	3233	6.58
	H52	5776	495	3575	7.47
	H81	6702	−2374	618	4.84
	H82	6135	−1119	117	5.67
	H121	4219	−1603	547	5.05
	H122	3286	−968	1230	2.68
	H123	3801	−1997	1714	4.33
	H141	5506	−2935	3440	8.32
	H142	4445	−2746	3107	4.93
	H143	4846	−2403	4421	9.58
	H151	7715	389	1693	7.15
	H152	7068	301	624	6.63
	H153	7908	−727	774	7.60
	H61	5941	210	1608	2.74
	H71	7118	−1292	2077	4.52
	H111	4594	−44	1194	1.35
Molecule II	H21	4327	−3223	9250	3.48
	H41	6459	−4156	8543	5.65
	H42	5944	−3469	9497	4.50
	H51	6913	−2573	8158	3.66
	H52	5811	−2115	8420	4.03
	H81	6629	−5077	5547	4.67
	H82	6046	−3765	4983	3.71
	H121	4166	−3993	5385	5.97
	H122	3283	−3396	6033	2.89
	H123	3755	−4391	6542	3.79
	H141	5461	−5515	8287	6.18
	H142	4470	−5215	7959	4.29
	H143	4792	−4991	9274	6.67
	H151	7700	−2237	6451	5.21
	H152	7062	−2415	5485	5.01
	H153	7749	−3422	5633	6.48
	H61	5984	−2375	6477	1.74
	H71	7164	−3877	6900	4.05
	H111	4606	−2526	6126	1.34

and isotropic thermal parameters of thirty-eight hydrogen atoms. The positional and thermal parameters of all non-hydrogen atoms and thirty-eight hydrogen atoms are listed in Tables 1 and 2 respectively.

III. DETERMINATION OF ABSOLUTE CONFIGURATION

The absolute configuration of suberogorgin molecules was determined by using the anomalous scattering method. Firstly, $F_c(hkl)$ and $F_c(\bar{h}\bar{k}\bar{l})$ were calculated by using the parameters listed in Tables 1 and 2 and the parameters of anomalous scattering effect (carbon atom: $\Delta f'_{\mathrm{CuK}\alpha} = 0.017$, $\Delta f''_{\mathrm{CuK}\alpha} = 0.009$. oxygen atom: $\Delta f'_{\mathrm{CuK}\alpha} = 0.047$, $\Delta f''_{\mathrm{CuK}\alpha} = 0.032$)[3]. After comparing $F_c(hkl)$ with $F_c(\bar{h}\bar{k}\bar{l})$, only 31 pairs of reflections with $|\Delta F_c| \geqslant 0.2$ were found (Table 3). Secondly, intensities measured were corrected by radiation damage factors as follows:

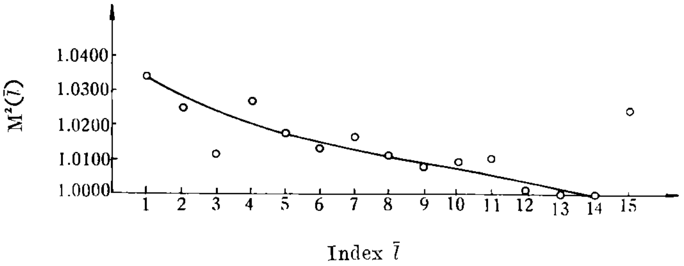


Fig. 2. The plot of radiation damage of suberogorgin crystal.

The radiation damage factors for each pair of l and $\bar{l}$ were calculated according to the following formula:

$$M(\bar{l}) = \left[\sum_{l} I_0(hkl) / \sum_{\bar{l}} I_0(\bar{h}\bar{k}\bar{l})\right]^{\frac{1}{2}}, \qquad (1)$$

then the plot of radiation damage was smoothed (Fig. 2). $F_0(\bar{h}\bar{k}\bar{l})$ was multiplied by $M(\bar{l})$ and $F_0(hkl)$ was not changed. Table 3 shows that there are 22 pairs of reflections with the negative or positive sign of ΔF_0 in accord with the ΔF_c before radiation damage correction and 27 pairs of reflections after radiation damage correction. The percentage of Bijvoet pairs with the same signs of ΔF_c increased from 71% to 87%. So the absolute configuration of the molecule was determined as illustated in Fig. 1 with the correct structure parameters listed in Tables 1 and 2.

Thirdly, the intensities of 31 Bijvoet pairs of reflections mentioned above were measured again with caution on the four-circle diffractometer by means of CuKα($\lambda = 1.5418$Å) radiation. The percentage of Bijvoet pairs with the same signs of ΔF_c is about 94% (Table 3).

Finally, a significant test on the R-factor was made by using Halmilton's method[4] for further verifying the above-mentioned molecular configuration. Using $F_0(hkl)$ containing anomalous scattering effect, two R-factors were calculated as follows:

Table 3

Anomalous Scattering Effect of Suberogorgin Crystal

Indices			Radiation Damage Factor				First Observation						Second Observation		
							Before radiation damage correction			After radiation damage correction					
h	k	l	$M(\bar{l})$	$F_c(hkl)$	$F_c(\bar{k}\bar{h}\bar{l})$	$\triangle F_c$	$F_0(hkl)$	$F_0(\bar{k}\bar{h}\bar{l})$	$\triangle F_0$	$F_0(hkl)$	$F_0(\bar{k}\bar{h}\bar{l})$	$\triangle F_0$	$F_0(hkl)$	$F_0(\bar{k}\bar{h}\bar{l})$	$\triangle F_0$
3	2	5	1.0092	65.2	65.4	−0.2	64.90	64.35	+0.55	64.90	64.94	−0.44	465.2	470.0	−
6	2	5	1.0092	23.0	23.2	−0.2	22.52	22.58	−0.06	22.52	22.79	−0.27	167.9	169.5	−
7	2	5	1.0092	14.9	14.7	+0.2	17.05	16.22	+0.83	17.05	16.37	+0.68	153.2	150.1	+
4	5	5	1.0092	27.4	27.6	−0.2	28.21	27.93	+0.28	28.21	28.18	+0.03	162.4	164.5	−
5	5	5	1.0092	33.8	34.0	−0.2	34.83	34.55	+0.28	34.83	34.87	−0.04	195.6	196.3	−
1	6	5	1.0092	41.6	41.4	+0.2	44.12	43.68	+0.44	44.12	44.08	+0.04	253.2	253.9	−
7	6	5	1.0092	9.6	9.8	−0.2	12.50	12.05	+0.45	12.50	12.16	+0.34	162.8	163.6	−
9	10	5	1.0092	13.3	13.1	+0.2	13.06	12.67	+0.39	13.06	12.79	+0.27	100.8	95.8	+
7	3	6	1.0082	16.7	16.9	−0.2	17.42	17.27	+0.15	17.42	17.41	+0.01	156.4	157.0	−
3	4	6	1.0082	16.7	16.5	+0.2	18.30	18.03	+0.27	18.30	18.18	+0.12	130.8	130.1	+
4	4	6	1.0082	25.4	25.7	−0.3	25.31	25.44	−0.13	25.31	25.65	−0.34	144.4	147.0	−
3	5	6	1.0082	19.1	18.9	+0.2	19.00	18.77	+0.23	19.00	18.92	+0.08	128.7	128.1	+
5	5	6	1.0082	30.0	30.2	−0.2	30.67	30.62	+0.05	30.67	30.87	−0.20	161.2	162.7	−
2	2	7	1.0070	33.9	34.1	−0.2	36.03	36.29	+0.26	36.03	36.54	−0.51	386.8	391.1	−
0	2	7	1.0070	12.4	12.6	−0.2	12.03	12.08	−0.15	12.03	12.16	−0.13	116.9	118.2	−
4	4	8	1.0060	43.4	43.6	−0.2	44.74	44.74	0.0	44.74	45.01	−0.27	393.7	396.7	−
4	1	1	1.0164	28.9	29.1	−0.2	29.97	29.53	+0.44	29.97	30.01	−0.04	307.9	311.6	−
1	3	1	1.0164	41.3	41.1	+0.2	43.49	43.11	+0.38	43.49	43.81	−0.32	846.9	856.9	−
4	3	1	1.0164	87.7	87.5	+0.2	82.21	80.78	+1.43	82.21	82.10	+0.11	780.5	777.3	+
2	5	1	1.0164	34.4	34.6	−0.2	33.64	33.26	+0.38	33.64	33.81	−0.17	478.3	486.7	−
7	5	1	1.0164	21.8	21.6	+0.2	22.59	22.15	+0.44	22.59	22.52	+0.07	286.2	283.6	+
3	6	1	1.0164	21.0	21.2	−0.2	19.29	19.57	−0.28	19.29	19.89	−0.60	221.3	230.4	−
8	10	1	1.0164	7.5	7.7	−0.2	6.80	6.92	−0.12	6.80	7.04	−0.24	115.2	121.3	−
4	1	2	1.0139	29.7	29.9	−0.2	32.55	32.17	+0.38	32.55	32.61	−0.06	307.9	310.0	−
1	3	2	1.0139	26.4	26.2	+0.2	29.39	28.86	+0.53	29.39	29.26	+0.13	285.0	283.5	+
8	4	2	1.0139	17.6	17.4	+0.2	19.75	19.23	+0.52	19.75	19.50	+0.25	143.6	142.0	+
4	8	2	1.0139	20.8	20.6	+0.2	22.88	22.39	+0.49	22.88	22.72	+0.16	147.8	146.5	+
3	2	3	1.0119	26.3	26.1	+0.2	26.42	26.00	+0.42	26.42	26.31	+0.11	408.2	407.3	+
7	5	4	1.0104	5.4	5.2	+0.2	5.84	5.65	+0.19	5.84	5.71	+0.13	134.5	117.1	+
4	9	4	1.0104	7.9	8.1	−0.2	7.94	8.07	−0.13	7.94	8.15	−0.21	143.4	145.2	−
3	1	5	1.0092	9.5	9.7	−0.2	10.99	11.11	−0.12	10.99	11.21	−0.22	137.9	141.2	−

$$R(+) = \sum |F_0(hkl) - F_c(hkl)| / \sum F_0(hkl) = 0.0585, \tag{2}$$

$$R(-) = \sum |F_0(hkl) - F_c(\bar{h}\bar{k}\bar{l})| / \sum F_0(hkl) = 0.0587. \tag{2'}$$

The R-factor ratio $\mathcal{R}$ is $R(-)/R(+) = 1.00342$. Because of $\mathcal{R} > \mathcal{R}_{1,2222,0.005} = 1.00184$, the probability that we would be wrong was only 0.5% if we accepted the molecular configuration as illustrated in Fig. 1. This was in accord with the above-mentioned experimental result.

IV. Description of the Structure

The main character of the suberogorgin molecule as illustrated in Fig. 1 is that it has a unique cyclopentapentalane skeleton rings (**A**, **B**, **C**) on which there are three methyl groups, a carboxyl group and a carbonyl group.

Each asymmetric unit contains two suberogorgin molecules. Between them there is a noncrystallographic symmetry, i.e. a translational of $\frac{1}{4}\boldsymbol{b}+\frac{1}{2}\boldsymbol{c}$ approximately. This pseudosystematic absence could be seen on the Weissenberg's photos. The two molecules related by the translational operator in the asymmetric unit should have the same absolute configuration.

The bond lengths and bond angles of the suberogorgin molecules are given in Tables 4 and 5. The difference of bond lengths as well as bond angles between two molecules of an asymmetric unit is small. The maximum difference of bond lengths between two molecules is 0.2Å and of bond angles, 1.5°. In the carboxyl group, $C(sp^2) - O$ bond has an average value of 1.276Å. In the carbonyl group, $C(sp^2) - O$ bond has an average value of 1.210Å. On the ring **A**, the average value of $C(sp^2) - C(sp^2)$ bond length is 1.326Å and of $C(sp^2) - C(sp^3)$, 1.520Å. All $C(sp^3) - C(sp^3)$ bonds have the average value of 1.530Å.

Table 4

The Bond Lengths (Å) of Suberogorgin Molecules in Asymmetric Unit

Molecule I				Molecule II			
C1—C2	1.328	C2—C3	1.526	C1—C2	1.323	C2—C3	1.522
C3—C4	1.538	C4—C5	1.493	C3—C4	1.543	C4—C5	1.513
C5—C6	1.549	C6—C7	1.534	C5—C6	1.549	C6—C7	1.534
C7—C8	1.542	C8—C9	1.500	C7—C8	1.545	C8—C9	1.496
C9—C10	1.507	C10—C11	1.568	C9—C10	1.513	C10—C11	1.567
C11—C12	1.526	C1—C13	1.455	C11—C12	1.534	C1—C13	1.464
C3—C14	1.518	C7—C15	1.524	C3—C14	1.515	C7—C15	1.518
C13—O1	1.278	C13—O2	1.272	C13—O1	1.260	C13—O2	1.295
C9—O3	1.211			C9—O3	1.209		

The mode of the close packing of the suberogorgin molecules in the unit cell is illustrated as in Fig. 3. The interactions between the molecules can be divided into two types. For one of them there is a hydrogen bond interaction between the carboxyl groups of the molecules related by noncrystallographic symmetry in the orthogonal direction of **c**. The hydrogen bond has an average length of 2.602Å. For another there are many van der Waals interactions between the molecules related by crystallographic symmetry in various directions. The shortest contacting distance has the value of 3.289Å. Those interactions make a network between each other and are present in all the unit cells and may play an important role in stabilizing the crystal structure.

Table 5

The Bond Angles (°) of Suberogorgin Molecules in Asymmetric Unit

Molecule I		Molecule II		Molecule I		Molecule II	
O1—C13—O2	122.2	O1—C13—O2	122.1	C10—C6—C7	106.2	C10—C6—C7	106.5
O1—C13—C1	119.9	O1—C13—O2	121.4	C6—C7—C8	103.0	C6—C7—C8	103.5
O2—C13—C1	117.9	O2—C13—C1	116.5	C6—C7—C15	114.2	C6—C7—C15	113.9
C13- C1—C2	124.8	C13—C1—C2	124.3	C15—C7—C8	114.9	C15—C7—C8	113.9
C13—C1—C11	122.2	C13—C1—C11	122.4	C7—C8—C9	102.3	C7—C8—C9	103.4
C2—C1—C11	113.0	C2—C1—C11	113.4	C8—C9—C10	109.5	C8—C9—C10	109.7
C1—C2—C3	113.0	C1—C2—C3	112.8	C8—C9—O3	124.6	C8—C9—O3	124.8
C2—C3—C14	109.7	C2—C3—C14	109.9	O3—C9—C10	125.9	O3—C9—C10	125.6
C2—C3—C10	100.9	C2—C3—C10	101.4	C9—C10—C6	103.8	C9—C10—C6	104.3
C14—C3—C4	114.5	C14—C3—C4	113.8	C9—C10—C11	112.0	C9—C10—C11	112.5
C10—C3—C4	103.7	C10—C3—C4	104.4	C6—C10—C3	105.1	C6—C10—C3	104.8
C3—C4—C5	105.5	C3—C4—C5	105.0	C3—C10—C11	106.1	C3—C10—C11	105.9
C4—C5—C6	103.7	C4—C5—C6	103.2	C1—C11—C10	101.3	C1—C11—C10	101.7
C5—C6—C7	112.2	C5—C6—C7	112.0	C10—C11—C12	116.2	C10—C11—C12	116.6
C5—C6—C10	106.1	C5—C6—C10	106.9	C1—C11—C12	110.1	C1—C11—C12	110.5

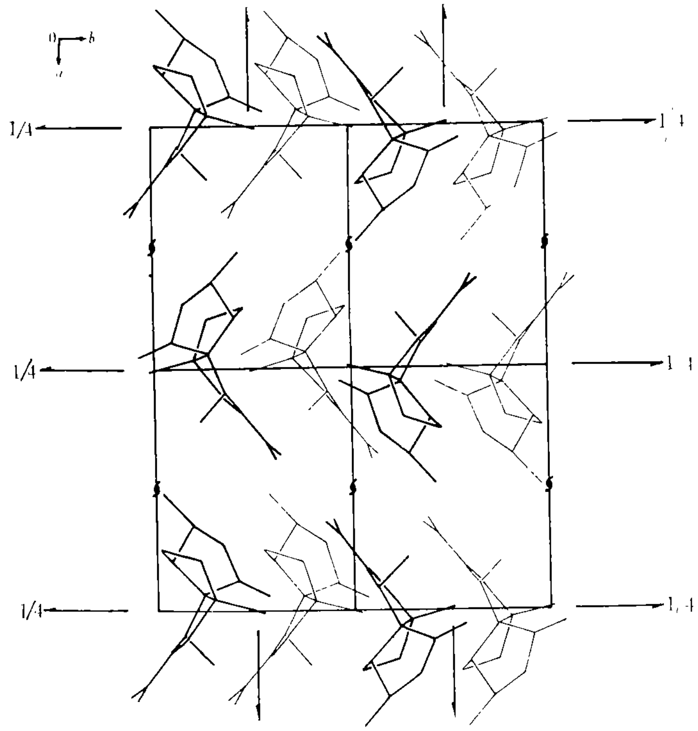


Fig. 3. Diagram of the close packing of the suberogorgin molecules (viewed along the *c* axis) in the unit cell.

V. DISCUSSION

1. *Imperfection of the Solvent Effect Theory of NMR*

In the study of suberogorgin the experimental results of NMR were used to determine the chemical structure of suberogorgin[1]. The signals of three methyl groups in the molecule were very clear. The C_{14}-methyl group appeared as a singlet. The C_{12}-methyl group coupled with C_{11}-proton and exhibited as a doublet. The C_{15}-methyl group was solvent dependent. Considering the theory of the solvent effect of NMR especially about variations in the chemical shifts of the neighboring group of the carbonyl group varying with the solvent[5,6], since C_{12}-methyl group has the solvent effect with $\Delta(\delta_{CDCl_3}-\delta_{C_6D_6}) = -0.1$, it can be thought that C_{12}-methyl group is little affected by the carbonyl group and that it deviates from the carbonyl group plane as far as possible. This is consistent with the results of the X-ray crystal structure analysis. The C_{15}-methyl group is not the case and the results of $\Delta(\delta_{CDCl_3} - \delta_{C_6D_6}) = 0.45$ indicate that this methyl group has a close relationship with the carbonyl group. According to the theory of NMR solvent effect, the C_{15}-methyl group would be in the carbonyl group plane. However, the C_{15}-methyl group cannot be in the carbonyl plane even though it is in α or β orientation, or the five-member ring with the carbonyl group is twisty.

Table 6

The Data of the Least Squares Planes of Suberogorgin Molecules in Asymmetric Unit

	Atom	C8	C9	C10	O3	C15	C12
Molecule I	Equation of the Plane	$(0.61161X) + (-0.34206Y) + (0.71339Z) = 0.0$					
	Deviations from the Plane (Å)	−0.0	0.0	−0.0	−0.0	0.67	−2.14
Molecule II	Equation of the Plane	$(0.56395X) + (-0.40578Y) + (0.71924Z) = 0.0$					
	Deviations from the Plane (Å)	−0.0	0.0	−0.0	−0.0	0.44	−2.11

The data of the least square planes related with ring ***C*** and the carbonyl group are listed in Table 6 in which it is shown that in the two molecules of asymmetric unit C_{15}-methyl groups deviate from the carbonyl group plane by 0.67Å and 0.44Å respectively and both C_{12}-methyl groups by 2.1Å, i.e. even though the C_{15}-methyl group has a deviation of 0.67Å from the carbonyl group plane, it can still give a significant solvent effect while the C_{12}-methyl group gives no solvent effect because it deviates 2.1Å from the plane. Therefore, when we describe the NMR solvent effect of the compounds containing the carbonyl groups, it is insufficient to consider whether the neighboring groups of the carbonyl group are in the carbonyl group plane. We should consider whether those groups are in the spatial region, which has the carbonyl group plane as a mirror plane. According to the data gained from the structure of suberogorgin, we can image this space has a mirror symmetry with respect to the carbonyl group plane as the mirror plane and is of a width of 0.67 × 2Å in which the carbonyl group has the close relationship with the neighboring groups and the significant solvent effect arises.

2. *Preliminary Investigation of the Relationship Between the Molecular Structure of Suberogorgin and Its Toxicity*

Suberogorgin is intensely toxic with the median lethal dose of mice of $LD_{50} = 22.8 \pm 1.8$mg/kg as measured with the intravenous injection of its crystallized sodium salt. This intense toxicity is very rare in the terpene compounds. Compared with the many sesquiterpene compounds used as perfumes, the toxicity of suberogorgin is noteworthy. On the basis of the symptoms of poisoned animals and some related experimental results, and taking into account that the distance between the carboxyl group anion and the carbonyl group in the suberogorgin molecule is 5.527 Å, which is similar to that of the active center of cholinergic acceptor, we can conclude that the neurophysiological activity of suberogorgin is probably the result of action of suberogorgin on the cholinergic acceptor. The molecule of a drug possessing the neurophysiological activity should contain a partial structure with nitrogen cation[7,8]. Nevertheless, suberogorgin is a terpene compound containing only C, H, O but no N, still it possesses intensely neurophysiological activity. This novel result reveals that the knowledge and theory about nerve impulse transmission probably contain more substantial content for further investigation.

We would like to express our gratitude to Wu Bomu and Dou Shiqi for their help in the collecting of diffraction intensities.

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