

The Crystal Structure of the Monoterpene *isoiridomyrmecin* C₁₀H₁₆O₂

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(Received 9 October 1961)

The crystal structure of *isoiridomyrmecin* has been determined at room temperature and at -130°C . The space group is $P2_1$ with $Z=2$, the unit-cell dimensions at -130°C . being

$$a = 10.09, b = 6.41, c = 7.50 \text{ \AA}, \beta = 96.4^{\circ}.$$

A structure derived by optical-transform techniques with the room temperature data failed to refine in projection below $R=0.20$. This failure was shown by the use of the low-temperature data to be due to an incorrect conformation of the lactone group. The correct structure refined smoothly to $R=0.14$ for $h0l$, $h1l$ and $h2l$ data. The lactone group, previously considered capable of accommodation in a six-membered ring with a chair conformation, is found to be planar, the six-membered ring adopting a skewed boat conformation. Discussion of the configuration of the molecule, of bond lengths and angles, and of the packing of the molecule is presented. Comment is also offered on the dangers of analysis using inadequate data.

Introduction

Recently a novel group of monoterpenoid compounds has been isolated possessing the dimethylisopropylcyclopentane skeleton, (Cavill, 1960) shown in Fig. 1. Current interest in these insect extractives rests in their unusual chemical structure and their biological activity, particularly the insecticidal activity of the cyclopentanoid lactones of insect origin. Although the chemical structures of the majority of these compounds have been elucidated and the stereochemistry of the iridolactones† derived from that of the closely

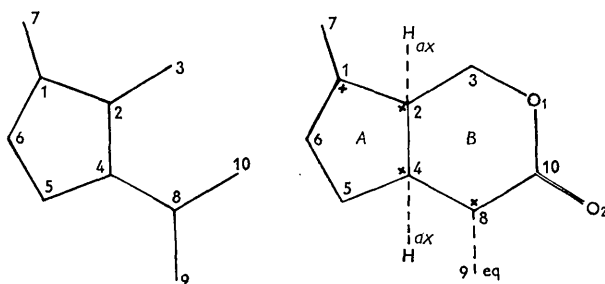


Fig. 1.

Fig. 2.

Fig. 1. The dimethylisopropylcyclopentane skeleton.

Fig. 2. *Isoiridomyrmecin*.

related nepetalinic acids (Fusco, Trave & Vercellone, 1955) certain doubts remained regarding the relative configuration of C₈. Conformational analysis (Cavill, 1960) has been used in an attempt to determine the

most likely structure from the possible choices, but a definite conclusion was not achieved. These uncertainties led to an independent investigation of the structures of the iridolactones by X-ray methods. The following presents the analysis and structure of *isoiridomyrmecin* (Fig. 2).

Experimental

Isoiridomyrmecin forms colourless crystals with a melting point of 58°C . and is soluble in water and most organic solvents. Slow evaporation from petroleum ether ($30\text{--}40^{\circ}$ fraction) at about 5°C . produced plate-like crystals which could be cleaved to a convenient size. Because of the high vapour pressure of *isoiridomyrmecin* at room temperature the crystal was sealed in a thin-walled Lindeman glass tube.

The unit-cell parameters and space group were determined from oscillation photographs about the b axis together with $h0l$, $hk0$, $h1l$ and $h2l$ Weissenberg photographs using $\text{Cu } K\alpha$ radiation, and $hk0$ and $0kl$ precession photographs using $\text{Mo } K\alpha$ radiation.

Crystal data

Isoiridomyrmecin C₁₀H₁₆O₂; m.p. = 58°C .

Monoclinic. Space group $P2_1$.

Unit cell (at -130°C .):

$$a = 10.09, b = 6.41, c = 7.50 \text{ \AA}, \beta = 96.4^{\circ}.$$

Optical activity $[\alpha]_D^{24} = -59^{\circ}$.

The only systematic absences were $0k0$ when k is odd. Because of its ready solubility the density was difficult to determine, but was established as in the range 1.1 to 1.2 g.cm.^{-3} . On the basis of two molecules in the unit cell, the calculated density is 1.172 g.cm.^{-3} (at low temperature). Since the molecule is asymmetric with a high optical activity, the space group can only be $P2_1$.

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† The term iridolactone is used to include both iridomyrmecin and *isoiridomyrmecin*. Originally, it described the naturally occurring *isoiridomyrmecin* only.

A multiple-film technique was used to determine the intensities which were estimated visually with the aid of a calibration strip and corrected for Lorentz and polarization effects. Correction for absorption was omitted due to the low linear absorption coefficient, $\mu = 6.4 \text{ cm}^{-1}$.

For the low-temperature exposures, the crystal, mounted in a Nonius Enraf integrating Weissenberg camera, was cooled to -130°C . by introducing along the axis of the camera dry nitrogen cooled by passage over solid CO_2 and through liquid nitrogen. Slow cooling was essential to prevent fracture of the crystal.

Structure determination at room temperature

The structure analysis of the compound was initiated with the room temperature data for the two zones (010) and (001). It was immediately obvious from the absence of reflections for $\sin \theta > 0.7$ that there was a high temperature effect. Optical-transform methods (Hanson, Lipson & Taylor, 1953) were applied to the data corresponding to the b axis projection. Inspection of the weighted $h0l$ reciprocal lattice (Fig. 3) suggested a projection corresponding to reasonably resolved atomic groups. From models representing the

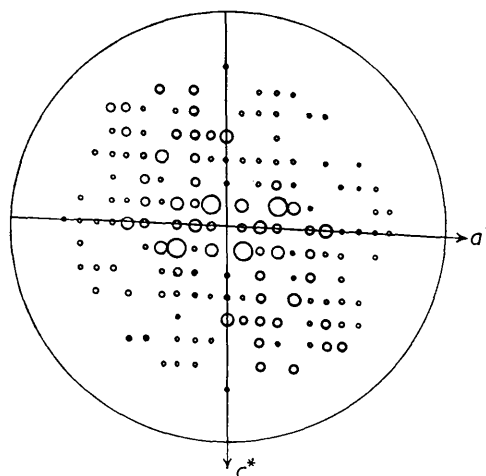


Fig. 3. $h0l$ weighted reciprocal-lattice section (room temperature). The large circle indicates the limit of observable reflections with $\text{Cu } K\alpha$.

possible configurational and conformational dispositions of the molecule, based on the deductions from chemical evidence (Cavill & Locksley, 1957), optical transforms were recorded for each type at various

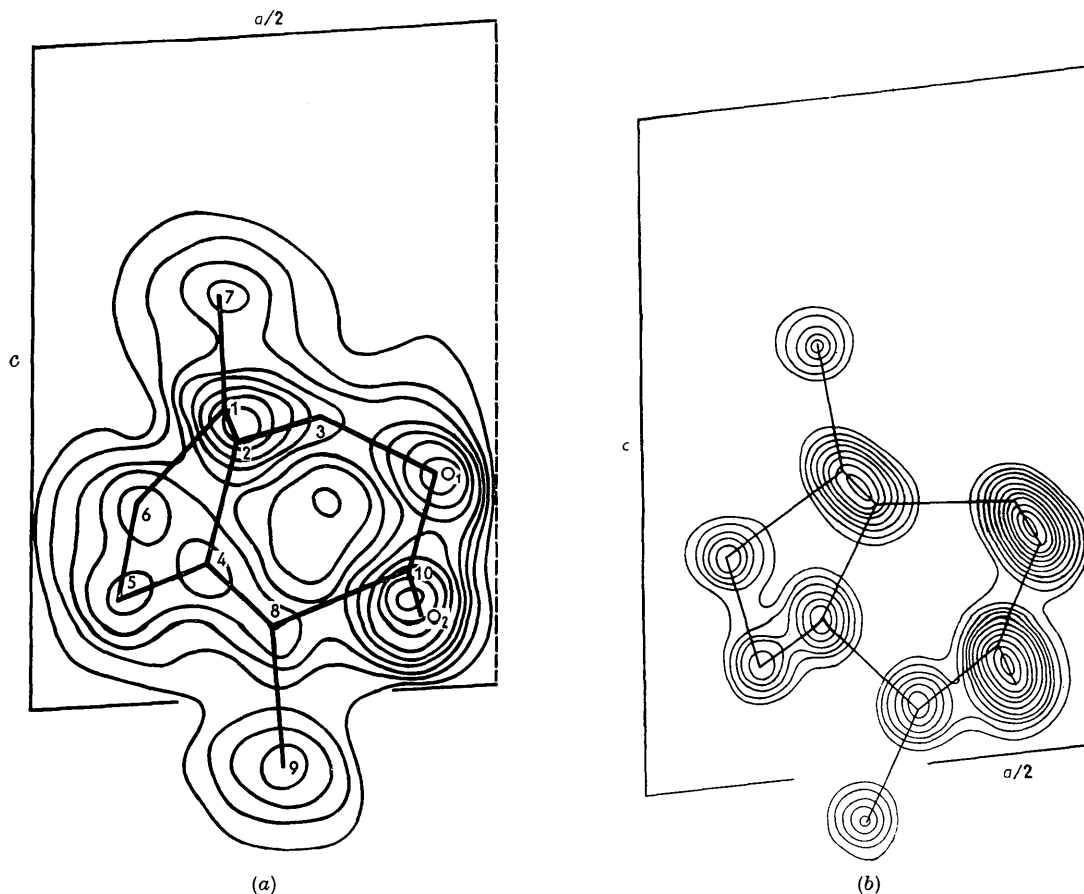


Fig. 4. (a) The erroneous electron-density projection along the b axis (20°). (b) The correct electron-density projection along the b axis (-130°C). Contours are given at intervals of $1 \text{ e.}\text{\AA}^{-2}$ starting with $1 \text{ e.}\text{\AA}^{-2}$.

angles of tilt with respect to [010]. In all 45 trial projections were tested.

From these a trial molecular structure in reasonable accord with the main features of the distribution was selected. The correct location of the molecule with respect to the origin was determined by Fourier-transform principles (Taylor, 1954). The structure was then refined by $\rho_0(x, z)$ and the corresponding $\Delta\rho(x, z)$ syntheses until R was reduced to 0.20 (McConnell & Schoenborn, 1960). This projection appeared to be in

accord with a chair conformation of the six-membered ring, proposed by Cavill (1960) on the basis of conformational analysis.

It was however difficult to reconcile this aspect of the structure with the evidence regarding the lactone group which has been obtained in the structure determinations of himbacine hydrobromide (Fridrichsons & Mathieson, 1960, 1961) and the bromodilactone from jacobine (Taylor, 1960). In both, the lactone group was found to be planar and it was concluded that this property is a characteristic of the lactone group (Mathieson & Taylor, 1961). Considered in conjunction with the rather high value of the reliability index for such limited data, this factor suggested that, although the general distribution of atoms in this structure may accord with that of the correct one, certain details required reassessment and readjustment. It was considered that the high value of 7.5 for the temperature factor B with its consequent severe limitation in the number of observable reflections would prevent any further progress with the room temperature data, and an investigation at low temperature was undertaken. The atomic positions derived from the room-temperature analysis are given in Table 1 and indicated on the erroneous electron-density distribution (Fig. 4(a)).

Table 1. *The atomic parameters of isoirdomyrmecin in fractions of cell edges*

	Erroneous structure (20 °C.)		Correct structure (-130 °C.)		
	<i>x</i>	<i>z</i>	<i>x</i>	<i>y</i>	<i>z</i>
C ₁	0.2080	0.5667	0.2197	0.7879	0.5598
C ₂	0.2185	0.6180	0.2603	0.5619	0.6023
C ₃	0.3167	0.5867	0.4080	0.5377	0.6274
C ₄	0.1857	0.8000	0.1987	0.4992	0.7734
C ₅	0.0905	0.8500	0.1316	0.7004	0.8285
C ₆	0.1100	0.7000	0.0949	0.8218	0.6583
C ₇	0.2000	0.3835	0.1978	0.8581	0.3592
C ₈	0.2670	0.9000	0.3045	0.4147	0.9186
C ₉	0.2800	0.1100	0.2445	0.3084	0.0755
C ₁₀	0.4060	0.8260	0.3915	0.2442	0.8379
O ₁	0.4333	0.6800	0.4433	0.3202	0.6912
O ₂	0.4200	0.9000	0.4160	0.0769	0.8988

Table 2. *Calculated and observed structure factors*

h	k	l	F _c	F _o	h	k	l	F _c	F _o	h	k	l	F _c	F _o
00	0	+2	1046	-	02	0	-9	228	-	07	0	-2	578	+ 1171
00	0	+3	973	-	02	0	+0	304	-	07	0	+4	1133	- 1148
00	0	+4	764	+ 817	04	0	+1	2318	- 2296	07	0	-5	1357	- 1138
00	0	+5	2571	- 2267	04	0	+2	696	+ 754	07	0	-6	223	+ 320
00	0	+6	355	- 479	04	0	+3	1054	+ 965	07	0	-7	81	+ 67
00	0	+7	1738	- 163	04	0	+4	874	+ 866	07	0	-8	144	+ 148
00	0	+8	580	- 537	04	0	+5	237	- 237	08	0	+0	335	- 435
00	0	+9	261	- 189	04	0	+6	419	- 381	08	0	+1	460	+ 378
01	0	+0	2384	- 2413	04	0	+7	92	- 253	08	0	+2	916	+ 826
01	0	+1	3257	+ 2948	04	0	+8	223	- 92	08	0	+3	49	+ 241
01	0	+2	1243	- 1234	04	0	+9	72	+ 817	08	0	+4	53	- 119
01	0	+3	554	+ 858	04	0	-2	1492	+ 1638	08	0	+5	107	+ 111
01	0	+4	257	- 532	04	0	-3	141	+ 445	08	0	+6	267	+ 277
01	0	+5	916	+ 855	04	0	-4	203	+ 100	08	0	+7	80	- 61
01	0	+6	118	+ 10	04	0	-5	211	+ 194	08	0	-1	198	- 248
01	0	+7	212	- 338	04	0	-6	1421	+ 1512	08	0	-2	294	- 202
01	0	+8	52	+ 107	04	0	-7	25	- 118	08	0	-3	1267	- 1524
01	0	+9	88	- 78	04	0	-8	52	- 101	08	0	-4	276	- 278
01	0	-1	5377	- 5438	04	0	-9	36	- 65	08	0	-5	664	+ 847
01	0	-2	1808	+ 1589	05	0	+0	1958	+ 1954	08	0	-6	58	- 79
01	0	-3	119	- 163	05	0	+1	474	+ 705	08	0	-7	578	+ 52
01	0	-4	937	+ 848	05	0	+2	1955	- 1534	09	0	+0	449	+ 444
01	0	-5	398	+ 201	05	0	+3	79	- 100	09	0	+1	737	- 858
01	0	-6	151	- 121	05	0	+4	53	- 110	09	0	+2	649	- 610
01	0	-7	66	- 109	05	0	+5	181	+ 258	09	0	+3	82	- 117
01	0	-8	231	+ 235	05	0	+6	421	- 267	09	0	+4	394	- 219
01	0	-9	2666	- 2607	05	0	+7	170	- 107	09	0	+5	567	- 486
02	0	+0	1268	- 1293	05	0	+8	243	+ 182	09	0	+6	61	+ 71
02	0	+1	1733	- 1682	05	0	-1	1064	- 1246	09	0	-1	215	+ 207
02	0	+2	1098	- 1130	05	0	-2	1477	+ 1781	09	0	-2	417	+ 320
02	0	+3	1101	- 1091	05	0	-3	571	- 695	09	0	-3	704	+ 607
02	0	+4	365	- 238	05	0	-4	661	- 547	09	0	-4	786	+ 900
02	0	+5	1119	+ 984	05	0	-5	283	+ 330	09	0	-5	19	+ 111
02	0	+6	798	+ 663	05	0	-6	142	+ 269	09	0	-6	10	+ 10
02	0	+7	96	+ 104	05	0	-7	132	+ 112	09	0	-7	208	- 62
02	0	+8	129	+ 73	05	0	-8	239	+ 206	10	0	+0	599	+ 508
02	0	+9	1740	+ 1517	05	0	-9	193	+ 150	10	0	+1	303	+ 450
02	0	-1	1039	- 1368	06	0	+0	2340	- 2294	10	0	+2	6	- 116
02	0	-2	2172	+ 2243	06	0	+1	246	+ 246	10	0	+3	160	- 160
02	0	-3	1346	+ 1507	06	0	+2	104	+ 228	10	0	+4	294	- 173
02	0	-4	1209	- 1193	06	0	+3	759	- 610	10	0	+5	133	+ 75
02	0	-5	730	+ 737	06	0	+4	25	- 110	10	0	-1	205	- 202
02	0	-6	15	- 121	06	0	+5	772	+ 537	10	0	-2	208	- 116
02	0	-7	50	+ 107	06	0	+6	117	+ 117	10	0	-3	268	- 268
02	0	-8	58	- 78	06	0	+7	73	- 97	10	0	-4	298	- 308
02	0	-9	1933	- 2161	06	0	+8	77	+ 185	10	0	-5	101	+ 177
03	0	+0	4358	+ 4430	06	0	-1	87	+ 960	10	0	-6	230	+ 112
03	0	+1	1941	+ 1810	06	0	-2	366	- 498	11	0	+0	283	- 277
03	0	+2	377	+ 267	06	0	-3	126	- 238	11	0	+1	236	- 102
03	0	+3	1386	+ 974	06	0	-4	2082	+ 1905	11	0	+2	229	+ 306
03	0	+4	1630	- 1439	06	0	-5	216	- 267	11	0	+3	465	+ 373
03	0	+5	436	- 377	06	0	-6	209	+ 119	11	0	+4	27	+ 49
03	0	+6	351	+ 370	06	0	-7	204	+ 107	11	0	+5	517	- 524
03	0	+7	157	- 100	07	0	+0	13	- 85	11	0	-2	825	- 825
03	0	+8	159	- 63	07	0	+1	621	+ 616	11	0	-3	442	+ 355
03	0	+9	2013	- 2338	07	0	+2	87	+ 107	11	0	-4	373	+ 370
03	0	-1	461	+ 581	07	0	+3	536	+ 316	11	0	-5	199	- 177
03	0	-2	951	- 816	07	0	+4	528	- 330	12	0	+0	11	- 68
03	0	-3	1905	- 2275	07	0	+5	122	+ 121	12	0	+1	51	+ 90
03	0	-4	1188	+ 1320	07	0	+6	437	+ 372	12	0	+2	13	+ 72
03	0	-5	244	- 263	07	0	+7	193	- 105	12	0	+3	41	- 49
03	0	-6	37	+ 268	07	0	+8	71	+ 63	12	0	-1	47	+ 53
03	0	-7	325	+ 148	07	0	-2	1247	- 989	12	0	-2	42	- 501
					07	0	-7	724	- 833	12	0	-3	469	+ 518

Table 2 (cont.)

h	k	l	F _c	A ₀	B ₀	h	k	l	F _c	A ₀	B ₀	h	k	l	F _c	A ₀	B ₀	h	k	l	F _c	A ₀	B ₀
000	1	+1	24008+	484	+2457	07	1	+5	478	+411	+427	03	2	+5	323	+99	+342	03	2	+5	323	+99	+342
000	1	+2	22336+	685	+2137	07	1	+6	481	+301	+55	03	2	+6	129	+367	+72	03	2	+6	129	+367	+72
000	1	+3	8774	-1486	-567	07	1	+7	158	-	-	03	2	+7	332	+327	+43	03	2	+7	332	+327	+43
000	1	+4	6280+	133	+477	07	1	+8	211	+271	-	03	2	+8	332	+327	+43	03	2	+8	332	+327	+43
000	1	+5	550	-655	-237	07	1	+9	842	-	+945	03	2	+9	332	+327	+43	03	2	+9	332	+327	+43
000	1	+6	902	-420	+931	07	1	-3	748	-752	+229	03	2	-3	332	+327	+43	03	2	-3	332	+327	+43
000	1	+7	171	-143	+320	07	1	-4	666	-777	+546	03	2	-4	332	+327	+43	03	2	-4	332	+327	+43
000	1	+8	111	-30	+103	07	1	-5	666	-465	+720	03	2	-5	332	+327	+43	03	2	-5	332	+327	+43
001	1	+0	2417+	401	-1556	07	1	-6	293	+333	-	03	2	-6	504	+278	+446	03	2	-6	504	+278	+446
01	1	+0	6158	-5643	-502	07	1	-7	162	-55	-67	03	2	-7	469	+305	+187	03	2	-7	469	+305	+187
01	1	+1	2451	-783	+2444	08	1	+0	656	-642	-215	03	2	-8	158	+123	+275	03	2	-8	158	+123	+275
01	1	+2	1853+	260	+332	08	1	+1	681	-630	-128	03	2	-9	1035	+393	+21	03	2	-9	1035	+393	+21
01	1	+3	771	-741	-497	08	1	+2	127	-630	-128	03	2	-10	1035	+393	+21	03	2	-10	1035	+393	+21
01	1	+4	1496+	1459	-212	08	1	+3	323	-148	-122	04	2	+1	1406	-114	-1556	04	2	+1	1406	-114	-1556
01	1	+5	841+	749	+287	08	1	+4	200	-188	-15	04	2	+2	1207	-1193	-1010	04	2	+2	1207	-1193	-1010
01	1	+6	316	-347	+37	08	1	+5	420	+95	-541	04	2	+3	751	-443	-630	04	2	+3	751	-443	-630
01	1	+7	119+	80	+57	08	1	+6	242	-89	-24	04	2	+4	264	-200	-273	04	2	+4	264	-200	-273
01	1	+8	552+	259	+118	08	1	+7	45	-50	+15	04	2	+5	811	+331	+580	04	2	+5	811	+331	+580
01	1	+9	231	-593	+11	08	1	+8	1319	+953	+202	04	2	+6	219	+72	-363	04	2	+6	219	+72	-363
01	1	-2	1706+	522	-1888	08	1	-2	210	-176	-70	04	2	+7	649	+465	+346	04	2	+7	649	+465	+346
01	1	-3	396+	109	+304	08	1	-3	751	+470	-626	04	2	+8	586	+299	+481	04	2	+8	586	+299	+481
01	1	-4	229	-53	+266	08	1	-4	923	+912	-84	04	2	+9	405	+238	+145	04	2	+9	405	+238	+145
01	1	-5	823+	386	-637	08	1	-5	176	-40	-106	04	2	+10	843	-863	+52	04	2	+10	843	-863	+52
01	1	-6	685	-82	+795	08	1	-6	61	-43	-84	04	2	+11	1568	-866	+671	04	2	+11	1568	-866	+671
01	1	-7	741+	627	+469	08	1	-7	150	+16	+71	04	2	+12	615	-45	+569	04	2	+12	615	-45	+569
01	1	-8	229	-53	+266	08	1	-8	205	+100	-100	04	2	+13	390	+441	-20	04	2	+13	390	+441	-20
02	1	+0	2596+	4665	+696	09	1	+1	140	-11	-	04	2	+14	1106	+6	+505	04	2	+14	1106	+6	+505
02	1	+1	3481+	1625	-1386	09	1	+2	363	-349	+4	04	2	+15	324	-238	-255	04	2	+15	324	-238	-255
02	1	+2	844	-639	-192	09	1	+3	804	-697	-301	04	2	+16	411	-219	-175	04	2	+16	411	-219	-175
02	1	+3	1481+	639	-192	09	1	+4	601	+451	+442	04	2	+17	137	+4	+32	04	2	+17	137	+4	+32
02	1	+4	953	-1208	-435	09	1	+5	164	-11	-62	04	2	+18	510	+4	+55	04	2	+18	510	+4	+55
02	1	+5	240	-208	+82	09	1	+6	458	+430	-1	05	2	+19	664	+130	+508	05	2	+19	664	+130	+508
02	1	+6	143+	233	-73	09	1	+7	475	+365	-495	05	2	+20	1070	+809	+699	05	2	+20	1070	+809	+699
02	1	+7	329+	210	+273	09	1	+8	327	-213	+274	05	2	+21	324	-78	-80	05	2	+21	324	-78	-80
02	1	+8	321	-255	-105	09	1	+9	429	+468	-58	05	2	+22	294	+114	+100	05	2	+22	294	+114	+100
02	1	+9	874	-852	-469	09	1	+10	112	+26	+108	05	2	+23	294	+114	+100	05	2	+23	294	+114	+100
02	1	-1	874	-852	-469	09	1	-1	69	-59	+52	05	2	+24	837	-573	-610	05	2	+24	837	-573	-610
02	1	-2	1387	-1823	+734	09	1	-2	403	+337	-207	05	2	+25	349	+361	-53	05	2	+25	349	+361	-53
02	1	-3	1120	-1361	+751	10	1	+0	184	+33	+236	05	2	+26	1307	-217	+960	05	2	+26	1307	-217	+960
02	1	-4	1120	-1299	-837	10	1	+1	184	+33	+236	05	2	+27	1307	-217	+960	05	2	+27	1307	-217	+960
02	1	-5	863	-817	+205	10	1	+2	597	+607	+233	05	2	+28	808	-254	-670	05	2	+28	808	-254	-670
02	1	-6	1282+	1261	+727	10	1	+3	122	-36	-167	05	2	+29	401	+204	-375	05	2	+29	401	+204	-375
02	1	-7	81	-68	-663	10	1	+4	659	-84	-5	05	2	+30	764	+309	-874	05	2	+30	764	+309	-874
02	1	-8	497	-490	-328	10	1	+5	2	-214	+57	05	2	+31	583	-316	-450	05	2	+31	583	-316	-450
02	1	-9	351+	195	-102	10	1	+6	223	-220	+98	05	2	+32	299	-215	-289	05	2	+32	299	-215	-289
03	1	+0	1789	-1201	+1429	10	1	+7	591	-666	+43	05	2	+33	299	+221	+126	05	2	+33	299	+221	+126
03	1	+1	1532+	1325	+778	10	1	+8	757	-831	-122	05	2	+34	367	+234	-301	05	2	+34	367	+234	-301
03	1	+2	1733	-2039	-638	10	1	+9	101	+120	-98	05	2	+35	874	+782	+386	05	2	+35	874	+782	+386
03	1	+3	700+	775	+343	10	1	+10	313	-27	-138	05	2	+36	703	+331	-331	05	2	+36	703	+331	-331
03	1	+4	595	-397	-26	10	1	+11	448	-27	-397	05	2	+37	713	-711	+749	05	2	+37	713	-711	+749
03	1	+5	262+	167	-159	11	1	+0	308	+165	-6	05	2	+38	1336	+609	+1171	05	2	+38	1336	+609	+1171
03	1	+6	827	-134	-875	11	1	+1	219	+100	+100	05	2	+39	522	-297	-221	05	2	+39	522	-297	-221
03	1	+7	497	-490	-328	11	1	+2	114	+169	+168	05	2	+40	492	+407	+424	05	2	+40	492	+407	+424
03	1	+8	126+	83	+35	11	1	+3	325	+196	+225	05	2	+41	948	-58	+19	05	2	+41	948	-58	+19
03	1	+9	2364+	777	+2573	11	1	+4	225	-155	-136	05	2	+42	616	-366	-813	05	2	+42	616	-366	-813
03	1	-1	1070	-1240	+335	11	1	+5	459	-321	-508	05	2	+43	78	-95	+43	05	2	+43	78	-95	+43
03	1	-2	1511	-317	-1931	11	1	+6	116	+89	-23	05	2	+44	574	+770	+73	05	2	+44	574	+770	+73
03	1	-3	1511	-317	-1931	11	1	+7	116	+89	-23	05	2	+45	364	+93	-436	05	2	+45	364	+93	-436
03	1	-4	501	-48	-395	11	1	+8	162	+303	+265	05	2	+46	113	-81	+5	05	2	+46	113	-81	+5
03	1	-5	501	-48	-395	11	1	+9	162	+303	+265	05	2	+47	275	-128	+333	05	2	+47	275	-128	+333
03	1	-6	590+	26	-492	11	1	+10	232	-160	-43	05	2	+48	82	-35	+92	05	2	+48	82	-35	+92
03	1	-7	766	-855	-133	11	1	+11	119	+71	+24	05	2	+49	183	-65	+57	05	2	+49	183	-65	+57
03	1	-8	623	-73	-61	12	1	+0	138	+64	-70	05	2	+50	748	+296	+571	05	2	+50	748	+296	+571
03	1	-9	263	-73	-61	12	1	+1	219	+100	+100	05	2	+51	549	-57	+62	05	2	+51	549	-57	+62
04	1	+0	659+	766	-237	12	1	+2	411	+326	+336	06	2	+0	1126	+1289	-389	06	2	+0	1126	+1289	-389
04	1	+1	574+	464	-618	12	1	+3	453	-200	+587	06	2	+1	591	-261	-586	06	2	+1	591	-261	-586
04	1	+2	1770	-1725	-1478	12	1	+4	126	+40	+44	06	2	+2	1078	-952	-691	06	2	+2	1078	-952	-691
04	1	+3	700	-189	-905	12	1	+5	126	+40	+44	06	2	+3	1125	-1125	-691	06					

Structure determination at low temperature

With the low-temperature data, calculations were initiated using the atomic parameters derived from the room-temperature analysis, the temperature factor B being adjusted to 2.5 for the calculation of structure factors. At this stage R was 0.35. On the basis of these atomic parameters, refinement by $\rho_0(x, z)$ and $\Delta/(x, z)$ projection was carried out. Small adjustments of atomic parameters were made until R dropped to 0.29, but at this point it was clear that no further improvement was possible. The difference map at this stage is shown in Fig. 5, which indicates a serious discrepancy at atomic position C_3 , while the $\rho_0(x, z)$ projection revealed at the O_1 position a higher density than expected. Atom C_3 was moved to the new location C_3^* as shown in Fig. 4 which also shows adjustments made in the positions of C_1 , C_2 and O_1 . Structure factors calculated from these parameters gave $R=0.33$. By means of four $\rho_0(x, z)$ and four difference syntheses the structure readily refined to $R=0.18$.

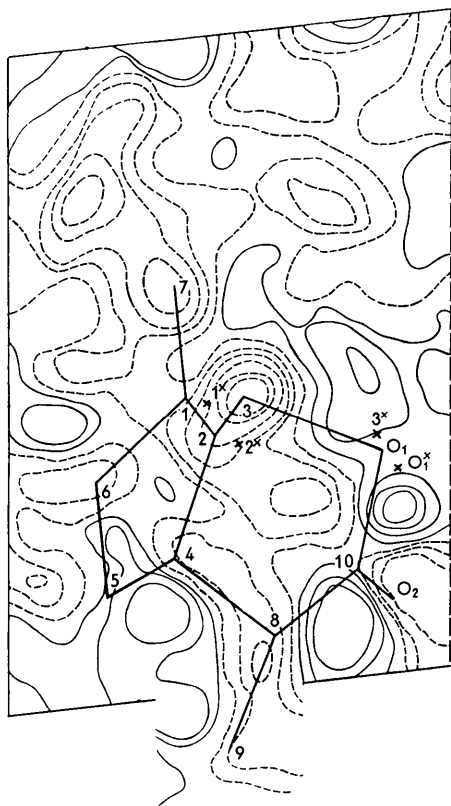


Fig. 5. The difference map, corrections indicated by + (-130°C). Contours are given at intervals of $0.5\text{ e}\cdot\text{\AA}^{-2}$, zero and negative contours dashed, positive contours solid lines.

The modification of atomic sites involved in these readjustments permits the re-interpretation of the projected electron density in terms of a molecular model with a planar lactone group.

The y parameters, initially derived approximately on the basis of the projection together with normal bond lengths and angles, were made more precise by the use of the cosine and sine components of generalized projections (Fridrichsons & Mathieson, 1955) for the $h1l$ and $h2l$ data. The final parameters (Table 1) were obtained from a least squares refinement. The reflections were weighted so that $\nu(w1)=1$ if $F_o \leq 8$ and $\nu(w1)=8/F_o$ for $F_o > 8$. The reliability indices dropped during six cycles to 0.13 ($h0l$), 0.15 ($h1l$) and 0.16 ($h2l$) with 0.14 overall; comparison between observed and calculated structure factors with an isotropic value of $B=2.5$ is given in Table 2. Bond lengths and bond angles are shown in Fig. 5 and approach distances in Fig. 7. The final correct electron-density distribution is shown in Fig. 4(b) and may be compared with the false distribution Fig. 4(a).

Discussion

The progress of the analysis of *isoiridomyrmecin* is of interest from two aspects:

- (1) that a structure may be refined (at least in projection) to a surprisingly low value of R (0.20) and yet be in considerable error in certain details;
- (2) that this possibility of an erroneous conclusion is less likely to appear acceptable when the diffraction data cover an adequate $\sin \theta$ range.

With respect to (1), it has been noted (Dunitz & Robertson, 1947) that the possibility of attaining a small value of R in such circumstances usually means a certain similarity with the true structure. Since then other examples have occurred. Thus in the analysis of the compound called 'cis naphthodioxan', Furberg & Hassel (1950) showed that it was not possible to refine below a certain value of R . Peculiarities in the electron density distribution and in bond lengths suggested an error in the proposed structure and the analysis finally revealed that the correct structure was 1,3,1',3'-tetraoxa-2,2'-bicyclopentane. Even for heavy-atom derivatives which at first appeared isomorphous Trommel & Bijvoet (1954) found that the hydrochloride and hydrobromide of D(-)-Isoleucine differed in the disposition of the methyl side-group. For triphenylene, the structure first proposed by Klug (1950) was again associated with unexpected features in the electron-density distribution and intermolecular approach distances. This was re-examined later by Vand & Pepinsky (1954) and by Pinnock, Taylor & Lipson (1956) showing that a gross shift of the molecule was required to produce the correct crystal structure. In the present case, the analysis proceeded to what could be regarded as a very satisfactory overall agreement between calculated and observed structure amplitudes but was however proved to be partly erroneous.

In all these structures, it appears that the main objection to acceptance was the inadequate chemical

sensibility of the end-result and when this aspect was investigated and rectified, the analysis could then proceed smoothly to an entirely satisfactory conclusion.

As has been noted earlier (Mathieson, 1955) all three main inter-related factors must be satisfied in a correct structure solution:

- (1) agreement between calculated and observed structure factors;
- (2) the electron-density distribution with peak heights and shapes of satisfactory form;
- (3) chemically sensible bond lengths, angles and approach distances.

Some of these aspects may not be capable of complete investigation in specific cases, such as those investigated only in projection. This is particularly likely with certain methods of analysis such as optical transform methods, and appropriate warnings have been made e.g. Pinnock, Taylor & Lipson (1956).

So far as the experimental data were concerned, these were limited in range at room temperature and this limitation had its effect on the apparent low value of R . Extension of the range of data by operation at a low temperature immediately raised R to 0.35 using the same atomic parameters, an aspect of the comparison of F_c with F_o noted earlier (Mathieson, 1955) for K-benzylpenicillin. Hence when making comparison of structure analyses of compounds of comparable complexity it is important to take into account the effective temperature factor and range of the experimental data. The range of data experimentally determined is of great significance not only with regard to the ultimate accuracy of the refinement (Cruickshank, 1960) but also for the primary procedure of locating the molecular skeleton (Fridrichsons & Mathieson, 1961).

In the present case in which the principal aim was to determine the molecular skeleton and the refinement for accurate atomic position was of less importance, it is clear that adequate data proved to be a prerequisite to assure the correct structure solution. The structure based on the temperature-limited data seemed to be in accord with an electron-density distribution of reasonable appearance, had $R=0.20$ and a chair conformation for the six-membered ring which was in satisfactory accord with what had been deduced on chemical grounds and conformational argument. The corresponding difference map suggested certain shifts, particularly at the carbonyl position (Fig. 5) but these shifts tended to increase rather than reduce R . The modified structure based on the low temperature data revealed that these shifts were in the correct direction but had been overshadowed by the failure to make the major shift C_3 to C_3^* .

The relative configuration of the asymmetric carbon atoms (starred) is shown in Fig. 2 and confirms that deduced for *isoiridomyrmecin* (Cavill & Locksley,

1957) from its relationship to nepetalactone and the nepetalinic acids. Furthermore it defines the configuration of C_8 (Cavill, 1960). The X-ray results provide a decision as to which of the two alternatives offered by Cavill & Locksley (1957) corresponds to *isoiridomyrmecin*. The other structural alternative corresponding to *iridomyrmecin* is also under investigation by the authors.

With regard to the detailed shape of the molecule, the five-membered ring has the expected conformation with four atoms nearly planar and the fifth out of this plane by 0.5 Å. The most important detail of the conformational aspect concerns the six-membered ring of which the lactone group forms part. On the basis of conventional conformational analysis it was deduced that this ring was in the chair conformation. This argument involved however the tacit assumption that the lactone group is sufficiently flexible to be accommodated in this manner. This structure analysis accords however with a planar conformation for the lactone group and this planarity forces a skew boat conformation on the six-membered ring. Evidence for the planarity of γ -lactone groups was first observed in himbacine hydrobromide (Fridrichsons & Mathieson, 1960, 1961) and for the δ -lactone groups in the bromodilactone of jacobine (Taylor, 1960), from which the conclusion was drawn that this planarity is a characteristic of lactone groups in general (Mathieson & Taylor, 1961). The data for *isoiridomyrmecin* provide further confirmation of this characteristic with respect to δ -lactone groups. We may note that the skew boat conformation of ring *B* requires a cis-junction between rings *A* and *B* as has been deduced by McElvain in more recent studies (Cavill & Locksley, 1957).

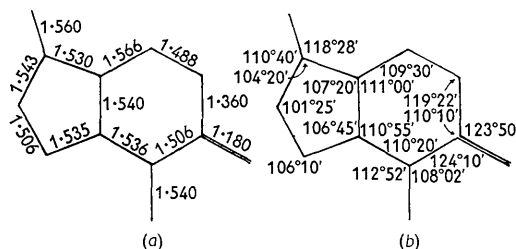


Fig. 6. (a) Bond lengths of *isoiridomyrmecin*.
(b) Bond angles of *isoiridomyrmecin*.

Bond lengths and angles are shown in Fig. 6. The average (not including C_8-C_{10}) C-C bond length is found to be 1.54 Å with a mean deviation of 0.012 Å which suggests a maximum inaccuracy of 0.03 Å for the measured values. The C_8-C_{10} bond adjacent to C=O is shorter (1.51 Å) as is to be expected. The bond lengths within the lactone group are of interest, with $C_{10}-O_1=1.36$ Å as against $C_3-O_1=1.49$ Å. The explanation for this difference may be given on the basis of either double-bond characteristics or the hybridization of atom C_{10} (Fridrichsons & Mathieson,

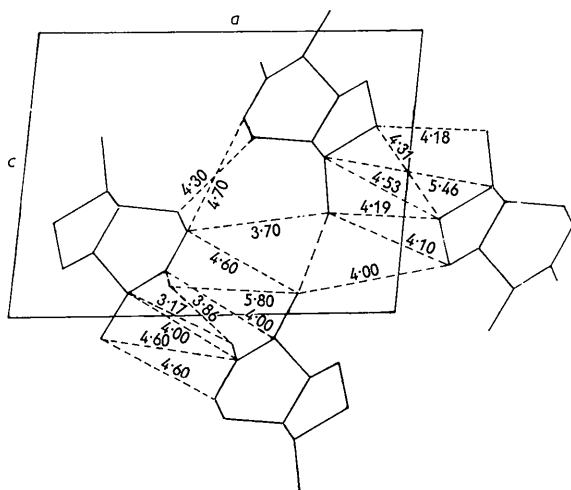


Fig. 7. The major inter-molecular approach distances.
Projection along the b axis.

1961). From either viewpoint it is evident that this dissymmetry in bond lengths is closely bound up with the planarity of the lactone group.

The molecules pack together in the crystal with the polar ends associated to form dipolar layers. The relatively neutral outer parts of the layers pack by van der Waals forces with rather larger approach distances (Fig. 7).

Note added in proof.—The structure of iridomyrmecin has now been completed and a comparison of the two structures has been submitted to Tetrahedron Letters (Conformation of Iridomyrmecin and Iso-iridomyrmecin, J. F. McConnell, A. McL. Mathieson and B. P. Schoenborn). The structure of iridomyrmecin will be submitted for publication shortly.

All structure factor, Fourier and least-squares calculations were carried out on UTECOM, a DEUCE computer at the University of New South Wales.

We are grateful for use of the coordinated set of programmes devised by Dr J. S. Rollett.

The authors wish to thank Dr A. McL. Mathieson of the Division of Chemical Physics, C.S.I.R.O., Melbourne, for pointing out at a critical stage of this analysis that the lactone group must be planar, and consequently restricts possible models, and for much other helpful advice. The authors are also indebted to Prof. G. W. K. Cavill of this University for providing a supply of *isoiridomyrmecin* and much chemical background.

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