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The Crystal and Molecular Structure of Miyaconitine Hydrobromide Dihydrate

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The structure of an *Aconitum* alkaloid, miyaconitine, $C_{23}H_{29}O_6N$, has been determined by the X-ray analysis of crystals of the hydrobromide dihydrate, which are monoclinic with four formula units in a unit cell of the dimensions; $a=10.41$, $b=13.85$, $c=9.63$ Å and $\beta=113.8°$; space group, $P2_1$. The structure was solved by the heavy-atom method and was refined by the least-squares method. The final R index was 0.151. The absolute configuration was determined using the anomalous dispersion effect of the bromine atom. It was thus established that miyaconitine is a novel type of *Aconitum* alkaloid.

Introduction

Miyaconitine, $C_{23}H_{29}O_6N$, was isolated from *Aconitum miyabei* Nakai as a major alkaloid; the first preliminary investigation of its structure by chemical methods was reported in 1950.[1] Since then the structure has been investigated by many workers,[2-4] but certain reactions still remained uninterpretable, thus precluding a conclusive elucidation of the structure. Miyaconitine seemed to have an unusual skeleton, capable of a facile cyclization. In view of this, an X-ray structure analysis was undertaken in cooperation with the chemical work by Ichinohe, Yamaguchi, Katsui, and Kakimoto.[5]

A heavy-atom derivative, miyaconitine hydrobromide dihydrate, was prepared and supplied by Professor Ichinohe. A preliminary report of the present X-ray work has already been published.[6]

Experimental

Crystals of miyaconitine hydrobromide dihydrate are colorless scales, the (001) plane being well developed. The unit-cell dimensions were determined from zero-layer Weissenberg photographs about the a and the b axes, calibrated with superimposed Al-powder photographs.

Multiple-film equi-inclination Weissenberg photographs were taken at room temperature for the layer lines from 0 to

1) H. Suginome, S. Furusawa, Y. Chiba, and S. Kakimoto, *J. Fac. Sci. Hokkaido Univ. Ser. III, Chem.*, **4**, 1 (1950).
2) S. Kakimoto, This Bulletin, **32**, 349 (1959).
3) H. Suginome and S. Kakimoto, *ibid.*, **32**, 352 (1959).
4) S. Kakimoto, N. Katsui, and Y. Ichinohe, *ibid.*, **32**, 1153 (1959).
5) Y. Ichinohe, M. Yamaguchi, N. Katsui, and S. Kakimoto, *Tetrahedron Lett.*, **1970**, 2323.
6) H. Shimanouchi, Y. Sasada, and T. Takeda, *ibid.*, **1970**, 2327.

7 about the a axis and from 0 to 9 about the b axis, using Cu$K\alpha$ radiation. The crystals used were square in cross-section, with rectangular dimensions of 0.02×0.002 cm and 0.05×0.002 cm for the a and b axis rotation respectively. Almost no reflections were observed with $2\theta>100°$. Therefore, only 1342 were indexed out of the 2900 possible independent reflections within the limiting sphere for Cu$K\alpha$. The intensities of those 1342 reflections were estimated by visual comparison with a standard scale prepared with the same crystal, of which 211 were unobserved above the background. The accuracies of the intensity data were rather low, because only very thin crystals were available. The corrections for the Lorentz and polarization factors were made in the usual way, and those for the spot-size variation in the high-layer photographs, by the method of Phillips.[7] The correction for absorption was omitted.

Crystal Data

The crystallographic and physical data obtained are: Miyaconitine hydrobromide dihydrate $C_{23}H_{29}O_6N\cdot HBr\cdot 2H_2O$, mp 270°C (decomp.). Monoclinic, $a=10.41$ Å, $b=13.85$ Å, $c=9.63$ Å and $\beta=113.8°$. Absent spectra, $(0k0)$ when k is odd. Space group, $P2_1$. Two molecules per unit cell. Volume of the unit cell, 1270.5 Å^3. Density (by flotation), 1.399 g·cm^{-3}. Density (calculated), 1.391 g·cm^{-3}. Linear absorption coefficient for Cu$K\alpha$ radiation, $\mu=28.4$ cm^{-1}. Total number of electrons per unit cell, $F(000)=556$.

Table 1. Final atomic coordinates and temperature factors

The anisotropic temperature factors are expressed in the form of

$$\exp\{-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)\}.$$

Atom	x/a	y/b	z/c
Br	0.1017	0.0000	0.1711
Atom	B_{11}	B_{22}	B_{33}
Br	0.01676	0.00446	0.02593
Atom	B_{12}	B_{13}	B_{23}
Br	0.00205	0.02904	0.00071

Atom	x/a	y/b	z/c	B(Å^2)
O(1)	0.4864	0.4022	0.3369	4.14
O(2)	0.1601	0.5844	0.6034	2.30
O(3)	0.2090	0.4567	0.8366	2.26
O(4)	0.0220	0.2954	0.4435	2.47
O(5)	0.5542	0.2117	0.7295	4.01
O(6)	0.5289	0.2757	0.2128	9.60
OW(1)	−0.0835	0.1781	0.1885	4.56
OW(2)	−0.2241	0.3130	−0.0098	11.37
N	0.3650	0.4897	0.6325	1.19
C(1)	0.2753	0.3216	0.3201	3.33
C(2)	0.3363	0.3907	0.2379	2.55
C(3)	0.2617	0.4902	0.2086	3.62
C(4)	0.2469	0.5300	0.3611	2.19
C(5)	0.1613	0.4618	0.4210	1.53
C(6)	0.2108	0.4886	0.5850	1.98
C(7)	0.1655	0.4241	0.6933	1.55
C(8)	0.2249	0.3173	0.6864	1.09
C(9)	0.1717	0.2880	0.5217	1.45
C(10)	0.2534	0.3559	0.4574	1.53
C(11)	0.2112	0.1744	0.5220	1.00
C(12)	0.3116	0.1502	0.6667	2.58
C(13)	0.4336	0.2222	0.7108	−0.84
C(14)	0.3830	0.3219	0.7334	1.21
C(15)	0.1847	0.2515	0.7933	2.73
C(16)	0.2607	0.1470	0.7904	4.62
C(17)	0.2554	0.0771	0.8885	3.58
C(18)	0.1439	0.6239	0.2817	4.05
C(19)	0.3824	0.5566	0.4981	3.05
C(20)	0.3868	0.3801	0.5970	2.27
C(21)	0.5935	0.3480	0.3265	7.78
C(22)	0.7281	0.3609	0.4408	10.50
C(23)	0.4570	0.5273	0.7868	4.02

7) D. C. Phillips, *Acta Cryst.*, **7**, 746 (1954).

Structure Determination

The three-dimensional sharpened Patterson function was synthesized, and the bromine atom was easily located. A three-dimensional Fourier synthesis was subsequently carried out using the phases of the bromine atom. The resulting map necessarily exhibited the space group symmetry of $P2_1/m$, causing the superposition of the real atoms with their related mirror-image peaks. The 108 peaks were picked out within the asymmetric unit; we then tried to assemble them together to give a three-dimensional molecular model. By studying the distances and angles between peaks, the twenty-three peaks were tentatively assigned to

Table 2. Estimated standard deviations ($\sigma(x)$, $\sigma(y)$, and $\sigma(z)$ in Å, $\sigma(B)$ in Å^2)

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
Br	0.005	0.000	0.005
Atom	$\sigma(B_{11})$	$\sigma(B_{22})$	$\sigma(B_{33})$
Br	0.0006	0.0002	0.0008
Atom	$\sigma(B_{12})$	$\sigma(B_{13})$	$\sigma(B_{23})$
Br	0.0008	0.0011	0.0009

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$	$\sigma(B)$
O(1)	0.025	0.025	0.026	0.53
O(2)	0.021	0.020	0.020	0.39
O(3)	0.021	0.019	0.021	0.39
O(4)	0.021	0.020	0.021	0.41
O(5)	0.026	0.024	0.025	0.52
O(6)	0.040	0.042	0.040	1.02
OW(1)	0.028	0.025	0.027	0.56
OW(2)	0.045	0.048	0.046	1.22
N	0.021	0.024	0.020	0.39
C(1)	0.037	0.034	0.036	0.72
C(2)	0.034	0.031	0.033	0.64
C(3)	0.034	0.043	0.033	0.71
C(4)	0.032	0.027	0.031	0.63
C(5)	0.030	0.026	0.029	0.54
C(6)	0.028	0.034	0.027	0.56
C(7)	0.030	0.027	0.029	0.55
C(8)	0.028	0.025	0.028	0.49
C(9)	0.029	0.026	0.028	0.52
C(10)	0.030	0.027	0.029	0.54
C(11)	0.028	0.025	0.027	0.48
C(12)	0.034	0.032	0.033	0.63
C(13)	0.025	0.021	0.023	0.41
C(14)	0.029	0.026	0.028	0.50
C(15)	0.034	0.032	0.034	0.66
C(16)	0.043	0.040	0.041	0.87
C(17)	0.038	0.036	0.036	0.74
C(18)	0.041	0.038	0.038	0.81
C(19)	0.036	0.033	0.035	0.70
C(20)	0.033	0.031	0.033	0.60
C(21)	0.056	0.053	0.057	1.31
C(22)	0.067	0.068	0.068	1.80
C(23)	0.040	0.035	0.038	0.82

TABLE 3. OBSERVED AND CALCULATED STRUCTURE FACTORS ($\times$ 7)

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
H,L= 0 8			1 100 115			11 0 21			10 81 75			12 0 52			10 139 137			9 0 72			2 229 242			H,L= -7 2		
0 78 84			2 95 48			12 61 50			11 0 10			13 44 101			11 0 41			10 67 110			3 33 19			0 184 161		
1 123 151			3 139 181			13 55 35			12 50 82			H,L= 6 2			12 0 79			11 89 68			4 212 215			1 184 179		
H,L= 2 8			4 89 67			H,L= 5 4			H,L= 6 3			0 95 78			13 72 86			12 100 108			5 89 99			2 117 85		
0 72 54			5 72 71			0 80 35			0 83 77			1 95 81			H,L= 6 1			13 72 52			6 229 232			3 206 192		
H,L= 3 8			6 123 129			1 78 64			1 83 90			2 85 87			0 87 72			H,L= 6 0			7 106 107			4 184 194		
0 0 37			7 100 113			2 106 124			2 102 101			3 100 83			1 80 98			0 150 145			8 117 84			5 139 105		
1 72 59			8 83 104			3 55 71			3 83 86			4 104 178			2 111 129			1 240 249			9 128 103			6 134 139		
2 72 27			9 78 71			4 111 107			4 111 138			5 128 100			3 83 79			2 95 96			10 195 107			7 206 166		
3 0 41			H,L= 3 5			5 78 87			5 55 71			6 111 101			4 0 24			3 134 141			11 83 117			8 134 138		
H,L= 0 7			0 72 26			6 0 9			6 95 63			7 95 27			5 100 105			4 139 126			12 100 112			9 0 65		
0 0 35			1 167 151			7 0 45			7 0 2			8 95 27			6 145 137			5 150 160			13 72 54			10 123 90		
1 72 41			2 95 106			8 0 17			8 111 97			9 89 71			7 117 120			6 324 294			H,L= -7 1			11 89 59		
2 55 75			3 167 146			9 100 141			9 0 20			10 0 44			8 100 95			7 134 100			0 178 186			H,L= -1 3		
3 128 130			4 0 60			10 0 29			10 0 77			11 0 28			9 0 15			8 111 112			1 83 23			0 632 672		
4 95 23			5 72 78			11 0 59			11 50 22			12 0 16			10 67 57			9 0 82			2 128 157			1 268 215		
H,L= 1 7			6 117 26			12 44 24			12 44 63			H,L= 7 2			11 0 85			10 0 52			3 123 103			2 302 308		
0 67 59			7 117 60			H,L= 6 4			H,L= 7 3			0 89 46			12 67 28			11 78 61			4 201 215			3 318 327		
1 78 92			8 0 31			0 95 29			0 78 47			1 89 51			13 72 42			12 83 56			5 167 185			4 274 233		
2 67 40			9 111 69			1 95 118			1 89 56			2 134 169			H,L= 7 1			13 78 59			6 111 79			5 206 144		
3 83 91			H,L= 4 5			2 72 72			2 100 76			3 100 62			0 67 51			14 67 37			7 218 176			6 268 247		
4 0 64			0 72 57			3 128 133			3 83 83			4 95 92			1 151 180			H,L= 7 0			8 123 99			7 223 216		
5 67 85			1 100 145			4 95 118			4 95 85			5 83 51			2 102 108			0 89 55			9 0 22			8 279 246		
H,L= 2 7			2 0 46			5 100 100			5 95 101			6 100 88			3 95 33			1 150 155			10 0 39			9 156 99		
0 72 42			3 139 200			6 0 22			6 95 55			7 100 91			4 150 145			2 128 120			11 67 39			10 357 324		
1 78 74			4 0 47			7 0 33			7 0 14			8 95 54			5 150 160			3 117 140			H,L= -1 2			11 234 238		
2 95 113			5 0 22			8 0 83			8 61 51			9 0 48			6 0 87			4 111 73			0 453 492			12 139 141		
3 134 71			6 0 47			9 0 50			H,L= 0 2			10 0 70			7 170 142			5 117 93			1 302 241			H,L= -2 3		
4 0 20			7 78 76			10 67 49			0 643 609			11 72 29			8 120 114			6 95 104			2 408 332			0 50 34		
5 55 33			8 0 36			H,L= 7 4			1 408 395			H,L= 0 1			9 0 41			7 0 18			3 542 535			1 374 370		
H,L= 3 7			9 0 98			0 78 8			2 178 121			0 520 569			10 67 24			8 0 33			4 229 143			2 257 224		
0 78 87			10 67 78			1 95 51			3 201 198			1 313 336			11 0 11			9 100 120			5 413 387			3 234 225		
1 55 103			11 50 21			2 61 10			4 346 347			2 285 249			H,L= 0 0			10 95 79			6 100 90			4 509 470		
2 89 111			H,L= 5 5			3 83 87			5 458 373			3 721 711			2 464 473			11 55 58			7 408 315			5 257 200		
3 0 35			0 61 18			4 83 76			6 201 191			4 313 284			3 0 0			H,L= -1 1			8 117 67			6 290 238		
4 0 69			1 72 54			5 89 40			7 223 227			5 419 354			4 447 427			0 44 4			9 285 254			7 223 170		
5 0 43			2 55 92			H,L= 0 6			8 206 181			6 95 77			5 0 0			1 341 306			10 246 206			8 0 65		
6 0 66			3 0 29			0 318 301			9 67 91			7 279 250			6 596 526			2 520 582			11 167 100			9 100 98		
7 72 32			4 55 51			1 246 207			10 223 209			8 156 113			7 0 0			3 469 434			12 95 105			10 162 164		
H,L= 4 7			5 0 32			2 402 339			11 139 71			9 95 82			8 190 166			4 262 273			13 117 134			11 123 116		
0 50 66			6 0 45			3 139 80			12 134 125			10 89 76			9 0 0			5 313 259			H,L= -2 2			12 78 89		
1 0 30			7 61 74			4 441 418			13 0 35			11 208 266			10 262 272			6 531 418			0 223 163			13 83 144		
H,L= 0 6			8 55 73			5 78 63			H,L= 1 2			12 78 90			11 0 0			7 335 228			1 357 383			H,L= -3 3		
0 167 175			9 50 46			6 279 226			0 83 24			13 0 88			12 190 152			8 380 347			2 447 432			0 206 199		
1 128 132			10 44 30			7 0 22			1 341 302			H,L= 1 1			H,L= 1 0			9 167 104			3 369 348			1 324 374		
2 123 104			11 39 40			8 156 166			2 503 526			0 447 412			0 95 64			10 240 197			4 318 250			2 0 72		
3 0 52			H,L= 6 5			9 206 193			3 61 18			1 822 915			1 542 575			11 78 75			5 402 327			3 676 671		
4 100 104			0 72 11			10 223 195			4 95 105			2 139 71			2 332 408			12 0 75			6 223 165			4 363 334		
5 0 70			1 55 37			11 0 57			5 318 346			3 178 154			3 117 91			13 95 86			7 134 116			5 223 230		
6 139 147			2 61 88			12 95 102			6 251 278			4 240 233			4 290 299			14 0 85			8 139 110			6 324 268		
7 0 12			3 89 39			13 95 70			7 139 116			5 363 387			5 67 58			13 67 34			9 355 320			7 408 368		
8 0 80			4 83 44			H,L= 1 6			8 268 208			6 139 62			6 497 414			H,L= -2 1			10 156 163			8 78 35		
9 78 117			5 83 49			0 251 311			9 0 25			7 0 34			7 274 236			0 453 573			11 257 277			9 234 231		
10 0 30			6 55 50			1 246 249			10 190 164			8 106 77			8 50 82			1 341 355			12 151 147			10 111 73		
11 0 8			7 78 32			2 178 164			11 139 149			9 268 297			9 89 99			2 447 461			13 100 108			11 83 99		
H,L= 5 6			8 72 78			3 134 109			12 173 223			10 139 111			10 178 161			3 89 65			H,L= -3 2			12 78 64		
0 89 59			H,L= 0 4			4 229 269			13 111 65			11 134 159			11 0 65			4 285 333			0 503 610			H,L= -4 3		
1 72 69			0 39 14			5 218 225			H,L= 2 2			12 123 98			12 111 140			5 178 143			1 268 252			0 178 156		
2 0 26			1 357 382			6 234 251			0 246 238			13 145 180			13 139 145			6 626 584			2 419 446			1 156 142		
3 72 72			2 408 435			7 100 68			1 206 188			H,L= 2 1			H,L= 2 0			7 380 389			3 302 292			2 201 195		
4 89 56			3 268 226			8 0 69			2 229 175			0 195 166			0 430 450			8 419 369			4 374 382			3 380 384		
5 0 62			4 83 75			9 184 167			3 218 167			1 391 377			1 257 308			9 173 149			5 223 175			4 206 187		
6 78 78			5 151 141			10 0 84			4 246 262			2 246 215			2 102 157			10 0 116			6 128 112			5 408 331		
7 78 112			6 89 93			11 134 145			5 156 142			3 318 296			3 469 497			11 78 33			7 190 143			6 234 197		
8 100 115			7 178 156			H,L= 2 5			6 212 198			4 290 299			4 240 237			12 78 133			8 234 259			7 223 196		
H,L= 2 6			8 123 122			0 72 53			7 123 138			5 102 177			5 456 428			13 78 46			9 0 38			8 72 85		
0 72 44			9 151 175			1 302 295			8 72 92			6 262 220			6 262 204			14 50 104			10 95 127			9 0 79		
1 100 132			10 0 84			2 111 109			9 0 18			7 352 322			7 369 364			H,L= -3 1			11 100 95			10 195 193		
2 0 59			11 78 70			3 251 274			10 145 165			8 218 202			8 162 110			0 111 140			12 55 82			11 0 47		
3 128 172			12 78 71			4 123 106			11 0 36			9 72 107			9 218 231			1 374 406			13 78 74			12 78 78		
4 0 48			H,L= 1 4			5 117 94			12 111 157			10 139 146			10 156 159			2 363 377			H,L= -4 2			13 78 90		
5 111 139			0 95 103			6 117 114			13 78 63			11 78 99			11 162 210			3 352 355			0 251 284			H,L= -5 3		
6 0 90			1 67 61			7 178 192			14 72 119			12 78 82			12 89 33			4 234 235			1 167 132			0 335 380		
H,L= 3 6			2 190 188			8 83 86			H,L= 3 2			13 100 104			13 78 83			5 190 179			2 268 276			1 139 75		
0 0 12			3 229 210			9 134 159			0 178 140			14 0 88			14 72 57			6 145 124			3 167 168			2 257 214		
1 111 163			4 55 46			10 78 52			1 296 328			H,L= 3 1			H,L= 3 0			7 178 161			4 206 239			3 0 11		
2 89 151			5 123 92			11 78 133			2 251 263			0 139 177			0 500 484			8 117 110			5 134 111			4 285 241		
3 0 35			6 128 88			12 55 18			3 324 347			1 95 114			1 296 355			9 78 88			6 279 267			5 67 65		
4 0 39			7 151 101			H,L= 3 5			4 78 71			2 206 216			2 145 142			10 123 134			7 145 111			6 318 282		
5 78 85			8 89 81			0 0 36			5 190 194			3 173 140			3 475 549			11 100 132			8 262 249			7 151 70		
6 0 30			9 78 91			1 128 138			6 156 172			4 240 222			4 274 250			12 78 95			9 134 112			8 296 259		
7 78 73			H,L= 2 4			2 67 47			7 111 123			5 89 76			5 335 328			13 78 80			10 0 85			9 61 32		
H,L= 4 6			0 111 89			3 134 164			8 106 130			6 201 208			6 151 127			H,L= -4 1			11 0 49			10 190 218		
0 72 57			1 78 94			4 106 109			9 123 131			7 0 25			7 290 297			0 324 333			12 0 92			11 61 50		
1 72 90			2 195 251			5 100 140			10 83 80			8 184 185			8 0 39			1 324 410			13 0 68			12 83 106		
2 83 108			3 151 190			6 111 130			11 0 51			9 106 108			9 167 199			2 257 261			H,L= -5 2			13 0 12		
3 0 52			4 195 220			7 134 160			12 55 59			10 78 85			10 78 52			3 206 235			0 0 43			H,L= -6 3		
4 55 75			5 83 82			8 95 129			H,L= 4 2			11 55 49			11 78 105			4 240 231			1 363 411			0 268 253		
5 0 18			6 0 44			9 145 180			0 0 50			12 55 70			12 83 84			5 380 344			2 83 64			1 151 162		
H,L= 0 5			7 139 172			H,L= 4 3			1 195 149			H,L= 4 1			13 95 114			6 212 174			3 262 232			2 223 225		
0 145 170			8 89 39			0 78 63			2 167 172			0 363 342			H,L= 4 0			7 201 234			4 201 156			3 178 173		
1 218 226			9 117 143			1 156 162			3 162 104			1 341 376			0 61 48			8 117 100			5 285 290			4 128 60		
2 262 260			H,L= 3 4			2 156 142			4 162 100			2 318 287			1 341 381			9 145 163			6 102 194			5 195 175		
3 184 144			0 134 124			3 134 122			5 178 209			3 0 67			2 324 330			10 0 27			7 218 202			6 123 130		
4 201 202			1 89 53			4 139 139			6 83 63			4 262 258			3 268 302			11 173 195			8 134 117			7 83 38		
5 195 196			2 173 225			5 100 111			7 106 145			5 123 119			4 190 165			12 55 68			9 123 128			8 106 73		
6 128 124			3 0 42			6 89 82			8 76 94			6 156 166			5 117 115			13 123 135			10 89 110			9 0 84		
7 100 95			4 117 110			7 0 34			9 0 17			7 89 58			6 89 99			H,L= -5 1			11 240 217			10 0 93		
8 151 192			5 0 54			8 0 79			10 100 80			8 145 134			7 117 100			0 285 292			12 55 31			11 67 41		
9 111 141			6 95 51			9 0 124			11 95 111			9 123 106			8 173 185			1 173 118			13 0 64			12 106 139		
10 111 131			7 111 25			10 100 103			12 61 69			10 111 138			9 89 72			2 123 144			H,L= -6 2			13 0 29		
11 0 40			8 0 66			11 72 47			13 0 62			11 106 122			10 111 121			3 134 133			0 162 122			H,L= -7 3		
12 0 51			9 123 147			12 0 46			H,L= 5 2			12 89 101			11 55 54			4 151 120			1 173 221			0 145 143		
H,L= 1 5			H,L= 4 4			13 44 28			0 357 308			13 72 87			12 67 90			5 307 279			2 83 71			1 234 268		
0 156 151			0 128 143			H,L= 5 3			1 156 147			H,L= 5 1			13 55 51			6 167 147			3 173 137			2 44 83		
1 178 206			1 78 36			0 0 23			2 178 155			0 257 254			H,L= 5 0			7 190 168			4 111 91			3 268 277		
2 123 99			2 117 91			1 100 102			3 72 48			1 218 234			0 44 15			8 123 88			5 246 249			4 162 164		
3 123 106			3 100 124			2 139 110			4 83 64			2 151 107			1 100 85			9 83 124			6 145 136			5 234 237		
4 162 182			4 106 119			3 100 144			5 0 5			3 246 238			2 234 247			10 111 100			7 184 159			6 55 28		
5 72 74			5 83 112			4 123 140			6 95 87			4 195 188			3 89 73			11 78 75			8 106 70			7 246 200		
6 123 127			6 78 109			5 61 29			7 162 157			5 167 154			4 95 100			12 0 19			9 89 76			8 55 31		
7 0 66			7 78 59			6 139 114			8 134 134			6 106 104			5 178 176			13 78 93			10 145 87			9 162 149		
8 55 19			8 123 148			7 0 57			9 128 129			7 55 76			6 195 178			H,L= -6 1			11 128 146			10 72 48		
H,L= 2 5			9 0 63			8 0 95			10 139 140			8 0 13			7 95 96			0 425 465			12 61 70			11 95 91		
0 117 84			10 95 130			9 106 112			11 55 80			9 111 129			8 229 222			1 184 154			13 111 120			H,L= -1 4		

TABLE 3. (Continued)

K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC	K	FO	FC
0	240	205	7	262	245	9	100	32	3	117	126	7	195	165	2	78	89	7	78	82	8	55	64	H,L=	-3	8
1	229	173	8	123	96	10	173	138	4	156	144	8	100	56	3	184	223	8	72	50	9	0	72	4	128	158
2	335	248	9	184	177	11	67	66	5	78	39	9	72	28	4	156	196	9	139	145	10	0	35	5	83	114
3	279	275	10	0	22	H,L=	-1	5	6	151	138	10	95	54	5	100	130	10	0	40	11	50	89	6	0	91
4	212	260	11	139	147	0	206	213	7	139	100	11	95	85	6	139	165	11	89	65	H,L=	-5	7	H,L=	-4	8
5	257	221	12	0	24	1	257	259	8	151	185	H,L=	-1	6	7	134	130	H,L=	-1	7	0	55	58	0	83	0
6	167	167	13	0	116	2	72	34	9	134	138	0	196	126	8	67	51	0	100	112	1	173	206	1	0	93
7	206	189	H,L=	-5	4	3	67	60	10	83	114	1	134	149	9	106	139	1	128	120	2	134	150	2	162	188
8	100	116	0	212	226	4	151	119	11	100	80	2	117	89	10	78	87	2	190	234	3	128	152	3	0	53
9	100	100	1	262	294	5	190	157	12	78	98	3	151	145	11	78	40	3	100	99	4	111	82	4	167	121
10	134	151	2	55	66	6	100	19	13	0	33	4	139	162	12	0	56	4	139	157	5	106	125	H,L=	-5	8
11	78	109	3	206	183	7	95	116	H,L=	-5	5	5	72	70	13	44	51	5	0	89	6	0	77	0	0	60
12	0	92	4	145	129	8	156	158	0	162	189	6	128	135	H,L=	-5	6	6	0	65	7	128	125	1	128	122
H,L=	-2	4	5	257	228	9	195	208	1	128	147	7	117	114	0	212	199	7	95	98	8	0	38	2	95	110
0	95	79	6	173	151	10	0	46	2	151	206	8	111	34	1	50	81	H,L=	-2	7	9	89	95	3	0	71
1	240	257	7	162	151	11	0	106	3	251	238	9	111	120	2	106	109	0	78	78	10	0	20	4	95	28
2	380	390	8	201	128	12	78	53	4	145	128	10	95	120	3	67	36	1	128	160	11	78	78	5	89	100
3	262	274	9	61	89	H,L=	-2	5	5	195	197	11	78	16	4	100	95	2	123	145	H,L=	-6	7	6	61	91
4	139	120	10	0	61	0	156	160	6	156	150	H,L=	-2	6	5	78	69	3	123	69	0	145	135	7	83	64
5	218	208	11	201	216	1	111	93	7	178	155	0	0	20	6	167	193	4	100	128	1	145	140	8	0	34
6	223	208	12	55	79	2	223	227	8	145	93	1	128	110	7	89	12	5	111	23	2	100	64	9	83	92
7	67	61	13	78	96	3	162	140	9	145	144	2	206	245	8	145	152	6	78	89	3	139	149	10	0	58
8	218	219	H,L=	-6	4	4	229	248	10	0	81	3	223	267	9	61	47	7	95	73	4	123	105	11	67	82
9	151	128	0	123	142	5	229	260	11	89	95	4	95	80	10	123	121	8	89	127	5	55	43	H,L=	-6	8
10	145	158	1	83	53	6	117	115	H,L=	-6	5	5	0	10	11	61	34	H,L=	-3	7	6	55	68	0	0	38
H,L=	-3	4	2	268	279	7	106	102	0	100	91	6	89	64	H,L=	-6	6	0	95	59	7	55	35	1	100	134
0	240	275	3	83	81	8	229	249	1	212	214	7	111	139	0	218	173	1	117	144	8	0	72	2	0	67
1	296	377	4	262	252	9	279	284	2	111	94	8	123	122	1	145	141	2	0	68	9	83	46	3	128	82
2	72	39	5	145	108	10	0	100	3	167	152	9	111	144	2	195	211	3	128	69	10	0	71	4	0	16
3	234	184	6	128	120	H,L=	-3	5	4	162	152	10	78	98	3	234	268	4	123	126	11	78	65	5	128	166
4	363	347	7	128	76	0	229	221	5	201	206	H,L=	-3	6	4	195	205	5	128	190	H,L=	-7	7	6	0	54
5	307	303	8	240	206	1	123	139	6	95	72	0	128	214	5	100	112	6	0	75	0	145	147	7	106	118
6	290	265	9	0	44	2	274	304	7	257	228	1	184	226	6	128	120	7	0	82	1	100	85	8	61	37
7	100	87	10	0	90	3	251	276	8	151	117	2	117	129	7	123	99	8	117	120	2	139	185	H,L=	-7	8
8	178	173	11	67	32	4	234	265	9	251	101	3	134	121	8	134	151	9	0	36	3	111	113	0	0	44
9	89	142	12	61	63	5	67	26	10	95	8	4	72	44	9	67	26	10	78	74	4	128	107	1	128	173
10	78	94	13	78	50	6	123	135	11	89	92	5	123	134	10	89	108	11	0	16	5	0	54	2	0	107
11	83	90	H,L=	-7	4	7	78	83	12	0	39	6	0	37	11	61	22	12	67	43	6	156	158	3	139	140
12	0	59	0	234	271	8	134	166	13	50	107	7	117	138	12	78	58	H,L=	-4	7	7	72	32	4	111	44
H,L=	-4	4	1	44	64	9	139	142	H,L=	-7	5	8	106	133	H,L=	-7	6	0	0	72	8	89	109	5	139	141
0	184	178	2	251	242	10	83	24	0	100	93	9	83	89	0	234	220	1	162	197	9	0	19	6	0	18
1	363	393	3	134	115	11	83	96	1	145	184	10	100	118	1	139	143	2	72	97	10	89	46	7	0	40
2	151	141	4	302	306	12	0	110	2	139	146	11	0	91	2	134	109	3	134	174	H,L=	-2	8	8	89	36
3	117	80	5	123	142	H,L=	-4	5	3	162	170	12	0	24	3	111	81	4	111	147	9	0	32	9	83	63
4	156	128	6	167	166	0	151	158	4	89	90	H,L=	-4	6	4	145	158	5	117	155	0	78	63	10	78	59
5	262	237	7	167	89	1	123	118	5	162	101	0	123	85	5	117	131	6	78	75	1	0	20	H,L=	-7	9
6	111	78	8	296	236	2	240	267	6	128	109	1	167	175	6	0	42	7	0	145	8	72	56	3	139	123

light atoms after many trials; nine of them were later found to be incorrect. The difficulty was the presence of many spurious peaks, probably because of the low accuracies of the diffraction data mentioned in the previous section. To find the remaining atoms, a successive Fourier synthesis and the least-squares refinement were executed in combination. The atoms whose temperature factors became unreasonably large in the least-squares refinement were abandoned. The atoms of the molecular skeleton were revealed step by step, but some of the atoms in the acetoxyl group and a water of crystallization did not appear in this stage. Finally, difference syntheses gave all the non-hydrogen atoms. The oxygen atoms were easily distinguished from the carbon atoms by inspecting the electron-density, the bond lengths, and the hydrogen bonding scheme, as will be described later.

Since the evidence for assigning the nitrogen atom was not conclusive at this stage, the electron-density values at the peaks and the chemical information were taken into account. This assignment is consistent with that of other related diterpenoid alkaloids of a known structure.[8-10]

The atomic parameters were refined by the block-diagonal matrix least-squares method. Anisotropic temperature factors, of the form $\exp\{-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)\}$, were applied to the bromine atom, while the thermal motion of the light atoms was assumed to be isotropic. The final discrepancy index, $R=\Sigma||F_o|-|F_c||/\Sigma|F_o|$, was 0.151 for the observed reflections. The atomic scattering factors used were taken from International Tables for X-ray Crystallography (1962).[11] The final atomic coordinates and temperature factors are given in Table 1, and their standard deviations, in Table 2. The ob-

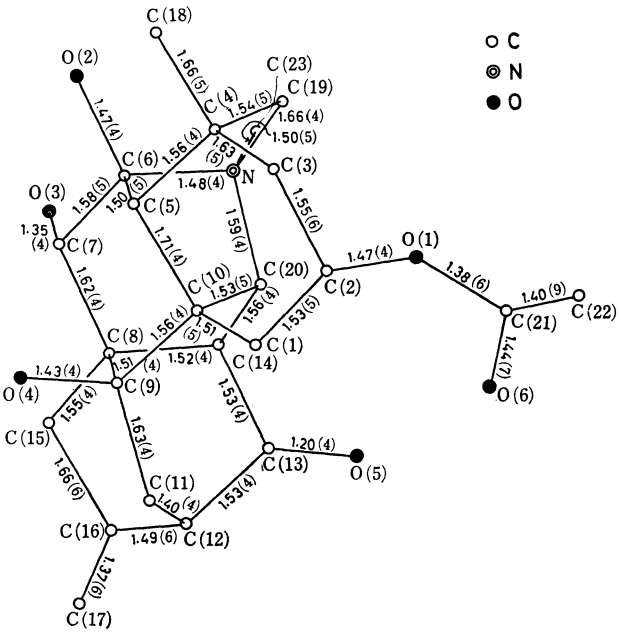


Fig. 1. Bond lengths (Å). The corresponding e.s.d.'s, given in parentheses, refer to the last decimal positions.

8) M. Przybylska, *Acta Cryst.*, **16**, 871 (1963).
9) S. W. Pelletier, L. H. Wright, M. G. Newton, and H. Wright, *Chem. Comm.*, **1970**, 98.
10) K. B. Birnbaum, *Tetrahedron Letters*, 5245 (1969).
11) "International Tables for X-ray Crystallography", Vol. 3, Kynoch Press, Birmingham, England (1962), p. 202.

TABLE 4. BOND ANGLES (deg.)
The corresponding e.s.d.'s, given in parentheses, refer to the last decimal positions.

C(21)	O(1)	C(2)	125(3)	C(9)	C(8)	C(15)	117(2)
C(23)	N	C(6)	119(3)	C(14)	C(8)	C(15)	112(2)
C(6)	N	C(20)	99(2)	C(8)	C(9)	O(4)	113(2)
C(19)	N	C(20)	107(2)	C(8)	C(9)	C(10)	103(2)
C(6)	N	C(19)	102(2)	C(10)	C(9)	C(11)	114(2)
C(19)	N	C(23)	111(2)	C(11)	C(9)	O(4)	107(2)
C(23)	N	C(20)	117(2)	O(4)	C(9)	C(10)	114(2)
C(2)	C(1)	C(10)	120(3)	C(11)	C(9)	C(8)	106(2)
O(1)	C(2)	C(1)	107(3)	C(5)	C(10)	C(9)	104(2)
O(1)	C(2)	C(3)	110(3)	C(5)	C(10)	C(20)	103(2)
C(1)	C(2)	C(3)	112(3)	C(1)	C(10)	C(20)	116(3)
C(2)	C(3)	C(4)	111(3)	C(1)	C(10)	C(9)	117(3)
C(3)	C(4)	C(19)	118(3)	C(9)	C(10)	C(20)	103(2)
C(3)	C(4)	C(5)	114(3)	C(1)	C(10)	C(5)	111(2)
C(5)	C(4)	C(18)	107(3)	C(9)	C(11)	C(12)	109(2)
C(18)	C(4)	C(19)	114(3)	C(11)	C(12)	C(13)	109(3)
C(19)	C(4)	C(5)	107(3)	C(11)	C(12)	C(16)	116(3)
C(3)	C(4)	C(18)	97(3)	C(13)	C(12)	C(16)	109(3)
C(4)	C(5)	C(10)	104(2)	O(5)	C(13)	C(12)	131(3)
C(6)	C(5)	C(4)	104(2)	O(5)	C(13)	C(14)	119(2)
C(6)	C(5)	C(10)	94(2)	C(12)	C(13)	C(14)	109(2)
N	C(6)	O(2)	111(2)	C(8)	C(14)	C(13)	108(2)
N	C(6)	C(5)	101(2)	C(8)	C(14)	C(20)	99(2)
C(5)	C(6)	C(7)	119(3)	C(13)	C(14)	C(20)	103(2)
C(7)	C(6)	O(2)	102(2)	C(8)	C(15)	C(16)	104(3)
O(2)	C(6)	C(5)	111(3)	C(12)	C(16)	C(15)	108(3)
N	C(6)	C(7)	112(3)	C(12)	C(16)	C(17)	135(4)
C(6)	C(7)	C(8)	106(2)	C(15)	C(16)	C(17)	117(3)
C(6)	C(7)	O(3)	115(2)	C(4)	C(19)	N	101(2)
C(8)	C(7)	O(3)	112(2)	N	C(20)	C(10)	104(2)
C(14)	C(8)	C(7)	110(2)	C(10)	C(20)	C(14)	108(3)
C(15)	C(8)	C(7)	107(2)	N	C(20)	C(14)	105(2)
C(9)	C(8)	C(14)	103(2)	O(1)	C(21)	O(6)	107(4)
C(9)	C(8)	C(7)	108(2)	O(1)	C(21)	C(22)	117(5)
				O(6)	C(21)	C(22)	134(5)

served and calculated structure factors are listed in Table 3.

The computations were done on a HITAC 5020E computer in the University of Tokyo, with programs written by Tamaichi Ashida [12]

TABLE 5. SOME LEAST-SQUARES PLANES

	Plane I		Plane II		Plane III	
l	−0.667		0.157		−0.445	
m	−0.334		0.207		−0.634	
n	−0.666		−0.966		0.632	
p	5.054		5.140		3.350	
	Deviation of atoms (Å)					
C(12)	0.01	O(5)	−0.00	O(1)	0.02	
C(16)	−0.03	C(12)	−0.00	O(6)	0.03	
C(15)	0.01	C(13)	0.00	C(21)	−0.07	
C(17)	0.01	C(14)	−0.00	C(22)	0.02	

The equations of the planes are expressed in the form of $lx'+my'+nz'+p=0$ where $x'=x+z\cos\beta$, $y'=y$ and $z'=z\sin\beta$.

12) T. Ashida, "HBLS-4, The Universal Crystallographic Computing System (I)", Japanese Crystallographic Association, Tokyo (1967), p. 65.

Validity of Assignment of Atomic Species

The intramolecular bond lengths and angles are shown in Fig. 1 and Table 4 respectively. Although the standard deviations were quite large, it is possible to distinguish the exocyclic C–O bonds from the C–C

TABLE 6. COMPARISON OF THE STRUCTURE FACTORS IN BIJVOET PAIRS

h	k	l	Calcd. $\lvert F(hkl)\rvert$		Calcd. $\lvert F(h\bar{k}l)\rvert$	Obs. $\lvert I(hkl)\rvert$		Obs. $\lvert I(h\bar{k}l)\rvert$
2	1	2	26.4	<	27.5		>	
2	1	4	13.2	>	12.6		<	
2	3	4	26.2	<	27.8		>	
3	1	4	7.6	>	7.5		<	
4	1	3	22.5	<	23.3		>	
4	2	1	39.1	<	42.1		>	
4	3	5	28.1	<	28.2		>	
5	1	2	20.2	<	20.8		>	
5	2	3	15.0	<	15.3		>	
6	3	4	18.5	<	19.1		>	
7	2	2	23.4	<	24.7		>	

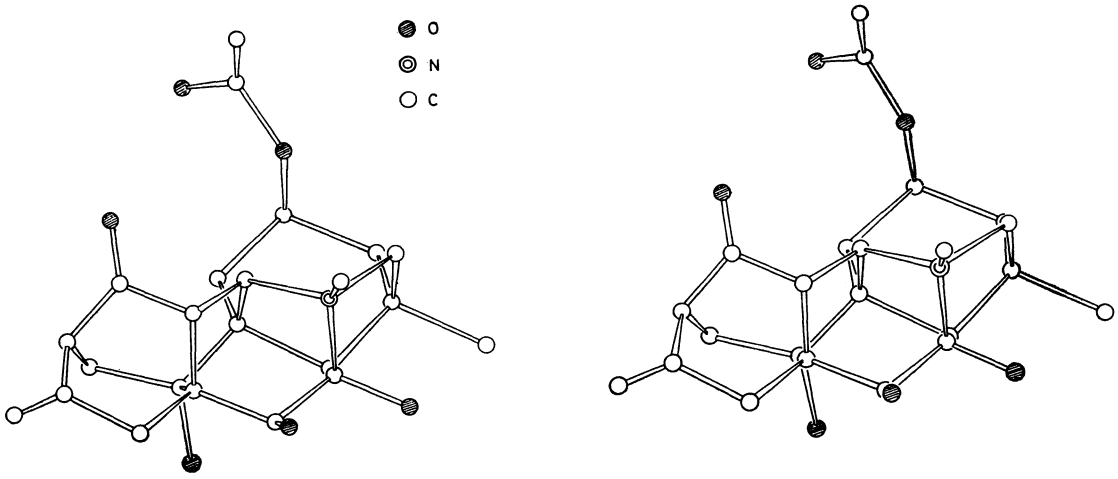
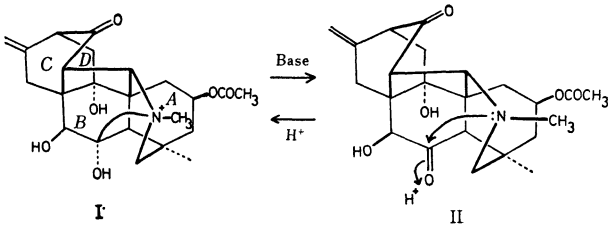


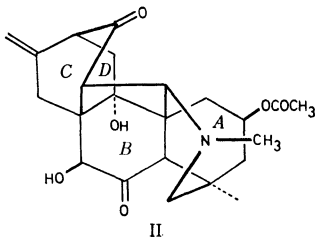
Fig. 2. Stereoscopic drawing of the structure.

bonds. That is, the C(sp^3)–O bond lengths are in the range of 1.35—1.47 Å, while the length of the C(4)—C(18) bond is 1.66 Å.

The equations for the least-squares planes of the planar groups are summarized in Table 5. The C(12), C(16), C(15), and C(17) atoms are essentially planar within the limits of error, and the O(5), C(12), C(13), and C(14) atoms are completely planar, showing that the C(13) and C(16) atoms are in the sp^2 hybridization. The bond lengths, 1.20 Å for C(13)–O(5) and 1.37 Å for C(16)–C(17), clearly distinguish the C=O group from the C=C bond.

The O(1), O(6), C(21), and C(22) atoms are also nearly planar, compatible with the identification of the acetoxyl group. Although there is no significant difference between the C(21)–O(6) and C(21)–C(22) distances, the peak of the electron-density of O(6) was higher than that of C(22) throughout all the stages of Fourier synthesis, so the oxygen atom can tentatively be assigned to the O(6).





Determination of Absolute Configuration

The absolute configuration of the present compound was determined by means of the anomalous scattering of the Cu$K\alpha$ radiation by the bromine atom. The Bijvoet pairs selected as most advantageous for visual comparison are given in Table 6. From these observations, it can be concluded that the atomic coordinates in Table 1 should be referred to a left-handed coordinate system. All the drawings in this paper are based on the correct absolute configuration. The absolute configuration found is in agreement with those of related compounds.[8–10]

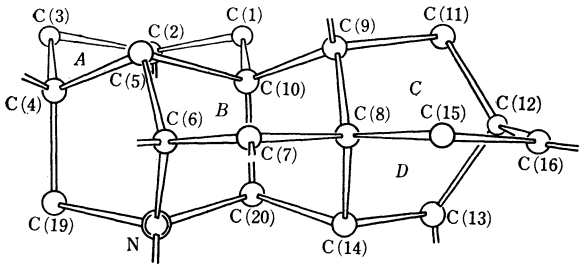


Fig. 3. Molecular skeleton, viewed down the vector between C(7) and the midpoint of C(10)–C(20).

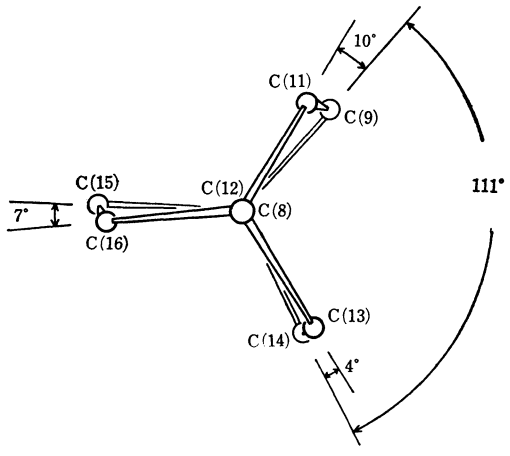


Fig. 4. Rings *C* and *D*, viewed down the C(12)···C(8) vector showing the twisting of the carbocycle.

Results and Discussion

From the X-ray analysis described in the preceding sections, the structure of the present molecule has been determined to be I, including the absolute configuration. A three-dimensional view of the molecule can be obtained from the stereodrawings in Fig. 2. On the basis of the present results, the structure of miyaconitine itself can be deduced to be II, which can easily be converted to I in acidic media.[5] Although the skeleton of the resultant hydrobromide molecule (I) is identical with those of hetisine[8] and kobusine methiodide,[9] the free alkaloid, miyaconitine itself (II), has a new type of skeleton. This is the first substance isolated as a biogenetic intermediate in the transformation from an atisine to a hetisine skeleton in *Aconitum* alkaloids.[5]

The drawing of the skeleton viewed along the vector between the C(7) and the midpoint of the C(10)–C(20) bond is shown in Fig. 3. The *A* ring takes the chair form, with the acetoxyl group in the axial position. If the fusion of the *A* ring and the difference in atomic species are disregarded, the main skeleton possesses an approximate mirror plane through the C(6), C(7), and C(8) atoms. The *C* and *D* rings make a bicyclo-[2,2,2]octane-like system, as is shown in Fig. 4. The conformation of this system is slightly staggered, with the projected angles ranging from 4° to 10°. The presence of a bridge between C(9) and C(14) through the C(10)–C(20) bond causes an appreciable closing of the projected angle, C(9)–C(8)–C(14) (111°). These indicate a significant deviation from D_3 symmetry.[13]

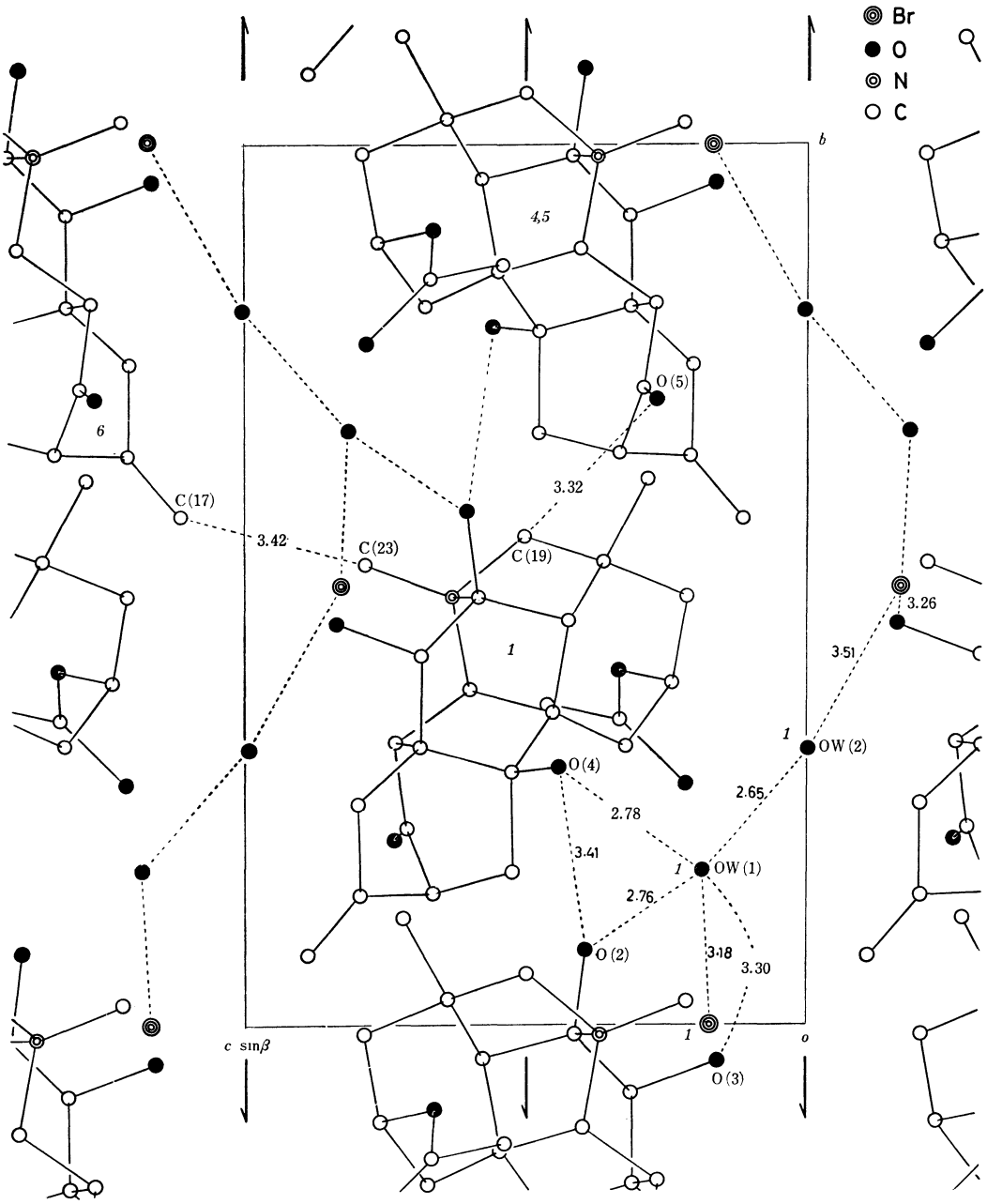


Fig. 5. The crystal structure projected along the a axis with some short intermolecular contacts in Å.

13) A. F. Cameron, G. Ferguson, and D. G. Morris, *J. Chem. Soc. (B)*, **1968**, 1249.

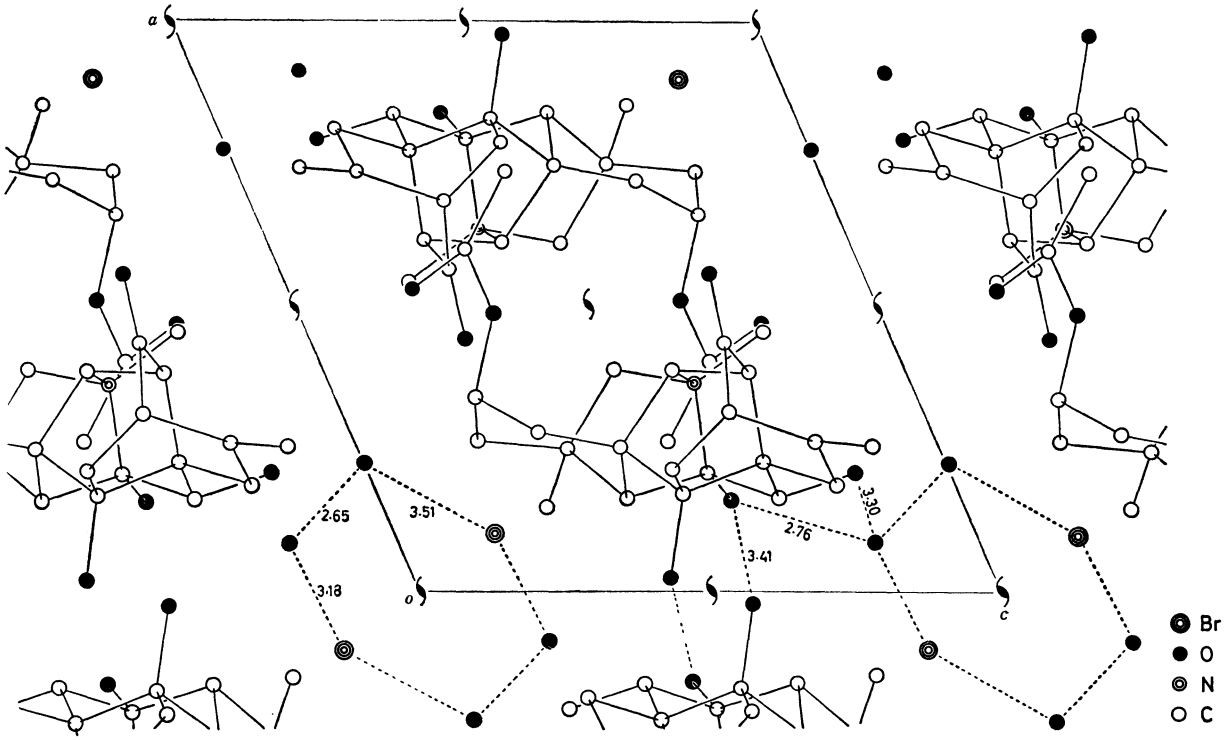


Fig. 6. The crystal structure projected along the b axis.

Table 7. Short intermolecular distances

Atom (position 1)	Atom	in position	Distance
	C···C shorter than 4.00 Å		
C(18)	C(16)	*4*	4.00 Å
C(18)	C(15)	*4*	3.66
C(18)	C(17)	*4*	3.86
C(23)	C(17)	*6*	3.42
	C···O shorter than 3.50 Å		
C(11)	OW(1)	*1*	3.43
O(3)	C(3)	*2*	3.43
C(19)	O(5)	*5*	3.32
C(23)	O(6)	*5*	3.44
C(18)	O(5)	*5*	3.41
	Br^-···C shorter than 4.00 Å		
Br	C(11)	*1*	3.93
C(17)	Br	*2*	3.82
C(7)	Br	*4*	3.67
C(22)	Br	*5*	3.93

Atom (position 1)	Atom	in position	Distance
	Br^-···O shorter than 4.00 Å		
Br	OW(1)	*1*	3.18
OW(2)	Br	*3*	3.51
O(3)	Br	*4*	3.26
	O···O shorter than 4.00 Å		
O(4)	OW(1)	*1*	2.78
OW(2)	OW(1)	*1*	2.65
O(3)	OW(1)	*4*	3.30
O(2)	O(4)	*4*	3.41
O(2)	OW(1)	*4*	2.76
Position[a)]	General coordinates		
1	x,	y,	z
2	x,	y,	$1+z$
3	$\bar{x}$,	$\frac{1}{2}+y$,	$\bar{z}$
4	$\bar{x}$,	$\frac{1}{2}+y$,	$1-z$
5	$1-x$,	$\frac{1}{2}+y$,	$1-z$
6	$1-x$,	$\frac{1}{2}+y$,	$2-z$

a) These are also indicated in Fig. 5.

The UV spectrum of this compound shows a somewhat higher intensity at 295 nm than that of normal saturated ketones.[5] This may correlate with the distance between, and the relative orientation of, the carbonyl and the exocyclic methylene groups; the C(13)···C(16) distance is 2.46 Å ,and the tilt of the C=O bond with respect to the C=C bond is 62°.

The packing diagrams of the crystal viewed along the a and b axes are shown in Figs. 5 and 6 respectively. The intermolecular distances are listed in Table 7.

All the C···C intermolecular distances can be considered to be normal: only four of them are shorter than 4 Å, the shortest being 3.42 Å of the C(sp^3)···C(sp^2) approach shown in Fig. 5. The closest C···O distance is 3.32 Å ,while the Br^-···C distances are all larger than 3.67 Å. The close Br^-···O and O···O approaches are also given in Fig. 5, suggesting that the hydrogen bonds may play an important role in the packing. The shortest N^+···Br^- distance is 5.09 Å, which might indicate no simple cation-anion interaction in the crystal structure.

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