Acta Cryst. (1965). **19**, 417

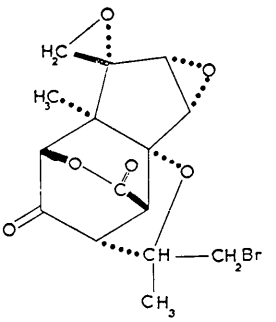
The Crystal Structure of α-Bromo-isotutinone at −150 °C

BY M. F. MACKAY
Department of Chemistry, University of Melbourne, Melbourne, Australia
AND A. MCL. MATHIESON
Chemical Physics Division, C.S.I.R.O., Chemical Research Laboratories, Melbourne, Australia

(*Received* 29 *December* 1964)

α-Bromo-isotutinone crystallizes in the orthorhombic space group $P2_12_12_1$ with $a=7{\cdot}35$, $b=14{\cdot}06$, $c=28{\cdot}06$ Å, at −150 °C, $Z=8$, 2 molecules in the asymmetric unit. Structure analysis based only on $h0l$, $0kl$, $1kl$ and $2kl$ was initiated by means of the heavy atoms, progressed with generalized Patterson projections about a, and was refined by difference, normal and generalized electron-density projections to an R index of 0·16.

(I)



The structure (I) found for this compound is in agreement with the structure found by Craven for the corresponding alcohol, α-bromo-isotutin.

Introduction

α-Bromo-isotutinone, $C_{15}H_{15}O_6Br$, is a derivative of tutin, $C_{15}H_{15}O_6$, the poisonous constituent of the New Zealand species of *Coriaria*, first isolated by Easterfield & Aston (1901). With picrotoxinin $C_{15}H_{16}O_6$, coriamyrtin, $C_{15}H_{18}O_5$ and mellitoxin, $C_{15}H_{18}O_7$, tutin forms a group of compounds similar in structure and physiological properties. The chemistry of these bitter principles has been studied extensively, leading in the case of picrotoxinin to the elucidation of its structure by Conroy (1951, 1957), while the crystal structure analysis of α_1-bromo-picrotoxinin by Craven (1960, 1962) assisted in defining many of the structural details in this group.

For the coriamyrtin series, structural proposals were made originally by Kariyone & Okuda (1953), these being replaced more recently by modified conclusions of Okuda & Yoshida (1964).

Structures have been proposed for tutin by Kariyone & Okuda (1953) and for tutin and its derivatives by Browne, Johns & Markham (1961) and by Johns & Markham (1961). X-ray analysis of α-bromo-isotutinone was undertaken to assist in establishing the structure of tutin. While the present analysis was nearing completion, we were informed by Dr Craven that he had carried out a three-dimensional analysis of the corresponding alcohol, α-bromo-isotutin (Craven, 1963, 1964). The results of this analysis of the keto compound are in essential agreement with those of the alcohol, and provide corroborative evidence which should aid in defining configurational and conformational details in the isotutin and, less directly, the tutin group.

A preliminary report of our result has been presented (Mackay & Mathieson, 1963).

Experimental

The crystals, colourless needles, were supplied by Dr R. B. Johns of the Chemistry Department, University of Melbourne, the material being that referred to earlier (Johns & Markham, 1961). In the preparation, the oxidative step, α-bromo-isotutin to α-bromo-isotutinone, was apparently not complete, with the result that a proportion of α-bromo-isotutin was incorporated in the crystals. The significance of this incomplete reaction on the interpretation of our results was only appreciated on completion of the X-ray analysis.

The unit-cell parameters were determined against a standard (Ag, $a=4{\cdot}0776$ Å) at *ca.* −150 °C, the density being determined (at room temperature) in a mixture of chloroform and bromoform. α-Bromo-isotutinone, $C_{15}H_{15}O_6Br$, is orthorhombic, $a=7{\cdot}35$, $b=14{\cdot}06$, $c=28{\cdot}06$ Å, $U=2910$ Å^3, $D_m=1{\cdot}69$, $D_x=1{\cdot}69$ for $Z=8$. The space group is $P2_12_12_1$ from systematic ex-

tinctions, the asymmetric unit being therefore two molecules.

The intensity data were recorded with filtered Cu $K\alpha$ radiation at −150 °C with the use of a low-temperature adaptor, in combination with a high-intensity X-ray source, the experimental conditions being as in Fridrichsons & Mathieson (1962). Equi-inclination Weissenberg photographs with multiple-film packs were recorded for the 0-, 1- and 2-layers about [100] and the 0-layer about [010]. For each layer, two packs of four films were exposed. Intensities were estimated visually against a set of timed exposures of a single reflexion, 1630 of 1860 possible terms being measured, ranging in relative intensity from 1 to 5100 (Table 1). Calculations were carried out on the University of Sydney computer SILLIAC (Freeman, 1957, 1958). Scattering factors employed in the calculation of structure factors were those of Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Veenendaal (1955) for C and O and of Thomas & Umeda (1957) for Br. No correction factors for absorption were applied. Scale factors and average temperature factors were determined from Wilson-type plots.

Table 1. *Comparison of number N_{obs} of terms observed and number N_{theor} theoretically observable in the respective layers*

R is the final value of the reliability index for each layer. Terms below the limit of observation were set at 3.

	N_{obs}	N_{theor}	R
$0kl$	428	521	0·14
$1kl$	487	543	0·16
$2kl$	481	522	0·17
$h0l$	234	274	0·17

Structure analysis

The x, y, z parameters of the two Br atoms in the asymmetric unit were derived from generalized Patterson functions (Cochran & Dyer, 1952) for the 0-, 1- and 2-layers about [100] with the aid of a sharpened Patterson synthesis, $P(0kl)$, which, by its improved resolution was useful in the selection of the Br–Br vectors.

With phases based on the contributions of the Br atoms and excluding terms for which $S_{B_r} < 0{\cdot}15$ of its maximum value, normal ($0kl$) and generalized ($1kl$ and $2kl$) Fourier syntheses were calculated, 1055 terms being included in these summations.

Attempt was made to derive from the cosine and sine compounds of the generalized Fourier syntheses the existence of the light atoms and an approximate estimate of their x parameters. With only 0-, 1- and 2-layers, the process, however, was by no means decisive. To extract the main features in a non-subjective manner, modulus projections (Fridrichsons & Mathieson, 1955) of the 1- and 2-layers were prepared by combination of the respective cosine and sine components. Since these modulus projections are effectively equivalent to the 0-layer projection, they were combined with it, to yield the maximum information regarding the structure in projection down a, the result being given in Fig. 1. Initially an attempt was made to improve this, the main projection, using where possible the generalized cosine and sine components to obtain approximate x parameters. In this projection, one region (later allocated to molecule B of the asymmetric unit) had a distribution of peaks which could, at this stage, be plausibly interpreted as atomic. With twenty-one such peaks taken as carbon and the two Br atoms, calculation of structure amplitudes yielded $R = 0{\cdot}42$ and the resultant Fourier and difference Fourier syntheses indicated correction of some allocations. However, certain features (taken in conjunction with the evidence of the generalized Fourier syntheses) appeared to be reasonably definite and rational, *e.g.* the lactone group and keto group in molecule B.

At this stage, it was possible to recognize in the projection that the overall distribution contained two re-

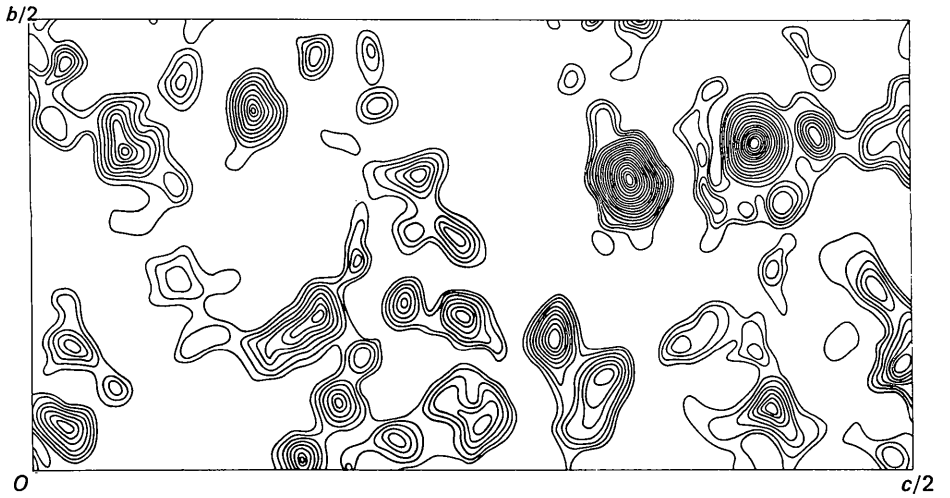


Fig. 1. Combination of the 0-layer electron-density [100] projection and the modulus projections derived from the 1- and 2-layer data.

gions which showed great similarity, and had the same relative disposition with respect to each Br atom. One region was rotated relative to the other, and had minor variations indicative of the same fundamental distribution in three-dimensions but slightly tilted with respect to [100]. It appeared likely that these two distributions represented the two molecules of the asymmetric unit as viewed along the *a* axis, one being at a slightly different orientation relative to the *a* axis. We could therefore assume that the two molecules were identical to a first approximation and this redundancy proved useful in the allocation of atom sites. On this basis, the main projection was refined by Fourier and difference procedures, five atoms of each molecule being differentiated as oxygen, and the index $R(0kl)$ was reduced to 0·19. Refinement of the $1kl$ and $2kl$ data in parallel with the 0-layer data established the three-dimensional skeletons of the two molecules except for O(2), O(3) and C(14), whose precise three-dimensional siting in respect of their x parameters re-

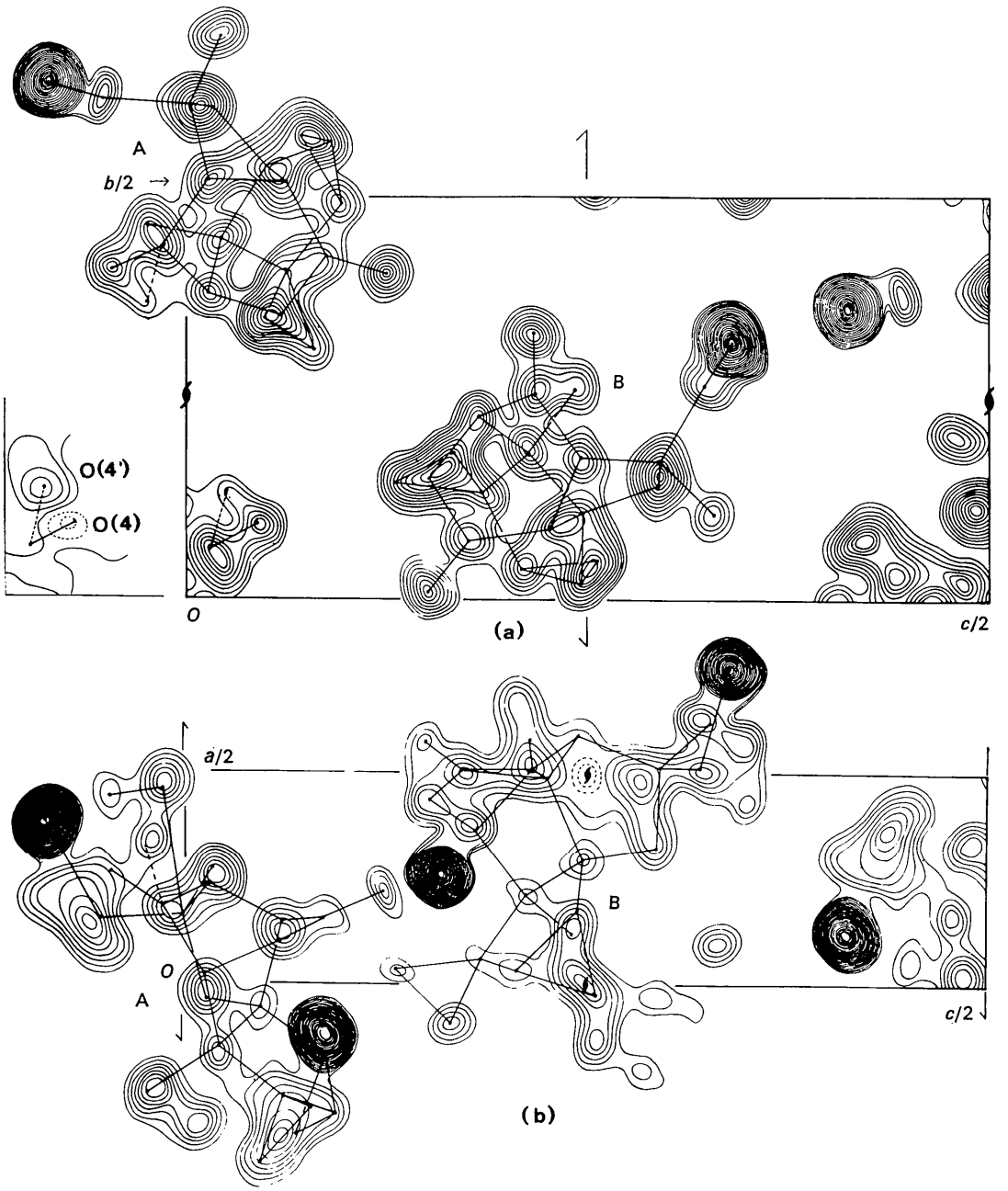


Fig. 2. Final electron-density distributions projected along (*a*) the *a* axis. The insert to the left is the portion of the difference map showing the location of O(4*A*) and O(4′*A*), site O(4*A*) having been assumed 100% occupied. (*b*) the *b* axis.

Table 2. *Atomic parameters of the asymmetric unit*

Atom (molecule *A*)	*x/a*	*y/b*	*z/c*
Br	0·116	0·3594	0·4125
C(1)	0·853	0·448	0·022
C(2)	0·019	0·381	0·013
C(3)	0·672	0·063	0·016
C(4)	0·762	0·020	0·487
C(5)	0·856	0·017	0·438
C(6)	0·056	0·034	0·452
C(7)	0·244	0·034	0·024
C(8)	0·341	0·384	0·499
C(9)	0·350	0·378	0·446
C(10)	0·734	0·198	0·481
C(11)	0·169	0·069	0·411
C(12)	0·694	0·492	0·095
C(13)	0·734	0·406	0·063
C(14)	0·709	0·308	0·080
C(15)	0·153	0·425	0·087
O(1)	0·038	0·109	0·485
O(2)	0·353	0·075	0·430
O(3)	0·578	0·347	0·048
O(4)	0·759	0·092	0·047
O(4′)	0·819	0·133	0·025
O(5)	0·216	0·406	0·124
O(6)	0·097	0·351	0·059

Table 2 (*cont.*)

Atom (molecule *B*)	*x/a*	*y/b*	*z/c*
Br	0·744	0·3203	0·3406
C(1)	0·206	0·183	0·213
C(2)	0·359	0·228	0·181
C(3)	0·506	0·256	0·217
C(4)	0·588	0·177	0·246
C(5)	0·484	0·088	0·227
C(6)	0·291	0·108	0·248
C(7)	0·116	0·261	0·242
C(8)	0·512	0·172	0·296
C(9)	0·519	0·266	0·323
C(10)	0·613	0·106	0·329
C(11)	0·172	0·019	0·245
C(12)	0·031	0·038	0·209
C(13)	0·056	0·131	0·184
C(14)	0·034	0·145	0·132
C(15)	0·506	0·070	0·175
O(1)	0·322	0·141	0·295
O(2)	0·975	0·047	0·257
O(3)	0·906	0·181	0·166
O(4)	0·578	0·333	0·216
O(5)	0·569	0·009	0·150
O(6)	0·431	0·150	0·152

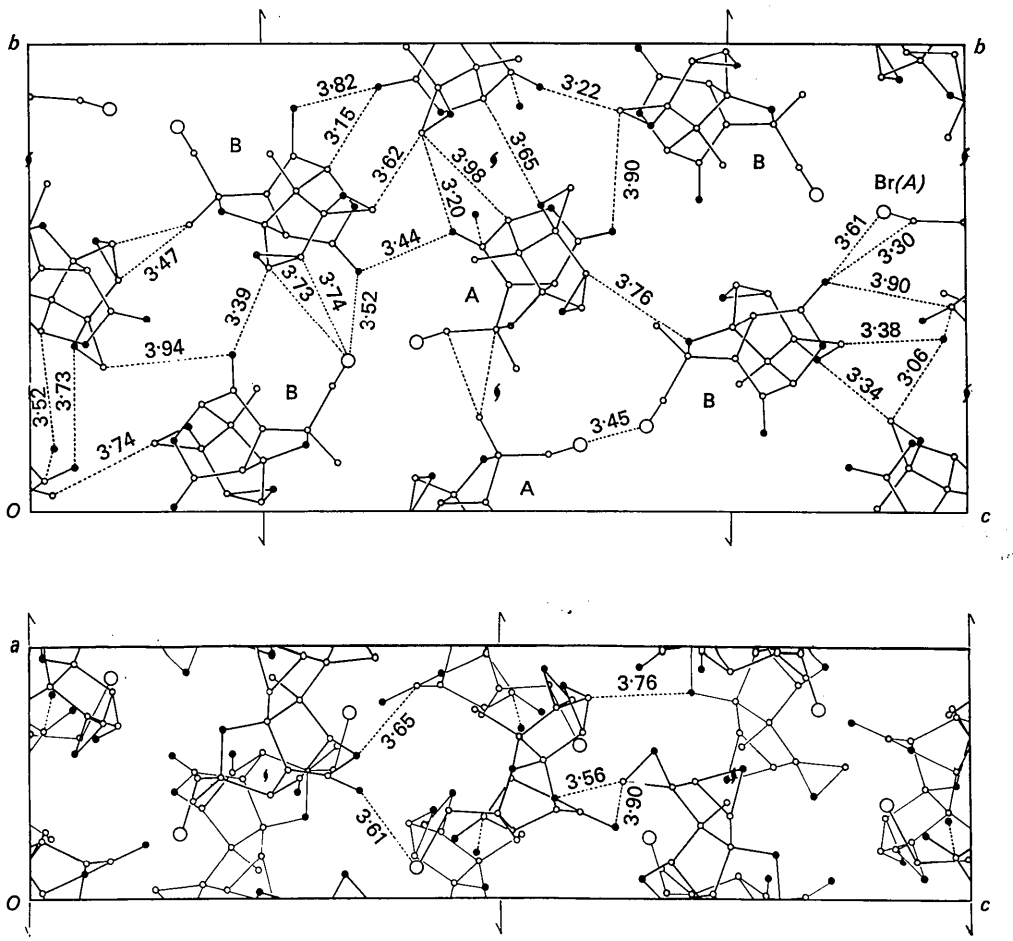


Fig. 3. Line diagrams of the structure as viewed along (*a*) the *a* axis and (*b*) the *b* axis. Larger open circles, Br; small open circles, C; small filled circles, O.

mained uncertain in both molecules. So far as the evidence in projection was concerned O(3) and C(14) lay close together but were separated from O(2) by more than 3 Å. It was evident that O(2), O(3) and C(14) could not be assembled to form a lactone group despite the earlier contention of Browne, Johns & Markham (1961) that 'the dilactone nature of tutin is demonstrated beyond reasonable doubt'. The possibility of the existence of epoxide rings had been considered by these authors and discarded in line with the conclusions mentioned above. A puzzling piece of evidence in relation to the crystals used for this anal-

Table 3. *Comparison of measured and calculated structure amplitudes*

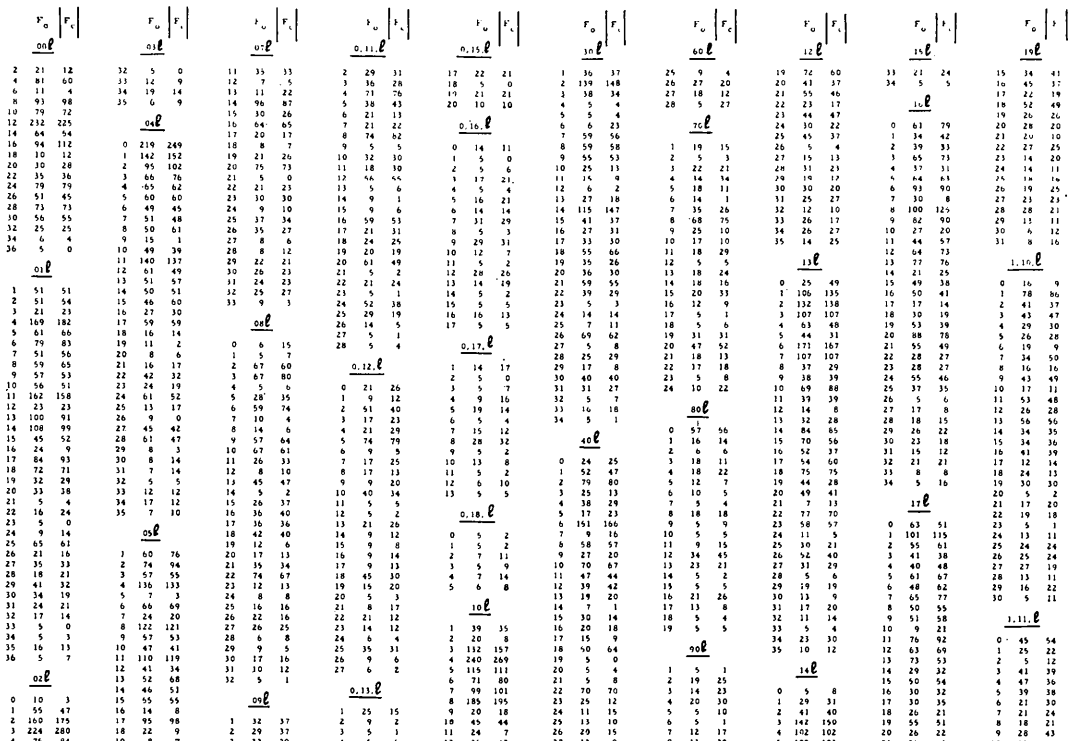
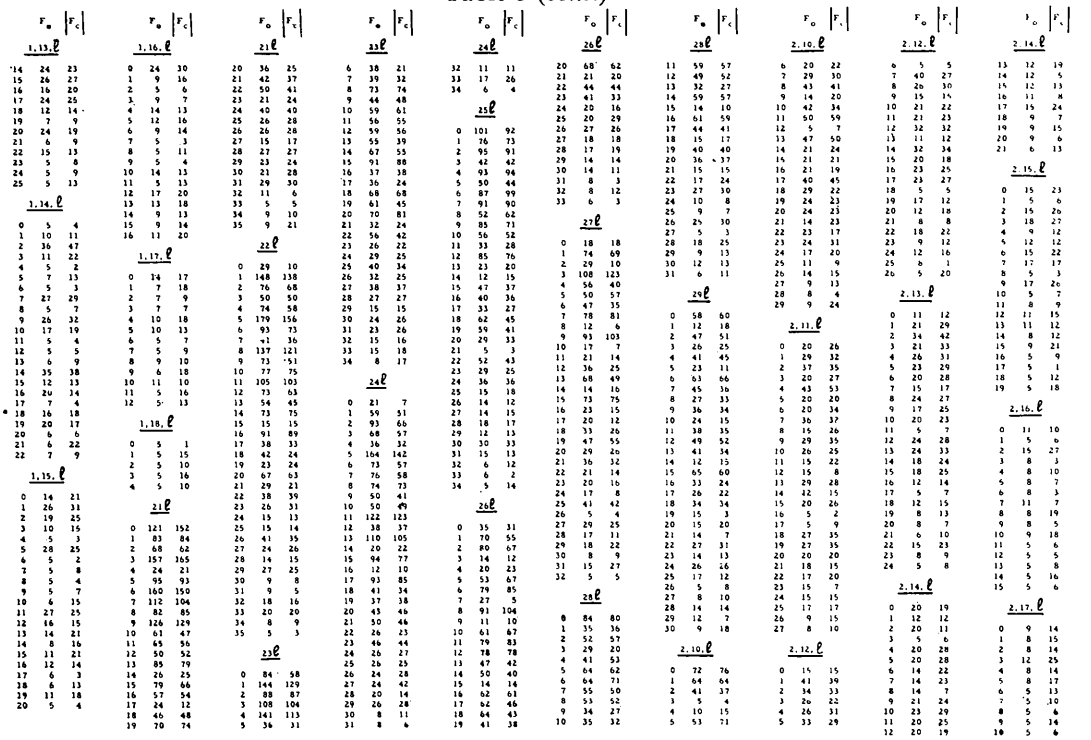


Table 3 (*cont.*)



ysis was that an infrared examination indicated the presence of a hydroxyl group. It was not possible to resolve the problem of the three-dimensional location of O(2), O(3) and C(14) from the data already dealt with, so the *b*-axis projection was investigated and this resolved the ambiguities showing that O(3) and C(14) formed a spiro epoxide ring with C(13), while O(2) formed a second epoxide ring linked, 1,2 with C(11) C(12).

Final steps in refinement were not quite straightforward because of an electron-density peak adjacent to molecule A of the asymmetric unit – a feature which had been persistent from the beginning. Difference syntheses based on 100% occupation of site O(4) by an oxygen atom yielded a negative peak there, and a positive peak at location 4′ (Fig. 2*a*). This could only be accounted for satisfactorily in terms of the existence of α-bromo-isotutin in molecule *A* site to the extent of approximately 25%. This was in accord with the infrared evidence for the hydroxyl group and was explicable in terms of the oxidative step in the preparation of α-bromo-isotutinone from α-bromo-isotutin being only partially complete. In accord with this argument, the configuration around C(3) of O(4′) relative to C(2) and C(4) is exactly the same as that given for α-bromo-isotutin by Craven (1963, 1964). In a sense, the present analysis constitutes a solution for both α-bromo-isotutinone and α-bromo-isotutin.

The electron-density projections down [100] and [010] are shown in Fig. 2(*a*) and (*b*) respectively, while corresponding line diagrams are given in Fig. 3. Atomic parameters are listed in Table 2, comparison of observed with calculated structure factors in Table 3. An isotropic temperature factor $B=2{\cdot}80$ was used for $0kl$, $1kl$ and $2kl$ and $B=2{\cdot}70$ for $h0l$. For Br(B) an

Table 4(*a*). *Bond lengths for the two molecules in the asymmetric unit*

	Molecule *A*	Molecule *B*	Average
Br–C(9)	1·98 Å	1·99 Å	1·98(5) Å
C(9)–C(8)	1·50	1·51	1·50(5)
C(8)–C(10)	1·51	1·52	1·51(5)
C(8)–C(4)	1·51	1·51	1·51
C(4)–C(5)	1·52	1·54	1·53
C(4)–C(3)	1·52	1·51	1·51(5)
C(3)–O(4)	1·21	1·21	1·21
C(3)–C(2)	1·56	1·52	1·54
C(2)–O(6)	1·47	1·46	1·46(5)
O(6)–C(15)	1·36	1·39	1·37(5)
C(15)–O(5)	1·20	1·20	1·20
C(15)–C(5)	1·48	1·48	1·48
C(5)–C(6)	1·57	1·57	1·57
C(2)–C(1)	1·56	1·57	1·56(5)
C(1)–C(6)	1·55	1·56	1·55(5)
C(6)–O(1)	1·41	1·40	1·40(5)
C(1)–C(7)	1·54	1·52	1·53
C(1)–C(13)	1·55	1·55	1·55
C(13)–C(12)	1·54	1·51	1·52(5)
C(12)–C(11)	1·49	1·48	1·48(5)
C(11)–C(6)	1·51	1·54	1·52(5)
C(12)–O(2)	1·40	1·42	1·41
C(13)–O(3)	1·47	1·40	1·43(5)
C(13)–C(14)	1·48	1·49	1·48(5)
O(2)–C(11)	1·45	1·46	1·45(5)
C(14)–O(3)	1·42	1·45	1·43(5)
C(3)–O(4′)	1·48	—	—
C(8)–O(1)	1·49	1·48	1·48(5)

Table 4(*b*). *Bond angles for the two molecules in the asymmetric unit*

	Molecule *A*	Molecule *B*	Average
Br–C(9)–C(8)	116°	118°	117°
C(9)–C(8)–O(1)	103	107	105
C(9)–C(8)–C(10)	110	104	107
C(9)–C(8)–C(4)	109	114	111(·5)
C(8)–O(1)–C(6)	109	106	107(·5)
C(8)–C(4)–C(5)	95	97	96
C(8)–C(4)–C(3)	115	113	114
O(1)–C(8)–C(10)	118	108	113
O(1)–C(8)–C(4)	103	110	106(·5)
O(1)–C(6)–C(11)	108	114	111
O(1)–C(6)–C(1)	109	115	112
O(1)–C(6)–C(5)	101	106	103(·5)
C(10)–C(8)–C(4)	114	115	114(·5)
C(4)–C(5)–C(6)	102	99	100(·5)
C(4)–C(3)–C(2)	110	116	113
C(4)–C(3)–O(4)	117	120	118(·5)
C(5)–C(6)–C(11)	113	110	111(·5)
C(5)–C(6)–C(1)	113	104	108(·5)
C(5)–C(15)–O(5)	129	136	132(·5)
C(5)–C(15)–O(6)	113	106	109(·5)
C(15)–O(6)–C(2)	114	120	117
C(15)–C(5)–C(6)	107	120	113(·5)
C(4)–C(5)–C(15)	115	115	115
O(5)–C(15)–O(6)	117	118	117(·5)
O(6)–C(2)–C(3)	108	108	108
O(6)–C(2)–C(1)	110	106	108
C(2)–C(3)–O(4)	127	122	124(·5)
C(2)–C(1)–C(7)	112	109	110(·5)
C(2)–C(1)–C(13)	109	113	111
C(2)–C(1)–C(6)	102	111	106(·5)
C(3)–C(2)–C(1)	109	104	106(·5)
O(2)–C(11)–C(12)	57	57	57
O(2)–C(11)–C(6)	106	108	107
O(2)–C(12)–C(11)	61	63	62
O(2)–C(12)–C(13)	114	113	113(·5)
C(11)–C(12)–C(13)	113	113	113
C(11)–O(2)–C(12)	60	59	59(·5)
C(12)–C(11)–C(6)	104	106	105
C(12)–C(13)–C(1)	104	106	105
C(12)–C(13)–C(14)	122	124	123
C(12)–C(13)–O(3)	117	121	119
C(13)–C(1)–C(7)	112	108	110
C(13)–C(1)–C(6)	102	106	104
C(13)–O(3)–C(14)	62	63	62(·5)
C(13)–C(14)–O(3)	61	57	59
C(14)–C(13)–O(3)	57	59	58
C(14)–C(13)–C(1)	132	122	127
C(1)–C(13)–O(3)	107	119	113
C(3)–C(4)–C(5)	107	105	106
C(1)–C(6)–C(11)	110	108	109
C(7)–C(1)–C(6)	118	110	114
C(4)–C(3)–O(4′)	112		
C(2)–C(3)–O(4′)	105		

approximation to anisotropic vibration with the limited computing facilities available was made by splitting the single site into two equally occupied sites (i) $y=0{\cdot}3305$, $z=0{\cdot}3402$, and (ii) $y=0{\cdot}3102$, $z=0{\cdot}3410$. Atoms O(4) and O(4′) were included as 0·75 and 0·25 respectively of an oxygen atom. The resultant $R(0kl)=0{\cdot}14$, $R(1kl)=0{\cdot}16$, $R(2kl)=0{\cdot}17$ and $R(h0l)=0{\cdot}17$, unobserved terms being allocated a value of three for these estimations.

Bond lengths and angles in molecules *A* and *B* with the mean values are listed in Table 4, the latter being also given in Fig. 4(*b*) and (*c*), while approach distances are in Table 5 and Fig. 3.

Table 5. *Intermolecular approach distances*

Br(*B*)–O(5*B*)	3·52 Å	O(6*B*)–O(4*A*)	3·90 Å
Br(*B*)–C(15*B*)	3·98	C(2*B*)–O(5*A*)	3·15
Br(*B*)–C(12*B*)	3·74	O(4*B*)–O(5*A*)	3·82
Br(*B*)–C(11*B*)	3·73	O(4*B*)–C(11*B*)	3·39
Br(*B*)–Br(*A*)	3·45	O(4*B*)–C(14*A*)	3·94
C(9*B*)–O(5*B*)	3·58	C(14*B*)–C(7*A*)	3·74
O(1*B*)–C(12*A*)	3·76	C(7*B*)–O(5*A*)	3·96
O(1*B*)–C(11*A*)	3·60	O(3*B*)–O(4*A*)	3·74
O(1*B*)–O(2*A*)	3·90	O(3*B*)–C(14*A*)	3·34
C(10*B*)–O(5*A*)	3·36	C(14*B*)–C(14*A*)	3·62
C(10*B*)–C(15*B*)	3·90	C(14*B*)–O(5*A*)	3·90
C(10*B*)–C(12*A*)	3·47	C(14*B*)–O(6*A*)	3·56
C(10*B*)–O(2*A*)	3·44	C(14*B*)–O(4*A*)	3·22
C(10*B*)–C(5*A*)	3·77	C(9*A*)–C(10*A*)	3·95
C(5*B*)–O(4*B*)	3·97	C(8*A*)–C(10*A*)	3·94
O(5*B*)–O(4*B*)	3·44	O(1*A*)–C(10*A*)	3·20
O(5*B*)–Br(*A*)	3·61	C(2*A*)–C(14*A*)	3·98
O(5*B*)–C(3*A*)	3·90	C(2*A*)–O(3*A*)	3·65
O(5*B*)–C(9*A*)	3·30	C(3*A*)–C(14*A*)	3·90
O(6*B*)–C(15*A*)	3·65	O(4*A*)–C(14*A*)	3·20
		O(4*A*)–O(3*A*)	3·73

Discussion

Analysis has shown that the two molecules of α-bromo-isotutinone in the asymmetric unit are to the first order identical in all conformational detail. In the majority of available examples of molecular multiplicity in the asymmetric unit this identity is to be expected where restrictions limit the possibility of alternative conformations, *e.g.* iodoacetate of epilimonol (Arnott, Davie, Robertson, Sim & Watson, 1960) and jacobine bromohydrin (Fridrichsons, Mathieson & Sutor, 1963). Where conformational alternatives exist for parts if not for the whole molecule, these alternatives are utilized on occasion and one molecule differs from another in a single crystal, *e.g.* ebelin lactone (Barclay, Eade, Simes, Simes & Taylor, 1963) or alternative conformations exist in closely allied derivatives, *e.g.* isoleucine (Bijvoet & Trommel, 1954). From the identity of the two molecules *A* and *B*, we may conclude that the molecule of α-bromo-isotutinone is an inflexible molecule and this is evident when we consider its structure (Fig. 4) which involves a rigid framework of ring systems. The bicyclic ring system C(6)C(1)C(2)C(3)O(4)C(4)C(5)C(15)O(5)O(6) has attached to it at C(1)C(6) a five-membered ring with two subsidiary epoxide rings, one spiro at C(13) and the other 1,2 at C(11)C(12). Another five-membered ring links across C(4) and C(6) with substituents C(10) and C(9)Br at C(8). A methyl group C(7) is attached to C(1). The only mobile skeletal atom is Br and its possible relocation is severely restricted by the close proximity of O(4) (molecule *A*, 3·60 Å, *B*, 3·78 Å) and C(10), (molecule *A*, 3·22 Å, *B*, 3·32 Å).

Because of the identity of the two molecules, the mean values of molecular dimensions (Fig. 4) derived from the two molecules may be regarded as slightly more reliable than the individual values. The C–C bond lengths are normal except for those in the epoxide rings which are 1·48 Å, slightly smaller than normal but in accord with the limited observations available on epoxides, the associated C–O bond lengths being

also correspondingly reduced to 1·43 Å. The lactone group exhibits the expected planarity and marked dissymmetry in C–O bond lengths, C(15)–O(6) = 1·37 Å, C(2)–O(6) = 1·46 Å (Mathieson & Taylor, 1961). Bond angles [Fig. 4(*c*)] are in accord with the strains arising from the ring linkages. Thus the closure of C(4) and C(6) by C(8)O(1) produces torque around C(1)C(6) of the bonds associated with C(1) and C(6), and the five-membered ring C(1)C(6)C(11)C(12)C(13) which might be expected to be planar due to the epoxide ring C(11)C(12)O(2) is found to be slightly distorted from planarity. Atoms C(6), C(11), C(12), C(13) are coplanar to within ±0·05 Å, while atom C(1) is approximately 0·5 Å from this plane on the same side as O(2).

The crystal structure is based on layers of *A* molecules interleaved with layers of *B* molecules, the layers lying parallel to (001) (Fig. 3). Approach distances are in the range of normal van der Waals values, the smaller values involving an oxygen atom. One close approach between Br atoms is 3·45 Å which is rather small but short values have been noted also in 1,4-dibromocycl(3,2,2)azine (Hanson, 1961).

The conventional formulation for α-bromo-isotutinone is given in Fig. 5(*a*) and that for isotutinone in Fig. 5(*b*). The structure of the carbon skeleton is in accord with the earlier proposals of Johns & Markham (1961) for isotutinone but the complete structure differs from their proposal, the difference being that, whereas they had arrived at the conclusion that the compound must be a dilactone, the X-ray analysis

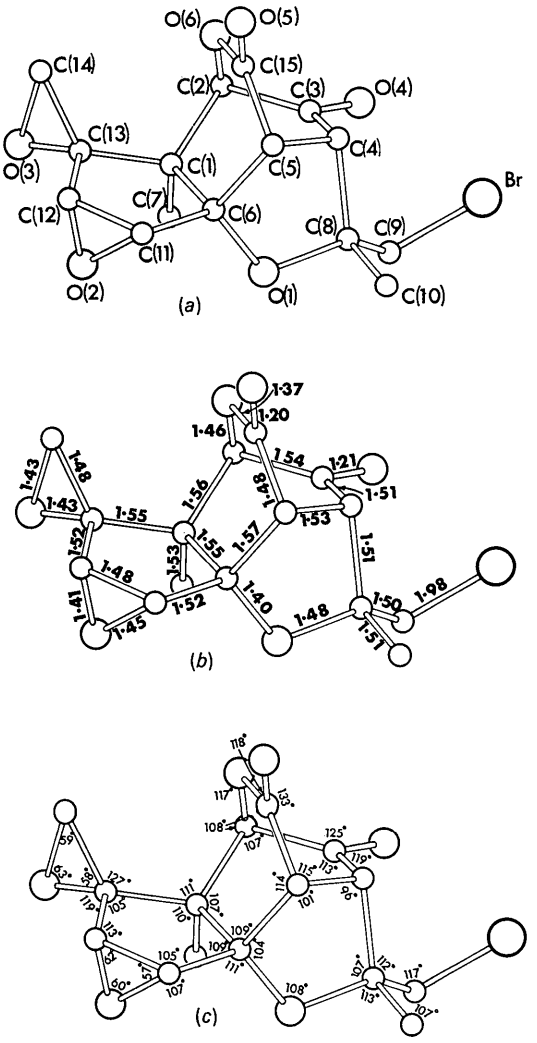


Fig. 4. Molecular skeleton of α-bromo-isotutinone. (*a*) The numbering of the atoms. (*b*) The average bond lengths. (*c*) The average bond angles.

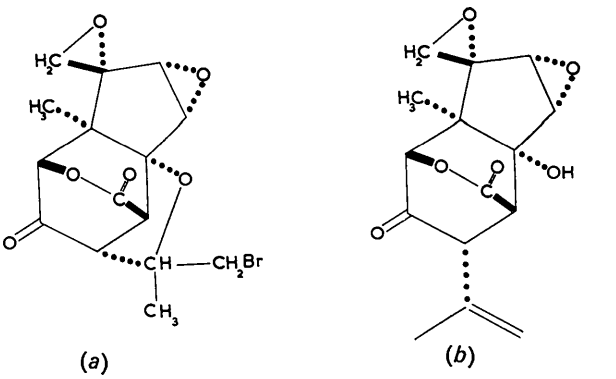


Fig. 5. The chemical formula for (*a*) α-bromo-isotutinone and that deduced for (*b*) iso-tutinone.

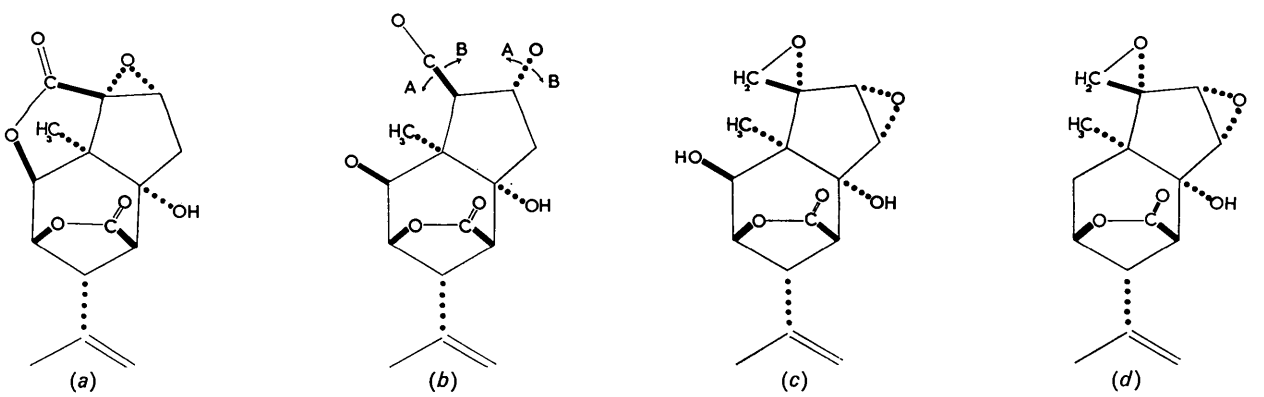


Fig. 6. The basic structure (*b*) from which picrotoxinin (*a*) can be derived by concerted moves *A* and tutin (*c*) by moves *B*. The structure proposed for coriamyrtin by Kariyone & Yoshida (1964) is shown in (*d*).

reveals that the atoms ascribed to the lactone function are involved instead in two epoxide rings. The structural results for both α-bromo-isotutinone (Mackay & Mathieson, 1963) and for α-bromo-isotutin (Craven, 1963) indicate the need for caution in the interpretation of infrared spectra with regard to oxygen functional groups since diagnostic features for epoxide rings are not well defined. Indeed for tutin the possible presence of epoxide rings first proposed by Kariyone & Okuda (1953) had been carefully considered by Browne, Johns & Markham (1961) and they concluded that the presence of epoxide rings could not be substantiated by the available infrared and chemical evidence. The failure to reveal at least one of the epoxide rings by chemical reaction is unexpected. C(11)C(12)O(2) would be protected from rearward attack but C(13)C(14)O(3) would appear capable of reaction.

If, as appears most probable, the isotutin series arises from the tutin series by the isomerization of the lactone group from C(5)–C(3) to C(5)–C(2) and no other major structural change occurs then the close structural relationship of the tutin and picrotoxinin series can be indicated by Fig. 6. The molecular skeleton [Fig. 6(*b*)] is basic to both series and can be converted by the concerted moves *A* to picrotoxinin [Fig. 6(*a*)] or alternative moves *B* to tutin [Fig. 6(*c*)]. If this be the case, the absolute configuration of both molecules is defined by that of α_1-bromo-picrotoxinin (Craven, 1958, 1962). Further the close relationship of coriamyrtin to these groups suggested that structurally it can be ascribed to a deoxygenated variant of Fig. 6(*b*) (Mackay & Mathieson, 1963). Okuda & Yoshida (1964) have re-appraised the earlier work and have substantiated this, concluding that coriamyrtin is as depicted in Fig. 6(*d*).

The authors are grateful to Dr R. B. Johns for the provision of crystals and for helpful discussion regarding the chemistry of the tutin and isotutin series. We wish to express our appreciation of Dr B. M. Craven's kindness in informing us of his analysis of α-bromo-isotutin and for his generous cooperation in the exchange of results. We also wish to thank Mr Fridrichsons for his assistance with the low-temperature exposures.

References

ARNOTT, S., DAVIE, A. W., ROBERTSON, J. M., SIM, G. A. & WATSON, D. G. (1960). *Experientia,* **16**, 49.
BARCLAY, G. A., EADE, R. A., SIMES, H. V., SIMES, J. J. H. & TAYLOR, J. C. (1963). *Chem. and Ind.*, p. 1206.
BERGHUIS, J., HAANAPPEL, IJ. M., POTTERS, M., LOOPSTRA, B. O., MACGILLAVRY, C. H. & VEENENDAAL, A. L. (1955). *Acta Cryst.* **8**, 478.
BIJVOET, J. M. & TROMMEL, J. (1954). *Acta Cryst.* **7**, 703.
BROWNE, G. F., JOHNS, R. B. & MARKHAM, K. R. (1961). *J. Chem. Soc.*, p. 3000.
COCHRAN, W. & DYER, H. B. (1952). *Acta Cryst.* **5**, 634.
CONROY, H. (1951). *J. Amer. Chem. Soc.* **73**, 1889.
CONROY, H. (1957). *J. Amer. Chem. Soc.* **79**, 5550.
CRAVEN, B. M. (1960). *Tetrahedron Letters,* No. 19, 21.
CRAVEN, B. M. (1962). *Acta Cryst.* **15**, 387.
CRAVEN, B. M. (1963). *Nature, Lond.* **197**, 1193.
CRAVEN, B. M. (1964). *Acta Cryst.* **17**, 396.
EASTERFIELD, T. H. & ASTON, B. C. (1901). *J. Chem. Soc.* **79**, 120.
FREEMAN, H. C. (1957). *Aust. J. Chem.* **10**, 95.
FREEMAN, H. C. (1958). *Aust. J. Chem.* **11**, 99.
FRIDRICHSONS, J. & MATHIESON, A. MCL. (1955). *Acta Cryst.* **8**, 761.
FRIDRICHSONS, J. & MATHIESON, A. MCL. (1962). *Acta Cryst.* **15**, 119.
FRIDRICHSONS, J., MATHIESON, A. MCL. & SUTOR, D. J. (1963). *Acta Cryst.* **16**, 1075.
HANSON, A. W. (1961). *Acta Cryst.* **14**, 124.
JOHNS, R. B. & MARKHAM, K. R. (1961). *J. Chem. Soc.* p. 3006.
KARIYONE, T. & OKUDA, T. (1953). *J. Pharm. Soc., Japan,* **73**, 930.
MACKAY, M. F. & MATHIESON, A. MCL. (1963). *Tetrahedron Letters,* No. 21, 1399.
MATHIESON, A. MCL. & TAYLOR, J. C. (1961). *Tetrahedron Letters,* No. 17, 590.
OKUDA, T. & YOSHIDA, T. (1964). *Tetrahedron Letters,* No. 9, 439. (Correction in *Tetrahedron Letters,* No. 12, 694).
THOMAS, L. H. & UMEDA, K. (1957). *J. Chem. Phys.* **26**, 293.