1046. *Salts of Amidines and Related Compounds. Part II.[1] An X-Ray Crystallographic Study of S-Methylthiouronium p-Chlorobenzoate: the Constancy of the Amidinium Carboxylate Grouping and its Importance for Protein Conformations.* ˙
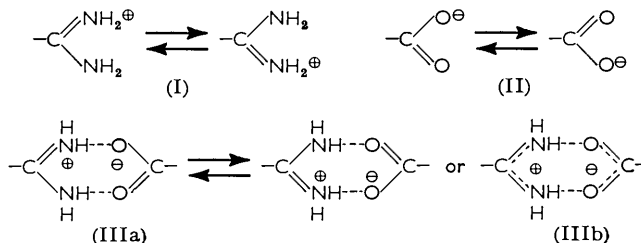
By (MRS.) OLGA KENNARD and JAMES WALKER.

A further review of the distribution of the melting points of S-arylmethyl-thiouronium salts of carboxylic acids has fortified the belief that a uniform mechanism underlies the capacity of substances containing the amidino-group to form characteristic crystalline salts with carboxylic acids. The mode of crystallisation previously predicted has been borne out by a three-dimensional X-ray crystallographic study of S-methylthiouronium p-chloro-benzoate.

A survey of recorded carbon–carbon bond lengths in mono- and 1,4-di-substituted benzene rings shows that greater apparent variation occurs in compounds in which anisotropic thermal movements have also been observed.

Other evidence bearing on the mode of crystallisation of amidinium salts of carboxylic acids is discussed, and the relevance of the present work to the participation of the guanidino-group of arginine in the maintenance of conformations in native proteins is noted.

IN a previous communication [1] one of us drew attention to the use of carboxylic acids for the characterisation of amidines unsubstituted in the amidino-group. This procedure was, of course, analogous with, and complementary to, the established use of S-benzyl-thiouronium salts for the characterisation of carboxylic acids, as the salt-forming amidino-group is common to both amidines and isothioureas. In considering this ready crystall-isation of the carboxylic acid salts of amidines and isothioureas, to which may be added isoureas and guanidines, it was noted that resonance in the cation (I) was complementary to that in the anion (II), and it was suggested that ionic bonds were formed simultaneously between the two oxygen atoms sharing the negative charge in the carboxylate ion and the two nitrogen atoms sharing the positive charge in the amidinium group. Furthermore, the coplanarity of the seven atoms comprising the amidinium group, arising as a conse-

quence of resonance stabilisation, led to the representation (III) for the amidine salt of a carboxylic acid, in which the seven atoms of the amidinium group, the three atoms of the ionised carboxyl group, and the respective atoms to which these groups are linked, *i.e.*, twelve atoms altogether, are coplanar and assume a relatively rigid configuration of mini-mum potential energy, the implicit hydrogen bonds being short and relatively strong. Such association *in solution* into doublet ion-pairs of a relatively rigid oriented type was considered to be the prelude to the formation of crystalline aggregates, which proceeded by hydrogen bonding between the lateral amidinium hydrogen atoms and the oxygen atoms of carboxylate groups in neighbouring doublet ion-pairs. A survey of the literature showed that the melting points of an extensive and heterogeneous range of S-benzyl-, 4-substituted S-benzyl-, and S-1-naphthylmethyl-thiouronium salts of carboxylic acids

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[1] Walker, *J.*, 1949, 1996; that paper is to be regarded as Part I.

covered only a small range of temperature, which suggested that the forces which held crystals of this type together were comparable in strength throughout the series and that the radicals attached to the $-S\cdot C(NH_2)\!:\!NH_2{}^{\oplus}$ and the $-C(\!:\!O)\cdot O^{\ominus}$ groups, respectively, made little or no contribution to the stability of the crystal. As purely chemical studies could not supply the proof of these suggestions, or show how hydrogen-bonding between the hypothetical doublet ion-pairs could be effected to give a three-dimensional structure, X-ray diffraction evidence was sought and is described below.

In the earlier work [1] the 193 known S-benzyl-, S-4-bromobenzyl-, S-4-chlorobenzyl-, and S-4-nitrobenzyl-thiouronium salts of carboxylic acids showed a mean melting point of 154° with a standard deviation of 18°, while the 149 known salts of the same bases with
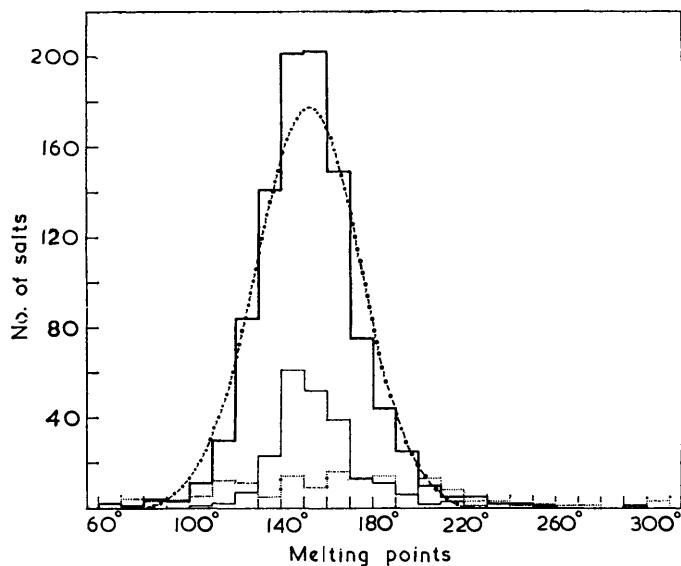
FIG. 1.　Distribution of m. p.s of arylmethylthiouronium salts of carboxylic and sulphonic acids.

—— Distribution of m. p.s (to end of 1959) of 998 S-benzyl- (772), S-4-bromobenzyl- (61), S-4-chlorobenzyl- (36), S-4-nitrobenzyl- (49), S-2,4-dinitrobenzyl- (34), S-1-naphthylmethyl- (42), and S-benzimidazol-2-ylmethyl-thiouronium (4) salts of carboxylic acids.

—— Distribution of m. p.s (to end of 1947) of 221 S-benzyl-, S-4-bromobenzyl-, S-4-chlorobenzyl-, S-4-nitrobenzyl-, and S-1-naphthylmethyl-thiouronium salts of carboxylic acids.

...... Distribution of m. p.s (to end of 1947) of 149 S-benzyl-, S-4-bromobenzyl-, S-4-chlorobenzyl-, and S-4-nitrobenzyl-thiouronium salts of sulphonic acids.

— · — · —　Theoretical normal curve for distribution of m. p.s of a sample of 998 salts having mean m. p. 152° with standard deviation 22°.

sulphonic acids showed a mean melting point of 165° with a standard deviation of 46°, indicating a less uniform pattern for the crystallisation of the salts formed with sulphonic acids. We have not taken our review of the salts of sulphonic acids further, but a large number of salts of carboxylic acids has been described in the interval. Up to the end of 1959, 1006 S-benzyl-, S-4-bromobenzyl-, S-4-chlorobenzyl-, S-4-nitrobenzyl-, S-2,4-dinitrobenzyl-, S-1-naphthylmethyl-, and S-benzimidazol-2-ylmethyl-thiouronium salts * had been described and the distribution of their melting points is analysed in Table 1 and in Fig. 1.

* These were traced through *Chemical Abstracts* and checked with the original literature sources whenever possible. Eight salts were omitted from further consideration, because either (i) melting points recorded by different observers showed considerable divergence, or (ii) poor analytical criteria were recorded, or (iii) a wide melting range was given.

TABLE 1.

Distribution of melting points of (A) S-benzyl-, (B) S-4-bromobenzyl-, (C) S-4-chloro-benzyl-, (D) S-4-nitrobenzyl-, (E) S-2,4-dinitrobenzyl-, (F) S-1-naphthylmethyl-, and (G) S-benzimidazol-2-ylmethyl-thiouronium salts of carboxylic acids, $RS \cdot C(:NH) \cdot NH_2, R' \cdot CO_2H$, showing the numbers of salts having melting points within the stated ranges.

M. p. range	A	B	C	D	E	F	G	Totals
60—70°	2	0	0	0	0	0	0	2
70—80	0	0	0	1	0	0	0	1
80—90	4	0	0	0	0	0	0	4
90—100	3	0	0	0	0	0	0	3
100—110	10	0	0	0	1	0	0	11
110—120	28	0	0	2	0	0	0	30
120—130	79	0	0	1	4	0	0	84
130—140	117	8	3	6	5	2	0	141
140—150	153	19	11	11	3	4	0	201
150—160	149	20	9	8	4	9	3	202
160—170	108	10	9	6	5	10	1	149
170—180	56	2	3	4	3	7	0	75
180—190	28	1	0	4	4	7	0	44
190—200	18	1	1	2	2	1	0	25
200—210	6	0	0	2	1	1	0	10
210—220	5	0	0	0	0	0	0	5
220—230	3	0	0	1	0	1	0	5
230—240	2	0	0	0	0	0	0	2
240—250	1	0	0	0	1	0	0	2
250—260	0	0	0	0	1	0	0	1
Over 260	0	0	0	1 *	0	0	0	1
Totals	772	61	36	49	34	42	4	998
Mean m. p.	150°	153°	156°	157°	162° (157° †)	168° (166° ‡)	—	152°
Standard deviation	22°	12°	13°	26°	33° (25° †)	18° (16° ‡)	—	22°

* M. p. 293°, omitted from statistical analysis. † Two salts of m. p. al   )° omitted.
‡ Salt of m. p. 220° omitted.

Table 1 shows the distribution of the melting points of these salts under the headings of the seven bases concerned and the aggregates are also given.   Except for the S-benz-imidazol-2-ylmethylthiouronium salts, where the sample size was insignificant, each column has been analysed statistically, and the degree of correspondence of the mean melting points for the benzyl-, S-4-bromobenzyl-, S-4-chlorobenzyl-, and S-4-nitrobenzyl-thiouronium salts is noteworthy.   The mean melting point (162°) of the S-2,4-dinitro-benzylthiouronium salts became of a similar order (157°) when two relatively high-melting salts were disregarded, illustrating the marked weighting effect of one or two isolated representatives on the wings on the statistical analysis.   The mean melting point (168°) calculated for the 42 S-1-naphthylmethylthiouronium salts was also higher than the general mean, and this could be due either to a real difference or to an accidental circum-stance of the fairly small number available for statistical analysis.   Fig. 1 shows the melting-point distribution for 998 salts of carboxylic acids in the form of a histogram and includes the results of the previous survey [1] for comparison; it also shows the calculated curve for a normal distribution of the sample size (998), mean (m. p. 152°), and standard deviation (22°) found experimentally.   The excellence of the fit of the theoretical normal distribution curve to the experimental results and the degree of symmetry of the latter about the mean are striking, and show clearly that a uniform mechanism underlies the crystallisation of these salts.   It should also be noted (Table 1) that, while the great majority were S-benzylthiouronium salts (772), five other bases were represented to significant extents; the carboxylic acids involved in the formation of these salts were, however, a completely heterogeneous series, as every available recorded salt of a carboxylic acid with these bases has been considered.   The uniformity of crystalline pattern we therefore consider to be a function of the amidinium and the carboxylate group which are common throughout the series, and we consider the radicals to which these groups are

respectively linked to make an insignificant contribution to the stability of the crystals. Although it has been noted by various authors [2] that the melting points of S-benzyl-thiouronium salts may vary with the rate of heating these variations are not of sufficient magnitude to affect appreciably the present treatment * of the data, which were obtained from the sources cited in the Appendix.

While the general picture concerning the melting points shown by compounds of this type is as shown in Table 1 and Fig. 1, significant trends were observable in particular groups. For example, comparison of the S-benzylthiouronium salts of the *o*-, *m*-, and *p*-bromo-, -chloro-, -methoxy-, -nitro-, -amino-, -2′-methoxyethoxy-, -2′-ethoxyethoxy-, -2′-butoxyethoxy-, -2′-phenoxyethoxy-, and -2′-2″-butoxyethoxyethoxy-benzoic acids and the toluic acids showed that the salt of the *p*-substituted acid had the highest melting point within each group, but with the hydroxybenzoic acids the *m*-substituted compound had the highest melting point. Among the S-4-bromo- and S-4-chloro-benzylthiouronium salts of the *o*-, *m*-, and *p*-bromo-, -chloro-, and -iodo-benzoic acids and the toluic acids there was only one exception to the rule that the salt of the *p*-substituted acid had the highest melting point in each group. Another trend was noted during the collection of data when the number of salts having melting points in the 120—130° range suddenly forged ahead and reached a level ahead of expectation. This was due to the melting points of the S-benzylthiouronium salts of 17 acids of the type $H \cdot [CH_2]_n \cdot CMe_2 \cdot CH_2 \cdot CO_2H$,[3] eleven of which had melting points in this particular range; this series also showed in part the alternation frequently noted in homologous series, although the same feature was less marked with the S-benzyl- and S-1-naphthylmethyl-thiouronium salts, and not at all with the known S-4-bromobenzylthiouronium salts, of the *n*-fatty acids. Although the S-benzyl- and substituted S-benzyl-thiouronium salts of carboxylic acids show a restricted melting-point range, and melting points should not be relied upon alone as criteria for the identification of acids, the presence of the heteroatoms (S, N) helps to make ultimate elementary analysis diagnostic, and the salts lend themselves to non-aqueous titration; [2b] their identification by means of X-ray powder diffraction patterns has also been employed.[4]

In course of determining the crystallographic constants [5] of a range of amidinium salts

TABLE 2.

Unit-cell dimensions of typical amidinium carboxylates.

Substance	*a* (Å)	*b* (Å)	*c* (Å)	α	β	γ	D_m *	D_c *	Z	Space group
Benzamidinium benzoate	28·9	35·8	9·9				1·25	1·25	32	*Ccc*2
3,5-Dibromobenzamidin- ium benzoate	15·21	9·64	12·34	110°	110°	100·7°	1·755	1·77	4	*P*1 or *P*Ī
3,5-Dibromobenzamidin- ium 3,5-dibromo- benzoate	23·8	32·1	4·85				2·10	2·00	8	
S-Methylthiouronium benzoate	9·52	20·29	5·61				1·28	1·30	4	$P2_12_12_1$
S-Methylthiouronium *p*-bromobenzoate	9·505	5·61	22·556		103·22°		1·625	1·651	4	$P2_1/c$
S-Methylthiouronium *p*-iodobenzoate	9·40	5·61	23·55		101·5°		1·82	1·85	4	$P2_1/c$ or $P2/c$

* In g./c.c.

* Where the same salt has been described from more than one laboratory the mean m. p. was taken, when the individual observations agreed within a few degrees, or the m. p. showing maximum agreement between authors was taken in a few cases where an isolated observation stood out from the others.

[2] *E.g.*, (a) Kass, Nichols, and Burr, *J. Amer. Chem. Soc.*, 1942, **64**, 1061; Crombie and Jacklin, *J.*, 1955, 1740; Berger and Uldall, *Acta Chem. Scand.*, 1962, **16**, 1811; (b) Berger, *ibid.*, 1954, **8**, 427; Friediger and Pedersen, *ibid.*, 1955, **9**, 1425.
[3] Kimura and Tanaka, *Chem. Pharm. Bull. (Japan)*, 1958, **6**, 9.
[4] Morita and Miles, *Analyt. Chem.*, 1956, **28**, 1081.
[5] Kennard and Walker, *Acta Cryst.*, 1961, **14**, 91.

of carboxylic acids it was noted that these compounds showed a marked physical similarity in the appearance of the crystals, which were usually tabular with a prominent cleavage, indicating the presence of alternate strong and weak directional binding forces. The unit-cell dimensions, which are summarised in Table 2, varied considerably, however, ranging from benzamidinium benzoate with 32 ion-pairs in an orthorhombic cell to 3,5-dibromobenz-amidinium benzoate with 4 ion-pairs in a triclinic cell. The isomorphous *S*-methylthiouro-nium *p*-chloro- and *p*-bromo-benzoates were chosen as most suitable for detailed analysis.* These salts were of additional interest in that they offered the possibility of an accurate determination of the paraffinic carbon–sulphur bond length for bivalent sulphur, as relatively few accurate values for this bond length had been reported in the literature.[6]

EXPERIMENTAL

The crystals of *S*-methylthiouronium *p*-chlorobenzoate [5] were mostly in the form of opaque tablets with marked striations parallel to the *b*-axis, which was also the direction of elongation. The tablets cleaved readily parallel to the (00*l*) plane. Cell dimensions were derived from layer-line spacings on rotation photographs taken about the *b*-axis, and from the 0,0,18 and 10,0,0 reflexions by using the θ method [7] for the other two axes and for the β angle. The density was measured at room temperature by centrifuging the crystals in a continuous-gradient-density column [8] calibrated with suitable liquids.

The crystal data were: *S*-Methylthiouronium *p*-chlorobenzoate; $C_2H_6N_2S,C_7H_5ClO_2$; $M = 246\cdot6$; m. p. 210—211° (decomp.). Monoclinic, $a = 9\cdot505 \pm 0\cdot005$, $b = 5\cdot61 \pm 0\cdot01$, $c = 22\cdot176 \pm 0\cdot010$ Å, $\beta = 103\cdot22° \pm 0\cdot05°$, $U = 1151$ Å³, $D_m = 1\cdot41 \pm 0\cdot01$ g./c.c., $Z = 4$, $D_c = 1\cdot422$ g./c.c. Absorption coefficient for *X*-rays ($\lambda = 1\cdot5418$ Å), $\mu = 44$ cm.⁻¹. Electrons per unit cell = F(000) = 512. Space group, $P2_1/c$. Reflexions absent for $h0l$ when *l* odd, and for $0k0$ when *k* odd.

Three-dimensional data were collected from an approximately cylindrical crystal (diameter, 0·16 mm.; length, 0·16 mm.). Weissenberg equi-inclination photographs were taken with Cu-K_α radiation for five layer lines about the *a*- and four about the *b*-axis. The *h0l* intensities were also derived from oscillation photographs of a very small crystal (<0·05 mm.) by using time-exposures on the same film pack. These intensities were correlated with the three-dimensional data. The intensities were measured on multiple film-packs by matching the reflexions visually against standard intensity charts. With the particular crystals used there was no marked change in spot-shape with equi-inclination angle, and no corrections were made for absorption or extinction. Only two reflexions, a very strong one from the plane (200) and a medium one from (100), appeared to have suffered markedly from extinction effects and these two planes were, therefore, omitted from the final stages of refinement. In all, 1066 non-equivalent reflexions were observed. The Lorentz and polarisation corrections were applied with a reciprocal chart,[9] and the intensities, $F_o{}^2$, were correlated and scaled by means of Wilson [10] plots of the basal reflexions. The square-roots of these values, $|F_o|$, were used in the structure analysis, and the factor converting them to an absolute scale was improved throughout this work, at first by making $\sum|F_o| = \sum|F_c|$ (with allowance for multiplicity) and later during the anisotropic refinement by including the scale factor as one of the variable parameters. The final scale factor was 0·79 times that derived from statistical tests.

During the two-dimensional analysis a desk computer was used in conjunction with Beevers–Lipson strips for the electron-density summations and specially prepared strips for structure-factor calculations. The three-dimensional isotropic refinement was carried out at the University of Manchester on a Ferranti mark I computer, and the anisotropic refinement on the Pegasus computer of the University of Leeds. The atomic scattering factors used were those

* A brief account of work on the *p*-bromobenzoate was given at the 3rd International Congress of Crystallography, Paris, July 1954 (Kennard and Walker, Resumés des Communications, p. 33; *Acta Cryst.*, 1954, **7**, 646).

[6] (*a*) Cox and Jeffrey, *Proc. Roy. Soc.*, 1951, *A*, **207**, 110; (*b*) Abrahams, *Quart. Rev.*, 1956, **10**, 407.
[7] Weisz, Cochran, and Cole, *Acta Cryst.*, 1948, **1**, 83.
[8] Low and Richards, *J. Amer. Chem. Soc.*, 1952, **74**, 1660.
[9] Cochran, *J. Sci. Instr.*, 1948, **25**, 253.
[10] Wilson, *Nature*, 1942, **150**, 152.

given by McWeeny [11] for carbon, oxygen, and nitrogen, and by James and Brindley [12] for sulphur and chlorine, multiplied by appropriate temperature factors. These theoretical scattering factors are independent of the thermal and bonding properties found in particular structures [13] and permit greater flexibility in refining the positional and thermal parameters. The three-dimensional calculations occupied a total computer time of 42·5 hours, and we are greatly indebted to Dr. D. W. J. Cruickshank and Miss Diana Pilling for the programmes used and for carrying out the computations.
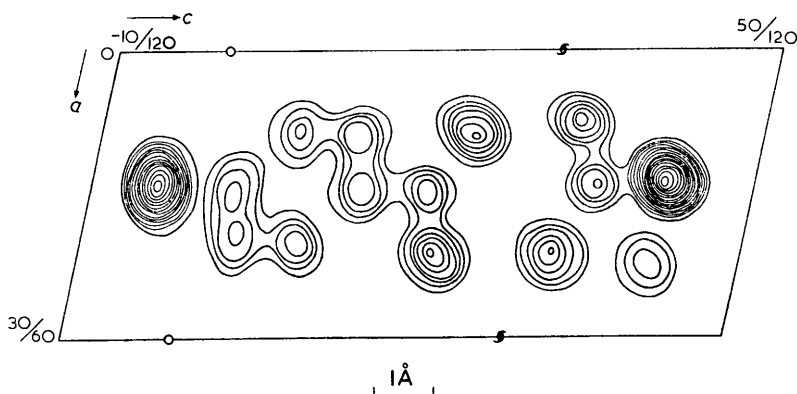
FIG. 2.   Electron-density projection on a plane normal to the *b*-axis.   (Each contour corresponds to a density interval of 1 eÅ^{-2}; the one-electron line is omitted.)
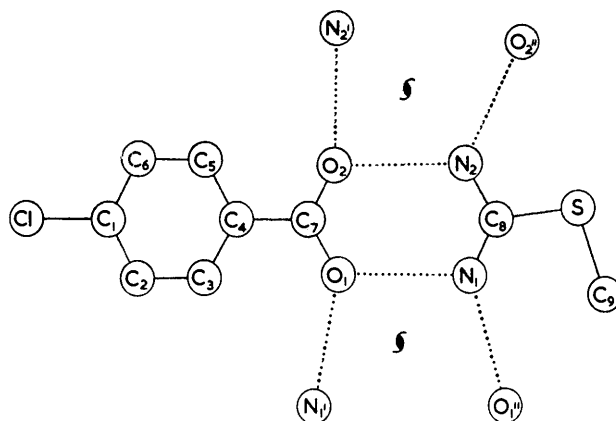
FIG. 3.   Numbering of atoms in doublet ion-pair, and of significant symmetry related atoms.

Structure Analysis.—Two-dimensional refinement.   The best view of the structure was to be expected from a projection down the short *b*-axis.   The approximate positions of the light atoms in this projection were derived from the isomorphous bromobenzoate [5] by the heavy-atom method.   With these co-ordinates as a starting-point the (*h0l*)projection of the chloro-benzoate was gradually refined through a series of Fourier and Fourier-difference maps, till all atoms, except hydrogen, appeared fully resolved.

The predicted type of structure [1] was readily discernible, and Fig. 2 shows the electron-density distribution in the doublet ion-pair which is steeply inclined to the plane of projection. The numbering of the atoms in the doublet ion-pair, and of significant symmetry related atoms.

[11] McWeeny, *Acta Cryst.*, 1951, **4**, 513.
[12] James and Brindley, " International Tables for the Determination of Crystal Structures," Borntraeger, Berlin, 1935.
[13] Cf. Cox, Gillot, and Jeffrey, *Acta Cryst.*, 1949, **2**, 356; Abrahams, *ibid.*, 1955, **8**, 661.

is shown in Fig. 3. The benzene ring is rotated about the chlorine–sulphur axis out of the plane cutting the plane of projection and having the chlorine–sulphur axis as its line of greatest slope. The carboxylate and amidinium groups are similarly rotated through several degrees. The elliptical contours around some of the atoms indicate considerable variations in the mean square vibration of these atoms in different directions. The chlorine atom in particular appears to execute a marked oscillation perpendicular to the $Cl-C_1$ bond and anisotropic thermal corrections had to be introduced in the structure-factor calculations at a comparatively early stage in the two-dimensional refinement.

The application of the heavy-atom technique to the other two projections was less straight-forward. The contribution of the halogen atom to about half of the reflexions was very small since the y-co-ordinate, deduced from Patterson maps, was found to be close to $b/4$. In addition the directions of projection resulted in considerable overlap of the various atoms, expecially on the c-axis projection where the doublet ion-pairs are viewed almost end-on. Finally, there was, at this stage, some uncertainty about the z-co-ordinates, since the b-axis projection does not distinguish between structures where the origin is placed at a centre of symmetry or at a
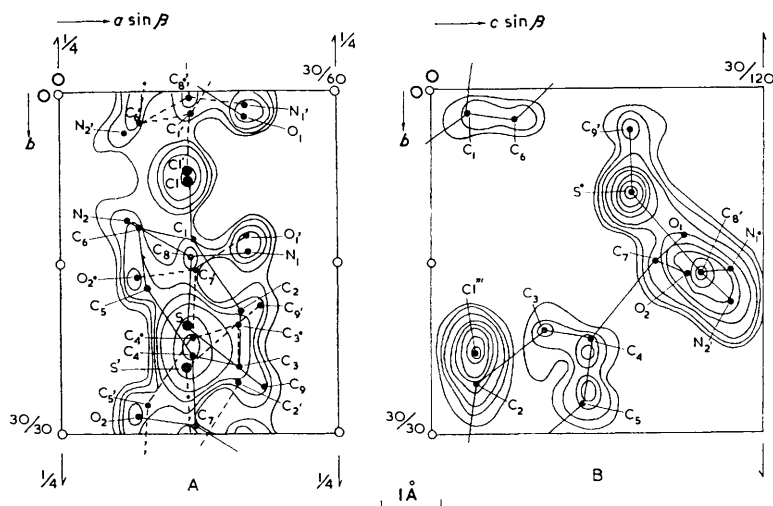
FIG. 4. (A) Electron-density projection on a plane normal to the c-axis (contours at arbitrary intervals). (B) Electron-density projection on a plane normal to the a-axis (contours at arbitrary intervals).

screw axis.[14] Initially, therefore, both alternatives had to be considered in the structure-factor calculations until one set of co-ordinates gave significantly better results. In spite of the considerable overlap of atoms in these projections the analytical application of Fourier difference maps [15] proved unexpectedly powerful in locating the positions of the light atoms and led to reasonable agreement between the observed and calculated structure factors. The reliability factor, R, defined as $\sum |(|F_o| - |F_c|)|/\sum|F_o|$, was reduced, at the end of the two-dimensional refinement, to 23% for each of the three basal zones of reflexions. In this sum, reflexions too weak to be observed were included as half the minimum observable value. Figs. 4A and B illustrate the resolution obtained in the electron density maps of the structure projected on $(hk0)$ and $(0kl)$.

Three-dimensional refinement (isotropic). Although the general features of the structure were clear from the three axial projections, the standard deviations of co-ordinates were high and no reliable deductions could be based on the bond-length values. With the availability of electronic computing facilities, however, a full three-dimensional analysis, utilising the 1064

[14] Donohue and Trueblood, *Acta Cryst.*, 1956, **9**, 960.
[15] Cf. Lipson and Cochran, " The Crystalline State. Vol. III. The Determination of Crystal Structures," G. Bell and Sons, Ltd., London, 1953, pp. 298 *et seq.*

observed *hkl* terms, became possible. The atomic co-ordinates were refined by calculation of differential syntheses [16] with backshift corrections to allow for finite series effects. In the first three cycles the atomic scattering factors were modified by a temperature factor in the form $\exp(-B \sin^2 \theta/\lambda^2)$ (for $\lambda = 1.5418$ Å) and the value of the numerical factor B was adjusted at each stage so as to reduce the difference between the observed and the calculated peak values of the electron-density distribution and the observed and the calculated mean curvatures $(\sigma^2\rho/\sigma x_i^2)$. The B factor used in the first cycle was derived from statistical tests of the $h0l$ reflexions, and, as shown in Table 3, represented a reasonable approximation. Table 3 shows

TABLE 3.

Progress of isotropic refinement of *S*-methylthiouronium *p*-chlorobenzoate.

Cycle	Temperature factor, B (Å^{-1})						Scale factor	Reliability factor, R (%)	Max. shift (Å)	Standard devn. of positional co-ordinates
	Cl	S	O	N	$C_{1, 2, 6, 9}$	$C_{3, 4, 5, 7, 8}$				
I_1	1·6	1·6	1·6	1·6	1·6	1·6	0·829	26·4	$N_2 \, y - 0·17$	0·019
I_2	1·80	1·63	1·70	1·68	1·68	1·68	0·827	19·5	$C_1 \, y + 0·035$	0·018
I_3	2·30	1·68	1·90	1·80	2·10	1·68	0·9375	16·8	$C_9 \, y + 0·027$	0·018

the progress of three cycles of isotropic refinement. A difference map calculated with the structure factors derived from the third cycle of the three-dimensional refinement indicated clearly that little further improvement could be expected from co-ordinate shifts alone and that allowances had to be made for the marked anisotropic vibrations of the majority of the atoms.

Three-dimensional refinement (anisotropic). Cruickshank [17] has shown that when the thermal displacement of an atom varies with direction the spherical distribution of displacement must be replaced by an ellipsoidal distribution. The directional variation of thermal oscillation for atoms in the present structure is evident from Table 4, which shows the ratios of the observed and the calculated electron-density curvatures along the three crystallographic axes. An allowance can be made for this effect by replacing the isotropic temperature factor, $\exp(-B^2 \theta/\lambda^2)$, by the expression

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

and the six thermal parameters, b_{ij}, can be included in the differential synthesis together with the scale factor. The course of four cycles of anisotropic refinement is shown in Table 5. The hydrogen atoms were included in these calculations, having been placed in chemically acceptable positions; the length of the C–H bond was assumed as 0·95 Å in the first cycle and 1·05 Å subsequently.

The observed values of the structure factors, F_o, were weighted by a factor, $\omega = 1/(a + bF_o + cF_o^2)$ in which $a = 8.0$, $b = 1.0$, $c = 1/128$, to allow for experimental errors in the measurement of intensities. In the final cycle (A_4) the influence of possible experimental inaccuracies on the interatomic distance values was examined by carrying out a second set of calculations in which 18 planes which showed maximum disagreement with calculated values were omitted. The two sets of calculations gave reliability factors of 10·13% and 9·46%, but no systematic variations were found in the interatomic distances derived from the two sets of calculations, and the differences between the two sets were always less than the standard deviations in the interatomic distances. The final co-ordinates and their standard deviations are listed in Table 6, the thermal parameters are given in Table 7, and the observed and calculated structure factors in Table 8; the standard deviations were calculated by Cruickshank's method.[18]

All interatomic distances less than 4 Å were calculated on the Mercury computer of the University of London Computing Centre; no abnormally short non-bonded distances were observed, except possibly the distance of 3·54 Å between the chlorine atom and a sulphur atom in a neighbouring unit cell, which is slightly less than the sum (3·65 Å) of the respective van

[16] Booth, *Trans. Faraday Soc.*, 1946, **42**, 44; *Proc. Roy. Soc.*, 1946, *A*, **188**, 77.
[17] Cruickshank, *Acta Cryst.*, 1956, **9**, 747.
[18] Cruickshank, *Acta Cryst.*, 1949, **2**, 65.

TABLE 4.

Observed electron density, ratio of observed to calculated electron density, and ratios
of observed and calculated electron density curvatures along the three crystal axes
(isotropic refinement, cycle I_3).

	ρ_0	ρ_0/ρ_c	$r(x_l)$	$r(y_l)$	$r(z_l)$		ρ_0	ρ_0/ρ_c	$r(x_l)$	$r(y_l)$	$r(z_l)$
Cl	20·632	0·956	0·828	0·997	1·034	C_3	7·088	1·023	1·035	1·045	1·042
S	25·447	1·027	1·031	1·003	1·044	C_4	8·037	1·059	1·078	1·018	1·114
O_1	10·505	1·021	1·163	0·991	1·019	C_5	6·935	0·990	0·995	1·032	1·024
O_2	10·061	0·987	1·114	0·944	1·003	C_6	6·783	1·023	1·049	1·024	1·020
N_1	9·211	1·058	1·161	1·116	1·032	C_7	7·789	1·034	1·166	1·125	1·103
N_2	8·358	0·992	1·038	0·957	0·967	C_8	7·726	1·040	1·119	0·942	1·053
C_1	6·906	1·003	0·921	1·042	1·027	C_9	5·922	1·022	0·996	0·925	0·999
C_2	6·481	1·049	0·991	1·142	1·096						

ρ_0, Observed electron density; ρ_c, calculated electron density; $r(x_l)$, $r(y_l)$, $r(z_l)$, ratio of observed
and calculated electron density curvatures along the x-, y-, and z-axes.

TABLE 5.

Progress of anisotropic refinement of S-methylthiouronium p-chlorobenzoate.

Cycle	Scale factor	Reliability factor, R (%)	Max. shift (Å)	Standard devn. of positional co-ordinates
A_1	0·8868	14·4	$C_8 z - 0.0328$	0·0137
A_2	0·8192	11·1	$C_2 x + 0.0323$	0·0135
A_3	0·8014	10·2	$C_8 x - 0.0197$	0·0100
A_4	0·7904	10·1	$C_6 z + 0.0077$	0·0118

TABLE 6.

Final atomic co-ordinates and standard deviations (Å).

	Co-ordinates			Standard deviations		
	x	y	z	x	y	z
Cl	2·1777	1·4065	10·3688	0·0045	0·0036	0·0034
S	2·1471	3·8416	18·8868	0·0031	0·0031	0·0030
O_1	3·3913	6·0616	15·2523	0·0064	0·0074	0·0074
O_2	1·3479	5·3762	15·4954	0·0065	0·0083	0·0080
N_1	3·3696	2·4822	17·1659	0·0075	0·0086	0·0088
N_2	1·1832	1·8716	17·2517	0·0082	0·0097	0·0096
C_1	2·2343	2·5568	11·6936	0·0133	0·0124	0·0108
C_2	3·1289	3·5591	11·8231	0·0127	0·0100	0·0116
C_3	3·1795	4·4506	12·9062	0·0110	0·0115	0·0113
C_4	2·2928	4·3205	13·8024	0·0094	0·0107	0·0101
C_5	1·4006	3·2825	13·6244	0·0114	0·0111	0·0107
C_6	1·3409	2·3547	12·5681	0·0126	0·0142	0·0118
C_7	2·3470	5·3277	14·9170	0·0090	0·0109	0·0099
C_8	2·2747	2·6711	17·6524	0·0097	0·0112	0·0098
C_9	3·5816	4·9180	18·8146	0·0120	0·0122	0·0122

TABLE 7.

Components of thermal vibration coefficients (b_{ij}); anisotropic refinement, cycle A_4.

	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
Cl	0·00380	0·00546	0·00030	0·00088	0·00050	−0·00066
S	0·00175	0·00418	0·00030	0·00015	0·00064	−0·00018
O_1	0·00090	0·00455	0·00035	−0·00018	0·00034	−0·00038
O_2	0·00108	0·00544	0·00042	−0·00128	0·00071	−0·00105
N_1	0·00096	0·00313	0·00036	−0·00012	0·00037	−0·00033
N_2	0·00099	0·00497	0·00037	−0·00045	0·00035	−0·00048
C_1	0·00284	0·00467	0·00022	0·00076	0·00010	−0·00027
C_2	0·00234	0·00332	0·00032	0·00054	0·00073	−0·00030
C_3	0·00142	0·00453	0·00032	0·00013	0·00034	0·00008
C_4	0·00102	0·00403	0·00026	−0·00042	0·00029	−0·00017
C_5	0·00205	0·00360	0·00026	−0·00012	0·00030	0·00022
C_6	0·00222	0·00600	0·00031	−0·00097	0·00042	−0·00039
C_7	0·00089	0·00430	0·00027	0·00130	0·00014	0·00034
C_8	0·00119	0·00419	0·00025	0·00108	0·00018	0·00032
C_9	0·00180	0·00458	0·00035	−0·00059	0·00037	−0·00057

TABLE 8.

Observed and calculated structure factors and weighted differences for S-methyl-thiouronium p-chlorobenzoate on ten times the absolute scale.

h	k	l	$|F_o|$	F_c	$\omega|F_o - F_c|$
0	0	0	—	5120	—
		4	65	61	1
		6	590	609	2
		8	201	−197	1
		10	201	−200	0
		12	408	−432	3
		16	305	−323	2
		18	247	−232	2
		20	85	−68	4
		22	97	−89	2
		24	79	−46	8
		26	85	92	2
0	1	1	142	164	4
		2	130	129	0
		3	925	1160	15
		4	668	678	1
		5	810	−859	4
		6	752	747	0
		7	493	489	0
		8	305	−263	6
		9	169	−139	5
		10	577	552	2
		11	156	−124	6
		12	428	399	3
		13	71	−66	1
		15	117	−103	3
		16	182	−163	3
		20	58	−49	2
		21	85	−76	2
		22	240	−237	0
0	2	0	142	−128	3
		1	221	−211	1
		2	616	−659	4
		3	259	274	2
		4	207	178	5
		5	447	−398	5
		6	58	−28	8
		7	104	111	2
		8	376	−359	2
		9	233	219	2
		10	441	442	0
		12	32	56	7
		15	104	−107	1
		16	227	224	0
		18	123	116	2
		19	130	−130	0
		22	39	−17	6
		26	45	−49	1
0	3	1	123	103	4
		2	97	−82	3
		3	85	−75	2
		4	350	−380	4
		5	207	−205	0
		6	207	−196	2
		7	253	232	3
		8	273	−266	1
		10	26	−21	2
		11	143	−112	6
		12	182	−165	3
		13	214	216	0
		17	85	−76	2
		20	91	95	1
		22	65	66	0
		24	29	46	5
0	4	0	142	133	2
		1	207	−200	1
		2	117	112	1
		4	130	116	3
		5	77	70	2
		7	194	−176	3
		9	130	−150	4
		11	117	123	1
		12	104	−88	3
		13	85	69	3
		14	97	−90	1
		15	117	−117	0
		18	52	−72	5
		19	71	69	0
0	5	1	169	−162	1
		2	188	171	3
		3	130	133	1
		4	58	−65	2
		5	58	52	2
		7	97	−90	1
		8	85	57	6
		10	85	73	3
		12	77	−20	13
0	6	0	52	−52	0
		2	77	−58	4
		5	91	−91	0
		10	91	−31	13
		12	104	40	13
0	7	4	39	−46	2
1	$\bar{6}$	$\bar{6}$	85	105	5
		$\bar{4}$	91	101	2
		$\bar{2}$	123	−143	4
		$\bar{1}$	71	103	8
1	$\bar{5}$	$\bar{10}$	110	−114	1
		$\bar{9}$	58	44	4
		$\bar{7}$	77	87	2
		$\bar{6}$	58	82	6
		$\bar{5}$	149	−164	3
		$\bar{4}$	77	112	8
		$\bar{2}$	123	131	2
		$\bar{1}$	58	68	2
		0	156	184	5
1	$\bar{4}$	$\bar{13}$	77	−74	1
		$\bar{12}$	110	−126	3
		$\bar{11}$	156	143	2
		$\bar{10}$	110	−129	4
		$\bar{9}$	77	78	0
		$\bar{8}$	162	−163	0
		$\bar{7}$	182	−189	1
		$\bar{6}$	117	−133	3
		$\bar{5}$	136	148	2
		$\bar{4}$	130	−135	1
		$\bar{3}$	201	214	2
		$\bar{1}$	117	−133	3
1	$\bar{3}$	$\bar{25}$	26	28	1
		$\bar{24}$	39	−45	2
		$\bar{16}$	130	139	2
		$\bar{15}$	143	−152	2
		$\bar{14}$	182	181	0
		$\bar{13}$	85	90	1
		$\bar{12}$	188	186	0
		$\bar{11}$	32	−27	1
		$\bar{9}$	123	−118	1
		$\bar{8}$	26	−16	3
		$\bar{7}$	77	−90	3
		$\bar{6}$	188	−200	2
		$\bar{5}$	318	322	0
		$\bar{4}$	311	−346	4
		$\bar{2}$	110	−130	4
		$\bar{1}$	91	−123	7
1	$\bar{2}$	$\bar{26}$	77	−108	7
		$\bar{20}$	85	−75	2
		$\bar{18}$	142	−142	0
		$\bar{17}$	123	−132	2
		$\bar{16}$	97	82	3
		$\bar{15}$	136	122	3
		$\bar{14}$	143	123	4
		$\bar{13}$	175	163	2
		$\bar{12}$	156	153	0
		$\bar{11}$	136	−121	3
		$\bar{10}$	182	203	4
		$\bar{9}$	123	−126	1
		$\bar{8}$	694	622	6
		$\bar{7}$	26	−12	4
		$\bar{6}$	370	321	6
		$\bar{5}$	519	−471	5
		$\bar{4}$	136	−118	3
		$\bar{3}$	104	77	6
		$\bar{2}$	545	586	4
		$\bar{1}$	58	75	4
		0	52	−67	4
1	$\bar{1}$	$\bar{25}$	71	−72	0
		$\bar{20}$	156	−145	2
		$\bar{17}$	85	41	10
		$\bar{16}$	117	−110	1
		$\bar{15}$	201	194	1
		$\bar{14}$	383	−379	0
		$\bar{13}$	149	−133	3
		$\bar{12}$	182	−171	2
		$\bar{11}$	169	165	1
		$\bar{10}$	292	268	3
1	0	$\bar{9}$	486	449	4
		$\bar{8}$	350	−330	2
		$\bar{7}$	376	−345	4
		$\bar{6}$	182	−176	1
		$\bar{5}$	318	292	3
		$\bar{4}$	855	873	1
		$\bar{3}$	273	253	3
		$\bar{2}$	428	402	3
		$\bar{1}$	206	202	1
		0	234	−218	2
1	0	$\bar{26}$	65	67	0
		$\bar{22}$	130	−128	0
		$\bar{20}$	71	87	4
		$\bar{18}$	369	387	2
		$\bar{16}$	130	−115	3
		$\bar{14}$	292	−264	4
		$\bar{12}$	376	382	1
		$\bar{10}$	488	−537	5
		$\bar{8}$	454	−473	2
		$\bar{6}$	207	−236	5
		$\bar{4}$	396	452	6
		$\bar{2}$	104	141	8
		2	104	−111	2
		4	305	−342	5
		8	395	418	3
		10	479	508	3
		12	564	−586	2
		14	285	295	1
		16	123	121	0
		18	247	−270	3
		24	53	−34	5
		26	58	−52	2
1	1	1	52	−58	2
		2	207	−183	2
		3	136	−126	2
		4	1304	−1469	8
		5	635	−615	2
		6	247	253	1
		7	58	61	1
		8	272	240	4
		9	383	−358	3
		11	65	−52	3
		12	273	258	2
		13	136	117	4
		14	253	244	1
		15	221	−182	6
		17	156	128	5
		20	110	132	5
1	2	1	156	−144	2
		2	292	−310	2
		3	182	184	0
		4	130	−129	0
		5	26	23	1
		6	408	−368	4
		7	383	−354	3
		8	713	−673	3
		9	389	375	2
		10	52	−43	3
		11	65	−65	0
		12	91	−94	1
		13	136	−127	2
		14	117	−100	3
		18	91	80	2
		20	85	85	0
		24	65	65	0
1	3	1	247	268	3
		2	330	390	7
		3	65	−51	3
		4	20	−20	0
		5	156	−173	3
		6	71	57	3
		7	162	162	0
		9	182	177	1
		10	117	−115	0
		11	194	−210	3
		12	39	−42	1
		13	39	47	2
		14	227	−233	1
		16	85	−82	1
1	4	3	253	−297	6
		4	182	146	6
		6	285	314	4
		8	77	70	2
		9	58	54	1
		10	77	79	0
		11	58	−59	0
		12	77	80	1
		13	77	79	0
1	5	1	110	−115	1
		2	97	−96	0
		3	110	115	1
		4	77	−104	6
		5	97	114	4
		6	58	−57	0
		7	77	−72	1
		10	77	88	3
		11	71	48	6
		13	117	29	18
1	6	1	65	−97	8
		4	65	−72	2
		7	77	−76	0
		10	65	−20	11
2	$\bar{6}$	$\bar{13}$	104	36	14
2	$\bar{5}$	$\bar{17}$	97	−80	4
		$\bar{15}$	110	100	2
		$\bar{10}$	110	−100	2
		$\bar{3}$	110	−118	2
		$\bar{1}$	65	84	5
		0	110	−113	1
2	$\bar{4}$	$\bar{15}$	123	114	2
		$\bar{12}$	142	128	3
		$\bar{9}$	162	180	3
		$\bar{7}$	85	−100	4
		$\bar{4}$	136	−155	4
		$\bar{2}$	110	−115	1
		$\bar{1}$	221	249	4
		0	221	−213	1
2	$\bar{3}$	$\bar{26}$	20	−40	6
		$\bar{23}$	110	−12	20
		$\bar{17}$	117	109	2
		$\bar{15}$	162	−127	6
		$\bar{14}$	71	62	2
		$\bar{13}$	123	−109	3
		$\bar{12}$	253	256	0
		$\bar{11}$	175	162	2
		$\bar{9}$	91	74	4
		$\bar{8}$	194	183	2
		$\bar{7}$	285	−263	3
		$\bar{6}$	182	192	2
		$\bar{5}$	234	209	4
		$\bar{4}$	266	262	1
		$\bar{3}$	194	214	3
		$\bar{2}$	207	230	4
		$\bar{1}$	402	−435	4
		0	234	−257	3
2	$\bar{2}$	$\bar{23}$	91	−86	1
		$\bar{19}$	110	107	1
		$\bar{18}$	149	−154	1
		$\bar{16}$	142	−140	0
		$\bar{14}$	58	61	1
		$\bar{13}$	85	97	3
		$\bar{12}$	188	−185	3
		$\bar{11}$	110	86	5
		$\bar{10}$	188	−179	1
		$\bar{9}$	493	−456	4
		$\bar{8}$	169	143	5
		$\bar{6}$	350	324	3
		$\bar{5}$	551	539	1
		$\bar{4}$	188	−173	3
		$\bar{3}$	299	−309	1
		$\bar{2}$	675	740	5
		$\bar{1}$	169	165	1
		0	337	341	1
2	$\bar{1}$	$\bar{28}$	39	56	5
		$\bar{24}$	91	75	3
		$\bar{21}$	77	78	0
		$\bar{19}$	97	87	2
		$\bar{18}$	149	−119	6
		$\bar{15}$	97	85	3
		$\bar{14}$	123	88	7
		$\bar{13}$	130	117	2
		$\bar{12}$	422	−394	3
		$\bar{11}$	85	−76	2
		$\bar{10}$	480	−424	6
		$\bar{9}$	104	−98	1

TABLE 8. (*Continued.*)

Column group 1

h	k	l	F_o	F_c	$\omega|F_o-F_c|$
		$\bar{8}$	97	−90	2
		$\bar{6}$	681	−689	1
		$\bar{5}$	71	−71	0
		$\bar{4}$	325	−309	2
		$\bar{3}$	259	−260	0
		$\bar{2}$	292	280	2
		$\bar{1}$	285	291	1
		0	364	319	5
2	0	$\bar{28}$	58	−62	1
		$\bar{22}$	123	129	1
		$\bar{20}$	156	173	3
		$\bar{18}$	292	309	2
		$\bar{16}$	270	281	1
		$\bar{12}$	168	169	0
		$\bar{10}$	336	351	2
		$\bar{8}$	225	−221	1
		$\bar{6}$	752	−922	13
		$\bar{4}$	77	−67	2
		$\bar{2}$	130	−143	3
		2	350	−366	2
		4	123	131	2
		6	273	−304	4
		8	168	179	2
		10	194	212	3
		12	298	308	1
		14	182	190	1
		16	233	252	3
		18	110	121	2
2	1	1	221	−187	5
		2	486	−456	3
		3	933	−1046	7
		4	713	−728	1
		5	479	424	6
		6	253	−224	4
		8	71	50	5
		10	194	−167	4
		11	169	136	6
		12	311	−310	0
		13	77	68	2
		15	85	83	0
		16	194	198	1
		20	85	85	0
		22	136	139	1
2	2	1	363	−342	3
		3	85	78	1
		4	156	−158	0
		5	85	−82	1
		6	136	−120	3
		8	278	267	1
		9	32	40	2
		10	402	−380	2
		11	130	111	4
		12	39	−25	4
		13	85	62	5
		14	97	−78	4
		15	85	−77	2
		16	123	−135	2
		17	91	78	3
		19	85	92	2
		21	77	−60	4
2	3	1	143	134	2
		2	149	−139	2
		4	383	377	1
		5	77	68	2
		6	130	128	0
		7	273	−278	1
		8	97	78	4
		10	311	328	2
		11	58	41	4
		12	39	51	3
		13	169	−177	1
		14	85	−76	2
		15	77	74	1
		21	65	−14	13
		24	39	−32	2
2	4	1	149	150	0
		2	58	−50	2
		3	58	66	2
		5	240	−276	5
		6	136	−126	2
		7	311	350	5
		10	111	−12	21
		13	110	−58	11
		15	104	65	8
2	5	1	97	112	3
		2	188	−237	8
		3	77	−102	6

Column group 2

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
		4	77	80	1
		7	91	77	3
2	6	3	91	27	14
		11	71	66	1
		13	58	23	9
3	$\bar{0}$	$\bar{12}$	71	−74	1
		$\bar{5}$	123	−25	19
		$\bar{1}$	136	−59	15
3	$\bar{5}$	$\bar{18}$	123	106	3
		$\bar{16}$	97	65	7
		$\bar{5}$	97	105	2
		$\bar{4}$	85	−77	2
		$\bar{3}$	104	−98	1
		$\bar{2}$	104	−124	4
		0	97	−91	1
3	$\bar{4}$	$\bar{21}$	110	88	4
		$\bar{15}$	104	106	1
		$\bar{14}$	104	116	3
		$\bar{12}$	91	91	0
		$\bar{11}$	207	−221	2
		$\bar{10}$	97	86	2
		$\bar{9}$	97	−112	3
		$\bar{8}$	130	132	0
		$\bar{7}$	162	196	6
		$\bar{6}$	77	54	5
		$\bar{5}$	123	−138	3
		$\bar{4}$	52	−40	3
		$\bar{3}$	77	−73	1
		$\bar{1}$	130	145	3
		0	104	−92	2
3	$\bar{3}$	$\bar{24}$	58	6	13
		$\bar{22}$	84	−16	15
		$\bar{20}$	104	−105	0
		$\bar{16}$	110	−94	3
		$\bar{15}$	207	208	0
		$\bar{14}$	110	−91	4
		$\bar{13}$	91	−80	2
		$\bar{12}$	85	−80	1
		$\bar{11}$	77	−60	4
		$\bar{10}$	116	128	2
		$\bar{9}$	194	186	1
		$\bar{8}$	85	−69	4
		$\bar{7}$	117	−103	3
		$\bar{6}$	142	141	0
		$\bar{5}$	370	−367	0
		$\bar{4}$	454	495	4
		$\bar{3}$	156	156	0
		$\bar{2}$	32	−32	0
		$\bar{1}$	52	−43	2
		0	26	43	5
3	$\bar{2}$	$\bar{27}$	58	−82	6
		$\bar{26}$	85	105	5
		$\bar{22}$	65	−65	0
		$\bar{21}$	91	−91	0
		$\bar{20}$	91	88	1
		$\bar{18}$	130	123	1
		$\bar{17}$	136	124	2
		$\bar{16}$	104	−89	3
		$\bar{14}$	292	−295	0
		$\bar{13}$	110	−98	3
		$\bar{11}$	338	338	0
		$\bar{10}$	305	−318	2
		$\bar{9}$	97	−89	2
		$\bar{8}$	486	−439	5
		$\bar{7}$	39	50	3
		$\bar{6}$	26	23	1
		$\bar{5}$	130	130	0
		$\bar{4}$	110	−99	2
		$\bar{3}$	305	300	1
		$\bar{2}$	247	−248	0
		$\bar{1}$	279	−254	3
		0	117	103	3
3	$\bar{1}$	$\bar{25}$	58	58	0
		$\bar{24}$	52	−55	1
		$\bar{22}$	39	60	6
		$\bar{20}$	77	72	1
		$\bar{19}$	221	226	1
		$\bar{18}$	77	70	2
		$\bar{17}$	266	−256	1
		$\bar{16}$	194	191	1
		$\bar{15}$	110	−103	1
		$\bar{14}$	441	430	1
		$\bar{12}$	58	−46	3
		$\bar{11}$	234	−218	2
		$\bar{10}$	299	−251	6
		$\bar{9}$	104	−103	0

Column group 3

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
		$\bar{8}$	214	194	3
		$\bar{7}$	110	−87	5
		$\bar{6}$	156	−139	3
		$\bar{5}$	331	349	2
		$\bar{4}$	247	−239	1
		$\bar{3}$	65	−61	1
		$\bar{2}$	441	−515	8
		$\bar{1}$	227	−239	2
		0	221	216	1
3	0	$\bar{28}$	33	−12	6
		$\bar{26}$	71	−67	1
		$\bar{24}$	85	−88	1
		$\bar{22}$	201	200	0
		$\bar{20}$	168	−165	1
		$\bar{18}$	247	−252	1
		$\bar{16}$	247	252	1
		$\bar{14}$	136	−141	1
		$\bar{12}$	253	241	2
		$\bar{10}$	39	33	1
		$\bar{8}$	247	255	1
		$\bar{6}$	134	177	8
		$\bar{4}$	182	224	7
		$\bar{2}$	285	304	3
		0	207	−243	6
		2	395	−361	4
		4	52	37	4
		6	221	−239	3
		8	294	−337	6
		12	149	152	0
		16	130	−133	1
		18	142	140	0
		20	59	34	6
		24	77	69	2
3	1	1	117	110	1
		2	571	541	3
		3	39	−36	1
		4	642	608	3
		5	26	45	6
		6	156	−145	2
		7	356	312	5
		8	85	−78	2
		11	58	58	0
		12	240	−229	2
		14	123	−122	0
		15	110	108	0
		18	91	−76	3
		21	77	72	1
3	2	1	343	288	7
		3	492	−451	4
		4	253	255	0
		5	304	282	3
		6	227	214	2
		7	434	411	2
		8	564	536	3
		9	182	−177	1
		10	32	−48	4
		13	97	89	2
		14	168	179	2
		15	110	−105	1
		16	91	−89	0
		20	52	−66	3
3	3	1	169	−153	3
		2	266	−259	1
		3	85	−70	3
		5	182	183	0
		6	110	103	1
		7	123	−126	1
		8	169	183	2
		9	142	−149	1
		10	136	137	0
		11	305	320	2
		12	71	−71	0
		13	77	−78	0
		14	162	150	2
		23	32	−19	4
3	4	3	182	181	0
		6	234	−261	4
		13	97	−75	5
3	5	1	97	100	1
		3	85	−65	4
		4	97	73	5
		12	142	−125	3
3	6	8	71	3	16
4	$\bar{6}$	$\bar{14}$	77	60	4
		$\bar{3}$	77	42	8

Column group 4

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
4	$\bar{5}$	$\bar{15}$	97	−100	1
		$\bar{10}$	85	62	5
		$\bar{7}$	85	−94	2
		$\bar{3}$	85	68	4
4	$\bar{4}$	$\bar{22}$	65	−53	3
		$\bar{19}$	117	120	3
		$\bar{14}$	85	−55	7
		$\bar{12}$	169	−92	14
		$\bar{9}$	97	−102	1
		$\bar{6}$	117	88	6
		$\bar{5}$	97	100	1
		$\bar{4}$	77	69	2
		$\bar{3}$	110	−120	2
		$\bar{2}$	52	67	4
		$\bar{1}$	149	−148	0
		0	234	242	1
4	3	$\bar{24}$	91	52	9
		$\bar{23}$	65	−61	1
		$\bar{22}$	104	98	1
		$\bar{21}$	85	78	1
		$\bar{17}$	97	−92	1
		$\bar{16}$	39	55	5
		$\bar{15}$	142	120	4
		$\bar{14}$	39	−40	0
		$\bar{13}$	39	37	0
		$\bar{12}$	156	−147	2
		$\bar{11}$	201	−203	0
		$\bar{10}$	259	−280	3
		$\bar{7}$	239	238	0
		$\bar{6}$	130	−123	0
		$\bar{5}$	149	−128	4
		$\bar{4}$	162	−149	2
		$\bar{3}$	85	−85	0
		$\bar{1}$	207	233	4
		0	136	126	2
4	2	$\bar{25}$	52	−28	6
		$\bar{24}$	91	98	2
		$\bar{23}$	71	79	2
		$\bar{19}$	45	−67	6
		$\bar{18}$	136	147	2
		$\bar{15}$	266	267	0
		$\bar{14}$	85	−78	2
		$\bar{13}$	227	−231	1
		$\bar{12}$	227	209	3
		$\bar{11}$	117	−121	1
		$\bar{10}$	71	56	4
		$\bar{9}$	214	215	0
		$\bar{8}$	201	−197	1
		$\bar{7}$	123	−121	0
		$\bar{6}$	207	−226	2
		$\bar{5}$	169	−160	2
		$\bar{4}$	26	26	0
		$\bar{3}$	71	72	0
		$\bar{2}$	259	−260	0
		$\bar{1}$	58	58	0
		0	460	−422	4
4	1	$\bar{28}$	39	−58	5
		$\bar{24}$	85	−88	1
		$\bar{22}$	123	−109	3
		$\bar{20}$	58	73	4
		$\bar{19}$	97	−93	1
		$\bar{18}$	194	170	4
		$\bar{16}$	39	−50	3
		$\bar{15}$	39	−53	4
		$\bar{13}$	123	−121	0
		$\bar{12}$	422	363	6
		$\bar{11}$	85	89	1
		$\bar{10}$	65	−56	2
		$\bar{9}$	259	225	5
		$\bar{8}$	318	312	1
		$\bar{7}$	402	−355	5
		$\bar{6}$	311	318	1
		$\bar{5}$	499	470	3
		$\bar{4}$	26	−38	4
		$\bar{3}$	32	−32	0
		$\bar{2}$	376	−401	3
		$\bar{1}$	169	−165	1
		0	26	21	2
4	0	$\bar{28}$	45	54	2
		$\bar{22}$	65	−53	3
		$\bar{20}$	97	−93	1
		$\bar{18}$	272	−296	3
		$\bar{16}$	123	−106	3
		$\bar{12}$	123	−115	2
		$\bar{10}$	402	−401	2
		$\bar{8}$	571	675	9
		$\bar{6}$	499	569	7
		$\bar{4}$	162	−153	2

TABLE 8. (Continued.)

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
		$\bar{2}$	765	785	2
		0	142	−102	8
		2	221	203	3
		4	240	−223	3
		6	279	318	5
		8	71	−86	4
		10	207	−224	3
		12	58	−52	2
		14	130	−134	1
		16	142	−177	7
		20	59	58	0
4	1	1	97	−78	4
		2	338	285	7
		3	247	212	5
		4	441	391	5
		5	194	158	6
		7	240	−212	4
		8	65	52	3
		9	123	118	1
		12	156	158	0
		14	156	−159	1
		16	110	−88	5
		20	77	−61	4
4	2	1	376	325	6
		2	194	162	5
		3	168	−152	3
		4	201	184	3
		5	149	133	3
		7	52	−33	5
		10	168	154	2
		11	221	−211	2
		12	71	75	1
		13	123	−112	2
		14	97	88	2
		15	91	140	11
4	3	2	91	60	7
		3	142	−120	4
		4	194	−227	5
		5	58	65	2
		7	175	220	8
		9	58	−61	1
		10	273	−318	6
4	4	1	136	−146	2
		5	175	176	0
		7	188	−186	0
4	5	2	110	109	0
		3	91	98	2
4	6	3	58	−40	5
5	$\bar{3}$	$\overline{24}$	97	46	11
		$\overline{20}$	130	123	1
		$\overline{15}$	104	−105	0
		$\overline{14}$	123	78	9
		$\overline{12}$	182	−183	0
		$\overline{11}$	221	193	4
		$\overline{10}$	52	−72	5
		$\bar{9}$	169	−176	1
		$\bar{8}$	77	74	1
		$\bar{7}$	221	212	1
		$\bar{6}$	52	−46	1
		$\bar{5}$	194	177	3
		$\bar{4}$	221	−214	1
		$\bar{3}$	156	−141	3
		$\bar{2}$	52	−38	4
		0	71	−54	4
5	$\bar{2}$	$\overline{26}$	71	−95	6
		$\overline{20}$	104	−123	4
		$\overline{15}$	58	−63	1
		$\overline{14}$	285	306	3
		$\overline{13}$	85	−68	4
		$\overline{12}$	85	−75	2
		$\overline{11}$	227	−235	1
		$\overline{10}$	221	211	2
		$\bar{8}$	253	280	4
		$\bar{7}$	156	139	3
		$\bar{6}$	142	−140	0
		$\bar{5}$	71	60	3
		$\bar{4}$	266	247	3
		$\bar{3}$	266	−283	2
		$\bar{2}$	52	−38	4
		$\bar{1}$	299	283	2
		0	110	−118	2
5	$\bar{1}$	$\overline{24}$	91	67	5
		$\overline{22}$	116	−120	1
		$\overline{21}$	85	76	2

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
		$\overline{19}$	201	−203	0
		$\overline{17}$	182	163	3
		$\overline{16}$	201	−188	2
		$\overline{15}$	58	55	1
		$\overline{14}$	292	−305	2
		$\overline{13}$	85	−56	6
		$\overline{12}$	123	132	2
		$\overline{11}$	175	152	4
		$\overline{10}$	169	144	4
		$\bar{9}$	117	−103	3
		$\bar{8}$	162	−153	2
		$\bar{7}$	240	231	1
		$\bar{5}$	201	−176	4
		$\bar{4}$	441	422	2
		$\bar{3}$	65	−65	0
		$\bar{2}$	221	184	6
		$\bar{1}$	130	89	8
		0	136	−112	5
5	0	$\overline{26}$	62	81	5
		$\overline{24}$	77	79	0
		$\overline{22}$	104	−116	3
		$\overline{20}$	182	188	1
		$\overline{18}$	91	76	3
		$\overline{16}$	305	−376	9
		$\overline{14}$	142	180	7
		$\overline{12}$	175	−185	2
		$\overline{10}$	98	−111	3
		$\bar{8}$	71	−59	3
		$\bar{6}$	97	93	1
		$\bar{4}$	182	−200	3
		$\bar{2}$	337	−377	5
		0	266	280	2
		2	408	383	3
		4	104	−113	2
		6	370	402	4
		8	117	142	5
		10	149	−198	9
		14	91	−87	1
		18	117	−127	2
5	1	1	194	−168	4
		2	557	−495	6
		3	162	119	8
		5	169	141	5
		6	175	155	3
		7	221	−206	2
		9	117	111	1
		12	156	149	1
		15	63	−68	1
		18	77	78	0
		19	91	97	1
5	2	1	123	−108	3
		2	104	−87	3
		3	214	208	1
		4	91	−79	3
		5	156	−149	1
		6	110	−106	1
		7	130	−155	5
		8	240	−255	2
		10	85	69	3
		14	136	−162	5
		15	85	98	3
5	3	1	71	95	6
		4	52	78	7
		5	97	−138	9
		6	58	−69	3
		7	58	82	6
		8	142	−189	9
		10	65	−77	3
		11	136	−167	6
6	$\bar{3}$	$\overline{21}$	77	−66	3
		$\overline{11}$	227	219	1
		$\overline{10}$	305	321	2
		$\bar{9}$	117	−107	2
		$\bar{7}$	137	−131	1
		$\bar{6}$	52	59	2
		$\bar{5}$	123	111	2
		$\bar{4}$	77	64	3
		$\bar{3}$	77	−71	2
		$\bar{2}$	177	−154	4
		0	110	101	2
6	$\bar{2}$	$\overline{24}$	71	−69	0
		$\overline{19}$	85	73	3
		$\overline{18}$	85	−78	2
		$\overline{15}$	182	−180	0
		$\overline{14}$	91	84	2
		$\overline{13}$	175	178	2
		$\overline{12}$	123	−123	0

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
		$\overline{10}$	104	−90	3
		$\bar{8}$	350	382	4
		$\bar{7}$	194	211	3
		$\bar{5}$	97	−91	1
		0	156	151	1
6	$\bar{1}$	$\overline{24}$	65	48	4
		$\overline{22}$	71	67	1
		$\overline{20}$	104	−98	1
		$\overline{18}$	110	−127	4
		$\overline{16}$	156	160	1
		$\overline{15}$	91	85	1
		$\overline{14}$	142	−127	3
		$\overline{12}$	299	−256	6
		$\overline{10}$	142	139	1
		$\bar{8}$	123	−119	1
		$\bar{7}$	156	140	3
		$\bar{6}$	156	−127	2
		$\bar{5}$	156	−96	11
		$\bar{4}$	201	175	4
		$\bar{3}$	201	−134	11
		$\bar{2}$	214	200	2
		$\bar{1}$	91	82	2
		0	110	−100	2
6	0	$\overline{26}$	66	58	2
		$\overline{24}$	92	96	1
		$\overline{18}$	190	201	2
		$\overline{12}$	188	206	3
		$\overline{10}$	142	143	0
		$\bar{8}$	330	−392	8
		$\bar{6}$	261	−249	2
		$\bar{4}$	168	177	1
		$\bar{2}$	350	−347	0
		0	91	−81	2
		2	233	193	6
		4	97	86	2
		6	227	−236	1
		10	142	154	2
		16	85	89	1
6	1	2	77	−64	3
		4	201	−176	1
		5	85	−78	1
		9	91	−73	4
		10	130	−120	2
		14	149	154	1
6	2	4	85	−90	1
		8	91	−89	0
		11	110	123	3
		12	85	−74	2
6	3	1	97	−93	1
		2	130	122	1
7	$\bar{3}$	$\overline{17}$	52	69	4
		$\overline{14}$	97	−89	2
		$\overline{12}$	214	225	2
		$\overline{11}$	123	−92	6
		$\bar{9}$	65	72	2
		$\bar{7}$	156	−148	1
		$\bar{3}$	58	67	2
7	$\bar{2}$	$\overline{20}$	104	98	1
		$\overline{19}$	97	94	1
		$\overline{14}$	110	−99	2
		$\overline{13}$	110	109	0
		$\overline{11}$	91	82	2
		$\overline{10}$	58	−52	2
		$\bar{9}$	85	84	0
		$\bar{8}$	104	−96	2
		$\bar{7}$	227	−219	1
		$\bar{5}$	85	75	2
		$\bar{4}$	136	−140	1
		$\bar{1}$	149	−151	0
		0	123	116	1
7	$\bar{1}$	$\overline{22}$	117	105	2
		$\overline{20}$	97	79	4
		$\overline{16}$	130	131	0
		$\overline{15}$	65	−75	2
		$\overline{14}$	91	93	0
		$\overline{13}$	142	133	2
		$\overline{12}$	91	−88	1
		$\overline{11}$	58	−58	0
		$\overline{10}$	123	−103	4
		$\bar{8}$	162	159	0
		$\bar{5}$	85	−78	2
		$\bar{4}$	486	−433	5
		$\bar{3}$	85	−72	3
		$\bar{2}$	58	51	2
		$\bar{1}$	58	74	4

h	k	l	$|F_o|$	F_c	$\omega|F_o-F_c|$
7	0	$\overline{26}$	92	−89	1
		$\overline{20}$	85	−82	1
		$\overline{16}$	213	278	10
		$\overline{12}$	110	−148	8
		$\overline{10}$	266	298	5
		$\bar{6}$	104	−126	5
		$\bar{4}$	82	81	0
		$\bar{2}$	130	139	2
		0	292	−287	1
		6	201	−215	2
		18	97	108	2
7	1	1	61	76	4
		2	234	173	9
		3	110	−116	1
		6	156	−148	1
7	2	8	85	86	0
7	3	1	110	−116	1
8	$\bar{3}$	$\overline{11}$	136	−138	0
		$\overline{10}$	77	−81	1
		$\bar{9}$	136	142	1
		$\bar{8}$	58	−48	3
		$\bar{7}$	58	72	3
		$\bar{5}$	142	−125	3
		$\bar{3}$	85	74	2
		$\bar{2}$	97	91	1
8	$\bar{2}$	$\overline{23}$	39	40	0
		$\overline{19}$	71	−75	1
		$\overline{17}$	77	87	2
		$\overline{14}$	58	−68	2
		$\overline{13}$	58	−65	2
		$\overline{12}$	58	59	0
		$\overline{11}$	58	29	7
		$\overline{10}$	91	90	0
		$\bar{8}$	325	−329	1
		$\bar{7}$	156	−167	2
		$\bar{6}$	91	67	5
		$\bar{5}$	91	65	6
		$\bar{4}$	65	56	2
		$\bar{3}$	65	80	4
		$\bar{2}$	65	−74	2
		$\bar{1}$	110	−95	3
		0	65	63	0
8	$\bar{1}$	$\overline{22}$	58	−64	1
		$\overline{20}$	91	91	0
		$\overline{19}$	77	69	2
		$\overline{16}$	123	−112	2
		$\overline{15}$	136	−118	3
		$\overline{14}$	110	95	3
		$\overline{13}$	110	107	1
		$\overline{12}$	130	111	4
		$\bar{9}$	110	−102	2
		$\bar{7}$	91	69	5
		$\bar{6}$	110	79	6
		$\bar{5}$	221	−199	3
		$\bar{4}$	182	−173	1
		$\bar{3}$	247	235	2
		$\bar{1}$	130	−112	3
		0	91	60	7
8	0	$\overline{24}$	82	−74	2
		$\overline{22}$	71	61	2
		$\overline{18}$	111	−114	1
		$\overline{12}$	177	−257	14
		$\overline{10}$	98	141	9
		$\bar{6}$	101	120	4
		$\bar{4}$	110	−122	3
		$\bar{2}$	98	−82	3
		0	330	385	7
		2	240	−277	5
		6	65	80	4
		16	52	−16	9
8	1	3	91	74	4
		4	110	103	1
		5	91	−117	6
		7	58	76	4
		8	58	−77	4
		11	110	−5	22
9	$\bar{3}$	$\overline{19}$	39	20	5
		$\overline{15}$	58	12	12
		$\overline{14}$	97	46	11
		$\overline{13}$	77	92	3
9	$\bar{2}$	$\overline{19}$	71	−74	0
		$\overline{16}$	71	70	0
		$\bar{7}$	104	98	1

TABLE 8. *(Continued.)*

h	k	l	$\lvert F_o\rvert$	F_c	$\omega\lvert F_o-F_c\rvert$	h	k	l	$\lvert F_o\rvert$	F_c	$\omega\lvert F_o-F_c\rvert$	h	k	l	$\lvert F_o\rvert$	F_c	$\omega\lvert F_o-F_c\rvert$	h	k	l	$\lvert F_o\rvert$	F_c	$\omega\lvert F_o-F_c\rvert$
		$\bar{5}$	123	−123	0			$\overline{14}$	58	−65	2			$\bar{9}$	71	−72	0			2	77	103	6
		$\bar{3}$	85	76	2			$\overline{12}$	123	141	3			$\bar{8}$	136	125	2			8	59	48	3
9	$\bar{1}$	$\overline{16}$	77	−72	1			$\overline{10}$	201	−204	1	10	$\bar{1}$	$\bar{5}$	117	106	2	10	1	3	91	−97	1
		$\overline{13}$	136	−121	3			0	211	220	1			$\bar{4}$	117	92	5			4	71	−72	0
		$\overline{12}$	85	76	2			2	110	−112	0			$\bar{3}$	85	−110	6			6	77	40	9
		$\bar{9}$	91	67	5			12	65	−85	5			$\bar{2}$	97	−46	11			8	52	20	8
		$\bar{8}$	156	−147	2	9	1	3	85	79	1			0	77	−56	5						
		$\bar{7}$	123	−132	2			5	104	−90	3	10	0	$\overline{18}$	58	80	5	11	0	$\overline{16}$	52	46	2
		$\bar{6}$	91	65	6			6	85	74	2			$\overline{16}$	65	−74	2			$\overline{14}$	58	−59	0
		$\bar{5}$	91	79	3			7	77	83	1			$\overline{12}$	117	133	3			$\bar{4}$	77	72	1
		$\bar{4}$	194	182	2	10	$\bar{2}$	$\overline{19}$	20	26	2			$\overline{10}$	117	−114	1			$\bar{2}$	65	−88	6
		$\bar{3}$	130	115	3			$\overline{18}$	52	−46	2			$\bar{4}$	104	90	3			0	91	−98	2
9	0	$\overline{16}$	117	−122	1									0	201	−214	2			2	77	78	0

der Waals radii. The final interatomic distances, together with their standard deviations, are listed in Table 9, where the values obtained at the end of the two-dimensional refinement are also given for comparison. On application of the significance test developed by Cruickshank [19] differences in the present structure of 0·028 Å in C–Cl, of 0·037 Å in C–C, of 0·033 Å in C–N, of 0·031 Å in C–O, and 0·027 Å in C–S would be at the level of possible significance. Bond angles are recorded in Table 10. The benzene ring was found to be planar within 0·006 Å. The eight-membered amidinium carboxylate ring was planar with an average deviation of 0·04 Å from the mean plane through the eight atoms. The environment about each of the hydrogen-bonded nitrogen atoms was also planar with an average deviation of 0·05 Å from the mean plane of $C_8, N_1, O_1, O_{1''}$ and of 0·04 Å from the mean plane of $C_8, N_2, O_2, O_{2''}$. The atoms C_8, N_1, N_2, S of the thiouronium cation were coplanar, and the methyl-carbon atom, C_9, lay 0·44 Å above (or below) the plane of the others, the S–C_9 bond being inclined to it at an angle of 14°.

TABLE 9.

Interatomic distances (Å).

	From two-dimensional refinement	From three-dimensional refinement (with standard devn.)			From two-dimensional refinement	From three-dimensional refinement (with standard devn.)	
Cl–C$_1$	1·61	1·746	(0·011)	S–C$_8$	1·64	1·727	(0·012)
C$_1$–C$_2$	1·40	1·330	(0·015)	S–C$_9$	1·66	1·808	(0·014)
C$_2$–C$_3$	1·38	1·395	(0·014)	C$_8$–N$_1$	1·30	1·310	(0·012)
C$_3$–C$_4$	1·40	1·404	(0·013)	C$_8$–N$_2$	1·22	1·338	(0·012)
C$_4$–C$_5$	1·39	1·354	(0·013)				
C$_5$–C$_6$	1·39	1·397	(0·015)	O$_1\cdots$N$_1$	2·92	2·794	(0·010)
C$_6$–C$_1$	1·39	1·401	(0·016)	O$_2\cdots$N$_2$	2·92	2·771	(0·010)
C$_4$–C$_7$	1·50	1·494	(0·012)	O$_1\cdots$N$_{1'}$	2·82	2·790	(0·010)
C$_7$–O$_1$	1·23	1·257	(0·011)	O$_2\cdots$N$_{2'}$	2·89	2·786	(0·010)
C$_7$–O$_2$	1·29	1·265	(0·011)				

TABLE 10.

Bond angles.

Cl–C$_1$–C$_2$ ...	118·35°	C$_6$–C$_1$–C$_2$ ...	123·98°	N$_1$–C$_8$–N$_2$ ...	119·77°	C$_7$–O$_1\cdots$N$_{1'}$ ...	128·17°
Cl–C$_1$–C$_6$ ...	117·66	C$_3$–C$_4$–C$_7$ ...	119·56	N$_1$–C$_8$–S	124·62	C$_7$–O$_2\cdots$N$_{2'}$ ...	157·15
C$_1$–C$_2$–C$_3$ ...	117·48	C$_5$–C$_4$–C$_7$ ...	121·71	N$_2$–C$_8$–S	115·49	N$_1\cdots$O$_1\cdots$N$_{1'}$	98·93
C$_2$–C$_3$–C$_4$ ...	121·37	C$_4$–C$_7$–O$_1$ ...	118·62	C$_8$–S–C$_9$	100·72	N$_2\cdots$O$_2\cdots$N$_{2'}$	83·40
C$_3$–C$_4$–C$_5$ ...	118·73	C$_4$–C$_7$–O$_2$ ...	117·97			C$_8$–N$_1\cdots$O$_{1''}$ ...	134·05
C$_4$–C$_5$–C$_6$ ...	121·44	O$_1$–C$_7$–O$_2$ ...	123·39	C$_7$–O$_1\cdots$N$_1$	118·10	C$_8$–N$_2\cdots$O$_{2''}$ ...	120·52
C$_5$–C$_6$–C$_1$ ...	116·96			C$_7$–O$_2\cdots$N$_2$	119·12	O$_1\cdots$N$_1\cdots$O$_{1''}$	104·37
				O$_1\cdots$N$_1$–C$_8$	119·83	O$_2\cdots$N$_2\cdots$O$_{2''}$	119·78
				O$_2\cdots$N$_2$–C$_8$	118·76		

DISCUSSION

In the crystal structure the two nitrogen atoms sharing the positive charge of each cation are opposed to the two oxygen atoms sharing the negative charge of one anion, each to each, and the strong hydrogen-bonded linkages postulated previously [1] are confirmed by the relatively short $O_1\cdots(H)N_1$ and $O_2\cdots(H)N_2$ bond lengths shown in

[19] Cruickshank, *Acta Cryst.*, 1953, **6**, 698.

Table 9. Each *S*-methylthiouronium group lying parallel to the *c* crystallographic axis is further linked laterally through comparatively short hydrogen bonds with the oxygen atoms of neighbouring chlorobenzoate anions in the manner predicted.[1] Each of these is in turn linked to two other *S*-methylthiouronium cations, one opposed and the other lateral, to form a system of O $\cdots$ (H)N hydrogen bonds extending in an infinite spiral about the screw axes parallel to *b*. Between these sheets consisting of firmly bonded ions the only cohesive forces are relatively weak van der Waals ones, as already indicated by the cleavage properties of the crystals. Plate 1 illustrates the structure viewed along the *b*-axis and shows the clockwise and anticlockwise disposition of spirals of O $\cdots$ (H)N hydrogen bonds; Plates 2 and 3 show a model of the structure viewed along the *c*- and the *a*-axis, respectively. This type of structure is probably characteristic of the whole class of *N*-unsubstituted amidinium carboxylates.

Abrahams [6b] gives a value of 1·82 Å as the length of a pure C–S single bond, and the S–C_9 bond length (1·808 Å) found in the present determination is in good agreement. The S–C_8 bond, however, is significantly shorter (1·727 Å), being slightly larger than the lengths quoted for the C–S bond in ethylenethiourea [20] and in thiourea,[21] and indicates, on the basis of Abrahams's curve,[6b] an approximately 50% double-bond character. Similar observations have recently been recorded for *S*-methylthiouronium sulphate.[22] Of greater interest perhaps is the difference of about 9° between the two N–C–S bond angles in the crystal structure of *S*-methylthiouronium *p*-chlorobenzoate. Precisely similar observations have been made on *S*-methylthiouronium sulphate [22] and on dithiodiformamidinium di-iodide [23] (IV; X = I), but to a less marked extent (3°) with dithiodiformamidinium dibromide [23] (IV; X = Br). In each case the larger angle is the one to which the remote substituent on the sulphur atom stands in a *syn*-relationship, and, in the present instance, inspection of a model and of a planar diagram drawn by using Pauling's van der Waals radii suggest that the distortion is due to the closeness of approach of the methyl group to the $(N_{1'}\text{-})$hydrogen-bonded oxygen atom $(O_{1''})$ of a neighbouring anion.

In view of the overall accuracy of the structure refinement we were surprised to note the irregular bond lengths in the benzene ring, and, in particular, the short C_1–C_2 interatomic distance. The test of omitting the planes with maximum disagreement described above suggested that this apparent shortening was not related to any overt experimental errors. This kind of observation has been made previously, for example, with benzoic acid [24] and dibenzyl hydrogen phosphate,[25] where the variations were rather less than those we have observed, and with the di-*p*-bromobenzoyl ester of iresin,[26] in which the variations are the largest we have traced. Although bond-length variations in simple benzene derivatives have been considered theoretically,[27] no satisfactory reason for them is yet available. In searching for an explanation of this effect we have made a survey of recorded C–C interatomic distances in compounds containing a mono- or 1,4-di-substituted benzene ring and a correlation with various structural features was attempted. Fig. 5 illustrates the observed scatter of C–C bond lengths in the form of histograms, and the results are analysed statistically in Table 11, which shows the probabilities of the observed variance ratios between different groups. It was found that substances containing heavy atoms showed a wider scatter of the C–C bond lengths in the benzene rings than did those with light atoms only, even when accurate three-dimensional analyses in the first group
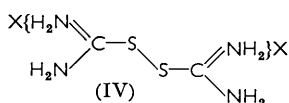
[20] Wheatley, *Acta Cryst.*, 1953, **6**, 369.
[21] Kunchur and Truter, *J.*, 1958, 2551.
[22] Stam, *Acta Cryst.*, 1962, **15**, 317.
[23] Foss, Johnsen, and Tvedten, *Acta Chem. Scand.*, 1958, **12**, 1782.
[24] Sim, Robertson, and Goodwin, *Acta Cryst.*, 1955, **8**, 157.
[25] Dunitz and Rollett, *Acta Cryst.*, 1956, **9**, 327.
[26] Rossmann and Lipscomb, *Tetrahedron*, 1958, **4**, 275.
[27] Cf. Trotter. *Tetrahedron*, 1960, **8**, 13.
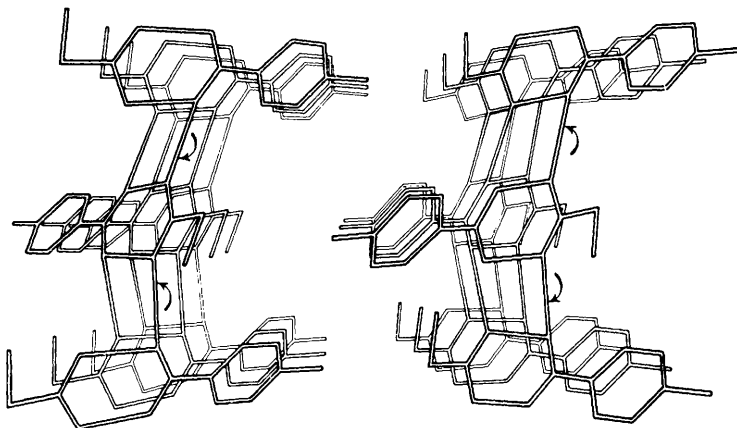
PLATE 1. Partly perspective drawing of skeleton model giving view along *b*-axis, and showing clockwise and anticlockwise disposition of spirals of O $\cdots$ HN hydrogen bonds.

The 00*l* cleavage plane passes through the clear space.
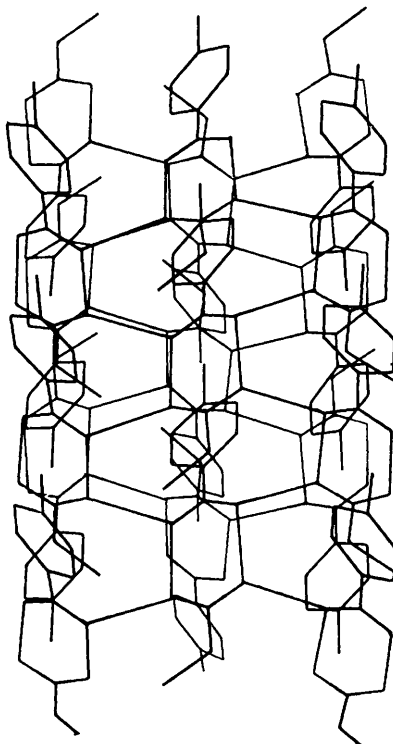
PLATE 2. Photograph of skeleton model showing view along *c*-axis.
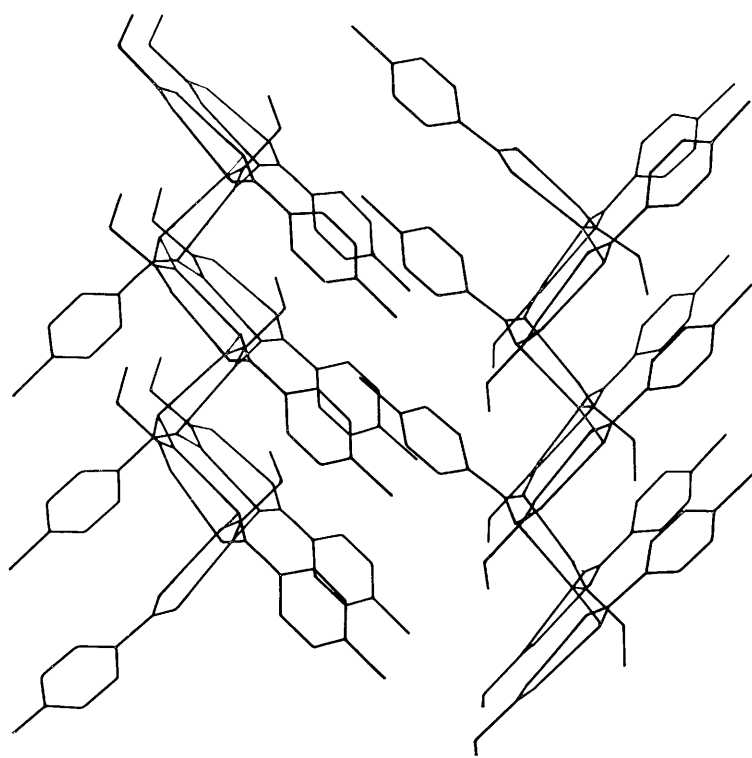
PLATE 3. Photograph of skeleton model showing view along *a*-axis.

were compared with less accurate two-dimensional analyses in the second group. An even more striking, and statistically highly significant, correlation was found when substances containing only atoms with isotropic thermal movement were compared with substances
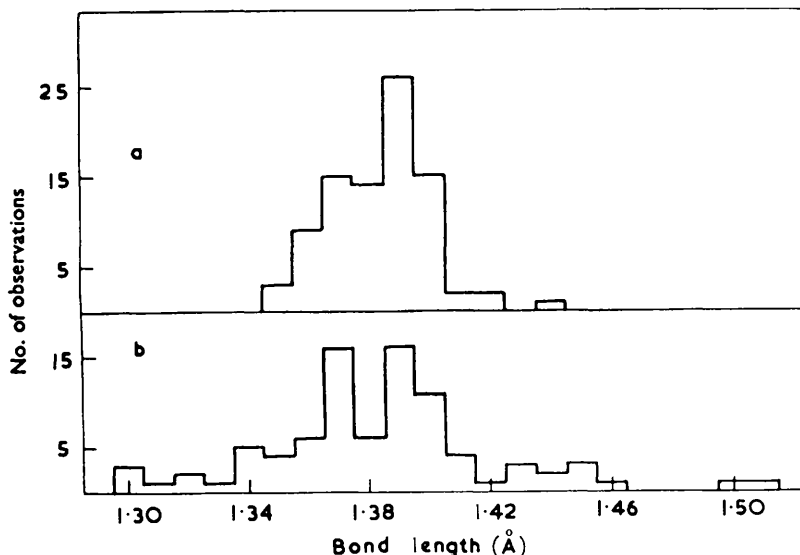
FIG. 5. Variation of recorded carbon–carbon bond lengths in mono- and 1,4-di-substituted benzene rings.

(a) In molecules in which all atoms vibrate isotropically (mean, 1·384 Å; variance, 0·000275). (b) In molecules in which certain atoms vibrate anisotropically (mean, 1·383 Å; variance, 0·001448).

containing one or more atoms executing marked anisotropic vibration, and the correlation was independent of the accuracy of the structure determination. In substances showing a scatter of C–C bond-length values there was also a tendency for the bond corresponding to our C_1–C_2 bond to be the shortest. We are unable to offer a theoretical explanation

TABLE 11.

Statistical analysis of variation in length of carbon–carbon bonds in mono- and 1,4-di-substituted benzene rings.

Thermal movement [atom(s) present]	No. of obsns.	Mean ring C–C bond length	Variance	Variance ratio		Probability of variance ratio
(1) Isotropic **	24	1·382	0·000241	(1) and (3)	1·17	>0·20
(2) Anisotropic **	36	1·386	0·001963	(2) and (4)	1·83	0·01—0·05
(3) Isotropic *	63	1·385	0·000282	(1) and (2)	8·15	<0·001
(4) Anisotropic *	51	1·381	0·001075	(3) and (4)	3·81	<0·001
(1 and 3) All isotropic	87	1·384	0·000275 }	(1 and 3) and	5·27	<0·001
(2 and 4) All anisotropic	87	1·383	0·001448 }	(2 and 4)		
(5) Isotropic [light atoms only]	54	1·384	0·000254	(5) and (7)	1·42	0·05—0·10
(6) Anisotropic [light atoms only]	18	1·382	0·000461	(6) and (8)	3·72	0·001—0·01
(7) Isotropic [heavy atom(s)]	33	1·389	0·000361	(5) and (6)	1·81	0·05
(8) Anisotropic [heavy atom(s)]	69	1·383	0·001714	(7) and (8)	4·75	<0·001
(9) Anisotropic ** [heavy atom(s)]	30	1·384	0·002290 }	(9) and (10)	1·80	0·01—0·05
(10) Anisotropic * [heavy atom(s)]	39	1·382	0·001269 }			

The grading signs (** and *) have the significance defined in " Tables of Interatomic Distances and Configurations in Molecules and Ions," Special Publ. No. 11, The Chemical Society, London, 1958 (pp. 14, 27), from which, together with the following supplementary sources, the data were obtained: present work; Webster, *J.*, 1956, 2841; Rossmann and Lipscomb, *Tetrahedron*, 1958, **4**, 275; Dunitz and Rollett, *Acta Cryst.*, 1956, **9**, 327; Penfold and White, *ibid.*, 1959, **12**, 130; Frasson, Garbuglio, and Bezzi, *ibid.*, p. 126; Houstry and Clastre, *ibid.*, 1957, **10**, 695.

of this effect but we should like to point out the close correlation between variations in the C–C bond lengths and the presence, especially, of a heavy atom as a *para*-substituent vibrating preferentially at right angles to the bond linking it with the benzene ring. It is very probable that this effect, which may be a simple mechanical resonance one, does not extend beyond the immediate environment of the atom showing anisotropic vibration and that reasonable deductions can be based on the remaining interatomic distance values.
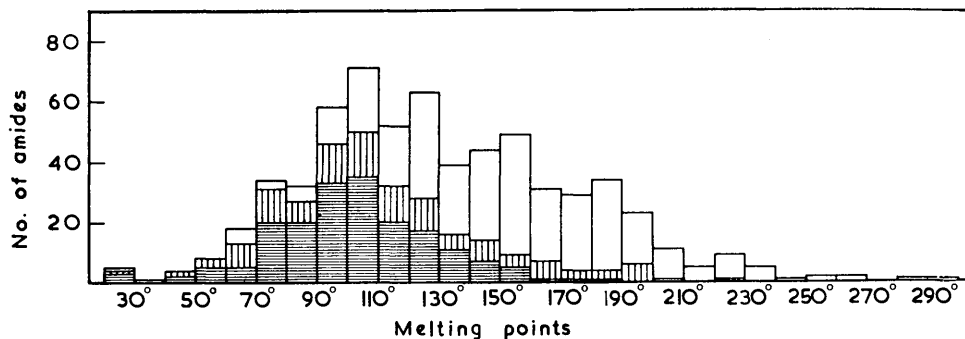
FIG. 6.   Distribution of m. p.s of 632 representative amides.

≡ 188 Amides of acyclic carboxylic acids (Beilstein's " Handbuch der organischen Chemie," 4te Aufl., Springer, Berlin, 1920, Bd. II).

‖‖‖ 118 Amides of acyclic hydroxy- and oxo-carboxylic acids (*op. cit.*, 1921, Bd. III).

□ 326 Amides of carbocyclic carboxylic acids (*op. cit.*, 1926, Bd. IX).

Monoamides derived from polybasic acids, other than those containing a free carboxyl group, are included.

The amidinium carboxylate doublet ion-pair (III) is formally reminiscent of the dimers (V) formed by carboxylic acids, but the latter, of course, lack hydrogen atoms available for lateral hydrogen bonding. It might be thought, however, that amides would show some resemblances in crystalline behaviour to the amidinium carboxylates, as, like the latter (III), the dimers (VI) that amides can form have two hydrogen atoms available for lateral bonding. A survey (Fig. 6) of the melting points of 632 representative amides shows no narrow spread of melting point such as that found (Table 1 and Fig. 1) for the *S*-arylmethylthiouronium salts of carboxylic acids, and suggests more latitude in the modes of crystallisation adopted by amides. Benzamide,[28] for example, forms dimers (VI; R = Ph) that subsequently form endless chains (VII), recalling the behaviour of dioxopiperazine,[29] but with nicotinamide [30] the ring-nitrogen atom participates in the hydrogen-bonding arrangements to give a two-dimensional network; acetamide shows still another arrangement [31] with continuous hydrogen-bonded chains forming loops of six molecules. The formation of chains has also been observed with carboxylic acids, for example, in formic acid,[32] in the α-form of oxalic acid,[33] and in nicotinic acid,[34] which forms chains of molecules linked by N······ HO bonds between the carboxyl group of one molecule and the nitrogen atom of the next. With the amidinium carboxylates, however. the presence of the specific ionic charges is responsible, we believe, for the formation of

[28] Penfold and White, *Acta Cryst.*, 1959, **12**, 130.

[29] Corey, *J. Amer. Chem. Soc.*, 1938, **60**, 1598.

[30] Wright and King, *Acta Cryst.*, 1954, **7**, 283.

[31] Senti and Harker, *J. Amer. Chem. Soc.*, 1940, **62**, 2008.

[32] Holtzberg, Post, and Fankuchen, *Acta Cryst.*, 1953, **6**, 127; in contrast, formamide associates in coplanar cyclic dimers (Ladell and Post, *ibid.*, 1954, **7**, 559).

[33] Hendricks, *Z. Krist.*, 1935, **91**, 48; Cox, Dougill, and Jeffrey, *J.*, 1952, 4854.

[34] Wright and King, *Acta Cryst.*, 1953, **6**, 305.

doublet ion-pairs (III) *in solution,* and their preliminary formation limits their subsequent aggregation into crystals to a uniform pattern.
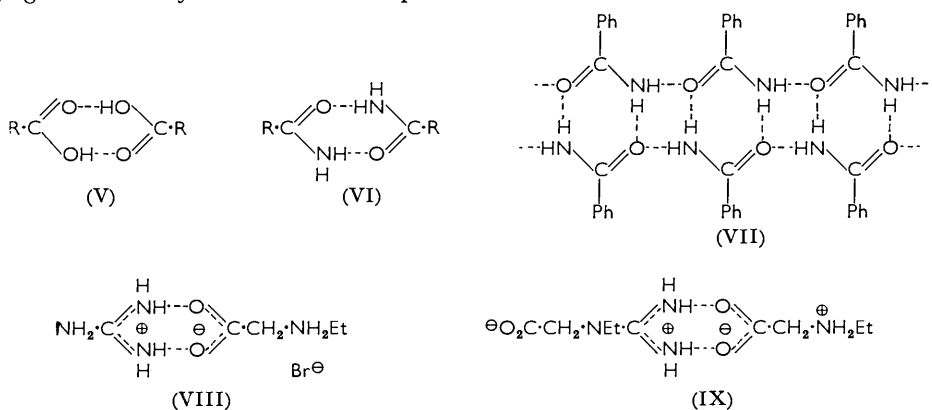
The amidinium carboxylate structure (III) is found [35] in the crystal structure of creatine monohydrate, $^{\ominus}O_2C \cdot CH_2 \cdot NMe \cdot C(\cdot NH_2) \overset{\oplus}{:} NH_2, H_2O$, but in this case the doublet ion-pairs form endless rows of end-to-end creatine molecules that are hydrogen-bonded laterally in layers held together by hydrogen-bonding involving the water of crystallisation between alternate rows. The structure (III) is almost certainly involved in the double salts formed between guanidines and amino-acids, such as *N*-ethylglycine–guanidinium bromide (VIII) and the *N*-ethylglycocyamine–*N*-ethylglycine complex (IX) described by Armstrong.[36] The present work and the above observations indicate a more precise picture of the probable mode of participation of the guanidino-group of arginine in the tertiary structures of proteins than has hitherto been available. In fact, the role of the guanidino-group of arginine in the tertiary structure of proteins has been grossly under-estimated, and, at times, even overlooked; [37] at best, it has been regarded merely as a basic group and considered in terms similar to those applied to the ε-amino-group of lysine. The guanidino-group of arginine (pK_a 12·5) is, however, the strongest cationic group found in proteins and must attract to itself suitably situated and orientated anionic groups. Barring small extraneous anions, these could, in the native protein, be the ionised carboxyl-terminal end of the peptide chain or, more probably, the distal ionised carboxyl groups of aspartic or glutamic acid residues in the peptide chain. The more exacting stereochemical requirements of the amidinium carboxylate structure (III), when applied to the guanidino-group of arginine in proteins, introduce constraints that are absent in the case of the ε-amino-group of lysine, and an amidinium carboxylate bridge formed between two well-separated arginine and glutamic, or aspartic, acid residues in a peptide chain will therefore confer a considerable degree of rigidity on the native protein, apart from the opportunity of further stabilisation resulting from cross-bracing of the bridge by lateral hydrogen bonding. It is to be expected [38] that the amino-acid side-chains will project from the main peptide chain in the fully staggered and extended all-*trans*-conformation,* and an amidinium carboxylate bridge (X) formed between the arginine-guanidino-group

* In the crystal structure of one form of free L-glutamic acid, however, there appears to be a gauche-conformation at the βγ-position (Hirokawa, *Acta Cryst.*, 1955, **8**, 637). A second form, probably the all-*trans*-one, has not yet been investigated.

[35] Mendel and Hodgkin, *Acta Cryst.*, 1954, **7**, 443.
[36] Armstrong, *J. Org. Chem.*, 1956, **21**, 503.
[37] Cf., *e.g.*, Linderstrøm-Lang and Schellman, in Boyer, Lardy, and Myrback's " The Enzymes," 2nd edn., Academic Press, Inc., New York, 1959, Vol. I, p. 451; Scheraga, " Protein Structure," Academic Press, Inc., New York, 1961.
[38] Kendrew, Watson, Strandberg, Dickerson, Phillips, and Shore, *Nature*, 1961, **190**, 666.

and the γ-carboxyl group of a glutamic acid residue, having its two ends pointing away from each other, could link two α-positions in the peptide chain separated by about 13·5—14·0 Å and having appropriately directed αβ-bonds; similarly, participation of aspartic acid would give a bridge that could link two α-carbon atoms in the peptide chain separated in space by up to 12·5 Å, again if we assume suitably directed αβ-bonds. A perfect example of a bridge of this nature is to be seen in a detailed three-dimensional structure proposed by Kendrew [39] for sperm-whale myoglobin, where the participating residues are arginine (" CD-3 ") and glutamic acid (" E-10 "); Kendrew's structure is of further interest to us here as the lateral amidinium carboxylate hydrogen atoms are shown employed in hydrogen-bonding with the β-carboxyl group of an aspartic acid residue (" E-3 ") and the carboxyl group of one of the 2-carboxyethyl side-chains of the hæm moiety, respectively, after the fashion we have emphasised for the pattern of crystallisation of amidinium salts of carboxylic acids. Thus, in addition to the fact of its own presence, the amidinium carboxylate bridge (X) in myoglobin is cross-braced laterally to two other parts of the chromoprotein to give a powerful coalition of forces for the maintenance of the protein in its native conformation. Moreover, the hydrogen-bonding to the hæm carboxyl group may have in myoglobin the further reciprocal purpose of stabilising the molecule for its respiratory function, since, in the case of hæmoglobin, artificial hæmoglobins prepared from hæms lacking free carboxyl groups, and therefore hydrogen-bonding capabilities, are relatively unstable.[40]

(X)

(XI)

(XII)
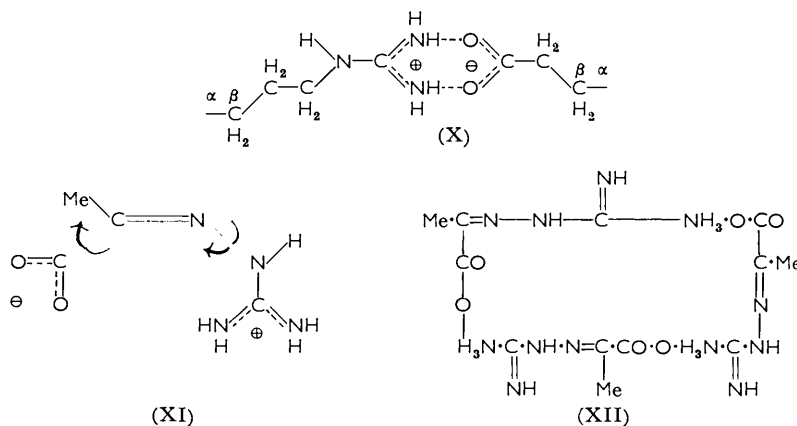
That native egg albumin may be stabilised by the presence of an amidinium carboxylate bridge is suggested by the fact that it can be titrated between pH 2·5 and 12·0 without denaturation, indicating that the basic group involved has pK_a greater than 12, thus excluding α- and ε-amino-groups and imidazole groups,[41] and rupture of an amidinium carboxylate bridge could, in this case, be the event leading to denaturation.. We believe that the amidinium carboxylate bridge may play a major role in maintaining the conformations of native proteins, and in a much more efficient manner than any other form of tertiary structure; thus, in addition to the existence of the bridge itself, its cross-bracing by lateral hydrogen-bond formation, as it appears to be present in myoglobin, may be a regular feature in maintaining the relative positions of separate helical regions of the peptide chain in globular proteins, and account, for example, for the compact and sparingly hydrated nature of the lysozyme molecule.[42] Amidinium carboxylate formation between discrete protein molecules could also account for association phenomena. The efficiency

[39] Kendrew, *Scientific American*, 1961, **205**, No. 6, 96.
[40] O'Hagan, *Biochem. J.*, 1960, **74**, 417; Harrap, Gratzer, and Doty, *Ann. Rev. Biochem.*, 1961, **30**, 269.
[41] Neuberger, *J. Sci. Food Agric.*, 1950, 80.
[42] Tanford and Wagner, *J. Amer. Chem. Soc.*, 1954, **76**, 3331.

of guanidine as a denaturing agent is, however, not necessarily related to any interaction with amidinium carboxylate bridges, as it is likely to interact even more readily with more accessible carboxyl groups involved in other forms of hydrogen-bonding in the tertiary structure of the protein. The amidinium carboxylate structure (III), moreover, probably possesses considerable thermal stability in solution in dissociating solvents, as suggested by the fact that the free amidinohydrazone (XI) of pyruvic acid has been found to be trimeric by the ebullioscopic method in glacial acetic acid.[43] This trimer was formulated by Wedekind and Bronstein [43] as the cyclic structure (XII), but a more acceptable cyclic structure results from rotation of the carboxylate and guanidinium groups in the monomer (XI) out of the plane of the paper in the directions shown through about 50° and 80°, respectively, and formation of a large ring containing three amidinium carboxylate (III) groups.

We have previously suggested [1] that amidinium carboxylate formation may underlie the diverse pharmacological and chemotherapeutic activities of amidines, guanidines, and isothioureas; these properties appear to be those of the amidinium cations,[44] which are presumably held ionically to cellular anionic groups by mechanisms such as those we have discussed above. It is also probable that the stereochemical consequences of amidinium carboxylate formation explain why replacement of the amidino-group by the amino-group in otherwise comparable structures may give substances with little or none of the biological activity of the amidines, although, on occasion, such substitution may give practically unimpaired biological activity.[45]

APPENDIX

The data analysed in Table 1 and Fig. 1 were obtained from the sources cited previously [1] and from the following supplementary sources:

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