values of 1·28 Å and 1·38 Å found for the C–N bonds in the amide groups of glutamine and acetamide respectively, taking into account the errors in these values. The amide group bond angles in nicotinamide, however, are very close to those found for the amide group in glutamine but differ from those found for acetamide. It may therefore be concluded that, as in the case of glutamine, the C–N bond of the amide group in nicotinamide has a greater degree of double-bond character than the corresponding bond in acetamide.

The C–O bond in nicotinamide appears to be shorter than the corresponding bonds in glutamine and acetamide. As the difference in length is of possible significance it may be inferred that the C–O bond in nicotinamide has greater double-bond character than the C–O bonds in the other two substances. Both in glutamine and acetamide, however, the evidence is in favour of the keto form for the amide group, and in view of this it seems even more probable that the amide group has the keto configuration in nicotinamide. This is confirmed in some measure by the hydrogen bonding arrangement, in which both hydrogen atoms available for bond formation are attached to atom N_2. Some indication of the positions of the hydrogen atoms is also given by the c-axis Fourier projection in which, if normal carbon to hydrogen and nitrogen to hydrogen bonds are used, the positions of the hydrogen atoms lie in regions of electron density of $1 \rightarrow 2$ e.Å^{-2}. It can be seen that there are two such regions around atom N_2.

Nicotinamide forms two hydrogen bonds, one of length 2·99 Å from atom N_2 to the oxygen atom of molecule M''', and the other of length 3·09 Å from atom N_2 to the ring nitrogen atom of molecule $_{\bar{x}\bar{z}}M'''$ (Fig. 4). The values are in agreement with those found

for bonds of the type N–H $\cdots$ N, which range from 2·94 Å to 3·30 Å, and for N–H $\cdots$ O, which have values ranging from 2·69 Å to 3·17 Å (Donohue, 1952). No other intermolecular distances are shorter than 3·2 Å. This arrangement of hydrogen bonds links each molecule to four other molecules in two-dimensional networks parallel to (010). The networks are held together by van der Waals forces only.

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The Structure of Tropine-Hydrobromide

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Tropine-hydrobromide is monoclinic with $a = 6·32$, $b = 20·2$, $c = 7·44$ Å, $\beta = 95°$; $Z = 4$; space group $P2_1/n$. The molecule has the *trans* chair configuration.

Introduction

The structure of tropinone and its derivatives was determined by a number of chemists in the period of 1880–1900 (see Willstätter & Bommer, 1921). The only remaining ambiguity was the structure of tropine and pseudotropine, both of which were obtained on reduction of tropinone. For these alcohols there are four possible structures (Fig. 1). We can expect

that I and II will easily be converted into each other; the same is true for III and IV. The tropinoles were not studied until 1951–2 when three independent groups published their work on these structures.

The first publication was that of Sixma, Siegmann & Beyerman (1951) who, by means of reaction rates, concluded that tropine has configuration IV and pseudotropine the configuration II (see also Siegmann,

1952). Fodor & Nádor (1952), from N–O acyl migration, drew exactly the opposite conclusion, namely that tropine has the configuration II and pseudotropine
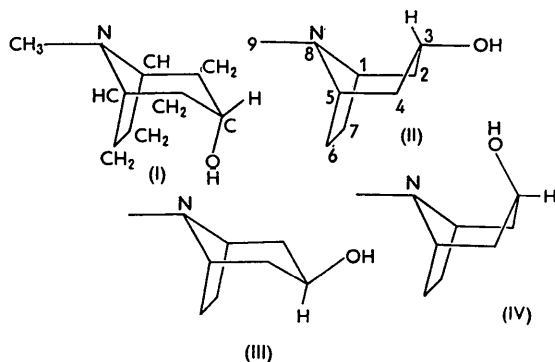

Fig. 1.

the configuration IV. At this point our investigation started. When it was well under way, Nickon & Fieser (1952), working independently and more thoroughly along the same lines as Fodor & Nádor, gave conclusive evidence which confirmed the results of these authors. Zenitz, Martini, Priznar & Nachod (1952) gave additional support by measurements of dipole moments, infra-red absorption and molecular refraction.

Although the structure of tropine seemed now to be beyond doubt, we decided to pursue our investigation in order to establish whether the constellation is the boat or the chair form.

Still later, Paddock (1953) confirmed the view of Sixma et al., whereas Clemo & Jack (1953) supported the work of Zenitz et al. While we were writing this paper we learnt of the publication of Hardegger & Ott (1953), who proved the cis configuration of nor-pseudotropine by building a bridge between N and O by means of p-nitro-benzaldehyde.

It is of interest to note that most of the chemical evidence points to a boat form for pseudotropine, whereas we find a chair form for tropine although it would seem to be sterically unfavourable.

The structure determination

Choice of compounds

Tropine-hydrobromide and tropine-hydrochloride were kindly put at our disposal by Dr H. C. Beyerman of the Laboratory of Organic Chemistry of the University of Amsterdam. The compounds are not isomorphous:

Tropine-hydrochloride

$a = 6.5, b = 11.2, c = 14.3$ Å, $\beta = 93°$;

$Z = 4$; space group (probably) $P2_1$.

Tropine-hydrobromide

$a = 6.32, b = 20.2, c = 7.44$ Å, $\beta = 95°$;

$Z = 4$; space group $P2_1/n$.

As the hydrobromide can be studied by the heavy-atom method and has a centrosymmetric space group with two short axes, we chose this compound rather than the chloride; the more so because the main purpose of this investigation was to distinguish between the configurations I, II, III and IV.

The crystals

The rather hygroscopic crystals were obtained by dissolving the amorphous mass of tropine-hydrobromide in a little alcohol, adding benzene and then carefully adding a separate layer of petrol-ether on to the liquid. After standing for one night at −10°C. crystals were obtained. These were long and flat, with easy cleavages making angles of 44° and 129° respectively with the length of the crystal (Fig. 2).
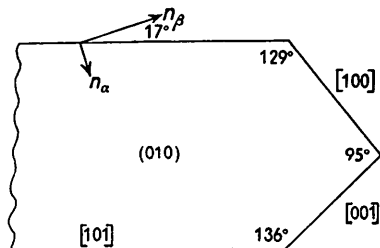

Fig. 2.

Optical properties

The crystals are biaxial and positive. In convergent light, falling on (010), both axes are visible, disposed symmetrically around the centre of the image. In parallel light, the larger refractive index (n_β) was found to make an angle of 17° with the length of the crystal (Fig. 2).

X-ray data

Weissenberg photographs of zero and first layers around the length of the crystal indicated that it was convenient to take the cleavage lines as the a and c axes (Fig. 2), the space group then being $P2_1/n$, with cell constants as given above. Crystals were cut along these axes and Weissenberg photographs were taken of zero layer lines, using the multiple-film technique and visual estimation of intensities. The crystal cut along the c axis was sufficiently small to need no absorption correction; the crystal along the a axis had a cross-section of 0.25×0.35 mm. A correction was applied, taking the crystal as a cylindrical rod of radius 0.15 mm. ($\mu = 57.1$ cm.$^{-1}$) and using data from the *International Tables*.

Structure determination

The Y and Z parameters of bromine were determined from the systematic peaks of a Patterson [100] projection. Structure factors were calculated using bromine positions only. A Fourier projection [100] was computed using those terms whose signs were
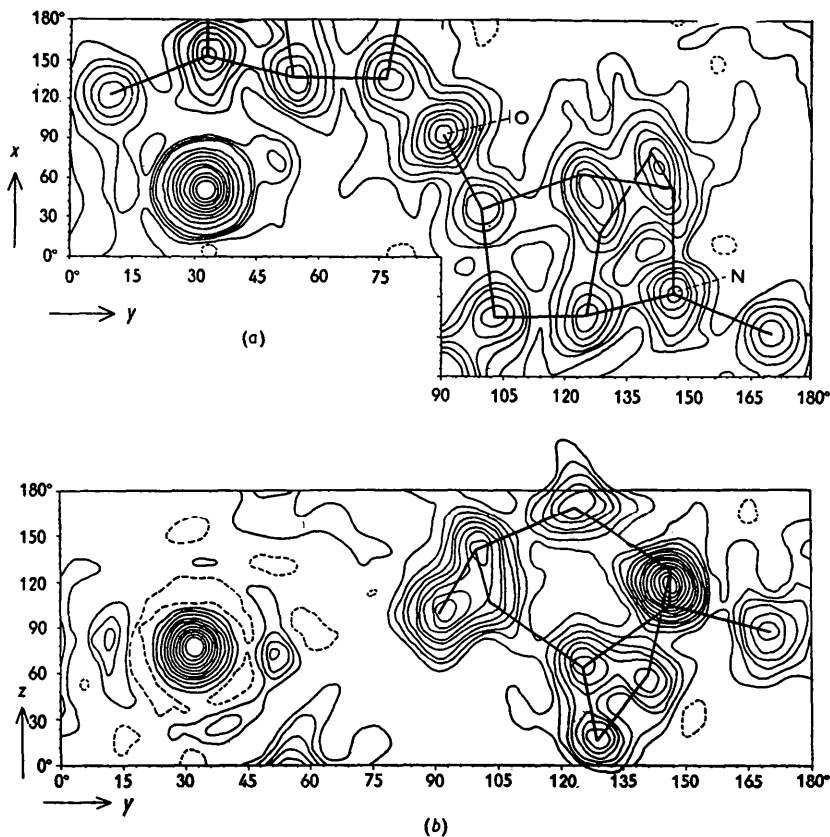
Fig. 3. Fourier projections of tropine-hydrobromide on an absolute scale. Broken lines indicate negative electron density. Full lines represent 1 e.Å^{-2}; first line drawn at 2 e.Å^{-2}. (a) [001] projection. Around the bromine ion lines are drawn at 2, 3, 4, 5, 10, 15, ... e.Å^{-2}. (b) [100] projection. Around the bromine ion lines are drawn at 5, 10, 15, ... e.Å^{-2}.

reasonably certain. Only a model of structure I (Fig.1) could be reconciled with this Fourier projection. Positions were assigned to the N, O and C atoms and the structure-factor calculation was repeated. After five refinements this process was stopped, the signs of all the F_o's being established.

Meanwhile, the X and Y parameters of bromine were independently determined directly from the [001] Weissenberg photographs. The [001] projection was treated in the same way as the [100] projection.

The F_o's were expressed on an absolute scale, temperature factor constants being 2·82 Å^2 for the

[100] projection and 3·88 Å^2 for the [001] projection. The difference between these temperature factors is clearly visible in the marked difference between the diffraction rings around the bromine atom in the two projections (Fig. 3).

The reliability-index, defined as $R = \Sigma||F_o|-|F_c|| \div \Sigma|F_o|$, was 0·151 for the [100] projection and 0·138 for the [001] projection. The reflexions 040, 060 and 002 from the a-axis crystal are strongly suspected to suffer from extinction. Without these three reflexions, the reliability index diminishes from 0·151 to 0·131.

Final co-ordinates are given in Table 1.

Table 1. Positions of the atoms

Atoms are numbered in accordance with chemical convention

Atom	X	Y	Z
Br	0·143	0·089	0·211
O	0·258	0·253	0·283
N	0·925	0·406	0·297
C_1	0·878	0·347	0·175
C_2	0·875	0·286	0·297
C_3	0·100	0·278	0·392
C_4	0·175	0·344	0·472
C_5	0·147	0·406	0·350
C_6	0·222	0·389	0·164
C_7	0·056	0·356	0·044
C_9	0·842	0·472	0·242

Discussion of the structure

Tropine has the *trans* configuration, in accordance with the results of Fodor & Nádor, Nickon & Fieser, Hardegger & Ott and others. Moreover, in the hydrobromide it has the chair form. The distances between oxygen and the carbon atoms of the 'bridge' (C_6 and C_7) are only 3·0 Å. Even when the errors in the atomic positions are estimated at somewhat less than 0·1 Å, this is still short of the normal value.

The position of the bromine ion is such that it completes a slightly distorted tetrahedral environment of the nitrogen atom. The distance N–Br (3·7 Å) is

rather long (3·5 Å in NH_4Br, 3·17 Å in strychnine-hydrobromide). This is possibly due to repulsion of the bromine ion by the CH_2 groups numbered C_2 and C_4, which in the chair form of the cyclohexane ring come much closer to bromine than the corresponding atoms in strychnine.

We are very grateful to Prof C. H. MacGillavry for her encouragement and never failing interest in the work. We are also much indebted to Mr A. Kreuger for his kind help in many ways, especially in the experimental work and the drawings. The experimental part of this work was carried out with the help of X-ray apparatus put at the disposal of this Laboratory by the Organization Z. W. O.

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The Crystal Structure of N,N'-Diglycyl-L-Cystine Dihydrate*

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The crystal structure of N,N'-diglycyl-L-cystine dihydrate has been determined by means of X-ray methods. The unit cell is monoclinic with $a = 12·26$, $b = 4·84$, $c = 17·17$ Å, and $\beta = 124°24'$ and contains two molecules. The space group is $A2$.

The structure of the molecule was deduced from Patterson projections and sections and refined by Fourier and least-squares methods. The bond distances and angles are similar to those found in related structures. Several unusual hydrogen bonds are reported, however. The possible effect of the very long hydrogen bond formed by the amide group on bond distances and planarity of that group is discussed. The structural features of the disulfide bridge in this molecule are also presented in some detail.

1. Introduction

Previous determinations of the crystal structures of simple amino acids, peptides, and related compounds have illustrated several structural features of these molecules which have been used as criteria in the deduction of the configurations of polypeptide chains. For example, the structures of N-acetylglycine (Carpenter & Donohue, 1950) and β-glycylglycine (Hughes & Moore, 1949) have suggested that resonance in the amide groups of peptide molecules forces these groups to assume a planar configuration and also results in a shortening of the C–N bond and a lengthening of the C=O bond from their normal values. All of the amino acid and peptide structures investigated to date have emphasized the importance of the role played by hydrogen bonding in determining the packing of these molecules. Therefore, by analogy, one might expect the packing of the polypeptide chains in proteins to be governed in part by similar considerations.

An interesting series of compounds from the point of view of possible application to protein structures is that consisting of cystine and peptides containing cystine. The $–CH_2–S–S–CH_2$-group (the disulfide bridge) common to the members of this series supposedly constitutes one of the more important means by which the polypeptide chains of proteins are held together. The fact that the peptide chain at one end of the bridge may be identical with that at the other end, a doubling back of the chain having taken place, also indicates that the configuration may provide a convenient method for holding polypeptide chains in a folded configuration. In an effort to determine the structural characteristics of the disulfide bridge an X-ray crystal structure investigation of the peptide N,N'-diglycyl-L-cystine dihydrate, $C_{10}N_4O_6H_{18}S_2.2H_2O$, has been completed. The details and results of this investigation are given in the following sections.

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