CRYSTAL AND MOLECULAR STRUCTURE OF 3-TRICHLOROMETHYL-4-CHLORO-5-ISOPROPOXYISOTHIAZOLE AND 4,5-DICHLOROISOTHIAZOLE-3-CARBOXYLIC ACID

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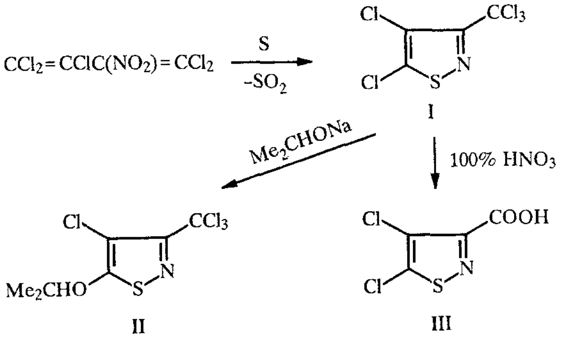
X-ray structural data are used to demonstrate that the chlorine in the 5-position of the heterocycle is replaced on reaction of 3-trichloromethyl-4,5-dichloroisothiazole with sodium isopropoxide. The S—N and C—S bond lengths are lengthened in the resulting 3-trichloromethyl-4-chloro-5-isopropoxyisothiazole whereas the C—N and C—C bonds are shortened compared with analogous bonds in 4,5-dichloroisothiazole-3-carboxylic acid. This is explained by conjugation of the carboxylic acid with the heterocycle.

Derivatives of isothiazole are widely used to prepare biologically active compounds such as pesticides, antibiotics, and hypertension agents [1]. We have discovered a convenient original path into the isothiazole system that is based on a new reaction of nitrocompounds, the reaction of 2-nitropentachloro-1,3-butadiene with sulfur [2]. The structure of the 3-trichloromethyl-4,5-dichloroisothiazole (I) formed was established by spectral methods and certain chemical transformations. The action of sodium isopropoxide on I was used to replace one Cl atom by an isopropoxide. On the basis of IR, NMR, and mass-spectral data, this was assigned the structure 3-trichloromethyl-4-chloro-5-isopropoxyisothiazole (II) [3]:



However, considering the large number of Cl atoms in I, a reaction involving the trichloromethyl group or the 4-position of the ring is possible. This would form isomeric compounds that differ little spectrally from II.

Reaction of I with fuming HNO_3 produced 4,5-dichloroisothiazole-3-carboxylic acid (III). This is a previously unknown structural isomer of 3,4- and 3,5-dichlorosubstituted isothiazolecarboxylic acids, which are effective growth regulators [4].

The nontrivial reaction of the isothiazole ring, the inability to establish accurately the structure of II on the basis of the spectral data used, and the importance of determining the molecular geometry of III in order to explain the mechanism of the biological action of isothiazolecarboxylic acids made it necessary to solve the x-ray structure of II and III (compound I is obtained as a liquid).

The studies confirmed the formation of II and III (Figs. 1 and 2 and Tables 1 and 2). In II, $C_{(4)}$, $C_{(5)}$, $S_{(1)}$, and $N_{(2)}$ of the isothiazole ring are located in a single plane A. Atom $C_{(3)}$ deviates from this plane by 0.010 Å. The dihedral angle between planes A and B (the plane of $N_{(2)}C_{(3)}C_{(4)}$) is 0.8°.

In III (Fig. 2), $N_{(2)}$, $C_{(3)}$, $C_{(4)}$, and $C_{(5)}$ are located in a single plane (C). Atom $S_{(1)}$ deviates from plane C by 0.003 Å. Planes C and D (plane of $N_{(2)}S_{(1)}C_{(5)}$) form an angle of 0.15°. Thus, the isothiazole fragments of II and III are practically planar.

Atom $Cl_{(10)}$ in II deviates from plane A by 0.005 Å; $O_{(6)}$, by 0.013 Å. The rotation around the $C_{(5)}—O_{(6)}$ bond of the isopropoxy group relative to plane A is 13.2(5)°. The bond angles in the trichloromethyl group are close to the tetrahedral values. In III, the Cl atoms are coplanar with plane C within 0.019 Å. The plane of the carboxyl group is twisted relative to

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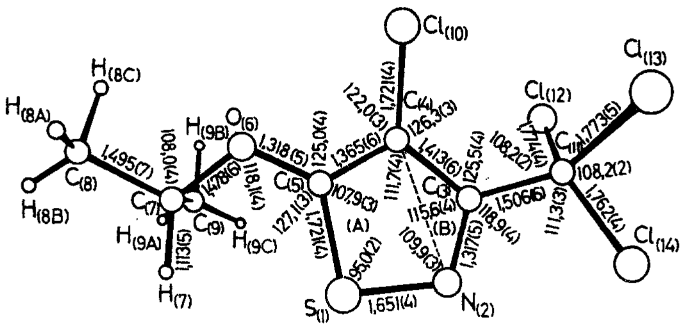

Fig. 1. Structure of II.

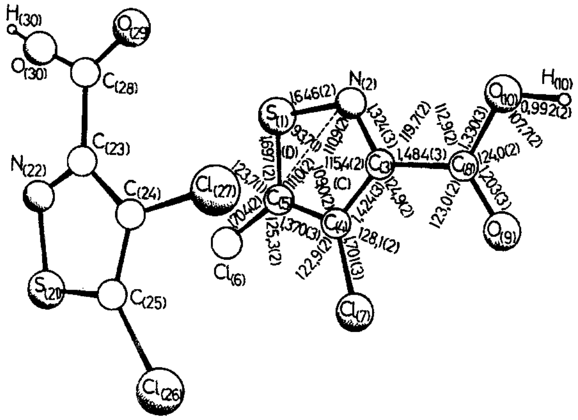

Fig. 2. Structure of the acid III and placement of molecules in the cell.

TABLE 1. Atomic Coordinates of II ($\times 10^4$, $\times 10^3$ for H)*

Atom	x	y	z	Atom	x	y	z
C(3)	4100(4)	1105(4)	6582(2)	Cl(12)	3793(1)	-835(1)	5705(1)
C(4)	3841(3)	2109(4)	6115(2)	Cl(13)	6136(1)	192(1)	6276(1)
C(5)	3285(4)	3048(4)	6385(2)	Cl(14)	4854(2)	-1100(1)	7159(1)
C(7)	2147(4)	4919(4)	6364(2)	H(7)	2359	4934	6944
C(8)	884(5)	4462(5)	6115(3)	H(8A)	372	4914	6221
C(9)	2321(5)	6182(5)	6093(3)	H(8B)	738	3537	6283
C(11)	4687(4)	-88(4)	6444(2)	H(8C)	704	4408	5523
N(2)	3758(3)	1240(3)	7176(2)	H(9A)	1915	6753	6274
O(6)	2955(3)	4106(3)	6070(2)	H(9B)	1939	6046	5453
S(1)	3120(1)	2604(1)	7199(1)	H(9C)	3125	6346	6147
Cl(10)	4163(1)	2198(1)	5301(1)				

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*Temperature factors can be obtained from the authors.

plane C along the $C_{(8)}$—$C_{(3)}$ axis by 1.5°. This does not prevent effective conjugation of the C=O and C=N bonds. Delocalization of π-electron density into III also produced certain differences in the geometric parameters of II and III.

The $N_{(2)}$—$S_{(1)}$ bond lengths in both compounds are intermediate between 1.53 Å for S=N and 1.76 Å for S—N [5]. The bonds $C_{(5)}$—$S_{(1)}$ are shortened compared with the literature values for C_{sp^2}—S (1.50 Å), especially in III. They are in agreement with data for thiazole [1.724(2) Å] and 1,3,4-thiadiazole [1.722(6) Å] [6]. The C=N and $C_{(3)}$—$C_{(4)}$ bond lengths also differ little from the known values in thiazole and thiadiazoles. The slightly shorter S—N and C—S bond lengths and the longer C—N and C=C bond lengths in III compared with II may be due to conjugation of the carboxylic group with the ring in III. As was noted previously for aromatic compounds [7], increasing the number of Cl atoms bonded to the ring shortens the corresponding C—Cl bonds. This is observed in III. The $C_{(11)}$—Cl bond lengths in II are typical of a trichloromethyl group. Replacing CCl_3

TABLE 2. Atomic Coordinates of Pairs of III ($\times 10^4$, $\times 10^3$ for H)*

Atom	x	y	z	Atom	x	y	z
$C_{(3)}$	10307(4)	1002(3)	-2711(2)	$O_{(10)}$	11753(3)	3339(2)	-1636(2)
$C_{(4)}$	10328(4)	-341(3)	-3615(2)	$O_{(29)}$	6048(3)	-1450(2)	391(2)
$C_{(5)}$	8270(4)	-1162(3)	-3545(2)	$O_{(30)}$	3338(3)	-3332(2)	34(2)
$C_{(8)}$	12225(4)	2187(3)	-2520(3)	$S_{(1)}$	6512(1)	-273(1)	-2418(1)
$C_{(23)}$	6755(4)	-3529(3)	-1174(3)	$S_{(21)}$	7736(1)	-5596(1)	-2848(1)
$C_{(24)}$	8998(4)	-3075(3)	-1576(3)	$Cl_{(6)}$	7527(1)	-2846(1)	-4465(1)
$C_{(25)}$	9770(4)	-4136(3)	-2528(3)	$Cl_{(7)}$	12477(1)	-917(1)	-4653(1)
$C_{(28)}$	5349(4)	-2650(3)	-163(3)	$Cl_{(26)}$	12346(1)	-4045(1)	-3321(1)
$N_{(2)}$	8390(4)	1169(2)	-2022(2)	$Cl_{(27)}$	10623(1)	-1465(1)	-1031(1)
$N_{(22)}$	5898(3)	-4843(2)	-1772(2)	$H_{(10)}$	13068	4103	-1634
$O_{(9)}$	14013(3)	2102(2)	-3109(2)	$H_{(30)}$	2436	-3174	119

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*Temperature factors can be obtained from the authors.

in II by CO_2H in III shortens the exocyclic $C_{(3)}$—$C_{(8)}$ bond owing to delocalization of π-electrons in the N=C—C=O system. The corresponding bond angles of both compounds differ by ~5°.

For II, shortened intermolecular contacts are not found. In III, shortened intermolecular contacts $H_{(10)}...N_{(2')}$ span neighboring cells. This indicates the existence of an intermolecular H-bond $H_{(10)}...N_{(2')} = 1.858$ Å.

EXPERIMENTAL

Crystals of II were grown from a mixture of acetone—$CHCl_3$—hexane—ethanol—H_2O (2:2:2:1:1). The crystals were destroyed and completely decomposed by the Mo Kα x-ray beam ($\lambda = 0.71069$ Å) under natural conditions. A specimen of dimensions 0.12 × 0.3 × 0.4 mm was selected for collection of the data set. It was sealed in a glass capillary with desiccant since II is hygroscopic. At 20°C $a = 11.354(4)$, $b = 10.834(4)$, $c = 19.666(6)$, $\beta = 102.62(3)$, $V = 2360.7(2)$ Å, $d_{calc} = 1.66$ g/cm^3, space group A2/a, Z = 8. Calculations were performed using the SHELX-83 programs. A total of 1318 reflections with $I \geq 2.5\delta$ were initially used. The experimental estimates were $R_{merge} = 0.035$ and $R_{sigma} = 0.019$ taking into account absorption. The structure of II was solved by direct methods using $E > 1.35$ for 262 normalized structure factors. After identifying the atoms and refining isotropically, R was 14%. Anisotropic block-diagonal refinement using 1221 structure factors and the weighting scheme (WGHT = 0.000001) gave final R = 0.043, $R_w = 0.042$ and $R_m = 0.044$.

Crystals of III were obtained by repeated heating to 70°C and subsequent slow cooling from a mixture of H_2O—ethano—$CHCl_3$ (6:3:1). The data set was collected using a crystal of dimensions 0.28 × 0.4 × 0.42 mm sealed in a capillary in the presence of mother liquor. At 22°C, $a = 6.372(2)$, $b = 10.321$ (4), $c = 11.366(3)$, $\alpha = 109.62(3)°$, $\beta = 78.00(2)°$, $\gamma = 104.85(3)°$, $V = 674.4(4)$ Å^3, $d_{calc} = 1.95$ g/cm^3, Z = 4, space group $P\bar{1}$, two molecules per asymmetric unit. After adjusting the peak profiles, an experimental estimate of the data was $R_{merge} = 0.027$ and $R_{sigma} = 0.015$.

The structure of III was solved by the TREF procedure in the SHELX-86 programs. Only $H_{(10)}$ on $O_{(10)}$ on one of the molecules was found in a difference Fourier. However, substantial differences in the C—O bond lengths for the second molecule most likely indicate the presence of an O—H bond in the molecule [8]. The H atom of the carboxylic group of the second molecule was fixed using a geometric construction program. Isotropic and then anisotropic refinement gave a final R = 0.032. A total of 2061 unique reflections with $F \geq 10\sigma$ was obtained for acid III.

The unit-cell constants of II and III and the data set were studied on a Nicolet P3 automated four-circle diffractometer using $\theta/2\theta$ scanning with $2\theta_{max} = 54°$ for II and $2\theta_{max} \leq 50°$ for III. Calculations were performed on a NOVA 3/12 computer.

The atomic coordinates of II and III are given in Tables 1 and 2, respectively.

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