Nature of the Isomerism in the Adducts of Diketen to Non-aromatic 2-Mercapto-1,3-Diazaheterocycles

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ON studying the reaction paths in non-aromatic heterocycles,[1] the problem arose of the nature of the pairs of products resulting from mono-addition of diketen to "cyclic isothioureas" in anhydrous conditions, one pair arising from each substrate (Ia, Ib, and possibly Ic; $R^1=H$ or Me).[2,3] Of other possible reaction products, the *N*-substituted adducts (II) and the cycloaddition–elimination derivative (III) were isolated, but only for particular values of *n* and R^2, when $R^1=H$.[2]

Physico-chemical properties show that each member of a pair belongs to one of two series[3,4] but none have cycloaddition structures like those assigned to the adducts of diketen and acyclic isothioureas.[5]

We have now obtained conclusive *X*-ray, chemical, and n.m.r. evidence that all the pairs of isomers studied are *cis*- and *trans*-crotonoylurea derivatives (IV and V), arising from a rather unusual reaction.

(i) The *X*-ray crystal structure analysis[3] was carried out on the higher m.p. isomer (132°), obtained by reacting (Ib; $R^1=Me$, $R^2=p\text{-}CH_2\text{-}C_6H_4Br$) with diketen. It showed that the compound has a crotonoylurea structure and that its configuration corresponds to the *trans*-isomer (Vb), as shown by the Figure.

The three-dimensional structure determination by the heavy-atom method indicates that the vinyl hydrogen is C-H–O hydrogen bonded with the ureic oxygen, in the direction of one of its lone-pair orbitals (C–O, 2·8, H–O, ~2 Å). The existence of C-H–O hydrogen bonding has been reported for several compounds,[6] including β-chlorocrotonic acid.[7] A short intramolecular S–O contact (2·8 Å) and molecular planarity and resonance from the ureic to the vinyl group, are additional characteristic features.

(ii) The observation that thiols add to compound (III), giving pairs of compounds identical to those from the reaction of (Ib) with diketen,[8] and the hypothesis that such addition might occur in the 1,6-position of the oxazine ring led to the suggestion of an independent synthesis. 1-Methyl-2-oxo-imidazolidine was condensed with *cis*- and *trans*-β-chloro-crotonoyl chlorides and the chlorine atom of the intermediate β-chlorocrotonoylurea derivatives was substituted by a benzyl mercaptide group. The crotonoyl urea structure was thus ascertained for both members of the pair. Of the resulting 3-(β-benzylthiocrotonoyl)-1-methyl-2-oxo-imidazolines (IVa and Va; $R^1=Me$; $R^2=CH_2Ph$), the *trans*-structure is assigned to the higher m.p. isomer, on the basis of the configuration of the β-chlorocrotonic acids,[7,9] in agreement with *X*-ray data on compound (Vb; $R^1=Me$, $R^2=p\text{-}CH_2\cdot C_6H_4Br$).

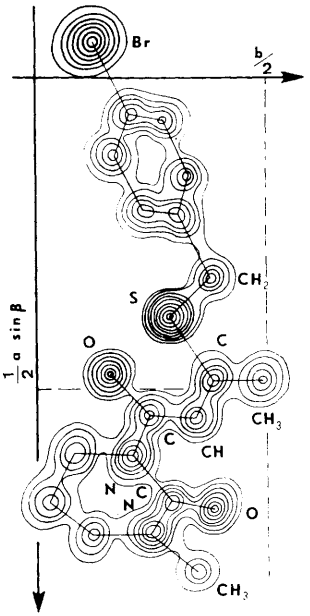
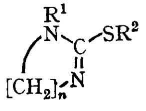


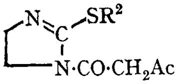
FIGURE. *Electron density projection on to* (001)

(iii) The n.m.r. data of several pairs led to the same conclusions and extended the structure assignment to all the pairs of isomers, independent of the values of R^1 and *n*. The protons of the CH_2, NH, and NMe groups are identical to those of the related cyclic ureas, and the chemical shifts and coupling constants of the crotonoyl moieties agree with those of model compounds such as *cis*- and *trans*-*NN*-dimethylcrotonamide. The chemical shifts of the vinyl hydrogens are found, on the contrary, at very low fields for both members of each pair (6·8—7·3 and 7·2—7·4 p.p.m., in $CDCl_3$ solution; δ values from tetramethylsilane). These data are interpreted as being due to C-H-O intramolecular hydrogen bonding, existing in the solution of each compound, as found in the crystalline state.

The formation of *N*-crotonoyl derivatives from diazaheterocycles, with or without a hydrogen atom at the nitrogen, extends the problem of the migration of the SR^2 group from the amidine ring-carbon to the side-chain one and gives more emphasis to the intercorrelation of the various reaction products.


(I)

(a, b, c: *n*=2, 3, 4)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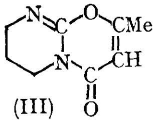
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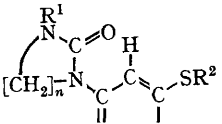
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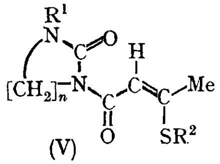
(V)

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