CHEMISTRY OF THE THIAZOLES

Part V. Fine Structure and Orientation

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(Received September 25, 1952)

1. INTRODUCTION

The thiazole ring system from the point of view of fine structure remains the least studied of the heterocyclic compounds. None of the customary physical or physico-chemical measurements which give us accurate ideas about the dispositions of the various atoms in the ring, the bond distances, the valency angles and the state of polarisation of the atoms, have been made with thiazole or any of its derivatives. So, to understand the fine structure of the thiazole derivatives, we have to rationalise \textit{a posteriori}, on the basis of the physical properties and the chemical reactivities of the various thiazole derivatives so far reported. This paper is an attempt in this direction.

2. POLARISATION (MESOMERISM) AND DISPOSITION OF THE ATOMS IN THE RING

There are some very characteristic properties of thiazole and its derivatives which should be reflected in their fine structure. Though thiazole is a five membered heterocyclic compound, in its properties such as the boiling point, basicity, solubility in water, odour, reactivity, isosterism and resistance to the attack of electrophilic reagents, it strikingly resembles the six-membered compound pyridine and also pyrimidine, and sharply differs from the five-membered heterocyclic compounds, thiophene, furan, oxazole, glyoxaline and pyrrole. There are some thiazole derivatives which, in their properties and behaviour, resemble the corresponding thiophene, furan, or glyoxaline derivatives rather than the pyridines. Next, the thiazole compounds fall into two groups: the first consists of thiazole and some derivatives which are stable and resist attack by electrophilic reagents, while the second group comprises of derivatives which show properties quite the reverse of this. Thirdly, in some substitution reactions, even with the reagents of the same category, there is a difference in the orientation of the incoming group; in the case of nitration and sulphonation, the position taken by the incoming group is different from that in halogenation. Lastly, the reactivities of the various groups or atoms present in thiazoles differ
markedly depending upon the position they occupy in the ring and also upon the substituents in the other positions.

To seek an explanation for these properties, one of the methods adopted is to rely on the resonant structures. Erlenmeyer et al. studied the deuterium and hydrogen exchange in 4-methylthiazole-5-carboxylic acid and postulated that thiazole exists in the resonant forms represented by the formula (I) and express the view that this postulation provides an explanation for an aromatic linkage between the carbon atoms 4 and 5 and for an "aromatic sulphur", i.e., a sulphur atom that does not behave as a thioether. On the basis of the general rules available for the postulation of the resonant structures and on analogy with the structures proposed for the other heterocyclic ring systems, we could write down a number of resonant formulae for thiazole also. But this does not help us because we cannot assess the contributions of the various forms due to lack of data to calculate the resonance energies, bond distances, or the character of the various bonds. On the other hand, we can get far ahead by examining the mesomeric influences in the thiazole ring, the polarisation of the various atoms, the nature of the bonds, and the effects of the substituents in the ring as revealed by the experimental results, as is shown below:

The system \( \text{N} \rightarrow \text{C} \rightarrow \text{S} \).—This system is taken together since these three atoms individually influence the properties of the other. Of the two heterocyclic atoms, nitrogen dominates in governing the properties of thiazole which is evidently because it has the lesser number of unshared electron pairs than sulphur. Depending upon the nature of the substituents at \( \text{C}_2 \), the ring nitrogen can function in two diametrically opposed roles, viz., (i) as an electron sink when the substituent at \( \text{C}_2 \) is an electron acceptor (nitro, carboxy, carbonyl, sulphonic, or cyano groups) or cannot tautomerise with the nitrogen (hydrogen, halogens) and (ii) as an electron source or a relay of electrons when the substituent at \( \text{C}_2 \) (amino, substituted amino, hydroxy, substituted hydroxy, mercapto, substituted mercapto groups) is an electron donor or can tautomerise with nitrogen (hydroxy, mercapto and amino groups). These two possibilities as regards the function of nitrogen account for the two types of effects resulting in the segregation of the thiazoles into the abovementioned two classes as shown below:

\[ \text{N} \rightarrow \text{C} \rightarrow \text{S} \]