The Isomerization of 2,4-Dinitrophenylhydrazones of α-Keto Acids

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Most of 2, 4-dinitrophenylhydrazones of α-keto acids derived from monocarboxylic amino acids have been observed to give two spots on the paper chromatogram except dimethylpyruvic acid (DMPA) and methylethylpyruvic acid[1]. Because of the confirmation of the presence of *cis*- and *trans*-isomers in 2, 4-dinitrophenylhydrazones of pyruvic acid (PA), a representative of α-keto acid giving two spots on the paper chromatogram, we have ascribed these two spots to geometrical isomers of the hydrazones[2]. Furthermore we have recognized that DMPA, a representative of α-keto acid giving one spot on the paper chromatogram, gave only one isomer in some conditions on account of rapid isomerization velocity[3]. Since then in our laboratory the isomerization of these hydrazones had been studied and it was found that the directions of the isomerization were determined by the polarity of solvent.

Each component in the isomeric mixtures of the hydrazones of PA was determined by Hayashi's method[4] based on the fact that only the *cis*-form is extracted by ethyl acetate-ether mixture (3:1) from 0.1% sodium carbonate solution containing 10% sodium chloride. In less-polar solvent such as ethyl acetate, acetone or ether, the isomerization did not occur but in a polar solvent such as water or glacial acetic acid, the *cis*-form converted into the *trans*-form and a part of the hydrazone decomposed. But the inversion in the opposite direction was not observed. Both isomerization and decomposition were greatly accelerated by hydrogen ions. The rates of isomerization and decomposition of the *cis*-form in 0.3 N hydrochloric acid at 18°C for 5 hours, for example, were 30% and 60% respectively. On the other hand, in a less-polar solvent, hydrogen ions accerelated the interconversion in either direction and an equilibrium state was estabilshed, the composition of which being determined by the kind of solvent used, by the water content of the solvent and by temperature. For example, when standing in ethyl acetate saturated with 6 N hydrochloric acid for 30 min. at 18°C, the equilibrium mixture consisted of 46% of the *cis*-form and 47% of the *trans*-form. Seven per cent was proved to decompose.

In the case of the hydrazone of DMPA, the isomerization is so rapid that the equilibrium state is attained as soon as the isomer is dissolved in a solvent, and the simultaneous measurements of spectra of both isomers in the same solvent is impossible. For this reason the paper chromatogram gives only one spot. The α-isomer, m. p. 198°C (decomp.) is stable in anhydrous less-polar solvent, whereas the β-isomer, m. p. 188°C (decomp.) is stable in polar solvent. In absolute alcohol, the absorption maximum of the α-isomer in visible region lay at 365 mμ but with the increase of water content of the solvent it shifted to a longer wave length until it reached 380 mμ where the component consisted of β-isomer. The same results were obtained when formamide was used instead of water. That the rearrangement of the configuration of the hydrazone of DMPA occurred very easily was shown as follows: the freshly precipitated hydrazone in hydrochloric acid for the most part, consisted of the α-form but changed to the β-form within a few hours. Furthermore, when the sodium salt of the β-form was acidified with dilute hydrochloric acid precipitated free hydrazone at first was found to be the α-form. The structures of two isomers of the hydrazones of DMPA, at present, are not fully elucidated and will be discussed elsewhere.

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