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Syntheses and Reactions of Metal Organics. VIII. The Formation of 2,5-Piperazinediones from Metal Alkoxides and α-Amino Acids

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In preliminary studies of the yellowing of wool by ultraviolet light[1] it was observed that the pretreatment of wool with an alkyl titanate, for example, tetra-*n*-butyl titanate, protects wool from yellowing. It has been proved that this protection is not due to the screening of wool from ultraviolet light by the titanate. Other observations have suggested that the titanates may react with proteins, peptides, and amino acids. Many reactions of metal (IV) alkoxides and metal (IV) chlorides with amines, amides, and carboxylic acids have been studied,[2] but few with amino acids have been studied. The present investigation is concerned with the reactions of titanium isopropoxide, *n*-butoxide, and zirconium isopropoxide with glycine and DL-α-alanine.

On heating α-amino acids, two moles of them condense to 2,5-piperazinediones, but the products are colorized by partial thermal decomposition. On the addition of metal alkoxides, they acted as dehydrating agents on α-amino acids in the presence of alcohols, but did not do so in hydrocarbon solvents.

The reactions proceeded as follows:

$$2H_2NCHRCOOH + 2M(OR')_4 \longrightarrow [RCHCONH]_2 + 2M(OR')_2O + 4R'OH$$

(R=H or Me, R'=^{i}Pr or ^{n}Bu, M=Zr or Ti)

Experimental

Reaction of Zirconium Isopropoxide with Glycine. A mixture of glycine (2.0 g, 27 mmol) and zirconium isopropoxide (13.1 g, 40 mmol) in 50 ml of ethyl alcohol was heated to boiling while being stirred. The glycine dissolved completely within 2 hr. On heating at the boiling point of the clear solution for 1.5 hr, some precipitates began to appear. Heating was continued for 20 hr in order to complete the precipitation. The white precipitates obtained were washed with cold ethyl alcohol and dried under a vacuum; yield, 1.1 g; mp 309 °C (decomp.). The product was identified with 2,5-piperazinedione by means of its melting point (lit,[3] mp 311—312 °C) and its IR spectrum.

Reaction of Zirconium Isopropoxide with DL-*α-Alanine.* The isolation of 3,6-dimethyl-2,5-piperazinedione (0.7 g) from DL-α-alanine (2.0 g, 22 mmol) and zirconium isopropoxide (11.0 g, 33 mmol) was accomplished in the same way as has been described for the preceding experiment; mp 268—269 °C (lit,[4] mp 271 °C). The IR spectrum of this product was identical with that of an authenic specimen.

Reactions of Titanium Alkoxides with Glycine. A mixture of glycine (2.0 g, 27 mmol) and titanium isopropoxide (11.3 g, 40 mmol) in 50 ml of isopropyl alcohol was heated to boiling with stirring. The glycine did not dissolve completely, but a light brown powder (1.5 g) was obtained after 20 hrs' heating; mp 307.5—308.5 °C (decomp.).

From the reaction of titanium *n*-butoxide (13.6 g, 40 mmol) and glycine (2.0 g, 27 mmol) in ethyl or isopropyl alcohol, a light brown powder (1.1—1.5 g) was also obtained. These products were identified with 2,5-piperazinedione.

Reaction of Titanium n*-Butoxide with* DL-*α-Alanine.* From the reaction of titanium *n*-butoxide (11.2 g, 33 mmol) and DL-α-alanine (2.0 g, 22 mmol) in 50 ml of methyl, ethyl, or isopropyl alcohol, colorless needles (0.7—0.8 g) were formed. All the products melted at 267 °C and were identified with 3,6-dimethyl-2,5-piperazinedione.

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