

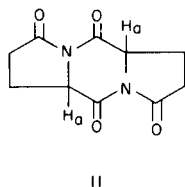
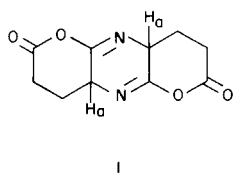
Structure of the Dehydration Product of Glutamic Acid.

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Sir:

A recent claim (1) that the high melting dehydration product of glutamic acid possesses a tricyclic lactone structure (I) rather than the tetraketo structure (II) previously assigned (2,3,4) is based upon an erroneous interpretation of infrared data.

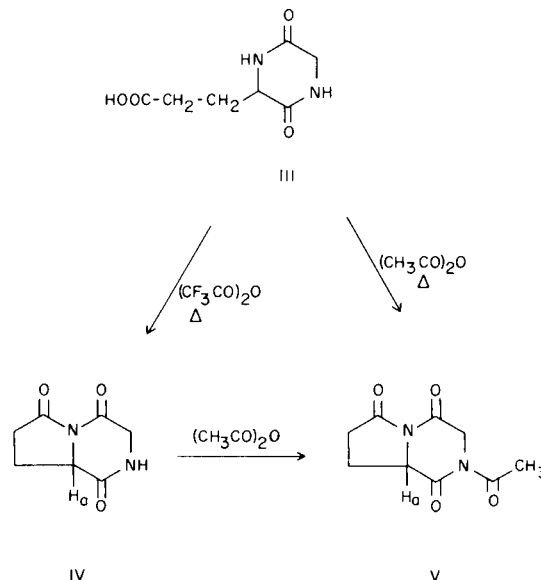


King and McMillan (2) prepared the compound in question by dehydration of glutamic acid, 3,6-dioxopiperazine-2,5-dipropionic acid and 5-pyrrolidone-2-carboxylic acid. Their results have been confirmed in this laboratory. The material (m.p. 337-340°) shows two distinct bands in the C=O stretching region, one fairly broad at 1760 cm^{-1} and one sharp at 1690 cm^{-1} .

The fact that the highest yield (60%) of the dehydration product was obtained from 5-pyrrolidone-2-carboxylic acid would seem to favor the structure (II) formulated by King and McMillan. However El-Zanfally and his coworkers (1) argue that whether the compound is obtained by dehydration of 3,6-dioxopiperazine-2,5-dipropionic acid or 5-pyrrolidone-2-carboxylic acid the lack of a strongly basic nitrogen in both of these compounds would make further dehydration to structure II highly improbable. They therefore favor structure I and claim that the infrared data supports their formulation since the 1760 cm^{-1} absorption indicates a δ -lactone structure rather than a γ -lactam. They assign the 1690 cm^{-1} band and bands at 1675 cm^{-1} and 1685 cm^{-1} which were not observed in the spectrum of the sample prepared in this laboratory, to C=N stretching. The carbonyl functions of structure II, however, are imide rather than simple lactam. Carbonyl absorptions of imides normally appear as two widely separated bands in the regions 1790-1720 cm^{-1} and 1710-1670 cm^{-1} (5).

Recently, the dehydration of 3,6-dioxopiperazine-2-

propionic acid (III) with carboxylic acid anhydrides has been investigated in this laboratory. With refluxing trifluoroacetic anhydride and acetic anhydride cyclization of the carboxyl function to the adjacent amido nitrogen occurs to give 1,4-diazabicyclo[4,3,0]nonane-2,5,9-trione (IV) and its *N*-acetyl derivative (V) respectively.



The structures of compounds IV and V were unequivocally proven from nmr data (6).

The infrared spectrum of IV shows C=O stretching bands at 1785 cm^{-1} (imide) and 1710 cm^{-1} (imide, lactam), and that of V at 1795 cm^{-1} (imide) and 1730 cm^{-1} (imide). Furthermore, when the nmr spectra of II, IV and V were determined in deuteriated dimethylsulphoxide, the Ha protons were found to have chemical shifts of $\delta=4.85$ ppm, 4.63 ppm and 4.93 ppm respectively and in each case was coupled to the adjacent methylene protons with $J=8$ Hz.

Comparison of the spectral data obtained for these compounds indicates therefore that structure II, originally assigned by King and McMillan, is indeed the correct structure for the dehydration product of glutamic acid.

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