Decarboxylation of 4-Pyridylacetic Acid Hydrochloride in Dimethyl Sulphoxide

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WE have found that 4-pyridylacetic acid hydrochloride (I) decarboxylates in dimethyl sulphoxide at moderate temperature.

The decarboxylation of 4-pyridylacetic acid have been observed on several occasions, but only at elevated temperatures and usually only under conditions where the free amine exists. Doering and Pasternak[1] found that a substituted 2-pyridylacetic acid decarboxylated smoothly in a boiling neutral aqueous solution, but was stable to prolonged boiling both in concentrated hydrochloric acid and strong alkali. In aqueous ammonia,[2] the 4-pyridyl acid was hydrogenated at moderate temperature with no loss by decarboxylation. Most decarboxylations of a 4-pyridyl acid involve high temperatures or dry distillations such as Singh's[3] dry distillation of a barium salt, and Koenigs's[4] dry distillation of an acid at 230° to obtain 4-methylpyridine. Koenigs and Fulde[5] found that diethyl 2-nitro-4-pyridylsodiomalonate decarboxylates in boiling hydrochloric acid. Gebauer[6] describes the decarboxylation of a 4-dicarboxylic acid, which is acidified with hydrochloric acid and evaporated to dryness, or until no more carbon dioxide is evolved. This probably involves a solid at high temperatures since Malan and Dean[7] were able to evaporate 4-pyridylacetic acid hydrochloride to dryness under reduced pressure without apparent loss through decarboxylation. We have prepared a compound (whose spectrum fits 4-pyridylacetic acid) from aqueous solution, by removing the water under reduced pressure.

The n.m.r. spectrum of (I) dissolved in [$^2H_6$]-dimethyl sulphoxide at 30°, has δ 15·11 (br s, acid protons) 8·13, 9·01 (J_{AB} 6·2 Hz AB quartet, ring protons), and 4·11s, methylene protons). When the solution of (I) in [$^2H_6$]dimethyl sulphoxide is heated, the downfield resonance δ 15·11 and the methylene resonance gradually decrease while three new resonances appear, δ 7·70, 8·66 (J_{AB} 6·8 Hz, AB quartet), and 2·11s. These results are consistent with decarboxylation, and both n.m.r. and i.r.[8] were used to follow the reaction. Excellent first-order plots were obtained which yielded a half-life at 30° of 4·1 hr. The n.m.r. spectrum of (I) dissolved in D_2O did not, however, change significantly, even after a prolonged period of heating (90°, 24 hr.).

Mass spectrometry showed a large increase of carbon dioxide in the gas above the heated solution of (I) in dimethyl sulphoxide. This was also substantiated by the fact that the carbon dioxide stretching frequency was the only absorption observed in the i.r. spectrum.

The only other product found after a solution of (I) in dimethyl sulphoxide was completely decarboxylated was 4-methylpyridine hydrochloride, which was isolated (>95%) and when compared with a prepared sample of 4-methylpyridine hydrochloride gave the same melting points and same n.m.r. spectrum in D_2O.

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