

O-Deuterio-Butanoic Acid

By H Maskill,

Chemistry Department, University of Stirling, Stirling FK9 4LA,  
Scotland.

Summary. A literature procedure for the preparation of O-deuterioacetic acid from the anhydride gives substantial deuterium incorporation at C-2 when used to prepare deuterio-butanoic acid. The enol form of butanoic anhydride is implicated as the intermediate which causes the isotopic scrambling. The required title compound was obtained by the reaction of butanoyl chloride and deuterium oxide.

In the course of our solvolytic studies, we required O-deuterio-butanoic acid (1). The first preparative attempt was the reaction of the anhydride with deuterium oxide; this method had been successful for the preparation of O-deuterioacetic acid (2). Deuterium oxide was heated under reflux with a small excess of butanoic anhydride and a catalytic amount of sulphuric acid for four hours. Integration of the  $^1\text{H}$  n.m.r. spectrum of the fractionally distilled butanoic acid unambiguously showed complete scrambling of the two hydrogens from the  $\alpha$ -carbon and the one on oxygen i.e.  $4/3$   $^1\text{H}$  and  $2/3$   $^2\text{H}$  on C-2 with  $2/3$   $^1\text{H}$  and  $1/3$   $^2\text{H}$  on oxygen. The routine i.r. spectrum of the carboxylic acid also indicated deuterium bonded to carbon by peaks at 2190 and 2260  $\text{cm}^{-1}$ . When this method was repeated without the sulphuric acid, some deuterium on carbon was detected but the n.m.r. spectrum did not indicate complete

scrambling. The required product was obtained by the reaction of butanoyl chloride with deuterium oxide (3) followed by fractional distillation. This establishes:

- 1, the rate of hydrolysis of the acyl chloride is much faster than its rate of enolization (which would cause scrambling);
- 2, once the O-deuterio-carboxylic acid is formed, its C-2 hydrogens and O-deuterium do not become scrambled to any appreciable extent, even at its boiling point in the presence of a strong acid. This is in agreement with an earlier report (4).

The isotopic scrambling in the preparation of deuterio-butanolic acid from the anhydride must, therefore, occur before the anhydride is hydrolysed. The most credible mechanism involves the enol tautomer of the anhydride. Since O-<sup>2</sup>H- acetic acid was obtained without isotopic scrambling (2), hydrolysis of acetic anhydride must be significantly faster than enolization. However, for butanolic anhydride the present results show that enolization is faster than hydrolysis in the presence of sulphuric acid, and comparable with it in the absence of the strong acid.

Experimental. Butanoyl chloride (125g, 1.17 mol.) was carefully added over 1½ hr to magnetically stirred, water-cooled deuterium oxide (26 cm<sup>3</sup>, 1.43 mol., 99.7% <sup>2</sup>H<sub>2</sub>O) under a reflux condenser. The system was protected from atmospheric H<sub>2</sub>O by a slow stream of dry nitrogen. When the addition was complete, the reflux condenser was replaced by a Dufton Column and the two-phase mixture was fractionally distilled. The first fraction comprised some product plus an immiscible layer of concentrated deuterio-hydrochloric acid. The next fraction (b.p. 162-163°C,

80g, 77%) was the required product. A test with aqueous silver nitrate confirmed the absence of any hydrochloric acid. Integration of the n.m.r. spectrum showed any <sup>1</sup>H on oxygen to be less than 5%. There was no evidence in the <sup>1</sup>H n.m.r. spectrum or i.r. spectrum of any <sup>2</sup>H on carbon.

#### References

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