Tetrahedron Letters No.43, pp. 4479-4480, 1968. Pergamon Press. Printed in Great Britain.

ONE STEP SYNTHESIS OF α-SULFO-β-ALANINE

Daniel Wagner, David Gertner and Albert Zilkha,
Department of Organic Chemistry, The Hebrew University,
Jerusalem, Israel.

(Received in UK 15 July 1968; accepted for publication 29 July 1968)

α-Sulfo-β-alanine was prepared by the oxidation of isocysteine (1) which in turn was prepared in low overall yield by multistep procedures, e.g. starting from an uracil derivative (2) or from β-alanine (3). Recently it was reported from this laboratory (4) that α-sulfo-β-alanine is obtained in low yield from the reaction of acrylonitrile with fuming sulfuric acid. We wish to describe a simple, one-step synthesis of this compound, comprising the direct sulfonation of β-alanine by fuming sulfuric acid. The best results were obtained using a large excess of oleum, the reaction being carried out at room temperature. Lower yields of the amino acid were obtained on reducing the amount of oleum or heating the reaction mixutre to 100°C.

Thus, oleum (33% SO_3) (40 ml) was added to β-alanine (2.67 g, 0.03 mole) with cooling in ice-salt bath, the reaction mixture was left at room temperature for 4 days, and then diluted cautiously with water (85 ml). The solution was boiled and left overnight at room temperature to crystallize. α-Sulfo-β-alanine (4.1 g, 81%) was collected and washed with ice-water, ethanol and ether. The filtrate was neutralized with barium hydroxide, filtered, and the precipitated barium sulfate was extracted with boiling water. Evaporation of the filtrate gave a further crop of the amino acid (0.8 g, 16%; total yield 97%).

On reducing the amount of oleum used in the reaction to 10 ml, the amino acid crystallized out in 72% yield on dilution of the reaction mixture, and a further 10% was isolated from the filtrate. The reaction mixture contained also unreacted β-alanine. The α-sulfo-β-alanine thus obtained was identified by comparison of its i.r. spectrum and R_f with that of an authentic sample and by elemental analysis. (Calculated values for $C_3H_7NO_5S$: C, 21.29; H,4.17; N, 8.28; S, 18.95. Found: C, 21.43; H, 4.10; N, 8.30; S, 18.97).

This sulfonation of amino acids having a β-amino group seems to be a general reaction as seen from preliminary experiments with other β-amino-acids such as β-amino butyric acid.

On the other hand, α-aminoacids did not yield α-sulfo derivatives, as could be expected from the instability of α-sulfo-α-amino acids (5).

A plausible explanation for the formation of α-sulfo-β-aminoacids seems to involve the addition of SO_3 to the double bond of the enol form of aminoacid.

Further investigations on the sulfonation of amino acids and on other methods for the preparation of α-sulfo-β-aminoacids are under way.

REFERENCES

1. S. Gabriel, Ber., 38, 642 (1905)
2. S. Gabriel, ibid, 38, 637 (1905)
3. A. Schoberl and H. Braun, Ann., 542, 274 (1939)
4. A. Zilkha, I. Barzilay, J. Naiman and B.A. Feit, J.Org.Chem. 33, 1686 (1968)
5. M. Frankel and P. Moses, Tetrahedron 9, 289 (1960)