354. *Preparation of the Simpler α-Alkylamino-acids. Part I.*

By Wesley Cocker.

The method used by Cocker and Lapworth (J., 1931, 1894) for the synthesis of sarcosine has been extended to the preparation of a number of other alkylamino-acids, and rendered more economical by the use of magnesium sulphate in place of zinc sulphate as precipitant for benzenesulphonic acid (compare Lapworth and Morriss, B.P. 14,402, 1915).

Although Cocker and Lapworth (*loc. cit.*) realised that in the preparation of sarcosine, after the hydrolysis of its benzenesulphonyl derivative, the benzenesulphonic acid could be removed as its magnesium salt (Lapworth and Morriss, *loc. cit.*), its removal as zinc salt was described because of difficulties in the complete precipitation of magnesium from solution. Later investigation has shown that magnesium hydroxide is insoluble in excess

of barium hydroxide solution and thus the excess of magnesium sulphate required to precipitate benzenesulphonic acid may be completely removed by excess of barium hydroxide. The preparations of *N*-ethyl- and *N*-propyl-glycine and *N*-methylalanine are quite straightforward. On the other hand, attempts to prepare *N*-benzylglycine yielded only glycine, and this is considered to be due to debenzylation of *N*-benzenesulphonyl-*N*-benzylglycine rather than *N*-benzylglycine. The only evidence for this view is the fact that treatment of the *N*-benzenesulphonyl-*N*-benzyl derivative with hydriodic acid yields benzyl iodide more quickly than phenyl mercaptan. Glycine was not obtained by hydrolysis of *N*-benzenesulphonyl-*N*-allylglycine with sulphuric acid.

Experimental.

Preparation of Sarcosine.—Benzenesulphonylsarcosine (40 g.) is hydrolysed with 60% sulphuric acid, and the product treated with magnesium sulphate (38 g.) in water (40 c.c.). The mixture is agitated and cooled to 0°, and the precipitated magnesium benzenesulphonate collected on glass wool and washed with a saturated solution of magnesium sulphate. The combined filtrates are made neutral to Congo-red, again filtered, concentrated to 50 c.c., and treated with barium hydroxide (70 g.). The precipitated magnesium hydroxide is removed, and sarcosine, m. p. 211—212°, isolated from the filtrate as described by Cocker and Lapworth (*loc. cit.*). Yield, 11·2—11·3 g. (74—76% of the theoretical).

Preparation of Other α-Alkylamino-acids.—(1) N-*Ethylglycine.* Benzenesulphonylglycine (25 g.) is dissolved in 3N-sodium hydroxide (80 c.c.) and shaken with ethyl iodide (32 g.; 2 mols.). The solution is acidified and the *N*-benzenesulphonyl-*N*-ethylglycine obtained is washed with a solution of sodium thiosulphate and with water, and recrystallised from hot water; m. p. 115·5—116° (compare Johnson and McCollum, *Amer. Chem. J.*, 1906, **35**, 61). Yield, 24·2 g. (85% of the theoretical).

The above compound (38·5 g.) is boiled under reflux for 5 hours with dilute sulphuric acid (42 c.c. of the conc. acid and 52 c.c. of water). After cooling, 6 g. of unhydrolysed material are removed. From the filtrate, *N*-ethylglycine is isolated by the method described above or by Cocker and Lapworth (*loc. cit.*). Yield, 9·47 g. (70%, calc. on the material hydrolysed); m. p. 180—182° (decomp.) [Heintz, *Annalen*, 1864, **129**, 35, gives m. p. 160° (decomp.)] (Found: N, 13·7. Calc.: N, 13·6%). The *phenylhydantoin*, prepared by the usual method, crystallises from benzene–ligroin in six-sided prisms, m. p. 110°, soluble in alcohol and benzene (Found: N, 14·1. $C_{11}H_{12}O_2N_2$ requires N, 13·7%).

(2) N-*Propylglycine.* Benzenesulphonylglycine (23·5 g.), dissolved in 3N-sodium hydroxide (75 c.c.), is refluxed for 24 hours with *n*-propyl iodide (24 g.; 1·5 mols.). From the solution, by acidification, *N*-benzenesulphonyl-*N*-propylglycine is obtained as a white solid; it is washed with water, dried in a vacuum, and recrystallised from benzene–ligroin. Yield, 20 g. (72% of the theoretical); m. p. 99—100° (compare Johnson and McCollum, *loc. cit.*) (Found: N, 5·45. Calc.: N, 5·45%).

The above compound (30 g.) is boiled under reflux for 12 hours with a mixture of 30 c.c. of concentrated sulphuric acid and 37 c.c. of water. From the solution, 13·7 g. (61% of the theoretical yield) of *N*-propylglycine are obtained in long prisms or needles, m. p. 196—198° (decomp.), readily soluble in water and hot alcohol (Found: N, 11·8. Calc.: N, 12·0%). Chancel (*Bull. Soc. chim.*, 1892, **7**, 410) prepared it from ethyl bromoacetate and *n*-propylamine, but gave no yield or m. p. The *benzoyl* derivative, readily prepared by the method described by Cocker and Lapworth (*loc. cit.*) for benzoylsarcosine, crystallises from benzene–ligroin in flat hexagonal plates, m. p. 89—90°, readily soluble in ether, water, and chloroform. In aqueous solution it is acid to litmus (Found: N, 6·4. $C_{12}H_{15}O_3N$ requires N, 6·3%). The phenylcarbamido-derivative, m. p. 132° (decomp.), forms colourless prisms, soluble in hot water and alcohol, but sparingly in benzene.

(3) N-*Methylalanine.* Benzenesulphonylalanine (16 g.), prepared from alanine in 80% yield, is methylated with methyl sulphate (18 g.), giving *N*-benzenesulphonyl-*N*-methylalanine (15·4 g.; 90%), m. p. 95—96°, in small needles or prisms which are readily recrystallised from benzene–ligroin.

The above compound (26·9 g.) is boiled under reflux with a mixture of 28·5 c.c. of concentrated sulphuric acid and 35 c.c. of water for 14 hours; after removal of 2 g. of unhydrolysed material, *N*-methylalanine (8·07 g.) is isolated from the filtrate in 81% yield (calc. on the material hydrolysed), m. p. 315—317° (decomp.). It is freely soluble in water but only sparingly in alcohol and is best purified from a mixture of the two (Found: N, 13·7. Calc.: N, 13·6%). Lindenberg

(*J. pr. Chem.*, 1875, **12**, 244) gives m. p. 260° (decomp.). The *benzoyl* derivative crystallises from benzene in flat, colourless, transparent plates, m. p. 129—129·5°, readily soluble in water, in which it gives an acid reaction (Found : N, 6·85. $C_{11}H_{13}O_3N$ requires N, 6·8%). The *benzenesulphonyl* derivative, m. p. 96—97°, forms long needles or prisms from benzene (Found : N, 5·6. $C_{11}H_{13}O_4NS$ requires N, 5·5%). The *phenylhydantoin* crystallises in colourless four-sided plates, m. p. 145—6°, from hot water (Found : N, 13·9. $C_{11}H_{12}O_2N_2$ requires N, 13·7%).

(4) *Attempts to prepare* N-*benzylglycine*. *N*-Benzenesulphonyl-*N*-benzylglycine is readily prepared in theoretical yield from benzenesulphonylglycine and benzyl iodide (2 mols.); with benzyl chloride (2 mols.), the yield is 62%. It crystallises from benzene or 75% alcohol in colourless silky needles, m. p. 124·5—125·5° (compare Johnson and McCollum, *loc. cit.*).

When the compound (30 g.) is refluxed for 10 hours with a mixture of 24 c.c. of concentrated sulphuric acid and 29 c.c. of water, 10 g. remain unhydrolysed and 3·5 g. of glycine, m. p. 255° (decomp.), are obtained (benzenesulphonyl derivative m. p. and mixed m. p. 165—166°).

The compound is unchanged by 45% sulphuric acid, and almost unchanged by dilute hydriodic acid (1 : 1) at water-bath temperature. With more concentrated hydriodic acid it yields benzyl iodide, quickly followed by phenyl mercaptan.

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