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SYNTHESES OF AMINO ALKYL SULPHONIC ACIDS AND THEIR PEPTIDE ANALOGUES[1]

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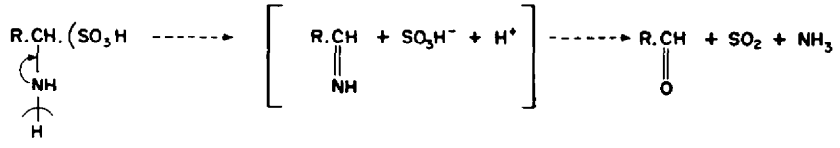
Abstract—New amino alkyl sulphonic acids have been synthesized, including some substituted derivatives and several peptide analogues containing the —CO·NH— group formed from amino acid and amino alkyl sulphonic acid components. Peptide-like compounds containing the —SO_2·NH— group were prepared from N-substituted taurine and esters of amino acids. Theoretical aspects underlying the reactions involved are discussed.

THE amino sulphonic acids, structurally related to amino acids, are of interest from the chemical and also the biological standpoint, e.g., as potential anti-metabolites.

Baker and Mulder[2] prepared a number of α-amino sulphonic acids and McIlwain[3] extended the study of these compounds and tested some for their inhibitory effect on the growth of micro-organisms.[4]

The aim of this investigation was the synthesis of new amino alkyl sulphonic acids and of peptide-like compounds derived from them. These compounds were tested for their inhibitory effect on the growth of micro-organisms; in addition, their effect on the growth of tumours are under investigation.

New amino alkyl sulphonic acids were obtained by modifications of the methods of McIlwain.[3] Unlike the α-amino acids, the α-amino alkyl sulphonic acids are unstable in acid and alkali solutions, decomposing to aldehyde, sulphur dioxide and ammonia. It is suggested that in these compounds the lability of the sulphonic acid group is further increased by the presence of the amino group; the free electron pair on the nitrogen atom is capable of undergoing electromeric shift to form the unstable imine,[5] with rupture of the carbon-sulphur bond and loss of proton.

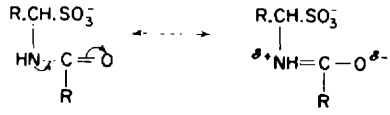


Acylation or benzoylation of the amino group greatly enhances the stability of these compounds; the electron pair of the nitrogen is able to participate in an electromeric shift with the carbonyl group, thus suppressing the tendency of the compound to revert to the unstable imine.[5]

The coupling of the α-amino alkyl sulphonic acids with a second amino acid

[1] Abstracted from a thesis submitted by P. Moses to the Senate of the Hebrew University in partial fulfilment of the requirements for the Ph.D. (1959).
[2] H. J. Backer and H. Mulder, *Rec. Trav. Chim.* **52**, 454 (1933); *Ibid.* **53**, 1120 (1934).
[3] H. McIlwain, *J. Chem. Soc.* 75 (1941).
[4] H. McIlwain, *Brit. J. Expt. Path.* **22**, 148 (1941).
[5] L. E. Hinkel, E. E. Ayling and J. H. Beynon, *J. Chem. Soc.* 184 (1936).

component, to form compounds analogous to peptides but containing the sulphonamide group was unsuccessful by adaptations of the known methods of peptide synthesis.[6–9] The failure of the α-amino alkyl sulphonic acids to couple with an amino acid is probably due to the instability of the former as well as to the relative lack of readiness on the part of the sulphur atom to act as an electron-acceptor towards the



amino group of the second amino acid component. This relative inactivity of the sulphur atom may be attributed to the limited polarisability of the sulphonic acid group as compared to that of the carbonyl group of the amino carboxylic acids.[10] The reluctance of the sulphur atom to form the sulphonamide bond is increased by the presence of an animo group in the molecule. This is demonstrated by the synthesis of benzene sulphonyl amino methane sulphonic acid, from benzene sulphonyl chloride and amino methane sulphonic acid, as compared to the failure of *p*-acetamino benzene sulphonyl chloride to react with amino methane sulphonic acid under like conditions. There are reasons to believe that the amino group in the amino sulphonic acid molecule provides internal compensation for any possible electron deficiency on the central sulphur atom of the acidic group, suppressing any inclination on the part of the sulphur atom to play the role of electron-acceptor towards an external source of binding electrons. Furthermore, this postulated inactivating effect of the amino group may depend upon its proximity to the acidic function. Thus the α-amino alkyl sulphonic acids do not form sulphonamides. The β-amino alkyl sulphonic acids do form sulphonamides but only to a limited extent, demonstrated by the readiness with which tauryl chloride derivatives react with amino carboxylic acid esters as against their failure to couple with the less reactive free amino acids and with amino alkyl sulphonic acids. With still further removal of the amino group from the acidic function, the electrophilic character of the central sulphur atom continues to increase and the molecule becomes capable of undergoing "peptide" coupling even with a second amino alkyl sulphonic acid component. Thus Helfeirch and Otten[11] caused carbobenzoxy-δ-amino-butane sulphonyl chloride to react with 1,4-amino butane sulphonic acid to form the corresponding "dipeptide".

In contradistinction to the negative results obtained with the α-amino alkyl sulphonic acids, we did succeed in preparing some "peptides" containing a β-amino alkyl sulphonic acid component, viz. taurine. Thus we were able to prepare the ethyl esters of phthaloyl-tauryl-glycine, carbobenzoxy-tauryl-glycine and phthaloyl-tauryl-glycyl-glycine. In these "peptides" the esteric end group could not be split off by hydrolysis without decomposition of the compounds. In attempts at removal of the phthaloyl group by means of alcoholic hydrazine, reaction did occur, but the final products isolated could not be identified.

[6] J. R. Vaughan, Jr., *J. Amer. Chem. Soc.* 73, 3547 (1951).
[7] J. C. Sheehan and C. P. Hess, *J. Amer. Chem. Soc.* 77, 1067 (1955).
[8] Y. Liwschitz and A. Zilkha, *J. Amer. Chem. Soc.* 76, 3698 (1954).
[9] E. Fischer, *Untersuchungen ueber Aminosaeuren, Polypeptide und Proteine* p. 326. Springer, Berlin (1906).
[10] W. Grossman and E. Wuensch, *Fortschritte der Chemie Organischer Naturstoffe* Vol. XIII, p. 452. Springer, Wien (1956); H. Gilman, *Organic Chemistry* Vol. I, p. 880. John Wiley, New York (1949).
[11] B. Helferich and G. Otten, *J. Prakt. Chem.* (NF), 1, 2 (1954).

Hippuryl chloride reacts smoothly with amino methane sulphonic acid to give the appropriate "di-peptide", but the benzoyl group could not be split off by hydrolysis without rupturing the peptide bond. The desired free "di-peptide" was, however, obtained from the corresponding carbobenzoxy derivative by splitting off the protecting group with an anhydrous solution of hydrogen bromide in acetic acid.

α-N-(carbobenzoxy glycyl)-amino ethane sulphonic acid was obtained in small yield by the mixed anhydride method,[6] using isobutyl chloroformate as the coupling agent.

β-Alanyl amino methane sulphonic acid was synthesized by reacting phthaloyl-β-alanine with amino methane sulphonic acid in the presence of n-butyl chloroformate with subsequent removal of the phthaloyl group with alcoholic hydrazine, according to the method of Ing and Manske.[12]

Although *p*-acetamino benzene sulphonyl chloride did not couple with an amino alkyl sulphonic acid to give the "di-peptide", it did couple with β-alanine, to give *p*-acetamino benzene sulphonyl-β-alanine.

Most of the compounds prepared were tested for their inhibitory effect on the growth of micro-organisms. The results will be reported elsewhere.

EXPERIMENTAL[13]

α-Amino-butane-sulphonic acid

To 24 g sodium metabisulphite in 40 ml water, 23 ml (slight excess) butyraldehyde was added with stirring, cooled to 0° and 20 ml conc ammonia slowly added with continued stirring at room temp for 1 hr, cooled to 0°, and acidified with 1:1 HCl to pH 4. The crystals were filtered, washed with a little cold water, 50% ethanol and finally 96% ethanol. The air-dried product was recrystallized from 15 ml hot (60°) water, to give 2 g, m.p. 120–121°. (Found: C, 31·3; H, 7·1; N, 9·0; S, 20·4. $C_4H_{11}NO_3S$ requires: C, 31·3; H, 7·1; N, 9·1; S, 20·9%).

α-Amino-heptane-sulphonic acid

The appropriate hydroxy sulphonate (19 g) was treated with 40 ml 1:1 ammonia, and the mixture warmed for ½ hr at 70°, filtered, cooled to 0° and acidified with conc HCl to pH 3. The pasty product was filtered, warmed with 50% ethanol and filtered. Yield 7·5 g (20%) m.p. 138–140°. (Found: C, 42·8; H, 8·9; N, 7·0; S, 16·3. $C_7H_{17}NO_3S$ requires: C, 43·1; H, 8·8; N, 7·2; S, 16·4%).

α-Amino-β-phenyl-ethane-sulphonic acid

On attempting the preparation of this compound by treating the hydroxy sulphonate (obtained from redistilled phenyl acetaldehyde and potassium bisulphite) with conc ammonia, N,N-di-(benzyl methylene sulphonic acid)-amine, mono K salt was obtained. (Found: C, 43·4; H, 4·7; N, 3·4; S, 14·0; K, 8·7. $C_{16}H_{18}NO_6S_2K \cdot H_2O$ requires: C, 43·5; H, 4·5; N, 3·2; S, 14·5; K, 8·8%).

The required product was obtained by adding the hydroxy sulphonate portion-wise to a cold (0°) excess of ammonia with vigorous stirring. The mixture was stirred at room temp for 10 min. acidified with conc HCl to pH 3, filtered and washed with water, followed by ethanol. The product was purified by dissolving in the calculated amount of 8% bicarbonate solution, warming with addition of Norit, and acidifying the filtered solution with 1:10 HCl. After several hours in ice, a small quantity of white crystals was collected, m.p. 138–140°. (Found: C, 47·9; H, 5·6; N, 7·0; S, 15·9. $C_8H_{11}NO_3S$ requires: C, 47·8; H, 5·5; N, 7·0; S, 15·9%).

α-Benzoylamido-ethane-sulphonic acid, K salt

To 5 g α-amino-ethane-sulphonic acid[8] in 40 ml 1:1 ethanol was added 6·9 g potassium carbonate and the mixture warmed to complete solution. Benzoyl chloride (8·4 g, 50% excess) was added to the cooled solution with stirring at 50° during 3 hr. The filtered solution was evaporated (water-bath) to

[12] H. R. Ing and R. H. F. Manske, *J. Chem. Soc.* 2348 (1926).
[13] Melting points determined on Fischer–Jones Apparatus; microanalysis by Weiler and Strauss, Oxford, England.

first appearance of crystals, 20 ml ethanol was added and cooled. After 10 min, the crystals were collected. On recrystallization from hot water, the salt was obtained in 35% yield. (Found: C, 38·1; H, 3·9; N, 4·9; S, 11·4. $C_9H_{10}NO_4SK \cdot H_2O$ requires: C, 37·9; H, 4·2; N, 4·9; S, 11·2%).

Benzoylamido-phenyl-methane-sulphonic acid, K salt

This was obtained by benzoylation of phenyl-amino-methane-sulphonic acid[3] by the above method. (Found: C, 48·1; H, 3·7; N, 4·3; S, 9·6. $C_{14}H_{12}NO_4SK \cdot H_2O$ requires: C, 48·4; H, 4·0; N, 4·0; S, 9·2%).

Carbobenzoxy-amino-methane-sulphonic acid, K salt

To 111 g of amino-methane-sulphonic acid suspended in 250 ml water and cooled in ice, were added 69 g potassium carbonate. To the cold, stirred mixture was added simultaneously, during 40 min, 69 g potassium carbonate in 250 ml water and 150 ml of a solution of carbobenzoxychloride in toluene. (Bergmann and Zervas).[14] The mixture was stirred with cooling for 1 hr, followed by 4 hr at room temp. The product was collected, washed with water, ethanol and ether, yield 74 g (26%) m.p. 240–245°. (Found: N, 4·7; S, 10·8. $C_9H_{10}NO_5SK \cdot H_2O$ requires: N, 4·6; S, 10·6%).

General preparation of α-benzylamino-alkyl-sulphonic acids

To sodium bisulphite (0·25 moles) in 40 ml water was added at room temp one equivalent of the appropriate aldehyde, and after cooling (10–20°), a 10% excess of benzylamine in an equal volume of water. The mixture was stirred ½ hr at 50–70°, cooled, acidified with 10 N sulphuric acid to pH 4, placed in ice overnight and filtered. Where necessary, ethanol was added to the acidified solution to facilitate crystallization. After trituration with ethanol, the products were analytically pure without further recrystallization.

α-Benzylamino-β-phenyl-ethane-sulphonic acid was obtained by adding the appropriate hydroxy sulphonate to a 100% excess of 50% aqueous benzylamine. The product separated out initially as an oil.

The following compounds were prepared by the above method:

Benzylamino-methane-sulphonic acid; α-benzylamino-ethane-sulphonic acid; α-benzylamino-butane-sulphonic acid; α-benzylamino-iso-pentane-sulphonic acid; α-benzylamino-heptane-sulphonic acid; α-benzylamino-β-ethyl-hexane-sulphonic acid; benzylamino-phenyl-methane-sulphonic acid; benzylamino-*p*-anisyl-methane-sulphonic acid and α-benzylamino-β-phenyl-ethane-sulphonic acid.

The experimental data are summarized in Table 1.

TABLE 1. SYNTHESES OF α-BENZYLAMINO-ALKYL-SULPHONIC ACIDS

$$\begin{array}{l} R\cdot CH\cdot SO_3H \\ \quad | \\ NH\cdot CH_2C_6H_5 \end{array}$$

R	M.p.	Yield (%)	Found (%)				Required (%)			
			C	H	N	S	C	H	N	S
H	139	23	47·6	5·4	6·7	15·8	47·8	5·5	7·0	15·9
CH_3	104–6	38	50·3	6·0	6·5	14·8	50·2	6·0	6·5	14·8
C_3H_7	87–92	60	54·0	7·0	5·8	13·5	54·3	7·0	5·8	13·2
$(CH_3)_2\cdot CH\cdot CH_2$	105–10	25	55·7	7·5	5·2	13·0	56·0	7·4	5·5	12·5
C_6H_{13}	95–100	20	59·2	8·0	4·9	10·7	59·0	8·1	4·9	11·2
$CH_3(CH_2)_3CH$ | H_5C_2	89–90	10	59·9	8·0			60·2	8·3		
C_6H_5	95–105	30	60·7	5·3	5·0	11·6	60·7	5·4	5·1	11·6
p-$CH_3OC_6H_4$	100–104	30	58·3	5·3		10·0	58·6	5·5		10·4
$C_6H_5CH_2$	84–85	20	61·6	6·0	4·8	11·3	61·9	5·9	4·8	11·0

[14] M. Bergmann and L. Zervas, *Ber. Dtsch. Chem. Ges.* **65**, 1192 (1932).

β-Benzylamino-β-phenyl-ethane-sulphonic acid

To 9·2 g 2-phenyl-ethene-1-sulphonic acid[15] in 40 ml water was added 15 ml benzylamine. After remaining at room temp for ten days and acidifying with 16 ml conc HCl, a heavy white precipitate separated, and on filtering, the desired product was obtained (40% yield), m.p. 184–186°. (Found: C, 61·6; H, 6·0; N, 4·7; S, 10·6. $C_{15}H_{17}NO_3S$ requires: C, 61·9; H, 5·8; N, 4·8; S, 11·0%).

N-(*benzoyl-glycyl*)-*amino-methane-sulphonic acid, K salt*

Amino-methane-sulphonic acid (5·6 g) was warmed with 25 ml 2 N potassium carbonate until evolution of CO_2 ceased. Hippuryl chloride[16] (9·9 g) and 25 ml 2 N potassium carbonate was added simultaneously during 1 hr to the cooled (0°) solution which was then stirred for 15 min, cooled, acidified with conc HCl and placed in ice overnight. Hippuric acid (1·7 g) was filtered and the filtrate concentrated in vacuo, yielding 9·7 g (63%) crude product, m.p. 235–250°. On recrystallization from water–ethanol, a pure product m.p. 258–260° was obtained. (Found: C, 36·9; H, 3·9; N, 8·4; S, 9·9. $C_{10}H_{11}N_2O_5SK \cdot H_2O$ requires: C, 36·6; H, 4·0; N, 8·5; S, 9·8%).

N-(*carbobenzoxy-glycyl*)-*amino-methane-sulphonic acid, K salt*

Method 1. Into a 250 ml flask fitted with a calcium-chloride tube, was introduced 10·5 g carbobenzoxy-glycine, 100 ml dry toluene and 5·1 g triethylamine. After cooling (−7°), 6·8 g isobutyl-chloroformate was added in one portion. The mixture kept at −10° for 20 min and then 5·6 g amino-methane sulphonic acid in 50 ml N potassium carbonate was added portionwise. After stirring vigorously at 0–10° for 1·5 hr, and for 2 hr at room temp, the aqueous layer was separated, washed with 3 portions of ether, acidified with 4·5 ml conc HCl and cooled in ice. After 4 hr, 7 g crude product, m.p. 150–170° was collected. The filtrate was concentrated and cooled, yielding 6·8 g (43%) of a pure product, m.p. 190–200°. Repeated recrystallization gave a product m.p. 208–210°. (Found: C, 38·5; H, 3·8; N, 8·1; S, 9·5. $C_{11}H_{13}N_2O_6SK$ requires: C, 38·8; H, 3·8; N, 8·2; S, 9·4%).

Method 2. To a mixture of 1·05 g carbobenzoxy-glycine and 1·03 g dicyclohexylcarbo-diimide[17] in 20 ml dry methylene chloride, was added 0·9 g (60% excess) amino-methane-sulphonic acid in 8 ml N potassium carbonate; 10 ml water was added and stirred at room temp for 7 hr. The dicyclohexyl-urea (1 g, m.p. 233–236°) was filtered, the aqueous layer separated, extracted with two portions of ether and acidified with 12 ml conc HCl to pH 1. After cooling, 500 mg of the desired compound, identified by mixed melting point, was collected.

Glycyl-amino-methane-sulphonic acid

Carbobenzoxy-glycyl-amino-methane-sulphonic acid (1·02 g) was treated with 5 ml HBr in glacial acetic acid (300 mg HBr/ml), and allowed to stand at room temp for 3 hr with frequent shaking. The small amount of undissolved material was filtered and the filtrate treated with ethanol to incipient cloudiness. The mixture was chilled, and the resulting flocculent precipitate coagulated. It was dissolved in 2–3 ml hot water and ethanol added until a gel separated, and on filtering and washing with ethanol, gave 100 mg of glycyl-amino-methane-sulphonic acid, which charred at 290° without melting. (Found: C, 21·3; H, 5·0; N, 16·4; S, 19·4. $C_3H_8N_2O_4S$ requires: C, 21·4; H, 4·7; N, 16·7; S, 19·0%).

N-(*carbobenzoxy-glycyl*)-α-*amino-ethane-sulphonic acid, K salt*

To a solution of 5·2 g carbobenzoxy-glycine in 50 ml dry toluene was added 4·6 g tributylamine, and, after cooling (−12°) 3·4 ml isobutyl chloroformate added in one portion. The solution was kept in a freezing mixture for 20 min, after which a solution of 3·1g α-amino-ethane-sulphonic acid[9] in 30 ml N potassium carbonate was added dropwise. The mixture was stirred (−5°) for ½ hr, 6 ml N potassium carbonate added, and stirring continued (1·5 hr). After filtering, the aqueous layer was separated extracted with 2 portions of ether and acidified with 5 ml conc HCl; 2 g carbobenzoxy-glycine was filtered and the filtrate concentrated in vacuo (40–50°) to first appearance of crystals. After cooling, filtering and washing with ethanol and ether, 800 mg of the potassium salt melting at

[15] F. C. Bordwell, C. M. Suter, J. M. Holbert and C. S. Rondestvedt, *J. Amer. Chem. Soc.* **68**, 139 (1946).
[16] E. Fischer, *Ber. Dtsch. Chem. Ges.* **38**, 612 (1905).
[17] G. Amiard and R. Heymes, *Bull. Soc. Chim. Fr.* 1360 (1956).

250–255° was obtained. (Found: C, 38·6; H, 4·5; N, 7·4; S, 9·0. $C_{13}H_{15}N_3O_6SK \cdot H_2O$ requires: C, 38·7; H, 4·6; N, 7·5; S, 8·6%).

Phthaloyl-β-alanyl-amino-methane-sulphonic acid, K salt

To a suspension of 22 g β-phthalimido-propionic acid[18] in 100 ml dry chloroform 14 ml triethylamine was added, and after cooling to −10°, 12·6 ml n-butyl-chloroformate was added. After standing (−5 to 0°) for 10 min, 11·1 g amino-methane-sulphonic acid in 50 ml 2 N potassium carbonate was added, stirred at room temp (2·5 hr) and filtered. After triturating with ethanol, 14·5 g (41%) of the salt, m.p. 266–268°, was obtained. After recrystallization (water–ethanol) the product melted at 268°. (Found: C, 40·9; H, 3·3; N, 8·0; S, 8·7; K, 11·0. $C_{13}H_{11}N_3O_6SK$ requires: C, 41·1; H, 3·1; N, 8·0; S, 9·1; K, 11·1%).

β-Alanyl-amino-methane-sulphonic acid

Phthaloyl-β-alanyl-amino-methane-sulphonic acid (7 g) in 30 ml water was refluxed with 20 ml N alcoholic hydrazine (1 hr), cooled, acidified with 2 ml conc HCl, and the phthalyl hydrazine filtered. After concentrating (vacuum) at 45–50° and diluting with ethanol, white crystals, giving a positive ninhydrin reaction, precipitated out, yield, 1·5 g, m.p. 283–285°. (Found: C, 26·2; H, 5·5; N, 15·2; S, 17·2. $C_6H_{10}N_2O_4S$ requires: C, 26·4; H, 5·5; N, 15·4; S, 17·6%).

Carbobenzoxy-tauryl-glycine, ethyl ester

Carbobenzoxy-tauryl-chloride[3] (2·8 g) was suspended in 1·4 g glycine ester HCl in 10 ml water; 1·7 g sodium bicarbonate was added, then 20 ml water and 10 ml ethanol. The mixture was stirred (room temp 6 hr), then left in ice (48 hr). Repeated recrystallization gave a small amount of white, tacky crystals. (Found: C, 48·5; H, 6·1; N, 7·8; EtO, 12·7. $C_{14}H_{20}N_2O_6S$ requires: C, 48·8; H, 5·8; N, 8·1; EtO, 13·1%).

Phthaloyl-tauryl-glycine, ethyl ester

Phthaloyl-tauryl chloride was prepared by refluxing potassium phthaloyl taurate[19] with 100% excess phosphorus pentachloride in benzene (water bath) for ½ hr. The phthaloyl tauryl chloride (84%) melted at 161–162°. (Found: N, 4·9; S, 11·9. Calc. for: $C_{10}H_8NO_4SCl$: N, 5·1; S, 11·7%).

Glycine ester HCl (14 g) in 50 ml 2 N potassium carbonate was added to 13·7 g phthaloyl-tauryl chloride in 100 ml benzene. After stirring (room temp 2 hr then 60° 3 hr), cooling and filtering, 8 g (57%) of white crystals, m.p. 126–127° were obtained. (Found: C, 49·2; H, 4·8; N, 8·1; S, 9·0; EtO, 13·2. $C_{14}H_{16}N_2O_6S$ requires: C, 49·4; H, 4·7; N, 8·2; S, 9·4; EtO, 13·2%).

Phthaloyl-tauryl-glycyl-glycine, ethyl ester

To 5·5 g phthaloyl-tauryl chloride in 35 ml benzene 4 g glycyl-glycine-ethyl ester HCl[20] was added followed by 1·1 g sodium carbonate in 5 ml water with stirring during 50 min. After stirring (4 hr) 2·8 g crude product was collected, dissolved in 60 ml ethyl acetate, filtered and precipitated with excess petrol ether. White crystals (1·2 g, 17%) m.p. 100–101° were obtained. (Found: C, 48·7; H, 4·6; N, 10·5; S, 7·7. $C_{16}H_{19}N_3O_7S$ requires: C, 48·4; H, 4·8; N, 10·6; S, 8·1%).

N-(p-*acetamido-benzene-sulphonyl*)-β-*alanine*

p-Acetamido-benzene-sulphonyl-chloride[21] (23·4 g) was added to a stirred solution of β-alanine (8·9 g) in 50 ml 2 N potassium carbonate, and then 2 N potassium carbonate (50 ml) added during 1 hr. After standing in ice (two weeks), 7 g (24%) crude product was filtered. After two recrystallizations (hot water), a pure product melting at 160° (slow heating) was obtained. (Found: C, 43·7; H, 5·3; N, 9·5; S, 10·1. $C_{11}H_{14}N_2O_5S \cdot H_2O$ requires: C, 43·4; H, 5·3; N, 9·2; S, 10·5%).

[18] S. Gabriel, *Ber. Dtsch. Chem. Ges.* **38**, 632 (1905).
[19] G. Pellizari and V. Matteucci, *Liebigs Ann.* **248**, 159 (1885).
[20] E. Fischer, *Untersuchungen ueber Aminosaeuren, Polypeptide und Proteine* p. 283. Springer, Berlin (1906).
[21] A. I. Vogel, *Practical Organic Chemistry* p. 871. Longmans, Green, London (1948).