97. *Hydroxyalkylamino-Acids. Part I.*

By Wesley Cocker.

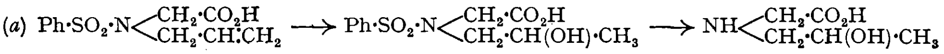
Hydrolysis of arylsulphonyl derivatives of *N*-allylglycine, *N*-allylalanine, and *N*-β-methylallylglycine with boiling 60% sulphuric acid gave N-β-*hydroxypropylglycine*, a syrup, and a quantitative yield of glycine and *iso*butaldehyde respectively.

N-β-*Hydroxy*iso*butylglycine* was obtained by hydrolysis of *mesitylenesulphonyl-β-methylallylglycine*, and N-β-*hydroxypropylalanine* by condensation of β-hydroxypropylamine with ethyl α-bromopropionate.

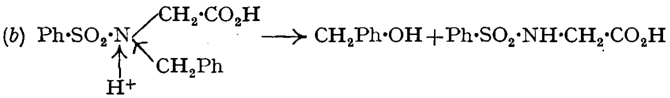
When treated with cold concentrated sulphuric acid, N-*benzenesulphonyl*-N-*allylglycine* gave N-*benzenesulphonyl*-6-*methyl*-2-*morpholone*, its p-*toluenesulphonyl* analogue gave N-p-*toluenesulphonyl*-N'-β-*hydroxypropylglycine*, and N-*benzene*- and N-p-*toluene-sulphonyl-β-methylallylglycines* gave the corresponding derivatives of 6 : 6-dimethyl-2-morpholone.

Bromination of the arylsulphonyl derivatives of *N*-allylglycine and their esters gave dibromides, decomposable by sodium hydroxide into arylsulphonylglycine and acraldehyde. Attempts to effect ring closure of the dibromides to yield *N*-arylsulphonyl-4-bromoproline were ineffective.

Previous investigation (Cocker, J., 1937, 1693) showed that debenzylation takes place when *N*-benzenesulphonyl-*N*-benzylglycine is treated with boiling 60% sulphuric acid. It has now been shown that, despite the similar directive effects of the allyl and the benzyl group, the main product of the similar treatment of N-*benzenesulphonyl*-N-*allylglycine* is dl-N-β-*hydroxypropylglycine* owing to hydration in the three-carbon chain; the odour of propaldehyde and acetone perceptible during the hydrolysis, however, indicates partial three-carbon chain elimination :



$$(a)\ \mathrm{Ph{\cdot}SO_2{\cdot}N}\!<\!\begin{matrix}\mathrm{CH_2{\cdot}CO_2H}\\ \mathrm{CH_2{\cdot}CH{:}CH_2}\end{matrix} \longrightarrow \mathrm{Ph{\cdot}SO_2{\cdot}N}\!<\!\begin{matrix}\mathrm{CH_2{\cdot}CO_2H}\\ \mathrm{CH_2{\cdot}CH(OH){\cdot}CH_3}\end{matrix} \longrightarrow \mathrm{NH}\!<\!\begin{matrix}\mathrm{CH_2{\cdot}CO_2H}\\ \mathrm{CH_2{\cdot}CH(OH){\cdot}CH_3}\end{matrix}$$



$$(b)\ \underset{\substack{\uparrow\\ \mathrm{H^+}}}{\mathrm{Ph{\cdot}SO_2{\cdot}N}}\!<\!\begin{matrix}\mathrm{CH_2{\cdot}CO_2H}\\ \\ \mathrm{CH_2Ph}\end{matrix} \longrightarrow \mathrm{CH_2Ph{\cdot}OH + Ph{\cdot}SO_2{\cdot}NH{\cdot}CH_2{\cdot}CO_2H}$$

Hydration in (*a*) takes place prior to the removal of the arylsulphonyl group, since *N*-allylglycine remains unchanged after prolonged boiling with 60% sulphuric acid.

N-Benzenesulphonyl-*N*-allylglycine, when treated with cold concentrated sulphuric acid, is converted into N-*benzenesulphonyl*-6-*methyl*-2-*morpholone* (the lactone of *N*-benzenesulphonyl-*N*-β-hydroxypropylglycine), but the p-*toluenesulphonyl* analogue gives the corresponding *hydroxy-acid*; both products yield *N*-β-hydroxypropylglycine with boiling 60% sulphuric acid. The *benzene*- and the p-*toluene-sulphonyl* derivative of β-methylallylglycine yield the corresponding derivatives of 6 : 6-dimethyl-2-morpholone, which are formed as soon as a solution of the sodium salt of the corresponding hydroxy-acid is acidified. Conversely, the unsubstituted morpholones are hydrolysed even by boiling water (Knorr, *Annalen*, 1899, **307**, 203).

The increased stability of the substituted morpholones is due to the electron-attracting arylsulphonyl group, which effect is greater in the benzenesulphonyl group than in the *p*-toluenesulphonyl group.

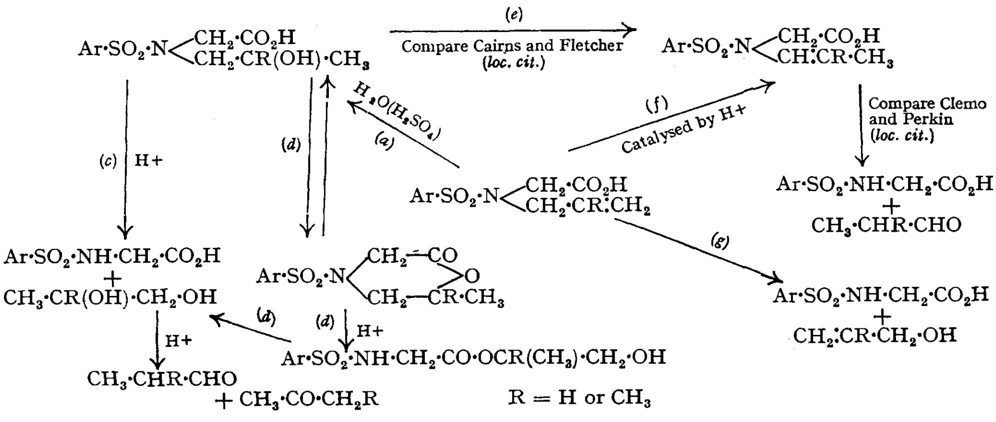
The hydration of allyl compounds has been observed by many workers (for references, see Burgin, Hearne, and Rust, *Ind. Eng. Chem.*, 1941, **33**, 385; Brachfelt and Smola, Austrian Pat. 135,351, 1935). In all cases secondary alcohols are produced.

In spite of the electron-attractive properties of the arylsulphonyl group the proton attached itself to the γ-carbon atom in all the hydrations performed. This was proved by oxidation of the hydration product of benzenesulphonylallylglycine with sodium hypoiodite, iodoform being obtained, and by the synthesis, by condensation of β-hydroxypropylamine with ethyl bromoacetate, of *N*-β-hydroxypropylglycine, the arylsulphonyl derivatives of which were identical with the hydration products of the corresponding arylsulphonylallylglycines. The constitution of the hydration product of the arylsulphonyl-β-methylallylglycines was similarly proved.

Attempts to add the elements of hydrogen chloride or bromide to the arylsulphonylallylglycines were unsuccessful; indeed, these compounds could be esterified with saturated alcoholic hydrogen chloride, but esterification of the arylsulphonyl-β-methylallylglycines under similar conditions yielded ethyl *N*-arylsulphonyl-*N*-β-chloro*iso*butylaminoacetates.

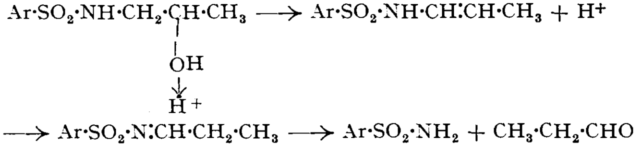
Unlike the arylsulphonylallyglycines, the corresponding β-methylallylglycines gave theoretical quantities of glycine on treatment with boiling 60% sulphuric acid, the side chain being removed as *iso*butaldehyde. Only a small proportion of the allylglycines suffered side-chain elimination and then as a mixture of acetone and propaldehyde.

The following reactions are possible in this three-carbon chain elimination.



Reaction (*c*) involves the attack of the proton at the tertiary nitrogen atom assisted by the electron-donating side chain. In view of the small difference in electron-releasing effect of the β-hydroxypropyl and the propyl group on the one hand and the β-hydroxy*iso*butyl and the *iso*butyl group on the other and the fact that the propyl and the *iso*butyl group are not eliminated in similar circumstances (compare Cocker and Harris, J., 1940, 1290), such a mechanism is not likely to lead to elimination of the three-carbon chain. Reaction (*d*) is similar to (*c*). Both reactions lead to aldehydic or ketonic products or both. When R = H, the glycol is methylethyleneglycol, which yields a mixture of acetone and propaldehyde on pinacolinic change; but when R = CH_3, only *iso*butaldehyde is formed (compare Nevrole, *Ber.*, 1876, **9**, 448; Eltekow, *Ber.*, 1878, **11**, 990).

Cairns and Fletcher (*J. Amer. Chem. Soc.*, 1941, **63**, 1034) showed that β-hydroxypropylarylbenzenesulphonamides readily give propaldehyde on treatment with acid according to the reaction



$$Ar{\cdot}SO_2{\cdot}NH{\cdot}CH_2{\cdot}\underset{\substack{|\\ OH\\ \downarrow\\ H^+}}{C}H{\cdot}CH_3 \longrightarrow Ar{\cdot}SO_2{\cdot}NH{\cdot}CH{:}CH{\cdot}CH_3 + H^+$$

$$\longrightarrow Ar{\cdot}SO_2{\cdot}N{:}CH{\cdot}CH_2{\cdot}CH_3 \longrightarrow Ar{\cdot}SO_2{\cdot}NH_2 + CH_3{\cdot}CH_2{\cdot}CHO$$

This suggests that when R = H, lactonisation as in (*d*) prevents the operation of reaction (*e*), which would lead to complete elimination of the three-carbon chain. Instead the removal of the arylsulphonyl group from the lactone proceeds normally, yielding the unstable free morpholone, which gives the hydroxy-acid. Traces of acetone and propaldehyde formed probably arise as shown in reaction (*d*).

None of the other reactions apply when R = H, as they lead to the production of only one carbonyl compound. Also unsubstituted allyl compounds undergo negligible tautomerism (compare Burgin, Hearne, and Rust, *loc. cit.*), which rules out reaction (*f*), and lactonisation is probably much more rapid than dehydration as in (*e*).

When R = CH_3, if the unsaturated acid is the starting material, reaction (*e*) or (*f*) is possible, although (*f*) is more likely, as conversion of β-methylallyl compounds into dimethylvinyl compounds is rapid and almost complete in the presence of hot sulphuric acid (compare Burgin and co-workers, *loc. cit.*). If the lactone is the starting material, it is possible that it reverts to the hydroxy-acid and then by reaction (*e*) to the dimethylvinyl compound.

The last stage of the mechanism of Cairns and Fletcher is not applicable, as we are dealing with a tertiary nitrogen atom, but it is unnecessary, since Clemo and Perkin (J., 1924, **125**, 1805) showed that vinyl derivatives of tertiary nitrogen compounds are readily decomposed under acid conditions, yielding aldehydes. This applies in compounds now under discussion.

Reaction (*g*) is also a possibility, but whereas β-methylallyl alcohol, produced when R = CH_3, is known to yield *iso*butaldehyde on treatment with acid, allyl alcohol, produced when R = H, is unaffected or yields acraldehyde.

No tautomerism takes place previous to treatment with acid, since it has been shown by ozonolysis that the arylsulphonyl-allyl- and -β-methylallyl-glycines are true allyl compounds. In every case the volatile compound from the decomposition of the ozonides was formaldehyde, and whilst the expected aldehyde from the other part of the ozonide of the former sulphonyl compound was not obtained crystalline, its 2 : 4-dinitrophenylhydrazone was isolated. The ketone from benzenesulphonyl-β-methylallylglycine was obtained in crystalline condition.

In view of the easy removal of the β-methylallyl group with sulphuric acid the hydrolysis of N-*mesitylenesulphonyl*-N-β-*methylallylglycine* was performed, a boiling mixture of glacial acetic and concentrated hydrochloric acids being used (compare Cocker, J., 1937, 1695). β-*Hydroxy*iso*butylglycine* was thus obtained. The reaction probably involves the addition of hydrogen chloride to the methylallyl group, followed by the removal of the mesitylenesulphonyl group and substitution of OH for Cl in the treatment with silver oxide to remove the excess of hydrochloric acid.

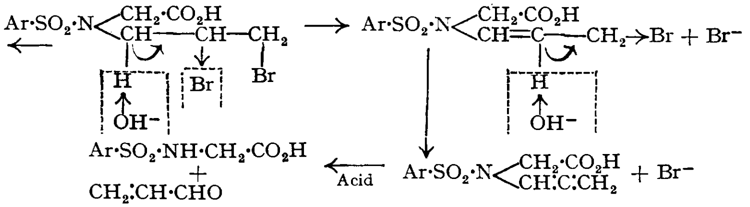
The arylsulphonylallylglycines readily give dibromides of the type $Ar{\cdot}SO_2{\cdot}N(CH_2{\cdot}CO_2H){\cdot}CH_2{\cdot}CHBr{\cdot}CH_2Br$. These lose bromine and become unsaturated on boiling with zinc and acetic acid, are reduced by Raney nickel and hydrogen at slightly above atmospheric pressure with the production of arylsulphonylpropylglycines, and are decomposed by hot dilute aqueous sodium hydroxide to give a solution containing bromidion which on acidification even at 0° yields a mixture of acraldehyde, arylsulphonylglycine, and a small quantity of a monobromo-compound.

The monobromo-compound from *p*-toluenesulphonylallylglycine is unsaturated, and is immediately decomposed by hot dilute mineral acid with the production of a mixture of acraldehyde and a substance with the odour of propaldehyde, most likely β-bromopropaldehyde. This reaction with acid suggests that the monobromo-compound is a vinyl compound (compare Clemo and Perkin, *loc. cit.*) and throws light on the mechanism of the decomposition of the dibromide. Only very small quantities of the monobromo-compound could be obtained, but ozonolysis experiments in sodium bicarbonate solution gave a volatile aldehyde from which a 2 : 4-dinitrophenylhydrazone containing no bromide was obtained. The bromine was no doubt removed by hydrolysis during the steam distillation of the alkaline solution.

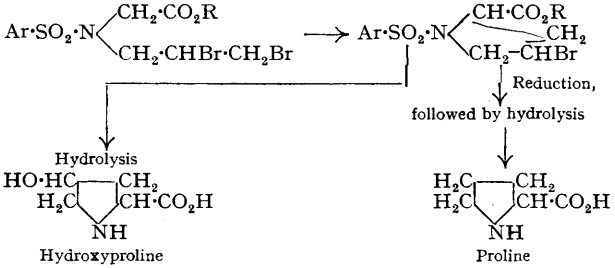
Analysis and m. p. of the 2 : 4-dinitrophenylhydrazone corresponded to that of glycollaldehyde 2 : 4-dinitrophenylhydrazone. The monobromo-compound is therefore probably

$$C_6H_4Me{\cdot}SO_2{\cdot}N(CH_2{\cdot}CO_2H){\cdot}CH{:}CH{\cdot}CH_2Br$$

and the mechanism of the decomposition of the dibromide now suggested is :



Since the dibromides were obtained in good yield, their possible ring closure was investigated with a view to the following transformations :



R = Me, Et, or H.

However, all attempts to cyclise the methyl or the ethyl esters or the free acids led either to the recovery of the starting material or to gums. The following condensing agents were used : silver oxide, sodium in boiling xylene, copper bronze in boiling nitrobenzene.

Attempts were also made to brominate the acetate chain so as to assist ring closure. α-Bromination was never successful and it seems that the α-hydrogen atom is firmly bound by a still basic nitrogen atom. The introduction of the *m*-nitrobenzenesulphonyl group did not influence the reactivity towards bromine.

Further work is proceeding with a view to obtain the γ-bromopropyl derivative of the arylsulphonylglycines, to which more vigorous methods of ring closure can be applied.

EXPERIMENTAL.

Benzene- and *p*-toluene-sulphonyl derivatives of the various amino-acids are described. The former are preferable in view of their greater readiness to crystallise, but at times benzenesulphonyl chloride was not available.

N-*Benzenesulphonyl*-N-*allylglycine* (I).—A mixture of benzenesulphonylglycine (3 g.) in 3N-sodium hydroxide (15 c.c.) and allyl bromide (3 g.) was refluxed for 3 hours on the water-bath, cooled to 0°, filtered, and acidified with concentrated hydrochloric acid, and the precipitate washed, dried, and crystallised from benzene, forming long colourless prisms (2·0 g.), m. p. 107° (Found : C, 51·8; H, 5·1; N, 5·6. $C_{11}H_{13}O_4NS$ requires C, 51·8; H, 5·1; N, 5·5%).

N-p-*Toluenesulphonyl*-N-*allylglycine* (II), prepared in the same way, formed long thin prisms, m. p. 109—110° (Found : C, 53·7; H, 5·9. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%).

The identity of the above compounds was confirmed as follows : (i) Both rapidly decolourised bromine water and alkaline permanganate. (ii) Compound (II) (1·5 g.), dissolved in chloroform (20 c.c.), was subjected to a stream of 8% ozonised oxygen for 5½ hours. The chloroform was then removed in a vacuum at 20°, the syrupy residue steam-distilled, and formaldehyde identified by the dimedon derivative, m. p. and mixed m. p. 191—192°. The residue from the steam-distillation was extracted several times with ether, from which an oil was obtained the 2 : 4-*dinitrophenylhydrazone* of which crystallised from dilute alcohol in orange micro-prisms, m. p. 173—174° (Found : C, 45·4; H, 3·4. $C_{17}H_{17}O_8N_5S$ requires C, 45·2; H, 3·8%). This agrees with the 2 : 4-dinitrophenylhydrazone of *N*-*p*-toluenesulphonyl-*N*-aldehydomethylglycine.

Ethyl *N*-benzenesulphonyl-*N*-allylaminoacetate (III), prepared by allylation of ethyl benzenesulphonamidoacetate with allyl chloride in sodium ethoxide solution or by esterification of (I), was a colourless oil, b. p. 172—173°/1 mm. Hydrolysis with dilute sodium hydroxide solution yielded (I).

dl-N-β-*Hydroxypropylglycine* (IV).—Compound (I) (9 g.) was refluxed (125°) with 60% sulphuric acid (9·4 c.c. of concentrated acid, 11·7 c.c. of water) for 4½ hours, and the mixture then treated according to Cocker and Lapworth (J., 1931, 1894). The required *amino-acid* crystallised from methyl alcohol in colourless rectangular prisms (2 g.), m. p. 194—195° (decomp.) (Found : C, 45·2; H, 8·0; N, 10·4. $C_5H_{11}O_3N$ requires C, 45·1; H, 8·3; N, 10·5%). The acid had a sweet taste, was readily soluble in water but only sparingly in boiling alcohol, was non-hygroscopic, and gave the usual deep coloration with copper acetate.

N-*Benzenesulphonyl*-6-*methyl*-2-*morpholone* (V).—Treatment of (IV) in alkaline solution with benzenesulphonyl chloride and acidification of the solution gave (V). It crystallised from dilute alcohol in colourless plates, m. p. 128—128·5°, which dissolved slowly in sodium hydroxide solution (Found : C, 51·6; H, 4·9; N, 5·7. $C_{11}H_{13}O_4NS$ requires C, 51·8; H, 5·1; N, 5·5%). Attempts to prepare the free acid yielded the lactone.

N-p-*Toluenesulphonyl*-N-β-*hydroxypropylglycine* (VI), obtained from (IV) on treatment with *p*-toluenesulphonyl chloride and sodium hydroxide, crystallised from hot water in transparent prisms, m. p. 138—139° (Found : C, 49·9; H, 5·9; N, 5·2; S, 11·6. $C_{12}H_{17}O_5NS$ requires C, 50·2; H, 5·9; N, 4·9; S, 11·2%). On drying in a vacuum at 120° for 8 hours it lost one equivalent of water and gave N-p-*toluenesulphonyl*-6-*methyl*-2-*morpholone* (VII). This crystallised from benzene–light petroleum in colourless needles, m. p. 92—93° (Found : C, 53·7; H, 5·6. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%). Lactonisation was also effected by treatment of (VI) with acetic anhydride (no acetyl compound was produced), thionyl chloride, or even boiling benzene. No other derivative of the new amino-acid has been obtained crystalline.

Hydration of (II).—0·5 G. was slowly stirred into 2 c.c. of concentrated sulphuric acid and after ½ hour the mixture was poured on ice. The oil obtained solidified on scratching; after crystallisation from hot water it had m. p. and mixed m. p. with (VI) 139°. The mother-liquors from the crystallisation of (VI) yielded a little (VII), m. p. 93°. The filtrate from the collection of the crude (VI) in the above hydration gave a mixture of 2 : 4-dinitrophenylhydrazones which could not be separated by crystallisation. The m. p. (137°) suggested a mixture of acetone- and propaldehyde-2 : 4-dinitrophenylhydrazones.

Compound (I) was similarly hydrated to the lactone (V).

Condensation of β-Hydroxypropylamine with Ethyl Bromoacetate.—The amine (Levene and Watt, *J. Biol. Chem.*, 1926, **71**, 461) was characterised as its *phenylcarbamyl* derivative [presumably $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}NH{\cdot}CO{\cdot}NHPh$], which was prepared by treating the amine (1 mol.) slowly with phenylcarbimide (1 mol.) at 0°. The mixture became glass-like and solidified on elutriation with benzene. It crystallised from ethyl acetate–benzene in colourless plates, m. p. 108—109° (Found : C, 62·2; H, 6·9. $C_{10}H_{14}O_2N_2$ requires C, 61·9; H, 7·2%). The *phenylurethane* of the phenylcarbamyl derivative was obtained by heating the latter with an excess of phenylcarbimide for ½ hour on the water-bath. After cooling, the mixture was repeatedly stirred with benzene, and the solid collected. It crystallised from ethyl acetate–benzene in clusters of colourless needles, m. p. 180—181° (Found : C, 65·0; H, 5·8. $C_{17}H_{19}O_3N_3$ requires C, 65·2; H, 6·1%).

β-Hydroxypropylamine (2 g.), cooled to 0°, was slowly treated, with stirring, with ethyl bromoacetate (2·2 g.). After 12 hours the mixture was poured into water, unchanged ester extracted with ether, and the aqueous solution just acidified to Congo-red with hydrochloric acid and heated on the water-bath for 1 hour. Hydrochloric acid was removed by silver oxide, silver by hydrogen sulphide, and the filtrate decolourised (charcoal) and evaporated to a syrup in a vacuum. It was stirred several times with acetone to remove the excess of β-hydroxypropylamine and once with methyl alcohol. The solid obtained crystallised from methyl alcohol–acetone in colourless rectangular prisms, m. p. 194—195° (Found : C, 45·4; H, 7·9%). It gave no depression in m. p. with compound (IV), and its *p*-toluenesulphonyl derivative was identical with (VI).

Oxidation of β-Hydroxypropylglycine.—Iodine (1·2 g.) was added to a solution of sodium carbonate (1·2 g.) and the amino-acid (0·2 g.) in 10 c.c. of water and the mixture was gently warmed for 10 minutes, cooled, and extracted with ether. From the ethereal solution, iodoform (0·05 g.), m. p. 119—120°, was isolated, but the other oxidation product (iminodiacetic acid) was not obtained crystalline.

N-*Benzenesulphonyl*-N-*β-methylallylglycine* (VIII).—A mixture of benzenesulphonylglycine (3 g.) in 3N-sodium hydroxide (25 c.c.) and β-methylallyl chloride (20 g.) was refluxed on the water-bath for 9 hours. The mixture was steam-distilled, cooled, treated with charcoal, and filtered. The well-stirred solution was acidified at 0°, and the product washed and dried. It crystallised from benzene–light petroleum (charcoal) in colourless prisms (3 g.), m. p. 91—92°. For analysis it was dried at 80° in a vacuum (Found : C, 53·9; H, 5·8. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%).

N-p-*Toluenesulphonyl*-N-*β-methylallylglycine* (IX), prepared in the same manner, crystallised from benzene in needles, m. p. varying from 92 to 106° according to the rate of heating. After being heated for 5 hours at 80° in a vacuum, it had m. p. 109—110° (Found : C, 55·0; H, 6·3. $C_{13}H_{17}O_4NS$ requires C, 55·1; H, 6·0%). The unheated crystals yielded benzene when warmed with water, indicating the presence of benzene of crystallisation. 5 G. of compound (IX), esterified with alcoholic hydrogen chloride, yielded 3 g. of product which crystallised from light petroleum in long silky needles, m. p. 67·5—68°. It contained bound chlorine and on treatment with dilute aqueous sodium hydroxide gave a solution containing sodium chloride. On acidification this yielded the lactone (XII). The ester was therefore *ethyl* N-p-*toluenesulphonyl*-N-*β-chloro*iso*butylaminoacetate* (X) (Found : C, 51·8; H, 6·5. $C_{15}H_{22}O_4NClS$ requires C, 51·9; H, 6·3%).

N-*Benzenesulphonyl*-6 : 6-*dimethyl*-2-*morpholone* (XI).—*N*-Benzenesulphonyl-*N*-β-methylallylglycine (0·5 g.) was hydrated with concentrated sulphuric acid (2 c.c.) at 0°; after ½ hour the mixture was poured on ice, and the crude morpholone collected. The combined aqueous filtrates were retained. The *morpholone* crystallised from hot water in long, felted, colourless needles (0·35 g.), m. p. 134—135° (Found : C, 53·9; H, 5·7. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%). It dissolved slowly in sodium hydroxide, but was insoluble in sodium carbonate solution.

The filtrates were treated with 2 : 4-dinitrophenylhydrazine, and the hydrazone collected. After crystallisation from alcohol it had m. p. and mixed m. p. with *iso*butaldehyde-2 : 4-dinitrophenylhydrazone 182° (Lindenbaum, *J. Amer. Chem. Soc.*, 1930, **52**, 2955, gives m. p. 182°; Ostertag, *ibid.*, 1932, **54**, 3758, gives m. p. 187°) (Found : C, 47·7; H, 4·6. Calc. for $C_{10}H_{12}O_4N_4$: C, 47·6; H, 4·6%).

N-p-*Toluenesulphonyl*-6 : 6-*dimethyl*-2-*morpholone* (XII), prepared similarly, formed long felted needles, m. p. 133—134° (Found : C, 55·3; H, 5·9. $C_{13}H_{17}O_4NS$ requires C, 55·1; H, 6·0%).

Ozonolysis of N-*Benzenesulphonyl*-N-*β-methylallylglycine.*—The compound (1·5 g.) in chloroform (25 c.c.) was ozonised as in the case of the allyl analogue. The formaldehyde–dimedon product had m. p. 188—189°. The residue from the steam-distillation was cooled and extracted with ether, from which N-*benzenesulphonyl*-N-*acetonylglycine* (1 g.) was obtained. This, crystallised from ethyl acetate–light petroleum and then from water, formed stout, colourless prisms, m. p. 123° (Found : C, 48·9; H, 5·0. $C_{11}H_{13}O_5NS$ requires C, 48·7; H, 4·8%). On treatment with iodine and sodium carbonate, iodoform was produced. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in golden felted needles and behaved as though it contained water of crystallisation (Found : C, 45·9; H, 4·4. $C_{17}H_{17}O_8N_5S,H_2O$ requires C, 46·3; H, 4·3%).

Hydrolysis of N-*Benzenesulphonyl*-6 : 6-*dimethyl*-2-*morpholone.*—A suspension of this compound (10 g.) in 60% sulphuric acid (18·8 c.c. of concentrated acid, 23·4 c.c. of water) was refluxed for 4 hours; the vapour, passed into a solution of 2 : 4-dinitrophenylhydrazine hydrochloride, gave *iso*butaldehyde-2 : 4-dinitrophenylhydrazone, m. p. 178°. From the hydrolysis liquor, glycine was isolated, identical with an authentic specimen, as also were the benzenesulphonyl and the phenylcarbamyl derivative.

N-*Mesitylenesulphonyl*-N-*β-methylallylglycine* (XIV).—The preparation from mesitylenesulphonylglycine in 2N-sodium hydroxide and β-methylallyl chloride, though it gave the desired *glycine* in colourless prisms, m. p. 117—118° (Found : C, 57·4; H, 7·0. $C_{15}H_{21}O_4NS$ requires C, 57·9; H, 6·8%), was unsatisfactory for the preparation of large batches and the following method was preferred. *Ethyl mesitylenesulphonamidoacetate* (XV) [large flat prisms, m. p. 43—44°, from benzene–light petroleum (Found : C, 52·5; H, 6·7. $C_{13}H_{19}O_4NS$ requires C, 52·2; H, 6·4%)] (10·7 g.) in alcohol (30 c.c.) was added to sodium ethoxide from sodium (0·8 g.) and alcohol (20 c.c.), followed by β-methylallyl chloride (4·3 g.), and the mixture was refluxed overnight. Alcohol was removed, the residue poured into water and extracted with ether, and the extract washed with dilute sodium hydroxide solution and with water and dried. The solvent was removed, and the residue hydrolysed with 10% methyl-alcoholic potash (50 c.c.), poured into water, and acidified. The solid obtained crystallised from dilute alcohol in colourless prisms (3·7 g.), m. p. 117—118°. Mesitylenesulphonylglycine was obtained from the alkaline extract.

N-*β-Hydroxy*iso*butylglycine* (XVI).—The compound (XIV) (20 g.) was refluxed for 4 hours with 50 c.c. of glacial acetic acid and 65 c.c. of concentrated hydrochloric acid, the mixture evaporated to dryness in a vacuum, and the residue dissolved in water and extracted with ether. The aqueous solution was evaporated to dryness in a vacuum, the remaining hydrochloric and sulphuric acids removed with litharge, followed by silver oxide, and lead and silver removed with hydrogen sulphide. From the filtrate a syrup was obtained which solidified on trituration with acetone and crystallised from alcohol–ether in long needles, m. p. 176° (decomp.) (Found : C, 48·9; H, 9·1; N, 9·2. $C_6H_{13}O_3N$ requires C, 49·0; H, 8·8; N, 9·5%). The *p*-toluenesulphonyl compound prepared from it gave no depression in m. p. with (XII).

Condensation of β-hydroxy*iso*butylamine (5 g.) in alcohol (5 c.c.) with ethyl bromoacetate (4·7 g.) in alcohol (5 c.c.) at 0° gave after 2 days a solution from which, after removal of the excess of bromo-ester with ether and of hydrochloric acid with silver oxide, the required amino-acid was obtained in small yield, m. p. 176°, identical in all respects with (XVI). The new amino-acid is hygroscopic, gives a deep blue coloration with copper acetate, and has a sweet taste.

Attempts to prepare Inactive N-*β-Hydroxypropylalanine.*—Benzenesulphonylalanine (Cocker and Harris, *loc. cit.*), when treated with allyl bromide, gave a mixture (m. p. 102—119°) which could not be separated by crystallisation. However, since on hydration the required compound was expected to give a lactone, 2·5 g. of the above mixture were treated at 0° with 9 c.c. of concentrated sulphuric acid and the mixture was poured on ice and slowly basified with sodium carbonate. The precipitated N-*benzenesulphonyl*-3 : 6-*dimethyl*-2-*morpholone* (XVII), after being washed and dried, crystallised from benzene–light petroleum in colourless micro-prisms (Found : C, 53·65; H, 5·5. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%). Propaldehyde also was identified in the mixture. The following method proved more satisfactory. *Ethyl benzenesulphonyl-α-aminopropionate* (32 g.) [colourless flat prisms, m. p. 61—62°, from light petroleum–benzene (Found : C, 51·7; H, 5·8. $C_{11}H_{15}O_4NS$ requires C, 51·4; H, 5·8%)], dissolved in alcohol (150 c.c.), was added to a solution of sodium (2·9 g.) in alcohol (50 c.c.) and allyl chloride (11·4 g.; 1·2 mols.) and the mixture was refluxed for 8 hours. Alcohol was removed, and the residue poured into dilute sodium hydroxide solution and extracted with ether. From the ether an oil (18 g.) was obtained, which was hydrolysed on the water-bath with 10% alcoholic potash during 3 hours; the mixture was poured into water and acidified, and the oil obtained was extracted with ether. From the extract a solid was obtained, crystallisation of which from benzene–light petroleum yielded N-*benzenesulphonyl*-N-*allylalanine* (XVIII) in colourless prisms (about 8 g.), m. p. 95° (Found : C, 53·7; H, 5·5. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%). 5·5 G. of (XVIII) were hydrolysed with 60% sulphuric acid (5·8 c.c. of acid, 7·1 c.c. of water); from the mixture a brown syrup of the required amino-acid was obtained, which gave a deep blue coloration with copper acetate.

Condensation of β-Hydroxypropylamine with Ethyl α-Bromopropionate.—The bromo-ester (1·8 g.) was added to a cooled solution of the amine (3 g.) in alcohol (20 c.c.); after 2 days the alcohol was removed, and the residue poured into water (20 c.c.) and extracted with ether. The aqueous solution was warmed with barium hydroxide for 1 hour and evaporated to dryness in a vacuum; the residue was dissolved in water, and barium removed by sulphuric acid, the excess of acid by litharge, and lead by hydrogen sulphide. The final solution was evaporated to dryness in a vacuum, leaving a syrup which became solid on trituration with acetone; on crystallisation from alcohol and ether *β-hydroxypropylalanine* was obtained in small colourless prisms, m. p. 214° (Found : C, 48·6; H, 8·9. $C_6H_{13}O_3N$ requires C, 49·0; H, 8·8%). The yield was very small. The benzenesulphonyl compound prepared from it was identical with (XVII).

The following compounds were prepared in unsuccessful efforts to obtain the above amino-acid : *Ethyl* p-*toluenesulphonyl-α-aminopropionate* crystallised from benzene–light petroleum in large colourless prisms, m. p. 66—67° (Found : C, 51·4; H, 6·0. $C_{12}H_{17}O_4NS$ requires C, 53·1; H, 6·3%), *mesitylenesulphonylalanine* from benzene in needles, m. p. 155—156° (Found : C, 53·1; H, 6·3. $C_{12}H_{17}O_4NS$ requires C, 53·1; H, 6·3%), and its *ethyl* ester from alcohol in large colourless prisms, m. p. 99° (Found : C, 56·5; H, 7·2. $C_{14}H_{21}O_4NS$ requires C, 56·2; H, 7·0%).

Bromination Experiments.—N-*Benzenesulphonyl*-N-*βγ-dibromopropylglycine* (XIX). Bromine (0·5 g.) in chloroform (5 c.c.) was slowly added to a stirred solution of *N*-benzenesulphonyl-*N*-allylglycine (0·5 g.) in chloroform (15 c.c.) at 0° and after 1 hour the mixture was washed with dilute sodium bisulphite solution and with water and dried over sodium sulphate. From the solution an oil was obtained which crystallised from benzene–light petroleum in colourless needles, m. p. 117—118° after drying at 80° in a vacuum (Found : C, 31·9; H, 3·4. $C_{11}H_{13}O_4NSBr_2$ requires C, 31·8; H, 3·1%). This compound retained solvent very tenaciously. The *methyl* ester (XX), prepared from (XIX), crystallised from methyl alcohol in long colourless needles, m. p. 101—102° (Found : C, 33·2; H, 3·4. $C_{12}H_{15}O_4NSBr_2$ requires C, 33·6; H, 3·5%). The *ethyl* ester, prepared from (XIX) and alcoholic hydrogen chloride or by bromination of (III), crystallised from alcohol in micro-needles, m. p. 72° (Found : C, 35·5; H, 4·0. $C_{13}H_{17}O_4NSBr_2$ requires C, 35·2; H, 3·8%). N-p-*Toluenesulphonyl*-N-*βγ-dibromopropylglycine* (XXII) crystallised from benzene–light petroleum in transparent prisms, m. p. 127—128° after drying at 80° in a vacuum (Found : C, 34·0; H, 3·4; Br, 37·7. $C_{12}H_{15}O_4NSBr_2$ requires C, 33·6; H, 3·5; Br, 37·5%).

Reduction of the bromo-compounds. Compound (XIX) (1 g.) in methyl alcohol (25 c.c.) was reduced with hydrogen in the presence of Raney nickel. From the alcohol a solid was obtained which crystallised from benzene–light petroleum in colourless prisms, m. p. 102°, not depressed by authentic *N*-benzenesulphonyl-*N*-propylglycine.

Compound (XXII) (1 g.) in 20 c.c. of glacial acetic acid was heated on the water-bath for 4 hours with zinc dust (5 g.). After filtration the acetic acid was removed in a vacuum, and the residue poured into water. The oil obtained solidified on scratching and crystallised from benzene in needles (0·4 g.), m. p. 111·5°, not depressed by *N*-*p*-toluenesulphonyl-*N*-allyglycine (Found : C, 53·7; H, 5·9. Calc. for $C_{12}H_{15}O_4NS$: C, 53·5; H, 5·6%).

Hydrolysis of N-p-*Toluenesulphonyl*-N-*βγ-dibromopropylglycine.*—20 G., dissolved in 200 c.c. of 5% sodium hydroxide solution, were heated on the water-bath for 3 hours, cooled, and acidified. At the moment when the solution became acid to Congo-red the smell of acraldehyde developed (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 165°) and a solid was deposited. This, crystallised from ethyl acetate, had m. p. and mixed m. p. with *p*-toluenesulphonylglycine 147°. From the ethyl acetate, by concentration and crystallisation from alcohol, a small quantity of colourless needles, m. p. 193°, was obtained. This compound was readily soluble in dilute sodium bicarbonate solution, readily decolourised bromine in acetic acid, and on treatment with hot dilute sulphuric acid immediately gave an odour reminiscent of a mixture of acraldehyde and propaldehyde (Found : C, 41·4; H, 3·9; Br, 23·3. $C_{12}H_{14}NSBr$ requires C, 41·4; H, 4·0; Br, 23·3%). Ozonolysis yielded a volatile compound which gave a 2 : 4-dinitrophenylhydrazone, m. p. 156° (Found : C, 40·0; H, 3·2. Calc. for $C_8H_8O_5N_4$: C, 40·0; H, 3·3%). This corresponds to the 2 : 4-dinitrophenylhydrazone of glycollaldehyde, m. p. 155—156° (corr.) (Collatz and Neuberg, *Biochem. Z.*, 1932, **255**, 27).

N-m-*Nitrobenzenesulphonylglycine* (XXIII).—A well-agitated solution of glycine (5 g.) in N-sodium hydroxide (200 c.c.) was treated at intervals during 4 hours with a solution of *m*-nitrobenzenesulphonyl chloride in benzene, until 15 g. of the chloride had been added. The aqueous layer was acidified, and the precipitate crystallised from ethyl acetate–ligroin, forming colourless hairy needles (8 g.), m. p. 149—150° (Found : C, 37·1; H, 3·2. $C_8H_8O_6N_2S$ requires C, 36·9; H, 3·1%). The *ethyl* ester (XXIV), prepared in the presence of concentrated sulphuric acid, crystallised from alcohol in long needles, m. p. 122° (Found : C, 41·7; H, 4·6. $C_{10}H_{12}O_6N_2S$ requires C, 41·7; H, 4·2%).

Ethyl N-m-*Nitrobenzenesulphonyl*-N-*allylaminoacetate.*—Compound (XXIV) (3 g.) was heated on the water-bath with a mixture of sodium ethoxide (from 0·24 g. of sodium and 20 c.c. of alcohol) and allyl chloride (1 c.c.) for 6 hours. Alcohol was removed, the residue poured into water containing a little sodium hydroxide, and the solid collected, washed, and dried. It crystallised from alcohol in colourless needles or prisms, m. p. 57·5—58° (Found : C, 47·6; H, 5·1. $C_{13}H_{16}O_6N_2S$ requires C, 47·6; H, 49%). The *dibromide* crystallised from alcohol in colourless tufts, m. p. 91—91·5° (Found : C, 33·0; H, 3·5. $C_{13}H_{16}O_6N_2SBr_2$ requires C, 32·9; H, 3·4%).

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