199. *The Action of Phthalide on Toluene*-p-*sulphonamide and its Derivatives.*

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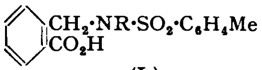
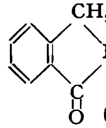
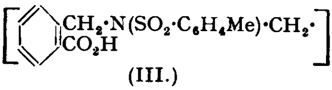
Wislicenus (*Ber.*, 1885, **18**, 172; *Annalen*, 1886, **233**, 101) showed that potassium cyanide reacted with phthalide at 180—200° to form *o*-carboxybenzyl cyanide. It has now been found that the sodium derivatives of toluene-*p*-sulphonamide and of several of its monosubstituted derivatives react similarly, to give *N*-*o*-carboxybenzyltoluene-*p*-sulphonamide and similar *N*-substituted amides. From these derivatives the *N*-aryl-1-keto*iso*indolines are readily prepared.

trans-1′-HYDROXY-2′-INDANYLACETIC ACID and the lactone of the *cis*-acid are not converted into amino-acids by the usual methods (Menon and Peacock, *J.*, **1934**, **1297**). In a search for other methods of converting lactones into amino-acids preliminary experiments with phthalide and the sodium derivative of toluene-*p*-sulphonamide have shown that the toluene-*p*-sulphonyl derivative of the amino-acid is formed. Potassium phthalimide reacted similarly, but ethyl sodiomalonate gave only condensation products of malonic ester. The lactone of *cis*-1′-hydroxy-2′-indanylacetic acid decomposed below the temperature necessary for reaction. In the present paper the reactions with toluene-*p*-sulphon-amide and -anilide and some similar compounds are described.

Wislicenus (*Ber.*, 1885, **18**, 172; *Annalen*, 1886, **233**, 101) showed that phthalide reacted at about 190° with potassium cyanide to form the potassium salt of *o*-carboxybenzyl cyanide. By analogy it would be expected that sodium or potassium, united with radicals capable of forming a stable linkage with carbon but not forming a too stable ion, might behave similarly.


(I.)


(II.)


(III.)

When the sodium derivative of toluene-*p*-sulphonamide was heated with phthalide at 180—200° the sodium salt of *N*-*o*-carboxybenzyltoluene-*p*-sulphonamide (I; R = H) was formed together with 1-keto-2-toluene-*p*-sulphonyl*iso*indoline (II; R = $SO_2{\cdot}C_6H_4Me$). The sodium derivatives of toluene-*p*-sulphon-anilide, -*p*-toluidide, and -ethylamide similarly gave the analogous compounds (I; R = Ph, C_6H_4Me, and Et, respectively). *NN′*-Ditoluene-*p*-sulphonamidoethane gave a mixture of (I; R = $CH_2{\cdot}CH_2{\cdot}NH{\cdot}SO_2{\cdot}C_6H_4Me$) and (III).

Compounds of the type (I; R = Ph or C_6H_4Me) are readily converted by cold concentrated sulphuric acid into compounds of type (II), displacement of the toluene-*p*-sulphonyl group occurring during cyclisation. No such reaction occurs when toluene-*p*-sulphonanilide is treated with benzoic acid in concentrated sulphuric acid.

The derivatives described could presumably all be prepared by conventional methods from *o*-cyano- or *o*-carboxy-benzyl chloride but phthalide is more readily accessible and the reaction is of interest as an example of alkyl–oxygen fission of an ester (Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686).

EXPERIMENTAL.

N-o-*Carboxybenzyltoluene*-p-*sulphonamide*.—The sodium derivative of toluene-*p*-sulphonamide (10·0 g.) and phthalide (20·0 g., *ca.* 3 mols.) were well mixed and heated for 5 hours at 190—200° (oil-bath). They formed a sticky mass at about 180°. The cooled product, pink and slightly sticky, was extracted with warm ether, leaving a hard, pale yellow solid, which was extracted with warm sodium hydrogen carbonate (5 g. in 200 c.c. of water) and filtered, to give a yellow solid and a pink filtrate. Acidification of the filtrate with acetic acid afforded oily N-o-*carboxybenzyltoluene*-p-*sulphonamide* (6·7 g.), which soon solidified and crystallised from methanol, ethanol, or acetic acid as colourless needles, m. p. 162° (Found: C, 58·3; H, 4·81; N, 4·4; S, 10·1; equiv., 304. $C_{15}H_{15}O_4NS$ requires C, 59·0; H, 4·9; N, 4·59; S, 10·5%; equiv., 305). The yellow solid was extracted with warm ethanol, and residual 1-*keto-2-toluene*-p-*sulphonylisoindoline* (3·7 g.) crystallised from acetic acid as colourless prisms, m. p. 211° (Found: C, 62·8; H, 4·8. $C_{15}H_{13}O_3NS$ requires C, 62·7; H, 4·5%), insoluble in aqueous sodium hydroxide.

N-o-*Carboxybenzyl*-N-*ethyltoluene*-p-*sulphonamide*.—The sodium derivative of *N*-ethyltoluene-*p*-sulphonamide (4·0 g.) was heated with phthalide (8·0 g.) for 3 hours at 170—190° (oil-bath). The product, worked up as above, gave N-o-*carboxybenzyl*-N-*ethyltoluene*-p-*sulphonamide* (4·1 g.), needles (from glacial acetic acid), m. p. 181° (Found: C, 61·1; H, 5·9. $C_{17}H_{19}O_4NS$ requires C, 61·2; H, 5·7%).

The Reaction applied to 1 : 2-*Ditoluene*-p-*sulphonamidoethane*.—The disodium derivative (4·0 g.) of this diamide and phthalide (8·0 g.) at 180—190° gave, in the usual way, a mixture of acids (5·0 g.). Extraction with alcohol left a residue. Addition of water to the alcoholic extract precipitated colourless 1-N-o-*carboxybenzyltoluene*-p-*sulphonamido-2-toluene*-p-*sulphonamidoethane* which, crystallised from acetone–benzene, had m. p. 166° (Found: C, 57·7; H, 4·9; N, 5·4. $C_{24}H_{26}O_6N_2S_2$ requires C, 57·3; H, 5·2; N, 5·6%). The residue from the alcohol, crystallised from acetic acid, afforded 1 : 2-*di*-(N-o-*carboxybenzyltoluene*-p-*sulphonamido*)*ethane*, m. p. 244° (decomp.; quick heating) (Found: C, 60·3; H, 5·0; N, 4·5. $C_{32}H_{32}O_8N_2S_2$ requires C, 60·3; H, 5·0; N, 4·4%).

N-o-*Carboxybenzyltoluene*-p-*sulphonanilide*.—The dry sodium derivative (4·0 g.) of toluene-*p*-sulphonanilide and phthalide (6·0 g.) at 170—190° (4 hours) gave the N-o-*carboxybenzyl* derivatve (3·2 g.), m. p. 181° (from aqueous acetic acid) (Found: C, 66·1; H, 5·0. $C_{21}H_{19}O_4NS$ requires C, 65·9; H 5·2%).

N-o-*Carboxybenzyltoluene*-p-*sulphon*-p-*toluidide* was prepared similarly in 65% yield; it had m. p. 191° (from acetic acid) (Found: C, 66·7; H, 5·3; N, 3·3. $C_{22}H_{21}O_4NS$ requires C, 66·8; H, 5·3; N, 3·5%).

Substituted 1-*Keto*isoindoline.—*N*-*o*-Carboxybenzyltoluene-*p*-sulphonanilide (0·4 g.) in ice-cold, concentrated sulphuric acid (2 ml.) was kept for 16 hours in a refrigerator. The mixture was then poured on ice and the 1-keto-2-phenyl*iso*indoline (0·3 g.) filtered off and crystallised from ethanol; it had m. p. 162° (Found: C, 79·8; H, 5·3. Calc. for $C_{14}H_{11}ON$: C, 80·4; H, 5·3%) (cf. Hessert, *Ber.*, 1877, **10**, 1450). The 2-p-*tolyl* derivative, prepared similarly, crystallised from alcohol in colourless plates, m. p. 140° (Found: C, 80·2; H, 5·8; N, 6·4. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·8; N, 6·3%). The same product was obtained by the action of thionyl chloride on *N*-*o*-carboxybenzyltoluene-*p*-sulphon-*p*-toluidide. *N*-*o*-Carboxybenzyltoluene-*p*-sulphonethylamide was recovered unchanged from a solution in concentrated sulphuric acid kept at 0°, but was decomposed when this was heated at 100°.

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