

## A General Method of Esterification using Trifluoroacetic Anhydride

For the synthesis of esters from carboxylic acids and alcohols or phenols, it is customary to heat the reactants for several hours in the presence of a strong mineral acid catalyst, or else to proceed via the acid chloride or the acid anhydride. We now report a method of esterification which obviates the necessity of a two-stage process and, at the same time, enables a rapid direct reaction to occur between the acid and the hydroxy-compound under mild conditions. The new method, which entails the use of the anhydride of trifluoroacetic acid, gives the purified esters in yields of 60–90 per cent.

The standard technique involves warming the carboxylic acid (1.5 moles) together with trifluoroacetic anhydride (1.5 moles) for a few minutes before adding the alcohol or phenol (1 mole for a mono-hydroxy-compound and a proportionate amount for a polyhydroxy-compound) and then maintaining the mixture at 40–60° for about 15 min. The resulting solution may then be poured into aqueous sodium bicarbonate and the ester isolated in the usual manner. By this method glyceryl tripalmitate, *p*-nitrobenzyl acetate and ethylene dibenzoate have been made. Minor modifications can be introduced to suit the individual case; for example, acetylations of mannitol and of  $\beta$ -naphthol proceed spontaneously and, without the application of any external heat, are complete in about three minutes.

An advantage of the method is that solid reactants do not require the introduction of a solvent, for we have isolated, by the standard technique, good yields of *p*-nitrobenzyl phenylacetate, diphenyl adipate and the benzoates of phenol,  $\beta$ -naphthol, *p*-nitrobenzyl alcohol and mannitol.

The conditions of the reaction are sufficiently mild to enable it to be employed for the esterification of glycosides; for example, for the acetylation of  $\alpha$ -methyl glucoside, trehalose and (with care) sucrose, and for the propionylation of  $\alpha$ -methyl glucoside and maltose. It is worthy of note that cellulose, starch and other polysaccharides can be acetylated and benzoylated in 60 min. or less at 50° to give essentially fully esterified products.

The new method would appear to be advantageous for the self-esterification of hydroxy-acids to give polyesters. We have prepared one such polyester by treating *p*-hydroxy-benzoic acid with trifluoroacetic anhydride at 75° for 15 min.

It is to be noted that two patents (B.P. 285,858 and 313,408) have described the use of monochloroacetic anhydride as an 'impeller' for the esterification of cellulose with carboxylic acids; but in these cases a catalyst, namely, magnesium perchlorate or sulphuric acid, was also employed. We have obtained various examples of other uses for trifluoroacetic anhydride as a condensing agent, and these will be described in a later communication. We are greatly indebted to Imperial Chemical Industries, Ltd., General Chemicals Division (Widnes), for supplies of trifluoroacetic acid.

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## Metal Catalysis of Indole Production

THE production of indole from tryptophan by the action of copper sulphate and 9 per cent (w/v) sodium hydroxide was reported by Herzfeld<sup>1</sup> and confirmed by Baker, Dawes and Happold<sup>2</sup> in an attempt to elucidate the mechanism of the tryptophanase enzyme system of *Esch. coli*<sup>3</sup>. Catalysis of indole production was shown to occur with copper and cobalt, but not with other metals (including iron, manganese, nickel, chromium, tin and cerium). This specific effect of copper and cobalt is detectable down to concentrations of  $5 \times 10^{-6} M$ , and both metals show approximately the same catalytic activity. Only indole formation was observed at that time.

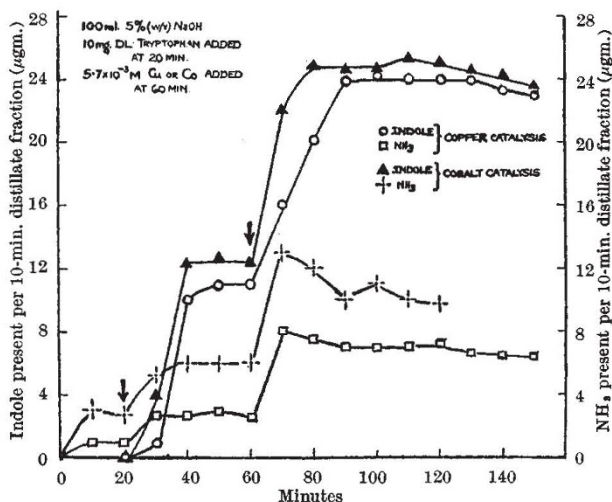


Fig. 1. Products of tryptophan decomposition with copper and cobalt catalysis

We now wish to record that the products of the reaction, other than indole, are ammonia and pyruvic acid (as with the enzyme-catalysed reaction<sup>4</sup>). Indole and ammonia production have been followed by determinations on successive fractions of distillate collected over 10-min. intervals, and pyruvate determined in the distillation flask residue. 100 ml. 5 per cent (w/v) sodium hydroxide was distilled and the volume kept constant by the addition of boiling distilled water. When the ammonia in the distillate had fallen to constant low level, 10 mgm. DL-tryptophan was added. Some indole was formed, due sometimes to trace metals present in the sodium hydroxide and always to trace metals resulting from the solvent action of the boiling alkali on the glass distillation vessel. The indole and ammonia distillation reach a constant level, and when this has occurred the appropriate salt is added to a concentration of  $5 \times 10^{-3} M$  and the distillation continued. This results in a very marked increase in indole and ammonia production (see Fig. 1). Ammonia production was invariably ahead of indole formation, which suggests that deamination occurs first, as found with certain enzyme preparations<sup>5</sup> (see table).

Substrate	Catalyst	Products per 10-minute distillate	
		Indole ( $\mu\text{mol.}$ )	NH <sub>3</sub> ( $\mu\text{mol.}$ )
Tryptophan	Cu	0.11	0.34
	Co	0.11	0.43
$\beta$ -Indolyl-3-ethylamine	Cu	0.35	0.68
	Co	0.10	0.43