THE MECHANISM AND APPLICATION OF THE FRIES ISOMERIZATION

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ABSTRACT

At the present time, the Fries reaction is the best means of obtaining the hydroxyaryl ketones which are important in a variety of organic syntheses. Fries and Finck,[1] in their study of the homologs of Cumarone, observed that when the chloroacetates of phenols were heated with aluminum chloride a rearrangement occurred readily and smoothly to the hydroxy-*omega*-chloroacetophenones.

This rearrangement of the aryl esters of carboxylic acids to hydroxyaryl ketones, as has been indicated by a large number of investigators, may also be accomplished by employing anhydrous ferric chloride and zinc chloride. However, it is apparent that anhydrous aluminum chloride is the most effective reagent for the conversion.

The technique of Fries and Finck was used until Rosenmund and Schnurr[2] recently announced that the Fries method could not be put to general application because of several complications and also observed that when the rearrangement is carried out in nitrobenzene solution a more rapid conversion occurs and in many cases with a better yield of product.

The reaction was generally assumed to be an intramolecular rearrangement of the phenyl ester into the hydroxyaryl ketone until recently when Rosenmund and Schnurr suggested that the reaction must be bimolecular. When they heated a mixture of o-chloro-p-cresyl acetate and p-cresyl benzoate with aluminum chloride for fifteen minutes at 150° C. they obtained all four possible products. An intramolecular change should produce only the two normal compounds o-acetyl-o-chloro-p-cresol and o-benzoyl-p-cresol. The subsequent work of Rosenmund and Lohfert[3] apparently gave further evidence that the Fries shifting does not occur within a single molecule. Auwers and co-workers[4] refuted these arguments and presented evidence to indicate that the Fries reaction is not a saponification and a subsequent resubstitution but a molecular rearrangement. It was reported recently by Cox[5] that some acetyl chloride was obtained when aluminum chloride acted on 2, 4, 6,-trichloro-phenyl acetate. This observation would support the contention that the reaction is bimolecular and that when the phenyl ester is acted upon by aluminum chloride, the free acid chloride is produced, which subsequently reacts with the phenol giving a ketone.

Fries and his co-workers[6] indicated that the reaction is a valuable synthetic method and the work of Auwers and his students[7] not only confirmed this but extended its usefulness to the preparation of a large number of monohydroxy-aryl ketones. Interesting syntheses in the poly-hydroxy-aryl ketone series were accomplished recently by Mauthner[8] employing the Fries method of transformation. It was shown by Fries[9] and later by Lederer[10] that when *alpha*-naphthyl acetate is rearranged by heating with aluminum chloride, 2-aceto-1-naphthol is formed. In the same manner the isomerization of *beta*-naphthyl acetate with aluminum chloride yielded chiefly 1-aceto-2-naphthol.

The Fries reaction has the possibility of becoming important in the commercial preparation of intermediates for antiseptics[11] and dyes.[12] It is also of theoretical interest because of its still uncertain and disputable mechanism.

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[1] Fries and Finck, Ber., *41,* 4271 (1908).
[2] Rosenmund and Schnurr, Ann., *460,* 56 (1928).
[3] Rosemund and Lohfert, Ber., *61,* 2601 (1928).
[4] Auwers and co-workers, Ber., *61,* 416, 1495 (1928) Ann., *464,* 293 (1928).
[5] Cox, J. Am. Chem. Soc., *52,* 352 (1930).
[6] Fries and co-workers, Ber., *43,* 212 (1910).
[7] Auwers and co-workers, Ber., *54,* 1543 (1921) ; *58,* 26, 36 (1925). Ann., *408,* 212 (1915).
[8] Mauthner, J. prakt. Chem., *118,* 314 (1928) ; *136,* 205, 213 (1933).
[9] Fries, Ber., *54,* 709 (1921) ; *58,* 2835 (1925).
[10] Lederer, J. prakt. Chem., *135,* 49 (1932).
[11] Coulthard, Marshall, and Pyman, J. Chem. Soc., *1930,* 280.
[12] E. P. 248 791 Chem. Zentr., *1927,* (II) 336.