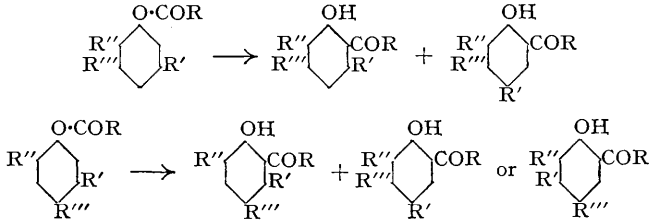
71. *The Fries Rearrangement and Subsequent Isomerisation.*

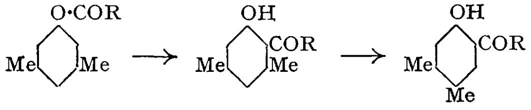
By G. Baddeley.

The migration of one alkyl group sometimes observed in the Fries rearrangement is not conditioned by the presence of another alkyl group in the *p*-position to it. The isomerisation has been studied kinetically.

Auwers (*Annalen*, 1928, **460**, 254) has tabulated a number of instances in which the normal product of the Fries rearrangement was accompanied by an isomeride, derived by displacement of an alkyl group from its original position :



Although in all the instances recorded by Auwers, a second alkyl group was in the *p*-position to that displaced, this is not essential. It has been shown that the acetate, propionate, and benzoate of *m*-5-xylenol are convertible quantitatively into either the corresponding 6-hydroxy-2 : 4-dimethylphenyl alkyl or aryl ketone (I) or its 3 : 4-dimethyl isomeride (II) according as only 1 mol. or 2 or more mols. of aluminium chloride are used. Auwers obtained mixtures of isomerides because he used 1—2 mols. of the chloride.



(I.) (II.)

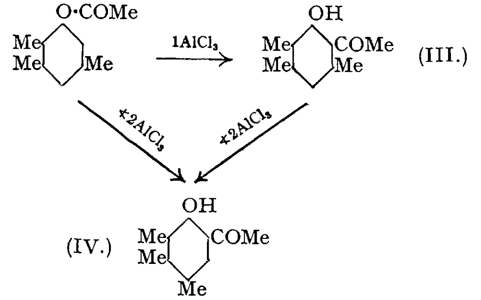
As would be expected from these results, hydroxy-ketones of type (I) undergo isomerisation when treated with 2 or more mols. of aluminium chloride. The reaction is bimolecular and the table summarises the results obtained with 3 and 3·5 mols. of reagent :

Phenol.	Acid.	Temp.	*k*.	*E* (Cals.).	Phenol.	Acid.	Temp.	*k*.	*E* (Cals.).
m-5-Xylenol	Propionic	140°	0·179	—	*m*-5-Xylenol	Benzoic	160°	0·107	—
		150	0·359	24·2			170	0·209	25·6
,,	Acetic	140	0·177	—	3 : 5-Diethylphenol	Acetic	110	0·405	—
		150	0·357	24·4			130	1·47	19·9

An experiment in which (I, R = Me) was isomerised in the presence of an added amount of (II, R = Me) showed that these hydroxy-ketones make respectively one and two molecules of reagent ineffective for producing the isomerisation.

The greater mobility of the ethyl than of the methyl group demonstrated by these results accords with various observations of Auwers, according to which, for example, both 2 : 5-dimethyl-4-ethyl- and 2 : 4-dimethyl-5-ethyl-phenyl acetates were isomerised to 6-hydroxy-3 : 5-dimethyl-4-ethylacetophenone.

More highly alkylated compounds are also subject to the above generalisations. For instance, *iso*-ψ-cumenyl acetate yields either 2 : 4 : 5- or 3 : 4 : 5-trimethyl-6-hydroxyacetophenone (III and IV respectively). In such cases the extra alkyl group so facilitates the isomerisation of the ketone first formed that this sets in before a homogeneous reaction mixture can be prepared, and, so far, has prevented a kinetic investigation of the change.



Discussion of the theoretical significance of the results is postponed pending an account of similar studies of the isomerisation by aluminium chloride on the one hand of alkyl ketones and on the other of alkyl phenols. Meanwhile it may be pointed out that, since the acetyl group can be removed from 2-hydroxyacetophenones by hydrolysis, a convenient method is available for preparing, for example, *o*-4-xylenol from *m*-5-xylenol.

EXPERIMENTAL.

The 6-hydroxy-2 : 4-dimethyl derivatives of the following ketones were obtained quantitatively from the corresponding esters and aluminium chloride (1 mol.) at 120—150° : Acetophenone, stout, pale yellow needles, m. p. 60°, from light petroleum (b. p. 40—60°) (Auwers and Borsche, *Ber.*, 1915, **48**, 1707, give m. p. 58°) ; propiophenone, colourless needles, m. p. 78°, from light petroleum (b. p. 60—80°) (Found : C, 74·1 ; H, 7·8. $C_{11}H_{14}O_2$ requires C, 74·2 ; H, 7·9%) ; benzophenone, colourless needles, m. p. 143°, from ethyl alcohol (Wittig, Oppermann, and Faber, *J. pr. Chem.*, 1941, **158**, 61, give m. p. 139—140°).

The 6-hydroxy-3 : 4-dimethyl derivatives of the following ketones were similarly obtained : Acetophenone, colourless hexagonal plates, m. p. 74°, from light petroleum (b. p. 60—80°) (Auwers, Bundesmann, and Weiners, *Annalen*, 1926, **447**, 176, give m. p. 71°) ; propiophenone, colourless plates, m. p. 60°, from light petroleum (b. p. 60—80°) (Found : C, 74·2 ; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·2 ; H, 7·9%) ; benzophenone, pale yellow plates, m. p. 111°, from ethyl alcohol (Found : C, 79·8 ; H, 6·1. $C_{15}H_{14}O_2$ requires C, 79·7 ; H, 6·2%).

Each of the above 6-hydroxy-2 : 4-dimethyl derivatives isomerised quantitatively to the corresponding 6-hydroxy-3 : 4-dimethyl derivative when heated for several hours with aluminium chloride (3 mols.) at 140—180°. Similarly, 6-hydroxy-2 : 4-diethylacetophenone [the *dibromo*-derivative crystallised from light petroleum (b. p. 60—80°) in large colourless prisms, m. p. 81° (Found : Br, 45·8. $C_{12}H_{14}O_2Br_2$ requires Br, 45·7%)] isomerised to the 6-hydroxy-3 : 4-diethyl derivative [the *monobromo*-derivative crystallised from light petroleum (b. p. 60—80°) in small, pale yellow prisms, m. p. 59° (Found : Br, 29·6. $C_{12}H_{15}O_2Br$ requires Br, 29·5%)].

Quantitative Investigations.—Isomerisation of 6-*hydroxy*-2 : 4- *to* 6-*hydroxy*-3 : 4-*dimethyl-acetophenone.* Preliminary experiments determined the procedure for the simultaneous dibromination of the former and monobromination of the latter ketone.

A mixture of *m*-5-xylenyl acetate (10·2 g.), aluminium chloride (24·6 g.), and sodium chloride (2·4 g.) was heated at 120° in a rotating flask ; the evolution of hydrogen chloride was complete in less than 30 minutes. The homogeneous liquid was divided between two flasks in thermostats at 140° and 150°. From time to time, portions of the mixture were transferred to a weighed flask and dissolved in 75% acetic acid (33·33 c.c./g. of mixture). The clear solution (5 c.c.) was pipetted into a 100 c.c. flask, 75% acetic acid (10 c.c.), carbon tetrachloride (3 c.c.), N/10-bromate–bromide (2·0—2·5 c.c. excess), and dilute hydrochloric acid (5 c.c.) added, and the mixture shaken for 3 minutes. Potassium iodide was added, followed, after 1 minute, by N/10-thiosulphate until the end-point was nearly reached ; the flask was then almost filled with water, starch solution added, and the titration completed.

Temperature = 140°.

Time, hours.	Mixture, g.	Dilution, 75% AcOH, c.c.	0·1N-Bromate, c.c.	*k*.
0	1·167	38·90	10·50	—
0·5	0·972	32·40	9·70	0·173
1·0	0·546	18·20	9·03	0·177
1·5	0·694	23·13	8·50	0·179
2·0	0·636	21·20	8·07	0·179
2·5	0·793	26·43	7·73	0·177
3·5	0·523	17·43	7·15	0·179
5·5	0·643	21·43	6·50	0·173
10·5	0·588	19·60	5·68	0·179
∞	—	—	5·25	—
				Mean 0·177

$$k = \frac{1}{t - t_0} \ln \frac{T_t(T_0 - T_\infty)}{T_0(T_t - T_\infty)}.$$

The velocity constants tabulated on p. 273 were similarly obtained.

Isomerisation of 6-*hydroxy*-2 : 4- *in presence of* 6-*hydroxy*-3 : 4-*dimethyl-acetophenone.* A mixture of *m*-5- and *o*-4-xylenyl acetates (5·1 g. of each), aluminium chloride (25·2 g.), and sodium chloride (2·4 g.) gave $k_{150^\circ} = 0·354$, the hydroxy-ketones being assumed to use up 1 and 2 mols. of reagent respectively.

iso-*ψ-Cumenyl Acetate and Aluminium Chloride.*—The Fries rearrangement with 1 mol. of reagent gave a product, m. p. 46°, which isomerised to 6-hydroxy-3 : 4 : 5-trimethylacetophenone, m. p. 42° (Auwers, Bundesmann, and Weiners, *loc. cit.*, give m. p. 42°), when heated with 2 mols. of reagent. A mixture of the two products showed a marked depression of m. p.

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