587. *The Fries Rearrangement. Part III.* Mechanism of the* ortho-*Migration.*

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Formation of 2-hydroxy-5-methylacetophenone from *p*-tolyl acetate by titanic chloride in nitrobenzene proceeds by way of a complex which decomposes by (*a*) an intramolecular transposition and (*b*) scission into an acyl and a phenolic component which then condense (cf. *o*-tolyl acetate [1]).

The *ortho*-rearrangement of *p*-tolyl acetate, catalysed by titanium tetrachloride, gave yields of up to 90% of 2-hydroxy-5-methylacetophenone; in addition *p*-cresol was obtained and in some experiments some of the original ester was recovered; all the products have been determined quantitatively. The reaction is slower than the *para*-migration observed for *o*-tolyl acetate [1] but it follows a similar pattern.

These experiments were carried out in homogeneous nitrobenzene solution; other solvents were found in general to be less effective, in the order nitrobenzene > ethylene dichloride > *s*-tetrachloroethane > chlorobenzene > benzene.

Illari [2] claimed that the course of the Fries rearrangement depends upon the proportion of catalyst employed, but in our work this was not so. Thus the rate of decomposition of the ester was the same for 2 and 3 mols. of titanic chloride (Table 1); a bimolecular reaction between the acetate and catalyst would have required that its rate should increase with a larger proportion of catalyst. We therefore conclude that the ester and titanic halide combine irreversively as soon as they are brought together and that the rate of decomposition of this complex is being measured.

Table 1.

Effect of temperature on velocity constant, k (10^{-5} sec.$^{-1}$)

Temp.	40°	50°	60°	*E* (kcal.)
Initial slope	3·79	9·26	22·6	18·4
Three-quarter life	3·77	9·14	21·6	19·2
Half life	3·38	8·33	20·9	18·4
First-order plot	—	9·14	21·8	18·8

Effect of volume of solvent at 60° *on velocity constant, k* (10^{-5} sec.$^{-1}$).

Nitrobenzene	100 c.c.	150 c.c.	200 c.c.
Initial slope	22·6	22·2	21·6
Three-quarter life	21·6	21·7	21·2
Half life	20·9	19·2	18·7
First-order plot	21·8	20·9	20·0

Effect of catalyst : ester ratio at 60° *on velocity constant, k* (10^{-5} *sec.*$^{-1}$).

Titanic chloride (molar ratio)	1	2	3
Initial slope	5·2	21·6	23·0
Three-quarter life	5·3	21·2	21·9
Half life	5·3	18·7	20·2
First-order plot	5·5	20·0	20·9

The curves showing the rate of disappearance of the ester were analysed by the method of initial slopes, and of three-quarter and half life, *i.e.*, when the concentration of ester had fallen to three-quarters and half respectively. The first-order plots approximated closely to straight lines while the second-order plots were markedly curved; hence the decomposition of *p*-tolyl acetate is a first-order process. From the rate constants the activation

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* Previous papers (*J.*, 1955, 3894; 1956, 2222) are regarded as Parts I and II.

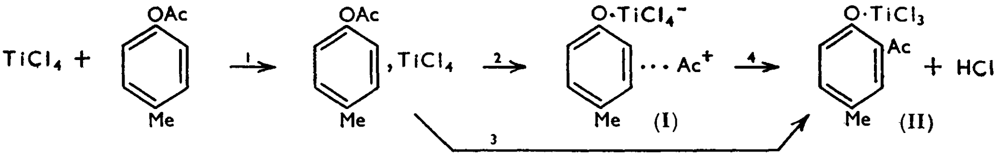
[1] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.

[2] Illari, *Gazzetta*, 1947, **77**, 339.

energy was evaluated (Table 1). This applies to the overall reaction, *i.e.*, the rearrangement of the ester by the two processes referred to below. The values for the separate reactions are also shown below.

The initial rates of formation of the hydroxy-ketone and cresol increased with the temperature, the former more rapidly, but the maximum yields were unaffected. As the cresol was formed at a finite rate at zero time it must have come directly from the ester complex by a first-order process. Since the curve exhibited a maximum the cresol must have undergone further change; the concentration of the hydroxy-ketone continued to rise in the region where the cresol concentration was still decreasing, and even after all the ester had disappeared.

Reaction 3 is required to account for the fact that the hydroxy-ketone was formed at a finite rate at zero time by the intramolecular rearrangement of the ester complex, this being confirmed by the fact that a 2-fold increase in the volume of solvent scarcely affected the rate of formation of the ketone (Table 1). As this was produced by the two reactions 3 and 4, *i.e.*, direct intramolecular migration and synthesis from the products of ester fission, each must be a first-order process. The latter can best be interpreted by assigning an ion-pair structure to these products (I) (this holds also for the *para*-isomerisation of *o*-tolyl acetate [1]). Reaction 3 is shown as irreversible for the overall reaction will only obey first-order kinetics if the reverse process is zero or negligible.



The fact that the maximum reaction rate is observed when the catalyst : ester molar ratio is 2 can be accounted for if we regard the product (II) as capable, like other ketones, of forming a complex with a further molecule of titanic chloride.

The effect of temperature on the velocity constants (k) and activation energies (E) of reactions 2, 3, and 4 is shown below. From the kinetics of the reaction the following equations can be derived:

$$-\mathrm{dA}/\mathrm{d}t = (k_2 + k_3)\mathrm{A} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (a)$$

$$\mathrm{dK}/\mathrm{d}t = k_3\mathrm{A} + k_4\mathrm{C} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (b)$$

$$\mathrm{dC}/\mathrm{d}t = k_2\mathrm{A} - k_4\mathrm{C} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (c)$$

Hence

$$-\mathrm{dA}/\mathrm{d}t = \mathrm{dK}/\mathrm{d}t + \mathrm{dC}/\mathrm{d}t \quad . \; . \; . \; . \; . \; . \; . \quad (d)$$

where A is the concentration of the *p*-tolyl acetate complex, C that of the fission products (I), and K that of the ketone (II). The sum of the constants ($k_2 + k_3$) is calculated from the plot of log mole % of ester against time. The constant k_3 is evaluated from the initial slope of the hydroxy-ketone curve; subtraction of k_3 from the above value of ($k_2 + k_3$) gives k_2; k_4 is obtained from eqn. (*b*) by using the above value of k_3, and from the slope of the hydroxy-ketone curve at a time when the concentration of ester has fallen to half. The constants together with the corresponding activation energies are listed below (k_2, k_3, and k_4 and E_2, E_3, and E_4 refer to reactions 2, 3, and 4 respectively).

Temp.	k_2	k_3 (10⁻⁵ sec.⁻¹)	k_4
40°	2·15	1·64	3·01
50	4·57	4·69	9·59
60	13·70	8·89	20·60

E_2 is 25·9, E_3 15·4, and E_4 18·4 kcal./mole.

The accuracy of the relation (*d*) is indicated in Table 2 for (*a*) 25% and (*b*) 50% decomposition of the ester complex, the slopes being expressed as mole change per second A = concn. of ester complex).

TABLE 2.

Temp.	-10^5 dA/d*t*	10^5 dC/d*t*	10^5 dK/d*t*	10^5 (dK/d*t* + dC/d*t*)
(*a*) 40°	2·99	1·04	1·42	2·46
50	6·86	2·08	4·35	6·43
60	16·20	6·67	7·78	14·50
(*b*) 40	1·69	0·22	1·30	1·55
50	4·17	0·60	3·98	4·58
60	10·50	3·47	7·33	10·80

EXPERIMENTAL

The materials were purified by standard methods.

Rearrangement of p-*Tolyl Acetate.*—The ester and nitrobenzene were introduced into the reaction vessel at 0°; titanic chloride was added during *ca.* 1 min. with continuous stirring, which was maintained throughout the experiment. The colour of the solution changed from pale yellow to reddish-brown. After the requisite time the product was cooled in ice and decomposed with 6N-hydrochloric acid. From the solvent layer 2N-sodium hydroxide took up the *p*-hydroxy-ketone and *p*-cresol, leaving the ester. Distillation removed traces of solvent from the alkaline extract which was then acidified with concentrated hydrochloric acid and kept cold for 12 hr.; 2-hydroxy-5-methylacetophenone separated in needles, which were dried to constant weight. Recrystallisation from ligroin gave m. p. 50°, in agreement with Rosenmund and Schnurr.[3] The small quantity of hydroxy-ketone remaining in solution was estimated by precipitation of an aliquot portion with 2 : 4-dinitrophenylhydrazine. After 12 hr. the *hydrazone* was dried at 110°. Recrystallised from benzene it yielded bright red prisms, m. p. 271° (Found: C, 54·8; H, 4·2; N, 17·2. $C_{15}H_{14}O_5N_4$ requires C, 54·6; H, 4·2; N, 17·0%). In another aliquot part *p*-cresol was analysed as follows : To 50 c.c. a large excess of concentrated hydrochloric acid was added and a standard solution containing potassium bromate (10 g./l.) and potassium bromide (25 g./l.) was run in at once until the liquid became yellow (a white turbidity due to bromocresol was also observed). Excess of a 10% solution of potassium iodide was then added and the liberated iodine titrated against standard sodium thiosulphate. Control experiments showed the results to be 3% too high. The very small amount of hydroxy-ketone present scarcely affected the accuracy. The organic layer was boiled under reflux for 4 hr. with 2N-sodium hydroxide (200 c.c.), the nitrobenzene distilled off in steam, and the residual liquor made acid with concentrated hydrochloric acid and again distilled with steam. The *p*-cresol thus formed by the hydrolysis of the original ester was analysed as described above. The residue from the steam-distillation contained a small quantity of resin which was taken up in acetone and weighed.

Effect of Temperature.—The components were *p*-tolyl acetate (0·1 mole), titanic chloride (0·2 mole), and nitrobenzene (100 c.c.) and the reactions were studied at 40°, 50°, and 60°. At 40° 11% of the ester remained after 17 hr.; the yield of cresol reached a maximum (17%) in 5½ hr., falling gradually to 9%. A 74% yield of *o*-hydroxy-ketone was obtained in 17 hr. At 50° the rate of decomposition of the ester was more rapid and it disappeared completely in 11 hr. Both the cresol and the hydroxy-ketone were formed more rapidly than at 40°, the yield of the former reaching a maximum of 14% in 2½ hr., falling afterwards to 3%, and of the latter being 92% in 13 hr. At 60° the reaction was still more rapid, the ester reacting completely in 6 hr., when the yield of ketone had become 88%.

Effect of Volume of Solvent.—The reaction between *p*-tolyl acetate (0·1 mole) and titanium tetrachloride (0·2 mole) in (*a*) 100 c.c., (*b*) 150 c.c., and (*c*) 200 c.c. of nitrobenzene was investigated at 60°. Very little difference was noted, the acetate disappearing completely in 6 hr., when the yield of the hydroxy-ketone had reached a maximum value of 90%. The yield of *p*-cresol rose to *ca.* 15—20%, subsequently falling to *ca.* 4%.

Effect of Catalyst : Ester Ratio.—*p*-Tolyl acetate (0·1 mole) in nitrobenzene (200 c.c.) was treated at 60° with (*a*) 0·1 mole, (*b*) 0·2 mole, and (*c*) 0·3 mole of titanic chloride. In (*a*), some ester (2·5%) remained after 13 hr., when an 85% yield of the hydroxy-ketone had been obtained.

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[3] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56.

The yield of the cresol reached a maximum of 13% in 4½ hr., with a gradual fall to 5% after 13 hr. In (*b*), the rate of disappearance of the acetate was higher and none remained after 6 hr., 2-hydroxy-5-methylacetophenone (88%) being formed in this time. The highest yield of the cresol (15%) was attained in 1 hr.; it fell to 5% in 6 hr. In (*c*) the reaction was almost identical with that in (*b*).

We thank Peter Spence and Sons Ltd. for a gift of titanium tetrachloride; one of us (B. F. R. E.) thanks the University of Wales for the award of a Post-graduate Studentship.

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