464. *Fries Reaction. Part II.* Effect of Hydrogen Chloride on the Isomerisation of Thymyl Acetate.*

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The rate of isomerisation of thymyl acetate to acetylthymol in the presence of anhydrous aluminium chloride and hydrogen chloride in homogeneous nitrobenzene solution increased with temperature, with the catalyst : ester ratio, and with the amount of hydrogen chloride present. The overall order of the reaction is ~2. It seems probable that hydrogen chloride exerts its effect partly by increasing the polarity of the solution, and partly by releasing the catalyst from its compounds, but it may have other effects, for the rate of the Fries migration increases in its presence even when aluminium chloride is present in excess. The present study indicates that hydrogen chloride may accelerate the rearrangement also by addition of a proton to the rearranging ester–aluminium chloride complex.

Pressure had but little effect on the isomerisation.

Unlike hydrogen fluoride, hydrogen chloride above does not catalyse the Fries rearrangement.
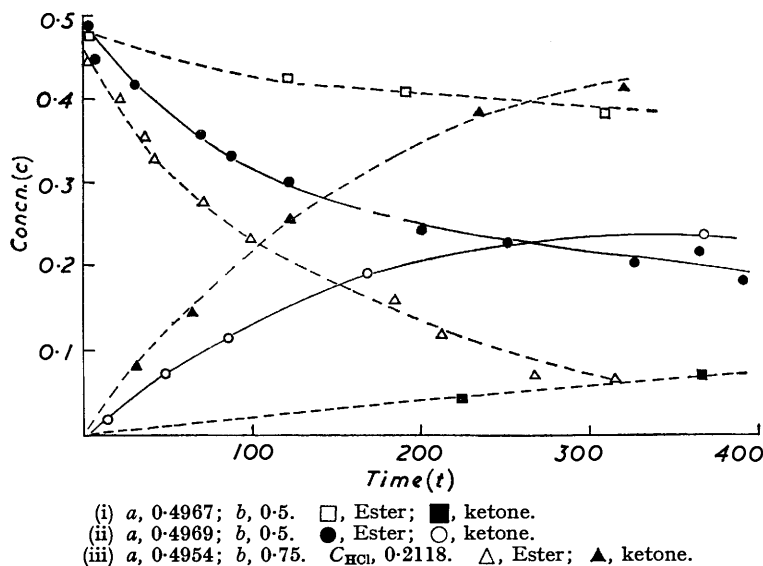
FOR many of the processes catalysed by aluminium chloride it is well known that the reactions are accelerated by the presence of hydrogen chloride, while catalysts free from

* Part I, preceding paper.

hydrogen chloride are less effective.[1,2,3] Thomas and his co-workers[3] endeavoured to explain this phenomenon by proton-catalysis. Until recently, no studies on this affect in the Fries reaction had been reported, though Skraup and Poller[4] opined that, at room temperature, *m*-tolyl acetate is rearranged only in the presence of hydrogen chloride, but their suggested mechanism does not account for this fact, and the observation was not confirmed by Baltzly *et al.*[5] Mechanisms proposed for the Fries reaction generally do not explain the rôle of hydrogen chloride: Amin and Shah[6] assumed proton-catalysis, but did not propose a mechanism.

It has been observed by Gerecs and his co-workers,[7,8] for several esters, that *para*-isomerisation is accelerated by the presence of hydrogen chloride, but when it is removed (*i.e., in vacuo*) or when substances reacting with it or hindering its dissociation (*e.g.*, NH_3, C_5H_5N, C_5H_5N,HCl, NaCl) are added together with aluminium chloride in equivalent amounts to the usual mixtures for Fries reactions, the *para*-shift is impeded. It has been demonstrated that this decelerating action is due to decrease of the proton concentration.

FIG. 1. *Effect of hydrogen chloride on disappearance of ester and on formation of ketone at 40°.*

(i) *a*, 0·4967; *b*, 0·5. □, Ester; ■, ketone.
(ii) *a*, 0·4969; *b*, 0·5. ●, Ester; ○, ketone.
(iii) *a*, 0·4954; *b*, 0·75. C_{HCl}, 0·2118. △, Ester; ▲, ketone.

It was assumed, therefore, by Gerecs *et al.* that the ester forms a proton-containing inter-mediate complex, which, when sufficiently polarised, becomes capable of acylating another molecule, but when relatively stable it is rearranged by an intramolecular process. It has been supposed that, in the latter case, the ether-oxygen of the ester must be a stronger proton-acceptor. Both of these processes yield hydroxy-ketone and proton.

The present work gives further results bearing on the rôle of hydrogen chloride in the Fries reaction.

General Considerations.—Theoretically, hydrogen chloride may exert its action in two ways: it can create more favourable conditions for some ionic process by increasing the

[1] Ipatieff and Grosse, *Ind. Eng. Chem.*, 1936, **28**, 461.
[2] Groggins, " Unit Processes in Organic Synthesis," 4th edtn., McGraw-Hill Publ. Co. Ltd., 1952, London.
[3] Thomas, " Anhydrous Aluminium Chloride in Organic Chemistry," Reinhold Publ. Corp., 1941, New York.
[4] Skraup and Poller, *Ber.*, 1924, **57**, 2033.
[5] Baltzly, Ide, and Phillips, *J. Amer. Chem. Soc.*, 1955, **77**, 2522.
[6] Amin and Shah, *J. Univ. Bombay*, 1948, **17**, *A*, 1.
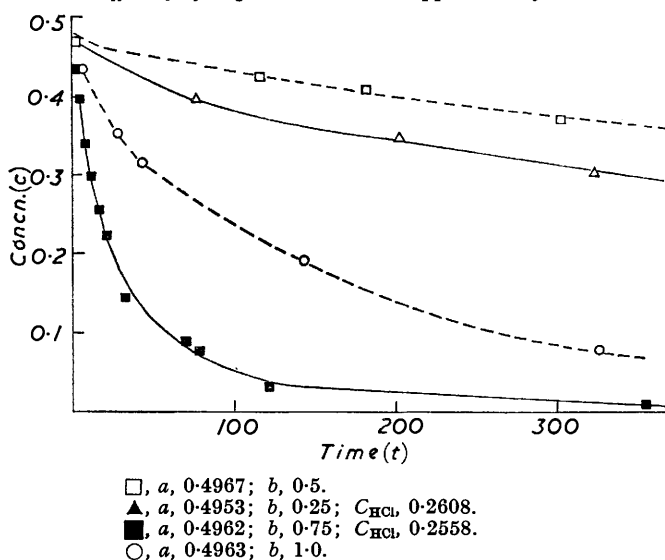[7] Gerecs, Széll, and Windholz, *Acta Chim. Acad. Sci. Hung.*, 1953, **3**, 459 (*Chem. Abs.*, 1955, 2361b).
[8] Gerecs and Windholz, *Naturwiss.*, 1955, **24**b, 414.

polarity of the medium, or it may play a direct part in the Fries reaction. Several results [5,9,10,11] indicate that the rate of formation of *para*-hydroxy-ketones is increased in solvents of higher dipole moment; it is therefore reasonable to suppose that hydrogen chloride exerts its effect, at least in part, by increasing the polarity of the medium. (We propose to determine the dielectric constants of the relevant media.)

We have therefore tried to test by kinetic methods the assumption that hydrogen chloride participates in the reaction. For this purpose the rearrangement of thymyl acetate to acetylthymol in the presence of aluminium chloride and hydrogen chloride in homogeneous nitrobenzene solution was investigated.

FIG. 2. *Effect of hydrogen chloride on disappearance of ester at 40°.*

□, a, 0·4967; b, 0·5.
▲, a, 0·4953; b, 0·25; C_{HCl}, 0·2608.
■, a, 0·4962; b, 0·75; C_{HCl}, 0·2558.
○, a, 0·4963; b, 1·0.

Results and Discussion.—The progress of the rearrangement of 0·5 mole l.$^{-1}$ of thymyl acetate was studied at different concentrations of hydrogen chloride (0·1—0·25M) and of catalyst (0·25, 0·5, 0·75, and 1·0M) and at temperatures of 33°, 40°, and 47°. The concentration of hydrogen chloride was varied within relatively narrow limits because its solubility is limited under the experimental conditions (see Table 2).

It was found that hydrogen chloride has a marked positive effect on both the rate of

TABLE 1. *Values of* 10^2k (min.$^{-1}$) *and* 10^2k (l. mole^{-1} min.$^{-1}$).

	$\tau/4$			$\tau/2$			Fig. 7			Average		
Calc. from	33°	40°	47°	33°	40°	47°	33°	40°	47°	33°	40°	47°
For 1st order ...	2·3	3·4	5·8	1·6	2·2	4·1	—	—	—	1·95	2·8	4·95
For 2nd order ...	5·6	8·2	13·9	5·0	7·4	13·3	4·6	7·2	15·2	5·05	7·7	14·15

disappearance of ester and the rate of formation of ketone (see Figs. 1 and 2).* It is seen that the normal reaction is generally more accelerated by addition of hydrogen chloride than by addition of further aluminium chloride in equivalent amount except at about a catalyst to ester ratio of 1·0—1·3, in which region the accelerating effect of aluminium chloride increases suddenly.[12]

We observed that the ester remains unchanged even during a prolonged period (1000

* The broken lines of Fig. 2 are taken from Part I for comparison. For symbolism, see Part I.
[9] Ralston, McCorkle, and Bauer, *J. Org. Chem.*, 1940, **5**, 645.
[10] Marey, Baddar, and Awad, *Nature*, 1953, **172**, 1186.
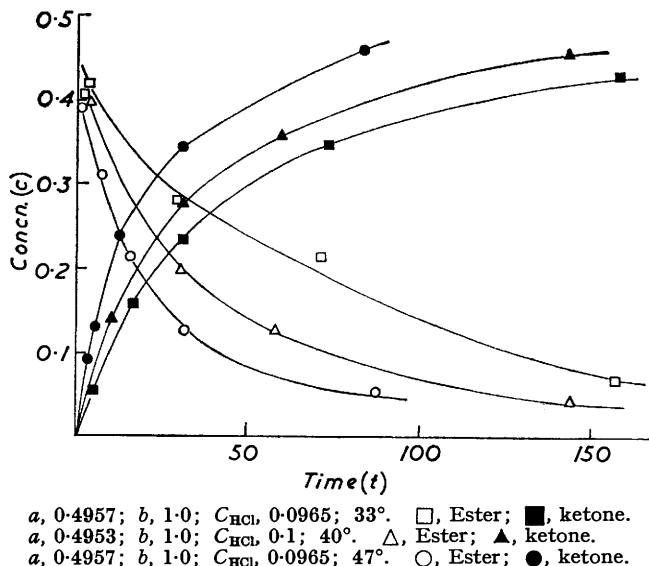[11] Cullinane and Edwards, *J.*, 1958, 2926.
[12] Furka and Széll, preceding paper.

TABLE 2. *Solubilities.*

Solvent: 100 g. of nitrobenzene (83·4 ml. at 25°).

AlCl₃ (mole)	Thymyl acetate (mole)	HCl-content of the saturated HCl–nitrobenzene solution (mole/100 g. of nitrobenzene)			
		10°	30°	50°	70°
—	—	0·0819	0·0672	0·0459	0·0278
—	0·09085	—	0·0895	0·0547	0·0348
0·1065	—	0·0934	0·0841	0·0685	0·0420
0·1180	0·0930	0·1400	0·1100	0·0850	0·0584

min.) when only hydrogen chloride was substituted for all the aluminium chloride, so hydrogen chloride alone, unlike hydrogen fluoride,[13,14] does not catalyse the isomerisation.

Results of reactions carried out at 33°, 40°, and 47° for a catalyst-ester ratio of 2 : 1 are summarised in Fig. 3. Second-order constants obtained at different temperatures by

FIG. 3. *Effect of temperature on disappearance of ester.*

a, 0·4957; b, 1·0; C_{HCl}, 0·0965; 33°. □, Ester; ■, ketone.
a, 0·4953; b, 1·0; C_{HCl}, 0·1; 40°. △, Ester; ▲, ketone.
a, 0·4957; b, 1·0; C_{HCl}, 0·0965; 47°. ○, Ester; ●, ketone.

alternative methods show a closer agreement than those of first order (Table 1). At given catalyst concentration the rate of formation of ketone depends on both the ester and the hydrogen chloride concentrations (Fig. 4).

In Fig. 5 the logarithm of the reaction rate is plotted against that of the initial hydrogen chloride concentration. For hydrogen chloride the partial order calculated from the slope of the straight line is 0·98. For the overall order of the reaction, application of van't Hoff's differential method to a single reaction (Fig. 6) gave values of 1·8 at 33° and 40° and 1·9 at 47°. From the above results, the reaction may be considered to be of roughly second order for formation of ketone. The first stage of the reaction, as well as plots for higher temperature, show a much closer approximation. These findings may be partly ascribed to the fact that hydrogen chloride, which appears to participate in the reaction, is present in lower concentration than the ester, and is only partly liberated again in the course of the reaction. Towards the end of the reaction, therefore, an approach to first order can be observed. The problem is further complicated by the fact that, inasmuch as the Fries reaction in the presence of hydrogen chloride should be regarded as a separate process, two competing isomerisations of comparable rates must be running, of which that in absence of hydrogen chloride is of first order.[12]

[13] Simons, Archer, and Randall, *J. Amer. Chem. Soc.*, 1940, **62**, 485.
[14] Dann and Mylius, *Annalen*, 1954, **587**, 1.

It has been suggested that the action of hydrogen chloride—in part at least—may consist in liberating the catalyst from its combination in some intermediate or end-

FIG. 4. *Dependence of the rate of formation of ketone on the initial concentration of hydrogen chloride at 40°.*
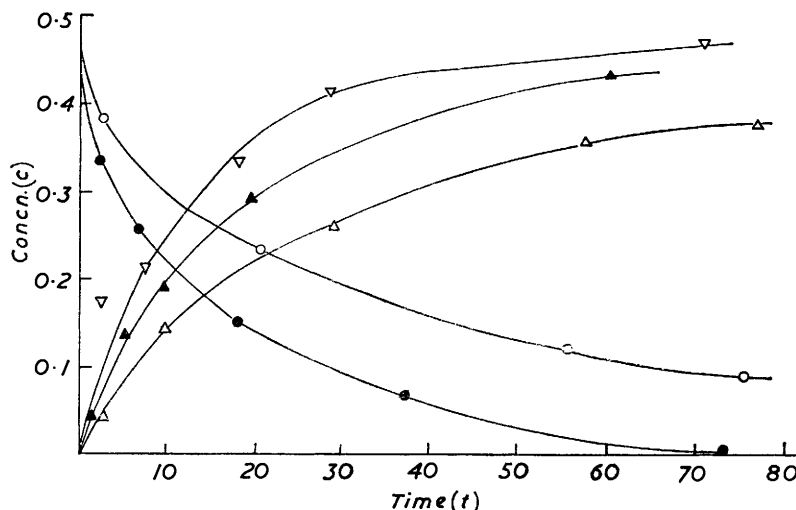
(i)   *a*, 0·4960; *b*, 1·0; C_{HCl}, 0·2418. $\triangledown$, Ketone.
(ii) *a*, 0·4953; *b*, 1·0; C_{HCl}, 0·10. $\bigcirc$, Ester; $\triangle$, ketone.
(iii) *a*, 0·4964; *b*, 1·0; C_{HCl}, 0·2418. $\bullet$, Ester.
(iv) *a*, 0·4962; *b*, 1·0; C_{HCl}, 0·2118. $\blacktriangle$, Ketone.

FIG. 5. *Dependence of the rate of formation of ketone on the initial concentration of hydrogen chloride.*
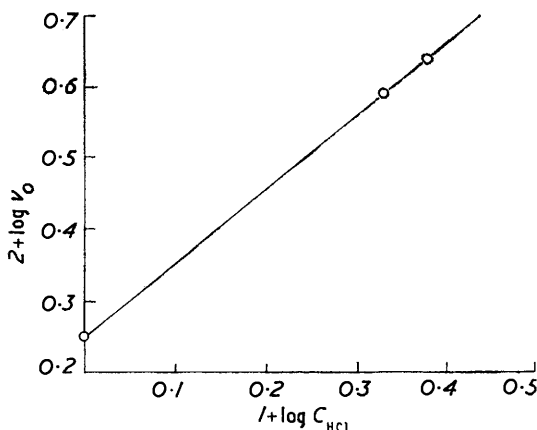
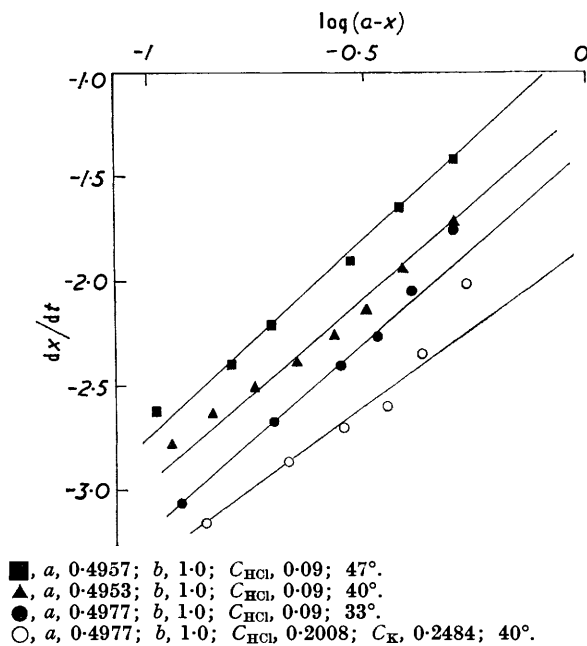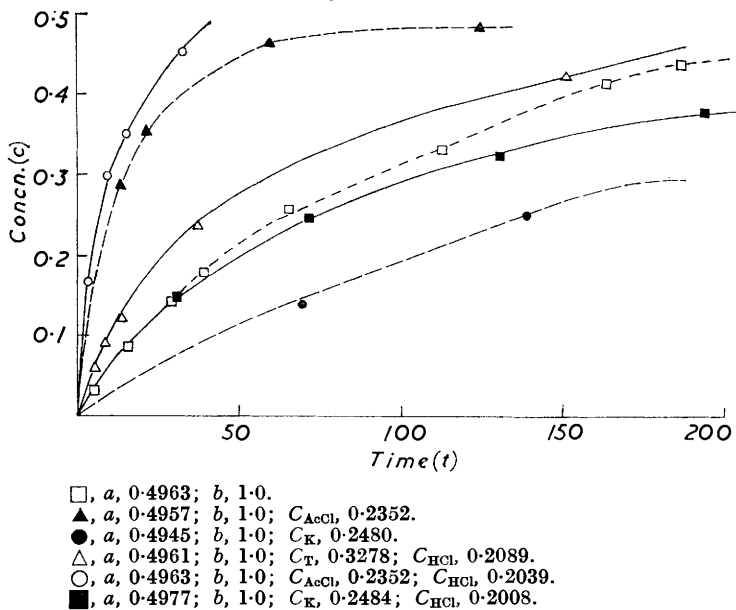*a*, 0·50; *b*, 1·0; C_{HCl} = 0·1000, 0·2118, and 0·2418.

product,* and our results do not seem inconsistent with this supposition, for it was found [12]

* There is reason to believe that, in systems such as those in Fries reactions, several types of aluminium compound occur in various amounts. Some authors [4,5,15,16] assumed that a compound of the type $ArO \cdot AlCl_2$ exists in such systems, which, in addition to acyl chloride, might be in equilibrium with the ester, and, in addition to hydrogen chloride, with the free hydroxy-compound and the catalyst.[7,17] Baltzly *et al.*[5] assumed the presence also of compounds of the type of $Cl_3AlO(H)Ar$ and $Cl_2AlOAr \cdot COR$. It is conceivable that an equilibrium established between hydrogen chloride and some such species may result in the increase of concentration, not only of the catalyst, but also of the more reactive species.

[15] Ralston, McCorkle, and Segebrecht, *J. Org. Chem.*, 1941, **6**, 750.
[16] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.
[17] Gerecs, *Magyar Tud. Akad. Kémiai Tudományok Osztály Közleményei*, 1953, **3**, 78.

FIG. 6. *van't Hoff's differential method applied to reactions carried out at different temperatures.*

■, *a*, 0·4957; *b*, 1·0; C_{HCl}, 0·09; 47°.
▲, *a*, 0·4953; *b*, 1·0; C_{HCl}, 0·09; 40°.
●, *a*, 0·4977; *b*, 1·0; C_{HCl}, 0·09; 33°.
○, *a*, 0·4977; *b*, 1·0; C_{HCl}, 0·2008; C_{K}, 0·2484; 40°.

FIG. 7. *Effect of thymol, acetylthymol, and acetyl chloride on the formation of this ketone in presence and in absence of hydrogen chloride at 40°.*

□, *a*, 0·4963; *b*, 1·0.
▲, *a*, 0·4957; *b*, 1·0; C_{AcCl}, 0·2352.
●, *a*, 0·4945; *b*, 1·0; C_{K}, 0·2480.
△, *a*, 0·4961; *b*, 1·0; C_{T}, 0·3278; C_{HCl}, 0·2089.
○, *a*, 0·4963; *b*, 1·0; C_{AcCl}, 0·2352; C_{HCl}, 0·2039.
■, *a*, 0·4977; *b*, 1·0; C_{K}, 0·2484; C_{HCl}, 0·2008.

that the rearrangement of thymyl acetate is considerably retarded in the presence of acetylthymol or thymol. When this rearrangement takes place in the presence of hydrogen chloride in amount equivalent to the above substances, however, they do not exert this

FIG. 8. *Effect of acetylthymol on the disappearance of ester in presence and in absence of hydrogen chloride at 40°.*
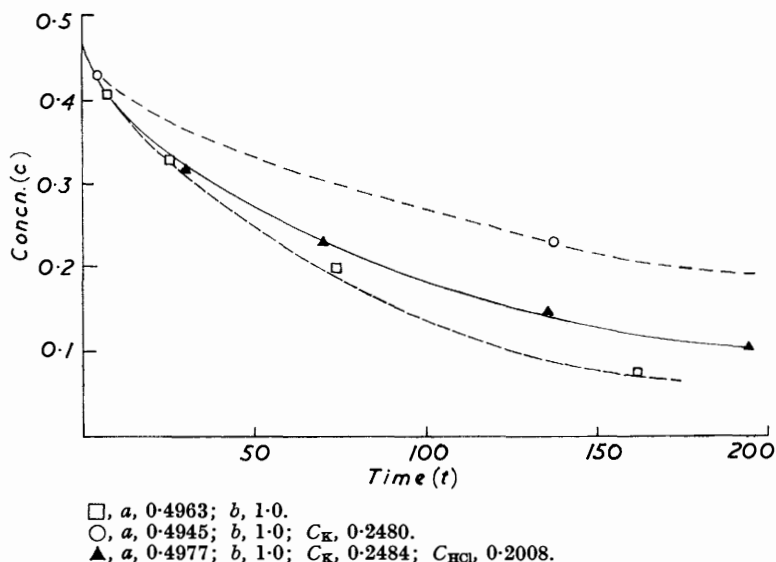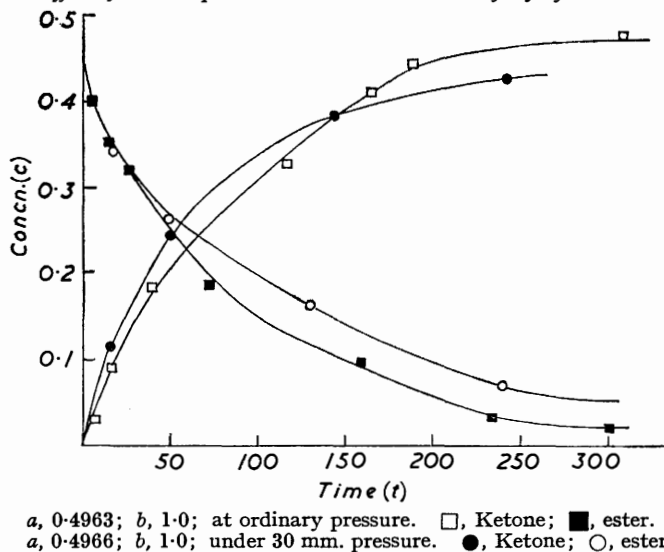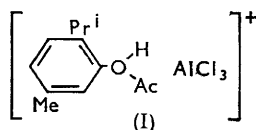

□, a, 0·4963; b, 1·0.
○, a, 0·4945; b, 1·0; C_K, 0·2480.
▲, a, 0·4977; b, 1·0; C_K, 0·2484; C_{HCl}, 0·2008.

FIG. 9. *Effect of reduced pressure on the isomerisation of thymyl acetate at 40°.*

a, 0·4963; b, 1·0; at ordinary pressure. □, Ketone; ■, ester.
a, 0·4966; b, 1·0; under 30 mm. pressure. ●, Ketone; ○, ester.

decelerating action, and at the same time no accelerating effect of hydrogen chloride is to be observed (Figs. 7 and 8 *).

* Fig. 7 also serves to demonstrate that under conditions when acetyl chloride is present, hydrogen chloride is still able to exert further accelerating influence.

Undoubtedly, however, hydrogen chloride does not only operate by increasing the concentration of the catalyst, because it has also a distinct effect, when aluminium chloride is present in great excess,[7] and our results are not inconsistent with this hypothesis, according to which the proton of hydrogen chloride can be partly added to the intermediate ester–aluminium chloride complex to give the protonated derivative (I); consequently, hydrogen chloride participates also in this way in the Fries reaction. In this case, this bimolecular reaction would be the rate-determining step.

Results of measurements contained in Table 2, which show that, according to the temperature, additional quantities of 0·54—0·19 mole l.$^{-1}$ of hydrogen chloride may be dissolved if the nitrobenzene contains both aluminium chloride and ester, are consistent with the above conception. (Note that Table 2 records moles per 100 g. of nitrobenzene, not moles per l.) Similarly, it may be in accord with our explanation that both hydrogen fluoride [13,14] (a recognised proton-donor) and catalysts promoting the formation of the hydrogen halides [18] are effective in the Fries reaction.

Contrary to reports on similar reactions,[7] the Fries migration of thymyl acetate does not become slower in a vacuum (Fig. 9), so we assume that decrease of pressure hinders only those *para*-shifts in which hydrogen chloride is formed (evolution of hydrogen chloride sometimes occurs in Fries reactions).

EXPERIMENTAL

Materials.—Solutions of hydrogen chloride in nitrobenzene were prepared by saturating the redistilled solvent at room temperature with the gas dried over phosphoric oxide; the hydrogen chloride content, as determined by alkalimetry in ethanol, varied between 0·47 and 0·70 mole l.$^{-1}$. Thymyl acetate and other materials were as described in the preceding paper.

Rearrangement of Thymyl Acetate.—Anhydrous aluminium chloride (B.D.H. and V.E.B. Feinchemie " for synth.") was dissolved in a known volume of the nitrobenzene containing hydrogen chloride, diluted as required with nitrobenzene, and placed in a thermostat ($\pm 0\cdot1°$), and after 20 min. (zero time) the solution was poured into a wide-necked, glass-stoppered, 25 ml. flask containing a weighed quantity of thymyl acetate, and the flask was filled to the mark.

Kinetic Measurements.—The progress of the reaction was followed by removing 2 ml. samples of the above mixture and analysing them as in the preceding paper. Concentrations are given in mole l.$^{-1}$. The reaction at reduced pressure was carried out in an apparatus provided with a water pump and protected against moisture. When samples were being taken, dry air was passed through the vessel. The acetylthymol obtained had m. p. 122·2—125° (uncorrected).

Solubility of Hydrogen Chloride in Nitrobenzene–Aluminium Chloride–Thymyl Acetate at Different Temperatures.—Gaseous hydrogen chloride, dried as described above, was passed into 16·74 g. of nitrobenzene (13·97 ml. at 25°) at 10° until constant weight was attained, and the solution was placed in a water-bath at 10°, 30°, 50°, or 70° until the weight again became constant. The increases in weight were 0·50, 0·41, 0·28, and 0·17 g., respectively.

Similarly, the other solubilities recorded in Table 2 were determined. When nitrobenzene alone or nitrobenzene containing aluminium chloride was heated from 10° to 70° without having been saturated with hydrogen chloride, a loss of weight of not more than 0·04 g. was observed per 100 g.

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[18] Klosa, *Arch. Pharm.*, 1956, **289**, 71.