596. *The Fries Rearrangement. Part V.* Effect of the Ring Substituent and the Acyl Group.*

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Rearrangements of phenyl, *o*-, *m*-, and *p*-tolyl acetate and benzoate were examined at high temperature in the absence of solvent, and at low temperature in solution. With the phenyl and *o*- and *m*-tolyl esters both *ortho*- and *para*-substitution took place, the benzoates giving a higher *para* : *ortho* ratio than the acetates. The *p*-tolyl esters underwent an *ortho*-shift only, and in the reactions in solution titanic chloride was a more active catalyst than aluminium chloride. Reactions in nitrobenzene were faster and gave a higher proportion of *p*-hydroxy-ketones than did the corresponding reactions in ethylene dichloride.

Phenyl acetate, propionate, *n*-butyrate, *iso*butyrate, and octanoate yielded mainly *para*-substituted products, the proportion of the *ortho*-isomer increasing with the size of the acyl group and with the branching of the chain.

The position of an alkyl group substituted in the ring has a considerable influence on the proportion of *o*- and *p*-hydroxy-ketones formed in the Fries rearrangement of phenol esters. The results of earlier work,[1] carried out mainly with aluminium chloride as catalyst, are not readily comparable since the experimental conditions varied widely, but it has been found in general that *o*-tolyl esters yield predominantly *p*-, and *m*-tolyl esters *o*-hydroxy-ketones, while *p*-tolyl esters give exclusively *o*-hydroxy-ketones.

In the present work phenyl, *o*-, *m*-, and *p*-tolyl acetate and benzoate were treated with aluminium chloride and titanic chloride (*a*) at high temperature in the absence of solvent and (*b*) at low temperature in homogeneous solution. In the high-temperature experiments considerable decomposition occurred with titanic chloride, especially in the transformation of acetates, and with both sets of esters this catalyst was less active than aluminium chloride. In general, the isomerisation of benzoates was the slower reaction and also less *ortho*-shift took place. Production of varying amounts of the phenol was observed in all the reactions studied. The products of the low-temperature experiments, where nitrobenzene and ethylene dichloride were the solvents, were determined quantitatively; it was found that more *ortho*-substituted ketone was obtained in the titanic chloride-catalysed migrations.

The phenyl esters gave both *o*- and *p*-hydroxy-ketones, chiefly the latter, especially in the benzoate rearrangements. *o*-Tolyl acetate underwent chiefly a *para*-shift, although at the higher temperature the proportion of the *ortho*-product increased; no *ortho*-migration occurred with the benzoate. *m*-Tolyl acetate and benzoate yielded predominantly the *ortho*-isomers at high temperature. In the low-temperature reactions mainly *para*-substitution was observed in the benzoate transformation with both catalysts; the acetate afforded mainly the *ortho*-product with the titanic and the *para*-product with the aluminium halide under these conditions. Only *ortho*-shifts occurred in the transformation of the *p*-tolyl esters; for the reactions in solution titanic chloride was found to be the more active agent.

For the rearrangement of phenyl octanoate Ralston, McCorkle, and Bauer [2] observed a higher *para* : *ortho*-ratio of hydroxy-ketones in nitrobenzene than in *s*-tetrachloroethane. We found that the solvent had a marked effect on this ratio, as well as on the rate of reaction. Thus in the aluminium chloride-catalysed reactions *m*-tolyl acetate, dissolved in the more

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* Part IV, *J.*, 1958, 434.

[1] Cf. Blatt, *Org. Reactions*, 1942, **1**, p. 342.

[2] Ralston, McCorkle, and Bauer, *J. Org. Chem.*, 1940, **5**, 645.

polar nitrobenzene, underwent in the main *para*-substitution, but use of ethylene dichloride led mainly to *ortho*-substitution, the reaction being slower in the latter medium. Titanic chloride induced *ortho*-substitution mainly in nitrobenzene and a still greater *ortho*-shift in ethylene dichloride. In general, aluminium chloride was a more powerful catalyst than titanic chloride, and caused a greater amount of *para*-migration.

Rearrangement of acetates.

(a) *In the absence of solvent.* (b) *In nitrobenzene solution.*

		(a) Phenol	(a) Hydroxy-ketones			(b) Phenol	(b) Hydroxy-ketones			Ester recovd.
	Catalyst	(%)	*o* (%)	*p* (%)	*o*/*p*	(%)	*o* (%)	*p* (%)	*o*/*p*	(%)
Phenyl	$AlCl_3$	0·0	46·4	41·7	1·2	11·6	11·4	72·8	0·16	0·0
	$TiCl_4$	29·3	19·7	14·9	1·3	18·3	11·3	65·6	0·17	0·0
o-Tolyl	$AlCl_3$	0·0	24·1	61·3	0·4	0·0	4·1	81·8	0·05	0·0
	$TiCl_4$	20·0	9·7	12·1	0·8	0·0	7·3	74·5	0·10	0·0
m-Tolyl	$AlCl_3$	0·0	89·0	6·5	14·0	4·0	43·9	46·0	1·0	0·0
	$TiCl_4$	16·1	34·3	1·0	34·0	4·6	72·5	13·9	5·2	0·0
p-Tolyl	$AlCl_3$	6·4	91·5	—	—	12·6	74·0	—	—	12·1
	$TiCl_4$	27·8	61·4	—	—	4·0	84·4	—	—	0·9

Rearrangement of benzoates.

(c) *In the absence of solvent.*

Benzoate	Catalyst	Phenol (%)	Hydroxy-ketones *o* (%)	*p* (%)	*o*/*p*	Ester recovd. (%)	Benzoic acid (%)
Phenyl	$AlCl_3$	0·0	27·4	69·6	0·4	0·0	0·0
	$TiCl_4$	11·4	23·1	58·0	0·4	0·0	10·8
o-Tolyl	$AlCl_3$	3·0	0·0	86·3	—	0·0	2·5
	$TiCl_4$	11·8	0·0	69·2	—	0·0	11·6
m-Tolyl	$AlCl_3$	0·0	89·0	3·0	30·0	0·0	0·0
	$TiCl_4$	10·1	82·3	0·0	—	0·0	9·7
p-Tolyl	$AlCl_3$	4·6	88·1	—	—	0·0	4·0
	$TiCl_4$	1·4	78·0	—	—	0·0	0·0

(d) *In nitrobenzene solution.*

Benzoate	Catalyst	Phenol (%)	Hydroxy-ketones *o* (%)	*p* (%)	*o*/*p*	Ester recovd. (%)	Benzoic acid (%)
Phenyl	$AlCl_3$	5·1	8·9	80·5	0·11	0·0	4·9
	$TiCl_4$	3·9	7·4	83·7	0·09	0·0	4·0
o-Tolyl	$AlCl_3$	6·2	0·0	91·1	—	0·0	6·0
	$TiCl_4$	5·5	0·0	89·0	—	0·0	5·2
m-Tolyl	$AlCl_3$	6·9	14·9	67·7	0·22	0·0	6·6
	$TiCl_4$	19·6	27·0	48·0	0·56	0·0	19·1
p-Tolyl	$AlCl_3$	12·7	38·0	—	—	32·0	12·3
	$TiCl_4$	9·2	57·2	—	—	14·8	8·9

Rearrangement of m-*tolyl acetate.*

Solvent	Catalyst	*m*-Cresol (%)	Hydroxy-ketones *o* (%)	*p* (%)	*o*/*p*	Ester recovd. (%)
Nitrobenzene	$AlCl_3$	1·5	27·7	66·1	0·4	0·0
Ethylene dichloride	$AlCl_3$	4·1	42·1	24·9	1·7	9·8
Nitrobenzene	$TiCl_4$	12·7	55·1	20·2	2·8	6·4
Ethylene dichloride	$TiCl_4$	4·0	43·1	4·2	10·0	42·7

Rearrangement of phenyl esters.

Ester	Phenol (%)	Hydroxy-ketones *o* (%)	*p* (%)	*o*/*p*	Ester	Phenol (%)	Hydroxy-ketones *o* (%)	*p* (%)	*o*/*p*
Acetate	4·2	10·4	76·5	0·15	*iso*Butyrate	6·1	24·6	61·7	0·40
Propionate ...	4·1	16·2	72·4	0·22	Octanoate ...	7·2	29·8	55·5	0·54
n-Butyrate ...	6·8	17·8	72·0	0·25	*iso*Valerate	4·3	23·5	68·1	0·35

For the transformation of certain aliphatic esters of *m*-cresol Coulthard, Marshall, and Pyman [3] stated that the length of the acyl chain had little effect on the *ortho* : *para* ratio

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[3] Coulthard, Marshall, and Pyman, *J.*, 1930, 280.

of products. Baltzly and Bass [4] obtained similar results except that the acetate gave a considerable yield of the *ortho*-isomer. For the phenol series Baltzly, Ide, and Phillips [5] observed that the butyl gave a higher proportion of the *o*-hydroxy-ketone than did the propyl ester, while in his study of 1-naphthyl esters Stoughton [6] reported that the amount of *ortho*-rearrangement decreased in the order acetate, propionate, butyrate, valerate.

While the above results are not strictly comparable, since the experimental conditions varied somewhat, in our experiments with phenyl esters in nitrobenzene solution, catalysed by aluminium chloride, a quantitative study has been made, all products including phenol being accounted for. We have found that the acetate, propionate, *n*-butyrate, and octanoate give chiefly *para*-substitution, but the proportion of *para* decreases and *ortho* increases with the size of the acyl group. We have also observed that replacement of *n*-butyl by *iso*butyl results in an increase in the *ortho* : *para* ratio.

EXPERIMENTAL

Materials.—The esters were dried and fractionally distilled. Phenyl propionate had b. p. 211°, *n*-butyrate 227°, *iso*butyrate 211°, *iso*valerate 235—236°, octanoate 293—294°. The ethylene dichloride was distilled with steam, and dried first over calcium chloride and then phosphoric oxide; the b. p. was 83°.

Rearrangement of Acetates.—(a) *In the absence of solvent*. The ester (0·033 mole) was well mixed with the catalyst (0·052 mole) and heated at 120° for 5 min., then at 165° for 15 min. 5N-Hydrochloric acid was added to the cooled product which was then shaken with nitrobenzene. Sodium hydroxide extracted the *p*- and *o*-hydroxy-ketone and the phenol, the last two compounds being volatile with steam. The latter ketone was converted into its 2 : 4-dinitrophenylhydrazone, in the filtrate from which phenol and *o*- and *m*-cresol were determined by formation of the bromo-derivatives [7, 8] and *p*-cresol by the potassium bromate–bromide process.[9] Decomposition occurred in some of these operations, especially with titanium tetrachloride; no ester was recovered in any experiment. The results are shown in Table *a*.

(b) *In nitrobenzene solution*. The ester (0·1 mole) and catalyst (0·2 mole) were heated for 5 hr. at 60°; homogeneous solutions were obtained in all the reactions studied. The products were worked up as described in previous papers of this series. The results are presented in Table *b*.

Rearrangement of Benzoates.—(a) *In the absence of solvent*. The ester (0·033 mole) and catalyst (0·052 mole) were heated at 140° for 15 min., and the products analysed by the method already described. The results are given in Table *c*.

(b) *In nitrobenzene solution*. The ester (0·1 mole), catalyst (0·2 mole), and solvent (100 c.c.) were heated at 60° for 18 hr., the products being separated in the usual way. The results are shown in Table *d*.

Effect of Solvents on the Rearrangement of m-*Tolyl Acetate*.—The ester (0·1 mole) was heated for 24 hr. at 25° with (*a*) anhydrous aluminium chloride (0·2 mole) and (*b*) titanic chloride (0·2 mole) in (*a*) nitrobenzene (100 c.c.) and (*b*) ethylene dichloride (100 c.c.). The products obtained are shown in Table *e*.

Effect of the Acyl Group on the Rearrangement of Phenyl Esters.—The ester (0·1 mole) and catalyst (0·2 mole) in nitrobenzene (100 c.c.) were heated at 50° for 18 hr. Homogeneous solutions were obtained in all reactions; the products were separated and analysed in the usual way, and the results are presented in Table *f*. No ester was recovered in any of the experiments.

Reaction Products.—The following ketones were prepared by rearrangement of the appropriate esters (2 : 4-dinitrophenylhydrazones in parentheses): 2-hydroxyacetophenone (orange needles, m. p. 213° [10]); 4-hydroxyacetophenone,[11] colourless needles (from hot water), m. p.

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[4] Baltzly and Bass, *J. Amer. Chem. Soc.*, 1933, **55**, 4292.
[5] Baltzly, Ide, and Phillips, *ibid.*, 1955, **77**, 2522.
[6] Stoughton, *J. Amer. Chem. Soc.*, 1935, **57**, 202.
[7] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.
[8] Cullinane and Edwards, *J.*, 1958, 434.
[9] *Idem, J.*, 1957, 3016.
[10] Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 2720.
[11] Mozingo, *Org. Synth.*, 1941, **21**, 45.

108° [deep red prisms (from alcohol), m. p. 269° [12]]; 2-hydroxy-3-methylacetophenone [red plates, m. p. 249° (decomp.) [13]]; 4-hydroxy-3-methylacetophenone,[7, 14] colourless plates (from hot water), m. p. 104° [red prisms, m. p. 276° (decomp.) [7]]; 2-hydroxy-4-methylacetophenone [8] [orange-red needles (from ethyl acetate), m. p. 244° [8]]; 4-hydroxy-2-methylacetophenone,[8] colourless needles, m. p. 127° (orange-red needles, m. p. 216° [8]); 2-hydroxy-5-methylacetophenone,[15] colourless needles (from ligroin), m. p. 50° (red prisms, m. p. 271° [9]); 2-hydroxybenzophenone,[16] m. p. 39° (brick-red plates, m. p. 260° [12]); 4-hydroxybenzophenone,[12] m. p. 135° (brick-red needles, m. p. 240° [12]); 4-hydroxy-3-methylbenzophenone,[17] pale yellow needles (from aqueous alcohol), m. p. 173°; 2-hydroxy-4-methylbenzophenone,[17] pale yellow needles (from aqueous alcohol), m. p. 63° (orange-red prisms, m. p. 235° [8]); 4-hydroxy-2-methylbenzophenone,[8] colourless needles, m. p. 129° (red needles, m. p. 224° [8]); 2-hydroxy-5-methylbenzophenone,[18] pale yellow needles (from aqueous alcohol), m. p. 85°; 2-hydroxypropiophenone (red needles, m. p. 189° [19]); 4-hydroxypropiophenone,[20] colourless prisms, m. p. 147—148° (red needles, m. p. 229° [19]); 2-hydroxybutyrophenone [red prisms (from ethyl acetate), m. p. 207° (Found: C, 56·0; H, 4·9; N, 16·2. $C_{16}H_{16}O_5N_4$ requires C, 56·0; H, 4·7; N, 16·3%)]; 4-hydroxybutyrophenone,[21] m. p. 91° [red prisms (from alcohol), m. p. 223° (Found: C, 56·0; H, 4·9; N, 16·2%)]; 2-hydroxy*iso*butyrophenone [red prisms, m. p. 186° (decomp.) [22]]; 4-hydroxy*iso*butyrophenone,[22] m. p. 54° [red needles, m. p. 166° (decomp.) [22]]; 2- (orange-red needles, m. p. 144° [2]), and 4-hydroxyoctanoylbenzene,[2] light brown prisms, m. p. 63° (red needles, m. p. 176° [2]); 2-hydroxy*iso*valerophenone [red plates (from ethyl acetate), m. p. 181° (Found: C, 57·1; H, 5·1; N, 15·4. $C_{17}H_{18}O_5N_4$ requires C, 57·0; H, 5·1; N, 15·6%)]; 4-hydroxy*iso*valerophenone,[23] light brown prisms, m. p. 95—96° [brick-red needles, m. p. 210° (Found: C, 57·0; H, 5·0; N, 15·4%)].

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