β-Aroylpropionic Acids. Part III.* Further Observation on the Fries Rearrangement.

By W. I. Awad, F. G. Baddar, and A. E. Marei.

[Reprint Order No. 5585.]

Phenyl and *o*-tolyl hydrogen succinate give a mixture of *o*- and *p*-hydroxy-keto-acids when heated with anhydrous aluminium chloride in nitrobenzene or *s*-tetrachloroethane, whereas *p*- and *m*-tolyl hydrogen succinate give only *o*-hydroxy-keto-acids. α- and β-Naphthyl hydrogen succinate give, in *s*-tetrachloroethane β-(1-hydroxy-2-naphthoyl)- and β-(2-hydroxy-1-naphthoyl)-propionic acid, respectively. When the solvent used in this rearrangement is susceptible to the electrophilic attack a certain amount of non-phenolic β-aroylpropionic acid is formed.

In continuation of the study of the mechanism of the Fries rearrangement (cf. Baddar and El-Assal, *J.*, 1950, 3606) a systematic investigation has been made of the effect of the medium on the rearrangement of phenyl, *o*-, *m*-, *p*-tolyl, and α- and β-naphthyl hydrogen succinate (I) in presence of anhydrous aluminium chloride under standardised conditions.

In nitrobenzene or *s*-tetrachloroethane phenyl and *o*-tolyl hydrogen succinate gave a mixture of *o*- and *p*-hydroxy-keto-acids (III and VI, respectively), but *p*- and *m*-tolyl hydrogen succinate gave only an *o*-hydroxy-keto-acid (III). α-Naphthyl hydrogen succinate gave mainly β-(1-hydroxy-2-naphthoyl)propionic acid, but a trace of β-(1-hydroxy-4-naphthoyl)propionic acid (cf. Berliner, Daniels, and Surmacka, *J. Amer. Chem. Soc.*, 1951, **73**, 4970) was isolated when nitrobenzene was used as a solvent; in *s*-tetrachloroethane or toluene another acid, m. p. 94°, was isolated, probably β-(1-hydroxy-8-naphthoyl)propionic acid since it gave with ferric chloride a violet colour. From β-naphthyl hydrogen succinate only β-(2-hydroxy-1-naphthoyl)propionic acid (cf. Berliner *et al.*, *loc. cit.*) was isolated.

With phenyl and *o*-tolyl hydrogen succinate the higher the dipole moment of the medium the greater was the proportion of the *p*-hydroxy-keto-acid (VI) (cf. the results with tetrachloroethane and nitrobenzene; Table 2). Similarly, from α-naphthyl hydrogen succinate a trace of β-(1-hydroxy-4-naphthoyl)propionic acid was obtained only when nitrobenzene was used as a medium (cf. Table 3).

When boiling benzene was used as a medium the esters studied in the present investigation were recovered unchanged.

Contrary to the report by Berliner *et al.* (*loc. cit.*), a mixture of β-naphthol and succinic anhydride with aluminium chloride under their conditions gave a mixture of β-naphthyl hydrogen succinate and β-(2-hydroxy-1-naphthoyl)propionic acid in which the former was predominant. It seems that the procedure adopted by these authors for the separation of the product caused complete hydrolysis of the ester, since it is easily hydrolysed especially in alkaline medium.

Raval, Bokil, and Nargund (*J. Univ. Bombay*, 1938, **7**, 184) considered that reaction between phenol, *o*-, *m*-, and *p*-cresol, and succinic anhydride in presence of aluminium chloride in tetrachloroethane proceeded by Friedel–Crafts mechanism. However, it was found in the present investigation that succinic anhydride and phenol or *m*- or *p*-cresol in tetrachloroethane at 0° afforded the corresponding hydrogen succinate. This shows that in the experiments of Raval *et al.* some of the ester was formed as an intermediate which rearranged to the hydroxy-keto-acid, *i.e.*, the process is probably a combination of the Fries and the Friedel–Crafts reaction.

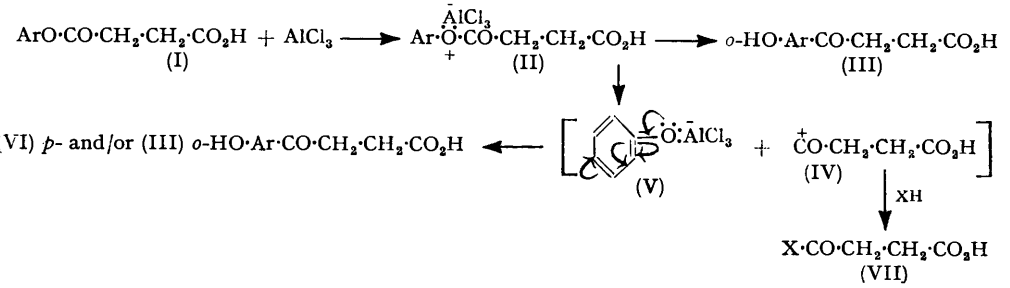
However, when a mixture of *o*-cresol and succinic anhydride was similarly treated, no ester was formed.

Berliner *et al.* (*loc. cit.*) discussed whether the succinoylation of the naphthols under their conditions took place by direct substitution or by a Fries rearrangement: we believe

* Part II, *J.*, 1951, 431.

that it is by direct substitution, since α- and β-naphthyl hydrogen succinate were recovered unchanged when treated under similar conditions.

The results of the present investigation showed that the ester (I) combines with aluminium chloride to give the complex (II), which either rearranges to give (III) by intramolecular rearrangement involving π-complexes (cf. Dewar, "Electronic Theory of



Organic Chemistry," Oxford, 1949, p. 229) or splits into an oxocarbonium ion (IV) and a phenoxyaluminium chloride complex (V). The oxocarbonium ion attacks both (V) and the solvent molecules (XH) to give rise to (III) and/or (VI), and β-aroylpropionic acid (VII), respectively. The proportion of (VII) in the reaction mixture depends on the relative susceptibility of XH to the electrophilic attack by the oxocarbonium ion. Such susceptibility increases with the increase in the electron-releasing power of the substituents. This explains the high percentage of β-aroylpropionic acid (VII) when *m*-xylene, anisole, and diphenyl ether were used as solvents, and its low percentage in the case of chlorobenzene.

The fact that β-aroylpropionic acids are formed mainly at the expense of the *p*-hydroxy-keto-acid (VI) (cf. Baddar and El-Assal, *loc. cit.*, and the result with *o*-tolyl hydrogen succinate in toluene, Table 2) indicates that the *p*-hydroxy-keto-acid is probably formed by an intermolecular mechanism, whereas the *o*-hydroxy-keto-acid (III) is probably formed by both the intra- and the inter-molecular mechanism (cf. Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56; Ralston *et al.*, *J. Org. Chem.*, 1940, **5**, 645; Gershzon, *J. Gen. Chem., U.S.S.R.*, 1943, **13**, 68; Cocker and Fateen, *J.*, 1951, 2632). A further support for the partial intramolecular nature of the Fries reaction is the fact that the rearrangement of α-naphthyl hydrogen succinate gave β-(1-hydroxy-2-naphthoyl)propionic acid, whereas direct substitution of α-naphthol by electrophilic reagents takes place mainly at position 4.

A similar scheme for α- and β-naphthyl hydrogen succinate could be proposed.

Gerecs, Windholz, and Sipos (*Acta Chim. Hung.*, 1954, **4**, 123) obtained evidence for the active role of hydrogen chloride in the Fries reaction. However, their results do not contradict our conclusions.

Experimental

Preparation of Aryl Hydrogen Succinates.—(*a*) The phenol (0·05 mole) and succinic anhydride (0·05 mole) were heated at 140—150° for 3 hr. (unless otherwise stated) and the product was worked up as stated by Baddar and El-Assal (*loc. cit.*). (*b*) To a cooled mixture of the phenol (0·1 mole) and succinic anhydride (0·1 mole) in tetrachloroethane (75 ml.), anhydrous aluminium chloride (0·12 mole) was gradually added and the reaction was carried out as stated by Baddar and El-Assal (*loc. cit.*). The mixture was diluted with ether and the organic layer was washed with water and extracted with cold concentrated sodium carbonate solution. The cold alkaline extract was acidified, and the precipitated product was filtered off and crystallised. The results are summarised in Table 1.

Fries Rearrangement.—This was carried out under standardised conditions, namely, the ester (0·033 mole), aluminium chloride (Prolabo-Produite pour Laboratoires, Rhone Poulenc) (0·067 mole), and solvent (0·462 mole) at 117° (boiling *n*-butyl alcohol bath) for 2·5 hr.

A stirred mixture of aryl hydrogen succinate and the solvent was heated at 117° and treated gradually with aluminium chloride during the first 30 min. The mixture was heated for further 2 hr., then hydrolysed with crushed ice and dilute hydrochloric acid. Ether was added, and the

ether solvent layer was separated, washed with water, and extracted with sodium carbonate solution. The alkaline extract was boiled to hydrolyse any unchanged ester (charcoal), filtered, and acidified with concentrated hydrochloric acid. In the cases of tetrachloroethane and nitrobenzene, the precipitated acids were separated as recorded in Table 2. For the other solvents the phenolic acids were separated from the non-phenolic acids by esterification with hydrogen chloride and ethyl alcohol in the normal way. The alcohol was removed, and the product was extracted with ether, and washed with sodium carbonate solution to remove unesterified acids, followed by sodium hydroxide solution to remove the phenolic esters (these were usually hydrolysed with sodium hydroxide during extraction). From the sodium hydroxide solution acidification precipitated the phenolic acids. The ester of the non-phenolic acid was hydrolysed by boiling 8% alcoholic potassium hydroxide for 3 hr. The precipitated non-phenolic acid (VII) was crystallised and identified by m. p. and mixed m. p. (cf. Tables 2 and 3).

TABLE 1.

Aryl hydrogen succinate	M. p.	Solvent for crystn.[1]	Yield (%)[2] (*a*)	(*b*)	Found (%) C	H	Formula	Required (%) C	H
p-Tolyl[3]	105—106°	C_6H_6–Pet (b. p. 30—50°)	50	43	63·95	5·6	$C_{11}H_{12}O_4$	63·45	5·8
m-Tolyl[4]	66—67	C_6H_6–Pet (b. p. 40—60°)	50	83	63·4	5·8			
o-Tolyl[5]	49—50	Pet (b. p. 30—50°)	43	—	63·1	5·7			
α-Naphthyl[6] ...	114	C_6H_6	57	40	68·5	5·0	$C_{14}H_{12}O_4$	68·9	4·95
β-Naphthyl[7] ...	135—136	C_6H_6	57	56	69·2	5·1			

[1] Pet = light petroleum. [2] Methods (*a*) and (*b*) (see text). [3] Traces of di-*p*-tolyl succinate were formed, m. p. 118—119° (from benzene–light petroleum) (Found C, 72·3; H, 6·0. Calc. for $C_{18}H_{16}O_4$: C, 72·5; H, 6·0%). [4] Fusion at 130° for 2·5 hr. [5] Method (*b*) gave only β-(2-hydroxy-3-toluoyl)-propionic acid, m. p. 184° (cf. Raval *et al.*, *loc. cit.*). [6] Method (*b*) gave a mixture of β-(1-hydroxy 4-naphthoyl)propionic acid and the ester. The former was separated by extraction with hot benzene in which it was insoluble, and was identified by m. p. and mixed m. p. (cf. Berliner *et al.*, *loc. cit.*). [7] The sodium carbonate (4%) extract should be immediately acidified, otherwise hydrolysis takes place.

TABLE 2. *Yields* (g.)

		Ar = Ph			Ar = *o*-C_6H_4Me			Ar = *p*-C_6H_4Me		Ar = *m*-C_6H_4Me	
Solvent	μ	VII	III *	VI *	VII	III †	VI †	VII	III	VII	III
$C_2H_2Cl_4$ ...	0	—	3·8[a]	Trace[b]	—	1·46[h]	1·83[i]	—	4·6[j]	—	2·85[k]
$PhNO_2$ ...	4·96	—	0·83	0·38	—	0·12	3·8	—	3·9	—	2·9
PhMe	0·37	0·9[c]	1·55	Trace	1·25	0·57	0·55	1·11	1·27	1·11	2·1
m-$C_6H_4Me_2$	0·4	3·1[d]	0·76	,,	1·72	0·15	0·7	2·68	0·3	1·85	3·05
PhOMe ...	1·2	1·98[e]	—	—	1·8	0·08	0·08	2·25	—	3·8	0·73
Ph_2O	1·17	5·16[f]	0·25	Trace	4·0	0·08	0·45	3·8	—	4·1	1·13
PhCl	1·54	0·55[g]	2·7	,,	Trace	1·15	1·4	0·63	2·65	0·11	3·01

* For Ar = Ph, acids (III) and (VI) were separated by means of diazomethane in ether (free from alcohol) (cf. Baddar and El-Assal, *loc. cit.*).

† For Ar = *o*-tolyl, acids (III) and (VI) were separated by use of nitrobenzene in which (VI) is less soluble (cf. Raval *et al.*, *loc. cit.*).

[a, h, i, j, k] Identified by m. p. and mixed m. p. (cf. Raval *et al.*, *loc. cit.*). [b] Identified as β-*p*-anisoyl-propionic acid by m. p. and mixed m. p. (cf. Mitter and Shyamakanta De, *J. Indian Chem. Soc.*, 1939, **16**, 35; Haworth and Sheldrick, *J.*, 1934, 1951). [c] β-*p*-Toluoylpropionic acid, m. p. and mixed m. p. 128° (cf. Barnett and Sanders, *J.*, 1933, 434). [d] β-(2 : 4-Dimethylbenzoyl)propionic acid, m. p. and mixed m. p. 109—110° (cf. Muhr, *Ber.*, 1895, **28**, 3216). [e] *p*-Anisoylpropionic acid, m. p. 149—150° (cf. Mitter and Shaymakanta De, *loc. cit.*; Haworth and Sheldrick, *loc. cit.*; Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1936, **58**, 2314; Rosenmund and Shapiro, *Arch. Pharm.*, 1934, **272**, 313). [f] β-4-Phenoxybenzoylpropionic acid, m. p. and mixed m. p. 117° (cf. Kipper, *Ber.*, 1905, **38**, 2491). [g] β-*p*-Chlorobenzoylpropionic acid, m. p. and mixed m. p. 131° (cf. Skraup and Schwamberger, *Annalen*, 1928, **462**, 148).

Action of Aluminium Chloride on a Mixture of β-Naphthol and Succinic Anhydride in Benzene.—A mixture of β-naphthol (18 g.), succinic anhydride (10 g.), aluminium chloride (26 g.), and dry benzene (80 ml.) was refluxed on the water-bath for 1 hr. (cf. Berliner *et al.*, *loc. cit.*). The product was hydrolysed with ice and hydrochloric acid, ether (*ca.* 90 ml.) was added, and the mixture was filtered off from the insoluble product (11 g.). This on crystallisation from benzene proved to be β-naphthyl hydrogen succinate (m. p. and mixed m. p.). The benzene–ether layer was extracted with sodium carbonate solution, which was boiled to decompose any unchanged

ester, then filtered from the precipitated β-naphthol, cooled, and acidified with concentrated hydrochloric acid. The precipitated product was extracted with hot benzene, filtered from traces of high-melting material, then crystallised from benzene–light petroleum (b. p. 40—60°) to give β-(2-hydroxy-1-naphthoyl)propionic acid (2 g.), identified by m. p. and mixed m. p.

TABLE 3. *Yields* (g.)

		Ar = α-$C_{10}H_7$				Ar = β-$C_{10}H_7$	
Solvent	μ	VII	Acid, m. p. 173° [a]	Acid, m. p. 94° [b]	Acid,[c] m. p. 232°	VII	Acid, m. p. 118—119° [d]
$C_2H_2Cl_4$	0	—	3·1	1·9	—	—	1·65
$PhNO_2$	4·96	—	0·8	—	Traces	—	0·2
PhMe	0·37	0·4	1·8	0·6	—	1·7	1·8
m-$C_6H_4Me_2$ ...	0·4	0·7	2·5	—	—	1·9	0·61
PhOMe	1·2	2·9	0·9	—	—	3·42	—
Ph_2O	1·17	1·75	1·9	—	—	1·98	0·58
PhCl	1·54	Traces	5·2	—	—	0·1	1·72

[a] Identified by m. p. and mixed m. p. with β-(1-hydroxy-2-naphthoyl)propionic acid (Berliner *et al., loc. cit.*). [b] The acid was separated from β-(1-hydroxy-2-naphthoyl)propionic acid by fractional crystallisation from methyl alcohol. [c] Separated from the acid, m. p. 173°, by crystallisation from methyl alcohol and identified as β-(1-hydroxy-4-naphthoyl)propionic acid by m. p. and mixed m. p. (*idem, ibid.*). [d] Identified by m. p. and mixed m. p. as β-(2-hydroxy-1-naphthoyl)propionic acid (*idem, ibid.*).

Action of Aluminium Chloride on β-Naphthyl Hydrogen Succinate at 100° *and on α- and β-Naphthyl Hydrogen Succinate in Boiling Benzene.*—Naphthyl hydrogen succinate (8·2 g.) and anhydrous aluminium chloride (9 g.) in tetrachloroethane (76·7) or benzene (36 g.) was stirred for 2 hr. on a steam-bath. The mixture was hydrolysed with ice and concentrated hydrochloric acid, ether was added, and the organic layer was extracted with cold dilute sodium carbonate solution, which was then immediately acidified. The precipitated products (4·0, 7·8, and 6·8 g., respectively) proved to be the unchanged ester (m. p. and mixed m. p.).

FACULTIES OF SCIENCE,
CAIRO UNIVERSITY, ORMAN,
IBRAHIM UNIVERSITY, ABBASSIA, CAIRO, EGYPT.

[*Received, July 26th*, 1954.]