

489. *Reactions in Fused Aluminium Chloride-Sodium Chloride.*

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It is shown that intramolecular cyclisations, Fries rearrangements, and condensation of quinol with various mono- and di-basic acids can be effected in two minutes by fusion in an aluminium chloride-sodium chloride melt at 180—200°. Condensation of quinol with γ -butyro- and valero-lactones gave indanones and not the expected tetralones.

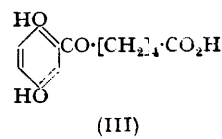
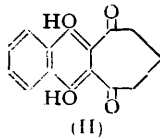
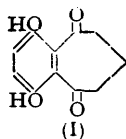
A MOLTEN mixture of aluminium chloride and sodium chloride has been used in the synthesis of naphthazarins and hydroxyanthraquinones by condensation of maleic and phthalic anhydrides with various phenols (Zahn and Ochwat, *Annalen*, 1928, **462**, 72; Kuroda and Wada, *Proc. Imp. Acad. Tokyo*, 1936, **12**, 239; Raudnitz, *Ber.*, 1929, **62**, 509; Waldmann and Mathiowetz, *J. pr. Chem.*, 1930, **126**, 250), and for the preparation of numerous more complex polycyclic quinones and ketones by cyclisation reactions involving dehydration and dehydrogenation (Scholl reactions). We now find that intramolecular cyclisations of aryl-substituted aliphatic acids, and Fries rearrangements, can be readily effected by this reagent by 2 minutes' heating at 180—200°. The method is convenient for small-scale (<10 g.) preparations but is limited by the fact that alkyl groups are known to migrate under such conditions (Auwers, *Annalen*, 1928, **460**, 254; Baddeley, *J.*, 1943, 273; 1944, 232; 1952, 2415). The yields recorded in the Table are similar to those obtained by more conventional procedures, any decrease being offset by the ease of operation in most cases.

Section (c) shows a number of ketones which were obtained by condensation of quinol with various carboxylic acids and lactones, and section (d) illustrates the cyclisation of aryl vinyl ketones under the same conditions. The condensation of quinols with dibasic acids

Reactants	Products	Yield, %
(a) <i>Cyclisation of aryl-substituted aliphatic acids</i> ¹		
β -Phenylpropionic acid	Indan-1-one	85
β - <i>m</i> -Hydroxyphenylpropionic acid	5-Hydroxyindan-1-one	60
	7-Hydroxyindan-1-one	15
β - <i>o</i> -Nitrophenylpropionic acid	4-Nitroindan-1-one	10
γ -Phenylbutyric acid	α -Tetralone	73
δ -Phenylvaleric acid	Benzosuberone	22
$\alpha\beta$ -Diphenylsuccinic acid	1-Keto-2-phenylindan-3-carboxylic acid	50
(b) <i>Fries rearrangements</i> ²		
Phenyl acetate	<i>o</i> -Hydroxyacetophenone	37
	<i>p</i> -Hydroxyacetophenone	35
Phenyl benzoate	<i>o</i> -Hydroxybenzophenone	17
	<i>p</i> -Hydroxybenzophenone	55
Quinol diacetate	2 : 5-Dihydroxyacetophenone	60
Quinol dibenzoate	2 : 5-Dihydroxybenzophenone	30
Quinol dicrotonate	4 : 7-Dihydroxy-3-methylindan-1-one	55
Phloroglucinol triacetate	Triacetylphloroglucinol	50
(c) <i>Phenol-acid condensations</i> (HQ = quinol)		
Phenol + benzoic acid	<i>o</i> -Hydroxybenzophenone	17
	<i>p</i> -Hydroxybenzophenone	55
HQ + benzoic acid	2 : 5-Dihydroxybenzophenone	33
HQ + <i>p</i> -bromobenzoic acid	4-Bromo-2' : 5'-dihydroxybenzophenone	32
HQ + crotonic acid	4 : 7-Dihydroxy-3-methylindan-1-one	30
HQ + γ -butyrolactone	4 : 7-Dihydroxy-3-methylindan-1-one	45
HQ + γ -valerolactone	3-Ethyl-4 : 7-dihydroxyindan-1-one	12
HQ + maleic acid	Naphthazarin	30
HQ + succinic acid	1 : 2 : 3 : 4-Tetrahydro-5 : 8-dihydroxy-1 : 4-diketonnaphthalene	25
HQ + glutaric acid	1' : 4'-Dihydroxy-1 : 2-benzocycloheptene-3 : 7-dione	33
1 : 4-Dihydroxynaphthalene + glutaric acid	1' : 4'-Dihydroxynaphtho(2' : 3'-1 : 2)cycloheptene-3 : 7-dione	7
HQ + adipic acid	δ -(2 : 5-Dihydroxybenzoyl)valeric acid	9
(d) <i>Cyclisation of aryl vinyl ketones</i> ³		
Chalcone	3-Phenylindan-1-one	60
2 : 5-Dihydroxyphenyl propenyl ketone	4 : 7-Dihydroxy-3-methylindan-1-one	90
β -Benzoylacrylic acid ⁴	1-Ketoindane-3-carboxylic acid	1
β -2-Naphthoylacrylic acid ⁵	1-Keto-4 : 5-benzindane-3-carboxylic acid	30

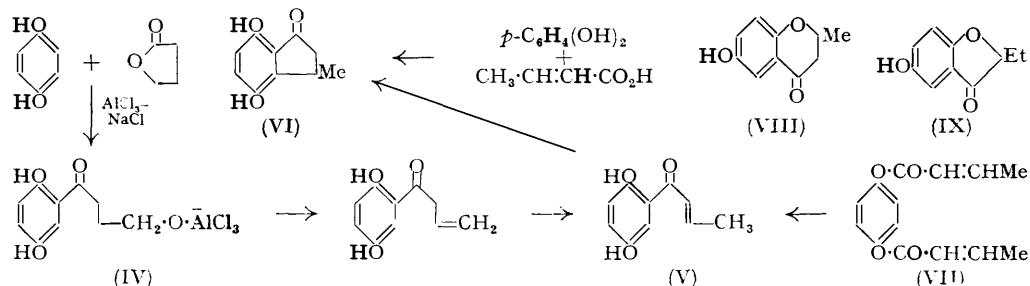
¹ Johnson, "Organic Reactions," Wiley, New York, 1944, Vol. II, p. 114. ² Blatt, *op. cit.*, 1942, Vol. I, p. 342. ³ Auwers and Risse, *Annalen*, 1933, 502, 282. ⁴ Cf. Baddeley, Holt, and Makar, *J.*, 1952, 3289. ⁵ Cf. Baddeley, Holt, Makar, and Ivinson, *J.*, 1952, 3605.

has been extended to glutaric acid to give the diketones (I) and (II) (a detailed study of these compounds will be reported later), but the only identifiable product obtained from the reaction with adipic acid was a little of the keto-acid (III).



The use of γ -lactones in Friedel-Crafts reactions for the preparation of γ -arylbutyric acids was first reported by Eijkmann (*Chem. Weekblad*, 1904, 1, 421 *et seq.*). Later, Mosby (*J. Amer. Chem. Soc.*, 1952, 74, 2564) observed the additional formation of tetralones when the reaction time was prolonged, and satisfactory yields of tetralones have been obtained by using excess of aluminium chloride (Arnold, Buckley, and Richter, *ibid.*, 1947, 69, 2322; Truce and Olson, *ibid.*, 1952, 74, 4721). We therefore expected no difficulty in preparing 5 : 8-dihydroxytetralone by condensing quinol with γ -butyrolactone in an aluminium chloride-sodium chloride melt, but in fact the product obtained, although

very similar in physical and chemical properties, was the isomeric ketone 4 : 7-dihydroxy-3-methylindanone (VI). It gave a positive reaction with Brady's reagent, a transient blue-green ferric colour, and a yellow alkaline solution [like all the quinol derivatives in section (c) of the Table], and formed a diacetate. The lactone ring can open in two ways : (a) to form a carbonium ion on the γ -carbon atom, subsequent reaction giving a γ -arylbutyric acid, and (b) to form a carbonium ion on the carbonyl carbon atom which gives



rise to the intermediate ketone (IV) and thence by elimination of the alcoholic group and shift of the double bond to form (V) and then (VI). In support of this we also obtained (VI) by cyclisation of 2 : 5-dihydroxyphenyl propenyl ketone (V), by a Fries rearrangement of quinol dicrotonate (VII), and by direct condensation of quinol with crotonic acid. Since the indanone forms a diacetate, the alternative monohydroxychromanone (VIII) and, less probable, coumaranone (IX) structures are eliminated (cf. von Auwers, *Annalen*, 1920, **421**, 1, and other papers). Valerolactone gave the ethyl homologue of (VI) but we could only isolate traces of 1 : 4-dihydroxyanthrone from the reaction between phthalide and quinol (formation of a five-membered ring is impossible in this case).

EXPERIMENTAL

General Procedure.—A mixture of anhydrous aluminium chloride (10 g.) and sodium chloride (2 g.) is melted in a beaker (100 c.c.) by direct heating over a flame, and stirred with a thermometer. The aromatic acid or ester (2 g.) is added at 140° , and the temperature raised rapidly to 180° and kept at $180\text{--}200^\circ$ for 2 min. The mixture is then cooled, decomposed with ice and hydrochloric acid, and worked up in the usual way. In cases where the product is chelated (especially quinol derivatives) it may be necessary to heat the hydrochloric acid mixture to the boil to decompose the complex. In condensation reactions involving two components the amount of aluminium chloride used is five times the combined weights of the two components, which are added as an intimate mixture to the melt. On a larger scale, addition of the organic material must be made gradually to avoid excessive frothing.

δ -(2 : 5-Dihydroxybenzoyl)valeric acid (III) formed pale yellow leaflets, m. p. 130° (from water) (Found : C, 60.5; H, 5.9. $\text{C}_{12}\text{H}_{14}\text{O}_5$ requires C, 60.5; H, 5.8%); its 2 : 4-dinitrophenylhydrazone formed orange plates, m. p. 194° (from alcohol) (Found : N, 13.3. $\text{C}_{18}\text{H}_{18}\text{O}_8\text{N}_4$ requires N, 13.4%).

4-Bromo-2' : 5'-dihydroxybenzophenone formed light yellow needles, m. p. 153° (from benzene-light petroleum) (Found : C, 53.2; H, 3.2. $\text{C}_{13}\text{H}_9\text{O}_3\text{Br}$ requires C, 53.25; H, 3.1%); its 2 : 4-dinitrophenylhydrazone formed orange-red plates, m. p. 314° (decomp.) (from glacial acetic acid) (Found : N, 11.8. $\text{C}_{19}\text{H}_{13}\text{O}_6\text{N}_4\text{Br}$ requires N, 11.8%).

1' : 4'-Dihydroxy-1 : 2-benzocycloheptene-3 : 7-dione (I).—This dione crystallises from light petroleum (b. p. $100\text{--}120^\circ$) in bright red needles and sublimes *in vacuo* as yellow crystals, m. p. 149° (Found : C, 64.05; H, 4.85. $\text{C}_{11}\text{H}_{10}\text{O}_4$ requires C, 64.05; H, 4.85%). The diacetate formed plates, m. p. 170° (from aqueous acetic acid) (Found : C, 62.2; H, 4.85. $\text{C}_{15}\text{H}_{14}\text{O}_6$ requires C, 62.05; H, 4.85%). The dimethyl ether, prepared by refluxing with methyl sulphate-acetone-potassium carbonate for 2 hr., crystallised from light petroleum in plates, m. p. 148° , soluble in concentrated hydrochloric acid (Found : C, 67.05; H, 6.05. $\text{C}_{13}\text{H}_{14}\text{O}_4$ requires C, 66.65; H, 6.0%). The *p*-nitrophenylhydrazone formed orange crystals, m. p. 218° (from aqueous alcohol) (Found : N, 12.4. $\text{C}_{17}\text{H}_{15}\text{O}_5\text{N}_3$ requires N, 12.3%).

1' : 4'-Dihydroxynaphtho(2' : 3'-1 : 2)cycloheptene-3 : 7-dione (II) formed yellow rosettes, m. p. 121° (from light petroleum) (Found : C, 70.45; H, 4.7. $\text{C}_{15}\text{H}_{12}\text{O}_4$ requires C, 70.3; H,

4.7%); its *dimethyl ether* crystallised from aqueous methanol in plates, m. p. 124° (Found: C, 71.5; H, 5.85. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.65%).

1-Keto-2-phenylindane-3-carboxylic Acid.—This crystallised from water as the *monohydrate*, needles, m. p. 116° Found: C, 70.95; H, 5.16. $C_{16}H_{12}O_3 \cdot H_2O$ requires C, 71.1; H, 5.2%). (It was first obtained by Dr. M. B. Watson by monocyclisation of $\alpha\beta$ -diphenylsuccinic acid with sulphuric acid; personal communication.) When the keto-acid was heated with concentrated sulphuric acid at 135° for 2 min. it cyclised to form *4b* : 5 : *9b* : 10-tetrahydroindeno(2 : 1*a*)indene-5 : 10-dione, which crystallised from alcohol in plates, m. p. 205°, undepressed by admixture with an authentic specimen. A little of this diketone was formed along with the keto-acid when diphenylsuccinic acid was fused with a larger amount of aluminium chloride-sodium chloride for 10 mins.

Quinol Dicrotonate (VII).—Quinol (1.1 g.) and crotonoyl chloride (5 g.) were refluxed together for 3 min. Crystals separated on cooling. The mixture was poured on ice, and the *ester* crystallised from alcohol in needles, m. p. 113° (94%) (Found: C, 68.15; H, 5.7. $C_{14}H_{14}O_4$ requires C, 68.25; H, 5.7%).

2 : 5-Dihydroxyphenyl Propenyl Ketone (V).—A suspension of 2 : 5-dihydroxyacetophenone (2 g.) in glacial acetic acid (40 c.c.) was saturated at 0° with dry hydrogen chloride, the passage of which was continued while acetaldehyde (20 c.c.) was added gradually (3 hr.). After 6 hr. the red solution was poured on ice. Next day, the dark viscous oil which had separated was washed repeatedly with water, taken up in chloroform, and then extracted with aqueous potassium hydroxide. The alkaline extract was acidified and again extracted with chloroform, and the latter dried ($CaCl_2$) and evaporated. The residue was sublimed at 175°/10 mm., and the sublimed *ketone* recrystallised from light petroleum (charcoal) in pale yellow needles, m. p. 154.5° (0.1 g.) (Found: C, 67.45; H, 5.8. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.65%).

4 : 7-Dihydroxy-3-methylindan-1-one (VI).—This *ketone* was obtained by the four methods indicated in the Table. It crystallised from light petroleum in clusters of pale yellow plates, m. p. 182—183° (Found: C, 67.45; H, 5.6. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.65%). The *diacetate* crystallised from light petroleum (b. p. 50—60°) in plates, m. p. 75° (Found: C, 63.95; H, 5.25. $C_{14}H_{14}O_5$ requires C, 64.1; H, 5.4%).

3-Ethyl-4 : 7-dihydroxyindan-1-one formed lemon-yellow needles, m. p. 199° (Found: C, 68.55; H, 6.25. $C_{11}H_{12}O_3$ requires C, 68.75; H, 6.3%), and its *diacetate* crystallised in needles, m. p. 102° (from alcohol) (Found: C, 65.15; H, 5.9. $C_{15}H_{16}O_5$ requires C, 65.2; H, 5.8%).

Some of the analyses are by Miss M. A. Buchanan. One of us (A. J. S. S.) thanks the Carnegie Trust for the Universities of Scotland for a scholarship.

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[Received, March 2nd, 1953.]