

STUDIES IN THE FRIEDEL-CRAFTS REACTION.

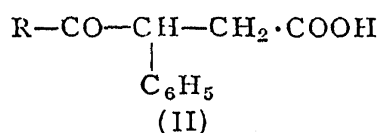
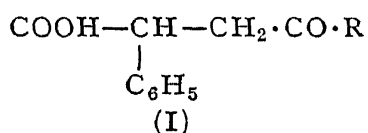
Part III. The Condensation of Succinic Anhydride with the Methyl Ethers of the Phenol and the Cresols.

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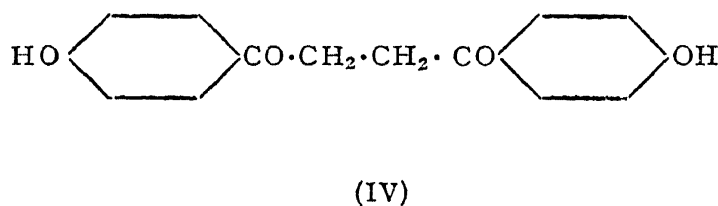
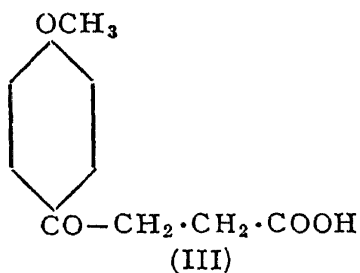
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WE have already described the condensation of phenylsuccinic anhydride with benzene and toluene with the result that two isomeric acids represented by formulæ I and II (where R = phenyl or *p*-tolyl) are always produced (see preceding paper). While extending this observation to anisole, we observed that complications arose owing to the condensation of anisole either in the *ortho* or *para* position to the methoxy group. In order to make sure of the position taken up in the benzene ring, we decided to repeat the observations of Rosenmund and Schapiro¹ on the condensation of succinic anhydride with the methyl ethers of the phenol, and the three isomeric cresols.



Succinic anhydride condensed with anisole, either in nitrobenzene or acetylene tetrachloride solution, giving β -(4-methoxy-benzoyl)-propionic acid (III) together with a small quantity of a phenolic product which was identified as α - β -4 : 4'-dihydroxydibenzoyl-ethane (IV), because it was oxidised by alkaline hypobromite to *p*-hydroxybenzoic acid and ethylenedibromide. The constitution of the acid (III) followed from the fact that oxidation with alkaline hypobromite gave *p*-methoxybenzoic acid. The Clemmensen reduction of this keto-acid gave γ -4-methoxyphenylbutyric acid.



Methyl-*o*-cresyl ether gave β -(3-methyl-4-methoxy-1-benzoyl)-propionic acid (V) as it was oxidised to 3-methyl-4-methoxybenzoic acid. The keto-acid was reduced to γ -(3-methyl-4-methoxyphenyl)-butyric acid. Methyl-*m*-cresyl ether yielded β -(2-methyl-4-methoxy-1-benzoyl)-propionic acid (VI),

aluminium chloride. On extending this observation to the anhydrides of α - α -dimethylsuccinic acid, 3-methylcyclopentane-1-carboxy-1-acetic acid and cyclohexane-1-carboxy-1-acetic acid, it was found that each of them gave only one keto-acid on condensing with benzene and toluene. An explanation has been offered on the electronic conception.

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Haworth and co-workers, *J.*, 1932, 1125, 1784, 2248, 2717 ; 1934, 54, 1950.
2. Anschütz and co-workers, *Annalen*, 1907, 354, 150.
3. Robinson and Young, *J.*, 1934, 1414.
4. Lapworth and Hann, *ibid.*, 1904, 1358.
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Perkin, Robinson and Turner, *J.*, 1908, 93, 1085.
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9. Lapworth and McRae, *ibid.*, 1922, 2741.
10. Rothstein and Thorpe, *ibid.*, 1926, 2011.
11. Desai, *ibid.*, 1931, 1218.
12. Higson and Thorpe, *ibid.*, 1906, 1465.

N. B.— The paper by Ahmad Ali, Desai, Hunter and Muhammad (*J.*, 1937, 1013) forms Part I of this series.

silky needles melting at 54° . [Found: C, 66.4; H, 5.8, $C_{16}H_{14}O_4H_2O$ requires C, 66.6; H, 5.5 per cent.]

Oxidation with sodium hypobromite.—The diketone (0.5 g.) dissolved in caustic soda solution was oxidised by the hypobromite (3 c.c.) as described above. The neutral product was extracted with ether, the alkaline solution was acidified with strong HCl and the resulting solid crystallised from alcohol. It melted at $209-210^{\circ}$ and was identified as *p*-hydroxybenzoic acid by comparison with an authentic specimen.

γ -(4-methoxyphenyl)-butyric acid.—A mixture of the keto-acid (2 g.) amalgamated zinc (20 g.) and concentrated HCl (25 c.c.) was heated under reflux on sand-bath for 12 hours. The resulting semi-solid acid was purified through solution in sodium carbonate, and crystallised from hexane when short, white needles melting at 62° were obtained. [Found: C, 67.9; H, 7.2: $C_{10}H_{14}O_3$ requires C, 68.0; H, 7.2 per cent.]

Condensation of succinic anhydride with o-cresol methyl ether.—This was carried out as usual using succinic anhydride (4 g.), *o*-cresyl methyl ether (5 g.), nitrobenzene (60 c.c.) and aluminium chloride (12 g.), and giving 60 hours for the reaction to complete. After the usual purification, β -(4-methoxy-3-methyl-1-benzoyl)-propionic acid crystallised from benzene in long white needles melting at 150° (Rosenmund gives 146°). When the keto-acid was oxidised by means of sodium hypobromite as usual, 3-methyl-4-methoxybenzoic acid² (m.p. $191-192^{\circ}$) was produced.

Reduction by amalgamated zinc gave γ -(3-methyl-4-methoxyphenyl)-butyric acid which crystallised from benzene in white, fine needles melting at $98-99^{\circ}$. [Found: C, 68.9; H, 7.4; $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7 per cent.]

The condensation of succinic anhydride with *m*-cresyl methyl ether gave β -(2-methyl-4-methoxy-1-benzoyl)-propionic acid; as it was oxidised by alkaline hypobromite to 2-methyl-4-methoxybenzoic acid² (m.p. $175-176^{\circ}$).

Reduction by the usual method gave γ -(2-methyl-4-methoxyphenyl)-butyric acid which crystallised from hexane in white, lustrous plates melting at 92° . [Found: C, 69.2; H, 7.6; $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7 per cent.].

p-Cresyl methyl ether and succinic anhydride gave β -(5-methyl-2-methoxy-1-benzoyl)-propionic acid, as it was oxidised by alkaline sodium hypobromite to 5-methyl-2-methoxybenzoic acid² (m.p. 70°).

Reduction of the keto-acid by the usual method gave γ -(5-methyl-2-methoxyphenyl)-butyric acid which crystallised from hexane in white needles, melting at 66° . [Found: C, 69.2; H, 7.7: $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7 per cent.]

We have great pleasure in expressing our thanks to Dr. R. F. Hunter for his kind interest in this investigation.

Summary of Part III.

The condensation of anisole with succinic anhydride gave β -(4-methoxybenzoyl)-propionic acid, and a small quantity of α - β -4 : 4'-dihydroxydibenzoylethane.

Similar condensation has been carried out with the methyl ethers of the three cresols. The constitution of these various keto-acids has been determined by oxidation. They have been also reduced to the corresponding substituted butyric acids.

REFERENCES.

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2. Schall, *Ber.*, 12, 825.