

## STUDIES IN FRIEDEL-CRAFTS' ACYLATION. PART I. FRIEDEL-CRAFTS' ACETYLATION OF ACETANILIDE AND ACETO-*o*-TOLUIDIDE

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Friedel-Crafts' acetylation of acetanilide and aceto-*o*-toluidide has been investigated using acetyl chloride. Acetanilide yielded *p*-acetaminoacetophenone, and aceto-*o*-toluidide, 3-acetamino-4-methylacetophenone (I). The constitution assigned to (I) has been confirmed by unambiguous synthesis.

Kunckeli *et al.* (*Ber.*, 1900, 33, 2641; 1907, 40, 3394; 1901, 34, 124) studied Friedel-Crafts' acylation of acetanilide and its derivatives using various acyl chlorides in presence of excess of anhydrous aluminium chloride and carbon disulphide as the solvent. They found that for the reaction to succeed, it was essential that the acyl halide should have boiling point exceeding 90° or that it should be halogenated. For instance, they reported that, in case of acetanilide, Friedel-Crafts' acetylation failed with acetyl chloride but furnished satisfactory results with acetyl bromide or chloroacetyl chloride. They did not investigate Friedel-Crafts' acetylation of any other acetanilide derivative.

We have, however, successfully carried out the Friedel-Crafts acetylation of acetanilide and aceto-*o*-toluidide using acetyl chloride as the acetylating agent. By investigating the reaction with different proportions of the components at 100° and in the absence of any solvent, it has been established that the acetaminoketone is obtained in good yield on using 1 : 1 : 3 parts by weight respectively of acetanilide (or aceto-*o*-toluidide), acetyl chloride and anhydrous aluminium chloride.

The constitution assigned to the acetaminoketone, obtained from aceto-*o*-toluidide, viz., 3-acetamino-4-methylacetophenone (I), has been confirmed by unambiguous synthesis in the following manner. *p*-Methylacetophenone on nitration afforded 3-nitro-4-methylacetophenone from which, on reduction with iron powder and acetic acid and subsequent N-acetylation with acetic anhydride, 3-acetamino-4-methylacetophenone was obtained, identical with the above product (I).

On oxidation with aqueous potassium permanganate, (I) furnished 3-acetamino-4-methylbenzoic acid, m.p. 267-70° (decomp.), which agreed with the melting point reported in literature for the same acid (Kunckell, *Chem. Zentr.*, 1912, I, 136).

### EXPERIMENTAL

*Acetylation of Acetanilide to p-Acetaminoacetophenone.*—To a cooled mixture of acetanilide (10 g.) and AlCl<sub>3</sub> (anhydrous, 30 g.) acetyl chloride (10 g.) was added in small lots with occasional stirring. It was left at room temperature for half an hour and then heated on a water-bath for 3 hours, cooled and decomposed with ice and HCl. The product was filtered and washed with water. It crystallised from boiling water in small plates, m.p. 166-67°, yield 2.5 g. Kunckell (*loc.cit.*, 1900) records the same melting point.

*Acetylation of Aceto-o-toluidide to 3-Acetamino-4-methylacetophenone (I).*—This reaction was similarly carried out. 3-Acetamino-4-methylacetophenone crystallised from boiling water in white shining plates, m.p.  $141-42^{\circ}$ , yield 6 g. (Found: N, 7.6.  $C_{11}H_{13}O_2N$  requires N, 7.3 per cent).

*3-Amino-4-methylacetophenone.*—The above acetaminoketone (I) was hydrolysed at  $100^{\circ}$  with excess of dilute HCl and the product crystallised from petroleum ether in yellowish small needles, m.p.  $83-84^{\circ}$ . (Found: N, 9.7.  $C_9H_{11}ON$  requires N, 9.4 per cent).

The oxime of the aminoketone crystallised from dilute alcohol in thin long needles, m.p.  $152-53^{\circ}$ . (Found: N, 17.3.  $C_9H_{12}ON_2$  requires N, 17.1 per cent).

The N-benzoyl derivative was prepared by heating the above aminoketone with a slight excess of benzoyl chloride in presence of dilute alkali. It crystallised from boiling water in white shining thin needles, m.p.  $124-25^{\circ}$ . (Found: N, 5.67.  $C_{16}H_{15}O_2N$  requires N, 5.5 per cent).

*Reduction of 3-Nitro-4-methylacetophenone: Formation 3-Amino-4-methylacetophenone.*—The suspension of 3-nitro-4-methylacetophenone (2 g.) (Errera, *Gazzetta*, 1891, 21, 92) in hot water (10 c.c.) was added in small portions to a well-stirred mixture of iron filings (7.5 g.), water (30 c.c.) and acetic acid (2 c.c.) at about  $80^{\circ}$ , and heating was then continued for half an hour, and the hot solution was filtered immediately. From the filtrate, 3-amino-4-methylacetophenone separated out on cooling. It crystallised from petroleum ether in yellowish small needles, m.p.  $83-84^{\circ}$ . It did not depress the melting point of the amino-ketone, described above.

*N-Acetylation of 3-Amino-4-methylacetophenone: Formation of 3-Acetamino-4-methylacetophenone.*—The above mentioned amino-ketone (2 g.) was heated on a water-bath with acetic anhydride (3 c.c.) for half an hour and poured in cold water. The white solid which separated after about half an hour was collected and crystallised from hot water in white shining plates, m.p.  $141-42^{\circ}$ . It did not depress the melting point of (I), described above.

*3-Acetamino-4-methylbenzoic Acid.*—3-Acetamino-4-methylacetophenone (2 g.) was heated on a water-bath with a 5% solution of potassium permanganate (120 c.c.) till oxidation was complete. The solution was filtered hot and the filtrate was evaporated on a water-bath to half its bulk. On acidifying it 3-acetamino-4-methylbenzoic acid separated out. It crystallised from boiling water in white small needles, m.p.  $267-70^{\circ}$  (decomp.). Kunckell [1902] records the same melting point. (Found: Equiv. 191.2. Calc for  $C_{16}H_{11}O_5N$  Equiv. 193.0).