

San-ya Akaboshi and Makoto Suzuki: Condensation of Methylsuccinic Anhydride with Monomethylaniline.

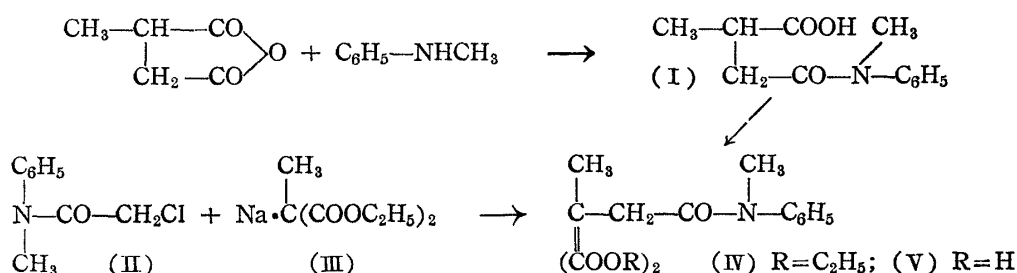
(Pharmaceutical Institute, Medical Faculty, University of Tokyo*)

In connection with other synthetical work now in progress in our hands we have to elucidate the structure of the condensation product of methylsuccinic anhydride with a secondary amine, a work not yet described in any literature.

The search of literature revealed, however, that the condensation between methylsuccinic anhydride and aniline has already been investigated by Morell.¹⁾ According to this author methylsuccinic anhydride and aniline gave a single methylsuccinilic acid of m.p. 159°, when the two components were heated either in benzene or in chloroform, but when N-phenylmethylsuccinimide, the condensation product of the two components at a higher temperature, was hydrolyzed, there were obtained two kinds of methylsuccinilic acids of m.p. 159° and 123°, depending upon the hydrolyzing conditions. He, however, did not determine the structure of these amido-acids.

Taking methylaniline as a typical example of aromatic secondary amines, it was heated with methylsuccinic anhydride in absolute benzene. A single substance of m.p. 157~159°, which was raised to 162~163° after purification from ethanol, was obtained in 85% yield. The presence of an isomeric amido-acid was examined in the filtrate and the ethanolic mother liquor of purification, but without effect, so we can assume that the reaction took the single course. The structure of the reaction product was proved to be β -carboxybutyryl-N-methylanilide (I) as follows.

Chloroaceto-N-methylanilide (II) was condensed with diethyl methylmalonate (III), furnishing β,β -bis(ethoxycarbonyl)butyryl-N-methylanilide (IV). The latter was hydrolyzed and then decarboxylated to give β -carboxybutyryl-N-methylanilide (I) of m.p. 162~163°, which was not depressed when admixed with the one of the same melting point mentioned above.



The behavior of methylsuccinic anhydride toward aliphatic secondary amines was studied taking ethyl sarcosinate as an example. Although the product was not analyzed, here again it was found that it was with a carboxyl group beta to the methyl substituent that took part in the amido-formation.

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Experimental

β -Carboxybutyryl-N-methylanilide (I)—(1) Condensation of methylsuccinic anhydride and

* Hongo, Tokyo (赤星三彌, 鈴木真言).

1) Morell: J. Chem. Soc., **105**, 2699(1914).

methylaniline : Methylsuccinic anhydride²⁾(5g.) and equimolecular proportion of methylaniline³⁾(4.7g.) were mixed in pure benzene (10 cc.) with evolution of heat. After some time crystalline solid begun to separate. The reaction was accelerated by heating ca. 3 hrs. on a steam bath. On cooling the resultant crystalline solid was collected on a filter and washed with a little cold benzene. The combined benzene solution was refluxed again, yielding some more solid and this procedure was repeated twice more, until separation of the solid was not observed. The solid substances from every batch were proved to be one and the same by direct comparison. Yield, ca. 85% of m.p. 157~159°. Purified from aq. EtOH, forming colorless minute pillars of m.p. 162~163° *Anal.* Calcd. for C₁₂H₁₅O₃N : C, 65.1; H, 6.8; N, 6.3. Found : C, 64.9; H, 6.9; N, 6.35.

(2) By synthesis : Na powder (0.15g.) prepared in abs. xylene was added with diethyl methylmalonate (4.3g.), forming yellowish fluffy sodium derivative of the latter. Chloroaceto-N-methylanilide (4.5g.) in xylene was now added slowly, causing vigorous reaction. The whole was then refluxed for 5 hrs., and then worked up as usual. The main product (IV) was a yellow viscous oil of b.p._{0.15} 174~176°; yield, 5.3g. or 68%.

When this ester was hydrolyzed by boiling with NaOH either in water or in EtOH, the amide linkage was also split off, recovering methylaniline. Selective hydrolysis of the ester groups was achieved by standing with 3% methanolic KOH at room temperature (15~18°) overnight. After addition of water, MeOH was evaporated *in vacuo*, acidified with dil. H₂SO₄, and the liberated acid (V) was extracted with ether, dried, and evaporated, leaving faint yellow viscous syrup. Since this acid or its salt was not obtained crystalline, the acid was directly decarboxylated by heating toward 160~170°. Vigorous effervescence ensued, which subsided after about 15 mins. On cooling, a semisolid substance was obtained, which solidified completely on being triturated with petroleum ether. Purified from aq. EtOH, forming colorless rhombic pillars of m.p. 161~162°, which was not depressed when admixed with the specimen obtained above.

Condensation of methylsuccinic anhydride with ethyl sarcosinate : Two components in equimolecular amounts were heated in xylene as in the former case. The product was not obtained in crystalline condition and so it was esterified and purified by distillation, giving faint yellow oil of b.p._{0.05} 153~154°, yield 67%. The hydrolysis of the ester was effected by standing with 3% methanolic NaOH, giving a dicarboxylic acid of m.p. 106~107°, after being purified from dil. EtOH, in a poor yield.

On the other hand, ethyl chloroacetosarcosinate (b.p.₅ 135~136°) was condensed with sodium salt of diethyl methylmalonate, the condensation product was then hydrolyzed, yielding a dicarboxylic acid of m.p. 104~105°, which remained at 103~105° when admixed with the specimen obtained above.

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2) cf. *Org. Syntheses*, **26**, 54.

3) Prepared according to Pachter : *J. Am. Chem. Soc.*, **74**, 1321(1952).