[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

DIACETYLATION OF *m*-XYLENE

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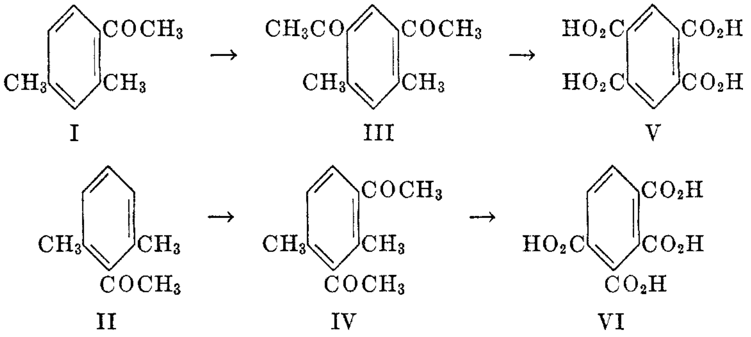
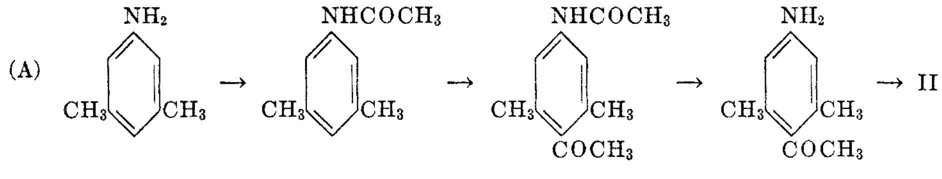
Acetylation of *m*-xylene with acetyl chloride and aluminum chloride produces, in addition to the expected 2,4-dimethylacetophenone (I), a small amount of a diacetyl compound believed by its discoverers, Meyer and Pavia, to be 1,3-diacetyl-2,4-dimethylbenzene (IV) (1). Reasoning by analogy with the ready formation of diacetylmesitylene (2), these investigators suggested that the diketone was formed by way of 2,6-dimethylacetophenone (II) which, unlike the major product, 2,4-dimethylacetophenone (I), might be expected to undergo acetylation readily. Additional evidence in favor of this structure for the ketone was provided by Klages and Lickroth (3). However, subsequent studies (4), including the preparation of the diketone from 2,4-dimethylacetophenone (I) (5) and degradation of the diketone to benzene-1,2,4,5-tetracarboxylic acid (V) (6), provide ample evidence that the compound prepared by Meyer and Pavia is in reality 1,3-diacetyl-4,6-dimethylbenzene (III).

The facile diacylation of mesitylene has been ascribed to steric inhibition of the resonance interaction of the carbonyl group and the ring (7, 8), which would operate to mitigate the deactivating effect of the acyl group of acetomesitylene. As a test of this hypothesis the two dimethylacetophenones, 2,4-dimethylacetophenone (I) and 2,6-dimethylacetophenone (II), have been compared with respect to ease of acetylation. Only in the latter is the carbonyl group prevented from resonating with the benzene ring (8).





2,6-Dimethylacetophenone (II), previously prepared by de Jong (9) from

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2,6-dimethylaniline, has been synthesized from 3,5-dimethylaniline by reaction sequence *A*. The two dimethylacetophenones were subjected to the action of a carbon disulfide solution of acetyl chloride in the presence of anhydrous aluminum chloride. The hindered ketone gave the diacetyl compound in a yield of 54.9 % whereas the unhindered ketone failed to react. These results are in accord with the experience that the introduction of a second acyl group into an aryl nucleus is facilitated if the acyl group already present is flanked by two *ortho*-methyl groups.

The physical properties of the two diketones prepared are summarized in Table I. The following evidence is presented to establish the structure of the diketone prepared from 2,6-dimethylacetophenone (II) as 1,3-diacetyl-2,4-dimethylbenzene (IV). The presence of a second augmented carbonyl infrared absorption band is strongly indicative of the presence of a hindered acyl group. Also, the formation of only a monoxime suggests that one of the carbonyl groups is hindered. The fact that the oxime, even after repeated recrystallization, did not have a sharp melting point may mean that it is a mixture of the *syn* and *anti* forms. The diacetyl compound was oxidized with alkaline potassium permanganate to the corresponding tetracarboxylic acid (VI), which was completely esterified by treatment with diazomethane to give white needles melting at 128.5–129°. The infrared spectrum of the neutral ester is identical with that of an authenic sample of tetramethyl benzene-1,2,3,4-tetracarboxylate and differs significantly from the isomeric tetramethyl benzenetetracarboxylates.

TABLE I

PHYSICAL PROPERTIES OF THE ISOMERIC DIKETONES

KETONE ACETYLATED	M.P., °C.	CRYST. FORM	INFRARED ABSORPTION BANDS IN CARBONYL REGION
2,4-Dimethylacetophenone	106–107°	Needles	1679 cm^{-1}
2,6-Dimethylacetophenone	66.5–67.5°	Plates	1675 cm^{-1} 1700 cm^{-1}

The authors wish to acknowledge the assistance of Dr. C. B. Purves, who kindly supplied authentic samples of the various tetramethyl benzenetetracarboxylates.

EXPERIMENTAL PART[2]

3,5-Dimethyl-4-acetylacetanilide. The acetylation of 10.0 g. of 3,5-dimethylaniline was effected by use of the procedure of Haller, Adams, and Wherry (11). The yield of 3,5-dimethylacetanilide was 11.4 g. (84.5%) of white plates; m.p. 138–140°. To 9.3 g. of the anilide and 7.0 g. of acetyl chloride in 60 ml. of dry carbon disulfide was added slowly, with stirring, 23 g. of anhydrous aluminum chloride. The resulting mixture was boiled under reflux, with stirring, for 30 minutes and allowed to stand 4 hours. The carbon disulfide

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[2] All melting points are corrected. Microanalyses are by Mrs. Katherine Pih, Miss Emily Davis, and Mrs. Jeanne Fortney. The infrared spectra were determined and interpreted by Miss Helen Miklas.

layer was decanted and the residual complex decomposed by pouring on a mixture of ice and hydrochloric acid. The solid, collected on a filter, was taken up in boiling ethanol and decolorized with Norit. The solvent was removed from the resulting solution under an air blast. The yield was 11.6 g. (98%) of light-cream colored solid; m.p. 143–146°. A portion of the material was recrystallized from ethanol to give white plates; m.p. 145–147°.

Anal. Calc'd for $C_{12}H_{15}NO_2$: C, 70.19; H, 7.36; N, 6.82.
Found: C, 70.43; H, 7.45; N, 6.92.

2,6-Dimethyl-4-aminoacetophenone. A solution of 10.0 g. of 3,5-dimethyl-4-acetylacetanilide in 40 ml. of ethanol and 30 ml. of concentrated hydrochloric acid was boiled under reflux for 15 hours. When the cold reaction mixture was made alkaline to litmus with 10% aqueous sodium hydroxide, 6.7 g. (85%) of light tan crystals precipitated; m.p. 112–115°. A solution of the material in boiling ethanol was decolorized with Norit. Recrystallization of the compound from an ethanol-water mixture gave white plates; m.p. 114–115.5°.

Anal. Calc'd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58.
Found: C, 73.79; H, 8.15; N, 8.40.

2,6-Dimethylacetophenone (9). To 9.0 g. of 2,6-dimethyl-4-aminoacetophenone in 25 ml. of ethanol and 80 ml. of concentrated hydrochloric acid, cooled to 0°, was added dropwise, with stirring, 3.8 g. of sodium nitrite in 25 ml. of water. To the resulting solution was added 52 ml. of 50% hypophosphorous acid. The mixture was gradually warmed to 95° and then steam-distilled until all the ketone was removed from the reaction mixture. The distillate was extracted with 200 ml. of ethyl ether and the extract dried over calcium chloride. The solvent was removed from the extract on a steam-bath and the residue distilled *in vacuo* to yield 4.76 g. (58%) of the colorless ketone; b.p. 96–99° (13 mm.); n_D^{20} 1.5150 (10). The material solidified only when cooled below room temperature. The melting point recorded by deJong is 23.0–23.6°.

Acetylation of 2,4-dimethylacetophenone. The 2,4-dimethylacetophenone was purified by distillation *in vacuo*; b.p. 107–108° (12 mm.); n_D^{20} 1.5330 (12). To 3.00 g. of the 2,4-dimethylacetophenone and 2.4 g. of acetyl chloride in 60 ml. of dry carbon disulfide was added, with stirring, 8 g. of anhydrous aluminum chloride. The mixture was boiled under reflux, with stirring, for 2 hours and allowed to stand 30 minutes. The carbon disulfide layer was decanted and the residual complex decomposed by pouring on a mixture of ice and hydrochloric acid. The resulting mixture was extracted with 200 ml. of ethyl ether, the extract dried over calcium chloride, and the solvent removed from the extract on a steam-bath. The residual brown oil was distilled *in vacuo* to yield 2.00 g. of colorless liquid; b.p. 106–110° (12 mm.); n_D^{20} 1.5337. The liquid remaining in the pot was taken up in boiling petroleum ether (b.p. 90–120°) and decolorized with Norit. No solid could be obtained, so the solvent was removed under an air blast. The liquid residue, distilled *in vacuo,* gave 0.1 g. of yellow oil; n_D^{20} 1.5340. The total amount of ketone recovered was 2.10 g. (70%). A trace of yellow needles, presumably the diketone, remained in the delivery tube after the distillation. The amount present was insufficient for purification and a subsequent melting point determination.

Acetylation of 2,6-dimethylacetophenone. To 4.61 g. of 2,6-dimethylacetophenone and 6.6 g. of acetyl chloride in 60 ml. of dry carbon disulfide was added, with stirring, 20.7 g. of anhydrous aluminum chloride. The mixture was boiled under reflux, with stirring, for 2 hours and allowed to stand for 30 minutes. After decantation of the carbon disulfide layer, the residual complex was decomposed by pouring on a mixture of ice and hydrochloric acid. The resulting mixture was extracted with 200 ml. of ethyl ether and the solvent was removed from the extract on a steam-bath. The residual oil, which solidified on standing, was taken up in boiling petroleum ether (b.p. 90–120°) and, after being decolorized with Norit, was chilled. It crystallized as white plates; yield 2.94 g. Evaporation of the mother liquor to one-half its original volume gave an additional crop of crystals weighing 0.10 g. The solvent was removed from the mother liquor under an air blast and the residue distilled *in vacuo* to give 0.88 g. (19%) of a colorless liquid; b.p. 99–108° (11 mm.); n_D^{20} 1.5238. As the refractive index indicates, the recovered ketone was impure. The residual material from the vacuum distillation was taken up in boiling petroleum ether (b.p. 90–120°) and decolorized with Norit. The cool solution deposited an additional 0.22 g. of crystalline product. The total yield was 3.26 g. (54.9%) of white plates; m.p. 66–67.5°. A second recrystallization from petroleum ether (b.p. 90–120°) gave white plates; m.p. 66.5–67.5°. The infrared spectrum of the diketone exhibits two absorption bands in the carbonyl region; one at 1675 cm^{-1} and the other at 1700 cm^{-1}.

Anal. Calc'd for $C_{12}H_{14}O_2$: C, 75.72; H, 7.41.
Found: C, 75.87; H, 7.55.

Preparation of the monoxime. A solution of 0.30 g. of the above diacetyl-*m*-xylene and 0.33 g. of hydroxylamine hydrochloride in 3 ml. of pyridine and 3 ml. of commercial absolute ethanol was boiled under reflux for 2 hours. The solvent was evaporated under an air blast and the residue extracted with boiling petroleum ether (b.p. 90–120°). The cool extract deposited white crystalline material melting at 119–129°. Two additional recrystallizations from petroleum ether (b.p. 90–120°) gave white plates; m.p. 120–129°. The infrared spectrum of the compound exhibits an absorption band at 1685 cm^{-1}, attributable to a carbonyl group; a second at 1647 cm^{-1}, attributable to an imino group; and a third at 3365 cm^{-1}, attributable to a hydroxyl group.

Anal. Calc'd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.83.
Found: C, 70.40; H, 7.55; N, 7.05.

1,3-Diacetyl-4,6-dimethylbenzene. The acetylation of 2,4-dimethylacetophenone was effected in very poor yield, according to the procedure of Wulff (5), to give colorless needles, m.p. 106–107°, after two recrystallizations from petroleum ether (b.p. 90–120°). The melting point previously recorded is 108° (1, 5). The only infrared absorption band in the carbonyl region is at 1679 cm^{-1}.

Oxidation of the lower-melting diacetyl-m-xylene and esterification of the resulting acid. A mixture of 1.00 g. of the diketone, 4.0 g. of potassium permanganate, 1 ml. of 10% aqueous sodium hydroxide, and 80 ml. of water was boiled under reflux for 2 hours. The reaction mixture was neutralized with concentrated hydrochloric acid, made alkaline to litmus with 10% aqueous sodium hydroxide, and filtered. To the filtrate was added an excess of aqueous barium chloride solution, and the precipitate was collected. The solid material was acidified with dilute hydrochloric acid and the resulting solution was continuously extracted with ethyl ether for 46 hours. After removal of the solvent from the extract on a steam-bath, the brown solid which remained was taken up in 100 ml. of ethyl ether and dried over magnesium sulfate. The dry ethereal solution, after being cooled, was added, drop-wise with shaking, to a cold ethereal solution of diazomethane, prepared from 7.0 g. of N-nitrosomethylurea (13). The reaction mixture was allowed to stand for 30 minutes, then warmed on a steam-bath to remove the ether and excess diazomethane. A methanol solution of the residue was decolorized with Norit after which the solvent was removed under an air blast. The material remaining was suspended in 75 ml. of 5% aqueous sodium bicarbonate and extracted with two 50-ml. portions of ethyl ether. The residue, obtained by removal of the solvent on a steam-bath, was taken up in a boiling methanol-water mixture and decolorized with Norit. The cool solution deposited white needles; m.p. 117–125°. Two additional recrystallizations from acetone-petroleum ether (b.p. 30–60°) mixtures gave long white needles; m.p. 128.5–129°. The infrared spectrum of the material was compared with the spectra of authentic samples of the neutral methyl esters of benzene-1,2,3,4-tetracarboxylic acid, benzene-1,2,3,5-tetracarboxylic acid, and benzene-1,2,4,5-tetracarboxylic acid and found to be identical with the 1,2,3,4-isomer. Previous melting points recorded for tetramethyl benzene-1,2,3,4-tetracarboxylate are 128–130° (14), 129–130° (15), 129–131° (16), 130–131° (17), 131–133° (18), and 133–135° (19).

SUMMARY

2,4-Dimethylacetophenone is not attacked by acetyl chloride under the conditions of Friedel and Crafts. Under comparable conditions, 2,6-dimethylace-

tophenone is readily acylated to give 1,3-diacetyl-2,4-dimethylbenzene whose structure has been established.

A new synthesis of 2,6-dimethylacetophenone has been developed.

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