

washed and dried; it distilled at 110 to 170° (ca. 0.5 mm.). The distillate was heated for three hours with a fresh 15-cc. portion of nitric acid. The product was isolated, dissolved in ether, washed and dried. Evaporation of the ether gave the bright yellow diketone, which was recrystallized from aqueous methyl alcohol, m. p. 58–59°.

Anal. Calcd. for $C_{15}H_{19}O_4N$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.87; H, 7.03; N, 5.15.

Like the xylyl analog this diketone failed to give a quinoxaline. Even after fifteen hours' treatment the diketone was almost entirely recovered.

β,β,β -Trimethylatrolactic Acid.—One cubic centimeter of *t*-butyl phenyl diketone was added to a solution of 2 g. of potassium hydroxide and 1 cc. of ethyl alcohol in 10 cc. of water. This mixture was refluxed until a clear solution was obtained (about six hours). Acidification with hydrochloric acid precipitated an oily material which was separated and treated with low-boiling petroleum ether. The white solid acid which separated was removed by filtration and recrystallized from high-boiling petroleum ether, m. p. 105–106°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75; neut. equiv., 208. Found: C, 69.33; H, 7.95; neut. equiv., 208.

Dibenzoate of *t*-Butylphenylacetylene Glycol.—A mixture of 0.26 g. of sodium, 20 cc. of dry toluene and 1 cc. of *t*-butyl phenyl diketone was refluxed in an atmosphere of nitrogen for two hours, with vigorous stirring. After addition of 1.25 cc. of benzoyl chloride, the dark brown reaction mixture was heated and stirred for a few minutes

and then cooled to room temperature. The excess sodium and the precipitated sodium chloride were removed by filtration and the filtrate was concentrated to a viscous brown oil. The dibenzoate was recrystallized from high-boiling petroleum ether, m. p. 138–139°.

Anal. Calcd. for $C_{26}H_{26}O_4$: C, 77.98; H, 6.04. Found: C, 77.96; H, 6.12.

Summary

t-Butylglyoxal condenses with benzene, toluene, *m*-xylene and mesitylene to give acyloins of the type $(CH_3)_3CCOCH(OH)Ar$. Oxidation with nitric acid converts the acyloins to the corresponding diketones. In the case of the mesityl compound the diketone is isolated in the form of its mononitro derivative.

The diketones derived from benzene and toluene react normally with *o*-phenylenediamine to give quinoxalines. This reaction could not be effected with the *m*-xylyl or mesityl diketones.

t-Butyl phenyl diketone undergoes the benzilic acid rearrangement to give β,β,β -trimethylatrolactic acid. The sodium derivative of this diketone reacts with benzoyl chloride to give the dibenzoate of *t*-butylphenylacetylene glycol. The two foregoing types of reaction hitherto had been restricted to benzils and aliphatic 1,2-diketones.

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The Methylation of β -Ketonitriles

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The discovery that α -cyanoacetomesitylene (IV) and α -cyanopropiomesitylene gave only O-methylation products¹ suggested that the steric hindrance present in these β -ketonitriles favored O-methylation.² As a test of this suggestion an unhindered β -ketonitrile, *p*-bromophenacyl cyanide (I), has been methylated under similar conditions. It reacted with methyl sulfate in the presence of aqueous potassium hydroxide to give the O-methyl ether (II). When the alkylating agent was methyl iodide in the presence of sodium ethoxide, a different compound, the C-methylated product (III), was formed.

The structure of the enol methyl ether (II) was established by analysis for methoxyl and by its

(1) Fuson, Ulyot and Gehrt, *THIS JOURNAL*, **60**, 1199 (1938).

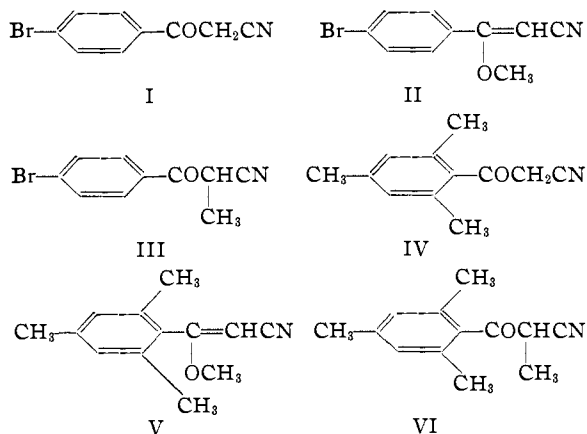
(2) This idea was developed by Kohler and his co-workers in connection with mesityl ketones. For a leading reference see Kohler and Thompson, *ibid.*, **59**, 887 (1937).

insolubility in alkali. Both the parent compound (I) and the C-methylated derivative (III) are soluble in 10% sodium hydroxide solution and in 10% sodium carbonate solution. Compound III was hydrolyzed easily to give *p*-bromobenzoic acid. When allowed to stand for some time it decomposed spontaneously, probably by auto-oxidation of its enol—a phenomenon previously noted for compounds of this type.³

The structure of the C-methylated product, α -(*p*-bromobenzoyl)-propionitrile (III), was established by synthesis, employing the method used by Dorsch and McElvain⁴ for similar compounds. Ethyl *p*-bromobenzoate was condensed with propionitrile in the presence of sodium ethoxide. The product proved to be α -(*p*-bromobenzoyl)-propionitrile (III).

(3) Jenkins, *ibid.*, **57**, 2733 (1935).

(4) Dorsch and McElvain, *ibid.*, **54**, 2960 (1932).



The formation of the O-methylated derivative (II) of an unhindered phenacyl cyanide is not without precedent since Arndt and his co-workers⁵ have reported recently that phenacyl cyanide reacts with diazomethane to give *trans*- β -methoxycinnamionitrile. The formation of the C-methylated derivative (III) by the method employed here seems to be a new reaction.

Inasmuch as the experimental conditions used in methylating *p*-bromophenacyl cyanide were not entirely parallel with those used by Fuson, Ulliot and Gehrt¹ in working with α -cyanoacetomesitylene, a further study was made of the latter (IV). It was found that when the methylating agent was methyl iodide in the presence of sodium ethoxide both O-methylated (V) and C-methylated (VI) derivatives were obtained in nearly equivalent amounts.

Two crystalline forms of the β -methoxy- β -methylacrylonitrile (V) were isolated. The identity of each was established by mixed melting points with authentic samples prepared by Fuson, Ulliot and Gehrt.¹ The structure of α -cyano-propomesitylene (VI) was established by the synthesis of this compound, using the method described by Fuson, Ulliot and Gehrt.¹

It therefore appears that the steric hindrance present in α -cyanoacetomesitylene favors O-methylation but not to the complete exclusion of C-methylation.

Experimental

***p*-Bromophenacyl Cyanide (I).**—The method used by Grothaus and Dains⁶ for the preparation of this compound from *p*-bromophenacyl chloride and sodium cyanide was not found satisfactory when *p*-bromophenacyl bromide

(5) Arndt, Loewe, Günter and Sepahi, *Ber.*, **71B**, 1627 (1938); Arndt, Loewe, Özsoy, Ogüt, Arslan and Bagevi, *ibid.*, **71B**, 1631 (1938).

(6) Grothaus and Dains, *THIS JOURNAL*, **58**, 1334 (1936).

was the starting material. The method accordingly was modified as follows. Ten grams of *p*-bromophenacyl bromide was dissolved in about 400 cc. of 95% ethanol. To this solution was added, dropwise and with stirring, a solution of 4.7 g. of potassium cyanide in the minimum amount of water. The reaction mixture was stirred for five hours at room temperature during which time a white crystalline precipitate formed, and then for one hour in an ice-salt bath. The precipitate was collected on a filter and dissolved in water. The cloudy aqueous solution was clarified with Darco. Treatment with hydrochloric acid gave 6 g. of a fine white precipitate of *p*-bromophenacyl cyanide (m. p. 162–163°) sufficiently pure for use.

Methylation of *p*-Bromophenacyl Cyanide with Methyl Sulfate.—A mixture of 2 g. of dry *p*-bromophenacyl cyanide and 4.6 g. of methyl sulfate was heated under reflux to 70° and 3 g. of potassium hydroxide in 40 cc. of water was added slowly, with stirring, over a fifteen-minute period while the bath temperature was raised from 70 to 130°. A yellow oil separated during the addition of potassium hydroxide solution. One and thirty-five hundredths grams of methyl sulfate was added and the heating continued for five minutes. The container was surrounded by an ice-bath and 1 g. of potassium hydroxide in 150 cc. of water was added. The yellow oil solidified leaving a clear solution. The oily solid was dried and treated with petroleum ether. The insoluble portion was starting material melting at 162–163°. The petroleum ether solution was washed with potassium carbonate solution and the solvent evaporated. The crude methoxy nitrile (II) weighed about 0.7 g. and melted at 56–58°. It was recrystallized twice from high boiling petroleum ether and melted at 58.5–59.5°.⁷

Anal. Calcd. for $C_{10}H_8BrNO$: C, 50.46; H, 3.39; OCH₃, 13.03. Found: C, 50.49; H, 3.33; OCH₃, 12.94, 12.92.

No other product could be detected.

Methylation of *p*-Bromophenacyl Cyanide with Methyl Iodide and Sodium Ethoxide.—To a solution of 0.35 g. of clean sodium in 100 cc. of absolute ethanol was added 3.45 g. of dry *p*-bromophenacyl cyanide. The reaction mixture was heated, with stirring, until it refluxed gently. Not all the solid was in solution. A solution of 3.5 cc. of methyl iodide in 40 cc. of absolute ethanol was added slowly, with stirring. The remaining solid dissolved. Refluxing was continued until samples of the reaction mixture gave a neutral test with moist litmus paper (one to one and a half hours).

The solution was concentrated to 25 cc. and the concentrate cooled to 0°. Forty cubic centimeters of ice water was added followed by 40 cc. of ether, and the solution was shaken to dissolve the solid. A few drops of 10% sodium hydroxide solution were necessary to bring about complete solution. The aqueous layer was separated and acidified with dilute sulfuric acid, giving a solid and an oil. Treatment with ether dissolved the precipitate. The ether extract was washed with saturated sodium bicarbonate solution to remove any *p*-bromobenzoic acid, then with water and finally was dried over anhydrous sodium sulfate. The solvent was evaporated yielding an oil which crystallized

(7) The melting points reported in this paper have all been corrected.

when cooled. The product was difficult to purify because when it was heated with methyl alcohol or aqueous sodium carbonate it decomposed to give *p*-bromobenzoic acid. Purification was accomplished by dissolving the solid in cold sodium carbonate solution (10%), decolorizing with Darco and very carefully precipitating the product by addition of dilute sulfuric acid to the solution at 0° until the first appearance of turbidity. A pure product was also obtained from aqueous methanol when heating was avoided. The pure ketonitrile (III) melted at 74.5–75.5°.

Anal. Calcd. for $C_{10}H_8BrNO$: C, 50.46; H, 3.39. Found: C, 51.06; H, 3.49.

A Zeisel determination showed the absence of a methoxy group.

The identity of the *p*-bromobenzoic acid resulting from the decomposition of the C-methyl derivative (III) was verified by a neutral equivalent determination and a mixed melting point with an authentic sample.

Synthesis of α -(*p*-Bromobenzoyl)-propionitrile (III).—A mixture of 23 g. of ethyl *p*-bromobenzoate and 6.8 g. of sodium ethoxide was warmed under reflux to 80° and stirred until it became homogeneous. Seven grams of propionitrile was added slowly, with stirring, to this mixture over a period of half an hour. Following the addition of propionitrile the temperature of the mixture was raised to 110–120° and maintained at this point for ten hours, with continuous stirring.

The reaction mixture was cooled to 0°, treated with 40 cc. of ice water and 100 cc. of ether, and shaken until the solid was dissolved. The aqueous layer was separated and acidified with dilute sulfuric acid, giving an oil and a white solid. The insoluble material was extracted with ether and washed three times with saturated sodium bicarbonate solution, then once with water, and the ether solution dried over anhydrous sodium sulfate.

When the ether was evaporated a tan oil was left which yielded crystals when cooled. The crude product was dissolved in 10% sodium carbonate solution, decolorized with Darco and precipitated by careful addition of dilute sulfuric acid to the ice cold solution until the appearance of turbidity. The melting point of the pure α -(*p*-bromobenzoyl)-propionitrile was 74.5–75.5°.

A mixed melting point with the ketonitrile (III) prepared by methylation of *p*-bromophenacyl cyanide was 74.5–75.5°.

Anal. Calcd. for $C_{10}H_8BrNO$: N, 5.89. Found: N, 5.83.

Methylation of α -Cyanoacetomesitylene with Methyl Iodide.—To a solution of 0.615 g. of clean sodium in 200 cc. of absolute ethanol was added 5 g. of α -cyanoacetomesitylene. The reaction mixture was stirred and heated until it refluxed gently, precautions being taken to preserve anhydrous conditions. To the refluxing solution was added slowly 6.7 cc. of methyl iodide dissolved in 25 cc. of absolute ethanol. Refluxing was continued for two hours following addition of the methyl iodide; at the end of this time the reaction mixture gave no basic test with moist red litmus paper.

The solution was concentrated to 50 cc., cooled in an ice-

bath and poured into 100 cc. of ice water to which 5 cc. of a 10% sodium hydroxide solution had been added. The mixture was shaken with 100 cc. of ether.

The ether layer was separated and shaken with a 10% sodium carbonate solution to take out any alkali-soluble material which might be present. The ether was then dried over sodium sulfate and evaporated, giving an oil. Crystallization was brought about when methanol was added and the solution was immersed in a dry-ice-acetone bath. The crude O-methylated product (V) thus obtained melted at 64–65.5° and weighed about 0.85 g. A small amount of oil remained from which no solid product could be obtained even on long standing dissolved in ligroin. Compound V was dissolved in ligroin and allowed to crystallize slowly. The first crop consisted of small rhombic crystals which melted at 65.5–66°. This was evidently the *cis* form identical with the low melting form obtained by Fuson, Ullyot and Gehrt.¹ A mixed melting point with a sample of their compound confirmed the identity. On longer standing a second crop of crystals appeared, this time in rosetts of needles melting at 68–69°. These were the mixed-crystal form consisting of both *cis* and *trans* isomers. A mixture with an authentic sample of the same form showed no lowering of the melting point.

The aqueous layer and the sodium carbonate solution employed to wash the ether layer above were treated as follows. The solution was acidified with dilute sulfuric acid and the precipitate extracted with ether. The ether was dried over sodium sulfate and evaporated, leaving an oil which crystallized to colorless plates on standing in an ice box. The crude material melted at about 126°. It was dissolved in cold 10% sodium carbonate solution, cooled in an ice-bath and acidified to the first permanent turbidity with dilute sulfuric acid. Approximately 0.9 g. of white crystals (VI) was thus obtained melting at 127–128.5°. Addition of more sulfuric acid caused the precipitation of about 0.5 g. more of solid material which proved to be mainly starting material. Compound VI was further purified by recrystallization from aqueous methanol giving small white crystals melting at 130–131°. A mixed melting point with a sample synthesized by the method of Fuson, Ullyot and Gehrt¹ showed no lowering.

Summary

1. It has been shown that *p*-bromophenacyl cyanide reacts with methyl sulfate in the presence of potassium hydroxide to yield the O-methyl ether (II). When the alkylating agent was methyl iodide in the presence of sodium ethoxide the C-methyl derivative (III) was obtained.

2. α -Cyanoacetomesitylene when treated with methyl iodide in the presence of sodium ethoxide has been found to yield roughly equal quantities of the O-methylated derivative (V) and the C-methylated derivative (VI).