yellow needles, m. p. 182–183° with preliminary softening. *Anal.* Calcd. for $C_{15}H_{10}O_3N_3Br$: Br, 22.2. Found: Br, 22.5.

3-(4-Bromoanilino)-5-phenylpyrazole.—The new pyrazole was prepared with hydrazine in a manner similar to that used for the isoxazole. The product after crystallization from chlorohydrin was dissolved in boiling alcohol and concd. hydrochloric acid added dropwise. The resulting colorless precipitate, filtered while warm, was washed thoroughly with water; yield 4–5 g. It separated from dilute alcohol as lustrous small plates, m. p. 176–177°. *Anal.* Calcd. for $C_{15}H_{12}N_3Br$: Br, 25.5. Found: Br, 25.4. Bromine changed this substance into a tribromo derivative identical with that obtained from the nonhalogenated pyrazole. Oxidation of this tribromo derivative in one instance using permanganate produced a small amount of material, probably the monoanilide of oxalic acid, soluble in alkali and precipitated by acid, m. p. approx. 130° with foaming. It was decomposed by boiling with dilute acid into 2,4-dibromoaniline identified by a mixed melting point and oxalic acid.

3-(2-Chloro-4-bromoanilino)-4-chloro-5-phenylpyrazole was prepared by the action of chlorine on the above pyrazole. It separated from alcohol as needles, m. p. 197–198°. *Anal.* Calcd. for $C_{15}H_{10}N_3BrCl_2$: Cl, 18.6. Found: Cl, 18.5. A nitro derivative was obtained from the pyrazole, but because of a poor analysis is not listed.

Summary

It has been shown that 3-anilino-5-phenylisoxazole and pyrazole form substitution products with chlorine or bromine and nitric acid in which position four of the heterocyclic ring and positions two and four of the aniline group are involved.

Medford, Mass. Received February 28, 1938

[Contribution from the Chemical Laboratory of the University of Illinois]

β-Methoxy-β-mesitylacrylonitriles

By Reynold C. Fuson, G. E. Ullyot and A. J. Gehrt

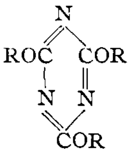
β-Alkoxyacrylonitriles (I) are little known, and no general method is available for their preparation. The present paper reports the synthesis of certain β-methoxy-β-mesitylacrylonitriles and gives a proof of their structures. This study was initiated with the hope of throwing some light on the behavior of the vinylogous alkyl cyanates (II) which have never been isolated. Apparently the cyanates trimerize rapidly to give alkyl cyanurates (III).

RO—CH=CH—CN

I

ROCN

II

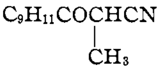


III

The method of synthesis is due to the discovery of Kohler and his co-workers[1] that the mesityl group favors O-alkylation. It was found, in fact, that α-cyanoacetomesitylene (IV) and α-cyanopropiomesitylene (V) gave exclusively O-methylation products.

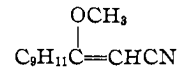
$C_9H_{11}COCH_2CN$

IV



$C_9H_{11}COCH(CH_3)CN$

V



$C_9H_{11}C(OCH_3)=CHCN$

VI (a, b, c)

While the mesityl group on the β-carbon atom would be expected to inhibit addition to the olefinic linkage, it was thought that the reactions due to the cyano group and to the methoxyl group might resemble those ascribed to methyl cyanates. This expectation was, however, not realized; the β-methoxy-β-mesitylacrylonitriles are very stable and, in particular, show no tendency to polymerize.

The unsubstituted β-mesityl-β-methoxyacrylonitriles (VI) were made by methylation of α-cyanoacetomesitylene prepared by the method of Fuson and Beveridge.[2] The reaction was carried out by two different procedures. The first involved the use of methyl sulfate in aqueous potassium hydroxide. It yielded two forms of the enol ether which melted at 66° (VIa) and 82.5–83.5° (VIb).

The second method of methylation consisted in treating IV with methyl iodide and silver oxide. Here, also, the product consisted of the isomers VIa and VIb. Under certain circumstances these forms appeared as a solid solution melting at 67–68° (VIc). For example, when a mixture of equal amounts of VIa and VIb was fused and then dissolved in high-boiling petroleum ether and the solution allowed to cool, the crystals which formed consisted entirely of VIc.

Treatment with alcoholic hydrochloric acid converted VIb and VIc into VIa. These three forms of the enol ether (VIa, VIb, VIc) when

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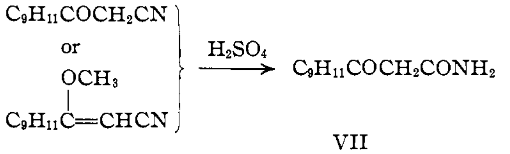
[1] Kohler, Tishler and Potter, This Journal, **57**, 2517 (1935); Kohler and Potter, *ibid.*, **58**, 2166 (1936); Kohler and Thompson, *ibid.*, **59**, 887 (1937).

[2] Fuson and Beveridge, *ibid.*, **53**, 1985 (1931).

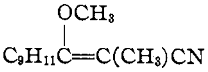
hydrolyzed by treatment with concentrated sulfuric acid gave the same product, 2,4,6-trimethylbenzoylacetamide (VII). This amide results when α-cyanoacetomesitylene itself is subjected to the sulfuric acid treatment. Zeisel determinations showed each form to have one methoxyl group. From these facts it was concluded that VIa and VIb are the *cis* and *trans* forms of the enol methyl ether.



$$\left.\begin{array}{l} C_9H_{11}COCH_2CN \\ \text{or} \\ C_9H_{11}\overset{OCH_3}{\overset{|}{C}}{=}CHCN \end{array}\right\} \xrightarrow{H_2SO_4} C_9H_{11}COCH_2CONH_2$$

VII

α-Cyanopropiomesitylene (V) was synthesized by condensing mesitylene with α-cyanopropionyl chloride. Methylation with methyl sulfate in aqueous potassium hydroxide gave a product which had one methoxyl group and to which was assigned the formula of the enol ether (VIII).



$$C_9H_{11}\overset{OCH_3}{\overset{|}{C}}{=}C(CH_3)CN$$

VIII

Experimental Part

β-Methoxy-β-mesitylacrylonitriles (VI).—These enol ethers were prepared by methylation of α-cyanoacetomesitylene (IV).

1. Methylation with Methyl Sulfate and Potassium Hydroxide.—One hundred cubic centimeters of water, 133.6 g. of methyl sulfate and 100 g. of IV were placed in a three-necked flask equipped with a mercury-sealed stirrer, a reflux condenser and a dropping funnel. Eighty-nine grams of potassium hydroxide dissolved in 800 cc. of water was added over a period of one hour to the well-stirred contents of the reaction flask. An oil formed on the surface of the reaction mixture and solidified on cooling. This was collected, dried and crystallized from high-boiling ligroin: yield, 88 g.; m. p. 67–68° (VIc).

Anal. Calcd. for $C_{13}H_{15}ON$: C, 77.67; H, 7.5; N, 6.96; OCH_3, 15.47; mol. wt., 201. Found: C, 77.6; H, 7.42; N, 7.07; OCH_3, 15.3, 15.0; mol. wt. (Rast), 206.7.

It was found that variations from the above procedure gave a product melting at 64–66° which consisted of a mixture of the compound melting at 67–68° (VIc) and an isomeric enol methyl ether (VIa), melting at 66°. The isomers were separated by slow crystallization from a considerable volume of hot high-boiling ligroin. The lower melting compound (VIa) crystallized in large clumps of prisms whereas the isomer (VIc) crystallized as small needles in the form of rosets.

Anal. of the compound melting at 66° (VIa). Calcd. for $C_{13}H_{15}ON$: C, 77.67; H, 7.50; N, 6.96; OCH_3, 15.47. Found: C, 77.4; H, 7.77; N, 7.06; OCH_3, 15.7, 15.25.

2. Methylation by the Use of Silver Oxide and Methyl Iodide.—Twelve grams of IV, 14.8 g. of freshly prepared dry silver oxide, and 150 cc. of dry ether were placed in a three-necked flask equipped with a reflux condenser and a mercury-sealed stirrer. The mixture was stirred constantly throughout the reaction. Fifteen cubic centimeters of methyl iodide dissolved in 50 cc. of dry ether was added and the flask was warmed until a reaction began to occur. The mixture was stirred for two hours without heating and then refluxed one hour. The insoluble silver salts were removed by filtration and the filtrate was evaporated. The residual oil was crystallized from high-boiling ligroin. Colorless needles were obtained: yield, 5.1 g.; m. p. 82.5–83.5° (VIb).

Anal. Calcd. for $C_{13}H_{15}ON$: C, 77.67; H, 7.50; N, 6.96; OCH_3, 15.47; mol. wt., 201. Found: C, 77.77; H, 7.69; N, 7.13; OCH_3, 15.96, 16.48; mol. wt. (Rast), 210.9.

The filtrates from two preparations were combined and evaporated. After standing several days the residual oil partially crystallized. Six grams of solid was obtained from which 2.5 g. of VIc was isolated on crystallization from high-boiling ligroin.

Preparation of VIc from VIa and VIb.—A mixture of 1 g. each of VIa and VIb was melted in a flask and the melt was crystallized from high-boiling ligroin. The characteristic crystals of VIc were obtained, melting at 66–68°. A mixed melting point determination with VIc showed no depression.

Rearrangement of VIc and VIb into VIa.—A solution of 1 g. of VIc in 16 cc. of alcohol and 5 cc. of concentrated hydrochloric acid was heated under reflux for six hours and allowed to stand overnight. The alcohol was evaporated and water was added to the residue. Seven-tenths of a gram of crystals in the form of clumps of prisms was obtained; m. p. 64.5–65.5°. This was shown to be VIa by a mixed melting point determination.

Similar results were obtained on subjecting VIb to the same treatment.

Hydrolysis of the β-Methoxy-β-mesitylacrylonitriles (VIa, VIb and VIc) and of ω-Cyanoacetomesitylene (IV).—The procedure was that of Berger and Olivier:[3] 2 g. of VIc was dissolved in a mixture of 18 cc. of concd. sulfuric acid and 2 cc. of water. The solution was warmed at 50–55° for one hour and then poured into a beaker of ice water. The mixture was extracted with ether; the ether solution was washed with water, then dilute sodium carbonate solution and dried over sodium sulfate. The ether was evaporated, and the residue was crystallized from benzene containing a small amount of ligroin: yield of VII, 1.2 g.; m. p. 126–127°.

Anal. Calcd. for $C_{12}H_{15}O_2N$: C, 70.21; H, 7.36; N, 6.82. Found: C, 70.05, 70.31; H, 7.52, 7.51; N, 6.9.

The same product was obtained from VIa, VIb and IV by this procedure. Identification was made by a mixed melting point determination.

α-Cyanopropiomesitylene.—A mixture of 44.9 g. of aluminum chloride, 35.9 g. of mesitylene, and 200 cc. of dry carbon disulfide was placed in a three-necked flask equipped with a reflux condenser, mercury-sealed stirrer and a dropping funnel. Thirty-two grams of α-cyanopropionyl chloride, dissolved in 100 cc. of carbon disulfide.

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[3] Berger and Olivier, *Rec. trav. chim.*, **46**, 600 (1927).

was added dropwise to the reaction flask, and the mixture was refluxed seven hours. Continuous stirring was maintained. The reaction mixture was decomposed with ice and a little hydrochloric acid. The carbon disulfide layer was separated and washed with water. The aqueous layer was extracted with ether, and the extract was washed with water. The ether and carbon disulfide solutions were combined and dried over sodium sulfate. Removal of the solvent by distillation gave a dark red oil. High-boiling ligroin was added, and the mixture was cooled. A brown crystalline solid was obtained. The filtrate was diluted with ether, extracted with 10% sodium hydroxide solution and dried over sodium sulfate. The ether was removed, and the residue was distilled at atmospheric pressure. A small amount of propionitrile (b. p. 95–102°) and 10 g. of mesitylene (b. p. 160–164°) were obtained.

The brown solid was dissolved in 10% sodium hydroxide solution and the solution was extracted with ether, the aqueous solution was acidified and the solid was collected. This was crystallized by dissolving it in hot methyl alcohol, adding a little water and cooling. Further purification was effected by crystallization from benzene diluted with a little ligroin: yield 11.6 g.; m. p. 127–128°.

Anal. Calcd. for $C_{13}H_{15}ON$: C, 77.67; H, 7.5; N, 6.96. Found: C, 77.73, 77.35; H, 7.73, 7.68; N, 6.93, 7.15.

α-Methyl-β-methoxy-β-mesitylacrylonitrile (VIII).—Ten grams of α-cyanopropiomesitylene was dissolved in a solution of 16.6 g. of potassium hydroxide in 150 cc. of water. The solution was heated to boiling and 33.5 g. of methyl sulfate was added dropwise. The reaction mixture was boiled twenty minutes after the methyl sulfate was added. The mixture was cooled, a small amount of 10% potassium hydroxide was added and the mixture was extracted with ether. The ether solution was dried over calcium chloride and evaporated. The residue was crystallized from ligroin. Four grams of a solid melting at 78–81° was obtained. Recrystallization raised the melting point to 83–84°. The aqueous filtrate was acidified, and 2.3 g. of starting material was recovered.

Anal. Calcd. for $C_{14}H_{17}ON$: C, 78.10; H, 7.95; N, 6.51; OCH_3, 14.42. Found: C, 78.73, 78.26; H, 7.9, 7.97; N, 6.69; OCH_3, 14.8.

Summary

β-Methoxy-β-mesitylacrylonitrile (VI) and α-methyl-β-methoxy-β-mesitylacrylonitrile (VIII) have been prepared by methylation, respectively, of α-cyanoacetomesitylene (IV) and α-cyanopropiomesitylene (V). In each instance only O-methylation occurred.

Two forms—presumably *cis* and *trans* modifications—were obtained of VI; they form a solid solution when mixed in equal proportions.

URBANA, ILLINOIS RECEIVED FEBRUARY 26, 1938

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Oxidation of Sugar Alcohols by *Acetobacter suboxydans*[1]

BY RAYMOND M. HANN, EVELYN B. TILDEN AND C. S. HUDSON

Through the coöperation of Messrs. H. T. Herrick and P. A. Wells, of the Industrial Farm Products Research Division of the Bureau of Chemistry and Soils, U. S. Department of Agriculture, we have been enabled to test the oxidizing action of *Acetobacter suboxydans*, in submerged growth, upon a series of rare sugar alcohols and some related derivatives.

The optimum cultural conditions for oxidation of perseitol were first determined, and were then applied to the other oxidations. The substance to be tested was made up in a 2% aqueous solution containing 0.5% of Difco yeast extract, 0.3% potassium acid phosphate, and 0.05% glucose as nutrients, and then sterilized in 500-cc. Jena glass gas-washing bottles. A bacterial suspension of *A. suboxydans* was added, and sterile air passed through the culture at a rate of 200 cc. per minute, the temperature being maintained at 30°. Copper reduction values were determined on 2-cc. sub-samples by the Shaffer–Hartmann method after six and twelve days. The results are summarized in Table I.

The oxidation of *d*-α-mannoheptitol (perseitol) to perseulose, first investigated by Bertrand[2] using *A. xylinum* and obtained in 45% yields, has been shown by copper reduction studies, using crystalline perseulose as a standard, to be quantitative with *A. suboxydans*. It was possible to isolate the ketose in crystalline condition in a yield of 95%, and studies detailing the production of perseulose under various bacteriological conditions and confirming its structure as *l*-galaheptulose have been completed.

Oxidized solutions of *d*-arabitol, following removal of the bacteria and a lead acetate purification, gave a specific rotation of −30° in good agreement with the rotation of *d*-xylulose, quoted by Schmidt and Treiber[3] as −33.2°. Upon treatment with phenylhydrazine the oxidized

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[1] Publication authorized by the Surgeon General, U. S. Public Health Service.

[2] Bertrand, *Compt. rend.*, **126**, 762 (1908).

[3] Schmidt and Treiber, *Ber.*, **66**, 1765 (1933).