Rudy, Schloesser and Watzel.[5] Similar precipitates are also formed with Al^{+++} and sodium triphosphate, but only in a certain range of concentrations. In some ranges the precipitate dissolves on standing, while in others an excess of one of the reactants is necessary. The effect with Al^{+++} salts was demonstrated for the range where precipitation does not occur as follows: 0.2 ml. of a 0.139 *M* solution of sodium triphosphate was mixed with 1.5 ml. of 0.033 *M* aluminum chloride and diluted to a volume of 4 ml. The resulting solution had a *p*H lower than 3.1 when measured with brom thymol blue indicator, whereas aluminum chloride solution alone at the same concentration had a *p*H of 3.6.

Mixtures of triphosphate with potassium fluoride were tested as representative of the monovalent cation salts. Its addition had no effect on the *p*H of sodium triphosphate solution.

A possible explanation for this effect is that polyvalent cations can form complex compounds with sodium triphosphate, even though the ordinary formulation of such a reaction would not account for the extent of the acid shift. Since a depression in *p*H has also been observed in a solution of sodium glycerophosphate on addition of magnesium chloride, it is not unlikely that similar complexes also occur with phosphoric esters other than the sodium triphosphate. This possibility should be taken into consideration when the effect of salts upon phosphatase activity is investigated.

The author wishes to express her thanks to Dr. J. Leibowitz for his kind advice and interest in this work.

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[5] H. Rudy, H. Schloesser and R. Watzel, *Chem. Abs.*, **35**, 1337 (1941).

CHEMICAL DEPARTMENT
CANCER RESEARCH LABORATORIES
THE HEBREW UNIVERSITY
JERUSALEM, PALESTINE
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The Condensation of α-Picoline Methiodide with Aromatic Aldehydes

BY C. F. KOELSCH

Many aromatic aldehydes have been condensed with α-picoline to form stilbazole derivatives. The conditions used for bringing about this reaction are drastic, usually a mixture of the reagents with zinc chloride is heated at 180–230°. The procedure of Shaw and Wagstaff[1] involves somewhat milder conditions, boiling with acetic anhydride for ten hours, but even this procedure might not be applicable to aldehydes containing acid-sensitive groups.

It has been shown[2] that whereas α-picoline will not react with *p*-nitrosodimethylaniline, α-picoline methiodide will do so readily. But only a few condensations of α-picoline methiodide with aromatic aldehydes have been recorded: with *p*-dimethylaminobenzaldehyde,[3] and with *m*-dimethyl-, diethyl- and dipropylbenzaldehyde.[4] It has now been found that such condensations generally can be brought about under very mild conditions. When a solution of equivalent amounts of an aromatic aldehyde and α-picoline methiodide in a small amount of alcohol is treated with a few drops of piperidine and then allowed to stand at room temperature for some time, it deposits the condensation product in a crystalline form.

3′-Nitro-α-stilbazole methiodide forms coarse yellow needles from water that sinter at 235° and melt with decomposition at 256°[5]; yield 88% after eight hours.

Anal. Calcd. for $C_{14}H_{13}IN_2O_2$: C, 45.7; H, 3.5. Found: C, 45.8; H, 3.7.

4′-Hydroxy-α-stilbazole methiodide forms bright yellow prisms from water, that fall to a yellow powder on drying at 100° and then melt at 268–270°; yield 33% after three weeks.

Anal. Calcd. for $C_{14}H_{14}INO$: C, 49.6; H, 4.1. Found: C, 49.4; H, 4.3.

4′-Methoxy-α-stilbazole methiodide forms yellow needles from water that fall to a powder on drying and then melt with decomposition at 235–240°; yield 50% after eight hours.

Anal. Calcd. for $C_{15}H_{16}INO$: C, 50.9; H, 4.5. Found: C, 50.9; H, 4.5.

Furfurylidene-α-picoline methiodide, yellow prisms from water, that fall to an orange-yellow powder on drying, darkens at 200° and melts to a red liquid at 204–206°; yield 67% after eight hours.

Anal. Calcd. for $C_{12}H_{12}INO$: C, 46.0; H, 3.8. Found: C, 46.3; H, 4.2.

When the methiodides so obtained are heated at about 250° under reduced pressure, they dissociate, and the resulting stilbazole distils. For example 4′-methoxy-α-stilbazole methodide yields 4′-methoxy-α-stilbazole, colorless plates from dilute alcohol, m. p. 76° (reported[6] 75°). And furfurylidene-α-picoline methiodide yields furfurylidene-α-picoline, tan needles from dilute alcohol, m. p. 65–66° (reported[7] 51–53°).

Anal. Calcd. for $C_{11}H_9NO$: C, 77.2; H, 5.3. Found: C, 77.2; H, 5.2.

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[1] Shaw and Wagstaff, *J. Chem. Soc.*, 77 (1933).

[2] Kaufmann and Vallette, *Ber.*, **45**, 1739 (1912); *cf.* Mills and Smith, *J. Chem. Soc.*, **121**, 2726 (1922).

[3] Mills and Pope, *ibid.*, **121**, 946 (1922); *cf.* Doja and Prasad, *J. Indian Chem. Soc.*, **19**, 125 (1942).

[4] Cocker and Turner, *J. Chem. Soc.*, 59 (1940).

[5] Temperatures are corrected.

[6] Bialon, *Ber.*, **35**, 2788 (1902).

[7] Merck, *ibid.*, **21**, 2709 (1888).

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS, MINNESOTA
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Catalytic Hydrogenation of Cyanoacetic Ethyl Ester

BY KEVIN E. KAVANAGH AND F. F. NORD

While the Hofmann degradation of succinimide is the best method for obtaining β-alanine used in the synthesis of pantothenic acid, it is rather tedious. Weygand[1] applied hydrogenation to an aliphatic nitrile, *viz.*, cyanoacetic ethyl ester, for this synthesis. He utilized platinum oxide (10%

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[1] F. Weygand, *Ber.*, **74B**, 256 (1941).

by weight of substrate) at 40 atmospheres of pressure. The applicability and high efficiency of the recently developed noble metal synthetic high polymer catalysts, described in previous papers[2,3,4,5] suggested that hydrogenation be attempted employing this type of catalyst. A palladium-polyvinyl alcohol (Pd-PVA) catalyst was prepared wherein the palladium was 0.5% by weight of substrate and cyanoacetic ethyl ester was successfully hydrogenated at atmospheric pressure.

Procedure

The Pd-PVA catalyst was composed of 30 mg. of Pd and 500 mg. of PVA in 100 cc. of 50% alcohol-water mixture which was 0.5 *N* in hydrochloric acid. The purpose of the high acidity was to minimize formation of secondary amines.[6] Six and four-tenths g. of cyanoacetic ester was introduced into the vessel with the catalyst and the whole shaken for twenty hours at room temperature and ordinary pressure. At the end of this time 1822 cc. of a theoretical 2580 cc. of hydrogen had been adsorbed. The rate of adsorption was very slow at this point, so the isolation of β-alanine was started.

The colloidal catalyst was flocculated by addition of about 500 cc. of ethanol. After filtering, the liquid was concentrated. Hereafter, a separation into two layers was noticed, the lower layer containing some unreduced starting material, which is insoluble in water. The latter was drawn off and to assure complete removal of unreduced cyanoacetic ethyl ester, the remaining aqueous layer was extracted twice with ether. The aqueous solution was then taken to dryness under reduced pressure. The residual salt was twice extracted with 35-cc. portions of hot 95% ethanol, filtered while hot and allowed to cool. On cooling crystallization of ammonium chloride, which had been extracted along with the β-alanine ethyl ester hydrochloride, occurred. This was filtered off and discarded. The filtrate was again evaporated to dryness *in vacuo*. The residual salt was extracted with 35-cc. portions of absolute ethanol and filtered. The filtrate was concentrated *in vacuo* and then diluted with about 20 cc. of water and hydrolyzed under reflux. After concentrating under reduced pressure to remove the excess hydrochloric acid, the residue was dissolved in water and made up to a volume of 30 cc. A 2-cc. portion was withdrawn for determination of total halide.[6] A suspension of silver oxide prepared from 10% more than the equivalent quantity of silver nitrate was added to the solution to bring about complete precipitation of halide.

After standing for some time, the precipitate was filtered, the filtrate concentrated and treated with hydrogen sulfide. The silver sulfide is centrifuged off, the solution treated with norite and filtered. The crystals of β-alanine may be obtained by concentrating the filtrate in a vacuum desiccator until crystallization begins. Upon recrystallization from water a product of m. p. 194–196° was obtained with the analysis calculated: N, 15.73; found: N, 15.56; yield, 15%.

No attempt was made to increase this yield as the primary purpose of the experiments was to demonstrate the ability of the colloidal noble metal synthetic high polymer catalysts to serve in the reduction of the nitrile group.

Acknowledgment.—These hydrogenations were carried out with the aid of grants of the Bache Fund of the National Academy of Sciences and the Penrose Fund of the American Philosophical Society. Analyses were performed by Mr. Joseph Alicino of the Squibb Institute for Medical Research, New Brunswick, N. J.

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(2) Louis D. Rampino and F. F. Nord, THIS JOURNAL, **63**, 2745, 3268 (1941).

(3) Rampino and Nord, *ibid.*, **65**, 429 (1943).

(4) Kevin E. Kavanagh, *ibid.*, **64**, 2721 (1942).

(5) Kevin E. Kavanagh and F. F. Nord, *ibid.*, **65**, 2121 (1943).

(6) "Organic Syntheses," Vol. 16, John Wiley and Son. Inc., New York. N. Y., 1936, p. 1.

Chlorination of Fluorene with Sulfuryl Chloride

BY ANDREW STREITWIESER

Sulfuryl chloride is being used increasingly as a chlorinating agent because of the ease with which it reacts and the high yields obtained. In 1939, Kharasch and Brown[1] treated fluorene with this reagent and reported that the fluorene was chlorinated in the nucleus. However, they did not report the position taken by the entering chlorine atom, nor did they give any yields or procedures. The purpose of this work was to determine the position of the entering chlorine and to find out whether this method is a convenient one for preparing the chloro compound.

The fluorene was chlorinated in ether solution with a slight excess of sulfuryl chloride. The product melted at 95–96°.[2] This compares favorably with the 2-chlorofluorene prepared simultaneously by Chanussot[3] and Courtot and Vignati,[4] m. p. 96–97°. Authentic 2-chlorofluorene was prepared by the method of Chanussot[3] from 2-aminofluorene by the Sandmeyer reaction. A mixed melting point determination showed the two to be identical. The following procedure is recommended as a quick, convenient method for preparing 2-chlorofluorene.

Experimental

2-Chlorofluorene from SO_2Cl_2.—Sixteen grams of fluorene and 120 cc. of anhydrous ether was placed in a distilling flask. Not all of the fluorene dissolved. The flask was stoppered with a rubber stopper carrying a separatory funnel containing 8 cc. (13.4 g.) sulfuryl chloride. The latter was added rapidly to the solution. When all was added, the ether was distilled off, and the residue recrystallized from alcohol. It can also be purified by steam distillation: yield, 85% of a white crystalline powder, m. p. 95–96°.

The author wishes to acknowledge the assistance of Mr. L. Friedman and Mr. E. Kosower in this work.

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(1) Kharasch and Brown, THIS JOURNAL, **61**, 2149 (1939).

(2) All melting points corrected.

(3) Chanussot, *Añales asocn. quim. Argentina*, **15**, 216 (1927).

(4) Courtot and Vignati, *Compt. rend.*, **184**, 1479 (1927).

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The Preparation of N-Alkyl Derivatives of *p*-Aminobenzoic Acid[1]

BY A. R. SURREY AND H. F. HAMMER

It has been reported that procaine hydrochloride and other local anesthetics which are

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(1) Presented before the Division of Medicinal Chemistry, A. C. S., Cleveland, Ohio, April, 1944.