rate of 2 to 3 bubbles/second. The cyanide accumulated in the alkaline solution in the wash bottle which was removed at the termination of the heating period. Yields in this step were quantitative.

In a series of four runs, using approximately 1 mmole. of barium carbonate, in which the magnesium excess ranged from 14 to 48% over the stoichiometric amount, and the carbon dioxide pressure from 278 to 385 mm., the yields of cyanide obtained were 67, 69, 72 and 59%. The value of 59% was obtained by radioactivity assay, the others by silver nitrate titration.

INSTITUTE OF RADIOBIOLOGY AND BIOPHYSICS
UNIVERSITY OF CHICAGO
CHICAGO 37, ILLINOIS

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2,4-Dinitrophenylhydrazones of Methoxy- and Methylcyclohexanones

BY HOMER ADKINS AND A. G. ROSSOW

Since the literature record of the melting points of these derivatives is confused and contradictory, we have re-examined the behavior of their ketones in the procedure described by Shriner and Fuson.[1]

2-Methoxycyclohexanone gave in our hands not the 2,4-dinitrophenylhydrazone, m. p. 135°, reported by others[2] but slowly and in low yield a red product, m. p. 218–219° uncor., whose analysis corresponded to cyclohexandione-1,2-bis-(2,4-dinitrophenyl)-osazone. *Anal.* Calcd. for $C_{18}H_{16}N_8O_8$: N, 23.72. Found: N, 23.62. This reaction is analogous to the prior[3] record for 3-methoxy-2-butanone. 3-Methoxycyclohexanone by similar treatment did not yield a 2,4-dinitrophenylhydrazone, m. p. 133.5°,[2] but instead gave rapidly in quantitative yield a product, m. p. 170–170.5° uncor., whose analysis indicated loss of methanol as well as water during the condensation. *Anal.* Calcd. for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.30; H, 4.42; N, 20.54. Our product may therefore be either a ring-closed derivative or cyclohexen-2-one 2,4-dinitrophenylhydrazone; the latter has previously been reported as m. p. 163[4] and 117°.[5] From the 4-methoxy ketone we obtained 4-methoxycyclohexanone 2,4-dinitrophenylhydrazone, orange crystals from ethanol, m. p. 142.5–143.5° uncor. *Anal.* Calcd. for $C_{13}H_{16}N_4O_5$: N, 18.18. Found: N, 18.20. This accords with the m. p. of 141.5–142.5°[6] but disagrees with the values of 150°[2,7] from the prior literature.

The behavior of 2-methylcyclohexanone was not examined, but its position isomers gave conventional results. 3-Methylcyclohexanone gave an orange-yellow 3-methylcyclohexanone 2,4-dinitrophenylhydrazone, m. p. 153.5–155.0° uncor., which appeared to be a mixture of stereoisomers. *Anal.* Calcd. for $C_{13}H_{16}N_4O_4$: N, 19.17. Found: N, 19.22. The same procedure on 4-methylcyclohexanone gave 4-methylcyclohexanone 2,4-dinitrophenylhydrazone, golden yellow crystals from ethanol, m. p. 134.7–135.1° uncor. *Anal.* Found: N, 19.47.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WIS.

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(1) Shriner and Fuson, "The Systematic Identification of Organic Compounds," p. 148, John Wiley and Sons, Inc., New York, N. Y., 1935; the preparation and properties of the ketones are given in another paper. Adkins, Elofson, Rossow and Robinson, THIS JOURNAL, **71**, 3622 (1949).

(2) Ferrante and Bloom, *Am. J. Pharm.*, **105**, 381 (1933).

(3) Aston, Clarke, Burgess and Greenburg, THIS JOURNAL, **64**, 300 (1942).

(4) Bartlett and Woods, *ibid.*, **62**, 2933 (1940).

(5) Whitmore and Pedlow, *ibid.*, **63**, 758 (1941).

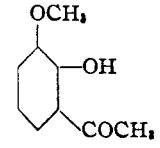
(6) Adamson and Kenner, *J. Chem. Soc.*, 188 (1939).

(7) Marvel and Walton, *J. Org. Chem.*, **7**, 92 (1942).

The Reaction of *o*-Veratronitrile with Methylmagnesium Iodide

BY E. D. AMSTUTZ

In the course of other work to be reported later relatively large quantities of *o*-acetovanillone (I) were required.



I

The usual method of synthesis involves the successive conversion of *o*-veratric aldehyde to the methylcarbinol,[1] acetophenone,[2] and demethylation.[3] It has now been found that several of these steps may be obviated with improvement in yield and facility. Although ether splitting is by no means new, the reaction of *o*-veratronitrile with methylmagnesium iodide has previously been reported[4] to yield the dimethoxyketone. Apparently the phenol formed escaped attention.

The present work has shown that the 2,3-dimethoxyacetophenone may be the main product of the reaction but also that conditions may be so arranged that it appears only as a minor product with 2-demethylated ketone assuming major importance. For example, using double the calculated quantity of Grignard reagent over a total reaction time of sixty hours the yield of *o*-acetovanillone rises to about 75% and the yield of non-phenolic ketone drops to about 18%.

Since the methoxyl group ortho to the acetyl is vinylogous with methyl acetate it is not inconceivable that it could have suffered hydrolysis during the acid treatment to destroy the magnesium complex. A sample of the solid magnesium-containing complex was therefore removed from the reaction mixture and rapidly decomposed with cold ammonium chloride solution. Ether extraction removed a yellow material which exhibited (in alc. soln.) a definitely positive test for the phenolic group with ferric chloride. Since it is hardly likely that the hydrolysis could have occurred under these mild conditions and in such a short interval of time, it appears necessary to suppose that the splitting occurred during the reaction of the Grignard reagent. The same conclusion is indicated by the fact that 2,3-dimethoxyacetophenone (in ether soln.) did not yield phenolic bodies on gentle warming and stirring for three hours with dilute hydrochloric acid, although it was obvious other changes were taking place. Also Fuson and Chadwick[5] have

(1) Pauly, *et al.*, *Ann.*, **383**, 317 (1911).

(2) Krannichfeldt, *Ber.*, **46**, 4016 (1913).

(3) Reichstein, *Helv. Chim. Acta*, **10**, 392 (1927).

(4) Richtzenhain and Nippus, *Ber.*, **77B**, 566 (1914); Baker and Smith, *J. Chem. Soc.*, 346 (1936).

(5) Fuson and Chadwick, *J. Org. Chem.*, **13**, 484 (1948).

shown that such hydrolysis is quite liable to remove the acyl group. The production of *o*-acetovanillone therefore appears to be analogous to the formation of isobutyl 3,5-dimethoxy-4-hydroxyphenyl ketone from 3,4,5-trimethoxybenzonitrile and isobutylmagnesium bromide.[6] It differs, however, in the fact that methylmagnesium iodide does not require high temperatures and apparently does not alkylate at the position of attachment of the *o*- or *p*-methoxyl group.

Similar observations have been made on 2-benzyloxy-3-methoxybenzonitrile in which the benzyl ether is split. Since there is no preparative advantage accruing to the use of the benzyl ether rather than the methyl ether, details of these experiments are omitted.

Experimental

An ether solution of 16.3 g. (0.1 mole) of *o*-veratronitrile was added rapidly to an ether solution of Grignard reagent prepared from 28.4 g. (0.2 mole) of methyl iodide and 4.8 g. (0.2 g.-atom) of magnesium. No refluxing was observed and no precipitate formed for about one hour. The solution was therefore refluxed and stirred for eight hours during a total time of about sixty hours. Although a small amount of Grignard reagent was still present the mixture was then worked up in the usual way with water, ammonium chloride solution and finally dilute hydrochloric acid. Phenolic material, removed from the ethereal solution with dilute alkali, proved to be almost pure *o*-acetovanillone and amounted to 12.36 g. (74.5%), m. p. 50–53.1°, mixed with authentic *o*-acetovanillone, m. p. 51.8–53°. The crude neutral material amounted to 3.25 g. (18%), $n^{30.5}D$ 1.5282, observed for authentic *o*-acetoveratrone $n^{26.5}D$ 1.5368. Starting material unaccounted for above was obtained as a water-, ether- and alkali-insoluble resinous gum.

A second run of the same size using a nitrile to Grignard ratio of 1:1.5, refluxing for one hour and standing overnight yielded some tar and 25.6% of *o*-acetovanillone (m. p. 51.8–53°; mixed with authentic, m. p. 51.8–53°) and 32.2% of *o*-acetoveratrone, $n^{26.5}D$ 1.5368. The neutral fraction yielded iodoform (m. p. 121–123°) and an acid, m. p. 118–120.4° (reported for *o*-veratric acid, m. p. 122°).[7] It also formed a 2,4-dinitrophenylhydrazone, m. p. 150–151.8° which did not depress the melting point of an authentic specimen.

(6) Hurd and Winberg, THIS JOURNAL, **64**, 2085 (1942).

(7) Perkin and Robinson, *J. Chem. Soc.*, **105**, 2383 (1914).

DEPT. OF CHEMISTRY
LEHIGH UNIVERSITY
BETHLEHEM, PENNSYLVANIA RECEIVED JULY 1, 1949

Purification of Xanthopterin[1]

BY A. G. ANDERSON, JR., AND JERRY A. NELSON

In connection with the studies on the physiological properties of xanthopterin in this Laboratory,[2] xanthopterin free of other pterin impurities was desired. A purification procedure satisfactory as a routine method for this purpose was not found in the literature. In this investigation xanthopterin has been purified *via* a new crystalline derivative, xanthopterin hydrochloride. Crystalline xanthopterin sulfate has also been prepared. The hydrochloride salt affords a simple, effective means for the purification of synthetic xanthopterin as prepared in this Laboratory. Purification was also effected by sublimation *in vacuo*. This procedure gave poor yields and thus was not practical.

(1) This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

(2) Norris and Majnarich, *Amer. J. Physiol.*, **152**, 175, 179, 652 (1948); **153**, 133, 483, 486, 492, 496 (1949); *Science*, **109**, 32, 33 (1949).

Experimental

Xanthopterin.—Leucopterin and, from it, xanthopterin were prepared by the procedures of Purrmann[3] and Totter,[4] respectively, as modified by Dauben and Goheen,[5] the modified procedure being similar to that recently reported by Hitchings and co-workers.[6] The xanthopterin so obtained was used in the experiments described below.

Xanthopterin Hydrochloride.—To 100 mg. of finely powdered xanthopterin was added 20 ml. of concentrated hydrochloric acid and the mixture heated on a steam-bath for ten minutes and filtered by suction while hot. The insoluble material (approximately 20 mg.) was largely xanthopterin hydrochloride and to this was added 5 ml. of hydrochloric acid and the mixture heated and filtered as before. The small quantity (5 mg.) of insoluble material was discarded. The two filtrates were placed in a refrigerator at −5° overnight. The hydrochloride precipitated as tiny, tan hexagonal plates which were separated by filtration, washed with a few ml. of cold alcohol, then with ether and dried. The yield from the first filtrate was 86 mg. (71.5%) and from the second filtrate 10 mg. (8.4%); total yield 96 mg. (79.9%). The salt was recrystallized from hydrochloric acid in corresponding yield. It was soluble in hot water or hot dilute hydrochloric acid but the hydrochloride could not be recovered from these solutions by cooling or concentration. On heating the crystals darkened at 200° and above but no melting point was observed up to 320°.

Anal. Calcd. for $C_6H_6O_2N_5Cl$: N, 32.48. Found: N, 32.41.

Amorphous xanthopterin was recovered quantitatively as a yellow solid on treatment of the hydrochloride with just sufficient 0.1 *N* ammonium hydroxide to effect solution (the xanthopterin began to precipitate a few seconds after the salt had dissolved) and then adjustment of the acidity to *p*H 5–6 by addition of dilute hydrochloric acid. The mixture was cooled, filtered and the collected precipitate washed with a few ml. of cold water, then acetone and dried.

Xanthopterin Sulfate.—Eighty-six mg. of finely powdered xanthopterin was dissolved in 2.3 ml. of sulfuric acid–water (1:1) solution by heating on a steam-bath. As the xanthopterin dissolved the solution became orange in color. On cooling the solution in tap water and scratching the sides of the flask, crystallization occurred and, after standing overnight in a refrigerator, the tiny, tan boat-shaped crystals were separated by filtration, washed with a few ml. of cold alcohol, then with ether and dried; yield 45 mg. (36%). The crystals gradually darkened and decomposed above 200° leaving a black residue at 280°. The sulfate could be recrystallized from the same sulfuric acid solution in corresponding yield. Attempts to obtain a second crop from the filtrate were unsuccessful. Xanthopterin sulfate is quite soluble in dilute or concentrated sulfuric acid and undergoes hydrolysis with water to precipitate amorphous xanthopterin. Recovery of xanthopterin from the sulfate was best effected in the manner described for the hydrochloride.

Anal. Calcd. for $C_6H_7O_6N_5S$: N, 25.27. Found: N, 25.80.

(3) Purrmann, *Ann.*, **544**, 182 (1940).

(4) Totter, *J. Biol. Chem.*, **154**, 105 (1944).

(5) Dauben and Goheen, private communication.

(6) Elion, Light and Hitchings, THIS JOURNAL, **71**, 741 (1949).