phase over the temperature range studied. This is in agreement with the results of Manchot and Ortner[10] for selenious acid.

Berzelius[1] viewed the normal selenite of barium as anhydrous. Nilson,[3] who prepared it by the rather extraordinary procedure of mixing solutions of barium nitrate and sodium biselenite, found it to be a monohydrate. We have attempted repeatedly to duplicate his work, but have obtained only the pyroselenite by this means, according to the X-ray diffraction pattern of the powdered material. We have also attempted to prepare the hydrate by precipitation of the normal selenite at 0° instead of the boiling point, but this yields the anhydrous salt, according to the diffraction pattern. Moreover, the anhydrous salt, even on exposure to water at 0° for several months, shows no change in form or appearance detectable under the microscope. We conclude that the hydrate, if it exists at all, is unstable above 0°.

TABLE II

SUMMARY OF SOLUBILITY DETERMINATIONS ON SELENIOUS ACID

Investigators	% SeO_2 in saturated solution at 0°	25°	50°
Étard[11]	47.3[a]	66.7[a]	78.2[a]
Manchot and Ortner[10]	65.9[a]	73.3[a]	79.2[a]
Neal and McCrosky	58.9	68.8	76.6

[a] Interpolated.

The only previous data available as a check upon our solubility measurements are upon selenious acid alone. The summary is given in Table II. We are unable to suggest an explanation for the discrepancy.

Summary

1. Data on the solid–solution equilibrium have been obtained for the ternary system selenium dioxide–barium selenite–water at 0, 25, and 50°.

2. At each temperature the stable solid phases prove to be selenious acid, H_2SeO_3, barium pyroselenite, $BaSe_2O_5$, and barium selenite, $BaSeO_3$, all three of which have long been known.

3. No indication of hitherto unknown acid salts or hydrates has been found within the temperature range studied.

4. The normal salt monohydrate $BaSeO_3 \cdot H_2O$ reported by Nilson cannot be confirmed.

SYRACUSE, N. Y. RECEIVED FEBRUARY 7, 1938

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(10) Manchot and Ortner, *Z. anorg. allgem. Chem.*, **120**, 300 (1922).

(11) Étard, *Ann. chim. phys.*, [7] **2**, 551 (1894).

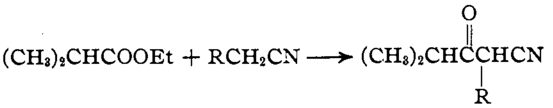
[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Reactions of β-Keto-nitriles with Hydrogen

BY RICHARD H. WILEY[1] AND HOMER ADKINS

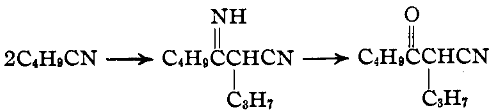
Recent papers from this Laboratory on the reactions of hydrogen by Sauer, Durland, Musser and Mozingo have been concerned with the selective hydrogenation of compounds containing two functional groups, *i. e.*, unsaturated esters, amido esters, imido amides, polynuclear aromatic compounds and unsaturated ketones. Attention is now directed toward the selective hydrogenation of keto-nitriles over Raney nickel. Both the keto and cyano groups accept hydrogen under rather mild conditions with this catalyst; in fact some ketones and cyanides have reacted with hydrogen at room temperatures.[2] However, the preferred range of temperature for the hydrogenation of cyanides is 120–140°, which is somewhat above that ordinarily used for the hydrogenation of ketones. There has been no information available, in so far as we know, with regard to which group over nickel would be hydrogenated first in the presence of the other.[3]

The keto-nitriles used in this investigation were prepared either by the condensation of an ester with a nitrile under the influence of sodium ethoxide, I, or through the condensation of two molecules of a cyanide by sodium followed by the hydrolysis of the imino nitrile, II.



$$(CH_3)_2CHCOOEt + RCH_2CN \longrightarrow (CH_3)_2CH\overset{O}{\overset{\|}{C}}\underset{R}{CH}CN$$

I



$$2C_4H_9CN \longrightarrow C_4H_9\overset{NH}{\overset{\|}{C}}\underset{C_3H_7}{CH}CN \longrightarrow C_4H_9\overset{O}{\overset{\|}{C}}\underset{C_3H_7}{CH}CN$$

II

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[1] Wisconsin Alumni Research Foundation Fellow, 1935–1937.

[2] Adkins and Covert, THIS JOURNAL, **54**, 4116 (1932).

[3] A thesis at Leipzig by F. R. Urlass on the hydrogenation of keto-nitriles over palladium is listed for 1931.

None of the keto-nitriles except where R is H have been prepared previously. The methods used were those of Kroeker and McElvain, and of von Meyer and Holzwart.[4]

Five keto esters were prepared by the first method, where R was H, methyl, ethyl, *n*-propyl or *n*-butyl, the yields in all cases being 40 ± 3%. The second method gave a yield of 44% of the keto-nitrile based upon the valeronitrile used. When ethyl trimethylacetate was substituted for ethyl isobutyrate in the first method the yield with butyl cyanide was only 6%.

Many unsuccessful attempts were made to hydrogenate these keto-nitriles which need not be described here. Hydrogen reacted with the keto-nitriles over a wide range of temperatures, but difficulty was encountered in isolating the products Ultimately it was found that fairly good results could be obtained if the hydrogenations were carried out (a) at 35–40° for one hour, during which time approximately one mole of hydrogen per mole of keto-nitrile was added, or (b) at 150–200° until the absorption of hydrogen had ceased. In the latter case, two to three moles of hydrogen per mole of keto-nitrile were taken up within two to three hours.

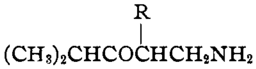
TABLE I

HYDROGENATION OF KETO-NITRILES OVER RANEY NICKEL

Ketonitrile	Temp., °C.	% Yield of product
2-*n*-Propyl-4-methyl-3-ketovaleronitrile	35	60 keto-amine
2-Ethyl-4-methyl-3-ketovaleronitrile	35	10 keto-amine
2,4-Dimethyl-3-ketovaleronitrile	35	35 keto-amine
4-Methyl-3-keto-valeronitrile	200	32 amino alcohol
2,4-Dimethyl-3-ketovaleronitrile	200	40 amino alcohol
2-Ethyl-4-methyl-3-ketovaleronitrile	150	58 amino alcohol
2-Ethyl-4-methyl-3-ketovaleronitrile	200	30 amino alcohol 20 cyclic ether[a]
2-*n*-Propyl-4-methyl-3-ketovaleronitrile[a]	150	54 amino alcohol 25 cyclic ether
2-*n*-Propyl-3-keto-enanthonitrile	170	50 amino alcohol 24 cyclic ether
2-*n*-Propyl-3-keto-enanthonitrile	150	23 amino alcohol 37 cyclic ether

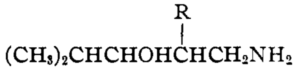
[a] In another hydrogenation a 40% yield of the cyclic ether was obtained but the yield of amino alcohol was not ascertained. These cyclic ethers contain no nitrogen and are apparently produced by rearrangement and loss of ammonia, with ring closure.

The low temperature hydrogenation is favorable to the formation of keto-amines III by the addition of two moles of hydrogen. The high temperature is favorable to the addition of three moles of hydrogen and the formation of amino alcohols, IV.



$$(CH_3)_2CHCO\overset{\overset{R}{|}}{C}HCH_2NH_2$$

III



$$(CH_3)_2CHCHOH\overset{\overset{R}{|}}{C}HCH_2NH_2$$

IV

Intermediate temperatures are unfavorable, apparently because the keto-amine first formed reacts with itself to give high molecular weight compounds that could not be isolated. For the same reason great care must be taken in attempting to isolate the keto-amine from the low temperature hydrogenation.

The nature of R in a keto-nitrile of formula I was a factor in determining the amount of keto-amine that could be isolated. Where R was *n*-propyl the yield of keto-amine III was 60%, when methyl, 35%, and ethyl, only 10%. No keto-amine could be isolated where R was H or *n*-butyl. No keto-amine could be obtained from the keto-nitrile II, which is not branched at the 3-carbon atom. Presumably branching at the carbon atoms adjacent to the carbonyl retards hydrogenation and condensation at the carbonyl and so makes it possible to obtain keto-amines.

The three keto-amines isolated were solids, which were soluble in acids but not in water or bases. They were sufficiently strong bases so that they could be titrated with hydrochloric acid, using a mixture of methylene blue and methyl red as an indicator. The acid had been standardized against triacetonealkamine as is customary in this Laboratory. The molecular weights so determined were 2 to 3% too high. The keto-amines gave a weak but definite enol test with ferric chloride. Two moles of methane were evolved per mole of keto-amine when they were treated with methylmagnesium iodide in a Zerewitinov analysis, thus indicating that under these conditions they react as enols. There was no addition of the Grignard reagent. The amount of hydrogen required for their preparation from keto-nitriles and the amount of hydrogen absorbed in their hydrogenation to amino alcohols, etc., was that to be expected upon the basis of the structure of the keto-amines. Neither of these transformations involves a single

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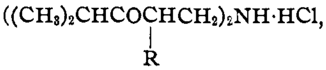
[4] Kroeker and McElvain, THIS JOURNAL, 56, 1172 (1934); Holzwart, *J. prakt. Chem.*, [2] 39, 230 (1889).

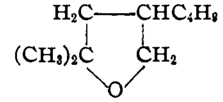
clear-cut reaction, so that quantitative hydrogenations could not be made. All three of the solid keto–amines turned to oils on standing. The most stable one was when R in formula III was methyl; this compound could be kept pure for a week or two. The compound where R is *n*-propyl began to "polymerize" within a few days.

From all of the hydrogenations made below 130° a fraction was obtained boiling 100–140° (1 mm.). This amounted in some cases to 4–6 g. from 15 g. of keto-nitrile. Several of these fractions from different runs were combined and fractionated. The chief fractions from two different keto-nitriles gave crystalline hydrochlorides, although the free bases gave no satisfactory neutral equivalents. The analyses of the hydrochlorides for nitrogen and chlorine (see Table II) agreed fairly well with the formula  $((CH_3)_2CHCO\underset{\displaystyle R}{\underset{|}{C}}HCH_2)_2NH\cdot HCl$, where R was hydrogen or ethyl. The formation of a secondary amine in the hydrogenation of a nitrile is a well-known reaction.[5]

Five of the keto-nitriles submitted to hydrogenation at 150–200° yielded amino alcohols. The yields, in three cases, were from 50 to 58%, while in two cases they were 32 to 40%. There is no particular difficulty in isolating the amino alcohols by fractional distillation. The low yields apparently are due to formation of high molecular weight compounds during the period of hydrogenation, and to cleavage. The formation of condensation products during the period of hydrogenation can be minimized by heating the reactants to the desired temperature as rapidly as possible. This avoids hydrogenation at a low temperature and thus the possibility of the keto-amine so formed condensing with keto-nitrile or with itself.

The other type of side reaction cannot be minimized so readily because the high temperature which is unfavorable to the formation of condensation products is particularly favorable to hydrogenolysis. In the case of one keto-nitrile of type I, where R is *n*-butyl, hydrogenolysis took place to such an extent that no amino alcohol could be isolated. It seems probable that for any given keto-nitrile temperatures can be found in the range 125 to 225° where either the amino alcohol or a hydrogenolysis product will be formed in yields of 30 to 60%.

The chief product of hydrogenolysis which has been isolated is an inert oxygen-containing compound. Four of these compounds have been isolated in yields of 20 to 40% from the hydrogenolysis of four different keto-nitriles. The compounds contain no nitrogen, are inert toward methylmagnesium iodide, and other reagents for an alcohol. They do not react with hydrogen over Raney nickel at 200°. Their analysis in each case indicates a cyclic ether. Their indices of refraction bear out this conclusion. A probable structure of the cyclic ether is that of a substituted tetrahydrofuran.. The structure of the ether from a keto-nitrile of type I where R is *n*-butyl would be



The formation of such a compound would involve in this case the migration of·an oxygen from a secondary to a tertiary carbon atom, as proposed by Ruzicka[6] for the first step in the Wagner rearrangement of tertiary alkyl carbinols, followed by the elimination of ammonia. The formation of these cyclic ethers during a hydrogenation in such relatively high yields is surprising. However, since evidence as to their exact structure is lacking, it seems useless to consider the matter further at this time.

Another product of hydrogenolysis contained nitrogen. Benzoyl and *p*-nitrobenzoyl derivatives of two of these amines were prepared and isolated. The analysis of the derivatives indicated that the carbon chain of the original keto-nitrile was intact and that the oxygen had been eliminated. However, the amounts of material isolated were too small to make it possible to establish with certainty whether the amines were open chain or cyclic compounds.

The hydrogenations were carried out in a steel reaction vessel having a void of 270 ml. The preparation of catalyst and general procedure were the usual ones used in this Laboratory.[7] The fractionations were carried out with electrical heating in Widmer or modified Widmer columns having spirals 15 cm. in length.[8]

Amino Ketones.—One-tenth mole of hydrogen was taken up within sixty minutes when 15.3 g. (0.1) mole of

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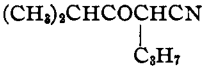
(5) Winans and Adkins, THIS JOURNAL, 54, 308 (1932).

(6) Ruzicka, *Helv. Chim. Acta*, 1, 130 (1918); 6, 267 (1923).

(7) Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, Wisconsin, 1937.

(8) Martha E. Smith and Adkins, THIS JOURNAL, 60, 657 (1938).


$(CH_3)_2CHCOCH(C_3H_7)CN$ in 110 ml. of methanol was shaken at 35° with hydrogen (120 atm.) over 10 g. of Raney nickel. The solvent was then removed at 30–50 mm. and the unreacted keto-nitrile (4 g.) removed as rapidly as possible through a modified Widmer at 1 mm., the oil pump being protected with a trap cooled in carbon dioxide. The temperature of the oil-bath was then raised rapidly to 170–180° and the column heater to 110°. The keto-amine was then distilled very slowly, sometimes as long as two days being required. The keto-amine, 9.2 g., solidified in the receiver. Keto-amine of good quality was not obtained if attempts were made to speed up the distillation. The keto-amine was dissolved in petroleum ether (b. p. 100–140°) without being melted, for recrystallization.

Amino Alcohols.—The hydrogenation (270 atm.) of keto-nitriles (0.1 mole) to amino alcohols was made in methanol (110 ml.) over Raney nickel (5 g.) at the temperatures indicated in Table I. The amino alcohols were isolated by fractionation at the temperatures and pressures shown in Table II. The analyses and neutral equivalents of the amino alcohols and the m. p. and analyses of their benzoyl or *p*-nitrobenzoyl derivatives are also given in Table II.

TABLE II

PHYSICAL PROPERTIES AND ANALYTICAL DATA

Compound	B. p.				M_D		Analyses,[a] %	
	°C.	Mm.	n^{25}_D	d_{24}	Calcd.	Found	Calcd.	Found
2,4-Dimethyl-3-ketovaleronitrile	95–96	24	1.4213	0.9253	34.3	34.3	11.20N	11.16
2-Ethyl-4-methyl-3-ketovaleronitrile	96.5	17	1.4273	.9172	38.9	38.9	10.07N	10.24
2-*n*-Propyl-4-methyl-3-ketovaleronitrile	91	7	1.4322	.9042	43.5	43.9	9.16N	9.23
2-*n*-Butyl-5-methyl-3-ketovaleronitrile	128	24	1.4337	.9003	48.2	48.3	8.38N	8.27
2-*n*-Propyl-3-ketoenanthonitrile	127	17	1.4360	.9089	48.2	48.0	8.38N	8.41
2-*n*-Propyl-4,4-dimethyl-3-ketovaleronitrile	122	22	1.4323	.8957	48.2	48.3	8.38N	8.29
2-*n*-Propyl-4-methyl-1-amino-3-pentanone			M. p. 79–80° (corr.)				8.92N	8.94
							157M	161
							2.00Z	2.02
2-Ethyl-4-methyl-1-amino-3-pentanone			M. p. 104–105° (corr.)				9.79N	9.85
							143M	146
							2.00Z	1.99
2,4-Dimethyl-1-amino-3-pentanone			M. p. 140–141° (corr.)				10.85N	11.01
							129M	132
							2.00Z	2.03
Hydrochloride of β,β'-diisobutyrylethylamine			M. p. 194–196° (corr.)				5.62N	5.59
							14.24Cl	14.98
							2.00Z	1.97
Hydrochloride of β,β'-diisobutyrylbutylamine			M. p. 185–187° (corr.)				4.58N	4.72
							11.53Cl	11.69
							2.00Z	2.05
2-*n*-Propyl-3-iminoenanthonitrile	125–126	3	1.4929	0.9011			16.88N	16.94
1-Amino-4-methyl-3-pentanol	104	23	1.4528	0.9159	35.0	34.5	11.96N	12.10
							117M	116
1-*p*-Nitrobenzoylamino-4-methyl-3-pentanol			M. p. 132–133° (corr.)				10.52N	10.57
1-Amino-2,4-dimethyl-3-pentanol	105	22	1.4513	0.9053	39.6	39.1	10.68N	10.60
							131M	133
1-(*p*-Nitrobenzoylamino)-2,4-dimethyl-3-pentanol			M. p. 181–182° (corr.)				10.00N	10.29
1-Amino-4-methyl-2-ethyl-3-pentanol	107	16	1.4611	0.9021	44.2	44.1	9.66N	9.75
							145M	146
1-Benzoylamino-4-methyl-2-ethyl-3-heptanol			M. p. 99–100° (corr.)				5.63N	5.70
1-Amino-4-methyl-2-*n*-propyl-3-pentanol	120	17	1.4512	0.8855	48.8	48.3	8.81N	8.90
							159M	159
1-Benzoylamino-4-methyl-2-*n*-propyl-3-heptanol			M. p. 107–108° (corr.)					
1-Amino-2-*n*-propyl-3-pentanol	147	22	1.4552	0.8910	53.5	52.5	8.09N	7.98
							173M	176
1-(*p*-Nitrobenzoylamino)-2-*n*-propyl-3-pentanol			M. p. 137–138° (corr.)				8.69N	8.70
A cyclic ether $C_9H_{16}O$	66–67	22	1.4122	0.8099	43.2	43.6	76.05C	75.78
							12.67H	12.88
A cyclic ether $C_{10}H_{18}O$	80–81	22	1.4164	.8146	47.8	48.1	76.92C	76.71
							12.82H	12.80
A cyclic ether $C_{10}H_{18}O$	88–89	22	1.4218	.8131	47.8	48.7	76.92C	77.10
							12.82H	13.05

[a] N, C, H, Cl, Z and M refer to nitrogen, carbon, hydrogen, chlorine, Zerewitinov analysis and molecular weight, respectively.

Cyclic Ethers.—These compounds were distilled at 65–90° (22) mm. from the reaction mixture after hydrogenation. The fractions so obtained contained some basic material which was extracted repeatedly with 10% hydrochloric acid. The ether was then washed with a 10% solution of sodium hydroxide and finally with distilled water. The ethers were then dried and fractionated.

Solid derivatives of the basic compounds distilling over with the ethers were obtained from the hydrogenation of $(CH_3)_2CHCOCH(C_3H_2)CN$ and $C_4H_9C(O)CH(C_3H_7)CN$. The benzoyl derivative of the amine from the former, m. p. 71.5–73.5°, corr., and the *p*-nitrobenzoyl derivative of the amine from the latter, m. p. 97.5–98.5°, corr., were obtained and analyzed.

Keto-nitriles from an Ester and a Nitrile.—One mole of sodium ethoxide was prepared by the standard procedure. The nitrile (1.2 moles) was added and the mixture stirred until it was homogeneous. It was then heated in an oil-bath at 90–100° and one mole of ethyl isobutyrate added during fifteen minutes. The bath was then raised to 120–130° and held there with stirring for three or four days, until the solution became clear. In the case of the higher boiling nitriles the alcohol formed by reaction was allowed to distil out, thus increasing the yields and decreasing the time required for reaction. The cold reaction mixture was poured slowly on 400 g. of finely crushed ice. The alkaline solution was extracted for the recovery of the unreacted nitrile. The alkaline solution was acidified with dilute sulfuric acid, the mixture being kept cold. A considerable portion of the keto-nitrile separated and was later added to ether extractions of the acid solution. The combined extracts were treated with Drierite. The keto-nitrile was obtained by fractionation, the yields being approximately 40% of the theoretical. The condensation of ethyl trimethylacetate with valeronitrile was run for five days, yet the yield of ketonitrile was only 6%.

2-*n*-Propyl-3-iminoenanthonitrile.—One mole of sodium after being powdered under xylene was placed under 400 ml. of dry ether in a three-necked one-liter flask provided with a stirrer, condenser and dropping funnel, the latter protected with calcium chloride tubes. Two moles (166 g.) of *n*-valeronitrile was added at such a rate as to maintain refluxing. The mixture was then refluxed until the mass became homogeneous in appearance; this required four to ten hours, depending on the fineness of division of the sodium. The reaction mixture was poured on ice with vigorous stirring, the ether and crude product were separated, treated with Drierite, and fractionated. The pure product, b. p. 125–126 (3 mm.), weighed 75 g. (45% yield).

2-*n*-Propyl-3-ketoenanthonitrile.—The imino-nitrile (114 g.) prepared as above was refluxed with 350 ml. of 10% sulfuric acid for two hours. The layer of keto-nitrile was separated and the acid layer extracted with ether. The ether extract combined with the crude keto-nitrile was treated with Drierite and fractionated. The yield of pure product, b. p. 127–128 (18 mm.), was 100 g. or 88% of the calculated amount. Considerable time may be saved by not fractionating the imino-nitrile, but hydrolyzing the crude product with 10% sulfuric acid. The over-all yield of keto-nitrile from 2 moles of valeronitrile was 71 g., or 42% of the theoretical. In addition, 45 g. of valeronitrile was recovered. The imine could not be hydrolyzed by refluxing the suspension of the salt in ether with dilute sulfuric acid.

Summary

Six β-keto-nitriles have been prepared and submitted to hydrogenation over Raney nickel. Reaction occurred under quite mild conditions, but difficulty was encountered in isolating the products, apparently because of the tendency of the first products of hydrogenation to undergo condensation. The cyano group is first hydrogenated in preference to the carbonyl group. This is shown by the fact that from three keto-nitriles hydrogenated at 35–40° the keto-amine was isolated in yields of 10 to 60%. Branching of the chain at the carbon atoms adjacent to the carbonyl is apparently favorable for the protection of the carbonyl group, during hydrogenation and isolation of the products. Hydrogenations carried out rapidly at 150–200° gave amino alcohols in yields of 32 to 58% from five keto-nitriles. Hydrogenations made at 40 to 150° yield only products of secondary reactions. Hydrogenolysis of the keto-nitriles occurred to some extent at 150–200°; the principal such product isolated in four cases was a cyclic ether of the same carbon content as the keto-nitrile.

MADISON, WISCONSIN RECEIVED JANUARY 31, 1938