777. *A Novel Reduction of Nitriles to Aldehydes.*

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Nitriles are conveniently reduced to aldehydes by sodium hypophosphite and Raney nickel in aqueous acetic acid or aqueous acetic acid–pyridine at room temperature and pressure. A modification of this procedure serves as a convenient qualitative test for nitriles.

THE reduction of nitriles to aldehydes has been reviewed in " Organic Reactions "[1] and in " Methoden der organischen Chemie; "[2] two principal procedures are used: (i) The well-known Stephen method,[3] in which stannous chloride and hydrogen chloride in ether, under anhydrous conditions, form the reagent (a procedure used six years earlier by Sonn and Müller[4] for the reduction of imidoyl chlorides to aldehydes but not mentioned by Stephen); this method gives excellent yields in very many cases, although both the above reviews mention certain limitations of the reaction; (ii) various hydrogenation procedures which are complicated by the fact that the aldehyde formed, as well as the intermediate aldimine, are liable to further reduction to the corresponding alcohol and amine; under suitable conditions the nitrile may in fact be reduced to the primary amine exclusively.[5] Improved yields of aldehyde have been reported by conducting the reduction in the presence of, for example, hydrazine,[6] phenylhydrazine,[7] or semicarbazide,[8] which removes the aldehyde from further reaction, but subsequent liberation of the aldehyde from the product may present difficulties.

As a result of an observation[9] that Raney nickel liberates hydrogen from water in the presence of sodium hypophosphite (which becomes oxidised to the phosphite) and at the same time retains its catalytic activity, we have successfully applied this reducing system to the synthesis of aldehydes directly from nitriles at room temperature and pressure. The procedure requires neither special apparatus nor particular precautions, and yields the free aldehyde as the sole product, making easy its isolation by conventional means. The yields of product, isolated as the phenylhydrazone and/or the 2,4-dinitrophenylhydrazone, and in several instances as the free aldehyde, are summarised in the accompanying Table. When low yields were obtained (*e.g.*, from *o*-tolunitrile and the apparently less readily hydrogenated aliphatic nitrile, hexanonitrile), the use of other solvent systems and reaction conditions, *e.g.*, temperature, time of stirring, or proportion of catalyst and of hypophosphite, might lead to improved reduction, but such variations have not been studied in detail.

Nitro-compounds appear not to react under the conditions used, and attempts to reduce *m*-nitrobenzonitrile and nitrobenzene led to their recovery unchanged.

Although aldehydes are readily hydrogenated to the corresponding alcohols[10] at room temperature and moderate pressures, no similar reduction appears to occur under the conditions described, and good yields of aldehyde resulted if a moderate excess of hypophosphite was used. The Raney nickel appears to become gradually deactivated during the reaction (in which the aldimine is rapidly hydrolysed) and performs the two-fold

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[1] Mosettig, *Org. Reactions*, 1954, **3**, 218.

[2] Houben-Weyl, " Methoden der organischen Chemie," Thieme Verlag, Stuttgart, 4th edn., Vol. VII, Part I, p. 299.

[3] Stephen, *J.*, 1925, **127**, 1874; 1930, 2786; 1956, 4695.

[4] Sonn and Müller, *Ber.*, 1919, **52**, 1927.

[5] Gould, Johnson, and Ferris, *J. Org. Chem.*, 1960, **25**, 1658.

[6] Pietra and Trinchera, *Gazzetta*, 1955, **85**, 1705.

[7] Ref. 2, p. 302; Gaiffe and Pallaud, *Compt. rend.*, 1961, **252**, 1339; 1962, **254**, 496.

[8] Plieninger and Werst, *Chem. Ber.*, 1955, **88**, 1956.

[9] " Newer Methods of Preparative Organic Chemistry," Interscience Publ., Inc., New York, 1948, p. 70.

[10] Weissberger, " Techniques of Organic Chemistry," Interscience Publ., Inc., New York, 1956, 2nd edn., Vol. II, p. 115.

Nitrile	Wt. used (g.)	Reaction time (hr.)	Yield (%)		
			2,4-D *	H †	A *
Ph	1	1	90	—	—
	5	2	—	85	85
o-$Me{\cdot}C_6H_4$	1	1	10	—	—
m-$Me{\cdot}C_6H_4$	1	1	—	70	—
p-$Me{\cdot}C_6H_4$	1	1	80	—	—
o-$Cl{\cdot}C_6H_4$	1	1	40	—	—
p-$Cl{\cdot}C_6H_4$	1	1·5	80	85	—
	3	2	75—80	—	80
p-$MeO{\cdot}C_6H_4$	1	1·5	80	80	—
α-$C_{10}H_7$	1	2·5	15	—	—
β-$C_{10}H_7$	1	1	80	—	75
	4	1·5	—	90	90
	10	4	—	55 †	—
p-$NH_2{\cdot}SO_2{\cdot}C_6H_4$	1	1	—	—	50 ‡
	5	1·5	—	—	60 ‡
n-C_7H_{15}	1	1	20	—	—
2-Cyanopyridine	1	1	—	70	—
$Ph{\cdot}CH{:}CH$	0·5	1	20 §	—	—

* 2,4-D = 2,4-Dinitrophenylhydrazone; H = phenylhydrazone; A = free aldehyde; m. p.s agree with reported values.[12] † 1·2 g. of Raney nickel. ‡ Isolated as the anil. § The double bond is not reduced.

function of decomposing water to furnish hydrogen and of catalysing the reduction of the nitrile, and a suitable weight of catalyst was found to be one-third to one-half of that of the nitrile.

A small-scale modification of the procedure was found to provide a convenient qualitative test for nitriles and proved to be satisfactory even for hindered compounds such as *o*-tolunitrile and α-naphthonitrile; a small quantity of the nitrile in orthophosphoric acid solution was treated with Raney nickel, and the aldehyde formed was converted into its 2,4-dinitrophenylhydrazone; the melting point of the uncrystallised product served for its identification.

EXPERIMENTAL

M. p.s were determined in an electrically heated copper block.

General Procedure: Reduction in aqueous acetic acid–pyridine. The nitrile (1 g.) and hydrated sodium hypophosphite (2 g.) in 1 : 1 : 2 water–acetic acid–pyridine (29 c.c.), complete dissolution being achieved by addition of a little additional acetic acid if necessary, were treated with Raney nickel (0·3—0·4 g.) and stirred at 40—45° for 1—1·5 hr. The mixture was filtered, the catalyst extracted with a little warm aqueous alcohol, and the extract added to the filtrate. For quantitative estimation an aliquot part of the filtrate was treated with phenylhydrazine or 2,4-dinitrophenylhydrazine in the usual manner. The remainder of the filtrate was diluted with water (which precipitated, for example, the sparingly soluble β-naphthaldehyde or *p*-chlorobenzaldehyde in good yield) and extracted with ether, and the extract was washed to remove pyridine and acetic acid and evaporated to furnish the aldehyde.

Using equimolecular quantities of nitrile and hypophosphite gave lower yields.

The amount of solvent used and the proportions of the components were arbitrary and not critical. The solution was acid to litmus.

The Raney nickel [11] was not especially reactive and was effective even after storage over ethanol in the ice-chest for many months.

When a magnetic stirrer was used the nickel tended to accumulate on the poles of the magnet, but test runs with a mechanical stirrer did not give significantly higher yields.

Little if any hydrogen was evolved during the initial stirring, but gas evolution became more evident when the reduction was complete. Immediate evolution of hydrogen occurred in those cases (*e.g.*, *o*-tolunitrile) in which reduction was relatively slow. In some instances reduction appeared to be complete in ~30 min. and the reaction time for a given nitrile was largely determined by the quantity of catalyst and the temperature used.

A number of reductions in aqueous acetic acid were studied at room temperature; it was

[11] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., London, 1959, 3rd edn., p. 870.

found that if the stirred solution was warmed the rate of deactivation of the catalyst increased and the results were erratic, unlike the result when pyridine was used in the solvent mixture.

Reduction in 50% *Acetic Acid* (v/v).—A solution of the nitrile (1 g.) and sodium phosphite (2 g.) in 50% acetic acid (40 c.c.) was stirred with Raney nickel (0·3—0·4 g.) for 4 hr. The following yields of aldehyde (as the 2,4-dinitrophenylhydrazone) were obtained: Ph 70—80%; *p*-$Me{\cdot}C_6H_4$ 80%; *o*-$Me{\cdot}C_6H_4$ 12%, 2 hr.; *m*-$Me{\cdot}C_6H_4$ 70%; *o*-$Cl{\cdot}C_6H_4$ 40%; *p*-$Cl{\cdot}C_6H_4$ 60—70%; *p*-$MeO{\cdot}C_6H_4$ 85%; *p*-$NH_2{\cdot}SO_2{\cdot}C_6H_4$ 55—65%, as the anil; Et, 25%, 2 hr. (4 g. of hypophosphite used).

Reduction in 75% *Acetic Acid* (v/v).—A solution of the nitrile (5 g.) and sodium hypophosphite (10 g.) in 75% acetic acid (40 c.c.) was stirred with Raney nickel (1·5—2 g.) for several hours. The following yields of aldehyde were obtained (as the 2,4-dinitrophenylhydrazone): Ph 65—70%, 3 hr.; *p*-$Me{\cdot}C_6H_4$ 75%, 3 hr.; *p*-$MeO{\cdot}C_6H_4$ 73%, 2 hr.; *p*-$Cl{\cdot}C_6H_4$ 71%, 3 hr.; β-$C_{10}H_7$, 70%, 5 hr. Poor yields (10—15%) were obtained from *o*-$Me{\cdot}C_6H_4{\cdot}CN$ and α-$C_{10}H_7{\cdot}CN$. Dioxan and acetic acid (10 c.c. each) were added to dissolve the last two nitriles of this list.

Qualitative Test for Nitriles.—Raney nickel (50—75 mg.) was added to the nitrile (50—75 mg.) dissolved or suspended in syrupy orthophosphoric acid (2 c.c.) in a small beaker or test-tube. The mixture was warmed on the water-bath (70—90°) for 10 min. with occasional shaking. 1 : 1 Aqueous alcohol (5 c.c.) was then added, the mixture filtered and treated with 2,4-dinitrophenylhydrazine reagent [13] (25 c.c.), the precipitate was filtered off, washed with hot water, and dried, and its m. p. determined. The following nitriles were tested, the m. p. of the crude 2,4-dinitrophenylhydrazone being recorded, followed by the reported m. p.: [12] Ph 234—237°, 239—240°; *o*-$Me{\cdot}C_6H_4$ 191—193°, 194°; *p*-$Me{\cdot}C_6H_4$ 236—239°, 233°; α-$C_{10}H_7$ 248—251°, 254°; β-$C_{10}H_7$ 264—268°, 270°; *o*-$Cl{\cdot}C_6H_4$ 205—209°, 209—210°; *p*-$Cl{\cdot}C_6H_4$ 264—268°, 269—270°; *p*-$MeO{\cdot}C_6H_4$ 249—252°, 253—254°; Pr 115—120°, 120—121°; $Ph{\cdot}CH{:}CH$ 240—246° (crystallised from acetic acid), 254—255°.

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[*Received, April 2nd*, 1962.]

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[12] Johnson, *J. Amer. Chem. Soc.*, 1953, **75**, 2720; also ref. 11, p. 723.
[13] Ref. 11, p. 1061.