Reductions with Raney Alloy in Alkaline Solution

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Improved yields of primary amines have been obtained by the reduction of nitriles and oximes with Raney alloy. Oximes can also be reduced with Raney nickel and sodium hypophosphite. Treatment of ketoximes with Raney nickel yields the ketones.

PAPA[1] and others[2-4] have described the reduction of a variety of compounds using Raney nickel alloy and aqueous alkali; the conversion of oximes[3] and nitriles[4] into primary amines was only moderately successful. By conducting the respective reductions without external heating we have obtained the amines in improved yields (see column A in Table). In some instances, the carbonyl compound and hydroxylamine hydrochloride reacted to form the oxime which was then reduced in solution without isolation (column B).

Reduction of oximes to the corresponding amines was effected also by means of sodium hypophosphite and Raney nickel in alkaline solution (column C); this method was, however, not successful with nitro-compounds, nitriles, aldehydes, and ketones which were recovered unchanged.

It is noteworthy that virtually complete deoximation to the carbonyl compound resulted on refluxing an oxime in alkaline solution with Raney nickel; it would appear that hydroxylamine, produced in the equilibrium

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[1] D. Papa, E. Schwenk, and B. Whitman, *J. Org. Chem.*, 1942, **7**, 587, and subsequent Papers.

[2] P. L. Cook, *J. Org. Chem.*, 1962, **27**, 3873.

[3] T. Kametani and Y. Nomura, *J. Pharm. Soc. Japan*, 1954, **74**, 413.

[4] T. Kametani and Y. Nomura, *J. Pharm. Soc. Japan*, 1954, **74**, 889.

shown, is decomposed by the catalyst with consequent liberation of the ketone:

$$RR_1C{=}NOH + H_2O \rightleftharpoons RR_1C{=}O + NH_2OH$$

Acetoacetanilide is converted into β-hydroxybutyranilide by Raney nickel and hydrogen under pressure[5] and by means of potassium borohydride;[6] the carbinol can also be conveniently obtained in good yield using Raney alloy and dilute alkali under normal conditions.

Yields of amines from reduction of oximes and nitriles

	Yield (%)		
Oxime	A	B	C
Benzophenone	89	85	89
Acetophenone	88	63	78
Propiophenone	92	78	60
Dibenzyl ketone	93		
p-Bromoacetophenone	77[a]		76
Cyclopentanone	82		52
Cyclohexanone	88	68	61
Acetone	44[b]		
Diacetyldioxime	8[c]		
Benzaldehyde		50	
Anisaldehyde		63	
p-Bromobenzaldehyde	62[a]	65[a]	72
n-Heptaldehyde		67	
Nitrile			
Benzo	62		
p-Methoxybenzo	79		
α-Naphtho	82		
Cinnamo	36[d]		
Phenylaceto	76		
Succino	9		
n-Capro	52		

[a] The bromine group was removed. [b] 3 g. of alloy used. [c] 6 g. of alloy used. [d] The double bond was reduced.

EXPERIMENTAL

Reduction to Amines.—(*a*) Raney alloy (1·5 g.) was added in one portion to a (magnetically) stirred solution of the appropriate oxime or nitrile (1 g.) in ethanol (20 ml.) and 2N-sodium hydroxide (20 ml.). No external cooling was used and the stirring was continued for 1 hr. The resulting amine was generally isolated by extraction of the mixture with chloroform and was characterised, if required, by conversion into a suitable derivative.

(*b*) A solution of the appropriate aldehyde or ketone (1 g.) and hydroxylamine hydrochloride (1 g.), in 30% sodium hydroxide (10 ml.) and ethanol (20 ml.) was boiled under reflux for 20 min., cooled, diluted with water (10 ml.), and treated with Raney alloy as in (*a*).

(*c*) The oxime (1 g.), ethanol (20 ml.), 2N-sodium hydroxide (20 ml.), and freshly prepared Raney nickel (~0·3 g.) were stirred magnetically and 1M-sodium hypophosphite (NaH_2PO_2,H_2O) solution added at such a rate that little hydrogen was evolved. The reduction was conducted at *ca.* 25 mm. above atmospheric pressure, and was complete when hydrogen was freely liberated. The amine was isolated as indicated above.

Deoximation by Raney Nickel.—The oxime (1 g.) dissolved in 2N-sodium hydroxide (10 ml.) and ethanol (10 ml.) was heated under reflux with Raney nickel (~1 g.) for 1 hr. The mixture was filtered and the ketone isolated by chloroform extraction of the filtrate and subsequent evaporation of the solvent. The following ketones were obtained in almost theoretical yield from the corresponding oximes: benzophenone, acetophenone, propiophenone, and dibenzyl ketone. In each case the crude product was shown to be free from oxime impurity by its infrared spectrum.

Reduction of Acetoacetanilide.—Raney alloy (2 g.) was added in one portion to a solution of acetoacetanilide (2 g.) in 2N-sodium hydroxide (60 ml.) and the mixture stirred without external cooling for 1 hr. Hydrogen was liberated and the sparingly soluble β-hydroxybutyranilide separated as a scum. The alkaline mixture, after being left overnight, was filtered and the insoluble residue extracted with warm chloroform. Evaporation of the solvent afforded the crude carbinol in ~60% yield; colourless crystals from dilute ethanol, m. p. 113—114° (lit.,[6] 112—113°). Similarly prepared in 60—70% yields were β-hydroxybutyr-*o*-toluidide, m. p. 89—90° (lit.,[6] 91°), and β-hydroxy-β-phenyl-propionanilide, m. p. 162—163° (lit.,[7] 160°). The identity of the product was confirmed in each case by its infrared spectrum.

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[5] M. Vesely, J. Horyna, V. Kmonicek, and M. Kramsky, Czech. P., 112,525/1964 (*Chem. Abs.*, 1965, **62**, 16,149).

[6] P. Pastour and E. Maréchal, *Compt. rend.*, 1956, **243**, 166.

[7] A. Darapsky, *J. prakt. Chem.*, 1917, [2], **96**, 327.