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PREPARATION OF OXIMES AND N-ALKYLHYDROXYLAMINES BY HYDROGENATION OF α-CHLORO NITRO COMPOUNDS

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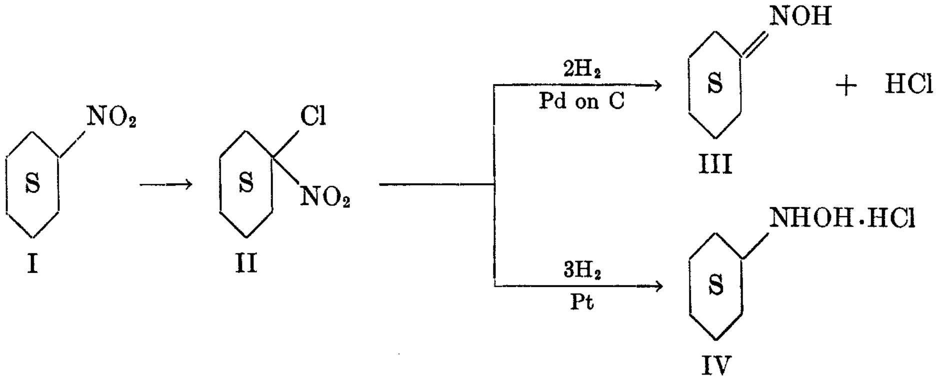
Various methods for the preparation of oximes and N-alkylhydroxylamines by partial reduction of aliphatic nitro compounds have been reported. For example, the potassium salt of aci-nitrocyclohexane has been treated with stannous chloride in hydrochloric acid to give an 80% yield of cyclohexanone oxime (1). Similarly, benzaldehyde oxime resulted from the reduction of the sodium salt of aci-phenylnitromethane with zinc or sodium amalgam (2). N-Alkylhydroxylamines have been the principal products obtained from the corresponding nitroparaffins by reduction with metals such as zinc (3) and tin (4), or with hydrogen in the presence of acid and a palladium catalyst (5). Other catalysts such as platinum (6) or nickel (7) have been used to hydrogenate nitroparaffins to amines and, according to a recent report, to oximes (8).

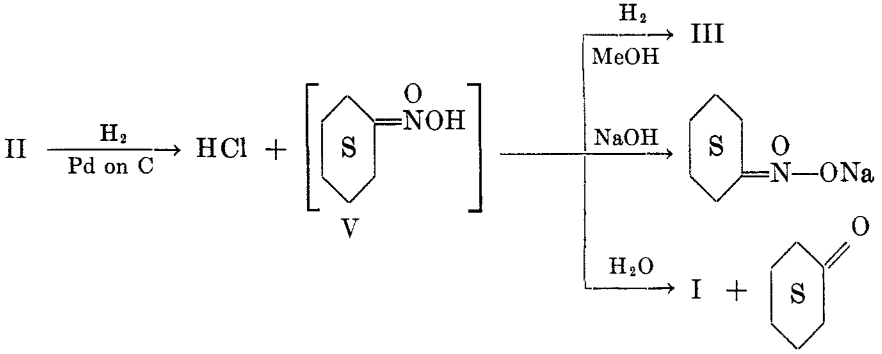
Recent work (9) has shown that nitro alkanes and nitro cycloalkanes can be converted to the corresponding oximes or N-alkylhydroxylamines by chlorination to α-chloro nitro alkanes and nitro cycloalkanes, and selective hydrogenation of these intermediates over specific catalysts.



In experiments with 1-chloro-1-nitrocyclohexane (II), which was prepared according to a method (10) described for nitroparaffins by chlorination of the sodium salt of aci-nitrocyclohexane, hydrogenation in methanol over a palladium-on-charcoal catalyst produced up to 80% yields of cyclohexanone oxime (III). The exothermic reduction started at room temperature and proceeded under 10–50 pounds hydrogen pressure until two mole equivalents of the gas had been absorbed. Cyclohexanone oxime was isolated by evaporating the solvent after neutralizing the hydrochloric acid formed in the reaction. The minimum catalyst concentration and hydrogen pressure employed were interdependent variables. Thus, a high yield of product and a practical rate of hydrogenation were achieved at 50 pounds or less hydrogen pressure only when at least 0.5% palladium based on 1-chloro-1-nitrocyclohexane was used, whereas 0.1% catalyst was sufficient to give equivalent results at 500 pounds hydrogen pressure.

When a platinum catalyst was substituted for palladium in the hydrogenation of 1-chloro-1-nitrocyclohexane, the reduction proceeded further to yield N-cyclohexylhydroxylamine hydrochloride (IV), which was converted to the free base with sodium hydroxide. N-Cyclohexylhydroxylamine was identified by the fact that it reduced Tollens' reagent, gave a neutral equivalent corresponding to the theoretical value, and was identical to a product obtained in an independent synthesis described previously (11).

In view of the fact that all previously reported reductions of nitroparaffins to oximes (1, 2) proceeded through the intermediate *aci* forms of the nitro compounds, it is postulated that the first step in the hydrogenation of 1-chloro-1-nitrocyclohexane involves removal of the halogen with the formation of aci-nitrocyclohexane (V). The extent to which further reduction proceeds to give different products depends on the selectivity of the catalyst used. It is not surprising that the reduction stopped at the oxime stage when palladium was employed, since it is known that oximes are not readily hydrogenated in the presence of acids with this catalyst (12).



The effect of various media on the course of the hydrogenation provided information on the mechanism of the reaction. Methanol and ethanol were suitable diluents for use in the hydrogenation of 1-chloro-1-nitrocyclohexane to cyclohexanone oxime, but when water was used the product consisted of a mixture of cyclohexanone and nitrocyclohexane. This is in agreement with the findings of previous investigators who reported that hydrogenation of α-chloro nitro alcohols over palladium catalysts in aqueous systems gave nitro alcohols (13) and hydroxycarbonyl compounds (14). The fact that no oximes were formed may be explained on the basis that, in the presence of aqueous acid, the intermediate aci-nitrocyclohexane hydrolyzed to the ketone and rearranged in part to the nitro compound.

Actual isolation of the proposed intermediate was achieved when a 75% yield of the sodium salt of aci-nitrocyclohexane was obtained from a hydrogenation of the chloro nitro compound over palladium in a 10% aqueous sodium hydroxide solution. In this reaction the halogen was removed initially and the labile aci-nitrocyclohexane was converted to the stable sodium salt.

To illustrate the general applicability of this new synthesis, 2-chloro-2-nitropropane was hydrogenated over palladium-on-charcoal in a similar manner to give a 35% yield of acetone oxime.

EXPERIMENTAL

1-Chloro-1-nitrocyclohexane. 1-Chloro-1-nitrocyclohexane was prepared in substantially quantitative yield from the sodium salt of aci-nitrocyclohexane by reaction with chlorine in aqueous solution at −5 to 0°, according to a procedure described for other nitroparaffins by Henry (10). A distilled sample, b.p. 81–82°/8 mm., gave the following analyses:

Anal. Calc'd for $C_6H_{10}ClNO_2$: N, 8.6; Cl, 21.7.
Found: N, 8.6; Cl, 21.3.

Hydrogenation of 1-chloro-1-nitrocyclohexane. Except where otherwise designated, the following hydrogenations were carried out in a laboratory Burgess-Parr hydrogenation apparatus equipped with "Pyrex" brand glass pressure bottles. The hydrogenation vessel was charged with 0.1 mole of the compound to be reduced, 100 ml. of solvent, and the catalyst. The vessel was evacuated and then pressured with 40–50 pounds of hydrogen. The hydrogenations proceeded at room temperature with agitation, and the vessels were repressured with hydrogen when the pressure fell below 15 pounds. When absorption of hydrogen had ceased, the contents of the bottle were removed and the various products obtained were isolated as described below.

Palladium-on-charcoal.[1] In the experiment which gave the highest yield of cyclohexanone oxime, 16.35 g. (0.1 mole) of 1-chloro-1-nitrocyclohexane was hydrogenated over 1.6 g. of 10% palladium-on-charcoal in 100 ml. of methanol as described above. After 0.2 mole of hydrogen was absorbed the reaction stopped; the filtrate was neutralized with 10% aqueous sodium carbonate and most of the methanol was evaporated under reduced pressure, at which point cyclohexanone oxime precipitated. The yield was 9 g., (80%). The product melted at 88°. A similar result was obtained in a stainless-steel bomb at 500 pounds hydrogen pressure using 0.16 g. of 10% palladium-on-charcoal catalyst.

The above hydrogenation was repeated exactly except that 10% aqueous sodium hydroxide solution was substituted for the methanol. Only 0.1 mole of hydrogen was absorbed. The catalyst was removed from the resulting clear, aqueous solution as before. Evaporation of the solvent under reduced pressure deposited a white solid, which proved to be the sodium salt of aci-nitrocyclohexane. Acidification of an aqueous solution of this salt with hydrochloric acid resulted in the separation of an oil, which was extracted with ether and distilled. Nine grams of nitrocyclohexane, b.p. 95°/22 mm., was obtained. In a similar run where water was employed instead of caustic solution, a total of 10 g. of liquid was obtained, which consisted of a mixture of cyclohexanone and nitrocyclohexane, which were identified by their boiling points.

A 0.1-mole sample of 2-chloro-2-nitropropane was hydrogenated in methanol over palladium-on-charcoal as described above for 1-chloro-1-nitrocyclohexane. A 36% yield of acetone oxime (m.p. 58°) was isolated.

Platinum. Using a procedure similar to that described for the preparation of cyclohexanone oxime, 1-chloro-1-nitrocyclohexane was hydrogenated in ethanol in the presence of a platinum oxide catalyst. Following the absorption of 0.3 mole of hydrogen, the catalyst was removed and the solution was evaporated to dryness under reduced pressure. The

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[1] This catalyst was purchased from Baker and Company, 113 Astor St., Newark, N. J., and consisted of 10% palladium supported on activated charcoal powder (Baker catalyst #25).

residual salt was recrystallized from ethyl acetate, was dissolved in water, and was made basic with 10% sodium hydroxide. The white, fluffy solid which precipitated was collected on a filter, dried, and was recrystallized from a 6:4 benzene-petroleum ether mixture. A 65% yield of N-cyclohexylhydroxylamine, m.p. 140° (11), was obtained. Neutral equivalent, calc'd 115; found 113. This compound reduced Tollens' reagent readily.

SUMMARY

1-Chloro-1-nitrocyclohexane has been hydrogenated to cyclohexanone oxime in high yield over a palladium-on-charcoal catalyst in nonaqueous systems. When a platinum catalyst was used, the reduction proceeded further to yield N-cyclohexylhydroxylamine hydrochloride.

Evidence is presented to show that the reaction proceeds through the intermediate aci-form of the nitro compound.

Acetone oxime was obtained from 2-chloro-2-nitropropane by hydrogenation over a palladium catalyst.

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REFERENCES

(1) KONOWALOFF, *J. Russ. phys.-chem. Soc.*, **30**, 960 (1898).
(2) HANTZSCH AND SCHULTZE, *Ber.*, **29**, 2251 (1896).
(3) BAMBERGER, *Ber.*, **27**, 1347 (1894).
(4) MEYER AND HOFFMAN, *Ber.*, **24**, 3528 (1891).
(5) SCHMIDT, ASCHERL, AND MAYER, *Ber.*, **58**, 2430 (1925).
(6) SCHALES, *Ber.*, **68**, 1579 (1935).
(7) JOHNSON, U. S. Patent 2,174,498.
(8) DOUMANI AND COE, U. S. Patent 2,423,180.
(9) ROBERTSON, U. S. Patent, 2,420,382.
(10) HENRY, *Chem. Zentr.*, **1898**, I, 192.
(11) VAVON AND BERTON, *Bull. soc. chim.*, **37**, 297 (1925).
(12) GULEVICH, *Ber.*, **57**, 1645 (1924).
(13) WILKENDORF AND TRENNEL, *Ber.*, **56**, 619 (1923).
(14) SCHMIDT AND ASCHERL, *Ber.*, **58**, 356 (1925).