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REDUCTION OF HEXACHLOROACETONE BY 1-BENZYL-1,4-DIHYDRONICOTINAMIDE[1]

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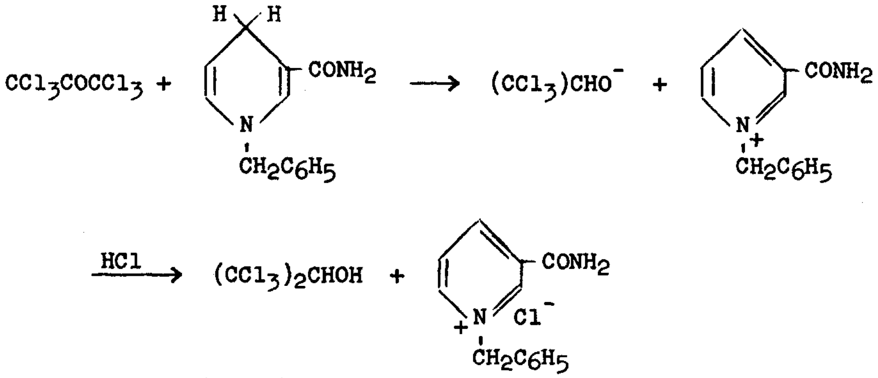
HEXACHLOROACETONE is very readily reduced to hexachloroisopropanol by 1-benzyl-1,4-dihydronicotinamide. The reduction goes violently at room temperature in the absence of solvent, is exothermic, and is accompanied by formation of a black tar. Even at 0° the reaction went vigorously.



Best yields (53-60%) were obtained in formamide in which the initial

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solubility of hexachloroacetone was low. The best yield of hexachloroisopropanol in the absence of solvent was 24%. Hydrolysis of the reaction mixtures with dilute hydrochloric acid gave hexachloroisopropanol (m.p. 87-87.5°), which was identified by its melting point, elemental analysis, infra-red spectrum, and mixed melting point with an authentic sample.[4] A blank run in formamide in which the dihydro compound was absent gave no hexachloroisopropanol. Nicotinamide-1-benzylochloride was identified by its melting point (232-238°), mixed melting point with an authentic sample (no depression), and by the identity of its infra-red spectrum with that of an authentic sample.

The reduction of a "true" ketone in good yield by a dihydronicotinamide model for the coenzyme, dihydrodiphosphopyridine nucleotide (dihydronicotinamide-adenine-dinucleotide), has not yet been accomplished. Pyruvic acid has been reduced to lactic acid in 5-7% yield by 5-(2,4-dinitrophenylthio)-1-(2,6-dichlorobenzyl)-1,4-dihydronicotinamide.[5] Alloxan is reduced rapidly, although in unstated yield, by 1-methyl or 1-n-propyl-1,4-dihydronicotinamide in water at 0° and pH 6-11.[6] Pyruvic acid,[6,7] benzoylformic acid[7] and benzil[8] are reduced in low yield by 2,6-dimethyl-3,5-dicarboethoxy-1,4-dihydropyridine, which is not strictly analogous to a 1-substituted dihydronicotinamide. The olefinic double bond of 1-phenyl-4,4,4-trifluoro-2-buten-1-one is reduced in good yield by 1,2,6-trimethyl-

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[4] M. Geiger, E. Usteri and C. Gränacher, Helv.Chim.Acta 34, 1335 (1951); W. Gerrard and B.K. Howe, J.Chem.Soc. 505 (1955); O. Neunhoeffer and A. Spange, Liebigs Ann. 632, 22 (1960).

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[7] R. Abeles and F.H. Westheimer, J.Amer.Chem.Soc. 80, 5459 (1958).

[8] E.A. Braude, J. Hannah and R. Linstead, J.Chem.Soc. 3257 (1960). The reduction of benzil in low yield by 1-benzyl-1,4-dihydronicotinamide in the absence of solvent has been observed by J.M. Kolyer, Ph.D. Thesis, University of Pennsylvania, p.159 (1960).

3,5-dicarboethoxy-1,4-dihydropyridine.[9]

The ready reduction of hexachloroacetone reported here may be attributed to an increase in the positive character of the carbonyl carbon. The facile reduction of thiobenzophenones by 1-benzyl-1,4-dihydronicotinamide is suggested as being caused by the greater polarity of the thiocarbonyl group.[10] Previous work on the reduction of aromatic nitro and nitroso compounds has indicated that the more electron-deficient the nitrogen atom was, the more readily the group was reduced by 1-substituted dihydronicotinamides.[11] The electron-withdrawing trifluoromethyl group promotes the nonenzymic reduction of a double bond by 1,2,6-trimethyl-3,5-dicarboethoxy-1,4-dihydropyridine.[9]

Chloral is reduced in 3% yield to 2,2,2-trichloroethanol by 1-benzyl-1,4-dihydronicotinamide in the absence of solvent or in chloroform or acetone. The alcohol was identified by gas chromatography and by comparison of its infra-red spectrum with that of an authentic sample.

When the reduction of hexachloracetone was done in acetone, nitromethane or cyclohexene, nicotinamide-1-benzylochloride precipitated quickly; in the case of cyclohexene a yield in excess of 90% was formed within 15 min but no hexachloroisopropanol was detected. The yield of chloride ion in cyclohexene solvent appears to be a function of the purity of the cyclohexene.

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[9] B.E. Norcross, P.E. Klinedinst, Jr. and F.H. Westheimer, Abstracts of Papers, p.74 Q. 140th Meeting, American Chemical Society, Chicago, Illinois, September, 1961.

[10] R.H. Abeles, R.F. Hutton and F.H. Westheimer, J.Amer.Chem.Soc. **79**, 712 (1957).

[11] D.C. Dittmer and J.M. Kolyer, J.Org.Chem. In press.