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SODIUM CYANOBOROHYDRIDE: A REAGENT FOR SELECTIVE REDUCTION OF THE OXAZOLIDINE RING OF C_{20}-DITERPENOID ALKALOIDS

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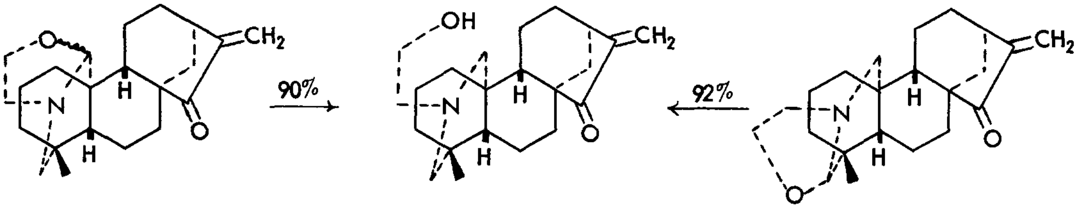
A very selective reduction of the oxazolidine ring of C_{20}*-diterpenoid alkaloid derivatives in the presence of other functional groups, e.g., an α,β unsaturated ketone or a simple ketone, has been achieved in almost quantitative yield using sodium cyanoborohydride.*

In connection with other work we required compounds containing the N-CH_2-CH_2-OH group in the presence of an α,β-unsaturated ketone, e.g., compound 1. Because protection of the carbonyl group in compounds such as 2 and 3 is very difficult, selective reduction of the oxazolidine ring in these compounds has not been heretofore achieved. By conventional methods, compound 1 can be synthesized from veatchine in five or six steps in poor yield. This situation prompted us to investigate the selective reducing properties of sodium cyanoborohydride[1] toward oxazolidine ring-containing compounds.

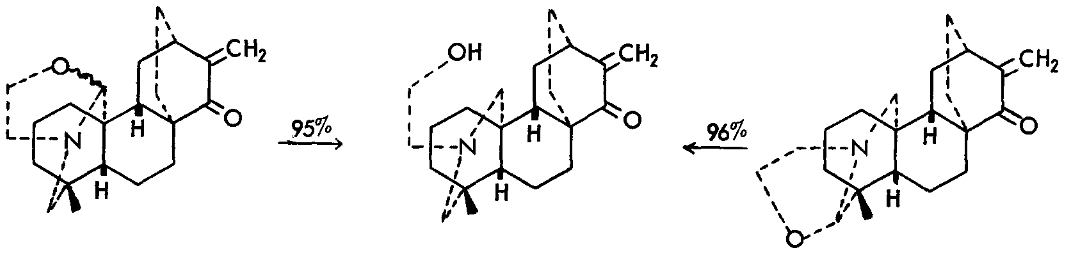


2 Veatchine

1 Dihydroveatchinone
HCl salt: mp. 198-201°

3 Garryinone

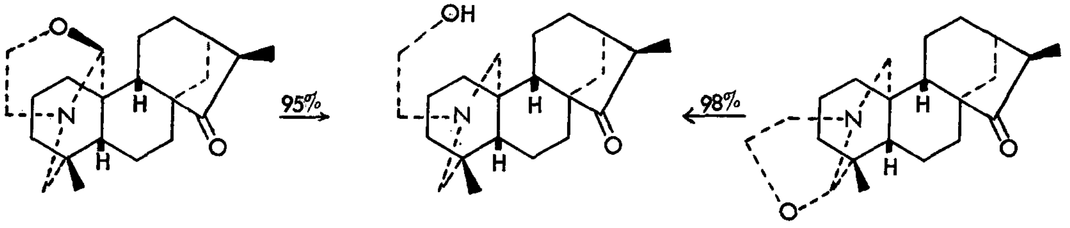
We report here a convenient and high-yield method using sodium cyanoborohydride for converting the oxazolidine ring-containing alkaloid derivatives into their N-CH_2-CH_2-OH group-containing derivatives. At pH 6 to 7 sodium cyanoborohydride reduces the oxazolidine ring in the presence of an α, β-unsaturated ketone or simple ketone with remarkable selectivity. The normal-type and iso-type oxazolidine ring-containing compounds, veatchinone, garryinone, atisinone, isoatisinone, cuauchichicine, isocuauchichicine, and ovatine were reduced to their dihydro derivatives[2] in almost quantitative yield at 25°C. No side products were detected during this reaction. Reduction of these compounds probably takes place via the immonium ions because the normal-type and iso-type oxazolidine rings are known[3] to form the corresponding immonium ions (e.g., 4 and 5) in the presence of ionic solvents or acids. In a typical experiment, to a solution of 60 mg of veatchinone and 60 mg of sodium cyanoborohydride in 10 ml of methanol was added few drops of 10% aq. hydrochloric acid to adjust pH of the reaction mixture between 6 and 7. The resulting solution was stirred continuously at 25°C for 3 hours and the pH of the reaction mixture was maintained between 6 and 7 by adding drops of 10% hydrochloric acid. The solvent was removed *in vacuo*, the residue was treated with 15 ml of sodium carbonate solution, and the mixture was extracted with three 10-ml portions of chloroform. The combined extracts were dried over anhydrous sodium sulphate and evaporated *in vacuo* to give amorphous dihydroveatchinone, in quantitative yield.



Atisinone

Dihydroatisinone
mp. 100–102°
HCl salt: mp. 213–215°

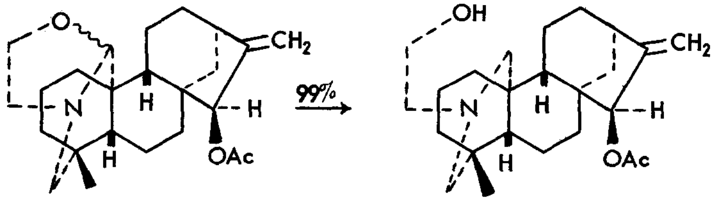
Isoatisinone



Cuauchichicine

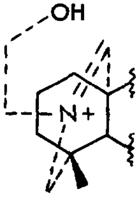
Dihydrocuauchichicine

Isocuauchichicine



Ovatine

Dihydroovatine
HCl salt: mp. 190–194°



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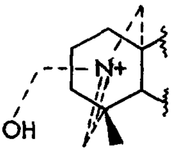

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1. For applications of sodium cyanoborohydride see R. F. Borch, M. D. Bernstein and M. D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971); R. O. Hutchins, C. A. Milewski and B. E. Maryanoff, *J. Am. Chem. Soc.*, **95**, 3662 (1973); R. O. Hutchins, D. Kandasamy, C. A. Maryanoff, D. Masilamani and B. E. Maryanoff, *J. Org. Chem.*, **42**, 82 (1977).
2. Each product was characterized by ^{1}H, ^{13}C NMR, and mass spectral analysis, or by comparison with an authentic sample.
3. S. W. Pelletier and N. V. Mody, *Tetrahedron Letters*, **1477** (1977); S. W. Pelletier and L. H. Keith in "The Alkaloids" Ed. R.H.F. Manske, vol. 12, chapter 2, Academic Press, New York, 1970.

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