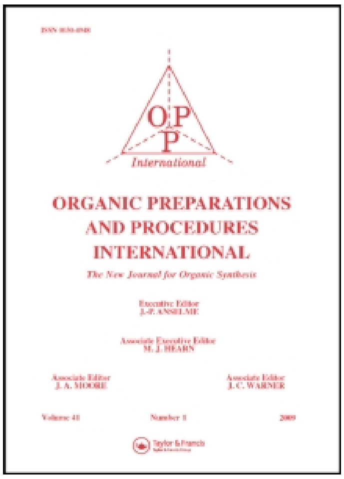


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

REDUCTION OF 5-HYDROXYMETHYL-1-AZA-3,7-DIOXABICYCLO[3.3.0]OCTANE AND OF 2-PHENYL-4,4-DIMETHYLOXAZOLIDINE WITH FORMIC ACID

S. Wawzonek[a]
[a] Department of Chemistry, The University of Iowa, Iowa City, Iowa

To cite this Article Wawzonek, S.(1981) 'REDUCTION OF 5-HYDROXYMETHYL-1-AZA-3,7-DIOXABICYCLO[3.3.0]OCTANE AND OF 2-PHENYL-4,4-DIMETHYLOXAZOLIDINE WITH FORMIC ACID', Organic Preparations and Procedures International, 13: 2, 126 — 129

To link to this Article: DOI: 10.1080/00304948109356109

URL: http://dx.doi.org/10.1080/00304948109356109

16B, 737 (1978).

4. N. D. Heindel and J. R. Reid, J. Heterocyclic Chem., 17 1087 (1980).
5. N. D. Heindel, J. R. Reid, and J. E. Willis, J. Medicin. Chem., 14, 453 (1971).
6. J. R. Reid and N. D. Heindel, J. Heterocyclic Chem., 13, 925 (1976).
7. R. M. Acheson, Advances in Heterocyclic Chemistry, Vol. 1, A. R. Katritzky, Ed., Academic Press, New York, 1963 pp. 143-157.

REDUCTION OF 5-HYDROXYMETHYL-1-AZA-3,7-DIOXABICYCLO[3.3.0]OCTANE AND OF 2-PHENYL-4,4-DIMETHYLOXAZOLIDINE WITH FORMIC ACID

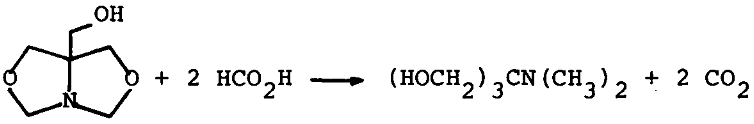
Submitted by (5/27/80) S. Wawzonek

Department of Chemistry
The University of Iowa
Iowa City, Iowa 52242

Amino alcohols which have an amino group or a monosubstituted amino group and an alcohol group attached to adjacent carbon react with aldehydes to give oxazolidines. Amino polyhydric alcohols with similar structures react with two moles of aldehydes to yield substituted 1-aza-3,7-dioxabicyclo[3.3.0]octanes. These heterocyclic compounds are useful for the preparation of monoalkyl or dialkylamino alcohols; reduction has been accomplished by hydrogenation using 1% palladium on charcoal as a catalyst at 100° and 1000 psi.[1]

The same type of reduction has been found to occur when 5-

hydroxymethyl-1-aza-3,7-dioxabicyclo[3.3.0]octane(I) prepared from tris(hydroxymethylamino)methane and formaldehyde was heated with 88% formic acid.



I II

The resulting tris(hydroxymethyl)-methyl dimethylamine(II) was isolated as the hydrochloride in a 93% yield. Direct treatment of tris(hydroxymethyl)methylaminomethane with formaldehyde and formic acid[2] as a method for preparing II was not satisfactory and afforded an impure product. The generality of this reduction was demonstrated by the conversion of 2-phenyl-4,4-dimethyloxazolidine(III) to 2-benzylamino-2-methyl-1-propanol(IV) in a 53-54% yield. This method had an advantage over the catalytic hydrogenation method[1] since debenzylation occurs in the latter unless a temperature of 35-45° is used. The amino alcohol IV once formed is debenzylated only slowly by formic acid; 88% of the amine IV was recovered unchanged after heating with 88% formic acid for 24 hrs.

III IV

EXPERIMENTAL

Melting points are uncorrected.

tris-(Hydroxymethyl)methyldimethylamine(II).- 5-Hydroxymethyl-

1-aza-3,7-dioxabicyclo[3.3.0]octane(I)[1] (73.5 g, 0.5 mole) was heated with 88% formic acid (110 ml) on a steam bath for 24 hrs. The product was treated with an excess of 6N hydrochloric acid and the resulting solution was evaporated to dryness under reduced pressure. The white solid obtained was triturated with methanol and gave 86.4 g of the hydrochloride, mp. (softening at 200°) 228° (dec.).

Anal. Calcd for $C_6H_{16}O_3NCl$: C, 38.81; H, 8.62; N, 7.55.
Found: C, 38.94; H, 8.41; N, 7.48.

The hydrochloride (92.7 g, 0.5 mole) upon basification with 10% sodium hydroxide followed by removal of water under reduced pressure gave a solid which was extracted with chloroform. Removal of the chloroform gave 68 g (91% yield) of II, mp. 90°.[1] The mp. of a mixture with a sample prepared by hydrogenation was undepressed.

2-Benzylamino-2-methyl-1-propanol(IV).- 2-Phenyl-4,4-dimethyloxazolidine(III)[1] (17.7 g, 0.1 mole) was heated with 88% formic acid (15 ml) on a steam bath for 24 hrs. The resulting solution was treated with 25 ml of 6N hydrochloric acid and the excess formic acid and hydrochloric acid were removed under reduced pressure. The oily solid obtained was heated with an additional 25 ml of 6 N hydrochloric acid on a steam bath for 8 hrs and the excess hydrochloric acid was removed using reduced pressure. The resulting solid upon triturating with benzene gave a solid hydrochloride (17.2 g) which was treated with excess 10% sodium hydroxide. Extraction with benzene followed by removal of the solvent gave 9.6 g of solid IV, mp. 68-70°, lit.[1] mp. 67.6°. Recrystallization from cyclohexane did not change the melting point. Structure IV was supported by elemental analysis and IR and NMR spectra. A mixture melting point with the starting material (III) occurred at 45-50°.

Amine IV after treatment with formic acid in the same manner was recovered in an 88% yield.

REFERENCES

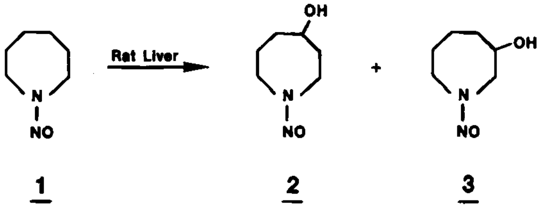
1. M. Senkus, J. Am. Chem. Soc., 67, 1515 (1945).
2. T. Clarke, B. Gillespie, and Z. Weisshaus, J. Am. Chem. Soc., 55, 4571 (1933).

REACTION OF DIAZOMETHANE WITH N-NITROSO-4-PIPERIDINONES

Submitted by (6/19/80) Joseph E. Saavedra

Chemical Carcinogenesis Program
NCI Frederick Cancer Research Center
Frederick, MD 21701

N-Nitrosohexahydroazepine 1 is a powerful liver and esophageal carcinogen in rats[1] and initial biochemical studies indicated that γ-hydroxylation to 2 and β-hydroxylation to 3 are major metabolic pathways (Scheme 1).



Scheme 1

In order to prepare metabolites 2 and 3 for use as synthetic standards,[2] we explored the ring expansion of some N-