Tetrahedron Letters, Vol. 33, No. 17, pp. 2361-2362, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Highly Selective Reduction of 2-Nitrocycloalkanones to 2-Nitrocycloalkanols with Zinc Borohydride in DME

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Key Words : Zinc borohydride; reduction of 2-nitrocycloalkanones; 2-nitrocycloalkanols.

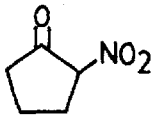
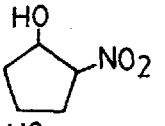
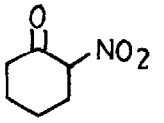
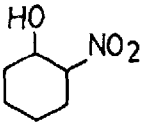
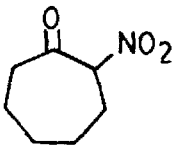
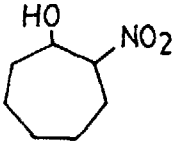
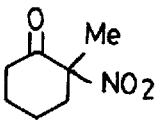
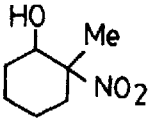
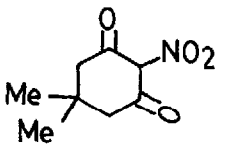
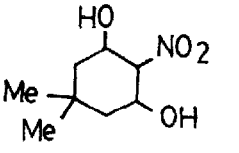
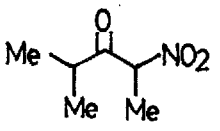
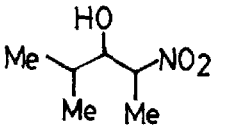
Abstract : Clean and efficient reduction of 2-nitrocycloalkanones to 2-nitrocycloalkanols has been achieved using zinc borohydride in 1,2-dimethoxyethane.

2-Nitrocycloalkanones are of great synthetic potential in organic chemistry.[1] In connection with another project we sought to reduce 2-nitrocycloalkanone to 2-nitrocycloalkanol. But, the reduction of 2-nitrocycloalkanones to the corresponding nitroalcohols is complicated because of a peculiar reactivity of these compounds which involves cleavages of the C(1)-C(2) bond and carbon-nitrogen bond by action of external nucleophiles under mild conditions.[1,2] Thus ring cleavage and/or denitration are frequently encountered during reduction of these compounds with many reducing agents.[1-3] Reduction of 2-nitrocycloalkanones with a stoichiometric amount of sodium borohydride has been reported to give the corresponding nitrocycloalkanols[4], whereas use of sodium borohydride in excess (5 equivalents) led to ring cleavage.[3] In light of these results, our recent endeavour of selective reductions using zinc borohydride[5] prompted us to investigate the reduction of 2-nitrocycloalkanones. We now report that zinc borohydride in 1,2-dimethoxyethane (DME)[6] cleanly reduces 2-nitrocycloalkanones to the corresponding nitrocycloalkanols without any ring cleavage or denitration.

In a typical general procedure, the 2-nitrocycloalkanone[7] (5 mmol) was stirred with zinc borohydride (5 mmol) in DME[6] at room temperature. The reaction was complete within 10 minutes. The reaction mixture was decomposed with H_2O and extracted with ether. Evaporation of solvent left the crude product which was purified by column chromatography over silica gel. The results are reported in Table 1.

As shown in Table 1, representative examples of different types of 2-nitrocycloalkanones were reduced with zinc borohydride in DME to give the corresponding 2-nitrocycloalkanols as mixture of stereoisomers[8] in high yields. Apparently, no significant selectivity for a particular stereoisomer was observed. The acyclic nitroketone (entry 6) was also reduced to the corresponding nitroalcohol. The reductions are reasonably fast. The experimental procedure is very simple compared to that with sodium borohydride.[4] Reduction with excess (10 equiv) zinc borohydride also afforded the same nitrocycloalkanol in similarly good yield without any ring cleavage. Thus this

Table 1: Reduction of α-nitroketones to the corresponding alcohols with $Zn(BH_4)_2$/DME.

entry	substrate	time	product	yield, %[a]	% of isomers[b]
1		5 min		73	40:60
2		5 min		69	35:65
3		10 min		88	30:70
4		5 min		84	55:45
5		10 min		74	10:30:60
6		5 min		90	

[a]yield of isolated products as mixtures of stereoisomers; [b]as determined by GC.

reagent avoids the disadvantages of sodium borohydride with regard to using excess reagent.[3] Moreover, zinc borohydride is neutral and compatible with a number of functional groups like carboxylic ester, nitrile, ketal etc.[5]

In conclusion, zinc borohydride offers significant advantages towards reduction of 2-nitrocycloalkanones to 2-nitrocycloalkanols over the existing methods[4] and recommends itself for the simplicity, reliability, the mild conditions needed and the high yields obtained.

Acknowledgement: Financial support from DST, New Delhi (Grant No. SP/S1/G-49/88) is gratefully acknowledged. A.R.D. thanks CSIR for his fellowship.

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7. The nitrocycloaokanones were prepared according to the procedure: Dampawan, P.; Zajac, Jr., W.W. Synthesis **1983**, 545.
8. The stereochemical assignment of each isomer is yet to be determined and will be disclosed in the full paper.

(Received in UK 11 February 1992)