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Reduction of Conjugated Nitroalkenes with Zinc Borohydride. A Mild Method for Converting Monosubstituted Nitroalkenes to Nitroalkanes and Disubstituted Ones to Oximes

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Abstract : Mono-β-substituted conjugated nitroalkenes are readily reduced by zinc borohydride in 1,2-dimethoxyethane to the corresponding nitroalkanes, whereas the disubstituted ones furnish the corresponding oximes in excellent yields.

Nitroalkenes are valuable precursors to a wide variety of building blocks and intermediates in organic synthesis.[1] The reduction of conjugated nitroalkenes is very interesting and complex. A variety of reducing agents have been used to give different results.[2] Lithium aluminium hydride produces a mixture of products containing saturated amine, nitroalkane, oxime and hydroxylamine,[3] whereas sodium borohydride, lithium borohydride and sodium trimethoxyborohydride, though, furnish primarily the corresponding nitroalkanes, these reduction reactions are often accompanied by consecutive processes in which Michael addition of the initial reduction product to the parent nitroalkene give salts of the corresponding 1,3-dinitroketones and related polynitroalkanes of higher molecular weights.[4] The secondary Michael addition in the reduction with sodium borohydride is prevented using aqueous ethanol or acetonitrile and maintaining the pH of the reduction medium between 3-6.[5] Similar results are also achieved with sodium borohydride in THF-MeOH[6] and ethanol.[7] Sodium borohydride supported on amberlite[8] and sodium cyanoborohydride[9] are also reported to reduce the conjugated nitroalkenes to the corresponding nitroalkanes, and on the other hand, borane together with sodium borohydride[10] furnish N-substituted hydroxylamines. In light of these results, our recent endeavour of selective reductions using zinc borohydride[11] prompted us to initiate a systematic investigation of the reduction of conjugated nitroalkenes with this reducing agent. Very interestingly, we have observed that mono-β-substituted conjugated nitroalkenes are reduced by zinc borohydride in DME to the corresponding nitroalkanes, whereas the disubstituted ones produced the corresponding oximes.[12]

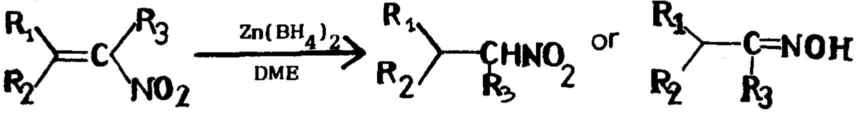


Table 1 : Reduction of Conjugated Nitroalkenes with Zinc Borohydride in DME

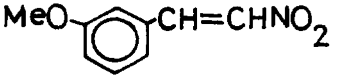
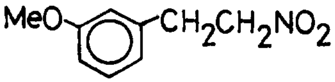
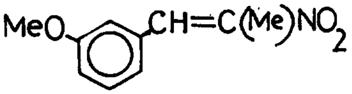
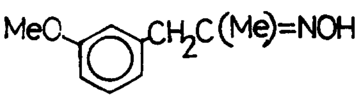
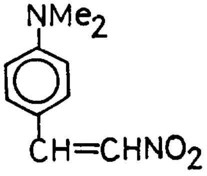
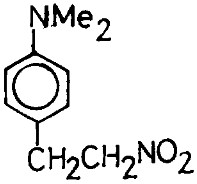
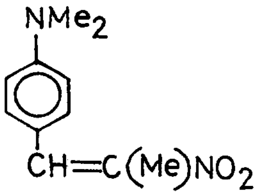
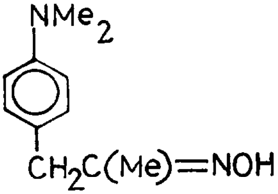
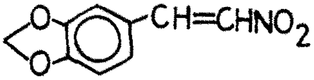
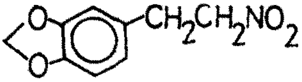
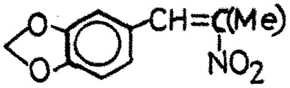
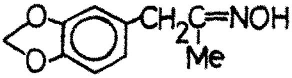
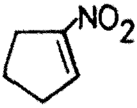
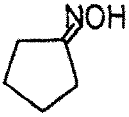
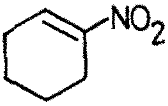
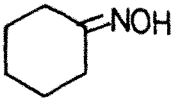
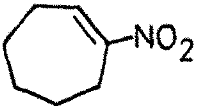
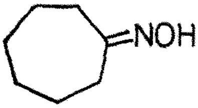
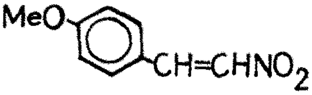
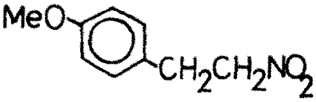
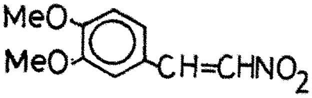
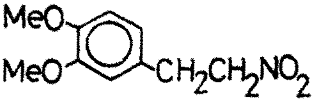
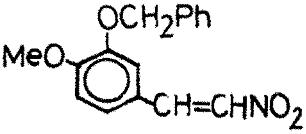
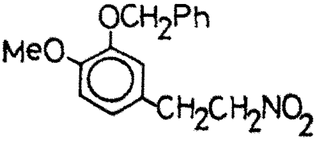
entry	conjugated nitroalkene	temp(°C)	time(h)	product[a]	yield(%)[b]
1	$\mathrm{PhCH{=}CHNO_2}$	0	6	$\mathrm{PhCH_2CH_2NO_2}$	88
2	$\mathrm{PhCH{=}C(Me)NO_2}$	25	6	$\mathrm{PhCH_2C(Me){=}NOH}$	81
3	$\mathrm{PhC(Me){=}CHNO_2}$	25	9	$\mathrm{PhCH(Me)CH{=}NOH}$	83
4	$\mathrm{PhC(Me){=}C(Me)NO_2}$	25	24	No reaction	
5		0	6		93
6		25	7		80
7		0	12		88
8		25	6		73

Table 1 (Contd...)

entry	conjugated nitroalkene	temp (°C)	time(h)	product[a]	yield(%)[b]
9		0	6		88
10		25	7		82
11		0	0.75		75
12		0	1		90
13		0	1.5		91
14		0	6		90
15		0	10		86
16		0	6		93

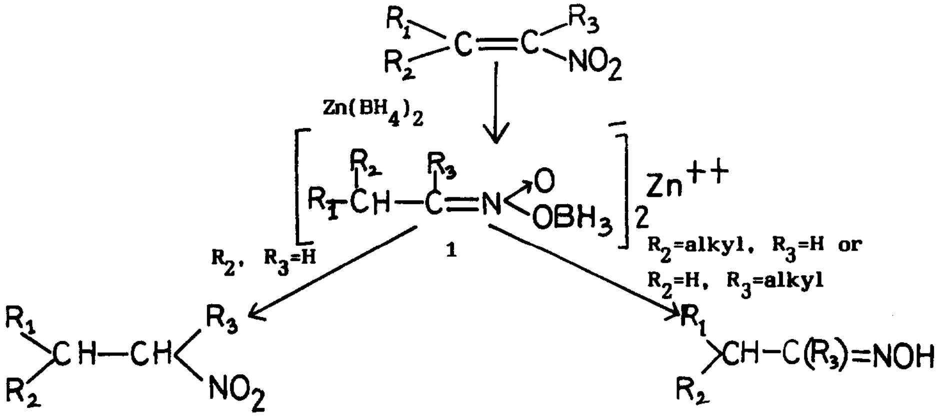
[a] oximes were obtained as mixture of E and Z isomers;

[b] yield of isolated pure products, fully characterized by their IR, NMR data.

In a typical general procedure, the conjugated nitroalkene[13] was stirred with zinc borohydride in DME till completion of the reaction, as monitored by TLC. The reaction mixture was decomposed with water and extracted with ether. Evaporation of solvent left the crude product which was then purified by column chromatography. The results are reported in Table 1.

As shown in Table 1, several structurally varied conjugated nitroalkenes were reduced with zinc borohydride in DME. In general, mono-β-substituted nitroalkenes (entries 1,5,7,9,14,15,16) underwent clean and smooth reductions to the corresponding nitroalkanes in excellent yields, whereas disubstituted nitroalkenes (entries 2,3,6,8,10,11,12,13) produced the corresponding oximes in good yields under similar treatment. The trisubstituted nitroolefin (entry 4) resisted the reduction even under a prolonged treatment.

Presumably, the reaction proceeds via a 1,4-addition of borohydride to the nitroalkene producing the corresponding nitronate 1 which then undergoes usual hydrolysis to give the nitroalkane if there is one substitution at the β-position, whereas additional substitution at the α-or β-position prevent the above course of hydrolysis and dictate the hydrolysis-step to produce the corresponding oxime. Obviously, the substitutions at the α- or β-position have vital role in the reduction of conjugated nitroalkenes with zinc borohydride. But, the precise functions of zinc cation and substituents at the α-or β-position towards governing the mode of hydrolysis are not fully clear to us.



Whatever be the reasons, this study of reduction of conjugated nitroalkene with zinc borohydride is very interesting as it shows marked difference in the course of reduction from those carried out with other borohydride reagents.[4-9] To the best of our knowledge isolation of oxime in the reduction of nitroalkenes with borohydride reducing agents is not reported. With regard to its synthetic utility, besides giving the usual reduction product nitroalkane, this procedure provides a facile and efficient route to oximes under a mild condition which is superior to the existing methods[14] of synthesis of oximes from nitroalkenes involving toxic and strong reagents. Moreover, zinc borohydride is neutral and can tolerate a number of sensitive functional groups like, carboxylic ester, nitro, halogen substituents on aromatic nuclei, ketal and nitrile.[11] These advantages make this procedure more useful for selective reduction of nitroalkene in polyfunctional molecules.

In conclusion, the reduction of conjugated nitroalkenes with zinc borohydride under the present condition producing nitroalkanes or oximes based on the substitution in nitroalkene is very interesting and synthetically useful.

Experimental

General : ^1H NMR spectra were recorded at 60 MHz on EM 360 spectrometers of Varian Associates in CCl_4 solutions with Me_4Si as an internal standard. IR spectra were recorded on a Perkin Elmer 298 spectrometer. Elemental analyses were performed on a Perkin Elmer 240C autoanalyser and by Mr. S. Sarkar of this laboratory. Thin layer chromatography was done on precoated silica gel plates (E. Merck). Silica gel (60-120 mesh) used for column chromatography was supplied by SRL, India. Zinc borohydride in 1,2-dimethoxyethane (DME) was prepared from zinc chloride and sodium borohydride according to the reported procedure.[15] Ether refers to diethyl ether.

General procedure for reduction of nitroalkenes : A solution of zinc borohydride (1 mmol) in DME was added to the conjugated nitroalkene (1 mmol) in DME (2 ml) with stirring at 0°C (ice-bath) or at room temperature (25°C) as indicated in Table 1.[16] The reaction mixture was then stirred at that temperature for a certain period of time (Table 1) as required for completion (monitored by TLC) and quenched with careful dropwise addition of water. The mixture was then extracted with ether (3 x 10 ml) and the ether extract was washed with brine, dried over anhydrous sodium sulphate and evaporated to leave a crude product which was purified by column chromatography over silica gel.

Although the procedure was written in 1 mmol scale, gram-scale reactions were also carried out and found to afford the corresponding products in analogously excellent yields.

The products were simple compounds and were easily indentified by their spectral (IR and ^1H NMR) and analytical data which are presented here for ready reference (products correspond to entries in Table 1).

1[6] : IR ($CHCl_3$) 1380, 1550 cm^{-1}; ^1H NMR δ 3.26 (2H, t, J = 8 Hz), 4.51 (2H, t, J = 8 Hz), 7.21 (5H, s).

2[14] : IR (neat) 1665, 3280 (broad) cm^{-1}; ^1H NMR δ 1.77 (3H, s), 3.43 and 3.66 (2H, 2s), 7.13 (5H, s).

3[17] : IR (neat) 1670, 3300 (broad) cm^{-1}; ^1H NMR δ 1.44 (3H, d, J = 7 Hz), 3.60 and 4.41 (1H, 2 quintets, J = 7 Hz), 7.23 (5H, s), 7.40 (1H, d, J = 7 Hz), 8.0-8.43 (1H, broad).

5 : IR (neat) 1380, 1550, 1585, 1605 cm^{-1}; ^1H NMR δ 3.20 (2H, t, J = 8 Hz), 3.73 (3H, s), 4.46 (2H, t, J = 8 Hz), 6.61-7.26 (4H, m). Anal. calcd. for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found : C, 59.42; H, 6.03; N, 7.79.

6 : IR (neat) 1585, 1600, 1685, 3300 (broad) cm^{-1}; ^1H NMR δ 1.79 (3H, s), 3.40 and 3.60 (2H, 2s), 3.74 (3H, s), 6.49-7.40 (4H, m). Anal. calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found : C, 66.84; H, 7.45; N, 7.71.

7 : IR ($CHCL_3$) 1365, 1550 cm^{-1}; ^1H NMR δ 2.90 (6H, s), 3.16 (2H, t, J = 8 Hz), 4.42 (2H, t, J = 8 Hz), 6.46-7.07 (4H, m). Anal. calcd. for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27; N, 14.42. Found : C, 61.88; H, 7.39; N, 14.59.

8 : IR (neat) 1520, 1600, 3280 (broad) cm^{-1}; ^1H NMR δ 1.73 (3H, s), 2.84 (6H, s), 3.31 and 3.56 (2H, 2s), 6.36-7.06 (4H, m). Anal. calcd. for $C_{11}H_{16}N_2O$: c, 68.72; H, 8.39; N, 14.57. Found : C, 68.53; H, 8.42; N, 14.32.

9 : IR (neat) 1380, 1550 cm^{-1}; ^1H NMR δ 3.18 (2H, t, J = 8 Hz), 4.45 (2H, t, J = 8 Hz), 5.90 (2H, s), 6.61 (3H, s). Anal. calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found : C, 55.46; H, 4.62; N, 7.04.

10 : IR (KBr) 1445, 1485, 1500 cm^{-1}; ^{1}H NMR δ 1.73 (3H, s), 3.30 and 3.53 (2H, 2s), 5.80 (2H, s), 6.56 (3H, s). Anal. calcd. for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.74; N, 7.25. Found : C, 62.02; H, 5.78; N, 7.36.

11[18] : ^{1}H NMR δ 1.30-2.07 (4H, m), 2.07-2.63 (4H, m), 8.43-9.76 (1H, broad s); m.p. 53°C (lit. 53-55°C).

12[18] : ^{1}H NMR δ 1.36-1.97 (6H, m), 1.97-2.64 (4H, m), 9.06-9.66 (1H, broad s), m.p. 89-90°C (lit. 89-91°C).

13[17] : ^{1}H NMR δ 1.32-2.13 (8H, m), 2.13-2.80 (4H, m).

14 : IR (neat) 1360, 1550 cm^{-1}; ^{1}H NMR δ 3.21 (2H, t, J = 7 Hz), 3.74 (3H, s), 4.52 (2H, t, J = 7 Hz), 6.46-7.26 (4H, m). Anal. calcd. for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found : C, 59.79; H, 6.15; N, 7.80.

15 : IR (neat) 1380, 1515, 1550 cm^{-1}; ^{1}H NMR δ 3.15 (2H, t, J = 8 Hz), 3.74 (6H, s), 4.43 (2H, t, J = 8 Hz), 6.51-6.73 (3H, m). Anal. calcd. for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found : C, 56.61; H, 6.18; N, 6.76.

16 : IR (neat) 1365, 1550 cm^{-1}; ^{1}H NMR δ 3.15 (2H, t, J = 8 Hz), 3.80 (3H, s), 4.40 (2H, t, J = 8 Hz), 5.0 (2H, s), 6.60-7.53 (8H, m). Anal. calcd. for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found : C, 66.62; H, 5.82; N, 5.04.

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