HETEROCYCLES, Vol 27, No 1, 1988

CONVENIENT METHOD FOR THE CHEMOSELECTIVE AND REGIOSELECTIVE REDUCTION OF OXIRANES WITH SODIUM BOROHYDRIDE IN SINGLE SOLVENT

Atsuhiro Ookawa, Masaya Kitade, and Kenso Soai*
Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Shinjuku, Tokyo 162, Japan

Abstract—Chemo- and regio-selective reduction of oxiranes to the corresponding alcohol are performed in high yields with sodium borohydride in single solvent (ethanol or 2-propanol).

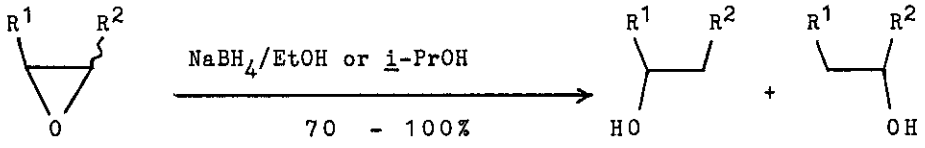
Sodium borohydride ($NaBH_4$) is a readily available, mild, and selective reagent for the reduction of ketones and aldehydes.[1] However, the reduction of oxiranes to the corresponding alcohols with $NaBH_4$ has long been considered to be very slow,[1] except for the oxiranes with neighboring functional groups such as nitro and hydroxy.[2]

On the other hand, reducing reagents such as lithium aluminum hydride and lithium triethylborohydride[3] have poor chemoselectivities.[1] Therefore chemoselective reduction of oxiranes in the presence of other reducible groups can not be performed with these reagents.

During our continuing study on the chemoselective reduction with complex metal borohydrides, we reported a chemoselective reduction of oxiranes with $NaBH_4$ in mixed solvent containing methanol.[4] The procedure requires a dropwise addition of a small amount of methanol over a period of 1 h.

We now report a chemoselective and regioselective reduction of oxiranes with $NaBH_4$ in single solvent such as ethanol and 2-propanol. The method is very convenient because it involves the use of single solvent. To the best of our knowledge, no systematic study has been reported on the reduction of oxiranes with sodium borohydride in these single solvents.

When 2-hexyloxirane(**1b**) was allowed to react with $NaBH_4$ in refluxing ethanol for 2 h, 2-octanol(**2b**) was obtained in 85% isolated yield as the sole product and 1-



1a–e **2a–e** **3a–e**

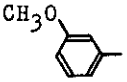
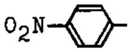
1, 2, 3	R^1	R^2
a	C_6H_5	H
b	$\underline{n}$-C_6H_{13}	H
c		H
d		H
e	CH_3	C_6H_5

Table 1. Reduction of Oxiranes **1a–e** with Sodium Borohydride in Single Solventa)

Entry	Oxirane 1	Solvent	Reaction time /h	Product 2, 3	Ratiob) /%	Yieldc) 2 : 3
1	**1a**d)	EtOH	2	**2a** **3a**	81 : 19	98
2	**1a**d)	2-propanol	2	**2a** **3a**	87 : 13	96
3	**1b**e)	EtOH	2	**2b** **3b**	100 : 0	85f)
4	**1c**d)	EtOH	2	**2c** **3c**	83 : 17	100
5	**1d**d)	EtOH	1	**2d** **3d**	42 : 58	89
6	**1e**d)	2-propanol	7g)	**2e** **3e**	66 : 34	70

a) Molar ratio; $NaBH_4$ / **1a–d** = 1.5 - 2.5, $NaBH_4$ / **1e** = 5. b) Determined by glc (**a,b,e**) and ^1H nmr (**c,d**) analyses. c) Isolated total yield of **2** and **3**. Structures of these products were determined by ^1H nmr, ir, and glc analyses as compared with those of authentic samples.[5] d) Small scale (1 mmol) reaction. e) Preparative scale (20 mmol) reaction. f) Bp 110 °C/25 mmHg (bath temperature). Lit.[5] bp 175 °C. g) Yield was 54% when the reaction time was 3 h.

octanol(**3b**) was not formed at all. This shows that the hydride(H^-) from $NaBH_4$ attacked regioselectively the less hindered carbon of the oxirane(**1b**). Results are summarized in Table 1. Reduction of 2-phenyloxirane(**1a**) with $NaBH_4$ (1.5 mol equivalent) afforded **2a** and **3a** (81 : 19) in 97% total yield.[5] 2-Propanol was also found to be an effective solvent, and the reduction of **1a** with $NaBH_4$ afforded **2a** and **3a** in 96% total yield (**2a** : **3a** = 87 : 13). Even the reduction of 2-methyl-3-phenyloxirane(**1e**), 2, 3-disubstituted oxirane, afforded 70% of alcohols (**2e** and **3e**).

In order to establish the synthetic utility of the present procedure, competitive reduction was examined. Competitive reduction of a mixture of equimolar amounts of **1a** and benzyl cyanide with $NaBH_4$ (1.5 molar equivalent) in refluxing 2-propanol for 1 h afforded **2a** and **3a** in 96%, whereas benzyl cyanide was recovered in 92 %. In a similar manner, benzoylglycine and isopropyl benzoate were recovered respectively in 100 and 81 %, whereas **1a** was reduced in 92 -95 %.

$$\mathbf{1a} + PhCH_2CN \xrightarrow[\underline{i}\text{-PrOH}]{NaBH_4} (\mathbf{2a} + \mathbf{3a}) + PhCH_2CN$$

96% 92% (Recovery)

$$\mathbf{1a} + PhCONHCH_2CO_2H \xrightarrow[\underline{i}\text{-PrOH}]{NaBH_4} (\mathbf{2a} + \mathbf{3a}) + PhCONHCH_2CO_2H$$

92% 100%(Recovery)

$$\mathbf{1a} + PhCO_2CH(CH_3)_2 \xrightarrow[\underline{i}\text{-PrOH}]{NaBH_4} (\mathbf{2a} + \mathbf{3a}) + PhCO_2CH(CH_3)_2$$

95% 81%(Recovery)

Thus the present facile procedure enabled chemo- and regio-selective reduction of oxiranes in the presence of other reducible groups such as nitro, nitrile, amide, carboxylic acid, or ester.

EXPERIMENTAL

2-Octanol (**2b**; R^1=n-C_6H_{13}, R^2=H); Typical Procedure:

A mixture of 2-hexyloxirane (**1b**; R^1=n-C_6H_{13}, R^2=H; 2.56 g, 20 mmol) and sodium borohydride (1.89 g, 50 mmol) in ethanol (40 ml) was refluxed for 2 h. The reaction was quenched with saturated aqueous ammonium chloride (40 ml). The resulting precipitate was filtered with suction and the cake was washed with ether. The filtrate was evaporated under reduced pressure. The residue was extracted with dichloromethane, dried over sodium sulfate. Organic solvent was evaporated under reduced pressure. Bulb-to-bulb distillation afforded **2b**; yield 2.21 g (85 %); bp 110 °C/25 mmHg (bath temperature), lit.[6] 175 °C.

REFERENCES

1. For reviews, see A. Hajos, "Complex Hydrides," Elsevier Scientific Publishing Co., Budapest (1979); H. C. Brown and S. Krishnamurthy, Tetrahedron, 1979, **35**, 567; E. H. R. Walker, Chem. Soc. Rev., 1976, **5**, 23.
2. H. H. Baer and C. B. Madumelu, Can. J. Chem., **56**, 1177 (1978); M. Bharucha, H. Jaeger, K. Meyer, T. Reichstein, and O. Schindler, Helv. Chim. Acta, 1959, **42**, 1395.
3. H. C. Brown, S. Narasimhan, and V. Somayaji, J. Org. Chem., 1983, **48**, 3091.
4. K. Soai, A. Ookawa, H. Oyamada, and M. Takase, Heterocycles, 1982, **19**, 1371; A. Ookawa, H. Hiratsuka, and K. Soai, Bull. Chem. Soc. Jpn., 1987, **60**, 1813. However the reduction of oxiranes with lithium borohydride in mixed solvent containing MeOH doesn't require the dropwise addition, see K. Soai and A. Ookawa, J. Org. Chem., 1986, **51**, 4000.
5. Regioselectivities of the ring opening of 2-aryloxiranes are explained by electronic effect. R. Fuchs and C. A. VanderWerf, J. Am. Chem. Soc., 1954, **76**, 1631.
6. The Aldrich Library of NMR Spectra, C. J. Pouchert, J. R. Campbell, Eds., Aldrich Chemical Co., Milwaukee (1974). The Aldrich Library of Infrared Spectra, C. J. Pouchert, Ed., Aldrich Chemical Co., Milwaukee (1975).

Received, 1st September, 1987