[Chem. Pharm. Bull. 26(9)2897—2898(1978)]

UDC 547.288.4.04 : 547.233.2.057

A Convenient Method for the Reduction of Oxime Ethers to the Corresponding Amines

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(Received March 1, 1978)

Sodium acyloxyborohydrides, [$NaBH_3(OCOR)$], prepared from an equivalent mol sodium borohydride and various carboxylic acids in tetrahydrofuran reduced oxime ethers to the corresponding amines. Particularly sodium trifluoroacetoxyborohydride gave best results.

Keywords——reduction; aromatic and aliphatic oxime ethers; primary and secondary amines; complex hydride; sodium trifluoroacetoxyborohydride

We have recently reported that sodium acyloxyborohydrides in tetrahydrofuran or dioxane converted carboxamides,[2] carbamates[2] or nitriles[3] to the corresponding amines in high yields and these reduction procedures were operationally simple and efficient.

Although the reduction of oximes with complex hydrides [$LiAlH_4$,[4] $NaBH_2S_3$,[5] $NaAlH_2(OCH_2CH_2OCH_3)_2$[6] *etc.*] to corresponding amines is known, they have disadvantages such as low yields owing to side reactions (formation of secondary amines, aziridines or hydroxylamines), and non-generality for both aryl and alkyl oximes. Feuer and his co-workers have described that oximes were reduced by diborane in diglyme-tetrahydrofuran to the corresponding amines at 105—110° and oxime ethers or oxime esters were also reduced to give the corresponding amines.[7–9]

Now, we wish to report that sodium acyloxyborohydrides prepared from an equivalent mol sodium borohydride and various carboxylic acids in tetrahydrofuran convert oxime

Table I. Reduction of Acetophenone Oxime Ether with $NaBH_3$ (OCOR) (5 equiv.) in Tetrahydrofuran

$\underset{\mathrm{CH_3}}{\mathrm{PhC{=}NOMe}}$	$NaBH_3$ (OCOR)	Yield of amine HCl %
	R=CH_3	10.8
	CH_2Cl	26.7
	$CHCl_2$	52.1
	CCl_3	51.7
	CF_3	90.2

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1) Location: *Kawagishi, Toda-shi, Saitama.*
2) N. Umino, T. Iwakuma and N. Itoh, *Tetrahedron Lett.*, **1976**, 763.
3) N. Umino, T. Iwakuma and N. Itoh, *Tetrahedron Lett.*, **1976**, 2875.
4) D.R. Smith, M. Maienthal and J. Tipton, *J. Org. Chem.*, **17**, 294 (1952).
5) J.M. Lalancette and J.R. Brindel, *Can. J. Chem.*, **48**, 735 (1970).
6) S.R. Landor, O.O. Sonola and A.R. Tatchell, *J. Chem. Soc., Perkin I*, **1974**, 1294.
7) H. Feuer, B.F. Vincent, Jr., and R.S. Bartlett, *J. Org. Chem.*, **30**, 2877 (1965).
8) H. Feuer, and D.M. Braustein, *J. Org. Chem.*, **34**, 1817 (1969).
9) A. Hassner and P. Catsoulacos have also shown that diborane in THF converted ketoxime acetates to the corresponding amines, *Chem. Commun.*, **1969**, 590.

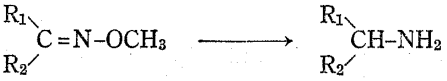
ethers to the corresponding amines and sodium trifluoroacetoxyborohydride provides a convenient method for the reduction of oxime ethers to the corresponding amines.[10)]

The reduction of acetophenone oxime ether to 1-phenylethylamine was tried by various sodium acyloxyborohydrides and the results were summarized in Table I.

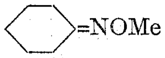
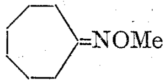
The excellent result of reduction of acetophenone oxime ether with sodium trifluoroacetoxyborohydride as shown in Table I prompted us to examine the reduction of other various oxime ethers.

As can be noted from the Table II, both aromatic and aliphatic oxime ethers were smoothly reduced by sodium trifluoroacetoxyborohydride, $NaBH_3(OCOCF_3)$, to the corresponding amines in high yields.

TABLE II. The Reduction of Oxime Ethers with $NaBH_3$ $(OCOCF_3)$ (5 equiv.) in Tetrahydrofuran



$$\begin{matrix}R_1\diagdown \\ \quad C{=}N\text{-}OCH_3 \\ R_2\diagup\end{matrix} \longrightarrow \begin{matrix}R_1\diagdown \\ \quad CH\text{-}NH_2 \\ R_2\diagup\end{matrix}$$

Oxime ether	Yield of amine HCl %	mp[a)] (°C) (lit.)
$CH_3(CH_2)_8CH{=}NOMe$	84.2	192—193 (194)[b)]
$PhCH_2CH_2CH{=}NOMe$	86.9	212—215 (218)[c)]
 =NOMe	90.0	201—203 (206—207)[c)]
 =NOMe	86.9	244—247 (242—246)[c)]
$PhCH{=}NOMe$	90.6	252—253 (253)[c)]
$(Ph)_2C{=}NOMe$	81.1	294—296 (293)[c)]

a) All melting points are uncorrected.
b) G. Komppa and Y. Talvitie, *J. Prakt. Chem.*, **135**, 193 (1932).
c) Dictionary of Organic Compounds, Eyre and Spottiswoods, London, 1965.

Experimental

Representative Reduction of an Oxime Ether with Sodium Trifluoroacetoxyborohydride——To the stirred suspension of $NaBH_4$ (1.9 g, 50 mmol) in tetrahydrofuran (50 ml) was added CF_3COOH (5.70 g, 50 mmol) in tetrahydrofuran (5 ml) over a period of 10 minutes at 20°. To this solution was added O-methyl acetophenone oxime (1.49 g, 10 mmol) in tetrahydrofuran (5 ml), the mixture was stirred at room temperature for 2 hr and then heated under reflux for 2 hr. The excess reagent was cautiously decomposed with water below 10° and the resulting mixture was concentrated to dryness *in vacuo* and extracted with methylene chloride. The extract was washed with brine and dried over anhydrous sodium sulfate. The methylene chloride solution was treated with dry hydrogen chloride, evaporated *in vacuo* and the residue was crystallized from methanol-ether to give 1-phenyl-ethylamine hydrochloride (1.42 g, 90.2%).

Acknowledgement We would like to express our thanks to Emertius Prof. S. Sugasawa of Tokyo University and Prof. Y. Ban of Hokkaido University for their helpfull discussions. We are also indebted to Mr. M. Yamazaki and Dr. S. Saito of this laboratory, for encouragement.

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10) Treatment of acetophenone oxime with $NaBH_3$ $(OCOCF_3)$(5 equiv.) in refluxing THF for 2 hr or in diglyme at 120° for 5 hr led to 1-phenylethylamine hydrochloride in 23.5% or 50.7% yield, respectively. Reduction of acetophenone oxime acetate in refluxing THF for 2 hr also gave a similar result (53.6%).