1 PERKIN
COMMUNICATION

Selective and rapid oxidation of primary, allylic and benzylic alcohols to the corresponding carbonyl compounds with $NaNO_2$–acetic anhydride under mild and solvent-free conditions

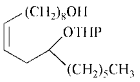
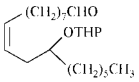
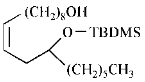
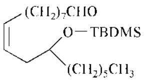
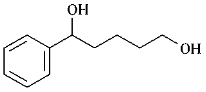
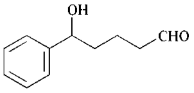
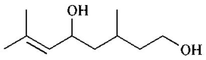
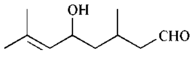
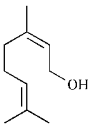
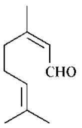
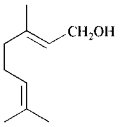
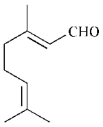
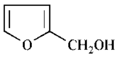
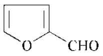
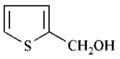
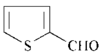
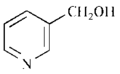
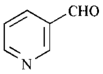
Babasaheb P. Bandgar,* Vaibhav S. Sadavarte and Lavkumar S. Uppalla

Organic Chemistry Research Laboratory, School of Chemical Sciences,
Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded-431 606, Maharashtra,
India. Fax: 0091-2462-29245; E-mail: upekam@hotmail.com

Received (in Cambridge, UK) 14th February 2000, Accepted 21st September 2000
First published as an Advance Article on the web 10th October 2000

Various primary, benzylic and allylic alcohols undergo selective and rapid oxidation to the corresponding carbonyl compounds using $NaNO_2$–acetic anhydride as a novel oxidant under mild and solvent free conditions.

Table 1 Selective and rapid oxidation of alcohols with $NaNO_2$–Ac_2O

Entry	Alcohol	Product	Yield (%)[a]
1	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	65
2	Butyl alcohol	Butanal	60
3	4-Chlorobenzyl alcohol	4-Chlorobenzaldehyde	65
4	4-Cyanobenzyl alcohol	4-Cyanobenzaldehyde	75
5	3,4-Dimethoxybenzyl alcohol	3,4-Dimethoxybenzaldehyde	82
6	4-(*N*,*N*-Dimethylamino)benzyl alcohol	4-(*N*,*N*-Dimethylamino)benzaldehyde	72
7	4-Methoxybenzyl alcohol	4-Methoxybenzaldehyde	80
8	3,4-Methylenedioxybenzyl alcohol	3,4-Methylenedioxybenzaldehyde	86
9	2-Nitrobenzyl alcohol	2-Nitroaldehyde	90
10	3-Nitrobenzyl alcohol	3-Nitroaldehyde	91
11	4-Nitrobenzyl alcohol	4-Nitroaldehyde	92
12	Cinnamyl alcohol	Cinnamaldehyde	85
13	Hexan-1-ol	Hexanal	75
14	Octane-1,8-diol	Octane-1,8-dial	75
15	Stearyl alcohol	Stearaldehyde	60
16	$(CH_3)_3COCONH-CH(CH_2OH)-COOCH_2C_6H_4NO_2$	$(CH_3)_3COCONH-CH(CHO)-COOCH_2C_6H_4NO_2$	90
17			87
18			82
19			89
20			93
21			84
22			94
23			94
24			97
25			95

[a] Unoptimized yields of pure isolated products that exhibited physical and spectral properties in accord with the assigned structure.

DOI: 10.1039/b001215g

Table 2 Oxidation of 4-nitrobenzyl alcohol (1 mmol) with different amounts of $NaNO_2$–Ac_2O

Entry	Amount of $NaNO_2$/mmol	Yield of 4-nitrobenzaldehyde (%)
1	0.5	40
2	1.0	55
3	1.5	70
4	2.0	80
5	2.5	87
6	3.0	92

The oxidation of alcohols into carbonyl compounds is an important transformation in organic synthesis.[1] Although a large number of reagents are known in the literature[2] for such transformations there still appears a need either to improve the existing oxidation methods[3] or to introduce newer reagents[4] to permit better selectivity under milder conditions. More recently, some novel reagents[5] have been used for this purpose to get relatively better results. Nitronium and nitrosonium fluoroborates are also reported as efficient reagents for similar oxidations[6–8] which are fast and exothermic.

We now report for the first time that $NaNO_2$ in acetic anhydride is a remarkably effective reagent for the rapid and selective oxidation of a variety of primary, allylic and benzylic alcohols into their corresponding carbonyl compounds under mild conditions.

$$RCH_2OH \xrightarrow[25\ ^\circ C,\ <1\ \text{min}]{NaNO_2\text{–}Ac_2O} RCHO$$

The rapid and selective formation of oxidation products demonstrates the efficiency of this new method. In all cases, the reactions are completed in <1 min. The results are summarized in Table 1. Interestingly, no overoxidation to carboxylic acids is observed (entries 1–15). Primary aliphatic alcohols (entries 2,13–15), a primary aliphatic diol (entry 14), allylic alcohols (entries 12, 21–22) and benzylic alcohols (entries 1, 3–11) are selectively oxidized to the corresponding carbonyl compounds. No isomerization of double bonds is observed in the oxidation of the α,β-unsaturated alcohols (entries 12, 21–22). Furthermore, cyano (entry 4), *tert*-amino (entry 6), THP ether (entry 17) and TBDMS (entry 18) groups remain unchanged during the oxidation. In addition, it is worth commenting that secondary alcohols like cyclohexanol, menthol and benzoin are not oxidized to the corresponding ketones under these reaction conditions. It is also important to note that a primary alcoholic group is oxidized selectively in the presence of a secondary benzyl alcoholic group (entry 19) under these reaction conditions. Therefore, it is a method of choice for the oxidation of primary, allylic and primary benzylic alcohols in the presence of secondary alcohols. Heterocyclic alcohols (entries 24, 25) are also selectively oxidized without oxidation of heteroatoms like N, S.

An oxidation study of 4-nitrobenzyl alcohol with different amounts of $NaNO_2$–Ac_2O is shown in Table 2. If a catalytic amount of $NaNO_2$–Ac_2O is used for oxidation of 4-nitrobenzyl alcohol, the reaction does not go to completion. Three equivalents of reagent are required for complete oxidation of 4-nitrobenzyl alcohol.

In conclusion, the present results demonstrate the novelty of the $NaNO_2$–Ac_2O system which shows unique selectivity and constitutes a useful alternative to the commonly accepted procedures for the oxidation of primary, allylic and benzylic alcohols. Moreover, this simple, inexpensive and rapid oxidation technique affords products in good yields without overoxidation to carboxylic acids.

Experimental

A typical procedure for oxidation of 4-nitrobenzyl alcohol: a mixture of $NaNO_2$ (1035 mg, 15 mmol) and 4-nitrobenzyl alcohol (5 mmol) in acetic anhydride (2 mmol) was stirred. A spontaneous exothermic reaction took place which was controlled by cooling the mixture in ice. After completion of the reaction (TLC), the product was extracted with ether (2 × 10 ml). Removal of the solvent under reduced pressure afforded crude 4-nitrobenzaldehyde which was further purified by column chromatography (petroleum ether–ethyl acetate, 9 : 1).

Acknowledgements

VSS thanks CSIR, New Delhi for a junior research fellowship.

References

1 S. V. Ley and A. Madin, in *Comprehensive Organic Synthesis*, eds. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 7, p. 251.

2 R. C. Larock, *Comprehensive Organic Transformations*, VCH, New York, 1989, p. 604.

3 S. Ait-Mohand, F. Henin and J. Muzart, *Tetrahedron*, 1995, **36**, 2473; A. P. de Oliveria Filho, B. G. Moreira, P. J. S. Moran and J. A. R. Rodrigues, *Tetrahedron Lett.*, 1996, **37**, 5029.

4 D. B. Dess and J. C. Martin, *J. Org. Chem.*, 1983, **48**, 4155.

5 R. Rosenau, A. Potthast, C. L. Chen and J. S. Gratzl, *Synth. Commun.*, 1996, **26**, 315; A. Shaabani and M. Ameri, *J. Chem. Res.* (*S*), 1998, 101; N. B. Barhate, M. Sasidharan, A. Sudali and R. D. Wakharkar, *Tetrahedron Lett.*, 1996, **37**, 2067; S. V. Pitre, M. V. R. Reddy and Y. D. Vankar, *J. Chem. Res.* (*S*), 1997, 462; T. Aoyama, N. Sonoda, M. Yamauchi, K. Toriyama, M. Anzai, A. Ando and T. Shioiri, *Synlett*, 1998, 35; R. S. Varma and R. K. Saini, *Tetrahedron Lett.*, 1998, **39**, 1481; K. S. Coleman, M. Coppe, C. Thomas and J. A. Osborn, *Tetrahedron Lett.*, 1999, **40**, 3723; M. M. Aghayan and M. M. Heravi, *Synth. Commun.*, 1999, **29**, 785; M. M. Heravi, D. Ajami and K. T. Heydar, *Synth. Commun.*, 1999, **29**, 163.

6 G. A. Olah and T. L. Ho, *Synthesis*, 1976, 616.

7 G. A. Olah and T. L. Ho, *Synthesis*, 1976, 609.

8 T. L. Ho and G. A. Olah, *J. Org. Chem.*, 1977, **42**, 3097.