

SHORT COMMUNICATION

Kinetics of catalytic Meerwein–Ponndorf–Verley reduction of aldehydes and ketones using boron triethoxide

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Received 30 April 2009; Revised 19 August 2009; Accepted 20 August 2009

Catalytic Meerwein–Ponndorf–Verley (MPV) reduction of various aliphatic, aromatic, and unsaturated aldehydes and ketones to corresponding alcohols (analyzed by GC-MS) in the presence of boron triethoxide ($B(OEt)_3$) were studied. Kinetics of this reduction reaction was also studied and the respective rate constants were determined. It was found that $B(OEt)_3$ catalyzes the reduction of aliphatic aldehydes and ketones to alcohols at room temperature while aromatic aldehydes and ketones were not reduced under the same conditions. In addition, MPV reduction using $B(OEt)_3$ was found to be chemoselective as unsaturated aldehydes and ketones afforded the corresponding alcohols without affecting unsaturated groups. The mechanism proposed involves a six-membered transition state in which both the alcohol and the carbonyl are coordinated to the same boron centre of a boron alkoxide catalyst.

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Keywords: boron triethoxide, chemoselective reduction, aldehydes, ketones, Meerwein–Ponndorf–Verley reduction

Synthesis of alcohols by the reduction of carbonyl compounds is one of the most widely used reactions in the synthetic organic, fine, and perfumery chemicals industries. Chemoselectivity of the reducing agent is very important because reduction of the carbonyl group without affecting other reducible groups present in the molecule is difficult. For that reason, new methods, catalysts and reagents providing higher activity and selectivity are permanently searched for.

The Meerwein–Ponndorf–Verley (MPV) reduction of carbonyl substrates to primary and secondary alcohols, discovered in 1925 (Meerwein & Schmidt, 1925), is a useful method for the reduction of carbonyl compounds because of its chemoselectivity. It is a mild method for the reduction of aldehydes and ketones in the presence of metal alkoxide catalysts (Klomp et al., 2004). Usually, metal *sec*-alkoxides are used as homogeneous catalysts in the MPV reduction of carbonyl compounds (van der Waal et al., 1998; Aramendia et al., 2001).

The MPV process provides a highly selective re-

duction of the carbonyl group in the presence of other reducible sites such as a conjugated double bond, a nitro group or a halogen atom (Furniss et al., 1989; Creighton et al., 1997a). Thus, this reduction process is an interesting pathway for the reduction of aldehydes and ketones to alcohols (Ruiz et al., 2006).

In an MPV reduction, the reaction proceeds with a hydride transfer to the carbonyl compound from alcohol, which is then coordinated to the metal center as an alkoxide (Liu et al., 2002). In the reaction, the secondary alcohol acts as a hydrogen donor and the carbonyl group of the substrate as the hydrogen acceptor. Generally, a stoichiometric amount of metal alkoxide is required to obtain good yields of the desired alcohols (Lermontov et al., 2003).

MPV reactions are usually catalyzed homogeneously by metal alkoxides such as aluminum isopropoxide ($Al(Oi-Pr)_3$) (Creighton et al., 1997b). The catalytic activity of these catalysts is related to their Lewis acidic character in combination with their ligand and exchange ability (Zhu et al., 2003). The hydro-

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Table 1. Reaction characteristics of MPV reduction of carbonyl compounds^a using B(OEt)₃

Carbonyl compound	Product	Yield ^b /%	Reaction time/h	Rate constant ($k \times 10^{-3}$)/min
Acetone	2-Propanol	88.0	7	4.402
1-Hexanal	1-Hexanol	88.8	8	4.378
1-Pentanal	1-Pentanol	89.1	8	4.128
2-Pentanone	2-Pentanol	86.8	8	3.713
2-Butanone	2-Butanol	87.0	8	3.858
Cyclopentanone	Cyclopentanol	90.3	8	4.563
Cinnamaldehyde	Cinnamyl alcohol	87.8	13	2.490
Geranial ^c	Geraniol	86.6	20	2.470
Neral ^d	Nerol	85.2	20	2.280

a) Aromatic carbonyl compounds: benzaldehyde, 2-hydroxybenzaldehyde, 2-chlorobenzaldehyde, acetophenone, and 4-nitroacetophenone were resistant to the reduction, no alcohol products were obtained; b) determined by GS-MS analysis of the reaction mixture; c) *trans*-citral; d) *cis*-citral.

gen donor is usually a secondary alcohol such as 2-propanol. In addition to the classical aluminum isopropoxide catalyst, catalytic applications of other isopropoxides, such as zirconium(IV) isopropoxide (Ishii et al., 1986; Knauer & Krohn, 1995) and lanthanide isopropoxides (Namy et al., 1984), in the MPV reaction have been reported.

Like metal alkoxides, boron alkoxides are also expected to catalyze MPV reductions. The boron atom in these compounds is in a trigonal coplanar state with sp^2 bond hybridization. A vacant p -orbital exists along the threefold axis perpendicular to the BO_3 plane. This vacant p -orbital readily accepts adjacent unshared electrons, acting electronically in a manner similar to the carbonyl group of an organic ester. Boron alkoxides are very susceptible to hydrolysis in the presence of water or, in some cases, atmospheric moisture (Kroschwitz & Howe-Grant, 1992).

Recently, it was shown that boron triisopropoxide reduces some aliphatic aldehydes and ketones (Cha & Park, 2002). This reduction can be considered as an MPV-type reduction. In a previous study, the effects of the catalytic characteristics of two kinds of boron alkoxides, boron triisopropoxide and boron tri-*sec*-butoxide on the reduction of aliphatic and aromatic aldehydes and ketones were showed (Uysal & Buyuktas, 2007).

There are no data in literature concerning the kinetics of chemoselective MPV reduction of aliphatic and aromatic aldehydes and ketones with boron triethoxide as catalyst. In this paper, an efficient and selective method for the reduction of aldehydes and ketones using boron triethoxide (B(OEt)₃) as the catalyst is described and kinetics of the MPV reduction of some carbonyl compounds were examined.

All chemicals were purchased from Merck, Darmstadt, Fluka, Buchs or Sigma–Aldrich, Taufkirchen, and used as received. All reactions were carried out under nitrogen atmosphere using modified Schlenk techniques.

GC-MS analyses were performed on a Varian CP 3800 gas-chromatograph equipped with a Varian Sat-

urn 2200 MS detector and a VF-5 ms capillary column (30 m × 0.25 mm × 0.25 mm).

As a general method, procedure for the reduction of 2-butanone to 2-butanol is given: The apparatus consisted of a 50 mL two-neck flask with a side stopcock equipped with a 50 cm condenser. Ethanol (1.76 mL, 30 mmol) was added dropwise to B(OEt)₃ (1.72 mL, 10 mmol) in the flask immersed in a water bath. The solution was stirred for 5 min, then 2-butanone (2.7 mL, 30 mmol) was injected into the solution, with slow stream of dry nitrogen passing just over the surface (to remove arising acetaldehyde), and the reaction mixture was stirred for 8 h at room temperature. The alcohol products were not isolated. Aliquots of the reaction mixture for the GC-MS analysis were taken at regular intervals to determine the corresponding alcohol content (non-isolated yields, Table 1).

The rate constant of each carbonyl compound reduction was determined. All aliphatic aldehydes and ketones exhibited linear correlation between the natural logarithm of the carbonyl group concentration and the reaction time. This suggests that the reaction is of the first order in the aldehyde concentration: $\ln(c_0/c) = kt$, where c_0 and c are the aldehyde concentrations at initial and at any time t , respectively, and k is the rate constant. A plot of $\ln(c_0/c)$ vs. t was used to determine the rate constant. The selected carbonyl compounds, the yields of the reduction products, and the rate constants of aliphatic aldehyde and ketones are summarized in Table 1. As can be seen, some differences in the reaction yields and the rate constants were observed, but reduction times were approximately 8 h for most carbonyl compounds except for acetone, cinnamaldehyde and citral. Lower rate constants of cinnamaldehyde and citral can be attributed to some steric hindrance and to the presence of a double bond conjugated to the carbonyl group.

It was found that the MPV reduction shows chemoselectivity for aromatic and aliphatic carbonyl compounds. Although aliphatic carbonyl compounds were reduced to alcohols smoothly, aromatic carbonyl

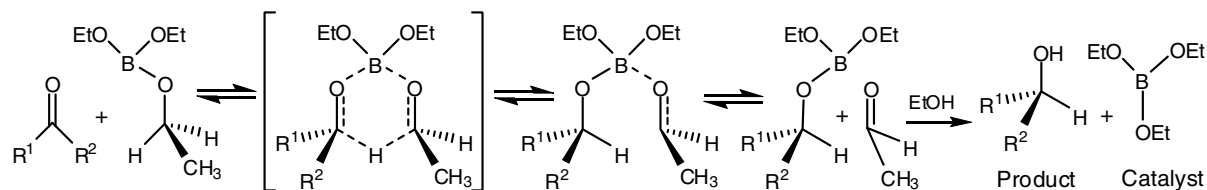


Fig. 1. Proposed reaction mechanism of MPV reduction of aliphatic ketones and aldehydes using $B(OEt)_3$.

compounds were found to be resistant to the MPV reduction in the presence of $B(OEt)_3$.

The MPV reduction of citral (3,7-dimethyl-2,6-octadienal) with $B(OEt)_3$ was also examined. In addition to the conjugated $C=C$ and $C=O$ bonds, this important aldehyde possesses also an isolated $C=C$ bond. The $C=C$ bonds are more readily hydrogenated by most usual techniques than the $C=O$ bonds (Narayanan, 2003). Although reduction of the $C=O$ bonds without affecting the $C=C$ bonds is sometimes very difficult, the $C=O$ bond of citral was selectively reduced using the $B(OEt)_3$ catalyst in this study (Table 1). Conversion higher than 85 % of *cis*- and *trans*-citral to nerol and geraniol (used in the fragrance industry for their pleasant rose-like odor), respectively, was achieved within 20 h. The preferential formation of geraniol as compared to nerol can be explained by a steric hindrance (Zhu et al., 2004). In case of geraniol, the carbonyl group is oriented *trans* to the bulky chain of the molecule minimizing thus the steric hindrance for the binding of $C=O$ to the boron center and therefore, the reaction rate for geraniol is higher than for nerol.

Proposed reaction mechanism of MPV reduction using $B(OEt)_3$ (Fig. 1) involves a cyclic six-membered transition state (de Graauw et al., 1994) and is analogous with the reaction mechanism for MPV reduction using boron triisopropoxide already published (Uysal & Buyuktas, 2007). Since the reduction is reversible, the produced acetaldehyde was removed from the reaction mixture by a slow stream of nitrogen, leading to the progress of the reaction towards the product (alcohols). Using a $B(OEt)_3$ catalyst, the alcohol yields are higher than those obtained using boron triisopropoxide and triisobutoxide, respectively; because the removal of acetone (b.p. $56^\circ C$) and 2-butanone (b.p. $81^\circ C$) is more difficult than the removal of acetaldehyde (b.p. $20.2^\circ C$).

Acknowledgements. The authors gratefully acknowledge The Scientific Research Projects Coordination Unit of the Akdeniz University for financial support.

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