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SHORT COMMUNICATION

Reduction of Aldehydes Using Sodium Borohydride under Ultrasonic Irradiation

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ABSTRACT

A simple, energy efficient, and relatively quick synthetic procedure for the reduction of aldehydes under ultrasonic irradiation is reported. Satisfactorily isolated yields (71-96%) were achieved confirming that the preparation of alcohol by aldehyde reduction is possible in green and sustainable fashion.

***Keywords**: green synthesis; ultrasound irradiation; aldehyde reduction; sodium borohydride*

ABSTRAK

Sintesis menggunakan prosedur sederhana, efisien energi, dan relatif cepat untuk mereduksi senyawa aldehida dengan radiasi ultrasonik telah dilaporkan. Hasil dengan rendemen yang sangat baik (71-96%) telah diperoleh menunjukkan bahwa reaksi reduksi aldehida menjadi alkohol dapat dilakukan dengan metode yang green dan berkelanjutan.

***Kata Kunci**: green sintesis; radiasi ultrasonik; reduksi aldehida; natrium borohidrida*

INTRODUCTION

Reduction of aldehydes into corresponding alcohols is an important transformation in organic synthesis. Conventionally, aldehyde reduction is usually done with flammable solvents such as ethanol, 2-propanol, and methanol, even though it is unstable in either methanol or ethanol because of solvolysis [1]. To only mention few examples, several reducing agents such as borohydride derivatives [2-5], organohydride [6], and Ni-nanoparticles [7] have been recently reported. Sodium borohydride is commonly employed since this reagent is low-priced, easy to handle, and environmentally benign reducing agent that quickly reduce ketones, acid chlorides, and aldehydes [1]. However, this traditional procedure has disadvantage for practical utility i.e. using a large amount of solvent, for a certain condition consuming a lot of energy for reflux, and requiring long reaction times [2].

From ecological point of view, demonstrating reactions without the use of solvent are not only interest for minimizing waste and energy usage, but in various cases, also offer significant synthetic advantages in term of simplicity, selectivity and yield [8]. Solvent-free organic reaction can be carried out at room temperature. In addition, it can be accelerated by grinding with mortar and pestle, heating, shaking, irradiating with microwaves or ultrasounds.

An example for aldehydes reduction with sodium borohydride under solvent free condition was reported [3]. The reduction of aldehydes with $NaBH_4$ activated by solid acids were performed by grinding using a mortar and pestle. A limitation in grinding with mortar and pestle is that small amount of samples might be essentially lost when ground into the surface of the mortar. This leads to poor yields since sample recovery is difficult. In addition, the energy could not be quantified since it is conducted by hand. Thus, strong and weak grinding could affect the reaction time and the obtained product.

As there is an increasing need for fine chemicals synthesis utilizing ''green'' methods, ultrasound has gained significance attention as a clean and valuable tool in accelerating chemical reactions when compared to conventional methods and thus, in the past three decades a tremendous number of organic reactions have been reported using this technology [9]. Ultrasound irradiation have some important advantages not only accelerating a chemical reaction but also providing beneficial in other ways like substantial decreases of reaction time, improved yield, increased selectivity, avoided forcing conditions like high

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temperature and high pressure, lower costs and simplicity in handling and processing, and reduced the number of steps in a reaction [9-10]. Thus, in this work, we present simple, efficient, and rapid reduction of aldehydes with sodium borohydride into alcohols under ultrasonic condition.

EXPERIMENTAL SECTION

Materials

Unless stated otherwise, most of the compounds used in this study were commercial products of high purity purchased from Merck such as: cinnamaldehyde, *p*-anisaldehyde, furfural, vanillin, sodium borohydride, dichloromethane, $NaHCO_3$, and anhydrous Na_2SO_4. Compound 4-ethoxy-3-methoxy benzaldehyde was prepared according to the previously reported method [11]. All technical grade solvents were purchased and used without further purification.

Instrumentation

Thin layer chromatography (TLC) was carried out on silica gel TLC-cards (layer thickness 0.20 mm, Merck). Permanganate reagent was employed as developing solution. ^{1}H-NMR spectra were recorded in $CDCl_3$ on Agilent V NMR spectrometer operating at 400 MHz. Chemical shifts (δ) are reported in parts per million relative to the internal standard tetramethylsilane (TMS, δ = 0.00 ppm). FTIR spectra were recorded on Shimadzu FTIR Prestige-21 spectrophotometer. All the reactions were studied using ultrasonic apparatus from Branson 1510 ultrasound cleaner working at 40 kHz of power 80 W (constant frequency) without mechanical stirring. Melting points were determined using electrothermal melting point apparatus Stuart MPS-10.

Procedure

General procedure for the reduction of aldehydes

A mixture of aldehyde (0.01 mol) and sodium borohydride (0.02 mol) was sonicated in a sonic bath (40 kHz) at room temperature until TLC showed complete disappearance of the starting materials. The reaction was stopped using a saturated aqueous solution of $NaHCO_3$. The reaction mixture was then extracted with dichloromethane (3 x 20 mL). The organic layer was dried with anhydrous Na_2SO_4 to be followed with evaporation of the solvent to give the corresponding alcohol. All of the products were characterized by FTIR and ^{1}H-NMR and by comparison with authentic sample on TLC. When the starting materials were solid i.e. vanillin and 4-ethoxy-3-methoxy benzaldehyde, a small amount of ethanol (~5 mL) was used to dissolve these materials.

RESULT AND DISCUSSION

Several aldehydes can be reduced by $NaBH_4$ without using a solvent or a small amount of ethanol under ultrasound irradiation at room temperature. The procedure is very simple, energy efficient, and converted the aldehydes into corresponding alcohols in relatively high yield. Moreover, in many cases, sonication reactions under ultrasound irradiation could be considered environmentally benign processes, employing either no solvent or small amount of solvents and being less energy consumer [12], which offers minimal side reactions [13]. This reduction method is expected as an alternative to replace the conventional reduction method that still use a large amount of solvent with a relatively high energy consumption.

We initially studied the reduction of benzaldehyde using sodium borohydride under ultrasound irradiation at room temperature. The reaction was checked by TLC until completion using hexane-ethyl acetate (4:1). As shown in Table 1, benzaldehyde was quickly reduced to benzyl alcohol in high yield for 15 min. Using the same procedure, we then examined the reduction of other aldehydes. Renewable aldehydes such as cinnamaldehyde, *p*-anisaldehyde, and furfural were chosen since these aldehydes could be potentially converted into other valuable materials. In this case, the reductions gave the corresponding alcohol in good yields (entries 2–4). All synthesized alcohols summarized in Table 1 were characterized by spectroscopic methods (^{1}H-NMR and FTIR).

Ultrasound promoted reduction of benzaldehyde and *p*-anisaldehyde with $NaBH_4$ using aprotic solvent i.e. tetrahydrofuran (THF) at room temperature was already reported [15]. In case of benzaldehyde reduction, It was reported that the reaction completed for 17 min with molar ratio $NaBH_4$/benzaldehyde = 1:1. Compared to our method, the use of THF in the ultrasound reduction is more effective than without solvent in term of $NaBH_4$ and benzaldehyde molar ratio. In case of *p*-anisaldehyde, reduction reaction using THF as the solvent needed 1.7 molar equivalent of $NaBH_4$ for completion to give the *p*-anisyl alcohol in 94 min. Thus, in comparison with solvent-free condition, the ultrasound reduction is much more effective since it needs 15 min for completion.

The employed method was successfully applied to reduce liquid aldehydes. Following the same methodology, we further investigated the prospective of this procedure to reduce solid aldehydes such as vanillin and 4-ethoxy-3-methoxy benzaldehyde. Initially

Table 1. Ultrasound assisted reduction of aldehydes using sodium borohydride

Entry	Aldehyde	Time (min)	Product	Yield (%)	M.p. (°C)	
					found	Lit. [14]
1	Benzaldehyde	15	Benzyl alcohol	96	-	-
2	*p*-Anisaldehyde	15	*p*-Anisyl alcohol	96	-	-
3	Furfural	15	Furfuryl alcohol	89	-	-
4	Cinnamaldehyde	20	Cinnamyl alcohol	71	n.a.[a]	30-33
5	Vanillin	20	Vanillyl alcohol	92	112-113	112-115
6	4-Ethoxy-3-methoxy benzaldehyde	20	4-Ethoxy-3-methoxy benzyl alcohol	94	56-57	54-59

[a]The obtained cinnamyl alcohol was liquid since the melting point is closer to the ambient room temperature

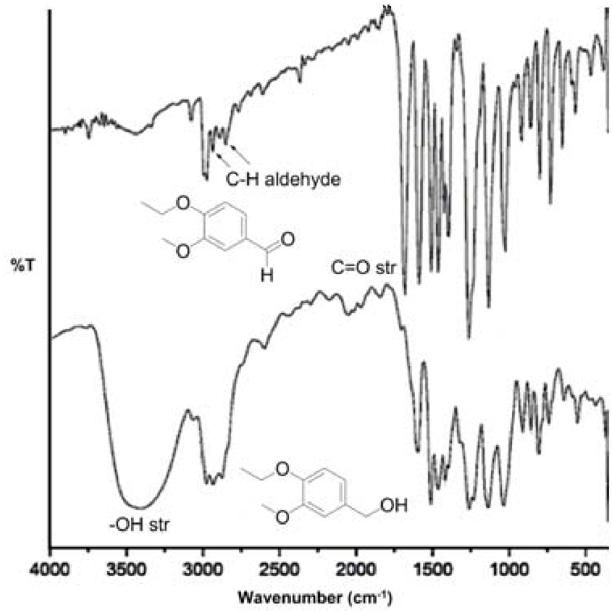

Fig 1. FTIR spectra of 4-ethoxy-3-methoxy benzaldehyde (top) and 4-ethoxy-3-methoxy benzyl alcohol (bottom)

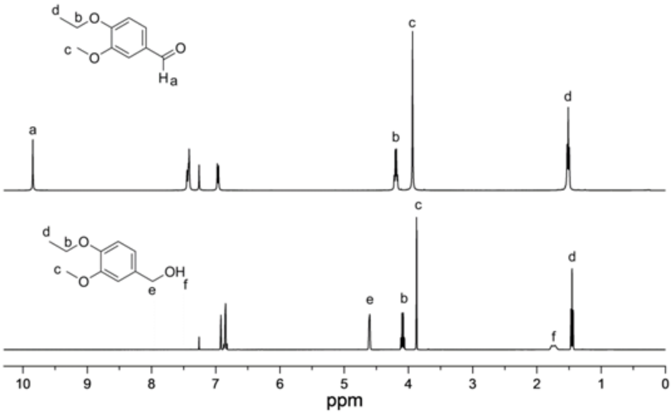

Fig 2. ^{1}H-NMR (400 MHz, $CDCl_3$) spectra of 4-ethoxy-3-methoxy benzaldehyde (top) and 4-ethoxy-3-methoxy benzyl alcohol (bottom)

the reaction was performed by ultrasonication of vanillin and sodium borohydride under solvent free condition at room temperature. Unfortunately, TLC analysis showed that the spot of starting material was not completely disappeared even after 2 h sonication. Thus, ultrasonication of aldehyde reduction using sodium borohydride in solid state condition was not working. Performing a reaction without the use of solvent usually has at least one compound in a liquid form acting as a semi-solvent. Therefore, further attempt was done by conducting the reduction in small amount of ethanol. Minimum amount of ethanol (~5 mL) was used to completely dissolve vanillin. Vanillin and sodium borohydride was dissolved in ethanol. The reaction mixture was then sonicated at room temperature. After 20 min of reaction, TLC analysis showed the successful of the reduction indicated by the disappearance of the vanillin spot and the appearance of new spot which was different with starting material. The reduction of vanillin gave vanillyl alcohol in 92% yield. Vanillyl alcohol, which can be obtained by vanillin reduction, proves promise as a renewable starting material for the synthesis of flavoring ingredients [16] and biologically active compounds [17-18].

We next examined the sonication reduction of 4-ethoxy-3-methoxy benzaldehyde under the same procedure as vanillin. Compound 4-ethoxy-3-methoxy benzaldehyde was synthesized by ethylation of vanillin following to the previous reported method [11]. TLC analysis of the reduction product using silica gel as stationary phase and hexane-ethyl acetate (4:1) as mobile phase showed the disappearance of starting material spot after 20 min reaction. Further analysis was done with FTIR spectrophotometer. FTIR spectra of the resulting product (Fig. 1) revealed the successful of the reduction. This was shown by the disappearance of carbonyl group around 1681 cm^{-1} and C–H aldehyde at 2854 and 2893 cm^{-1}. The appearance of broad absorption peak at 3417 cm^{-1} indicates the presence of hydroxyl group of alcohol.

To ensure that the synthesized product is 4-ethoxy-3-methoxybenzyl alcohol, the resulted product was then analyzed using ^{1}H-NMR spectrometer. ^{1}H-NMR spectra of the synthesized alcohol is presented in Fig. 2. The complete reduction was revealed by the ^{1}H-NMR spectra of 4-ethoxy-3-methoxybenzyl alcohol (bottom), at which no C–H aldehyde signal around 9.85 ppm was observed and the new peaks at 4.60 ppm and

1.82–1.61 ppm corresponding to the proton of $–CH_2–$ (e) and hydroxyl –OH (f), respectively appeared. The reduction of 4-ethoxy-3-methoxy benzaldehyde afforded 4-ethoxy-3-methoxybenzyl alcohol in 94% yield.

CONCLUSION

In summary, we develop an efficient, green, fast, and convenient method for the reduction of aldehydes into corresponding alcohols under ultrasound irradiation. The method presented here is green alternative to publish procedure of aldehyde reduction. Compared with conventional methods, present procedures offer advantages such as good yield, mild reaction condition, shorter reaction time, and ease of execution and economic viability.

REFERENCES

1. Paquette, L., 1995, *Reagents for Organic Synthesis*, Wiley, New York.
2. Azizi, N., Batebi, E., Bagherpour, S., and Ghafuri, H., 2012, *RSC Adv.*, 2 (6), 2289–2293.
3. Cho, B.T., Kang, S.K., Kim, M.S., Ryu, S.R., and An, D.K., 2006, *Tetrahedron*, 62 (34), 8164–8168.
4. Chandrasekhar, S., and Shrinidhi, A., 2014, *Synth. Commun*., 44 (14), 2051–2056.
5. Kuroiwa, Y., Matsumura, S., and Toshima, K., 2008, *Synlett*, 16, 2523–2525.
6. Brogan, A.P., Dickerson, T.J., and Janda, K.D., 2007, *Chem. Commun*., 46, 4952–4954.
7. Kidwai, M., Bansal, V., Saxena, A., Shankar, R., and Mozumdar, S., 2006, *Tetrahedron Lett*., 47 (25), 4161–4165.
8. Tanaka, K., and Toda, F., 2000, *Chem. Rev*., 100 (3), 1025–1074.
9. Naik, R., Nizam, A., Siddekha, A., and Pasha, M.A., 2011, *Ultrason. Sonochem*., 18 (5), 1124–1127.
10. Nikpassand, M., Fekri, L.Z., and Farokhian, P., 2016, *Ultrason. Sonochem*., 28, 341–345.
11. Jumina, Siswanta, D., and Zulkarnain, A.K., 2001, *Indones. J. Pharm*., 12, 24–35.
12. Zbancioc, G., Florea, O., Jones, P.G., and Mangalagiu, I.I., 2012, *Ultrason. Sonochem.*, 19 (3), 399–403.
13. Hallett, J.P., and Welton, T., 2011, *Chem. Rev*., 111 (5), 3508–3576.
14. Budavari, S., 1989, *The Merck index, an encyclopedia of chemicals, drugs, and biologicals*, 11th Ed., John Wiley and Sons Inc., New York.
15. Zeynizadeh, B., and Yahyaei, S., 2004, *Z. Naturforsch*, 59 (6), 704–710.
16. Gupta, M.S., and Venkatachalam, V.V., 2006, *Asian J. Chem*., 18 (4), 2993–2996.
17. Kim, I.S., Choi, D.K., and Jung, H.J., 2011, *Molecules*, 16 (7), 5349–5361.
18. Jung, H.J., Song, Y.S., Lim, C.J., and Park, E.H., 2008, *Arch. Pharmacal Res*., 31 (10), 1275–1279.