

Deprotection of benzyl ethers using 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) under photoirradiation

Mohammad Abdur Rahim, Shuichi Matsumura and Kazunobu Toshima*

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan

Received 30 July 2005; revised 26 August 2005; accepted 26 August 2005

Available online 12 September 2005

Abstract—The deprotection of benzyl ethers was effectively realized in the presence of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in MeCN under photoirradiation using a long wavelength UV light.
© 2005 Elsevier Ltd. All rights reserved.

The popularity and extensive use of benzyl (Bn) ethers as protecting groups for alcohols arise from their ease of formation and removal, and their stability under wide range of reaction conditions.¹ A variety of methods have been developed for their removal. Catalytic hydrogenolysis using Pd–C, Raney–Ni or Rh–Al₂O₃ is the most common for deprotecting benzyl ethers. As an alternative method, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) was reported to be a good reagent in the presence or absence of water.^{2,3} However, the use of DDQ for deprotecting benzyl ethers cannot be always applicable. In view of the importance of benzyl ethers in organic synthesis, the search for novel methods for the effective deprotection is of considerable importance. On the other hand, a photochemical reaction using DDQ has been reported for deprotecting thioacetals and ketals.⁴ DDQ is a well-known electron acceptor and forms charge transfer (CT) complexes with a variety of donors.⁵ Based on these facts, we were interested in the investigation of benzyl ethers as donors and quinones as acceptors leading to the photochemical deprotection of benzyl ethers. Herein, we report a novel deprotection method of benzyl ethers using DDQ under photoirradiation (Fig. 1).

Based on our hypothesis, we first examined the deprotection of benzyl ether in **1**, possessing a pivaloyl (Pv)

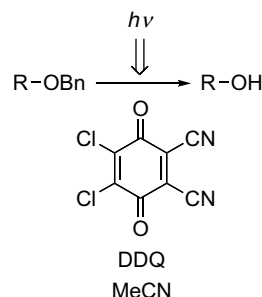


Figure 1. Photodeprotection of benzyl ethers using DDQ.

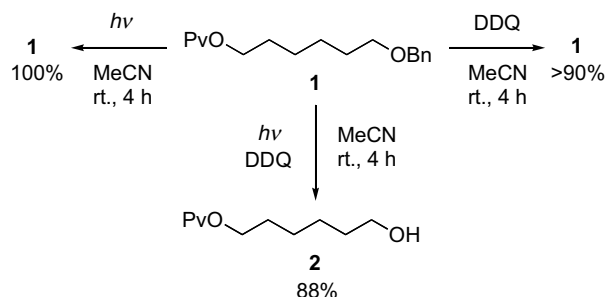


Figure 2. Photodeprotection of the benzyl ether in **1** using DDQ.

Keywords: Protecting group; Benzyl ether; 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone; Photoirradiation; Alcohol.

*Corresponding author. Tel.: +81 45 566 1576; fax: +81 45 566 1576; e-mail: toshima@applc.keio.ac.jp

ester as another protecting group, using DDQ in MeCN with or without photoirradiation (Fig. 2). The photoirradiation was carried out using a long wavelength

UV light (365 nm, 100 W) placed at 15 cm from the reaction mixture. We found, for the first time, that the deprotection of the benzyl ether in **1** using 1.5 equiv of DDQ in MeCN at room temperature during the photoirradiation proceeded smoothly to give the alcohol **2** in 88% yield. In drastic contrast, it was found that the deprotection of the benzyl ether in **1** using DDQ in MeCN without the photoirradiation occurred very slightly, and the reactant **1** was recovered in more than 90% yield. Furthermore, it was confirmed that the deprotection of the benzyl ether in **1** in MeCN during the photoirradiation in the absence of DDQ was not performed at all. These results clearly indicated that the combined use of DDQ and the photoirradiation is indispensable, and the UV light functioned as a trigger to initiate the benzyl group deprotection using DDQ. In addition, it was revealed that MeCN was quite superior to other solvents such as MeOH, THF and PhMe. Actually, the photodeprotection using DDQ proceeded very slowly or did not take place at all in MeOH, THF and PhMe.

With these results in hand, we investigated the scope and limitation of the photodeprotection reaction. For this purpose, we first examined the deprotections of the benzyl ethers of several substances **3–6**, each of which possesses a primary or a secondary benzyl ether. These results are summarized in Table 1. We found that all the deprotection reactions using DDQ and photoirradiation proceeded smoothly to give the corresponding alcohols in good yields. These results also showed that the deprotection method is applicable to not only primary benzyl ethers but also to secondary ones. In addition, it was found that the addition of BaCO₃ is sometimes effective (entries 1 and 4 in Table 1), probably due to the quenching effect for small amounts of acidic products coming from the minor DDQ decomposition under the reaction conditions.

We next tested the deprotections of the benzyl ethers of several compounds **7–12**, which possess another protecting group, such as benzoyl (Bz), methoxymethyl

(MOM), carbonate or isopropylidene group, or a functional group, such as double or triple bond. These results are summarized in Table 2. It was found that the deprotections of the benzyl ethers in **7–9** effectively proceeded, as well as **1**, to provide the corresponding alcohols in good to high yields. In the cases of **10** and **11** possessing an isopropylidene group and a double bond, respectively, the yields were not very high and even moderate in the presence of BaCO₃. Unfortunately, it was confirmed that a triple bond is not a good substrate for the deprotection reaction as shown in the reaction using **12**. These unfavorable results came from the partial deprotection of the isopropylidene group in **10**, and the generation of the significant amounts of by-products from **11** and **12**. Furthermore, as Tanemura et al. have demonstrated,⁶ silyl groups were readily deprotected by DDQ with and without photoirradiation.

We finally compared the reactivity of the benzyl ether with that of the *p*-methoxybenzyl ether (MPM) using **13**, which had both benzyl and *p*-methoxybenzyl ethers, under the stated reaction conditions (Fig. 3). *p*-Methoxybenzyl ether is well known to be easily deprotected by DDQ in the presence of water.⁷ It was found that the *p*-methoxybenzyl ether in **13** was selectively removed using DDQ in MeCN under the photoirradiation and anhydrous conditions within a short time to give the monool **14** in high yield. In addition, it was confirmed that a longer reaction time led to the deprotection of both benzyl and *p*-methoxybenzyl ethers in **13** that produces the diol **15** in good yield.

The typical experimental protocol for the deprotection of the benzyl ether in **1**: To a stirred solution of **1** (0.1 mmol) in dry MeCN (15 mL) was added DDQ (0.15 mmol). After stirring at room temperature for 4 h under the photoirradiation using a UV lamp (365 nm, 100 W) placed at 15 cm from the reaction mixture, the mixture was poured into saturated aqueous NaHCO₃ solution and then the resulting mixture was extracted with CHCl₃. The extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Purifica-

Table 1. Photodeprotection of the benzyl ethers in **3–6** using DDQ

$\text{R-OBn} \xrightarrow[\text{MeCN, rt.}]{\text{DDQ, } h\nu} \text{R-OH}$					
Entry	R-OBn	DDQ (equiv)	BaCO ₃ (equiv)	Time/h	Yield/%
1	3	1.1	1.1	24	78
2	4	1.5	—	15	76
3	5	1.5	—	16	74
4	6	1.1	1.1	22	75

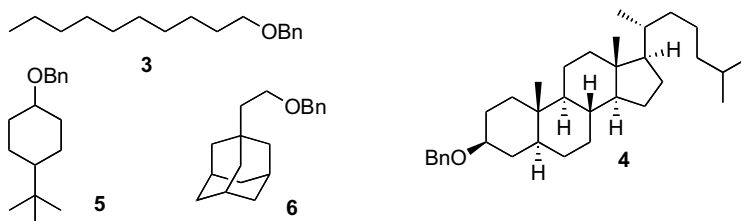
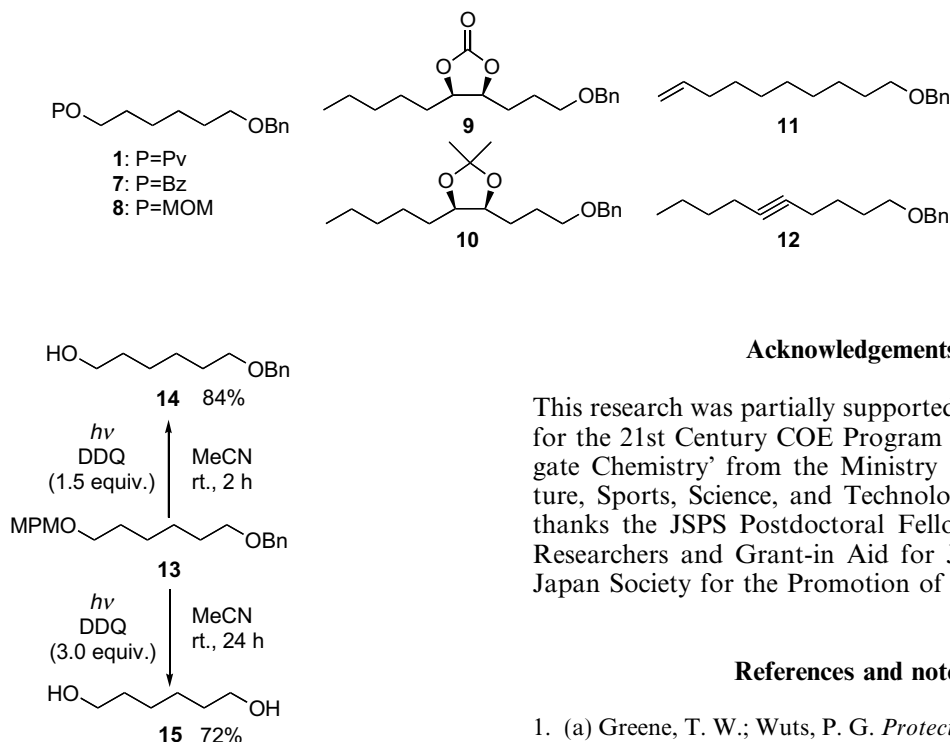


Table 2. Photodeprotection of the benzyl ethers in **1** and **7–12** using DDQ

$\text{R-OBn} \xrightarrow[\text{DDQ, MeCN, rt.}]{h\nu} \text{R-OH}$					
Entry	R-OBn	DDQ (equiv)	BaCO ₃ (equiv)	Time/h	Yield/%
1	1	1.5	—	4	88
2	7	1.1	—	8	87
3	8	1.5	—	5	93
4	9	1.5	—	5	97
5	10	1.5	1.5	10	65
6	11	1.5	1.5	16	52
7	12	1.5	—	5	12

**Figure 3.** Deprotection of the benzyl and *p*-methoxybenzyl ethers in **13** using DDQ with photoirradiation.

tion of the residue by column chromatography (2:1 hexane–ethyl acetate) gave the alcohol **2** in 88% yield.

In summary, we demonstrated here, for the first time, the novel photodeprotection method of benzyl ethers using DDQ in MeCN under photoirradiation using a long wavelength UV light. DDQ, MeCN and the photoirradiation were found to be indispensable for the deprotection reaction. Although the precise reaction mechanism is not clear at this stage, and the present method has some limitations, this novel photodeprotection protocol of benzyl ethers should find alternative applications in organic synthesis.

Acknowledgements

This research was partially supported by a Grant-in-Aid for the 21st Century COE Program ‘KEIO Life Conjugate Chemistry’ from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. M.A.R. thanks the JSPS Postdoctoral Fellowship for Foreign Researchers and Grant-in Aid for JSPS Fellows from Japan Society for the Promotion of Science (JSPS).

References and notes

- (a) Greene, T. W.; Wuts, P. G. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1999; (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, 1994.
- (a) Tanaka, T.; Oikawa, Y.; Nakajima, N.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bull.* **1987**, *35*, 2203; (b) Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Borodkin, V. S.; Kochetkov, N. K. *Tetrahedron Lett.* **1987**, *28*, 3839; (c) Vedejs, E.; Buchanan, R. A.; Watanabe, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8430.
- Ikemoto, N.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 2524.
- Mathew, L.; Sankararaman, S. *J. Org. Chem.* **1993**, *58*, 7576.
- (a) Foster, R. *Organic Charge Transfer Complexes*; Academic Press: New York, 1969; (b) Foster, R.; Foreman, M. L. In *The Chemistry of the Quinonoid Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1974; Part 1, pp 257–333.
- Tanemura, K.; Suzuki, T.; Horaguchi, T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2997.
- Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885.