Tetrahedron Letters 54 (2013) 2412-2414

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Benzoyl peroxide-imidazole: a novel and efficient reagent for the mild conversion of alcohols or phenols into benzoates

Najmeh Nowrouzi*, Seyedeh Zahra Alizadeh

Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169, Iran

ARTICLE INFO

ABSTRACT

Article history: Received 29 November 2012 Revised 9 February 2013 Accepted 28 February 2013 Available online 7 March 2013

Keywords: Benzoyl peroxide Imidazole Esterification

Esterification is a frequently used reaction due to its broad utility.¹ Typically, the esterification reaction is an acid-catalyzed process, in which the conventional acid catalysts are sulfuric acid and hydrochloric acid, and needs either of two methods to shift the equilibrium between the reactants and products. One is removal of water (azeotropically or using dehydrating agents) generated as the reaction proceeds, and the other involves the use of a large excess of one of the reactants. Classical methods have several disadvantages that include equipment corrosion, formation of unwanted side products, environmental problems, and difficulties in catalyst recovery and loss of the catalyst. To date, a variety of esterification conditions have been developed.²⁻¹³ However, most procedures require either the presence of strong acids, bases, or other catalysts. Accordingly, the further development of simple methods for direct esterification under mild conditions is desirable. In 2003, Palaniappan and Ram employed benzoyl peroxide in the presence of sulfuric acid and sodium lauryl sulfate as a surfactant, to convert aniline into a polyaniline salt that was then used as the catalyst in the esterification of carboxylic acids with methanol at 70 °C.¹⁴ Herein, we describe a simple and mild method for the conversion of alcohols into benzoates that uses benzoyl peroxide and imidazole as a novel reagent without the need for any acidic catalyst.

Initially, the reaction conditions were optimized using benzyl alcohol as a model compound.

Reaction of benzoyl peroxide (1.5 equiv) and imidazole (4.0 equiv), followed by the addition of 1.0 equiv of benzyl alcohol

in refluxing acetonitrile gave the best result; the benzoate was obtained in 88% yield after purification (Scheme 1).

© 2013 Elsevier Ltd. All rights reserved.

A very mild, one-pot, and expedient protocol for the conversion of alcohols and phenols into their

corresponding benzoates using imidazole and benzoyl peroxide as a novel reagent is described.

Based on this outcome, the conversion of different alcohols into benzoates was performed and the results are listed in Table 1.

This reagent system was suitable for the conversion of primary, secondary, and benzylic alcohols into their corresponding benzoates. The reaction with primary alcohols was faster in comparison to those of more bulky secondary alcohols. For example, 2-phenylethanol (Table 1, entry 6), underwent the reaction much faster and in higher yield than 1-phenylethanol (Table 1, entry 7).

In the case of a sterically hindered tertiary alcohol (Table 1, entry 11), no desired product was formed even after reflux for a prolonged time.

Having successfully converted various alcohols into benzoates, we sought to extend this methodology to the direct preparation of phenolic benzoates. Hence, reactions between benzoyl peroxide, imidazole, and various phenols were carried out to afford the desired products. As can be seen in entries 12–17 in Table 1, the reactions proceeded quite well with phenols. Phenols with electron-donating or electron-withdrawing groups reacted smoothly under mild conditions to afford the corresponding benzoates in moderate to high yields.

The reaction of benzoyl peroxide and imidazole with the electron-rich phenol, 4-methoxyphenol (Table 1, entry 16) was









^{*} Corresponding author. Tel.: +98 771 4222341; fax: +98 771 4541494. *E-mail address:* nowrouzi@pgu.ac.ir (N. Nowrouzi).

^{0040-4039/\$ -} see front matter @ 2013 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.tetlet.2013.02.101

Table 1

Synthesis of alkyl and phenolic $\underline{benzoates}$ using benzoyl peroxide and imidazole in refluxing acetonitrile



Table 1 (continued)



^a Isolated yield.

^b 4-Methoxybenzaldehyde was obtained as a by-product.



successful and gave 4-methoxyphenyl benzoate in 85% yield after 2 h, but lower yields and longer reaction times were observed with phenols bearing electron-withdrawing groups on the phenyl moiety. Analysis of the results of the reactions with nitro phenols (Table 1, entries 14 and 15), revealed that the nitro group had a negative effect on the rate and yield of the reaction, as the electron-withdrawing properties of the nitro substituent(s) reduce the nucleophilic character of phenol. In addition to the electronic factors, steric factors also affected the reaction in terms of time and yield. Comparison of entries 13 and 14 indicated that the presence of an *ortho* substituent on the phenol ring decreased the yield and increased the reaction time.

The stereochemical outcome of the reaction was then probed utilizing (–)-menthol as a secondary, chiral alcohol. Using benzoyl peroxide, imidazole, and (–)-menthol, we obtained menthyl benzoate in 50% yield with complete retention of configuration.¹⁵ The retention of configuration is thought to arise through a direct attack of the alcohol on the carbonyl carbon atom of the intermediate **II** (Scheme 2).

Although benzoyl peroxide is a radical initiator, nevertheless, there are many reports in the literature that use benzoyl peroxide in a polar mechanism.¹⁶ Several observations support the proposed pathway outlined in Scheme 2. (1) Optimization experiments showed that polar solvents, which are unfavorable for free radical reactions, increased the rates of these reactions. (2) Imidazole

shows a useful promoting ability in this system and increasing its molar ratio accelerates the rate of the reaction. It appears that imidazole enhances the reactivity of the reagent system with the formation of intermediates **I** and **II** and also neutralizes the liberated carboxylic acid. (3) The overall yields of these reactions depend mostly on the electronic nature of the substituents on the benzyl alcohols or phenols in such a manner that electron-donating groups increase the yield of the benzoate formation and the presence of electron-withdrawing groups diminishes the yield. (4) We observed that (–)-menthol was converted into its benzoate with retention of the configuration of the stereogenic center. (5) The products of these reactions do not correspond to those of the known radical decomposition of peroxides.

In addition to the above observations, the product of the reaction of *cis*-3-hexen-1-ol (an alcohol with a C=C bond), also confirmed the polar mechanism. Thus, *cis*-3-hexen-1-ol was added to a mixture of imidazole and benzoyl peroxide under the optimized conditions. After 6 h, (*Z*)-hex-3-enyl benzoate was obtained in 70% yield (Table 1, entry 18). Formation of this product is consistent with the proposed mechanism shown in Scheme 2. Therefore, a free radical mechanism for these reactions does not seem likely.

In conclusion, a simple and mild one-pot protocol for the conversion of alcohols and phenols into benzoates using benzoyl peroxide and imidazole as a novel reagent has been developed.¹⁷ The reactions do not require a dehydrating agent nor azeotropic removal of water. Furthermore, the simple procedure, availability, safety, and ease of handling of the reagents, no requirement for additives, and no neutralization or washing steps during the work-up are advantages of this reagent system.

Acknowledgement

We thank the Persian Gulf University Research Council for generous partial financial support of this study (Code: PGU/FS/7-1/1391/842).

References and notes

- (a) Otera, J. Esterification Methods. Reactions and Applications; Wiley-VCH: Weinheim, Germany, 2003; (b) Larock, R. C. Comprehensive Organic Transformations, 2nd ed.; VCH: New York, 1999; (c) Franklin, A. S. J. Chem. Soc., Perkin Trans. 1 1998, 2451; (d) Franklin, A. S. J. Chem. Soc., Perkin Trans. 1 1999, 3537.
- Iranpoor, N.; Firouzabadi, H.; Khalili, D.; Motevalli, S. J. Org. Chem. 2008, 73, 4882.
- Soltani Rad, M. N.; Behrouz, S.; Faghihi, M. A.; Khalafi-Nezhad, A. Tetrahedron Lett. 2008, 49, 1115.
- Saito, Y.; Yamaki, T.; Kohashi, F.; Watanabe, T.; Ouchi, H.; Takahata, H. Tetrahedron Lett. 2005, 46, 1277.
- 5. Manabe, K.; Sun, X.; Kobayashi, S. J. Am. Chem. Soc. 2001, 123, 10101.
- Sejidov, F. T.; Mansoori, Y.; Goodarzi, N. J. Mol. Catal. A: Chem. 2005, 240, 186.
 Sharma, P.; Vyas, S.; Patel, A. J. Mol. Catal. A: Chem. 2004, 214, 281.
- Wakasugi, K.; Nakamura, A.; Iida, A.; Nishii, Y.; Nakatani, N.; Fukushima, S.; Tanabe, Y. *Tetrahedron* **2003**, *59*, 5337.
- 9. Won, J.; Kim, H.; Kim, J.; Yim, H.; Kim, M.; Kang, S.; Chung, H.; Lee, S.; Yoon, Y. *Tetrahedron* **2007**, 63, 12720.
- 10. Salome, C.; Kohn, H. Tetrahedron 2009, 65, 456.
- 11. Nowrouzi, N.; Mehranpour, A. M.; Ameri Rad, J. Tetrahedron 2010, 66, 9596.
- 12. Mukaiyama, T.; Shintou, T.; Kikuchi, W. Chem. Lett. 2002, 1126.
- 13. Sarpong, R.; Heller, S. T. *Tetrahedron* **2011**, 67, 8851.
- 14. Ram, M. S.; Palaniappan, S. J. Mol. Catal. A: Chem. 2003, 201, 289.
- (a) McNulty, J.; Capretta, A.; Laritchev, V.; Dyck, J.; Robertson, A. J. J. Org. Chem. 2003, 68, 1597; (b) Silverman, R. B.; Forrester, M. T.; Gomez-Vidal, J. A. Org. Lett. 2001, 3, 2477.
- (a) Challenger, F.; Wilson, V. J. Chem. Soc. **1927**, 209; (b) Greenbaum, M. A.; Denny, D. B.; Hoffmann, K. J. Am. Chem. Soc. **1956**, 78, 2563; (c) Pautard, A. M.; Evans, S. A., Jr. J. Org. Chem. **1988**, 53, 2300; (d) Grierson, L.; Perkins, M. J. Tetrahedron Lett. **1993**, 34, 7463.
- 17. Typical procedure for the synthesis of benzyl benzoate (1): Benzyl alcohol (0.1 mL, 1 mmol) was added to a stirred solution of imidazole (0.272 g, 4.0 mmol) and benzoyl peroxide (0.363 g, 1.5 mmol) in 5 mL of CH₃CN at reflux. The reaction was monitored by TLC. After completion of the reaction (3 h), the solvent was evaporated and the residue was subjected to purification on a short column of silica gel, using *n*-hexane/EtOAc (4:1) as the eluent to give benzyl benzoate (0.186 g, 88%) as a colourless oil; $\delta_{\rm H}$ (250 MHz, CDCl₃) 7.98 (dd, 2H, *J* 8.4, 1.5 Hz, Ph), 7.44-7.24 (m, 8H, Ph), 5.26 (s, 2H, CH₂); $\delta_{\rm C}$ (62.9 MHz, CDCl₃) 166.4, 136.1, 133.1, 130.2, 129.7, 128.6, 128.4, 128.3, 128.2, 66.7.