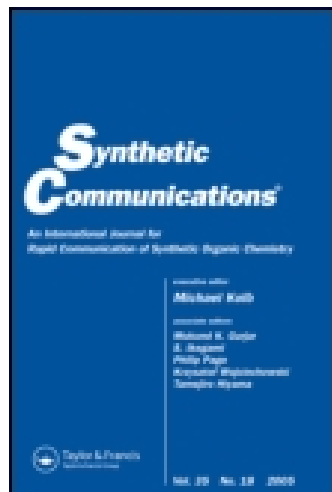


This article was downloaded by: [Santosh G. Tilve]

On: 13 July 2015, At: 22:52

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: 5 Howick Place, London, SW1P 1WG



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

PDC-Mediated Tandem Oxidative-Wittig Olefination

Kashinath L. Dhumaskar^a, Chinmay Bhat^a & Santosh G. Tilve^a

^a Department of Chemistry, Goa University, Goa, India

Accepted author version posted online: 10 Feb 2014. Published online: 29 Apr 2014.



[Click for updates](#)

To cite this article: Kashinath L. Dhumaskar, Chinmay Bhat & Santosh G. Tilve (2014) PDC-Mediated Tandem Oxidative-Wittig Olefination, *Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry*, 44:10, 1501-1506, DOI: [10.1080/00397911.2013.862725](https://doi.org/10.1080/00397911.2013.862725)

To link to this article: <http://dx.doi.org/10.1080/00397911.2013.862725>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms &

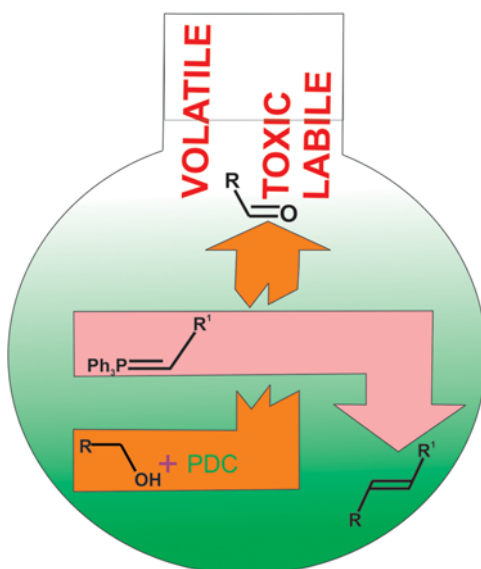
Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

PDC-MEDIATED TANDEM OXIDATIVE–WITTIG OLEFINATION

Kashinath L. Dhumaskar, Chinmay Bhat, and Santosh G. Tilve

Department of Chemistry, Goa University, Goa, India

GRAPHICAL ABSTRACT



Abstract A convenient tandem oxidative–Wittig olefination of a primary alcohols to α,β -unsaturated compounds using pyridinium dichromate (PDC) is described.

Keywords Olefination; oxidation; PDC; tandem; Wittig reaction

INTRODUCTION

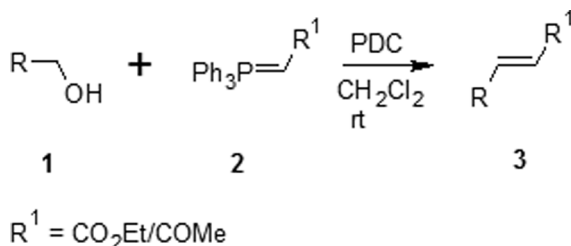
One of the routine organic transformations in organic synthesis for the homologation sequence is the oxidation of primary alcohol to aldehyde and further condensation with an appropriate Wittig reagent to get an α,β -unsaturated compound. The

Received August 27, 2013.

Address correspondence to Santosh Tilve, Department of Chemistry, Goa University, Goa 403 206, India. E-mail: stilve@unigoa.ac.in

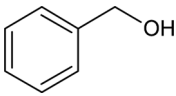
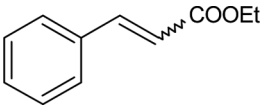
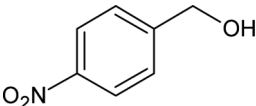
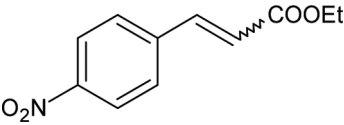
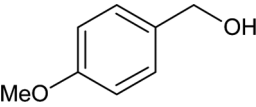
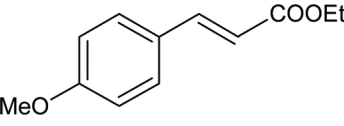
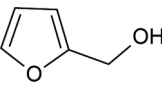
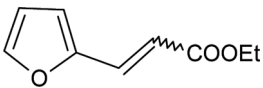
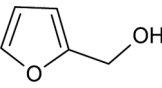
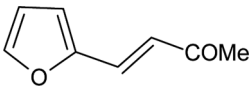
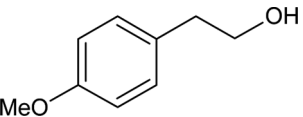
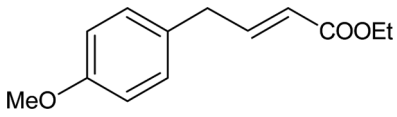
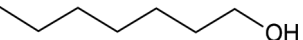
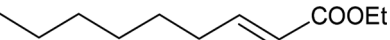
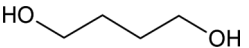
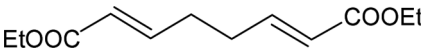
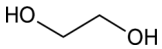
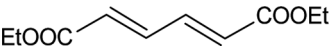
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/lsyc.

problem associated with this sequence is the handling of the intermediate aldehyde, particularly in the case of aldehydes, which are unstable, volatile, and toxic. This problem has been overcome to a great extent by the development of what is called as tandem oxidative procedure^[1] (TOP) or domino reactions. These reactions slightly differ from the “one-pot” procedures wherein first aldehyde is obtained and then immediately reacted with a stabilized Wittig reagent.^[2] In TOP, oxidation is carried out in the presence of a Wittig reagent so that as soon as aldehyde is formed it can further condense with the Wittig reagent. In this procedure the crucial part is the choice of the oxidizing agent, as it should not react with the Wittig reagent to oxidize it or overoxidize the initial alcohol further to an acid or ester. There are several reagents available for the selective oxidation of a primary alcohol to aldehyde but all cannot be used for TOP. For example, the most popular Swern oxidation^[2] has to be used in a sequential manner and not in TOP as intermediate oxalyl chloride readily reacts with phosphorane. The first such TOP was reported by Barrett et al. in 1997 wherein primary alcohol was condensed with stable phosphorane in the presence of Dess–Martin periodinane^[3] as an oxidizing agent. Benzoic acid was added to the reaction mixture to expedite the reaction in dimethylsulfoxide (DMSO)–CH₂Cl₂ (1:6) solvent mixture. In 1998 Wie and Taylor reported TOP for activated alcohols such as allylic, benzylic, and propargylic alcohols using excess of MnO₂.^[1] The procedure is suitable for sensitive aldehydes that are normally difficult to isolate. In the same year Shuto and coworkers used BaMnO₄^[4] again for activated alcohol in TOP. In 1999 Davies and McKervey extended the MnO₂ TOP for *N*-protected β-amino alcohols^[5] under refluxing acetonitrile conditions. In the same year Crich and Mo reported use of iodoxybenzoic acid (IBX)^[6] in dimethylsulfoxide (DMSO) for homologation of nucleosides. Catalytic aerobic oxidation using Ru^[7] catalyst for TOP was reported by Kim et al. in 2001. The popular Corey reagent pyridinium chlorochromate (PCC)^[8] in combination with NaOAc was reported from our laboratory in 2004. Recently Karama et al. in 2010 reported synthesis of α-bromo-α,β-unsaturated esters using a combination *N*-bromosuccinimide (NBS),^[9] stable Wittig reagent, and primary alcohol under ultrasonic conditions. Because PCC is not a choice of reagent for the oxidations of allylic and propargylic alcohols, we were interested in using pyridinium dichromate (PDC) for such TOP. It was reported by Shuto^[4] and coworkers that PDC is not suitable for such TOP. Hence we thought of investigating this reaction as it would be complementary to our PCC methodology for synthesizing homologated compounds of activated alcohols. In this article, we describe PDC-mediated tandem oxidative Wittig reaction procedure for the synthesis of α,β-unsaturated esters.



Scheme 1. Tandem oxidative Wittig reaction.

Table 1 PDC-mediated tandem oxidation Wittig reaction

Entry	Reactant 1	Product 3	Yield ^a
a			90 (<i>E-Z</i> = 17:1)
b			82 (<i>E-Z</i> = 17:1)
c			81 (<i>E</i>)
d			98 (<i>E-Z</i> = 20:1)
e			96 (<i>E</i>)
f			54 (<i>E</i>)
g			87 (<i>E</i>)
h			62 (<i>E</i>)
i			40 (<i>E</i>)

(Continued)

Table 1. Continued

Entry	Reactant 1	Product 3	Yield ^a
j			66 (<i>E</i>)
k			73 (<i>E</i>)
l			70 (<i>E</i>)
m			56 (<i>E</i>)
n			84 (<i>E</i>)

^aIsolated using column chromatographic technique with 2% EtOAc in petroleum ether. *E-Z* ratio derived from NMR data.

RESULTS AND DISCUSSION

In our efforts, initially we tried the reaction of benzyl alcohol **1a** with ethyl (triphenylphosphoranylidene)acetate in the presence of PDC in CH₂Cl₂. The reaction was found to be complete after prolonged stirring (24 h), comparatively longer than the PCC method. The yield of ethyl cinnamate **3a** (*E-Z*, 95:5) was found to be 90%. After this success we tested this protocol with various other alcohols (Table 1). Benzyl alcohol, having an electron-withdrawing group *p*-nitrobenzyl alcohol **1b**, gave the corresponding *E*-homologated product **3b** exclusively in 82% yield. Benzyl alcohol, having an electron-donating group *p*-methoxybenzyl alcohol **1c**, gave the corresponding *E*-homologated product **3c** exclusively in 81% yield. Acid-sensitive furfuryl alcohol **1d** with ethyl (triphenylphosphoranylidene)acetate and (triphenylphosphoran ylidene)acetone gave the products **3d** and **3e** in 98% and 96% yields respectively. Next the protocol was checked for aliphatic alcohols *n*-heptanol **1g** and isobutyl alcohol **1j**. In both the cases the homologated product **3g** and **3j** were obtained in good yield. 1,4-Butanediol **1h** with 2 equivalents of Wittig

reagent and oxidizing agent gave *bis*-homologated product **3h** in 62% yield, while ethanediol **1i** gave the corresponding product **3i** in only 40% yield. We then subjected this protocol to allylic alcohols. Cinnamyl alcohol **1k** gave the corresponding product **3k** in 73% yield. The allyl alcohol **1l**, which is a poor substrate for PCC, gave the product **3l** in 70% yield. Propagyl alcohol **1m**, which is not amenable to PCC, gave the product **3m** in moderate yield of 56%. *p*-Methoxy homobenzyl alcohol **1f** gave homologated product **3f** in 54% yield. In this reaction formation of a trace amount of *p*-methoxy benzaldehyde was also observed on thin-layer chromatography (TLC). Boc-protected prolinol **1n** an, amino alcohol that is sensitive to the acidic PCC, gave the product **3n** successfully in 84% yield. However, Cbz-prolinol did not give the homologated product as the Cbz group was found to get knocked off, resulting in formation of ethyl cinnamate due to the formation of intermediate benzaldehyde and decomposition of prolinol.

CONCLUSION

In conclusion, we have developed a PDC-mediated tandem oxidative Wittig olefination procedure for the homologation of primary alcohols. The present procedure is complementary to our PCC-mediated protocol wherein nonactivated alcohols can be more effectively homologated.

EXPERIMENTAL

Flash chromatography was performed on silica gel (230–400 mesh). Infrared (IR) spectra were recorded on a Shimadzu FT-IR spectrophotometer. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) were recorded on a Bruker instrument. Chemical shifts (ppm) are relative to the internal standard Me₄Si (0 ppm).

Wittig reagent (1.85 mmol) in anhydrous CH₂Cl₂ (10 mL) and alcohol (1.85 mmol) in anhydrous CH₂Cl₂(10 mL) were added in one portion to a magnetically stirred suspension of pyridinium dichromate (1.85 mmol). The reaction mixture was stirred at rt for 24 h. Et₂O (30 mL) was added to the reaction mixture and filtered. The residue was washed with ether (2 × 5 mL) and dried over anhydrous Na₂SO₄. The combined filtrate was then evaporated to give the crude product. Further purification by column chromatography using petroleum ether as an eluent gave the product.

FUNDING

The authors thank the Department of Science and Technology and the Council of Scientific and Industrial Research (CSIR), New Delhi, for financial assistance. K.L.D. and C.B. thank CSIR for awards of National Eligibility Test (NET) Senior research fellowships.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

REFERENCES

1. Wei, X.; Taylor, R. J. K. In situ alcohol oxidation–Wittig reactions. *Tetrahedron Lett.* **1998**, *39*, 3815–3818.
2. Ireland, R. E.; Norbeck, D. W. Application of the Swern oxidation to the manipulation of highly reactive carbonyl compounds. *J. Org. Chem.* **1985**, *50*, 2198–2200.
3. Barrett, A. G. M.; Hamprecht, D.; Ohkubo, M. Dess–Martin periodinane oxidation of alcohols in the presence of stabilized phosphorus ylides: A convenient method for the homologation of alcohols via unstable aldehydes. *J. Org. Chem.* **1997**, *62*, 9376–9378.
4. Shuto, S.; Niizuma, S.; Matsuda, A. One-pot conversion of α,β -unsaturated alcohols into the corresponding carbon-elongated dienes with a stable phosphorus ylide–BaMnO₄ system: Synthesis of 6'-methylene derivatives of neplanocin A as potential antiviral nucleosides: New neplanocin analogues. *J. Org. Chem.* **1998**, *63*, 4489–4493.
5. Davies, S. B.; McKervey, M. A. Convenient in situ synthesis of nonracemic *N*-protected β -amino aldehydes from β -amino acids: Applications in Wittig reactions and heterocycle synthesis. *Tetrahedron Lett.* **1999**, *40*, 1229–1232.
6. Crich, D.; Mo, X.-S. One-pot Selective 5'-oxidation/olefination of 2'-deoxynucleosides. *Synlett* **1999**, *1*, 67–68.
7. Kim, G.; Lee, D. G.; Chang, S. In situ aerobic alcohol oxidation–Wittig reactions. *Bull. Korean Chem. Soc.* **2001**, *22*, 943.
8. Shet, J.; Desai, V.; Tilve, S. G. Domino primary alcohol oxidation–Wittig reaction: Total synthesis of ABT-418 and (*E*)-4-oxonon-2-enoic acid. *Synthesis* **2004**, *11*, 1859–1863.
9. Karama, U.; Al-Othman, Z.; Al-Majid, A.; Almansour, A. A facile one-pot synthesis of α -bromo- α,β -unsaturated esters from alcohols. *Molecules* **2010**, *15*, 3276–3280.