http://pubs.acs.org/journal/acsodf

Article

Yb(OTf)$_3$-Catalyzed and Di-*tert*-butyl Dicarbonate-Mediated Decarboxylative Etherification and Esterification Reactions

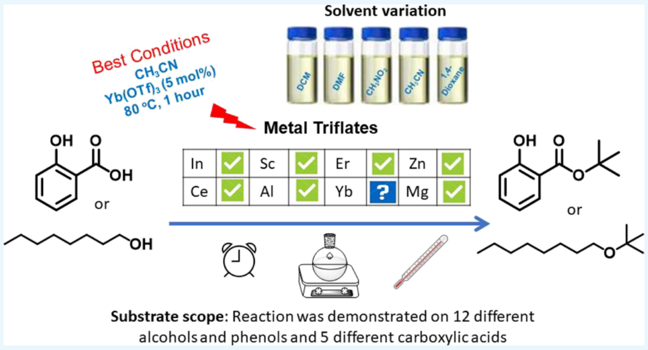
Arshpreet Kaur, Arshdeep Pannu, Deshkanwar S. Brar, Surinder K. Mehta, and Deepak B. Salunke*

Cite This: *ACS Omega* 2020, 5, 21007−21014

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Protecting group chemistry has invariably captured the fascination of chemists because of its extensive viability in chemical synthesis. The present report describes our pioneer work of applying ytterbium triflate as a catalyst, for the reaction of alcohols with di-*tert*-butyl dicarbonate (Boc$_2$O) leading to the formation of *tert*-butyl ethers. There exists no recorded evidence for the use of Yb(OTf)$_3$ as a catalyst for the protection of alcohols to *tert*-butyl ethers, despite its excellent utility in various reactions. Yb(OTf)$_3$ has been used predominantly in the catalytic deprotection studies such as selective deprotection of *tert*-butyl esters to carboxylic acids as well as prenyl ethers to alcohols. This study involved the critical evaluation of solvent, time, and temperature that finally led to an efficient protocol for the formation of *tert*-butyl ethers. Yb(OTf)$_3$ catalyzed the formation of *tert*-butyl ethers, notably reducing the reaction time, which is exemplified by the achievement of up to 92% conversion of alcohols to *tert*-butyl ethers within an hour. Additionally, the report demonstrates the utility of this synthetic protocol for the protection of carboxylic acids.



1. INTRODUCTION

Various protecting groups like esters, silyl ethers, alkoxy alkyl ethers, and so forth have been reported for the protection of alcohols (Figure 1).[1] However, *tert*-butyl ether is one of the most versatile protecting group because of its extreme stability in basic conditions.[2] It can be successfully employed to aliphatic alcohols as well as phenols and is compatible with other protecting groups and functionalities such as carbonyls, nitriles, hydroxyl moieties, and esters. Bartoli's mild and chemoselective deprotection strategy using anhydrous CeCl$_3$ and NaI in acetonitrile contributed to the popularity of the *tert*-butyl ether as a desirable protecting group for alcohols.[3]

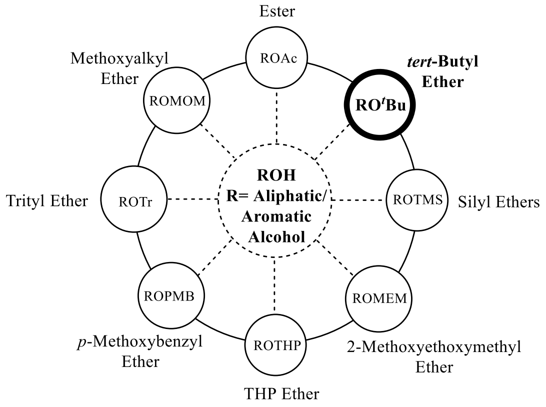


Figure 1. Protecting groups for hydroxy functionality.

Protection of alcohols to *tert*-butyl ethers using isobutene in the presence of strong acids came into the limelight during the 1980s.[4] However, this conventional route did not work well in the case of aromatic alcohols as it preferentially resulted in Friedel−Craft ring alkylation. Bartoli *et al.* evaluated various Lewis acid catalysts for the protection of alcohols using *tert*-butyl dicarbonate (Boc$_2$O) as the reagent to replace harsh conditions for the formation of *tert*-butyl ethers.[5] During their investigation, it was observed that the catalytic amount (10 mol %) of perchlorates [Ce(ClO$_4$)$_3$, Zn(ClO$_4$)$_2$, Mg(ClO$_4$)$_2$, Ca(ClO$_4$)$_2$, and HClO$_4$] and triflates [In(OTf)$_3$, Sc(OTf)$_3$, Al(OTf)$_3$, Ce(OTf)$_3$, Zn(OTf)$_2$, and Mg(OTf)$_2$] resulted in *tert*-butyl ethers with more than 94% yield in each case. Mg(ClO$_4$)$_2$ stood out to be the best in terms of cost and efficiency of the reaction, while in the case of aromatic alcohols, Sc(OTf)$_3$ was found to be the best choice as *tert*-butyl ethers are not much stable in the case of perchlorates.

Received: May 28, 2020
Accepted: July 31, 2020
Published: August 13, 2020

117.5 (C3, ArCH), 118.8 (C5, ArCH), 130.1 (C6, ArCH), 135.1 (C4, ArCH), 161.8 (C2, ArC−), 169.8 (C═O). The ^{1}H NMR and ^{13}C NMR were consistent with that reported in the literature.[28]

*5.1.1.15. tert-Butyl Dodecanoate (**16**).*[29] It was obtained as colorless oil; yield (47%, 0.061 g); R_f (5% ethylacetate/hexane): 0.70.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.9 Hz, 3H, C12H, CH_3), 1.26 (br s, 16H, C4H, C5H, C6H, C7H, C8H, C9H, C10H, C11H, CH_2), 1.50 (s, 9H, C2′H, CH_3), 1.52−1.63 (m, 2H, C3H, CH_2), 2.20 (t, J = 7.5 Hz, 2H, C2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C12, CH_3), 22.7 (C3, CH_2), 25.1 (C10, CH_2), 28.1 (C2′, $-C(\underline{C}H_3)_3$), 29.1, 29.3, 29.3, 29.5, 29.6, 31.9 (C4, C5, C6, C7, C8, C10, C11, CH_2), 35.6 (C2, CH_2), 79.8 (C1′, $-\underline{C}(CH_3)_3$), 173.3 (C═O).

*5.1.1.16. tert-Butyl Oleate (**17**).* It was obtained as colorless oil; yield (35%, 0.042 g); R_f (2% ethylacetate/hexane): 0.50.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3H, C18H), 1.22−1.36 (m, 20H, C4H, C5H, C6H, C7H, C12H, C13H, C14H, C15H, C16H, C17H), 1.44 (s, 9H, C2′H, CH_3), 1.52−1.62 (m, 2H, C3H, CH_2), 2.07−1.89 (m, 4H, C8H, C11H), 2.20 (t, J = 7.5 Hz, 2H, C2H, CH_2), 5.28−5.40 (m, 2H, C10H, HC═CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C18, CH_3), 22.7 (C17, CH_2), 25.1 (C3, CH_2), 27.18, 27.22 (C8, C11, CH_2), 28.1 (C2′, CH_3), 29.1, 29.1, 29.2, 29.3, 29.5, 29.7, 29.7, 31.9 (C4, C5, C6, C7, C12, C13, C14, C15, C16, CH_2), 35.6 (C2, $\underline{C}H_2$−CO), 79.9, 129.8 (C1′, CH_3), 129.9 (C9, C10), 173.3 (C═O). The ^{1}H NMR and ^{13}C NMR were consistent with that reported in the literature.[30]

*5.1.1.17. tert-Butyl Cinnamate (**18**).* It was obtained as colorless oil; yield (58%, 0.04 g); R_f (5% ethylacetate/hexane): 0.50.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 9H, C2″H, CH_3), 6.37 (d, J = 16.0 Hz, 1H, C2H, ═CH), 7.33−7.43 (m, 3H, ArH, C3′H, C4′H, C5′H), 7.51 (dd, J = 6.5, 3.1 Hz, 2H, ArH, C2′H, C6′H), 7.59 (d, J = 16.0 Hz, 1H, C3H, HC═). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.2 (C2″, $\underline{C}H_3$), 80.5 (C1″), 120.2 (C2, ═$\underline{C}$H−CO), 128.0 (C1′, ArC), 128.8 (C2′, C6′, ArCH), 130.0 (C3′, C5′, ArCH), 134.7 (C4′, ArCH), 143.6 (C3, ═$\underline{C}$H−C), 166.4 (CO). The ^{1}H NMR and ^{13}C NMR were consistent with that reported in the literature.[31]

*5.1.1.18. tert-Butyl N^2-(((9H-Fluoren-9-yl)methoxy)carbonyl)-N^6-(tert-butoxycarbonyl)-L-lysinate (**19**).* It was obtained as white solid; yield (89%, 0.1 g); R_f (20% ethylacetate/hexane): 0.4.

IR (neat, cm^{-1}) ν: 3311 (s), 3042 (s), 2979 (s), 1686 (s), 1534 (m), 1451 (m), 1271.9 (m), 1154 (m), 744 (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H, $-C(CH_3)_3$, Boc), 1.47 (s, 9H, $-C(CH_3)_3$, COO^{t}Bu), 1.52−1.94 (m, 4H, CH_2), 3.11 (d, J = 5.8 Hz, 2H, CH_2), 4.15−4.30 (m, 2H, CH), 4.34−4.45 (m, 2H, CH_2O), 4.56 (s, 1H, NH), 5.38 (d, J = 7.6 Hz, 1H, NH), 7.32 (td, J = 7.4, 1.0 Hz, 2H, ArH), 7.40 (t, J = 7.5 Hz, 2H, ArH), 7.61 (d, J = 7.4 Hz, 2H, ArH), 7.76 (d, J = 7.5 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3 (CH_2), 28.0 (CH_3), 28.4 (CH_3), 29.6 (CH_2), 32.4 (CH_2), 40.2 (CH_2), 47.2 (CH), 54.2 (CH), 66.9 (CH_2), 79.1 ($-\underline{C}(CH_3)_3$), 82.1 ($-\underline{C}(CH_3)_3$), 120.0 (ArCH), 125.1 (ArCH), 127.0 (ArCH), 128.0 (ArCH), 141.3 (ArC═), 143.8 (ArC═), 144.0 (ArC═), 156.0 (C═O), 156.0 (C═O), 171.6 ($\underline{C}$OO^{t}Bu). ESI-MS: calcd for $C_{30}H_{41}N_2O_6^+$, 525.29; found, 525.30 $[M + H]^+$. The ^{1}H NMR was consistent with that reported in the literature.[32]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c02516.

> Spectral data for compounds **2−19** including IR, ^{1}H NMR, ^{13}C NMR, DEPT-135, MS (ESI), HSQC, COSY, and comparison list for spectral data with the literature (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Deepak B. Salunke − *Department of Chemistry and Centre for Advanced Studies in Chemistry and National Interdisciplinary Centre of Vaccines, Immunotherapeutics and Antimicrobials, Panjab University, Chandigarh 160014, India;* orcid.org/0000-0002-1241-9146; Email: salunke@pu.ac.in

Authors

Arshpreet Kaur − *Department of Chemistry and Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh 160014, India*

Arshdeep Pannu − *Department of Chemistry and Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh 160014, India*

Deshkanwar S. Brar − *Department of Chemistry and Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh 160014, India*

Surinder K. Mehta − *Department of Chemistry and Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh 160014, India;* orcid.org/0000-0002-1623-7745

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.0c02516

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

D.B.S. is thankful to DBT New Delhi for the award of Ramalingaswami Fellowship (BT/RLF/Re-entry/16/2013). The support from UGC-CAS and Panjab University Development fund is gratefully acknowledged. A.K. is thankful to UGC, New Delhi, for the award of Junior and Senior Research Fellowships.

■ REFERENCES

(1) Sartori, G.; Maggi, R. Update 1 of: Protection (and Deprotection) of Functional Groups in Organic Synthesis by Heterogeneous Catalysis. *Chem. Rev.* **2010**, *110*, PR1−PR54.

(2) Bisel, P.; Al-Momani, L.; Müller, M. The *tert*-butyl group in Chemistry and Biology. *Org. Biomol. Chem.* **2008**, *6*, 2655−2665.

(3) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. Tert-Butyl Ethers: Renaissance of an Alcohol Protecting Group. Facile Cleavage with Cerium(III) Chloride/Sodium Iodide. *Adv. Synth. Catal.* **2006**, *348*, 905−910.

(4) (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999; pp 1−65. (b) Holcombe, J. L.; Livinghouse, T. A New and Specific Method for the Protection of Phenols as the Corresponding *tert*-Butyl Ethers. *J. Org. Chem.* **1986**, *51*, 111−113.

(5) Bartoli, G.; Bosco, M.; Carlone, A.; Dalpozzo, R.; Locatelli, M.; Melchiorre, P.; Sambri, L. Alcohols and Di-*tert*-butyl Dicarbonate: How the Nature of the Lewis Acid Catalyst May Address the reaction