Complimentary and personal copy



SYNFACTS Highlights in Current Synthetic Organic Chemistry

This electronic reprint is provided for noncommercial and personal use only: this reprint may be forwarded to individual colleagues or may be used on the author's homepage. This reprint is not provided for distribution in repositories, including social and scientific networks and platforms.

Publishing House and Copyright: © 2015 by Georg Thieme Verlag KG Rüdigerstraße 14 70469 Stuttgart ISSN 1861-1958

Any further use only by permission of the Publishing House



www.thieme.com

S. TONG, Q. WANG, M.-X. WANG, J. ZHU* (ÉCOLE POLYTECHNIQUE FEDERALE DE LAUSANNE, SWITZERLAND AND TSINGHUA UNIVERSITY, BEIJING, P. R. OF CHINA) Tuning the Reactivity of Isocyano Group: Synthesis of Imidazoles and Imidazoliums from Propargylamines and Isonitriles in the Presence of Multiple Catalysts *Angew. Chem. Int. Ed.* **2015**, *54*, 1293–1297.

Imidazoles and Imidazoliums from Propargylamines and Isonitriles



Significance: Reported is a multicatalytic methodology for the synthesis of 1,4,5-trisubstituted imidazoles 3 from the reaction of isonitriles 1 with propargylamines 2 in the presence of catalytic amounts of Yb(OTf)₃ and AgOTf. The same reaction of 2 with the primary, secondary, and aryl isonitriles 1 in the presence of Yb(OTf)₃, AgOTf, and KOTf affords 1,3,4,5-tetrasubstituted imidazoliums 4 in good to excellent yields. Compounds 1 and 2, with bulky alkyl groups and with aryl groups with different electronic properties, including heterocycles, were found to be well tolerated and led to various substituted imidazoles and imidazoliums. In addition, chiral propargylamines 2 were converted into enantioenriched imidazoles without racemization. Imidazole 3a was elaborated into the polycyclic compound 6.

Comment: Imidazoles 3 and imidazolium salts 4 are important classes of heterocycles which are widely used in pharmaceuticals and organic synthesis (see Review below). The reported method involves a one-pot substrate-specific multiple metal salt catalytic route to a wide range of multisubstituted 3 and 4. The synthesis of a bioactive compound, 1-benzyl-5,6-dihydro-imidazo[5,1-a]isoquinoline (7), by the developed method is reported. A possible mechanism is proposed based on the quantitative isolation and identification of the intermediate 5 and X-ray crystal analysis of 3 $(R^1 = R^2 = Ph; R^3 = Bn)$ and **6**. Intramolecular nucleophilic addition of the amidine nitrogen atom in 5 to the silver-coordinated triple bond through a 5-exo-dig cyclization to 3 is proposed. Further investigation of the reaction mechanism and applications of this methodology are encouraged.

SYNFACTS Contributors: Victor Snieckus, M. A. Jalil Miah Synfacts 2015, 11(4), 0359 Published online: 18.03.2015 DOI: 10.1055/s-0034-1380365; Reg-No.: V02015SF

 Review:
 P. K. Maji, R. U. Islam, S. K. Bera Heterocycles 2014, 89, 869–962.

Category

Synthesis of Heterocycles

Key words

propargylamines isonitriles ytterbium triflate silver triflate cyclization imidazoles

imidazoliums