Tetrahedron Letters xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Iodine catalyzed solvent-free cross-dehydrogenative coupling of arylamines and H-phosphonates for the synthesis of N-arylphosphoramidates under atmospheric conditions

Bashir Ahmad Dar [a], Nisar A. Dangroo [a,b], Amit Gupta [a], Aarti Wali [a], Mohammad Akbar Khuroo [b], Ram A. Vishwakarma [a,*], Baldev Singh [a,*]

[a] Indian Institute of Integrative Medicine (CSIR), Canal Road, Jammu 180001, India
[b] Department of Chemistry, University of Kashmir, Hazratbal, Srinigar 190006, India

ARTICLE INFO

Article history:
Received 2 December 2013
Revised 13 January 2014
Accepted 15 January 2014
Available online xxxx

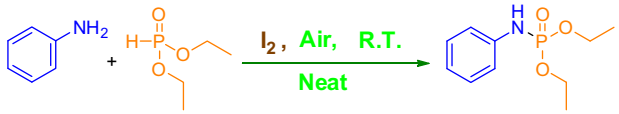
Keywords:
Phosphoramidates
Molecular iodine
Anilines
Neat conditions
Room temperature

ABSTRACT

Aerobic oxidative coupling of various arylamines and H-phosphonates to the corresponding N-arylphosphoramidates has been achieved under solvent-free conditions using molecular iodine. This protocol works at room temperature furnishing the corresponding P–N coupling products in moderate to high yields.

© 2014 Published by Elsevier Ltd.

Phosphoramidates are present as structural motifs in a number of biologically active natural products like agrocin 84,[1] phosmidosine,[2] and microcin C7.[3] Bioactive compounds like N-phosphoryl peptides, N-phosphoryl amino acids, and phosphoramidate substituted nucleosides also contain phosphoramidate functional groups as a key structural unit.[4] Phosphoramidates are used in industry as pharmaceutical prodrugs.[5] Several aryloxy triester phosphoramidates (GS-9140, GS-9131, thymectacin (NB1011), and stampidine) are in clinical trials.[6] In the domain of medicinal chemistry, phosphonamidates have been used as surrogates for amide bonds in the synthesis of pharmaceutically active peptide-based protease inhibitors since the P(=O)—NH moiety mimics the tetrahedral transition state during amide bond hydrolysis.[7] Phosphoramidates are also used as flame retardants[8] and are being used in analytical chemistry to improve ionization efficiency and suppress matrix-related ion effects in MALDI-TOF mass spectrometry.[9] N-arylphosphoramidates have also been employed for the synthesis of azetidines,[10] aziridines,[11] imines[12] and various heterocycles such as quinazolinediones.[13] As a consequence of their broad range applications, a plethora of methods have been developed for phosphoramidate synthesis. The two most common standard procedures used extensively for the synthesis of phosphoramidates are (i) reactions of amines with dibenzyl or dialkyl phosphites using CCl_4 or a better activating agent[14] and (ii) reaction of amines with phosphorodichloridates or phosphorochloridates using a base.[4b,15] Other methods include the oxidation of phosphite triesters with I_2 in the presence of alkylamines and the reduction of nitroarenes with triethyl phophite followed by phosphorylation with triethyl phosphite.[16] These procedures are all based on the prefunctionalization–defunctionalization strategy. Consequently these procedures use additional active agents or produce undesired by-products. Preparation and handling of hazardous phosphoryl halides, stoichiometric use of CCl_4, use of excess base and long reaction time present an obvious limitation. The Staudinger-phosphite reaction offers one alternative for phosphoramidate synthesis,[17] but this method is not ideal as it relies on the preparation and use of organic azides. More recently Cu(I) salts like CuBr[18] and CuI[19] have successfully been employed for oxidative coupling of amines and H-phosphonates to generate phosphoramidates.



Scheme 1.

* Corresponding authors. Tel.: +91 (0191) 2572002; fax: +91 (0191) 2548607.
E-mail address: drbaldev1@gmail.com (B. Singh).

0040-4039/$ - see front matter © 2014 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.tetlet.2014.01.064