Concise Report

Cross-coupling, Synthetic methods, *t*BuXPhos, Ketoxime ethers, Chalcone oxime ethers

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An Easy Access to Oxime Ethers by Pd-Catalyzed C—O Cross-Coupling of Activated Aryl Bromides with Ketoximes and Chalcone Oximes

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Summary of main observation and conclusion An efficient Pd-catalyzed method for C—O cross-coupling of ketoximes and chalcone oximes with activated aryl bromides and bromo-chalcones has been developed. All oxime ethers were obtained in good to excellent yields by [(π-allyl)PdCl]$_2$/*t*BuXPhos (**L7**) catalyst system. TrixiePhos (**L11**) was also found to be effective for the oxime coupling. This method offers an easy and smooth coupling of chalcone oximes with activated aryl bromides and bromo-chalcones, which has not been previously explored.

Background and Originality Content

Oxime ethers are one of the most important structural motifs in organic chemistry, which continue to beguile the chemists' interest thanks to their pharmaceutical and agricultural applications.[1] Examples concerning the biological importance of oxime ethers (Figure 1) are as potent inhibitors of transthyretin amyloid fibril formation,[1a] antibiotic (Cefmenoxime,[1b] Aztreonam,[1c] Roxithromycin),[1d] anti-inflammatory (Ridogrel),[1e] antifungal (Oxiconazole),[1f] neuroleptic activity,[1g] immunosuppressive agents,[1h] antihistamine (**1a**),[1i] therapeutic agent for insomnia (Eplivanserin) (**1b**),[1j,k] melanin-concentrating hormone1 receptor antagonists (**1c**),[1l] antiplasmodial property,[1m] monamine oxidase and Acethylcholinesterase inhibitors (**1d**),[1n] insecticidal,[1o] fungicidal,[1p,q] herbicidal,[1r] *etc*. Moreover, oxime ethers are served as important and versatile intermediates in the synthesis of various structural motifs.[2] The *O*-aryl oxime ethers have been paid much attention due to their accessibility to a myriad of medicinally and synthetically important organic compounds,[2] such as benzoxazole,[3a-c] dihydrobenzofuran,[3d,e] benzofurans,[3e-j,p] phenols,[3k,l] quinolines,[3m] 3-aminobenzisoxazoles,[3n] pyrroles,[3o] *etc*.

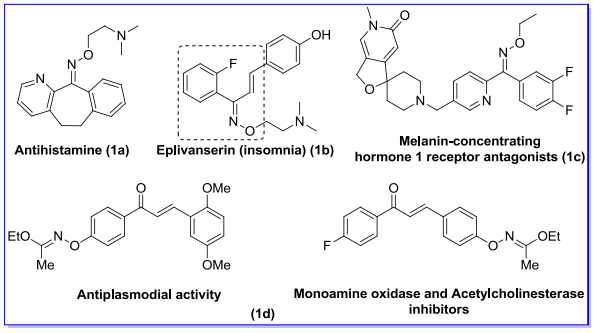
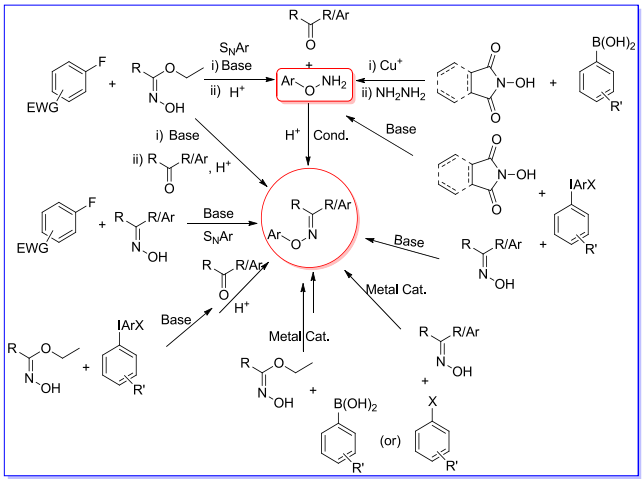


Figure 1 Examples of pharmaceutical molecules containing oxime ethers structural motif.

Moreover, *O*-aryl oxime ethers could also be used as a ligand in Pd-catalyzed Suzuki-Miyaura coupling reaction to synthesize biaryls.[4] Conventionally, the syntheses of *O*-aryl oxime ethers were achieved by i) condensation of *O*-aryloxyamines with carbonyl compounds,[1a,3e,f,5] and ii) *O*-arylation of oximes with activated nitro- or fluoroarene derivatives in the presence of a strong base *via* S_NAr type process.[1a,3e,5a,6]

The *O*-aryloxyamines could be obtained from an amine exchange reaction of 2,4-dinitrophenoxyamine with phenols[3f,7] and *O*-arylation of ethyl acetohyroxamate,[1a,5d,8] or *N*-protected hydroxylamine[9] by S_NAr type process, and subsequent hydrolysis with acid (Scheme 1).

Scheme 1 Previous synthetic routes to oxime ethers



Other methods describing the synthesis of alkoxy and aryloxyamines are the oxyaziridines as an aminating agent for a wide range of alcohols as nucleophile.[10]

In the recent past, several other improved methods for the synthesis of *O*-aryloxyamines developed are i) copper-catalyzed coupling of phenylboronic acids with *N*-hydroxyphthalimide,[11] ii) base promoted *O*-arylation of *N*-hydroxyphthalimide and *N*-hydroxysuccinimide with diaryliodonium salts[12] and subsequent cleavage with hydrazine, hydroxylamine or ammonia, and iii) *O*-arylation of ethyl acetohydroxamate or oximes either with aryl

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