An efficient synthesis of *O*-aryloxime ethers by copper fluorapatite catalyzed cross-coupling of aryloximes with arylboronic acids

Shafeek A.R. Mulla, Santosh S. Chavan, Suleman M. Inamdar, Mohsinkhan Y. Pathan, Taufeekaslam M.Y. Shaikh

PII: S0040-4039(14)01220-9
DOI: http://dx.doi.org/10.1016/j.tetlet.2014.07.056
Reference: TETL 44899

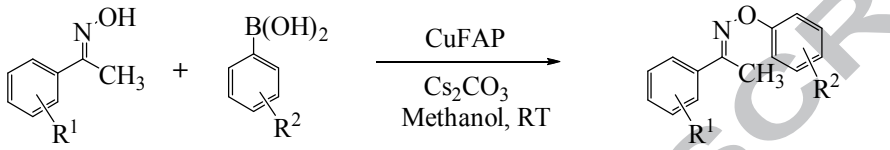
To appear in: *Tetrahedron Letters*

Received Date: 28 May 2014
Revised Date: 16 July 2014
Accepted Date: 16 July 2014

Please cite this article as: Mulla, S.A.R., Chavan, S.S., Inamdar, S.M., Pathan, M.Y., Shaikh, T.M.Y., An efficient synthesis of *O*-aryloxime ethers by copper fluorapatite catalyzed cross-coupling of aryloximes with arylboronic acids, *Tetrahedron Letters* (2014), doi: http://dx.doi.org/10.1016/j.tetlet.2014.07.056

An efficient synthesis of *O*-aryloxime ethers by copper fluorapatite catalyzed cross-coupling of aryloximes with arylboronic acids

Shafeek A. R. Mulla[a]*, Santosh S. Chavan[a], Suleman M. Inamdar, Mohsinkhan Y. Pathan, Taufeekaslam M. Y. Shaikh[a]



R^1= H, isobutyl,$PhCH_2O$, Me, OMe, NO_2, Halogen, etc

R^2=Me, OMe, CHO, CF_3, etc

An efficient synthesis of *O*-aryloxime ethers by copper fluorapatite catalyzed cross-coupling of aryloximes with arylboronic acids

Shafeek A. R. Mulla[a]*, Santosh S. Chavan[a], Suleman M. Inamdar, Mohsinkhan Y. Pathan, Taufeekaslam M. Y. Shaikh[a]

[a]*Academy of Scientific & Innovative Research (AcSIR)*

Chemical Engineering and Process Development Division, National Chemical Laboratory, Pashan Road, Pune 411 008, INDIA

*Corresponding author.Tel: +91-20-25902316; Fax: +91-20-25902676; e-mail: sa.mulla@ncl.res.in

Abstract: A novel, highly efficient and mild protocol has been developed for the synthesis of *O*-aryloxime ethers in good to excellent yield at ambient reaction conditions. This is the first report in which =N-O-Ar linkage was achieved with ecofriendly, recyclable, heterogeneous copper fluorapatite (CuFAP) catalyst via C-O cross coupling of aryloxime with aryboronic acid in the presence of Cs_2CO_3 as base and methanol as solvent.

Keywords: Copper fluorapatite, *O*-aryl oxime ethers, Aryl boronic acid, Aryl oxime.

The *O*-aryloxime ethers are not only core structural constituents of a variety of natural products, pharmaceuticals, agricultural chemicals and molecular drug design,[1] but also an important and/ or precious precursors for the synthesis of various motifs such as benzooxazole,[2] benzofurans/dihydrobenzofuran,[3] pyrrolidines, piperidines, indolizidine alkaloids,[4] chiral primary amines,[5] substituted pyrroles,[6] trisubstituted isoxazoles,[7] amino acids,[8,5b] *cis*-1,2-amino alcohols,[9,5b] fluorenones[10] and so on. These synthesized motifs show wide range of biological activities such as inhibitors of protein chaperone Hsp 90,[11a] monoamine oxidase,[11b] cytokinin-like,[11c] neuroleptic,[11d] and anticholinesterase.[11e] However, 1,2-oxazines and 6-aryl-3,6-dihydro-1,2-oxazines are NO-prodrugs,[11f] and

mGluR1 receptor antagonists,[11g] respectively. Recently, bisaryloxime ethers were found to be potent inhibitors of transthyraten amyloid fibril formation.[12]

Owing to potential and/or wider application of *O*-aryloxime ethers in life sciences, pharmaceuticals, agricultural chemicals as well as in bioorganic chemistry, researchers have aspired to develop various methods of their synthesis by reacting oximes and/ or sodium salt of an oxime with alkenes,[13] alkyl or aryl halides,[14] aryl nitrates,[15a] allylic sp^3 C-H bonds,[15b] or esters,[15c] alcohols,[16] methyl sulfate,[17a] activated olefins,[17b] fluorobenzene derivatives,[17c] nitro- or fluoroarene derivatives,[14b] aryl nitrates,[18a] diazonium salts[18b] etc. Moreover, the *O*-aryloxime ethers are synthesized conventionally by condensation reaction of commercially available carbonyl compounds with *O*-aryloxyamines,[19] which must be prepared prior to its use. Due to arylboronic acid motifs being stable and non-toxic compared to aryl halide, its use to introduce the phenyl ring in various biologically active compounds,[20] as well as copper catalyzed cross-coupling of C-N and C-O bond forming reactions with –NH and/ or -OH functional group containing various substrates were well documented.[21] To the best of our knowledge so far only four research groups, Meyer *et al*,[22a] Huang *et al*,[22b] Bora *et al*,[22c] and Cai *et al*,[22d] have reported the synthesis of *O*-aryloxime ether via cross coupling of aryloxime with arylboronic acid over $Cu(OAc)_2$ and polymer-supported copper complex. However, all these methods reported so far by reacting oxime with various substrates[13-19] and/ or arylboronic acid[22a-d] for the synthesis of *O*-aryloxime ethers lack general applicability along with one/or other limitations and drawbacks such as use of expensive aryl or alky halides, ligands, chlorinated solvents, high concentration of base, oxidants, moisture-free

atmosphere, high temperature, and long reaction time resulting in the formation of many side products, hence lower yield to desired product.

As *O*-aryloxime ethers motifs are key constituents of structural backbone of many pharmaceutical compounds, the construction of its structural unit by developing more general and cost effective protocol using non-toxic, cheap, commercially available substrates, environmentally benign solvents, cost effective recyclable catalysts at milder reaction condition is still challenging and an active research area. As we were inspired from our research work for the synthesis of diaryl ether over CuFAP catalyst,[23a-b] herein, we further investigated an application of CuFAP catalyst and we present the first report to achieve =N-O-Ar linkage using heterogeneous copper fluoroapatite CuFAP catalyst for an efficient synthesis of *O*-aryloxime ethers via C-O cross coupling of aryloxime with aryboronic acid in the presence of Cs_2CO_3 as base and methanol as solvent at ambient reaction conditions (Scheme 1).

To develop the protocol for the synthesis of *O*-aryloxime ethers via cross coupling reaction, acetophenone oxime (1 mmol) and phenyl boronic acid (1.5 mmol) was initially treated with CuFAP (100 mg) catalyst in the presence of Cs_2CO_3 as base in methanol solvent under ambient conditions to give 90 % yields to *O*-aryloxime ethers (Table 1 entry 1). Initially, the C-O cross coupling reaction was screened in various solvents such as methanol, ethanol, dimethyl sulfoxide, dimethylformamide, toluene, tetrahydrofuran, acetonitrile, dichloromethane, and dichloroethane. However, methanol gave the cross-coupling product in high yield (Table 1, entry 1) as compared to other solvents (Table 1, entries 2 and 6). The formation of desired coupling product was not observed using dimethyl sulfoxide, dimethylformamide, toluene, acetonitrile, dichloromethane, and

dichloroethane as solvents (Table 1, entries 3-5 and 7-9). After the promising results in methanol as a solvent, studies were undertaken to investigate the influence of various bases/catalyst loading on the C-O cross coupling reaction. The Cs_2CO_3 shows excellent performance as base to achieve desired product in high yield (Table 2 entry 3) as compared to Na_2CO_3, K_2CO_3, and NaOH (Table 2, entries 1-2 and 4). However, the organic bases such as diisopropylethylamine, pyridine, and triethylamine (Table 2, entries 5-6) were ineffective to form the desired product. Influence of catalyst loading was investigated, by lowering the catalyst loading from 100 mg to 75 mg and 50 mg, resulting in a drastic decrease in the yield from 90% to 73% and 39%, respectively, (Table 2, entries 7, 8).

The excellent results on the optimized reaction conditions using Cs_2CO_3 base in methanol over the CuFAP catalyst encouraged us to investigate the scope of this protocol by coupling the wide range of substituted aryl oxime with substituted aryl boronic acid as coupling partner for the synthesis of *O*-aryloxime ethers. The various substituted aryl oximes possessing a variety of an electron donating and/ or electron withdrawing functional groups reacted smoothly with various substituted phenyl boronic acid under ambient reaction conditions to get various *O*-aryloxime ethers as desired products in good to excellent yield (Table 3, entries 2-31). However, the formation of desired product was not observed under the same reaction condition in the presence of CuFAP catalyst without base and vice versa (Table 3, entry 1). The electron-rich acetophenone oximes such as 4-methoxyacetophenone oxime, 4-methylacetophenone oxime, 4-isobutylacetophenone oxime, and 4-benzyloxyacetophenone oxime coupled successfully with phenyl boronic acid providing the corresponding cross coupling products in good

(83-88%) yield (Table 3, entries 3-6) and the electron-deficient acetophenone oximes such as 4-nitroacetophenone oxime, and 4-fluoroacetophenone oxime provided the corresponding cross coupling products in excellent (95%) yield (Table 3, entry 7, 8).

To widen the scope of this protocol a variety of substituted phenyl boronic acid with electron donating/ electron withdrawing group such as 2-methoxy phenyl boronic acid, 2,3,4-trimethoxyphenylboronic acid, 4-carboxyl phenyl boronic acid, (4-methoxy-3,5-dimethylphenyl)boronic acid, (3,5-bis(trifluoromethyl)phenyl)boronic acid were coupled smoothly without any problem with acetophenone oxime/substituted acetophenone oxime having electron donating/ electron withdrawing group such as 4-methyl acetophenone oxime, 4-methoxy acetophenone oxime, 4-isobutyl acetophenone oxime, 3-nitro acetophenone oxime, 4-nitro acetophenone oxime, 2-bromo acetophenone oxime 4-bromo acetophenone oxime, 4-fluoro acetophenone oxime, 4-phenyl ether acetophenone oxime. These reactions furnished desired cross coupling products in good to excellent (76-96%) yield (Table 3 entries 9-29). Surprisingly, diverse coupling partners with electron rich and deficient centre (Table 3, entries 5, 11-13, 16, 19, 20, 24,25, 27, 28) coupled smoothly to achieve desired product via =N-O-Ar linkage in presence of CuFAP catalyst. The promising results on diverse coupling partners prompted us to investigate the feasibility of this protocol to hetrocyclic boronic acids. Accordingly, benzothiophene-2-boronic acid and thiophene-2-boronic acid coupled smoothly with acetophenone oxime under our optimized reaction conditions and delivered the desired cross coupling products in moderate to good yield in 24 h (Table 3, entry 30, 31). The results in Table 3 indicate that a wide range of aryloximes and arylboronic acids were compatible to achieve =N-O-Ar linkage over ecofriendly, recyclable, heterogeneous copper fluorapatite

(CuFAP) catalyst for an efficient synthesis of *O*-aryloxime ethers via cross coupling of aryloxime with aryboronic acid in the presence of Cs_2CO_3 as base and methanol as solvent at ambient temperature. However, the yields obtained are dependent on the nature of substituents on the aryl oxime as well as on the aryl boronic acids.

According to our and the previous research work on O-arylation[22b,23a,b] and N-arylation,[24] respectively, a possible mechanism is proposed in Scheme 2. The plausible mechanism for cross coupling reaction may involve the coordination of acetophenone oxime with CuFAP catalyst that proceeds via formation of the Cu(II) complex **I**. Subsequent reaction of complex **I** with phenyl boronic acid formed Cu(II) complex **(II)** followed by instantaneous formation of linkage =N-O-Ar to release the *O*-aryloxime ethers product **(III)** as well as CuFAP catalyst to recycle.

The recyclability of CuFAP catalyst for an efficient synthesis of O-aryl oxime ether via C-O cross coupling reaction was studied using acetophenone oxime and phenyl boronic acid in the presence of Cs_2CO_3 as base and methanol as solvent at ambient reaction condition, the results are shown in Table 4. The catalyst was recovered quantitatively by filtration and reused several times without loss of catalytic activity (Table 4).

In conclusion, a highly efficient, cost effective, general and milder protocol has been developed for the synthesis of *O*-aryloxime ethers in good to excellent yield via C-O cross coupling reactions of a wide range of substituted aryl oximes with substituted aryl boronic acids using inexpensive, ecofriendly, heterogeneous, reusable copper fluorapatite (CuFAP) catalyst in the presence of Cs_2CO_3 as base, in methanol solvent at ambient reaction conditions. This may be a practical approach for the synthesis of various natural

products, pharmaceuticals, agricultural chemicals motifs containing *O*-aryloxime ethers units.

Acknowledgements

SSC, SMI, MYP and TMYS thank CSIR and UGC New Delhi for SRF and JRF. The authors also thank to Dr. V. V. Ranade, Chair, CE-PD for their encouragement and support.

References and notes:

1. (a) Cozzi, P.; Carganico, G.; Fusar, D.; Grossoni, M.; Menichincheri, M.; Pinciroli, V.; Tanani, R.; Vaghi, F.; Salvati, P. *J. Med. Chem.* **1993**, *36*, 2964.; (b) Huang, J. X.; Jia, Y. M.; Liang, X. M.; Zhu, W. J.; Zhang, J. J.; Dong, Y. H; Yuan, H. Z.; Qi, S. H.; Wu, J. P.; Chen, F. H.; Wang, D. Q. *J. Agric, Food Chem.* **2007**, *55*, 10857; (c) Tu, S.; Xu, L. H.; Ye, L. Y.; Wang, X.; Sha, Y.; Xiao, Z. Y. *J. Agric. Food Chem.* **2008**, *56*, 5247; (d) Sun, R.; Lv, M.; Chen, L.; Li, Q.; Song, H.; Bi, F.; Huang, R. *J. Agric. Food Chem.* **2008**, *56*, 11376; (e) Bhandari, K.; Srinivas, N.; Keshava, G. B. S.; Shukla, P. K. *Eur. J. Med. Chem.* **2009**, *44*, 437; (f) Johnson, S. M.; Petrassi, H. M.; Palaninathan, S. K.; Mohamed mohaideen, N. N.; Purkey, H. E.; Nichols, C.; Chiang, K. P.; Walkup, T. Sacchettini, J. C.; Sharpless, K. B.; Kelly, J. W. *J. Med. Chem*. **2005**, *48*, 1576; (g) Karakurt, A.; Dalkara, S.; Ozalp, M.; Ozbey, S.; Kendi, E.; Stables, J. P. *Eur. J. Med. Chem*. **2001**, *36*, 421.

2. (a) Shutske, G. M. *J. Org. Chem.* **1984**, *49*, 180; (b) Shutske, G. M.; Kapples, K. J. *J. Heterocyclic Chem.* **1984**, *49*, 180.

3. (a) Sheradsky, T. *Tetrahedron Lett*. **1966**, *43*, 5225; (b) Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 4399.

4. Miyata, O.; Takahashi, S.; Tamura, A.; Ueda M.; Naito, T. *Tetrahedron.* **2008**, *64*, 1270.

5. (a) Huang, X.; Marciales, M. O.; Huang, K.; Stepanenko, V.; Merced, F. G.; Ayala, A. M.; Correa, W.; De Jesús, M. *Org. Lett.* **2007**, *9*, 1793-1795; (b) Moody, C. J. *Chem. Commun.* **2004**, 1341-1351.

6. Wang, H.-Y.; Mueller, D. S.; Sachwani, R. M.; Londino, H. N.; Anderson, L. L. *Org. Lett.* **2010**, *12*, 2290-2293.

7. Ueda, M.; Sato, A.; Ikeda, Y.; Miyoshi, T.; Naito, T.; Miyata, O. *Org. Lett.* **2010**, *12*, 2594-2597.

8. Miyabe, H.; Fujii, K.; Naito, T. *Org. Lett.* **1999**, *1*, 569-572.

9. Ghosh, A. K.; Mckee, S. P.; Sanders, W. M. *Tetrahedron Lett.* **1991**, *32*, 711-714.

10. Thirunavukkarasu, V. S.; Parthasarathy, K.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2008**, *47*, 9462-9465.

11. (a) Mailliet, P.; Ruxer, J. M.; Thompson, F.; Luc, C. C. New 3-aryl- 1,2-benzisoxazole derivatives, compositions containing them and their use for treating cancer. French Patent FR 288236, August 25, 2006; (b) Yoshimi, K.; Kozuka, M.; Sakai, J.; Lizawa, T.; Shimizu, Y.; Kaniko, I.; Kojima, K.; Iwata, N. *Jpn. J. Pharmacol.* **2002**, *88*, 174; (c) Ricci, A.; Carra, A.; Torelli, A.; Maggiali, C. A.; Vicini, P.; Zani, F.; Branca, C. *Plant Growth Regul.* **2001**, *34*, 167; (d) Strupczewski, J. T.; Allen, R. C.; Gardner, B. A.; Schmid, B. L.; Stache, U.; Glamkowski, E. J.; Jones, M. C.; Ellis, D. B.; Huger, F. P.; Dunn, R. W. *J. Med. Chem.* **1985**, *28*, 761; (e) Yu, Q-s; Zhu, X.; Holloway, H. W.; Whittaker, N. F.; Brossi, A.; Greig, N. H. *J. Med. Chem.* **2002**, *45*, 3684; (f) Chakrapani, H.; Toone, E. J. *Abstracts of Papers*. 230th ACS National Meeting; Washington, DC, Aug 28-Sept 1, 2005; American Chemical Society: Washington, DC, 2005; MED-414; (g) Clark, B. P.; Harris, J.; Richard; K.; Ann, E. Preparation of 6-aryl-3,6-dihydro-1,2-oxazines as mGluR1 receptor antagonists. UK Patent WO 2000026199, May 11, 2000.

12. (a) Johnson, S. M.; Petrassi, H. M.; Palaninathan, S. K.; Mohamedmohaideen, N. N.; Purkey, H. E.; Nichols, C.; Chiang, K. P.; Walkup, T.; Sacchettini, J. C.; Sharpless, K. B. and Kelly, J. W. *J. Med. Chem.* **2005**, *48*, 1576. (b) Blake, J. A.; Pratt, D. A; Lin, S.; Walton, J. C.; Mulder, P.; Ingold, K. U. *J. Org. Chem.* **2004**, *69*, 3112.

13. (a) Meshram, H. M.; Eeshwaraiah, B.; Sreenivas, M.; Aravind, D.; Sundar, B. S.; Yadav, J. S. *Synth. Commun.* **2009**, *39*, 1857–1863.

14. (a) De, P. Nonappa; Pandurangan, K.; Maitra, U.; Wailes, S. *Org. Lett.* **2007**, *9*, 2767-2770; (b) Mooradian, A.; Dupont, P. E. *J. Heterocycl. Chem.* **1967**, *4*, 441-444; (c) Jia, X.; Wang, X.; Yang, C.; Da, Y.; Yang, L.; Liu, Z. *Tetrahedron* **2009**, *65*, 2334-2338; (d) Abele, E.; Abele, R.; Rubina, K.; Popelis, J.; Sleiksa, I.; Lukevics, E. *Synth. Commun.* **1998**, *28*, 2621-2633; (e) Yamada, T.; Goto, K.; Mitsuda, Y.; Tsuji, J. *Tetrahedron Lett.* **1987**, *28*, 4557-4560; (f) Merkas, S.; Litvic, M.; Cepanec, I.; Vinkovic, V. *Molecules* **2005**, *10*, 1429-1437; (g) Banerjee, T.; Dureja, P. *Molecules* **2005**, *10*, 990–

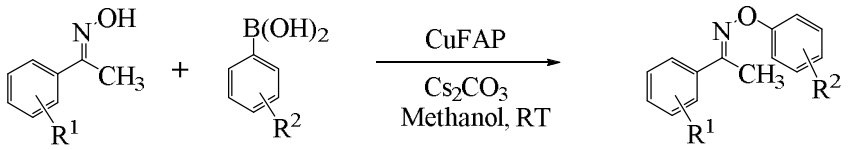
999; (h) Kubmarawa, D.; Barminas, J. T.; Aliyu, A. O. C. Archives of Applied Science Research **2011**, *3*, 126-130.

15. (a) Baumann, J. B. *Synthesis* **1975**, 782; (b) Jin, J.; Li, Y.; Wang, Z.-J.; Qian, W.-X.; Bao, W.-L. Eur. *J. Org. Chem.* **2010**, 1235–1238; (c) Miyabe, H.; Yoshida, K.; Reddy, V. K.; Matsumura, A.; Takemoto, Y. *J. Org. Chem*. **2005**, *70*, 5630–5635.
16. (a) Bittner, S.; Grinberg, S. J. Chem. Soc., *Perkin Trans*. **1976**, *1*, 1708-1711; (b) Rad, M. N. S.; Nezhad, A. K.; Karimitabar, F.; Behrouz, S. *Synthesis* **2010**, *10*, 1724-1730.
17. (a) Li, C. B.; Cui, Y.; Zhang, W. Q.; Li, J. L.; Zhang, S. M.; Choi, M. C. K.; Chan, A. S. *Chin. Chem. Lett.* **2002**, *13*, 95-96; (b) Stefani, A.; Lacher, J.; Park, J. *J. Org. Chem.* **1960**, *25*, 676; (c) Kaminsky, D.; Shavel, J., Jr.; Meltzer, R. I. *Tetrahedron Lett*. **1967**, *10*, 859–861.
18. (a) Jacob, B. B.; Synthesis. **1975**, 782; (b) Nesynov, E. P.; Zh. Org. Khim.**1976**, 12, 1965.
19. (a) Goda, H.; Ihara, H.; hirayama, C.; Sato, M.; *Tetrahedron Lett*.**1994**, *35*, 1565; (b) Abele, E.; Lukevics, E. *Org. Prep. Proced. Int.* **2000**, *32*, 235; (c) Rad, M. N. S.; Behrour, S.; Dianat, M. *Synthesis*. **2008**, 2055.
20. (a) Mori, S.; Nagata, M.; Nakahata,Y.; Yasuta, K.; Goto, R.; Kimura, M.; Taya, M. *J. Am. Chem. Soc.* **2010**, *132*, 4054; (b) Wang, J.; Medina, C.; Radomski M.; Gilmer, M. J. F. *Bioorg. Med. Chem*. **2011**, *19*, 4985; (c) K. Dodo, A. Aoyama, T. Noguchi-Yachide, M. Makishima, H. Miyachia and Y. Hashimoto, *Bioorg. Med. Chem.* **2008**, *16*, 4272; (d) Speicher, A.; Matthias, G.; Hennrich M.; Huynh, A.-M. *Eur. J. Org. Chem*. **2010**, 6760; (e) Kilitoglu, B.; Arndt, H.-D. *Synlett*, **2009**, 720; (f) Ullah, E.; McNulty, J.; Kennedy, C. Robertson A. *Org. Biomol. Chem.* **2011**, *9,* 4421.
21. (a) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Averill, K. M.; Chan, D. M. T.; Combs, A. *Synlett.* **2000** 674; (b) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Averill, K. M.; Chan, D. M. T.; Combs, *Tetrahedron Lett*. **1998**, *39*, 2941; (c) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett*. **1998**, *39*, 2937; (d) Chan, D. M. T.; Monaco, K. L.; Wang, R. P.; Winters, M. P. *Tetrahedron Lett*. **1998**, *39*, 2933; (e) Lam, P. Y. S.; Deudon, S.; Hauptman, E.; Clark, C. G. *Tetrahedron Lett*. **2001**, *42*, 2427; (f) Lam, P. Y. S.; Deudon, S.; Averill, K. M.; Li, R.; He, M. Y.; Desong, P.; Clark, C. G. *J. Am. Chem. Soc*. **2000**, *122*, 7600.

22. (a) Ali, A.; Meyer, A. G.; Tuckb, K. L. *Synlett.* **2009**, *6*, 0955-0959; (b) Feng, X-H.; Zhang, G-Z.; Chen, C-Q.; Yang, M-Y.; Xu, X-Y.; Huang.; G.-S. *Synth. Commun*. **2009,** *39*, 1768-1780; (c) Mondal, M.; Sarmah, G.; Gogoi, K.; Bora, U. *Tetrahedron Lett*. **2012**, *53* 6219-6222; (d) Wang, L.; Huang, C.; Cai, C. *Catal. Commun*. **2010,** *11*, 532-536.

23. (a) Mulla, S. A. R.; Inamdar, S. M.; Pathan, M. Y.; Chavan, S. S. *Tetrahedron Lett*. **2012**, *53***,** 1826; (b) Mulla, S. A. R.; Inamdar**,** S. M.; Pathan, M. Y.; Chavan, S. S. *RSC Adv.,* **2012,** *2***,** 12818.

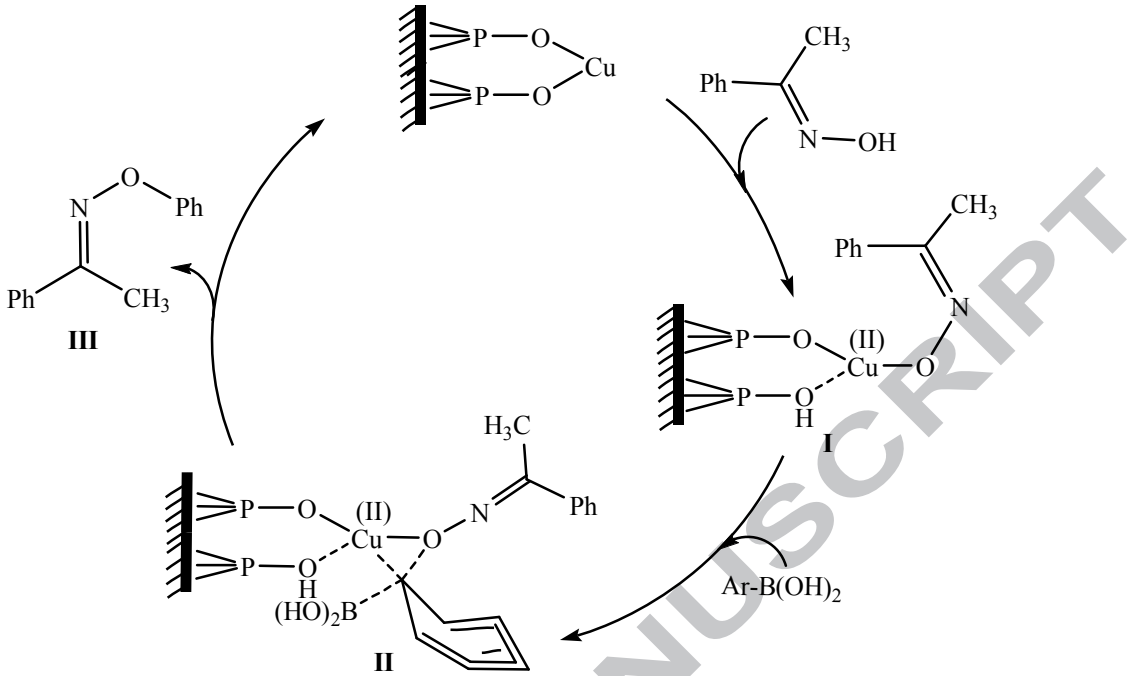
24. (a) Choudhary, B. M.; Sridhar, C.; Kantam, M. L.; Venkanna, G. T.; Sreedhar. B. *J. Am. Chem. Soc.* **2005**, *127*, 9948; (b) Kantam, M. L.; Venkanna, G. T.; Sridhar, C. H.; Shiva Kumar K. B. *Tetrahedron Lett*. **2006**, *47*, 3897.



R^1= H, isobutyl,$PhCH_2O$, Me, OMe, NO_2, Halogen, etc

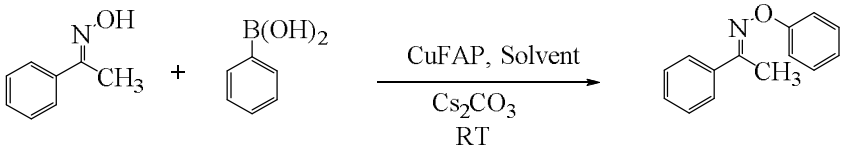
R^2=Me, OMe, CHO, CF_3, etc

Scheme 1: Synthesis of *O*-aryl oxime ethers over CuFAP catalyst.



Scheme 2: Possible mechanism over CuFAP catalyst for the *O*-aryl oxime synthesis

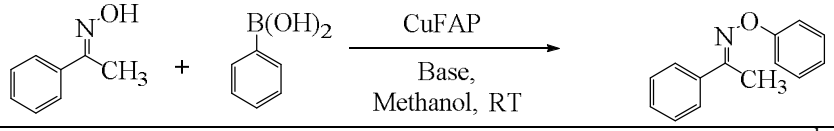
Table 1: Effect of solvents on CuFAP catalyzed O-arylation of acetophenone oxime with phenylboronic acid[a]



Entry	Solvent	Yield[b] (%)
1	Methanol	90
2	Ethanol	76
3	DMSO	N.R.[c]
4	DMF	N.R.[c]
5	Toluene	N.R.[c]
6	THF	18
7	Acetonitrile	N.R.[c]
8	Dichloroethane	N.R.[c]
9	Dichloromethane	N.R.[c]

[a] Reaction conditions: Acetophenone oxime (1 mmol), phenyl boronic acid (1.5 mmol), Cs_2CO_3 (1.5 mmol), solvent (5 mL), 100 mg CuFAP catalyst (Cu content 0.73 $mmolg^{-1}$), at room temperatures, 15 h.
[b] Isolated yields.
[c] No reactions
.

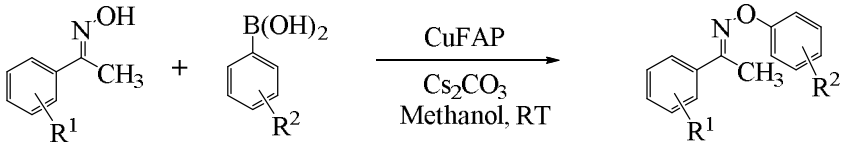
Table 2: Effect of base/catalyst loading on the O-arylation of acetophenone oxime with phenylboronic acid[a]



Entry	Base/catalyst loading	Yield[b] (%)
1	Na_2CO_3	43
2	K_2CO_3	64
3	Cs_2CO_3	90
4	NaOH	N.R.[c]
5	Diisopropylethylamine	N.R.[c]
6	Pyridine	N.R.[c]
7[d]	CuFAP (75 mg)	73
8[e]	CuFAP (50 mg)	39

[a] Reaction conditions : Acetophenone oxime (1 mmol), phenyl boronic acid (1.5 mmol), Base (1.5 mmol), Methanol (5 mL), 100 mg CuFAP catalyst (Cu content 0.73 mmolg^{-1}), at room temperatures, 15 h.
[b] Isolated yields.
[c] No reactions.
[d,e]Effect of catalyst loading, Cs_2CO_3 base was used.

Table 3: CuFAP catalyzed O-arylation of substituted acetophenone oxime with substituted arylboronic acids[a]



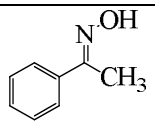
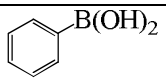
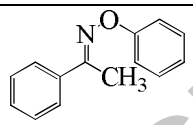
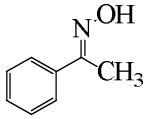
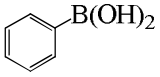
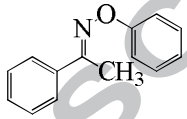
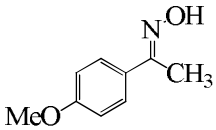
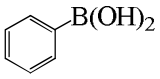
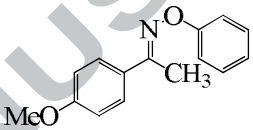
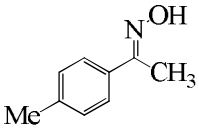
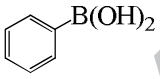
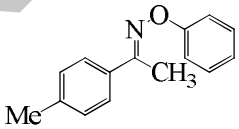
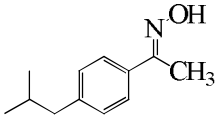
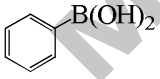
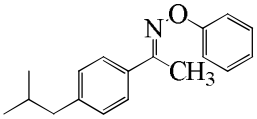
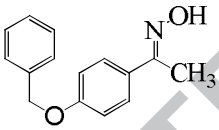
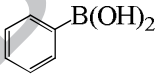
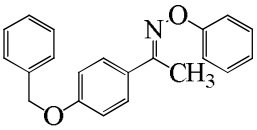
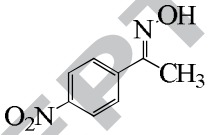
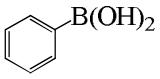
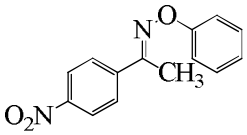
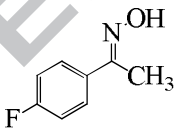
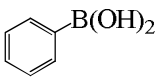
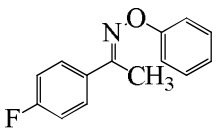
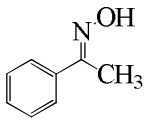
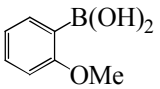
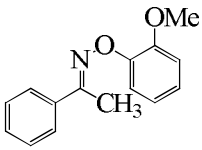
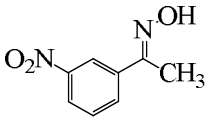
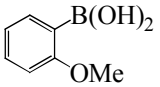
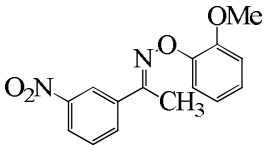
Sr. No.	Oximes	Boronic acids	Products	Yield (%)[b]
1				N.R.[c]
2				90
3				83
4				88
5				87
6				86
7				95
8				95
9				95
10				89

Table 3 continue

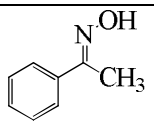
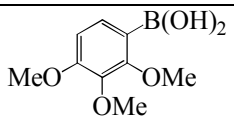
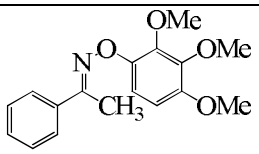
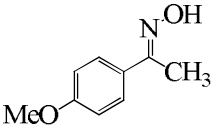
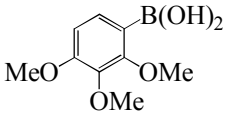
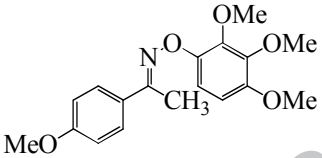
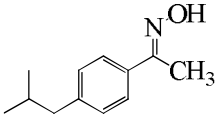
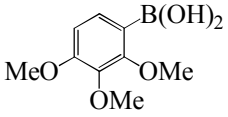
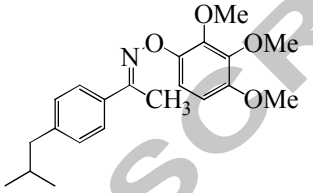
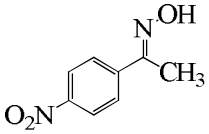
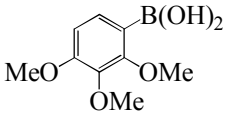
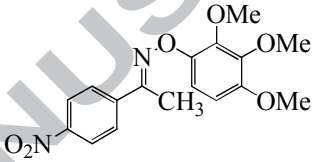
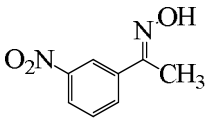
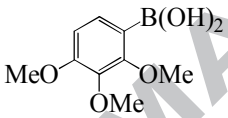
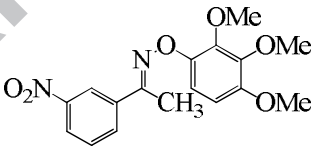
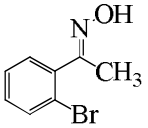
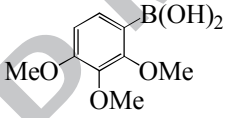
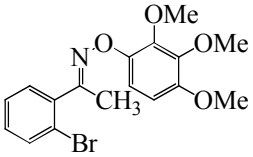
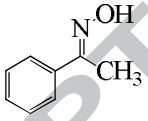
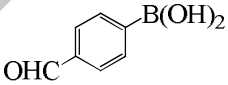
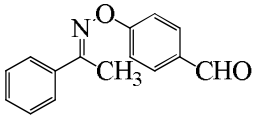
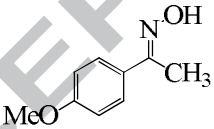
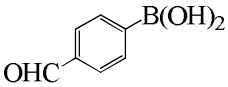
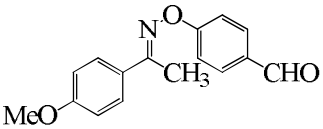
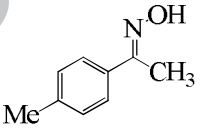
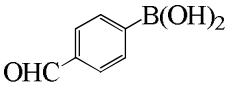
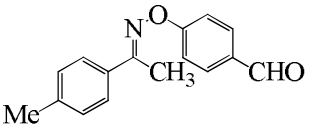
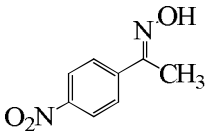
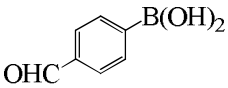
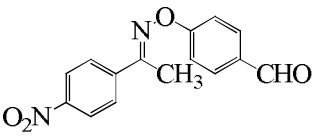
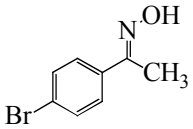
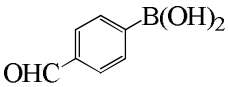
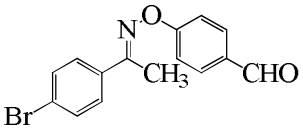
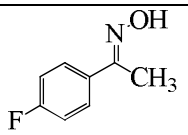
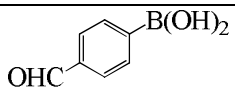
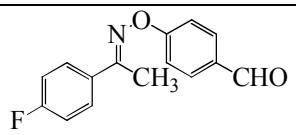
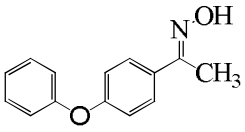
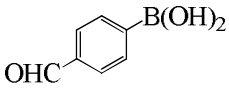
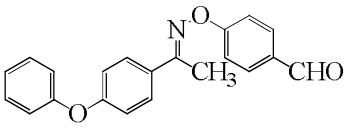
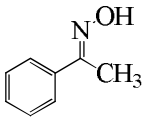
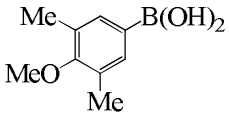
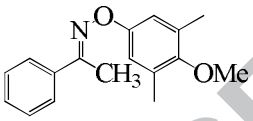
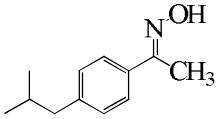
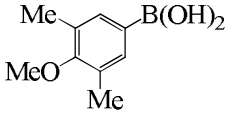
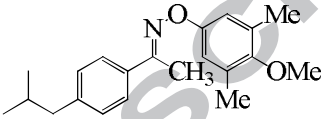
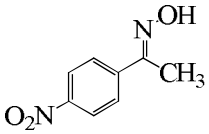
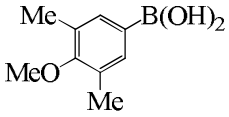
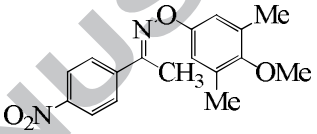
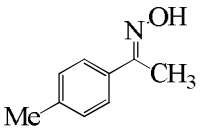
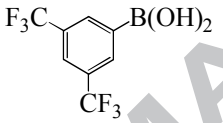
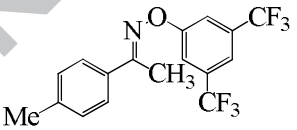
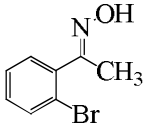
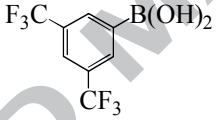
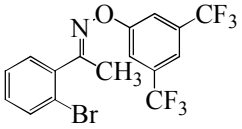
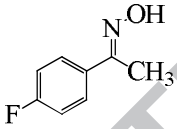
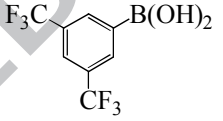
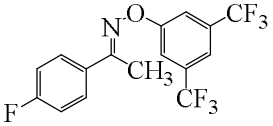
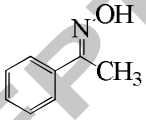
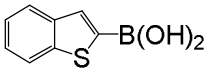
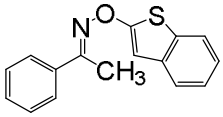
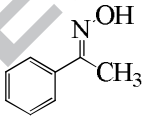
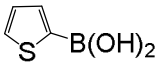
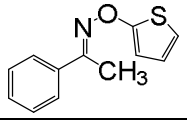
11				96
12				85
13				92
14				85
15				84
16				82
17				86
18				79
19				90
20				86
21				76

Table 3 continue

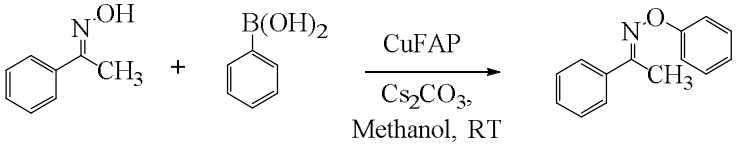
22				79
23				84
24				94
25				85
26				83
27				83
28				85
29				81
30				74
31				61

[a] Reaction conditions: substituted acetophenone oximes (1 mmol), substituted arylboronic acid (1.5 mmol), Cs_2CO_3 (1.5 mmol), Methanol (5 mL), 100 mg CuFAP catalyst (Cu content 0.73 $mmolg^{-1}$), at room temperatures, 15 h.

[b] Isolated yields.

[c] No reaction with base (Cs_2CO_3) without CuFAP catalyst and vice versa.

Table 4: Recyclability study of CuFAP catalyzed C-O cross coupling of acetophenone oxime with phenyl boronic acid[a]



Entry	Yield[b] (%)
1	90
2	89
3	88
4	89

[a] Reaction conditions: Acetophenone oxime (1 mmol), phenyl boronic acid (1.5 mmol), Cs_2CO_3 (1.5 mmol), Methanol (5 mL), 100 mg CuFAP catalyst (Cu content 0.73 $mmolg^{-1}$), at room temperatures, 15h.

[b] Isolated yields,