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CuI/L-proline-catalyzed selective one-step mono-acylation of styrenes and stilbenes

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ABSTRACT

Vicinal di-oxygenation of styrene-type olefins was achieved with cheaper, less toxic CuI in the presence of L-proline as ligand and $NaIO_4$ as the oxidant. This approach provides a straightforward and efficient access to mono-acylated diols from both styrene and stilbene derivatives with good to excellent yields and diastereoselectivity.

Vicinal di-functionalizations are attractive synthetic tools as they can be used to transform simple and readily available alkenes into value added products. Transition metal-catalyzed vicinal di-functionalizations of alkenes are among the most powerful techniques for the synthesis of several organic building blocks.[1] By employing this strategy, in one-step, functionalized molecules can be generated by methods such as di-amination, amino-oxygenation, di-oxygenation, and di-methoxylation of olefins in a highly regio- and enantio-selective manner.[2] Among them, di-oxygenation of alkenes gains its importance with the development of the Sharpless asymmetric di-hydroxylation (ADH), where both enantiomers of the *syn* di-oxygenated products could selectively be accessed.[3] The main disadvantage of the Sharpless procedure is the toxicity associated with the osmium metal and its expensive nature.

This led to the development of alternate routes for di-oxygenation, employing cheaper and environmentally benign catalytic systems. Several groups have reported Pd-catalyzed di-oxygenation of alkenes, viz., hydroxyl acetoxylation of alkenes using cationic Pd catalyst,[4] Pd(II)-catalyzed aerobic di-alkoxylation of styrene derivatives containing an *o*-phenol[5] and aerobic di-acetoxylation of alkenes with Pd(II) catalyst[6] to name a few. A conceptually different approach, where a metal-free di-hydroxylation of alkenes employing LiBr as the catalyst in presence of commercially available $NaIO_4$ or $PhI(OAc)_2$ as oxidants has also been reported.[7]

Recently, there has been a surge in reports of organic transformations catalyzed by cheaper and more benign metals such as copper and iron that are predominantly found in metallo-enzymes which play important roles in biological di-oxygen metabolism.[8] The low cost, ample supply of Cu salts combined with their environmentally benign nature and lack of toxicity make them ideal for an industrial scale synthesis of specialty chemicals.[9] Aminohydroxylation of styrenes and activated olefins by $Cu(TFA)_2$,[10] copper-catalyzed allylic oxidation of olefins with peresters,[11] and copper-catalyzed enantio-selective intramolecular amino-oxygenation of olefins[12] were a few notable olefin oxidations mediated by Copper. Till recently, di-oxygenation of olefins with Cu proved to be of great challenge.[13]

Herein, we report a facile and highly selective synthesis of mono-acylated diols from styrenes and stilbenes using inexpensive CuI/L-proline catalytic system. This strategy represents an efficient, convenient, and direct one-pot synthesis of mono-acylated diols from styrene-type olefins.

Our initial aim was to develop a simple catalytic system for di-hydroxylation of stilbenes with Cu salts. For the optimization studies, *trans*-stilbene was taken as the model substrate in presence of $NaIO_4$ as the oxidant. With various non-polar solvents, we could not observe the desired product and polar solvents such as AcOH, DMSO, and DMF were also screened. Among them AcOH proved to be the best solvent and the analysis of final product revealed that one of the hydroxyl group was selectively converted into –OAc in the presence of AcOH. Inspired by this result, we optimized the conditions for selective one-pot mono-acylation of stilbenes and styrenes by treating *trans*-stilbene with several oxidants and

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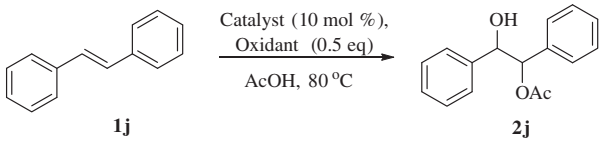
Table 1
Optimization conditions for mono-acylation of *trans*-stilbene[a]



1j **2j**

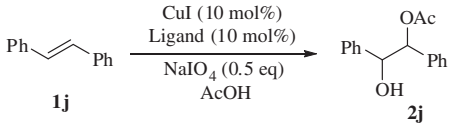
Entry	Oxidant[b]	Catalyst	Yield (%)	
			GC[c]	Isolated[d]
1	$NaIO_4$	—	NR[e]	—
2	$NaIO_4$	CuCl	45	35
3	$NaIO_4$	$CuSO_4$	29	15
4	$NaIO_4$	$Cu(OAc)_2$	40	25
5	$NaIO_4$	CuBr	50	35
6	$NaIO_4$	CuI	60	45
7	NaOCl	CuI	—	—
8	*m*CPBA	CuI	NR[e]	—
9	Oxone	CuI	10	5
10	$PhI(OAc)_2$	CuI	38	25
11	H_2O_2	CuI	43	30

[a] Reaction conditions: substrate **1j** (1 mmol), oxidant (0.5–1 equiv), catalyst (10 mol %), AcOH (3 mL), 80 °C, 18 h.
[b] $NaIO_4$ = 0.5 equiv; NaOCl or oxone or *m*CPBA or $PhI(OAc)_2$ or H_2O_2 = 1.0 equiv.
[c] Determined by GC integration of crude product.
[d] Isolated yield of **2j**.
[e] Benzaldehyde was observed as the major product.

copper salts and the results are summarized in Table 1. The reaction fails to yield the desired product in the absence of copper (entry 1). Screening of various copper salts shows that CuI was the suitable catalyst for this reaction in terms of both conversion and selectivity (entries 2–6). Several oxidants were screened and among them NaOCl and *m*CPBA do not afford the desired product (entries 7 and 8). With oxone as the oxidant, only oxidatively cleaved product, that is, benzaldehyde was observed as the major product (entry 9). When $PhI(OAc)_2$ and H_2O_2 were taken as the oxidants, the yield and selectivity were appreciable (entries 10 and 11) but lower than that of $NaIO_4$ (entry 6). Thus we can conclude that CuI acts as the best catalyst and $NaIO_4$ as the best oxidant for this selective mono-acylation of olefins.

Despite the moderate conversion and selectivity for mono-acylation of *trans*-stilbene with CuI/$NaIO_4$, the yields were very low. To improve the over-all conversion and yield, we have screened several ligands for this reaction (Table 2). Among them, L-proline

Table 2
Effect of ligands on mono-acylation of *trans*-stilbene[a]



1j **2j**

Entry	Ligand	Time (h)	Yield[b] (%)
1	—	24	45
2	L-Valine	24	15
3	Diaminocyclohexane	72	5
4	L-Proline	18	74
5	Picolinic acid	24	8
6	Ethylene diamine	24	10
7	2-Amino pyridine	24	20
8	1,2-Diamino benzene	24	7

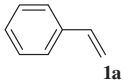
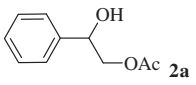
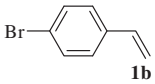
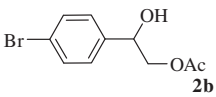
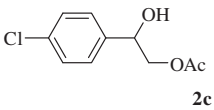
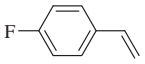
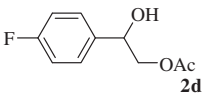
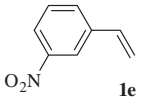
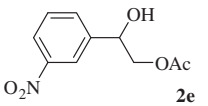
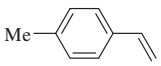
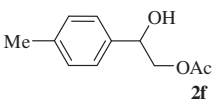
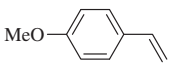
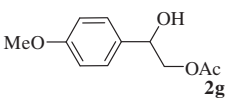
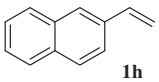
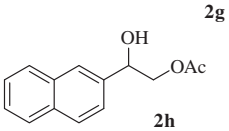
[a] All reactions were carried out on a 1 mmol reaction scale of (**1j**) using $NaIO_4$ (0.5 equiv), CuI (10 mol %), AcOH (3 mL) at 80 °C.
[b] Isolated yield.

afforded improved yield compared to that of ligand-free condition (entry 4). Varying different ligands does not produce any appreciable increase in the yield. Thus the optimized reaction condition for mono-acylation of olefins was fixed and CuI/L-proline system was proved to be the suitable catalytic system for this reaction.

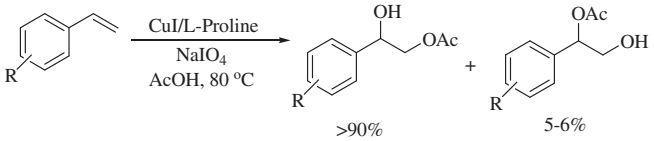
With the optimized reaction condition in hand, the general applicability of this reaction was tested with substituted styrenes, di-substituted alkenes (*trans*-stilbenes), and a tri-substituted alkene and the results are summarized in Table 3. As expected, the reaction was found to be faster with styrenes compared to stilbenes, which can be explained in terms of steric factors. In case of styrenes, we focused our attention on the regioisomeric distribution of monoesters and found that acetylation was more favorable at the least hindered site. Thus mono-acylation preferably occurs at the primary carbon rather than at the sterically crowded secondary position (Scheme 1). Irrespective of the electronic nature of the substituted styrenes, the reaction proceeds smoothly to give the desired product in good to excellent yields (Table 3, entries 1–8).

When stilbene derivatives were taken as the substrates, there is slight decrease in yield and the rate of the reaction (Table 4).

Table 3
CuI/L-proline-catalyzed mono-acylation of terminal olefins[a]

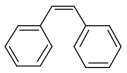
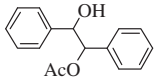
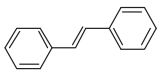
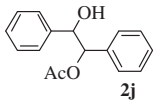
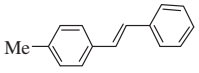
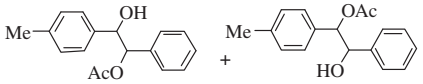
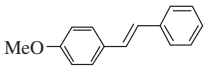
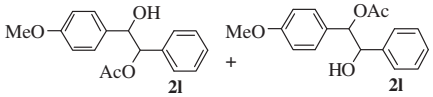
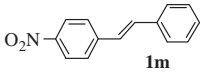
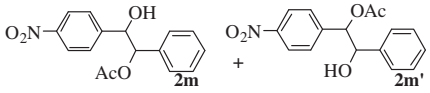
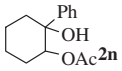
Entry	Olefin	Product	Yield[b] (%)
1	 **1a**	 **2a**	79
2	 **1b**	 **2b**	85
3	 **1c**	 **2c**	82
4	 **1d**	 **2d**	80
5	 **1e**	 **2e**	79
6	 **1f**	 **2f**	75
7	 **1g**	 **2g**	72
8	 **1h**	 **2h**	76

[a] All reactions were carried out in 1 mmol scale in acetic acid solvent system at 80 °C, $NaIO_4$ (0.5 equiv), CuI (10 mol %), L-proline (10 mol %), 18 h.
[b] Isolated yield.

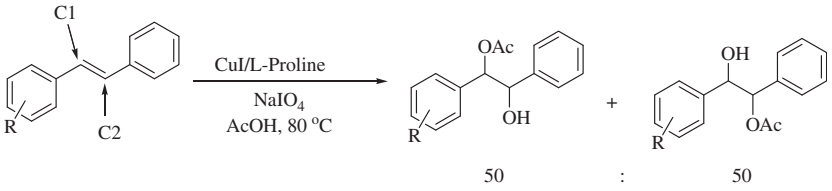


Scheme 1. Cu-catalyzed mono-acylation of styrenes.

Table 4
CuI/L-proline-catalyzed mono-acylation of internal olefins[a]

Entry	Olefin	Product	Yield[b] (%)
1	 **1i**	 **2i**	72
2	 **1j**	 **2j**	74
3	 **1k**	 **2k** + **2k'**	75
4	 **1l**	 **2l** + **2l**	76
5	 **1m**	 **2m** + **2m'**	70
6	 **1n**	 **2n**	62

[a] All reactions were carried out in 1 mmol scale in acetic acid solvent system at 80 °C, $NaIO_4$ (0.5 equiv), CuI (10 mol %), L-proline (10 mol %).
[b] Isolated yield.

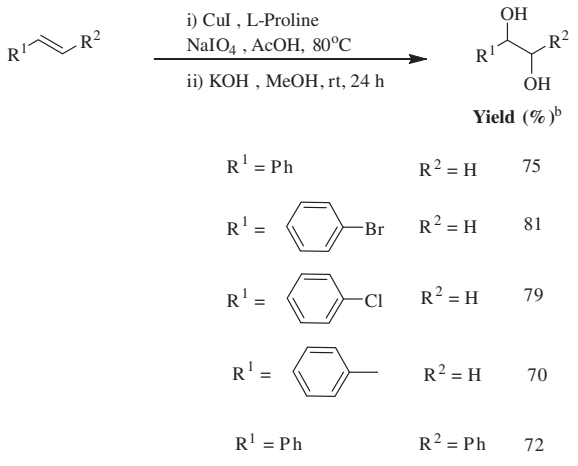


Scheme 2. Cu-catalyzed mono-acylation of stilbenes.

Remarkably, in the case of stilbenes, *anti*-isomers of the corresponding mono-acetylated derivatives with dr >90% (entries 1–6) were obtained exclusively. Both *cis*- and *trans*-stilbene gave the *anti*-product in moderate yield (Table 4, entries 1 and 2). In case of substituted stilbenes, mono-acylation can be possible at both the position; C1 and C2, leading to two different regio-isomers. In our case, we observed an inseparable mixture of both the isomers in equal ratio (Table 4, entries 3–5 and Scheme 2). When a tri-substituted olefin was taken, the reaction followed the similar trend leading to the *anti*-product, but with lesser yield (Table 4, entry 6).

The mono-acylated product thus obtained can be easily converted into their respective diols in good yields by treatment with simple base, that is, KOH in MeOH. The yields were good for both styrene and stilbene derivatives (Scheme 3).

In summary we have developed a straightforward and efficient method to generate mono-acylated diols from styrenes and stilbenes using a simple, eco-economically friendly catalytic system, that is, CuI/L-proline and a cheap oxidant $NaIO_4$. Structurally diverse styrenes and stilbenes were selectively converted into mono-acylated product with good to excellent yields, and excellent diastereoselectivity. Finally, the mono-acylated products, thus obtained, can be easily converted into their corresponding diols by a simple base treatment.



Scheme 3. CuI/L-proline catalyzed di-hydroxylation of styrenes and *trans*-stilbene[a]. Reagents: All reactions were carried out in 1 mmol scale in acetic acid at 80 °C, $NaIO_4$ (0.5 equiv), CuI (10 mol %), L-proline (10 mol %), 24 h. [b]Isolated yield.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.084.

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