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Cesium hydroxide catalyzed addition of alcohols and amine derivatives to alkynes and styrene

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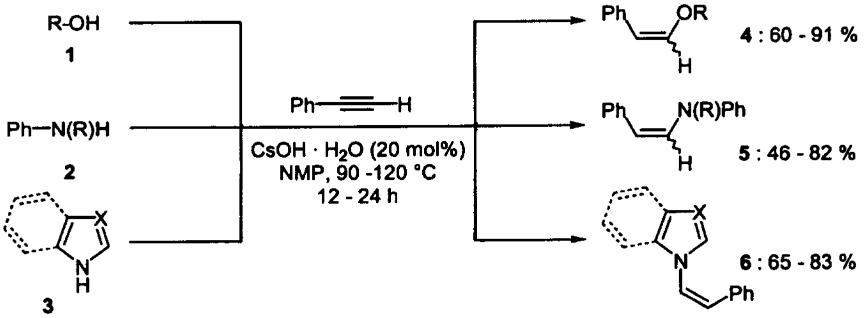
Abstract

In the presence of catalytic amounts of cesium hydroxide ($CsOH \cdot H_2O$), alcohols, substituted anilines and heterocyclic amines undergo an addition in NMP to phenylacetylene leading to functionalized enol ethers and enamines. Anilines add to styrene (90–120°C, 12–14 h) leading to *N*-substituted anilines in satisfactory yields.

The addition of heteroatoms to alkynes and alkenes is a thermodynamically favored reaction, however, it requires a high activation energy preventing these additions occurring under uncatalyzed reaction conditions.[1] However, a few catalytic systems are known which allow the addition of alcohols to alkynes[2] and the addition of amines to alkynes[1b,3] or to styrenes.[4] Recently, we have found that $CsOH \cdot H_2O$ is an excellent catalyst for the catalytic alkynylation of aldehydes and ketones.[5,6] Herein, we wish to report that cesium hydroxide also catalyzes the addition of alcohols of type **1** and secondary aromatic or heterocyclic amines of types **2** or **3** to phenylacetylene in NMP leading to enol ethers of type **4** and enamines of types **5** or **6** (Scheme 1 and Table 1).



Scheme 1.

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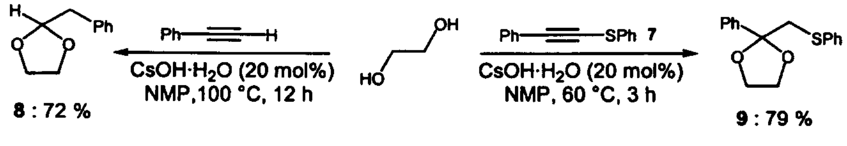
Table 1
Enol ethers **4a–g** and enamines **5a,b** and **6a–d** obtained by the cesium hydroxide catalyzed addition of alcohols and secondary amines or *N*-heterocycles to phenylacetylene in NMP (see also Scheme 1)

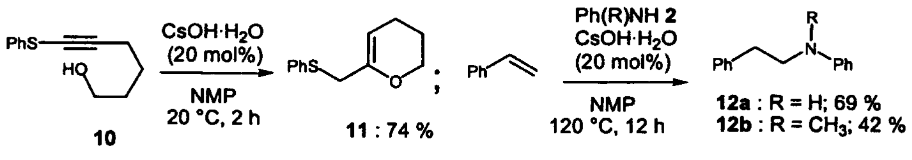
Entry	Alcohol or amine	Product of type 4-6	Cis-trans ratio	Yield (%)[a]
1	MeOH **1a**	**4a**: R = Me	75:25	90
2	EtOH **1b**	**4b**: R = Et	90:10	82
3	*i*-PrOH **1c**	**4c**: R = *i*-Pr	70:30	63
4	BuOH **1d**	**4d**: R = Bu	75:25	91
5	$PhCH_2OH$ **1e**	**4e**: R = $PhCH_2$	67:33	75
6	$(i\text{-}Pr)_2CHOH$ **1f**	**4f**: R = $CH(i\text{-}Pr)_2$	67:33	60
7	$HOCH_2CH_2NH_2$ **1g**	**4g**: R = $CH_2CH_2NH_2$	70:30	76
8	Ph_2NH **2a**	**5a**: R = Ph	75:25	82
9	Ph(Me)NH **2b**	**5b**: R = Me	50:50	46
10	pyrrole **3a**	**6a**: X = CH	100:0	79
11	imidazole **3b**	**6b**: X = N	100:0	83
12	indole **3c**	**6c**: X = CH	92:8	65
13	benzimidazole **3d**	**6d**: X = N	100:0	73

[a] Isolated yield of analytically pure compounds.

Methanol gives the best results in the addition reaction (NMP, 100°C, 12 h, 90% yield, entry 1 of Table 1). Under these reaction conditions, various primary and secondary alcohols add to phenylacetylene in satisfactory yields (60–91% yield; entries 2–6). Interestingly, ethanolamine (**1g**)[2b] adds to phenylacetylene forming a C–O bond and not a C–N bond showing that primary alcohols preferentially add to yield the functionalized enol ether **4g** (entry 7). All these enol ethers were obtained as *cis*:*trans* mixtures which may be a result of the relatively high reaction temperature required for the addition (100°C, 12 h). Substituted anilines like diphenylamine **2a** or *N*-methylaniline **2b** also undergo the addition reaction leading to enamines like **5a** and **5b** in 82% and 46% yield (see entries 8 and 9). Especially attractive is the addition of various *N*-heterocycles to phenylacetylene resulting in the formation of the heterocyclic enamine derivatives **6a–d** in 65–79% yield (see entries 10–13). With several of these substrates, only the *cis*-enamine is obtained (entries 10, 11 and 13). Phenylacetylene and 2-phenylthio-1-phenylacetylene **7** react with ethylene glycol, furnishing the double addition products **8** and **9** in 72–79% yield (Scheme 2). The regioselectivity of the addition product **9** was proved by the acid catalyzed hydrolysis (TsOH cat., THF:H_2O, 60°C, 6 h) which provided phenylthiomethyl phenyl ketone as sole product (90% yield). By using the hydroxyalkyne **10**, a cyclization followed by an isomerization of the double bond takes place, affording the dihydropyran **11** in 74% yield (CsOH·H_2O (20 mol%), NMP, 20°C, 2 h) (Scheme 3).



Scheme 2.



Scheme 3.

Finally, we have found that CsOH·H_2O catalyzes the addition of various substituted anilines to styrene leading to the amines **12** in moderate yields[1b,3,4] (42–69%; Scheme 3). We are currently investigating extension of these reactions to intramolecular reactions.[7]

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References

1. (a) Taube, R. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B.; Herrmann, W. A., Eds.; VCH, 1996; pp. 507–520; (b) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675.
2. (a) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1415; (b) Kukharev, B. F.; Stankevich, V. K.; Klimenko, G. R. *Russ. J. Org. Chem.* **1993**, *29*, 2005.
3. Heider, M.; Henkelmann, J.; Ruehl, T. Eur. Pat. Appl. EP 646,571 (*Chem. Abst.* **1995**, *123*, 229254s).
4. (a) Beller, M.; Eichberger, M.; Trauthwein, H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2225; (b) Beller, M.; Breindl, C.; Riermeier, T. H.; Eichberger, M.; Trauthwein, H. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3389; (c) Settambolo, R.; Mariani, M.; Caiazzo, A. *J. Org. Chem.* **1998**, *63*, 10022; (d) Beller, M.; Thiel, O. R.; Trauthwein, H. *Synlett* **1999**, 243.
5. Tzalis, D.; Knochel, P. *Angew. Chem.* **1999**, *111*, in press.
6. For recent publications using cesium hydroxide: (a) Dueno, E. E.; Chu, F.; Kim, S.-I.; Jung, K. W. *Tetrahedron Lett.* **1999**, *40*, 1843; (b) Chu, F.; Dueno, E. E.; Jung, K. W. *Tetrahedron Lett.* **1999**, *40*, 1847; (c) Busch-Petersen, J.; Bo, Y.; Corey, E. J. *Tetrahedron Lett.* **1999**, *40*, 2065.
7. **Typical procedure**: Preparation of 2-methoxyethenylbenzene (**4a**; entry 1 of Table 1): A Schlenk flask was charged with CsOH·H_2O (329 mg, 1.96 mmol). NMP (10 mL), methanol (0.6 mL, 14.7 mmol) and phenylacetylene (1.00 g, 9.8 mmol) was successively added. The reaction mixture was vigorously stirred and heated to 100°C for 12 h. After cooling to rt, the solution was poured into brine and washed with ether. The combined etheral layer was extracted with water and dried ($MgSO_4$). After evaporation of the solvent, the desired product was purified by flash chromatography on basic alumina (pentane:ethyl acetate, 19:1) to yield as a colorless oil (1.18 g, 90% yield). Preparation of 1-(2-phenyl-1-ethenyl)-1*H*-imidazole (**6b**; entry 11 of Table 1): A Schlenk flask was charged with CsOH·H_2O (300 mg, 1.8 mmol). NMP (5 mL) and imidazole (650 mg, 9.6 mmol) was successively added. The reaction mixture was vigorously stirred and phenylacetylene (1 mL, 9.1 mmol) was slowly added and the mixture stirred for 24 h at 120°C. The reaction mixture was poured into ether and washed with H_2O. The etheral layer was dried ($MgSO_4$). The product was recrystallized from ether to yield **6b** as white needles (1.28 g, 83% yield; mp=92–94°C).