

SYNLETT Spotlight 296

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

CsOH·H₂O in Organic Synthesis

Compiled by Filipa Siopa

Filipa Siopa was born in Portugal. She received her chemistry degree from Faculdade de Ciências of Universidade de Lisboa in 2003, and is now working towards her PhD under the supervision of Prof. Paula Branco at the Faculdade de Ciências e Tecnologia of Universidade Nova de Lisboa. Her current research is focused on understanding the role of catecholamines in several biological processes, namely the synthesis of catecholamine adducts of amino acids, nucleosides, and small peptides.

REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, 2829-516 Caparica, Portugal

E-mail: fsiopa@dq.fct.unl.pt



Introduction

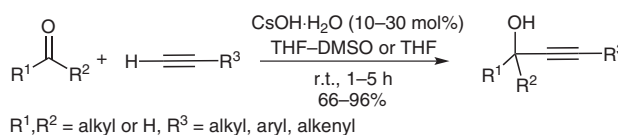
Cesium hydroxide monohydrate (CsOH·H₂O) is an important reagent in organic synthesis being applied in a diversity of reactions. It is a solid strong base, commercially available, and it can be used in an assortment of solvents and reaction conditions.

Cesium hydroxide monohydrate allows the catalytic generation of highly reactive anions, which are able to add to

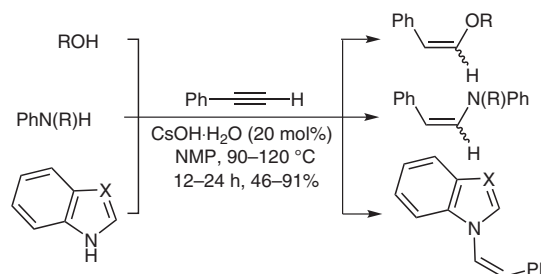
carbonyl groups or carbon–carbon multiple bonds. Its great versatility as a base can be seen in a range of reactions as those involving carbon–carbon and carbon–heteroatom bond formation. The increasing interest on CsOH·H₂O over the last few years, is patent on the diversity of applications, and the increased number of publications reporting its powerful basicity.

Abstracts

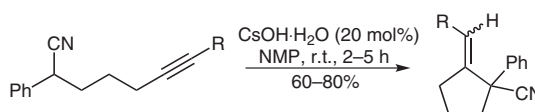
(A) The exceptional activity of cesium hydroxide monohydrate as a base can be observed on the catalytic generation of highly nucleophilic, stabilized organometallic species derived from alkynes. Under these conditions, terminal alkynes undergo a smooth addition to secondary or tertiary aliphatic aldehydes or aliphatic ketones to give the corresponding propargylic alcohols in good yields.¹



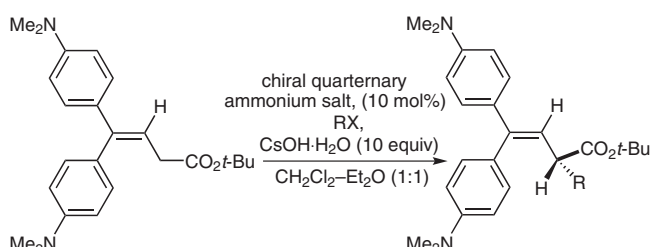
(B) Enol ethers and enamines can be obtained by the CsOH·H₂O catalyzed addition of alcohols, and secondary or heterocyclic amines to phenylacetylene in the presence of NMP in satisfactory to good yields.²



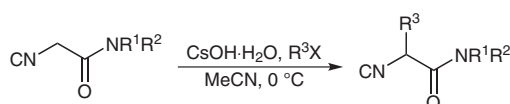
(C) Intramolecular addition of benzylic carbons to alkynes can be performed with CsOH·H₂O. Benzyl cyanides allow intramolecular reactions with alkynes in the presence of catalytic amounts of CsOH·H₂O using NMP as solvent providing functionalized olefins with good regio- and *E*-stereoselectivities.³



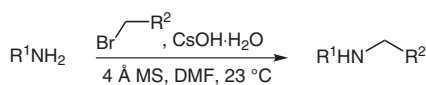
(D) Corey and co-workers developed the use of solid CsOH·H₂O, in liquid-phase transfer conditions with a chiral quaternary ammonium salt and its applications in catalytic enantioselective alkylation and Michael reactions. CsOH·H₂O is used as the basic phase to minimize the possibility of water in the organic phase and allow the use of lower temperatures, which permits the reaction to proceed smoothly, with good yields, and high enantioselectivities (ee >94%). With this methodology the synthesis of a variety of chiral building blocks is achieved easily.⁴



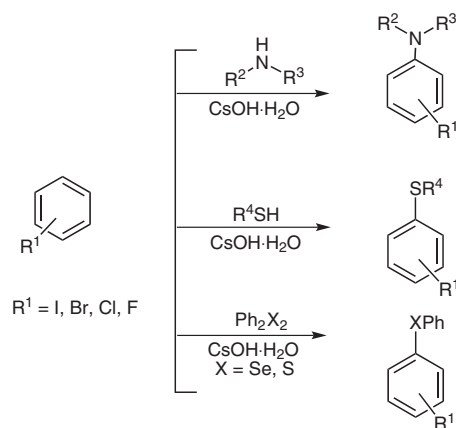
(E) The use of CsOH·H₂O was described for the monoalkylation of α -isocyano acetamides to their higher homologues. The importance of this reaction is unquestionable due to the importance of functionalized isonitriles for the synthesis of heterocycles.⁵



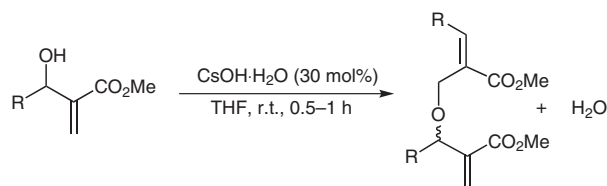
(F) CsOH·H₂O can be used to promote the direct mono-N-alkylation of primary amides, diamines, and polyamines, to prepare secondary amines efficiently.⁶



(G) Adapa and co-workers reported that CsOH·H₂O promotes the direct coupling reaction of aryl halides with *sec*-alicyclic amines, thiols, and Ph₂Se₂.⁷ The direct cross-coupling of aryl halides was performed using CsOH·H₂O in good yields without a transition metal catalyst. Salvatore et al. described an efficient coupling of secondary phosphines with alkyl halides using CsOH·H₂O as base.⁸



(H) In the literature there is a range of methods for the preparation of stereo-defined trisubstituted alkenes which are a significant group of building blocks in natural products. CsOH·H₂O in catalytic amount promoted the dimerization of Baylis–Hillman adducts which result in the formation of unsymmetrical bis-allyl ethers consisting of an *E*-allylic unit and a terminal allylic unit as the only product. Selective formation of the *E*-allylic unit in the product and water being the only by-product add to the reaction high stereo-selectivity and atom-economy.⁹



References

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