Tetrahedron Letters 51 (2010) 4281–4283

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Silica-supported $HgSO_4/H_2SO_4$: a convenient reagent for the hydration of alkynes under mild conditions

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ARTICLE INFO

Article history:
Received 6 May 2010
Revised 4 June 2010
Accepted 8 June 2010
Available online 12 June 2010

Keywords:
Hydration
Alkynes
Mercury
Catalysis
Supported catalyst

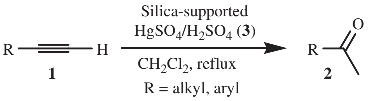
ABSTRACT

The silica-supported aqueous-phase catalyst (SAPC) approach has proven convenient for efficiently performing the hydration of alkynes with $HgSO_4/H_2SO_4$ to give the corresponding carbonyl compounds in dichloromethane under mild conditions. The use of this solid reagent significantly improves the reaction work-up as it merely involves filtering and evaporating the solvent.

Hydration of C–C triple bonds of unsymmetrically substituted alkynes (**1**) to give substituted ketones (**2**) or aldehydes is of fundamental importance in synthetic organic chemistry.[1] Transition metals[1,2] such as mercury,[3] ruthenium, rhodium, palladium, platinum, and gold, as well as Brönsted acids[4] catalyze these reactions. Among these catalysts, Hg(II) salts are the most efficient and reliable to activate alkynes toward nucleophiles and are still used in organic synthesis for these reasons.[1] For instance, Nishizawa et al. have reported[5] highly efficient and selective addition and C–C bond-forming reactions of alkynes catalyzed by $Hg(OSO_2CF_3)_2$ and its tetramethylurea complex.[5]

Solid-supported Hg(II) catalysts[6] have been developed to improve the reaction work-up and to minimize metal residues in the reaction products. Recently, Nishizawa and co-workers have developed[6a] a solid-supported phenylmercuric triflate which efficiently catalyzed most $Hg(OSO_2CF_3)$-catalyzed reactions. In this context, a supported aqueous-phase catalyst (SAPC) approach,[7] in which a water phase containing the catalyst is maintained on a hydrophilic support such as silica and the reaction takes place at the interface, would be particularly well suited for the Hg(II)-catalyzed alkyne hydration given the water solubility of Hg(II) salts.

We herein report that hydrated silica-supported $HgSO_4/H_2SO_4$ (**3**) is an efficient reagent for performing the hydration of alkynes (**1**) in dichloromethane under mild conditions to give the corresponding carbonyl compounds (**2**) (Eq. 1). The reaction takes place at the hydrophilic silica surface where the water molecules coordinating to the acidic sites are nucleophilic enough to perform the reaction. The reaction work-up involves filtering the solution and evaporating the solvent, and avoids the usual extraction steps required for homogeneous reactions carried out in aqueous organic solvents.



(1)

Silica-supported reagent **3** was prepared by adding chromatographic grade silica to an aqueous solution of $HgSO_4$ and H_2SO_4 and by evaporating the solvent under vacuum at room temperature until it reached a constant weight. This procedure yielded a free flowing, white, hygroscopic solid which can be stored at room temperature for months in a desiccator without loss of activity or change in appearance. The mass balance indicated a 22% w/w of water content and a load of 0.27 mmol of $HgSO_4$, 1.5 mmol of H_2SO_4, and 12.5 mmol of H_2O per gram of material (molar ratio $HgSO_4/H_2SO_4/H_2O$ 1:5.5:46).

The hydration reactions were carried out by adding the silica-supported catalyst (5 mol %) to a dichloromethane solution of the alkyne **1** and by heating to reflux. The reactions were monitored by gas chromatography and stopped once the substrate conversion was complete. The product was obtained by filtering the solid and evaporating the solvent under vacuum. The results are shown in Table 1.[8,9]

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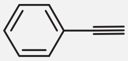
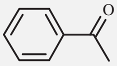
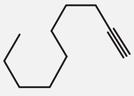
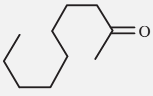
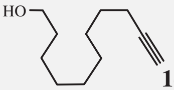
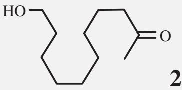
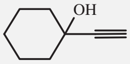
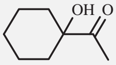
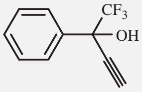
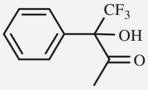
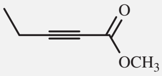
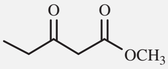
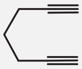
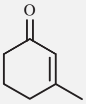
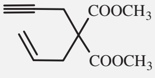
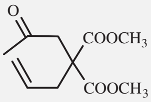
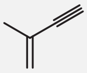
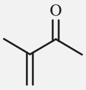
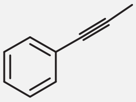
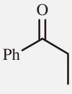
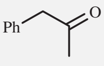
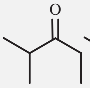
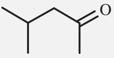
doi:10.1016/j.tetlet.2010.06.042

Table 1
Hydration of alkynes (**1**) with hydrated silica-supported $HgSO_4/H_2SO_4$ (**3**)[a]

Entry	1	2	t (h)	Yield[b] (%)
1	 **1a**	 **2a**	2	91
2	 **1b**	 **2b**	2	91
3[b]	 **1c**	 **2c**	2	90
4	 **1d**	 **2d**	24	87
5	 **1e**	 **2e**	24	89
6	 **1f**	 **2f**	5	86
7	 **1g**	 **2g**	6	85[c]
8	 **1h**	 **2h**	17[d]	95
9	 **1i**	 **2i**	20[e]	57[e]
10	 **1j**	 **2j**  **2j'**	16[d]	99[f]
11	 **1k**	 **2k**  **2k'**	15[d]	99[f]

[a] Reactions carried out in dichloromethane at 40 °C with hydrated **3** (5 mol % of $HgSO_4$) except where noticed; substrate conversion was complete in all cases.

[b] Isolated yield after removing the solvent.

[c] The reaction mixture contained a 7% of 2,6-heptadione.

[d] 10 mol % of $HgSO_4$.

[e] Reaction with 10 mol % of $HgSO_4$ at room temperature in a closed vial; GC analysis showed complete conversion to give **2i** as the only product.

[f] Ratios **2j**/**2j'** and **2k**/**2k'** 8.1:1 and 1.8:1, respectively.

The results show that silica-supported $HgSO_4/H_2SO_4$ (**3**) is very efficient to perform the hydration of alkynes under these conditions. The reaction work-up significantly improved compared to those procedures which use soluble Hg(II) salts under biphasic conditions or in aqueous solvents. The solid which was recovered once the reaction had been completed is olive green in color with a loose appearance and can be reused at least three times with a similar activity.

The reaction is very efficient for the alkynes with electron-withdrawing or sterically hindered substituents (Table 1, entries 4 and 5). For instance, phenylacetylene (**1a**) reacts in 2 h while methyl 2-pentinoate **1h** reacts in 5–6 h (Table 1, entries 1 and 6), and both 1-ethynylcyclohexanol (**1d**) and 1,1,1-trifluoro-2-phenyl-3-butynol (**1e**) react in 24 h (Table 1, entries 4 and 5). Internal alkynes react more slowly than their terminal counterparts, which is probably due to the steric or hydrophobic shielding of the substituents to the interaction of the C–C triple bond with the catalysts on the hydrophilic silica surface (Table 1, entries 10 and 11).

The hydration of 1,6-heptadiyne (**1g**) led to 3-methyl-2-cyclopentenone (**2g**) as the main product with small amounts of 2,6-heptadione (Table 1, entry 7). These results could be attributed to either Hg-catalyzed diyne cyclization or the intramolecular acid-catalyzed aldol condensation of the corresponding diketone on the acidic silica surface. The absence of acid-catalyzed side reactions for the tertiary alcohol **1d** or the enyne **1i** suggest that 3-methyl-2-cyclopentenone (**2g**) might be formed mainly through a Hg-catalyzed C–C-bond formation.

The results show that the water molecules coordinated with the acidic sites of the silica surface (7.2 water molecules per sulfate anion) are sufficiently nucleophilic to react with the electrophilic species involved in the reaction. Higher loads of water on the supported reagent led to slower reactions. For instance, the reaction of phenylacetylene (**1a**) with a sample of 38% w/w hydrated **3** (molar ratio $HgSO_4/H_2SO_4/H_2O$ 1:5.5:79) required 6 h for completion. These results suggest that excess water diminishes the mass transfer efficiency at the water/dichloromethane interface which acts as a barrier by inhibiting the access of the substrate to the catalytic sites on the silica surface. The induction period observed for substrates **1h**, **1j**, and **1k** (entries 8, 10, and 11) was attributed to this factor. Higher loads of $HgSO_4/H_2SO_4$ did not improve the reaction efficiency, but led to an extensive reduction of the metal on the silica surface. Lower $HgSO_4/H_2SO_4$ ratios led to the formation of HgO on the silica surface and to the formation of an inactive yellow solid. Silica-supported $HAuCl_4$ and $FeCl_3$ (20% hydrated, 1 and 3 mmol per gram of material, respectively) were found inactive under the same conditions (conversions 6% and 7%, respectively, after 24 h). Brönsted acids were more effective, thus the reaction of phenylacetylene (**1a**) with silica-supported H_2SO_4 (2.5 mmol per gram of material) under the same conditions led to the complete conversion of the substrate after 120 h. The strongly hygroscopic nature of this solid material prevented a precise determination of water content. It is likely that the highly hydrated silica surface both diminished the acidity of the catalysts and hindered the approach of the substrate to the catalytic sites.

In summary, hydrated silica-supported $HgSO_4/H_2SO_4$ is an adequate and inexpensive reagent to perform the hydration of alkynes (**1**). The reaction proceeds efficiently in dichloromethane under mild conditions, and the isolation of products involves filtering and evaporating the solvent. The results show that supported aqueous-phase catalyst (SAPC) is a suitable approach to perform the hydration of alkynes with water-soluble mercury salts in an acid medium.

Acknowledgments

Financial support from the Spanish Dirección General de Investigación and Fondos Feder, (CTQ2007-65251/BQU) and Consolider Ingenio 2010 (CSD2007-00006) is gratefully acknowledged. A.A.A. thanks the Spanish Ministerio de Educación y Ciencia for fellowships. We also thank the SCSIE (Universidad de Valencia) for allowing us access to their instruments and facilities.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.042.

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8. *Silica-supported $HgSO_4/H_2SO_4$* (**3**). *General procedure*. To a stirred aqueous solution of 2.71 mL of concentrated sulfuric acid (50.8 mmol) and 2.74 g of mercuric sulfate (9.24 mmol) in 100 mL of water, 20 g of chromatographic grade silica (Merck silicagel 60, 0.040–0.063 mm, specific surface area 480–540 $m^2\,g^{-1}$, pore volume 0.74–0.84 $mL\,g^{-1}$) was added. The mixture was stirred for 15 min at room temperature and then the solvent was removed under vacuum (3–5 10^{-2} mbar) at room temperature until it reached a constant weight. The supported reagent was obtained as a free flowing white solid (34.52 g). *Caution: silica-supported $HgSO_4/H_2SO_4$ is a poisonous and corrosive solid which must be handled with care.*
9. *Hydration of alkynes* **1** *with silica-supported $HgSO_4/H_2SO_4$* (**3**). *General procedure*. To a stirred solution of 0.1 mL (0.91 mmol) of phenylacetylene (**1a**) in 10 mL of methylene chloride, 0.1 g of the silica-supported $HgSO_4/H_2SO_4$ (0.46 mmol of $HgSO_4$ and 2.54 mmol of H_2SO_4 per gram of reagent, 5 mol %) was added. The reaction mixture was heated to reflux for 24 h under stirring. The mixture was filtered and the solid washed with methylene chloride. The organic solvent was removed under vacuum to obtain 0.10 g (91% yield) of a colorless oil.