Metal-Catalyzed Alkyne Cyclotrimerizations in Supercritical Water

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This work demonstrates that supercritical water can be utilized as a benign solvent for traditional, synthetic organometallic chemistry. The cobalt(I) complex $CpCo(CO)_2$ catalyzed cyclotrimerizations of 1-hexyne, phenylacetylene, and 2-butyne to their respective benzene derivatives in water at 374 °C. Product yields and regiochemistries were in good agreement with those reported for analogous cyclizations in organic solvents. Participation by water did not interfere with the cyclizations, and hydrolysis of the alkynes was observed only in the presence of acid. Unreacted alkyne was recovered in the absence of added catalyst. Cyclizations attempted in water at 140 °C proceeded slowly and gave a multitude of products. Thus, alkyne cyclization proved to be a viable reaction in supercritical water but not in the lower temperature water. Pyridine synthesis via the coupling of alkynes and acetonitrile under supercritical conditions was also observed but was less effective due to relatively facile hydrolysis of the acetonitrile.

Introduction

Environmental concerns are making disposal of organic wastes increasingly difficult. Reaction solvents are one major source of such waste; therefore means of minimizing the amount of organic solvents entering the waste stream are of great current interest. Replacement of these solvents with water is an attractive alternative, provided the desired reactions can be enabled in water. This approach has been successfully applied to a limited number of homogeneous organometallic reactions in which the catalysts and reagents are naturally water soluble[1,2] or have been modified to be water soluble.[3,4] We have become interested in developing a more general method whereby unmodified organotransition metal catalysts and hydrophobic organic reagents can be readily solubilized in water.

Supercritical water has excellent potential for achieving this goal. It possesses a high solubility for organic molecules[5] and is reasonably accessible, with a critical temperature and pressure of 374 °C and 3205 psi, respectively. The water returns to its liquid state upon cooling, thus facilitating product separation. Reactions in supercritical water have thus far been primarily targeted toward the destruction of toxic and carcinogenic wastes[6] while the use of supercritical water as a solvent for transition-metal-catalyzed organic synthesis remains largely unexplored.[7]

We have undertaken a brief exploration of alkyne chemistry to examine the viability of traditional synthetic organometallic reactions in supercritical water.[8] The purpose of this study was to determine (1) whether synthetically useful reactions could successfully compete with hydrolysis in water at 374 °C and (2) whether

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(4) Phase-transfer reactions are not included in this consideration since they still rely on the presence of an organic solvent.

(5) The critical density of water is 0.32 g/mL. (a) Franck, E. U. *Pure Appl. Chem.* **1985**, *8*, 1065. (b) Johnston, K. P. In *Supercritical Fluid Science and Technology*; Johnston, K. P., Penninger, J. M. L., Eds.; ACS Symposium Series 406; American Chemical Society: Washington, DC, 1989; Chapter 1.

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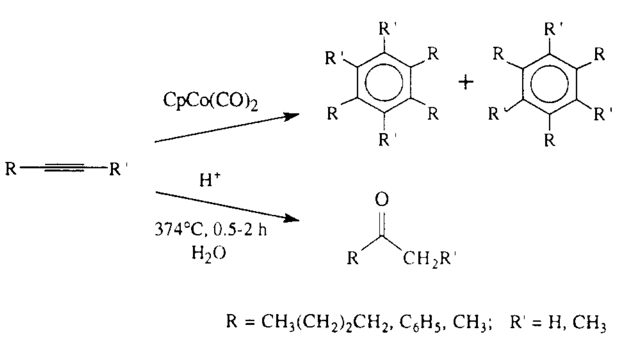
supercritical water can act as a benign solvent for carrying out previously developed reactions. Alkynes provide a convenient test system in which to probe these considerations, since they undergo both acid-catalyzed hydration[9] and well-developed coupling reactions. Also, several alkyne coupling catalysts are reported to be water sensitive[8a,c] and, in some cases, thermally sensitive,[10] and it was not known whether they would continue to function in water at 374 °C. As reported below, the answer to both these questions is affirmative for alkyne trimerization catalyzed by $CpCo(CO)_2$[11] under supercritical water conditions. The analogous cyclization of alkynes and acetonitrile to form pyridines also occurs but is somewhat inhibited due to more facile hydrolysis of the acetonitrile. Test reactions were carried out using 1-hexyne, phenylacetylene, and 2-butyne.

Results and Discussion

In each of the alkyne reactions, alkyne, water, and catalyst were sealed in quartz tubes which were then heated at 374 °C for 2 h. Alkyne conversion and product yields were determined relative to an internal benzene standard, and recoveries of 100 ± 5% were obtained in all cases. Neither introduction of air into the reaction tubes nor the amount of time the reaction mixture was held at liquid water temperature made an observable difference in the products obtained. Control reactions in which no catalyst (either metal salt or protic acid) was present led to complete recovery of unreacted 1-hexyne and 2-butyne. Although we observed no uncatalyzed hydrolysis of phenylacetylene, some low molecular weight oligomers[12] were obtained after 2 h at 374 °C. Katritzky and Siskin[13] report complete conversion of phenylacetylene after 5 days in 250 °C water, with hydrolysis to acetophenone accounting for 51% of the products. The longer reaction time may account for the observation of hydrolysis in their system; however, their hydrolysis may also result from acid catalysis (see below) since preliminary water neutralization was not specifically reported. The lack of benzene-derivative formation in our control experiments also indicates that uncatalyzed alkyne cyclization does not occur in water at 374 °C. However, neat 1-hexyne at 374 °C produced a moderate yield of the tributylbenzenes.[14] This suggests that water protects the alkyne from oligomerization, possibly by inhibiting contact between alkyne molecules through simple dilution.

One of the primary questions addressed by this study was whether or not synthetically useful reactions could successfully compete with hydrolysis in supercritical water. Hydrolysis is a very common reaction in supercritical water; therefore, the scope and limitations of this process are important considerations in developing competing synthetic processes. Acid-catalyzed hydrolysis of the alkynes to ketones occurred in the presence of protic acids or acidic metal salts (eq 1). In the case of hexyne, reaction in water at pH 6 yielded 10–14% 2-hexanone while the yield of 2-hexanone from the metal chloride reactions correlated well with the pK_a's of the metal aqua complexes. No ketone was obtained from reactions involving NaCl or $CaCl_2$, followed by increasing yields of ketone with increasing metal ion pK_a's until essentially 100% 2-hexanone was obtained from reactions with $CuCl_2$ and $SnCl_2$. 2-Butyne and phenylacetylene followed the same trends, producing nearly quantitative yields of acetophenone and 2-butanone, respectively, in the presence of $SnCl_2$. Katritzky and Siskin's proposal[15] that chloride ion acts as a strong base in superheated water is improbable and is not consistent with the acid catalysis seen here. Basic ligands such as acetate and carbonate ($CoCO_3$ and $Co(OAc)_2$) did inhibit the hydrolysis, however, and unreacted alkyne was recovered from reactions with these complexes.[16] Cobalt(II) nitrate also produced a 10% yield of 2-hexanone along with 4% hexanoic acid. The acid is presumably formed by nitrate-induced oxidation of hexanal resulting from anti-Markovnikov addition of water to the alkyne. A small amount of anti-Markovnikov addition product was also observed in the reaction of hexyne and Cu_2Cl_2, which yielded approximately 2% hexanal along with the hexanone.



(1)

The cobalt(I) complex $CpCo(CO)_2$ is an efficient alkyne cyclization catalyst in organic solvents.[17] Although it is heat sensitive, this sensitivity involves loss of the carbonyl ligands, a step which necessarily precedes alkyne coordination and cyclization and may in fact lead to more active catalytic species.[18,19a] The catalyst maintained its activity in 374 °C water, resulting in cyclotrimerization of the alkynes to form their respective benzene derivatives (eq 1). Hexyne produced a quantitative yield of 1,3,5-tributylbenzene and 1,2,4-tributylbenzene (1:3 ratio), while phenylacetylene yielded 1,3,5-triphenylbenzene and 1,2,4-triphenylbenzene in a 1:6 ratio (Table 1). These isomer ratios are in agreement with the ratios from similar reactions carried out in organic solvents.[8a] The quanti-

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[11] Abbreviations: Cp, η^5-cyclopentadienyl anion; OAc, acetate ion.

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Table I. Cyclotrimerization of Alkynes Effected by $CpCo(CO)_2$ in Supercritical Water[a]

	conversion (%)[b]	benzene(s) total (%)	isomer ratio	
			1,3,5	1,2,4
$CH_3(CH_2)_3C{\equiv}CH$	>95	>95	1	3
$C_6H_5C{\equiv}CH$	>95	>95	1	6
$CH_3C{\equiv}CCH_3$	40	5		

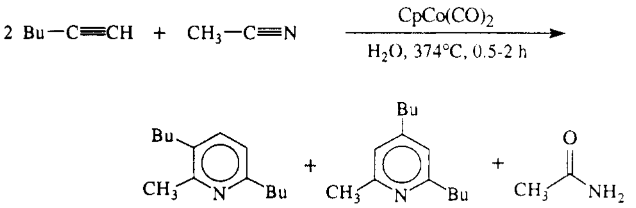
[a] 0.3 mmol of catalyst, 0.1 mL of alkyne, 0.4 mL of water at 374 °C for 2 h. [b] Relative to a benzene internal standard.

tative yields of substituted benzenes obtained from these alkynes indicate that water does not destroy the catalyst prior to completion of the reaction. 2-Butyne produced a much lower yield of hexamethylbenzene (5%). The remaining 2-butyne was recovered unreacted (60%) or was incorporated into cobalt complexes (35%). Although the hexamethylbenzene yield was lower than has been observed in organic solvents,[20] formation of coordinated species and subsequent restriction of the reaction have been observed previously.[21]

The product similarities observed between reactions run in organic solvents and those in supercritical water indicate that any participation by water in the reaction does not significantly affect the reaction pathway. Strongly coordinating solvents such as alcohols are known to inhibit alkyne complexation and therefore lower the rate of cyclization catalyzed by cobalt(I) complexes.[19b] At 374 °C, conversion of hexyne to tributylbenzenes was complete within 30 min (the shortest reaction time examined), which suggests either that water does not coordinate strongly under the reaction conditions or that the reaction is inhibited but still complete within this timeframe. The same reaction at 140 °C resulted in 33% conversion of the hexyne and yielded only 16% of the tributylbenzene isomers after 12 h. Presumably the cyclization reaction was sufficiently slow at the lower temperature that a variety of other reactions were able to successfully compete with the cyclotrimerization. The result is that cyclization is not a viable synthetic reaction in hot water, while it is in supercritical water.

$Co_2(CO)_8$ is only a moderately active cyclization catalyst in organic solvents[8a] and was significantly less active in water at 374 °C. Low tributylbenzene yields (approximately 16%, combined) were obtained from hexyne, probably due to destruction of the "unprotected" $Co_2(CO)_8$. In contrast, $CpCo(CO)_2$ is stabilized as an active cyclopentadienylcobalt(I) species by its cyclopentadienyl ligand in organic solvents and a similar stabilization is almost certainly in effect in the supercritical water.[19b] This cyclopentadienyl ligand protection may prove useful in designing catalysts for other reactions in supercritical water, as well.

Extension of the alkyne cyclizations to include pyridine formation[19] by coupling two alkynes with an acetonitrile was not productive due to rapid hydrolysis of the acetonitrile. Acetamide formation was much more rapid than hydrolysis of the alkynes and even occurred to a limited extent in neutral water. In the presence of hexyne and $CpCo(CO)_2$ as catalyst, a 15% yield of the pyridine isomers 2,4-dibutyl-6-methylpyridine and 3,6-dibutyl-2-methylpyridine in a 1:1 ratio was obtained (eq 2). This is in contrast



(2)

to pyridine yields of 40–58% (approximately 2:1, 2,4,6-trialkylpyridine to 2,3,6-trialkylpyridine) reported for similar reactions in organic solvents at 130 °C.[19b,22] The major products from the coupling reaction in supercritical water were again the benzene isomers expected from simple hexyne cyclization, while the remaining acetonitrile was converted to acetamide.

Conclusion

This work demonstrates that supercritical water can act as a benign solvent for traditional organometallic chemistry even when that chemistry involves extremely hydrophobic reagents. The water did not interfere with alkyne cyclizations catalyzed by $CpCo(CO)_2$, neither deactivating the catalyst nor hydrolyzing the alkynes. In fact, alkyne hydrolysis was observed only in the presence of acid, which reinforces the general acid-catalyzed nature of hydrolytic processes in supercritical water.[6,13,15] Not surprisingly, traditional metal-mediated alkyne chemistry is not 100% adaptable to supercritical water, as evidenced by the successful competition of acetonitrile hydrolysis with its respective cyclization reactions. On the basis of the success of the alkyne trimerizations, however, we are confident that further studies will reveal a wide variety of organometallic reactions which are directly portable to this medium.

Experimental Section

Water was distilled from basic potassium permanganate and then neutralized by vigorous boiling under a stream of purified argon and degassed under vacuum. Alkyne (100 μL), catalyst (0.3 mmol), and water (400 μL) were sealed in a quartz tube having a total volume of 1.5 mL. Up to 11 tubes were then placed in a Parr bomb which was counterpressured to 3000 psi with argon. The bomb was placed in a tube furnace and heated to 374 °C for 0.5–2 h. Following the reaction, the tubes were cracked and the organic layer was separated and analyzed. Yields were determined relative to an internal benzene standard and recoveries of 100 ± 5% were obtained in all cases. Several experiments were run in D_2O and monitored directly by ^1H NMR for water-soluble products. A minimum of three trials were performed to confirm the reproducibility of each experiment.

Postreaction cobalt species resulting from $CpCo(CO)_2$ and $Co_2(CO)_8$ were observed in both the aqueous and organic layers by X-ray fluorescence spectroscopy. The identities of these species were not determined. In most cases the amount of cobalt present in the organic layer was insufficient to interfere with subsequent analyses; however, it could be removed by vacuum transfer when necessary. Neither the cobalt in the aqueous layer nor the cobalt in the organic layer was capable of catalyzing further cyclizations. We currently have no means of determining whether deactivation occurs under supercritical conditions or during the subsequent cool down period.

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