FeCl$_3$-H$_2$O: a specific system for arylacetylene hydration

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Abstract

FeCl$_3$ has been found to be very specifically effective in the hydration of terminal aromatic alkynes to the corresponding methylketones.

Keywords: Iron; Alkyne; Hydration

1. Introduction

Hydration is one of the most useful methods of functionalizing unactivated alkynes, and has found considerable synthetic use [1]. The reaction is classically carried out in dilute acidic conditions with mercury ion salts as catalyst [2]. However, the loss of the catalyst during the reaction and environmental problems are severe limits to this method. Numerous attempts have been made to develop non-mercury alkyne hydration systems; metal catalysts, including Cu(II), Pd(II) [3,4], Pt(II) [5–7], Ru(0) [8], Os(II) [9], Au(III) [10], or Rh(III) [11] have been used with varying degrees of success.

During our investigation of the reaction of alkynes with iron complexes, we serendipitously found that phenylacetylene, in the presence of FeCl$_3$, was very easily hydrated to acetophenone in the presence of mere traces of water. This reaction, to the best of our knowledge, has not been reported so far. This led us to experiment with the FeCl$_3$-H$_2$O system as a new alkyne hydration procedure and we found it to be remarkably specific.

2. Experimental section

All solvents were of reagent quality and were distilled before use. The alkyne substrates were purchased from Aldrich. The iron complexes were obtained from Aldrich.

Elemental analyses were performed by the Service Central de Microanalyses of the CNRS. Infrared spectra were recorded on a Bruker FT-IFS 45 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AC 200 spectrometer. Mass spectra were obtained with a Finnigan MAT INCOS 500E spectrometer (GC-MS). The GC analyses were performed on a Delsi-300 chromatograph (column SE 30, 10%, 3 m × 3/8") and on a Varian-3400 chromatograph (capillary column DB-1, 25 m).

2.1. General procedure for alkyne hydration

To 1.26 g anhydrous FeCl$_3$ (7.77 mmol) solution in CH$_2$Cl$_2$ (40 ml), 0.42 ml (23.30 mmol) of H$_2$O were added. Phenylacetylene (0.793 g; 7.77 mmol) was then added to the resulting yellow-orange solution, together with n-octane (0.17 g; 1.51 mmol) as an internal standard for GC. The reaction mixture was stirred for 24 h at room temperature. After extraction with an H$_2$O-Et$_2$O 1 : 1 mixture, the organic phase was separated and analysed. This general procedure was applied to the alkynes listed in Table 1.

3. Results

Phenylacetylene, when allowed to react with 3 equivalents of water in the presence of 1 equivalent of FeCl$_3$, cleanly gave quantitative conversion into acetophenone

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Table 1
Alkyne hydration in the presence of FeCl₃

Entry	Alkyne	Temperature (°)	Time (h)	Ketone (%)	Chloroalkene (%)
1	PhC≡CH	22	24	92	—
2	H₉C₄C≡CH	65	24	52	10
3	H₁₃C₆C≡CH	65	24	50	20
4	EtC(OH)MeC≡CH	70	24	0	0
5	PhC(OH)MeC≡CH	70	24	0	0
6	H₇C₃C≡CC₃H₇	70	72	10	53
7	PhC≡CPh	70	72	0	—

within 24 h at room temperature (Table 1, entry 1). The same reaction procedure was then experimented with for various alkynes and our results are listed in Table 1.

Terminal aliphatic alkynes, exemplified by 1-hexyne (entry 2) and 1-octyne (entry 3) were also totally converted under the same conditions. However, the selectivity towards the hydration product, i.e. the corresponding methylketone amounted to ca. 50%, the second major product being the 2-chloroalkene. A different behaviour was observed with 3-methylpent-1-yn-3-ol (entry 4) and 3-phenylpent-1-yn-3-ol (entry 5), aliphatic terminal alkynes bearing an α-hydroxy function. No ketone and no chloroalkene could be detected in the resulting products of the reaction, which consisted of intractable polymers.

With 4-octyne (entry 6), taken as a typical internal aliphatic alkyne, the reaction was slowed down (87% conversion after 72 h at 70°C), and 4-chlorooct-2-ene (53%) was favoured over the ketone (10%). No reproducible results could be obtained for diphenylacetylene (entry 7): the corresponding chloroalkene, but no ketone, were detected in the reaction products.

The results in Table 1 indicate a net selectivity, of the FeCl₃-assisted hydration process, for terminal aromatic alkynes such as phenylacetylene. This was further illustrated through the following competition reactions. In a first experiment, phenylacetylene and 1-hexyne in a 1:1 molar ratio were simultaneously reacted with H₂O (3 equivalents) and FeCl₃ (1 equivalent) in dichloromethane for 72 h at room temperature: phenylacetylene was totally converted to acetophenone, while 90% of 1-hexyne remained unchanged. Similar results were obtained when simultaneously reacting phenylacetylene and diphenylacetylene: acetophenone and diphenylacetylene were the only compounds detected in the reaction medium after 48 h contact at room temperature.

4. Influence of the iron complex and of the solvent

We selected phenylacetylene, as a typical terminal aromatic alkyne, and attempted to perform its hydration

in the presence of various iron derivatives. The hydration reaction was found to be totally inhibited in the presence of coordinated iron(III) chloride such as the aquo [FeCl₃ · 6H₂O] complex, or the [FeCl₃(L)₂] derivatives with L = PPh₃ or OPPh₃. Furthermore, iron(II) compounds such as anhydrous FeCl₂ or [FeCl₂ · 4H₂O] were not capable of promoting phenylacetylene hydration in our conditions. In all these experiments, phenylacetylene remained unchanged after 24 h contact at room temperature in marked contrast with its total conversion to acetophenone in the presence of FeCl₃ under the same experimental conditions.

In agreement with these results, no reaction occurred when phenylacetylene was allowed to react with the FeCl₃ + H₂O system in coordinating solvents such as acetonitrile. The hydration of phenylacetylene proceeded very slowly in pentane or diethyl ether where FeCl₃ is only poorly soluble.

We take these results to indicate that coordination of the terminal alkyne to iron(III) is a prerequisite for its hydration.

5. Kinetics of the hydration reaction

Fig. 1 displays the alkyne consumption (curve 1a) with time, together with the formation and evolution of the reaction products during the course of phenylacetylene hydration in dichloromethane at room temperature in the presence of FeCl₃. The data in Fig. 1 were determined by monitoring the concentrations of the various compounds by GC in the presence of n-octane as an internal standard.

Fig. 1 shows that, in our experimental conditions, the alkyne was totally converted after 4 h. It also shows the simultaneous formation of both methylketone and chloroalkene from the very beginning of the reaction. The concentration in 2-chlorostyrene went through a maximum (35%) after 3 h contact between the reactants and then decreased to the benefit of acetophenone. Acetophenone was the only organic compound detected in the reaction medium after 20 h.
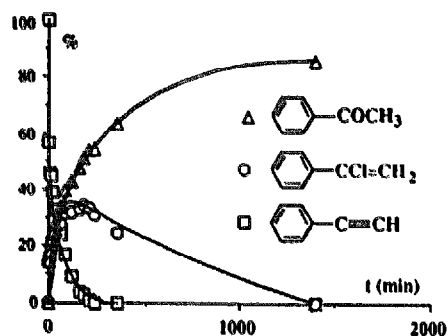

Fig. 1. Kinetics of phenylacetylene transformation in FeCl₃-promoted hydration.

The data presented here clearly indicate that two reactions are operating, one leading directly to the ketone and the other to the chloroalkene. This latter reaction appears to be very similar to that observed in anhydrous conditions [11,12]: intermediate formation of a π-alkyne–$FeCl_3$ adduct has been proposed which evolves towards the chloroalkene together with reduction of iron(III) to iron(II). Hydrolysis of the chloroalkene, which has been shown to be rather slow [12], affords acetophenone. The rapid formation of the ketone, i.e. the former reaction, could imply hydrolysis of the same π-bonded intermediate, like classical mercury-catalyzed procedures [13], the higher reactivity of phenylacetylene being related to its higher electrophilic character when compared with the other alkynes in this study. It could also, as has been shown for the phenylmercuric hydroxide hydration system [14], go through reaction of the acidic terminal acetylenic proton with the Fe–Cl moiety. The rapid hydrolysis of the resulting σ-acetylide $FeCl_2$ adduct would then bring acetophenone. σ-Acetylide iron complex formation, is only possible for terminal acetylenes; further, it is likely to be favoured for the more acidic phenylacetylene, which brings acetophenone quantitatively, as compared with alkylalkynes for which a mixture of chloroalkene, ketone and polymers are obtained.

However, no definite evidence for either a π- or a σ-bonded intermediate has so far been found in the infrared of the reaction medium. Further, it should be noted that a radical mechanism can not, at this stage, be eliminated.

6. Conclusion

We have experimented with a new, easy process for terminal alkyne hydration which uses stoichiometric amounts of $FeCl_3$ and water in dichloromethane. The most striking feature for this process is certainly its specificity: (i) $FeCl_3$ is capable of promoting this reaction, but not the $[FeCl_3 \cdot 6H_2O]$ aquo complex nor iron(II) chloride; (ii) only terminal alkynes are hydrated in this process, the hydration of arylalkynes being much faster than that of aliphatic alkynes.

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