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Alkyne hydration using Pt(II) catalysts

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Abstract

A series of Pt(II) derivatives has been found to be quite effective as alkyne hydration catalysts. These are new and differ from many other hydration catalysts in that there is no need to add protonic acids to or as the media. They are effective for hydration of electron rich alkynes but not useful for electron deficient systems. Finally, using unsymmetrically substituted alkynes, slight regioselectivity is observed with the carbonyl moiety preferring the position closer to the bulky substituent. When substituents have heteroatoms such as oxygen or sulfur, a chelation control process seems to govern the regiochemistry and high selectivities may be obtained.

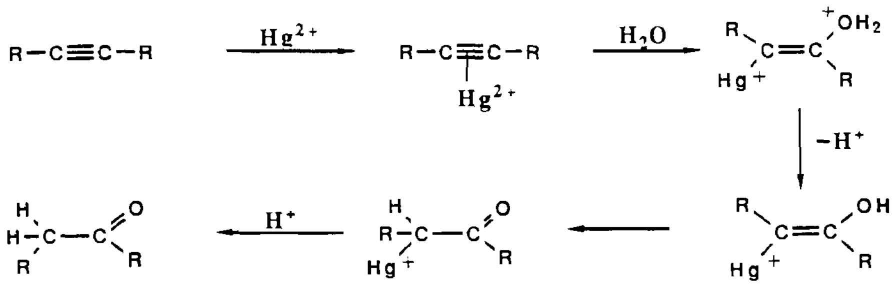
Key words: Catalysis; Alkyne hydration; Platinum complexes; Regioselectivity; Mercury complexes

Introduction

Unactivated alkynes are abundant as a hydrocarbon source and in organic syntheses. Subsequent hydration often represents an excellent means of functionalization or further elaboration. The hydration catalyst of choice to yield ketones is Hg(II) complexes with catalytic amounts of H_2SO_4 or pTsOH [1, 2]. Other metal catalysts that have been employed with varying degrees of success include Cu(I) [3], Ag(I) [3], Pd(II) [3], Ru(III) [3], Rh(III) [3] and Os(II) [4]. These reactions are accelerated with protonic acids. One convenient reagent is Nafion-H impregnated with mercuric oxide [5]. This resinous combination is also quite acidic. Equation (1) describes the reaction with Hg(II) as it is presently perceived [1]. For terminal alkynes, only methyl ketones are obtained in accordance to Markovnikov's rule. However, there are numerous side products. The reaction is also catalyzed with regioselectivity through use of an Au(III) catalyst [6].

With regard to platinum-facilitated addition reactions with alkynes, other investigators have concentrated on the addition of methanol to cationic complexes [7, 8]. Jensen and Trogler [9] have reported the analogous hydration of nitriles with a hydridoplatinum(II) hydroxide complex. Finally, in a paper by Chatt *et al.* [10] in 1961, dealing with the preparation of alkyne derivatives of Pt(II) complexes, it was reported that ethanolic $Na_2PtCl_4 \cdot 4H_2O$ reacted with several alkynes to form ketones. They speculated that hydration was catalyzed by colloidal platinum generated by reduction of the above-mentioned salt.

In this paper, we wish to elaborate on our recent results which demonstrate that Pt(II) is an excellent hydration catalyst for unactivated alkynes [11]. Further, efforts to control the regiochemistry of hydration with unsymmetrically substituted alkynes will be discussed.



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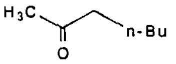
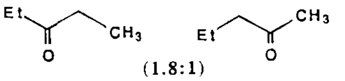
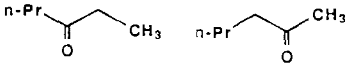
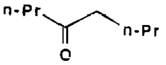
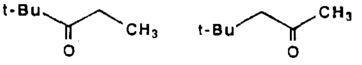
Results and discussion

Specific results on alkyl-substituted alkynes are listed in Table 1. It can be seen that the catalyst works quite well with unactivated (electron rich) alkynes but is not effective for activated (electron poor) alkynes. There is some regioselectivity but it is not impressive. It should be noted, however, that the regioselectivity always results in the carbonyl moiety being nearer the sterically encumbered side except for the terminal alkyne entry.

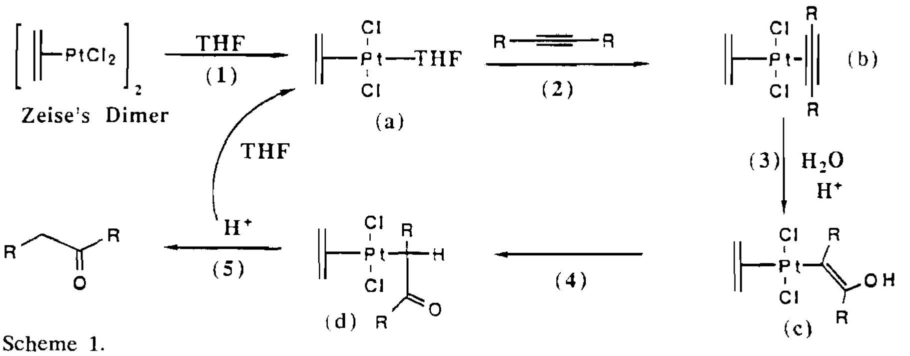
With regard to additional mechanistic insight, the following results were obtained. The reactions obey pseudo first order kinetics with regard to [alkyne] over the majority of the time span. However, in the first portion, there is an inhibition period suggesting that the Pt(II) source (Zeise's dimer) is a precatalyst. There is *no* kinetic isotope effect using D_2O and protonic acids *do not* accelerate the reaction. Finally, efforts to capture the intermediate as an enol ether using an alcohol rather than water have been unsuccessful. In fact, there is no evidence that alcohols, acetic acid, amines or phenols add to alkynes via Zeise's dimer catalysis. In other words, the reaction appears to be chemospecific for H_2O. With these results in mind, the pathway shown in Scheme 1 represents a preliminary hypothesis.

There are several suggestions/conclusions to be made from Scheme 1. First, it looks as though simple platinum(II) halides might be effective catalysts (i.e. $PtCl_2$). Second, the reason for the chemospecificity for water appears to be that step (3) is reversible when tautomerization is prevented, as in the cases of RXH additions ($X = O, N$). Third, the regioselectivity observed (Table 1) is rationalized via the detailed structure of intermediate (b). We propose that the regiochemistry is derived from the metal atom being unsymmetrically bound to the alkyne due to steric repulsion. This places more cationic charge on the carbon atom nearest the

TABLE 1. Substrates catalytically hydrated with Zeise's dimer[a]

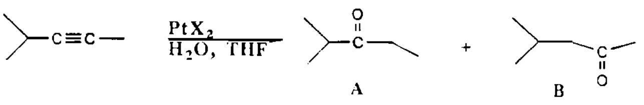
Alkyne	Product (ratio)	Extent of reaction[b] (%) (isolated yield, %)
1-Heptyne		93 (85)
2-Pentyne	 (1.8:1)	100 (88)
2-Hexyne	 (2:1)	100 (84)
4-Octyne		100 (93)
4,4-Dimethyl-2-pentyne	 (2.7:1)	95 (89)
Dimethylacetylene-dicarboxylate	a myriad of products in extremely low yield	<10

[a] $[PtCl_2(C_2H_4)]_2$. [b] From ^1H NMR spectroscopy.



Scheme 1.

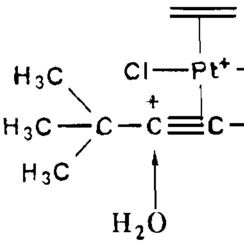
TABLE 2. Regioselectivity for hydration of 4-methyl-2-pentyne using PtX_2 complexes



	A	B	$t_{1/2}$ (h)
ZD	71	29	4.0
$PtCl_2$	64	36	3.8
$PtBr_2$	74	26	
PtI_2	78	22	14.8
Hg(II)	31	69	

Conversion in all cases is greater than 94% with isolated yields near 87%.

steric bulk and hence the bonding of water to that carbon (see structure below). If this is true, perhaps means other than steric effects can be employed to give higher regiospecificity. The two subsequent sections address the issues of simple platinum halide catalysis and chelation control for enhanced regioselectivity.



(b)

Simple platinum(II) complexes

As stated above, intermediate (b) looks a great deal like platinum(II) chloride. And since platinum halides are both less expensive than Zeise's dimer and more accessible, we have begun to investigate simple platinum(II) species. Table 2 shows the comparative results. As with Zeise's dimer, these simple platinum halides are quite effective catalysts giving high yield and exhibiting modest regioselectivity. Clearly higher regioselectivity results from lower rates (i.e. PtI_2). It is interesting that mercury leads to a reversal in regioselectivity [12].

Chelation control for enhancing regioselectivity

The question arose as to whether a heteroatom in the alkyne substrate could profoundly affect the regioselectivity via chelation as shown in the following structure. Data are listed in Table 3 which clearly show that chelation control is effective. Having the heteroatom beta or gamma to the alkyne is the most effective. The lack of complete regiospecificity is not clear. Perhaps rotation of the ethyl 'tail' of the ethoxy moiety is inhibiting complete chelation control or, in THF, the intramolecular oxygen may not be as competitive as expected. Results from reactions (2) and (3) appear to confirm that both hypotheses play a role in the observed regioselectivity. By reducing the ethyl 'tail' to a methyl moiety substantial improvement in regioselectivity was observed (eqn. (2)). Further, by replacing the oxygen with a better chelating element, S, again the regioselectivity was increased.

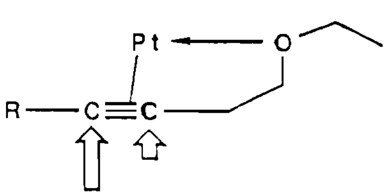
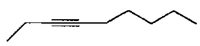
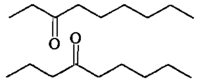
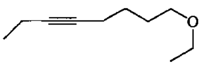
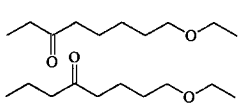
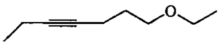
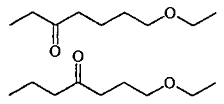
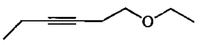
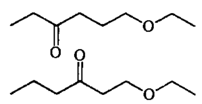
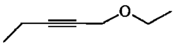
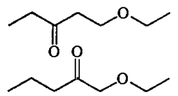
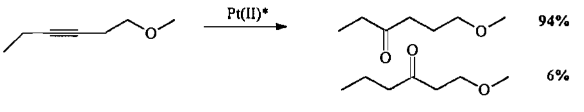


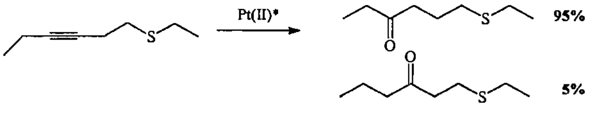
TABLE 3. Regioselectivity enhancement using chelation control[a]

Alkyne	Products[b] (ratio %)
(1) 	 (40) (60)
(2) 	 (55) (45)
(3) 	 (65) (35)
(4) 	 (86) (14)
(5) 	 (88) (12)

[a]Zeise's dimer as catalyst. [b]Conversions are >95%.

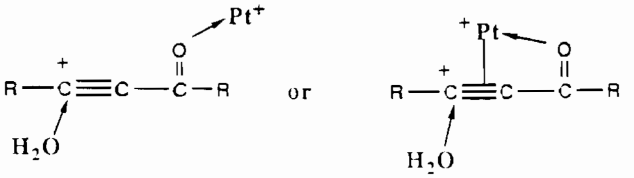


(2)



(3)

Finally, three other substrate types were tried in an effort to find additional means of controlling regioselectivity, eqns. (4), (5) and (6). The results shown in eqn. (4) indicate regiospecificity with high yields. These data can be rationalized as a result of either Lewis acid catalysis or chelation control combined with a Lewis acid contribution as shown below. Unfortunately, at this time it is not possible to make the correct choice between these alternatives. Thus, reaction (5) was run. While it is not as regiospecific as that shown in eqn. (4), its selectivity is quite high suggesting that chelation control by carbonyl oxygen is slightly better than ether oxygen (entry 4 in Table 3).



Equation (6) represents the final example to be reported in our attempts to find additional means for controlling regioselectivity. The question was whether the water would attack the terminal carbon of the alkyne to give a π allyl platinum complex or choose the inner carbon because the platinum atom is pushed to the terminal alkyne carbon by steric factors. This latter postulate has merit as it simultaneously results in some allylic cation stabilization. Obviously, from the results, the latter postulate appears to be the correct interpretation as regiospecificity is observed.

Conclusions

New, simple alkyne hydration catalysts have been elaborated using a limited number of unactivated alkynes. These platinum(II) complexes offer some distinct advantages over Hg(II) catalysts in that cleaner reaction products are obtained and enhanced regioselectivity is observed with some substrates.

Experimental

General

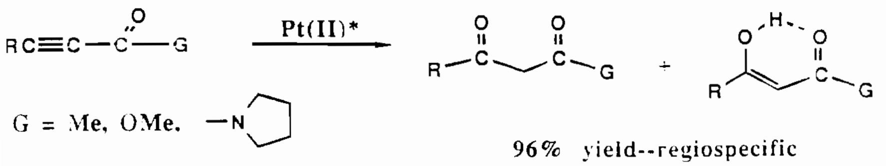
Product ratios were obtained using a Varian 3500 capillary gas chromatograph with an Alltech SE-54 capillary column. Kinetic studies were conducted using a Bruker 250 MHz NMR spectrometer with temperature probe ±3 °C. Zeise's dimer was prepared from K_2PtCl_4 generously loaned from Johnson Matthey. Platinum(II) chloride and platinum(II) iodide were used as purchased from Strem Chemicals. The alkyne substrates 2-hexyne, 4-methyl-2-pentyne and 4,4-dimethyl-2-pentyne were used as purchased from Lancaster Synthesis.

Platinum(II) chloride, bromide and iodide catalyzed hydration of alkyne substrates

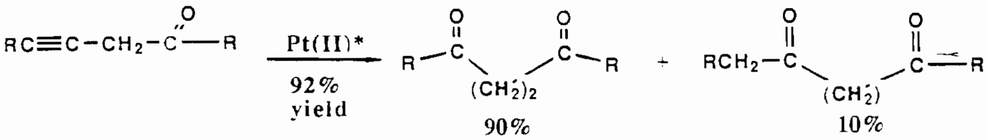
In a 25 ml round bottomed flask were placed THF (10 ml), $PtCl_2$ (0.095 mmol) (or $PtBr_2$ or PtI_2), alkyne (13.5 mmol) and water (22 mmol). The reaction mixture was stirred at reflux (*c.* 60 °C) for 12 h. The platinum(II) catalyst was removed from the reaction mixture by Kugelrohr distillation. Product ratios for the resulting distillates were determined by capillary GC and are listed in Table 2.

Kinetic studies on the platinum(II) catalyzed hydration of 4-methyl-2-pentyne

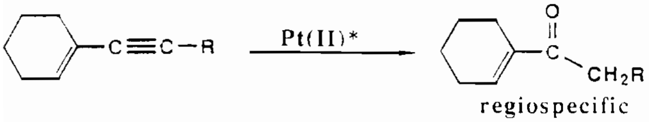
In a 5 mm NMR tube were placed d_8-THF (0.5 ml), 4-methyl-2-pentyne (0.675 mmol), platinum(II) catalyst



(4)



(5)



(6)

* Zeise's Dimer

(0.005 mmol), water (1.1 mmol) and $CHCl_3$ (0.33 mmol, internal standard). The sample was then placed in the Bruker 250 MHz NMR spectrometer at a temperature of 50 °C and data collected for more than 12 h. Integration of the spectra, with respect to the peak of 1.65(s) ppm which corresponds to the C-1 methyl of the alkyne, allowed for monitoring the disappearance of 4-methyl-2-pentyne. First order kinetic treatment of these data afforded half-lives which are listed in Table 2.

Mercury(II) catalyzed hydration of alkyne substrates [13, 14]

In a 5 ml round bottomed flask were placed methanol (1.0 ml), red HgO (0.046 mmol), alkyne (2.2 mmol), water (0.4 ml) and conc. H_2SO_4 (0.2 ml). The reaction mixture was stirred at reflux (*c.* 60 °C) for 12 h. Water (2 ml) was then added followed by NaCl (0.3 g) to salt out the products. The mixture was subsequently decanted from the undissolved salts and extracted with 1 ml of methylene chloride. These extractions were Kugelrohr distilled and the distillate dried with anhydrous $MgSO_4$. Product ratios were determined by capillary GC and are listed in Table 2.

Syntheses

1-Ethoxy-2-pentyne, 1-ethoxy-3-hexyne, 1-ethoxy-4-heptyne and 1-ethoxy-5-octyne

To a 250 ml round bottomed flask equipped with Claisen adapter, condenser and stirbar, were added 223 mmol $NaNH_2$, 60 ml dry THF and 267 mmol ethyl iodide. The mixture was brought to 50 °C with stirring followed by dropwise addition of a solution of 89.2 mmol of the appropriate alkynyl alcohol (propargyl alcohol, 3-butyn-1-ol or 5-hexyn-1-ol) in 10 ml dry THF. The reaction mixture was allowed to stir at 50 °C for 5 h. Water was then added to completely dissolve the white precipitate and form two distinct clear layers. The aqueous layer was removed and extracted with two 20 ml portions of ether. All organics were then combined, dried over Na_2SO_4 and solvent removed by rotoevaporation. The remaining liquid was then Kugelrohr distilled to afford a colorless, clear product (95%).

1-Methoxy-3-hexyne

To a 200 ml round bottom flask equipped with Claisen adapter, condenser and stirbar, were added 67.5 mmol $NaNH_2$, 30 ml dry THF and 67.5 mmol methyl iodide. The mixture was brought to 50 °C with stirring followed by slow addition of a solution of 45 mmol 3-hexyn-1-ol in 5 ml dry THF. The reaction mixture was allowed to stir at 50 °C for 2 h. Water was then added to completely dissolve the precipitate. The aqueous layer was removed and washed twice with ether. The organics were then combined and dried over $MgSO_4$. Removal of the solvent in vacuo afforded the pure product in 94% yield.

Ethyl 3-hexynyl sulfide

To a 250 ml round bottom flask were added 100 mmol 3-hexyn-1-ol, 175 mmol triethyl amine and 100 ml dry CH_2Cl_2. The flask was then immersed in a dry ice/acetone bath. Methanesulfonyl chloride (125 mmol) was then added to the reaction mixture dropwise over a 10 min period. The reaction mixture was then allowed to warm to 0 °C and washed once with ice cold water, and then with ice cold HCl solution (3 M), and then again with water. The organic layer was dried with $MgSO_4$, rotoevaporated to remove solvent and yield the alkynyl sulfonate ester. The sulfonate ester was then added slowly to a stirring solution of 120 mmol NaOH and 120 mmol ethyl mercaptan in 30 ml ethanol/H_2O (5:1) cooled in an ice bath. A precipitate formed and after 1 h of stirring, 100 ml of brine were added and the mixture transferred to a separatory funnel. The mixture was extracted three times with 20 ml portions of pentane. The organics were then combined, dried over $MgSO_4$ and solvent removed *in vacuo*. Short-path distillation afforded the pure product in 82% yield.

3-Nonyn-2-one

To a 100 ml round bottomed flask equipped with Claisen adapter, condenser and magnetic stirbar were added 2.45 g (100 ml) Mg turnings, a few iodine crystals and 20 ml dry ether. To this stirring mixture 13.1 g (120 mmol) ethyl bromide were added dropwise via syringe. After all the Mg was digested, 7.55 g (80 mmol) 1-heptyne were added dropwise. After *c.* 15 min 4.4 g (100 mmol) acetaldehyde in 5 ml dry ether were added to the reaction mixture and then allowed to stir for 1 h. HCl (3 M) was added slowly to quench the reaction until two distinct layers were visible. The organic layer was isolated and combined with ether extractions of the aqueous layer. The combined organics were dried with $MgSO_4$ and the solvent removed by rotoevaporation to yield the 3-nonyn-2-ol. Subsequent oxidation of this ynol by Jones' reagent afforded the 3-nonyn-2-one product (89% yield).

N-(2-Octynoyl) pyrrolidine [15]

To a 250 ml round bottomed flask fitted with condenser were added 1.84 g (25.9 mmol) pyrrolidine in 50 ml dry CH_2Cl_2 followed by slow addition of 13 ml of 2.0 M $Al(CH_3)_3$ in hexane. This mixture was stirred for 20 min at room temperature followed by dropwise addition of 3.96 g (25.7 mmol) methyl 2-octynoate. The reaction mixture was then warmed to 41 °C and stirred for 36 h. Reaction was quenched by careful addition of dilute HCl. The organic layer was isolated and combined with CH_2Cl_2 extractions of the aqueous layer, dried over $MgSO_4$ and the solvent removed by rotoevaporation to afford 2.5 g of the ynamide.

4-Heptyn-2-one

To a 250 ml Erlenmeyer flask were added 50 ml acetone and 2.5 g of 4-heptyn-2-ol. The mixture was submerged in an ice bath and stirred while being titrated with Jones' reagent. Acetone was then removed by rotoevaporation followed by ether extraction of the residue. The combined ether extracts were dried over Na_2SO_4 and the solvent removed by rotoevaporation, affording 2.2 g of 4-heptyn-2-one (89.7% yield).

1-Propynyl cyclohexene

To a 250 ml round bottomed flask equipped with Claisen adapter and condenser and magnetic stirbar were added 4.86 g (0.124 mmol) $NaNH_2$, 17.56 g (124.0 mmol) methyl iodide and 50 ml dry THF. The mixture was stirred and brought to 50 °C followed by slow addition of 8.76 g (82.5 mmol) 1-ethynyl cyclohexene. The reaction mixture was allowed to stir for 5 h at 50 °C followed by quenching by addition of distilled water until two distinct clear layers were observed. The organic layer was isolated and later combined with two 20 ml ether washings of the aqueous layer. The combined organics were dried with Na_2SO_4 and the solvent removed by rotoevaporation, affording 9.12 g of the pure product (92% yield).

General procedure for hydration experiments

To a 50 ml round bottomed flask were added 20 ml THF, 9.0 mmol alkyne substrate, 15 mmol H_2O and 1–4 mol% Pt(II) in the form of Zeise's dimer. The reaction mixture was then allowed to stir at reflux for 24–48 h. The solvent was removed by rotoevaporation and the sample analyzed by NMR spectroscopy.

Acknowledgements

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