



Platinum (II) catalyzed addition of water and alcohols to alkynes
by John Wesley Hartman

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in
Chemistry

Montana State University

© Copyright by John Wesley Hartman (1996)

Abstract:

An alternative catalytic method of adding water and alcohols to alkynes was examined. Platinum(II) in the form of Zeises Dimer, simple platinum halides, and platinate salts have been successfully employed as mild and selective catalysts. The hydration conditions require only 1 mol% platinum(II), alkyne, water, and THF solvent, and can be run at ambient temperature or at reflux. The catalytic system displays modest to excellent regioselectivity. A novel and facile route to α,β -unsaturated ketones is encountered when hydrating secondary and tertiary α -hydroxy- or α -methoxy-alkynes. Alcohol additions are effected under identical mild conditions when using Na_2SO_4 or 2,6-di-*t*-butylpyridine as a co-catalyst. Alcohol addition to conjugated alkynyl ketones and alkynyl esters provides a facile protocol for keto-enol ether synthesis. Four major mechanisms, depending upon the identity of the alkyne substrate, have been developed and evaluated based on the results of this investigation.

PLATINUM(II) CATALYZED ADDITION OF WATER
AND ALCOHOLS TO ALKYNES

by

John Wesley Hartman

A thesis submitted in partial fulfillment
of the requirements for the degree

of

Doctor of Philosophy

in

Chemistry

MONTANA STATE UNIVERSITY-BOZEMAN
Bozeman, Montana

August 1996

© Copyright

by

John Wesley Hartman

1996

All Rights Reserved

D378
H2559

APPROVAL

of a thesis submitted by

John Wesley Hartman

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

Paul W. Jennings

Dr. P. W. Jennings
(Signature)

8/30/96
Date

Approved for the Department of Chemistry

David M. Dooley

David M. Dooley
(Signature)

9/25/96
Date

Approved for the College of Graduate Studies

Robert Brown

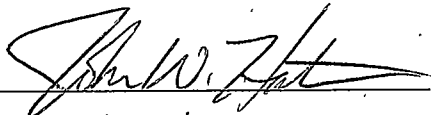
R. Brown
(Signature)

10/23/94
Date

STATEMENT OF PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for a doctoral degree at Montana State University-Bozeman, I agree that the Library shall make it available to borrowers under rules of the Library. I further agree that copying of this thesis is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U.S. Copyright Law. Requests for extensive copying or reproduction of this thesis should be referred to University Microfilms International, 300 North Zeeb Road, Ann Arbor, Michigan 48106, to whom I have granted "the exclusive right to reproduce and distribute my dissertation in and from microform along with the non-exclusive right to reproduce and distribute my abstract in any format in whole or in part."

Signature



Date

8/30/96

ACKNOWLEDGEMENTS

For the help received both inside and outside the lab, and in the preparation of this thesis, I owe a debt of sincere gratitude to the following people: God, Saint Mary, and Saint Jude; my Mom and Dad; my wife Denise and our beautiful children; my sisters Mary Pat and Jennifer; Don and JoAnn Marks; past and present members of the Jennings Research Group: Dr. Fred Stewart, Dr. Brian Williams, Mark Dimke, and Steve Eversoll; my talented undergraduate researchers Jennifer Calkins, Victoria Koelzer, Denise Brokke, and Rashed Abdullah; and Professors David Dooley, Arnold Craig, and Wyn Jennings for the opportunity of experiencing the trials and tribulations associated with teaching the evergreen subject of chemistry.

In addition, I gratefully acknowledge financial support from the National Science Foundation, the Petroleum Research Fund administered by the American Chemical Society, the Department of Energy's Experimental Program for Stimulating Competitive Research (EPSCoR), and Johnson Matthey for their generous loan of platinum salts.

TABLE OF CONTENTS

	Page
APPROVAL.....	ii
STATEMENT OF PERMISSION TO USE.....	iii
ACKNOWLEDGEMENTS.....	iv
TABLE OF CONTENTS.....	v
LIST OF TABLES.....	vii
LIST OF FIGURES.....	viii
ABSTRACT.....	xii
INTRODUCTION.....	1
Background.....	3
Hydration of Alkynes.....	3
Alcohol Addition to Alkynes.....	15
Mechanism.....	19
RESULTS AND DISCUSSION.....	25
Alkyne Hydration with Platinum(II) Halides.....	25
Clean Reaction Mixtures.....	32
Kinetic Studies.....	34
Other Pt(II) Complexes.....	36
Acid-Sensitive Substrates.....	43
Alkynyl Alcohols.....	44
Mechanism of Hydration-Elimination.....	49
Ketals and Acetals.....	56
Alkynyl Carbonyl Substrates.....	60
Alcohol Protecting Groups.....	62
Alkoxy Alkynes.....	62

Conjugated Alkenyl and Aryl Acetylenes.....	68
Alcohol Additions to Alkynes.....	70
Addition of Ethylene Glycol.....	75
Role of Sulphate.....	75
Regioselectivity.....	77
Kinetic study on Alcohol Addition.....	78
Alcohol Addition to Alkynyl Ketones and Esters.....	81
Conclusion.....	90
EXPERIMENTAL.....	91
REFERENCES.....	117
APPENDICES.....	122
Appendix A: Hydration Kinetic Data.....	123
Appendix B: Alcohol Addition Kinetic Data.....	129

LIST OF TABLES

Table 1. Selected Alkyne Substrates, Products, and Yields	11
Table 2. Hydration of 2-hexyne.....	27
Table 3. Hydration of 4-methyl-2-pentyne.....	28
Table 4. Hydration of 4,4-dimethyl-2-pentyne.....	29
Table 5. Alkyne half-lives with selected catalysts	35
Table 6. Hydration of selected alkynyl alcohols.....	44
Table 7. Alkyne and Alkoxy Alkyne Hydrations.....	63
Table 8. Addition of various alcohols to 4-octyne	74
Table 9. Different bases as co-catalysts.....	76
Table 10. Regioselectivity using various alcohols on 2-hexyne	78

LIST OF FIGURES

Figure 1. Nucleophilic additions to alkynes.....	1
Figure 2. Mechanism for Hg(II) catalyzed hydration	4
Figure 3. Hydration products of acetylenic compounds.....	4
Figure 4. Alkynyl ketones (n = 2 or 3) and alkynyl ester	5
Figure 5. Regiospecificity via carbonyl participation.	6
Figure 6. Hydration of alkynes using formic acid.	7
Figure 7. Alkynone threshold for Pd(II) catalyzed hydration.	8
Figure 8. Hydroboration of 1-cyclohexylpropyne with catecholborane.....	9
Figure 9. Zeise's Dimer.....	10
Figure 10. Platinum-catalyzed alkyne hydration	10
Figure 11. Explanation of platinum(II) regioselectivity.....	12
Figure 12. Chatt-Dewar-Duncanson bonding model.....	12
Figure 13. Dichloroplatinum(tetrapropylcyclobutadiene).....	13
Figure 14. Proposed mechanism of Pt(II) catalyzed hydration	14
Figure 15. Enol ethers and ketals from alkynes.....	15
Figure 16. Mercury(II) facilitated alkynyl alcohol cyclizations.....	16
Figure 17. Catalytic variation on mercury(II) cyclization.....	16

Figure 18. Methanol addition to a cationic platinum(II) acetylene complex (L = phosphine).....	17
Figure 19. Methanol addition to 1-heptyne.	18
Figure 20. Michaelis-Menten catalytic model.....	20
Figure 21. Osmium facilitated additions to alkynes.....	22
Figure 22. Rehybridization in metallacyclopropene extreme	23
Figure 23. Acetoxymercuration of 3-hexyne.	24
Figure 24. 4,4-Dimethyl-2-pentyne derivatives of Z.D.....	30
Figure 25. Bonding and back-bonding modes in platinum-alkyne complexes. ...	30
Figure 26. Spacefilling model comparison of two catalysts.....	31
Figure 27. ¹ H NMR comparison of hydration reaction mixtures.	33
Figure 28. First-order plot of Pt(II) catalyzed hydration using Z.D.....	35
Figure 29. Ligand substitution on platinum(II) halide complexes (X = Cl, Br)	36
Figure 30. (1,5-cyclooctadiene)Platinum(II) complexes	38
Figure 31. Platinum(II) mesityl bromide complex.....	39
Figure 32. (Norbornadiene)platinum(II) complexes.....	39
Figure 33. (Dicyclopentadienyl)platinum(II) chloride	40
Figure 34. Bis(benzyl)(nbd)platinum(II).....	41
Figure 35. Methoxy-bridged platinum(II) dimer.	42
Figure 36. (DMSO) ₂ Dimethylplatinum(II)	42

Figure 37. Effects of acidic water on sensitive functional groups	43
Figure 38. Hydration of 3-hexyn-2-ol	45
Figure 39. Hydration of 4-heptyn-2-ol	46
Figure 40. 1-Methylcyclohexanol test for acid sensitivity	48
Figure 41. Preliminary hydration-elimination mechanism	52
Figure 42. Detailed mechanism of the hydration-elimination reaction	54
Figure 43. Examples of stereoselective elimination	55
Figure 44. Acetal/ketal formation from carbonyls ($R' = H$ or alkyl)	56
Figure 45. Hydration protocol acidity - ketal sensitivity	57
Figure 46. Hydration of 2-heptyn-1-ol diethyl acetal	59
Figure 47. Conjugated alkynyl carbonyl substrates	60
Figure 48. Hydration of 4-heptyne-2-one	61
Figure 49. Chelation control from 4-heptyn-2-one	61
Figure 50. Hydration of 1-(trimethylsilyloxy)-3-hexyne	62
Figure 51. Chelation control by alkoxy alkynes	64
Figure 52. Resonance structures of ethoxy acetylene	65
Figure 53. Regiospecificity of the Michael addition reaction	65
Figure 54. Hydration of 1-methoxy-3-hexyne	67
Figure 55. Hydration of ethyl 3-hexynyl sulfide	68
Figure 56. Hydration of propynylbenzene	68

Figure 57. Hydration of 1-(1-propynyl)cyclohexene.	69
Figure 58. Platinum(II) and methanol inactive on ketones.....	70
Figure 59. Reversibility of initial alcohol addition.....	72
Figure 60. Methanol addition to 4-octyne.....	73
Figure 61. Addition of ethylene glycol to 4-octyne.....	75
Figure 62. First-order kinetics of methanol addition to 4-octyne.....	79
Figure 63. Different mechanistic paths for double alcohol addition.....	80
Figure 64. Methanol addition to 2,3-dihydropyran.....	81
Figure 65. β -Dimethoxy ketones from alkynyl ketones.....	81
Figure 66. E and Z isomers of enol ethers.....	82
Figure 67. Enol ethers from 3-hexyn-2-one.....	83
Figure 68. Platinum catalyzed rearrangement of alkynones.....	83
Figure 69. ^1H NMR spectrum of 3-hexyn-2-one methanol addition.....	84
Figure 70. Detailed mechanism for alcohol addition to 3-hexyn-2-one.....	86
Figure 71. Methanol addition to methyl 2-butynoate.....	87
Figure 72. Regiospecificity of methanol addition to alkynyl ester.....	87
Figure 73. ^1H NMR spectrum of methyl 2-butynoate methanol addition.....	88
Figure 74. ^1H NMR Spectrum of 1-Ethoxy-3-hexyne.....	95

ABSTRACT

An alternative catalytic method of adding water and alcohols to alkynes was examined. Platinum(II) in the form of Zeise's Dimer, simple platinum halides, and platinate salts have been successfully employed as mild and selective catalysts. The hydration conditions require only 1 mol% platinum(II), alkyne, water, and THF solvent, and can be run at ambient temperature or at reflux. The catalytic system displays modest to excellent regioselectivity. A novel and facile route to α,β -unsaturated ketones is encountered when hydrating secondary and tertiary α -hydroxy- or α -methoxy-alkynes. Alcohol additions are effected under identical mild conditions when using Na_2SO_4 or 2,6-di-*t*-butylpyridine as a co-catalyst. Alcohol addition to conjugated alkynyl ketones and alkynyl esters provides a facile protocol for keto-enol ether synthesis. Four major mechanisms, depending upon the identity of the alkyne substrate, have been developed and evaluated based on the results of this investigation.

INTRODUCTION

Alkynes are an abundant hydrocarbon resource, comprising at least 30% of the compounds isolated in petroleum distillation.¹ Methods for conversion of acetylenic compounds into other products are beneficial for both industry and synthetic organic research, and have received considerable attention. Perhaps the simplest means of converting alkynes are by addition of water (hydration) and addition of alcohol, to yield ketones and ketals, respectively (Figure 1). Several different metal complexes have been reported to effect these alkyne transformations.² However, the objective of finding a generally versatile, selective, and mild catalytic method for these functionalizations has been elusive.

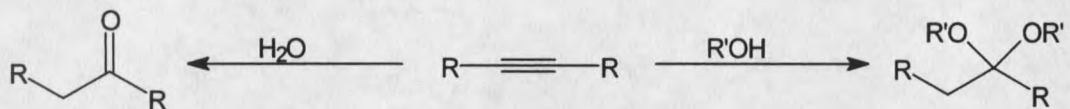


Figure 1. Nucleophilic additions to alkynes.

Platinum has shown versatility as a catalytic reagent in organic synthesis by providing a mild and selective procedure for the hydration of alkynes.³ Though narrowly defined previously, this system has been more broadly applied and had its horizons expanded. These elaborations and new mechanistic insights are the focus of this thesis.

Background

Hydration of Alkynes

One of the earliest reports of the hydration of unsaturated hydrocarbons was by Brooks and Humphrey⁴ in 1918. The use of concentrated sulphuric acid solutions to hydrate alkynes was common although the extremely acidic conditions and requisite high temperatures provided a large amount of polymeric by-products in addition to the desired ketones.

Mercuric salts were then found to catalyze the hydration of alkynes, thereby avoiding the need for high temperatures and requiring relatively small amounts of mineral acids. Further investigation into the catalytic system by Thomas *et al.*⁵ verified that the mercuric salt is necessary for the reaction, as well as additional amounts of mineral acid, in order for the reaction to proceed. The accepted mechanism of the reaction is illustrated in Figure 2. The reaction is regiospecific for terminal alkynes, obeying Markovnikof's rule and yielding methyl ketones (Figure 3). Aldehyde can be obtained if the substrate is acetylene. However, hydrations of internal alkynes yield both

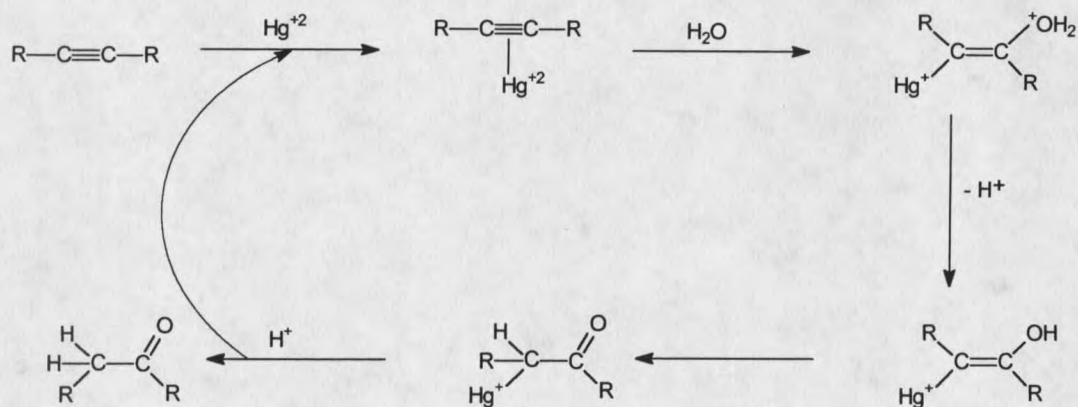
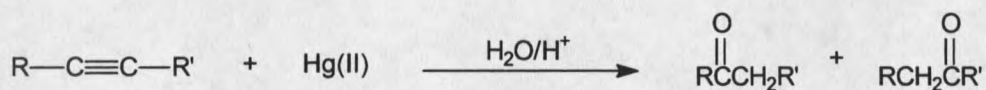
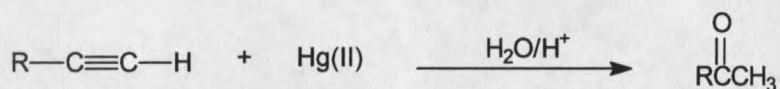
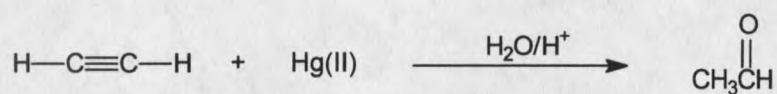


Figure 2. Mechanism for Hg(II) catalyzed hydration

possible ketones with little or no regioselectivity. Through the use of this catalytic system, more ketone products could be isolated than through the former acid method, yet oligomers, polymers, and mercuration products were still observed in significant amounts. Despite these by-products, mercury(II) catalysis remains the traditional method of alkyne hydration.

Figure 3. Hydration products of acetylenic compounds.



Variations on the classical method have provided simpler and sometimes more selective routes. Olah and Meidar⁶ successfully synthesized a solid support, super-acid resin (Nafion™) impregnated with mercury(II), which was then used to hydrate alkynes with yields ranging from 65% to 94%. With the catalytic species on the solid support, the work-up for the reaction was reduced to a mere filtration step, however the activity of the catalyst was found to deteriorate upon heating.

Regiospecific hydration using mercury(II) catalysis has been observed in the syntheses of 1,4- and 1,5-diketones⁷, and γ -keto esters⁸. The substrates employed were alkynyl ketones or alkynyl esters as shown in Figure 4. Regiospecificity is obtained by participation of the carbonyl during the reaction as illustrated in Figure 5. Consequently, the product arises not from attack by water on the π -bound alkyne, but rather through addition to the carbonyl carbon and formation of a cyclic intermediate, indicating that water addition is the rate determining step.

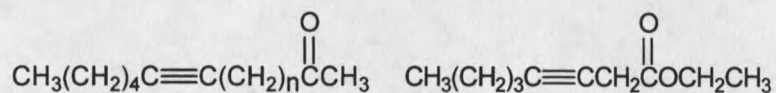


Figure 4. Alkynyl ketones ($n = 2$ or 3) and alkynyl ester

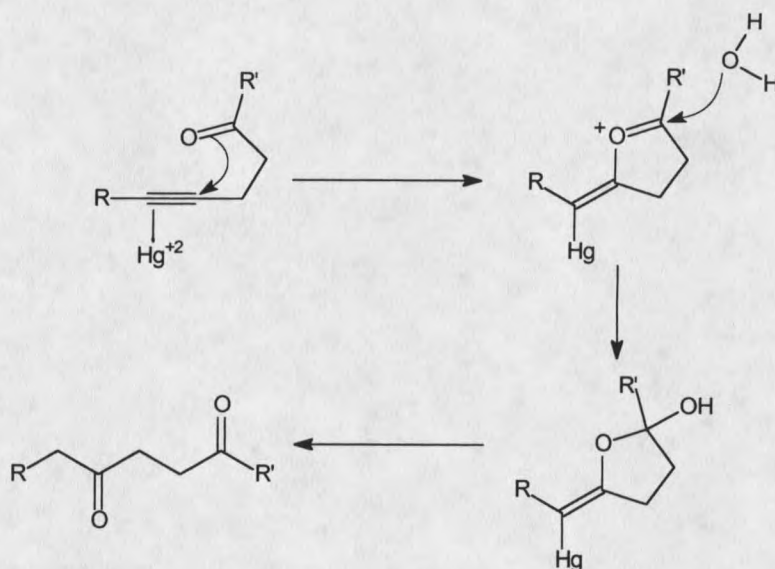


Figure 5. Regiospecificity via carbonyl participation.

The only example of alkyne hydration with a mercury(II) species without the need for additional mineral acid was reported by Janout and Regen.⁹ Phenyl mercuric hydroxide was found to hydrate a small number of terminal alkynes in yields ranging from 49% to 65%. Equally disappointing to the low yields obtained is the fact that the reaction is stoichiometric with the mercuric species. The method is also completely unreactive with internal alkynes.

Other metals have also been found to effect the hydration of alkynes. In 1961, ruthenium(III) chloride was found to catalyze the reaction, although aqueous HCl solutions were required and the system demonstrated an

