

Mercuric Triflate-Catalyzed Reaction of Propargyl Acetates with Water Leading Vinyl Ketones

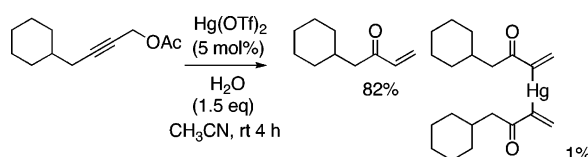
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ABSTRACT



Reaction of propargyl acetate with water catalyzed by Hg(OTf)₂ afforded vinyl ketone as the major product along with a dimeric vinyl mercuric product and normal hydration products in small amounts. The reaction is an alternative to the Meyer–Schuster and Rupe rearrangement applicable to primary alcohols, although the mechanism is entirely different.

Acid-catalyzed rearrangement of propargyl alcohol to an α,β -unsaturated ketone is known as the Meyer–Schuster and Rupe rearrangement. Unfortunately, this reaction has only been usable for *tert*- and *sec*-alcohols.¹ In this communication, we describe the reaction of propargyl acetate and water to give vinyl ketones under very mild conditions, catalyzed by mercury(II) trifluoromethanesulfonate [mercuric triflate, hereafter referred to as Hg(OTf)₂], as an alternative to the Meyer–Schuster and Rupe rearrangement applicable to primary alcohols, although the mechanism is entirely different. Conversion of primary propargyl alcohols to vinyl ketones was reported by Yadav using 6 equiv of Hg(OAc)₂ followed by H₂S treatment^{2a} and by Alami using CF₃CO₂H at 100 °C.^{2b} Trahanovsky also reported enone synthesis by pyrolysis of propargyl esters at very high temperature (around

650 °C).^{2c} We originally developed Hg(OTf)₂ as a highly efficient olefin cyclization agent,³ and we applied it to the synthesis of polycyclic terpenoids.⁴ Recently, we found that the Hg(OTf)₂ and Hg(OTf)₂–tetramethylurea (TMU) complexes showed highly efficient catalytic activity in several

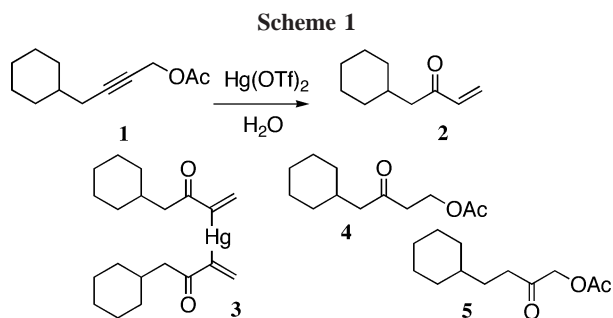
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reactions including hydroxylative 1,6-enyne cyclization to give exomethylene five-membered ring products,⁵ cyclization of 1-alkyn-5-ones leading to 2-methylfurans,⁶ arylalkyne cyclization leading to dihydronaphthalene derivatives,⁷ and biomimetic tandem cyclization of aryl-ene-yne derivatives to give polycarbocycles.⁸ We have also reported that Hg(OTf)₂·(TMU)₂ showed highly efficient catalytic activity for the hydration of terminal alkynes to give methyl ketones under very mild conditions.⁹ That reaction is far more efficient than the more commonly used general procedure, which employs a significant amount of HgO and H₂SO₄ in refluxing aqueous methanol.¹⁰ It is well-known that the hydration of internal alkyne bonds produces a regioisomeric mixture of ketones, and thus, it is a practically useless reaction. Consequently, we tried to control the regioselectivity of Hg(OTf)₂-catalyzed hydration of internal alkynes by using neighboring group participation and examined the reaction of propargyl acetate **1** with water in the presence of a catalytic amount of Hg(OTf)₂ (Scheme 1). Contrary to



expectation, the major product was not the expected hydration products **4** or **5** but was vinyl ketone **2**.^{11a,b} A strange dimeric vinyl mercuric product **3** was also detected in low yield.^{11c}

To characterize the reaction, we first examined a reaction of propargyl acetate **1** with 1.5 equiv of H₂O in the presence of Hg(OTf)₂ (5 mol %) in acetonitrile at room temperature.¹² The reaction was completed within 4 h, and vinyl ketone **2** was obtained in 84% yield after column chromatography on silica gel. The yield before purification, as measured by NMR, was 82%. Additional products included the dimeric

mercuric product **3** (1% yield) as well as ketones **4** (4%) and **5** (4%) (Table 1, entry 1).¹¹ The effects of varying the

Table 1. Hg(OTf)₂-Catalyzed Reaction of **1** and H₂O^a

entry	Hg(OTf) ₂ (mol %)	solvent	H ₂ O equiv	yield (%) ^b				
				2	3	4	5	1
1	5	CH ₃ CN	1.5	82	1	4	4	
2	5	CH ₃ CN	1.1	71	2	3	4	
3	5	CH ₃ CN	3.0	66	4	3	9	1
4	5	CH ₃ CN	5.0	53	5	4	14	12
5	5	CH ₂ Cl ₂	1.5	14	2			72
6	5	C ₆ H ₅ CH ₃	1.5	16	2	4		68
7	5	CH ₃ NO ₂	1.5	64				
8	1	CH ₃ CN	1.5	16	1			75
9	5 ^c	CH ₃ CN	1.5	74	4	3	3	5

^a Reactions were carried out at room temperature for 4 h. ^b NMR yield using mesitylene as the internal standard. ^c Reaction in the presence of TMU (5 mol %).

amount of water on the yield of vinyl ketone were investigated at 1.5, 1.1, 3, and 5 equiv, and the 1.5 equiv was shown to be the best (Table 1, entries 1–4). Water insoluble dichloromethane and toluene were shown to be useless as solvent affording significant amounts of starting material (Table 1, entries 5 and 6), and nitromethane was not as good as acetonitrile (Table 1, entry 7). One mol % of catalyst was not enough to complete the reaction (Table 1, entry 8). Reaction in the presence of TMU (5 mol %) produced a higher quantity of **3**, and the yield of vinyl ketone **2** was 74% at room temperature for 4 h (Table 1, entry 9).

Next, we investigated the reactions of a variety of 4-cyclohexyl-2-butyne esters **6a–k** (Scheme 2). By comparison with acetate **1** (Table 1, entry 1), 2-methylpropionate **6a** was converted to enone **2** in lower yield (73%) along with **3** (2%) and ketones **7a** (5%) and **8a** (5%) (Table 2, entry 1). Pivalate **6b**, methoxy acetate **6c**, and monochloroacetate **6d** also produced enone **2** in moderate yield within several hours (Table 2, entries 2–4). *p*-Methoxybenzoate **6e**, *p*-nitrobenzoate **6f**, and pentafluorobenzoate **6g** formed product **2** only in poor to moderate yield after 24 h (Table 2, entries 5–7). Surprisingly, benzoate **6h** and 2,4,6-trichlorobenzoate **6i** produced no trace of products at all (Table 2, entries 8 and 9). On the other hand, formate **6j** produced **2** in 51% yield along with **3** (2%) and ketones **7j** (2%) and **8j** (4%) (Table 2, entry 10). The mother alcohol **6k** was entirely inert under the standard reaction conditions, and all starting materials were recovered (Table 2, entry 11).

(12) Typical experimental procedure is as follows. To a stirred solution of propargyl acetate **1** (194 mg, 1.0 mmol) and water (27 mg, 1.5 mmol, 1.5 equiv) in acetonitrile (9.5 mL) was added 0.5 mL of 0.1 M Hg(OTf)₂ (0.5 mL, 5 mol %) in acetonitrile at room temperature under argon, and the mixture was allowed to stir at the same temperature for 4 h. After addition of aqueous NaHCO₃, the organic material was extracted with ether. Dried and concentrated material was subjected to a column chromatography on silica gel using pentane and ether as eluent to give enone **2** (128 mg, 84% yield, NMR yield 82%) and a mixture of dimeric mercury compound **3** (NMR yield 1%, determined by using mesitylene as an internal standard), ketones **4** (NMR yield 2%), and ketone **5** (NMR yield 6%).

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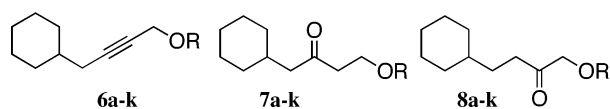
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Scheme 2



Together, these results indicated that the reactions were affected by neither electronic nor steric factors of leaving groups, and we concluded that acetate is the leaving group of choice.

We then examined the reaction of 2-decanoyl acetate (**9**) with 1.5 equiv of water in CH₃CN at room temperature for 3.5 h in the presence of 5 mol % Hg(OTf)₂. Enone **10**^{11a} was obtained in 70% yield (as measured by NMR; isolated yield was 59%) along with dimeric mercuric product **11** (2%) and a mixture of hydrated ketones (7%) (Table 3). Phenylpropargyl acetate **12** formed enone **13**^{2c,11a,11d} in 51% yield (isolated yield 53%), and 3-oxo-3-phenylpropanoyl acetate (18%), but no dimeric mercuric product, was detected. Reaction of propargyl acetate containing *tert*-alcohol **14** afforded only Meyer–Schuster product **15** in 76% yield (isolated yield 74%), and the acetate group did not affect the reaction. Reaction of secondary acetate **16** took place smoothly to give (*E*)-enone **17** selectively in 84% yield (isolated yield 80%) along with dimeric mercuric product **18** (2% yield). Stereochemistries of **17** and **18** were established to be *E* and *Z*, respectively, on the basis of nuclear Overhauser effect (NOE) experiments. When the same reaction was carried out using 1 mol % of Hg(OTf)₂, enone **17** was obtained in 88% yield after 114 h. The reaction of *tert*-acetate **19** was completed within 6 min and afforded enone **20**^{11e} in 67% yield (isolated yield 60%) along with an enyne **21** in 13% yield. When water was added to the mixture of **19** and Hg(OTf)₂, the yield of **20** and **21** changed to 15% and 60%, respectively, as measured by NMR. When diacetate **22** was treated with 5 mol % of Hg(OTf)₂ and H₂O (1.5 equiv), enones **23** and **24** were obtained in 70% yield (isolated yield 61%) and 18% yield (isolated yield 15%), respectively, along with a 1:5 mixture of dimeric products

Table 3. Hg(OTf)₂-Catalyzed Reaction of Acetate with H₂O

Substrate	Time (h)	Product ^a
	4	10 (70%) 11 (2%)
	2	13 (51%)
	1	
	1	17 (84%) ^b 18 (2%) ^c
	0.1	20 (67%) 21 (13%)
	5	23 (70%) 24 (18%) 25 (0.5%) 26 (2.5%)

^a NMR yield using mesitylene as an internal standard. ^b NMR yield using naphthalene as an internal standard. ^c Isolated yield.

25 and **26** in 3% yield that was difficult to separate. Stereochemistries of **24** and **26** were established to be *E* and *Z*, respectively, on the basis of NOE experiments.

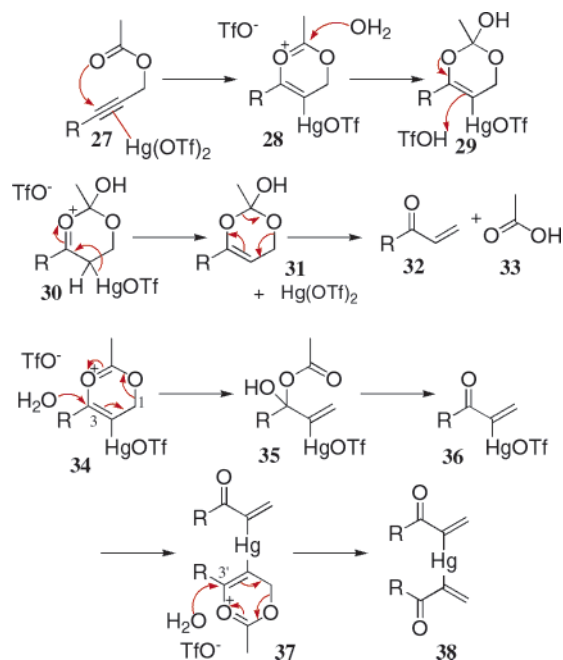
Taken together, these results are consistent with the following mechanism (Scheme 3). The reaction is initiated by π -complexation of alkyne with Hg(OTf)₂, as shown in **27**. Oxonium cation **28** is attacked by water to generate intermediate **29** along with TfOH. Protonation of **29** forms alternative oxonium cation **30**, which undergoes demercuration to produce the second intermediate **31** and the catalyst Hg(OTf)₂. A 6π electrocyclic reaction should yield the enone **32**, along with acetic acid **33**. If water attacks carbon 3 of the oxonium cation as indicated in **34**, an alternate intermediate **35** could form. The corresponding ketone **36** cannot be demercurated because protonation would convert it to an unstable primary cation. However, **36** may react slowly with a second propargyl acetate molecule, creating another oxonium cation **37**, which becomes the stable vinyl mercury product **38**. Therefore, this process contains a novel suicide mechanism for the catalyst Hg(OTf)₂. This could explain why we could not achieve the very high catalytic turnover for vinyl ketone formation that we observed for

Table 2. Hg(OTf)₂-Catalyzed Reaction of **6** with H₂O^a

entry	R	time (h)	yield (%) ^b				
			2	3	7	8	6
1	a: COCH(CH ₃) ₂	2	73	2	5	5	
2	b: COC(CH ₃) ₃	2	67	2	16	6	
3	c: COCH ₂ OCH ₃	4	68	3	4	2	2
4	d: COCH ₂ Cl	4	61	3	7	1	8
5	e: COC ₆ H ₄ - <i>p</i> -OCH ₃	24	30		5	1	64
6	f: COC ₆ H ₄ - <i>p</i> -NO ₂	24	53	3	10		18
7	g: COC ₆ F ₅	24	14	1			65
8	h: COC ₆ H ₅	24					100
9	i: COC ₆ H ₂ -2,4,6-Cl ₃	24					100
10	j: COH	4	51	2	2	4	14
11	k: H	24					100

^a Reaction with 1.5 equiv of H₂O in CH₃CN at room temperature. ^b NMR yield using mesitylene as an internal standard.

Scheme 3



enyne cyclization,⁵ arylyne cyclization,⁷ and biomimetic tandem cyclization.⁸

In summary, we have developed a novel reaction between propargyl acetate and water catalyzed by $\text{Hg}(\text{OTf})_2$ to produce synthetically useful conjugated ketones under very mild conditions. The reaction behaves like a variation of the Meyer–Schuster and Rupe rearrangement, but it is applicable to primary alcohols. Toxicity of organomercuric compounds is a serious concern, particularly with respect to their use in industrial synthetic application. Although, CH_3HgCl and $(\text{CH}_3)_2\text{Hg}$ are extremely dangerous and can cause serious damage to the central nervous system, most organomercuric compounds are not that toxic. Phenylmercuric acetate used to be employed as agrochemicals for rice fields, and mercurochrome is an excellent antiseptic for wounds. It is important to distinguish between useful mercuric compounds and the highly toxic methylmercuric chloride.

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Supporting Information Available: Spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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