

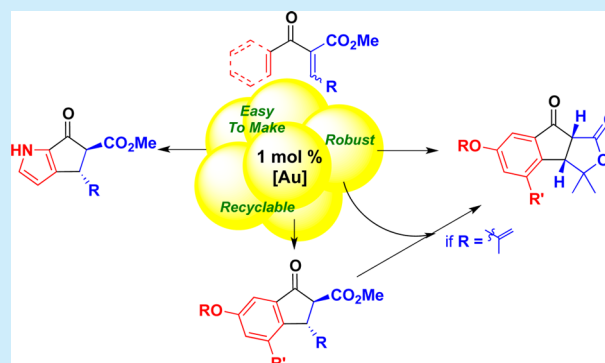
Cationic Cyclizations and Rearrangements Promoted by a Heterogeneous Gold Catalyst

Tulaza Vaidya, Ryan Cheng, Peter N. Carlsen, Alison J. Frontier,* and Richard Eisenberg*

Department of Chemistry, University of Rochester, Rochester, New York 14627-0216, United States

S Supporting Information

ABSTRACT: A heterogeneous gold catalyst with remarkable activity for promoting the electrophilic reactions of aryl vinyl ketones and aryl dienyl ketones is described. The catalyst is easy to prepare, is robust, and can be recycled. Low loadings are effective for different types of cationic reactions, including Nazarov cyclizations, lactonizations, and [1,2] shifts.

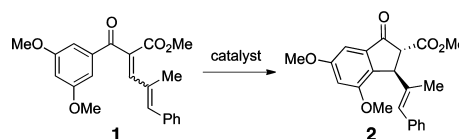


Catalysis of pericyclic reactions using coinage metals (Cu, Ag, Au) is a rapidly evolving field. In this context, catalysis of the Nazarov electrocyclozation of aryl and vinyl enones has been studied with numerous Cu(II) complexes¹ and with Ag(I).^{2–4} Homogeneous Au(I) and Au(III) complexes have been reported to promote both *iso*-Nazarov cyclizations⁵ and the cyclization of more typical divinyl ketone substrates.^{6,7} When considering effective catalysts for the Nazarov cyclization of less reactive aryl enones,^{1c} the Ir(III) complexes developed in our group demonstrate unique reactivity, promoting Nazarov cyclization and novel electrophilic chemistry of otherwise inert aryl and heteroaryl enones.^{8,9} However, multistep reaction sequences are necessary to prepare the dicationic and tricationic Ir(III) complexes.

Several reports have detailed the *in situ* generation of a catalytically active [Au] species from gold(III) chloride (AuCl₃) and silver(I) salts for catalysis of arene and alkene functionalization reactions,^{10–15} as well as Nazarov cyclization.^{6,7} However, the identity of the active catalyst in these reactions is unknown.¹⁶ We describe here a related gold catalyst that is generated *in situ* from a combination of AuCl₃ and silver(I) hexafluoroantimonate (AgSbF₆). This catalyst is convenient to prepare, heterogeneous, recyclable, and comparable in activity to the Ir(III) complexes for the catalysis of Nazarov cyclization and other electrophilic chemistry of aryl vinyl ketones.

The catalyst was identified during a screen performed to identify gold(III) complexes able to promote the Nazarov cyclization of aryl enone **1**, a polarized,^{17,18} but relatively unreactive substrate (Table 1). The addition of AgSbF₆ to AuCl₃ was intended to abstract gold-bound chloride ions to generate an unsaturated, cationic Au(III) species.¹⁰ The suspension obtained upon addition of AgSbF₆ (2–3 mol %) to AuCl₃ (1 mol %) was found to be highly active, promoting the cyclization of **1** at room

Table 1. Gold-Catalyzed Nazarov Cyclizations Aryl Enone **1^a**



entry	catalyst	temp (°C)	time (h)	yield (%) ^b
1	AuCl ₃ /AgSbF ₆ (1:3)	rt	0.5	>99
2	AuCl ₃ /AgSbF ₆ (1:2)	rt	0.5	>99
3	AuCl ₃ /AgSbF ₆ (1:1)	rt	0.5	— ^d
4	AuCl ₃ /AgSbF ₆ (1:2) recycled once	rt	0.5	>99
5	AuCl ₃ /AgSbF ₆ (1:2) recycled twice	rt	0.5	97
6	(AuCl ₃) ₂ dppe/AgSbF ₆	rt	24	NR
7	AuCl ₃ /Na[BAr ^F ₄] (1:2)	rt	0.5	>99
8	AuCl ₃ /AgSbF ₆ (1:2) + Proton-sponge ^e	rt	1	>99
9	AuCl ₃ ^c	60	24	— ^d
10	AgSbF ₆ ^c	60	24	— ^d

^aReaction conditions: 1 mol % of AuCl₃ was used; catalyst was premixed for 0.5 h prior to reaction in dichloromethane or toluene; reactions containing AgSbF₆ were run under minimal light conditions.

^bIsolated yields. ^c15 mol % was used. ^dIncomplete reactions monitored by thin layer chromatography (<50% conversion). ^e100 mol % was used. NR = no reaction, dppe = 1,2-bis(diphenylphosphino)ethane, [BAr^F₄][−] = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate, Proton-sponge = 1,8-bis(dimethylamino)naphthalene.

temperature within 0.5 h with >99% yield (entries 1 and 2). In an earlier study, cyclization of a similar substrate using Cu(ClO₄)₂

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required heating at 45 °C for 8 h to achieve cyclization (80% yield).¹⁷

A 1:1 mixture of AuCl₃ and AgSbF₆ shows diminished activity with incomplete conversion over 0.5 h (entry 3). The dark precipitate generated from the 1:2 mixture can be recovered after the reaction by filtration through Celite and reused in the presence of Celite for catalysis with negligible loss in activity. The filtrate is not catalytically active. Subsequent cyclizations were performed with the recovered heterogeneous substance, giving >99% after the first recycle (entry 4) and 97% after the second recycle (entry 5).

Cyclization does not occur upon exposure to a combination of (AuCl)₂dppe (dppe = 1,2-bis(diphenylphosphino)ethane) with AgSbF₆ (Au/Ag = 1:1) (entry 6). However, a CH₂Cl₂ mixture of AuCl₃/Na[BarF₄][−] ([BarF₄][−] = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate) in a 1:2 ratio (entry 7) has the same catalytic activity as the optimal catalyst formed from AuCl₃/AgSbF₆ (1:2), indicating that silver does not play a significant role in the catalysis. A CH₂Cl₂ mixture of AuCl₃/AgSbF₆ (1:2) with Proton-sponge (100 mol %; Proton-sponge = 1,8-bis(dimethyl-amino)naphthalene) gives a quantitative yield of cyclized product but requires a slightly longer reaction time (entry 8). Thus, trace amounts of H⁺ may aid in the catalysis, but the effect is not great. Finally, neither AuCl₃ (15 mol %) nor AgSbF₆ (15 mol %) used alone exhibits high activity (entries 9 and 10), giving incomplete conversions after 24 h at 60 °C.

To determine the reaction scope and look for new reactivity patterns, the aryl vinyl and aryl dienyl ketones shown in Table 2 were exposed to the electrophilic heterogeneous gold catalyst (Au(III) loading = 1 mol %). We observed rapid and quantitative cyclizations of aryl dienone **3** as well as dienones having aromatic β -substituents such as PMP (*p*-methoxyphenyl) **5** and TMP (2,4,6-trimethoxyphenyl) **7** (entries 2 and 3, respectively). While aryl enone **9** provides Nazarov cyclopentenone **10** (entry 4), aryl γ -cyclobutyl enone **11** affords electrocyclized product **12** and unexpected naphthalenol **13** (entry 5). Similarly, the aryl γ -cyclopropyl enone **14** provides both electrocyclized product **15** and tricycle **16** (entry 6).

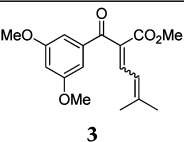
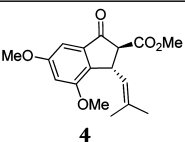
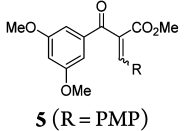
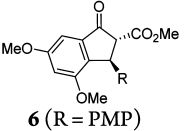
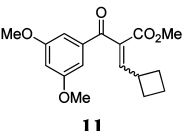
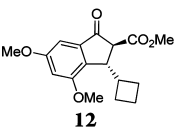
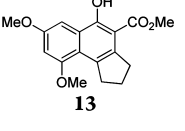
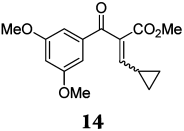
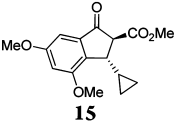
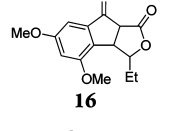
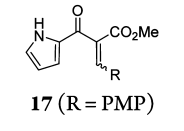
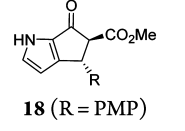
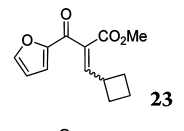
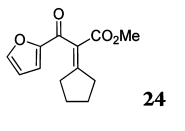
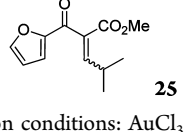
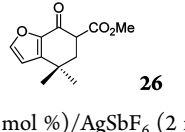
The gold catalyst is effective for electrocyclizations of unprotected pyrroles **17**, **19**, and **21**, promoting efficient cyclization using 1 mol % of the gold complex under mild conditions (entries 7–9). In comparison, cyclization of **19** using Sc(OTf)₃ (5 mol %) and LiClO₄ (1 equiv) requires heating at 80 °C for 8.5 h.¹⁸

The electrophilic nature of the heterogeneous gold catalyst ([Au]) is evident in its ability to promote [1,2] rearrangement chemistry, which was previously only possible using a tricationic Ir(III) complex.⁹ For example, rearrangement of **23** produced tetrasubstituted enone **24** (entry 10), and furyl enone **25** rearranges and cyclizes to afford **26** in 50% yield (entry 11).¹⁹ These results also suggest that product **13** is produced from **11** via a [1,2]-alkyl shift/Friedel–Crafts annulation,⁹ followed by aromatization upon air oxidation.

Exposure of aryl enone **27a** to the [Au] catalyst for 5 h at room temperature exclusively generates tricyclic lactone **29a**, via a novel Nazarov cyclization/lactonization cascade (Table 3, entry 1).²⁰ Aryl vinyl enone **14** undergoes a related, but less efficient, cyclization/lactonization (Table 2, entry 6). Similarly, cyclization of precursors **27b–d** produces lactones **29a–c**, respectively, but requires heating in a mixture of dichloromethane/toluene and a longer reaction time (entries 2–4).

Probing the reaction further, when enone **27c** is added to a solution containing the heterogeneous gold catalyst in the

Table 2. Cyclization of Aryl and Heteroaryl Enones with the Heterogeneous Gold Catalyst [Au]^a

no.	substrate	product	time (h) ^b	yield (%) ^c
1			1	>99
2			0.5	>99
3	7 (R = TMP)	8 (R = TMP)	0.5	>99
4	9 (R = <i>i</i> -Pr)	10 (R = <i>i</i> -Pr)	0.5	>99
5		 	16	64 ^d 30 ^d
6		 	16	68 24
7			12	>99
8	19 (R = <i>n</i> -Pr)	20 (R = <i>n</i> -Pr)	16	>99 ^e
9	21 (R = cyclobutyl)	22 (R = cyclobutyl)	4	74 ^d
10			0.5	95 ^d
11			18	50 ^{d,f}

^aReaction conditions: AuCl₃ (1 mol %)/AgSbF₆ (2 mol %), premixed prior to reaction, CH₂Cl₂ or toluene, rt unless otherwise indicated, minimal light conditions. ^bReactions monitored using thin layer chromatography. ^cIsolated yields. ^dReactions at 80 °C. ^eReaction at 60 °C. ^f10 mol % catalyst. PMP = *para*-methoxyphenyl, TMS = trimethylsilyl, TMP = 2,4,6-trimethoxyphenyl.

presence of Proton-sponge, no reaction is observed (entry 5). On the other hand, enone **27c** cyclizes to give **28b**, but not lactone

Table 3. Nazarov/Lactonization Cascade Reactions of Aryl Vinyl Enones with Heterogeneous Gold Catalyst^a

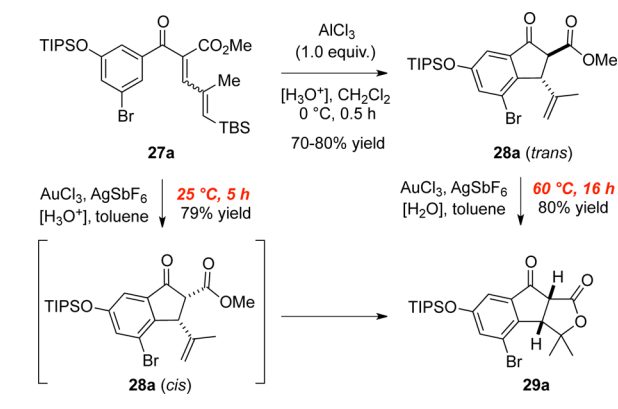
no.	dienone	R ¹	R ²	R ³	time ^b (h)	temp (°C)	solvent	additive	product	yield ^c (%)
1	27a	TIPS	Br	TBS	5	rt	CH ₂ Cl ₂	none	29a	79
2	27b	TIPS	Br	TMS	20	60	CH ₂ Cl ₂ /PhMe (1:1)	none	29a	82
3	27c	Me	OMe	TBS	24	60	CH ₂ Cl ₂ /PhMe (1:1)	none	29b	83
4	27d	Me	H	TMS	24	60	CH ₂ Cl ₂ /PhMe (1:1)	none	29c	88
5	27c	Me	OMe	TBS	24	60	CH ₂ Cl ₂ /PhMe (1:1)	Proton-sponge ^d	—	NR
6	27c	Me	OMe	TBS	24	60	CH ₂ Cl ₂ /PhMe (1:1)	3 Å mol sieves	28b	80
7	27c	Me	OMe	TBS	24	60	CH ₂ Cl ₂ /PhMe (1:1)	HOTf (1 equiv) ^e	27e (R ₃ =H)	92

^aReaction conditions (unless otherwise specified): 1 mol % of AuCl₃ was used; catalyst was premixed prior to reaction; reactions were protected from light. ^bReactions monitored using thin layer chromatography. ^cIsolated yields. ^d100 mol %. ^eReaction was conducted without the AuCl₃/AgSbF₆ catalyst. TBS = *tert*-butyldimethylsilyl, TIPS = triisopropylsilyl, TMS = trimethylsilyl, Proton-sponge = 1,8-bis(dimethylamino)naphthalene. NR = no reaction, HOTf = triflic acid.

29b, when molecular sieves are added to the reaction (entry 6). Furthermore, treating 27c with HOTf effects protodesilylation without cyclization (entry 7). From these experiments, it can be deduced that protic acid must effect protodesilylation of 27 before cyclization can occur and that water is necessary for the lactonization (conversion of 28 to 29).

Aryl enone 27a can be cyclized with stoichiometric amounts of AlCl₃, allowing isolation of intermediate 28a (Scheme 1).^{8b,21} Subsequently, heating cyclopentanone 28a with [Au] at 60 °C furnishes tricycle 29a in 80% yield. However, heating 28a to 60 °C in wet 1,2-dichloroethane for 16 h did not produce lactone 29a. This finding, along with the result in Table 3, entry 6, indicates that both water and [Au] are required for lactone formation. The isolation of product 16 (Table 2, entry 6) is additional evidence that [Au] promotes lactone formation, although the mechanism for formation of 16 is not yet clear to us.

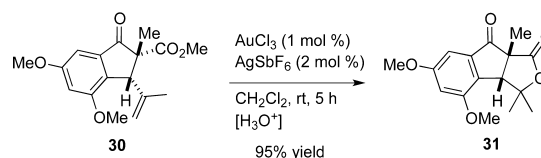
Scheme 1. Stepwise Nazarov Electrocyclization/Lactonization



There is a significant rate difference between the one-step cyclization/lactonization and the stepwise version (Scheme 1). We propose that the one-pot sequence occurs via the kinetically favored 28a (*cis*),²² which is rapidly converted to 29a. However, in the stepwise reaction sequence, elevated temperature and extended reaction times are required for the isomerization of 28a (*trans*) to 28a (*cis*) which has the geometry necessary for lactone formation.

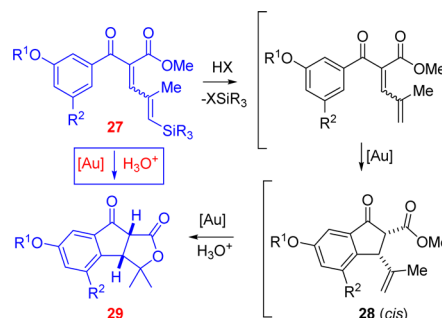
To test this hypothesis, 28b was methylated at the α position to lock the ester and olefin groups of cyclopentanone 30 in the *cis* conformation (Scheme 2). Indeed, the lactonization of 30 occurs at room temperature to give 31 in near-quantitative yield.

Scheme 2. Room Temperature Conversion of Nazarov Product to Lactone



A tentative mechanism for the multistep transformation of the Nazarov cyclization/lactonization cascade is presented in Scheme 3. The serendipitous discovery of the cascade is due to the adventitious presence of water and acid in the reaction medium. Thus, the sequence begins with protodesilylation, promoted by trace amounts of acid in the reaction mixture. The Nazarov cyclization step only occurs upon exposure to the gold catalyst: protic acid alone does not promote cyclization, and cyclization was also efficient when water was excluded from the reaction using molecular sieves. Lactone formation, however, requires the presence of both the [Au] catalyst and water.

Scheme 3. Proposed Mechanism for the Nazarov Cyclization/Lactonization Cascade



In conclusion, we report an electrophilic heterogeneous gold catalyst that promotes cationic reactions of relatively unreactive

polarized dienones. The reactivity of the gold catalyst is comparable to the unusually reactive Ir(III) tricationic complex,⁶ but the gold catalyst is easily prepared and can be recycled, and only 1 mol % of AuCl₃ is used as the catalyst precursor. Aryl and heteroaryl enones with diverse functionalities are readily cyclized, and other cationic reaction chemistry is also observed, including [1,2]-rearrangements and an unexpected lactonization.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, preparation, and characterization of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: frontier@chem.rochester.edu.

*E-mail: eisenberg@chem.rochester.edu.

Notes

The authors declare no competing financial interest.

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