Cationic Au(I)-Catalyzed Cycloisomerization of Aromatic Enynes for the Synthesis of Substituted Naphthalenes

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Abstract: A cationic Au(I) complex catalyzed the cycloisomerization of aromatic enynes that possess a substituent on their alkyne terminus. Cyclization of the 6-*endo*-dig type proceeded dominantly to give 1,3-di- and 1,2,3-trisubstituted naphthalenes.

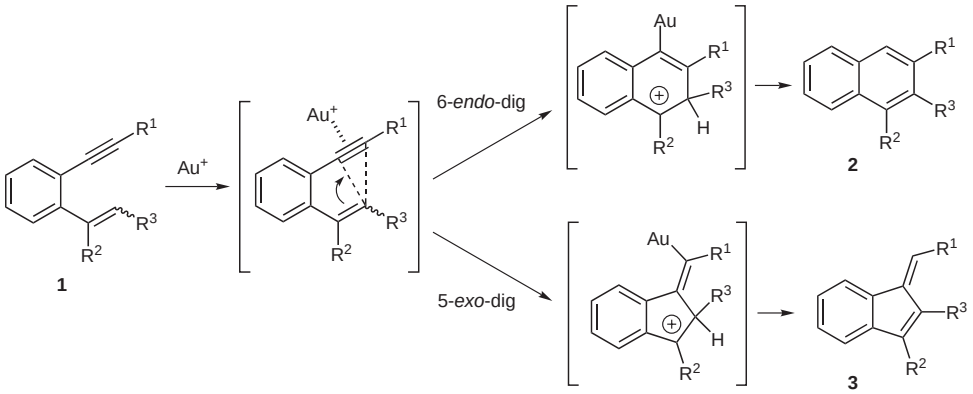
Key words: cycloisomerization, catalysis, enynes, gold, indenes, naphthalenes

Recently, activation of alkyne moiety by a metal complex has been an attractive strategy for the development of new catalytic carbon–carbon bond forming reactions and gold-catalyzed cyclization has been intensively studied, which gives various types of carbo- and heterocyclic skeletons.[1,2] In particular, Au(I)-catalyzed cycloisomerization of enynes draws much attention in these days.[3] We here disclose Au(I)-catalyzed cycloisomerization of aromatic enynes, which have a substituent on their alkyne terminus, under mild reaction conditions.

Catalytic benzannulation of aromatic enynes is a well-known protocol for the synthesis of naphthalene derivatives and various metal complexes, including Ru(II),[4–6] Pt(II),[4,5] Pd(II),[4] Rh(I),[4] Au(III),[4,5] Ag(I),[4] W(0),[7] and In(III),[8] have already been reported as efficient catalysts. In the Ru(II)- and W(0)-catalyzed reactions, however, aromatic enynes with no substituent on their alkyne terminus were used. The authors explained the reason that the formation of vinylidene complexes, prepared from unsubstituted alkynes and metal catalysts, triggers the following cycloisomerization.[6,7a] In the reactions of enynes with a substituent on their alkyne terminus, electron-donating ene components, such as a silyl enol ether, were submitted to the cycloisomerization.[4]

We here examined Au(I)-catalyzed cycloisomerization of aromatic enynes. When alkyne moiety of aromatic enyne **1** is activated by a cationic Au(I) catalyst, 6-*endo*-dig- or 5-*exo*-dig-type cyclization proceeds and the following deprotonation gives substituted naphthalene **2** or 1-methylene-1*H*-indene derivative **3** (Scheme 1).

We chose 1-(1-hexynyl)-2-isopropenylbenzene (**1a**) as a model aromatic enyne and examined a Au(I)-catalyzed cycloisomerization under various reaction conditions (Table 1). No reaction proceeded at room temperature using $AuCl(PPh_3)$ (entry 1); however, the addition of Ag salts increased the catalytic activity of Au(I) complex and aromatic enyne **1a** was consumed within one hour. Cyclization proceeded exclusively in a 6-*endo*-dig-type manner regardless of counter anions of Ag salts and 3-butyl-1-methylnaphthalene (**2a**) was obtained in high yield (entries 2–4). Ag salt itself did not work at all as a catalyst even at 40 °C (entry 5). High yield was achieved using only 1 mol% catalyst (entry 6) and it is noteworthy that the cyclization efficiently proceeded even under an atmosphere of air (entry 7). In the presence of 10 mol% of $TsOH{\cdot}H_2O$ as a protic acid catalyst, naphthalene **2a** could not be detected, which means that the cationic Au(I) complex worked as an effective catalyst in the present cycloisomerization.[9,10]



Scheme 1

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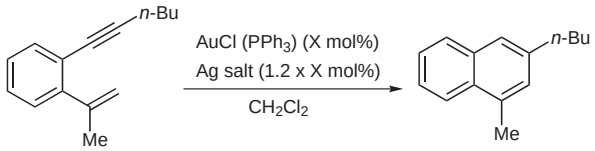
Table 1 Screening of Reaction Conditions Using Cationic Au(I) Catalysts



Entry	Ag salt	X (mol%)	Time (h)	Yield (%)
1	None	5	1	NR[c]
2	$AgBF_4$	5	1	93
3	$AgSbF_6$	5	1	92
4	AgOTf	5	1	92
5[a]	AgOTf	5	1	NR[c]
6	AgOTf	1	1.5	94
7[b]	AgOTf	1	1.5	96

[a] The reaction was examined without $AuCl(PPh_3)$ at 40 °C.
[b] The reaction was examined under an atmosphere of air.
[c] NR = no reaction.

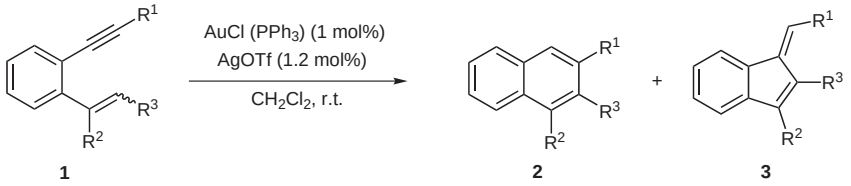
Under the above reaction conditions (Table 1, entry 6), various aromatic enynes were examined (Table 2).[11] An aryl group was tolerable as a substituent of the alkyne terminus and enyne **1b** was transformed into the biaryl compound **2b** exclusively (entry 1). When oxygen-functionalized enyne **1c** was subjected to the present cycloisomerization, a small amount of 5-*exo*-dig-type product **3c** was detected (entry 2). $AgSbF_6$ induced a more active catalyst and cyclized products **2c**/**3c** were obtained in higher yield at the lower temperature (entry 3). Protective groups of hydroxyl substituent controlled the reaction pathway and almost no 5-*exo*-dig-type product **3** was detected in the case of TIPS-protected propargyl alcohol **1e** (entries 4 and 5). Moreover, the protection of a hydroxyl substituent was unnecessary and (2-naphthyl)methanol (**2f**) was exclusively obtained from propargyl alcohol **1f** (entry 6).[12] The cyclization of nitrogen-functionalized enyne **1g** also proceeded, however, a significant amount of 5-*exo*-dig-type product **3g**[13] was obtained (entry 7). An aryl group on the alkene moiety was acceptable (entry 8). Aromatic enyne **1i** possessing trisubstituted alkene moiety was also a good substrate and 1,2,3-trisubstituted naphthalene **2i** was obtained (entry 9).

An *o*-alkynyl biphenyl, with an aryl group as ene moiety in aromatic enyne, was also a good substrate: Au(I)-catalyzed cyclization of 2-(1-hexynyl)biphenyl (**1j**) proceeded at higher reaction temperature and 9-butylphenanthrene (**2j**) was a major product (Equation 1). Different from the previous examples,[5,8] electron-donating substituents, such as a methoxy or methyl group, were not needed.[14]

Double cyclization of dienediyne **1k** efficiently proceeded under the typical reaction conditions and 2,2′-binaphthyl compound **2k** was obtained in good yield (Equation 2).

When aromatic enyne **1l**, having no substituent on its alkyne terminus, was examined, 5-*exo*-dig-type cycliza-

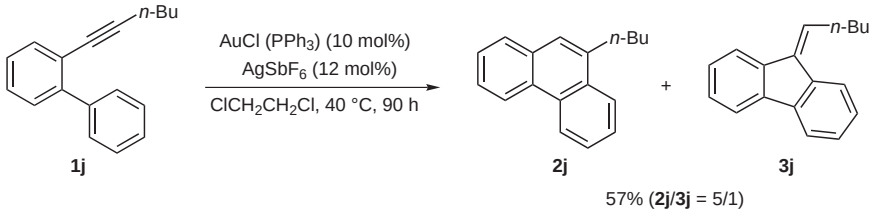
Table 2 Au(I)-Catalyzed Cycloisomerization of Various Aromatic Enynes **1**



1 **2** **3**

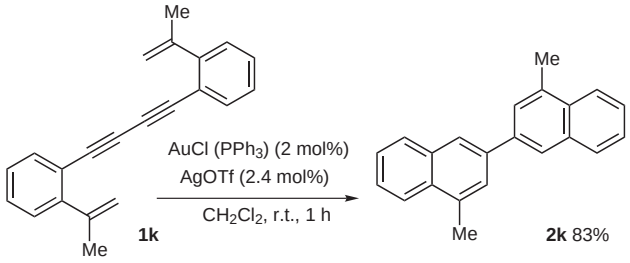
Entry	R^1	R^2	R^3	Enyne	Time (h)	Yield (%)	Product ratio **2**/**3**
1	Ph	Me	H	**1b**	2	87	>20:1
2	CH_2OMe	Me	H	**1c**	1	71	7:1
3[a]	CH_2OMe	Me	H	**1c**	2	87	7:1
4	CH_2OTBS	Me	H	**1d**	1	78[b]	20:1
5	CH_2OTIPS	Me	H	**1e**	1	73[b]	>20:1
6	CH_2OH	Me	H	**1f**	1	93	>20:1
7	CH_2NMeTs	Me	H	**1g**	2	84	2:1
8	*n*-Bu	Ph	H	**1h**	1	86	>20:1
9	*n*-Bu	Me	Me[c]	**1i**	1	97	5:1

[a] $AgSbF_6$ was used in place of AgOTf and the reaction was examined at 0 °C.
[b] Some product (ca. 20%) was obtained as desilylated alcohol **2f**.
[c] *E*/*Z* ratio was ca. 1:1.

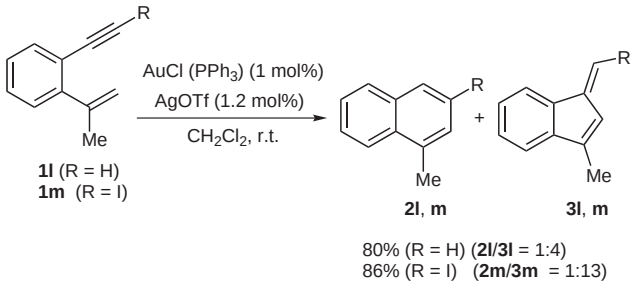


Equation 1

tion proceeded and 1-methylene-1*H*-indene (**3l**) was a major product. In the case of iodo-substituted enyne **1m**, vinyl iodide **3m** was dominantly obtained[15,16] and only a small amount of naphthalene derivative **2m** was detected (Equation 3). These results strikingly contrast with the reported examples, where enyne **1l** gave naphthalene **2l**[6,7a] and iodo migration occurred from iodoalkynes.[7b]



Equation 2



Equation 3

In summary, we disclosed a cationic Au(I) complex-catalyzed cycloisomerization of aromatic enynes. Enynes with an alkyl- or aryl-substituted alkyne terminus underwent 6-*endo*-dig-type cyclization to give various 1,3-di-, and 1,2,3-trisubstituted naphthalenes. The enyne with an iodo-substituted alkyne terminus underwent 5-*exo*-dig-type cyclization, which provides a new protocol for the construction of an indene skeleton.

Acknowledgment

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(9) Using $AuCl_3$ (1 mol%) as a catalyst in toluene (see ref. 4), the cycloisomerization of **1a** did not proceed at r.t. and it did at 100 °C for 24 h to give **2a** yet in ca. 30% yield. Moreover, $AuCl(PPh_3)$ is more stable and easy to handle than hygroscopic $AuCl_3$.

(10) Cationic platinum, which was prepared from $PtCl_2$ (1 mol%) and AgOTf (2.5 mol%), did not work as a catalyst even in refluxed CH_2Cl_2.

(11) **Typical Experimental Procedure (Table 2).** $AuCl(PPh_3)$ (1.2 mg, 0.0024 mmol) was placed in a flask and a CH_2Cl_2 solution (2.5 mL) of aromatic enyne (0.25 mmol) was added. To the resulting mixture was added AgOTf (0.8 mg, 0.0030 mmol) and the mixture was stirred at r.t. for 1–2 h. After completion of the reaction, the mixture was quenched with H_2O and extracted with CH_2Cl_2 three times. The combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude products were purified by thin-layer chromatography.

(12) (1-Methylnaphthalen-3-yl)methanol (**2f**): yellow oil. IR (neat): 3350, 872, 773, 748 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.92 (br s, 1 H), 2.68 (s, 3 H), 4.79 (s, 2 H), 7.31 (s, 1 H), 7.47–7.52 (m, 2 H), 7.64 (s, 1 H), 7.81–7.82 (m, 1 H), 7.96–7.97 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 65.4, 123.7, 123.9, 125.6, 125.7, 125.8, 128.4, 132.0, 133.4, 134.7, 137.8. HRMS (FAB): *m/z* calcd for $C_{12}H_{12}O$ [M^+]: 172.0888; found: 172.0891.

(13) The stereochemistry of alkene moiety was determined by NOE observation (Figure 1).

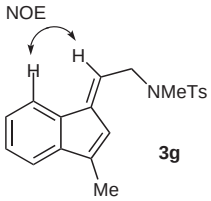

Figure 1

(14) In the presence of $AuCl_3$ (5 mol%) as a catalyst, almost no cycloisomerization of **1j** proceeded even at 80 °C in toluene (see ref. 5).

(15) (1*E*)-1-(Iodomethylene)-3-methyl-1*H*-indene (**3m**): yellow oil. IR (neat): 1110, 1079, 1019 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.16 (s, 3 H), 6.35 (s, 1 H), 7.14–7.29 (m, 4 H), 7.39 (d, 1 H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 79.1, 119.1, 125.1, 125.7, 126.5, 127.8, 135.6, 144.3, 145.9, 150.0. HRMS (FAB): *m/z* calcd for $C_{11}H_9I$ [M^+]: 267.9749; found: 267.9747.

(16) During the purification of the products, some vinyl iodide (*E*)-**3m** was isomerized to (*Z*)-**3m**.