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Gold-catalyzed consecutive [1,2] alkyl migration-oxygen transfer reaction of 2-alkynyl-1-tetralones

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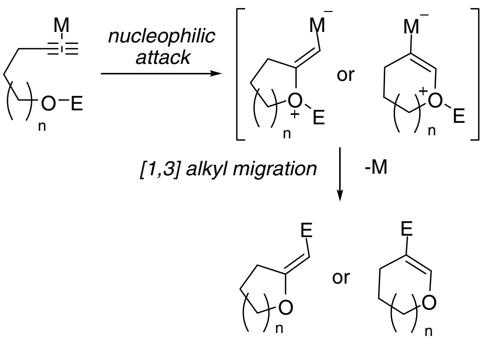
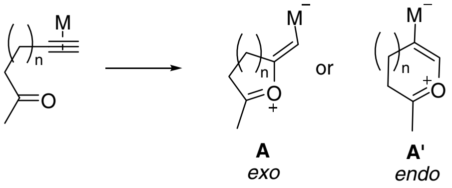
ABSTRACT

Gold-catalyzed isomerization of 2-alkynyl-1-tetralones afforded the corresponding 2-naphthylmethyl ketones in good to high yields. For example, the reaction of 2-{4-(methoxyphenyl)methyl}-2-(phenylethynyl)-3,4-dihydronaphthalen-1(2*H*)-one and 2-benzyl-2-(phenylethynyl)-3,4-dihydronaphthalen-1(2*H*)-one in the presence of 5 mol % of $(Ph_3P)AuCl$ and 5 mol % of AgOTf in THF at 50 °C gave 2-{1-(4-methoxyphenylmethyl)naphthalen-2-yl}-1-(4-methoxyphenyl)ethanone and 2-(1-benzylnaphthalen-2-yl)-1-phenylethanone in 85% and 96% yields, respectively. The present reaction proceeds through [1,2] alkyl migration followed by oxygen transfer.

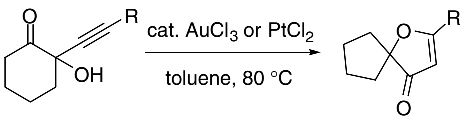
The employment of domino reaction in rearrangement is especially important for the access of complex frameworks.[1] Several groups, including ours, have recently reported domino reactions proceeding through consecutive nucleophilic attack of an alkoxy sp^3-oxygen atom to a C–C triple bond, which were activated by π-acidic transition metal complex, followed by [1,3] alkyl migration (Scheme 1).[2] We envisioned that the use of carbonyl sp^2-oxygen nucleophile instead of ether sp^3-oxygen nucleophiles would lead us to new domino reactions incorporating carbon–oxygen bond formation and carbon group migration (Scheme 2). It has been revealed that the resulting oxonium-containing vinylmetal intermediate **A** and **A′** undergoes various transformations, such as isomerization to vinyl carbenoids,[3] [3,3] rearrangement,[4] proton shift involving protodemetalation,[5] trapping with external nucleophiles,[6] ring expansion,[7] oxygen transfer (hetero-enyne metathesis),[8] and cycloaddition.[9] Recently, Kirsch et al. reported gold- and platinum-catalyzed domino reactions consisting of heterocyclization and [1,2] alkyl migration (Eq. 1).[10,11] In their reaction, the oxygen lone pair of the hydroxy group provides the critical driving force in the reaction allowing this kind of acyloin rearrangements to take place under mild conditions. Herein, we report that the gold-catalyzed reaction of 2-alkynyl-1-tetralones **1** proceeds through consecutive [1,2] alkyl migration-oxygen transfer producing 1,2-disubstituted naphthalenes **2** in good to excellent yields (Eq. 2).[12]



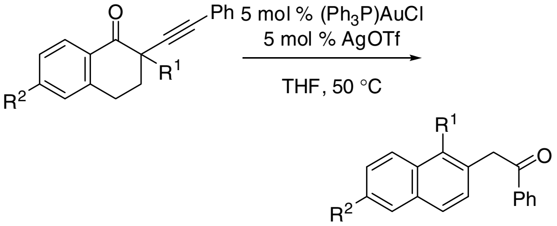
Scheme 1. Intramolecular nucleophilic attack of an alkoxy oxygen atom followed by [1,3] alkyl migration catalyzed by π-acidic transition metal (M).



Scheme 2. Intramolecular nucleophilic attack of a carbonyl oxygen atom catalyzed by π-acidic transition metal (M).



(1)



(2)

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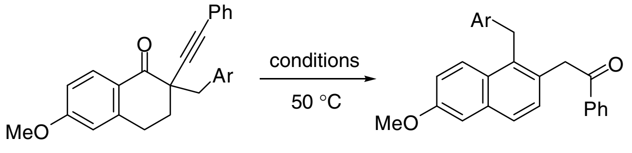
Table 1
Catalytic activity for isomerization of **1a**

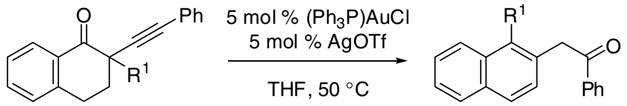


1a (Ar = *p*-anisyl) **2a** (Ar = *p*-anisyl)

Entry	Catalyst (mol %)	Solvent	Yield/%[a]
1	$(Ph_3P)AuCl$ (5) + AgOTf (5)	THF	89
2[b]	$(Ph_3P)AuCl$ (5) + AgOTf (5)	THF	73
3	$(tBu_2PhP)AuCl$ (5) + AgOTf (5)	THF	63
4	{(*p*-Anisyl)Ph_2P}AuCl (5) + AgOTf (5)	THF	57
5	{(*p*-$F_3CC_6H_4$)Ph_2P}AuCl (5) + AgOTf (5)	THF	69
6	$(Ph_3P)AuCl$ (5) + $AgBF_4$ (5)	THF	57
7	$(Ph_3P)AuCl$ (5) + $AgSbF_6$ (5)	THF	16[c]
8	$(Ph_3P)AuCl$ (5) + $AgNTf_2$ (5)	THF	11[d]
9	$(Ph_3P)AuCl$ (5) + AgOTf (5)	Toluene	80
10[b]	$(Ph_3P)AuCl$ (5) + AgOTf (5)	CH_2Cl_2	18[e]
11[b]	$(Ph_3P)AuCl$ (5) + AgOTf (5)	MeCN	5[f]
12[b]	$(Ph_3P)AuCl$ (5) + AgOTf (5)	$MeNO_2$	5[g]
13	$(Ph_3P)AuCl$ (10)	Toluene	Nr[h]
14[b]	AgOTf (10)	Toluene	43
15	TfOH (20)	Toluene	—[i]

[a] ^1H NMR yield using dibromomethane as an internal standard.
[b] At 35 °C.
[c] 42% of **3** was obtained.
[d] 53% of **3** was obtained.
[e] 48% of **1a** was recovered.
[f] 16% of **1a** was recovered.
[g] 57% of **1a** was recovered.
[h] Nr: no reaction.
[i] Decomposition of **1a** was observed.

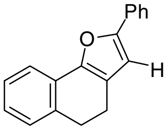
Table 2
Gold-catalyzed consecutive [1,2] alkyl migration-oxygen transfer reaction of **1**[a]



Entry	1	R^1	Time	2	Yield/%[b]
1	**1b**	benzyl	20 min	**2b**	96
2	**1c**	(*p*-Tolyl)CH_2	20 min	**2c**	Quant
3	**1d**	(*p*-Anisyl)CH_2	20 min	**2d**	85
4	**1e**	{2,5-$(MeO)_2C_6H_3$}CH_2	21 h	**2e**	59
5	**1f**	Me	12 h	**—**	No reaction
6	**1g**	Et	1 h	**2g**	12
7[c]	**1h**	*i*-Pr	14.5 h	**2h**	21

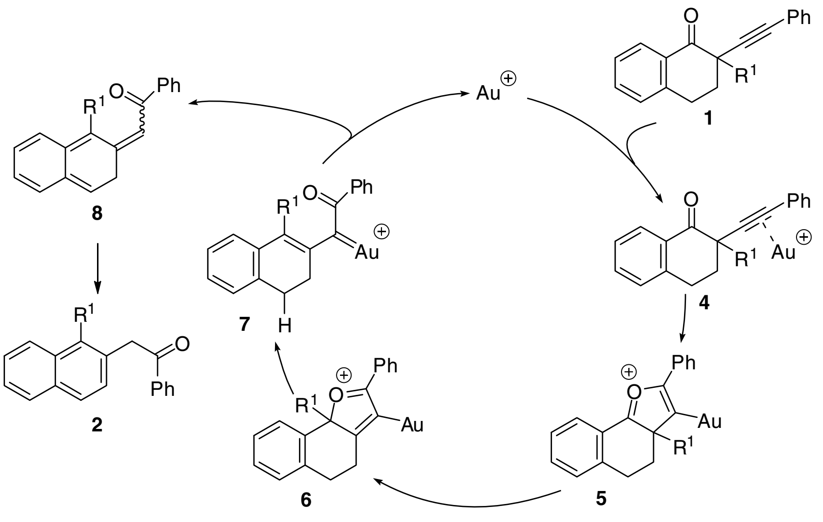
[a] The reaction of **1** (0.2 mmol) was carried out in the presence of 5 mol % of $(Ph_3P)AuCl$ and 5 mol % of AgOTf in THF (0.4 mL) at 50 °C.
[b] Isolated yield.
[c] The reaction of **1h** was carried out in the presence of 5 mol % of AuCl at 70 °C.

First, we optimized the reaction conditions using **1a** as the substrate. The results are summarized in Table 1. The reaction of **1a** in the presence of 5 mol % of $(Ph_3P)AuCl$ and 5 mol % of AgOTf in THF at 50 °C gave **2a** in 89% yield (entry 1).[13] The reaction at 35 °C afforded **2a** in 73% yield (entry 2). The use of other gold-phosphine complexes, such as $(tBu_2PhP)AuCl$, {(*p*-anisyl)Ph_2P}AuCl,[14] and {(*p*-$F_3CC_6H_4$)Ph_2P}AuCl[14] instead of $(Ph_3P)AuCl$, afforded **2a** in lower yields (entries 3–5). The present reaction was significantly affected by the counteranion of the silver salt; when silver salts having weakly coordinating anions, such as bis(trifluorosulfonyl)amide and hexafluoroantimonate, were used, the yield of **2a** decreased, forming a large amount of byproduct **3** (entries 7 and 8).[15] The reaction of **1a** using toluene instead of THF gave **2a** in 80% yield, whereas CH_2Cl_2, acetonitrile, and nitromethane were less effective (entries 9–12). The reaction in the absence of silver salts did not proceed at all (entry 13). The reaction using AgOTf as catalyst afforded **2a** in a lower yield, although TfOH led to decomposition of the starting material **1a** (entries 14 and 15).



3

We applied the optimal conditions (Table 1, entry 1) to various substrates (Eq. 2). The results are summarized in Table 2. The reaction of 1b and 1c, which had a benzyl and p-tolylmethyl group, respectively, as a migrating group, completed within 20 min, giving 2b and 2c in good to excellent yields (entries 1 and 2). The reaction of 1d bearing a (p-methoxyphenyl)methyl group at R1 proceeded smoothly, while that of 1e having a (2,4-dimethoxyphenyl)methyl group took 21 h due to steric hindrance of the migration group (R1) (entries 3 and 4). As expected, methyl and ethyl groups proved to be poor migrators; formation of gold mirror was observed (entries 5 and 6). The substrate 1h having an isopropyl group at



Scheme 3. Plausible mechanism.

R1 was instead converted to 2h by the use of AuCl as catalyst and by elevating the reaction temperature to 70 °C, though the chemical yield was low (entry 7).

A plausible mechanism of the reaction of **1** is illustrated in Scheme 3. The cationic gold catalyst first coordinates to the alkynyl moiety of **1**. The then triggered intramolecular nucleophilic attack of the carbonyl group to the electron-deficient triple bond leads to the formation of cyclic intermediate **6**. [1,2] Alkyl migration would be followed by C–O bond cleavage, forming the gold carbenoid intermediate **7**.[16,17] Finally, hydrogen transfer leads to elimination of the gold catalyst, and aromatization of **8** would give **2**. Formation of **3** as a byproduct clearly suggests intermediacy of the furyl-gold species **5**.[18]

In conclusion, we are now in the position to synthesize 2-naphthylmethyl aryl ketones by using cationic gold catalysts. This present reaction, which proceeds via carbon functional group migration on an oxonium ion, is a useful methodology to synthesize complex compounds in an efficient and atom-economic manner. Further investigations including mechanistic studies are currently on going in our laboratory.

Acknowledgment

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Supplementary data

Experimental procedures and characterization of the products **2** and **3**. This material is available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.10.129.

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13. *General procedure*: A stock solution of $(Ph_3P)AuOTf$ (0.05 M) was prepared by mixing stoichiometric amounts of $(Ph_3P)AuCl$ and AgOTf in THF under argon at room temperature for 5 min, and was allowed to stand for another 10 min for gravitational sedimentation to take place. To a 1 dram vial with a threaded cap containing a magnetic stir bar and **1b** (73.2 mg, 1 equiv) in 0.2 mL of THF at 50 °C under argon was added 0.2 mL of the pre-generated solution of $(Ph_3P)AuOTf$ by a microsyringe. The mixture was stirred at 50 °C and monitored by TLC analysis. Upon completion, the mixture was filtered through a short silica plug and eluted with ethyl acetate. The solvent was removed under reduced pressure, and the crude product was chromatographed with hexanes–EtOAc (20:1 v/v) to afford **2b** as pale yellow solid.
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17. Alternatively, it is possible that the transformation from **5** to **6** proceeds through 1,5-alkyl migration.
18. Presumably, a trace amount of water would capture **5** to form the byproduct **3**.