

# Organic & Biomolecular Chemistry

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

*Accepted Manuscripts* are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

## ARTICLE

# Gold-catalyzed Carboalkoxylations of 2-Ethynylbenzyl Ethers to Form 1- and 3-Substituted 2-Methoxy-1-*H*-indenes: Brønsted Acid Versus Gold Catalysis

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,

Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Chun-Hao Chen, Chiou-Dong Wang, Yi-Feng Hsieh and Rai-Shung Liu\*,

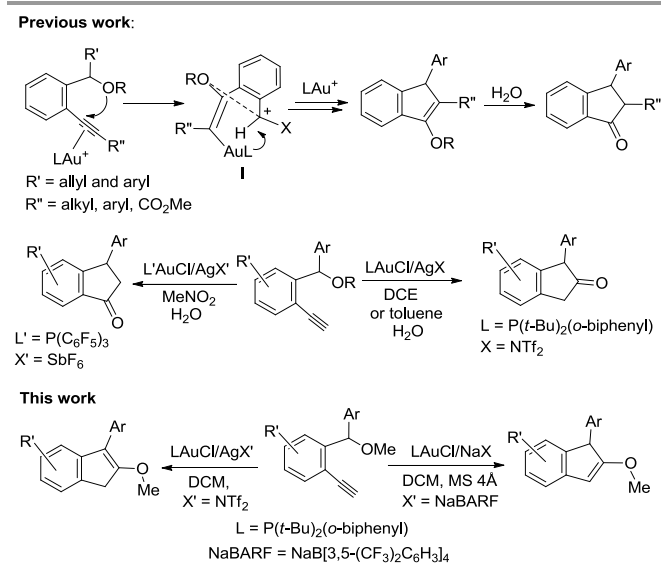
Selective synthesis of 1- and 3-substituted 2-methoxyindenes from the carboalkoxylations of 2-ethynylbenzyl ethers is described; the former is obtained efficiently with  $P(t\text{-Bu})_2(o\text{-biphenyl})\text{AuCl}/\text{NaBARF}$  in DCM/MS 4Å whereas the latter is produced preferably with  $P(t\text{-Bu})_2(o\text{-biphenyl})\text{AuCl}/\text{AgNTf}_2$  in pre-dried DCM. Both 1- and 3-substituted 2-indenyl ethers are subjected to ozone oxidations to afford two distinct carbonyl products. Our new data indicate that 1-substituted 2-indenyl ethers are generated from gold catalysts whereas their 3-substituted analogues arise from Brønsted acid.

## Introduction

The Au- and Pt-catalyzed carboalkoxylations of alkynes are powerful tools to access 1,2-difunctionalized molecules as both C-C and C-O bonds can be introduced onto the alkyne functionality.<sup>1-4</sup> Toste and co-workers reported the carboalkoxylations of 2-alkynylbenzyl ethers bearing internal alkynes, to generate carbocation-like intermediates **I**, ultimately

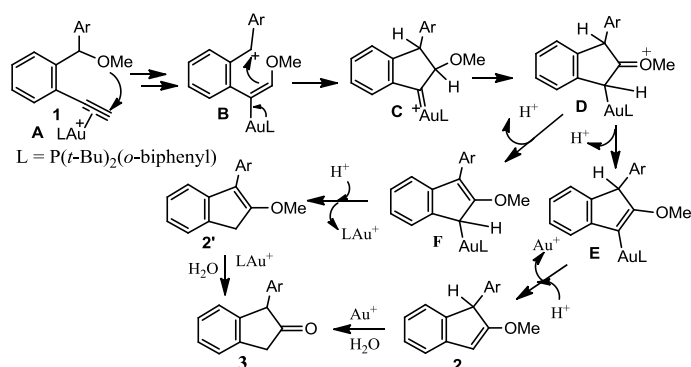
giving 1-indanone products.<sup>4a,b</sup> With their terminal alkyne analogues, we reported the selective synthesis of 1- and 2-indanones through the modifications of gold catalysts and reaction solvents.<sup>4c</sup> Herein,  $P(\text{C}_6\text{F}_5)_3\text{AuCl}/\text{AgSbF}_6$  in  $\text{CH}_3\text{NO}_2$  preferably produced 1-indanones whereas  $P(t\text{-Bu})_2(o\text{-biphenyl})\text{AuCl}/\text{AgNTf}_2$  in dichloromethane (DCM) gave mainly 2-indanones;<sup>4c</sup> both 1- and 2-indanones were postulated to derive from initial gold- $\pi$ -alkyne species via 5-*exo-dig* and 6-*endo-dig* cyclizations respectively. Such chemoselective synthesis is highly dependent on the phosphine ligands and solvents.<sup>5</sup> In this work, we demonstrate the effects of water and the MX as in  $P(t\text{-Bu})_2(o\text{-biphenyl})\text{Cl}/\text{MX}$ , to control the regioselective formation of 1- or 3-aryl-2-methoxy-1-*H*-indenes from the same 2-alkynylbenzyl ethers; the two 2-indenyl ethers are subjected to the ozone oxidations<sup>6</sup> to afford two distinct carbonyl products to highlight the synthetic utility.

Scheme 2 depicts a postulated mechanism to rationalize the formation of 2-indanones using  $\text{LAuCl}/\text{AgNTf}_2$  [ $\text{L} = P(t\text{-Bu})_2(o\text{-biphenyl})$ ] in DCM according to our previous data.<sup>4c</sup> An initial 6-*endo-dig* cyclization of gold- $\pi$ -alkynes **A** generates benzylic cations **B** to achieve an intramolecular carbocyclization, yielding gold carbenes **C**. In dichloromethane, this carbocyclization provides 2-indanones **3** together with 1- or 3-aryl-2-methoxyindenes **2** and **2'**. We tentatively postulate that gold carbenes **C** undergo a 1,2-hydride shift to form new oxonium species **D** that likely lose a proton from the two adjacent C-H moieties to yield two 2-indenyl ethers **2** and **2'** respectively. To gain insight into this mechanism, we sought optimized conditions to generate the two 2-indenyl ethers **2'**



**Scheme 1.** Carboalkoxylations of 2-ethynylbenzyl ethers

and **2** chemoselectively. The counter anion sources (MX) of P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/MX<sup>7</sup> (MX = AgNTf<sub>2</sub>, NaBARF) and the presence of water<sup>8,9</sup> are found to be the major factors to affect the reaction chemoselectivity. These optimized conditions enable us to revise the mechanisms more accurately. More importantly, two indenyl ethers **2** and **2'** seem to arise from Brønsted acid<sup>8,9</sup> and Au(I) complexes respectively.



**Scheme 2.** Postulated routes to regioisomeric 2-indenyl ethers

## Results and Discussions

Our previously investigation<sup>4c</sup> disclosed that the use of LAuCl/AgNTf<sub>2</sub> [L = P(*t*-Bu)<sub>2</sub>*o*-biphenyl] in DCE or DCM provides 2-indanones **3** with optimized yields. Here, we examine the effects of counter anions in DCM at 28°C to yield 1- or 3-phenyl 2-indenyl ethers **2a** and **2a'** efficiently. The workup of solution followed immediately after initial **1a** had just disappeared; a protracted period in the solution led to the formation of 2-indanone **3a** slowly due to presence of residual water. After isolation, the two 2-indenyl ethers were stable on a silica chromatograph. As shown in entry 1 (Table 1), with the use of AgNTf<sub>2</sub> as the anion source, we obtained 3-phenyl-2-indenyl ether **2a'** and 2-indanone **3a** in 71% and 20% respectively, and 1-phenyl-2-indenyl ether **2a** in 5% yield. AgOTf and AgSbF<sub>6</sub> gave a mixture of desired **2a'** in 20-40% yields, together with 1- and 2-indanones **3a** (33-39%) and **4a** (19-35%) in appreciable amount. In contrast, a mixture of P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/AgBF<sub>4</sub> in DCM preferably gave 1-indanone **4a** as the major product (69% yield). We aimed to decrease the formation of 2-indanone **3a**; MS 4Å was introduced to the DCM solution containing LAuCl/AgNTf<sub>2</sub>, seriously inhibiting the reaction seriously to give unreacted **1a** and 2-indanone **3a** in 70% recovery and 19% yield (entry 5). Starting **1a** was recovered in 82% if the reaction was run in toluene in which water was present in a trace proportion. This observation suggests that both water and P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/AgNTf<sub>2</sub> were essentially required to complete the carboalkoxylation reaction of substrate **1a**. A distinct behavior was observed for NaBARF (BARF = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate) as the anion source. The mixture of LAuCl/NaBARF in DCM gave a mixture of

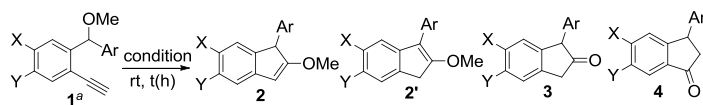
**Table 1.** Effects of counter anions in various solvents

Entry	MX	Solvent/additive <sup>a,b</sup>	time (h)	compounds (yields, %) <sup>c</sup>				
				<b>1a</b>	<b>2a</b>	<b>2a'</b>	<b>3a</b>	<b>4a</b>
1	AgNTf <sub>2</sub>	DCM	3.5	0	5	71	20	0
2	AgOTf	DCM	5	0	0	20	33	35
3	AgSbF <sub>6</sub>	DCM	0.25	0	0	40	39	19
4	AgBF <sub>4</sub>	DCM	1.5	0	6	0	21	69
5	AgNTf <sub>2</sub>	DCM /MS 4Å	24	70	0	0	19	0
6	AgNTf <sub>2</sub>	toluene	5	82	6	0	0	0
7	AgNTf <sub>2</sub>	DCE	4	0	25	61	0	0
8	NaBARF	DCM	0.5	0	47	23	22	0
9	NaBARF	DCM /MS 4Å	0.5	0	90	0	0	0
10	NaBARF	DCE /MS 4Å	0.5	0	85	0	0	0
11	NaBARF	toluene /MS 4Å	1.5	40	48	0	0	0

<sup>a</sup>[**1a**] = 0.1 M. <sup>b</sup>Water is present in trace amount for those solvents without MS 4Å. <sup>c</sup>Product yields are reported after separation from a silica column.

2-indenyl ethers **2a** (47%) and **2a'** (23%) in addition to 2-indanone **3a** (22%). Surprisingly, the presence of MS 4Å in this DCM solution yielded only 1-phenyl-2-methoxyindene **2a** with a yield up to 90% (entry 9). Excellent chemoselectivity was also achieved in DCE/MS 4Å, in which the same **2a** was isolated in 85% yield (entry 10). When toluene/MS 4Å was the solvent; a 60% conversion was attained after 1.5 h, yielding unreacted **1a** and desired **2a** in 40% and 48% yields respectively (entry 11).

We tested the feasibility of such regioselective syntheses over additional 2-ethnylbenzyl ethers **1b-1i** under the optimized conditions **A** and **B**. Condition **A** refers to the use of P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/NaBARF in DCM/MS 4Å whereas **B** involves the use of P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/AgNTf<sub>2</sub> in dried DCM. In condition **B**, water is required to initiate the reaction, thus leading to the partial hydrolysis of indenyl ethers **2'** or **2** to 2-indanones **3**. These starting substrates exclude X = OMe or Y = OMe, which tend to form undesired 1-indanone **4** products preferably.<sup>4c</sup> For ethers **1b** and **1c** bearing X = F or Y = F, their 1-phenyl-substituted ethers **2b** and **2c** were formed exclusively in 93 and 92% yields under condition **A**. In contrast, only ether **1b** (X = F) gave a 82% yield of desired 3-phenyl-2-methoxyindene **2b'** whereas ether **1c** (Y = F) gave a mixture of **2c** (40%) and **2c'** (25%), together with 2-indanone **3c** in 30% yield (entries 1-2). For substrates **1d** and **1e**, conditions **A** and **B** gave desired indenyl ethers **2d-2e** and **2d'-2e'** in 84-91% and 50-60% yields respectively (entries 3-4). For unsubstituted ether (X = Y = H), their corresponding indenyl ethers **2f** and **2f'** were obtained in 94% and 89% yields respectively (entry 5).

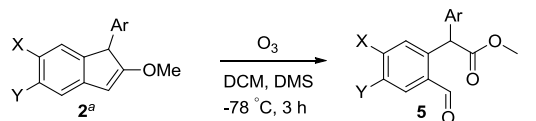
**Table 2.** Formation of two indenyl ethers.

entry	substrates			Condition A		Condition B <sup>b</sup>		
	1	X	Y	Ar	t (h)	Yields(%) <sup>b</sup>	t (h)	Yields(%) <sup>c</sup>
1	1b	F	H	Ph	0.3	2b (93)	3	2b (7) 2b' (82)
2	1c	H	F	Ph	0.3	2c (92)	1.5	2c (40) 2c' (25) 3c (30)
3	1d	H	Cl	Ph	0.5	2d (91)	1	2d' (50) 3d (43)
4	1e	H	Br	Ph	0.3	2e (84)	1.8	2e' (60) 3e (34)
5	1f	H	H	Ph	2	2f (94)	1	2f' (89)
6	1g	Me	H	Ph	0.2	2g (86)	2	2g' (62) 3g (27)
7	1h	<i>t</i> -Bu	H	Ph	0.1	2h (82)	2	2h' (82) 3h (15)
8	1i	H	Me	Ph	0.1	2i (87)	1	2i' (62) 3i (33)
9	1j	H	<i>t</i> -Bu	Ph	0.5	2j (89)	2.5	2j' (77) 3j (17)
10	1k	Cl	H	4-MeC <sub>6</sub> H <sub>4</sub>	0.5	2k (89)	1	2k' (66) 3k (25)
11	1l	Cl	H	4-ClC <sub>6</sub> H <sub>4</sub>	1	2l (88)	1.5	2l' (68) 3l (23)

Condition A : P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuBARF (BARF = B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>)/DCM, MS 4Å. Condition B : P(*t*-Bu)<sub>2</sub>(*o*-biphenyl) AuNTf<sub>2</sub>/DCM. <sup>a</sup>[1] = 0.1 M, 5 mol % catalyst. <sup>b</sup>Water is present in trace amount in Condition B.

<sup>c</sup>Product yields are reported after separation from a silica column.

We tested also the two conditions on alkyl-substituted benzyl ethers **1g-1j** (X = Me, *t*-Bu or Y = Me, *t*-Bu); condition A afforded 1-phenyl-2-methoxyindenes **2g-2j** in 82-89% yields whereas condition B provided their 3-phenyl regioisomers **2g'**

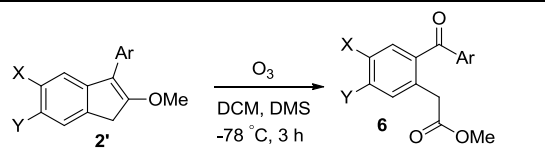
**Table 3.** The ozonolysis of 1-aryl-2-methoxyindenes

entry	substrates				Yields(%) <sup>b</sup>
	2	X	Y	Ar	
1	2a	Cl	H	Ph	5a (81)
2	2b	F	H	Ph	5b (85)
3	2c	H	F	Ph	5c (86)
4	2d	H	Cl	Ph	5d (83)
5	2e	H	Br	Ph	5e (77)
6	2f	H	H	Ph	5f (91)
7	2g	Me	H	Ph	5g (83)
8	2h	<i>t</i> -Bu	H	Ph	5h (88)
9	2i	H	Me	Ph	5i (86)
10	2j	H	<i>t</i> -Bu	Ph	5j (57)
11	2k	Cl	H	4-MeC <sub>6</sub> H <sub>4</sub>	5k (80)
12	2l	Cl	H	4-ClC <sub>6</sub> H <sub>4</sub>	5l (79)

<sup>a</sup>[2] = 0.2 M DMS (1.5 equiv). <sup>b</sup>Product yields are reported after separation from a silica column.

**-2j'** in 62-82% yields (entries 6-9). For benzylethers **1k** and **1l** bearing varied aryl groups (Ar = 4-Cl and 4-MeC<sub>6</sub>H<sub>4</sub>), their corresponding indenyl ethers **2k-2l** and **2k'-2l'** were obtained in 88-89% and 66-68% yields respectively (entries 10-11). For most substrates, two indenyl ethers can be selectively prepared under two optimized conditions, manifesting the utility of these reactions.

We employed ozone oxidations<sup>6</sup> of 1- and 3-aryl methoxyindenes **2** and **2'** to afford distinct aldehyde and ketone derivatives **5** and **6** to highlight their synthetic utility; the results are summarized in Tables 3-4 respectively. For 1-aryl-2-indenyl ethers **2a-2e** bearing X = F, Cl or Y = F, Cl and Br, as shown in Table 3, the oxidative cleavage of these ethers with O<sub>3</sub> in cold DCM at -78 °C (3 h) delivered aldehyde derivatives **5a-5e** in 77-86% yields (entries 1-5, Table 3). This ozonolysis was also extendible to unsubstituted indenyl ether **2f** to give the desired aldehyde **5f** in 91% yield. Such ozone oxidations were compatible with 2-indenyl ethers **2g-2j** bearing X or Y = Me or *t*-Bu, affording the corresponding aldehyde derivatives **2g-2j** in 57-88% yields (entries 7-10, Table 3). For indenyl ethers **2k** and **2l** with Ar = 4-MeC<sub>6</sub>H<sub>4</sub> or 4-ClC<sub>6</sub>H<sub>4</sub>, their ozonolysis reactions provided expected aldehydes **5k** and **5l** in 79-80% yields respectively (entries 11-12).

**Table 4.** The ozonolysis of 3-aryl-2-methoxyindenes

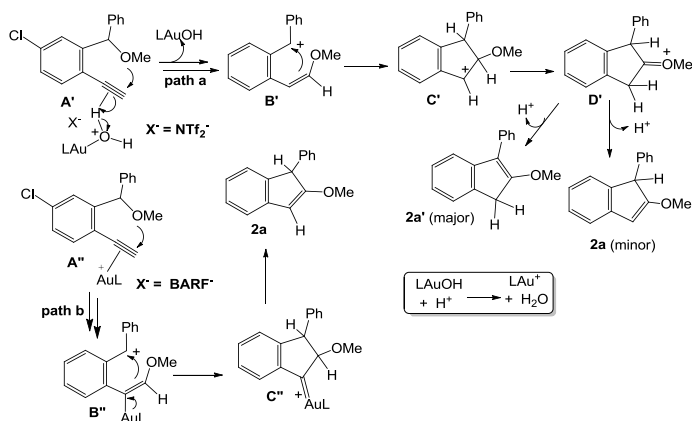
entry	substrates				Yields(%) <sup>b</sup>
	2'	X	Y	Ar	
1	2a'	Cl	H	Ph	6a (78)
2	2b'	F	H	Ph	6b (81)
3	2c'	H	F	Ph	6c (77)
4	2d'	H	Cl	Ph	6d (80)
5	2e'	H	Br	Ph	6e (79)
6	2f'	H	H	Ph	6f (82)
7	2g'	Me	H	Ph	6g (77)
8	2h'	<i>t</i> -Bu	H	Ph	6h (75)
9	2i'	H	Me	Ph	6i (62)
10	2j'	H	<i>t</i> -Bu	Ph	6j (69)
11	2k'	Cl	H	4-MeC <sub>6</sub> H <sub>4</sub>	6k (58)
12	2l'	Cl	H	4-ClC <sub>6</sub> H <sub>4</sub>	6l (61)

<sup>a</sup>[2'] = 0.2 M DMS (1.5 equiv). <sup>b</sup>Product yields are reported after separation from a silica column.

Table 4 shows the same ozone oxidations on 3-aryl-2-methoxyindenes **2'**, but yielding distinct ketone products **6** instead. The reactions were amenable to indenyl ethers **2a'-2e'** bearing X = Cl, Br or Y = F, Cl and Br, yielding the ketone derivatives **6a-6e** in 77-81% yields respectively (entries 1-5). The ozonolysis of unsubstituted indenyl ethers **2'f** yielded the

desired ketone **6f** in 82% (entry 6). These oxidative cleavage reactions were compatible with those indenyl ethers **2g**–**2j** bearing X or Y = Me, *t*-Bu, giving ketone derivatives **6g**–**6j** in 62–77% yields. (entries 7–10). For ethers **2k** and **2l** bearing varied aryl groups, their ozone reactions delivered ketone compounds **6k** and **6l** in 58% and 61% yields respectively (entries 11–12).

With new data in Table 1, we revise the reaction mechanisms more precisely to rationalize chemoselectivity toward **2** and **2'**, as water is required to activate the reaction for P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)AuCl/AgNTf<sub>2</sub>. Herein, LAu<sup>+</sup> and its anion NTF<sub>2</sub><sup>-</sup> will greatly increase the acidity of water as in LAu(H<sub>2</sub>O)<sup>+</sup> via a Lewis-acid activated Brønsted acid model.<sup>9</sup> Accordingly, we postulate that LAu(H<sub>2</sub>O)<sup>+</sup> is likely the active species in the initial carbocyclizations (path a), as depicted in Scheme 3, forming an intermediate **C'** that undergoes Pinacol-type 1,2-hydride shift<sup>10–11</sup> to generate an oxonium species **D'**. The *CHPh* proton of species **D'** is more acidic than that of the methylene protons, thus giving 3-phenyl-substituted **2a'** as the major product, consistent with our results. In contrast, the use of LAuCl/NaBARF provides a gold- $\pi$ -alkyne intermediate to initiate the carbocyclization reaction (path b), generating gold-carbene intermediate **C''** that undergoes a well known 1,2-hydride shift<sup>11</sup> to form 1-phenyl-substituted **d**<sub>1</sub>-**2a** as the major or exclusive product.



**Scheme 3.** Revised mechanisms for the effects of counter anions.

## Conclusions

In summary, we have found two optimized conditions to obtain 1- and 3-aryl-2-methoxyindenes **2** and **2'**<sup>12–14</sup> from the carboalkoxylation reactions of 2-ethynylbenzyl ethers **1** using LAuCl/NaBARF and LAuCl/AgNTf<sub>2</sub> respectively. These two indenyl ethers are further oxidatively cleaved with ozone in cold DCM to yield two distinct aldehyde and ketone products. The new data together with our re-analysis of previous deuterium experiments reveal that 1-aryl-2-methoxyindenes **2** are produced from gold- $\pi$ -alkyne species whereas 3-aryl-2-methoxyindenes **2'** are catalyzed mainly from Brønsted acid, presumably in the form of LAu(H<sub>2</sub>O)NTF<sub>2</sub>.<sup>13,14</sup>

## Experimental

### General procedure

Unless otherwise noted, the preparations of the substrates were performed in oven-dried glassware under nitrogen atmosphere with freshly distilled solvents. Catalytic reactions were performed under an argon atmosphere. DCE and DCM were distilled from CaH<sub>2</sub> under nitrogen. THF and toluene were distilled from Na metal under nitrogen. Commercial reagents were used without further purification. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Varian 400 MHz, Bruker 400, Bruker 500 and 600 MHz Spectrometers using chloroform-*d* (CDCl<sub>3</sub>) as the internal standards.

### Typical Procedure for the synthesis of 1-phenyl-2-methoxyindene (**2a**):

After adding 4 Å molecular sieves (60 mg), a dichloromethane (1.0 mL) solution of AuCl(*t*-Bu)<sub>2</sub>P(*o*-biphenyl) (6.2 mg, 5 mol %) and NaBARF (10.3 mg, 5 mol %) was stirred at rt for 10 min, and to this solution was slowly added a dichloromethane (1.3 mL) solution of 4-chloro-1-ethynyl-2-(methoxy(phenyl)methyl)benzene (**1a**) (60 mg, 0.2 mmol) at rt. The solution was stirred for 0.5 h before it was filtered over a Celite bed. The solvent was evaporated under reduced pressure, and the residue was purified on a flash silica-gel column to give compound **2a** (54 mg, 0.2 mmol, 90% yield) as a yellow oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  7.27–7.30 (m, 2H), 7.23–7.26 (m, 1H), 7.05–7.14 (m, 4H), 6.98 (br, 1H), 5.69 (s, 1H), 4.45 (s, 1H), 3.75 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  170.1, 143.4, 142.3, 137.7, 128.8, 128.5, 128.1, 127.3, 127.2, 124.0, 119.8, 98.4, 57.7, 54.7. HRMS(EI) calcd. for C<sub>16</sub>H<sub>13</sub>ClO: 256.0655, found 256.0654.

### Typical Procedure for the synthesis of 3-phenyl-2-methoxyindene (**2a'**):

A dichloromethane (1.0 mL) solution of AuCl(*t*-Bu)<sub>2</sub>P(*o*-biphenyl) (6.2 mg, 5 mol %) and AgNTf<sub>2</sub> (4.4 mg, 5 mol %) was stirred at rt for 10 min; to this solution was slowly added a dichloromethane (1.3 mL) solution of 4-chloro-1-ethynyl-2-(methoxy(phenyl)methyl)benzene (**1a**) (60 mg, 0.2 mmol) at rt. The solution was stirred for 3.5 h before it was filtered over a Celite bed. The solvent was evaporated under reduced pressure; the residue was purified on a flash silica-gel column to give compound **2a'** (42.6 mg, 0.17 mmol, 71% yield) as yellow oil and **3a** (14.2 mg, 0.06 mmol, 25%) as a yellow oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  7.51–7.53 (m, 2H), 7.41–7.44 (m, 2H), 7.28–7.31 (m, 1H), 7.22–7.25 (m, 2H), 7.03 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.82 (s, 3H), 3.55 (s, 2H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  161.7, 147.1, 133.6, 133.1, 132.8, 128.7, 128.4, 126.9, 124.2, 122.5, 118.5, 116.4, 57.9, 34.8. HRMS(EI) calcd. for C<sub>16</sub>H<sub>13</sub>ClO: 256.0655, found 256.0648.

### Procedure for ozonolysis of 1-phenyl-2-methoxy indene (5a):

A dichloromethane (2.3 ml) solution of compound **2a** (60 mg, 0.2 mmol) was cooled to  $-78\text{ }^{\circ}\text{C}$ , and to this solution was introduced with a stream of  $\text{O}_3/\text{O}_2$  ( $\sim 1$  mmol/min of  $\text{O}_3$ ) for 1.0 min. The solution was stirred at rt for 1 h. The resulting mixture was cooled to  $-78\text{ }^{\circ}\text{C}$  and carefully quenched by addition of dimethylsulfide (21.8 mg, 0.4 mmol). After 1 h, the solvent was evaporated under reduced pressure; the residue was purified on a flash silica-gel column to give compound **5a** (54.7 mg, 0.19 mmol, 81% yield) as a yellow oil.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.05 (s, 1H), 7.75 (d,  $J = 8.4$  Hz, 1H), 7.44 (dd,  $J = 7.8, 1.8$  Hz, 1H), 7.35–7.38 (m, 2H), 7.30–7.33 (m, 1H), 7.23–7.24 (m, 2H), 7.15 (d,  $J = 1.8$  Hz, 1H), 6.00 (s, 1H), 3.73 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  192.0, 172.3, 141.9, 140.5, 136.8, 136.2, 132.1, 130.8, 129.1, 129.0, 128.0, 127.8, 52.5 ( $\text{CH}_3 \times 1$ ,  $\text{CH} \times 1$ ). HRMS(ESI) calcd. for  $\text{C}_{16}\text{H}_{13}\text{ClNaO}_3^+$  ( $\text{M}+\text{Na}$ ) $^+$  311.0445, found 311.0446.

### Procedure for ozonolysis of 3-phenyl-2-methoxy indene (6a):

A dichloromethane (2.3 ml) solution of compound **2a'** (60 mg, 0.2 mmol) was cooled to  $-78\text{ }^{\circ}\text{C}$ , and to this solution was introduced with a stream of  $\text{O}_3/\text{O}_2$  ( $\sim 1$  mmol/min of  $\text{O}_3$ ) for 1 min. The solution was stirred at rt for 1 h. The resulting mixture was cooled  $-78\text{ }^{\circ}\text{C}$  and carefully quenched by addition of dimethylsulfide (21.8 mg, 0.4 mmol). After 1 h, the solvent was evaporated under reduced pressure; the residue was purified on a flash silica-gel column to give compound **6a** (52.6 mg, 0.18 mmol, 78% yield) as a yellow oil.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.79 (dd,  $J = 8.4, 1.8$  Hz, 2H), 7.58–7.61 (m, 1H), 7.45–7.48 (m, 2H), 7.43 (dd,  $J = 8.4, 2.4$  Hz, 1H), 7.35 (d,  $J = 2.4$  Hz, 1H), 7.29 (d,  $J = 8.4$  Hz, 1H), 3.82 (s, 2H), 3.53 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  196.5, 171.2, 139.9, 137.0, 133.4, 133.1, 132.7, 132.2, 130.8, 130.3, 129.6, 128.5, 52.0, 38.0. HRMS(ESI) calcd. for  $\text{C}_{16}\text{H}_{14}\text{ClO}_3^+$  ( $\text{M}+\text{H}$ ) $^+$  289.0626, found 289.0627.

## Acknowledgements

The authors wish to thank the National Science Council, Taiwan, and the Ministry of Education for supporting this work.

## Notes and References

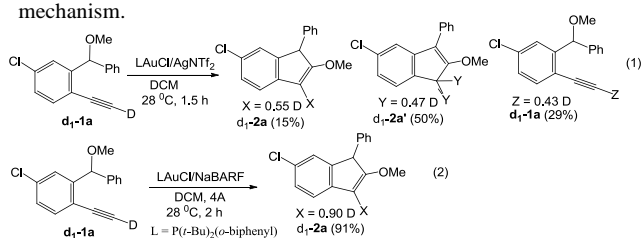
Department of Chemistry, National Tsing-Hua University, Hsinchu, Taiwan, ROC.

E-mail: rslu@mx.nthu.edu.tw

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

- (a) A. Fürstner, P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410–3449; (b) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896–7936; (c) I. Nakamura, Y. Yamamoto, *Chem. Rev.*, 2004, **104**, 2127–2198; (d) N. T. Patil, Y. Yamamoto, *Chem. Rev.*, 2008, **108**, 3395–3442; (e) A. Corma, A. Leyva-Pérez, M. J. Sabater, *Chem. Rev.*, 2011, **111**, 1657–1712; (f) M. Bandini, *Chem. Soc. Rev.*, 2011, **40**, 1358–1367; (g) A. S. K. Hashmi, M. Bührle, *Aldrichimica Acta*, 2010, **43**, 27–33; (h) C. Nevado, *Chimia*, 2010, **64**, 247–251; (i) A. Fürstner, *Chem. Soc. Rev.*, 2009, **38**, 3208–3221.
- For Pt(II) and Pd(I) catalysts, see: (a) I. Nakamura, G. B. Bajracharya, Y. Mizushima, Y. Yamamoto, *Angew. Chem., Int. Ed.*, 2002, **41**, 4328–4331; (b) I. Nakamura, G. B. Bajracharya, H. Wu, K. Oishi, Y. Mizushima, I. D. Gridnev, Y. Yamamoto, *J. Am. Chem. Soc.*, 2004, **126**, 15423–15430; (c) T. Shimada, I. Nakamura, Y. Yamamoto, *J. Am. Chem. Soc.*, 2004, **126**, 10546–10547; (d) I. Nakamura, C. W. Chan, T. Araki, M. Terada, Y. Yamamoto, *Org. Lett.*, 2008, **10**, 309–312; (e) I. Nakamura, Y. Mizushima, Y. Yamamoto, *J. Am. Chem. Soc.*, 2005, **127**, 15022–15023; (f) A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.*, 2000, **122**, 6785–6786; (g) A. Fürstner, P. W. Davies, *J. Am. Chem. Soc.*, 2005, **127**, 15024–15025; (h) C.-M. Ting, C.-D. Wang, R. Chaudhuri, R.-S. Liu, *Org. Lett.*, 2011, **13**, 1702–1705; (i) A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.*, 2001, **123**, 11863–11869; (j) S. Cacchi, G. Fabrizi, P. Pace, *J. Org. Chem.*, 1998, **63**, 1001–1007; (k) I. Nakamura, Y. Mizushima, U. Yamagishi, Y. Yamamoto, *Tetrahedron*, 2007, **63**, 8670–8676; (l) A. Fürstner, E. Heilmann, P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 4760–4763.
- For gold catalysts, see: (a) I. Nakamura, T. Sato, Y. Yamamoto, *Angew. Chem., Int. Ed.*, 2006, **45**, 4473–4475; (b) H. J. Bae, B. Baskar, S. E. An, J. Y. Cheong, D. T. Thangadurai, I.-C. Hwang, Y. H. Rhee, *Angew. Chem., Int. Ed.*, 2008, **47**, 2263–2266; (c) C. Kim, H. J. Bae, J. H. Lee, W. Jeong, H. Kim, V. Sampath, Y. H. Rhee, *J. Am. Chem. Soc.*, 2009, **131**, 14660–14661; (d) H. Kim, Y. H. Rhee, *J. Am. Chem. Soc.*, 2012, **134**, 4011–4014; (e) D. M. Schultz, N. R. Babij, J. P. Wolfe, *Adv. Synth. Catal.*, 2012, **354**, 3451–3455; (f) M. Zhang, Y. Wang, Y. Yang, X. Hu, *Adv. Synth. Catal.*, 2012, **354**, 981–985.
- (a) P. Dube, F. D. Toste, *J. Am. Chem. Soc.*, 2006, **128**, 12062–12063; (b) W. Zi, F. D. Toste, *J. Am. Chem. Soc.*, 2013, **135**, 12600–12603; (c) C.-D. Wang, Y.-F. Hsieh, R.-S. Liu, *Adv. Synth. Catal.*, 2014, **356**, 144–152.
- The effect of ligands on the chemoselectivity of gold catalysis, see selected reviews: (a) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351–3378; (b) N. D. Shapiro, F. D. Toste, *Synlett*, 2010, 675–691.
- For  $\text{O}_3$ -oxidative cleavage, see selected examples: (a) D. A. Bleasdale, D. W. Jones, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1683–1692; (b) C. Schwartz, J. Raible, K. Mott, P. H. Dussault, *Org. Lett.*, 2006, **8**, 3199–3201; (c) R. Willand-Charnley, P. H. Dussault, *J. Org. Chem.*, 2013, **78**, 42–47; (d) S. G. V. Ornum, R. M. Champeau, R. Pariza, *Chem. Rev.*, 2006, **106**, 2990–3001; (e) N. M. Cain, E. R. T. Tiekink, D. K. Taylor, *J. Org. Chem.*, 2012, **77**, 3808–3819.
- For the “silver effects” of gold catalysts, see: (a) D. Wang, R. Cai, S. Sharma, J. Jirak, S. K. Thummanapelli, N. G. Akhmedov, H. Zhang, X. Liu, J. L. Petersen, X. Shi, *J. Am. Chem. Soc.*, 2012, **134**, 9012–9019; (b) S. R. Patrick, I. I. F. Boogaerts, S. Gaillard, A. M. Z. Slawin, Nolan, S. P. Beilstein, *J. Org. Chem.*, 2011, **7**, 892–896.
- In the presence of Au(I) catalysts, the role of Brønsted acid is highly pronounced. See selected examples: (a) C. H. Cheon, O. Kanno, F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 13248–13251; (b) O. Kanno, W.

- Kuriyama, Z. J. Wang, F. D. Toste, *Angew. Chem., Int. Ed.*, 2011, **50**, 9919-9922.
- 9 The acidity of H<sub>2</sub>O can be increased significantly in the presence of Lewis acids; see selected examples (a) H. Yamamoto, K. Futatsugi, *Angew. Chem., Int. Ed.*, 2005, **44**, 1924-1942. (b) H. Ishibashi, K. Ishihara, H. Yamamoto, *Chem. Rec.*, 2002, **2**, 177-188.
- 10 Pinacol-type reactions: (a) T. Bach, F. Eilers, *J. Org. Chem.*, 1999, **64**, 8041-8044; (b) L. E. Overman, E. J. Velthuisen, *J. Org. Chem.*, 2006, **71**, 1581-1587; (c) N. Hanaki, J. T. Link, D. W. C. MacMillan, L. E. Overman, W. G. Trankle, J. A. Wurster, *Org. Lett.*, 2000, **2**, 223-226; (d) S. Matsubara, H. Yamamoto, K. Oshima, *Angew. Chem., Int. Ed.*, 2002, **41**, 2837-2840; (e) S. A. Snyder, S. B. Thomas, A. C. Mayer, S. P. Breazzano, *Angew. Chem., Int. Ed.*, 2012, **51**, 4080-4084.
- 11 See selected examples: (a) S. F. Kirsch, J. T. Binder, B. Crone, A. Duscheck, T. T. Haug, C. Liebert, H. Menz, *Angew. Chem., Int. Ed.*, 2007, **46**, 2310-2313; (b) J.-M. Tang, S. Bhunia, S. M. Abu Sohel, M.-Y. Lin, H.-Y. Liao, S. Datta, A. Das, R.-S. Liu, *J. Am. Chem. Soc.*, 2007, **129**, 15677-15683; (c) V. V. Pagar, A. M. Jadhav; R.-S. Liu, *J. Org. Chem.*, 2013, **78**, 5711-5716; (d) A. M. Jadhav, V. V. Pagar; R.-S. Liu, *Angew. Chem., Int. Ed.*, 2012, **51**, 11809-11813; (e) A. S. K. Hashmi, W. Yang, F. Romminger, *Angew. Chem., Int. Ed.*, 2011, **50**, 5762-5765.
- 12 For metal-catalyzed synthesis of 1- or 2-indenyl ethers see ref 4 and selected examples: (a) I. Nakamura, G. B. Bajracharya, H. Wu, K. Oishi, Y. Mizushima, I. D. Gridnev, Y. Yamamoto, *J. Am. Chem. Soc.*, 2004, **126**, 15423-15430; (b) Y. Nakanishi, K. Miki, K. Ohe, *Tetrahedron.*, 2007, **63**, 12138-12148; (c) J. Zhao, D. A. Clark, *Org. Lett.*, 2012, **14**, 1668-1671; (d) M. Asikainen, S. Woodard, *Tetrahedron.*, 2012, **68**, 5492-5497; (e) P. Becker, D. L. Priebbenow, R. Pierwerdjan, C. Bolm, *Angew. Chem., Int. Ed.*, 2014, **53**, 269-271.
- 13 Our previous work reports deuterium labelling results that are related to this work. As recovered d<sub>1</sub>-**1a** lost significant amount of deuterium content, an exchange with external H<sub>2</sub>O and starting d<sub>1</sub>-**1a** might proceed much faster than the rates in carbalkoxylation reactions. These data did not support or oppose to our newly revised mechanism.



- 14 In a separate experiment, indenyl ether **2a** was treated with P(*t*-Bu)<sub>2</sub>(*o*-biphenyl)Cl/AgNTf<sub>2</sub> (5 mol %) in CD<sub>2</sub>Cl<sub>2</sub> (25 °C, 0.5 – 3 h). As monitored by <sup>1</sup>H NMR, we only observed the NMR peaks of unreacted **2a** and 2-indanone **3a** whereas the other indenyl ether **2a'** was not detectable during this period. We can not obtain the evidence that species **2a** is generated initially to undergo a subsequent isomerization to the other isomer **2a'**. This possibility can not be excluded.