



HAL
open science

Regioselective Synthesis of Indene from 3-Aryl Propargylic gem -Divalates Catalyzed by N -Heterocyclic Carbene Gold(I) Complexes

Damien Hueber, Matthieu Teci, Eric Brenner, Dominique Matt, Jean-Marc Weibel, Patrick Pale, Aurélien Blanc

► **To cite this version:**

Damien Hueber, Matthieu Teci, Eric Brenner, Dominique Matt, Jean-Marc Weibel, et al.. Regioselective Synthesis of Indene from 3-Aryl Propargylic gem -Divalates Catalyzed by N -Heterocyclic Carbene Gold(I) Complexes. *Advanced Synthesis and Catalysis*, 2018, 360 (13), pp.2453-2459. 10.1002/adsc.201800305 . hal-02348174

HAL Id: hal-02348174

<https://hal.science/hal-02348174>

Submitted on 5 Nov 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Regioselective Synthesis of Indene from 3-Aryl Propargylic *gem*-Divaloylates Catalyzed by *N*-Heterocyclic Carbene Gold(I) Complexes

Damien Hueber,^a Matthieu Teci,^b Eric Brenner,^b Dominique Matt,^b Jean-Marc Weibel,^a Patrick Pale,^{a,*} and Aurélien Blanc^{a,*}

^a Laboratoire de Synthèse, Réactivité Organiques, et Catalyse, Institut de Chimie, UMR 7177 CNRS, Université de Strasbourg, 4 rue Blaise Pascal, 67070 Strasbourg, France.

E-mail: ppale@unistra.fr; ablanc@unistra.fr

^b Laboratoire de Chimie Inorganique Moléculaire et Catalyse, Institut de Chimie, UMR 7177 CNRS, Université de Strasbourg, 4 rue Blaise Pascal, 67070 Strasbourg, France.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/adsc.201#####>. ((Please delete if not appropriate))

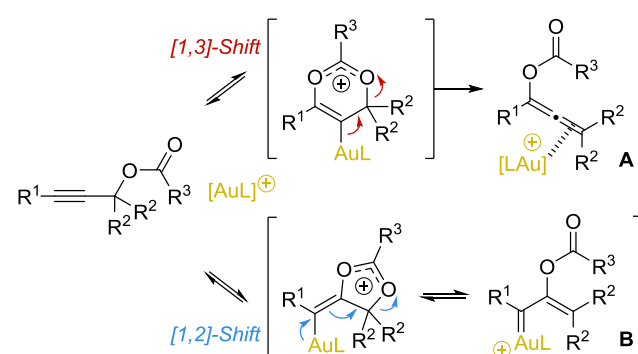
Abstract. 1-Aryl-3,3-bis(pivaloyloxy)propynes can be converted in good to high yields into either 1,3- or 1,2-bis(pivaloyloxy)indenes, depending on the *N*-heterocyclic carbene (NHC) gold(I) hexafluoroantimonate catalyst used. Almost exclusive formation of 1,3-di(oxycarbonyl)indene derivatives was achieved with cationic gold complexes containing the embracing *N,N'*-1,3-bis(9-butylfluorenyl)benzimidazolylidene ligand (ⁿBuFNHC). The regioselective issue of the reaction was rationalized by the specific spatial distribution of the steric bulk in the ⁿBuFNHC ligand. In contrast, only modest selectivities in favor of 1,2-disubstituted indenes were observed with more classical NHC gold complexes, the best selectivity being then obtained with *N,N'*-1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazolylidene gold chloride (SIPrAuCl) as precatalyst.

Keywords: Gold(I); *N*-heterocyclic carbenes; Homogeneous catalysis; Indenes; Rearrangement

Homogeneous gold catalysis has emerged at the turn of the XXIst century, and has rapidly grown through a kind of new “gold rush”,^[1] providing access to numerous compounds under (very) mild conditions, but also offering to the chemical community various new reactions, especially rearrangements.^[2] Among the latter, gold-catalyzed 1,2- and 1,3-acyl migrations of propargylic esters have been a milestone,^[3] considering the various applications,^[4] the complexity associated to decipher the exact mechanism^[5] and the difficulty to tune the selectivity of the 1,2- or 1,3 shift (Scheme 1). This rearrangement is initiated by endo- or exo-dig cyclization of the carboxylate group upon gold coordination to the alkyne moiety, followed by 1,3- or 1,2-migration, leading respectively to a gold

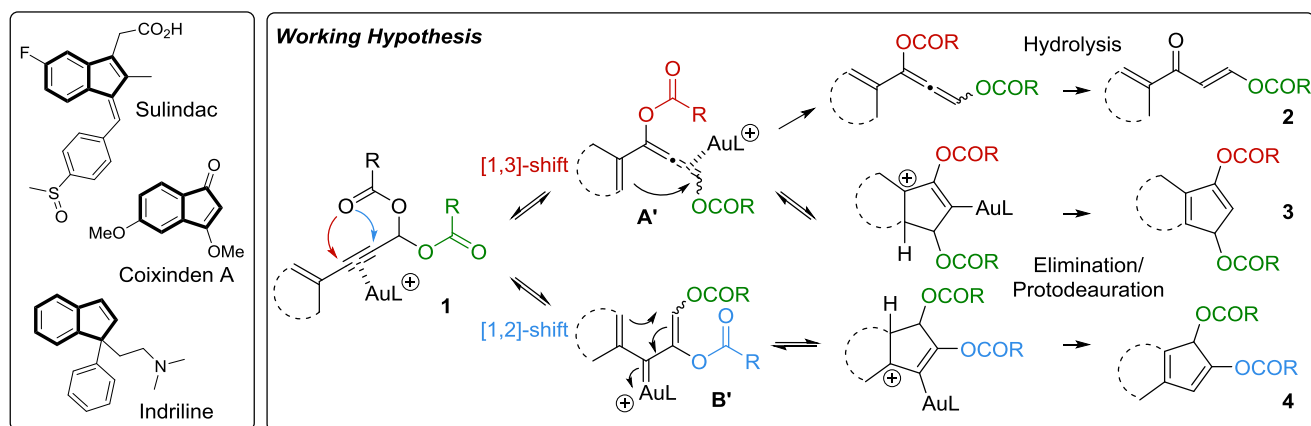
coordinated allene (**A** in Scheme 1) or to a gold carbene (**B** in Scheme 1), which can further evolve. All these intermediates seem to be in equilibrium and of close energy,^[5] and the selectivity towards one or the other pathway seems to be dictated by the **R**¹⁻³ substituents of the propargylic ester.^[6]

Furthermore, it has been shown that alkenyl or aryl propargylic esters (**R**¹ = alkenyl or aryl) lead under gold catalysis to valuable cyclized products upon participation of the unsaturated group to further reactions with intermediates **A** or **B**.^[7] It was also shown that the outcome of such reactions could be adjusted towards one or another product depending on the presence or not of water, of silver salt, and on the ligand nature.^[8]



Scheme 1. Gold(I) Catalyzed Rearrangements of Propargylic Esters.

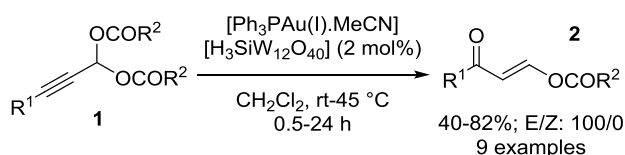
Indenes are recurrent motifs in many pharmaceuticals and natural products (Scheme 2) such as Sulindac, an efficient non-steroidal anti-inflammatory drug, Coixinden A, an antimicrobial substance or Indriline, an antidepressant agent.^[9] Considering the potent biological activities of this



Scheme 2. Selected Natural or Bioactive Products Containing Indene Motifs and Mechanistic Hypothesis for Gold-Catalyzed Transformation of Propargylic *gem*-Diester **1**.

class of molecules, various synthetic methods dedicated to the preparation of indene derivatives have been reported in the literature, including gold catalysis.^[8a,10] We thus wondered if alkenyl or aryl propargylic *gem*-diesters **1** could be engaged in 1,2- or 1,3-migration processes catalyzed by gold, leading to polyfunctionalized building blocks such as indenenes **3** or **4** in only one step (Scheme 2).

In this context, we started investigating the behavior of propargylic *gem*-diesters (**1**) under Au-catalysis and we have already demonstrated that such diesters highly selectively provide (*E*)-3-carboxyloxy enones **2** in good to high yields in the presence of [(triphenylphosphino)gold(I) silicotungstate as non-conventional and recyclable catalyst (Scheme 3).^[11]

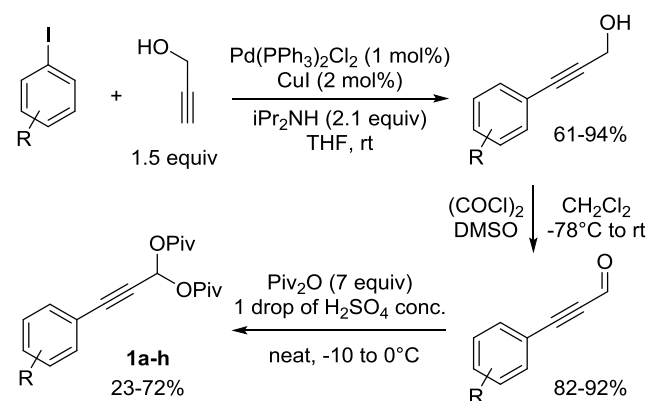


Scheme 3. Polyoxometalate-Gold(I) Catalyzed Stereoselective Rearrangement of Propargylic *gem*-Diesters **1** into (*E*)-Enones.¹⁰

In the present work, we show that certain NHC-gold complexes catalyze the almost exclusive formation of 1,3-di(carboxyloxy)indene derivatives (**3** in Scheme 2) from 3-arylpropargylic *gem*-diesters.

The starting 3-arylpropargylic *gem*-dipivalates **1a-h** were conveniently produced through a three-step sequence from propargyl alcohol and iodo aryl derivatives (Scheme 4). From the latter, a Sonogashira coupling followed by a Swern oxidation allowed the formation of various 3-arylprop-2-yn-1-als. These aldehydes could be converted to their ester acetals in the presence of an excess of anhydride and sulfuric acid as catalyst.^[12] This strategy allows readily varying the aryl moiety, while keeping the

number of steps as short as possible within a scalable sequence.



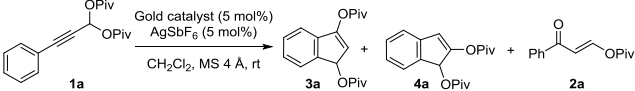
Scheme 4. Three Step Synthesis of Propargyl *gem*-Dipivalates **1a-h**.

The reaction optimization was performed with one of the simplest of these propargylic *gem*-diesters, *i.e.* the 1-phenyl-3,3-bis(pivaloyloxy)propyne (**1a**). The latter was submitted to various gold catalysts, activated or not by silver salt, in dichloromethane at room temperature. These reactions were performed in the presence of anhydrous molecular sieves to trap any adventitious water and thus limiting hydration or hydrolysis side-reactions (Table 1). Despite these precautions, the common (triphenylphosphino)gold catalyst mostly gave mainly the (*E*)-1-phenyl-3-pivaloyloxyprop-2-en-1-one (**2a**), (Table 1, entry 1).^[11,13] The same trend also occurred with less donating phosphite ligand on gold, although with a diminished reactivity (Table 1, entry 2 vs 1). Interestingly, shifting to more donating *o*-biarylphosphines reversed this selectivity in favor of the 1,3-di(pivaloyloxy)indene **3a**, but to the detriment of the kinetic of the reaction (Table 1, entry 3). Rewardingly, gold catalysts carrying even more

donating NHC-type ligand^[14] restored the reactivity, with reaction times mostly below 1 h (Table 1, entries 4-9). Furthermore, depending on NHC substitution, the selectivity towards **3a** could be reinforced, up to the almost exclusive formation of this compound (Table 1, entry 9). NHC ligands also allowed the formation of the 1,2-di(pivaloyloxy)indene **4a**, more or less selectively depending on their nature (Table 1, entries 5-7).^[15]

SIPr and IPr ligands with a high hindrance, measured as the percentage of buried volume (%V_{Bur}), seem to favour the formation of the 1,2-di(pivaloyloxy)indene **4a** (Table 1, entries 6 and 7). However, using this factor, no clear correlation between ligand size and product yields could be found. ~~as demonstrated by the large difference of selectivities (3a/4a) obtained with IrBu and IAd ligands possessing almost the same %V_{Bur} (entry 5 vs 8). On the other hand, the formation of 1,3-disubstituted indene **3a** is particularly erratic when correlated to ligand bulkiness.~~ In contrast, the formation of enone **2a** is almost constant, whatever the NHC used, although with large variations (16±12%). The latter could be due to the more or less important presence of water, brought by the silver salt used to activate the gold chloride catalyst. It is worth noticing here that the highly hygroscopic silver hexafluoroantimonate alone promoted the sole formation of **2a** to an extent of 20% (Table 1, entry 11).

Table 1. Optimization of Gold(I)-Catalyzed Rearrangement of Propargylic *gem*-Dipivalate **1a** in Indene Derivatives **2a** or **3a**.



Entry	Gold Complex (%V _{Bur} for NHC)	Time (h)	Yield 3a ^a	Yield 4a ^a	Yield 2a ^a
1	Ph ₃ PAuCl	0.5	8	-	33
2	PhosphiteAuCl 5 ^b	5	9	-	18
3	JohnPhosAuCl	24	32	-	17
4	IMesAuCl (36.5)	0.25	10	5	28
5	IrBuAuCl (39.3)	0.25	45	28	10
6	IPrAuCl (46.6)	1	25	42	16
7	SIPrAuCl (47.4)	0.75	20	55	18
8	IAdAuCl (39.8)	0.25	41	2	3
9	ⁿ BuFNHC-AuCl 6 ^c (39.4)	0.5	85	6	-
10	ⁿ BuFNHC-AuNTf ₂ 7 ^d (42.6)	3.5	70	15	-
11	AgSbF ₆	24	-	-	20

^a) Calculated yields from ¹H NMR integration relative to an internal standard (hexamethylbenzene). ^b) **5** = tris(2,4-*tert*-butylphenyl)phosphite. ^c) **6** = (1,3-bis(9-butyl-9H-fluoren-9-yl)benzimidazol-2-ylidene)gold(I) chloride. ^d) Reaction run without AgSbF₆, **7** = (1,3-bis(9-butyl-9H-fluoren-9-yl)benzimidazol-2-ylidene) gold(I) triflimide.^[16]

For NHC ligands, the spatial distribution of the steric bulk can easily be depicted by a topographic

steric map (TSM).^[17] Recently, this parameter proved to be a more accurate criterion than the buried volume to rationalize results and selectivity in gold catalysis (Figure 1).^[18]

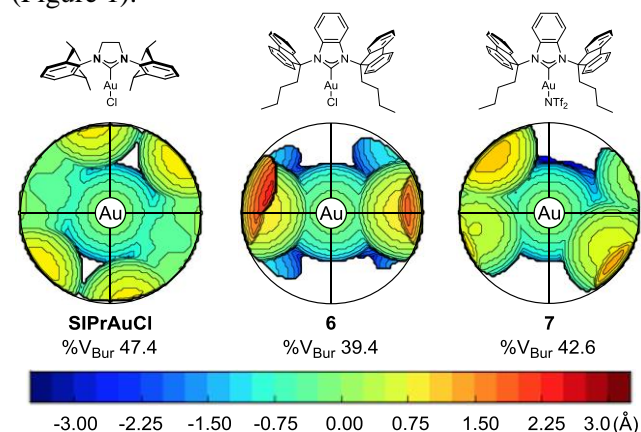
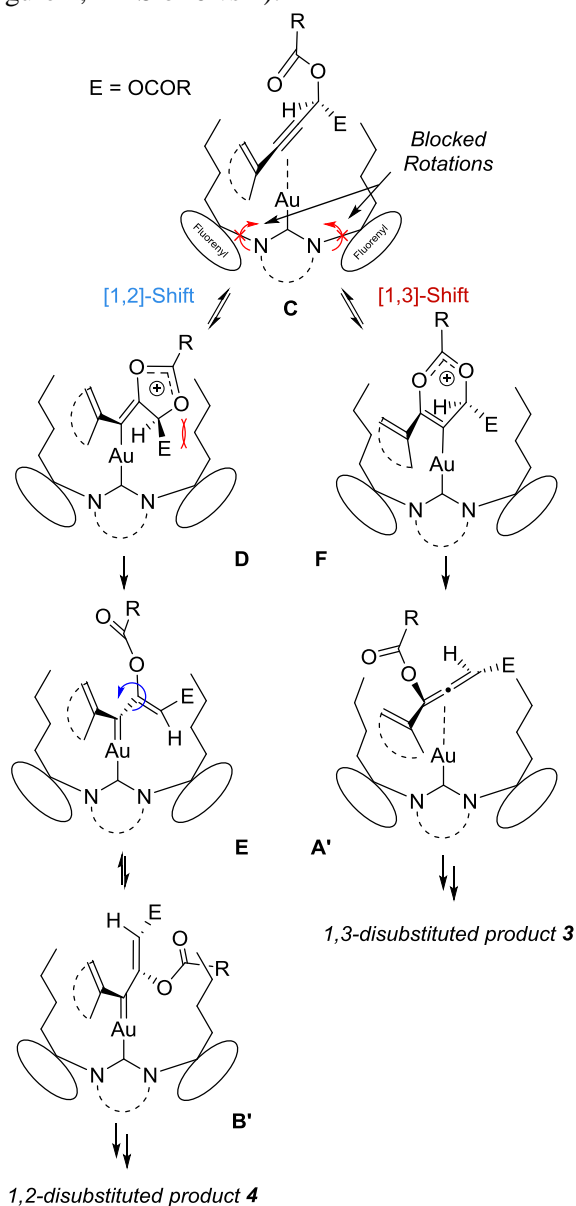


Figure 1. Structures and topographic steric maps (TSM)^[17] of SIPrAuCl, *N,N'*-bis(9-butylfluorenyl)benzimidazolyliedene gold(I) chloride and triflimide complexes **6** and **7**.

The *N,N'*-bis(9-butylfluorenyl)benzimidazolyliedene ligand^[19] (ⁿBuFNHC) outperformed all the evaluated ligands, providing a very high selectivity in favour of the 1,3-disubstituted indene **3a** (Table 1, entry 9 vs 4-8). As already observed for other reactions,^[18b] the strong embracing character of this ligand is likely responsible for the observed selectivity. Indeed, TSM of the gold complex **6** shows that the two butyl chains of the ligand are facing the metal, creating a pocket, which is clearly not the case for the [1,2]-selective SIPr ligand (Figure 1 and Table 1, entry 6 vs 9). The in situ formed cationic [AuL]⁺ complex can thus bind the alkyne bond of **1a** between these two chains, in an orthogonal position relative to the benzimidazole moiety (complex **C** in Scheme 5). It is worth reminding here that π coordination is largely controlled by steric factors.^[20] The coordination induces the subsequent formation of cyclic intermediates **D** or/and **F** (Scheme 5). The latter can easily evolve towards the complex **A'** allene and subsequently to product **3**. In contrast, intermediate **D** already suffered from strong steric interactions between the oxolanium moiety and one butyl side chain, limiting its evolution towards the carbenic intermediate **E**, which is not the case on the intermediate **F**.^[21] Even if formed, intermediate **E** does not have the right conformation to proceed through a Nazarov-type cyclization to the final product. To reach this conformation (intermediate **B'**), a rotation around the C-C bond adjacent to the newly created carbene is required; however, this rotation seems hampered by severe clashes with the butyl side chains. The difficulties to form both intermediates **D** and **B'** are factors that may prevent the formation of the corresponding 1,2-disubstituted product, explaining the high selectivity in favor of the 1,3-disubstituted product.

Of note, the slightly lower selectivity observed using the ⁿBuFNHC gold(I) triflimide **7** could be attributed to the presence of the large NTF₂ counter anion, distorting the clamp formed around gold atom (Figure 1, TMS of **6** vs **7**).



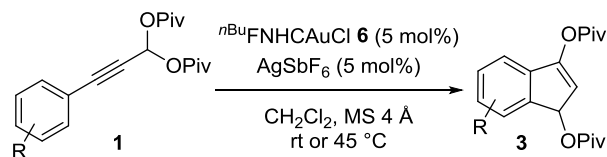
Scheme 5. Simplified view of the developed interactions during the formation of 1,2- or 1,3-disubstituted products within the *N,N'*-bis(9-butylfluorenyl)benzimidazolylidene gold(I)-complex (E = OCOR).

Having identified the best gold catalyst and best conditions to provide 1,3-di(pivaloyloxy)indene **3**, we then explored the scope and limitations of this transformation. Various propargylic *gem*-dipivalates **1a-h** were submitted to the conditions set above (Table 2).

The coordination of the alkynyl moiety to the metal will probably be influenced by the electronic properties of the substituent on the aryl group adjacent to the insaturation. This phenomenon was clearly observed by comparing the *para*-chlorophenyl

derivative **1b** and the methylphenyl derivatives **1d-e**. The former proved to be unreactive (Table 2, entry 2 vs 1) due to its electron-withdrawing substituent, while the latter quantitatively gave the corresponding indenenes **3d-e** (Table 2, entries 4-5 vs 1). With a better electron-donating group, such as in the methoxylated **1c**, the 1,3-regioselectivity slightly decreased, leading to an inseparable mixture of **3c** and **4c** in a ratio of 83:17, but with a steady overall yield of 75% (Table 2, entry 3 vs 1).

Table 2. Scope of *N,N'*-bis(9-Butyl)fluorenyl-NHC Gold(I)-Complex **6** in Catalyzed Transformation of Propargylic *gem*-Diester **1** in 1,3-Di(pivaloyloxy)indene Derivatives **3**.



Entry	Substrate 1	Time (h)	Indene 3	Yield (%) ^a
1	1a (R = H)	1	3a	75
2	1b (R = <i>p</i> Cl)	24	3b	– ^{b,c}
3	1c (R = <i>p</i> OMe)	2	3c	63 ^d
4	1d (R = <i>p</i> Me)	3	3d	98
5	1e (R = <i>m</i> Me)	2	3e + 3e'	98 (3e/3e' 89:11)
6	1f (R = <i>o</i> Me)	24	3f	22 ^{c,e}
7	1g (1-naphtyl)	1	3g	92
8	1h (2-naphtyl)	5	3h	85

^{a)} Isolated yield. ^{b)} No reaction, starting material recovered.

^{c)} Reaction run at 45 °C. ^{d)} Isolated with 12% of 1,2-di(carbonyloxy)indene derivative **4c** (See SI). ^{e)} Along with 74% of unreacted starting material.

To tackle the hindrance issue discussed above, we screened the effect of the substituent position (Table 2, entries 4-6). In the methyl series, the *para* derivative **1d** readily reacted, as expected (Table 2, entry 4), while the *meta* derivative **1e** reacted as efficiently but provided two regioisomers **3e/3e'** in, respectively, a ratio of 89:11 (Table 2, entry 5). As suspected from our model and hindrance developed in Scheme 5, the

ortho derivative **1f** reacted only very slowly, probably because of the steric hindrance generated by the methyl group located close to the insaturation, giving only 22% of the expected product along with the remaining starting material, even after extended reaction time and heating (Table 2, entry 6). These results reasonably fit with our hypothesis: in *para* position, the substituent probably does not feel any constraint, while in *ortho* position, steric interactions with the NHC butyl chain are highly probable. In the *meta* position, less interactions should apply, but in one rotamer the methyl substituent may experience some clash with one butyl chain, thus leading preferentially to one regioisomer.

For the same reason, we also examined the behaviour of the 1- or 2-naphthyl substituted propargylic *gem*-diesters **1g-h** (Table 2, entries 7-8). As expected, both electron rich naphthyl derivatives lead to the formation of two indenenes **3g** and **3h** in high yields. It is noteworthy to mention that the 2-naphthyl derivative **1h** affords exclusively the regioisomer **3h** resulting from selective addition of the naphthyl group in position one.

In summary, we have demonstrated that the spatial repartition of hindrance imparted by ⁿBuFNHC ligand around the gold atom is a key factor in the regioselective conversion in good to high yields of 1-aryl-3,3-bis(pivaloyloxy)-propynes (**1**) into 1,3-di(oxy carbonyl)indene derivatives (**3**). In contrast, only modest selectivity in favor of 1,2-disubstituted indenenes **4** was observed with more classical NHC gold complexes, the best selectivity in this series being then achieved with SIPrAuCl/AgSbF₆ as catalyst.

Further works on the improvement of the [1,2]-migration selectivity as well as on the development of chiral version of *N*-alkylfluorenyl NHC ligands are ongoing in our laboratories.

Experimental Section

General Information. Proton (¹H NMR) and carbon (¹³C NMR) nuclear magnetic resonance spectra were recorded on 300, 400 or 500 MHz instruments. Chemical shifts are given in part per million (ppm) on the delta scale. The solvent peak was used as reference value. For ¹H NMR: CHCl₃ = 7.26 ppm. For ¹³C NMR: CHCl₃ = 77.16 ppm. High resolution mass spectra (HRMS) data were recorded on a microTOF spectrometer equipped with orthogonal electrospray interface (ESI). The parent ions [M]⁺, [M+H]⁺, [M+Li]⁺ or [M+Na]⁺ are quoted. Analytical thin layer chromatography (TLC) was carried out on silica gel 60 F₂₅₄ plates or basic alumina (63–200 μm) with visualization by ultraviolet light or potassium permanganate dip. Flash column chromatography was carried out using silica gel 60 (40–63 μm) or basic Al₂O₃ (63–200 μm) and the procedure included the subsequent evaporation of solvents *in vacuo*. Reagents and solvents were purified using standard means. Dichloromethane (CH₂Cl₂), acetonitrile (CH₃CN), tetrahydrofuran (THF) and diethyl ether (Et₂O) were dried over activated alumina column (DryStation). All other chemicals were used as received, and all extractive procedures were performed using non-distilled solvents and all aqueous solutions used were saturated unless details are given.

General Procedure 1 for the gold-catalyzed rearrangement of propargylic *gem*-dipivalates 2 in 1,3-dipivaloxyindene derivatives 3: AgSbF₆ (5 mol%) was added to a solution of *N,N'*-bis(9-butylfluorenyl)NHCuCl^[18b] **6** (5 mol%) and MS 4A in dry dichloromethane. The resulting mixture was stirred at room temperature for 1 hour. The *gem*-dipivalates (≈ 0.3 mmol) were added to the catalytic solution and stirred at room temperature until completion (NMR monitoring). The reaction mixture was then evaporated, and the crude residue was purified by flash column chromatography over silica gel (Cyclohexane/EA 5%) to afford the desired products.

1*H*-Indene-1,3-diyl bis(2,2-dimethyl-propanoate) 3a: Prepared according General procedure 1 from 0.316 mmol of **1a**; yield: 75% (75.2 mg, 0.238 mmol); yellow oil; TLC *R*_f 0.65 (Cyclohexane/EA 20%); ¹H NMR (400 MHz, CDCl₃) δ 1.23 (s, 9H), 1.38 (s, 9H), 6.26 (d, *J* = 2.3 Hz, 1H), 6.30 (d, *J* = 2.3 Hz, 1H), 7.22–7.29 (m, 2H), 7.30–7.37 (m, 1H), 7.38–7.41 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 27.2, 39.0, 39.7, 74.6, 113.9, 118.5, 124.3, 127.3, 128.7, 138.5, 141.0, 151.3, 175.1, 179.0; HR-MS [M+Na]⁺ 339.1540 [C₁₉H₂₄O₄Na], calculated 339.1567.

6-Methoxy-1*H*-indene-1,3-diyl bis(2,2-dimethyl-propanoate) 3c: Prepared according General procedure 1 from 0.1 mmol of **1c**; yield: 63% (26 mg, 0.075 mmol) as an inseparable mixture with **4c** (12%); colorless oil; TLC *R*_f 0.53 (Cyclohexane/EA 20%); ¹H NMR (400 MHz, CDCl₃) δ 1.23 (s, 9H), 1.37 (s, 9H), 3.81 (s, 3H), 6.13 (d, *J* = 2.4 Hz, 1H), 6.24 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 7.12 (d, *J* = 8.3 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 27.2, 27.2, 39.0, 39.6, 55.7, 74.4, 111.5, 111.9, 113.3, 131.1, 143.0, 151.3, 159.7, 175.1, 179.0; HR-MS [M+Na]⁺ 369.1624 [C₂₀H₂₆O₅Na], calculated 369.1672.

6-Methyl-1*H*-indene-1,3-diyl bis(2,2-dimethyl-propanoate) 3d: Prepared according General procedure 1 from 0.272 mmol of **1d**; yield: 98%, 88.8 mg, 0.269 mmol; yellow oil; TLC *R*_f 0.63 (Cyclohexane/EA 20%); ¹H NMR (400 MHz, CDCl₃) δ 1.27 (s, 9H), 1.37 (s, 9H), 2.38 (s, 3H), 6.18 (d, *J* = 2.4 Hz, 1H), 6.25 (d, *J* = 2.4 Hz, 1H), 7.10–7.16 (m, 2H), 7.21 (s, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 21.6, 27.2, 27.2, 39.0, 39.6, 74.6, 113.0, 118.1, 125.3, 129.2, 135.8, 137.4, 141.2, 151.4, 175.2, 179.1; HR-MS [M+Na]⁺ 353.1769 [C₂₀H₂₆O₄Na], calculated 353.1723.

5-Methyl-1*H*-indene-1,3-diyl bis(2,2-dimethyl-propanoate) 3e: Prepared according General procedure 1 from 0.303 mmol of **1e**, in mixture with 11 mg of 7-methyl-1*H*-indene-1,3-diyl bis(2,2-dimethyl-propanoate) **2c'**; yield: 87% (87 mg, 0.297 mmol); yellow oil; TLC *R*_f 0.63 (Cyclohexane/EA 20%); ¹H NMR (400 MHz, CDCl₃) δ 1.22 (s, 9H), 1.38 (s, 9H), 2.39 (s, 3H), 6.24 (d, *J* = 2.4 Hz, 1H), 6.26 (d, *J* = 2.4 Hz, 1H), 7.03 (brs, 1H), 7.04–7.09 (m, 1H), 7.28 (d, *J* = 7.6 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 21.6, 27.2, 27.2, 39.0, 39.7, 74.4, 114.1, 119.2, 124.1, 127.9, 138.1, 138.7, 151.3, 175.2, 179.0; HR-MS [M+Na]⁺ 353.1711 [C₂₀H₂₆O₄Na], calculated 353.1723.

4-methyl-1*H*-indene-1,3-diyl bis(2,2-dimethyl-propanoate) 3f: Prepared according General procedure 1 from 0.303 mmol of **1f**; yield: 22% (22 mg, 0.067 mmol); yellow oil; TLC *R*_f 0.64 (Cyclohexane/EA 20%); ¹H NMR (400 MHz, CDCl₃) δ 1.23 (s, 9H), 1.36 (s, 9H), 2.52 (s, 3H), 6.24 (d, *J* = 2.4 Hz, 1H), 6.30 (d, *J* = 2.4 Hz, 1H), 7.06–7.10 (m, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.20–7.23 (m, 1H, H₅); ¹³C NMR (126 MHz, CDCl₃) δ 19.4, 27.1, 27.2, 39.0, 39.4, 74.0, 114.1, 121.9, 127.2, 130.6, 131.5, 136.0, 141.6, 153.1, 175.5, 179.0. HR-MS [M+Na]⁺ 353.1720 [C₂₀H₂₆O₄Na], calculated 353.1723.

3*H*-Cyclopenta[*a*]naphthalene-1,3-diyl bis(2,2-dimethylpropanoate) 3g: Prepared according General procedure 1 from 0.273 mmol of **1g**; yield: 92% (91.7 mg,

0.25 mmol); yellow oil; TLC R_f 0.64 (Cyclohexane/EA 20%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.26 (s, 9H), 1.48 (s, 9H), 6.37 (d, $J = 2.3$ Hz, 1H), 6.52 (d, $J = 2.3$ Hz, 1H), 7.46–7.55 (m, 3H), 7.78 (d, $J = 8.3$ Hz, 1H), 7.86–7.90 (m, 1H), 8.62 (d, $J = 8.5$ Hz, 1H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 27.3, 27.3, 39.1, 39.7, 74.3, 114.5, 121.6, 123.9, 125.9, 126.4, 127.3, 128.0, 128.8, 133.5, 134.3, 139.9, 153.2, 175.3, 179.1; HR-MS $[\text{M}+\text{Na}]^+$ 389.1732 $[\text{C}_{23}\text{H}_{26}\text{O}_4\text{Na}]$, calculated 389.1723.

1H-Cyclopenta[a]naphthalene-1,3-diyl bis(2,2-dimethylpropanoate) 3h: Prepared according General procedure 1 from 0.330 mmol of **1h**; yield: 85% (102.4 mg, 0.279 mmol); yellow oil; TLC R_f 0.64 (Cyclohexane/EA 20%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.27 (s, 9H), 1.42 (s, 9H), 6.39 (d, $J = 2.3$ Hz, 1H), 6.64 (d, $J = 2.3$ Hz, 1H), 7.41–7.54 (m, 3H), 7.77–7.82 (m, 1H), 7.86–7.92 (m, 2H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 27.2, 27.3, 39.2, 39.7, 74.2, 113.5, 117.0, 123.4, 125.6, 127.0, 129.0, 129.3, 129.8, 133.1, 136.4, 136.7, 151.4, 175.2, 178.7; HR-MS $[\text{M}+\text{Na}]^+$ 389.1683 $[\text{C}_{23}\text{H}_{26}\text{O}_4\text{Na}]$, calculated 389.1723.

1H-indene-1,2-diyl bis(2,2-dimethylpropanoate) (4a): By-product obtained during the optimization study (table 1); yellow oil; TLC R_f 0.70 (Cyclohexane/EA 20%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 1.30 (s, 9H), 6.81 (d, $J = 12.3$ Hz, 1H), 7.44–7.50 (m, 2H), 7.54–7.59 (m, 1H), 7.90–7.94 (m, 2H), 8.41 (d, $J = 12.3$ Hz, 1H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 26.8, 39.0, 109.9, 128.4, 128.7, 133.0, 138.0, 151.0, 174.6, 190.5; HR-MS $[\text{M}+\text{Na}]^+$ 255.0980 $[\text{C}_{14}\text{H}_{16}\text{O}_3\text{Na}]$, calculated 255.0992.

(E)-3-Oxo-3-phenylprop-1-en-1-yl pivalate (2a): ^[11a] By-product obtained during the optimization study (table 1); yellow oil; TLC R_f 0.45 (Cyclohexane/EA 20%); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 1.30 (s, 9H), 6.81 (d, $J = 12.3$ Hz, 1H), 7.44–7.50 (m, 2H), 7.54–7.59 (m, 1H), 7.90–7.94 (m, 2H), 8.41 (d, $J = 12.3$ Hz, 1H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 26.8, 39.0, 109.9, 128.4, 128.7, 133.0, 138.0, 151.0, 174.6, 190.5; HR-MS $[\text{M}+\text{Na}]^+$ 255.0980 $[\text{C}_{14}\text{H}_{16}\text{O}_3\text{Na}]$, calculated 255.0992.

Acknowledgements

We gratefully acknowledge the CNRS and the French Ministry of Research. D.H. thanks the Agence Nationale de la Recherche (Grant ANR-11-JS07-001-01 SynthetAu) for a PhD fellowship.

References

- [1] a) A. S. K. Hashmi, *Gold Bull.* **2004**, *37*, 51-65; b) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2005**, *44*, 6990-6993; c) S. P. Nolan, *Nature* **2007**, *445*, 496-497; d) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208-3221. e) *Modern Gold Catalyzed Synthesis* (Eds.: F. D. Toste, A. S. K. Hashmi), Wiley-VCH, Weinheim, **2012**. f) *Gold Catalysis: An Homogeneous Approach, Catalytic Science Series, Vol. 13* (Eds.: F. D. Toste, V. Michelet), Imperial College Press, London, **2014**.
- [2] For recent reviews, see: a) A. M. Asiri, A. S. K. Hashmi, *Chem. Soc. Rev.* **2016**, *45*, 4471-4503; b) D. Pflästerer, A. S. K. Hashmi, *Chem. Soc. Rev.* **2016**, *45*, 1331-1367; c) W. Zi, F. Dean Toste, *Chem. Soc. Rev.* **2016**, *45*, 4567-4589; d) Z. Zheng, Z. Wang, Y. Wang, L. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 4448-4458; e) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028-9072; f) B. Ranieri, I. Escofet, A. M. Echavarren, *Org. Biomol. Chem.* **2015**, *13*, 7103-7118.
- [3] a) V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654-8655; b) A. Fürstner, P. Hannen, *Chem. Commun.* **2004**, 2546-2547. c) Y. Harrak, C. Blaszykowski, M. Bernard, K. Cariou, E. Mainetti, V. Mouries, A.-L. Dhimane, L. Fensterbank, M. Malacria *J. Am. Chem. Soc.* **2004**, *126*, 8656-8657.
- [4] For reviews, see: a) N. Marion, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 2750-2752; b) R. K. Shiroodi, V. Gevorgyan, *Chem. Soc. Rev.* **2013**, *42*, 4991-5001.
- [5] A. Correa, N. Marion, L. Fensterbank, M. Malacria, S. P. Nolan, L. Cavallo, *Angew. Chem. Int. Ed.* **2008**, *47*, 718-721.
- [6] J. Jiang, Y. Liu, C. Hou, Y. Li, Z. Luan, C. Zhao, Z. Ke *Org. Biomol. Chem.* **2016**, *14*, 3558-3563.
- [7] For selected examples see: a) L. Zhang, S. Wang *J. Am. Chem. Soc.*, **2006**, *128*, 1442-1443. b) J. Zhao, C. O. Hughes, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 7436-7437; c) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**, *128*, 12614-12615; d) E. Soriano, J. Marco-Contelles, *Chem. Eur. J.* **2007**, *13*, 1350-1357; e) T. Schwier, A. W. Sromek, D. M. L. Yap, D. Chernyak, V. Gevorgyan, *J. Am. Chem. Soc.* **2007**, *129*, 9868-9878. e) D. Leboeuf, A. Simonneau, C. Aubert, M. Malacria, V. Gandon, L. Fensterbank, *Angew. Chem. Int. Ed.* **2011**, *51*, 6868-6871.
- [8] a) N. Marion, S. Diez-Gonzalez, P. de Frémont, A. R. Noble, S. P. Nolan, *Angew. Chem. Int. Ed.* **2006**, *45*, 3647-3650; b) N. Marion, P. Carlqvist, R. Gealagas, P. de Frémont, F. Maseras, S. P. Nolan, *Chem. Eur. J.* **2007**, *13*, 6437-6451; c) P. Nun, S. Gaillard, A. M. Z. Slawin, S. P. Nolan, *Chem. Commun.* **2010**, *46*, 9113-9115; d) A. Gomez-Suarez, R. S. Ramon, O. Songis, A. M. Z. Slawin, C. S. J. Cazin, S. P. Nolan, *Organometallics* **2011**, *30*, 5463-5470; e) P. Nun, S. Gaillard, A. Poater, L. Cavallo, S. P. Nolan, *Org. Biomol. Chem.* **2011**, *9*, 101-104.
- [9] a) H. Buschmann, T. Christoph, in *Analgesics*; H. Buschmann, T. Christoph, E. Friderichs, C. Maul, B. Sundermann, Eds.; Wiley-VCH: Weinheim, **2002**, 106 and references cited therein; b) Y. Ishiguro, K. Okamoto, H. Sakamoto, Y. Sonoda, *Nippon Nogei Kagaku Kaishi* **1993**, *67*, 1405-1410; c) M. P. Young, O. C. Idowu, P. McKeown, (e-Therapeutics Ple, UK), *US Patent* 20110212173, A1 20110901, **2011**.
- [10] For a review on the synthesis of indenenes derivatives, see: a) B. Gabriele, R. Mancuso, L. Veltri, *Chem. Eur. J.* **2016**, *22*, 5056-5094; For selected recent examples in gold catalysis, see: b) X. Yin, M. Mato, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2017**, *56*, 14591-14595; c) M. Alvarez-Perez, M. Frutos, A. Viso, R. Fernandez de la Pradilla, M. C. de la Torre, M. A. Sierra, H. Gornitzka, C. Hemmert, *J. Org. Chem.* **2017**, *82*, 7546-7554; d) A. M. Sanjuan, C. Virumbrales, P. Garcia-Garcia, M. A. Fernandez-Rodriguez, R. Sanz, *Org. Lett.* **2016**, *18*, 1072-1075; e) A. Preinfalk, A. Misale, N. Maulide, *Chem. Eur. J.* **2016**, *22*, 14471-14474; f) N. Morita, M. Miyamoto, A. Yoda, M. Yamamoto, S. Ban, Y. Hashimoto, O. Tamura, *Tetrahedron Lett.* **2016**, *57*, 4460-4463; g) B. Ma, Z.

- Wu, B. Huang, L. Liu, J. Zhang, *Chem. Commun.* **2016**, 52, 9351-9354.
- [11] a) D. Hueber, M. Hoffmann, B. Louis, P. Pale, A. Blanc, *Chem. Eur. J.* **2014**, 20, 3903-3907; b) D. Hueber, M. Hoffmann, P. de Frémont, P. Pale, A. Blanc, *Organometallics* **2015**, 34, 5065-5072.
- [12] F. Wille, W. Schwab *Monatsh. Chem.* **1978**, 109, 337-355.
- [13] Compound **2a** probably results from the hydrolysis of the allenyl diester intermediate **A'** (see Scheme 2).
- [14] P. de Frémont, N. M. Scott, E. D. Stevens, S. P. Nolan *Organometallics* **2005**, 24, 2411-2418.
- [15] For selected examples where the ligand on gold change the outcome of a reaction, see: a) Pablo Mauleón, Rachel M. Zeldin, Ana Z. González and F. Dean Toste *J. Am. Chem. Soc.* **2009**, 131, 6348-6349; b) I. Alonso, B. Trillo, F. Lopez, S. Montserrat, G. Ujaque, L. Castedo, A. Lledos, J. L. Mascarenas *J. Am. Chem. Soc.* **2009**, 131, 13020-13030; c) M. Alcarazo, T. Stork, A. Anoop, W. Thiel, A. Fürstner, *Angew. Chem. Int. Ed.* **2010**, 49, 2542-2546.
- [16] CCDC number for compound **7**: 1549989.
- [17] <https://www.molnac.unisa.it/OMtools/sambvca2.0>. a) A. Poater, F. Ragone, R. Mariz, R. Dorta, L. Cavallo, *Chem. Eur. J.* **2010**, 16, 14348-14353; b) L. Falivene, R. Credendino, A. Poater, A. Petta, L. Serra, R. Oliva, V. Scarano, L. Cavallo, *Organometallics* **2016**, 35, 2286-2293.
- [18] a) A. Gómez-Suárez, D. J. Nelson, S. P. Nolan, *Chem. Commun.* **2017**, 53, 2650-2660. b) M. Teci, D. Hueber, P. Pale, L. Toupet, A. Blanc, E. Brenner, D. Matt, *Chem. Eur. J.* **2017**, 23, 7809-7818.
- [19] M. Teci, E. Brenner, D. Matt, C. Gourlaouen, L. Toupet, *Chem. Eur. J.* **2015**, 21, 10997-11000.
- [20] a) T. J. Brown, M. G. Dickens, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2009**, 131, 6350-6351; b) S. Flügge, A. Anoop, R. Goddard, W. Thiel, A. Fürstner, *Chem. Eur. J.* **2009**, 15, 8558-8565.
- [21] Preliminary calculations (PM6 Spartan) revealed a **68 kJ/mol** difference between the two intermediates **D** and **F** (R = Me).

Regioselective Synthesis of Indene from 3-Aryl Propargylic *gem*-Divalates Catalyzed by *N*-Heterocyclic Carbene Gold(I) Complexes*Adv. Synth. Catal.* **Year**, *Volume*, Page – PageDamien Hueber,^a Matthieu Teci,^b Eric Brenner,^b Dominique Matt,^b Jean-Marc Weibel,^a Patrick Pale,^{a,*} and Aurélien Blanc^{a,*}