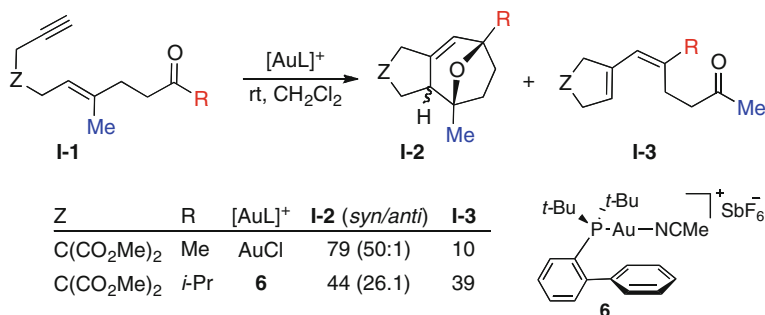


Chapter 2

Gold(I)-Catalyzed Reactions of 1,6-Enynes with Aldehydes: Cycloaddition Versus Metathesis-Type Reactions

2.1 Introduction

The intra- and intermolecular nucleophilic trapping of gold intermediates starting from 1,*n*-enynes, allows the synthesis of very complicated structures in a highly efficient and selective manner (See general introduction) [Ref. 155 in Chap. 1]. In this context, 1,6-enynes with a carbonyl group at the alkenyl side chain such as **I-1** react in the presence of AuCl and other gold(I) catalysts to give oxatricyclic compounds **I-2** by a domino process in which two C–C bonds and one C–O bond are formed (Scheme 2.1) [Ref. 223 Chap. 1]. Fragmentation products **I-3** are also obtained as minor products.

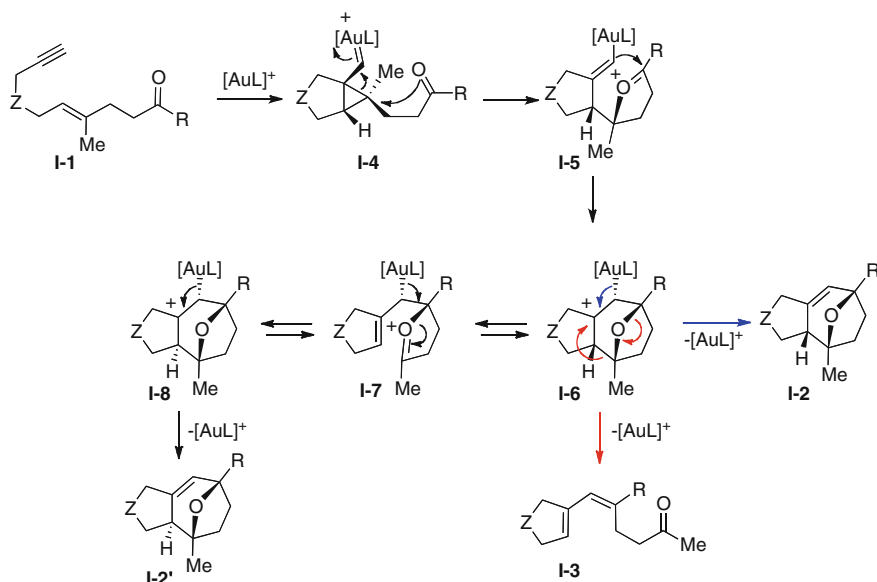


Scheme 2.1 Gold(I)-catalyzed cyclization of **I-1** enynes

This formal [2+2+2] alkyne/alkene/carbonyl cycloaddition proceeds through the opening of the cyclopropyl carbene intermediate **I-4** by the carbonyl group to form oxonium cation **I-5**, which undergoes nucleophilic attack by the vinylgold intermediates in a Prins-type cyclization to give tetrahydropyranyl cation **I-6**.

Part of these results have been published in: Escribano-Cuesta, A.; López-Carrillo, V.; Janssen, D.; Echavarren, A. M. *Chem. Eur. J.* **2009**, *15*, 5646–5650.

Intermediate **I-6** can evolve by metal loss to give tricyclic compound **I-2**, or by fragmentation to form methyl ketone **I-3** (Scheme 2.2). The competitive 2-oxonia-Cope rearrangement of intermediate **I-6** via **I-7** forms **I-8**, which results in the minor epimer **I-2'** of the tricyclic compound. As other gold(I)-catalyzed reactions of enynes, this reaction is stereospecific [Refs. 4, 8, 154 in Chap. 1] [1].



Scheme 2.2 Proposed mechanism for the cyclization of **I-1** enynes

This is a powerful method to increase molecular complexity in one step, which has been applied as a key step in the total synthesis of natural products like (\pm)-pubinernoid B [Ref. 224 in Chap. 1], (+)-orientalol F [Ref. 224 in Chap. 1], and (–)-englerin A and B [Ref. 225 in Chap. 1] (Fig. 2.1).

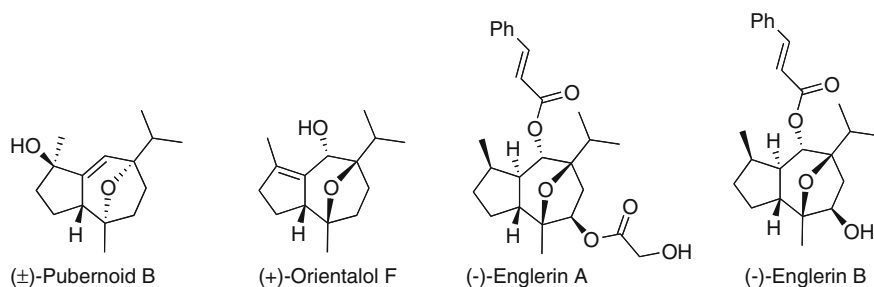
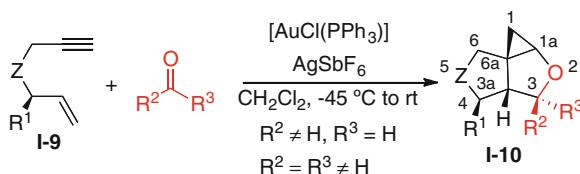


Fig. 2.1 Structures of (\pm)-pubinernoid B, (+)-orientalol F, (–)-englerin A and (–)-englerin B

Intermolecular addition of aldehydes and ketones to 1,6-enynes is also feasible. 1,6-Enynes with a terminally monosubstituted alkene **I-9** react with carbonyl compounds to give tricyclic derivatives of type **I-10** with a highly diastereoselective control (Scheme 2.3) [Ref. 229 in Chap. 1]. The reaction proceeds with complete diastereoselectivity with respect to the stereogenic centers C1a, C3, C3a, and C6a.



Scheme 2.3 Gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enynes

The reaction proceeds with 1,6- and 1,7-enynes in the presence of aromatic and aliphatic aldehydes, but remarkably also with ketones. Selected examples using this methodology are shown in Fig. 2.2.

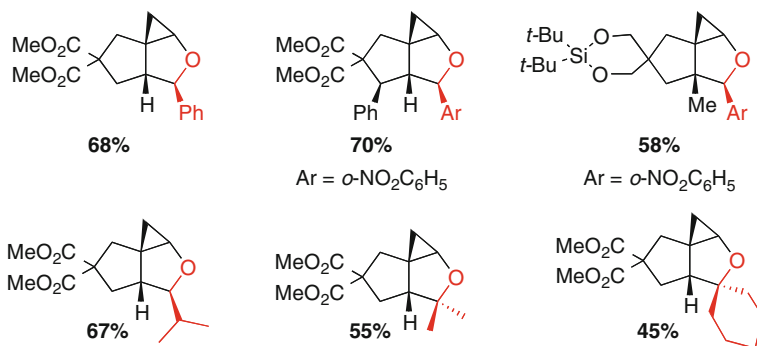
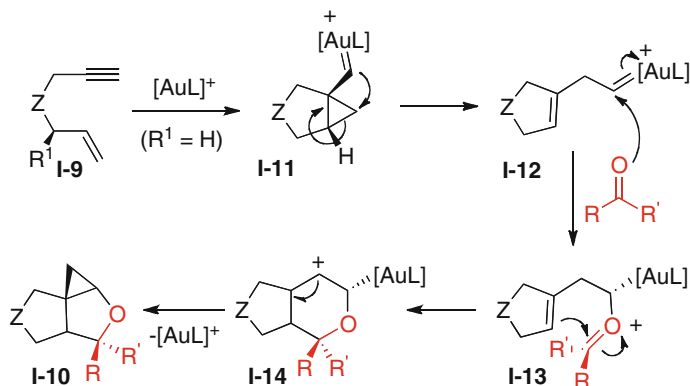


Fig. 2.2 Products of the intermolecular addition of different aldehydes and ketones to 1,6-enynes **I-9**

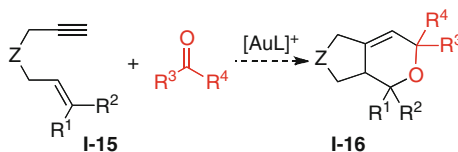
The gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enyne **I-9** presumably proceeds by trapping rearranged gold carbene intermediate **I-12** with the carbonyl compounds (Scheme 2.4). Thereby forming the oxonium cation **I-13**, which undergoes a Prins-type reaction to give **I-10**, probably via intermediate **I-14**.



Scheme 2.4 Proposed mechanism for the gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enynes **I-9**

2.2 Objective

The precedent results shown in Scheme 2.3 suggested that aldehydes could react intermolecularly with 1,6-enynes possessing a terminal alkene moiety through cyclopropyl carbene **I-12** see (Scheme 2.4). Nevertheless, based on our observation of the intramolecular reaction of carbonyl compounds with 1,6-enynes **I-1** possessing a tri-substituted olefinic group (Scheme 2.1), we instead postulated that 1,6-enynes of type **I-15** give bicyclic compounds **I-16** in a formal [2+2+2] cycloaddition (Scheme 2.5).



Scheme 2.5 Proposal for the study of the gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enynes **I-15**

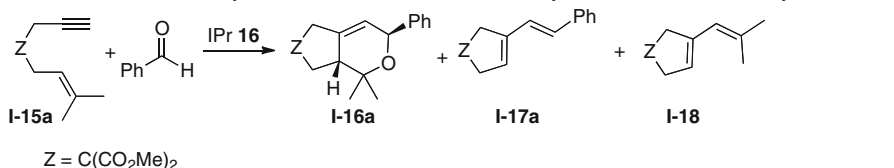
Therefore, the aim of the research was to study the intermolecular addition of carbonyl compounds to 1,6-enynes bearing a tri-substituted alkene (**I-15**) catalyzed by gold(I) complexes. This would provide a new methodology for the synthesis of bicyclic compounds of type **I-16**.

2.3 Results and Discussion

2.3.1 Optimization of the Reaction Conditions

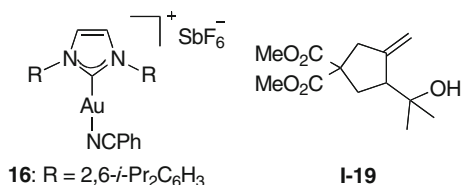
To study the gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enynes substituted at the alkene, like in **I-15**, we used enyne **I-15a** and benzaldehyde as our model (Table 2.1). Using the standard conditions for the intermolecular trapping of 1,6-enynes with nucleophiles, [Ref. 31 in Chap. 1] the formation of the expected [2+2+2] product **I-16a** and the skeletal rearrangement product **I-18** was observed. Surprisingly, an unpredicted metathesis-type product **I-17a** was also detected (Table 2.1, entry 1). Interestingly, we were able to decrease the yield of **I-18** by increasing the reaction time to 12 h at $-40\text{ }^{\circ}\text{C}$ (Table 2.1, entry 2). It should be noted that when this reaction was tested at room temperature, only the skeletal rearrangement product **I-18** was formed.

Table 2.1 Gold(I)-catalyzed intermolecular reaction of enyne **I-15a** and benzaldehyde

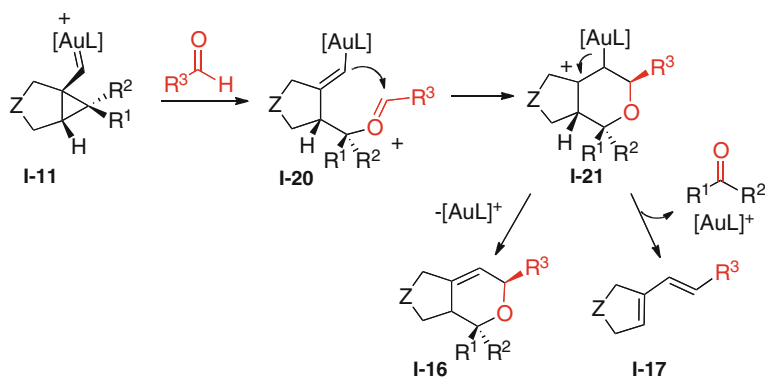


Entry	Equiv aldehyde	Conditions	Conv. (%)	I-16a : I-17a : I-18 ratio ^a
1	2	$-40\text{ }^{\circ}\text{C}$ (2 h) to rt (10 h)	100	28:18:55
2	5	$-40\text{ }^{\circ}\text{C}$ (12 h) to rt (10 h)	100	50:33:17 ^b

Reaction conditions: Aldehyde (5 equiv) and IPr gold(I) **16** (5 mol %) in 0.1 M CH_2Cl_2 from $-40\text{ }^{\circ}\text{C}$ (12 h) to rt (10 h). ^a Ratios determined by $^1\text{H-NMR}$; ^b Traces of hydroxycyclization **I-19** were observed



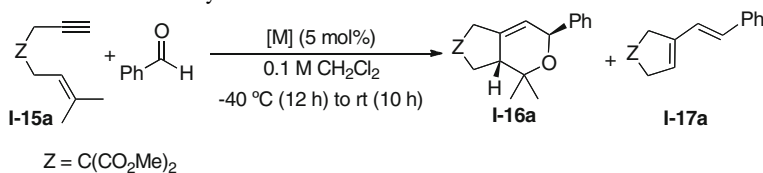
The mechanism for this reaction is analogous to its intramolecular version [Ref. 223 in Chap. 1], and starts with the formation of the cyclopropyl carbene **I-11** (Scheme 2.6). Direct attack of the aldehyde to the cyclopropyl gold(I) intermediate **I-11** leads to the oxonium cation **I-20**, which suffers Prins-type cyclization to give tetrahydropyranyl cation **I-21**. Intermediate **I-21** can undergo metalation to yield bicycle **I-16** or can evolve by a fragmentation reaction to form 1,3-diene **I-17**.



Scheme 2.6 Proposed mechanism for the gold(I)-catalyzed intermolecular addition of carbonyl compounds to 1,6-enynes substituted at the alkene **I-15**

In order to optimize the reaction conditions, a series of complexes were screened (Table 2.2). The best ratios were obtained with cationic gold(I) complexes (Table 2.2, entries 1–3). $[\text{AuCl}(\text{PPh}_3)]/\text{AgSbF}_6$ gave a nearly 1:1 mixture of dihydropyran **I-16a** and metathesis-type product **I-17a** (Table 2.2, entry 1). However, a similar ratios of **I-16a**/**I-17a** = 2.3:1 were observed with phosphine gold(I) **16** and phosphite gold(I) **20** (Table 2.2, entries 2–3). No difference between the results with the cationic phosphite gold(I) **20** and the in situ form

Table 2.2 Screening of catalysts for the gold(I)-catalyzed intermolecular reaction of enyne **I-15a** with benzaldehyde



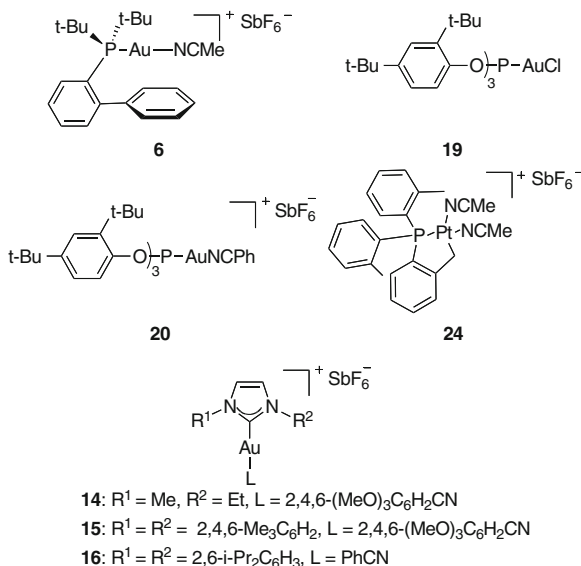
Entry	[M]	Conv. (%)	I-16 : I-17a : I-18 ratio ^b	Entry	[M]	Conv. (%)	I-16 : I-17a : I-18 ratio ^a
1	$[\text{AuCl}(\text{PPh}_3)]/\text{AgSbF}_6$	100	41:59:0	8	PtCl_2	0	–
2	6	100	37:63:0	9	PtCl_4	0	–
3	19 / AgSbF_6 or 20	100	33:67:0	10	24	100	13:8:63 ^b
4	14	100	35:48:16	11	PdCl_2	0	–
5	15	100	38:27:35	12	AgSbF_6	0	–
6	16	100	50:33:17	13	InCl_3	7	0:71:29
7	AuCl	100	0:0:100	14	GaCl_3	5	0:95:5

Reaction conditions: Aldehyde (5 equiv) and [M] (5 mol %) in 0.1 M CH_2Cl_2 from -40°C (12 h) to rt (10 h)

^a Ratios determined by $^1\text{H-NMR}$

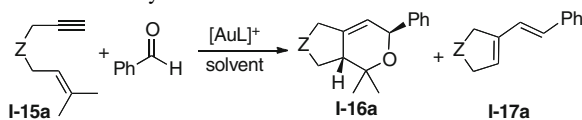
^b Traces of hydroxycyclization product **I-19** were observed

19/AgSbF₆ were found (Table 2.2, entry 3). In the examples with gold(I) carbene complexes **14**, **15**, and **16** quantitative conversion was observed but with low selectivity (Table 2.2, entries 4–6).



In the reaction catalyzed by AuCl and platinacycle **24** [Ref. 29 in Chap. 1] the rearranged product **I-18** was observed as the major product (Table 2.2, entries 7 and 10), whereas very low conversions ($\leq 7\%$) were obtained when using PtCl₂, PtCl₄, PdCl₂, AgSbF₆, InCl₃, or GaCl₃ as catalysts (Table 2.2, entries 8, 9, 11–14).

The choice of solvent influenced both the activity and the selectivity of the catalytic system. Consequently, the reactions with the best cationic complexes phosphine gold(I) **6**, phosphite gold(I) **20**, and IPr gold(I) **16** were tested in different solvents (Table 2.3). In CH₂Cl₂, phosphine complex **6** gave a similar ratio to phosphite complex **20** (Table 2.3, entries 1 and 6), but in Et₂O the major product was the hydroxycyclization product **I-19**, due to traces of residual water (Table 2.3, entry 2). DMF completely inhibited the reaction of all the complexes (Table 2.3, entries 4, 9, and 13).

Table 2.3 Screening of solvents for the gold(I)-catalyzed intermolecular reaction of enyne **I-15a** with benzaldehyde

Entry	[AuL] ⁺	Solvent	Conv. (%)	I-16 : I-17a : I-18 ratio ^a
1	6	CH ₂ Cl ₂	100	38:63:0
2		Et ₂ O	100	18:15:0 ^{b,c}
3		DCE	50	23:32:45
4		DMF	0	—
5 ^d		Dioxane	50	—
6	20	CH ₂ Cl ₂	100	33:67:0
7		Et ₂ O	44	38:62:0
8		DCE	100	33:67:0
9		DMF	5	0:0:100 ^d
10	16	CH ₂ Cl ₂	100	38:27:35
11		Et ₂ O	58	72:29:0 ^b
12		DCE	100	26:21:53
13		DMF	0	—

Reaction conditions: Aldehyde (5 equiv) and [AuL]SbF₆ (5 mol %) in 0.1 M solution from −40 °C (12 h) to rt (10 h)

^a Ratios determined by ¹H-NMR

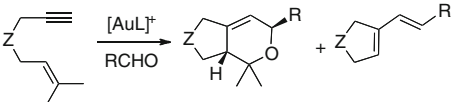
^b Complex mixture

^c 67 % of hydroxycyclization **I-19**. ^d rt (12 h) only hydroxycyclization product **I-19**

In CH₂Cl₂, Et₂O and DCE, the use of phosphite complex **20** gave the metathesis-type product **I-17a** as the major product (Table 2.3, entries 6–8), whereas low conversion of **I-15a** was observed in Et₂O (Table 2.3, entry 7).

2.3.2 Scope of the Reaction

Once we determined the best reaction conditions, the scope was explored. Products **I-16a-h** of [2+2+2] cycloaddition were isolated from enyne **I-15a** in 21–85 % yield, along with 1,3-dienes **I-17a-h** (Table 2.4). The reaction proceeded readily with electron-rich aldehydes. Conversely, in the reaction of **I-15a** with *o*-nitrobenzaldehyde, no adduct was formed (Table 2.4, entry 17), which is in contrast with the previously reported results for 1,6-enynes bearing a terminal alkene moiety **I-9** [Refs. 226, 228 in Chap. 1].

Table 2.4 Study of the gold(I)-catalyzed intermolecular reaction of enyne **I-15a** with different aldehydes


Entry	R	[AuL] ⁺	I-16 yield (%)	I-17 yield (%)
1	Ph	6	I-16a (35) ^a	I-17a (25) ^{b,c}
2		16	I-16a (21) ^a	I-17a (11) ^{b,c}
3		20	I-16a (29) ^a	I-17a (61)
4	4-MeC ₆ H ₄	16	I-16b (41)	I-17b (21) ^{b,c}
5		20	I-16b (22)	I-17b (71)
6	2,4-Me ₂ C ₆ H ₃	16	I-16c (77)	I-17c (19)
7		20	I-16c (41)	I-17c (59) ^b
8	2,4,6-Me ₃ C ₆ H ₂	16	I-16d (85)	I-17d (39)
9		20	I-16d (53)	I-17d (9)
10	4-MeOC ₆ H ₄	6	I-16e (25)	I-17e (27)
11		16	I-16e (58)	I-17e (12)
12		20	I-16e (30)	I-17e (23)
13	2,4-(MeO) ₂ C ₆ H ₃	16	I-16f (63)	I-17f (29)
14		20	I-16f (50)	I-17f (34) ^b
15	2,4,6-(MeO) ₃ C ₆ H ₂	16	I-16g (39)	I-17g (57)
16		20	I-16g (22)	I-17g (76)
17	4-O ₂ NC ₆ H ₄	20	–	–
18	<i>c</i> -C ₃ H ₅	20	I-16h (24)	I-17h (70)

Reaction conditions: Aldehyde (2 equiv) and [AuL]SbF₆ (2 mol %) in 0.1 M CH₂Cl₂ at –40 °C, 12 h

^a 9:1–1:1 mixture of **I-16** and its Δ^[4a,5] isomer

^b Yield determined by ¹H-NMR spectroscopy (1,3,5-trimethoxybenzene as standard)

^c Skeletal rearrangement product was also formed (10–50 % yield)

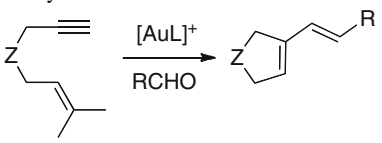
The metathesis-type products **I-17a–c** and **I-17g** were the major products observed with benzaldehyde, 4-methylbenzaldehyde, 2,4-dimethylbenzaldehyde, and 2,4,6-trimethoxy-benzaldehyde using phosphite complex **20** as catalyst (Table 2.4, entries 3, 5, 7, and 16). In contrast, with 2,4-dimethylbenzaldehyde, 2,4,6-trimethylbenzaldehyde, 4-methoxybenzaldehyde, and 2,4-dimethoxybenzaldehyde, the major products were the dihydropyran **I-16c–f** using IPr NHC complex **16** (Table 2.4, entries 6, 8, 11 and 13).

In general, we observed an increase in the yield of the dihydropyran products **I-16** using IPr gold(I) complex **16** (Table 2.4, entries 4, 6, 8, 13, 16 and 18). On the other hand, using phosphite complex **20**, the metathesis product **I-17** is favored (Table 2.4, entries 3, 5, 7 and 16).

On the other hand, complete selectivity toward 1,6-dienes **I-17** was obtained with 1,6-enynes **I-15b–c**, which only differ from **I-15a** in the heteroatom in the

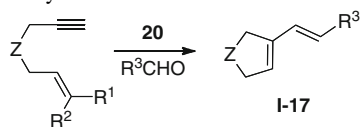
enyne backbone (Table 2.5) [2]. Enynes **I-15b-c**, which in the absence of nucleophiles reacted by a 6-*endo-dig* pathway, reacted here by a 5-*exo-dig* process to give 1,3-dienes **I-17** [Refs. 28, 29, 154 in Chap. 1] [3], in moderate to good yields (Table 2.5, entries 1–7). It is worth mentioning that 1,6-enyne **I-15b** react with *p*-bromobenzaldehyde, which is the only example involving a deactivated aldehyde, in 67 % yield (Table 2.5, entry 4). Reactions were carried out routinely with two equivalents of aldehyde. Although acetone was released in the metathesis-like reactions of substrates **I-15a-c**, this ketone did not compete with the aldehydes. Consequently, this reaction can be applied to the ready synthesis of C1-substituted 1,3-dienes **I-17**, which would be otherwise difficult to prepare by other methods. For example, the reaction of 1,6-enynes **I-15b** with 1-pyrenecarboxaldehyde in the presence of phosphine gold(I) complex **6** (2 mol %) at -40°C gave prenyl pyrenyl diene **I-17o** in 76 % yield (Table 2.5, entry 5).

Table 2.5 Study of the gold(I)-catalyzed intermolecular reaction of enyne **I-15b-c** with different aldehydes

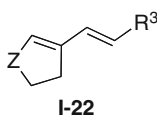
				
I-15b Z = NTs I-17				
I-15c Z = O				
Entry	I-15	[AuL] ⁺	R	I-17 yield (%)
1	b	20	Ph	I-17i (65)
2		20	4-MeC ₆ H ₄	I-17j (63)
3		20	2,4,6-Me ₃ C ₆ H ₂	I-17 k (91)
4		20	4-BrC ₆ H ₄	I-17 l (67)
5		6	1-pyrenyl	I-17 m (76)
6	c	20	4-MeC ₆ H ₄	I-17n (34)
7			2,4,6-Me ₃ C ₆ H ₂	I-17o (60)

Reaction conditions: Aldehyde (2 equiv) and [AuL]SbF₆ (2 mol %) in 0.1 M CH₂Cl₂ at -40°C , 12 h

In addition, enynes **I-15d-f** with an aryl substituent at the alkene exclusively gave 1,3-dienes **I-17** by intermolecular metathesis with aldehydes in good yields (Table 2.6, entries 1–6) [Ref. 173 in Chap. 1]. Surprisingly, electron-rich aldehydes, such as 4-methoxybenzaldehyde or 3,4-dimethoxy-benzaldehyde, only led to decomposition or low yield using enynes with an aryl substituent at the alkene **I-15b-f** (Tables 2.5 and 2.6).

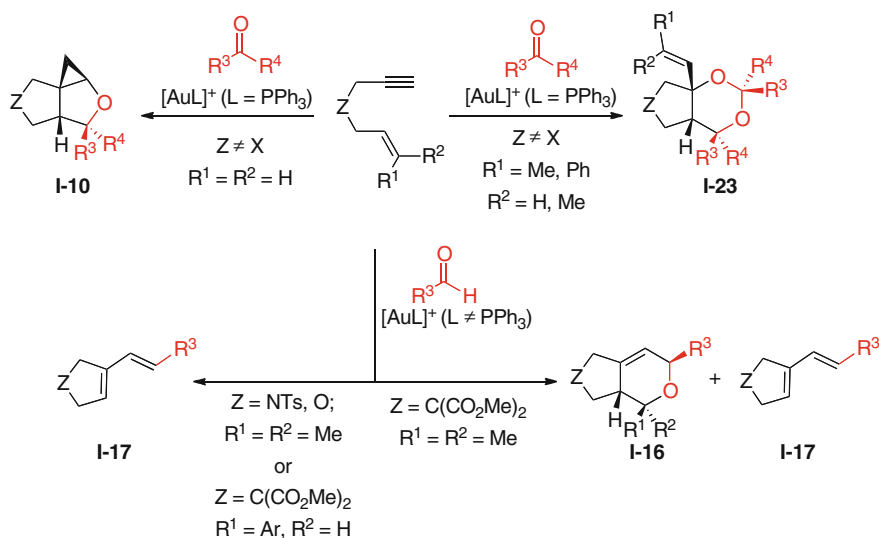
Table 2.6 Study of the gold(I)-catalyzed intermolecular reaction of enyne **I-15d-f** with different aldehydes**I-15d** Z = C(CO₂Me)₂, R¹ = Ph, R² = H**I-15e** Z = C(CO₂Me)₂, R¹ = 3,4-(MeO)₂C₆H₃, R² = H**I-15f** Z = C(CO₂Me)₂, R¹ = 3,4,5-(MeO)₃C₆H₂, R² = H

Entry	I-15	R ³	I-17 yield (%)
1	d	4-MeC ₆ H ₄	I-17b (78) ^a
2		2,4-Me ₂ C ₆ H ₃	I-17c (58) ^b
3		2,4,6-Me ₃ C ₆ H ₂	I-17d (75) ^b
4	e	2,4,6-Me ₃ C ₆ H ₂	I-17d (70)
5	f	4-MeC ₆ H ₄	I-17b (41)
6		2,4,6-Me ₃ C ₆ H ₂	I-17d (81)

Reaction conditions: Aldehyde (2 equiv) and **20** (2 mol %) in 0.1 M CH₂Cl₂ at -40 °C, 12 h^a 1:1 mixture of **I-17** and **I-22** isomer^b 1:5 mixture of **I-17** and **I-22** isomer

2.4 Conclusions

In summary, a clearer picture of the intertwined reaction pathways at play in the intermolecular gold(I)-catalyzed addition of carbonyl compounds to 1,6-enynes has emerged from this study. Ultimately, this work complements the investigations leading to tricyclic compound **I-10** and 1,3-dioxolanes **I-23** reported by the Helmchen group (Scheme 2.7) [Ref. 226, 228 in Chap. 1].

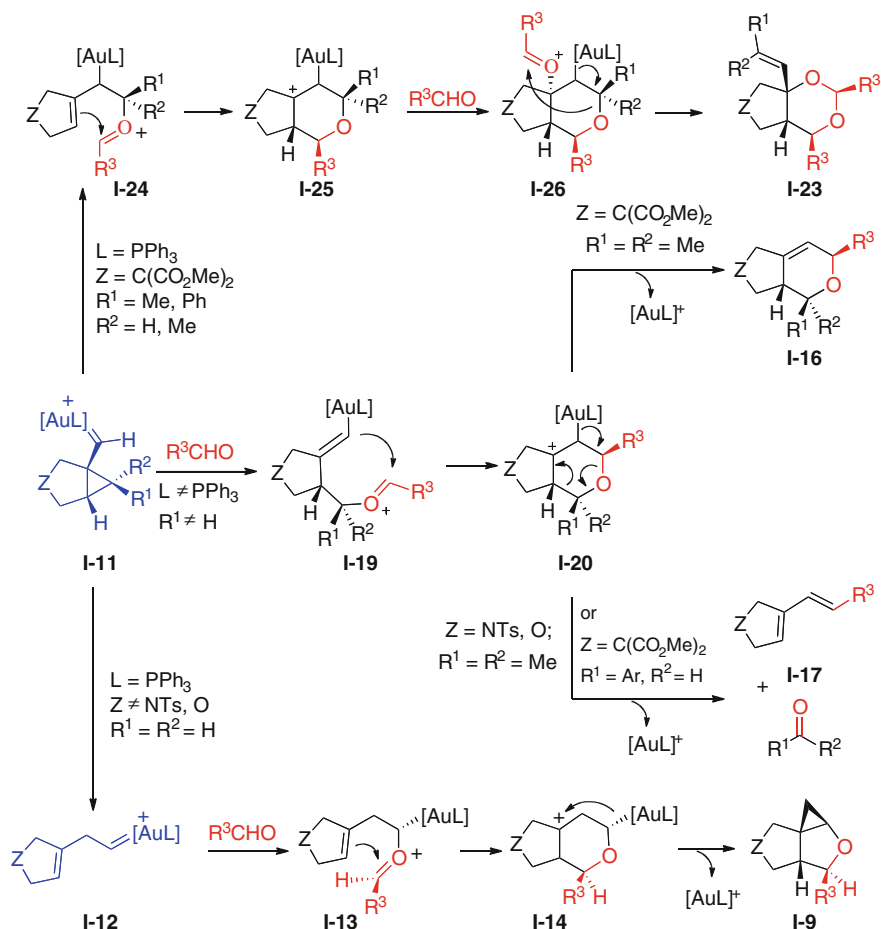


Scheme 2.7 General overview of the gold(I)-catalyzed addition of carbonyl compounds to 1,6-enynes

We conclude that changing the substitution pattern of the alkene, the heteroatom in the tether, or using different gold(I) complexes has a tremendous influence in the selective formation of tricyclic compound **I-10**, the product of formal [2+2+2] cycloaddition **I-16**, 1,3-dienes **I-17** or 1,3-dioxolanes **I-23** [Ref. 226 in Chap. 1].

Depending on the substitution pattern of different 1,6-enynes used and the ligand on the gold(I) complex, either gold carbene **I-11** or **I-12** could be trapped, thus giving different type of products (Scheme 2.8). In the case of 1,6-enynes substituted at the alkene, the formation of three different products is possible, the [2+2+2] cycloaddition product **I-16**, the 1,3-diene **I-17** and the 1,3-dioxolanes **I-23**.

Using 1,6-enynes **I-15** ($\text{Z} = \text{C(CO}_2\text{Me)}_2$, $\text{R}^1 \neq \text{H}$, $\text{R}^2 \neq \text{H}$), the formation of the expected [2+2+2] cycloaddition product **I-16** was observed in a mixture with 1,3-diene **I-17** from 1,6-dienes **I-15a** ($\text{Z} = \text{C(CO}_2\text{Me)}_2$, $\text{R}^1 = \text{R}^2 = \text{Me}$). However, 1,3-dienes **I-17** were synthesized selectively in moderate to high yields using 1,6-enynes with a heteroatom in the enyne backbone **I-17b-c** ($\text{Z} = \text{NTs, O}$, $\text{R}^1 = \text{R}^2 = \text{Me}$) or 1,6-enynes with an electron-donating aryl substituent at the alkene **I-15d-f** ($\text{Z} = \text{C(CO}_2\text{Me)}_2$, $\text{R}^1 = \text{Ar}$, $\text{R}^2 = \text{H}$). This reaction proceeds by a fragmentation of the tetrahydropyranyl cation **I-20** formed by an intramolecular Prins reaction.



Scheme 2.8 Mechanism hypothesis concerning the formation of the different products from 1,6-enynes and carbonyl compounds

On the other hand, in the case of enynes substituted at the alkene the double addition of aldehydes is also possible, although it is not a general process. Addition of the carbonyl compound to the gold cyclopropyl carbene **I-11** gives the oxonium cation **I-24**. Subsequent Prins-type addition leads to the gold stabilized carbocation **I-25**, which suffers nucleophilic attack by a second carbonyl compound. Then, the oxonium cation **I-26** rearranges to the final 1,3-dioxolane **I-23**.

To conclude, a wide array of products can be synthesized via intermolecular gold(I)-catalyzed addition of carbonyl compounds to 1,6-enynes by changing the substitution pattern of the alkene, the heteroatom in the tether, or using different gold(I) complexes. Within this work, we have shed some light into the necessary conditions to selectively synthesize these compounds.

2.5 Experimental Section

2.5.1 General Methods

All reactions were carried out under Ar in solvents dried using a Solvent Purification System (SPS). Extractive workup refers to portioning of the crude reaction between an organic solvent and water, phase separation, drying (Na_2SO_4 or MgSO_4), and evaporation under reduced pressure.

Thin layer chromatography was carried out using TLC-aluminum sheets with 0.2 mm of silica gel (Merk GF₂₅₄). Chromatography purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40–60 μm). HPLC chromatography was performed on an Agilent Technologies Series 1100 chromatograph with UV detector.

NMR spectra were recorded at 23 °C on a Bruker Advance 400 Ultrashield apparatus.

Mass spectra were recorded on Waters LCT Premier (ESI) and Waters GCT (EI, CI) spectrometers. Elemental analyses were performed on a LECO CHNS 932 micro-analyzer at the Universidad Complutense de Madrid. Melting points were determined using a Büchi melting point apparatus. Optical rotations were recorded on a P-1030 polarimeter from Jasco at the sodium D line.

2.5.2 Preparation of Substrates

The metal salts AuCl (Strem), PdCl_2 (Johnson Matthey), InCl_3 (SDS), GaCl_3 (Aldrich), PtCl_2 (Johnson Matthey), AgSbF_6 (Aldrich), complex $[\text{AuCl}(\text{PPh}_3)]$ (Strem) and phosphine complex **6** (Aldrich) were used as received. Complex IME gold(I) **14** [Ref. 43 in Chap. 1], IMes gold(I) **15** [Ref. 43 in Chap. 1] IPr gold(I) **16** [Ref. 43 in Chap. 1], phosphite gold(I) **19** [Ref. 31 in Chap. 1] cationic phosphite gold(I) **20** [Ref. 42 in Chap. 1], platinacycle **24** [Ref. 29 in Chap. 1] were prepared according to the reported procedure.

The starting 1,6-enynes were synthesized following the literature procedures: **I-15a** [4], **I-15b** [5], **I-15c** [6], **I-15d** [7], **I-15e**, [Ref. 173 in Chap. 1] and **I-15d** [Ref. 173 in Chap. 1].

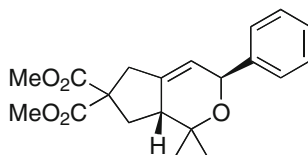
2.5.3 Cyclization Products

General procedure for the reaction of 1,6-enynes with aldehydes (Table 2.1). A solution of 1,6-enyne (80 mg) and the corresponding aldehyde (2 equiv) in CH_2Cl_2 (concentration. ca. 0.1 M) was cooled to $-40\text{ }^\circ\text{C}$ and the gold complex **6**, **16** or **20** (2 mol %) was added after 15 min. The solution was kept at $-40\text{ }^\circ\text{C}$ for 12 h.

A 0.1 M solution of Et₃N in hexane was added and the solution was filtered through Celite. After evaporation, the crude was chromatographed.

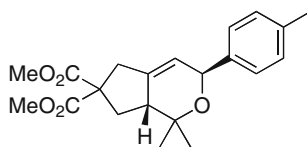
Characterization of the following compounds have been reported previously: **I-17a** [8], **I-17c** [Ref. 173 in Chap. 1], **I-17e**, [Ref. 28 in Chap. 1] **I-17f**, [Ref. 173 in Chap. 1], **I-17g** [Ref. 173 in Chap. 1], and **I-17h** [Ref. 173 in Chap. 1].

Dimethyl 1,1-dimethyl-3-phenyl-3,5,7,7a-tetrahydrocyclopenta[*c*]pyran-6,6(1*H*)-dicarboxylate (I-16a).



Compound **I-16a** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (82.0 mg, 0.34 mmol) and benzaldehyde (0.07 mL, 0.69 mmol) with catalyst **20**. The residue was purified by column chromatography (from 12:1 to 10:1 hexane/EtOAc) to give 34.1 mg of the compound **I-16a** (29 %, 1:0.16 mixture of estereoisomers) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.31 (m, 5H), 5.51 (quintuplet, *J* = 2.1 Hz, 1H), 5.01 (quintuplet, *J* = 2.7 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.14 (br d, *J* = 17.5 Hz, 1H), 2.95 (dq, *J* = 17.5 Hz, *J* = 2.1 Hz, 1H), 2.70–2.63 (m, 1H), 2.54 (dd, *J* = 12.8 Hz, *J* = 7.6 Hz, 1H), 1.81 (t, *J* = 12.4 Hz, 1H), 1.34 (s, 3H), 1.19 (s, 3H). ¹³C NMR (125 MHz, CDCl₃; PENDANT) Mixture of isomers δ 172.5 (C), 172.4 (C), 141.9 (C), 136.9 (C), 128.6 (2CH), 127.8 (CH), 127.4 (2CH), 120.4 (CH), 74.4 (C), 73.4 (CH), 58.1 (C), 53.1 (CH₃), 53.0 (CH₃), 47.5 (CH), 38.7 (CH₂), 36.3 (CH₂), 29.6 (CH₃), 19.0 (CH₃). HRMS-ESI *m/z* calcd for C₂₀H₂₄O₅Na [*M*+Na]⁺ 367.1521, found 367.1537. The structure was confirmed by HMBC, HSQC and COSY experiments and configuration assigned by NOESY.

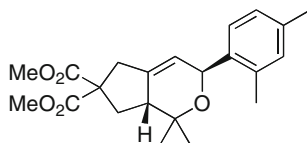
Dimethyl 1,1-dimethyl-3-*p*-tolyl-3,5,7,7a-tetrahydrocyclopenta [*c*] pyran-6,6(1*H*)-dicarboxylate (I-16b).



Compound **I-16b** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (91.2 mg, 0.38 mmol) and *p*-tolualdehyde (0.09 mL, 0.77 mmol) with catalyst **20**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 30.3 mg of the compound **I-16b** (22 %) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.21 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.50 (quintuplet, *J* = 2.1 Hz, 1H), 4.98 (quintuplet, *J* = 2.9 Hz 1H), 3.77(s, 3H), 3.74 (s, 3H), 3.13 (br d, *J* = 17.2 Hz, 1H), 2.95 (dq, *J* = 17.4, 2.1 Hz, 1H), 2.68–2.61 (m, 1H), 2.53 (dd,

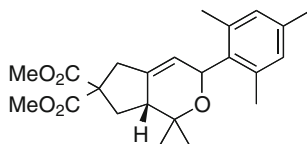
$J = 12.4, 7.9$ Hz, 1H), 2.32 (s, 3H), 1.80 (t, $J = 12.4$ Hz, 1H), 1.33 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3 , PENDANT) δ 172.5 (C), 172.4 (C), 138.9 (C), 137.5 (C), 136.8 (C), 129.3 (CH), 127.4 (2CH), 120.5 (CH), 74.4 (C), 73.2 (CH), 58.1 (C), 53.1 (CH_3), 53.0 (CH_3), 47.5 (CH), 38.7 (CH_2), 36.3 (CH_2), 29.6 (CH_3), 21.3 (CH_3), 19.0 (CH_3); HRMS-ESI m/z calcd for $\text{C}_{21}\text{H}_{26}\text{O}_5\text{Na}$ [$M+\text{Na}$] $^+$ 381.1678, found 381.1694. The structure was confirmed by HMBC, HSQC and COSY experiments and configuration assigned by NOESY.

Dimethyl 3-(2,4-dimethylphenyl)-1,1-dimethyl-3,5,7,7a-tetrahydro-cyclopenta[*c*]pyran-6,6(1*H*)-dicarboxylate (I-16c).



Compound **3ac** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (82.6 mg, 0.35 mmol) and 2,4-dimethylbenzaldehyde (0.10 mL, 0.69 mmol) with catalyst **16**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 99.8 mg of the compound **I-16c** (77 %) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.20 (d, $J = 7.6$ Hz, 1H), 6.98–6.95 (m, 2H), 5.51 (quintuplet, $J = 1.9$ Hz, 1H), 5.19 (quintuplet, $J = 3.0$ Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.15 (br d, $J = 17.3$ Hz, 1H), 2.96 (br dd, $J = 17.4, 2.0$ Hz, 1H), 2.67–2.60 (m, 1H), 2.34 (s, 3H), 2.27 (s, 3H), 1.82 (t, $J = 12.3$ Hz, 1H), 1.32 (s, 3H), 1.19 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 ; PENDANT) δ 172.5 (C), 172.4 (C), 137.3 (C), 137.3 (C), 136.3 (C), 136.2 (C), 131.6 (CH), 128.0 (CH), 126.9 (CH), 119.4 (CH), 74.4 (C), 70.5 (CH), 58.1 (C), 53.1 (CH_3), 53.0 (CH_3), 47.4 (CH), 38.8 (CH_2), 36.2 (CH_2), 29.6 (CH_3), 21.2 (CH_3), 19.1 (CH_3), 19.0 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_5\text{Na}$ [$M+\text{Na}$] $^+$ 395.1834, found 395.1848. The structure was confirmed by HMBC, HSQC and COSY experiments and configuration assigned by NOESY.

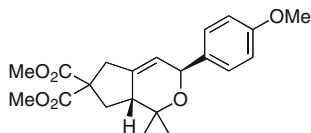
Dimethyl 3-mesityl-1,1-dimethyl-3,5,7,7a-tetrahydrocyclopenta[*c*]pyran-6,6(1*H*)-dicarboxylate (I-16d).



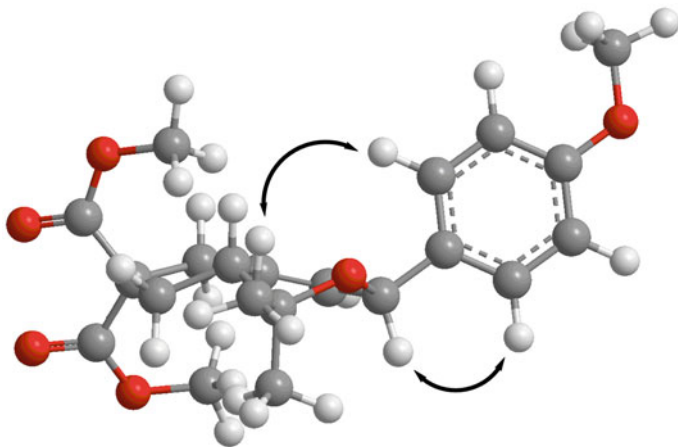
Compound **I-16d** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (84.6 mg, 0.36 mmol) and mesitaldehyde (0.11 mL, 0.71 mmol) with catalyst **16**. The residue was purified by column chromatography (15:1 hexane/EtOAc) to give 116.2 mg of the compound **I-16d** (85 %) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.80 (s, 2H), 5.47–5.44 (m, 2H), 3.78 (s, 3H), 3.75 (s, 3H), 3.13 (br d, $J = 17.7$ Hz, 1H),

2.93 (br d, $J = 13.3$ Hz, 1H), 2.66–2.61 (m, 1H), 2.53 (dd, $J = 12.5, 7.9$ Hz, 1H), 2.32 (s, 6H), 2.23 (s, 3H), 1.89 (t, $J = 12.2$ Hz, 1H), 1.32 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 ; PENDANT) δ 172.5 (C), 172.4 (C), 137.1 (C), 136.8 (C), 133.2 (C), 130.0 (CH), 118.7 (CH), 74.4 (C), 69.1 (CH), 58.1 (C), 53.1 (CH_3), 53.0 (CH_3), 46.9 (CH), 38.6 (CH_2), 36.2 (CH_2), 29.4 (CH_3), 20.9 (CH_3), 20.4 (CH_3), 19.3 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{23}\text{H}_{30}\text{O}_5\text{Na}$ [$M+\text{Na}$] $^+$ 409.1991, found 409.1987. The structure was confirmed by HMBC, HSQC and COSY experiments.

Dimethyl 3-(4-methoxyphenyl)-1,1-dimethyl-3,5,7,7a-tetrahydro-cyclopenta[*c*] pyran-6,6(1*H*)-dicarboxylate (I-16e).

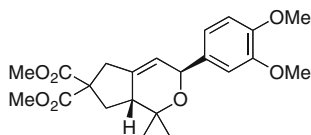


Compound **3ae** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (92.5 mg, 0.39 mmol) and *p*-methoxybenzaldehyde (0.10 mL, 0.78 mmol) with catalyst **16**. The residue was purified by column chromatography (7:1 hexane/EtOAc) to give 84.6 mg of the compound **I-16e** (58 %) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.24 (d, $J = 8.6$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 5.48 (quintuplet, $J = 2.3$ Hz, 1H), 4.96 (quintuplet, $J = 2.7$ Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.74 (s, 3H), 3.14 (br d, $J = 17.4$ Hz, 1H), 2.95 (dq, $J = 17.4, 2.0$ Hz, 1H), 2.67–2.61 (m, 1H), 2.52 (dd, $J = 12.6, 7.8$ Hz, 1H), 1.80 (t, $J = 12.5$ Hz, 1H), 1.32 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , PENDANT) δ 172.5 (C), 172.4 (C), 159.4 (C), 136.9 (C), 134.0 (C), 128.8 (CH), 120.5 (CH), 114.0 (CH), 74.4 (C), 72.9 (CH), 58.1 (C), 55.5 (CH_3), 53.1 (CH_3), 53.0 (CH_3), 47.5 (CH), 38.7 (CH_2), 36.3 (CH_2), 29.6 (CH_3), 19.0 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{21}\text{H}_{26}\text{O}_6\text{Na}$ [$M+\text{Na}$] $^+$ 397.1627, found 397.1631. The structure was confirmed by HMBC, HSQC and COSY experiments and configuration assigned by NOESY.



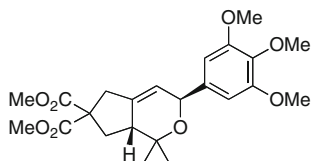
NOE effects shown in **I-16e** (conformation minimized by MM2).

Dimethyl 3-(3,4-dimethoxyphenyl)-1,1-dimethyl-3,5,7,7a-tetrahydro-cyclopenta[c]-pyran-6,6(1H)-dicarboxylate (I-16f).



Compound **I-16f** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (85.9 mg, 0.36 mmol) and 3,4-dimethoxybenzaldehyde (0.12 g, 0.72 mmol) with catalyst **16**. The residue was purified by column chromatography (from 5:1 to 3:1 hexane/EtOAc) to give 92.5 mg of the compound **I-16f** (63 %) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.98–6.80 (m, 3H), 5.50 (br s, 1H), 4.95 (br s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.76 (d, $J = 0.9$ Hz, 3H), 3.74 (d, $J = 0.8$ Hz, 3H), 3.14 (d, $J = 17.5$ Hz, 1H), 2.96 (d, $J = 17.4$, 1H), 2.68–2.63 (m, 1H), 2.53 (dd, $J = 12.7, 7.8$ Hz, 1H), 1.80 (t, $J = 12.5$ Hz, 1H), 1.33 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 ; PENDANT) δ 172.5 (C), 172.4 (C), 149.2 (C), 148.8 (C), 137.1 (C), 134.5 (C), 120.4 (CH), 119.9 (CH), 111.3 (CH), 110.8 (CH), 74.5 (C), 73.2 (CH), 58.1 (C), 56.1 (CH_3), 56.0 (CH_3), 53.1 (CH_3), 53.0 (CH_3), 47.5 (CH), 38.7 (CH_2), 36.2 (CH_2), 29.6 (CH_3), 19.0 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{22}\text{H}_{28}\text{O}_7\text{Na}$ [$M + \text{Na}$] $^+$ 427.1733, found 427.1737. The structure was confirmed by HMBC, HSQC and COSY experiments and configuration assigned by NOESY.

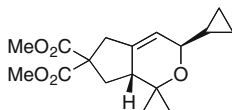
Dimethyl 1,1-dimethyl-3-(3,4,5-trimethoxyphenyl)-3,5,7,7a-tetrahydro-cyclopenta[c]pyran-6,6(1H)-dicarboxylate (I-16g).



Compound **I-16g** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (96.4 mg, 0.40 mmol) and 3,4,5-trimethoxybenzaldehyde (0.16 g, 0.81 mmol) with catalyst **20**. The residue was purified by column chromatography (from 4:1 to 3:1 hexane/EtOAc) to give 115.8 mg of the compound **I-16g** (76 %) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 6.55 (s, 2H), 5.51 (quintuplet, $J = 2.1$ Hz, 1H), 4.94 (quintuplet, $J = 3.0$ Hz, 1H), 3.86 (s, 6H), 3.80 (s, 3H), 3.77 (s, 3H), 3.74 (s, 3H), 3.15 (br d, $J = 17.2$ Hz, 1H), 2.97 (dq, $J = 17.4, 1.9$ Hz, 1H), 2.69–2.63 (m, 1H), 2.53 (dd, $J = 12.7, 7.8$ Hz, 1H), 1.80 (t, $J = 12.4$ Hz, 1H), 1.35 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 ; PENDANT) δ 172.5 (C), 172.3 (C), 153.5 (2C), 137.4 (C), 137.4 (C), 120.1 (CH), 104.5 (CH), 74.6 (C), 73.5 (CH), 60.9 (CH_3), 58.0 (C),

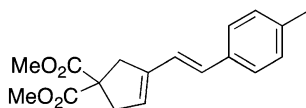
56.3 (CH₃), 53.1 (CH₃), 53.0 (CH₃), 47.4 (CH), 38.7 (CH₂), 36.2 (CH₂), 29.3 (CH₃), 19.0(CH₃). HRMS-ESI m/z calcd for C₂₃H₃₀O₈Na [$M+Na$]⁺ 457.1838, found 457.1843. The structure was confirmed by HMBC, HSQC and COSY experiments.

Dimethyl 3-cyclopropyl-1,1-dimethyl-3,5,7a-tetrahydrocyclopenta[c]pyran-6,6(1*H*)-dicarboxylate (I-16h).



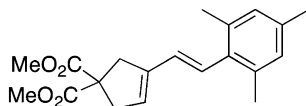
Compound **I-16h** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (90.0 mg, 0.38 mmol) and cyclopropanecarboxaldehyde (0.14 mL, 1.89 mmol) with catalyst **20**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 32.9 mg of the compound **I-16h** (24 %) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.49 (quintuplet, J = 2.1 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.22 (dd, J = 5.8, 3.0 Hz, 1H), 3.10 (dt, J = 17.4 Hz, 2.5 Hz, 1H), 2.89 (dq, J = 17.3, 2.0 Hz, 1H), 2.51–2.42 (m, 2H), 1.72 (t, J = 11.2 Hz, 1H), 1.28 (s, 3H), 0.96 (s, 3H), 0.89–0.81 (m, 1H), 0.59–0.52 (m, 1H), 0.49–0.42 (m, 1H), 0.37–0.31 (m, 1H), 0.22–0.16 (m, 1H). ¹³C NMR (125 MHz, CDCl₃; PENDANT) δ 172.5 (C), 172.5 (C), 137.5 (C), 119.4 (CH), 75.2 (CH), 73.4 (C), 58.2 (C), 53.1 (CH₃), 53.0 (CH₃), 47.6 (CH), 38.6 (CH₂), 36.2 (CH₂), 29.6 (CH₃), 18.8 (CH₃), 15.7 (CH), 3.8 (CH₂), 1.2 (CH₂). HRMS-ESI m/z calcd for C₁₇H₂₄O₅Na [$M+Na$]⁺ 331.1521, found 331.1505. The structure was confirmed by HMBC, HSQC and COSY experiments.

(E)-Dimethyl 3-(4-methylstyryl)cyclopent-3-ene-1,1-dicarboxylate (I-17b).



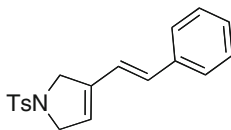
Compound **I-17b** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (91.2 mg, 0.38 mmol) and *p*-tolualdehyde (0.09 mL, 0.77 mmol) with catalyst **20**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 70.1 mg of the compound **I-17b** (71 %) as colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 6.85 (d, J = 16.2 Hz, 1H), 6.42 (d, J = 16.2 Hz, 1H), 5.67 (br s, 1H), 3.76 (s, 6H), 3.26 (br s, 2H), 3.16 (br s, 2H), 2.34 (s, 3H). ¹³C NMR (125 MHz, CDCl₃; PENDANT) δ 172.7 (C), 140.0 (C), 137.6 (C), 134.6 (C), 130.2 (CH), 129.5 (CH), 127.0 (CH), 126.5 (CH), 123.5 (CH), 59.0 (C), 53.0 (2CH₃), 41.2 (CH₂), 39.9 (CH₂), 21.9 (CH₃). HRMS-ESI m/z calcd for C₁₈H₂₀O₄Na [$M+Na$]⁺ 323.1259, found 323.1265. The structure was confirmed by HMBC, HSQC and COSY experiments.

(*E*)-Dimethyl 3-(2,4,6-trimethylstyryl)cyclopent-3-ene-1,1-dicarboxylate (I-17d).



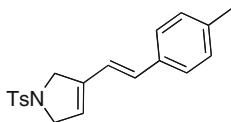
Compound **I-17d** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15a** (84.6 mg, 0.36 mmol) and mesitaldehyde (0.11 mL, 0.71 mmol) with catalyst **16**. The residue was purified by column chromatography (15:1 hexane/EtOAc) to give 9.9 mg of the compound **I-17d** (9 %) as a colorless white solid: mp 126–127 °C. ^1H NMR (400 MHz, CDCl_3) δ 6.86 (s, 2H), 6.44 (d, J = 16.6 Hz, 1H), 6.38 (d, J = 16.6 Hz, 1H), 5.59 (br s, 1H), 3.78 (s, 6H), 3.29 (d, J = 1.5 Hz, 2H), 3.16 (d, J = 1.4 Hz, 2H), 2.28 (s, 6H), 2.27 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 ; PENDANT) δ 172.8 (C), 140.0 (C), 136.4 (C), 136.1 (2C), 133.8 (C), 129.5 (CH), 128.9 (CH), 128.3 (CH), 126.4 (CH), 58.9 (C), 53.1 (CH_3), 41.2 (CH_2), 39.8 (CH_2), 21.2 (CH_3), 21.1 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{20}\text{H}_{24}\text{O}_4\text{Na}$ [$M+\text{Na}$] $^+$ 351.1572, found 351.1573. The structure was confirmed by HMBC, HSQC and COSY experiments.

(*E*)-3-Styryl-1-tosyl-2,5-dihydro-1H-pyrrole (I-17i).



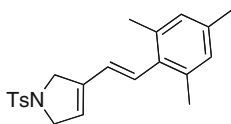
Compound **I-17i** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15b** (83.4 mg, 0.30 mmol) and benzaldehyde (64.3 mg, 0.60 mmol) with catalyst **20**. The residue was purified by column chromatography (5:1 hexane/EtOAc) to give 63.5 mg of compound **I-17i** (65 %) as an oil. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.38–7.29 (m, 6H), 7.26–7.22 (m, 1H), 6.76 (d, J = 16.4 Hz, 1H), 6.32 (d, J = 16.3 Hz, 1H), 5.68 (t, J = 1.8 Hz, 1H), 4.34–4.32 (m, 2H), 4.23–4.21 (m, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.7 (C), 137.3 (C), 136.5 (C), 134.2 (C), 131.5 (CH), 130.0 (CH), 128.8 (2CH), 128.3 (CH), 127.6 (CH), 126.6 (CH), 123.5 (CH), 121.6 (CH), 55.3 (CH_2), 53.9 (CH_2), 21.6 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{19}\text{H}_{19}\text{NNaO}_2\text{S}$ [$M+\text{Na}$] $^+$ 348.1040, found 348.1034.

(*E*)-3-(4-Methylstyryl)-1-tosyl-2,5-dihydro-1H-pyrrole (I-17j).



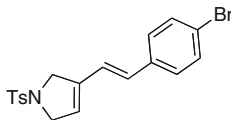
Compound **I-17j** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15b** (83.4 mg, 0.30 mmol) and *p*-tolualdehyde (72.1 mg, 0.60 mmol) with catalyst **20**. The residue was purified by column chromatography (5:1 hexane/EtOAc) to give 64.6 mg of the compound **I-17j** (63 %) as an oil. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.71 (d, J = 16.3 Hz, 1H), 6.30 (d, J = 16.2 Hz, 1H), 5.65 (bt, J = 1.9 Hz, 1H), 4.34–4.31 (m, 2H), 4.23–4.20 (m, 2H), 2.41 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.6 (C), 138.3 (C), 137.4 (C), 134.3 (C), 133.7 (C), 131.4 (CH), 129.9 (CH), 129.6 (CH), 127.6 (CH), 126.5 (CH), 122.9 (CH), 120.7 (CH), 55.3 (CH_2), 53.9 (CH_2), 21.6 (CH_3), 21.4 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{20}\text{H}_{21}\text{NNaO}_2\text{S}$ [$M+\text{Na}$] $^+$ 362.1191, found 362.1179.

(*E*)-1-Tosyl-3-(2,4,6-trimethylstyryl)-2,5-dihydro-1*H*-pyrrole (**I-17k**).



Compound **I-17k** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15b** (83.9 mg, 0.30 mmol) and mesitaldehyde (89.8 mg, 0.60 mmol) with catalyst **6**. The residue was purified by column chromatography (5:1 hexane/EtOAc) to give 100.3 mg of compound **I-17k** (91 %) as an oil. ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 6.86 (s, 2H), 6.34 (d, J = 16.5 Hz, 1H), 6.26 (d, J = 16.7 Hz, 1H), 5.61 (bs, 1H), 4.37–4.35 (m, 2H), 4.23–4.20 (m, 2H), 2.43 (s, 3H), 2.26 (s, 3H), 2.24 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.6 (C), 137.5 (C), 136.9 (C), 136.0 (2C), 134.4 (C), 133.0 (C), 129.9 (CH), 129.8 (CH), 128.9 (CH), 127.6 (CH), 126.9 (CH), 122.7 (CH), 55.1 (CH_2), 53.7 (CH_2), 21.7 (CH_3), 21.1 (3 CH_3). HRMS-ESI m/z calcd for $\text{C}_{22}\text{H}_{25}\text{NNaO}_2\text{S}$ [$M+\text{Na}$] $^+$ 390.1504, found 390.1521.

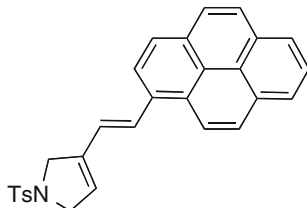
(*E*)-3-(4-Bromostyryl)-1-tosyl-2,5-dihydro-1*H*-pyrrole (**I-17l**).



Compound **I-17l** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15b** (83.6 mg, 0.30 mmol) and *p*-bromobenzaldehyde (111.1 mg, 0.60 mmol) with catalyst **6**. The residue was purified by column chromatography (5:1 hexane/EtOAc) to give 81.2 mg of compound **I-17l** (67 %) as an oil. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 16.4 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.71 (bt, J = 2.0 Hz, 1H), 4.32–4.30 (m, 2H), 4.23–4.20 (m, 2H), 2.42 (s, 3H). ^{13}C

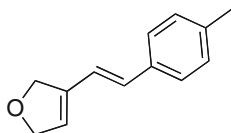
NMR (100 MHz, CDCl_3) δ 143.7 (C), 137.1 (C), 135.5 (C), 134.2 (C), 132.0 (CH), 130.2 (CH), 130.0 (CH), 128.0 (CH), 127.6 (CH), 124.3 (CH), 122.3 (CH), 122.1 (C), 55.3 (CH_2), 53.7 (CH_2), 21.6 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{19}\text{H}_{18}\text{BrN-NaO}_2\text{S}$ [$M+\text{Na}$] $^+$ 426.0139, found 426.0143.

(*E*)-3-(2-(pyren-1-yl)vinyl)-1-tosyl-2,5-dihydro-1*H*-pyrrole (I-17m).



Compound **I-17m** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15b** (83.3 mg, 0.30 mmol) and 1-pyrenecarboxaldehyde (138.4 mg, 0.60 mmol) with catalyst **6**. The residue was purified by column chromatography (100 % CH_2Cl_2) to give 103.5 mg of compound **I-17o** (76 %) as a yellow solid: mp 213–215 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.30 (d, $J = 9.3$ Hz, 1H), 8.18 (d, $J = 7.7$ Hz, 1H), 8.17 (d, $J = 7.7$ Hz, 1H), 8.11 (d, $J = 8.6$ Hz, 2H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.04 (d, $J = 8.9$ Hz, 1H), 8.00 (d, $J = 8.9$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 7.99 (t, $J = 7.6$ Hz, 1H), 7.84 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 15.8$ Hz, 1H), 7.35 (d, $J = 8.6$ Hz, 2H), 6.98 (d, $J = 16.0$ Hz, 1H), 5.77 (t, $J = 1.8$ Hz, 1H), 4.55–4.53 (m, 2H), 4.30–4.27 (m, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.7 (C), 137.8 (C), 134.3 (C), 131.6 (C), 131.3 (C), 131.0 (C), 130.7 (C), 130.0 (2CH), 128.5 (C), 128.2 (CH), 128.0 (CH), 127.7 (2CH), 127.6 (CH), 127.5 (CH), 126.2 (CH), 125.6 (CH), 125.4 (CH), 125.2 (CH), 125.1 (C), 125.0 (C), 124.4 (CH), 124.0 (CH), 123.4 (CH), 122.7 (CH), 55.4 (CH_2), 54.0 (CH_2), 21.7 (CH_3). HRMS-ESI m/z calcd for $\text{C}_{29}\text{H}_{23}\text{NNaO}_2\text{S}$ [$M+\text{Na}$] $^+$ 472.1347, found 472.1346. UV–Vis (CH_2Cl_2) λ_{max} (ϵ_{max}) 388 nm (28830), 371 (31780), 289 (23470), 237 (34990). Fluorescence (395 nm excitation, c 0.05 M, CH_2Cl_2) 437 nm (2.88), 414 (4.12).

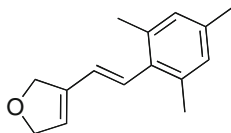
(*E*)-3-(4-Methylstyryl)-2,5-dihydrofuran (I-17n).



Compound **I-17n** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15c** (50.5 mg, 0.40 mmol) and *p*-tolualdehyde (96.3 mg, 0.80 mmol) with catalyst **6**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 13.5 mg of compound **I-17n** (34 %) as an oil. ^1H NMR (400 MHz, CDCl_3) δ 7.29 (d, $J = 7.8$ Hz, 2H), 7.13 (d, $J = 7.8$ Hz, 2H), 6.88 (d, $J = 16.4$ Hz, 1H), 6.26 (d, $J = 16.4$ Hz, 1H), 5.90 (s, 1H), 4.86–4.84 (m, 2H), 4.76–4.74 (m, 2H), 2.34 (s, 3H). ^{13}C NMR

(100 MHz, CDCl₃) δ 138.4 (C), 137.9 (C), 134.2 (C), 130.9 (CH), 129.5 (CH), 126.4 (CH), 124.7 (CH), 120.2 (CH), 76.2 (CH₂), 74.4 (CH₂), 21.4 (CH₃). HRMS-APCI m/z calcd for C₁₃H₁₅O [$M+H$]⁺ 187.1123, found 187.1124.

(E)-3-(2,4,6-Trimethylstyryl)-2,5-dihydrofuran (I-17o)



Compound **I-17o** was synthesized following the general procedure for the reaction of 1,6-enynes with aldehydes, starting from **I-15c** (50.1 mg, 0.40 mmol) and mesitaldehyde (119.5 mg, 0.80 mmol) with catalyst **6**. The residue was purified by column chromatography (10:1 hexane/EtOAc) to give 51.8 mg of compound **I-17o** (59 %) as an oil. ¹H NMR (400 MHz, CDCl₃) δ 6.94 (s, 2H), 6.50 (d, J = 16.7 Hz, 1H), 6.37 (d, J = 16.6 Hz, 1H), 5.92 (bt, J = 1.8 Hz, 1H), 4.99–4.96 (m, 2H), 4.85–4.83 (m, 2H), 2.35 (s, 3H), 2.34 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 138.5 (C), 136.6 (C), 136.0 (C), 133.5 (C), 129.2 (CH), 128.9 (CH), 126.4 (CH), 124.4 (CH), 76.1 (CH₂), 74.4 (CH₂), 21.0 (3CH₃). HRMS-APCI m/z calcd for C₁₅H₁₉O [$M+H$]⁺ 215.1436, found 215.1431.

References

1. Gorin, D.J., Sherry, B.D., Toste, F.D.: Chem. Rev. **108**, 3351–3378 (2008)
2. Results carried out in collaboration with Dr. D. Janssen
3. Nevado, C., Cárdenas, D.J., Echavarren, A.M.: Chem. Eur. J. **9**, 2627–2635 (2003)
4. Trost, B.M., Braslau, R.: Tetrahedron Lett. **29**, 1231–1234 (1988)
5. Trost, B.M., Toste, F.D.: J. Am. Chem. Soc. **124**, 5025–5036 (2002)
6. Kataoka, T.; Yoshimatsu, M.; Noda, Y.; Sato, T.; Shimizu, H.; Hori, M.: J. Chem. Soc., Perkin. Trans. 1 **1993**, 121–129
7. Chatani, N., Morimoto, T., Muto, T., Murai, S.: J. Am. Chem. Soc. **116**, 6049–6050 (1994)
8. Ma, S., Jiao, N., Zhao, S., Hou, H.: J. Org. Chem. **67**, 2837–2847 (2002)

New Gold-Catalyzed Reactions and Applications for the
Synthesis of Alkaloids

Escribano Cuesta, A.

2013, XIII, 195 p., Hardcover

ISBN: 978-3-319-00701-4