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Gold(I)-Catalyzed Intermolecular Cycloaddition of Allenamides with α,β-Unsaturated Hydrazones: Efficient Access to Highly Substituted Cyclobutanes

Paloma Bernal-Albert,[†] Hélio Faustino,[†] Ana Gimeno,[§] Gregorio Asensio,[§] José L. Mascareñas,*[,†] and Fernando López*[,†,‡]

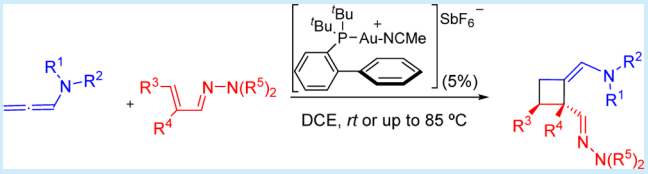
[†]Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Orgánica, Universidad de Santiago de Compostela, 15782, Santiago de Compostela, Spain

[‡]Instituto de Química Orgánica General CSIC, Juan de la Cierva 3, 28006, Madrid, Spain

[§]Departamento de Química Orgánica, Universidad de Valencia, Avda. Vicent Andrés Estellés s/n, 46100-Burjassot, Valencia, Spain

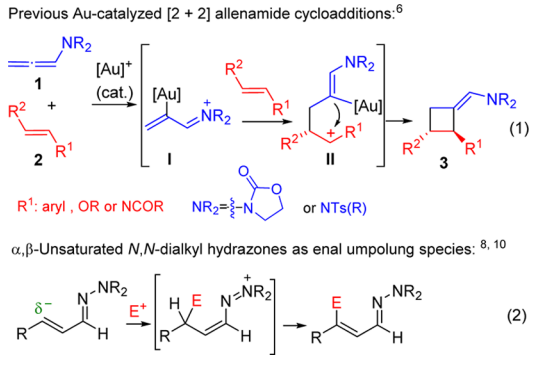
Supporting Information

ABSTRACT: α,β-Unsaturated *N*,*N*-dialkyl hydrazones undergo a mild [2 + 2] cycloaddition to allenamides when treated with a suitable gold catalyst. The method, which represents the first application of *N*,*N*-dialkyl hydrazones in gold catalysis, is compatible with a wide variety of substituents at the alkenyl moiety of the hydrazone component, proceeds with excellent levels of regio- and diastereoselectivity, and provides densely substituted cyclobutanes with good to excellent yields.



Cyclobutanes not only constitute the basic structural motif of a wide range of biologically active products but, owing to their inherent strain energy, are also highly valuable synthetic building blocks.[1,2] The most common strategies to assemble cyclobutanes are based on [2 + 2] cycloadditions of unsaturated precursors, reactions which are typically carried out under photochemical conditions,[3] although in some cases they can also be promoted by Lewis acids.[4] Alternatively, transition metal catalysis has recently emerged as a powerful tool for uncovering new types of [2 + 2] annulations.[5] In this context, the groups of Chen, González, and ours have independently reported an efficient approach to cyclobutanes based on the Au(I)-catalyzed intermolecular [2 + 2] cycloadditions between allenamides and electron-rich alkenes (Scheme 1, eq 1).[6] Despite the relevance of these methods, their success is associated with the use of styrenes, enol ethers, or enamides as reaction partners, which restricts the type of substituents (R^1/R^2) that can be incorporated in the resulting cyclobutanes, as well as access to cyclobutanes with quaternary stereocenters.[6]

Scheme 1. Au-Catalyzed [2 + 2] Cycloadditions and Umpolung Reactivity of Conjugate Hydrazones



Considering the mechanism proposed for these cycloadditions,[6,7] which involves the formation of intermediates **I** and **II**, we were curious to analyze the behavior of other types of electron-rich alkenes that could afford alternative, diversely substituted cyclobutanes. In particular, we focused our attention on α,β-unsaturated *N*,*N*-dialkyl hydrazones, a relatively unexplored class of substrates that are easily prepared from *N*,*N*-dialkylhydrazines and enals.[8] Although these species have been typically used as azadienes in hetero-Diels–Alder cycloadditions,[9] the electron-donor characteristics of the *N*,*N*-dialkylamino group convert them into umpoled enals (vinylogous aza-enamines, Scheme 1, eq 2).[8] Curiously, this umpolung reactivity has been scarcely exploited[10,11] and, to the best of our knowledge, remains essentially unexplored in transition metal catalyzed processes.[12] Herein, we report that α,β-unsaturated *N*,*N*-dialkyl hydrazones are excellent two-carbon partners in gold-catalyzed cycloadditions with allenamides, providing for the efficient assembly of highly substituted cyclobutanes with excellent regio- and diastereoselectivities.[13]

We started our research by analyzing the reactivity of allenamide **1a** with the *N*,*N*-diisopropylhydrazone **2a** in the presence of several Au or Pt catalysts. As can be seen in Table 1, Pt(II) complexes, such as $PtCl_2$, $PtBr_2$, or $[PtCl_2(C_2H_4)]_2$/P(*o*-

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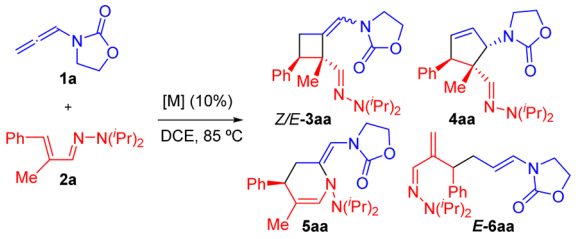
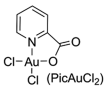
Table 1. Preliminary Screening with Pt and Au Catalysts[a]



entry	[M]	time[b]	*Z*-**3aa**	*E*-**3aa**	**4aa**	**5aa**	**6aa**
1	$PtCl_2$	5 h	0	7	3	1	0
2	$PtBr_2$	3 h	0	12	3	1	0
3	$[PtCl_2(C_2H_4)]_2$/P(o-Tol)$_3$	5 h	0	13	1	1	0
4	AuCl	6 h	1	5	0	0	0
5	 (PicAuCl$_2$)	16 h	1	9	0	0	0
6[c]	$Ph_3PAuNTf_2$	20 h	7	0	0	0	3
7[c,d]	 (**Au1**)	0.1 h	1[e]	0	0	0	0

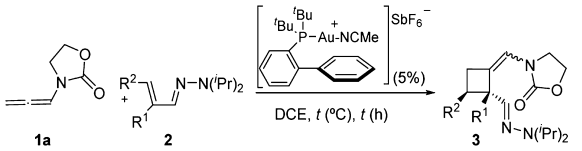
[a]**1a** (1 equiv), **2a** (2 equiv) and [M] (10%) were heated at 85 °C (0.25 M in DCE), unless otherwise noted. The table indicates the proportion of products as deduced from ^{1}H NMR of the crude mixtures. [b]Conversions >99% after the indicated time. [c]Carried out at rt. [d]Carried out with 5% catalyst. [e]*Z*-**3aa** isolated in 99% yield.

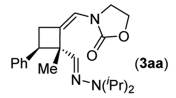
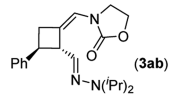
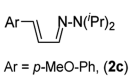
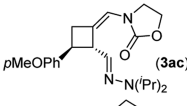
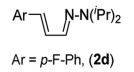
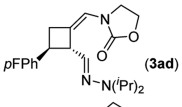
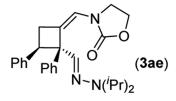
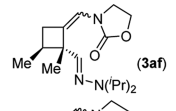
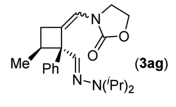
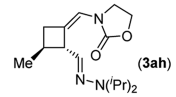
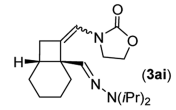
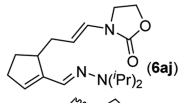
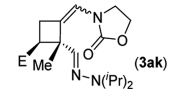
Tol)$_3$, promote intermolecular annulations between the conjugated hydrazone and the allenamide to yield, after a few hours at 85 °C, the [2 + 2] cycloadduct *E*-**3aa**, together with minor amounts of the [3 + 2] and [4 + 2] adducts **4aa** and **5aa**, respectively (Table 1, entries 1−3). On the other hand, the use of AuCl or the gold(III) complex $PicAuCl_2$ led exclusively to the [2 + 2] cycloadducts **3aa**, as 5:1 and 9:1 mixtures of *E*/*Z* isomers (entries 4 and 5). Gratifyingly, cationic Au(I) complexes were also active catalysts for the cycloaddition. Thus, while $Ph_3PAuNTf_2$ provided the [2 + 2] adduct *Z*-**3aa**, together with the acyclic product **6aa** (7:3 ratio, entry 6), the Johnphos-based gold(I) complex **Au1** exclusively provided *Z*-**3aa**, which was isolated after 10 min at rt, in 99% yield using just 5% of the catalyst (entry 7). The structure and stereochemical identity of this adduct could be further corroborated by X-ray analysis, which confirmed the *cis* disposition of the Ph and Me groups and the *Z* configuration of the enamide (Figure S2, Supporting Information).

Noteworthy, the cyclobutanes **3aa** incorporate the phenyl substituent at the *β*-positon of the *exo*-enamide and, therefore, can be considered as regioisomers of those obtained in the previous annulations of allenamides and styrenes.[6]

We next analyzed the scope of the process. The *N*,*N*-diisopropyl hydrazone derived from cinnamaldehyde (**2b**) did also participate in the cycloaddition, although full conversions required heating at 55 °C and longer reaction times (Table 2, entry 2). In any case, the corresponding cyclobutane, Z-**3ab**, was isolated in good yield and with complete stereoselectivity. The reaction tolerated electron-rich (e.g., *p*-OMe) or electron-poor (e.g., *p*-F) substituents at the hydrazone-phenyl moiety (entries 3 and 4). On the other hand, the introduction of a phenyl group at the *α*-position of the conjugate hydrazone (**2e**) allows the reaction to be completed at rt in <1 h; the [2 + 2] adduct **3ae** was obtained in 95% yield (*Z*/*E* ratio = 6:4, entry 5).

Table 2. Scope of the [2 + 2] Au-Catalyzed Cycloaddition[a]



entry	hydrazone (**2**)	*t* (°C)	*t* (h)	cycloadduct (**3**)	*Z*:*E*[b]	yield[c]
1	 (**2a**)	23	0.1	 (**3aa**)	1:0	99%
2	 (**2b**)	55	1.5	 (**3ab**)	1:0	62%
3	 Ar = *p*-MeO-Ph, (**2c**)	55	2.5	 (**3ac**)	1:0	88%
4	 Ar = *p*-F-Ph, (**2d**)	55	3.5	 (**3ad**)	1:0	55%
5	 (**2e**)	rt	0.6	 (**3ae**)	6:4	95%
6	 (**2f**)	55	0.6	 (**3af**)	8:2	87%
7	 (**2g**)	55	2	 (**3ag**)	6:4	94%
8[d]	 (**2h**)	85	16	 (**3ah**)	1:0	95%
9	 (**2i**)	55	0.6	 (**3ai**)	7:3	90%
10	 (**2j**)	45	16	 (**6aj**)	-	65%
11	 E = CO_2Et, (**2k**)	55	0.6	 (**3ak**)	7:3	83%

[a]**1a** (1 equiv) was added to a mixture of **2b**−**k** (2 equiv) and **Au1** (5%) in DCE (0.25 M) and heated at the indicated temperature. [b]*Z*/*E* ratios determined by ^{1}H NMR of the crude mixtures. [c]Isolated combined yield of *Z* and *E* isomers. [d]Carried out with 10% catalyst.

The reaction is also efficient with *α*,*β*-unsaturated hydrazones bearing alkyl substituents at the *β*-position. Thus, hydrazones **2f** and **2g**, with a methyl substituent, provided the corresponding [2 + 2] adducts, **3af** and **3ag**, in excellent yields, as 8:2 and 6:4 mixtures of *Z* and *E* isomers, respectively (entries 6 and 7). In consonance with the lower reactivity of the *α*-unsubstituted hydrazone **2b** with respect to its *α*-methylated analog **2a**, inducing the reaction of hydrazone **2h**, derived from crotonaldehyde, also required more drastic conditions (16 h at 85 °C and 10% of the catalyst). Using these conditions, the expected product was obtained in 95% yield and with complete *Z* selectivity (entry 8). Gratifyingly, hydrazone **2i**, derived from cyclohexene-1-carbaldehyde, also participated in the [2 + 2]

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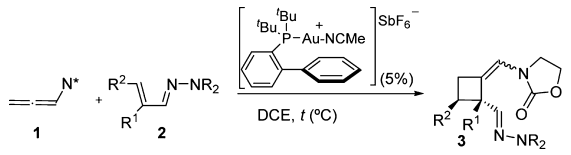
cycloaddition providing, in excellent yield and complete *syn* selectivity at the ring fusion, the bicyclo[4.2.0]octane product **3ai**, an attractive bicyclic scaffold quite common in many natural products (entry 9).[14] The analog hydrazone **2j**, derived from cyclopentenecarbaldehyde, did not afford the bicyclo[3.2.0]-heptane adduct (**3aj**), presumably because of the higher strain associated with the formation of this bicyclic system. Instead, the acyclic product **6aj** was isolated in 65% yield (entry 10). Electron-withdrawing groups at the β-position of the hydrazone are tolerated. Indeed, **2k**, featuring an ethyl carboxylate at this position, provided the [2 + 2] adduct **3ak** in 83% yield (entry 11).

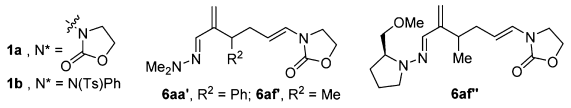
The annulation reaction is not restricted to *N*,*N*-diisopropyl hydrazones. As can be seen in Table 3, *N*,*N*-dimethyl hydrazones

Table 3. Scope of the Hydrazone and Allenamide[a]



entry	1	R^2, R^1	2	NR_2	t (°C)	t (h)	3	yield (dr)[b]
1	**1a**	Ph, Me	**2a'**	NMe_2	55	3.5	**3aa'**	76%[c]
2	**1a**	Ph, H	**2b'**	NMe_2	65	7	**3ab'**	53%
3	**1a**	*p*OMePh, H	**2c'**	NMe_2	65	4	**3ac'**	41%
4	**1a**	Me, Me	**2f'**	NMe_2	55	1	**3af'**	47%[d,e]
5	**1a**	EtO_2C, Me	**2k'**	NMe_2	55	0.5	**3ak'**	63%
6	**1a**	Ph, Me	**2a''**		55	1	**3aa''**	85% (7:3)
7	**1a**	Me, Me	**2f''**		55	1	**3af''**	63%[f] (6:4)
8	**1b**	Ph, Me	**2a**	$N(^iPr)_2$	85	0.2	**3ba**	95%
9	**1b**	Ph, H	**2b**	$N(^iPr)_2$	85	16	**3bb**	97%

[a] **1** (1 equiv) was added to a mixture of **2** (2 equiv) and **Au1** (5%) in DCE (0.25 M), unless otherwise noted. [b] *Z*/*E* ratios (determined by ^{1}H NMR spectroscopy of the crude mixtures) are 1:0 unless otherwise noted. [c] **6aa'** (6%) was also isolated. [d] **6af'** (21%) was also isolated. [e] *Z*/*E* ratio = 9.3:0.7. [f] **6af''** (9%) was also isolated.

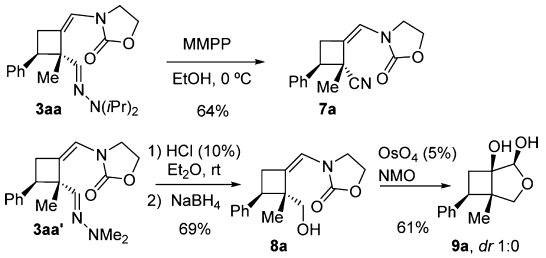


with aryl or alkyl substituents at the alkene (**2a′**−**c′**,**f′**,**k′**) provided the [2 + 2] cycloadducts, although the reactions required slightly higher reaction times and temperatures (Table 3, entries 1−5). For example, while the cycloaddition of the diisopropyl hydrazone **2a** occurred at rt in 5 min (99% yield, Table 2, entry 1), that of its *N*,*N*-dimethyl analog **2a′**, which gives **3aa′**, required 3.5 h at 55 °C (76% yield, Table 3, entry 1). Small amounts of the acyclic products of type **6** were also isolated in some cases (entries 1 and 4).[15] The SAMP-derived chiral hydrazone **2a″** also participated in the process providing the corresponding [2 + 2] cycloadduct in 85% yield and moderate diastereoselectivity (dr = 7:3, entry 6). Similarly, the SAMP-hydrazone **2f″** provided the expected adduct as a 6:4 mixture of diastereomers. Thus, these preliminary results suggest that further modifications in the chiral hydrazone moiety might allow the development of asymmetric versions of the reaction.

The current methodology is not restricted to oxazolidinone-derived allenamides such as **1a**. As can be seen in entries 8 and 9, the *N*-tosyl phenyl allenamide **1b** also participated in the cycloaddition, providing the expected cycloadducts with complete selectivity and excellent yields (95−97% yield).

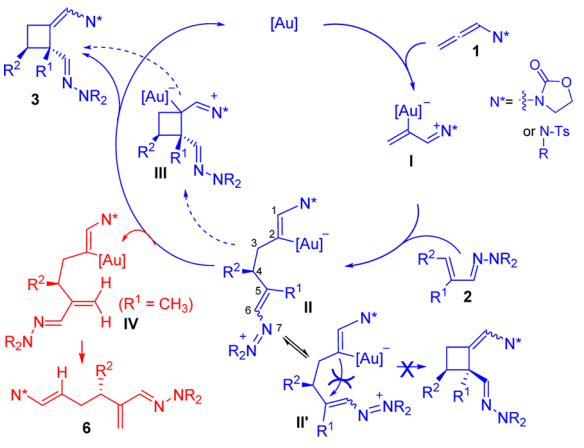
The cyclobutane adducts obtained in the above cycloadditions offer interesting potential for further manipulations (Scheme 2). Thus, the hydrazone moiety of **3aa** can be converted into a nitrile by treatment with magnesium monoperoxiphthalate (MMPP). Alternatively, hydrolysis and subsequent reduction allow the hydrazone to be readily converted into the alcohol **8a** in a good overall yield. Interestingly, a catalytic dihydroxylation of the *exo*-enamide of **8a** afforded, with total diastereoselection, the cyclobutane-fused γ-lactol **9a**, a type of scaffold that recalls the core of biologically relevant products.[16]

Scheme 2. Preliminary Manipulation of the Cycloadducts



A plausible mechanism for the cycloaddition reaction is proposed in Scheme 3. An initial activation of the allenamide by the carbophilic catalyst would provide the zwitterionic intermediate **I**, species that has been theoretically located in the context of intermolecular [4 + 2] Au-catalyzed cycloadditions between dienes and allenamides.[7] Regioselective interception of **I** by the nucleophilic β-carbon of the alkenylhydrazone affords the acyclic intermediate **II**, which might evolve to the final cycloadduct **3** by direct cyclization with concomitant elimination of the catalyst.[7] Alternatively, the cyclization might proceed through the alkyl gold intermediate **III**, which would explain the formation of *Z*/*E* mixtures of **3**.[17] The diastereoselectivity of the reaction, to give cyclobutanes in which R^1 and R^2 are in a *cis* disposition, is consistent with an approach of the vinyl gold moiety of **II** from the opposite face to that of the R^2 group. A cyclization via rotamer **II′**, leading to a hypothetical *trans* isomer, should be less favorable due to steric reasons. Finally, the

Scheme 3. Mechanistic Proposal



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formation of acyclic side products of type **6** can be explained by assuming a hydrogen abstraction in intermediate **II** (i.e., R^1 = CH_3) followed by protodeauration of the resulting acyclic species **IV**.[19] In consonance with this mechanistic proposal and the involvement of species of type **II**, we have found that the cycloaddition of *Z*-**2b** provides the same cycloadduct (*Z*-**3ab**) that is obtained from *E*-**2b**.[18]

In summary, we have developed a new gold-catalyzed cycloaddition which involves allenamides and conjugate *N,N*-dialkyl hydrazones. The reaction provides densely substituted cyclobutanes in good yields with excellent levels of regio- and diastereoselectivity. To the best of our knowledge, this method constitutes the first transition-metal-catalyzed process in which this type of α,β-unsaturated hydrazones exhibits azaenamine vinylogous reactivity. Consequently, in just three simple steps, it is now possible to transform an enal into a highly substituted cyclobutane that incorporates a quaternary stereocenter.

■ ASSOCIATED CONTENT

Supporting Information

Full experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: joseluis.mascareñas@usc.es.
*E-mail: fernando.lopez@csic.es.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Dembitsky, V. *J. Nat. Prod.* **2008**, *62*, 1. (b) Hansen, T. V.; Stenstrom, Y. *Organic Synthesis: Theory and Applications* **2001**, *5*, 1.

(2) (a) Namyslo, J. C.; Kaufmann, D. *Chem. Rev.* **2003**, *103*, 1485. (b) Fu, N.-Y.; Chan, S.-H.; Wong, H. N. C. In *The Chemistry of Cyclobutanes*; Rappoport, Z., Liebman, J. F., Eds.; John Wiley & Sons: West Sussex, 2005; Vol. *1*, Chapter 9.

(3) (a) Baldwin, J. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. *5*, p 63. (b) Crimmins, M. T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol *5*, p 123. (c) Lee-Ruff, E. In *The Chemistry of Cyclobutanes*; Rappoport, Z., Liebman, J. F., Eds.; John Wiley & Sons, Ltd.: West Sussex, 2005; Vol. *1*, Chapter 8. (d) Hehn, J. P.; Müller, C.; Bach, T. In *Handbook of Synthetic Photochemistry*; Wiley-VCH: Weinheim, 2010; p 171.

(4) For selected examples, see: (a) Inanaga, K.; Takasu, K.; Ihara, M. *J. Am. Chem. Soc.* **2004**, *126*, 1352. (b) Schmidt, A. W.; Knölker, H.-J. *Synlett* **2010**, 2207. (c) Brimioulle, R.; Bach, T. *Science* **2013**, *342*, 840.

(5) (a) Parthasarathy, K.; Cheng, C. H. In *Comprehensive Organic Synthesis II*, 2nd ed.; Knochel, P., Molander, G. A., Eds.; Elsevier: Amsterdam, 2014; p 222. (b) Tam, W.; Goodreid, J.; Cockburn, N. *Curr. Org. Synth.* **2014**, *6*, 219. (c) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Soc. Rev.* **2010**, *39*, 783. (d) Gulías, M.; Collado, A.; Trillo, B.; López, F.; Oñate, E.; Esteruelas, M. A.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2011**, *133*, 7660.

(6) (a) Li, X. X.; Zhu, L. L.; Zhou, W.; Chen, Z. L. *Org. Lett.* **2012**, *14*, 436. (b) Suárez-Pantiga, S.; Hernández-Díaz, C.; Piedrafita, M.; Rubio, E.; González, J. M. *Adv. Synth. Catal.* **2012**, *354*, 1651. (c) Faustino, H.; Bernal, P.; Castedo, L.; López, F.; Mascareñas, J. L. *Adv. Synth. Catal.* **2012**, *354*, 1658. (d) Suárez-Pantiga, S.; Hernández-Díaz, C.; Rubio, E.; González, J. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 11552.

(7) Montserrat, S.; Faustino, H.; Lledós, A.; Mascareñas, J. L.; López, F.; Ujaque, G. *Chem.—Eur. J.* **2013**, *19*, 15248.

(8) Lazny, R.; Nodzewska, A. *Chem. Rev.* **2010**, *110*, 1386.

(9) For a review, see: (a) Behforouz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259. See also: (b) Lomberget, T.; Baragona, F.; Fenet, B.; Barret, R. *Org. Lett.* **2006**, *8*, 3919.

(10) For examples of this umpolung reactivity using acid catalysis, see: (a) Hashimoto, T.; Omote, M.; Maruoka, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 3489. (b) Hashimoto, T.; Kimura, H.; Maruoka, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 6844. (c) Sridharan, V.; Ribelles, P.; Estévez, V.; Villacampa, M.; Ramos, M. T.; Perumal, P. T.; Menéndez, J. C. *Chem.—Eur. J.* **2012**, *18*, 5056. For representative stoichiometric examples, see: (d) Kamitori, Y.; Hojo, M.; Msuda, R.; Yoshida, T.; Ohara, S.; Yamada, K.; Yoshikawa, N. *J. Org. Chem.* **1988**, *53*, 519. (e) Hegedus, L. S.; Sestrick, M. R.; Michaelson, E. T.; Harrington, P. J. *J. Org. Chem.* **1989**, *54*, 4141.

(11) In contrast to the α,β-unsaturated *N,N*-dialkyl hydrazones, the homologues derived from formaldehyde have been widely used as umpoled species in catalysis, see: (a) Brehme, R.; Enders, D.; Fernández, R.; Lassaletta, J. M. *Eur. J. Org. Chem.* **2007**, 5629. (b) Crespo-Pelna, A.; Monge, D.; Martín-Zamora, E.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 12912.

(12) *N,N*-Dialkyl hydrazones are typically used as ancillary ligands in transition metal catalysis.[8] For isolated examples of their use as reactants, see: (a) Ros, A.; López-Rodríguez, R.; Estepa, B.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 4573. (b) Pair, E.; Monteiro, N.; Bouyssi, D.; Baudoin, O. *Angew. Chem., Int. Ed.* **2013**, *52*, 5346. (c) Prieto, A.; Jeamet, E.; Monteiro, N.; Bouyssi, D.; Baudoin, O. *Org. Lett.* **2014**, *16*, 4770. For a report involving transition metal Lewis acid catalysis, see: (d) Monge, D.; Martín-Zamora, E.; Vázquez, J.; Alcarazo, M.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Org. Lett.* **2007**, *9*, 2867.

(13) For previous Au-catalyzed annulations of allenamides, see ref 6 and: (a) Faustino, H.; López, F.; Castedo, L.; Mascareñas, J. L. *Chem. Sci.* **2011**, *2*, 633. (b) Faustino, H.; Alonso, I.; Mascareñas, J. L.; López, F. *Angew. Chem., Int. Ed.* **2013**, *52*, 6526. (c) Zhou, W.; Li, X. X.; Li, G. H.; Wu, Y.; Chen, Z. *Chem. Commun.* **2013**, *49*, 3552. (d) Li, G. H.; Zhou, W.; Li, X. X.; Bi, Q. W.; Wang, Z.; Zhao, Z. G.; Hu, W. X.; Chen, Z. *Chem. Commun.* **2013**, *49*, 4770. For a recent review on allenamides, see: (e) Lu, T.; Lu, Z. J.; Ma, Z. X.; Zhang, Y.; Hsung, R. P. *Chem. Rev.* **2013**, *113*, 4862. For a cycloaddition leading to products related to **5aa**, see: Berry, C. R.; Hsung, R. P. *Tetrahedron* **2004**, *60*, 7629.

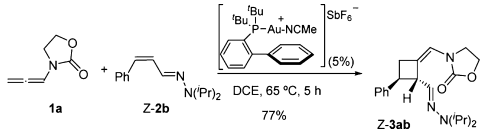
(14) Braun, I.; Rudroff, F.; Mihovilovic, M. D.; Bach, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 5541 and references therein.

(15) The structure of **3ac′** was also confirmed by X-ray analysis (see the Supporting Information (SI))

(16) (a) Lu, P.; Bach, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 1261. (b) Alibes, R.; Álvarez-Larena, A.; de March, P.; Figueredo, M.; Font, J.; Parella, T.; Rustullet, A. *Org. Lett.* **2006**, *8*, 491.

(17) Alternative closures in species **II**, either between C1 and C5 or C2 and N7, could respectively explain the formation of the [3 + 2] and [4 + 3] adducts **4aa** and **5aa**, observed under Pt catalysis (Table 1).

(18) For further details on the cycloaddition of *Z*-**2b**, see the SI.



(19) For gold-catalyzed hydrofunctionalizations of allenamides, see: (a) Kimber, M. C. *Org. Lett.* **2010**, *12*, 1128. (b) Hill, A. W.; Elsegood, M. R.; Kimber, M. C. *J. Org. Chem.* **2010**, *75*, 5406.