

## Gold-catalyzed oxycyclization of allenic carbamates: expeditious synthesis of 1,3-oxazin-2-ones

Benito Alcaide<sup>\*1</sup>, Pedro Almendros<sup>\*2</sup>, M. Teresa Quirós<sup>1</sup>  
and Israel Fernández<sup>3</sup>

### Full Research Paper

Open Access

#### Address:

<sup>1</sup>Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica I, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid, Spain, <sup>2</sup>Instituto de Química Orgánica General (IQOG), Consejo Superior de Investigaciones Científicas (CSIC), Juan de la Cierva 3, 28006-Madrid, Spain and <sup>3</sup>Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid, Spain

#### Email:

Benito Alcaide<sup>\*</sup> - [alcaideb@quim.ucm.es](mailto:alcaideb@quim.ucm.es); Pedro Almendros<sup>\*</sup> - [palmendros@iqog.csic.es](mailto:palmendros@iqog.csic.es)

\* Corresponding author

#### Keywords:

allenes; computational chemistry; gold; gold catalysis; heterocycles; reaction mechanisms

*Beilstein J. Org. Chem.* **2013**, *9*, 818–826.

doi:10.3762/bjoc.9.93

Received: 08 February 2013

Accepted: 26 March 2013

Published: 26 April 2013

This article is part of the Thematic Series "Gold catalysis for organic synthesis II".

Guest Editor: F. D. Toste

© 2013 Alcaide et al; licensee Beilstein-Institut.

License and terms: see end of document.

## Abstract

A combined experimental and computational study on regioselective gold-catalyzed synthetic routes to 1,3-oxazin-2-ones (kinetically controlled products) and 1,3-oxazin-2-one derivatives (thermodynamically favored) from easily accessible allenic carbamates has been carried out.

## Introduction

The search for new synthetic routes to 1,3-oxazin-2-one derivatives [1] is of interest because of the biological activity of these molecules [2-7]. Carretero and colleagues have published the Au(I)-catalyzed cyclization of *N*-Boc-3-butyn-1-amines to afford six-membered 2-oxazinones, namely, 6-methylene-1,3-oxazin-2-ones involving a 6-*exo-dig* cyclization [1]. This interesting method avoids complicated prefunctionalization of starting materials and minimizes the formation of byproducts; however, it is used just for the preparation of four simple examples. 1,3-Oxazin-2-ones are also used as valuable intermediates

in organic synthesis [8-14]. Recently, allenes have attracted much attention as they have been used for the preparation of both biologically relevant drugs as well as advanced materials [15-27]. However, regioselectivity problems are significant (*endo-trig* versus *endo-dig* versus *exo-dig* versus *exo-trig* cyclization). Great effort is currently being made in the search for a variety of reactions promoted by gold salts due to their impressive catalytic properties [28-41]. The Boc protective group has been widely used in allene chemistry, being an inert and recommended partner in gold- and palladium-catalyzed

aminocyclizations of allenes [42]. On the other hand, reports of gold-catalyzed cyclizations leading to heterocycles that contain more than one heteroatom are rare [43–48]. Besides, it has been reported very recently that the Au(I)-catalyzed cyclization of a *N*-phenethyl-*N*-Boc-protected allenamide failed [49]. Despite the above precedents, but in continuation of our interest in heterocyclic and allene chemistry [50–55], we decided to examine the gold-catalyzed cyclization of *N*-Boc-allenes with the aim of establishing a protocol for the synthesis of 1,3-oxazin-2-one derivatives in which the carbamate group should serve as the source of CO<sub>2</sub>.

## Results and Discussion

To explore the effects of various substrates on gold-catalyzed oxycyclization reactions, a number of new allenic carbamates were synthesized as shown in Scheme 1. Starting materials, *tert*-butyl (prop-2-ynyl)carbamates **1a–j**, were obtained both in the racemic form and in optically pure form by using standard methodologies. Thus, alkynylcarbamates **1a–g** were prepared through reductive amination of the appropriate aldehyde with propargylamine, followed by Boc<sub>2</sub>O treatment of the corresponding *N*-substituted prop-2-yn-1-amine. Alkynylcarbamate **1h** was prepared from Garner's aldehyde following a literature report [56,57]. Alkynylcarbamate **1i** was readily accessed from (*S*)-prolinol by using a modified known procedure [58]. Alkynylcarbamate **1j** was achieved through the reaction of 3-bromo-1*H*-indole-2-carbaldehyde with the Ohira–Bestmann reagent followed by the addition of Boc<sub>2</sub>O. Terminal alkynes **1** were conveniently converted into allenic carbamates **2** by treatment with paraformaldehyde in the presence of diisopropylamine and copper(I) bromide (Crabbé reaction) [59,60].

We employed three different gold salts in our initial screening of catalysts for the model system, allenic carbamate **2a**. Initially, the use of AuCl<sub>3</sub> and AuCl were tested, but both failed to catalyze the reaction. Fortunately, we found that [AuClPPH<sub>3</sub>]/AgOTf was an excellent catalyst for our purpose. To our delight, the reaction of allenic carbamate **2a** at room temperature afforded 3-benzyl-6-methylene-1,3-oxazinan-2-one (**3a**) bearing an exocyclic double bond as the sole product (Scheme 2). Adding a catalytic amount of Brønsted acid (PTSA) into the reaction system did slightly improve the yield of **3a**. Solvent screening demonstrated that dichloromethane was the best choice in the reaction.

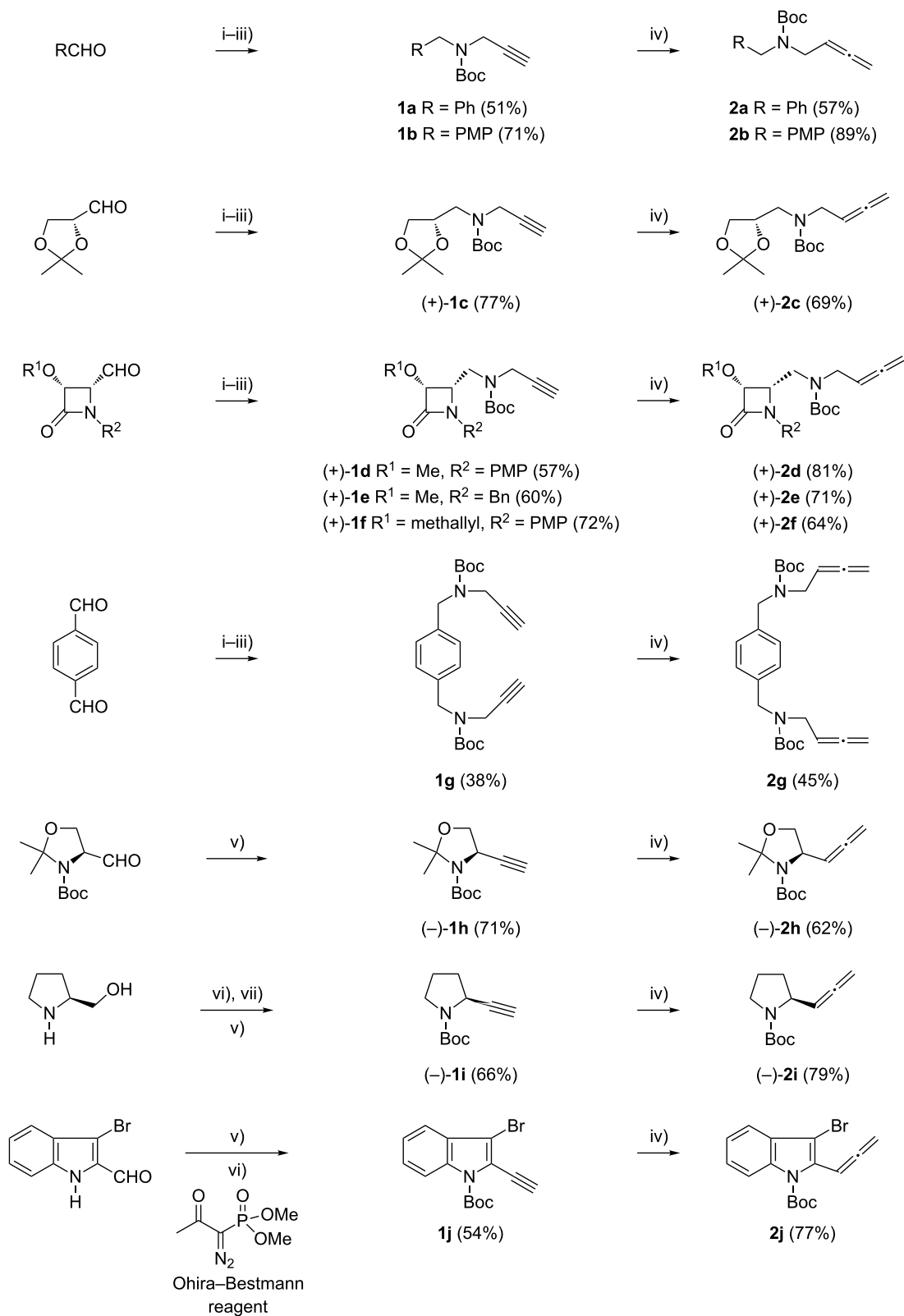
As revealed in Scheme 2, a variety of allenic carbamates **2** were also suitable for such heterocyclization reactions to afford 1,3-oxazinan-2-ones **3**. To increase the molecular diversity by incorporating more 1,3-oxazin-2-ones in the molecule, compound **2g** having two allenic carbamate units was used. Notably, bis(allenic carbamate) **2g** also undergoes this interest-

ing transformation to give bis(6-methylene-1,3-oxazinan-2-one) **3g** through a two-fold cyclization. This product particularly underlines the power of the present cyclization reaction, as none of the conventional methods would allow its synthesis with such great ease.

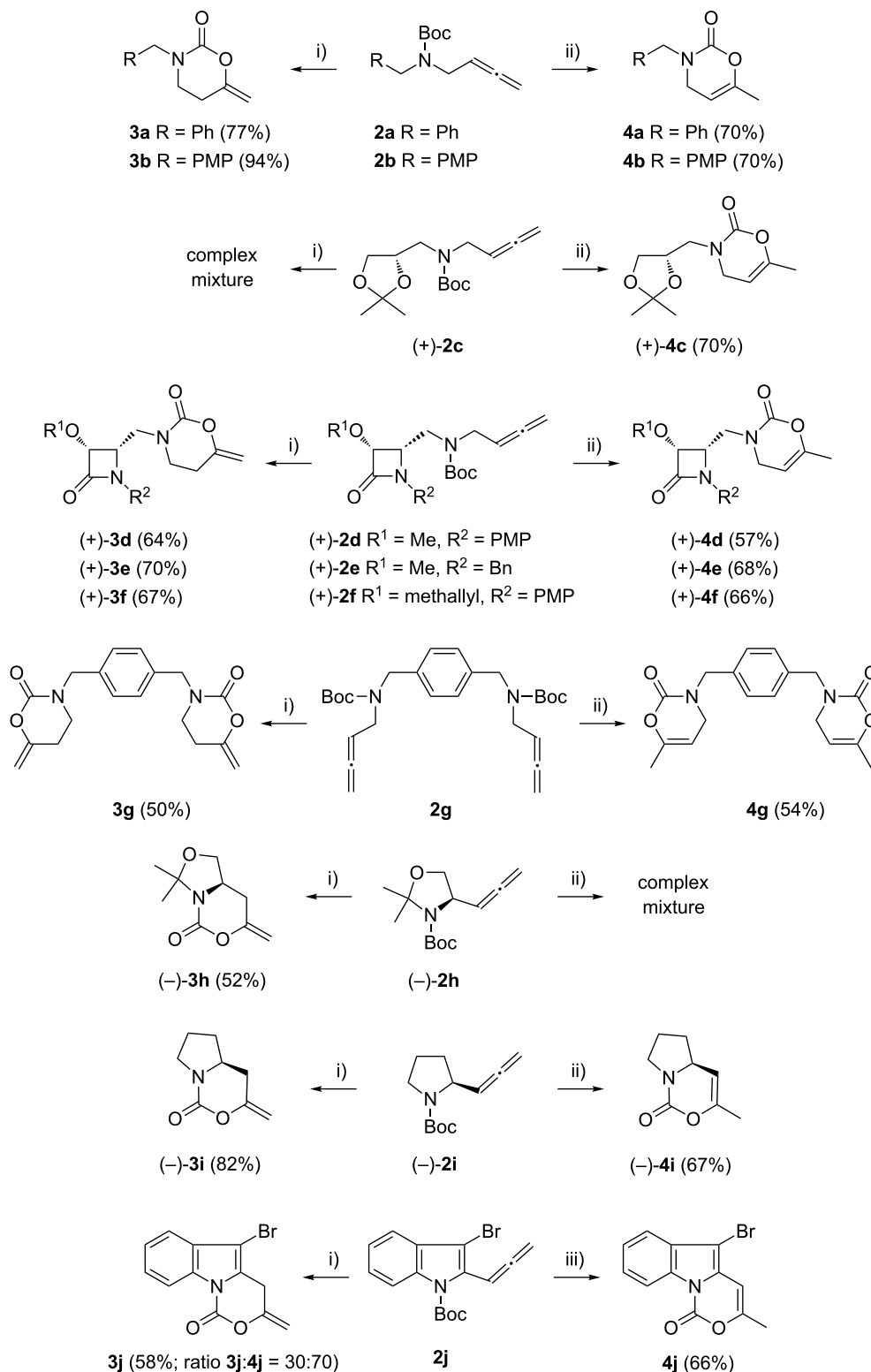
Interestingly, as a first try, we were pleased to notice that the reaction of allenyl derivative **2a** in dichloromethane at 90 °C, afforded 1,3-oxazin-2-one **4a** bearing an endocyclic double bond as the major component, and 1,3-oxazinan-2-one **3a** was also isolated as a minor component. Notably, starting from allenic carbamates **2a–j** and performing the reaction in dichloromethane at 130 °C, a series of 6-methyl-3-substituted 3,4-dihydro-2*H*-1,3-oxazin-2-ones **4a–j** were exclusively formed (Scheme 2) [61–68]. The observed regioselectivity is worthy of note, because under our reaction conditions only 1,3-oxazinan-2-ones **3** (arising from 6-*endo-dig* cyclization) or 3,4-dihydro-2*H*-1,3-oxazin-2-ones **4** (arising from 6-*exo-dig* cyclization) were achieved, with the nucleophilic oxygen attacking the central allene carbon atom in each case. This is an interesting result, because the available examples on related metal-catalyzed allene heterocyclizations usually lead to 5-*exo-trig* cyclization [69,70]; only Hashmi et al. have recently reported an attack at the central position of the allene in allenylamides [44].

Thus, it is possible to suppress the formation of the 1,3-oxazinan-2-one ring by performing the reaction at higher temperature, yielding the 1,3-oxazin-2-one as the exclusive product. A general trend can be deduced on the basis of these results: heterocycle **4** is the thermodynamically controlled product while heterocycle **3** is the kinetically controlled product [71–73]. Probably, double-bond migration in compounds **3** results in the formation of the 1,3-oxazin-2-one **4**. In order to verify the role of the Au(I) catalyst in the double-bond migration process, we set up two experiments. Heating a mixture of **3a** with Au(OTf)PPH<sub>3</sub> at a loading of 2.5 mol % in dichloromethane for 1.5 h at 130 °C resulted in full conversion into **4a**. Running the same reaction in the absence of any catalyst resulted in 30% conversion after two days, as determined by <sup>1</sup>H NMR. Treatment of 1,3-oxazinan-2-one **3a** with 5 mol % TfOH in CH<sub>2</sub>Cl<sub>2</sub> at room temperature did not proceed to give an appreciable amount of 3,4-dihydro-2*H*-1,3-oxazin-2-one **4a** after 2 h. This indicates that the Au(I) catalyst might participate in the double-bond migration process; being a possible intermediate, the  $\pi$ -allyl complex **5** is depicted in Scheme 3 [74]. Despite that, the isomerization process can be also viewed as an intramolecular 1,3-H shift assisted by gold.

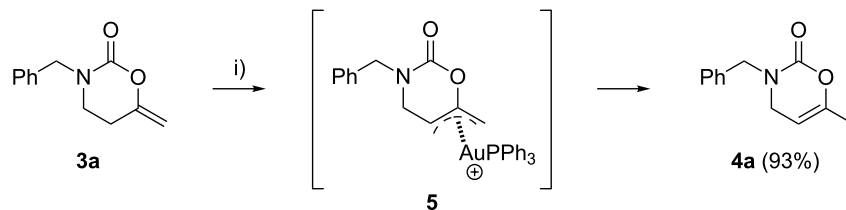
A possible pathway for the gold-catalyzed achievement of heterocycles **3** from allenyl-tethered carbamates **2** may initially



**Scheme 1:** Preparation of allenic carbamates **2a–j**. Reagents and conditions: (i) Propargylamine, MgSO<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 15 h. (ii) NaBH<sub>4</sub>, MeOH, rt, 0.5 h. (iii) Boc<sub>2</sub>O, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, rt, 2–15 h. (iv) (CH<sub>2</sub>O)<sub>n</sub>, iPr<sub>2</sub>NH, CuBr, 1,4-dioxane, reflux, 1 h. (v) Ohira–Bestmann reagent, K<sub>2</sub>CO<sub>3</sub>, MeOH, rt, 15 h. (vi) Boc<sub>2</sub>O, DMAP, CH<sub>3</sub>CN, rt, 2 h. (vii) Dess–Martin periodinane, CH<sub>2</sub>Cl<sub>2</sub>, rt. PMP = 4-MeOC<sub>6</sub>H<sub>4</sub>.



**Scheme 2:** Controlled oxycyclization reactions of allenic carbamates **2** to 1,3-oxazinan-2-ones **3** and 1,3-oxazin-2-ones **4** under selective gold-catalyzed conditions. Reagents and conditions: (i) 2.5 mol % [AuClPPH<sub>3</sub>], 2.5 mol % AgOTf, 10 mol % PTSA, CH<sub>2</sub>Cl<sub>2</sub>, rt, **3a**: 6 h; **3b**: 7 h; **3d**: 6 h; **3e**: 8 h; **3f**: 7 h; **3g**: 5.5 h; **3h**: 5 h; **3i**: 7 h; **3j**: 2 h. (ii) 2.5 mol % [AuClPPH<sub>3</sub>], 2.5 mol % AgOTf, 10 mol % PTSA, CH<sub>2</sub>Cl<sub>2</sub>, sealed tube, 130 °C, **4a**: 1.5 h; **4b**: 2 h, **4c**: 4 h; **4d**: 6 h; **4e**: 4 h; **4f**: 0.5 h; **4g**: 5.5 h; **4i**: 2 h. (iii) 2.5 mol % [AuClPPH<sub>3</sub>], 2.5 mol % AgOTf, 10 mol % PTSA, CH<sub>2</sub>Cl<sub>2</sub>, sealed tube, 80 °C, **4j**: 2 h. PMP = 4-MeOC<sub>6</sub>H<sub>4</sub>.

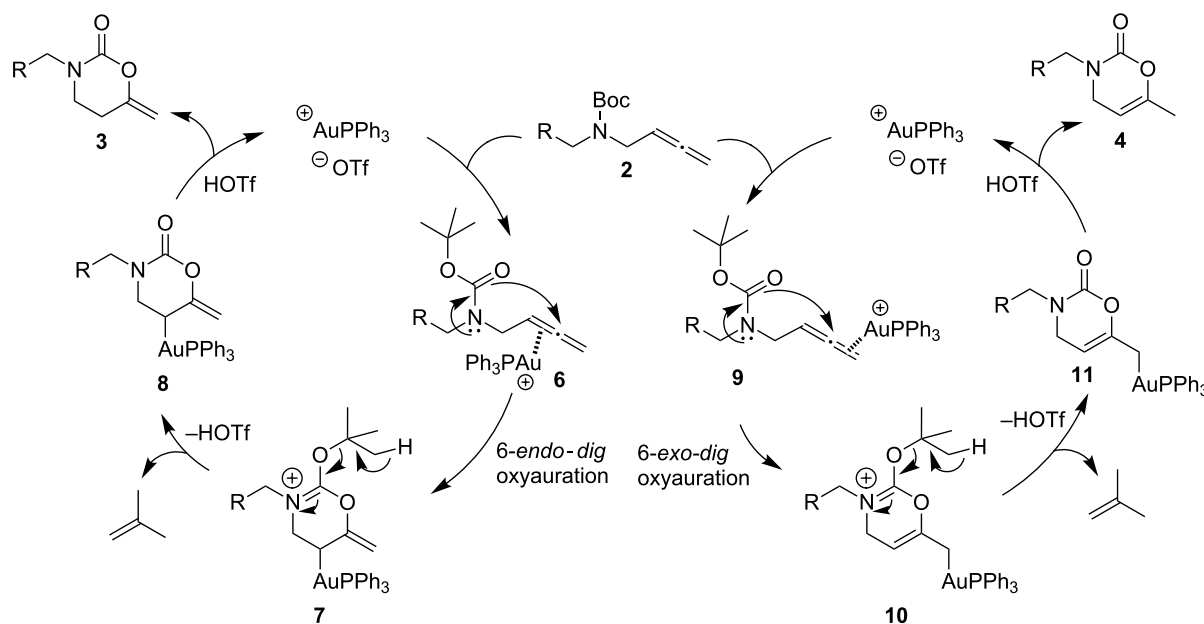


**Scheme 3:** Possible explanation for the gold-catalyzed isomerization reaction of 1,3-oxazinan-2-one **3a** into 1,3-oxazin-2-one **4a**. Reagents and conditions: (i) 2.5 mol % [AuClPPh<sub>3</sub>], 2.5 mol % AgOTf, 10 mol % PTSA, CH<sub>2</sub>Cl<sub>2</sub>, sealed tube, 130 °C, 1.5 h.

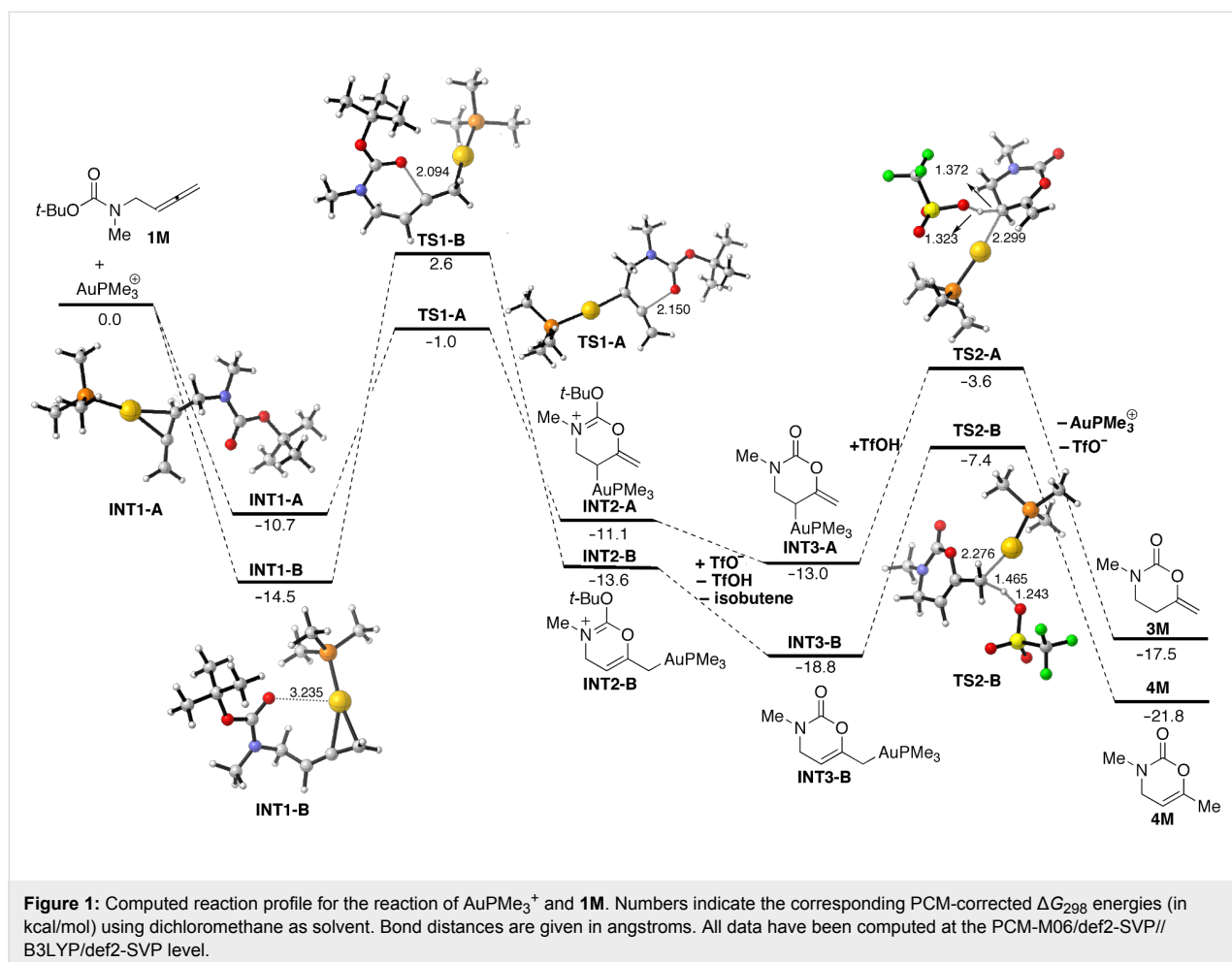
involve the formation of a complex **6** through coordination of the gold salt to the proximal allenic double bond. Next, chemo- and regioselective 6-*endo-dig* oxyauration of the carbamate carbonyl moiety forms species **7**. Attack of the carbamate carbonyl group occurs as a result of the stability of the intermediate ammonium cation type **7**. Loss of proton linked to 2-methylprop-1-ene release [75–78], generates neutral species **8**, which followed by protonolysis of the carbon–gold bond affords 6-methylene-1,3-oxazinan-2-ones **3** with concurrent regeneration of the gold catalyst (Scheme 4, left catalytic cycle). In line with the above mechanistic proposal, the easy breakage of the *tert*-butyl group at species **7** is essential for the formation of 1,3-oxazinan-2-ones **3**. Besides, the replacement of the *tert*-butyl group in allenic carbamates **2** by other alkyl functions, such as methyl, did not allow the preparation of heterocycles **3**. In addition to the double-bond isomerization that transforms

products **3** into the thermodynamically more favored compounds **4**, a mechanistic scenario involving the initial coordination of the gold to the distal allenic double bond leading to complex **9**, followed by a 6-*exo-dig* oxyauration is likely for the achievement of 1,3-oxazin-2-ones **4** from allenic carbamates **2** (Scheme 4, right-hand catalytic cycle).

Density functional theory (DFT) calculations (see Supporting Information File 1) have been carried out at the PCM-M06/def2-SVP//B3LYP/def2-SVP level to gain more insight into the reaction mechanism of the above discussed gold-catalyzed divergent oxycyclization reaction. The corresponding computed reaction profiles of the model allene **1M** with the model gold catalyst AuPMe<sub>3</sub>(OTf) are shown in Figure 1, which gathers the respective free energies (computed at 298 K) in CH<sub>2</sub>Cl<sub>2</sub> solution.



**Scheme 4:** Mechanistic explanation for the gold-catalyzed oxycyclization reactions of allenic carbamates **2** into 6-methylene-1,3-oxazinan-2-ones **3** or into 3-substituted-3,4-dihydro-2*H*-1,3-oxazin-2-ones **4**.



As initially envisaged, two different coordination modes of the metal fragment to the allenic double bond of **1M**, i.e., distal versus proximal, are possible. Our calculations indicate that the distal coordination leading to **INT1-B** is favored over the proximal coordination mode, which forms **INT1-A** ( $\Delta\Delta G = 3.8$  kcal/mol). This is mainly due to the presence of a two-electron stabilizing interaction established by donation of electronic density from the lone pair of the oxygen atom of the carbonyl moiety to a vacant d atomic orbital of the gold atom in **INT1-B** [79]. Both complexes can undergo the corresponding oxyauration cyclization reaction. Thus, **INT1-A** is converted into **INT2-A** in a slightly exergonic process ( $\Delta G_{R,298} = -0.4$  kcal/mol) through the saddle point **TS1-A**, which is associated with the 6-*endo-dig* cyclization. Similarly, **INT1-B** is transformed into **INT2-B** in a slightly endergonic process ( $\Delta G_{R,298} = +0.9$  kcal/mol) via **TS1-B**, associated with the 6-*exo-dig* cyclization reaction.

From the data in Figure 1, it becomes obvious that the 6-*endo-dig* transformation is kinetically favored over the 6-*exo-dig* reaction in view of the computed lower activation barrier of the former process ( $\Delta\Delta G^\ddagger_{298} = +7.4$  kcal/mol). However, the cyclic

reaction product **INT2-B** is thermodynamically more stable than the counterpart **INT2-A** ( $\Delta\Delta G = 2.5$  kcal/mol), which is in agreement with the experimental findings (see above). The next step of the process involves the  $\text{TfO}^-$  promoted elimination of isobutene to form the corresponding **INT3** complexes. The driving force of this process is clearly related to the thermodynamically favored release of isobutene ( $\Delta G_{R,298} = -1.9$  and  $-5.2$  kcal/mol from **INT3-A** and **INT3-B**, respectively). Finally, the protonolysis reaction of the carbon–gold bond by  $\text{TfOH}$  renders the final products **3M** and **4M** regenerating the catalyst. This step occurs through the transition states **TS2-A** and **TS2-B**, respectively, in an exergonic transformation ( $\Delta G_{R,298} = -4.5$  and  $-3.0$  kcal/mol from **INT3-A** and **INT3-B**, respectively). Again, the data in Figure 1 indicate that the final product **4M** is thermodynamically more stable than **3M**, which is in line with the experimentally observed conversion of **3a** into **4a** by heating in the presence and also in the absence of the gold-catalyst. From the computed reaction profile, it can be concluded that the observed divergent cyclization finds its origin in the initial 6-*endo* versus 6-*exo* oxyauration reaction steps, with the former being kinetically favored whereas the

latter is thermodynamically favored. At this point, it cannot be safely discarded that the formation of the thermodynamically more stable 6-*exo-dig* products is the result of the simple thermally promoted isomerization of the less stable 6-*endo-dig* species.

## Conclusion

In conclusion, efficient gold-catalyzed synthetic routes to 1,3-oxazinan-2-one and 1,3-oxazin-2-one derivatives from easily accessible allenic carbamates under mild conditions have been reported. The oxycyclization reactions were found to proceed with complete control of regioselectivity. The mechanism of these processes has additionally been investigated by a computational study showing that heterocycles **3** are the kinetically controlled products whereas heterocycles **4** are thermodynamically favored.

## Experimental

### General Information

<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on 700, 500, 300, or 200 MHz spectrometers. NMR spectra were recorded in CDCl<sub>3</sub> solutions, except where otherwise stated. Chemical shifts are given in parts per million relative to TMS (<sup>1</sup>H, 0.0 ppm) or CDCl<sub>3</sub> (<sup>13</sup>C, 76.9 ppm). Low- and high-resolution mass spectra were taken on a QTOF LC-MS spectrometer using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation [ $\alpha$ ]<sub>D</sub> is given in 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup> at 20 °C, and the concentration (*c*) is expressed in grams per 100 mL. All commercially available compounds were used without further purification.

### Typical procedure for the Au(I)-catalyzed preparation of 1,3-oxazin-2-ones, **4**

[AuClPPH<sub>3</sub>] (0.00475 mmol), AgOTf (0.00475 mmol), and *p*-toluenesulfonic acid (0.019 mmol) were sequentially added to a stirred solution of the allenic carbamate **2a** (50 mg, 0.19 mmol) in dichloromethane (1.9 mL). The resulting mixture was heated in a sealed tube at 130 °C until disappearance of the starting material (TLC, 1.5 h). The reaction was allowed to cool to room temperature and filtered through a pack of celite. The filtrate was extracted with dichloromethane (3 × 5 mL), and the combined extracts were washed twice with brine. The organic layer was dried (MgSO<sub>4</sub>), concentrated under reduced pressure, and purified by flash column chromatography on silica gel (hexanes/ethyl acetate 4:1) to afford product **4a** (27 mg, 70%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25 °C)  $\delta$  7.33 (m, 2H), 4.76 (m, 1H), 4.58 (s, 2H), 3.68 (dq, *J* = 3.2, 1.9 Hz, 2H), 1.86 (td, *J* = 1.9, 1.2 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 25 °C)  $\delta$  150.9, 148.1, 135.6, 128.7, 128.2, 127.9, 94.4, 52.1, 44.6, 18.3; IR (CHCl<sub>3</sub>)  $\nu$ : 1685 cm<sup>-1</sup>; HRMS-ES (*m/z*): [M]<sup>+</sup> calcd for C<sub>12</sub>H<sub>13</sub>NO<sub>2</sub>, 203.0946; found, 203.0952.

## Supporting Information

### Supporting Information File 1

Experimental details, analytical data of new compounds, copies of <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra and computational details.

[<http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-9-93-S1.pdf>]

## Acknowledgements

Financial support from the MINECO [Projects CTQ2012-33664-C02-01, CTQ2012-33664-C02-02, CTQ2010-20714-C02-01, and Consolider-Ingenio 2010 (CSD2007-00006)] and Comunidad Autónoma de Madrid (Projects S2009/PPQ-1752 and S2009/PPQ-1634) are gratefully acknowledged. M. T. Q. thanks MEC for a predoctoral grant.

## References

- Robles-Machin, R.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2006**, *71*, 5023. doi:10.1021/jo060520y  
See for the synthesis of oxazinones from *N*-Boc-(3-butyn)-1-amines.
- Eichner, S.; Knobloch, T.; Floss, H. G.; Fohrer, J.; Harmrolfs, K.; Hermans, J.; Schulz, A.; Sasse, F.; Spittler, P.; Taft, F.; Kirschning, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 752. doi:10.1002/anie.201106249
- Wolfe, A. L.; Duncan, K. K.; Parekar, N. K.; Weir, S. J.; Vielhauer, G. A.; Boger, D. L. *J. Med. Chem.* **2012**, *55*, 5878. doi:10.1021/jm300330b
- Taft, F.; Harmrolfs, K.; Nickeleit, I.; Heutling, A.; Kiene, M.; Malek, N.; Sasse, F.; Kirschning, A. *Chem.-Eur. J.* **2012**, *18*, 880. doi:10.1002/chem.201101640
- Chinkov, N.; Warm, A.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 2957. doi:10.1002/anie.201006689
- Fishkin, N.; Maloney, E. K.; Chari, R. V. J.; Singh, R. *Chem. Commun.* **2011**, *47*, 10752. doi:10.1039/c1cc14164c
- Zhang, F.; Qian, L.; Flood, P. M.; Shi, J.-S.; Hong, J.-S.; Gao, H.-M. *J. Pharmacol. Exp. Ther.* **2010**, *333*, 822. doi:10.1124/jpet.110.165829
- Richter, H.; Fröhlich, R.; Daniliuc, C.-G.; García-Mancheño, O. *Angew. Chem., Int. Ed.* **2012**, *51*, 8656. doi:10.1002/anie.201202379
- Kuznetsov, N. Yu.; Maleev, V. I.; Khrustalev, V. N.; Mkrtchyan, A. F.; Godovikov, I. A.; Strelkova, T. V.; Bubnov, Y. N. *Eur. J. Org. Chem.* **2012**, 334. doi:10.1002/ejoc.201101114
- Shpak-Kraievskiy, P.; Yin, B.; Martel, A.; Dhal, R.; Dujardin, G.; Laurent, M. Y. *Tetrahedron* **2012**, *68*, 2179. doi:10.1016/j.tet.2012.01.002
- Tian, C.; Jiao, X.; Liu, X.; Li, R.; Dong, L.; Liu, X.; Zhang, Z.; Xu, J.; Xu, M.; Xie, P. *Tetrahedron Lett.* **2012**, *53*, 4892. doi:10.1016/j.tetlet.2012.07.011
- Zhou, H.-B.; Lee, J. H.; Mayne, C. G.; Carlson, K. E.; Katzenellenbogen, J. A. *J. Med. Chem.* **2010**, *53*, 3349. doi:10.1021/jm100052k
- Sato, S.; Shibuya, M.; Kanoh, N.; Iwabuchi, Y. *Chem. Commun.* **2009**, 6264. doi:10.1039/b913770j
- Osa, Y.; Hikima, Y.; Sato, Y.; Takino, K.; Ida, Y.; Hirono, S.; Nagase, H. *J. Org. Chem.* **2005**, *70*, 5737. doi:10.1021/jo0501644

15. Yu, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3074. doi:10.1002/anie.201101460
16. Rivera-Fuentes, P.; Diederich, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 2818. doi:10.1002/anie.201108001
17. Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994. doi:10.1021/cr1004088
18. Alcaide, B.; Almendros, P. *Chem. Rec.* **2011**, *11*, 311. doi:10.1002/tcr.201100011
19. Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Soc. Rev.* **2010**, *39*, 783. doi:10.1039/b913749a
20. Brasholz, M.; Reissig, H.-U.; Zimmer, R. *Acc. Chem. Res.* **2009**, *42*, 45. doi:10.1021/ar800011h
21. Krause, N., Ed. *Compounds with all carbon functions: Cumulenes and Allenes; Science of Synthesis*; Georg Thieme: Stuttgart, Germany, 2007; Vol. 44.
22. Ma, S. *Chem. Rev.* **2005**, *105*, 2829. doi:10.1021/cr020024j
23. Krause, N.; Hashmi, A. S. K., Eds. *Modern Allene Chemistry*; Wiley-VCH: Weinheim, Germany, 2004.
24. Alcaide, B.; Almendros, P. *Eur. J. Org. Chem.* **2004**, 3377. doi:10.1002/ejoc.200400023
25. Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. doi:10.1039/b103904k
26. Zimmer, R.; Dinesh, C. U.; Nandan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. doi:10.1021/cr9902796
27. Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. doi:10.1002/1521-3773(20001016)39:20<3590::AID-ANIE3590>3.0.CO;2-L
28. Hashmi, A. S. K.; Toste, F. D., Eds. *Modern Gold Catalyzed Synthesis*; Wiley-VCH: Weinheim, Germany, 2012.
29. Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. doi:10.1039/c1cs15279c
30. Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657. doi:10.1021/cr100414u
31. Rudolph, M.; Hashmi, A. S. K. *Chem. Commun.* **2011**, *47*, 6536. doi:10.1039/c1cc10780a
32. Alcaide, B.; Almendros, P.; Alonso, J. M. *Org. Biomol. Chem.* **2011**, *9*, 4405. doi:10.1039/c1ob05249g
33. Bandini, M. *Chem. Soc. Rev.* **2011**, *40*, 1358. doi:10.1039/c0cs00041h
34. Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 5232. doi:10.1002/anie.200907078
35. Lipshutz, B.; Yamamoto, Y., Eds. *Coinage Metals in Organic Synthesis*. *Chem. Rev.* **2008**, *108*, 2793–3442.
36. Hutchings, G. J.; Brust, M.; Schmidbaur, H., Eds. *Gold – Chemistry, Materials and Catalysis*. *Chem. Soc. Rev.* **2008**, *37*, 1745–2140.
37. Muzart, J. *Tetrahedron* **2008**, *64*, 5815. doi:10.1016/j.tet.2008.04.018
38. Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. doi:10.1021/cr000436x
39. Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. doi:10.1039/b612008c
40. Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. doi:10.1002/anie.200602454
41. Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. doi:10.1002/adsc.200600368  
See for a review.
42. Alcaide, B.; Almendros, P. *Adv. Synth. Catal.* **2011**, *353*, 2561. doi:10.1002/adsc.201100160
43. Higginbotham, M. C. M.; Bebbington, M. W. P. *Chem. Commun.* **2012**, *48*, 7565. doi:10.1039/c2cc33711h
44. Hashmi, A. S. K.; Schuster, A. M.; Litters, S.; Rominger, F.; Pernpointner, M. *Chem.–Eur. J.* **2011**, *17*, 5661. doi:10.1002/chem.201100132
45. LaLonde, R. L.; Wang, Z. J.; Mba, M.; Lackner, A. D.; Toste, F. D. *Angew. Chem., Int. Ed.* **2010**, *49*, 598. doi:10.1002/anie.200905000
46. Li, H.; Widenhoefer, R. A. *Org. Lett.* **2009**, *11*, 2671. doi:10.1021/ol900730w
47. Winter, C.; Krause, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6339. doi:10.1002/anie.200902355
48. Yeom, H.-S.; Lee, E.-S.; Shin, S. *Synlett* **2007**, 2292. doi:10.1055/s-2007-985571
49. Singh, S.; Elsegood, M. R. J.; Kimber, M. C. *Synlett* **2012**, 565. doi:10.1055/s-0031-1290335
50. Alcaide, B.; Almendros, P.; Quirós, M. T.; López, R.; Menéndez, M. I.; Sochacka-Ćwikła, A. J. *Am. Chem. Soc.* **2013**, *135*, 898. doi:10.1021/ja3108966
51. Alcaide, B.; Almendros, P.; Cembellín, S.; Martínez del Campo, T.; Fernández, I. *Chem. Commun.* **2013**, *49*, 1282. doi:10.1039/c2cc37872h
52. Alcaide, B.; Almendros, P.; Alonso, J. M.; Fernández, I. *Chem. Commun.* **2012**, *48*, 6604. doi:10.1039/c2cc32015k
53. Alcaide, B.; Almendros, P.; Aragoncillo, C.; Gómez-Campillos, G.; Arnó, M.; Domingo, L. R. *ChemPlusChem* **2012**, *77*, 563. doi:10.1002/cplu.201200090
54. Alcaide, B.; Almendros, P.; Alonso, J. M.; Quirós, M. T.; Gadziński, P. *Adv. Synth. Catal.* **2011**, *353*, 1871. doi:10.1002/adsc.201100209
55. Alcaide, B.; Almendros, P.; Carrascosa, R. *Chem.–Eur. J.* **2011**, *17*, 4968. doi:10.1002/chem.201100139
56. Bélanger, D.; Tong, X.; Soumaré, S.; Dory, Y. L.; Zhao, Y. *Chem.–Eur. J.* **2009**, *15*, 4428. doi:10.1002/chem.200802337
57. Spangenberg, T.; Schoenfelder, A.; Breit, B.; Mann, A. *Eur. J. Org. Chem.* **2010**, 6005. doi:10.1002/ejoc.201000865
58. Paul, A.; Bittermann, H.; Gmeiner, P. *Tetrahedron* **2006**, *62*, 8919. doi:10.1016/j.tet.2006.07.007  
We used the Dess–Martin oxidation and the Ohira–Bestmann reagent instead of the reported Swern oxidation and Corey–Fuchs olefination.
59. Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859. doi:10.1039/C39790000859
60. Kuang, J.; Ma, S. *J. Org. Chem.* **2009**, *74*, 1763. doi:10.1021/jo802391x
61. Decker, M. *Curr. Med. Chem.* **2011**, *18*, 1464. doi:10.2174/092986711795328355  
Compounds **3d–f** and **4d–f** can be considered as hybrid scaffolds, i.e., as a combination of the biologically relevant  $\beta$ -lactam and oxazinone frameworks. See for a review on hybrid chemical entities.
62. Tsogoeva, S. B. *Mini-Rev. Med. Chem.* **2010**, *10*, 773. doi:10.2174/138955710791608280
63. Meunier, B. *Acc. Chem. Res.* **2008**, *41*, 69. doi:10.1021/ar7000843
64. Tietze, L. F.; Bell, H. P.; Chandrasekhar, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3996. doi:10.1002/anie.200200553
65. Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489. doi:10.1021/cr900211p  
Fused tricyclic 3,4-dihydro-2H-1,3-oxazin-2-one **4j** was more efficiently obtained by performing the reaction at 80 °C. Fused indole derivatives are represented in numerous natural alkaloids and synthetic pharmaceuticals, which display a number of interesting biological activities.
66. Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608. doi:10.1002/anie.200901843
67. Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. doi:10.1021/cr0505270



68. Except for fused 6-methylene-1,3-oxazinan-2-one, **3j**, heterocycles **3** or **4** were exclusively obtained. Surprisingly, the exposure of tert-butyl allenic carbamate **2j** to the gold-catalyzed conditions at room temperature afforded the 1,3-oxazin-2-one **4j** as the major adduct, with the corresponding 1,3-oxazinan-2-one adduct **3j** being the minor component.
69. Chen, B.; Wang, N.; Fan, W.; Ma, S. *Org. Biomol. Chem.* **2012**, *10*, 8465. doi:10.1039/c2ob26291f
70. Shu, W.; Yu, Q.; Jia, G.; Ma, S. *Chem.–Eur. J.* **2011**, *17*, 4720. doi:10.1002/chem.201003611
71. Lee, P. H.; Kang, D.; Choi, S.; Kim, S. *Org. Lett.* **2011**, *13*, 3470. doi:10.1021/ol2012132
72. Mo, J.; Kang, D.; Eom, D.; Kim, S. H.; Lee, P. H. *Org. Lett.* **2013**, *15*, 26. doi:10.1021/ol3029274
73. Lee, P. H.; Kim, S.; Kang, D.; Park, A.; Chary, B. C.; Kim, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 6806. doi:10.1002/anie.201001799
74. Komiya, S.; Ozaki, S. *Chem. Lett.* **1988**, *17*, 1431. doi:10.1246/cl.1988.1431  
See for the isolation of an allylic gold complex.
75. <sup>1</sup>H NMR of the reaction mixtures revealed the presence of 2-methylprop-1-ene, which is likely formed from the tert-butyl fragmentation. For pioneering work on the introduction of tert-butyl carbonates as a cation-trapping group in gold catalysis, see references [76-78].
76. Buzas, A.; Gagosz, F. *Org. Lett.* **2006**, *8*, 515. doi:10.1021/ol053100o
77. Kang, J.-E.; Shin, S. *Synlett* **2006**, 717. doi:10.1055/s-2006-933110
78. Shin, S.-H. *Bull. Korean Chem. Soc.* **2005**, *26*, 1925. doi:10.5012/bkcs.2005.26.12.1925
79. The corresponding second-order perturbation energy from the NBO method associated with this LP(O) → d(Au) delocalization was computed to be ca. –5 kcal/mol.

## License and Terms

This is an Open Access article under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The license is subject to the *Beilstein Journal of Organic Chemistry* terms and conditions: (<http://www.beilstein-journals.org/bjoc>)

The definitive version of this article is the electronic one which can be found at:  
[doi:10.3762/bjoc.9.93](https://doi.org/10.3762/bjoc.9.93)