



HAL
open science

Silver(I) Oxide-/DBU-Promoted Synthesis of Dihydrofuran Units through Allenyl Silver Formation

Bao Yu, Anna Perfetto, Luca Allievi, Sabrina Dhambri, Marie-noelle Rager, Mohamed Selkti, Ilaria Ciofini, Marie-Isabelle Lannou, Geoffroy Sorin

► **To cite this version:**

Bao Yu, Anna Perfetto, Luca Allievi, Sabrina Dhambri, Marie-noelle Rager, et al.. Silver(I) Oxide-/DBU-Promoted Synthesis of Dihydrofuran Units through Allenyl Silver Formation. Chemistry - A European Journal, In press, 10.1002/chem.202002696 . hal-03044183

HAL Id: hal-03044183

<https://hal.science/hal-03044183>

Submitted on 7 Dec 2020

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

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

Silver(I) oxide - /DBU - promoted synthesis of dihydrofuran units through allenyl silver formation

Bao Yu^[a], Anna Perfetto^[b], Luca Allievi^[a], Sabrina Dhambri^[a], Marie-Noelle Rager^[b], Mohamed Selkti^[a], Ilaria Ciofini^[b], Marie-Isabelle Lannou^{*[a]}, and Geoffroy Sorin ^{*[a]}

[a] B. Yu, S. Dr. L. Allievi, S. Dhambri, Dr. M. Selkti, Dr. M.-I. Lannou, Dr. G. Sorin)
Faculté des Sciences Pharmaceutiques et Biologiques
Unité CNRS UMR 8038 CiTCoM
4 avenue de l'observatoire, 75270 Paris cedex 06 (France)
E-mail: marie-isabelle.lannou@parisdescartes.fr
geoffroy.sorin@parisdescartes.fr

[b] A. Perfetto, M.-N. Rager, Dr. I. Ciofini
Chimie ParisTech, PSL University
Unité CNRS FRE 2027
Institute of Chemistry for Life and Health Science (i-CLeHS)
11, rue Pierre et Marie Curie, 75005 Paris (France)
E-mail : ilaria.ciofini@chimie-paristech.fr

Abstract: A formal [3+2] cyclization mediated by silver(I) oxide and DBU is described herein. Through a broad variety of carbonyl compounds, this system can promote cyclization reactions with high yield (up to 85%) and diastereoselectivity (up to 95:5) for a straightforward access to complex and congested dihydrofuran derivatives in one step using smooth conditions. Based on DFT studies, the proposed mechanism would involve an allenyl silver intermediate.

Introduction

2,3-Dihydrofuran sub-units can be encountered in a wide range of natural and synthetic products exhibiting, in some cases, biologically interesting profiles.^[1] Additionally, such scaffolds can also be regarded as attractive precursors in an array of organic transformations.^[2] Based on these considerations, considerable efforts have been devoted to the development of efficient accesses to 2,3-dihydrofuran units by various approaches.^[3, 4, 5] Among them, intra- or intermolecular [3+2] cycloadditions constitute a powerful tool to reach such heterocycles^[6] and more generally, heterocyclic 5-membered rings. In this field, the vast majority of transformations encountered implies hetero 1,3-dipolar reagents or their synthetic equivalent for reaching a broad variety of heterocyclic molecules.^[7] However, access to cyclic frameworks by means of cycloadditions reveals to be much more challenging in cases where all-carbon 1,3-dipoles are involved due to the difficulty to generate such species.^[8] To overcome this issue, the activation of double or triple bonds by means of transition metals appears to be an attractive method. However, very specific substrates are required, which constitutes a main drawback and narrows the application field.^[8] One area of improvement could consist in taking advantage of the strong alkynophilicity of "coinage metals", to carry out such kind of cyclizations.

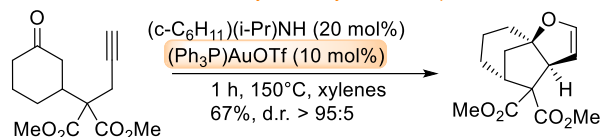
Indeed, in 2007 Zhang's group reported an elegant [3+2] cycloaddition for the diastereoselective synthesis of cyclopentanone enol ethers using enones and allenyl MOM ethers mediated by gold catalysis.^[9] One year later, the same group published the synthesis of different 2,5-dihydrofuran motifs through Au-containing all-carbon 1,3-dipoles from propargylic ketals, showing the ability of gold to promote such cyclizations.^[10] In the course of their work on dual organocatalysis combining gold and aminocatalysis, Kirsch *et al.* unexpectedly obtained a tricyclic *cis*-fused dihydrofuran adduct by using a co-catalytic amount of (Ph₃P)AuOTf (10 mol%) and (*c*-C₆H₁₁)(*i*-Pr)NH (20 mol%) in xylenes at 150°C for 1h (Figure 1).^[11] Surprisingly, this transformation has only been underlined in a single case by the authors and, to the best of our knowledge, has not been reported again in literature. Interestingly, in 2010, Zhang *et al.* demonstrated that the combination of Ag₂O and KOH was able to promote formal intramolecular [3+2] cycloaddition reactions, generating all-carbon 1,3-dipoles, under conventional heating^[12] or microwaves conditions.^[13] However, the scope of this transformation remains restricted to *N*-propargylamides bearing an electron withdrawing group on the nitrogen atom (Figure 1).

In the work developed herein, we expect to reach bi- or tricyclic complex structures containing 2,3-dihydrofuran cores in a single step from readily accessible compounds bearing an inactivated alkyne moiety. This reaction will proceed via a formal Ag(I) mediated [3+2] cyclization involving all-carbon 1,3-dipoles. This approach appears to be particularly challenging, since we envisioned to attain allenyl silver species through an unprecedented alkyne isomerization mediated by Ag(I) (Figure 1). As far as we know, the formation of an allenyl silver has only been reported by the Vermeer group through a 1,4-conjugated addition of an alkyl silver onto an ene-yne system (path a) or by transmetalation of an allenyl lithium species (path b).^[14] Moreover, the reactivity of such species has been little

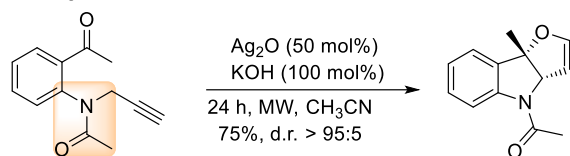
FULL PAPER

studied and the intramolecular cyclization targeted herein is unprecedented in literature (Figure 1).

S. Kirsch et al. - Gold catalysis / only one example described



Q. Zhang et al. - Amide moiety required for cyclization



P. Vermeer et al. - Allenyl silver formations reported to date

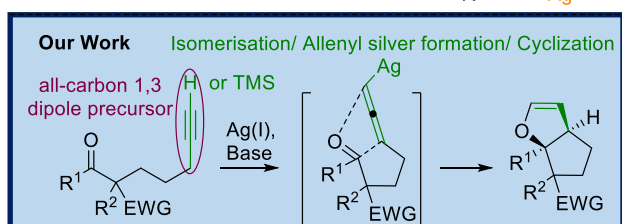
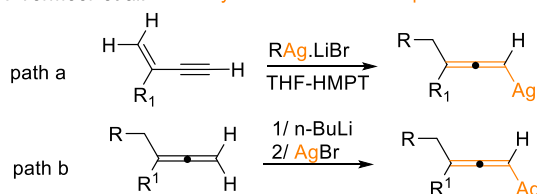
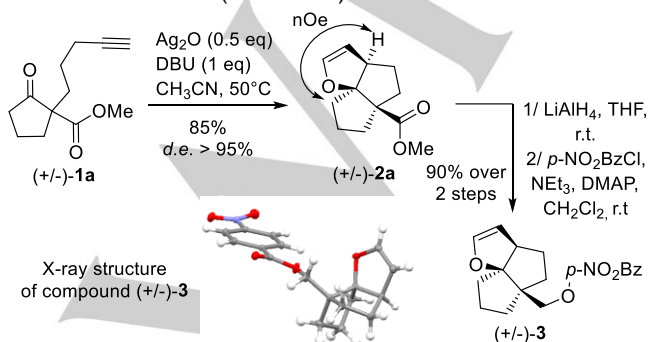


Figure 1 Silver/Base mediated alkyne isomerization/[3+2] cyclization reaction

Results and discussion

Silver was chosen as metal catalyst in this transformation since it is both significantly less expensive and more abundant than gold and less prone to undergo side-reactions than copper (*i.e.* Glaser-Hay coupling). Indeed, due to its [Kr] 4d¹⁰ 5s¹ configuration, silver possesses a strong alkynophilicity and its ability to π -coordinate to unsaturated systems having low-lying empty orbitals makes it extremely interesting especially in the field of alkyne-based chemistry.^[15] In a preliminary survey, we chose the combination of Ag₂O/DBU in acetonitrile and 1,3-keto ester **1a** as the substrate (Scheme 1).

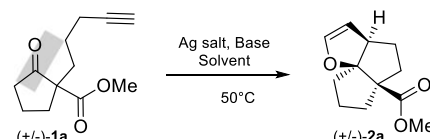


Scheme 1 Adduct **2a**: Structure and stereochemistry determination

We were pleased to find a complete and clean conversion of **1a** into the tricyclic compound **2a** at 50°C after 2h. The cyclized product was obtained in 85% yield with a total diastereoselectivity in favour of the *cis*-adduct without detection of the homo-coupling product.^[16] The stereochemistry was determined by NOE experiments and further confirmed by a single-crystal X-ray diffraction analysis of *p*-nitrobenzoyl derivative **3**,^[17] obtained after reduction of ester **2a** and subsequent esterification of the resulting alcohol with *p*-nitrobenzoyl chloride (90% yield over two steps, Scheme 1).

Encouraged by this preliminary result, we focused on the optimization the reaction conditions (Table 1). A short screening of silver salts highlighted the ability of inexpensive silver(I) oxide to cleanly promote the cyclization after 2 h with a satisfying yield (85%, Entry 1). Silver nitrate and silver antimonate afforded **2a** albeit in moderate yields, respectively 64% and 63% (Entry 2 and 4) whereas silver sulfate furnished only 32% of the desired product (Entry 3).

Table 1: Reaction optimization. Full data optimization is available in the ESI.



Entry	Metal (eq.)	Base ^a	Solvent	Time, Yield ^b %
1	Ag ₂ O (0.5)	DBU	MeCN	2h, 85%
2	AgNO ₃ (1.0)	DBU	MeCN	2h, 64%
3	Ag ₂ SO ₄ (0.5)	DBU	MeCN	3h, 32%
4	AgSbF ₆ (1.0)	DBU	MeCN	30h, 63%
5	Ag ₂ O (0.5)	K ₂ CO ₃	MeCN	12h, 80%
6	Ag ₂ O (0.5)	Pyrrolidine	MeCN	20h, 80%
7	Ag ₂ O (0.5)	NEt ₃	MeCN	20h, - ^c
8	Ag ₂ O (0.5)	DBU	DMF	2h, 76%
9	Ag ₂ O (0.5)	DBU	Toluene	2h, 85%
10	Ag ₂ O (0.5)	DBU	THF	2h, 84%
11	Ag ₂ O (0.5)	-	MeCN	24h, n.r
12	-	DBU	MeCN	24h, n.r
13	Ag ₂ O (0.25)	DBU	MeCN	48h, 78% ^d
14	Ag ₂ O (0.25)	DBU	MeCN	24h, 83% ^e
15	Ag ₂ O (0.5)	DBU	MeCN	24h, n.r. ^f
16	P(Ph) ₃ AuOTf (0.1)	pyrrolidine	toluene	2h, n.r. ^g

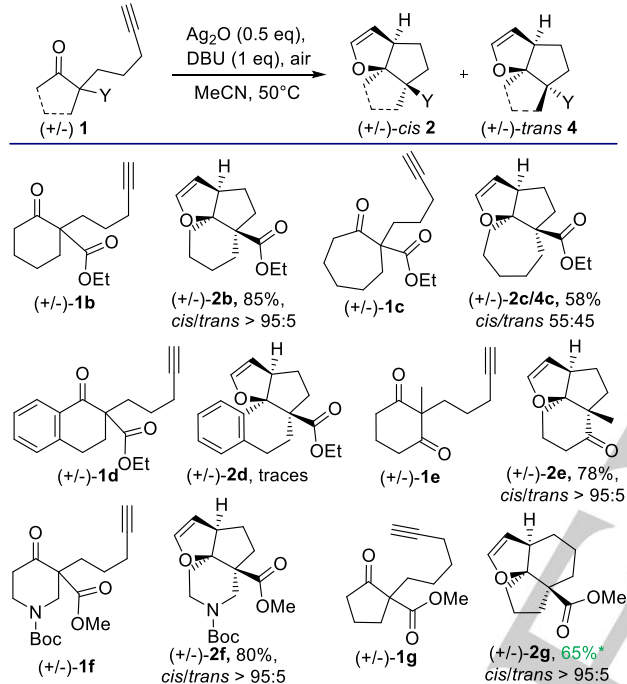
^a Each attempt was conducted with 1 eq. of base. ^b Isolated Yield. ^c Only traces of expected product were detected by ¹H NMR after 20h. ^d Reaction carried out under ambient atmosphere. ^e Reaction carried out with O₂ balloon. ^f Reaction performed at r.t instead of 50°C. ^g Reaction performed at 110°C

The reaction proceeded smoothly with K₂CO₃ as a base (80%, Entry 5) and pyrrolidine (80%, Entry 6) but only traces of the cyclized product were detected after 20h by using NEt₃ (Entry 7). Interestingly, the reaction is able to proceed in a wide range of solvents, providing **2a** in satisfying yields (Entry 8-10, see SI). Finally, without DBU (Entry 11) or silver(I) oxide (Entry 12) no reaction was observed, establishing that the combination of silver reagent and base is mandatory to promote such cyclization (Entry 11 and 12). Using 0.25 eq. of Ag₂O under air atmosphere afforded **2a** (78%, Entry 13) after a prolonged reaction time (48 h) which can be dramatically reduced to 24 h by conducting the reaction under O₂ atmosphere (83%, Entry 14). Interestingly,

FULL PAPER

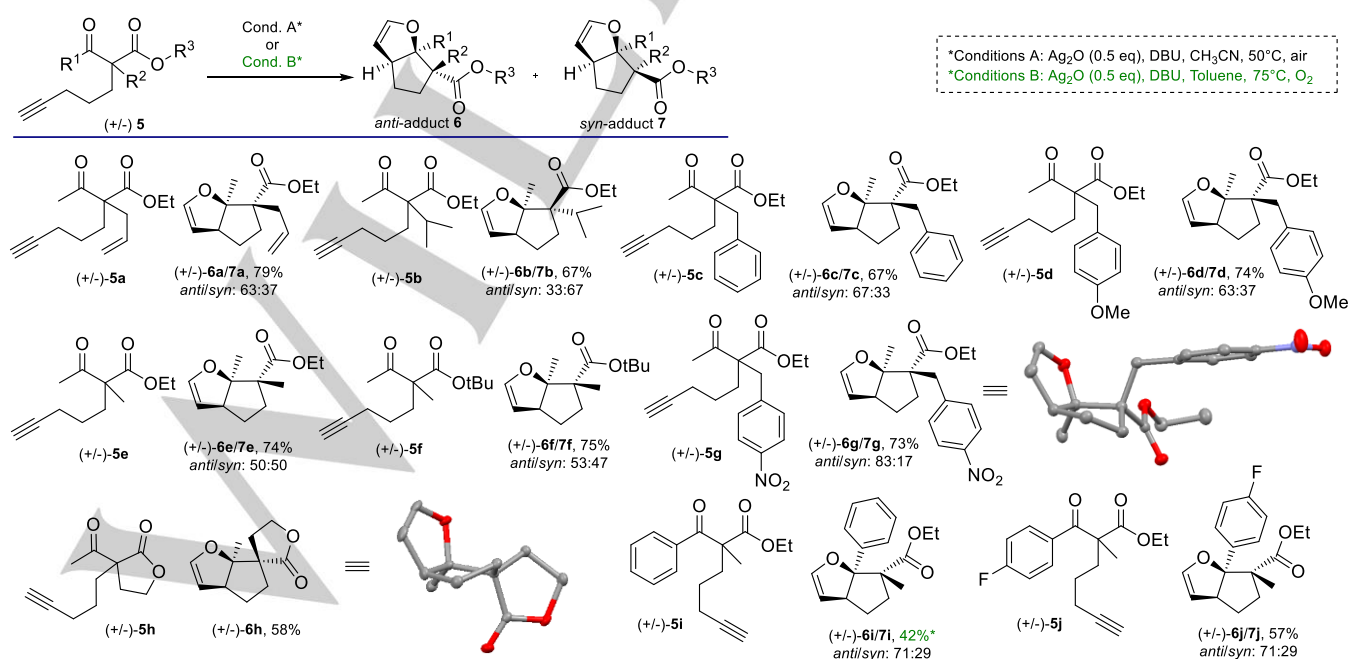
reactions can also be run with a catalytic amount of DBU (0.1 eq) without significant lengthening of the reaction time (3 h instead of 2 h). However, for accuracy and reproducibility considerations, we chose to perform the reactions with 1 equivalent of DBU instead of 0.1. Optimized conditions do not provide the product when the reaction is conducted at r.t (Entry 15). Also, we performed the reaction under conditions close to those reported by Kirsch but no product was detected (Entry 16)

Next, the scope of the reaction was examined: Our optimized conditions (Ag_2O : 0.5 eq., DBU: 1 eq. in MeCN, $[\text{C}] = 0.24 \text{ M}$) were first applied to various cyclic ketones (Scheme 2).



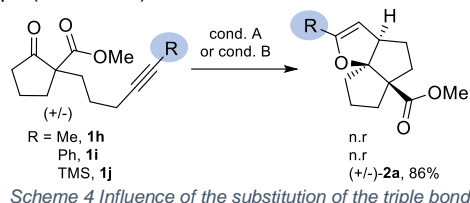
Scheme 2 Cyclization reactions of cyclic ketones ***2g** was obtained under Condition B (see Scheme 3)

The cyclization of five (**1a**) or six-membered ring substrates (**1b**) occurred under mild conditions and good yields were obtained (up to 85%) with a total diastereoselectivity in favour of the *cis*-adduct. We assumed that the selectivity is imposed by the configuration at the spiro carbon. Hence, for geometry and distance considerations, the ketone can be only attacked in a *syn*-periplanar fashion leading to the (+/-)-*cis*-isomer. Surprisingly, seven-membered ring analog **1c** was reluctant to cyclize and two equivalents of silver were necessary to attain a good conversion. Additionally, the cyclized products **2c/4c** were obtained as a mixture of two diastereoisomers (55:45 by ^1H NMR) probably due to a higher conformational flexibility. Starting from the naphthalenone derivative **1d**, no cyclization occurred even under heating in a sealed tube at 100°C .^[18] Tricyclic ketone **2e** was obtained in 78% yield from the corresponding symmetrical diketone **1e**. Noteworthy, these cyclization conditions were also suitable to heterocyclic compounds and piperidine derivative **2f** could be isolated in satisfying yield (80%). To our delight, using conditions B (see Scheme 3) allowed the extension to substrate with longer chain (**1g**) in order to reach six-membered-ring analog with good yield and high selectivity for the *cis*-isomer **2g**. The reactivity of linear ketones was next surveyed by varying the substitution of the malonate, the nature of the ketone and/or the influence of the functional group in beta position. We first studied the behaviour of different linear compounds towards the optimized cyclization conditions by tuning the nature of the substituent in alpha position to the ketone (R^2). Substitution by an allylic chain (compound **5a**) as well as neutral- (**5c**) or enriched- (**5d**) benzylic chains was not deleterious to the reaction and good reactivities were observed along with modest selectivities in favour of the *anti*-adduct (63:37, 67:33 and 63:37, respectively). Astonishingly, the diastereo-



Scheme 3 Cyclization reactions of linear ketones

-meric ratio raised to 83:17 when the aromatic moiety was substituted by a *p*-nitro group (**5g**).^[17] A bulkier isopropyl chain **5b** delivered the corresponding bicyclic compound in 67% yield with inversion of the diastereomeric ratio in favour of the *syn*-adduct (**7b**), evidencing that the steric hindrance at this position is not detrimental to the reaction but strongly influences the selectivity. Modification of the size of the ester provided the expected 2,3-dihydrofurans in good yields, however without notable improvement of the diastereoselectivity. On the contrary, the *anti* isomer **6h** was exclusively obtained with 58% yield when the lactone **5h** was used.^[17] Unlike benzylic ketone **5j**, ketone **5i** was reluctant to cyclize under conditions A while applying conditions B afforded good conversion, providing bicyclic compounds **6i/7i** and **6j/7j** (in 42 and 57% yield, respectively) with a similar selectivity towards the *anti*-isomer, along with degradation products. Finally, the substitution pattern of the triple bond was examined. To this aim, the reaction was conducted onto different substituted alkynes bearing either methyl (**1h**), phenyl (**1i**) or TMS (**1j**) groups (Scheme 4)



Reactions onto **1h** or **1i** were ineffective under both conditions (A or B). On the contrary, when trimethylsilylalkyne **1j** was submitted to conditions A, it was smoothly converted into the cyclized product **2a** (R = H). This result suggests a preliminary insertion of silver into the C-Si bond, which is consistent with the well-known propensity of terminal alkynes and TMS alkynes to undergo a metalation step under similar conditions.^[19,20]

In order to provide insights into the mechanism and to provide a rationale for the diastereoselectivity, we studied the first five steps of the Ag(I) mediated cycloaddition reaction mechanism by means of Density Functional Theory (DFT) approaches.^[21] The computed reaction path together is presented in Figure 2, while computational details together with the labelling scheme are reported in Supporting Information. Two most probable isomers of BH^+ and the two most probable approaches of **B** to Ag have been computed (see supporting information for the related structures). We would like to underline that other trials starting from other B to Ag geometry always lead to one of the two species here reported. The data discussed here correspond to the arrangements of the **B/BH⁺** and reactants providing the lowest energies.

A multistep pathway is proposed to explain the reaction mechanism up to the first cyclization process involving the carbonyl group and carbons of alkyne residue (Figure 1). The analyzed reaction mechanism proceeds through five steps. Starting from the very stable silver alkynyl intermediate (**I**), the initial step corresponds to the proton transfer from conjugated acid of DBU (BH^+ in Figure 2) to **I** leading to the formation of intermediate **II**. This step proceeds with a barrier of 14.40 kcal/mol (Table 1 in Supporting Information) and leads to the formation of stable intermediate **II**. A subsequent proton transfer from **II** to DBU

(**B** in Figure 2) generates the silver allenyl intermediate (**III**). The energetic barrier to overcome for its formation is found to be 12.07 kcal/mol (Figure 2). Of note the back reaction from **II** to **I** is characterized by a very small barrier so that we can assume that **I** is easily reformed. Following the energetic span model,^[22] we can therefore assume that the energy span is related to the difference between the energy of **I** and **TS2**, leading to an effective barrier of 22.45 kcal/mol determining the reaction turnover. The **III** allenyl intermediate is characterized by practically equivalent C₁-C₂ and C₂-C₃ bonds (1.30 Å). From this intermediate, a first cyclization occurs *via* the **TS3** transition state: the C₃-C₄ bond decrease achieving a value

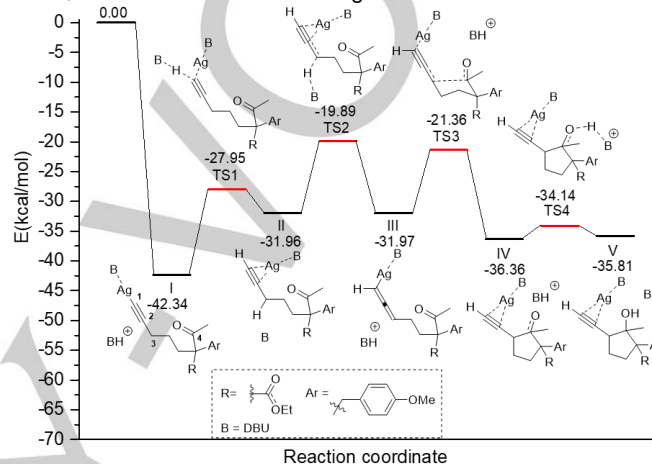


Figure 2 Computed reaction mechanism (ΔE in kcal/mol of all stationary points are reported with respect to the sum of all isolated species participating to the reaction).

of 2.20 Å and suggesting the closure of the cycle. **TS3** lies at 10.61 kcal/mol higher in energy with respect to the **III** and leads to the formation of intermediate **IV**, characterized by a C₃-C₄ bond of 1.57 Å and thus by a fully formed 5-carbon cycle. Of note in **IV** the silver atom approaches the oxygen (Ag-O bond of 2.15 Å), while C₁-Ag and C₂-Ag are elongating up to 2.70 Å. Comparing the atomic (Mulliken) charges computed for the **TS3** and the **IV**, it is found that C₄ becomes more electrophilic (from -1.91 |e⁻| to -0.22 |e⁻|), while the oxygen becomes more nucleophilic (from -0.34 |e⁻| and -0.49 |e⁻|). This makes possible to envisage a proton transfer from the conjugated acid BH^+ of DBU to the oxygen atom of **IV**. The very low energy barrier (2.23 kcal/mol) computed for this reaction confirmed this hypothesis.

In the corresponding transition state (**TS4**), the Ag atom is found to bridge the oxygen and the alkynyl lateral group (C₁-Ag, C₂-Ag, Ag-O bonds in the 2.30-2.40 Å range), while the C₄-O bond is elongated up to 1.41 Å and the O-H bond is forming (1.21 Å). Indeed, the **V** intermediate shows a proton bonded to the oxygen (O-H bond 1.02 Å) and the silver atom coordinated to the carbons of alkynyl residue (C₁-Ag, C₂-Ag around 2.30-2.35 Å).

At this stage, the reaction proceeds *via* a second cyclization process involving the alkynyl lateral group and the oxygen to form the dihydrofuran cycle^[23] which actually we computed to be extremely thermodynamically favored ($\Delta E = -119.16$ Kcal/mol, see S1).

In order to disclose the origin of the diastereoselectivity, we computed the first three steps of the reaction mechanism following two approaches leading to *anti* or *syn* diastereoisomers

FULL PAPER

(Figure 3; all computational details are reported in the Supporting Information). All computed energy barriers are similar for both diastereoisomers paths nonetheless we observe that **IIa** is effectively more stable than **IIb** of 4.19 kcal/mol. Indeed, the destabilizing interaction between the oxygen lone pairs of both carbonyls (O-O bond 2.80 Å) disfavors the *syn* adduct. With the aim of further validating the hypothesis that regioselectivity may be related to the presence (or absence) steric interactions for one of the adducts, we extended the study of reaction step II to compound **5e**. (see Figure 3 in the Supporting Information).

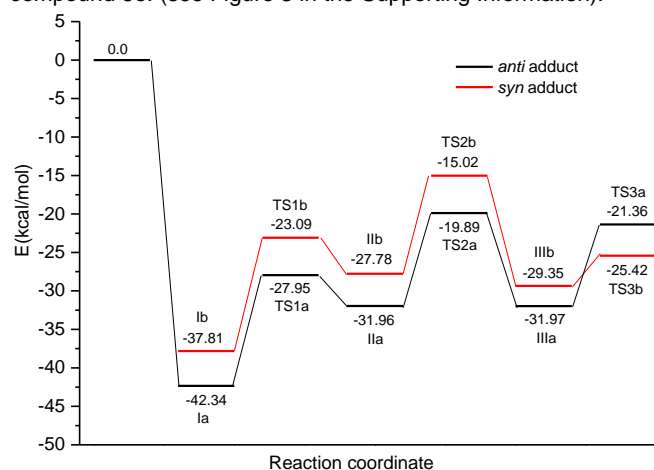
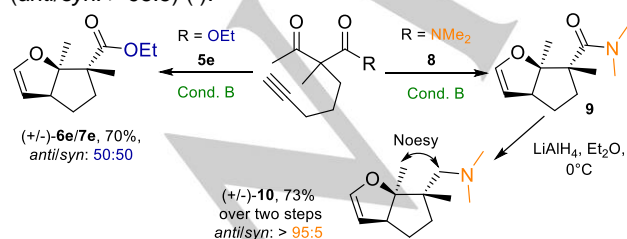


Figure 3 Computed ΔE of the first three steps of the reaction mechanism for the *anti/syn* adducts.

The reaction then proceeds with similar barriers both along the a and b pathway, suggesting that the final product depends on the most favorable initial intermediate. Indeed, with the aim of further validating our hypothesis, we extended the study of the reaction steps of compound **5d**. In this case, comparing the two optimized diastereoisomers, it is worth to notice that while the energy difference between the *anti/syn* adducts for the first step is similar to the value observed for compound **5e** (3.43 kcal/mol), it decreases down to 1.39 kcal/mol at step II. Since such energy difference is very low, we can assume that this is the origin of the absence of diastereoselectivity. Indeed, for this compound, the destabilizing interaction is substantially decreased upon substitution with less sterically-hindered methyl group, since the oxygen lone pairs of both carbonyls are located further apart in this case (O-O bond 3.00 Å see Figure 3 in the SI). Experimentally, we ran the reaction on bulkier amide **8** moiety leading to a drastic enhancement of the diastereomeric ratio (*anti/syn*: > 95:5) ().



Scheme 5 Selectivity on β -keto amide versus β -keto ester

However, we were unable to confirm the stereochemistry at this stage. In order to determine the relative configuration of the cyclized product, the amide **9** was subsequently reduced into the corresponding amine **10** in 73% yield over two steps. A NOE

experiment unambiguously evidenced *anti* adduct **10** as the major compound. In parallel, performing the reaction on ethyl ester **5e** under conditions B did not allow improvement of the diastereomeric ratio (50:50), underlining the primary importance of the nature of the electron withdrawing group on the diastereoselectivity. Noteworthy, conditions B allowed a better conversion without influencing the diastereoselectivity.

Conclusion

This unprecedented formal silver mediated [3+2] cyclization appears as a valuable tool for the synthesis of complex and/or congested polycyclic dihydrofurans. As an example, the approach developed herein would permit a straightforward access to precursor natural compounds, which possess an angularly fused tricyclic lactone backbone like alliacol or teucrolivin, under smooth conditions (Figure 4)

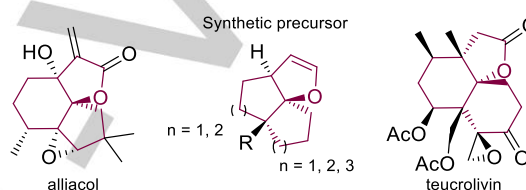


Figure 4 Dihydrofuran core as useful synthetic intermediate in natural products synthesis

In summary, we have developed a new formal [3+2] cyclization promoted by silver(I) oxide and DBU from readily available starting β -dicarbonyl compounds. The reaction is broad in scope, proceeds in mild conditions and allows an access to complex and congested molecules in a single step. This transformation is highly tolerant towards a wide range of solvents and bases (in stoichiometric or in catalytic amounts), thus facilitating its adaptation to structurally diverse, and potentially sensitive substrates. DFT calculations have demonstrated the formation of an allenyl silver intermediate by isomerization of the corresponding alkyne. Although the description of this species remains particularly scarce in the literature, its formation is a prerequisite in the promotion of the reaction. Moreover, DFT calculations have also allowed to determine the thermodynamic origin of the *syn/anti* diastereoselectivity for β -dicarbonyl compounds bearing an ester group. More generally, through this methodology, we highlighted a new reactivity of silver salts towards terminal alkyne. Thanks to this unprecedented isomerization reaction, we opened the way to a new field of transformations. The peculiar reactivity of allenyl silver species is currently under investigation in our laboratory.

Experimental Section

See supporting informations.

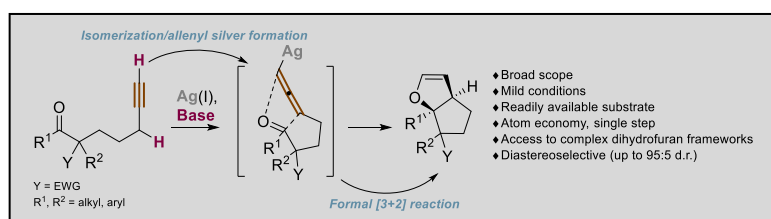
Acknowledgements

B. Y. thanks the China Scholarship Council for Ph.D grant. I.C. and A.P. thank the European Research Council (ERC) for funding under the European Union's Horizon 2020 research and innovation programme (grant agreement No 648558, STRIGES CoG grant). We would like to thank Pr. P. Belmont for fruitful discussions and single-crystal X-ray diffraction service from ICMMO-UMR8182 Orsay.

Keywords: Allenyl silver • dihydrofuran • isomerization • intramolecular cyclization

- [1] T. G. Kilroy, T. P. O'Sullivan, P. J. Guiry, *Eur. J. Org. Chem.*, **2005**, 23, 4929–4949.
- [2] B. H. Lipshutz, *Chem. Rev.*, **1986**, 86, 795–819. b) B. M. Fraga, *Nat. Prod. Rep.*, **1992**, 9, 217–241. c) A. T. Merritt, S. B. Ley, Clerodane, *Nat. Prod. Rep.*, **1992**, 9, 243–287. d) M. M. Faul, B. E. Huff, *Chem. Rev.*, **2000**, 100, 2407–2474. e) M. C. Elliott, *J. Chem. Soc. Perkin Trans. 1*, **2002**, 2301–2323. f) F. Garzino, A. Méou, P. Brun, *Synthesis*, **2003**, 0598–0602. g) T. G. Kilroy, T. P. O'Sullivan, P. J. Guiry, *Eur. J. Org. Chem.*, **2005**, 4929–4949. (h) R. A. Brawn, J. S. Panek, *Org. Lett.*, **2010**, 12, 4624–4627.
- [3] For some reactions using chiral auxiliaries and precursors, see: a) H. J. Gais, L. R. Reddy, G. S. Babu, G. Raabe, *J. Am. Chem. Soc.*, **2004**, 126, 4859–4864. b) W. Xia, C. Yang, B. O. Patrick, J. R. Scheffer, C. Scott, *J. Am. Chem. Soc.*, **2005**, 127, 2725–2730. c) R. K. Bowman, J. S. Johnson, *Org. Lett.*, **2006**, 8, 573–576. d) J.-C. Zheng, C.-Y. Zhu, X.-L. Sun, Y. Tang, L.-X. Dai, *J. Org. Chem.*, **2008**, 73, 6909–6912.
- [4] For some metal-mediated cyclization reactions, see: a) H. M. L. Davies, G. Ahmed, R. L. Calvo, M. R. Churchill, D. G. Churchill, *J. Org. Chem.*, **1998**, 63, 2641–2645. b) D. A. Evans, Z. K. Sweeney, T. Rovis, J. S. Tedrow, *J. Am. Chem. Soc.*, **2001**, 123, 12095–12096. c) S. Son, G. C. Fu, *J. Am. Chem. Soc.*, **2007**, 129, 1046–1047. d) J.-L. Zhou, L.-J. Wang, H. Xu, X.-L. Sun, Y. Tang, *ACS Catal.*, **2013**, 3, 685–688. e) D. Sinha, A. Biswas, V. K. Singh, *Org. Lett.*, **2015**, 17, 3302–3305. f) Y. Zhou, F.-L. Zhu, Z.-T. Liu, X.-M. Zhou, X.-P. Hu, *Org. Lett.*, **2016**, 18, 2734–2737. g) J. Reece, P. Ritashree, A. P. Nicholas, C. E. Sear, P. W. Smith, A. Ribaucourt, D. M. Hodgson, *Org. Biomol. Chem.*, **2016**, 14, 5875–5893. h) O. El-Sepelgy, A. Brzozowska, J. Sklyaruk, Y. K. Jang, V. Zubar, M. Rueping, *Org. Lett.*, **2018**, 20, 696–699.
- [5] For some organocatalytic reactions, see: a) R.-Q. Mei, X.-Y. Xu, L. Peng, F. Wang, F. Tian, L.-X. Wang, *Org. Biomol. Chem.*, **2013**, 11, 1286–1289. b) N.-J. Zhong, F. Wei, Q.-Q. Xuan, L. Liu, D. Wang, Y.-J. Chen, *Chem. Commun.*, **2013**, 49, 11071–11073. c) M. A. Calter, A. Korotkov, *Org. Lett.*, **2015**, 17, 1385–1388. d) Y. Cheng, Y. Han, P. Li, *Org. Lett.*, **2017**, 19, 4774–4777.
- [6] For some representatives [3+2] reactions, see: a) J. Tsuji, I. Watanabe, I. Minami, I. Shimizu, *J. Am. Chem. Soc.*, **1985**, 107, 2196–2198. b) I. Minami, M. Yuhara, I. Watanabe, J. Tsuji, *J. Organomet. Chem.*, **1987**, 334, 225–242. c) F.-L. Zhu, Y.-H. Wang, D.-Y. Zhang, J. Xu, X.-P. Hu, *Angew. Chem. Int. Ed.*, **2014**, 53, 10223–10227. d) Y. Zhou, F.-L. Zhu, Z.-T. Liu, X.-M. Zhou, X.-P. Hu, *Org. Lett.*, **2016**, 18, 2734–2737.
- [7] For selected reviews, see: a) T. Hashimoto, K. Maruoka, *Chem. Rev.*, **2018**, 115, 5366–5412. b) L. M. Stanley, M.P. Sibi, *Chem. Rev.*, **2008**, 118, 2887–2902. c) H. Pélissier, *Tetrahedron*, **2007**, 63, 3235–3285. d) V. Nair, T. D. Suja, *Tetrahedron*, **2007**, 63, 12247–12275. e) K. Harju, J. Yli-Kauhaluoma, *Mol. Divers.*, **2005**, 9, 187–207. f) K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.*, **1998**, 98, 863–909. g) M. S. Singh, S. Chowdhury, S. Koley, *Tetrahedron*, **2016**, 72, 1603–1644. h) C. Nájera, J. M. Sansano, *J. Organomet. Chem.*, **2014**, 771, 78–92.
- [8] For selected reviews and books, see: a) D. M. T. Chan, in *Comprehensive Organic Synthesis* 1st ed. (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, New York, **1991**, pp. 271–314. b) N. Iwasawa, in *Comprehensive Organic Synthesis* 2nd ed. (Eds.: P. Knochel, G. A. Molander), Elsevier, Oxford, New York, **2014**, pp. 273–350. c) S. Yamago, E. Nakamura, *Org. React.*, **2002**, 61, 1–217. d) P. Le Marquand, W. Tam, *Angew. Chem. Int. Ed.*, **2008**, 47, 2926–2928. e) M. E. Welker, *Chem. Rev.* **1992**, 92, 97–112.
- [9] X. Huang, L. Zhang, *J. Am. Chem. Soc.* **2007**, 129, 6398–6399. For key reviews on homogeneous gold catalysis, see: a) D. Pflaesterer, A. S. K. Hashmi, *Chem. Soc. Rev.*, **2016**, 45, 1331–1367. b) A. S. K. Hashmi, *Chem. Rev.*, **2007**, 107, 3180–3211. c) A. S. K. Hashmi, G. J. Hutchings, *Angew. Chem. Int. Ed.*, **2006**, 45, 7896–7936.
- [10] G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2008**, 130, 12598–12599.
- [11] J. T. Binder, B. Crone, T. T. Haug, H. Menz, S. F. Kirsch, *Org. Lett.*, **2008**, 10, 1025–1028. For a highlight on the combination of gold catalysis and organocatalysis, see: A. S. K. Hashmi, C. Hubbert, *Angew. Chem. Int. Ed.*, **2010**, 49, 1010–1012.
- [12] Z. Zhang, Q. Zhang, Z. Ni, Q. Liu, *Chem. Commun.*, **2010**, 46, 1269–1271.
- [13] Z. Zhang, S. Fang, Q. Liu, G. Zhang, *Adv. Synth. Catal.*, **2012**, 354, 927–932.
- [14] H. Westmijze, H. Kleijn, H.J.T. Bos, P. Vermeer, *J. Organomet. Chem.*, **1980**, 199, 293–297. b) H. Westmijze, K. Ruitenbergh, J. Meijer, P. Vermeer, *Tetrahedron. Lett.*, **1980**, 21, 1771–1772. c) J. Meijer, K. Ruitenbergh, H. Westmijze, P. Vermeer, *Synthesis*, **1981**, 551–554.
- [15] For recent results on silver-catalyzed conversions of alkynes, see: a) S. Dabral, U. Licht, P. Rudolf, G. Bollmann, A. S. K. Hashmi, T. Schaub, *Green Chem.*, **2020**, 22, 1553–1558. b) A. Ahrens, N. F. Heinrich, S. R. Kohl, M. Hokamp, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.*, **2019**, 361, 5605–5615. c) Y.-Y. Yang, P. Antoni, M. Zimmer, K. Sekine, F.F. Mulks, L. Hu, L. Zhang, M. Rudolph, F. Rominger, A.S.K. Hashmi, *Angew. Chem. Int. Ed.*, **2019**, 58, 5129–5133. d) S. Dabral, B. Bayarmagnai, M. Hermesen, J. Schiefl, V. Mormul, A. S. K. Hashmi, T. Schaub, *Org. Lett.*, **2019**, 21, 1422–1425. e) F. Chen, A. S. K. Hashmi, *Org. Lett.*, **2016**, 18, 2880–2882.
- [16] For selected Ag catalysed Glaser-Hay coupling, see: a) Y.-Q. Zhang, N. Kepčija, M. Kleinschrodt, K. Diller, S. Fischer, A. C. Papageorgiou, F. Allegretti, J. Björk, S. Klyatskaya, F. Klappenberger, M. Ruben, J. V. Barth, *Nat. Commun.*, **2012**, 3, 1286–1293. b) H.-Y. Gao, H. Wagner, D.-Y. Zhong, J.-H. Franke, A. Studer, H. Fuchs, *Angew. Chem.*, **2013**, 52, 4024–4028. c) H.-Y. Gao, H. Wagner, D.-Y. Zhong, J.-H. Franke, A. Studer, H. Fuchs, *Angew. Chem. Int. Ed.*, **2013**, 125, 4116–4120.
- [17] Crystallographic data are available from the Cambridge Crystallographic Data Centre: a) Compound **3**, reference CCDC no. 1972313. b) Compound **6g**, reference CCDC no. 1972314. c) Compound **6h**, reference CCDC no. 1972315.
- [18] Only traces of **2d** along with degradation products were observed by ¹H NMR
- [19] A. Vitèrisi, A. Orsini, J.-M. Weibel, P. Pale, *Tett. Lett.*, **2006**, 47, 2779–2781.
- [20] U. Létinois-Halbes, P. Pale, S. Berger, *J. Org. Chem.*, **2005**, 70, 9185–9190.
- [21] In all calculations, Ag⁺ counterion was not taken into account.
- [22] S. Kozuch, S. Shaik *Acc. Chem. Res.* **2011**, 44, 101–110.
- [23] For such cycloetherification mediated by silver see for example: B. Alcaide, P. Almendros, T. Martinez del Campo, R. Carrascosa, *Eur. J. Org. Chem.* **2010**, 4912–4919.

Entry for the Table of Contents



An unprecedented isomerization/allenyl silver formation/[3+2] cyclization promoted by a combination of silver salts and base are presented. The reaction allows the straightforward and diastereoselective (up to 95:5 d.r.) synthesis of complex dihydrofuran frameworks, under mild conditions from easily accessible substrates and is broad in scope.