



HAL
open science

Visible light-mediated gold-catalyzed alkynylative cyclization of allenates with iodoalkynes for the synthesis of β -alkynyl- γ butenolides

Yuanhao He, Yu Zhong, Maria Ballarin Marion, Jorge C Herrera, Wanping Ma, Yanfei Hu, Cyril Ollivier, Virginie Mouriès-Mansuy, Louis Fensterbank, Fen Zhao, et al.

► To cite this version:

Yuanhao He, Yu Zhong, Maria Ballarin Marion, Jorge C Herrera, Wanping Ma, et al.. Visible light-mediated gold-catalyzed alkynylative cyclization of allenates with iodoalkynes for the synthesis of β -alkynyl- γ butenolides. *Organic Chemistry Frontiers*, 2024, 11, pp.5695. <10.1039/D4QO01153H>. <hal-04797045>

HAL Id: hal-04797045

<https://hal.science/hal-04797045v1>

Submitted on 22 Nov 2024

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.



HAL Authorization

ARTICLE

Visible light-mediated gold-catalyzed alkynylative cyclization of allenates with iodoalkynes for the synthesis of β -alkynyl- γ -butenolides

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Yuanhao He,^a Yu Zhong,^a Maria Ballarin Marion,^c Jorge C. Herrera Luna,^c Wanping Ma,^a Yanfei Hu,^a Cyril Ollivier,^c Virginie Mouriès-Mansuy,^c Louis Fensterbank,^{c,d} Fen Zhao,^{*a} Zhonghua Xia,^{*b} and Baomin Fan^{*a}

A method for the tandem cyclization/alkynylation of allenates with iodoalkynes *via* gold catalysis under light irradiation is described. This transformation features a broad substrate scope, good functional group tolerance, and compatibility with heterocyclic substrates. The reaction proceeds smoothly at room temperature by using cheap, readily available acriflavine (ACF) as a photocatalyst, and offers β -alkynyl- γ -butenolides derivatives in moderate to good yields. Initial mechanistic studies suggest that a vinylgold(I) complex acts as a key intermediate, which would undergo photosensitization from the ACF singlet excited state. The corresponding energy transfer would promote the oxidative addition of the iodoalkyne partner to deliver C(sp²)-C(sp) coupling products after reductive elimination.

Introduction

Homogenous gold catalysis has emerged as a powerful and versatile tool for a broad range of chemical transformations during the past decades. In these reactions, either gold(I) or gold(III) complexes most frequently act as a carbophilic π -acidity that activates carbon-carbon multiple bonds (such as alkenes, allenes, and especially alkynes) towards nucleophilic attack. The gold center does not change the oxidation state in the whole catalytic cycle.¹ Over the past few years, there has been intense interest in developing Au(I)/Au(III) catalytic processes to expand the scope of gold-catalyzed processes.² Due to the high redox potential of the Au(I)/Au(III) couple (1.41 V) (compared to Pd(0)/Pd(II)),³ stoichiometric and strong external oxidants are usually required to access Au(I)/Au(III) catalytic processes.⁴ However, some of the transformations require harsh conditions, costly and hazardous reagents. Therefore, there has been a necessity to devise new pathways that are more efficient to promote it.⁵ Firstly, the ligand design for gold(I) has emerged as a viable alternative, especially the use of hemilabile (P, N) ligands for versatile catalytic cross-coupling reactions that have been recently developed.⁶ Secondly, the groups of Glorius,⁷ Toste,⁸ and Hashmi⁹ have devised dual gold/photoredox catalytic systems, using aryl diazonium or iodonium salts easy to reduce as SET partners, to allow Au(I)/Au(III) catalytic cycles in arylation reactions under mild conditions. This methodology has been applied to various substrates, including *ortho*-alkynyl phenols as a flexible synthesis of 3-aryl benzofurans,¹⁰ while some of these reactions can proceed smoothly without photocatalysts.^{11, 12}

Overall, the development of these dual gold/photoredox-catalyzed processes has been limited by the need for easily reduced radical precursors.

On the other hand, haloalkynes are widely used in synthetic chemistry, particularly as effective partners in transition metal-catalyzed cross-coupling reactions.¹³ Haloalkynes have been utilized in gold-catalyzed transformations without light activation or under light activation.¹⁴ In 2019, the Fensterbank group successfully replaced aryl diazoniums with alkynyl iodide partners in dual photo/gold-catalyzed alkynylative cyclization of *o*-alkynylphenols leading to valuable alkynylbenzofuran scaffolds. Further mechanistic and modeling studies support that photosensitized energy transfer takes place, rather than an electron transfer pathway, enabling the oxidative addition of iodoalkynes onto organogold intermediates in their excited triplet state (Scheme 1a, A).¹⁵ Recently, access to 2,3-disubstituted indoles from *o*-alkynyl aniline and iodoalkyne derivatives *via* a gold-catalyzed sequence under visible-light irradiation and in the absence of an exogenous photocatalyst was also developed. Mechanistic studies converge on the formation of potassium sulfonylamide emissive aggregates in the reaction medium (Scheme 1a, B).¹⁶ Extending the scope of possible partners for these transformations is highly desirable, particularly for the visible cyclization/alkynylation tandem of allenates with iodoalkynes to generate β -alkynyl- γ -butenolides.

To date, several research groups have developed the synthesis of β -alkynyl- γ -butenolides via gold catalysis. In 2010, the Gouverneur group reported a gold(I)-catalyzed cascade cyclization-oxidative alkynylation of allenates with various terminal alkynes using selectfluor acting as an external oxidant to prepare β -alkynyl- γ -butenolides (Scheme 1b, A).¹⁷ A few years later, the Hashmi group improved this method to avoid the use of any external oxidant. The cyclization-alkynylation reaction of allenates was established for various alkynyl bromides *via* gold catalysis at 50 °C for 4 days (Scheme 1b, B).¹⁸ The Patil group reported the electrochemical redox gold catalysis for the oxy-alkynylation of allenates with terminal

^a Yunnan Key Laboratory of Chiral Functional Substance Research and Application, Yunnan Minzu University, Kunming 650500, Yunnan, China.

^b School of Materials Science & Engineering, Beijing Institute of Technology, Beijing 100081, China

^c Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, Paris, France

^d Collège de France, Chaire Activations en Chimie Moléculaire, Paris, France

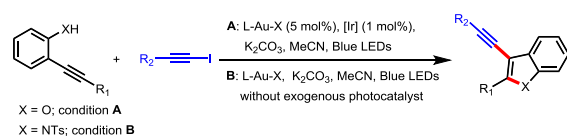
Email: fenzhao@ymu.edu.cn (F. Z.); zhonghua.xia@bit.edu.cn (Z. X.);

adams.bmf@hotmail.com (B. F.)

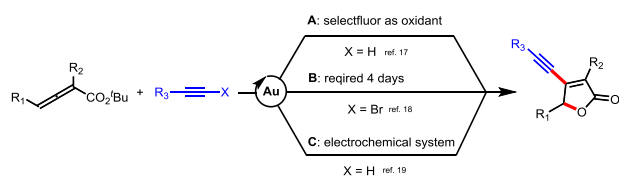
Electronic Supplementary Information (ESI) available: Experimental details, compound characterization, and NMR spectra. See DOI: 10.1039/x0xx00000x

alkynes (Scheme 1b, C).¹⁹ However, these approaches still suffered from the use of a strong external oxidant¹⁷, long reaction time (4 days)¹⁸, or a special electrochemical system¹⁹ required. Very recently, Ma and co-workers developed Rh(III)/Cu(I) co-catalyzed cyclic oxy-alkynylation of 2,3-allenoic acids with alkyl alkynes to construct 4-alkynyl furan-2(5*H*)-one derivatives. Also, aryl-substituted acetylenes were able to produce the target products smoothly but with a lower yield.²⁰ Interestingly, our preliminary study^{15a} showed the feasibility of the photosensitized cross-coupling of the corresponding vinylgold(I) intermediate with an iodoalkyne to produce β -alkynyl- γ -butenolides. Herein, we report the successful development of a dual gold and photocatalytic system applicable to the intramolecular alkynylative cyclization of allenates with iodoalkynes (Scheme 1c). In this work, we use cheap, readily available acriflavine (ACF) as a photocatalyst, and common gold complexes as catalysts, under visible light irradiation to achieve β -alkynyl- γ -butenolides derivatives.

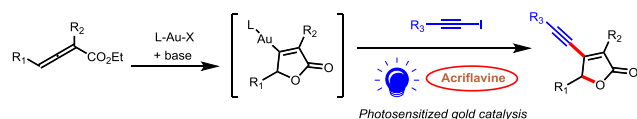
(a) Previous works: photosensitized alkynylative *O/N*-cyclization using gold catalysis



(b) The synthesis of β -alkynyl- γ -butenolides via gold catalysis (Known)



(c) This Work: Gold catalyzed cross-coupling of allenates with iodoalkynes under visible light irradiation



Scheme 1. Gold-catalyzed tandem cyclization/alkynylation.

Results and discussion

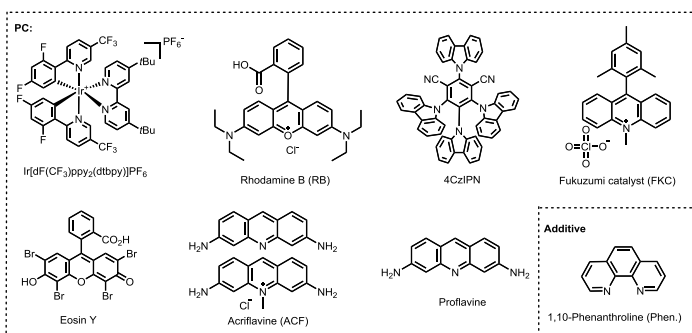
We initiated our investigation by utilizing ethyl 2-methyldeca-2,3-dienoate **1a** and 1-fluoro-4-(iodoethynyl)benzene **2a** as model substrates for this transformation under various conditions (see Supplementary Section III for detailed conditions optimization). Based on the previous work protocol, using (*p*-CF₃)₃PAuCl as gold catalyst, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ ([Ir-F]) as photocatalyst, K₂CO₃ as base in MeOH resulted in alkynylation product **3a** yield of 37%, accompanied by a 23% of iodoindole **3aa** as iodocyclization by-product (Table 1, entry 1). Subsequently, we explored

alternative conditions which led to an increased yield of product **3a** to 46% in the presence of Ph₃PAuCl (10 mol%), and Rhodamine B (RB) (5 mol%) in degassed MeOH (0.1 M) under blue LEDs irradiation (Table 1, entry 2). Other organic photocatalysts such as Eosin Y, 4CzIPN and Fukuzumi catalyst (FKC, 9-mesitylene-10-methylacridinium perchlorate) et al. were examined but they did not result in an improvement of the yield of **3a** (Table 1, entries 3-5) (Detail see Supplementary Section III. 1). We then turned our attention to acriflavine (ACF), a mixture of 3,6-diamino-10-methylacridinium chloride

Table 1. Optimization of reaction conditions.^a

Entry	[Au]	[PC]	Base	Ad.	3a yield (%)	3aa yield (%)
1 ^b	[Au-CF ₃]	[Ir-F]	K ₂ CO ₃	—	37	23
2	Ph ₃ PAuCl	RB	NaHCO ₃	—	46	17
3	Ph ₃ PAuCl	Eosin Y	NaHCO ₃	—	35	14
4	Ph ₃ PAuCl	4CzIPN	NaHCO ₃	—	45	20
5	Ph ₃ PAuCl	FKC	NaHCO ₃	—	40	16
6	Ph ₃ PAuCl	ACF	NaHCO ₃	—	53	18
7	Ph ₃ PAuCl	ACF	Na ₂ CO ₃	—	19	10
8	Ph ₃ PAuCl	ACF	Cs ₂ CO ₃	—	39	16
9	Ph ₃ PAuCl	ACF	K ₂ HPO ₄	—	23	12
10	Ph ₃ PAuNTf ₂	ACF	NaHCO ₃	—	55	18
11	Ph ₃ PAuOTf	ACF	NaHCO ₃	—	61	20
12	Ph ₃ PAuOTf	ACF	NaHCO ₃	Phen.	80 (78) ^f	15
13 ^c	Ph ₃ PAuOTf	ACF	NaHCO ₃	Phen.	50	13
14	Ph ₃ PAuOTf	Proflavine	NaHCO ₃	Phen.	27	12
15	Ph ₃ PAuOTf	—	NaHCO ₃	Phen.	25	12
16	—	ACF	NaHCO ₃	Phen.	Nr	10
17	Ph ₃ PAuOTf	—	NaHCO ₃	—	16	20
18	Ph ₃ PAuOTf	ACF	—	Phen.	15	10
19 ^d	Ph ₃ PAuOTf	ACF	NaHCO ₃	Phen.	20	14
20 ^{d,e}	Ph ₃ PAuOTf	ACF	NaHCO ₃	Phen.	40	16

Journal Name

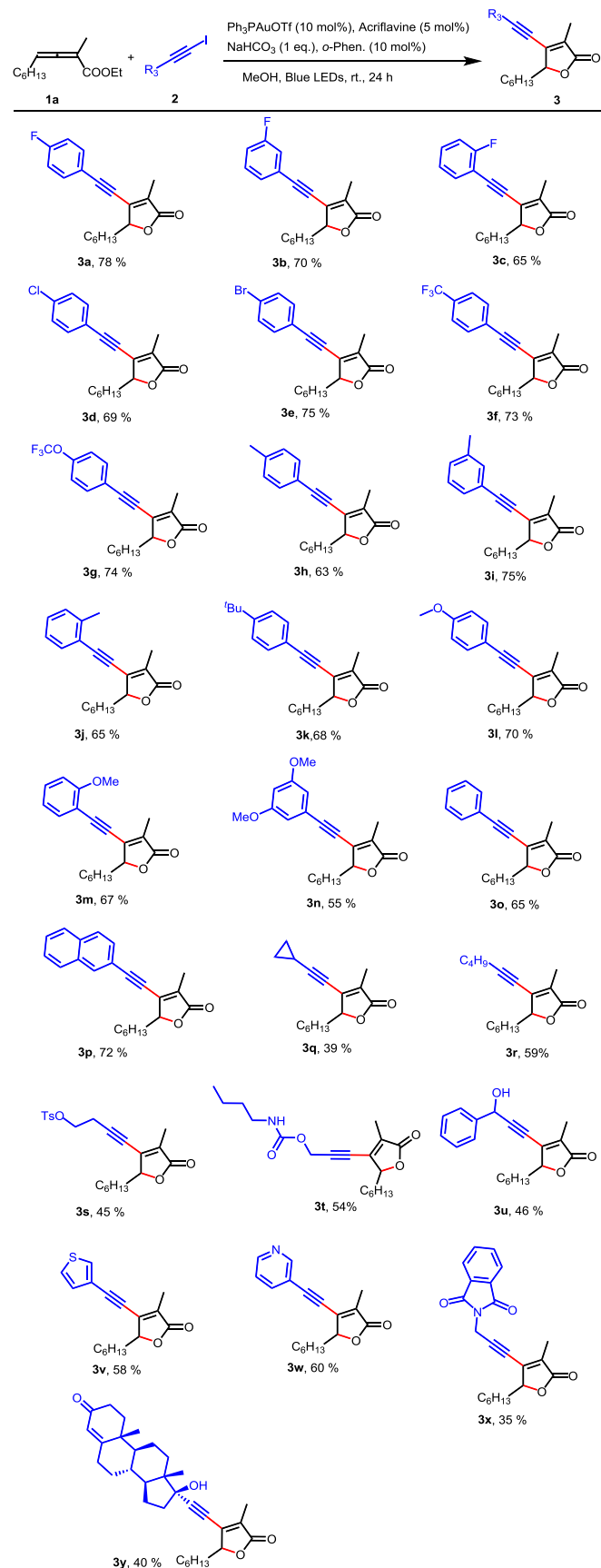


^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol, 1.5 eq.), catalyst (10 mol%), photocatalyst (5 mol%), base (0.2 mmol, 1 eq.), additive (10 mol%), MeOH (2.0 mL), room temperature, blue LEDs, 24 h. Yields were determined by ¹H NMR using 1,3,5-trimethoxybenzene as the internal standard, the yield in parentheses is the isolated yield. ^b [Au-CF₃] = (*p*-CF₃Ph)₃PAuCl (5 mol%); [Ir-F] = Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (1 mol%); ^c 5 mol% of Ph₃PAuOTf was used; ^d Reaction performed under darkness. ^e Reaction performed at 50 °C. ^f Isolated yield.

(tryptaflavine) and 3,6-diaminoacridine (proflavine) in a 1:6 molar ratio. ACF is an old drug that was previously used as a trypanocidal agent during World War II,²¹ which has been extensively researched in the field of biomedical chemistry,²² yet its use as photosensitizer has not been reported in organic synthesis. The use of ACF increased the yield to 53% (Table 1, entry 6). Keeping with ACF, lower yields were obtained when NaHCO₃ was replaced by Na₂CO₃, Cs₂CO₃, or K₂HPO₄ (Table 1, entries 7-9). When cationic Au(I) complexes, such as Ph₃PAuNTf₂ and Ph₃PAuOTf, were utilized in the reaction, 55% and 61% yield of **3a** were obtained respectively (Table 1, entries 10-11). The addition of 10 mol% of 1,10-phenanthroline as an additive increased the yield to 78% (Table 1, entry 12), possibly due to some halogen bonding between phenanthroline and the alkynyl iodides might be at work.²³ Similarly, other amines such as 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were tested without improving the reaction (see Supplementary Section III. 3). When the amount of gold catalyst was decreased to 5 mol%, yield of **3a** was reduced to 50% (Table 1, entry 13). In the control experiment, using proflavine (previously employed as photosensitizer)²⁴ instead of acriflavine reduced the yield of product **3a** to 27% (Table 1, entry 14). The result is similar to that obtained without a PC (Table 1, entry 15). Furthermore, no product was detected when the reaction was performed in the absence of the gold catalyst (Table 1, entry 16). Additionally, significantly reduced yields of **3a** were observed when acriflavine, 1,10-phenanthroline, or NaHCO₃ were absent (Table 1, entries 17-18). It is apparent that visible light and temperature play essential roles in this reaction. When the reaction was conducted in the dark at room temperature, only a 20% yield of product **3a** was obtained (Table 1, entry 19), while increasing the temperature to 50 °C led to a yield of 40% (Table 1, entry 20).

With the optimized reaction conditions in hand, summarized in Table 1, entry 12, we then explored the scope of this transformation, as shown in Table 2. Initially, a series of substituted aryl iodoalkynes **2** were reacted with ethyl 2-methyldeca-2,3-dienoate **1a**. Aryl iodoalkynes **2** bearing electron-withdrawing groups such as F, Cl, Br, CF₃, and OCF₃,

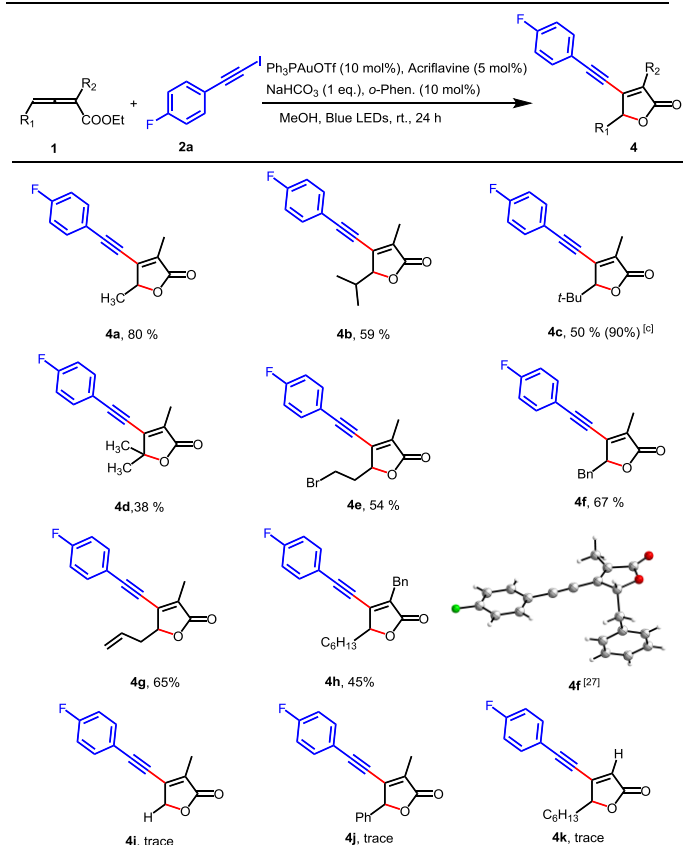
were coupled with allenoates **1a** affording the corresponding products in good yields (Table 2, **3a-3g**). The best results were obtained with aryl iodoalkynes **2** containing halogen substituent in the *para* position compared with the *ortho* or *meta* positions (**3a** vs **3b**, **3c**). The presence of electron-donating groups (Me, *t*-Bu, OMe) or the absence of substitution, led the β -alkynyl- γ -butenolides in moderate (**3n**) to good (**3h-3m**, **3o**) yields. When 2-(iodoethynyl)naphthalene was used, the corresponding product was formed in moderate yields (**3p**). We next explored various aliphatic iodoalkynes bearing sterically diversified alkyl groups to give target products in fairly good yields (**3q-3v**). Notably, aliphatic iodoalkyne substituted with a strongly electron-withdrawing group (OTs) worked well to give the desired **3s** products in 45% yield. Even, aliphatic iodoalkynes bearing a benzylic alcohol and O-acyl hydroxylamine groups were also tolerated to afford the product in moderate yields (**3t-3v**). In addition, we were pleased to find that 3-(iodoethynyl)thiophene and 3-(iodoethynyl)pyridine also gave in moderate yields of the

Table 2. Scope of iodoalkynes.^{a, b}

^a Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol, 1.5 eq.), Ph₃PAuOTf (10 mol%), Acriflavine (5 mol%), NaHCO₃ (0.2 mmol, 1 eq.), 1,10-phenanthroline (10 mol%), MeOH (2.0 mL), room temperature, blue LEDs, 24 h. ^b Isolated yield.

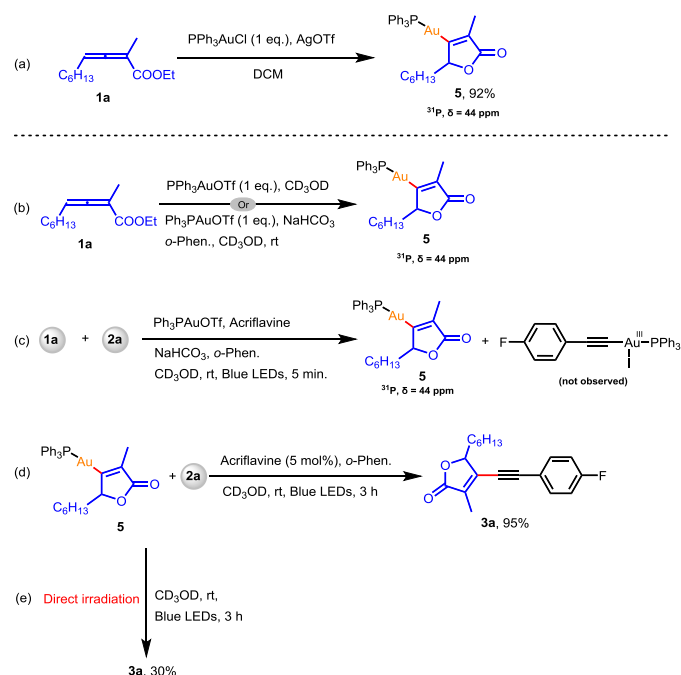
corresponding product **3w** and **3x**. Gratifyingly, this method is also effective when applied to iodinated ethisterone derivative, producing the corresponding product **3y** in 40% yield.

In a second step, the scope and limitations of the reaction of various allenates **1** with 1-fluoro-4-(iodoethynyl)benzene **2a** were explored, as shown in Table 3. Various sterically alkyl-substituted allenates in the R1 position afforded the corresponding products (**4a-4d**) in yields ranging from 38 to 80%. When using the methyl-substituted allenate at R1, the corresponding product **4a** was obtained in 80% yield. However, when the allenate was substituted by two methyl groups at this position, the reaction gave the expected product **4c** in lower yield. In particular, allenate substituted with a bulky *tert*-butyl group gives the desired product **4c** in moderate yield. To our delight, when we used allenic acids instead of allenates, providing desired product **4c** in 90% yield. Furthermore, allenates with other substituents in the R1 position, such as bromoethyl, benzyl and allyl, provided the corresponding alkynylating cyclization products (**4e-4g**) in equally appreciable yields. And the structure of product **4f** was confirmed by X-ray diffraction analysis, Cambridge Crystallographic Data Centre (CCDC) accession code no. 2374591. Interestingly, when the methyl group was replaced by benzyl in the R2 position of the allenates, the reaction

Table 3. Scope of allenates.^{a, b}

^a Reactions were performed with allenates **1**, unless otherwise noted. Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol, 1.5 eq.), Ph₃PAuOTf (10 mol%), Acriflavine (5 mol%), NaHCO₃ (0.2 mmol, 1 eq.), 1,10-phenanthroline (10 mol%), MeOH (2.0 mL), room temperature, blue LEDs, 24 h. ^b Isolated yield. ^c Allenic acids instead of allenates.

proceeded smoothly and gave the desired product in a 45% yield (**4h**). We also tested phenylated or unsubstituted allenates in position R1, but only a trace amount of corresponding products (**4i-4j**) was formed under these reaction conditions. A similar result was obtained when R2 was replaced by H-atom (**4k**).



Scheme 2. Control experiments.

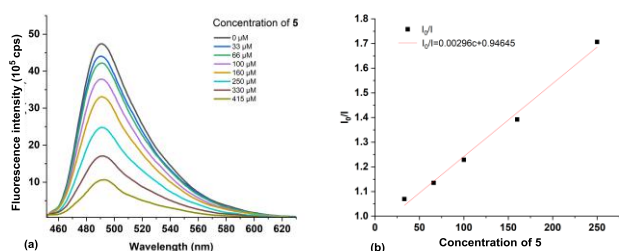
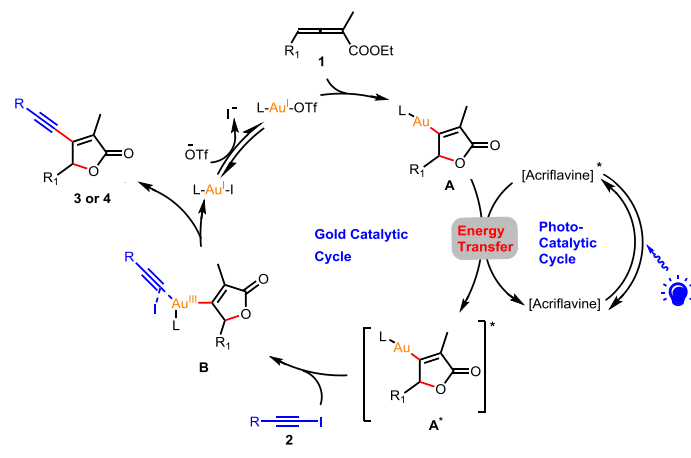


Figure 1. Mechanistic investigations: (a) Quenching of acriflavine by vinylgold(I) complex **5** monitored by steady-state fluorimetry; (b) Stern-Volmer linear fitting of the quenching described in panel (a).

In order to find a reasonable mechanism for this transformation, a series of control experiments was carried out (Scheme 2). Firstly, vinylgold(I) complex **5** was prepared in 92% yield by an independent route involving **1a**, PPh₃AuCl and AgOTf,^{15a,25} as shown in Scheme 2a. ³¹P NMR spectroscopy showed the expected single peak at 44 ppm. We were then able to confirm the formation of **5** using PPh₃AuOTf as the source of gold(I) by ³¹P NMR spectroscopy and the same peak at 44 ppm was observed (Scheme 2b). Finally, we showed that **5** was instantaneously and selectively formed from allenate **1a** under standard reaction conditions in the presence of iodoalkyne **2a**. Accordingly, we did not observe by ³¹P NMR any peak corresponding to gold(III)-acetylide (Scheme 2c). These results indicated that vinylgold(I) complex **5** was a key intermediate for this transformation. Secondly, we performed the experiment of vinylgold(I) complex **5** with iodoalkyne **2a** under photocatalyzed conditions for 3 h, yielding target product **3a** almost quantitatively (Scheme 2d). However, a

lower yield of **3a** was obtained under direct irradiation conditions (without acriflavine) (Scheme 2e and entry 15, Table 1). Consistent with previous reports,^{15,16} these results suggest that the reaction involves an energy transfer process. Finally, we observed a decrease in the acriflavine luminescence signal when the concentration of vinylgold **5** was increased, suggesting that **5** acts as a quencher of the acriflavine excited state (Figure 1a). We also determined that the lifetime of acriflavine, obtained from the fluorescence lifetime decay (λ_{ex} = 450 nm, λ_{em} = 636 nm) curve of acriflavine, was 3.18 ns (See Supplementary V.3), which suggests that the excited state of acriflavine is a singlet state. The corresponding Stern-Volmer linear plot is shown in Figure 1b. The value of the kq bimolecular quenching rate constant was estimated at $6.65 \times 10^{11} \text{ mol}^{-1} \cdot \text{L} \cdot \text{s}^{-1}$ from respectively the luminescence intensity (I_0/I) and lifetime (t_0/t) Stern-Volmer plots (See inset of Figure 1b and Supplementary Section V.3). This very high value, is reminiscent of our precedent study that established a static quenching instead of a dynamic one.¹⁶ Moreover, we also conducted the light/dark experiment, the desired product **3a** formed only under continuous irradiation (See inset of Figure 8 and Supplementary Section V.6).

Taking all these results into account, and based on literature precedents for visible-light-mediated energy transfer catalysis including our reported work,^{15, 16, 26} a possible mechanism cycle has been proposed, as shown in Scheme 3. First, the gold(I) species coordinates to allenate **1**, and cyclization leads to the organogold(I) complex **A** in the presence of the base. Meanwhile, acriflavine acts as a photosensitizer, absorbing visible light to produce the excited singlet state. At this stage, energy transfer can take place to produce electronically excited gold(I) species **A*** in its singlet state while simultaneously regenerating the ground state of acriflavine. After easy intersystem crossing due to the heavy atom effect of gold, the triplet excited gold(I) species **A*** undergoes oxidative addition to iodoalkynes **2** to produce the gold(III) complex **B**. Subsequent reductive elimination provides β -alkynyl- γ -butenolides **3** and the active catalyst through the formation of the new C-C bond, and complete the catalytic cycle.



Scheme 3. Proposed reaction mechanism.

Conclusions

We have reported an original approach to β -alkynyl- γ -butenolides by gold-catalyzed tandem cyclization/alkynylation of allenolates with iodoalkynes under visible light irradiation at room temperature. This transformation features a broad substrate scope, good functional group tolerance, and compatibility with heterocyclic substrates. Mechanistic studies suggest that acriflavine acts as a photosensitizer, promoting the excitation of the vinylgold(I) intermediate through an energy transfer process and aiding the oxidative addition of an iodoalkyne. Such a dual catalytic process opens a new method for the synthesis of β -alkynyl- γ -butenolides with potential biological activity.

Author Contributions

Y. H., Y. Z., M.B.M., J.C.H.L., W. M. and Y. H. performed the synthetic experiments, prepared the starting materials and purified the products. M. B. M., J. H. L., C.O., V.M.M. and L.F. verified the experiment. C.O., V.M.M., L.F., F. Z., Z. X. and B. F. designed the experiments. All authors analyzed the data, discussed the results, commented on the manuscript, and approved the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support from the National Natural Science Foundation of China (22201019; 22061048), and Yunnan Provincial Science and Technology Department (202401CF070075, 202401BC070018), and Yunnan Key Laboratory of Chiral Functional Substance Research and Application (202402AN360010). We thank also Sorbonne Université, CNRS, IUF, ANR-20-CE07-0038 LuxOr, and Generalitat Valenciana (CIAPOS/2022/174) for financial support.

References

- (a) J. Xie, C. Pan, A. Abdulkadera, C. Zhu, Gold-catalyzed C(sp³)-H bond functionalization, *Chem. Soc. Rev.* **2014**, *43*, 5245-5256; (b) Z. Zheng, X. Ma, X. Cheng, K. Zhao, K. Gutman, T. Li, L. Zhang, Homogeneous gold-catalyzed oxidation reactions, *Chem. Rev.* **2021**, *121*, 8979-9038; (c) L. Rocchigiani, M. Bochmann, Recent advances in gold(III) chemistry: structure, bonding, reactivity, and role in homogeneous catalysis, *Chem. Rev.* **2021**, *121*, 8364-8451; (d) A. Nijamudheen, A. Datta, Gold-catalyzed cross-coupling reactions: an overview of design strategies, mechanistic studies, and applications, *Chem. Eur. J.* **2020**, *26*, 1442-1487; (e) S. Bhakta, T. Ghosh, Gold-catalyzed carboxylative cyclization reactions: recent advances, *Asian. J. Org. Chem.* **2021**, *10*, 496-505; (f) R. Dorel, A. M. Echavarren, Gold(I)-catalyzed activation of alkynes for the construction of molecular complexity, *Chem. Rev.* **2015**, *115*, 9028-9072; (g) D. Pflästerer, A. S. K. Hashmi, Gold catalysis in total synthesis-recent achievements, *Chem. Soc. Rev.* **2016**, *45*, 1331-1367.
- M. N. Hopkinson, A. D. Gee, V. Gouverneur, Au^I/Au^{III} catalysis: an alternative approach for C-C oxidative coupling, *Chem. Eur. J.* **2011**, *17*, 8248-8262.
- S. G. Bratsch, Standard electrode potentials and temperature coefficients in water at 298.15 K, *J. Phys. Chem. Ref.* **1989**, *18*, 1-21.
- (a) W. Wang, J. Jasinski, G. B. Hammond, B. Xu, Fluorine-enabled cationic gold catalysis: functionalized hydration of alkynes, *Angew. Chem. Int. Ed.* **2010**, *49*, 7247-7252; (b) P. Garcia, M. Malacria, C. Aubert, V. Gandon, L. Fensterbank, Gold-catalyzed cross-couplings: new opportunities for C-C bond formation, *Chem. Cat. Chem.* **2010**, *2*, 493-497; (c) M. N. Hopkinson, A. D. Gee, V. Gouverneur, Au^I/Au^{III} catalysis: an alternative approach for C-C oxidative coupling, *Chem. Eur. J.* **2011**, *17*, 8248-8262; (d) L. T. Ball, G. C. Lloyd-Jones, C. A. Russell, Gold-catalyzed direct arylation, *Science*, **2012**, *337*, 1644-1648; (e) L. T. Ball, G. C. Lloyd-Jones, C. A. Russell, Gold-catalyzed oxidative coupling of arylsilanes and arenes: origin of selectivity and improved precatalyst, *J. Am. Chem. Soc.* **2014**, *136*, 254-264.
- (a) M. N. Hopkinson, A. Tlahuext-Aca, F. Glorius, Merging visible light photoredox and gold catalysis, *Acc. Chem. Res.* **2016**, *49*, 2261-2272; (b) M. Joost, A. Amgoune, D. Bourissou, Reactivity of gold complexes towards elementary organometallic reactions, *Angew. Chem. Int. Ed.* **2015**, *54*, 15022-15045; (c) P. Font, X. Ribas, Fundamental basis for implementing oxidant-free Au(I)/Au(III) catalysis, *Eur. J. Inorg. Chem.* **2021**, *2021*, 2556-2569; (d) V. W. Bhojare, A. G. Tathe, A. Das, C. C. Chintawar, N. T. Patil, The interplay of carbophilic activation and Au(I)/Au(III) catalysis: an emerging technique for 1,2-difunctionalization of C-C multiple bonds, *Chem. Soc. Rev.* **2021**, *50*, 10422-10450.
- (a) J. A. Cadge, H. A. Sparkes, J. F. Bower, C. A. Russell, Oxidative addition of alkenyl and alkynyl iodides to an Au^I complex, *Angew. Chem. Int. Ed.* **2020**, *59*, 6617-6621; (b) M. Rigoulet, O. T. D. Boullay, A. Amgoune, D. Bourissou, Gold(I)/gold(III) catalysis that merges oxidative addition and π -alkene activation, *Angew. Chem. Int. Ed.* **2020**, *59*, 16625-16630. (c) A. G. Tathe, N. T. Patil, Ligand-Enabled gold-catalyzed C(sp²)-S cross-coupling reactions, *Org. Lett.* **2022**, *24*, 4459-4463. (d) C. C. Chintawar, V. W. Boyare, M. V. Mane, N. Patil, Enantioselective Au(I)/Au(III) Redox Catalysis Enabled by Chiral (P,N)-Ligands, *J. Am. Chem. Soc.* **2022**, *144*, 7089-7095. (e) A. Das, N. T. Patil, Ligand-Enabled gold-catalyzed C(sp²)-O cross-coupling reactions, *ACS Catal.* **2023**, *13*, 3847-3853. (f) P. Font, H. Valdés, X. Ribas, Consolidation of the oxidant-free Au(I)/Au(III) catalysis enabled by the hemilabile ligand strategy, *Angew. Chem. Int. Ed.* **2024**, doi:org/10.1002/ange.202405824.
- (a) B. Sahoo, M. N. Hopkinson, F. Glorius, Combining gold and photoredox catalysis: visible light-mediated oxy- and aminoarylation of alkenes, *J. Am. Chem. Soc.* **2013**, *135*, 5505-5508; (b) A. Tlahuext-Aca, M. N. Hopkinson, B. Sahoo, F. Glorius, Dual gold/ photoredox-catalyzed C(sp)-H arylation of terminal alkynes with diazonium salts, *Chem. Sci.* **2016**, *7*, 89-93; (c) M. N. Hopkinson, B. Sahoo, F. Glorius, Dual photoredox and gold catalysis: intermolecular multicomponent oxyarylation of alkenes, *Adv. Synth. Catal.* **2014**, *356*, 2794-2800; (d) B. Sahoo, M. N. Hopkinson, F. Glorius, Combining gold and photoredox catalysis: visible light-mediated oxy- and aminoarylation of alkenes, *J. Am. Chem. Soc.* **2013**, *135*, 5505-5508.
- (a) Y. He, H. Wu, F. D. Toste, A dual catalytic strategy for carbon-phosphorus cross-coupling via gold and photoredox catalysis, *Chem. Sci.* **2015**, *6*, 1194-1198; (b) S. Kim, J. Rojas-Martin, F. D. Toste, Visible light-mediated gold-catalyzed carbon(sp²)-carbon(sp) cross-coupling, *Chem. Sci.* **2016**, *7*, 85-88; (c) X.-Z. Shu, M. Zhang, Y. He, H. Frei, F. D. Toste, Dual visible light photoredox and gold-catalyzed arylation ring expansion, *J. Am. Chem. Soc.* **2014**, *136*, 5844-5847; (d) M. D. Levin, S. Kim, F. D. Toste, Photoredox catalysis unlocks single-

- electron elementary steps in transition metal catalyzed cross-coupling, *ACS Cent. Sci.* **2016**, *2*, 293-301.
- 9 (a) J. Xie, T. Zhang, F. Chen, N. Mehrkens, F. Rominger, M. Rudolph, A. S. K. Hashmi, Gold-catalyzed highly selective photoredox C(sp²)-H difluoroalkylation and perfluoroalkylation of hydrazones, *Angew. Chem. Int. Ed.* **2016**, *55*, 2934-2938; (b) L. Huang, M. Rudolph, F. Rominger, A. S. K. Hashmi, Photosensitizer-free visible-light-mediated gold-catalyzed 1,2-difunctionalization of alkynes, *Angew. Chem. Int. Ed.* **2016**, *55*, 4808-4813.
 - 10 Z. Xia, O. Khaled, V. Mouriès-Mansuy, C. Ollivier, L. Fensterbank, Dual photoredox/gold catalysis aryative cyclization of *o*-alkynylphenols with aryldiazonium salts: a flexible synthesis of benzofurans, *J. Org. Chem.* **2016**, *81*, 7182-7190.
 - 11 (a) L. Huang, M. Rudolph, F. Rominger, A. S. K. Hashmi, Photosensitizer-free visible-light-mediated gold-catalyzed 1,2-difunctionalization of alkynes, *Angew. Chem. Int. Ed.* **2016**, *55*, 4808-4813; (b) S. Taschinski, R. Döpp, M. Ackermann, F. Rominger, F. D. Vries, M. F. S. J. Menger, M. Rudolph, A. S. K. Hashmi, J. E. M. N. Klein, Light-induced mechanistic divergence in gold(I) catalysis: revisiting the reactivity of diazonium salts, *Angew. Chem. Int. Ed.* **2019**, *58*, 16988-16993; (c) S. Witzel, A. S. K. Hashmi, J. Xie, Light in gold catalysis, *Chem. Rev.* **2021**, *121*, 8868-8925; (d) G. Revol, T. McCallum, M. Morin, F. Gagosz, L. Barriault, Photoredox transformations with dimeric gold complexes, *Angew. Chem. Int. Ed.* **2013**, *52*, 13342-13345; (e) L. Huang, F. Rominger, M. Rudolph, A. S. K. Hashmi, A general access to organogold(III) complexes by oxidative addition of diazonium salts, *Chem. Commun.* **2016**, *52*, 6435-6438.
 - 12 S. Witzel, A. S. K. Hashmi, J. Xie, Light in gold catalysis, *Chem. Rev.* **2021**, *121*, 8868-8925.
 - 13 W. Wu, H. Jiang, Haloalkynes: a powerful and versatile building block in organic synthesis, *Acc. Chem. Res.* **2014**, *47*, 2483-2504.
 - 14 (a) S. Mader, L. Molinari, M. Rudolph, F. Rominger, A. S. K. Hashmi, Dual gold-catalyzed head-to-tail coupling of iodoalkynes, *Chem. Eur. J.* **2015**, *21*, 3910-3913; (b) P. Morá n-Poladura, S. Suárez Pantiga, M. Piedrafita, E. Rubio, J. M. González, Regiocontrolled gold(I)-catalyzed cyclization reactions of *N*-(3-iodoprop-2-ynyl)-*N*-tosylanilines, *J. Organomet. Chem.* **2011**, *696*, 12-15; (c) V. Mamane, P. Hannen, A. Furstner, Synthesis of phenanthrenes and polycyclic heteroarenes by transition-metal catalyzed cycloisomerization reactions, *Chem. Eur. J.* **2004**, *10*, 4556-4575; (d) J. Xie, S. shi, T. Zhang, N. Mehrkens, M. Rudolph, A. S. K. Hashmi, A highly efficient gold-catalyzed photoredox α -C(sp³)-H alkylation of tertiary aliphatic amines with sunlight, *Angew. Chem. Int. Ed.* **2015**, *54*, 6046-6050.
 - 15 (a) Z. Xia, V. Corcé, F. Zhao, C. Przybylski, A. Espagne, L. Jullien, T. L. Saux, Y. Gimbert, H. Dossmann, V. Mouriès-Mansuy, C. Ollivier, L. Fensterbank, Photosensitized oxidative addition to gold(I) enables alkynylative cyclization of *o*-alkynylphenols with iodoalkynes, *Nat. Chem.* **2019**, *11*, 797-805; (b) E. B. McLean, A.-L. Lee, Golden potential, *Nat. Chem.* **2019**, *11*, 760-761.
 - 16 F. Zhao, M. Abdellaoui, W. Hagui, M. Ballarin-Marion, J. Berthet, V. Corcé, S. Delbaere, H. Dossmann, A. Espagne, J. Forté, L. Jullien, T. L. Saux, V. Mouriès-Mansuy, C. Ollivier, L. Fensterbank, Reactant-induced photoactivation of in situ generated organogold intermediates leading to alkynylated indoles via Csp²-Csp cross-coupling, *Nat. Commun.* **2022**, *13*, 2295-2305.
 - 17 M. N. Hopkinson, J. E. Ross, G. T. Giuffredi, A. D. Gee, V. Gouverneur, Gold-catalyzed cascade cyclization-oxidative alkylation of allenolates, *Org. Lett.* **2010**, *12*, 4904-4907.
 - 18 Y. Yang, J. Schiebl, S. Zallouz, V. Göker, J. Gross, M. Rudolph, F. Rominger, A. S. K. Hashmi, Gold-catalyzed C(sp²)-C(sp) coupling by alkynylation through oxidative Addition of bromoalkynes, *Chem. Eur. J.* **2019**, *25*, 9624-9628.
 - 19 A. Kumar, K. Shukla, S. Ahsan, A. Paul, N. T. Patil, Electrochemical gold-catalyzed 1,2-difunctionalization of C-C multiple bonds, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308636.
 - 20 J. Fan, D. Zhang, Y. Shi, C. Fu, S. Ma, Aerobic bimetallic catalysis for oxy-alkynylation of allenes, *Org. Chem. Front.* **2024**, *11*, 3842-3848.
 - 21 M. Wainwright, Acridine-A neglected antibacterial chromophore. *J. Antimicrob. Chemother.* **2001**, *47*, 1-13.
 - 22 (a) K. Piorecka, J. Kurjata, W. A. Stanczyk, Acriflavine, an acridine derivative for biomedical application: current state of the art. *J. Med. Chem.* **2022**, *65*, 11415-11432. (b) D. Sabolova, P. Kristian, M. Kozurkova, Proflavine/acriflavine derivatives with versatile biological activities, *J. Appl. Toxicol.* **2020**, *40*, 64-71.
 - 23 Dumele, D. Wu, N. Trapp, N. Gorof, F. Diederich, Halogen bonding of (iodoethynyl)benzene derivatives in solution, *Org. Lett.* **2014**, *16*, 4722-4725.
 - 24 (a) K. Kalyanasundaram, D. Dung, Role of proflavin as a photosensitizer for the light-induced hydrogen evolution from water, *J. Phys. Chem.* **1980**, *84*, 2551-2556; (b) J. Ong, J. W. L. Loke, H. L. Koh, W. Y. Fan. Proflavine-catalysed trifluoromethylation of α,β -unsaturated carbonyls. *Mol. Catal.* **2022**, *530*, 112587; (c) T. Ghosh, T. Slanina, B. König, Visible light photocatalytic reduction of aldehydes by Rh(III)-H: a detailed mechanistic study, *Chem. Sci.* **2015**, *6*, 2027-2034. (d) F. Mohamadpour, A. M. Amani, Proflavine (PFH⁺): as a photosensitizer (PS) biocatalyst for the visible-light-induced synthesis of pyrano [2,3-*d*] pyrimidine scaffolds, *Front. Chem.* **2024**, *12*, org/10.3389/fchem.2024.1304850.
 - 25 L. -P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, Synthesis and structural characterization of stable organogold(I) compounds. evidence for the mechanism of gold-catalyzed cyclizations, *J. Am. Chem. Soc.* **2008**, *130*, 17642-17643.
 - 26 (a) F. Strieth-Kalthof, M. J. James, M. Teders, L. Pitzer, F. Glorius, Energy transfer catalysis mediated by visible light: principles, applications, directions, *Chem. Soc. Rev.* **2018**, *47*, 7190-7202; (b) Z. Lu, T. P. Yoon, Visible light photocatalysis of [2+2] styrene cycloadditions by energy transfer, *Angew. Chem. Int. Ed.* **2012**, *51*, 10329-10332; (c) E. R. Weilin, C. C. Le, D. M. Arias-Rotondo, J. K. McCusker, D. W. C. MacMillan, Photosensitized, energy transfer-mediated organometallic catalysis through electronically excited nickel(II), *Science.* **2017**, *355*, 380-385.
 - 27 CCDC 2374591 (4f) contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.