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Introduction

Nucleophilic addition to carbonyl groups represents one of the most classic reactions for accessing ubiquitous C–C bonds. The C=O double bonds accept the attack of nucleophiles to form an alkoxide intermediate, followed by protonation to afford alcohol products (Scheme 1a). In contrast, the radical addition to carbonyls can generate a more reactive and versatile alkoxy radical intermediate that may undergo a reduction, 1,2-hydrogen atom transfer (1,2-HAT), or β -fragmentation to produce structurally diverse products (Scheme 1b), such as alcohols,¹ ketones,^{2,3} or aldehydes.^{4,5} In addition, the radical-mediated reaction usually occurs under mild, neutral conditions, thus tolerating many sensitive functional groups which are incompatible with the ionic reaction. Despite its apparent advantages, the addition of radicals to carbonyl compounds has been much less investigated due to the production of thermodynamically unfavorable alkoxy radicals.⁶ In this respect, we have established an aldehyde-to-ketone methodology² with 1,2-HAT of alkoxy radicals as the key step. However, the known

Solvent-controlled photocatalytic divergent cyclization of alkynyl aldehydes: access to cyclopentenones and dihydropyransols†‡

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Divergent synthesis is a powerful strategy for the fast assembly of different molecular scaffolds from identical starting materials. We describe here a solvent-controlled photocatalytic divergent cyclization of alkynyl aldehydes with sulfonyl chlorides for the direct construction of highly functionalized cyclopentenones and dihydropyransols that widely exist in bioactive molecules and natural products. Density functional theory calculations suggest that a unique *N,N*-dimethylacetamide-assisted 1,2-hydrogen transfer of alkoxy radicals is responsible for the cyclopentenone formation, whereas a C–C cleavage accounts for the selective production of dihydropyransols in acetonitrile and water at 50 °C. Given the simple and mild reaction conditions, excellent functional group compatibility, forming up to four chemical bonds, and tunable selectivity, it may find wide applications in synthetic chemistry.

methods are limited to aryl or alkenyl aldehydes ($R^1 = \text{Ar}$, alkenyl), and the transformation of alkyl aldehydes ($R^1 = \text{alkyl}$) is still unknown owing to the lack of spin delocalization in the formed ketyl radical. Recently, Liu⁴ and Zhu⁵ reported an elegant intramolecular formyl migration reaction *via* the β -scission of alkoxy radicals. Key to this transformation is the release of a much more stable radical ($R^{1\cdot}$), and therefore, it is a substrate-dependent process. So far, only α -hydroxy aldehydes work for this reaction, and the formyl shift from the more common alkyl aldehydes remains unexplored.

As fundamental structural scaffolds, cyclopentenones⁷ and dihydropyransols⁸ widely exist in numerous natural products and biologically active compounds, such as the inhibitor of cyclooxygenase-2 (COX-2) **A**,^{9a} potent anticancer agent **B**,^{9b} and herbicides **C**^{9c} (Scheme 1c). Consequently, the development of efficient methods for assembling these two motifs is highly desirable. Pursuing our recent interests in the aldehyde-to-ketone methodology,² we envisioned that an intramolecular addition of alkenyl radicals to alkyl aldehydes would allow us to access the more reactive alkoxy radicals (Scheme 1d). If we could control the reaction pathways of the *in situ* generated alkoxy radicals, a divergent synthesis of cyclopentenones and dihydropyransols would be established. Herein, we disclose a visible light-induced sulfonylative cyclization of alkynyl aldehydes using commercially available sulfonyl chlorides as the sulfonylation reagent.¹⁰ The reaction offers a facile access to various structurally diverse cyclopentenones, dihydropyransols, and dihydropyransols under very mild conditions. Density Functional Theory (DFT) calculations provide insights into this unique solvent-controlled divergent transformation. Specifically, the cyclopentenone formation proceeds *via* a novel DMA-

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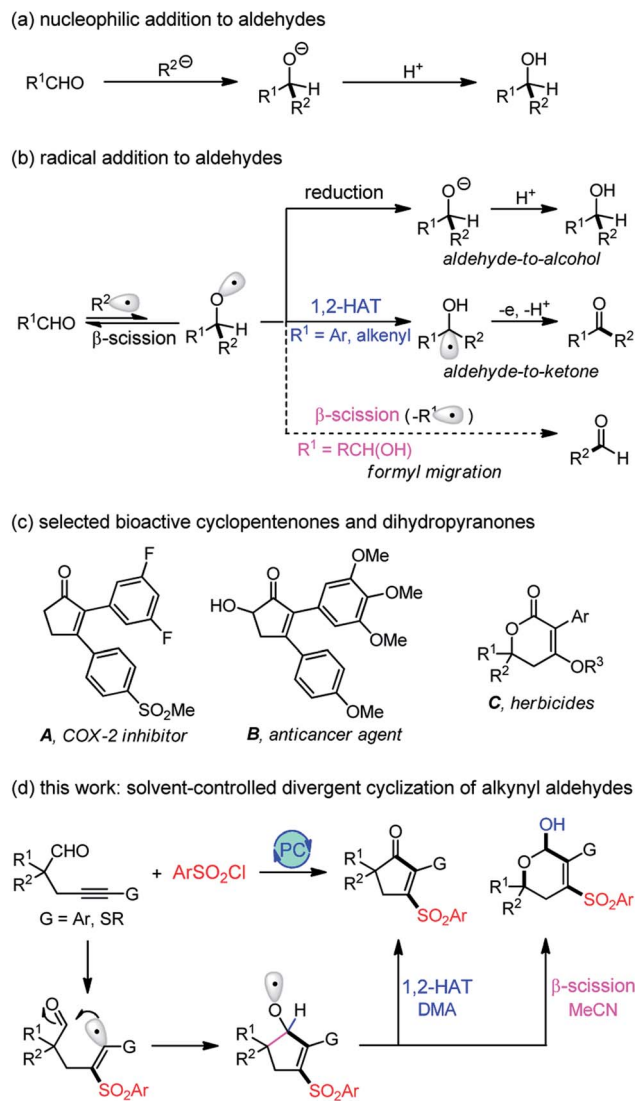
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† In memory of Prof. Ei-ichi Negishi.

‡ Electronic supplementary information (ESI) available: Data for all the products, experimental procedures, and computational data. CCDC 2060837 and 2060838. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1sc03416b

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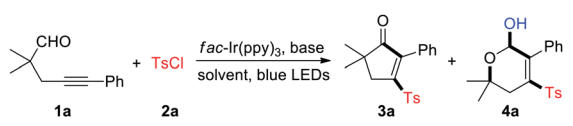


Scheme 1 Background and summary of this work.

assisted 1,2-hydrogen transfer, while the β -scission of alkoxy radicals accounts for the selective production of dihydropyranols with MeCN as the solvent. In contrast to the existing photocatalysis divergent synthesis^{11–13} which is generally restricted to the substrate¹¹ or catalyst-controlled¹² system, the solvent-controlled strategy developed here provides an operationally simple and highly efficient means for divergent synthesis.

Results and discussion

Initially, alkynyl aldehyde **1a** and TsCl (**2a**) were chosen as model substrates for evaluating the reaction conditions. In the presence of 2 mol% of *fac*-Ir(ppy)₃ and 2.0 equiv. of K₂CO₃, the 3-sulfonyl cyclopentenone **3a** was isolated in 66% yield after 5 h of irradiation with 15 W of blue LEDs in DMA at 25 °C (Table 1, entry 1). Base screening revealed that Na₂CO₃ was the most efficient choice, delivering **3a** in 76% yield (entries 2–5).

Table 1 Conditions optimization for the divergent cyclization^a


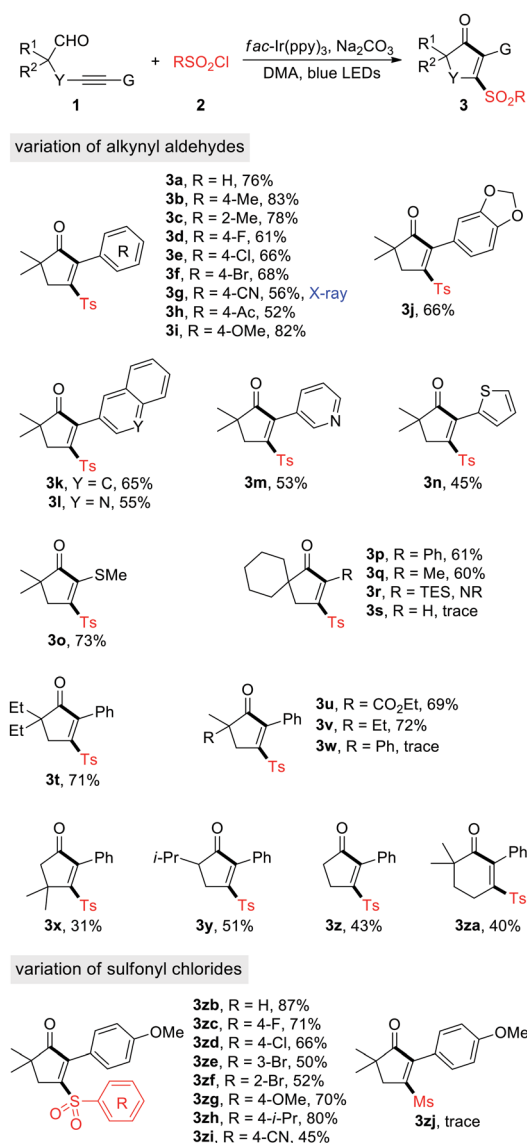
Entry	Base	Solvent	Yield of 3a ^b (%)	Yield of 4a ^b (%)
1	K ₂ CO ₃	DMA	66	Trace
2	K ₂ HPO ₄	DMA	65	Trace
3	K ₃ PO ₄	DMA	66	Trace
4	Et ₃ N	DMA	74	Trace
5	Na ₂ CO ₃	DMA	76	Trace
6	Na ₂ CO ₃	MeCN	5	57
7	Na ₂ HPO ₄	MeCN	30	30
8	K ₃ PO ₄	MeCN	10	25
9	Na ₂ CO ₃	MeNO ₂	5	51
10	Na ₂ CO ₃	DCM	Trace	48
11	Na ₂ CO ₃	DMSO	NR	NR
12	Na ₂ CO ₃	DMF	31	Trace
13 ^c	Na ₂ CO ₃	MeCN	Trace	73

^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), *fac*-Ir(ppy)₃ (2 mol%), base (0.4 mmol), H₂O (0.4 mmol), solvent, 25 °C, 5 h. ^b Isolated yield. ^c Run at 50 °C. DMA = *N,N*-dimethylacetamide, DCM = dichloromethane, DMSO = dimethyl sulfoxide, DMF = *N,N*-dimethylformamide, NR = no reaction.

Switching the solvent from DMA to MeCN led to **3a** in only 5% yield, and interestingly, the 4-sulfonyl dihydropyranol **4a** was isolated in 57% yield (entry 6). Encouraged by the result, we examined other bases and solvents for the dihydropyranol production, however, the reaction yields were not improved (entries 7–12). To our delight, running the reaction at 50 °C resulted in full conversion of **1a** and produced **4a** in 73% yield (entry 13).

With the optimized reaction conditions in hands, we set about evaluating the scope of this cyclopentenone formation protocol with DMA as the solvent (Table 2). In general, the transformation proceeded efficiently to form densely substituted cyclopentenones in moderate to high yields (**3a–3w**). A broad array of functional groups, such as F, Cl, Br, CN, Ac, OMe, quinoline, pyridine, and thiofuran, are well tolerated under the reaction conditions, which may be utilized for the downtown transformations. Although both the electron-rich and -deficient substituents were accommodated on the benzene ring of **1**, relatively lower yields were observed for the latter cases (**3g** and **3h**). In addition to arylalkynyl substrates (G = Ar), the thioalkynyl aldehyde **1o** reacted with **2a** as well to produce the desired product **3o** in 73% yield. Direct construction of spirocyclopentenones was also feasible, as exemplified by the production of **3p**. The alkylalkynyl aldehyde **1q** (G = Me) served as a viable substrate, while aldehydes **1r** and **1s** (G = SiEt₃ and H) were not engaged in this reaction (**3q–3s**). The reaction of **1u**, a dicarbonyl substrate, took place uneventfully to afford **3u** in 69% yield. Substitution at the propargyl position with two methyl groups led to **3x** in a low yield, which may be attributed to the increased hindrance for the radical sulfonation of C–C triple bonds. After succeeding in synthesizing tetrasubstituted



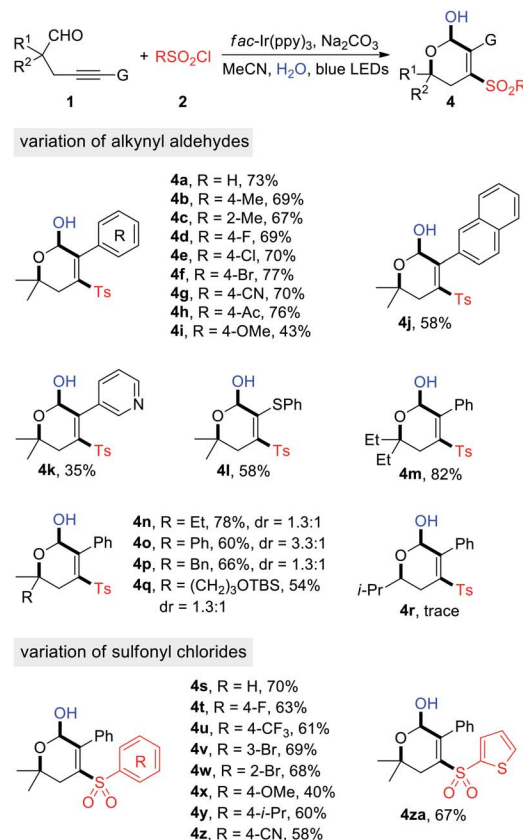
Table 2 Scope of the cyclopentenone formation^a

^a Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), *fac*-Ir(ppy)₃ (2 mol%), Na₂CO₃ (0.4 mmol), H₂O (0.4 mmol), DMA, 25 °C, 5 h. Isolated yields are given.

cyclopentenones, we then examined the feasibility of assembling tri- or disubstituted cyclopentenones. Starting from the α -secondary and α -primary aldehydes **1y** and **1z**, the 2,3,5-trisubstituted and 2,3-disubstituted cyclopentenones were successfully constructed (**3y** and **3z**). The reaction was also amenable to the access of sulfonylated cyclohexenones, albeit in a moderate yield (**3za**). In contrast, construction of cyclobutenone or cycloheptenone *via* this method was unsuccessful at the current stage. In the meantime, sulfonyl chlorides **2** were varied with **1i** as the coupling partner. Pleasingly, various arylsulfonyl chlorides proved to be efficient substrates and produced the corresponding sulfonyl cyclopentenones in medium to high yields (**3zb–3zi**). Unfortunately, MeSO₂Cl was

not engaged in this reaction (**3zj**). The X-ray crystallographic analysis of **3g**¹⁴ clearly indicated the structure of 3-sulfonyl cyclopentenones.

The generality of photoredox-catalyzed synthesis of dihydropyranols was then explored with MeCN as the solvent (Table 3). Alkynyl aldehydes bearing different substituents such as Me, F, Cl, Br, CN, Ac, and OMe served as competent substrates, delivering a variety of 4-sulfonyl dihydropyranols in moderate to high yields (**4a–4i**). The electron effects appeared to have an impact on the reaction efficiency. Specifically, the transformation of substrates **1g** and **1h**, having electron-withdrawing CN and Ac substituents on the benzene ring, produced the desired products **4g** and **4h** in 70% and 76% yield, respectively, while a moderate yield (42%) was observed in the case of **1i**, bearing an electron-donating OMe group (**4i**). Substituents at the α -position of aldehydes were evaluated. In particular, α -tertiary aldehydes worked well for this reaction (**4m–4q**), whereas the α -secondary aldehyde failed to provide the corresponding product (**4r**), presumably due to the reduced stability of secondary alkyl radicals. Aldehydes **1q–1s** were ineffective for the dihydropyranol formation. Additionally, the scope with respect to sulfonyl chlorides was investigated. A wide range of arylsulfonyl chlorides, substituted by groups such as F, CF₃, Br,

Table 3 Scope of the dihydropyranol formation^a

^a Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), *fac*-Ir(ppy)₃ (2 mol%), Na₂CO₃ (0.4 mmol), H₂O (0.4 mmol), MeCN, 50 °C, 5 h. Isolated yields are given.



OMe, *i*-Pr, and CN, underwent the reaction smoothly to generate functionalized dihydropyranols in promising yields (**4s–4z**). Similarly, 2-furansulfonyl chloride served as an efficient sulfonylation reagent (**4za**). It's noteworthy that four new chemical bonds are concurrently created under the reaction conditions, thus highlighting the high bond-forming efficiency of this method.

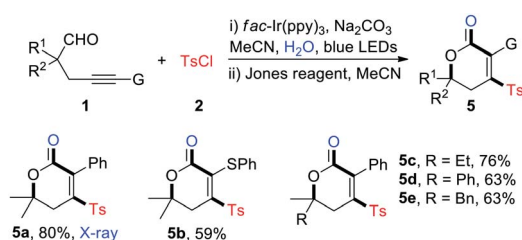
Meanwhile, the one-pot synthesis of polysubstituted dihydropyranones was explored (Table 4). As expected, the reaction furnished a set of sulfonylated dihydropyranones in medium to high yields with good functional group tolerance (**5a–5e**). The structure of 4-sulfonyl dihydropyranones was unambiguously identified by the X-ray crystallographic analysis of **5a**.¹⁴

To demonstrate the synthetic utility of this divergent transformation of alkynyl aldehydes, we carried out the derivatization of obtained products (Scheme 2). Substitution

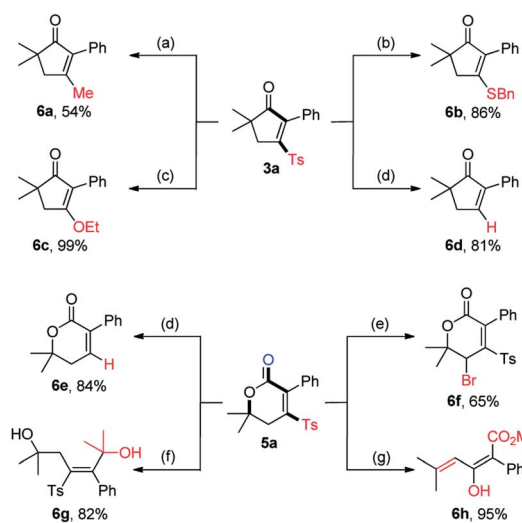
of the Ts group of **3a** by a methyl group with MeMgCl catalyzed by Ni(acac)₂ afforded **6a** in 54% yield.¹⁵ Michael addition of BnSH or NaOEt to **3a** followed by an elimination of sulfinate formed **6b** and **6c** in 86% and 99% yield, respectively. Following Orita's protocol,¹⁶ photocatalytic desulfonylation of both **3a** and **5a** occurred readily to give **6d** and **6e** in high yields. Bromination at the allylic position of **5a** with NBS and BPO produced **6f** in a good yield. Given the significant importance of tetrasubstituted alkenes in organic synthesis, the attempts to establish stereodefined tetrasubstituted alkenes were also performed. Nucleophilic attack of MeMgCl to **5a** delivered the tetrasubstituted (*E*)-alkene **6g** in 82% yield. Furthermore, the (*E*)-enol **6h** was selectively assembled in almost quantitative yield upon treatment of **5a** with K₂CO₃ in MeOH at 55 °C for 10 h.

To gain insights into the reaction mechanism, some control experiments were performed, and the results are summarized in Scheme 3. In the presence of butylated hydroxytoluene (BHT, 2.0 equiv.), neither **3a** nor **4a** could be obtained in a noticeable yield, and instead, the sulfonyl compound **7** was isolated in 11% and 48% yield, respectively. Likewise, adding 2,2,6,6-tetramethylpiperidinoxy (TMEPO, 2.0 equiv.) to the standard conditions shut down the reaction (not shown). These results suggested a radical pathway. Additionally, the ¹⁸O isotope labeling experiments were conducted. With the addition of 5.0 equiv. of H₂¹⁸O, **4a-¹⁸O** was isolated in 69% yield with 89% ¹⁸O incorporation. In addition to the signal of [M + Na]⁺ ion of **4a-¹⁸O**, a signal matched with [M + Na - H₂¹⁸O]⁺ ion was observed by the HRMS analysis, thus indicating that the hydroxy group of

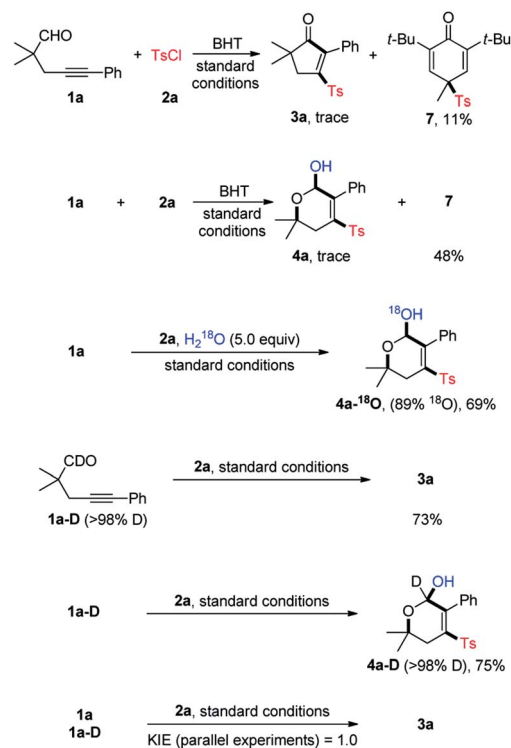
Table 4 One-pot synthesis of dihydropyranones^a



^a Reaction conditions: (i) see Table 3. (ii) Jones reagent (0.4 mmol), MeCN, 25 °C, 5 h. Isolated yields are given.



Scheme 2 Transformation of selected products. Reaction conditions: (a) MeMgCl (1.2 equiv.), Ni(acac)₂ (10 mol%), THF, 25 °C, 10 h; (b) BnSH (2.0 equiv.), DBU (2.0 equiv.), CHCl₃, 25 °C, 10 h; (c) NaOEt (2.0 equiv.), THF, 25 °C, 10 h; (d) perylene (5 mol%), *i*-Pr₂NEt (8.0 equiv.), MeCN/THF (5 : 1), blue LEDs, 25 °C, 10 h; (e) BPO (20 mol%), NBS (3.0 equiv.), CCl₄, 95 °C, 24 h; (f) MeMgCl (3.0 equiv.), THF, 10 h; (g) K₂CO₃ (4.0 equiv.), MeOH, 55 °C, 10 h. THF = tetrahydrofuran, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, BPO = dibenzoyl peroxide, NBS = *N*-bromosuccinimide.



Scheme 3 Mechanistic studies.

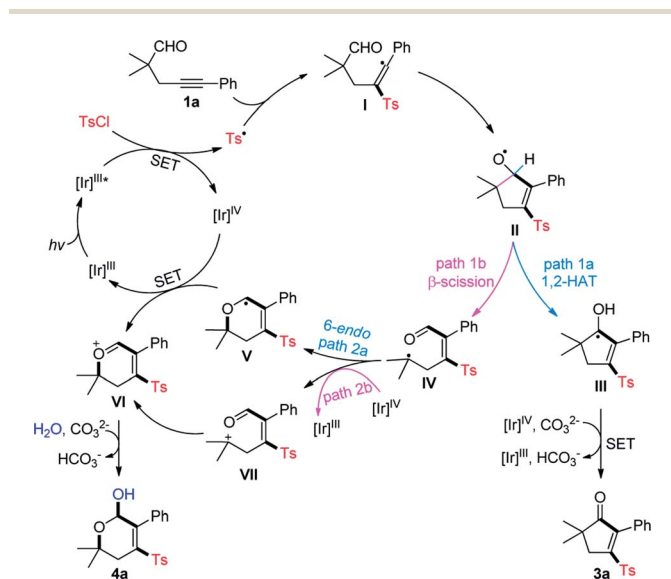


4a is originated from water (see ESI† for details). Under the standard conditions, the reaction of aldehyde **1a-D** performed well to deliver **3a** and **4a-D** in 73% and 75% yield, respectively.

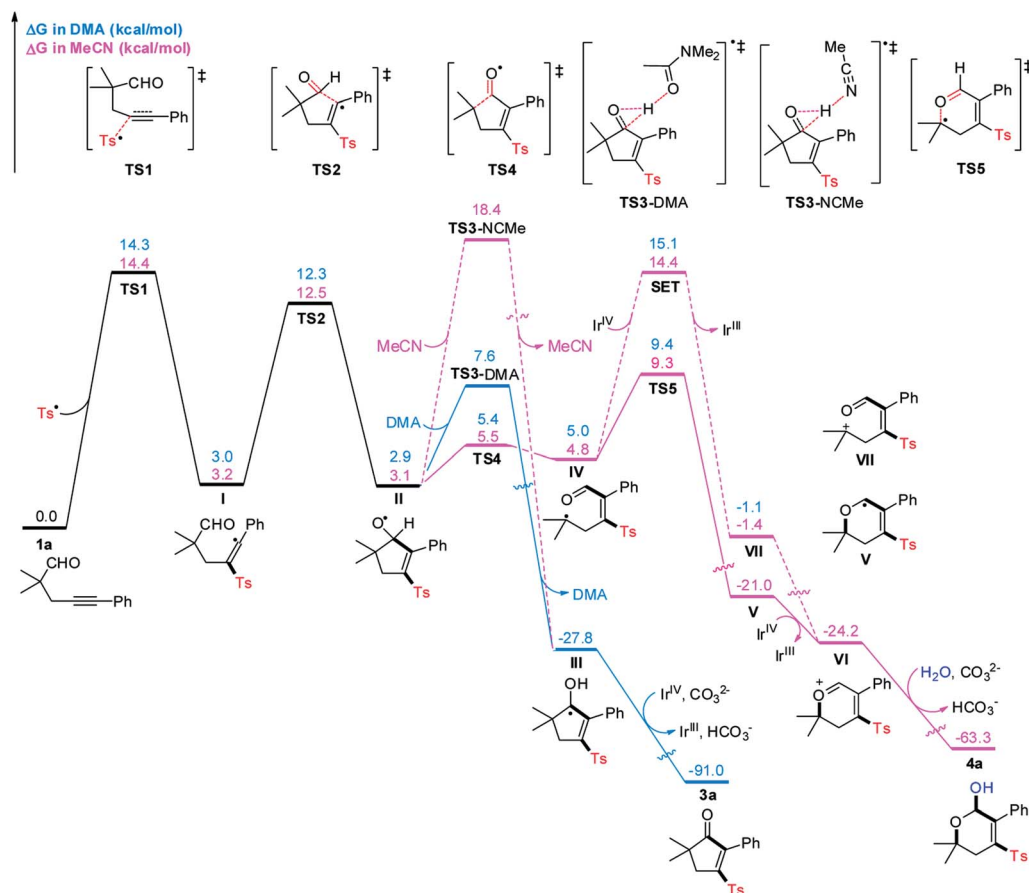
Parallel intermolecular kinetic isotopic effect experiments were then conducted, and a KIE value of 1.0 was determined, implying that the aldehydic C–H cleavage may not be the rate-determining step.

Based on the above results and previous reports,^{2,4,5} a mechanistic proposal for the divergent cyclization of **1a** is summarized in Scheme 4. Initially, the single electron transfer (SET) between the excited photocatalysis Ir(III)* and TsCl affords a Ir(IV) species and sulfonyl radical Ts•. Radical sulfonylation of the C–C triple bond of **1a** and a subsequent addition of vinyl radical **I** to the intramolecular CHO group produces a cyclopentenyl radical **II**. It may undergo a 1,2-HAT to deliver the neutral ketyl radical **III**, followed by SET with Ir(IV) and deprotonation to provide **3a** (path 1a). Alternatively, the β-C–C cleavage of **II**¹⁷ may take place to form a tertiary alkyl radical **IV** (path 1b), which can be converted into the oxonium ion **VI** via a 6-endo radical cyclization (path 2a)/SET oxidation sequence. Additionally, a radical oxidation to the cation **VII** (path 2b) followed by intramolecular nucleophilic attack may also lead to the generation of **VI**. Finally, the nucleophilic attack of **VI** by H₂O generates **4a** as the product.

To shed light on the unique role of solvent in tuning the reaction pathways, we carried out computational studies using DFT calculations, and the results are presented in Scheme 5. As



Scheme 4 Proposed mechanism.



Scheme 5 The calculated relative Gibbs free energies for the intermediates and transition-states of the model reaction in DMA (in blue) and MeCN (in pink) at the wb97xd/def2tzvp-SMD//B3LYP-D3(BJ)/6-31G(d,p) level of theory.



for the reaction performed in DMA, radical sulfonylation of **1a** occurring *via* transition state **TS1** requires an activation free energy of 14.3 kcal mol⁻¹, which is viable under the reaction conditions. Subsequently, radical addition to the intramolecular CHO group proceeds *via* a five-membered ring transition state **TS2** to give the radical **II**. This step has a free energy barrier of 9.3 kcal mol⁻¹. Starting from **II**, an unprecedented DMA-assisted 1,2-hydrogen transfer¹⁸ (*via* **TS3**-DMA, with a free energy of 7.6 kcal mol⁻¹) is favoured over the 6-*endo* radical cyclization (*via* **TS5**, with a free energy of 9.4 kcal mol⁻¹) by 1.8 kcal mol⁻¹, thus giving rise to the ketyl radical **III**. Formation of **III** is highly exergonic by 30.7 kcal mol⁻¹ and is therefore an irreversible process. Followed by SET oxidation and deprotonation, **3a** can be constructed together with the regeneration of photocatalysis Ir(III), which is strongly exergonic by 63.2 kcal mol⁻¹.

With MeCN as the solvent, the MeCN-assisted 1,2-hydrogen transfer of **II** (*via* **TS3**-NCMe) has a higher energy barrier of 15.3 kcal mol⁻¹, which is unlikely to compete with the β-C-C cleavage/6-*endo* cyclization sequence. Moreover, the 6-*endo* radical cyclization of **IV** requiring a free energy barrier of 4.5 kcal mol⁻¹ is favoured over the SET oxidation, with a free energy barrier of 9.6 kcal mol⁻¹, by 5.1 kcal mol⁻¹. Therefore, a stable allyl radical **V** that lies 25.8 kcal mol⁻¹ lower in energy than **IV** is selectively formed. Spin delocalization to the neighboring C-C double bond should be responsible for the increased stability of **V**, which provides a driving force for the C-C bond cleavage and uncommon addition of alkyl radical to the carbonyl oxygen atom¹⁹ in the 6-*endo* radical cyclization step. Subsequently, the radical **V** is oxidized by Ir(IV) to form an oxonium ion intermediate **VI**, followed by nucleophilic attack of water to produce **4a**, which is strongly exergonic by 39.1 kcal mol⁻¹.

Conclusions

In conclusion, a photocatalytic divergent coupling of alkynyl aldehydes with sulfonyl chlorides is developed. The reaction provides a straightforward and highly selective method for the assembly of structurally diverse cyclopentenones, dihydropyrans, and dihydropyranones that are important building blocks in organic and medicinal chemistry. Up to four new chemical bonds are concurrently constructed under mild reaction conditions, thus highlighting the high efficiency of this method. DFT calculations reveal that a DMA-assisted 1,2-HAT of alkoxy radicals is responsible for the production of cyclopentenones, whereas a β-C-C cleavage followed by 6-*endo* radical cyclization to formyl group accounts for the generation of dihydropyrans in MeCN. Tuneable selectivity for 1,2-HAT and β-fragmentation of alkoxy radicals is realized by change of the solvent, thus providing a novel strategy for the selective activation of inert C-H and C-C bonds.

Data availability

The data supporting this article have been uploaded as part of the ESI.†

Author contributions

H. Z., J. Z., and J. F. conducted the experiments. H. Z., and X.-S. X. carried out the theoretical calculations and wrote the manuscript. L. K., and F. Z. characterized the compounds and analyzed the data. G. Z. designed the project, analyzed the results and wrote the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

- For selected reports, see: (a) T. Kawamoto, T. Fukuyama and I. Ryu, *J. Am. Chem. Soc.*, 2012, **134**, 875; (b) L. Pitzer, F. Sandfort, F. Strieth-Kalthoff and F. Glorius, *J. Am. Chem. Soc.*, 2017, **139**, 13652; (c) G. Wang, J. Cao, L. Gao, W. Chen, W. Huang, X. Cheng and S. Li, *J. Am. Chem. Soc.*, 2017, **139**, 3904; (d) M. Saladrigas, C. Bosch, G. V. Saborit, J. Bonjoch and B. Bradshaw, *Angew. Chem., Int. Ed.*, 2018, **57**, 182; (e) S. Xie, D. Li, H. Huang, F. Zhang and Y. Chen, *J. Am. Chem. Soc.*, 2019, **141**, 16237; (f) J. Y. Kim, Y. S. Lee, Y. Choi and D. H. Ryu, *ACS Catal.*, 2020, **10**, 10585.
- (a) C. Che, Q. Huang, H. Zheng and G. Zhu, *Chem. Sci.*, 2016, **7**, 4134; (b) Y. Zhang, D. Guo, S. Ye, Z. Liu and G. Zhu, *Org. Lett.*, 2017, **19**, 1302; (c) D. Lu, Y. Wan, L. Kong and G. Zhu, *Org. Lett.*, 2017, **19**, 2929; (d) Y. Chen, C. Shu, F. Luo, X. Xiao and G. Zhu, *Chem. Commun.*, 2018, **54**, 5373; (e) Y. Zhou, Z. Xiong, J. Qiu, L. Kong and G. Zhu, *Org. Chem. Front.*, 2019, **6**, 1022. For a review, see: (f) L. Kong, Y. Zhou, F. Luo and G. Zhu, *Chin. J. Org. Chem.*, 2018, **38**, 2858.
- For selected reports from other groups, see: (a) W.-C. Yang, P. Dai, K. Luo, Y.-G. Ji and L. Wu, *Adv. Synth. Catal.*, 2017, **359**, 2390; (b) H. Hu, X. Chen, K. Sun, J. Wang, Y. Liu, H. Liu, L. Fan, B. Yu, Y. Sun, L. Qu and Y. Zhao, *Org. Lett.*, 2018, **20**, 6157; (c) X.-K. He, B.-G. Cai, Q.-Q. Yang, L. Wang and J. Xuan, *Chem.-Asian J.*, 2019, **14**, 3269; (d) Y. Mei, L. Zhao, Q. Liu, S. Ruan, L. Wang and P. Li, *Green Chem.*, 2020, **22**, 2270.
- Z.-L. Li, X.-H. Li, N. Wang, N.-Y. Yang and X.-Y. Liu, *Angew. Chem., Int. Ed.*, 2016, **55**, 15100.
- J. Yu, D. Wang, Y. Xu, Z. Wu and C. Zhu, *Adv. Synth. Catal.*, 2018, **360**, 744.
- S. Wilsey, P. Dowd and K. N. Houk, *J. Org. Chem.*, 1999, **64**, 8801.



- 7 For selected reviews, see: (a) S. P. Simeonov, J. P. M. Nunes, K. Guerra, V. B. Kurteva and C. A. M. Afonso, *Chem. Rev.*, 2016, **116**, 5744; (b) A. J. Frontier and J. J. Hernandez, *Acc. Chem. Res.*, 2020, **53**, 1822. For recent reports, see: (c) K. Wang, C. Jiang, Z. Zhang, C. Han, X. Wang, Y. Li, K. Chen and J. Zhao, *Chem. Commun.*, 2020, **56**, 12817; (d) M. J. Hensinger, N. J. Dodge and M. Brewer, *Org. Lett.*, 2020, **22**, 497; (e) J. Li, Y. Xu, X. Hu, S. Zhu and L. Liu, *Org. Lett.*, 2020, **22**, 9478; (f) Y. H. Lee, E. H. Denton and B. Morandi, *J. Am. Chem. Soc.*, 2020, **142**, 20948 and references cited therein.
- 8 For selected reviews, see: (a) J. A. Marco, M. Carda, J. Murga and E. Falomir, *Tetrahedron*, 2007, **63**, 2929; (b) X.-Y. Chen, Q. Liu, P. Chauhan and D. Enders, *Angew. Chem., Int. Ed.*, 2018, **57**, 3862. For selected reports, see: (c) H.-S. Yeom, J. Koo, H.-S. Park, Y. Wang, Y. Liang, Z.-X. Yu and S. Shin, *J. Am. Chem. Soc.*, 2012, **134**, 208; (d) H. Kim, S. Y. Choi and S. Shin, *Angew. Chem., Int. Ed.*, 2018, **57**, 13130; (e) D. D. Borisov, R. A. Novikov, A. S. Eltyшева, Y. V. Tkachev and Y. V. Tomilov, *Org. Lett.*, 2017, **19**, 3731; (f) H.-J. Zhang and L. Yin, *J. Am. Chem. Soc.*, 2018, **140**, 12270.
- 9 (a) W. C. Black, C. Brideau, C.-C. Chan, S. Charleson, N. Charet, D. Claveau, D. Ethier, R. Gordon, G. Greig, J. Guay, G. Hughes, P. Jolicoeur, Y. Leblanc, D. Nicoll-Griffith, N. Ouimet, D. Riendeau, D. Visco, Z. Wang, L. Xu and P. Prasit, *J. Med. Chem.*, 1999, **42**, 1274; (b) M. K. Gurjar, R. D. Wakharkar, A. T. Singh, M. Jaggi, H. B. Borate, P. D. Shinde, R. Verma, P. Rajendran, S. Dutt, G. Singh, V. K. Sanna, M. K. Singh, S. K. Srivastava, V. A. Mahajan, V. H. Jadhav, K. Dutta, K. Krishnan, A. Chaudhary, S. K. Agarwal, R. Mukherjee and A. C. Burman, *J. Med. Chem.*, 2007, **50**, 1744; (c) Y. Nakashima and Y. Jin, WO2014/084407A1, 2014.
- 10 For selected reports on radical sulfonylation of alkynes with sulfonyl chlorides, see: (a) X. Zeng, L. Iliés and E. Nakamura, *Org. Lett.*, 2012, **14**, 954; (b) L. Wang, H. Zhu, J. Che, Y. Yang and G. Zhu, *Tetrahedron Lett.*, 2014, **55**, 1011; (c) A. García-Domínguez, S. Müller and C. Nevado, *Angew. Chem., Int. Ed.*, 2017, **56**, 9949; (d) P. Chakrasali, K. Kim, Y.-S. Jung, H. Kim and S. B. Han, *Org. Lett.*, 2018, **20**, 7509; (e) A. Hossain, S. Engl, E. Lutsker and O. Reiser, *ACS Catal.*, 2019, **9**, 1103.
- 11 For selected reports, see: (a) H. Jiang, Y. Cheng, Y. Zhang and S. Yu, *Org. Lett.*, 2013, **15**, 4884; (b) D. B. Bagal, G. Kachkovskiy, M. Knorn, T. Rawner, B. M. Bhanage and O. Reiser, *Angew. Chem., Int. Ed.*, 2015, **54**, 6999; (c) J. Cheng, Y. Cheng, J. Xie and C. Zhu, *Org. Lett.*, 2017, **19**, 6452; (d) Y. Liu, R.-J. Song, S. Luo and J.-H. Li, *Org. Lett.*, 2018, **20**, 212; (e) H. Liang, G.-Q. Xu, Z.-T. Feng, Z.-Y. Wang and P.-F. Xu, *J. Org. Chem.*, 2019, **84**, 60; (f) J. Ma, F. Schäfers, C. Daniliuc, K. Bergander, C. A. Strassert and F. Glorius, *Angew. Chem., Int. Ed.*, 2020, **59**, 9639; (g) Z.-S. Wang, Y.-B. Chen, H.-W. Zhang, Z. Sun, C. Zhu and L.-W. Ye, *J. Am. Chem. Soc.*, 2020, **142**, 3636.
- 12 For selected reports, see: (a) A. Singh, C. J. Fennell and J. D. Weaver, *Chem. Sci.*, 2016, **7**, 6796; (b) M. J. James, J. L. Schwarz, F. Strieth-Kalthoff, B. Wibbeling and F. Glorius, *J. Am. Chem. Soc.*, 2018, **140**, 8624; (c) J. Li, Y. Luo, H. W. Cheo, Y. Lan and J. Wu, *Chem*, 2019, **5**, 192; (d) M. Mei, D. Anand and L. Zhou, *Org. Lett.*, 2019, **21**, 3548.
- 13 (a) S. Zhu, A. Das, L. Bui, H. Zhou, D. P. Curran and M. Rueping, *J. Am. Chem. Soc.*, 2013, **135**, 1823; (b) C. Zhang, S. Li, F. Bureš, R. Lee, X. Ye and Z. Jiang, *ACS Catal.*, 2016, **6**, 6853; (c) Y. Tsuchiya, R. Onai, D. Uruguchi and T. Ooi, *Chem. Commun.*, 2020, **56**, 11014.
- 14 Crystallographic data for products **3g** and **5a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 2060837 and 2060838.
- 15 J. L. Fabre, M. Julia and J. N. Verpeaux, *Tetrahedron Lett.*, 1982, **23**, 2469.
- 16 H. Watanabe, M. Takemoto, K. Adachi, Y. Okuda, A. Dakegata, T. Fukuyama, I. Ryu, K. Wakamatsu and A. Orita, *Chem. Lett.*, 2020, **49**, 409.
- 17 For selected reports on ring opening of unstrained cycloalkanols via β -scission of alkoxy radicals, see: (a) H. G. Yayla, H. Wang, K. T. Tarantino, H. S. Orbe and R. R. Knowles, *J. Am. Chem. Soc.*, 2016, **138**, 10794; (b) E. Ota, H. Wang, N. L. Frye and R. R. Knowles, *J. Am. Chem. Soc.*, 2019, **141**, 1457; (c) J.-J. Guo, A. Hu, Y. Chen, J. Sun, H. Tang and Z. Zuo, *Angew. Chem., Int. Ed.*, 2016, **55**, 15319; (d) A. Hu, Y. Chen, J.-J. Guo, N. Yu, Q. An and Z. Zuo, *J. Am. Chem. Soc.*, 2018, **140**, 13580; (e) D. Wang, J. Mao and C. Zhu, *Chem. Sci.*, 2018, **9**, 5805; (f) M. Wang, M. Li, S. Yang, X.-S. Xue, X. Wu and C. Zhu, *Nat. Commun.*, 2020, **11**, 672; (g) L. Huang, T. Ji and M. Rueping, *J. Am. Chem. Soc.*, 2020, **142**, 3532. For selected reviews, see: (h) X. Wu and C. Zhu, *Chem. Commun.*, 2019, **55**, 9747; (i) S.-H. Shi, Y. Liang and N. Jiao, *Chem. Rev.*, 2021, **121**, 485; (j) X.-Y. Yu, J.-R. Chen and W.-J. Xiao, *Chem. Rev.*, 2021, **121**, 506.
- 18 For selected reports on solvent-assisted 1,2-HAT of alkoxy radicals, see: (a) K. G. Konya, T. Paul, S. Lin, J. Luszytk and K. U. Ingold, *J. Am. Chem. Soc.*, 2000, **122**, 7518; (b) C. Che, Z. Qian, M. Wu, Y. Zhao and G. Zhu, *J. Org. Chem.*, 2018, **83**, 5665; (c) J. Zhang, D. Liu, S. Liu, Y. Ge, Y. Lan and Y. Chen, *iScience*, 2020, **23**, 100755. However, our calculations indicated that water-assisted 1,2-HAT is less likely for this work, see Fig. S1 and S2[†] of ESI for details.
- 19 For selected reports on addition of alkyl radicals to the carbonyl oxygen atom, see: (a) D. Liu, S. Tang, H. Yi, C. Liu, X. Qi, Y. Lan and A. Lei, *Chem.-Eur. J.*, 2014, **20**, 15605; (b) L. Lv, S. Lu, Q. Guo, B. Shen and Z. Li, *J. Org. Chem.*, 2015, **80**, 698; (c) L.-N. Guo, S. Wang, X.-H. Duan and S.-L. Zhou, *Chem. Commun.*, 2015, **51**, 4803.

