

RESEARCH ARTICLE

View Article Online
View Journal | View IssueCite this: *Org. Chem. Front.*, 2021, **8**, 5092

Copper-catalyzed [3 + 2]/[3 + 2] carboannulation of dienyne and arylsulfonyl chlorides enabled by Smiles rearrangement: access to cyclopenta[*a*]indene-fused quinolinones†

Liwei Zhou,^{‡,a} Xiaodong Liu,^{‡,a} Haiyan Lu,^a Guobo Deng,^{id} ^a Yun Liang,^{id} ^{*a} Yuan Yang,^{id} ^{*a} and Jin-Heng Li,^{id} ^{*a,b,c}

On one hand, the construction of two fused five-membered carbocyclic rings remains an extremely challenging topic in organic synthesis. On the other hand, transition-metal-catalyzed diyne cycloaddition reactions have become one of the most powerful methods for the construction of diverse cyclic frameworks. Nevertheless, these methods are limited to noble transition-metal catalysis and non-radical cycloaddition modes. Here, a radical Smiles rearrangement strategy for allowing an unprecedented [3 + 2]/[3 + 2] carboannulation of dienyne with arylsulfonyl chlorides using cheap copper catalysis is described. This cascade method represents a novel cycloaddition mode for diyne chemistry, which occurs by the sequence of addition of arylsulfonyl radical to a diyne, a Smiles rearrangement and radical annulation to access cyclopenta[*a*]indene-fused quinolinones with excellent diastereoselectivity.

Received 4th May 2021,
Accepted 11th July 2021

DOI: 10.1039/d1qo00703c

rsc.li/frontiers-organic

Introduction

Until now, the construction of two fused five-membered carbocyclic rings, especially with two vicinal chiral carbon atoms, has remained an extremely challenging topic in organic synthesis. Conventional methods often require multiple steps with low overall yields or the use of cyclopentane-based starting materials.¹ Therefore, the development of one-pot strategies for directly accessing two fused five-membered carbocyclic frameworks is in great demand.

The cycloaddition reaction is well-known and recognized as one of the most powerful and straightforward methodologies for efficient access to cyclic compounds in a single step, often along with the generation of multiple diastereocenters.² In

the past several decades, cycloaddition of dienyne (generally alkyne-tethered 1,3-dienes) has received considerable attention because this methodology is particularly appealing for rapid construction of diverse complex carbo- and hetero-cyclic structures, including the challenging seven- to nine-membered ring systems.^{3–6} Typical methodologies can be divided into three types of non-radical annulation modes (Scheme 1a), including (i) Diels–Alder reaction *via* intramolecular [4 + 2] cycloaddition/isomerization,⁴ (ii) intramolecular cycloisomerization/Cope rearrangement,⁵ and (iii) intermolecular [4 + 2 + *n*] annulation.⁶ However, these methods require expensive transition metal catalysts (such as Rh, Au, Pt, and Ni) and/or harsh

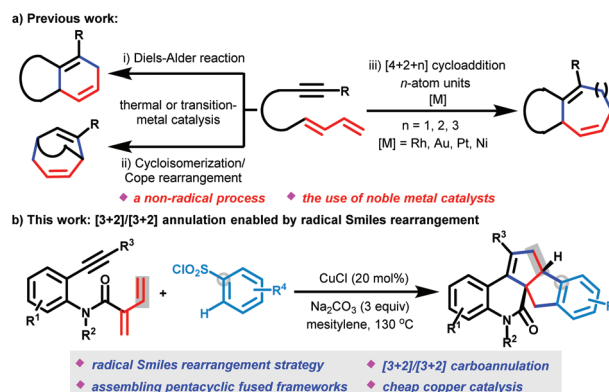
^aNational & Local Joint Engineering Laboratory for New Petro-chemical Materials and Fine Utilization of Resources, Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research (Ministry of Education), and Key Laboratory of the Assembly and Application of Organic Functional Molecules of Hunan Province, Hunan Normal University, Changsha 410081, China. E-mail: yliang@hunnu.edu.cn, yuanyang@hunnu.edu.cn, jhli@hnu.edu.cn

^bKey Laboratory of Jiangxi Province for Persistent Pollutants Control and Resources Recycle, Nanchang Hangkong University, Nanchang 330063, China

^cState Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

† Electronic supplementary information (ESI) available. CCDC 2059099. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1qo00703c

‡ The authors contributed equally.



Scheme 1 Annulation modes of dienyne.

thermal conditions. Although the last $[4 + 2 + n]$ cycloaddition of dienynes with external n -atom units can readily incorporate functional groups as well as controllably tune the ring scaffolds and has been well investigated, the scope of external n -atom units (such as carbene units, alkyne, ethyl cyclopropylideneacetate, and boryl(isopropoxy)silane) is limited. To the best of our knowledge, approaches that employ dienynes to undergo cycloaddition with external x -atom units for the construction of five-membered carbocyclic frameworks, especially those including two carbocyclic rings in a single step, have never been reported. Thus, the development of novel dienyne cycloaddition modes, especially including mechanistically distinguishable strategies using inexpensive transition metal catalysis, to widely expand the dienyne applications is desirable.

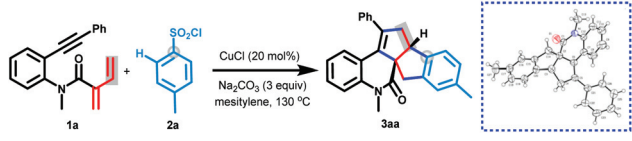
The Smiles rearrangement has emerged as one of the most powerful methods for the formation of chemical bonds in synthesis, and has been applied to difunctionalization of unsaturated hydrocarbons (such as alkenes and alkynes) by releasing SO_2 in recent years.^{7–11} In a pioneering study, the group of Nevado has reported a new Smiles rearrangement tactic for enabling the addition of various radicals across the $\text{C}=\text{C}$ bonds of N -(arylsulfonyl)acrylamides and their derivatives through radical addition/aryl migration/desulfonylation cascades to produce diverse N -heterocycles.⁸ However, these methods largely rely on tailored acryl sulfonamide motifs.^{8,9} Recently, Stephenson^{11a} and Zhu^{11b–e} made a significant breakthrough in the radical Smiles rearrangement to realize two-component difunctionalization of alkenes, in which external sulfonyl-based starting materials are converted to nitrogen- or sp^3 hybridized carbon-center radicals, and then they undergo addition across the $\text{C}=\text{C}$ bonds and Smiles rearrangement cascades. On this basis, we envisioned that by the addition of the external sulfonyl radicals across the $\text{C}=\text{C}$ bonds of the dienynes would arise an unprecedented cycloaddition reaction for the construction of new cyclic systems.

Here, we report an unprecedented copper-catalyzed $[3 + 2]/[3 + 2]$ carboannulation of dienynes with arylsulfonyl chlorides for diastereoselectively producing cyclopenta[a]indene-fused quinolinones (Scheme 1b). This method enables one-pot formation of four new $\text{C}-\text{C}$ bonds in a single step *via* radical addition cyclization, Smiles rearrangement and annulation cascades, and represents a new dienyne annulation mode to form two fused five-membered carbocyclic rings in a single step.

Results and discussion

We commenced our studies with the reaction of N -methyl-2-methylene- N -(2-(phenylethynyl)phenyl)but-3-enamide **1a** with 4-methylbenzenesulfonyl chloride **2a** in the presence of copper catalysts (Table 1). After investigating various reaction parameters, we were pleased to find that the $[3 + 2]/[3 + 2]$ carboannulation could be successfully achieved by a simple catalytic system composed of CuCl (10 mol%), Na_2CO_3 (3 equiv.), and mesitylene at 130 °C, leading to the formation of **3aa** in 58%

Table 1 Optimization of reaction conditions^a

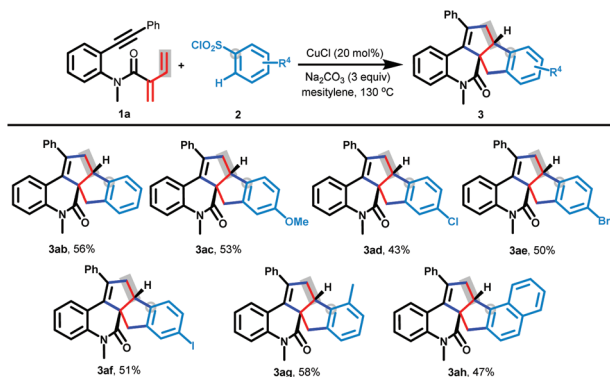


Entry	Variation from the optimal conditions	Yield (%) ^b
1	None	58 (46) ^c
2	CuBr instead of CuCl	13
3	Cu ₂ O instead of CuCl	36
4	CuOAc instead of CuCl	21
5	CuCl ₂ instead of CuCl	33
6	K ₂ CO ₃ instead of Na ₂ CO ₃	15
7	K ₃ PO ₄ instead of Na ₂ CO ₃	16
8	NaOAc instead of Na ₂ CO ₃	26
9	Cs ₂ CO ₃ instead of Na ₂ CO ₃	Trace
10	<i>o</i> -Xylene instead of mesitylene	40
11	<i>m</i> -Xylene instead of mesitylene	33
12	<i>p</i> -Xylene instead of mesitylene	35
13	DMF instead of mesitylene	0
14	At 120 °C	38
15	At 140 °C	49

^a Standard conditions: **1a** (0.15 mmol), **2a** (0.3 mmol), CuCl (20 mol%), Na_2CO_3 (3 equiv.), and mesitylene (1.5 mL) at 130 °C under a N_2 atmosphere for 12 h. Only the *cis*-diastereoisomer (dr >20 : 1) was obtained, which is determined by ¹H NMR and GC-MS analyses of the crude product. ^b Yield of the isolated product. ^c **1a** (1 mmol) and mesitylene (8 mL).

yield (entry 1). The structure of **3aa** was clearly confirmed by X-ray crystallography. Other alternative copper catalysts, including monovalent (CuBr , Cu_2O , and CuOAc) and bivalent copper salts (CuCl_2), did not give better results (entries 2–5). Further examination of other bases, including K_2CO_3 , K_3PO_4 , NaOAc , and Cs_2CO_3 , revealed that all of them were less effective than Na_2CO_3 (entries 6–9). Solvents were proved to have a vital effect on this reaction: using toluene derivatives such as *o*-xylene, *m*-xylene, and *p*-xylene as media could smoothly afford the target products, albeit with greatly reduced yields (entries 10–12). However, no desired product was observed when mesitylene was replaced by DMF as medium (entry 13). Finally, this reaction showed lower conversion efficiency on changing the reaction temperature to 120 °C or 140 °C (entries 14 and 15). Notably, we attempted to perform the reaction scaling up to 1 mmol of **1a**, delivering the product **3aa** in a 46% yield (entry 1).

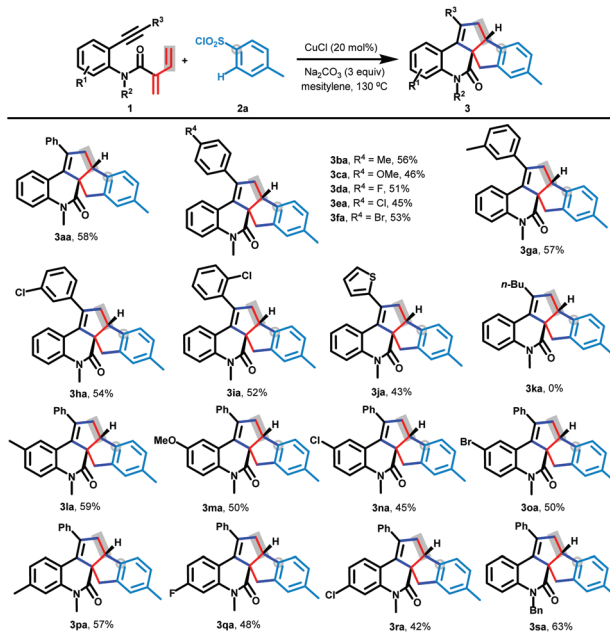
With the optimal reaction conditions identified, we set out to examine the substrate scope of this protocol with respect to arylsulfonyl chlorides. As shown in Scheme 2, a range of arylsulfonyl chlorides **2b–h** were subjected to $[3 + 2]/[3 + 2]$ carboannulation with aniline-linked conjugated dienynes **1a** to furnish the desired products **3ab–ah** in moderate yields. For example, benzenesulfonyl chloride could afford benzo[4,5]pentaleno[6a,1-c]quinolin-12-one **3ab** in a 56% yield. Electron-donating methoxy and methyl substituted sulfonyl chlorides were also competent substrates, delivering the target products in 53% and 58% yields (**3ac** and **3ag**). Importantly, halogen atom substituted sulfonyl chlorides at the *para*-position of the



Scheme 2 Variations of the arylsulfonyl chlorides (**2**). Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), CuCl (20 mol%), Na₂CO₃ (3 equiv.), and mesitylene (2 mL) at 130 °C under a N₂ atmosphere for 12 h; d.r. >20 : 1.

benzene ring were smoothly converted into products **3ad–af**, which could provide a promising opportunity for further manipulation. Gratifyingly, the reaction of naphthalene-1-sulfonyl chloride **2h** with **1a** proceeded favorably, resulting in a 47% yield of **3ah**.

We next turned our attention to the investigation of the scope of aniline-linked conjugated dienynes **1**. To our delight, the [3 + 2]/[3 + 2] carboannulation was applicable to a wide range of conjugated dienynes **1**, thus furnishing the target products **3ba–ta** in moderate yields (Scheme 3). Initially, the alkyne moiety of conjugated dienynes **1** was studied in detail.

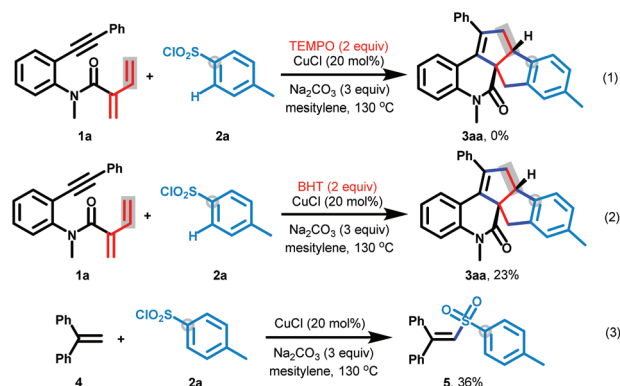


Scheme 3 Variations of the dienynes (**1**). Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), CuCl (20 mol%), Na₂CO₃ (3 equiv.), and mesitylene (2 mL) at 130 °C under a N₂ atmosphere for 12 h; d.r. >20 : 1.

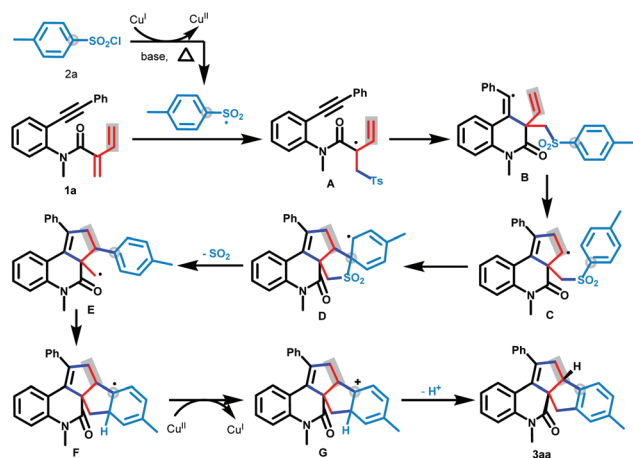
The reaction tolerated a variety of substrates **1b–i** with different aromatic substituents (4-MeC₆H₄, 4-OMeC₆H₄, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 3-MeC₆H₄, 3-ClC₆H₄, and 2-ClC₆H₄) at the alkyne terminus, furnishing pentacyclic-fused quinolin-12-one **3ba–ia** in moderate yields. The electronic and steric effects of substituents on the benzene ring had no significant influence on the cascade reaction. The heterocyclic thienyl group could also survive, delivering quinolin-12-one **3ja** in 43% yield. Unfortunately, chain alkynes did not give the desired product **3ka**. Afterward, we tested the variations in the aniline moiety. To our delight, various substituents such as electron-donating groups (Me and OMe) and electron-withdrawing groups (F, Cl, and Br) on the benzene ring were all well tolerated (**3la–ra**). When the methyl group on the nitrogen atom was replaced by a benzyl group, the anticipated product **3sa** could be obtained in 63% yield.

Several control experiments were carried out to explore if a radical process was involved in this reaction (Scheme 4). First, the formation of product **3aa** was greatly suppressed when a stoichiometric amount of radical inhibitors such as TEMPO and BHT was added to the model reaction of **1a** with **2a** under the standard conditions (eqn (1) and (2)). 1,1-Diphenyl ethylene **4** and 4-methylbenzenesulfonyl chloride **2a** were next subjected to the above optimal reaction conditions, leading to the generation of (2-tosylethene-1,1-diyl)dibenzene **5** in 36% yield (eqn (3)). These results indicated that the [3 + 2]/[3 + 2] carboannulation possibly involved a radical pathway, which was initiated by arylsulfonyl radicals generated from arylsulfonyl chlorides **2**.

On the basis of the above results and previous reports,¹⁰ a possible mechanism for the [3 + 2]/[3 + 2] carboannulation protocol is presented in Scheme 5. Initially, the reaction is triggered by a single electron transfer process of 4-methylbenzenesulfonyl chloride and Cu^I species under heating and basic conditions, thus producing 4-methylbenzenesulfonyl radicals and Cu^{II} species. Subsequently, the addition of the 4-methylbenzenesulfonyl radical to the C=C double bond of conjugated dienynes generates the allyl radical intermediate **A**, which continues to undergo a radical addition/annulation tandem reaction to form intermediate **C**. Then, the Smiles



Scheme 4 Mechanistic experiments.



Scheme 5 Proposed mechanism of [3 + 2]/[3 + 2] carboannulation.

rearrangement of intermediate C, including *ipso*-cyclization, 1,4-arylmigration, and SO₂-release, occurs to afford the alkyl radical intermediate E. The intramolecular radical addition to the vicinal benzene ring results in a cyclization of intermediate E to form intermediate F. Eventually, intermediate F undergoes a sequence of single electron oxidation with the Cu^{II} species and deprotonation to afford the desired fused pentacyclic product 3aa.

Conclusions

In summary, we have developed an unprecedented copper-catalyzed [3 + 2]/[3 + 2] carboannulation of dienyynes with arylsulfonyl chlorides *via* a radical Smiles rearrangement strategy. In this protocol, arylsulfonyl radicals generated from readily available arylsulfonyl chlorides undergo a radical cyclization/Smiles rearrangement/ring closure sequence to achieve [3 + 2]/[3 + 2] carbocyclization of dienyynes, thus providing cyclopenta[*a*]indene-fused quinolinone pentacyclic frameworks with excellent diastereoselectivity. Note that four C–C bonds can be formed by this complex radical cascade process. Further applications of the dienyynes are still in progress in our laboratory.

Conflicts of interest

The authors declare no competing interests.

Acknowledgements

The authors thank the National Natural Science Foundation of China (No. 21625203, 21871126, 21901071 and 21971061) and the Science and Technology Planning Project of Hunan Province (2018TP1017) for financial support.

Notes and references

- (a) C. Varela, K. Nilsson, M. Torneiro and A. Mourin, Synthesis of Tetracyclic Analogues of Calcitriol (1 α ,25-Dihydroxyvitamin D3) with Side-Chain-Locked Spatial Orientations at C(20), *Helv. Chim. Acta*, 2002, **85**, 3251–3261; (b) J. Holtsclaw and M. Koreeda, A Ring-Rearrangement Metathesis Approach toward the Synthesis of Cyclopenta- and Cyclohexa[*c*]indene Systems, *Org. Lett.*, 2004, **6**, 3719–3722; (c) E. Moman, D. Nicoletti and A. Mouriño, Strained Polycycles by H⁵C^{5x} Free-Radical Cascades, *Org. Lett.*, 2006, **8**, 1249–1251; (d) S. A. Snyder, in *Biomimetic Organic Synthesis*, ed. E. Poupon and B. Nay, Wiley-VCH, Weinheim, 2011; (e) B. S. Matsuura, M. H. Keylor, B. Li, Y. Lin, S. Allison, D. A. Pratt and C. R. J. Stephenson, A Scalable Biomimetic Synthesis of Resveratrol Dimers and Systematic Evaluation of their Antioxidant Activities, *Angew. Chem., Int. Ed.*, 2015, **54**, 3754–3757.
- (a) *Cycloaddition Reactions in Organic Synthesis*, ed. S. Kobayashi and K. A. Jorgensen, Wiley-VCH Verlag GmbH, Weinheim, Germany, 2002; (b) *Methods and Applications of Cycloaddition Reactions in Organic Syntheses*, ed. N. Nishiwaki, Wiley-VCH, Hoboken, 2014; (c) G. Dyker, Transition Metal Catalyzed Synthesis of Seven-Membered Carbocyclic Rings, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2223–2224; (d) M. Lautens, W. Klute and W. Tam, Transition Metal-Mediated Cycloaddition Reactions, *Chem. Rev.*, 1996, **96**, 49–92; (e) H.-W. Frühauf, Metal-Assisted Cycloaddition Reactions in Organotransition Metal Chemistry, *Chem. Rev.*, 1997, **97**, 523–596; (f) J.-J. Feng and J. Zhang, Synthesis of Unsaturated N-Heterocycles by Cycloadditions of Aziridines and Alkynes, *ACS Catal.*, 2016, **6**, 6651–6661; (g) H. Pellissier, Recent Developments in the [5 + 2] Cycloaddition, *Adv. Synth. Catal.*, 2018, **360**, 1551–1583; (h) P. Gandeepan, T. Mueller, D. Zell, G. Cera, S. Warratz and L. Ackermann, 3d Transition Metals for C–H Activation, *Chem. Rev.*, 2019, **119**, 2192–2452; (i) S. Rej, Y. Ano and N. Chatani, Bidentate Directing Groups: An Efficient Tool in C–H Bond Functionalization Chemistry for the Expedient Construction of C–C Bonds, *Chem. Rev.*, 2020, **120**, 1788–1887; (j) J.-H. Qin, J.-H. Li and D.-L. An, Recent Advances in Cycloaddition Reactions with Alkynes to Construct Heterocycles, *Synthesis*, 2020, **52**, 3818–3836.
- For reviews, see: (a) V. Michelet, P. Y. Toullec and J.-P. Genêt, Cycloisomerization of 1,*n*-Enynes: Challenging Metal-Catalyzed Rearrangements and Mechanistic Insights, *Angew. Chem., Int. Ed.*, 2008, **47**, 4268–4315; (b) L.-N. Wang and Z.-X. Yu, Transition-Metal-Catalyzed Cycloadditions for the Synthesis of Eight-Membered Carbocycles: an Update from 2010 to 2020, *Chin. J. Org. Chem.*, 2020, **40**, 3536–3558.
- For papers on Diels–Alder cycloaddition of dienyynes, see: (a) P. A. Wender and T. E. Jenkins, Nickel-catalyzed intramolecular [4 + 2] dienyne cycloadditions: an efficient new method for the synthesis of polycycles containing cyclo-

- hexa-1,4-dienes, *J. Am. Chem. Soc.*, 1989, **111**, 6432–6434; (b) R. S. Jolly, G. Luedtke, D. Sheehan and T. Livinghouse, Novel cyclization reactions on transition metal templates. The catalysis of intramolecular [4 + 2] cycloadditions by low-valent rhodium complexes, *J. Am. Chem. Soc.*, 1990, **112**, 4965–4966; (c) S. R. Gilbertson, G. S. Hoge and D. G. Genov, Rhodium-Catalyzed Asymmetric [4 + 2] Cycloisomerization Reactions, *J. Org. Chem.*, 1998, **63**, 10077–10080; (d) S.-J. Paik, S. U. Son and Y. K. Chung, Highly Efficient Intra- and Intermolecular [4 + 2] Cycloaddition Reaction Catalyzed by Rhodium Complex, *Org. Lett.*, 1999, **1**, 2045–2047; (e) B. Wang, P. Cao and X. Zhang, An efficient Rh-catalyst system for the intramolecular [4 + 2] and [5 + 2] cycloaddition reactions, *Tetrahedron Lett.*, 2000, **41**, 8041–8044; (f) D. Motoda, H. Kinoshita, H. Shinokubo and K. Oshima, Phosphane-Free Rhodium Catalyst in an Anionic Micellar System for [4 + 2] Annulation of Dienes, *Angew. Chem., Int. Ed.*, 2004, **43**, 1860–1862; (g) S. I. Lee, S. Y. Park, J. H. Park, I. G. Jung, S. Y. Choi, Y. K. Chung and B. Y. Lee, Rhodium *N*-Heterocyclic Carbene-Catalyzed [4 + 2] and [5 + 2] Cycloaddition Reactions, *J. Org. Chem.*, 2006, **71**, 91–96; (h) S. M. Kim, J. H. Park and Y. K. Chung, Au(PPh₃)OPOF₂-catalyzed intramolecular [4 + 2] cycloaddition reaction of dienes, *Chem. Commun.*, 2011, **47**, 6719–6722; (i) N. J. Kramer, T. T. Hoang and G. B. Dudley, Reaction Discovery Using Neopentylene-Tethered Coupling Partners: Cycloisomerization/Oxidation of Electron-Deficient Dienes, *Org. Lett.*, 2017, **19**, 4636–4639.
- 5 For papers on intramolecular cycloisomerization/Cope rearrangement of dienes, see: (a) H. Kusama, Y. Onizawa and N. Iwasawa, W(CO)₅(L)-Catalyzed Tandem Intramolecular Cyclopropanation/Cope Rearrangement for the Stereoselective Construction of Bicyclo[5.3.0]decane Framework, *J. Am. Chem. Soc.*, 2006, **128**, 16500–16501; (b) A. Furstner and C. C. Stimson, Two Manifolds for Metal-Catalyzed Intramolecular Diels-Alder Reactions of Unactivated Alkynes, *Angew. Chem., Int. Ed.*, 2007, **46**, 8845–8849; (c) Y. Onizawa, M. Hara, T. Hashimoto, H. Kusama and N. Iwasawa, Synthetic Studies on and Mechanistic Insight into [W(CO)₅(L)]-Catalyzed Stereoselective Construction of Functionalized Bicyclo[5.3.0]decane Frameworks, *Chem. – Eur. J.*, 2010, **16**, 10785–10796; (d) S. Y. Kim, Y. Park and Y. K. Chung, Sequential Platinum-Catalyzed Cycloisomerization and Cope Rearrangement of Dienes, *Angew. Chem., Int. Ed.*, 2010, **49**, 415–418; (e) Z. Cao and F. Gagosz, Gold-Catalyzed Tandem Cycloisomerization/Cope Rearrangement: An Efficient Access to the Hydroazulenic Motif, *Angew. Chem., Int. Ed.*, 2013, **52**, 9014–9018; (f) P.-J. Cai, Y. Wang, C.-H. Liu and Z.-X. Yu, Gold(I)-Catalyzed Polycyclization of Linear Dienes to Seven-Membered Ring-Containing Polycycles via Tandem Cyclopropanation/Cope Rearrangement/C-H Activation, *Org. Lett.*, 2014, **16**, 5898–5901; (g) Y. Wang, P.-J. Cai and Z.-X. Yu, Mechanistic Study on Gold-Catalyzed Cycloisomerization of Dienes Involving Aliphatic C-H Functionalization and Inspiration for Developing a New Strategy to Access Polycarbocycles, *J. Am. Chem. Soc.*, 2020, **142**, 2777–2786.
- 6 For papers on intermolecular [4 + 2 + x] carboannulation of dienes, see: (a) A. Padwa, K. E. Krumpe, Y. Gareau and U. Chiacchio, Rhodium(III)-Catalyzed Cyclization Reactions of Alkynyl-Substituted α -DiazoKetones, *J. Org. Chem.*, 1991, **56**, 2523–2530; (b) D. F. Harvey and K. P. Lund, Cyclization Reactions of a Molybdenum Carbene Complex with 1,3-Nonadien-8-yne, *J. Am. Chem. Soc.*, 1991, **113**, 5066–5068; (c) D. F. Harvey, E. M. Grenzer and P. K. Gantzel, Effect of Alkene Substituents on Molybdenum and Chromium Carbene Complex Mediated Cyclization Reactions, *J. Am. Chem. Soc.*, 1994, **116**, 6719–6732; (d) S. R. Gilbertson and B. DeBoef, Rhodium Catalyzed [4 + 2 + 2] Cycloaddition and Alkyne Insertion: A New Route to Eight-Membered Rings, *J. Am. Chem. Soc.*, 2002, **124**, 8784–8785; (e) Y. Ni and J. Montgomery, An Efficient [4 + 2 + 1] Entry to Seven-Membered Rings, *J. Am. Chem. Soc.*, 2004, **126**, 11162–11163; (f) Y. Ni and J. Montgomery, Synthetic Studies and Mechanistic Insight in Nickel-Catalyzed [4 + 2 + 1] Cycloadditions, *J. Am. Chem. Soc.*, 2006, **128**, 2609–2614; (g) B. DeBoef, W. R. Counts and S. R. Gilbertson, Rhodium-Catalyzed Synthesis of Eight-Membered Rings, *J. Org. Chem.*, 2007, **72**, 799–804; (h) S. Saito, K. Maeda, R. Yamasaki, T. Kitamura, M. Nakagawa, K. Kato, I. Azumaya and H. Masu, Synthesis of Nine-Membered Carbocycles by the [4 + 3 + 2] Cycloaddition Reaction of Ethyl Cyclopropylideneacetate and Dienes, *Angew. Chem., Int. Ed.*, 2010, **49**, 1830–1833; (i) R. Yamasaki, M. Ohashi, K. Maeda, T. Kitamura, M. Nakagawa, K. Kato, T. Fujita, R. Kamura, K. Kinoshita, H. Masu, I. Azumaya, S. Ogoshi and S. Saito, Ni-Catalyzed [4 + 3 + 2] Cycloaddition of Ethyl Cyclopropylideneacetate and Dienes: Scope and Mechanistic Insights, *Chem. – Eur. J.*, 2013, **19**, 3415–3425; (j) I. Sasaki, T. Ohmura and M. Sugimoto, Construction of Silicon-Containing Seven-Membered Rings by Catalytic [4 + 2 + 1] Cycloaddition through Rhodium Silylenoid, *Org. Lett.*, 2020, **22**, 2961–2966.
- 7 For selected reviews, see: (a) A. Studer and M. Bossart, Radical aryl migration reactions, *Tetrahedron*, 2001, **57**, 9649–9667; (b) Z.-M. Chen, X.-M. Zhang and Y.-Q. Tu, Radical aryl migration reactions and synthetic applications, *Chem. Soc. Rev.*, 2015, **44**, 5220–5245; (c) C. M. Holden and M. F. Greaney, Modern Aspects of the Smiles Rearrangement, *Chem. – Eur. J.*, 2017, **23**, 8992–9008.
- 8 (a) W. Kong, M. Casimiro, E. Merino and C. Nevado, Copper-Catalyzed One-Pot Trifluoromethylation/Aryl Migration/Desulfonylation and C(sp²)-N Bond Formation of Conjugated Tosyl Amides, *J. Am. Chem. Soc.*, 2013, **135**, 14480–14483; (b) W. Kong, M. Casimiro, N. Fuentes, E. Merino and C. Nevado, Metal-Free Aryltrifluoromethylation of Activated Alkenes, *Angew. Chem., Int. Ed.*, 2013, **52**, 13086–13090; (c) W. Kong, E. Merino and C. Nevado, Arylphosphonylation and Arylazidation of Activated Alkenes, *Angew. Chem., Int. Ed.*,

- 2014, **53**, 5078–5082; (d) N. Fuentes, W. Kong, L. Fernandez-Sanchez, E. Merino and C. Nevado, Cyclization Cascades via N-Amidyl Radicals toward Highly Functionalized Heterocyclic Scaffolds, *J. Am. Chem. Soc.*, 2015, **137**, 964–973; (e) W. Kong, N. Fuentes, A. García-Domínguez, E. Merino and C. Nevado, Stereoselective Synthesis of Highly Functionalized Indanes and Dibenzocycloheptadienes through Complex Radical Cascade Reactions, *Angew. Chem., Int. Ed.*, 2015, **54**, 2487–2491.
- 9 For selected examples, see: (a) M. Pudlo, I. Allart-Simon, B. Tinant, S. Gérard and J. Sapi, First domino radical cyclisation/Smiles rearrangement combination, *Chem. Commun.*, 2012, **48**, 2442–2445; For other selected examples, see: (b) Z. He, P. Tan, C. Ni and J. Hu, Fluoroalkylative Aryl Migration of Conjugated N-Arylsulfonylated Amides Using Easily Accessible Sodium Di- and Monofluoroalkanesulfinates, *Org. Lett.*, 2015, **17**, 1838–1841; (c) H. Zhang, C. Pan, N. Jin, Z. Gu, H. Hu and C. Zhu, Metal-free cascade construction of C-C bonds by activation of inert C(sp³)-H bonds, *Chem. Commun.*, 2015, **51**, 1320–1323; (d) Y.-L. Zhu, B. Jiang, W.-J. Hao, J.-K. Qiu, J. Sun, D.-C. Wang, P. Wei, A.-F. Wang, G. Li and S.-J. Tu, Catalytic Arylsulfonyl Radical Triggered 1,7-Enyne Bicyclizations, *Org. Lett.*, 2015, **17**, 6078–6081; (e) Z. Ni, X. Huang and Y. Pan, Metal-Free Mediated Meerwein-Type Reaction: A Radical Cascade Arylation/Aryl Migration/Desulfonylation of Conjugated Alkenes, *Org. Lett.*, 2016, **18**, 2612–2615; (f) F.-L. Tan, R.-J. Song, M. Hu and J.-H. Li, Metal-Free Oxidative 1,2-Arylmethylation Cascades of N-(Arylsulfonyl) acrylamides Using Peroxides as the Methyl Resource, *Org. Lett.*, 2016, **18**, 3198–3201; (g) X.-F. Xia, S.-L. Zhu, C. Chen, H. Wang and Y.-M. Liang, Silver-Catalyzed Decarboxylative Addition/Cyclization of Activated Alkenes with Aliphatic Carboxylic Acids, *J. Org. Chem.*, 2016, **81**, 1277–1284; (h) K. Liu, L.-C. Sui, Q. Jin, D.-Y. Li and P.-N. Liu, CuBr-mediated radical cascade difluoroacetamidation of acrylamides using α,α -difluoro- α -(TMS)-acetamides, *Org. Chem. Front.*, 2017, **4**, 1606–1611; (i) H. Huang and Y. Li, Sustainable Difluoroalkylation Cyclization Cascades of 1,8-Enynes, *J. Org. Chem.*, 2017, **82**, 4449–4457; (j) D. M. Whalley, H. A. Duong and M. F. Greaney, Alkene Carboarylation through Catalyst-Free, Visible Light-Mediated Smiles Rearrangement, *Chem. – Eur. J.*, 2019, **25**, 1927–1930; (k) M. Li, C.-T. Wang, Q.-F. Bao, Y.-F. Qiu, W.-X. Wei, X.-S. Li, Y.-Z. Wang, Z. Zhang, J.-L. Wang and Y.-M. Liang, Copper-Catalyzed Radical Aryl Migration Approach for the Preparation of Cyanoalkylsulfonylated Oxindoles/Cyanoalkyl Amides, *Org. Lett.*, 2021, **23**, 751–756.
- 10 (a) J. Zheng, Y. Li, J. Han, T. Xiong and Q. Zhang, Radical cascade reaction of alkynes with N-fluoroarylsulfonimides and alcohols, *Nat. Commun.*, 2015, **6**, 7011–7019; (b) E. Brachet, L. Marzo, M. Selkti, B. König and P. Belmont, Visible light amination/Smiles cascade: access to phthalazine derivatives, *Chem. Sci.*, 2016, **7**, 5002–5006; (c) Z.-S. Wang, Y.-B. Chen, H.-W. Zhang, Z. Sun, C. Zhu and L.-W. Ye, Ynamide Smiles Rearrangement Triggered by Visible-Light-Mediated Regioselective Ketyl-Ynamide Coupling: Rapid Access to Functionalized Indoles and Isoquinolines, *J. Am. Chem. Soc.*, 2020, **142**, 3636–3644; (d) J. Yan, H. W. Cheo, W. K. Teo, X. Shi, H. Wu, S. B. Idres, L.-W. Deng and J. Wu, A Radical Smiles Rearrangement Promoted by Neutral Eosin Y as a Direct Hydrogen Atom Transfer Photocatalyst, *J. Am. Chem. Soc.*, 2020, **142**, 11357–11362; (e) J. J. Douglas, H. Albright, M. J. Sevrin, K. P. Cole and C. R. J. Stephenson, A Visible-Light-Mediated Radical Smiles Rearrangement and its Application to the Synthesis of a Difluoro-Substituted Spirocyclic ORL-1 Antagonist, *Angew. Chem., Int. Ed.*, 2015, **54**, 14898–14902; (f) D. Alpers, K. P. Cole and C. R. J. Stephenson, Visible Light Mediated Aryl Migration by Homolytic C-N Cleavage of Aryl Amines, *Angew. Chem., Int. Ed.*, 2018, **57**, 12167–12170.
- 11 (a) T. M. Monos, R. C. McAtee and C. R. J. Stephenson, Arylsulfonylacetamides as bifunctional reagents for alkene aminoarylation, *Science*, 2018, **361**, 1369–1373; (b) J. Yu, Z. Wu and C. Zhu, Efficient Docking-Migration Strategy for Selective Radical Difluoromethylation of Alkenes, *Angew. Chem., Int. Ed.*, 2018, **57**, 17156–17160; (c) M. Wang, H. Zhang, J. Liu, X. Wu and C. Zhu, Radical Monofluoroalkylative Alkynylation of Olefins by a Docking-Migration Strategy, *Angew. Chem., Int. Ed.*, 2019, **58**, 17646–17650; (d) J. Liu, S. Wu, J. Yu, C. Lu, Z. Wu, X. Wu, X.-S. Xue and C. Zhu, Polarity Umpolung Strategy for the Radical Alkylation of Alkenes, *Angew. Chem., Int. Ed.*, 2020, **59**, 8195–8202; (e) H. Zhang, M. Wang, X. Wu and C. Zhu, Heterocyclization Reagents for Rapid Assembly of N-Fused Heteroarenes from Alkenes, *Angew. Chem., Int. Ed.*, 2021, **60**, 3714–3719.