Check for updates

How to cite: *Angew. Chem. Int. Ed.* **2024**, *63*, e202317299
doi.org/10.1002/anie.202317299

Organic Chemistry

Hydrated [3+2] Cyclotelomerization of Butafulvenes to Create Multiple Contiguous Fully Substituted Carbon Centers

*Bo-Chao Zhou, Bing-Zhi Chen, Ting-Ting Song, Yang Yang, Li-Ming Zhang, Ding-Wei Ji, Boshun Wan, and Qing-An Chen**

Abstract: The construction of multiple continuous fully substituted carbon centers, which serve as unique structural motif in natural products, is a challenging topic in organic synthesis. Herein, we report a hydrated [3+2] cyclotelomerization of butafulvenes to create contiguous fully substituted carbon backbone. In the presence of scandium triflate, all-carbon skeleton with spiro fused tricyclic ring can be constructed in high diastereoselectivity by utilizing butafulvene as the synthon. Mechanistic studies suggest that this atom-economic reaction probably proceeds through a synergistic process containing butafulvenes dimerization and nucleophilic attack by water. In addition, the tricyclic product can undergo a series of synthetic derivatizations, which highlights the potential applications of this strategy. The recyclability of $Sc(OTf)_3$ has also been demonstrated to show its robust performance in this hydrated cyclotelomerization.

Introduction

Fully substituted carbon, possessing sp^3-rich chemical space, is a predominant structural feature of natural products and drugs, which accounts for one of the most synthetically challenging blocks due to its conformational rigidity and bulky three-dimensional environment.[1] The synthetic difficulty increases exponentially when continuous fully substituted carbon centers moieties are present and even embedded in polyfused/bridged ring systems.[2] Using traditional synthetic strategy, the construction of uninterrupted multiple fully substituted carbon core frameworks required well-designed routes but consumed a lot of time and materials to accomplish (Figure 1a).[3]

During the past decade, owing to the significant progress in synthetic methodologies, several strategies for the construction of vicinal fully substituted carbon centers have been documented.[4] The traditional approach to obtain multiple contiguous fully substituted carbon centers (three and more) generally relies on stepwise introduction of fully substituted carbon centers onto pre-prepared substrate containing fully substituted carbon through multistep synthesis process.[5] To date, there have been rare reports on the one-pot synthesis of multiple contiguous fully substituted carbon frameworks, and reported methods primarily focused on light-induced cycloadditions (Figure 1b). For example, in 2018 and 2020 respectively, Bach and Dell'Amico groups achieved the synthesis of three contiguous fully substituted carbon centers polyfused rings products via intermolecular [2+2] dearomative cycloadditions.[6] Subsequently, You and Xu groups developed intramolecular [4+2]/[2+2] dearomative cycloaddition to access three and four contiguous fully substituted carbon centers using pre-designed substrates.[7] Therefore, the development of a new approach to create contiguous multiple fully substituted carbon center frameworks in one step is still highly desirable.

Owing to their varied structural diversity and conformational constraints, five-membered carbocycles containing fully substituted carbon center are prevalent and play significant roles in natural compounds and drugs.[8] Hence, their synthesis is always an important topic in organic synthesis. A commonly employed strategy is to effectuate [3+2] cycloaddition reactions via the alignment of polarities between 1,3-dipoles and dipolarophiles. Common 1,3-dipoles have been classified into the following categories (i) the zwitterionic allyl-palladium intermediates,[9] (ii) the phosphine-allenoate zwitterionic intermediates,[10] and (iii) the zwitterionic intermediates for ring-opening of cyclopropanes.[11] Butafulvene is a constitutional isomer of benzene, featuring a triple conjugated system that providing numerous potential reaction sites. Collaborating with Ma group, our group have reported an efficient synthesis of butafulvenes from readily available materials under Pd-catalysis.[12] Herein, we employed butafulvene as a synthon to create a polycyclic scaffold featuring multiple continuous fully substituted carbon centers via a hydrated [3+2] cyclotelomerization reaction, thus achieving a transformation from 2D to 3D molecular structures.

Results and Discussion

Initially, unsymmetric butafulvene (**1a**) was chosen as the model substrate to optimize the reaction condition (Ta-

[*] B.-C. Zhou, B.-Z. Chen, T.-T. Song, Y. Yang, L.-M. Zhang, D.-W. Ji, B. Wan, Q.-A. Chen
Dalian Institute of Chemical Physics, Chinese Academy of Sciences
457 Zhongshan Road, Dalian 116023 (China)
E-mail: qachen@dicp.ac.cn
Homepage: www.lbcs.dicp.ac.cn
B.-C. Zhou, B.-Z. Chen, L.-M. Zhang, B. Wan, Q.-A. Chen
University of Chinese Academy of Sciences
Beijing 100049 (China)

© 2023 Wiley-VCH GmbH

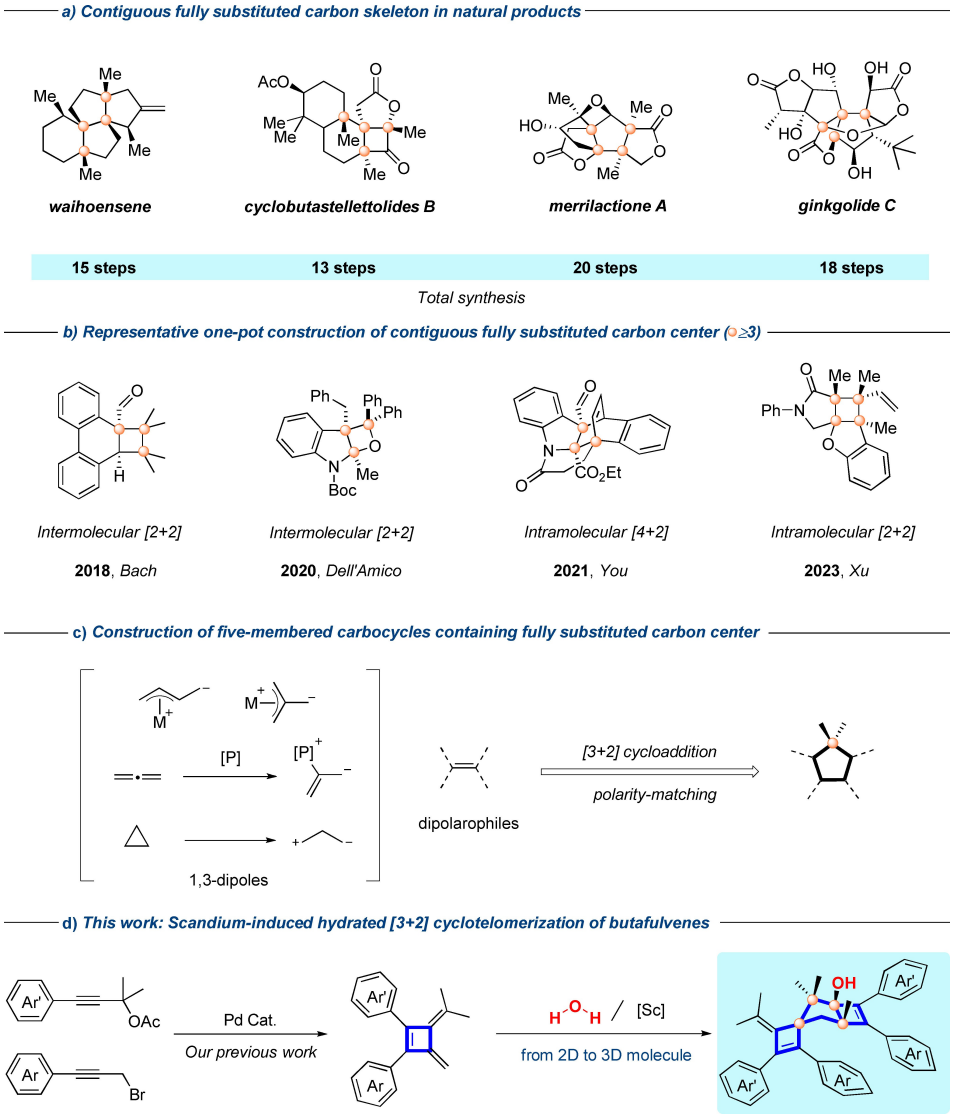


Figure 1. Hydrated [3+2] cyclotelomerization of butafulvenes.

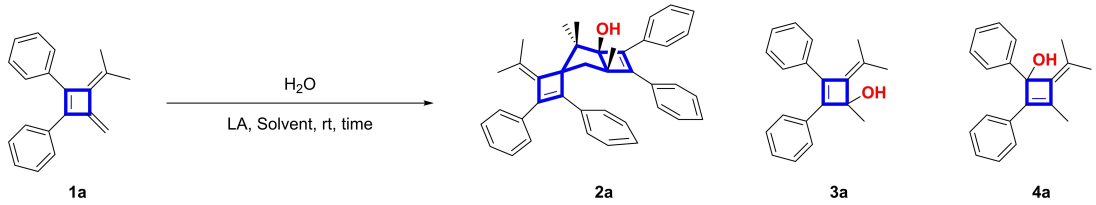
ble 1). When the reaction was performed in MeCN at room temperature (rt) for 12 h with $In(OTf)_3$ as a promoter, hydrated telomer **2a** was obtained in 48 % yield, together with trace amount of cyclobutanol **3a**/**4a** (Entry 1). The structure of **2a** was confirmed by single-crystal X-ray crystallography (CCDC: 2282886).[13] The further investigation on the Lewis acids (LA) indicated that $Sc(OTf)_3$ was the best promoter (Entries 2–5). No better result was observed from the evaluation of other solvents (Entries 6–8). When the loading of $Sc(OTf)_3$ was increased to 1.0 eq., the yield of the hydrated telomer **2a** was greatly improved to 86 % (Entries 9–11). While adding additional 1.0 eq. H_2O to the reaction system, the yield of **2a** was decreased to 56 % accompanied by some side product **3a** (Entry 12). To our delight, the use of naphthalene additive could significantly enhance the solubility of **1a** in acetonitrile (Entry 13), which shortened the reaction time to 6 h and further increased the yield of **2a** to 98 % (isolated yield 89 %). Without the presence of naphthalene, the solubility of **1a** decreased and only gave desired product **2a** in 50 % yield (Entry 14). The use of other aromatic additives such as toluene, benzene and chlorobenzene gave lower yields (see the Supporting Information, Table S2 for details).

With the optimized conditions in hand, we then evaluated the substrate scope for this scandium-induced hydrated [3+2] cyclotelomerization of substituted butafulvenes (Figure 2). Unsymmetric butafulvenes **1** bearing methyl group at the *para* and *meta* positions of phenyl motif, afforded the products **2b**–**2c** in moderate yields. Due to the steric cumbrance, the substrate with *ortho*-methyl substitution (**2d**) was delivered only in 25 % yield. Replacing methyl with other alkyl groups, such as ethyl (**2e**) and *tert*-butyl (**2f**), the substituted butafulvenes were amenable under the standard condition, giving target products in 67 % and 39 % yields, respectively. The reaction of substrates with halogen substituents all proceeded smoothly to afford the desired products in 55–83 % yields (**2g**–**2j**). The presence of strong electron-donating group (OMe) still gave the product **2k** in

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Optimization of Reaction Conditions.



1a **2a** **3a** **4a**

Entry	Lewis acid	Solvent[a]	Time	2a (%)	3a (%)	4a (%)
1	$In(OTf)_3$ (0.20 eq.)	MeCN	12 h	48	<5	<5
2	$Sc(OTf)_3$ (0.20 eq.)	MeCN	12 h	64	<5	<5
3	$AlCl_3$ (0.20 eq.)	MeCN	12 h	<5	<5	<5
4	$BF_3 \cdot Et_2O$ (0.20 eq.)	MeCN	12 h	nd	5	<5.
5	$Zn(OTf)_2$ (0.20 eq.)	MeCN	12 h	nd	nd	nd
6	$Sc(OTf)_3$ (0.20 eq.)	DCM	12 h	30	<5	<5
7	$Sc(OTf)_3$ (0.20 eq.)	MeOH	12 h	nd	nd	nd
8[c]	$Sc(OTf)_3$ (0.20 eq.)	THF	12 h	16	<5	<5
9	$Sc(OTf)_3$ (0.50 eq.)	MeCN	12 h	68	<5	<5
10	$Sc(OTf)_3$ (1.00 eq.)	MeCN	12 h	86	<5	<5
11	$Sc(OTf)_3$ (1.25 eq.)	MeCN	12 h	80	<5	<5
12[d]	$Sc(OTf)_3$ (1.00 eq.)	MeCN	12 h	56	8	<5
13[e]	$Sc(OTf)_3$ (1.00 eq.)	MeCN	6 h	98 (89)[b]	<5	<5
14	$Sc(OTf)_3$ (1.00 eq.)	MeCN	6 h	50	<5	<5

Standard condition: **1a** (0.10 mmol), $Sc(OTf)_3$ (0.10 mmol), naphthalene (0.05 mmol), MeCN (1.0 mL), rt, 6 h. Yields were determined by ^1H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [a]Water content of MeCN or THF = 0.16 mmol/mL or 0.027 mmol/mL. [b]Isolated yield. [c]Water content of THF = 0.027 mmol/mL, additional H_2O (0.10 mmol) was added. [d]Additional H_2O (0.10 mmol) was added. [e]Naphthalene = 0.05 mmol. nd = no detection.

42 % yield. However, substrates with electron-withdrawing groups, such as Ac and CO_2Me, delivered the products **2l** and **2m** respectively in decreased yields. When introducing a phenyl at the *para* position of the benzene ring, a highly aryl substituted spiro product **2n** could be obtained in 53 % yield. The structure of **2h** was further confirmed by single-crystal X-ray crystallography.

Subsequently, substituent effect on the upper aromatic ring of unsymmetric butafulvenes **5** was investigated (Figure 3). The presence of alkyl groups, such as methyl, ethyl, *tert*-butyl, at the *para* and *meta* positions were all tolerated to give the products in decent yields (**6a–6d**). Substrates possessing halides were also compatible under current standard reaction conditions (**6e–6f**). The presence of strong electron-withdrawing group delivered product **6g** in a low yield. However, highly aryl substituted spiro product **6h** was obtained in a higher yield. The presence of 1-naphthyl group led to the formation of a pair of diastereoisomers (**6i**). Naturally abundant 1,3-benzodioxole motif was compatible to give the target product **6j** in 58 % yield. Probably owing to the weakened coordination ability heteroatom with $Sc(OTf)_3$, substrates with the thienyl group underwent the current reaction inefficiently (**6k–6l**). When a phenyl group was introduced onto the exocyclic double bond of butafulvenes **5**, it reacted at the cyclic olefinic bond to give a different regioisomer **6m**. Replacing methyl with bulky *n*-propyl group (**6n**) led to a decrease in reactivity. The reaction with alkyl-substituted butafulvene **5o** failed to yield the corresponding product. The structures of **6f** and **6m** were further confirmed by single-crystal X-ray crystallography.

Corresponding control experiments were carried out to shed light on mechanistic insights (Figure 4). A mixture of butafulvene **1g**, $Sc(OTf)_3$ (1.0 eq.) and naphthalene (0.5 eq.) in MeCN were stirred for 6 h, and the desired product **2g** was obtained in 83 % yield (Figure 4a, Entry 1). No conversion was found in the absence of $Sc(OTf)_3$, indicating its indispensable role (Figure 4a, Entry 2). The product **2g** was formed in only a slightly decreased yield (80 %) without naphthalene. It is attributed to the influence of the *para*-F substituent on increasing the solubility of **1g** in MeCN during the reaction process (Figure 4a, Entry 3). When adding additional H_2O (0.1 mmol), a significant decrease on the yield of **2g** was observed. Meanwhile, it increased the formation of side product **3g** (Figure 4a, Entry 4). As expected, no reaction occurred by adding 50 mg 4 Å molecular sieve (Figure 4a, Entry 5). Then, an isotopic labeling experiment was conducted to determine the origin of oxygen atom on **2g**. When additional $H_2{}^{18}O$ (98 atom% ^{18}O) was added to the reaction system, 56 % yield of **2g** with 42 % ^{18}O-labeled incorporation was obtained (Figure 4a, Entry 6 and see the Supporting Information, Figure S1 and S2 for details).

Kinetic studies were conducted to further figure out the reaction process. With the increase of the reaction time, the yield of **2g** increased slowly and the trace product **3g** was detected during this period (Figure 4b-I). As shown in Figure 4b-II, the product yields of **1g** and **2g** exhibited a gradual increase when **3g** was consumed, ultimately culminating around 4.5 h. Control experiments have indicated **3a** could be transformed back to butafulvene **1a** under acidic condition (see the Supporting Information, Table S4 for

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

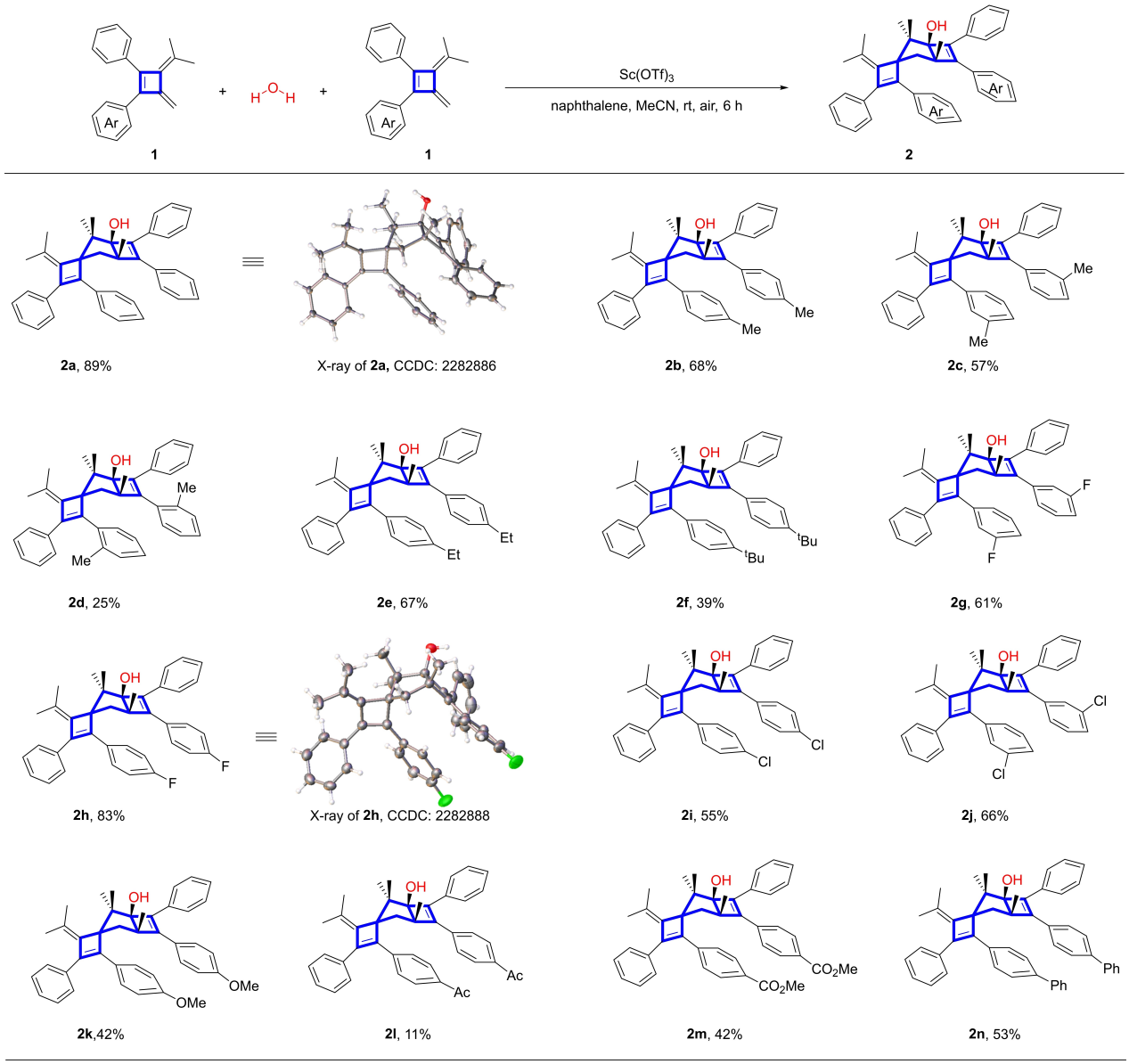


Figure 2. Substrate scope for unsymmetric butafulvenes **1**. Conditions: **1** (0.20 mmol), $Sc(OTf)_3$ (0.20 mmol), naphthalene (0.10 mmol), MeCN (2.0 mL), air, rt, 6 h. Water content of MeCN = 0.16 mmol/mL.

details). These results not only indicate alcohol **3** is not a necessary intermediate in the reaction, but also suggest that a potential reversible pathway between starting material **1** and side product **3**.

Based on the mechanistic investigations and previous works,[14] a proposed mechanism is shown in Figure 4c. Initially, butafulvene **1a** coordinates with $Sc(OTf)_3$ to form intermediate **A**. A subsequent electrophilic addition of intermediate **A** and another butafulvene **1a** releases trifluoromethanesulfonic anion and generates the complex **B**. Then, the complex **B** undergoes a ring-closure process through intramolecular electrophilic addition to furnish carbocation **C**. Next, the trifluoromethanesulfonic anion coordinates with the scandium in carbocation **C** to produce the zwitterionic intermediate **D**. Meanwhile, H_2O coordinates the scandium atom in the zwitterionic intermediate **D** to afford the hydration Sc complex **E**. A final protonolysis of the hydration Sc complex **E** delivers the target product **2a**. The diastereoselectivity is probably regulated by steric repulsion of phenyl group and close packing of ion pairs based on density functional theory (DFT) calculations (see the Supporting Information, Figure S3 for details). It is notable that intermediate **A** could also be hydrated to afford side product cyclobutanol **3a**. However, a reversal dehydration of cyclobutanol **3a** will regenerate **1a** to reenter the desired main reaction. Due to potential steric hindrance of phenyl group on exocyclic double bond of **5m**, another molecular **5m** will attack the formed **5m**-Sc complex in an 1,4-conjugated fashion to afford a different regioisomer **6m**.

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

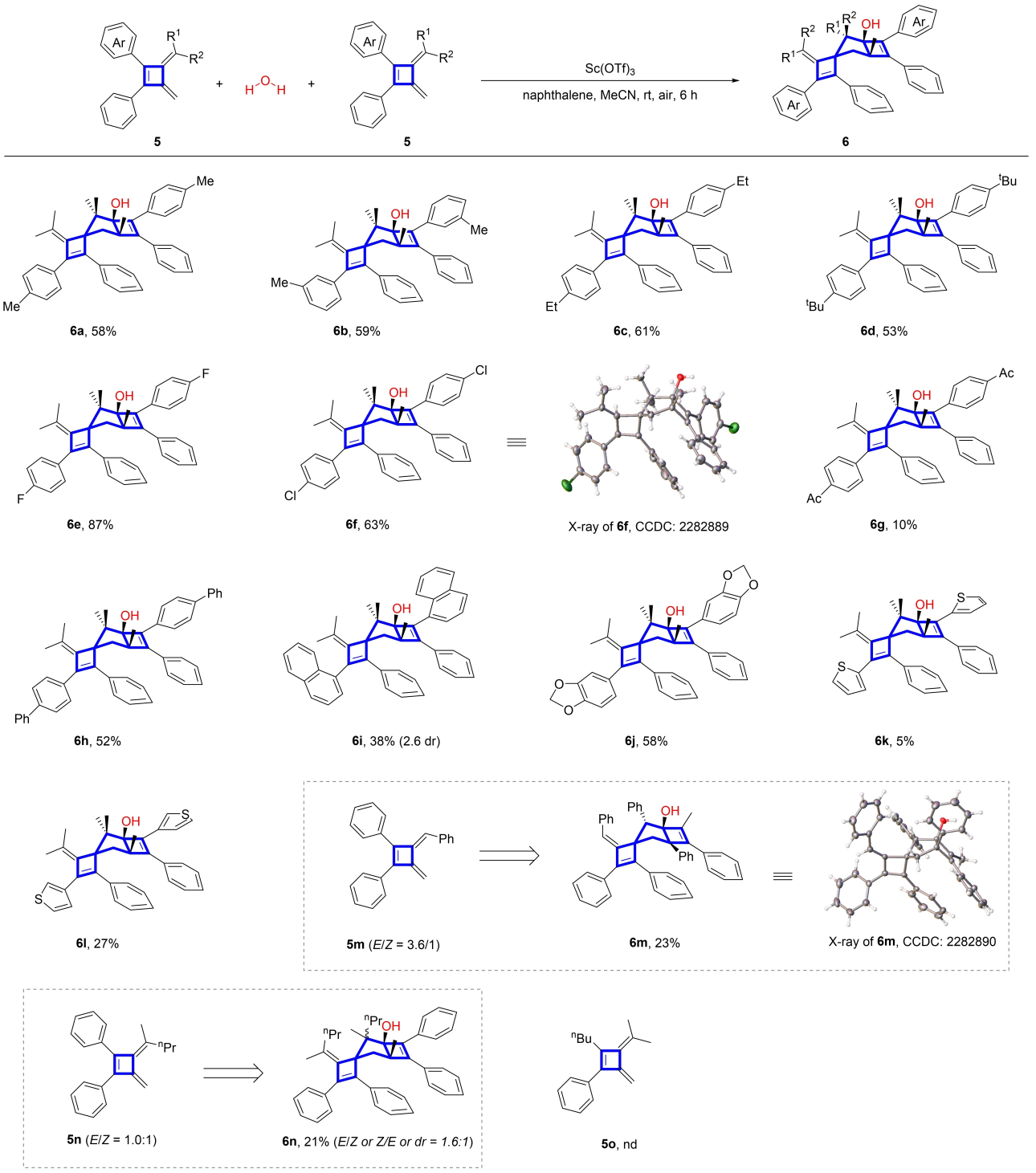


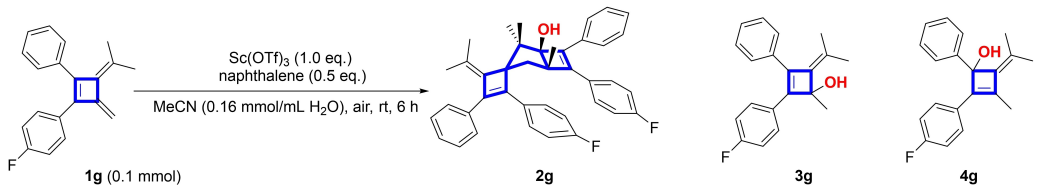
Figure 3. Substrate scope for unsymmetric butafulvenes **5**. Conditions: **5** (0.20 mmol), $Sc(OTf)_3$ (0.20 mmol), naphthalene (0.10 mmol), MeCN (2.0 mL), air, rt, 6 h. Water content of MeCN = 0.16 mmol/mL.

To further demonstrate the synthetic utility of this cyclotelomerization process, scale-up experiment and additional transformations were carried out. As shown in Figure 5a, the target product **2a** was successfully isolated in 1.05 g with 78 % yield under the standard condition. A methyl protection on hydroxyl group of **2a** occurred smoothly to afford a sterically-congested product **7** in 61 % yield.[15] In the presence of NaN_3, the nucleophilic substitution of **2a** efficiently delivered the azide product **8** in 41 % yield.[16] On the other hand, the epoxidation reaction of exocyclic double bond also proceeded efficiently with *m*-CPBA to give epoxide **9** in 65 % yield.[17] In addition, the

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

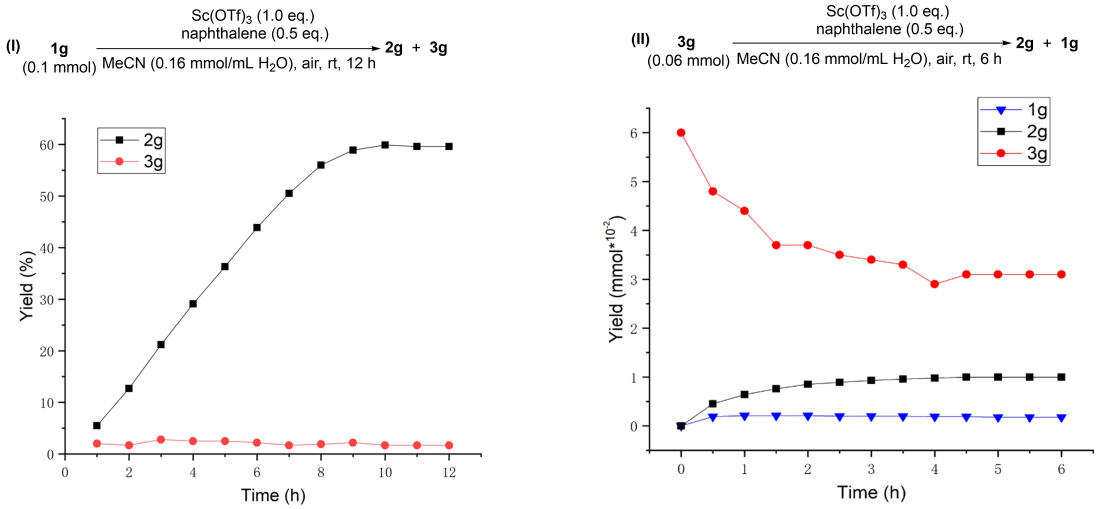
a) Control experiments



Entry	deviation from standard condition	yield of **2g**	yield of **3g**	yield of **4g**
1	none	83%	<5%	<5%
2	no $Sc(OTf)_3$	nd	nd	nd
3	no naphthalene	80%	<5%	<5%
4	with extra H_2O (0.10 mmol)	32%	12%	<5%
5	4 Å MS (50 mg)	nd	nd	nd
6	with extra $H_2{}^{18}O$ (0.10 mmol, N_2)	56% (42% ^{18}O)	15% (23% ^{18}O)	<5%

Yield was determined by ^1H NMR analysis of crude mixture.

b) Kinetic studies



c) Proposed mechanism

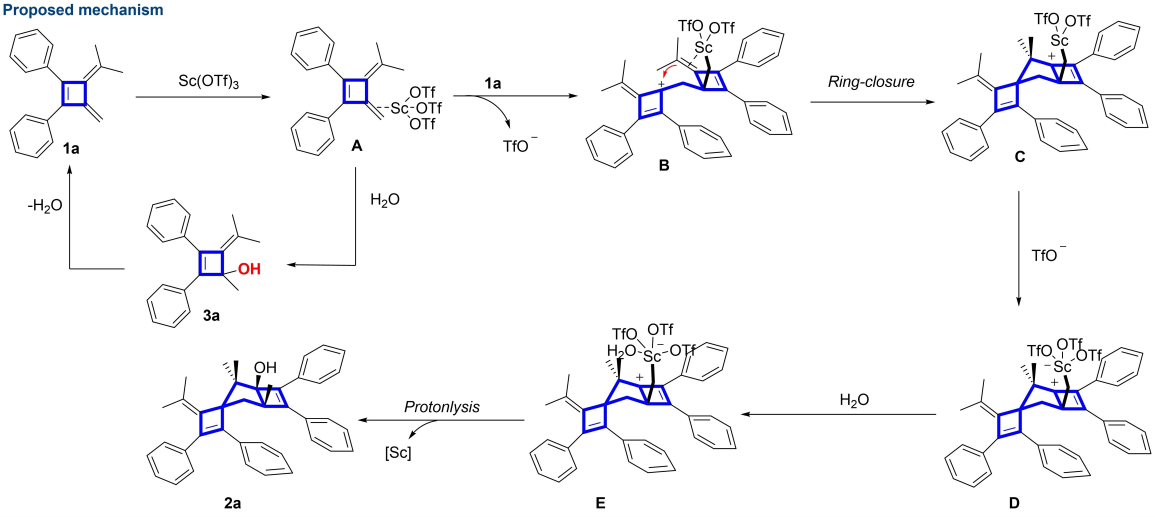


Figure 4. Mechanistic studies and proposed mechanism.

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

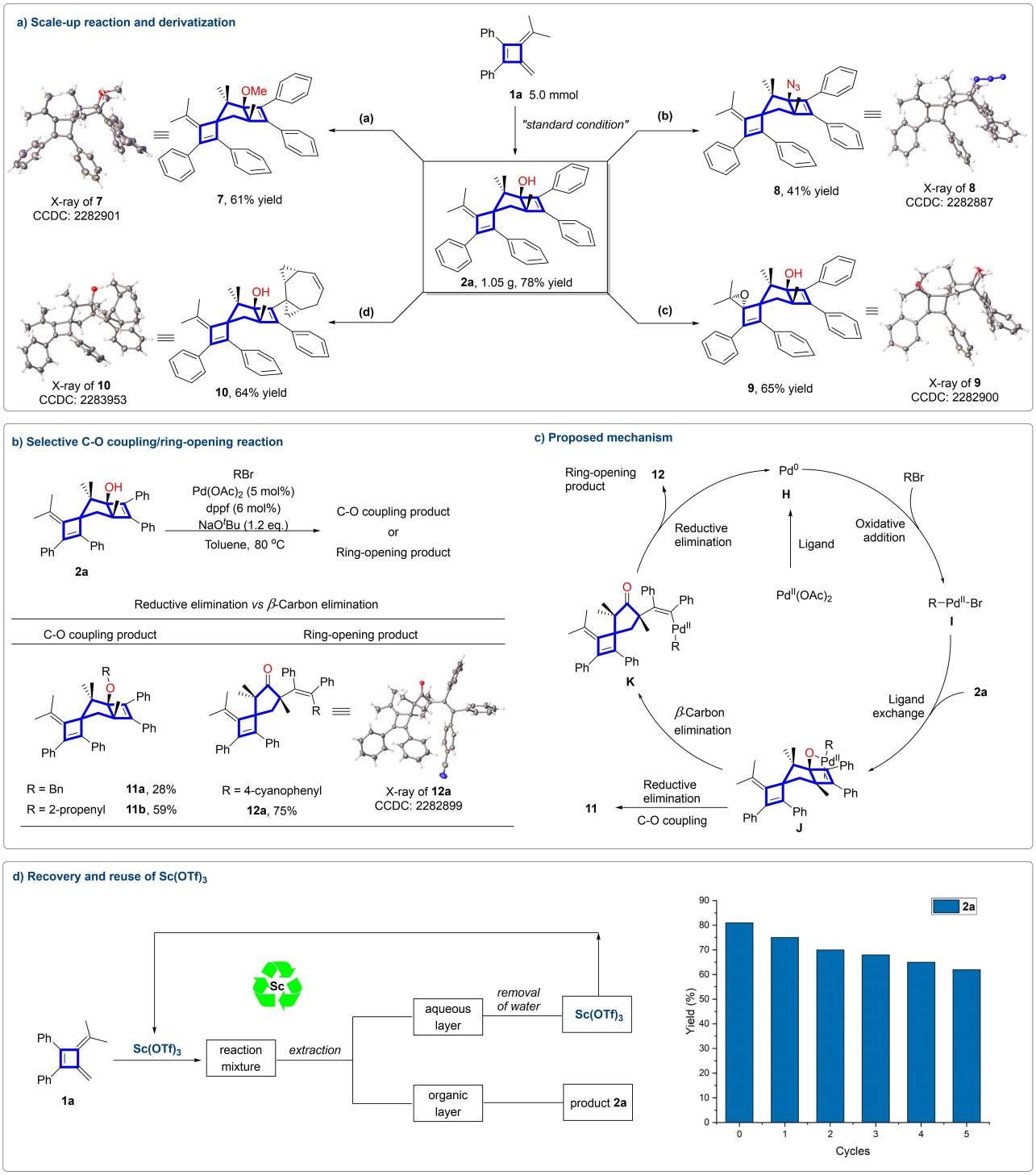


Figure 5. Scale up preparation and synthetic transformations. Conditions: (a) **2a** (0.10 mmol), NaH (0.3 mmol), CH_3I (0.3 mmol), DMF (1.0 mL), rt, N_2. (b) **2a** (0.10 mmol), NaN_3 (0.22 mmol), TFA (0.84 mmol), DCM (1.0 mL), 0 °C, N_2, 3 h. (c) **2a** (0.10 mmol), *m*-CPBA (0.11 mmol), $NaHCO_3$ (0.11 mmol), DCM/H_2O (1.5 mL, 1/1), 0 °C, N_2, 16 h. (d) **2a** (0.10 mmol), CH_2I_2 (0.40 mmol), Et_2Zn (0.40 mmol), DCM (1.0 mL), rt, N_2, 6 h. Yield of **10** was determined by ^1H NMR.

Simmons–Smith reaction of **2a** furnished dearomative cyclopropanation ring expansion product **10** with 64 % yield. This unexpected site selectivity control of the dearomative cyclopropanation may be attributed to the coordination between the hydroxyl group and the metal. Moreover, product **2a** underwent a selective C–O coupling/ring-opening reaction with organic bromide under Pd catalysis (Figure 5b).[18] When R was Bn or 2-propenyl, C–O coupling products **11a** and **11b** were delivered in 28 % and 59 % yields, respectively. Additionally, **2a** could selectively give ring-opening

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

product **12a** in 75 % yield through β-carbon elimination with phenyl bromide. It probably resulted from the stronger migration ability of phenyl group. Therefore, a plausible mechanism was proposed to interpret this chemoselectivity switch (Figure 5c). First, $Pd(OAc)_2$ is reduced to Pd^0 **H** by ligand,[19] which then undergoes oxidative addition with bromide to afford the Pd^{II} species **I**. A subsequent ligand exchange of Pd^{II} species **I** with **2a** generates the oxypalladium complex **J**. When R is an alkyl or alkenyl group, the oxypalladium complex **J** experiences direct reductive elimination, resulting in the formation of C–O coupling product **11**. Bearing phenyl instead of alkyl or alkenyl group, β-carbon elimination of the oxypalladium complex **J** proceeds to produce the intermediate **K**, which gives the ring-opening product **12** and regenerates catalyst Pd^0 **H**.

It is known that $Sc(OTf)_3$ exhibits higher solubility in water than organic solvent. Therefore, it could be recovered with nearly quantitative yield from the aqueous layer after the completion of the reaction under mild conditions (Figure 5d).[20] With the recovered $Sc(OTf)_3$, we have demonstrated its performance with up to 5 recycles for this hydrated cyclotelomerization. And no significant loss of the reactivity was observed during recyclability trial.

Conclusion

In summary, we have developed a hydrated [3+2] cyclotelomerization strategy for one-pot construction of multiple continuous fully substituted carbon centers. This protocol employed butafulvenes as synthon and $Sc(OTf)_3$ as recyclable promoter to deliver tricyclic skeleton compounds. Mechanistic studies showed that the hydration product of monobutafulvene was not the intermediate during the reaction process and the hydroxyl group in the product was derived from water. The synthetic utility of the cyclotelomerization products is demonstrated in a scale-up experiment and a series of transformations. The recyclability of $Sc(OTf)_3$ has also been demonstrated to show its robust performance in this hydrated cyclotelomerization.

Supporting Information

The authors have cited additional references within the Supporting Information[21–28] and crystallographic data are available in the Supporting Information and listed within reference [13].

Acknowledgements

Financial support from Dalian Institute of Chemical Physics (DICP I202309), Dalian Outstanding Young Scientific Talent (2020RJ05), and National Natural Science Foundation of China (22071239) is greatly appreciated.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Butafulvene · Cyclotelomerization · Fully Substituted Carbon · Hydration · Spiro Compound

[1] a) J. A. Burkhard, G. Wuitschik, M. Rogers-Evans, K. Müller, E. M. Carreira, *Angew. Chem. Int. Ed.* **2010**, *49*, 9052–9067; b) T. T. Talele, *J. Med. Chem.* **2020**, *63*, 13291–13315.

[2] a) M. Büschleb, S. Dorich, S. Hanessian, D. Tao, K. B. Schenthal, L. E. Overman, *Angew. Chem. Int. Ed.* **2016**, *55*, 4156–4156; b) A. Eggert, C. Etling, D. Lubken, M. Saxarra, M. Kalesse, *Molecules* **2020**, *25*, 3841; c) Z. Xin, H. Wang, H. He, S. Gao, *Tetrahedron Lett.* **2021**, *71*, 153029.

[3] a) S. A. Kolesnikova, E. G. Lyakhova, A. I. Kalinovsky, D. V. Berdyshev, E. A. Pislyagin, R. S. Popov, B. B. Grebnev, T. N. Makarieva, C. V. Minh, V. A. Stonik, *J. Nat. Prod.* **2019**, *82*, 3196–3200; b) Y. Qu, Z. Wang, Z. Zhang, W. Zhang, J. Huang, Z. Yang, *J. Am. Chem. Soc.* **2020**, *142*, 6511–6515; c) Y. Shen, L. Li, X. Xiao, S. Yang, Y. Hua, Y. Wang, Y. W. Zhang, Y. Zhang, *J. Am. Chem. Soc.* **2021**, *143*, 3256–3263; d) Z. Zhang, S. Chen, F. Tang, K. Guo, X. T. Liang, J. Huang, Z. Yang, *J. Am. Chem. Soc.* **2021**, *143*, 18287–18293; e) M. Hébert, G. Bellavance, L. Barriault, *J. Am. Chem. Soc.* **2022**, *144*, 17792–17796.

[4] a) R. Long, J. Huang, J. Gong, Z. Yang, *Nat. Prod. Rep.* **2015**, *32*, 1584–1601; b) F. Zhou, L. Zhu, B. W. Pan, Y. Shi, Y. L. Liu, J. Zhou, *Chem. Sci.* **2020**, *11*, 9341–9365; c) D. Pierrot, I. Marek, *Angew. Chem. Int. Ed.* **2020**, *59*, 36–49; d) P. Yan, J. Zhang, L. Lu, H. Fang, P. Lu, *ACS Catal.* **2022**, *12*, 15416–15423.

[5] a) C. G. Watson, A. Balanta, T. G. Elford, S. Essafi, J. N. Harvey, V. K. Aggarwal, *J. Am. Chem. Soc.* **2014**, *136*, 17370–17373; b) R. Alam, C. Diner, S. Jonker, L. Eriksson, K. J. Szabó, *Angew. Chem. Int. Ed.* **2016**, *55*, 14417–14421.

[6] a) S. Stegbauer, C. Jandl, T. Bach, *Angew. Chem. Int. Ed.* **2018**, *57*, 14593–14596; b) J. Mateos, A. Vega-Peñaloza, P. Franceschi, F. Rigodanza, P. Andreetta, X. Companyó, G. Pelosi, M. Bonchio, L. Dell'Amico, *Chem. Sci.* **2020**, *11*, 6532–6538.

[7] a) M. Zhu, H. Xu, X. Zhang, C. Zheng, S. L. You, *Angew. Chem. Int. Ed.* **2021**, *60*, 7036–7040; b) X. Wang, F. Liu, T. Xu, *Chin. Chem. Lett.* **2023**, *34*, 107624.

[8] a) D. Bora, A. Kaushal, N. Shankaraiah, *Eur. J. Med. Chem.* **2021**, *215*, 113263; b) A. Deepthi, M. Mohan, M. C. Balachandran, *SynOpen* **2022**, *6*, 270–285.

[9] a) Y. Zheng, T. Qin, W. Zi, *J. Am. Chem. Soc.* **2021**, *143*, 1038–1045; b) C. Gao, T. Zhang, X. Li, J.-D. Wu, J. Liu, *Org. Chem. Front.* **2022**, *9*, 2121–2128; c) J. Du, Y.-F. Li, C.-H. Ding, *Chin. Chem. Lett.* **2023**, *34*, 108401; d) H. Sun, Y. He, W. Guo, *Org. Chem. Front.* **2022**, *9*, 4861–4866; "(3+2) Cycloadditions Via Zwitterionic π-Allylmetal Species": e) B. Mao, H. Guo, *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering*, Elsevier, Amsterdam, **2022**; f) B. Niu, Y. Wei, M. Shi, *Org. Chem. Front.* **2021**, *8*, 3475–3501.

[10] a) Y. Wei, M. Shi, *Org. Chem. Front.* **2017**, *4*, 1876–1890; b) H. Ni, W. L. Chan, Y. Lu, *Chem. Rev.* **2018**, *118*, 9344–9411; c) H. Guo, Y. C. Fan, Z. Sun, Y. Wu, O. Kwon, *Chem. Rev.* **2018**,

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

118, 10049–10293; d) H. Li, Y. Lu, *Asian J. Org. Chem.* **2017**, *6*, 1130–1145.
[11] a) S. Chandrasekaran, V. Ganesh, *Synthesis* **2016**, *48*, 4347–4380; b) D. K. Brownsey, E. Gorobets, D. J. Derksen, *Org. Biomol. Chem.* **2018**, *16*, 3506–3523; c) V. Pirenne, B. Muriel, J. Waser, *Chem. Rev.* **2021**, *121*, 227–263; d) N. Radhoff, C. G. Daniliuc, A. Studer, *Angew. Chem. Int. Ed.* **2023**, *62*, e202304771.
[12] X. Huang, B. Z. Chen, P. Li, D. W. Ji, J. Liu, H. Zheng, S. N. Yang, Y. C. Hu, B. Wan, X. P. Hu, C. Fu, Y. Huang, J. Zheng, Q. A. Chen, S. Ma, *Nat. Chem.* **2022**, *14*, 1185–1192.
[13] Deposition numbers 2282886 (for **2a**), 2282888 (for **2h**), 2282889 (for **6f**), 2282890 (for **6m**), 2282901 (for **7**), 2282887 (for **8**), 2282900 (for **9**), 2283953 (for **10**) and 2282899 (for **12a**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.
[14] a) J. Dai, J. Wu, G. Zhao, W. M. Dai, *Chem. Eur. J.* **2011**, *17*, 8290–8293; b) S. Tang, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2020**, *142*, 5980–5984.
[15] M. Mazur, B. Dymek, R. Koralewski, P. Sklepkiewicz, S. Olejniczak, M. Mazurkiewicz, M. Piotrowicz, M. Salamon, K. Jedrzejczak, A. Zagozdzon, W. Czestkowski, K. Matyszewski, B. Borek, A. Bartoszewicz, E. Pluta, A. Rymaszewska, W. Mozga, F. Stefaniak, P. Dobrzanski, K. Dzwonek, J. Golab, A. Golebiowski, J. Olczak, *J. Med. Chem.* **2019**, *62*, 7126–7145.
[16] M. Kapoor, P. Chand-Thakuri, M. C. Young, *J. Am. Chem. Soc.* **2019**, *141*, 7980–7989.
[17] Y. Han, A. Qin, Q. Zhang, X. Zhang, H. Qian, S. Ma, *Angew. Chem. Int. Ed.* **2022**, *61*, e202211635.
[18] M. Palucki, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1996**, *118*, 10333–10334.
[19] a) Z. Csákai, R. Skoda-Földes, L. Kollár, *Inorg. Chim. Acta* **1999**, *286*, 93–97 ; b) C. Amatore, L. El Kaïm, L. Grimaud, A. Jutand, A. Meignié, G. Romanov, *Eur. J. Org. Chem.* **2014**, 4709–4713.
[20] S. Kobayashi, *Eur. J. Org. Chem.* **1999**, 15–27.
[21] M. J. Frisch, et al., Gaussian 16, Revision C01, Gaussian, Inc., Wallingford CT, **2016**.
[22] F. Furche, J. P. Perdew, *J. Chem. Phys.* **2006**, *124*, 044103.
[23] a) F. Weigend, *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057–1065; b) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.
[24] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104.
[25] M. Walker, A. J. Harvey, A. Sen, C. E. Dessent, *J. Phys. Chem. A* **2013**, *117*, 12590–12600.
[26] K. Eichkorn, F. Weigend, O. Treutler, R. Ahlrichs, *Theor. Chem. Acc.* **1997**, *97*, 6.
[27] A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 19.
[28] C. Y. Legault, CYLview, 1.0b, Universite de Sherbrooke, Quebec, Montreal, Canada, **2009**.

Manuscript received: November 14, 2023
Accepted manuscript online: December 17, 2023
Version of record online: January 2, 2024

© 2023 Wiley-VCH GmbH

15213773, 2024, 6, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/anie.202317299 by Dalian Institute Of Chemical, Wiley Online Library on [01/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License