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# Intermolecular oxidative decarbonylative [2 + 2 + 2] carbocyclization of *N*-(2-ethynylaryl)acrylamides with tertiary and secondary alkyl aldehydes involving C(sp<sup>3</sup>)-H functionalization†

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A new metal-free oxidative decarbonylative [2 + 2 + 2] carbocyclization of *N*-(2-ethynylaryl)acrylamides with tertiary and secondary alkyl aldehydes is described. This reaction enables the formation of three new C–C bonds in a single reaction by a sequence of oxidative decarbonylation, radical addition across C–C unsaturated bonds, C–H functionalization and annulation, and represents the first oxidative decarbonylative [2 + 2 + 2] carbocyclization approach using tertiary and secondary alkyl aldehydes as a two carbon unit for assembling six-membered carbocycle-fused polycycles.

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## Introduction

High-order carbocyclization reactions represent one of the most powerful methods for building complex carbocyclic frameworks. In this field, one particularly fascinating area is the intermolecular [2 + 2 + *m*] carbocyclization of 1,*n*-enynes, which continues to gain much attention due to its straightforward and highly atom-economic features.<sup>1–4</sup> Significant achievements include the [2 + 2 + 2] carbocyclization strategy which can allow the formation of a six-membered carbocycle within a complex polycyclic system by introducing a two-carbon unit across 1,*n*-enynes.<sup>2,3</sup> Despite these advances, there are still limitations with the available transformations, such as the requirement for noble metal catalysts and narrow two-carbon unit scope (*e.g.*, alkynes,<sup>3a–e</sup> alkenes<sup>3h–m</sup> and arylsulfonyl chlorides<sup>3n</sup>). Therefore, it would be welcomed to develop more efficient methods, especially metal-free use of new two-carbon unit strategies, to achieve the [2 + 2 + 2] carbocyclization of 1,*n*-enynes, which unfortunately remains a great challenge.

The decarbonylation reaction has proven among the most important methods for the formation of diverse chemical bonds in synthesis, the majority of which focus on the cleavage of C–CHO bonds by extrusion of carbon monoxide (CO) gas and

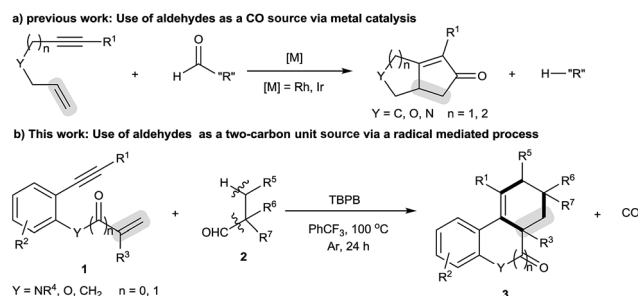
then transformation through radical<sup>5</sup> and anionic intermediates.<sup>6,7</sup> Such successful transformations include transition metal-catalyzed Pauson–Khand-type reactions of 1,*n*-enynes using aldehydes as the carbon monoxide (CO) source (Scheme 1a).<sup>7</sup> To our knowledge, however, approaches for carbocyclization of 1,*n*-enynes with aldehydes as the “R” source have never been reported.<sup>5g</sup> Intrigued by these results, we envisioned that extension of the decarbonylation concept to the combination of *N*-(2-ethynylaryl)acrylamides and alkyl aldehydes would offer a novel method to assemble six-membered carbocycle-fused polycyclic architectures. Herein, we report a novel oxidative radical decarbonylative [2 + 2 + 2] carbocyclization of *N*-(2-ethynylaryl)acrylamides with tertiary and secondary alkyl aldehydes that can be achieved under metal-free conditions through a sequence of oxidative decarbonylation, radical addition across C–C unsaturated bonds, C–H functionalization and annulation (Scheme 1b).<sup>10</sup> To the best of our knowledge, this method is the first metal-free radical-mediated decarbonylative [2 + 2 + 2] carbocyclization reaction of *N*-(2-ethynylaryl)acrylamides with

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Scheme 1 [2 + 2 + *m*] carbocyclization of 1,*n*-enynes with aldehydes.



tertiary alkyl aldehydes as a two carbon unit, which provides selective and straightforward access to important six-membered carbocycle-fused polycyclic skeletons, including tetrahydrophenanthridin-6(5*H*)-ones, 6*H*-indeno[1,2-*c*]quinolin-6-one, 6*H*-benzo[*c*]chromen-6-one and 1*H*-fluorene.<sup>9</sup> Moreover, this reaction is applicable to secondary alkyl aldehydes and the selectivity is shifted towards the decarbonylative [2 + 2 + 1] carbocyclization with *N*-(2-ethynyl)acrylamides.

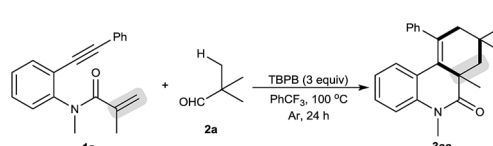
## Results and discussion

Our initial investigations focused on optimization of the decarbonylative [2 + 2 + 2] carbocyclization between *N*-methyl-*N*-(2-(phenylethynyl)phenyl)methacrylamide (**1a**) and pivalaldehyde (**2a**) (Table 1).<sup>11</sup> When amide **1a** and aldehyde **2a** were subjected to *tert*-butyl perbenzoate (TBPB) oxidation in PhCF<sub>3</sub> at 100 °C for 24 h, the desired decarbonylative [2 + 2 + 2] carbocyclization product **3aa** was obtained in 81% yield (entry 1). Inspired by this result, a series of other oxidants, including *tert*-butyl hydroperoxide (TBHP), di-*tert*-butyl peroxide (DTBP) and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, were examined (entries 2–4): they showed lower activity for the reaction than TBPB in terms of yields. A screening of the amount of TBPB revealed that 3 equiv. of TBPB was the best choice for further optimization (entries 5 and 6). We found that while a higher reaction temperature (110 °C) slightly affected the reaction (entry 7), a lower reaction temperature (90 °C) had an obviously negative effect (entry 8). Other solvents, including MeCN (entry 9), MeCONMe<sub>2</sub> (entry 10) and PhCl (entry 11), were found to be less effective than PhCF<sub>3</sub>, thus giving diminished yields. Gratifyingly, the reaction could

be satisfactorily performed at a 1 gram scale of amide **1a**, providing **3aa** in moderate yield (entry 12).

The scope of this decarbonylative [2 + 2 + 2] carbocyclization protocol was probed with regard to both the *N*-(2-ethynyl)acrylamide **1** and aldehyde **2** (Table 2). Gratifyingly, a variety of *N*-(2-ethynyl)acrylamides **1b–s** underwent the reaction with pivalaldehyde (**2a**) and TBPB to afford phenanthridin-6(5*H*)-ones **3** in moderate to good yields. We found that amides **1b–e** bearing a wide range of *N*-substituents, such as *N*-Bn, *N*-allyl, *N*-Ts and even free *N*-H, were viable substrates to assemble **3ba–ea** in moderate yields. With respect to the alkyne moiety in *N*-(2-ethynyl)acrylamides, the reaction was perfectly tolerant of various aryl substituents, namely 4-MeC<sub>6</sub>H<sub>4</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>, 4-BrC<sub>6</sub>H<sub>4</sub>, 4-ClC<sub>6</sub>H<sub>4</sub>, 4-FC<sub>6</sub>H<sub>4</sub>, 4-CNC<sub>6</sub>H<sub>4</sub>, 3-MeC<sub>6</sub>H<sub>4</sub>, 3-BrC<sub>6</sub>H<sub>4</sub> and pyridin-3-yl groups, at the terminal alkyne, and the nature of the aryl group had no detrimental effect on the reaction (**3fa–na**).<sup>11</sup> It was noted that in the case of the alkyl-substituted alkyne **1o** a moderate yield of the product (**3oa**) was still achieved. It is important to emphasize that amides **1p–r** with substituents, such as Me and Cl, on the 4- or 5-position of the *N*-aryl moiety were smoothly converted to **3pa–ra** in 70–75% yields. To our surprise, amide **1s** with a phenyl group on the 2-position of the acrylamide moiety shifted the selectivity towards

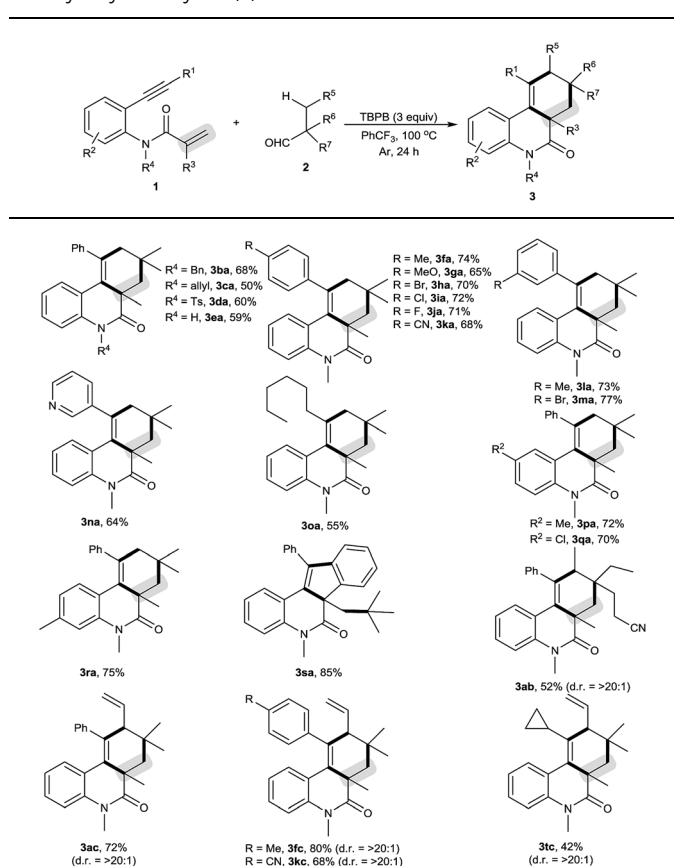
Table 1 Screening of optimal reaction conditions<sup>a</sup>



Entry	Variation from the standard conditions	Isolated yield (%)
1	None	81
2	TBHP instead of TBPB	10
3	DTBP instead of TBPB	22
4	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub> instead of TBPB	Trace
5	TBPB (3.5 equiv.)	80
6	TBPB (2.5 equiv.)	71
7	At 110 °C	80
8	At 90 °C	62
9	MeCN instead of PhCF <sub>3</sub>	67
10	MeCONMe <sub>2</sub> instead of PhCF <sub>3</sub>	20
11	PhCl instead of PhCF <sub>3</sub>	40
12 <sup>b</sup>	None	73

<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (2 equiv.), TBPB (3 equiv.), PhCF<sub>3</sub> (2 mL), argon, 100 °C for 24 h. TBHP (5 M in decane). Some by-products, including vinyl C–N bond-decomposition products, were observed. <sup>b</sup> **1a** (1 g, 3.64 mmol) and PhCF<sub>3</sub> (5 mL) for 48 h.

Table 2 Carbocyclization of *N*-(2-ethynyl)acrylamides (**1**) with tertiary alkyl aldehydes (**2**)<sup>a</sup>



<sup>a</sup> Reaction conditions: **1** (0.2 mmol), **2a** (2 equiv.), TBPB (3 equiv.), PhCF<sub>3</sub> (2 mL), argon, 100 °C for 24 h.

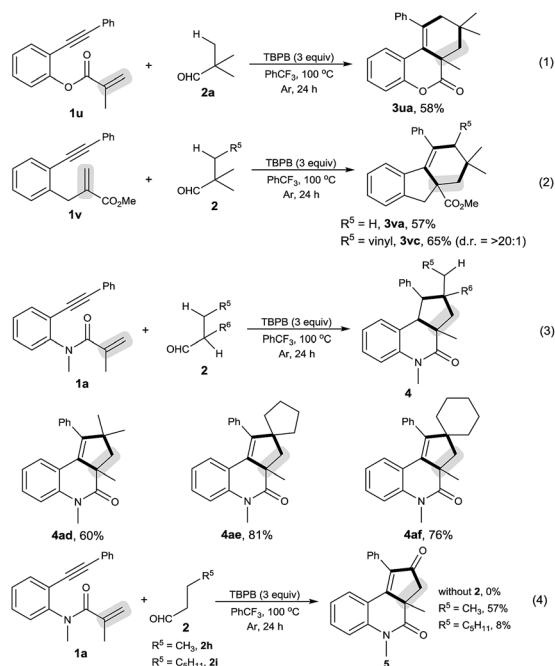


functionalization of the phenyl C(sp<sup>2</sup>)-H bond, not the *tert*-butyl C(sp<sup>3</sup>)-H bond, thus furnishing 6*H*-indeno[1,2-*c*]quinolin-6-one **3sa** rather than the phenanthridin-6(5*H*)-one.

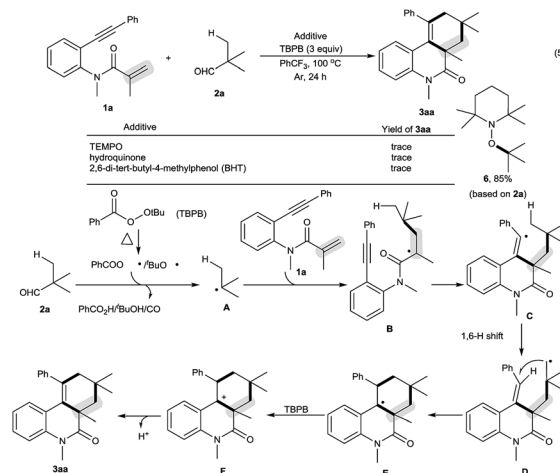
In the presence of amide **1a** and TBPB, tertiary alkyl aldehydes, namely 3-ethyl-3-formylpentanenitrile (**2b**) and 2,2-dimethylpent-4-enal (**2c**), were also found to be viable substrates to produce the decarbonylative [2 + 2 + 2] carbocyclization products **3ab** and **3ac**. Notably, in the case of 2,2-dimethylpent-4-enal (**2c**) the functionalization of the more active allyl C(sp<sup>3</sup>)-H bond takes precedence over the methyl C(sp<sup>3</sup>)-H bond: 2,2-dimethylpent-4-enal (**2c**) successfully underwent the reaction with *N*-(2-ethynylaryl)acrylamides **1f**, **1k** and **1t**, affording **3fc**, **3kc** and **3tc** in moderate to good yields with high diastereoselectivity.

As shown in Scheme 2, the decarbonylative [2 + 2 + 2] carbocyclization protocol also allowed the formation of useful 6*H*-benzo[*c*]chromen-6-one **3ua** (eqn (1)) and 1*H*-fluorenes **3va** and **3vc** (eqn (2)) from the corresponding 2-(phenylethynyl)phenyl methacrylate (**1u**) and methyl 2-(2-(phenylethynyl)benzyl)acrylate (**1v**), but a linear enyne, 4-methyl-*N*-(2-methylallyl)-*N*-(3-phenylprop-2-yn-1-yl)-benzenesulfonamide (**1w**), was not a suitable substrate.

We found that secondary alkyl aldehydes **2d-f** were viable substrates to perform the decarbonylative carbocyclization reaction, but the selectivity was shifted towards the functionalization of the C(sp<sup>3</sup>)-H bond adjacent to the aldehyde group, resulting in the construction of five-membered carbocycle-fused polycyclic skeletons (eqn (3)). For example, isobutyraldehyde (**2d**) underwent the decarbonylative [2 + 2 + 1] carbocyclization reaction to afford 4*H*-cyclopenta[*c*]quinolin-4-one **4ad** in 60% yield. Using cyclopentanecarbaldehyde (**2e**) or cyclohexanecarbaldehyde (**2f**)



Scheme 2 Variation of other 1,*n*-enynes and secondary alkyl aldehydes.



Scheme 3 Control experiments and possible reaction mechanism.

also delivered the decarbonylative [2 + 2 + 1] carbocyclization products **4ae** and **4af** with a spirocyclic scaffold. Unfortunately, cyclopropane aldehyde (**2g**) was not a suitable aldehyde. Attempts to carbocyclize primary alkyl aldehydes, such as butyraldehyde (**2h**) and caprylic aldehyde (**2i**), failed to give the desired products, but instead provided the CO-inserted Pauson-Khand-type product, 3*a*,5-dimethyl-1-phenyl-3,3*a*-dihydro-2*H*-cyclopenta[*c*]quinoline-2,4(5*H*)-dione (**5**), in 57% and 8% yields, respectively (eqn (4)).<sup>7</sup>

To understand the mechanism, the control reaction of amide **1a** with aldehyde **2a** and TBPB was completely suppressed by a stoichiometric amount of radical inhibitors, including TEMPO, hydroquinone and BHT. Moreover, aldehyde **2a** was converted into 1-(*tert*-butoxy)-2,2,6,6-tetramethylpiperidine (**6**) by reacting with TEMPO (eqn (5) in Scheme 3). These results implied that the decarbonylative [2 + 2 + 2] carbocyclization protocol involves a radical process. Therefore, the mechanism of this reaction is presented in Scheme 3.<sup>4,5,8,10</sup> Aldehyde **2a** is converted into alkyl radical **A** via oxidative decarbonylation with the aid of TBPB.<sup>5</sup> Addition of the alkyl radical **A** across the C-C double bond in amide **1a** affords new alkyl radical intermediate **B**, followed by cyclization to produce unstable vinyl radical intermediate **C**.<sup>4,10</sup> The intermediate **C** readily undergoes a 1,6-H shift followed by annulation to form intermediate **E**.<sup>8</sup> Oxidation of intermediate **E** by TBPB affords the cationic intermediate **F**.<sup>4,5,8</sup> Finally, deprotonation of intermediate **F** results in the formation of the product **3aa**.

## Conclusions

In summary, we have developed the first oxidative decarbonylative [2 + 2 + *m*] annulation reaction of 1,*n*-enynes with tertiary and secondary alkyl aldehydes as a two-carbon unit source for the synthesis of diverse six-membered carbocycle-fused polycycles under metal-free conditions. This method proceeds through a sequence of oxidative decarbonylation, 1,6-H shift and annulation, and allows the one-step formation of three new



C–C bonds with broad substrate scope and excellent functional group tolerance. Moreover, this method is applicable to secondary alkyl aldehydes leading to five-membered carbocyclic-ring-fused polycycles. Further studies will focus on the development of enantioselective aspects and other 1,*n*-enyne oxidative radical annulation reactions.

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## Notes and references

- For selected reviews, see: (a) P. A. Wender, V. A. Verma, T. H. Paxton and T. H. Pillow, *Acc. Chem. Res.*, 2008, **41**, 40; (b) M. Lautens, W. Klute and W. Tam, *Chem. Rev.*, 1996, **96**, 49; (c) P. A. Inglesby and P. A. Evans, *Chem. Soc. Rev.*, 2010, **39**, 2791; (d) D. P. Curran and M. Harmata, *Advances in Cycloaddition*, JAI Press, Greenwich, CT, 1988–1999, vol. 1–6; (e) W. Carruthers, *Cycloaddition Reactions in Organic Synthesis, Tetrahedron Organic Chemistry Series*, Pergamon, Elmsford, NY, 1990; (f) L. Yet, *Chem. Rev.*, 2000, **100**, 2963; (g) C. Aubert, O. Buisine and M. Malacria, *Chem. Rev.*, 2002, **102**, 813.
- For reviews on [2 + 2 + 2] cycloaddition reactions, see: (a) J. Varela and C. Saá, *Chem. Rev.*, 2003, **103**, 3787; (b) S. Kotha, E. Brahmachary and K. Lahiri, *Eur. J. Org. Chem.*, 2005, 4741; (c) K. Tanaka, *Chem.-Asian J.*, 2009, **4**, 508; (d) B. R. Galan and T. Rovis, *Angew. Chem., Int. Ed.*, 2009, **48**, 2830; (e) G. Dominguez and J. Perez-Castells, *Chem. Soc. Rev.*, 2011, **40**, 3430; (f) N. Weding and M. Hapke, *Chem. Soc. Rev.*, 2011, **40**, 4525.
- (a) R. Grigg, R. Scott and P. J. Stevenson, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1357; (b) C. H. Oh, H. R. Sung, S. H. Jung and Y. M. Lim, *Tetrahedron Lett.*, 2001, **42**, 5493; (c) S. Kezuka, T. Okado, E. Niou and R. Takeuchi, *Org. Lett.*, 2005, **7**, 1711; (d) P. A. Evans, J. R. Sawyer, K. W. Lai and J. C. Huffman, *Chem. Commun.*, 2005, 3971; (e) C.-A. Chang, J. A. King Jr and K. P. C. Vollhardt, *J. Chem. Soc.*, 1981, 53; (f) P. A. Evans, K. W. Lai and J. R. Sawyer, *J. Am. Chem. Soc.*, 2005, **127**, 12466; (g) S. García-Rubín, C. González-Rodríguez, C. García-Yebra, J. A. Varela, M. A. Esteruelas and C. Saá, *Angew. Chem., Int. Ed.*, 2014, **53**, 1841; (h) B. M. Trost, K. Imi and A. F. Indolese, *J. Am. Chem. Soc.*, 1993, **115**, 8831; (i) J. Seo, H. M. P. Chui, M. J. Heeg and J. Montgomery, *J. Am. Chem. Soc.*, 1999, **121**, 476; (j) J. A. Varela, S. G. Rubín, C. González-Rodríguez, L. Castedo and C. Saá, *J. Am. Chem. Soc.*, 2006, **128**, 9262; (k) T. Shibata and Y. Tahara, *J. Am. Chem. Soc.*, 2006, **128**, 11766; (l) D. Tanaka, Y. Sato and M. Mori, *J. Am. Chem. Soc.*, 2007, **129**, 7730; (m) M. Schelwies, A. Farwick, F. Rominger and G. Helmchen, *J. Org. Chem.*, 2010, **75**, 7917; (n) G.-B. Deng, Z.-Q. Wang, J.-D. Xia, P.-C. Qian, R.-J. Song, M. Hu, L.-B. Gong and J.-H. Li, *Angew. Chem., Int. Ed.*, 2013, **52**, 1535.
- (a) M. Hu, J.-H. Fan, Y. Liu, X.-H. Ouyang, R.-J. Song and J.-H. Li, *Angew. Chem., Int. Ed.*, 2015, **54**, 9577; (b) J.-K. Qiu, B. Jiang, Y.-L. Zhu, W.-J. Hao, D.-C. Wang, J. Sun, P. Wei, S.-J. Tu and G. Li, *J. Am. Chem. Soc.*, 2015, **137**, 8928; (c) Z.-Z. Chen, S. Liu, W.-J. Hao, G. Xu, S. Wu, J.-N. Miao, B. Jiang, S.-L. Wang, S.-J. Tu and G. Li, *Chem. Sci.*, 2015, **6**, 6654; (d) Y.-N. Wu, R. Fu, N.-N. Wang, W.-J. Hao, G. Li, S.-J. Tu and B. Jiang, *J. Org. Chem.*, 2016, **81**, 4762; (e) M. Hu, R.-J. Song, X.-H. Ouyang, F.-L. Tan, W.-T. Wei and J.-H. Li, *Chem. Commun.*, 2016, **52**, 3328; (f) L.-Y. Lv and Z.-P. Li, *Org. Lett.*, 2016, **18**, 2264.
- For a review and selected papers, see: (a) J. W. Wilt, in *Free Radicals*, ed. J. K. Kochi, Wiley-Interscience, New York, N.Y., 1973, vol. 1, ch. 8, pp. 346–356; (b) J. W. Wilt and H. Philip, *J. Org. Chem.*, 1960, **25**, 891; (c) J. W. Wilt and M. P. Stumpf, *J. Org. Chem.*, 1965, **30**, 1256; (d) J. W. Wilt and W. W. Pawlikowski, Jr, *J. Org. Chem.*, 1975, **40**, 3641; (e) J. R. Hwu and P. S. Furth, *J. Am. Chem. Soc.*, 1989, **111**, 8834; (f) A. Poloukhine and V. V. Popik, *J. Org. Chem.*, 2005, **70**, 1297; For a paper on the use of aldehydes as the “R” source for the cyclization of *N*-aryl acrylamides, see: (g) L. Yang, W. Lu, W. Zhou and F. Zhang, *Green Chem.*, 2016, **18**, 2941.
- For reviews and representative papers, see: (a) M. A. Garralda, *Dalton Trans.*, 2009, 3635; (b) T. Patra, S. Manna and D. Maiti, *Angew. Chem., Int. Ed.*, 2011, **50**, 12140; (c) K. Ohno and J. Tsuji, *J. Am. Chem. Soc.*, 1968, **90**, 99; (d) M. Kreis, A. Palmelund, L. Bunch and R. Madsen, *Adv. Synth. Catal.*, 2006, **348**, 2148; (e) T. Iwai, T. Fujihara and Y. Tsuji, *Chem. Commun.*, 2008, 6215; (f) P. Fristrup, M. Kreis, A. Palmelund, P. O. Norrby and R. Madsen, *J. Am. Chem. Soc.*, 2008, **130**, 5206; (g) K. Sen and J. C. Hackett, *J. Am. Chem. Soc.*, 2010, **132**, 10293; (h) A. Schirmer, M. A. Rude, X. Z. Li, E. Popova and S. B. del Cardayre, *Science*, 2010, **329**, 559; (i) T. C. Fessard, S. P. Andrews, H. Motoyoshi and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2007, **46**, 9331; (j) B. Gutmann, P. Elsner, T. Glasnov, D. M. Roberge and C. O. Kappe, *Angew. Chem., Int. Ed.*, 2014, **53**, 11557; (k) E. I. Gürbüz, D. D. Hibbitts and E. Iglesia, *J. Am. Chem. Soc.*, 2015, **137**, 11984; (l) J. A. Varela, C. González-Rodríguez, S. G. Rubín, L. Castedo and C. Saá, *J. Am. Chem. Soc.*, 2006, **128**, 9576; (m) X. Guo, J. Wang and C.-J. Li, *J. Am. Chem. Soc.*, 2009, **131**, 15092; (n) P. Wang, H. Rao, F. Zhou, R. Hua and C.-J. Li, *J. Am. Chem. Soc.*, 2012, **134**, 16468; (o) Q. Shuai, L. Yang, X. Guo, O. Baslé and C.-J. Li, *J. Am. Chem. Soc.*, 2010, **132**, 12212.
- (a) T. Morimoto, K. Fuji and K. Tsutsumi, *J. Am. Chem. Soc.*, 2002, **124**, 3806; (b) T. Shibata, N. Toshiada and K. Takagi, *J. Org. Chem.*, 2002, **67**, 7446; (c) K. Fuji, T. Morimoto and K. Tsutsumi, *Angew. Chem., Int. Ed.*, 2003, **42**, 2409; (d) J. H. Park, Y. Cho and Y. K. Chung, *Angew. Chem., Int. Ed.*, 2010, **49**, 5138; (e) F. Chahdoura, L. K. Fourmy, J. Durand, D. Madec and M. Gómez, *Eur. J. Org. Chem.*, 2013, 29; (f) T. Furusawa, T. Morimoto, K. Ikeda, H. Tanimoto,



- Y. Nishiyama, K. Kakiuchi and N. Jeong, *Tetrahedron*, 2015, **71**, 875.
- 8 For reviews, see: (a) P. Mátyus, O. Eliás, P. Tapolcsányi, A. Polonka-Bálint and B. Halász-Dajka, *Synthesis*, 2006, 2625; (b) M. C. Haibach and D. Seidel, *Angew. Chem., Int. Ed.*, 2014, **53**, 5010; (c) U. Wille, *Chem. Rev.*, 2013, **113**, 813; For representative papers on radical hydride shift, see: (d) E. Bosch and M. D. Bachi, *J. Org. Chem.*, 1993, **58**, 5581; (e) T. Hashimoto, D. Hirose and T. Taniguchi, *Angew. Chem., Int. Ed.*, 2014, **53**, 2730; (f) K. Wang, S. M. Villano and A. M. Dean, *J. Phys. Chem. A*, 2015, **119**, 7205; (g) P. Yu, J.-S. Lin, L. Li, S.-C. Zheng, Y.-P. Xiong, L.-J. Zhao, B. Tan and X.-Y. Liu, *Angew. Chem., Int. Ed.*, 2014, **53**, 11890; (h) P. Yu, S.-C. Zheng, N.-Y. Yang, B. Tan and X.-Y. Liu, *Angew. Chem., Int. Ed.*, 2015, **54**, 4041.
- 9 For selected reviews and papers, see: (a) M. A. Lago, J. I. Luengo, C. E. Peishoff and J. D. Elliot, in *Annual Reports in Medicinal Chemistry*, ed. J. A. Bristol, Academic Press, San Diego, 1996, vol. 31, p. 81; (b) S. F. Martin, in *The Alkaloids*, ed. A. R. Brossi, Academic Press, New York, 1987, vol. 30, pp. 251–376; (c) L. Ingrassia, F. Lefranc, J. Dewelle, L. Pottier, V. Mathieu, S. Spiegl-Kreinecker, S. Sauvage, M. E. Yazidi, M. Dehoux, W. Berger, E. Van Quaquebeke and R. Kiss, *J. Med. Chem.*, 2009, **52**, 1100; (d) J. P. Cueva, A. Gallardo-Godoy, J. I. Juncosa Jr, P. A. Vidi, M. A. Lill, V. J. Watts and D. E. Nichols, *J. Med. Chem.*, 2011, **54**, 5508; (e) K. C. Nicolaou, J. A. Pfefferkorn, A. J. Roecker, G.-Q. Cao, S. Barluenga and H. J. Mitchell, *J. Am. Chem. Soc.*, 2000, **122**, 9939; (f) C. Xue, V. R. R. Donuru and H. Liu, *Macromolecules*, 2006, **39**, 5747; (g) G. Majetich and J. M. Shimkus, *J. Nat. Prod.*, 2010, **73**, 284.
- 10 For papers on the common radical cyclization of 1,*n*-enynes, see: (a) I. Ryu, H. Miyazato, H. Kuriyama, K. Matsu, M. Tojino, T. Fukuyama, S. Minakata and M. Komatsu, *J. Am. Chem. Soc.*, 2003, **125**, 5632; (b) H. M. Ko, C. W. Lee, H. K. Kwon, H. S. Chung, S. Y. Choi, Y. K. Chung and E. Lee, *Angew. Chem., Int. Ed.*, 2009, **48**, 2364; (c) S. Mondal, B. Gold, R. K. Mohamed and I. V. Alabugin, *Chem.–Eur. J.*, 2014, **20**, 8664; (d) N. Fuentes, W. Kong, L. Fernández-Sánchez, E. Merino and C. Nevado, *J. Am. Chem. Soc.*, 2015, **137**, 964; (e) J.-Y. Luo, H.-L. Hua, Z.-S. Chen, Z.-Z. Zhou, Y.-F. Yang, P.-X. Zhou, Y.-T. He, X.-Y. Liu and Y.-M. Liang, *Chem. Commun.*, 2014, **50**, 1564.
- 11 CCDC 1438591 (**3ha**) contains the supplementary crystallographic data for this paper.†

