

Cite this: *Chem. Sci.*, 2024, 15, 16216

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 30th July 2024
Accepted 3rd September 2024

DOI: 10.1039/d4sc05067c

rsc.li/chemical-science

CCC pincer Ru complex-catalyzed C–H vinylation/ 6π -E-cyclization of aldimines for constructing 4*H*-pyrido[1,2-*a*]pyrimidines†

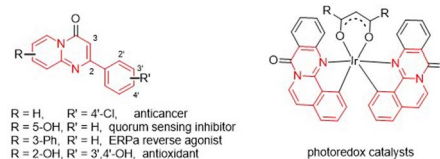
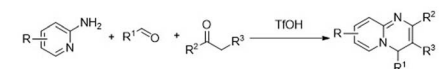
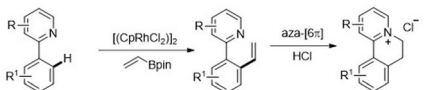
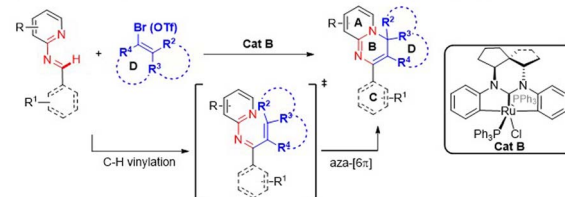
Heng Cai,^a Yong-Qiang Tu,^b Qiang Niu,^c Wen-Ping Xie,^b Bin Wang,^a Ka Lu,^a Zi-Hao Li,^b Fu-Min Zhang^a and Xiao-Ming Zhang^a

An unusual cascade C–H activation, vinylation and 6π -electrocyclization of 2-pyridyl aldimines with vinyl bromides/triflates was achieved using catalysis with a unique CCC pincer NHC–Ru(III) complex (Cat B). This reaction was found to enable a rapid and diverse synthesis of polycyclic 4*H*-pyrido[1,2-*a*]pyrimidine derivatives in mostly good to high yields, and with a broad substrate scope. A mechanistic study suggested the formation of a semi-opened Ru(III) intermediate chelating/activating the aldimine, and the occurrence of single-electron transfer (SET) to generate a vinyl radical, followed by vinylation and then an intramolecular 6π -electrocyclization of 1*N*,3*N*-hexatriene to form the product. This protocol provides a convenient approach for preparing and seeking new drug candidates.

Introduction

Organic *N*-heteropolycycles often play substantial roles in pharmaceuticals, bioactive molecules, and functional materials.¹ The 4*H*-pyrido[1,2-*a*]pyrimidine derivatives represent a large class of versatile *N*-heterocyclic molecules. At least ten members have been used as clinical drugs, having antidepressant,² anticancer,³ antiallergic,⁴ antioxidant,⁵ quorum sensing inhibition,⁶ and other functions.⁷ Additionally, some other derivatives show utility in other fields, such as photocatalysis (Scheme 1a).⁸ Over the past decades, however, only a few methods for constructing these *N*-heteropolycycles have been developed, and commonly involve the catalytic cyclization of multiple components or use of substrates premade in multiple steps (Scheme 1b).⁹ Some of the approaches also show limitations: poor diversity or functionality of generated products, requirement of pre-installation and post-removal of activating/directing groups (DGs), *etc.*¹⁰ Thus alternative development of a more efficient strategy is necessary for constructing diverse derivatives of this *N*-heterocyclic framework to meet the demands of multiple research fields.

The transition-metal-catalyzed C–H vinylation (Heck reaction) and annulation of arenes with vinyl species is recognized as a useful approach in organic synthesis.¹¹ To the best of our knowledge, there have hardly been any effective approaches reported for C–H vinylation and aza-cyclization to construct

a) Representative functional molecules with 2-substituted 4*H*-pyrido[1,2-*a*]pyrimidinesb) Previous: three-component reaction to provide 4*H*-pyrido[1,2-*a*]pyrimidinesc) Previous: 2-step synthesis of heterocycle via vinylation / 6π -electrocyclizationsd) This work: 1-step construction of diverse multi-substituted 4*H*-pyrido[1,2-*a*]pyrimidinesScheme 1 Features of multi-substituted 4*H*-pyrido[1,2-*a*]pyrimidines.

^aState Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P. R. China. E-mail: tuyq@lzu.edu.cn

^bSchool of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, Shanghai 200240, P. R. China. E-mail: tuyq@sjtu.edu.cn

^cNational Enterprise Technology Center, Inner Mongolia Erdos Electric Power and Metallurgy Group Co., Ltd, Ordos, 016064, Inner Mongolia, China

† Electronic supplementary information (ESI) available. CCDC 2340955, 2340956, 2340957, 2340958, 2340960 and 2340961. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d4sc05067c>



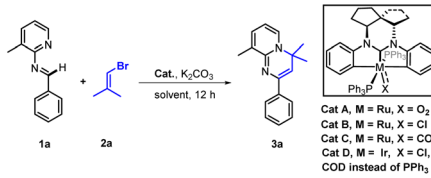
these *N*-heteropolycycles, except for the few examples using the simple vinyl partner (Scheme 1c).¹² To effectively access diverse multi-substituted 4*H*-pyrido[1,2-*a*]pyrimidine derivatives, we hope to find a suitable catalyst system to investigate a more effective cascade strategy involving C–H activation, vinylation and aza-cyclization from aldimine and unactivated multi-substituted vinyl species (Scheme 1d). Here the aldimine substrates can be readily assembled from commercial aldehyde and amine materials, and importantly the N-atom of the pyridine moiety can serve as both a transient guide for C–H vinylation and the reaction site for 6π-electrocyclization, avoiding the use of an extra DG. In this approach, however, there may exist some challenges that would need to be overcome: an undesired C–H vinylation may take place competitively at aromatic ring C under direction of the N-atom of the aldimine;¹³ and if the vinyl partners are unactivated and multi-functionalized for achieving product diversity, such as more rings B/D, a sufficiently powerful catalyst system would be required. Given our successful development of transition-metal (Ir, Ru) NHC pincer catalysts, which have proven to robustly enable C–H activation/functionalization,¹⁴ here we set out to evaluate this series of catalysts to achieve our goal of being able to synthesize diverse polycyclic 4*H*-pyrido[1,2-*a*]pyrimidine derivatives.

Results and discussion

We began our study with the preparation of representative spirocycle-fused NHC pincer Ru and Ir complexes, **Cat A–D**, according to methods we reported.^{14a,d} Then we tried to realize a model cascade reaction by screening the transition-metal catalysts and reaction conditions with *N*-(3-methylpyridin-2-yl)-1-phenylmethanimine (**1a**) as a substrate and the unactivated 1-bromo-2-methylpropene (**2a**) as its vinylation partner. Initially using the conditions described in Table 1 (see ESI† for details), to our delight we obtained the desired product **3a**, albeit in 40% yield, with **Cat A**, and a little better 43% yield with **Cat B**. In contrast, using **Cat C** or **D** failed to give product **3a** (entries 1–2 vs. 3–4). Fortunately, we did not detect the undesired product of C–H vinylation at aromatic ring C in this model reaction. This selectivity could be explained by the results of density functional theory (DFT) calculations, which indicated that the desired activation of the aldimine C–H (energy barrier $\Delta G = 28.0 \text{ kcal mol}^{-1}$) was easier than that ($\Delta G = 37.3 \text{ kcal mol}^{-1}$) of the undesired reaction (see ESI, Fig. S8†). Since **Cat A** and **B** gave the positive results (entries 1–2), additional commercial Ru-catalysts were examined, but no reaction was observed (entries 5–9). A control experiment without any catalyst resulted in no product. Subsequently we turned our attention to investigating the effect of solvent (entries 10–12), and found that 1,4-dioxane gave the better result (entry 12). Finally, the best 96% yield of **3a** was obtained by raising the reaction temperature to 130 °C, and the loading of **Cat B** to 5 mol% (entry 13).

With the optimal conditions (Table 1, entry 13) in hand, we then set out to expand the substrate **1** scope first by testing various substituents on ring A. The experimental results

Table 1 Screening of catalysts and reaction conditions^a



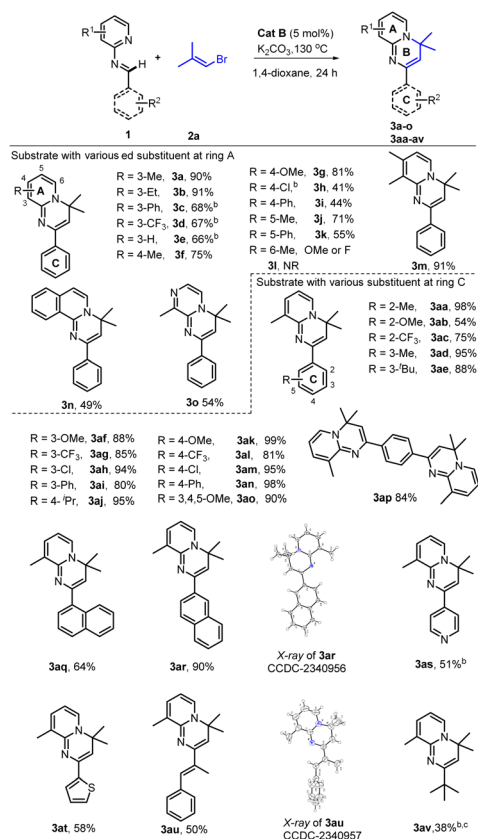
Entry	Cat	Solvent	Yield ^b /%
1	A	Toluene	40
2	B	Toluene	43
3	C	Toluene	NR
4	D	Toluene	NR
5	Ru(bpy) ₃ Cl ₂	Toluene	NR
6	Cp(PPh ₃) ₂ RuCl	Toluene	NR
7	RuCl ₃	Toluene	NR
8	Ru(acac) ₃	Toluene	NR
9	RuO ₂	Toluene	NR
10	B	DMSO	NR
11	B	MeCN	12
12 ^c	B	1,4-Dioxane	89
13 ^{cd}	B	1,4-Dioxane	96

^a General conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), **Cat** (3 mol%), K₂CO₃ (0.15 mmol) and solvent (1 mL), 110 °C for 12 h under argon.
^b Yields determined from ¹H NMR results. ^c 130 °C. ^d **Cat B** (5 mol%).

indicated that substitution with C3-alkyls, Ph, CF₃, and H gave medium to high yields of desired products **3a–3e** (Table 2), with the C3–Et substitution giving the best yield (**3b**). C4- (**3f–3i**) and C5-substitutions (**3j**, **3k**) gave on average lower yields of products than did the C-3 substitutions, with examples (**3f**, **3g**, **3j**) bearing electron-donating groups (EDGs) giving higher yields than those (**3h**, **3i**, **3k**) bearing electron-withdrawing groups (EWGs). The lower yield on average with EWGs was possibly due to a resulting decreased ability of the N-atom on ring A to coordinate with the Ru-catalyst. When a substituent (Me, OMe or F) was placed at the C6 position of the pyridine moiety, no reaction was observed, possibly due to steric hindrance from the neighboring C6 substituent. Furthermore, a 3,4-dimethyl substituent on ring A gave a high 91% yield of **3m**, whereas fusing benzene to ring A in one experiment and replacing A with 3-methyl-pyrazine in another experiment gave only modest yields of **3n** and **3o**, respectively. In short, substitution with an EDG at C3, C4 or C5 of ring A could favor this reaction, while any substitution at C6 disfavored it.

Subsequently we examined the substrate scope with 3-methyl-pyridyl fixed as ring A and testing various substitutions at C2–C4 of ring C. The experimental results demonstrated wide tolerance of the reaction to EDG (Me, Et, ⁱPr, or OMe), neutral phenyl, and EWG (Cl, CF₃) substituents here, generating mostly good to excellent yields of products (**3aa**, **3ad–3ao**)—except for **3ab** and **3ac**, which gave products with only moderate yields. Further replacing ring C with 1,4-disubstituted phenyl, α - or β -naphthalene, and 4-pyridyl or 2-thio-phenyl or phenylalkenyl, was still effective for this reaction, generating moderate (**3aq**, **3as–3au**) to good (**3ap**) and high (**3ar**) yields of desired products.



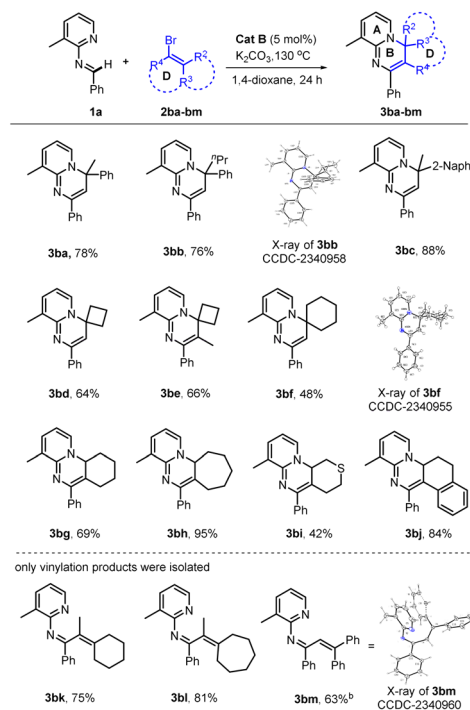
Table 2 Substrates with various substituents at rings A and C^a

^a Unless otherwise specified, reactions with **1** (0.2 mmol), **2a** (0.4 mmol), **Cat B** (5 mol%) and K₂CO₃ (0.3 mmol) in 1,4-dioxane (2 mL) at 130 °C under Ar for 24 h, isolated yield. ^b 150 °C. ^c **Cat B** (10 mol%).

Additionally, even a non-aromatic tertiary-butyl aldimine could be effective with this catalytic system, generating the corresponding product **3av**, albeit with a relatively low yield of 38%.

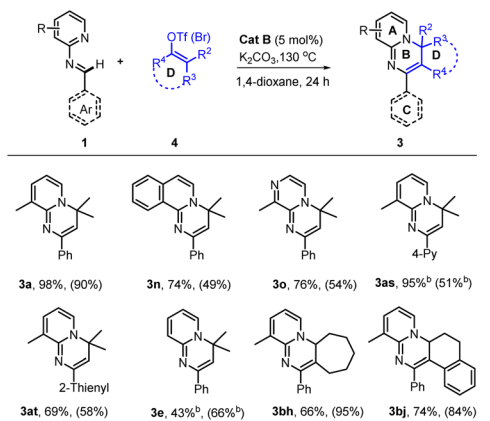
Of particular note, this catalyst system showed a robust ability to activate many unactivated vinyl partners **2**, enabling construction of diverse versions of ring B, even those bearing a spiro- or fused-ring D in many cases. As indicated in Table 3, this catalytic reaction could tolerate both acyclic and even cyclic vinyl species, smoothly generating tetra- (**3ba**, **3bb**, **3bd**–**3bi**) and pentacyclic (**3bc** and **3bj**) products with up to five rings in medium to good yields. However, when the vinyl species carried tri- or large 2,2-disubstituents, only the vinylation products were isolated, without further 6π-electrocyclization observed, possibly due to their greater steric hindrance at the terminus of the 1,3-diazo-1,3,5-triene moiety (**3bk**–**3bm**). This observation also confirmed that the reaction process underwent a 6π-electrocyclization of a diazo-triene intermediate instead of a azo-[4 + 2] D–A type cyclization of aldimides **1** with vinyl species **2** followed by dehydrobromination.

As the vinyl trifluoromethyl sulphonate (triflate, OTf) reagent is usually easier to prepare from ketone or aldehyde precursors, but less active than the bromide, we also examined the performance of the catalyst with some vinyl triflates **4**. As indicated in Table 4, the reaction efficiencies of several examples were

Table 3 Various vinyl species for constructing rings B/D^a

^a Unless otherwise specified, reactions with **1a** (0.2 mmol), **2** (0.4 mmol), **Cat B** (5 mol%) and K₂CO₃ (0.3 mmol) in 1,4-dioxane (2 mL) at 130 °C under argon for 24 h, isolated yield. ^b 150 °C.

examined, and a significant substrate dependence was found. When **1a** with 3-Me at ring A, **1n** with benzene-fused ring A, **1o** with 3-Me-pyrazine as ring A, **1as** with 4-pyridine as ring C, and **1at** with 2-thiophene as ring C, were subjected to the cascade reaction separately with 2,2-dimethyl vinyl triflates, they all gave the higher yields of products (**3a**, **3n**, **3o**, **3as** and **3at**) than they respectively did with the corresponding bromide. While **1e** was used to reaction, a reverse result was obtained (**3e**). Importantly, when cyclic vinyl triflates (**4bh** and **4bj**) were examined with **1a**,

Table 4 Results with vinyl triflates instead vinyl bromides^a

^a Unless otherwise specified, reactions with **1** (0.2 mmol), **4** (0.4 mmol), **Cat B** (5 mol%) and K₂CO₃ (0.3 mmol) in 1,4-dioxane (2 mL) at 130 °C under argon for 24 h, isolated yield. ^b 150 °C.



moderate yields were observed but lower than those with corresponding vinyl bromides. This result provided valuable information for seeking a reaction yield as high as possible, namely by screening vinyl partners, though a clear structure-efficiency relationship has not yet been identified.

In order to obtain insight into the mechanism of this reaction, several supporting experiments and DFT calculations were conducted. Initially, inspection of the model reaction of **1a** with **2a** under catalysis of 20 mol% **Cat B** with *in situ* high-resolution mass spectroscopy (HRMS) after one hour revealed the presence of the bromide **Cat E**, and Ru-species **I**, **III**, **IV** and **VI** (see ESI, Fig. S2†), whose structures are shown in Fig. 1. The molecular peak of **Cat B** was not detected in this case. A repeated experiment of this model reaction with 5 mol% **Cat E** instead of **Cat B** led to **3a** with a yield of 95% (Scheme 2a). This result indicated that **Cat E** participated in the catalytic cycle in the standard conditions with 2.0 equivalents of vinyl bromide **2**. We nevertheless still used **Cat B** instead of **Cat E** as the catalyst in this work, since the former was easier to prepare. When the deuterium-labeled-**1a** (**D-1a**) was subjected to the model reaction with 20 mol% **Cat B** or **Cat E** separately, two fragments with Ru-species **D-IV** and **2D-IV** were indicated by the HRMS data (see ESI, Fig. S3 and S5†) in each case, suggesting that a D-atom of **D-1a** was transferred onto the phenyl(s) of Ru-species **IV**. These results showed that reaction process underwent a semi-opening of Ru-species **I** and then re-cyclization after trapping aldimine substrate (**I** → **III**) *via* Ru intermediate **II**. Subsequently, a radical-trapping experiment with 2.0 equivalents of TEMPO was carried out, and found to form the TEMPO-linked vinyl product with a trace of **3a** formed, detected both using TLC and HRMS (Scheme 2b). This result showed that the C–Br bond cleavage of **2a** generated the vinyl radical, which was proposed based on the DFT calculations ($\Delta G = 33.2 \text{ kcal mol}^{-1}$, see ESI, Fig. S9†) to be the rate-determining step of the whole reaction. Finally, a kinetic isotope effect (KIE) experiment revealed a primary KIE of 1.05 (Scheme 2c), suggesting that C–H cleavage of aldimine was not the rate-determining step in this transformation.¹⁵

On the basis of the acquired evidence together with the related literature,^{14,16} a plausible mechanism was proposed (Fig. 1).

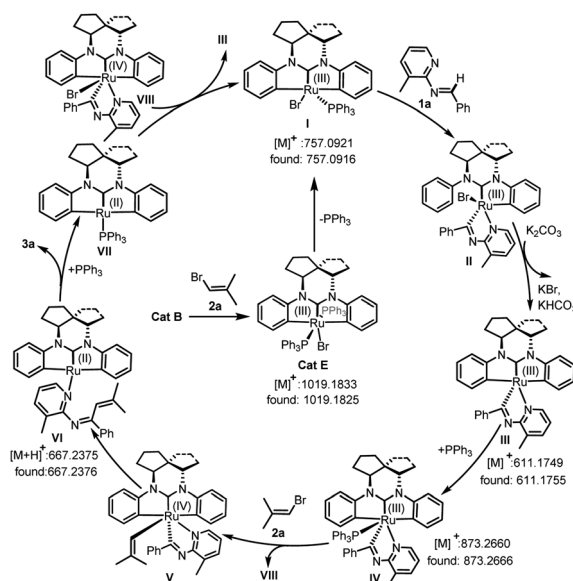


Fig. 1 Proposed reaction mechanism.

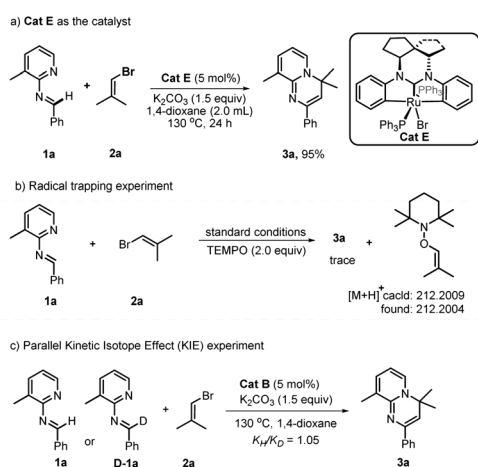
Initially, according to this mechanism, **Cat B** was *in situ* transferred to **Cat E**, which released a PPh_3 ligand to form the Ru-species **I**. Then the central Ru of **I** complexed substrate **1a**, which was accompanied with a Ru–Ph bond breaking and transfer of the aldimine H to Ph to form the semi-opened Ru(III) species **II**. After releasing the second PPh_3 ligand, eliminating HBr under assistance of K_2CO_3 and re-formation of a Ru–Ph bond, Ru-species **III** was formed. Complexation of **III** with PPh_3 formed the Ru intermediate **IV**, which combined with the SET-generated vinyl and Br radicals to form Ru(IV)-species **V** and **VIII**, respectively. Intramolecular reductive vinylation in **V** gave the Ru(II)-chelated 1*N*,3*N*-hexatriene **VI**, which generated **3a** and Ru(II)-species **VII** after 6 π -electrocyclization/ PPh_3 -ligand exchange. Subsequently, the Ru(II) species **VII** received a Br from **VIII** to regenerate species **I** and **III** for repeating the catalytic cycle.

Conclusions

In conclusion, we have developed a CCC pincer NHC–Ru(III)-catalyzed cascade C–H vinylation/6 π -electrocyclization of pyridyl aldimines with a series of unactivated vinyl bromides/triflates. This procedure displays advantages of broad substrate scope and multiple product functionality. A range of *N*-heteropolycycles have been produced efficiently, which we believe will find good potential utility in medicinal chemistry. Preliminary mechanistic studies indicated that this reaction proceeds through a radical pathway and a semi-opened Ru(III) intermediate. This success displays again one more powerful reactivity of our catalyst series, and inspires us to further the catalytic research and its applications.

Data availability

All data supporting the findings of this study are available within the article and its ESI† file.



Scheme 2 Mechanistic experiments.



Author contributions

H. Cai performed all of the experiments and prepared the ESI.† B. Wang prepared materials and catalysts for this reaction. K. Lu and Z.-H. Li performed the DFT calculations. Q. Niu, W.-P. Xie, F.-M. Zhang and X.-M. Zhang discussed the results and commented on the manuscript. Y.-Q. Tu wrote the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank prof. W.-X. Zhang (Peking University) for his helpful discussion of the reaction mechanism. We also acknowledge the “National Key R&D Program of China” (2023YFA1506400, 2023YFA1506403); NSFC (92256303); Shanghai Science and Technology Committee (19JC1430100) and Shanghai Jiao Tong University (WH410111001) for financial support.

Notes and references

- (a) T. Kametani, C. V. Loc, T. Higa, M. Koizumi, M. Ihara and K. Fukumoto, *J. Am. Chem. Soc.*, 1977, **99**, 2306–2309; (b) A. Witt and J. Bergman, *Curr. Org. Chem.*, 2003, **7**, 659–677; (c) T. Xu and H. Alper, *Org. Lett.*, 2015, **17**, 1569–1572; (d) M. Stępień, E. Gońka, M. Żyła and N. Sprutta, *Chem. Rev.*, 2017, **117**, 3479–3716; (e) T. Sena, K. Neog, S. Sarma, P. Manna, H. P. D. Boruah, P. Gogoi and A. K. Singha, *Bioorg. Med. Chem.*, 2018, **26**, 4942–4951; (f) K. P. Rakesh, H. K. Kumara, H. M. Manukumar and D. C. Gowad, *Bioorg. Chem.*, 2019, **87**, 252–264; (g) U. H. F. Bunz and J. Freudenberg, *Acc. Chem. Res.*, 2019, **52**, 1575–1587; (h) J. Zhang, X. Wang, D. Chen, Y. Kang, Y. Ma and M. Szostak, *J. Org. Chem.*, 2020, **85**, 3192–3201; (i) L. Lv and C.-J. Li, *Chem. Sci.*, 2021, **12**, 2870–2875; (j) T. Wesp, T. Bruckhoff, J. Petry, H. Wadepohl and L. H. Gade, *Chem.–Eur. J.*, 2022, **28**, e202200129; (k) Y. Zhang, S. Ling, P. Li, Z. Chen and X. F. Wu, *Org. Lett.*, 2022, **24**, 8864–8869; (l) Z. Luo, J. Jiang, L. Zou, X. Zhou, J. Liu, Z. Ke, F. Chen, H. Jiang and W. Zeng, *Sci. China Chem.*, 2024, **67**, 374–382; (m) Y. Gao, H. Li, S. Yang, Y. Huo, Q. Chen, X. Li, Z. Wang and X.-Q. Hu, *Sci. China Chem.*, 2024, **67**, 595–603.
- (a) M. V. Mey, A. D. Windhorst, R. P. Klok, J. D. M. Herscheid, L. E. Kennis, F. Bischoff, M. Bakker, X. Langlois, L. Heylen, M. Jurzakb and J. E. Leysen, *Med. Chem.*, 2006, **14**, 4526–4534; (b) L. E. J. Kennis, F. P. Bischoff, C. J. Mertens, C. J. Love, F. A. F. V. Keybus, S. Pieters, M. Braeken, A. A. H. P. Megens and J. E. Leysen, *Bioorg. Med. Chem.*, 2000, **10**, 71–74.
- G. Priyadarshani, S. Amrutkar, A. Nayak, U. C. Banerjee, C. N. Kundu and S. K. Guchhait, *Eur. J. Med. Chem.*, 2016, **122**, 43–54.
- Y. Yanagihara, H. Kasai, T. Kawashima and T. Shida, *Jpn. J. Pharmacol.*, 1988, **48**, 91–101.
- C. L. Motta, S. Sartini, L. Mugnaini, F. Simorini, S. Taliani, S. Salerno, A. M. Marini, F. D. Settimo, A. Lavecchia, E. Novellino, M. Cantore, P. Failli and M. Ciuffi, *J. Med. Chem.*, 2007, **50**, 4917–4927.
- S. Hiroaki and J. Igarashi, *WO Pat.*, WO2009063901, 2009.
- (a) F. Awouters, J. Vermeire, F. Smeyers, P. Vermote, R. Beek and C. J. E. Niemegeers, *Drug Dev. Res.*, 1986, **8**, 95–102; (b) P. Molina, E. Aller, A. Lorenzo, P. López-Cremades, I. Rioja, A. Ubeda, M. C. Terencio and M. J. Alcaraz, *J. Med. Chem.*, 2001, **44**, 1011–1014; (c) D. G. Shulman, L. Amdahl, C. Washington and A. Graves, *Clin. Therapeut.*, 2003, **25**, 1096–1106; (d) R. J. Perner, C. H. Lee, M. Jiang, Y.-G. Gu, S. DiDomenico, E. K. Bayburt, K. M. Alexander, K. L. Kohlhaas, M. F. Jarvis, E. L. Kowaluk and S. S. Bhagwat, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 2803–2807; (e) C. L. Motta, S. Sartini, L. Mugnaini, F. Simorini, S. Taliani, S. Salerno, A. M. Marini, F. D. Settimo, A. Lavecchia, E. Novellino, M. Cantore, P. Failli and M. Ciuffi, *J. Med. Chem.*, 2007, **50**, 4917–4927; (f) M. Donghi, O. D. Kinzel and V. Summa, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 1930–1934; (g) J. S. Debenham, C. B. Madsen-Duggan, J. Wang, X. Tong, J. Lao, T. M. Fong, M.-T. Schaeffer, J. C. Xiao, C. C. R.-R. Huang, C.-P. Shen, D. S. Stribling, L. P. Shearman, A. M. Strack, D. E. MacIntyre, J. J. Hale and T. F. Walsh, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 2591–2594; (h) L. Peng, X. Gao, L. Duan, X. Ren, D. Wu and K. Ding, *J. Med. Chem.*, 2011, **54**, 7729–7733; (i) P. Bhutani, G. Joshi, N. Raja, N. Bachhav, P. K. Rajanna, H. Bhutani, A. T. Paul and R. Kumar, *J. Med. Chem.*, 2021, **64**, 2339–2381.
- (a) S. Philipp, B. Esther and J. Dominik, *WO Pat.*, WO2011044988, 2011; (b) T. Hisato, W. Osamu, H. Hiromitsu, M. Makoto and T. Seiji, *JP Pat.*, JP2000156288, 2000.
- K. Yang, J. Xiang, G. Bao, Q. Dang and X. Bai, *ACS Comb. Sci.*, 2013, **15**, 519–524.
- (a) Y. Xie, T. Chen, S. Fu, H. Jiang and W. Zeng, *Chem. Commun.*, 2015, **51**, 9377–9380; (b) Y.-F. Liang, R. Steinbock, A. Münch, D. Stalke and L. Ackermann, *Angew. Chem., Int. Ed.*, 2018, **130**, 5482–5486; (c) R. T. Bhawale, A. S. Chillal and U. A. Kshirsagar, *J. Heterocycl. Chem.*, 2023, **60**, 1356–1373.
- (a) A. B. Dounay and L. E. Overman, *Chem. Rev.*, 2003, **103**, 2945–2964; (b) S. Jagtap, *Catalysts*, 2017, **7**, 267–319; (c) D. Paul, S. Das, S. Saha, H. Sharma and K. R. Goswami, *Eur. J. Org. Chem.*, 2021, **14**, 2057–2076; (d) R.-X. Liang and Y.-X. Jia, *Acc. Chem. Res.*, 2022, **55**, 734–745; (e) J. Cai, B. Sun, S. Yu, H. Zhang and W. Zhang, *Int. J. Mol. Sci.*, 2023, **24**, 8252–8280.
- X. Jiang, Z. Zeng, Y. Hua, B. Xu, Y. Shen, J. Xiong, H. Qiu, Y. Wu, T. Hu and Y. Zhang, *J. Am. Chem. Soc.*, 2020, **142**, 15585–15594.
- (a) B. Li, C. B. Bheeter, C. Darcel and P. H. Dixneuf, *ACS Catal.*, 2011, **1**, 1221–1224; (b) H. Wang, S. Yu, Z. Qi and X. Li, *Org. Lett.*, 2015, **17**, 2812–2815; (c) Y.-F. Liang, X. Wang, Y. Yuan, Y. Liang, X. Li and N. Jiao, *ACS Catal.*, 2015, **5**, 6148–6152; (d) C. Ma, C.-Q. Zhao, L.-P. Li, X.-T. Xu,



- K. Zhang and T.-S. Mei, *Chem. Commun.*, 2017, **53**, 12189–12192; (e) J. Li, K. Korvorapun, S. D. Sarkar, T. Rogge, D. J. Burns, S. Warratz and L. Ackermann, *Nat. Commun.*, 2017, **8**, 15430–15437; (f) K. Korvorapun, N. Kaplaneris, T. Rogge, S. Warratz, A. C. f. Stückl and L. Ackermann, *ACS Catal.*, 2018, **8**, 886–892; (g) M. T. Findlay, A. S. Hogg, J. J. Douglas and I. Larrosa, *Green Chem.*, 2023, **25**, 2394–2400; (h) X. Cong, Q. Zhuo, N. Hao, A. Mishra, M. Nishiura and Z. Hou, *Angew. Chem., Int. Ed.*, 2024, **63**, e202318203; (i) X. Cong, N. Hao, A. Mishra, Q. Zhuo, K. An, M. Nishiura and Z. Hou, *J. Am. Chem. Soc.*, 2024, **146**, 10187–10198.
- 14 (a) Z.-B. Yan, K.-L. Dai, B.-M. Yang, Z.-H. Li, Y.-Q. Tu, F.-M. Zhang, X.-M. Zhang, M. Peng, Q.-L. Chen and Z.-R. Jing, *Sci. China Chem.*, 2020, **63**, 1761–1766; (b) Z.-B. Yan, M. Peng, Q.-L. Chen, K. Lu, Y.-Q. Tu, K.-L. Dai, F.-M. Zhang and X.-M. Zhang, *Chem. Sci.*, 2021, **12**, 9748–9753; (c) K.-L. Dai, Q.-L. Chen, W.-P. Xie, K. Lu, Z.-B. Yan, M. Peng, C.-K. Li, Y.-Q. Tu and T.-M. Ding, *Angew. Chem., Int. Ed.*, 2022, **61**, e202206446; (d) H. Cai, Y.-Q. Tu, K. Lu, Q.-L. Chen, F.-M. Zhang, X.-M. Zhang, Y.-J. Pan and Z.-B. Yan, *Sci. China Chem.*, 2023, **66**, 2791–2796; (e) W.-F. Wang, K. Lu, P.-R. Liu, H.-H. Zeng, L.-M. Yang, A.-J. Ma, Y.-Q. Tu and J.-B. Peng, *ACS Catal.*, 2024, **14**, 5156–5166.
- 15 M. Gómez-Gallego and M. A. Sierra, *Chem. Rev.*, 2011, **111**, 4857–4963.
- 16 (a) N. Hofmann and L. Ackermann, *J. Am. Chem. Soc.*, 2013, **135**, 5877–5884; (b) Z. Shi, M. Suri and F. Glorius, *Angew. Chem., Int. Ed.*, 2013, **52**, 4892–4896; (c) J. H. Kim, S. Greßies and F. Glorius, *Angew. Chem., Int. Ed.*, 2016, **55**, 5577–5581; (d) H. Wang, M. M. Lorion and L. Ackermann, *Angew. Chem., Int. Ed.*, 2016, **55**, 10386–10390; (e) Y.-F. Liang, V. Mgller, W. Liu, A. Mgnch, D. Stalke and L. Ackermann, *Angew. Chem., Int. Ed.*, 2017, **56**, 9415–9419; (f) H. Wang, M. M. Lorion and L. Ackermann, *ACS Catal.*, 2017, **7**, 3430–3433; (g) K. Korvorapun, R. C. Samanta, T. Rogge and L. Ackermann, *Synthesis*, 2021, **53**, 2911–2934; (h) M. T. Findlay, P. Domingo-Legarda, G. McArthur, A. Yen and I. Larrosa, *Chem. Sci.*, 2022, **13**, 3335–3362; (i) J. H. Docherty, T. M. Lister, G. McArthur, M. T. Findlay, P. Domingo-Legarda, J. Kenyon, S. Choudhary and I. Larrosa, *Chem. Rev.*, 2023, **123**, 7692–7760; (j) S. Kamio, M. Nakamoto, T. Yamagishi, M. Oestreich and H. Yoshida, *Chem. Commun.*, 2024, **60**, 6379–6382.

