Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/d4ob01174k

Construction of axially chiral 2-arylpyrroles using catalytic asymmetric Suzuki–Miyaura cross-coupling: an efficient approach to esaxerenone†

Ling Jia,[a] Bing Li,[a] Xi Wang,[a] Jinfeng Zhao,[b] Jingping Qu [c] and Yuhan Zhou *[a]

Received 16th July 2024,
Accepted 14th August 2024

DOI: 10.1039/d4ob01174k

rsc.li/obc

A general and efficient method has been developed to access axially chiral 2-arylpyrroles using catalytic asymmetric Suzuki–Miyaura cross-coupling. A wide range of axially chiral arylpyrroles were obtained in high yields with good to excellent enantioselectivities. The key to success is the use of a combined catalytic system involving a palladium catalyst and chiral ferrocene diphosphine ligand for achieving effective enantiocontrol. More importantly, this axially chiral CF_3-substituted 2-arylpyrrole serves as a key intermediate in the preparation of the anti-hypertensive and diabetic nephropathy drug esaxerenone. It was directly asymmetrically synthesized with high enantioselectivity (92% ee). Thus, a new strategy is provided for the catalytic asymmetric synthesis of esaxerenone.

1 Introduction

Axially chiral molecules, particularly aryl-based molecules, are widely found in natural products, bioactive compounds, chiral catalysts or ligands, and functional materials.[1–5] Therefore, the catalytic atroposelective synthesis of axially chiral molecules has received a substantial amount of attention from chemists in recent years.[6–8] In previous studies, a number of strategies have been established for the atroposelective synthesis of axially chiral biaryls, especially those with six-membered biaryl skeletons. Efficient enantioselective transformations, including *de novo* synthesis of arenes, central to axial chirality transfer, kinetic resolution and desymmetrization of biaryls, Michael addition and ring-opening reactions, as well as cross-coupling, were developed to construct axially chiral biaryls.[9–19] In sharp contrast, there have been few studies on the asymmetric assembly of a chiral axis between a five-membered heterocycle and an aryl group.[20] Asymmetric assembly of atropisomers bearing five-membered heterocyclic rings was considered to be a difficult challenge, mainly due to the reduced rotational barriers and conformational instability caused by the increased distances between aryl substituents (Fig. 1a).[21,22]

As one of the most prominent classes of heterocyclic compounds, pyrroles are key structural motifs in biologically active compounds and useful building blocks in the synthesis of natural products, as well as in materials science.[23–25] It is noteworthy that arylpyrrole is considered to be an important active structural fragment in drug development.[26] For example, atorvastatin is used to treat conditions such as hypercholesterolemia and coronary heart disease.[27] Licofelone, an approved

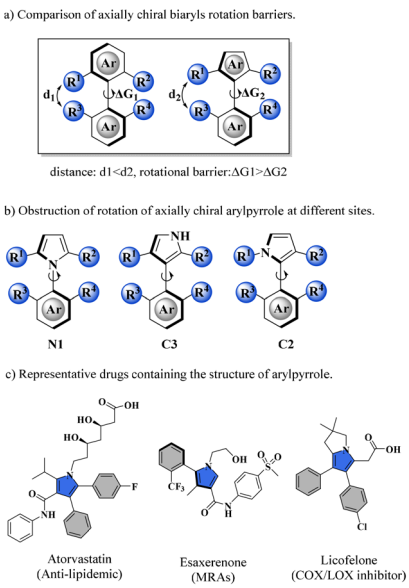


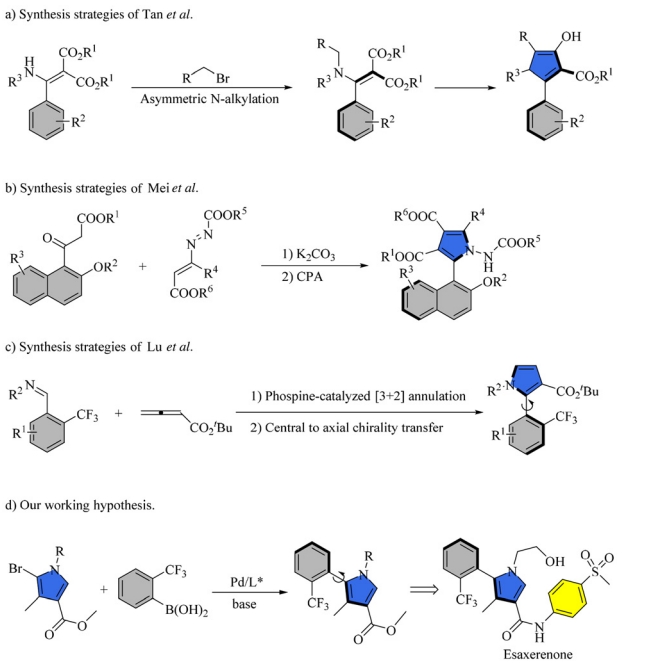
Fig. 1 Comparison of different structures of arylpyrrole and its application in medicine.

[a]State Key Laboratory of Fine Chemicals, Department of Pharmaceutical Engineering, School of Chemical Engineering, Dalian University of Technology, 2 Linggong Road, Dalian 116024, China. E-mail: zhouyh@dlut.edu.cn
[b]Instrumental Analysis Center, Dalian University of Technology, 2 Linggong Road, Dalian 116024, China
[c]State Key Laboratory of Fine Chemicals, School of Chemical Engineering, Dalian University of Technology, 2 Linggong Road, Dalian 116024, China

†Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d4ob01174k

osteoarthritis drug, and esaxerenone, a mineralocorticoid receptor antagonist (MRA) approved to treat hypertension, both contain arylpyrrole active structures.[28,29] In this case, the atropisomerism of arylpyrrole and its derivatives is particularly important for the advancement of drug development and organic synthesis. In the past reports, the catalytic asymmetric syntheses of axially chiral N1-arylpyrroles and axially chiral C3-arylpyrroles have been relatively well covered.[22,30–35] In contrast, direct catalytic asymmetric synthesis of axially chiral C2-arylpyrroles has been poorly reported (Fig. 1b). Tan *et al.* were the first to report an organocatalyzed asymmetric *N*-alkylation reaction, in which an enantioenriched 2-arylpyrrole framework was generated by cyclization (Scheme 1a).[36] Subsequently, 1-(1-amino-pyrrol-2-yl)naphthalen-2-ols (NPNOLs) with an axially chiral C2-arylpyrrole skeleton were prepared by a chiral phosphoric acid-catalyzed asymmetric Attanasi reaction reported by Mei *et al.* (Scheme 1b).[22] Recently, an axially chiral 2-arylpyrrole skeleton structure was creatively obtained by Lu *et al.* through a sequential phosphine-catalyzed asymmetric [3 + 2] annulation of aldimines with allenoates combined with an oxidative central-to-axial chirality transfer strategy (Scheme 1c).[20] Cross-coupling reactions catalyzed by transition metals play an important role in the field of organic synthesis, among which Suzuki–Miyaura cross-coupling is considered to be a highly versatile reaction for C–C bond formation.[37–41] The construction of six-membered biaryl skeletons using enantioselective Suzuki–Miyaura cross-coupling has been intensively reported.[42–47] In contrast, the direct construction of five-membered heterocyclic rings and aryl groups by enantioselective Suzuki–Miyaura cross-coupling has been rarely reported, and the enantioselectivity was poor.[48–52] It must be mentioned that the successful synthesis of axial chiral arylpyrroles by enantioselective Suzuki–Miyaura cross-coupling has not been reported to date.

Among numerous pyrrole-containing drugs, esaxerenone is a novel oral, non-steroidal, selective mineralocorticoid receptor blocker that was launched in 2019 for the treatment of hypertension.[53] It has good efficacy and safety in patients with essential hypertension, and can significantly reduce the urine protein of diabetic nephropathy patients.[54–57] Its antihypertensive effect is significantly better than that of eplerenone and can be used in mono-therapy or combined with a calcium channel blocker or renin angiotensin system inhibitors.[58] Thus, esaxerenone is regarded as a milestone in the treatment of hypertension. However, it is worth noting that there has been limited documentation on the synthesis of esaxerenone, and the key axial chiral monoisomers are mainly obtained through chiral resolution, which is criticised for its low atom economy.[59–61] The sole report on the asymmetric catalytic synthesis of esaxerenone was published by Ullah and Lu. Based on the strategy of asymmetric catalytic construction of central chirality and its further transfer to axis chirality, esaxerenone was obtained in a 10-step reaction with 7.6% yield and 90% ee.[20] As part of our ongoing interest in the optimization of synthetic pathways for esaxerenone,[62] we became interested in designing an effective strategy for the rapid construction of axially chiral 2-arylpyrroles. Herein, we describe a novel synthesis strategy using Suzuki–Miyaura cross-coupling (Scheme 1d). Direct asymmetric catalytic synthesis of axial chiral pyrrole, a key intermediate of esaxerenone, was realized. Because of its simplicity and efficiency, the newly designed synthesis route will provide new valuable information for the synthesis of numerous structurally diverse axial chiral arylpyrroles.

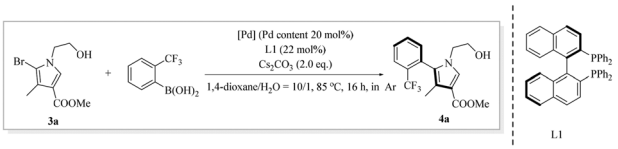


Scheme 1 Asymmetric synthesis strategies of 2-arylpyrroles and our working hypothesis.

2 Results and discussion

Initially, compound **3a**, prepared from *trans*-methyl crotonate and tosylmethyl isocyanide in three steps (see the ESI†), and (2-(trifluoromethyl)phenyl)boronic acid were selected as model substrates for the optimization of the reaction conditions. Firstly, the metal catalyst was screened. A mixture of $Pd(OAc)_2$ (20 mol%), **L1** (22 mol%), compound **3a** (1.0 equiv.), (2-(trifluoromethyl)phenyl)boronic acid (2.0 equiv.), and Cs_2CO_3 (2.0 equiv.) was stirred in the solvent 1,4-dioxane/H_2O = 10/1 at 85 °C for 16 h and the target product **4** was obtained in 85% yield with 51% ee (Table 1, entry 1). When $Pd(OAc)_2$ was replaced by $[Pd(C_3H_5)Cl]_2$ (10 mol% and Pd content 20 mol%), the target product was obtained in 6% yield with 73% ee (Table 1, entry 2). When $Pd(OAc)_2$ was replaced by PdI_2, $Pd(CF_3COO)_2$, and $Pd[(CO_2(CH_3)_3)]_2$, the yields of the target product were 62%, 71%, and 72%, and the ee values were 48%, 50%, and 51%, respectively (Table 1, entries 3–5). When $Pd(OAc)_2$ was replaced by $[Pd(C_3H_5)Cl]_2$ and **L1** was replaced by **L2**, the target product was obtained in 49% yield with 84%

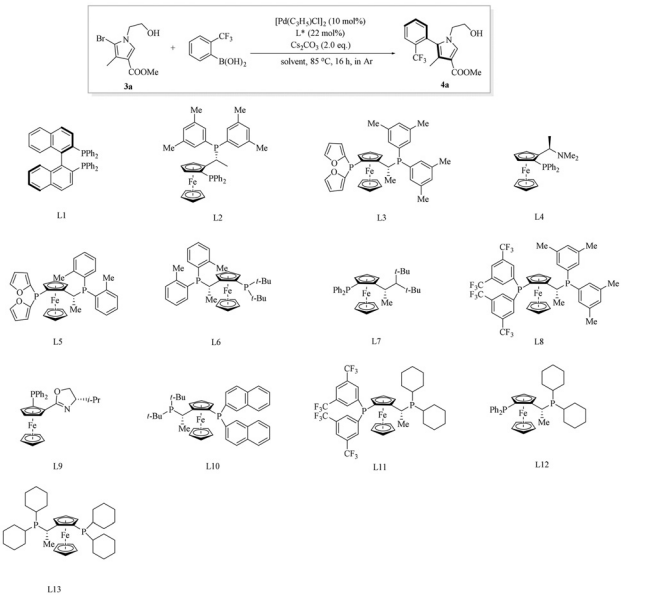
Table 1 Optimization of the catalyst[a]



Entry	Catalyst	Yield[b] [%]	ee[c] [%]
1	$Pd(OAc)_2$	85[d]	51
2	$[Pd(C_3H_5)Cl]_2$	6	73
3	PdI_2	62	48
4	$Pd(CF_3COO)_2$	71	50
5	$Pd[(CH_3)_3CCO_2]_2$	72	51
6	$Pd(PPh_3)_4$	3	0
7	$Pd_2(dba)_3$	41	51
8	$Pd(t\text{-}Bu_3P)_2$	22	25
9	$[Pd(C_3H_5)(con)]BF_4$	12	38
10	$PdCl_2$	NR	
11	$[Ir(cod)Cl]_2$	NR	

[a] Reaction conditions: under an argon atmosphere, compound **3a** (0.100 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.200 mmol), cat. (Pd content 0.020 mmol), ligand **L1** (0.022 mmol) and Cs_2CO_3 (0.200 mmol) in the solvent 1,4-dioxane/H_2O = 10/1 (3.000 mL) at 85 °C for 16 h (react in a heavy-wall pressure bottle). [b] The yields were determined by ^1H NMR analysis of the crude materials using *o*-phenanthroline as an internal standard. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Isolated yields after chromatography.

Table 2 Optimization of the ligand[a]



Entry	Solvent[b]	Ligand	Yield[c] [%]	ee[d] [%]
1	A	L2	49	88
2	A	L3	18	97
3	B	L2	92[e]	78
4	B	L3	89[e]	92
5	B	L4	63	60
6	B	L5	79	81
7	B	L6	47	86
8	B	L7	NR	
9	B	L8	NR	
10	B	L9	NR	
11	B	L10	NR	
12	B	L11	NR	
13	B	L12	NR	
14	B	L13	NR	

[a] Reaction conditions: under an argon atmosphere, compound **3a** (0.100 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.200 mmol), $[Pd(C_3H_5)Cl]_2$ (Pd content 0.020 mmol), ligand (0.022 mmol) and Cs_2CO_3 (0.200 mmol) in the solvent (3.000 mL) at 85 °C for 16 h (react in a heavy-wall pressure bottle). [b] Solvent A is 1,4-dioxane/H_2O = 10/1 and solvent B is Et_2O (with 0.2 mmol of H_2O). [c] The yields were determined by ^1H NMR analysis of the crude materials using *o*-phenanthroline as an internal standard. [d] Determined by HPLC analysis on a chiral stationary phase. [e] Isolated yields after chromatography.

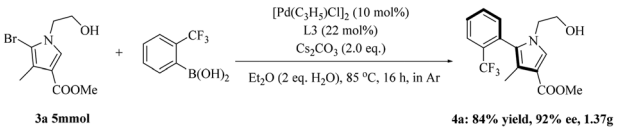
ee (Table 1, entry 13). Other palladium and iridium catalysts were screened under the same conditions, and no more satisfactory results were obtained (Table 1, entries 6–12 and entries 14–18).

Choosing 1,4-dioxane/H_2O = 10/1 as the solvent and $[Pd(C_3H_5)Cl]_2$ as the catalyst, the ligands were further screened. When ligands **L2**, **L3**, and **L8** were used, ee values greater than or equal to 85% were obtained, but all were obtained in low yields (Table 2, entries 1 and 2). To our excitement, when $[Pd(C_3H_5)Cl]_2$ was paired with **L2**, a high enantioselectivity of 88% ee was achieved, while the yield remained at a medium level of 49% (Table 2, entry 1). The combination of **L2** and $[Pd(C_3H_5)Cl]_2$ in ether solvent (adding 0.2 mmol of H_2O) gave exciting results of 92% yield and 78% ee (Table 2, entry 5). When **L3** was paired with $[Pd(C_3H_5)Cl]_2$, the enantioselectivity was further improved to 92% ee with 89% yield (Table 2, entry 4). The complete screening of ligands can be found in Table S1† (see Table S1 in the ESI†).

Based on the above results, the influence of other reaction factors on the reaction was further studied. The screening of solvents and bases revealed that the reaction in ether (2 equivalent H_2O) with Cs_2CO_3 as the base provided the best outcomes and the results are presented in Tables S2 and S3.† Based on the conventional Suzuki–Miyaura cross-coupling mechanism, it was speculated that the addition of water seems to increase the catalytic activity of the complex formed by $[Pd(C_3H_5)Cl]_2$ and ligand **L3**, resulting in increased yield and ee values.

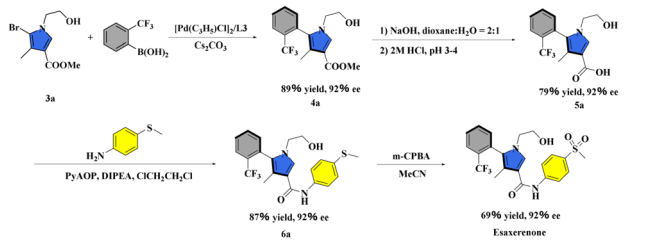
To demonstrate the practicability of this method, a gram-scale synthesis was performed. Compound **3** was reacted at 5 mmol, and the yield and enantioselectivity of product **4** (84% yield and 92% ee) were maintained compared to the small scale (89% yield and 92% ee) (Scheme 2).

5a was obtained by the hydrolysis of the key intermediate **4a** with yields of 79% and 92% ee. **5a** was further condensed



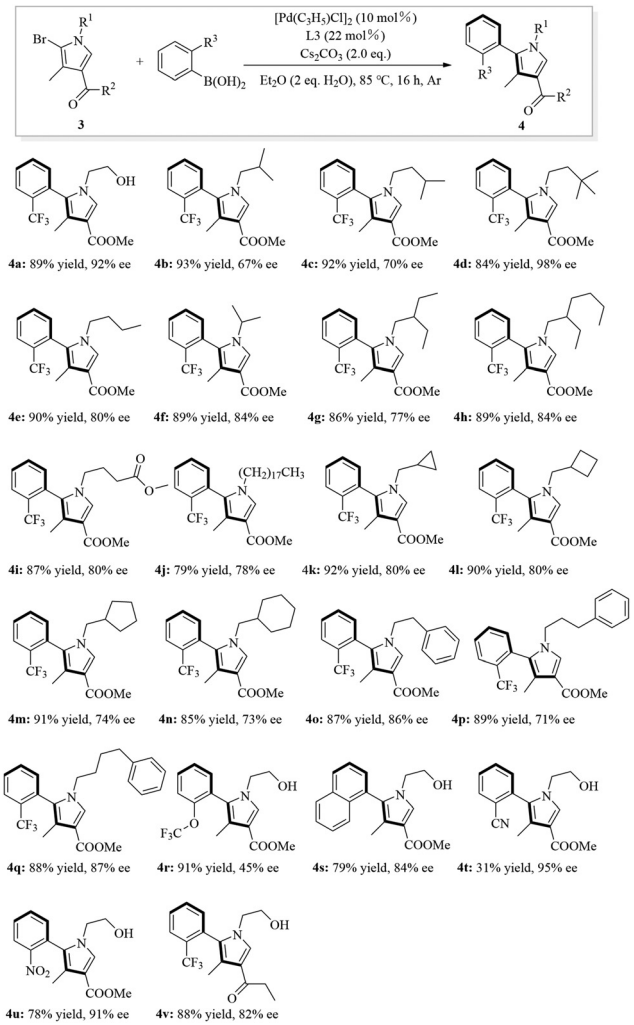
Scheme 2 Large-scale reaction of key intermediate **4a**.

with 4-amino thioanisole, and **6a** was obtained with 87% yield and 92% ee, and finally esaxerenone was successfully synthesized by an oxidation reaction (69% yield and 92% ee) (Scheme 3). Based on the commercially available starting materials *trans*-methyl crotonate and tosylmethyl isocyanide, the total yield of the seven-step reaction was 20%.



Scheme 3 Synthesis of esaxerenone.

Table 3 Substrate scope[a]



[a] Reaction conditions: under an argon atmosphere, **3** (0.100 mmol), (2-(trifluoromethyl)phenyl)boronic acid (0.200 mmol), $[Pd(C_3H_5)Cl]_2$ (0.010 mmol), **L3** (0.022 mmol) and Cs_2CO_3 (0.200 mmol) in the solvent Et_2O (0.200 mmol H_2O) (3.000 mL) at 85 °C for 16 h (react in a heavy-wall pressure bottle). Isolated yields. The ee values were determined by HPLC analysis on a chiral stationary phase.

With the standard reaction conditions for the palladium-catalyzed asymmetric Suzuki–Miyaura cross-coupling of pyrrole bromide with (2-(trifluoromethyl) phenyl)boronic acid in hand, the generality of different alkylation substrates in the proposed catalytic system was systematically investigated. Good tolerance was provided by various substituents on N in pyrroles, affording the desired products **4a–4q** (Table 3). When the hydroxyethyl group was replaced by other alkyl groups, a significant steric hindrance effect was observed. The enantioselectivity of the product was gradually enhanced with the increase of steric hindrance. In the case of *N*-(3,3-dimethyl) butyl pyrrole, the large steric effect results in an excellent enantioselectivity of 98% ee (**4d**). The yields of compounds **4k–4n** with monocyclic alkyl groups ranged from 85–92% and enantioselectivities of 73–80% ee. Besides, methoxycarbonyl butyl and long-chain alkyl substituted pyrroles can also undergo the reaction to afford the desired products with good yields and enantioselectivities (**4i**, 87% yield and 80% ee; **4j**, 79% yield and 78% ee). The ester site was then replaced with ketone, and compound **4v** was obtained with 88% yield and 82% ee. Notably, the replacement of phenylboronic acid was also explored. When the trifluoromethyl group was replaced by the trifluoromethoxy group, a high yield of 91% was achieved, but unfortunately no high enantioselectivity was obtained. When the trifluoromethyl group was replaced by electron-withdrawing groups such as the cyano or the nitro group, the target product was obtained with 95% ee and 91% ee, respectively, but the yield was lower when the trifluoromethyl group was replaced by the cyano group (**4t**). Furthermore, substitution of trifluoromethyl phenylboronic acid with halogens at other positions hinders the normal progression of the reaction. When 2-(trifluoromethyl)phenylboronic acid was replaced by 1-naphthylboric acid, the product was obtained with good yield and enantioselectivity (**4s**). The range of applicable substrates will be further investigated in subsequent studies.

3 Conclusions

In summary, asymmetric Suzuki–Miyaura cross-coupling catalyzed by a palladium/chiral diphosphine ligand has been successfully developed to incorporate pyrrole heterocyclic rings and construct axially chiral biaryl compounds. Using commercially available *trans*-methyl crotonate and tosylmethyl isocyanide as raw materials, esaxerenone was successfully prepared in a 7-step reaction with 20% total yield and 92% ee. The key intermediate **4a**, an axially chiral CF_3-substituted 2-arylpyrrole, was obtained directly by asymmetric catalysis. Using this suitable method, a variety of axially chiral 2-arylpyrroles were prepared under relatively mild conditions with high yields (up to 92%) and moderate to excellent enantioselectivities (up to 98% ee). The method developed in this paper plays a powerful role in promoting the selective synthesis of chiral 2-arylpyrrole derivatives.

Author contributions

Conceptualization, supervision, and writing – review & editing were carried out by Yuhan Zhou. Data curation, formal analysis, investigation, and writing – original draft were carried out by Ling Jia. Funding acquisition and project administration were carried out by Yuhan Zhou and Jingping Qu. The visualization was performed by Yuhan Zhou and Ling Jia. The validation was carried out by Ling Jia, Bing Li, Xi Wang and Jinfeng Zhao. All authors provided critical feedback and helped shape the research, analysis and manuscript.

Data availability

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

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support for this work was provided by the National Natural Science Foundation of China (No. 22278060).

References

1 G. Bringmann, T. Gulder, T. A. M. Gulder and M. Breuning, *Chem. Rev.*, 2011, **111**, 563–639.
2 A. C. C. Carlsson, S. Karlsson, R. H. Munday and M. R. Tatton, *Acc. Chem. Res.*, 2022, **55**, 2938–2948.
3 Y.-J. Wu, G. Liao and B.-F. Shi, *Green Synth. Catal.*, 2022, **3**, 117–136.
4 K.-W. Chen, Z.-H. Chen, S. Yang, S.-F. Wu, Y.-C. Zhang and F. Shi, *Angew. Chem., Int. Ed.*, 2022, **61**, e202116829.
5 K. Wang and Y. Xiao, *Chirality*, 2021, **33**, 424–446.
6 G. Liao, T. Zhou, Q.-J. Yao and B.-F. Shi, *Chem. Commun.*, 2019, **55**, 8514–8523.
7 J. A. Carmona, C. Rodríguez-Franco, R. Fernández, V. Hornillos and J. M. Lassaletta, *Chem. Soc. Rev.*, 2021, **50**, 2968–2983.
8 J.-K. Cheng, S.-H. Xiang, S. Li, L. Ye and B. Tan, *Chem. Rev.*, 2021, **121**, 4805–4902.
9 Z.-X. Zhang, L.-G. Liu, Y.-X. Liu, J. Lin, X. Lu, L.-W. Ye and B. Zhou, *Chem. Sci.*, 2023, **14**, 5918–5924.
10 D. Xu, S.-L. Huang, F.-L. Hu, L. Peng, S.-Q. Jia, H. Mao, X.-G. Gong, F.-L. Li, W.-L. Qin and H.-L. Yan, *CCS Chem.*, 2022, **4**, 2686–2697.
11 J. Yang, J.-W. Zhang, W. Bao, S.-Q. Qiu, S. Li, S.-H. Xiang, J. Song, J. Zhang and B. Tan, *J. Am. Chem. Soc.*, 2021, **143**, 12924–12929.
12 Y.-H. Guo, M.-M. Liu, X.-J. Zhu, L.-R. Zhu and C. He, *Angew. Chem., Int. Ed.*, 2021, **60**, 13887–13891.
13 B.-B. Zhan, L. Wang, J. Luo, X.-F. Lin and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2020, **59**, 3568–3572.
14 L.-L. Dai, Y.-H. Liu, Q. Xu, M.-F. Wang, Q.-H. Zhu, P.-Y. Yu, G.-F. Zhong and X.-F. Zeng, *Angew. Chem., Int. Ed.*, 2023, **62**, e202216534.
15 Q.-J. An, W. Xia, W.-Y. Ding, H.-H. Liu, S.-H. Xiang, Y.-B. Wang, G. Zhong and B. Tan, *Angew. Chem., Int. Ed.*, 2021, **60**, 24888–24893.
16 J. Wang, X.-T. Qi, X.-L. Min, W.-B. Yi, P. Liu and Y. He, *J. Am. Chem. Soc.*, 2021, **143**, 10686–10694.
17 S.-Y. Yan, W. Xia, S.-Y. Li, Q.-L. Song, S.-H. Xiang and B. Tan, *J. Am. Chem. Soc.*, 2020, **142**, 7322–7327.
18 J.-Z. Wang, J. Zhou, C. Xu, H.-B. Sun, L. Kürti and Q.-L. Xu, *J. Am. Chem. Soc.*, 2016, **138**, 5202–5205.
19 K. Zhao, S. Yang, Q. Gong, L.-H. Duan and Z.-H. Gu, *Angew. Chem., Int. Ed.*, 2021, **60**, 5788–5793.
20 C.-X.-A. Tan, R. Li, F.-H. Zhang, L. Dai, N. Ullan and Y.-X. Lu, *Angew. Chem., Int. Ed.*, 2022, **61**, e202209494.
21 Y.-B. Chen, Y.-N. Yang, X.-Z. Huo, L.-W. Ye and B. Zhou, *Sci. China: Chem.*, 2023, **66**, 2480–2491.
22 T.-J. Han, Z.-X. Zhang, M.-C. Wang, L.-P. Xu and G.-J. Mei, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207517.
23 J. He, L.-X. Luo, S.-D. Xu, F.-Y. Yang and W.-F. Zhu, *Chem. Biol. Drug Des.*, 2023, **101**, 195–217.
24 N. Singh, S. Singh, S. Kohli, A. Singh, H. Asiki, G. Rathee, R. Chandra and E. A. Anderson, *Org. Chem. Front.*, 2021, **8**, 5550–5573.
25 J. García-Ramírez, L. A. González-Cortés and L. D. Miranda, *Org. Lett.*, 2022, **24**, 8093–8097.
26 D. Patel, D. S. Shah, K. Patel, A. Patel, T. Bambharoliya, A. Mahavar and A. Patel, *Mini-Rev. Org. Chem.*, 2024, **21**, 717–741.
27 F.-C. Gong, Q. Shi, X.-J. Mou, K. Wang, Q.-Q. Wang and H.-T. Wang, *Aging*, 2023, **15**, 13669–13679.
28 V. Bhardwaj, D. Gumber, V. Abbot, S. Dhiman and P. Sharma, *RSC Adv.*, 2015, **5**, 15233–15266.
29 D. Akbaslar, E. S. Giray and O. Algul, *Mol. Divers.*, 2021, **25**, 2321–2338.
30 L. Zhang, J. Zhang, J. Ma, D.-J. Cheng and B. Tan, *J. Am. Chem. Soc.*, 2017, **139**, 1714–1717.
31 L. Zhang, S.-H. Xiang, J. Wang, J. Xiao, J.-Q. Wang and B. Tan, *Nat. Commun.*, 2019, **10**, 566.
32 U. Dhawa, C. Tian, T. Wdowik, J. C. A. Oliveira, J. Hao and L. Ackermann, *Angew. Chem., Int. Ed.*, 2020, **59**, 13451–13457.
33 Y. Gao, L.-Y. Wang, T. Zhang, B.-M. Yang and Y. Zhao, *Angew. Chem., Int. Ed.*, 2022, **61**, e202200371.
34 K.-W. Chen, Z.-H. Chen, S. Yang, S.-F. Wu, Y.-C. Zhang and F. Shi, *Angew. Chem., Int. Ed.*, 2022, **61**, e202116829.
35 S.-C. Zheng, Q. Wang and J.-P. Zhu, *Angew. Chem., Int. Ed.*, 2019, **58**, 9215–9219.
36 Y.-B. Wang, Q.-H. Wu, Z.-P. Zhou, S.-H. Xiang, Y. Cui, P.-Y. Yu and B. Tan, *Angew. Chem., Int. Ed.*, 2019, **58**, 13443–13447.

37 R. Jana, T. P. Pathak and M. S. Sigman, *Chem. Rev.*, 2011, **111**, 1417–1492.
38 I. P. Beletskaya and V. P. Ananikov, *Chem. Rev.*, 2011, **111**, 1596–1636.
39 A. A. Thomas and S. E. Denmark, *Science*, 2016, **352**, 329–332.
40 N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457–2483.
41 K. B. Gan, R.-L. Zhong, Z.-W. Zhang and F. Y. Kwong, *J. Am. Chem. Soc.*, 2022, **144**, 14864–14873.
42 P. Devendar, R.-Y. Qu, W.-M. Kang, B. He and G.-F. Yang, *J. Agric. Food Chem.*, 2018, **66**, 8914–8934.
43 W.-Q. Ji, H.-L. Wu and J.-L. Zhang, *ACS Catal.*, 2020, **10**, 1548–1554.
44 A. Chatterjee and T. R. Ward, *Catal. Lett.*, 2016, **146**, 820–840.
45 B. A. Baviskar, P. V. Ajmire, D. S. Chumbhale, M. S. Khan, V. G. Kuchake, M. Singupuram and P. R. Laddha, *Sustainable Chem. Pharm.*, 2023, **32**, 2352–5541.
46 S.-Q. Qiu, Y. Chen, X.-J. Peng, S.-J. He, J. K. E. Cheng, Y.-B. Wang, S.-H. Xiang, J. Song, P.-Y. Yu and J.-M. Zhang, *Angew. Chem., Int. Ed.*, 2022, **61**, e202211211.
47 R. Pearce-Higgins, L. N. Hogenhout, P. J. Docherty, D. M. Whalley, P. Chuentragool, N. Lee, N. Y. S. Lam, T. M. McGuire, D. Valette and R. J. Phipps, *J. Am. Chem. Soc.*, 2022, **144**, 15026–15032.
48 X.-Q. Guo, Y.-N. Wang, D. Wang, L.-H. Cai, Z. X. Chen and X. F. Hou, *Dalton Trans.*, 2012, **41**, 14557–14567.
49 N. A. LaBerge and J. A. Love, *Eur. J. Org. Chem.*, 2015, 5546–5553.
50 K. Muto, J. Yamaguchi, D. G. Musaev and K. Itami, *Nat. Commun.*, 2015, **6**, 7508.
51 C. A. Malapit, J. R. Bour, C. E. Brigham and M. S. Sanford, *Nature*, 2018, **563**, 100–104.
52 S.-C. Shi, G.-R. Meng and M. Szostak, *Angew. Chem., Int. Ed.*, 2016, **55**, 6959–6963.
53 S. Duggan, *Drugs*, 2019, **79**, 477–481.
54 M. Kato, H. Furuie, T. Shimizu, A. Miyazaki, F. Kobayashi and H. Ishizuka, *Br. J. Clin. Pharmacol.*, 2018, **84**, 1821–1829.
55 P. Kolkhof and L. Bärfacker, *J. Endocrinol.*, 2017, **234**, 125–140.
56 S. Ito, H. Itoh, H. Rakugi, Y. Okuda and S. Yamakawa, *J. Hum. Hypertens.*, 2019, **33**, 542–551.
57 W.-T. Chang and S.-N. Wu, *Biomedicines*, 2021, **9**, 549.
58 H. Rakugi, S. Ito, H. Itoh, Y. Okuda and S. Yamakawa, *Hypertens. Res.*, 2019, **42**, 1932–1941.
59 B. L. Canne, J. Chen, L. E. Dalrymple, B. T. Flatt, T. P. Forsyth, X. H. Gu, M. B. Mac, L. W. Mann, G. Mann, R. Martin, R. Mohan, B. Murphy, M. C. Nyman, W. C. J. Stevens, T. L. Wang, Y. Wong and J. H. Wu, WO2006012642A2, 2006.
60 L. C. Banne, J. Chen, L. E. Dalrymple, B. T. Flatt, T. P. Forsyth, X.-H. Gu, M. B. Mac, L. W. Mann, G. Mann, R. Martin, R. Mohan, B. Murphy, M. C. Nyman, W. C. Stevens, T.-L. Wang, Y. Wang and J. H. Wu, US20110301128A1, 2011.
61 M. Watanabe, H. Nagasawa and N. Sato, 2019, US10308604B2, 2019.
62 Y. Zhou, P. Liao and J. Qu, CN114456098B, 2024.