ACS Catalysis

pubs.acs.org/acscatalysis Letter

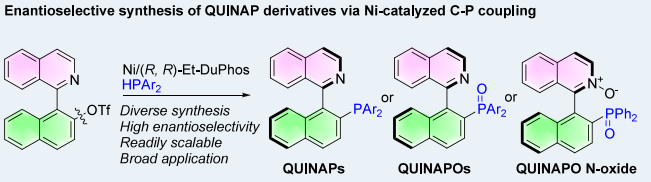
Modular Assembly of Axially Chiral QUINAP Derivatives via Nickel-Catalyzed Enantioselective C−P Cross-Coupling

Zhiping Yang, Xiaodong Gu, Li-Biao Han, and Jun Wang*

Cite This: ACS Catal. 2025, 15, 8268−8273 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: QUINAPs represent a powerful class of ligands with broad applications in a diverse array of synthetically important asymmetric transformations. However, their broader utilization is often constrained by a limited substrate scope and high cost associated with their multistep synthesis. Consequently, a highly efficient dynamic kinetic asymmetric transformation of *N*-heterobiaryl derivatives has been developed through Ni-catalyzed asymmetric C−P cross-coupling. This method provides versatile access to a wide range of substituted QUINAP derivatives with good yields and high enantioselectivities, which are successfully applied in both transition-metal catalysis and organocatalysis.



KEYWORDS: *Axial Chirality, C−P coupling, Ni-catalysis, QUINAP, DYKAT*

Axially chiral phosphine ligands have become fundamentally important in modern organic chemistry due to their pivotal role in catalytic processes, where they significantly influence both catalytic activity and selectivity.[1] Among these, axially chiral *P,N*-ligands, such as QUINAP and Quinazolinap, have emerged as a particularly powerful class, with notable recent advances in their synthesis, resolution, and application to a broad spectrum of synthetically important asymmetric transformations (Scheme 1a).[1e,f] However, the synthesis of axially chiral *P,N*-ligands has predominantly relied on intricate, multistep procedures and resolution methods, which limit the ability to systematically modify the steric and electronic properties of the catalyst.[1e]

N-Heterobiaryl derivatives are widely employed in classical dynamic kinetic asymmetric transformation (DYKAT) systems, primarily through the formation of intermediate metallacycles. Over the past decades, noble metal-catalyzed DYKATs, utilizing metals such as Pd, Rh, and Ir, have demonstrated remarkable efficacy in synthesizing axially chiral heterobiaryls.[2] In 2013, Lassaletta ingeniously developed a dynamic kinetic Suzuki−Miyaura cross-coupling method, employing heterobiaryl triflates and chiral palladium complexes.[2a] This strategy was subsequently extended to construct a variety of C−C,[2b−e] C−N,[2f] and C−P[2g−i] bonds in a series of axially chiral heterobiaryl compounds. Notably, Rh-catalyzed[3] or Ir-catalyzed[4] C−H bond activation strategies in DYKAT chemistry have also achieved significant advancements, further propelling the development of this field.

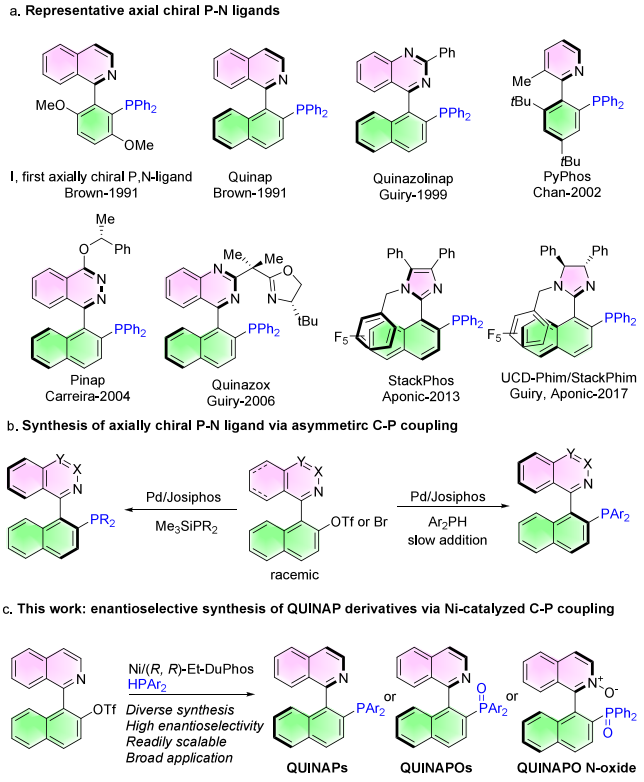
In the realm of earth-abundant metal-catalyzed DYKAT chemistry, the Tang group recently achieved notable breakthroughs, including a photomediated cobalt-catalyzed asymmetric radical coupling reaction and 1,4-addition reactions.[5] Meanwhile, Wang reported a significant advancement with the development of a cobalt-catalyzed asymmetric reductive alkenylation and arylation of heterobiaryl tosylates.[6] More recently, Liang introduced a groundbreaking dynamic kinetic reductive Grignard-type addition for the simultaneous construction of axial and central chirality through Co-catalysis.[7] Additionally, Cao developed a pioneering nickel-catalyzed enantio-convergent transformation of *N*-heterobiaryl derivatives using Grignard reagents.[8] Lately, Yu reported an innovative nickel-catalyzed enantio-convergent carboxylation of aza-biaryl triflates with CO_2, enabling the synthesis of atropisomeric carboxylic acids.[9] Despite these advancements, there have been no reported examples of asymmetric C−P bond construction for axially chiral *P,N*-ligands through Ni catalysis.

Asymmetric C−P bond construction represents a versatile and practical strategy for synthesizing axially chiral phosphorus compounds. This includes methodologies such as asymmetric C−P coupling,[2g−i] allenylation of phosphorus nucleophiles,[10] addition of phosphorus nucleophiles to alkynes,[11] and ring-opening reactions.[12] Despite the development of numerous methods for the preparation of axially chiral phosphorus compounds, the direct construction of C−P bonds through transition-metal-catalyzed approaches to synthesize axially chiral *P,N*-ligands remains a significant challenge. This challenge likely stems from the strong coordination between phosphorus nucleophiles and metal catalysts. The asymmetric synthesis of chiral QUINAP was not achieved until 2013, when

Received: March 5, 2025
Revised: April 29, 2025
Accepted: April 29, 2025

https://doi.org/10.1021/acscatal.5c01663
ACS Catal. 2025, 15, 8268−8273

Scheme 1. Ni-Catalyzed Asymmetric C−P Coupling for Synthesis of Chiral QUINAP Derivatives

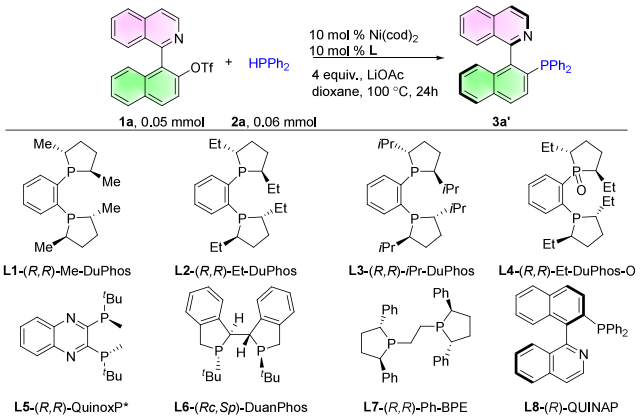


Stoltz and Virgil reported the kinetic resolution of aryl bromides and dynamic kinetic resolution of aryl-triflates asymmetric using Pd-catalyzed C−P coupling.[2g] Subsequent research has focused on synthesizing axially chiral P, N ligands via DKR process involving C−P coupling with aryl triflates (Scheme 1b).[2h,i] However, these methods suffer from significant limitations, including poor substrate generality, the reliance on expensive masked phosphine sources ($TMSPAr_2$), and the need for prolonged addition of $HPAr_2$ to minimize coordination between phosphine and metal catalysts. Additionally, the Tan group developed a kinetic resolution method for synthesis of axially chiral QUINAP derivatives through ketone-catalyzed enantioselective oxidation.[13]

Herein, building on traditional Ni-catalyzed C−P cross-coupling[14] and our group's previous work in chiral phosphorus chemistry,[10d,11b,15] we have developed a Ni-catalyzed DYKAT for the C−P coupling of *N*-heterobiaryl triflates and $HPAr_2$. This method provides a highly efficient approach for the structurally diverse construction of chiral QUINAP derivatives in high yields with excellent enantioselectivities (Scheme 1c).

We initially achieved Ni-catalyzed asymmetric C−P cross-coupling through dynamic kinetic asymmetric transformations using *N*-heterobiaryl triflate (**1a**) and $HPPh_2$ (**2a**) as model substrates in the presence of $Ni(cod)_2$ and chiral phosphine ligands (**L1**-**L8**) (Table 1). After optimization of the chiral ligands, we found that (*R*,*R*)-Et-DuPhos (**L2**) gave the best enantioselectivity (entries 1−8). (*R*,*R*)-Et-DuPhos-O (**L4**) was able to catalyze the reaction with a suboptimal result. Interestingly, (*R*)-QUINAP (**L8**) afforded 13% yield and 1% ee, suggesting that the product **3a′** can act as a ligand to some extent, thereby influencing enantioselectivity. This observation explains the challenges of achieving higher enantioselectivity. Then, using NaOAc instead of LiOAc increased the

Table 1. Optimization of the Reaction Conditions[a]



Entry	L	Base	Yield (%)	Ee (%)
1	**L1**	LiOAc	45	7
2	**L2**	LiOAc	73	68
3	**L3**	LiOAc	42	7
4	**L4**	LiOAc	49	13
5	**L5**	LiOAc	10	27
6	**L6**	LiOAc	67	49
7	**L7**	LiOAc	26	19
8	**L8**	LiOAc	13	1
9	**L2**	NaOAc	85	72
10	**L2**	KOAc	85	41
11[b]	**L2**	NaOAc	84	77
12[b,c]	**L2**	NaOAc	84	80
13[b,d]	**L2**	NaOAc	80	77
14[b,c,e]	**L2**	NaOAc	85	80
15[b,c,e,f]	**L2**	NaOAc	81	80

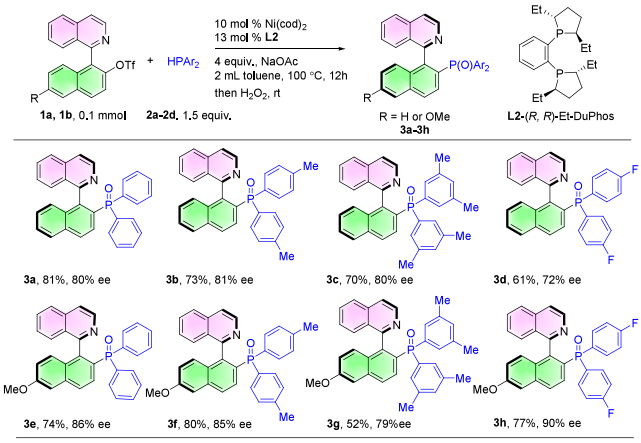
[a]Reaction conditions: **1a** (0.05 mmol), **2a** (0.06 mmol), 10 mol % $Ni(cod)_2$, 10 mol % **L**, in 1 mL of dioxane, 100 °C, 24 h. Yield (**3a′**) was based on ^{31}P NMR analysis with PPh_3 as internal standard. Ee was determined by HPLC analysis. [b]Toluene was used instead of dioxane. [c]13 mol % **L2**, 12 h. [d]5 mol % $Ni(cod)_2$, 6.5 mol % **L2**, 12 h. [e]0.075 mmol **2a**. [f]A scale of 0.1 mmol. Then 4 equiv of H_2O_2 was added. Isolated yield of QUINAPO **3a**.

enantioselectivity to 72% and KOAc gave poor enantioselectivity (entries 2, 9, and 10). Toluene outperformed 1,4-dioxane (entry 9 vs 11). Reducing the reaction time and increasing the loading of **L2** enhanced the enantioselectivity to 80% (entry 12). However, reducing the loading of $Ni(cod)_2$ and **L2** led to a decrease in the enantioselectivity (entry 13). The yield improved slightly when the amount of **2a** was increased to 1.5 equiv (entry 14). Finally, under the optimized conditions at a scale of 0.1 mmol and further oxidation by H_2O_2, QUINAPO **3a** was obtained in 81% isolated yield and 80% ee (entry 15). The configuration of the product (**3a′**) was consistent with that of commercially available (*R*)-QUINAP.

Having established the optimal conditions for this dynamic kinetic asymmetric C−P coupling, we initially explored various $HPAr_2$ (Table 2 **2a**−**2d**) with **1a**, yielding promising results (**3a**−**3d**, 61−81% yield, 72−81% ee). Furthermore, 6-MeO-substituted *N*-heterobiaryl triflates (**1b**) reacted with different $HPAr_2$ (**2**) to give improved yields and ee values (**3e**−**3h**, 52−80% yield, 79−90% ee) compared to **1a**. Various substituents on the naphthalene ring of *N*-heterobiaryl triflates were also investigated (Table 3). The presence of an ester group led to a decrease in enantioselectivity (**3l**, 79% yield, 75% ee), while the electron donating group enhanced enantioselectivity (**3i**−

https://doi.org/10.1021/acscatal.5c01663
ACS Catal. 2025, 15, 8268−8273

Table 2. Evaluation of the Substrate Scope of $HPAr_2$[a]

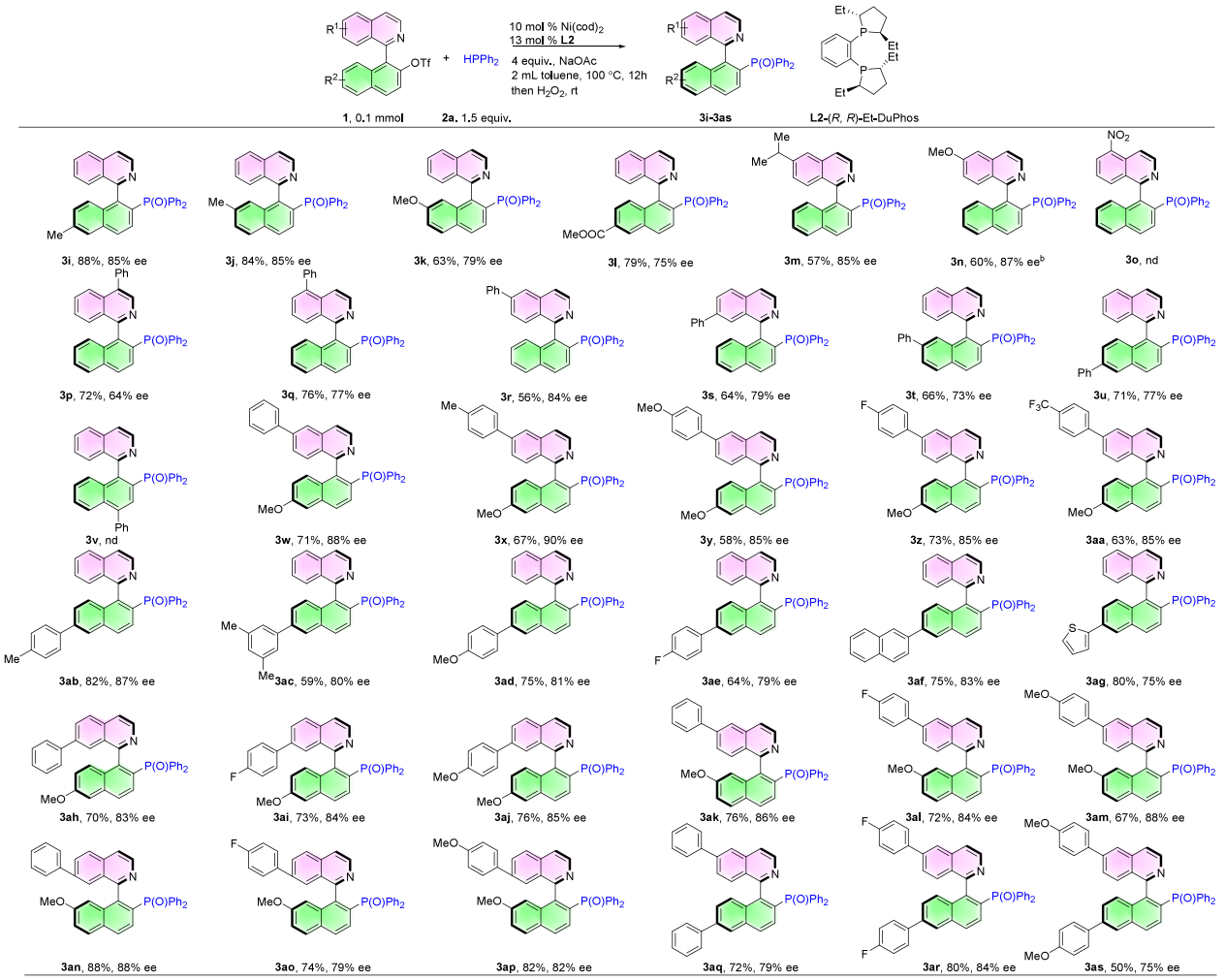


[a]Reaction conditions: **1a** (R = H) or **1b** (R = OMe) (0.1 mmol), **2a**−**2d** (0.15 mmol), 10 mol % $Ni(cod)_2$, 13 mol % **L2** in 2 mL of toluene, 100 °C, 12 h. Then 4 equiv of H_2O_2 was added. Isolated yield. Ee was determined by HPLC analysis.

3k, 63−88% yield, 79%−85% ee). 6-Substituent isoquinoline-based *N*-heterobiaryl triflates were also compatible with the reaction, although the electron-donating group slightly reduced yields (**3m** and **3n**, 57−60% yield, 85−87% ee). A strong electron withdrawing group (−NO_2, **3o**) resulted in a complex reactivity.

Next, the introduction of a phenyl group to the naphthalene or isoquinoline ring resulted in good yield and enantioselectivity (Table 3, **3p**−**3u**, 56−76% yield, 64−84% ee). However, 4-Ph-naphthalene triflates failed to react, likely due to steric hindrance (**3v**). To further explore the scope of the reaction, we selected 6-MeO-naphthalene as a constant and examined the effect of various substituents on the isoquinoline ring. Both electron-donating groups (Me and OMe) and electron-withdrawing groups (F and CF_3) were well-tolerated, yielding satisfactory results (**3w**−**3aa**, 58−73% yield, 85−90% ee). Moreover, *N*-heterobiaryl triflates bearing electron-donating groups (Me and OMe), electron-withdrawing groups (F), as well as 2-naphthalene or thiophene on the naphthalene ring, also produced QUINAPOs efficiently (**3ab**−**3ag**, 59−82% yield, 75−87% ee). Furthermore, different −Ar groups and −OMe positioned at various locations on *N*-heterobiaryl triflates also showed good practicality (**3ah**−**3ap**, 67−88%

Table 3. Evaluation of the Substrate Scope of Heterobiaryl Triflates with Different Substituents[a]



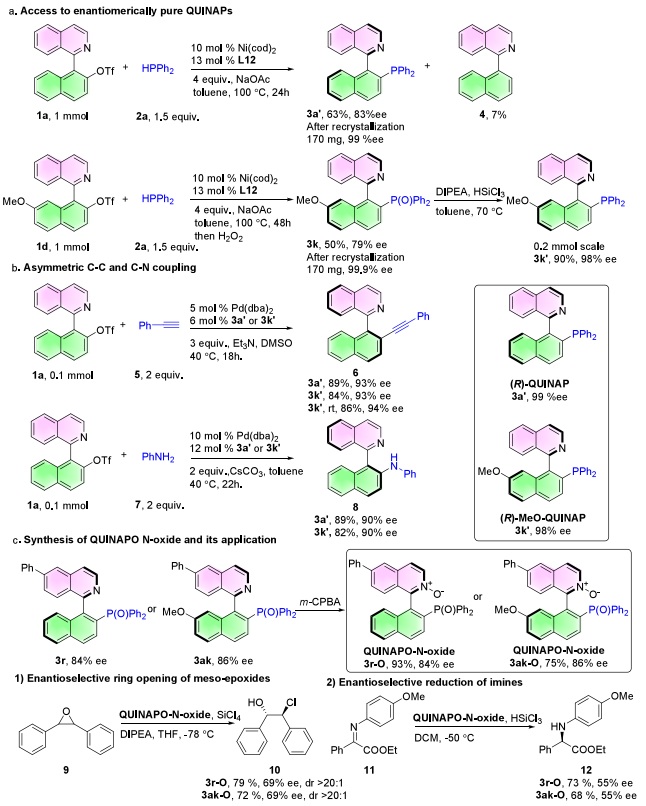
[a]Reaction conditions: **4** (0.1 mmol), **2a** (0.15 mmol), 10 mol % $Ni(cod)_2$, 13 mol % **L2** in 2 mL of toluene, 100 °C, 12 h. Then 4 equiv of H_2O_2 was added. Isolated yield. Ee was determined by HPLC analysis. [b]24 h.

https://doi.org/10.1021/acscatal.5c01663
ACS Catal. 2025, 15, 8268−8273

yield, 79−88% ee). Finally, substrates featuring 6-Ar-naphthalene and 6-Ar-isoquinoline also smoothly yielded the desired products (**3aq**−**3as**, 50−80% yield, 75−84% ee).

To evaluate the efficiency of the current method, a 1 mmol scale reaction was conducted, yielding **3a′** (63%, 83% ee) and **3k** (50%, 79% ee). During the scale-up reaction, we observed detriflate and protonation products (**4**), which are common side products in transition metal-catalyzed C−P coupling reactions.[16] Products (**3a′** and **3k**) with 99% ee were obtained after recrystallization. Compound **3k** was further transformed via reduction with $HSiCl_3$, affording **3k′** in 90% yield with 98% ee (Scheme 2a). (*R*)-MeO-QUINAP (**3k′**) demonstrated

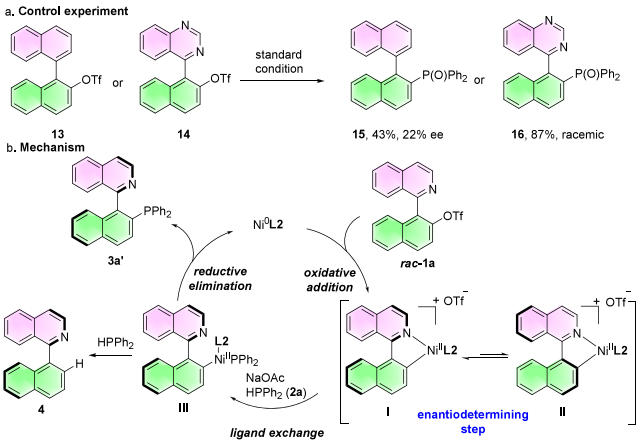
Scheme 2. Access to Enantiomerically Pure QUINAPs and Applications in Enantioselective and Diastereoselective Catalysis



catalytic activity comparable to that of (*R*)-QUINAP (**3a′**) in asymmetric C−C and C−N coupling reactions, showcasing excellent catalytic efficiency (Scheme 2b). Additionally, compounds (**3r** and **3ak**) were oxidized by *m*-CPBA to synthesize (*R*)-QUINAPO *N*-oxide **3r-O** and **3ak-O** in good yields without loss of enantioselectivity, which shows potential application in enantioselective and diastereoselective ring opening of meso-epoxides and reduction of imines in good yields and moderate enantioselectivities without condition optimization (Scheme 2c).

To gain insight into the nickel-catalyzed asymmetric C−P coupling reaction, control experiments were conducted. The yield and enantioselectivity decreased significantly in the absence of a nitrogen atom (**15**, 43%, 22% ee), suggesting that the formation of a five-membered nickelacycle is essential for this asymmetric transformation. The quinazoline skeleton gave racemic product (**16**, 87% yield, racemic), likely due to the weak coordination of the nitrogen atom in quinazoline to the Ni catalysis and its quickly racemization in high temperature (see the Supporting Information) (Scheme 3a).

Scheme 3. Mechanistic Investigations



Based on recent work about asymmetric synthesis of *N*-heterobiaryl derivatives via Ni-catalysis[8,9] and the control experiment, a possible mechanism is proposed as follows. First, the coordination of the nitrogen atom in isoquinoline to the generated $Ni^{(0)}$**L2** complex facilitates the oxidative addition of the C−O bond in triflates (**1a**) to $Ni^{(0)}$**L2**, forming 5-membered cationic nickelacycle (Ar−$Ni^{(II)}$**L2**) diastereoisomers **I** and **II**, which was the enantiodetermining step. These intermediates are prone to epimerization.[17] Following a ligand exchange step, intermediate **III** is generated, which undergoes competitive protonolysis of the Ni−C bond within the biaryl entity. This protonolysis leads to the formation of a byproduct (**4**). The primary pathway involves a reductive elimination, yielding **3a′** while regenerating the $Ni^{(0)}$**L2** complex (Scheme 3b).

In summary, we have developed an atroposelective DYKATs strategy for the asymmetric synthesis of QUINAP derivatives by using a Ni/(*R*,*R*)-Et-DuPhos catalyzed C−P cross-coupling approach. A wide range of *N*-heterobiaryl triflates and $HPAr_2$ participated efficiently in the reaction, generating chiral QUINAPs and QUINAPOs in high yield (up to 88%) and enantioselectivities (up to 90% ee). Moreover, we demonstrated the utility of these QUINAP derivatives in asymmetric metal catalysis and organocatalysis, exhibiting good catalytic activity. Future studies will focus on expanding the QUINAP ligand toolbox to address challenging problems in asymmetric catalysis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.5c01663.

Experimental details and procedures, characterization data, HPLC chromatograms and NMR spectra of isolated compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Jun Wang − *Department of Chemistry, Hong Kong Baptist University, Kowloon, Hong Kong 999077, China;*

https://doi.org/10.1021/acscatal.5c01663
ACS Catal. 2025, 15, 8268−8273

orcid.org/0000-0001-9723-4054; Email: junwang@hkbu.edu.hk

Authors

Zhiping Yang − *Department of Chemistry, Hong Kong Baptist University, Kowloon, Hong Kong 999077, China; Yunnan Key Laboratory of Chiral Functional Substance Research and Application, Yunnan Minzu University, Kunming 650500, China*

Xiaodong Gu − *Department of Chemistry, Hong Kong Baptist University, Kowloon, Hong Kong 999077, China*

Li-Biao Han − *Research Center of Advanced Catalytic Materials & Functional Molecular Synthesis, College of Chemistry & Chemical Engineering, Shaoxing University, Shaoxing 312000, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acscatal.5c01663

Author Contributions

Dr. Z. Yang conceived the project, performed the experiments, and prepared the Supporting Information. Mr. X. Gu repeated some experiments and collected some data. Prof. L.-B. Han contributed to the mechanism study. Prof. J. Wang directed the project. Dr. Z. Yang and Prof. J. Wang wrote the paper with input from all other authors.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the University Grants Committee (Hong Kong) (GRF 12303422), National Natural Science Foundation of China (NSFC 22271241), and HKBU RC-SFCRG/23-24 for financial support. Z. Yang thanks the support of Yunnan Key Laboratory of Chiral Functional Substance Research and Application (202402AN360010) and K. C. Wong Education Foundation. L-B Han thanks the support of Leading Innovative and Entrepreneur Team Introduction Program of Zhejiang (2022R01021).

■ REFERENCES

(1) (a) Kočovský, P.; Vyskočil, Š.; Smrčina, M. Non-Symmetrically Substituted 1,1'-Binaphthyls in Enantioselective Catalysis. *Chem. Rev.* **2003**, *103*, 3213−3246. (b) Carroll, M. P.; Guiry, P. J. P, N Ligands in Asymmetric Catalysis. *Chem. Soc. Rev.* **2014**, *43*, 819−833. (c) Fernandez, E.; Guiry, P. J.; Connole, K. P. T.; Brown, J. M. Quinap and Congeners: Atropos PN ligands for Asymmetric Catalysis. *J. Org. Chem.* **2014**, *79*, 5391−5400. (d) Wencel-Delord, J.; Panossian, A.; Leroux, F. R.; Colobert, F. Recent Advances and New Concepts for the Synthesis of Axially Stereoenriched Biaryls. *Chem. Soc. Rev.* **2015**, *44*, 3418−3430. (e) Rokade, B. V.; Guiry, P. J. Axially Chiral P,N-Ligands: Some Recent Twists and Turns. *ACS Catal.* **2018**, *8*, 624−643. (f) Rokade, B. V.; Barker, J.; Guiry, P. J. Development of and Recent Advances in Asymmetric A3 Coupling. *Chem. Soc. Rev.* **2019**, *48*, 4766−4790. (g) Carmona, J. A.; Rodriguez-Franco, C.; Fernandez, R.; Hornillos, V.; Lassaletta, J. M. Atroposelective Transformation of Axially Chiral (Hetero)biaryls. From Desymmetrization to Modern Resolution Strategies. *Chem. Soc. Rev.* **2021**, *50*, 2968−2983.

(2) (a) Ros, A.; Estepa, B.; Ramirez-Lopez, P.; Alvarez, E.; Fernandez, R.; Lassaletta, J. M. Dynamic Kinetic Cross-Coupling Strategy for the Asymmetric Synthesis of Axially Chiral Heterobiaryls. *J. Am. Chem. Soc.* **2013**, *135*, 15730−15733. (b) Hornillos, V.; Ros, A.; Ramirez-Lopez, P.; Iglesias-Siguenza, J.; Fernandez, R.; Lassaletta, J. M. Synthesis of Axially Chiral Heterobiaryl Alkynes via Dynamic Kinetic Asymmetric Alkynylation. *Chem. Commun.* **2016**, *52*, 14121−14124. (c) Sun, Y.-W.; Zhao, J.-H.; Yan, X.-Y.; Ji, C.-L.; Feng, H.; Gao, D.-W. Asymmetric Synthesis of Atropisomers Featuring Cyclobutane Boronic Esters Facilitated by Ring-strained B-ate Complexes. *Nat. Commun.* **2024**, *15*, 10810. (d) Su, L.; Gao, S.; Liu, J. Enantioconvergent Synthesis of Axially Chiral Amides Enabled by Pd-catalyzed Dynamic Kinetic Asymmetric Aminocarbonylation. *Nat. Commun.* **2024**, *15*, 7248−7261. (e) Ye, B.; Su, L.; Zheng, K.; Gao, S.; Liu, J. Synergistic Photoredox/Palladium Catalyzed Enantioconvergent Carboxylation of Racemic Heterobiaryl (Pseudo)-Halides with CO(2). *Angew. Chem., Int. Ed.* **2024**, *64*, No. e202413949. (f) Ramirez-Lopez, P.; Ros, A.; Romero-Arenas, A.; Iglesias-Siguenza, J.; Fernandez, R.; Lassaletta, J. M. Synthesis of IAN-type N,N-Ligands via Dynamic Kinetic Asymmetric Buchwald-Hartwig Amination. *J. Am. Chem. Soc.* **2016**, *138*, 12053−12056. (g) Bhat, V.; Wang, S.; Stoltz, B. M.; Virgil, S. C. Asymmetric Synthesis of QUINAP via Dynamic Kinetic Resolution. *J. Am. Chem. Soc.* **2013**, *135*, 16829−16832. (h) Ramirez-Lopez, P.; Ros, A.; Estepa, B.; Fernandez, R.; Fiser, B.; Gomez-Bengoa, E.; Lassaletta, J. M. A Dynamic Kinetic C-P Cross-Coupling for the Asymmetric Synthesis of Axially Chiral P,N Ligands. *ACS Catal.* **2016**, *6*, 3955−3964. (i) Han, S.-J.; Bhat, V.; Stoltz, B. M.; Virgil, S. C. Atroposelective Synthesis of PINAP via Dynamic Kinetic Asymmetric Transformation. *Adv. Synth. Catal.* **2019**, *361*, 441−444.

(3) (a) Wang, Q.; Cai, Z.-J.; Liu, C.-X.; Gu, Q.; You, S.-L. Rhodium-Catalyzed Atroposelective C-H Arylation: Efficient Synthesis of Axially Chiral Heterobiaryls. *J. Am. Chem. Soc.* **2019**, *141*, 9504−9510. (b) Wang, Q.; Zhang, W.-W.; Song, H.; Wang, J.; Zheng, C.; Gu, Q.; You, S.-L. Rhodium-Catalyzed Atroposelective Oxidative C-H/C-H Cross-Coupling Reaction of 1-Aryl Isoquinoline Derivatives with Electron-Rich Heteroarenes. *J. Am. Chem. Soc.* **2020**, *142*, 15678−15685. (c) Zheng, D.-S.; Zhang, W.-W.; Gu, Q.; You, S.-L. Rh(III)-Catalyzed Atroposelective C-H Iodination of 1-Aryl Isoquinolines. *ACS Catal.* **2023**, *13*, 5127−5134. (d) Zheng, D.-S.; Zheng, J.; Wang, Q.; Gu, Q.; You, S.-L. Rhodium(III)-Catalyzed Atroposelective C—H Indolylization of 1-Aryl Isoquinolines with 3-Indolylphenyliodonium Salts. *Chin. J. Chem.* **2023**, *41*, 2684−2690. (e) Zheng, D.-S.; Xie, P.-P.; Zhao, F.; Zheng, C.; Gu, Q.; You, S.-L. Rh(III)-Catalyzed Atroposelective C−H Selenylation of 1-Aryl Isoquinolines. *ACS Catal.* **2024**, *14*, 6009−6015.

(4) (a) Romero-Arenas, A.; Hornillos, V.; Iglesias-Siguenza, J.; Fernandez, R.; Lopez-Serrano, J.; Ros, A.; Lassaletta, J. M. Ir-Catalyzed Atroposelective Desymmetrization of Heterobiaryls: Hydroarylation of Vinyl Ethers and Bicycloalkenes. *J. Am. Chem. Soc.* **2020**, *142*, 2628−2639. (b) Li, F.; Luo, Y.; Ren, J.; Yuan, Q.; Yan, D.; Zhang, W. Iridium-Catalyzed Asymmetric Hydroarylation of Unactivated Alkenes with Heterobiaryls: Simultaneous Construction of Axial and Central Chirality. *Org. Lett.* **2024**, *26*, 6835−6840. (c) Xiong, M.; Yan, Z.; Chen, S.-C.; Tang, J.; Yang, F.; Xing, D. Iridium-Catalyzed Regiodivergent Atroposelective C−H Alkylation of Heterobiaryls with Alkenes. *ACS Catal.* **2024**, *14*, 7243−7255.

(5) (a) Jiang, X.; Xiong, W.; Deng, S.; Lu, F.-D.; Jia, Y.; Yang, Q.; Xue, L.-Y.; Qi, X.; Tunge, J. A.; Lu, L.-Q.; Xiao, W.-J. Construction of Axial Chirality via Asymmetric Radical Trapping by Cobalt under Visible Light. *Nat. Catal.* **2022**, *5*, 788−797. (b) Xiong, W.; Jiang, X.; Wang, W.-C.; Cheng, Y.; Lu, L.-Q.; Gao, K.; Xiao, W.-J. Dynamic Kinetic Reductive Conjugate Addition for Construction of Axial Chirality Enabled by Synergistic Photoredox/Cobalt Catalysis. *J. Am. Chem. Soc.* **2023**, *145*, 7983−7991.

(6) Dong, H.; Wang, C. Cobalt-Catalyzed Asymmetric Reductive Alkenylation and Arylation of Heterobiaryl Tosylates: Kinetic Resolution or Dynamic Kinetic Resolution? *J. Am. Chem. Soc.* **2023**, *145*, 26747−26755.

(7) Shao, Y.-P.; Liang, Y.-M. Dynamic Kinetic Reductive Grignard-Type Addition for the Construction of Axial and Central Chirality. *ACS Catal.* **2025**, *15*, 1147−1157.

(8) Sun, T.; Zhang, Z.; Su, Y.; Cao, H.; Zhou, Y.; Luo, G.; Cao, Z.-C. Nickel-Catalyzed Enantioconvergent Transformation of Anisole Derivatives via Cleavage of C−OMe Bond. *J. Am. Chem. Soc.* **2023**, *145*, 15721−15728.

(9) Chen, X.-W.; Li, C.; Gui, Y.-Y.; Yue, J.-P.; Zhou, Q.; Liao, L.-L.; Yang, J.-W.; Ye, J.-H.; Yu, D.-G. Atropisomeric Carboxylic Acids Synthesis via Nickel-Catalyzed Enantioconvergent Carboxylation of Aza-Biaryl Triflates with CO2. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202403401.
(10) (a) Zhang, J.; Chang, X.; Xu, X.; Wang, H.; Peng, L.; Guo, C. Nickel-catalyzed Switchable 1,3-Dienylation and Enantioselective Allenylation of Phosphine Oxides. *Nat. Commun.* **2022**, *13*, 7049−7059. (b) Wang, W.-H.; Wu, Y.; Wang, H.-T.; Qi, P.-J.; Lan, W.-N.; Zhang, Q.-W. Enantioselective Synthesis of P-Stereogenic Allenylphosphines through Ni-catalysed Propargylic Substitution. *Nat. Synth.* **2022**, *1*, 738−747. (c) Wang, H.; Qian, H.; Zhang, J.; Ma, S. Catalytic Asymmetric Axially Chiral Allenyl C−P Bond Formation. *J. Am. Chem. Soc.* **2022**, *144*, 12619−12626. (d) Gu, X.; Ngai, K. Y.; Wang, W.; Li, B.; Wang, J. Ni-catalyzed Propargylic Substitution Reaction: A General and Versatile Tool to Assemble Axially Chiral Phosphorus-containing Allenes. *Chem. Catal* **2024**, *4*, 100903−100916.
(11) (a) Ji, D.; Jing, J.; Wang, Y.; Qi, Z.; Wang, F.; Zhang, X.; Wang, Y.; Li, X. Palladium-catalyzed Asymmetric Hydrophosphination of Internal Alkynes: Atroposelective access to Phosphine-functionalized Olefins. *Chem.* **2022**, *8*, 3346−3362. (b) Cai, B.; Cui, Y.; Zhou, J.; Wang, Y. B.; Yang, L.; Tan, B.; Wang, J. J. Asymmetric Hydrophosphinylation of Alkynes: Facile Access to Axially Chiral Styrene-Phosphines. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202215820.
(12) (a) Pang, L.; Sun, Q.; Huang, Z.; Li, G.; Liu, J.; Guo, J.; Yao, C.; Yu, J.; Li, Q. Palladium-Catalyzed Stereoselective Cleavage of C-P Bond: Enantioselective Construction of Atropisomers Containing a P-Stereogenic Center. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202211710. (b) Pang, L.; Huang, Z.; Sun, Q.; Li, G.; Liu, J.; Li, B.; Ma, C.; Guo, J.; Yao, C.; Yu, J.; Li, Q. Diversity-oriented Synthesis of P-Stereogenic and Axially Chiral Monodentate Biaryl Phosphines Enabled by C-P bond Cleavage. *Nat. Commun.* **2023**, *14*, 4437−4447. (c) Pang, L.; Wang, C.; Ma, C.; Liu, J.; Shi, M.; Yao, C.; Yu, J.; Li, Q. Palladium-Catalyzed Modular Assembly of P-Stereogenic and Axially Chiral Phosphinooxazoles (PHOX) Ligands by C-P Bond Cleavage/Intermolecular C(sp(2))-H Bond Functionalization. *Org. Lett.* **2023**, *25*, 7705−7710. (d) Sun, J.; Yan, Y.; Chen, X.; Huang, Z.; Huang, Y. Palladium-Catalyzed Regio- and Stereoselective Phosphination of Cyclic Biarylsulfonium Salts to Access Atropoisomeric Phosphines. *Chem. Sci.* **2024**, *15*, 6943−6948.
(13) Jiang, P.-Y.; Wu, S.; Wang, G.-J.; Xiang, S.-H.; Tan, B. Synthesis of Axially Chiral QUINAP Derivatives by Ketone-Catalyzed Enantioselective Oxidation. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202309272.
(14) (a) Zhang, X.-H.; Liu, H.-Z.; Hu, X.-M.; Tang, G.; Zhu, J.; Zhao, Y.-F. Ni(II)/Zn Catalyzed Reductive Coupling of Aryl Halides with Diphenylphosphine Oxide in Water. *Org. Lett.* **2011**, *13*, 3478−3481. (b) Yang, J.; Chen, T.; Han, L.-B. C-P Bond-Forming Reactions via C-O/P-H Cross-Coupling Catalyzed by Nickel. *J. Am. Chem. Soc.* **2015**, *137*, 1782−1785. (c) Yang, J.; Xiao, J.; Chen, T.; Han, L.-B. Nickel-Catalyzed Phosphorylation of Phenol Derivatives via C-O/P-H Cross-Coupling. *J. Org. Chem.* **2016**, *81*, 3911−3916.
(15) (a) Lu, Z.; Zhang, H.; Yang, Z.; Ding, N.; Meng, L.; Wang, J. Asymmetric Hydrophosphination of Heterobicyclic Alkenes: Facile Access to Phosphine Ligands for Asymmetric Catalysis. *ACS Catal.* **2019**, *9*, 1457−1463. (b) Yang, Z.; Gu, X.; Han, L.-B.; Wang, J. Palladium-catalyzed Asymmetric Hydrophosphorylation of Alkynes: Facile access to P-Stereogenic Phosphinates. *Chem. Sci.* **2020**, *11*, 7451−7455. (c) Yang, Z.; Wang, J. Enantioselective Palladium-Catalyzed Hydrophosphinylation of Allenes with Phosphine Oxides: Access to Chiral Allylic Phosphine Oxides. *Angew. Chem., Int. Ed.* **2021**, *60*, 27288−27292. (d) Yang, Z.; Du, Q.; Jiang, Y.; Wang, J. Asymmetric Access of γ-Amino Acids and γ-Amino Phosphonic Acid Derivatives via Copper-Catalyzed Enantioselective and Regioselective Hydroamination. *CCS Chem.* **2022**, *4*, 1901−1911. (e) Zhang, Y.; Jiang, Y.; Li, M.; Huang, Z.; Wang, J. Palladium-catalyzed Diastereo- and Enantioselective Desymmetric Hydrophosphination of Cyclopropenes. *Chem. Catal* **2022**, *2*, 3163−3173. (f) Zhou, J.; Yang, Q.; Lee, C. S.; Wang, J. Enantio- and Regioselective Construction of 1,4-Diamines via Cascade Hydroamination of Methylene Cyclopropanes. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202202160. (g) Jiang, Y.; Cheng, K. W.; Zhang, H.; Yang, Z.; Wang, J. Palladium/Azaphos-Catalyzed Asymmetric Suzuki−Miyaura Coupling. *Synthesis* **2023**, *55*, 2537−2542. (h) Yang, Q.; Zhou, J.; Wang, J. J. Enantioselective Copper-catalyzed Hydrophosphination of Alkenyl Isoquinolines. *Chem. Sci.* **2023**, *14*, 4413−4417. (i) Zhou, J.; Meng, L.; Lin, S.; Cai, B.; Wang, J. J. Palladium-Catalyzed Enantio- and Regioselective Ring-Opening Hydrophosphinylation of Methylenecyclopropanes. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202303727. (j) Zhou, J.; Meng, L.; Yang, Z.; Wang, J. Enantio- and Regioselective Cascade Hydroboration of Methylenecyclopropanes for Facile Access to Chiral 1,3- and 1,4-Bis(boronates). *Adv. Sci.* **2024**, *11*, 2400096−2400104. (k) Jiang, Y.; Cheng, K. W.; Yang, Z.; Wang, J. Pd-catalyzed Enantioselective and Regioselective Asymmetric Hydrophosphorylation and Hydrophosphinylation of Enynes. *Chin. Chem. Lett.* **2025**, *36*, 110231−110237. (l) Luo, S.; Yuan, X.; Cheng, J.; Yang, Z.; Huang, Z.; Wang, J. *Chem. Sci.* **2025**, *16*, 7051−7056.
(16) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. Synthesis and Resolution of 1-(2-Diphenylphosphino-1-naphthyl)isoquinoline; a Phosphorus-nitrogen Chelating Ligand for Asymmetric Catalysis. *Tetrahedron: Asymmetry* **1993**, *4*, 743−756.
(17) Su, Y.; Cao, Z.-C. Metal-Catalyzed Enantioselective Cleavage of Aromatic C-O Bonds. *ChemCatChem.* **2024**, *16*, No. e202301566.

https://doi.org/10.1021/acscatal.5c01663
ACS Catal. 2025, 15, 8268−8273