Chemical
Science

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: X. Zhu, R. Mi, J. Yin, F. Wang and X. Li, *Chem. Sci.*, 2023, DOI: 10.1039/D3SC02714G.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemical-science

View Article Online
DOI: 10.1039/D3SC02714G

ARTICLE

Rhodium-Catalyzed Atroposelective Access to Trisubstituted Olefins via C-H Bond Olefination of Diverse Arenes

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Xiaohan Zhu, Ruijie Mi, Jie Yin, Fen Wang* and Xingwei Li*

The atroposelective synthesis of axially chiral acyclic olefins remains a daunting challenge due to their relatively lower racemerization barriers, especially for trisubstituted ones. In this work, atroposelective C-H olefination has been realized for synthesis of open-chain trisubstituted olefins via C-H activation of two classes of (hetero)arenes in the coupling with sterically hindered alkynes. The employment of phenyl *N*-methoxycarbamates as arene reagents afforded phenol-tethered olefins, with the carbamate being a traceless directing group. The olefination of *N*-methoxy-2-indolylcarboxamides afforded the corresponding chiral olefin by circumventing the redox-neutral [4+2] annulation. The reactions proceeded with excellent *Z*/*E* selectivity, chemoselectivity, regioselectivity, and enantioselectivity in both hydroarylation systems.

Introduction

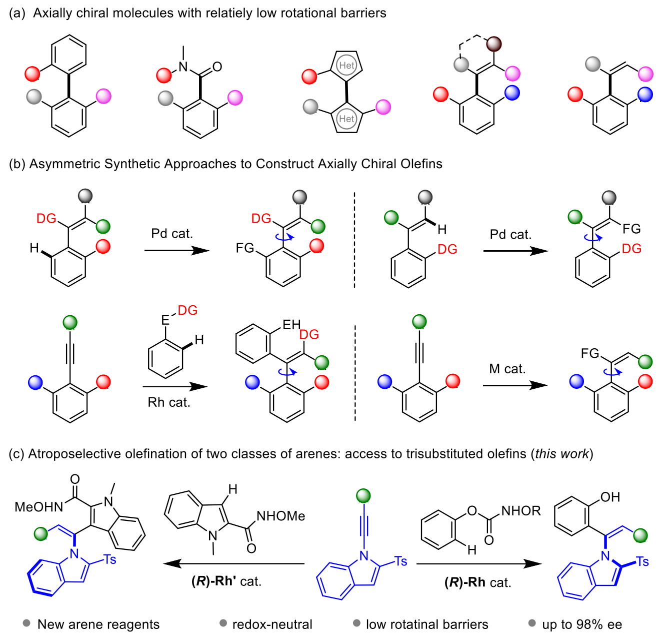
As an important phenomenon of chirality, atropisomerism that results from hindered rotation along a single bond has received increasing attention. Axially chiral structures have found tremendous applications in synthetic chemistry, pharmaceutical chemistry, catalysis, and material sciences.[1] As a result, catalytic asymmetric construction of axially chiral scaffolds has attracted great attention in the past several decades.[2-6] Previous studies have been primarily devoted to synthesis of binaphthalene-based atropisomers and other related 6-6 biaryl systems.[3] However, the investigation of axially chiral molecules with a relatively lower rotational energy barrier lags behind, such as five-membered biaryls,[4] chiral amides,[5] and axially chiral olefins.[6] Particularly, atroposelective construction of axially chiral styrenes remains daunting in modern asymmetric organic synthesis. This is ascribed to limited synthetic methods and low configurational stability of the styrenes that are prone to racemization. In addition, a specific *E*/*Z* geometry is necessary to maintain the atropo-stability.

Given the high reactivity and abundance of unsaturated reagents,[7-9] alkenes[8] and alkynes[9] have been widely applied as substrates in C-H bond asymmetric catalysis. In particular, metal-catalyzed C-H functionalization of arenes with unsaturated reagents has provided tremendous synthetic methods in atroposelective catalysis. Transformations of an existing olefin moiety constitutes a straightforward approach to access axially chiral olefins. In this context, Shi[10] realized *ortho* C-H functionalization of the arene ring assisted by a directing group tethered to a tetrasubstituted olefin, resulting in size-increase along the C-C axis (Scheme 1b). Alternatively, the same group realized C(vinyl)-H functionalization of trisubstituted olefins, leading to tetrasubstituted product.[11] Asymmetric functionalization of alkynes provides another straightforward avenue for construction of axially chiral olefins, where sterically hindered alkynes are typically employed to ensure atropo-stability of the olefin product. In 2021, our group reported 1,2-dicarbofunctionlization of sterically hindered alkynes via C-H activation of arenes bearing two classes of migratable directing groups.[12] The Song group recently tackled the limitation of sterically hindered alkynes and disclosed copper- and palladium-catalyzed atroposelective arylboration of simple diarylacetylenes using sterically hindered aryl bromides.[13] Metal-catalyzed hydrofunctionalization of alkynes offers a convenient approach to prepare trisubstituted olefins. Our group realized palladium-catalyzed atroposelective hydrophosphination of 1-indoylacetylenes, affording vinylphosphines that are potentially chiral ligands.[14] Later, Wang reported related hydrophosphinylation of 1-alkynylnaphthol via copper catalysis.[15] The Zhu group reported hydroarylation of 1-alkynylnaphthalene via Ni-catalyzed reductive coupling between alkyne and aryl halides.[16] Alternatively, organocatalysis delivers powerful protocols to access axially chiral styrenes via addition of a relatively bulky nucleophile (such as sulfinate) to sterically hindered and electronically activated alkyne such as 1-alkynyl-2-napthanol and variants, which reacts via a vinylidene-quinone methide,[17] as have been elegantly reported by Yan. In addition, Tan reported the first atroposelective addition of C-based nucleophiles to sterically hindered alkynals via an iminium ion intermediate.[18]

---

[a] School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an 710062 (China)
E-mail: lixw@snnu.edu.cn

†Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



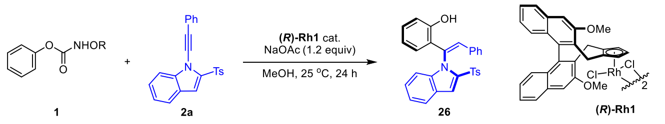
Scheme 1. Axially Chiral Olefins via C-H activation of Functionalization of Alkynes.

C-H bond activation has emerged as a powerful strategy in modern asymmetric synthesis owing to the abundance of hydrocarbons.[19] While increasing reports on asymmetric synthesis of chiral olefins have been documented via this strategy, these systems are mostly restricted to tetrasubstituted ones starting from a pre-existing olefin unit.[20] In contrast, *trisubstituted* olefins generally bear a much lower racemization barrier due to molecular fluxionality and distortion of the C=C bond. Consequently, they have been largely underexplored due to the synthetic challenges: the reaction kinetic barrier must be lower than that of the subsequent racemization. Although hydroarylation of alkenes have been extensively studied,[21] the atroposelective hydroarylation of alkynes is highly challenging because internal alkynes are necessary, and the alkene product may suffer from low atropo-stability with the introduced of a relatively small aryl group. We focused on hydroarylation of sterically hindered and electronically activated alkynes such as *N*-alkynylindoles via substrate activation. Meanwhile, (hetero)arenes bearing a functionalizable directing group are employed as suitable reagents, especially by a traceless directing group. We hereby report Rh^{III}-catalyzed atroposelective C-H olefination of two classes of arenes with excellent Z/E selectivity and enantioselectivity under mild conditions (Scheme 1c).

Results and Discussion

Extensive studies were conducted to explore the olefination of diverse arenes using alkyne **2a** as a coupling reagent. Various directing group such as pyridine (oxide), isoquinoline, amide and nitrone all failed to give efficient coupling or promising enantioselectivity. To enhance the effectiveness and applicability of the directing group in arenes, *O*-phenyl carbamate with a traceless directing group was investigated. The *N*-group was screened in the coupling with alkyne **2a** (Table 1). No olefination product was detectable when simple phenyl hydroxycarbamate was employed. A series of *N*-substituted phenyl carbamate were then extensively investigated. Indeed, some *N*-alkoxy carbamates exhibited activity, affording an *ortho*-alkenylated phenol product with the carbamate being a traceless directing group. *O*-phenyl-*N*-methoxy carbamate was identified as a suitable substrate with good yield and promising enantioselectivity (88:12 e.r.).

Table 1. Initial Optimization on the Phenyl Carbamate Directing Group

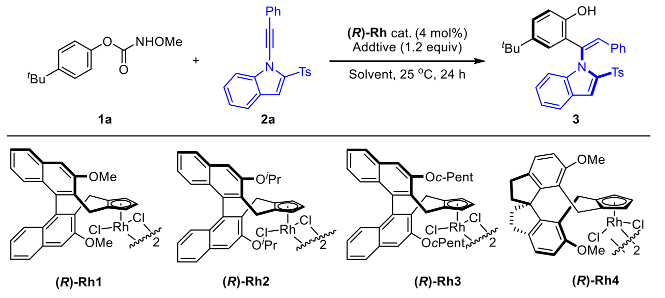


R	H	Me	^{i}Pr	^{t}Bu	Ph	Boc	Bn
Yield (%)	N.D.	67	46	N.D.	N.D.	N.D.	23
e.r.	-	88:12	85:15	-	-	-	70:30

[a] Reaction conditions: **1** (0.12 mmol), **2a** (0.1 mmol), ***(R)*-Rh1** cat. (4 mol%) and NaOAc (0.12 mmol) in MeOH (2 mL) at 25 °C for 24 h. The e.r. was determined by HPLC analysis using a chiral stationary phase.

Encouraged by the preliminary results, we next examined the effect of the chiral catalyst on the reaction of a *para* ^{t}Bu-substituted carbamate (Table 2), and the reaction proceeded with high yield and enantioselectivity to afford product **3** under the same reaction conditions when catalyzed by the ***(R)*-Rh1** catalyst, indicative of the substrate effect. Switching to other catalysts (***(R)*-Rh2-4**) only led to inferior reactivity and enantioselectivity (entries 2-4). Further investigation of solvent effects revealed that MeOH outperformed other common solvents (entries 5-8). The screening of base additives showed that some common carboxylates of sodium, potassium, and cesium slightly increased the enantioselectivity (entries 9-11). Decreasing the temperature to 10 °C resulted in higher enantioselectivity (96.5:3.5 e.r., entry 12). Further prolonging the reaction time to 48 h led to excellent yield with no change of the enantioselectivity (entry 14, Conditions A).

Table 2. Further optimization studies using phenyl carbamate **1a**.



Entry	Cat.	Additive	Solvent	Yield (%)	e.r.
1	***(R)*-Rh1**	NaOAc	MeOH	84	95:5

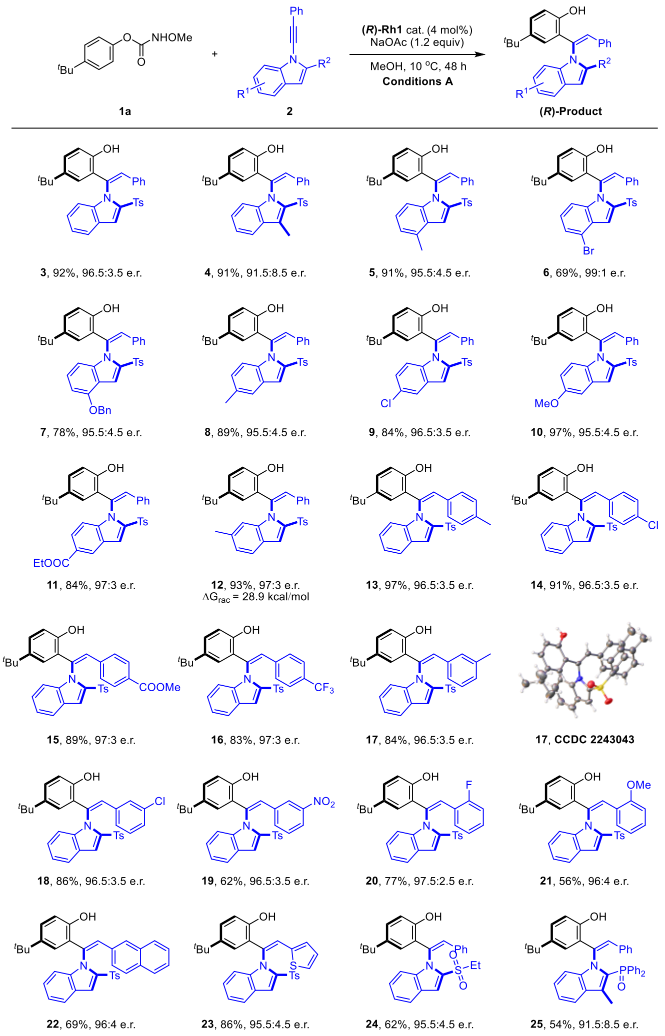
View Article Online
DOI: 10.1039/D3SC02714G

2	**(*R*)-Rh2**	NaOAc	MeOH	52	90:10
3	**(*R*)-Rh3**	NaOAc	MeOH	31	91:9
4	**(*R*)-Rh4**	NaOAc	MeOH	36	14:86
5	**(*R*)-Rh1**	NaOAc	PhMe	28	93.5:6.5
6	**(*R*)-Rh1**	NaOAc	DCE	46	94:6
7	**(*R*)-Rh1**	NaOAc	TFE	20	87.5:12.5
8	**(*R*)-Rh1**	NaOAc	EA	19	91:9
9	**(*R*)-Rh1**	NaOPiv	MeOH	80	95:5
10	**(*R*)-Rh1**	KOAc	MeOH	83	95.5:4.5
11	**(*R*)-Rh1**	CsOAc	MeOH	82	95.5:4.5
12[b]	**(*R*)-Rh1**	NaOAc	MeOH	81	96.5:3.5
13[c]	**(*R*)-Rh1**	NaOAc	MeOH	72	96.5:3.5
14[d]	**(*R*)-Rh1**	NaOAc	MeOH	92	96.5:3.5

[a] Reaction conditions: **1** (0.12 mmol), **2a** (0.1 mmol), **(*R*)-Rh** cat. (4 mol%) and NaOAc (0.12 mmol) in MeOH (2 mL), 25 °C, 24 h, isolated yield. The e.r. was determined by HPLC analysis using a chiral stationary phase. [b] 10 °C. [c] 0 °C. [d] 10 °C, 48 h. N.D. = not detectable

With the optimal conditions in hand, we next explored the scope and limitation of this coupling system. Initially, the scope of the 1-indolylacetylenes was investigated (Scheme 2). The coupling of these alkynes with electron-donating (alkyl and alkoxyl), electron-withdrawing (ester), and halogen (Cl and Br) groups at different positions of the indole ring afforded the axially chiral olefins in excellent yields and enantioselectivities (**4-12,** 91.5:8.5 to 99:1 e.r.). Extension of the alkyne terminus to phenyl groups bearing a large rang of electron-donating, -withdrawing, and halogen substituents at the meta and para positions were fully compatible (**13**-**23**). Of note, alkynes bearing an *ortho*-substituted phenyl was also compatible despite the somewhat enhanced steric effect, giving the desired product in excellent enantioselectivity and efficiency (**20** and **21,** > 96:4 e.r.). The alkyne terminus was also successfully expanded to a 2-thienyl, affording the corresponding product **23** in 86% yield and 95.5:4.5 e.r.. The bulky 2-substituent in the indole was not restricted to a sulfonyl group, and *N*-alkynylindoles bearing a 2-diphenylphosphoryl group also reacted smoothly in high enantioselectivity under the standard reaction conditions (**25**, 91.5:8.5 e.r.). The absolute configuration of the product **17** was determined by X-ray crystallography (CCDC 2243043) to be (*R*), and the rest were assigned by analogy. To obtain the conformational stability of this class of product, racemization studies have been conducted for **12**, and a $\Delta G^{\neq}_{rac}$ = 28.9 kcal/mol was obtained in PhMe at 80 °C, indicating the relatively low stability.

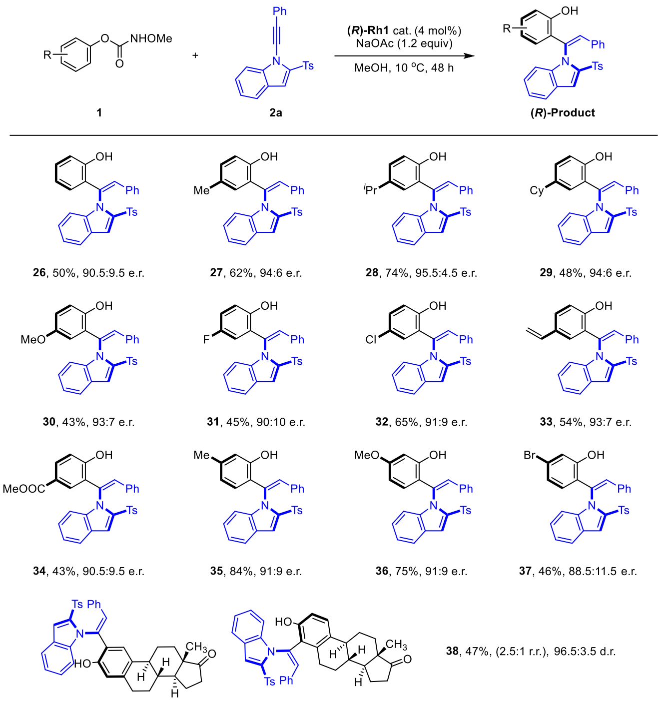
We next evaluated the generality of phenyl methoxycarbamate in the coupling with alkyne **2a** under the optimal conditions, where pronounced substituent effects were observed (Scheme 3). Simple phenyl methoxycarbamate was tolerated in this reaction and attenuated enantioselectivity was obtained (**26**, 90.5:9.5 e.r.). Carbamates bearing an electron-donating group at *para* position of the benzene ring tend to react with high yield and enantiomeric ratios (**27-30**). Similarly, carbamates with a halogen, vinyl, or ester group at the *para* position all tend to react in good yields and slightly lower atroposelectivities **(31-34)**. The presence of *meta* Me, OMe, and Br groups was also well tolerated, and the corresponding product was obtained with good yield and enantioselective control (**35-37**). Overall, the reaction enantioselectivity is affected by both the steric and electronic effects of the substituent. Moreover, an estrone-derived carbamate also proved effective in this coupling system with high d.r., albeit with a moderate conversion and a low regioselectivity, and the product (**38**) could be potentially useful in pharmaceutical development. Unfortunately, no reaction occurred when an *ortho*-substituted *O*-phenyl methoxycarbamate was employed as a substrate even under harsh conditions.



Scheme 2. Scope of the alkynes in hydroarylation reactions.

[a] Reaction conditions A: **1a** (0.12 mmol), **2** (0.1 mmol), **(*R*)-Rh1** cat. (4 mol%) and NaOAc (0.12 mmol) in MeOH (2 mL), 10 °C, 48 h, isolated yield. The e.r. was determined by HPLC analysis using a chiral stationary phase.

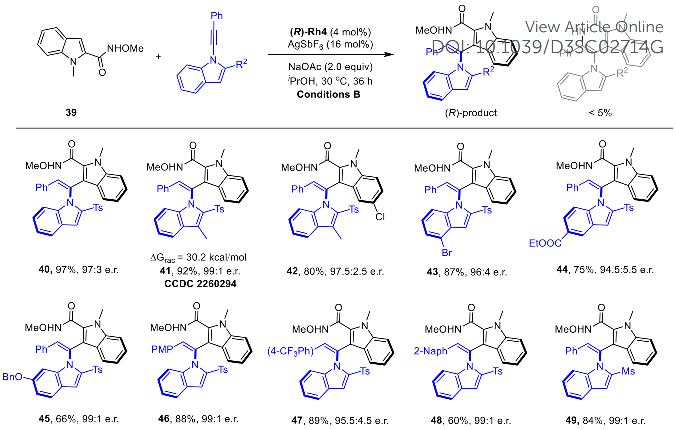
View Article Online
DOI: 10.1039/D3SC02714G



Scheme 3. Scope with respect to phenyl methoxycarbamates in C-H Olefination.

[a] Reaction conditions A: **1a** (0.12 mmol), **2** (0.1 mmol), **(*R*)-Rh1** cat. (4 mol%) and NaOAc (0.12 mmol) in MeOH (2 mL), 10 ºC, 48 h, isolated yield. The e.r. was determined by HPLC analysis using a chiral stationary phase.

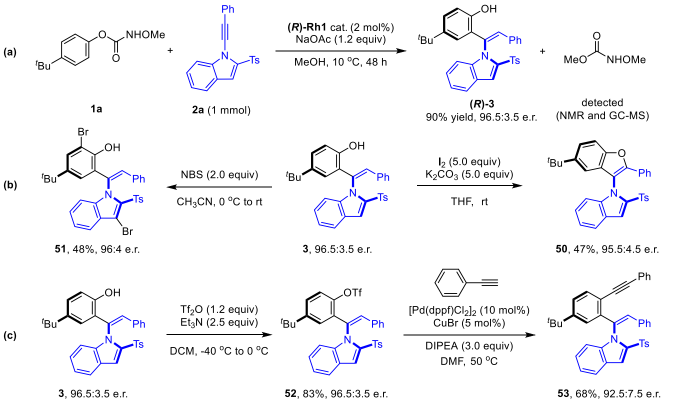
To better explore the scope of arene reagents in atroposeective C-H olefination, typically reactive heteroarenes such as indoles have been investigated. We have identified *N*-methoxy-2-indolylcarboxamide (**39**) as a suitable candidate (Scheme 4). Extensive studies have been conducted to control both the enantioselectivity and the chemical selectivity because it readily underwent redox-neutral [4+2] annulation via cleavage of an internal oxidizing N-OMe bond. Optimizations of the catalyst, solvent, and additive revealed that the rhodium spirocyclic Cp catalyst **(*R*)-Rh4**[22] outperformed the rest, and the choice of ^{i}PrOH solvent was essential to suppress the [4+2] side reaction (see Supporting Information). Both excellent enantioselectivity and reactivity were realized under these conditions. The scope of this atroposelective system was briefly explored by using various alkyne reagents. It was found that introduction of alkyl, alkoxyl, halogen, ester, and CF_3 group to the different positions of the alkyne has been well-tolerated, and excellent enantioselectivities ranging from 94.5:5.5 to 99:1 e.r. have been realized (**40-49**). The absolution configuration of product **41** was determined to be (*R*) by X-ray crystallography (CCDC 2260294). The conformational stability of product **41** was also investigated (90 ºC, toluene), and a racemization barrier of 30.2 kcal/mol was obtained, which is only slightly higher than that of the product **12**. In contrast to the high reactivity of the indolyl *N*-Me substrate, no reaction was observed when the corresponding protic NH reagent was used, likely due to the N-N chelation that inhibited subsequent C-H activation (substrate inhibition).



Scheme 4. Atroposelective C-H Olefination of 2-Indolylcarboxamides.

[a] Reaction Conditions B: indolylcarboxamide (0.1 mmol), alkyne **2** (0.12 mmol), **(*R*)-Rh4** (4 mol%), $AgSbF_6$ (16 mol%), and NaOAc (0.2 mmol) in iPrOH (2 mL), 30 ºC, 36 h, isolated yield. The e.r. was determined by HPLC analysis using a chiral stationary phase.

Synthetic applications of representative products were next demonstrated (Scheme 5). To explore the scalability of this protocol, the reaction of carbamate **1a** was performed at a mmol scale under a reduced catalyst leading, affording (*R*)-**3** in 90% yield with 96.5:3.5 e.r.. Oxidative C-O cyclization has been realized when the (*R*)-**3** was treated with I_2 under mild conditions, affording a C-N axially chiral biaryl **50** in a moderate yield (47%) and excellent enantioselectivity (95.5:4.5 e.r.). Electrophilic bromination of **3** with NBS was accomplished in 68% yield with 92.5:7.5 e.r. of the product **51**. *O*-Triflation (**52**) of the axially chiral indole-phenol with Tf_2O followed by the Sonogashira coupling with phenylacetylene afforded alkyne **53** in good yield. In all cases, only slight erosion of enantiopurity was detected.

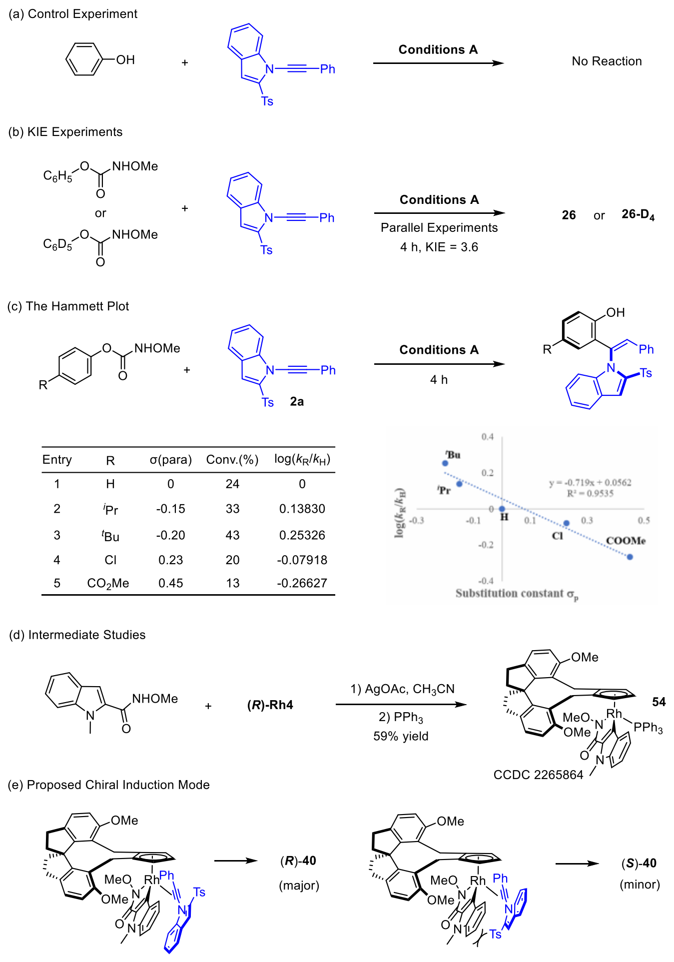


Scheme 5. Scale-Up Synthesis and Transformations of Selected Products.

Experimental studies have been briefly conducted to gain some insight into the mechanism of this reaction (Scheme 6). A control experiment using simple phenol as a substrate has been conducted under the standard conditions, but no desired product was detected (Scheme 6a). This observation indicated necessity of the carbamate directing group, and the phenol moiety was derived from decay of this traceless directing group. Indeed, an OMe carbamate was detected as a co-product (See

View Article Online
DOI: 10.1039/D3SC02714G

Scheme 5a). The reaction likely follows a C–H activation pathway based on previously related reports of phenols bearing a heterocyclic directing group, and kinetic isotope effect (KIE) was then determined from two parallel reactions using **1** and **1-*d*$_5$**. A rather large value of KIE = 3.6 was obtained based ^{1}H NMR analysis of the coupled products, indicating that the cleavage of the C–H bond is involved in the rate-limiting step (Scheme 6b). A Hammett plot of log(k_R/k_H) for various *para*-substituted phenyl methoxycarbamates revealed a decent linear correlation with a slight negative slope (Scheme 6c), suggesting stabilization of positive charge in the transition state of the turnover-limiting step. This is consistent with a C-H activation process where a more electron-rich arene is more susceptible to C-H activation. To explore the mechanism of the indolylcarboxamide system, a stoichiometric C-H activation reaction between the amide **39** and the **Rh-4** complex was conducted in the presence of a base followed by saturation with PPh$_3$,[9b] affording the 18-electron complex **54** in high yield as a single stereoisomer (Scheme 6d) that has been characterized by X-ray crystallography (CCDC 2265864). Complex **54** was indeed catalytically active when designated as a catalyst for the coupling of amide **39** and **2a**, affording coupled product **40** in high yield with 98.5:1.5 e.r. In complex **54**, the bulky amide directing group is pointed inward for minimized repulsions with the chiral ligand, which will then dictate the orientation of an incoming alkyne **2a** in the catalytic cycle (replacement of the PPh$_3$ by the alkyne). A stereochemical control model[9b,12, 23] is then proposed to account for the observed enantioselectivity of the product **40** when catalyzed by the (*R*)-**Rh4** catalyst on the basis of our previous report (Scheme 6e). The 2-Ts group of the alkyne is aligned upward, as dictated by the chiral environment of the rhodacycle for minimized steric repulsions with the arene ring. Enantio-determining migratory insertion of the Rh-C bond is followed by protonolysis of the resulting rhodium vinyl bond, affording the observed (*R*) product.



Entry	R	σ(para)	Conv.(%)	log(k_R/k_H)
1	H	0	24	0
2	^{i}Pr	-0.15	33	0.13830
3	^{t}Bu	-0.20	43	0.25326
4	Cl	0.23	20	-0.07918
5	CO$_2$Me	0.45	13	-0.26627

Scheme 6. Mechanistic Studies.

Conclusions

In conclusion, we have successfully developed an efficient and redox-neutral approach for atroposelective synthesis of axially chiral trisubstituted styrenes using two classes of arenes. The coupling systems proceeded via C-H activation-olefination of the arene with a sterically hindered alkynes as a result of dynamic kinetic transformation of the alkyne. In the case of O-phenyl carbamate substrates, the carbamate servers as a traceless directing group, affording synthetically useful phenols. One the other hand, efficient C-H olefination of 2-indolylcarboxamide was realized by successful suppression of the [4+2] redox-neutral annulation reaction. Relatively low atropo-stability of these chiral olefins have been evoked. In both systems, the hydroarylation reactions proceeded with excellent Z/E-selectivity, chemoselectivity, regioselectivity, and enantioselectivity. This coupling system provides a potentially useful protocol to access chiral olefins that may find applications in asymmetric synthesis.

Data availability

Further details of the experimental procedure, ^{1}H, and ^{13}C NMR, HPLC spectra, and X-ray crystallographic data for products **17**, **41** and **54** are available in the ESI.

Author Contributions

X. L. and F.W. conceived the idea and directed the project. X. Zhu, R. Mi and J. Yin performed the experiments. X. L. and F. W. wrote the manuscript.

Conflicts of interest

The authors declare no competing financial interests.

Acknowledgements

Financial support from the NSFC (22101167) and the SNNU is gratefully acknowledged.

Notes and references

View Article Online
DOI: 10.1039/D3SC02714G

1 For recent reviews, see: (a) E. Kumarasamy, R. Raghunathan; M. P. Sibi and J. Sivaguru, *Chem. Rev.*, 2015, **115**, 11239-11300; (b) J. E. Smyth, N. M. Butler and P. A. Keller, *Nat. Prod. Rep.*, 2015, **32**, 1562-1583; (c) G. Bringmann, T. Gulder, T. A. M. Gulder and M. Breuning, *Chem. Rev.*, 2011, **111**, 563-639; (d) Y.-M. Li, F.-Y. Kwong, W.-Y. Yu and A. Chan, *Coord. Chem. Rev.*, 2007, **251**, 2119-2144; (e) S. Erbas-Cakmak, D. A. Leigh, C. T. McTernan and A. L. Nussbaumer, *Chem. Rev.*, 2015, **115**, 10081-10206; (f) S. T. Toenjes and J. L. Gustafson, *Future Med. Chem.*, 2018, **10**, 409-422; (g) X.-Z. Bao, J. Rodriguez and D. Bonne, *Angew. Chem., Int. Ed.*, 2020, **59**, 12623-12634. (h) J. Clayden, W. J. Moran, P. J. Edwards and S. R. Laplante, *Angew. Chem., Int. Ed.*, 2009, **48**, 6398-6401.

2 For some recent reviews: (a) D. Bonne and J. Rodriguez, *Chem. Commun.*, 2017, **53**, 12385-12393; (b) D. Bonne and J. Rodriguez, *Eur. J. Org. Chem.*, 2018, **2018**, 2417-2431; (c) S. Zhang, G. Liao and B.-F. Shi, *Chin. J. Org. Chem.*, 2019, **39**, 1522-1528; (d) G. Liao, T. Zhou, Q.-J. Yao and B.-F. Shi, *Chem. Commun.*, 2019, **55**, 8514-8523; (e) T.-Z. Li, S.- J. Liu, W. Tan, and F. Shi, *Chem. Eur. J.*, 2020, **26**, 15779-15792; (f) B.-C. Da, S.-H. Xiang, S. Li, and B. Tan, *Chin. J. Chem.*, 2021, **39**, 1787-1796; (g) J. K. Cheng, S.-H. Xiang, S.-Y. Li, L. Ye, and B. Tan, *Chem. Rev.*, 2021, **121**, 4805-4902; (h) J. K. Cheng, S.-H. Xiang and B. Tan, *Acc. Chem. Res.*, 2022, **55**, 2920-2937. (i) H.-H. Zhang and F. Shi, *Acc. Chem. Res.*, 2022, **55**, 2562-2580.

3 For some representative reviews: (a) J. Wencel-Delord, A. Panossian, F. R. Leroux and F. Colobert, *Chem. Soc. Rev.*, 2015, **44**, 3418-3430; (b) A. Link and C. Sparr, *Chem. Soc. Rev.*, 2018, **47**, 3804-3815; (c) P. Loxq, E. Manoury, R. Poli, E. Deydier and A. Labande, *Coord. Chem. Rev.*, 2016, **308**, 131-190.

4 G. Centonze, C. Portolani, P. Righi and G. Bencivenni, *Angew. Chem., Int. Ed.*, 2023, e202303966.

5 (a) V. C. Fäseke and C. Sparr, *Angew. Chem., Int. Ed.*, 2016, **55**, 7261-7264; (b) A. J. Fugard, A. S. K. Lahdenperä, J. S. J. Tan, A. Mekareeya, R. S. Paton and M. D. Smith, *Angew. Chem., Int. Ed.*, 2019, **58**, 2795-2798. (c) Q.-J. Yao, P.-P. Xie, Y.-J. Wu, Y.-L. Feng, M.-Y. Teng, X. Hong, B.-F. Shi, *J. Am. Chem. Soc.*, 2020, **142**, 18266-18276.

6 For some representative reviews on axially chiral olefins: (a) J. Feng and Z.-H. Gu, *SynOpen*, 2021, **05**, 68-85; (b) S. Wu, S.-H. Xiang, J. K. Cheng and B. Tan, *Tetrahedron Chem.*, 2022, **1**, 100009.

7 (a) Y.-S. Jang, Ł. Woźniak, J. Pedroni and N. Cramer, *Angew. Chem., Int. Ed.*, 2018, **57**, 12901-12905; (b) S.-G. Wang, Y. Liu and N. Cramer, *Angew. Chem., Int. Ed.*, 2019, **58**, 18136-18140; (c) L. Liu; H. Song, Y.-H. Liu, L.-S. Wu, and B.-F. Shi, *ACS Catal.*, 2020, **10**, 7117-7122; (d) P.-J. Hu, B.-X. Liu, F. Wang, R.-J. Mi, X.-X. Li and X.-W. Li, *ACS Catal.*, 2022, **12**, 13884-13896. (e) J.-Y. Li, P.-P. Xie, T. Zhou, P.-F. Qian, Y.-B. Zhou, H.-C. Li, X. Hong and B.-F. Shi, *ACS Catal.*, 2022, **12**, 9083-9091.

8 (a) Z.-J. Jia, C. Merten, R. Gontla, C. G. Daniliuc, A. P. Antonchick and H. Waldmann, *Angew. Chem., Int. Ed.*, 2017, **56**, 2429-2434; (b) E. A. Trifonova, N. M. Ankudinov, A. A. Mikhaylov, D. A. Chusov, Y. V. Nelyubina and D. S. Perekalin, *Angew. Chem., Int. Ed.*, 2018, **57**, 7714-7718; (c) X.-F. Yang, G.-F. Zheng, X.-W. Li, *Angew. Chem., Int. Ed.*, 2019, **58**, 322-326; (d) W.-J. Cui, Z.-J. Wu, Q. Gu and S.-L. You, *J. Am. Chem. Soc.*, 2020, **142**, 7379-7385. (e) G.-Z. Li, X.-Q. Yan, J.-J. Jiang, H. Liang, C. Zhou, and J. Wang, *Angew. Chem., Int. Ed.*, 2020, **59**, 22436-22440; (e) R.-J. Mi, Z.-Y. Ding, S.-J. Yu, R. H. Crabtree and X. Li, *J. Am. Chem. Soc.*, 2023, **145**, 8150-8162.

9 (a) M.-M. Tian, D.-C. Bai, G.-F. Zheng, J.-B. Chang and X.-W. Li, *J. Am. Chem. Soc.*, 2019, **141**, 9527-9532; (b) F. Wang, Z.-S. Qi, Y.-X. Zhao, S.-L. Zhai, G.-F. Zheng, R.-J. Mi, Z.-Y. Huang, X.-L. Zhu, X.-M. He and X.-W. Li, *Angew. Chem., Int. Ed.*, 2020, **59**, 13288-13294; (c) P.-J. Hu, L.-H. Kong, F. Wang, X.-L. Zhu and X.-W. Li, *Angew. Chem., Int. Ed.*, 2021, **60**, 20424-20429. (d) W.-W. Zhang, Q. Wang, S.-Z. Zhang, C. Zheng and S.-L. You, *Angew. Chem., Int. Ed.*, 2023, **62**, e202214460.

10 H. Song, Y. Li, Q.-J. Yao, L. Jin, L. Liu, Y.-H. Liu and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2020, **59**, 6576-6580.

11 L. Jin, Q.-J. Yao, P.-P. Xie, Y. Li, B.-B. Zhan, Y.-Q. Han, X. Hong and B.-F. Shi, *Chem*, 2020, **6**, 497-511.

12 R.-J. Mi, H.-H. Chen, X.-K. Zhou, N. Li, D.-Q. Ji, F. Wang, Y. Lan and X.-W. Li, *Angew. Chem., Int. Ed.*, 2022, **61**, e202111860.

13 W.-Y. Li, S.-L. Chen, J.-H. Xie, Z.-W. Fan, K. Yang and Q.-L. Song, *Nat. Syn.*, 2023, **2**, 140-151.

14 D.-Q. Ji, J.-R. Jing, Y. Wang, Z.-S. Qi, F. Wang, X.-P. Zhang, Y. Wang and X.-W. Li, *Chem*, 2022, **8**, 3346-3362.

15 C. Yang, T.-R. Wu, Y. Li, B.-B. Wu, R.-X. Jin, D.-D. Hu, Y.-B. Li, K.-J. Bian and X.-S. Wang, *Chem. Sci.*, 2021, **12**, 3726-3732.

16 F.-T. Sheng, S.-C. Wang, J.-Q. Zhou, C.-P. Cheng, Y. Wang and S.-L. Zhu, *ACS Catal.*, 2023, **13**, 3841-3846.

17 (a) S.-Q. Jia, Z.-L. Chen, N. Zhang, Y. Tan, Y.-D. Liu, J. Deng and H.-L. Yan, *J. Am. Chem. Soc.*, 2018, **140**, 7056-7060; (b) Y. Tan, S.-Q. Jia, F.-L. Hu, Y.-D. Liu, L. Peng, D.-M. Li and H.-L. Yan, *J. Am. Chem. Soc.*, 2018, **140**, 16893-16898; (c) S. Li, D. Xu, F.-L. Hu, D.-M. Li, W.-L. Qin and H.-L. Yan, *Org. Lett.*, 2018, **20**, 7665-7669; (d) Y.-B. Wang, P.-Y. Yu, Z.-P. Zhou, J. Zhang, J. Wang, S.-H. Luo, Q.-S. Gu, K.N. Houk and B. Tan. *Nat. Catal.*, 2019, **2**, 504-513; (e) A.-Q. Huang, L.-L. Zhang, D.-M. Li, Y.-D. Liu, H.-L. Yan and W.-J. Li, *Org. Lett.*, 2019, **21**, 95-99.

18 S.-C. Zheng, S. Wu, Q.-H. Zhou, L. W.Chung, L. Ye and B. Tan, *Nat. Commun.*, 2017, **8**, 15238-15245.

19 For reviews on asymmetric C−H functionalization: (a) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel and J.-Q. Yu, *Chem. Soc. Rev.*, 2009, **38**, 3242-3272; (b) C. Zheng and S.-L. You, *RSC Adv.*, 2014, **4**, 6173-6214; (c) C. G. Newton, S.-G. Wang, C. C. Oliveira and N. Cramer, *Chem. Rev.* 2017, **117**, 8908-8976; (d) T. G. Saint-Denis, R.-Y. Zhu, G. Chen, Q.-F. Wu and J.-Q. Yu, *Science*, 2018, **359**, No. eaao 4798; (e) Q. Zhang, and B.-F. Shi, *Chin. J. Chem.*, 2019, **37**, 647-656; (f) J. Loup, U. Dhawa, F. Pesciaioli, J. Wencel-Delord and L. Ackermann, *Angew. Chem., Int. Ed.*, 2019, **58**, 12803-12818; (g) Ł. Woźniak and N. Cramer, *Trends in Chemistry*, 2019, **1**, 471-484; (h) T. Yoshino, S. Satake and S. Matsunaga, *Chem. Eur. J.*, 2020, **26**, 7346-7357; (i) G. Liao, T. Zhang, Z.-K. Lin and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2020, **59**, 19773-19786; (j) P.-S. Wang and L.-Z. Gong, *Acc. Chem. Res.*, 2020, **53**, 2841-2854; (k) T. K. Achar, S. Maiti, S. Jana and D. Maiti, *ACS Catal.*, 2020, **10**, 13748-13793; (m) C.-X. Liu, W.-W. Zhang, S.-Y. Yin,

View Article Online
DOI: 10.1039/D3SC02714G

Q. Gu and S.-L. You, *J. Am. Chem. Soc.*, 2021, **143**, 14025-14040.

20 (a) J. Feng, B. Li, J.-L. Jiang, M.-K. Zhang, W.-B. Ouyang, C.-Y. Li, Y. Fu and Z.-H. Gu, *Chin. J. Chem.*, 2018, **36**, 11-14; (b) 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; (c) Y.-Y. Liang, J.-Y. Ji, X.-Y. Zhang, Q.-B. Jiang, J. Luo and X.-D. Zhao, *Angew. Chem., Int. Ed.*, 2020, **59**, 4959-4964; (d) C. Ma, F.-T. Sheng, H.-Q. Wang, S. Deng, Y.-C. Zhang, Y.-C. Jiao, W. Tan and F. Shi, *J. Am. Chem. Soc.*, 2020, **142**, 15686-15696; (e) J. D. Jolliffe, R. J. Armstrong and M. D. Smith, *Nat. Chem.*, 2017, **9**, 558-562.

21 (a) B.-H. Ye, P. A. Donets and N. Cramer, *Angew. Chem., Int. Ed.*, 2014, **53**, 507-511; (b) C. M. Filloux and T. Rovis, *J. Am. Chem. Soc.*, 2015, **137**, 508-517; (c) S. Satake, T. Kurihara, K. Nishikawa, T. Mochizuki, M. Hatano, K. Ishihara, T. Yoshino and S. Matsunaga, *Nat. Catal.*, 2018, **1**, 585-591; (d) V. S. Shinde, M. V. Mane, L. Cavallo and M. Rueping, *Chem. Eur. J.*, 2020, **26**, 8308-8313; (e) S.-J. Lou, Z.-B. Mo, M. Nishiura and Z.-M. Hou, *J. Am. Chem. Soc.*, 2020, **142**, 1200-1205; (f) A. Carral-Menoyo, N. Sotomayor and E. Lete, *ACS Omega*, 2020, **5**, 24974-24993; (g) Y.-H. Liu, P.-P. Xie, L. Liu, J. Fan, Z.-Z. Zhang, X. Hong and B.-F. Shi, *J. Am. Chem. Soc.*, 2021, **143**, 19112-19120.

22 J. Zheng, W.-J. Cui, C. Zheng, S.-L. You, *J. Am. Chem. Soc.*, 2016, **138**, 5242-5245.

23 (a) B.-H. Ye and N. Cramer, *Science*, 2012, **338**, 504-506; (b) B.-H. Ye and N. Cramer, *J. Am. Chem. Soc.*, 2013, **135**, 636-639.