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CATALYTIC ENANTIOSELECTIVE CONSTRUCTION OF *trans*-FUSED 2,3,3a,4,5,9b-HEXAHYDRO-1*H*-PYRROLO[3,2-*c*]QUINOLINE DERIVATIVES BY INTRAMOLECULAR [3+2]-CYCLOADDITION

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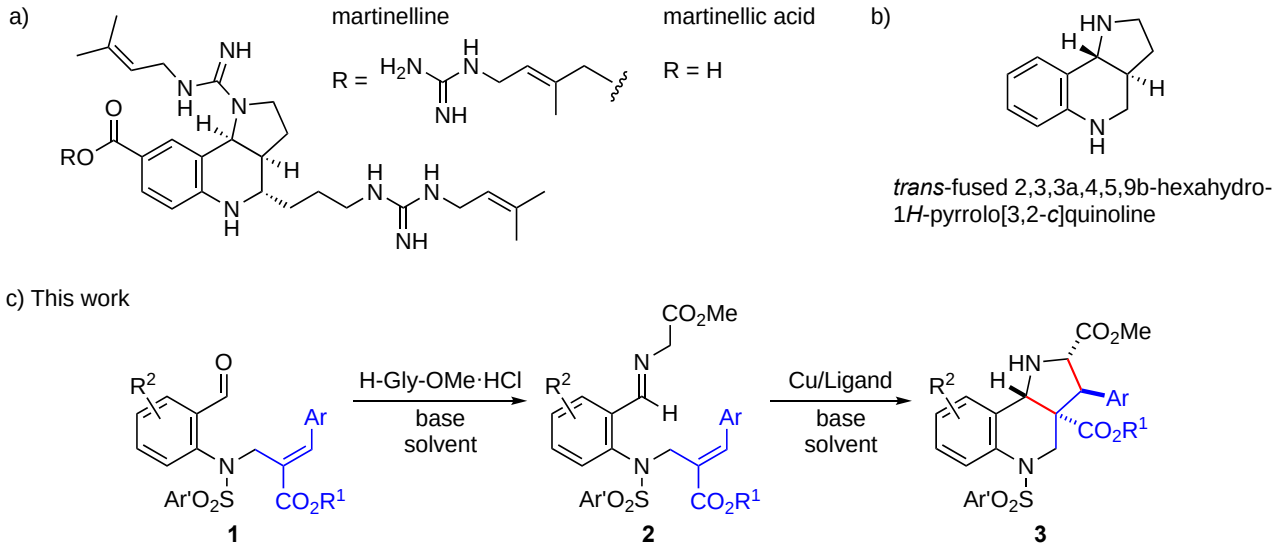
Abstract – An enantioselective construction of *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolines via Cu-catalyzed asymmetric intramolecular [3+2]-cycloaddition is described. The method entails the use of glycine ester imines bearing trisubstituted activated olefins derived from the adducts of Morita-Baylis-Hillman reactions as substrates to afford the desired cycloadducts as single diastereomers. A series of *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline derivatives were obtained in 19%–93% yield and 80%–93% ee. These results demonstrate that trisubstituted activated olefins are effective dipolarophiles in asymmetric intramolecular [3+2]-cycloadditions.

Transition metal-catalyzed asymmetric [3+2]-cycloaddition of azomethine ylides with activated alkenes is among the most effective synthetic methods for accessing enantioenriched polysubstituted pyrrolidines.[1] Over the past two decades, efficient catalytic systems have been developed to improve the structural scope and regio- and stereoselectivity of catalytic asymmetric intermolecular [3+2]-cycloadditions.[2] The intramolecular version of this type of reaction enables the formation of nitrogen-containing polycyclic scaffolds.[3] However, only minimal attention has been devoted to exploring catalytic asymmetric intramolecular [3+2]-cycloaddition compared to intermolecular cycloadditions.[4] In 2005, Pfaltz et al. developed an Ag^{I}/Phox-catalyzed highly diastereo- and enantioselective synthesis of hexahydrocromenopyrrolidines as the first example of asymmetric intramolecular [3+2]-cycloaddition.[4a] Recently, del Pozo and Adrio et al. reported the use of fluorinated dipolarophiles in Cu^{I}-catalyzed

asymmetric intramolecular [3+2]-cycloaddition of azomethine ylides.[4d] In these studies, azomethine ylides derived from aldehydes bearing disubstituted olefins as dipolarophiles on the side chain underwent metal-catalyzed intramolecular [3+2]-cycloaddition in a diastereo- and enantioselective manner. Considering the potential application of enantioenriched nitrogen-containing polycyclic compounds in the development of novel biologically active molecules, further exploration of this type of intramolecular cycloaddition is valuable.

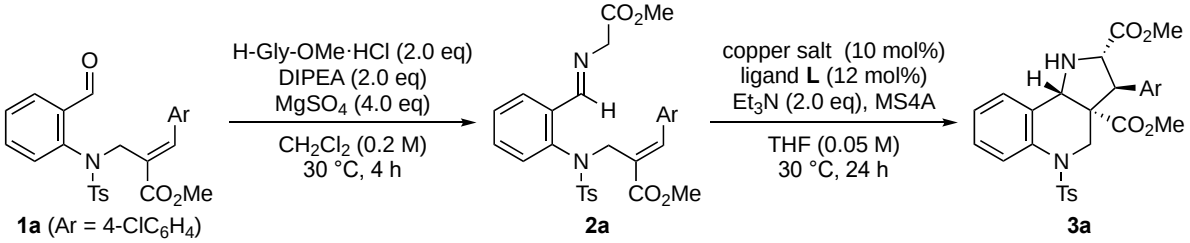
The *cis*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline scaffold is an attractive structural motif found in martinelline, martinellic acid, and related natural products (Scheme 1a).[5] Due to the interesting biological activity of these natural products, several synthetic methods for accessing the scaffold have been developed.[6] Compared to the efforts devoted to *cis*-fused derivatives, studies on the enantioselective construction of *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolines have been limited (Scheme 1b).[4d,7] Hence, we envisaged that imines **2**, prepared from aldehydes **1**, derived from Morita-Baylis-Hillman adducts,[8] would be suitable substrates for asymmetric intramolecular [3+2]-cycloaddition to afford *trans*-fused nitrogen-containing polycyclic products **3** (Scheme 1c). To the best of our knowledge, only one example of the use of trisubstituted activated olefin as dipolarophile in the catalytic asymmetric intramolecular [3+2]-cycloaddition of azomethine ylides has been reported to date.[4d,9] The trisubstituted olefins in **2** were expected to induce appropriate facial selection to afford the desired product **3** in an enantioselective manner. Herein, we report the enantioselective synthesis of *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline derivatives **3** via the copper-catalyzed intramolecular [3+2]-cycloaddition of **2**.



Scheme 1. a) The structures of martinelline and martinellic acid, b) *trans*-Fused scaffold, c) Schematic representation of the asymmetric intramolecular [3+2]-cycloaddition of **2**

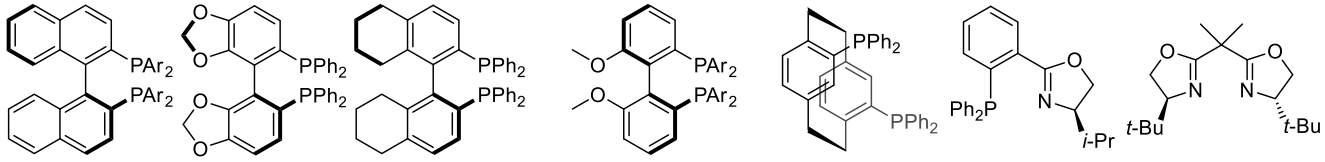
Our initial investigation entailed the Cu-catalyzed asymmetric intramolecular [3+2]-cycloaddition of imine **2a** as a model substrate. **2a** was readily prepared by condensation of aldehyde **1a** with glycine methyl ester hydrochloride in the presence of *N*,*N*-diisopropylethylamine (DIPEA) and $MgSO_4$. Treatment of crude **2a** with 10 mol% of $Cu(MeCN)_4BF_4$ and 12 mol% of (*S*)-BINAP **L1** in the presence of 2.0 equiv of triethylamine (Et_3N) and 4Å molecular sieves in THF at 30 °C afforded the desired cycloadduct **3a** as a single diastereomer in 89% yield and 68% ee (Table 1, entry 1). To elevate the enantioselectivity, a variety of ligands were screened (entries 2–9). (*S*)-TolBINAP **L2** and (*S*)-Segphos **L3** did not result in improvement (entries 2 and 3). (*S*)-H8-BINAP **L4** with an 5,5',6,6',7,7',8,8'-octahydro-binaphthyl backbone performed effectively, and desired **3a** was obtained in 91% yield and 75% ee (entry 4). On the other hand, bisphosphines **L5** and **L6** with a biphenyl backbone were found to be ineffective in this reaction (entries 5–6). A series of chiral ligands, **L7**–**L9**, were then examined, but they failed to improve the enantioselectivity (entries 7–9). Next, the effects of copper salts were investigated using **L4** to establish an optimal catalytic system (entries 10–12). Among the copper salts tested, $Cu(MeCN)_4OTf$ delivered the best results in terms of enantioselectivity (77% ee, entry 11).

Table 1. Screening of chiral ligands and copper salts[a]



Entry	**L**	Copper salt	Yield of **3a**/%[b]	ee/%[c]
1	**L1**	$Cu(MeCN)_4BF_4$	89	68
2	**L2**	$Cu(MeCN)_4BF_4$	83	63
3	**L3**	$Cu(MeCN)_4BF_4$	79	31
4	**L4**	$Cu(MeCN)_4BF_4$	91	75
5	**L5**	$Cu(MeCN)_4BF_4$	68	10
6	**L6**	$Cu(MeCN)_4BF_4$	89	23
7	**L7**	$Cu(MeCN)_4BF_4$	86	6
8	**L8**	$Cu(MeCN)_4BF_4$	86	1
9	**L9**	$Cu(MeCN)_4BF_4$	89	1
10	**L4**	$Cu(MeCN)_4PF_6$	81	63
11	**L4**	$Cu(MeCN)_4OTf$	86	77
12	**L4**	$Cu(OTf)_2$	90	27

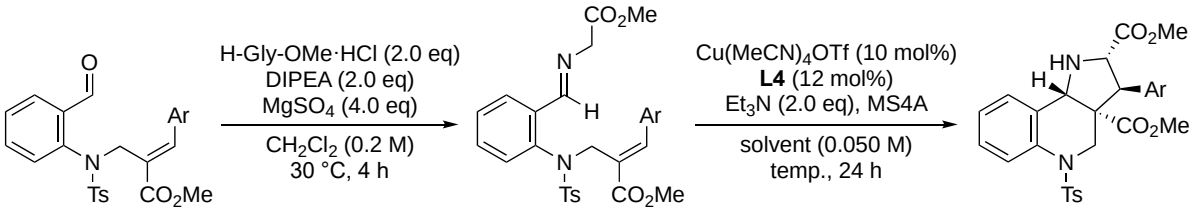
[a] Reaction conditions: **1a** (0.10 mmol), H-Gly-OMe·HCl (0.20 mmol), DIPEA (0.20 mmol), $MgSO_4$ (0.40 mmol), and CH_2Cl_2 (0.50 mL) were used for imine formation. Then, all reactions of crude **2a** were performed in the presence of copper salt (10 mol%), ligand **L** (12 mol%), Et_3N (0.20 mmol), and activated MS4A powder at 30 °C in THF (2.0 mL) under an argon atmosphere. [b] Isolated yield of **3a** from **1a**.
[c] Determined by HPLC analysis.



L1 (Ar = Ph) **L3** **L4** **L5** (Ar = Ph) **L7** **L8** **L9**
L2 (Ar = *p*-tol) **L6** (Ar = 3,4,5-$(MeO)_3C_6H_2$)

The reaction conditions with respect to the reaction solvent and temperature were then optimized using $Cu(MeCN)_4OTf$ and **L4** (Table 2). Among the reaction solvents examined (entries 1–7), the asymmetric intramolecular [3+2]-cycloaddition of **2a** proceeded smoothly in 1,4-dioxane and toluene to afford the desired product **3a** in 87% yield and 83% ee, and 85% yield and 80% ee, respectively (entries 3 and 5). Furthermore, the enantioselectivity increased slightly to 85% ee when the reaction was conducted in 1,4-dioxane at 15 °C (entry 8). Finally, performing the reaction at 0 °C in a binary solvent system consisting of 1,4-dioxane and toluene (4:1) afforded **3a** in 83% yield and 88% ee (entry 10). Optically pure **3a** was readily accessed by recrystallization of the enantioenriched product from CH_2Cl_2, Et_2O, and hexane. X-Ray crystallographic analysis of **3a** unambiguously revealed its *trans*-fused skeleton, and the absolute configuration of **3a** was determined to be (2*S*,3*S*,3a*R*,9b*S*) on the basis of the Flack parameter (Figure 1).[10]

Table 2. Optimization of reaction conditions[a]



1a (Ar = 4-ClC_6H_4) **2a** **3a**

Entry	Solvent	Temp./°C	Yield of **3a**/%[b]	ee/%[c]
1	THF	30	86	77
2	Et_2O	30	75	70
3	1,4-dioxane	30	87	83
4	CH_2Cl_2	30	30	32
5	toluene	30	85	80
6	MeOH	30	33	6
7	MeCN	30	13	2
8	1,4-dioxane	15	88	85
9	1,4-dioxane–toluene (1:1)	0	83	87
10	1,4-dioxane–toluene (4:1)	0	83	88 (>99)[d]
11	1,4-dioxane–toluene (6:1)	0	79	87

[a] Reaction conditions: **1a** (0.10 mmol), H-Gly-OMe·HCl (0.20 mmol), DIPEA (0.20 mmol), $MgSO_4$ (0.40 mmol), and CH_2Cl_2 (0.50 mL) were used for imine formation. Then, all reactions of crude **2a** were performed in the presence of $Cu(MeCN)_4OTf$ (10 mol%), **L4** (12 mol%), Et_3N (0.20 mmol), and activated MS4A powder at indicated temperature in solvent (2.0 mL) under an argon atmosphere.
[b] Isolated yield of **3a** from **1a**. [c] Determined by HPLC analysis. [d] After recrystallization.

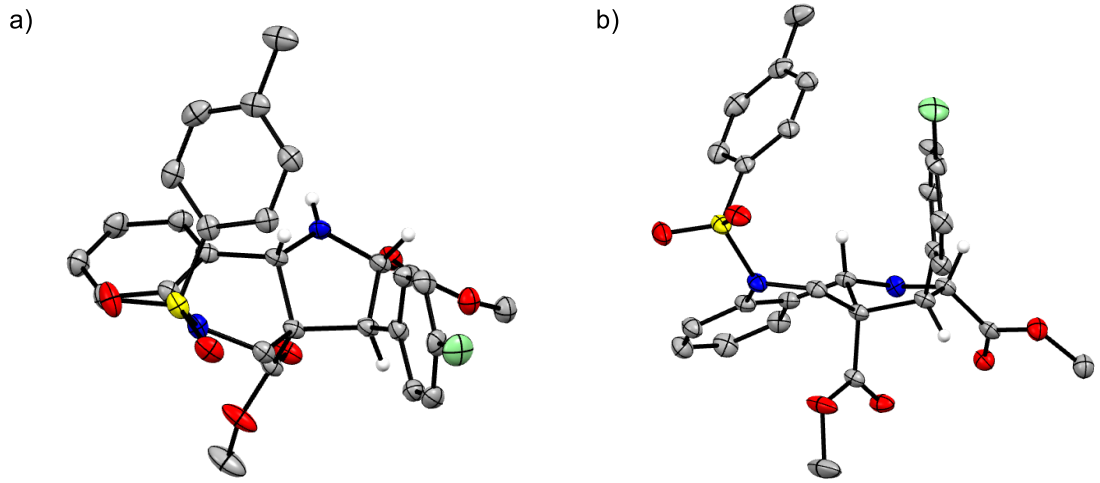
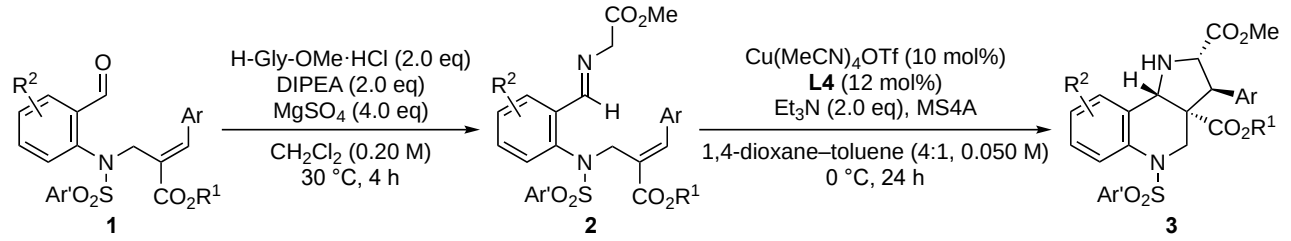
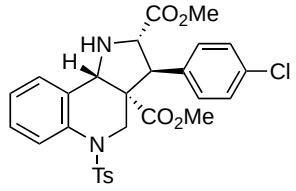


Figure 1. POV-Ray drawing of **3a** with probability ellipsoids drawn at the 50% level. Hydrogen atoms, except for important ones, are omitted for clarity. (a) Top view and (b) front view.

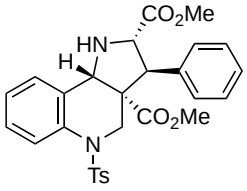
With the optimal reaction conditions in hand, the substrate scope of this transformation was studied (Table 3). Imines bearing a phenyl group (**2b**) and electron deficient aromatic rings (**2d** and **2e**) at the β-position of the α,β-unsaturated ester proved to be excellent substrates, affording the corresponding cycloadducts **3b**, **3d**, and **3e** in 87%–93% yield and 87%–89% ee. Furthermore, excellent results were obtained with chlorinated aromatic imines **2j** and **2k**, and the corresponding cycloadducts **3j** and **3k** formed in 75% and 77% yield, and 85% ee and 92% ee, respectively. Similar to the tosyl group of **2b**, *N*-arylsulfonyl groups, including *o*-nitrobenzenesulfonyl (**2n**), mesitylenesulfonyl (**2o**), and 1-naphthalenesulfonyl (**2p**) were tolerated as protecting groups, leading to the formation of the corresponding cycloadducts **3n**, **3o**, and **3p** in 53%–77% yield and 80%–89% ee. In addition, **2c** bearing an electron donating aromatic ring at the β-position of the α,β-unsaturated ester moiety, benzyl ester **2h**, and **2l** comprising a 1,3-benzodioxole skeleton, participated in this cycloaddition to afford cycloadducts **3c**, **3h**, and **3l** in 88%–93% ee, albeit in low to moderate chemical yields. In contrast, substrates **2f**, **2i**, and **2m** containing 1-naphthyl, *tert*-butyl ester, or electron rich aromatic substituents performed poorly due to their low reactivity, and the desired cycloadducts **3f**, **3i**, and **3m** were not formed. Additionally, the reaction of substrate **2g**, which lacked an aromatic ring at the β-position of the α,β-unsaturated ester, resulted in a complex mixture.

Table 3. Scope of the asymmetric intramolecular [3+2]-cycloaddition[a]

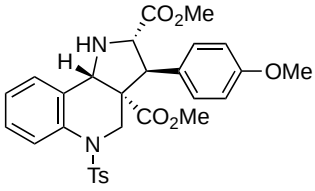




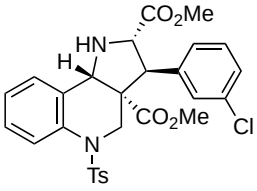
3a
83%, 88% ee



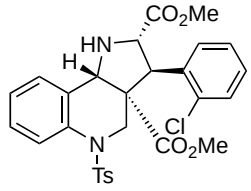
3b
87%, 89% ee (95% ee)[b]



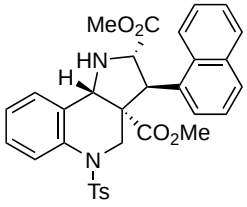
3c
25%, 88% ee



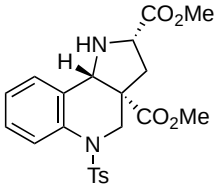
3d
90%, 88% ee



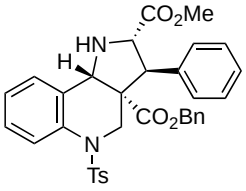
3e
93%, 87% ee



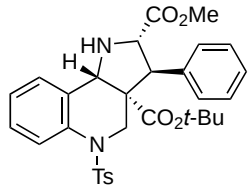
3f
trace



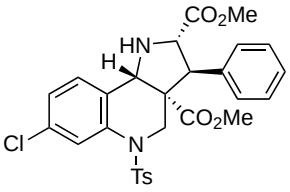
3g
complex mixture



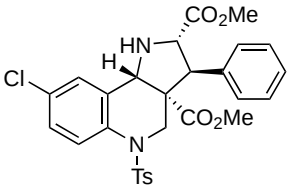
3h
67%, 90% ee



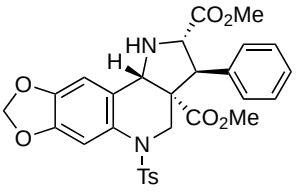
3i
trace



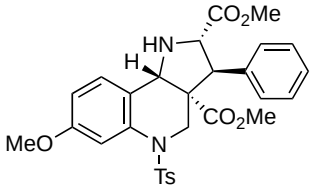
3j
75%, 85% ee



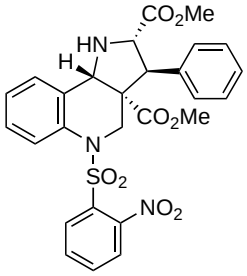
3k
77%, 92% ee



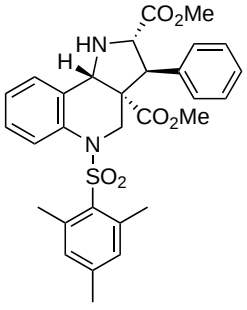
3l
19%, 93% ee



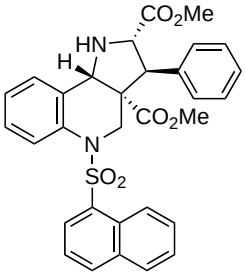
3m
trace



3n
53%, 80% ee



3o
75%, 81% ee



3p
77%, 89% ee

[a] Reaction conditions: **1** (0.10 mmol), H-Gly-OMe·HCl (0.20 mmol), DIPEA (0.20 mmol), $MgSO_4$ (0.40 mmol), and CH_2Cl_2 (0.50 mL) were used for imine formation. Then, all reactions of crude **2** were performed in the presence of $Cu(MeCN)_4OTf$ (10 mol%), **L4** (12 mol%), Et_3N (0.20 mmol), and activated MS4A powder at 0 °C in 1,4-dioxane–toluene (4:1, 2.0 mL) under an argon atmosphere. Yields of **3** were isolated yields from **1**. Enantiomeric excesses were determined by HPLC analysis. [b] After recrystallization.

To explain the stereochemical outcome of Cu-(*S*)-H8-BINAP **L4**-catalyzed asymmetric intramolecular [3+2]-cycloaddition of **2**, a plausible stereochemical pathway based on the experimental results and the absolute configuration of **3b** is proposed in Figure 2. Cu(I) is coordinated by the bidentate phosphine ligand **L4** and glycine ester imine **2** in a tetrahedral arrangement.[4c,4d,11] Deprotonation by Et_3N generates the azomethine ylide, which undergoes [3+2]-cycloaddition with the intramolecularly tethered trisubstituted activated olefin. The cycloaddition proceeds from the back side of the azomethine ylide to avoid unfavorable steric interactions between the diphenylphosphino group of **L4** and the arylsulfonamide moiety of **2**.[4d] Facial differentiation of the trisubstituted activated olefin is achieved by means of the C2-symmetric environment created by the two diphenylphosphino groups of (*S*)-H8-BINAP **L4**. Cycloaddition onto the trisubstituted olefin face opposite to that shown in Figure 2 would result in unfavorable interactions between the aryl group at the β-position of the α,β-unsaturated ester and the phenyl group pointing towards the back.

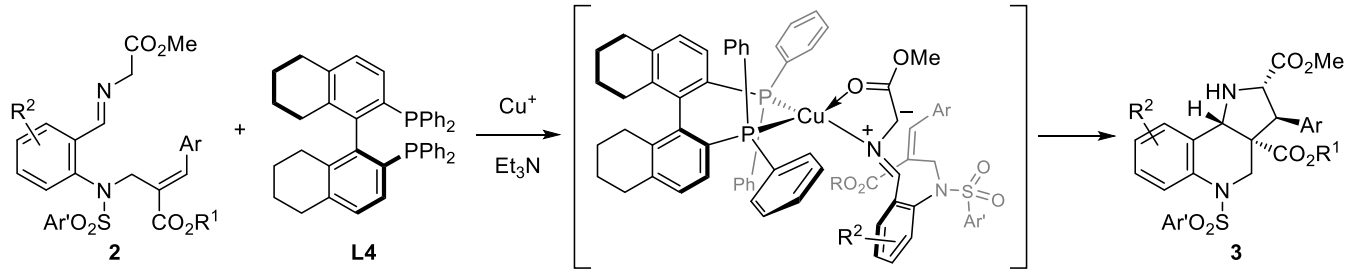
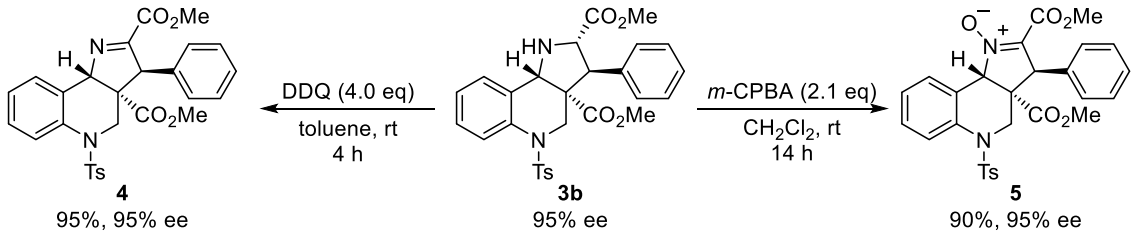


Figure 2. A plausible stereochemical pathway for the asymmetric intramolecular [3+2]-cycloaddition of **2** catalyzed by Cu-(*S*)-H8-BINAP **L4**

With the successful enantioselective construction of the *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline scaffold, further derivatizations of **3b** were examined (Scheme 2). DDQ-mediated dehydrogenation of the pyrrolidine moiety in **3b** was performed.[7c,12] Owing to the polyfunctional structure of the pyrrolidine ring of **3b**, partial dehydrogenation proceeded to afford cyclic iminoester **4** in 95% yield. Moreover, treatment of **3b** with *m*-CPBA delivered the nitrone **5** in 90% yield.[13] Notably, the enantiopurity of starting material **3b** was maintained in the products. Furthermore, **4** and **5** are amenable to further functionalization of the scaffold via nucleophilic addition or cycloaddition.[14,15]



Scheme 2. Synthetic transformations of **3b**

In summary, we have developed a Cu-catalyzed asymmetric intramolecular [3+2]-cycloaddition of azomethine ylides using trisubstituted activated olefins as dipolarophiles. Our method provides facile access to *trans*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolines in high enantiomeric excess. This method is expected to be applicable in the synthesis of biologically active pyrrolo[3,2-*c*]quinoline-based polycyclic compounds.

EXPERIMENTAL

Typical Procedure for Cu-catalyzed asymmetric intramolecular [3+2]-cycloaddition of 2.

Dimethyl (2*S*,3*S*,3a*R*,9b*S*)-3-(4-chlorophenyl)-5-(4-methylbenzene-1-sulfonyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline-2,3a-dicarboxylate (**3a**). To a round bottom flask charged with aldehyde **1a** (48.4 mg, 0.10 mmol), glycine methyl ester hydrochloride (25.1 mg, 0.20 mmol), and anhydrous $MgSO_4$ (48.1 mg, 0.40 mmol) under the Ar atmosphere, dry CH_2Cl_2 (0.50 mL, 0.20 M) and DIPEA (34.5 μL, 0.20 mmol) were added. The reaction mixture was stirred at 30 °C for 4 h. The reaction mixture was filtered and washed with water. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in *vacuo* to give crude imine **2a**. To a Schlenk flask charged with $Cu(MeCN)_4OTf$ (3.8 mg, 0.010 mmol), (*S*)-H8-BINAP **L4** (7.6 mg, 0.012 mol), and activated MS4A (80.0 mg) under the Ar atmosphere, dry 1,4-dioxane–toluene (4:1, 0.50 mL) were added. The reaction mixture was stirred at 30 °C for 30 min and cooled to 0 °C. To this mixture, the solution of crude imine **2a** in dry 1,4-dioxane–toluene (4:1, 1.5 mL) was added. After addition of triethylamine (27.7 μL, 0.20 mmol), the entire mixture was stirred at 0 °C for 24 h. The reaction mixture was filtered through a short plug of silica gel, which was rinsed with *n*-hexane and EtOAc (1:1). The filtrate was evaporated in *vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane : EtOAc = 3:1 to 1:1) to afford **3a** (46.3 mg, 0.083 mmol, 83%) as pale yellow amorphous solid; IR (KBr): 3310, 2953, 1740, 1599, 1492, 1354, 1218, 1167, 829, 814, 759 cm^{-1}; $[\alpha]_D^{22}$ +75.5 (*c* 1.00, $CHCl_3$, 88% ee); ^1H NMR (500 MHz, $CDCl_3$): δ 2.44 (s, 3 H), 2.83 (d, J = 11.9 Hz, 1 H), 3.25–3.27 (m, 4 H), 3.36–3.41 (m, 1 H), 3.73 (s, 3 H), 3.83 (d, J = 4.8 Hz, 1 H), 3.91 (d, J = 11.9 Hz, 1 H), 4.20 (dd, J = 8.9 Hz, 4.8 Hz, 1 H), 6.91 (br d, J = 8.3 Hz, 2 H), 7.12 (br d, J = 8.3 Hz, 2 H), 7.18 (br d, J = 8.3 Hz, 2 H), 7.216–7.225 (m, 2 H), 7.31–7.35 (m, 3 H), 7.74 (br d, J = 8.0 Hz, 1 H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 21.6, 50.2, 52.2, 52.6, 56.4, 60.1, 64.6, 69.7, 122.3, 125.8, 126.2, 126.8, 128.1, 129.5, 129.6, 129.9, 130.3, 134.0, 134.90, 134.92, 136.7, 143.9, 171.9, 173.1; HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{28}H_{27}{}^{35}ClN_2NaO_6S$, 577.1171; found, 577.1172; The enantiomeric excess was determined by HPLC analysis to be 88% ee, t_R = 26.6 min (minor), t_R = 42.9 min (major) (Chiralpak AS-H, *n*-hexane/*i*-PrOH = 2/1, flow rate = 0.5 mL/min, λ = 254 nm).

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REFERENCES AND NOTES

1. L. M. Harwood and R. J. Vickers, 'Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products: Azomethine Ylides,' Vol. 59, ed. by A. Padwa and W. H. Pearson, John Wiley & Sons, Inc., New York, 2002, pp. 169-252.
2. For recent reviews, see: (a) J. Adrio and J. C. Carretero, *Chem. Commun*., 2014, **50**, 12434; (b) R. Narayan, M. Potowski, Z.-J. Jia, A. P. Antonchick, and H. Waldmann, *Acc. Chem. Res*., 2014, **47**, 1296; (c) T. Hashimoto and K. Maruoka, *Chem. Rev*., 2015, **115**, 5366; (d) B. Bdiri, B.-J. Zhao, and Z.-M. Zhou, *Tetrahedron: Asymmetry*, 2017, **28**, 876; (e) X. Fang and C.-J. Wang, *Org. Biomol. Chem*., 2018, **16**, 2591; (f) J. Adrio and J. C. Carretero, *Chem. Commun*., 2019, **55**, 11979; (g) L. Wei, X. Chang, and C.-J. Wang, *Acc. Chem. Res*., 2020, **53**, 1084.
3. I. Coldham and R. Hufton, *Chem. Rev*., 2005, **105**, 2765.
4. (a) R. Stohler, F. Wahl, and A. Pfaltz, *Synthesis*, 2005, 1431; (b) Y. Oderaotoshi, H. Miyata, S. Minakata, and M. Komatsu, *Heterocycles*, 2006, **68**, 2465; (c) S. R. Vidadala, C. Golz, C. Strohmann, C.-G. Daniliuc, and H. Waldmann, *Angew. Chem. Int. Ed*., 2015, **54**, 651; (d) C. Cristóbal, D. Gaviña, I. Alonso, M. Ribagorda, J. C. Carretero, C. del Pozo, and J. Adrio, *Chem. Commun*., 2022, **58**, 7805.
5. Recent review: M. B. Haarr and M. O. Sydnes, *Molecules*, 2021, **26**, 341.
6. Selected reports: (a) Z. Chen, B. Wang, Z. Wang, G. Zhu, and J. Sun, *Angew. Chem. Int. Ed*., 2013, **52**, 2027; (b) Y.-J. Yang, H.-R. Zhang, S.-Y. Zhu, P. Zhu, and X.-P. Hui, *Org. Lett*., 2014, **16**, 5048; (c) M. Pappoppula and A. Aponick, *Angew. Chem. Int. Ed*., 2015, **54**, 15827; (d) H. Wang, C. Wang, K. Huang, L. Liu, W. Chang, and J. Li, *Org. Lett*., 2016, **18**, 2367; (e) X.-L. Yu, L. Kuang, S. Chen, X.-L. Zhu, Z.-L. Li, B. Tan, and X.-Y. Liu, *ACS Catal*., 2016, **6**, 6182; (f) J. Wang, Y. Li, J. Sun, H. Wang, Z. Jin, and Y. R. Chi, *ACS Catal*., 2018, **8**, 9859.
7. (a) C. E. Masse, P. Y. Ng, Y. Fukase, M. Sánchez-Roselló, and J. T. Shaw, *J. Comb. Chem*., 2006, **8**, 293; (b) C. S. Pavan Kumar, K. B. Harsha, N. C. Sandhya, A. B. Ramesha, K. Mantelingu, and K. S. Rangappa, *New J. Chem*., 2015, **39**, 8397; (c) J. Liu, G. S. Cremosnik, F. Otte, A. Pahl, S. Sievers, C. Strohmann, and H. Waldmann, *Angew. Chem. Int. Ed*., 2021, **60**, 4648.
8. Selected examples of intramolecular cycloadditions for the racemic synthesis of nitrogen-containing polycyclic compounds using the adducts of Morita-Baylis-Hillman reactions, see: (a) M. Bakthadoss,

A. Devaraj, and D. Kannan, *Eur. J. Org. Chem*., 2014, 1505; (b) M. Bakthadoss and D. Kannan, *RSC Adv*., 2014, **4**, 11723; (c) M. Bakthadoss and A. Devaraj, *Tetrahedron Lett*., 2015, **56**, 3954; (d) M. Bakthadoss, D. Kannan, J. Srinivasan, and V. Vinayagam, *Org. Biomol. Chem*., 2015, **13**, 2870; (e) M. Bakthadoss and V. Vinayagam, *Org. Biomol. Chem*., 2015, **13**, 10007; (f) M. Bakthadoss, V. Vinayagam, V. Agarwal, and D. S. Sharada, *ChemistrySelect*, 2019, **4**, 7996; (g) M. Bakthadoss and V. Agarwal, *J. Org. Chem*., 2020, **85**, 15221.

9. Racemic syntheses of *cis*-fused 2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinolines via intramolecular cycloaddition of azomethine ylides with the trisubstituted activated olefins have been reported. See reference 8d.
10. Complete crystallographic data for the structure analysis in this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 2214513 (**3a**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).
11. (a) M. Potowski, A. P. Antonchick, and H. Waldmann, *Chem. Commun*., 2013, **49**, 7800; (b) J. Corpas, A. Ponce, J. Adrio, and J. C. Carretero, *Org. Lett*., 2018, **20**, 3179.
12. I. Satyanarayana, D.-Y. Yang, and T.-J. Liou, *RSC Adv*., 2020, **10**, 43168.
13. B. Xu, Z.-M. Zhang, B. Liu, S. Xu, L.-J. Zhou, and J. Zhang, *Chem. Commun*., 2017, **53**, 8152.
14. N. Yasukawa, A. Yamanoue, T. Takehara, T. Suzuki, and S. Nakamura, *Chem. Commun*., 2022, **58**, 1318.
15. S.-I. Murahashi and Y. Imada, *Chem. Rev*., 2019, **119**, 4684.