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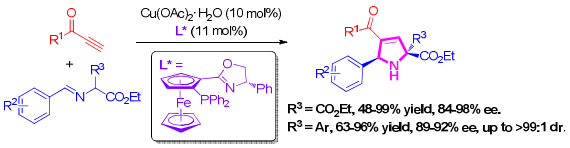

Cu(OAc)$_2$/FOXAP catalyzed asymmetric 1,3-dipolar cycloaddition of azomethine ylides to ethynyl ketones, affording 2,5-dihydropyrroles in good to excellent yields and excellent enantioselectivities.

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$Cu(OAc)_2$/FOXAP complex catalyzed construction of 2,5-dihydropyrrole derivatives via asymmetric 1,3-dipolar cycloaddition of azomethine ylides with ethynyl ketones

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A catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides to ethynyl ketones catalyzed by $Cu(OAc)_2$/FOXAP(ferrocenyl oxazolinylphosphine) complex was developed, affording 2,5-dihydropyrrole derivatives in good to excellent yields (up to 99%) and excellent level of enantioselectivities (up to 98% ee). This highly efficient chiral *N,P*-ligand/$Cu(OAc)_2$ catalytic system was also applicable for the 1,3-dipolar cycloaddition of α-arylglycine ester-generated azomethine ylides with ynones affording exclusive quaternary carbon-containing *cis*-2,5-dihydropyrroles in excellent enantioselectivities (89-92% ee).

Introduction

As a privileged structure for pharmaceutical activity in drug discovery, the 2,5-dihydropyrrole skeleton is the core structure of numerous natural products[1] and biologically relevant compounds exhibiting significant activities such as anti-tumor,[2] anti-microbial,[3] anti-inflammatory,[4] anti-oxidant[5] (Figure 1). Meanwhile, 2,5-dihydropyrroles could be served as important building blocks by means of the rich chemistry in the functionalization of its carbon-carbon double bond.[6] In consideration of the importance of 2,5-dihydropyrroles, our continuous interest in natural product-like compounds prompted us to devote our efforts for developing efficient synthetic methods for the construction of 2,5-dihydropyrroles, with the potential to deliver biological activities and better drug-like properties.

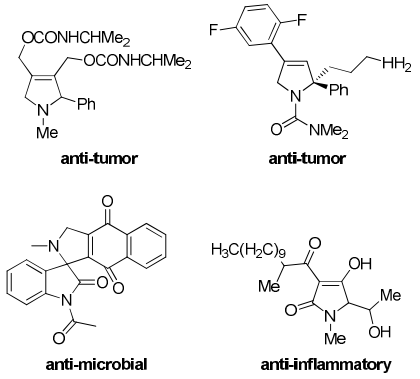
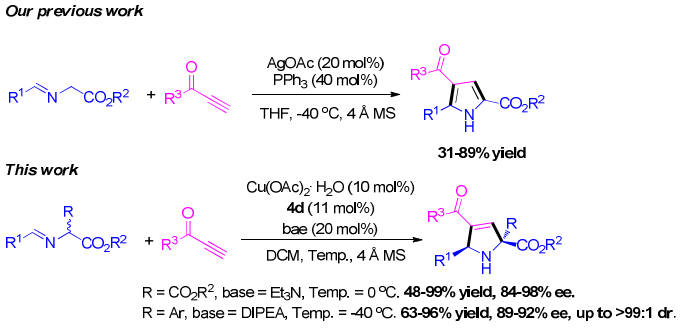


Figure 1. A selection of bioactive molecules with 2,5-dihydropyrrole skeletons

Recently, many efforts have been made towards the development of novel and highly efficient synthetic protocols for the synthesis of 2,5-dihydropyrroles.[7] Among which the 1,3-dipolar cycloaddition has arguably been one of the most ideal synthetic strategies.[8] The first catalytic asymmetric [3+2] cycloaddition of azomethine ylides with alkynes as dipolarophiles using chiral phosphoric acids as catalysts has been reported by Shi and Gong,[9] affording corresponding 2,5-dihydropyrroles in excellent enantioselectivities, however for the case of 2,5-dihydropyrroles with one quaternary stereogenic center, poor diastereoselectivities were observed.

We have recently established a series of 1,3-dipolar cycloadditions of azomethine ylides to both activated alkenes[10] and alkynes (Scheme 1)[11] as dipolarophiles, providing the corresponding [3+2] adducts. Inspired by the previous success from Shi/Gong and our own group, and the importance of 2,5-dihydropyrroles, we envisioned to use a metal/chiral ligand system to control the stereoselectivity of the titled reaction. Herein, we would like to disclose our latest results for the asymmetric synthesis of 2,5-dihydropyrrole derivatives via [3+2] cycloaddition of azomethine ylides to ethynyl ketones catalyzed by a $Cu(OAc)_2$/FOXAP complex.

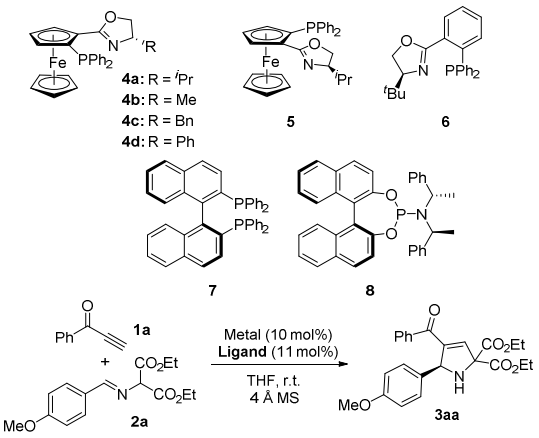


Scheme 1. [3+2] cycloaddition of azomethine ylides with alkynes

Results and discussion

Initially, ethynyl ketone **1a** and azomethine ylide **2a** were chosen as the model substrates to test the feasibility of the approach by using AgOAc (10 mol%) and FOXAP (**4a**) (11 mol%) in THF at room temperature according to our previous report.[10a] Fortunately, the reaction proceeded smoothly to afford the corresponding cycloaddition adduct **3aa** in 70% yield, 76% ee (Table 1, entry 1). Screening of metal salts revealed $Cu(OAc)_2 \cdot H_2O$ was the optimal metal of choice (Table 1, entries 1-4). FOXAP analogues **4b**-**4d** were then tested and **4d** was found to be optimal in terms of achievable yields and enantioselectivities (Table 1, entries 5-7). Other ligands **5**-**8** all led to an inactive catalytic system or lower stereoselectivities (Table 1, entries 8-11). Reaction with the ligand **4d** alone led to insignificant amount of the desired product **3aa** (Table 1, entry 12).

Table 1. Catalyst complexes screening for asymmetric 1,3-dipolar cycloaddition of ethynyl ketone **1a** with azomethine ylide **2a**[a]



Entry	Metal	Ligand	Yield (%)[b]	ee (%)[c]
1	AgOAc	**4a**	70	76
2	$AgBF_4$	**4a**	80	73
3	$Cu(CH_3CN)_4BF_4$	**4a**	86	76
4	$Cu(OAc)_2 \cdot H_2O$	**4a**	90	78
5	$Cu(OAc)_2 \cdot H_2O$	**4b**	83	48
6	$Cu(OAc)_2 \cdot H_2O$	**4c**	83	65
7	$Cu(OAc)_2 \cdot H_2O$	**4d**	93	85
8	$Cu(OAc)_2 \cdot H_2O$	**5**	81	-75
9	$Cu(OAc)_2 \cdot H_2O$	**6**	74	-64
10	$Cu(OAc)_2 \cdot H_2O$	**7**	62	40
11	$Cu(OAc)_2 \cdot H_2O$	**8**	48	0
12	-	**4d**	trace	-

[a] Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in THF (1 mL) with 4 Å MS at room temperature, and the ratio of **1a**:**2a** was 1:2.5. [b] Isolated yields based on ethynyl ketone **1a**. [c] Determined by HPLC.

Next, we turned our attention to optimization of other reaction parameters. Bases and solvents were systematically investigated, where $Cu(OAc)_2$/FOXAP (**4d**) complex was employed as the catalyst system. Base screening revealed that the organic bases Et_3N and DIPEA appeared to be more suitable for the reaction and same enantioselectivities of 87% ee could be achieved in THF (Table 2, entries 5-6). Further screening of solvents demonstrated that DCM was the best choice (Table 2, entry 10). Other solvents such as CH_3CN, toluene, Et_2O, gave unsatisfactory results (Table 2, entries 7-9). Lowing the temperature to 0 °C in DCM led to a significant enhancement of the enantioselectivity (97% ee, Table 2, entry 11), but further lowering the temperature to -20 °C offered no further improvement in enantioselectivity and only served to lower the yield (Table 2, entry 12). Reaction with the base alone led to insignificant amount of the desired product **3aa** (Table 2, entry 13). When the reaciton performed in the absence of the base, both of the yield and enantioselectivity decreased (Table 2, entry 14).

Table 2. Optimization for asymmetric 1,3-dipolar cycloaddition of ethynyl ketone **1a** with azomethine ylide **2a**[a]

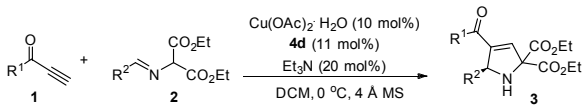
Entry	Base (mol%)	Solvent	T (°C)	Yield (%)[b]	ee (%)[c]
1	-	THF	RT	93	85
2	KO^{t}Bu (10)	THF	RT	83	87
3	K_2CO_3 (200)	THF	RT	90	86
4	DBU (20)	THF	RT	33	84
5	Et_3N (20)	THF	RT	93	87
6	DIPEA (20)	THF	RT	93	87
7	Et_3N (20)	CH_3CN	RT	50	94
8	Et_3N (20)	Toluene	RT	76	73
9	Et_3N (20)	Et_2O	RT	88	80
10	Et_3N (20)	DCM	RT	88	94
11	Et_3N (20)	DCM	0	90	97
12	Et_3N (20)	DCM	-20	35	96
13[d]	Et_3N (20)	DCM	0	trace	-
14	-	DCM	0	80	95

[a] Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in solvent (1 mL) with 4 Å MS, and the ratio of **1a**:**2a** was 1:2.5. [b] Isolated yields based on ethynyl ketone **1a**. [c] Determined by HPLC. [d] Without catalyst and ligand.

The above optimization identified optimal conditions as: 10 mol% of $Cu(OAc)_2 \cdot H_2O$, 11 mol% of chiral FOXAP (**4d**), 20 mol% of Et_3N, and addition of 4 Å MS (50 mg/mL), DCM as solvent at 0 °C. The generality and substrate scope were then investigated using a series of ethynyl ketone **1** and diethyl 2-aminomalonate-derived azomethine ylides **2**, as shown in Table 3. At the outset, diethyl 2-aminomalonate-derived azomethine ylides **2** bearing electron-rich (Table 3, entry 1), electron-deficient (Table 3, entries 2-6), and electronically-neutral groups (Table 3, entries 7-8) on the aryl ring all reacted with ethynyl ketone **1a** smoothly affording the corresponding 2,5-dihydropyrroles **3** exclusively in good to excellent yields (48-99%), and excellent enantioselectivities (94-97% ee). For instance, 4-bromo-substituted azomethine ylide **2e** reacted with ethynyl ketone **1a** effectively, leading to the 2,5-dihydropyrrole **3ae** in 96% yield, and 96% ee (Table 3, entry 5). Lower yield was obtained when 4-nitro-subtituted azomethine ylide **2b** was employed (Table 3, entry 2) instead of 3-nitro-subtituted azomethine ylide **2c** (Table 3, entry 3), mainly due to the instability of azomethine ylide. The heteroaryl substituted azomethine ylide **2i** derived from 2-thiophenylaldehyde was also suitable for this transformation, leading to the desired product **3ai** in 90% yield and 90% ee (Table 3, entry 9). Additionally, less reactive alkyl substituted azomethine ylide **2j** was tolerated in this transformation affording 2,5-dihydropyrrole **3aj**, albeit in a slightly lower enantioselectivity (entry 10, 89% yield and 84% ee). We next turned our attention to different ethynyl ketone **1** (Table 3, entries 11-15). ethynyl ketone **1** with both electron-withdrawing (Table 3, entry 11) and electron-donating

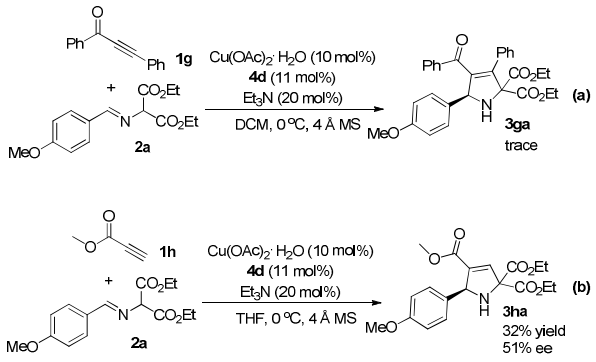
substituents (Table 3, entry 12) on the aromatic ring were tolerated, resulting in formation of the corresponding 2,5-dihydropyrrole **3** in excellent enantioselectivities (96% ee and 98% ee, respectively). Remarkably, ethynyl ketone **1** with 2-naphthyl, 2-thiophenyl substituents (Table 3, entries 13-14) and alkyl substituent (Table 3, entry 15) were also able to undergo the asymmetric 1,3-dipolar cycloadditions providing the desired 2,5-dihydropyrroles **3da-3fa** in excellent enantiomeric excesses (90-95% ee). It should be pointed out that our catalytic system is highly efficient in terms of not only the yields and enantioselectivities but also the shorter reaction times, for most of tried cases in Table 3, reaction can be finished within half hour, which is much faster than that of chiral phosphoric acids system (36 h is required for most cases) reported by Shi and Gong.[9] However, internal alkyne **1g** was not applicable for this reaction (Scheme 2a). Terminal alkynyl ester **1h** afforded the desired product **3ha** in low yield (32%) and poor enantioselectivity (51% ee) (Scheme 2b).

Table 3. The scope of asymmetric 1,3-dipolar cycloaddition of ethynyl ketones **1** with diethyl 2-aminomalonate-derived azomethine ylides **2**[a]



Entry	R^1	R^2	Product	Yield (%)[b]	ee (%)[c]
1	Ph (**1a**)	4-MeOC_6H_4 (**2a**)	**3aa**	90	97
2	Ph (**1a**)	4-$NO_2C_6H_4$ (**2b**)	**3ab**	48	95
3	Ph (**1a**)	3-$NO_2C_6H_4$ (**2c**)	**3ac**	77	95
4	Ph (**1a**)	4-CNC_6H_4 (**2d**)	**3ad**	70	95
5	Ph (**1a**)	4-BrC_6H_4 (**2e**)	**3ae**	96	96
6	Ph (**1a**)	3,4-$Cl_2C_6H_3$ (**2f**)	**3af**	99	94
7	Ph (**1a**)	Ph (**2g**)	**3ag**	90	94
8	Ph (**1a**)	2-Naphthy (**2h**)	**3ah**	91	94
9	Ph (**1a**)	2-Thiophenyl (**2i**)	**3ai**	90	90
10	Ph (**1a**)	Isopropyl (**2j**)	**3aj**	89	84
11[d]	4-FC_6H_4 (**1b**)	4-MeOC_6H_4 (**2a**)	**3ba**	80	96
12	4-MeOC_6H_4 (**1c**)	4-MeOC_6H_4 (**2a**)	**3ca**	91	98
13	2-Naphthyl (**1d**)	4-MeOC_6H_4 (**2a**)	**3da**	77	95
14[d]	2-Thiophenyl (**1e**)	4-MeOC_6H_4 (**2a**)	**3ea**	77	93
15	CH_3 (**1f**)	4-MeOC_6H_4 (**2a**)	**3fa**	83	90

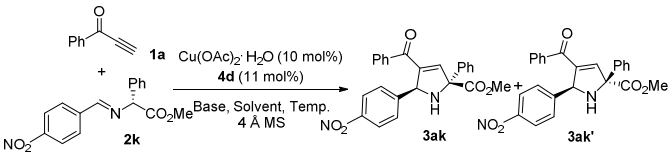
[a] Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in DCM (1 mL) with 4 Å MS at 0 °C for 0.5 h, and the ratio of **1**:**2** was 1:2.5. [b] Isolated yields based on ethynyl ketones **1**. [c] Determined by HPLC. [d] No base was used.



Scheme 2. [3+2] cycloaddition of azomethine ylide **2a** with internal alkyne **1g** or terminal alkynyl ester **1h**.

The catalytic asymmetric 1,3-dipolar cycloaddition of α-arylglycine ester-generated azomethine ylides with alkynes catalyzed by chiral phosphoric acid was reported.[9b] While that reaction led to the construction of 2,5-dihydropyrroles with one quaternary stereogenic center, serious limitations remained: both 2,5-dihydropyrrole diastereomers were generated simultaneously with low diastereoselectivities (1:1 to 1:3), and only 67-93% ees were obtained for *cis*-diastereomers, while up to 99% ee can be obtained for the major *trans*-diastereomers; Although, the diastereoselectivities can reversed by changing the ratio of starting materials, the two factors of yield and enantioselectivity were obviously restricted by each other, and a compromise between them should be made to afford *trans*-diastereoisomer as major product but in lower enantioselectivities. In view of high efficient catalytic activity, the $Cu(OAc)_2$/FOXAP (**4d**) system was further applied to the asymmetric 1,3-dipolar cycloaddition for the synthesis of 2,5-dihydropyrroles with one quaternary stereogenic center (Table 4).

Table 4. Optimization for asymmetric 1,3-dipolar cycloaddition of ethynyl ketone **1a** with α-arylglycine esters-derived azomethine ylide **2k**[a]



Entry	Base (mol%)	Solvent	T (°C)	Yield (%)[b]	dr (%)[c]	ee (%)[c]
1	Et_3N (20)	THF (1 mL)	0	65	89:11	59
2	Et_3N (20)	Et_2O (1 mL)	0	54	87:13	24
3	Et_3N (20)	CH_3CN (1 mL)	0	35	24:76	<10
4	Et_3N (20)	Toluene (1 mL)	0	<30	40:60	<10
5	Et_3N (20)	DCM (1 mL)	0	45	91:9	65
6	NaHMDS (10)	DCM (1 mL)	0	50	>99:1	69
7	Proton Sponge (20)	DCM (1 mL)	0	35	>99:1	68
8	Cs_2CO_3 (20)	DCM (1 mL)	0	63	96:4	70
9	DIPEA (20)	DCM (1 mL)	0	99	99:1	73
10	DIPEA (20)	DCM (1 mL)	-20	95	99:1	81
11	DIPEA (20)	DCM (2 mL)	-40	96	>99:1	90
12	DIPEA (20)	DCM (4 mL)	-40	90	>99:1	89
13[d]	DIPEA (20)	DCM (2 mL)	-40	96	>99:1	90
14[e]	DIPEA (20)	DCM (2 mL)	-40	96	>99:1	90

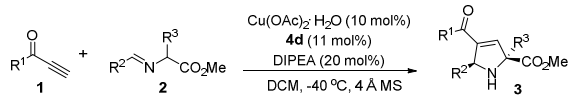
[a] Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale with 4 Å MS, and the ratio of **1a**:**2k** was 1:2. [b] Isolated yields based on ethynyl ketones **1a**. [c] Determined by HPLC. [d] (*S*)-**2k** was used. [e] *rac*-**2k** was used.

α-Arylglycine esters-derived azomethine ylide (*R*)-**2k** was selected as the dipolar and ethynyl ketone **1a** as the dipolarophile in the presence of 10 mol% of $Cu(OAc)_2 \cdot H_2O$ and 11 mol% of chiral FOXAP (**4d**) in 1 mL solvent at 0 °C. The choice of base and solvent was optimized as shown in Table 4. DIPEA as base and DCM as solvent were found to be optimal to afford **3ak** as an exclusive *cis*-diastereoisomer in excellent yield and enantioselectivity (99% yield, 73% ee, Table 4, entry 9). Lowering the temperature to -20 °C offered improvement in enantioselectivity (81% ee, Table 4, entry 10). Further lowering the temperature to -40 °C in 2 mL DCM led to a significant enhancement of the enantioselectivity for *cis*-diastereoisomer (90% ee, Table 4, entry 11). But increasing the volume of DCM to 4 mL offered no further improvement in enantioselectivity and only served to lower the yield (Table 4, entry 12). Interestingly, both (*S*)-**2k** (Table 4, entry 13) and *rac*-**2k** (Table 4, entry 14) afforded the desired product **3ak** in excellent

diastereoselectivities (>99:1 dr) and high enantioselectivities (90% ee), which revealed that there is no kinetic resolution involved in the reaction. Therefore, racemic azomethine ylides were utilized in the investigation of the reaction scope.

The generality of this $Cu(OAc)_2$/FOXAP(**4d**) complex catalyzed asymmetric 1,3-dipolar cycloaddition was then explored under the optimized conditions [$Cu(OAc)_2 \cdot H_2O$ (10 mol%), FOXAP **4d** (11 mol%), DIPEA (20 mol%), 4 Å MS (50 mg/mL), DCM (2 mL), -40°C] for the synthesis of 2,5-dihydropyrroles with one quaternary stereogenic center (Table 5). It was found that the reaction proceeded efficiently and smoothly to afford the desired product **3** in good to excellent yields (63-96%), excellent diastereoselectivities (98:2->99:1 dr) and high enantioselectivities (89-92% ee). A huge improvement has been achieved compared to the previous work reported by Shi.[9b]

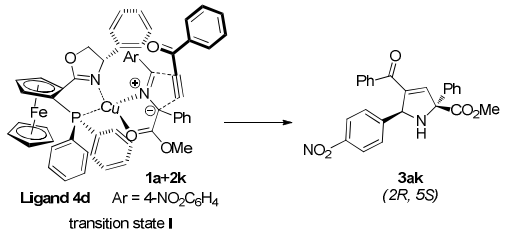
Table 5. The scope of asymmetric 1,3-dipolar cycloaddition of ethynyl ketones **1** with α-arylglycine esters-derived azomethine ylides **2**[a]



Entry	R^1	R^2/R^3	Product	Yield (%)[b]	dr (%)[c]	ee (%)[c]
1	Ph (**1a**)	4-$NO_2C_6H_4$/Ph (**2k**)	**3ak**	96	>99:1	90
2	Ph (**1a**)	4-$NO_2C_6H_4$/4-ClC_6H_4 (**2l**)	**3al**	86	>99:1	91
3	Ph (**1a**)	4-$NO_2C_6H_4$/4-$MeOC_6H_4$ (**2m**)	**3am**	63	98:2	92
4	Ph (**1a**)	4-$CO_2MeC_6H_4$/Ph (**2n**)	**3an**	68	>99:1	92
5	Ph (**1a**)	4-CNC_6H_4/Ph (**2o**)	**3ao**	90	>99:1	91
6	4-FC_6H_4 (**1b**)	4-$NO_2C_6H_4$/Ph (**2k**)	**3bk**	64	>99:1	89
7	4-$MeOC_6H_4$ (**1c**)	4-$NO_2C_6H_4$/Ph (**2k**)	**3ck**	70	99:1	92

[a] Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in DCM (2 mL) with 4 Å MS at -40 °C, and the ratio of **1**:**2** was 1:2. [b] Isolated yields based on ethynyl ketones **1**. [c] Determined by HPLC.

It should be pointed out that all the analytical data of corresponding major products **3** including proton NMR, chiral HPLC and the sign of optical rotation are well consistent with that of literature report,[9] thus the absolute configuration of **3** were established as (*5S*) and (*2R*, *5S*), respectively.



Scheme 3. Proposed transition state leading to the major product **3ak**.

The excellent diastereoselectivities and enantioselectivities observed in this 1,3-dipolar cycloaddition can be rationalized by considering the proposed transition state **I** shown in Scheme 3. Two phenyl groups adjacent to the phosphorus and phenyl group substituted on the dihydrooxazole ring in the ligand might block the dipolarophile's approach from the "bottom" face (as drawn), forming (2*R*,5*S*)-**3ak** through approach from the "top" face.

Conclusions

In conclusion, a catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylides to ethynyl ketones catalyzed by $Cu(OAc)_2$/FOXAP complex was developed, affording 2,5-dihydropyrrole derivatives in good to excellent yields (up to 99%) and excellent level of enantioselectivities (up to 98% ee). This highly efficient chiral *N*,*P*-ligand/$Cu(OAc)_2$ catalytic system was found also applicable to synthetically more challenging α-arylglycine ester derived azomethine ylides to provide *cis*-quaternary carbon-containing 2,5-dihydropyrroles **3** in extremely high diastereoselectivities (98:2->99:1) and excellent enantioselectivities (89-92%). Notably, our copper-catalyzed asymmetric protocol is not only the first example of metal-catalyzed asymmetric 1,3-dipolar cycloaddition of azomethine ylides to ethynyl ketones, but also greatly complementary to Shi and Gong's phosphoric acid system. Further investigations in the area of pyrrole derivatives synthesis and applications are ongoing in our laboratories.

Experimental

General Information

All Chemicals were purchased from commercial sources and they were used without further purification unless otherwise specified. ^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectra are interpreted as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, qd = quartet of doublets, m = multiplet. Optical rotations were measured on AUTOPOL V at λ = 589 nm. Diastereomeric ratios and enantiomeric excesses were determined by analysis of HPLC traces, obtained by using chiralpak AD-H, OD-H, IA or IF columns purchased from Daicel Chemical Industries, LTD.

General procedure for synthesis of 2,5-dihydropyrroles 3 via 1, 3-dipolar cycloadditions of diethyl 2-aminomalonate-derived azomethine ylides with ethynyl ketones

Under a nitrogen atmosphere, $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 0.01 mmol), ligand **4d** (5.7 mg, 0.011 mmol) and 4Å MS were dissolved in DCM (1 mL), and stirred at room temperature for approximately 0.5 h. Then, the mixture was cooled to 0 °C, azomethine ylide **2** (0.25 mmol), Et_3N (2.8 μL, 0.02 mmol) and ynone **1** (0.1 mmol) were added sequentially. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography to give the corresponding cycloaddition product **3**. The NMR data are consistent with that of the literature report.[9c,9d]

Diethyl 4-benzoyl-5-(4-methoxyphenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3aa). 38.0 mg; yield: 90%; colorless oil; $[\alpha]^{25}_D$ = +70.2 ($CHCl_3$, *c* = 1.50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.46 (d, *J* = 2.0 Hz, 1H), 5.66 (s, 1H), 4.40-4.19 (m, 4H), 3.73 (s, 3H), 3.58 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 97%; HPLC (Daicel Chiralpak IA, *n*-hexane/isopropanol = 80/20, 0.8 mL/min, 254 nm): t_R = 13.66 min (major), t_R = 17.84 min (minor).

Diethyl 4-benzoyl-5-(4-nitrophenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ab). 21.0 mg; yield: 48%; colorless oil; $[\alpha]^{25}_D$ = +59.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.7 Hz, 2H), 7.79 (d, *J* = 7.3 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 7.57

(t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.53 (d, *J* = 2.0 Hz, 1H), 5.83 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.41-4.21 (m, 4H), 3.79 (d, *J* = 6.3 Hz, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 95%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R = 16.68 min (major), t_R = 41.08 min (minor).

Diethyl 4-benzoyl-5-(3-nitrophenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ac). 33.8 mg; yield: 77%; yellow oil; $[\alpha]^{25}_D$ = +65.5 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (t, *J* = 2.0 Hz, 1H), 8.06 (dd, *J* = 7.8, 2.3 Hz, 1H), 7.81-7.77 (m, 3H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.45 (td, *J* = 7.8, 3.8 Hz, 3H), 6.55 (d, *J* = 2.1 Hz, 1H), 5.84 (s, 1H), 4.45-4.22 (m, 4H), 3.82 (s, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 95%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 14.34 min (major), t_R = 17.76 min (minor).

Diethyl 4-benzoyl-5-(4-cyanophenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ad). 29.3 mg; yield: 70%; colorless oil; $[\alpha]^{25}_D$ = +66.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.59-7.56 (m, 5H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.52 (d, *J* = 2.1 Hz, 1H), 5.77 (d, *J* = 2.1 Hz, 1H), 4.42-4.20 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); Enantiomeric excess: 95%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 16.77 min (major), t_R = 22.49 min (minor).

Diethyl 4-benzoyl-5-(4-bromophenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ae). 45.0 mg; yield: 96%; colorless oil; $[\alpha]^{25}_D$ = +54.7 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.3 Hz, 2H), 7.58-7.53 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.48 (d, *J* = 2.0 Hz, 1H), 5.68 (d, *J* = 1.9 Hz, 1H), 4.40-4.19 (m, 4H), 3.66 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 96%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R = 10.33 min (major), t_R = 14.79 min (minor).

Diethyl 4-benzoyl-5-(3,4-dichlorophenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3af). 45.5 mg; yield: 99%; colorless oil; $[\alpha]^{25}_D$ = +51.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CHCl_3$) δ 7.82-7.79 (m, 2H), 7.60-7.55 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 6.49 (d, *J* = 2.1 Hz, 1H), 5.68 (d, *J* = 2.1 Hz, 1H), 4.42-4.20 (m, 4H), 3.71 (s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 94%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 9.84 min (major), t_R = 13.36 min (minor).

Diethyl 4-benzoyl-5-phenyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ag). 35.2 mg; yield: 90%; colorless oil; $[\alpha]^{25}_D$ = +37.2 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.1 Hz, 2H), 7.58-7.51 (m, 1H), 7.46-7.39 (m, 4H), 7.39-7.24 (m, 2H), 7.21-7.16 (m, 1H), 6.48 (d, *J* = 2.1 Hz, 1H), 5.71 (d, *J* = 2.1 Hz, 1H), 4.40-4.21 (m, 4H), 3.65 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 94%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 90/10, 1.0 mL/min, 254 nm): t_R = 18.13 min (minor), t_R = 19.12 min (major).

Diethyl 4-benzoyl-5-(naphthalen-2-yl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ah). 40.1 mg; yield: 91%; colorless oil; $[\alpha]^{25}_D$ = +82.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.73 (m, 6H), 7.55 (d, *J* = 1.7 Hz, 1H), 7.53-7.51 (m, 1H), 7.43-7.38 (m, 4H), 6.52 (d, *J* = 2.1 Hz, 1H), 5.89 (d, *J* = 2.1 Hz, 1H), 4.43-4.22 (m, 4H), 3.74(s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 94%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 16.18 min (minor), t_R = 20.43 min (major).

Diethyl 4-benzoyl-5-(thiophen-2-yl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ai). 36.0 mg; yield: 90%; colorless oil; $[\alpha]^{25}_D$ = +11.2 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.60-7.55 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.14 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.04-7.03 (m, 1H), 6.87 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.45 (d, *J* = 2.1 Hz, 1H), 6.05 (d, *J* = 2.0 Hz, 1H), 4.39-4.20 (m, 4H), 3.78 (s, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 90%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 0.8 mL/min, 254 nm): t_R = 10.96 min (major), t_R = 12.77 min (minor).

Diethyl 4-benzoyl-5-isopropyl-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3aj). 32.0 mg; yield: 89%; colorless oil; $[\alpha]^{25}_D$ = -22.7 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.1 Hz, 2H), 7.62-7.58 (m, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 6.36 (d, *J* = 2.0 Hz, 1H), 4.66 (t, *J* = 2.6 Hz, 1H), 4.34-4.16 (m, 4H), 3.20 (s, 1H), 2.07 (pd, *J* = 6.8, 3.0 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H); Enantiomeric excess: 84%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 100/5, 1.0 mL/min, 254 nm): t_R = 8.51 min (minor), t_R = 9.24 min (major).

Diethyl 4-(4-fluorobenzoyl)-5-(4-methoxyphenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ba). 35.3 mg; yield: 80%; colorless oil; $[\alpha]^{25}_D$ = +73.6 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.42 (d, *J* = 1.9 Hz, 1H), 5.65 (s, 1H), 4.40-4.21 (m, 4H), 3.73 (s, 3H), 3.59 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 96%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 0.8 mL/min, 254 nm): t_R = 14.09 min (major), t_R = 19.71 min (minor).

Diethyl 4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ca). 41.0 mg; yield: 91%; yellow oil; $[\alpha]^{25}_D$ = +56.4 ($CHCl_3$, *c* = 1.10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.38 (d, *J* = 1.9 Hz, 1H), 5.66 (d, *J* = 1.8 Hz, 1H), 4.40-4.20 (m, 4H), 3.85 (s, 3H), 3.73 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 98%; HPLC (Daicel Chirapak IF, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 15.45 min (major), t_R = 17.52 min (minor).

Diethyl 4-(2-naphthoyl)-5-(4-methoxyphenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3da). 36.5 mg; yield: 77%; colorless oil; $[\alpha]^{25}_D$ = +66.3 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.89-7.83 (m, 3H), 7.62-7.52 (m, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.53 (d, *J* = 1.9 Hz, 1H), 5.73 (d, *J* = 1.7 Hz, 1H), 4.44-4.20 (m, 4H), 3.72 (s, 3H), 3.63 (s, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 95%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 19.84 min (minor), t_R = 23.05 min (major).

Diethyl 5-(4-methoxyphenyl)-4-(thiophene-2-carbonyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3ea). 33.1 mg; yield: 77%; colorless oil; $[\alpha]^{25}_D$ = +45.2 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.65 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.11 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.63 (d, *J* = 2.1 Hz, 1H), 5.65 (d, *J* = 2.1 Hz, 1H), 4.40-4.21 (m, 4H), 3.74 (s, 3H), 3.55 (s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); Enantiomeric excess: 93%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 0.8 mL/min, 254 nm): t_R = 16.15 min (major), t_R = 21.92 min (minor).

Diethyl 4-acetyl-5-(4-methoxyphenyl)-1*H*-pyrrole-2,2(5*H*)-dicarboxylate (3fa). 30.0 mg; yield: 83%; colorless oil; $[\alpha]^{25}_D$ = +95.1 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 2.0 Hz, 1H), 5.35 (d, *J* = 2.0 Hz, 1H), 4.34-4.22 (m, 4H), 3.77 (s, 3H), 2.26 (s, 3H), 1.31 (dt, *J* = 7.2, 3.6 Hz, 6H); Enantiomeric excess: 90%; HPLC (Daicel Chirapak OD-H, *n*-hexane/isopropanol = 100/5, 1.0 mL/min, 254 nm): t_R = 15.60 min (major), t_R = 18.50 min (minor).

2,2-diethyl 4-methyl 5-(4-methoxyphenyl)-1,5-dihydro-2H-pyrrole-2,2,4-tricarboxylate (3ha). 12.0 mg; yield: 32%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.85(s,

1H), 6.84 (d, *J* = 11.8 Hz, 2H), 5.32 (d, *J* = 2.1 Hz, 1H), 4.28 (dq, *J* = 12.2, 7.1 Hz, 4H), 3.78 (s, 3H), 3.63 (s, 3H), 3.39 (s, 1H), 1.30 (td, *J* = 7.1, 4.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.64, 169.30 , 163.17 , 159.36 , 140.53 , 135.82 , 133.76 , 128.89 , 113.98 , 78.94 , 68.02 , 62.65 , 62.63 , 55.34 , 51.95 , 14.17, 14.17. Enantiomeric excess: 51%; HPLC **(**Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R = 7.47 min (major), t_R = 17.92 min (minor).

General procedure for synthesis of 2,5-dihydropyrroles 3 via 1, 3-dipolar cycloadditions of α-arylglycine esters-derived azomethine ylides with ethynyl ketones

Under a nitrogen atmosphere, $Cu(OAc)_2 \cdot H_2O$ (2.0 mg, 0.01 mmol), ligand **4d** (5.7 mg, 0.011 mmol) and 4Å MS were dissolved in DCM (2 mL), and stirred at room temperature for approximately 0.5 h. Then, the mixture was cooled to -40 °C, azomethine ylide **2** (0.2 mmol), DIPEA (3.5 μL, 0.02 mmol) and ynone **1** (0.1 mmol) were added sequentially. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography to give the corresponding cycloaddition product **3**. The NMR data are consistent with the literature report.[9b]

Methyl 4-benzoyl-5-(4-nitrophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-Carboxylate (3ak). Reaction time = 30 hrs; dr > 99:1; 41.1 mg; yield: 96%. yellow oil; $[\alpha]^{25}_D$ = +57.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.77-7.74 (m, 2H), 7.61-7.56 (m, 3H), 7.50-7.44 (m, 4H), 7.40-7.37 (m, 2H), 7.35-7.31 (m, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 5.73 (d, *J* = 2.0 Hz, 1H), 3.87 (s, 3H), 3.19 (s, 1H); Enantiomeric excess: 90%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 15.64 min (major), t_R = 38.24 min (minor).

4-benzoyl-2-(4-chlorophenyl)-5-(4-nitrophenyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3al). Reaction time = 17 hrs; dr > 99:1; 39.8 mg; yield: 86%. yellow oil; $[\alpha]^{25}_D$ = +66.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.7 Hz, 2H), 7.75-7.73(m, 2H), 7.61-7.55 (m, 3H), 7.49-7.44 (m, 4H), 7.35 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 2.0 Hz, 1H), 5.69 (s, 1H), 3.87 (s, 3H), 3.18 (s, 1H); Enantiomeric excess: 91%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R =23.28 min (major), t_R = 43.58 min (minor).

4-benzoyl-2-(4-methoxyphenyl)-5-(4-nitrophenyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3am). Reaction time = 70 hrs; dr = 98:2; 28.9 mg; yield: 63%. yellow oil; $[\alpha]^{25}_D$ = +61.0 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.8 Hz, 2H), 7.76-7.74 (m, 2H), 7.61-7.56 (m, 3H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.41-7.38 (m, 2H), 6.93-6.89 (m, 3H), 5.72 (d, *J* = 2.0 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H); Enantiomeric excess: 92%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R = 35.86 min (major), t_R = 143.10 min (minor).

4-benzoyl-5-(4-(methoxycarbonyl)phenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3an). Reaction time = 80 hrs; dr > 99:1; 30.0 mg; yield: 68%. colorless oil; $[\alpha]^{25}_D$ = +54.8 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.98 (m, 2H), 7.78-7.75 (m, 2H), 7.58-7.49 (m, 3H), 7.47-7.43 (m, 4H), 7.39-7.29 (m, 3H), 6.92 (d, *J* = 2.0 Hz, 1H), 5.66 (d, *J* = 2.0 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H); Enantiomeric excess: 92%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 80/20, 1.0 mL/min, 254 nm): t_R = 16.36 min (major), t_R = 20.32 min (minor).

Methyl 4-benzoyl-5-(4-cyanophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-Carboxylate (3ao). Reaction time = 48 hrs; dr > 99:1; 36.8 mg; yield: 90%. colorless oil; $[\alpha]^{25}_D$ = +62.3 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.74 (m, 2H), 7.63-7.59 (m, 2H), 7.58-7.56 (m, 1H), 7.54-7.52 (m, 2H), 7.49-7.44 (m, 4H), 7.40-7.30 (m, 3H), 6.93 (d, *J* = 2.0 Hz, 1H), 5.67 (d, *J* = 2.0 Hz, 1H), 3.86 (s, 3H), 3.20 (s, 1H); Enantiomeric excess: 91%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 14.36 min (major), t_R = 23.99 min (minor).

4-(4-fluorobenzoyl)-5-(4-nitrophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3bk). Reaction time = 70 hrs; dr > 99:1; 28.6 mg; yield: 64%. yellow oil; $[\alpha]^{25}_D$ = +67.7 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.17 (m, 2H), 7.82-7.77 (m, 2H), 7.61-7.57 (m, 2H), 7.50-7.47 (m, 2H), 7.42-7.32 (m, 3H), 7.16-7.11 (m, 2H), 6.90 (d, *J* = 2.0 Hz, 1H), 5.73 (d, *J* = 2.0 Hz, 1H), 3.88 (s, 3H), 3.19 (s, 1H); Enantiomeric excess: 89%; HPLC (Daicel Chirapak IA, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 18.03 min (major), t_R = 48.37 min (minor).

4-(4-methoxybenzoyl)-5-(4-nitrophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3ck). Reaction time = 20 hrs; dr = 99:1; 32.1 mg; yield: 70%. yellow oil; $[\alpha]^{25}_D$ = +59.3 ($CHCl_3$, *c* = 1.00); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19-8.15 (m, 2H), 7.80-7.77 (m, 2H), 7.61-7.57 (m, 2H), 7.49-7.47 (m, 2H), 7.41-7.33 (m, 3H), 6.95-6.91 (m, 2H), 6.87 (d, *J* = 2.0 Hz, 1H), 5.74 (d, *J* = 2.0 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.23 (s, 1H); Enantiomeric excess: 92%; HPLC (Daicel Chirapak AD-H, *n*-hexane/ isopropanol = 70/30, 1.0 mL/min, 254 nm): t_R = 44.77 min (major), t_R = 65.72 min (minor).

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Notes and references

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