Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2018, **16**, 742

Decarboxylation-promoted Pd-catalyzed asymmetric propargylic [3 + 2] annulation for the enantioselective construction of a quaternary stereocenter in 2,3-dihydrofurans†

Kun Li,[a,b] Fu-Lin Zhu,[b] Zhen-Ting Liu,[b] Jing Tong*[a] and Xiang-Ping Hu *[b]

Received 13th November 2017,
Accepted 29th December 2017

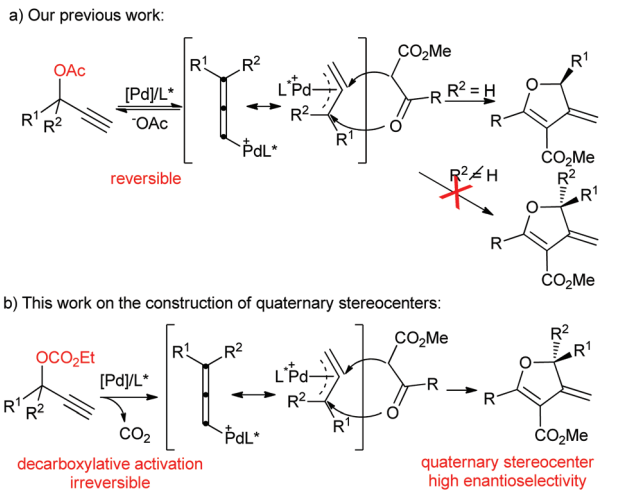
DOI: 10.1039/c7ob02778h

rsc.li/obc

The enantioselective construction of a quaternary stereocenter in 2,3-dihydrofuran frameworks has been realized *via* the palladium-catalyzed asymmetric [3 + 2] cycloaddition of tertiary propargylic carbonates with β-ketoesters enabled by a chiral ferrocene/benzimidazole-based bidentate P,N-ligand. The reaction was significantly promoted by loss of CO_2 to irreversibly form π-propargylpalladium or allenylpalladium intermediates. This protocol features a good tolerance of functional groups in both tertiary propargylic carbonates and β-ketoesters, thereby delivering a variety of highly functionalized chiral 2,3-dihydrofurans bearing a quaternary stereocenter at the 2-position and an exocyclic double bond at the 3-position in good chemical yields and high enantioselectivities (up to 98% ee).

Introduction

Palladium-catalyzed annulation of propargylic compounds with bis-nucleophiles has become a strategically important and powerful process for the construction of structurally diverse carbo- and heterocyclic frameworks[1] since the pioneering work of Tsuji and co-workers reported in the 1980s.[2] The reaction proceeds *via* the π-propargylpalladium or allenylpalladium intermediates, which are attacked consecutively by two nucleophilic atoms of bis-nucleophiles to give the cycloadducts bearing an exocyclic double bond. Due to the instability of the exocyclic double bond under the reaction conditions, it is readily isomerized into the more stable endocyclic double bond, thereby converting the adjacent sp^3 carbon atom into a non-chiral sp^2 carbon atom, which greatly limits its value in asymmetric catalysis. It is therefore appreciable that the asymmetric version of this methodology is rarely studied.[3] However, when a tertiary propargylic ester is used as the reaction partner, this isomerization process could be completely inhibited by the formation of a quaternary carbon center adjacent to the exocyclic double bond. We therefore envisioned that this methodology may provide an efficient and powerful access to optically active cyclic frameworks decorated with a quaternary stereocenter (Scheme 1). The construction of quaternary stereocenters in cyclic frameworks still represents one of the key challenges in organic synthesis, especially in a catalytic, enantioselective fashion.[4] To the best of our knowledge, none has explored the potential of this methodology in the employment of tertiary propargylic compounds for the construction of quaternary stereocenters with a control of the absolute stereochemistry. In this context, we wished to demonstrate the



Scheme 1 Decarboxylation-promoted palladium-catalyzed asymmetric propargylic [3 + 2] annulation with β-ketoesters for the construction of quaternary stereocenters.

[a]*Liaoning University, College of Chemistry, Shenyang 110036, Liaoning, China. E-mail: tongjinglnu@sina.com*
[b]*Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, Liaoning, China. E-mail: xiangping@dicp.ac.cn*

†Electronic supplementary information (ESI) available. CCDC 1469918. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ob02778h

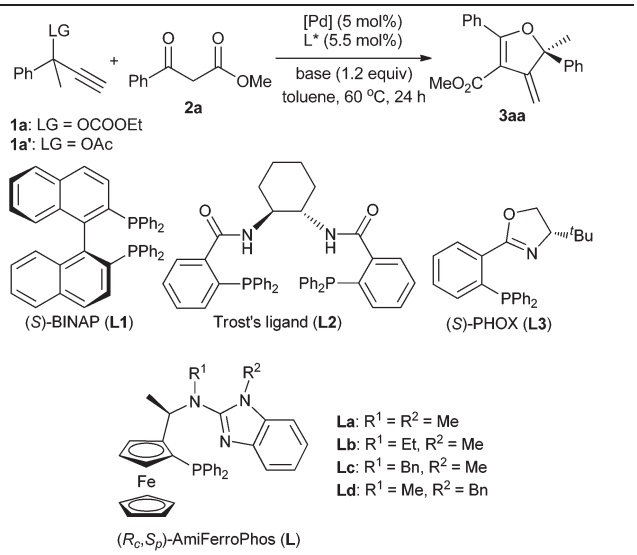
potential of this methodology in the enantioselective construction of quaternary stereocenters in cyclic frameworks.

In our recent study, we have disclosed an enantioselective palladium-catalyzed [3 + 2] cycloaddition of secondary propargylic acetates with β-ketoesters enabled by chiral ferrocene/benzimidazole-based bidentate P,N-ligands (AmiFerroPhos, **L**) developed by our group,[5] which led to biologically important chiral dihydrofurans (Scheme 1a).[6] It is therefore envisioned that this reaction protocol should be also suitable for tertiary propargylic acetates. However, an initial attempt led to very disappointing results in which no [3 + 2] adduct was detected. The reason might be the congested nature of tertiary propargylic acetates and their reversible conversion into π-propargylpalladium or allenylpalladium intermediates. We therefore presumed that tertiary propargylic carbonates should be a better choice for the reaction since they could irreversibly form π-propargylpalladium or allenylpalladium intermediates by the loss of CO_2 (Scheme 1b). As a result, herein we wish to describe the first highly enantioselective palladium-catalyzed decarboxylative [3 + 2] cycloaddition of tertiary propargylic carbonates with β-ketoesters, which gave rise to highly functionalized chiral 3-methylidene-2,3-dihydrofurans with a quaternary stereocenter at the 2-position in good chemical yields and high enatioselectivities (up to 98% ee).

Results and discussion

Experiments designed to evaluate a series of ligands employed ethyl (2-phenylbut-3-yn-2-yl)carbonate (**1a**), methyl benzoylacetate (**2a**, 1.0 equiv.), and Cs_2CO_3 (1.2 equiv.) in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) and the ligand (5.5 mol%) in toluene at 60 °C for 24 h, and the results are summarized in Table 1. The initial screening of the reaction with BINAP (**L1**)[7] gave rise to moderate enantioselectivity (entry 1). In sharp contrast, a very low conversion was achieved by the use of propargylic acetate **1a′** instead of the corresponding carbonate **1a** as the substrate (entry 2). This result demonstrated the important role of the decarboxylation-activated strategy in the development of this challenging propargylic [3 + 2] cycloaddition. Further ligand-screening showed that Trost's ligand (**L2**)[8] and PHOX (**L3**),[9] the privileged ligands for palladium-catalyzed asymmetric allylic transformation, led to disappointing performance (entries 3 and 4). The results of Table 1 disclosed that a chiral P,N-ligand class (AmiFerroPhos, **L**) developed by our group was indeed highly efficient in this palladium-catalyzed cycloaddition with ligand **La** to give the desired cycloadduct **3aa** in 90% yield and up to 96% ee (entry 6), significantly superior to those with ligands **L1–3**. Again, propargylic acetate **1a′** didn't lead to any cycloadduct with ligand **La** (entry 5). Further modification of the ligand structure did not improve the reaction performance (entries 7–9). We next investigated the influence of the reaction conditions on the reaction performance. The catalyst precursor exerted a large influence on the reactivity but had less influence on the enantioselectivity. Thus, the use of $Pd(PPh_3)_4$ and $Pd(OAc)_2$ instead of

Table 1 Optimization of the reaction conditions[a]



Entry	[Pd]	L	Base	Yield[b] (%)	ee[c] (%)
1	$Pd_2(dba)_3{\cdot}CHCl_3$	**L1**	Cs_2CO_3	92	59
2[d]	$Pd_2(dba)_3{\cdot}CHCl_3$	**L1**	Cs_2CO_3	—	—[e]
3	$Pd_2(dba)_3{\cdot}CHCl_3$	**L2**	Cs_2CO_3	—	—[e]
4	$Pd_2(dba)_3{\cdot}CHCl_3$	**L3**	Cs_2CO_3	—	—[e]
5[d]	$Pd_2(dba)_3{\cdot}CHCl_3$	**La**	Cs_2CO_3	—	—[e]
6	$Pd_2(dba)_3{\cdot}CHCl_3$	**La**	Cs_2CO_3	90	96
7	$Pd_2(dba)_3{\cdot}CHCl_3$	**Lb**	Cs_2CO_3	86	80
8	$Pd_2(dba)_3{\cdot}CHCl_3$	**Lc**	Cs_2CO_3	86	96
9	$Pd(dba)_3{\cdot}CHCl_3$	**Ld**	Cs_2CO_3	83	96
10	$Pd_2(dba)_3{\cdot}CHCl_3$	—	Cs_2CO_3	—	—[e]
11	$Pd(PPh_3)_4$	—	Cs_2CO_3	—	—[e]
12	$Pd(PPh_3)_4$	**La**	Cs_2CO_3	68	93
13	$Pd(OAc)_2$	**La**	Cs_2CO_3	65	96
14	$Pd(dba)_3{\cdot}CHCl_3$	**La**	None	56	95
15	$Pd(dba)_3{\cdot}CHCl_3$	**La**	Et_3N	65	96
16	$Pd(dba)_3{\cdot}CHCl_3$	**La**	K_3PO_4	88	96
17	$Pd(dba)_3{\cdot}CHCl_3$	**La**	^{t}BuOK	73	95
18[f]	$Pd_2(dba)_3{\cdot}CHCl_3$	**La**	Cs_2CO_3	38	87
19[g]	$Pd_2(dba)_3{\cdot}CHCl_3$	**La**	Cs_2CO_3	90	95

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), [Pd] (0.015 mmol, 5 mol%), **L*** (0.0165 mmol, 5.5 mol%), base (0.36 mmol), and 3 mL of toluene unless otherwise specified, 60 °C, 24 h. [b] Yield of the isolated product. [c] Determined by HPLC using a chiral stationary phase. [d] Acetate **1a′** was used instead of carbonate **1a**. [e] Not determined due to low conversion. [f] DMSO as the solvent. [g] $ClCH_2CH_2Cl$ as the solvent.

$Pd_2(dba)_3{\cdot}CHCl_3$ led to a clear decrease in the yields but gave rise to the almost maintained enantioselectivities (entries 12 and 13). However, no Pd-catalyst precursors in the absence of P,N-ligand **La** showed reactivity for the model reaction (entries 10 and 11). The base additive was not necessary for the reaction since the reaction could proceed in its absence although at a lower reaction rate (entry 14). However, the presence of an appropriate base such as Cs_2CO_3 could significantly promote the reactivity (entry 6). The variation of the base had a clear effect on the reactivity. Thus, the use of Et_3N and ^{t}BuOK clearly reduced the reactivity (entries 15 and 17), while K_3PO_4 gave good performance (entry 16). The nature of the solvent had a significant influence on both the yield and the enantio-

selectivity. DMSO proved to be an inferior solvent for the reaction, giving the cycloadduct in only 38% yield and 87% ee (entry 18). Using $ClCH_2CH_2Cl$ as the solvent, a similar result to that for toluene was obtained (entry 19).

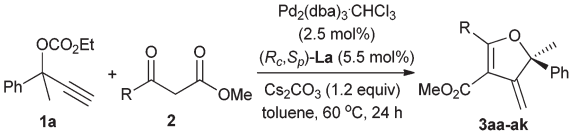
With the optimal reaction conditions in hand, various methyl β-ketoesters were explored to investigate the generality of this cycloaddition, and the results are summarized in Table 2. The electronic properties of the substituent at the *para* position of the phenyl ring had little effect on the enantioselectivity (entries 2–5), but showed some influence on the reactivity with the 4-methoxy group, leading to a decreased yield of 74% (entry 3). The reaction was highly sensitive to the substitution pattern on the phenyl ring. Thus, either a 4-Cl or 3-Cl substituted substrate (**2e** or **2f**) gave good yields and high enantioselectivities (entries 5 and 6), while the substrate **2g** bearing a 2-Cl substituent resulted in clearly reduced yield and enantioselectivity (entry 7). The 2-naphthyl substituted substrate **2h** worked well, giving the cycloadduct **3ah** in 92% yield and 95% ee (entry 8). Heteroaromatic substrate **2i** was also a suitable reaction partner, providing the cycloadduct **3ai** in 89% yield and 97% ee (entry 9). Remarkably, aliphatic β-ketoesters were also well tolerated in this process, providing the corresponding cycloadducts **3aj** and **3ak** in good enantioselectivities although with decreased yields (entries 10 and 11).

Next, the tolerance of tertiary propargylic esters in the cycloaddition was studied, and the results are shown in Table 3. To our delight, high to excellent enantioselectivities were observed regardless of the electronic properties and positions of the substituents at the *para* position of the phenyl ring (entries 1–5). However, the substitution pattern on the phenyl ring showed some influence on the reactivity (entries 5–7). Thus, the 2-Cl substituted substrate **1g** led to a reduced yield of 62% (entry 7). 2-Naphthyl (**1h**) and 2-furyl (**1i**) substrates also served well for this cycloaddition, thus giving the corresponding cycloadducts **3ha** and **3ia** in good results (entries 8 and 9). Besides the methyl group, other aliphatic chains such as the R^2 group were also tolerated in the reaction (entries 10 and 11). However, the substrate **1l** bearing two different alkyl groups (R^1 = Et, R^2 = Me) gave low enantioselectivity (entry 12). The absolute configuration of the [3 + 2] cycloadducts was unambiguously determined by X-ray structure analysis of **3da**, which is assigned as having an *S* configuration.[10]

Based on the experimental results, we proposed a plausible mechanism to explain the observed stereochemistry (Fig. 1). There are two possible orientations present in square-planar Pd-allyl intermediates: M-type and W-type, in which M-type (**A**) is favored due to steric hindrance. The regioselective attack at the more congested π-allyl terminus according to the report by Larock[11] and the *trans*-effect[12] gives (*S*)-**3aa** as a major cycloadduct.

The robustness and practicality of the current methodology could be further demonstrated by large-scale synthesis. Thus, the cycloaddition between **1a** and **2a** on a gram-scale delivered the corresponding cycloadduct **3aa** in 89% yield and 95% ee.

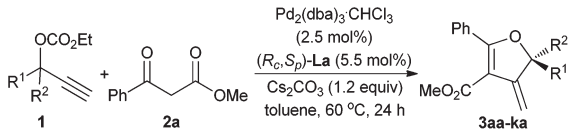
Table 2 Scope with respect to β-ketoesters[a]



Entry	Substrate (R)	Product (**3**)	Yield[b] (%)	ee[c] (%)
1	**2a**: R = Ph	**3aa**	90	96
2	**2b**: R = 4-MeC_6H_4	**3ab**	92	90
3	**2c**: R = 4-$MeOC_6H_4$	**3ac**	74	97
4	**2d**: R = 4-FC_6H_4	**3ad**	93	96
5	**2e**: R = 4-ClC_6H_4	**3ae**	92	94
6	**2f**: R = 3-ClC_6H_4	**3af**	90	92
7	**2g**: R = 2-ClC_6H_4	**3ag**	64	85
8	**2h**: R = 2-naphthyl	**3ah**	92	95
9	**2i**: R = 2-thienyl	**3ai**	89	97
10	**2j**: R = Me	**3aj**	72	87
11	**2k**: R = ^{i}Pr	**3ak**	66	89

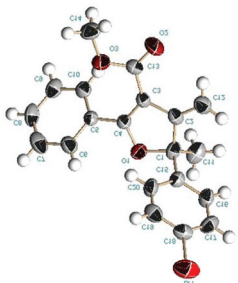
[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.3 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.0075 mmol, 2.5 mol%), (R_c,S_p)-**La** (0.0165 mmol, 5.5 mol%), Cs_2CO_3 (0.36 mmol, 1.2 equiv.), and 3 mL of toluene, 60 °C, 24 h. [b] Yield of the isolated product. [c] Determined by HPLC using a chiral stationary phase.

Table 3 Scope with respect to propargylic carbonates[a]



Entry	Substrate (R^1, R^2)	Product (**3**)	Yield[b] (%)	ee[c] (%)
1	**1a**: R^1 = Ph, R^2 = Me	**3aa**	90	96
2	**1b**: R^1 = 4-MeC_6H_4, R^2 = Me	**3ba**	93	90
3	**1c**: R^1 = 4-FC_6H_4, R^2 = Me	**3ca**	92	92
4	**1d**: R^1 = 4-BrC_6H_4, R^2 = Me	**3da**	76	94
5	**1e**: R^1 = 4-ClC_6H_4, R^2 = Me	**3ea**	86	93
6	**1f**: R^1 = 3-ClC_6H_4, R^2 = Me	**3fa**	85	95
7	**1g**: R^1 = 2-ClC_6H_4, R^2 = Me	**3ga**	62	98
8	**1h**: R^1 = 2-naphthyl, R^2 = Me	**3ha**	90	90
9	**1i**: R^1 = 2-furyl, R^2 = Me	**3ia**	85	86
10	**1j**: R^1 = Ph, R^2 = Et	**3ja**	81	93
11	**1k**: R^1 = Ph, R^2 = Pr	**3ka**	61	94
12	**1l**: R^1 = Et, R^2 = Me	**3la**	75	22

[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.3 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.0075 mmol, 2.5 mol%), (R_c,S_p)-**La** (0.0165 mmol, 5.5 mol%), Cs_2CO_3 (0.36 mmol, 1.2 equiv.), and 3 mL of toluene, 60 °C, 24 h. [b] Yield of the isolated product. [c] Determined by HPLC using a chiral stationary phase.



(*S*)-**3da**

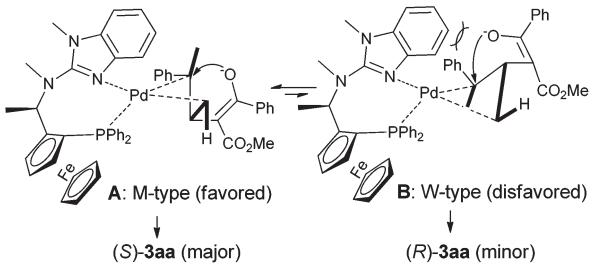
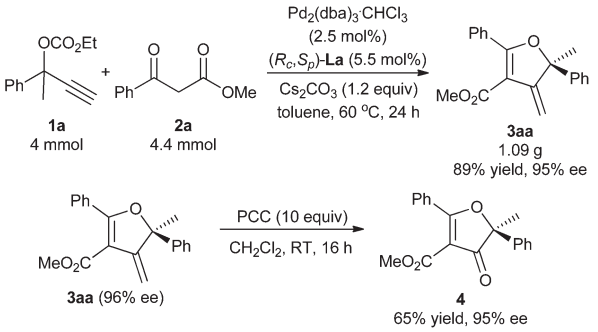


Fig. 1 The proposed transition state for stereochemistry.



Scheme 2 Synthetic application.

The resulting 2,3-dihydrofurans could be used for further functionalization and should be highly useful synthons. For example, the exocyclic double bond of **3aa** could be readily oxidized by PCC in CH_2Cl_2 at room temperature to provide the corresponding furan-3(2*H*)-one **4** without a clear erosion in the optical purity (Scheme 2).

Conclusions

In conclusion, we have developed a highly enantioselective Pd-catalyzed decarboxylative propargylic [3 + 2] cycloaddition of tertiary propargylic carbonates with methyl β-ketoesters, leading to highly functionalized 2,3-dihydrofurans bearing a quaternary stereocenter at the 2-position in good yields and high enantioselectivities (up to 98% ee). Chiral ferrocene/benzimidazole-based bidentate P,N-ligands developed by our group and the decarboxylation-activated strategy for irreversible formation of π-propargylpalladium or allenylpalladium intermediates should be responsible for the first realization of this cycloaddition in an enantioselective manner. The reaction tolerates a wide range of functional groups with respect to both tertiary propargylic esters and β-ketoesters, and represents an attractive and practical approach for the construction of chiral quaternary stereocenters in heterocyclic frameworks. The robustness and practicality of this method were demonstrated by large-scale synthesis and the formation of optically active furan-3(2*H*)-ones through the oxidation of the exocyclic double bond of cycloadducts. The development of a new asymmetric propargylic annulation is the subject of ongoing research in our laboratory.[13]

Experimental

General methods

All reactions were carried out under a nitrogen atmosphere. Solvents were purified by a standard procedure before use. Commercial reagents were used without further purification. Flash chromatography was performed on silica gel 60 (40–63 μm, 60 Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with an F254 indicator. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer. The chemical shifts (δ) and coupling constants (J) are expressed in parts per million (ppm) and hertz (Hz), respectively. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in hertz (Hz), integration. Enantiomeric ratios were determined by chiral HPLC using *n*-hexane and i-PrOH as solvents. Optical rotations were recorded on a JASCO P-1020 polarimeter. Tertiary propargylic esters **1**,[14] β-ketoesters **2**[15] and AmiFerroPhos **L**[5,16] were prepared following a method reported in the literature.

General procedure for Pd-catalyzed asymmetric [3 + 2] cycloaddition of β-ketoesters with tertiary propargylic esters

A solution of $Pd_2(dba)_3{\cdot}CHCl_3$ (7.8 mg, 0.0075 mmol) and (R_c,S_p)-**La** (9.2 mg, 0.0165 mmol) in 1 mL of anhydrous toluene placed in an oven-dried Schlenk flask was stirred at room temperature under a nitrogen atmosphere for 1 h. A solution of propargylic esters **1** (0.3 mmol), β-ketoesters **2** (0.3 mmol) and Cs_2CO_3 (117.3 mg, 0.36 mmol) in 2 mL of anhydrous toluene was added. The mixture was stirred at 60 °C for 24 h. The reaction mixture was purified by silica gel chromatography to afford dihydrofuran products **3**.

Methyl (*S*)-5-methyl-4-methylene-2,5-diphenyl-4,5-dihydrofuran-3-carboxylate (3aa). A pale yellow oil was obtained in 90% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 8.9 min, t_R (minor) = 6.0 min. $[\alpha]_D^{27}$ = +13.2 (c = 1.11, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74–7.72 (m, 2H), 7.55–7.31 (m, 8H), 5.53 (s, 1H), 4.84 (s, 1H), 3.63 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.5, 164.5, 152.6, 143.5, 131.5, 130.2, 129.4, 129.0, 128.5, 128.4, 125.1, 105.6, 103.0, 91.4, 51.5, 27.7; HRMS (ESI): m/z calcd for $C_{20}H_{19}O_3$ [M + H] 307.1334, found 307.1332.

Methyl (*S*)-5-methyl-4-methylene-5-phenyl-2-(*p*-tolyl)-4,5-dihydrofuran-3-carboxylate (3ab). A yellow oil was obtained in 92% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 90% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 16.9 min,

t_R (minor) = 7.5 min. $[\alpha]_D^{23}$ = −14.3 (*c* = 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65–7.63 (m, 2H), 7.50–7.28 (m, 7H), 5.50 (s, 1H), 4.82 (s, 1H), 3.63 (s, 3H), 2.37 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.6, 164.6, 152.8, 143.6, 141.5, 129.4, 129.0, 129.0, 128.3, 127.3, 125.1, 105.1, 102.6, 91.1, 51.4, 27.7, 21.6; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{21}O_3$ [M + H] 321.1491, found 321.1488.

Methyl (*S*)-2-(4-methoxyphenyl)-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ac). A yellow oil was obtained in 74% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 50/1). 97% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 80/20, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 17.5 min, t_R (minor) = 7.5 min. $[\alpha]_D^{29}$ = +10.9 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75–7.73 (m, 2H), 7.49–7.33 (m, 5H), 7.04–7.02 (m, 2H), 5.46 (s, 1H), 4.79 (s, 1H), 3.83 (s, 3H), 3.65 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.7, 161.9, 152.8, 143.7, 131.3, 129.0, 128.3, 125.1, 122.2, 113.9, 104.2, 102.3, 90.9, 55.8, 51.4, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{21}O_4$ [M + H] 337.1440, found 337.1438.

Methyl (*S*)-2-(4-fluorophenyl)-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ad). A yellow oil was obtained in 93% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 11.1 min, t_R (minor) = 6.7 min. $[\alpha]_D^{26}$ = −22.6 (*c* = 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83–7.80 (m, 2H), 7.50–7.29 (m, 7H), 5.53 (s, 1H), 4.83 (s, 1H), 3.64 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.6, 164.4, 163.9 (d, *J* = 249.4 Hz) 152.5, 143.4, 132.1 (d, *J* = 8.9 Hz), 129.0, 128.4, 126.6 (d, *J* = 3.2 Hz), 125.1, 115.6 (d, *J* = 21.9 Hz), 105.6, 103.2, 91.5, 51.5, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}FO_3$ [M + H] 325.1240, found 325.1241.

Methyl (*S*)-2-(4-chlorophenyl)-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ae). A yellow oil was obtained in 92% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 94% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 13.8 min, t_R (minor) = 6.9 min. $[\alpha]_D^{27}$ = −23.9 (*c* = 0.77, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77–7.75 (m, 2H), 7.56–7.32 (m, 7H), 5.54 (s, 1H), 4.85 (s, 1H), 3.64 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.3, 164.3, 152.4, 143.4, 136.2, 131.3, 129.0, 128.9, 128.6, 128.4, 125.1 106.1, 103.6, 91.6, 51.5, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0944.

Methyl (*S*)-2-(3-chlorophenyl)-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3af). A yellow oil was obtained in 90% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 92% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 7.1 min, t_R (minor) = 6.0 min. $[\alpha]_D^{26}$ = −36.7 (*c* = 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.78–7.58 (m, 3H), 7.50–7.33 (m, 6H), 5.56 (s, 1H), 4.84 (s, 1H), 3.64 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.8, 164.2, 152.2, 143.3, 133.2, 132.2, 131.2, 130.4, 129.1, 129.0, 128.4, 128.1, 125.2, 106.5, 103.9, 91.8, 51.6, 27.6; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0942.

Methyl (*S*)-2-(2-chlorophenyl)-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ag). A yellow oil was obtained in 64% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 85% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 95/5, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 8.2 min, t_R (minor) = 7.1 min. $[\alpha]_D^{29}$ = −17.4 (*c* = 1.04, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60–7.33 (m, 9H), 5.61 (s, 1H), 4.81 (s, 1H), 3.51 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.7, 163.7, 151.7, 142.9, 132.4, 132.1, 131.2, 130.8, 129.9, 128.9, 128.5, 127.5, 125.4, 108.2, 103.5, 92.9, 51.4, 27.6; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0941.

Methyl (*S*)-5-methyl-4-methylene-2-(naphthalen-2-yl)-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ah). A pale yellow solid was obtained in 92% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 50/1). M.p.: 97–98 °C. 95% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 80/20, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 10.3 min, t_R (minor) = 6.9 min. $[\alpha]_D^{24}$ = +35.4 (*c* = 0.95, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.07–7.96 (m, 3H), 7.78 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.63–7.54 (m, 4H), 7.44–7.32 (m, 3H), 5.57 (s, 1H), 4.86 (s, 1H), 3.65 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.5, 152.7, 143.6, 134.3, 132.5, 129.7, 129.3, 129.0, 128.4, 128.3, 128.1, 127.8, 127.6, 127.2, 126.2, 125.2, 106.0, 103.1, 91.5, 51.5, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{21}O_3$ [M + H] 357.1491, found 357.1486.

Methyl (*S*)-5-methyl-4-methylene-5-phenyl-2-(thiophen-2-yl)-4,5-dihydrofuran-3-carboxylate (3ai). A yellow oil was obtained in 89% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 97% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 80/20, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 6.9 min, t_R (minor) = 5.7 min. $[\alpha]_D^{24}$ = +102.9 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (dd, *J* = 3.9, 1.2 Hz, 1H), 7.95 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.47–7.24 (m, 7H), 5.54 (s, 1H), 4.87 (s, 1H), 3.78 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.5, 162.0, 152.0, 143.7, 133.8, 133.4, 131.0, 129.0, 128.4, 128.3, 125.0, 103.8, 103.7, 90.9, 51.6, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}O_3S$ [M + H] 313.0898, found 313.0895.

Methyl (*S*)-2,5-dimethyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3aj). A yellow oil was obtained in 72% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 87% ee was determined by chiral HPLC (Chiralcel OJ-H, *n*-hexane/i-PrOH = 50/50, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 8.6 min, t_R (minor) = 18.7 min. $[\alpha]_D^{29}$ = +88.1 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41–7.32 (m, 5H), 5.39 (s, 1H), 4.63 (s, 1H), 3.71 (s, 3H), 2.40 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.3, 164.9, 151.7, 143.3, 128.9, 128.3, 125.2, 105.1,

100.9, 92.0, 51.3, 27.5, 15.9; HRMS (ESI): *m*/*z* calcd for $C_{15}H_{17}O_3$ [M + H] 245.1178, found 245.1175.

Methyl (*S*)-2-isopropyl-5-methyl-4-methylene-5-phenyl-4,5-dihydrofuran-3-carboxylate (3ak). A yellow oil was obtained in 66% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 89% ee was determined by chiral HPLC (Chiralcel OJ-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 10.6 min, t_R (minor) = 11.7 min. $[\alpha]_D^{22}$ = −77.8 (*c* = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.41–7.30 (m, 5H), 5.38 (s, 1H), 4.62 (s, 1H), 3.76–3.70 (m, 4H), 1.73 (s, 3H), 1.19 (dd, *J* = 12.8, 6.9 Hz, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.0, 164.8, 152.0, 143.5, 128.9, 128.2, 124.9, 103.3, 101.2, 91.4, 51.3, 27.8, 27.5, 19.9, 19.8; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{21}O_3$ [M + H] 273.1491, found 273.1493.

Methyl (*S*)-5-methyl-4-methylene-2-phenyl-5-(*p*-tolyl)-4,5-dihydrofuran-3-carboxylate (3ba). A pale yellow solid was obtained in 93% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 90% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 9.5 min, t_R (minor) = 6.4 min. $[\alpha]_D^{29}$ = −48.1 (*c* = 1.04, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.72–7.69 (m, 2H), 7.54–7.36 (m, 5H), 7.21–7.19 (m, 2H), 5.51 (s, 1H), 4.78 (s, 1H), 3.62 (s, 3H), 2.29 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.6, 164.5, 152.8, 140.6, 137.7, 131.4, 130.3, 129.5, 129.4, 128.4, 125.2, 105.6, 102.8, 91.4, 51.4, 27.6, 21.1; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{21}O_3$ [M + H] 321.1491, found 321.1487.

Methyl (*S*)-5-(4-fluorophenyl)-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3ca). A yellow oil was obtained in 92% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 92% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 8.3 min, t_R (minor) = 6.2 min. $[\alpha]_D^{27}$ = −52.2 (*c* = 1.07, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.72–7.70 (m, 2H), 7.54–7.47 (m, 5H), 7.25–7.20 (m, 2H), 5.53 (s, 1H), 4.83 (s, 1H), 3.63 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.4, 162.2 (d, *J* = 244.6 Hz), 152.5, 139.8 (d, *J* = 3.0 Hz), 131.5, 130.1, 129.4, 128.5, 127.5 (d, *J* = 8.4 Hz), 115.8 (d, *J* = 21.5 Hz), 105.6, 103.2, 90.9, 51.4, 27.7; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}FO_3$ [M + H] 325.1240, found 325.1238.

Methyl (*S*)-5-(4-bromophenyl)-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3da). A pale yellow solid was obtained in 76% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). M.p.: 100–101 °C. 94% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 10.3 min, t_R (minor) = 7.0 min. $[\alpha]_D^{23}$ = −32.9 (*c* = 1.02, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.72–7.70 (m, 2H), 7.61–7.43 (m, 7H), 5.52 (s, 1H), 4.85 (s, 1H), 3.62 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.4, 152.2, 142.9, 132.0, 131.5, 130.0, 129.4, 128.5, 127.5, 121.8, 105.6, 103.4, 90.8, 51.5, 27.5; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}BrO_3$ [M + H] 385.0439, found 385.0436.

Methyl (*S*)-5-(4-chlorophenyl)-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3ea). A yellow oil was obtained in 86% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 93% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 9.5 min, t_R (minor) = 6.7 min. $[\alpha]_D^{27}$ = −56.9 (*c* = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.73–7.71 (m, 2H), 7.53–7.45 (m, 7H), 5.53 (s, 1H), 4.86 (s, 1H), 3.63 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.4, 152.3, 142.5, 133.2, 131.5, 130.0, 129.4, 129.0, 128.5, 127.2, 105.6, 103.3, 90.8, 51.5, 27.6; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0944.

Methyl (*S*)-5-(3-chlorophenyl)-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3fa). A yellow oil was obtained in 85% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 95% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 7.9 min, t_R (minor) = 5.6 min. $[\alpha]_D^{27}$ = −39.1 (*c* = 0.88, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.73–7.71 (m, 2H), 7.55–7.39 (m, 7H), 5.54 (s, 1H), 4.92 (s, 1H), 3.63 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.3, 164.3, 152.1, 145.9, 133.8, 131.6, 131.1, 129.9, 129.4, 128.5, 128.4, 125.0, 123.9, 105.7, 103.6, 90.7, 51.5, 27.5; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0944.

Methyl (*S*)-5-(2-chlorophenyl)-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3ga). A pale yellow solid was obtained in 62% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). M.p.: 96–97 °C. 98% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 9.7 min, t_R (minor) = 6.7 min. $[\alpha]_D^{29}$ = −28.8 (*c* = 1.13, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.79–7.67 (m, 3H), 7.53–7.41 (m, 6H), 5.44 (s, 1H), 4.41 (s, 1H), 3.65 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.9, 164.6, 152.4, 138.1, 134.2, 131.8, 131.3, 131.0, 130.6, 129.7, 129.3, 128.4, 127.4, 106.7, 102.0, 90.8, 51.4, 28.6; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}ClO_3$ [M + H] 341.0944, found 341.0939.

Methyl (*S*)-5-methyl4-methylene-5-(naphthalen-2-yl)-2-phenyl-4,5-dihydrofuran-3-carboxylate (3ha). A yellow oil was obtained in 90% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 50/1). 90% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 12.9 min, t_R (minor) = 8.4 min. $[\alpha]_D^{28}$ = −37.3 (*c* = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 8.07–7.75 (m, 6H), 7.59–7.46 (m, 6H), 5.58 (s, 1H), 4.86 (s, 1H), 3.65 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.8, 164.5, 152.6, 140.7, 133.0, 132.9, 131.5, 130.2, 129.5, 128.9, 128.8, 128.5, 127.9, 127.0, 126.9, 123.9, 123.7, 105.8, 103.3, 91.6, 51.5, 27.6; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{21}O_3$ [M + H] 357.1491, found 357.1489.

Methyl (*S*)-2-methyl-3-methylene-5-phenyl-2,3-dihydro-[2,2′-bifuran]-4-carboxylate (3ia). A yellow oil was obtained in 85%

yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 70/1). 86% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 8.1 min, t_R (minor) = 6.1 min. $[\alpha]_D^{22}$ = −59.1 (*c* = 1.13, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, *J* = 0.7 Hz, 1H), 7.64–7.62 (m, 3H), 7.53–7.43 (m, 3H), 6.56 (d, *J* = 3.3 Hz, 1H), 6.47 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.57 (s, 1H), 4.73 (s, 1H), 3.65 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 164.4, 154.3, 149.9, 144.4, 131.5, 130.1, 129.4, 128.4, 110.9, 108.7, 105.5, 103.3, 86.8, 51.5, 26.0; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}O_4$ [M + H] 297.1127, found 297.1124.

Methyl (*S*)-5-ethyl-4-methylene-2,5-diphenyl-4,5-dihydrofuran-3-carboxylate (3ja). A yellow oil was obtained in 81% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 93% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 7.4 min, t_R (minor) = 6.0 min. $[\alpha]_D^{18}$ = +55.3 (*c* = 0.93, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.77–7.75 (m, 2H), 7.56–7.29 (m, 8H), 5.57 (s, 1H), 4.93 (s, 1H), 3.61 (s, 3H), 2.31–2.13 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.0, 164.4, 150.7, 143.2, 131.5, 130.1, 129.3, 129.0, 128.5, 128.1, 124.8, 106.5, 102.9, 94.0, 51.4, 33.4, 8.3; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{21}O_3$ [M + H] 321.1491, found 321.1492.

Methyl (*S*)-4-methylene-2,5-diphenyl-5-propyl-4,5-dihydrofuran-3-carboxylate (3ka). A yellow oil was obtained in 61% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 94% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 95/5, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 7.8 min, t_R (minor) = 6.6 min. $[\alpha]_D^{22}$ = +99.1 (*c* = 0.40, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.75–7.73 (m, 2H), 7.57–7.30 (m, 8H), 5.51 (s, 1H), 4.94 (s, 1H), 3.61 (s, 3H), 2.26–2.08 (m, 2H), 1.43–1.21 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.8, 164.4, 151.1, 143.3, 131.5, 130.1, 129.3, 129.0, 128.6, 128.1, 124.8, 106.3, 102.8, 93.7, 51.5, 42.7, 17.1, 14.4; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{23}O_3$ [M + H] 335.1647, found 335.1648.

Methyl (*S*)-5-ethyl-5-methyl-4-methylene-2-phenyl-4,5-dihydrofuran-3-carboxylate (3la). A yellow oil was obtained in 75% yield after purification by column chromatography on silica gel (hexanes/ethyl acetate, 100/1). 22% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 98/2, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 9.5 min, t_R (minor) = 7.0 min. $[\alpha]_D^{19}$ = −16.7 (*c* = 1.10, CH_2Cl_2). ^1H NMR (400 MHz, DMSO-d_6) δ 7.64–7.62 (m, 2H), 7.52–7.43 (m, 3H), 5.45 (s, 1H), 4.72 (s, 1H), 3.61 (s, 3H), 1.83 (dq, *J* = 14.5, 7.3 Hz, 1H), 1.69 (dq, *J* = 14.5, 7.3 Hz, 1H), 1.42 (s, 3H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.2, 164.6, 151.5, 131.2, 130.6, 129.2, 128.3, 106.3, 100.2, 92.0, 51.2, 34.2, 27.4, 7.9; HRMS (ESI): *m*/*z* calcd for $C_{16}H_{18}O_3$ [M + H] 259.1334, found 259.1326.

Synthetic application of cycloadduct 3aa

To a solution of **3aa** (61.3 mg, 0.20 mmol) in 4 mL of anhydrous dichloromethane was added PCC (pyridinium chlorochromate 431.1 mg, 2.0 mmol), and the resulting solution was stirred at room temperature for 16 h. After the filtration of undissolved solids, the filtrate was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (hexanes/ethyl acetate, 20/1) to afford **4** (40.1 mg, 65% yield) as a colorless oil. 95% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/i-PrOH = 90/10, 0.8 mL min^{-1}, 254 nm, 40 °C): t_R (major) = 13.7 min, t_R (minor) = 11.6 min. $[\alpha]_D^{22}$ = +16.9 (*c* = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 2H), 7.64–7.33 (m, 8H), 3.82 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.0, 187.6, 163.3, 137.4, 133.5, 129.5, 128.8, 128.7, 128.5, 128.4, 124.6, 106.4, 90.7, 52.0, 24.8; HRMS (ESI): *m*/*z* calcd for $C_{19}H_{17}O_4$ [M + H] 309.1127, found 309.1127.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors are grateful to the National Natural Science Foundation of China (Grant No. 21572226 and 21772196) and Dalian Institute of Chemical Physics (DICP ZZBS201707) for financial support.

Notes and references

1 For reviews, see: (*a*) J. Tsuji and T. Mandai, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2589; (*b*) S. Ma, *Eur. J. Org. Chem.*, 2004, 1175; (*c*) L.-N. Guo, X.-H. Duan and Y.-M. Liang, *Acc. Chem. Res.*, 2011, **44**, 111; (*d*) M. Yoshida, *Chem. Pharm. Bull.*, 2012, **60**, 285; (*e*) M. Yoshida, *Heterocycles*, 2013, **87**, 1835; (*f*) J. Ye and S. Ma, *Acc. Chem. Res.*, 2014, **47**, 989; (*g*) X.-H. Hu, Z.-T. Liu, L. Shao and X.-P. Hu, *Synthesis*, 2015, **47**, 913. For recent examples, see: (*h*) M. Yoshida, S. Ohno and K. Shishido, *Chem. – Eur. J.*, 2012, **18**, 1604; (*i*) M. Yoshida, S. Ohno and K. Namba, *Angew. Chem., Int. Ed.*, 2013, **52**, 13597; (*j*) M. Yoshida and C. Sugimura, *Tetrahedron Lett.*, 2013, **54**, 2082; (*k*) M. Yoshida, T. Nakagawa, K. Kinoshita and K. Shishido, *J. Org. Chem.*, 2013, **78**, 1687; (*l*) T. D. Montgomery, A. E. Nibbs, Y. Zhu and V. H. Rawal, *Org. Lett.*, 2014, **16**, 3480; (*m*) R.-D. Gao, C. Liu, L.-X. Dai, W. Zhang and S.-L. You, *Org. Lett.*, 2014, **16**, 3919; (*n*) T. D. Montgomery and V. H. Rawal, *Org. Lett.*, 2016, **18**, 740.

2 (*a*) J. Tsuji, I. Watanabe, I. Minami and I. Shimizu, *J. Am. Chem. Soc.*, 1985, **107**, 2196; (*b*) I. Minami, M. Yuhara, I. Watanabe and J. Tsuji, *J. Organomet. Chem.*, 1987, **334**, 225.

3 (*a*) J.-R. Labrosse, P. Lhoste and D. Sinou, *Org. Lett.*, 2000, **2**, 527; (*b*) C. Damez, J.-R. Labrosse, P. Lhoste and D. Sinou, *Tetrahedron Lett.*, 2003, **44**, 557; (*c*) M. Yoshida, M. Higuchi and K. Shishido, *Org. Lett.*, 2009, **11**, 4752; (*d*) A. E. Nibbs,

T. D. Montgomery, Y. Zhu and V. H. Rawal, *J. Org. Chem.*, 2015, **80**, 4928.

4 For selected reviews, see: (*a*) *Quaternary Stereocentres: Challenges and Solutions for Organic Synthesis*, ed. J. Christoffers and A. Baro, Wiley-VCH, Weinheim, 2005; (*b*) B. M. Trost and C. Jiang, *Synthesis*, 2006, 369; (*c*) P. G. Cozzi, R. Hilgraf and N. Zimmermann, *Eur. J. Org. Chem.*, 2007, 5969; (*d*) I. Marek and G. Sklute, *Chem. Commun.*, 2007, 1683; (*e*) C. Hawner and A. Alexakis, *Chem. Commun.*, 2010, **46**, 7295; (*f*) J. P. Das and I. Marek, *Chem. Commun.*, 2011, **47**, 4593; (*g*) A. Y. Hong and B. M. Stoltz, *Eur. J. Org. Chem.*, 2013, 2745; (*h*) I. Marek, Y. Minko, M. Pasco, T. Mejuch, N. Gilboa, H. Chechik and J. P. Das, *J. Am. Chem. Soc.*, 2014, **136**, 2682; (*i*) K. W. Quasdorf and L. E. Overman, *Nature*, 2014, **516**, 181; (*j*) M. Buschleb, S. Dorich, S. Hanessian, D. Tao, K. B. Schenthal and L. E. Oerman, *Angew. Chem., Int. Ed.*, 2016, **55**, 4156.

5 Y. Zhou, F.-L. Zhu, Z.-T. Liu, X.-M. Zhou and X.-P. Hu, *Org. Lett.*, 2016, **18**, 2734.

6 (*a*) B. H. Lipshutz, *Chem. Rev.*, 1986, **86**, 795; (*b*) A. T. Merritt and S. B. Ley, *Nat. Prod. Rep.*, 1992, **9**, 243; (*c*) B. M. Fraga, *Nat. Prod. Rep.*, 1992, **9**, 217; (*d*) M. M. Faul and B. E. Huff, *Chem. Rev.*, 2000, **100**, 2407; (*e*) T. G. Kilroy, T. P. O'Sullivan and P. J. Guiry, *Eur. J. Org. Chem.*, 2005, 4929; (*f*) X.-L. Hou, Z. Yang, K.-S. Yeung and H. N. C. Wong, *Prog. Heterocycl. Chem.*, 2005, **17**, 142.

7 *Privileged Chiral Ligands and Catalysts*, ed. Q.-L. Zhou, Wiley-VCH, Weinheim, 2011.

8 B. M. Trost, M. R. Machacek and A. Aponick, *Acc. Chem. Res.*, 2006, **39**, 747.

9 G. Helmchen and A. Pfaltz, *Acc. Chem. Res.*, 2000, **33**, 336.

10 CCDC 1469918 ((*S*)-**3da**) contains the supplementary crystallographic data for this paper.

11 R. C. Larock, N. G. Berrios-Peña and C. A. Fried, *J. Org. Chem.*, 1991, **56**, 2615.

12 S. Murray and F. Hartiey, *Chem. Rev.*, 1981, **81**, 365.

13 For our recent works on asymmetric propargylic annulation, see: (*a*) C. Zhang, X.-H. Hu, Y.-H. Wang, Z. Zheng, J. Xu and X.-P. Hu, *J. Am. Chem. Soc.*, 2012, **134**, 9585; (*b*) F.-L. Zhu, Y.-H. Wang, D.-Y. Zhang, J. Xu and X.-P. Hu, *Angew. Chem., Int. Ed.*, 2014, **53**, 10223; (*c*) D.-Y. Zhang, L. Shao, J. Xu and X.-P. Hu, *ACS Catal.*, 2015, **5**, 5026; (*d*) Z.-T. Liu, Y.-H. Wang, F.-L. Zhu and X.-P. Hu, *Org. Lett.*, 2016, **18**, 1190; (*e*) L. Shao, Y.-H. Wang, D.-Y. Zhang, J. Xu and X.-P. Hu, *Angew. Chem., Int. Ed.*, 2016, **55**, 5014.

14 J.-B. Zhao and D. A. Clark, *Org. Lett.*, 2012, **14**, 1668.

15 C. N. EidJr and J. P. Konopelski, *Tetrahedron*, 1991, **47**, 975.

16 For selected reviews on chiral ferrocene ligands, see: (*a*) R. G. Arrayás, J. Adrio and J. C. Carretero, *Angew. Chem., Int. Ed.*, 2006, **45**, 7674; (*b*) *Chiral Ferrocenes in Asymmetric Catalysis*, ed. L.-X. Dai and X.-L. Hou, Wiley-VCH, Weinheim, 2010; (*c*) T. Noel and J. V. der Eycken, *Green Process. Synth.*, 2013, **2**, 297. For the synthesis of AmiFerroPhos analogues and key intermediates, see: (*d*) T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Konishi, K. Yamamoto and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1138; (*e*) X. Hu, H. Chen, H. Dai, X. Hu and Z. Zheng, *Tetrahedron: Asymmetry*, 2003, **14**, 2073; (*f*) X.-P. Hu, H.-L. Chen and Z. Zheng, *Adv. Synth. Catal.*, 2005, **347**, 541; (*g*) Y. Sheng, C. Zhang, Y.-H. Wang, Z. Cao, Z. Zheng and X.-P. Hu, *Tetrahedron Lett.*, 2013, **54**, 3669.