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Catalytic and highly enantioselective Friedel–Crafts type reactions of heteroaromatic compounds with trifluoropyruvate and glyoxylate by a dicationic palladium complex

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ABSTRACT

The highly enantioselective Friedel–Crafts alkylation of furan and thiophene derivatives with trifluoropyruvate, which have never provided the high level of asymmetric induction and yield until now, was achieved by using dicationic palladium complexes as Lewis acid catalysts. Moreover, glyoxylate instead of trifluoropyruvate as an electrophile led to complete change of regioselectivity with 2-trimethylsilylated furan, thiophene, and pyrrole derivatives to give the corresponding heteroarylated products in high yields and enantioselectivities. The respective products with trifluoropyruvate and glyoxylate could also be obtained via sequential catalytic reaction; intramolecular cyclization of alkynyldiols using cationic Au catalyst followed by Friedel–Crafts type reactions using dicationic Pd catalyst.

1. Introduction

Organofluorine compounds, which are extremely rare in Nature, have received considerable attention in the fields of pharmaceuticals, agrochemicals, and organic materials due to their unique chemical, biological, and physical properties.[1] In modern medicinal chemistry, trifluoromethyl-substituted compounds are widely employed, because trifluoromethyl (CF_3) groups can bring higher metabolic stability, increased lipophilicity, and stronger dipole moments to druglike compounds.[1] Therefore, a variety of synthetic methods to introduce the CF_3 group into organic compounds have been reported to readily produce the corresponding compounds, even in optically active forms. Optically active α-trifluoromethyl-substituted tertiary alcohols prepared via catalytic asymmetric synthesis have attracted widespread interest due to their unique biological activities, as typically shown in the anti-HIV agent (Efavirenz)[2] and nonsteroidal glucocorticoid receptor (GR) agonists.[3]

The Friedel–Crafts alkylation is one of the most fundamental carbon—carbon bond forming reactions in modern organic synthesis.[4] Chiral transition-metal catalysts as well as organocatalysts have been developed for the Friedel–Crafts alkylations of (hetero)aromatic compounds with carbonyl and imine compounds.[4] The Friedel–Crafts alkylations by treatment of trifluoropyruvate as a carbonyl compound, which is a versatile and commercially available reagent for the CF_3 building block method, can lead to optically active α-trifluoromethyl-substituted tertiary alcohols in high yields and enantioselectivities.[5–8] However, the high level of asymmetric induction is limited to indole, pyrrole, and activated aromatic derivatives as nucleophiles with higher reactivity,[5] as compared with furan and thiophene derivatives. Herein, we report the highly enantioselective Friedel–Crafts alkylations of furan and thiophene derivatives with trifluoropyruvate with high levels of asymmetric induction and yield using dicationic palladium complexes as Lewis acid catalysts (Scheme 1-1). We also report that the combination of 2-trimethylsilylated furan, thiophene, and pyrrole derivatives and glyoxylate leads to a complete change of regioselectivity to afford the heteroarylated products at the 2-position along with high asymmetric induction (Scheme 1-2).[9]

2. Results and discussion

Initially, the Friedel–Crafts type reaction of 2-trimethylsilyl furan **4a** as a nucleophile was examined in the presence of dicationic Pd-catalyst **1a** (5 mol %) prepared in situ from the corresponding dichloride complex and two equivalents of $AgSbF_6$[10] (Scheme 2). As shown in the literature,[9] the reactions with ethyl glyoxylate **3** proceeded regioselectively at the 2-position even at −40 °C to give product **6a** in excellent yield and enantioselectivity after the desilylation of siloxy product **6a′** (Scheme 2, Eq. 2). In sharp contrast to ethyl glyoxylate **3**, it was found that the reaction with ethyl trifluoropyruvate **2** provided the Friedel–Crafts product

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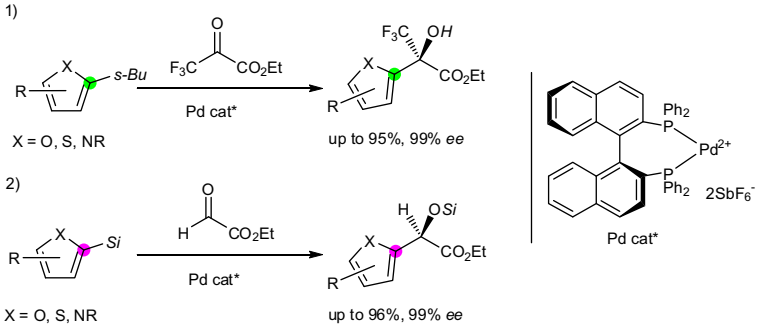
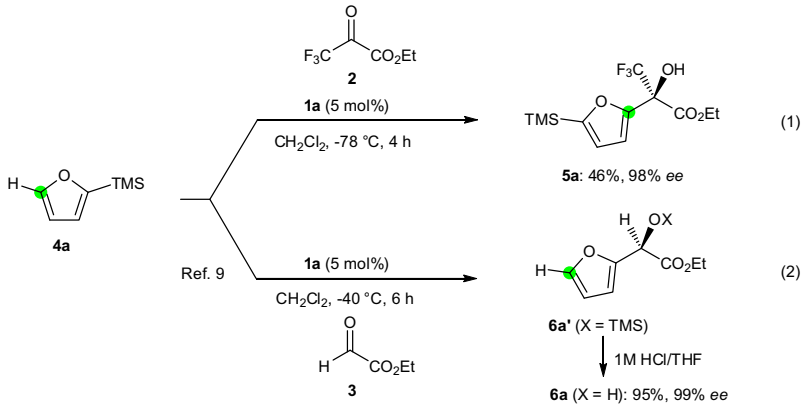


Scheme 1. Regio- and enantioselective Friedel–Crafts type reactions with dicationic palladium catalyst.



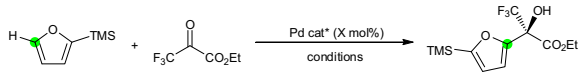
Scheme 2. Complete change of regioselectivity in reaction with 2-trimethylsilyl furan and carbonyl compounds.

5a at the 5-position with high levels of enantioselectivity but moderate yield, although **6a** and **6a′** were not observed at all (Scheme 2, Eq. 1). It is supposed that the complete change of regioselectivity originates from the steric repulsion between the trimethylsilyl and trifluoromethyl groups. The absolute configuration at the created carbon center of **5a** and **6a** was determined to be the same (*R*) by comparison with the specific rotation of the reported data.[5b,9]

Encouraged by the excellent enantioselectivity (98% ee) obtained even with simple mono-substituted furan, we attempted to optimize the Friedel–Crafts alkylation (Table 1). (*S*)-BINAP and (*S*)-SEGPHOS exhibited excellent enantioselectivities, while the yields were moderate (entries 1 and 2). The more sterically demanding ligand, (*S*)-DTBM-SEGPHOS led to an almost racemic product (entry 3). (*R*,*R*)-QuinoxP*[11] also gave high levels of enantioselectivity (entry 4). With the aim of enhancing the yield, we investigated the effect of the co-solvent. The use of toluene as a co-solvent did not increase the yield (entries 5 and 6). The combination of CH_2Cl_2 and the coordinating solvent Et_2O, which generally lowers the reactivity of Lewis acid catalysts, catalyzed the reaction to provide product **5a** in high yields, while maintaining excellent enantioselectivities (entries 7 and 8). Additionally, the yield and enantioselectivity could be maintained even with a lower catalyst loading of 1 and 2 mol % (90–93% yields, 99% ee) (entries 9 and 10). The use of THF or CH_3CN provided no products (entries 11 and 12).

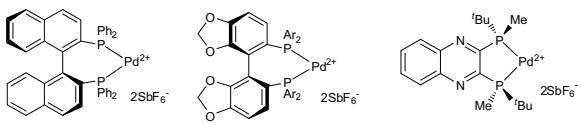
To extend the scope of the substrates, the Friedel–Crafts alkylation was further examined under the optimized reaction conditions in hand (Table 2). Non-substituted furan **4b** exhibited excellent results (95% and 99% ee), although it was hard to attain both high yield and enantioselectivity as in the previous reports.[5a,b] Furans **4c–e** bearing aliphatic and aromatic substituents at the

Table 1
Catalytic asymmetric Friedel–Crafts alkylation of 2-trimethylsilyl furan with trifluoropyruvate[a]



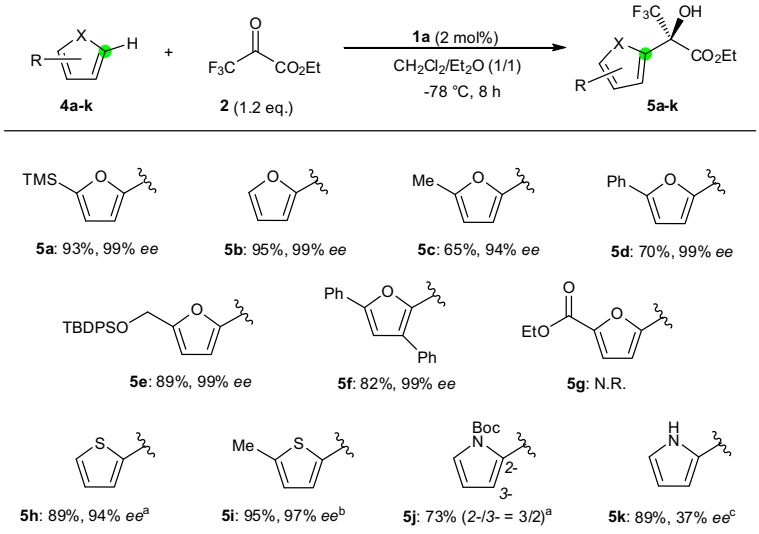
entry	Pd cat*	X	conditions	yield (%)[b]	*ee* (%)[c]
1	**1a**	5	CH_2Cl_2, -78 °C, 4 h	46	98
2	**1b**	5	CH_2Cl_2, -78 °C, 4 h	52	97
3	**1c**	5	CH_2Cl_2, -40 °C, 4 h	92	2
4	**1d**	5	CH_2Cl_2, -40 °C, 4 h	76	95[d]
5	**1a**	5	CH_2Cl_2/toluene (1/1), -78 °C, 8 h	48	94
6	**1d**	5	CH_2Cl_2/toluene (1/1), -78 °C, 8 h	55	96[d]
7	**1a**	5	CH_2Cl_2/Et_2O (1/1), -78 °C, 8 h	92	99
8	**1d**	5	CH_2Cl_2/Et_2O (1/1), -78 °C, 8 h	83	99[d]
9[e]	**1a**	2	CH_2Cl_2/Et_2O (1/1), -78 °C, 8 h	93	99
10[e]	**1a**	1	CH_2Cl_2/Et_2O (1/1), -40 °C, 8 h	90	99
11	**1a**	5	CH_2Cl_2/THF (1/1), -20 °C, 24 h	trace	-
12	**1a**	5	CH_2Cl_2/MeCN (1/1), -20 °C, 24 h	0	-

[a]3 equivalents of **2** were used. [b]Isolated yield. [c]Enantiopurity was determined by chiral HPLC anlysis.
[d]Opposite enantiomer (*S*) was obtained. [e]1.2 equivalents of **2** were used.



(*S*)-BINAP-Pd: **1a** (*S*)-SEGPHOS-Pd (Ar = Ph): **1b** (*S*)-DTBM-SEGPHOS-Pd: **1c** (Ar = 3,5-^{t}Bu$_2$-4-OMe-C$_6$H$_2$) (*R*,*R*)-QuinoxP*: **1d**

Table 2
Scope of substrates in the catalytic enantioselective Friedel–Crafts alkylation



[a]Conditions: 0 °C, 24 h. [b]Conditions: -40 °C, 24 h. [c]Conditions: -78 °C, 24 h.

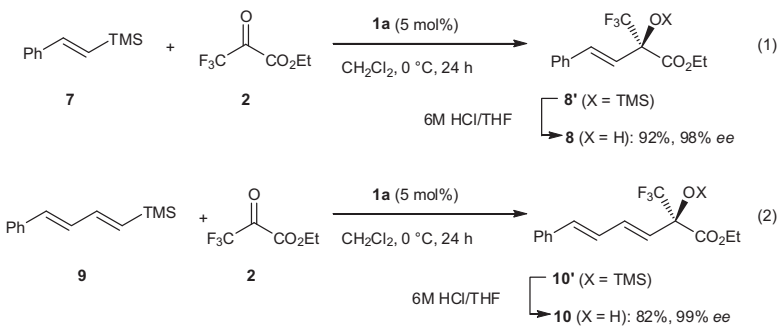
5-position also gave the good results, but **4c** decreased both the yield and enantioselectivity. Furan **4f** with a phenyl group at the 3,5-positions could be employed regardless of steric hindrance (82% and 99% ee). The reaction of furan **4g** with an electron-withdrawing ester group did not proceed even under the reflux conditions. Non- or methyl-substituted thiophenes **4h–i** were amenable to the highly enantioselective Friedel–Crafts reaction. The *tert*-butoxycarbonyl (Boc) group of pyrrole **4j** had a deteriorating effect on the regioselectivity and gave a mixture of a 3:2 ratio in the 2- and 3-positions. Treatment of N-unprotected pyrrole **4k** led to a single product at the 2-position but the enantioselectivity was low (89% and 37% ee).

In sharp contrast to a heteroaromatic system, the combination of vinylsilane **7** as a nucleophile and ethyl trifluoropyruvate **2** afforded the alkenylated product **8** in 92% yield and with 98% ee after desilylation, due to the smaller steric repulsion between **7** and the trifluoromethyl group compared to **4a** (Scheme 3, Eq. 1). Dienylsilane **9** also gave the dienylated product **10** in 82% and with 99% ee (Scheme 3, Eq. 2).

We also investigated the scope of the substrates in catalytic asymmetric Friedel–Crafts type reactions of 2-trimethylsilylated heteroaromatic compounds with ethyl glyoxylate **3** (Table 3). All substrates gave products **6** bonded onto the trimethylsilylated carbon with high enantioselectivity. Not only mono-substituted furan **4a**[12] but also 2,5-disubstituted **11b–d** provided with high to excellent enantioselectivities (94–99% ee). The reaction of 2,3,5-trisubstituted furans **11e** provided the product in high yield, but the enantioselectivity decreased with a deleterious effect on the steric hindrance (95% and 82% ee). 2,4,5-Trisubstituted furans **11f** facilitated the reactions to give excellent results (89% and 99% ee). Additionally, the reactions with mono- and disubstituted thiophenes **11g–j** also gave high yields and enantioselectivites (85–93% and 98–99% ee). The combination of Boc-pyrroles **11k–n** and **3** led to complete regioselectivity at the 2-position and high enantioselectivities (96–99% ee), while the regioisomers at the 2- and 3-positions were obtained in the Friedel–Crafts alkylation with Boc-pyrrole **4j** and **2**.

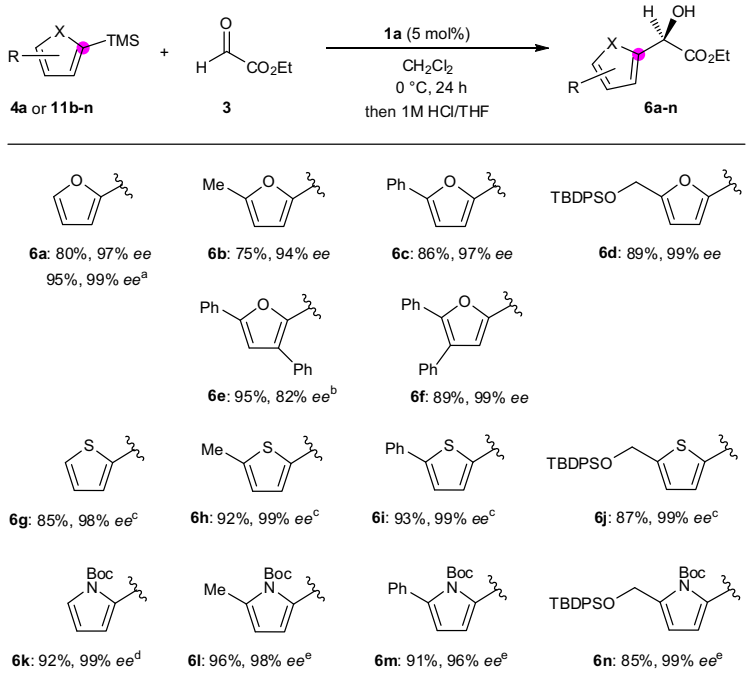
With these positive results for a wide range of 5-membered heteroaromatic nucleophiles, we utilized the heteroarylated products as chiral building blocks for the enantioselective synthesis of pyranone[13] (Scheme 4). Reduction[14] with **6a** followed by pivaloyl protection provided the corresponding alcohol **13** in good yield. Reaction of NBS with **13** in the presence of NaOAc and $NaHCO_3$ led to pyranone **14** via an Achmatowicz rearrangement.[15] Finally, Bz-protection of a hemiacetal proceeded to give the protected pyranone **15**[13b] in a 4:1 ratio of *trans* and *cis*-stereoisomer in 86% yield for two steps.

The palladium-catalyzed methodology was then expanded for a two-directional reaction (Scheme 5). Following the Friedel–Crafts alkylation of furan **4a** with trifluoropyruvate **2** in the presence of

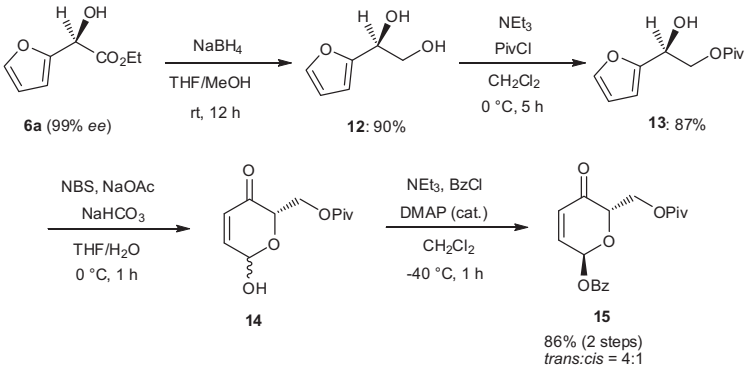


Scheme 3. Catalytic asymmetric alkenylation and dienylation.

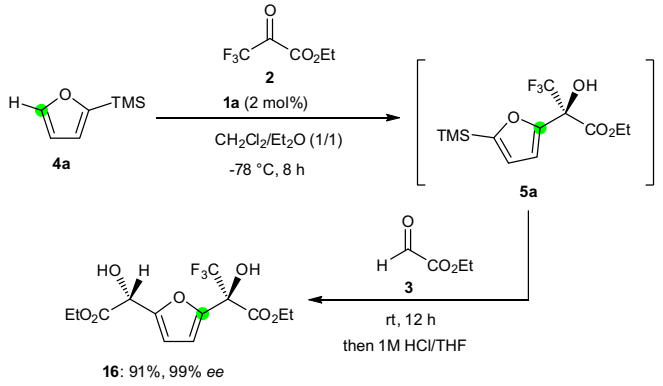
Table 3
Catalytic asymmetric Friedel–Crafts type reaction of 2-trimethylsilylated furan, thiophene, and pyrrole derivatives with ethyl glyoxylate



[a]Conditions: -40 °C, 6 h. [b]Conditions: -40 °C, 12 h. [c]Conditions: 0 °C, 12 h.
[d]Conditions: -78 °C, 5 h. [e]Conditions: -40 °C, 24 h.



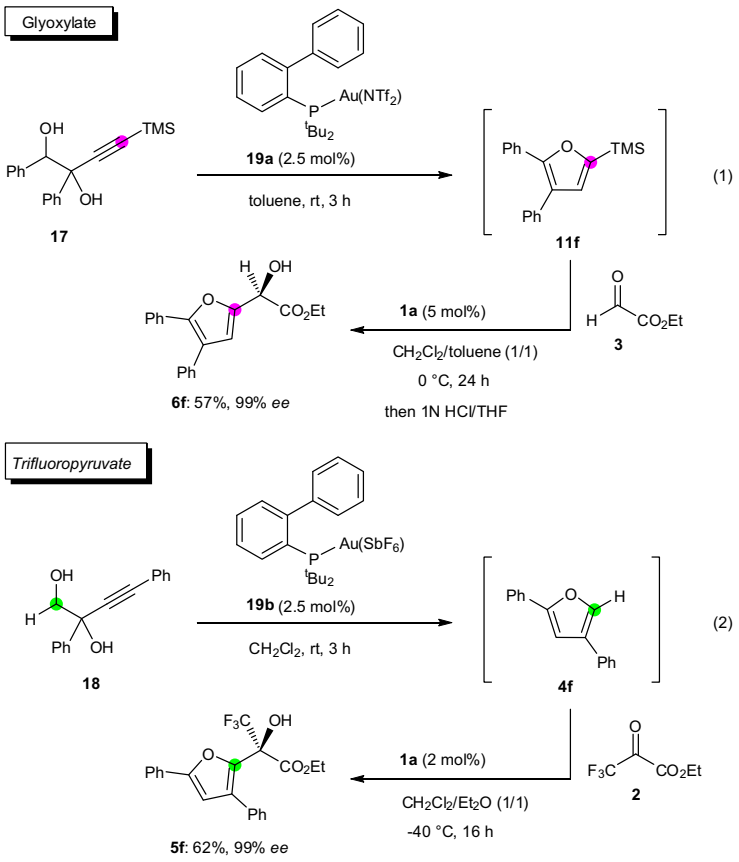
Scheme 4. Synthesis of a chiral pyranone from furan via an Achmatowicz rearrangement.



Scheme 5. Two-directional reaction of furan **4a** with ethyl trifluoropyruvate followed by ethyl glyoxylate.

1a (2 mol %) under the optimized reaction conditions, the reaction of glyoxylate **3** to intermediate **5a** led to the two-directional adduct **16** in 91% yield with 99% ee as a single diastereomer without the formation of the undesired *meso* type product.

We also attempted to transform alkynyldiols, which can be readily synthesized from α-hydroxy ketones, to α-hydroxy esters by a one-pot operation (Scheme 6). Alkynyldiol **17** in toluene was converted in situ to 2-trimethylsilylated furan **11f** via intramolecular cyclization by a cationic Au catalyst **19a**.[16,17] After the solution of ethyl glyoxylate **3** and dicationic Pd catalyst **1a** in dichloromethane was transferred to a solution of **17**, the Friedel–Crafts type reaction proceeded to produce the heteroarylated product **6f** in 57% yield and with 99% ee (Scheme 6, Eq. 1). In a similar manner to the glyoxylate system, intramolecular cyclization with alkynyldiol **18** by Au catalyst **19b** followed by Friedel–Crafts reaction with trifluoropyruvate **2** using Pd catalyst **1a** led to product **5f** in 62% yield and with 99% ee (Scheme 6, Eq. 2).



Scheme 6. Sequential catalytic intramolecular cyclization by an Au catalyst followed by Friedel–Crafts type reactions by a Pd catalyst.

3. Conclusion

In conclusion, we have reported on the highly enantioselective Friedel–Crafts reactions of furan and thiophene derivatives with trifluoropyruvate by using dicationic palladium complexes as Lewis acid catalysts. Moreover, the Friedel–Crafts type reaction of 2-trimethylsilylated furan, thiophene, and pyrrole derivatives with glyoxylate led to a complete change of regioselectivity to give the heteroarylated products in high yields and enantioselectivities. Additionally, the catalytic intramolecular cyclization of alkynyldiols by a cationic gold catalyst followed by Friedel–Crafts type reactions with trifluoropyruvate or glyoxylate by a dicationic palladium catalyst gave the corresponding products with high enantioselectivities. The development of novel and practical reactions to provide optically active α-fluoromethyl-substituted tertiary alcohols is currently ongoing in our laboratory.

4. Experimental

4.1. General

^{1}H, ^{13}C, and ^{19}F NMR spectra were measured on Bruker AV300M (300 MHz) spectrometers. The chemical shifts of ^{1}H NMR are expressed in parts per million relative to the singlet (δ = 7.26) for $CDCl_3$. The chemical shifts of ^{13}C NMR are expressed in parts per million relative to the central line of the triplet (δ = 77.0) for $CDCl_3$. The chemical shifts of ^{19}F NMR are expressed in parts per million relative to the singlet (δ = −63.24) for benzotrifluoride (BTF) as an internal standard. Optical rotations were measured on a JASCO P-1020. Mass spectra were measured on a JEOL JMS-T100CS (Accu-TOF) spectrometer. IR spectra were measured on a JASCO FT/IR-4200 spectrometer. High performance liquid chromatography (HPLC) was conducted on JASCO PU-980, LG-980-02, DG-980-50, MD-2010, and CO-966 instrument equipped with model UV-975 spectrometers as an ultra violet light. Dichloromethane (dehydrate), toluene (dehydrate), and diethyl ether (dehydrate) were purchased from Kanto Chemical Co., Inc. Ethyl trifluoropyruvate was provided by Central Glass Co., Ltd. Silver hexafluoroantimonate and ethyl glyoxylate polymer form (~50 wt % in toluene) were purchased from Aldrich. $PdCl_2$[(*S*)-BINAP] was synthesized according to the literature procedure.[18] Heteroarylsilanes **4a**,[19] **11b**,[20] **11c**,[21] **11g**,[22] **11h**,[23] **11k**,[24] vinylsilane **7**,[25] and dienylsilane **9**[26] were also synthesized according to the literature procedures.

4.2. General procedure for the catalytic asymmetric Friedel–Crafts reaction with trifluoropyruvate (Table 2)

To a solution of $PdCl_2$[(*S*)-BINAP] (3.2 mg, 0.004 mmol) in CH_2Cl_2 (1.0 mL) was added $AgSbF_6$ (3.0 mg, 0.0088 mmol) at room temperature under an argon atmosphere. After stirring for 30 min, Et_2O (1.0 mL), ethyl trifluoropyruvate **2** (32 μL, 0.24 mmol), and heteroaryl compounds **4** (0.2 mmol) were added at −78 °C. The reaction mixture was stirred at −78 °C for 8 h, and then loaded directly onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. Purification by a silica-gel chromatography (hexane/AcOEt = 9:1) gave the corresponding alcohol product **5**. The enantiomeric excess was determined by chiral HPLC analysis.

4.2.1. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(5-(trimethylsilyl)-furan-2-yl)propanoate 5a

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 9H), 1.34 (t, *J* = 7.2 Hz, 3H), 4.36–4.44 (m, 2H), 4.37 (s, 1H), 6.57 (d, *J* = 3.3 Hz, 1H), 6.60 (d,

J = 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.3, 13.9, 64.4, 75.3 (q, J_{C-F} = 31.5 Hz), 110.2, 120.2, 122.4 (q, J_{C-F} = 284 Hz), 149.8, 162.5, 167.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.2; FT-IR (KBr pellet, cm^{-1}) 3479, 2963, 1744, 1300, 1253, 1176, 1111, 1020, 932, 842; HRMS (ESI-TOF) calcd for $C_{12}H_{17}F_3NaO_4Si$ $[M+Na]^+$: 333.0746, found: 333.0749; $[\alpha]_D^{25}$ = −15.2 (c 1.3, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 11.8 min, t_R of major isomer 19.2 min. The absolute configuration was determined to be (R) in comparison with the specific rotation of the reported data.[5b]

4.2.2. (*R*)-Ethyl 3,3,3-trifluoro-2-(furan-2-yl)-2-hydroxypropanoate 5b

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, J = 7.2 Hz, 3H), 4.37–4.46 (m, 2H), 4.39 (s, 1H), 6.42 (d, J = 3.0 Hz, 1H), 6.62 (d, J = 3.0 Hz, 1H), 7.46 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 64.7, 75.3 (q, J_{C-F} = 30.5 Hz), 110.6, 110.7, 122.3 (q, J_{C-F} = 284 Hz), 143.9, 145.9, 167.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.4; FT-IR (KBr pellet, cm^{-1}) 3473, 2992, 2946, 1746, 1372, 1308, 1249, 1189, 1155, 1015, 968, 751; HRMS (ESI-TOF) calcd for $C_9H_9F_3NaO_4$ $[M+Na]^+$: 261.0351, found: 261.0363; $[\alpha]_D^{25}$ = −20.3 (c 0.80, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 32.2 min, t_R of major isomer 46.4 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.3. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(5-methylfuran-2-yl)propanoate 5c

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, J = 7.2 Hz, 3H), 2.29 (s, 3H), 4.35 (s, 1H), 4.35–4.46 (m, 2H), 5.99 (d, J = 3.0 Hz, 1H), 6.47 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 13.8, 64.5, 75.1 (q, J_{C-F} = 30.5 Hz), 106.7, 111.4, 122.4 (q, J_{C-F} = 284 Hz), 143.9, 153.9, 167.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.3; FT-IR (KBr pellet, cm^{-1}) 3474, 2988, 2929, 1749, 1371, 1305, 1261, 1178, 1113, 1021, 791; HRMS (ESI-TOF) calcd for $C_{10}H_{11}F_3NaO_4$ $[M+Na]^+$: 275.0507, found: 275.0495; $[\alpha]_D^{25}$ = −10.7 (c 0.7, $CHCl_3$), 94% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 20.7 min, t_R of major isomer 22.7 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.4. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(5-phenylfuran-2-yl)propanoate 5d

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, J = 7.2 Hz, 3H), 4.42–4.50 (m, 2H), 4.43 (s, 1H), 6.65 (d, J = 3.6 Hz, 1H), 6.69 (d, J = 3.6 Hz, 1H), 7.29–7.39 (m, 3H), 7.66 (d, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 64.7, 75.1 (q, J_{C-F} = 32.0 Hz), 105.7, 112.5, 122.4 (q, J_{C-F} = 284 Hz), 124.0, 128.1, 128.7, 130.0, 145.2, 155.3, 167.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.2; FT-IR (KBr pellet, cm^{-1}) 3475, 2986, 2933, 1745, 1486, 1371, 1304, 1179, 1115, 1017, 760, 691; HRMS (ESI-TOF) calcd for $C_{15}H_{13}F_3NaO_4$ $[M+Na]^+$: 337.0664, found: 337.0654; $[\alpha]_D^{25}$ = −35.2 (c 1.2, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 29.4 min, t_R of major isomer 42.4 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.5. (*R*)-Ethyl 2-(5-(((*tert*-butyldiphenylsilyl)oxy)methyl)-furan-2-yl)-3,3,3-trifluoro-2-hydroxypropanoate 5e

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H), 4.32 (s, 1H), 4.32–4.47 (m, 2H), 4.62 (s, 2H), 6.17 (d, J = 3.3 Hz, 1H), 6.52 (d, J = 3.3 Hz, 1H), 7.36–7.44 (m, 6H), 7.68 (d, J = 7.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 19.2, 26.6, 58.7, 64.6, 75.1 (q, J_{C-F} = 32.0 Hz), 108.2, 111.2, 122.3 (q, J_{C-F} = 284 Hz), 127.7, 129.8, 133.1, 135.6, 145.2, 155.6, 167.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.6; FT-IR (KBr pellet, cm^{-1}) 3479, 2957, 2932, 2858, 1745, 1428, 1308, 1178, 1111, 1019, 823, 703; HRMS (ESI-TOF) calcd for $C_{26}H_{29}F_3KO_5Si$ $[M+K]^+$: 545.1373, found: 545.1355; $[\alpha]_D^{25}$ = −19.0 (c 0.7, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 18.4 min, t_R of major isomer 20.1 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.6. (*R*)-Ethyl 2-(3,5-diphenylfuran-2-yl)-3,3,3-trifluoro-2-hydroxypropanoate 5f

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, J = 7.2 Hz, 3H), 3.61–3.67 (m, 1H), 4.01–4.07 (m, 1H), 4.52 (s, 1H), 6.76 (s, 1H), 7.34–7.47 (m, 8H), 7.75 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 64.4, 75.3 (q, J_{C-F} = 31.0 Hz), 108.3, 122.6 (q, J_{C-F} = 284 Hz), 124.1, 127.9, 128.2 (2C), 128.8, 129.1, 129.4, 129.7, 132.3, 140.6, 153.7, 167.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.3; FT-IR (KBr pellet, cm^{-1}) 3465, 3059, 2985, 1743, 1299, 1221, 1167, 1143, 916, 760, 700, 691, 673; HRMS (ESI-TOF) calcd for $C_{21}H_{17}F_3NaO_4$ $[M+Na]^+$: 413.0977, found: 413.0991; $[\alpha]_D^{25}$ = −23.3 (c 1.3, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of major isomer 33.9 min, t_R of minor isomer 55.7 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.7. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(thiophen-2-yl)-propanoate 5h

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 3H), 4.38–4.48 (m, 2H), 4.63 (s, 1H), 7.05 (dd, J = 5.1, 3.6 Hz, 1H), 7.36–7.39 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 64.8, 76.7 (q, J_{C-F} = 31.2 Hz), 122.4 (q, J_{C-F} = 284 Hz), 127.2, 127.3, 127.5, 135.9, 168.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0; FT-IR (KBr pellet, cm^{-1}) 3469, 2988, 2942, 1743, 1306, 1236, 1190, 1166, 1011, 856, 711; HRMS (ESI-TOF) calcd for $C_9H_9F_3NaO_3S$ $[M+Na]^+$: 277.0122, found: 277.0116; $[\alpha]_D^{25}$ = −14.5 (c 1.4, $CHCl_3$), 94% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 17.2 min, t_R of major isomer 22.8 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.8. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(5-methylthiophen-2-yl)propanoate 5i

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 3H), 2.47 (s, 3H), 4.38–4.47 (m, 2H), 4.55 (s, 1H), 6.69 (d, J = 3.6 Hz, 1H), 7.16 (d, J = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 16.1, 64.6, 76.6 (q, J_{C-F} = 32.4 Hz), 122.4 (q, J_{C-F} = 284 Hz), 125.5, 127.5, 132.9, 141.9, 168.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.0; FT-IR (KBr pellet, cm^{-1}) 3475, 2987, 2928, 1741, 1372, 1301, 1242, 1188, 1131, 1014, 805, 671; HRMS (ESI-TOF) calcd for $C_{10}H_{11}F_3NaO_3S$ $[M+Na]^+$: 291.0279, found: 291.0270; $[\alpha]_D^{25}$ = −10.6 (c 0.8, $CHCl_3$), 97% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 99:1, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 18.6 min, t_R of major isomer 23.0 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.2.9. *tert*-Butyl 2-(3-ethoxy-1,1,1-trifluoro-2-hydroxy-3-oxopropan-2-yl)-1*H*-pyrrole-1-carboxylate 5j

^{1}H NMR (300 MHz, $CDCl_3$) 2-substituted product: δ 1.28 (t, J = 7.2 Hz, 3H), 1.58 (s, 9H), 4.26–4.33 (m, 2H), 4.27 (s, 1H), 6.43 (m, 1H), 6.56 (m, 1H), 7.48 (t, J = 2.1 Hz, 1H); 3-substituted product: δ 1.38 (t, J = 7.2 Hz, 3H), 1.61 (s, 9H), 4.38–4.46 (m, 2H), 5.18 (s, 1H), 6.19 (t, J = 3.6 Hz, 1H), 7.22–7.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) a mixture of 2- and 3-substituted products: δ 13.84, 13.88, 27.8, 27.9, 63.2, 64.2, 75.3 (q, J_{C-F} = 31.5 Hz), 76.4 (q, J_{C-F} = 31.3 Hz), 84.3, 85.4, 110.4, 110.9, 116.2, 119.6, 120.2, 120.5, 122.9 (q, J_{C-F} = 284 Hz), 123.1 (q, J_{C-F} = 286 Hz), 148.3,

149.9, 167.4, 168.8; ^{19}F NMR (282 MHz, $CDCl_3$) 2-substituted product: δ −78.4, 3-substituted product: δ −74.0; FT-IR (KBr pellet, cm^{-1}) 3482, 2984, 2938, 1749, 1371, 1231, 1175, 1141, 978, 846, 772; HRMS (ESI-TOF) calcd for $C_{14}H_{18}F_3KNO_5$ [M+K]: 376.0774, found: 376.0764.

4.2.10. (*R*)-Ethyl 3,3,3-trifluoro-2-hydroxy-2-(1*H*-pyrrol-2-yl)-propanoate 5k

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (t, J = 7.2 Hz, 3H), 4.41–4.47 (m, 2H), 6.24 (d, J = 3.3 Hz, 1H), 6.48 (s, 1H), 6.83 (s, 1H), 8.79 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 64.6, 75.1 (q, J_{C-F} = 32.5 Hz), 108.9, 109.3, 118.8, 121.7, 122.5 (q, J_{C-F} = 284 Hz), 168.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.4; FT-IR (KBr pellet, cm^{-1}) 3435, 3367, 3123, 2991, 1738, 1265, 1226, 1182, 817, 746; HRMS (ESI-TOF) calcd for $C_9H_9F_3NO_3$ $[M-H]^-$: 236.0535, found: 236.0528; $[\alpha]_D^{25}$ = −8.6 (*c* 0.8, $CHCl_3$), 37% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 97:3, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 38.9 min, t_R of major isomer 45.7 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.3. Procedure for the catalytic asymmetric alkenylation and dienylation with trifluoropyruvate (Scheme 3)

To a solution of $PdCl_2$[(*S*)-BINAP] (8.0 mg, 0.01 mmol) in CH_2Cl_2 (2.0 mL) was added $AgSbF_6$ (7.6 mg, 0.022 mmol) at room temperature under an argon atmosphere. After stirring for 30 min, ethyl trifluoropyruvate **2** (53 μL, 0.4 mmol) and vinylsilane **8** or dienylsilane **9** (0.2 mmol) were added at 0 °C. The reaction mixture was stirred at 0 °C for 24 h, and then loaded directly onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. To a solution of the crude product in THF (1.0 mL) was added 6 M HCl (1.0 mL). After stirring for 4 h at room temperature, saturated aqueous $NaHCO_3$ (2.0 mL) was added, and then the mixture was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by a short silica-gel chromatography (hexane/AcOEt = 5:1) gave the corresponding alcohol products. The enantiomeric excess was determined by chiral HPLC analysis.

4.3.1. (*E*,*R*)-2-Hydroxy-4-phenyl-2-trifluoromethyl-but-3-enoic acid ethyl ester 8

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (t, J = 7.2 Hz, 3H), 4.14 (s, 1H), 4.30–4.51 (m, 2H), 6.35 (d, J = 15.9 Hz, 1H), 7.12 (d, J = 15.9 Hz, 1H), 7.30–7.38 (m, 3H), 7.43–7.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 64.4, 77.1 (q, J_{C-F} = 31.0 Hz), 119.3, 122.8 (q, J_{C-F} = 286 Hz), 127.1, 128.69, 128.72, 134.8, 135.2, 168.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −78.07; FT-IR (neat, cm^{-1}) 3484, 3063, 3024, 2988, 2932, 1741, 1650, 1448, 1368, 1305, 1166, 1043, 856; HRMS (ESI-TOF) calcd for $C_{13}H_{13}F_3NaO_3$ $[M+Na]^+$: 297.0715, found: 297.0710; $[\alpha]_D^{23}$ = −68.6 (*c* 1.6, $CHCl_3$), 98% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 97:3, flow rate 0.6 mL/min, 20 °C, detection UV 254 nm) t_R of major isomer 21.2 min, t_R of minor isomer 25.6 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.[10d]

4.3.2. (*R*,3*E*,5*E*)-Ethyl 2-hydroxy-6-phenyl-2-(trifluoromethyl)-hexa-3,5-dienoate 10

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, J = 7.2 Hz, 3H), 4.07 (s, 1H), 4.32–4.46 (m, 2H), 5.96 (d, J = 4.1 Hz, 1H), 6.67–7.00 (m, 3H), 7.23–7.43 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 64.3, 76.3 (q, J_{C-F} = 33.8 Hz), 122.7, 122.9 (q, J_{C-F} = 282 Hz), 126.6, 126.7, 128.2, 128.7, 134.9, 135.9, 136.6, 168.9; FT-IR (neat, cm^{-1}) 3490, 2919, 2845, 1731, 1634, 1589, 1453, 1311, 1283, 1011; HRMS (APCI-TOF) calcd for $C_{15}H_{15}NaF_3NaO_3$ $[M+Na]^+$: 323.0871, found: 323.0866; $[\alpha]_D^{25}$ = −33.7 (*c* 2.16, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 97:3, flow rate 0.6 mL/min, 20 °C, detection UV 254 nm) t_R of minor isomer 19.8 min, t_R of major isomer 27.1 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.[10d]

4.4. Synthesis of 2-trimethylsilylated heteroarylsilanes

General procedure A: To a solution of the corresponding heteroaryl compound (5.0 mmol) in THF (20 mL) was slowly added *n*-BuLi in hexane (1.6 M) (3.44 mL, 5.5 mmol) at −78 °C. The mixture was then allowed to warm up slowly to room temperature and stirred for 1 h, after which chlorotrimethylsilane (694 μL, 5.5 mmol) was added to the reaction mixture at −78 °C. The reaction mixture was allowed to warm slowly to room temperature, stirred for 4 h, and then quenched with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the corresponding heteroarylsilane products.

General procedure B: Freshly distilled diisopropylamine (0.94 mL, 6.6 mmol, 1.1 equiv) in THF (10 mL) was cooled to −78 °C. Next, *n*-BuLi in hexane (1.6 M) (4.12 mL, 6.6 mmol, 1.1 equiv) was slowly added to the THF solution at −78 °C, and the mixture was allowed to warm up to 0 °C. The mixture was stirred for 1 h at 0 °C before recooling to −78 °C. A solution of 1-*tert*-butyl pyrrole carboxylate derivative (6.0 mmol, 1.0 equiv) in THF (20 mL) was cooled to −78 °C. The LDA solution was added via cannula over 20 min at −78 °C. The mixture was stirred at −78 °C for a further 6 h before trimethylsilylchloride (1.0 mL, 7.2 mmol, 1.2 equiv) was added. The reaction mixture was allowed to warm up slowly to 0 °C and stirred for 10 h. The reaction mixture was poured into ice cold water. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the corresponding heteroarylsilane products.

4.4.1. *tert*-Butyldiphenyl((5-(trimethylsilyl)furan-2-yl)- methoxy)silane 11d

The title compound was synthesized from **4e** according to general procedure A (yield 60%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.29 (s, 9H), 1.10 (s, 9H), 4.73 (s, 2H), 6.18 (d, J = 3.3 Hz, 1H), 6.56 (d, J = 3.0 Hz, 1H), 7.38–7.70 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.6, 19.3, 26.7, 59.1, 107.2, 120.1, 127.6, 129.6, 133.5, 135.6, 158.2, 159.7; FT-IR (neat, cm^{-1}) 3074, 2962, 2936, 2857, 1476, 1427, 1250, 1115, 908, 833, 735; HRMS (ESI-TOF) calcd for $C_{24}H_{32}NaO_2Si_2$ $[M+Na]^+$: 431.1838, found: 431.1822.

4.4.2. (3,5-Diphenylfuran-2-yl)trimethylsilane 11e

The title compound was synthesized from **4f** according to general procedure A (yield 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.33 (s, 9H), 6.83 (s, 1H), 7.28–7.49 (m, 8H), 7.77 (d, J = 2.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.6, 114.0, 123.9, 126.3, 126.9, 127.4, 128.3, 128.5, 128.6, 131.5, 134.7, 152.4, 159.2; FT-IR (neat, cm^{-1}) 3059, 2957, 1604, 1502, 1446, 1269, 1246, 942, 840, 761, 698; HRMS (ESI-TOF) calcd for $C_{19}H_{21}OSi$ $[M+H]^+$: 293.1361, found: 293.1348.

4.4.3. Trimethyl(5-phenylthiophen-2-yl)silane 11i

The title compound was synthesized from 2-phenylthiophene according to general procedure A (yield 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.31 (s, 9H), 7.18 (d, J = 3.3 Hz, 1H), 7.23 (d, J = 4.8 Hz, 1H), 7.31–7.37 (m, 3H), 7.59 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.09, 124.4, 126.0, 127.4, 128.8, 134.4, 135.0,

140.1, 149.6; FT-IR (neat, cm^{-1}) 3059, 2954, 2894, 1596, 1483, 1430, 1246, 1078, 995, 840, 754, 690, 637; HRMS (ESI-TOF) calcd for $C_{13}H_{17}SSi$ $[M+H]^+$: 233.0820, found: 233.0824.

4.4.4. *tert*-Butyldiphenyl((5-(trimethylsilyl)thiophen-2-yl)-meth oxy)silane 11j

The title compound was synthesized from *tert*-butyldiphenyl(thiophen-2-ylmethoxy)silane according to general procedure A (yield 89%). ^1H NMR (300 MHz, $CDCl_3$) δ 0.33 (s, 9H), 1.10 (s, 9H), 4.92 (s, 2H), 6.92 (d, J = 3.3 Hz, 1H), 7.09 (d, J = 3.3 Hz, 1H), 7.37–7.44 (m, 6H), 7.71 (d, J = 7.5 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.01, 19.3, 26.8, 61.5, 125.1, 127.7, 129.7, 133.3, 133.6, 135.6, 139.3, 144.9; FT-IR (neat, cm^{-1}) 3074, 2954, 2857, 1743, 1472, 1427, 1371, 1250, 1111, 995, 836, 704; HRMS (ESI-TOF) calcd for $C_{24}H_{32}NaOSSi_2$ $[M+Na]^+$: 447.1610, found: 447.1606.

4.4.5. *tert*-Butyl 2-methyl-5-(trimethylsilyl)-1*H*-pyrrole-1-carboxylate 11l

The title compound was synthesized from *tert*-butyl 2-methyl-1*H*-pyrrole-1-carboxylate according to general procedure B (yield 52%). ^1H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 9H), 1.60 (s, 9H), 2.38 (s, 3H), 5.96 (d, J = 3.0 Hz, 1H), 6.34 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.06, 16.6, 27.9, 83.5, 112.9, 122.1, 134.8, 135.8, 150.8; FT-IR (neat, cm^{-1}) 2984, 2901, 1727, 1570, 1468, 1351, 1239, 1111, 916, 848, 735; HRMS (ESI-TOF) calcd for $C_{13}H_{24}NNaO_2Si$ $[M+Na]^+$: 254.1576, found: 254.1566.

4.4.6. *tert*-Butyl 2-phenyl-5-(trimethylsilyl)-1*H*-pyrrole-1-carboxylate 11m

The title compound was synthesized from *tert*-butyl 2-phenyl-1*H*-pyrrole-1-carboxylate according to general procedure B (yield 80%). ^1H NMR (300 MHz, $CDCl_3$) δ 0.33 (s, 9H), 1.21 (s, 9H), 6.24 (d, J = 3.3 Hz, 1H), 6.50 (d, J = 3.3 Hz, 1H), 7.30–7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.14, 27.2, 83.2, 114.2, 122.0, 126.9, 127.6, 128.9, 135.5, 137.1, 138.8, 150.8; FT-IR (neat, cm^{-1}) 3063, 2976, 2901, 1739, 1457, 1337, 1242, 1149, 1054, 998, 848, 757, 701; HRMS (ESI-TOF) calcd for $C_{18}H_{25}NNaO_2Si$ $[M+Na]^+$: 338.1552, found: 338.1552.

4.4.7. *tert*-Butyl 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)-5-(trimethylsilyl)-1*H*-pyrrole-1-carboxylate 11n

The title compound was synthesized from *tert*-butyl 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)-1*H*-pyrrole-1-carboxylate according to general procedure B (yield 27%). ^1H NMR (300 MHz, $CDCl_3$) δ 0.26 (s, 9H), 1.10 (s, 9H), 1.36 (s, 9H), 4.80 (s, 2H), 6.40 (d, J = 3.3 Hz, 1H), 6.44 (d, J = 3.3 Hz, 1H), 7.35–7.42 (m, 6H), 7.68 (d, J = 5.4 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.02, 19.3, 26.8, 27.7, 62.1, 83.8, 111.7, 122.4, 127.7, 129.7, 133.5, 135.6, 136.2, 138.5, 150.2; FT-IR (neat, cm^{-1}) 3048, 2958, 2857, 1731, 1476, 1341, 1262, 1167, 1111, 844, 739, 701; HRMS (ESI-TOF) calcd for $C_{29}H_{41}NNaO_3Si_2$ $[M+Na]^+$: 530.2522, found: 530.2518.

4.4.8. (4,5-Diphenylfuran-2-yl)trimethylsilane 11f

To a solution of the neutral Au chloride complex (3.9 mg, 0.005 mmol), which can lead to the corresponding cationic complex **19a**, and $AgNTf_2$ (1.9 mg, 0.005 mmol) in toluene (1.0 mL) was added diol **17** (62.0 mg, 0.20 mmol) at room temperature and the reaction mixture was stirred for 3 h. The reaction mixture was directly loaded onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. Purification by silica-gel column chromatography (hexane/AcOEt = 20:1) gave the product (85% yield). ^1H NMR (300 MHz, $CDCl_3$) δ 0.38 (s, 9H), 6.79 (s, 1H), 7.30–7.61 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.6, 114.0, 123.9, 126.3, 126.9, 127.4, 128.3, 128.5, 128.6, 131.5, 134.7, 152.4, 159.2; FT-IR (neat, cm^{-1}) 3059, 2957, 1604, 1502, 1446, 1269, 1246, 942, 840, 761, 698; HRMS (ESI-TOF) calcd for $C_{19}H_{21}OSi$ $[M+H]^+$: 293.1361, found: 293.1348.

4.5. General procedure for the catalytic asymmetric Friedel–Crafts type reaction with glyoxylate (Table 3)

To a solution of $PdCl_2$[(*S*)-BINAP] (8.0 mg, 0.01 mmol) in CH_2Cl_2 (2.0 mL) was added $AgSbF_6$ (7.6 mg, 0.022 mmol) at room temperature under an argon atmosphere. After stirring for 30 min, freshly distilled ethyl glyoxylate **3** (61.3 mg, 0.6 mmol) and 2-trimethylsilylated heteroaromatic compound **4a** or **11** (0.2 mmol) were added at −78 to 0 °C. The reaction mixture was stirred at −78 to 0 °C for 5–24 h, and then directly loaded onto a silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. To a solution of the crude product in THF (2.0 mL) was added 1 M HCl (1.0 mL). After stirring for 1 h at room temperature, the mixture was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (hexane/AcOEt = 4:1) gave the corresponding alcohol products **6**. The enantiomeric excess was determined by chiral HPLC analysis.

4.5.1. (*R*)-Ethyl 2-(furan-2-yl)-2-hydroxyacetate 6a[9]

^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 3H), 3.33 (d, J = 6.6 Hz, 1H), 4.25–4.33 (m, 2H), 5.17 (d, J = 5.7 Hz, 1H), 6.35–6.38 (m, 2H), 7.40 (dd, J = 1.8, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 62.4, 66.9, 108.5, 110.5, 142.9, 151.0, 171.5; FT-IR (KBr pellet, cm^{-1}) 3422, 2976, 2954, 2359, 1737, 1589, 1495, 1456, 1363, 1292, 1133, 1001, 892, 831; HRMS (APCI-TOF) calcd for $C_8H_{11}O_4$ $[M+H]^+$: 171.0657, found: 171.0651; $[\alpha]_D^{25}$ = −108.3 (*c* 0.80, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 11.2 min, t_R of major isomer 14.1 min. The absolute configuration was determined to be (*R*) in comparison with the specific rotation of the reported data.[9]

4.5.2. (*R*)-Ethyl 2-hydroxy-2-(5-methylfuran-2-yl)acetate 6b

^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 3H), 2.27 (s, 3H), 3.32 (br s, 1H), 4.25–4.33 (m, 2H), 5.11 (s, 1H), 5.93 (d, J = 2.4 Hz, 1H), 6.24 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 14.0, 62.4, 66.9, 106.4, 109.6, 149.1, 152.9, 171.7; FT-IR (KBr pellet, cm^{-1}) 3466, 2984, 2924, 1743, 1563, 1266, 1216, 1074, 1022, 791; HRMS (ESI-TOF) calcd for $C_9H_{13}O_4$ $[M+H]^+$: 185.0814, found: 185.0808; $[\alpha]_D^{25}$ = −42.3 (*c* 1.1, $CHCl_3$), 94% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 ml/min, 20 °C, detection UV 210 nm) t_R of minor isomer 12.5 min, t_R of major isomer 14.7 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.3. (*R*)-Ethyl 2-hydroxy-2-(5-phenylfuran-2-yl)acetate 6c

^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.41 (d, J = 7.8 Hz, 1H), 4.26–4.35 (m, 2H), 5.22 (d, J = 7.8 Hz, 1H), 6.45 (d, J = 3.3 Hz, 1H), 6.61 (d, J = 3.3 Hz, 1H), 7.24–7.40 (m, 3H), 7.65 (d, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, CDCl3) δ 14.0, 62.6, 67.0, 105.7, 110.7, 123.9, 127.7, 128.7, 130.4, 150.4, 154.4, 171.5; FT-IR (KBr pellet, cm^{-1}) 3462, 2981, 2927, 1739, 1484, 1448, 1263, 1211, 1074, 1023, 758, 695; HRMS (ESI-TOF) calcd for $C_{14}H_{14}NaO_4$ $[M+Na]^+$: 269.0790, found: 269.0803; $[\alpha]_D^{25}$ = −44.4 (*c* 0.86, $CHCl_3$), 97% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 15.9 min, t_R of major isomer 22.4 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.4. (*R*)-Ethyl 2-(5-(((*tert*-butyldiphenylsilyl)oxy)methyl)-furan-2-yl)-2-hydroxyacetate 6d

^{1}H NMR (300 MHz, CDCl3) δ 1.05 (s, 9H), 1.26 (t, J = 7.2 Hz, 3H), 3.30 (br s, 1H), 4.21–4.33 (m, 2H), 4.62 (s, 1H), 5.14 (s, 2H), 6.12 (d, J = 3.3 Hz, 1H), 6.29 (d, J = 3.3 Hz, 1H), 7.38–7.70 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 19.2, 26.7, 58.9, 62.5, 67.0, 108.2, 109.3, 127.6, 129.7, 133.2, 135.6, 150.3, 154.6, 171.5; FT-IR (KBr pellet, cm^{-1}) 3488, 2959, 2931, 2857, 1739, 1428, 1219, 1110, 1073, 1015, 823, 701, 610; HRMS (ESI-TOF) calcd for $C_{25}H_{30}NaO_5Si$ $[M+Na]^+$: 461.1760, found: 461.1772; $[\alpha]_D^{25} = -35.6$ (c 1.1, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 17.2 min, t_R of major isomer 20.6 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.5. (*R*)-Ethyl 2-(3,5-diphenylfuran-2-yl)-2-hydroxyacetate 6e

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, J = 7.2 Hz, 3H), 3.60 (d, J = 6.0 Hz, 1H), 4.25–4.33 (m, 2H), 5.35 (d, J = 6.0 Hz, 1H), 6.83 (s, 1H), 7.28–7.49 (m, 6H), 7.58 (d, J = 2.4 Hz, 2H), 7.59 (d, J = 2.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 62.6, 65.5, 106.8, 124.0, 127.6, 127.89, 127.94, 128.2, 128.7, 128.8, 130.1, 132.5, 145.5, 153.5, 171.6; FT-IR (KBr pellet, cm^{-1}) 3481, 3059, 2980, 1739, 1486, 1451, 1264, 1222, 1071, 758, 696; HRMS (ESI-TOF) calcd for $C_{20}H_{18}KO_4$ $[M+K]^+$: 361.0842, found: 361.0830; $[\alpha]_D^{25} = -19.5$ (c 1.05, $CHCl_3$), 82% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of major isomer 25.8 min, t_R of minor isomer 37.6 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.6. (*R*)-Ethyl 2-(4,5-diphenylfuran-2-yl)-2-hydroxyacetate 6f

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, J = 7.2 Hz, 3H), 3.40 (br s, 1H), 4.27–4.40 (m, 2H), 5.25 (s, 1H), 6.53 (s, 1H), 7.30–7.52 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 62.7, 67.0, 112.8, 123.0, 126.3, 127.3, 127.8, 128.4, 128.63, 128.64, 130.7, 133.9, 148.9, 149.8, 171.4; FT-IR (KBr pellet, cm^{-1}) 3390, 2920, 2853, 1743, 1671, 1446, 1252, 1188, 764, 697; HRMS (ESI-TOF) calcd for $C_{20}H_{18}NaO_4$ $[M+Na]^+$: 345.1103, found: 345.1116; $[\alpha]_D^{25} = -36.1$ (c 0.88, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 18.2 min, t_R of major isomer 26.2 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.7. (*R*)-Ethyl 2-hydroxy-2-(thiophen-2-yl)acetate 6g[9]

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.54 (d, J = 6.3 Hz, 1H), 4.21–4.36 (m, 2H), 5.40 (d, J = 6.3 Hz, 1H), 6.99 (dd, J = 5.1, 3.6 Hz 1H), 7.10 (d, J = 3.6 Hz, 1H), 7.28 (dd, J = 5.1, 1.2 Hz 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 62.6, 69.1, 125.3, 125.6, 126.9, 141.5, 172.6; FT-IR (neat, cm^{-1}) 3453, 3012, 2961, 2912, 1751, 1685, 1512, 1399, 1328, 1249, 1188, 1090, 1032, 918, 873; HRMS (APCI-TOF) calcd for $C_8H_{10}NaO_3S$ $[M+Na]^+$: 209.0248, found: 209.0250; $[\alpha]_D^{25} = -73.8$ (c 0.55, $CHCl_3$), 98% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 15.8 min, t_R of major isomer 17.7 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.8. (*R*)-Ethyl 2-hydroxy-2-(5-methylthiophen-2-yl)acetate 6h

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 2.45 (s, 3H), 3.42 (d, J = 6.6 Hz, 1H), 4.21–4.35 (m, 2H), 5.30 (d, J = 6.6 Hz, 1H), 6.62 (d, J = 3.6 Hz, 1H), 6.87 (d, J = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 15.3, 62.4, 69.1, 124.9, 125.4, 138.8, 140.5, 172.6; FT-IR (neat, cm^{-1}) 3480, 2982, 2923, 1735, 1448, 1367, 1267, 1213, 1072, 1022, 799; HRMS (ESI-TOF) calcd for $C_9H_{12}NaO_3S$ $[M+Na]^+$: 223.0405, found: 223.0394; $[\alpha]_D^{25} = -59.7$ (c 1.16, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 97:3, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 35.2 min, t_R of major isomer 39.6 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.9. (*R*)-Ethyl 2-hydroxy-2-(5-phenylthiophen-2-yl)acetate 6i

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (t, J = 7.2 Hz, 3H), 3.58 (d, J = 6.0 Hz, 1H), 4.30–4.35 (m, 2H), 5.41 (d, J = 4.8 Hz, 1H), 7.08 (d, J = 3.9 Hz, 1H), 7.20 (d, J = 3.6 Hz, 1H), 7.28–7.42 (m, 3H), 7.40 (dd, J = 7.2, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 62.7, 69.2, 122.8, 125.7, 126.3, 127.7, 128.9, 134.1, 140.6, 144.7, 172.6; FT-IR (KBr pellet, cm^{-1}) 3454, 2980, 2932, 1727, 1460, 1382, 1213, 1196, 1083, 1022, 751, 685; HRMS (ESI-TOF) calcd for $C_{14}H_{14}NaO_3S$ $[M+Na]^+$: 285.0561, found: 285.0573; $[\alpha]_D^{25} = -13.6$ (c 1.00, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 18.1 min, t_R of major isomer 22.0 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.10. (*R*)-Ethyl 2-(5-(((*tert*-butyldiphenylsilyl)oxy)- methyl)-thiophen-2-yl)-2-hydroxyacetate 6j

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H), 3.46 (d, J = 6.6 Hz, 1H), 4.26–4.34 (m, 2H), 4.83 (s, 2H), 5.36 (d, J = 6.3 Hz, 1H), 6.70 (d, J = 3.6 Hz, 1H), 6.92 (d, J = 3.6 Hz, 1H), 7.37–7.44 (m, 6H), 7.69 (d, J = 7.8 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 19.2, 26.7, 61.6, 62.5, 69.2, 123.3, 124.9, 127.7, 129.7, 133.1, 135.6, 140.3, 145.4, 172.5; FT-IR (KBr pellet, cm^{-1}) 3487, 3068, 2934, 2856, 1739, 1428, 1268, 1211, 1107, 1076, 826, 705; HRMS (ESI-TOF) calcd for $C_{25}H_{30}NaO_4SSi$ $[M+Na]^+$: 477.1532, found: 477.1544; $[\alpha]_D^{25} = -24.5$ (c 1.12, $CHCl_3$), 99% ee; HPLC (column, CHIRALCEL OD-H, Hexane/2-Propanol = 96:4, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 19.5 min, t_R of major isomer 43.2 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.11. (*R*)-*tert*-Butyl 2-(2-ethoxy-1-hydroxy-2-oxoethyl)-1*H*-pyrrole-1-carboxylate 6k[9]

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, J = 7.2 Hz, 3H), 1.57 (s, 9H), 4.04 (d, J = 8.1 Hz, 1H), 4.18–4.26 (m, 2H), 5.37 (d, J = 7.5 Hz, 1H), 6.12 (dd, J = 3.6, 3.3 Hz, 1H), 6.25 (dd, J = 3.3, 1.5 Hz, 1H), 7.38 (dd, J = 3.6, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 27.9, 61.6, 67.8, 84.8, 110.4, 115.5, 122.5, 131.7, 149.8, 171.6; FT-IR (neat, cm^{-1}) 3491, 3154, 2982, 2938, 1739, 1478, 1423, 1395, 1350, 1240, 1145, 1053, 950, 847; HRMS (ESI-TOF) calcd for $C_{13}H_{19}NNaO_5$ $[M+Na]^+$: 292.1161, found: 292.1160; $[\alpha]_D^{25} = -50.7$ (c 0.96, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 97:3, flow rate 1.0 mL/min, 20 °C, detection UV 254 nm) t_R of minor isomer 18.0 min, t_R of major isomer 22.6 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.12. (*R*)-*tert*-Butyl 2-(2-ethoxy-1-hydroxy-2-oxoethyl)-5-methyl-1*H*-pyrrole-1-carboxylate 6l

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3H), 1.58 (s, 9H), 4.05 (d, J = 9.3 Hz, 1H), 4.18–4.25 (m, 2H), 5.27 (d, J = 9.3 Hz, 1H), 5.87 (d, J = 3.3 Hz, 1H), 6.12 (dd, J = 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 16.7, 28.0, 61.6, 68.6, 85.0, 110.1, 114.3, 131.8, 132.9, 151.0, 171.9; FT-IR (neat, cm^{-1}) 3504, 2978, 2931, 1739, 1392, 1347, 1259, 1129, 1071, 850, 788; HRMS (ESI-TOF) calcd for $C_{14}H_{21}NNaO_5$ $[M+Na]^+$: 306.1317, found: 306.1317; $[\alpha]_D^{25} = -40.3$ (c 0.86, $CHCl_3$), 98% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 97:3, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 13.5 min, t_R of major

isomer 15.5 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.13. (*R*)-*tert*-Butyl 2-(2-ethoxy-1-hydroxy-2-oxoethyl)-5-phenyl-1*H*-pyrrole-1-carboxylate 6m

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 9H), 1.29 (t, J = 7.2 Hz, 3H), 4.17–4.30 (m, 3H), 5.37 (d, J = 9.0 Hz, 1H), 6.12 (d, J = 3.3 Hz, 1H), 6.27 (d, J = 3.3 Hz, 1H), 7.27–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 27.1, 61.7, 68.4, 84.8, 112.6, 113.9, 127.2, 127.7, 128.8, 133.0, 134.8, 136.7, 150.9, 171.7; FT-IR (neat, cm^{-1}) 3488, 2979, 2928, 1738, 1370, 1313, 1145, 848, 758, 700; HRMS (ESI-TOF) calcd for $C_{19}H_{23}KNO_5$ [M+K]$^+$: 384.1213, found: 384.1214; $[\alpha]_D^{25}$ = −15.2 (*c* 0.64, $CHCl_3$), 96% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 97:3, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 15.1 min, t_R of major isomer 17.4 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.5.14. (*R*)-*tert*-Butyl 2-(((*tert*-butyldiphenylsilyl)oxy)methyl)-5(2-ethoxy-1-hydroxy-2-oxoethyl)-1*H*-pyrrole-1-carboxylate 6n

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09 (s, 9H), 1.27 (t, J = 7.2 Hz, 3H), 4.03 (d, J = 9.0 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 4.75 (s, 2H), 5.31 (d, J = 9.0 Hz, 1H), 6.22 (d, J = 3.3 Hz, 1H), 6.28 (d, J = 3.3 Hz, 1H), 7.35–7.43 (m, 6H), 7.64–7.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 19.3, 26.8, 27.6, 61.6, 61.8, 68.5, 85.3, 110.2, 114.7, 127.7, 129.7 132.4, 133.3, 135.5, 136.3, 150.4, 171.7; FT-IR (neat, cm^{-1}) 3530, 3070, 2931, 2857, 1736, 1427, 1371, 1335, 1256, 1111, 704; HRMS (ESI-TOF) calcd for $C_{30}H_{39}NNaO_5Si$ [M+Na]$^+$: 560.2444, found: 560.2437; $[\alpha]_D^{25}$ = −25.6 (*c* 1.03, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-H, Hexane/2-Propanol = 97:3, flow rate 1.0 mL/min, 20 °C, detection UV 210 nm) t_R of minor isomer 12.4 min, t_R of major isomer 14.9 min. The absolute configuration was tentatively assigned by analogy of the specific rotation.

4.6. Synthesis of pyranone (Scheme 4)

To a solution of **6a** (851 mg, 5.0 mmol, 99% ee) in THF (30 mL) and MeOH (5.0 mL) at 0 °C was added $NaBH_4$ (605 mg, 16 mmol) under an argon atmosphere, and the reaction mixture was warmed up to room temperature. After stirring for 12 h, saturated aqueous NH_4Cl was added. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (hexane/AcOEt = 1:1) gave the diol **12** (90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.54 (br, 1H), 3.76–3.80 (br s, 2H), 3.95 (br, 1H), 4.75 (d, J = 5.9 Hz, 1H), 6.23 (dd, J = 4.0, 0.6 Hz, 1H), 6.27 (dd, J = 4.0, 1.8 Hz, 1H), 7.30 (dd, J = 1.8, 0.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.0, 68.3, 106.9, 110.3, 142.2, 153.6.

To a solution of diol **12** (256 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) were added triethylamine (554 μL, 4.0 mmol) and pivaloyl chloride (270 μL, 2.2 mmol) at −78 °C under an argon atmosphere. After the reaction mixture was allowed to slowly warm to 0 °C and stirred for 5 h, saturated aqueous $NaHCO_3$ was added. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (hexane/AcOEt = 5:1) gave the piv-protected product **13** (87% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (s, 9H), 3.07 (br, 1H), 4.30 (dd, J = 5.7, 4.8 Hz, 1H), 4.33 (dd, J = 5.7, 4.8 Hz, 1H), 4.90 (dd, J = 5.7, 5.7 Hz, 1H), 6.26–6.32 (m, 2H), 7.34 (dd, J = 1.8, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 38.8, 66.2, 66.3, 107.1, 110.2, 142.3, 153.2, 178.6.

An Achmatowicz rearrangement was attempted in this step according to O'Doherty's procedure.[13b] To a solution of **13** (212 mg, 1.0 mmol), $NaOAc{\cdot}3H_2O$ (149 mg, 1.1 mmol), and $NaHCO_3$ (167 mg 2.0 mmol) in THF (2.0 mL) and H_2O (1.0 mL) was added NBS (195 mg, 1.1 mmol) at 0 °C. After stirring for 1 h, the mixture was quenched by saturated aqueous $NaHCO_3$ and extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Crude **14** was obtained and used for the next step without further purification. *trans*-**14**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 4.41–4.49 (m, 2H), 4.73 (dd, J = 4.2, 4.2 Hz, 1H), 5.61 (d, J = 7.5 Hz, 1H), 6.08 (d, J = 10.9 Hz, 1H), 6.91 (dd, J = 10.9, 7.5 Hz, 1H). To a solution of **14** (without purification) and DMAP (cat.) in CH_2Cl_2 (5.0 mL) were added triethylamine (277 μL, 2.0 mmol) and benzoyl chloride (127 μL, 1.1 mmol) at −78 °C under an argon atmosphere. After stirring for 1 h at −40 °C, saturated aqueous $NaHCO_3$ was added. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (hexane/AcOEt = 5:1) gave pyranone **15**[13b] (86% yield, *trans*/*cis* 4:1, 2 steps). *trans*-**15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 4.50–4.55 (m, 2H), 4.82 (dd, J = 5.7, 5.7 Hz, 1H), 6.31 (d, J = 10.5 Hz, 1H), 6.83 (d, J = 6.6 Hz, 1H), 7.02 (dd, J = 10.5, 6.6 Hz, 1H), 7.41–7.50 (m, 2H), 7.61–7.67 (m, 1H), 8.01 (dd, J = 8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 38.7, 62.2, 74.5, 87.3, 128.6, 128.8, 128.9, 129.9, 133.8, 142.2, 164.8, 177.9, 192.3.; FT-IR (neat, cm^{-1}) 3433, 2951, 2911, 2833, 1721, 1600, 1438, 1361, 1203, 1003, 882; HRMS (APCI-TOF) calcd for $C_{13}H_{11}NaO_4$ [M+Na]$^+$: 254.0555, found: 254.0553; $[\alpha]_D^{25}$ = −82.1 (*c* 1.25, $CHCl_3$).

4.7. Two-directional reaction (Scheme 5)

To a solution of $PdCl_2$[(*S*)-BINAP] (3.2 mg, 0.004 mmol) in CH_2Cl_2 (1.0 mL) was added $AgSbF_6$ (3.0 mg, 0.0088 mmol) at room temperature under an argon atmosphere. After stirring for 30 min, Et_2O (1.0 mL), ethyl trifluoropyruvate **2**, (32 μL, 0.24 mmol) and **4a** (32 μL, 0.2 mmol) were added to the mixture at −78 °C. The reaction mixture was stirred at −78 °C for 8 h, and then freshly distilled ethyl glyoxylate (61.3 mg, 0.6 mmol) was added at −78 °C. After stirring for 12 h at room temperature, the reaction mixture was directly loaded onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. To a solution of the crude product in THF (2.0 mL) was added 1 M HCl (1.0 mL). After stirring for 1 h at room temperature, the mixture was extracted with ether. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by a silica-gel column chromatography (hexane/AcOEt = 2:1) gave the corresponding (*R*,*R*)-diol **16** (91% yield). The enantiomeric excess was determined by chiral HPLC analysis (99% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 3.48 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 4.37–4.46 (m, 2H), 4.44 (s, 1H), 5.16 (s, 1H), 6.39 (d, J = 3.3 Hz, 1H), 6.57 (d, J = 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.9, 62.7, 64.6, 66.7, 75.0 (q, J_{C-F} = 32 Hz), 109.4, 111.4, 122.1 (q, J_{C-F} = 284 Hz), 146.2, 152.4, 166.9, 171.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −76.4; FT-IR (KBr pellet, cm^{-1}) 3500, 3055, 2984, 1739, 1423, 1266, 1224, 1017, 896, 742, 704; HRMS (ESI-TOF) calcd for $C_{13}H_{15}F_3NaO_7$ [M+Na]$^+$: 363.0667, found: 363.0663; $[\alpha]_D^{25}$ = −52.3 (*c* 0.72, $CHCl_3$), 99% ee; HPLC (column, CHIRALPAK AD-3, Hexane/2-Propanol = 90:10, flow rate 0.6 mL/min, 20 °C, detection UV 210 nm) t_R of major isomer 35.2 min, t_R of minor isomer 41.6 min. The absolute configuration was tentatively assigned by analogy.

4.8. Sequential catalytic reactions (Scheme 6)

4.8.1. Sequential catalytic reaction with glyoxylate by Au and Pd catalysts

To a solution of the neutral Au chloride complex (3.9 mg, 0.005 mmol), which can lead to the corresponding cationic complex **19a**, and $AgNTf_2$ (1.9 mg, 0.005 mmol) in toluene (1.0 mL) was added diol **17** (62.0 mg, 0.20 mmol) at room temperature and the reaction mixture was stirred for 3 h. At the same time, a solution of $PdCl_2$[(*S*)-BINAP] (8.0 mg, 0.01 mmol), $AgSbF_6$ (7.6 mg, 0.022 mmol), and ethyl glyoxylate **3** (61.3 mg, 0.6 mmol) in CH_2Cl_2 (1.0 mL) was prepared according to the general procedure. The solution of glyoxylate **3** was then transferred to a solution of diol **17** with a syringe at −20 °C. After stirring for 24 h at 0 °C, the reaction mixture was loaded directly onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. To a solution of the crude product in THF (2.0 mL) was added 1 M HCl (1.0 mL). After stirring for 1 h at room temperature, the mixture was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (hexane/AcOEt = 5:1) gave the corresponding alcohol product **6f** (57% yield). The enantiomeric excess was determined by chiral HPLC analysis (99% ee).

4.8.2. Sequential catalytic reaction with trifluoropyruvate by Au and Pd catalysts

To a solution of the neutral Au chloride complex (3.9 mg, 0.005 mmol), which can lead to the corresponding cationic complex **19a**, and $AgSbF_6$ (1.7 mg, 0.005 mmol) in CH_2Cl_2 (0.5 mL) was added diol **18** (47.6 mg, 0.2 mmol) at room temperature and the reaction mixture was stirred for 1 h. At the same time, a solution of $PdCl_2$[(*S*)-BINAP] (8.0 mg, 0.010 mmol), $AgSbF_6$ (7.6 mg, 0.022 mmol), and trifluoropyruvate **2** (32 μL, 0.24 mmol) in CH_2Cl_2 (0.5 mL) was prepared according to the general procedure. Ether (1.0 mL) and a solution of trifluoropyruvate **2** were added to the solution of diol **18** via a syringe at −40 °C. After stirring for 16 h at −40 °C, the reaction mixture was loaded directly onto a short silica-gel column (hexane/AcOEt = 1:1) to remove the catalyst. Purification by a silica-gel chromatography (hexane/AcOEt = 5:1) gave the corresponding alcohol product **5f** (62% yield). The enantiomeric excess was determined by chiral HPLC analysis (99% ee).

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References

1. For reviews, see: (a) Mikami, K.; Itoh, Y.; Yamanaka, M. *Chem. Rev.* **2004**, *104*, 1; (b) Ma, J.-A.; Cahard, D. *J. Fluorine Chem.* **2007**, *128*, 975; (c) Shibata, N.; Mizuta, S.; Kawai, H. *Tetrahedron: Asymmetry* **2008**, *19*, 2633; (d) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1; (e) Nie, J.; Guo, H.-C.; Cahard, D.; Ma, J.-A. *Chem. Rev.* **2011**, *111*, 455.
2. Corbett, J. W.; Ko, S. S.; Rodgers, J. M.; Gearhart, L. A.; Magnus, N. A.; Bacheler, L. T.; Diamond, S.; Jeffrey, S.; Klabe, R. M.; Cordova, B. C.; Garber, S.; Logue, K.; Trainor, G. L.; Anderson, P. S.; Erickson-Viitanen, S. K. *J. Med. Chem.* **2000**, *43*, 2019.
3. (a) Schäcke, H.; Schottelius, A.; Döcke, W.-D.; Strehlke, P.; Jaroch, S.; Schmees, N.; Rehwinkel, H.; Hennekes, H.; Asadullah, K. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 227; (b) Betageri, R.; Zhang, Y.; Zindell, R. M.; Kuzmich, D.; Kirrane, T. M.; Bentzien, J.; Cardozo, M.; Capolino, A. J.; Fadra, T. N.; Nelson, R. M.; Paw, Z.; Shih, D.-T.; Shih, C.-K.; Zuvela-Jelaska, L.; Nabozny, G.; Thomson, D. S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4761; (c) Lee, T. W.; Proudfoot, J. R.; Thomson, D. S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 654; (d) Song, J. J.; Tan, Z.; Xu, J.; Reeves, J. T.; Yee, N. K.; Ramdas, R.; Gallou, F.; Kuzmich, K.; DeLattre, L.; Lee, H.; Feng, X.; Senanayake, C. H. *J. Org. Chem.* **2007**, *72*, 292; (e) Biggadike, K.; Bledsoe, R. K.; Coe, D. M.; Cooper, T. W. J.; House, D.; Iannone, M. A.; Macdonald, S. J. F.; Madauss, K. P.; McLay, I. M.; Shipley, T. J.; Taylor, S. J.; Tran, T. B.; Uings, I. J.; Weller, V.; Williams, S. P. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 18114; (f) Sumiyoshi, T.; Tojo, K.; Urabe, D.; Tobe, M. *Tetrahedron: Asymmetry* **2011**, *22*, 153.
4. For reviews, see: (a) Bandini, M.; Melloni, A.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 550; (b) Bandini, M.; Melloni, A.; Umani-Ronchi, A. *Synlett* **2005**, 1199; (c) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701; (d) Poulsen, T. B.; Jørgensen, K. A. *Chem. Rev.* **2008**, *108*, 2903; (e) You, S.-L.; Cai, Q.; Zeng, M. *Chem. Soc. Rev.* **2009**, *38*, 2190; (f) Zeng, M.; You, S.-L. *Synlett* **2010**, 1289; (g) Terrasson, V.; de Figueiredo, R. M.; Campagne, J. M. *Eur. J. Org. Chem.* **2010**, 2635; (h) Rueping, M.; Nachtsheim, B. J. *Beilstein J. Org. Chem.* **2010**, *6*.
5. For catalytic asymmetric Friedel–Crafts alkylation using trifluoropyruvate, see: (a) Gathergood, N.; Zhuang, W.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2000**, *122*, 12517; (b) Zhuang, W.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2001**, *66*, 1009; (c) Corma, A.; García, H.; Moussaif, A.; Sabater, M. J.; Zniber, R.; Redouane, A. *Chem. Commun.* **2002**, 1058; (d) Török, B.; Abid, M.; London, G.; Esquibel, J.; Török, M.; Mhadgut, S. C.; Yan, P.; Prakash, G. K. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 3086; (e) Lyle, M. P. A.; Draper, N. D.; Wilson, P. D. *Org. Lett.* **2005**, *7*, 901; (f) Zhuang, W.; Poulsen, T. B.; Jørgensen, K. A. *Org. Biomol. Chem.* **2005**, *3*, 3284; (g) Zhao, J.-L.; Liu, L.; Sui, Y.; Liu, Y.-L.; Wang, D.; Chen, Y.-J. *Org. Lett.* **2006**, *8*, 6127; (h) Dong, H.-M.; Lu, H.-H.; Lu, L.-Q.; Chen, C.-B.; Xiao, W.-J. *Adv. Synth. Catal.* **2007**, *349*, 1597; (i) Nakamura, S.; Hyodo, K.; Nakamura, Y.; Shibata, N. *Adv. Synth. Catal.* **2008**, *350*, 1443; (j) Zhao, J.-L.; Liu, L.; Gu, C.-L.; Wang, D.; Chen, Y.-J. *Tetrahedron Lett.* **2008**, *49*, 1476; (k) Nie, J.; Zhang, G.-W.; Wang, L.; Zheng, D.-H.; Zheng, Y.; Ma, J.-A. *Eur. J. Org. Chem.* **2009**, 3145; (l) Hui, Y.; Chen, W.; Wang, W.; Jiang, J.; Cai, Y.; Lin, L.; Liu, X.; Feng, X. *Adv. Synth. Catal.* **2010**, *352*, 3174; (m) Kashikura, W.; Itoh, J.; Mori, K.; Akiyama, T. *Chem. Asian J.* **2010**, *5*, 470; (n) Wolf, C.; Zhang, P. *Adv. Synth. Catal.* **2011**, *353*, 760; (o) Doherty, S.; Knight, J. G.; Mehdi-Zodeh, H. *Tetrahedron: Asymmetry* **2012**, *23*, 209.
6. Catalytic asymmetric Friedel–Crafts alkylation using fluoral, see: Ishii, A.; Soloshonok, V. A.; Mikami, K. *J. Org. Chem.* **2000**, *65*, 1597.
7. Catalytic asymmetric Friedel–Crafts alkylation using trifluoromethyl ketones, see: Blay, G.; Fernández, I.; Monleón, A.; Pedro, J. R.; Vila, C. *Org. Lett.* **2009**, *11*, 441.
8. Catalytic asymmetric Friedel–Crafts alkylation using glyoxylate, see: (a) Yuan, Y.; Wang, X.; Li, X.; Ding, K. *J. Org. Chem.* **2004**, *69*, 146; (b) Li, H.; Wang, Y.-Q.; Deng, L. *Org. Lett.* **2006**, *8*, 4063; (c) Majer, J.; Kwiatkowski, P.; Jurczak, J. *Org. Lett.* **2009**, *11*, 4636; For the use of perfluoroalkyl glyoxylate, see: (d) Tonoi, T.; Mikami, K. *Eur. J. Org. Chem.* **2007**, 1730.
9. Aikawa, K.; Hioki, Y.; Mikami, K. *Chem. Asian J.* **2010**, *5*, 2346.
10. (a) Aikawa, K.; Kainuma, S.; Hatano, M.; Mikami, K. *Tetrahedron Lett.* **2004**, *45*, 183; (b) Mikami, K.; Kawakami, Y.; Akiyama, K.; Aikawa, K. *J. Am. Chem. Soc.* **2007**, *129*, 12950; (c) Aikawa, K.; Hioki, Y.; Mikami, K. *J. Am. Chem. Soc.* **2009**, *131*, 13922; (d) Aikawa, K.; Hioki, Y.; Mikami, K. *Org. Lett.* **2010**, *12*, 5716; (e) Aikawa, K.; Mimura, S.; Numata, Y.; Mikami, K. *Eur. J. Org. Chem.* **2011**, 62; (f) Aikawa, K.; Honda, K.; Mimura, S.; Mikami, K. *Tetrahedron Lett.* **2011**, *52*, 6682; (g) Mikami, K.; Aikawa, K.; Aida, J. *Synlett* **2011**, 2719; (h) Aikawa, K.; Hioki, Y.; Shimizu, N.; Mikami, K. *J. Am. Chem. Soc.* **2011**, *133*, 20092.
11. QuinoxP*: Imamoto, T.; Sugita, K.; Yoshida, K. *J. Am. Chem. Soc.* **2005**, *127*, 11934.
12. See, Ref. 9; Even in the presence of 0.005 and 0.002 mol % Pd complex, the Friedel–Crafts type reaction with **4a** proceeded to give product **6a** in 75%, 98% ee and 46%, 98% ee, respectively (reaction conditions: toluene, 0 °C, 72 h).
13. (a) Harris, J. M.; Karanen, M. D.; O'Doherty, G. A. *J. Org. Chem.* **1999**, *64*, 2982; (b) Harris, J. M.; O'Doherty, G. A. *Tetrahedron Lett.* **2000**, *41*, 183; (c) Burke, M. D.; Berger, E. M.; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 14095; (d) Li, M.; Scott, J.; O'Doherty, G. A. *Tetrahedron Lett.* **2004**, *45*, 1005; (e) Babu, R. S.; Guppi, S. R.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 1605; (f) Cheng, K.; Kelly, A. R.; Kohn, R. A.; Dweck, J. F.; Walsh, P. J. *Org. Lett.* **2009**, *11*, 2703; (g) Nicolaou, K. C.; Aversa, R. J.; Jin, J.; Rivas, F. *J. Am. Chem. Soc.* **2010**, *132*, 6855; (h) Burke, C. P.; Swingle, M. R.; Honkanen, R. E.; Boger, D. L. *J. Org. Chem.* **2010**, *75*, 7505; (i) Noutsias, D.; Kouridaki, A.; Vassilikogiannakis, G. *Org. Lett.* **2011**, *13*, 1166.
14. Paolucci, C.; Rosini, G. *Tetrahedron: Asymmetry* **2007**, *18*, 2923.
15. (a) Achmatowicz, O.; Bukowski, P.; Szechner, B.; Zamojski, A. *Tetrahedron* **1971**, *27*, 1973; (b) Achmatowicz, O.; Bielski, R. *Carbohydr. Res.* **1977**, *55*, 165.
16. Egi, M.; Azechi, K.; Akai, S. *Org. Lett.* **2009**, *11*, 5002.
17. (a) Hashmi, A. S. K.; Sinha, P. *Adv. Synth. Catal.* **2004**, *346*, 432; (b) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164; (c) Zhang, J.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **2006**, *45*, 6704; (d) Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868; (e) Bew, S. P.; El-Taeb, G. M. M.; Jones, S.; Knight, D. W.; Tan, W.-F. *Eur. J. Org. Chem.* **2007**, 5759; (f) Xiao, Y.; Zhang, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1903; (g) Kramer, S.; Madsen, J. L. H.; Rottländer, M.; Skrydstrup, T. *Org. Lett.* **2010**, *12*, 2758; (h) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766; (i) Kramer, S.; Skrydstrup, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 4681.

18. (a) Ozawa, F.; Kubo, A.; Matsumoto, Y.; Hayashi, T.; Nishioka, E.; Yanagi, K.; Moriguchi, K. *Organometallics* **1988**, *7*, 1761; (b) Aikawa, K.; Miyazaki, Y.; Mikami, K. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 201.
19. Tamsyn, M.; Nikoletta, S.; Manolis, S.; Maria, T.; Georgios, V. *Org. Lett.* **2005**, *7*, 2357.
20. Yu, Y. P.; Liepin'sh, E. E.; Bruveris, Z. P.; Lukevits, E. *Chem. Heterocycl. Compd.* **1990**, *26*, 495.
21. Guillard, J.; Lamazzi, C.; Meth-Cohn, O.; Rees, C. W.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1304.
22. Albertin, L.; Bertarelli, C.; Capelli, C. S.; Gallazzi, C. M.; Meille, V. S. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1752.
23. Giancarlo, A.; Colin, E.; John, G. S. *J. Organomet. Chem.* **1981**, *204*, 153.
24. Elizabeth, M. B.; Matthew, J. G.; Richard, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 3004.
25. Jeffery, T. *Tetrahedron Lett.* **1999**, *40*, 1673.
26. Lee, B. S.; Gil, J. M.; Oh, D. Y. *Tetrahedron Lett.* **2001**, *42*, 2345.