JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

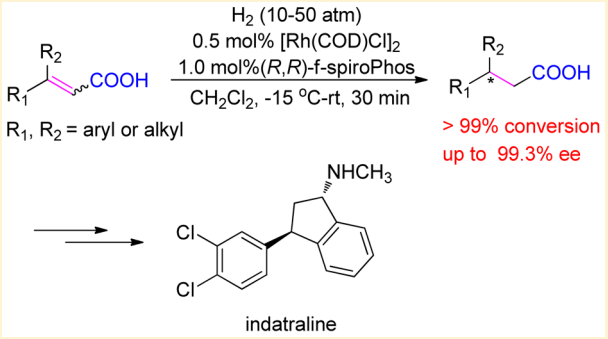
Enantioselective Hydrogenation of β,β-Disubstituted Unsaturated Carboxylic Acids under Base-Free Conditions

Qiaozhi Yan, Duanyang Kong, Wei Zhao, Guofu Zi, and Guohua Hou*

Key Laboratory of Radiopharmaceuticals, College of Chemistry, Beijing Normal University, Beijing 100875, China

Supporting Information

ABSTRACT: An additive-free enantioselective hydrogenation of β,β-disubstituted unsaturated carboxylic acids catalyzed by the Rh−(*R*,*R*)-f-spiroPhos complex has been developed. Under mild conditions, a wide scope of β,β-disubstituted unsaturated carboxylic acids were hydrogenated to the corresponding chiral carboxylic acids with excellent enantioselectivities (up to 99.3% ee). This methodology was also successfully applied to the synthesis of the pharmaceutical molecule indatraline.



INTRODUCTION

Optically active β,β-disubstituted propionic acids are important structural moieties which widely exist in many biologically active compounds and pharmaceuticals, including Lyrica,[1] baclofen,[2] ar-turmerone,[3] indatraline,[4] R-106578, and natural products, such as cherylline[5] and heliannuols[6] (Figure 1). Accordingly, the development of methodologies for the enantioselective synthesis of chiral β,β-disubstituted propionic acids is highly desirable and has attracted a lot of attention from synthetic chemists.

Up to now, there have been many methods for approaching chiral β,β-disubstituted propionic acids,[7] such as Cu-, Co-, or Rh-catalyzed asymmetric 1,4-reduction of β,β-disubstituted unsaturated acrylates or nitriles using moisture-sensitive hydrosilane derivatives or borohydride reagents,[8] and asymmetric 1,4-additions of nucleophilic reagents to α,β-unsaturated carbonyl compounds catalyzed by Pd, Rh, or Cu complexes.[9] Among these, the direct enantioselective hydrogenation of β,β-disubstituted unsaturated acrylic acids is the most straightforward and efficient method for chiral β,β-disubstituted propionic acids in spite of the asymmetric hydrogenation of β-arylbut-3-enoic acids and β,β-disubstituted unsaturated acrylates.[10] However, contrasted with the asymmetric hydrogenation of α-substituted unsaturated acrylic acids,[10i,11] the enantioselective hydrogenation of β,β-disubstituted unsaturated acrylic acids still remains a challenge and is less explored. Rh catalysts with chiral phosphine ligands and the Ru−Binap complex were developed for asymmetric hydrogenations of β,β-disubstituted unsaturated acrylic acids with good enantioselectivity.[12] A Pd catalyst with cinchona alkaloid could also be used in the hydrogenation of β-CF_3-substituted acrylic acids, but poor enantioselectivities were obtained.[13] Recently, Ding and co-workers developed a Rh catalyst containing a chiral monodentate phosphine (SPO) ligand and an achiral Ph_3P ligand, which exhibited excellent enantioselectivity for the asymmetric hydrogenation of β,β-diarylacrylic acids and β-CF_3-substituted acrylic acids.[11f,14] Whereas in most of the reported cases of the asymmetric hydrogenation of unsaturated acrylic acids, a base additive (NEt_3 or morpholine) was required to achieve high efficiency and enantioselectivity.[11−14] Accordingly, the development of more efficient catalysts for the asymmetric hydrogenation of β,β-disubstituted acrylic acids is highly desirable. Inspired by the excellent performance of the chiral diphosphine ligand f-spiroPhos in Rh- or Ir-catalyzed asymmetric hydrogenations of α,β-unsaturated nitriles and nitroolefins,[15] we evaluated this ligand for the hydrogenation of β,β-disubstituted unsaturated acrylic acids, including sterically similar β,β-diaryl unsaturated acrylic acids, and found that its Rh complex showed excellent enantioselectivities (up to 99.3% ee) under mild reaction conditions without any additive (Scheme 1).

RESULTS AND DISCUSSION

To optimize the reaction conditions, (*E*)-3-phenylbut-2-enoic acid (**1a**) was used as the model substrate, and the hydrogenation was initially performed without any additive using the complex of (*R*,*R*)-f-spiroPhos and $[Rh(COD)Cl]_2$ or $[Ir(COD)Cl]_2$ as the catalyst under 50 atm of H_2 in CH_2Cl_2 at room temperature for 6 h. To our delight, the Rh−(*R*,*R*)-f-spiroPhos catalyst provided a full conversion and high enantioselectivity, 93% ee (Table 1, entry 1), which was attributed to the electron-rich property and rigidity of the ligand, whereas poor results, 26% conversion and 35% ee, were observed using the $[Ir(COD)Cl]_2$ precursor. Subsequently, some other chiral phosphorus ligands illustrated in Figure 2 were investigated, and the results revealed that most of them were not efficient for this transformation, giving either low conversions or poor enantioselectivities (entries 2−5), except for

Received: January 4, 2016
Published: February 5, 2016

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

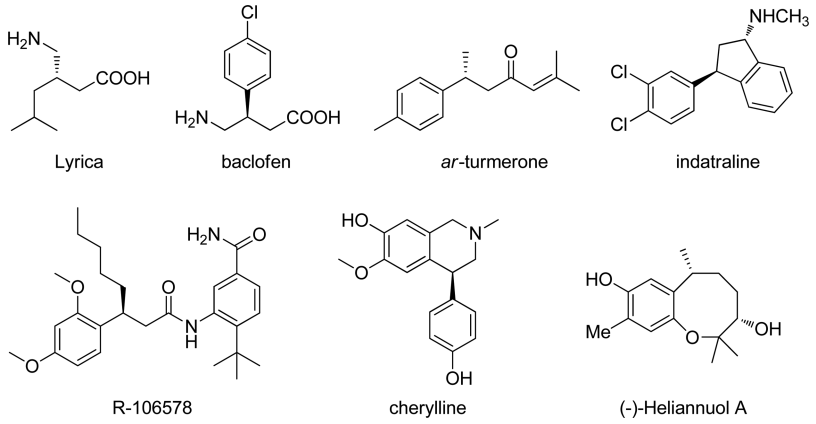


Figure 1. Key structural elements in chiral pharmaceuticals and natural products.

Scheme 1

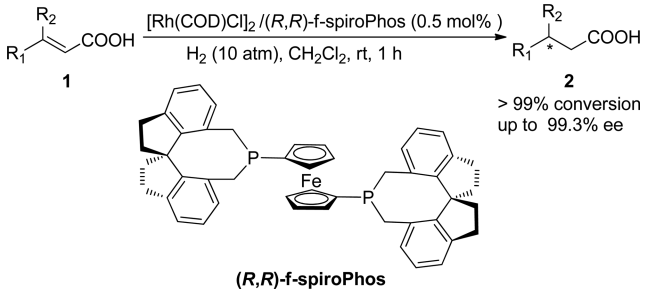
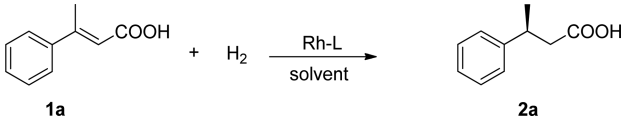


Table 1. Asymmetric Hydrogenation of (*E*)-3-Phenylbut-2-enoic Acid (1a), Optimizing the Reaction Conditions[a]



entry	ligand	solvent	conversion[b] (%)	ee[c] (%)
1	(*R*,*R*)-f-spiroPhos	CH_2Cl_2	>99	93
2	(*S*)-Binap	CH_2Cl_2	2	42
3	(*S*,*R*)-DuanPhos	CH_2Cl_2	2	14
4	(*R*)-JosiPhos-1	CH_2Cl_2	37	15
5	(*S*)-MonoPhos	CH_2Cl_2	0.4	ND
6	(*S*,*S*)-f-Binaphane	CH_2Cl_2	79	86
7	(*R*,*R*)-f-spiroPhos	THF	98	60
8	(*R*,*R*)-f-spiroPhos	MeOH	>99	86
9	(*R*,*R*)-f-spiroPhos	toluene	97	91
10	(*R*,*R*)-f-spiroPhos	DME	95	88
11	(*R*,*R*)-f-spiroPhos	dioxane	95	94
12[d]	(*R*,*R*)-f-spiroPhos	CH_2Cl_2	>99	94
13[e]	(*R*,*R*)-f-spiroPhos	CH_2Cl_2	>99	97

[a]Reaction conditions: $[Rh(COD)Cl]_2$:diphosphine (monophosphine):substrate = 0.5:1.1 (2.1):100, 50 atm of H_2, 6 h, rt. [b]Determined by chiral GC. [c]Determined by chiral GC using a Supelco γ-Dex 225 column (30 m × 0.25 mm × 0.25 μm). [d]Reaction conditions: 10 atm of H_2, 1 h. [e]Reaction conditions: 10 atm of H_2, −15 °C, 6 h.

(*S*,*S*)-f-Binaphane, which provided a good conversion and enantioselectivty (entry 6). Good enantioselectivities and almost full conversions could be achieved in most of the solvents, such as THF, MeOH, toluene, and DME (entries 7−10). In addition to CH_2Cl_2, 1,4-dioxane could also afford a similar enantioselectivity despite incomplete conversion (entry 11). Moreover, decreasing the hydrogen pressure from 50 to 10 atm, this transformation

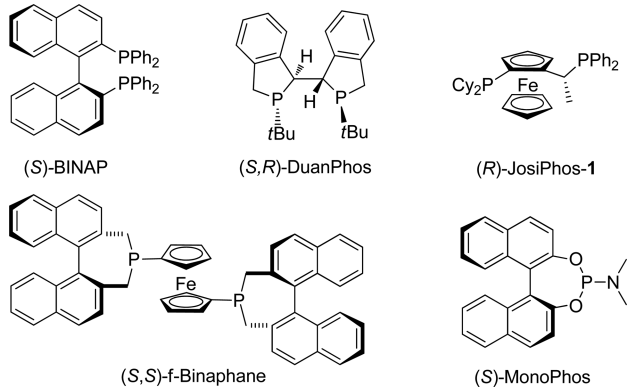


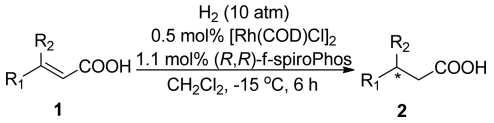
Figure 2. Phosphine ligands tested for the hydrogenation of (*E*)-3-phenylbut-2-enoic acid (**1a**).

could still be completed in 1 h with a slightly higher enantioselectivity (entry 12). A lower reaction temperature resulted in a much higher ee value, 97%, in spite of the little longer time required for the full conversion (entry 13). Finally, we evaluated the effect of an added base (5 mol % NEt_3) on the catalyst performance under the optimized conditions; a moderate enantioselectivity and incomplete conversion (72% ee, 27% conversion) were obtained. The asymmetric hydrogenation of the corresponding (*E*)-methyl 3-phenylbut-2-enoate was also investigated, but a very poor reactivity (<1% conversion) was observed. These results revealed that this catalyst should be more suitable for the free acids and has good tolerance for acidic conditions.

Encouraged by the promising results obtained in the hydrogenation of substrate **1a**, a series of β,β-disubstituted unsaturated carboxylic acids **1b**−**1t** were successfully hydrogenated under optimized reaction conditions to provide the corresponding chiral acids with excellent ee values, up to 99.3% ee, and complete conversions, regardless of the position or electronic properties of the substituents on the phenyl ring (Table 2). For example, substrates bearing an electron-withdrawing substituent, F, Cl, Br, or NO_2, or an electron-donating substituent, Me or MeO, at the *para*-, *meta*-, or *ortho*-position of the phenyl group were hydrogenated with excellent enatioselectivities, up to 99.3% ee (entries 1−11). The substrate **1j** with a methyl group at the *ortho*-position of the phenyl ring provided **2j** with the highest enantioselectivity, 99.3% ee, presumably due to the steric hindrance. A similar effect was also observed for substrates **1k** with an *o*-nitro group and **1l** with

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

Table 2. Rh-Catalyzed Asymmetric Hydrogenation of *β,β*-Disubstituted Unsaturated Carboxylic Acids 1[a]



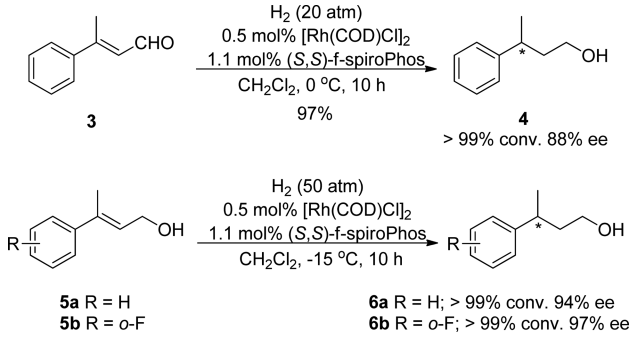
entry	R_1	R_2	product	conversion[b] (%)	ee[c] (%)
1	(*E*)-C_6H_5 (**1a**)	Me	**2a**	>99	97 (*S*)
2	(*E*)-4-ClC_6H_4 (**1b**)	Me	**2b**	>99	95 (+)
3	(*E*)-4-$NO_2C_6H_4$ (**1c**)	Me	**2c**	>99	97 (+)
4	(*E*)-3-FC_6H_4 (**1d**)	Me	**2d**	>99	96 (+)
5	(*E*)-3-BrC_6H_4 (**1e**)	Me	**2e**	>99	97 (+)
6	(*E*)-3-$NO_2C_6H_4$ (**1f**)	Me	**2f**	>99	97 (+)
7	(*E*)-3-$MeOC_6H_4$ (**1g**)	Me	**2g**	>99	91 (+)
8	(*E*)-2-FC_6H_4 (**1h**)	Me	**2h**	>99	96 (+)
9	(*E*)-2-ClC_6H_4 (**1i**)	Me	**2i**	>99	93 (−)
10	(*E*)-2-MeC_6H_4 (**1j**)	Me	**2j**	>99	99.3 (+)
11[d]	(*E*)-2-$NO_2C_6H_4$ (**1k**)	Me	**2k**	>99	97 (−)
12[d]	(*E*)-1-naphthyl (**1l**)	Me	**2l**	>99	98 (*S*)
13[d]	(*E*)-C_6H_5 (**1m**)	Et	**2m**	>99	94 (*S*)
14[d]	(*E*)-C_6H_5 (**1n**)	^{i}Pr	**2n**	>99	97 (*S*)
15[d]	(*E*)-C_6H_5 (**1o**)	C_6H_{11}	**2o**	>99	98 (*S*)
16[d]	(*E*)-$C_6H_5(CH_2)_2$ (**1p**)	Me	**2p**	>99	66 (*R*)
17[d]	(*E*)-C_6H_{11} (**1q**)	Me	**2q**	91	73 (−)
18[e]	(*Z*)-3,4-ClC_6H_4 (**1r**)	C_6H_5	**2r**	>99	97 (*S*)
19[e]	(*Z*)-2-FC_6H_4 (**1s**)	C_6H_5	**2s**	>99	94 (*S*)
20[e]	(*Z*)-3-ClC_6H_4 (**1t**)	C_6H_5	**2t**	>99	97 (−)
21[f]	(*E*)-4-ClC_6H_4 (**1b**)	Me	**2b**	>99	95 (+)

[a]Unless otherwise mentioned, all reactions were carried out with a $[Rh(COD)Cl]_2$:(*R,R*)-f-spiroPhos:substrate ratio of 0.5:1.1:100, CH_2Cl_2, and 10 atm of H_2 at −15 °C for 6 h. [b]Determined by ^{1}H NMR spectroscopy or GC analysis. [c]Determined by HPLC analysis using a chiral stationary phase or chiral GC analysis. [d]Reaction conditions: rt, 10 atm of H_2, 1 h. [e]Reaction conditions: 0 °C, 10 atm of H_2, 4 h. [f]A 1.5 g mass of substrate was used.

a 1-naphthyl group, and excellent enantioselectivities were provided even at room temperature (entries 11 and 12). Gratifyingly, excellent ee values, 97% and 98%, respectively, were also obtained for the substrates with a larger alkyl group, ^{i}Pr or cyclohexyl (entries 14 and 15). However, for the dialkyl substrates **1p** and **1q**, only moderate enantioselectivities were observed, possibly attributed to the flexibility of the alkyl groups (entries 16 and 17). It is notable that this catalyst system was also efficient for the asymmetric hydrogenation of challenging substrates *β,β*-diarylacrylic acids due to the difficult differentiation of a stereogenic center with two sterically similar aryl groups, providing the corresponding *β,β*-diarylpropionic acids with excellent enantioselectivities (entries 18−20). In addition, a large-scale (1.5 g) hydrogenation of **1b** could be performed smoothly with a full conversion and constant ee value (entry 21).

To our delight, in addition to *β,β*-disubstituted unsaturated carboxylic acids, this catalyst system exhibited excellent enantioselectivity for the asymmetric hydrogenation of *β,β*-disubstituted unsaturated aldehydes and *γ,γ*-disubstituted unsaturated alcohols. Under the mild reaction conditions, the unsaturated aldehyde **3** and *γ,γ*-disubstituted unsaturated alcohols **5a** and **5b** were successfully hydrogenated, affording chiral alcohols **4** and **6** in full conversions and excellent enantioselectivities, up to 97% ee (Scheme 2). However, when this catalyst was applied to the substrates bearing a neighboring polar group, such as an ester ((*E*)-4-methoxy-4-oxo-3-phenylbut-2-enoic acid) or amide ((*Z*)-4-oxo-3-phenyl-4-(phenylamino)but-2-enoic acid) group, very poor reactivities (<10% conversion) were observed for both substrates presumably due to the effect on the electronic properties of the C═C bond by two polar groups.

Scheme 2

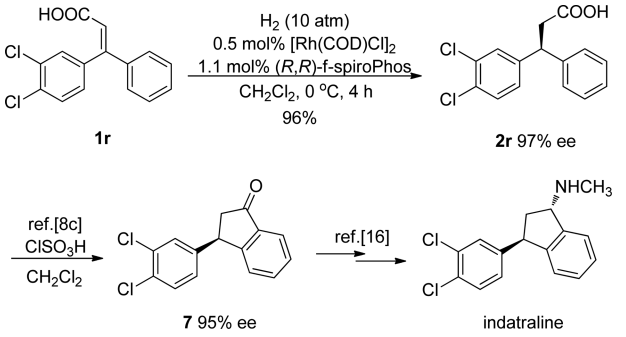


To demonstrate the application of this method, this catalyst system was applied to the preparation of the key intermediate **7** for the synthesis of indatraline, a nonselective monoamine reuptake inhibitor.[4] It could be readily afforded by this method from the hydrogenation product *β,β*-diarylacrylic acid **1r** in high yield and excellent enantioselectivity, 95% ee (Scheme 3).[8c,16]

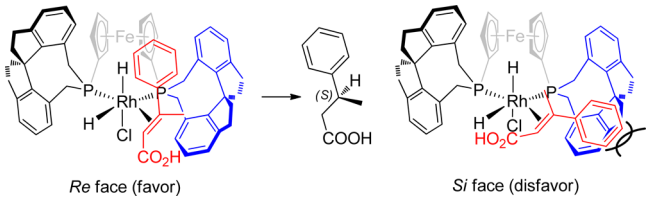
According to the reported mechanism of rhodium-catalyzed asymmetric hydrogenation of unsaturated nitriles,[15a] a possible enantio-determining transition model was also proposed (Scheme 4). The different bulk of two substituents at the *β*-carbon atom possibly had an influence on the coordination of the substrate to rhodium. It was revealed that the coordination from the *Re*-face of the substrates was much more favorable, resulting in the (*S*) products, which was in agreement with the absolute configuration outcome of the hydrogenation products. For 3,3-diaryl-substituted substrates, the primary recognition element responsible for enantioselection probably was the *α*-C atom

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

Scheme 3



Scheme 4



bearing a small H atom and a significantly larger carboxylic group. The enantioselectivity probably mainly depends on the steric bulk difference between the two substituents on the α-C atom.[10h,11g]

CONCLUSIONS

In conclusion, we have developed a method for Rh-catalyzed asymmetric hydrogenation of β,β-disubstituted unsaturated carboxylic acids without any additive with high activities and excellent enantioselectivities. This catalyst system is tolerant toward steric hindrance and is also very efficient for the asymmetric hydrogenation of β,β-diarylacrylic acids, β,β-disubstituted unsaturated aldehydes, and γ,γ-disubstituted unsaturated alcohols with excellent enantioselectives.

EXPERIMENTAL SECTION

General Information. All the air- or moisture-sensitive reactions and manipulations were performed by using standard Schlenk techniques and in a nitrogen-filled glovebox. DME, THF, dioxane, and toluene were distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from calcium hydride. Anhydrous MeOH was distilled from magnesium. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer. ^{13}C NMR (proton-decoupled) spectra were obtained at 100 MHz. $CDCl_3$ or DMSO-d_6 was the solvent used for the NMR analysis, with tetramethylsilane as the internal standard. Chemical shifts were reported upfield of TMS (0.00 ppm) for ^{1}H NMR. Optical rotation was determined using a polarimeter. HRMS spectra were recorded on a mass spectrometer with APCI.

General Procedure for the Synthesis and Characterization Data for Compounds 1. To a suspension of sodium hydride (0.7−1.5 g, 20.9−43.7 mmol, 1.5 equiv, 70% in mineral oil) in THF (140 mL) was added dropwise the corresponding triethyl phosphonoacetate (4.7−9.8 g, 20.9−43.7 mmol, 1.5 equiv) at 0 °C. The resulting solution was stirred for 3.0 h until gas evolution had ceased, and the corresponding ketone (3.5 g, 13.9−29.1 mmol, 1.0 equiv) in THF (14 mL) was added via syringe. The solution was stirred at room temperature until no starting material was detected by TLC. Then the reaction mixture was quenched with saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous phase was extracted with diethyl ether. The combined organic layers were washed with saturated aqueous NaCl solution, dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography (PE:EA = 50:1 to 20:1) afforded the corresponding acrylate.

The corresponding acrylate (500.0 mg, 1.6−2.6 mmol) was placed in a 50 mL round-bottom flask, then EtOH (5.4 mL) was added, the reaction mixture was stirred, and NaOH (10%, 10.8 mL) was added. The reaction mixture was stirred at room temperature until no starting material was detected by TLC. Then the pH was adjusted to 1.0 with HCl (1 N). The mixture was extracted with diethyl ether. The combined organic layer was washed with saturated aqueous NaCl solution, dried over Na_2SO_4, and concentrated in vacuo. Purification by recrystallization provided the corresponding carboxylic acid **1**.[17]

*(E)-3-Phenylbut-2-enoic Acid (**1a**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 423 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 12.01 (s, 1H), 7.53−7.50 (m, 2H), 7.44−7.39 (m, 3H), 6.20 (d, J = 0.9 Hz, 1H), 2.63 (d, J = 0.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.7, 158.5, 141.9, 129.3, 128.5, 126.3, 116.5, 18.2; mp 90−92 °C. The analytical data are consistent with the literature.[14]

*(E)-3-(4-Chlorophenyl)but-2-enoic Acid (**1b**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 434 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44−7.42 (m, 2H), 7.38−7.35 (m, 2H), 6.15 (d, J = 1.2 Hz, 1H), 2.58 (d, J = 1.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.5, 157.2, 140.3, 135.4, 128.8, 127.8, 116.8, 18.2; mp 130−132 °C. The analytical data are consistent with the literature.[18]

*(E)-3-(4-Nitrophenyl)but-2-enoic Acid (**1c**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 437 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27−8.25 (m, 2H), 7.65−7.63 (m, 2H), 6.22 (d, J = 1.3 Hz, 1H), 2.62 (d, J = 1.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 171.4, 155.9, 148.2, 148.1, 127.4, 123.9, 119.2, 18.4; mp 164−166 °C. The analytical data are consistent with the literature.[19]

*(E)-3-(3-Fluorophenyl)but-2-enoic Acid (**1d**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 430 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39−7.33 (m, 1H), 7.20−7.19 (m, 1H), 7.18−7.17 (m, 1H), 7.11−7.06 (m, 1H), 6.17 (d, J = 1.2 Hz, 1H), 2.58 (d, J = 1.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.3, 162.7 (d, $^1J_{C-F}$ = 245.0 Hz), 156.9, 144.1 (d, J = 7.2 Hz), 130.1 (d, J = 8.2 Hz), 122.1 (d, J = 2.6 Hz), 117.3, 116.1 (d, J = 21.1 Hz), 113.5 (d, J = 22.2 Hz), 18.2; mp 129−131 °C. The analytical data are consistent with the literature.[20]

*(E)-3-(3-Bromophenyl)but-2-enoic Acid (**1e**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 446 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63−7.62 (m, 1H), 7.53−7.50 (m, 1H), 7.43−7.40 (m, 1H), 7.29−7.25 (m, 1H), 6.15 (d, J = 1.2 Hz, 1H), 2.57 (d, J = 1.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ = 167.8, 152.4, 144.4, 132.2, 131.1, 129.3, 125.8, 122.5, 119.3, 17.6; mp 156−158 °C. The analytical data are consistent with the literature.[21]

*(E)-3-(3-Nitrophenyl)but-2-enoic Acid (**1f**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 430 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.36 (m, 1H), 8.26−8.24 (m, 1H), 7.83−7.81 (m, 1H), 7.61−7.57 (m, 1H), 6.25 (s, 1H), 2.64 (d, J = 0.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 167.8, 151.5, 148.5, 143.5, 133.2, 130.6, 124.0, 121.3, 120.2, 17.6; mp 188−190 °C. The analytical data are consistent with the literature.[22]

*(E)-3-(3-Methoxyphenyl)but-2-enoic Acid (**1g**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 430 mg, 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33−7.29 (m, 1H), 7.10−7.07 (m, 1H), 7.01−7.00 (m, 1H), 6.94−6.92 (m, 1H), 6.17 (d, J = 1.3 Hz, 1H), 3.84 (s, 3H), 2.59 (d, J = 1.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.5, 159.6, 158.4, 143.5, 129.5, 118.8, 116.6, 114.7, 112.1, 55.3, 18.4; mp 94−96 °C. The analytical data are consistent with the literature.[23]

*(E)-3-(2-Fluorophenyl)but-2-enoic Acid (**1h**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 434 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36−7.28 (m, 2H), 7.17−7.07 (m, 2H), 6.05 (d, J = 1.2 Hz, 1H), 2.56 (t, J = 1.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.2, 159.4 (d, $^1J_{C-F}$ = 248.4 Hz), 155.1, 130.7 (d, J = 13.1 Hz), 130.3 (d, J = 8.5 Hz), 129.1 (d, J = 3.5

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

Hz), 124.2 (d, J = 2.4 Hz), 119.8 (d, J = 2.4 Hz), 116.1 (d, J = 22.1 Hz), 19.8 (d, J = 3.6 Hz); mp 90−92 °C. The analytical data are consistent with the literature.[20]

*(E)-3-(2-Chlorophenyl)but-2-enoic Acid (**1i**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 240 mg, 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41−7.39 (m, 1H), 7.28−7.25 (m, 2H), 7.20−7.17 (m, 2H), 5.88 (d, J = 1.4 Hz,1H), 2.52 (d, J = 1.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.2, 158.9, 142.4, 131.1, 129.9, 129.3, 128.8, 126.8, 120.1, 20.6; mp 102−104 °C. The analytical data are consistent with the literature.[24]

*(E)-3-(o-Tolyl)but-2-enoic Acid (**1j**).* Purification by column chromatography (PE:EA = 2:1) afforded the product as a light yellow solid: yield 140 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25−7.16 (m, 3H), 7.09−7.08 (m, 1H), 5.82 (d, J = 1.1 Hz, 1H), 2.47 (d, J = 1.3 Hz, 3H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.4, 161.4, 143.7, 133.7, 130.5, 127.9, 126.9, 125.8, 118.9, 21.2, 19.7; mp 83−85 °C. The analytical data are consistent with the literature.[25]

*(E)-3-(2-Nitrophenyl)but-2-enoic Acid (**1k**).* Purification by recrystallization (EA/PE) afforded the product as a light orange solid: yield 440 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08−8.05 (m, 1H), 7.66−7.62 (m, 1H), 7.54−7.50 (m, 1H), 7.33−7.31 (m, 1H), 5.84 (d, J = 1.4 Hz, 1H), 2.48 (d, J = 1.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 171.5, 158.0, 146.7, 139.3, 133.6, 129.8, 129.1, 124.8, 118.4, 20.8; mp 122−124 °C; APCI-HRMS calcd for $C_{10}H_{10}NO_4$ [M + H$^+$] 208.0304, found 208.0308.

*(E)-3-(Naphthalen-1-yl)but-2-enoic Acid (**1l**).* Purification by recrystallization (EA/PE) afforded the product as a light yellow solid: yield 398 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93−7.83 (m, 3H), 7.55−7.45 (m, 3H), 7.33−7.32 (m, 1H), 6.08−6.07 (m, 1H), 2.69−2.68 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.5, 160.3, 141.8, 133.6, 129.8, 128.5, 128.4, 126.4, 126.0, 125.1, 124.1, 120.0, 22.0; mp 90−92 °C. The analytical data are consistent with the literature.[26]

*(E)-3-Phenylpent-2-enoic Acid (**1m**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 410 mg, 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48−7.46 (m, 2H), 7.41−7.38 (m, 3H), 6.06 (s, 1H), 3.16−3.11 (m, 2H), 1.09 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.3, 165.0, 140.8, 129.2, 128.5, 126.7, 116.1, 24.5, 13.6; mp 94−96 °C. The analytical data are consistent with the literature.[27]

*(E)-4-Methyl-3-phenylpent-2-enoic Acid (**1n**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 353 mg, 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36−7.32 (m, 3H), 7.22−7.20 (m, 2H), 5.75 (s, 1H), 4.18−4.09 (m, 1H), 1.10 (d, J = 7.0 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.0, 170.2, 140.5, 127.8, 127.7, 127.5, 117.9, 29.7, 21.3; mp 96−98 °C. The analytical data are consistent with the literature.[25]

*(E)-3-Cyclohexyl-3-phenylacrylic Acid (**1o**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 160 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35−7.29 (m, 3H), 7.10−7.07 (m, 2H), 5.82 (d, J = 0.9 Hz, 1H), 2.28−2.22 (m, 1H), 1.80−1.75 (m, 4H), 1.26−1.10 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 171.6, 167.0, 139.9, 127.7, 127.4, 127.0, 115.2, 47.7, 31.6, 26.4, 26.0; mp 140−142 °C. The analytical data are consistent with the literature.[28]

*(E)-3-Methyl-5-phenylpent-2-enoic Acid (**1p**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 427 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34−7.31 (m, 2H), 7.23−7.20 (m, 3H), 5.74 (s, 1H), 2.85−2.81 (m, 2H), 2.53−2.49 (m, 2H), 2.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 172.6, 162.3, 140.9, 128.6, 128.3, 126.2, 115.7, 43.0, 33.9, 19.4; mp 50−52 °C. The analytical data are consistent with the literature.[29]

*(E)-3-Cyclohexylbut-2-enoic Acid (**1q**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 427 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.68 (t, J = 1.0 Hz, 1H), 2.15 (d, J = 1.2 Hz, 3H), 2.04−1.98 (m, 1H), 1.84−1.69 (m, 5H), 1.37−1.11 (m, 5H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 173.0, 168.1, 113.5, 49.0, 31.2, 26.3, 26.0, 17.7; mp 74−76 °C. The analytical data are consistent with the literature.[30]

*(Z)-3-(3,4-Dichlorophenyl)-3-phenylacrylic Acid (**1r**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 447 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47−7.07 (m, 8H), 6.38 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ = 166.8, 152.0, 140.1, 139.7, 131.2, 131.1, 131.0, 130.6, 130.1, 129.8, 129.2, 128.3, 120.2; mp 174−176 °C. The analytical data are consistent with the literature.[14]

*(Z)-3-(2-Fluorophenyl)-3-phenylacrylic Acid (**1s**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 358 mg, 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40−7.30 (m, 6H), 7.18−7.08 (m, 3H), 6.48 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 170.9, 159.4 (d, $^1J_{C-F}$ = 246.1 Hz), 152.2, 139.5, 130.7, 130.1 (d, J = 8.0 Hz), 129.9, 128.5, 127.8, 126.0 (d, J = 15.8 Hz), 123.7, 118.5, 115.4 (d, J = 21.8 Hz); mp 156−158 °C. The analytical data are consistent with the literature.[14]

*(Z)-3-(3-Chlorophenyl)-3-phenylacrylic Acid (**1t**).* Purification by recrystallization (EA/PE) afforded the product as a white solid: yield 263 mg, >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38−7.28 (m, 5H), 7.24−7.23 (m, 2H), 7.16 (s, 1H), 7.09−7.07 (m, 1H), 6.32 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 171.2, 157.5, 140.0, 139.9, 133.8, 130.0, 129.2, 129.0, 128.5, 128.4, 128.3, 127.4, 117.0; mp 137−139 °C; APCI-HRMS calcd for $C_{15}H_{12}ClO_2$ [M + H$^+$] 259.0520, found 259.0523.

Procedure for the Synthesis and Characterization Data for Compound 3. (*E*)-3-Phenylbut-2-enenitrile (500.0 mg, 3.5 mmol, 1.0 equiv)[15a] was placed in an oven-dried 50 mL, three-neck round-bottom flask. THF (5 mL) was added under nitrogen. The reaction mixture was cooled, and DIBAL-H (5.2 mL, 1.0 M, 5.2 mmol, 1.5 equiv) was added dropwise with stirring at −10 °C. The solution was stirred at rt for 2.0 h. Then the reaction mixture was quenched with water and HCl (5%) slowly, maintaining the temperature at −10 °C. The mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography (PE:EA = 15:1) on silica gel to give **3** (yellow liquid, 240.3 mg, 47.1%):[31] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.2 (d, J = 7.9 Hz, 1H), 7.55−7.53 (m, 2H), 7.42−7.41 (m, 3H), 6.39 (d, J = 7.9 Hz, 1H), 2.57 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 191.1, 157.5, 140.3, 129.9, 128.5, 127.0, 126.1, 16.1. The analytical data are consistent with the literature.[32]

General Procedure for the Synthesis and Characterization Data for Compounds 5. The corresponding acrylate (0.7 g, 3.7 mmol, for **5a**; 0.9 g, 4.1 mmol, for **5b**) was placed in an oven-dried 50 mL, three-neck round-bottom flask. THF (20 mL) was added under nitrogen. The reaction mixture was cooled, and $LiAlH_4$ (140 mg for **5a**, 150 mg for **5b**, 1.0 equiv) was added dropwise with stirring at −78 °C. The solution was stirred at room temperature for 1 h. Then the reaction mixture was quenched with water and HCl (5%) slowly, maintaining the temperature at −78 °C. The mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography (PE:EA = 5:1) on silica gel to give **5a** (400 mg of colorless liquid, 73.4%) and **5b** (646 mg of colorless liquid, 95%).[17a,31c]

*(E)-3-Phenylbut-2-en-1-ol (**5a**).* Yield 400 mg, 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29−7.27 (m, 2H), 7.21−7.18 (m, 2H), 7.15−7.11 (m, 1H), 5.84 (t, J = 6.6 Hz, 1H), 4.23 (d, J = 6.6 Hz, 2H), 1.95 (s, 3H), 1.42 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 142.6, 136.9, 128.0, 126.9, 126.5, 125.5, 59.4, 15.7; The analytical data are consistent with the literature.[33]

*(E)-3-(2-Fluorophenyl)but-2-en-1-ol (**5b**).* Yield 646 mg, 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.12−7.07 (m, 2H), 6.97−6.93 (m, 1H), 6.91−6.86 (m, 1H), 5.67 (t, J = 6.3 Hz, 1H), 4.21 (d, J = 5.3 Hz, 2H), 1.91 (s, 3H), 1.60 (s, 1H); ^{13}C{^{1}H} NMR (400 MHz, $CDCl_3$) δ = 159.8 (d, $^1J_{C-F}$ = 245.5 Hz), 134.1, 131.7 (d, J = 14.0 Hz), 130.0, 129.6 (d, J = 4.1 Hz), 128.6 (d, J = 8.2 Hz), 124.0 (d, J = 3.2 Hz), 115.7 (d, J = 22.5 Hz), 59.3, 17.1 (d, J = 3.6 Hz); APCI-HRMS calcd for $C_{10}H_{12}FO$ [M + H$^+$] 167.0872, found 167.0873.

General Procedure for Asymmetric Hydrogenation and Characterization Data for the Products. A stock solution was made by mixing $[Rh(COD)Cl]_2$ (1.3 mg) with (*R*,*R*)-f-spiroPhos (4.3 mg) in a 1:2.2 molar ratio in CH_2Cl_2 (4.0 mL) at room temperature for 20 min in a nitrogen-filled glovebox. An aliquot of the catalyst solution (1.0 mL, 0.00132 mmol) was transferred by syringe into the vials

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

charged with different substrates (0.125 mmol for each) in anhydrous CH_2Cl_2 (2.0 mL). The vials were subsequently transferred into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H_2 (10 atm) at −15 °C for 6 h. The hydrogen gas was released slowly and carefully. The solution was passed through a short column of silica gel to remove the metal complex and then concentrated in vacuo. The residue was dissolved in CH_2Cl_2, and then aniline, EDC, and DMAP were added at 0 °C. The solution was stirred for 4−10 h. The residue was purified by chromatography. The ee values of the amides were determined by HPLC analysis on a chiral stationary phase.

Procedure for the Large-Scale Asymmetric Hydrogenation of 1b. The catalyst solution was made by mixing $[Rh(COD)Cl]_2$ (17.1 mg, 0.035 mmol) with (*R*,*R*)-f-spiroPhos (56.5 mg, 0.0765 mmol) in a 1:2.2 molar ratio in CH_2Cl_2 (2.0 mL) at room temperature for 20 min in a nitrogen-filled glovebox and then transferred by syringe into the vials charged with **1b** (1.5 g, 7.65 mmol) in anhydrous CH_2Cl_2 (4.0 mL). The vials were subsequently placed into an autoclave into which hydrogen gas was charged. The reaction was then stirred under H_2 (10 atm) at −15 °C for 6 h. The resulting solution was passed through a short column of silica gel to remove the metal complex and then concentrated in vacuo. The residue was dissolved in CH_2Cl_2, followed by addition of aniline, EDC, and DMAP at 0 °C, and stirred for 10 h. The corresponding amide was purified by chromatography. The ee value was determined by HPLC analysis on a chiral stationary phase.

*Data for (S)-3-phenylbutanoic acid (**2a**):* light yellow liquid; yield 20.1 mg, 98%; 97% ee; $[\alpha]_D^{20}$ = +12.2 (*c* = 0.7, CH_2Cl_2); GC condition (Supelco γ-Dex 225 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 100 °C, 1 °C/min, 200 °C, 50 min) t_R = 44.5 min (major), t_R = 45.2 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 11.37 (s, 1H), 7.23−7.20 (m, 2H), 7.14−7.10 (m, 3H), 3.22−3.14 (m, 1H), 2.60−2.45 (m, 2H), 1.23 (d, *J* = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.1, 145.3, 128.5, 126.6, 126.5, 42.6, 36.0, 21.8. The absolute configuration of (*S*)-**2a** was determined by comparison with optical rotation data from the reported literature.[10d]

*Data for (+)-3-(4-chlorophenyl)butanoic acid (**2b**):* light yellow solid; yield 24.1 mg, 97%; 95% ee; $[\alpha]_D^{20}$ = +44.94 (*c* = 1.07, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 7.5 min (minor), t_R = 9.1 min (major); ^{1}H NMR (400 MHz, CDCl3) δ = 10.19 (s, 1H), 7.21−7.19 (m, 2H), 7.09−7.07 (m, 2H), 3.22−3.13 (m, 1H), 2.59−2.47 (m, 2H), 1.22 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.6, 143.8, 132.1, 128.7, 128.1, 42.4, 35.6, 21.9; mp 60−62 °C. The analytical data are consistent with the literature.[10c]

*Data for (+)-3-(4-nitrophenyl)butanoic acid (**2c**):* light yellow solid; yield 25.1 mg, 96%; 97% ee; $[\alpha]_D^{20}$ = +45.8 (*c* = 1.3, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 12.6 min (minor), t_R = 19.3 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17−8.15 (m, 2H), 7.40−7.37 (m, 2H), 3.43−3.34 (m, 1H), 2.72−2.61 (m, 2H), 1.34 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 177.8, 152.8, 146.7, 127.7, 123.9, 41.8, 36.0, 21.7; mp 120−122 °C. The analytical data are consistent with the literature.[34]

*Data for (+)-3-(3-fluorophenyl)butanoic acid (**2d**):* light yellow liquid; yield 22.1 mg, 97%; 96% ee; $[\alpha]_D^{20}$ = +25.5 (*c* = 1.1, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 7.6 min (minor), t_R = 9.0 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.16−7.11 (m, 1H), 6.89−6.87 (m, 1H), 6.82−6.75 (m, 2H), 3.20−3.11 (m, 1H), 2.56−2.42 (m, 2H), 1.19 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.6, 162.9 (d, $^1J_{C-F}$ = 243.8 Hz), 148.0 (d, *J* = 6.7 Hz), 130.0 (d, *J* = 8.2 Hz), 122.4, 113.6 (d, *J* = 21.2 Hz), 113.4 (d, *J* = 21.1 Hz), 42.3, 35.9, 21.7. The analytical data are consistent with the literature.[10c]

*Data for (+)-3-(3-bromophenyl)butanoic acid (**2e**):* light yellow liquid; yield 29.2 mg, 96%; 97% ee; $[\alpha]_D^{20}$ = +28.4 (*c* = 1.6, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 10:90, 0.5 mL/min, 254 nm) t_R = 40.6 min (minor), t_R = 42.4 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36−7.33 (m, 2H), 7.19−7.14 (m, 2H), 3.29−3.20 (m, 1H), 2.68−2.54 (m, 2H), 1.31 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.5, 147.7, 130.1, 129.9, 129.6, 125.4, 122.6, 42.3, 35.8, 21.7. The analytical data are consistent with the literature.[35]

*Data for (+)-3-(3-nitrophenyl)butanoic acid (**2f**):* light yellow solid; yield 25.6 mg, 98%; 97% ee; $[\alpha]_D^{20}$ = +28.7 (*c* = 1.3, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 10.1 min (minor), t_R = 13.1 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09−8.06 (m, 2H), 7.57−7.55 (m, 1H), 7.49−7.45 (m, 1H), 3.43−3.34 (m, 1H), 2.73−2.60 (m, 2H), 1.36 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.3, 148.4, 147.4, 133.3, 129.6, 121.7, 42.1, 35.8, 21.7; mp 164−166 °C. The analytical data are consistent with the literature.[36]

*Data for (+)-3-(3-methoxyphenyl)butanoic acid (**2g**):* light yellow liquid; yield 23.8 mg, 98%; 91% ee; $[\alpha]_D^{20}$ = +30.2 (*c* = 1.2, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 11.7 min (minor), t_R = 16.2 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.31 (s, 1H), 7.35−7.30 (m, 1H), 6.93−6.91 (m, 1H), 6.87−6.84 (m, 2H), 3.89 (s, 3H), 3.39−3.32 (m, 1H), 2.79−2.63 (m, 2H), 1.41 (d, *J* = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.9, 159.6, 147.1, 129.5, 119.0, 112.7, 111.5, 55.1, 42.5, 36.1, 21.7. The analytical data are consistent with the literature.[10c]

*Data for (+)-3-(2-fluorophenyl)butanoic acid (**2h**):* light yellow liquid; yield 22.3 mg, 98%; 96% ee; $[\alpha]_D^{20}$ = +18.4 (*c* = 1.14, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 5:95, 1 mL/min, 254 nm) t_R = 41.1 min (minor), t_R = 43.1 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26−7.17 (m, 2H), 7.11−7.07 (m, 1H), 7.04−7.00 (m, 1H), 3.61−3.52 (m, 1H), 2.78−2.60 (m, 2H), 1.34 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.7, 160.6 (d, $^1J_{C-F}$ = 244.2 Hz), 131.9 (d, *J* = 14.1 Hz), 128.0 (d, *J* = 1.8 Hz), 127.9 (d, *J* = 5.6 Hz), 124.2 (d, *J* = 3.4 Hz), 115.6 (d, *J* = 22.3 Hz), 40.8, 30.1, 20.4. The analytical data are consistent with the literature.[37]

*Data for (−)-3-(2-chlorophenyl)butanoic acid (**2i**):* light yellow liquid; yield 24.3 mg, 98%; 93% ee; $[\alpha]_D^{20}$ = −16.4 (*c* = 1.22, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 10.1 min (major), t_R = 11.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38−7.27 (m, 1H), 7.25−7.22 (m, 2H), 7.18−7.14 (m, 1H), 3.85−3.76 (m, 1H), 2.79−2.53 (m, 2H), 1.33 (d, *J* = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 178.6, 142.4, 133.5, 129.8, 127.6, 127.1, 126.9, 41.0, 32.1, 20.2. The analytical data are consistent with the literature.[38]

*Data for (+)-3-(o-tolyl)butanoic acid (**2j**):* light yellow solid; yield 21.8 mg, 98%; 99.3% ee; $[\alpha]_D^{20}$ = +16.2 (*c* = 1.11, CH_2Cl_2) [lit.[13] $[\alpha]_D^{20}$ = +8.8 (*c* = 1.00 $CHCl_3$) for 16% ee]; HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 10:90, 1 mL/min, 254 nm) t_R = 21.0 min (major), t_R = 22.9 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.52 (s, 1H), 7.21−7.117 (m, 4H), 3.60−3.51 (m, 1H), 2.73−2.55 (m, 2H), 2.39 (s, 3H), 1.30 (d, *J* = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.4, 143.7, 135.3, 130.6, 126.4, 126.2, 125.0, 42.1, 31.3, 21.3, 19.5; mp 41−43 °C. The analytical data are consistent with the literature.[10d]

*Data for (−)-3-(2-nitrophenyl)butanoic acid (**2k**):* light yellow liquid; yield 25.4 mg, 97%; 97% ee; $[\alpha]_D^{20}$ = −93.5 (*c* = 1.0, CH_2Cl_2); HPLC (Lux 5u Cellulose-3 (250 × 4.60 mm), ipa:hex = 8:92, 1 mL/min, 254 nm) t_R = 39.6 min (minor), t_R = 43.6 min (major); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.68−7.66 (m, 1H), 7.50−7.46 (m, 1H), 7.36−7.34 (m, 1H), 7.29−7.25 (m, 1H), 3.77−3.68 (m, 1H), 2.72−2.52 (m, 2H), 1.30 (d, *J* = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 177.9, 149.8, 139.4, 132.8, 127.7, 127.2, 124.2, 41.7, 30.3, 21.3. The analytical data are consistent with the literature.[10d]

*Data for (S)-3-(naphthalen-1-yl)butanoic acid (**2l**):* light yellow solid; yield 26.0 mg, 97%; 98% ee; $[\alpha]_D^{20}$ = +7.3 (*c* = 1.2, CH_2Cl_2), HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 10.5 min (major), t_R = 14.4 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.70 (s,1H), 8.20−7.19 (m, 1H), 7.91−7.89 (m, 1H), 7.77−7.75 (m, 1H), 7.59−7.52 (m, 3H), 7.50−7.41 (m, 1H), 4.24−4.16 (m, 1H), 2.96−2.91 (m, 1H), 2.72−2.66 (m, 1H), 1.50 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.5, 141.4, 134.1, 131.1, 129.1, 127.1, 126.2, 125.6, 123.0, 122.4, 42.3, 30.6, 21.2; mp 82−84 °C. The analytical data are consistent with the literature.[10d]

*Data for (S)-3-phenylpentanoic acid (**2m**):* light yellow liquid; yield 21.8 mg, 98%; 94% ee; $[\alpha]_D^{20}$ = +22.5 (*c* = 1.1, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 8.5 min (major), t_R = 9.4 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32−7.28 (m, 2H), 7.23−7.17 (m, 3H), 3.03−2.96 (m, 1H), 2.70−2.59

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

(m, 2H), 1.78−1.58 (m, 2H), 0.80 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.0, 143.7, 128.3, 127.4, 126.4, 43.5, 41.5, 29.0, 11.8. The analytical data are consistent with the literature.[39]

*Data for (S)-4-methyl-3-phenylpentanoic acid (**2n**):* light yellow liquid; yield 23.6 mg, 98%; 97% ee; $[\alpha]_D^{20}$ = −23.5 (c = 1.2, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 6.5 min (major), t_R = 9.0 min (minor); ^1H NMR (400 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 7.05−7.01 (m, 2H), 6.97−6.95 (m, 1H), 6.93−6.89 (m, 2H), 2.66−2.52 (m, 2H), 2.39−2.33 (m, 1H), 1.66−1.58 (m, 1H), 0.70 (d, J = 6.7 Hz, 3H), 0.52 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.1, 142.5, 128.2, 128.1, 126.4, 48.3, 38.1, 33.0, 20.5, 20.1. The analytical data are consistent with the literature.[40]

*Data for (S)-3-cyclohexyl-3-phenylpropanoic acid (**2o**):* light yellow solid; yield 28.5 mg, 98%; 98% ee; $[\alpha]_D^{20}$ = −58.2 (c = 1.3, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 6.9 min (minor), t_R = 9.7 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.29−7.25 (m, 2H), 7.21−7.17 (m, 1H), 7.13−7.12 (m, 2H), 2.91−2.80 (m, 2H), 2.62−2.55 (m, 1H), 1.82−1.72 (m, 2H), 1.62−1.59 (m, 2H), 1.52−1.43 (m, 2H), 1.27−1.16 (m, 1H), 1.13−1.05 (m, 2H), 1.02−0.89 (m, 1H), 0.87−0.75 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ = 174.3, 143.8, 128.7, 128.3, 126.4, 47.9, 42.7, 38.1, 30.9, 30.6, 26.4, 26.3; mp 92−94 °C. The analytical data are consistent with the literature.[39]

*Data for (R)-(+)-3-methyl-5-phenylpentanoic acid (**2p**):* light yellow liquid; yield 23.6 mg, 98%; 66% ee; $[\alpha]_D^{20}$ = +1.2 (c = 1.3, CH_2Cl_2); HPLC (Lux 5u Cellulose-3 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 7.2 min (minor), t_R = 8.7 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32−7.28 (m, 2H), 7.21−7.19 (m, 3H), 2.74−2.58 (m, 2H), 2.46−2.41 (m, 1H), 2.26−2.21 (m, 1H), 2.10−2.01 (m, 1H), 1.77−1.68 (m, 1H), 1.62−1.52 (m, 1H), 1.07 (d, J = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 179.7, 142.2, 128.3, 128.2, 125.7, 41.7, 38.4, 33.2, 29.9, 19.5. The analytical data are consistent with the literature.[41]

*Data for (−)-3-cyclohexylbutanoic acid (**2q**):* light yellow liquid; yield 20.9 mg, 98%; 73% ee; $[\alpha]_D^{20}$ = −22.8 (c = 1.1, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 6.6 min (minor), t_R = 8.1 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.1 (s, 1H), 2.44 (m, 1H), 2.16 (m, 1H), 1.85 (s, 1H), 1.73 (m, 2H), 1.63 (m, 3H), 1.25−1.08 (m, 4H), 1.00−0.94 (m, 2H), 0.92−0.90 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 180.5, 42.6, 39.7, 35.3, 30.2, 28.9, 26.7, 26.6, 26.6, 16.4. The analytical data are consistent with the literature.[42]

*Data for (S)-3-(3,4-dichlorophenyl)-3-phenylpropanoic acid (**2r**).* light yellow liquid; yield 36.2 mg, 98%; 97% ee; $[\alpha]_D^{20}$ = −1.0 (c = 1.4, CH_2Cl_2); HPLC (Lux 5u Cellulose-3 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 12.5 min (major), t_R = 15.8 min (minor); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.29−7.22 (m, 4H), 7.19−7.11 (m, 3H), 7.02−7.00 (m, 1H), 4.41 (t, J = 7.9 Hz, 1H), 3.04−2.93 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 177.5, 143.4, 141.9, 132.6, 130.7, 130.5, 129.6, 128.9, 127.4, 127.1, 127.0, 45.7, 40.0. The analytical data are consistent with the literature.[14]

*Data for (S)-3-(2-fluorophenyl)-3-phenylpropanoic acid (**2s**):* light yellow solid; yield 29.3 mg, 96%; 94% ee; $[\alpha]_D^{25}$ = +5.2 (c = 1.36, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 20:80, 1 mL/min, 254 nm) t_R = 12.1 min (major), t_R = 13.4 min (minor); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.25−7.10 (m, 7H), 7.04−7.00 (m, 1H), 6.97−6.92 (m, 1H), 4.76 (t, J = 7.9 Hz, 1H), 3.06 (d, J = 8.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 177.9, 160.4 (d, $^1J_{C-F}$ = 244.9 Hz), 141.9, 130.2 (d, J = 14.2 Hz), 128.6, 128.4 (d, J = 4.2 Hz), 128.3 (d, J = 8.4 Hz), 127.6, 126.8, 124.2 (d, J = 3.4 Hz), 115.7 (d, J = 22.4 Hz), 40.0, 39.2; mp 120−122 °C. The analytical data are consistent with the literature.[14]

*Data for (−)-3-(3-chlorophenyl)-3-phenylpropanoic acid (**2t**):* light yellow solid; yield 31.6 mg, 97%; 97% ee; $[\alpha]_D^{20}$ = −12.3 (c = 1.62, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 10:90, 1 mL/min, 254 nm) t_R = 28.9 min (major), t_R = 31.9 min (minor); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32−7.29 (m, 2H), 7.24−7.17 (m, 6H), 7.14−7.12 (m, 1H), 4.50 (t, J = 7.9 Hz, 1H), 3.07 (d, J = 7.9 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 177.8, 145.2, 142.4, 134.4, 129.9, 128.8, 127.8, 127.5, 126.9, 126.9, 125.8, 46.2, 40.1; mp 112−114 °C. The analytical data are consistent with the literature.[4]

*Data for (S)-3-phenylbutan-1-ol (**4**):* light yellow liquid; yield 18.4 mg, 98%; 88% ee; $[\alpha]_D^{20}$ = −10.5 (c = 0.6, CH_2Cl_2); GC (Supelco α-Dex 120 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 90 °C, 0.5 °C/min, 200 °C, 50 min) t_R = 50.8 min (minor), t_R = 51.5 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.31−7.29 (m, 2H), 7.23−7.19 (m, 3H), 3.61−3.50 (m, 2H), 2.94−2.85 (m, 1H), 1.89−1.84 (m, 2H), 1.29 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 146.8, 128.3, 126.8, 125.9, 60.7, 40.7, 36.2, 22.2. The analytical data are consistent with the literature.[43]

*Data for (S)-3-phenylbutan-1-ol (**6a**):* light yellow liquid; yield 18.4 mg, 98%; 94% ee; $[\alpha]_D^{20}$ = −11.5 (c = 0.6, CH_2Cl_2); GC (Supelco α-Dex 120 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 90 °C, 0.5 °C/min, 200 °C, 50 min; t_R = 50.8 min (minor), t_R = 51.6 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.31−7.29 (m, 2H), 7.23−7.19 (m, 3H), 3.61−3.50 (m, 2H), 2.94−2.85 (m, 1H), 1.89−1.84 (m, 2H), 1.29 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 146.8, 128.3, 126.8, 125.9, 60.7, 40.7, 36.2, 22.2. The analytical data are consistent with the literature.[43]

*Data for (−)-3-(2-fluorophenyl)butan-1-ol (**6b**):* light yellow liquid; yield 20.2 mg, 96%; 97% ee; $[\alpha]_D^{20}$ = −11.5 (c = 0.8, CH_2Cl_2), GC (Supelco γ-Dex 120 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 100 °C, 0.5 °C/min, 200 °C, 50 min) t_R = 43.9 min (minor), t_R = 44.4 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.11−7.00 (m, 2H), 6.97−6.93 (m, 1H), 6.89−6.84 (m, 1H), 3.43−3.42 (m, 2H), 3.15−3.06 (m, 1H), 1.76−1.71 (m, 2H), 1.41 (d, J = 16.6 Hz, 1H), 1.15 (d, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 160.6 (d, $^1J_{C-F}$ = 242.7 Hz), 133.0 (d, J = 14.4 Hz), 127.9 (d, J = 5.2 Hz), 127.2 (d, J = 8.3 Hz), 124.1 (d, J = 3.4 Hz), 115.2 (d, J = 22.9 Hz), 60.9, 39.7, 29.1, 20.8. The analytical data are consistent with the literature.[44]

Synthesis of (−)-Indatraline Precursor 7. Chlorosulfonic acid (0.1 mL, 2.1 mmol) was slowly added by a syringe to a solution of the acid **2r** (54.0 mg, 0.18 mmol) in CH_2Cl_2 (2.0 mL) at room temperature under nitrogen. After the starting material was completely consumed, the resulting mixture was then quenched with water and extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated by a rotary evaporator. The residue was subsequently purified by column chromatography (PE:EtOAc = 10:1) to give compound 7 as a white solid (46.6 mg, 95%): mp 107−109 °C; 95% ee; $[\alpha]_D^{20}$ = −43.8 (c = 0.5, CH_2Cl_2); HPLC (Lux 5u Cellulose-1 (250 × 4.60 mm), ipa:hex = 10:90, 1.0 mL/min, 230 nm) t_R = 9.1 min (minor), t_R = 10.5 min (major); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, J = 7.7 Hz, 1H), 7.61 (m, 1H), 7.46 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.27−7.25 (m, 1H), 7.22 (d, J = 2.1 Hz, 1H), 6.95 (dd, J_1 = 8.3 Hz, J_2 = 2.1 Hz, 1H), 4.55 (dd, J_1 = 8.1 Hz, J_2 = 3.8 Hz, 1H), 3.23 (dd, J_1 = 19.2 Hz, J_2 = 8.2 Hz, 1H), 2.62 (dd, J_1 = 19.2 Hz, J_2 = 3.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 204.5, 156.3, 143.8, 136.5, 135.1, 132.6, 130.8, 130.7, 129.4, 128.1, 126.9, 126.5, 123.4, 46.2, 43.3. The analytical data are consistent with the literature.[15a,16a]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00018.

NMR, GC, and HPLC spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: ghhou@bnu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Grant Nos. 21272026, 21172022, and 21472013), the Ministry of Education of China (Fundamental Research Funds for the

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077

Central Universities, Specialized Research Fund for the Doctoral Program of Higher Education of China, Program for Changjiang Scholars and Innovative Research Team in University), and Beijing Municipal Commission of Education for generous financial support.

REFERENCES

(1) Jeong, K. H.; Woo, H. S.; Kim, C. J.; Lee, K. H.; Jeon, J. Y.; Lee, S. Y.; Kang, J.-H.; Lee, S.; Choi, Y. W. *Int. J. Pharm.* **2015**, *495*, 1.
(2) Paraskar, A. S.; Sudalai, A. *Tetrahedron* **2006**, *62*, 4907.
(3) Rupe, H.; Gassmann, A. *Helv. Chim. Acta* **1936**, *19*, 569.
(4) Bøgesø, K. P.; Christensen, A. V.; Hyttel, J.; Liljefors, T. *J. Med. Chem.* **1985**, *28*, 1817.
(5) Brossi, A.; Grethe, G.; Teitel, S.; Wildman, W. C.; Bailey, D. T. *J. Org. Chem.* **1970**, *35*, 1100.
(6) Manabe, Y.; Kanematsu, M.; Osaka, M.; Yoshida, M.; Shishido, K. *Heterocycles* **2014**, *88*, 441.
(7) (a) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771. (b) Takaya, Y.; Senda, T.; Kurushima, H.; Ogasawara, M.; Hayashi, T. *Tetrahedron: Asymmetry* **1999**, *10*, 4047. (c) Sakuma, S.; Sakai, M.; Itooka, R.; Miyaura, N. *J. Org. Chem.* **2000**, *65*, 5951. (d) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (e) Hillier, M. C.; Desrosiers, J.-N.; Marcoux, J.-F.; Grabowski, E. J. J. *Org. Lett.* **2004**, *6*, 573.
(8) (a) Taylor, J. G.; Correia, C. R. D. *J. Org. Chem.* **2011**, *76*, 857. (b) Itoh, K.; Tsuruta, A.; Ito, J.; Yamamoto, Y.; Nishiyama, H. *J. Org. Chem.* **2012**, *77*, 10914. (c) Yoo, K.; Kim, H.; Yun, J. *Chem. - Eur. J.* **2009**, *15*, 11134. (d) Shuto, Y.; Yamamura, T.; Tanaka, S.; Yoshimura, M.; Kitamura, M. *ChemCatChem* **2015**, *7*, 1547.
(9) For reviews, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (b) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453. (c) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796.
(10) (a) Uemura, T.; Zhang, X.; Matsumura, K.; Sayo, N.; Kumobayashi, H.; Ohta, T.; Nozaki, K.; Takaya, H. *J. Org. Chem.* **1996**, *61*, 5510. (b) Saburi, M.; Takeuchi, H.; Ogasawara, M.; Tsukahara, T.; Ishii, Y.; Ikariya, T.; Takahashi, T.; Uchida, Y. *J. Organomet. Chem.* **1992**, *428*, 155. (c) Sun, X.; Zhou, L.; Wang, C.-J.; Zhang, X. *Angew. Chem., Int. Ed.* **2007**, *46*, 2623. (d) Dong, K.; Li, Y.; Wang, Z.; Ding, K. *Org. Chem. Front.* **2014**, *1*, 155. (e) Mazuela, J.; Norrby, P.-O.; Andersson, P. G.; Pàmies, O.; Diéguez, M. *J. Am. Chem. Soc.* **2011**, *133*, 13634. (f) Diéguez, M.; Mazuela, J.; Pàmies, O.; Verendel, J. J.; Andersson, P. G. *J. Am. Chem. Soc.* **2008**, *130*, 7208. (g) Rageot, D.; Woodmansee, D. H.; Pugin, B.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 9598. (h) Li, J.-Q.; Quan, X.; Andersson, P. G. *Chem. - Eur. J.* **2012**, *18*, 10609. (i) Khumsubdee, S.; Fan, Y.; Burgess, K. *J. Org. Chem.* **2013**, *78*, 9969.
(11) (a) Cheng, X.; Zhang, Q.; Xie, J.-H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2005**, *44*, 1118. (b) Yamada, I.; Yamaguchi, M.; Yamagishi, T. *Tetrahedron: Asymmetry* **1996**, *7*, 3339. (c) Zirakzadeh, A.; Groß, M. A.; Wang, Y.; Mereiter, K.; Weissensteiner, W. *Organometallics* **2014**, *33*, 1945. (d) Li, S.; Zhu, S.-F.; Zhang, C.-M.; Song, S.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2008**, *130*, 8584. (e) Hoen, R.; Boogers, J. A. F.; Bernsmann, H.; Minnaard, A. J.; Meetsma, A.; Tiemersma-Wegman, T. D.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4209. (f) Dong, K.; Li, Y.; Wang, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 14191. (g) Verendel, J. J.; Pàmies, O.; Diéguez, M.; Andersson, P. G. *Chem. Rev.* **2014**, *114*, 2130.
(12) (a) Morrison, J. D.; Burnett, R. E.; Aguiar, A. M.; Morrow, C. J.; Phillips, C. *J. Am. Chem. Soc.* **1971**, *93*, 1301. (b) Ikemoto, T.; Nagata, T.; Yamano, M.; Ito, T.; Mizuno, Y.; Tomimatsu, K. *Tetrahedron Lett.* **2004**, *45*, 7757. (c) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174. (d) Yoshimura, M.; Ishibashi, Y.; Miyata, K.; Bessho, Y.; Tsukamoto, M.; Kitamura, M. *Tetrahedron* **2007**, *63*, 11399.
(13) Szőllősi, G.; Varga, T.; Felföldi, K.; Cserényi, S.; Bartók, M. *Catal. Commun.* **2008**, *9*, 421.
(14) Li, Y.; Dong, K.; Wang, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 6748.
(15) (a) Yan, Q.; Kong, D.; Li, M.; Hou, G.; Zi, G. *J. Am. Chem. Soc.* **2015**, *137*, 10177. (b) Yan, Q.; Liu, M.; Kong, D.; Zi, G.; Hou, G. *Chem. Commun.* **2014**, *50*, 12870. (c) Liu, M.; Kong, D.; Li, M.; Zi, G.; Hou, G. *Adv. Synth. Catal.* **2015**, *357*, 3875.
(16) (a) Davies, H. M. L.; Gregg, T. M. *Tetrahedron Lett.* **2002**, *43*, 4951. (b) Wei, W.-T.; Yeh, J.-Y.; Kuo, T.-S.; Wu, H.-L. *Chem. - Eur. J.* **2011**, *17*, 11405. (c) Takatsu, K.; Shintani, R.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 5548.
(17) (a) Hu, X.-H.; Zhang, J.; Yang, X.-F.; Xu, Y.-H.; Loh, T.-P. *J. Am. Chem. Soc.* **2015**, *137*, 3169. (b) Abe, M.; Nishikawa, K.; Fukuda, H.; Nakanishi, K.; Tazawa, Y.; Taniguchi, T.; Park, S.-y.; Hiradate, S.; Fujii, Y.; Okuda, K.; Shindo, M. *Phytochemistry* **2012**, *84*, 56.
(18) Yin, J.; Li, Y.; Zhang, R.; Jin, K.; Duan, C. *Synthesis* **2014**, *46*, 607.
(19) Gupta, M.; Wakhloo, B. P. *Arkivoc* **2007**, 94.
(20) Wiley, R. H.; Van der Plas, H. C. *J. Chem. Eng. Data* **1965**, *10*, 72.
(21) Edwards, P. D.; Albert, J. S.; Sylvester, M.; Aharony, D.; Andisik, D.; Callaghan, O.; Campbell, J. B.; Carr, R. A.; Chessari, G.; Congreve, M.; Frederickson, M.; Folmer, R. H. A.; Geschwindner, S.; Koether, G.; Kolmodin, K.; Krumrine, J.; Mauger, R. C.; Murray, C. W.; Olsson, L.-L.; Patel, S.; Spear, N.; Tian, G. *J. Med. Chem.* **2007**, *50*, 5912.
(22) Kadin, S. B. U.S. Patent US 4331683 A, 1982.
(23) Birch, A. J.; Corrie, J. E. T.; Macdonald, P. L.; Subba Rao, G. *J. Chem. Soc., Perkin Trans. 1* **1972**, *1*, 1186.
(24) Jia, W.-Q.; Zhang, H.-M.; Zhang, C.-L.; Gao, Z.-H.; Ye, S. *Org. Chem. Front.* **2016**, *3*, 77.
(25) Budhram, R. S.; Palaniswamy, V. A.; Eisenbraun, E. J. *J. Org. Chem.* **1986**, *51*, 1402.
(26) Barrera i Costa, H. *Ann. Chim.* **1949**, *4*, 84.
(27) Estévez, M.-C.; Galve, R.; Sánchez-Baeza, F.; Marco, M.-P. *Anal. Chem.* **2005**, *77*, 5283.
(28) Jalander, L.; Broms, M. *Org. Chem. Biochem.* **1982**, *B36*, 371.
(29) Woodmansee, D. H.; Müller, M.-A.; Neuburger, M.; Pfaltz, A. *Chem. Sci.* **2010**, *1*, 72.
(30) Young, S. T.; Turner, J. R.; Tarbell, D. S. *J. Org. Chem.* **1963**, *28*, 928.
(31) (a) Müller, M.-A.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 8668. (b) Lee, D.; Kim, D.; Yun, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2785. (c) Fronza, G.; Fuganti, C.; Serra, S. *Eur. J. Org. Chem.* **2009**, *2009*, 6160.
(32) Wang, T.; Xiang, S.-K.; Qin, C.; Ma, J.-A.; Zhang, L.-H.; Jiao, N. *Tetrahedron Lett.* **2011**, *52*, 3208.
(33) Mantilli, L.; Gérard, D.; Torche, S.; Besnard, C.; Mazet, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 5143.
(34) Carceller, E.; Salas, J.; Merlos, M.; Giral, M.; Ferrando, R.; Escamilla, I.; Ramis, J.; García-Rafanell, J.; Forn, J. *J. Med. Chem.* **2001**, *44*, 3001.
(35) Kuchar, M.; Rejholec, V.; Brunova, B.; Jelinkova, M. *J. Chromatogr.* **1980**, *195*, 329.
(36) Bott, K. *Tetrahedron Lett.* **1968**, *9*, 4979.
(37) Piano, V.; Benjamin, D. I.; Valente, S.; Nenci, S.; Marrocco, B.; Mai, A.; Aliverti, A.; Nomura, D. K.; Mattevi, A. *ACS Chem. Biol.* **2015**, *10*, 2589.
(38) Sato, K.; Lin, Y.-S.; Amakasu, T. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2600.
(39) Murakata, M.; Tsutsui, H.; Hoshino, O. *Org. Lett.* **2001**, *3*, 299.
(40) Sibi, M. P.; Ji, J. *J. Org. Chem.* **1997**, *62*, 3800.
(41) Sugiyama, S.; Satoh, T. *Tetrahedron: Asymmetry* **2005**, *16*, 665.
(42) Tomioka, K.; Suenaga, T.; Koga, K. *Tetrahedron Lett.* **1986**, *27*, 369.
(43) Ito, H.; Nagahara, T.; Ishihara, K.; Saito, S.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 994.
(44) Romanov-Michailidis, F.; Pupier, M.; Guénée, L.; Alexakis, A. *Chem. Commun.* **2014**, *50*, 13461.

DOI: 10.1021/acs.joc.6b00018
J. Org. Chem. 2016, 81, 2070−2077