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Asymmetric 1,4-addition of aryltrialkoxysilanes to α,β-unsaturated esters and amides catalyzed by a chiral rhodium complex

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Abstract—A highly enantioselective 1,4-addition of aryltrialkoxysilanes to α,β-unsaturated esters and amides was successfully catalyzed by a chiral rhodium complex generated from $[Rh(cod)(MeCN)_2]BF_4$ and (*S*)-BINAP.

1. Introduction

Transition metal-catalyzed transformations using organometallic reagents are of great importance in modern organic chemistry.[1] In particular, asymmetric carbon–carbon bond forming processes are being emphasized in advanced materials and pharmaceuticals. The asymmetric 1,4-conjugate addition of organometallic reagents to α,β-unsaturated carbonyl compounds is widely used for carbon–carbon bond formation, with a new stereogenic center being introduced at the β-position of the saturated carbonyl compounds formed.[2] Rhodium-catalyzed asymmetric 1,4-addition of organoboronic acids[3] was first reported by Hayashi and Miyaura[4] and has been widely studied.[5,6] Other organometallic reagents, such as organo-titanium,[7] -zirconium,[8,9] -zinc,[10] and -tin[11,12] have also been applied successfully for the rhodium-catalyzed 1,4-addition.

Organosilicon reagents are playing a growing role in organic synthesis due to their low cost, low toxicity, ease of handling, tolerance to a variety of functional groups, and simplicity of by-product removal.[13] A synthetic advantage is that the organosilicon reagents are readily prepared in one step by a variety of methods. For example, β-substituted *E*- and *Z*-vinylsilanes[14] and α-substituted ones[15] can be prepared by regio- and stereoselective hydrosilylation of alkynes, and acyl-, alkyl-, vinyl-, and arylsilanes can be prepared by cross-coupling reaction of the corresponding organic halides with disilanes[16] or hydrosilanes.[17] With regard to the rhodium-catalyzed reaction of organosilicon reagents, we have reported the addition of phenylmethyldifluorosilane to aldehydes.[18] The addition of diaryldichlorosilanes to unsaturated carbonyl compounds,[19] and the addition of arylmethylsilanediols to unsaturated carbonyl compounds and aldehydes[20] have been also reported. We[21] and Murata and Masuda[22] reported the 1,4-addition of organotrialkoxysilanes to α,β-unsaturated ketones catalyzed by rhodium complexes, which was then expanded to an asymmetric version by the use of rhodium–BINAP complexes as asymmetric catalysts.[23,24] The 1,4-addition of organosilicon compounds has also been found to be catalyzed by palladium complexes.[25] Herein, we report that the rhodium–BINAP complex-catalyzed asymmetric 1,4-addition of aryltrialkoxysilanes can be successfully applied to α,β-unsaturated esters and amides.

2. Results and discussion

2.1. Asymmetric addition to α,β-unsaturated esters

The reactions of aryltrialkoxysilanes with α,β-unsaturated esters were performed in the presence of a cationic rhodium complex, $[Rh(cod)(MeCN)_2]BF_4$ (4 mol %), and (*S*)-BINAP (6 mol %) in 1,4-dioxane/water (10:1) at 90 °C for 20 h. Results are summarized in Table 1. In the reactions of phenyltrimethoxysilane **2a** with linear α,β-unsaturated esters, enantioselectivity and reactivity

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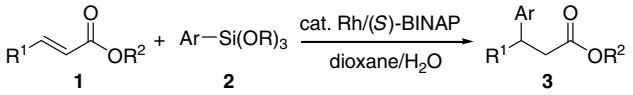
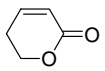
Table 1. Asymmetric 1,4-addition of aryltrialkoxysilanes to α,β-unsaturated esters[a]



1 2 3

1a: R^1=Me, R^2=Me
1b: R^1=Me, R^2=Et
1c: R^1=Me, R^2=Pr^i
1d: R^1=Pr^n, R^2=Me
1e: R^1=Pr^n, R^2=Pr^i
1f: R^1=Pr^i, R^2=Me
1g: R^1=Pr^i, R^2=Pr^i

1h: 

2a: Ar=Ph, R=Me
2b: Ar=4-MeO-C_6H_4, R=Et
2c: Ar=4-Cl-C_6H_4, R=Et

Entry	1	2	Product	Yield (%)[b]	ee (%)[c]
1	**1a**	**2a**	**3aa**	93	84 (*R*)
2	**1b**	**2a**	**3ba**	70	89 (*R*)
3	**1c**	**2a**	**3ca**	76	93
4	**1d**	**2a**	**3da**	70	85
5	**1e**	**2a**	**3ea**	76	93
6	**1f**	**2a**	**3fa**	36	94 (*S*)
7	**1g**	**2a**	**3ga**	28	97 (*S*)
8	**1h**	**2a**	**3ha**	64	99 (*S*)
9	**1c**	**2b**	**3cb**	84	88
10	**1c**	**2c**	**3cc**	80	93

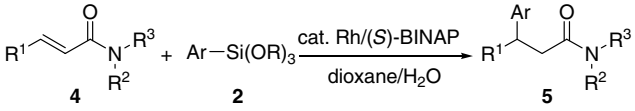
[a] Common reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), $[Rh(cod)(MeCN)_2]BF_4$ (0.04 mmol), (*S*)-BINAP (0.06 mmol), 2.2 mL of dioxane/H_2O (10:1), 90 °C, 20 h, N_2 atmosphere.
[b] Isolated yield.
[c] Determined by HPLC using chiral stationary phase column: Daicel Chiralcel OD-H (**3aa**, **3ba**, **3ca**, **3da**, **3ea**, **3fa**, **3ga**, **3cb**) (hexane/2-propanol = 100:1), OG (**3ha**) (hexane/2-propanol = 90:10), OB-H (**3cc**) (hexane). Absolute configuration is shown in parenthesis.

were affected by the bulkiness of both the substituents on the olefin terminal and the alkoxycarbonyl moiety. Generally, the bulkiness of these substituents heightened the enantioselectivity but lowered the yield. For example, the reaction of methyl (*E*)-4-methyl-2-pentenoate **1f**, which has an isopropyl group at the olefin terminal (R^1 = Pr^i) showed a higher enantioselectivity (94% ee) than that of methyl crotonate **1a** (84% ee) having a methyl group at the olefin terminal (R^1 = Me), while the yield was lower in the case of **1f** (36%) than **1a** (93%) (entries 1 and 6). Similarly, the reaction of isopropyl crotonate **1c** (R^2 = Pr^i) showed a higher enantioselectivity (93% ee) than that of methyl crotonate **1a** (R^2 = Me, 84% ee), while the yield was lower in the case of **1c** (76%) than **1a** (93%) (entries 1 and 3). Therefore, the highest enantioselectivity and the lowest yield in the linear substrate was observed in the reaction of **1g** ($R^1 = R^2$ = Pr^i) (97% ee and 28% yield) (entry 7). On the other hand, the reaction of cyclic substrate **1h** showed excellent enantioselectivity, affording product **3ha** in 64% yield with 99% ee (entry 8). The reaction of **1c** with 4-substituted phenyltriethoxysilane **2b** and **2c** also proceeded well, affording the corresponding products **3cb** and **3cc** in good yield (84% and 80%, respectively) with high enantioselectivity (88% ee and 93% ee, respectively) (entries 9 and 10).

2.2. Asymmetric addition to α,β-unsaturated amides

The asymmetric 1,4-addition of aryltrialkoxysilane was then applied to α,β-unsaturated amides. Results are summarized in Table 2. The reactivity of the α,β-unsaturated amides were slightly lower than that of esters. Thus the yields were lower than those of the esters derived from the corresponding carboxylic acids. The reaction of phenyltrimethoxysilane **2a** with (*E*)-2-butenamide **4a** gave the corresponding product **5aa** in 75% yield and 81% ee, while the reaction of **2a** with (*E*)-2-hexenamide **4b** gave the product **5ab** in 59% yield with a higher enantioselectivity of 91% ee (entries 1 and 2). The reaction of **2a** with **4c** having an isopropyl group at the olefin terminal (R^1 = Pr^i) did not proceed with the steric hindrance of the isopropyl group (entry 3). Substituents on the nitrogen atom of an amide moiety affected the enantioselectivity. The *N*,*N*-dimethyl amide of crotonic acid **4d** showed a lower enantioselectivity of 72% ee than that of **4a** (81% ee, entry 1), while *N*-benzyl amide **4e** showed a higher enantioselectivity of 92% ee (entries 4 and 5). The reaction of **4e** with 4-substituted phenyltriethoxysilane (**2b** and **2c**) proceeded well, affording the corresponding products **5eb** and **5ec** in moderate yield (30% and 54%, respectively) with high enantioselectivity (90% ee and 92% ee, respectively) (entries 6 and 7).

Table 2. Asymmetric 1,4-addition of aryltrialkoxysilanes to α,β-unsaturated amides[a]



4 2 5

4a: R^1=Me, R^2=R^3=H
4b: R^1=Pr^n, R^2=R^3=H
4c: R^1=Pr^i, R^2=R^3=H
4d: R^1=R^2=R^3=Me
4e: R^1=Me, R^2=H, R^3=CH_2Ph

2a: Ar=Ph, R=Me
2b: Ar=4-MeO-C_6H_4, R=Et
2c: Ar=4-Cl-C_6H_4, R=Et

Entry	4	2	Product	Yield (%)[b]	ee (%)[c]
1	**4a**	**2a**	**5aa**	75	81 (*R*)
2	**4b**	**2a**	**5ba**	59	91
3	**4c**	**2a**	**5ca**	Trace	
4	**4d**	**2a**	**5da**	61	72 (*R*)
5	**4e**	**2a**	**5ea**	70	92
6	**4e**	**2b**	**5eb**	30	90
7	**4e**	**2c**	**5ec**	54	92

[a] Common reaction conditions: **4** (1.0 mmol), **2** (2.0 mmol), $[Rh(cod)(MeCN)_2]BF_4$ (0.04 mmol), (*S*)-BINAP (0.06 mmol), 2.2 mL of dioxane/H_2O (10:1), 90 °C, 20 h, N_2 atmosphere.
[b] Isolated yield.
[c] Determined by HPLC using chiral stationary phase column: Daicel Chiralpak AD (hexane/2-propanol = 95:5). Absolute configuration is shown in parenthesis.

3. Conclusion

Enantioselective 1,4-addition of aryltrialkoxysilanes to α,β-unsaturated esters and amides, catalyzed by a chiral

rhodium complex generated from $[Rh(cod)(MeCN)_2]BF_4$ and (*S*)-BINAP is described. Aryl groups can be introduced easily and enantioselectively at the β-position of a variety of esters and amides. Enantioselectivity and chemical yield were affected by the bulkiness of the substituents on olefin terminal and also by the ester or amide moiety.

4. Experimental

4.1. General

Infrared (IR) spectra were recorded on JASCO FT/IR-350 Fourier transform infrared spectrophotometer. NMR spectra were recorded on Bruker DPX-400 or DRX-500 spectrometer using TMS as an internal standard. All reactions were carried out in Schlenk tubes under N_2. Flash chromatographies were performed using spherical silica gel (40–100 μm, Kanto Chemical). Elemental analyses were performed by the Microanalytical Laboratory of the Institute for Chemical Reaction Science, Tohoku University.

4.2. Materials

1,4-Dioxane was distilled and stored under N_2. The cationic rhodium complex, $[Rh(cod)(MeCN)_2]BF_4$, was prepared as described in the literature.[26] Phenyltrimethoxysilane **2a** was purchased from TCI Co., Ltd. *p*-Chlorophenyltriethoxysilane **2b** and *p*-methoxyphenyltriethoxysilane **2c** were prepared by cross-coupling reaction of the corresponding aryl bromide with triethoxysilane as described in the literature.[17d]

4.3. General procedure for rhodium-catalyzed asymmetric 1,4-addition

To a mixture of $[Rh(cod)(MeCN)_2]BF_4$ (15.2 mg, 0.04 mmol) and (*S*)-BINAP (37.4 mg, 0.06 mmol) in 1,4-dioxane (2 mL) was added α,β-unsaturated carbonyl compound **1** or **4** (1.0 mmol), aryltrialkoxysilane **2** (2.0 mmol), and then water (0.2 mL). The mixture was stirred at 90 °C for 20 h. Hexane (100–150 mL) was added to the reaction mixture and the resulting precipitate removed by filtration. The solvent was removed in vacuo and the residue purified by flash chromatography (hexane/AcOEt) to give the 1,4-addition product **3** or **5**.

4.3.1. 3-Phenylbutanoic acid methyl ester 3aa.[27] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.16 (m, 5H), 3.61 (s, 3H), 3.28 (sext, $J = 7.5$ Hz, 1H), 2.58 (m, 2H), 1.29 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 145.7, 130.8, 128.5, 128.2, 126.7, 126.4, 51.4, 42.7, 36.4, 21.7. $[\alpha]_D^{26} = -26$ (*c* 1.00, $CHCl_3$) 84% ee (*R*) {lit.[28] $[\alpha]_D^{24} = -25.3$ (*c* 1.07, $CHCl_3$) 95% ee (*R*)}.

4.3.2. 3-Phenylbutanoic acid ethyl ester 3ba.[29] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.17 (m, 5H), 4.07 (q, $J = 7.5$ Hz, 2H), 3.27 (sext, $J = 8.0$ Hz), 2.60 (dd, $J = 15$, 7 Hz, 1H), 2.53 (dd, $J = 15$, 7 Hz, 1H), 1.30 (d, $J = 7.2$ Hz, 3H), 1.17 (t, $J = 7$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 145.7, 128.4, 126.7, 126.4, 60.2, 43.0, 36.5, 21.8, 14.1. $[\alpha]_D^{24} = -29$ (*c* 1.05, Et_2O) 89% ee (*R*) (lit.[29] $[\alpha]_D^{22} = +21.4$ (*c* 1.538, Et_2O) 95% ee (*S*)).

4.3.3. 3-Phenylbutanoic acid isopropyl ester 3ca.[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.16 (m, 5H), 4.94 (sep, $J = 6.4$ Hz, 1H), 3.26 (sext, $J = 7.2$ Hz, 1H), 2.60–2.48 (m, 2H), 1.29 (d, $J = 6.8$ Hz, 3H), 1.16 (d, $J = 6.4$ Hz, 3H), 1.11 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 145.7, 128.4, 126.8, 126.3, 67.5, 43.3, 36.6, 21.8, 21.7, 21.6. $[\alpha]_D^{24} = -25$ (*c* 1.03, $CHCl_3$) 93% ee.

4.3.4. 3-Phenylhexanoic acid methyl ester 3da.[6a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.17 (m, 5H), 3.58 (s, 3H), 3.10 (quint, $J = 6.8$ Hz, 1H), 2.66–2.54 (m, 2H), 1.63–1.57 (m, 2H), 1.21–1.13 (m, 2H), 0.85 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 144.1, 128.4, 127.4, 126.4, 51.4, 41.9, 41.6, 38.4, 20.4, 13.9. $[\alpha]_D^{21} = -15$ (*c* 0.97, $CHCl_3$) 85% ee {lit.[6a] $[\alpha]_D^{20} = -20$ (*c* 0.90, $CHCl_3$) > 99% ee}.

4.3.5. 3-Phenylhexanoic acid isopropyl ester 3ea.[6a] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.16 (m, 5H), 4.89 (sept, $J = 6.5$ Hz, 1H), 3.12–3.06 (m, 1H), 2.58 (dd, $J = 15$, 7 Hz, 1H), 2.51 (dd, $J = 15$, 7 Hz, 1H), 1.63–1.57 (m, 2H), 1.21–1.16 (m, 2H), 1.12 (d, $J = 6$ Hz, 3H), 1.05 (d, $J = 6$ Hz, 3H), 0.85 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 144.1, 128.3, 127.5, 126.3, 67.4, 42.1, 42.1, 38.5, 21.7, 21.6, 20.4, 13.9. $[\alpha]_D^{22} = -17$ (*c* 0.98, $CHCl_3$) 93% ee {lit.[6a] $[\alpha]_D^{24} = -18$ (*c* 1.09, $CHCl_3$) 95% ee}.

4.3.6. 4-Methyl-3-phenylpentanoic acid methyl ester 3fa.[31] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.13 (m, 5H), 3.51 (s, 3H), 2.89 (ddd, $J = 10$, 7.6, 5.6 Hz, 1H), 2.79 (dd, $J = 15$, 5.6 Hz, 1H), 2.6 (dd, $J = 15$, 8.4 Hz, 1H), 1.86 (oct, $J = 7.6$ Hz, 1H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.75 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 142.8, 128.1, 128.0, 126.3, 51.4, 48.8, 38.3, 33.0, 20.6, 20.3. $[\alpha]_D^{22} = -26$ (*c* 0.97, $CHCl_3$) 94% ee (*S*) {lit.[32] $[\alpha]_D^{25} = +33.5$ (neat) (*R*)}.

4.3.7. 4-Methyl-3-phenylpentanoic acid isopropyl ester 3ga.[6a] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.13 (m, 5H), 4.82 (sept, 6 Hz, 1H), 2.85 (ddd, $J = 10.5$, 7.5, 5.5 Hz, 1H), 2.74 (dd, $J = 14.5$, 5.5 Hz, 1H), 2.55 (dd, $J = 14.5$, 10 Hz, 1H), 1.84 (oct, $J = 7$ Hz, 1H), 1.06 (d, $J = 6.5$ Hz, 3H), 0.97 (d, $J = 6.2$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.76 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 142.8, 128.3, 128.0, 126.2, 67.3, 49.1, 38.9, 33.3, 21.6, 21.5, 20.6, 20.4. $[\alpha]_D^{22} = -23$ (*c* 1.02, $CHCl_3$) 97% ee (*S*) {lit.[6a] $[\alpha]_D^{20} = -23$ (*c* 1.19, $CHCl_3$) 98% ee(*S*)}.

4.3.8. 4-(Phenyl)tetrahydro-2*H*-pyran-2-one 3ha.[6a] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.33 (m, 2H), 7.28–7.25 (m, 1H), 7.21–7.17 (m, 2H), 4.48 (ddd, $J = 11.4$, 4.7, 3.9 Hz, 1H), 4.39–4.33 (m, 1H), 3.24–3.18 (m, 1H), 2.89 (ddd, $J = 17.6$, 6, 1.7 Hz, 1H), 2.61 (dd, $J = 17.6$, 10.6 Hz, 1H), 2.18–2.12 (m, 1H), 2.05–1.97 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 142.7, 128.9, 127.2, 126.4, 68.6, 37.4, 37.3, 30.2. $[\alpha]_D^{20} = +4.4$ (*c* 2.70, $CHCl_3$) 99% ee (*S*) {lit.[6a] $[\alpha]_D^{20} = +4.0$ (*c* 2.70, $CHCl_3$) 98% ee (*S*)}.

4.3.9. 3-(4-Methoxyphenyl)butanoic acid isopropyl ester 3cb.[6d] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, $J = 9$ Hz, 2H), 6.83 (d, $J = 9$ Hz, 2H), 4.99 (sept, $J = 6.3$ Hz, 1H), 3.77 (s, 3H), 3.22 (sext, $J = 7.1$ Hz), 2.53 (dd, $J = 14.5$, 7.3 Hz, 1H), 2.48 (dd, $J = 14.5$, 7.5 Hz, 1H), 1.27 (d, $J = 7$ Hz, 3H), 1.17 (d, $J = 6.5$ Hz, 3H), 1.12 (d, $J = 6.3$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 158.0, 137.8, 127.7, 113.7, 67.4, 55.2, 43.5, 35.8, 22.0, 21.7, 21.7. $[\alpha]_D^{23} = -25$ (*c* 0.96, $CHCl_3$) 88% ee {lit.[6d] $[\alpha]_D^{20} = -21.6$ (*c* 0.99, $CHCl_3$) 92% ee}.

4.3.10. 3-(4-Chlorophenyl)butanoic acid isopropyl ester 3cc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2H), 7.17–7.13 (m, 2H), 4.93 (sept, $J = 7.5$ Hz, 1H), 3.24 (sext, $J = 7.2$ Hz, 1H), 2.53 (dd, $J = 14.8$, 7.6 Hz, 1H), 2.49 (dd, $J = 14.8$, 7.6 Hz, 1H), 1.26 (d, $J = 7$ Hz, 3H), 1.16 (dd, $J = 6.2$ Hz, 3H), 1.11 (dd, $J = 6.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 144.1, 131.8, 128.5, 128.1, 67.6, 43.0, 36.0, 21.8, 21.7, 21.6. IR (neat) 1730, 1261, 1108, 1013 cm^{-1}. Anal. Calcd for $C_{13}H_{17}O_2Cl$: C, 64.86; H, 7.12; Cl, 14.73. Found: C, 64.60; H, 6.94; Cl, 14.60. $[\alpha]_D^{23} = -26$ (*c* 1.02, $CHCl_3$) 93% ee.

4.3.11. 3-Phenylbutyramide 5aa.[6g] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.19 (m, 5H), 5.67 (s, 1H), 5.37 (s, 1H), 3.27 (sext, $J = 7.1$ Hz, 1H), 2.53–2.40 (m, 2H), 1.32 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 145.7, 128.6, 126.7, 126.5, 44.7, 36.7, 21.7. $[\alpha]_D^{24} = -36$ (*c* 1.01, $CHCl_3$) 81% ee (*R*) {lit.[6g] $[\alpha]_D^{20} = -30.9$ (*c* 1.01, $CHCl_3$) 89% ee (*R*)}.

4.3.12. 3-Phenylhexanamide 5ba. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.18 (m, 5H), 5.52 (s, 1H), 5.26 (s, 1H), 3.12–3.04 (m, 1H), 2.51 (dd, $J = 14.3$, 6.6 Hz, 1H), 2.44 (dd, $J = 14.3$, 8.4 Hz, 1H), 1.71–1.54 (m, 2H), 1.25–1.10 (m, 2H), 0.85 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 144.2, 128.5, 127.4, 126.5, 43.8, 42.4, 38.4, 20.5, 13.9. IR (KBr) 3408, 3196, 1655, 1406 cm^{-1}. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.16; H, 9.05; N, 7.16. $[\alpha]_D^{24} = -29$ (*c* 1.00, $CHCl_3$) 91% ee.

4.3.13. *N*,*N*-Dimethyl-3-phenylbutyramide 5da.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.17 (m, 5H), 3.36 (sext, $J = 6.9$ Hz, 1H), 2.90 (s, 3H), 2.86 (s, 3H), 2.61 (dd, $J = 15$, 6.2 Hz, 1H), 2.51 (dd, $J = 15$, 8 Hz, 1H), 1.33 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 146.5, 128.3, 126.8, 126.1, 41.7, 37.2, 36.4, 35.3, 21.5. $[\alpha]_D^{21} = -16$ (*c* 1.02, $CHCl_3$) 72% ee (*R*) (lit.[33] $[\alpha]_D^{25} = +40.1$ (*c* 4.66, EtOH) (*S*)).

4.3.14. *N*-Benzyl-3-phenylbutyramide 5ea.[6g] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.19 (m, 8H), 7.02–7.00 (m, 2H), 5.64 (s, 1H), 4.35 (dd, $J = 14.8$, 6 Hz, 1H), 4.26 (dd, $J = 14.8$, 5.5 Hz, 1H), 3.32 (sext, $J = 7.1$ Hz, 1H), 2.45 (d, $J = 7.6$ Hz, 2H), 1.31 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 145.7, 138.1, 128.6, 128.5, 127.5, 127.3, 126.8, 126.4, 45.8, 43.4, 37.0, 21.8. $[\alpha]_D^{20} = -13$ (c 1.01, $CDCl_3$) 92% ee (lit.[6g] $[\alpha]_D^{20} = -12.1$ (*c* 1.00, $CDCl_3$) 93% ee).

4.3.15. *N*-Benzyl-3-(4-Methoxyphenyl)butyramide 5eb.[6g] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.22 (m, 3H), 7.15–7.12 (m, 2H), 7.02–7.00 (m, 2H), 6.85–6.80 (m, 2H), 5.49 (s, 1H), 4.38 (dd, $J = 14.5$, 6.3 Hz, 1H), 4.27 (dd, $J = 14.5$, 5.4 Hz, 1H), 3.78 (s, 3H), 3.28 (sext, $J = 7.5$ Hz, 1H), 2.45 (dd, $J = 13.5$, 6.5 Hz, 1H), 2.39 (dd, $J = 13.5$, 8.3 Hz, 1H), 1.30 (d, $J = 7$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 158.2, 138.1, 127.8, 128.5, 127.7, 127.6, 127.3, 114.0, 55.2, 46.2, 43.4, 36.3, 22.0. $[\alpha]_D^{24} = -3.3$ (*c* 1.04, $CDCl_3$) 90% ee (lit.[6g] $[\alpha]_D^{20} = -11.6$ (*c* 1.00, $CDCl_3$) 87% ee).

4.3.16. *N*-Benzyl-3-(4-Chlorophenyl)butyramide 5ec. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.22 (m, 5H), 7.15–7.12 (m, 2H), 7.02–6.98 (m, 2H), 5.61 (s, 1H), 4.40 (dd, $J = 14.8$, 6.4H, 1H), 4.23 (dd, $J = 14.8$, 5.2 Hz, 1H), 3.32 (sext, $J = 8$ Hz, 1H), 2.45 (dd, $J = 14$, 6.8 Hz, 1H), 2.37 (dd, $J = 14$, 8.3 Hz, 1H), 1.29 (d, $J = 7$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 144.1, 128.0, 132.1, 128.7, 128.6, 128.2, 127.5, 127.4, 45.7, 43.4, 36.5, 21.7. IR (KBr) 3309, 3081, 1644, 1552, 1495, 1252 cm^{-1}. Anal. Calcd for $C_{17}H_{18}NOCl$: C, 70.95; H, 6.30; N, 4.87; Cl, 12.32. Found: C, 70.89; H, 6.51; N, 4.73; Cl, 12.18. $[\alpha]_D^{24} = -8.8$ (*c* 0.99, $CDCl_3$) 92% ee.

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