 

# Enantioselective Trifluoromethylation of Ketones with (Trifluoromethyl)trimethylsilane Catalyzed by Chiral Quaternary Ammonium Phenoxides[#]

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Chiral quaternary ammonium phenoxides were prepared readily from commercially available cinchona alkaloids and employed as novel useful asymmetric organocatalysts. Among these chiral quaternary ammonium phenoxides, a cinchonidine-derived phenoxide that possesses a sterically hindered *N*(1)-3,5-bis[3,5-bis(trifluoromethyl)phenyl]benzyl group was the most effective for asymmetric trifluoromethylation. In the presence of a catalytic amount of Lewis bases, such as cinchonidine-derived quaternary ammonium phenoxides, catalyzed the reaction of various ketones with (trifluoromethyl)trimethylsilane to afford the corresponding trifluoromethylated adducts in high yields and with moderate to high enantioselectivities.

In recent years, trifluoromethylated compounds[1] have attracted much interest in the fields of pharmacy and agrochemistry, because their physical, chemical, and biological properties are changed by introducing a strong electron-withdrawing trifluoromethyl group. This group has an electronegativity similar to that of oxygen, and it is highly hydrophobic. Discovery of medicines, such as Befloxatone (antidepressant)[2] and Efavirenz (anti-HIV),[3] of which the trifluoromethyl moiety is located at the asymmetric center, added to the importance of synthesizing of chiral trifluoromethylated compounds. The trifluoroacetyl moiety is usually employed in asymmetric reduction or nucleophilic addition for the synthesis of such compounds as having trifluoromethylated asymmetric carbon moieties.[4] On the other hand, a few methods have been reported on the asymmetric nucleophilic addition of a trifluoromethyl group to ketones.[5] The scope of these methods, however, has remained moderate concerning enantiomeric excess or substrate specificity.

(Trifluoromethyl)trimethylsilane ($TMSCF_3$) is generally known as a useful nucleophilic trifluoromethylating reagent, because the trifluoromethyl anion is extremely labile, liberating a difluorocarbene together with a fluoride ion.[6] As have shown in our previous papers, nitrogen- or oxygen-containing anions are effective Lewis base catalysts in trifluoromethylation for the activation of the carbon–silicon bond of $TMSCF_3$.[7] Recently, we have reported that new types of chiral quaternary ammonium phenoxides can be prepared from commercially available cinchona alkaloids and that the phenoxides thus formed can be employed as asymmetric Lewis base catalysts.[8]

In order to establish an efficient method for the preparation of chiral trifluoromethylated-alcohols and to extend the applicability of this ammonium phenoxides, asymmetric trifluoromethylation of ketones was considered.[9] In this paper, our detailed studies on enantioselective trifluoromethylation of ketones with (trifluoromethyl)trimethylsilane by using cinchonidine-derived quanternary ammonium phenoxides are described.

## Results and Discussion

**Enantioselective Trifluoromethylation of Acetophenones Catalyzed by Cinchonidine-Derived Quaternary Ammonium Phenoxides.** In order to examine catalytic efficiency of the cinchonidine-derived chiral quaternary ammonium phenoxides, reactions of 3-nitroacetophenone (**2a**) with $TMSCF_3$ were performed at $-78\,^{\circ}C$ for 1 h in the presence of 0.1 molar amount of *N*-arylmethylated cinchonidinium phenoxides **1a**–**1j**[8d,10] (Table 1). When catalyst **1a** having a simple phenyl group was used, trifluoromethylation proceeded smoothly to afford trimethyl-$\alpha$-(trifluoromethyl)-$\alpha$-methyl-3-nitorobenzyloxysilane (**3a**) in 93% yield, although the enantioselectivity turned out to be poor (13% ee) (Entry 1). However, the enantioselectivity increased when substituents, such as 2-naphthyl (**1d**), 3,5-dimethoxyphenyl (**1e**), 3,5-bis(trifluoromethyl)phenyl (**1g**), and 3,5-diphenylphenyl (**1h**) groups, were introduced (Entries 4, 5, 7, and 8). It was shown next that the enantiomeric excess of **5a** increased up to 60% ee when catalysts having bulky substituents on the nitrogen atom of cinchonidine, such as **1i** (Ar = 3,5-bis(3,5-di-*tert*-butylphenyl)phenyl or **1j** (Ar = 3,5-bis[3,5-bis(trifluoromethyl)phenyl]phenyl), were used (Entries 9 and 10).

The effects of solvents were then examined (Table 2). When the catalyst **1j** was used in toluene at $-78\,^{\circ}C$, trifluoromethylation did not occur, because the catalyst scarcely dissolved in this solvent (Entry 1). When polar solvents, such as EtCN or THF, were used **3a** was obtained with low enantioselectivity (19% ee or 58% ee, Entries 4 and 5). The enantiomeric excess

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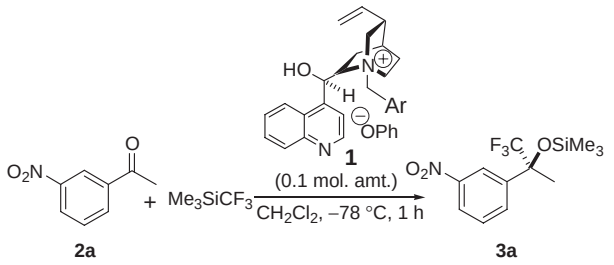
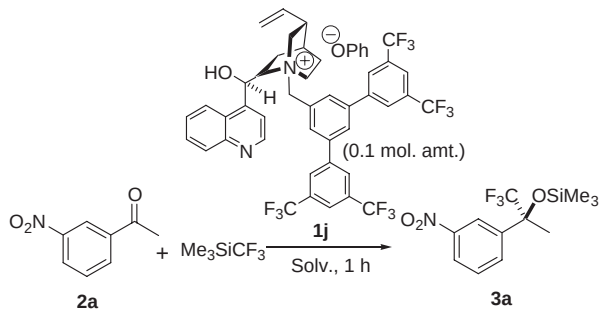
Table 1. Effects of Catalysts




| Entry | Catalyst | Yield[a]/% | ee[b),c]/% |
|---|---|---|---|
| 1 | **1a**: Ar = Ph | 93 | 13 |
| 2 | **1b**: Ar = 2,6-$F_2C_6H_3$ | 98 | 8 |
| 3 | **1c**: Ar = 1-Naphthyl | 99 | 11 |
| 4 | **1d**: Ar = 2-Naphthyl | 97 | 26 |
| 5 | **1e**: Ar = 3,5-$(MeO)_2C_6H_3$ | 97 | 29 |
| 6 | **1f**: Ar = 3,5-$(t\text{-}Bu)_2C_6H_3$ | 96 | 17 |
| 7 | **1g**: Ar = 3,5-$(CF_3)_2C_6H_3$ | 95 | 34 |
| 8 | **1h**: Ar = 3,5-$(Ph)_2C_6H_3$ | 95 | 50 |
| 9 | **1i**: Ar = 3,5-[3,5-$(t\text{-}Bu)_2C_6H_3]_2C_6H_3$ | 99 | 61 |
| 10 | **1j**: Ar = 3,5-[3,5-$(CF_3)_2C_6H_3]_2C_6H_3$ | 99 | 62 |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H) with hexane/2-propanol (volume ratio = 20/1) as an eluent. c) Enantiomeric excess was measured after desilylation of **3a**.

Table 2. Effects of Solvents

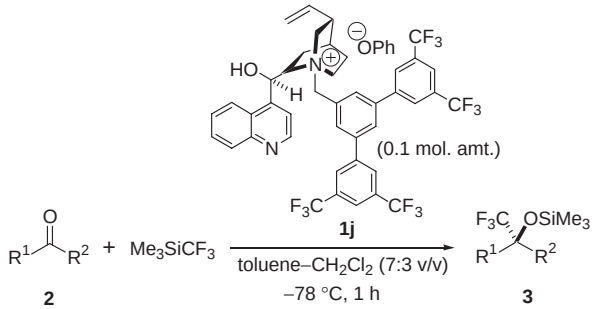



| Entry | Solv. | Temp/°C | Yield[a]/% | ee[b),c]/% |
|---|---|---|---|---|
| 1 | Toluene | −78 | N.R. | — |
| 2 | Toluene | −20 | 99 | 79 |
| 3 | $CH_2Cl_2$ | −20 | 99 | 62 |
| 4 | EtCN | −20 | 65 | 19 |
| 5 | THF | −78 | 92 | 58 |
| 6 | Toluene/$CH_2Cl_2$ = 7/3 | −78 | 98 | 87 |
| 7 | Toluene/$CH_2Cl_2$ = 7/3 | −78 | 90 | 79[d] |
| 8 | Toluene/$CH_2Cl_2$ = 7/3 | −78 | 56 | 71[e] |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H) with hexane/2-propanol (volume ratio = 20:1) as an eluent. c) Enantiomeric excess was measured after desilylation of **3a**. d) Catalyst **1j** (0.05 mol. amt.) was used. e) Catalyst **1j** (0.03 mol. amt.) was used.

of **3a** also increased up to 79% ee in a less-polar solvent, such as toluene at −20 °C (Entry 2). In order to carry out the reaction successfully at lower temperature (−78 °C), the use of a mixed-solvent was examined, and a mixture of toluene–$CH_2Cl_2$ (v/v = 7/3) was found to be most effective, yielding **3a** in 98% yield with a high enantioselectivity (87% ee, Entry 6). Both the yield and the enantioselectivity of this trifluoromethylation decreased when the amount of the catalyst **1j** was reduced (Entries 7 and 8).

Table 3. Enantioselective Synthesis of Trifluoromethylated Silyl Ethers by Using Catalyst **1j**

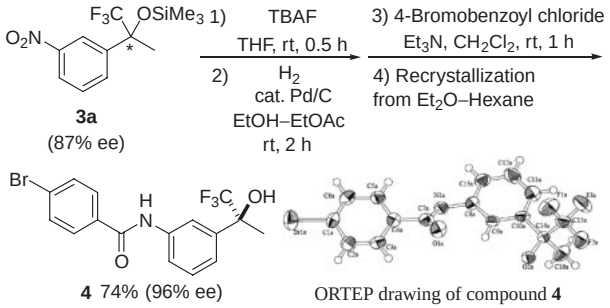



| Entry | $R^1$ | $R^2$ | Product | Yield[a]/% | ee[b]/% |
|---|---|---|---|---|---|
| 1 | 2-$(NO_2)C_6H_4$ | Me | **3b** | 93 | 71[c] |
| 2 | 4-$(NO_2)C_6H_4$ | Me | **3c** | 97 | 73[c] |
| 3 | 3-$(CN)C_6H_4$ | Me | **3d** | 96 | 71[c] |
| 4 | 3-$BrC_6H_4$ | Me | **3e** | 97 | 61[c] |
| 5 | 4-$BrC_6H_4$ | Me | **3f** | 97 | 44[c] |
| 6 | 3-$(MeO)C_6H_4$ | Me | **3g** | 90 | 59[c] |
| 7 | 1-Naphthyl | Me | **3h** | 91 | 51[c] |
| 8 | 2-Naphthyl | Me | **3i** | 95 | 77[c] |
| 9 | 3-Pyridyl | Me | **3j** | 90 | 46 |
| 10 | 4-Pyridyl | Me | **3k** | 93 | 60 |
| 11 | 2-Thienyl | Me | **3l** | 72 | 33[c] |
| 12 | 3-$(NO_2)C_6H_4$ | Et | **3m** | 99 | 64[c] |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H or Chiralpak AD-H) with hexane/2-propanol (volume ratio = 20:1 or 30:1) as an eluent. c) Enantiomeric excess was measured after desilylation of **3**.

Next, reactions of $TMSCF_3$ with various ketones were performed in the presence of cinchonidine-derived quaternary ammonium phenoxide **1j** in toluene–$CH_2Cl_2$ (v/v = 7/3) at −78 °C for 1 h (Table 3). In most cases, acetophenones **2** having electron-withdrawing or -donating group reacted smoothly to afford the corresponding trifluoromethylated silyl ethers in high yields with moderate to good enantioselectivities (Entries 1–6). When ketones having naphthyl group were employed, enantioselectivities were influenced by the naphthyl group on the linked position (Entries 7 and 8). Further, ketones having heteroaromatic rings, such as pyridyl group or thienyl group, afforded the corresponding trifluoromethylated adducts in good yields with moderate enantioselectivities (Entries 9–11), whereas the use of 3-nitropropiophenone decreased the enantioselectivity.

The absolute configuration of trifluoromethylated compound **3a** was determined to be *S* by X-ray crystallographic analysis, after being derivatized to the corresponding carboxamide **4**, as shown in Scheme 1. Desilylation of the adduct **3a** was accomplished by using TBAF, followed by catalytic hydrogenation using Pd/C under hydrogen atmosphere and subsequently acylation with 4-bromobenzoyl chloride. Recrystallization from $Et_2O$/hexane afforded 4-bromobenzoate




Scheme 1. Conversion of **3a** to carboxamide **4** and determination of their absolute configurations.

derivative **4** as a crystalline compound, which was clearly identified by X-ray crystallographic analysis.[11]

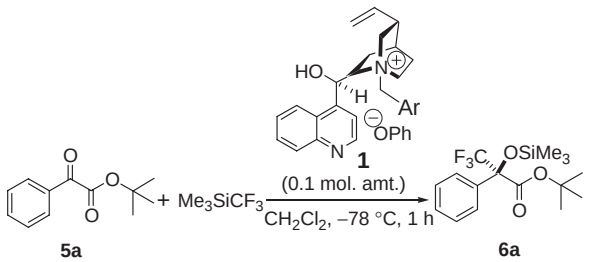
**Enantioselective Trifluoromethylation of α-Ketoesters Catalyzed by Cinchonidine-Derived Quaternary Ammonium Phenoxides.** Mosher's acid (MTPA) is a quite useful reagent for determining the enantiomeric excess of alcohols or amines, and many preparative methods have been reported.[12] Although MTPA acts as a convenient reagent, it is not extensively used, because the signals of certain diastereotopic groups from the MTPA overlap each other. Since a few chiral MTPA analogues[13,14] have successfully been employed, enantioselective trifluoromethylation of α-ketoesters was considered next for establishing an efficient method of preparating MTPA derivatives.

First, reaction of *t*-butyl 2-oxo-2-phenylacetate (**5a**)[15] with $TMSCF_3$ in the presence of 0.1 molar amount of various cinchonidine-derived quaternary ammonium phenoxides **1a**–**1j** in $CH_2Cl_2$ at −78 °C for 1 h were tried (Table 4). When catalysts **1** having substituents on the nitrogen atom of cinchonidine, such as benzyl group (**1a**), 2,6-difluorophenyl group (**1b**), 1-naphthylmethyl group (**1c**), or 2-naphthylmethyl group (**1d**), were used, trifluoromethylation proceeded smoothly to afford the corresponding trifluoromethylated adduct **6a** in high yields with poor enantioselectivities (Entries 1–4). Introduction of substituents, such as 3,5-dimethoxyphenyl group (**1e**), 3,5-bis(trifluoromethyl)phenyl group (**1g**), 3,5-diphenylphenyl group (**1h**), or 3,5-bis(3,5-di-*tert*-butylphenyl)phenyl group (**1i**) to aromatic substituents (Ar), enhanced the enantioselectivities slightly (Entries 5 and 7–9). Further, cinchonidine-derived catalyst **1j** that possessed a *N*(1)-3,5-bis[3,5-bis(trifluoromethyl)-phenyl]benzyl group was found to be most effective, affording (*R*)-(+)-**6a**[12c,16] in 99% yield with 60% ee (Entry 10). Trifluoromethylation with 0.05 molar amount of the catalyst **1j** and a longer reaction time (6 h) did not influence the yield or the enantioselectivity (Entry 11). Also, the trifluoromethylated adduct **6a** was not detected when amount of the catalyst **1j** was reduced to 0.03 molar amount (Entry 12).

Next, effects of solvents were examined (Table 5) and better results were obtained when $CH_2Cl_2$ was used. On the other hand, the enantioselectivities decreased when solvents such as toluene, THF, $Et_2O$, or AcOEt were used (21% ee, 34% ee, 49% ee, or 42% ee, Entries 1–4). Then, the reaction was attempted in a less-polar solvent such as hexane/$CH_2Cl_2$ (v/v = 1/1); however, no significant improvement in enantiomeric excess was observed (Entry 6).

Effects of the alkyl substituents (R) contained in the α-ketoesters were studied next in order to improve the enantioselectivity of the above-mentioned reaction (Table 6). Introduction of less hindered substituents, such as methyl group

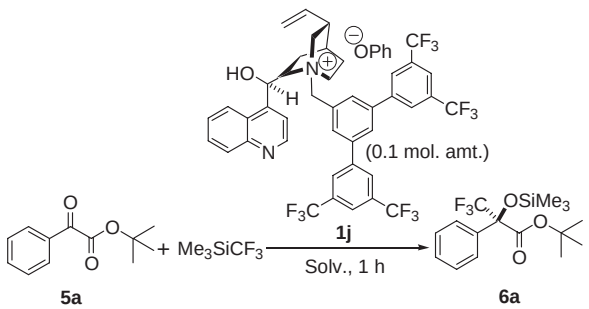
Table 4. Effects of Catalysts




| Entry | Catalyst | Yield[a] /% | ee[b),c] /% |
|---|---|---|---|
| 1 | **1a**: Ar = Ph | 86 | 10 |
| 2 | **1b**: Ar = 2,6-$F_2C_6H_3$ | 96 | 3 |
| 3 | **1c**: Ar = 1-Naphthyl | 92 | 15 |
| 4 | **1d**: Ar = 2-Naphthyl | 95 | 20 |
| 5 | **1e**: Ar = 3,5-$(MeO)_2C_6H_3$ | 77 | 31 |
| 6 | **1f**: Ar = 3,5-(*t*-Bu)$_2C_6H_3$ | 77 | 11 |
| 7 | **1g**: Ar = 3,5-$(CF_3)_2C_6H_3$ | 89 | 31 |
| 8 | **1h**: Ar = 3,5-$(Ph)_2C_6H_3$ | 84 | 37 |
| 9 | **1i**: Ar = 3,5-[3,5-(*t*-Bu)$_2C_6H_3$]$_2C_6H_3$ | 95 | 31 |
| 10 | **1j**: Ar = 3,5-[3,5-$(CF_3)_2C_6H_3$]$_2C_6H_3$ | 99 | 60 |
| 11 | **1j**: Ar = 3,5-[3,5-$(CF_3)_2C_6H_3$]$_2C_6H_3$ | 94 | 58[d),e] |
| 12 | **1j**: Ar = 3,5-[3,5-$(CF_3)_2C_6H_3$]$_2C_6H_3$ | N.D.[f] | — |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralpak AD-H) with hexane/2-propanol (volume ratio = 50:1) as an eluent. c) Enantiomeric excess was measured after desilylation of **6a**. d) Catalyst (0.05 mol. amt.) was used. e) Reaction was carried out for 6 h. f) Catalyst (0.03 mol. amt.) was used.

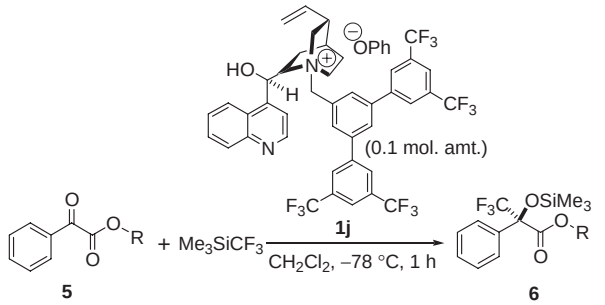
Table 5. Effects of Solvents




| Entry | Solv. | Temp/°C | Yield[a] /% | ee[b),c] /% |
|---|---|---|---|---|
| 1 | Toluene | −20 | 99 | 21 |
| 2 | THF | −78 | 99 | 34 |
| 3 | $Et_2O$ | −60 | 99 | 49 |
| 4 | AcOEt | −78 | 98 | 42 |
| 5 | $CH_2Cl_2$ | −78 | 99 | 60 |
| 6 | Hexane/$CH_2Cl_2$ = 1/1 | −65 | 95 | 45 |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralpak AD-H) with hexane/2-propanol (volume ratio = 50:1) as an eluent. c) Enantiomeric excess was measured after desilylation of **6a**.

Table 6. Effects of Alkyl Substituents R in $\alpha$-Ketoesters




5 6

| Entry | | R | Product | Yield[a]/% | ee[b),c)]/% |
|---|---|---|---|---|---|
| 1 | **5b**: | Me | **6b** | 90 | 31 |
| 2 | **5c**: | Et | **6c** | 86 | 38 |
| 3 | **5a**: | *t*-Bu | **6a** | 99 | 60 |
| 4 | **5d**: | $C(Me)_2CH_2CH_2Ph$ | **6d** | 91 | 33 |
| 5 | **5e**: | 1-Adamantyl | **6e** | 93 | 14 |

a) Isolated yield. b) Enantiomeric excess was determined by HPLC analysis using a chiral column (DAICEL Chiralpak AD-H) with hexane/2-propanol (volume ratio = 50:1) as an eluent. c) Enantiomeric excess was measured after desilylation of **6**.

(**5b**) or ethyl group (**5c**) instead of *tert*-butyl group (**5a**), decreased the enantioselectivity (Entries 1 and 2). On the other hand, the enantiomeric excess of **6** decreased considerably compared to that of **5a** when $\alpha$-ketoesters having a bulky substituent, such as 1-adamantyl (**5e**) group were used (Entry 5). In other words, the alkyl substituents R in the $\alpha$-ketoesters play important roles in controlling the enantioselectivities of this asymmetric trifluoromethylation.

## Conclusion

Enantioselective trifluoromethylation of various ketones with (trifluoromethyl)trimethylsilane was established. A cinchonidine-derived catalyst with a sterically hindered *N*(1)-3,5-bis[3,5-bis(trifluoromethyl)phenyl]benzyl group was found to work effectively as a chiral Lewis base catalyst in this asymmetric nucleophilic addition of a trifluoromethyl group via activation of the carbon–silicon bond of $TMSCF_3$. Optically active trifluoromethylated silyl ethers were synthesized in high yields with moderate to high enantioselectivities. Further studies on the use of chiral quaternary ammonium phenoxides in other catalytic asymmetric reactions, particularly the use of organosilicon reagents, are now in progress.

## Experimental

**General.** All melting points were determined on a Yanagimoto micro melting apparatus (Yanaco MP-S3) and are uncorrected. Infrared (IR) spectra were recorded by using an attenuated total reflection (ATR) method on a SensIR Technologies Travel *IR*™ spectrometer. $^1$H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts ($\delta$) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. $^{13}$C NMR spectra were recorded on EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane, with the solvent resonance as the internal standard ($CDCl_3$; $\delta$ 77.0, DMSO-$d_6$; $\delta$ 39.5), High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700V mass instrument or a micromass Q-Tof-2 instrument. Elemental analyses were conducted using a Yanaco MT-5 CHN Corder. Analytical high-performance liquid chromatography (HPLC) was performed on a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator. Enantiomeric excess (ee) was determined by HPLC analysis using a chiral column (DAICEL Chiralcel OD-H or Chiralpak AD-H, $\Phi 4.6 \times 250$ mm) with hexane/2-propanol as an eluent. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Column chromatography was carried out on Merck silica gel 60 (0.063–0.200 mm) or Kanto silica gel 60 N (neutral). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise noted. Dehydrated solvents were purchased from Kanto Chemical. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, Wako Pure Chemical Industries, or Aldrich. (Trifluoromethyl)trimethylsilane was purchased from Tokyo Kasei Kogyo and used without further purification. Cinchonidine-derived chiral quaternary ammonium phenoxides were prepared according to the reported procedures.[8d] $\alpha$-Ketoesters (**5a**, **5d**, and **5e**) were prepared by using the literature procedures.[15]

**Typical Experimental Procedure for Asymmetric Trifluoromethylation of Acetophenones by Using Cinchonidine-Derived Catalyst 1j (Table 2, Entry 5).** To a stirred solution of **1j** (27 mg, 0.03 mmol) in toluene–$CH_2Cl_2$ (7:3, 0.6 mL) were successively added a solution of 3-nitroacetophenone (49.5 mg, 0.3 mmol) in toluene–$CH_2Cl_2$ (7:3, 0.8 mL) and a solution of (trifluoromethyl)trimethylsilane (59.7 mg, 0.42 mmol) in toluene–$CH_2Cl_2$ (7:3, 0.8 mL) at $-78$ °C. After the mixture was stirred for 1 h at the same temperature, it was quenched with sat. $NH_4Cl$ (aq), and the mixture was extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, and the solvent was evaporated. The crude product was purified by preparative TLC (hexane/EtOAc = 8/1) to give the corresponding adduct **3a** (90.3 mg, 98% yield). The enantiomeric excess was measured after desilylation of **3a** and determined by HPLC analysis (87% ee).

**Trimethyl-$\alpha$-(trifluoromethyl)-$\alpha$-methyl-3-nitrobenzyloxysilane (3a):** Colorless oil; $[\alpha]_D^{13} = +25.4°$ ($c = 1.00$ in $CHCl_3$, 87% ee); IR (ATR) 2962, 1532, 1349, 1163, 841 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 8.42 (s, 1H), 8.22 (d, $J = 8.0$ Hz, 1H), 7.90 (d, $J = 8.0$ Hz, 1H), 7.58 (t, $J = 8.0$ Hz, 1H), 1.88 (s, 3H), 0.20 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 148.0, 142.3, 132.8, 129.0, 124.6 (q, $J_{C-F} = 286$ Hz), 123.4, 122.0, 76.8 (q, $J_{C-C-F} = 30$ Hz), 22.7, 2.0; Anal. Calcd for $C_{12}H_{16}F_3NO_3Si$: C, 46.90; H, 5.25; N, 4.56%. Found: C, 46.68; H, 5.02; N, 4.52%; HPLC analysis (The enantiomeric excess was measured after desilylation of **3a**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 12.3 min (minor) and 15.2 min (major).

**Trimethyl-$\alpha$-(trifluoromethyl)-$\alpha$-methyl-2-nitrobenzyloxysilane (3b):** Colorless oil; $[\alpha]_D^{17} = +46.9°$ ($c = 0.76$ in $CHCl_3$, 71% ee); IR (ATR) 2962, 1539, 1163, 843 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.54–7.40 (m, 3H), 7.38–7.29 (m, 1H), 1.87 (s, 3H), 0.21 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 150.4, 131.0, 129.8, 129.5, 128.7, 124.7 (q, $J_{C-F} = 287$ Hz), 123.9, 78.1 (q, $J_{C-C-F} = 30$ Hz), 24.0, 1.5; Anal. Calcd for $C_{12}H_{16}F_3NO_3Si$: C, 46.90; H, 5.25; N, 4.56%. Found: C, 46.58; H, 4.87; N, 4.72%; HPLC analysis (The enantiomeric excess was measured after

desilylation of **3b**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 13.8 min (minor) and 18.7 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-4-nitrobenzyloxysilane (3c):** Colorless oil; $[\alpha]_D^{17} = +17.6^\circ$ ($c = 0.92$ in $CHCl_3$, 73% ee); IR (ATR) 2962, 1525, 1163, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 8.23 (d, $J$ = 8.6 Hz, 2H), 7.73 (d, $J$ = 8.6 Hz, 2H), 1.87 (s, 3H), 0.20 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 147.9, 147.0, 127.8, 124.6 (q, $J_{C-F}$ = 285 Hz), 123.1, 77.1 (q, $J_{C-C-F}$ = 30 Hz), 22.8, 2.1; Anal. Calcd for $C_{12}H_{16}F_3NO_3Si$: C, 46.90; H, 5.25; N, 4.56%. Found: C, 46.82; H, 5.38; N, 4.58%; HPLC analysis (The enantiomeric excess was measured after desilylation of **3c**): DAICEL Chiralcel OD-H, hexane/2-propanol = 30/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 17.6 min (minor) and 19.2 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-3-cyanobenzyloxysilane (3d):** Colorless oil; $[\alpha]_D^{14} = +28.0^\circ$ ($c = 0.74$ in $CHCl_3$, 71% ee); IR (ATR) 2962, 2232, 1164, 842 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.84 (s, 1H), 7.78 (d, $J$ = 7.9 Hz, 1H), 7.65 (d, $J$ = 7.9 Hz, 1H), 7.50 (t, $J$ = 7.9 Hz, 1H), 1.83 (s, 3H), 0.23 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 141.6, 131.9, 131.1, 130.5, 128.8, 124.6 (q, $J_{C-F}$ = 286 Hz), 118.5, 112.3, 76.7 (q, $J_{C-C-F}$ = 30 Hz), 22.5, 2.0; Anal. Calcd for $C_{13}H_{16}F_3NOSi$: C, 54.34; H, 5.61; N, 4.87%. Found: C, 54.39; H, 5.51; N, 4.92%; HPLC analysis (The enantiomeric excess was measured after desilylation of **3d**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 14.1 min (minor) and 19.6 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-3-bromobenzyloxysilane (3e):** Colorless oil; $[\alpha]_D^{17} = +23.7^\circ$ ($c = 1.10$ in $CHCl_3$, 61% ee); IR (ATR) 2961, 1160, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.67 (s, 1H), 7.53–7.44 (m, 2H), 7.28–7.24 (m, 1H), 1.80 (s, 3H), 0.16 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 142.3, 131.4, 130.0, 129.5, 125.4, 124.8 (q, $J_{C-F}$ = 285 Hz), 122.1, 76.8 (q, $J_{C-C-F}$ = 30 Hz), 22.7, 2.1; HRMS (EI positive) calcd for $C_{12}H_{16}BrF_3OSi$ M$^+$ 340.0106, found $m/z$ 340.0108; HPLC analysis (The enantiomeric excess was measured after desilylation of **3e**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 7.8 min (minor) and 11.3 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-4-bromobenzyloxysilane (3f):** Colorless oil; $[\alpha]_D^{26} = +22.1^\circ$ ($c = 1.04$ in $CHCl_3$, 44% ee); IR (ATR) 2961, 1161, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.50 (d, $J$ = 8.4 Hz, 2H), 7.41 (d, $J$ = 8.4 Hz, 2H), 1.80 (s, 3H), 0.15 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 139.1, 131.1, 128.6, 124.9 (q, $J_{C-F}$ = 285 Hz), 122.7, 76.9 (q, $J_{C-C-F}$ = 30 Hz), 22.6, 2.1; Anal. Calcd for $C_{12}H_{16}BrF_3OSi$: C, 42.24; H, 4.73%. Found: C, 41.91; H, 4.57%; HPLC analysis (The enantiomeric excess was measured after desilylation of **3f**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 7.2 min (minor) and 8.9 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-3-methoxybenzyloxysilane (3g):** Colorless oil; $[\alpha]_D^{17} = +27.3^\circ$ ($c = 1.14$ in $CHCl_3$, 59% ee); IR (ATR) 2959, 1163, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.32–7.25 (m, 1H), 7.16–7.06 (m, 1H), 6.92–6.85 (m, 1H), 3.82 (s, 3H), 1.81 (s, 3H), 0.15 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 159.1, 141.5, 128.8, 125.1 (q, $J_{C-F}$ = 285 Hz), 119.0, 113.3, 113.1, 77.0 (q, $J_{C-C-F}$ = 29 Hz), 55.1, 22.8, 2.0; HRMS (EI positive) calcd for $C_{13}H_{19}F_3O_2Si$ M$^+$ 292.1106, found $m/z$ 292.1112; HPLC analysis (The enantiomeric excess was measured after desilylation of **3g**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 13.8 min (minor) and 23.4 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-1-naphthylmethyloxysilane (3h):** Colorless oil; $[\alpha]_D^{17} = +43.0^\circ$ ($c = 0.53$ in $CHCl_3$, 51% ee); IR (ATR) 2962, 1155, 1099, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 8.93–8.84 (m, 1H), 7.84 (d, $J$ = 7.3 Hz, 2H), 7.62–7.38 (m, 4H), 2.06 (s, 3H), −0.05 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 135.1, 134.5, 132.0, 130.2, 128.6, 128.3, 126.3, 126.2, 125.4, 124.3, 123.7 (q, $J_{C-F}$ = 287 Hz), 79.8 (q, $J_{C-C-F}$ = 30 Hz), 25.3, 1.6; HRMS (EI positive) calcd for $C_{16}H_{19}F_3OSi$ M$^+$ 312.1157, found $m/z$ 312.1154; HPLC analysis (The enantiomeric excess was measured after desilylation of **3h**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 14.4 min (minor) and 26.2 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-2-naphthylmethyloxysilane (3i):** Colorless oil; $[\alpha]_D^{15} = +34.4^\circ$ ($c = 0.53$ in $CHCl_3$, 77% ee); IR (ATR) 2961, 1159, 1100, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.98 (s, 1H), 7.95–7.82 (m, 3H), 7.68 (d, $J$ = 8.6 Hz, 1H), 7.58–7.45 (m, 2H), 1.94 (s, 3H), 0.17 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 137.3, 132.9, 132.6, 128.3, 127.5, 127.4, 126.4, 126.1, 126.0, 125.2 (q, $J_{C-F}$ = 286 Hz), 124.5, 77.2 (q, $J_{C-C-F}$ = 29 Hz), 22.8, 2.1; HRMS (EI positive) calcd for $C_{16}H_{19}F_3OSi$ M$^+$ 312.1157, found $m/z$ 312.1154; HPLC analysis (The enantiomeric excess was measured after desilylation of **3i**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 14.6 min (minor) and 25.2 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-3-pyridylmethyloxysilane (3j):** Colorless oil; $[\alpha]_D^{16} = +18.1^\circ$ ($c = 0.97$ in $CHCl_3$, 46% ee); IR (ATR) 2961, 1162, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 8.78 (s, 1H), 8.59 (d, $J$ = 4.8 Hz, 1H), 7.85 (d, $J$ = 8.1 Hz, 1H), 7.37–7.28 (m, 1H), 1.85 (s, 3H), 0.17 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 149.3, 148.0, 135.4, 134.3, 124.7 (q, $J_{C-F}$ = 285 Hz), 122.6, 76.0 (q, $J_{C-C-F}$ = 30 Hz), 22.8, 2.1; HRMS (EI positive) calcd for $C_{11}H_{16}F_3NOSi$ M$^+$ 263.0953, found $m/z$ 263.0956; HPLC analysis: DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 6.1 min (minor) and 8.4 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-4-pyridylmethyloxysilane (3k):** Colorless oil; $[\alpha]_D^{14} = +21.6^\circ$ ($c = 1.00$ in $CHCl_3$, 60% ee); IR (ATR) 2962, 1163, 841 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 8.63 (d, $J$ = 5.4 Hz, 2H), 7.43 (d, $J$ = 5.4 Hz, 2H), 1.80 (s, 3H), 0.19 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 149.6, 148.9, 124.6 (q, $J_{C-F}$ = 285 Hz), 121.4, 76.6 (q, $J_{C-C-F}$ = 30 Hz), 22.4, 2.0; HRMS (EI positive) calcd for $C_{11}H_{16}F_3NOSi$ M$^+$ 263.0953, found $m/z$ 263.0962; HPLC analysis: DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 6.1 min (minor) and 8.7 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-2-thienylmethyloxysilane (3l):** Colorless oil; $[\alpha]_D^{27} = +25.2^\circ$ ($c = 0.80$ in $CHCl_3$, 33% ee); IR (ATR) 2962, 1163, 1101, 840 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.35–7.29 (m, 1H), 7.09–7.05 (m, 1H), 7.03–6.96 (m, 1H), 1.85 (s, 3H), 0.15 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 144.5, 126.7, 125.8, 125.5, 124.6 (q, $J_{C-F}$ = 285 Hz), 76.1 (q, $J_{C-C-F}$ = 31 Hz), 23.8, 1.9; HRMS (EI positive) calcd for $C_{10}H_{15}F_3OSSi$ M$^+$ 268.0565, found $m/z$ 268.0573; HPLC analysis (The enantiomeric excess was measured after desilylation of **3l**): DAICEL Chiralpak AD-H, hexane/2-propanol = 20/1, $\lambda$ = 254 nm, flow rate = 1.0 mL min$^{-1}$, retention time = 7.9 min (minor) and 8.7 min (major).

**Trimethyl-α-(trifluoromethyl)-α-methyl-3-nitrophenylethyl-**

**oxysilane (3m):** Colorless oil; $[\alpha]_D^{16} = -6.0^\circ$ ($c = 0.91$ in $CHCl_3$, 64% ee); IR (ATR) 2961, 1533, 1163, 842 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 8.39 (s, 1H), 8.21 (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 8.0$ Hz, 2H), 7.56 (t, $J = 8.0$ Hz, 1H), 2.30–2.09 (m, 2H), 0.71 (t, $J = 7.4$ Hz, 3H), 0.29 (s, 9H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 148.1, 140.3, 132.8, 129.0, 125.1 (q, $J_{C-F} = 287$ Hz), 123.1, 122.1, 80.4 (q, $J_{C-C-F} = 29$ Hz), 27.2, 6.9, 1.7; Anal. Calcd for $C_{13}H_{18}F_3NO_3Si$: C, 48.59; H, 5.65; N, 4.36%. Found: C, 48.63; H, 5.49; N, 4.44%; HPLC analysis (The enantiomeric excess was measured after desilylation of **3m**): DAICEL Chiralcel OD-H, hexane/2-propanol = 20/1, $\lambda = 254$ nm, flow rate = 1.0 mL $min^{-1}$, retention time = 14.1 min (major) and 16.2 min (minor).

**3′-(2,2,2-Trifluoro-1-hydroxy-1-methylethyl)-4-bromobenzanilide (4).** To a stirred solution of **3a** (600 mg, 1.95 mmol, 87% ee) in THF (6 mL) was added tetrabutylammonium fluoride (1 mol $L^{-1}$ in THF; 3.9 mL, 3.9 mmol) at room temperature. After the mixture was stirred for 0.5 h at the same temperature, it was quenched with sat. $NH_4Cl$ (aq), and the mixture was extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, and the solvent was evaporated. Pd/C (10%; 46 mg) was added to a solution of the residue in EtOH/AcOEt (1:1; 6 mL), and the mixture was stirred under hydrogen at ambient temperature for 2 h. The reaction mixture was then filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. 4-Bromobenzoyl chloride (450 mg, 2.05 mmol) and triethylamine (326 μL, 2.34 mmol) were added successively to a solution of the residue in $CH_2Cl_2$ (6 mL) at 0 °C. The mixture was stirred for 1 h at the same temperature, quenched with sat. $NH_4Cl$ (aq), and extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, and the solvent was evaporated. The crude product was purified by column chromatography ($SiO_2$; hexane/EtOAc = 2/1) and recrystallized from $Et_2O$/hexane to afford the corresponding carboxamide **4** (560 mg, 74% yield) as colorless crystals. $[\alpha]_D^{17} = -4.3^\circ$ ($c = 0.35$ in $CHCl_3$, 96% ee); IR (ATR) 3339, 1657, 1531, 1484, 1433, 1307, 1287, 1257, 1172, 1154, 1085, 1069, 1007 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.87–7.72 (m, 5H), 7.64 (d, $J = 7.7$ Hz, 2H), 7.45–7.32 (m, 2H), 2.58 (s, 1H), 1.81 (s, 3H); $^{13}C$ NMR (68 MHz, DMSO-$d_6$) $\delta$ 164.4, 140.3, 138.6, 133.7, 131.2, 129.7, 128.1, 125.3, 124.9 (q, $J_{C-F} = 286$ Hz), 121.8, 120.0, 118.6, 73.2 (q, $J_{C-C-F} = 29$ Hz), 23.1; Anal. Calcd for $C_{16}H_{13}BrF_3NO_2$: C, 49.51; H, 3.38; N, 3.61%. Found: C, 49.52; H, 3.41; N, 3.55%; HPLC analysis: DAICEL Chiralpak AD-H, hexane/2-propanol = 10/1, $\lambda = 254$ nm, flow rate = 1.0 mL $min^{-1}$, retention time = 24.4 min (*R*) and 37.6 min (*S*).

**X-ray Crystal Structure Analyses of 4:** $C_{16}H_{13}BrF_3NO_2$ (FW: 388.18), monoclinic, $P2_1$, $a = 13.089(5)$ Å, $b = 6.456(2)$ Å, $c = 18.059(5)$ Å, $\beta = 93.74(3)^\circ$, $V = 1522.7(9)$ $Å^3$, $Z = 4.0$, $D_{calcd} = 1.693$ g $cm^{-3}$, $T = 295$ K. X-ray intensities were measured on a Rigaku AFC-5S diffractometer with graphite-monochromated Mo K$\alpha$ radiation ($\lambda = 0.710690$ Å). The final *R* factors was 0.043 ($Rw = 0.130$ for all data) for 3441 reflections with $I > 2\sigma(I)$. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition number CCDC-655383. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

***t*-Butyl 2-Oxo-2-phenylacetate (5a).**[15] Colorless oil; IR (ATR) 1726, 1688, 1212, 1147, 983 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 8.00–7.93 (m, 2H), 7.67–7.59 (m, 1H), 7.54–7.45 (m, 2H), 1.63 (s, 9H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 186.5, 163.5, 134.4, 132.2, 129.6, 128.6, 84.6, 28.0.

**1,1-Dimethyl-3-phenylpropyl 2-Oxo-2-phenylacetate (5d).** Colorless oil; IR (ATR) 1725, 1688, 1198, 1167, 981 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 8.02–7.96 (m, 2H), 7.68–7.60 (m, 1H), 7.55–7.46 (m, 2H), 7.32–7.14 (m, 5H), 2.77–2.66 (m, 2H), 2.25–2.15 (m, 2H), 1.70 (s, 6H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 186.5, 163.5, 141.4, 134.6, 132.3, 129.8, 128.8, 128.3, 128.2, 125.8, 86.5, 42.9, 30.3, 26.1; HRMS (FAB+) calcd for $C_{19}H_{21}O_3$ $[M + H]^+$ 297.1491, found 297.1510.

**1-Adamantyl 2-Oxo-2-phenylacetate (5e).** White powder; mp 65–66 °C; IR (ATR) 2909, 1720, 1684, 1202, 1175 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 8.02–7.92 (m, 2H), 7.69–7.59 (m, 1H), 7.55–7.45 (m, 2H), 2.34–2.18 (m, 9H), 1.77–1.65 (m, 2H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 186.5, 163.5, 141.4, 134.6, 132.3, 129.8, 128.8, 128.3, 128.2, 125.8, 86.5, 42.9, 30.3, 26.1; Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09%. Found: C, 75.91; H, 7.05%.

**Typical Experimental Procedure for Asymmetric Trifluoromethylation of α-Ketoesters by Using Cinchonidine-Derived Catalyst 1j (Table 4, Entry 10).** To a stirred solution of **1j** (27 mg, 0.03 mmol) in $CH_2Cl_2$ (0.6 mL) were successively added a solution of *t*-butyl 2-oxo-2-phenylacetate (61.9 mg, 0.3 mmol) in $CH_2Cl_2$ (0.8 mL) and a solution of (trifluoromethyl)trimethylsilane (59.7 mg, 0.42 mmol) in $CH_2Cl_2$ (0.8 mL) at −78 °C. After the mixture was stirred for 1 h at the same temperature, it was quenched with sat. $NH_4Cl$ (aq), and the mixture was extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$, and the solvent was evaporated. The crude product was purified by preparative TLC (hexane/EtOAc = 8/1) to give the corresponding adduct **6a** (103.4 mg, 99% yield). The enantiomeric excess was measured after desilylation of **6a** and determined by HPLC analysis (60% ee).

***t*-Butyl 3,3,3-Trifluoro-2-(trimethylsiloxy)-2-phenylpropanoate (6a):** Colorless oil; $[\alpha]_D^{28} = +22.7^\circ$ ($c = 1.00$ in $CHCl_3$, 60% ee); IR (ATR) 2981, 1747, 1251, 1180, 1148, 839 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.64–7.55 (m, 2H), 7.41–7.34 (m, 3H), 1.55 (s, 9H), 0.20 (s, 9H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 166.5, 135.4, 129.0, 128.1, 126.5, 126.4, 123.3 (q, $J_{C-F} = 286$ Hz), 84.3, 81.4 (q, $J_{C-C-F} = 29$ Hz), 27.9, 1.8; HRMS (ESI positive) calcd for $C_{16}H_{23}F_3O_3SiNa$ $[M + Na]^+$ 371.1266, found *m/z* 371.1273; HPLC analysis (The enantiomeric excess was measured after desilylation of **6a**): DAICEL Chiralpak AD-H, hexane/2-propanol = 50/1, $\lambda = 254$ nm, flow rate = 1.0 mL $min^{-1}$, retention time = 8.3 min (minor) and 9.5 min (major).

**Methyl 3,3,3-Trifluoro-2-(trimethylsiloxy)-2-phenylpropanoate (6b):** Colorless oil; $[\alpha]_D^{27} = +22.3^\circ$ ($c = 1.23$ in $CHCl_3$, 31% ee); IR (ATR) 2959, 1755, 1252, 1182, 1152, 843 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.58–7.50 (m, 2H), 7.41–7.34 (m, 3H), 3.86 (s, 3H); 0.17 (s, 9H); $^{13}C$ NMR (68 MHz, $CDCl_3$) $\delta$ 168.1, 134.7, 129.3, 128.2, 126.4, 126.3, 123.0 (q, $J_{C-F} = 286$ Hz), 81.2 (q, $J_{C-C-F} = 29$ Hz), 52.9, 1.4; HRMS (ESI positive) calcd for $C_{13}H_{18}F_3O_3Si$ $[M + H]^+$ 307.0977, found *m/z* 307.0976; HPLC analysis (The enantiomeric excess was measured after desilylation of **6b**): DAICEL Chiralpak AD-H, hexane/2-propanol = 50/1, $\lambda = 254$ nm, flow rate = 1.0 mL $min^{-1}$, retention time = 11.6 min (minor) and 14.0 min (major).

**Ethyl 3,3,3-Trifluoro-2-(trimethylsiloxy)-2-phenylpropanoate (6c):** Colorless oil; $[\alpha]_D^{27} = +23.8^\circ$ ($c = 1.14$ in $CHCl_3$, 38% ee); IR (ATR) 2962, 1752, 1250, 1183, 1153, 844 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.61–7.45 (m, 2H), 7.41–7.32 (m, 3H), 4.42–4.22 (m, 2H), 1.33 (t, $J = 7.1$ Hz, 3H), 0.18 (s, 9H); $^{13}C$ NMR

(68 MHz, $CDCl_3$) $\delta$ 167.7, 134.9, 129.2, 128.2, 126.4, 126.3, 123.1 (q, $J_{C-F} = 286$ Hz), 81.2 (q, $J_{C-C-F} = 30$ Hz), 62.6, 14.0, 1.6; HRMS (ESI positive) calcd for $C_{23}H_{29}F_3O_3SiNa$ $[M + Na]^+$ 461.1736, found $m/z$ 461.1744; HPLC analysis (The enantiomeric excess was measured after desilylation of **6c**): DAICEL Chiralpak AD-H, hexane/2-propanol = 50/1, $\lambda = 254$ nm, flow rate = 1.0 mL min$^{-1}$, retention time = 10.5 min (minor) and 12.0 min (major).

**1,1-Dimethyl-3-phenylpropyl 3,3,3-Trifluoro-2-(trimethylsiloxy)-2-phenylpropanoate (6d):** Colorless oil; $[\alpha]_D^{27} = +12.8^\circ$ ($c = 1.19$ in $CHCl_3$, 33% ee); IR (ATR) 2958, 1746, 1250, 1183, 1153, 842 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.68–7.60 (m, 2H), 7.41–7.35 (m, 3H), 7.32–7.09 (m, 6H), 2.63 (t, $J = 8.6$ Hz, 2H), 2.18–1.97 (m, 2H), 1.62 (s, 6H), 0.21 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 166.6, 141.6, 135.4, 129.1, 128.3, 128.2, 128.1, 126.5, 125.8, 123.4 (q, $J_{C-F} = 286$ Hz), 86.2, 81.5 (q, $J_{C-C-F} = 30$ Hz), 43.7, 30.1, 25.8, 25.5, 1.8; HRMS (ESI positive) calcd for $C_{14}H_{20}F_3O_3Si$ $[M + H]^+$ 321.1134, found $m/z$ 321.1135; HPLC analysis (The enantiomeric excess was measured after desilylation of **6d**): DAICEL Chiralpak AD-H, hexane/2-propanol = 50/1, $\lambda = 254$ nm, flow rate = 1.0 mL min$^{-1}$, retention time = 14.7 min (minor) and 16.7 min (major).

**1-Adamantyl 3,3,3-Trifluoro-2-(trimethylsiloxy)-2-phenylpropanoate (6e):** White powder; mp 61–63 °C; $[\alpha]_D^{27} = +6.9^\circ$ ($c = 0.80$ in $CHCl_3$, 14% ee); IR (ATR) 2913, 1741, 1249, 1180, 1152, 841 cm$^{-1}$; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 7.71–7.60 (m, 2H), 7.46–7.35 (m, 3H), 2.28–2.16 (m, 9H), 1.76–1.63 (m, 6H), 0.23 (s, 9H); $^{13}$C NMR (68 MHz, $CDCl_3$) $\delta$ 166.1, 135.4, 129.0, 128.0, 126.5, 123.2 (q, $J_{C-F} = 286$ Hz), 84.4, 81.4 (q, $J_{C-C-F} = 30$ Hz), 41.1, 36.0, 31.0, 1.9; Anal. Calcd for $C_{22}H_{29}F_3O_3Si$: C, 61.95; H, 6.85%. Found: C, 61.76; H, 6.58%; HPLC analysis (The enantiomeric excess was measured after desilylation of **6e**): DAICEL Chiralpak AD-H, hexane/2-propanol = 50/1, $\lambda = 254$ nm, flow rate = 1.0 mL min$^{-1}$, retention time = 9.7 min (minor) and 10.5 min (major).

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## References


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