spectrum (assignment, relative intensity) 373 (MH^+, 7.4), 372 (M^+, 28.3), 358 (MH^+-CH_3, 32.4), 357 (M^+-CH_3, 100), 343 (MH^+-$2CH_3$, 12.9), 315 (M^+-$(CH_3)_3C$, 38.2), 303 (16.3), 295 (M^+-Ph, 5.5), 221 (15.0), 201 (26.5), 183 (52.3). Oxide form of **11e**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70-7.27 (m, 14H, $2C_6H_5$ & C_6H_4), 6.46 (d, J=16.0 Hz, 1H, β-CH to CO), 6.17 (d, J=16.0 Hz, 1H, α-CH to CO), 1.04 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.44 (CO), 134.87-123.36 (Cs of three phenyl group), 33.99 (γ-C to CO), 28.39 (3Cs of $3CH_3$); IR spectrum (neat) 3059, 2967, 2875, 1966, 1664 (CO), 1571, 1440, 1368, 1302, 1124, 1032, 861, 755, 703 cm^{-1}; mass spectrum (assignment, relative intensity) 389 (MH^+, 8.1), 388 (M^+, 17.8), 373 (M^+-CH_3, 17.4), 332 (MH^+-$C(CH_3)_3$, 16.9), 331 (M^+-$C(CH_3)_3$, 53.5), 319 (11.8), 311 (M^+-C_6H_5, 21.4), 305 ($Ph_2P(=O)C_6H_4CO^+$, 50.4), 303 (27.7), 295 (14.2), 289 (19.0), 277 ($Ph_2P(=O)C_6H_4^+$, 36.0) 227 (28.,2), 201 (20.0), 183 (32.8), 152 (50.0), 77 (100); HRMS calcd for $C_{25}H_{25}O_2P$ (M^+): 388.1594. Found: 388.1569.

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An Efficient and Enantioselective Synthesis of A Chiral Primary Amine II[1]

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Chiral amines have received considerable attention because of their potential as a key intermediate for synthetic drugs such as **1**, which was developed in our lab as a potent and irreversible HIV-1 protease inhibitor.[2]

In our continuing effort to optimize C-terminal of this novel series of inactivators, it was necessary to develop an efficient method for the preparation of optically active primary amines such as **5**. We, herein, report an efficient and enantioselective synthesis of a chiral primary amine using a naturally occurring amino acid as the starting material.

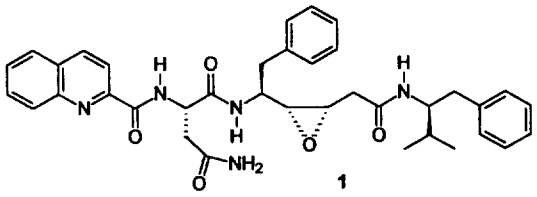
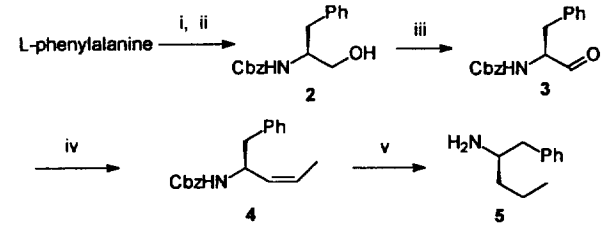
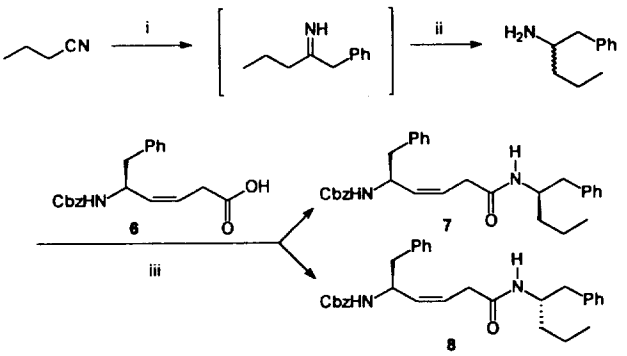


Figure 1. Structure of Irreversible HIV-1 Protease Inactivator.



Scheme 1. Reagents: i) $NaBH_4$, H_2SO_4, 96%; ii) CbzCl, Na_2CO_3, 95%; iii) $(COCl)_2$, DMSO, $^iPr_2NEt$, 98%; iv) ethyltriphenylphosphonium bromide, KHMDS, toluene, −20 ℃, 92%; v) Pd/C, H_2, MeOH, 99%.



Scheme 2. Reagents: i) $PhCH_2MgCl$, THF, reflux; ii) $NaBH_4$, THF/MeOH; iii) isobutyl chloroformate, N-methylmorpholine, CH_2Cl_2, −20 ℃.

As shown in Scheme 1, the target amine **5** was synthesized from L-phenylalanine. Cbz-protected phenylalaninol **2** was readily obtained from L-phenylalanine by $NaBH_4$-H_2SO_4 reduction[3] and subsequent Cbz-protection. Oxidation of **2** was performed under the modified condition[4] of Moffat-Swern oxidation at −20 ℃. Olefination of **3** was effected by use of potassium bis(trimethylsilyl)amide in toluene at −20 ℃ to give **4** without racemization. As a final step, hydrogenation with 10% Pd/C catalyst afforded the target compound **5**. The yields of all the steps in Scheme 1 were higher than 90% (81% overall yield).

The racemic amine was prepared from butyronitrile by the addition of benzylmagnesium chloride and the subsequent $NaBH_4$ reduction of the ketemine intermediate.[1] The coupling of the resulting racemic amine with **6** gave two diastereomers **7** and **8** which can be easily separated[5] on silica gel column chromatography as depicted in Scheme 2.

The coupling of amine **5** from Scheme 1 with **6** gave exclusively one diastereomer **7**, which proved that the reaction sequence shown in Scheme 1 was an efficient and enantioselective method for the preparation of optically active amine **5**.[6]

Various alkyltriphenylphosphonium salts were subjected to the same method in Scheme 1 to provide optically active amines as follows:

Studies are in progress for the extension of this method to prepare various optically active amines by the combination of L- or D-amino acids and alkyltriphenylphosphonium salts.

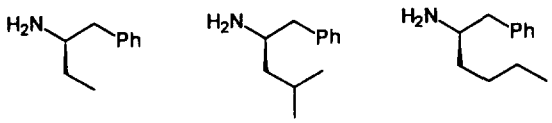


Figure 2. Structures of various optically pure primary amines.

Thus, we have developed a simple, practical and enantioselective method for the synthesis of a chiral primary amine using L- or D-amino acid as a starting material.

Acknowledgment. The authors thank Dr. Jong Hoa Ok for helpful discussion and acknowledge the encouragement and support of Dr. Yong-Zu Kim.

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5. R_f Value of **7** and **8** was 0.35 and 0.20 in 30% ethyl acetate in n-hexane, respectively.
   7 : ^{1}H NMR ($CDCl_3$) δ 0.81 (t, 3H), 1.25 (m, 2H), 1.34 (m, 2H), 2.44 (m, 1H), 2.68 (dd, 1H), 2.66 (m, 2H), 2.77 (dd, 1H), 3.16 (dd, 1H), 4.03 (m, 1H), 4.41 (m, 1H), 4.82 (s, 1H), 4.92 (m, 2H), 5.42 (m, 1H), 5.51 (dd, 1H), 6.54 (d, 1H), 7.07-7.31 (m, 10H).
   8 : ^{1}H NMR ($CDCl_3$) δ 0.80 (t, 3H), 1.16-1.29 (m, 3H), 1.39 (m, 1H), 2.60-2.81 (m, 6H), 4.03 (m, 1H), 4.28 (m, 1H), 4.71 (s, 1H), 4.94 (m, 2H), 5.40 (m, 1H), 5.49 (dd, 1H), 5.63 (d, 1H), 7.03-7.28 (m, 10H).
6. $[\alpha]_D = -30.6$ (c=0.05, CH_2Cl_2).
   ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.16 (s, 2H), 1.41 (m, 2H), 1.50 (m, 2H), 2.48 (m, 2H), 2.81 (m, 1H), 3.01 (m, 1H), 7.18-7.33 (m, 5H).

Assignment of Heme Proton Signals of Cytochrome c_3 of *Desulfovibrio vulgaris* Miyazaki F by ^{1}H NMR

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Cytochrome c_3 (cyt c_3) isolated from a sulfate-reducing bacterium, possesses four *c*-type heme groups per molecule. It is involved in the electron-transport system in the bacteria, as a partner of hydrogenase. Since the crystal structure of cyt c_3 from *Desulfovibrio vulgaris* Miyazaki F (*Dv*MF) is available at 0.18 nm resolution,[1] the relationship between its structure and redox behavior can be discussed in detail. The final goal is to elucidate the structural factors which determine the redox potentials of each of the four hemes. In this study, the total assignment of heme methyl and propionate signals was carried out.

*Dv*MF was cultured in medium C.[2] Cyt c_3 was purified according to the procedure reported previously.[3] In NMR experiments, a trace amount of hydrogenase was add to a 1.3 mM cyt c_3 solution (molar ratio, *ca.* 0.001) as a redox catalyst. The hydrogenase was purified from *Dv*MF cells according to the reported method.[4] Partial reduction (referred to as the intermediate redox stage hereafter) of a cyt c_3 solution was achieved by controlling the ratio of hydrogen and argon gases in an NMR tube. ^{1}H NMR spectra were obtained on a Bruker AM 400 NMR spectrometers at 30 ℃. Chemical shifts are presented in parts per million relative to an internal standard of 2.2-dimethyl-2-silpentane-5-sulfonate (DSS). Saturation transfer experiments were carried out for various intermediate redox stages in order to assign heme methyl resonances in the five macroscopic oxidation states. Sixteen free induction decays (FID) were accumulated alternately under on-resonance and off-resonance irradiation for 1s. Nuclear Overhauser effect (NOE) experiments were performed with typically 0.1s preirradiation and accumulation of 8000 transients. One thousand transients were accumulated for each FID. Two-dimensional (2D) TOCSY(HOHAHA) spectra were measured at 30 ℃ with a data size of 512x2048, spectral width of 8064 Hz and mixing time of 26.6 ms. 2D NOESY spectra were measured with the same data size, spectra width of 12820 Hz and mixing time 60 ms.

The NMR spectra of *Dv*MF cyt c_3 in various redox stages were discussed previously.[5,6] The assignment of 13 heme methyl signals (designated as A-M) has been performed.[3,7] Among them, signals J (13.46 ppm) and L (10.30 ppm) were classified to each heme groups on the basis of the first and second reduction fractions, R^I and R^{II},[5] (the term of electron distribution probability was used in the reference). Unfortunately, they did not include the major reduction step ($R^i > 0.5$). It was shown for cyt c_3 from *D. vulgaris* Hildenborough (*Dv*H) that the reduction behavior of signal J is unusual.[8] Since J was the key signal in the heme assignment,[7] our assignment for hemes 2 and 3 was questioned.[8] Our assignment for hemes 1 and 4 was consistent signals A, H, I, K (heme 4) and B, F, G, M (heme 1) are on the firm basis. To make the correct assignment, we have carried out the total assignment of the heme methyl and propionate signals.

Saturation transfer experiments have been carried out again for signal J at p^{2}H 7.0 to determine the chemical shifts of heme methyl J in all reduction steps (macroscopic oxidation states). As shown in Figure 1, signal J could be identified in the five macroscopic oxidation states.

The chemical shifts were 13.46, 13.86, 11.45, 12.10 and about 4.7 ppm for the fully oxidized (S_0), one-electron reduced (S_1), two-electron reduced (S_2), three-electron reduced (S_3) and fully reduced (S_4) states, respectively. The chemical shift for the fully reduced state was also confirmed in the assignment of the heme protons of ferrocytochrome c_3 (unpublished data). The unusual behavior of signal J was similar