Arch Pharm Res Vol 22, No 6, 624-628, 1999 Medicinal Chemistry

A Formal Asymmetric Synthesis of Mugineic Acid: An Efficient Synthetic Route Through Chiral Oxazolidinone

Young Hoon Jung and Chang Min Kim

Laboratory of Organic Medicinal Chemistry, College of Pharmacy, Sungkyunkwan University, Suwon 440-746, Korea

(Received August 17, 1999)

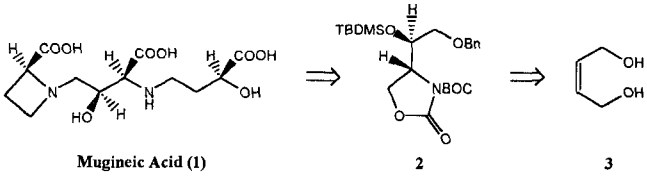
A formal asymmetric synthesis of Mugineic acid was accomplished from cis-2-butene-1,4-diol through catalytic Sharpless epoxidation oxidations and coupling reaction.

Key words: Mugineic acid, Phytosiderophore, Angiotensin converting enzyme, Oxazole, Amino acids, Homoserine, Oxazolidinone, Formal asymmetric total synthesis

INTRODUCTION

Mugineic acid **1** is a typical phytosiderophore excreted from the root of barley (Hordeum vulgare L. var. Minorimugi) which promotes uptake and transport of iron in higher plants and stimulates chlorophyll synthesis (Takemoto, *et al.*, 1978). Recently, it has been reported that mugineic acid shows an inhibitory effect against angiotensin converting enzyme (Funahashi, *et al.*, 1984). Its importance in plant physiology and interesting amino acid structure have led several groups to synthesize it. The first total synthesis of **1** was achieved by Shioiri group (Hamada, *et al.*, 1986) using oxazole route and then other several synthetic methodologies have been developed using various acids or sugars as a starting materials (Hamada, *et al.*, 1990, Matsuura, *et al.*, 1993, Carreaux, et al., 1992). A detailed review of the previous syntheses was reported (Shioiri, *et al.*, 1995).

As part of our program aimed at formation of various amino acids, we reported earlier the synthesis of protected homoserine which can be used as building blocks for mugineic acid (Jung, *et al.*, 1993). In this paper, we report a formal asymmetric total synthesis of mugineic acid through chiral oxazolidinone. Our synthetic strategy toward **1** is illustrated in Scheme 1.



Mugineic Acid (1) 2 3

Scheme 1. The retrosynthesis of Mugineic acid

MATERIALS AND METHODS

Commercially available reagents were used without additional purification unless otherwise stated. Solvents were routinely distilled prior to use. All reactions were performed under an inert atmosphere of nitrogen or argon. Melting points were measured on a Gallenkamp melting point apparatus and were not corrected. Nuclear magnetic resonance spectra (^{1}H, and ^{13}C NMR) were recorded on a Varian Unity Inova 500 MHz spectrometer and chemical shifts are reported as part per million (ppm) from the internal standard, tetramethylsilane (TMS). Resonance pattern are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation b is used to indicate a broad signal. Coupling constants (*J*) are reported in hertz (Hz). IR spectra were recorded on a Nicolet 205 Infrared spectrophotometer as a liquid film (neat) or a Nujol mull and reported as cm^{-1}. Optical rotations were measured on JASCO DIP 1020 digital polarimeter and reported as $[\alpha]_D$. Thin layer chromatography was carried out using plates coated with Kieselgel $60F_{254}$ (Merck). Flash column chromatography was carried out on silica gel 60 (230-400 mesh, Merck).

4-[2'-(Benzyloxy-1'-(benzoyloxyethyl)]-2-oxazolidinone (5)

To a stirred solution of threo-4-(benzyloxy)-2,3-epoxy-1-butanol (986 mg, 5.08 mmol) in THF (15 ml) was added benzoyl isocyanate (702 mg, 5.59 mmol) at room temperature. After 20 min stirring, sodium hydride (30

Correspondence to: Professor Young Hoon Jung, Sungkyunkwan University, Laboratory of Organic Medicinal Chemistry, College of Pharmacy 300 Chonchon-Dong, Changan-Ku, Suwon 440-746, Kyonggi-Do
E-mail: yhjung@skku.ac.kr

mg, 1.27 mmol) and imidazole (86 mg, 1.27 mmol) was added to the reaction mixture. After refluxing over-night, the reaction mixture was quenched with satu- rated ammonium chloride solution, taken up in ethyl acetate, washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc : hexane=3 : 2) to afford 1.34 g (77.4%) of the pure oxazolidinone ester **5** as a colorless oil.

R_f: 0.45 (EtOAc : Hexane=10 : 1); IR (neat) cm^{-1}: 3240, 1758, 1721, 1271 ; ^1H NMR (500MHz, $CDCl_3$) δ : 8.02-7.99 (m 2 H), 7.60-7.42 (m, 3H), 7.35-7.26 (m, 5 H), 6.08 (s, 1H), 5.28-5.25 (m, 1H), 4.54-4.50 (m, 4H), 4.30-4.26 (m, 1H), 3.77-3.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.51, 160.65, 138.16, 134.11, 130.27, 129.46, 128.83, 77.93, 74.18, 73.66, 69.16, 67.38, 56.50, 54.01; $[\alpha]_D^{26.6}$ +41.2° (c0.82, $CHCl_3$).

4-[2'-(Benzyloxy-1'-(hydoxyethyl)]-2-oxazolidinone(6) and *cis*-4-[2'-(hydroxymethyl-5-(benzyloxymethyl)]-2-oxazolidinone (7)

To a stirred solution of oxazolidinone **5** (1.16 g, 3.39 mmol) in MeOH (20 ml) was added a catalytic amount of sodium methoxide and the reaction mixture was stirred at room temperature overnight. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate, washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography ($CHCl_3$: MeOH=10 : 1) to afford 577 mg (71.8%) of oxazolidinone alcohol **6** mg (5.1%) of oxazolidinone alcohol **7** as colorless oils.

Oxazolidinone alcohol 6

R_f: 0.47 ($CHCl_3$: MeOH=10 : 1); IR (neat) cm^{-1}: 3316, 1746, 1409 ; ^1H NMR (500 MHz, $CDCl_3$): δ 7.37-7.31 (m, 5H), 6.49 (s, 1 H), 4.52 (s, 2 H), 4.46-4.40 (m, 1 H), 4.38 (t, 1 H, *J*=9Hz) 3.93-3.89 (m, 1 H), 3.81-3.79 (m, 1 H), 3.54-3.48 (m, 2 H), 3.42 (d, 1 H, *J*=5Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.50, 138.20, 129.24, 128.62, 77.83, 74.29, 71.37, 67.31, 55.34; $[\alpha]_D^{26.6}$ -15.7° (c 0.20, $CHCl_3$).

Oxazolidinone alcohol 7

R_f: 0.37 ($CHCl_3$: MeOH=10 : 1); IR (nujol) cm^{-1}: 3278, 1710, 1459 ; ^1H NMR (500 MHz, $CDCl_3$): δ 7.39-7.31 (m, 5H), 5.90 (bs, 1 H), 4.83-4.79 (m, 1 H), 4.63-4.58 (m, 2H), 3.96-3.92 (m, 1 H), 3.88-3.85 (m, 1 H), 3.80-3.77 (m, 1 H), 3.70 (bd, 2 H, *J*=2.5 Hz), 3.19 (bs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.62, 137.59, 129.32, 128.79, 77.75, 74.66, 67.68, 61.61, 56.83; $[\alpha]_D^{24.6}$ +1.933° (c=0.20, $CHCl_3$).

3-*tert*-Butyloxycarbonyl-4-[2'-(Benzyloxy-1'-(*tert*-butyldimethylsilyloxyethyl)]-2-oxazolidinone (2)

To a stirred solution of oxazolidinone alcohol **6** (1.53 g, 6.43 mmol) in DMF (40 ml) was added *tert*-butyldimethylsilyl chloride (1.94 g, 12.86 mmol), imidazole (1.09 g, 16.1 mmol) and dimethylaminopyridine (157 mg, 1.29 mmol) at 0°C and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was diluted with brine (60 ml), taken up in ethyl acetate (50 ml × 3), washed with 5% HCl, saturated $NaHCO_3$, water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc : hexane=1 : 2) to afford 2.0 g (88.4%) of silyl compound as a colorless solid. To a stirred solution of silyl compound (263 mg, 0.75 mmol) in CH_2Cl_2 (10 ml) was added triethylamine (0.11 ml, 0.75 mmol), dimethylaminopyridine (91 mg, 0.75 mmol) and di-*tert*-butyl dicarbonate (357 mg, 1.65 mmol) at room temperature and the reaction mixture was stirred for 10 h. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate, washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc : hexane=1 : 4) to afford 330 mg g (97.6%) of N-BOC-oxazolidinone **2** as a colorless oil.

R_f: 0.38 (EtOAc : hexane=1 : 4); IR (neat) cm^{-1}: 1819, 1795, 1719, 1330, 1091 ; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38-7.29 (m, 5 H), 4.56 (d, 1 H, *J*=15 Hz), 4.51-4.45 (m, 4H), 4.38-4.35 (m, 1 H), 4.15 (t, 1 H, *J*=8 Hz), 3.49 (dd, 1 H, *J*=4.5, 10 Hz), 3.35 (dd, 1H, *J*=7, 10Hz), 1.55 (s, 9 H), 0.87 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.07, 150.40, 138.31, 129.18, 128.40, 88.46, 77.73, 74.12, 71.68, 69.61, 62.20, 57.92, 28.91, 26.41, 18.48, -4.00, -4.49; $[\alpha]_D^{23.9}$ +44.0° (c 0.04, $CHCl_3$).

***erythro*-[4-(Benzyloxy)-3-(*tert*-butyldimethylsilyloxy)-2-(*tert*-butylcarboxamido)]-butyric acid methyl ester (8)**

To a stirred solution of oxazolidinone **2** (325 mg, 0.72 mmol) in MeOH (30 ml) was added cesium carbonate (94 mg, 0.29 mmol) and the reaction mixture was stirring at room temperature overnight. After neutralization with 10% aqueous citric acid solution, the solvent was evaporated under reduced pressure. The residue was extracted with ethyl acetate, washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc : hexane=3 : 2) to afford 245 mg (79.8%) of *N*-BOC-aminoalcohol as colorless oils. To a stirred solution of oxalyl chloride (0.22 ml, 2.54 mmol) in methylene chloride (12 ml) was added the solution of DMSO (0.39 ml, 5.54 mmol) in methylene chloride (8 ml) at -78°C and the reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added *N*-BOC-amino alcohol (984 mg, 2.31 mmol) in methylene chloride (20 ml) through cannular at -78°C. The resulting mixture was stirred for 15 min at the same temperature, and then

diisopropylethylamine (2.02 ml, 11.6 mmol) was added. The reaction mixture was allowed to room tem-perature, stirred for additional 20 min after addition of water (15 ml), extracted with methylene chloride (30 ml × 3), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by short column chromatography (EtOAc : hexane=1 : 5) to afford 880 mg (89.9%) of aldehyde as colorless oils. The aldehyde (880 mg, 2.07 mmol) wad added to a mixed solution of *tert*-butyl alcohol (40 ml) and 2-methyl-2-butene (17.6 ml). To this solution was added a mixed aqueous solution of sodium chlorite (1.97 g, 17.2 mmol) and sodium dihydrogen phosphate (2.06 g, 17.2 mmol), and then this reaction mixture was stirred at room temperature overnight. The solvent was evaporated under reduced pressure and then the residue was extracted with ethyl acetate after addition of water (30 ml) and the aqueous layer was extracted with ether after addition of 6N-HCl. The combined organic layer was washed with cold water, brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Without further purification, the residue was treated with diazomethane and purified by column chromatography (EtO Ac : hexane=1 : 6) to afford 600 mg (63.7%) of methyl ester **8** as colorless oils.

R_f: 0.40 (EtOAc : hexane=1 : 6); IR (neat) cm^{-1}: 3446, 1748, 1719, 1498, 1366 ; ^1H NMR (500 MHz, $CDCl_3$): δ 7.35-7.27 (m, 5 H), 5.39 (bd, 1 H, *J*=8Hz), 4.56-4.49 (m, 3 H), 4.20 (bd, 1 H, *J*=3 Hz), 3.68 (s, 3 H), 3.57 (dd, 1 H, *J*=6, 10 Hz), 3.47 (dd, 1 H, *J*=6, 10 Hz), 1.45 (s, 9 H), 0.86 (s, 9 H), 0.78 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.20, 155.88, 138.63, 129.02, 128.41, 80.42, 77.73, 74.12, 73.05, 72.43, 57.55, 52.80, 29.04, 26.38, 18.72, -3.91, -4.44; $[\alpha]_D^{23.3}$ +29.5° (c 0.04, $CHCl_3$).

erythro-Methyl-[4-(hydroxy)-3-*tert*-butyldimethylsilyloxy)-2-(*tert*-butylcarboxamido)]-butyric acid methyl ester (9) and *cis*-[4-(*tert*-butyldimethylsilyloxy)-3-(*tert*-butylcarboxamido)]-2-lactone (10)

Methyl ester **8** (600 mg, 1.32 mg) was dissolved in ethyl acetate (50 ml) and palladium on carbon (60 mg) was added to the solution. The reaction flask was charged with nitrogen first and then charged to a hydrogen current by using a hydrogen-filled balloon and stirred at room temperature overnight. The reaction mixture was filtered through a plug of Celite and concentrated *in* vacuo. The residue was purified by column chromatography ($CHCl_3$: MeOH=20 : 1) to afford 381 mg (79.5%) of methyl ester **9** and 52 mg (10.7%) of lactone **10**.

Butyric acid methyl ester **9**

R_f: 0.56 ($CHCl_3$: MeOH=20 : 1); IR (neat) cm^{-1}: 3444, 1746, 1720, 1504, 1366 ; ^1H NMR (500 MHz, $CDCl_3$): δ 5.40 (bd, 1 H, *J*=8 Hz), 4.52-4.49 (m, 1 H), 4.00-3.97 (m, 1 H), 3.76 (s, 3 H), 3.74 (bs, 2 H), 3.60 (bs, 1 H), 1.44 (s, 9 H), 0.86 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.66, 156.01, 81.23, 80.87, 77.60, 74.39, 64.47, 56.93, 52.97, 28.99, 26.35, 18.68, -4.15; $[\alpha]_D^{25.3}$ +20.5° (c 0.18, $CHCl_3$).

Lactone **10**

R_f: 0.62 ($CHCl_3$: MeOH=20 : 1); ^1H NMR (500 MHz, $CDCl_3$): δ 5.00 (bd, 1 H, *J*=8 Hz), 4.55-4.50 (m, 2 H), 4.37 (dd, 1 H, *J*=2.5, 10Hz), 4.21 (d, 1 H, *J*=10 Hz), 1.46 (s, 9 H), 0.88 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.70, 156.00, 81.28, 81.23, 77.74, 74.18, 70.16, 55.21, 28.97, 26.30, 18.79, -4.33; $[\alpha]_D^{25.3}$ +20.5° (c 0.18, $CHCl_3$).

erythro-[4-Oxo-3-(*tert*-butyldimethylsilyloxy)-2-(*tert*-butylcarboxamido)]-butyric acid methyl ester (11)

To a stirred solution of oxalyl chloride (0.05 ml, 0.62 mmol) in methylene chloride (3 ml) was added the solution of DMSO (0.01 ml, 1.35 mmol) in methylene chloride (2 ml) at -78°C and the reaction mixture was stirred at room temperature for 10 min. To this reaction mix-ture was added methyl ester **9** (205 mg, 0.56 mmol) in methylene chloride (5 ml) through cannular at -78°C. The resulting mixture was stirred for 15 min at the same temperature, and then diisopropylethylamine (0.49 ml, 2.84 mmol) was added. The reaction mixture was allowed to room temperature, stirred for additional 20 min after addition of water (3 ml), extracted with methylene chloride (30 ml × 3), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography ($CHCl_3$: MeOH=20 : 1) to afford 193 mg (94.8%) of aldehyde as colorless oils.

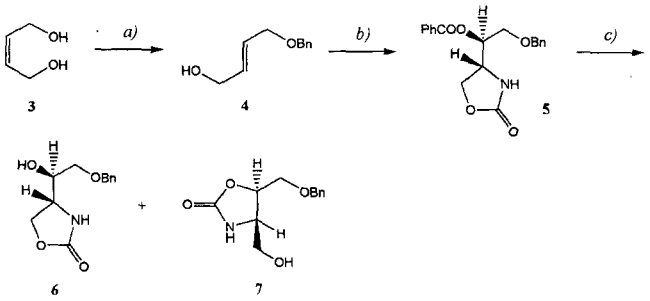
R_f: 0.65 ($CHCl_3$: MeOH=20 : 1); IR (neat) cm^{-1}: 3447, 1720, 1502, 1366 ; ^1H NMR (500MHz, $CDCl_3$): δ 9.63 (s, 1 H), 5.40 (bd, 1 H, *J*=6.5 Hz), 4.79 (bd, 1 H, *J*=2, 7 Hz), 4.43 (d, 1 H, *J*=2.5 Hz), 3.76 (s, 3 H), 1.46 (s, 9 H), 0.86 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.93, 169.76, 155.42, 81.10, 79.07, 77.75, 57.31, 53.33, 29.00, 26.30, 18.79, -4.23; $[\alpha]_D^{23.2}$ +22.33° (c 0.10, $CHCl_3$).

RESULTS AND DISCUSSION

According to the known method (Roush, *et al.*, 1991), monobenzyl allylic alcohol **4** was prepared from diol **3** in a 66% overall yield for three steps. Treatment of the allylic alcohol **4** with 2 equiv. of *tert*-butyl hydroperoxide and 0.05 equiv. of titanium tetraisopropoxide in methylene chloride at -23°C in the presence of 0.07 equiv. of L-(+)-diisopropyl tartrate afforded the corresponding chiral epoxy alcohol (98.4% e.e) (Gao, *et al.*, 1987) which was further transformed to oxazolidinone **5** by reaction with phenyl isocyanate and cyclization using sodium hydride (Roush, *et al.*, 1985). The overall yield was 71% for three steps. Basic hydrolysis of the benzo-

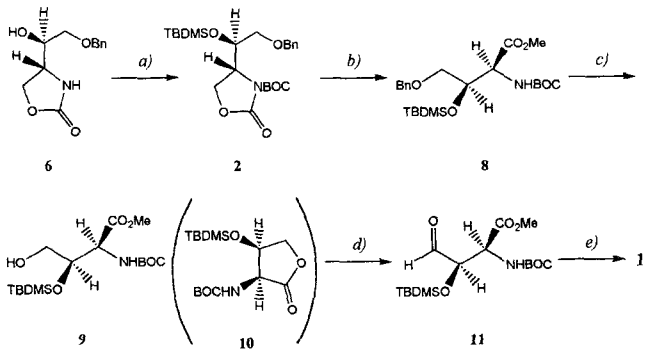
ate in the oxazolidinone **5** with sodium methoxide in methanol proceeded in a 77% yield to give the mixture of the oxa-zolidinone alcohol **6** and **7** in a 14:1 ratio. (Scheme. 2) This result can be explained on the basis of the difference of the stability of the product. The oxzolidinone alcohol **7** is unstable due to the steric hindrance between the hydroxy methyl and benzyloxy methyl moiety of the oxazolidinone ring (*cis* configuration), even though the primary alkoxide, which leads to **7**, is more stable than the secondary one.

Protection of alcohol **6** with *tert*-butyldimethylsilyl chloride and imidazole in dimethylformamide afforded the corresponding silyl ether compound, which was treated with di-*tert*-butyldicarbonate and triethylamine in tetrahydrofuran to give the *N*-*tert*-butoxycarbonyl oxazolidinone **2** in a 86% overall yield. Ring cleavage of **2** was carried out with a catalytic amount of cesium carbonate in methanol to obtain amino alcohol, which



Reagents and conditions: a) ref. (Roush, *et al.*, 1991); b) i) L-(+)-DIPT, $Ti(O\text{-}iPr)_4$, TBHP, 4Å Molecular sieve, CH_2Cl_2, -78°C -0°C, 92%; ii) PhCONCO, THF, RT, then NaH, imidazole, reflux, 77%; c)NaOMe, MeOH, RT, 77% (**6**:**7**=14:1).

Scheme 2. The preparation of the optically active oxazolidnone **6** and **7**



Reagents and conditions: a) i) TBDMSCl, imidazole, DMAP, DMF, RT, 88%; ii) $(BOC)_2O$, Et_3N, DMAP, CH_2Cl_2, RT, 98%; b) i) Cs_2CO_3, MeOH, RT, 80%; ii) $(COCl)_2$, DMSO, DIPEA, CH_2Cl_2, -78°C ~RT, 90%; iii) $NaClO_2$, 2-methyl-2-butene, NaH_2PO_4, *t*-BuOH, RT; then CH_2N_2, ether, 0°C ~RT, 64%; c) 10% Pd/C, H_2, EtOAc, RT, 90% (**9**:**10**=7.4:1); d) $(COCl)_2$, DMSO, DIPEA, CH_2Cl_2, -78°C ~RT, 95%; e) ref. (Hamada, *et al.*, 1990).

Scheme 3. The formal synthesis of Mugineic acid.

was oxidiz-ed to give the corresponding ester **8** through Swern oxidation, $NaClO_2$ oxidation, and treatment of diazome-thane. The overall yield was 46% for four steps. Debenzylation of the oxazolidinone ester **8** was performed by catalytic hydrogenolysis with hydrogen in the presence of palladium on charcoal to give the corresponding alcohol **9**, which was oxidized to aldehyde **11** using the Swern oxidation in a 75% overall yield. During debenzylation, a small amount of lactone **10** was produced as a side product. The conversion of **11** to mugineic acid **1** has been earlier reported by Shioiri group (Hamada, *et al.*, 1990). (Scheme. 3)

In summary, we accomplished a stereoselective synthesis of aldehyde **11** from *cis*-2-butene-1,4-diol as a starting material through 14 steps involving catalytic Sharpless epoxidation, oxazolidinone formation using isocyanate, ring cleavage and oxidations. Aldehyde **11** had previously been transformed into mugineic acid, thus completing the formal asymmetric total synthesis.

ACKNOWLEDGEMENTS

This paper was supported by Faculty Research Fund, Sungkyunkwan University, 1998, and Grant of the KPRC of Sunkyunkwan University.

REFERENCES CITED

Carreaux, F., Dureault, A., and Depezay, J. C., Tartaric acid derived aziridines as chiral precursors of 3-amino-3-deoxy and 2-amino-2-deoxy tetroses: An efficient approach toward mugineic acid. *Synlett.*, 527-529 (1992).

Funahashi, K., Tanaka, H., Muramatsu, M., Sato, F., Nomoto, K., Abstract of papers, 104th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, March 426 (1984).

Gao, Y., Hanson, R. M., Klunder, J. M., Ko, S. Y., Masamune, H., and Sharpless, K. B., Catalytic asymmetric epoxidation and kinetic resolution: Modified procedure including in situ derivatization. *J. Am. Chem. Soc.*, 109, 5765-5780 (1987).

Hamada, Y. and Shioiri, T., Synthesis of Mugineic through Direct C-Acylation Using Diphenyl Phosphorazidate. *J. Org. Chem.*, 51, 5489-5490 (1986).

Hamada, Y., Iwai, K., and Shioiri, T., A new stereoselective synthesis of a γ-azetidinyl-β-hydroxy-α-amino acid moiety of mugineic acid. A formal synthesis of mugineic acid. *Tetrahedron Lett.*, 31, 5041-5042 (1990).

Jung, Y. H., and Won, S. R., Synthesis of β-hydroxyhomoserine, constituent of mugineic acid. *Yakhak Hoeji*, 37, 437-441 (1993).

Matsuura, F., Hamada, Y., and Shioiri, T., Total synthesis of mugineic acid. Efficient use of the phenyl group as the carboxyl synthon. *Tetrahedron*, 49, 8211-8222 (1993).

Roush, W. R. and Adam, M. A., Directed openings of 2,3-epoxy alcohols via reactions with isocyanates: Synthesis of (+)-*erythro*-dihydrosphingosine. *J. Org. Chem.*, 50, 3752-3757 (1985).

Roush, W. R., Straub, J. A., and Vannieuwenhze, M. S., A stereochemically general synthesis of 2-deoxyhexoses via the asymmetric allylboration of 2,3-epoxyaldehyde. *J. Org. Chem.*, 56, 1636-1648 (1991).

Shioiri, T., Hamada, Y., and Matsuura, F., Total synthesis of phytosiderophores. *Tetrahedron*, 51, 3939-3958 (1995).

Takemoto, T., Nomoto, K., Fushiya, S., Ouchi, R., Kusano, G., Hikino, H., Takagi, S., Jatsuura, Y., Kakudo, M., Structure of mugineic acid, a new amino acid possessing an iron-chelating activity from root washings of water-cultured Hordeum vulgare L.. *Proc. Jpn. Acad. Ser.* B., 54, 469-473 (1978).