Notes

A New Stereo- and Enantioselective Approach to the N-Terminal Amino Acid Moiety of Nikkomycins B and B_X

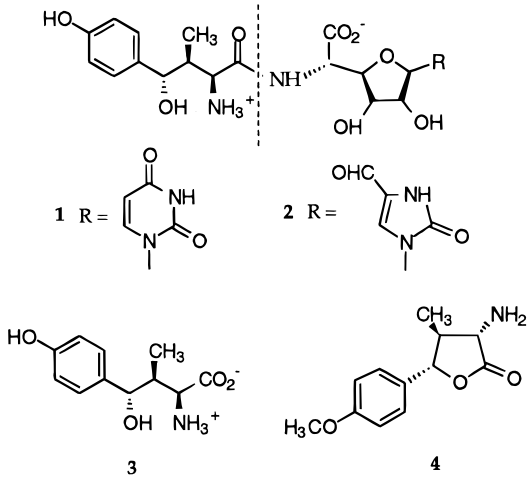
Gérard Mandville, Mohammed Ahmar, and Robert Bloch*

Laboratoire des Carbocycles, URA CNRS 478, Institut de Chimie Moléculaire d'Orsay, Bât. 420, Université de Paris-Sud, 91405 Orsay, France

Received August 7, 1995

Nikkomycins are peptidyl nucleoside antibiotics, structurally related to polyoxins, which have been isolated from fermentation broths of both *streptomyces tendae* and *streptomyces cacaoi* ssp. *asoensis*. The purification of these substances, as well as the determination of their chemical structures and pharmacological activities, have been described by König and Isono.[1,2] These compounds are potent competitive inhibitors of chitin synthetase and exhibit antifungal, acaricidal, and insecticidal activities. Due to their interesting pharmaceutical properties, much effort has been devoted to the total synthesis of nikkomycins B **1**[3] and B_X **2**,[4] mainly by coupling the C-terminal nucleoside amino acid with the N-terminal amino acid component **3**. The presence of three consecutive stereogenic centers in **3** is a synthetic challenge, and several approaches to this amino acid **3** or its lactone derivative **4**, in either racemic[5] or optically active form,[6] have been recently reported.

In the course of our work directed toward the development of stereoselective reactions induced by a thermolabile group, we have described the conditions under which very high steric control is achieved in the addition of alkyl organometallic reagents to Diels−Alder adducts of furan.[7] This method is useful for the synthesis of enantiomerically pure 4-alkyl-but-2-enolides. However, its scope of application has been limited by the modest yields in the oxidation step.[8] We report here an improved procedure for the preparation of 4-arylbut-2-enolides and the incorporation of this methodology into a short and highly stereoselective synthesis of (2*S*,3*S*,4*S*)-2-amino-4-(*p*-methoxyphenyl)-3-methyl-4-butanolide (**4**), a potential precursor of the N-terminal amino acid unit of



3 **4**

nikkomycins B and B_X. The synthetic pathway is outlined in Scheme 1.

Chelation-controlled addition of (*p*-methoxyphenyl)-magnesium bromide to the enantiomerically pure lactol **5**[9] led to the corresponding diols as a 20:1 mixture of two diastereomers. The product ratio was estimated by integration of the ^{1}H NMR signals for the bridgehead protons which appear as singlets at $\delta = 4.99$ and 5.08 ppm for **6** and at $\delta = 4.82$ and 4.94 ppm for its stereomer. The major component **6** was obtained pure as a colorless solid in 73% yield by simple trituration of the crude product mixture with ether. Oxidation of diol **6** [4-methylmorpholine *N*-oxide (NMO), tetrapropylammonium perruthenate (TPAP)][10] gave the tricyclic lactone **7** which, by cycloreversion in refluxing toluene, afforded the enantiomerically pure butenolide **8** [ee > 95% determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$]. The stereoselective introduction of the methyl group via Michael addition proved to be quite critical, since both the selectivity and the chemical yield were greatly dependent on the reaction conditions (temperature, nature of the cuprate and of the solvent). We found that excellent yield (85%) and stereoselectivity (a single product was detected) could be attained if the reaction was carried out at −78 °C in ether using 3 equiv of lithium dimethyl cuprate in the presence of chlorotrimethylsilane. Electrophilic amination of the lithium enolate of the disubstituted lactone **9** was then tried with several reagents. In our hands, di-*tert*-butylazodicarboxylate[11] or 1-chloro-1-nitrosocyclohexane[12] did not give

(1) (a) Dähn U.; Hagenmaier, H.; Höhne, M.; König, W. A.; Wolf, G.; Zähner, H. *Arch. Microbiol.* **1976**, *107*, 249. (b) Hagenmaier, H.; Keckeisen, A.; Zähner, H.; König, W. A. *Liebigs Ann. Chem.* **1979**, 1494. (c) König, W. A.; Hass, W.; Dehler, W.; Fiedler, H. P.; Zähner, H. *Liebigs Ann. Chem.* **1980**, 622. (d) Hagenmaier, H.; Keckeisen, A.; Dehler, W.; Fiedler, H. P.; Zähner, H.; König, W. A. *Liebigs Ann. Chem.* **1981**, 1018.

(2) (a) Kobinata, K.; Uramoto, M.; Nishii, M.; Kusakabe, H.; Nakamura, G.; Isono, K. *Agric. Biol. Chem.* **1980**, *44*, 1709. (b) Uramoto, M.; Kobinata, K.; Isono, K.; Higashijima, T.; Miyazawa, T.; Jenkins, E. E.; McCloskey, J. A. *Tetrahedron Lett.* **1980**, *21*, 3395. (c) Uramoto, M.; Kobinata, K.; Isono, K.; Higashijima, T.; Miyazawa, T.; Jenkins, E. E. McCloskey, J. A. *Tetrahedron* **1982**, *38*, 1599.

(3) Barrett, A. G. M.; Lebold, S. A. *J. Org. Chem.* **1991**, *56*, 4875.

(4) Hahn, H.; Heitsch, H.; Rathmann, R.; Zimmerman, G.; Bormann, C.; Zähner, H.; König, W. A. *Liebigs Ann. Chem.* **1987**, 803.

(5) (a) Hass, W.; König, W. A. *Liebigs Ann. Chem.* **1982**, 1615. (b) Jäger, W.; Grund, H.; Buss, V.; Schwab, W.; Müller, I.; Schohe, R.; Franz, R.; Ehrler, R. *Bull. Soc. Chim. Belg.* **1983**, *92*, 1039. (c) Banks, B.; Barrett, A. G. M.; Russell, M. A.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1983**, 873. (d) Melnick, M. J.; Weinreb, S. M. *J. Org. Chem.* **1988**, *53*, 850. (e) Barrett, A. G. M.; Dhanak, D.; Lebold, S. A.; Russell, M. A. *J. Org. Chem.* **1991**, *56*, 1894.

(6) (a) Zimmerman, G.; Hass, W.; Faash, H.; Schmalle, H.; König, W. A. *Liebigs Ann. Chem.* **1985**, 2165. (b) Barrett, A. G. M.; Lebold, S. A. *J. Org. Chem.* **1990**, *55*, 5818. (c) Barluenga, J.; Viado, A. L.; Aguilar, E.; Fustero, S.; Olano, B. *J. Org. Chem.* **1993**, *58*, 5972. (d) Mukai, C.; Miyakawa, M.; Hanaoka, M. *Synlett* **1994**, 165.

(7) (a) Bloch, R.; Gilbert, L. *Tetrahedron Lett.* **1987**, *28*, 423. (b) Bloch, R.; Brillet, C. *Tetrahedron: Asymmetry*, **1992**, *3*, 333.

(8) Bloch, R.; Gilbert, L. *J. Org. Chem.* **1987**, *52*, 4603.

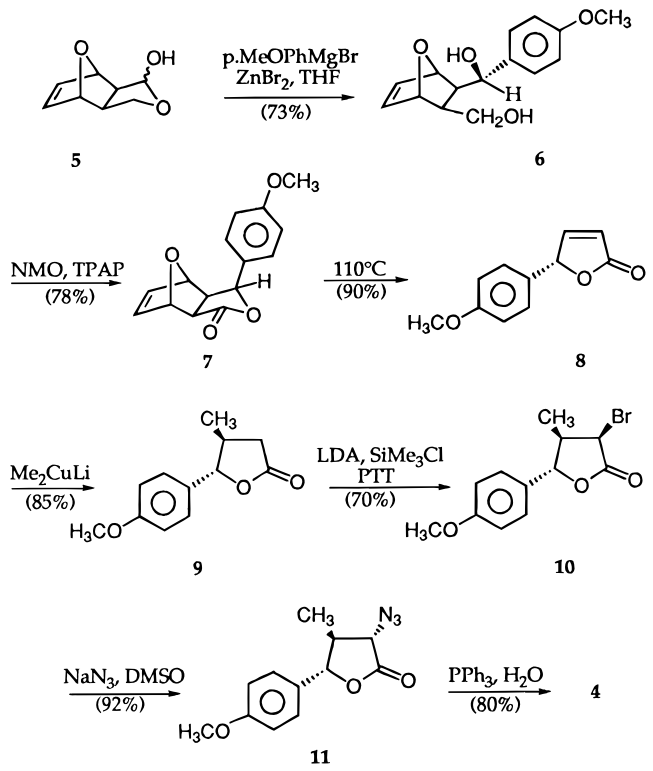
(9) Lactol **5** is readily available from the Diels−Alder adduct of furan and maleic anhydride either via an enzymatic desymmetrization (Bloch, R.; Guibé-Jampel, E.; Girard; C. *Tetrahedron Lett.* **1985**, *26*, 4087) or by an asymmetric reduction: Matsuki, K.; Inoue, H.; Takeda, M.*Tetrahedron Lett.* **1993**, *34*, 1167.

(10) (a) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639. (b) Bloch, R.; Brillet, C. *Synlett* **1991**, 829.

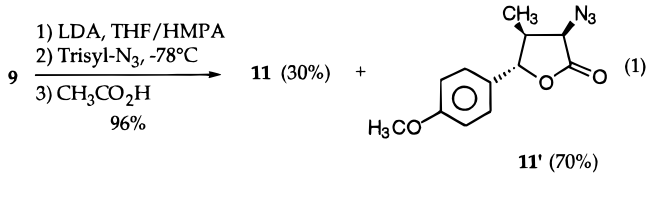
(11) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539 and references therein.

0022-3263/96/1961-1122$12.00/0

Scheme 1



good results, mainly due to the conditions necessary for the regeneration of the free amine after alkylation. In contrast, excellent yields of azides **11** and **11′** were obtained when the lithium enolate of **9** was treated with arenesulfonyl azides in the presence of a small amount of HMPA. The use of a sterically demanding sulfonyl-azide such as 2,4,6-triisopropylbenzenesulfonyl azide (or trisyl azide) developed by Evans[13] led to a fairly stereoselective reaction as shown in eq 1.



In contrast to reported results involving similar transformations of trans disubstituted butyrolactones,[14] the major diastereomer formed was the undesired azide **11′**. This indicates that during the approach of the electrophile 1,3-interactions with the aryl group were stronger than 1,2-interactions with the methyl group. The respective stereochemistry of the stereomers **11** and **11′** was easily assigned by comparison of their ^{1}H NMR spectra with the corresponding data for known lactone **11**.[15] We then decided to take advantage of the stereochemical course of this reaction to obtain stereoselectively the desired azide **11** via the corresponding bromide **10**. Effectively, electrophilic bromination of the trimethylsilyl enol ether of lactone **9** with the bulky reagent phenyltrimethylammonium tribromide (PTT) generated stereoselectively bromide **10** as the major component of a mixture containing also a small amount of its diastereomer (ratio 92/8). After purification by crystallization, the bromo lactone **10** was treated with sodium azide in dimethyl sulfoxide at 0 °C to give, in excellent yield and without any epimerization during the course of azide displacement, the desired compound **11**. Finally, transformation of the azido group to the primary amino group was achieved by reduction with triphenylphosphine/water to give the target compound, butanolide **4**.[15]

In conclusion, we have accomplished a short and efficient synthesis (seven steps, 23% from lactol **5**) of (2*S*,3*S*,4*S*)-2-amino-4-(*p*-methoxyphenyl)-3-methyl-4-butanolide, a potential precursor of the N-terminal amino acid moiety of nikkomycins B and B_X.

Experimental Section[16]

(1*R*,2*R*,3*S*,4*S*,1′*S*)-2-[1′-(*p*-Methoxyphenyl)hydroxymethyl]-3-(hydroxymethyl)-7-oxabicyclo[2.2.1]-5-heptene (6). To a solution of the Grignard reagent prepared from 4-bromoanisole (8.5 g, 45.4 mmol) and Mg (1.1 g, 0.042 g·atoms) in THF (10 mL) at 0 °C was added anhydrous $ZnBr_2$ (2.05 g, 9.09 mmol). The suspension was stirred for 10 min, and a solution of lactol **5** (1.4 g, 9.09 mmol) in THF (50 mL) was added dropwise at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. The solution was cooled to 0 °C, diluted with saturated aqueous NH_4Cl (50 mL), extracted with ether (2 × 50 mL) and CH_2Cl_2 (2 × 50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was triturated with hexane (10 mL). The solid formed was decanted, washed with ether (25 mL), and isolated by filtration. The filtrate was concentrated in vacuo and the residue triturated with a small amount of ether (5 mL) to give a second crop of solid after filtration: total yield 1.75 g (73%) of diol **6** as a white solid; mp 155 °C; $[\alpha]^{20}_D$ +5.7° (*c* 1.06, $CHCl_3$); IR (KBr) 3440, 1615, 1540 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.88 (m, 1H), 2.11 (m, 1H), 2.3 (bs, 1H), 3.15 (bs, 1H), 3.7−3.9 (m, 2H), 3.81 (s, 3H), 4.9 (d, J = 5.3 Hz, 1H), 4.99 (s, 1H), 5.08 (s, 1H), 6.33 (m, 1H), 6.49 (m, 1H), 6.9 (m, 2H), 7.32 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 42.2, 46.3, 55.3, 62.1, 71.2, 79.2, 80.9, 113.9, 127.2, 135.8, 136.2, 136.4, 158.9; CIMS (NH_3) *m*/*z* (relative intensity) 262 (M^+, 2), 196 (30), 180 (60), 179 (100), 177 (65). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.46; H, 7.07.

(1*S*,2*R*,5*S*,6*S*,7*R*)-4,10-Dioxa-5-(*p*-methoxyphenyl)tricyclo-[5.2.1.0^{2,6}]dec-8-en-3-one (7). To a solution of diol **6** (985 mg, 3.75 mmol) in CH_2Cl_2 (20 mL) were added activated 4 Å molecular sieve powder (1 g) and 4-methylmorpholine *N*-oxide (1.32 g, 11.25 mmol). After the mixture was stirred for 10 min, tetrapropylammonium perruthenate (39 mg, 0.11 mmol) was added. The mixture was stirred at rt for 1 h and was then filtered through a pad of silica gel. The solid was washed with CH_2Cl_2 (20 mL) and EtOAc (100 mL). The solvents were removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/CH_2Cl_2/CH_3CO_2Et 1/1/1) to give 757 mg (78%) of lactone **7** as a white solid: mp 135−136 °C; $[\alpha]^{20}_D$ +4.3° (*c* 1.2, $CHCl_3$); IR (KBr) 1770, 1620, 1590 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.78 (dd, J = 7.8, 7.8 Hz, 1H), 3.03 (d, J = 7.8 Hz, 1H), 3.83 (s, 3H), 4.43 (bs, 1H), 5.36 (bs, 1H), 5.69 (d, J = 7.8 Hz, 1H), 6.34 (m, 1H), 6.47 (m, 1H), 6.94 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 46.3, 49.1, 55.3, 80.4, 81.6, 113.9, 127.4, 128.0, 136.9, 137.7, 159.6, 175.5; CIMS (NH_3) *m*/*z* (relative intensity) 276 (MNH_4^+, 71), 258 (M^+, 3), 208 (49), 191 (100). Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.71; H, 5.49.

(12) Oppolzer, W.; Tamura, O.; Deerberg, J. *Helv. Chim. Acta* **1992**, *75*, 1965.

(13) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 4011.

(14) Hanessian, S.; Murray, P. J. *J. Org. Chem.* **1987**, *52*, 1170.

(15) ^{1}H NMR spectra of **11** and **4** were in excellent agreement with those of the products already described in ref 6d. We thank Professor C. Mukai for sending us these documents. However, we found much higher values of optical rotations for these products than the one reported in this reference: **11**, $[\alpha]^{20}_D$ −141° (*c* 1.0, $CHCl_3$) (lit.[6d] $[\alpha]^{19}_D$ −90.4° (*c* 0.50, $CHCl_3$)); **4**, $[\alpha]^{20}_D$ −32° (*c* 0.57, $CHCl_3$) (lit.[6d] $[\alpha]^{19}_D$ −27.3° (*c* 0.50, $CHCl_3$)). In order to confirm the enantiomeric purity of our product, **4** was chemically transformed in its *N*-Boc derivative: $[\alpha]^{20}_D$ +20.7° (*c* 0.24, $CHCl_3$) (lit.[6c] $[\alpha]^{23}_D$ +20.1° (*c* 0.82, $CHCl_3$)).

(16) For a general description of experimental parameters see: Bloch, R.; Bortolussi, M.; Girard, C.; Seck, M. *Tetrahedron* **1992**, *48*, 453.

(4*S*)-4-(*p*-Methoxyphenyl)but-2-enolide (8). A solution of tricyclic adduct **7** (740 mg, 2.85 mmol) in toluene (10 mL) was heated under reflux for 2 h. The toluene was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/CH_2Cl_2/EtOAc: 50/30/20) to give 487 mg (90%) of butenolide **8** as a white solid: mp 88 °C; $[\alpha]^{20}_D$ −266° (*c* 1, $CHCl_3$); IR (KBr) 1775, 1750, 1620 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.82 (s, 3H), 5.98 (t, J = 1.6 Hz, 1H), 6.24 (dd, J = 5.6, 2 Hz, 1H), 6.92 (m, 2H), 7.19 (m, 2H), 7.51 (dd, J = 5.6, 1.6 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 55.0, 84.0, 114.1, 120.6, 125.7, 128.0, 155.8, 160.1, 173.0; CIMS (NH_3) m/z (relative intensity) 208 (MNH_4^+, 28), 191 (MH^+, 100). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.29. Found: C, 69.13; H, 5.10.

(3*S*,4*S*)-4-(*p*-Methoxyphenyl)-3-methyl-4-butanolide (9). To a suspension of CuI (660 mg, 3.47 mmol) in ether (10 mL) cooled at −20 °C was added dropwise a solution of methyllithium 1.5 M in ether (4.63 mL, 6.94 mmol). The reaction mixture was warmed to 0 °C and stirred at this temperature until a colorless clear solution was obtained. To this solution cooled at −78 °C was added dropwise freshly distilled chlorotrimethylsilane (440 μL, 376 mg, 3.47 mmol) followed by a solution of butenolide **8** (220 mg, 1.16 mmol) in ether (40 mL). After addition completion, the mixture was stirred for an additional 4 h at −78 °C and the temperature was allowed to rise gradually to −30 °C. A saturated NH_4Cl aqueous solution (20 mL) was then added at this temperature, and the reaction mixture was warmed to rt, extracted with CH_2Cl_2 (3 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (ether/hexane: 70/30) to afford 203 mg (85%) of butanolide **9** as a white solid: mp 109 °C; $[\alpha]^{20}_D$ +11.8° (*c* 1.0, $CHCl_3$); IR (KBr) 1780, 1770, 1730, 1610 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.17 (d, J = 6.4 Hz, 3H), 2.34 (dd, J = 16.3, 10.7 Hz, 1H), 2.5 (m, 1H), 2.80 (dd, J = 16.3, 7.1 Hz, 1H), 3.83 (s, 3H), 4.90 (d, J = 8.4 Hz, 1H), 6.92 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 16.2, 37.4, 39.6, 55.3, 88.1, 114.0, 127.5, 129.6, 159.9, 176.1; CIMS (NH_3) m/z (relative intensity) 224 (MNH_4^+, 96), 207 (MH^+, 100), 206 (M^+, 10). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.82; H, 6.90.

(2*R*,3*R*,4*S*)-2-Bromo-4-(*p*-methoxyphenyl)-3-methyl-4-butanolide (10). To a solution of diisopropylamine (63 μL, 0, 48 mmol) in THF (1 mL) cooled at 0 °C was added dropwise a solution of butyllithium 1.6 M in hexane (302 μL, 0.48 mmol). To this mixture, cooled at −78 °C was added dropwise a solution of butanolide **9** (83 mg, 0.40 mmol) in THF (2 mL). The solution was stirred for an additional 30 min at −78 °C, and the temperature was allowed to rise gradually to −40 °C. To the solution cooled again at −78 °C were added successively freshly distilled chlorotrimethylsilane (102 μL, 0.80 mmol) and a solution of phenyltrimethylammonium tribromide (227 mg, 0.6 mmol) in THF (2 mL). The solution was stirred for an additional 3 h at −78 °C, quenched at this temperature by the addition of saturated aqueous NH_4Cl (5 mL), and warmed to ambient temperature. The organic layer was separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 mL) and water (5 mL) and dried over $MgSO_4$. Concentration in vacuo and purification of the residue by silica gel chromatography (ether/hexane: 60/40) gave 80 mg (70%) of a mixture of two stereomers (92/8). Recrystallization from ether/hexane 50/50 (1 mL) afforded 64 mg of pure bromo lactone **10** as a white solid: mp 82 °C; $[\alpha]^{20}_D$ +46° (*c* 1.0, $CHCl_3$); IR (KBr) 1805, 1785, 1620 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.15 (d, J = 6.5 Hz, 3H), 2.42 (m, 1H), 3.83 (s, 3H), 4.56 (d, J = 5.7 Hz, 1H), 5.07 (d, J = 9.5 Hz, 1H), 6.94 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.6, 44.6, 47.9, 55.3, 86.0, 114.2, 127.0, 128.1, 160.6, 172.0; CIMS (NH_3) m/z (relative intensity): 304 and 302 (MNH_4^+, 64 and 77), 287 and 285 (MH^+, 99 and100). Anal. Calcd for $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.64; H, 4.57.

(2*S*,3*S*,4*S*)-2-Azido-4-(*p*-methoxyphenyl)-3-methyl-4-butanolide (11). To a solution of bromobutanolide **10** (64 mg, 0, 22 mmol) in dimethyl sulfoxide (1 mL), cooled at 0 °C was added sodium azide (58 mg, 0.9 mmol). The mixture was stirred for 1 h, and the reaction was quenched with water (1 mL). After extraction with CH_2Cl_2 (3 × 5 mL), the organic layers were dried over $MgSO_4$. The solvent was removed in vacuo and the residue was purified by chromatography on silica gel (ether/hexane: 60/40) to give 51 mg (92%) of compound **11** as a white solid: mp 93 °C; $[\alpha]^{20}_D$ −141° (*c* 1.0, $CHCl_3$); IR (KBr) 2140, 1805, 1795, 1620 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.21 (d, J = 6.7 Hz, 3H), 2.32 (m, 1H), 3.84 (s, 3H), 4.04 (d, J = 11.5 Hz, 1H), 4.86 (d, J = 10.1 Hz, 1H), 6.94 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.5, 45.8, 55.3, 64.4, 84.7, 114.2, 127.4, 128.1, 160.4, 172.3; CIMS (NH_3) m/z (relative intensity) 265 (MNH_4^+, 66), 248 (MH^+, 71), 222 (57), 220 (100). Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30. Found: C, 58.17; H, 5.45.

(2*S*,3*S*,4*S*)-2-Amino-4-(*p*-methoxyphenyl)-3-methyl-4-butanolide (4). To a solution of azide **11** (44 mg, 0.18 mmol) in THF (1 mL) was added triphenylphosphine (58 mg, 0.22 mmol), and this solution was stirred at room temperature until no more nitrogen was released (∼15 min). After addition of water (200 μL), the mixture was heated at 60 °C for 4 h (monitored by TLC). The solution was cooled, diluted with water (5 mL), extracted with ethyl acetate (5 × 5 mL), and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by chromatography on silica gel (EtOAc/CH_3OH: 95/5, aqueous NH_4OH 1/1000) to give 32 mg (80%) of amino lactone **4** as an oil: $[\alpha]^{20}_D$ −32.2° (*c* 0.57, $CHCl_3$); IR ($CDCl_3$) 3450, 1790, 1650, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.19 (d, J = 6.5 Hz, 3H), 1.66 (bs, 2H), 2.12 (m, 1H), 3.41 (d, J = 11.4 Hz, 1H), 3.83 (s, 3H), 4.80 (d, J = 10.1 Hz, 1H), 6.93 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.6, 48.3, 55.2, 58.8, 84.6, 114.0, 128.1, 128.5, 160.1, 177. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 65.03; H, 6.97.

JO9514533