ditional 16.3 mg of **3** as a white powder for a combined yield of 93%: R_f 0.05 (silica gel, 40:60:4:0.2 chloroform–methanol–water–15 M ammonium hydroxide); $[\alpha]^{22}_D$ +44.6° (*c* 0.505, H_2O); ^1H NMR (D_2O, HOD = 4.80 ppm) δ 2.09 (dd, 1 H, *J* = 17 Hz, *J'* = 15 Hz, PC*H*HC), 2.12 (dd, 1 H, *J* = *J'* = 13 Hz, CC*H*HCH), 2.15 (dd, 1 H, *J* = 17 Hz, *J'* = 15 Hz, PC*H*HCH), 2.39 (dd, 1 H, *J* = 13 Hz, *J'* = 5 Hz, CCH*H*CH), 3.37 (d, 1 H, *J* = 8 Hz, $HOCH_2CHCHCH$), 3.70 (dd, 1 H, *J* = 9 Hz, *J'* = 4 Hz, HOC*H*HCH), 3.75 (ddd, 1 H, *J* = 13 Hz, *J'* = 5 Hz, *J''* = 3 Hz, CCH_2CHCH), 3.80–3.90 (m, 3 H, HOCH*H*CH, $HOCH_2CHCH$, $POCH_2CHCH$), 4.04 (ddd, 1 H, *J* = 12 Hz, *J'* = 6 Hz, *J''* = 2 Hz, POC*H*HCH), 4.17 (ddd, 1 H, *J* = 12 Hz, *J'* = 4 Hz, *J''* = 2 Hz, POCH*H*CH), 4.25 (br s, 1 H, $CCH_2CHCHCH$), 4.26–4.34 (m, 2 H, NC*H*CHCH), 5.93 (d, 1 H, *J* = 3 Hz, NC*H*CH), 6.17 (d, 1 H, *J* = 7 Hz, NCH=C*H*), 8.09 (d, 1 H, *J* = 7 Hz, NC*H*=CH); ^{13}C NMR (D_2O, 125.76 MHz) δ 33.75, 36.67 (d, *J* = 133.4 Hz), 62.41 (d, *J* = 4.5 Hz), 63.96, 66.40, 67.70, 68.96, 69.05, 74.22, 74.38, 79.41 (br s), 82.82 (d, *J* = 6.8 Hz), 89.48, 95.98, 142.32, 154.46, 163.72, 178.98 (br s); FAB MS, *m/z* 542 $(M + H)^+$, 564 $(M + Na)^+$; exact mass calcd for $C_{18}H_{28}N_3O_{14}PNa$ $(M + Na)^+$ 564.1207, found 564.1224.

Phosphonate 17. To a stirred solution of 55 mg (0.105 mmol) of the phosphonate **11** in 3 mL of methanol was added 0.6 mL of aqueous 1 N NaOH. After 5 h at 50 °C, the reaction was cooled, diluted with 3 mL of water, brought to pH 2 with Dowex HCR-S resin, filtered, and concentrated under reduced pressure. The residue was dissolved in 3.0 mL of water and allowed to stand at room temperature for 38 h. TLC (silica gel, 4:3:1 chloroform–methanol–15 M ammonium hydroxide) indicated conversion of a diacid (R_f 0.11) to the triacid **17** (R_f 0.01). The reaction mixture was concentrated under reduced pressure. Chromatography of the residue on 5 g of Baker (aminopropyl)silane-bonded silica gel with 60:40:2 methanol–water–15 M ammonium hydroxide and lyophilization afforded 30.1 mg (78%) of the phosphonate **17** as a white solid: R_f 0.08 (EM Science, HPTLC-NH_2, F-254, 60:40:2 methanol–water–15 M ammonium hydroxide); $[\alpha]^{22}_D$ 49.4° (*c* 0.64, H_2O); ^1H NMR (D_2O, HOD = 4.80 ppm) δ 2.04 (dd, 1 H, *J* = 21 Hz, *J'* = 15 Hz, PC*H*HC), 2.08 (dd, 1 H, *J* = *J'* = 13 Hz, CC*H*CH), 2.10 (dd, 1 H, *J* = 21 Hz, *J'* = 15 Hz, PCH*H*C), 2.35 (dd, 1 H, *J* = 13 Hz, *J'* = 5 Hz, CCH*H*CH), 3.38 (d, 1 H, *J* = 9 Hz, $OCH_2CHCHCH$), 3.68–3.90 (m, 5 H); ^{13}C NMR (D_2O, CH_3CN = 1.40 ppm) δ 34.49 (d, *J* = 3.8 Hz), 38.82 (d, *J* = 129.8 Hz), 64.58, 66.89, 68.25, 69.65, 75.17, 80.06 (d, *J* = 4.5 Hz), 179.96 (d, *J* = 9 Hz); FAB MS, *m/z* 317 $(M + H)^+$; exact mass calcd for $C_9H_{18}O_{10}P$ $(M + H)^+$ 317.0638, found 317.0645.

Acknowledgment is made to the Abbott Analytical Group for assistance in obtaining spectral data.

A 1,3-Dipolar Cycloaddition Route to the 3(*R*)- and 3(*S*)-Hydroxy-(2*S*)-arginines

John Wityak, Steven J. Gould,*[1] Scott J. Hein, and Douglas A. Keszler*

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331

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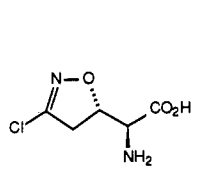
The 3(*R*)- and 3(*S*)-hydroxy-(2*S*)-arginines (**4a** and **4b**) were prepared from the corresponding β-hydroxyornithines (**3a** and **3b**) via the methyl 2(*S*)-[2-benzyl-(5(*R*,*S*)-isoxazolidinyl][*N*-((benzyloxy)carbonyl)amino]acetates (**5a** and **5b**). The isoxazolidines **5** were prepared from the 1,3-dipolar cycloaddition of 2(*S*)-vinylglycine derivative **6** with a nitrone generated in situ from *N*-benzylhydroxylamine and paraformaldehyde.

Our studies on the biosynthesis of acivicin (**1**)[2] and streptothricin F (**2**)[3] required the synthesis of the (2*S*,3*R*)- and (2*S*,3*S*)-β-hydroxyornithines (**3a** and **3b**) and the corresponding β-hydroxyarginines (**4a** and **4b**), respectively. Syntheses of the *threo*- and *erythro*-β-hydroxy-



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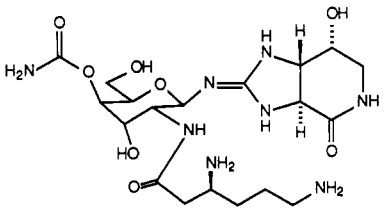

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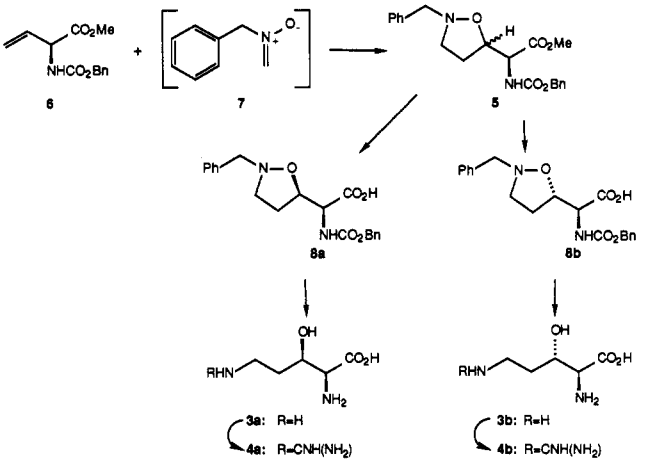
ornithines have previously been reported,[4] although only in racemic form; furthermore, these syntheses were either lengthy or not amenable to the introduction of isotope labels.

Noting that isoxazolines can be reduced to afford β-amino alcohols,[5] we found that **3b** could be obtained in 78% yield from a catalytic reduction of **1**. Since acivicin and its C3 diastereomer have been synthesized from 2-(*S*)-(*N*-phthalimidovinyl)glycine,[6] this would constitute a formal synthesis of **3a** and **3b**. Removing what would be extraneous functionality for our purpose, we focused on

Scheme I



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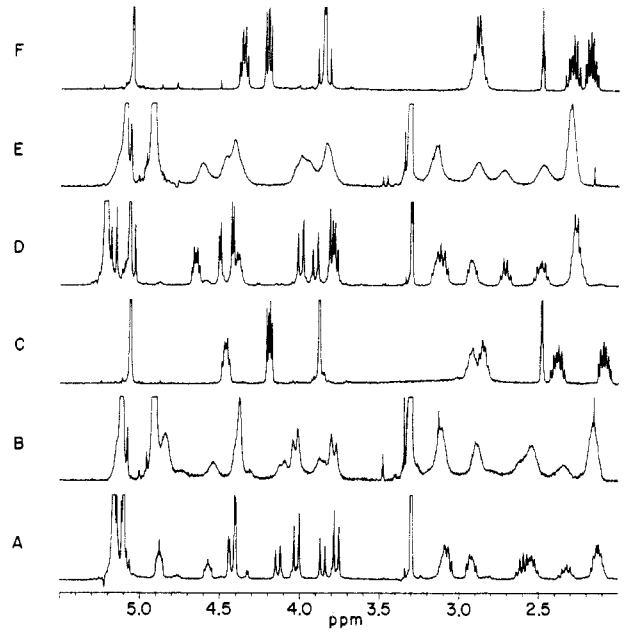


Figure 1. ^{1}H NMR of **8a** at 270 (a) and 298 K (b) in methanol and at 348 K (c) in Me_2SO and of **8b** at 270 (d) and 298 K (e) in methanol and at 350 K (f) in Me_2SO.

the synthesis of isoxazolidines **5a** and **5b**.

As shown in Scheme I, in the presence of protected 2(*S*)-vinylglycine (**6**),[7] nitrone **7** was generated in situ from *N*-benzylhydroxylamine[8] and paraformaldehyde. Dipolar cycloaddition of **6** and **7** then afforded a 92% yield of **5** in a diastereomer ratio of 1.6:1.0. These proved difficult to separate. Careful hydrolysis with lithium hydroxide, however, gave the acids **8a** and **8b** in almost quantitative yield, which were separable by flash chromatography.

The ^{1}H and ^{13}C NMR spectra of the esters (**5a** and **5b**) and the acids (**8a** and **8b**) exhibited only broad, ill-defined resonances at room temperature (Figure 1, parts b, **8a**, and e, **8b**). Such NMR dynamics may be due to hindered rotation about the carbamate C–N bond[9] or due to multiple ring conformations arising from inversion at the isoxazolidine nitrogen.[10] Acquisition of the ^{1}H NMR spectrum of the major isomer of the acids **8** at 270 K then produced a fully resolved spectrum (Figure 1, parts a, **8a**, and d, **8b**) of conformers in an apparent ratio of 1.74:1.00 (in methanol). At temperatures of 348 K for **8a** and 350 K for **8b** (in Me_2SO), however, interconversion was sufficiently rapid to afford fully resolved, averaged spectra (Figure 1, parts c, **8a**, and f, **8b**).

From the low-temperature ^{1}H NMR and two-dimensional shift-correlated NMR (COSY) experiments (Figure 2) the coupling constants could be measured and tentative stereochemical assignments made. Thus, it was determined that H2 (δ 4.42) of the major conformer of the major isomer was coupled to H3 (δ 4.90) with J = 2.8 Hz, while in the major conformer of the minor isomer the coupling constant between H2 (δ 4.41) and H3 (δ 4.65) was 5.3 Hz. By analogy to the coupling constants reported for the known structures **1**,[11] **9**,[12] **10**,[13] and **11**,[13] we were tempted

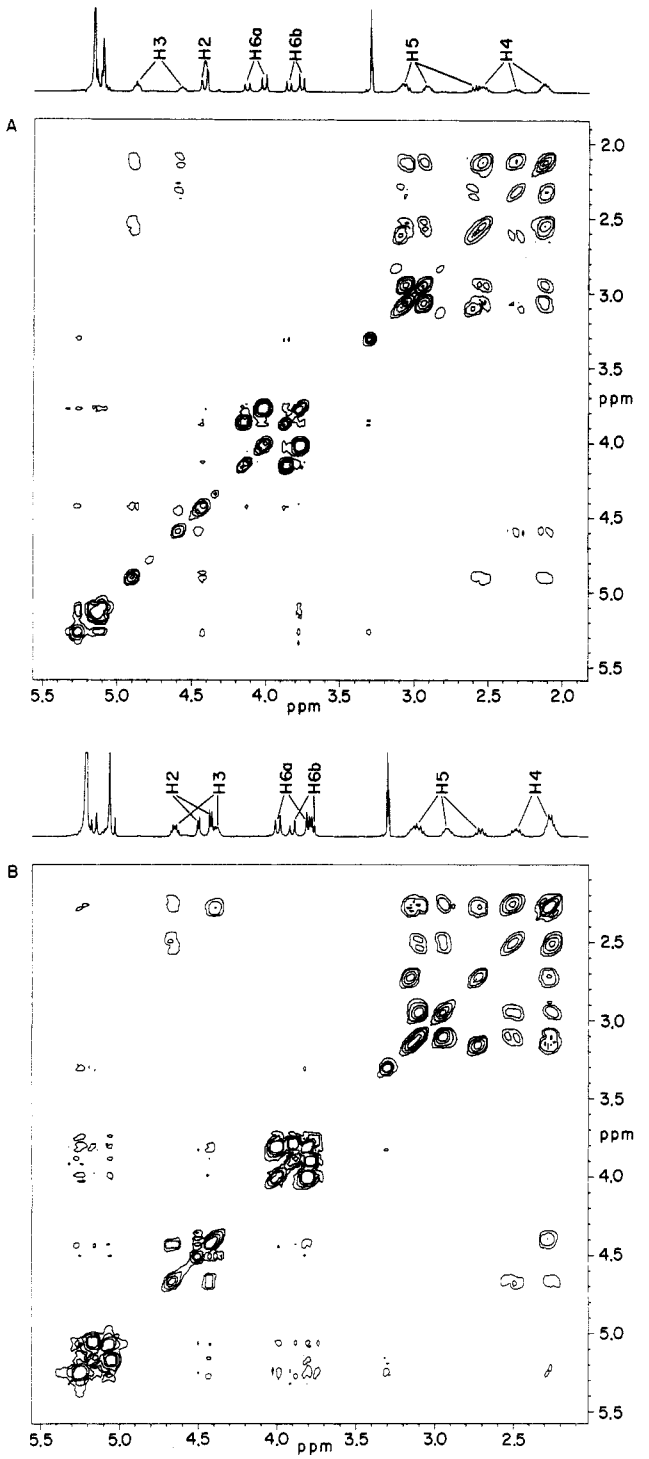
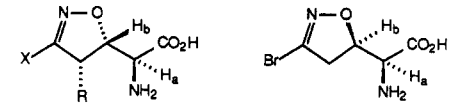


Figure 2. Two-dimensional shift-correlated spectra of **8a** (a) and **8b** (b) in methanol at 270 K.

to assign the major and minor isomers as the erythro and threo stereochemistries, respectively; however, subsequent evidence would refute this assignment.



1: R = H, X = Cl, J_{ab} = 3.5 Hz
9: R = OH, X = Cl, J_{ab} = 4.0 Hz
10: R = H, X = Br, J_{ab} = 3.5 Hz

11: J_{ab} = 7.4 Hz

Isoxazolidine **8a** proved more difficult to reduce catalytically than had acivicin. Attempted hydrogenolysis under a variety of conditions afforded a mixture of prod-

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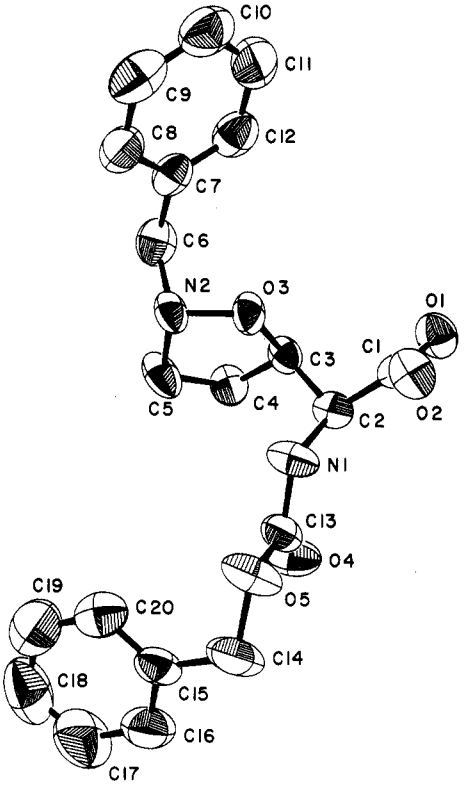
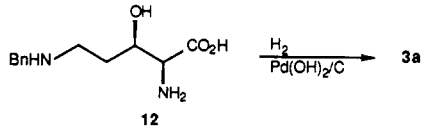


Figure 3. ORTEP drawing from the single-crystal X-ray structure determination of **8a**. Hydrogens have been omitted for clarity.

ucts of which β-hydroxyornithine was a minor component. Dissolving metal reduction using sodium in ammonia then gave N^5-benzyl-β-hydroxyornithine (**12**). This compound was presumed to be the major product from the previous catalytic reductions. Hydrogenolysis of **12** over Pearlman's catalyst ($Pd(OH)_2/C$) afforded β-hydroxyornithine; however, this material was not identical with the (2*S*,3*S*)-*erythro*-β-hydroxyornithine from the previous catalytic reduction of **1**. Therefore the assignment of stereochemistry of the adducts from the cycloaddition was revised, making the major isomer the threo isomer. Indeed, reduction of **8b** using Pearlman's catalyst gave the *erythro*-β-hydroxyornithine (**3b**) in 78% yield, identical in all respects with **3b** obtained from **1**, except for a small difference in optical rotation. Reduction of **8a** similarly afforded the *threo*-β-hydroxyornithine (**3a**) in 80% yield.



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The structure of **1** had been established as erythro by single-crystal X-ray analysis.[11] Thus it appeared that our comparison of coupling constants was misleading. This was clarified with a single-crystal X-ray analysis of **8a**. The ORTEP drawing in Figure 3 clearly shows the threo relationship in **8a**, confirming the results from reductions of **8a**, **8b**, **1**, and **12**. Interestingly, using the value of 67.8° obtained for the dihedral angle (H2–C2–C3–H3), the Karplus equation[14] predicts a $^3J_{HH}$ of 3.0 Hz, nearly identical with the coupling of 2.8 Hz found in solution.

It was anticipated that the conversion of **3a** and **3b** to the corresponding β-hydroxyarginines **4a** and **4b** could be obtained via the copper complexes. β-Hydroxy amino acids such as the *threo*- and *erythro*-phenylserines were believed to behave as tridentate ligands, complexing the amino, carboxyl, and hydroxyl groups to copper.[15] Initially, small-scale reaction of such complexes of **3a** or **3b** with *O*-methyl isourea tosylate[16] met with sluggish reaction rates and modest yields of amino acids. Reaction with *S*-methyl isothiourea sulfate[17] markedly increased the reaction rate, but also quite understandably precipitated all of the copper from these attempts after 2 h. Efforts to improve on this conversion were unsuccessful and resulted in yields of only 15–30% until the reactions were scaled-up, whereupon reactions of the **3a** and **3b** copper complexes with *S*-methyl isothiourea sulfate now afforded **4a** and **4b** in 57% and 60% yields, respectively, and with no structural isomers detected.

Experimental Section

Melting points were determined on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on either a Perkin-Elmer 727B infrared spectrophotometer or a Nicolet 5DXB FT-IR spectrophotometer. UV spectra were obtained on an IBM 9420 UV–vis spectrophotometer. ^1H NMR spectra were obtained on either a Varian FT-80A instrument at 80 MHz or a Bruker AM 400 spectrometer at 400.13 MHz with Me_4Si (δ 0.0) or *t*-BuOH (δ 1.27) as internal standard. ^{13}C NMR spectra were determined on a Bruker AM 400 spectrometer at 100.61 MHz with Me_4Si (δ 0.0) or MeCN (δ 1.3) as internal standard. Mass spectra were obtained on a Varian MAT CH7 spectrometer with a System Industries 150 data system. High-resolution mass spectra were taken on a Kratos MS 50 TC spectrometer. Optical rotations were determined on a Perkin-Elmer 243 polarimeter. All solvents were distilled prior to use. Thin-layer chromatography was done on either EM Reagents 5729-6 silica gel 60 F_{254} glass-backed or Eastman 13254 cellulose plastic-backed plates. All preparative flash chromatography was carried out with E. Merck 230–400 mesh, 9385 silica gel 60. Pearlman's catalyst and Adam's catalyst were purchased from Aldrich. Elemental analyses were performed by MicAnal, Organic Microanalysis, Tucson, AZ.

3(*S*)-Hydroxy-(2*S*)-ornithine, Hydrochloride (3b). Into a 50-mL round-bottomed flask was placed the isoxazoline **1** (90 mg, 0.5 mmol) along with platinum oxide (40 mg) and glacial acetic acid (20 mL). The mixture was hydrogenated at room temperature and atmospheric pressure for 1 day, after which time the catalyst was filtered off with the aid of Celite and washed with water. The combined filtrates were concentrated in vacuo, and the residue was taken up in a small volume of water. Following adjustment to pH 6.5, the hydrochloride was crystallized by the addition of ethanol, affording 70 mg (78%) of **3b**: TLC (4:2:1 *n*-BuOH/H_2O/AcOH on cellulose, 0.3% ethanolic ninhydrin spray) R_f 0.34; $[\alpha]^{25}_D$ +1.0° (*c* 3, H_2O), +20.5° (c 2, 6 N HCl); ^1H NMR (D_2O, 400 MHz) δ 4.28 (1 H, m), 3.91 (1 H, d, *J* = 3.7 Hz), 3.20 (2 H, m), 2.01 (1 H, m), 1.88 (1 H, m).

Methyl 2(*S*)-[2-Benzyl-5(*R*,*S*)-isoxazolidinyl][*N*-((benzyloxy)carbonyl)amino]acetate (5a and 5b). The olefin **6** (989 mg, 3.968 mmol), paraformaldehyde (595 mg, 5 equiv), *N*-benzylhydroxylamine[8] (525 mg, 4.26 mmol, 1.1 equiv), 4-Å molecular sieves (1.22 g), and benzene (65 mL) were placed into a 100-mL round-bottomed flask fitted with a condenser. The reaction was heated at 85 °C in an oil bath for 12 h, followed by removal of the sieves by filtration. Concentration of the combined filtrates in vacuo afforded a golden syrup which was purified by flash chromatography (1:4:95 MeOH/EtOAc/benzene, 3 × 26 cm column), affording 1.411 g (92%) of the partially separated isoxazolidines as a light yellow oil in a ratio of 1.4:1.0 (threo/erythro) for the diastereomers [TLC (2:1:87 MeOH/EtOAc/benzene on silica gel 60, 3% $(NH_4)_2Ce(NO_3)_6$ in 2 N H_2SO_4 spray) R_f 0.28 (threo), 0.23 (erythro)]. A small amount of nearly pure threo isomer **5a** could routinely be obtained after chromatography:

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IR (neat) 3340, 3090, 2900, 1760, 1720, 1510 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 270 K, major conformer) δ 7.38 (5 H, s), 7.32 (5 H, s), 6.24 (1 H, d, J = 8.8 Hz), 5.15 (2 H, s), 4.81 (1 H, ddd, J = 8.8, 5.2, 2.2 Hz), 4.41 (1 H, dd, J = 8.8, 2.2 Hz), 4.11 (1 H, d, J = 12.5 Hz), 3.74 (3 H, s), 3.72 (1 H, d, J = 12.5 Hz), 3.16 (1 H, m), 2.68 (1 H, m), 2.52 (1 H, m), 2.24 (1 H, m); mass spectrum (70 eV), m/z (relative intensity) 386 (M + 2, 0.8), 385 (M + 1, 4.1), 384 (M^+, 22.0).

2(*S*)-[2-Benzyl-5(*S*)- and 2(*S*)-[2-Benzyl-5(*R*)-isoxazolidinyl][*N*-((benzyloxy)carbonyl)amino]acetic acids (8a and 8b). The esters **5a** and **5b** (932 mg, 2.42 mmol, 1.4:1.0 threo/erythro) were dissolved in THF (30 mL) and cooled to 5 °C in an ice–water bath. To this was added 0.56 N LiOH (10 mL) and the reaction stirred vigorously for 2 h. The mixture was concentrated in vacuo at 35 °C to a volume of 10 mL, followed by pH adjustment to 5.6 with 10% HCl and saturation with ammonium sulfate. Extraction of the resulting mixture with EtOAc and concentration of the combined, dried ($MgSO_4$) organic extracts gave a yellow syrup, which was purified by flash chromatography (1:7:92 AcOH/MeOH/$CHCl_3$, 2.7 × 30 cm column). Combination of the appropriate fractions followed by crystallization of each diastereomer from methanol–water afforded 518 mg of **8a** and 375 mg of **8b** (99% combined). Data for threo isomer **8a**: TLC (1:7:92 AcOH/MeOH/$CHCl_3$ on silica gel 60) R_f 0.30; mp 129 °C dec; $[\alpha]^{25}_D$ −9.1° (*c* 2, MeOH); IR (1% KBr) 3440, 3325, 1720, 1700, 1500 cm^{-1}; ^1H NMR (MeOH-d_4, 400 MHz, 270 K, major conformer) δ 7.3 (10 H, m), 5.09 (2 H, d, J = 2.4 Hz), 4.9 (1 H, m), 4.42 (1 H, d, J = 2.8 Hz), 4.01 (1 H, d, J = 12.6 Hz), 3.76 (1 H, d, J = 12.6 Hz), 3.07 (1 H, m), 2.95 (1 H, m), 2.56 (1 H, m), 2.10 (1 H, m); FABMS (glycerol) m/z (relative intensity) 371 (M + H, 28.4), 370 (M^+, 1.5), 91 (100). Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.73; H, 5.95; N, 7.52. Data for erythro isomer **8b**: TLC R_f 0.24; mp 122 °C dec; IR (1% KBr) 3300, 1710, 1680, 1520 cm^{-1}; ^1H NMR (MeOH-d_4, 400 MHz, 270 K, major conformer) δ 7.3 (10 H, m), 5.07 (2 H, s), 4.65 (1 H, m), 4.41 (1 H, d, J = 5.3 Hz), 3.96 (1 H, d, J = 12.8 Hz), 3.81 (1 H, d, J = 12.8 Hz), 3.13 (1 H, m), 2.94 (1 H, m), 2.50 (1 H, m), 2.27 (1 H, m); $[\alpha]^{25}_D$ +17.4° (*c* 2, MeOH); FABMS (glycerol), m/z (relative intensity) 371 (M + H, 4.3), 115 (36.2), 91 (100). Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.87; H, 6.02; N, 7.39.

The two-dimensional shift-correlated (COSY-45) data for **8a** was acquired at 270 K and at a sweep width of 3600 Hz (1024 data points) in the $F2$ domain; 256 spectra (eight scans each) were accumulated with 0.278-ms increments across the interval 3 μs to 71.17 ms. A 1-s recycle delay was inserted between scans to allow for spin relaxation. The digital resolution was 7.026 Hz/dp after zero filling in $F1$. Resolution enhancement was accomplished by applying a $\pi/2$-shifted sinebell window function to $F1$ and $F2$ prior to Fourier transformation. The COSY-45 data for **8b** was acquired and processed in an identical fashion except as follows: a sweep width of 3700 Hz and a 0.268-ms increment across the interval 3 μs to 68.61 ms was used. The digital resolution was 7.288 Hz/dp.

***threo*-N^5-Benzyl-β-hydroxy-L-ornithine, Hydrochloride Monohydrate (12).** An oven-dried assemblage consisting of a 100-mL three-neck flask, stirrer, and Dewar condenser was placed under a nitrogen atmosphere followed by introduction of the isoxazolidine **8a** (200 mg, 0.540 mmol). A dry ice–acetone mixture was placed in the Dewar and the flask was also immersed in a dry ice–acetone bath. Ammonia gas was condensed into the flask to a volume of 40 mL and freshly shaved sodium metal (120 mg, 5 mmol) added, causing the solution to immediately turn a deep blue. After 3 h the ammonia was allowed to evaporate, leaving a white residue, which was taken up in water followed by adjustment to pH 6.5. Inorganic salts were precipitated by the addition of ethanol and acetone and were removed by centrifugation. The supernatant was then brought to the cloud point with additional acetone, affording 115 mg (73%) of **12**: TLC (4:1:1 *n*-BuOH/AcOH/H_2O on cellulose, 0.3% ethanolic ninhydrin spray) R_f 0.45; mp 212.5 °C dec; $[\alpha]^{25}_D$ +11.6° (*c* 0.9, H_2O); FTIR (1% KBr) 3418, 2943, 1652 cm^{-1}; UV [*c* 7.286 × 10^{-5} M (H_2O)] λ_{max} (ε) 256.0 (329), 205.4 (6615); ^1H NMR (D_2O, 400 MHz) δ 7.53 (5 H, s), 4.31 (2 H, s), 4.16 (1 H, ddd, J = 9.4, 5.9, 3.5 Hz), 3.68 (1 H, d, J = 5.9 Hz), 3.31 (2 H, m), 2.13 (1 H, m), 2.0 (1 H, m); ^{13}C NMR (D_2O, 100 MHz) δ 172.42, 131.05, 130.22, 130.15, 129.73, 68.03, 59.75, 51.61, 44.69, 30.37. Anal. Calcd for $C_{12}H_{21}N_2O_4Cl$: C, 49.23; H, 7.23; N, 9.56; Cl, 12.10. Found C, 49.23; H, 7.15; N, 9.54; Cl, 12.10.

Reduction of threo-N^5-Benzyl-β-hydroxy-L-ornithine, Hydrochloride Monohydrate (12). To the benzylamine **12** (10 mg, 0.034 mmol) were added 20% $Pd(OH)_2/C$ (30 mg), 95% ethanol (2 mL), and 1.2 N HCl (57 μL, 2 equiv). The mixture was hydrogenated at room temperature and atmospheric pressure for 6 days, after which the catalyst was filtered and washed with water, and the combined filtrates were concentrated to a residue. Crystallization of the residue from ethanol–water at pH 6.5 gave 3 mg (48%) of **3a**: TLC (4:2:1 *n*-BuOH/H_2O/AcOH on cellulose, 0.3% ethanolic ninhydrin spray) Rf 0.34.

3(*R*)-Hydroxy-(2*S*)-ornithine, Hydrochloride (3a). To the isoxazolidine **8a** (379 mg, 1.02 mmol) were added 20% $Pd(OH)_2/C$ (400 mg), absolute ethanol (20 mL), and 6 N HCl (0.35 mL, 2.1 mmol). The mixture was then hydrogenated at atmospheric pressure and room temperature. After 4 days the reaction was stopped and filtered through Celite followed by water wash. The pH was then adjusted to 6.6 with NH_4OH followed by concentration in vacuo to a volume of 0.5 mL. To this was added ethanol, which caused the amino acid to crystallize, affording 138 mg (73%) of **3a**: TLC (4:2:1 *n*-BuOH/H_2O/AcOH on cellulose, 0.3% ethanolic ninhydrin spray) Rf 0.33; mp 123 °C dec (lit.[4b] mp for D,L 189–190 °C dec); $[\alpha]^{25}_D$ +2.9° (*c* 3, H_2O), +9.6° (*c* 2, 6 N HCl); IR (1% KBr) 3350, 2950, 1580 cm^{-1}; ^1H NMR (D_2O, 400 MHz) δ 4.22 (1 H, ddd, J = 8.4, 5.1, 3.3 Hz), 3.72 (1 H, d, J = 5.1 Hz), 3.23 (2 H, m), 2.08 (1 H, m), 1.97 (1 H, m); ^{13}C NMR (D_2O, 100 MHz) δ 172.37, 68.00, 59.62, 37.24, 31.30; FABMS (monothioglycerol + HCl), m/z (relative intensity) 150 (M + 1 − Cl, 6.3), 149 (M^+ − Cl, 100).

3(*S*)-Hydroxy-(2*S*)-ornithine, Hydrochloride (3b). This was prepared as per **3a** except as follows. The isoxazolidineacetic acid **8b** (200 mg, 0.540 mmol) afforded 78 mg (78%) of **3b**: TLC (4:2:1 *n*-BuOH/H_2O/AcOH on cellulose, 0.3% ethanolic ninhydrin spray) R_f 0.34; mp 232 °C dec (lit.[4b] mp for D,L 225 °C dec); $[\alpha]^{25}_D$ +0.4° (*c* 3, H_2O), +18.0° (*c* 2, 6 N HCl); IR (1% KBr) 2900 (b), 1600, 1500, 1320, 1140 cm^{-1}; ^1H NMR (D_2O, 400 MHz) identical with that of the product from reduction of **1**; ^{13}C NMR (D_2O, 100 MHz) δ 171.39, 67.88, 59.41, 37.60, 29.03; FABMS (monothioglycerol + HCl), m/z (relative intensity) 150 (M + 1 − Cl, 14.9), 149 (M^+ − Cl, 100).

3(*R*)-Hydroxy-(2*S*)-arginine, Hydrochloride (4a). To the amino acid **3a** (580 mg, 3.14 mmol) in water (15 mL) was added basic copper carbonate (1.4 g, 6.3 mmol) and the resulting mixture heated to near boiling for several minutes. The excess copper salts were removed by filtration and washed with water. To the combined filtrates was added *S*-methyl isothiourea sulfate[17] (960 mg, 3.44 mmol, 1.1 equiv) followed by adjustment to pH 9.7 with 10% NaOH. After 2 h, most of the blue color had faded and was replaced by a yellow precipitate of copper methylthiolate. This precipitate was removed by filtration after 4 days and washed with water. The combined filtrates were adjusted to pH 5.5 with 10% HCl and lyophilized. The resulting lyophilizate was dissolved in water and adjusted to pH 2.5 followed by passage through a column of Dowex 50W-X8 (H^+ form, 100 mesh, 1.5 × 8.5 cm column, 100 mL of H_2O → 6 N NH_4OH (linear gradient)). Combination and lyophilization of the appropriate fractions then afforded 400 mg of a white powder, which was crystallized from ethanol–water at pH 6.6 to give 404 mg (57%) of the amino acid hydrochloride **4a**: TLC (2:2:2:1 *n*-BuOH/H_2O/acetone/Et_2NH on cellulose, Sakaguchi[18] spray) R_f 0.42; mp 212 °C dec; $[\alpha]^{25}_D$ +10.4° (*c* 2, H_2O); IR (1% KBr) 3400, 3200, 1700, 1660, 1640 cm^{-1}; ^1H NMR (D_2O, 400 MHz) δ 4.14 (1 H, m), 3.67 (1 H, d, J = 5.3 Hz), 3.40 (2 H, m), 2.00 (1 H, m), 1.84 (1 H, m); ^{13}C NMR (D_2O, 100 MHz) δ 172.64, 157.24, 67.52, 59.92, 38.16, 32.83; HRMS (FAB, monothioglycerol + HCl), m/z 191.1185, calcd for $C_6H_{15}N_4O_3$ 191.1144.

3(*S*)-Hydroxy-(2*S*)-arginine, Hydrochloride (4b). This was prepared in a similar fashion to **4a** except as follows. **3b** (430 mg, 2.33 mmol) afforded 317 mg (60%) of **4b**: TLC (2:2:2:1 *n*-BuOH/H_2O/acetone/Et_2NH on cellulose, Sakaguchi spray) R_f 0.42; mp 204 °C dec; $[\alpha]^{25}_D$ −3.8° (*c* 2, H_2O); FTIR (1% KBr) 3400,

(18) Acher, R.; Crocker, C. *Biochim. Biophys. Acta* **1952**, *9*, 704.

3200, 3100, 1677, 1641 cm^{-1}; ^{1}H NMR (D_2O, 400 MHz) δ 4.22 (1 H, m), 3.90 (1 H, d, J = 2.6 Hz), 3.39 (2 H, m), 1.83 (2 H, m); ^{13}C NMR (D_2O, 100 MHz) δ 172.87, 158.40, 71.29, 60.81, 39.58, 31.78; HRMS (FAB, monothioglycerol + HCl) 191.1170, calcd for $C_6H_{15}N_4O_3$ 191.1144.

X-ray Crystallography of $C_{20}N_2O_5H_{22}$ (8a). Examination of the crystal by Weissenberg photography established that it belongs to the orthorhombic system. The systematic absences ($h01$, $l = 2n + 1$; $0kl$, $l = 2n + 1$) and the chirality of the molecule are uniquely accommodated by the space group $Pca2_1$. Intensity data were collected at Molecular Structure Corporation with Cu Kα radiation on a Rigaku AFC6 diffractometer equipped with a graphite crystal, incident beam monochromator, and 12-kW rotating anode generator. The intensities of three representative reflections, measured after every 150 reflections throughout data collection, were constant.

The structure was solved and refined with use of the TEXSAN crystallographic software package. With the exception of C14 and C17, the positions of the C, N, and O atoms were determined from the direct methods program MITHRIL. The atoms C14 and C17 were located from an ensuing electron density synthesis. Eleven of the H atoms were located on difference electron density syntheses following partial refinement. All H atoms were subsequently placed in calculated positions and assigned isotropic thermal parameters of value one greater than that of the atom to which it binds, with the exception of the H atom bound to the carboxyl group which was not located. An absorption correction was not applied. The final cycle of refinement with anisotropic thermal parameters for the non-hydrogen atoms affords a value of 0.050 for the conventional index R on F for those 1045 reflections having $F_o^2 \geq 3\sigma(F_o^2)$. The final difference electron density map contains no features greater than 1.9% of the height of an O atom. Analysis of F_o^2 vs. F_c^2 as a function of F_o^2, $\lambda^{-1}\sin\theta$, and Miller indices reveals no unusual trends.

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Supplementary Material Available: Tables of relevant details of the X-ray crystallographic studies (Table I) and Tables of final atomic parameters, anisotropic thermal parameters, and selected bond distances and bond angles (Tables II, III, and V) (4 pages); table of structure amplitudes (8 pages). Ordering information is given on any current masthead page.

Reaction of 1,8-Bis(phenylethynyl)naphthalene with Phenylchlorocarbene: Formation of an Intramolecular Cyclization Product from the Carbene Monoadduct and of 1,8-Naphthylenebis(diphenylcyclopropenylium) Dication from the Bisadduct

Koichi Komatsu,[1a] Mikiro Arai,[1a] Yoshiyuki Hattori,[1a] Keiichi Fukuyama,[1b] Yukiteru Katsube,[1b,c] and Kunio Okamoto*[1a]

Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto 606, Japan, and Faculty of Engineering, Tottori University, Koyamacho, Tottori 680, Japan

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The reactions of 1,8-bis(phenylethynyl)naphthalene (**4**) with phenylchloro- and dichlorocarbenes and chemistry of the obtained products have been studied. The reaction of **4** with 1 equiv of phenylchlorocarbene exclusively affords spirocyclopropene **8**, whose structure has been determined by X-ray crystallography. The formation of **8** is interpreted by intramolecular "ene"-type cyclization of the carbene monoadduct **5**. Upon thermolysis, **8** cleanly rearranges into chloro-8*H*-cyclopent[*a*]acenaphthylene **7** by way of cyclopropene ring cleavage. From the results of kinetic studies, the activation energy for this rearrangement has been determined as 23.8 kcal/mol. The reaction of **4** with dichlorocarbene generated under the phase-transfer catalytic conditions affords cyclopropenone **12a**, which undergoes thermal rearrangement to acecyclone (**14**) in addition to decarbonylation. Hydroxycyclopropenylium ion **19a** has been generated from **12a** and characterized with ^{13}C NMR. The reaction of **4** with 2 equiv or an excess of phenylchlorocarbene affords dicyclopropenylnaphthalene **6** or **21**, which can be converted to the new face-to-face dication **3**. The effects of electrostatic repulsion of the two cationic rings in **3** upon the properties of the monocation unit is discussed based on ^{13}C NMR data and values of pK_{R^+} and reduction potential. The zinc reduction of dication **3** smoothly affords fluoranthene **30**, which has been produced supposedly by way of intramolecular coupling of cyclopropenyl radicals followed by bis(cyclopropenyl)–benzene rearrangement.

The compounds containing two or more π-electronic systems which are held in a face-to-face conformation can serve as fundamental models for study of intermolecular π-electronic interaction. Especially when the interacting π-systems can act as a pair of electron donor and acceptor, the whole system is regarded as an undissociable charge-transfer complex.[2,3] Among various compounds with such structural features, 1,8-disubstituted naphthalenes are characteristic in that the σ-bonds at the 1,8-positions stand

(1) (a) Kyoto University. (b) Tottori University. (c) Present address: Institute for Protein Research, Osaka University, Suita, Osaka 565, Japan.

(2) For example, see: O'Connor, J. G.; Keehn, P. M. *J. Am. Chem. Soc.* **1976**, *98*, 8446. Horita, H.; Otsubo, T.; Sakata, Y.; Misumi, S. *Tetrahedron Lett.* **1976**, 3899. Nakazawa, T.; Murata, I. *J. Am. Chem. Soc.* **1977**, *99*, 1996. Komatsu, K.; Takahashi, K.; Okamoto, K. *Tetrahedron Lett.* **1979**, 4747. Yamamura, K.; Nakasuji, K.; Murata, I.; Inagaki, S. *J. Chem. Soc., Chem. Commun.* **1982**, 396. Staab, H. A.; Hinz, R.; Knaus, G. H.; Krieger, C. *Chem. Ber.* **1983**, *116*, 2835 and the earlier publications.

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