and any excess HCl were removed in vacuo, and the solid residue was treated with ether (850 mL). After the mixture was stirred for 30 min at room temperature the crystalline imidate **5** was filtered, washed with ether, and vacuum-dried at 25 °C to yield 100.2 g (90%). GC assay on the corresponding imino ether[18] indicated 99.2% purity (0.2% benzonitrile, 0.4% benzamide).

Methyl (*S*)-2-Phenyl-2-oxazoline-4-carboxylate (3A). In a 250-mL three-neck flask under N_2 were placed methylbenzimidate hydrochloride (**5**) (11.6 g 74.5 mmol), methyl (*S*)-serinate hydrochloride (12.8, 74.5 mmol), and CH_2Cl_2 (150 mL). The stirred mixture was treated with Et_3N (10.4 mL, 74.5 mmol) and stirred overnight at ambient temperature. The resulting suspension was diluted with CH_2Cl_2 (150 mL) and washed with H_2O (3 × 50 mL). The organic layer was dried ($MgSO_4$) and vacuum concentrated to an oil, which was Kugelrohr distilled [95 °C (0.05 mm)] to produce **3a** as a low-melting solid (9.74 g, 65%).

Methyl (*R,S*)-2-Phenyl-2-oxazoline-4-*d*-4-carboxylate [(*RS*)-4A]. (By Statistical Exchange.) Oxazoline **3A** (6.5 g, 31.7 mmol) was dissolved in 99% CH_3OD (20 mL) at 15–20 °C and treated with 50 mg of sodium methoxide. After the mixture was stirred for 2 h the partially exchanged CH_3OD was removed by vacuum distillation and replaced with fresh 99% CH_3OD (20 mL). After 2 h the $NaOCH_3$ was quenched by adding CH_3CO_2D (1.0 mL) and the mixture concentrated to an oil. The residue was Kugelrohr distilled [105 °C (0.05 mm)] to produce 6.1 g (94%) of >98% deuteriated, racemic oxazoline **4A**: ^1H NMR ($CDCl_3$) δ 3.81 (3 H, S), 4.6 (2 H, center of AB, ^2J = 9 Hz), 7.4 (2 H, m, meta), 7.5 (1 H, m, para), 7.98 (2 H, m, ortho).

(*RS*)-Serine-2-*d*. Deuteriooxazoline **4a** (6.1 g, 29.6 mmol) was refluxed for 2.5 h in 15 mL of 6 N HCl. After cooling to room temperature the crystalline benzoic acid was removed by washing with CH_2Cl_2 (2 × 25 mL). The aqueous layer was vacuum concentrated to a small volume, treated with H_2O (25 mL), and concentrated to ca. 8 mL. The resulting solution was diluted to 15 mL with H_2O and the pH adjusted to 5.1 with Et_3N. The free amino acid was crystallized by adding 75 mL of isopropyl alcohol. The product was filtered, washed with isopropyl alcohol (25 mL) and hexane (25 mL), and vacuum-dried to yield 2.83 g (90%) of >99% deuteriated, racemic serine (mp 233–234 °C), HPLC purity ≥98%.[26]

Registry No. **1**, 35523-45-6; **2**, 103292-62-2; **3a**, 78715-83-0; **3c**, 103292-60-0; (±)-**4a**, 103292-63-3; (±)-**4c**, 103292-61-1; (*R*)-**4c**, 103365-57-7; **5**, 5873-90-5; **10**, 103420-05-9; H-DL-Ser-OH, 302-84-1; H-DL-Ser-OPr-*i*·HCl, 103292-59-7; PhCN, 100-47-0; Ph_3CH, 519-73-3; Ph_3CLi, 733-90-4; H-L-Ser-OH, 56-45-1; H-L-Ser-OMe·HCl, 5680-80-8; DL-Serine-2-*d*, 53170-89-1; (+)-ammonium bromocamphorsulfonate, 14575-84-9; (+)-α-bromocamphorsulfonic acid, 5344-58-1.

(26) Amino acid HPLC analysis was run on an E. Merck RP-18 column under ion-pairing conditions: elution with aqueous sodium heptanesulfonate adjusted to pH 2.2; 210 nm; 1.5 mL/min. Serine, t_r 5.0 min; fluoralanine, t_r 4.1 min.

Three New Diterpene Isonitriles from a Palauan Sponge of the Genus *Halichondria*

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Three new diterpenes (3*S**,4*R**,7*S**,8*R**,11*S**,12*R**,13*S**)-7-isocyano-1-cycloamphilectene (**1**), (1*S**,3*S**,4*R**,7*S**,8*R**,13*R**)-7-isocyano-11-cycloamphilectene (**2**), and 8-isocyano-10,14-amphilectadiene (**3**) were isolated from the Palauan sponge *Halichondria sp.* The major metabolite of this sponge, (3*S**,4*R**,7*S**,8*S**,11*S**,13*R**)-8-isocyano-1(12)-cycloamphilectene (**4**), had previously been isolated from a sponge of the genus *Amphimedon* (ex. *Adocia*) and had been assigned an incorrect structure **5**. The structures of **1**, **2**, and **7**, the formamide derived from isonitrile **4**, were all determined by X-ray analysis.

Isonitriles are rare in nature, yet they are frequently found in sponges of the order Halichondrida[1] and in the dorsal mantle of nudibranchs that eat Halichondrid sponges.[2] Diterpene isonitriles have been found in *Amphimedon sp.* (ex. *Adocia sp.*),[3] *Hymeniacidon amphilecta*,[4] and *Acanthella sp.*[5] The Palauan sponge *Halichondria sp.* has now been found to contain four diterpene isonitriles, one which had physical and spectral properties identical with a compound previously reported by Kazlauskas et al.[3b] In this paper, we report the structural elucidation of 7-isocyano-1-cycloamphilectene (**1**), 7-isocyano-11-cycloamphilectene (**2**), 8-isocyano-10,14-amphilectadiene (**3**), and 8-isocyano-1(12)-cycloamphilectene (**4**), a compound that was previously assigned the structure 8-isocyano-11-cycloamphilectene (**5**). 7-Isocyano-1-cycloamphilectene (**1**) and 7-isocyano-11-cycloamphilectene (**2**) are unique among the diterpene isonitriles because they have cis-fused ring junctions.

Sequential solvent extraction of the freeze-dried sponge yielded a hexane extract that inhibited the growth of the microorganisms *Staphylococcus aureus* and *Bacillus subtilis*. Two antimicrobial fractions from flash chromatography on silica gel were further purified by HPLC on Partisil to obtain 7-isocyano-1-cycloamphilectene (**1**; 0.028% dry weight), 7-isocyano-11-cycloamphilectene (**2**; 0.018% dry weight), 8-isocyano-10,14-amphilectadiene (**3**; 0.006% dry weight), and 8-isocyano-1(12)-cyclo-

(1) For recent reviews, see: (a) Faulkner, D. J. *Nat. Prod. Rep.* **1986**, *3*, 1. (b) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 551. (c) Faulkner D. J. *Tetrahedron* **1977**, *33*, 1421.

(2) For reviews, see: Schulte, G. R.; Scheuer, P. J. *Tetrahedron* **1982**, *38*, 1857. Thompson, J. E.; Walker, R. P.; Wratten, S. J.; Faulkner, D. J. *Tetrahedron* **1982**, *38*, 1865. Faulkner, D. J.; Ghiselin, M. T. *Mar. Ecol.: Prog. Ser.* **1983**, *13*, 295 and ref 1b.

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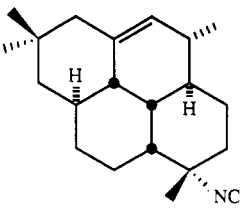

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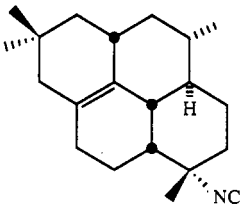

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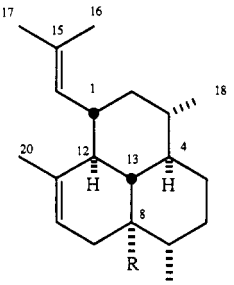
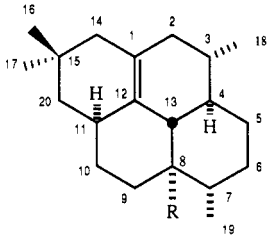
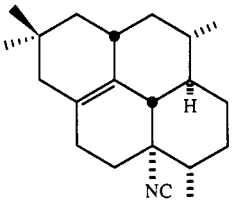


3 R= NC
6 R= NHCHO



4 R= NC
7 R= NHCHO



5

amphilectene (**4**; 0.23% dry weight).

The minor isonitriles **1** and **2** both have the same molecular formula, $C_{21}H_{31}N$. The infrared spectra of both compounds have bands at 2130 cm^{-1} assigned to the isonitrile functionality. The ^1H NMR spectrum of isonitrile **1** contained methyl signals at δ 0.81 (s, 3 H), 0.94 (s, 3 H), 0.97 (d, 3 H, J = 7 Hz), and 1.54 (br s, 3 H) and an olefinic proton signal at δ 4.99 (s, 1 H). The ^1H NMR spectrum of isonitrile **2** [δ 0.81 (s, 3 H), 0.85 (d, 3 H, J = 7 Hz), 0.92 (s, 3 H), 1.54 (br s, 3 H)] was quite similar to that of isonitrile **1**, except that it lacked an olefinic proton signal. The ^{13}C NMR spectra contained signals for a CH_3CNC moiety in each molecule and confirmed the presence of a trisubstituted olefin in isonitrile **1** and a tetrasubstituted olefin in isonitrile **2**. These data implied that the isonitriles **1** and **2** might differ simply in the position of the double bond, but further spectral interpretation did not allow unambiguous assignment of either structure. Fortunately, both isonitriles gave good crystals from hexane, allowing the structures to be determined by X-ray crystallography.

Computer-generated perspective drawings of (3*S**,4*R**,7*S**,8*R**,11*S**,12*R**,13*S**)-7-isocyano-1-cycloamphilectene (**1**) and (1*S**,3*S**,4*R**,7*S**,8*R**,13*R**)-7-isocyano-11-cycloamphilectene (**2**) are given in Figures 1 and 2, respectively. Hydrogens are omitted for clarity, and since the X-ray experiment did not define the absolute configuration, the enantiomer shown is an arbitrary choice. The molecules differ in the placement of the double bond; it is between C1 and C2 in isonitrile **1** and between C11 and C12 in isonitrile **2**. This apparently small change, together with the cis fusion of some rings, gives the overall molecule a distinctly different shape in each case. Isonitrile **2** is relatively flat, while isonitrile **1** is rather convex. One of the difficulties in establishing the structure of isonitrile **1** by interpretation of ^1H NMR data was the absence of coupling between H2 and H3. In retrospect this is not surprising, since the dihedral angle H2–C2–C3–H3 is ~85°. In general, the bond distances and angles agree well with accepted values.

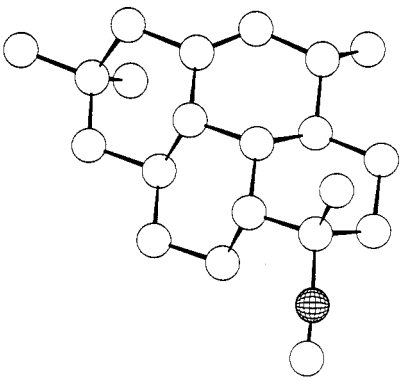


Figure 1. Computer-generated perspective drawing of the final X-ray model of 7-isocyano-1-cycloamphilectene (**1**). Hydrogens are omitted for clarity, and no absolute configuration is implied.

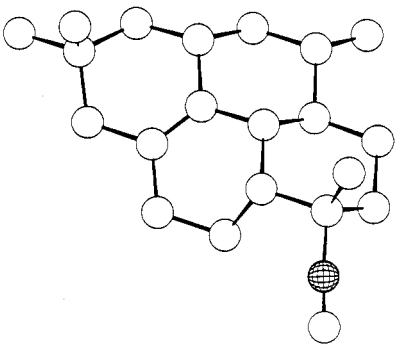


Figure 2. Computer-generated perspective drawing of the final X-ray model of 7-isocyano-11-cycloamphilectene (**2**). Hydrogens are omitted for clarity, and no absolute configuration is implied.

The isonitrile **3** is an isomer of **1** and **2** but contains two olefinic bonds and must therefore have a tricyclic ring system. The ^{13}C NMR spectrum of **3** contains signals at δ 154.5 (br s) and 63.3 (br s), due to the tertiary isonitrile group, and olefinic carbon signals at δ 137.6 (s), 133.4 (d), 126.6 (s), and 118.8 (d). The ^1H NMR data that included ^1H COSY and decoupling experiments revealed the presence of an isobutenyl group that gave rise to signals at δ 1.66 (d, 3 H, J = 1 Hz), 1.57 (d, 3 H, J = 1 Hz), and 5.15 (br, d, 1 H, J = 7 Hz). The signal at δ 5.15 is coupled to a signal at δ 2.24 (m, 1 H, J = 12, 12, 7, 4 Hz), which was assigned to an axial proton on a six-membered ring that is coupled to one equatorial and two axial protons. This is exactly the situation for the isobutenyl side chain in the amphilectane ring system. Furthermore, the signal at δ 2.24 is coupled to a partially obscured signal at δ 2.04 (br t, 1 H, $J \cong$ 12 Hz) that can be assigned to an allylic proton at C12. The second olefinic proton signal at δ 5.26 (br s, 1 H) is coupled to signals at δ 2.45 (br d, 1 H, C9), 2.04 (C12), ca. 2.0 (obscured, C9), and 1.69 (br d, 3 H, J = 1 Hz, C20). These data, together with the two methyl signals at δ 0.88 (d, 3 H, J = 6.3 Hz) and 1.02 (d, 3 H, J = 6 Hz), are all compatible with the proposed structure, 8-isocyano-10,14-amphilectadiene (**3**). The most likely stereochemistry is 1*S**,3*S**,4*R**,7*S**,8*R**,12*S**,13*S**, because the C3–C8 stereochemistry is identical in all other amphilectenes. Isonitrile **3** affords a crystalline formamide **6** (mp 78–80 °C) upon treatment with aqueous acetic acid, but repeated attempts to obtain suitable crystals for X-ray diffraction were unsuccessful.

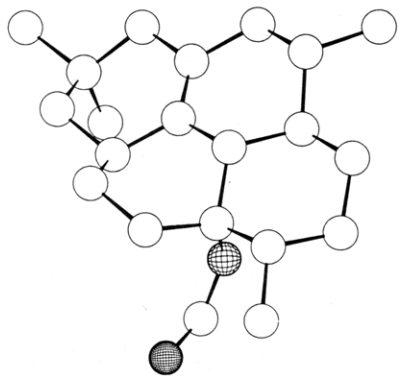


Figure 3. Computer-generated perspective drawing of the final X-ray model of formamide **7**. Hydrogens are omitted for clarity, and no absolute configuration is implied.

The major metabolite **4** was in all respects identical with a compound that had previously been assigned the structure **5** on the basis of the interpretation of very limited spectral data, which simply implied that **5** was a double-bond isomer of 8-isocyano-10-cycloamphilectene, for which the structure had been determined by X-ray analysis.[3b] Since the evidence for structure **5** was not very convincing, a crystalline formamide **7** (mp 165–166 °C) was prepared by treatment of the isonitrile **4** with aqueous acetic acid. The structure of the formamide **7** was determined by X-ray analysis. A computer-generated perspective drawing of the final X-ray model less hydrogens is given in Figure 3.

It is possible that acid treatment of the isonitrile might have caused a double-bond migration, but comparison of the ^{13}C NMR spectra of isonitrile **4** and formamide **7** revealed only those differences in chemical shift that might be expected to result from changing the isonitrile group to a formamide group. Thus, we have reassigned the structure of the major isonitrile from 8-isocyano-11-cycloamphilectene (**5**) to (3*S**,4*R**,7*S**,8*S**,11*S**,13*R**)-8-isocyano-1(12)-cycloamphilectene (**4**).

Antimicrobial screening of the purified isonitriles **1**–**4** revealed that the activity of the crude extract was due primarily to the major metabolite, 8-isocyano-1(12)-cycloamphilectene (**4**), and one of the minor constituents, 8-isocyano-10,14-amphilectadiene (**3**), both of which inhibited *S. aureus* and *B. subtilis* at 5 μg/disk in the standard disk assay. In contrast to all isonitriles in the adociane, amphilectene, and cycloamphilectene series for which X-ray structure determinations show all-trans ring junctions,[3] the isonitriles **1** and **2** both have cis ring junctions. It may therefore be necessary to reexamine those diterpene isonitriles[3b] for which the all-trans geometry was assumed.

Experimental Section

Extraction and Chromatography. The sponge *Halichondria sp.* (81-053) was collected from a marine lake in Palau by hand using SCUBA (–2 m, March 1981) and immediately frozen. The freeze-dried sponge (30.9 g) was extracted sequentially with hexane, dichloromethane, ethyl acetate, and methanol. Biological testing showed that the antimicrobial activity resided in the hexane extract.

The hexane extract was concentrated to give a brown oil (459 mg), which was separated by flash chromatography (silica, 43–63 μm, hexane/ethyl ether mixtures). Fractions eluted with 3–10% ether/hexane were combined, concentrated, and separated by repeated HPLC (Partisil M9/50, 2:3 dichloromethane/hexane) to yield 8-isocyano-1(12)-cycloamphilectene (**4**; 71.5 mg, 0.23% of dry weight) and 8-isocyano-10,14-amphilectadiene (**3**; 20.5 mg, 0.066% of dry weight) and 8-isocyano-10,14-amphilectadiene (**3**; 20.5 mg, 0.066% of dry weight). 8-Isocyano-10,14-amphilectadiene (**3**) decomposed slowly on storage at –20 °C.

Additional fractions eluted by flash chromatography (10% ether/hexane) were combined and concentrated, whereupon colorless needles of 7-isocyano-1-cycloamphilectene (**1**; 6.7 mg) separated. Further separation of the mother liquors (Partisil M9/50, 1% ethyl ether/hexane followed by 5% isopropyl ether/hexane) gave additional 7-isocyano-1-cycloamphilectene (**1**; 1.5 mg, combined yield 8.3 mg, 0.028% of dry weight), 7-isocyano-11-cycloamphilectene (**2**; 5.3 mg, 0.018% of dry weight), and several unresolved minor components.

7-Isocyano-1-cycloamphilectene (1): colorless needles from hexane, mp 182–183 °C; $[\alpha]_D$ –14° (c = 0.41, $CHCl_3$); IR ($CHCl_3$) 2130 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 0.81 (s, 3 H), 0.94 (s, 3 H), 0.97 (d, 3 H, J = 7 Hz), 1.54 (br s, 3 H), 4.99 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.1 (q), 23.5 (t), 25.3 (q), 26.4 (q), 26.7 (t), 32.3 (q), 33.1 (t), 33.4 (s), 33.7 (t), 34.6 (d), 36.0 (d), 36.4 (d), 38.0 (d), 45.3 (d), 46.9 (d), 47.7 (t), 49.0 (t), 61.5 (br s), 124.9 (d), 137.9 (s), 153.2 (br s), EIMS, m/z 297 (M^+, 8%), 270 (91), 255 (100); exact-mass EIMS measured 297.2453, $C_{21}H_{31}N$ requires 297.2456.

7-Isocyano-11-cycloamphilectene (2): colorless prisms from hexanes, mp 134 °C; IR ($CHCl_3$) 2130 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 0.81 (s, 3 H), 0.85 (d, 3 H, J = 6.5 Hz), 0.92 (s, 3 H), 1.54 (br s, 3 H); EIMS, m/z 297 (M^+, 13%), 270 (11), 255 (83), 214 (40); exact-mass EIMS measured 297.2445, $C_{21}H_{31}N$ requires 297.2456.

8-Isocyano-10,14-amphilectadiene (3): oil, $[\alpha]_D$ –79.8° (c = 2.0, $CHCl_3$); IR ($CHCl_3$) 2130 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 0.88 (d, 3 H, J = 6.3 Hz), 1.02 (d, 3 H, J = 6.0 Hz), 1.57 (d, 3 H, J = 1.1 Hz), 1.66 (d, 3 H, J = 1.0 Hz), 1.69 (d, 3 H, J = 0.9 Hz), 2.0 (m, 2 H), 2.04 (m, 1 H), 2.24 (m, 1 H, J = 12, 12, 7, 4 Hz), 2.45 (br dd, 1 H, J = 17, 4.4 Hz), 5.15 (br d, 1 H, J = 9 Hz), 5.26 (m, 1 H, $w_{1/2}$ = 11 Hz); ^{13}C NMR ($CDCl_3$, 50.3 Hz) δ 15.4 (q), 17.6 (q), 19.6 (q), 25.1 (q), 25.7 (q), 29.2 (t), 29.8 (t), 37.2 (d), 37.9 (t), 40.6 (d), 41.4 (d), 42.1 (d), 43.5 (t), 44.8 (d), 49.6 (d), 63.3 (br s), 118.8 (d), 126.6 (s), 133.4 (d), 137.6 (s), 154.5 (br s); EIMS, m/z 297 (M^+, 6%), 270 (M^+ – HNC, 36), 255 (26), 186 (26), 159 (100), 109 (60), 105 (25); exact-mass EIMS measured 297.2444, $C_{21}H_{31}N$ requires 297.2456.

Single-Crystal X-ray Analysis of 7-Isocyano-1-cycloamphilectene (1). Suitable crystals were grown by slow evaporation of a hexane solution. Preliminary X-ray diffraction photographs displayed orthorhombic symmetry, and accurate lattice constants of a = 8.831 (2), b = 6.068 (1), and c = 33.744 (5) Å were determined by a least-squares fit of 15 diffractometer-measured 2θ values. The systematic extinctions, crystal density (~1.09 g/cm^3), and optical activity were uniquely accommodated by space group $P2_12_12_1$ with 1 molecule of composition $C_{21}H_{31}N$ forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected from variable-speed, 1° ω scans and graphite-monochromated Cu Kᾱ radiation (1.541 78 Å). Of the 1498 reflections measured in this fashion, 704 (47%) were judged observed ($F_o \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[6] A phasing model was found through an initial multisolution tangent formula approach followed by tangent formula recycling of a plausible molecular fragment.[7] All of the non-hydrogen atoms were located this way. The hydrogen atoms were located in a ΔF synthesis, following partial refinement of the non-hydrogen atoms. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic

(6) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed: Leonowicz, M. E. REDUCE and UNIQUE, data reduction programs, Cornell University, 1978. Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses), University of York, England, 1979 and 1980. Beurskens, P. T. et al. DIRDIF, University of Nijmegen, The Netherlands, 1981. Gilmore, C. J. MITHRIL, an automatic solution package, University of Galsgow, Scotland, 1983. Hirotsu, K. K.; Arnold, E. BLS78A, an anisotropic block-diagonal least-squares refinement, Cornell Univerisity, 1980. Motherwell, W. D. S. PLUTO78, a crystallographic illustration program, Cambridge Crystallographic Data Centre, 1978. Hirotsu, K. BOND, a program to calculate molecular parameters and prepare tables, Cornell University, 1978.

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(fixed) hydrogens have converged to a conventional crystallographic residual of 0.073 (R_w = 0.090) for the observed reflections. Crystallographic results are available as supplementary material.

Single-Crystal X-ray Analysis of 7-Isocyano-11-cycloamphilectene (2). Crystals were grown from a hexane solution by slow evaporation. Preliminary X-ray photographs showed orthorhombic symmetry, and accurate lattice constants of a = 8.1169 (7), b = 13.299 (2), and c = 16.962 (2) Å were determined from a least-squares fit of 15 diffractometer-measured 2θ values. The systematic extinctions, crystal density (~1.08 g/cm^3), and optical activity were uniquely accommodated by space group $P2_12_12_1$ with 1 molecule of $C_{21}H_{31}N$ forming the asymmetric unit. All diffraction maxima with $2\theta \leq 114°$ plus a subset of maxima with $2\theta \leq 156°$ were collected on a computer-controlled diffractometer using variable-speed, 1° ω scans and graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.541 78 Å). Of the 1821 reflections measured in this fashion, 1170 (64%) were judged observed ($F_o \geq 3\sigma(F_o)$) after correcting for background, Lorentz, and polarization effects.[6] The structure was solved uneventfully by using a multisolution tangent formula approach, and hydrogens were located on a ΔF synthesis after partial refinement. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic (fixed) hydrogens have converged to a conventional crystallographic residual of 0.054 (R_w = 0.061) for the observed reflections. Additional crystallographic results are described in the supplementary material.

Preparation of Formamide from Isonitrile. General Procedure. The isonitrile (ca. 2–10 mg) was dissolved in a mixture of glacial acetic acid (0.5 mL) and water (two drops) and left at 30 °C for 24 h. Solvent was removed under vacuum and the residue dissolved in toluene (0.5 mL) and reevaporated. The residue was then dissolved in warm hexane and left standing at a temperature of −20 °C until crystals of formamide appeared.

Formamide 6: colorless prisms, mp 78–80 °C; IR ($CHCl_3$) 3440, 1662 cm^{-1}; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 0.87 (d, 3 H, J = 6.2 Hz), 0.88 (d, 3 H, J = 6.5 Hz), 1.57 (br s, 3 H), 1.64 (br s, 3 H), 1.68 (br s, 3 H), 2.25 (m, 1 H), 2.50 (m, 1 H), 5.07 (br d, 1 H, J = 9 Hz), 5.30 (m, 1 H), 5.61 (br d, 1 H, J = 12 Hz), 7.99 (d, 1 H, J = 12 Hz); EIMS, m/z 315 (M^+, 2%), 270 (45), 186 (49), 159 (100); exact-mass EIMS measured 315.2652, $C_{21}H_{33}NO$ requires 315.2562.

Formamide 7: colorless needles, mp 165–166 °C; IR ($CHCl_3$) 3380, 1665 cm^{-1}; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 0.84 (s, 3 H), 0.90, 0.91, 0.92 (2 d, s overlapping, 9 H), 2.28 (m, 3 H), 5.47 (br d, 1 H, J = 12 Hz), 8.37 (d, 1 H, J = 12 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 15.0 (q), 19.1 (q), 26.1 (t), 26.5 (q), 29.2 (t), 29.3 (s), 29.8 (t), 29.8 (q), 33.0 (d), 34.7 (d), 39.9 (t), 40.1 (d), 43.8 (t), 44.3 (d), 44.7 (t), 47.5 (d), 56.2 (s), 127.8 (s), 129.3 (s), 164.2 (d); exact-mass EIMS measured 315.2573, $C_{21}H_{33}NO$ requires 315.2562.

Single-Crystal X-ray Analysis of Formamide 7. The formamide 7 crystallized as stout rods and a crystal of approximate dimensions 0.4 × 0.4 × 0.6 mm was selected for further analysis. Preliminary X-ray diffraction photographs displayed orthorhombic symmetry, and precise lattice constants of a = 8.785 (2), b = 9.480 (2), and c = 22.521 (4) Å were determined from a least-squares fit of 15 diffractometer-measured 2θ values. The systematic extinctions, crystal density, and optical activity were uniquely accommodated by space group $P2_12_12_1$ with 1 molecule of composition $C_{21}H_{33}NO$ forming the asymmetric unit. All unique diffraction maxima with $2\theta < 114°$ were collected with graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.541 78 Å) and variable-speed, 1° ω scans. Of the 1483 reflections measured in this way, 1242 (84%) were judged observed after correction for Lorentz, polarization, and background effects.[6] No absorption (μ = 4.8 cm^{-1}) or decomposition corrections were made. The structure was solved with the MULTAN family of programs. Hydrogens were located on a ΔF synthesis or, in a few instances, calculated. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a crystallographic residual of 0.077 for the observed data. Additional crystallographic details are available as supplementary material.

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Supplementary Material Available: Lists of crystal data and data collection parameters and tables of fractional coordinates, thermal parameters, interatomic distances, interatomic angles, and torsional angles for 7-isocyano-1-cycloamphilectene (1), 7-isocyano-11-cycloamphilectene (2), and formamide 7 (15 pages). Ordering information is given on any current masthead page.

Total Synthesis of (+)-Nojirimycin and (+)-1-Deoxynojirimycin

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An efficient chiral total synthesis of (+)-nojirimycin (1) and (+)-1-deoxynojirimycin (2) has been achieved in optically pure form via the common intermediate 11 derived from the nonsugar chiral pool. The monosilyl derivative 4 of 2,3-*O*-isopropylidene-L-threitol (3) was converted to the (*E*)-allyl alcohol 8, which upon asymmetric epoxidation provided the syn epoxide 9. Regio- and stereoselective epoxide opening reaction of 9 followed by methoxymethylation yielded the azide 11, which afforded in five steps (+)-1-deoxynojirimycin (2). The azide 11 could also serve as the intermediate for the synthesis of (+)-nojirimycin (1), which was thus derived from 11 in six steps.

The antibiotic nojirimycin (1) was first isolated from several strains of Streptomyces[1,2] and then from Bacillus.[3] Nojirimycin was the first member of the "heterose" discovered in nature and has remarkable biological activity against drug-resistant strains of *Sarcina lutea*, *Shigella flexneri*, and *Xanthomonas oryzae*.[1] 1-Deoxynojirimycin

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