Single-Crystal X-ray Diffraction Analysis of Urea 5. Preliminary X-ray photographs displayed tetragonal symmetry. Accurate lattice parameters of $a = b = 18.306$ (4) and $c = 9.611$ (2) Å were determined from a least-squares fit of 15 diffractometer-measured 2θ values. The systematic extinctions, optical rotation, and crystal density were uniquely accommodated by space group $P4_2$ with four molecules of composition $C_{31}H_{52}N_2O$ comprising the unit cell. All unique diffraction maxima with $2\theta \leq 114°$ were measured on a computer-controlled four-circle diffractometer using variable speed, 1° ω-scans and graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å). Of the 2328 reflections surveyed in this fashion, only 756 (33%) were judged observed after correction for Lorentz, polarization, and background effects ($|F_o| \geq 3\sigma(F_o)$). A phasing model was found with some difficulty, and the use of the program DIRDIF for phase recycling was crucial.[3] Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and calculated hydrogens have converged to a standard crystallographic residual of 0.078 for the observed reflections. Additional crystallographic information is available and is described in the paragraph entitled Supplementary Material Available at the end of this paper.

Dehydrogenation of Guaia-1(5),6-diene (7). Palladium on carbon (10%) catalyst (~5 mg) was added to a solution of the diene **7** (12 mg, 0.06 mmol) in xylene (5 mL) and the mixture was boiled under reflux for 36 h. The product was filtered, the solvent was evaporated, and the residue was chromatographed on silica gel to obtain guaiazulene, identical in all respects with an authentic sample.

Oxidation of Guaia-1(5),6-diene (7) with Singlet Oxygen. A solution of the diene **7** (90 mg, 0.44 mmol) and rose bengal (2 mg) in 95:5 dichloromethane–methanol (20 mg) was irradiated with a 200-W incandescent lamp under an atmosphere of oxygen for 6 h. The reaction mixture was evaporated and redissolved in ether, and the solution was filtered through a plug of silica gel to remove the catalyst. The crude product (100 mg) was separated by LC on μ-Partisil using 15% ether in hexane as eluant to obtain two isomeric peroxides, **8a** (11 mg, 10% theoretical) and **8b** (23 mg, 20% theoretical).

Peroxide 8a: oil; ^{1}H NMR ($CDCl_3$) δ 0.99 (d, 6 H, J = 7 Hz), 1.06 (d, 3 H, J = 7 Hz), 1.19 (d, 3 H, J = 7 Hz), 2.65 (m, 1 H), 5.72 (d, 1 H, J = 2.3 Hz).

Peroxide 8b: oil; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3 H, J = 7 Hz), 0.96 (d, 3 H, J = 7 Hz), 0.97 (d, 3 H, J = 7 Hz), 1.13 (d, 3 H, J = 7 Hz), 2.87 (m, 1 H), 6.0 (d, 1 H, J = 2.2 Hz).

Acknowledgment. We thank Dr. Klaus Rützler for identifying the sponge. Screening data was provided by Lilly Research Laboratories and bioassays were performed by Mary Kay Harper. This research was supported by funds from the National Institutes of Health (AI11969 to D.J.F. and CA24487 to J.C.), the California Sea Grant College Program (NA85AA-D-SG140, R/MP-30), and the New York State Sea Grant Program (to J.C.).

Registry No. **3**, 105281-43-4; **4**, 105281-44-5; **5**, 105281-45-6; **6**, 105281-46-7; **7**, 105369-35-5; **8**, 105281-47-8; (6*R*,7*E*)-α-bisabolene, 70286-31-6; guaiazulene, 489-84-9.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

(3) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data programs by M. E. Leonowicz, Cornell University, 1978; 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) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P. T. Buerskens et al., University of Nijmegan, Netherlands, 1981; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978, and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.

Nitrogenous Bisabolene Sesquiterpenes from Marine Invertebrates

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Three bisabolene sesquiterpenes, an amine hydrochloride (**8**), an isocyanate (**9**), and an isocyano derivative (**16**), were isolated from a sponge, *Ciocalypta* sp. The structure of the isocyanate was proven by X-ray diffraction of its (*p*-bromobenzyl)urea derivative. From a nudibranch, *Phyllidia* sp., from Sri Lanka, we isolated the previously unreported 3-isocyanotheonellin (**11**).

Bisabolene sesquiterpenes are widely distributed in nature. A notable terrestrial representative is hernandulcin, the sweet principle of *Lippia dulcis* (Verbenaceae).[2] Marine bisabolenes include an alcohol from a gorgonian,[3] 3-isothiocyanato- (**1**) and 3-formamidotheonellin (**2**) from a sponge, *Theonella* cf. *swinhoei*,[4] and four nitrogenous derivatives from a sponge, *Halichondria* sp., which were isolated in Faulkner's laboratory and are described in the accompanying paper.[5] The *Halichondria* metabolites are a 7(*S*)-amine (**3**) and its hydrochloride salt (**4**), a 7(*S*)-isothiocyanate (**5**), and a urea bisdihydrobisabolene (**6**).

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(2) Compadre, C. M.; Pezzuto, J. M.; Kinghorn, A. D.; Kamath, S. K. *Science (Washington, D.C.)* **1985**, *227*, 417-419.

(3) Look, S. A.; Buchholz, K.; Fenical, W. *Experientia* **1984**, *40*, 931-933.

(4) Nakamura, H.; Kobayashi, J.; Ohizumi, Y.; Hirata, Y. *Tetrahedron Lett.* **1984**, *25*, 5401-5404.

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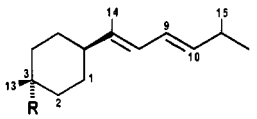
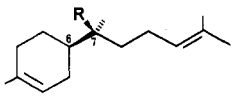
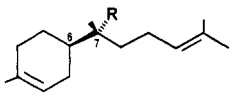
0022-3263/86/1951-5136$01.50/0



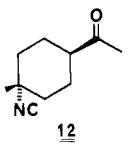
1 R = NCS
2 R = NHCHO
11 R = NC



3 R = NH_2
4 R = NH_3^+ Cl^-
5 R = NCS
6 R = NHCONH–$C_{15}H_{25}$



7 R = NH_2
8 R = NH_3^+ Cl^-
9 R = NCO
10 R = NHCONHCH$_2$– 
14 R = NHAc
15 R = NHCONH– 
16 R = NC



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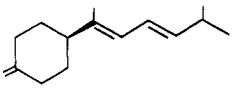

13

In a *Ciocalypta* sp., a sponge genus also belonging to the order Halichondrida, we encountered a bisabolene amine (**7**) as its hydrochloride salt (**8**), and an unprecedented isocyanate (**9**). X-ray diffraction of Faulkner's urea (**6**) and of our (*p*-bromobenzyl)urea (**10**) prepared from **9** unexpectedly revealed that the two series of bisabolene derivatives from **9** have *R* stereochemistry at C-6 but are epimeric at the nitrogen-bearing carbon C-7. Another bisabolene, 3-isocyanotheonellin (**11**), proved to be the major metabolite in a *Phyllidia* sp. nudibranch from Sri Lanka. This compound was absent in the Okinawan sponge *Theonella* cf. *swinhoei*.[4]

The nudibranchs (40 specimens, 300 g) furnished 400 mg of a methanol/methylene chloride extract that after silica gel chromatography yielded 120 mg of a colorless optically inactive oil of composition $C_{16}H_{25}N$. Spectral data established an isocyano function (ν_{max} 2130 cm^{-1}) with a geminal methyl (δ 1.42) and a conjugated diene (λ_{max} 232 sh, 239 nm). Proposed structure **11** was proven by ozonolysis of **11**, which yielded 1-acetyl-4-isocyano-4-methylcyclohexane (**12**). *E,E* stereochemistry of the conjugated diene follows from a 15-Hz coupling constant between H-9 and H-10, a 15.1 ppm chemical shift for C-14, and an NOE at H-9 upon irradiation of Me-15.

Evidence for the stereochemistry at C-3 stems from an NOE experiment on Me-13 (δ 0.95 in C_6D_6), which affects the axial protons (δ 1.3) at C-1 and C-5. Hence the methyl at C-3 is axial. This was confirmed by LAH reduction of the isocyano to methylamine, treatment with excess MeI, and Hofmann elimination yielding a single hydrocarbon, 1-(1,5-dimethyl-1,3-hexadienyl)-4-methylenecyclohexane (**13**). Only an equatorial isocyano group could have given rise to the exo methylene isomer, consistent with our results in an earlier case.[6]

Our discovery of a bisabolene isocyanate (**9**) in *Ciocalypta* sp.[7] resulted from a detailed search for minor metabolites in this sponge and the observation of three infrared bands between 2500 and 2000 cm^{-1} in a hexane extract of the Pupukea, O'ahu sponge, at 2260, 2130, and 2120 (sh) cm^{-1}. The low frequency bands were assigned to NC and NCS functions, but the 2260 cm^{-1} band was outside the normal range for NC or NCS.[8] We initially thought that the high frequency band was due to a cyano function that had originated from isocyano by thermal rearrangement. However, GC-MS analysis of the *Ciocalypta* hexane extract revealed a major component of molecular weight 247 daltons, or $C_{16}H_{25}NO$. Exhaustive treatment of the hexane extract with 1% silver nitrate in 50% aqueous methanol removed all 231 dalton ($C_{16}H_{25}N$) material from the hexane, while retaining the compound with the 2260-cm^{-1} infrared band. TLC separation of microgram quantities and HRMS proved that the 2260-cm^{-1} absorption arose from a compound $C_{16}H_{25}NO$. A large-scale isolation from 1.4 kg (wet) of *Ciocalypta* sp. yielded 33 mg of 7-isocyanato-7,8-dihydro-α-bisabolene (**9**) as a colorless oil, $[\alpha]_D$ –24.3°.

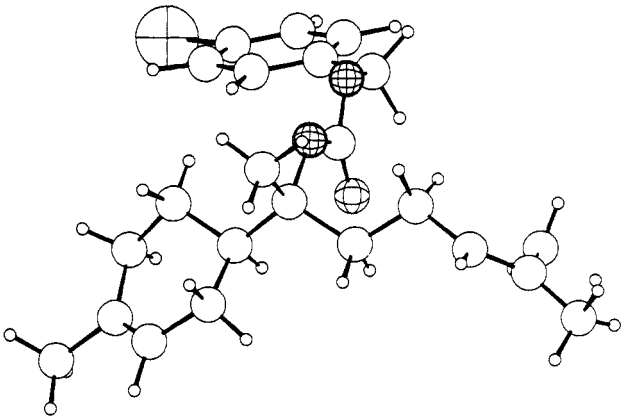

Figure 1. Computer-generated perspective drawing of the final X-ray model of 7-[(*p*-bromobenzyl)ureido]-7,8-dihydro-α-bisabolene (**15**). No absolute configuration is implied. Heteroatoms are indicated by cross-hatching.

The major spectral features, four C-methyls and four olefinic carbons, suggested a monocyclic sesquiterpene, possibly having a bisabolane skeleton. A ^{13}C singlet at δ 63.7 and a quartet at δ 25.7 described the functional moiety without revealing the function itself. A fifth low-field carbon singlet at δ 120.2 was unique in our experience when compared with approximately 150 ppm for NC and 130 ppm for NCS. While the chemical shift was compatible with CN, the oxygen atom in the molecular formula was best accommodated by an unprecedented NCO function.

We proved the presence of the isocyanate function by reacting **9** with *p*-bromobenzylamine in methylene chloride, which yielded after chromatography the corresponding (*p*-bromobenzyl)urea (**10**), mp 113 °C, $[\alpha]_D$ –36.8°.

Crystals suitable for a single-crystal X-ray diffraction analysis were grown from aqueous methanol: a = 9.622 (1), b = 24.697 (5), and c = 10.660 (1) Å, β = 113.80 (1)°, $P2_1$ with *two* $C_{23}H_{33}BrN_2O$ molecules forming the asymmetric unit (Z = 4), $2\theta \leq 114°$, Cu Kα, 2819 of 3221 reflections with $F_o \geq 3\sigma(F_o)$ used.[9] Bromine positions were

(6) Burreson, B. J.; Christophersen, C.; Scheuer, P. J. *J. Am. Chem. Soc.* **1975**, *97*, 201–202.

(7) The sponge was previously [Hagadone, M. R.; Scheuer, P. J.; Holm, A. *J. Am. Chem. Soc.* **1984**, *106*, 2447–2448] believed to be *Hymeniacidon* sp. We thank Professor P. Bergquist for correct identification.

(8) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Strukturaufklärung organischer Verbindungen*, 2nd ed.; Springer: Berlin, 1981; pp I65–80.

Table I. ^{13}C NMR Spectral Data of 7-[(*p*-Bromobenzyl)ureido]- and 7-[(*p*-Bromophenyl)ureido]-7,8-dihydro-α-bisabolene (10 and 15) (300 MHz, $CDCl_3$)

carbon no.	δ, multiplicity 10	15
1	26.6 t	26.5 t
2	120.6 d	120.5 d
3	131.4 s	131.6 s
4	31.2 t	31.2 t
5	22.4 t	22.4 t
6	41.0 d	40.9 d
7	57.9 s	58.5 s
8	36.5 t	36.2 t
9	23.9 t	24.0 t
10	124.5 d	124.3 d
11	134.0 s	134.0 s
12	23.3 q	23.3 q
13	21.1 q	21.0 q
14	25.7 q	25.7 q
15	17.6 q	not observed
16	156.9 s	154.4 s
1′	121.0 s	115.0 s
2′,6′	131.7 d	121.9 d
3′,5′	129.1 d	132.1 d
4′	138.7 s	138.1 s
7′	43.9 t	

found by Patterson synthesis, and their structure was extended using DIRDIF.[9] Hydrogen atoms were in part located on ΔF-syntheses and in part put in at calculated positions. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and heavily damped isotropic hydrogens have converged with $R = 0.0807$. Sixteen reflections appear to suffer from extinction effects and were removed from the final cycles of refinement. Additional crystallographic details are described in the paragraph entitled Supplementary Material Available at the end of this paper.

Figure 1 is a computer-generated perspective drawing of the final X-ray model of the (*p*-bromobenzyl)urea (**10**). There are two independent molecules in the crystal, but, since they have the same configuration and conformation, only one is shown. An attempt was made to determine the absolute configuration by using the anomalous dispersion of bromine, but the results were ambiguous so the enantiomer shown represents an arbitrary choice. The cyclohexene ring has the expected half-chair conformation and the urea the syn,syn conformation. The side chain shows very large thermal motions and may be partially disordered. In general, interatomic distances and angles agree with accepted values.

In the course of our preparative *Ciocalypta* sp. workup, we examined the polar phase of an acetone followed by methanol extraction, after hexane partition had removed all nonpolar constituents. Successive chromatographies (BioSil A, Sephadex LH-20, RP-18 BondElut) resulted in a pale yellow oil, $[\alpha]_D$ −8.3°, which appeared to be an amine salt as indicated by a broad IR absorption at 3266 cm^{-1} and precipitate formation with silver nitrate. The salt **8** could be converted to the free amine **7** by base treatment. This transformation was accompanied by a dramatic change in the chemical shift of the geminal Me-14 from 1.31 to 0.97 ppm in the ^1H NMR spectrum.[10] The amine hydrochloride was also converted to the acetamide (**14**) and the (*p*-bromophenyl)urea (**15**). ^{13}C NMR chemical shifts of **15** and of the (*p*-bromobenzyl)urea (**10**) prepared from the isocyanate **9** are virtually identical (Table I) except for the missing benzyl carbon in **15**, thus proving the bisabolene structure of **8**.

Our interest in the biological origin of the isocyano function in sponges[7] had prompted us to search for trace metabolites in *Ciocalypta* sp., whose predominant sesquiterpenes possess the pupukeanane skeleton.[11,12] The isocyanatobisabolene, as judged by a GC-MS spectrum of the hexane extract of the sponge is clearly the major isocyanate, but by no means the only one in the sponge.

In another *Ciocalypta* sp. specimen from Kaneohe Bay, O'ahu, we found that the isocyanopupukeananes were not the predominant metabolites. This sponge sample contained a 1:1 mixture of 9-isocyanopupukeanane[11,12] and 7-isocyano-7,8-dihydrobisabolene (**16**), which could be separated by reversed phase HPLC ($MeCN/H_2O$, 85:15), from which it eluted first as an oil, ν_{max} 2128 cm^{-1}, $[\alpha]_D$ −49.9°.

Perhaps of biogenetic significance is the antipodal nature of functionalized C-7 in the compounds from *Halichondria* sp.[5] and *Ciocalypta* sp. This would imply that an sp_2-hybridized C-7 is the immediate precursor of the nitrogeneous metabolites.

3-Isocyanotheonellin (**11**) and 7-ammonio-7,8-dihydro-α-bisabolene chloride (**8**) display in vitro growth inhibition of *Bacillus subtilis*.

Experimental Section

3-Isocyanotheonellin (11). *Phyllidia* sp. (40 specimens, 300 g) were collected near Colombo, Sri Lanka, at −10 m in January, 1984. Extraction with $MeOH/CH_2Cl_2$ (1:1) furnished 400 mg of residue, which after silica gel chromatography (hexane/CH_2Cl_2, 3:2) yielded a trace isothiocyanate, a major isocyano, and a sterol fraction. Rechromatography of the major fraction under identical conditions resulted in 120 mg of a colorless oil, $[\alpha^{25}]_D$ 0.0 (*c* 0.44, $CHCl_3$).

HRMS: *m/z* 231.1975, calcd for $C_{16}H_{25}N$ 231.1987. UV (MeOH): λ_{max} 203 (6400), 232 sh (1100), 239 nm (ε 11 600). IR (neat): ν_{max} 3040, 2970, 2950, 2880, 2130, 1470, 1385, 1128, 965 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.2 (ddd, *J* = 15, 10.8, 1 Hz) H-9, 5.79 (d, *J* = 10.8 Hz) H-8, 5.58 (dd, *J* = 15, 6.8 Hz) H-10, 2.33 (mult, *J* = 6.8, 1 Hz) H-11, 1.7 (br s) Me-14, 1.42 (t, *J* = 2 Hz, coupled to ^{14}N) Me-13, 0.99 (d, *J* = 6.8 Hz) Me-12,15; (C_6D_6): 6.29 (ddd, *J* = 15, 10.8, 1 Hz), H-9; 5.77 (d, *J* = 10.8 Hz) H-8, 5.59 (dd, *J* = 15, 6.8 Hz), 2.29 (mult, *J* = 6.8, 1 Hz) H-11, 1.48 (br s) Me-14, 0.99 (d, *J* = 6.8 Hz) Me-12,15, 0.95 (t, *J* = 2 Hz) Me-13, 1.6-1.0 (complex). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.3 (C-1,5), 38.1 (C-2,4), 56.6 (t, coupled to ^{14}N) C-3, 44.6 (C-6), 138.4 (C-7), 123.7, 123.3 (C-8, 9), 140.5 (C-10), 31.5 (C-11), 22.4 (C-12,15), 15.1 (C-14), 152.2 (coupled to ^{14}N) C-16; (C_6D_6): δ 26.6 (C-1,5), 38.3 C-2,4), 56.6 (t, coupled to ^{14}N) C-3, 44.8 (C-6), 138.4 (C-7), 124.5 (C-8), 124.2 (C-9), 140.3 (C-10), 31.8 (C-11), 22.8 (C-12,15), 15.1 (C-14), 139.3 (t, coupled to ^{14}N) C-16.

1-Acetyl-4-isocyano-4-methylcyclohexane (12): EIMS, *m/z* (relative intensity) 165 (M^+, 0.8); IR (neat) ν_{max} 2980, 2950, 2870,

(9) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; 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) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1980; DIRDIF written by P. T. Beurskens et al., University of Nijmegen, Netherlands, 1981; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a locally modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

(10) An even larger shift (0.5–1 ppm) is observed for protons bonded to N-bearing carbon when N is protonated [Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon: Oxford, 1969; p 180.

(11) Burreson, B. J.; Scheuer, P. J.; Finer, J.; Clardy, J. *J. Am. Chem. Soc.* **1975**, *97*, 4763–4764.

(12) Hagadone, M. R.; Burreson, B. J.; Scheuer, P. J.; Finer, J. S.; Clardy, J. *Helv. Chim. Acta* **1979**, *62*, 2484–2494.

2130, 1705, 1355, 1135 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (1 H, sept, J = 5 Hz), 2.15 (3 H s), 1.96–1.5 (unresolved), 1.38 (3 H, s).

Hofmann Degradation of 11. 3-Isocyanotheonellin (**11**, 30 mg) was reduced to the methylamine by LAH in THF, resulting in 24 mg of amine [m/z 235 $M^{\bullet+}$; IR (neat) ν_{max} 3460–3160, transparent between 2860 and 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (3 H, s)]. Amine was treated with MeI in KOH/MeOH yielding Me_3N^+ (30 mg) [^1H NMR ($CDCl_3$): δ 3.31 (9 H, s)]. Trimethylammonium iodide heated with Ag_2O in aqueous MeOH to 170 °C under N_2 for 15 min; purified by Bond Elut (hexane) yielding 8 mg of **13**.

1-(1,5-Dimethyl-1,3-hexadienyl)-4-methylenecyclohexane (13): IR (neat) ν_{max} 3070, 3020, 2960, 2939, 2865, 1645, 1445, 965, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.24 (1 H, ddd, J = 15, 10.8, 1 Hz), 5.81 (1 H, d, J = 10.8 Hz), 5.55 (1 H, dd, J = 15, 6.8 Hz), 4.59 (2 H, s), 2.32 (3 H, m), 2.04–1.75 unresolved, 1.55 (3 H, s), 1.3 (2 H, m), 1.01 (6 H, d, J = 6.8 Hz); HREIMS, m/z 204.1851, calcd for $C_{15}H_{24}$ 204.1878.

7-Isocyanato-7,8-dihydro-α-bisabolene (9): colorless oil, $[\alpha]^{25}_D$ −24.3° (c 0.094, hexane); UV (hexane) λ_{max} 205 (5000), 248 (ϵ 500) nm; IR (film on NaCl) 2967, 2926, 2255, 2081 (br), 1453, 1377 cm^{-1}; EIMS, m/z (relative intensity) 247 (19) $M^{\bullet+}$, 205 (34), 204 (37), 189 (20), 95 (64), 82 (46), 69 (99), 41 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (1 H, br s), 5.07 (1 H t, J = 7 Hz), 2.07–1.5 (11 H, unresolved), 1.68 (3 H, s), 1.63 (3 H, s), 1.60 (3 H, s), 1.23 (3 H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.1 s (C-11), 132.2 s (C-3), 123.4 d (C-10), 120.2 s (C-16), 119.9 d (C-2), 63.7 s (C-7), 42.9 d (C-6), 40.4 t (C-8), 30.9 t (C-8), 26.6 t (C-11), 25.7 q (C-14), 24.2 q (C-12), 24.0 t (C-3), 23.2 q (C-13), 22.7 t (C-5), 17.7 q (C-15).

7-[(p-Bromobenzyl)ureido]-7,8-dihydro-α-bisabolene (10). Compound **9** (7 mg) was treated with p-bromobenzylamine (11 mg) in 0.5 mL of methylene chloride (3 h, room temperature, N_2) and the product was purified over Bond Elut (hexane/EtOAc) and Partisil-10 (same solvents), yielding 8 mg of **10**: mp 113 °C; $[\alpha]^{22}_D$ −36.8° (c 0.19, MeOH); UV (MeOH) λ_{max} 204 (36 500), 229 (ϵ 15 000) nm; IR (film on NaCl) 3349 br, 2959, 2926, 2853, 1638, 1561, 1487 cm^{-1}; EIMS, m/z (relative intensity) 434 (22), 432 (23), 351 (4), 349 (4), 339 (37), 337 (39), 231 (20), 229 (22), 204 (25), 171 (32), 169 (32), 126 (100); HREIMS, m/z 432.17486, calcd for $C_{23}H_{33}{}^{79}BrN_2O$ 432.17762; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (2 H, d, J = 8.3 Hz), 7.14 (2 H, d, J = 8.3 Hz), 5.33 (1 H, br s), 5.08 (1 H, t, J = 6.8 Hz), 4.64 (1 H, t, J = 5.8 Hz), 4.22 (2 H, d, J = 5.8 Hz), 4.17 (1 H, s), 2.15–1.45 (11 H, unresolved), 1.65 (3 H, s), 1.61 (3 H, s), 1.56 (3 H, s), 1.15 (3 H, s).

7-Ammonio-7,8-dihydro-α-bisabolene Chloride (8). *Ciocalypta* sp. (1.4 kg wet) was collected at Pupukea, O'ahu, and extracted with Me_2CO and then MeOH. Aqueous acetone was extracted with hexane; the aqueous phase was combined with MeOH extract and concentrated. The residue was dissolved in water and extracted with EtOAc. The EtOAc-soluble residue (750 mg) was chromatographed on BioSil A (200–400 mesh) first with a hexane/EtOAc gradient and then with MeOH. The MeOH-eluted fractions were combined and chromatographed on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1). Fractions were monitored by ^1H NMR and the amine material was further purified on RP-18 BondElut (MeCN/H_2O, 85:15), yielding a yellow oil, 15 mg: $[\alpha]^{23}_D$ −8.3° (c 0.5, MeOH); IR (AgCl) 3266 (br), 2922, 1618, 1518, 1449, 1387 cm^{-1}; ^1H NMR ($CDCl_3$) 8.3 (2 H, br s), 5.31 (1 H, br s), 5.04 (1 H, t, J = 5.7 Hz), 1.62 (3 H, s), 1.59 (3 H, s), 1.57 (3 H, s), 1.31 (3 H, s); EIMS, m/z (relative intensity) 221 (9.3) $M^{\bullet+}$, 204 (18.8), 138 (75.9), 126 (100), 95 (31.3); EIHRMS, m/z obsd 221.21207, $C_{15}H_{27}N$ requires 221.214354; m/z obsd 126.12690, $C_8H_{16}N$ requires 126.128277; m/z obsd 95.083012, C_7H_{11} requires 95.086077.

7-Amino-7,8-dihydro-α-bisabolene (7). The HCl salt (**8**, 4.8 mg) in 1 mL of $CHCl_3$ was shaken with 1 N KOH (1 mL). The amine (4 mg) was an oil: $[\alpha]_D$ −15° (c 0.4, MeOH); IR (NaCl) ν_{max} 3320 (br), 2930, 1454, 1379 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.37 (1 H, br s), 5.09 (1 H, t, J = 6.6), 1.66 (3 H, s), 1.62 (3 H, s), 1.59 (3 H, s), 0.97 (3 H, s).

7-Acetamido-7,8-dihydro-α-bisabolene (14). Compound **8** (3 mg) was reacted with excess Ac_2O and DMAP at room temperature for 1 h. The reaction mixture was dried under vacuum and passed through BondElut (EtOAc/hexane, 1:1) and then subjected to HPLC on a 5-μm silica gel column with the same solvent system, resulting in **14** (2.5 mg), oil, $[\alpha]^{23}_D$ −33° (c 0.06, $CHCl_3$): UV (hexane) λ_{max} 201 nm (ϵ 10 000); IR (NaCl) 3308 (br), 2920, 1649, 1551, 1442, 1372, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) 5.33 (1 H, br s), 5.09 (2 H, br m), 1.92 (3 H, s), 1.65 (3 H, s), 1.61 (3 H, s), 1.58 (3 H, s), 1.19 (3 H, s); EIMS, m/z (relative intensity) 263 (100), 204 (56), 119 (86.7); EIHRMS, m/z obsd 263.22390, $C_{17}H_{29}NO$ requires 263.224920; m/z obsd 204.18787, $C_{15}H_{24}$ requires 204.187805.

7-[(p-Bromophenyl)ureido]-7,8-dihydro-α-bisabolene (15). Compound **8** (5 mg) was refluxed for 12 h with p-bromophenyl isocyanate (10 mg) in benzene (2 mL) with DMAP. The reaction mixture was dried under vacuum and the residue was dissolved in $CHCl_3$ and filtered. The filtrate was dried with a stream of N_2 and passed through BondElut (hexane/EtOAc, 95:5) and then further purified by HPLC on a 5-μm silica gel column with the same solvent system to obtain the (p-bromophenyl)urea derivative **15** (4 mg), pale yellow oil: $[\alpha]^{23}_D$ −37.5° (c 0.16, MeOH); IR (AgCl) 3345, 2959, 2922, 1653, 1597, 1547, 1487, 1393 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (2 H, d, J = 8.6 Hz), 7.18 (2 H, d, J = 8.7 Hz), 6.12 (1 H, br s), 5.35 (1 H, br s), 5.11 (1 H, br s), 4.37 (1 H, s), 1.64 (3 H, s), 1.61 (3 H, s), 1.57 (3 H, s), 1.22 (3 H, s); UV (MeOH) λ_{max} 204.2 (46 300), 249.7 (ϵ 28 900) nm; EIMS, m/z (relative intensity) 420 (16.1), 418 (17.4), 337 (12.3), 335 (12.6), 325 (100), 323 (100), 269 (8.1), 267 (8.2), 257 (7.9), 255 (8.7), 248 (75.6), 217 (60.5), 215 (61.0), 204 (69.6), 199 (53.1), 197 (53.8), 173 (91.6), 171 (92.3); EIHRMS, m/z observed 418.16195, $C_{22}H_{31}N_2O^{79}Br$ requires 418.161973.

7-Isocyano-7,8-dihydro-α-bisabolene (16). The hexane partition fraction of a single *Ciocalypta* sp. specimen from Kaneohe Bay, O'ahu, was chromatographed on silica gel (hexane/EtOAc, 99:1) to separate hydrocarbons, isocyanos, and isothiocyanates as a single fraction. HPLC (SiO_2, hexane/benzene, 99:1) separated the isocyano compounds, which by reversed phase HPLC (MeCN/H_2O, 85:15) proved to be **16** and 9-isocyanopupukeanane. **16**: oil, $[\alpha]^{22}_D$ −49.9° (c 0.033, hexane); λ_{max} (hexane) 195 nm (ϵ 14 500); IR (CCl_4) ν_{max} 2969, 2930, 2128, 1679, 1448, 1382, 915, 883 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.87 (tqq, J = 7.1, 1.5, 1.5 Hz), 5.54 (m), 2.13 (bq, J = 7 Hz), 1.79 (3 H, m), 1.67 (3 H, m), 1.63 (3 H, m), 2.05–1.35 (9 H, m), 1.32 (3 H, t, J = 3.9 Hz); ^{13}C NMR ($CDCl_3$) 134.2 s, 132.6 s, 123.0 d, 119.6, 63.7 (J_{NC} = 5 Hz), 42.0 d, 38.9 t, 30.8 t, 26.2 t, 25.6 q, 23.9 t, 23.1 (2) q, 22.6 t, 17.7 q; EIMS, m/z (relative intensity) 231 (2, $M^{\bullet+}$), 204 (90), 189 (11), 161 (24), 147 (10), 135 (25), 121 (72), 109 (47), 107 (48), 93 (100); HREIMS, m/z 231.1991, $C_{16}H_{25}N$ requires 231.1987.

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Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances and angles, and torsional angles for 7-[(p-bromobenzyl)ureido]-7,8-dihydro-α-bisabolene (**15**) (8 pages). Ordering information is given on any current masthead page.