Articles

A Sesquiterpene Thiocyanate and Three Sesquiterpene Isothiocyanates from the Sponge *Trachyopsis aplysinoides*

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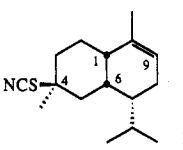
The Palauan sponge *Trachyopsis aplysinoides* contains a unique sesquiterpene thiocyanate, (1*S**,4*S**,6*S**,7*R**)-4-thiocyanato-9-cadinene (**1**), three isothiocyanates, 2-isothiocyanatotrachyopsane (**2**), (2*R**,5*R**,10*R**)-2-isothiocyanato-6-axene (**3**), and (1*S**,4*S**,5*R**,10*S**)-10-isothiocyanatoguaia-6-ene (**4**), and a formamide, (2*R**,5*R**,10*R**)-2-formamido-6-axene (**5**). The structures of the thiocyanate **1** and isothiocyanate **2** were determined by X-ray analysis, and the remaining structures were elucidated by interpretation of spectral data. The carbon skeleton of isothiocyanate **2** had not previously been reported.

Marine sponges of the order Halichondrida often contain mixtures of sesquiterpene isonitriles, isothiocyanates, and formamides.[1] In many prior studies, particularly those on *Axinella cannabina*,[2] investigators described isonitrile–isothiocyanate–formamide trios based on sesquiterpene skeletons that could be interrelated by the type of carbonium ion rearrangements commonly proposed in sesquiterpene biosynthesis. Although the biosynthetic origin of the isonitrile group remains an area of active research,[3] earlier biosynthetic studies indicated that the isothiocyanates and formamides are derived from isonitriles.[4] Recently, however, certain sesquiterpene isothiocyanates were found in marine sponges that did not contain the corresponding isonitriles[5] and vice versa.[6] In this paper we describe the isolation of a unique sesquiterpene thiocyanate, three sesquiterpene isothiocyanates, and a sesquiterpene formamide from a marine sponge.

A small specimen of the sponge *Trachyopsis aplysinoides* was collected in Palau, Western Caroline Islands. Silica gel chromatography of material extracted from the lyophilized sponge with 30% ethyl acetate in hexane gave a mixture of three isothiocyanates, the thiocyanate **1** (25 mg, 0.13% dry weight), and the formamide **5** (35 mg, 0.18% dry weight). The mixture of isothiocyanates was separated by repeated application of HPLC on Partisil with 2% ether in hexane as eluant to obtain isothiocyanate **2** (15 mg, 0.08% dry weight), isothiocyanate **3** (6 mg, 0.03% dry weight), and isothiocyanate **4** (13 mg, 0.07% dry weight).



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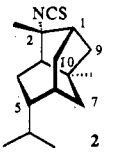

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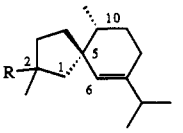
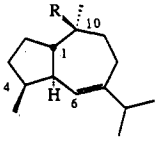


3 R = NCS
5 R = NHCHO



4 R = NCS
6 R = $NHCH_3$

The thiocyanate **1** was isolated as white crystals, mp 67–68 °C. The molecular formula, $C_{16}H_{25}NS$, which was determined by high-resolution mass measurement, is typical of the more familiar sesquiterpene isothiocyanates. The ^1H NMR spectrum contained signals at δ 5.46 (br s, 1 H) and 1.64 (br d, 3 H, J = 1 Hz) that were assigned to a cyclic trisubstituted olefin bearing a methyl group and three additional methyl signals at 1.60 (s, 3 H), 0.93 (d, 3 H, J = 7 Hz), and 0.88 (d, 3 H, J = 7 Hz). The remaining signals in the $CDCl_3$ spectrum overlapped so badly that their assignment was out of the question. When first recorded, the ^{13}C NMR spectrum contained only 15 signals, but it confirmed the presence of a trisubstituted olefin in a bicyclic ring system. We initially assumed that we were

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Table I. ^{1}H NMR Spectral Data [Chemical Shift (Multiplicity, Coupling Constants in Hertz)] of Compounds 1, 2, 4, 3, and 5

H	1 (acetone-d_6)	2 ($CDCl_3$)	4 (acetone-d_6)	3 (acetone-d_6)	5 (acetone-d_6)
1	2.36 (br s)	2.12 (m)	2.31 (dt, 5.4, 9.7)	1.77 (d, 14.8), 2.10 (d, 14.8)	1.63 (d, 14.5), 2.17 (d, 14.5)
2	1.78 (m)		1.70 (m)		
	1.74 (m)		1.91 (m)		
3	1.44 (dd, 14.4, 10.8), 2.02 (dd, 14.4, 6.8, 3.2)	1.93 (m)	1.70 (m), 1.42 (m)		
4		1.71 (m), 1.07 (m)	2.25 (m)		
5	1.51 (dd, 14.4, 12.6), 1.62 (m)	1.07 (m)	2.41 (br dd, 9.7, 7.2)		
6	2.26 (br ddd, 12.6, 7.9, 4.0)	1.93 (m)	5.53 (br d, 2.9)	5.30 (s)	5.33 (br s)
7	1.27 (m)	1.24 (br s)			
8	2.17 (br d, 16.0), 1.63 (m)		2.09 (br dd, 16.5, 9.7), 2.25 (m)	1.85 (dt, 18.0, 4.7), 1.99 (m)	
9	5.47 (br s)	2.08 (br d, 11.7), 1.29 (d, 11.7)	1.93 (ddd, 14.0, 9.4, 1.4), 1.83 (ddd, 14.0, 9.7, 1.4)		
10		1.78 (ddd, 14.4, 6.5, 3.2), 1.38 (br d, 14.4)		1.72 (m)	
11	1.41 (oct, 6.8)	1.35 (m)	2.27 (m)	2.14 (sept, 6.8)	2.14 (sept, 6.8)
12	0.94 (d, 6.8)	0.87 (d, 6.5)	0.99 (d, 6.8)	0.98 (d, 6.8)	0.98 (d, 6.8)
13	0.98 (d, 6.8)	0.87 (d, 6.5)	0.98 (d, 6.8)	0.98 (d, 6.8)	0.98 (d, 6.8)
14	1.60 (s)	1.55 (s)	0.90 (d, 7.2)	1.53 (s)	1.44 (s)
15	1.65 (br s)	1.04 (s)	1.44 (s)	0.93 (d, 6.8)	0.88 (d, 6.8)
NHCHO					7.00 (br s), 7.99 (s)

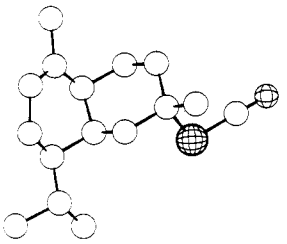


Figure 1. Computer-generated perspective drawing of the final X-ray model of thiocyanate **1**. Hydrogens are omitted for clarity, and no absolute configuration is implied.

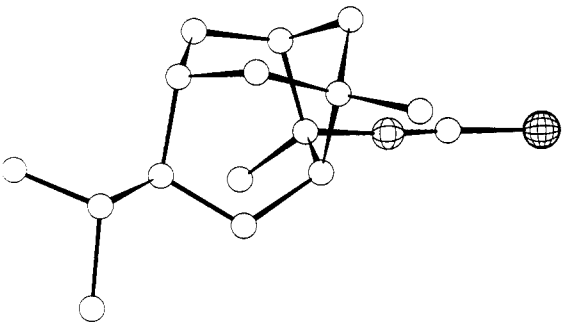


Figure 2. Computer-generated perspective drawing of the final X-ray model of isothiocyanate **2**. Hydrogens are omitted for clarity, and no absolute configuration is implied.

dealing with a sesquiterpene isothiocyanate and that the isothiocyanate signal was too weak to be observed in the ^{13}C NMR spectrum, but the infrared spectrum contained a band at 2142 cm^{-1} that was much weaker in intensity than expected for an isothiocyanate.

The structure of the thiocyanate **1** was determined by X-ray diffraction analysis. Figure 1 is a computer-generated perspective drawing of the final X-ray model of the thiocyanate with the hydrogens omitted for clarity. The enantiomer shown was arbitrarily selected. The most significant structural feature is the attachment of S, not N, to the sesquiterpene core. The bond angle around S is 102°. The rest of the structure is unexceptional.

The ^{1}H NMR spectrum of thiocyanate **1** recorded in acetone-d_6 (Table I) was assigned by interpretation of a 2D COSY experiment. The ^{13}C NMR spectrum was recorded with use of a longer delay time (5 s) to reveal the thiocyanate carbon signal at δ 111.8 (s): the signal at δ 58.5 (s) was assigned to the carbon atom bearing the thiocyanate group. However, the data that most clearly differentiate the thiocyanate and isothiocyanate groups are the intensities of the respective infrared bands at ~2150 cm^{-1}. The formal name of the thiocyanate **1** is (1*S**,4*S**,6*S**,7*R**)-4-thiocyanato-9-cadinene.

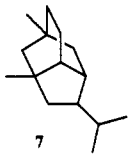
The isothiocyanate **2** was obtained as colorless needles, mp 52 °C. The mass spectral data (m/z = 263.1690) indicated a molecular formula of $C_{16}H_{25}NS$, which is isomeric with the thiocyanate **1**. The ^{13}C NMR spectrum contained 15 aliphatic carbon signals, indicating that isothiocyanate **2** has a tricyclic carbon skeleton. Signals in the ^{1}H NMR spectrum were assigned by interpretation of a 2D COSY experiment (see Table I), but the assignment did not result in the unambiguous elucidation of the carbon skeleton.[7]

The structure of isothiocyanate **2** was determined by a single-crystal X-ray experiment. A computer-generated perspective drawing of the final X-ray model of isothiocyanate **2** is given in Figure 2. The crystal contained two independent but essentially identical molecules and only one is shown for clarity. The absolute configuration shown is arbitrary. The coordination of the NCS group is clearly through nitrogen, and the C2–N–C angle is 174° and 156° for the two independent molecules. The tricyclic cores of both independent molecules are much more alike. The five-membered ring C1, C2, C3, C8, and C9 has an approximate envelope conformation with C1 as the flap atom. One of the six-membered rings, C3–C8, has a twist chair conformation while the other, C1 and C6–C10, has a flattened chair conformation. The isothiocyanate has been named 2-isothiocyanatotrachyopsane (**2**) and has a novel "trachyopsane" carbon skeleton.

The isothiocyanate **3**, which was isolated as an oil, also has the molecular formula $C_{16}H_{25}NS$. The strong infrared bands at 2112 and 2108 cm^{-1} clearly defined the isothiocyanate group. The ^{13}C NMR spectrum contained olefinic signals at δ 140.5 (s) and 127.3 (d) and an isothiocyanate signal at 127.2 (s), which was partially obscured by the

(7) The data was incompatible with the pupukaenane (**7**), neopupukaenane (Scheuer, P. J., personal communication) and closely related carbon skeletons.

adjacent olefinic signal. The ^{1}H NMR spectrum (Table I) recorded in acetone-d_6 contained mutually coupled signals at δ 0.98 (d, 6 H, J = 6.8 Hz) and 2.14 (septet, 1 H, J = 6.8 Hz) that were assigned to an isopropyl group on a cyclic olefin. The olefinic proton signal at δ 5.30 (s, 1 H), is quite sharp, suggesting that there are no vicinal couplings. Further analysis of the NMR spectra allowed the ^{13}C signal at δ 68.0 (s) to be assigned to the carbon atom bearing both the isothiocyanate group and a methyl group [δ 28.4 (q), 1.53 (s, 3 H)] and indicated that the ^{13}C signal at 46.4 (s) must be assigned to the spiro ring junction adjacent to the olefinic bond. The ^{1}H NMR spectrum contained signals at δ 2.10 (d, 1 H, J = 14.5 Hz) and 1.77 (d, 1 H, J = 14.5 Hz) that are assigned to a methylene group between the two fully substituted aliphatic carbon atoms and a methyl signal at δ 0.93 (d, 3 H, J = 6.8 Hz). These data constitute compelling evidence that the isothiocyanate **3** has the "axane" skeleton found in axisonitrile 3 (**8**).[2d]



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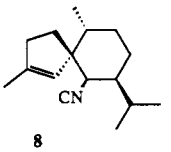

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The stereochemistry was elucidated by using a series of NOEDS experiments. Irradiation of the olefinic proton caused an enhancement of the H-1 proton signal at δ 1.77, which is coupled to a signal at 2.10. The methylene proton signal at δ 2.10 is shifted downfield from its partner by the influence of the proximal isothiocyanate group, an observation that was confirmed by NOEDS measurements on the corresponding formamide **5**. The stereochemistry at C-10 was also determined by a NOEDS measurement on the formamide **5** (see below). The isothiocyanate is therefore (2*R**,5*R**,10*R**)-2-isothiocyanato-6-axene (**3**) and has the same relative stereochemistry at C-5 and C-10 as axisonitrile 3 (**8**).

Isothiocyanate **4** was obtained as a colorless oil. The mass spectral data indicated that isothiocyanate **4** was isomeric with compounds **1**–**3** and the strong infrared band centered at 2127 cm^{-1} was clearly due to an isothiocyanate group. The ^{13}C NMR spectrum contained olefinic carbon signals at δ 148.0 (s) and 124.0 (d) and an isothiocyanate signal at 127.8 (s), which was partially obscured by the solvent. Isothiocyanate **4** therefore has a bicyclic carbon skeleton. The ^{1}H NMR spectrum (Table I) recorded in acetone-d_6 was completely assigned by interpretation of a 2D COSY experiment and indicated that the isothiocyanate **4** was an isomer of 10-isothiocyanatoguaia-6-ene. The ^{13}C NMR data was in agreement with that structure. The relative stereochemistry of **4** was determined by analysis of NOEDS experiments. Irradiation of the olefinic proton signal at δ 5.53 caused enhancement of the methyl doublet at δ 0.90 while irradiation of the methyl doublet caused enhancement of both the olefinic proton signal and the H-1 signal at δ 2.31. These data confirm the trans ring junction which was suggested by the coupling constant $J_{1,5}$ = 9.7 Hz. Irradiation of the CH_3-15 signal at δ 1.44 could not be accomplished without irradiation of other signals but reduction of the isothiocyanate **4** with lithium aluminum hydride in refluxing ether gave an amine **6** in which the CH_3-15 signal at δ 1.03 was cleanly irradiated to produce an enhancement of the H-5 signal at δ 2.41. These data define the isothiocyanate as (1*S**,4*S**,5*R**,10*S**)-10-isothiocyanatoguaia-6-ene (**4**).

The formamide **5** was obtained as small colorless needles, mp 66–67 °C. The molecular formula, $C_{16}H_{27}NO$, was determined from mass spectral data. The ^{1}H and ^{13}C NMR spectra contained many signals that were "doubled", indicating the presence of a mixture of cis and trans geometrical isomers of a formamide. The exact ratio of the isomeric signals varied sightly according to the polarity of the solvent: in $CDCl_3$ solution the cis:trans ratio was 6:4 while in acetone-d_6 solution (Table I) the ratio was nearer 9:1. Comparison of the spectral data of formamide **5** with those of isothiocyanate **3** revealed that both compounds had an identical carbon skeleton and stereochemistry. The ^{13}C NMR spectra of compounds **3** and **5** were assigned (Table II) by using COLOC experiments and by assuming that differences in chemical shift of the signals due to the cis and trans geometrical isomers of the formamide **5** were related to the proximity of the formamido group.

Table II. ^{13}C NMR ($CDCl_3$) Spectral Data of Compounds 3 and 5

C	3	5
1	55.50 (t)	55.54 (t),[a] 54.16 (t)[b]
2	67.96 (s)	61.14 (s),[b] 60.05 (s)[a]
3	41.21 (t)	41.00 (t),[a] 39.72 (t)[b]
4	34.93 (t)	34.39 (t),[b] 34.31 (t)[a]
5	46.43 (s)	46.12 (s)
6	127.28 (d)	128.08 (d),[b] 127.81 (d)[a]
7	140.57 (s)	138.80 (s)
8	27.78 (t)	27.83 (d)
9	22.51 (t)	22.87 (t)
10	35.01 (d)	34.85 (d)
11	36.81 (d)	37.03 (d)
12	21.58 (q)[c]	21.43 (q)
13	21.44 (q)[c]	21.43 (q)
14	28.42 (q)	30.23 (q),[a] 27.08 (q)[b]
15	15.13 (q)	15.30 (q)
NHCHO		163.60 (d),[a] 160.44 (d)[b]

[a] *trans*-Formamide (40%). [b] *cis*-Formamide (60%). [c] Signals may be interchanged.

The stereochemistry of both the formamide **5** and isothiocyanate **3** were determined by interpretation of NOEDS experiments performed on the formamide **5** in acetone-d_6 solution, which, despite the doubling of signals, gave a spectrum in which the signals were better separated. Irradiation of the formamide NH signal at δ 7.00 caused an enhancement of the adjacent H-1 signal at δ 2.18. Irradiation of the methyl signal at δ 0.88 caused a 4% enhancement of the same H-1 signal and an unusual difference spectrum in the region of δ 1.65 that appears to be the combination of a strong positive enhancement of the H-10 signal and a weaker negative enhancement of the second H-1 signal. The formamide is therefore (2*R**,5*R**,10*R**)-2-formamido-6-axene (**5**).

The discovery of a sesquiterpene thiocyanate and three unrelated isothiocyanates in a sponge that appears devoid of isonitriles[8] raises a challenge to the generality of the current hypothesis concerning the biosynthesis of these metabolites. Although the biosynthetic conversion of an isonitrile to an isothiocyanate is quite feasible, the direct conversion of an isonitrile to the corresponding thiocyanate seems unlikely. The isolation of both a thiocyanate and isothiocyanates from the same sponge suggests the possible involvement of a thiocyanate ion or a biosynthetic equivalent in their formation.

Experimental Section

Extraction and Isolation. The sponge *Trachyopsis aplysinoides* was collected in Palau (–20 m) and immediately frozen.

(8) It is not possible at this time to eliminate the trivial explanation that the corresponding isonitriles were sufficiently volatile to be lost during freeze-drying, but we know that other sesquiterpene isonitriles have survived this isolation procedure.

The freeze-dried sponge (19.8 g) was sliced and extracted three times for 2 days with hexane–EtOAc (7:3). The combined extracts were filtered, and the solvent was removed under reduced pressure. The residual brown oil (0.6 g) was chromatographed on a silica gel column, eluting with a solvent gradient from hexane to ethyl acetate. The hexane fraction gave a mixture of isothiocyanates. Repeated separation by HPLC (hexane–Et_2O, 99.8:0.2) afforded pure isothiocyanates **2** (15 mg), **3** (6 mg), and **4** (13 mg). The hexane–EtOAc (98:2) and hexane–EtOAc (70:30) fractions gave thiocyanate **1** (25 mg) and formamide **5** (35 mg), respectively, after further purification by HPLC (hexane–Et_2O, 98:2, and hexane–EtOAc, 40:60).

(1*S,4*S**,6*S**,7*R**)-4-Thiocyanato-9-cadinene (1)**: cuboid crystals; mp 67–68 °C; $[\alpha]_D$ −13.7° (*c* 0.27, $CHCl_3$); UV (MeOH) 240 nm (ε 1440); IR ($CHCl_3$) 2142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.46 (br s, 1 H), 1.64 (br d, 3 H, *J* = 1.1 Hz), 1.60 (s, 3 H), 0.93 (d, 3 H, *J* = 7.2 Hz) 0.88 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 132.6 (s), 124.0 (d), 111.8 (s), 58.5 (s), 44.5 (d), 39.0 (d), 33.8 (t), 32.7 (t), 32.7 (q), 32.4 (d), 29.5 (d), 27.3 (t), 24.3 (t), 21.1 (q), 20.6 (q), 20.6 (q); EIMS *m/z* 263.1707 ($C_{16}H_{25}NS$ requires *m/z* 263.1702).

2-Isothiocyanatotrachyopsane (2): needles; mp 52 °C; $[\alpha]_D$ +123.5° (*c* 0.54, $CHCl_3$); UV (MeOH) 244 nm (ε 1570); IR ($CHCl_3$) 2134, 2110 cm^{-1}; ^1H NMR, see Table I; ^{13}C NMR (C_6D_6) δ 128.3 (s), 74.8 (s), 53.8 (d), 48.0 (d), 46.9 (d), 45.1 (t), 39.1 (s), 37.2 (t), 34.5 (t), 32.0 (d), 31.5 (d), 26.9 (q), 24.9 (t), 22.0 (q), 21.4 (q), 20.8 (q); EIMS *m/z* 263.1690 ($C_{16}H_{25}NS$ requires *m/z* 263.1702).

(2*R,5*R**,10*R**)-2-Isothiocyanato-6-axene (3)**: colorless oil; $[\alpha]_D$ −13.0° (*c* 0.27, $CHCl_3$); UV (MeOH) 244 nm (ε 1545); IR ($CHCl_3$) 2112, 2108 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.18 (br s, 1 H), 1.51 (s, 3 H), 0.96 (d, 6 H, *J* = 6.8 Hz), 0.91 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 140.5 (s), 127.3 (d), 127.2 (s), 68.0 (s), 55.5 (t), 46.4 (s), 41.2 (t), 36.8 (d), 35.0 (t), 34.9 (d), 28.4 (q), 27.8 (t), 22.5 (t), 21.5 (q), 21.4 (q), 15.1 (q); EIMS *m/z* 263.1679 ($C_{16}H_{25}NS$ requires *m/z* 263.1702).

(1*S,4*S**,5*R**,10*S**)-10-Isothiocyanatoguaia-6-ene (4)**: colorless oil; $[\alpha]_D$ −33.9° (*c* 0.28, $CHCl_3$); UV (MeOH) 244 nm (ε 1564); IR ($CHCl_3$) 2127, 2100, 2085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.46 (br s, 1 H), 1.38 (s, 3 H), 0.98 (d, 3 H, *J* = 6.8 Hz), 0.96 (d, 3 H, *J* = 6.8 Hz), 0.88 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR (C_6D_6) δ 148.0 (s), 124.0 (d), 66.8 (s), 51.0 (d), 42.9 (d), 41.6 (t), 38.1 (d), 37.3 (d), 33.0 (t), 25.1 (t), 24.9 (t), 21.6 (q), 21.3 (q), 20.6 (q), 15.2 (q); EIMS *m/z* 263.1701 ($C_{16}H_{25}NS$ requires *m/z* 263.1702).

(2*R,5*R**,10*R**)-2-Formamido-6-axene (5)**: small needles; mp 66–67 °C; $[\alpha]_D$ +14.8° (*c* 1.5 $CHCl_3$); IR ($CHCl_3$) 1762 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.26 (d, *J* = 12.1 Hz [CHO, trans]), 8.04 (d, *J* = 1.4 Hz [CHO, cis]), 5.84 (br d, *J* = 12 Hz [HNCO, trans]), 5.41 (br s [HNCO, cis]), 5.21 (br s, 1 H), 2.12 (m, 1 H, *J* = 6.8 Hz), 2.04 (d, 1 H, *J* = 13.7 Hz), 1.75 (d, *J* = 13.7 Hz [1-Hα, cis formamide]), 1.74 (d, *J* = 13.7 Hz, [1-Hα, trans formamide]), 0.97 (d, 6 H, *J* = 6.8 Hz), 0.86 (d, 3 H, *J* = 6.8 Hz); EIMS *m/z* 249.2089 ($C_{16}H_{27}NO$ requires *m/z* 249.2093).

Amine 6. A solution of isothiocyanate **4** (3.6 mg) and lithium aluminum hydride (4 mg) in ether (1.5 mL) was refluxed for 3.5 h. After careful addition of water, the mixture was extracted with ether, which was then washed with water and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed on a silica gel column and eluted with hexane–EtOAc–Et_3N (8:1:0.3) to yield the amine **6** (2.3 mg) as a colorless oil: ^1H NMR ($CDCl_3$) δ 5.45 (br s, 1 H, H-2), 2.41 (br dd, 1 H, *J* = 10.0, 6.8 Hz, H-1), 2.29 (s, 3 H, NCH_3), 1.03 (s, 3 H, CH_3-14), 0.95, (d, 3 H, *J* = 6.8 Hz), 0.94 (d, 3 H, *J* = 6.8 Hz), 0.80 (d, 3 H, *J* = 6.8 Hz, CH_3-15); EIMS *m/z* 235.2296 ($C_{16}H_{29}NS$ requires *m/z* 235.2300).

Single-Crystal X-ray Diffraction Analysis of Thiocyanate 1. Crystals belonged to the orthorhombic system with *a* = 7.166 (2), *b* = 13.320 (5), and *c* = 16.333 (7) Å. The combination of crystal density, systematic absences, and optical activity uniquely required space group $P2_12_12_1$ with one molecule of composition $C_{16}H_{25}NS$. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using Cu Kα (1.541 78 Å) and variable-speed 1° ω-scans. Of the 1239 unique data, 1068 (86%) were judged observed after correction for Lorentz, polarization, and background effects.[9] Structure solution via direct methods was uneventful, and block-diagonal least-squares refinements with anisotropic heavy atoms and fixed hydrogens have converged to a conventional crystallographic residual of 0.087 for the observed reflections.[10] Additional crystallographic details are described in the supplementary material.

Single-Crystal X-ray Diffraction Analysis of Isothiocyanate 2. Crystals formed in the monoclinic system with *a* = 13.211 (3), *b* = 10.962 (2), and *c* = 10.861 (2) Å, and β = 95.05 (1)°. Systematic absences, crystal density, and optical activity were uniquely accommodated in space group $P2_1$ and *two* molecules of composition $C_{16}H_{25}NS$ forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using Cu Kα radiation (1.541 78 Å) and variable speed 1° ω-scans. Of the 1920 reflections surveyed, only 1191 (65%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[9] The structure was phased by direct methods, and the initial phasing model was extended by tangent formula recycling.[10] Hydrogens were included at ideal positions after partial refinement. The final model had anisotropic non-hydrogen atoms and fixed hydrogens and refined to a conventional crystallographic residual of 0.085. Additional crystallographic details are described in the supplementary material.

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Supplementary Material Available: Tables of fractional coordinates, interatomic distances, interatomic angles, and torsional angles for thiocyanate **1** and isothiocyanate **2** (9 pages). Ordering information is given on any current masthead page.

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