Tetrahedron Letters, Vol. 33, No. 12, pp. 1593-1596, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press Ltd

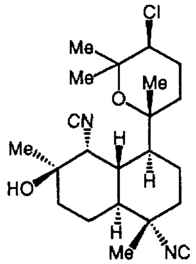
# Two New Diterpene Isocyanides from a Sponge of the Family *Adocidae*

**Hari A. Sharma, Jun-ichi Tanaka, and Tatsuo Higa***
Department of Marine Sciences, University of the Ryukyus, Nishihara, Okinawa 903-01, Japan
**Anna Lithgow**
PharmaMar Research Institution, 28086 Tres Cantos, Madrid, Spain
**Gérald Bernardinelli and Charles W. Jefford***
Department of Organic Chemistry, University of Geneva, 1211 Geneva 4, Switzerland

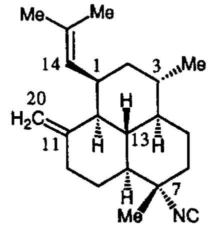
*Key Words*: Neoamphilectane, spirocyclic diterpene, isocyanide, X-ray structure

***Abstract**. 10-Isothiocyanatobiflora-4,15-diene* (**4**) *and 7-isocyanoneoamphilecta-11,15-diene* (**5**) *have been isolated together with known amphilectene diterpenes from a sponge belonging to the family Adocidae. The structures of* **4** *and* **5** *were determined by spectroscopic methods and X-ray respectively.*

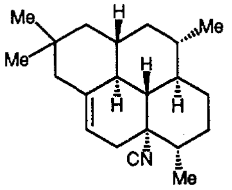
Diterpene isocyanides and related derivatives originating from sponges fall into two distinct structural classes. The first class, represented by the kalihinols (*e.g.* **1**) occurring in *Acanthella* sp.[1] and *A. carvenosa*,[2] is characterized by a highly functionalized bicyclic carbon framework. The second class features three or four rings bearing only one or two isocyanide or related functions. Typical members are the amphilectenes and cycloamphilectenes (*e.g.* **2** and **3**) which are found in *Amphimedon* sp.,[3] *Hymeniacidon amphilecta*[4] and *Halichondria* sp..[5] We now report the isolation of two new diterpenes, the structures of which constitute a significant divergence from the above classification.



**1**



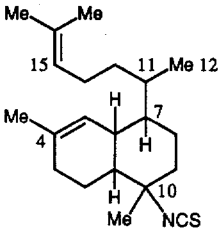
**2**



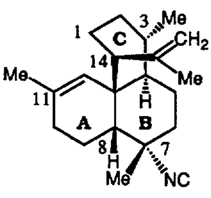
**3**

A sponge (4 kg, wet weight) belonging to the family *Adocidae*,[6] collected off the island of Miyako, was extracted with acetone. After concentration the residue was extracted with ethyl acetate to give an oil (39 g) which was separated by flash chromatography ($SiO_2$, hexane/$CH_2Cl_2$/MeOH).[7] The non-polar fractions were repeatedly submitted to chromatography (HPLC) to give **4** (12 mg) and **5** (72 mg) together with six previously reported compounds: 8-isocyano-10-cycloamphilectene (**3**, 1.28 g), 8-isocyano-1(12)-cycloamphilectene (80 mg), 7-isocyano-1-cycloamphilectene (5.2 mg), diisocyanoadociane (26 mg), 7-isocyano-11(20),14-epi-amphilectadiene (**2**, 15 mg), and 7,15-diisocyano-11(20)-epiamphilectene (28 mg). The known compounds were readily identified by comparing their spectral data with the published values.[3-5]

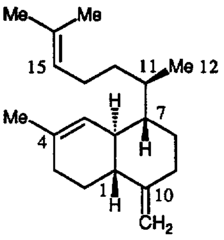
Compound **4** was obtained as an oil, $[\alpha]_D$ +97° (c 0.085, $CHCl_3$), and was analyzed for $C_{21}H_{33}NS$ by HR EIMS [m/z 331.2323 ($M^+$, Δ1.1 mmu; 272.2500 $(M-HNCS)^+$, Δ0.4 mmu). A strong, broad absorption band at 2090 $cm^{-1}$ in the IR spectrum and signals at δ 129.3 and 64.9 in the $^{13}C$ NMR spectrum are indicative of an isothiocyanato group attached to a quaternary carbon atom. The presence of two trisubstituted double bonds was revealed by the characteristic $^1H$- and $^{13}$-NMR data (δ 5.47 (d, $J$ = 5.9 Hz, 1H), 5.08 (t, $J$ = 7.1 Hz, 1H) and δ 134.5 (s), 131.2 (s), 124.6 (d), 123.4 (d)) respectively. Thus, compound **4** must be a bicyclic molecule. The $^1H$ NMR spectrum also exhibited signals for five methyl groups. Three were attached to vinyl carbon atoms as evidenced by their chemical shifts (δ 1.68 (s), 1.67 (s) and 1.60 (s)), one was geminal to the isothiocyanate group (δ 1.52 (s)), and another was located on a secondary carbon atom (δ 0.8 (d, $J$ = 7.3 Hz)). These deductions, in conjunction with the $^{13}C$ NMR data,[8] enable the structure of **4** to be elucidated as that depicted, but without assignment of configuration. Compound **4** finds a precedent[9,10] in a metabolite isolated from a termite soldier, biflora-4,10(19),15-triene (**6**).[8] Accordingly, it is appropriate to name **4** as 10-isothiocyanatobiflora-4,15-diene.



**4**



**5**



**6**

Compound **5** was obtained as colorless crystals, mp 109-110°C, $[\alpha]_D$ +31.8° (c 2.3, $CHCl_3$). The formula $C_{21}H_{31}N$ was secured by HR FABMS [m/z 298.2528 (M + H), Δ0.7 mmu]. A strong, sharp absorption band at 2140 $cm^{-1}$ in the IR spectrum indicated the presence of an isocyano function. The molecule contains one trisubstituted double bond (δ 4.95 (s), 136.0 (s), 129.4 (d)) and one exo-cyclic methylene group (δ 4.84 (s), 4.69 (s); δ 149.0 (s), 114.5 (t)). This finding together with the unsaturation required by the formula means that **5** must be tricyclic. Similar spectroscopic features[9] with those of compounds **2** and **4** suggest that **5** is related to the tricyclic amphilectenes. However, scrutiny of the $^{13}C$ NMR data[11] shows that it is different from the amphilectenes since it contains six methylene (δ 36.3, 35.4, 28.4, 27.0, 19.9, 19.5), four methine (δ 55.4, 51.9, 38.1, 29.0), and two quaternary carbon atoms (δ 60.8, 43.8) instead of five, six, and one such atoms as is the case for compound **2**. The NMR spectra of **5** are accommodated by its chemical formula, but were insufficient to provide any details about the configuration of the molecule. Fortunately, recourse to X-ray analysis[12] furnished the desired stereochemical information. The relative configuration of **5** was elucidated and it is seen to be a new kind of amphilectene diterpene in which ring C is spirocyclic to the cyclohexene ring (A) (Fig.).

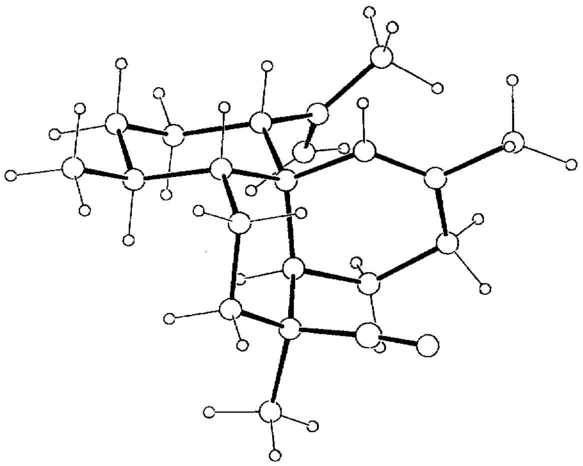


Fig. X-ray structure of compound **5**

The fusion between rings A and B is *cis*. Ring A adopts an envelope conformation (minimum value of $\Delta C_s = 0.048(4)^{15}$) in which C8 lies out of the plane. Rings B and C are also *cis*-fused and fixed in chair conformations like *cis*-decalin. Consequently, by keeping the numbering system used for the amphilectenes, and taking **2** as a structural reference, compound **5** can be designated as (3S*,4R*,7S*,8R*,13R*,14R*)-7-isocyanoneoamphilecta-11,15-diene.

The fact that compounds **4** and **5** are found together with the amphilectenes and cycloamphilectenes in the same source suggests that their biogenesis[3] involves the stepwise cyclization of a common linear precursor such as geranylgeraniol. The skeleton of **4** is new to the amphilectane class of diterpenes and is a much less substituted version of kalihinol A (**1**). The neoamphilectene skeleton of **5**, although tricyclic, may be due to a diversion from the usual biogenetic pathway or might be the result of adventitious rearrangement of a precursor to **2**.

*Acknowledgments.* We thank Professor Paul J. Scheuer, Wesley Y. Yoshida, and Toshio Ichiba of the University of Hawaii and Professor Isao Kitagawa of Osaka University for recording NMR and MS spectra.

### *References and Notes*

1. Chang, C.W.J.; Patra, A.; Roll, D.M.; Scheuer, P.J.; Matsumoto, G.M.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 4644. Patra, A.; Chang, C.W.J.; Scheuer, P.J.; van Duyne, G.D.; Matsumoto, G.M.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 7981. Chang, C.W.J.; Patra, A.; Baker, J.A.; Scheuer, P.J. *J. Am. Chem. Soc.* **1987**, *109*, 6119.
2. Omar, S.; Albert, C.; Fanni, T.; Crews, P. *J. Org. Chem.* **1988**, *53*, 5971.
3. Baker, J.T.; Wells, R.J.; Oberhansli, W.E.; Hawes, G.B. *J. Am. Chem. Soc.* **1976**, *98*, 4010. Kazlauskas, R.; Murphy, P.T.; Blount, J.F. *Tetrahedron Lett.* **1980**, *21*, 315. Fookes, C.J.R.; Garson, M.J.; MacLeod, J.K.; Skelton, B.W.; White, A.H. *J. Chem. Soc. Perkin Trans. I* **1988**, 1003.
4. Wratten, J.S.; Faulkner, D.J.; Hirotsu, K.; Clardy, J. *Tetrahedron Lett.* **1978**, 4345.
5. Molinski, T.F.; Faulkner, D.J. *J. Org. Chem.* **1987**, *52*, 3334.

6. A specimen has been examined by Dr. Ole Tendal, Zoological Museum, University of Copenhagen.
7. Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
8. Compound **4**: $^{13}$C NMR ($CDCl_3$) $\delta$ 134.5 (s), 131.2 (s), 129.3 (s), 124.6 (d), 123.4 (d), 64.9 (s), 44.6 (d), 41.7 (d), 35.7 (t), 35.0 (d), 34.4 (t), 31.1 (d), 30.9 (t), 26.9 (q), 26.1 (t), 25.7 (q), 23.5 (q), 20.54 (t), 20.45 (t), 17.6 (q), 13.3 (q).
9. Wiemer, D.F.; Meinwald, J.; Prestwich, G.D.; Solheim, B.A.; Clardy, J. *J. Org. Chem.* **1980**, *45*, 191.
10. A hydrocarbon of similar structure was also isolated in minute amounts (< 10 mg) from the soft coral *Xenia obscuronata* (Grohweis, A.; Kashman, Y. *Tetrahedron* **1983**, *39*, 3385).
11. Compound **5**: $^{1}$H NMR ($CDCl_3$) $\delta$ 4.95 (s, 1H), 4.84 (s, 1H), 4.69 (s, 1H), 1.72 (s, 3H), 1.65 (s, 3H), 1.49 (s, 3H), and 0.84 (d, $J$ = 6.4 Hz), 3H). $^{13}$C NMR ($CDCl_3$) $\delta$ 154.0 (s), 149.0 (s), 136.0 (s), 129.4 (d), 114.5 (t), 60.8 (s), 55.4 (d), 51.9 (d), 43.8 (s), 38.1 (d), 36.3 (t), 35.4 (t), 31.7 (q), 29.0 (d), 28.4 (t), 27.0 (t), 25.1 (q), 23.4 (q), 20.0 (q), 19.9 (t), and 19.5 (t).
12. Crystal data for compound **5**, recrystallized from hexane. Cell dimensions and intensities were measured at room temperature on a Philips PW1100 diffractometer with graphite-monochromated $MoK_{\alpha}$ radiation. The structure was solved by direct methods (MULTAN-87)[13] and refined by full-matrix least-squares (X-TAL 3.0)[14]: $C_{21}H_{31}N$, Mr = 297.5, mp 109-110°, orthorhombic, $P2_12_12_1$, a = 11.478(3), b = 12.453(3), c = 12.859(3) Å from 21 reflections ($19° < 2\theta < 30°$, V = 1838.0(8) Å$^3$, Z = 4, $D_c$ = 1.08 gr·cm$^{-3}$, Fooo = 656, $\mu$(MoK$\alpha$) = 0.057 mm$^{-1}$. R = $\omega$R = 0.081 ($\omega$ = 1) for 1071 observed reflections ($|Fo| > 4\sigma(Fo)$). Hydrogen atoms were placed in calculated positions and the other atoms were refined with anisotropic displacement parameters. The final Fourier difference synthesis showed a maximum and minimum of +0.38 and -0.47 e.A$^{-3}$ respectively. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre.
13. Main, P.; Fiske, S.J.; Hull, S.E.; Lessinger, L.; Germain, D.; Declerq, J.P.; Woolfson, M.M. *"MULTAN 87"*, Universities of York, England, and Louvain-la-Neuve, Belgium, **1987**.
14. Hall, S.R.; Stewart, J.M., Eds. *"XTAL 3.0 User's Manual"*, Universities of Western Australia and Maryland, USA, **1989**.
15. Nardelli, M.. *Acta Crystallogr.* **1983**, *C39*, 1141.

(Received in Germany 5 November 1991)