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UDOTEAL, A LINEAR DITERPENOID FEEDING DETERRENT FROM THE TROPICAL GREEN ALGA *UDOTEA FLABELLUM**

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Key Word Index—*Udotea flabellum*; Codiaceae; Chlorophyta; marine diterpenoids; algal feeding deterrents.

Abstract—The structure of a new linear diterpenoid, udoteal, has been determined by chemical and spectral methods. Udoteal induced feeding avoidance behavior in the herbivorous fish *Eupomacentrus leucostictus*.

INTRODUCTION

Tropical green seaweeds of the families Caulerpaceae and Codiaceae (phylum Chlorophyta) are found in conspicuous abundance in marine ecosystems of intense herbivore activity [1]. Several chemical studies of the genera *Caulerpa* [2, 3], *Chlorodesmus* [4] and *Rhipocephalus* [5] have shown these algae to produce terpenoid 1,4-diacetoxybutadiene-containing metabolities which apparently function as chemical defense agents. In an attempt to define the biological properties of molecules of this latter type, we earlier showed that the metabolities of the related alga *Rhipocephalus phoenix* induce pronounced feeding avoidance in the herbivorous fish *Eupomacentrus leucostictus* [5]. In this short report we wish to describe the structure of a related metabolite, udoteal (1), from the Caribbean alga *Udotea flabellum* (Ellis and Solander). Udoteal induced significant feeding avoidance in the herbivorous fish *Pomacentrus coeruleus*, using a previously described bioassay [5, 6].

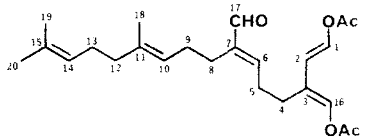
RESULTS AND DISCUSSION

Udoteal (1) was the major lipid component of freshly extracted *U. flabellum*, but could not be detected in extracts of isopropanol-preserved specimens. Once isolated, udoteal was moderately stable.

A molecular formula of $C_{24}H_{34}O_5$ was established for 1 by high resolution mass measurement of the M^+-HOAc, $-CH_2CO$ fragments taken in conjunction with ^{13}C NMR features. IR absorptions at 1770 and 1740 cm^{-1} indicated the *bis*-enol-acetate functionality to be present, as already fully defined in several related compounds [3–6]. This assignment was supported by two ^{13}C NMR ester carbonyl bands at 167.3 and 166.5 ppm, and by a ^1H NMR band at δ 2.18 (integrating for 6H) assigned to two acetate methyl groups. The ^1H NMR spectrum also illustrated the olefinic AB pattern at δ 7.43 (d, $J = 13$ Hz) and 5.95 (d, $J = 13$ Hz), and the olefinic singlet at δ 7.27 (C-16 proton), characteristic of the *E,E*-1,4-diacetoxybutadiene functionality.

The IR spectrum of 1 further indicated the presence of an α,β-unsaturated aldehyde group ($\gamma_{CO} = 1680$ cm^{-1}) in udoteal, and this assignment was confirmed by the expected ^1H NMR bands at δ 9.34 (s) and 6.45 (t, $J = 7$ Hz), and by a ^{13}C NMR off-resonance doublet carbon at 193.9 ppm. The remaining ^{13}C NMR features illustrated two additional double bonds to be present in 1. Consideration of the molecular formula and the overall unsaturation delineated above showed udoteal to be a linear diterpenoid.

Treatment of 1 with the dieneophile 4 - phenyl - 1,2,4 - triazoline - 3,5 - dione gave the adduct 2 in high yield. The ^1H NMR features of this compound were highly analogous to those from a similar adduct produced from rhipocephalin [6], thus reinforcing our initial spectral assignment of the *E,E*-diacetoxybutadiene functional group. What remained for the final assignment of udoteal was the location of the



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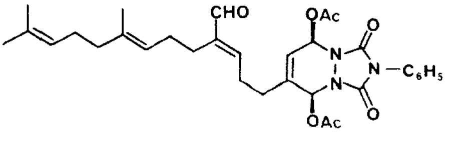

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α,β-unsaturated aldehyde and the stereochemistry of the associated double bond. In this circumstance, MS and ^{13}C NMR data allowed a confident assignment of the aldehyde at C-17 and the associated unsaturation at C-6–C-7. A prominent fragment at *m/z* 137.1329, which calculated for $C_{10}H_{17}$, showed that cleavage of the *bis*-allylic C-8–C-9 bond occurred to yield a hydrocarbon fragment. Secondly, the ^{13}C NMR features of **1**, from C-8 to C-15, and including the methyl carbons C-18–C-20, were virtually identical with those of appropriate linear terpenoid models [7]. The stereochemistry of the C-6–C-7 olefin was assigned as *E* based upon both ^{1}H and ^{13}C NMR features. The aldehyde proton was observed at δ 9.34 (*br s*) conforming to the slightly shielded values recognized for the *E* configuration (*E* = δ 9.3–9.4, *Z* = 10.0–10.1) [8] of this functional group. Also, the ^{13}C NMR value for the C-17 aldehyde carbon (193.9 ppm) in **1** is in close accord to the shift of the *E* isomer in the morellin–isomorellin antibiotics [7].

Biological testing showed udoteal to induce significant avoidance in the herbivorous fish *Pomacentrus coeruleus* at the 800-ppm level. This would appear to be environmentally significant as udoteal occurs in *ca* 6000 ppm (dry wt) in *U. flabellum*. Contrary to other linear terpenes of this type [5], udoteal shows little ichthyotoxicity even at the 10 μg/ml seawater level.

EXPERIMENTAL

Isolation of udoteal (**1**). Freshly collected *U. flabellum* (Carrie Bow Cay, Belize, May 1978) was ground with a hand-grinder and the resulting mush was extracted repeatedly with Et_2O (3×). *Ca* 1 kg (wet wt) yielded 5 g residual extract after solvent removal by evaporation. TLC of the extract illustrated one major relatively non-polar component which turned purple-red upon H_2SO_4 charring. Fractionation of the extract over Si gel gave 0.9 g udoteal as a bright yellow oil. If the crude extract was allowed to stand, udoteal was observed to decompose over a period of several days. Extracts of isopropanol-preserved *U. flabellum* were found not to contain udoteal. Udoteal was fully purified to a mobile and colorless oil by Si HPLC (15% EtOAc in isooctane) and showed the following spectral characteristics: $[\alpha]_D$ 0°, (*c* 1.8, $CHCl_3$); ^{1}H NMR (220 MHz, $CDCl_3$) δ 9.34 (1H, *s*), 7.43 (1H, *d*, *J* = 13 Hz), 7.27 (1H, *s*), 6.45 (1H, *t*, *J* = 7 Hz), 5.95 (1H, *d*, *J* = 13 Hz), 5.09 (2H, mult), 2.55 (4H, mult), 2.27 (2H, mult), 2.18 (6H, *s*), 2.05 (6H, mult), 1.77 (3H, *s*), 1.61 (3H, *s*), 1.59 (3H, *s*); ^{13}C NMR (20 MHz, C_6D_6) δ 193.9 (*d*), 167.3 (*s*), 166.5 (*s*), 152.2 (*d*), 144.1 (*s*), 136.1 (*d*, *s*), 135.5 (*d*), 131.1 (*s*), 124.8 (*d*), 124.0 (*d*), 119.9 (*s*), 113.0 (*d*), 40.1 (*t*), 27.5 (*t*, *t*), 27.1 (*t*), 25.8 (*q*), 24.5 (*t*), 24.3 (*t*), 20.0 (*q*, *q*), 17.7 (*q*), 16.0 (*q*); IR ($CHCl_3$) 1770, 1740, 1680, 930 cm^{-1}; UV (MeOH) λ_{max} = 247 nm, ϵ = 22,500; HRMS *m/z* 300.2103, calc. for $C_{20}H_{28})_2$ (M^+–HOAc, –CH_2CO) = 300.2082.

Diels–Alder adduct **2**. 4-Phenyl-1,2,4-triazoline-3,5-dione (22.0 mg, 0.124 mmol) in 2 ml $CHCl_3$ was slowly added to udoteal (50 mg, 0.124 mmol) in 3 ml $CHCl_3$ at room temp. The solution immediately decolorized, and after 1 min the solvent was removed under pressure to yield the adduct **2** (65 mg, 91%) as a colorless oil. The adduct showed the following spectral features: ^{1}H NMR (220 MHz, $CDCl_3$) δ 9.36 (1H, *s*), 7.5 (5H, mult), 7.09 (1H, *s*), 6.9 (1H, *d*, *J* = 5 Hz), 6.4 (1H, *t*, *J* = 7 Hz), 6.0 (1H, *d*, *J* = 5 Hz), 5.1 (2H, mult), 2.6 (2H, mult), 2.34 (4H, mult), 2.22 (3H, *s*), 2.18 (3H, *s*), 2.05 (6H, mult), 1.68 (3H, *s*), 1.63 (3H, *s*), 1.60 (3H, *s*), IR ($CHCl_3$) 2930, 2850, 1750–1720 *br*, 1680, 1410, 1370, 1140, and 1000 cm^{-1}.

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