3.95 (s, 1), 4.58 (d, J = 8 Hz, 2), 5.1–5.5 (m, 6-H and 28-H, 2); MS m/z 654 (M^+ – AcOH and (*tert*-butyldimethylsilyl)oxy).

To the acetate (200 mg, 0.28 mmol) was added 1.5 mL of tetrabutylammonium fluoride solution in THF (1.5 mmol). The mixture was stirred for 5 h at room temperature, diluted with water (100 mL), and extracted with CH_2Cl_2 (2 × 120 mL). The extract was dried ($MgSO_4$) and the solvent removed, leaving the crude product which on chromatography with ethyl acetate–chloroform (2:1) gave the diol acetate 11: 100 mg; mp 100–102 °C. It consisted essentially of the 7β-hydroxy isomer only. On recrystallization from ethyl acetate the compound had the following: mp 102–103 °C; IR 3310–3100, 1730 cm^{-1}; NMR δ 0.69 (s, 3), 1.02 (d, J = 7 Hz, 6), 1.05 (s, 3), 2.03 (s, 3), 3.3–3.95 (m, 3-H and 7-H, 2), 4.56 (d, J = 7 Hz, 2), 5.27 (m, 6-H and 28-H, 2); MS m/z (relative intensity) 484 (M^+, 1), 468 (1), 450 (1), 426 (M^+ – AcOH, 3).

3β,29-Dihydroxystigmasta-5,24(28)(*E*)-dien-7-one (12). (a) 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (112 mg, 0.5 mmol) was added to a solution of the diol (11, 80 mg, 0.16 mmol) in 3 mL of dry benzene and the mixture was shaken at room temperature for 24 h. It was diluted with benzene and filtered through a short column of silica gel. The crude product was chromatographed with ethyl acetate–chloroform (1:2), yielding the enone: 63 mg (0.13 mmol); semicrystalline solid; IR 3300–3100, 1732, 1670 cm^{-1}; UV (CH_3OH) λ_{max} 233 nm (ϵ 10200); NMR δ 0.67 (s, 3), 1.00 (d, J = 6 Hz, 6), 1.18 (s, 3), 2.03 (s, 3), 3.4–3.9 (m, 1), 4.57 (d, J = 7 Hz, 2), 5.28 (t, J = 7 Hz, 1), 5.66 (s, 1); MS m/z (relative intensity) 484 (M^+, 4).

The enone (58 mg) was dissolved in THF (1 mL) and methanol (8 mL) and a 10% solution of K_2CO_3 (in 3:2 methanol–water, 0.35 mL) added. After the solution was stirred overnight, solid NH_4Cl was added, and the solvent was removed in a stream of N_2. The residue was chromatographed with chloroform–ethyl acetate (1:1) to give the diol 12: 50 mg; mp 170–180 °C; NMR ($CDCl_3$–CD_3OD) δ 0.67 (s, 3), 0.97 (d, J = 7 Hz, 3), 0.99 (d, J = 6 Hz, 6), 1.17 (s, 3), 4.11 (d, J = 6 Hz, 29-H of *E* isomer), 4.13 (d, J = 6 Hz, 29-H of *Z* isomer), 5.30 (t, J = 6 Hz), 5.64 (s, 1). The signals for 29-H in the *E* and *Z* isomers could be seen clearly in the expanded spectrum (5-ppm sweep width). The *Z* isomer was estimated to amount to less than 15% of the mixture.

Recrystallization from ethyl acetate gave pure *E* isomer: 33 mg; mp 188–191 °C; the purity was confirmed by the 360-MHz NMR spectrum; IR 3450–3150, 2950, 1670, 1645, 1475, 1380, 1230, 1050 cm^{-1}; UV (CH_3OH) λ_{max} 234 nm (ϵ 11000); MS m/z (relative intensity) 442.3452 [M^+ (calcd 442.3435), 2], 329.2452 [M^+ – $C_7H_{13}O$ (fragment from allylic cleavage at C(22)–C(23), 9]. Anal. Calcd for $C_{29}H_{46}O_3$: C, 78.67; H, 10.48; O, 10.84. Found: C, 78.68; H, 10.25; O, 10.80.

(b) 3,5-Dimethylpyrazole (309 mg, 3.2 mmol) was added to chromium trioxide (322 mg, dried in vacuo at 100 °C overnight) suspended in dry methylene chloride (1.5 mL) at –15 °C. The mixture was stirred for 10 min, and 29-hydroxyfucosterol 3β,29-diacetate (110 mg, 0.2 mmol) was added in one portion. Stirring was continued for 5 h while the temperature was maintained between –10 and –20 °C. Sodium hydroxide solution (1 mL, 5 N) was next added, and after a further 1 h at 0 °C, methylene chloride was added, and the organic phase was separated, washed with dilute hydrochloric acid and water, and dried ($MgSO_4$). Removal of the solvent and chromatography of the residue with ethyl acetate–hexanes (1:4) gave the ketone 13 (60 mg) and unreacted 29-hydroxyfucosterol diacetate (40 mg). Ketone 13 was recrystallized from methanol: mp 151–153 °C; UV (CH_3OH) 235 nm (ϵ 12000); IR 2950, 1730, 1660, 1370, 1240, 1030 cm^{-1}; NMR δ 0.68 (s, 3), 0.98 (s, 3), 1.05 (s, 3), 1.19 (s, 3), 2.03 (s, 6), 4.58 (d, J = 7 Hz, 2), 5.30 (t, J = 7 Hz, 1), 5.66 (s, 1); MS m/z (relative intensity) 526 (M^+, 1), 466 (M^+ – AcOH, 2).

To a stirred solution of ketone 13 (10 mg, 0.02 mmol) in 0.3 mL of THF and 2 mL of methanol was added 10% K_2CO_3 solution (in 60% CH_3OH/40% H_2O, 0.1 mL). The reaction mixture was kept at room temperature for 20 h and then evaporated to dryness. Chloroform was added and the mixture filtered. On evaporation of the solvent, the filtrate yielded the product (12) which was recrystallized from ethyl acetate: mp 188–191 °C; 5 mg.

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Registry No. 1, 10211-88-8; (*E*)-2, 32230-64-1; 3, 20981-59-3; 4, 13254-10-9; (*E*)-5, 81256-53-3; (*Z*)-5, 81256-54-4; (*E*)-5 alcohol, 81256-55-5; (*Z*)-5 alcohol, 81256-56-6; (*E*)-6, 52065-17-5; (*Z*)-6, 81256-57-7; (*E*)-7, 81256-58-8; (*Z*)-7, 81256-59-9; (*E*)-7 acetate, 81256-60-2; (*E*)-7 diacetate, 81256-61-3; (*E*)-8, 81256-62-4; (*Z*)-8, 81256-63-5; (*E*)-9, 81256-64-6; (Z)-9, 81256-65-7; 9 diether, 81256-66-8; 10, 81256-67-9; 10 acetate, 81256-68-0; 11, 81256-69-1; 11 enone, 81256-70-4; (*E*)-12, 81256-71-5; (*Z*)-12, 81256-72-6; 13, 81256-73-7; diethyl (3-methyl-2-oxobutyl)phosphonate, 7751-67-9; vinyl bromide, 106-95-6; saringosterol, 6901-60-6.

Triophamine, a Unique Diacylguanidine from the Dorid Nudibranch *Triopha catalinae* (Cooper)

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Triophamine (1), a symmetrical diacylguanidine, has been isolated from skin extracts of the dorid nudibranch *Triopha catalinae*. The proposed structure of 1 was based on interpretation of the mass, IR, UV, ^1H NMR, and ^{13}C NMR spectra. It was verified by comparison with diacetylguanidine (3) and by base-catalyzed hydrolysis to guanidine and 2,4-diethyl-4-hexenoic acid (6).

Dorid nudibranchs are delicate, shell-less, and often strikingly colored marine molluscs that despite their conspicuousness and vulnerability have almost no known predators.[1] A number of dorids utilize chemical antifeedants obtained from their sponge diets as one component of their defensive arsenal. Several well-documented examples include albicanyl acetate[2] and furodysinin[2,3] from *Cadlina luteomarginata*, 9-isocyanopupukeanane from *Phyllidea varicosa*,[4] and nakafuran-8 and nakafuran-9 from *Hypselodoris godeffroyana* and *Chromodoris mari-*

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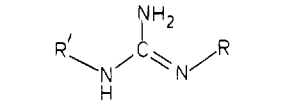
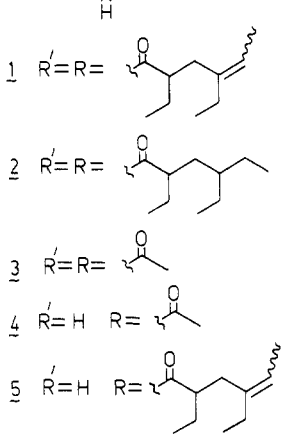
0022-3263/82/1947-2167$01.25/0

dadilus.[5] Many other fascinating metabolites, to which no defensive role is ascribed, have also been isolated from dorids.[6] As part of an ongoing program to study the skin extracts of soft-bodied marine molluscs,[2,7] we have examined *Triopha catalinae*, a common British Columbia dorid that feeds exclusively on bryozoans.[8] We report herein the structure of triophamine (1), a novel diacylguanidine that is the major component of *T. catalinae* extracts.

T. catalinae was collected by hand, using SCUBA (−1 to −5 m), in Barkley Sound, British Columbia. Freshly collected specimens were extracted whole in acetone at room temperature for 24–48 h at which time the solvent was decanted and evaporated in vacuo to give an aqueous suspension. Silica gel column ($CHCl_3$) and preparative thin-layer chromatography (1:1 hexane/ether, $R_f \sim 0.5$) of the chloroform-soluble fraction of the suspension gave triophamine (1) as a light yellow oil.

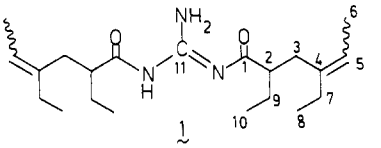




Triophamine (1) is optically active ($[\alpha]_D$ −7.0° (*c* 1.7, MeOH)) and it contains a UV chromophore with a λ_{max} = 251 nm (ϵ 12 000, MeOH). Treatment with acid causes a hypsochromic shift in the λ_{max} to 214 nm (ϵ 14 500, MeOH/HCl), while treatment with base (MeOH/NaOH) converts triophamine to a new substance with λ_{max} = 232 nm ($T_{1/2} \simeq 30$ min, ϵ 10 000).

Electron-impact high resolution mass spectrometry indicated a molecular formula of $C_{21}H_{37}N_3O_2$ (M^+, *m/z* 363.2885, calcd 363.2885) for triophamine and it showed major fragment ions resulting from loss of CH_3 (*m/z* 348), C_5H_5 (*m/z* 334), C_6H_{10} (*m/z* 281) and C_9H_{17} (*m/z* 238) residues. The ^1H NMR spectra (400 MHz, $CDCl_3$) of 1 clearly showed well-resolved resonances for only 17 nonexchangeable protons (Table I). The same sample run in Me_2SO-d_6 showed one additional exchangeable proton at δ 9.4 and a very broad exchangeable signal at δ 11 which integrates for less than one proton. We concluded, therefore, that triophamine (1) must contain an element of symmetry on the NMR timescale and that each resonance must account for double the number of protons

Table I

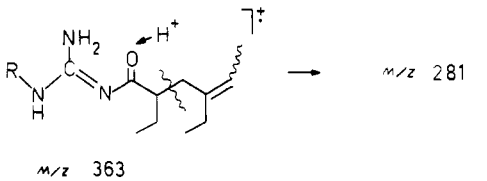


carbon	^1H NMR,[a] δ	^{13}C NMR,[b] δ
1, 1′		185.6 (s)
2, 2′	2.30–2.48 (1 H, m)	50.3 (d)
3, 3′	2.12 (1 H, dd, *J* = 6, 13 Hz), 2.30–2.42 (1 H, m)	40.1 (t)
4, 4′		140.4 (s)
5, 5′	5.21 (1 H, q, *J* = 7 Hz)	120.5 (d)
6, 6′	1.56 (3 H, d, *J* = 7 Hz)	12.1 (q)
7, 7′	2.01 (2 H, q, *J* = 7 Hz)	23.2 (t)[e]
8, 8′	0.95 (3 H, t, *J* = 7 Hz)	12.9 (q)[d]
9, 9′	1.46–1.67 (2 H, m)	26.1 (t)[e]
10, 10′	0.91 (3 H, t, *J* = 7 Hz)	13.1 (q)[d]
11		158.9 (s)
NH_2[c]	9.4 (1 H, br)	
NH[c]	11.0 (0.5 H, br)	

[a] 400 MHz, $CDCl_3$. [b] 100 MHz, acetone-d_6. [c] 100 MHz, Me_2SO-d_6. [d] May be reversed. [e] May be reversed.

indicated by integration. As expected then, the ^{13}C NMR spectra showed only 11 carbon resonances, 10 of them accounting for 2 carbons each (Table I). An SFORD experiment demonstrated that the 17 nonexchangeable protons were bonded to a 9-carbon segment in each half of the molecule.

Detailed analysis of the ^1H NMR spectra allowed us to assign a structure to the C_9H_{17} residue. A one-proton quartet at δ 5.21 (*J* = 7 Hz) coupled to a three-proton doublet at 1.56 (*J* = 7 Hz) indicated that a proton and a methyl were attached to the same carbon of a trisubstituted olefin. Resonances at δ 2.01 (2 H, q, *J* = 7 Hz) and 0.95 (3 H, t, *J* = 7 Hz) revealed that the third substituent was an ethyl group. Decoupling experiments demonstrated that the remaining proton resonances at δ 2.30–2.48 (m, 2 H), 2.12 (dd, 1 H, *J* = 13, 6 Hz), 1.46–1.67 (m, 2 H), and 0.91 (t, 3 H, *J* = 7 Hz) belonged to a linear four carbon fragment CH_2–CH–CH_2–CH_3 which must be attached to the olefinic carbon either via the methylene or methine carbon. Catalytic hydrogenation (Pd/C, EtOH) of triophamine (1) gave tetrahydrotriophamine (2; M^+, *m/z* 367). An ^1H NMR analysis of 2 revealed that the protons on the methylene carbon had undergone an upfield shift proving that this was the point of attachment to the olefin.[9] An intense fragment at *m/z* 281 in the mass spectrum of 1 supports this assignment.



The remaining portion of triophamine (1) consisted of $C_3H_3N_3O_2$, and it had to incorporate three units of unsaturation. A ^{13}C NMR resonance at δ 185.6 and an IR absorption at 1700 cm^{-1} implied the presence of two carbonyl carbons, and the remaining ^{13}C NMR resonance at

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(6) For example, see: (a) Hochlowski, J. E.; Faulkner, D. J. *Tetrahedron Lett.* **1981**, *22*, 271. (b) Walker, R.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 1475. (c) Castiello, D.; Cimino, G.; De Rosa, S.; De Stefano, S.; Sodano, G. *Tetrahedron Lett.* **1980**, *21*, 5047. (d) Cimino, G.; De Rosa, S.; De Stefano, S.; Sodano, G. *Ibid.* **1981**, *22*, 1271.

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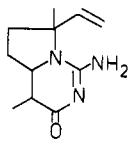
(9) Compound 2 shows the following: high-resolution mass spectrum, *m/z* 367.3198 (M^+; calcd for $C_{21}H_{41}N_3O_2$, 367.3198) 338, 296, 283 (base peak), 240; ^1H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7 Hz, 6 H), 0.84 (t, *J* = 7 Hz, 6 H), 0.93 (t, *J* = 7 Hz, 6 H), 1.40–1.15 (m, 12 H); 1.55 (m, 2 H), 1.65 (m, 4 H), 2.79 (m, 2 H).

158.9 was highly suggestive of a guanidine moiety. Assembling these fragments led to the hypothesis that triophamine was the diacylguanidine 1 which is in rapid tautomeric equilibrium.[10]

Authentic diacetylguanidine (3) was prepared as a model compound.[11] It has UV characteristics [λ_{max} 248 nm (ϵ 16 800, MeOH) λ_{max} 212 nm (ϵ 19 900, MeOH/HCl)] and ^{13}C NMR resonances[12] (δ 159.0 and 180.1) in good agreement with triophamine (1). Diacetylguanidine (3) undergoes rapid base-catalyzed hydrolysis (MeOH/NaOH, room temperature) to give monoacetylguanidine (4) (λ_{max} 230 nm (ϵ 14 300, MeOH)]. Triophamine (1) is converted to the monoacylguanidine 5 under the same reaction conditions [5: UV (MeOH) λ_{max} 232 nm (ϵ 10 000); mass spectrum, m/z 211 (M^+)]. Final proof of the structure was obtained by base-catalyzed hydrolysis of 1 (CH_3OH/NaOH, 48 h) which gave guanidine (identified as its 4,6-dimethylpyrimidine derivative[13]) and the carboxylic acid 6.[14]



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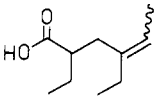

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(10) Monoacylguanidines exist almost exclusively as the acyl imine tautomer. Masumoto, K.; Rapoport, H. *J. Org. Chem.* **1968**, *33*, 552.
(11) Greenhalgh, R.; Bannard, R. A. B. *Can. J. Chem.* **1959**, *37*, 1810.
(12) The deshielding of the carbonyl carbons in triophamine (1) relative to diacetylguanidine (3) is almost equal in magnitude to the difference between propionamide (δ 177.2) and acetamide (δ 172.7). Levy, G. C.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists"; Wiley-Interscience: New York, 1972; p 123.
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A number of marine natural products contain guanidine functionalities. These include the acarnidines,[15] the polyandrocarpidines,[16] ptilocaulin,[17] saxitoxin,[18] and tetrodotoxin,[19] Triophamine, however, is to the best of our knowledge the first example of a naturally occurring diacylguanidine. Arenaine (7),[20] a terrestrial monoterpenoid alkaloid, is one example of a naturally occurring monoacylguanidine. The acyl residues found in triophamine also contain ten carbon atoms, but it is difficult to rationalize their biogenesis from a terpenoid pathway.

Acknowledgment. We acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada. We thank Mike LeBlanc and the staff at the Bamfield Marine Station for assistance in collecting *Triopha catalinae*. We thank Dr. D. J. Faulkner for helpful discussions about guanidine chemistry and Sandra Millen for identifying the nudibranch.

Registry No. 1, 81256-25-9; 2, 81256-26-0; 3, 81256-27-1; 4, 5699-40-1; 5, 81256-28-2; 6, 81256-29-3; guanidine, 113-00-8.

(14) Acid 6 shows the following: high-resolution mass spectrum, m/z 170.1298 (M^+; calcd for $C_{10}H_{18}O_2$, 170.1307); ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7 Hz, 3 H), 0.95 (t, J = 7 Hz, 3 H), 1.57 (d, J = 7 Hz, 3 H), 1.52–1.62 (m, 2 H), 2.04 (q, J = 7 Hz, 2 H), 2.14 (dd, J = 7, 15 Hz, 1 H), 2.33 (dd, J = 9, 15 Hz, 1 H), 2.47 (m, 1 H), 5.23 (q, J = 7 Hz, 1 H).
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Synthesis of Benzannelated Pyranosides†

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Ethyl and benzyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-uloses (e.g., 9–11) were prepared from D-glucal. The enones reacted with 1-methoxy-1,3-butadiene or 1-[(trimethylsilyl)oxy]-1,3-butadiene to afford the corresponding [4 + 2] cycloadducts. DDQ aromatization and subsequent elaboration of the cycloadducts gave benzannelated pyranosides. Amino sugar derivatives also were prepared. Aromatization of the (trimethylsilyl)oxy adducts directly afforded the corresponding phenols, but the reaction was found to be of limited scope. The stereochemistry of intermediates and products and subtleties of the DDQ reaction are discussed.

The importance of deoxy sugars as both synthetic and biological intermediates[1] promoted us to investigate the synthesis of functionalized derivatives. As part of a program concerned with the annelation of carbohydrate moieties, we have examined the cycloaddition reactions of some unsaturated sugars and the synthesis of benzannelated pyranosides. This paper reports the results of our study.

Ethyl and benzyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-uloses were chosen as initial substrates because of their ease of preparation and the position of the desired unsaturation. The synthesis of enones 9–11 is essentially that of Fraser-Reid[2] with some modifications (Scheme I). Diacetates 2 and 3 were prepared from tri-*O*-acetyl-D-glucal according to the method of Ferrier,[3] and although 2 was isolated directly as the α anomer, 3 was obtained as a 9/1 (α/β) mixture. This mixture was separated at the diol

† Contribution No. 2983.

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