δ 0.04 (br d, 1 H), 0.95 (br d, 6 H), 1.58 (s, 3 H), 1.68 (s, 3 H), 2.00 (s, 3 H), 3.38 (s, 6 H), 5.05 (br t, 1 H), 5.28 (s, 1 H), 5.44 (s, 1 H); ^{13}C NMR ($CDCl_3$, 24 °C) δ 8.1 (t), 12.6 (d), 17.7 (q), 21.5 (q), 25.7 (q), 26.6 (t), 32.1 (d), 35.4 (t), 45.9 (d), 53.5 (q), 54.5 (q), 73.6 (d), 109.3 (d), 124.5 (d), 131.5 (s), 169.8 (s). The others were unobserved possibly due to broadening. Crenulacetal D (6): colorless oil; IR ($CHCl_3$) 1720, 1080, 1000 cm^{-1}; high resolution mass spectrum, $C_{24}H_{38}O_5$ (M^+) *m/e* obsd 406.2717, calcd 406.2720; ^1H NMR ($CDCl_3$, 24 °C) δ 0.40 (m, 1 H), 0.96 (br d, 6 H), 1.58 (s, 3 H), 1.66 (s, 3 H), 2.00 (s, 3 H), 2.82 (m, 1 H), 3.34 (s, 6 H), 5.06 (br t, 1 H), 5.66 (s, 2 H). This extract was extremely rich in terpenoids, and the following ten other diterpenes were isolated: dictyoxide (17 mg),[14] pachydictyol A (150 mg),[11] isodictyoacetal (92 mg),[12] 19α- and 19β-methoxyisodictyoacetals (50 mg),[15] acetyldictyolal (4 mg),[9a,15] dictyolactone (2 mg),[13] acetylsanadaol (3 mg),[16] dictyone (10 mg),[10] and 18-hydroxy-2,7-dolabelladiene (18 mg).[17]

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Acid Hydrolysis of Crenulacetal C (5). A solution of **5** (15 mg) in MeOH (0.75 mL) was treated with 0.08 mL of 35% hydrochloric acid, and the mixture was allowed to stand at room temperature for 21 h. The mixture was neutralized with an aqueous saturated solution of sodium bicarbonate, and the product was taken up in CH_2Cl_2. After being dried over sodium sulfate, the CH_2Cl_2 solution was concentrated into an oily residue (11.8 mg), which was separated by preparative TLC (Merck, Kieselgel 60, GF_{254}; hexane/acetone, 9:1) to give **1** (4.6 mg) and hydroxycrenulide (1.5 mg). The products were identified by comparison of their ^1H and ^{13}C NMR data as well as R_f values of TLC with those of authentic samples. Crenulacetals A (**3**), B (**4**), and D (**6**) also afforded the same products under the same reaction conditions. In another experiment, a solution of **5** (10 mg) in tetradeuteriomethanol (0.5 mL) was treated with deuteriochloric acid (12 M; 0.06 mL), and after 10 h, the mixture was neutralized with a sodium bicarbonate solution in D_2O. Workup as described above afforded **1** (5 mg), whose ^1H NMR spectrum exhibited a broad singlet due to 18-CH_2 (δ 4.82). The intensity of this signal corresponded to exactly two protons.

Acknowledgment. We thank Dr. Hiroshi Yamamoto, Ibaraki University, for measurement of the high resolution mass spectra, and Miki Murata for her collaboration on this work.

Hydration of Diacetylene Compounds. Synthesis of a Marine Natural Product: (±)-1-(2,6,6-Trimethyl-4-hydroxycyclohexenyl)-1,3-butanedione

Mauricio G. Constantino,*,† Paulo M. Donate,‡ and Nicola Petragnani‡

Departamento de Química, FFCLRP-USP, Av. Bandeirantes s/n, 14.100-Ribeirão Preto-SP, Brazil, and Instituto de Química, USP, Caixa Postal 20.780, São Paulo-SP, Brazil

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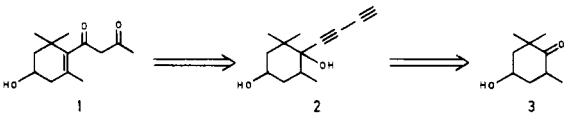
The marine natural product (±)-1-(2,6,6-trimethyl-4-hydroxycyclohexenyl)-1,3-butanedione (**1**) was synthesized from the known keto alcohol **3** and 1,4-dichlorobut-2-yne. The synthetic sequence involves dehydration of the diyne tertiary alcohol **2** and hydration of the diyne system to give the β-diketone moiety. This reaction was accomplished in excellent yield by using 85% formic acid as also demonstrated with a simple model substrate.

In the course of our studies on the synthesis of biologically active natural products structurally related to carotenoids, we became interested in the recently described marine natural product **1**, 1-(2,6,6-trimethyl-4-hydroxycyclohexenyl)-1,3-butanedione, isolated from cultures of the dinoflagellate *Prorocentrum minimum* by Andersen, Le Blanc, and Sum.[1] They pointed out the structural relation between **1** and compounds believed to be degradation products of carotenoids, suggesting that zeaxanthin could be a precursor of **1**. These authors showed also that compound **1** has in vitro antibiotic activity against *Staphylococcus aureus*.

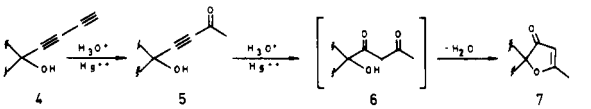
In our preliminary communication[2] on the synthesis of (±)-**1**, the retrosynthetic planning depicted in Scheme I drew our attention to the problem of hydration of diacetylene alcohols.

Diacetylene alcohols such as **2** are relatively unstable compounds; however, they can be satisfactorily stored in solution at low temperatures. The hydration of these compounds in the presence of mercury salts and acid results, through a stepwise addition of water, in hydroxylated β-diketone **6**, which gives, by cyclization and water elimination, a furanone **7** (Schene II).[3] To obtain an unsaturated β-diketone such as **1** it would seem necessary to eliminate the tertiary hydroxyl group of compound **2** before hydration of the diacetylene.

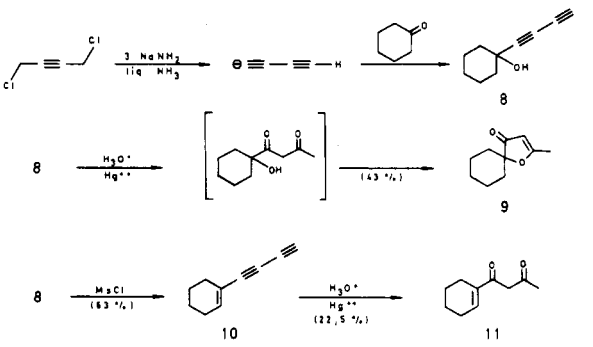
Scheme I



Scheme II



Scheme III



† FFCLRP-USP.
‡ IQ-USP.

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Scheme IV

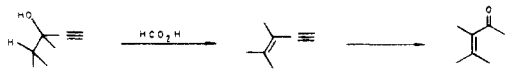


Table I. Hydration of Diacetylene Compounds with Formic Acid

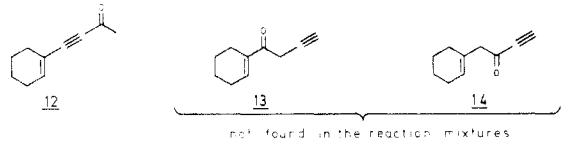
compd hydrated	HCO_2H concn, %	reactn time, h	yield, %	prod (ratio)
10	85	2	53.5	11
8	85	2	77	11
8	70	1		12 + 11 (60:40)[a]
8	70	0.5		8 + 10 + 12 + 11 (35:40:15:10)[b]

[a] By NMR analysis. [b] By preparative TLC.

A model study was carried out with cyclohexanone as the starting material (Scheme III). The monoanion of butadiyne, prepared by treating 1,4-dichlorobut-2-yne with 3 equiv of sodium amide in liquid ammonia,[4] reacted readily with cyclohexanone to furnish the diacetylene alcohol **8**, which was extracted and purified while maintaining the product always in solution. Hydration of **8** in the presence of acid and mercury salt produced the furanone **9** in 43% yield, while hydration after elimination of the tertiary hydroxyl group furnished the β-diketone **11** in 22% yield; the low yield is due mainly to extensive polymerization of **10** during the hydration.

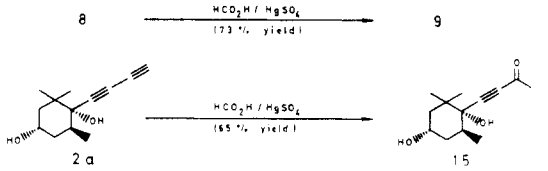
Seeking a more efficient method to transform **8** into **11**, we decided to try an adaptation of the Rupe "rearrangement" to these diacetylene compounds. The Rupe reaction, previously believed to be a rearrangement, consists of elimination of water followed by hydration of acetylenic alcohols to give α,β-unsaturated ketones[5] as indicated in Scheme IV.

The results we obtained when treating compounds **8** or **10** with formic acid (Table I) are in agreement with this mechanism. Hydration of **10** could be effected in much better yield with 85% formic acid than with mercury salts, probably because the hydrocarbon **10** is soluble in formic acid, thus reducing the polymerization during the hydration process. A still better yield of the product **11** can be obtained by treating **8** directly with 85% formic acid. By using more dilute formic acid and shorter reaction times we could isolate the intermediate **12** but not compounds **13** or **14**. This strongly suggests that the terminal triple

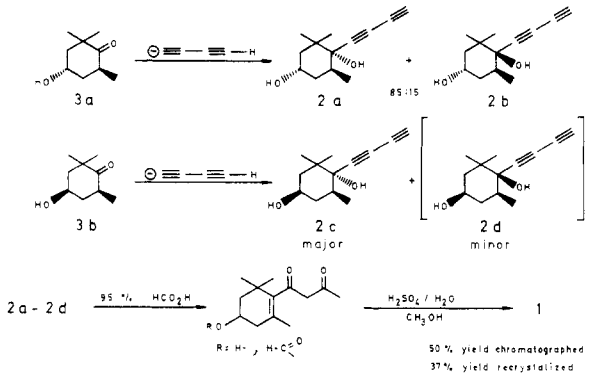


bond is hydrated before the internal one and no cyclic rearrangement involving the tertiary hydroxyl group and the internal triple bond occurs. The successful use of formic acid in hydration of diacetylenes led us to consider the use of this acid together with mercury salts to increase solubility and hydrating power. Mercury salts are reduced by formic acid but, as shown in the examples in Scheme V, some hydration reactions are faster than the reduction process. The spirofuranone **9** could be obtained in considerably better yield than before, and the diacetylene diol **2a** was hydrated only at the terminal acetylene, without elimination of the hydroxyl group.

Scheme V



Scheme VI



The synthesis of compound **1** was effected as depicted in Scheme VI. For analytical purposes, each isomer of **3**[6] was separately reacted with the monoanion of butadiyne and three of the four possible isomeric products were separated and analyzed. The supposed fourth isomer **2d** was obtained only in very small amounts and was not purified. Compounds **2a**, **2b**, and **2c** decomposed on attempted distillation, but they could be purified by column chromatography and kept reasonably well in solution at low temperatures.

Since the stereochemistry of compounds **2a** to **2d** is not relevant in the synthesis of racemic **1**, a mixture of **3a** and **3b** was reacted with the butadiyne monoanion to obtain the mixture **2a** to **2d** in 78.6% yield after purification from resinous byproducts by column chromatography. This mixture was treated with 95% refluxing formic acid to give a complex mixture of products containing **1** and its formic acid ester. After hydrolysis of the ester with dilute sulfuric acid at room temperature and purification by column chromatography, compound **1** was obtained in 50% yield with acceptable purity, as indicated by ^1H and ^{13}C NMR spectra; recrystallization from water gave pure **1** in 37% yield.

Experimental Section

Melting points were determined on a Reichert Kofler block melting point apparatus. All melting points and boiling points are uncorrected. Infrared (IR) spectra were determined on Perkin-Elmer 467 and 280 spectrometers. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at 60 MHz (Varian T-60) or 90 MHz (Varian EM-390). Chemical shifts are reported in parts per million (δ) relative to Me_4Si as an internal standard, with conventional nomenclature for splitting and coupling constants. The ^{13}C NMR spectra were recorded on a FT-80 spectrometer. Mass spectra were recorded on a HP-5985-B spectrometer. Microanalyses were performed in the Microanalytical Laboratory, IQ-USP, Brazil. Analytical gas chromatography

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(GLC) separations were performed on a Varian 2800 gas chromatograph.

The extraction of products was performed in the following manner: dilution of the reaction mixture at room temperature with water and ethyl ether; separation of the organic layer, which was then washed with dilute HCl (only when the reaction mixture was strongly alkaline), water, saturated $NaHCO_3$ and saturated brine and dried over $MgSO_4$; evaporation of the solvent to give the crude product. All distillations were carried out with a Kugelrohr apparatus.

1. Preparation of Diacetylene Alcohols. a. 1-(1-Hydroxycyclohexyl)-1,3-butadiyne (8). Sodium amide (300 mmol) was prepared by adding sodium (6.9 g, 0.3 mol) in small portions to a solution of ferric nitrate (≃0.1 g) in liquid ammonia (500 mL). 1,4-Dichlorobut-2-yne (12.3 g, 100 mmol) was added slowly (a vigorously exothermic reaction ensued), and then a solution of cyclohexanone (4.9 g, 50 mmol) in dry tetrahydrofuran (100 mL) was added dropwise. After having been stirred for 30 min, the ammonia was evaporated quickly by warming, while maintaining the original volume by addition of ether. During this process 6 mL of H_2O in 20 mL of THF was added to protonate the alkoxide formed. Water (100 mL) was added, and the reaction mixture was extracted. Due to its instability the product was always maintained in solution. To determine the yield an aliquot was evaporated, and the residue was weighed; the yield was 6.9 g (93%) of **8**.

An analytical sample was prepared by purification on a column of silica gel, by elution with chloroform–ethyl acetate (1:1). After removal of its solvent, the purest fraction was distilled at 50–55 °C under reduced pressure (0.025 mmHg). Freezing of the distillate produced crystals which were recrystallized from a mixture of ethyl ether and *n*-hexane to give an unstable white crystalline solid: mp 38–39 °C dec; IR ($CHCl_3$) 3350, 3295, 2210, 2045, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.93 (br s, 1 H), 2.23 (s, 1 H), 2.1–1.2 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 80.3 (s), 69.0 (s), 58.4 (d, $J_1 \simeq 5\ J_2$), 67.8 (d, J_2), 39.6 (t), 25.1 (t), 23.1 (t). Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.02; H, 8.28.

b. 1-(2,6,6-Trimethyl-1,4-dihydroxycyclohexyl)-1,3-butadiyne (2). In the same way as described above (experiment 1a), the mixture of isomers **3a** and **3b** (5.2 g, 33.3 mmol) was treated with the monoanion of butadiyne, prepared from 1,4-dichlorobut-2-yne (12.3 g, 100 mmol). After extraction, the crude product was purified from resinous byproducts by column chromatography through silica gel, by using a mixture of chloroform and ethyl ether (7:3) as eluent, to give 5.4 g (78.6%) of a mixture of the stereoisomers **2a**, **2b**, **2c**, and probably **2d**. Since all isomers give the same desired final product, the mixture was used in the subsequent step. Analytical samples of the three main isomers were prepared by column chromatography.

Careful elution with the same mixture of solvents used above furnished pure compound **2a** and a mixture of **2b** and **2c**. This mixture was separated by column chromatography in silica gel, eluting with benzene and ethyl acetate (7:3). The major isomer **2a** was recrystallized from a mixture of chloroform and *n*-hexane to give a relatively unstable white crystalline solid: mp 100–102 °C dec. The isomer **2c** was recrystallized from chloroform and ethyl ether as a crystalline solid which darkens quickly: mp 139–141 °C dec. The isomer **2b** was not recrystallized. **2a**: IR (KBr) 3400, 3300, 2210, 2040, 1050, 1010, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.05 (m, Σ_J = 13 Hz, 1 H), 2.23 (s, 1 H), 2.4–1.5 (m, 5 H), 1.22 (s, 3 H), 1.13 (s, 3 H), 1.08 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 79.2 (s), 77.3 (s), 71.2 (s), 67.9 (d, $J_3 \simeq 5J_2$), 67.7 (d, J_2), 66.6 (d, $J_1 \simeq 3.2J_2$), 44.2 (t), 39.8 (t), 39.2 (s), 32.4 (d), 27.4 (q), 23.1 (q), 16.0 (q).

2b: IR ($CHCl_3$) 3610, 3300, 2210, 2045, 1020, 995, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.07 (m, Σ_J = 13 Hz, 1 H), 2.20 (s, 1 H), 2.4–1.4 (m, 5 H), 1.33 (s, 3 H), 1.12 (d, J = 6 Hz, 3 H), 1.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 78.6 (s), 76.8 (s), 69.8 (s), 67.9 (d, $J_3 \simeq 5\ J_2$), 67.6 (d, J_2), 66.9 (d, $J_1 \simeq 3.5J_2$), 40.2 (t), 38.5 (s), 35.6 (t), 30.9 (d), 26.9 (q), 26.7 (q), 16.7 (q).

2c: IR (KBr) 3350, 3290, 2500, 2060, 1065, 1030, 975 cm^{-1}; ^1H NMR [$(CD_3)_2CO$] δ 4.16 (m, Σ_J = 32 Hz, 1 H), 2.90 (s, 1 H), 2.2–1.3 (m, 5 H), 1.15 (s, 3 H), 1.09 (d, J = 6 Hz, 3 H), 1.03 (s, 3 H); ^{13}C NMR ($CDCl_3$ + CH_3OD) δ 78.3 (s), 77.1 (s), 71.5 (s), 68.1 (d, $J_3 \simeq 5J_2$), 67.7 (d, J_2), 65.8 (d, $J_1 \simeq 3J_2$), 46.6 (t), 41.4 (t), 40.3 (s), 36.3 (d), 27.0 (q), 20.9 (q), 16.4 (q).

2. 1-(1-Cyclohexenyl)-1,3-butadiyne (10). To a solution of compound **8** (3.10 g, 21 mmol) in pyridine (100 mL) was added methanesulfonyl chloride (6.7 g, 58 mmol). After stirring at room temperature for 48 h, extraction gave 1.72 g (63%) of compound **10** as a colorless oil which darkens quickly at room temperature. An analytical sample was prepared by elution through a column of silica gel with a mixture of *n*-hexane and ethyl acetate (8:2): IR (film) 3300, 3020, 2210, 2200, 1620, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.4–6.1 (m, 1 H), 2.39 (s, 1 H), 2.4–1.9 (m, 4 H), 1.8–1.4 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 139.8 (d), 119.3 (s), 77.5 (s), 70.3 (d, $J_1 \simeq 5\ J_2$), 68.5 (d, J_2), 28.5 (t), 25.9 (t), 22.1 (t), 21.3 (t).

3. Hydration of Diacetylene Compounds. a. 2-Methyl-4-oxo-1-oxaspiro[4.5]dec-2-ene (9). Method A. To a solution of compound **8** (370 mg, 2.5 mmol) in acetic acid (4 mL) was added a solution of mercuric sulfate[7] (6 mL), and the mixture was refluxed for 2 h. After cooling, extraction and distillation at 50–60 °C (0.05 mm) gave 177 mg (43%) of **9**. The distillate was crystallized from a mixture of ethyl ether and *n*-hexane to furnish a stable white crystalline solid: mp 64–65 °C; IR (KBr) 3090, 1690, 1595, 1210, 1060, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.40 (s, 1 H), 2.25 (s, 3 H), 2.0–1.1 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 207.2 (s), 188.1 (s), 102.5 (d), 90.8 (s), 31.7 (t), 24.6 (t), 21.8 (t), 17.0 (q). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.03; H, 8.73.

Method B. To a solution of compound **8** (1.63 g, 11 mmol) in 85% formic acid (60 mL) was added a solution of mercuric sulfate[7] (90 mL). The mixture was stirred at room temperature for 1 h and was refluxed for another 1 h. After cooling and extraction, the residue was distilled and recrystallized as above to give 1.34 g (73%) of **9**.

b. 1-(1-Cyclohexenyl)-1,3-butanedione (11). Method A (from 10). To a solution of compound **10** (250 mg, 1.9 mmol) in methanol (5 mL) was added slowly a solution of mercuric sulfate[7] (10 mL). After the solution was stirred at room temperature for 1 h, the product was extracted, and the crude residue was distilled to give 72 mg (22.5%) of **11**: bp 80–90 °C (0.5 mm); IR (film) 1720, 1640, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) enol form δ 7.0–6.6 (m, 1 H), 5.83 (s, 1 H), 2.12 (s, 3 H); keto form δ 3.77 (s, 2 H), 2.23 (s, 3 H); both forms δ 2.5–2.1(m, 4 H), 1.9–1.5 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ enol form 194.2 (s), 182.6 (s), 136.3 (d), 133.8 (s), 95.7 (d), 26.0 (q + t), 23.6 (t), 22.6 (t), 21.7 (t). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.04; H, 8.35.

Method B (from 10). The compound **10** (228 mg, 1.75 mmol) was dissolved in 85% formic acid (15 mL) and refluxed for 2 h, whereupon extraction and distillation as above gave 156 mg (53.5%) of **11**.

Method C (from 8). The compound **8** (151 mg, 1.02 mmol) was dissolved in 85% formic acid (15 mL) and refluxed for 2 h, whereupon extraction and distillation gave 131 mg (77%) of compound **11**.

c. 1-(1-Cyclohexenyl)-1-butyn-3-one (12). The compound **8** (163 mg, 1.1 mmol) was dissolved in 70% formic acid (16 mL) and refluxed for 1 h. After cooling, extraction yielded a residue (170 mg) which consisted of a ca. 4:6 mixture (NMR analysis) of compound **11** and the partially hydrated compound **12**, respectively. This mixture was partially purified by elution through a column of silica gel with a mixture of *n*-hexane and ethyl acetate (95:5). It was then chromatographed on a column of silica impregnated with $FeCl_3$, with mixtures of *n*-hexane and ethyl acetate (8:2 and 1:1) and, finally, pure ethyl acetate as eluant. The initial fraction (yellow) was concentrated, dissolved in ethyl ether, washed with water, 10% oxalic acid solution, water again, and saturated $NaHCO_3$, and dried ($MgSO_4$). Removal of the solvent gave 85 mg (52%) of compound **12**: IR ($CHCl_3$) 2250, 2180, 1660, 1620, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.48 (m, 1 H), 2.32 (s, 3 H), 2.3–2.0 (m, 4 H), 1.8–1.4 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 184.6 (s), 142.2 (d), 119.0 (s), 86.7 (s), 77.2 (d), 32.6 (q), 28.4 (t), 26.2 (t), 22.0 (t), 21.2 (t). Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.38; H, 8.34.

The second fraction (red) treated as above furnished 65 mg (35%) of pure compound **11**.

d. 1-(2,6,6-Trimethyl-4-hydroxycyclohexenyl)-1,3-butanedione (1). A mixture of the four isomers **2a–2d** (930 mg, 4.5 mmol) was dissolved in 95% formic acid (100 mL) and refluxed

(7) The hydrating solution was prepared from concentrated sulfuric acid (10.5 mL), water (39.5 mL), and red mercuric oxide (2.0 g).

for 1 h, cooled, diluted with water, and extracted with ethyl ether. The solvent was evaporated, and the residue was then dissolved in methanol (25 mL); 20% sulfuric acid solution (15 mL) was added, and the reaction solution was stirred for 1 h at room temperature. After extraction, purification of the crude material by elution with a mixture of benzene and ethyl ether (7:3), on a column of silica gel, gave a semicrystalline yellow product (500 mg), which was recrystallized from water to give 373 mg (37%) of compound **1** as a stable white crystalline solid: mp 64–65 °C (lit.[8] mp 68.5 °C); IR (KBr) 3400, 1600, 1370, 1070, 1035, 990, 955 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.45 (s, 1 H), 4.3–3.6 (m, 1 H), 2.08 (s, 3 H), 1.67 (s, 3 H), 1.17 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 193.5 (s), 189.3 (s), 137.5 (s), 130.1 (s), 103.4 (d), 64.1 (d), 47.9 (t), 41.1 (t), 36.3 (s), 29.6 (q), 28.9 (q), 25.7 (q), 20.9 (q). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.71; H, 9.01.

e. 1-(2,6,6-Trimethyl-1,4-dihydroxycyclohexyl)-1-butyn-3-one (15). To a solution of pure isomer **2a** (250 mg, 1.2 mmol) in 85% formic acid (5 mL) was added a solution of mercuric sulfate[7] (12 mL). After 5 min of stirring at room temperature, the solution was refluxed for 2 h. After separation of the precipitated metallic mercury, the reaction mixture was extracted and hydrolyzed as above. The residue obtained was then purified by elution with *n*-hexane–ethyl acetate (1:1) on preparative TLC to give 176 mg (65%) of compound **15**: IR ($CHCl_3$) 3450, 2950, 2200, 1665, 1600, 1460, 1360, 1230, 1035, 965, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10 (m, 1 H), 2.38 (s, 3 H), 2.4–1.3 (m, 5 H), 1.25 (s, 3 H), 1.15 (s, 3 H), 1.10 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 184.2 (s), 86.8 (s), 79.0 (s), 77.3 (s), 66.5 (d), 44.2 (t), 39.9 (t), 39.0 (s), 32.9 (d), 32.2 (q), 27.4 (q), 23.0 (q), 16.0 (q); mass spectrum, *m/e* (relative intensity) 224 (M^+, 1), 209 (1), 206 (6), 191 (5), 96 (61), 43 (100).

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Alkaloids from *Delphinium geyeri*. Three New C_{20}-Diterpenoid Alkaloids

Jonas A. Grina, Daniel R. Schroeder, Edward T. Wydallis, and Frank R. Stermitz*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

Jonathan Melman and John L. Capinera

Department of Entomology, Colorado State University, Fort Collins, Colorado 80523

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Three new C_{20}-diterpenoid alkaloids related to hetisinone were isolated from *Delphinium geyeri* (Ranunculaceae) and their structures determined by spectroscopic methods. The major new alkaloid, dubbed geyerine, was found to be 6-hydroxy-11-*O*-(2-methylbutanoyl)hetisinone. The two minor new alkaloids were 6-hydroxy-13-*O*-acetylhetisinone (geyeridine) and 3-acetoxy-6-hydroxy-11-*O*-(2-methylbutanoyl)hetisine (geyerinine). In addition to these substances, the known C_{19}-diterpenoid alkaloids dictyocarpine, glaucenine, delcosine, browniine, 14-acetyldelcosine, 14-acetylbrowniine, 14-dehydrobrowniine, and delphatine were isolated. The total alkaloid mixture was shown to have feeding deterrent activity against the migratory grasshopper, but results on some of the purified alkaloids were equivocal.

Delphinium geyeri, a Colorado larkspur, has been known for some time[1] to be toxic to range animals. Three alkaloids were isolated[1] as Hg complexes, but no structural characterizations were carried out. Considerable data are available[2,3] on the toxicity and biological activity of alkaloids from other Delphinium species. A grasshopper (*Melanoplus sanguinipes*) feeding deterrent screening[4] of 5-g range plant extracts showed the highest activity for *D. geyeri* and field observations[4,5] indicated little, if any, plant consumption by herbivorous insects. This research was undertaken to isolate and characterize the alkaloids of *D. geyeri* and to determine if they were responsible for the insect feeding deterrence.

Results and Discussion

A total of 11 alkaloids were isolated and characterized. Eight of these were known C_{19}-diterpenoid alkaloids, while three were C_{20}-diterpenoid alkaloids, all new. Table I lists the isolated alkaloids in an approximate order of decreasing concentration. Most of the known alkaloids were identified by spectral and TLC comparison with standard samples. Standards were not available for a few and the structures of these rest on spectral comparisons with the literature data. The new C_{20} alkaloids were identified as follows.

Table I. Relative Abundance of the Alkaloids Isolated from *D. geyeri*[a]

alkaloid	occurrence	type
browniine	major	C_{19}
14-acetylbrowniine	major	C_{19}
geyerine (1)	major	C_{20}
14-dehydrobrowniine	major	C_{19}
14-acetyldelcosine	moderate	C_{19}
delcosine	moderate	C_{19}
delphatine	minor	C_{19}
dictyocarpine	minor	C_{19}
geyeridine (2)	minor	C_{20}
geyerinine (3)	minor	C_{20}
glaucenine	minor	C_{19}

[a] Listed from top to bottom as most to least abundant.

The major new alkaloid, dubbed geyerine, was shown by HREIMS to have the molecular formula $C_{25}H_{33}NO_5$ (M_r

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