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CHEMICAL DEFENSE MECHANISMS OF ARTHROPODS XXXVI. STEREOSPECIFIC SYNTHESIS OF GYRINIDAL, A NOR-SESQUITERPENOID ALDEHYDE FROM GYRINID BEETLES

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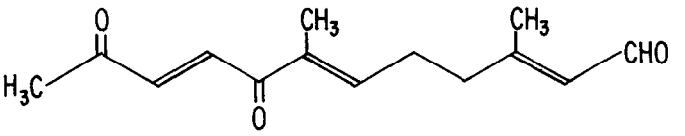
The familiar "whirligig" water beetles of the family Gyrinidae possess a pair of abdominal glands which secrete a milky, odorous fluid when the insect is handled or otherwise mistreated. Recently, Schildknecht and co-workers[2] (studying Gyrinus natator) and Meinwald and co-workers[3] (studying G ventralis, Dineutes hornii and D serrulatus) have independently isolated and characterized the novel, highly oxygenated, nor-sesquiterpenoid gyrinidal (1), (E,E,E)-3,7-dimethyl-8,11-dioxo-2,6,9-dodecatrienal, as a major constituent of these secretions



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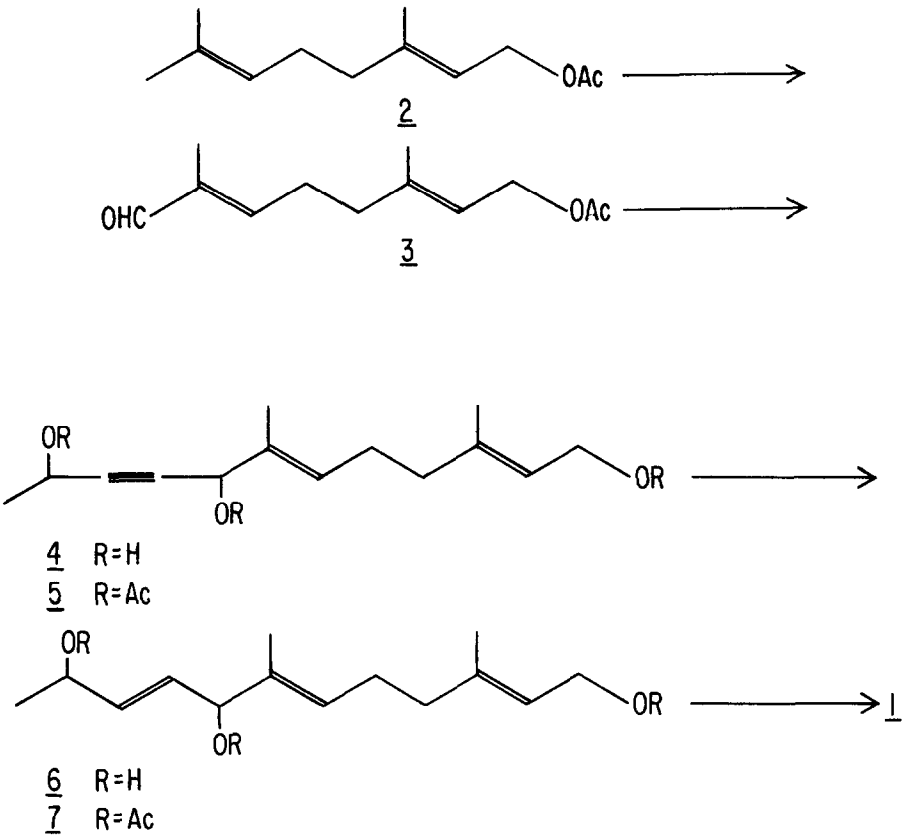
In order to provide further confirmation of this structure and to supply quantities of gyrinidal required for a study of its biological potentialities, notably its high repellent effe on some fishes[4], it was necessary to synthesize this rather labile compound We wish here to report a short, stereospecific synthesis of gyrinidal as outlined below An important feature of the synthetic plan is the generation of the highly reactive 1,4-diene-3,6-dione system as the final step in our sequence.



Geranyl acetate (2) was oxidized with freshly sublimed selenium dioxide in refluxing 97% aqueous ethanol[5] to give, after chromatography on Florisil, aldehyde 3[6] in 54% yield, IR(CCl_4) 2720(w), 1750(s), 1690(s) cm^{-1}, NMR(CCl_4) δ 1 75(s,6H), 1.97(s,3H), 2 35(m,4H), 4 55(d,J=7Hz,2H), 5 40(broad t,J=7Hz,1H), 6.42(broad t,J=6Hz,1H), 9 38(s,1H), MS(70eV) m/e 150(M-HOAc), chemical ionization MS(CH_4,500eV) m/e 211(M+1)

Addition of 3 to ten molar equivalents of the dilithio salt of 3-butyn-2-ol in tetrahydrofur (formed by the reaction of two moles of methyl lithium with 3-butyn-2-ol) produced the acetylenic triol 4 in 62% yield (after Florisil chromatography); IR($CHCl_3$) 3580(sharp), 3400(broad) cm^{-1}, NMR($CDCl_3$) δ 1 44(d,J=6Hz,3H), 1 65,1 72(overlapping s,6H), 2 13(broad s,4H), 4.00-4.87(complex overlapping m,d,4 12,J=6Hz,7H), 5 17-5 85(m,2H) Acetic anhydride/pyridine acetylation of 4 provided the corresponding triacetate 5, IR(CCl_4) 1740,1230 cm^{-1}, NMR(CCl_4) δ 1 45(d,J=7Hz,3H),

1.70(broad,s,6H), 1.95-2.29(1 95s, 2.00s, 2.10m, 13H), 4.48(d,J=7Hz,2H), 5.11-5.78(m,4H), MS(70eV) m/e 305(M-OAc)

Reduction of 4 with an excess of sodium in liquid ammonia/tetrahydrofuran (3 8/1) and a trace of ethanol for 2 hr yielded the triene 6 (29% based on 4 consumed, after purification on Florisil); IR($CHCl_3$) 3560(sharp), 3390(broad), 970(s) cm^{-1}, NMR($CDCl_3$) δ 1 27(d,J=6Hz,3H), 1.62,1.67(two s,6H), 2.13(broad s,4H), 3 45-4.82(overlapping absorptions, 4 13 d,J=6Hz,~7H), 5.18-5.82(m,4H) Acetic anhydride/pyridine acetylation of 6 gave the triacetate 7, IR(CCl_4) 1745,1230 cm^{-1}, NMR(CCl_4) δ 1 32(d,J=7Hz,3H), 1.53-1 82(1 6s,1.72s,6H), 2.00-2 32(2.00s,2 04s,2.14m,13H), 4.53(d,J=7Hz,2H), 5 07-5 73(m,6H); MS(70eV) m/e 307(M-OAc).

Oxidation of 6 with activated manganese dioxide (Winthrop Laboratories, New York, N.Y) at 0° in chloroform provided crude gymnidal (1), which was obtained pure in 17% yield after preparative TLC on silica gel (E Merck, GF-254) and aluminum oxide (E. Merck, GF-254). The IR, NMR, UV, and GLC/MS spectra, as well as the TLC behavior of synthetic 1, were identical to those of the natural product, IR(CCl_4) 2720(w), 1675(s), 1650(s), 1635(sh), 1610 cm^{-1}, NMR(CCl_4) δ 1 82(d,J~1Hz,3H), 2 12-2 75(2.18d,J~1 5Hz,2 27s, 2.31m,10 H), 5 78(d,J=8Hz,1H), 6 42-6 90(6.60m,6.90d,J=16Hz,2H), 7 33(d,J=16Hz,1H), 9 95(d,J=8Hz,1H), MS(70eV) m/e 234, 219, 191, 125, 109, 43, UV λmax(MeOH)=237nm, ε=22,500

Gymnidal is a powerful feeding deterrent to large mouth bass (Micropterus salmoides) The threshold of rejection, determined on the basis of acceptability to the fish of mealworms coated with varying quantities of the material, ranged broadly and depended on the state of satiation of the animal (minimum threshold = 0 4μg/mealworm). Evaluation of synthetic material showed its deterrence to match that of the purified natural product [4]

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Footnotes and References

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