Biomimetic Synthesis of the *Fucus* Pheromone, Fucoserraten

A Contribution to the Heterolytic Fragmentation of Unsaturated 1,5-Diols

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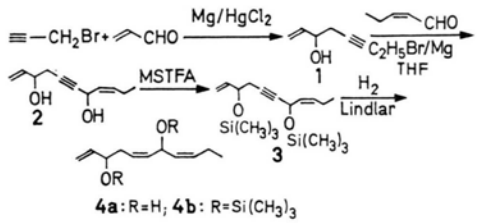
Fucoserraten (1,3-*trans*, 5-*cis*-octatriene), the sex-attractant of *Fucus serratus* and *F. vesiculosus*, was obtained by heating bis-trimethylsilyl-1,5-*cis*, 8-*cis*-undecatrien-3,7-diol in an acidic milieu, showing simultaneously that also 3-unsaturated 1,5-diols undergo heterolytic fragmentation. As expected, the reaction proceeds without isomerization and under *trans*-elimination of the leaving group.

As the initiating step in the mating act of the gametes of brown algae (phaeophytes), the mature female reproductive cell (gynogamete) secretes a low-molecular, volatile chemical messenger into the medium to lure the motile spermatozoids (androgametes) within their vicinity [1].

The sex-attractants or pheromones of the brown algae investigated so far [1 c] are rather hydrophobic, polyunsaturated, linear or cyclic hydrocarbons, structurally closely related. They all end with a *cis*-butenyl moiety and possess three double bonds, but no other functional groups. Their close relationship to highly unsaturated fatty acids which occur widely in algae (and in their gametes) let us postulate a common biogenetic origin of the lures from an intermediate of linolenic acid metabolism [2], thus making of a normal metabolic product a messenger by a process of ritualization or sematicization. β-Oxidation of linolenic acid – or possibly also direct synthesis [3] – forms a dodecatrienoic acid. This can be oxidatively decarboxylated to a C_{11}-trienol which, after (pyro)phosphorylation at the C-3 OH and subsequent removal of the leaving group, generates an intermediate cation. This now may stabilize and cyclize under proper catalytic action to the $C_{11}H_{16}$ hydrocarbons of *Dictyopteris*, *Cutleria*, and *Ectocarpus*. Furthermore, hydroxylation of the C_{11}-trienol at the allylic C-7 CH_2 would give the undecatrien-3,7-diol (**4 a**), a compound which may be split by heterolytic fragmentation [4] to acrolein and the C-8 hydrocarbon fucoserraten (1,3-*trans*-, 5-*cis*-octatriene) (**6**) [5], the lure of the Fucales [6]. The occurrence of 1,5-octadien-3-ol, a compound clearly related to the proposed biogenetic intermediate **4 a**, in the essential oil of the red alga *Chondrococcus hornemani* [7], gives support to this conception.

To control our hypothesis, we studied the behaviour of the postulated precursors under biomimetic conditions and wish to report here on the successful *in vitro* preparation of fucoserraten (**6**) from 1,5-*cis*-, 8-cis-undecatrien-3,7-diol (**4 a**) by the fragmentation method.

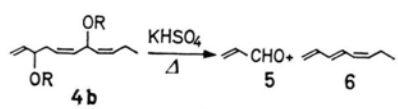
The starting material of unambiguous stereochemistry was synthesized as follows (Scheme I):



Scheme I: Synthesis of 1,5-*cis*, 8-*cis*-undecatrien-3,7-diol (**4 a**).

Propargyl bromide was condensed [8] with acrolein to 1-hexen-5-yn-3-ol (**1**), which after isolation and purification was reacted with 2-*cis*-penten-1-al (containing 15% of the *trans* isomer) to *cis*-1,8-undecadien-5-yn-3,7-diol (**2**). The unstable **2** was derivatized with MSTFA to form the stable bis(trimethylsilylether (**3**). The acetylenic bond at C-5 was hydrogenated stereoselectively to the all-*cis* ether **4 b** using a Lindlar catalyst. The free alcohol **4 a** was obtained by trans-silylation of **4 b** in methanol/TMSCl. However, it prooved too unstable in acidic or basic conditions to be useful in fragmentation studies. Therefore, this reaction was carried out with the above bis(trimethylsilyl) ether **4 b**.

A solution of **4 b** in dry ether was heated with fused $KHSO_4$. At 100 °C (bath temperature) the compound begins to fragmentate quickly, yielding – besides an as yet unidentified major product (50%) – 1,3-*trans*-, 5-*cis*-octatriene (**6**) (15%) and acrolein (Scheme II).



Scheme II: Heterolytic fragmentation of 1,5-*cis*-8-*cis*-undecatriene-3,7-diol-bis(trimethylsilyl) ether (**4 b**) to fucoserraten (**6**) and acrolein (**5**). (In both, **4 b** and **6**, the butenyl double bond was actually 85% *cis* and 15% *trans*.)

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The stereochemistry of the octatriene **6** was unequivocally proven by physical comparison to be identical with the natural sex-attractant fucoserraten, as shown by the following data:

(i) *Kovàts index:*	10% PEG 4000/ 52 °C	10% Apiezon L + 1% Igepal/62 °C
isolated triene:	1013.3	884.4
fucoserraten:	1013.2	885.0

(ii) *UV-spectrum (ether)* (λ_{max})

isolated triene:	252.3	*262.0*	272.3 nm
fucoserraten:	252.3	*262.0*	272.3 nm

(iii) *GC-MS*, 2% OV-17; temp. 100 – 260 °C, 15 °C/min; inject. 250 °C; 70 eV

isolated triene: $m/e = 65$ (12.8%), 66 (14.6%), 77 (59.8%), 79 (100%), 80 (11.2%), 91 (50.3%), 93 (14.9%), 105 (2.5%), 108 (32%), 109 (3%).

fucoserraten: $m/e = 65$ (14.8%), 66 (14%), 77 (63%), 79 (100%), 80 (11.4%), 91 (37.6%), 93 (15.5%), 105 (1.2%), 108 (31.4%), 109 (2.9%).

The product **6** was a mixture of 85% 1,3-trans,5-*cis*-octartriene (fucoserraten) and 15% all-*trans*-1,3,5-octatriene, exactly corresponding to the starting material **4 a**. Thus, fragmentation proceeds without isomerization, and HOR is eliminated *trans*.

For the identification of acrolein, another sample of **4 b** was treated as described. The volatile products of the reaction were collected at 0 °C in a tetraline trap by means of a stream of N_2. Glc analysis of the trap contents on 20% PEG 4000 and 15% SE-30 columns identified the isolate as acrolein. Due to losses by the flushing procedure and work-up, exact stoicheiometry cannot be given.

The heterolytic fragmentation of 1,3-diols is well established in the literature (see [3 c]). With the fragmentation of **4 b** we believe to have demonstrated for the first time that also 3-unsaturated 1,5-diols react in the same fashion.

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Experimental

Boiling points are uncorrected. Infrared spectra: Perkin-Elmer 337 IR-spectrometer on neat liquid samples; UV-spectra: Varian Cary 14; NMR-spectra: Varian 90 MHz spectrometer, internal standard: tetramethylsilane (we thank Mrs. U. Baumann for the analyses); MS-spectra: Hewlett-Packard GC-MS, 5992 A (we thank Prof. Dr. M. Donike for giving us access to his instrument); vapor phase chromatographic analyses were carried out on a Hewlett-Packard, model 5750 G, FID, with glass capillary columns, 1.5 m × 3 mm. For the preparative glc separations, a Wilkens Aerograph, model 1520 with 2 m × 4 mm columns was used. Data on column packings are specified in each case.

1,8-cis-undecadien-5-yn-3,7-diol (**2**)

To a solution of 0.4 mol ethyl magnesium bromide in THF 19.2 g (0.2 mol) 1-hexen-5-yn-3-ol (**1**) [8] were added slowly at 0 °C. After complete addition, 8.4 g (0.1 mol) 2-*cis*-penten-1-al was added and the mixture kept boiling overnight. It was then allowed to cool, and hydrolyzed with 50% (v/v) THF in H_2O. After acidification with solid ammonium chloride and extraction, vacuum destillation yielded 15.3 g (85%) of the colorless, viscous diol **2**, bp. 129 – 132 °C/0.6 mm.

IR: 3340 cm^{-1} (s), 3080 (m), 2140 (w), 1660 (m), 1125 (m), 1035 (s), 995 (s), 970 (m), 930 (s), 845 (m).

^{1}H-NMR (CCl_4/TMS): 1.0 ppm (t) ($-CH_3$), 2.2 (q) ($-CH_2-CH_3$), 2.5 (d) ($-CH_2-$), 4.3 (q) (*tert.*-H), 4.5 (s) (–OH), 4.8 (d) (*tert.*-H), 5.3 (m) ($=CH_2$), 6.0 (m) ($=CH-$).

GC-MS (OV-1; temp. 130 – 250 °C; 8 °C/min; 70 eV): $m/e = 57$ (82%), 65 (18%), 67 (20%), 77 (25%), 79 (20%), 84 (28%), 91 (100%), 95 (18%), 105 (25%), 106 (19%), 123 (3%), 134 (5%), 149 (4%), 151 (1%).

1,8-cis-undecadien-5-yn-3,7-bis-trimethylsilyl ether (**3**)

The diol **2** was silylated with N-methyl-N-trifluoro acetamide (MSTFA) in a homogeneous reaction at room temperature. The silyl ether **3** was purified on a preparative glc column which was pre-treated with a 9 : 1 mixture of MSTFA/TMSCl.

1,5-cis,8-cisundecatrien-3,7-bis-trimethylsilyl ether (**4 b**) *($R = Si(CH_3)_3$)*

700 mg of **3** were dissolved in 15 ml of ethylacetate, 20 µl quinoline and Lindlar catalyst added, and hydrogenated under atmospheric pressure.

Progress of the reaction was monitored by glc on a 20% PEG 4000 column. When the reaction was complete, the product **4 b** was isolated and purified on a preparative PEG 4000 column. To prevent desilylation of the product, the column-material was washed with alkali and preteated as above with MSTFA/TMSCl. **4 b** could also be purified on neutral Al_2O_3 plates, treated with 5% HMDS in cyclohexane/ethylacetate (9 : 1); however, in this case some desilylation occurs.

IR: 3080 cm^{-1} (w), 3020 (m), 2970 (s), 1245 (s), 1060 (s), 870 (m), 840 (s), 750 (s).

^{1}H-NMR (CCl_4/TMS): 0.9 ppm (t) ($-CH_3$) 2.0 (m) (4 H; $-CH_2-$), 4.0 (q) (*tert.*-H), 4.7 (t) (*tert.*-H), 5.0 – 6.0 (m) (7 H; olefinic).

GC-MS (2% OV-17; temp. 100 – 250 °C, 10 °C/min; 70 eV, intensities down to 2% recorded): $m/e = 73$ (100%), 75 (21%), 79 (5.3%), 91 (3.3%), 129 (72%), 131 (17%), 147 (5.2%).

Heterolytic fragmentation of (**4 b**)

In a two-neck round bottom flask, 0.45 g (3.3 mmol) of fused $KHSO_4$ was added to 1.1 g (3.3 mmol) of **4 b**, dissolved in 25 ml of dry ether. The flask which was equipped with a powerful condenser was heated in an oil bath to 100 °C. The reaction started right after the temperature of the bath reached that value and the ocatriene formation was complete within 60 min. Further heating did not influence the composition of the products. After filtration, the products were isolated and purified by glc on a preparative SE-30 column. The yield of the octatriene **6** after isolation was 49.8 mg (15%).

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