Biomimetic Synthesis of the Fucus Pheromone, Fucoserraten

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

Konstantin Seferiadis and Lothar Jaenicke

Institut für Biochemie der Universität zu Köln

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Fucoserraten (1,3-trans, 5-cis-octatriene), the sex-attractor of Fucus serratus and F. vesiculosus, was obtained by heating bis-trimethylsilyl-1,3-cis, 8-cis-undecatrien-3,7-diol in an acidic milieu, showing simultaneously that also 3-ununsaturated 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 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-butynyl moiety and possess three double bonds, but

bic, polyunsaturated, linear or cyclic hydrocarbons,

making of a normal metabolic product a messenger for the mating act. The above bis(trimethylsilyl) ether 4 b.

to l-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(trimethylsilyl)ether (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 proved 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).

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):

\[
\begin{align*}
\text{CH}_3\text{Br} & \rightarrow \text{CHO} \\
\text{Mg/HgCl}_2 & \rightarrow \text{OH} \\
\text{THF} & \rightarrow \text{H}_2
\end{align*}
\]

\[
\begin{align*}
\text{CHO} & \rightarrow \text{CHO} \\
\text{Lindlar} & \rightarrow \text{CHO}
\end{align*}
\]

4a: R = H, 4b: R = Si(CH 3 ) 3

Scheme I: Synthesis of 1,3-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(trimethylsilyl)ether (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 proved 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).

\[
\begin{align*}
\text{OR} & \rightarrow \text{KHSO}_4 \\
\text{H}_2\text{O} & \rightarrow \text{CH}_3\text{OH}
\end{align*}
\]

4b

Scheme II: Heterolytic fragmentation of 1,5-cis-8-cis-undecatrien-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.)
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) Kováts index: 10% PEG 4000/52 °C
isolated triene: 1013.3
fucoserraten: 1013.2

(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 (2.9%).
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-octatriene (fucoserraten) and 15% all-trans-1,3,5-octatriene, exactly corresponding to the starting material 4a. Thus, fragmentation proceeds without isomerization, and HOR is eliminated trans.

For the identification of acrolein, another sample of 4b 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 N2. 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 stoichiometry cannot be given.

The heterolytic fragmentation of 1,3-diols is well established in the literature (see [3c]). With the fragmentation of 4b 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, 5992A (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-ol was added and the mixture kept boiling overnight. It was then allowed to cool, and hydrolyzed with 50% (v/v) THF in H2O. After acidification with solid ammonium chloride and extraction, vacuum distillation 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), 970 (m), 930 (s), 845 (m).

¹H-NMR (CC14/TMS): 1.0 ppm (t) (-CH₃), 2.2 (q) (-CH₂-CH₃), 2.5 (d) (-CH₂-), 4.3 (q) (tert.-H), 4.5 (s) (-OH), 4.8 (d) (tert.-H), 5.3 (m) (-CH₃), 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-trifluoroacetamide (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 (4b) (R = Si(CH₃)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 pre-treated as above with MSTFA/TMSCl. \(4\ b\) could also be purified on neutral Al\(_2\)O\(_3\) 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) (\(-\text{CH}_3\)) 2.0 (m) (4 H; \(-\text{CH}_2\)), 4.0 (q) (\text{tert.-H}), 4.7 (t) (\text{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 KH\(_2\)SO\(_4\) 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 octatriene 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%).