

THE SYNTHESIS OF 3-n-HEXYLDITHIACYCLOHEPTAN-5-ONE, A NOVEL  
CYCLIC KETODISULFIDE FROM DICTYOPTERIS

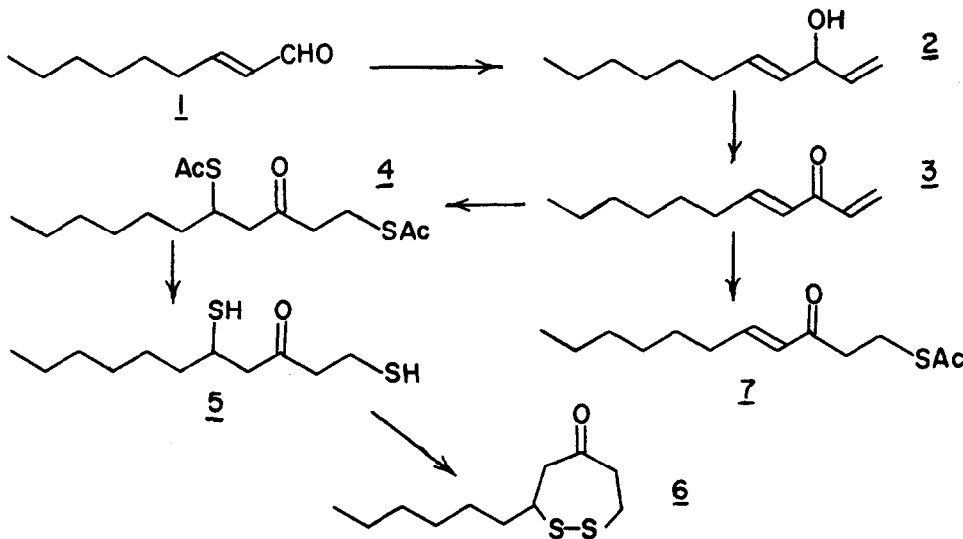
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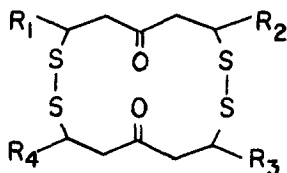
We have previously reported that the Hawaiian algae Dictyopteris plagiogramma and D. australis contain a wide variety of highly unsaturated C<sub>11</sub> hydrocarbons<sup>1a-c</sup>, one of which, dictyopterene D', is identical to the sperm attractant produced by the female gametes of the brown seaweed Ectocarpus siliculosus<sup>2</sup>. In addition, several sulfur-containing compounds which bear an obvious structural and apparent biogenetic relationship to the C<sub>11</sub> hydrocarbons have been isolated and identified from these odoriferous seaweeds<sup>3a,b</sup>. One of the sulfur compounds is the novel seven-membered cyclic ketodisulfide, 3-n-hexyldithiacycloheptan-5-one, 6.<sup>3a</sup> We now wish to describe an efficient and unambiguous synthesis<sup>4</sup> (Scheme 1) of 6.

Scheme 1



The reaction of 2-nonenal<sup>5</sup>, 1, with ethereal vinylolithium (2 h, -30°) gave 1,4-undecadien-3-ol, 2, bp 67-8°/0.6 torr. Oxidation of 2 with DDQ in dichloromethane (2 h, r.t.) followed by column chromatography on neutral alumina with the same solvent yielded the highly reactive cross-conjugated ketone, 1,4-undecadien-3-one, 3. Subsequent overnight treatment of the crude divinyl ketone 3 with 2 mol equiv of thiolacetic acid<sup>6</sup> followed by gel filtration on Sephadex LH-20 using CHCl<sub>3</sub>-CH<sub>3</sub>OH (1:1) afforded 1,5-bis-acetylthio-3-undecanone, 4, as a pale yellow oil. Transesterification of the bis-thioacetate 4 with 3% methanolic HCl<sup>7</sup> (1.5 h, 75°) gave 1,5-dimercapto-3-undecanone, 5, which was purified in the same manner as compound 4. Lastly, oxidative coupling of dithiol 5 using 1.1 equiv of iodine and 2.2 equiv of pyridine (5 min, r.t.) in ether gave the desired cyclic ketodisulfide, 6, as a colorless oil in 66-70% yield after purification by gel filtration on Sephadex LH-20 (1:1 CHCl<sub>3</sub>-CH<sub>3</sub>OH).

A colorless crystalline solid (mass spectrum m/e 464) was also obtained in 6-10% yield from the cyclization of dithiol 5. Preliminary studies indicate that this solid is a mixture of isomeric macrocyclic bis-disulfides, 8a and 8b.



8a: R<sub>1</sub> = R<sub>3</sub> = n-hexyl; R<sub>2</sub> = R<sub>4</sub> = H

8b: R<sub>1</sub> = R<sub>4</sub> = n-hexyl; R<sub>2</sub> = R<sub>3</sub> = H

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#### FOOTNOTES AND REFERENCES

- (a) R. E. Moore, J. A. Pettus, Jr. and M. S. Doty, *Tetrahedron Lett.*, 4787 (1968); (b) J. A. Pettus, Jr. and R. E. Moore, *Chem. Comm.*, 1093 (1970); J. A. Pettus, Jr. and R. E. Moore, *J. Amer. Chem. Soc.*, 93, 3087 (1971).
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- (a) P. Roller, K. Au and R. E. Moore, *Chem. Comm.*, 503 (1971); (b) R. E. Moore, *Chem. Comm.*, 1168 (1971).
- Satisfactory analytical data were obtained for all compounds prepared in this study.
- This compound was prepared from 1,1,3-triethoxynonane essentially according to the procedure of O. Isler, H. Lindlar, M. Montavon, R. Ruegg and P. Zeller, *Helv. Chim. Acta*, 39, 249 (1956).
- With 1 equiv of thiolacetic acid, ketone 3 underwent facile stereospecific addition to the terminal double bond to give S-(3-oxoundec-4-enyl) thioacetate, 7, which was identical in all respects to the natural product isolated from *Dictyopteris*.
- L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, John Wiley and Sons, New York, N. Y., 1967, p. 668.
- Naturally occurring 3-n-hexyldithiacycloheptan-5-one is optically active with  $[\alpha]_D^{25} = -65^\circ$ .