

## Total Synthesis of Astaxanthin and Hydroxyechinenone

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ASTAXANTHIN (I, R = *d*) occurs in *Crustacea* and other animals;<sup>1,2</sup> together with its esters, it constitutes the principal prosthetic group of the carotenoproteins.<sup>1,3,4</sup> Attempts to isolate astaxanthin frequently yield the corresponding diosphenol, astacene (I, R = *b*).<sup>1</sup> The latter may readily be obtained by autoxidation of canthaxanthin (I, R = *a*),<sup>5,6</sup> for which a number of syntheses have been developed.<sup>7</sup> We now report the conversion of astacene into astaxanthin by reduction with potassium borohydride, and oxidation of the resulting mixture of tetraols (I, R = *c*) with

manganese dioxide or, preferably, 2,3-dichloro-5,6-dicyanoquinone.

The product, which exhibited a molecular ion† corresponding to  $C_{40}H_{52}O_4$ , was identified by direct comparison with an authentic specimen‡ from the common lobster, *Homarus gammarus* L. (mixed thin-layer chromatograms on Kieselgel H). Both had  $\lambda_{\max}$  (CS<sub>2</sub>) 503 m $\mu$ ,  $\lambda_{\max}$  (CHCl<sub>3</sub>) 485 m $\mu$ ,  $\lambda_{\max}$  (MeOH) 472 m $\mu$ ,  $\nu_{\max}$  (CHCl<sub>3</sub>) 3520 and 1660 cm.<sup>-1</sup>,  $\tau$  (CDCl<sub>3</sub>)\* 8.74, 8.06, and 8.02, and yielded astacene on autoxidation.

Synthetic astaxanthin combined‡ with the

† Precision mass spectrometry on an A.E.I. MS9 spectrometer with sample directly inserted into source (Dr. E. S. Waight).

\* Methyl bands only.

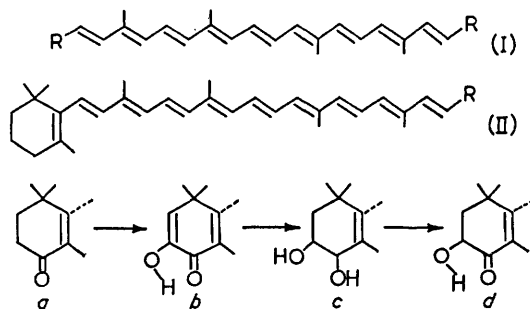
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appropriate apoprotein from the lobster carapace to give the characteristic blue colour,  $\lambda_{\max}$  (phosphate buffer, pH 7) 630 m $\mu$ , of  $\alpha$ -crustacyanin.<sup>4</sup>

Autoxidation of echinenone (II, R = a) gave 3-oxoechinenone (II, R = b).<sup>6</sup> Reduction of the latter with potassium borohydride, and oxidation of the resulting glycols (II, R = c) with 2,3-dichloro-5,6-dicyanoquinone or, preferably, acetone and aluminium t-butoxide, gave 3-hydroxyechinenone (II, R = d), m.p. (evac. capillary) 156—157°. This exhibited the expected spectral properties,  $\lambda_{\max}$  (C<sub>6</sub>H<sub>6</sub>) 472 m $\mu$ ,  $\lambda_{\max}$  (CHCl<sub>3</sub>) 472 m $\mu$ ,  $\lambda_{\max}$  (EtOH) 460 m $\mu$ ,  $\lambda_{\max}$  (petrol) 457 m $\mu$ ,  $\nu_{\max}$  (CCl<sub>4</sub>) 3520 and 1665 cm<sup>-1</sup>,  $\tau$  (CDCl<sub>3</sub>)\* 8.96, 8.74, 8.28, 8.06, and 8.02, and a molecular ion† corresponding to C<sub>40</sub>H<sub>54</sub>O<sub>2</sub>.

A pigment in *Adonis annua* has been formulated

as (II, R = d);<sup>8</sup> this structure has now been confirmed by mixed chromatograms¶ of the derived diosphenol with 3-oxoechinenone.



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<sup>4</sup> D. F. Cheesman, P. F. Zagalsky, and H. J. Ceccaldi, *Proc. Roy. Soc.*, 1966, **B**, **164**, 130.

<sup>5</sup> J. B. Davis and B. C. L. Weedon, *Proc. Chem. Soc.*, 1960, 182.

<sup>6</sup> Cf., B. C. L. Weedon in "Chemistry and Biochemistry of Plant Pigments", ed. T. W. Goodwin, Academic Press, London, 1965.

<sup>7</sup> Cf., M. Akhtar and B. C. L. Weedon, *J. Chem. Soc.*, 1959, 4058.

<sup>8</sup> K. Egger, *Phytochemistry*, 1965, **4**, 609.