Total Synthesis of Astaxanthin and Hydroxyechinenone

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ASTAXANTHIN (I, R = *d*) occurs in *Crustacea* and other animals;[1,2] together with its esters, it constitutes the principal prosthetic group of the carotenoproteins.[1,3,4] Attempts to isolate astaxanthin frequently yield the corresponding diosphenol, astacene (I, R = *b*).[1] The latter may readily be obtained by autoxidation of canthaxanthin (I, R = *a*),[5,6] for which a number of syntheses have been developed.[7] 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 λ_{max} (CS_2) 503 mμ, λ_{max} ($CHCl_3$) 485 mμ, λ_{max} (MeOH) 472 mμ, ν_{max} ($CHCl_3$) 3520 and 1660 cm.$^{-1}$, τ ($CDCl_3$)* 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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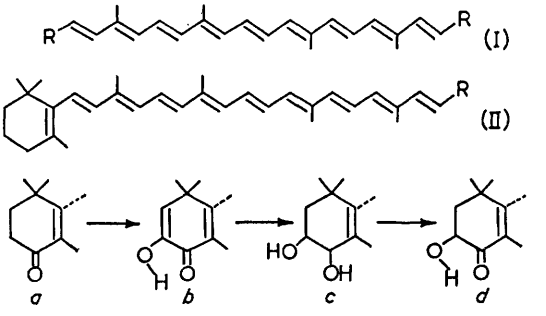
appropriate apoprotein from the lobster carapace to give the characteristic blue colour, λ_{max} (phosphate buffer, pH 7) 630 mμ, of α-crustacyanin.[4]

Autoxidation of echinenone (II, R = *a*) gave 3-oxoechinenone (II, R = *b*).[6] 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, λ_{max} (C_6H_6) 472 mμ, λ_{max} ($CHCl_3$) 472 mμ, λ_{max} (EtOH) 460 mμ, λ_{max} (petrol) 457 mμ, ν_{max} (CCl_4) 3520 and 1665 cm^{-1}, τ ($CDCl_3$)* 8·96, 8·74, 8·28, 8·06, and 8·02, and a molecular ion† corresponding to $C_{40}H_{54}O_2$.

A pigment in *Adonis annua* has been formulated as (II, R = *d*);[8] this structure has now been confirmed by mixed chromatograms¶ of the derived diosphenol with 3-oxoechinenone.



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