Electrochemical Reductive Acylation of the Carotenoid Canthaxanthin

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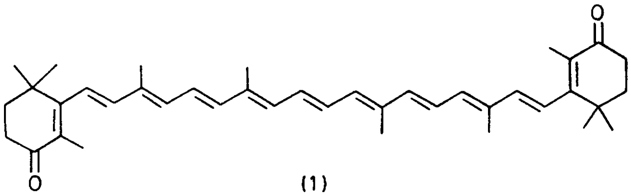
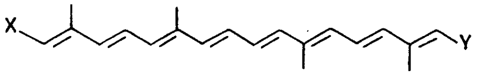
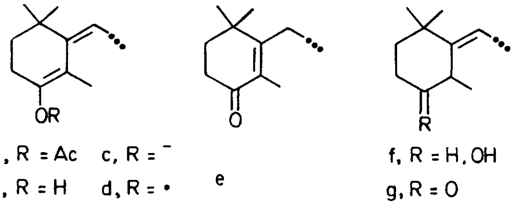
Summary The *in situ* acylation of nucleophiles generated cathodically from canthaxanthin (**1**) provides a novel and convenient route to the retro-diacetate (**2**) and the corresponding retro-monoacetate (**3**); these are hydrolysed to respectively, 5,5′-dihydrocanthaxanthin (**8**) and 7,7′-dihydrocanthaxanthin (**4**).

The smooth and convenient acylation and alkylation of electrogenerated radical-anions and dianions have recently been described for several model compounds.[1] In particular, *O*-acetylation follows cathodic reduction of benzophenone in the presence of acetic anhydride.[2] Polyene carbonyl compounds show electrochemical behaviour similar to that of structurally simpler aromatic ketones and aldehydes; *e.g.* α- and β-ionones and retinal form pinacols cathodically at readily accessible potentials.[3] The electrochemical method offers therefore considerable scope for effecting transformations in polyene and carotenoid chemistry. The electrochemical reactions reported herein for the reductive acylation of canthaxanthin (**1**) encourage this view.



(1)





(**2**) X = Y = a
(**3**) X = a, Y = b
(**4**) X = Y = e
(**5**) X = Y = c
(**6**) X = a, Y = d
(**7**) X = Y = f
(**8**) X = Y = g

Cyclic voltammetry of canthaxanthin [Hg drop, CH_2Cl_2, Bu_4NBF_4 (0·1M), 80—200 mV s^{-1}] showed reversible reduction with E_p — 1·13 V (*vs.* standard calomel electrode). Similar behaviour was found for CH_2Cl_2–MeCN solution (1 : 3) with E_p — 1·08 V (*vs.* Ag wire), and —1·52 V from the ferricinium reduction peak. Addition of small amounts of acetic, benzoic, trimethylacetic, and trifluoroacetic anhydrides caused reduction of (**1**) to become irreversible but with no change in peak current.

In the controlled potential electrolysis at mercury [CH_2Cl_2–Bu_4NBF_4 (0·1M), —1·15 V (*vs.* Ag wire)] of canthaxanthin (2 × 10^{-2} mol l^{-1}) in the presence of an excess of acetic anhydride the current dropped to the background value after the passage of 1·8 F mol^{-1}. T.l.c. analysis showed a major product which proved to be the retro-diacetate (**2**). Traces of the retro-monoacetate (**3**) and 7,7′-dihydrocanthaxanthin (**4**) were also present. Treatment of (**3**) with aqueous methanol gave (**4**).

The formation of (**2**) and the consumption of 1·8 F mol^{-1} suggests either an ECE reaction or that the retro-dianion (**5**) is an intermediate. The ECE route would require a doubling of peak current upon addition of the anhydrides in the cyclic voltammetric experiments. The coulometry was also studied at low concentration (*ca.* 4 × 10^{-4} mol l^{-1}) by comparing cyclic voltammetric peak currents for a series of concentrations of (**1**) with those for known concentrations of ferrocene. From these experiments n = 1·06 suggesting a different route at low concentration of starting material. Controlled potential reduction in the presence of acetic anhydride with relatively low concentrations of canthaxanthin (10^{-3} mol l^{-1}) gave (**4**) as the major isolated product after consumption of 1·4 F mol^{-1}. The reaction was monitored by t.l.c. analysis which showed that (**3**) is the first-formed product which is converted into (**4**) during isolation.

The voltammetric and coulometric results together with the nature of the products and their dependence on concentration of (**1**) are well rationalised by the mechanism depicted in the Scheme. It is suggested that at the higher concentrations a key step is disproportionation to the highly stabilised retro-dianion (**5**). At low concentration hydrogen abstraction from the solvent by the oxygen radical (**6**) leads to monoacetate formation (**3**).

$$\begin{tikzcd}
2\,(\mathbf{1}) \arrow[r, shift left, "2e"] & 2\,(\mathbf{1})\cdot \arrow[l, shift left] \arrow[r, shift left, "\text{slow}"] \arrow[d, "2Ac_2O"] & (\mathbf{1}) + (\mathbf{5})^{2-} \arrow[l, shift left] \arrow[d, "2Ac_2O"] \\
 & 2\,(\mathbf{6})\cdot \arrow[d] & (\mathbf{2}),\ 2\ \text{F mol}^{-1} \\
 & 2\,(\mathbf{3}),\ 1\ \text{F mol}^{-1} &
\end{tikzcd}$$

Scheme

The retro-diacetate (**2**) is surprisingly unreactive; treatment of (**2**) at room temperature for two days with $LiAlH_4$ in ether gave partial cleavage to 5,5′-dihydroisozeaxanthin (**7**). To introduce more labile acyl groups cathodic reduction of canthaxanthin was effected in the presence of trifluoroacetic anhydride (TFAA). In cyclic voltammetry TFAA quenched, without increasing peak currents, the reversibility of the canthaxanthin reduction. Following controlled potential reduction in the presence of TFAA 5,5′-dihydrocanthaxanthin (**8**) was isolated as the only significant product. The most convenient route to (**8**) was by controlled potential reduction of (**1**) in 1 : 1 MeCN–CH_2Cl_2 solution with acetic anhydride present and using $LiClO_4$

(0·2M) as electrolyte. In these conditions 2 F mol^{-1} were consumed and, following removal of electrolyte with water, (**8**) was isolated in 92% yield. Treatment of (**8**) in ethanol, with a trace of potassium hydroxide led to rapid and complete conversion into (**4**) (as shown by u.v. spectroscopy). Satisfactory spectroscopic data were obtained for all new compounds.

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