Electrochemical Reductive Acylation of Astacene; a Route to the Carotenoid Astaxanthin

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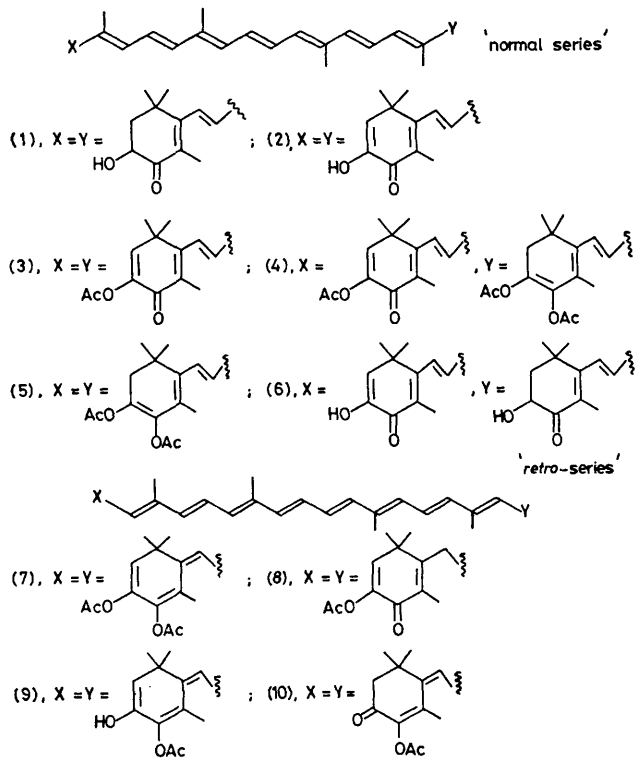
Summary Controlled potential electrolysis of astacene (**2**) gives, in the presence of acetic anhydride, either 2e or 4e reduction depending upon the potential and the solvent-supporting electrolyte system, a new *retro*-tetra-acetate (**7**) resulting from 2e reduction; by 4e reduction, astaxanthin tetra-acetate (**5**) is obtained which may be hydrolysed to astaxanthin (**1**).

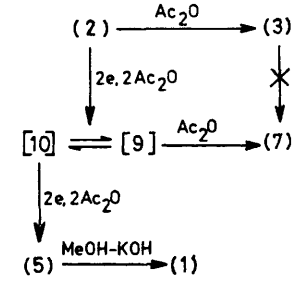
METHODS for the synthesis of the important carotenoid astaxanthin (**1**) are scarce.[1] We report on an electrochemical study of the reduction of astacene (**2**) because, in principle, a 4 F mol^{-1} hydrogenation of this readily available pigment is a route to astaxanthin.

According to single sweep cyclic voltammetry [Hg cathode, Bu_4NBF_4 (0·1M) in CH_2Cl_2] astacene shows complex quasi-reversible behaviour with a reduction peak at −1·12 V (*vs.* S.C.E.). On the reverse scan oxidation peaks at −1·05, −0·90, and −0·72 V are observed. Addition of acetic anhydride quenches reversibility and reduction peaks are seen at −1·00, −1·24, and −1·50 V.

Controlled potential electrolysis to 2 F mol^{-1} of astacene (*ca.* 2×10^{-3} mol l^{-1}) in a divided cell at a mercury cathode [−0·95 V (*vs.* Ag wire), CH_2Cl_2–Bu_4NBF_4 (0·1M)], in the presence of acetic anhydride, gave the *retro*-tetra-acetate (**7**). Hydrolysis of this product in mildly alkaline conditions gave back astacene, probably *via* 5,5′-, 5,7′-, and 7,7′-dihydroastacene and air oxidation during work-up. Traces of the dihydro-compounds were detected. In similar reductions[2] of canthaxanthin important differences in product distribution were found for reduction using $LiClO_4$ as supporting electrolyte *vis à vis* Bu_4NBF_4. With astacene rapid chemical acylation to astacene diacetate (**3**) occurs in CH_2Cl_2–MeCN (3 : 1) containing $LiClO_4$ (0·1M) and acetic anhydride; Bu_4NBF_4 does not induce chemical acylation. Controlled potential reduction of astacene diacetate [CH_2Cl_2–MeCN–$LiClO_4$ (0·1M)] gave unstable products which re-oxidised on work-up to give back starting material. In other conditions [−0·95 V (*vs.* Ag wire), CH_2Cl_2–Bu_4NBF_4 (0·1M), Ac_2O] similar electrolysis gave as the major product the unstable 7,7′-dihydroastacene diacetate (**8**).



In an attempt to force reduction to the 4 F mol^{-1} level, and in view of the more cathodic peaks seen in voltammetry, reduction was carried out at −1·5 V (*vs.* Ag wire) in each of the solvent–electrolyte systems. In CH_2Cl_2–Bu_4NBF_4, 4 F mol^{-1} were passed but a complex mixture of unstable products was obtained. In CH_2Cl_2–MeCN–$LiClO_4$, passage of 4 F mol^{-1} gave the three products, (**3**), (**4**), and (**5**). Astacene diacetate (**3**) is presumably formed chemically and (**4**) may be considered as acylated chemically at one end group and cathodically at the other. The third product, astaxanthin tetra-acetate (**5**), could be isolated in 25% yield and is at the oxidation level of astaxanthin. Using a two-fold excess of acetic anhydride, work-up in slightly acidic conditions, and with precautions against air-oxidation, astaxanthin tetra-acetate, according to t.l.c., becomes the major product. The product mixture from such an electrolysis was, without separation of the components, treated with methanol and a trace of potassium hydroxide. When hydrolysis was judged to be complete (t.l.c.) acidic work-up gave astaxanthin (**1**; 10% based on astacene), astacene (**2**; 25%) and 2,3-didehydroastaxanthin (**6**; 40%). The latter compound has been reported to occur in nature.[3] With larger excess of acetic anhydride astacene diacetate is formed predominantly; in view of experiments outlined above it is unlikely that reduction proceeds *via* astacene diacetate. A working mechanistic hypothesis is embodied in the Scheme, details of which, together with further



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evidence, will be elaborated in a full paper. Satisfactory spectroscopic data were obtained for the compounds (**1**)—(**7**); the presence of (**8**) is inferred from the u.v. absorption characteristic for the chromophore.

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