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1987Selective Allylic Electro-oxidation of α - and β -Ionones

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Allylic ring substitution of α - and β -ionones by, respectively, anodically generated cobalt(III) acetate and bromine, is selective and efficient; in contrast direct anodic oxidation is unselective but provides a route to the novel, rearranged, carotenoid end group (7).

The ring substitution of α - and β -ionones is important for their use in carotenoid synthesis. Many important carotenoids are oxygenated at the 3- and 4-positions¹ and the ionones are often used as end group synthons. Previously used methods for the introduction of 3- and 4-substituents include allylic bromination² and chromate oxidations.³ By analogy with simpler alkenes, the ionones should be reactive toward anodic substitution; such electrochemical reactions have been much studied⁴ and key intermediates are usually allylic cations formed by an electron transfer–deprotonation–electron transfer sequence (*ECE* reaction). However, competing reactions are addition and coupling. The cathodic reactions of the ionones⁵ proved to be surprisingly selective because of the steric constraints imposed by the methyl group substitution; this encouraged the hope that the anodic chemistry might similarly be clean.

In this context we herein report on voltammetric experiments which indicate the relative ease of oxidation of the ionones and on preparative-scale experiments involving both direct and indirect anodic oxidation.

β -Ionone (1) is oxidised at accessible potentials; cyclic voltammetry at a platinum microelectrode [MeCN–Bu₄NClO₄ (0.1 M), 0.235 V s⁻¹] indicated two irreversible peaks at E_p 1.34 and 2.00 V (*vs.* Ag/Ag⁺). By contrast α -ionone (2) is difficult to oxidise and the first oxidation peak is merged with the solvent oxidation limit at >2.00 V.

β -Ionone was conveniently oxidised on a preparative scale in acetic acid solution in the presence of sodium acetate. The results of direct anodic oxidation at controlled potential and at constant current were similar and are summarised in Table 1. The major products were the 4-acetoxy- β -ionone (3), corresponding to substitution, and the diol derivative (4), which arises from addition. The relative yields of the substitution and addition products were essentially independent of reaction conditions. It is mechanistically significant that only the *cis*-isomer of the addition product (4) is formed (see below). It is also noteworthy that in the presence of water (Table 1, entry 3) there is no significant formation of 4-hydroxy- β -ionone or of the 5,6-dihydroxylated product.

Efficient substitution is best achieved by indirect anodic oxidation. For β -ionone this involves *in situ* generation of

bromine in acetic acid–sodium acetate medium (Table 1, entries 5 and 6). In contrast to the direct method the product distribution is very sensitive to electrolyte composition; in the presence of water (entry 6) the total yield of 4-substituted- β -ionone is 81% with a 100% current efficiency (based on an assumption of 2 F mol⁻¹ for complete conversion).

In an attempt to effect direct anodic hydroxylation of β -ionone, electrolyses were conducted in largely aqueous electrolytes with non-nucleophilic co-solvents: *i.e.* acetone–H₂O (2.75:1 v/v), containing H₂SO₄ (*ca.* 0.04 M), and tetrahydrofuran (THF)–H₂O (2.50:1 v/v) containing LiClO₄ (*ca.* 0.3 M) with solid CaCO₃ to maintain neutrality. Anodic oxidation was performed at constant current in a divided cell and at a Pt mesh anode (aqueous acetone: 0.13 A cm⁻², 3 F mol⁻¹; aqueous THF: 0.075 A cm⁻², 4 F mol⁻¹). In each case the products were the compounds (5)–(8) and the distribution was similar for both acidic and neutral conditions. Yields (%) for the acetone–H₂O and THF–H₂O conditions are: respectively: (5), 20, 32; (6), 28, 19; (7), 26, 24; (8), 15, 11.

Table 1. Anodic oxidation of β -ionone (1).

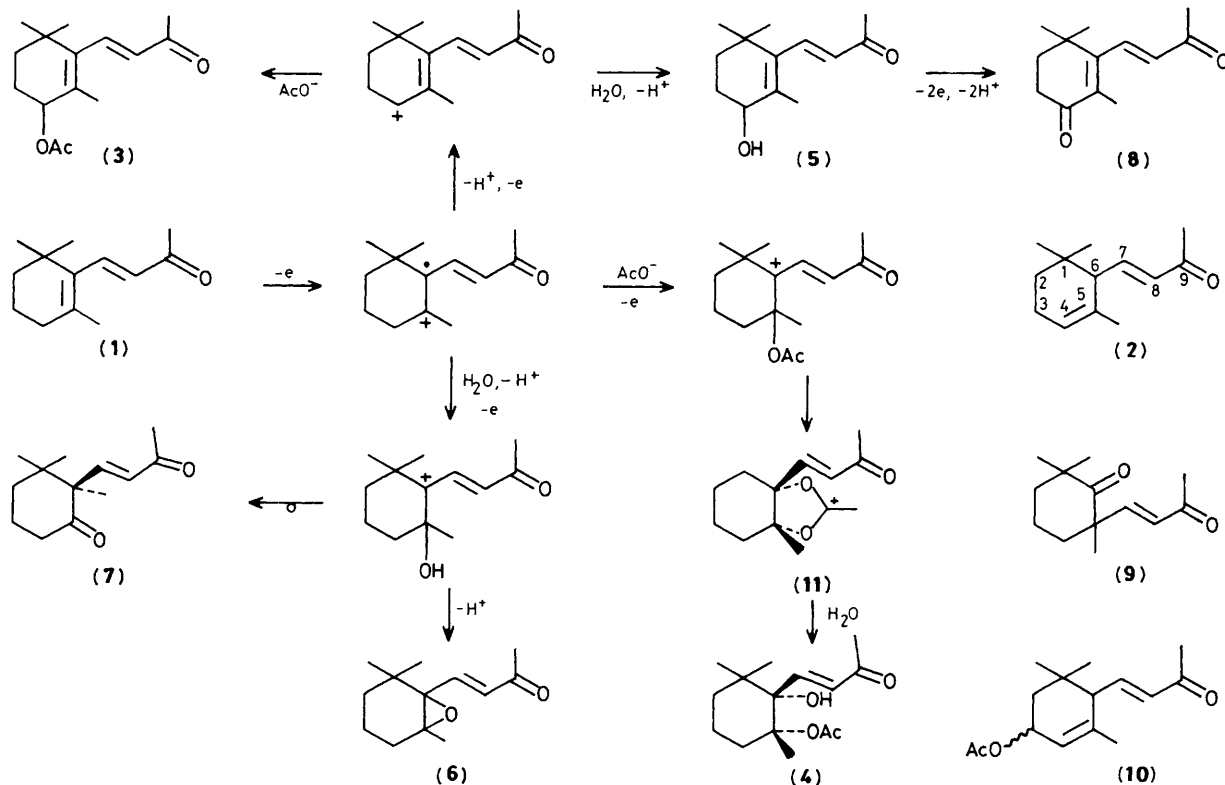
Entry	Electrolysis conditions ⁱ	% Yield ^b	
		(3)	(4)
1 ^a	2.7 [1.7 V (<i>vs.</i> Ag/Ag ⁺)]	38	31
2 ^c	3.0; <i>ca.</i> 0.025	39	28
3 ^d	3.0; <i>ca.</i> 0.11	38	33
4 ^{e,f}	8.0; <i>ca.</i> 0.083	34	30
5 ^g	2.5; <i>ca.</i> 0.013	77	—
6 ^h	1.6; <i>ca.</i> 0.025	24 ⁱ	—

^a Undivided cell; Pt mesh anode (*ca.* 12 cm² nominal area), carbon cathode; electrolyte, HOAc–NaOAc (0.55 M)–LiClO₄ (0.09 M).

^b Isolated product; yields with respect to consumed starting material.

^c HOAc–NaOAc (0.52 M). ^d HOAc–NaOAc (0.52 M)–H₂O (4 M).

^e MeCN–HOAc (*ca.* 1 M)–Bu₃N (*ca.* 1 M). ^f Substrate, the ethylene acetal of (1). ^g HOAc–NaOAc (0.6 M)–LiBr (0.3 M). ^h HOAc–NaOAc (0.5 M)–LiBr (0.5 M)–H₂O (1.5 M). ⁱ Electricity passed/F mol⁻¹; current density/A cm⁻². ^j +57% of (5).



Scheme 1

The modest yields offer no preparative advantage for compounds (5), (6), and (8). However, compound (7) is a novel carotenoid end group which is not likely to be readily accessible by other routes; for instance, acid-catalysed ring opening of the epoxide (6), followed by rearrangement gives only the alternative isomer (9), and that in low yield.⁶

α -Ionone is oxidised with difficulty and attempted direct electrolysis (constant current, HOAc–NaOAc) gave after 10 F mol⁻¹ very low conversion, the only significant products being traces of the *cis*- and *trans*-isomers of (10). Indirect oxidation was achieved by *in situ* anodic oxidation of cobalt(II) acetate in acetic acid solution.⁷ In a typical experiment α -ionone (0.01 mol), Co(OAc)₂·4H₂O (0.017 mol), acetic acid (100 cm³), and KOAc (0.017 mol) were oxidised at 0.025 A cm⁻² in an undivided cell at a Pt mesh anode. The cell temperature was kept at 60 °C and 6.5 F mol⁻¹ was passed, with respect to the α -ionone. Only one product was detected (t.l.c.) which was isolated in 67% yield and identified as the isomers of 3-acetoxy- α -ionone (10).

For both α - and β -ionones the indirect methods of anodic oxidation are clearly superior, giving selective and efficient substitution. The practical convenience of the method makes it an attractive alternative to existing routes to 3- and 4-oxygenated carotenoid end groups [cf. compounds (3), (5), and (10)].

The direct oxidations involve interesting conversions and the preparation of the rearranged product (7) is possibly important. The results of the preparative experiments are plausibly accommodated in the mechanism in Scheme 1.

There is good precedent in carbohydrate chemistry⁸ for intermediates of the type (11). The involvement of (11) is required for an explanation of the stereoselective formation of (4) as the *cis*-isomer only.

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