

Electro-organic Reactions. Part V.† Cathodic Pinacolisation of α - and β -Ionones

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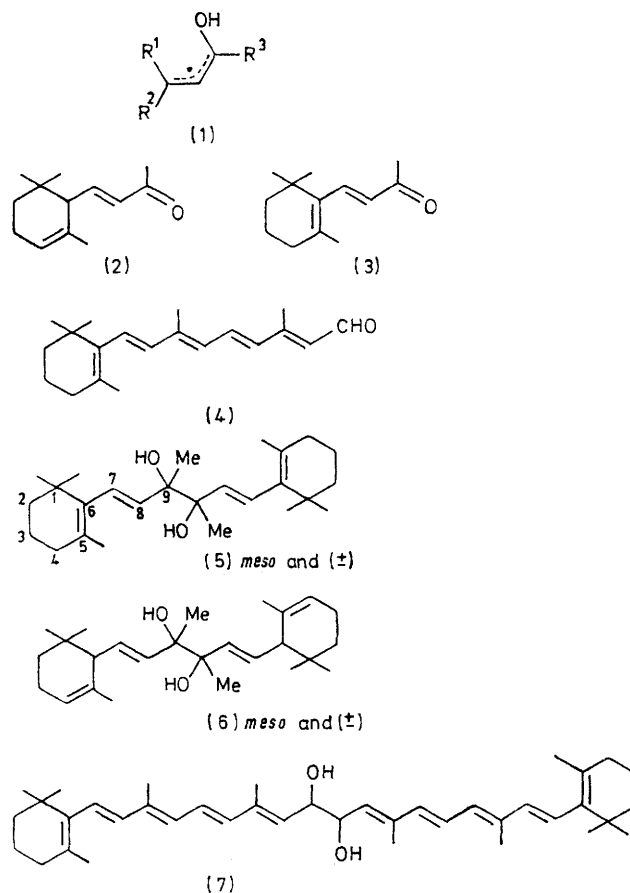
Controlled potential electrolysis at a mercury cathode of α - and β -ionone gives, in aqueous dimethylformamide, the corresponding pinacols in ca. 50% chemical yield. By electrolysis in acetonitrile with acetic acid as proton donor β -ionone is converted smoothly into the pinacol (70% isolated yield), and retinal is pinacolised in ca. 10% yield.

$\alpha\beta$ -UNSATURATED carbonyl compounds may be coupled cathodically, but the major product usually involves combination at the β -carbon atoms to give a hydro-dimer.¹ Coupling at the carbonyl carbon atoms is relatively inefficient; for instance reductive coupling of methyl vinyl ketone at a mercury cathode gives a low (10%) yield of α -glycol, whereas an 80% yield is obtained by reduction with magnesium amalgam.² Detailed polarographic investigation of the mechanism of electro-reduction of $\alpha\beta$ -unsaturated carbonyl compounds suggests that in both protic³ and, with added proton donor, aprotic⁴ solvents the coupling reaction involves neutral radicals such as (1). Examples of unsaturated carbonyl compounds which are hindered at the β -carbon atom, and which therefore undergo at the cathode increased dimerisation at the carbonyl group, are 3-methylcrotonaldehyde⁵ and certain (highly hindered) 3-oxo- Δ^4 -steroids and 3-oxo- $\Delta^{1,4}$ -steroids.⁶

The cathodic reduction of α -ionone (2) and β -ionone (3) should, because of hindrance in the ring and side chain, give some pinacol. Several polarographic studies of the electroreduction of α - and β -ionones have been reported⁷ and the cathodic generation in tetrahydrofuran solution of the relatively stable radical anions of the ionones (2) and (3) has been achieved.⁸ The stability in tetrahydrofuran of these radical anions suggested that rapid coupling at C-5 or C-7 ‡ was indeed sterically precluded because in other systems where charge is well delocalised in the radical anions rapid coupling is observed.⁹ Coupling of radical anions at the carbonyl carbon atoms is discouraged by coulombic repulsion and prior protonation to give neutral radicals [e.g. (1)] is necessary.

For the ionones (2) and (3) no macro-scale electrolyses and product analyses have been reported previously. β -Ionone has been pinacolised chemically¹⁰ but the pinacol of α -ionone was unknown prior to the work herein described. Vitamin A aldehyde (retinal) (4) is reported to undergo pinacolisation chemically¹¹ following

reduction at a mercury-zinc amalgam. This chemical method failed, in our hands, to give a significant yield



of the pinacol. The preparative scale electroreduction of retinal has not been reported previously. Methods of coupling polyene units are of considerable preparative significance and in particular production of C_{40} molecules

† Part IV, L. A. Avaca and J. H. P. Utley, *J.C.S. Perkin I*, 1975, 971.

‡ Carotenoid numbering is used here and in the Table.

¹ 'Organic Electrochemistry,' ed. M. M. Baizer, Dekker, New York, 1973, pp. 399 *et seq.*

² J. Wiemann, M. R. Monot, and J. Gourdan, *Compt. rend.*, 1957, **245**, 172.

³ P. Zuman, D. Barnes, and A. Ryslova-Kejharova, *Discuss. Faraday Soc.*, 1968, **45**, 202.

⁴ J. Simonet, *Bull. Soc. chim. France*, 1970, 1533.

⁵ D. Miller, L. Mandell, and R. A. Day, *J. Org. Chem.*, 1971, **36**, 1683.

⁶ H. Lund, *Acta Chem. Scand.*, 1957, **11**, 283.

⁷ K. Schwabe and H. Berg, *Z. Elektrochem.*, 1952, **56**, 961; M. Cernoch, J. Dokoupil, and B. Chutny, *Chem. listy*, 1953, **47**, 269; H. Sato, *Bull. Nat. Hyg. Laboratory, Tokyo*, 1959, **77**, 51; V. G. Mairanovski, *Med. Promysl. S.S.S.R.*, 1964, **18**, 37.

⁸ J. Harbour and A. V. Guzzo, *Mol. Phys.*, 1971, **20**, 565.

⁹ E. Lamy, L. Nadjo, and J. M. Savéant, *J. Electroanal. Chem. Interfacial Electrochem.*, 1973, **42**, 223; V. J. Puglisi and A. J. Bard, *J. Electrochem. Soc.*, 1973, **120**, 748.

¹⁰ V. Teterim and A. Ivanov, *Compt. rend. Acad. Sci. S.S.S.R.*, 1935, **2**, 259.

¹¹ Eastman Kodak Co., B.P. 1,097,497/1968.

from C₂₀ units provides a route to carotenoids. For instance a recently reported synthesis of β -carotene by reduction of retinal is believed to involve a pinacol intermediate.¹²

RESULTS AND DISCUSSION

Voltammetry.—Cyclic voltammetry of β -ionone [Hg drop; ca. 30 mm; dimethylformamide containing tetra-n-butylammonium iodide (0.1M)] gave, at 0.1 V s⁻¹, a quasi-reversible reduction-oxidation couple (R₁-O₁) at peak potentials of -1.48 V (*vs.* Ag/AgI) (R₁) and -1.25 V (O₁). A second, and irreversible reduction peak (R₂) occurred at -2.19 V. It is not certain whether R₂ is associated with further reduction of the species produced at R₁, or whether it represents reduction of a product formed at R₁. The uncertainty arises from the relatively low peak current at R₂: $i_p(R_2)/i_p(R_1) = 0.6$. The species formed at R₁ undergoes slow chemical reaction; with a platinum micro-electrode, repeated scan cyclic voltammetry (at 0.03 V s⁻¹) shows diminution of the couple at R₁-O₁ and growth of an oxidation peak (O₃) at -0.05 V.

The experiments were repeated with α -ionone and the results were similar except for the absence of a second reduction peak. The corresponding peak potentials

was isolated in 56% yield by t.l.c. It exhibited the expected u.v. and i.r. absorption properties (see Table). Its n.m.r. spectrum (Table), in addition to the bands expected for the ring methyl groups and the protons of the carbon-carbon double bonds, exhibited a strong singlet at δ 1.29 attributable to the two methyl groups on the α -glycol system. The mass spectrum included the expected molecular ion [m/e 386.318 (C₂₈H₄₂O₂)], a fragment ion at m/e 368 corresponding to the loss of water, and a strong line at m/e 193 corresponding to symmetrical fission of the glycol. Further proof of structure was obtained by periodate fission of the product to β -ionone. Electrolysis at -1.55 V in acetonitrile-tetra-n-butylammonium acetate (Bu₄NOAc, HOAc 0.1M) gave much cleaner conversion into the pinacol which was isolated (by t.l.c.) in 71% yield.

Subsequent t.l.c. analysis of the pinacol suggested the presence of two isomers in the ratio ca. 2 : 1 (see Experimental section). These are presumably the *meso*- and (\pm)-forms; much effort has been devoted to elucidating factors which control the *meso* : (\pm) ratio in pinacols formed from structurally simple aldehydes and ketones and these factors are quite well understood.¹³ The β -ionone system might prove to be a useful substrate for the routine extension of such studies but because of

Characterisation of pinacols ^a (4) and (5)

	¹ H N.m.r. [δ (CCl ₄) 100 MHz]						$\lambda_{\max.}$ (cyclohexane)/ nm (ϵ)
	1-Me	5-Me	9-Me	9-OH	7-H	8-H	
β, β -Pinacol (5)	1.00 (6 H, s)	1.64 (3 H, s)	1.29 (3 H, s)	2.18 (1 H, s)	6.10 (1 H, d, J 16 Hz) 6.10 (J 16 Hz)	5.45 (1 H, d, J 16 Hz) 5.41 (J 16 Hz)	233 (19 000)
β -Ionol ^b	0.98	1.64	1.24				
α, α -Pinacol (6)	0.84 (3 H, s) 0.90 (3 H, s)	1.56 (3 H, s)	1.21 (3 H, s)	2.81 (1 H, s)		5.46 (2 H, m)	210 (end absorption)
α -Ionol ^c	0.80 (s) } (3 H) 0.82 (s) } 0.89 (3 H, s)	1.56 (3 H, s)	1.20 (3 H, d, J 6 Hz)			5.38 (2 H, m)	

^a Major features of n.m.r. spectra; for both (5) and (6) i.r. spectra (CCl₄) showed ν_{OH} 3 600 cm⁻¹. ^b V. Ramamurthy, G. Tustin, C. C. Yau, and R. S. H. Liu, *Tetrahedron*, 1975, **31**, 193 (in CDCl₃). ^c Mixture of diastereoisomers, in CCl₄.

were R₁ -1.65 V, O₁ -1.50 V, O₃ -0.07 V. Cyclic voltammetry of retinal (4) [Hg drop; acetonitrile containing tetra-n-butylammonium iodide (0.1M)] gave, at 0.1 V s⁻¹, quasi-reversible reduction at R₁ -0.93 V (*vs.* Ag-AgI) and O₁ -0.72 V.

Preparative-scale Electrolyses.—The potentials for macro-scale electrolysis were chosen on the basis of the voltammetric experiments. Both α - and β -ionone were electrolysed at controlled potential (-1.50 V, *vs.* Ag-AgI) at a mercury pool cathode with tetra-n-butylammonium iodide (0.55M) in dimethylformamide, aqueous dimethylformamide (20% v/v H₂O), and methanolic dimethylformamide (20% v/v MeOH), and with tetra-n-butylammonium acetate (Bu₄NOAc, HOAc 0.1M) in acetonitrile. The best yield of pinacol was obtained by using the latter solvent system. For β -ionone in 20% aqueous dimethylformamide passage of 1.3 F mol⁻¹ led to a mixture of products from which the pinacol (5)

the overall synthetic purpose of the present work the stereochemical aspect has not been pursued.

Similar controlled-potential electrolysis of α -ionone gave the corresponding pinacol (6) in 46% yield. Accurate mass measurement on the molecular ion (m/e 386.318) confirmed the molecular formula. Spectroscopic evidence for structure (6) is given in the Table.

Retinal was electrolysed at -1.00 V in acetonitrile-tetra-n-butylammonium acetate (Bu₄NOAc, HOAc 0.1M). The pinacol (7), isolated by t.l.c. in 11% yield, exhibited $\lambda_{\max.}$ (ethanol) 324 nm (lit.,¹¹ 325 nm). The mass spectrum gave a molecular ion corresponding to retinal pinacol (m/e 570), and fragment ions at m/e 552 (loss of water) and 285 (symmetrical fission of the pinacol).

EXPERIMENTAL

Materials and Solvents.—The ionones were manufactured products as supplied by International Flavors and Fra-

¹² J. E. McMurray and M. P. Fleming, *J. Amer. Chem. Soc.*, 1974, **96**, 4708.

¹³ J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 1968, **33**, 2145; A. Bewick and H. P. Cleghorn, *J.C.S. Perkin II*, 1973, 1410.

grances. Retinal was supplied by Roche Products Ltd. (Welwyn). Dimethylformamide (B.D.H., as supplied for spectroscopy), tetra-*n*-butylammonium iodide (B.D.H.), and acetonitrile (Hopkins and Williams) were also used without further purification. Tetra-*n*-butylammonium acetate ($\text{Bu}_4\text{NOAc,HOAc}$) was prepared by a standard method.¹⁴

Apparatus.—Conventional H cells, with sintered glass separators, were used. For cyclic voltammetry the cells were equipped with a hanging mercury drop cathode or a platinum bead. Electrode potentials were measured or controlled against reference electrodes composed of a silver wire immersed in a 0.1M-solution of tetra-*n*-butylammonium iodide in dimethylformamide. Preparative-scale electrolyses were carried out at mercury pool cathodes, and a Chemical Electronics Ltd. TR2A potentiostat was used with an electronic current integrator. For voltammetry the potentiostat was combined with a type RB1 waveform generator and a Hewlett-Packard 1035B X-Y recorder.

Preparative Scale Electrolyses.—**Cathodic reduction of β -ionone.** (i) *Aqueous dimethylformamide.* β -Ionone (3.4 g, 0.018 mol) was added to aqueous dimethylformamide (20% v/v H_2O) with tetra-*n*-butylammonium iodide (0.55M) in the cathode compartment of an H cell (catholyte volume ca. 50 ml) and electrolysed at a mercury pool at -1.5 V (*vs.* Ag-AgI). A carbon rod anode was used. The initial current density was ca. 0.015 A cm^{-2} , which fell after the passage of 1.3 F mol^{-1} to ca. 0.001 A cm^{-2} . The catholyte was diluted with water and the crude product extracted into benzene. The extract was washed (H_2O) and dried (MgSO_4). After concentration the mixture was subjected to preparative scale t.l.c. (40×40 cm plate; silica gel) and elution with light petroleum (85%; b.p. $60-80^\circ$)-acetone (15%). Six bands were obtained and the pinacol (5) (R_F 0.40) was isolated as an oil. The yield was 64% of the organic material collected from the plate and 56% based on the amount of β -ionone subjected to electrolysis.

(ii) *Acetonitrile-tetra-*n*-butylammonium acetate.* β -Ionone (0.95 g, 0.005 mol) in acetonitrile-tetra-*n*-butylammonium acetate ($\text{Bu}_4\text{NOAc,HOAc}$) (0.1M) was similarly reduced (-1.55 V) to yield a crude product (0.87 g, 91%) from which the pure pinacol was obtained [t.l.c.; elution with light petroleum (80%)-acetone (20%)] giving an overall isolated yield of 71%.

Further t.l.c. analysis of the pinacol so obtained (20×20 cm plate; silica gel) allowed partial separation after

elution with light petroleum (80%; b.p. $60-80^\circ$)-acetone (20%) of two components with similar R_F values and closely similar i.r. spectra. The amount of the component of slightly lower R_F value was, by weight, about twice that of the second component.

Cathodic reduction of α -ionone. α -Ionone (3.36 g, 0.017 mol) was electrolysed in aqueous dimethylformamide as described above at -1.5 V (*vs.* Ag-AgI), the initial current density being 0.008 A cm^{-2} . Similar work-up gave a crude product from which the pinacol (6) was isolated as an oil by t.l.c. (conditions as above; R_F 0.45). The pinacol (6) constituted, by weight, 57% of the organic material collected from the plate and the yield was 46% based on the amount of starting material.

Cathodic reduction of retinal. Retinal (1.1 g, 0.004 mol) was added to acetonitrile with tetra-*n*-butylammonium acetate ($\text{Bu}_4\text{NOAc,HOAc}$) (0.1M) in the cathode compartment of an H cell (catholyte volume ca. 25 ml) and electrolysed at -1.0 V. The initial current density was ca. 0.009 A cm^{-2} , which fell after the passage of 0.73 F mol^{-1} to ca. 0.0005 A cm^{-2} . The catholyte was diluted with water and extracted into ether. The ether layer was washed with water ($\times 4$), dried (Na_2SO_4), and evaporated. The mixture was purified by preparative scale t.l.c. on silica gel [light petroleum ether (80%)-acetone (20%)]. The product (7) was isolated as a yellow oil in 11% yield.

Fission of the Pinacol (5) by Periodate.—The pinacol (5) (0.58 g) was treated with potassium periodate (1 g) in aqueous ethanol (30 ml; 30% v/v H_2O) containing concentrated sulphuric acid (1 ml). After 20 min at room temperature more periodate (1 g) was added and the mixture was left for a further 2 h and then kept at 90°C for 20 min. The mixture was cooled and diluted with water and the crude product (0.48 g) extracted with benzene. The major product was a ketone (ν_{CO} 1680 cm^{-1}) which did not separate from β -ionone on t.l.c. [silica gel; light petroleum (85%; b.p. $60-80^\circ$)-acetone (15%)].

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¹⁴ H. O. House, E. Feng, and N. P. Peet, *J. Org. Chem.*, 1971, **36**, 2371.