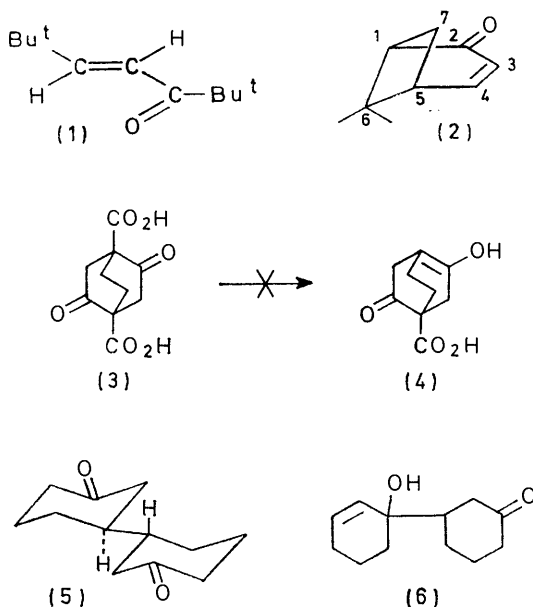


Electrochemical Reactions. Part XI.¹ Reduction of Apoverbenone (6,6-Dimethylnorpin-3-en-2-one)

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In a cyclic voltammetric study of apoverbenone in anhydrous dimethylformamide no indication was obtained of reduction to a stable anion radical at temperatures varying from 298 to 196 K. Electrochemical reduction in aqueous dimethylformamide afforded two diketonic dimers and a small amount of a triketonic trimer. The dimers are stereoisomers formed by the union of two 6,6-dimethyl-4-oxonorpinan-2-yl radicals, the more abundant dimer being formed by union of radicals from the less hindered side. Reduction in anhydrous dimethylformamide gave an isomeric triketonic trimer.

REDUCTION in dimethylformamide of 2,2,6,6-tetramethylhept-4-en-3-one (1) has been shown² to give a sufficiently long-lived anion radical for its e.s.r. and u.v. characteristics to be recorded. One reason for the stability of this anion radical in the presence of excess of ketone is the absence of enolisable hydrogen atoms in the latter so that the radical is not protonated from this source. Apoverbenone (2) would not be expected to enolise because the formation of its enol violates Bredt's rule; it was therefore expected to form a long-lived anion radical. The observation, in a recent re-examination of Bredt's rule,³ that decarboxylation of the acid (3) does not proceed *via* the enol (4) in a normal Westheimer-type reaction, reinforces the expectation that apoverbenone will not readily enolise.



Cyclic triangular wave voltammetry was used in an attempt to demonstrate the reversible transfer of one electron to apoverbenone to give the anion radical. Various aprotic solvents were used at room temperature and dimethylformamide at temperatures from 298 to

196 K. Reduction occurred in one step. The cyclic voltammetric traces at various scan rates (v) showed only one cathodic peak (height i_{pc}) which could be due to reduction to the anion radical but there was no anodic peak on the reverse scan corresponding to oxidation of this anion radical back to apoverbenone. At the greatest sweep rates, the time interval between reduction of apoverbenone and attempted detection of the anion radical by an electrochemical test was 0.6 s. Thus the half-life for this anion radical is less than 0.6 s. The function $i_{pc}/v^{1/2}$ for this cathodic peak was independent of v (Table 2) within experimental error, indicating a diffusion-controlled reduction process.⁴

Electrochemical reduction of cyclohexenone has given the *meso*-diketonic dimer (5) as the major product along with the corresponding (\pm)-diketone and the ketol (6).⁵ Such products are usual from reduction of enones. Reduction of apoverbenone in aqueous dimethylformamide gave two isomeric diketonic dimers A and B and a small amount of a trimer X. Each dimer gave a dioxime and had mass spectral and analytical data consistent with the molecular formula $C_{18}H_{26}O_2$. Their i.r. and n.m.r. spectra (Table 1) are consistent with the presence in each of two 6,6-dimethyl-4-oxonorpinan-4-yl radicals.

TABLE I

Chemical shifts [$\tau(CDCl_3)$] of methyl resonances and their relative intensities

Compound	τ		
6,6-Dimethylnorpinan-2-one	8.66(1)		9.15(1)
Dimer A	8.62(2)		9.14(2)
Dimer B	8.65(2)	9.01(1)	9.19(1)
Trimer Y	8.61(3)	8.96(1)	9.14(2)
Trimer X	8.64(3)	9.03(1)	9.19(2)

We assume that the electrochemical reduction of apoverbenone gives a short-lived anion radical which is protonated in the presence of water to form the radical (7). This may dimerise and revert to the ketonic products or it may first form radical (8). Three stereoisomeric reduction products are possible from apoverbenone [(9)—(11)]. In the 6,6-dimethylnorpinan-2-one

¹ Part X, K. Al-Wair, J. F. Archer, and J. Grimshaw, *J.C.S. Perkin II*, 1972, 1663.

² K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, D. K. Roe, and K. Kronberger, *J. Amer. Chem. Soc.*, 1970, **92**, 2783.

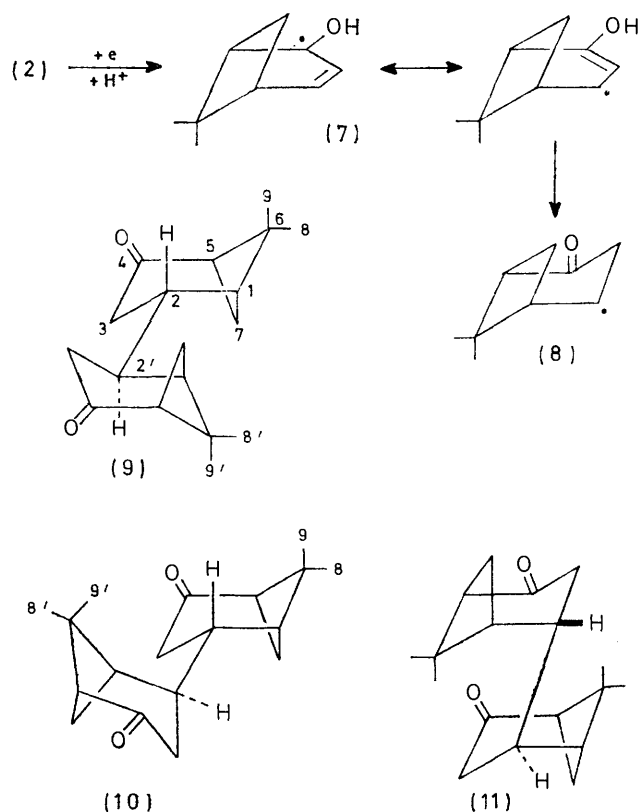
³ G. L. Buchanan, N. B. Kean, and R. Taylor, *J.C.S. Chem. Comm.*, 1972, 201.

⁴ R. S. Nicholson and I. Shain, *Analyt. Chem.*, 1964, **36**, 706.

⁵ E. Touboul, F. Weisbuch, and J. Wiemann, *Compt. rend.*, 1969, **268C**, 1170; T. S. Ivcher, E. N. Zil'berman, and E. M. Perepelchikova, *Trudy Khim. i khim. Technol.*, 1968, 100.

molecule (2) (numbered as shown) the cyclohexane ring formed by carbon atoms 1—6 has been shown to adopt a flattened chair conformation⁶ and the methyl groups are magnetically nonequivalent. Assignment of structures to dimers A and B can be made with reference to previous studies on the ¹H n.m.r. spectra of pinane derivatives.⁷ The signal of the methyl group which faces the cyclobutane ring is downfield and is almost unaffected by substituents, whereas that of the methyl group which faces the cyclohexane ring is upfield and is sensitive to the stereochemistry of the substituents (methyl or acetoxy) at carbon atoms 2, 3, and 4. It is brought relatively downfield by *cis*- in comparison with *trans*-substituents.⁷

Dimer A has two resonances corresponding to the four methyl groups and the chemical shifts are almost identical with those of the methyl groups in 6,6-dimethylnorpinan-2-one. It must have one of the more symmetrical structures [(9) or (11)]. Dimer B, in contrast, shows three resonances due to methyl groups



and must have the unsymmetrical structure (10). In structure (9) the dimer 2,2'-bond is *trans* to the methyl groups 9 and 9' and will therefore have little effect on their chemical shift relative to the corresponding methyl groups of 6,6-dimethylnorpinan-2-one. Dimer A is therefore given structure (9).

⁶ A. J. Abraham, F. H. Bottom, M. A. Cooper, J. R. Salmon, and D. Whittaker, *Org. Magnetic Resonance*, 1969, **1**, 51.

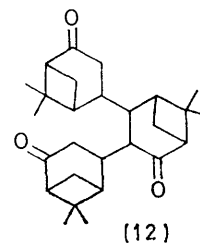
⁷ A. J. Baretta, C. W. Jefford, and B. Waegell, *Bull. Soc. chim. France*, 1970, 3985.

Of the three resonances due to methyl groups in dimer B, the one most downfield is assigned to the groups 8 and 8', facing cyclobutane rings. The remaining two lines are assigned to the methyl groups facing cyclohexane rings. Of these, group 9 is *trans* to the 2,2'-bond and gives rise to the upfield line, and the middle line is assigned to the 9'-group which is *cis* to the 2,2'-bond.

The third possible dimer (11) has not been isolated. It should show two resonances of equal intensity due to four methyl groups. The two methyl groups 9 and 9' are *cis* to the 2,2'-bond, so the line at higher field would be shifted to lower field relative to the spectrum of 6,6-dimethylnorpinan-2-one. Dimer A is formed in greater amount, which is in accord with the steric control of the approach of two radicals (7) or (8), so that dimerisation occurs preferentially on the less hindered side opposite the *gem*-dimethyl system. Formation of dimer (11) would involve approach of both halves from the more hindered sides.

During the reduction of apoverbenone in unbuffered solution the reaction mixture becomes alkaline; the dimerisation of cyclohexenones by alkali in a Michael-type reaction is well known.⁸ A mixture of apoverbenone and nopinone (6,6-dimethylnorpinan-2-one) when treated with alkali under vigorous conditions gave none of dimers A and B. Apoverbenone is slowly decomposed by alkali but the rate of this decomposition is less than the rate of the electrochemical reduction; however the yields of dimers will be affected.

Reduction of apoverbenone in anhydrous dimethylformamide afforded a crystalline trimer Y, C₂₇H₃₈O₃, not identical with the trimer X already obtained. Trimer Y shows no i.r. band due to OH and is assumed to be a triketone. It contains six methyl groups. The trimerisation and further polymerisation of enones during electrochemical reduction in aprotic solvents has been demonstrated by other workers,⁹ who have assumed that reduction first gives a dimer whose enolate ion condenses with the starting material in a Michael-type reaction. Thus we suggest that the trimers are



stereoisomers of structure (12). Attempts to carry out a reversed Michael reaction on trimer Y led to no

⁸ W. A. Ayer, and W. I. Taylor, *J. Chem. Soc.*, 1955, 2227; G. Büchi, J. H. Hansen, D. Knutson, and E. Koller, *J. Amer. Chem. Soc.*, 1958, **80**, 5517; J. E. Engelhart and J. R. McDivitt, *J. Org. Chem.*, 1971, **36**, 752.

⁹ S. Wawzonek and A. Gundersen, *J. Electrochem. Soc.*, 1964, **111**, 324; J. Simonet, *Compt. rend.*, 1966, **263C**, 1546.

crystalline product and resulted in extensive decomposition to an acidic material.

EXPERIMENTAL

All electrode potentials were measured with respect to an aqueous saturated calomel electrode/1.0M-sodium nitrate/salt bridge containing the electrolyte solution. The electrochemical apparatus has been described previously.¹ Nitrogen was deoxygenated with the BTS-catalyst¹⁰ and dried over molecular sieve. Dimethylformamide was dried successively over sodium sulphate and copper sulphate then distilled under nitrogen (b.p. 43° at 12 mmHg).¹¹

(+)-Apoverbenone was prepared as previously described; $[\alpha]_D + 319^\circ$ (*c* 2.4 in CHCl_3).¹²

Polarography.—A solution of apoverbenone ($1.0 \times 10^{-3}\text{M}$) and tetrapropylammonium perchlorate (0.1M) in dimethylformamide showed one polarographic wave, $E_{\frac{1}{2}} - 2.04$ V. A similar solution with dimethylformamide (9.0 ml) and aqueous 10% tetrapropylammonium hydroxide (1.0 ml) had $E_{\frac{1}{2}} - 1.86$ V, but after about 1 h, the height of the wave had decreased by half owing to decomposition of the apoverbenone by alkali.

Cyclic Voltammetry.—The cathode was a platinum sphere (*ca.* 1.5 mm diam.) prepared by melting platinum wire in a hydrogen-oxygen flame, supported in soft glass and coated by dipping into mercury. When necessary the cathode was cleaned in a hydrogen-oxygen flame. The first scan from cyclic triangular wave voltammetry was recorded; scan rate *v*, cathodic peak height i_{pc} , and cathodic peak potential E_{pc} . A solution of apoverbenone ($1.0 \times 10^{-3}\text{M}$) and tetrapropylammonium perchlorate (0.1M) in dimethylformamide showed one cathodic peak and no corresponding anodic peak at any temperature between 196 and 298 K. The results at 298 K are given in Table 2. The same result was obtained in dimethylacetamide, acetonitrile, dimethyl sulphoxide, or hexamethylphosphoric triamide at 298 K. As a test of solvent purity, reversible electron transfer could be demonstrated at scan rates of 0.05 V s^{-1} at 298 K in all these solvents with benzophenone and the formed radical anion and in dimethylformamide and dimethyl sulphoxide (the other solvents were not tried) with pyrene and the formed radical anion.

TABLE 2

Single-scan cyclic triangular wave voltammetry of apoverbenone in anhydrous dimethylformamide

v/Vs^{-1}	$i_{pc}/\mu\text{A}$	$i_{pc}/v^{\frac{1}{2}}$	$-E_{pc}/\text{V}$
0.043	13.4	64	2.10
0.086	18.2	62	2.11
0.172	25.0	60	2.13
0.860	53.0	57	2.16
1.315	73.5	56	2.21

Stability of Apoverbenone.—Solutions of the ketone were stored for some time, then diluted with water, and the ketone was recovered in ether. *p*-Isopropylphenol (t_R 17.5 min) was used as internal standard and the remaining apoverbenone (t_R 8.5 min) was estimated by g.l.c. (F-11 instrument; 1.5% silicone gum rubber, 2 m \times $\frac{1}{8}$ in column). The results showed 92% recovery from aqueous dimethylformamide after 18 h; 21% recovery from di-

methylformamide (22.5 ml) and aqueous 10% tetrapropylammonium hydroxide (2.5 ml) after 18 h.

Reduction of Apoverbenone in Dimethylformamide.—The electrolyte, 0.1M-tetrapropylammonium perchlorate in dimethylformamide, was used as anolyte with a platinum anode. A solution of apoverbenone (0.75 g) in the electrolyte (25 ml) was reduced at the mercury cathode (area 6.2 cm² and initial current 8×10^{-3} A) at -1.8 to -2.1 V for 5–6 h; a sample then showed a negligible concentration of apoverbenone (by cyclic voltammetry). The mixture was diluted with water, acidified with hydrochloric acid, and extracted with ether. The extract was washed with sodium hydrogen carbonate solution and water, dried (MgSO_4), and evaporated. The residue crystallised from ether to give trimer Y (0.45 g), m.p. 290–292° (sealed tube; sublimes) (Found: C, 78.7; H, 9.5. $\text{C}_{27}\text{H}_{38}\text{O}_3$ requires C, 79.0; H, 9.3%), ν_{CO} (CS_2) 1706 cm⁻¹ (no OH stretching band), $[\alpha]_D + 194^\circ$ (*c* 1.0 in CHCl_3), *m/e* 410 (50%, M^+), 95 (17), 91 (17), and 83 (100). Attempts to prepare the oxime appeared to give mixtures of the di- and tri-oximes.

Reduction of Apoverbenone in Aqueous Dimethylformamide.—The foregoing experiment was repeated with aqueous 10% dimethylformamide and the reduction was carried on for 10–12 h. The mixture was worked up to yield a semisolid which was separated by crystallisation from ether and chromatography over alumina into two dimers. The most insoluble was dimer A (0.375 g, 50%), m.p. 190–191° (Found: C, 79.0; H, 9.5. $\text{C}_{18}\text{H}_{26}\text{O}_2$ requires C, 78.8; H, 9.6%), ν_{CO} (KBr) 1715 cm⁻¹, $[\alpha]_D + 59.3^\circ$ (*c* 1.0 in CHCl_3), *m/e* 274 (14%, M^+), 137 (51), 109 (35), 95 (40), and 83 (100). Some was recovered by direct crystallisation and the remainder by chromatography.

Dimer A (0.30 g) and hydroxylamine hydrochloride (0.36 g) in ethanol (3.0 ml) and pyridine (2.0 ml) were refluxed for 10 h. The dioxime (0.30 g) precipitated and formed prisms, m.p. 282–284° (decomp.) (from ethanol) (Found: C, 71.0; H, 9.4; N, 9.2. $\text{C}_{13}\text{H}_{23}\text{N}_2\text{O}_2$ requires C, 71.0; H, 9.3; N, 9.2%).

The residue from crystallisation of dimer A was evaporated to small bulk and deposited a solid. This was chromatographed on alumina [elution with pentane-ether (4 : 1)] to yield dimer B (0.075 g, 10%), m.p. 142–143° (Found: C, 78.9; H, 9.8%), ν_{CO} (KBr) 1710 cm⁻¹, $[\alpha]_D + 81^\circ$ (*c* 1 in CHCl_3), *m/e* 294 (9%, M^+), 137 (35), 109 (31), 95 (35), and 83 (100). The same solvent mixture next eluted dimer A. Dimer B dioxime formed prisms, m.p. 298–300° (decomp.) (from aqueous ethanol) (Found: C, 71.0; H, 9.4; N, 9.1%) depressed to m.p. 265–270° on admixture with dimer A oxime.

The final residues from reduction of apoverbenone (4.0 g) after some time deposited trimer X (0.020 g, 0.5%), needles (from ether), m.p. 275–276° (Found: C, 78.9; H, 9.6%) (a mixture with trimer Y had m.p. 220–230°), ν_{CO} (KBr) 1714 cm⁻¹, $[\alpha]_D + 62.0^\circ$ (*c* 1 in CHCl_3), *m/e* 410 (30%, M^+), 137 (83), 109 (40), 108 (39), 95 (33), and 83 (100). No further crystalline material was obtained.

Action of Base on Dimer A, Apoverbenone, and Nopinone.—Dimer A (0.2 g) and apoverbenone (0.2 g) were refluxed for 4 h with methanolic 10% sodium methoxide (4 ml) and the products were isolated with ether. Dimer A, m.p. 190–191°, was recovered and apoverbenone was detected by g.l.c. No trimer X or Y was isolated. This

¹⁰ M. Schütze, *Angew. Chem.*, 1958, **70**, 697.

¹¹ C. K. Mann, *Electroanalyt. Chem.*, 1969, **3**, 57.

¹² J. Grimshaw, J. T. Grimshaw, and H. R. Juneja, *J.C.S. Perkin I*, 1972, 50.

negative result was also obtained when 5% potassium t-butoxide in t-butyl alcohol was used as base.

Nopinone (0.30 g) and apoverbenone (0.60 g) in 5% sodium methoxide (5 ml) were kept for 48 h at room temperature and the products were isolated with ether. No dimer A or B or trimer X or Y was isolated. G.l.c.

(at 70°) indicated the presence of starting materials and two other volatile products.

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