

Electrochemical Reduction of Bicyclo[3,3,1]nonadienediones: Synthesis of Substituted Barbaralanes

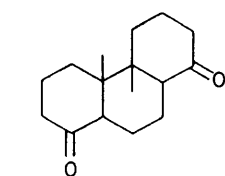
By John M. Mellor,* B. Stanley Pons, and John H. A. Stibbard, Department of Chemistry, The University, Southampton SO9 5NH

Electrochemical reduction of 4,8-dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione in the first cathodic wave at -2.0 V gave dihydro-dimer products. In contrast, reduction in the second cathodic wave at -2.75 V in the presence of acetic anhydride gave a substituted barbaralane, 2,6-diacetoxy-4,8-dimethyltricyclo[3.3.1.0^{2,8}]nona-3,6-diene. Similarly by reduction of 4,6-dimethylbicyclo[3.3.1]nona-4,6-diene-2,8-dione in the second wave at -2.75 V, a further substituted barbaralane, 4,6-diacetoxy-2,8-dimethyltricyclo[3.3.1.0^{2,8}]nona-3,6-diene was obtained. The effect of substituents on the stability of the valence isomers of barbaralanes is discussed. The mechanism of electrochemical reduction is analysed on the basis of data obtained from cyclic voltammetry, and chronamperometry.

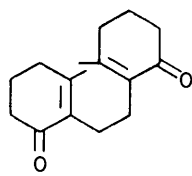
CONTROLLED-POTENTIAL preparative electrochemistry permits the selection of a potential at the working electrode so that electrolysis in the first voltammetric wave can give products different from those of the second voltammetric wave. We have described¹ preparative anodic oxidations in the second wave, where products, different from those of a first wave oxidation, were obtained. We now describe cathodic reductions of unsaturated ketones, which lead by first-wave reduction to dihydro-dimers, products of a one-electron reduction process, and by second-wave reduction to monomeric products of an overall two-electron reduction process.

The cathodic reduction of $\alpha\beta$ -unsaturated ketones to give dihydro-dimers by coupling of an intermediate anion radical is well described. Three possible couplings leading to vicinal diols, 1,6-diketones or 1,4-keto-alcohols can occur. Typically, intermolecular coupling to give 1,6-diketones² is dominant but steric constraints as in the ionones³ may lead preferentially to diols. With dicarbonyl compounds as precursors either intramolecular coupling⁴ giving a 1,6-diketone (1) from (2) without

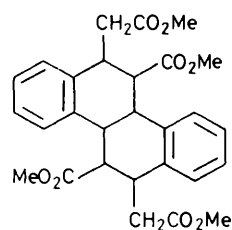
dimerisation, or intermolecular coupling⁵ to give the dihydro-dimer (3) from (4) is possible. In all the above cases, products arise from cathodic reductions in the first voltammetric wave. The initially formed anion radical, which can be observed with suitable⁶ $\alpha\beta$ -unsaturated ketones, can undergo either rapid intermolecular coupling as in the case of the ionones or, as with dicarbonyl compounds, intramolecular coupling. In the presence of suitable electrophiles the reaction course can



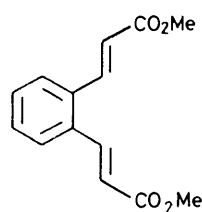
(1)



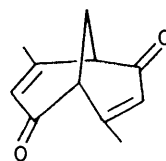
(2)



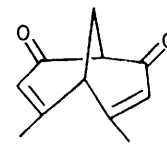
(3)



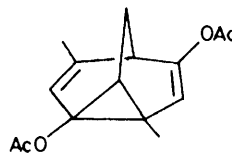
(4)



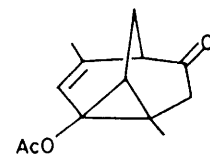
(5)



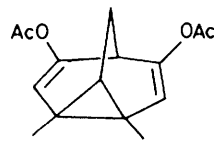
(6)



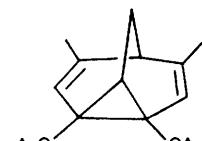
(7)



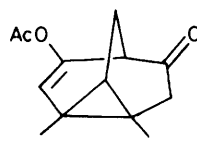
(8)



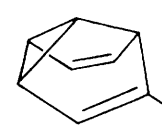
(9a)



(9b)



(10)



(11)

be diverted; in hydroxylic solvents alcohols⁷ may be obtained and in acetonitrile containing acetic anhydride reductive acylation⁸ is possible. Such reductive acylations feature reaction of the acetic anhydride with the electrogenerated anion radical to give a radical capable of further reduction.^{8,9} Alternatively successive electron transfers lead to a dianion¹⁰ then quenched with acetic anhydride. In a related process¹¹ reductive acylation of 1,3-diketones gives cyclopropyl acetates. By a study of the electrochemical reduction of the readily available¹² diketones (5) and (6) we have both distinguished between the fate of intermediate anion radicals and intermediate dianions, and also developed a novel route to substituted barbaralanes.

RESULTS

Cyclic voltammograms were recorded for the diketones (5) and (6) in acetonitrile. For both compounds a reversible first wave at *ca.* 1.7 V [versus Ag/Ag⁺ (0.01M-AgNO₃) electrode] (Figures 1 and 2) and a second irreversible wave at *ca.* 2.75 V (Figure 3) were observed.

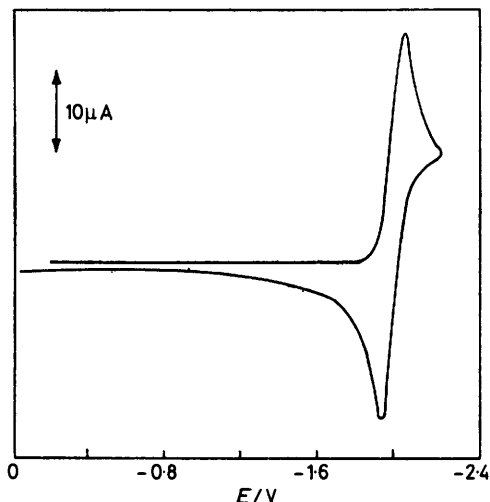


FIGURE 1 Cyclic voltammogram of 4,8-dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione in MeCN between 0 and -2.2 V at 0.5 V s⁻¹

Chronamperometric results were obtained on 5 mmol solutions of (5) and (6) and related to the behaviour of phenazine, known to be reduced by successive one-electron transfers. Appropriate plots were made of I vs $t^{-1/2}$ from the $I-t$ transient data. Linear plots were obtained for the ketones at a potential of -2.15 V and for phenazine at -1.30 V with similar gradients. Hence one electron is associated with the first wave reduction of compounds (6) and (5). A chronamperometric study at the remote cathodic potential of the second wave was not made.

Preparative electrolysis of compounds (5) and (6) (fully described in the Experimental section) were carried out at -2.0 V (in the first wave) and at -2.75 in the second wave. Products of first-wave studies were isolated by preparative t.l.c., and products of second-wave studies isolated either by preparative t.l.c. or by a combination of direct distillation of the electrolysis mixture and preparative g.l.c. Structural assignments follow from the observed spectroscopic

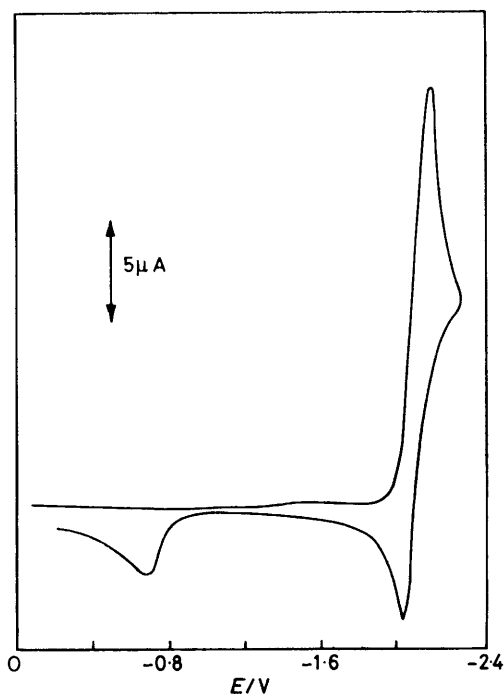


FIGURE 2 Cyclic voltammogram of 4,6-dimethylbicyclo[3.3.1]nona-4,6-diene-2,8-dione in MeCN between 0 and -2.2 V at 0.3 V s⁻¹

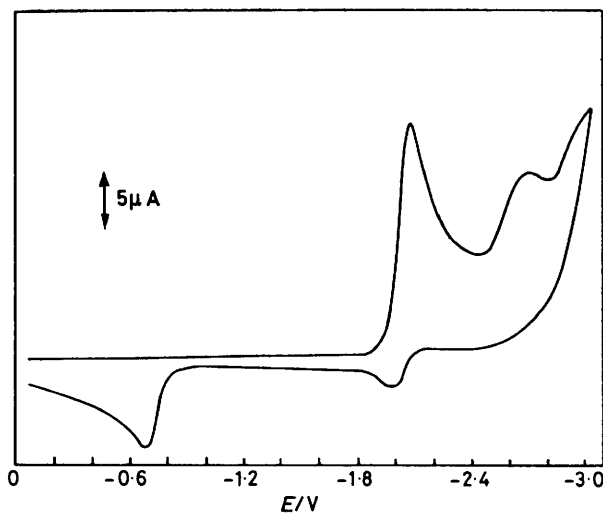


FIGURE 3 Cyclic voltammogram of 4,6-dimethylbicyclo[3.3.1]nona-4,6-diene-2,8-dione in MeCN between 0 and -2.9 V at 0.3 V s⁻¹

data. The spectra of the barbaralanes are fully discussed below.

DISCUSSION

The more complete product study with the diketone (5) shows that in both the presence or the absence of acetic anhydride cathodic reduction leads to coupling products at -2.0 V but at the more cathodic potential -2.75 V in the presence of acetic anhydride these products are of little significance. The major product is the substituted barbaralane (7), which is unstable and on

chromatography is converted into the ketoacetate (8). With the diketone (6) similar results are obtained. At -2.75 V in the presence of acetic anhydride the analogous barbaralane (9) can be isolated, but again the instability of (9) leads to isolation of a keto-acetate (10) when chromatography on silica gel is used. The instability of compounds (7) and (9) may possibly be attributed to a ready acid-catalysed hydrolysis on silica gel. Conversion of (7) into (8) was also observed on g.l.c. columns above 220 °C. The explanation for this unusual conversion was not determined.

Our results suggest that reduction of the diketone (5) at -2.0 V produces the intermediate anion radical. Racemic compound (5) can give a large number of possible dihydro-dimers. These arise from choice of enantiomers in formation of dihydro-dimers, choice of coupling site (ketone, ketone or ketone, alkene, or alkene, alkene) and stereoselection leading to *exo*- or *endo*-modes of coupling. Although previous results¹³ clearly suggest that products will arise from attack from the *exo*-face, the complexity of the n.m.r. spectra associated with chromatographic fractions tentatively identified as dihydro-dimers, prevents further structural assignment. In the presence of acetic anhydride at -2.0 V electrolysis of the diketone (5) gives similar results.

Further evidence that the dihydro-dimers are derived from an anion radical intermediate stems from the cyclic voltammetry and chronamperometry (reversible one-electron wave) and the observation of a strong e.s.r. signal associated with the electrogenerated intermediate.

In contrast, electrochemical reduction of compound (5) in the presence of acetic anhydride at -2.75 V leads to only traces of dihydro-dimers. Work-up by preparative t.l.c. of the catholyte affords the keto-acetate (8), but work-up by distillation followed by preparative g.l.c. permits isolation of the rather unstable diacetate (7). In the second wave, further reduction of the intermediate anion radical gives a dianion quenched by acetic anhydride to give the diacetate (7) directly. In a similar manner reduction of the diketone (6) gives a diacetate (9) in the second wave. The importance of these results lies in their showing that interesting products may be obtained by cathodic acylation in the second wave by avoiding the normal products of reduction in the first wave. Extension to intramolecular coupling, with avoidance of intermolecular coupling, of other polyfunctional systems is suggested.

The valence isomerisation of barbaralanes and related systems has stimulated considerable discussion. The ^1H n.m.r. spectrum of compound (7) is unexceptional. At ambient temperatures, a fast equilibration *via* a divinylcyclopropane rearrangement, related equivalent molecular species. In contrast in compound (9) the fast equilibrium at ambient temperatures interconverts the non-equivalent molecular species (9a) and (9b). Observation of the ^1H n.m.r. spectrum of (9) shows that (9a) is the dominant structure. This accords with earlier predictions.¹⁴ Extended Hückel calculations indicated that in semibullvalenes substitution at the 2, 4, 6, and 8

positions with π -electron donors should strengthen the 2,8-bond and conversely π -electron acceptors should weaken it. Studies¹⁵ with various semibullvalenes have shown that the position of equilibrium is influenced by subtle remote substituent effects. In (9) comparison is made between the relative substituent effects of methyl and acetoxy. The preference for a methyl substituent at the sp^2 rather than sp^3 site has been established in methylsemibullvalene¹⁶ (11), in methylbarbaralones¹⁷ and methylbullvalenes.¹⁸ The result from compound (9) is the first experimental demonstration that the methyl substituent effect is weaker than the acetoxy-substituent effect. By use of either differently substituted bicyclo-[3.3.1]nonadienediones or by reductive acylation with other acylating agents this approach offers the opportunity of comparing other substituent effects.

EXPERIMENTAL

General experimental details were as reported in a previous paper.¹

Cyclic Voltammetry.—An undivided cell was washed with distilled water and acetone, and dried at 110 °C before use. The working electrode was a 1-cm platinum wire of area 0.16 cm². The secondary electrode was a cylindrical platinum gauze positioned concentric to the working electrode. The luggin capillary leading to the reference compartment passed through the cylindrical gauze to within 0.5 mm of the working electrode. A silver wire reference electrode was used in 10^{-2}M silver nitrate. The cell was driven by a Chemical Electronics Potentiostat Type TR 70/2A and either the Hi-Tek Instruments Waveform Generator PP R1 or a Chemical Electronics Waveform Generator Type RB1. Voltammograms were recorded for sweep speeds of up to 2 V s⁻¹ on a Hewlett-Packard 7015 BxY recorder and for higher sweep speeds on a Teliquipment D 61 A oscilloscope. In dry acetonitrile voltammograms were obtained using 0.4M -Bu₄NBF₄ as electrolyte in solutions of the diketones (*ca.* 10 mM).

Chronoamperometry.—The above cell was used in conjunction with a Hi-Tek Instruments Waveform Generator PPR1 and a Hi-Tek Instruments Multi-purpose Signal Averager Type AA1. The *I-t* transients were recorded on the Hewlett-Packard XY recorder. Compounds were examined as 5mM-solutions in dry acetonitrile and between successive runs the working electrode was flamed and the solutions deoxygenated by bubbling with nitrogen.

Preparative Electrolysis in Acetonitrile.—Acetonitrile (Fisons HPLC Grade Reagent) was dried over aluminium oxide (ICN Pharmaceuticals Activity Grade Super 1 W 200 Neutral) and used directly. Both anolyte and catholyte compartments were 0.1M-solutions of Bu₄NBF₄ and to the catholyte (30 ml) acetic anhydride (1 ml) was added. The acetic anhydride was purified by distillation and by subsequent storage over aluminium oxide (ICN Grade as above). Satisfactory results were obtained using such freshly prepared acetic anhydride. Storage of acetic anhydride for prolonged periods over aluminium oxide led to the formation of impurities reduced at potentials above -2.75 V.

In a divided cell a working electrode of platinum gauze (4.5 cm²) and a secondary electrode of platinum gauze (3 cm²) were used. Compartments were divided by Number 4 glass frits. The potentiostatic equipment was as described above.

In a typical experiment before addition of substrate trace impurities were removed by prior electrolysis at -2.6 V to give a residual background current of *ca.* 10 mA. Following addition of the substrate (*ca.* 300 mg) the solution was gently stirred with a Teflon magnetic follower, flushed with dry nitrogen, and maintained in an anhydrous condition by addition of aluminium oxide. Typical currents of *ca.* 100 mA followed addition of substrate. Electrolysis was continued until the current had dropped to the initial background current and the total charge passed was measured using an integrator. Two work-up procedures were used. In method A the catholyte (30 ml) was poured into water (50 ml). After filtration organic products were isolated by extraction with ether (3×50 ml). The combined organic extracts were washed with water (2×50 ml), dried, and evaporated to give products. In method B the catholyte was evaporated to dryness under reduced pressure. The residual solid was taken up in chloroform (2 ml) and ether (60 ml) was slowly added with constant swirling to precipitate the base electrolyte. After filtration the residue was taken up in chloroform (2 ml) and the process repeated. Evaporation of the combined filtrates afforded the organic products.

Electroreduction of 4,8-Dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) in the First Wave.—4,8-Dimethyl[3.3.1]nona-3,7-diene-2,6-dione¹² (5) (228 mg) in dry acetonitrile was reduced at -2.0 V. An initial current of 40.5 mA was observed which fell after passage of 1.5 F mol^{-1} to a final current of 1.9 mA. Work-up by method A followed by preparative t.l.c. using ether–light petroleum (4 : 1) as eluant afforded four fractions; R_F 0.5 unchanged 4,8-dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) (48 mg) and three oily fractions having R_F 0.25, 0.15, and 0.10. Each of the oily fractions was characterised by an apparent M^+ 354. Since racemic compound (5) can lead to a number of dihydro-dimer diastereoisomers by the three possible coupling modes (ketone, ketone or ketone, alkene or alkene, alkene) and the observed n.m.r. spectra of the three fractions were complex, structures were not assigned. However it is tentatively concluded that the three fractions are dihydro-dimers of (5).

In a further experiment 4,8-dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) (176 mg) was similarly reduced in dry acetonitrile containing acetic anhydride. An initial current of 56.4 mA was observed which fell after passage of 1.6 F mol^{-1} to a final current of 3.1 mA. Work-up by method A followed by preparative t.l.c. using ether as eluant afforded unchanged 4,8-dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) (52 mg) and the above dimeric reduction products.

Electroreduction of 4,6-Dimethylbicyclo[3.3.1]nona-3,6-diene-2,8-dione (6) in the First Wave.—4,6-Dimethylbicyclo[3.3.1]nona-3,6-diene-2,8-dione (6) (250 mg) in dry acetonitrile was similarly reduced at -2.0 V. After passage of 1.5 F mol^{-1} work-up by method A followed by preparative t.l.c. failed to give any reaction products—only starting material was recovered.

Electroreduction of 4,8-Dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) in the Second Wave.—4,8-Dimethylbicyclo[3.3.1]nona-3,7-diene-2,6-dione (5) (176 mg) in dry acetonitrile containing acetic anhydride was reduced at -2.75 V. An initial current of 210 mA was observed, which fell after passage of 2.66 F mol^{-1} to a final current of 6 mA. Work-up by method A, followed by preparative t.l.c. using light petroleum–ether (3 : 2) as eluant afforded two major fractions; the fraction R_F 0.5 was shown to be a mixture (g.l.c. and analytical t.l.c.) and the second fraction

R_F 0.4 was 2-acetoxy-4,8-dimethyltricyclo[3.3.1.0^{2,8}]nona-3-en-6-one (8) (73 mg), M^+ 220.1244 ($\text{C}_{13}\text{H}_{16}\text{O}_3$ requires 220.1099) (7%), 192 (9%), 178 (56%), 150 (73%), 43 (100%); ν_{max} 1 730 and 1 710 cm^{-1} ; τ 4.06 (1 H, m, H-3), 7.20 (1 H, m, H-5), 7.45 (2 H, dd J 20 Hz, H-7), 7.86 (3 H, s, MeCO_2), 8.05 (2 H, m, H-9), 8.25 (3 H, d, 4-Me), 8.50 (1 H, m, H-1), and 8.81 (3 H, s, 8-Me). G.l.c. (10% OV 17, 220 °C) showed a single peak.

In a further experiment the reaction mixture was worked up by procedure B, and the products were distilled (130 °C/0.1 mmHg). G.l.c. showed that the distillate contained mainly keto-acetate (8) and the diacetate (7) (ratio *ca.* 1 : 1) and a third minor unidentified product. Preparative g.l.c. (250 °C) of the distillate afforded a low yield of 2,6-diacetoxy-4,8-dimethyltricyclo[3.3.1.0^{2,8}]nona-3,6-diene (7) M^+ 262.1328 ($\text{C}_{15}\text{H}_{18}\text{O}_4$ requires 262.1205) (2%), 220 (23%), 192 (2%), 178 (77%), and 43 (100%); τ 4.82 (2 H, m, H-3 and H-7), 8.00 (2 H, t, J 3 Hz, H-1 and H-5), 7.95 (6 H, s, MeCO_2), 8.41 (6 H, d, 4- and 8-Me), and 8.65 (2 H, d J 3 Hz, H-9). Using a column (10 ft) of 10% OV 17 a successful separation was achieved at 220 °C; above this temperature thermal conversion of (7) into (8) was observed.

Electroreduction of 4,6-Dimethylbicyclo[3.3.1]nona-3,6-diene-2,8-dione (6) in the Second Wave.—4,6-Dimethylbicyclo[3.3.1]nona-3,6-diene-2,8-dione¹² (6) (176 mg) in dry acetonitrile containing acetic anhydride was reduced at -2.75 V. An initial current of 220 mA was observed, which fell after passage of 2.6 F mol^{-1} to 5.8 mA. Work-up by method A, followed by preparative t.l.c. using light petroleum–ether (3 : 2) as eluant afforded two major fractions; the fraction R_F 0.9 was shown to be a mixture (g.l.c. and analytical t.l.c.) and the second fraction R_F 0.8 was 4-acetoxy-2,8-dimethyltricyclo[3.3.1.0^{2,8}]non-3-en-6-one (10) (41 mg), M^+ 220.1148 ($\text{C}_{13}\text{H}_{16}\text{O}_3$ requires 220.1099) 5%, 192 (2%), 178 (100%), 150 (47%), and 43 (83%); ν_{max} 1 740 and 1 705 cm^{-1} ; τ 4.33 (1 H, m, H-3), 7.26 (1 H, m, H-5), 7.37 (2 H, dd J 20 Hz, H-7), 7.90 (3 H, s, MeCO_2), 8.08 (2 H, m, H-9), 8.65 (3 H, s, 2-Me), 8.80 (3 H, s, 8-Me), and 8.95 (1 H, m, H-1). G.l.c. (10% OV 17, 220 °C) showed a single peak.

In a further experiment the reaction mixture was worked up by procedure B and the products were distilled (130 °C/0.1 mmHg). G.l.c. showed that the distillate contained mainly the keto-acetate (10) and the diacetate (9) (ratio *ca.* 1 : 1) and a third minor unidentified product. Preparative g.l.c. of the distillate afforded a low yield of 4,6-diacetoxy-2,8-dimethyltricyclo[3.3.1.0^{2,8}]nona-3,6-diene (9), M^+ 262.1214 ($\text{C}_{15}\text{H}_{18}\text{O}_4$ requires 262.1205) (1%), 220 (27%), 178 (85%), and 43 (100%); τ 4.94 (2 H, m, H-3 and H-7), 8.06 (1 H, t, J 3 Hz, H-5), 8.12 (6 H, s, MeCO_2), 8.83 (2 H, t, J 3 Hz, H-9), 8.90 (6 H, s, 2- and 8-Me), and 9.07 (1 H, t, J 3 Hz, H-1).

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