

Electrochemical Difunctionalisation of Adamantane and Further Oxidation of Substituted Adamantanes

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Anodic oxidation of adamantane in trifluoroacetic acid at a potential shown by cyclic voltammetry to be in the second wave, gives after hydrolytic work up adamantane-1,3-diol (70%). Similar oxidation in acetonitrile gives *NN'*-adamantane-1,3-diyl)bisacetamide (58%). Electroanalytical techniques are used to define the oxidation mechanism, and oxidations of some substituted adamantanes at high anodic potentials are described.

THERE are few methods available for direct introduction of polyfunctionality into saturated hydrocarbons.¹ We have previously reported studies of controlled electrolysis conducted in the first oxidation wave. Here we report in full the results of oxidation in the second anodic wave, which for the first time establish that direct electrochemical difunctionalisation of hydrocarbons is possible in preparatively significant yields.

RESULTS

As in earlier studies we have examined hydrocarbons expected to give stable primary products of oxidation. By using adamantanes, the formation of olefins, capable of rapid further oxidation, is avoided.

Voltammetric data from linear potential sweep measurements for a series of adamantanes are reported in Table 1. Long-lived transient intermediates, for example cation radicals or dications produced in the anodic sweep, were not detected: in the reverse cathodic sweep no wave was observed. For adamantane in trifluoroacetic acid three separate oxidation waves were detected, whereas in acetonitrile only two waves were observed.

The results of preparative electrochemical oxidation of adamantane in the first anodic wave both in trifluoroacetic acid and in acetonitrile have been described.^{2,3} Table 2 shows the results of preparative electrolysis in the second anodic wave. Product yields were determined either by g.l.c. or by isolation of products (see Experimental section).

¹ Preliminary report, A. Bewick, G. J. Edwards, S. R. Jones, and J. M. Mellor, *Tetrahedron Letters*, 1976, 631.

² G. J. Edwards, S. R. Jones, and J. M. Mellor, *J.C.S. Perkin II*, 1977, 505.

The nature of the oxidative process in the second wave was investigated both by coulometry and by additional voltammetric studies. Oxidation of adamantane in acetonitrile at 2.4 V (the first anodic wave) against an Ag|Ag⁺

TABLE 1
Voltammetric data for substituted adamantanes

Compound	Solvent	$E_{p/2}^1/V$	$E_{p/2}^2/V$
Adamantane	MeCN	2.38	2.86
1-t-Butyladamantane	MeCN	2.33	2.81
1,3-Dimethyladamantane	MeCN	2.42	2.87
<i>N</i> -(1-Adamantyl)acetamide ³	MeCN	1.90	
Adamantane	CF ₃ CO ₂ H	1.86	2.35 (2.75)
Adamantan-1-ol ^b	CF ₃ CO ₂ H	2.30	2.76
3,5-Dimethyladamantan-1-ol ^b	CF ₃ CO ₂ H	2.28	2.67
Adamantanone	CF ₃ CO ₂ H	1.75	2.55
<i>N</i> -(1-Adamantyl)acetamide	CF ₃ CO ₂ H	2.34	2.90
1-Adamantylamine	CF ₃ CO ₂ H	2.38	2.67
1-Adamantylammonium tetrafluoroborate	CF ₃ CO ₂ H	2.46	2.89

^a In acetonitrile the reference electrode was Ag|AgNO₃ (0.01M) in MeCN. In trifluoroacetic acid the reference electrode was a silver wire in CF₃CO₂H. Sweep rate 0.1 V s⁻¹ ([substrate] 10 mM); electrolyte BuⁿNBF₄. ^b Dissolution of alcohols in CF₃CO₂H leads to rapid formation of the trifluoroacetates.

(0.01M) electrode in acetonitrile led to a linear plot of current versus Faradays mol⁻¹, which only deviated from linearity towards the end of electrolysis. The slope of the early linear portion gave an *n* value of 2.0–2.2 Faradays mol⁻¹. Similarly in the second wave at 3.0 V, linearity was observed for >50% electrolysis and the *n* value was 4.0–4.3

³ V. R. Koch and L. L. Miller, *J. Amer. Chem. Soc.*, 1973, **95**, 8631.

Faradays mol⁻¹. More closely linear plots were observed for electrolyses in trifluoroacetic acid, where the background current was very low. In oxidation of adamantane *n* values were determined from these good linear plots. Oxidation at 1.8 V (first anodic wave) (silver wire reference electrode) gave an *n* value of 1.9–2.0 Faradays mol⁻¹ and at 2.3 V (second anodic wave) a value of 3.8–4.0 Faradays mol⁻¹. In a separate experiment 1.9 Faradays mol⁻¹ were passed at 1.8 V and then a further 2 Faradays mol⁻¹ at 2.3 V. In both anodic regions linear plots indicating the passage of 2 Faradays mol⁻¹ in each wave were obtained.

TABLE 2

Electrochemical oxidation of adamantane and derivatives ^a

Compound	Solvent	Potential (V)	Products (%)
Adamantane	MeCN ^b	3.0	(3) (6); (5) (58)
Adamantane	MeCN ^c	3.0	(3) (24); (5) (20)
Adamantane	CF ₃ CO ₂ H	2.3	(9) (12); (10) (2); (11) (51); (12) (5); (13) (1)
Adamantane	CF ₃ CO ₂ H ^d	2.3	(9) (4); (11) (70)
Adamantan-2-ol	CF ₃ CO ₂ H	2.3	(13) (11); (12) (44)
Adamantan-1-ol	CF ₃ CO ₂ H	2.3	(11) (50)
<i>N</i> -(1-Adamantyl)-acetamide	MeCN	2.8	(3) (83); 5 (<3)
<i>N</i> -(1-Adamantyl)-acetamide	CF ₃ CO ₂ H	2.4	(9) (8); (11) (68)
Adamantan-1-ol	CF ₃ CO ₂ H ^e	2.3	(5) (80)

^a Background electrolyte Bu₄NBF₄. ^b Yields determined by g.l.c. analysis. ^c Yields of isolated products; background electrolyte Me₄NBF₄. ^d For details see Experimental section. ^e Work-up with MeCN-H⁺ (see Experimental section).

These conclusions were substantiated by further voltammetric experiments. In cyclic voltammetry linear plots passing through the origin of a peak current density *versus* (sweep rate)[‡] plot were obtained for both first and second anodic waves in acetonitrile. Comparison of the values of the current function VF [equation (i)] with that obtained

$$VF = \frac{I/A \text{ cm}^{-2}}{(\nu^{\ddagger}/V^{\ddagger} \text{ s}^{-\ddagger}) \times (c/\text{mol l}^{-1})} \quad (\text{i})$$

for *NN*-bis-(2,4,6-trimethoxyphenyl)methylamine (1), a compound known to undergo reversible one-electron oxidation, showed that the transfer of two electrons was associated with each wave for adamantane [VF values 2.9 for adamantane (first wave); 2.9 for adamantane (second wave); 1.3 for (1)]. Similar waves in trifluoroacetic acid showed plots of current density *versus* (sweep rate)[‡] which were linear, and had the same slope, passing through the origin.

Similar conclusions were derived from studies at a rotating disc electrode. Values of the current function RF [equation (ii)] were obtained for rotation speeds

$$RF = \frac{I/A \text{ cm}^{-2}}{(\omega^{\ddagger}/\text{rad}^{\ddagger} \text{ s}^{-\ddagger}) \times (c/\text{mol l}^{-1})} \quad (\text{ii})$$

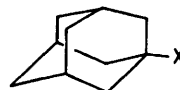
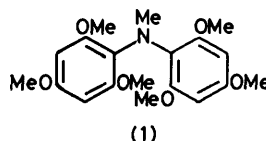
between 500 and 5 000 rev. min⁻¹. Comparison of the RF value for the standard (1) (0.09) with those of the first wave (0.24) and the second wave (0.45) for adamantane in acetonitrile, making some allowance ⁴ for the difference in diffusion coefficients, indicates that the transfer of two electrons is associated with the first wave, and the transfer of an additional two with the second.

The oxidations of a number of substituted adamantanes

were examined with regard to synthetic utility. Voltammetric results are shown in Table 1 and product studies in Table 2, and further voltammetric and coulometric experiments are noted in the Discussion section.

DISCUSSION

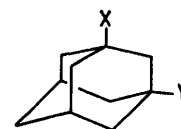
Coulometry and voltammetry establish that for adamantane in either trifluoroacetic acid or acetonitrile anodic oxidation leads to removal of two electrons in the first wave and a further two in the second. Earlier preparative studies ^{2,3} have shown that in the first wave the trifluoroacetate of adamantan-1-ol (2) is the major product in trifluoroacetic acid, and *N*-(1-adamantyl)-acetamide (3) the major product in acetonitrile. Oxidation of adamantane in trifluoroacetic acid in the second

(2) X = O₂C·CF₃

(3) X = NHAc

(6) X = N:ĊMe

(9) X = OH

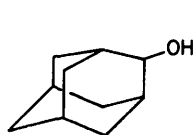
(4) X = Y = O₂C·CF₃

(5) X = Y = NHAc

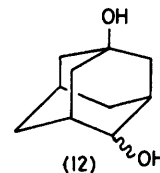
(7) X = Y = N:ĊMe

(8) X = NHAc, Y = O₂C·CF₃

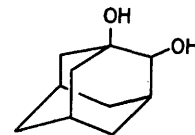
(11) X = Y = OH



(10)



(12)



(13)

wave at 2.3 V gives a high yield of the bistrifluoroacetate (4), and similarly, after work-up of the solution from oxidation of adamantane in acetonitrile in the second wave at 3.0 V, the diamide (5) is obtained (see Table 2). These results are the first electrochemical difunctionalisations of saturated hydrocarbons to be reported. Interestingly, in trifluoroacetic acid higher yields of disubstituted products are obtained by passage of 2 Faradays mol⁻¹ at 1.8 V and then a further 2 Faradays mol⁻¹ at 2.3 V. Two aspects of this work deserve discussion: the mechanistic aspects of the oxidation in the second wave, and the generality of a process which permits either direct introduction of two functional groups into a hydrocarbon, or further functionalisation of a monofunctionalised substrate.

In the case of *N*-(1-adamantyl)acetamide (3) at 2.8 V, although oxidation of the substrate occurs, as shown by the large increase in electrode current on addition of the amide, isolation of the products leads largely to unchanged amide (83%), and the diamide (5) is only

⁴ V. D. Parker, *Electrochim. Acta*, 1973, **18**, 519.

obtained in trace quantities (<3%). This shows that the diamide (5) is not obtained in the second wave oxidation of adamantane *via* the monoamide (3) as intermediate. This is substantiated by voltammetry of the amide (3), which shows peak positions considerably displaced from those of adamantane. A simple explanation of these results is that oxidation of the amide (3) electrochemically leads to the 1-adamantyl cation by oxidation of the amide side chain. Capture of this cation by solvent then leads to the nitrilium ion (6), and with water this gives back the amide (3). Overall the process represents an oxidation of acetonitrile. In oxidation of adamantane in the second wave the crucial intermediate is the nitrilium ion (6). In the rigorous absence of water no amide can be formed and hence the electroactive species in the second wave must be the mononitrilium ion (6), which on further oxidation gives the dinitrilium ion (7). Quenching with water then gives the diamide (5). The difference between the potentials of the first and second waves of adamantane is explained by the deactivation of further electron withdrawal afforded by the positively charged nitrilium substituent. This analysis accords well with the earlier observation³ that in the first wave adamantane is oxidised to give a nitrilium ion in acetonitrile.

Oxidation of adamantane in trifluoroacetic acid is mechanistically more straightforward. In the second wave the product of oxidation of the first wave, 1-adamantyl trifluoroacetate, is further oxidised to give directly the diester (4). Adamantan-1-ol can be electrolysed in trifluoroacetic acid to give the diester (4). Again the difference between the potentials of the first and second waves of adamantane in trifluoroacetic acid is explained by the deactivation effect of the substituent, here the trifluoroacetoxy-group. We note a confirmation of this analysis in the similar $E_{p/2}$ values from cyclic voltammetry of the second wave of adamantane and the first wave of adamantan-1-ol in trifluoroacetic acid (*i.e.* 1-adamantyl trifluoroacetate). In such cases successive functionalisation is possible by appropriate increase in the applied potential. Polyamides are obtained in dry nitrile solvents, polyesters in trifluoroacetic acid.

Although the amide (3) is oxidised in acetonitrile by loss of electrons from the functional group, we thought it possible that in trifluoroacetic acid protonation of the functional group might lead to preferential oxidation of the hydrocarbon moiety. Oxidations of some substituted adamantanes have been reported,^{3,5} and both oxidation of the substituent and difunctionalisation have been observed. Oxidation of the amide (3) at 2.4 V in trifluoroacetic acid containing trifluoroacetic anhydride (5%) gave the diester (4). The formation of this ester was explained when the amide (3) was observed to dissolve in the above solvent in the absence of an applied current. Solvolytic cleavage gave the ester (2) in

high yield. Precedent for solvolytic conversion of an amide into ester exists.⁶ Trifluoroacetamides undergo ready solvolysis.⁷ Solvolyses of derivatives of *N*-t-butylacetamide and of *N*-(1-adamantyl)acetamide are markedly facilitated by the stability of the tertiary carbocation formed. Here it permits efficient passage from a bridgehead amide to bridgehead alcohol.

Electrolysis of the amide (3) in trifluoroacetic acid alone gave the amide ester (8) in poor yield. Further electrolyses of other substituted adamantanes are described in the Experimental section. Oxidation of adamantanol is an efficient route to diesters and diamides.

The major problems in the electrochemical polyfunctionalisation of saturated hydrocarbons are (*a*) the need to use high anode potentials and (*b*) the efficient capture of reaction intermediates by nucleophilic substitution to prevent olefin formation and hence complex secondary oxidation processes. This work shows that in both acetonitrile and trifluoroacetic acid the problems associated with the use of high anode potentials are not important. By using bridged hydrocarbons, unable to form olefins, the second constraint is removed and hence difunctionalisation proceeds in a satisfactory manner. To make such polyfunctionalisations more general requires methods for more efficient capture of intermediate carbocations.

EXPERIMENTAL

General experimental details⁸ and electrochemical techniques² have been reported in previous papers. Procedures for purification of solvents and the electrolyte² and of adamantane⁸ have been described. Adamantan-1-ol (Cambrian), adamantan-2-ol (Aldrich), 1-adamantylamine hydrochloride (Cambrian), and adamantan-2-one (Aldrich) were used as supplied. Preparations of 1-t-butyladamantane, *N*-(1-adamantyl)acetamide, and 3,5-dimethyladamantan-1-ol have been described.^{2,8}

Electrolysis of Adamantane in Acetonitrile at 3.0 V.—Adamantane (71 mg) was oxidised at 3.0 V in acetonitrile with tetramethylammonium tetrafluoroborate (0.1M) as electrolyte. In the absence of added adamantane a background current of 6 mA was recorded. Addition of adamantane led to a current of 50 mA which fell to 8 mA. Water (0.2 ml) was then added to the anolyte and the solvent removed under reduced pressure. The residue was washed with water and then dichloromethane, and the aqueous layer was further extracted continuously with dichloromethane. The organic extracts were dried and evaporated to leave a white solid (90 mg). Preparative t.l.c. (ethyl acetate as eluant) afforded *N*-(1-adamantyl)acetamide (3) (23 mg), identical with an authentic sample and *NN'*-(adamantane-1,3-diyl)bisacetamide (5) (25 mg), which was recrystallised from ethyl acetate, m.p. 226—227° (lit.,⁹ 226—227°), δ 1.60 (2 H, t), 1.88 (s) and 1.96br (total 14 H), 2.22br (2 H), 2.28 (2 H, s), and 5.27br (NH); m/e 250 (60%, M^+), 207 (100, $M - C_5H_5O$), 193 (61, $M - 57$), 149 (22), 148 (21), 136 (33), 108 (22), and 43 (48); ν_{max} . (CHCl₃) 3 400, 1 660, 1 520, and 1 300 cm⁻¹.

⁷ J. B. Hendrickson, R. Bergeron, A. Giga, and D. Sternbach, *J. Amer. Chem. Soc.*, 1973, **95**, 3412.

⁸ S. R. Jones and J. M. Mellor, *J.C.S. Perkin I*, 1976, 2576.

⁹ H. Stetter and C. Wulff, *Chem. Ber.*, 1960, **93**, 1366.

⁵ F. Vincent, R. Tardivel, and P. Mison, *Tetrahedron*, 1976, **32**, 1681.

⁶ R. N. Lacey, *J. Chem. Soc.*, 1960, 1633.

In a further experiment product yields were determined directly by g.l.c. analysis. Thus adamantane (29 mg) was oxidised at 3.0 V with tetrabutylammonium tetrafluoroborate as electrolyte until the current had fallen to the background value. Water (0.2 ml) was added. Direct g.l.c. analysis (with added internal standard) indicated the formation of *N*-(1-adamantyl)acetamide (3) (6%) and *NN'*-(adamantane-1,3-diyl)bisacetamide (5) (58%).

Electrolysis of Adamantane in Trifluoroacetic Acid at 2.3 V.—Adamantane (47.8 mg) was oxidised at 2.3 V in trifluoroacetic acid with added trifluoroacetic anhydride (1%) and tetrabutylammonium tetrafluoroborate (0.1M) as electrolyte. In the absence of added adamantane a background current of 0.6 mA was recorded. Addition of adamantane led to a current of 55 mA which fell to 5 mA. After electrolysis the anolyte was poured onto ice-water covered with ether and the acidity was quenched by slow addition of sodium hydrogen carbonate. The ether solution was separated, dried (MgSO₄), and evaporated, and the residue was hydrolysed as previously described.⁸ G.l.c. analysis of the hydrolysate showed the presence of adamantan-1-ol (12%), adamantan-2-ol (2%), adamantane-1,3-diol (51%), adamantane-1,4-diol (mixture of isomers; 5%), and adamantane-1,2-diol (1%) (by comparison with authentic samples).

In a further experiment adamantane (52 mg) was oxidised under similar conditions but at 1.8 V for the passage of 2 Faradays mol⁻¹ and then at 2.3 V for the passage of a further 2 Faradays mol⁻¹. The initial current was 29 mA and the final current 1.7 mA (background 0.1 mA). Work-up and hydrolysis as above afforded a mixture of alcohols separated by preparative t.l.c. Elution with ethyl acetate gave adamantan-1-ol (2 mg, 4%) and adamantane-1,3-diol (45 mg, 70%). Recrystallisation from ethyl acetate-ethyl alcohol (9 : 1) afforded pure adamantane-1,3-diol, m.p. 330° (lit.,¹⁰ 325–330°); δ [(CD₃)₂SO] 1.49 (12 H, m), 2.12 (2 H, s), and 4.37 (2 H, s); *m/e* 168 (19%, *M*⁺), 150 (4, *M* - H₂O), 112 (8), 111 (100), 110 (5), 109 (4), 108 (4), and 95 (16); ν_{\max} (KBr) 3 220, 2 930, 2 850, 1 580, 1 443, 1 327, 1 295, 1 200, 1 131, and 1 024 cm⁻¹. Other, minor products of the previous experiment were not observed here.

Electrolysis of Adamantan-1-ol in Trifluoroacetic Acid at 2.3 V.—Adamantan-1-ol (100 mg) was oxidised at 2.3 V in trifluoroacetic acid with added trifluoroacetic anhydride (1%) and tetrabutylammonium tetrafluoroborate (0.1M) as electrolyte. An undivided preparative cell was used. The initial current (42 mA) fell to 8 mA for the passage of 2 Faradays mol⁻¹. The potential was pulsed to 1.0 V anodic for 1 in every 30 s. After electrolysis the solution was worked up to give a mixture of products analysed by g.l.c. Before hydrolysis no alcohols were observed and the only products were adamantane (a trace), the bistrifluoroacetate of adamantane-1,3-diol (50%), and some 1-adamantyl trifluoroacetate which was not oxidised.

Electrolysis of Adamantan-2-ol in Trifluoroacetic Acid at 2.3 V.—Adamantan-2-ol (49 mg) was oxidised at 2.3 V in trifluoroacetic acid with added trifluoroacetic anhydride (1%) and tetrabutylammonium tetrafluoroborate (0.1M) as electrolyte. The initial current (14.7 mA) had fallen to 3.3 mA at the end of electrolysis. The potential was pulsed to 1.0 V anodic for 1 in every 30 s. After electro-

lysis the anolyte was worked up to give a mixture of products, which were separated by preparative t.l.c. Elution with ethyl acetate afforded adamantane-1,2-diol (7 mg, 11%) and a mixture of adamantane-1,4-diols (23 mg, 44%), identified by comparison with authentic samples obtained by reduction (LiAlH₄) of 5-hydroxyadamantanone.

Trifluoroacetolysis of N-(1-Adamantyl)acetamide (3).—*N*-(1-Adamantyl)acetamide (3) (25 mg) dissolved in trifluoroacetic acid-trifluoroacetic anhydride (19 : 1) was set aside at room temperature for 3 h. G.l.c. analysis then showed the presence of a little unchanged amide but substantial formation of 1-adamantyl trifluoroacetate (1) (>80%). In trifluoroacetic acid alone after 3 h g.l.c. analysis showed little (<5%) formation of 1-adamantyl trifluoroacetate (1).

Electrolysis of N-(1-Adamantyl)acetamide (3) in Trifluoroacetic Acid at 2.4 V.—*N*-(1-Adamantyl)acetamide (3) (176 mg) was oxidised at 2.4 V in trifluoroacetic acid with added trifluoroacetic anhydride (1%) and tetrabutylammonium tetrafluoroborate as electrolyte. After electrolysis in which 2 Faradays mol⁻¹ were passed and the current fell from 28 to 0.7 mA the solution was worked up as above. G.l.c. analysis showed formation of (2) and (4) as the major products. The products were hydrolysed as described above and the hydrolysis products were analysed by g.l.c. and subsequently crystallised. Analysis showed the presence of adamantan-1-ol (8%) and adamantane-1,3-diol (68%). Recrystallisation afforded pure adamantane-1,3-diol.

Electrolysis of N-(1-Adamantyl)acetamide (3) in Acetonitrile at 2.8 V.—*N*-(1-Adamantyl)acetamide (17.7 mg) was oxidised at 2.8 V in acetonitrile with tetrabutylammonium tetrafluoroborate as electrolyte. Electrolysis as described above and work-up provided a sample for g.l.c. analysis. This showed that the starting material was largely unchanged (83% recovery) and little diamide (<3%) was obtained even after the passage of 2 Faradays mol⁻¹.

Electrolysis of Adamantan-1-ol in Trifluoroacetic Acid at 2.3 V and Reaction of the Products with Acetonitrile.—Adamantan-1-ol (208 mg) was oxidised at 2.3 V in trifluoroacetic acid as above. After the passage of 2 Faradays mol⁻¹ work-up was effected by extraction with ether from a solution of the anolyte in ice-water. The acid was neutralised by slow addition of sodium carbonate. The residual yellow oil was heated at 95 °C with stirring for 48 h with acetonitrile (4 ml), trifluoroacetic acid (8 ml), sulphuric acid (98%; 0.8 ml), and water (0.1 ml). The cold solution was poured into water (80 ml) and chloroform (80 ml), sodium carbonate was added, and the aqueous layer was further extracted with chloroform. The combined chloroform extracts were dried and evaporated and the solid residue was analysed by g.l.c. and recrystallised. Analysis showed the presence of *NN'*-(adamantane-1,3-diyl)bisacetamide (5) as major product (80%). Recrystallisation from ethyl acetate afforded pure diamide (5), m.p. 224–225° (144 mg, 42%).

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¹⁰ H. W. Geluk and J. L. M. A. Schlatmann, *Tetrahedron*, 1968, **24**, 5369.