Studies on Electrolytic Substitution Reactions. XX.* The Anodic Acetoxylation of Fluorene — A Mechanistic Study

LENNART EBERSON** and ANDREW WEBBER ***

Division of Organic Chemistry 3, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund 7, Sweden

A re-investigation of the very ineffective anodic acetoxylation of fluorene, using 9,9-dideuterio-fluorene or non-deuterated fluorene in acetic acid or perdeuterioacetic acid, respectively, disproves a previously proposed cyclic mechanism. It is found that anode passivation occurs in tetrabutyl tetra-fluoroborate—acetic acid solutions. In acetate-containing media nuclear and side-chain substitution do occur but do not account for all of the reacted fluorene. Thus, it is concluded that another, as yet unidentified, oxidation process competes with acetoxylation. The nature of this reaction is briefly discussed.

The anodic acetoxylation of fluorene (FHH, 1) is expected to yield nuclear, as opposed to side-chain, substituted acetates due to the anti-aromatic nature of the cation intermediate FH⁺ shown in Scheme 1.¹ In media where acetate ion is not present, nuclear substitution is known to be inhibited ² as the cation

radical, FHH⁺, loses a proton instead of undergoing attack by the nucleophilic acetate ion. In the case of fluorene and other aromatics possessing a side-chain, the proton loss is expected to occur at the benzylic site to give ultimately, in this particular case, 9-acetoxyfluorene (2). An earlier paper in this series 1 showed that these expectations are borne out to some degree. In 0.1 M Bu₄NBF₄ - acetic acid only 9-acetoxyfluorene is formed (0.5 % current yield), whereas both nuclear and side-chain acetates are produced when fluorene is oxidized in 1 M NaOAc-acetic acid. In the latter case the ratio of nuclear to side-chain substitution is indeed high as compared to "normal" alkylbenzenes. However, the total current yield is only 15 % for all of the acetates combined. To explain this the mechanism depicted in Scheme 2 was proposed, whereby the fluorenyl radical, FH, abstracts a hydrogen atom from the medium to regenerate fluorene. The antiaromatic nature of the fluorenyl cation, FH⁺, was thought to be responsible for favouring hydrogen atom abstraction over further oxidation of the radical.

We decided to test this mechanism by investigating the anodic oxidation of 9,9-dideuterio-fluorene (FDD) in acetic acid and of fluorene

FHH
$$\xrightarrow{-e^{-}}$$
 FHH'+ $\xrightarrow{-H^{+}}$ FH' $\xrightarrow{-e^{-}}$ FH+ $\xrightarrow{OAc^{-}}$ FH-OAc

OAc

A'r \xrightarrow{OAc} Ar-OAc

Scheme 1.

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^{**}Author to whom correspondence should be addressed.

^{***} Present address: Chemistry Department, State University of New York at Buffalo, Buffalo, N.Y. 14214, U.S.A.

FHH
$$\xrightarrow{-e^{-}}$$
 FHH $\xrightarrow{+}$ FH $\xrightarrow{-e^{-}}$ FH+

Scheme 2.

(FHH) in perdeuterioacetic acid, using sodium acetate (perdeuterioacetate) or tetrabutylammonium tetrafluoroborate as supporting electrolyte. The mechanism predicts that the substrate should undergo hydrogen—deuterium exchange at the position of proton loss from the radical cation FHH⁻⁺, i.e., the benzylic 9-position.

RESULTS AND DISCUSSION

Oxidation of fluorene in 1 M sodium acetate—acetic acid. Cyclic voltammetry at a platinum bead electrode gave an irreversible wave with a peak potential of +1.70 V vs. s.c.e.. Comparison of the peak height with that of ferrocene suggested that the process was a two-electron oxidation. However, caution should be exercised when comparing such dissimilar electrode processes. Further electroanalytical investigation in this medium was not attempted and preparative scale electrolyses with subsequent product determination were used in this study.

FDD was oxidized at both constant potential (+1.7 V vs. s.c.e.) and constant current (5 mA cm⁻²). Table 1 gives some typical examples of the product distribution. Concentrations from 7 to 200 mM

were employed. The product distribution appears to be independent of concentration, current density and whether constant current or controlled potential conditions were used. The mixture was worked-up and analyzed by GLC/MS and ¹H NMR spectroscopy. Note that when the internal standard was added directly to the crude electrolyte, GLC analysis gave yields identical to those determined by addition of the standard to the ethereal extract of the electrolyte. Thus, it is ascertained that none of the products listed in Table 1 are lost in the work-up procedure.

It was thought possible that dimeric products could be formed from either the relatively stable fluorenyl radicals or the cation radicals. Dimerization of fluorenvl radicals has been reported.³ albeit in non-nucleophilic media. However, the medium used here is too nucleophilic to allow formation of 9,9'-bifluorenyl or other dimeric products. Oxidation of fluorene to fluorenone was also considered a possibility and small amounts of fluorenone were indeed found in the product mixture. The major products detected were nuclear and, to a lesser extent, side-chain acetates, the identities of which were confirmed by ¹H NMR, comparison of their retention times with authentic samples and GLC/ MS (the latter of which distinguishes between nuclear and side-chain acetates when the substrate is FDD but not FHH). The exact identity of the isomer(s) "1,3,4-acetoxyfluorene" is not known. The ratio of nuclear to side-chain acetoxylation is high, as previously reported.1

We also note, as before, that the total current yield of identified products is low, around 20 %,

Table 1. Typical product distributions from the anodic oxidation of fluorene (FHH or FDD).

Substrate (conc./mM)	Electrolyte	Charge passed/F mol ⁻¹	Recovered fluorene/%	,	, 0	2-OAc	1,3,4-OAc	Material not accounted for/%
FDD (200) ^b	CH3COOH/CH3COONa	2.0	69 ^s	≈0.1	0.2	16	1.9	12.8
FDD (94)°	CH3COOH/CH3COONa	2.0	64 ^g	0.6	0.2	17	2.0	16.2
FHH (8.2)°	CD ₃ COOD/CD ₃ COONa	1.0	73 ^g	6.0	0.5	5.9	0.6	14.0
FHH (7.0)c,e	CD ₃ COOD/CD ₃ COONa	1.0	73 ^g	6.8	1.6	3.4	_	15.2
FDD (38) ^d	CH ₃ COOD/Bu ₄ NBF ₄	2.0	77 9	_	_	_	_	23
FHH (36) ^d	CD ₃ COOD/Bu ₄ NBF ₄	2.0	67 ^f	4.8	0.9	2.9	_	24.4

^a Undivided cell, Pt electrodes (1 cm² each). ^b Constant current electrolysis (c.c.e.) at 5 mA cm⁻². ^c C.p.e. at 1.7 V vs. s.c.e. ^d C.c.e. at 0.5 mA cm⁻². ^e Divided cell. ^f Yield determined by analysis of the ethereal extract of the electrolyte. ^g Yield determined by analysis of the crude electrolyte. ^h F = O is fluorenone, 9-OAc is 9-acetoxyfluorene, etc. Yields are based on the amount of starting fluorene.

which now at least partly can be ascribed to the fact that ca. 15 % of the starting material cannot be accounted for in the analysis. Isotope analysis of the recovered fluorene (GLC/MS and ¹H NMR) showed that no H-D exchange had occurred, even in experiments in which charges up to 8 F mol⁻¹ has been passed through the electrolyte. Thus the cyclic mechanism proposed earlier (Scheme 2) is refuted. This mechanism in principle can only account for low current yields (i.e. inefficient oxidation) but of course not for missing material. Oxidation of FDD in a divided cell gave results virtually identical to those discussed above where an undivided cell was used. Thus the possibility of some cathodic mechanism being responsible for the lost material is excluded.

Nondeuterated fluorene, FHH, was also oxidized in 1 M NaOOCD $_3$ -CD $_3$ COOD (Table 1). Product analysis again confirmed that no H-D exchange had occurred and the yields of the products were similar to those from the oxidation of FDD in nondeuterated medium. Due to the weaker C-H bond at the side-chain position, it was expected that higher yields of fluorenone and 9-acetoxyfluorene would be found and this is in fact observed (see Table 1).

Oxidation of fluorene in 0.1 M Bu₄NBF₄-acetic acid. FDD was oxidized at both constant current (current densities from 0.3 to 10 mA cm⁻²) and controlled potential (initially +1.6 V, then +1.8 V vs. s.c.e.) until 2 F mol⁻¹ had been passed. In every case the anode became coated with a black film. In the controlled potential experiments this resulted in a rapid initial decrease in current and continual switching of the potentials of the counter and working electrodes only partly alleviated this problem. Removal and cleaning of the anode temporarily restored the current to its original value. Concentrations of FDD ranging from 20 to 170 mM were used. In every case GLC/MS and ¹H NMR examination of the electrolysis product showed that the isotopic composition of the fluorene was unchanged, no FDH or FHH being present. The ¹H NMR analysis gave a "clean" spectrum of FDD with no other signals present. No acetates, fluorenone, bifluorenyl or bifluorenylidene could be detected by GLC. However, only about 75 % of the substrate, FDD, was recovered at the end of the electrolysis. Control experiments in the absence of FDD showed that the blackening and associated anode passivation only occurred when FDD was present. We believe that this film may be either the results of polymerization of a fluorene radical species (FDD + or FD) or of attack of such a species on the substrate and/or supporting electrolyte and that the formation of the film probably accounts for the missing material.

Oxidation of FHH at constant current in 0.1 M $Bu_4NBF_4-CD_3COOD$ gave similar results (i.e., no H-D exchange). However, fluorenone, 9-acetoxyfluorene and 2-acetoxyfluorene were formed in low yields (Table 1). That neither fluorenone nor 9-acetoxyfluorene were detected when FDD was oxidized can presumably be attributed to the stronger C-D bond at the 9-position.

Further evidence of electrode passivation was supplied by cyclic voltammetry of fluorene (4.5 × 10⁻³ M) in 0.1 M Bu₄NBF₄-acetic acid at a platinum bead electrode. An irreversible peak with a peak potential of +1.61 V vs. s.c.e. was observed. Repetitive cycling of the electrode potential resulted in a markedly greater than normal drop in peak current, shifting of the peak to less anodic potentials and a crossing-over of the anodic and cathodic branches at +2.0 V vs. s.c.e.. Furthermore, subsequent stirring of the solution and resweeping did not fully restore the peak current to the original value. Removal and cleaning of the electrode did however accomplish this. No such effects were observed in sodium acetate - acetic acid solutions. The peak height was virtually the same as that for the same concentration of fluorene in 1 M NaOAcacetic acid.

From the above-mentioned results we conclude that the cyclic mechanism proposed earlier¹ (Scheme 2) to account for the low current yields of acetates is incorrect. One can support this conclusion by an estimate of the energy of activation for hydrogen abstraction by FH on a C-H bond of acetic acid. Using the benzyl radical as a model for FH' (necessitated by the lack of data for the FH' system) the bond energy-bond order (BEBO)⁴ and equibonding⁵ method both give $E_a = ca$. 20 kcal mol⁻¹ for attack on H-CH₂COOH.⁶ To compare, the much more reactive methyl radical has an experimental E_a of 10.2 kcal mol⁻¹ for the same process,7 and it is known that anodically generated methyl radical just barely can effect hydrogen abstraction from H-CH₂COOH.8

In Bu₄NBF₄-acetic acid media electrode passivation occurs and the oxidation is inhibited. It is probable that the film formation accounts for part or all of the lost fluorene in this medium. In NaOAcacetic solutions nuclear acetoxylation is favoured over side-chain acetoxylation.² However, this process is in competition with another, as yet unidentified, process. Our results suggest that the product(s) of this/these other reaction(s) are water-soluble, non-volatile or thermally unstable (since no unidentified peaks were observed in the GLC analysis). The formation of carboxylic acids or aldehydes is considered a possibility, although no direct evidence for their formation is available at present.

MATERIALS AND METHODS

Calculations. A computer program was written to calculate the final isotopic distribution of FHH, FDH and FDD after passage of a known amount of charge, based on the mechanism proposed in Scheme 2. Two cases were considered; oxidation of FHH in deuterated medium and oxidation of FDD in non-deuterated medium. Scheme 3 shows the system for the oxidation of FDD in non-deuterated medium. The program is based upon the following assumptions: The oxidation has a current efficiency of 100 %. The probability of electron transfer to each fluorene species is solely dependent on their relative concentrations. Abstraction of a deuterium atom from non-deuterated medium and of a hydrogen atom from deuterated medium is negligible. The relative probability of loss of D⁺, as opposed to loss of H+, from the radical cation FDH⁺ is estimated 9 to be 0.2. Note that each step in Scheme 3 involves oxidation to a radical cation, loss of a proton (or deuterium ion) and subsequent abstraction of a hydrogen atom. Thus, passage of 2 F mol⁻¹ through a solution of FDD in nondeuterated medium is predicted to give a product ratio for FDD:FDH:FHH of 14:67:20, whereas the same ratio for oxidation of FHH in deuterated medium is 53:33:14. Using values for the probability of loss of D⁺ as opposed to H⁺ of 0.15 or 0.25 gave results that differed only slightly from those above. Even if the process were only, e.g., 20% efficient, any significant H-D exchange would easily have been detected.

Calculations according to the BEBO and equibonding method were performed as described earlier.⁶

EXPERIMENTAL

Equipment and materials. The cyclic voltammetry equipment has been described previously. ¹⁰ Controlled potential and constant current electrolyses were carried out using an AMEL 552 potentiostat/galvanostat in conjunction with a coulometer built in this Department. GLC analyses were performed using either a Hewlett Packard model 3380A or 5830A gas chromatograph.

Fluorene (B.D.H., England) was recrystallized from methanol prior to use. Fluorene-9,9-d₂ and fluorene-9-d were prepared according to published procedures, 11,12 the latter being shown (MS, 1H NMR) to contain 69.5 % FDH and 30.5 % FDD.

NMR) to contain 69.5 % FDH and 30.5 % FDD. GLC examination of all three fluorene samples showed that they contained less than 0.1 % fluorenone or acetoxyfluorenes. All compounds gave satisfactory mass and ¹H NMR spectra. The relative abundancies of the peaks at m/e values M-2, M-1, M+1 and M+2 were found to be independent of whether the direct or GLC inlet was employed. A simple computer program was written to calculate the distribution of FHH, FDH and FDD from the relative abundancies of the peaks at m/e 166, 167 and 168. ¹H NMR spectroscopy was also used and gave results in agreement with the MS-method. However, analysis of a known mixture of FDD and FHH indicated that the MS method was more accurate (error $<\pm 1\%$). It was established that FDD did not undergo any H-D exchange when stirred at room temperature in 0.5 KOAc – acetic acid for 48 h. The limits of detection of the various products by GLC was typically 0.1 %.

Bifluorenyl, bifluorenylidene, 2- and 9-acetoxy-fluorenes were synthesized according to known methods. 13-16 Fluorenone (Fluka, Buchs, Switzerland) was used as received. Pentamethylbenzyl acetate, used as standard for GLC analysis, was prepared by the anodic oxidation of hexamethylbenzene. 17

Electrolyses. Oxidations were carried out in a small (ca. 5 cm³ electrolyte) undivided glass cell

FDD
$$\xrightarrow{-e^-, -D^+, +H^-}$$
 FDH $\xrightarrow{-e^-, -D^+, +H^-}$ FHH $\xrightarrow{-e^-, -H^+, +H^-}$

Scheme 3.

with platinum electrodes (1 cm²) at room temperature. At the end of the electrolysis the electrolyte was slowly pipetted into a separating funnel containing saturated sodium bicarbonate solution and diethyl ether. The aqueous phase was extracted with two more portions of ether and the combined ethereal extracts were then washed with saturated sodium bicarbonate solution and water (twice). Drying (anhydrous sodium sulfate) and concentration gave a solution suitable for analysis by GLC (2 m×0.3 mm 5 % neopentylglycol succinate on Chromosorb W at 210 °C with pentamethylbenzyl acetate as an internal standard). Isotopic analyses were carried out by GLC/MS. Subsequently the solvent was removed and the residue examined by both ¹H NMR and MS. The yields of fluorene and the acetoxyfluorenes, as determined by ¹H NMR were in agreement with those found by GLC. Note that the GLC/MS method was capable of distinguishing between nuclear and side-chain acetates when the substrate was the dideuterio form, FDD. The identities of all peaks observed on analysis by GLC were confirmed by GLC/MS and comparison of their retention times with authentic samples. The absence (less than 0.1 %) of bifluorenyl and bifluorenylidene was confirmed by GLC (3 % OV1 on Chromosorb W at 270 °C). The efficiency of the extraction procedure was determined by extraction of three samples of fluorene in 0.1 M Bu₄NBF₄acetic acid. GLC analysis gave an average "vield" of 102 %. In addition analysis of various electrolysis products before and after extraction gave virtually identical results.

A few experiments were carried out in a divided cell with a platinum foil anode (1 cm²) and a working compartment containing 15 cm³ of solution. The work-up and analysis procedure was identical to that described above. Analysis of the catholyte showed that virtually no diffusion of the substrate into the cathode compartment had occurred.

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