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Anodic Synthesis of Bimesityl by Oxidation of Mesitylene

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Anodic oxidation of mesitylene in acetonitrile containing different supporting electrolytes produces bimesityl. The reaction was found to be dependent on the concentration of mesitylene as well as on the choice of supporting electrolyte and anode material. The addition of water reduces the yield of bimesityl markedly. The optimum yield is obtained by electrolyzing a 2 M solution of mesitylene in acetonitrile containing tetrabutylammonium tetrafluoroborate at a platinum anode. On a preparative basis bimesityl is isolated in 49 % yield. Also formed is a nonamethyl-*m*-terphenyl (termesityl).

Anodic oxidation of aromatic compounds in the presence of different nucleophiles have been extensively studied from both mechanistic and preparative points of view in the last decade.[1] The over-all reaction is represented by the transfer of two electrons from the aromatic compound and substitution by a nucleophile (1 and 2).

Nuclear substitution:

$$ArH + Nu^- \longrightarrow ArNu + 2\,e + H^+ \quad (1)$$

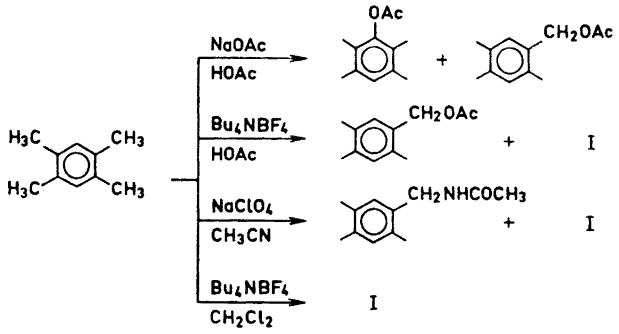
Side-chain substitution:

$$ArCH_3 + Nu^- \longrightarrow ArCH_2Nu + 2\,e + H^+ \quad (2)$$

Depending on the nucleophilic strength of the electrolysis medium either (1) or (2) or a mixed reaction will take place (for a substrate where both reactions are possible). If the nucleophile is cyanide ion, (1) takes place exclusively.[2–4] Oxidation in the presence of acetate ions results in both nuclear and side-chain substitution,[5–8] while oxidation in acetic acid with no acetate ions present results exclusively in side-chain substitution.[8,9] Reaction (2) is also the predominant reaction path in anodic acetamidation, where the main products are *N*-benzylacetamides.[10,11] However, in the last two reactions dehydrodimeric hydrocarbons (mainly diphenylmethanes) are also formed (3).

$$ArCH_3 \xrightarrow[-2e,\,-H^+]{} ArCH_2^+ \xrightarrow[-H^+]{ArCH_3} \text{diphenylmethanes} \quad (3)$$

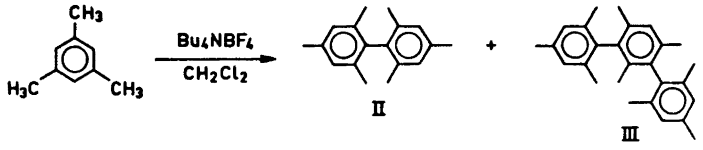
If the reaction medium is made less nucleophilic by using methylene chloride as solvent, anodic oxidation of durene produces 2,4,5,2′,3′,5′,6′,-heptmethyldiphenylmethane, I, as the major product.[12] The change in electrolysis product by the change in the electrolysis medium is shown in Scheme 1, when



Scheme 1

durene is the substrate (minor products have been omitted). It is seen that I is formed in increasing amounts when the medium is made less nucleophilic (I is formed in larger amounts in acetonitrile than in acetic acid).

A similar scheme may be drawn for mesitylene although some data are lacking. Anodic acetoxylation of mesitylene in sodium acetate/acetic acid gives mainly nuclear substitution whereas in acetic acid/Bu_4NBF_4 only side-chain substitution takes place.[9] Formation of a small amount of 2,4,6,2′,4′,6′-hexamethylbiphenyl (bimesityl), II, is also observed. In methylene chloride anodic oxidation of mesitylene produces two main products, bimesityl and 1,3,5,2′,4′,6′,2″,4″,6″-nonamethyl-*m*-terphenyl (termesityl), III, in addition to some chloro compounds (Scheme 2).[12]



Scheme 2

Thus in addition to the reactions outlined in (1) – (3) a fourth major path for anodic oxidation of aromatic compounds is represented by (4).

$$\mathrm{ArH} \xrightarrow[-e]{} \mathrm{ArH}^{\cdot+} \xrightarrow[-e,\ -2H^+]{\mathrm{ArH}} \text{biphenyls} \qquad (4)$$

Acetonitrile is less nucleophilic than acetic acid but more so than methylene chloride; therefore it was of interest to investigate anodic oxidation of mesitylene in acetonitrile. If bimesityl is formed, the reaction may be of preparative value. From a mechanistic point of view it is of interest to compare the behaviour of mesitylene with that of other alkylbenzenes.

RESULTS

Anodic oxidation of mesitylene was first carried out following the directions given by Eberson and Olofsson.[11] When mesitylene (0.2 M) in 50 ml 0.5 M $NaClO_4/CH_3CN$ was oxidized at a platinum anode at an anode potential of 1.60 V (*vs.* the saturated calomel electrode, SCE) until 0.2 F per mol of mesitylene had passed, the following products were detected: 3,5-dimethylbenzaldehyde, *N*-3,5-dimethylbenzylacetamide, 2,4,6,2′,4′,6′-hexamethyldiphenylmethane, 2,4,6,3′,5′-pentamethyldiphenylmethane, bimesityl, and termesityl. The major product was bimesityl but the current yield of this was only 3 %. From the results of Eberson and Olofsson [11] it can be seen that the major product in the anodic oxidation of several methylbenzenes in acetonitrile were the corresponding *N*-benzylacetamides and the current yields were in the range 30 – 70 %.

Since anodic coupling of mesitylene to bimesityl in methylene chloride is dependent on the concentration of mesitylene [12] the same would be expected in acetonitrile. In Table 1 it is seen that increasing the mesitylene concentration from 0.2 M to 1.0 M results in a yield of 25 % for bimesityl when sodium perchlorate is used as supporting electrolyte. In order to see if there is any difference in the reaction yield by using different electroinactive supporting electrolytes, the oxidation of mesitylene was run in the presence of five different salts. The results are given in Table 1 and indeed show that selecting the proper salt is important. Tetrabutylammonium tetrafluoroborate is the salt for optimizing the yield of bimesityl. From Table 1 it is also seen that the ratio of bimesityl to termesityl is constant.

Table 1. The effect of the supporting electrolyte on anodic oxidation of mesitylene (1.0 M) in acetonitrile at a platinum anode.

Supporting electrolyte[a]	% Current yield of II[b]	% Current yield of III[b]
$LiClO_4$[c]	25	3
$NaClO_4$[c]	25	3
Bu_4NPF_6[d]	23	4
Bu_4NClO_4[d]	32	5
Bu_4NBF_4[d]	39	6

[a] 0.2 M.
[a] Calculated after 0.2 F per mol mesitylene had passed.
[b] Anode potential 1.80 V.
[c] Anode potential 1.90 V.

By increasing the concentration of mesitylene no corresponding increase in the yield of by-products was observed. Instead, polymeric material was formed and coated the anode surface partially. However, this did not affect the electrolyses in any negative way. Similar behaviour was noted in the methylene chloride case.[12]

Since the best yield of coupling products was obtained using Bu_4NBF_4 as supporting electrolyte, a number of experiments were carried out in order to optimize the reaction conditions for obtaining bimesityl and termesityl. The results are shown in Table 2. First it should be noted that the yield of

Table 2. Anodic oxidation of mesitylene in 0.2 M Bu_4NBF_4/CH_3CN. The effect of mesitylene concentration and the anode material.

Mesitylene conc. (M)	Anode material	% Current yield of II[a]	% Current yield of III[a]
4.0[b]	Pt	37	6
2.0[b]	»	71	6
1.0[b]	»	39	6
4.0[c]	C	22	2
2.0[d]	»	30	2
1.0[b]	»	14	1
0.2[b]	»	3	–

[a] Calculated after 0.2 F per mol mesitylene had passed.
[b] Anode potential 1.90 V.
[c] Anode potential 1.60 V.
[d] Anode potential 1.50 V.

bimesityl reaches a plateau value when the mesitylene concentration is increased and the highest yield is obtained by using 2.0 M solutions. This is the case both on platinum and carbon anodes. However, the yields on the carbon anode are significantly lower than those on the platinum anode. It should also be noted that the ratio of bimesityl to termesityl is higher at the carbon anode. Thus, to be an anodic reaction, a remarkably high yield is obtained by selecting the proper reaction conditions.

The effect of added water on the yield of *N*-benzylacetamides was investigated by Eberson and Olofsson,[11] who found the reactions to be surprisingly insensitive to the water concentration. There is of course a major difference in that reaction and the mesitylene oxidation, since the intermediate in the formation of *N*-benzylacetamides is a benzyl cation, whereas a cation radical is the intermediate in the formation of bimesityl. It was, however, of interest to test the mesitylene oxidation in the presence of varying amounts of water. The reactions were carried out using both Bu_4NBF_4 and Bu_4NClO_4 as supporting electrolytes in order to see if there was any significant difference in the results obtained with these salts. Difference in substitution behaviour has been observed for oxidation of hexamethylbenzene in the presence of these salts.[13]

From the results in Table 3 it is clear that the formation of bimesityl is decreased considerably even at rather low water concentrations. Comparing the results obtained at a platinum and a carbon anode show that the effect of added water is more important at a platinum than at a carbon anode. Although bimesityl is formed in a larger amount at a platinum anode in anhydrous acetonitrile than at a carbon anode, the addition of water gives a sharp decrease in the yield at a platinum anode in contrast to the carbon

Table 3. Anodic oxidation of mesitylene (1.0 M) in acetonitrile. The effect of added water.

Added water conc. (M)	Anode potential	Anode material	Supporting electrolyte[a]	% Current yield of II[b]	Ratio II to IV[c]
0.1	2.2 V	Pt	Bu_4NBF_4	36	99:1
0.2	2.4	»	»	11	93:7
0.5	2.4	»	»	2	51:49
1.0	2.4	»	»	1	24:76
0	1.9	C	»	14	99:1
0.5	1.5	»	»	8	90:10
1.0	1.5	»	»	8	76:24
4.0	1.5	»	»	4	67:33
0.5	2.3	Pt	Bu_4NClO_4	3	74:26
0.5	1.5	C	»	15	97:3

[a] 0.2 M.
[c] Calculated after 0.2 F per mol of mesitylene had passed.
[b] IV includes 3,5-dimethylbenzaldehyde, 3,5-dimethylbenzyl alcohol and 2,4,6-trimethylphenol.

anode. The ratio of bimesityl to oxygen containing products is also higher at the carbon anode at the same concentration level. No particular change is observed by substituting perchlorate ion for tetrafluoroborate ion.

The formation of bimesityl in such a large yield is of course interesting from a preparative point of view. For that reason the reaction was run on a larger scale. When a 500 ml solution containing 1 mol of mesitylene and 0.05 mol of Bu_4NBF_4 in acetonitrile was electrolyzed at an anode potential of 2.0 V at a platinum anode, an isolated yield of 49 % bimesityl and 10 % termesityl was obtained. The reaction was run until 0.4 F per mol of mesitylene had passed. If the reaction was run to higher conversion the yield of bimesityl dropped due to polymer formation and further oxidation. Although the controlled potential conditions give a high yield of bimesityl, the reaction can be conveniently run under controlled current conditions with only a slight decrease in the yield.

A known chemical oxidation of mesitylene to bimesityl is the ferric chloride oxidation.[14] This reaction was repeated under the conditions used by Kovacic and Wu[14] and the yield of bimesityl was found to correspond to their reported value (30 – 38 %). However, it was found difficult to get pure bimesityl in this way due to the formation of chlorinated bimesityl. Interestingly, GLC analysis indicated that termesityl was also formed in this reaction.

DISCUSSION

The study of anodic oxidation of alkylbenzenes in acetonitrile by Eberson and Olofsson[1] showed that the major product in all cases was the corresponding *N*-benzylacetamide. Therefore it might be surprising to find that mesitylene does not follow the same reaction path. Using the same reaction conditions as they did *N*-3,5-dimethylbenzylacetamide was formed, but only as minor

product, instead the major product was bimesityl. It is quite clear that bimesityl is formed in a coupling reaction and therefore one would expect the highest yield at a high concentration of mesitylene, which is also borne out by the results.

Alkali metal perchlorates or tetra-alkylammonium perchlorates are the most commonly used supporting electrolytes in the study of anodic oxidation processes, when an electro inactive and a non-nucleophilic salt is desired. The results presented show that it can be important to change the nature of the anion. Tetrabutylammonium tetrafluoroborate is now easily available and seems to have promising qualities for use in anodic oxidation. It is more difficult to oxidize than perchlorates[15] and the hazard of distilling mixtures where perchlorates might be present is avoided.

The highest yield of bimesityl and termesityl is obtained by using a mesitylene concentration of 2.0 M, whereas still higher concentrations lead to a significant decrease in the yield, probably due to extensive polymer formation. Although polymers are formed in all oxidations of mesitylene in acetonitrile, too high a concentration of mesitylene might prevent the product (or intermediate) from leaving the vicinity of the anode and therefore the possibility of further oxidation of product or attack by a charged species on the product will increase. It is also of interest to note from Table 2 that the use of carbon as anode results in markedly lower yields of bimesityl. This is probably due to a weaker adsorption of mesitylene on carbon than on platinum. An adsorption effect can also explain the fact that the ratio of bimesityl to termesityl is higher when carbon is used as anode.

The cation radical generated by anodic oxidation of mesitylene will certainly be expected to react rapidly with water and therefore the results in Table 3 should not be unexpected. However, it should be remembered that Eberson and Olofsson[11] found that the formation of *N*-benzylacetamides by anodic oxidation of alkylbenzenes in acetonitrile containing sodium perchlorate was rather unaffected by the presence of water. They found that on oxidation of *p*-xylene the yield of *N*-4-methylbenzylacetamide dropped from 71 % to 38 % when the water content was increased from 0.1 M to about 3 M. In Table 3 it is seen that when the added water concentration was increased from 0.1 M to 1.0 M a considerable decrease in the yield of bimesityl takes place from 36 % to 1 %. Thus it is no doubt that in the coupling reaction the effect of added water is large and completely prevents the desired reaction even in rather low concentration. It is of interest to note that this effect is smaller on a carbon anode. It has already been mentioned that polymer formation accompanies the formation of bimesityl. When the reactions with added water were carried out, large amounts of polymeric material were also formed. However, one might suspect that in the latter case the polymers were of different type. In the anhydrous solvent they are probably composed of methylsubstituted polyphenyls. As is seen in the last column of Table 3, the ratio of bimesityl to oxygen containing products decreases as the water concentration increases but not enough to account for the loss in the bimesityl yield. If the cation radical reacts with water the product may either form mesitol or a charged species (or a radical after loss of a proton.) Mesitol is oxidized vary rapidly at the potential employed and could end up as poly-

mers. In the same way the charged species (or radical) may also end up as polymers.

In the work concerning anodic oxidation of mesitylene in methylene chloride[12] the different possible reaction paths leading to bimesityl were discussed and it was suggested that bimesityl was formed either by coupling of two cation radicals or by attack of a cation radical on the starting material. The same paths could also be responsible for the formation of bimesityl in acetonitrile.

$$ArH \xrightarrow{\text{oxid.}} ArH^{\cdot+} \xrightarrow[\text{attack on mesitylene}]{\text{coupling or}} Ar-Ar$$

That the second route is operating was shown by carrying out oxidation of mesitylene in the presence of benzene and the result showed that in addition to bimesityl a mixed biphenyl was formed and this was identified as 2,4,6-trimethylbiphenyl. Since benzene is not oxidized at the potential employed, the trimethylbiphenyl must be formed by attack of the mesitylene cation radical on benzene.

If benzene is oxidized in acetonitrile, no biphenyl is detected and only polyphenyls are formed[16]. This is no doubt due to the fact that biphenyl is oxidized at much lower potential than is benzene and would therefore be consumed very fast. Bimesityl on the other hand is oxidized in the same potential region as mesitylene and therefore has a good chance to survive further oxidation. The bimesityl molecule can be regarded as two separate mesityl units with little overlap between the π-electrons, due to the steric hindrance for rotation at the pivot bond, and therefore the oxidation potential will not be lower than mesitylene in contrast to the behaviour of the biphenyl-benzene pair.

The preparative value of anodic coupling of aromatic hydrocarbons is evident. In this work it is shown that bimesityl can be conveniently prepared by oxidation of mesitylene in acetonitrile and work is in progress to extend the reaction to other aromatic hydrocarbons. Although the preparation of bimesityl can be carried out under controlled potential conditions, only a small reduction in the yield was noted if controlled current was used. The latter way may be more convenient since no potentiostat or integrator is necessary to control the reaction.

Two other methods for the preparation of bimesityl were used in order to compare the yields. The Ullman reaction with 2,4,6-trimethyliodobenzene produced bimesityl in 31 % yield. The ferric chloride oxidation of mesitylene that has been studied by Kovacic and Wu[14] gave a yield of about the same magnitude as the electrolytic method, but it was difficult to obtain pure bimesityl due to the formation of chlorobimesityl.

EXPERIMENTAL

The electrolyses were carried out in a water-jacketed cell (volume 60 ml) equipped with a cylindrical platinum anode (surface area 50 cm^2) or a carbon plate anode (surface area 27 cm^2) and a platinum foil cathode (or a carbon cathode) and with stirring using a magnetic stirrer. The saturated calomel electrode was used as a reference electrode. The cell temperature was maintained at about 25°. The anode potential was controlled by means of the Model 557 potentiostat from Amel, Milan, Italy. The amount of charge

passed through the electrolyte was measured by an Amel Model 558 integrator. For constant current electrolysis a 60 V/2 A power supply from Radiak was used. Gas chromatographic analysis was carried out with a Perkin-Elmer Model 880 instrument, equipped with a Perkin-Elmer Model D 24 integrator, on a 2 m × 0.3 cm 5 % NPGS on Chromosorb W column. Mass spectrometric analysis was carried out with an LKB 9000 mass spectrometer in combination with GLC at 70 eV. NMR spectra were recorded with a Varian A 60 A NMR spectrometer.

Materials. Mesitylene, acetonitrile (0.02 % water) and lithium perchlorate were used without further purification. Anhydrous sodium perchlorate was prepared from commercial sodium perchlorate ($NaClO_4.3\ H_2O$) by dissolving it in a large amount of water at 150° and then allowing it to crystallize at 100°. The tetrabutylammonium salts were prepared by mixing equivalent amounts of tetrabutylammonium hydrogensulphate (AB Hässle, Gothenburg, Sweden) and the appropriate alkali metal salt in water. The precipitate was taken up in methylene chloride. The methylene chloride solution was washed with water, dried over molecular sieves and finally evaporated *in vacuo* to dryness. The solid residue was washed with ether and dried.

Electrolysis. For small scale electrolysis 50 ml solutions were made up from the appropriate amount of mesitylene and supporting electrolyte in acetonitrile. The electrolysis was then run using the anode potentials specified in the tables until 0.2 F per mol of mesitylene had passed through the solution. Acetonitrile was then removed by evaporation *in vacuo*. Ether was added to the residue and the insoluble salts were filtered off. The ether solution was washed with water, dried and finally reduced to a small volume and analyzed by GLC. 3,5-Dimethylbenzaldehyde, 3,5-dimethylbenzyl alcohol, and 2,4,6-trimethylphenol were identified by comparison with authentic samples. N-3,5-Dimethylbenzylacetamide (*m/e* 177), 2,4,6,3′,5′-pentamethyldiphenylmethane (*m/e* 238), and 2,4,6,2′,4′,6′-hexamethyldiphenylmethane (*m/e* 252) were identified solely by mass spectrometry. The yields of bimesityl and termesityl were calculated using biphenyl as standard.

Preparation of bimesityl and termesityl by electrolysis. A 500 ml solution, made up from mesitylene (1 mol) and tetrabutylammonium tetrafluoroborate (0.05 mol) in acetonitrile, was electrolyzed in a water-jacketed cell between a platinum anode and a carbon plate cathode at an anode potential of 2.0 V (*vs.* SCE) and with a current of about 0.7 A at a temperature of 25°. When 0.4 F per mol of mesitylene had passed, the electrolysis. was interrupted and acetonitrile and mesitylene were removed by distillation at reduced pressure. Ether was added to the residue in order to precipitate the salt (if the salt did not precipitate the ether layer was decanted), which was removed by filtration. The ether solution was evaporated *in vacuo* and the residue was distilled at reduced pressure. At 150 – 160°/11 mm bimesityl was collected (23.5 g, 49 % current yield, m.p. 102 – 102.5°) and the purity was found to be better than 99 % by GLC. When the pressure was reduced to 0.3 mm, 6 g of a semisolid product was obtained at 165 – 190°. This product was dissolved in pentane and subjected to column chromatography on alumina. After elution with pentane and removal of the solvent, the white crystalline solid was recrystallized from ethanol and gave 1,3,5,2′,4′,6′,2″,4″,6″-nonamethyl-*m*-terphenyl,[17] III, m.p. 124 – 127°. The mass spectrum gave peaks at m/e 356 (100 % abundance), 341 (48 %), 326 (13 %), and 311 (9 %). The NMR spectrum (in $CDCl_3$) showed signals at δ-values of 1.45 ppm (CH_3 in the 2′-position), 1.90 ppm (CH_3 in the 3,5,4′,6′,2″,6″-positions), 2.32 ppm (CH_3 in the 1- and 4″-positions), 6.94 ppm (H in the 2,6,3″,5″-positions), and 7.07 ppm (H in the 5′-position).

When the electrolysis was repeated using controlled current conditions, the current yield of bimesityl was 43 % at a current of 1 A and 44 % at 0.5 A.

Ullman reaction of 2,4,6-trimethyliodobenzene. Iodomesitylene (14 g) and 40 g of copper-bronze were intimately mixed and then heated up to 270° and maintained for 4 h. After cooling ether was added and the mixture was filtered and washed several times with ether. The residue, after removal of ether, was distilled to give bimesityl (2.1 g: 31 %) at 155°/15 mm.

Ferric chloride oxidation of mesitylene. Following the procedure of Kovacic and Wu [14] mesitylene (1 mol) was oxidized with ferric chloride (0.5 mol) under an argon atmosphere at about 20°. After work-up bimesityl was isolated by distillation at 155 – 170°/15 mm (21.1 g). After three crystallizations from ethanol the amount of chlorobimesityl was found to be 4 % (by GLC).

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