

Anodic Oxidative Functionalization of Toluene Derivatives

by

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Class of 2009

A thesis submitted to the
faculty of Wesleyan University
in partial fulfillment of the requirements for the
Degree of Bachelor of Arts
with Departmental Honors in Chemistry

ABSTRACT

Electrochemical oxidation is a powerful alternative to standard chemical oxidations in that it can often circumvent experimental limitations of synthetic organic chemistry. The goal of this project is to investigate the side chain functionalization of aryl methyl groups via electrochemical oxidation. Anodic oxidations of toluene, 4-chlorotoluene, 2,4-dichlorotoluene, methyl p-toluate, 4, 4'-dimethylbiphenyl, 4,4'-dimethyl-2-nitro-1,1'-biphenyl, N-benzylacetamide, and N-(4-chlorobenzyl)-acetamide were carried out, some under direct oxidation and others via electrocatalysis.

Under the conditions the electrolyses were carried out, the following are observed: 1) chlorination of substrates with two proposed mechanisms to explain the phenomenon: a) oxidation of the substrate bearing a chlorine group or b) the generation of Cl^+ by the catalyst employed in the indirect oxidation; 2) as more coulombs pass through the electrolysis solution, the subsequent side chain oxidation of an amide to an aldehyde functional group is observed; and 3) the ratio of formation of an aldehyde to that of an amide is dependent on the water concentration in the electrolysis cell.

“Attitude is a small thing that makes a big difference.”

ACKNOWLEDGEMENTS

I would like to extend my gratitude to Dr. Fry for the opportunity to conduct research in his lab; it has been an honor and an enriching experience. Thank you for your unwavering support, guidance, wisdom, and humor through the years as my advisor and mentor.

Thanks to the rest of the Fry Group for making this an interesting learning experience. Special thanks to Anthony Davis and Peter Lambert. Thank you to Anthony for constantly taking time and going out of his way to help and encourage me for the entirety of this project. Thank you to Peter for his company and keeping up with me in the lab. In addition, many thanks to Anthony for carrying out the *ab initio* calculations on the ionization potentials of the compounds.

Thanks to the faculty of the Wesleyan Chemistry Department for all the events that have fueled me through the years.

Thanks to Professor Laurel Appel, Santos Cayetano, and the other fellows of the Ronald E. McNair Program for their support. Also thanks for the opportunities presented to me by the Ronald E. McNair Program.

Financial support by the Ronald E. McNair and Howard Hughes Programs are greatly appreciated.

Thanks to my housemates and friends for acting as a support group and cheerleaders.

Finally, thanks to my parents for ultimately allowing me to make my choice without which I would not be writing this thesis.

List of Tables:

| <u>Table</u> | | <u>Page</u> |
|--------------|--|-------------|
| 1 | Structures and names of compounds to be anodically oxidized..... | 5 |
| 2 | Calculations for ionization potential of 1-6 and peak oxidation potential values from CV..... | 23 |
| 3 | Retention times of the oxidized product and the two synthesized amides from acylation..... | 77 |

List of Figures

| <u>Figure</u> | <u>Page</u> |
|---------------|---|
| 1 | Reaction pathways for the anodic oxidation of hydrocarbons.....3 |
| 2 | Electrolysis setup: Compounds are oxidized in a 3-neck 10 mL round bottom flask with ports for the counter, working, and reference electrodes.....7 |
| 3 | Scheme of electrocatalysis.....12 |
| 4 | Organic redox catalysts.....13 |
| 5 | Plot of I.P. vs E_p24 |
| 6 | GC of electrolysis of toluene after 424.6 coulombs of current were passed.....26 |
| 7 | GC of anodic oxidation of toluene, post work-up.....27 |
| 8 | Mass spectrum of N-benzylacetamide.....28 |
| 9 | Mass spectrum of benzoic acid.....29 |
| 10 | GC of oxidation of toluene with the addition of water.....30 |
| 11 | Mass spectrum of benzaldehyde.....30 |
| 12 | GC of oxidation of 1:1 mol 4-chlorotoluene (2) and 2,4- dichlorotoluene (3).....31 |
| 13 | Mass spectrum of 4-chlorotoluene.....32 |
| 14 | Mass spectrum of 2,4-dichlorotoluene.....33 |
| 15 | Mass spectrum of 4-chlorobenzaldehyde.....34 |
| 16 | Mass spectrum of 4-chlorotoluene; post 297 coulombs.....35 |
| 17 | Mass spectrum of 4-chlorobenzaldehyde; post 297 coulombs.....36 |
| 18 | Mass spectrum of 2,4-dichlorotoluene; post 297 coulombs.....37 |
| 19 | Mass spectrum of N-(4-chlorobenzyl)-acetamide; post 297 coulombs.....38 |
| 20 | GC of 4-chlorotoluene from electrolysis; post-workup.....39 |

| | | |
|----|--|----|
| 21 | Mass spectrum of 2,4-dichlorobenzaldehyde..... | 41 |
| 22 | Mass spectrum of 2,4,6-trichlorotoluene..... | 42 |
| 23 | Mass spectrum of benzaldehyde..... | 43 |
| 24 | Mass spectrum of phenyl acetate..... | 44 |
| 25 | Mass spectrum of phenol from post-workup of oxidation of N-benzylacetamide..... | 45 |
| 26 | GC of crude product from synthesis of 2a | 46 |
| 27 | Mass spectrum of 2a in the crude product mixture..... | 47 |
| 28 | Mass spectrum of diacylated N-chlorobenzylamine in the crude product mixture..... | 47 |
| 29 | GC post flash column chromatography indicating 2a as the isolated product..... | 48 |
| 30 | Mass spectrum of 4-chlorobenzaldehyde (r.t. different than that from electrolysis of 4-chlorotoluene because of a different GC/MS method)..... | 49 |
| 31 | Mass spectrum of methyl 3-chloro-4-methylbenzoate; post 1040 coulombs..... | 51 |
| 32 | Mass spectrum of methyl 3,5-dichloro-4-methylbenzoate, post 1559 coulombs..... | 52 |
| 33 | Mass spectrum of 7a , methyl 3-chloro-4-methylbenzoate..... | 54 |
| 34 | Mass spectrum of 7b , methyl 4-(chloromethyl) benzoate..... | 55 |
| 35 | Structures of 7b and 4 and table of ¹ H NMR data values for 7b and 4 that was present in the ¹ H NMR sample..... | 55 |
| 36 | Mass spectrum of 4-(4-methylphenyl)benzaldehyde, purchased from Fisher (5d')..... | 57 |
| 37 | Mass spectrum of 4-(4-methylphenyl)benzaldehyde (5d)..... | 58 |
| 38 | Mass spectrum of 4-(4-methylphenyl)benzoic acid (5e)..... | 59 |
| 39 | Mass spectrum of biphenyl-4, 4'-dicarboxylic acid (5f)..... | 60 |
| 40 | Mass spectrum of 4, 4'-biphenyldicarboxaldehyde (5g)..... | 61 |

| | | |
|----|--|----|
| 41 | Mass spectrum of a compound with a mass of biphenyl-4, 4'-dicarboxylic acid methyl ester (5j)..... | 62 |
| 42 | Mass spectrum of N-([1,1'-biphenyl]-4-ylmethyl,4'methyl)-acetamide (5k) | 64 |
| 43 | Mass spectrum of 4,4'-dimethyl-2-nitro-1,1'-biphenyl (6)..... | 65 |
| 44 | ¹ H NMR spectrum of 4, 4'-dimethyl-2-nitro-1, 1'-biphenyl (6)..... | 66 |
| 45 | 2D COSY spectrum of 6 | 67 |
| 46 | Expansion of figure 45 aromatic region of 2D COSY of 6 | 68 |
| 47 | Mass spectrum of 4-aldehyde, 4'methyl-2'-nitro-1, 1'-biphenyl (6a)..... | 70 |
| 48 | ¹ H NMR spectrum of 4-aldehyde, 4'methyl-2-nitro-1, 1'-biphenyl..... | 71 |
| 49 | Three trends observed in the overall anodic oxidation of studied compounds where C ₆ H ₅ RR' represents compounds 1-6 , 1a , and 2a | 72 |
| 50 | Aromatic iodination ¹ and side chain acetamidation..... | 73 |
| 51 | Mass spectrum of N-benzylacetamide from synthesis; scheme 2; r.t.: 7.703min..... | 76 |
| 52 | Mass spectrum of N-benzylacetamide post electrolysis; r.t.: 7.784min..... | 76 |
| 53 | Proposed mechanism for electrolysis of toluene to N-benzylacetamide..... | 78 |
| 54 | Anodic oxidation of 1 to benzaldehyde..... | 79 |
| 55 | Anodic oxidation of 2 to 4-chlorobenzaldehyde..... | 81 |
| 56 | GC from electrolysis of 4-chlorotoluene; post 152.44coulombs..... | 83 |
| 57 | GC from electrolysis of 4-chlorotoluene; post 297coulombs..... | 83 |
| 58 | Mechanism for oxidation of N-(4-chlorobenzyl)-acetamide to 4-4-chlorobenzaldehyde..... | 84 |
| 59 | Proposed mechanism for the formation of Cl ⁺ from substrate..... | 85 |
| 60 | An alternate proposed mechanism of chlorination via the catalyst as chlorine donor..... | 86 |
| 61 | Dimerization of 4,4'-dichloro-2,2',2''-trinitrotriphenylamine (Q)..... | 87 |

| | | |
|----|--|-----|
| 62 | Indirect oxidation of 3 , post 168 coulombs..... | 89 |
| 63 | Indirect oxidation of 3 , post 250 coulombs, noting the absence of N-[(2, 4-dichlorophenyl)-methyl]-acetamide..... | 89 |
| 64 | Mass spectrum of N-[(2, 4-dichlorophenyl)-methyl]-acetamide..... | 90 |
| 65 | TLC plate of electrolysis solution, 3 against benzaldehyde, 1 & phenyl acetate, 2 | 92 |
| 66 | GC of mixture of phenyl acetate (synthesized) and that of the electrolysis solution from oxidation of 4-benzylacetamide..... | 93 |
| 67 | Mass spectrum of methyl 3-chloro-4-methylbenzoate, purchased from Fisher..... | 99 |
| 68 | Structures of compounds 7b , 7a , and 4a | 100 |
| 69 | Anodic oxidation of 5 to its respective aldehydes and acids: 4-(4 methylphenyl)benzaldehyde (5d), 4-(4-methylphenyl)benzoic acid (5e), biphenyl-4, 4'-dicarboxylic acid (5f), 4, 4'-biphenyldicarboxaldehyde (5g)..... | 102 |
| 70 | Scheme for oxidation of an aldehyde to a methyl ester via acetate..... | 103 |
| 71 | Indirect oxidation of 5 to 5k | 104 |
| 72 | Anodic oxidation of 6 | 107 |

List of Abbreviations

| <u>Abbreviation</u> | <u>Definition</u> |
|--------------------------|---|
| A | ampere |
| μL | microliter |
| ^1H | hydrogen (atomic mass = 1 amu) |
| Ac_2O | acetic anhydride |
| amu | atomic mass units |
| CD_3CN | acetonitrile |
| CH_2Cl_2 | methylene chloride |
| E_p | oxidation potential |
| eq. | equivalent |
| EtOAc | ethyl acetate |
| F | Faraday, equals 96,485 C / mol(e) |
| g | gram |
| G/C | gas chromatography |
| I.P. | ionization potential |
| M | molarity= mole per liter |
| m.p. | melting point |
| m/z | the mass of an ion divided by the electrical charge of the ion. Normally, the charge is +1. m/e is used synonymously |
| mg | milligram |
| MHz | megahertz |
| mL | milliliter |

mmol

milli mole

NaHCO_3

sodium bicarbonate

r.t.

retention time

TABLE OF CONTENTS

| | <u>Page</u> |
|--|-------------|
| Abstract..... | i |
| Acknowledgments..... | iii |
| List of Tables..... | iv |
| List of Figures..... | v |
| List of Abbreviations..... | ix |
| I. Introduction..... | 1 |
| A. Objective for Research..... | 1 |
| B. Brief Explanation of Oxidation..... | 6 |
| C. A Brief Introduction of Electrolysis..... | 8 |
| D. Potential-Controlled Electrolysis..... | 10 |
| E. Indirect Electrolysis: Electrocatalysis..... | 11 |
| F. Organic Electrocatalysts..... | 12 |
| II. Results..... | 14 |
| A. Cyclic Voltammetry..... | 14 |
| B. Substituent Effects on Redox Potentials..... | 23 |
| C. Syntheses and Preparative Scale Electrolyses: Anodic Oxidation of : | 26 |
| (1). Toluene (1)..... | 26 |
| (2). 1:1 mol 4-chlorotoluene: 2,4-dichlorotoluene..... | 31 |
| (3). 4-chlorotoluene (2)..... | 35 |

| | | |
|-------|---|-----|
| (4) | 2,4-dichlorotoluene (3)..... | 40 |
| (5) | N-benzylacetamide (1a)..... | 43 |
| (6) | Synthesis of N-(4-chlorobenzyl)-acetamide (2a)..... | 46 |
| (7) | N-(4-chlorobenzyl)-acetamide (2a)..... | 49 |
| (8) | Methyl p-toluate (4)..... | 50 |
| (9) | Synthesis of methyl 4-(chloromethyl) benzoate (7b)..... | 53 |
| (10a) | 4,4'-Dimethylbiphenyl (5)..... | 56 |
| (10b) | 4, 4'Dimethylbiphenyl (5) with 4, 4', 4''-trichloro-2-nitrotriphenylamine..... | 63 |
| (11) | Synthesis of 4,4'-Dimethyl-2-nitro-1,1'-biphenyl (6)..... | 65 |
| (12) | 4, 4'-dimethyl-2-nitro-1,1'-biphenyl (6)..... | 69 |
| III. | Discussion..... | 72 |
| IV. | Experimental..... | 108 |
| A. | Synthesis..... | 108 |
| B. | Electrolysis..... | 113 |
| V. | References..... | 122 |

INTRODUCTION

A. Objective for Research

Our interest lies in the anodic functionalizations of substituted toluene derivatives. There is much interest in the oxidation of methyl groups on aromatic rings as it is a frequently used procedure in organic synthesis and is of industrial importance; for example, the oxygenates are valuable intermediates in the production of polymers, rubbers, and resins.¹ However, many oxidations of methyl aromatics are carried out by the routes given in classic organic chemistry, which employs transition metal oxidants and harsh reaction conditions,² while also generating large amounts of byproducts and waste. For example, *p*-methoxy benzaldehyde, a valuable fragrance, is manufactured by oxidation of anisole using potassium permanganate.³ In addition, the workup and isolation of the products are also tedious and call for use of additional chemical reagents and thus generate more waste. The methodology of electrochemical oxidations, on the other hand, provides a basis for environmentally friendly techniques as it often uses less toxic raw materials, safer solvents, employs more atom-efficient processes, greatly reduces the emission of waste, and provides easier methods for the isolation of products.⁴

Besides the necessity of environmentally friendly processes, selective oxidations of methyl groups on aryl rings are often difficult using conventional organic oxidations. For example, the initial oxidation products are often more susceptible to oxidation than the substrate; the methyl group is likely to be over-oxidized to the carboxylic acid. Thus, in an attempt to overcome environmental issues and oxidation difficulties often encountered in traditional organic synthesis,

electrochemical oxidation was employed in this study to investigate functionalization of aryl methyl groups.

The initiation step in the anodic oxidation of aromatic hydrocarbons is commonly the removal of an electron from the π -electron system to form a cation radical. The cation radical is recognized as the first formed intermediate and the reaction mechanism is inferred from the follow-up chemical or electrochemical reaction. This is called the ECE mechanism⁵ (the letter E symbolizes the electrochemical step and C the chemical step) where the electron transfer is followed by a fast chemical reaction and the product undergoes further oxidation at the same applied potential.

For the anodic oxidation of methyl (hydrocarbon) groups, the reaction paths that can follow from the initial electron transfer to a cation radical are shown in figure 1: the cation radical can transfer a proton to a suitable base to yield a radical, and the radical can proceed to lose an electron to the anode to give a monocation (path 2), or alternatively, the cation radical can transfer a second electron to form a dication (path 1)*. The cation radical, dication and the monocation can all be subjected to attack by nucleophiles; the nature and reactivity can be controlled by the conditions of the electrolysis setup. The cation radical, **a**, and the radical, **b** can also undergo pathways available to radical species.

* this pathway has been disputed as unlikely to occur due to the very small disproportionation equilibrium constants of the usual cations, but may occur in some situations.⁶

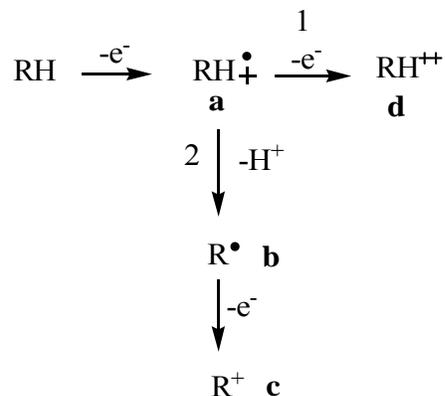


Figure 1: Reaction pathways for the anodic oxidation of hydrocarbons.

It comes as no surprise that the four reactive intermediates, **a-d**, can lead to a wide spectrum of products. The nature of the products obtained from a particular electrolysis will depend on 1) the relative stabilities of the four intermediates (more or less dependent on the nature of the substrate); 2) the potential at which the electrolysis is carried out (discussed later); 3) the nature and concentration of the nucleophiles in the system; and 4) the availability of proton acceptors. Thus, electrochemical oxidations offer fluidity and a range of controllable parameters to affect experimental outcomes fit to the desired outcome of the researcher: parameters 2-4 are fully subjected to the control of the researcher. For example, Steckhan, et al ⁷ studied the indirect side chain oxidation of alkyl aromatic compounds and presented that methyl benzoates were obtained electrochemically under neutral or slightly acidic conditions and orthobenzoic acid trimethyl esters were formed using slightly basic conditions at low potentials in ethanol using tris(2,4-dibromophenyl)amine as a redox catalyst. Additionally, his study on the oxidation of benzylic alcohols illustrated that at low potentials, benzaldehydes are formed in high yield using catalytic amounts of triarylamine cation radicals as electron transfer agents.⁸ When

the reaction takes place in methanol as opposed to acetonitrile, aldehyde is formed as the major product, if small amounts of Na_2CO_3 are present. In the absence of an added base, either 2,6-lutidine or Na_2CO_3 , dimethyl acetal predominates. As presented, Steckhan found that the material of the cathode also influenced the outcome of the results: cathodic formations of dimeric benzaldehyde were suppressed when a platinum cathode was used while carrying out the oxidation under neutral conditions. Furthermore, in the anodic oxidation of toluene in acetonitrile by Parker and Burget,⁹ the distribution of the five products observed was dependent on the anode potential and the concentration of water.

Thus, it is clear that the fate of the cation radical or any of the other three intermediates, **c-d**, and hence the nature of the product formed is dependent on the conditions of the electrolysis system.

Anodic oxidation to transform the functionality of the methyl groups was carried out on the substrates of interest, table 1. Cyclic voltammograms were taken to obtain the oxidation peak potentials of the compounds and preparative electrochemical oxidations were carried out, some in the presence of a redox catalyst and some via direct electrolysis (discussed later in this section) in 0.1M lithium perchlorate in acetonitrile. Synthesis was performed throughout the project when necessary to compare products from electrolysis or to prepare substrates of interest.

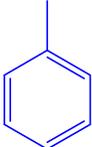
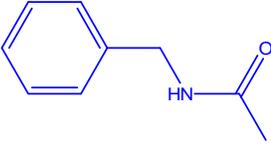
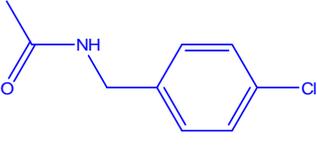
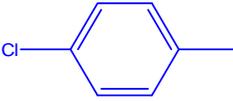
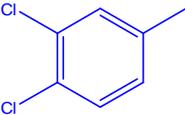
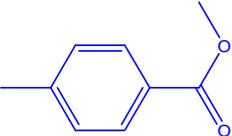
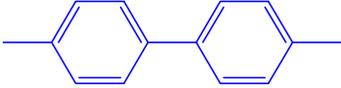
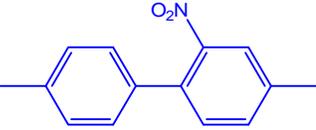
| | | |
|--|---|---|
| (1) Toluene | (1a) N-benzylacetamide | (2a) N-(4-chlorobenzyl)-acetamide |
|  |  |  |
| (2) 4-chlorotoluene | (3) 2, 4-dichlorotoluene | (4) Methyl p-toluate |
|  |  |  |
| (5) 4, 4'-dimethylbiphenyl | (6) 4,4'-dimethyl-2-nitro-1,1'-biphenyl | |
|  |  | |

Table 1: Structures and names of compounds to be anodically oxidized.

B. Brief Explanation of Oxidation

What does a freshly cut fruit that turns brown have in common with a copper penny that suddenly turns green or a bicycle fender that becomes rusty? They are all part of a process called oxidation. Oxidation is the interaction between oxygen molecules and any other substances that they may come into contact with. However, with the discovery of electrons, oxidation is technically defined as the loss of at least one electron when two or more substances come into contact and the substances may or may not contain oxygen. Oxidation does not necessarily have to be a bad thing; it is used in a wide variety of industries such as in the production of cleaning products and oxidizing ammonia to produce nitric acid, which is used in most fertilizers. Other times, oxidation can be destructive, such as the rusting of an automobile part or the spoiling of fresh fruit. Oxidation can also be extended to include the loss of hydrogen, the gain of oxygen or an increase in the oxidation number of an atom.

True oxidation happens on a molecular level — we only see the large-scale effects as the oxygen causes free radicals on the surface to break away. Because electrons are neither created nor destroyed in a chemical reaction, reduction is inherently linked to oxidation. Reduction describes the gain of electrons/ hydrogen, loss of oxygen or a decrease in the oxidation number of an atom/ion, or molecule.

The oxidation of compounds studied here is performed in electrolytic cells. Electrochemical galvanic cells are powered by redox reactions which are spontaneous and the electrical energy produced is harnessed in a battery. The reverse reaction is non spontaneous and requires electrical energy to occur and are termed electrolytic cells. The free energy is supplied in the form of electrical work done on the system by the surroundings whereas for galvanic cells, the free energy as a result of the cell

reaction is extracted as work done on the surroundings—this is the fundamental difference between the two.

Electrolytic cells are widely used to produce certain metals like aluminum from their oxides or ores and also to electroplate gold and silver onto jewelries. Below is a depiction of an electrolytic cell used in the oxidation of studied compounds:

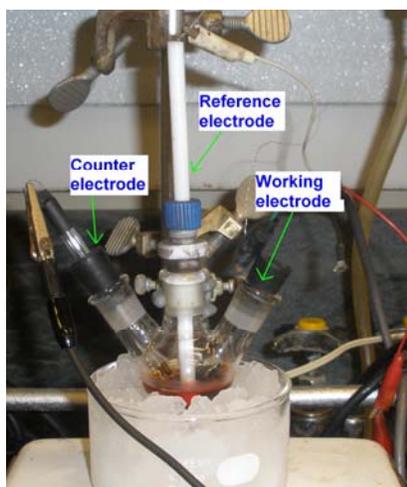


Figure 2: Electrolysis setup: Compounds are oxidized in a 3-neck 10 mL round bottom flask with ports for the counter, working, and reference electrodes.

The working electrode consists of a 1 cm x 3 cm piece of carbon cloth through which a 10 cm platinum wire transverses. The counter electrode consists of a piece of platinum supported by a platinum wire. The reference electrode is composed of a silver wire fitted in a Teflon tube sealed with porous glass plug and contains a solution of 0.1M silver nitrate (AgNO_3) in acetonitrile, CH_3CN .¹⁰ In the cell, 10mL of 0.1M lithium perchlorate (LiClO_4)_{in} CH_3CN is used as the supporting salt electrolyte.

C. A Brief Introduction of Electrolysis

Electrochemistry studies the chemical effects of electricity and electrolysis is one of its main forms—a chemical reaction that proceeds directly under the influence of an electric current. An electrochemical reaction is a heterogeneous redox reaction¹¹—anodic and cathodic reactions that occur at the electrodes and involve electron transfer to or from an electroactive species at metal-solution interfaces. The anode and the cathode are the positive and negative metal conductors, respectively, and reduction occurs at the cathode, whereas oxidation, at the anode. The most easily oxidized species supply electrons to the positive charge developed on the anode and similarly, the most easily reduced species accept electrons from the negative charge that develops on the cathode.

Current is carried through the electrolysis cell by 1) electronic conduction through the metal electrodes and external connectors; 2) transfer of electrons across metal-solution boundary; and 3) the ionic conduction across the solution between the electrodes.

The electrode potential is a crucial factor in electrochemical reactions in the conversion of substrates to desired products. Haber in his studies of electro-reduction of nitrobenzene was the first to realize the importance of the electrode potential. He identified phenylhydroxylamine at low negative potentials and aniline at more-negative potentials.¹² Electro-oxidations of many organic compounds proceed in stepwise fashion: the loss of electrons followed by a chemical reaction. Thus, to obtain selective products, it is important to produce the desired reactive species in the electrolysis stage—mediated by the electrode potential, and having the appropriate constituents in the electrolysis media, such as the electrode, solvent, or other

additives such that the reactive species produced by the loss of electrons can be directed to the desired product.

Faraday in his studies of oxidation of acetic acid in the early nineteenth century illustrated the important consequences of the passage of current in an electrolysis and summed them up in what are known as Faraday's laws of electrolysis: first, the amount of substrate that undergoes chemical change or reaction at an electrode is proportional to the quantity of electricity passed and second, the amounts of chemical changes produced by the same quantity of electricity to different substances are proportional to their formula weights.

Electric charge, q , is measured in coulombs. The amount of charge carried by one mole, or Avogadro's number of electrons is known as the faraday, F ; expressed in coulombs per mole. For most purposes, 96,500 coulombs is used as the value of the Faraday. The electric charge on an electron = 1.602×10^{-19} C or 1.602×10^{-19} A s. For one coulomb to pass a given point, the number of electrons passing = $1 / 1.602 \times 10^{-19}$ or 6.24×10^{18} .

- $F = \frac{\text{the number of electrons per mole}}{\text{by the number of electrons per coulomb}} = 96,485 \text{ C / mol(e)}$
- $\text{Total Charge (C)} = \text{\#mol(e)} \times 96485 \text{ C / mol(e)}$

D. Potential- Controlled Electrolysis

Electrochemical oxidation and reduction are powerful alternatives to standard synthetic chemistry: 1) It can often circumvent experimental limitations of synthetic organic chemistry; 2) High selectivity can occur with milder conditions, does not require any harsh chemical redox reagents, and also produces less toxic waste; thus is environmentally benign; and 3) Isolation of products is easier.⁴

The compounds of interest were studied via preparative scale electrolysis. Two techniques are often employed for preparative scale electrolyses: constant-current and constant-potential. The electrochemical oxidations of the compounds discussed here were all carried out at constant-potential. As its name implies, constant-potential electro-oxidation consists of an experiment in which the electro-reaction is allowed to occur at an electrode whose potential is controlled to a desired value. The potentiostat is the instrument used to affect the constant-potential power supply. The potential at which the electro-oxidation is to be run is chosen from results of potentiostatic steady-state measurements or cyclic voltammetry. In the three-cell electrolysis employed for the studies of compounds of interest, the desired potential on the working electrode is maintained relative to the reference electrode. The current that flows between the working and the counter electrode is indicated on the ammeter and the current passing between the reference and the working electrode is negligible. Controlled-electrode potential electro-oxidations are allowed to proceed until the current has dropped to some low value near the background's current or when the substrate of interest has disappeared.

E. Indirect Electrolysis: Electrocatalysis

Some of the electro-oxidations of the compounds of interest were studied via direct oxidation. For some, indirect electrolysis or electrocatalysis were performed. This process is called indirect electro-oxidation because an electrochemical reaction is affected on substance A to create a chemical transformation on substance B: oxidation (or reduction) of substance A forms a species that subsequently reacts with the substrate of interest (B) to generate the desired product. Thus the function of A is to mediate electron transfer which will result in the chemical transformation of B. Substance A is also known as an electrogenerated reagent—it is continuously regenerated in its active form at the surface of the electrode and is only needed in catalytic amounts, figure4.

Indirect catalysis is a kinetic, rather than a thermodynamic phenomenon. Substrate B undergoes a redox conversion at a lower potential than what is required for its direct oxidation because one or more steps in the mediated process are generally faster than those in direct electrolysis. The electrochemical formation and regeneration of redox agents widens the potential range of electro-oxidation, as well as affording higher or totally different selectivities with lower levels of energy input. Thus, the choice of an electrocatalyst is important; when indirect catalysis was employed in studying the substrate of interest, the oxidation potential of the catalyst chosen needed to be close enough to that of the substrate ($\pm 0.4V$) for the catalyst to be able to chemically oxidize the substrate.

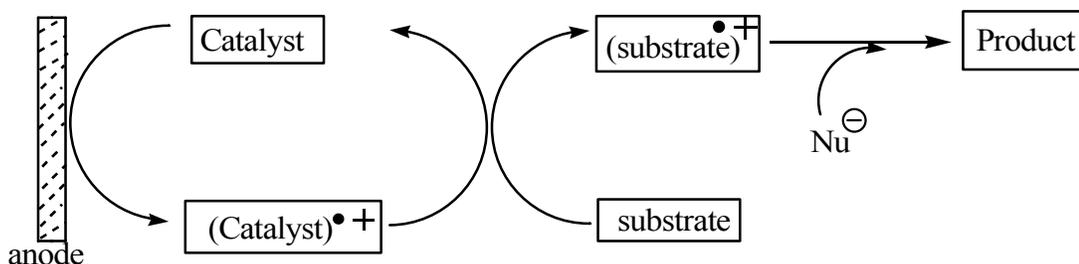


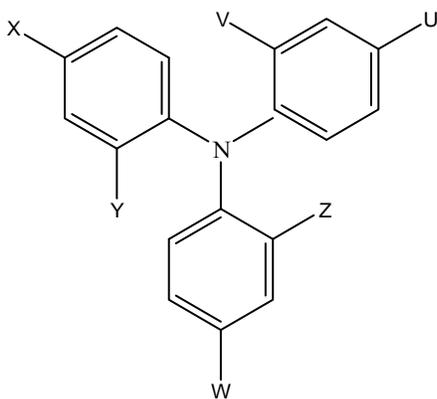
Figure 3: Scheme of electrocatalysis.

F. Organic Electrocatalysts

Electrocatalysts partake in both its own electrolysis at the electrode and the chemical redox reaction of the substrate. As mentioned, the choice of which electrocatalyst to employ in an indirect electrocatalysis is crucial. Our group has studied and synthesized^{13,14,15} a series of substituted triphenylamines as electrocatalysts for redox electro-reactions. Some of the desirable properties of electrocatalysts that are sought after are: First, the stability of the electrocatalyst in both its reduced and oxidized forms in the electrolysis cell. The destruction of the active form of the catalyst would render it catalytically inactive. Second, the electrocatalyst, in both its reduced and oxidized forms should be soluble in the electrolysis solution. Third, the active form of the catalyst be selective for the substrate of interest rather than other constituents in the electrolysis medium. For example, the oxidized catalyst should have more ease at oxidizing the substrate than the solvent. Lastly, the redox process of electrocatalyst should be as irreversible as possible to ensure a rapid electron exchange with the electrode and again with the substrate, so as to minimize any occurrence of other side reactions.

Schmidt & Steckhan,¹⁶ along with our groups' studies have shown that the oxidation potential of electrocatalysts increase with the increasing amount of electron-withdrawing groups as substituents. The presence of such electrocatalysts in electrolysis allows for oxidation to occur at lower potentials—crucial in making anodic oxidations widely applicable.

The catalysts used in this study, synthesized and studied extensively via computational method by our lab^{13,14} are shown below, with their oxidation potentials:



Catalyst 1: tris-(4-bromophenyl)-amine ($E_p=0.781V$): $X=U=W=Br$; $Y=V=Z=H$
 Catalyst 2: 4,4',4''-Trimethyl-2,2',2''-trinitrotriphenylamine, ($E_p=1.281V$) : $X=U=W=Me$; $Y=V=Z=NO_2$
 Catalyst 3: 4,4',4''-Trichloro-2,2',2''-trinitrotriphenylamine, ($E_p=1.563V$): $X=U=W=Cl$; $Y=V=Z=NO_2$
 Catalyst 4: 4,4',4''-Trichloro-2-nitrotriphenylamine, ($E_p=0.960V$): $X=U=W=Cl$; $Y=NO_2$

Figure 4: Organic redox catalysts.

RESULTS

A. Cyclic Voltammetry (CV)

CV is an attractive method that enables us to obtain the basic characteristics of a compound's mechanism of electrode reactions in a relatively short period of time.

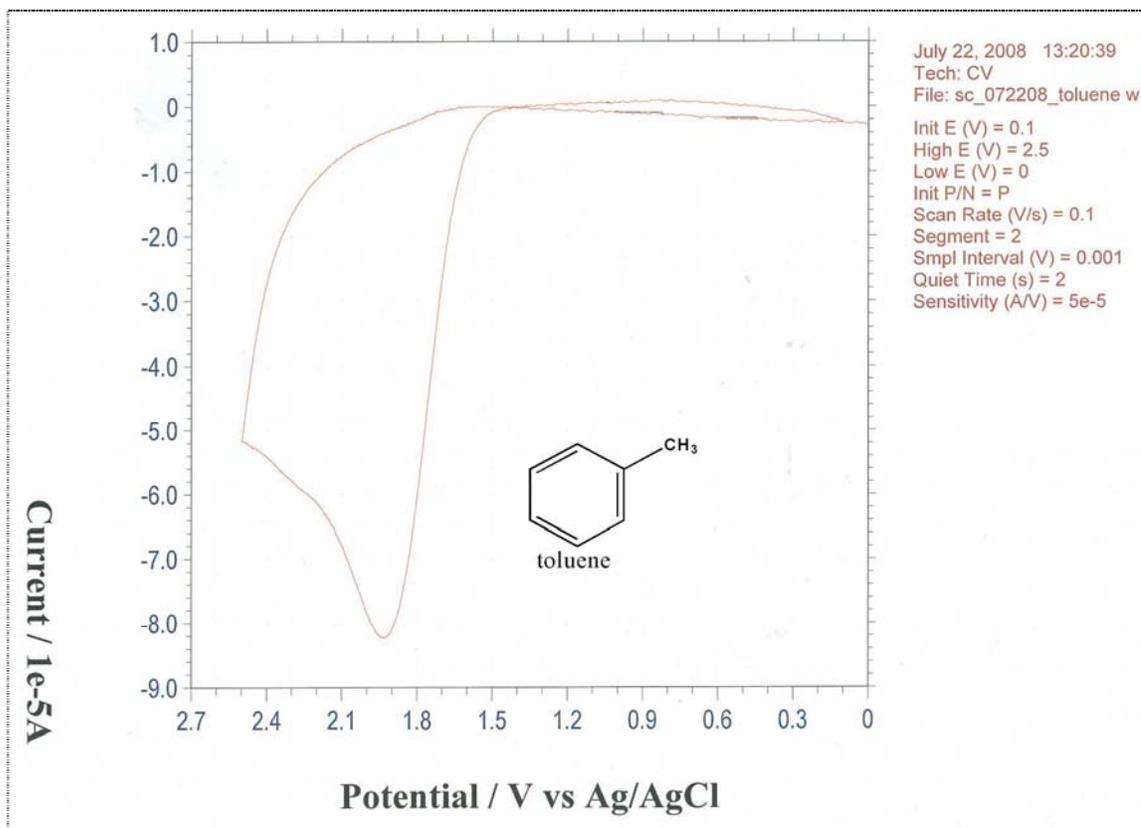
Some of the useful characteristics of the studied compound that can be extracted from a CV: 1. The oxidation potential of the compound

2. Whether the studied compound's oxidation is reversible or irreversible, i.e., whether the initial intermediate is long- or short-lived.

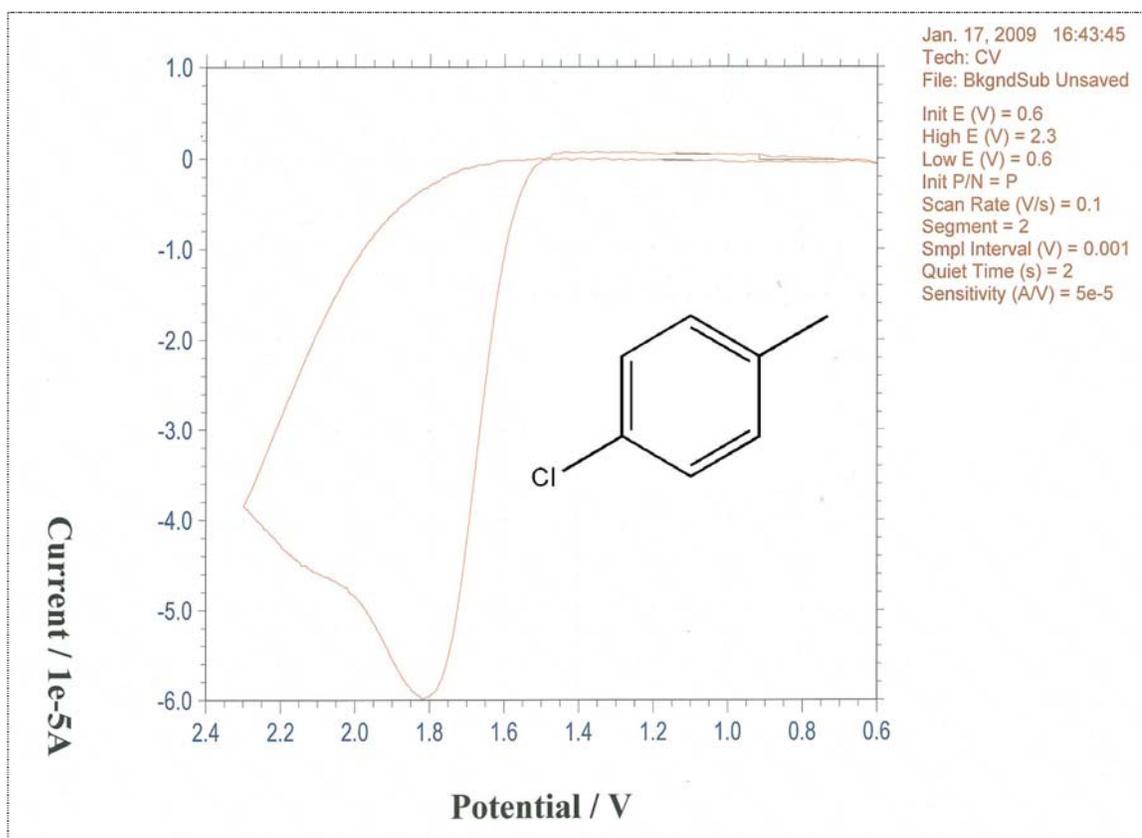
Cyclic voltammetry experiments are all carried out in a supporting salt electrolyte, 0.1M lithium perchlorate in acetonitrile at a scan rate of 0.1 V sec^{-1} . Carbon and platinum wires were used the anode and the cathode, respectively. A silver wire in 0.1M silver nitrate solution in acetonitrile was used as a reference electrode.

All cyclic voltammograms were scanned over a range of potentials. Backgrounds, (the supporting electrolyte solution) were first scanned and were subsequently overlaid or subtracted from the studied compound's scan. In the following pages, the CVs of the studied compounds are shown.

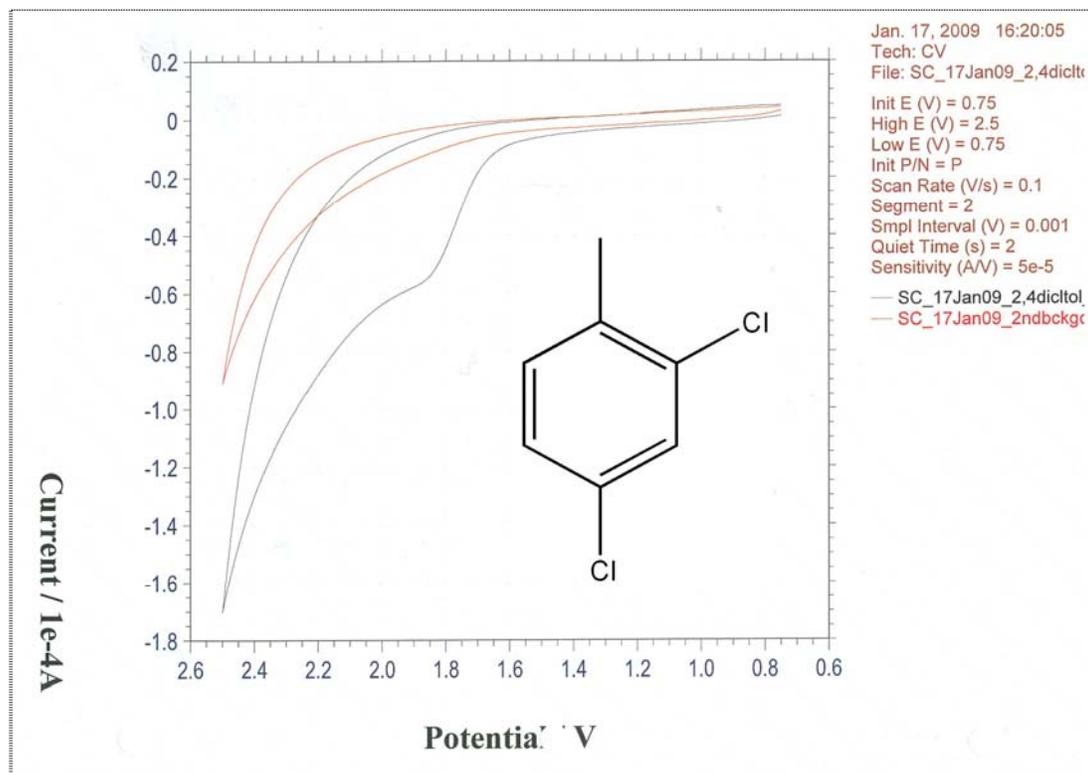
Toluene (1) produces the following cyclic voltammogram (with background subtracted). It exhibits an anodic oxidation peak potential at +1.93V. The absence of a corresponding reduction peak indicates that its oxidation is irreversible.



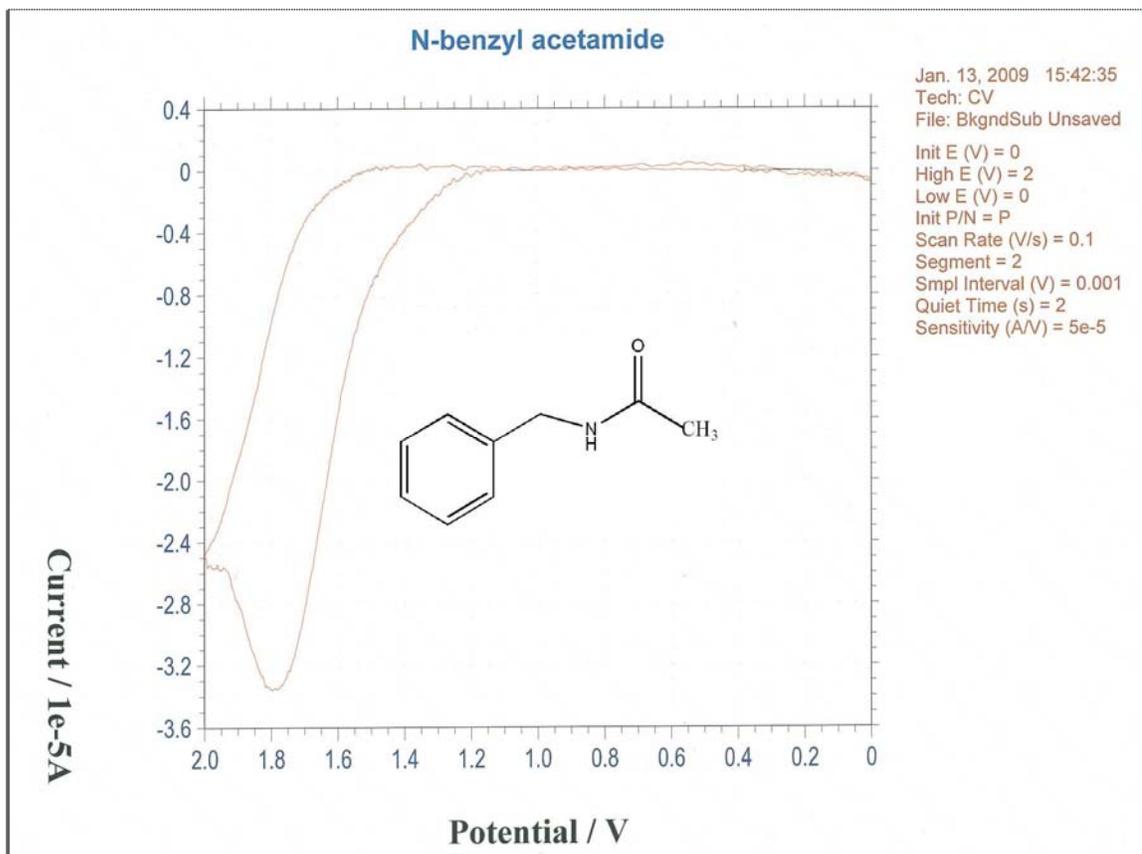
4-Chlorotoluene (2): The CV of 4-chlorotoluene is shown below with an oxidation peak at +1.75V vs. Ag/0.1M AgNO₃. This is also irreversible as indicated by the absence of the corresponding reduction peak. (The background is subtracted)



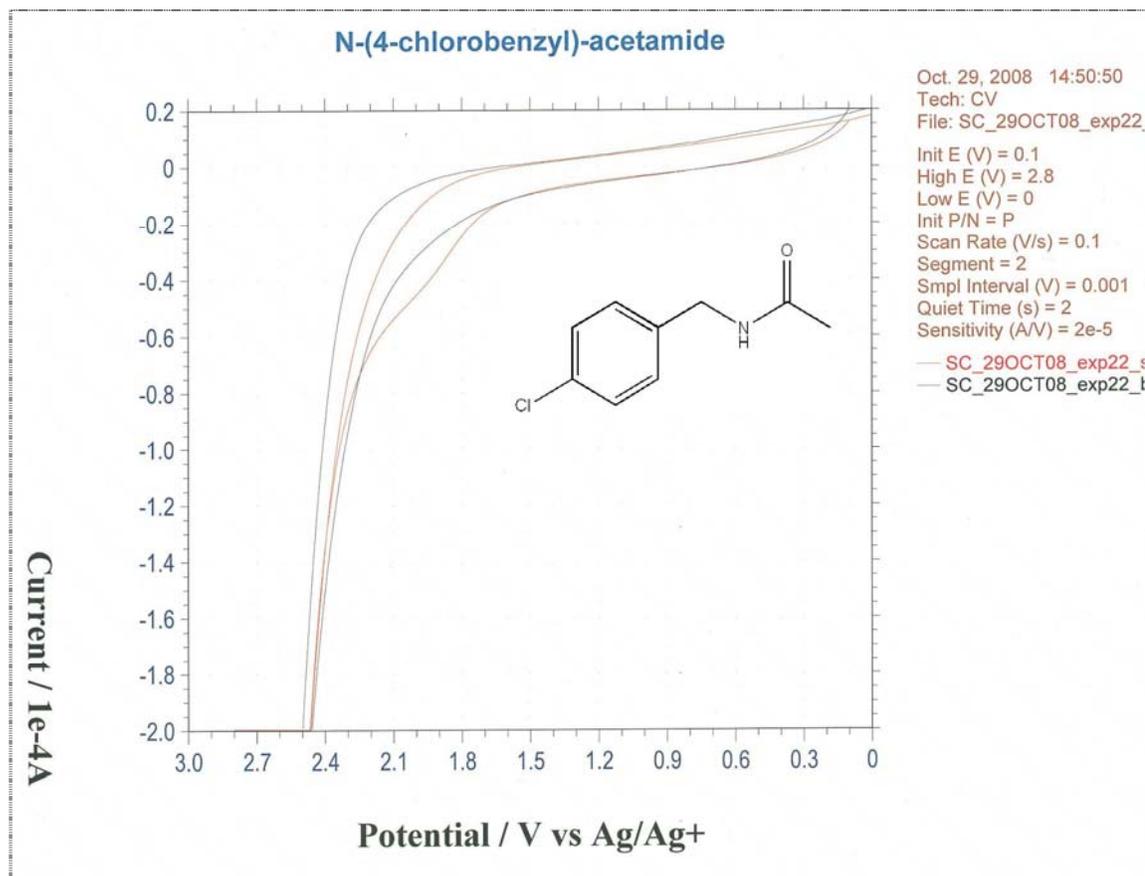
2,4-Dichlorotoluene (3) shows an oxidation potential at +1.82V. The absence of a cathodic sweep in the negative direction indicates the oxidation of **3** is irreversible.



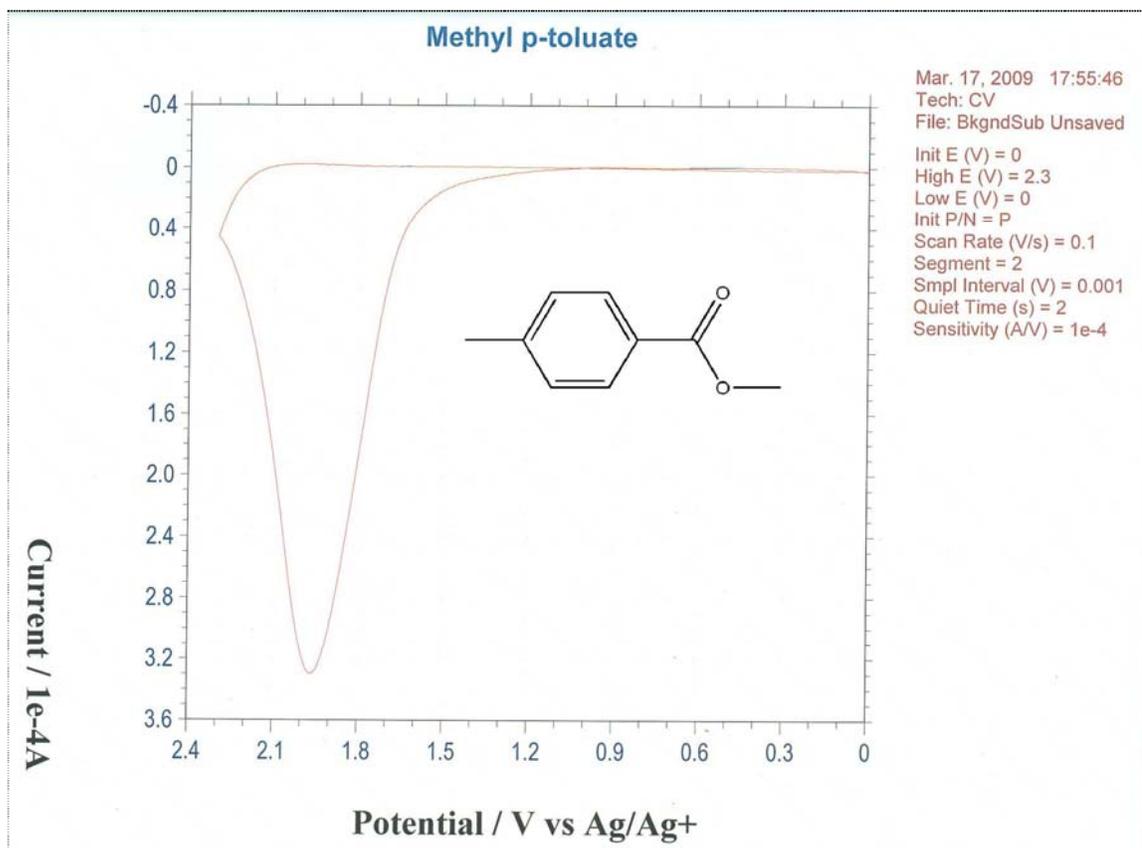
N-benzylacetamide (1a) exhibits an oxidation peak at +1.80. The absence of a corresponding reverse cathodic peak shows that oxidation of N-benzylacetamide is irreversible. (The background is subtracted).



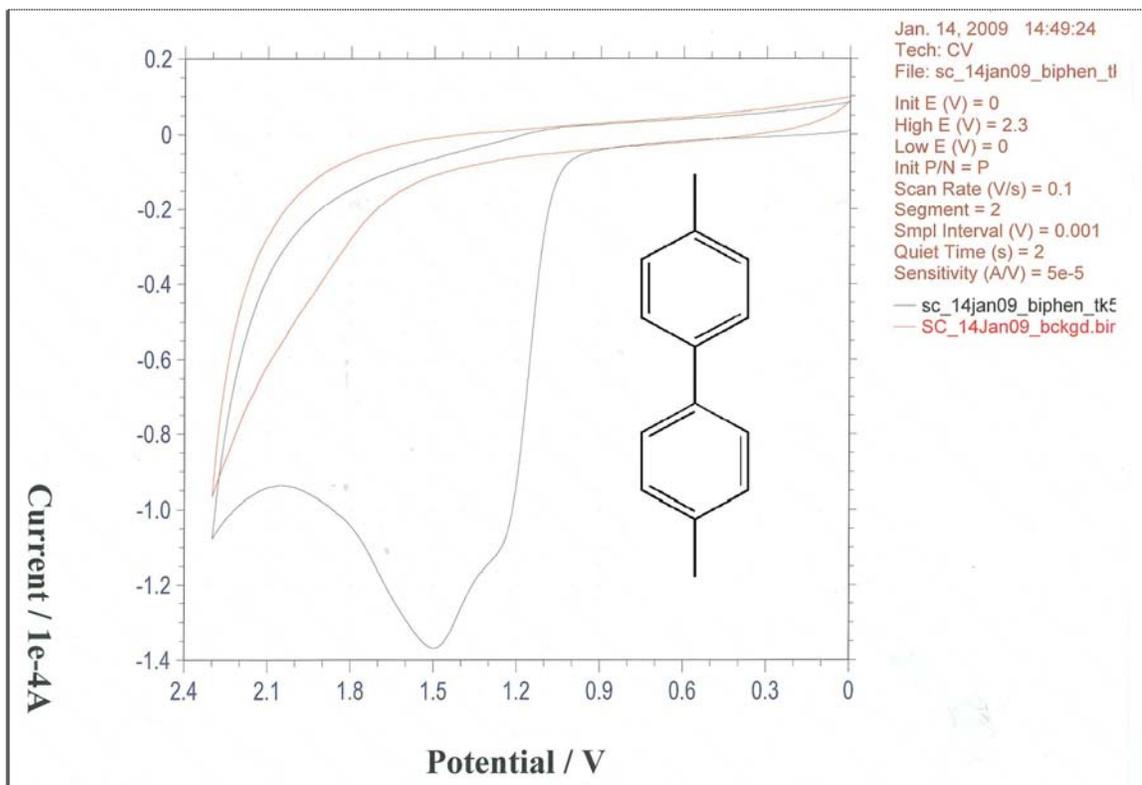
N-(4-chlorobenzyl)-acetamide (2a) generates the following CV. It has an oxidation potential of +2.0V and the absence of a corresponding reduction peak upon scan indicates an irreversible oxidation.



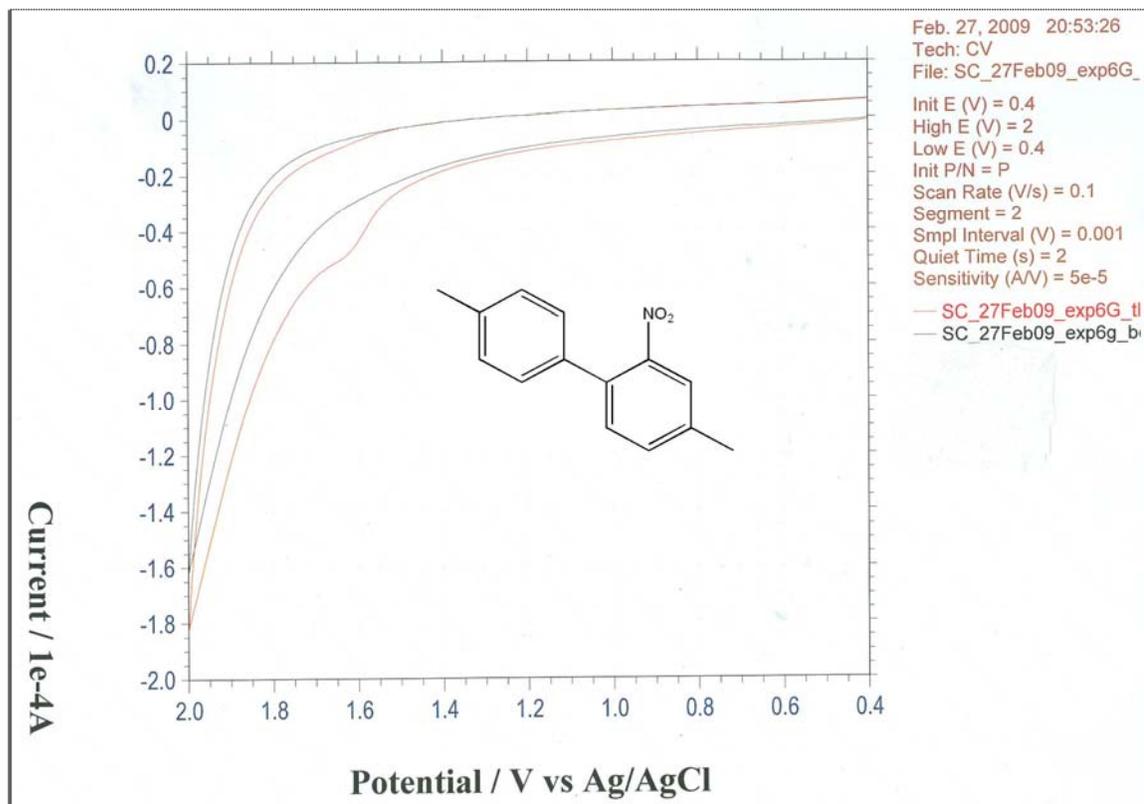
Methyl p-toluate (4) produces the following cyclic voltammogram—with the background subtracted. The oxidation peak is observed at +1.96V. The absence of a corresponding reduction peak for the reverse scan indicates that the oxidation of **4** is irreversible.



4,4'-Dimethylbiphenyl (5) depicts an irreversible oxidation peak at +1.50V.



4,4'-dimethyl-2-nitro-1,1'-biphenyl (6) generates the following CV. It exhibits an oxidation peak at +1.64V; the lack of a corresponding reduction peak indicates that the oxidation is irreversible.



Fig___: Cyclic voltammogram of 4,4'-dimethyl-2-nitro-1,1'-biphenyl

B. Substituent Effects on Redox Potentials

Oxidation potentials of compounds **1-6** were measured by cyclic voltammetry in acetonitrile using Ag/0.1M AgNO₃ as reference. Ionization potentials (I. P.) of compounds **1-6** were calculated by density functional theory (DFT), employing the B3LYP functional and the 6-31G basis set, with *d*-orbital polarization functions. In an effort to closely match the conditions carried out in cyclic voltammetry, solvation energies in acetonitrile were also included in the computation. Geometries of both the neutral and the radical cation of **1-6** were fully optimized and the ionization potential was computed as the difference between the enthalpy of the cation and that of the neutral compound:

$$\text{I.P.} = \text{enthalpy}_{\text{cation}} - \text{enthalpy}_{\text{neutral}}$$

Table 2 presents the data obtained from the calculation of I.P.; E_p is the oxidation potential of the compounds as indicated by cyclic voltammetry:

| | Compound # | neutral (hartrees) | cation (hartrees) | I.P. (hartrees) | I.P. (eV)* | E _p (V) |
|-------------------------------------|------------|-----------------------|----------------------|--------------------|---------------|--------------------|
| 4,4'-Dimethylbiphenyl | 5 | -541.9495477 | -541.7447913 | 0.2047564 | 5.53 | 1.5 |
| 4,4'-Dimethyl-2-nitro-1,1'-biphenyl | 6 | -746.4472291 | -746.226454 | 0.2207751 | 5.96 | 1.64 |
| 4-Chlorotoluene | 2 | -731.1685335 | -730.9364104 | 0.2321231 | 6.27 | 1.75 |
| Toluene | 1 | -271.5711913 | -271.3385858 | 0.2326055 | 6.28 | 1.93 |
| 2,4-dichlorotoluene | 3 | -1190.763315 | -1190.524979 | 0.2383358 | 6.44 | 1.82 |
| Methyl p-toluate | 4 | -499.4555662 | -499.2111491 | 0.2444171 | 6.60 | 1.96 |

Table 2: Calculations for ionization potential of **1-6** and peak oxidation potential values from CV.

* There is a conversion factor of 27 from hartrees to electron-volts

In order to assess the correlation between I.P. and E_p , a plot of the two properties was prepared. There exists a fairly good linear correlation between the two properties ($R = 0.926$) (figure 5).

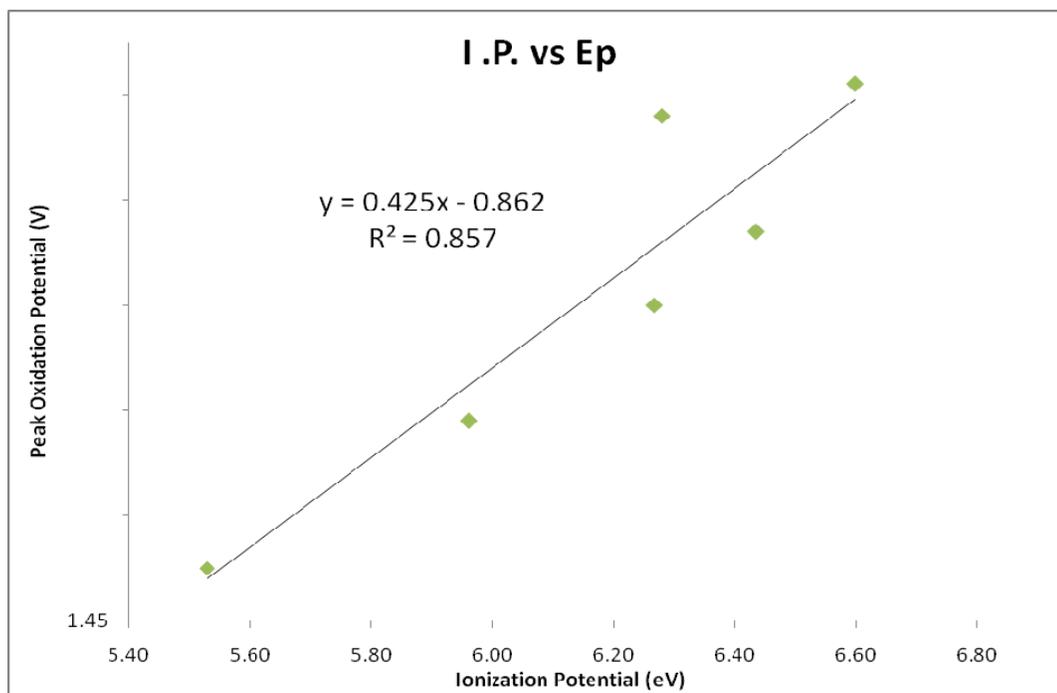


Figure 5: Plot of I.P. vs E_p .

The table and the plot of I.P. and E_p reveal certain substituent effects on the redox potentials. It can be observed that oxidation potentials increase with the increasing degree of electron-withdrawing groups on the compound, as observed between 4-chlorotoluene and 2,4-dichlorotoluene. This is in accordance with the results obtained by Steckhan on bromine substituents.¹⁶ Methyl p-toluate has the highest E_p and therefore I.P. among the molecules listed, and 4,4'-dimethylbiphenyl has the lowest I.P. and therefore E_p due to its two electron-releasing substituents. This is as expected because electron-donating substituents decrease the oxidation potential (and I.P.) of a compound, whereas electron-withdrawing groups increase E_p (and I.P.) by removing electron density from the π system and thus more energy is needed to

remove an electron. Hammett constants relate the nature of the substituent to their effect on chemical reactivity and also other physical properties; it has been demonstrated that for compounds bearing more than one substituent, the effect of the substituents are additive upon oxidation,¹⁷ i.e., the overall electronic electron effect is given by the sum of Hammett constants of all substituents. This can explain why 4-chlorotoluene would be easier to oxidize than 2,4-dichlorotoluene as it is easier to oxidize 4,4'-dimethylbiphenyl than toluene.

C. Syntheses and Preparative Scale Electrolyses: Anodic Oxidation

Preparative Scale Electrolysis of toluene (1): The anodic oxidation of toluene (**1**) in 0.1M LiClO₄ at +1.4V vs. Ag/0.1M AgNO₃ was monitored at regular intervals for the consumption of **1**. As illustrated by the GC in figure 6, **1** was completely oxidized after 424.6 coulombs or when 1.95 eq. of the calculated amount of electrons were utilized. The electrolysis yielded mainly N-benzylacetamide (**1a**), GC: r.t. (%):7.697min, (89%) and a small amount of benzoic acid as seen in the MS with M⁺ of 122, GC: r.t. (%):3.729 min, (11%) (Figure 6). Benzoic acid was a result of over-oxidation. The other peaks in the GC are either minor by-products or artifacts from the column of the mass spectrometer; they are unimportant as the workup eradicated them. The GC of post-workup did not show the benzoic acid peak and only the presence of N-benzylacetamide, figure 7.

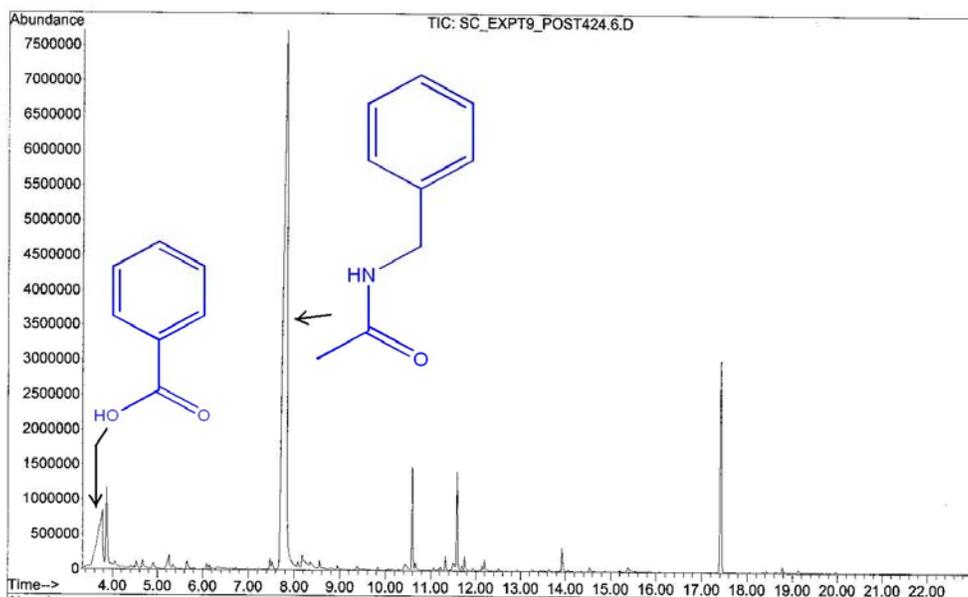


Figure 6: GC of electrolysis of toluene after 424.6 coulombs of current were passed.

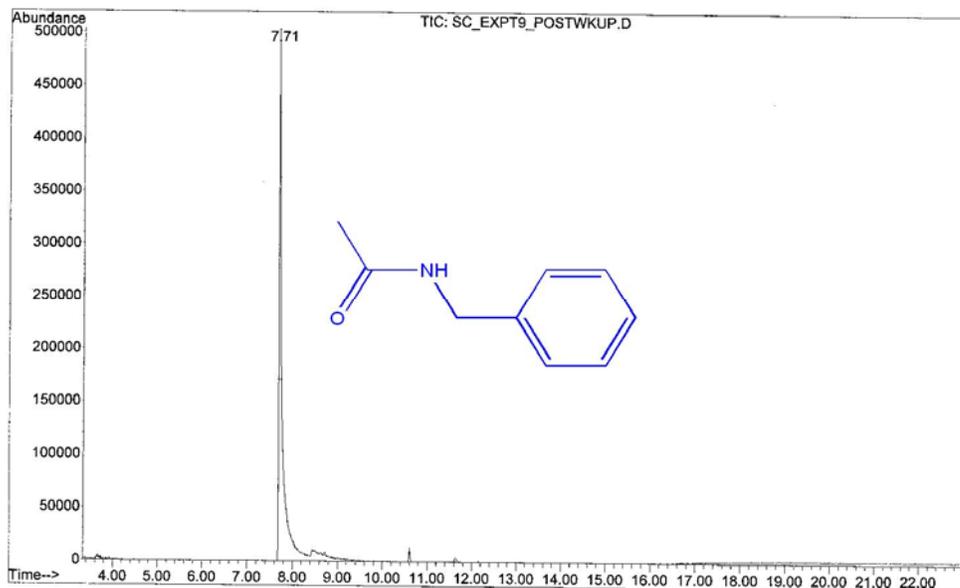


Figure 7: GC of anodic oxidation of toluene, post work-up.

7.784 minutes. (Figure 6) The GC peak at 7.784 minutes was assigned as N-benzylacetamide (**1a**) (Discussion). MS: m/z (%) = 149 (81), 106 (100), 91 (30), 79 (14), 77(14). The mass spectrum data is given on the following page and the identification of **1a** is verified upon synthesis and GC/MS comparison to that of the synthesized product. Furthermore, since the molecular ion peak has an odd mass, it suggests a nitrogen-containing compound, thus supporting the presence of the acetamide. The base peak at m/z 106 corresponds to the cation **13** and m/z 91 corresponds to cation **14**:



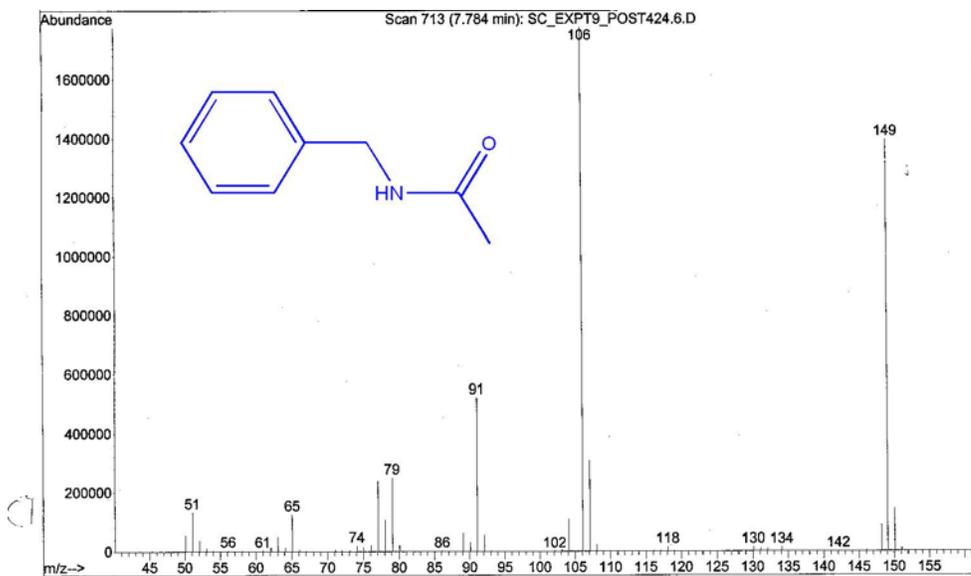
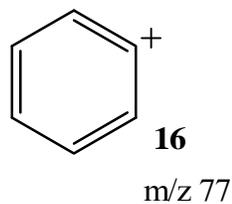
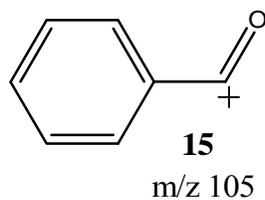


Figure 8: Mass spectrum of N-benzylacetamide.

3.729 minutes. The GC peak at 3.729 minutes corresponds to benzoic acid. MS: m/z (%) = 122 (90), 105 (100), 77 (70), 51(30). The mass spectrum is shown on the next page. The base peak at m/z 105 corresponds to the cation **15** and the m/z 77 corresponds to cation **16**:



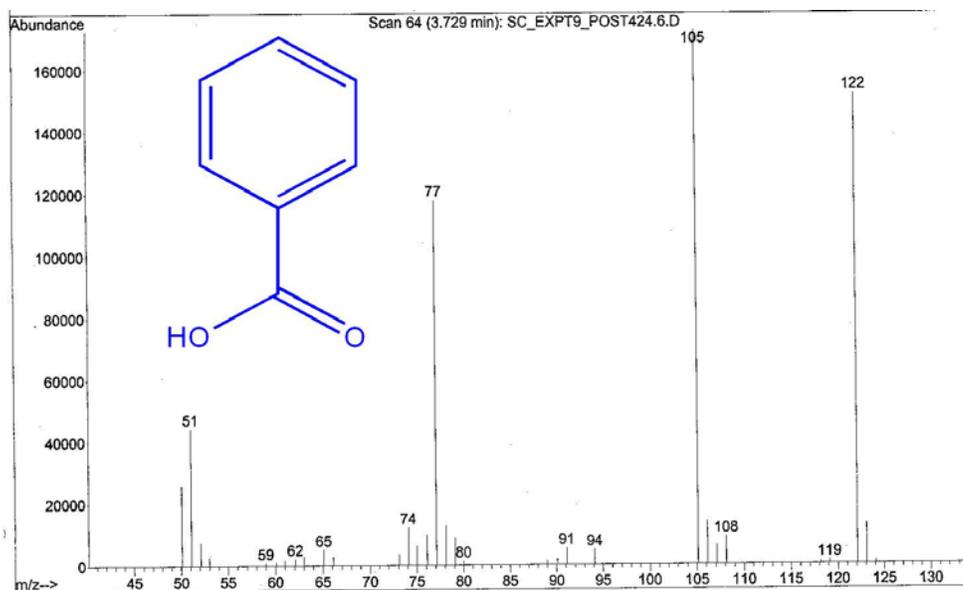


Figure 9: Mass spectrum of benzoic acid.

Preparative scale electrolysis of toluene with additional drops of water was carried out to test the dependence of water concentration in the oxidation of toluene. The oxidation yielded primarily benzaldehyde and a small amount of **1a** as opposed to mainly **1a** and minor amounts of benzoic acid, as observed in the previous electrolysis without the addition of water. GC/MS of this electrolysis utilized a different method, hence the different retention times of **1a**. The mass fragmentations, however, are identical (same fragmentation as figure 8). The GC shown in figure 10 represents the electrolysis solution after 1.95 eq. of the calculated amount of electrons were utilized; r.t. (%): benzaldehyde, 4.94 min, (52%) and N-benzylacetamide, 9.08min, (26%).

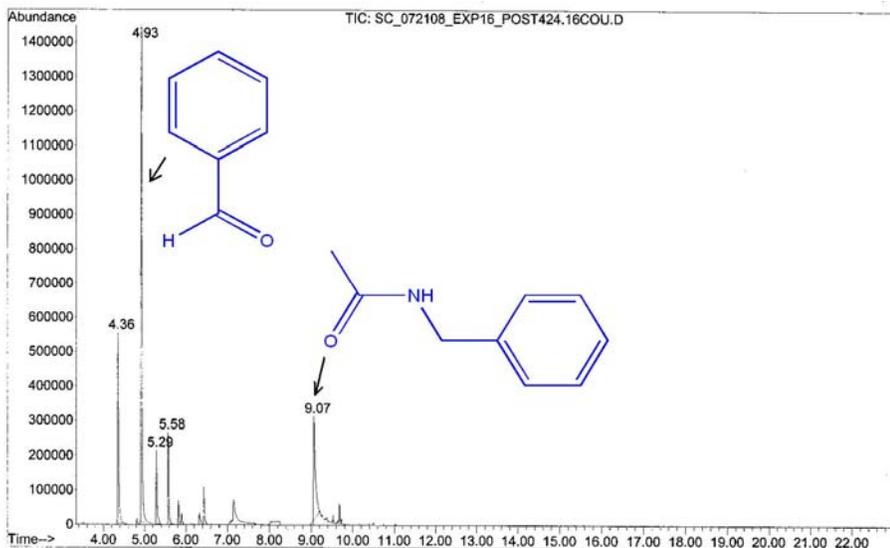


Figure 10: GC of oxidation of toluene with the addition of water.

4.929 minutes. The GC peak at 4.929 minutes and m/z at 106 corresponds to benzaldehyde; the mass spectrum is shown below. The m/z at 77 corresponds to cation **14**:

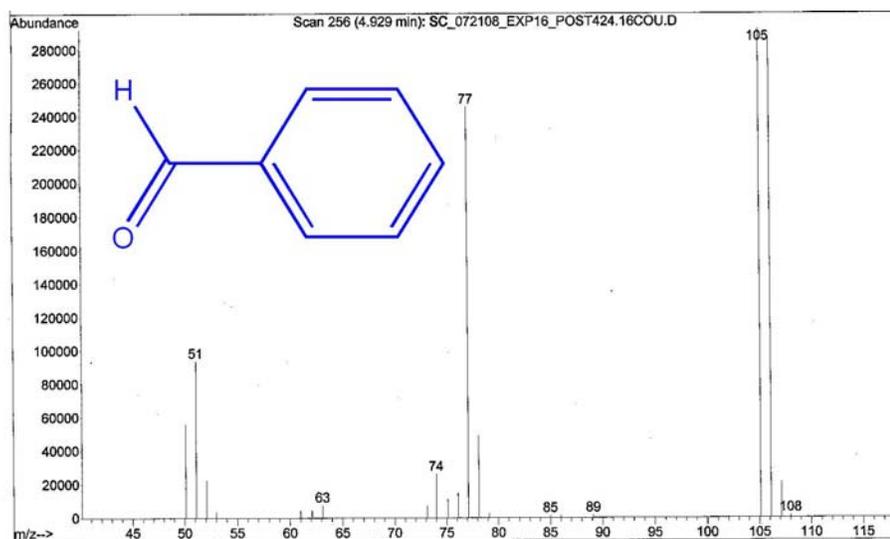
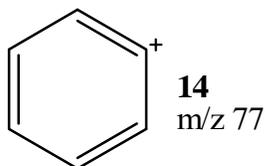


Figure 11: Mass spectrum of benzaldehyde.

Preparative scale catalytic electrolysis of 1:1 mol 4-chlorotoluene (2**): 2,4-dichlorotoluene (**3**) with 4,4',4''-trimethyl-2,2',2''-trinitrotriphenylamine**

(catalyst **2)**: This electrolysis was carried out to observe the products that can be obtained from the oxidation of aromatic compounds bearing electron-withdrawing substituents. The cell ran at +1.6V and GC/MS of the electrolysis solution was taken every 2F/mol to monitor the progress of **2** and **3**. The electrolysis was stopped after 130 minutes and 76.24 coulombs electrons had been utilized. GC/MS (figure 12) showed only the oxidation of 4-chlorotoluene to 4-chlorobenzaldehyde and the presence of **2** and **3**, with more of **3** than **2**. GC: r.t. (%): 4-chlorotoluene, 3.88 min, (35%); MS (figure 13): m/z (%)= 126 (38), 91 (100); 2,4-dichlorotoluene, 8.75 min, (55%); MS: m/z (%)=164 (3.8), 162 (23.8), 127 (31), 125(100), 89 (25); 4-chlorobenzaldehyde, 9.05min, (9%); MS: m/z (%)= 142 (23), 140 (72), 139 (100), 111 (50), 75 (24).

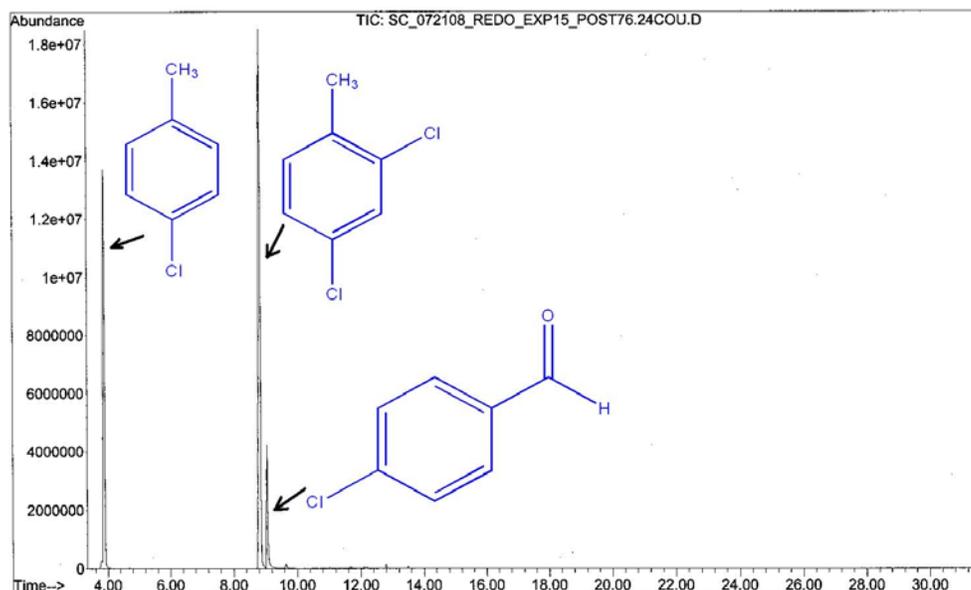


Figure 12: GC of oxidation of 1:1 mol 4-chlorotoluene (**2**) and 2,4-dichlorotoluene (**3**).

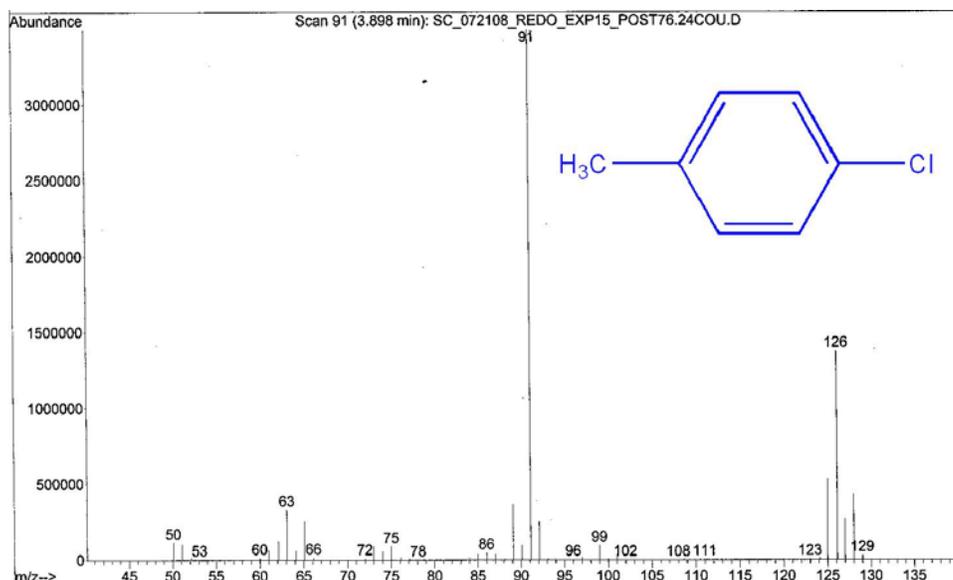


Figure 13: Mass spectrum of 4-chlorotoluene.

8.753 minutes. The GC peak at 8.753 minutes corresponds to 2,4-dichlorotoluene (**3**). There are two isotopes of chlorine (one of the five $A+2$ elements) in nature, ^{35}Cl and ^{37}Cl , in roughly a 3:1 ratio. Therefore if there is one chlorine present in a compound, the MS will indicate a pair of lines, separated by 2 amu, and in a relative abundance ratio of about 3:1 (which can be observed in the mass spectrum of 4-chlorotoluene: m/z 126 and m/z 128, figure 13). The mass spectrum of 2,4-dichlorotoluene is given on the following page and analysis of the spectrum suggests that the compound contains two chlorines, as indicated by the isotopically shifted lines, separated also by 2 amu, and in a relative abundance of 1: 2/3: 1/9. In the mass spectrum, the base peak at m/z 125, 127 corresponds to cation **17** and the m/z 91 corresponds to cation **18**:

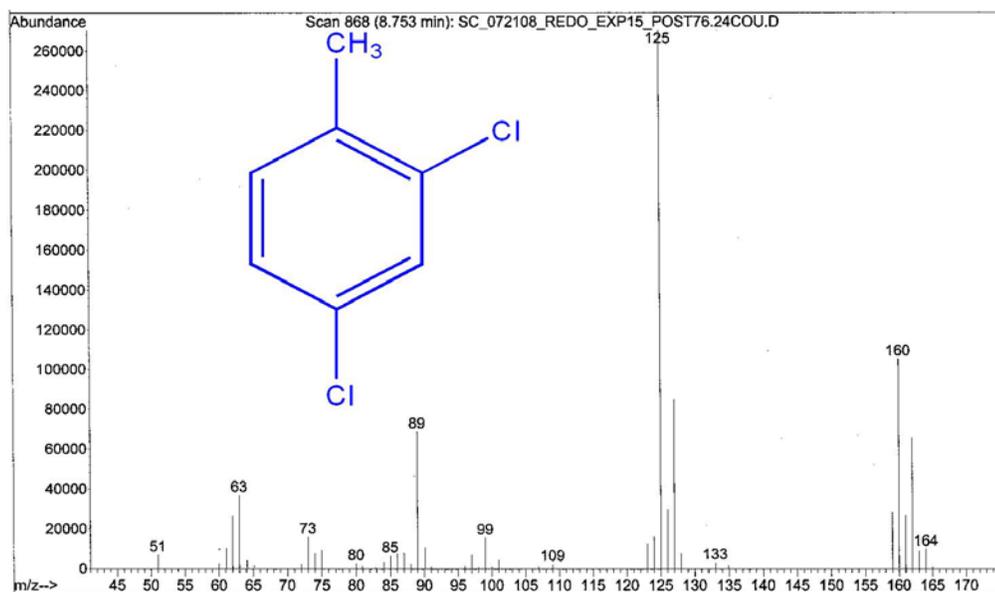
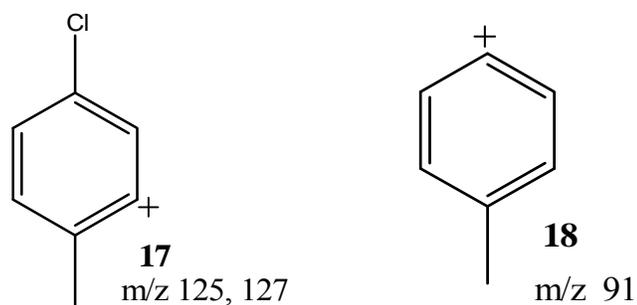
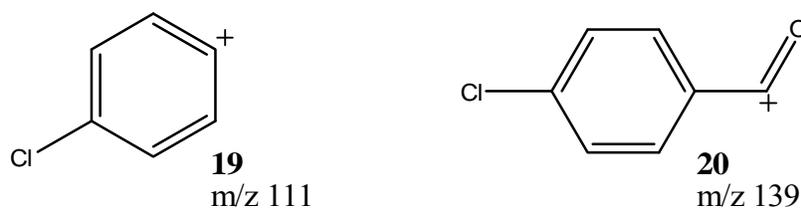


Figure 14: Mass spectrum of 2,4-dichlorotoluene.

9.053 minutes. The GC peak at 9.053 minutes was assigned 4-chlorobenzaldehyde. The mass spectrum is shown on the following page. The m/z at 111 corresponds to cation **19**. The base peak at m/z 139 corresponds to the cation **20**:



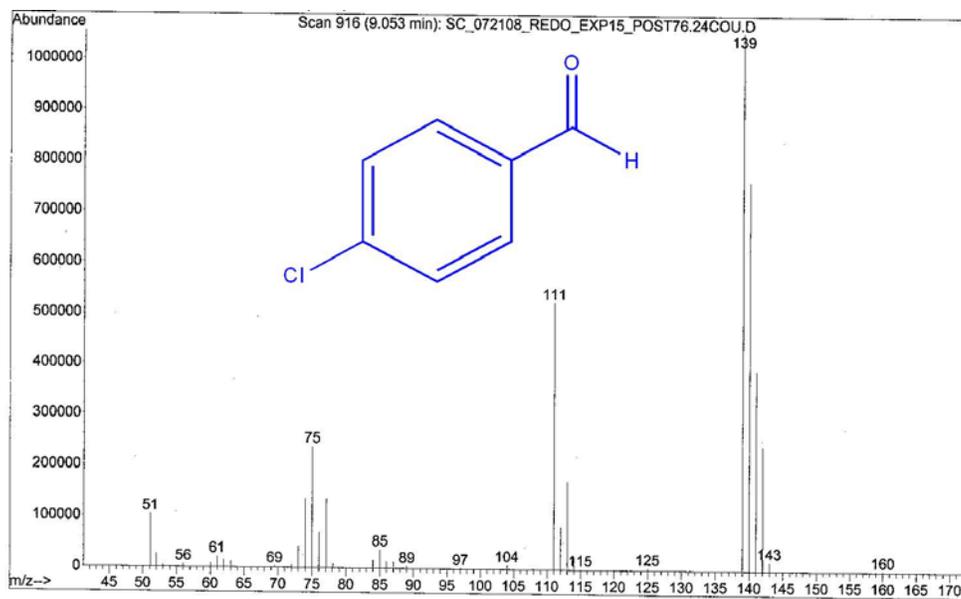


Figure 15: Mass spectrum of 4-chlorobenzaldehyde.

Preparative scale catalytic electrolysis of 4-chlorotoluene (2) with 4,4',4''-Trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): To resolve the technical error of the previous electrolysis (Discussion), electrolyses of the substrates of interest, **2** and **3**, were carried out separately. The electrolysis of **2** ran at +1.60 volts vs. Ag/0.1M AgNO₃ and was stopped after 297 coulombs (8F/mol), i.e., 3.90 eq. of the calculated amount of electrons were utilized. A post-electrolysis GC/MS was obtained for analysis.

3.89 minutes. The GC peak at 3.89 minutes was assigned 4-chlorotoluene because it exhibits a similar retention time and mass fragmentation as the 4-chlorotoluene observed in mass spectrum shown in figure 13. The mass spectrum is shown below:
MS: m/z (%)= 128 (13), 126 (38), 91 (100).

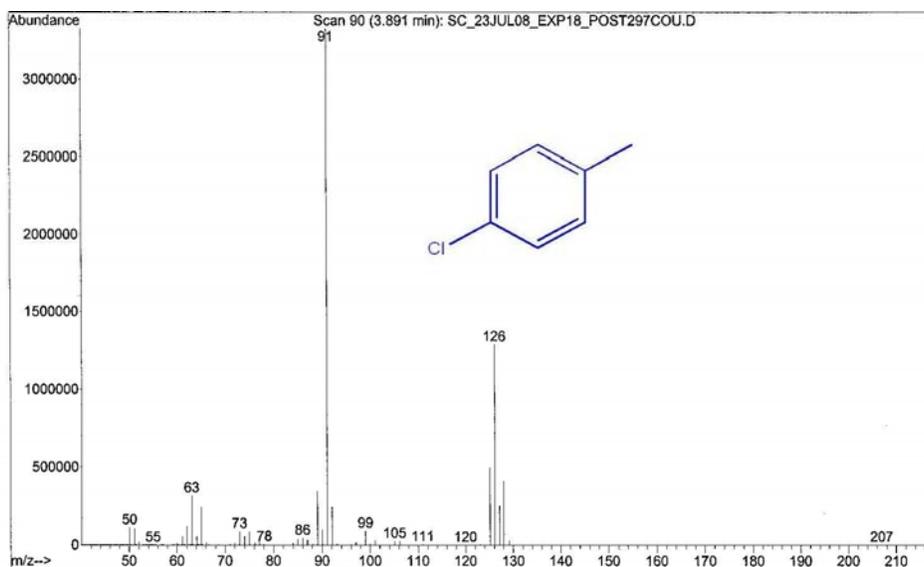


Figure 16: Mass spectrum of 4-chlorotoluene; post 297 coulombs.

7.928 minutes. The GC peak at 7.928 minutes was identified as 4-chlorobenzaldehyde because it exhibits the same mass fragmentation as the 4-chlorobenzaldehyde in figure 15; MS: m/z (%)=142 (22), 140 (70), 139 (100), 113 (16), 111 (50), 77 (13), 75 (22).

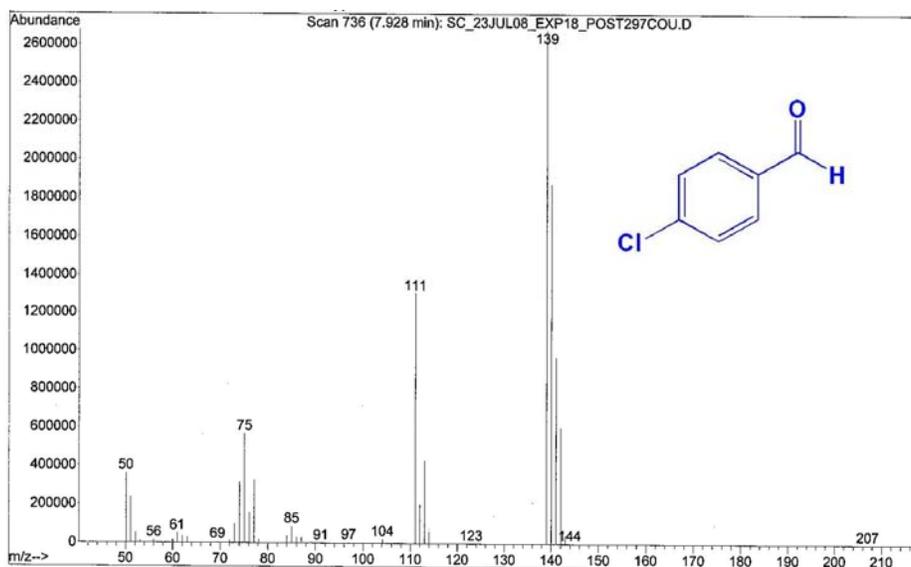


Figure 17: Mass spectrum of 4-chlorobenzaldehyde; post 297 coulombs.

9.403 minutes. The GC peak at 9.403 minutes was assigned as 2,4-dichlorotoluene because it exhibits identical mass fragmentation as the mass spectrum of **3** shown in figure 14; MS: m/z (%)=162 (14), 160 (20), 127 (32), 125 (100), 89 (17), figure 18.

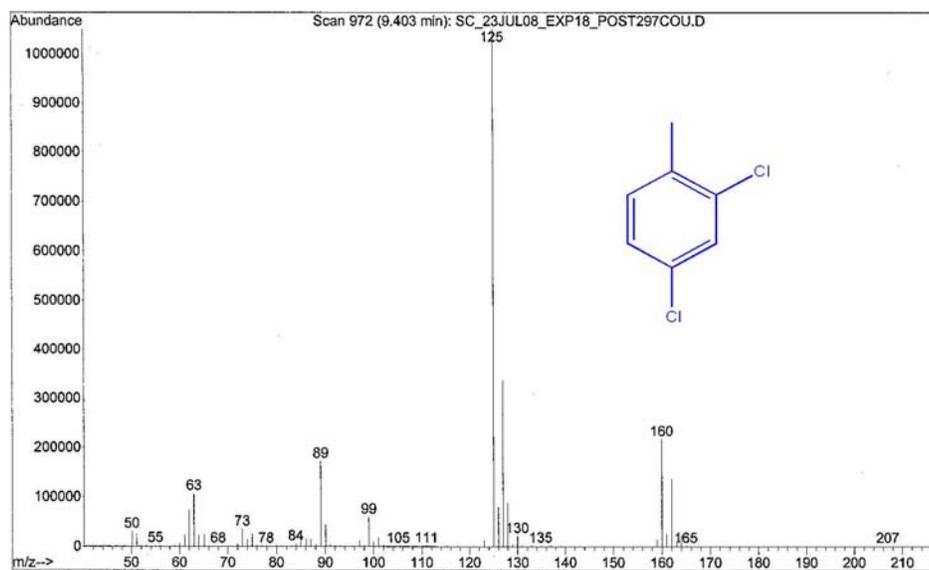


Figure 18: Mass spectrum of 2,4-dichlorotoluene; post 297 coulombs.

15.706minutes. The GC peak at 15.706 minutes was identified as N-(4-chlorobenzyl)-acetamide (**2a**) (11%); MS: m/z (%) = 185 (31), 183 (97), 140 (63), 125 (43), 106 (100), 77 (20). The mass spectrum appears below. M⁺ of 183 suggests a nitrogen-containing compound and the base peak at m/z 106 corresponds to cation **21**, m/z 140 corresponds to cation **22**, m/z 125 corresponds to cation **23**, and m/z 106 corresponds to cation **24**:

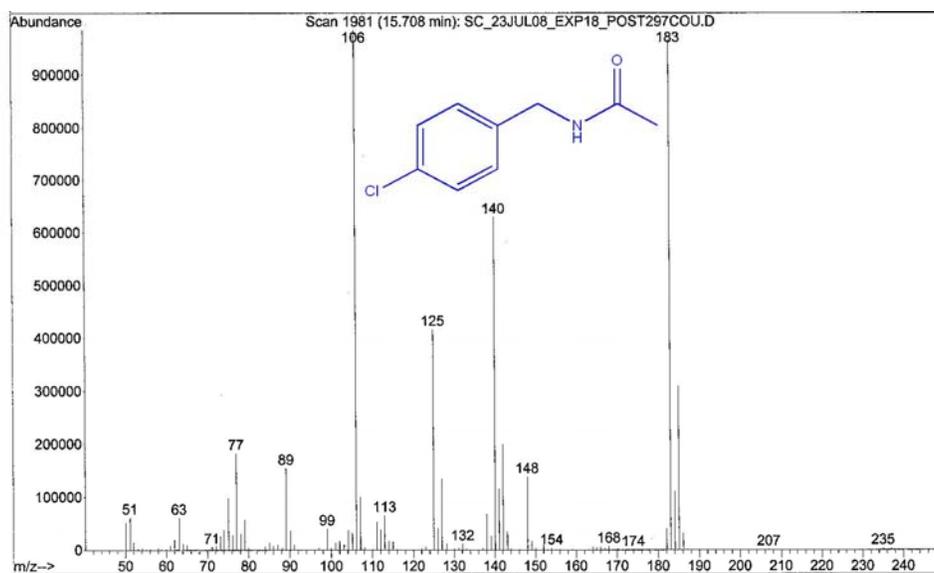
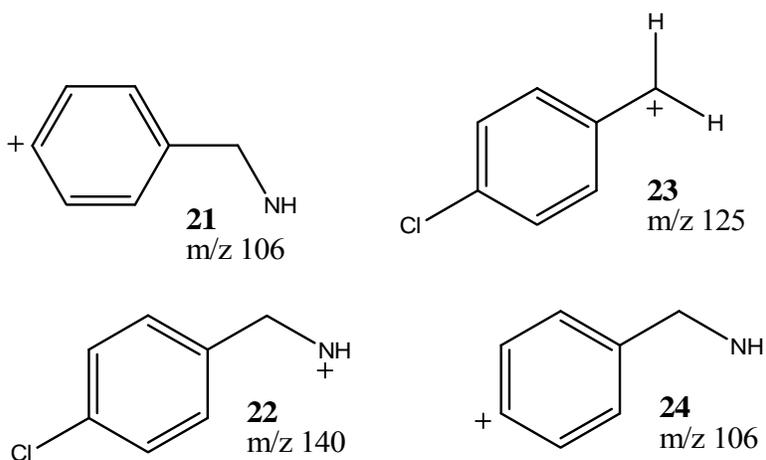


Figure 19: Mass spectrum of N-(4-chlorobenzyl)-acetamide; post 297 coulombs.

A GC/MS was obtained after working-up the electrolysis solution and only indicates the presence of **2** and 4-chlorobenzaldehyde (figure 20); the peak at 28min is an artifact from mass spectrometer's column ($M^+=429$). GC: r.t. (%): 4-chlorotoluene, 3.96 min, (15%) and 4-chlorobenzaldehyde, 7.76 min, (85%).

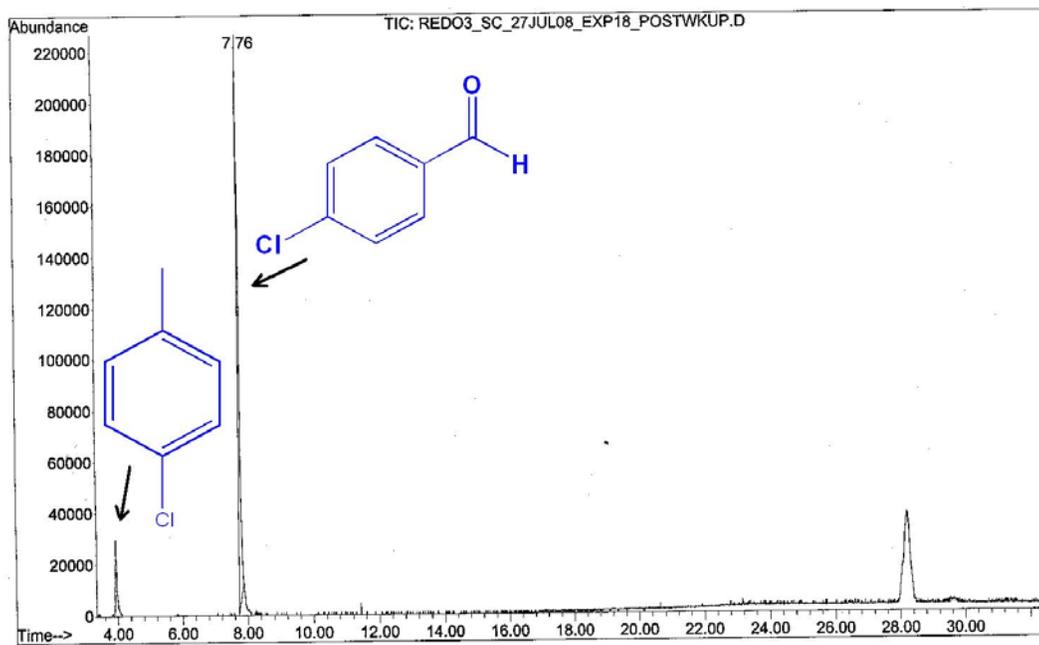
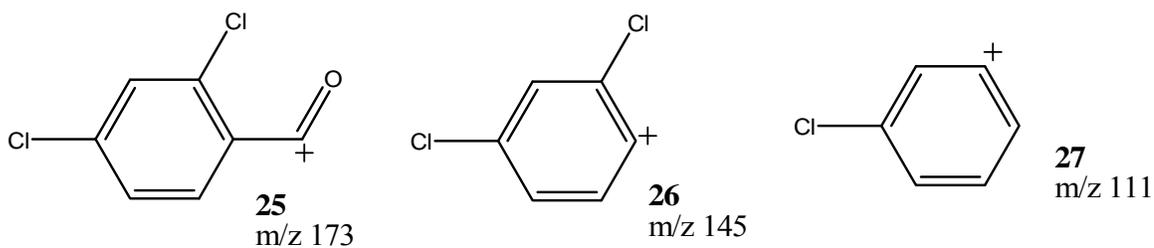


Figure 20: GC of 4-chlorotoluene from electrolysis; post-workup.

Indirect electrolysis of 2,4-dichlorotoluene (3) with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): Since the electrolysis with 1:1 mole ratio of **3** and **2** did not oxidize **3** due to technical errors, this separate electrolysis of **3** was carried out in an attempt to resolve them. The electrolysis of **3** ran at +1.7V and its progress was followed by extracting samples of the electrolysis solution at regular intervals to be analyzed by GC/MS. The electrolysis was stopped after **3** was almost completely consumed, i.e. after 5.9 eq. of the calculated amount of electrons (12F/mol). GC/MS identified the presence of 2,4-dichlorobenzaldehyde (70%) and 2,4,6-trichlorotoluene (20%).

10.378 minutes. The GC peak at 10.378 minutes was assigned as 2,4-dichlorobenzaldehyde (70%); MS: m/z (%) = 178 (7), 176 (39), 174 (61), 173 (100), 149 (3), 147 (16), 145 (25). The mass spectrum is given on the following page. The base peak at m/z 173 corresponds to cation **25**, m/z 145 corresponds to cation **26**, and m/z 111 corresponds to cation **27**:



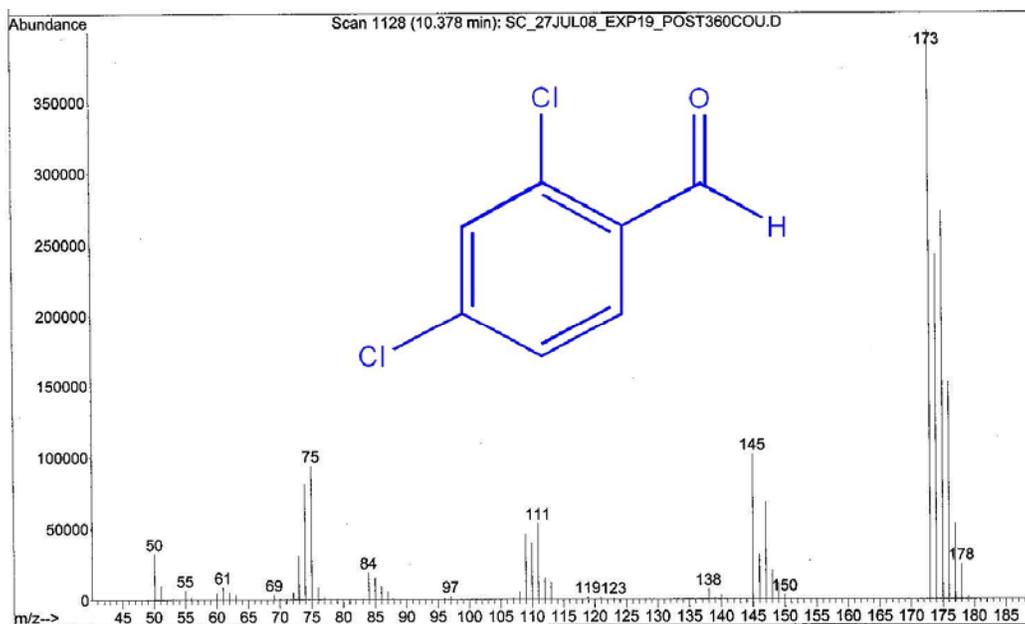
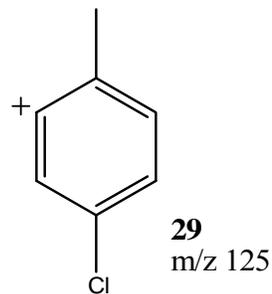
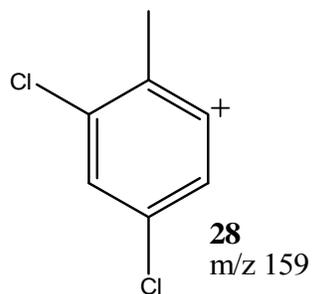


Figure 21: Mass spectrum of 2,4-dichlorobenzaldehyde.

11.802 minutes. The GC peak at 11.802 minutes is believed to be 2,4,6-trichlorotoluene; MS: m/z (%) = 198 (6), 196 (17), 194 (18), 163 (11), 161 (65), 163 (100). The mass spectrum appears on the following page. The molecular ion peak at m/z 194 is identified as the 2,4,6-trichlorotoluene; the isotopic lines, each separated by 2 amu and in a relative abundance ratio of 1:1:1/3:1/27 indicates the presence of three chlorines in the compound (the 1/27 abundance is weak and therefore was not picked up by the mass detector). The base peak at m/z 159 corresponds to the cation **28** and m/z 125 corresponds to the cation **29**:



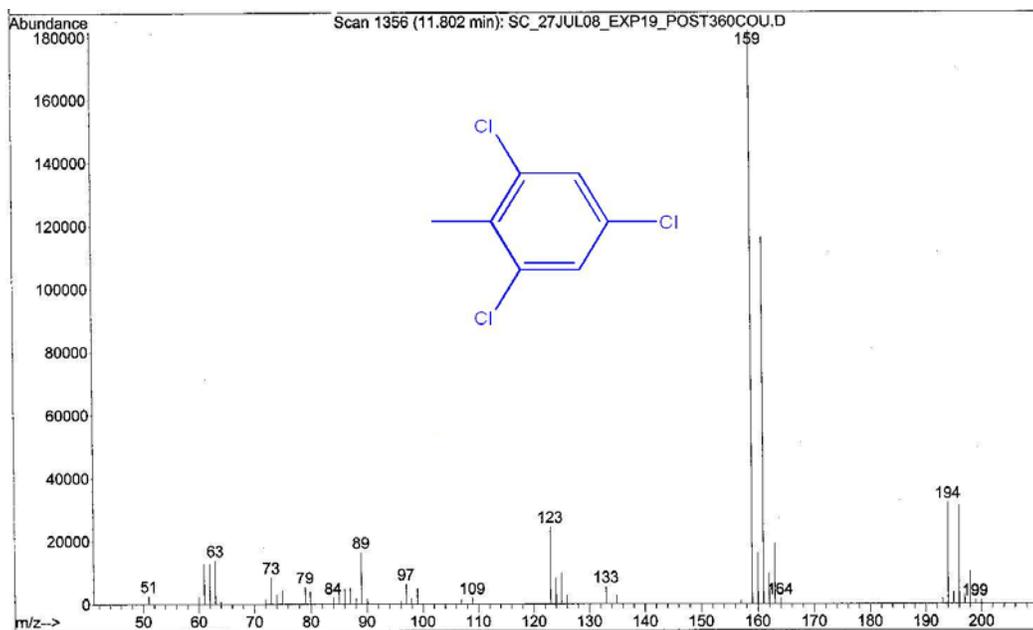


Figure 22: Mass spectrum of 2,4,6-trichlorotoluene.

Preparative scale electrolysis of N-benzylacetamide (1a): This electrolysis was carried out to verify that an amide can be anodically oxidized to an aldehyde; as the results of the electrolysis of 4-chlorotoluene indicated. The electrolysis of **1a** was run at +1.40V in 0.1M lithium perchlorate in acetonitrile and several samples of the electrolysis solution were analyzed by GC/MS to monitor the disappearance of **1a**. The electrolysis was stopped after **1a** was no longer present; after 220 minutes and 157 coulombs (12F/mol) had passed. GC/MS identified benzaldehyde and phenyl acetate (**9**).

3.691 minutes. The GC peak at 3.691 minutes was assigned to be benzaldehyde; MS: m/z (%) = 106 (100), 105 (100), 77 (100), 51 (43), 50 (26). The mass spectrum is given below and the base peak at m/z 77 corresponds to cation **32**:

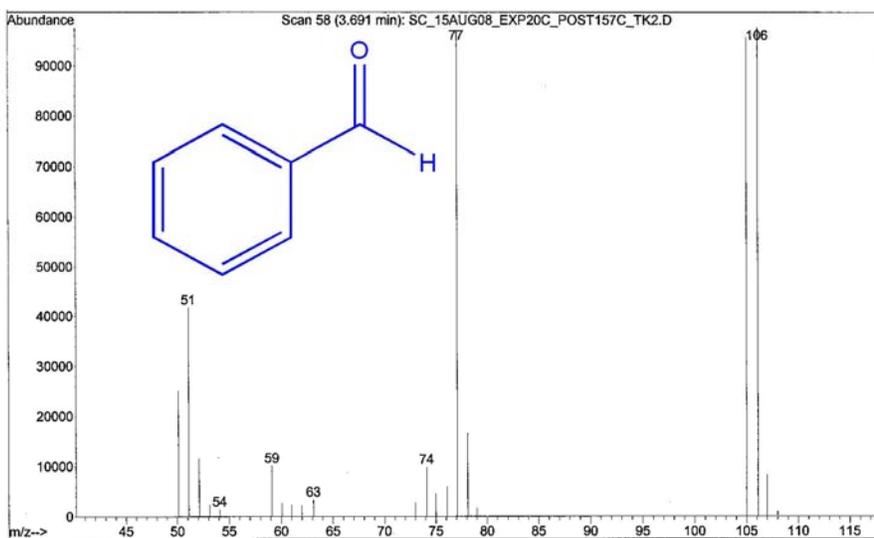
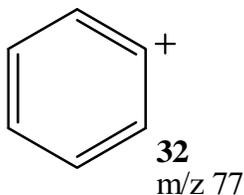


Figure 23: Mass spectrum of benzaldehyde.

5.941 minutes. The GC peak at 5.941 minutes was believed to be phenyl acetate; MS: m/z (%) = 136 (13), 94 (100). The mass spectrum is given below and the base peak at m/z 94 corresponds to cation radical **33**:

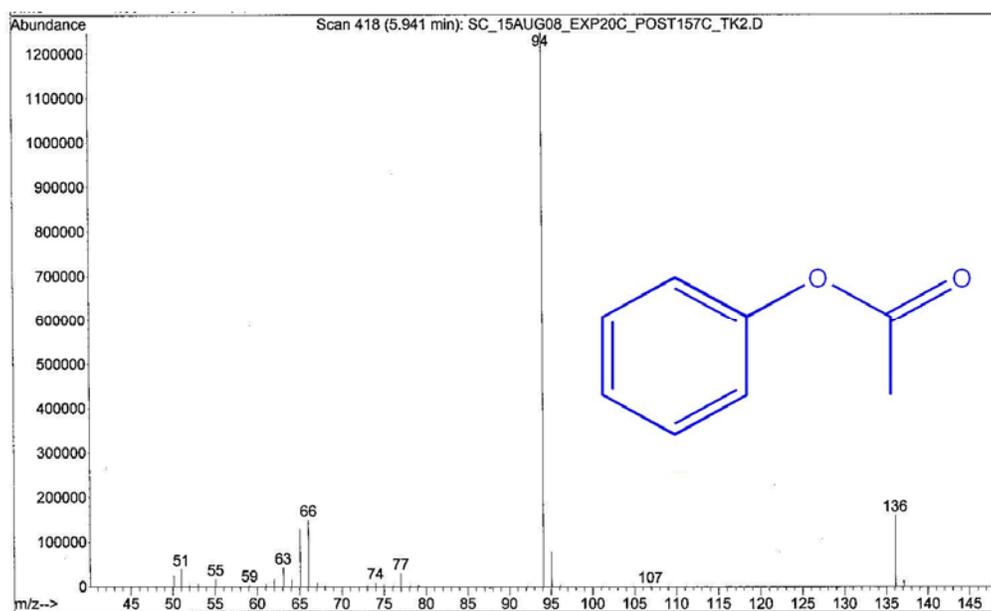
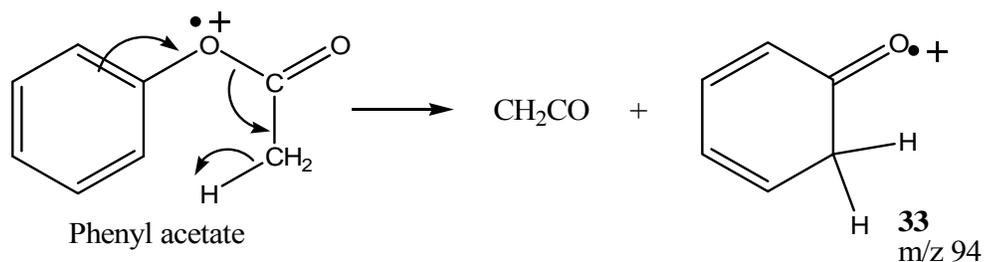


Figure 24: Mass spectrum of phenyl acetate.

The GC/MS post-work up showed a decrease in the amount of phenyl acetate and the presence of phenol and benzaldehyde. The assignments of phenyl acetate and benzaldehyde were based upon the retention times and mass fragmentations as illustrated in figures 23 and 24, respectively.

4.022 minutes. The GC peak (post electrolysis) at 4.022 minutes and molecular ion peak at m/z 94 was identified as phenol because it exhibits a similar retention time and an identical mass fragmentation pattern as a standard phenol sample.

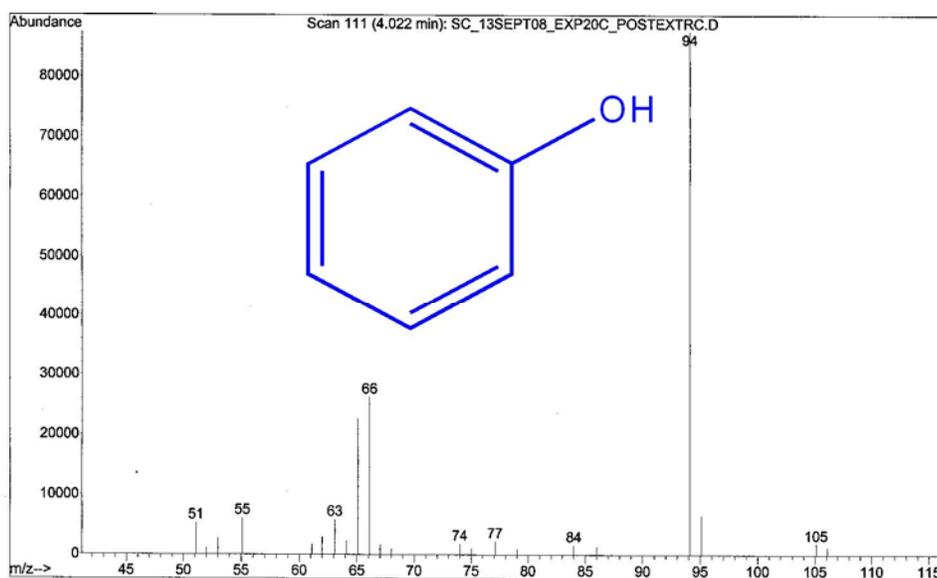


Figure 25: Mass spectrum of phenol from post-workup of oxidation of N-benzylacetamide.

Synthesis of N-(4-chlorobenzyl)-acetamide (2a): The synthesis of **2a** was carried out so that its electrolysis can be conducted to: First, verify that an amide can be functionally oxidized to an aldehyde; as observed in the electrolysis of **2**; and second, because of our interest in the electrochemical behavior upon oxidation of a substrate bearing an electron-withdrawing substituent and comparing this result to that of **1a**. The GC in figure 26 shows the presence of two products in the crude sample: mono- and di-acylated N-chlorobenzylamine. GC: r.t. (%): N-(4-chlorobenzyl)-acetamide, 11.64 min (53%); diacylated N-benzylamine, 12.19 min (47%). Figures 27 and 28 on the following page illustrate the mass spectrometries of the products in the crude product mixture. Purification by flash chromatography using silica with 60% ethyl acetate in hexanes as the eluent yielded 0.11 g of almost-white solid of **2a**. m.p. 107-112°C (lit. 106-108°C).¹⁸ GC (figure 29): r.t. (%): N-(4-chlorobenzyl)-acetamide, 11.46min (100%).

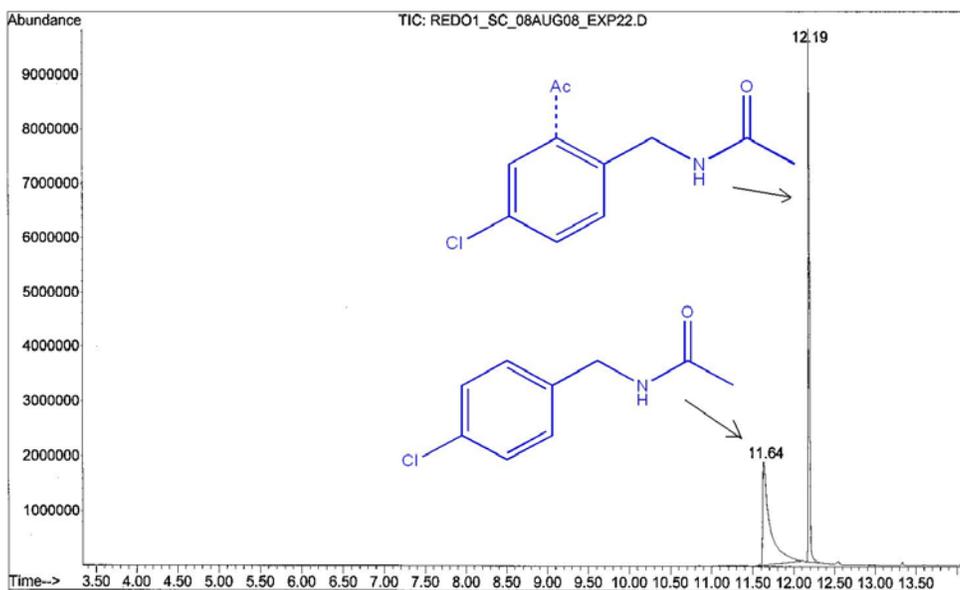


Figure 26: GC of crude product from synthesis of **2a**.

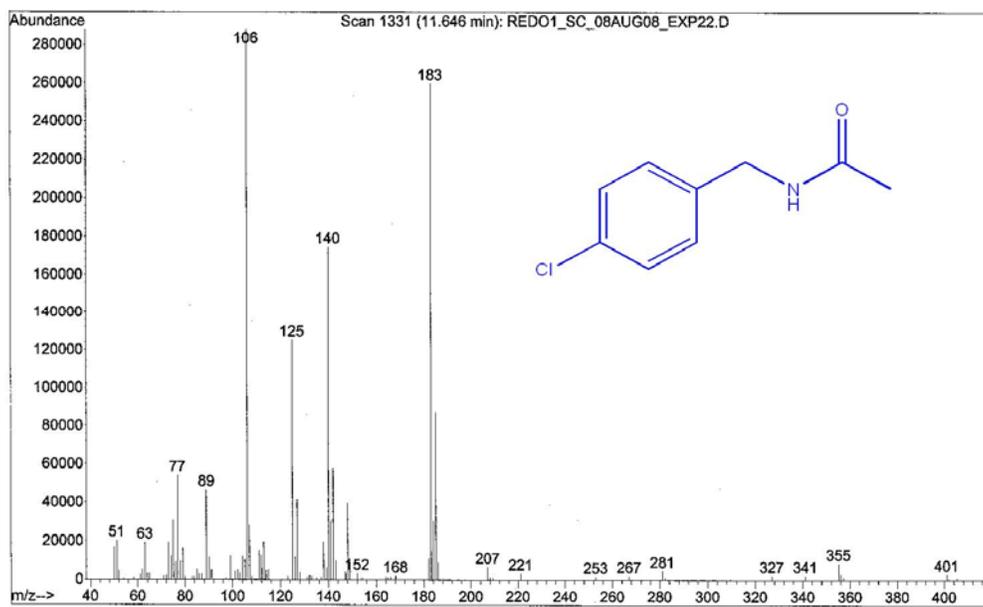


Figure 27: Mass spectrum of **2a** in the crude product mixture.

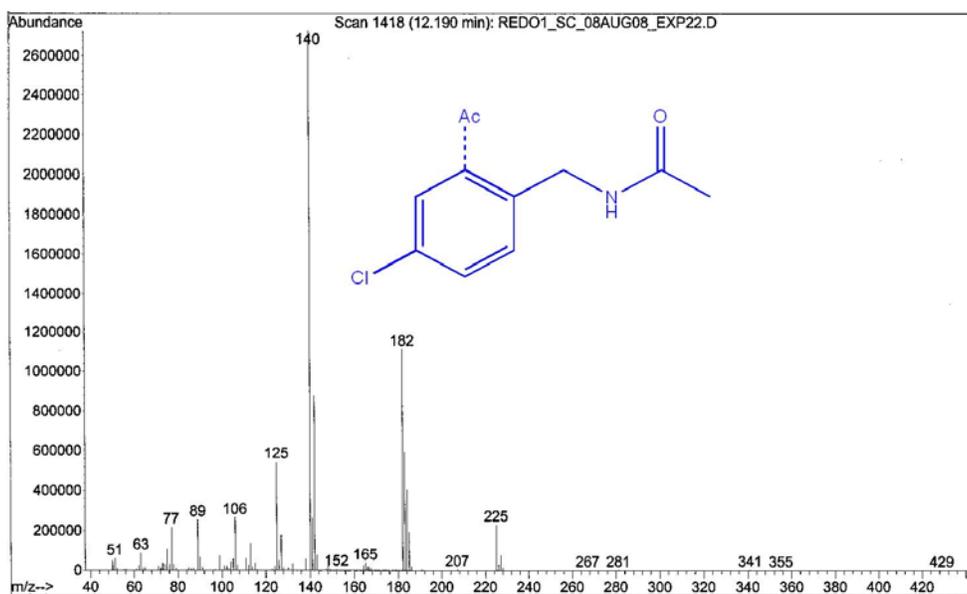


Figure 28: Mass spectrum of diacylated N-chlorobenzylamine in the crude product mixture.

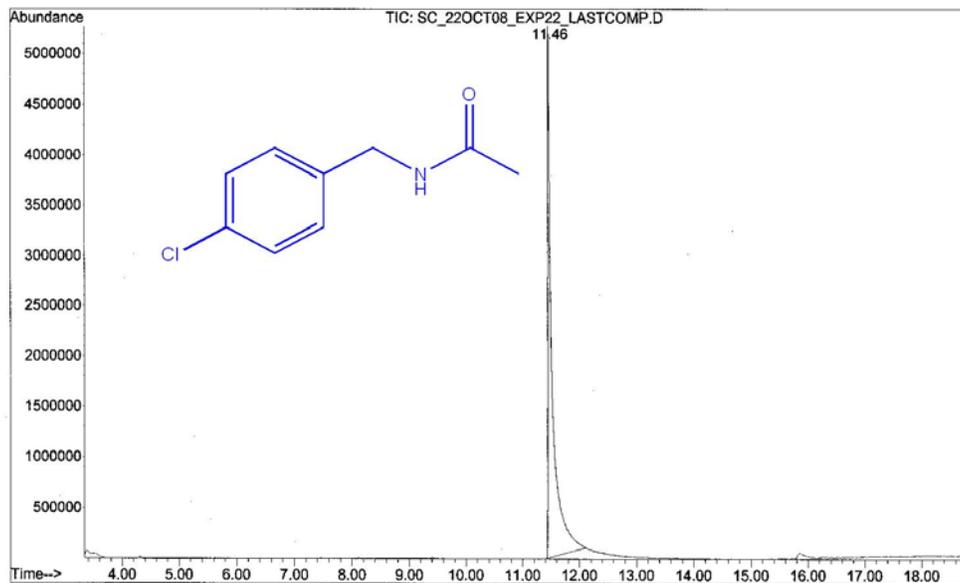


Figure 29: GC post flash column chromatography indicating **2a** as the isolated product.

Preparative scale electrolysis of N-(4-chlorobenzyl)-acetamide (2a): The electrolysis of **2a** was run at +2.00V in a supporting electrolyte of 0.1 M lithium perchlorate in acetonitrile. The oxidation was stopped after 263 coulombs, i.e. after 4.9 eq. of the calculated amount of electrons were utilized. GC/MS showed 100% conversion to 4-chlorobenzaldehyde. GC: r.t. (%): 4-chlorobenzaldehyde, 7.07 min, (100%).

7.066 minutes. The peak at 7.066 minutes was assigned 4-chlorobenzaldehyde because it exhibits identical mass fragmentation as that in the mass spectrum in figures 15 and 17; MS: m/z (%) = 142 (23), 141 (39), 140 (74), 139 (100), 113 (17), 111 (51), 77 (14), 75 (27), 50 (20).

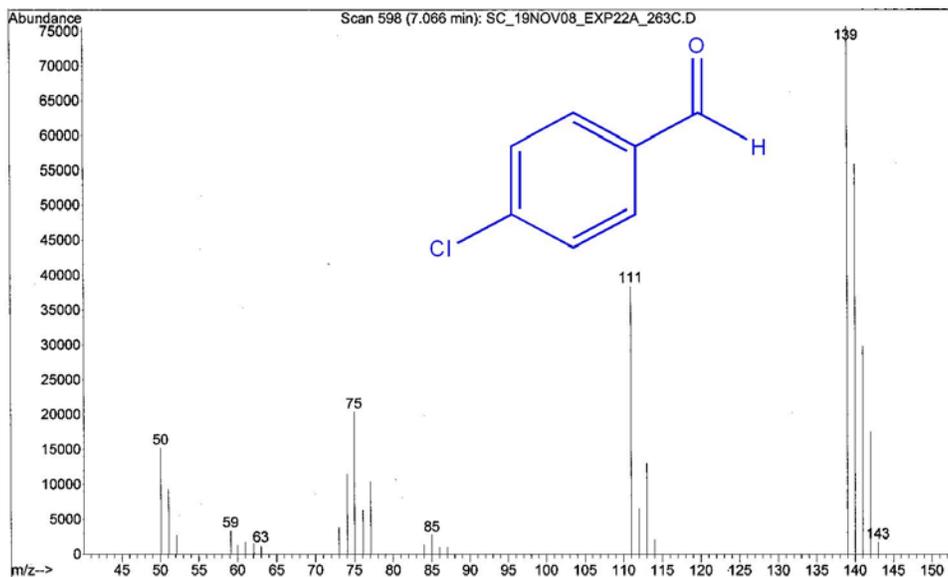
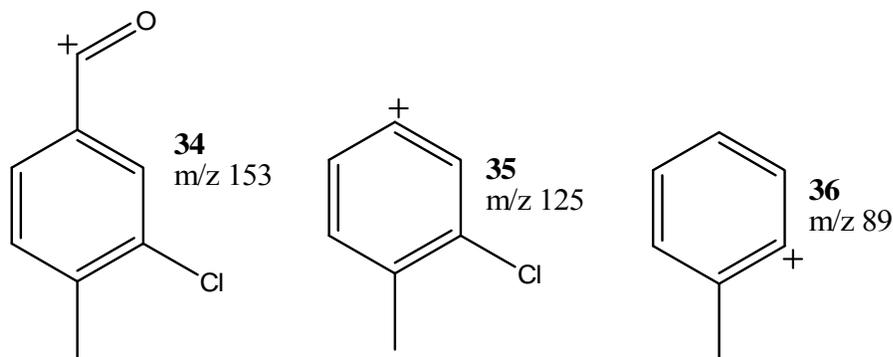


Figure 30: Mass spectrum of 4-chlorobenzaldehyde (r.t. different than that from electrolysis of 4-chlorotoluene because of a different GC/MS method).

Preparative scale catalytic electrolysis of methyl p-toluate (4) with 4,4',4''-trichloro-2,2',2'' nitrotriphenylamine, (catalyst 3): The different properties of the substituents on **4**: an electron-donating methyl group and an electron-withdrawing methoxy carbonyl, prompted us to study its electrochemical behaviors upon anodic oxidation. The electrolysis of **4** was carried out at + 1.5V in a supporting electrolyte of 0.1M lithium perchlorate in acetonitrile and its progress monitored by taking 1 μ L of the sample at regular intervals. GC/MS shows the appearance of a compound with the mass of methyl 3-chloro-4-methylbenzoate post 1040 coulombs (Discussion). After 1559 coulombs, methyl 3,5-dichloro-4-methylbenzoate was observed by GC/MS, but formed no greater than 5% by the end of 2810 coulombs. Starting material was still present after 2810 coulombs.

9.678 minutes. The peak at 9.678 minutes was assigned methyl 3-chloro-4-methylbenzoate (Discussion); MS: m/z (%)= 186 (11), 184 (32), 155 (34), 153 (100), 127 (10), 125 (33), 89 (24) The mass spectrum is shown on the following page. The base peak at m/z 153 corresponds to the cation **34**, m/z 125 corresponds to cation **35**, and m/z 89 corresponds to cation **36**:



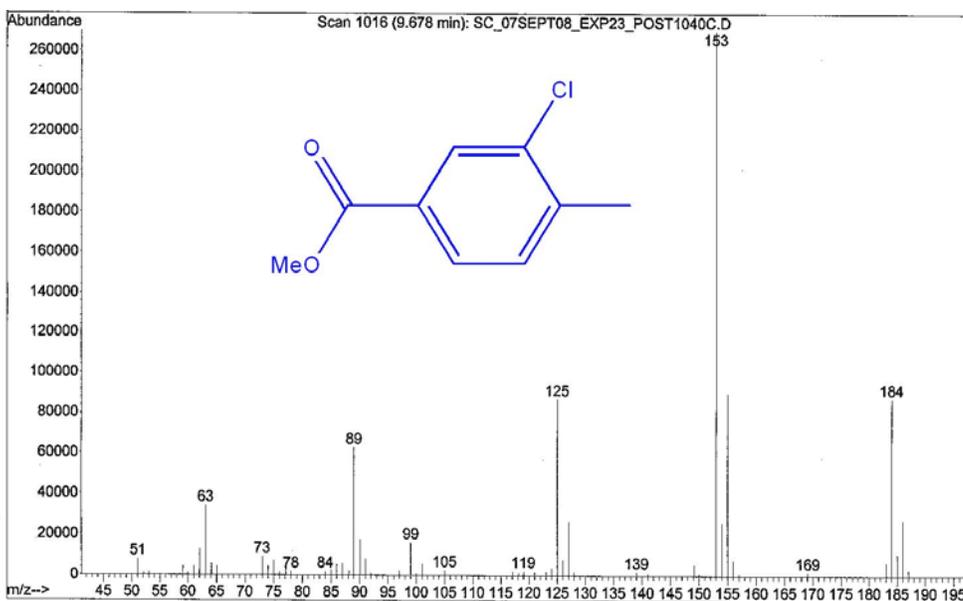
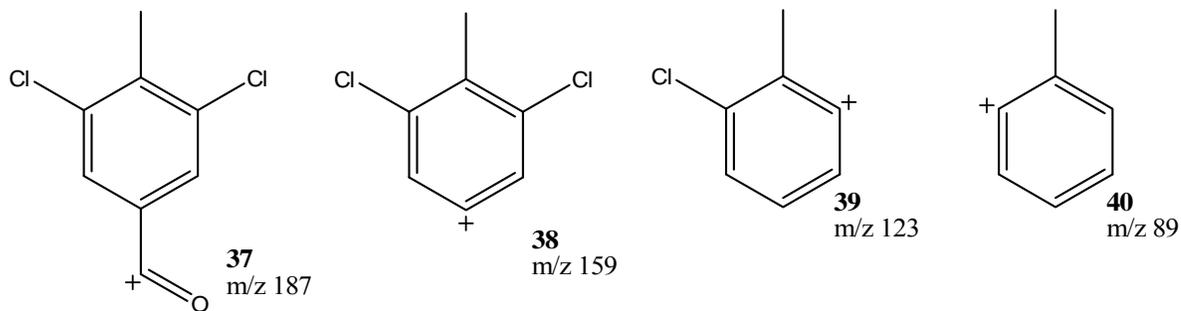


Figure 31: Mass spectrum of methyl 3-chloro-4-methylbenzoate; post 1040 coulombs.

10.921 minutes. The peak at 10.921 minutes was identified as 3,5-dichloro-4-methylbenzoate; MS: m/z (%)= 220 (19), 218 (26), 191 (13), 189 (62), 187 (100). The mass spectrum is shown on the following page. The base peak at m/z 187 corresponds to the cation **37**, m/z 159 corresponds to cation **38**, m/z 123 corresponds to cation **39**, and m/z 89 corresponds to cation **40**:



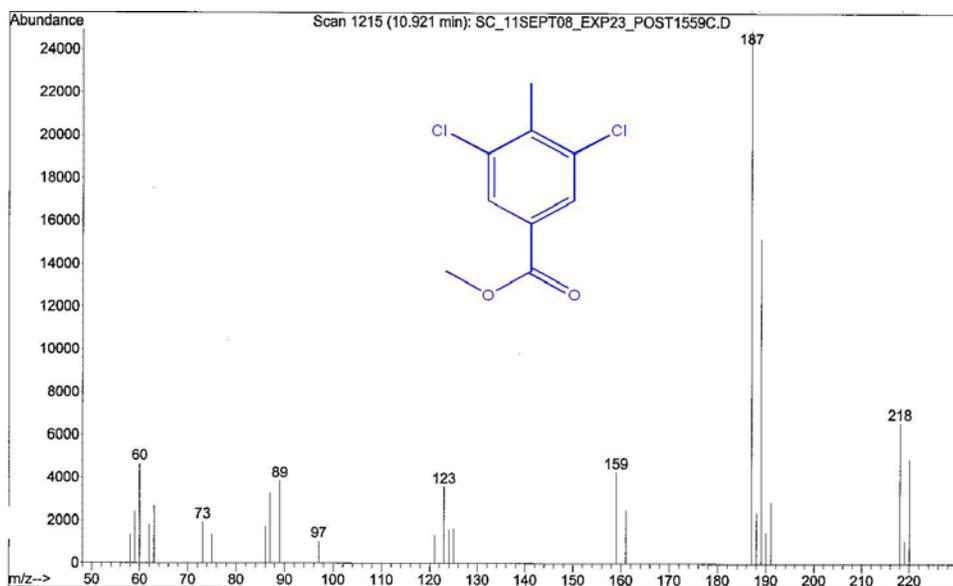


Figure 32: Mass spectrum of methyl 3,5-dichloro-4-methylbenzoate, post 1559 coulombs.

Methyl 4-(chloromethyl) benzoate (7b): Halogenation of methyl p-toluate (**4**) was carried out with *N*-chlorosuccinimide¹⁹ (NCS) and FeCl₃ to test a chlorinated product from the electrolysis of **4** (Discussion). The main isomer, methyl 4-(chloromethyl) benzoate (**7b**) was isolated by flash chromatography (15% EtOAc in hexanes) and yielded 0.07g of yellow liquid. The other isomer, methyl 3-chloro-4-methylbenzoate (**7a**) was isolated from the crude mixture by 10% EtOAc and yielded 0.03g of clear liquid. The proton NMR sample of **7b** illustrated a small trace of the starting material, methyl p-toluate.

9.671 minutes. The GC peak at 9.671 minutes was identified as methyl 3-chloro-4-methylbenzoate (**7a**) (59%); M/S: m/z: (%) = 186 (17), 184 (50), 155 (47), 153 (100), 127 (14), 125 (44), 80 (26). The mass spectrum is shown on the next page; the base peak at m/z 153 corresponds to cation **34**, m/z 125 corresponds to cation **35** and m/z 89 corresponds to cation **36** (p. 50):

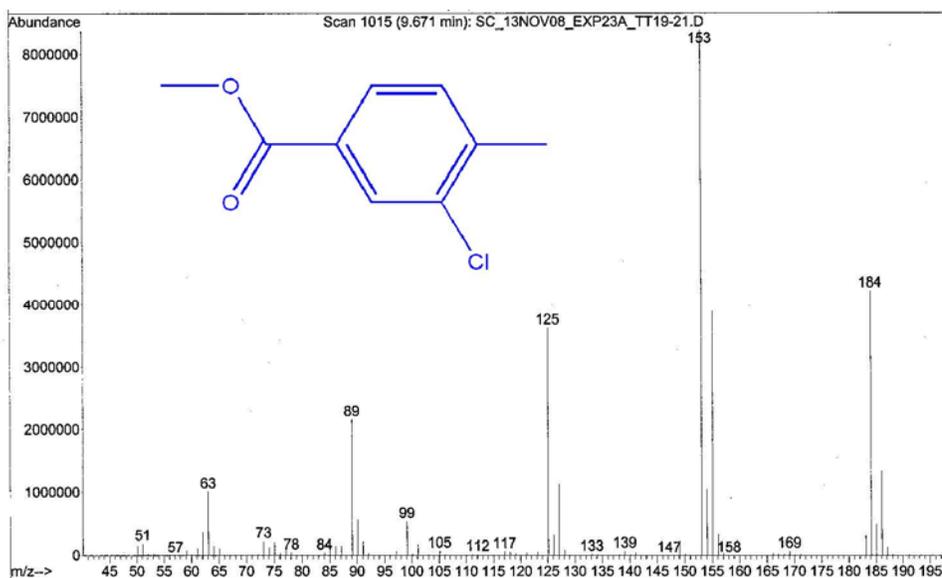
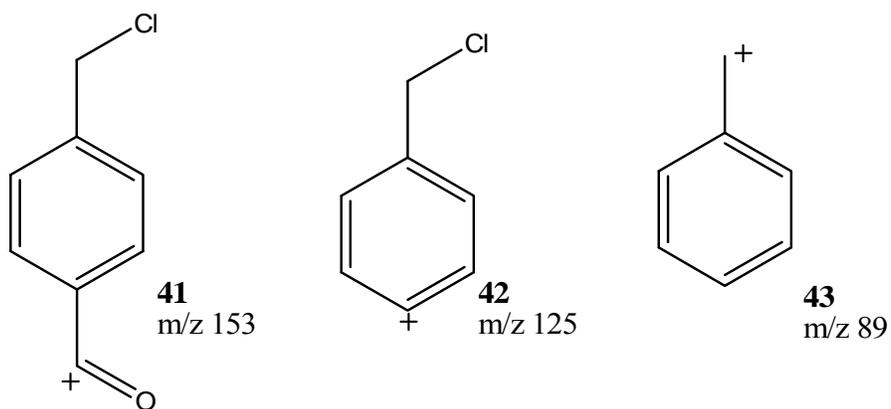


Figure 33: Mass spectrum of **7a**, methyl 3-chloro-4-methylbenzoate.

10.278 minutes. The GC peak at 10.278 minutes was identified as **7b** (78%); M/S: m/z: (%) = 186 (13), 184 (41), 155 (35), 153 (100), 149 (55), 125 (34), 89 (20). The mass spectrum is given on the following page and the base peak at m/z 153 corresponds to cation **41**, m/z 125 to cation **42**, and m/z 89 to cation **43**:



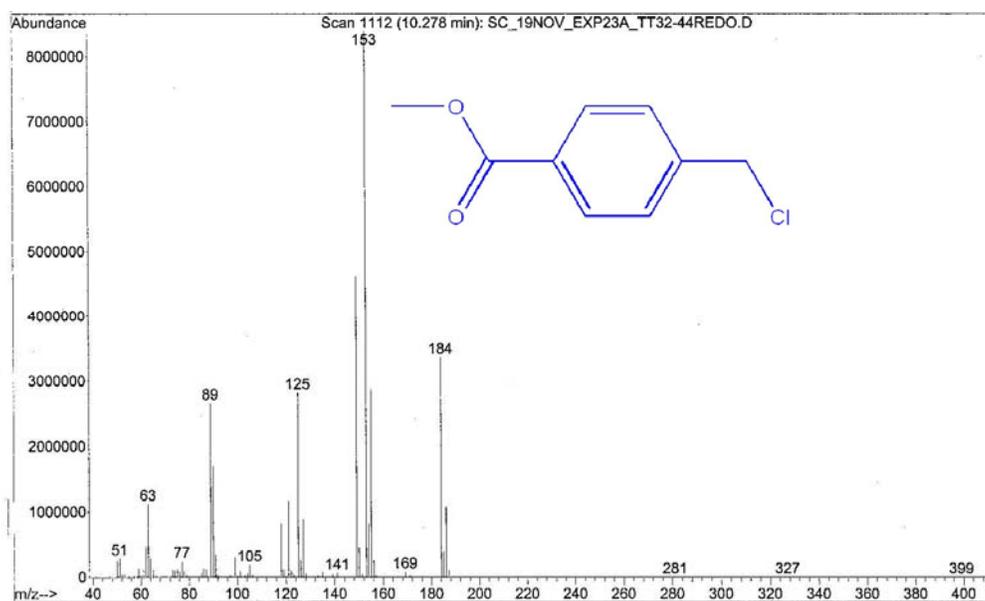
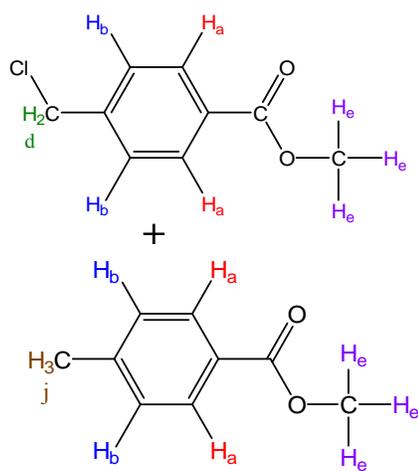


Figure 34: Mass spectrum of **7b**, methyl 4-(chloromethyl) benzoate.



| δ (ppm) | # of H | Coupling (J in Hz) | Assignment |
|----------------|--------|--------------------|----------------|
| 8.03 | 2 | s (0) | H _d |
| 7.46 | 2 + 2 | d (7.5) | H _a |
| 7.26 | 2 + 2 | d (6.9) | H _b |
| 4.61 | 3 + 3 | s(0) | H _e |
| 3.92 | 3 | s(0) | H _j |

Figure 35: Structures of **7b** and **4** and table of ¹H NMR data values for **7b** and **4** that was present in the ¹H NMR sample.

Preparative scale direct electrolysis of 4, 4'-dimethylbiphenyl (5): The electrolysis of **5** was conducted to compare if any similarities or differences will arise from this compound that is similar yet more complex than toluene. The oxidation of **5** was carried out in a solution of 0.1 M lithium perchlorate in acetonitrile. A potential of + 1.5V vs. Ag/0.1M AgNO₃ was applied as the cell was stirred at room temperature. The progress of the oxidation was monitored at regular intervals by taking 1 μ L samples and assessed by GC/MS. The electrolysis was stopped when the starting material (**5**) was consumed, after 1434 coulombs (54F/mol) or 27.5 eq. of the calculated amount of electrons were passed. Flash column chromatography was employed to isolate the different products from the electrolysis: 0.01g of yellow crystals as 4-(4-methylphenyl)benzaldehyde (**5d**) from 5% EtOAc in hexanes, 0.01g of yellow crystals of 4-(4-methylphenyl)benzoic acid (**5e**) from 10% EtOAc in hexanes, 4.8mg of yellow film containing biphenyl-4,4'-dicarboxylic acid (**5f**) and 4,4'-biphenyldicarboxaldehyde (**5g**) from 35% EtOAc in hexanes. The last component from the flash column chromatography was obtained by elution with 100% EtOAc and has a mass that is the same as that of biphenyl-4,4'-dicarboxylic acid methyl ester (**5j**), though this product is unlikely (Discussion). A ¹H NMR spectrum of **5j** cannot be obtained as there was a negligible amount of the sample after ethyl acetate was removed under pressure.

12.081 minutes. The GC peak at 12.081 minutes was assigned as **5d'** (100%);

M/S: m/z (%) = 196 (100), 195 (88), 167 (20), 165 (36), 152 (40). It was purchased from Fisher to compare the mass fragmentation of **5d**.

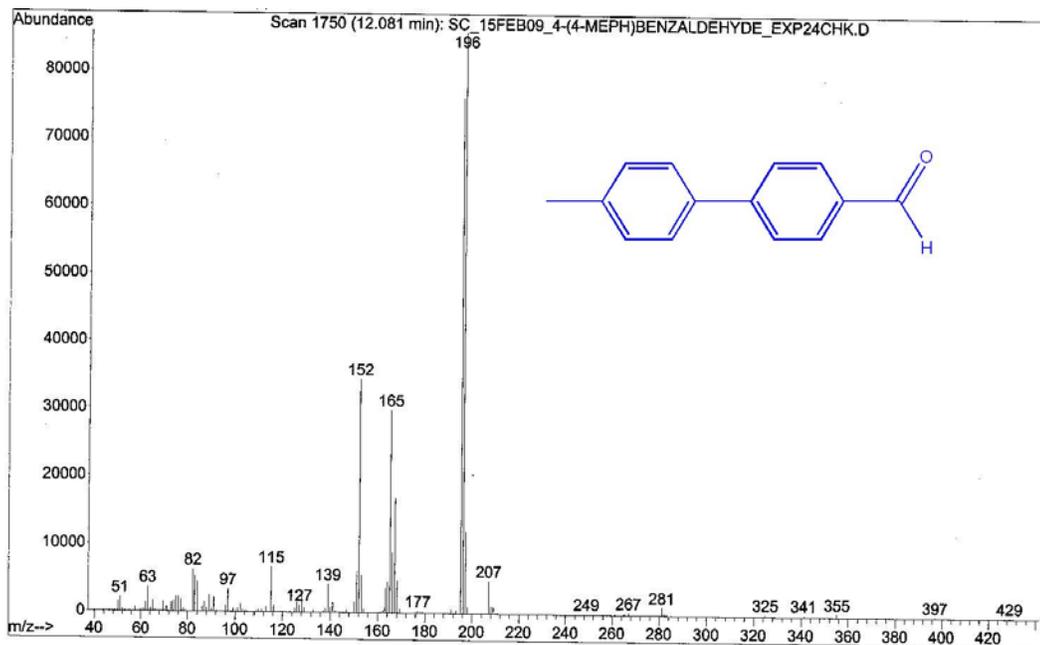


Figure 36: Mass spectrum of 4-(4-methylphenyl)benzaldehyde, purchased from Fisher (**5d'**).

12.534 minutes. The GC peak at 12.534 minutes was assigned as **5d**: M/S: m/z: (%)= 196 (100), 195 (88), 167 (19), 165 (34), 152 (40) because it exhibits the same mass fragmentation as **5d'**. The mass spectrum is shown below. The m/z at 167 corresponds to cation **45** and m/z at 153 to cation **46**:

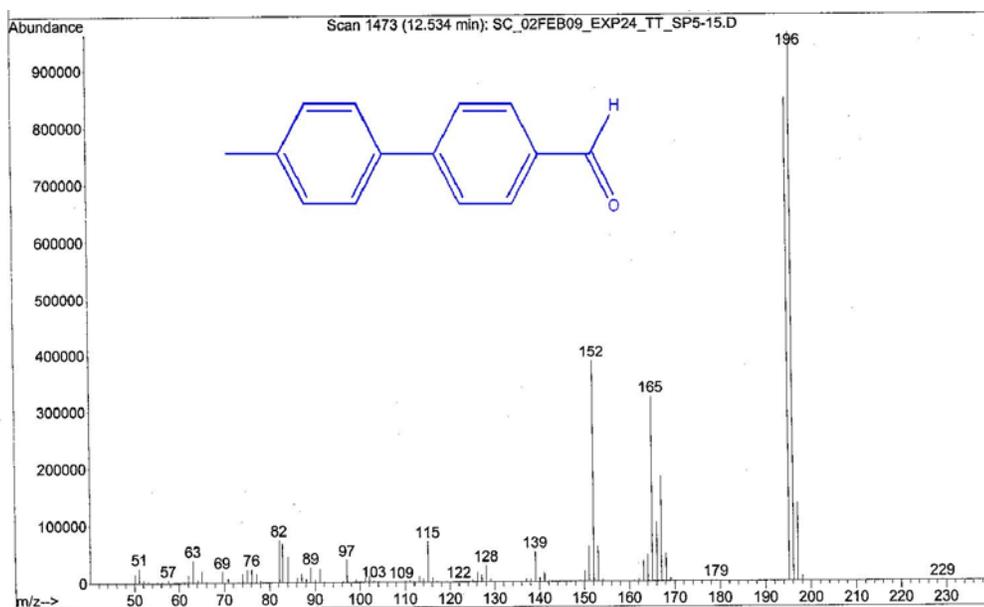
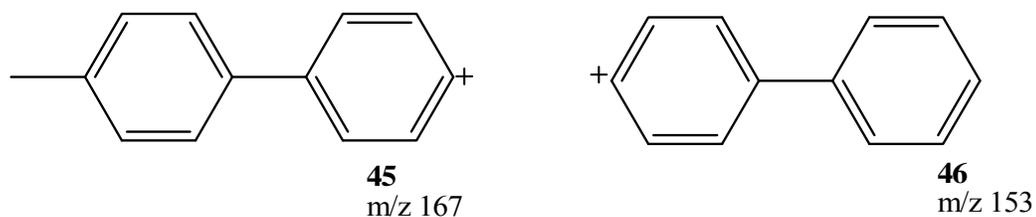


Fig 37: Mass spectrum of 4-(4-methylphenyl)benzaldehyde (**5d**).

12.071 minutes. The peak at 12.071 minutes was identified as **5e**; M/S: m/z (%)= 212 (100), 211 (26), 197 (51), 184 (24), 183 (37), 169 (24), 130 (24), 129, (30), 128 (31), 115 (58), 82 (21). The mass spectrum is shown below. The peak at m/z 197 corresponds to cation **47**:

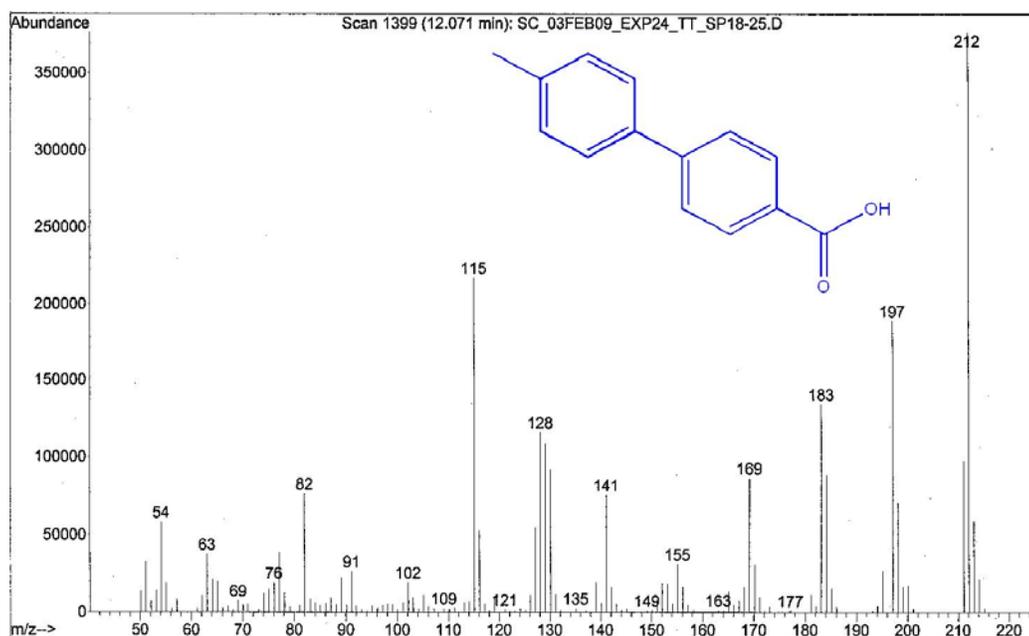
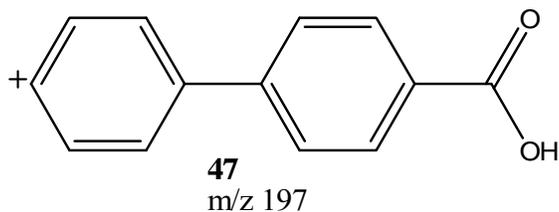


Figure 38: Mass spectrum of 4-(4-methylphenyl)benzoic acid (**5e**).

13.508 minutes. The GC peak at 13.508 minutes was identified as **5f**; M/S: m/z: (%)= 242 (10), 200 (100). The mass spectrum is shown below. The molecular ion of 200 corresponds to the expected mass of **5f**.

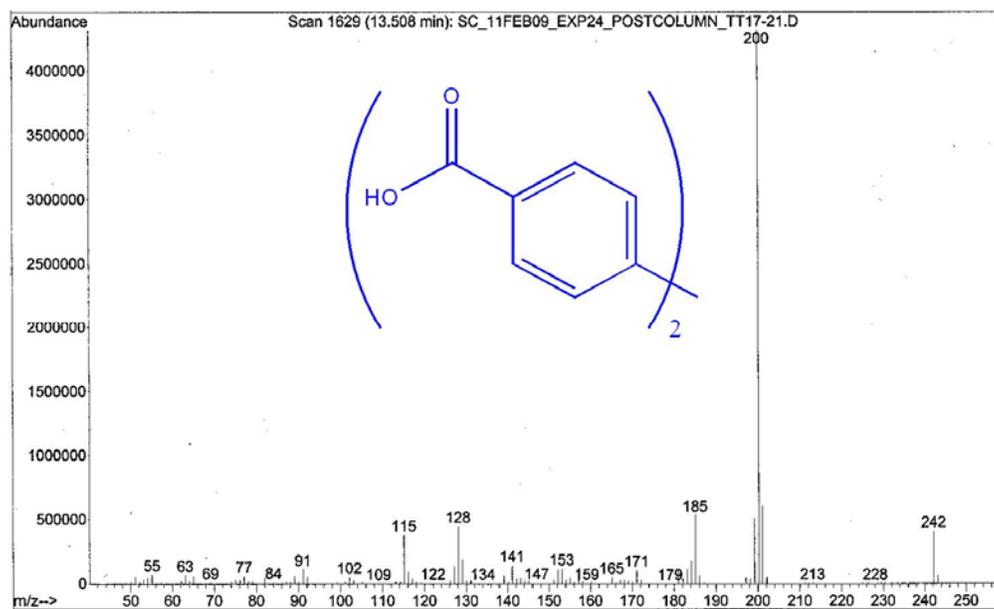


Figure 39: Mass spectrum of biphenyl-4,4'-dicarboxylic acid (**5f**).

13.658 minutes. The GC peak at 13.658 minutes and the base peak at m/z 209 was assigned as **5g**; M/S: m/z : (%) = 210 (94), 209 (100), 153 (25), 152 (67). The mass spectrum is shown below; m/z at 152 corresponds to cation **49**:

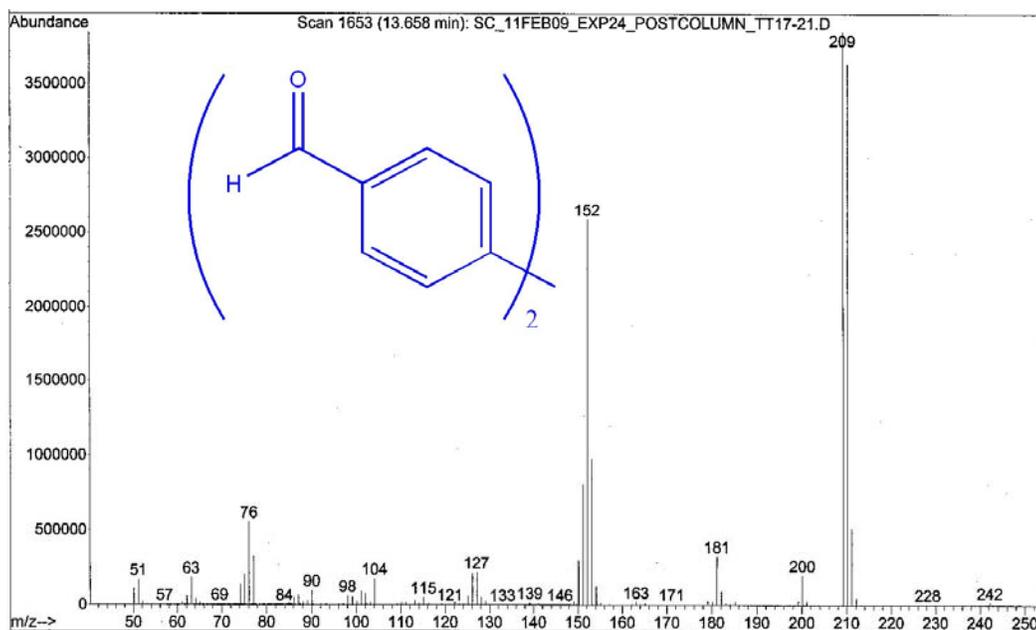
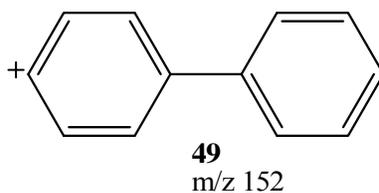


Figure 40: Mass spectrum of 4, 4'-biphenyldicarboxaldehyde (**5g**).

15.358 minutes. The GC peak was speculated to be biphenyl-4, 4'-dicarboxylic acid methyl ester. The mass spectrum is given below; the m/z at 212 corresponds to **50**, m/z at 197 corresponds to cation **51**, m/z at 181 corresponds to cation **52**, and m/z 153 corresponds to cation **53**:

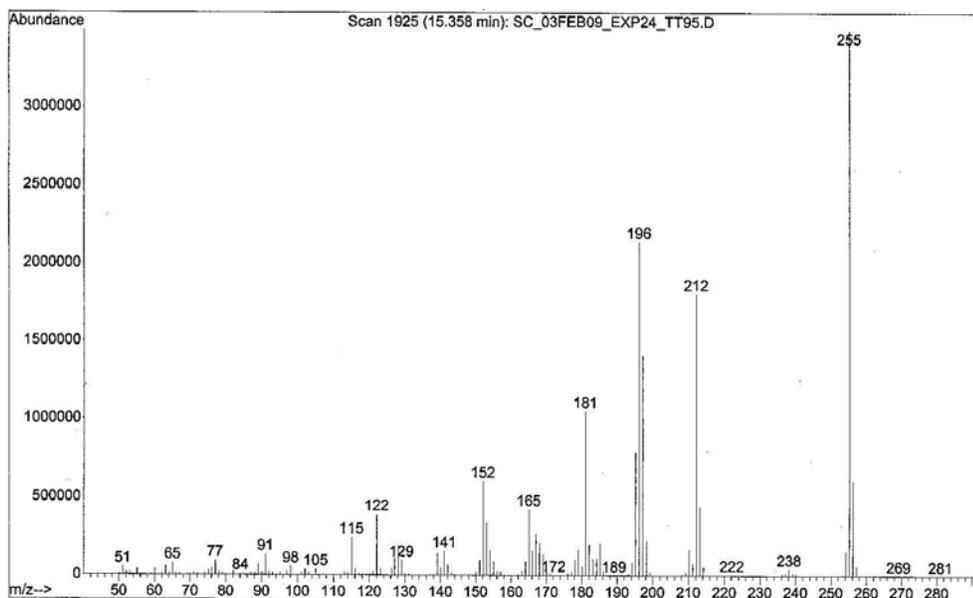
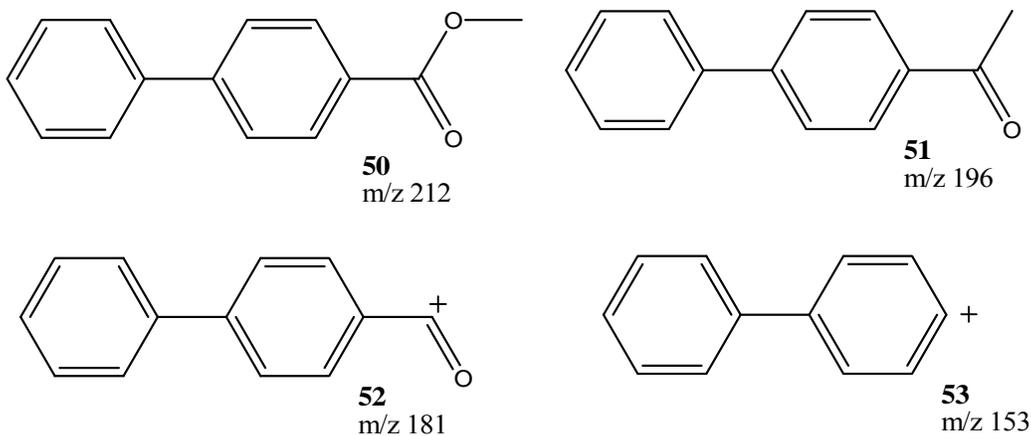


Figure 41: Mass spectrum of a compound with a mass of biphenyl-4, 4'-dicarboxylic acid methyl ester (**5j**).

Preparative scale catalytic electrolysis of 4, 4'-dimethylbiphenyl (5) with 4, 4', 4'-trichloro-2-nitrotriphenylamine (catalyst 4): The cyclic voltammogram of **5** indicates that one electron oxidation occurs at +1.2V (p. 21). Thus an indirect oxidation was performed with **catalyst 4**, which has an oxidation potential of +0.960V, to compare products and behaviors observed in this electrolysis to the direct electrolysis of **5**. The oxidation potential of **catalyst 4** is within $\pm 0.5V$ of the substrate to effectively oxidize one electron of **5**. **Catalyst 4** and **5** were mixed in a solution of 0.1M lithium perchlorate in acetonitrile as the supporting electrolyte. The cell was stirred at room temperature while +1.00 V was applied to the electrolysis system. To monitor the disappearance of the starting material, 1 μ L samples were taken from the electrolysis solution at regular intervals and analyzed by GC/MS. The electrolysis was stopped after 9 hours, after 151.16 coulombs were passed or after 5 eq. of the calculated amount of electrons. The GC/MS showed the presence of **5d** and **5e**, and also N-([1,1'-biphenyl]-4-ylmethyl,4'methyl)-acetamide (**5k**). **5d** and **5e** were assigned according to the mass fragmentation patterns observe in figures 36 and 38, respectively.

12.996 minutes. The GC peak at 12.996 minutes was believed to correspond to **5k** (MW: 239); M/S: m/z (%)=227 (41), 210, 195 (34), 196 (39), 184, 115 (20), 182 (46), 181 (24), 170, 167 (27), 166 (22), 165 (100), 152 (30). The M⁺ of 239 is absent perhaps due a relatively low abundance. The m/z at 196 corresponds to cation **54**; m/z at 181 corresponds to cation **55**, m/z 167 to cation **56**, and m/z 153 to cation **57**:

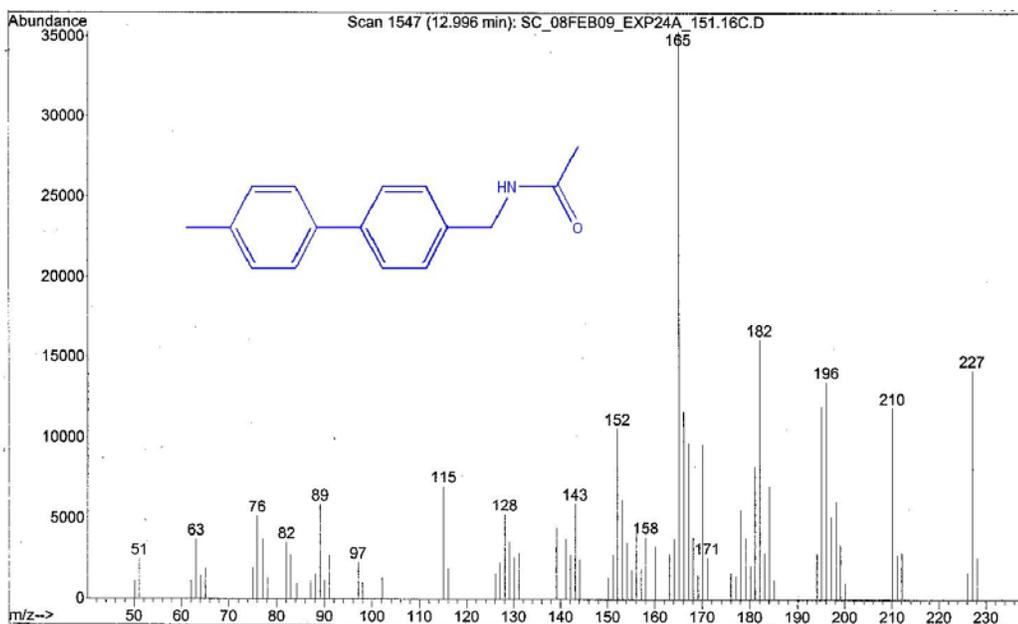
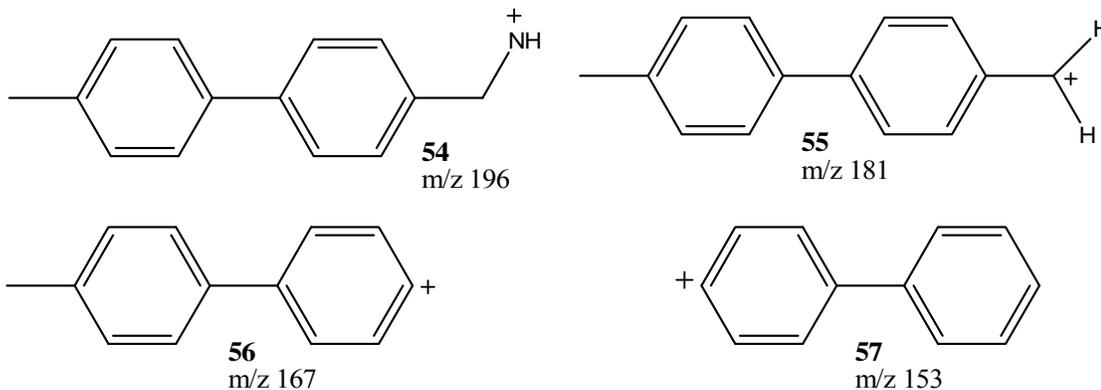


Figure 42: Mass spectrum of **5k**, N-(1,1'-biphenyl)-4-ylmethyl,4'-methyl)-acetamide.

4,4'-dimethyl-2-nitro-1,1'-biphenyl (6) was synthesized to investigate the effects of anodic oxidation of **5** with the introduction of an electron-withdrawing group. The reaction was carried out by nitrating 4,4'-dimethylbiphenyl in the presence of potassium dihydrogen phosphate; the reaction was stirred at room temperature for 20 minutes after which it was worked up. Flash chromatography was employed to isolate the two components: 0.42g of **5** (5% EtOAc in hexanes); M/S: m/z (%)= 182 (100), 181 (27), 167 (48), 165 (38); **6** (5-10% EtOAc in hexanes); 0.18g of yellow liquid which was then recrystallized with 95% EtOH to yield 91.2mg of yellow crystals (9% yield); M/S: m/z (%)= 227 (43), 210 (38), 184 (21), 182 (50), 170 (30), 166 (32), 165 (100).) ¹H NMR (CD₃CN, 300MHz): δ 7.68 (s, 1H), 7.49, 7.39 (J_{AB}= 7.8Hz), 7.25, 7.21 (J_{AB}=8.1Hz), 2.45 (s, 3H), 2.38 (s,3H), 2.13 (s) is H₂O in CD₃CN and 2.08 (s) is acetone. ²⁰; m.p. 68-69°C (lit. 67-68°C)²¹

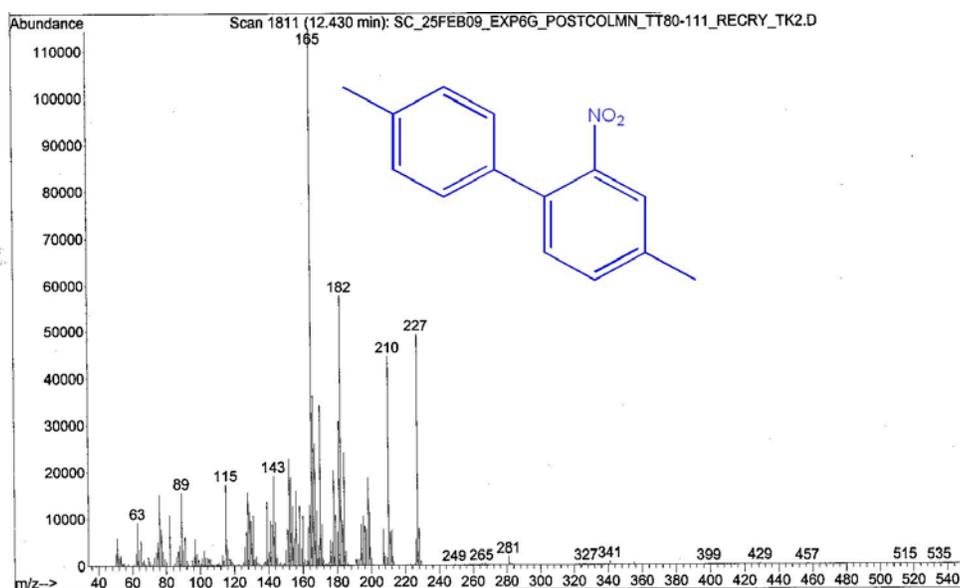


Figure 43: Mass spectrum of 4,4'-dimethyl-2-nitro-1,1'-biphenyl (**6**).

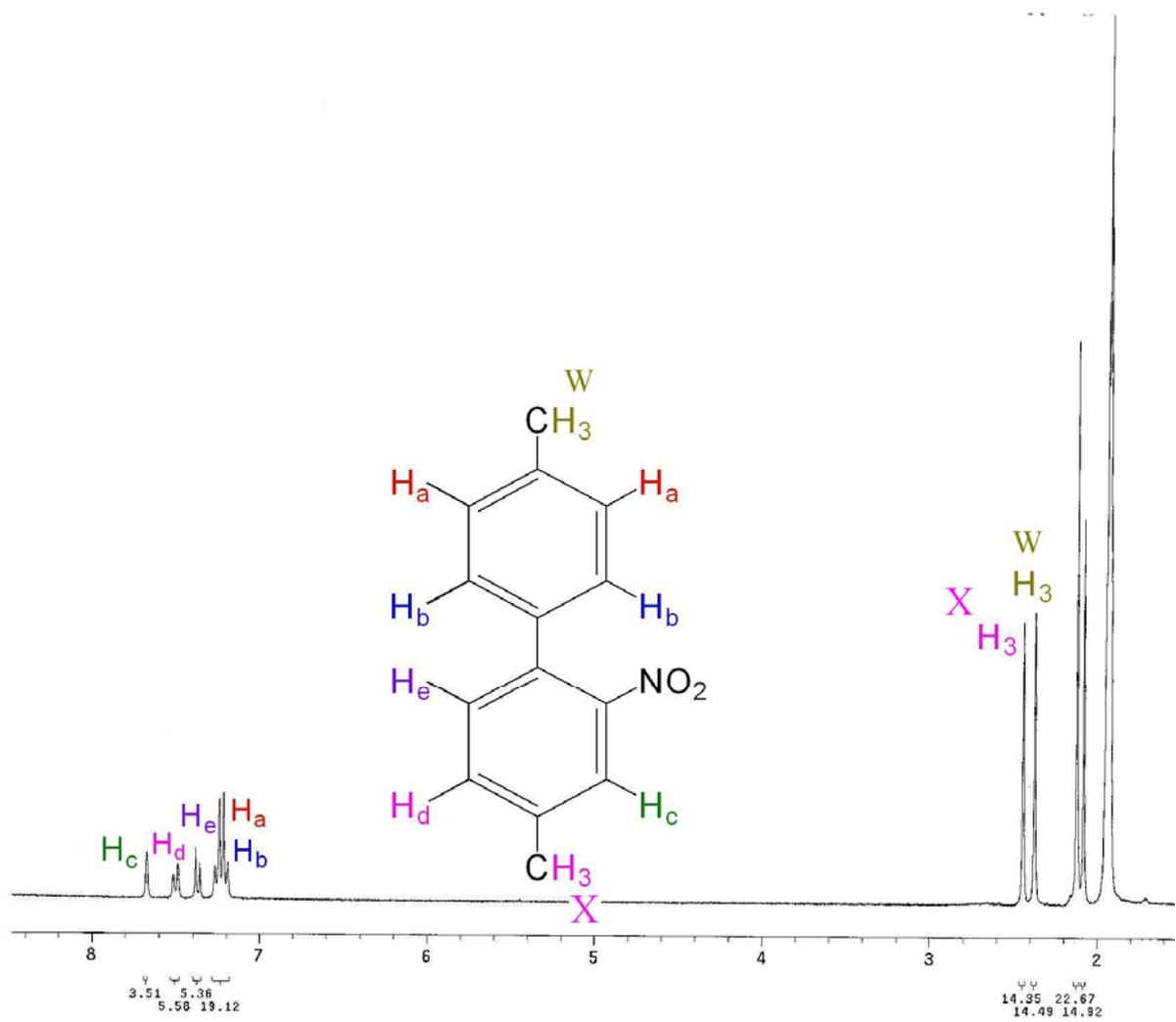


Figure 44: ^1H NMR spectrum of 4,4'-dimethyl-2-nitro-1,1'-biphenyl (**6**).

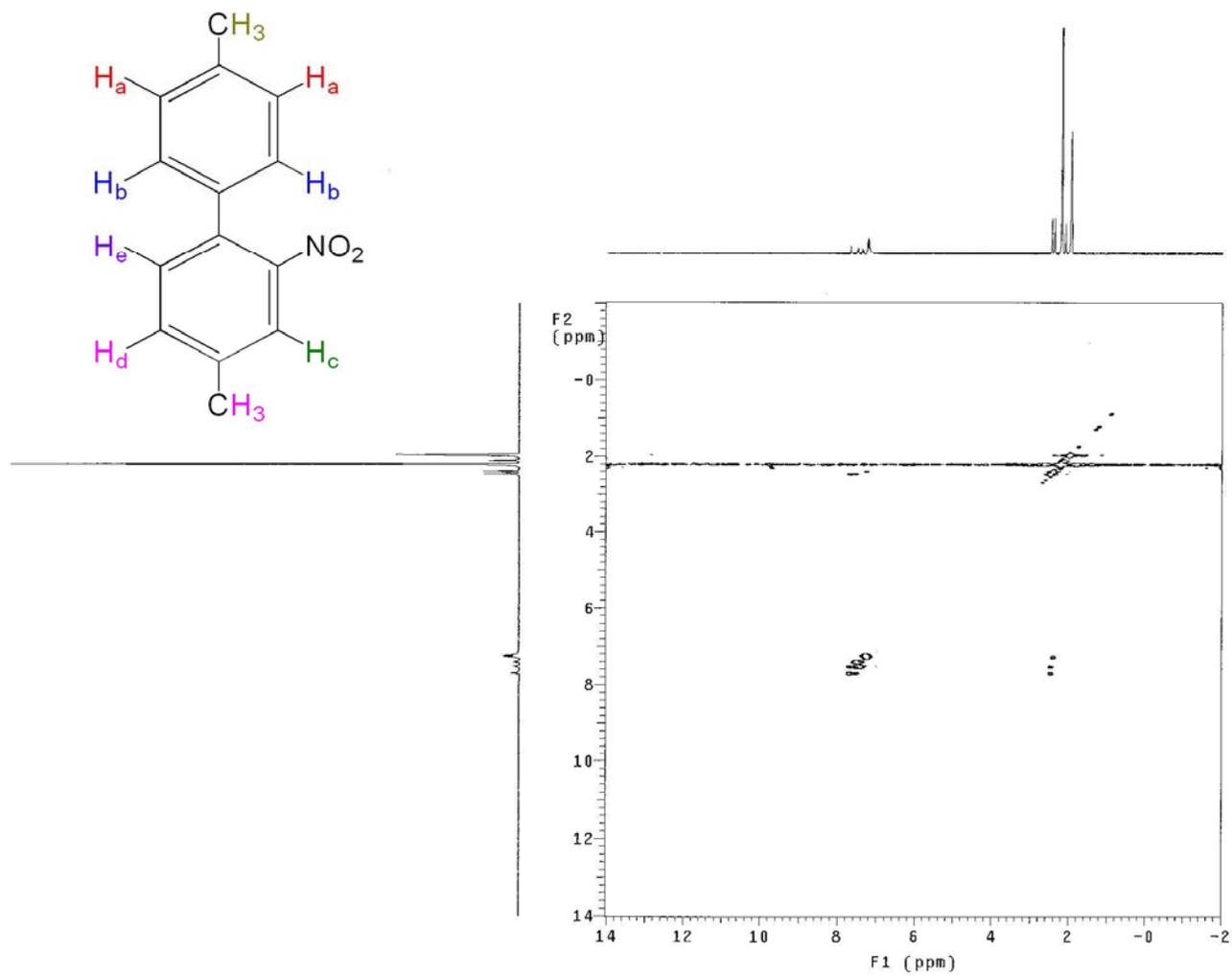


Figure 45: 2D COSY spectrum of **6**.

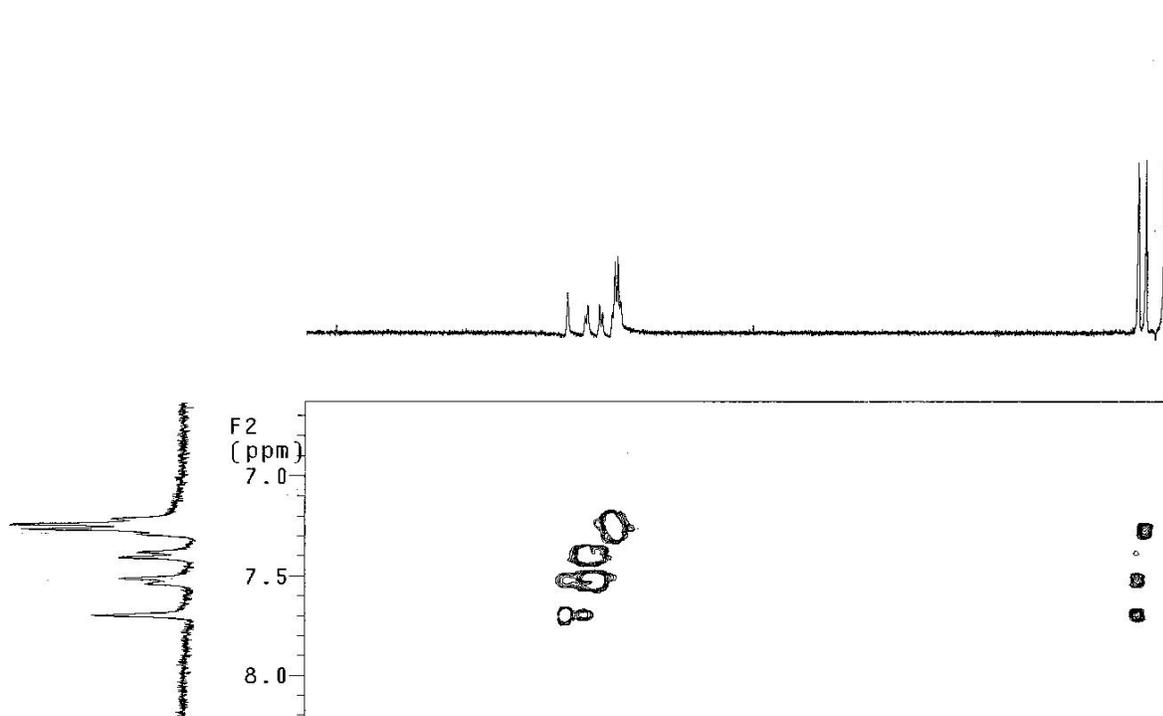
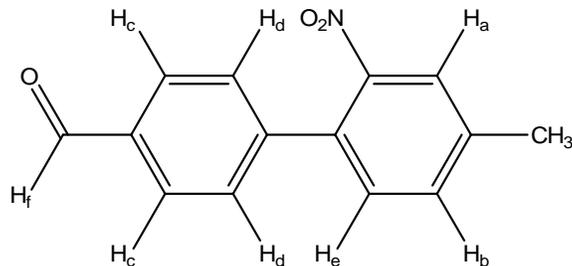


Figure 46: Expansion of figure 45, aromatic region of 2D COSY of **6**.

Preparative scale direct electrolysis of 4, 4'-dimethyl-2-nitro-1,1'-biphenyl (6):

Synthesis and subsequently the electrolysis of **6** were conducted to study the electrochemical behaviors of a compound that is similar but also a bit more complex than toluene with the addition of a ring-deactivating group. The electrolysis of **6** was carried out at room temperature with the application of +1.6V in 0.1M lithium perchlorate in acetonitrile as the supporting electrolyte. The oxidation was stopped after **6** was no longer present, after 7.22 coulombs or 2.9 eq. of the calculated amount of current had passed. Workup yielded 3.5mg of caramel color film. **6a**: M/S: m/z (%)= 241 (34), 213 (41), 196 (36), 184 (48), 168 (69), 166 (28), 165 (100), 156 (34), 152 (64), 139 (27); ¹H NMR (CD₃CN, 300MHz): δ 10.05(s, 1H_f), 7.93 (H_c), 7.55 (H_d) (J_{AB}=7.65Hz), 7.82 (s, 1H_a), 7.58 (H_b), 7.42 (H_e) (J_{AB}= 7.2Hz), 2.48 (s, 3H, 4-CH₃).



13.516 minutes. The GC peak at 13.516 minutes corresponds to **6a**; M/S: m/z (%)= 241 (34), 213 (41), 196 (36), 184 (48), 168 (69), 166 (28), 165 (100), 156 (34), 152 (64), 139 (27). The mass spectrum is shown below; the m/z at 213 corresponds to cation **58**, m/z at 167 corresponds to cation **59**, and m/z at 153 corresponds to cation **60**:

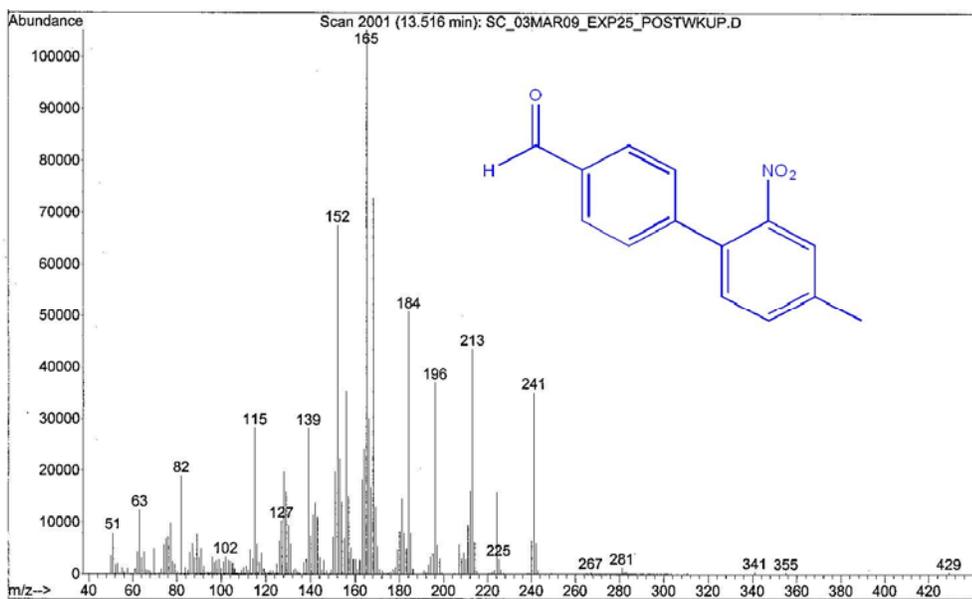
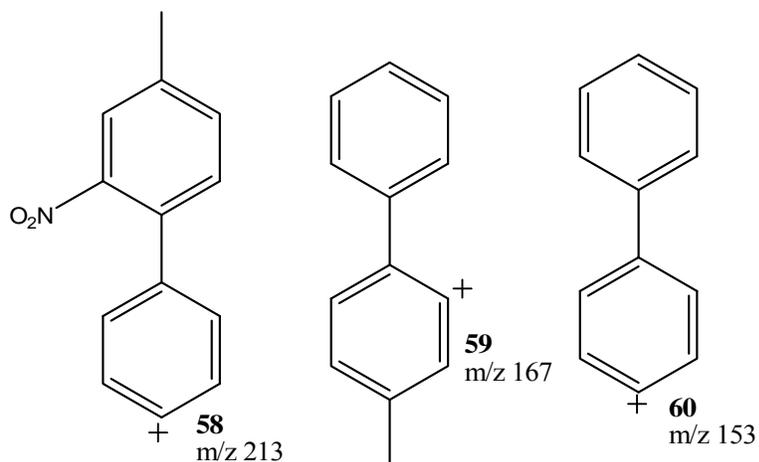


Figure 47: Mass spectrum of 4-aldehyde, 4'-methyl-2'-nitro-1,1'-biphenyl (**6a**).

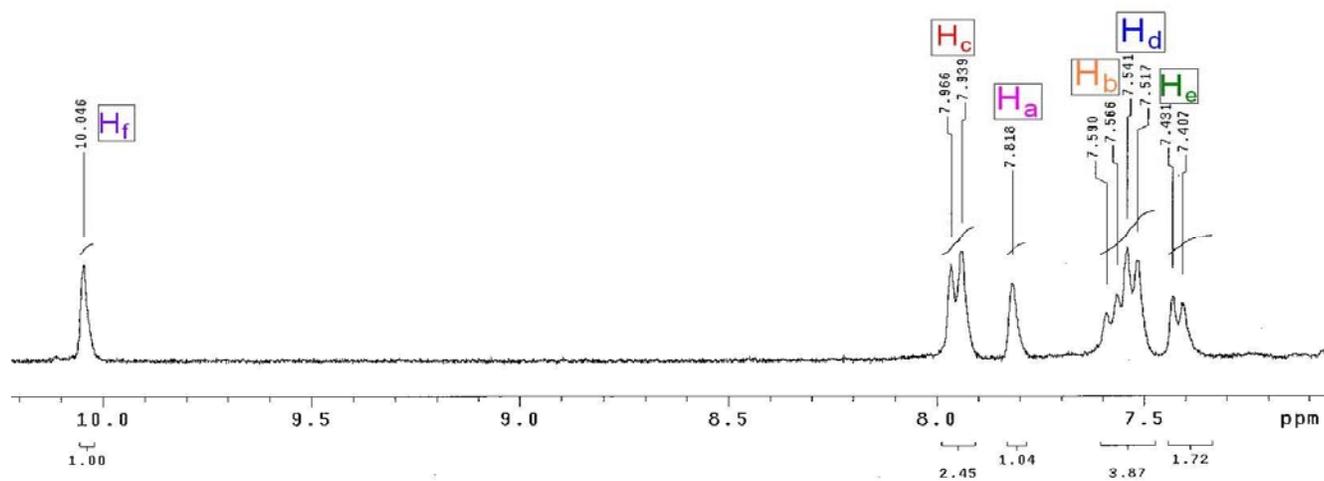
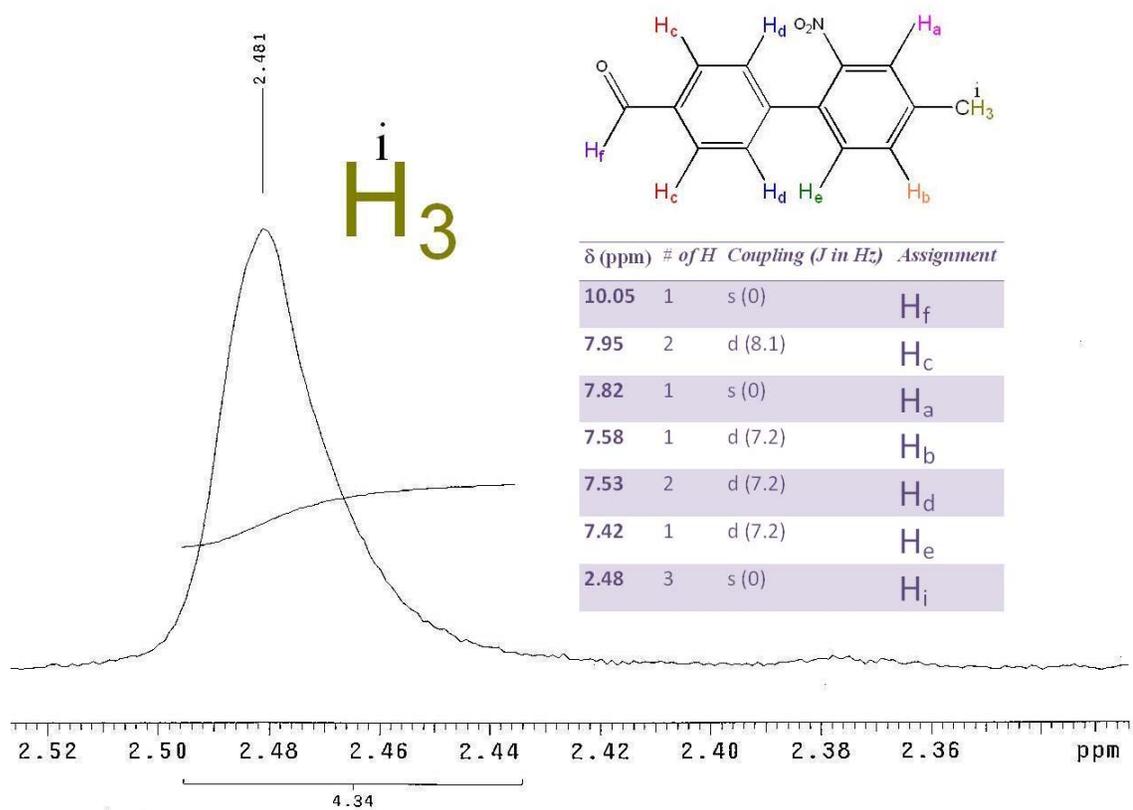


Figure 48: ¹H NMR spectrum of 4-aldehyde, 4'-methyl-2-nitro-1,1'-biphenyl.

DISCUSSION

Three broad patterns are observed from the anodic oxidation of compounds **1-6**, **1a**, and **2a**: (a) chlorination of substrates; two mechanisms are proposed to explain the origin of the Cl^+ or Cl^+ equivalent that apparently leads to the chlorination: 1) from the substrate containing a chlorine group that is being oxidized or 2) Cl^+ generated by the catalyst, figures 59 and 60; (b) anodic oxidation of side chain substituents to either the aldehyde or the amide with the concentration of water as a variable, as observed in the anodic oxidation of toluene, and (c) anodic oxidation to an aldehyde functional group at the expense of the amide as more current is passed through the electrolysis (figure 58).

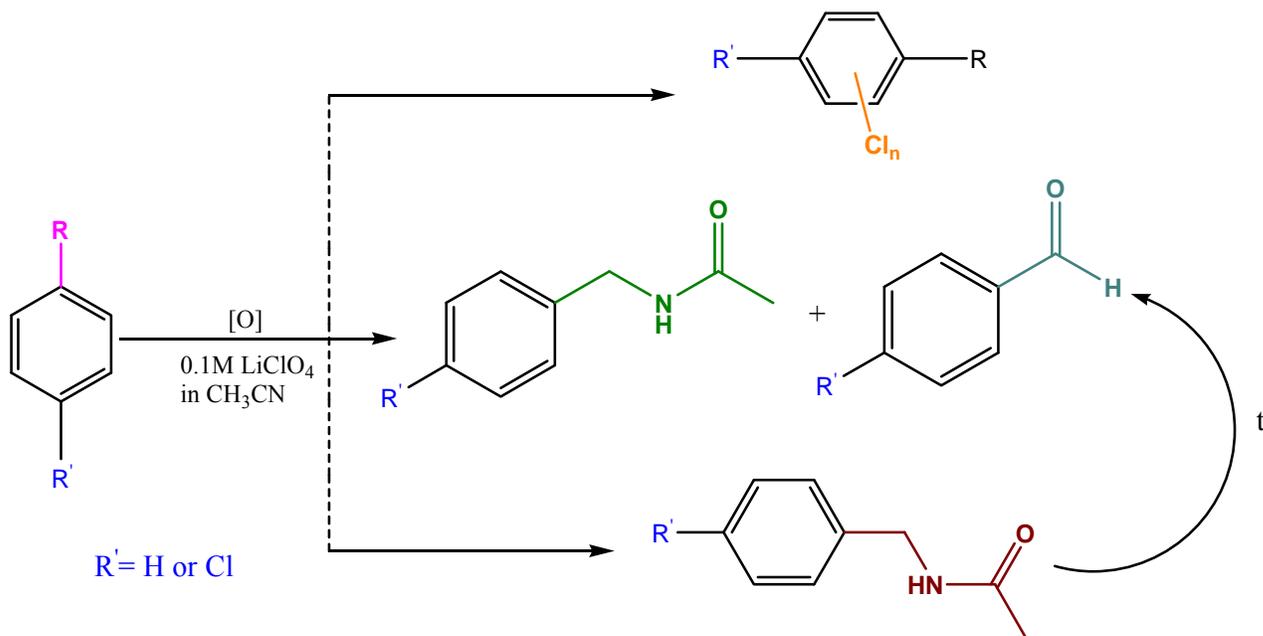


Figure 49: Three trends observed in the overall anodic oxidation of studied compounds: where $\text{C}_6\text{H}_5\text{RR}'$ represents compounds **1-6**, **1a**, and **2a**.

Miller²² presented successful aromatic iodination of a number of simple aromatic compounds, most likely via initial iodine oxidation followed by electrophilic substitution by a positive iodine species. In the case of several alkyl substituted aromatics, acetamidation as a side chain substitution was observed:

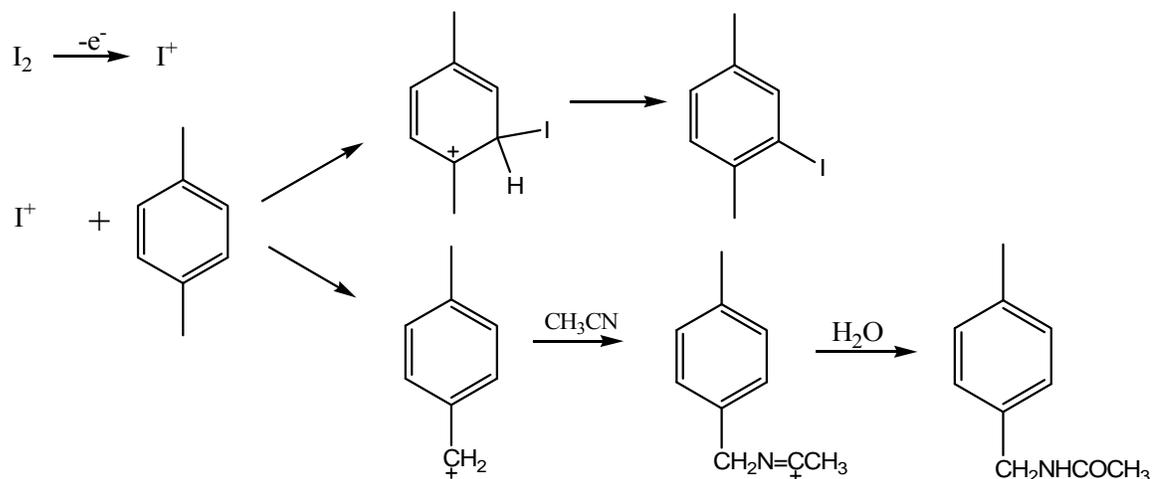
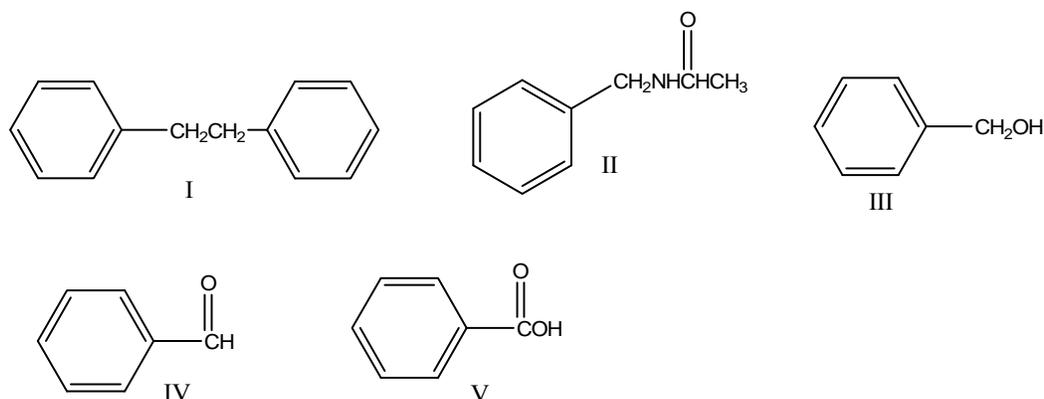


Figure 50: Aromatic iodination²² and side chain acetamidation.

These results are similar in nature to those observed in the electrolyses of **2** and **3**: chlorination of the aromatic compound and the occurrence of a side chain acetamidation reaction. The amide is formed by reaction of the benzylic cation in acetonitrile, and in our case, the positive chlorine species can stem from either oxidation of the substrate or of the catalyst.

The anodic acetamidation of toluene was also found by Parker and Burget:²³ it was found that anodic oxidation of toluene in acetonitrile results in five products (I-V), and the distribution of the five products was dependent on the anode potential and the concentration of water.

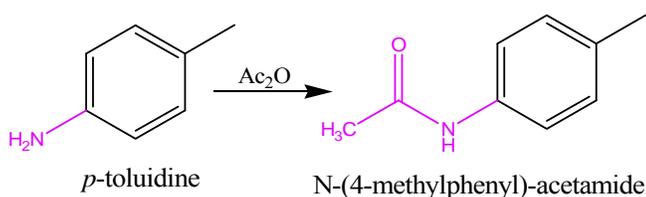


Parker found that at a given potential, with an increase in the concentration of water in the electrolyte, the ratio of IV: II increased. Ebersson's²⁴ studies on anodic acetamidation also supports that in the presence of water, the yields of both III and IV increase at the expense of N-benzylacetamide (II). Our results obtained from the anodic oxidation of toluene also concur with the results: in the presence of higher water concentration and as more coulombs are passed through the solution, the benzaldehyde product increased as the amide decreased (observed in the oxidation of **2** and **3** and confirmed by the oxidations of **1a** and **2a**; discussed below).

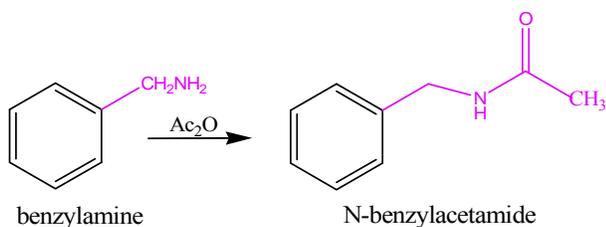
Ebersson also noted an interesting phenomenon in his studies of anodic acetamidation: cations generated in anodic oxidation have different preferentiality toward the available nucleophiles (water and acetonitrile) than those formed in homogenous chemical reaction. In homogenous chemical reactions, the more stable cations showed greater selectivity toward the stronger nucleophile (water), whereas cations generated in anodic oxidation react preferentially towards the weaker nucleophile, acetonitrile. Mayeda and Miller later suggested that the behavior was not reflection of a kinetic competition for the benzyl cation, but rather was the result of the chosen supporting electrolyte²⁵.

Preparative Scale Electrolysis of toluene (1) under two different conditions: Two separate electrolyses of toluene were carried out: one relying on traces of moisture from the wet acetonitrile in 0.1 M lithium perchlorate solution and the other with 5 additional drops of water in the electrolysis solution. The electrolysis performed without additional water yielded primarily a product with a M^+ of 149 and minor amounts of benzoic acid. On the contrary, the main product from the electrolysis with the 5 additional drops of water was benzaldehyde and the minor product with a molecular ion of 149 (with the same fragmentation patterns as the M^+ of 149 from the electrolysis of toluene without the addition of water).

The molecular ion of 149 present in both mass spectrometries from the two separate electrolyses suggests the presence of an amide. However, a M^+ of 149 could be either of two amides: N-(4-methylphenyl) acetamide or N-benzylacetamide. To distinguish, both were synthesized by direct acylation, schemes 1 and 2, and GC/MS obtained to match the unique fragmentation pattern and retention time to that of the oxidized product.



Scheme 1: Acylation of *p*-toluidine



Scheme 2: Acylation of benzylamine

7.703 minutes. The GC peak at 7.703 minutes corresponds to N-benzylacetamide, the product obtained from scheme 2. The mass spectrum is shown below in figure 51; it contains the same fragmentation observed in the mass spectrum of the product from oxidation, figure 8, reproduced below in figure 52. The m/z at 106 corresponds to cation **13** and m/z 91 to cation **14** (Results p.27-28).

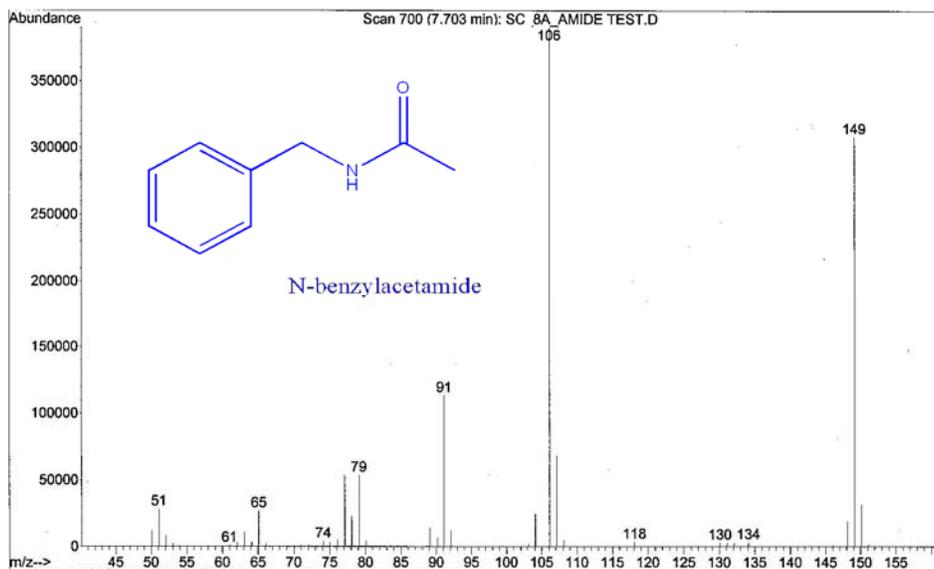


Figure 51: Mass spectrum of N-benzylacetamide from synthesis; scheme 2; r.t.: 7.703min.

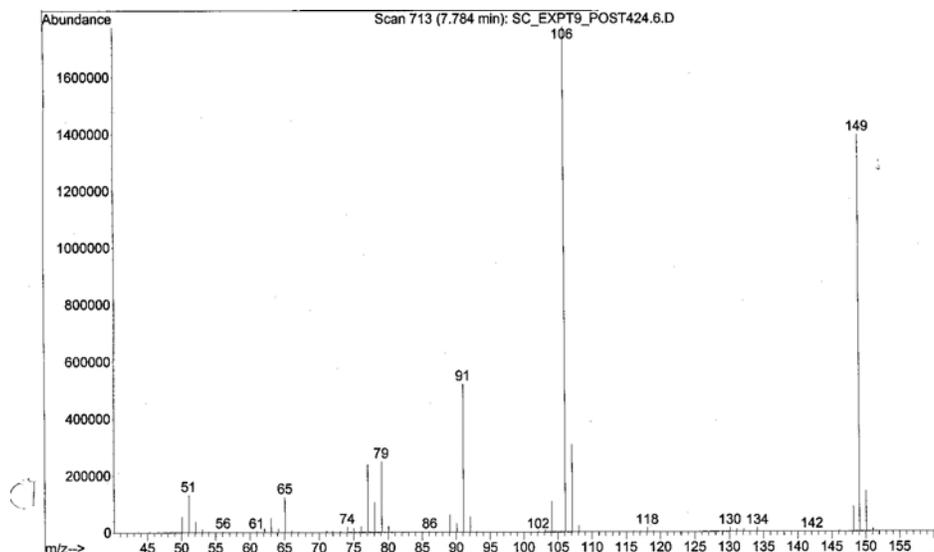


Figure 52: Mass spectrum of N-benzylacetamide post electrolysis; r.t.: 7.784min.

| Compound | Retention time in GC (min) | M+ |
|---|----------------------------|-----|
| Product from oxidation | 7.784 | 149 |
| <u>N-benzylacetamide</u> from acylation of benzylamine | 7.703 | 149 |
| <u>N-(4-methylphenyl)-acetamide</u> from acylation of <i>p</i> -toluidine | 8.634 | 149 |

Table 3: Retention times of the oxidized product and the two synthesized amides from acylation.

The retention time difference between that of the synthetic sample of N-benzylacetamide and that of the oxidized product (table 3) is 1.4 msec, a negligible difference; thus the two retention times are considered identical. In addition, a m/z of 91, present in both synthesis of scheme 2 and the mass spectrum of the electrolysis product strongly suggest a benzyl radical and was absent in the mass spectrum of N-(4-methylphenyl) acetamide. All this strongly confirms that the molecular ion of 149 from the two separate electrolyses of toluene is N-benzylacetamide.⁹

The proposed mechanism for the formation of N-benzylacetamide from the electrolysis of toluene is given in figure 53: an electron is removed from the ring, producing a cation radical corresponding to **1**. Then a loss of proton leaves a radical **2**. This can then be oxidized again to make a carbocation **3** which in turn will undergo nucleophilic attack by acetonitrile and in the presence of water, to afford **4**. The enol then tautomerizes to N-benzylacetamide. The reaction of carbocations with nitriles to form amides is a well known process, the Ritter reaction.²⁶

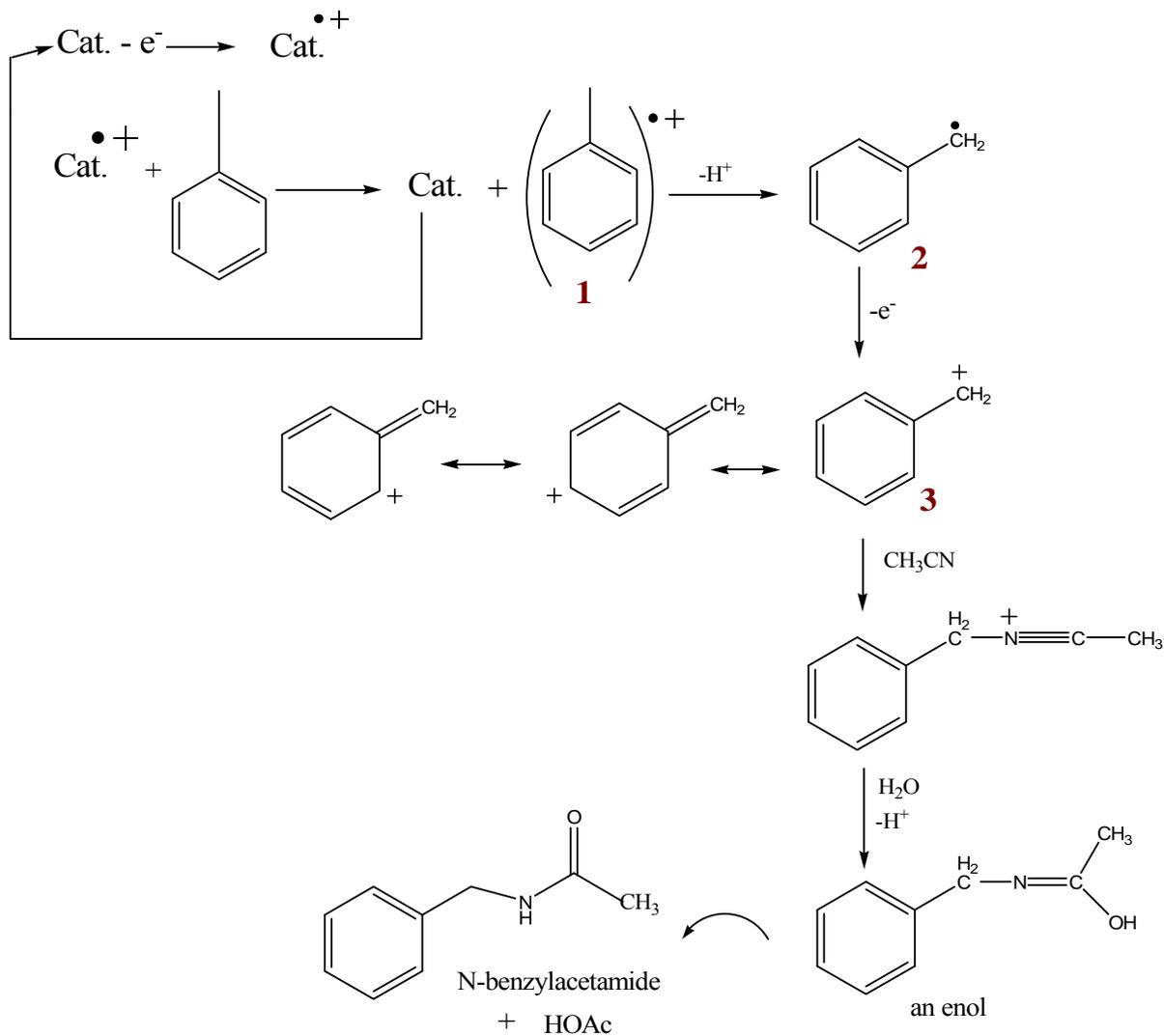


Figure 53: Proposed mechanism for electrolysis of toluene to N-benzylacetamide.

Electro-oxidation of polyalkylbenzenes, and other related compounds in various media have lead to the corresponding acetoxyated, alkoxyated, and acetamidated derivatives;²⁷ the electrolysis of toluene to N-benzylacetamide confirms that electro-oxidation of alkylbenzenes can occur at the side chain. On the contrary, electro-oxidation of benzene and other condensed aromatic compounds is necessarily restricted to the nucleus because they lack side chains. For alkylbenzenes,

whether side-chain or nucleus oxidation occurs depends on the system employed. The solvent utilized in this electrolysis acted as the nucleophile and afforded an easy route to produce a benzyl cation intermediate, which was trapped with the nucleophilic acetonitrile to yielded N-benzylacetamide.

The other oxidation product, benzaldehyde, arises from the subsequent oxidation of benzyl alcohol (figure 54). The two electrolyses performed, one relying on traces of moisture for water and the other with 5 additional drops of water illustrated that the concentration of water in the supporting electrolyte affects the ratio of amide and aldehyde formed;⁹ higher concentration of water favors trapping of the benzyl cation by water and thus a higher quantitative yield of benzaldehyde.

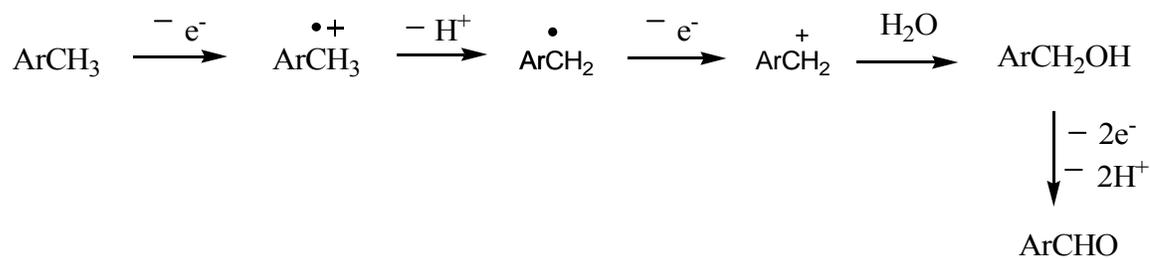


Figure 54: Anodic oxidation of **1** to benzaldehyde.

Preparative scale catalytic electrolysis of 1:1 mol 4-chlorotoluene (2): 2,4-dichlorotoluene (3) with 4,4',4''-trimethyl-2,2',2''-trinitrotriphenylamine as a catalyst: This electrolysis was carried out to study the electrochemical behavior of aromatic compounds bearing ring-deactivating substituents. The anodic oxidations of **2** and **3** in particular were carried out to compare the results and behaviors between a substrate bearing one and two electronegative groups, respectively.

The electrolysis was carried out in 0.1M lithium perchlorate in acetonitrile as the supporting electrolyte. It was run at +1.6V and stopped after 130 minutes, when 76.24 coulombs electrons had been utilized, i.e., after 2 eq. of the calculated amount of electrons. Although starting materials, **2** and **3** were present after 76.24 coulombs, it was evident from GC/MS that some of **2** was oxidized to 4-chlorobenzaldehyde. Also, there was more unreacted **3** than **2**.

The electrode potential at which the electrolysis was run can explain why 2,4-dichlorotoluene (**3**) was not oxidized; the E_p of 4-chlorotoluene is +1.75V and that of 2,4dichlorotoluene is +1.82V. It is well established that the electrode potential determines whether enough energy is being supplied for electron transfer to occur and the applied potential (+1.6V) was in fact not high enough to oxidize **3**. In addition, the catalyst utilized was within the $\pm 0.4/0.5V$ range for the E_p of 4-chlorotoluene but not that of 2,4-dichlorotoluene; which can also attribute to why 2,4-dichlorotoluene was not oxidized in this electrolysis setup.

The mechanism wherein the methyl group of 4-chlorotoluene is oxidized to an aldehyde functional group is shown below in figure 55:

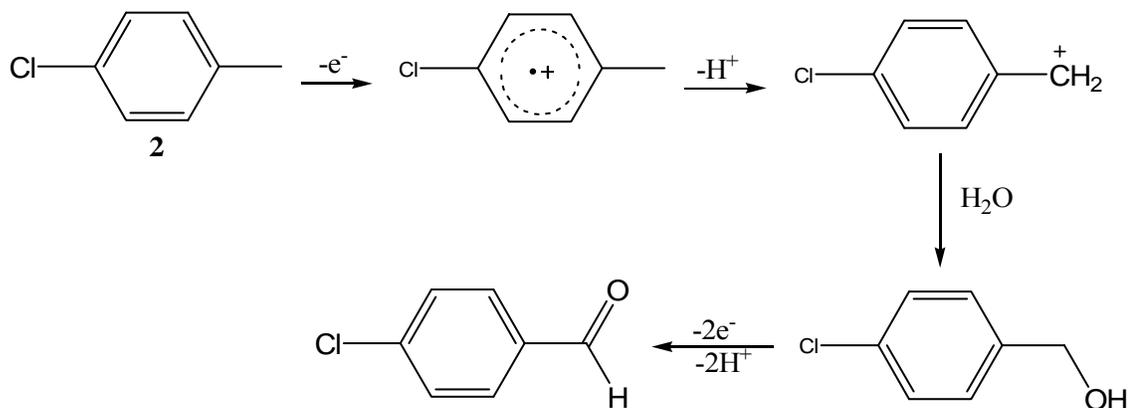


Figure 55: Anodic oxidation of **2** to 4-chlorobenzaldehyde.

In summary, the setup of this indirect electrolysis was erred because the potential was not run at the oxidation potential of the catalyst, +1.28V. In order to study this electrolysis correctly in the future, the electrolysis should be carried out at the potential of the catalyst.

Preparative scale catalytic electrolysis of 4-chlorotoluene (2) with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): This electrolysis was carried out in an attempt to resolve the technical errors executed in the previous electrolysis: applying the appropriate voltage so that the electrode potential is sufficient to cause a reaction. The electrolysis of **2** ran at +1.60 volts vs. Ag/0.1M AgNO₃ and was stopped after 297 coulombs (8F/mol), i.e., 3.90 eq. of the calculated amount of electrons were utilized. GC/MS illustrated some starting material (**2**), 4-chlorobenzaldehyde, 2,4-dichlorotoluene, and N-(4-chlorobenzyl)-acetamide (figure 56). Post work-up GC/MS showed mainly 4-chlorobenzaldehyde and a small amount of **2**.

As the electrolysis of **2** was carried out, GC/MS was utilized to monitor the disappearance of the starting material. After 76.29 coulombs had passed, three compounds were present in solution: 4-chlorobenzaldehyde, (**2**), and N-(4-chlorobenzyl)acetamide (**2a**). It was observed by GC/MS that as more coulombs passed, the amide product decreased as the aldehyde functional group product increased. Apparently, the amide was further oxidized into an aldehyde functional group as time and current increased, (figures 56 and 57); the mechanism of oxidation of N-(4-chlorobenzyl)-acetamide to 4-chlorobenzaldehyde is proposed below in figure 58.

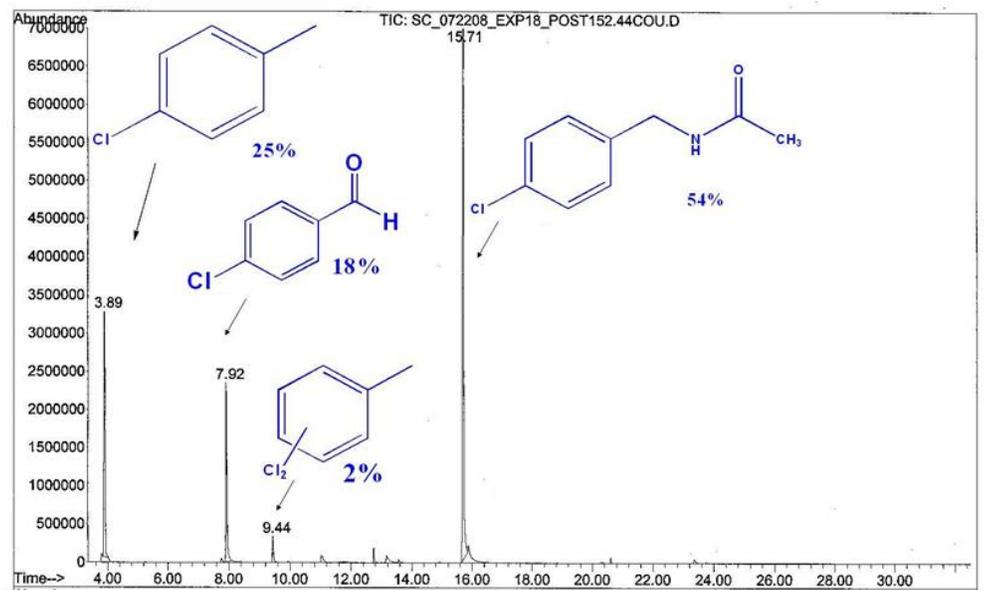


Figure 56: GC from electrolysis of 4-chlorotoluene; post 152.44coulombs.

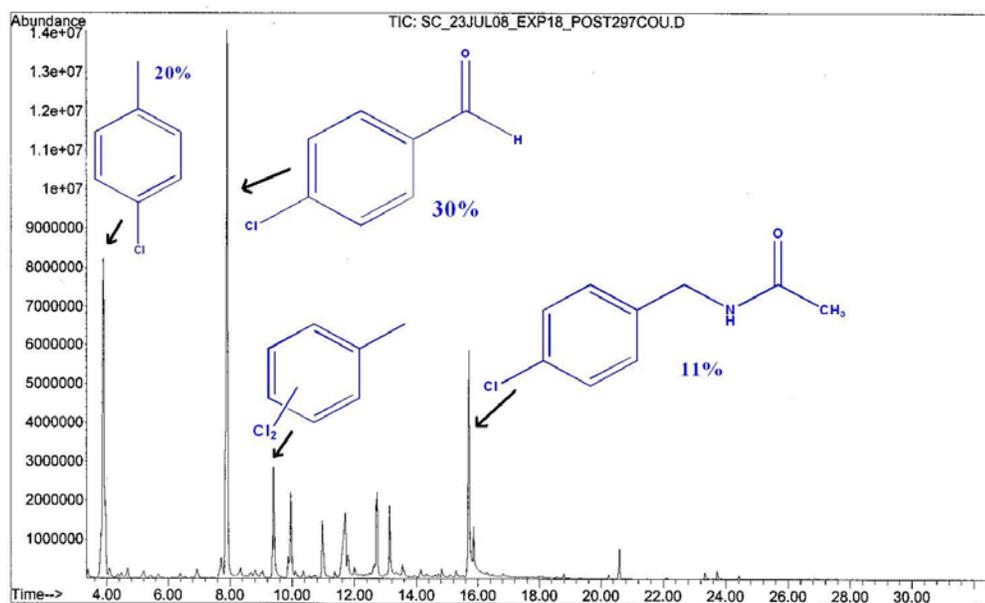


Figure 57: GC from electrolysis of 4-chlorotoluene; post 297coulombs. *Note the increase in 4-chlorobenzaldehyde and the decrease of N-(4-chlorobenzyl)-acetamide.

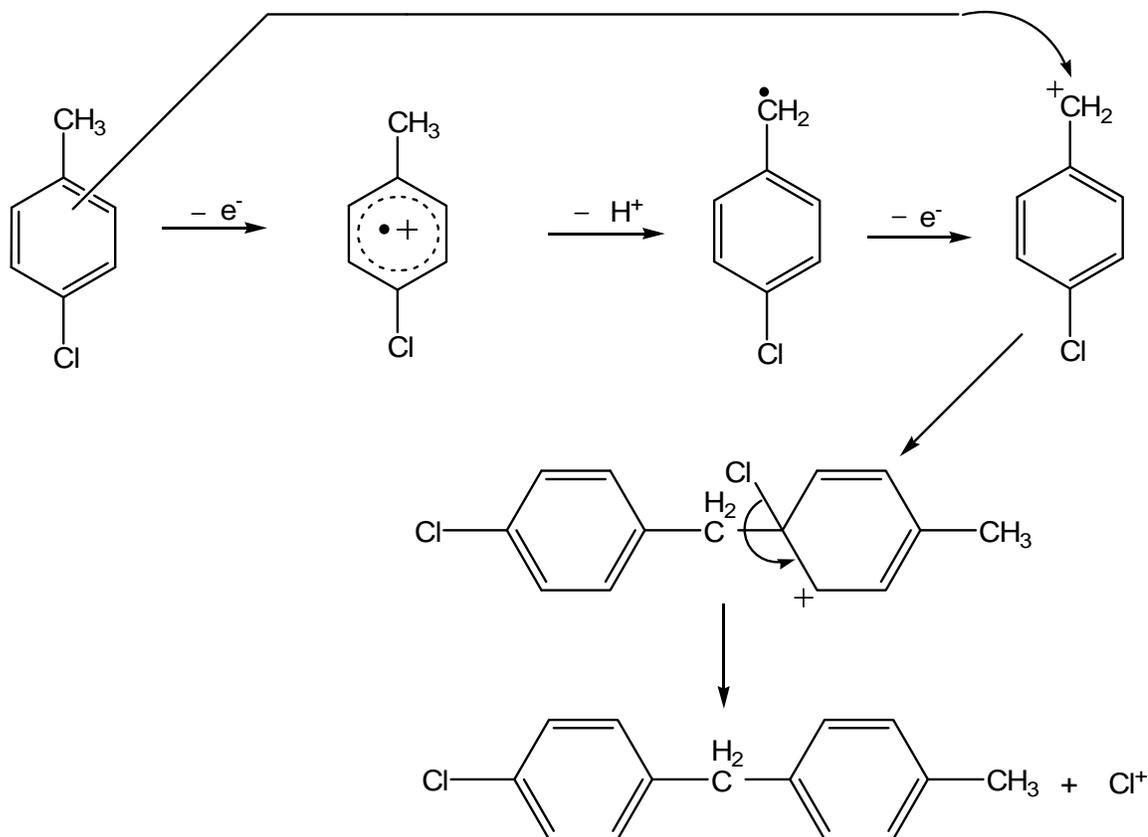


Figure 59: Proposed mechanism for the formation of Cl^+ from substrate.

However, it is also worthy to note that chlorination of the substrate can also arise from the catalyst employed in the electrolysis, which also contains chlorine atoms that can subsequently lead to the formation of Cl^+ to perform an electrophilic aromatic substitution. Figure 60 shows a proposed mechanism; 4,4'-dichloro-2,2',2''-trinitrotriphenylamine (**Q**) produced will then proceed to dimerize and the dimer would not be detected by the mass spectrometry due its high mass (figure 61). The catalyst will be rendered ineffective after the formation of Cl^+ since cyclic voltammograms of products such as these were studied by our lab and show irreversible oxidation potentials. A test that can be carried out to confirm which of the two proposed mechanisms actually occurs to result in chlorination would be to use

catalyst 1 and observe if the substrate becomes brominated, since Br^+ is more stable than Cl^+ . If 4-chlorotoluene is brominated while using the bromine-containing catalyst, then it would show that a neutral 4-chlorotoluene does not yield the Cl^+ needed for the electrophilic aromatic substitution (figure 59) and that chlorination is a result of chlorine transfer from the catalyst (figure 60).

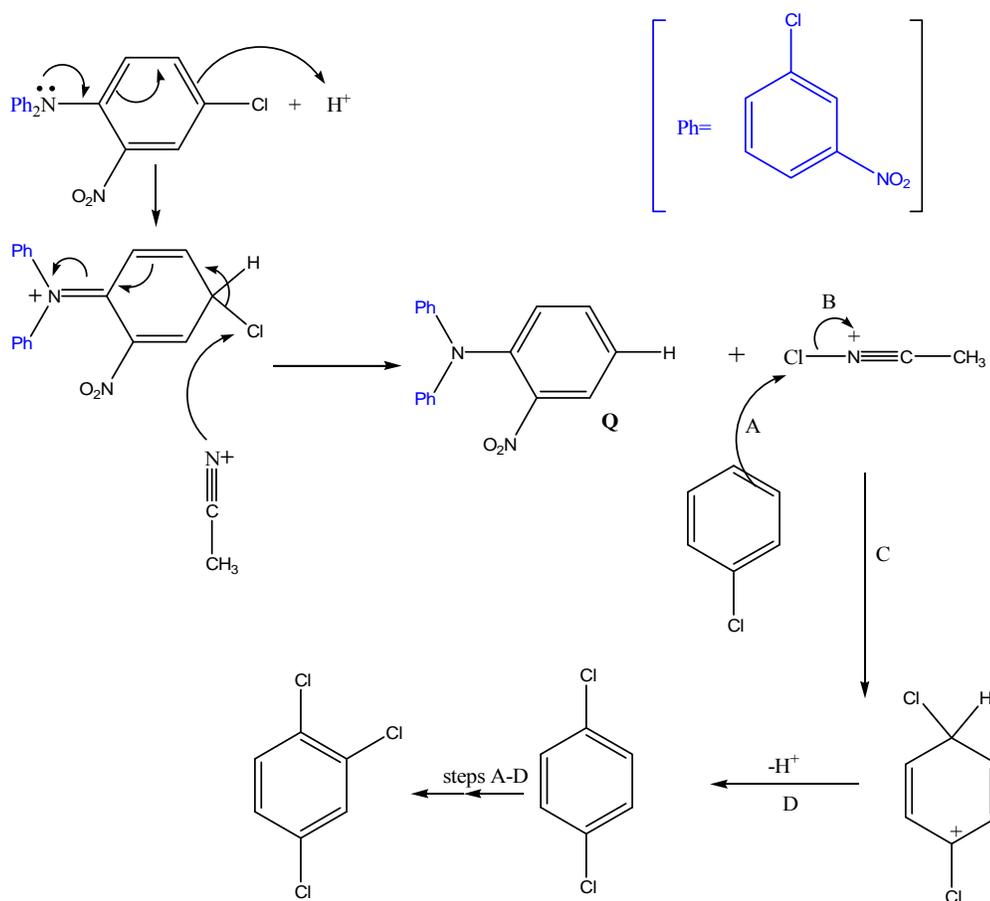


Figure 60: An alternate proposed mechanism of chlorination via the catalyst as chlorine donor.

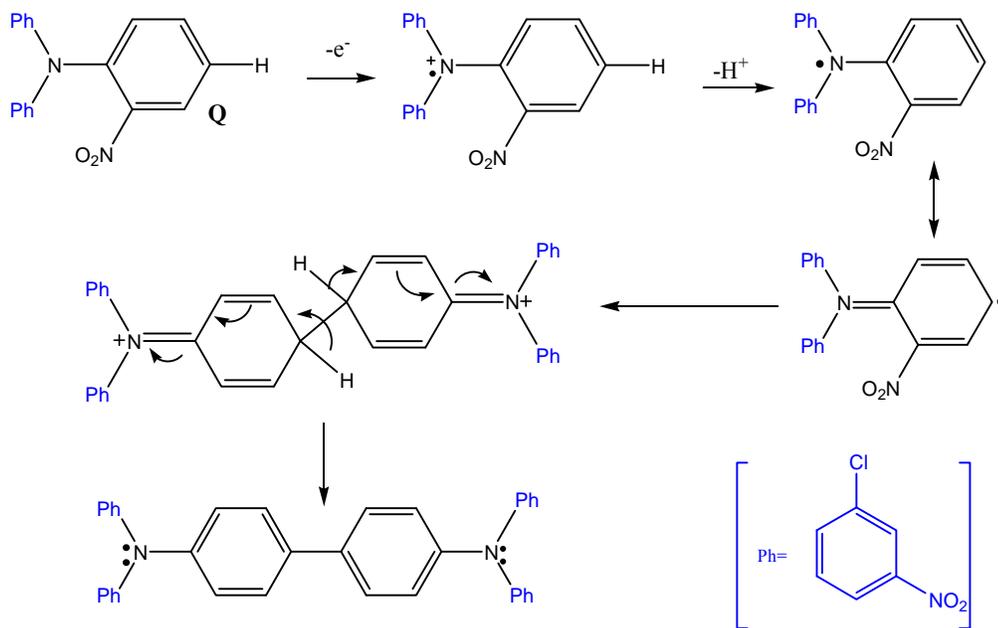


Figure 61: Dimerization of 4,4'-dichloro-2,2',2''-trinitrotriphenylamine (**Q**).

Indirect electrolysis of 2,4-dichlorotoluene (3) with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): Again, this electrolysis was carried out to resolve the technical mistake that occurred in the electrolysis of 1:1 mol of 2: 3. The electrolysis of 3 was run at +1.7V in 0.1M lithium perchlorate in acetonitrile as the supporting electrolyte and was stopped after 5.9 eq. electrons were consumed. GC/MS post 168 coulombs indicates the presence of starting material (3), 2,4-dichlorobenzaldehyde, 2,4,6-trichlorotoluene, and N-[(2,4-dichlorophenyl)-methyl]-acetamide. However, as more current is passed through the solution as a function of time, the GC indicates the formation of 2,4-dichlorobenzaldehyde at the expense of N-[(2,4-dichlorophenyl)-methyl]-acetamide (figures 62 and 63). This result is consistent with that of the indirect oxidation of 4-chlorotoluene (2): as the oxidation time increases and more coulombs are passed, the amide is functionally oxidized to the aldehyde (same scheme as figure 58). Below are the GC's (figure 62 and 63) of the electrolysis solution after different coulombs, 168 and 250, illustrating the absence of the amide product peak at 250 coulombs and the increase in the formation of the aldehyde product. Figure 64 illustrates the MS of N-[(2, 4-dichlorophenyl)-methyl]-acetamide, GC: r.t. (%): 16.79 min, (25%); MS: m/z (%)= 217, 186, 184 (33), 182 (100), 178 (2), 176 (9). 174 (15), 163, 161 (12), 159 (17), 141 (32). The presence of 2,4,6-trichlorotoluene can also be attributed to the same mechanisms speculated for the formation of 2,4-dichlorotoluene in the electrolysis of 4-chlorotoluene (2): Cl⁺ electrophilic aromatic substitution generated either by the substrate or catalyst 3, figures 59 and 60, respectively.

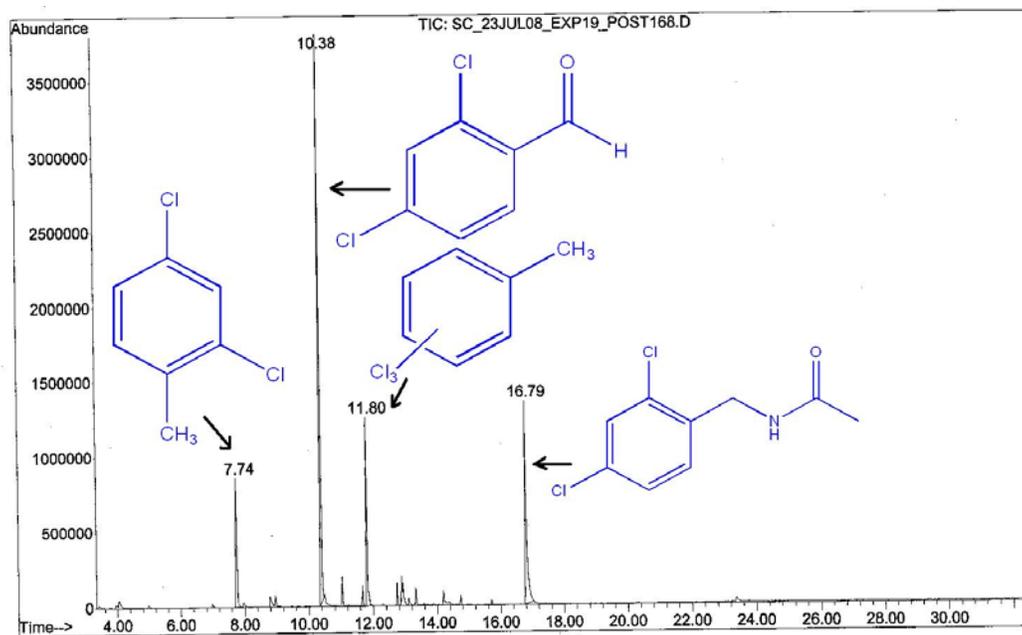


Figure 62: Indirect oxidation of **3**, post 168coulombs.

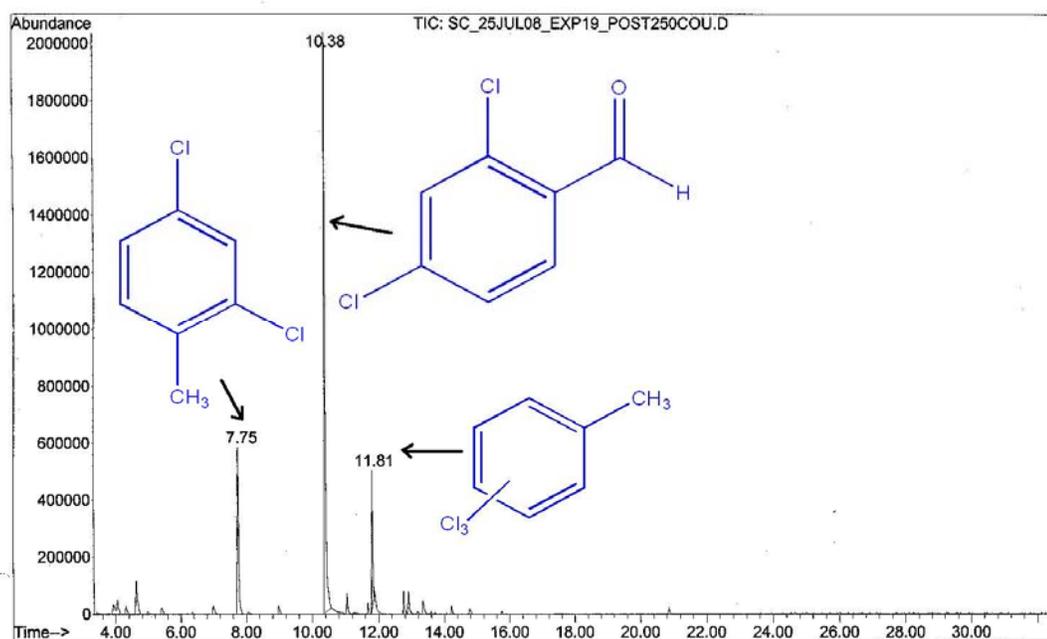


Figure 63: Indirect oxidation of **3**, post 250 coulombs, noting the absence of N-[(2, 4-dichlorophenyl)-methyl]-acetamide.

16.808 minutes. The GC peak at 16.808 minutes was believed to correspond to N-[(2, 4-dichlorophenyl)-methyl]-acetamide. According to m/z 182, the compound contains two chlorines, since the isotopically shifted lines are each separated by 2 amu and are in a relative abundance of 1: 2/3: 1/9. The mass spectrum is given below: the molecular ion peak of 217 is hypothesized to be absent because of its low abundance, hence the mass detector could not register the peak. The base peak at m/z 182 corresponds to cation **30** and m/z 140 corresponds to cation **31**:

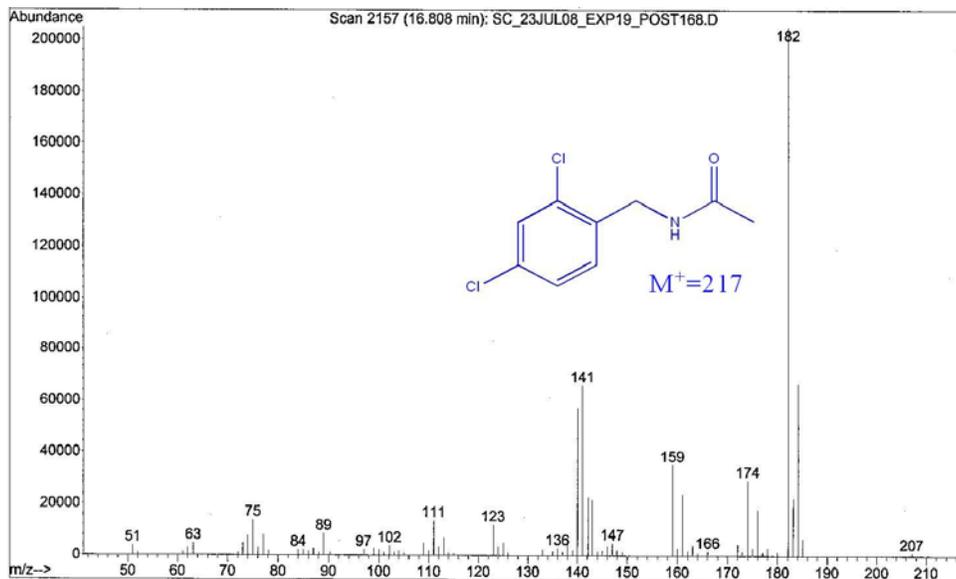
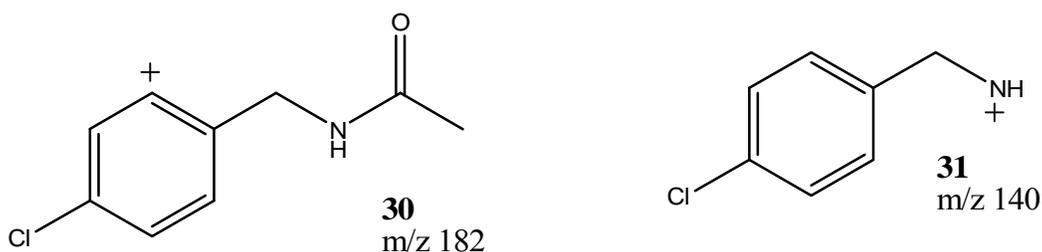


Figure 64: Mass spectrum of N-[(2, 4-dichlorophenyl)-methyl]-acetamide.

Preparative scale electrolysis of N-benzylacetamide (1a): Since both the indirect electrolyses of **2** and **3** saw the transformation of an amide functional group to one of benzaldehyde as a function of time and current, this experiment was conducted to confirm that an amide can be electrochemically oxidized to an aldehyde. Synthesis of **1a** was carried out (Experimental and Results) so this electrolysis can be performed. The electrolysis of **1a** was run at +1.40V in an electrolysis cell with 0.1M of lithium perchlorate as the supporting electrolyte. The electrolysis of **1a** did yield benzaldehyde, although not an appreciable amount of it and the main product was phenyl acetate. GC/MS identified benzaldehyde and phenyl acetate after the electrolysis was stopped after 220 minutes or when 157 coulombs (12F/mol) had passed through the solution. The GC/MS post work-up showed a decrease in the amount of phenyl acetate and the presence of phenol and benzaldehyde. Please see Results section for the GC/MS of these products.

The obtainment of phenyl acetate came as a surprise, thus three tests were performed to confirm that phenyl acetate was present from the electrolysis of **1a**: 1) phenyl acetate (**9**) was synthesized with phenol and Ac_2O and its GC's retention time and MS's fragmentation pattern compared to that from electrolysis; 2) a small amount of the synthesized phenyl acetate was added to that from the electrolysis solution to observe if there would only be one peak in the GC for this phenyl acetate mixture; and 3) the solution from electrolysis was TLC spotted against benzaldehyde and the synthesized phenyl acetate in 20% ethyl acetate in hexanes, figure 65.

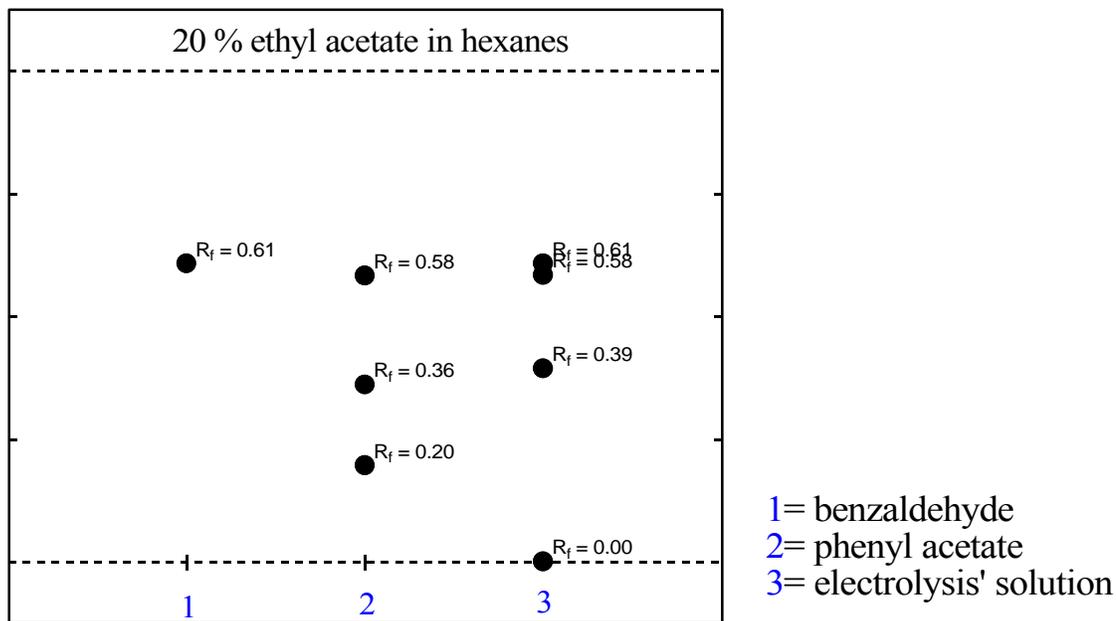


Figure 65: TLC plate of electrolysis solution 3 against benzaldehyde 1 & phenyl acetate 2.

The GC/MS of the synthesized phenyl acetate has a retention time difference of 5.7msec from that of electrolysis—a negligible difference. The 5.7msec difference can be attributed to the amount and concentration of the injected sample. The GC/MS of the mixture of phenyl acetate, figure 66, shows only one peak, indicating that the phenyl acetate from synthesis and electrolysis are identical and suggests the presence of phenyl acetate as a product from electrolysis. A ^1H NMR of the phenyl acetate could not be obtained as the product was hydrolyzed to phenol, its presence was further suggested by the strong characteristic smell of phenols. Post workup of the electrolysis solution was analyzed by GC/MS and only indicated the presence of phenol and benzaldehyde. Additionally, the TLC given in figure 65 suggests that the electrolysis product contains both benzaldehyde and phenyl acetate, as denoted by the matching R_f values to the standards (1 and 2).

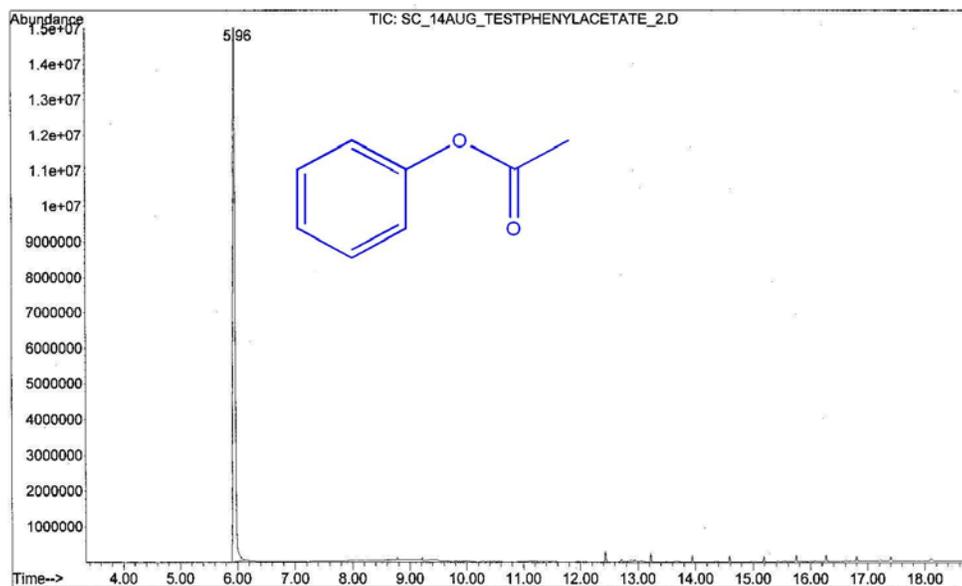


Figure 66: GC of mixture of phenyl acetate (synthesized) and that of the electrolysis solution from oxidation of 4-benzylacetamide.

During the electrolysis of N-benzylacetamide (**1a**), the presence of benzaldehyde— from its initial appearance to when all of the starting material was oxidized, did not increase to any significant amount. After 50.6 coulombs were passed through the solution, or ~ 2 eq. of the calculated amount of electrons, there were mainly the starting material (97%), phenyl acetate (3%), and a minute amount of benzaldehyde in the electrolysis solution. After 103.4 coulombs, i.e., ~ 4 eq. of the calculated amount of electrons, there was an appreciable amount of increase in phenyl acetate and a slight increase in benzaldehyde. Finally, the electrolysis solution post 128.7 coulombs or after 5 eq. of the calculated amount of electrons were utilized, noted a dramatic decrease in starting material, phenyl acetate as the predominant product, and the final amount of benzaldehyde was not altered appreciably. This suggests that the oxidation to phenyl acetate is preferred over the formation of the aldehyde in the anodic oxidation of N-benzylacetamide under the given electrolysis

setup. The absence of an ample amount of water concentration in the electrolysis can partly explain why phenyl acetate was formed at the expense of the aldehyde since benzaldehyde formations are favored in the presence of liberal amounts of moisture.⁹ However, a mechanism cannot be proposed as of now to take into account the formation of phenyl acetate due to the unusual C-C bond cleavage under the conditions of this electrolysis.

Studies of the oxidation of N-benzylacetamide, catalyzed by N-Hydroxyphthalimide and $\text{Co}(\text{OAc})_2$ ²⁸ leads either to imides and minor amounts of aromatic amounts of aldehydes or to carboxylic acids and variable amounts of imides, depending on the temperature and the reaction solvent. A possible explanation as to why we did not obtain imides can be explained by the fact that our oxidation was carried out electrochemically and thus the constituents of the reaction were different, thus resulting in different products.

The electrochemical oxidation of N-benzylacetamide was carried out a total of three times to test the consistency of appearance of M^+ of 136. Indeed, the GC/MS of each separate electrolysis shows the presence of $M^+ = 136$ with identical retention times and mass fragmentation patterns. In addition, the mass spectrum of phenyl acetate shows the common fragmentation pattern observed for simple methyl esters, figure 24 (Results p.44).

Preparative scale electrolysis of N-(4-chlorobenzyl)-acetamide (2a): The electrolysis of **2a** was also carried out to verify that an amide can be electrochemically oxidized to an aldehyde functional group; since N-(4-chlorobenzyl)-acetamide was a product from the electrolysis of **3** and was subsequently oxidized to 2,4-dichlorobenzaldehyde (Results of electrolysis of **3**). In addition, this electrolysis was also performed to study the electrochemical behavior of an electron-withdrawing substituent on an aromatic ring, thus **2a** was synthesized (Experimental and Results) and an electrolysis carried out to compare its oxidation products and electrochemical behaviors to that of N-benzylacetamide (**1a**).

The direct anodic oxidation of N-(4-chlorobenzyl)-acetamide, after 4.9 eq. of the calculated amount of electrons were utilized, saw the 100% conversion to 4-chlorobenzaldehyde. This result is analogous to the indirect electrolysis of 2,4-dichlorotoluene with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine ([catalyst 3](#)) and the electrolysis of 4-chlorotoluene, wherein the amide formed was subsequently oxidized to the aldehyde as more current is passed through the solution (figure 58). The formation of the aldehyde is clearly from the hydrolysis of the chloro-hydroxyamide: $\text{Cl-Ar-CHOH-NHCOCH}_3 \rightarrow \text{Cl-Ar-CHOH} + \text{CH}_3\text{-CONH}_2$.

In comparing the electrolyses of N-benzylacetamide and N-(4-chlorobenzyl)-acetamide, there are some noteworthy and yet puzzling differences: in the indirect electro-oxidation of **1a** ($E_p=1.80\text{V}$), ran at +1.4V, phenyl acetate was the major product (71%) and benzaldehyde, the minor product (27%) (Percentage values are prior to work-up of the electrolysis solution). Conversely, in the direct electrolysis of **2a** ($E_p=2.0\text{V}$), the only product observed was 4-chlorobenzaldehyde. What accounts for the difference? The only difference between the two substrates, **1a** and **2a** is the

additional chlorine atom on **2a**. Indeed, the reactivity and oxidation of the substrate is significantly affected by the addition and the position of chlorine on the aromatic ring. Chlorine, an electron withdrawing atom that is also *ortho*-/*para*- directing, produces an inductive electron-withdrawing as well as resonance donating effects (lone pair donation). The inductive effect lowers the reactivity and the resonance effect controls the regiochemistry due to the stability of the intermediates. The oxidation rate constant is decreased by s-electron withdrawing conductive effects,²⁹ but at the same time, the *ortho*- or *para*-substituted chlorines also increases the oxidation rate constant by p-electron donating conjugative effect and can counteract some of the negative impact as a result of the conductive effect. Nevertheless, in this electrolysis, the results were not expected to differ by obtaining two distinct products so much so as how the potential of the electrolyses would affect the oxidization of the two different substrates as a result of an additional chlorine on one substrate. Next, the electrolyses constituents of N-benzylacetamide and N-(4-chlorobenzyl)-acetamide were identical: the setup, apparatus, the amount and the type of electrolyte solution. Hence, such discrepancies in products formed post electrolyses came as a surprise.

The other possible variable that could have contributed to the differences observed for the products of the electrolyses of these two substrates is the electrode potential. The electrode potential determines whether enough energy is supplied for electron transfer to occur which in turn essentially governs the mode and rate of the reaction. Also, the electrode potential may affect the reaction by changing the adsorption characteristics of the substrate, intermediates, or the products of the electrolysis.³⁰ The results suggest that direct oxidation afforded a cleaner route (as in the 100% conversion of **2a** to 4-dichlorobenzaldehyde) as opposed to indirect

electrolysis where more than one product was formed and further oxidation of one of the products can dominate as more current is passed through the solution; as in the case of N-benzylacetamide with the dominant formation of phenyl acetate over the benzaldehyde as the starting material was consumed.

In summary, although the three electrolyses of N-benzylacetamide yielded consistent results, it can nevertheless be set up better: for indirect electrolysis, the electrode potential should be set to the oxidation potential of the catalyst, 1.28V as opposed to 1.40V. Also, a direct anodic oxidation of N-benzylacetamide should be carried out and its products compared to those from indirect electrolysis.

Preparative scale catalytic electrolysis of methyl p-toluate (4) with 4, 4', 4''-trichloro-2,2',2'' trinitrotriphenylamine, (catalyst 3): The electrolysis of **4** was carried out because of the interest in the electrochemical behavior of the compound bearing one electron-donating and the one electron-withdrawing substituent. The oxidation of **4** was run at + 1.5V in a supporting electrolyte of 0.1M lithium perchlorate in acetonitrile and its progress monitored by taking 1 μ L of the sample at regular intervals. The electrolysis was stopped after passing 2810 coulombs or 70.7 eq. of the calculated amount of electrons. GC/MS shows the appearance of a compound with the mass of methyl 3-chloro-4-methylbenzoate post 1040 coulombs. After 1559 coulombs, methyl 3,5-dichloro-4-methylbenzoate was observed by GC/MS; but formed no greater than 5% by the end of 2810 coulombs. Starting material was still present after 2810 coulombs.

The presence of the chlorinated methyl p-toluate from electrolysis was hypothesized to be methyl 3-chloro-4-methylbenzoate (**4a**), a result of nuclear halogenation, with methyl as an *ortho* director and the deactivating methoxy carbonyl as a *meta* director.

To confirm this, halogenation of **4** was carried out with N-chlorosuccinimide (NCS) and FeCl₃ (Results and Experimental). It was hypothesized that methyl 4-(chloromethyl) benzoate would be the main product from halogenation of **4** as a result of NCS generating a Cl⁺ and thus halogenating the side chain as opposed to the aromatic ring of **4**. The main isomer from synthesis, methyl 4-(chloromethyl) benzoate (**7b**) was isolated by flash chromatography (15% EtOAc in hexanes) and yielded 0.07g of yellow liquid. The other isomer, **7a**, was a minor product and was

isolated from the crude mixture by 10% EtOAc and yielded 0.03g of clear liquid.

(Results and Experimental)

The mass spectrum of **7b** (figure 34), the main isomer from halogenation of **4**, differs from that of **4a** (figure 31), the chlorinated product from the electrolysis; whereas the mass spectrum of **7a** (figure 33), the minor isomer from halogenation of **4**, is identical to that of the **4a**, thereby confirming the structure of **4a** as shown in figure 68. Also, in the mass spectrum of **7b** (figure 34), the M^+ of 149 from 184 indicates a loss of chlorine, which is more likely to be ionized off the side chain, $-CH_2Cl_2$ as opposed from the aromatic ring. Furthermore, methyl 3-chloro-4-methylbenzoate was purchased (Fisher) and a GC/MS taken to compare to **4a** (shown below in figure 67). The retention time difference between the purchased chemical (9.64min) to the product from the electrolysis (9.68min) is negligible, 0.67msec, and the mass fragmentations are identical, thus confirming **4a** and **7a** as methyl 3-chloro-4-methylbenzoate and **7b** as methyl 4-(chloromethyl) benzoate.

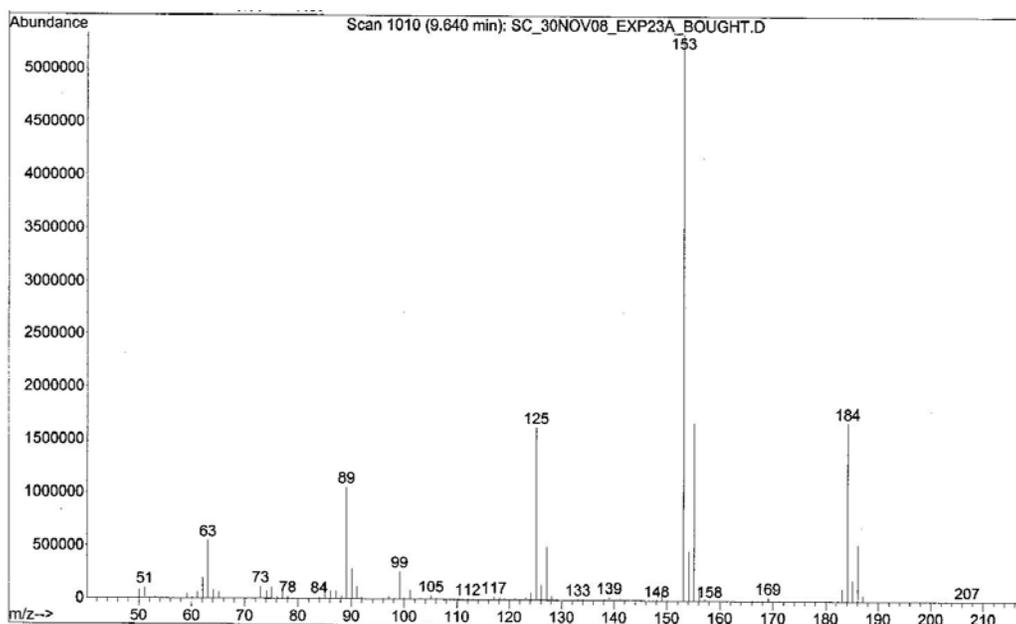


Figure 67: Mass spectrum of methyl 3-chloro-4-methylbenzoate, purchased from Fisher.

In summary, nuclear halogenation occurred during electrolysis with **catalyst 3** to yield methyl 3-chloro-4-methylbenzoate (**4a**), methyl 4-(chloromethyl) benzoate (**7b**) and methyl 3-chloro-4-methylbenzoate (**7a**) are the major and minor isomers from synthesis, respectively. Despite that **4** was not oxidized, this electrolysis suggests another likelihood that **catalyst 3** could be chlorinating substrates (figure 60).

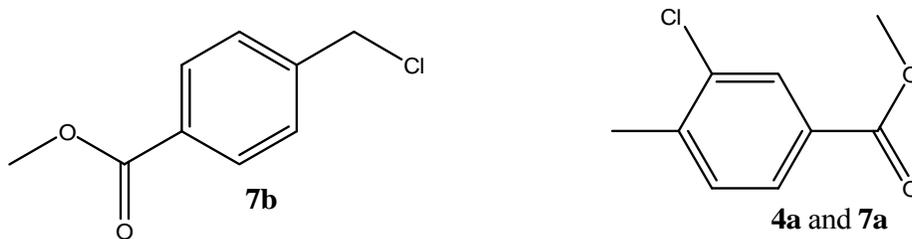


Figure 68: Structures of compounds **7b**, **7a**, and **4a**.

Preparative scale direct electrolysis of 4, 4'-dimethylbiphenyl (5): The electrolysis of **5** was carried out to study the electrochemical behavior of a compound that is to some extent similar to toluene, but a bit more complex. The electrolysis resulted in the oxidation of one methyl group to the aldehyde and then to the subsequent acid. As more current was passed in an attempt to completely consume the starting material, the oxidation of the other methyl group on the second ring was also oxidized to the aldehyde and then also to its respective acid before the complete consumption of the starting material. The mechanisms for oxidation of **5** to its respective aldehydes and acids (figure 69) are identical to the oxidations of **1**, **2**, and **3** to their respective aldehydes. 4-(4-methylphenyl)benzaldehyde (97%) (**5d'**) (figure 36) was purchased from Fisher to compare the GC retention time and mass fragmentation patterns to those from the electrolysis. The molecular ions peaks present in the purchased **5d'** are also present in **5d** and there is only a 7.3msec retention time difference between the two; thus it confirms **5d** as one of the products from the electrolysis of **5**.

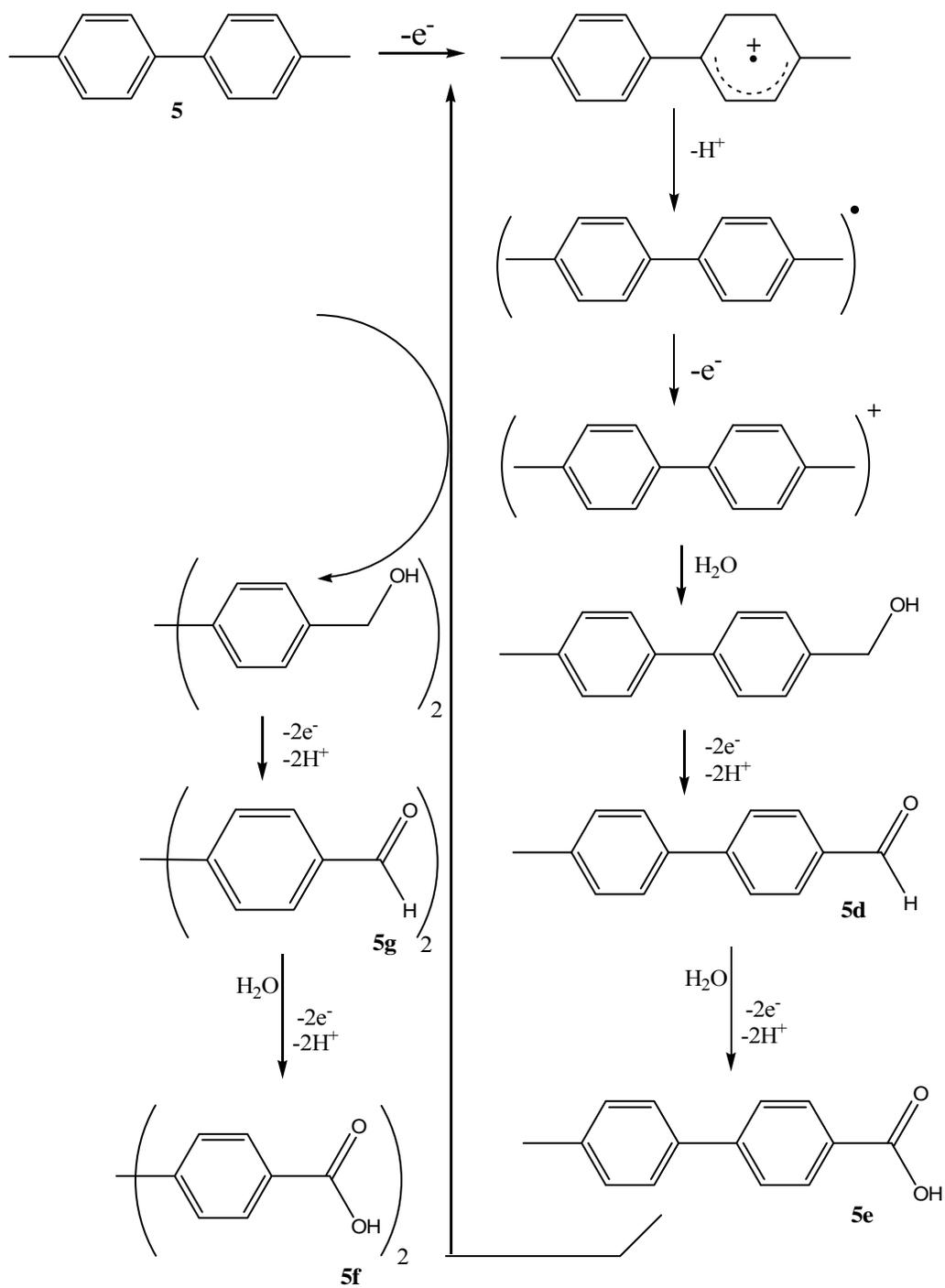


Figure 69: Anodic oxidation of **5** to its respective aldehydes and acids: 4-(4-methylphenyl)benzaldehyde (**5d**), 4-(4-methylphenyl)benzoic acid (**5e**), biphenyl-4, 4'-dicarboxylic acid (**5f**), 4, 4'-biphenyldicarboxaldehyde (**5g**).

A compound with the same mass as biphenyl-4,4'-dicarboxylic acid methyl ester was isolated from the flash column chromatography using 100% EtOAc as the eluent. However its presence as a product from electrolysis is questionable. It is reasonable to suggest that the methyl ester could be formed from the oxidation of the aldehyde to the acid with subsequent esterification with an addition of a methyl group (figure 70). However, due to the lack of a methyl source in the electrolysis medium, the formation of the methyl ester seems unlikely. A test can be carried out by the esterification of **5f** in methanol and comparing the GC retention time and mass fragmentation of this synthetic sample to the speculated methyl ester from electrolysis, **5j**, figure 41 (Results p. 62).

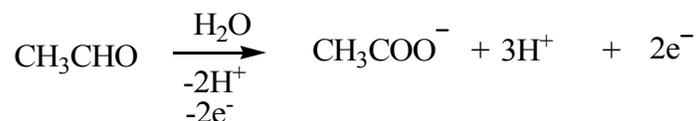


Figure70: Scheme for oxidation of an aldehyde to a methyl ester via acetate.

Indirect electrolysis of 4,4'-dimethylbiphenyl (5) with 4,4',4''-trichloro-2-nitrotriphenylamine (catalyst 4): According to the cyclic voltammogram of **5**, one electron oxidation will occur at +1.2V, thus this electrolysis was carried out to see if different products will be formed if **5** were allowed to oxidize with only the loss of an electron. Indirect oxidation was performed with **catalyst 4** and the results are similar to the electrolysis of toluene, wherein (one of) the methyl group is functionalized to an acetamide, mechanism proposed in figures 53. 4-(4-methylphenyl)benzaldehyde (**5d**) and 4-(4-methylphenyl)benzoic acid (**5e**) were also identified as products in this electrolysis and were confirmed by comparison of GC/MS to **5d**' and **5e** obtained from Fisher and direct electrolysis of **5**, respectively (figures 36 and 38).

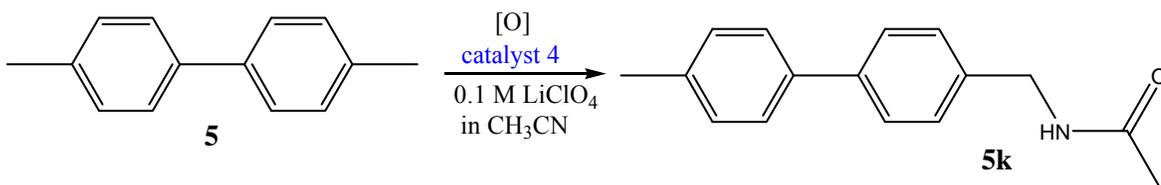


Figure 71: Indirect oxidation of **5** to **5k**.

4,4'-dimethyl-2-nitro-1,1'-biphenyl (6): The synthesis of **6** was conducted to study the electrochemical behavior of **5** with an addition of an electronegative substituent. The nitration³¹ of 4,4'-dimethylbiphenyl was carried out in the presence of potassium dihydrogen phosphate at room temperature as opposed to 60° C as presented by the paper. The reaction was also carried out for a shorter period of time than indicated by the paper because di-nitrated products appeared at the temperature and reaction time given by the paper. The reaction mixture was monitored to prevent over-nitration and was stopped after stirring at room temperature for 20 minutes. Flash chromatography was employed to isolate the two components in the crude: 0.42g fine white crystals of **5** (5% EtOAc in hexanes) and 0.18g of yellow liquid (5-10% EtOAc in hexanes) that was subsequently recrystallized in 95% EtOH to yield 91.2mg of yellow crystals, **6**. 2D COSY (figures 45 and 46) was taken to confirm the position of the nitro group. The 2D COSY hydrogen correlated spectrum will not give rise to any cross signals for protons that are three chemical bonds apart because the ⁴J coupling constants are close to 0. Therefore, the only signals of protons that arise will be from protons that are two or three bonds apart. The COSY spectrum shows that H_c and H_d are coupled with methyl protons on the ring with the nitro group and H_e, which is more than four bonds away, will not be couple with the methyl group on the ring with the nitro group. The 2D COSY actually shows a very weak spin-spin coupling between the two. Also, the spectrum shows that only H_a and H_b, the AB quartet at 7.25 and 7.21 with J_{AB}=8.1Hz, are the only aromatic protons coupled to the lower field methyl protons—which are the methyl groups on the ring without the nitro group.

Preparative scale direct electrolysis of 4, 4'-dimethyl-2-nitro-1,1'-biphenyl (6):

As mentioned earlier, in order to examine the electrochemical behavior of **5** with an electron-withdrawing group, **6** was synthesized so that its electrolysis can be carried out to investigate the functionalization of the methyl group upon anodic oxidation. The electrolysis was carried out at +1.6V in a 0.1M lithium perchlorate in acetonitrile solution and was stopped after **6** was no longer present, after 7.22 coulombs or 2.9 eq. of the calculated amount of current had passed. Workup yielded 3.5mg of caramel color film. GC/MS indicates 100 percent conversion to one product, 4-aldehyde,4'-methyl-2'-nitro-1,1'-biphenyl (**6a**). The chemical shifts and proton integration from ¹H NMR also confirm the presence of only one product and the position of the aldehyde functional group on the ring without the nitro group. Furthermore, comparing with the ¹H NMR of benzaldehyde and 3-nitrobenzaldehyde, it is clear that the aldehyde group of **6a** is on the ring without the nitro group: in benzaldehyde, the proton ortho to the aldehyde functional group has a chemical shift of 7.87ppm; whereas for 3-nitrobenzaldehyde, the proton ortho to the aldehyde and nitro group is of chemical shift 8.7ppm. The absence of a chemical shift in the 8ppm range further confirms that the aldehyde functional group is on the ring without the nitro group.

The figure below describes the mechanism to the oxidation of **6a**: since nitro is an electron-withdrawing group, it will destabilize the formation of the benzyl cation, J, thus it is coherently logical that the methyl group that is oxidized is on the ring without the nitro group.

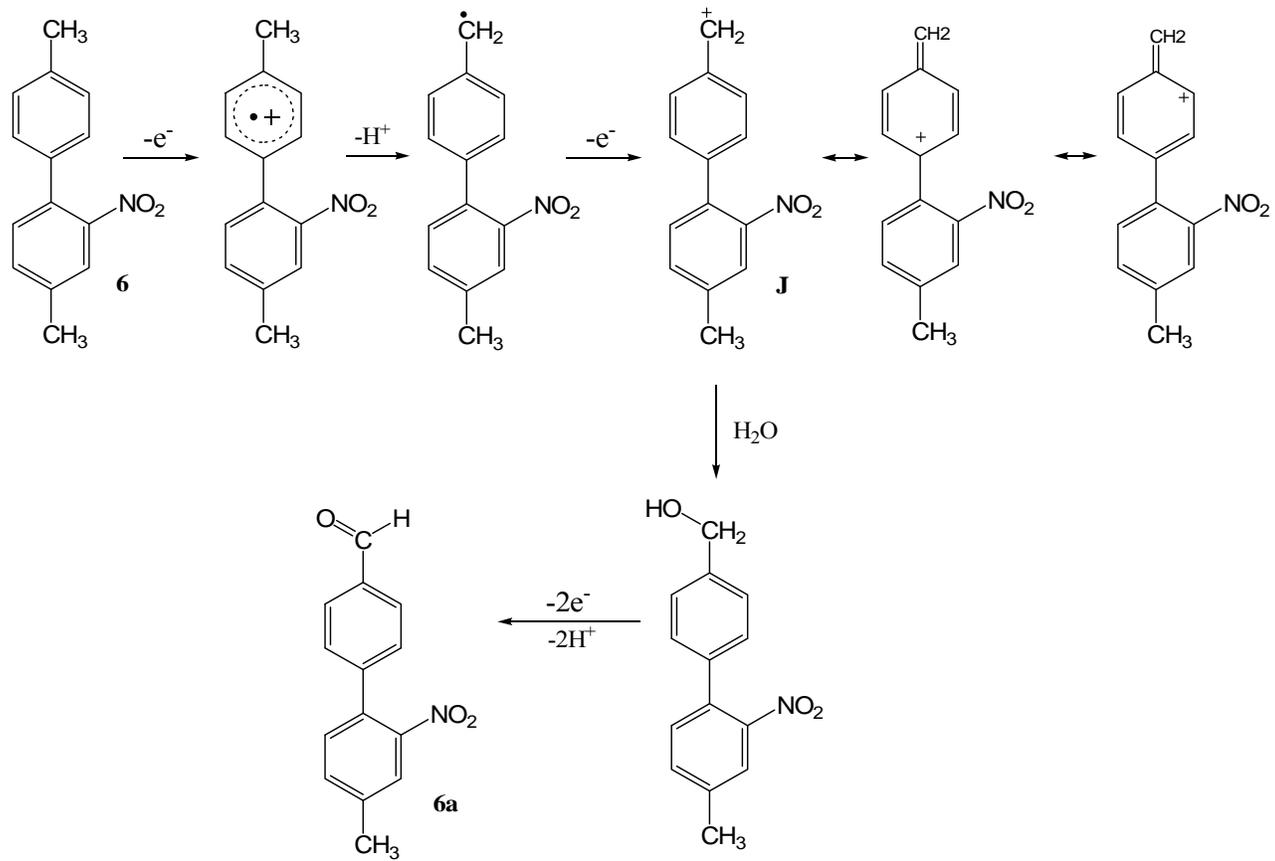


Figure 72: Anodic oxidation of **6**.

EXPERIMENTAL

Instrumentation:

GC/MS acquired for analysis were obtained from Agilent Technologies 5979 Network mass selective detector with 6890N network GC system. Two different methods were employed: 1) the run started at 75°C, where it was held for five minutes. The temperature of the oven then increased 20°C/min for ten minutes to 300°C, where it is then held for 3 minutes—resulting in a total of 19.24 minutes for a GC/MS; 2) the run started at 100°C for 3 minutes and then increased 10°C/min until the temperature reached 250°C and was held there for an additional 5 minutes.

Cyclic voltammetry was performed on a CHI650A (Austin, TX, USA) computer-based electrochemistry system. All the experiments are all carried out in a solution of 0.1M lithium perchlorate in acetonitrile at a scan rate of 0.1 V sec⁻¹.

A. Synthesis

The aim of this research is to study the functionalization of aryl methyl groups on toluene derivatives via anodic oxidation. Syntheses were carried out to either to confirm products from electrolyses or prepared as substrates for electrochemical study. Unless otherwise stated, all reagents used were obtained from commercial sources. Methyl 3-chloro-4-methylbenzoate and 4-(4-methylphenyl)benzaldehyde were purchased from Fisher to confirm products from electrolyses.

N-benzylacetamide (1a): In a 25mL round bottom flask equipped with a stir bar, 0.98g (1 mL, 9.15 mmol) of benzylamine was added to 7mL (7.57g, 74.2 mmol) of acetic anhydride, Ac_2O . The reaction was exothermic and immediately turned yellow; the mixture was then stirred at room temperature for 17 hours. 20mL of water was added to the reaction solution and the organic layer extracted with pentane (2x10mL). The organic layers were combined and added to 70mL of NaHCO_3 and stirred to neutralize. The organic layer was then separated from the aqueous and dried over Na_2SO_4 . Solvent was removed under reduced pressure to yield 0.65g of fine white crystals (66% yield). GC: r.t. (%): N-benzylacetamide (**8a**), 7.741 min (100%); MS: m/z (%) = 149 (80), 106 (100), 91 (30), 79 (15), 77 (15).

Phenyl acetate (9): 35mL (37.45g, 397.9mmol) of phenol was added to 35mL (37.87g, 370.9mmol) of Ac_2O . The mixture was refluxed for an hour after which it turned yellow. The reaction mixture was quenched with distilled water (25mL) and extracted with methylene chloride, CH_2Cl_2 (2x 20mL). The organic layers were combined and added to 125mL of saturated sodium bicarbonate after which the organic layer was extracted and then dried over Na_2SO_4 . CH_2Cl_2 was removed under reduced pressure to yield 2.78g of pale yellow liquid (lit. colorless liquid) (yield=6%). GC: r.t. (%): phenol, 4.29min (40%); MS: m/z (%)= 94 (100), 66 (290, 65 (22); phenyl acetate, 6.28min (60%); MS: m/z (%)= 136 (17), 94 (100), 66 (15), 65 (11). ^1H NMR (CDCl_3 , 300MHz): δ 7.42 (d, 2H), 7.25 (d, 1H), 7.08 (t, 2H), 2.32 (s, 3H).

N-(4-chlorobenzyl)-acetamide (2a): 1.15mL (1.25g, 123mmol) of Ac₂O was added to 1.5mL (1.74g, 123mmol) of 4-chlorobenzylamine. An additional 0.50mL of Ac₂O was added because not enough solvent was present to dissolve all of the starting material. Upon addition of Ac₂O, white fumes and the formation of an off-white solid were observed. As time passed, while applying heat, the cream solid became a transparent yellow liquid and the mixture was allowed to reflux overnight. The reaction was quenched with distilled water (20mL), and extracted with CH₂Cl₂ (2x20mL). The organic fractions were combined and washed with saturated sodium bicarbonate (150mL); it was then extracted and dried over Na₂SO₄. Methylene chloride was removed by rotary evaporation and yielded 1.08g of cream/peach solid (crude yield= 5%). GC/MS shows the presence of two products: both the mono- and di- acylated 4-chlorobenzylamine. Purification by flash chromatography using silica with 60% ethyl acetate in hexanes as the eluent yielded 0.11g of off-white solid. m.p. 107-112°C (lit. 106-108°C).¹⁸ GC: r.t. (%): N-(4-chlorobenzyl)-acetamide, 11.46min (100%); MS: m/z (%) = (185) 21, 183 (92), 142 (20), 140 (62), 127 (13), 125 (41), 106 (100).

Halogenation of methyl p-toluate with N-chlorosuccinimide¹⁹: methyl 4-(chloromethyl)benzoate (7b): In a one-necked flask equipped with a stir bar and a reflux condenser, a mixture of 1.51g (10mmol) of **4**, 1.35g (10mmol) of N-chlorosuccinimide (NCS), and 0.17g (1mmol) of FeCl₃ were added to 5mL of acetonitrile. The flask was heated to and maintained at 100°C. 1μL samples of the reaction solution were taken at regular intervals and analyzed by GC/MS to monitor

the progress of the reaction. After refluxing the reaction mixture for 33 hours and 15 minutes at 100°C, GC/MS still showed an appreciable amount of starting material, along with two isomers of chlorinated **4**. An additional 1.34g (10mmol) of NCS, 0.17g (1mmol) of FeCl₃, and 2mL of acetonitrile were added and refluxed for another 58 hours. GC/MS still showed the presence of starting material and not a significant increase of the chlorinated **4** isomers. The reaction solution was washed with distilled water (15mL) and extracted with chloroform (2x 15mL). The organic layers were combined and dried over Na₂SO₄ and the solvent was removed under reduced pressure to yield 1.31g of yellow liquid (yield=71%). The main isomer, methyl 4-(chloromethyl) benzoate (**7b**) was isolated by flash chromatography (15% EtOAc in hexanes) and yielded 0.07g of yellow liquid. GC: r.t.: (%): **7b**, 10.28min, (78%); M/S: m/z: (%) = 186 (13), 184 (41), 155 (35), 153 (100), 149 (55), 125 (34), 89 (20). The other isomer, methyl 3-chloro-4-methylbenzoate (**7a**), was isolated from the crude mixture by 10% EtOAc and yielded 0.03g of clear liquid. GC: r.t.: (%): methyl 3-chloro-4-methylbenzoate, 9.68min, (59%); M/S: m/z: (%) = 186 (17), 184 (50), 155 (47), 153 (100), 127 (14), 125 (44), 80 (26). The proton NMR illustrated the presence of methyl 3-chloro-4-methylbenzoate plus a small trace of the starting material, methyl p-toluate: ¹H NMR (CDCl₃, 300MHz): δ 8.03(d, 2H), 7.46 (d, 2H), 7.26 (d, 2H), 4.61 (s, 3H), 3.92 (s, 3H). (lit. **4**: δ 7.92 (d, 2H), 7.23 (d, 2H), 3.886 (s, 3H), 2.394 (s, 3H).³²

4,4'-dimethyl-2-nitro-1,1'-biphenyl (6): To a mixture of 0.08g (5.2×10^{-4} mol) of CCl_4 , 0.61g (6.0mmol) of acetic anhydride, 56mg (4.11×10^{-4} mol) of potassium dihydrogen phosphate in a 20mL flask equipped with a stir bar were added 0.12g (1.9mmol) of 70% nitric acid and 0.80g (4.4mmol) of 4,4'-dimethylbiphenyl. The reaction mixture was exothermic and immediately turned yellow/orange in color; it was allowed to stir at room temperature for 20minutes after which it was worked up. The solution was washed with distilled water (25mL) and extracted with CH_2Cl_2 (10mL). Then it was washed with 5% sodium bicarbonate. The organic layer was extracted with CH_2Cl_2 (3x 15mL) and then with distilled water (70mL). The organic layer was then dried over Na_2SO_4 and CH_2Cl_2 removed under reduced pressure to yield 0.86g (crude yield=86%) of crude yellow solid and crystals. Flash chromatography was employed to isolate the two components: 0.42g of 4,4'-dimethylbiphenyl (5% EtOAc in hexanes); GC: r.t. (%): 10.73min (100%); M/S: m/z (%)= 182 (100), 181 (27), 167 (48), 165 (38) and 0.18g of **6**, a yellow liquid (5-10% EtOAc in hexanes) which was then recrystallized with 95% EtOH to yield 91.2mg of yellow crystals (9% yield); GC: r.t. (%): 12.43min (100); M/S: m/z (%)= 227 (43), 210 (38), 184 (21), 182 (50), 170 (30), 166 (32), 165 (100).) $^1\text{H NMR}$ (CD_3CN , 300MHz,): δ 7.68 (s, 1H), 7.49, 7.39 ($J_{\text{AB}}=7.8\text{Hz}$), 7.25, 7.21 ($J_{\text{AB}}=8.1\text{Hz}$), 2.45 (s, 3H), 2.38 (s,3H); m.p. 68-69°C (lit. 67-68°C)²¹.

B. ELECTROLYSIS

Reference electrode: The reference electrode consisted of a silver wire fitted in a Teflon tube sealed with porous glass plug and stored in a solution of 0.1M silver nitrate (AgNO_3) in acetonitrile, CH_3CN .¹⁰

Working Electrode: The working electrode consisted of a 1 cm x 3 cm piece of carbon cloth supported by a 10 cm platinum wire.

Counter Electrode: The counter electrode consisted of a piece of platinum supported by a platinum wire.

Electrolysis cell: The electrolysis cell consisted of a 25mL 3-neck round bottom flask with ports for the working, reference, and counter electrode. Anodic electrolyses were performed with 10mL of 0.1 M lithium perchlorate in acetonitrile.

Preparative scale electrolysis of toluene (1): The electrolysis of toluene (**1**) (0.12mL, 103.9mg, 1.13mmol) ran at +1.4V vs. Ag/0.1M AgNO_3 in 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) in the electrolysis cell described above. The cell was stirred at room temperature and the progress of the electrolysis was monitored by taking 1 μL sample of material every 212coulombs for analysis by GC/MS. After 4F/mol, or 424.6 coulomb electrons had been passed, i.e., 1.95 eq. of the calculated amount of electrons, the GC/MS illustrated absence of (**1**) and the electrolysis was stopped and the reaction solution worked up and analyzed.

Workup consisted of washing with distilled water (20mL) and extracting with CH_2Cl_2 (2x15mL). The organic layers were then combined and dried over Na_2SO_4 .

The solvent was removed under reduced pressure and yielded 0.21 g of brown solid. The product was analyzed via GC/MS. Thin layer chromatography indicates only one product. GC/MS shows mainly N-benzylacetamide (**1a**) and a minor amount of benzoic acid. Identified peaks, in order of retention time; GC: r.t. (%): benzoic acid, 3.729 min, (11%); MS: m/z (%) = 122 (90), 105 (100), 77 (70), 51(30). N-benzylacetamide (**1a**), 7.697min, (89%); MS: m/z (%) = 149 (81), 106 (100), 91 (30), 79 (14), 77(14). The GC/MS of compound post-workup did not show the benzoic acid peak; GC: r.t. (%): 7.766min, (100%); MS: m/z (%) = 149 (81), 106 (100), 91 (30), 79 (13), 77 (15).

Preparative scale electrolysis of toluene (1): electrolysis setup and workup were the same as above but with the exception that 5 drops of water were added to this electrolysis. The electrolysis yielded more benzaldehyde than N-benzylacetamide when compared to the previous electrolysis without the addition of water. The electrolysis yielded 33.2mg of a brown solid. GC utilized a different method, hence the different retention times from the GC in figure 6. The mass spectrum, however, is identical to the N-benzylacetamide from the previous electrolysis. GC: r.t. (%): benzaldehyde, 4.94 min, (52%); MS: m/z (%)=106 (100), 105 (100), 77 (86), 51 (33); N-benzylacetamide, 9.08min, (26%); MS: m/z (%)= 149 (85), 106 (100), 91 (33), 79 (15), 77(15). The GC/MS of product post-workup contained less benzaldehyde and more of the amide product than prior to the work-up: GC: r.t. (%): benzaldehyde, 4.94 min, (13%); MS: m/z (%)= 106 (99), 105 (100), 77 (84), 51 (31); N-benzylacetamide, 9.06min, (78%); MS: m/z (%)=149 (85), 106 (100), 91 (31), 79 (15), 77(15).

Preparative scale catalytic electrolysis of 1:1 mol 4-chlorotoluene (2): 2,4-dichlorotoluene (3) with 4,4',4''-trimethyl-2,2',2''-trinitrotriphenylamine (catalyst 2): 47 μL (50.3mg, $3.97\text{e-}04$ mol) of 4-chlorotoluene (**2**), 40.5 μL (50.2mg, $3.12\text{e-}04$ mol) of 2,4-dichlorotoluene (**3**), and 3.9mg ($3.11\text{e-}05$ mol) of **catalyst 2** were mixed along with 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) in the electrolysis cell described above. The cell was stirred at room temperature and ran at +1.6V. GC/MS of the reaction was taken every 2F/mol to monitor the progress of **2** and **3**. The electrolysis was stopped after 130 minutes and 76.24 coulombs electrons had been utilized, this corresponds to 2 eq. of the calculated amount of electrons. The GC (figure 12) showed only the oxidation of 4-chlorotoluene to 4-chlorobenzaldehyde and the presence of **2** and **3**—with more of **3** than **2**. GC: r.t. (%): 4-chlorotoluene, 3.88 min, (35%); MS: m/z (%)= 126 (38), 91 (100); 2,4-dichlorotoluene, 8.75 min, (55%); MS: m/z (%)=164 (3.8), 162 (23.8), 127 (31), 125(100), 89 (25); 4-chlorobenzaldehyde, 9.05min, (9%); MS: m/z (%)= 142 (23), 140 (72), 139 (100), 111 (50), 75 (24).

Preparative scale catalytic electrolysis of 4-chlorotoluene (2) with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): 50mg ($3.94\text{e-}04$ mol, 47 μL) of 4-chlorotoluene and 19.2mg ($3.98\text{e-}05\text{mol}$) of **catalyst 3**—trichlorotrinitrotriphenylamine were mixed along with 10mL of supporting electrolyte, (0.1M lithium perchlorate in acetonitrile) in a 3-neck electrolysis cell (describe above). The electrolysis ran at +1.60 volts vs. Ag/0.1M AgNO_3 while stirring at room temperature. The progress of the electrolysis was monitored every 76.22 coulombs by GC/MS for the consumption of **2**. It was stopped after 297 coulombs (8F/mol), i.e., 3.90 eq. of the calculated amount of electrons and a post-

electrolysis GC/MS obtained for analysis. GC: r.t. (%): 4-chlorotoluene, 3.89 min, (20%); MS: m/z (%)= 128 (13), 126 (38), 91 (100); 4-chlorobenzaldehyde, 7.92 min, (30%); MS: m/z (%)=142 (22), 140 (70), 139 (100), 113 (16), 111 (50), 77 (13), 75 (22); 2,4-chlorotoluene, 9.40 min; MS: m/z (%)=162 (14), 160 (20), 127 (32), 125 (100), 89 (17); N-(4-chlorobenzyl)-acetamide (**2a**), 15.71 min, (11%); MS: m/z (%)= 185 (31), 183 (97), 140 (63), 125 (43), 106 (100), 77 (20). The solution was washed with distilled water (20mL) and extracted with CH₂Cl₂ (2 x 20mL). The organic layers were then combined and dried over Na₂SO₄ and CH₂Cl₂. CHCl₂ was removed under reduced pressure. The post-workup GC/MS showed mainly 4-chlorobenzaldehyde and a small amount of **2**. GC: r.t. (%): 4-chlorotoluene, 3.96 min, (15%); MS: m/z (%) = 128 (16), 126 (47), 91 (100); 4-chlorobenzaldehyde, 7.76 min, (85%); MS: m/z (%) = 162 (27), 160 (38), 127 (30), 125 (100), 89 (23).

Indirect electrolysis of 2,4-dichlorotoluene (3) with 4,4',4''-trichloro-2,2',2''-trinitrotriphenylamine (catalyst 3): 41 μL (50.8mg, 3.16e-04 mol) of **3** was mixed with 15mg (3.11e-05mol) of **catalyst 3** in a stirring electrolysis cell with 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) at room temperature. The electrolysis ran at +1.7V and its progress was followed by extracting samples of the electrolysis solution at regular intervals to be analyzed by GC/MS. The electrolysis was stopped when **3** was almost completely consumed, 360 coulombs, i.e., 5.9 eq. of the calculated amount of electrons or (12F/mol). GC/MS identified peaks, in the order of retention time (%): 2,4-dichlorobenzaldehyde, 10.8 min, (70%); MS: m/z (%) = 178 (7), 176 (39), 174 (61), 173 (100), 149 (3), 147 (16), 145 (25); 2,4,6-trichlorotoluene, 11.80 min, (20%); MS: m/z (%)= 198 (6), 196 (17), 194 (18), 163 (11), 161 (65), 163 (100).

Preparative scale electrolysis of N-benzylacetamide (1a): 19.7 mg (1.32×10^{-4} mol) of **1a** was added to 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) in an electrolysis cell describe above. The cell was stirred at room temperature with the application of +1.40V. Several samples of the electrolysis solution were analyzed by GC/MS as the electrolysis was carried out to monitor the disappearance of **1a**. The electrolysis was stopped after **1a** was no longer present; after 220 minutes—when 157 coulombs (12F/mol) had passed. GC/MS identified peaks, in the order of retention time: (%): benzaldehyde, 3.69 min, (27%); MS: m/z (%) = 106 (100), 105 (100), 77 (100), 51 (43), 50 (26); phenyl acetate, 5.94 min, (71%); MS: m/z (%) = 136 (13), 94 (100).

The electrolysis solution was washed with distilled water (20mL) and extracted with CH_2Cl_2 (2x 20mL). Then the combined organic later was dried over Na_2SO_4 , and CH_2Cl_2 was removed under reduced pressure to yield 0.01g of pale brown crystals. The GC/MS showed a decrease in the amount of phenyl acetate and the presence of phenol and benzaldehyde. GC: r.t. (%): benzaldehyde, 3.72 min, (48%); MS: m/z (%)= 106 (100), 105 (98), 77 (96), 51 (4.5), 50 (24); phenol, 4.02 min; MS: m/z (%)= 94 (100), 66 (31), 65 (26); phenyl acetate, 5.95min, (52%); MS: m/z (%)= 136 (13), 94 (100), 66 (13), 65 (12).

Preparative scale electrolysis of N-(4-chlorobenzyl)-acetamide (2a): 50.8mg (2.77×10^{-4} mol) of **2a** was added to 10mL of supporting electrolyte solution (0.1 M lithium perchlorate in acetonitrile) in an electrolysis cell described above. The cell was stirred at room temperature and +2.00V was applied. The progress of the electrolysis was assessed by GC/MS by extracting 1 μL of the sample at regular

intervals. The electrolysis was stopped after 263 coulombs (10F/mol), i.e., 4.9 eq. of the calculated amount of electrons. GC/MS showed 100% conversion to 4-chlorobenzaldehyde. GC: r.t. (%): 4-chlorobenzaldehyde, 7.07 min, (100%); MS: m/z (%) = 142 (23), 141 (39), 140 (74), 139 (100), 113 (17), 111 (51), 77 (14), 75 (27), 50 (20).

Preparative scale catalytic electrolysis of methyl p-toluate (4) with 4,4',4''-trichloro-2,2',2''trinitrotriphenylamine, (catalyst 3): 31 mg (2.06e-04 mol) of methyl p-toluate and 1.7 mg (3.96e-05 mol) of catalyst 3 were mixed along with 10 mL of supporting electrolyte solution (0.1 M lithium perchlorate in acetonitrile) in an electrolysis cell described above. + 1.5 V was applied while the cell stirred at room temperature. The progress of the electrolysis was monitored by taking 1 μ L of the sample at regular intervals. The electrolysis was stopped after passing 2810 coulombs or 70.7 eq. of the calculated amount of electrons. Methyl 3-chloro-4-methylbenzoate formed post 1040 coulombs. After 1559 coulombs, methyl 3,5-dichloro-4-methylbenzoate was observed by GC/MS; but formed no greater than 5% by the end of 2810 coulombs. Starting material was still present after 2810 coulombs. GC: r.t. (%): methyl 3-chloro-4-methylbenzoate, 9.68 min, (17%); MS: m/z (%) = 186 (11), 184 (32), 155 (34), 153 (100), 127 (10), 125 (33), 89 (24); ; Methyl 3,5-dichloro-4-methylbenzoate, 10.92 min; MS: m/z (%) = 220 (19), 218 (26), 191 (13), 189 (62), 187 (100).

Preparative scale direct electrolysis of 4,4'-dimethylbiphenyl (5):

4,4'-dimethylbiphenyl (5) (50 mg, 2.74e-4 mol) was added to 10 mL of supporting

electrolyte solution (0.1 M lithium perchlorate in acetonitrile) in an electrolysis cell described above. The cell was stirred at room temperature while applying + 1.5V vs. Ag/0.1M AgNO₃. The progress of the reaction was monitored at regular intervals by taking 1 μ L samples to be assessed by GC/MS. The electrolysis was stopped when starting material (**5**) was consumed, after 1434 coulombs (54F/mol) or 27.5 eq. of the calculated amount of electrons were passed. The electrolysis solution was washed with distilled water (20mL) and extracted with methylene chloride (3x20mL). The organic layers were then combined and dried over sodium sulfate. Methylene chloride was removed under reduced pressure to yield 0.05g of brown film with a yellow hint. Flash column chromatography was employed to isolate the different products from electrolysis: 4-(4-Methylphenyl)benzaldehyde (**5d**); (5% EtOAc in hexanes), 0.01g of yellow crystals; GC: r.t. (%): 12.52min, (69%); M/S: m/z: (%)= 196 (100), 195 (88), 167 (19), 165 (34), 152 (40); 4-(4-methylphenyl)benzoic acid (**5e**); (10% EtOAc in hexanes), 0.01 of yellow crystals; GC: r.t. (%): 11.99min, (85%); M/S: m/z (%)= 212 (100), 211 (26), 197 (51), 184 (24), 183 (37), 169 (24), 130 (24), 129, (30), 128 (31), 115 (58), 82 (21); biphenyl-4,4'-dicarboxylic acid (**5f**) and 4,4'-biphenyldicarboxaldehyde (**5g**), (35% EtOAc in hexanes), 4.8mg of yellow film; GC: r.t. (%): **5f**: 13.51min (43%); M/S: m/z: (%)= 242 (10), 200 (100); **5g**: 13.66min (25%); M/S: m/z: (%)= 210 (94), 209 (100), 153 (25), 152 (67); a mass that indicates the presence of biphenyl-4,4'-dicarboxylic acid methyl ester (**5j**), (100% EtOAc); GC: r.t. (%): 15.36min (78%); M/S: m/z: (%)= 256 (17), 255 (100), 212 (53), 197 (40), 196 (63), 195 (23), 181 (31).

Preparative scale catalytic electrolysis of 4, 4'-dimethylbiphenyl (5) with 4,4',4'-trichloro-2-nitrotriphenylamine (catalyst 4): 28.5mg (1.56e-04 mol) of **5** and 6.9mg (1.76e-05) of **catalyst 4** were added to 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) in an electrolysis cell described above. The cell was stirred at room temperature while applying +1.00V to the electrolysis system. 1 μ L samples were taken from the electrolysis solution at regular intervals and analyzed by GC/MS to monitor the progress of the electrolysis. The electrolysis was stopped after 9 hours, after 151.16 coulombs were passed or after 5 eq. of the calculated amount of electrons were passed. The solution was washed with distilled water (20mL) and extracted with methylene chloride (3x 20mL). Then the combined organic layers were washed once more with water, after which it was dried over sodium sulfate. Methylene chloride was removed under reduced pressure to yield 40mg of red brown film with a hint of yellow. The GC/MS showed **5d** and **5e** and also N-([1,1'-biphenyl]-4-ylmethyl,4'methyl)-acetamide (**5k**). GC: r.t. (%): **5d**, 12.55min (88%); M/S: m/z (%)= 196 (100), 195 (88), 167 (20), 165 (36), 152 (42); **5e**, 12.60min; M/S: m/z (%)= 214 (22), 212 (25), 196 (100), 195 (89), 167 (20), 165 (38), 152 (94), 115 (25); N-([1,1'-biphenyl]-4-ylmethyl,4'methyl)-acetamide (**5k**), 13.00min (13%); M/S: m/z (%)=227 (41), 210, 195 (34), 196 (39), 184, 115 (20), 182 (46), 181 (24), 170, 167 (27), 166 (22), 165 (100), 152 (30)

Preparative scale direct electrolysis of 4,4'-dimethyl-2-nitro-1,1'-biphenyl (6): 2.9mg(1.28e-05mol) of **6** was added to 10mL of supporting electrolyte solution (0.1M lithium perchlorate in acetonitrile) in the electrolysis cell described above. +1.6V was applied to the cell as it was stirred at room temperature. The progress of

the electrolysis was monitored by taking 1 μ L samples of the solution at regular intervals. The electrolysis was stopped when **6** was longer present—after 7.22 coulombs or 2.9 eq. of the calculated amount of current had been utilized. The solution was washed with distilled water (20mL) and extracted with methylene chloride (2 x 20mL). Then the organic layers were combined and extracted once more with distilled water (40mL) and then subsequently dried over sodium sulfate. Methylene chloride was removed under reduced pressure to yield 3.5mg of caramel color film. GC: r.t. (%):4-aldehyde,4'-methyl-2'-nitro-1,1'-biphenyl (**6a**), (13.52min) (100%); M/S: m/z (%)= 241 (34), 213 (41), 196 (36), 184 (48), 168 (69), 166 (28), 165 (100), 156 (34), 152 (64), 139 (27); ^1H NMR (CD_3CN , 300MHz): δ 10.05(s, 1H_f), 7.93 (H_c),7.55 (H_d) ($J_{\text{AB}}=7.65\text{Hz}$), 7.82 (s,1H_a), 7.58 (H_b), 7.42 (H_e) ($J_{\text{AB}}=7.2\text{Hz}$), 2.48 (s,3H, 4-CH₃).

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