This is to certify that the

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Conversion of 2,3-Pentanedione to
Value-Added Chemicals

presented by

Melissa A. Thiel

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Dennis J Miller
Major professor

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CONVERSION OF 2,3-PENTANEDIONE TO VALUE-ADDED CHEMICALS

By

Melissa A. Thiel

A THESIS

Submitted to
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ABSTRACT

CONVERSION OF 2,3-PENTANEDIONE TO VALUE-ADDED CHEMICALS

By

Melissa A. Thiel

Possible downstream reaction products and intermediates from 2,3-pentanedione, a high value specialty chemical made from crop-derived lactic acid, were studied. Yield of duroquinone, a product from the self-condensation of 2,3-pentanedione, was produced in yields as high as 29% by reacting 2,3-pentanedione in basic solutions. Low yield can be attributed to duroquinone degredation, favoring of undesired species, and 2,3-pentanedione polymerization before condensation. Duroquinone has possible antioxidant uses.

Pyrazines were produced by reacting 2,3-pentanedione with vicinal diamines to form dihydropyrazines which were then oxidized. 2-Ethyl-3-methyl pyrazine was produced in 72.4% yield and a mixture of 2-ethyl-3,5-dimethyl pyrazine and 3-ethyl-2,5-dimethyl pyrazine was produced in 93% yield. Pyrazines are used as nutty, roasted flavorings.

2-Ethyl-3-methyl quinoxaline was produced in 98% yield from o-phenylenediamine and 2,3-pentanedione. Quinoxalines are used as antibacterial and antifungal agents.

Conversion of 2,3-pentanedione to value-added chemicals was successful.

This work is dedicated to Scott and Vicki, who still have theses to write!

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A special thanks goes to Mom, Dad, Vicki, and Larry for helping me to realize my dreams.

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Chapter 1

INTRODUCTION AND BACKGROUND

1.1 Introduction

Lactic acid is a bifunctional, optically active chemical typically used in the food industry which is derived from fermentation of biomass feedstocks. It can be converted to other valuable products such as acetaldehyde, acrylic acid, propanoic acid, and 2,3-pentanedione (1). Conversion to 2,3-pentanedione is achieved by condensation of lactic acid and was first discovered in our laboratory at Michigan State University. Our process is environmentally favorable due to the combination of low lactic acid cost, reduction of petroleum use, and low toxicity of the catalysts used for condensation. Producing value-added fine chemicals from 2,3-pentanedione is the focus of this work.

2,3-Pentanedione is a high-value fine chemical ($40/lb) that is currently produced in limited quantities (5000 lbs/yr) through multi-step synthesis or via dairy waste recovery. The demand and uses for 2,3-pentanedione are confined because of its high price, but its potential low cost production from lactic acid provides an opportunity to produce a new clas

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class of chemical products from biomass. It is currently used as a butter flavoring ingredient in foods ranging from candy to cereal. It is also used in coffee products to enhance flavor and aroma (2). Outside of the food industry, 2,3-pentanedione can be used as a viable photopolymerization initiator and as a biodegradeable solvent (3). 2,3-Pentanedione also has potential for use as a feedstock (4), solvent (5), or as a fuel additive. Its isomer, 2,4-pentanedione, is a well known chelating agent (6).

The primary focus of this work is to examine possible downstream reaction products and intermediates from 2,3-pentanedione and to optimize yields of promising products. Figure 1.1 shows the reaction pathways of interest to this work. The α-diketone function makes 2,3-pentanedione a valuable starting material for producing heterocyclic aromatic compounds. It undergoes a self-condensation reaction to duroquinone (2,3,5,6-tetramethyl-2,5 cyclohexadiene-1,4 dione) (7). The condensation of 2,3-pentanedione with diamines to alkyl pyrazines proceeds through a dihydropyrazine, in the presence of sodium or potassium hydroxide (8). α-Diketones may be characterized by means of their crystalline condensation products, especially the quinoxalines obtained with o-phenylenediamine (9). Although we did not investigate it in this work, 2,3-pentanedione can be sequentially dimerized in the presence of an aldol condensation catalyst and then hydrolyzed in the presence of an acid or cationic resin to give 2,5-dialkyldihydrofuranones and 2,4,5-trialkyldihydrofuranones (10). These compounds can be used to enhance caramel flavor in foods.

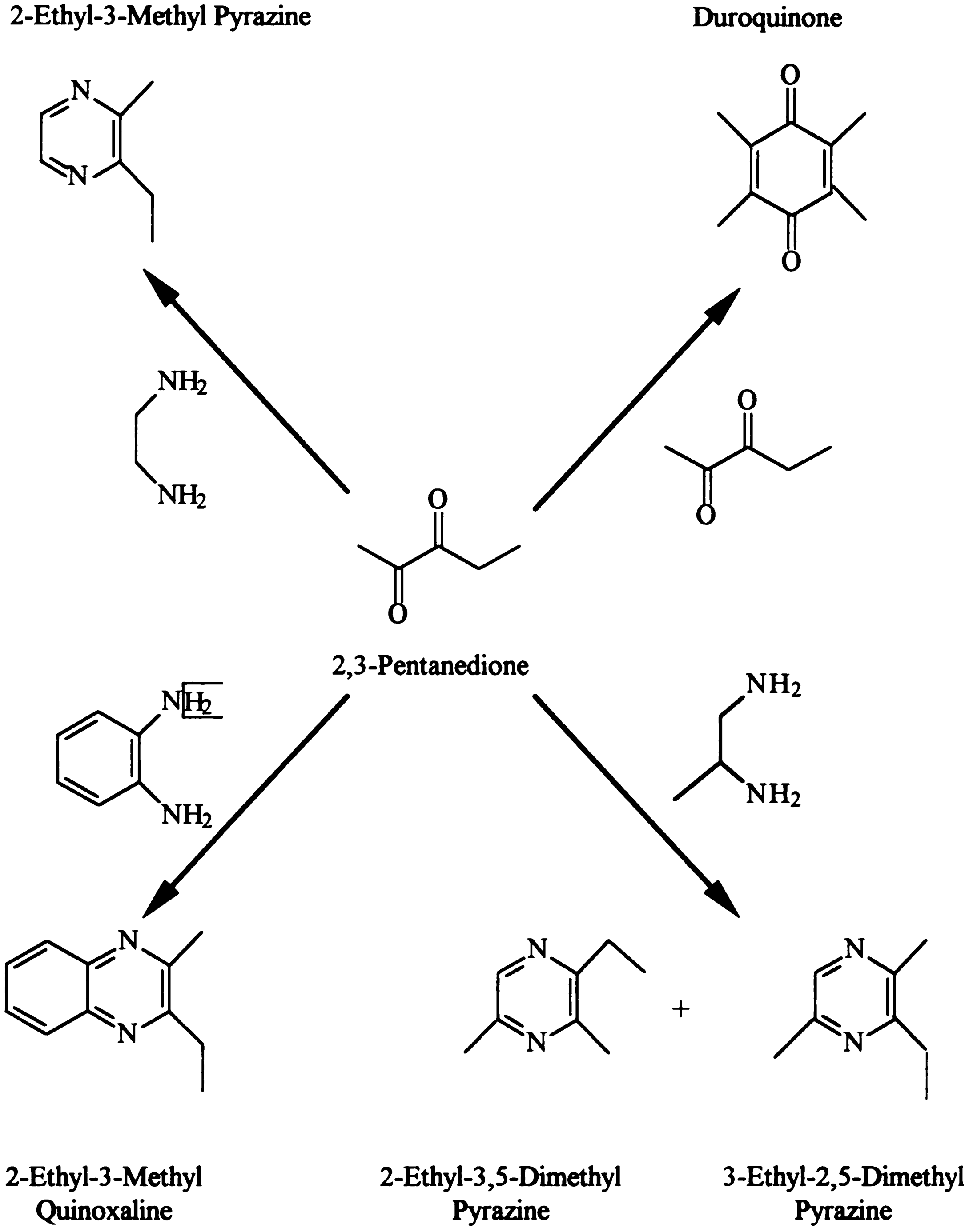

Figure 1.1
Conversion Pathways of 2,3-Pentanedione

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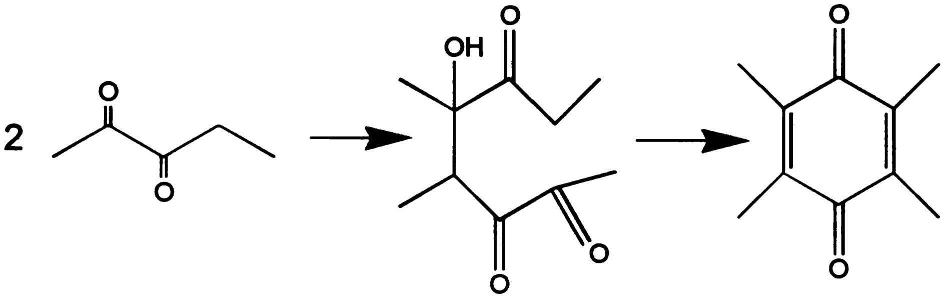
1.2 Literature Review

1.2.1 Duroquinone

As mentioned, 2,3-pentanedione undergoes a self-condensation to form duroquinone. The procedure described in the literature gives a 10% yield of duroquinone from 2,3-pentanedione and aqueous NAOH upon heating (7). The pathway displayed below shows the intermediate formation (9).



Duroquinone is currently produced by converting durene into dinitrodurene with fuming nitric acid and then reducing the dinitro compound (11). When pure durene is used as the feed, the reaction yields 90% duroquinone. Duroquinone can also be produced by oxidation of 1,2,4,5-tetramethylbenzene in the presence of 0.24 wt% Pd(II)-sulfonated polystyrene type resin in acetic acid and aqueous hydrogen peroxide (12). Conversion was reported as 74.8% with a 8.4% yield of duroquinone. Tetramethyl benzene with high temperature and high concentration of hydrogen peroxide gave yields of duroquinone on the order of 19% (13). A third reaction involving tetramethyl benzene was found. It involves m-chloroperbenzoic acid oxidation resulting in a duroquinone yield of 20% (14). Starting with 2,3,5,6-tetramethyl phenol, duroquinone is produced in 59%

yield by a modified two-phase Jones oxidation procedure (ether/aqueous chromic acid) (15). Durohydroquinone can be oxidized with hydrogen peroxide in methanolic solution with catalytic amounts of iodine to produce duroquinone in 92% yield (16). All of these methods for producing duroquinone are different from the condensation reaction we worked with because they start with a compound similar in structure to duroquinone itself.

Quinones, in general, are an important class of compounds in industry. The literature contains several applications for duroquinone and similar quinones as antioxidants, as photosensitive materials, in holographic recording media, as sensitizing and stabilizing agents, as electron acceptors for storing solar energy, and as oxidizing agents for catalyst recovery (17 - 20). tert-Butyl hydroquinone (TBHQ) was approved by the FDA in 1972 as an antioxidant that can be used in foods (21). With duroquinone as the starting product, antioxidants similar to TBHQ can be produced. It can also be used to produce N, N'-dicyano-p-quinodiimine (DCNQI) in 55% yield (22). This compound readily forms charge-transfer complexes and radical anion salts which have high electrical conductivity. Duroquinone can be used as a starting material for the growth of linear multiring polyquinoidal polyacenes (23). These compounds are of interest because of their electronic properties. By controlling which quinone and hydroquinone structure appear in the molecular framework of these compounds, reactivity and optical, magnetic, and electrical properties can be controlled.

Hydroquinone and its derivatives are used principally as photographic developers, antioxidants of fats and oils, and inhibitors of polymerization (24). Tetramethyl hydroquinone is formed easily from duroquinone by reduction with alloxatin (20). It can also be produced by reduction with vanadium (II) chloride in 96% yield (25).

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1.2.2 Pyrazines and Quinoxalines

2,3-Pentanedione can undergo a two step reaction, formation of dihydropyrazine and subsequent oxidation, with a number of α,β-diamino compounds, including ethylenediamine and propylenediamine, to give pyrazines in high yields (26). Starting from pure dihydropyrazine, dehydrogenation with CuO gave nearly 80% yields of pyrazines (27). The condensation of α,β-diamino compounds with 2,3-pentanedione has been used for synthesis of quinoxalines from o-phenylenediamine (28). This is the most widely used route to synthesize quinoxalines since simple changes such as using substituted o-phenylenediamine can make almost all the quinoxalines. Quinoxaline has also been prepared in 85-90% yield by reaction of o-phenylenediamine with glyoxal sodium bisulfate (29).

There are many food products that contain pyrazines. Fried beef, coffee, roasted barley, and potato chips are a few examples (29). Generally, pyrazines give a nutty, roasted flavor. Pyrazines also have a large number of biological and medicinal applications, ranging from herbicidal to antibiotic activities (30). Quinoxalines are rarely found in natural products; however, they exhibit good antibacterial and antifungal uses (27). Quinoxalines and their simple derivatives can be converted into both mono- and di-N-oxides by oxidation with peracids; they also form quaternary salts (31).

1.3 Research Objectives

The first objective of this research was to review the available methods for duroquinone, pyrazine, and quinoxaline production. Secondly, a set of experiments were performed to optimize the formation of duroquinone from the base catalyzed self-condensation of 2,3-pentanedione by changing reaction vessels, temperatures, bases, and concentrations of reactants. The third objective was to investigate reactions of 2,3-pentanedione with vicinal diamines to produce pyrazines and quinoxalines.

Chapter 2

DUROQUINONE STUDIES

2.1 Introduction

This chapter describes the methods and procedures used to optimize the yield of duroquinone formed via the self-condensation of 2,3-pentanedione. General experimental methods are first described, followed by a progression of procedures that evolved over the course of the research. Results are incorporated in the pertinent sections. The NMR spectra shown are a representative sampling of the work that was done. Additional results, calculations, and spectra are given in the Appendices.

2.2 Materials

High purity 2,3-pentanedione (Aldrich, 97%) was used as a starting material in each reaction in predetermined concentration in aqueous solution. Basic solutions of sodium hydroxide (MCB), triethylamine (Baker), cesium hydroxide (Aldrich, 50 wt%), and lithium hydroxide (Aldrich, 99%) were utilized as indicated in each section. Solutions

of hydrogen chloride (Mallinckrodt, 37%) were used as neutralizing agents. All dilutions were made using HPLC water (Sigma-Aldrich). Duroquinone (Aldrich, 97%) was used as a standard. Other solvents and chemicals specific to each analytical technique are indicated in the appropriate sections.

2.3 Duroquinone Extraction Technique

Although the procedure for duroquinone formation from 2,3-pentanedione changed over the course of the project, the extraction technique for duroquinone recovery can be generalized. A typical reaction procedure involved 2,3-pentanedione addition to a basic aqueous solution. The mixture was allowed to react for a specific amount of time. Since duroquinone is insoluble in water, it precipitated out as it was formed. In order to recover the duroquinone after the reaction, toluene was added to the reaction vessel. The resulting two phase mixture was transferred to a separatory funnel. The reaction vessel was washed with a measured amount of water followed by toluene to ensure all the sample was transferred. After vigorous shaking, the aqueous layer was separated from the organic layer and set aside. The organic layer was emptied from the separatory funnel and dried over sodium sulfate. A rotary evaporator was used to distill off the toluene and leave the organic products, including duroquinone.

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2.4 Analytical Methods

2.4.1 NMR Spectroscopy

^{1}H Nuclear Magnetic Resonance (NMR) spectra, obtained on a Varian VXR-300 spectrometer, were used to obtain information on the structure and concentration of reaction products by weighted Fourier Transform of free induction decays (FID's). Qualitatively, NMR spectra show how hydrogen atoms in organic molecules absorb radiofrequency and change the direction of their nuclear spin. Combined hydrogens on different types of molecules absorb at slightly different frequencies or "chemical shifts" due to the electronic or chemical character of the hydrogen (32). This method gives both quantitative results from peak areas and qualitative structural information from peak location. Peaks of interest were integrated so the relative amounts of hydrogen present could be calculated. The area of the spectral peaks is directly proportional to the number of protons involved. When the concentration of a species is calculated using NMR spectra, a standard is used with a known concentration and number of hydrogens. By comparison of the peak areas of the standard and unknown, the unknown concentration can be found.

Deuterated toluene (Isotec, 99% D), deuterated water (Cambridge Isotope Laboratories, 99% D), and deuterated chloroform (Isotec, 99% D), were used as solvents because the substitution of D (deuterium) for H (hydrogen) eliminates unwanted H signal. Tetramethylsilane (TMS) (Aldrich, 99.9+%) was used for quantification because it has a recognized chemical shift of 0 ppm. Chloroform (Aldrich) and methanol (Mallinckrodt) were used as standards and were added as indicated in 10 microliter quantities.

Spectra were obtained at room temperature by first loading the sample tube into the magnet bore. Standard acquisition parameters were chosen according to the solvent used. Manual as well as automatic “shimming” was performed to reduce line broadening. Typical operating parameters for normal data acquisition for deuterated toluene are shown in Table 2.1.

Table 2.1 NMR Operating Parameters

Acquisition	Setting
Frequency	299.949
Type	^{1}H
Attenuation	3.499
Number of Passes	32000
Scan Width	4573.0
Baseline	16
Filter Bandwidth	2600
Power	8.0
Tof	786.8
Number of Scans	16

NMR spectra were obtained as references for 2,3-pentanedione and duroquinone. Peak identifications for these chemicals in various solvents are listed in Table 2.2. Sample spectra shown throughout this document contain a number of peaks for chemicals which are not listed here and have not been assigned. The spectra have overlapping peaks due to the complexity of the structures involved and the number of species in the sample.

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Table 2.2 NMR Peak Assignments For Duroquinone Studies

Chemical (Solvent)	δ (ppm)
2,3-Pentanedione (deuterated toluene)	0.86 triplet (methyl) 1.95 singlet (methyl) 2.39 quartet (methylene)
2,3-Pentanedione (deuterated chloroform)	1.09 triplet 2.34 singlet 2.77 quartet
Duroquinone (deuterated toluene)	1.69 singlet
Duroquinone (deuterated chloroform)	2.00 singlet
Tetramethylsilane	0.00 singlet
Chloroform (deuterated toluene)	6.14 singlet
Methanol (deuterated toluene)	3.05 singlet
Deuterated Toluene	2.08 triplet 7.01 multiplet

2.4.2 High Pressure Liquid Chromatography

High pressure liquid chromatography (HPLC) was used to identify and separate reaction mixtures into their components. Hardware included a Nucleosil C18 column (Sigma-Aldrich, 4.6mm x 250mm) connected to a V^4 Absorbance Detector (Isco) with a deuterium lamp. A ten microliter sample loop was utilized with a manual injection port (Valco Instruments). An Isco Model 2350 dual piston HPLC pump was used for flow of the mobile phase, which was chosen to be 75% acetonitrile (EM), 25% 0.1M H_3PO_4 (Mallinckrodt) in HPLC water. Samples were dissolved in mobile phase and flushed through the injection port. Chromatograms were recorded using a Waters 745 Data Module. Typical operating parameters can be seen in Table 2.3. Standards of 2,3-

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pentanedione and duroquinone were used to identify peaks. 2,3-Pentanedione appears at 11.4 minutes and duroquinone appears at 17.5 minutes, as seen in Figure 2.1.

Table 2.3 HPLC Operating Parameters

Variable	Conditions
Mobile phase flow rate	0.3 ml/minute
Run time	30 minutes
Sensitivity (Detector)	1.0% Transmittance
UV wavelength	210 nm
Attenuation	512
Chart speed	0.5 cm/ minute

2.4.3 Gas Chromatography

A Varian 3700 Gas Chromatograph with flame ionization detection and a 4% Carbowax 80/100 carbopack B-DA (Supelco) glass column was used for identification and concentration analyses for 2,3-pentanedione. A Hewlett Packard HP3394 Integrator was used to record and integrate the chromatograms. In preparation for injection, samples were diluted one to one with a solution containing 10.0 g/l 2-propanol as an internal standard and 0.06M oxalic acid for column conditioning. Sample injection size was one microliter. Once an injection was made, the needle was left in the port for one minute to assure vaporization of the sample. Each run started at 100°C and ramped at 25°C per minute until it reached 200°C. At the conditions described, 2,3-pentanedione appears at 9.4 minutes and 2-propanol appears at 3.0 minutes.

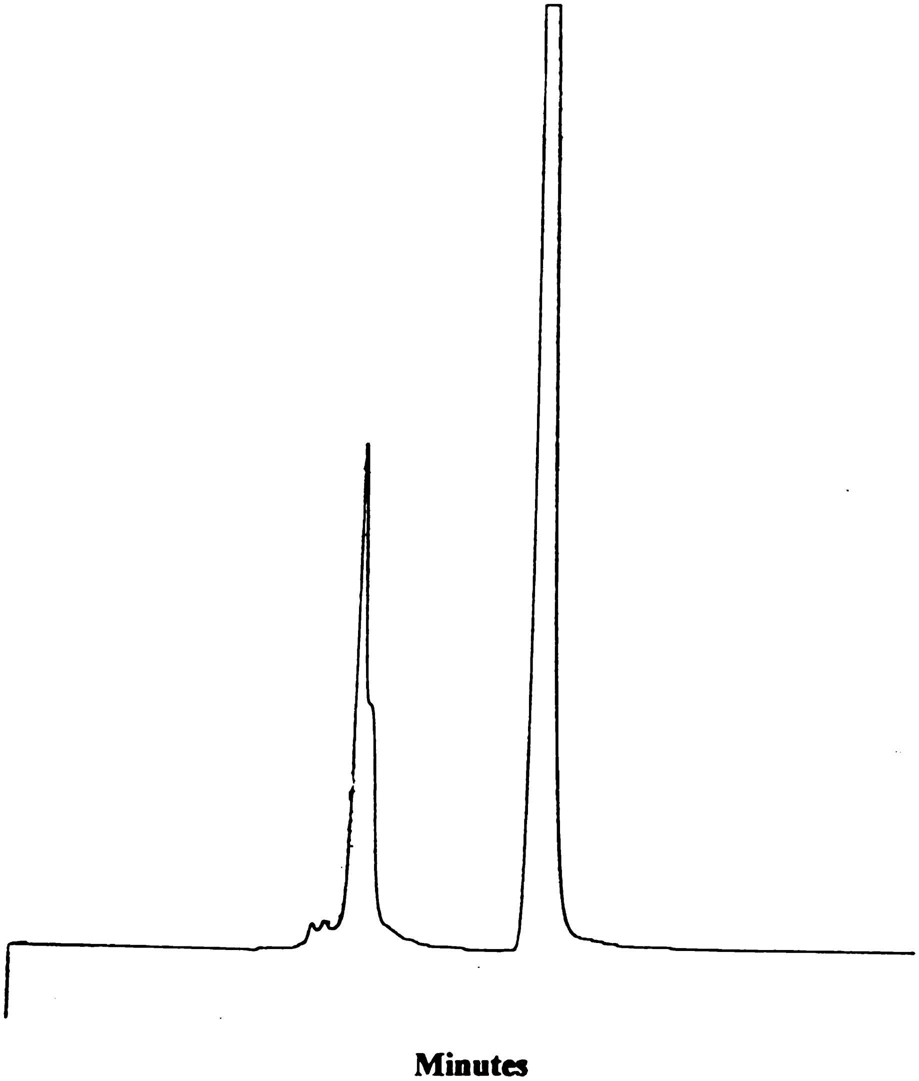


Figure 2.1
HPLC of Duroquinone and 2,3-Pentanedione (5/3/96)

2.4.4 Thin Layer Chromatography

Thin Layer Chromatography (TLC) was used to separate fractions of organic residues from reactions. Silica gel (SiO_2) was the substrate used on the plates. By trial and error, a mobile phase of 75% hexanes and 25% ethyl acetate was determined to move and separate the sample components based on polarity. The solvent was placed in the developing chamber, covered, and allowed to equilibrate. On large silica gel 60 F-254 plates, samples were spotted on the bottom of a plate and allowed to dry. The plate was placed in the developing chamber and covered. The mobile phase rose to the top of the plate carrying with it the sample components. After the plate was carefully removed and thoroughly dried, a UV light at 254nm was used to locate the sample spots. A spatula was used to scrape off the spots; the gel from each spot was collected and put in a vial where it was redissolved in mobile phase. The mixture was filtered and the filtrate was then dried and analyzed by NMR spectroscopy.

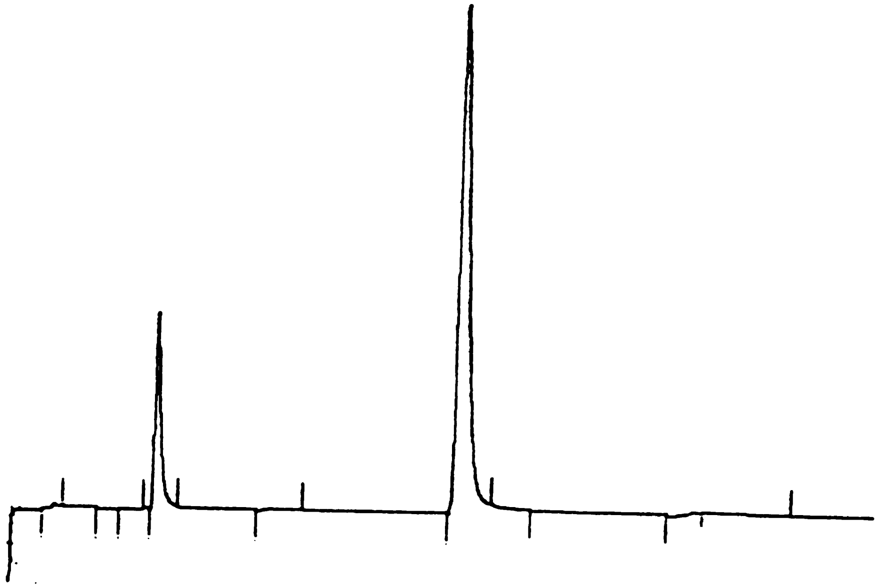
2.5 Examination of Species Recovery

2.5.1 Analysis and Recovery of 2,3-Pentanedione

To examine the reliability of the experimental methods, a check of 2,3-pentanedione recovery was conducted using both NMR spectroscopy and gas chromatography (GC). To determine the response factor for 2,3-pentanedione, the diketone was dissolved in toluene (0.02016 g/ml) and water (0.04019 g/ml) and injected into the gas chromatograph. Response factors for 2,3-pentanedione were determined for each solvent. For the toluene standard, the response factor was 1.15 ± 0.03; for the water standard the response factor was 1.14 ± 0.03. Typical gas chromatograms for 2,3-pentanedione in water and in toluene can be seen in Figures 2.2 and 2.3, respectively.

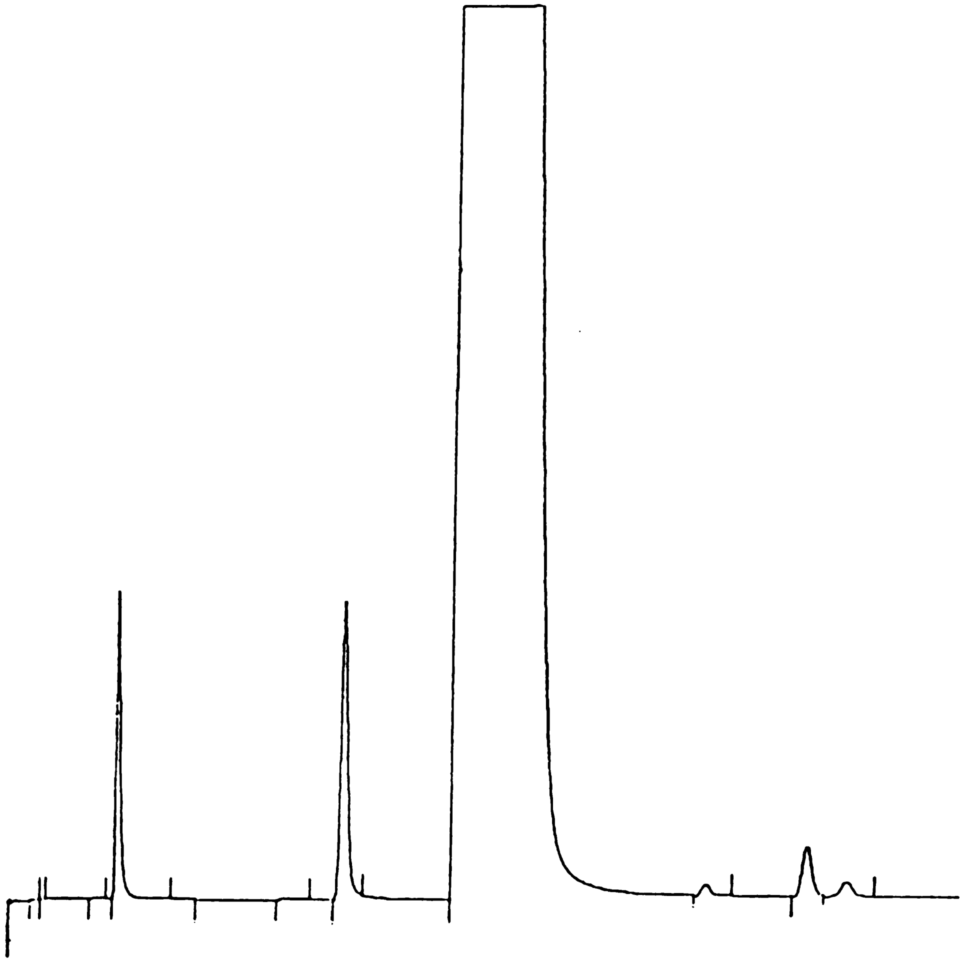
Three solutions of 2,3-pentanedione in water with concentrations of 0.0197 g/ml, 0.0391 g/ml, 0.0586 g/ml were made. Each was injected straight into the GC to check for linearity and reliability of the determined response factor. As seen in Table 2.4, recoveries were on the order of 95%, based on concentration of the original solution.

Next, each solution was subjected to extraction with toluene. The organic layer was injected into the GC and also run on the NMR spectrometer. A typical NMR spectrum of 2,3-pentanedione dissolved in deuterated toluene can be seen in Figure 2.4. The singlet CH_3 peak at 1.95 ppm was used for quantitation of 2,3-pentanedione. Ten microliters of chloroform were used as the standard. All aqueous solutions were also injected into the GC and recoveries of 2,3-pentanedione together from both phases were high, as seen in Table 2.4. When GC is used to determine the amount of 2,3-pentanedione in toluene, recoveries are not as high as when NMR is used. Toluene appears as a large peak on the GC chromatograms, so it may affect other peak integrations. This is consistent with the organic layer set of runs which were run on the NMR. The same sample, dissolved in deuterated toluene, was then injected into the GC. These results differed by an average of 20%, as seen in Table B.1. An NMR spectrum (Figure B.1) and gas chromatograms (Figure B.2 and B.3) can be found in Appendix B.



Minutes

Figure 2.2
GC of 2,3-Pentanedione in Water (7/31/95)



Minutes

Figure 2.3
GC of 2,3-Pentanedione in Toluene (7/13/95)

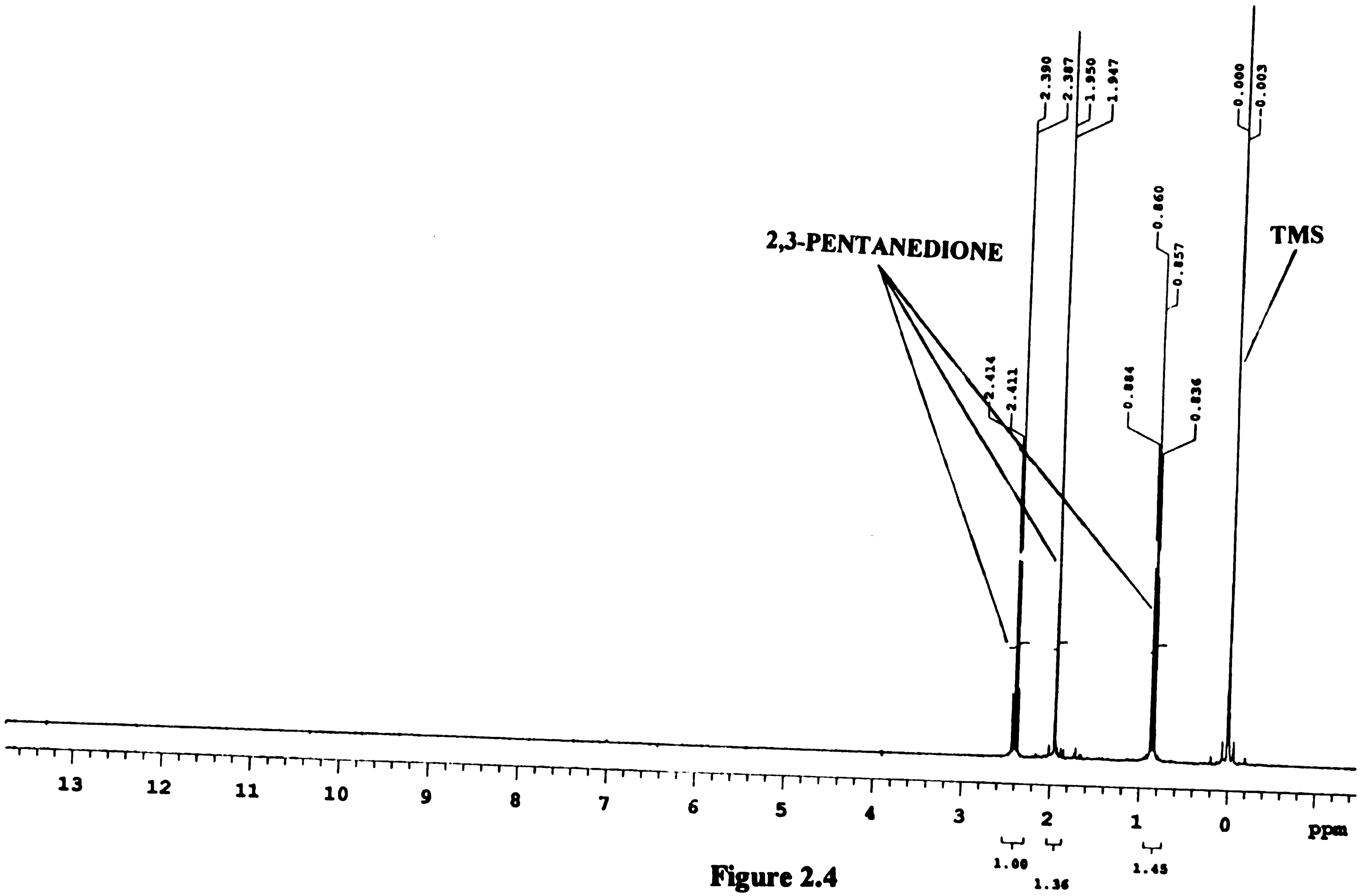


Figure 2.4
NMR Spectrum of 2,3-Pentanedione in Deuterated Toluene (3/14/95)

Table 2.4 GC and NMR Recoveries

Solution *	Recovery **	Method
1 2 3	94% 95% 97%	Inject sample straight into GC
1 2 3	115% 125% 153%	Extract with toluene, Inject aqueous on GC, Run organic on NMR spectrometer
1 2 3	88% 81% 83%	Extract with toluene, Inject aqueous and organic on GC

* 2,3-pentanedione in water solutions: 1- 0.0197 g/ml, 2 - 0.0392 g/ml, 3 - 0.0586 g/ml.
** Recoveries are based on the analysis for both the aqueous and organic phases.

2.5.2 Efficiency of Toluene Extraction for Recovering Duroquinone

Since duroquinone has a low solubility in water, extraction of product was relatively simple. The products were collected by separating aqueous and organic layers. However, since base was present, a small amount of duroquinone dissolved in the aqueous phase. To determine the efficiency of toluene extraction, 0.02g of duroquinone was weighed and added to 10 ml of a 0.5M NaOH aqueous solution From a visual inspection, it did not appear the duroquinone dissolved. Ten ml of toluene were added and the layers were shaken and separated using a separatory funnel. The organic layer was run over sodium sulfate to remove excess water. The organic species were then either put in the rotary evaporator to dry and the residue weighed, or put in an NMR tube and analyzed to determine concentration by peak comparison with chloroform. Results are listed in Table

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2.5. A typical NMR spectrum of duroquinone dissolved in d-toluene can be seen in Figure 2.5.

Table 2.5 Duroquinone Recovery

Run	Duroquinone Added (g)	Residue (g)	Recovery
1	0.0213	0.0189	89%
2	0.0227	0.0206	91%
3	0.0206	0.0190	92%
4 (081)	0.0821	NMR	88%
5 (082)	0.0821	NMR	89%

Since duroquinone is not volatile, GC was not used to analyze the aqueous phases associated with these experiments. It is seen that about 90% of the initial duroquinone is recovered via toluene extraction. The remaining 10% dissolved in the basic solution.

2.6 Experimental Results

2.6.1 Confirmation of Literature Methods

Duplicate reactions to those described in the literature by H. von Pechmann (7) were conducted using a three-neck flask, a heating mantle, and a condenser. An aqueous 5% solution of 2,3-pentanedione (20.0 ml) was put in the flask and 2.0 ml of 3.0 M NaOH were added as catalyst. The mixture was refluxed with an organic layer of benzene for 10 minutes at 100°C. Many color changes occurred over the course of the reaction. The solution was initially light yellow. As the reaction progressed, a dark brown color appeared. Upon cooling, the organic layer was separated from the aqueous layer, and

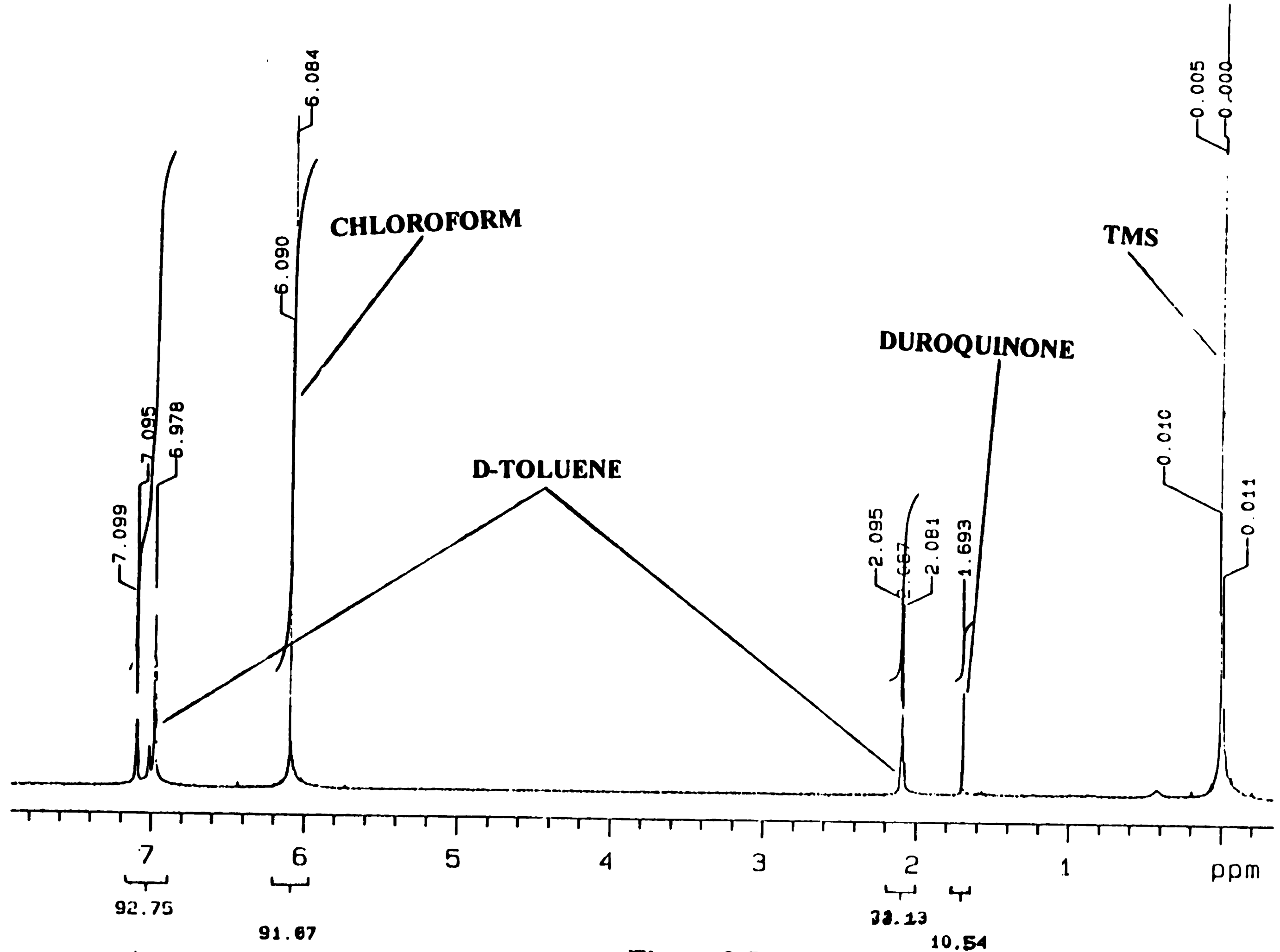

Figure 2.5
NMR Spectrum of Duroquinone in Deuterated Toluene (3/14/95)

benzene was distilled off, leaving an oily dark brown liquid. ^{1}H-NMR spectroscopy was used to analyze the reaction product; a sample NMR spectrum can be seen in Figure A.1. The highest yield from the three runs completed (experiment numbers A1 - A3) was around 7%. This procedure was abandoned due to low yield.

2.6.2 NMR Tube Reactions

A set of experiments was performed in standard NMR tubes so the reaction mixture could be directly analyzed by NMR spectroscopy. It was also thought small quantities of 2,3-pentanedione in the condensation reaction would induce dimers and trimers but no larger chains. Initially, deuterated chloroform was used as a solvent. When the reaction samples of 2,3-pentanedione in aqueous NaOH were analyzed, it was determined that chloroform and base may react, so the solvent was switched to deuterated toluene.

A typical NMR tube experiment involved adding 50 microliters of 2,3-pentanedione to 0.5 ml deuterated toluene in an NMR tube. Once it dissolved, 20 microliters of varying concentrations of NaOH (0.5 M to 3.0 M) in water were added, and the tube was vigorously shaken. The reaction mixtures were allowed to sit overnight, and were then run on the NMR spectrometer. Figure 2.6 shows the NMR spectrum of the above reaction using 10 microliters of 3.0 M NaOH in water. Even with this strong base concentration, very little reaction occurred. Peaks at 0.822 ppm, 1.869 ppm, and 2.334 ppm show the presence of 2,3-pentanedione. Since the base and deuterated toluene are in

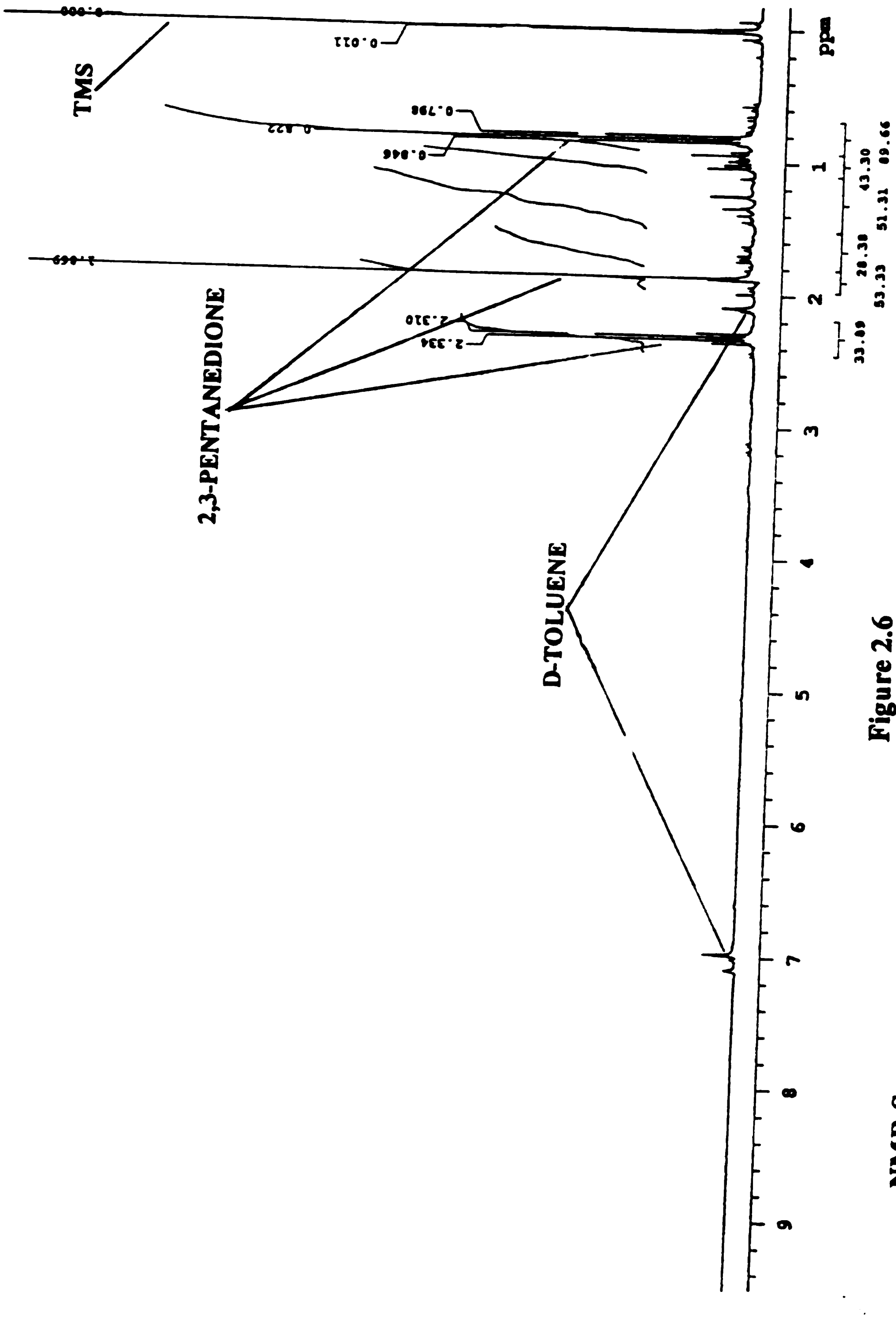

Figure 2.6
NMR Spectrum of Organic Species Formed in NMR Tube Reaction (T8, 3/22/95)

separate phases, it was thought there was a partitioning problem. This means the 2,3-pentanedione was concentrated in the organic phase, while the base remained in the aqueous phase, reducing their contact and subsequent reaction. To reduce partitioning of 2,3-pentanedione between the aqueous and organic phases and to decrease the ratio of 2,3-pentanedione to base, the amount of 2,3-pentanedione added was lowered to 25 μl.

A typical NMR spectrum in which 25 microliters of 2,3-pentanedione and 20 microliters of 3.0 M aqueous NaOH were reacted in 0.5 ml of deuterated toluene can be seen in Figure 2.7. Numerous peaks appear, most of which are as of yet unassociated with identified chemical species. Duroquinone can be identified at 1.695 ppm, but it is present only in low concentration. At this small volume of reaction, contact between the base (20 microliters) and the 2,3-pentanedione (25 microliters dissolved in 0.5 ml deuterated toluene) was minimal. It was difficult to tell what qualities and color changes the solution underwent during reaction.

2.6.3 Vials as Reaction Vessels

2.6.3.1 Effects of Base Concentration

After the NMR tube experiments, 20 dram vials were used as reaction vessels. The reaction of 2,3-pentanedione to duroquinone is base catalyzed, so varying the amount of base present in the mixture was investigated. Two sets of experiments were completed using 2.0 ml reaction volumes and 10.0 ml reaction volumes. For the first set, reactions consisted of adding 1.0 ml of 5% aqueous 2,3-pentanedione solution and 1.0 ml of varying base concentrations of aqueous NaOH, ranging from 0.5 M to 3.0 M. The two were

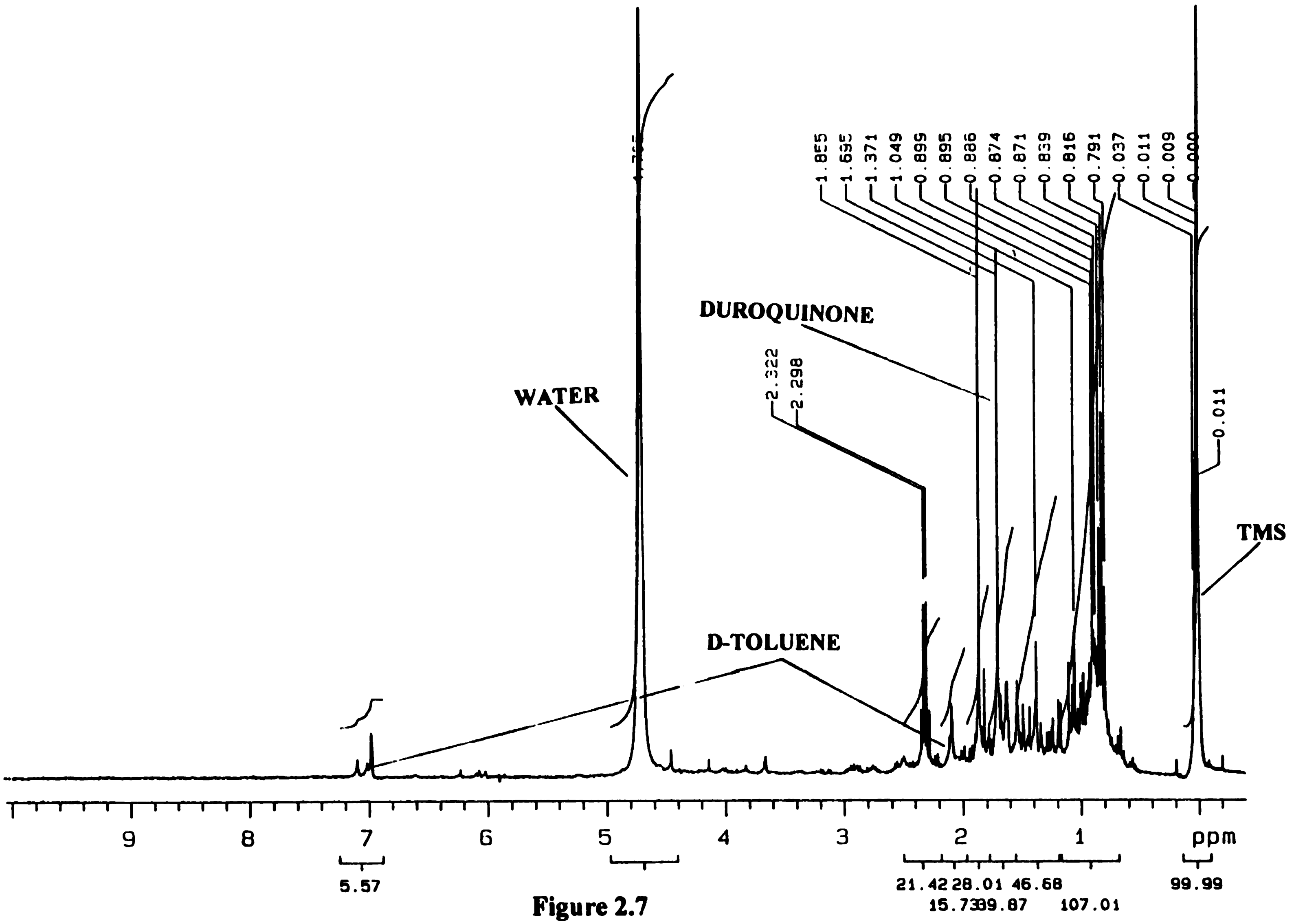

Figure 2.7
NMR Spectrum of Organic Species Formed in NMR Tube Reaction (T14, 3/22/95)

mixed well and allowed to react for 30 minutes. As the base concentration was increased, the solution appeared darker over time. Yellow duroquinone crystals, insoluble in water, precipitated out over the course of the reaction. At the end of the reaction time, 1.0 ml of deuterated toluene was added to the reaction mixture to extract the organic species. The deuterated toluene was separated from the aqueous solution and run over sodium sulfate for drying. It was then put in a NMR tube with 10 microliters of methanol for quantification and analyzed. The highest yield was observed at a solution base concentration of 0.5 M (Table 2.6). At higher molarities, the mixture became more viscous.

Table 2.6 Duroquinone Yields from NaOH

Reaction Volume (ml)	Final Molarity of NaOH in solution	Reaction Time	% Yield of Duroquinone
2.0	0.250	30 minutes	16.2
2.0	0.500	30 minutes	21.1
2.0	0.750	30 minutes	19.6
2.0	1.500	30 minutes	11.4
10.0	0.005	overnight	0
10.0	0.020	overnight	0
10.0	0.032	3 days	9.5
10.0	0.076	3 days	6.8
10.0	0.380	overnight	11.6
10.0	1.900	overnight	11.7

The second set of experiments were conducted by adding 5.0 ml of 5% 2,3-pentanedione solution and 5.0 ml of NaOH aqueous solutions in various concentrations to vials and mixing. The reaction was allowed to progress for a specified amount of time, and then 1.5 ml of deuterated toluene were added. The deuterated toluene was separated after mixing with the reaction phase and placed in an NMR tube. Chloroform or methanol (10 microliters) was added to the tube as a standard for quantitation. With a base concentration of 0.005 M and 0.020 M, no reaction occurred. When the base concentration was increased to 0.032 M, the reaction yielded no duroquinone after one hour, a yield of 4.2% after one day, 9.5% after three days, and 8.7% after six days. These NMR spectra were complicated and likely represent many species. Figure 2.8 contains an NMR spectrum of the organic species formed after just five minutes. No duroquinone was present yet, but 2,3-pentanedione peaks appear at 0.8 ppm (triplet), 1.9 ppm (singlet), and 2.3 ppm (quartet). This sample was taken right when the reaction started changing color from light yellow to dark brown. In comparison, Figure 2.9 shows the organic species from the same reaction after it had progressed for six days. There is no longer 2,3-pentanedione present and the duroquinone peak appears at 1.69 ppm. This is not, however, a clean NMR spectrum. Peaks very similar to those in Figure 2.8 also appear in Figure 2.9. This method was successful at tracking the progress of the reaction, but since none of the intermediate species present can be conclusively identified, no further information on intermediates and other products was gained.

Next, an experiment with a base concentration of 0.076 M was run using the same procedures. Figure 2.10 shows the NMR spectrum of the organic species formed after three days. Yield of duroquinone for this run, which was the maximum for this ratio, was 6.79%. The duroquinone peak is identifiable at 1.69 ppm. A strong peak at 0.43 ppm and

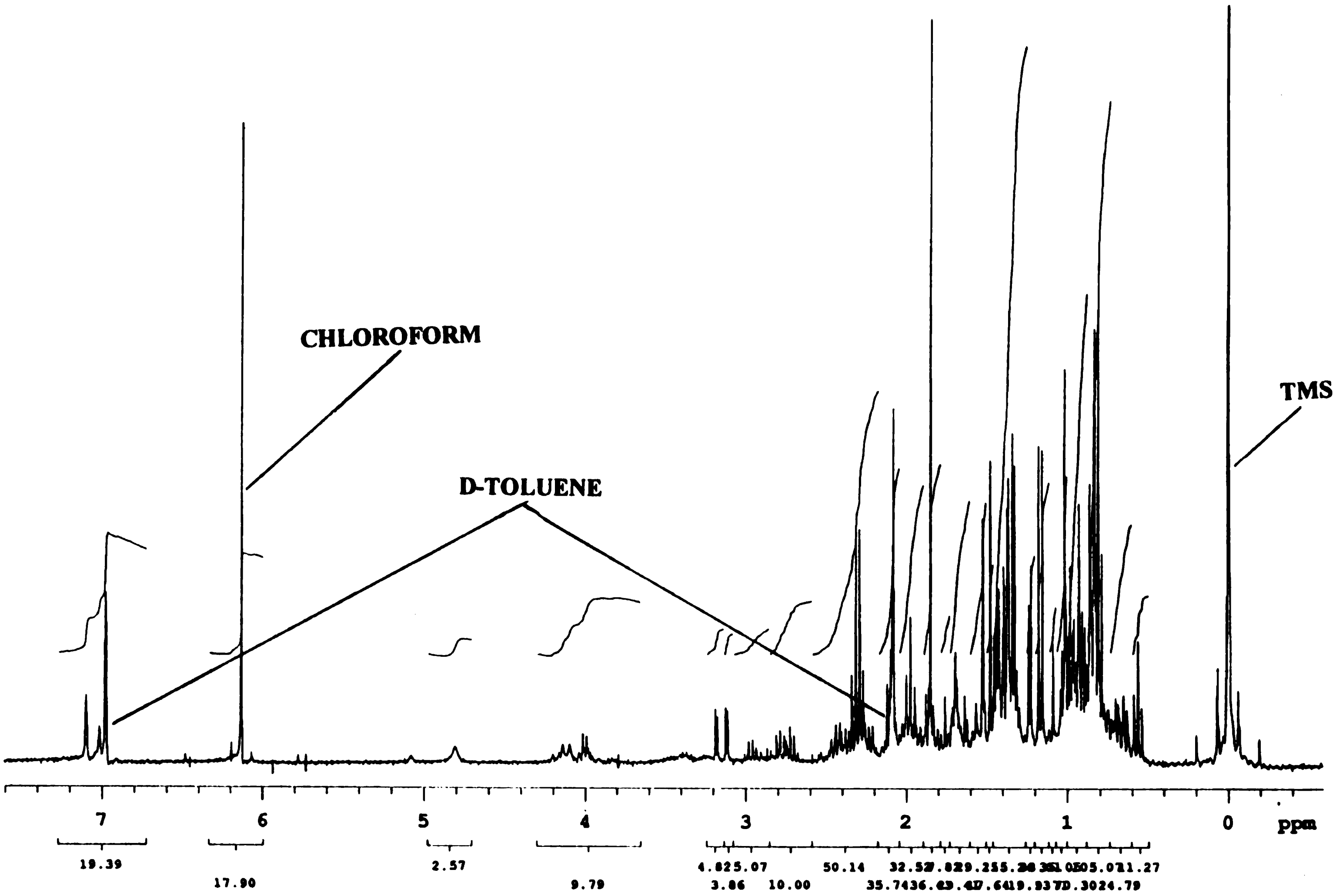

Figure 2.8
NMR Spectrum of Organic Species Formed After 5 Minutes in Reaction
(M 8195 0.1M 019, 8/1/95)

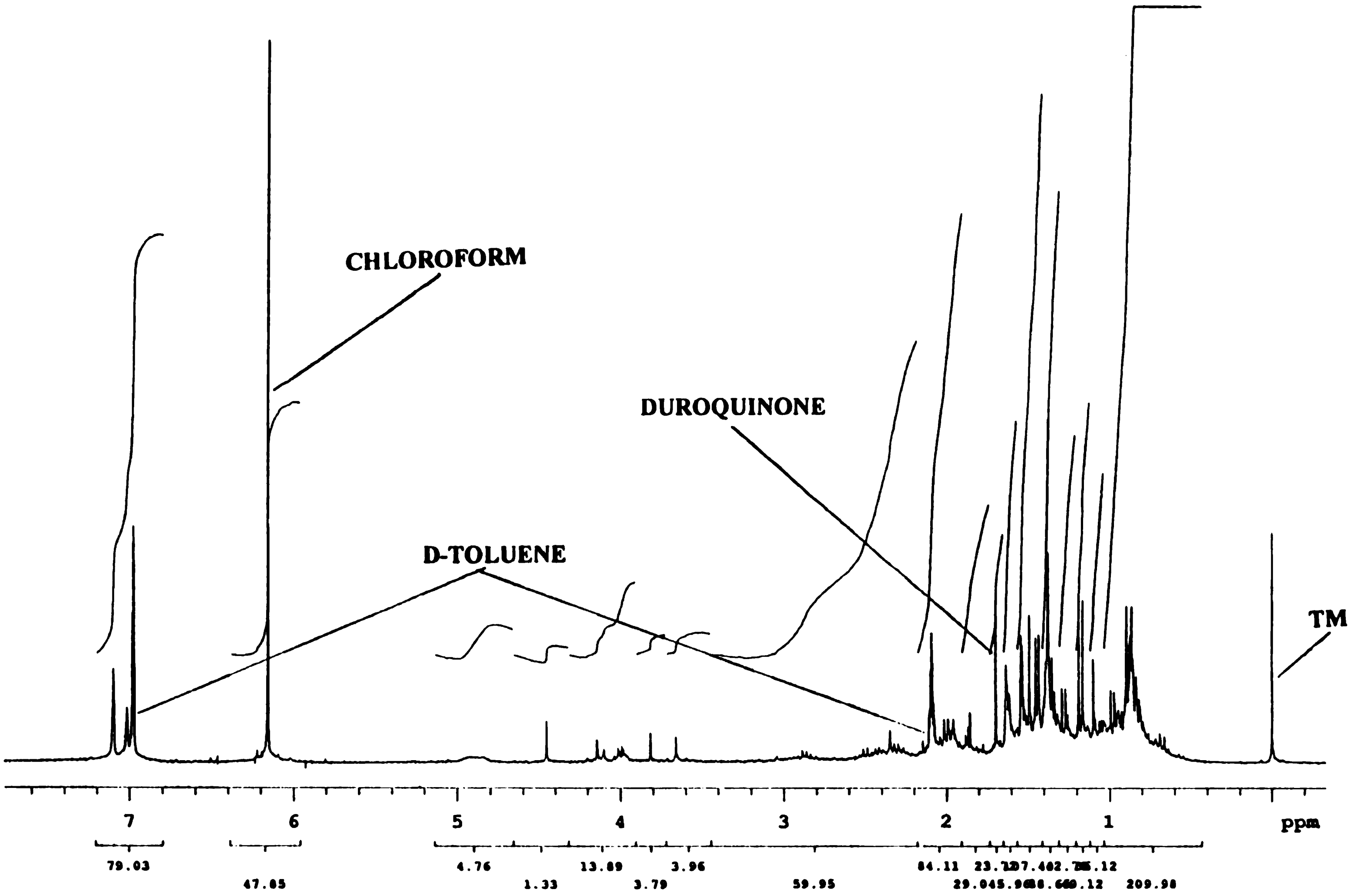

Figure 2.9
NMR Spectrum of Organic Species Formed After 6 Days in Reaction
(M 8195 0.1M 025, 8/1/95)

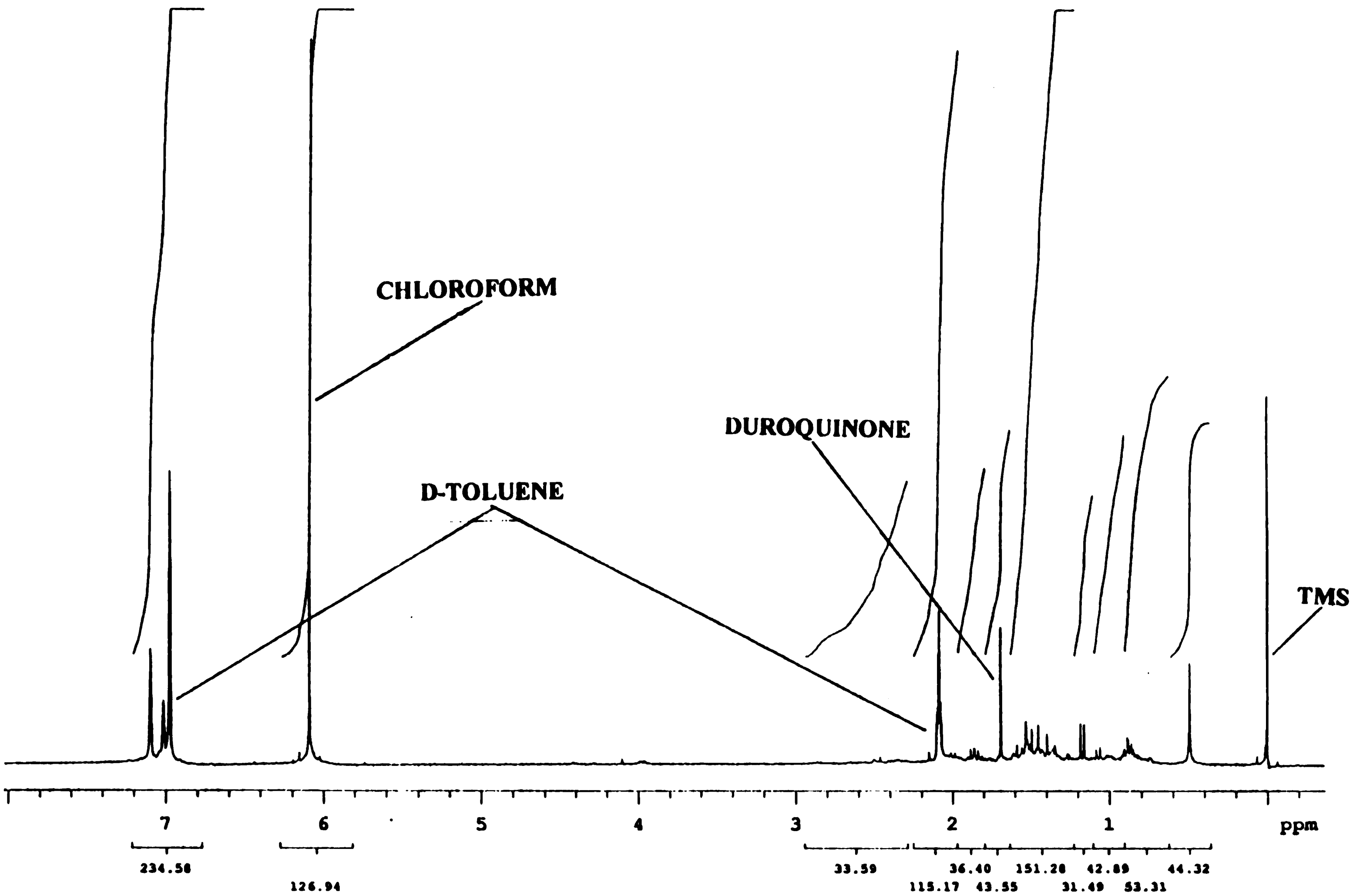

Figure 2.10
NMR Spectrum of Organic Species Formed After 3 Days in Reaction
(M 8195 0.1M 002, 8/1/95)

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many other small peaks appear, which have not been assigned. For experiments using 0.380 M NaOH, organic species gave clean NMR spectra with a duroquinone yield of 11.57% of theoretical. The lowest molarity tried was 1.900 M, which resulted in a duroquinone yield of 11.73%. These lower ratio runs gave cleaner spectra and higher yields of duroquinone, which implies that fewer unwanted species were forming. The trend of 2,3-pentanedione to base ratio suggested that with less 2,3-pentanedione available, more duroquinone was formed (Table 2.6). This observation led us to change the experimental procedure to dropwise addition of 2,3-pentanedione over time into base instead of just mixing the reactants together.

2.6.3.2 Duroquinone Degradation

Before experiments could be completed to investigate temperature effects on the reaction, the effect of heating duroquinone in base needed examination. Duroquinone (0.1 g) was added to 1.0 ml of 3.0 M NaOH in water with stirring and heated to 95°C. These conditions were considered the harshest a reaction might undergo. Figure 2.11 shows the resulting NMR spectrum. Based on NMR peak areas, there was substantial degradation of the duroquinone upon heating at these conditions. The peaks at 1.5 ppm, 1.26 ppm, and 0.4 ppm are unassigned, but must represent degradation products of duroquinone. When duroquinone was heated to 50°C with 1.0 M NaOH, very little decomposition occurred. Degradation in base is important because the reaction of 2,3-pentanedione in base is exothermic and product degradation could occur without external heating.

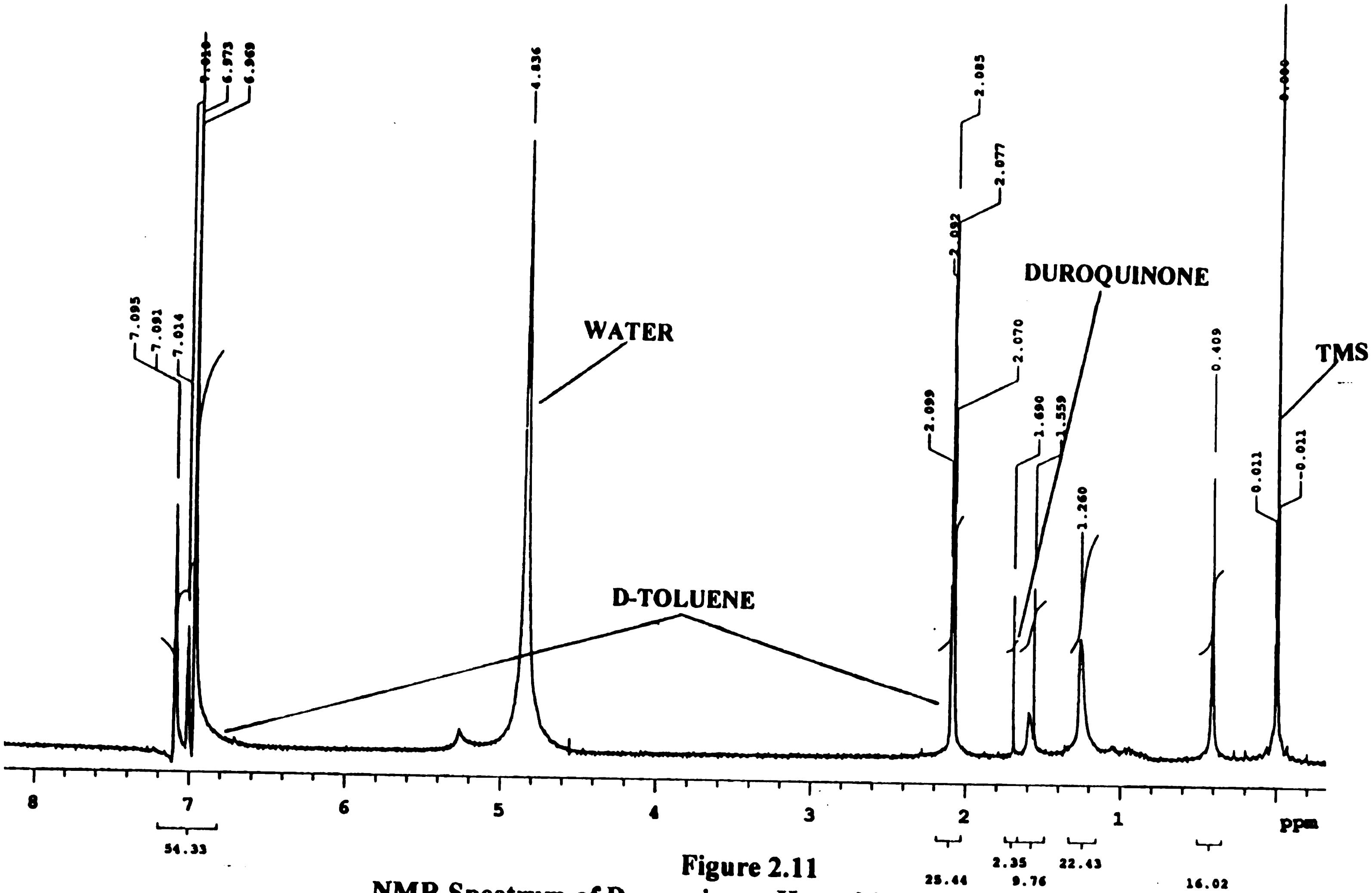

Figure 2.11
NMR Spectrum of Duroquinone Heated in Base (D1, 4/19/96)

2.6.3.3 Effects of Temperature on Duroquinone Yield

It was discovered that the reaction of 2,3-pentanedione in the presence of base to yield duroquinone is exothermic by the following method. Two ml of 2,3-pentanedione and 2.0 ml of 1.0 M NaOH in water were added to a vial. Initially, the mixture was at 22°C. After four minutes, it reached its maximum temperature of 45°C and then slowly returned to room temperature. The solution was light brown in color and small duroquinone crystals could be seen floating on the surface. A similar experiment was done with 3.0 M base, also initially at 22°C. After one minute, the reaction mixture reached a maximum temperature of 83°C. This reaction mixture looked very dark brown with suspended solids in it. No precipitate was observed floating on top. It was thought that polymerization occurred at these strong base conditions, but the solution could not be analyzed by our methods to confirm this. Since the reaction is exothermic, experiments were performed with temperature variations to observe temperature sensitivity and its effect on duroquinone formation.

Experiments were performed with the idea that dropping the reaction temperature, or at least keeping it constant, might decrease the extent of polymerization. To a vial on ice, 1.0 ml of pure 2,3-pentanedione was added. The initial reaction temperature was 5°C. Slowly, 1.0 ml of aqueous 1.0 M NaOH was added and the solution was allowed to react for a specific amount of time. NMR samples were prepared by adding 50 microliters of the reaction mixture to an NMR tube with 1.0 ml of deuterated toluene. As seen in Figure 2.12, the main constituent was still 2,3-pentanedione, but other peaks appeared,

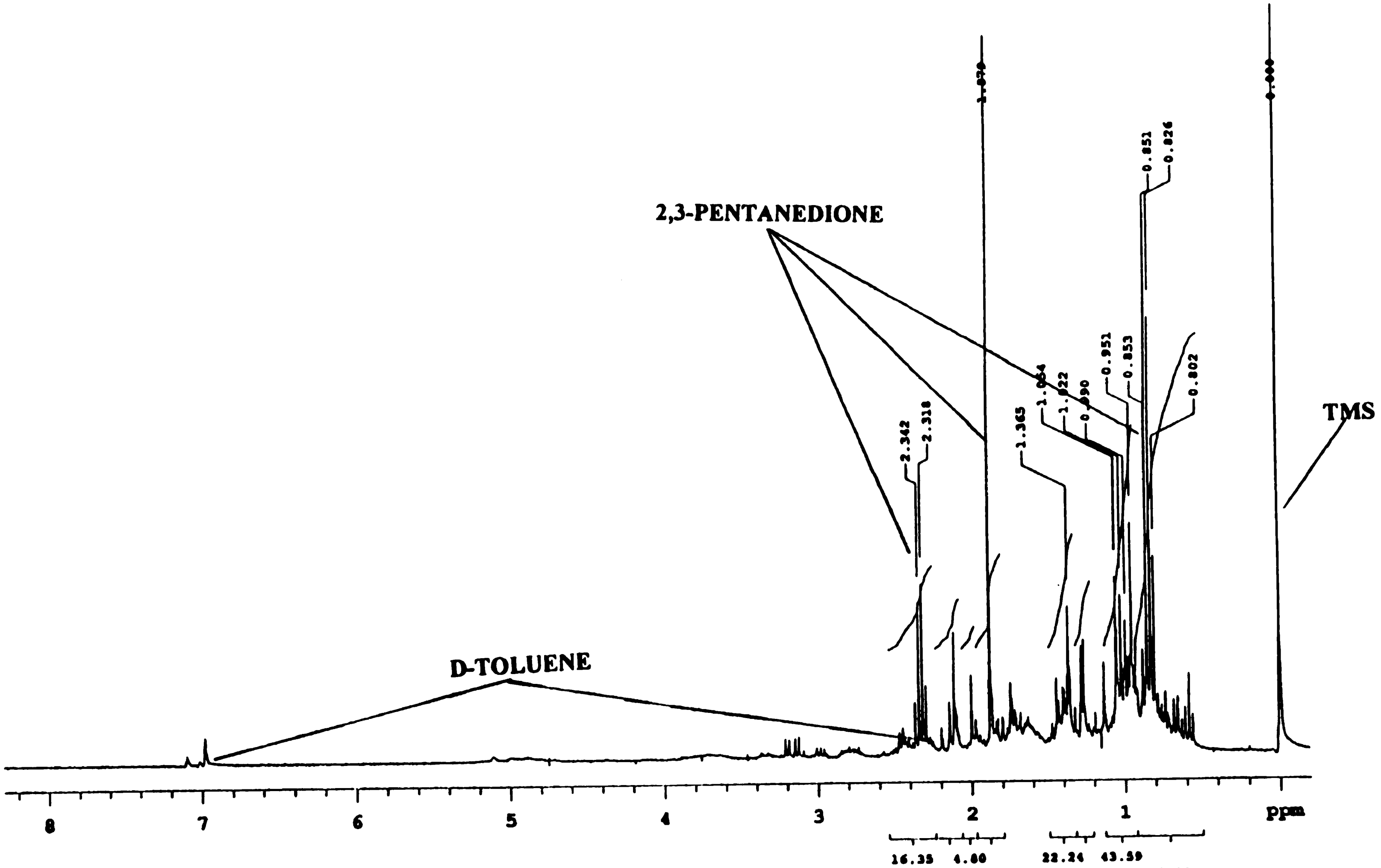

Figure 2.12
NMR Spectrum of Organic Species Formed in Ice Reaction I2 (4/19/96)

suggesting a reaction had or still was occurring. In fact, a color change from light yellow to dark brown was observed. The reaction mixture was allowed to sit overnight and a new NMR spectrum was taken. Again, 2,3-pentanedione was present in similar concentration, so the reaction had stopped prior to reaching complete conversion.

Once it was known where degradation products of duroquinone appeared in NMR spectra, experiments were done that involved heating the reaction. In a vial, 0.5 ml of 5% 2,3-pentanedione were mixed with 0.5 ml of either 1.0 M, 1.5 M, or 3.0 M aqueous NaOH solution. The mixture was heated in a water bath for 15 minutes. Two water bath temperatures, 50°C and 80°C, were examined. Deuterated toluene was added, mixed, and separated. Figure 2.13 shows the NMR spectrum of the organics formed in a heated run. The spectrum is clean, with a split peak appearing for duroquinone at 1.690 ppm and 1.707 ppm; possibly due to the beginnings of duroquinone degradation products. Duroquinone yield for this set of runs was on the order of 8%. Table D.4 in the Appendix contains the calculations for these runs.

Analysis of this subset of data shows that temperature is a factor in the condensation reaction. The ice bath experiments did not react to the desired duroquinone product. Coinciding with literature results, heating the reaction mixture did yield duroquinone, but there was no increase in yield over prior experiments at room temperature, as seen in Figure 2.14. The highest yield of duroquinone was observed when the reaction was allowed to generate its own heat at room temperature; these conditions were used for the next set of experiments.

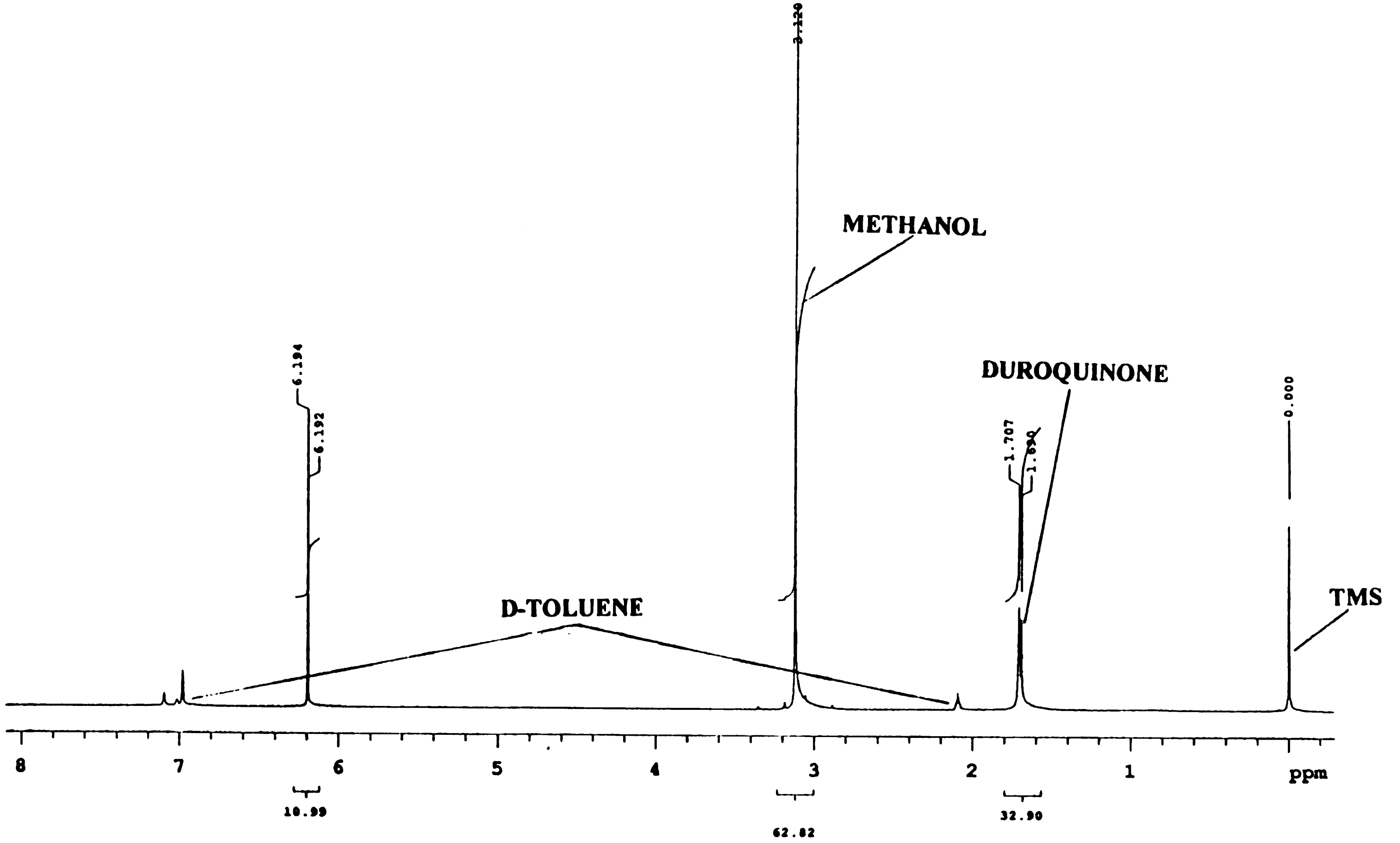

Figure 2.13
NMR Spectrum of Organics Formed in Heated Reaction (H1, 6/19/95)

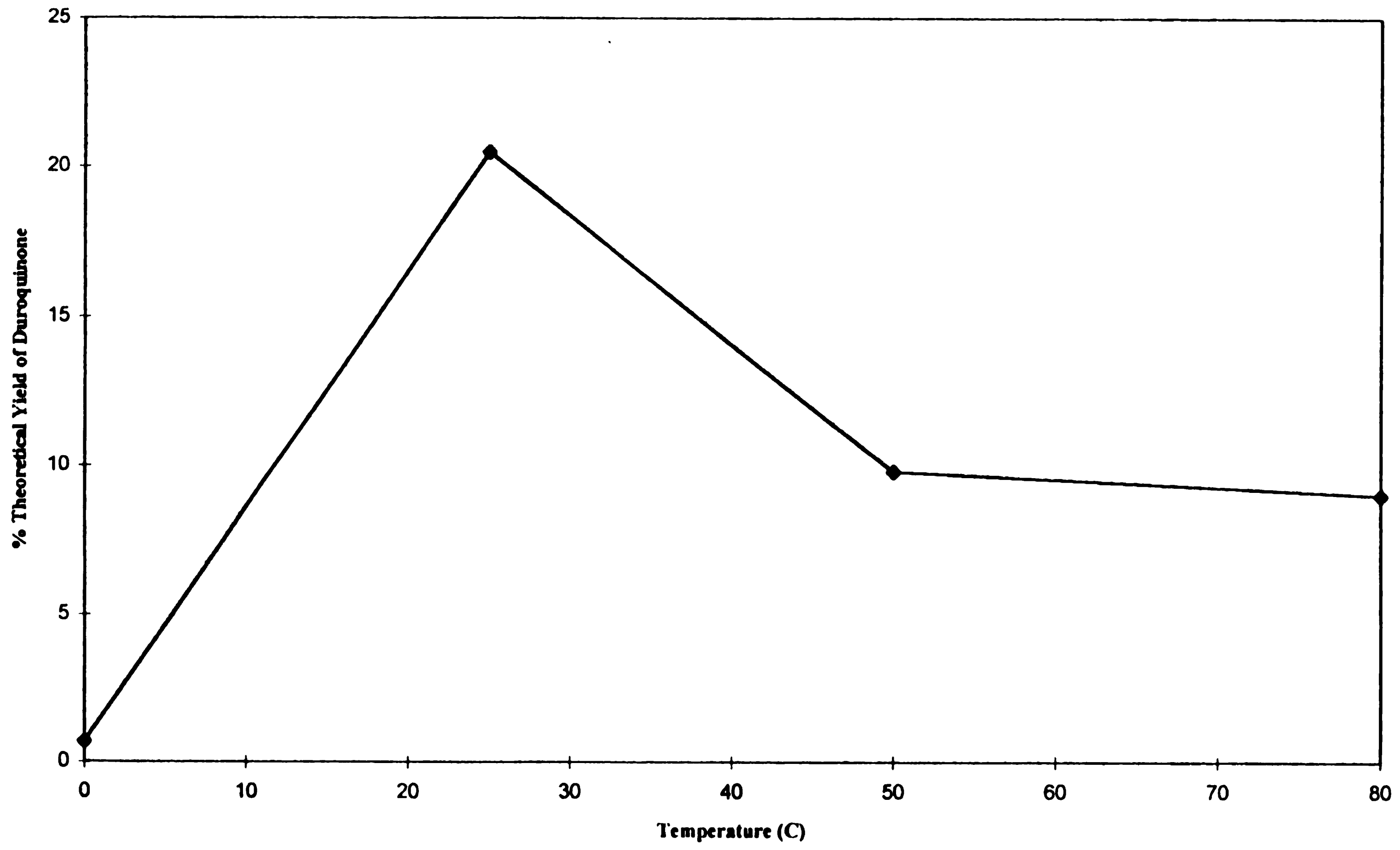

Figure 2.14
Duroquinone Yield Vs. Temperature of Reaction

2.6.3.4 Dropwise Addition of 2,3-Pentanedione

To try to improve yields based on the initial experiments, 2,3-pentanedione was dripped from a buret into base with stirring over the course of the reaction. Figure 2.15 shows the trend that was observed by dripping 5.0 ml of 5% 2,3-pentanedione with drip rates of 0 ml/min to 3.8 ml/min. Yields were increased from when the reactants were just mixed, but the drip rate did not affect yield of duroquinone significantly over a wide range. Drip rates of 0.5 to 1.0 ml solution per minute were deemed appropriate for future work.

2.6.3.5 Reaction Time Effects

To investigate the effect reaction time had on the yield of duroquinone, four solutions containing 5%, 2.5%, 1%, and 0.5% 2,3-pentanedione in water by weight were put into separate burets. To four flasks containing 5.0 ml of aqueous 1.0 M NaOH, 5.0 ml of each of the 2,3-pentanedione solutions were added dropwise over the course of ten minutes with stirring to separate flasks. Reaction time began when the first drop of 2,3-pentanedione hit the basic solution. When the allotted time of the reaction approached, 10.0 ml of toluene were added to the flask and mixed well. The solution was transferred to a separatory funnel and the organic species were recovered using the general extraction procedure described earlier. Along with the known weight of organic species formed, yields were calculated using NMR spectra and were based on the theoretical yield possible from conversion of 2,3-pentanedione to duroquinone. Figure 2.16 shows the trend that

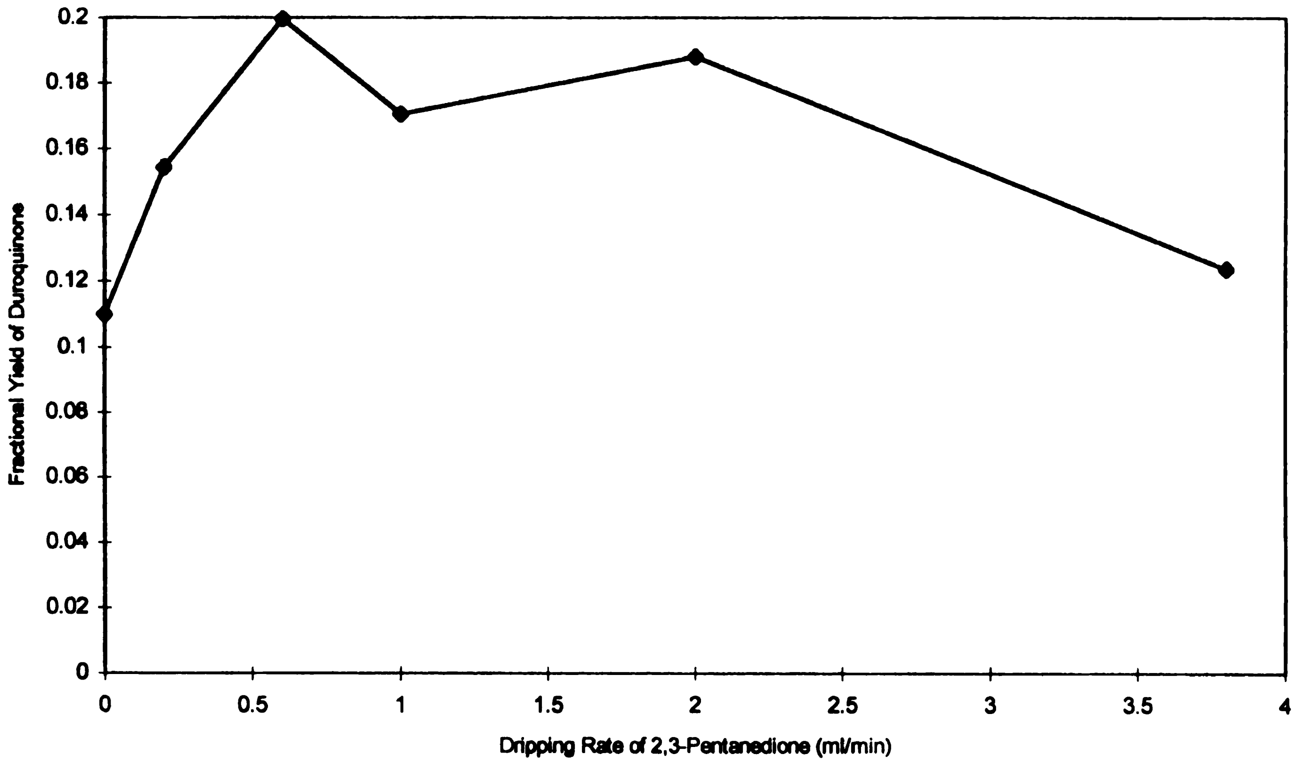

Figure 2.15
Duroquinone Yield Vs. Dropwise Addition Rate of 2,3-Pentanedione

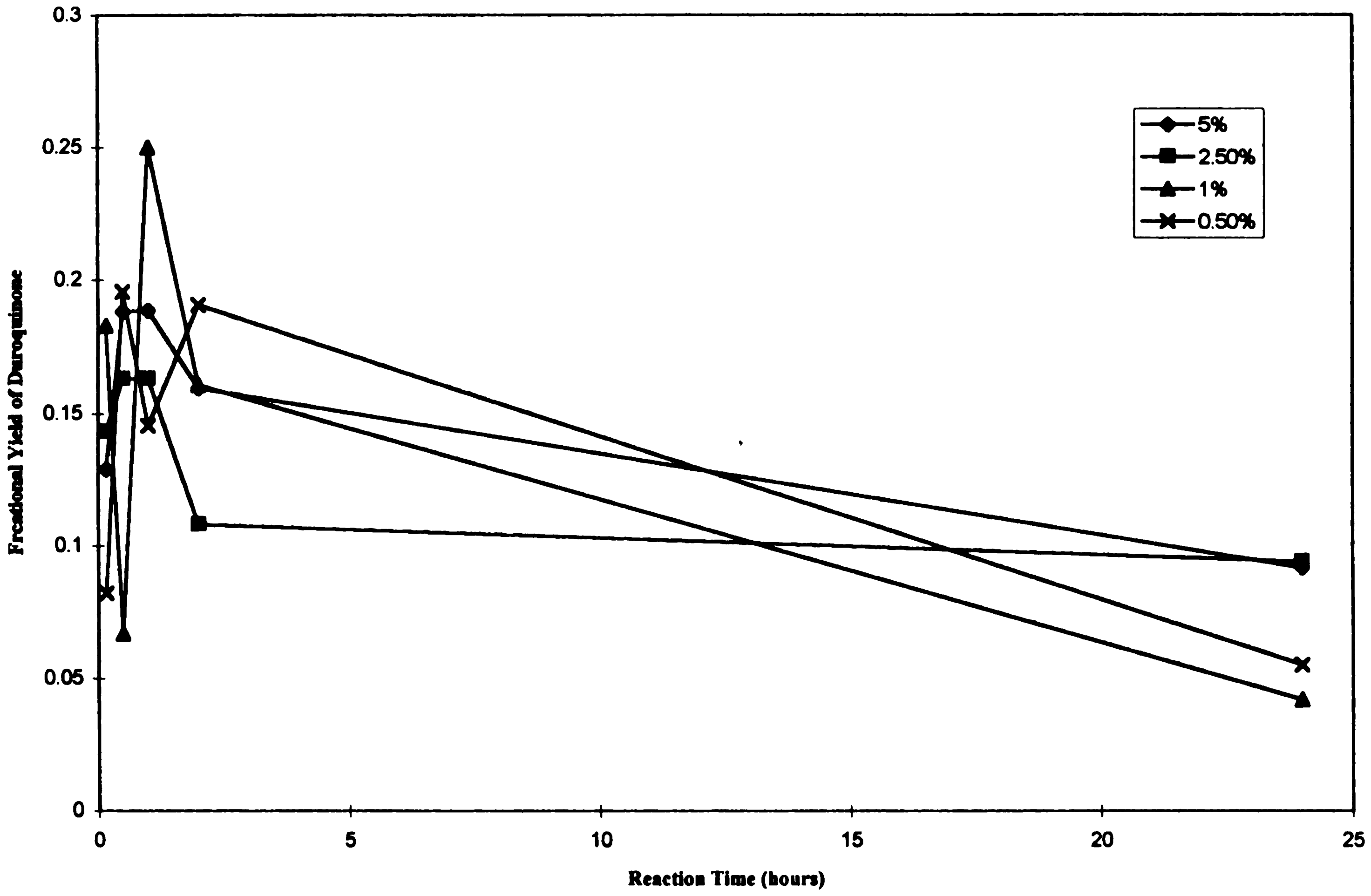

Figure 2.16
Yield of Duroquinone from Different Concentrations of 2,3-Pentanedione Solutions

was observed in the data. As a reminder, only one toluene extraction was done on the aqueous layer, which may result in up to 10% loss in yield. This set of data shows that the highest yield of duroquinone (25%) was obtained from a 1% 2,3-pentanedione solution after two hours of reaction. However, after sitting overnight, yield decreased to 5%. This may be due to degradation of duroquinone or formation of new products from it, equilibrium in the reaction, or due to more duroquinone dissolving into the basic aqueous solution at this length of time.

To help identify species that may be present in other parts of the mixture, basic aqueous reaction layers were dried to concentrate them and remove water which would interfere with NMR interpretation. A known amount of the resulting viscous, black tar was dissolved in deuterated water and NMR spectra, like that seen in Figure 2.17, were obtained. Duroquinone appears on the spectra at 2.00 ppm. The large peak at 4.6 ppm is water; the other peaks are unidentified. 2,3-Pentanedione does not appear to be present in the aqueous spectra, or in the organic phase, indicating it has all reacted.

To stop the reaction at a desired time, the procedure was modified to include addition of stoichiometric amounts of 1.0 M HCl to neutralize the solution. Higher recovery and thus higher yields were anticipated since duroquinone has a slight solubility in basic solutions. Neutralization was initially checked with pH paper, and then a pH meter was utilized. As neutralized occurred, it changed from a clear dark brown in color to cloudy yellowish orange. Two runs, both initially starting with 5.0 ml each of 5% 2,3-pentanedione and aqueous 1.0 M NaOH, were neutralized with HCl after a reaction time of one hour. Figure 2.18 shows the NMR spectrum of the organic species

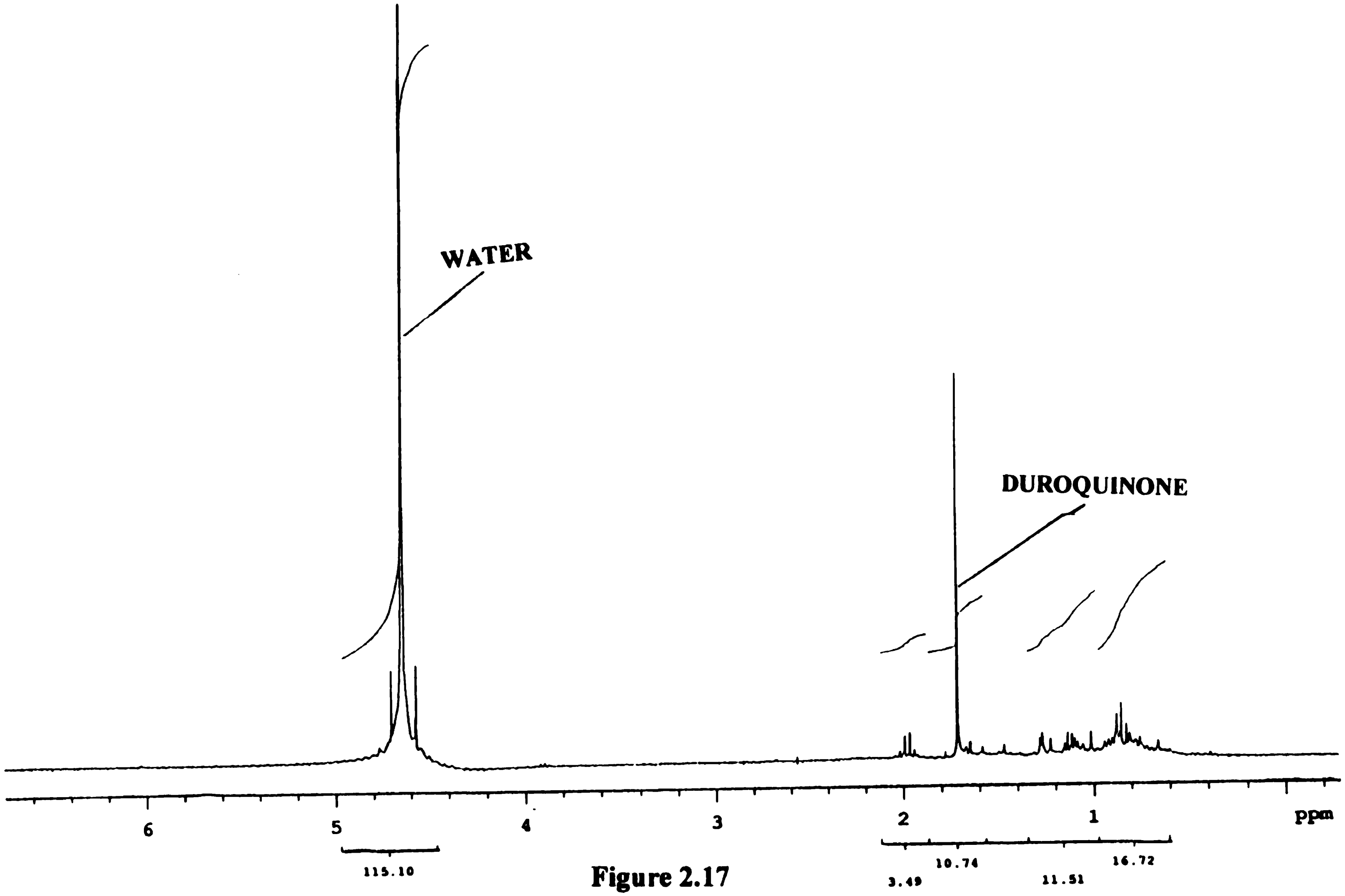

Figure 2.17
NMR Spectrum of the Neutralized Aqueous Layer from NaOH Reaction
(086, 10/30/95)

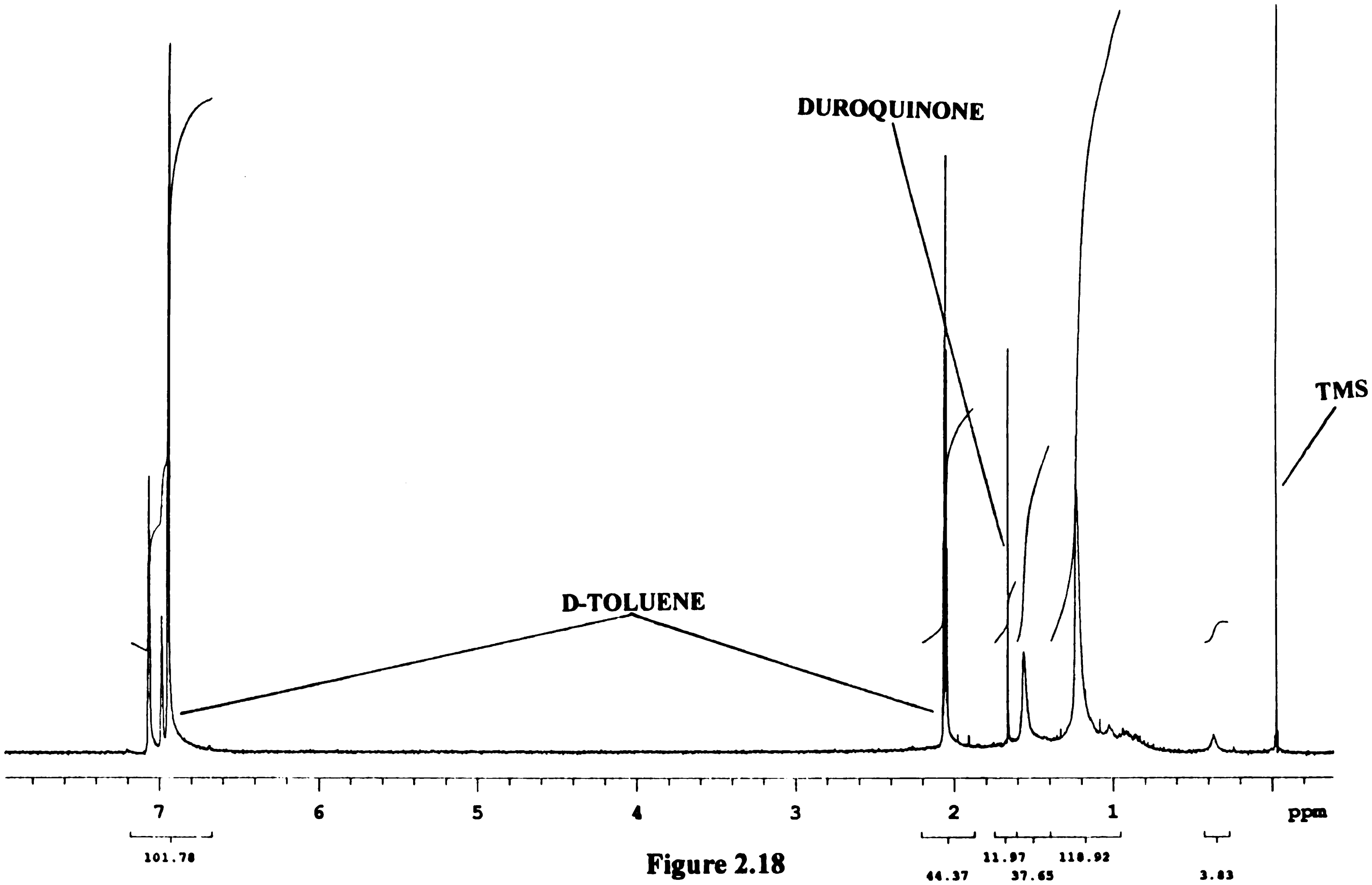

Figure 2.18
NMR Spectrum of Organic Species Formed in Neutralization Reaction
(101, 1/15/96)

for one of these runs prepared as described previously. The duroquinone peak appears as expected at 1.69 ppm, but there are two other large peaks, at 1.2 ppm and 1.58 ppm, and a small peak at 0.4 ppm, that have not been assigned, but look to be duroquinone degradation products. Figure 2.19 shows the spectrum of a duplicate reaction. The peak at 0.4 ppm is no longer present, but the other peaks also appear to be duroquinone degradation products. Yields for these runs were 29.36% and 20.57%, based on the theoretical amount of duroquinone possible. These yields are slightly higher than when the mixture was basic, which is in agreement with the fact that duroquinone slightly partitions into basic solutions. The timed neutralization experiments were done to follow progress of the reaction and to see if intermediates disappeared over time. Duroquinone formation did increase over time, but unidentified species grew as well. No peaks disappeared as time of reaction increased, so these peaks are not associated with intermediate species, but with other products formed in the reaction.

2.6.4 Effects of Various Base Catalysts

Until this point, only aqueous NaOH solutions with molarities ranging from 0.5 M to 3.0 M had been used as the base catalyst. In an effort to increase the yield of duroquinone formed from the self-condensation of 2,3-pentanedione, the catalyst base was changed from NaOH to LiOH and CsOH. One organic base, triethylamine, was also investigated. Changing the alkali metal changes the reactivity of the base and was hoped to increase the yield of duroquinone. Since the base was changed through these runs, a

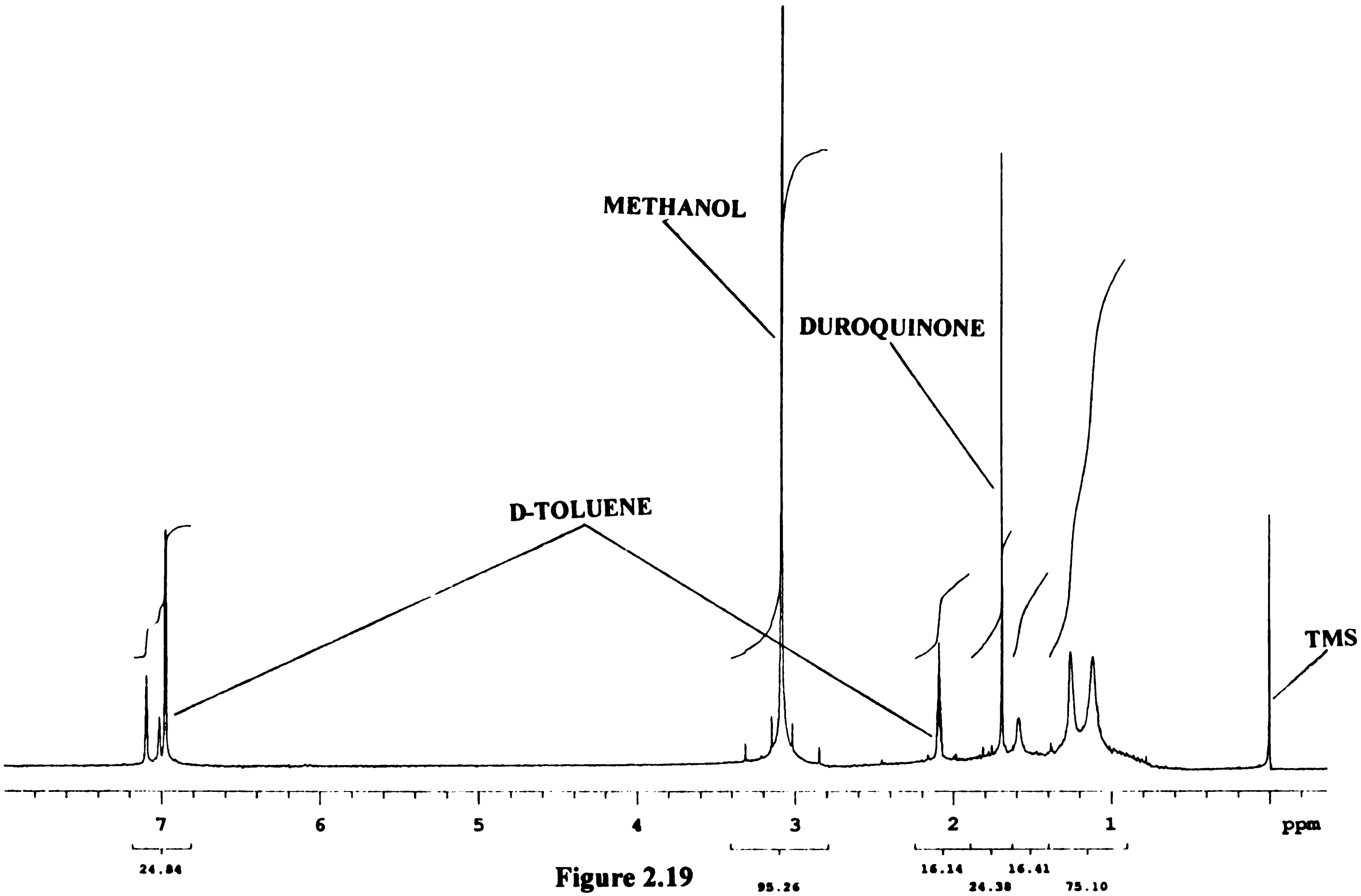

Figure 2.19
NMR Spectrum of Organic Species Formed in Neutralization Reaction
(107, 1/15/96)

standard procedure was established, keeping all other variables constant. To an Erlenmeyer flask, 10.00 ml of a 1.0 M base solution was added, although the triethylamine could only be made at 0.67 M due to solubility limits. Next, 10.00 ml of 5% 2,3-pentanedione were added dropwise to the flask over a ten minute interval with stirring. The reaction was allowed to proceed for one hour, when 10.0 ml of toluene were added. Standard extraction procedures were used as described previously. NMR samples of the organic species were prepared and yields of duroquinone were obtained, as listed in Table 2.7.

Table 2.7 Duroquinone Yields From Different Bases

Base	% Yield of Duroquinone Based on Theoretical
NaOH	21.25
LiOH	11.31
CsOH	5.14
Triethylamine	7.22

Unfortunately, yields were lower or about the same as those obtained with NaOH so no significant increase was obtained by changing the catalyst. Figure 2.20 shows a typical NMR spectrum of organic species formed in a run with NaOH as the base. Some small peaks appear to unidentified species, but its main constituent is duroquinone. Figure 2.21 shows the NMR spectrum of organic species formed in a reaction with LiOH as the base. Again, duroquinone is the largest peak, but a stray peak appears at 1.19 ppm that is unidentified. Figure 2.22 is the NMR spectrum of the organic species formed from a run with CsOH as the base. Chloroform was used as a standard and appears at 6.4 ppm.

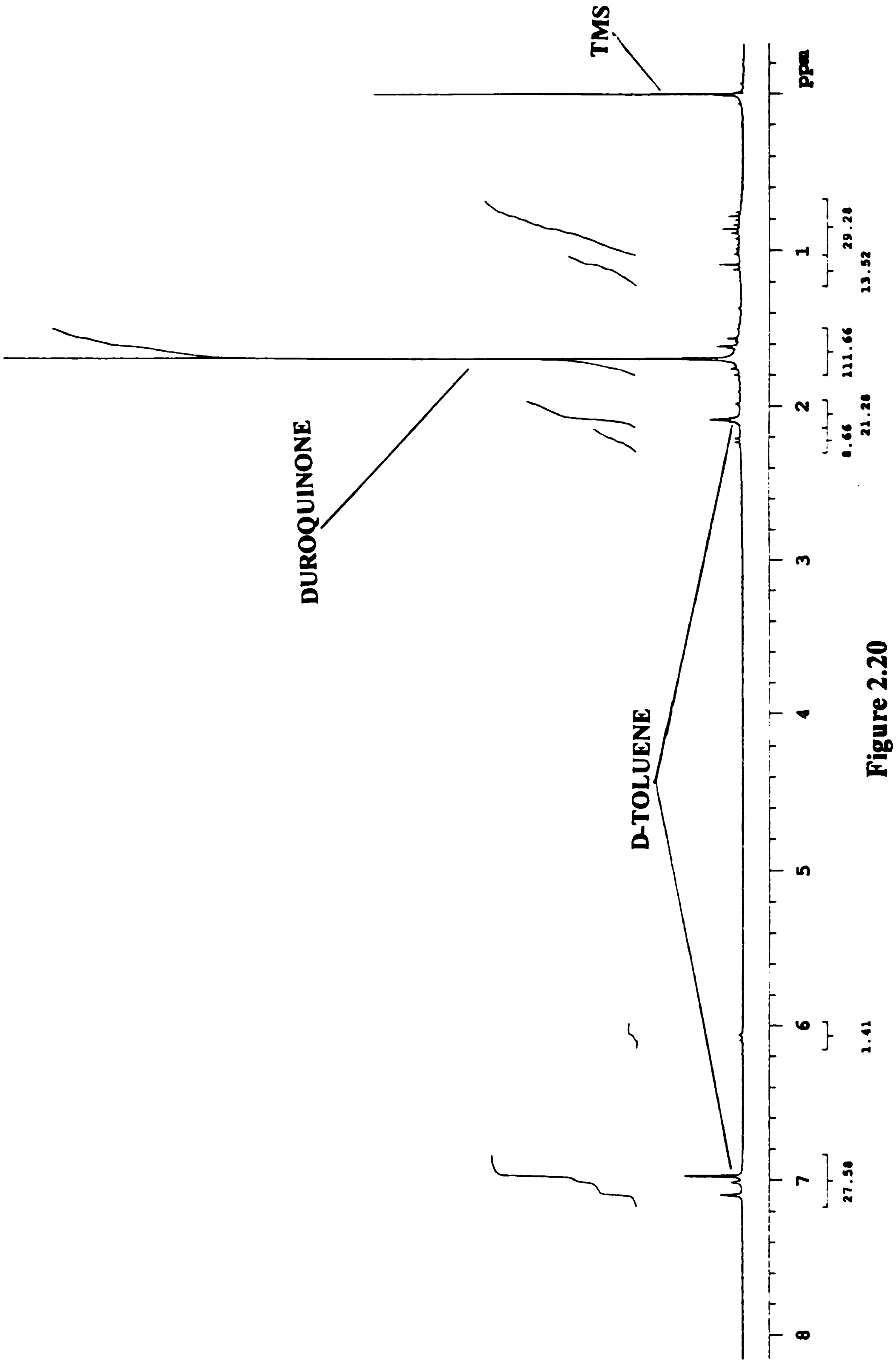

Figure 2.20
NMR Spectrum of Organic Species Formed from NaOH Reaction (108, 2/12/96)

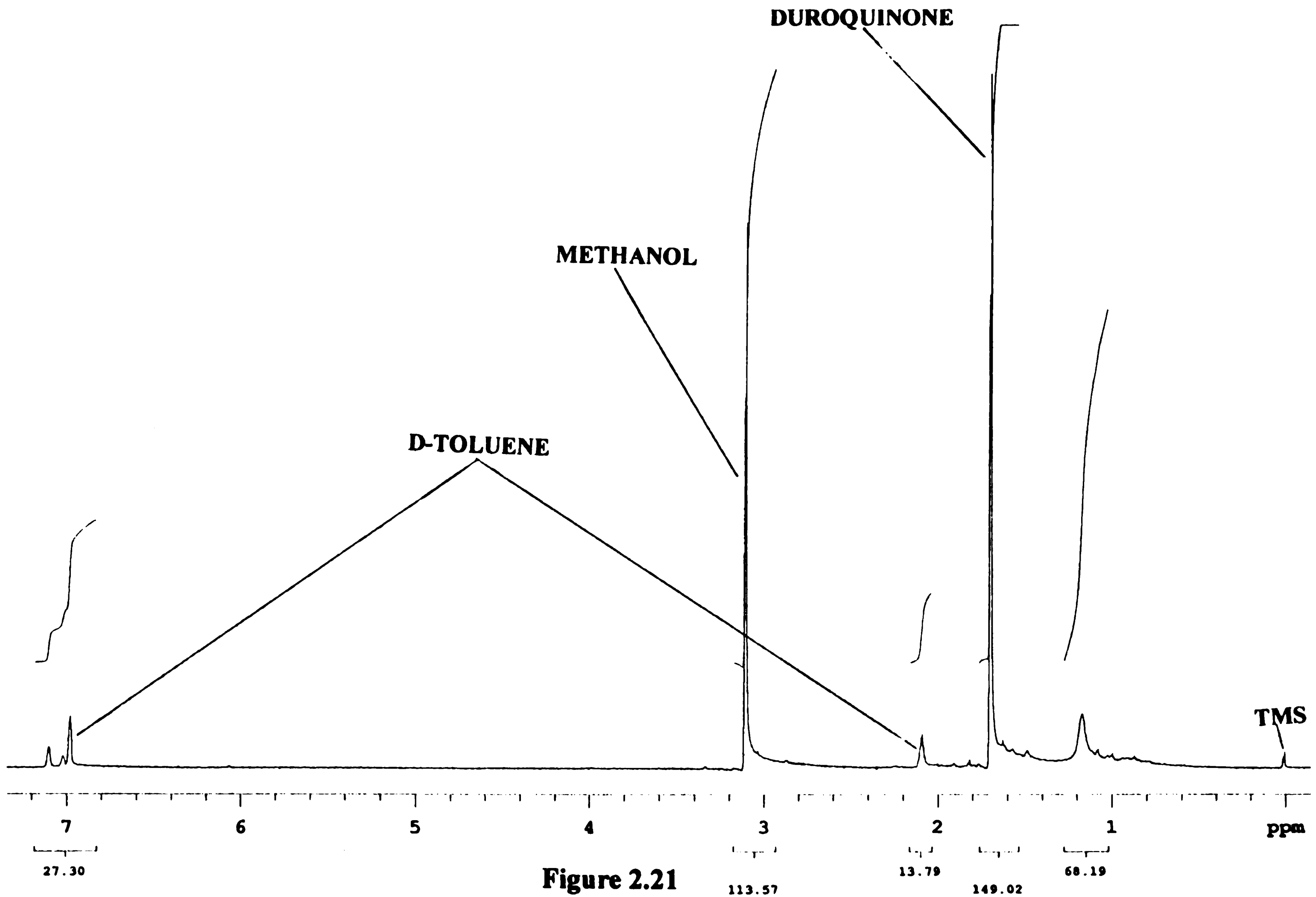

Figure 2.21
NMR Spectrum of Organic Species Formed in LiOH Reaction (2, 8/12/96)

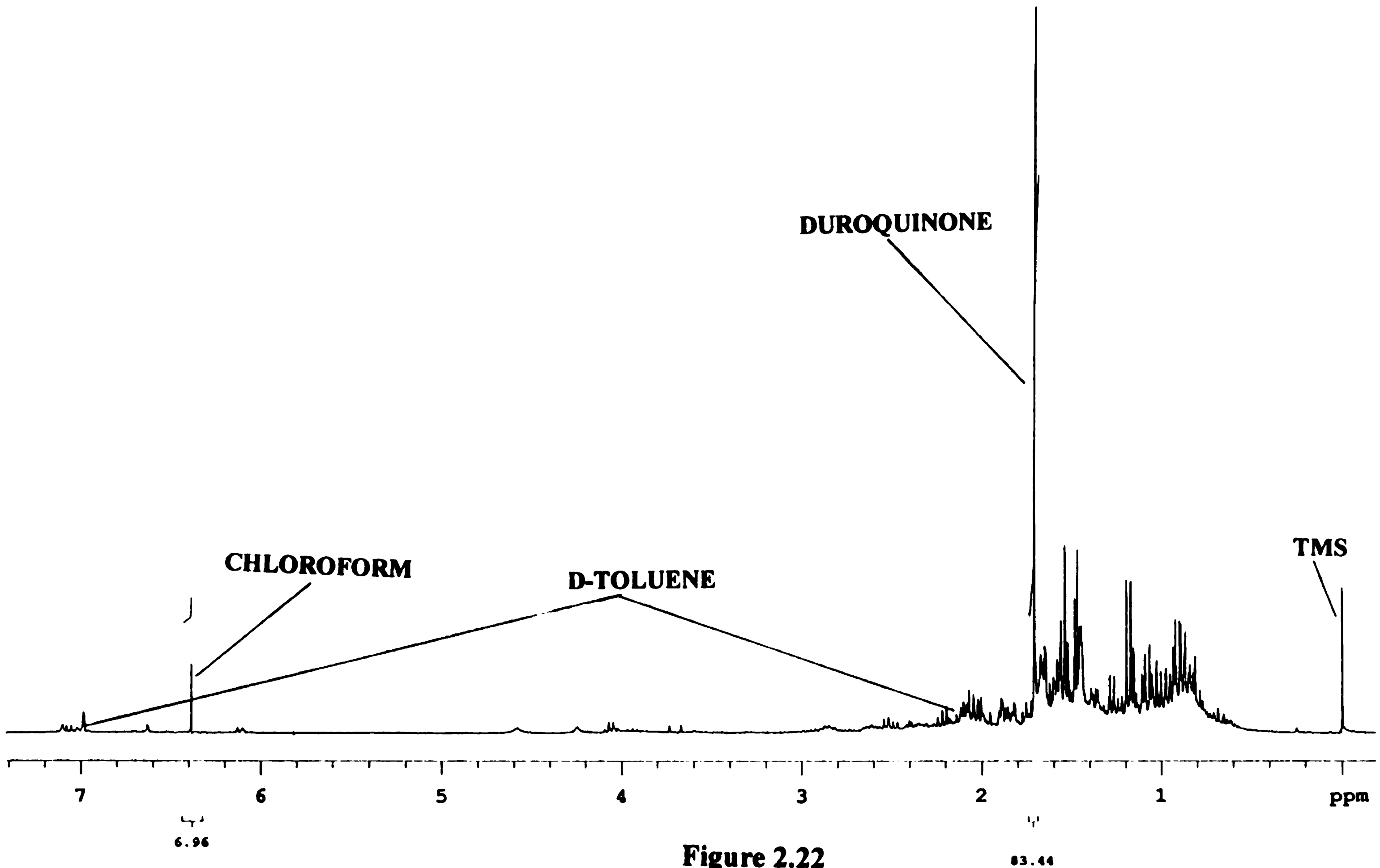

Figure 2.22
NMR Spectrum of Organic Species Formed in CsOH Reaction (133A, 6/12/96)

There are many sharp peaks in this spectrum, some of which can be identified as doublets and quartets, but the compounds they come from are unknown. Of the four bases, CsOH appears to give the largest number of side products, which coincides with its low yield. Figure 2.23 shows the NMR spectrum of organic species formed in the reaction with triethylamine as the base. The hydrogens associated with the triethylamine appear as the triplet and quartet at 0.9 ppm and 2.4 ppm respectively. Duroquinone appears at 1.69 ppm and the chloroform standard appears at 6.1 ppm.

2.6.5 Fractionation of Organic and Aqueous Products

Because many of the NMR spectra that were obtained from these reactions were very complex, HPLC was used to purify samples. Both the aqueous and organic phases were analyzed using this method. Reaction procedures were performed as described earlier, with dropwise addition of 50.0 ml of 5% 2,3-pentanedione in water into 50.0 ml aqueous 1.0 M NaOH solution. Toluene was added and the standard extraction procedure was followed. Both the organic and aqueous phase solvents were evaporated. In order to increase the concentration of each fraction separated by the HPLC, the mobile phase was saturated with sample and injected. This high concentration of sample resulted in peaks that exceed the scale of the chromatogram. Figure 2.24 shows a typical chromatogram of the organic species formed in the reaction. Duroquinone is present as evidenced by its peak at 16.48 minutes. Large peaks also appear between 9 minutes to 11.4 minutes. 2,3-Pentanedione elutes during that time, but a positive identification was

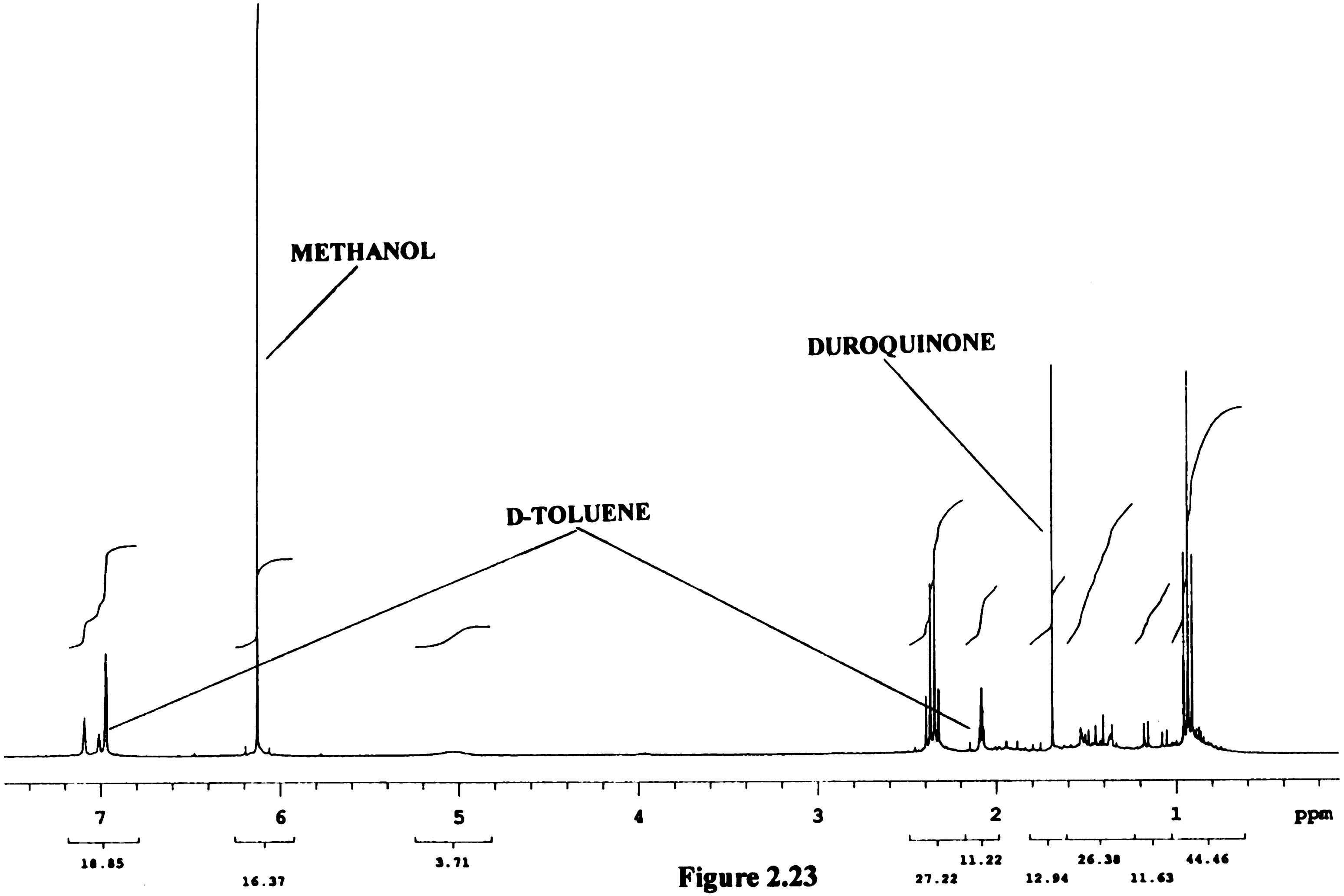

Figure 2.23
NMR Spectrum of Organic Species Formed in Triethylamine Reaction
(054, 8/22/95)

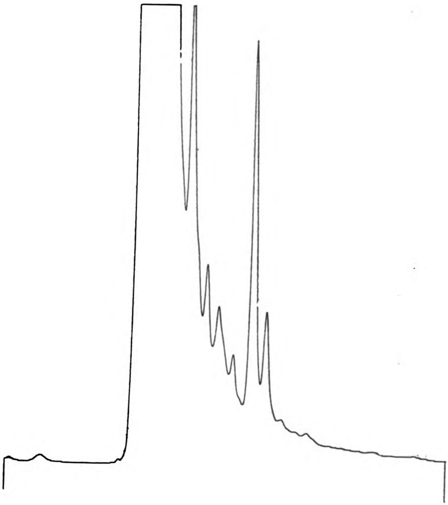

Figure 2.24
HPLC of Organic Species Formed in NaOH Reaction (126, 3/7/96)

not possible due to the large number of peaks in that area. NMR spectra of the organic species did not show the presence of 2,3-pentanedione. No peak species were identified except for duroquinone. Figure 2.25 shows a chromatogram for the aqueous constituents present in the reaction mixture. A small amount of duroquinone is present (16.64 minutes), as confirmed by NMR spectra. The largest peaks on the chromatogram appear before 2,3-pentanedione is expected (11.4 minutes). None of these peaks have been assigned to species. Using HPLC for analysis shows there are many significant compounds being formed in the reaction of 2,3-pentanedione in basic solution.

The next step was to collect fractions of these samples after they eluted on the HPLC to purify them for further analysis. Referring back to Figure 2.24, four fractions were taken of the organic species roughly between the times of 9 to 12 minutes, 12 to 15 minutes, 15 to 19 minutes, and 19 to 25 minutes. Since the sample injection size is only 10 microliters, these fractions were collected three times. Referring to Figure 2.25, the aqueous phase was separated into three fractions between the times of 7 to 10 minutes, 10 to 15 minutes, and 15 to 21 minutes. The fractions were individually re-injected into the HPLC to check for separation; it was successful. The fractions were prepared and run on the NMR spectrometer. Unfortunately, even with three collections, the species were so minute they did not appear on the spectra.

TLC was investigated as an alternative to using HPLC fractionation because it can handle much larger sample loads. Organic compounds formed from 2,3-pentanedione in basic solution (1.0 g) were dissolved in acetone and spotted on a TLC plate. Pure duroquinone was also spotted as a standard. The procedures described in Section 2.4.4

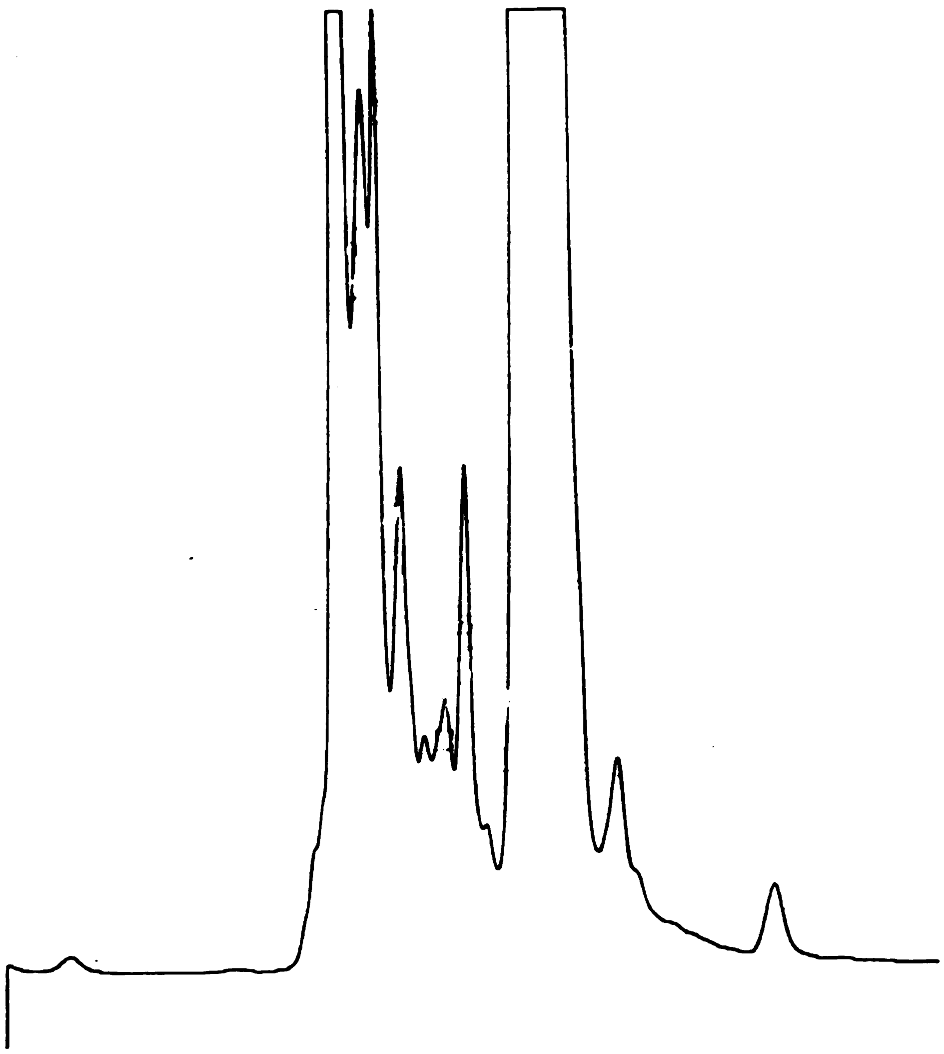

Figure 2.25
HPLC of Organic Species Formed in NaOH Reaction (126, 3/7/96)

were used to develop the plate. Duroquinone separated into two fractions and the organic sample separated into four fractions. The largest quantity of material traveled to the two highest fractions. Figure 2.26 shows the NMR spectrum for the highest fraction of the organic sample. It is interesting to note that upon first glance, it appears 2,3-pentanedione is present in the sample at 0.86 ppm, 1.95 ppm, and 2.28 ppm. The presence of 2,3-pentanedione after the reaction has been completed had not been found in previous results and would suggest that conversion to other products was not 100%. In Figure 2.27, the NMR spectrum of the fraction below the highest one, only two of the three peaks appear proportionately in smaller concentration. The quartet at 2.3 ppm is not present, suggesting the triplet around 0.8 ppm and the singlet around 1.9 ppm are not associated with 2,3-pentanedione. The other fractions showed no other identifiable peaks.

Solid Probe Mass Spectroscopy was used to analyze the TLC fractions. Figure 2.28 shows the spectrum for the organic fraction that traveled highest up the plate. Figure 2.29 shows the spectrum of the second highest fraction. No discernible matches to the spectra in the mass spectrometer database were found on chemicals present in either case.

2.6.6 Mass and Carbon Balances

Total mass balances, excluding solvents, were completed to check precision and accuracy of the reaction procedure. For this experiment, 5% 2,3-pentanedione in water was dripped into 1.0 M NaOH in water with stirring. Neutralization of the basic solution with 1.0 M HCl followed. This step was necessary to ensure removal of all the water in

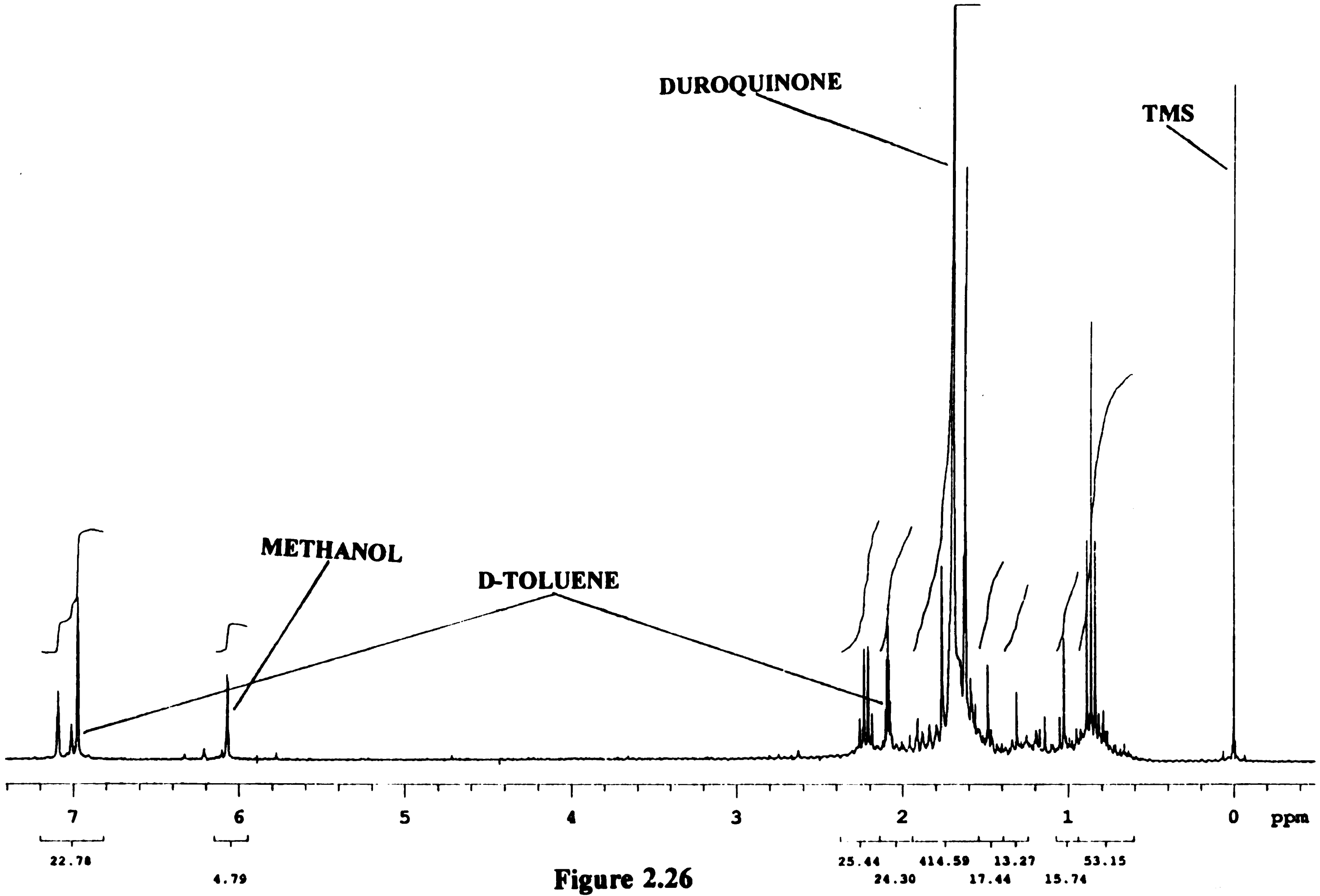

Figure 2.26
NMR Spectrum of Species in TLC Fraction #1 (4/9/96)

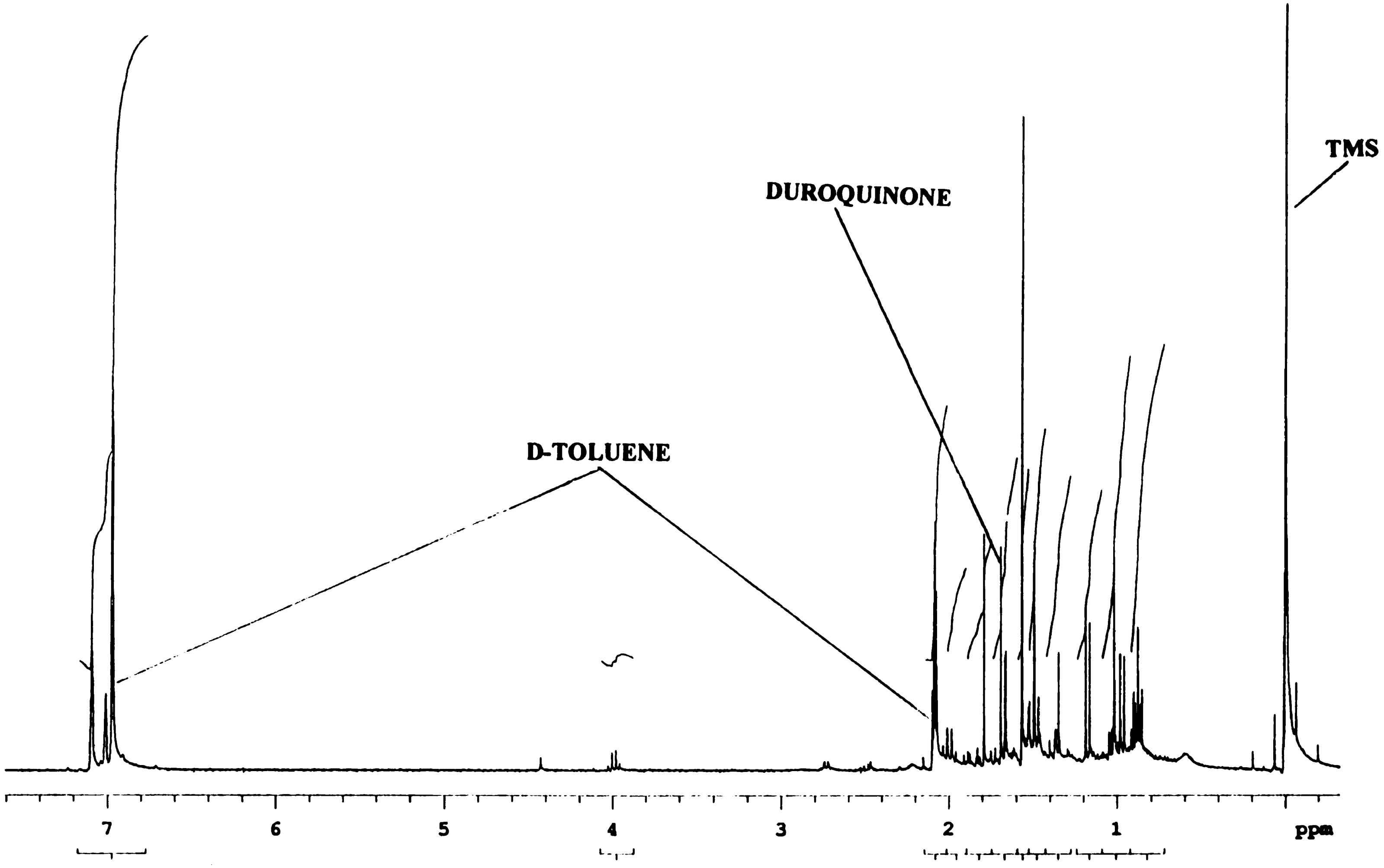

Figure 2.27
NMR Spectrum of Species in TLC Fraction #2 (4/9/96)

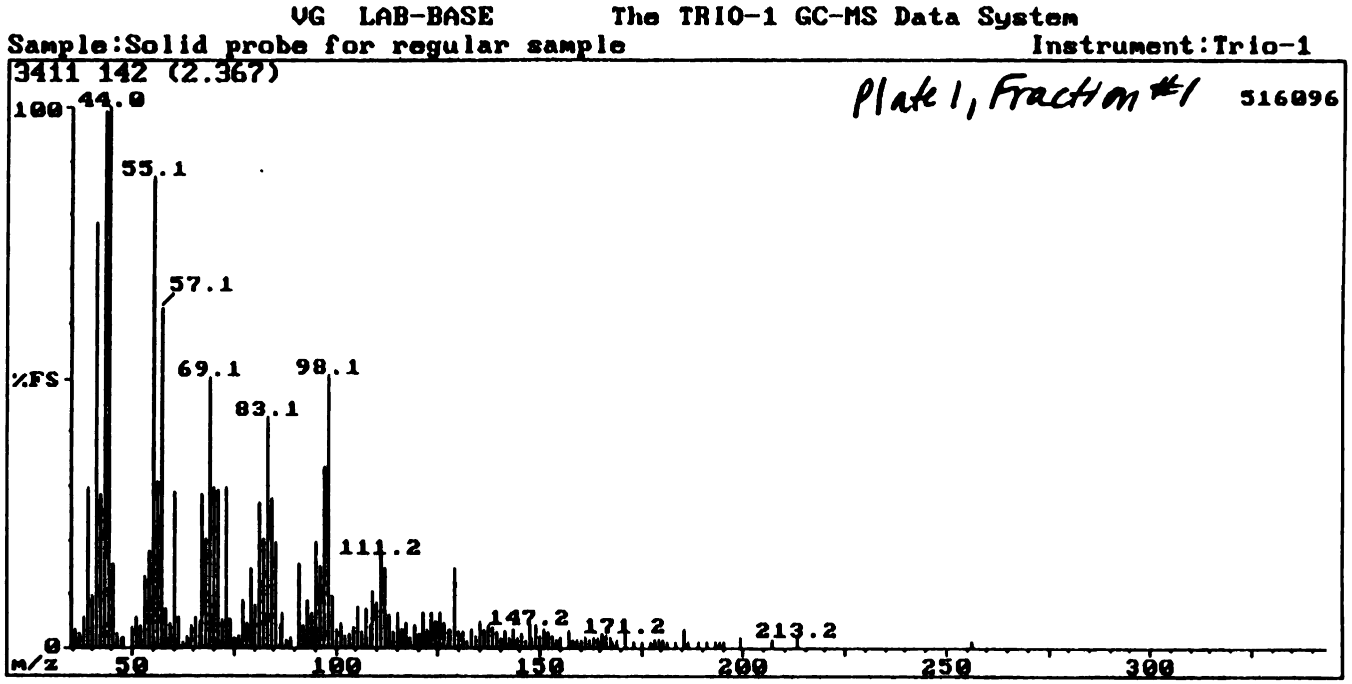

Figure 2.28
Solid Probe Mass Spectrum of TLC Fraction #1 (4/25/96)

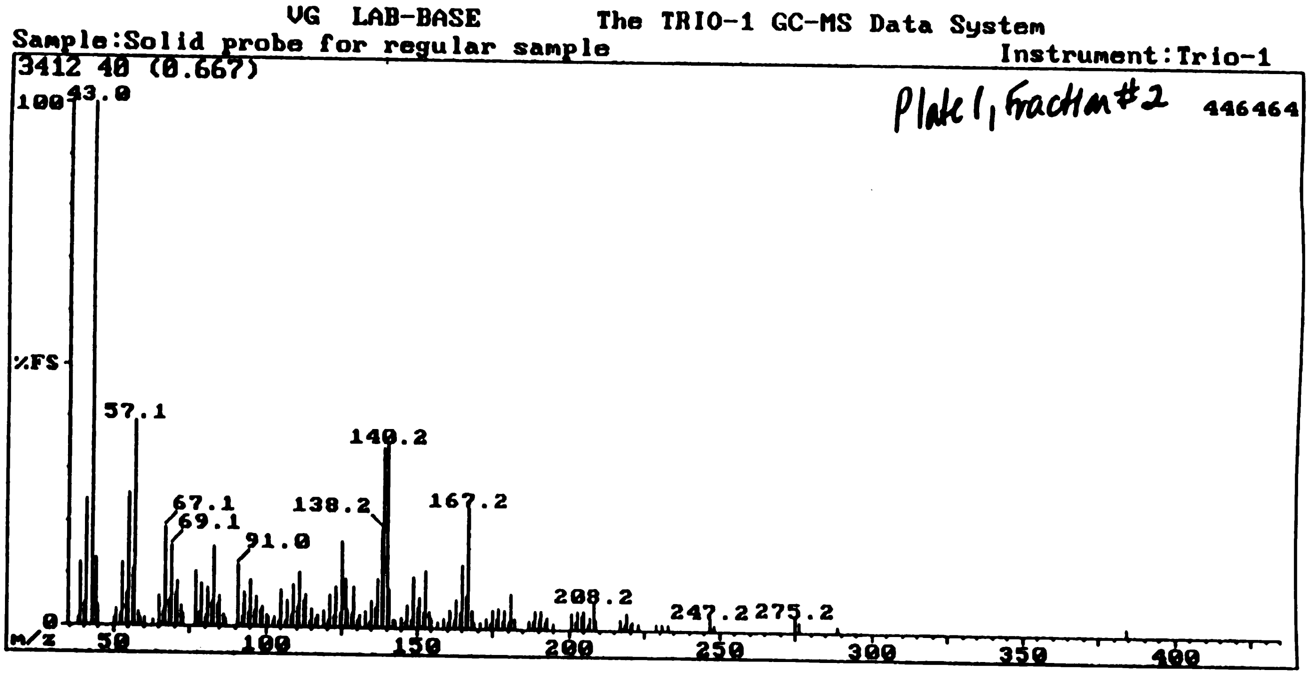

Plate 1, Fraction #2

Figure 2.29
Solid Probe Mass Spectrum of TLC Fraction #2 (4/25/96)

the aqueous phase. The organic and aqueous phases were separated as described previously. Run 132, using 50 ml of base and 50 ml of a 5% 2,3-pentanedione solution, resulted in 0.3018 g organic species and 5.651g aqueous species. The total expected weight of product plus catalyst, based on theoretical yield, was 6.0234g, resulting in 98.82% recovery. There is some error involved with this calculation because the theoretical result assumes duroquinone is the only organic recovered and NMR spectra show the presence of low concentrations of other unidentified chemicals. A sample calculation can be found in Table C.3 in the Appendices.

The same procedure was performed with 1.0 M aqueous LiOH as the base, giving a recovery of 87%. When aqueous 1.0 M CsOH was used a the base, calculations show a 92% recovery. Triethylamine runs resulted in 94% recovery. Mass balances were within acceptable limits of closure for all four bases used.

A carbon balance was completed for Run 132 (conditions described earlier). Elemental analysis (carbon, nitrogen, and hydrogen) was performed on the dried residues from the aqueous and organic phases. The aqueous residue contained 30.7% carbon and weighed 5.2489 g, which is most of the available carbon. The organic residue contained 71.51% carbon and weighed 0.3018 g, which is consistent with duroquinone (73.08% carbon). This results in a 119% recovery (Table C.1 in Appendices), which implies no carbon was lost due to formation of gases in the reaction. As usual, the products of the reaction were separated by toluene addition, so it is possible toluene was still present in the aqueous residue even though it was dried.

2.6.7 ^{13}Carbon Prediction

To examine possible intermediates and products formed in the self-condensation of 2,3-pentanedione, ChemWindows ^{13}C prediction was used. Table 2.8 shows the prediction and experimental data for a group of standards. The ^{13}C NMR spectrum for 2,3-pentanedione in deuterated chloroform can be seen in Figure 2.30.

Table 2.8 Prediction Vs. Experimental ^{13}C Results

Compound	ChemWindows Prediction	Experimental ^{13}C
$CDCl_3$		77.3 76.9 76.4
Duroquinone	187.0 (C-1) 144.3 (C-2) 11.7 ($C\text{-}CH_3$)	187.5 140.3 12.2
2,3-Pentanedione	197.6 (C-3) 196.5 (C-2) 33.6 (C-4) 24.8 (C-1) 7.6 (C-5)	199.6 197.3 29.0 23.5 6.7

Since ChemWindows gave a reasonable prediction of where the carbons appeared in these standards, it was used to predict where carbons of possible product structures would appear. Figure 2.31 shows the structure and prediction for each compound examined. Unfortunately, most of the different structures that may be forming have carbons that appear in the same places that duroquinone carbons would appear in a ^{13}C spectrum. A ^{13}C spectrum requires a large concentration of ^{13}carbon atoms for strong

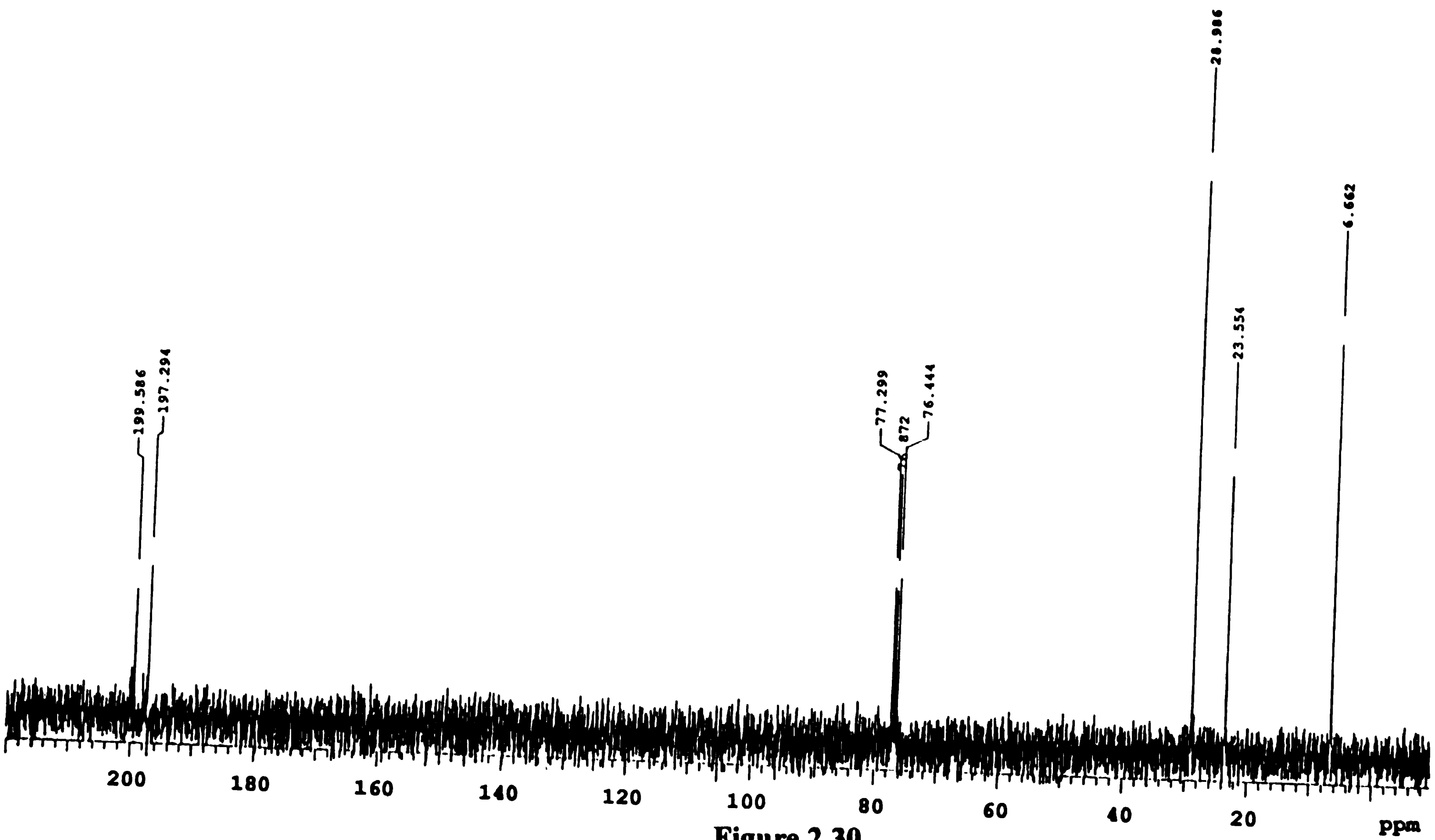

Figure 2.30
^{13}C for 2,3-Pentanedione (5/9/95)

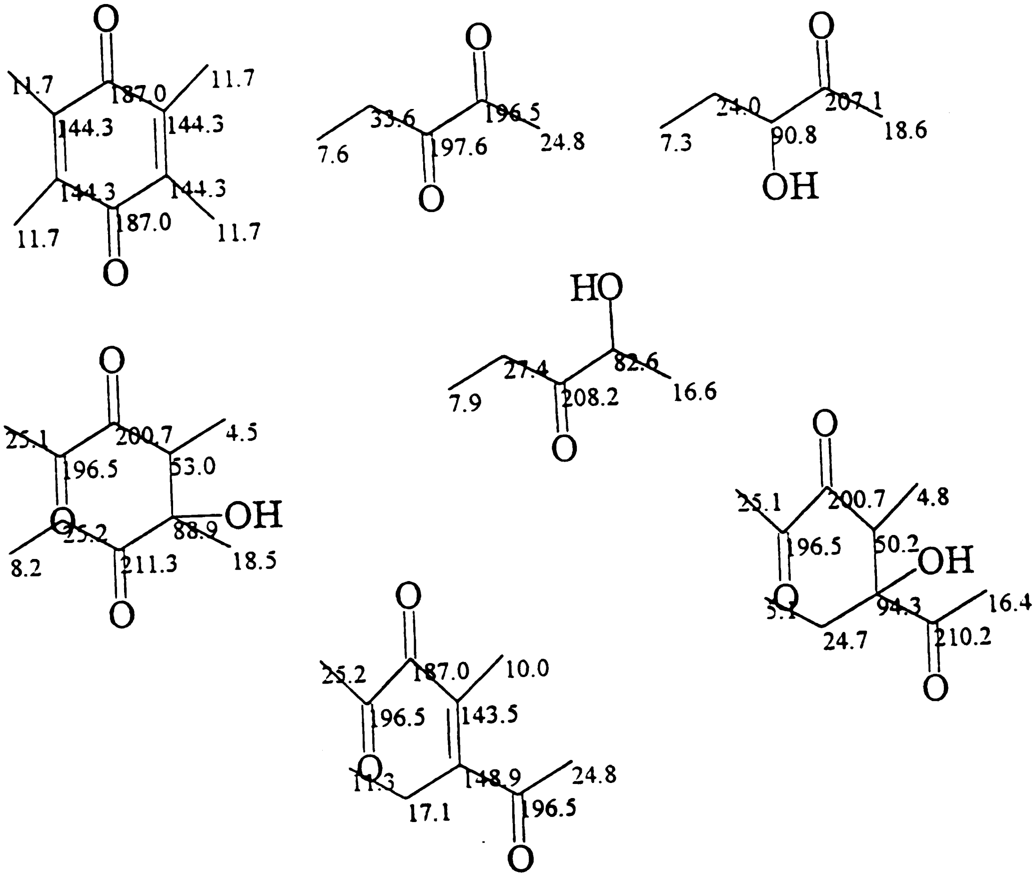

Figure 2.31
^{13}C Structure Prediction

peaks to appear. When ^{13}C spectra for organic samples were analyzed, no strong peaks appeared. The peaks that did appear could not distinguish between the various forms shown in Figure 2.31.

2.6.8 Discussion of Duroquinone Formation

Condensation of 2,3-pentanedione to duroquinone was more difficult than expected. Analysis of the aqueous phase of the reaction mixtures showed no 2,3-pentanedione remains in the mixture in its original form. When strong base (3.0 M) is used, it looks qualitatively as though polymerization occurs. The organic phase analysis shows duroquinone as the main constituent, but no other products were identified. The highest yield was increased from 7%, using the literature procedures, to 25% consistently using methods described here.

There are a number of reasons why duroquinone yield is low from the condensation of 2,3-pentanedione. Since the reaction is exothermic, duroquinone could be degrading or it could be reacting further. Part of the recovery procedure of the organic products formed in the reaction involves rotary evaporation to remove solvents. Although the temperature required to evaporate toluene is much lower under vacuum, it still may be enough to cause degradation. The carbon analysis of the organic and aqueous species shows the majority of the carbon present in the system is in the aqueous constituents. The organic phase carbon analysis is consistent with duroquinone. At best, the yield of duroquinone was 29% and contained trace impurities. This leaves the majority of the reaction products in the aqueous phase. The aqueous phase constituents were analyzed by NMR, GC, and HPLC, as previously seen, and no identification of species were made. If 2,3-pentanedione is dimerizing or forming larger chains, it would inhibit production of duroquinone and might stay in the aqueous phase.

For duroquinone production, the two 2,3-pentanedione molecules have to align and condense as shown in the proposed mechanism (Figure 2.32). Figure 2.33 shows both the desired and undesired species that could be forming. If the desired and undesired species were formed in equal amounts, a theoretical yield of 50% duroquinone would be possible. It is not known if either form is favorable, at what ratio one intermediate forms to the other, or how consistently the intermediates are formed in this ratio. If the desired and undesired species are formed in equal amounts, the lower yield obtained in this work (25%) is due to the degradation reasons discussed previously.

Figure 2.33 shows many structures that may be present in the condensation of 2,3-pentanedione. These products have not been confirmed by the analytical techniques used here, but are reasonable possibilities because the many unassigned peaks appear in locations that these species would appear in. If these compounds are present, it would be hard to distinguish between them based on spectra and chromatograms because their signals would be similar. There are no standards available for these chemicals that could be used to verify their formation.

The reaction intermediates and products, other than duroquinone, still have not been identified. Short-term experiments were completed, as discussed with Figure 2.8. Figure 2.34 shows an enlargement of the peaks that appeared between 0.5 and 3.2 ppm.

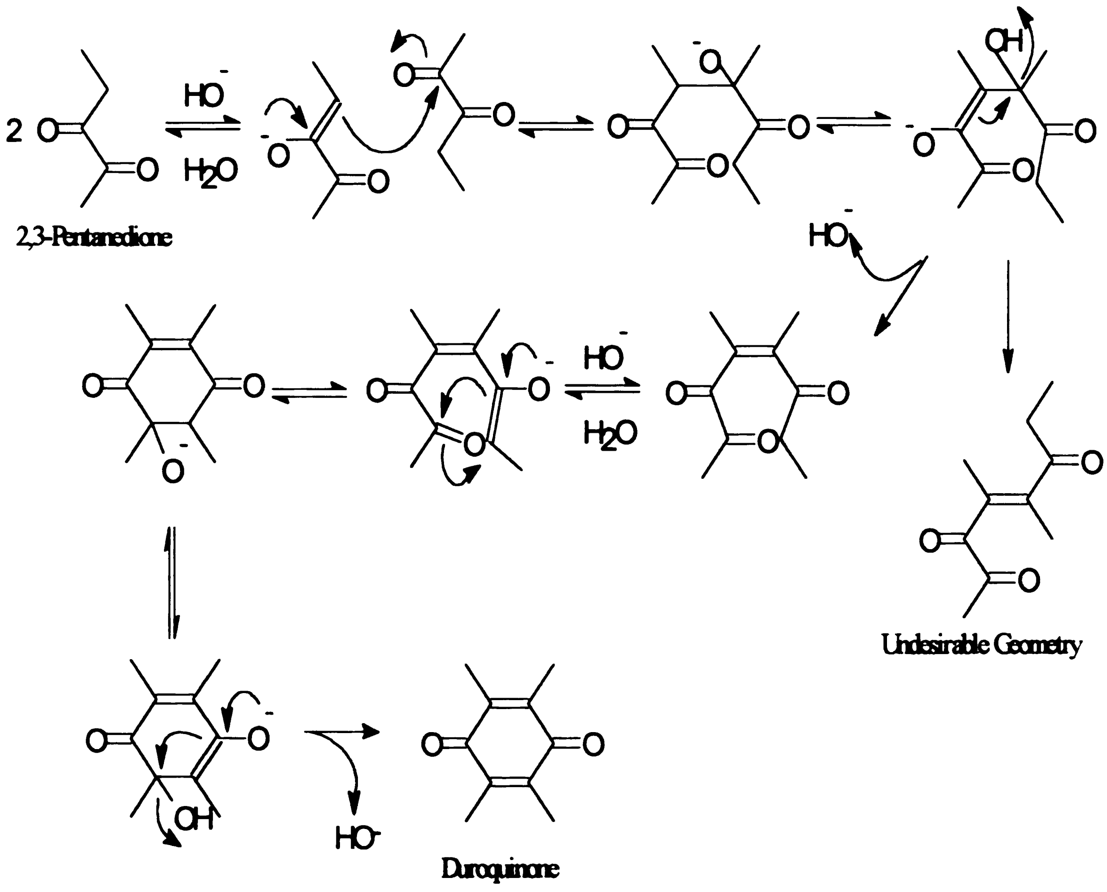

Figure 2.32
Proposed Mechanism for Duroquinone Formation

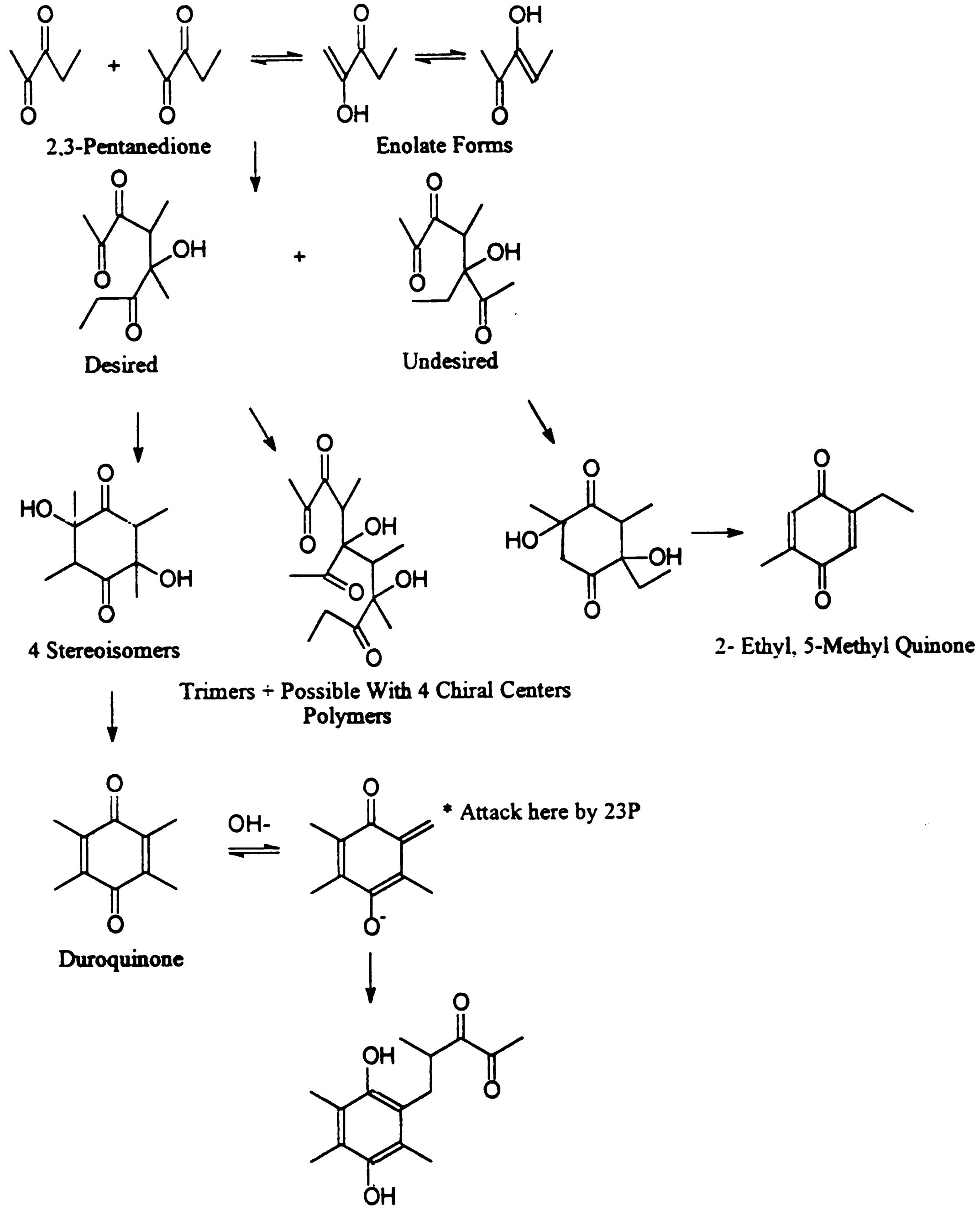

Figure 2.33
Possible Formations from self-Condensation of 2,3-Pentanedione

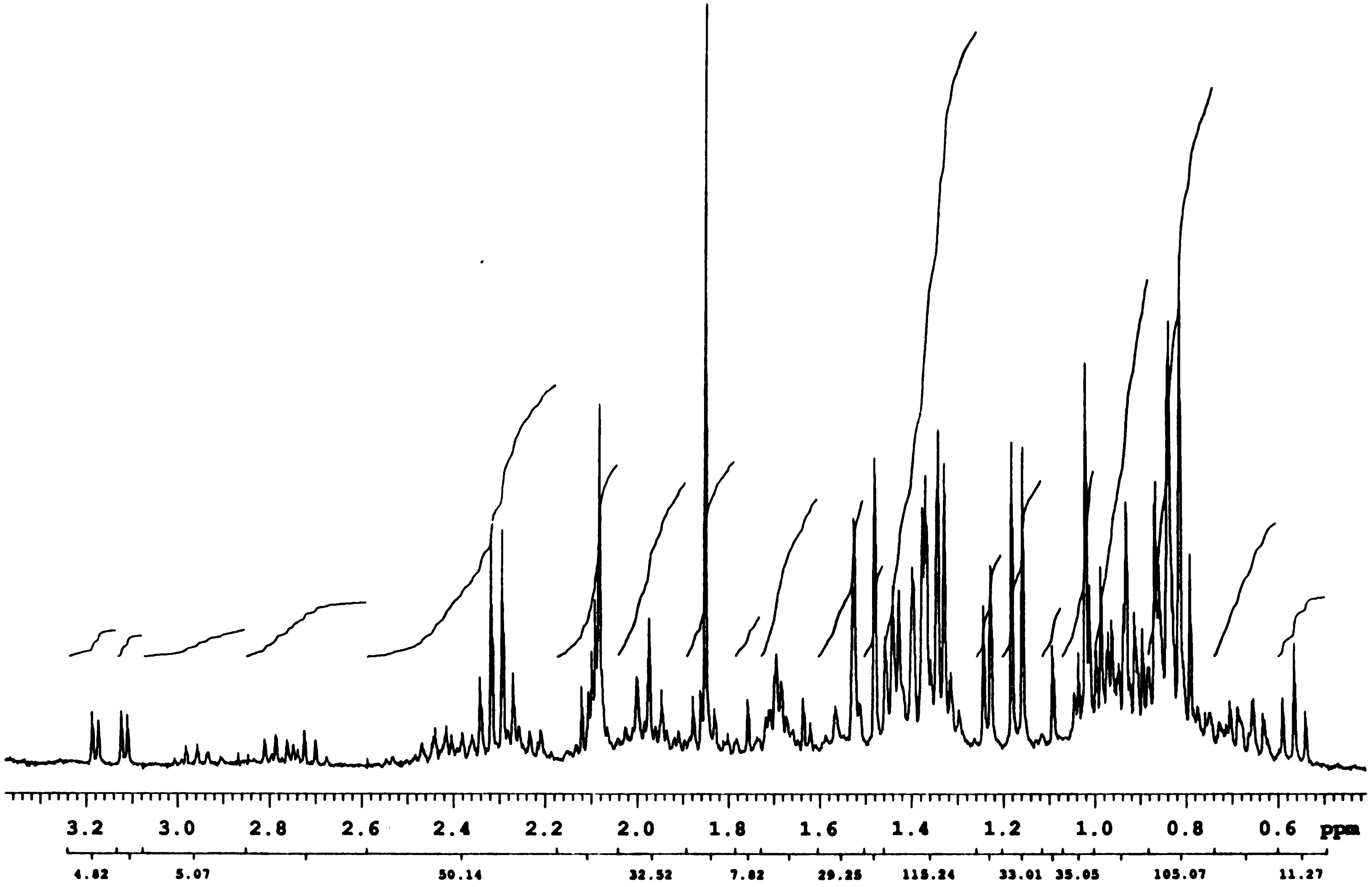

Figure 2.34

Enlargement of NMR Spectrum of Organic Species Formed After 5 Minutes in Reaction (M 8195 0.1M 019, 8/1/95)

Table 2.9 shows the number of each type of peak, not including the deuterated toluene peaks at 2.1 ppm.

Table 2.9 Short Term Organic Species Formation - NMR Peak Assignments

Type of Peak	**Number of Peaks on Figure 2.33**
Singlet	23
Doublet	8
Triplet	5
Quartet	3
5 +	1

The number of hydrogens associated with each peak is harder to estimate. Because peaks appear according to how many hydrogens are bonded to the surrounding carbons plus one, a singlet can appear from a methyl group (three hydrogens) attached to a carbon with no hydrogens, such as the singlet in 2,3-pentanedione, or similarly from a CH_2 group or CH group bonded to carbons with no hydrogens. Without knowing which peaks are from the same compound, it is impossible to estimate the number of hydrogens present in this sample. Thus, no intermediate or reaction products besides duroquinone could be identified.

Chapter 3

PYRAZINES AND QUINOXALINE STUDIES

3.1 Introduction

This chapter describes the analytical methods and procedures used for reactions of 2,3-pentanedione with substituted diamines. Chemical structures can be referred to in Figure 1.1. Pyrazine formation involved a two step process through a dihydropyrazine intermediate. Ethylenediamine was used to produce 2-ethyl-3-methyl pyrazine. Propylenediamine was used to produce a mixture of 2-ethyl-3,5-dimethyl pyrazine and 3-ethyl-2,5-dimethyl pyrazine. Phenylenediamine was used to produce 2-ethyl-3-methyl quinoxaline.

3.2 Materials

2,3-Pentanedione (Aldrich, 97%) in 5 wt% aqueous solution was used in all reactions. o-Phenylenediamine (Aldrich, 99%) was used in 2-ethyl-3-methyl quinoxaline production. Propylenediamine (Aldrich, 99%) and ethylenediamine (Baker) were used in pyrazine production. Quinoxaline (Aldrich) was used as a standard for NMR spectra.

3.3 Analytical Methods

3.3.1 NMR Spectroscopy

NMR spectra were used to confirm the presence of pyrazines and for quantitation of 2-ethyl-3-methyl quinoxaline. The method and its operating parameters are described in detail in Section 2.4.1. NMR standard spectra, found in Appendix A, were obtained as references for 2,3-pentanedione (Figure A.2), ethylenediamine(Figure A.6), 2-ethyl-3-methyl dihydropyrazine (Figure A.7) 2-ethyl-3-methyl pyrazine (Figure A.8), and o-phenylenediamine (Figure 3.5) using deuterated toluene as the solvent for all.

Table 3.1 NMR Peak Identifications for Pyrazine Studies

Chemical	δ (ppm)
2-ethyl-3-methyl pyrazine	1.31 triplet (methyl on 2-ethyl)
	2.56 singlet (3-methyl)
	2.85 quartet (methylene in 2-ethyl)
	8.28 singlet (aromatic)
	8.33 singlet (aromatic)
2-ethyl-3-methyl quinoxaline	1.55 triplet (methyl on 2-ethyl)
	3.19 singlet (3-methyl)
	3.32 quartet (methylene)
	8.00 doublet (H on benzene)
	8.42, 8.67 doublets (H on benzene)
ethylenediamine	1.17 singlet
	2.74 singlet
phenylenediamine	4.71 triplet
	7.22 singlet

Table 3.1 gives the NMR peak asssignments for chemicals used in the pyrazine studies.

3.3.2 Gas Chromatography

A Varian Model 3300 Gas Chromatograph equipped with a FID was used for pyrazine analyses. Sample injection size was 5 microliters. The detector oven and injector were kept at constant temperatures of 290°C and 250°C, respectively. The column utilized was a Supelco fused silica capillary column (SPB-1) 0.53 mm ID and helium was used as a carrier gas. A Perkin Elmer Single Channel Interface collected the output signal. 1-Hexanol (70 g/l) was used as a standard in methanol and response factors for each eluted compound expected were determined. At the conditions described, peaks of interest appear at the times listed in Table 3.2.

Table 3.2 GC Peak Identification For Pyrazine Studies

Chemical	Elution (minutes)	Response Factor
2,3-pentanedione	3.92	1.00
2-ethyl-3-methyl pyrazine	10.70	1.06
2-ethyl-3,5-dimethyl pyrazine	10.20	1.06
2-ethyl-3-methyl dihydro pyrazine	11.45	0.87
ethylenediamine	3.56	7.13
propylenediamine	4.38	6.28
1-hexanol	7.56	1.00

3.4 Experimental Methods

Three different substituted pyrazines and one substituted quinoxaline were formed via reaction of 2,3-pentanedione with vicinal diamines. The procedure for all the reactions is similar, but the pyrazine formation requires a two step process through an intermediate dihydropyrazine. For pyrazine production, 10.0 g 2,3-pentanedione was dissolved in 30.0 ml ethyl ether and a stoichiometric quantity of diamine was dissolved in 40.0 ml ethyl ether. Ethyl ether was chosen as a solvent because, with its low boiling point (34.6°C), it is easy to separate from the products. Diamine in solvent was placed in a 125 ml Erlenmeyer flask with a stir bar on a stirrer/hot plate. The 2,3-pentanedione in solvent was dripped in to the reaction flask from a buret over a ten minute interval. At this point, the mixture was cloudy white in appearance. A condenser was then placed on top of the flask, the mixture was heated to 35°C, and the reaction was allowed to reflux for 90 minutes. Within five minutes of when heating began, the mixture turned a clear yellow. As the reaction progressed and water was formed, a dark brown phase appeared in the bottom of the flask. The quantity of water expected for complete conversion was 3.5 ml. After the refluxed mixture cooled, it was transferred to a rotary evaporator flask. Ethyl ether was evaporated, leaving dark brown products dissolved in the water formed from condensation. The products were weighed, and then dissolved in 70.0 ml methanol. The solution was transferred to a 125ml Erlenmeyer flask in preparation for the oxidation step.

As suggested by the literature (7), a 3:1 molar ratio of copper(II) oxide to dihydropyrazine was used for the oxidation, with a 1:1 molar ratio of KOH to dihydropyrazine used to facilitate the reaction. With these components in the flask, the mixture was heated on a hot plate with stirring and allowed to reflux for 5 hours. The mixture appeared black in color through the whole reaction. To ensure the oxidation was complete, a 0.5 ml sample was taken. It was diluted 1:1 with a standard solution of 70 g/l

1-hexanol in methanol and injected into the GC. Once complete oxidation was confirmed, the reaction mixture was filtered using gravity filtration and Whatman 2 filter paper and washed with methanol. The volume of the solution was measured, and a 0.5 ml sample was removed. The sample was diluted 1:1 with a standard solution of 70 g/l 1-hexanol in methanol and injected into the GC. The concentration of pyrazine in the sample was calculated from the peak integration on the chromatogram, and the overall yield of pyrazine was obtained. A sample calculation can be found in Appendix E, Table E.1.

The quinoxaline reaction utilized a similar procedure as the pyrazine reaction, but required a higher temperature to form the desired product. Methanol, in similar quantities to ether, was used as the solvent. To make 2-ethyl-3-methyl quinoxaline, 10.0 g of 2,3-pentanedione was dissolved in 30.0 ml of methanol and a stoichiometric amount of o-phenylenediamine was dissolved in 40.0 ml methanol. The 2,3-pentanedione solution was added dropwise to the o-phenylenediamine solution over ten minutes with stirring. The solution looked ruddy. A condenser was placed on the flask, the mixture was heated, and allowed to reflux for 90 minutes. Upon cooling, the solution was transferred to a rotary evaporator flask. The methanol and water formed in the reaction was distilled off and the product weighed. A measured amount (0.02 g) of the product were dissolved in 1.0 ml of deuterated chloroform and an NMR spectrum was obtained. Calculations of yield were based on weight of the product collected in the flasks (Appendix E, Table E.3).

3.5 Pyrazine Results

Once standards and response factors were entered into the method on the GC, chromatograms of unknown concentrations were obtained. Figure 3.1 shows the chromatogram of the 2-ethyl-3-methyl dihydropyrazine formed from 2,3-pentanedione and ethylenediamine. The small impurity at 9.28 min is an unknown. Figure 3.2 shows the chromatogram of the oxidized product. Again, a few small peaks appear totaling 0.61 % of the total area, showing the product is essentially pure. Figure 3.3 is the NMR spectrum of the oxidized product dissolved in deuterated chloroform. Table 3.1 lists the peak assignments for 2-ethyl-3-methyl pyrazine. NMR spectral results were not used for quantitation, but to confirm the presence of the pyrazine and examine the impurities that were present in the sample. From the gas chromatograms, it was determined that the yield, based on the possible theoretical amount of the 2-ethyl-3-methyl dihydropyrazine, was 83.2% and the overall yield of the 2-ethyl-3-methyl pyrazine produced was 72.4%.

When propylenediamine was used as a reactant, the same procedure, conditions, and quantities described previously were used. At these conditions, when a drop of the 2,3-pentanedione solution was added to the flask, the mixture reacted violently. To alleviate this occurrence, solvent quantities were doubled to 60.0 ml ether to dissolve the 2,3-pentanedione and 80.0 ml ether to dissolve the propylenediamine. Other than this change, the same procedure was used for the reaction. Figure 3.4 shows the chromatogram of the mixture of 2-ethyl-3,5 dimethyl dihydropyrazine and 3-ethyl-2,5-dimethyl pyrazine, which was produced in 93.6% yield. The peak at 10.16 minutes is

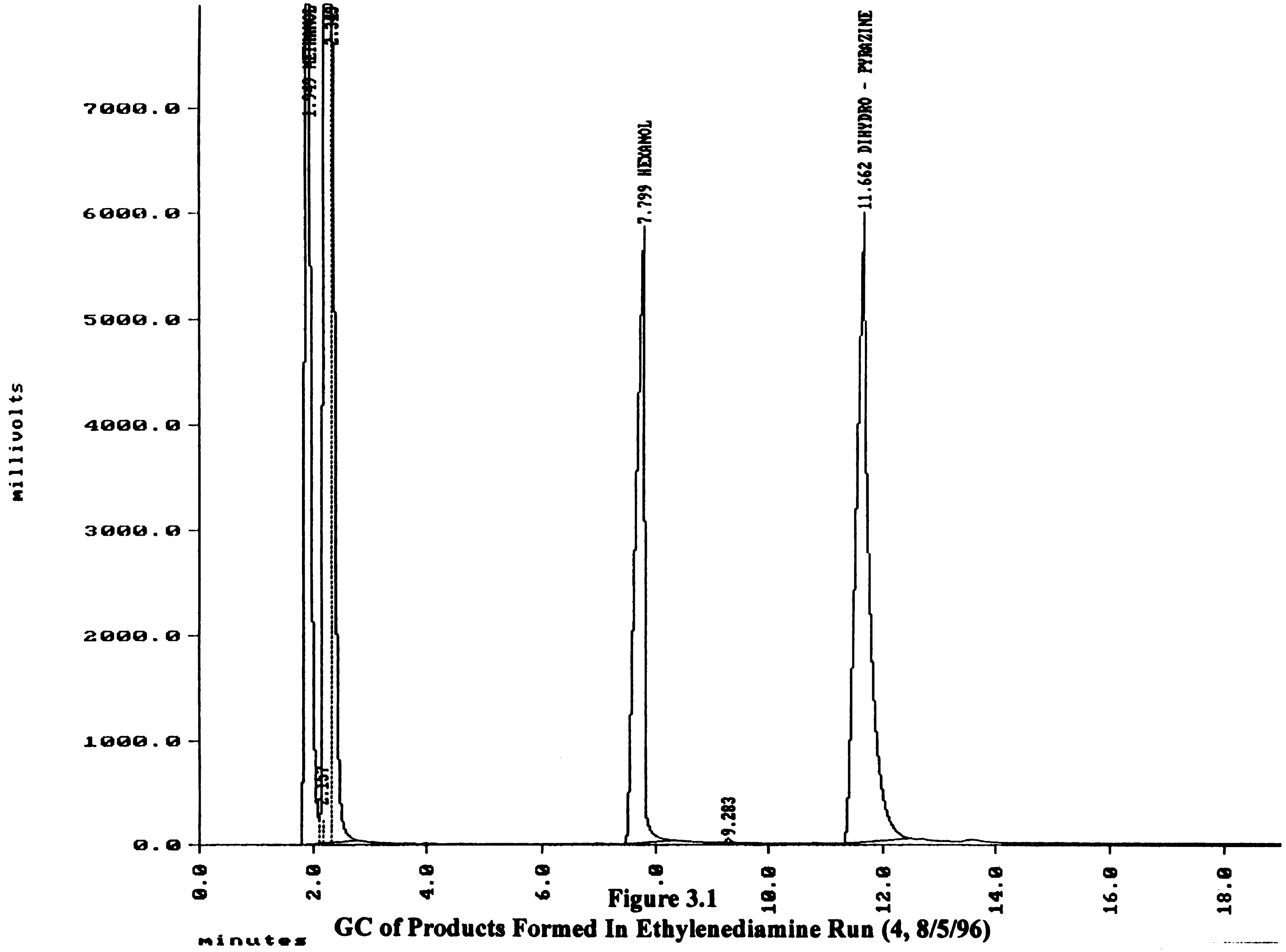

Figure 3.1
GC of Products Formed In Ethylenediamine Run (4, 8/5/96)

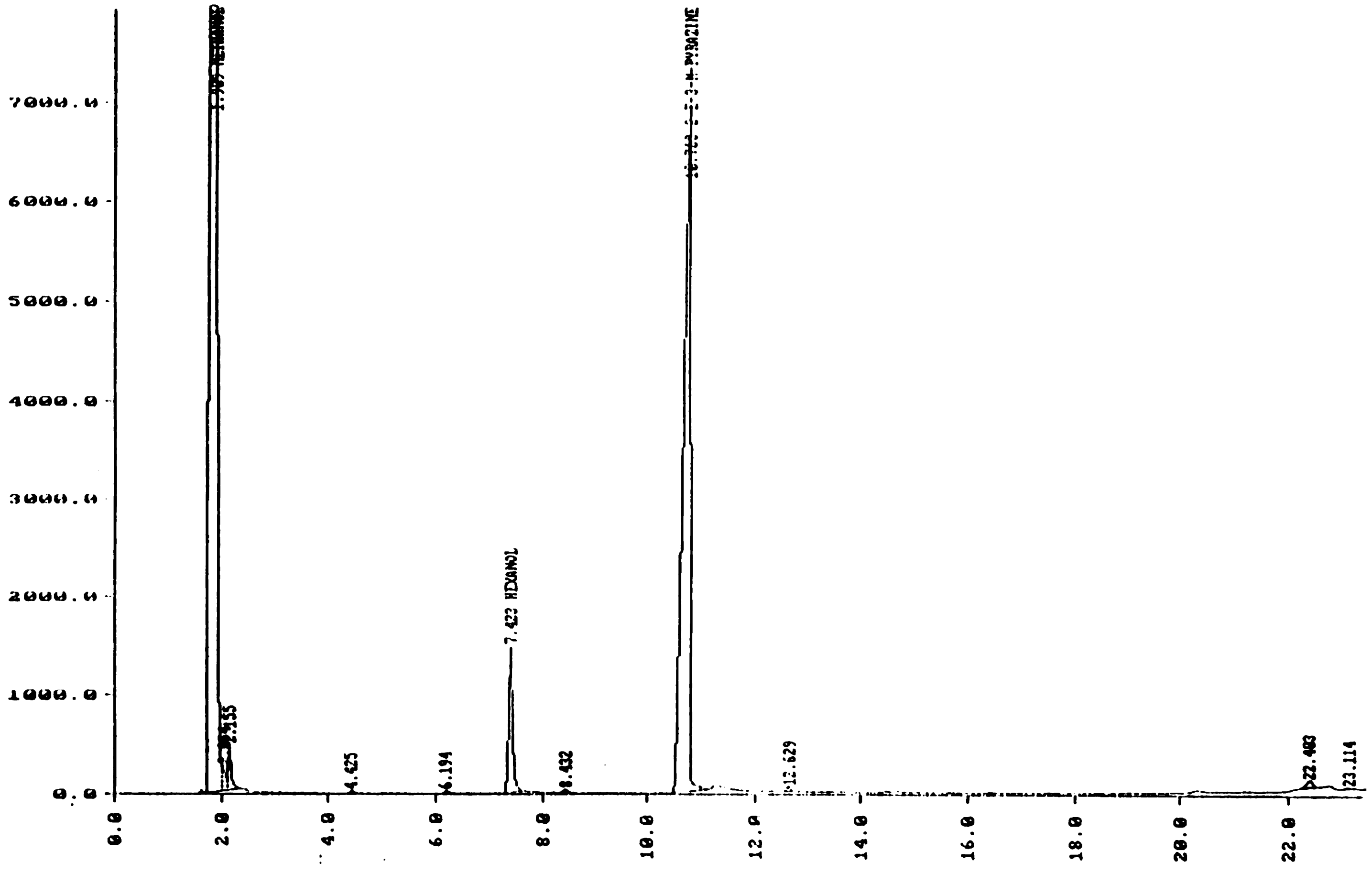

Figure 3.2
GC of Oxidized Product Formed In Ethylenediamine Run (3, 7/22/96)

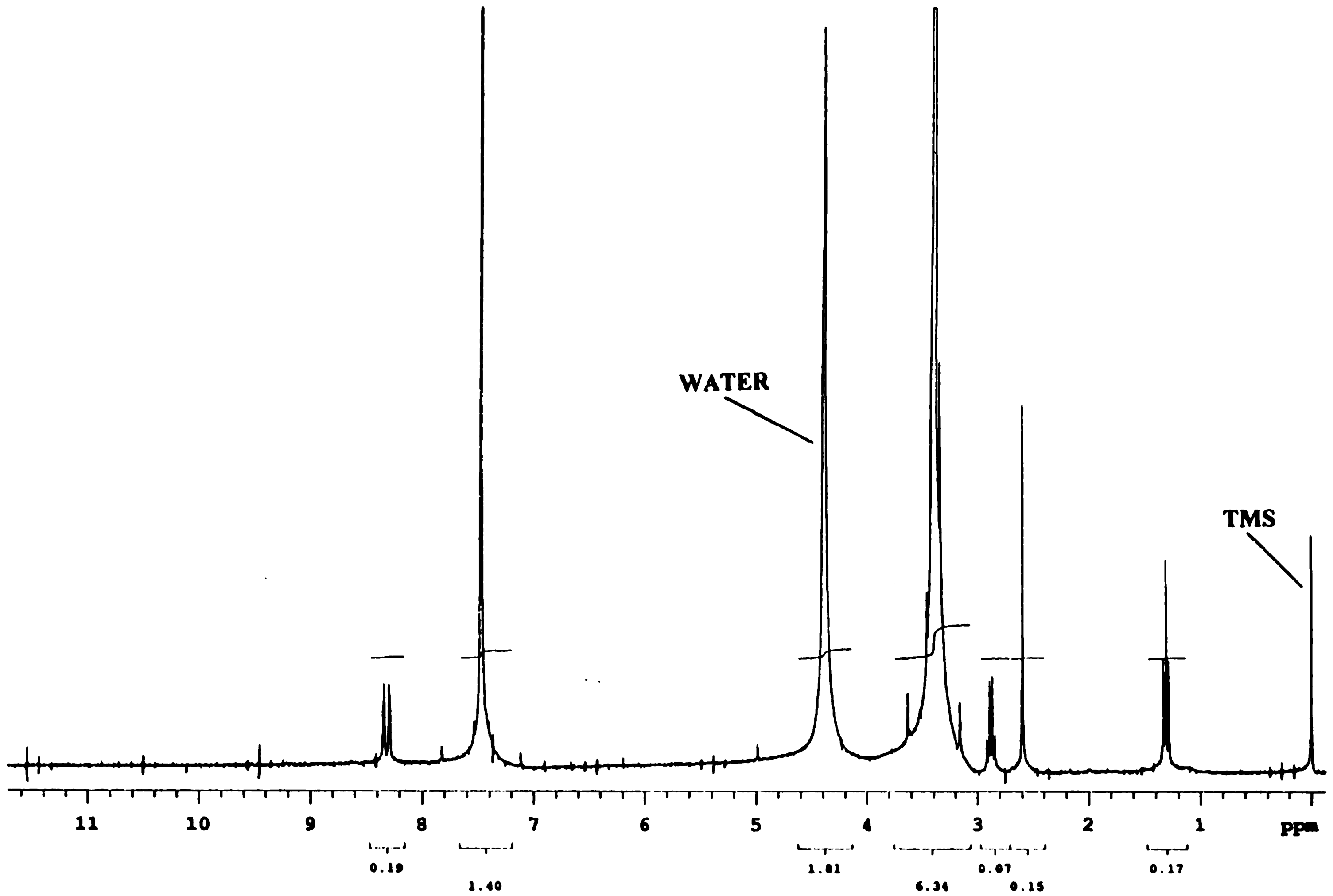

Figure 3.3
NMR Spectrum of Oxidized Product Formed In Ethylenediamine Run (2, 7/17/96)

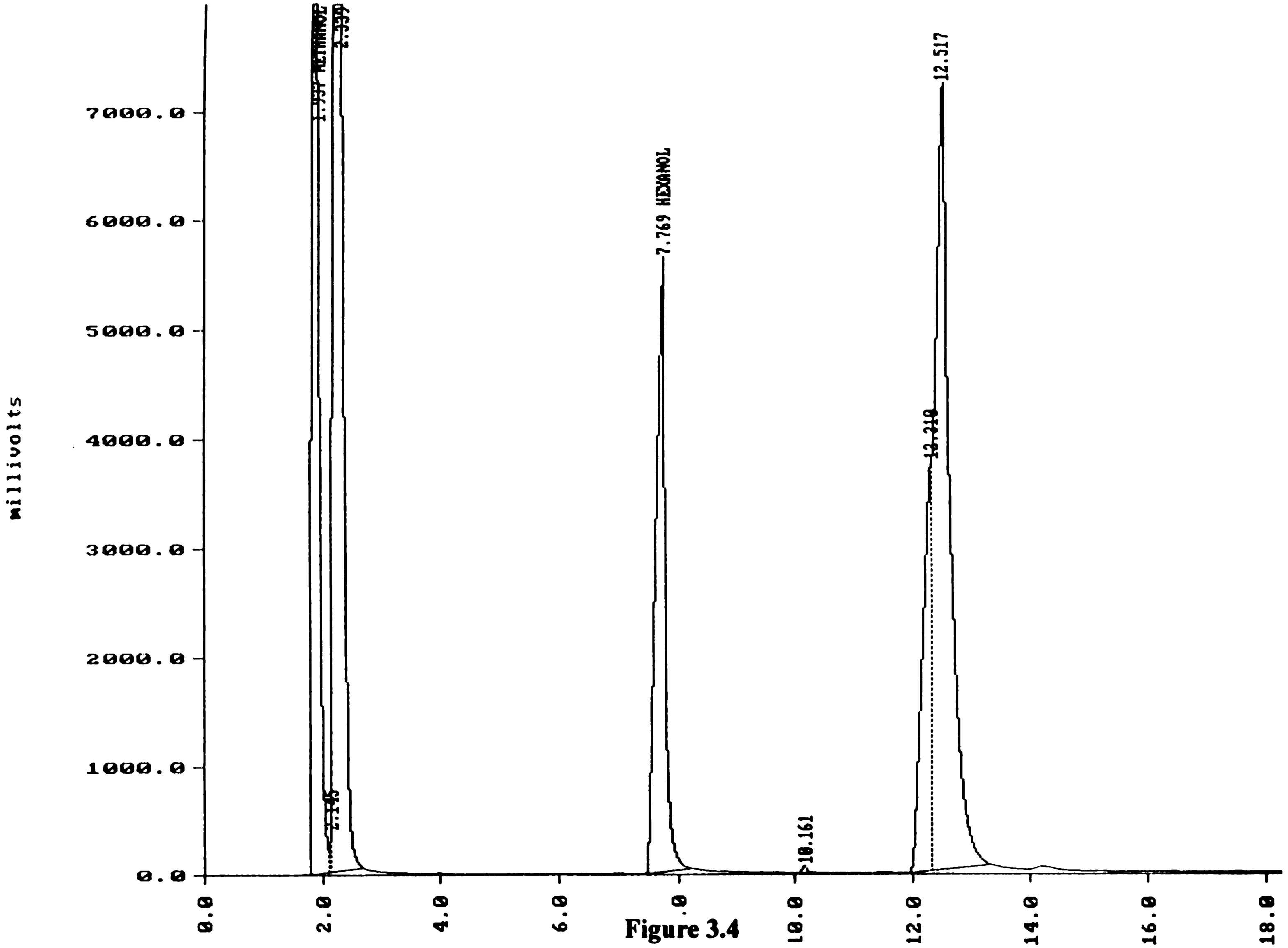

Figure 3.4
GC of Products Formed In Propylenediamine Run (1, 8/5/96)

unassigned and the peak at 2.34 minutes is ethyl ether. The broad peak is from the two forms of dihydropyrazine produced, which have different elution times, giving one broad peak instead of two fine peaks. The solution was oxidized using the same method and an overall yield of 2-ethyl-3,5-dimethyl pyrazine and 3-ethyl-2,5-dimethyl pyrazine of 87.0% as determined by GC analysis using the response factor for 2-ethyl-3-methyl pyrazine.

3.6 2-Ethyl-3-Methyl Quinoxaline Results

An NMR spectrum of phenylenediamine can be seen in Figure 3.5. o-Phenylenediamine was used to form 2-ethyl-3-methyl quinoxaline as described in the procedure in 98% yield, based on weight. The NMR spectrum of the product dissolved in d-toluene with methanol standard can be seen in Figure 3.6. The only unidentified peak not associated with the quinoxaline or the solvent and standard appears to be water at 1.65 ppm. Since yield was based on weight and there is a low concentration of impurity, yield is slightly lower than the reported 98.0%. A GC/MS was run on the sample to try to identify impurities and can be seen in Figure 3.7. The mass spectrometric correlation between the reaction sample and the standard saved in the databank is good. No other reasonable impurities were identified by this method.

3.7 Discussion of Pyrazine and Quinoxaline Formation

The reaction of 2,3-pentanedione with vicinal diamines to form pyrazines produces high yields of the desired products. The spectra and chromatograms show relatively small

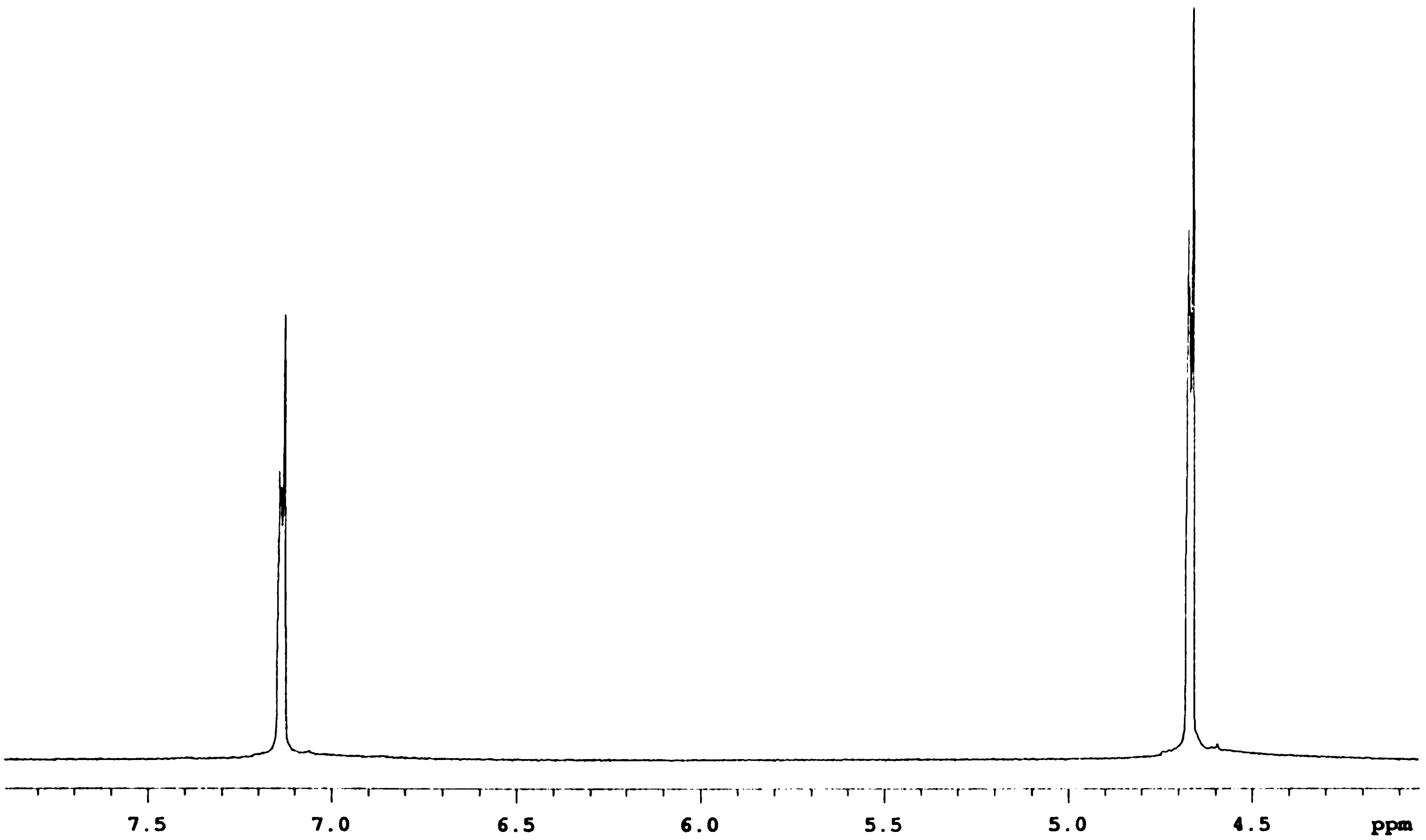

Figure 3.5
NMR Spectrum of Phenylenediamine (8/5/96)

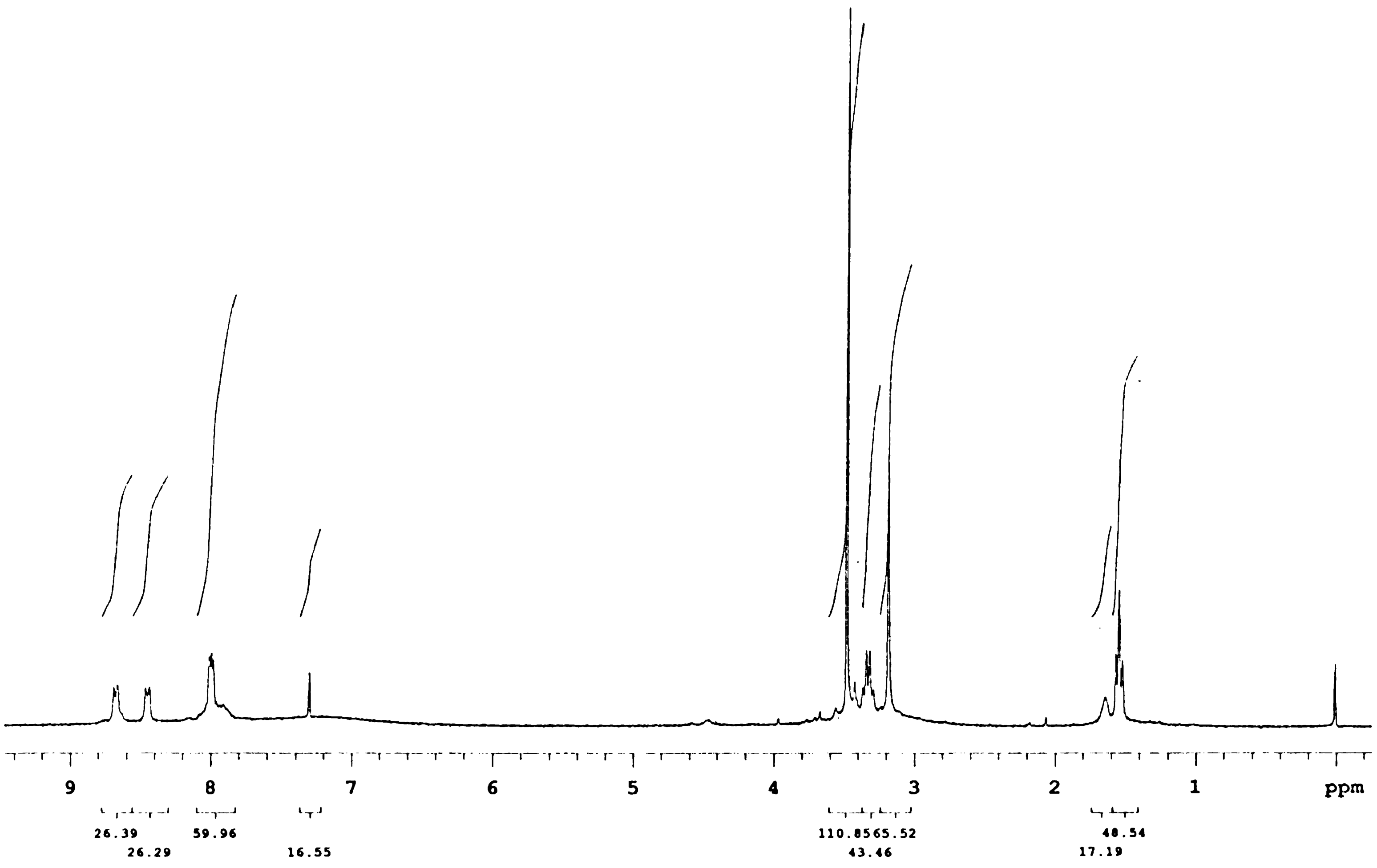

Figure 3.6
NMR Spectrum of 2-Ethyl, 3-Methyl Quinoxaline (2, 8/12/96)

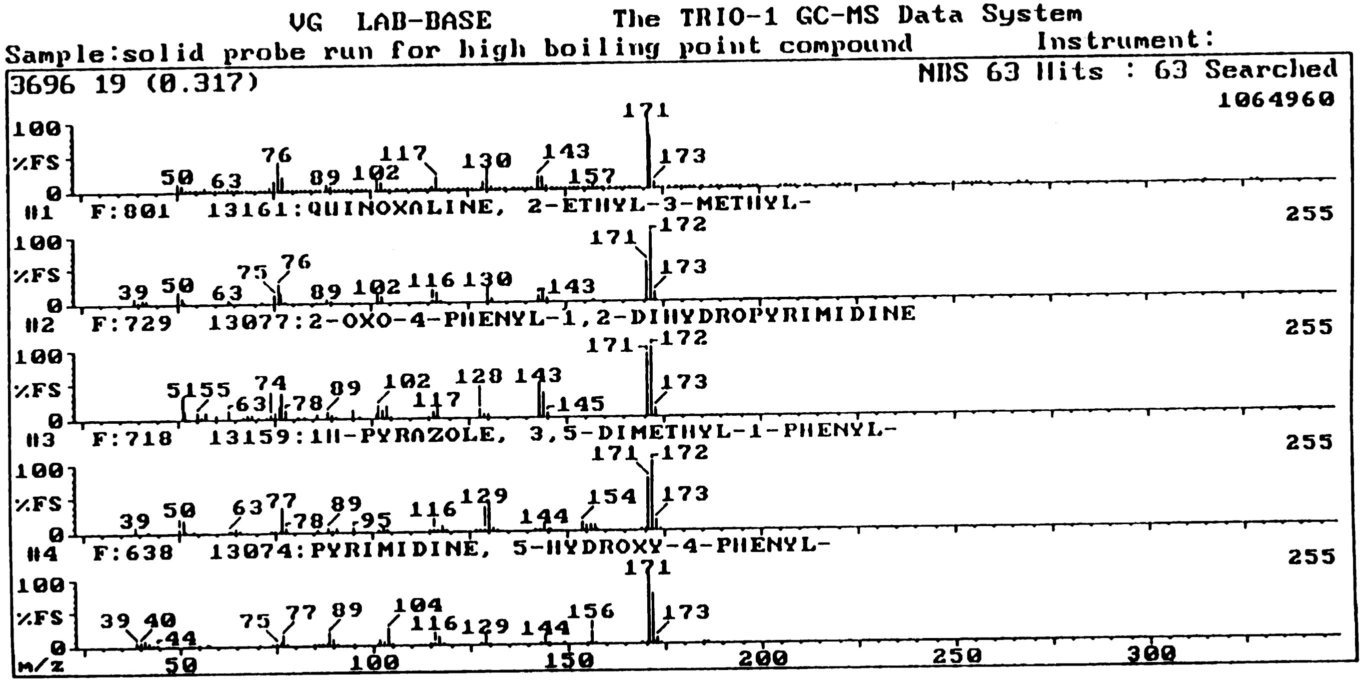

Figure 3.7
Solid Probe Mass Spectrum of 2-Ethyl-3-Methyl Quinoxaline (2, 8/12/96)

amounts of impurities present in the reaction products. Ethylenediamine was used as a reactant to produce 2-ethyl-3-methyl pyrazine in 72.4% yield. Propylenediamine was reacted with 2,3-pentanedione to produce a mixture of 2-ethyl-3,5-dimethyl pyrazine and 3-ethyl-2,5-dimethyl pyrazine in 87.0% yield. Both yields were based on GC analysis. 2-Ethyl-3-methyl quinoxaline was produced in 98%, based on weight.

Chapter 4

SUMMARY AND RECOMMENDATIONS

4.1 Summary and Conclusions

4.1.1 Duroquinone Studies

This work has shown the downstream processing of 2,3-pentanedione is favorable. Although no in-depth cost breakdown was completed on these chemicals, an initial economic analysis gives insight to the factors that might influence the success of these processes. Current costs of chemicals cited here are taken from market quotations. 2,3-Pentanedione (97%) currently sells for about $40/lb and we project it can be produced in our processes for around $4 - 6/lb. Duroquinone (97%) sells for $500/lb in Aldrich and is currently produced from durene. The cost of durene is $52/lb. Although the optimal yield obtained for duroquinone from 2,3-pentanedione was only 25%, it can be easily separated and could be considered a natural product from this route. An estimate of what we might be able to produce duroquinone for is $45/lb. Durohydroquinone is not readily available, but it is produced from duroquinone in high yield. Its competition as an antioxidant is tert-butyl hydroquinone (TBHQ), which sells for $165/lb. A further in-depth

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depth study of these processes needs to be completed before a reasonable judgment can be made on the future of this method of production for duroquinone. Since duroquinone is so valuable, this route may be viable, but waste disposal costs from this process would be high (since the aqueous phase contents are unknown) and have not been investigated.

The highest yield of duroquinone obtained from the condensation of 2,3-pentanedione was 29%, which is three times that obtained in the literature. This was achieved by adding a neutralization step before toluene was added to remove the organic products. Without the neutralization step, yields on the order of 25% duroquinone can be expected. As discussed in Chapter 2, if the desired intermediate for duroquinone formation was formed in a 1:1 ratio with the undesired species, duroquinone yield would theoretically be 50%. This yield was not obtained and may be due to the exothermicity of the reaction and heat sensitivity of duroquinone in basic solution. Duroquinone could be degrading or reacting further. It also may be due to polymerization of 2,3-pentanedione before it reacts to form duroquinone. The spectra and chromatograms seen here show there are other species being formed in the reaction which have not been identified by the methods used in this work.

4.1.2 Pyrazine and Quinoxaline Studies

2,3-Pentanedione was reacted with ethylenediamine, $1.39/lb, to produce 2-ethyl, 3-methyl pyrazine (99%) which is sold for $200/lb. Unsubstituted quinoxaline (99%) sells for $10/lb , which is formed from the reaction of 2,3-pentanedione and

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o-phenylenediamine ($3.77/lb). Using our process to produce 2,3-pentanedione, pyrazine and quinoxaline production looks to be feasible and economically favorable. The reaction of 2,3-pentanedione with vicinal diamines produces high yields of the desired pyrazines and quinoxalines. By reacting different diamines with 2,3-pentanedione, targeted chemicals were produced and verified by GC and NMR spectra. These pathways show the versatility and greatly increase the marketability of 2,3-pentanedione.

4.2 Recommendations

Duroquinone production from 2,3-pentanedione condensation has been investigated in great detail. It is recommended that the aqueous phase constituents be further investigated if production of duroquinone from this procedure is desired since they are the key to a complete understanding of this reaction. Since the aqueous species formed were not identified by the methods described here, other wet chemical methods would need to be used. If these species were identified and valuable, the process would be more practicable. A further in-depth cost analysis is also recommended.

The pyrazine and quinoxaline reactions were not optimized as completely as the reaction to duroquinone. Although this work shows these reactions are possible, higher yields might be obtained with method improvement. The literature suggested the oxidation step yields more desirable product if the dihydropyrazine has a higher purity (33). Another possibility in pyrazine production is to try to oxidize the dihydropyrazine as it is being formed to eliminate loss of product from transfer. Methods to remove impurities before oxidation might increase overall yields.

There are many other possible reactions that 2,3-pentanedione can be involved in besides those investigated here. Because of its current high cost, 2,3-pentanedione has not been utilized for all its potentials. A reaction of interest is furanone production from dimerization of 2,3-pentanedione in the presence of an aldol condensation catalyst to yield 2,5-dialkyldihydrofuranones.

APPENDICIES

APPENDIX A

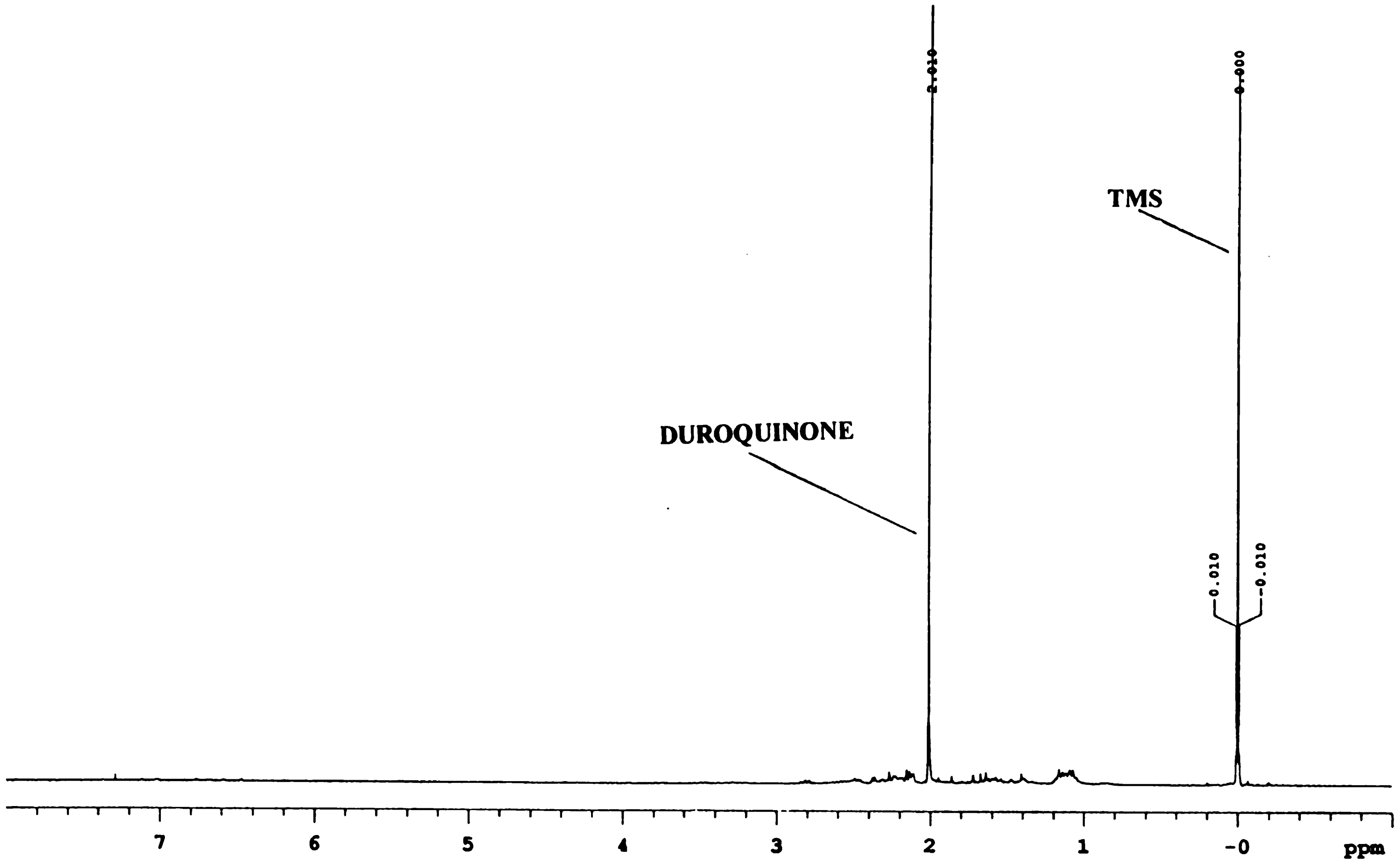


Figure A.1
NMR Spectrum of Organic Species Formed in Literature Confirmation Run (D1, 4/5/95)

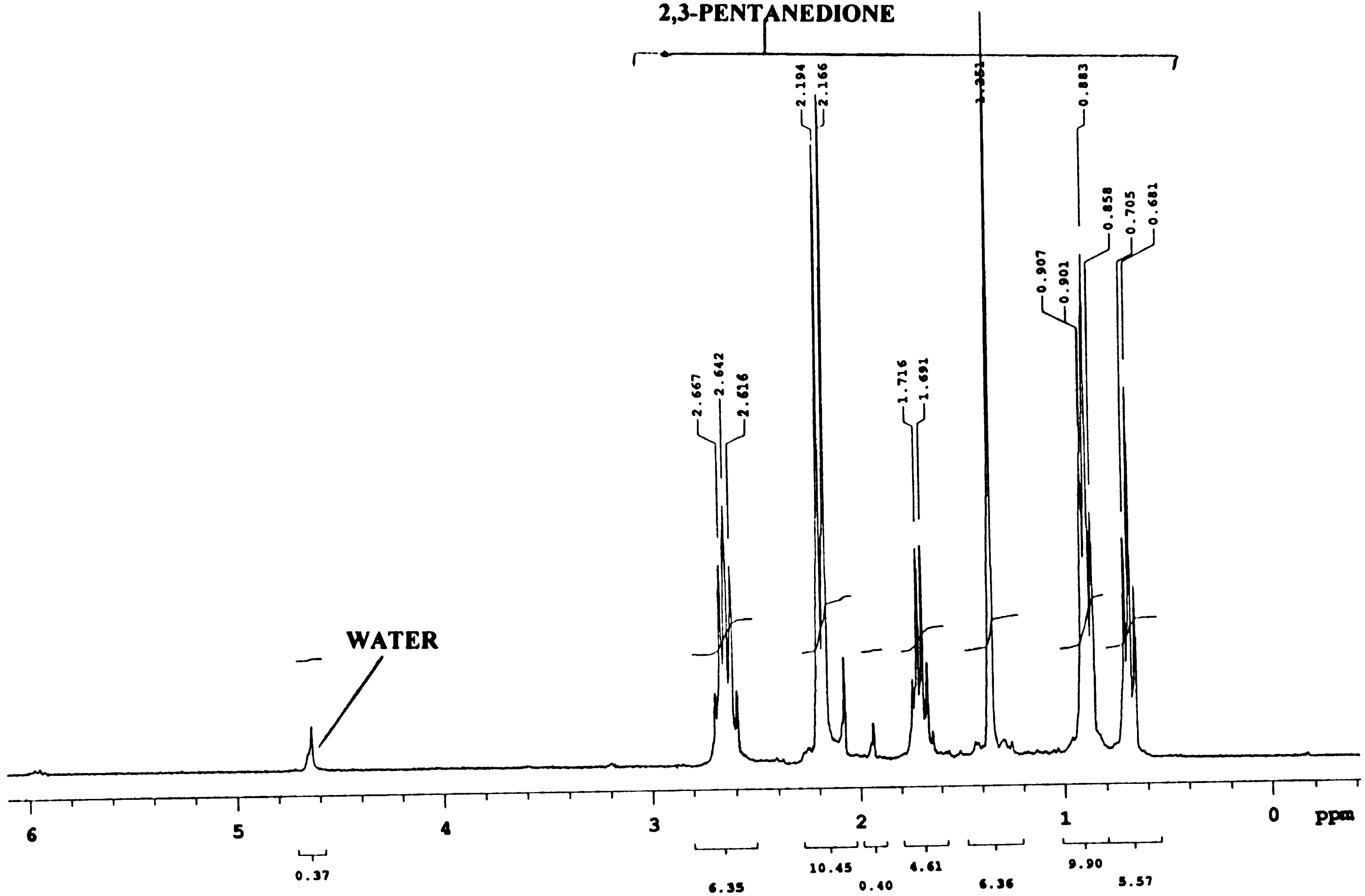


Figure A.2
NMR Spectrum of 2,3-Pentanedione in Water (2/23/96)

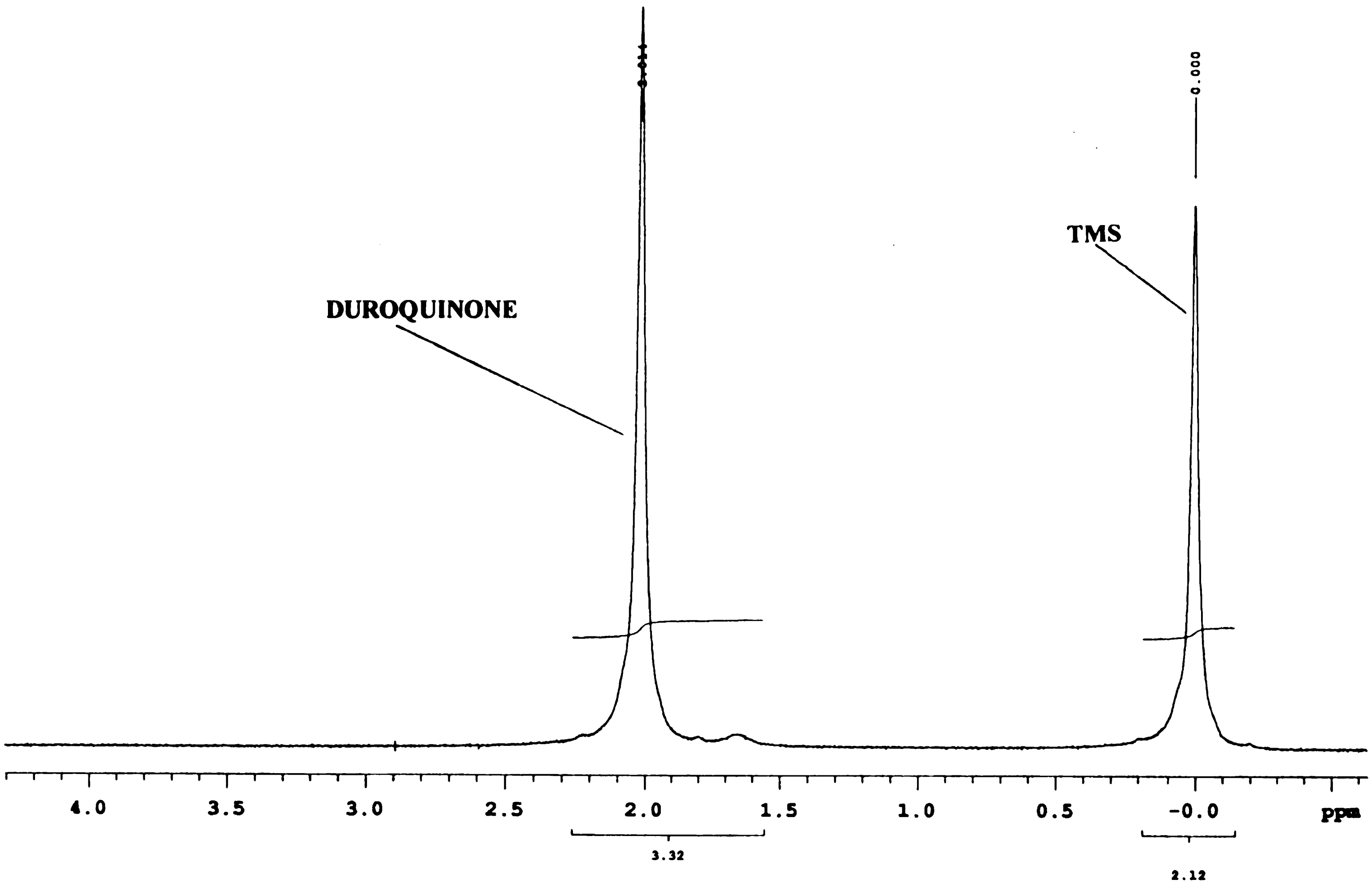


Figure A.3
NMR Spectrum of Duroquinone in Chloroform (2/23/96)

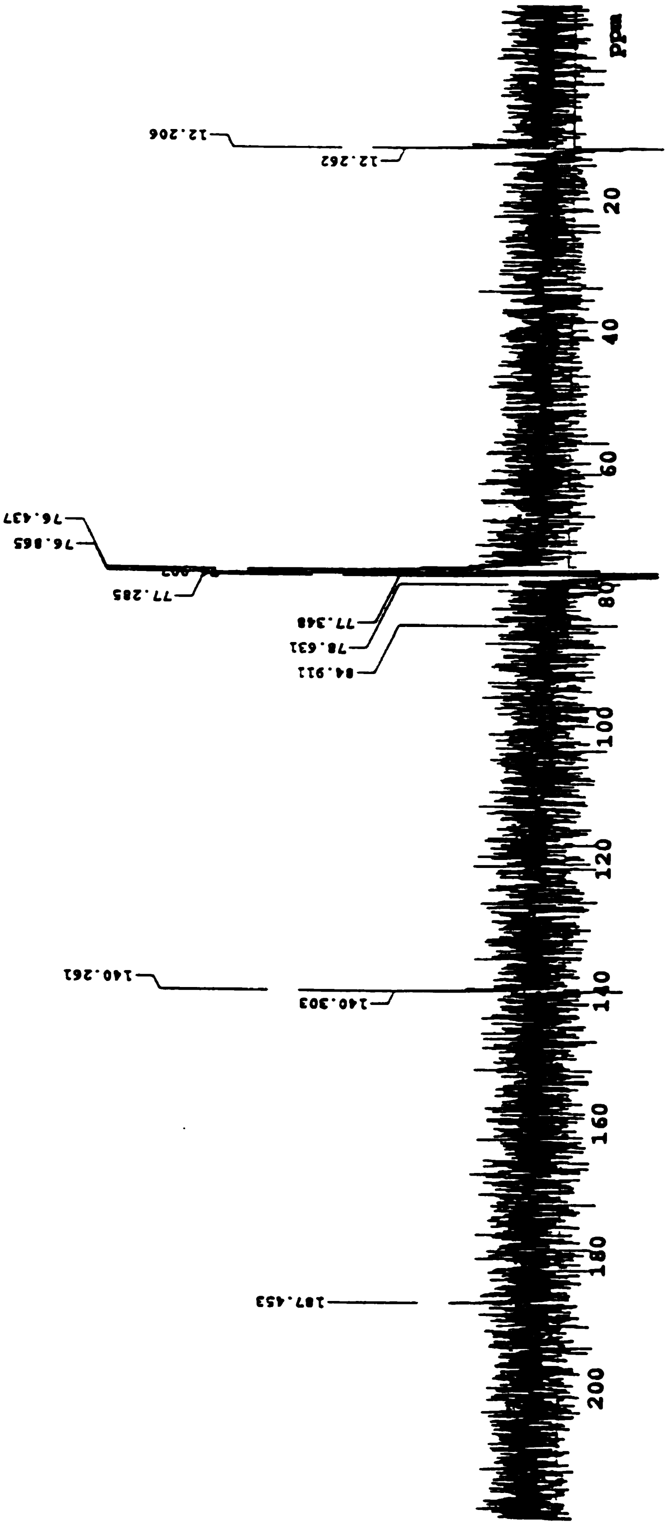


Figure A.4
C-13 Spectrum of Duroquinone in Chloroform (5/9/96)

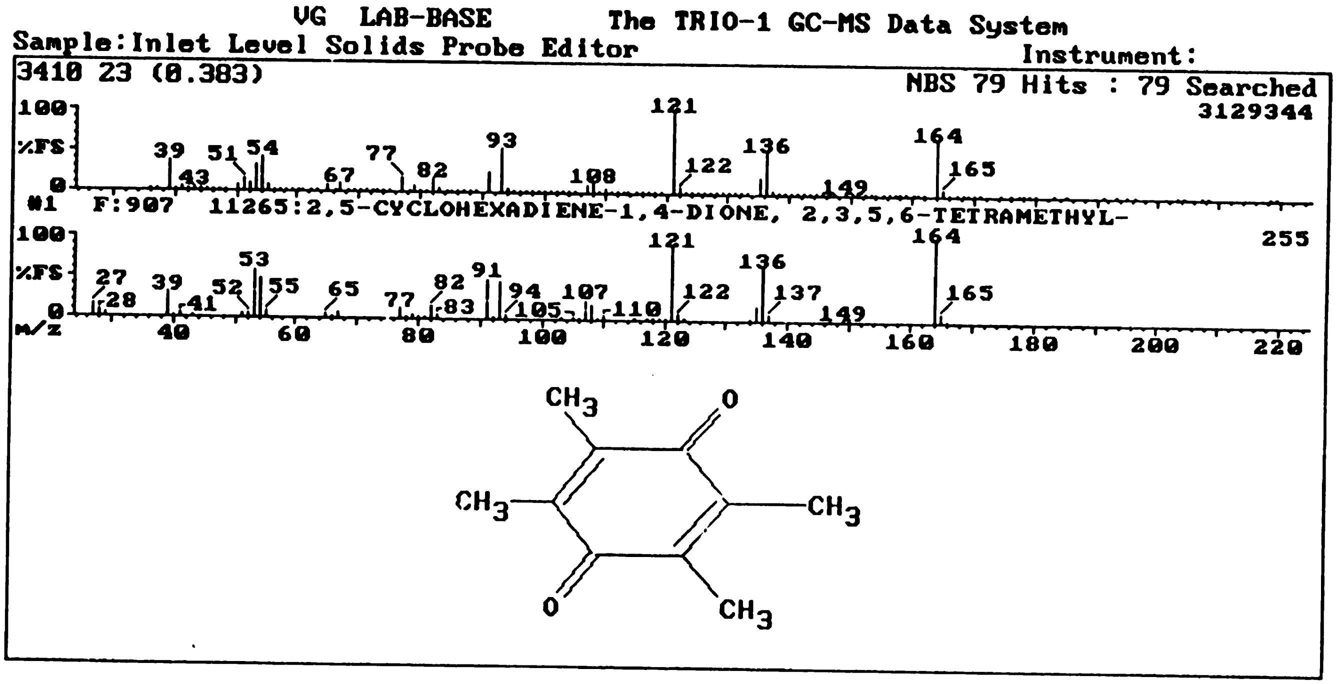


Figure A.5
Solid Probe Mass Spectrum of Duroquinone (4/25/96)

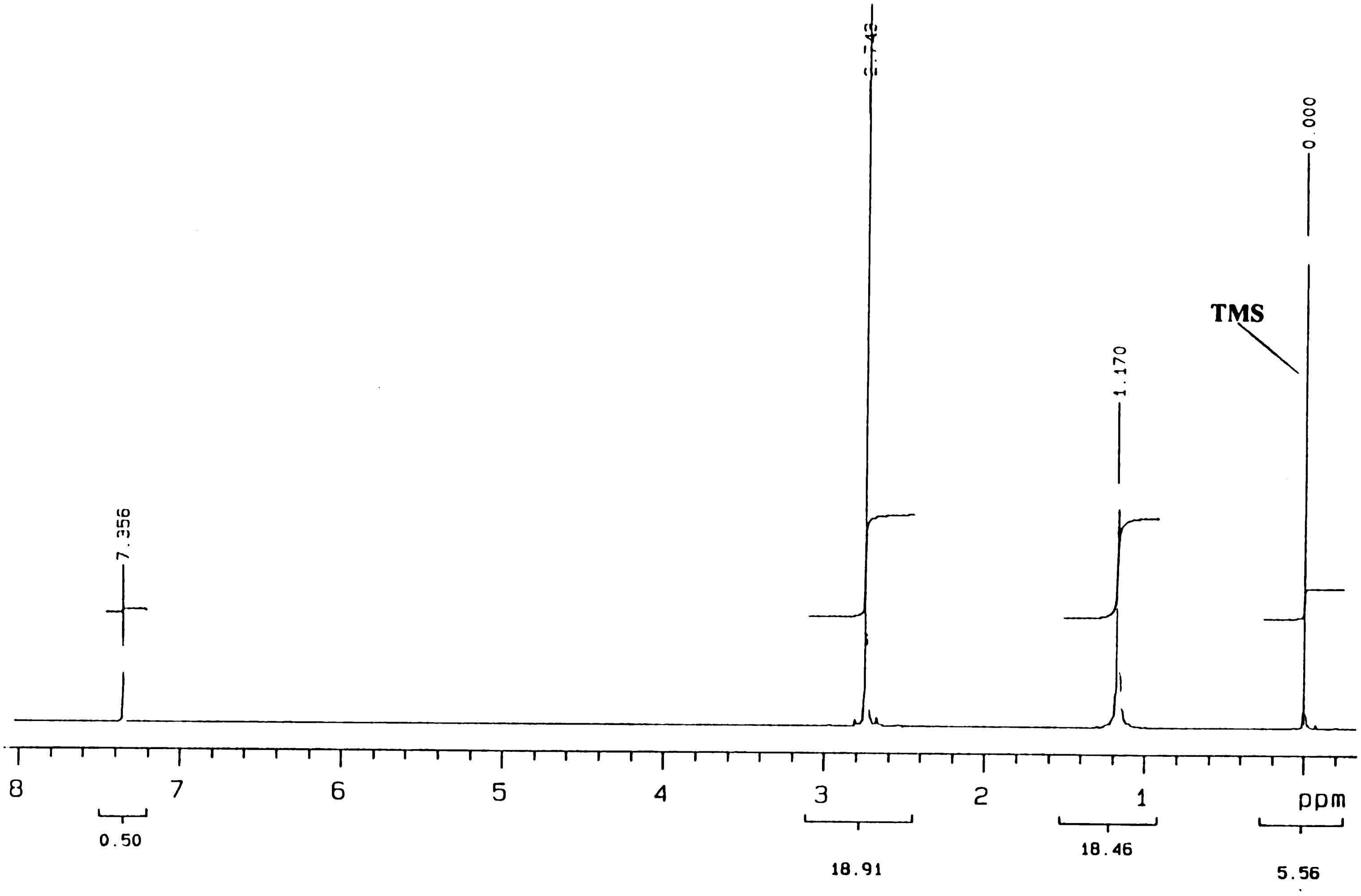


Figure A.6
NMR Spectrum of Ethylene Diamine (7/22/96)

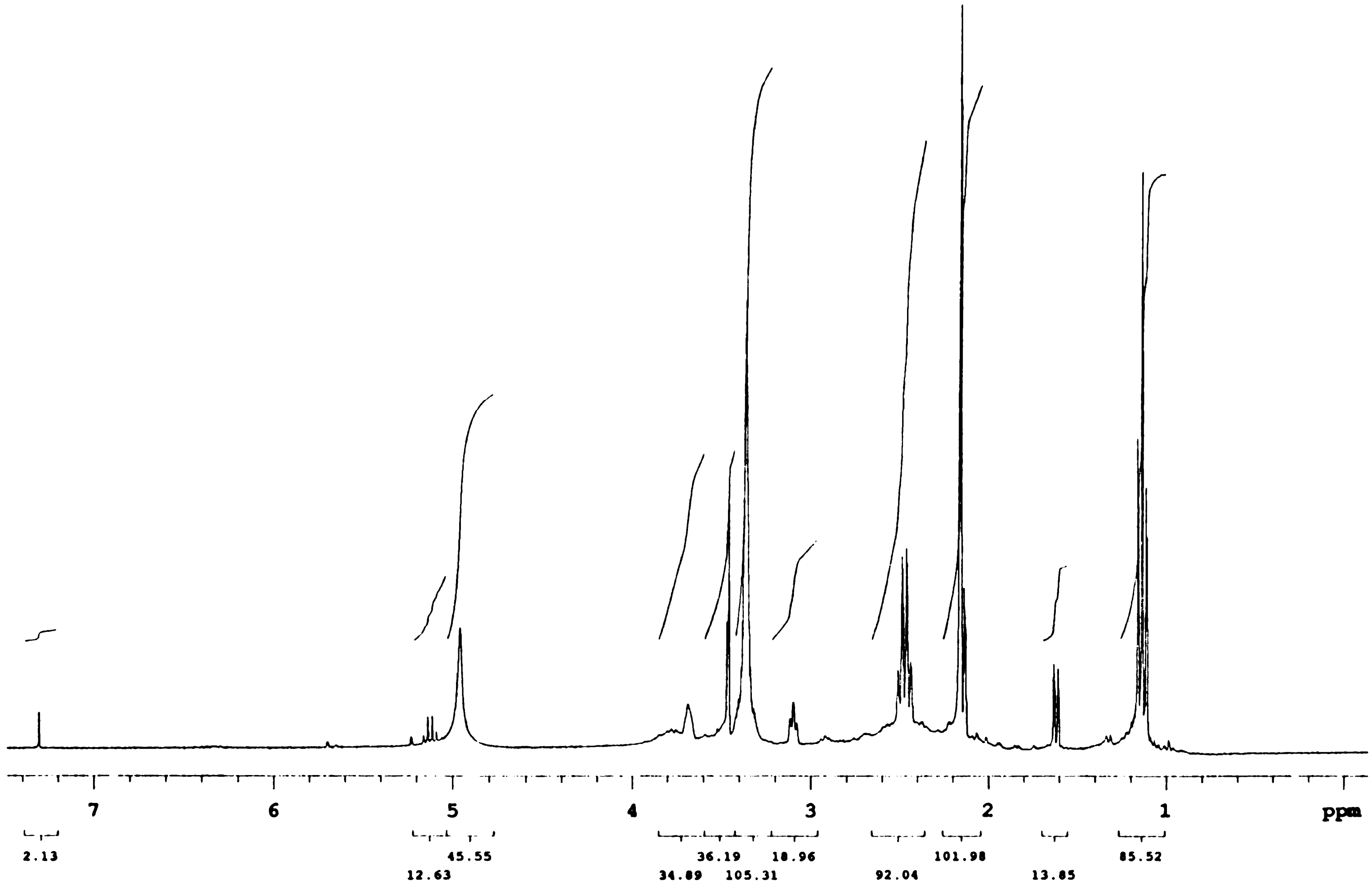


Figure A.7
NMR Spectrum of 2-Ethyl, 3-Methyl Dihydropyrazine From Run 3

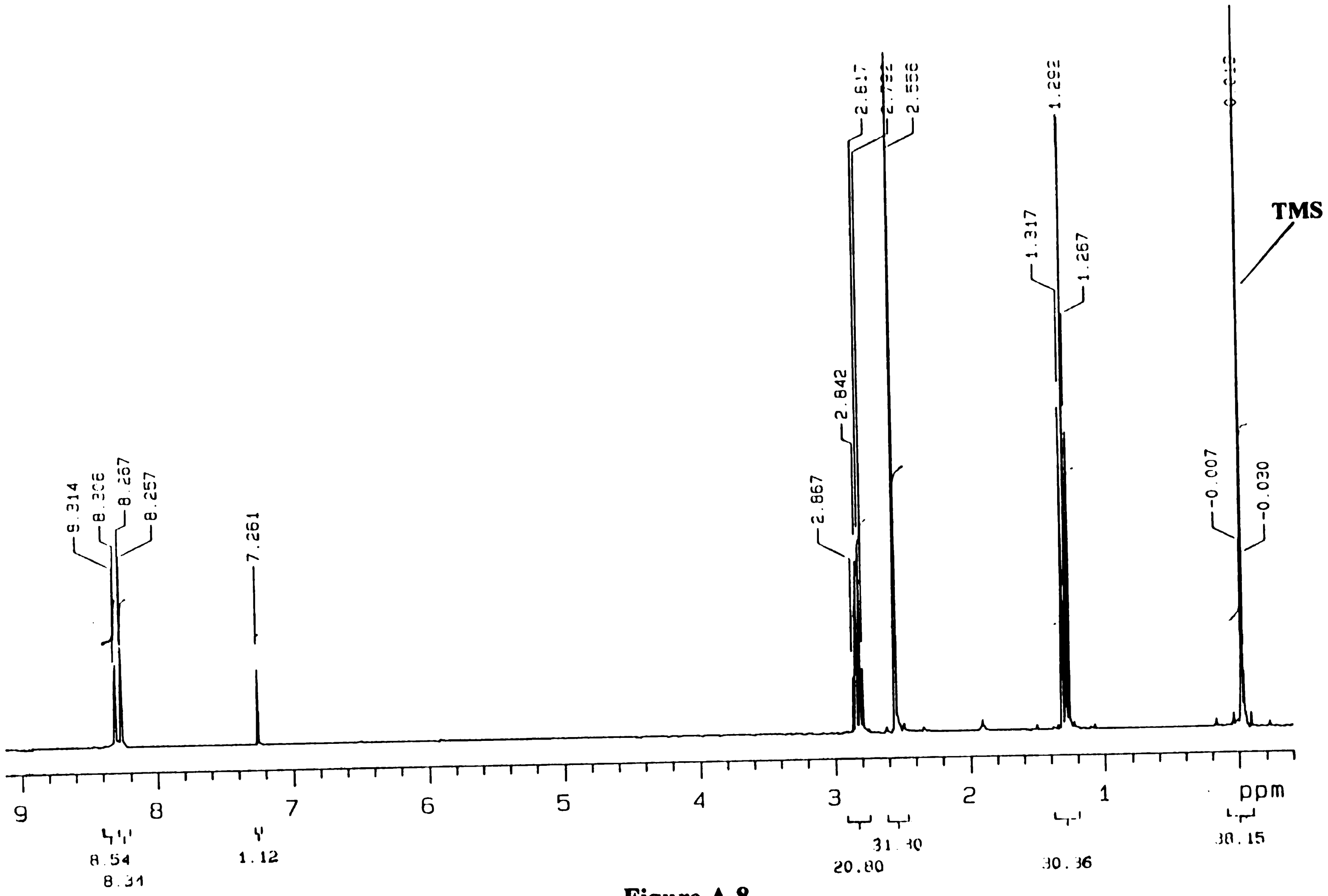


Figure A.8
NMR Spectrum of 2-Ethyl, 3-Methyl Pyrazine (7/22/96)

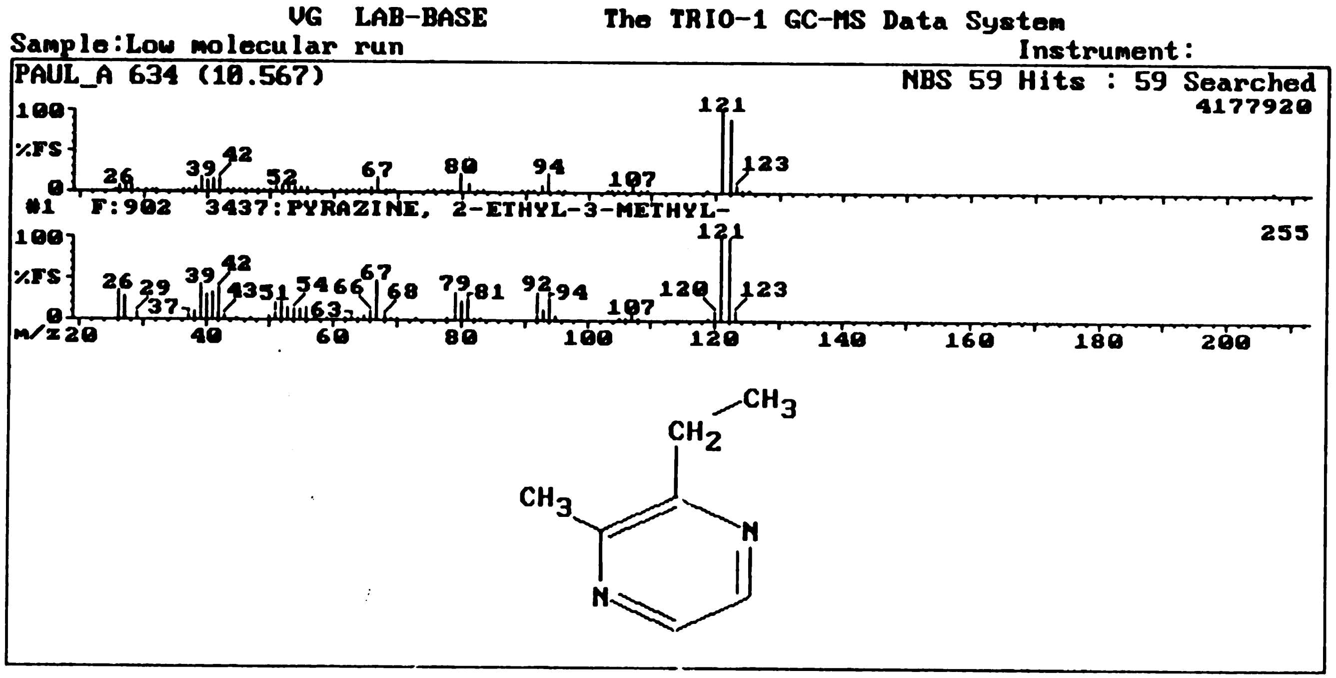


Figure A.9
Solid Probe Mass Spectrum of 2-Ethyl, 3-Methyl Pyrazine (3/8/96)

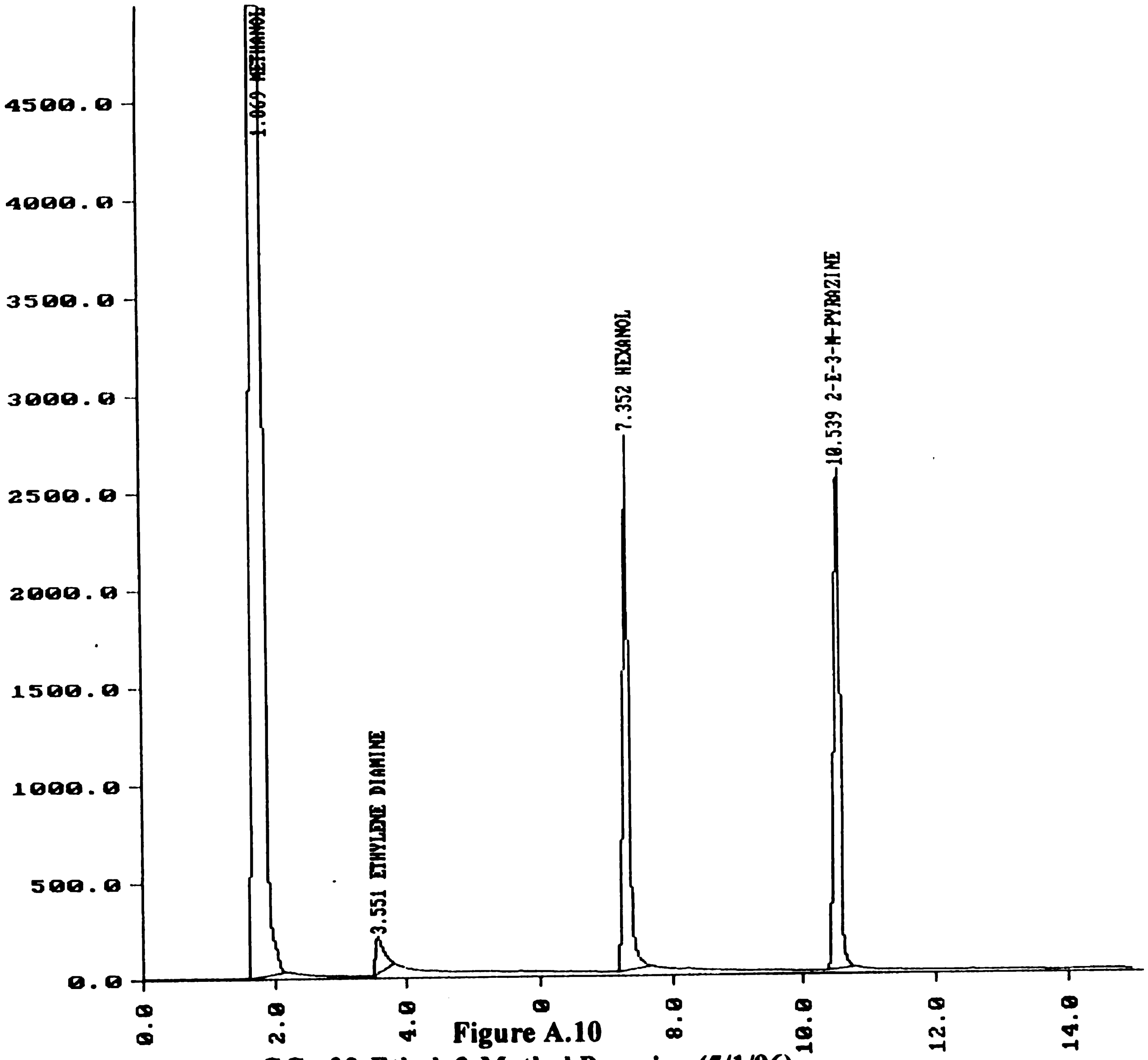


Figure A.10
GC of 2-Ethyl, 3-Methyl Pyrazine (5/1/96)

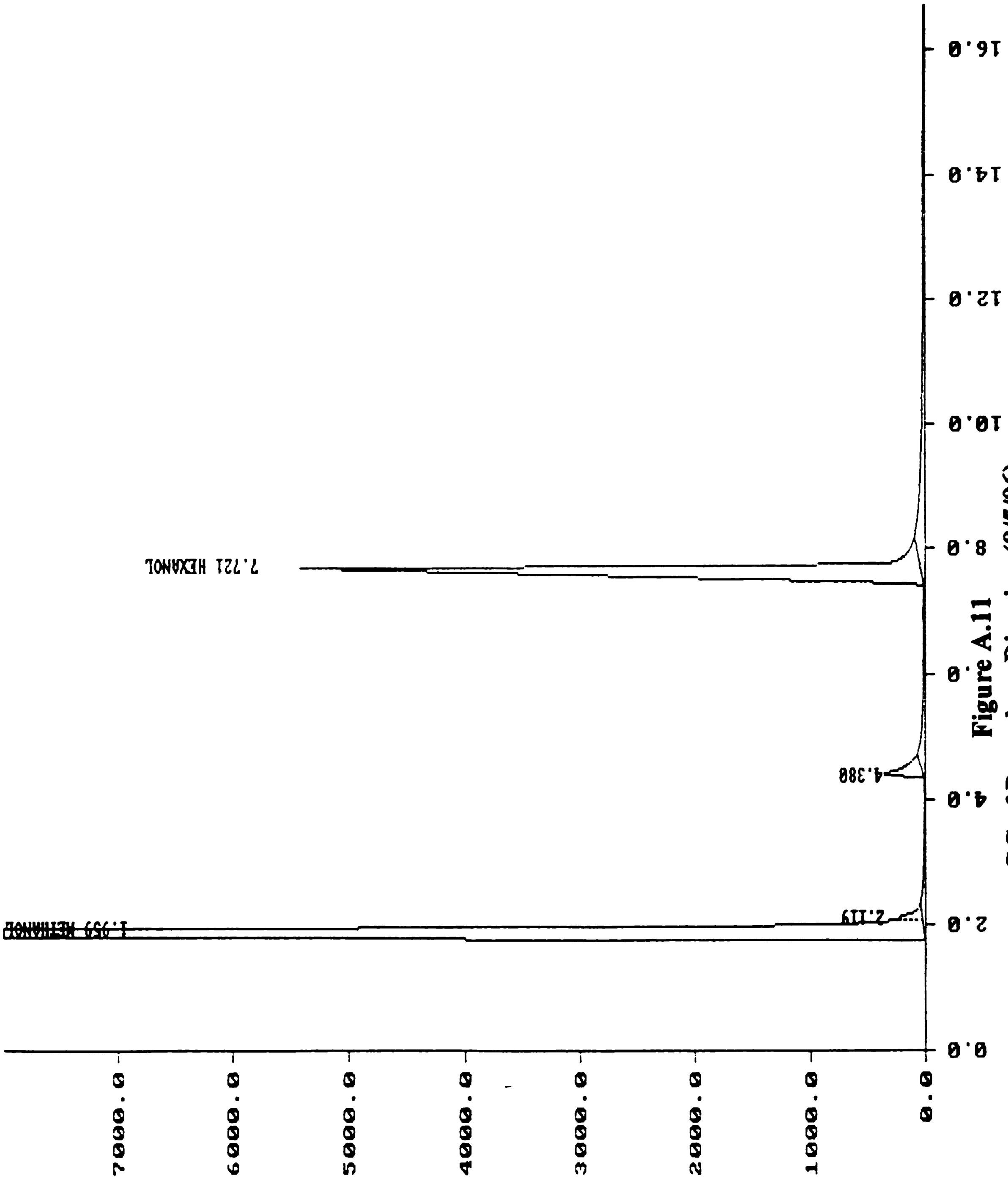


Figure A.11
GC of Propylene Diamine (8/5/96)

APPENDIX B

			Table B.1						
		2,3-Pentanedione Recovery (0.5g, 1.0g, 1.5g)							
					Response Factor Calculation				
									RF
Solution 1	0.01970	g/ml 23Pentanedione			Aqueous Standard:		RF using dtol/tol:		1.2517555
Solution 2	0.03917	g/ml			0.06 M oxalic acid				1.1938937
Solution 3	0.05863	g/ml			10 g/l 2-propanol				1.1333641
									1.0533003
GC Calcs					Rf (tol/tol)	2.24890		average	1.1580784
RF= area iso/area 23p * conc 23p/conc iso					RF =	1.15808			
Standard:	0.0401192	g/ml Pent in water		**Use for samples extracted onto toluene layer and run					
	0.02016	g/ml iso in toluene		on GC					
*Use CH3 singlet of 23P for peak area on NMR									
*Concentrations are in units of g/ml									
Run the three solutions straight in the GC (no extract in tol)									
Solution	Conc 23P		Should Be	Recovery					
0.5	1.86E-02	g/ml	0.01970	94%					
1	3.33E-02	g/ml	0.03917	85%	** I wonder if these solutions did not dissolve all the				
1.5	0.050481	g/ml	0.05863	86%	** pentanedione				
Extract into tol layer and run on GC:									
	Organic dtol		Left in aqu from GC:		Should be	total	Recovery	Rec fr str	
Solution	Conc 23P		Solution	Conc 23P				GC run	
.5g	0.009270	g/ml	.5g	0.00816	0.01970	0.01743	88%	94%	
1g	0.0180327	g/ml	1g	0.013674	0.03917	0.03171	81%	95%	
1.5g	0.0337695	g/ml	1.5g	0.01501	0.05863	0.04878	83%	97%	
Run extracted dtol layer on NMR and aqueous layer on GC									
Aqueous layer:			Dtol layer:						
Solution	Conc 23P		area chloro	area meoh	area 23p	conc meoh	conc chloro		
.5g	0.0034125	g	15.54	84.37	85.94	0.0209562	0.019199		
1g	0.009106		18.88	112.74	108.53	0.0396101	0.0399128		
1.5g	0.009609		15.05	103.46	173.15	0.0688628	0.0798823		
Should be	total(meoh)	recovered		Chloro	recov chlor				
0.01970	0.0243687	124%		0.0226115	115%				
0.03917	0.0487161	124%		0.0490188	125%				
0.05863	0.0784718	134%		0.0894913	153%				
Run dtol layer that I ran in the NMR in the GC to compare:									
	GC			Add Aqueous from					
Solution	Conc 23P			above	Total	Should be	Recovered		
.5g	0.02291	g/ml		0.0034125	0.02633	0.01970	134%	** Redid	
1g	0.03190	g/ml		0.009106	0.04101	0.03917	105%		
1.5g	0.04778	g/ml		0.009609	0.05739	0.05863	98%		
Try 0.5g solution again									
.5g	Conc 23P	Aqu	Total	should be	recovered				
	0.01604	0.0034125	0.0194533	0.01970	99%				

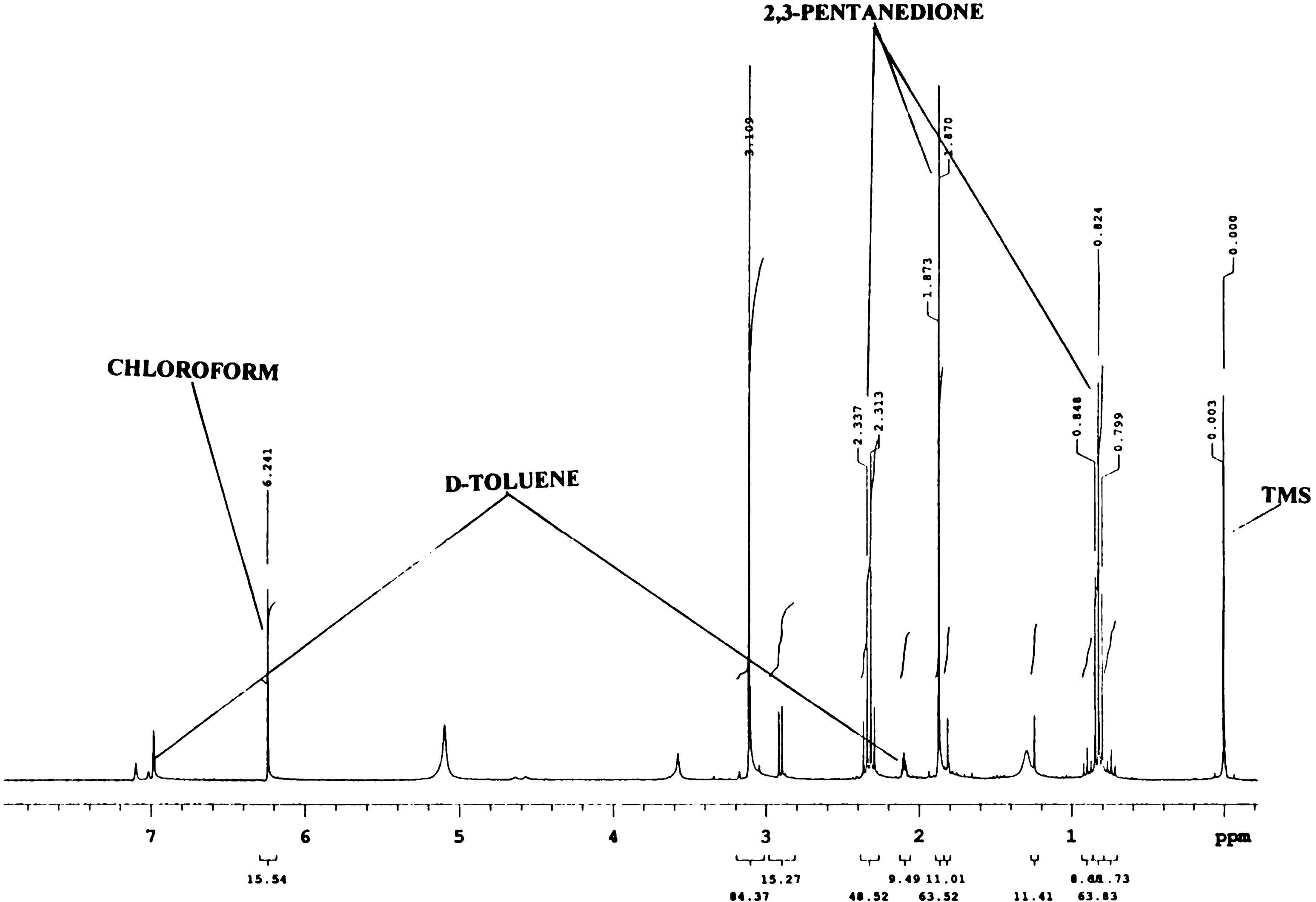


Figure B.1
Calibration NMR Spectrum of 2,3-Pentanedione (7/13/96)

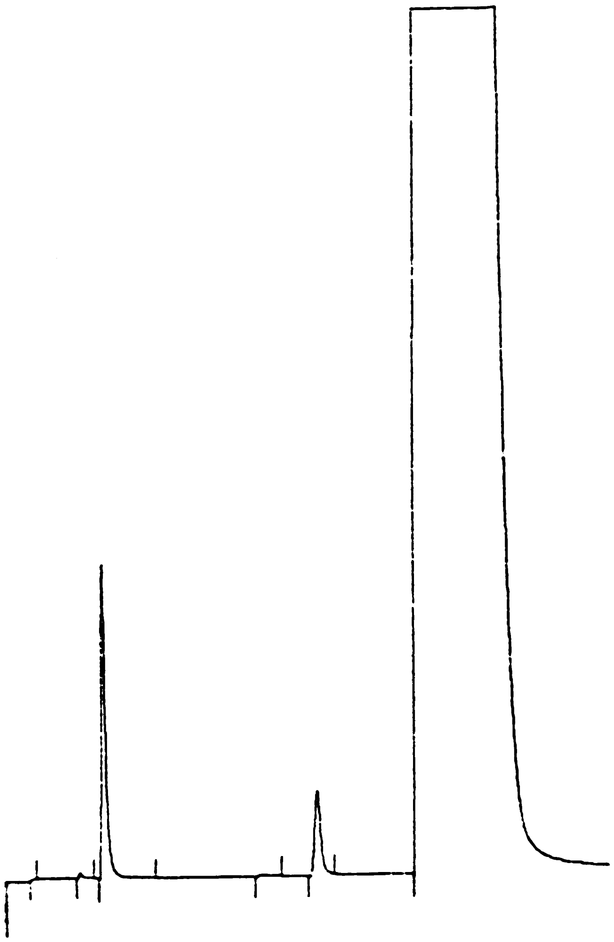


Figure B.2
Calibration GC of Aqueous Layer (7/13/96)

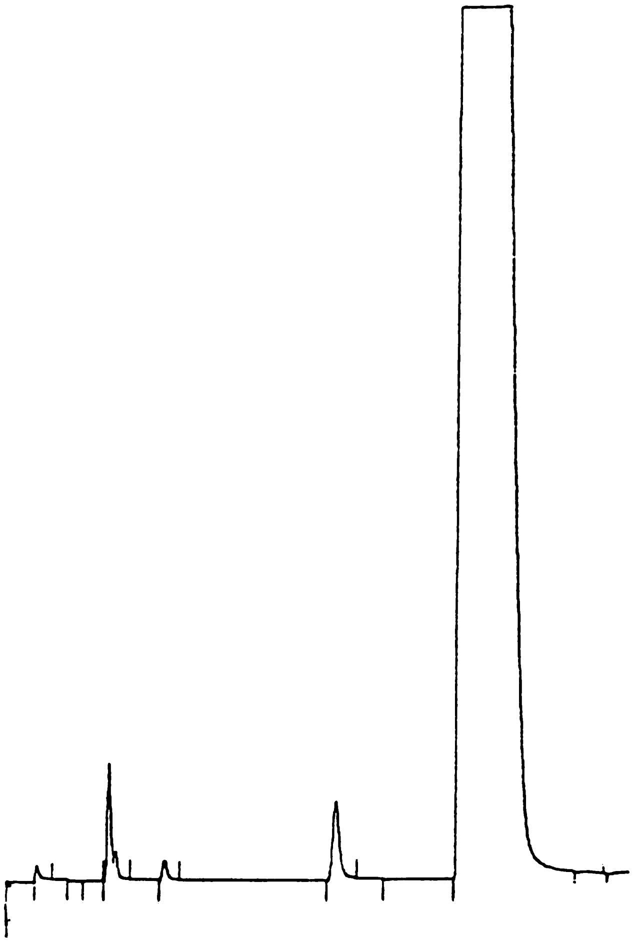
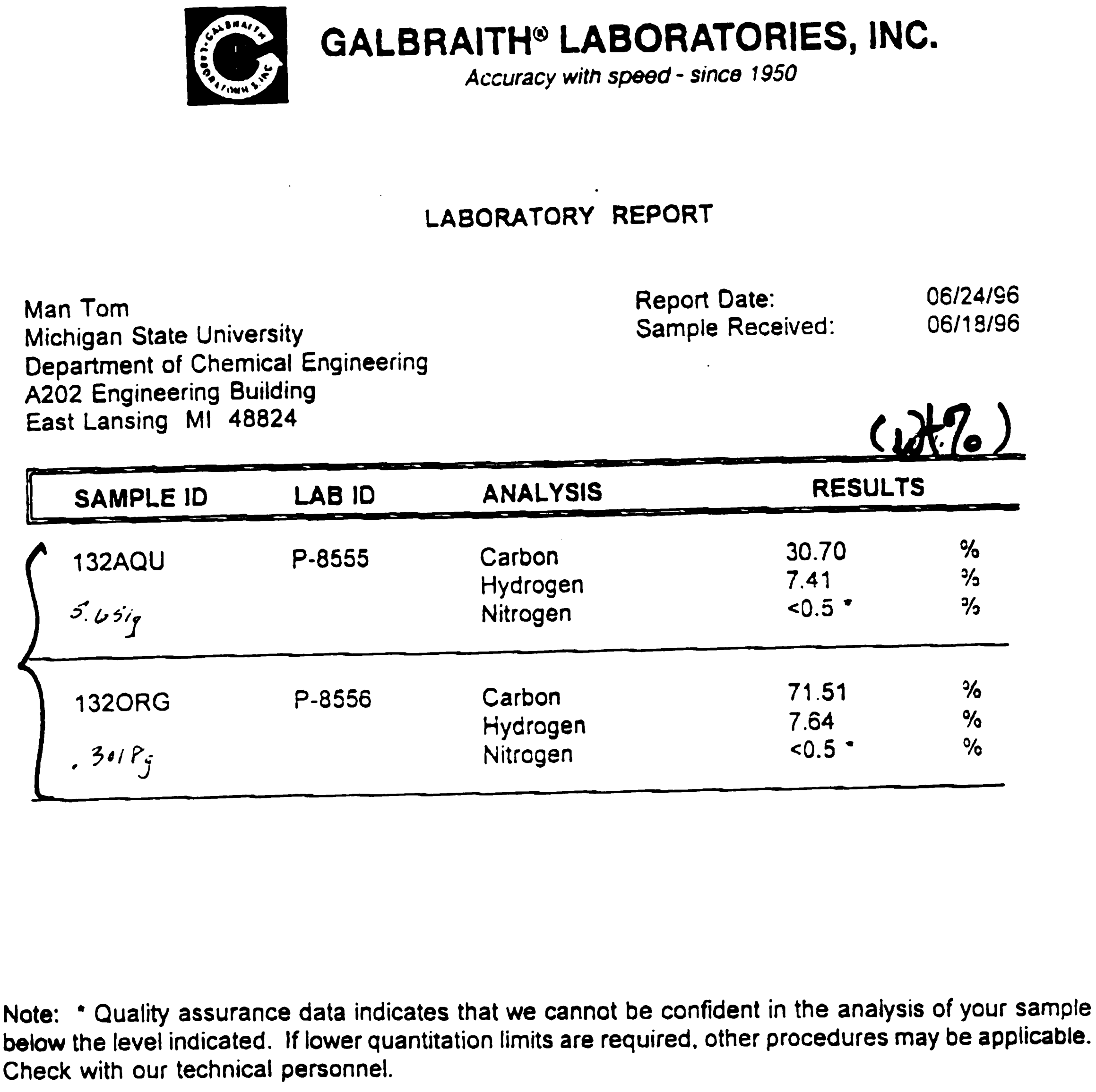


Figure B.3
Calibration GC of Toluene Layer (7/20/96)

APPENDIX C

				Table C.1						
		Carbon Balance Calculation (132, 6/1/96)								
From CHN Analysis,										
				The experiment was run along with the standard extraction procedure.						
Aqueous	carbon	30.7	%	Once separated, both the aqueous and organic layers were rotary						
	hydrogen	7.41	%	evaporated to remove the solvents.						
	nitrogen	<0.5	%							
Organic	carbon	71.51	%							
	hydrogen	7.64	%							
	nitrogen	<0.5	%							
From Reaction #132,										
Aqueous Species Produced:			5.2489	g	*0.3070 =	1.611412	g			
Organic Species Produced:			0.3018	g	*0.7151 =	0.215817	g			
					Total	**1.827229**	**g carbon present in product**			
50 ml of 5.081g23P/100ml water were used, in which carbon is 60% of the 23P.										
50ml *5.081g23P/100mlwater*0.60=				**1.5243**	**g carbon present in feed**					
	Results in 1.827/1.523 =			1.198734						
So, 119% of the carbon that was started with was recovered.										



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LABORATORY REPORT

Man Tom
Michigan State University
Department of Chemical Engineering
A202 Engineering Building
East Lansing MI 48824

Report Date: 06/24/96
Sample Received: 06/18/96

(wt%)

SAMPLE ID	LAB ID	ANALYSIS	RESULTS	
132AQU	P-8555	Carbon	30.70	%
		Hydrogen	7.41	%
5.651g		Nitrogen	<0.5 *	%
132ORG	P-8556	Carbon	71.51	%
		Hydrogen	7.64	%
.3018g		Nitrogen	<0.5 *	%

Note: * Quality assurance data indicates that we cannot be confident in the analysis of your sample below the level indicated. If lower quantitation limits are required, other procedures may be applicable. Check with our technical personnel.

Figure C.1
CHN Analysis for Run 132, Aqueous and Organic Species (6/18/96)

				Table C.2				
	Mass Balance Calculation For CsOH Reaction (133, 6/12/96)							
5% 23P Solution	5.0069g * .97 purity 23P/100ml solution * 25ml used /100.12 g/mol = 0.012141 mols							
1.0 M CsOH Solution	7.4626 g CsOH/100ml solution *25ml used *0.5 purity /149.9 g/mol = 0.00622 mols CsOH							
1.0 M HCl Solution	8.6ml conc.HCl/100ml solution*5.1ml used*.85 purity*1.2 g/ml HCl*1/36.45 g/mol = 0.01227 mol							
CsOH + HCl ->	**CsCl + H_2O**		1 mol CsCl formed for every mol CsOH					
0.00622 mol CsCl * 168.35 g/mol = 1.0471 g CsCl can possibly be formed								
0.01227 mol HCl - 0.00622 mol CsOH = 0.00605 mol excess HCl								
0.00605 mol excess *36.45 g/mol = 0.2205 g HCl present								
2 23P -> Duroquinone + 2 H_2O								
0.012141 mol 23P (1 mol Duro /2 mol 23P)*164.2 g/mol = 0.9966 g Duroquinone Possible								
0.012141 mol 23P (1 mol water/1mol 23P)*18 g/mol = 0.21853 g water possible								
So,	Dried Organic Species		0.9966g					
	Dried Aqueous Species		1.2676 g	(not including water added or formed in the reaction)				
			———					
			2.2642 g dry constituents expected					
Actually Formed:								
	organic:	0.1444 g collected		aqueous:	1.9494 g collected			
			Total	2.0938 g				
		2.0938/2.2642 = 0.9247 Recovered.						

			Table C.3					
	Mass Balance Calculation For NaOH Reaction (132, 6/12/96)							
5% 23P Solution		5.0081g 23P* .97 purity */100ml solution* 50ml used /100.12 g/mol = 0.024289 mols						
1.0 M NaOH Solution		4.0369 g NaOH */100 ml solution *50 ml used /40 g/mol = 0.05046 mols NaOH						
1.0 M HCl Solution		8.6ml HCl/100ml soln*35ml used*.85 purity*1.2 g/ml HCl/36.45 g/mol = 0.08423 m						
NaOH + HCl	**-> NaCl + H2O**							
0.05046 mol NaCl * 58.45 g/mol = 2.94938 g NaCl possible								
0.08423 mols HCl - 0.05046 mols NaOH = 0.02963 mols excess HCl								
0.02963 moles excess *36.45 g/mol HCl = 1.08 g HCl								
2 23P -> Duroquinone + 2 H2O								
0.024289 mol 23P* 1mol duro/ 2mol 23P *164.2 g/mol = 1.9940 g Duroquinone possible								
0.024289 mol 23P * 1mol water/1mol 23P * 18 g/mol = 0.4372 g water possible								
So,	Dried Organic Species		1.994	g				
	Dried Aqueous Species		2.949 +1.08	g not including water				
			———					
			6.0234 g dry constituents expected					
Actually Formed :								
	organic:	0.3018 g collected		aqueous:	0.0731 + 0.0329 + 5.2489 g			
			Total	5.9528 g				
		5.9528g/6.02342 g = 0.9882 Recovered						

APPENDIX D

Table D.1

Different Base Concentration Calculations (3 -14, 7/19/95)

					Density g/ml	MW	(Aldrich)	
				23P	0.957	100.12	(97%23p)	
Concentrations in mol/ml				MeOH	0.791	32.04		
				Chloroform	1.492	119.38		
				Dtol	0.943	100.21		
				Duroquinone		164.2		
*Duroquinone peak areas come from integrals on NMR spectra at 1.69 ppm.								
*MeOH Conc Duro mol/ml means duroquinone yield concentration according to methanol standard peak.								
NaOH					MeoH Conc	Chloro Conc		Chloro
Molarity	NMR#	Area Duro	Area Meoh	Area Chlor	Duro mol/ml	Duro mol/ml		Total
.5M	3	12.69	114.25	46.36	4.5703E-06	5.702E-06		5.702E-06
1M	2	10.29	70.69	25.82	5.9895E-06	8.301E-06		9.844E-06
1.5M	4	15.41	113.89	39.44	5.5674E-06	8.139E-06		1.056E-05
3M	5	6.44	82.11	13.82	3.2272E-06	9.707E-06		
Other #2		26.91	70.09	12.43	1.5798E-05	4.509E-05		
Other #5		5.89	84.27		2.8759E-06		*Don't trust this one.	
Second Extract						Chloro Conc		
Molarity	NMR#	Area Duro		Area Chlor		Duro mol/ml		
1M	2a	0.08		1.08		1.543E-06		
1.5M	4a	10.64		91.67		2.418E-06		
Started with 2.4302E-4 mol/ml 23Pent. 2mol 23P-> 1 mol Duro						0.0001215	mol/ml duro 100% yld	
(97% Solution)			Chloro	MeOH		Solution is 0.7ml		
			Yield	Yield				
		3	0.0670393	0.1612082				
		2	0.1157464	0.2112706				
		4	0.124119	0.1963806				
		5	0.1141272	0.1138338				
Second Set of Experiments					meoh	chloro		
Molarity	NMR#	Area Duro	Area Meoh	Area Chlor	Conc Duro	Conc Duro		
1.5M	11	18.26	47.95	6.66	1.3058E-05	4.759E-05		
1M	12	6.28	78.64	11.48	2.7382E-06	9.496E-06		
2M	13	5.03	102.96	15.09	1.6751E-06	5.786E-06		
3M	14	9.51	102.55	19.14	3.1798E-06	8.625E-06		
	Chloro	Meoh						
	Yield	Yield						
11	0.559573	0.4605879						
12	0.1116472	0.0965865						
13	0.0680313	0.0590881		**Rxn Time of ABOUT 25 min.				
14	0.1014072	0.1121619						

Table D.2

Different 2,3-Pentanedione to Base Ratio Experiments (M8195 0.1M 001 - 0026, 8/5/95)

	From NMR peak integrations.					From GC peak integration.			
Exp 2.5:1		**Area Chloro**	**Area Duro**	**Area 23P**	**Mols Duro**	**Yield**			**GC 23P**
M81950.1M 001		78.79	17.02		3.4612E-06	0.038031			0.366
2		126.94	43.55		5.4971E-06	0.060401			1.01
3		53.03	17.37		5.25E-06	0.057358			
(9.5:1)									
M81950.01M004		94.51		71.55					1.175
5		38.05		34.32					0.998
6		173.15		116.27					1.093
7		180.49		79.78					0.913
8		108.53		58.76					0.826
9		106.4		69.93					0.86
10		129.72		52.04					
11		73.79		50.69					
12	1day	118.49		52.88					0.886
13	3 days	195.81		55.6					1.654
14	6 days	72.33		17.79					
15	straight	49.81		41.73					4.004
(5.86:1)									
M81950.1M016		0.67		65.3					
17		13.87		63.07					3.014
18		8.51		27.68					2.071
19		17.9		36.43					1.096
20		15.26		12.09					0.557
21		14.37							
22		18.41							
23		52.07	12.45		3.8311E-06	0.042095			
24		21.47	11.57		8.6346E-06	0.094875			0.272
25		47.85	23.72		7.94E-06	0.0868			
26		4.66		57.43					15.734

Table D.3

Low 2,3-Pentanedione to Base Ratios (M 8195 036 - 045, 8/16/95)

Amount of 23P 0.0485341 g/ml Use 1ml each time.

2,3-Pentanedione area from NMR spectra integral for CH3 peak.

Duroquinone peak integral at 1.69ppm is compared to choloform standard peak for concentration.

	NaOH Base Conc	23P Area	Duro Area	Chloro Are	Duro mols	Duro Yield
M81595036	strght	118.82		12.23		
M81595037	strght-heat	21.17		0.3		
M81595038	1M-heated		23.15	19.22	1.93E-05	0.106038
M81595039	1M		25.74	13.45	3.066E-05	0.1684807
M81595040	0.1M heat		17.49	11.54	2.428E-05	0.1334283
M81595041	0.1M		20.19	50.7	6.381E-06	0.0350584
M81595042	0.01M heat	12.21	12.21	19.63		
M81595043	0.01M	14.14				
M81595044	3M heated		120.66	95.49	2.025E-05	0.1112421
M81595045	3M		116.83	71.61	2.614E-05	0.1436298

		Table D.4					
Time and Heat Experimental Runs (15 - 20, h1 - h6, 6/1/95)							
Duroquinone yield based on peak integral compared to methanol and chloroform standards.							
	NaOH				**Chloro Conc**		
Time(min)	**Molarity**	**NMR#**	**Area Duro**	**Area Chloro**	**Duro mol/ml**	**Yield**	
1	1.5M	15	13.29	68.04	4.0686E-06	0.0334865	
3	1.5M	16	13.93	92.77	3.1277E-06	0.0257426	
5	1.5M	17	14.84	56.65	5.4566E-06	0.04491	
10	1.5M	18	16.12	56.34	5.9598E-06	0.0490521	
20	1.5M	19	18.53	48.75	7.9175E-06	0.0651644	
30	1.5M	20	21.82	55.95	8.1234E-06	0.0668597	0.0001215
Heated Runs							
					MeOH Conc	**Chloro Conc**	
Molarity	**NMR#**	**Area Duro**	**Area Meoh**	**Area Chlor**	**Duro mol/ml**	**Duro mol/ml**	
1M	h1	32.9	62.84	10.99	1.7952E-05	5.196E-05	Heat at 50C
1.5M	h2	2.49	33.14	4.85	2.5763E-06	8.912E-06	
3.M	h3	2.3	26.43	5.08	2.9839E-06	7.859E-06	
1M	h4	2.19	35.86	5.67	2.0941E-06	6.704E-06	Heat at 80C
1.5M	h5	5.01	85.91	14.01	1.9996E-06	6.207E-06	
3M	h6	5.64	102.75	14.48	1.8821E-06	6.761E-06	
		Chloro	**Meoh**				
		Yield	**Yield**				
	1M	0.610982	0.6332279	*Wrong integral for duro peak			
	1.5M	0.1047823	0.0908756				
	3M	0.0924048	0.1052522				
	1M	0.07883	0.0738642				
	1.5M	0.0729844	0.0705333				
	3M	0.0794952	0.0663892				

			Table D.5				
		Time Experiments (T1 - T21, 7/24/95)					
Time experiments using 0.1M NaOH/H20							
At allotted time, add stoichiometric amount of HCl.							
Ratio 23P to base:		**2.5:1**					
NMR:				**Singlet**			
Time (min)	**Number**	**areaCHCl3**	**area duro**	**area 23P**			
1	t1	75.61		22.68			
3	t2	40.31		6.44			
5	t3	46.81					
10	t4	47.74		**mols duro**	**Yield**		
15	t5	85.03	20.95	4.28E-06	0.0503488		
20	t6	105.42	35.05	5.77E-06	0.0679426		
25	t7	13.79	9.14	1.15E-05	0.1354439		
30	t8	17.71	5.18	5.08E-06	0.0597707		
night	t10	1.62	1.69	1.81E-05	0.2131813		
7/26/95							
Use solution of 0.019026 g/ml made on 7/12/95.							
Use 0.5ml, or 9.502e-5 mols.							
Add 0.5ml 0.01M NaoH, 5e-6 mols.				**Ratio=**	**19.004**	**23P to base**	
Add 0.5ml 0.01M HCL to stop reaction							
Time experiments							
		GC Results: (aqu)		**NMR Results: (Dtol)**			**GC+NMR**
Time (Min	**Number**	**Conc 23P**		**Area Chlor**	**Area 23P**	**Area Duro**	**Recovery**
ASAP	t11	2.281		19.52	16.98	None	120.2
1	t12	1.359		93.79	72.32		71.8
2	t13	1.672		83.63	45.73		88.1
3	t14	1.772		73.41	50.61		93.4
10	t16	1.583		95.88	59.47		83.5
15	t17	1.499		111.04	82.62		79.1
20	t18	1.425		133.12	88.79		75.2
30	t19	1.45		128.39	85.93		76.5
50	t20			90.43	75.31		36.5
24hrs	t21	2.684		108.29	34.48		141.2
	straight	13.448		90.35	63.13		
	no reaction						

Table D.6

Conversion of 2,3-Pentanedione to Duroquinone

Dropwise Experiments (100 - 127, 1/14/96)

Calculate amount of 2,3P in each solution:							
				Ratio of 2,3P to base:			
5%	0.0004853	mol/ml		5%	0.4852716		
2.50%	0.0002432	mol/ml		2.50%	0.2432275		
1%	9.841E-05	mol/ml		1%	0.0984065		
0.50%	4.851E-05	mol/ml		0.50%	0.0485097		
				duroquinone formed (g)	**duroquinone form(mols)**	**Fractional yield**	**Extraction Corrected**
Run #	**%23Pent**	**Notes...**					
100	5	overnight		0.0183	0.00011145	0.0918656	0.1010522
101	5	1 hr, neutralize, NMR		0.0585	0.00035627	0.2936688	0.3230357
102	2.5	overnight		0.0094	5.7247E-05	0.094146	0.1035606
103	2.5	1 hour, neutralize		0.0302	0.00018392	0.3024692	0.3327161
104	1	overnight		0.0017	1.0353E-05	0.0420835	0.0462919
105	1	1 hour, neutralize		0.0091	5.542E-05	0.2125194	0.2337713
106	0.5	overnight NMR		0.0011	6.6991E-06	0.0552397	0.0607636
107	0.5	1 hour, neutralize		0.0059	3.5932E-05	0.2057538	0.2263291
108	5	2 hrs		0.0318	0.00019367	0.1596354	0.1755989
109	2.5	2 hrs		0.0108	6.5773E-05	0.1081678	0.1189846
110	5	10 min		0.0257	0.00015652	0.1290135	0.1419148
111	2.5	1 hr		0.0163	9.9269E-05	0.1632532	0.1795785
112	1	2 hrs		0.0065	3.9586E-05	0.1609075	0.1769983
113	0.5	2 hrs		0.0038	2.3143E-05	0.1908279	0.2099107
114	1	1 hr		0.0101	6.151E-05	0.2500256	0.2750281
115	5	30min		0.039	0.00023752	0.1882492	0.2070742
116	5	1 hr		0.0376	0.00022899	0.1887512	0.2076264
117	2.5	10 min		0.0143	8.7089E-05	0.1432222	0.1575444
118	0.5	1 hr		0.0029	1.7661E-05	0.1456318	0.160195
119	0.5	10 min		0.0018	1.0962E-05	0.0821747	0.0903922
120	1	30 min		0.00271	1.6504E-05	0.0670861	0.0737947
121	2.5	30 min		0.0163	9.9269E-05	0.1632532	0.1795785
122	0.5	30 min		0.0039	2.3752E-05	0.1958497	0.2154346
123	1	10 min		0.0074	4.5067E-05	0.1831871	0.2015058
Dripping Rate Runs							
124	5	1 min drip, 30 min		0.0308	0.00018758	0.1546154	0.1700769
125	5	3 min drip, 30 min		0.0398	0.00024239	0.1997952	0.2197747
126	5	5 min drip, 30 min		0.034	0.00020706	0.1706793	0.1877472
		10min drip, 40 min				0.1882492	0.2070742
127	5	19 min drip, 30 min		0.0257	0.00015652	0.1240514	0.1364566

APPENDIX E

Table E.1

2-Ethyl-3-Methyl Pyrazine Yield Calculation (4, 8/6/96)

Based on amount of 2,3-pentanedione (23P), calculate stoichiometric amounts of other species:

9.7213 g 23P *0.97 purity/100.12 g/mol *2mol water/1mol 23P*18 g/mol = 3.39 g water possible

9.7213 g 23P*0.97 purity/100.12 g/mol*124 g/mol = 11.679 g 2-ethyl-3methyl dihydropyrazine possible

9.7213g 23P *0.97 purity/100.12 g/mol* 60.1g = 5.66 g ethylenediamine needed

9.7213g 23P*0.97 purity/100.12 g/mol *122 g/mol = 11.490 g 2-ethyl-3-methyl pyrazine

Actually Used: See Notebook for Further Details.

ethylendiamine: 5.8910 g measured, needed 5.66, 0.231 g excess ethylenediamine

Weight flask: 69.3665 g

Weight stir bar: 1.7181 g

React and rotovap off ether, 64.8260 g in flask - 52.2932 tare weight = 12.5328 g Product

Cold trap in rotovap set up contained yellow chemical, so inject into GC.

GC Results: 11.0298 g/L 2-ethyl-3-methyl pyrazine in trap*19.95ml soln/1000ml = 0.220 g Product

So, formed 12.7528 g product

From GC integration, 710.01 g/l dihydro*13.390ml/1000ml=9.508g dihydropyrazine

9.728g /11.679 g = 0.8335 Fractional Conversion of 2-ethyl-3-methyl dihydropyrazine

Remove 0.515 g product,left with 12.0178g product (0.515g*.833 = 0.4289g dihydro removed)

Oxidation Step:

12.0178g dihydro/124g/mol*3mol CuO/1mol dihydro*79.84 g/mol*.98 purity = 22.7494 g CuO needed

12.0178 g dihydro/124 g/mol *56.11 g/mol = 5.438 g KOH needed.

Actually used an excess of CuO of 0.4311 g and a KOH excess of 0.036 g

Oxidize and filter, From GC integration,

109.457 g/l pyrazine*76 ml /1000 ml = 8.318 g pyrazine formed

8.318/11.490 g = 0.724 Pyrazine Yield

Table E.2

2-Ethyl-3,5-Dimethyl Pyrazine Yield Calculation (1, 8/6/96)

***This procedure gives a mixture of 2-ethyl-3,5-dimethyl pyrazine and 3-ethyl-2,5-dimethyl pyrazine.**

Based on the amount of 2,3-Pentanedione used, calculate stoichiometric amounts of other species:

14.9911 g 23P/100.12 g/mol *.97 purity *137 g/mol = 19.8977 g pyrazine possible
14.9911 g 23P/100.12 g/mol *.97 purity *139 g/mol = 20.18827 g dihydropyrazine possible
14.9911g 23P/100.12 g/mol*.97 purity*74.13 g/mol = 10.766 g propylenediamine needed
14.9911 g 23P/100.12 g/mol*.97 purity*2mol water/1mol 23P*18g/mol = 5.2286 g water possible

Actually used 11.006*.99 purity = 10.8959 g, excess of 0.12934 g
React following described procedure, evap off ether

Formed 22.0971 g product
From GC integration, 688.25 g/l dihydro *27.4551 ml/1000ml = 18.8962 g dihydro formed

Yield dihydro is 18.8962/20.18827 = 0.936

Oxidation Step:

18.8962 g dihydro/139 g/mol *3mol CuO/1 mol dihydro *79.84 g/mol *.98 purity =31.734 g CuO needed
18.8962 g dihydro /139 g/mol *56.11 g/mol = 7.6278 g KOH needed

Actually Used: 35.1526 g CuO, 8.0842 g KOH Excesses of 3.4186 g CuO and 0.4564 g KOH

From GC integration, 115.40 g/l * 150 ml/ 1000ml = 17.311 g pyrazine formed

17.311/19.8977 = 0.87 Fractional Yield of Pyrazine

Table E.3

2-Ethyl-3-Methyl Quinoxaline Yield Calculation (2, 7/31/96)

Calculate stoichiometric amounts of speciess based on 2,3-Pentanedione

7.0080 g 23P/100.12 *.97 purity *181.1 g/mol = 12.296 g o-phenylenediamine needed

7.0080 g 23P/100.12 *.97 purity*2 mol water/ 1mol 23P * 18 g/mol = 2.44 g water possible

7.0080 g 23P/100.12 *.97 purity*172 g/mol = 12.0393 g 2-ethyl-3-methyl quinoxaline possible

Actually Used 12/3200 g phenylenediamine, excess of 0.024 g

56 ml MeOH * 0.79 g/ml = 44.24 g methanol used

Rotovap off water and methanol.

67.1420 - 55.290 = 11.852 g quinoxaline formed

11.852/12.0393 = .98 Fractional yield of quinoxaline fomred

Yield is based on weight, not GC like pyrazines. Confirmed by NMR spectra.

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