Synthesis, copolymerization and characterization of novel n-substituted phenyl maleimides

Victor Vandell
SYNTHESIS, COPOLYMERIZATION AND CHARACTERIZATION

OF NOVEL

N-SUBSTITUTED PHENYL MALEIMIDES

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I. ABSTRACT

Six target N-substituted maleimides were synthesized using a modified synthetic procedure. The six target maleimides synthesized and their yields were N-phenyl maleimide (40.8%), p-Chloro maleimide (33.3%), m-Nitro maleimide (59%), p-Methoxy maleimide (11.5%), p-Nitro maleimide (53.9%), and the Fast Garnet Azo Dye maleimide (2.2%). Of these six maleimides the m-Nitro and Fast Garnet derivatives are novel compounds.

Three of the maleimides were copolymerized with styrene to show that these N-substituted maleimides can be incorporated into a polymer backbone. The three maleimides polymerized with styrene were the p-Chloro, m-Nitro, and Fast Garnet derivatives. Percent incorporation of maleimides into the subsequent copolymers was calculated to be 34%, 33%, and 23% respectively.

Computer aided modeling through the program Computer Aided Chemistry (CaChe™) was also conducted. Dihedral rotational energy plots and optimized geometric conformation data was compiled and reported as unpublished results. This data was offered as a foundation for future work with this reaction system.
II. INTRODUCTION

Maleic Anhydride [1] and the chemistry which can be performed upon it has been of great interest to researchers for more than one hundred and seventy years. Maleic anhydride's multifunctionality makes it a prime candidate as a precursor for many more complex molecules. Not surprisingly there are many uses for maleic anhydride and it's derivatives. N-substituted maleimides have been used successfully as insecticidal and fungicidal agents. They have been used as cottonseed preserving agents and as modifying agents for the synthesis of rubber products1. Maleimides have been also studied for anticancer activity. Brookes and Lawely2 reported the cytotoxic activity of maleimides, resulting from it's imide functionality. The imido carbonyl group is nucleophilically attacked by the 7-position nitrogen of guanine. Acylation at this particular site causes mis-matching of nucleotide base pairs, which ultimately stops cell growth. The mechanism for these types of reactions are similair
to that of the nitrogen mustards which are currently being used as antitumor reagents\textsuperscript{2}. N-substituted maleimides are currently used as blocking agents which prevent crosslinking of sulfur groups in protein folding. This ultimately renders tumor cells more sensitive to irradiation.

Imides in general have been one of the primary monomers used in a variety of polymerization reactions for years. Polyimides are characterized by their oxidative, hydrolytic and thermal stability. They have been researched and developed industrially for a variety of engineering applications such as high strength composites, molding composites, and adhesives\textsuperscript{3}. Polymers of this nature are generally made with main chain imides rather than maleimides. Some of the more commonly known uses are the synthesis of resins, deemulsifying reagents, adhesives and various copolymers. A multitude of derivatives of maleic anhydride have been synthesized, ranging from reactions at the olefinic ethylene site to yield benzylsuccinic anhydride\textsuperscript{4} \cite{2} to nucleophilic attack upon the carbonyls to yield N-phenyl maleimide\textsuperscript{5} \cite{3}. The latter type of compound is of great interest to
our group and is thus the topic of our study.

The work which pioneered the synthesis of maleimides was that of N.E. Searle\textsuperscript{6} in 1948. Searle reported the dehydration of the maleamic acid \textsuperscript{4} to the maleimide in the presence of acetic anhydride and sodium acetate at temperatures of 150 °C.

This work was later followed by P. O. Tawney et. al.\textsuperscript{7} who reported, in 1960, the pyrolytic decomposition of phthalimide to the maleimide. Tawney's work also reported the synthesis of several types of N-substituted maleimides, via nucleophilic displacement reactions performed on maleimides, in which the nitrogen contained a fairly good leaving group (e.g. methoxy, acetyl, etc.). More notably this work presented the copolymerization of the maleimides with monomers like styrene,
methyl methacrylate, vinyl chloride, and isobutylene. The olefinic carbon bond of the maleimide is highly reactive to vinyl monomers in free-radical initiated polymerizations. In fact, the reactivity of the maleimide olefinic bond is so high that, unlike maleic anhydride, the maleimide was found to undergo homopolymerization [5]. From the series of polymerization reactions run by Tawney, the monomer reactivity ratios of maleimide and styrene were assigned as 0.02 and 0.05 respectively. These values were supported by Mayo and Walling who initially conducted studies on systems similar to that of Tawney. The reactivity ratios suggested that the copolymeric system displayed an alternating pattern.

The more commonly used strategy for maleimide synthesis, with various modifications, was that of Searle. The synthesis of N-phenyl maleimides was started by the formation of the maleanilic acid [6] precursor. Nucleophilic attack by an amine or an amine derivative was reported to produce the ring-opened product in relatively high yields (93%-97%) [5]. Subsequent dehydration of the maleanilic acid in acetic anhydride along with sodium acetate
reportedly gave the crude ring-closed maleimide product in good yields (75%-80%)\textsuperscript{5}. It has been reported that the synthesis of the unsubstituted N-phenyl maleimide goes towards completion with little or no production of isomers. Two probable mechanisms for this overall process can be viewed in Scheme 1 and Scheme 2.

The objective of this project was to develop a synthetic route to N-substituted maleimides. In the literature there has been many reported procedures for the synthesis of maleimides. These methods were employed and modified in our study of the imidization of maleanilic acids. Various N-substituted anilines were used in our study to make a variety of known and novel maleimides. The large-scale synthesis of the known maleimides were reported as a one pot reaction. Isolation of the maleanilic acid was not part of the reported reaction procedure protocol.
Proposed Mechanism of Maleimide Formation (Scheme 1)

Aniline + Ether $\xrightarrow{25 \, ^\circ C}$ Maleic Anhydride 

$\text{N-Phenyl Maleimide} + 2 \text{CH}_3\text{CO}_2\text{H}$
Aniline

Proposed Mechanism of Maleimide Formation (Scheme 2)

Maleic Anhydride

H₂O

Maleic Anhydride

N-phenyl Maleamic Acid

Acetic Anhydride

N-phenyl Maleimide
It was our intent to isolate the maleanilic acids so as to monitor for possible electronic effects in maleimide formation. Several of the synthesized maleimides are subsequently copolymerized with styrene. These polymers will be later used in fluorescence probe studies.

A. Synthetic Routes To N-Substituted Maleimides

In the literature, Yang and Wang\textsuperscript{9} reported the synthesis of N-phenyl maleimide in Dimethylformamide (DMF) at 30 °C. This was a one pot reaction done in a constant temperature bath.

The synthesis of N-phenyl maleimide in relatively high yields (75%-80%) was reported by Cava et. al.\textsuperscript{5} The Cava procedure called for the use of the polar aprotic solvent, ether, at room temperature to synthesize the maleanilic acid. Subsequent formation of the maleimide was then performed in a large excess of acetic anhydride, along with sodium acetate acting as a catalyst.

From numerous attempts to synthesize various substituted N-phenyl maleimides following the Yang and Wang, or the Cava procedures, it seemed that maleimide formation was dependent
on the presence of bulky and/or electronically active groups. The formation of unidentified isomers prompted our group to take a closer look at the possibilities of electronic and steric effects which might affect the ring closure reaction. Various aniline derivatives were used to introduce the electronic and/or steric effects desired.

As stated earlier temperature control is very crucial in control of unwanted isomers, thus Tetrahydrofuran (b.p. 68 °C) was employed as the reaction solvent. The necessity of the sodium acetate was tested and found to offer no contribution to the success of the ring closure reaction. It was also observed that the sodium acetate was not necessary for maleimide formation, subsequently it was deleted from the reactant protocol. Finally, all of the ring closure reactions were refluxed in an acetic anhydride-THF solution for 24 hours as an attempt to assure further success of the reactions.

Up to this point, the procedures for maleimide synthesis were not very consistent nor applicable to the synthesis of substituted N-phenyl maleimides which were of interest to our
group. Studies on the electronic or steric effects of substituents on the phenyl ring and how they may or may not influence the dehydration step to form maleimides had also not been reported in the literature. **Therefore it was the intent of our group to investigate the formation and purification of substituted N-phenyl maleimides and find a straightforward way to synthetically produce them, and subsequently purify them.** The details to this investigation have been disclosed in full in the results and discussion section of this report. General background information, nomenclature, and spectroscopic characterization of maleimides has been reported in the introduction segment of this report.

**B. Synthetic Routes to Copolymers of Maleimides**

Maleimides are known for the highly reactive olefinic bond in the presence of a free radical initiator\(^7,10\). Copolymerization reactions of maleimides with vinyl monomers like styrene, methyl methacrylate, and vinylidene chloride were performed in an inert atmosphere. The reactions were heated anywhere from 70 to 90
°C in a variety of solvents and free radical initiators.

The copolymerizations of maleimide [7] and several vinyl monomers were performed by VanPaesschen and Timmerman\textsuperscript{10} at 75°C in cyclohexanone with azo-bis-isobutyronitrile (AIBN) as the free radical initiator. The reactions were performed in an evacuated sealed glass tube. The resultant polymers were precipitated in crude form from diethyl ether. The polymer was then recrystallized from tetrahydrofuran.

Tawney et.al.\textsuperscript{7} performed copolymerization reactions similar to Van Paesschen. This group however conducted the reactions in chlorobenzene at 90 °C in the presence of benzoyl peroxide.

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\text{N} \\
\text{O} \\
\end{array}
\]

Due to the high reactivity of the olefinic bond of N-substituted maleimides, copolymerization with a vinyl monomers are seemingly rapid. The N-substituted maleimides used in the literature were substituted with aliphatic chains no longer than five carbons or less. The method employed by our group is
similiar to the methods previously discussed. The reactions were run though, under a nitrogen blanket as opposed to the sealed glass tube as called for by the literature.10

C. **Nomenclature and Physical Properties**

Maleimide is the trivial name for a class of compounds that are members of the pyrrol family. The prefix "male" in the name maleimide is derived from it's precursor maleic anhydride (2,5-furandione). The root "imide" is representative of the carbonyl-nitrogen-carbonyl functionality. Maleamic acids, formed from the reaction of maleic anhydride with ammonia, primary, or secondary amines, are the ring-opened, acid precursors to maleimides. If the amine used to form the acid has aromatic character, then the ring-opened product is reffered to as maleanilic acid6 [6], while if an alkyl amine is used then the ring opened product is reffered to as a maleamic acid. Systematic naming of the ring-opened maleanilic acids calls for the assignment of the root of the name to the acid family. The stereochemical
orientation of the olefinic region (i.e. cis or trans orientation) of the molecule must also be taken into account. Hence, structure [4] would be named 1-N-phenyl-cis-butenedioic acid. If the phenyl ring is substituted with some substituent (e.g. chlorine, nitro, etc.) then brackets should be used between the "N" and the "cis" wording. For example, if p-chloroaniline were used to form the maleanilic acid it would be systematically named 1-N-[4-chlorophenyl]-cis-butenoic acid. Systematic naming of the maleimides is not such a straightforward task due to the nature of the imido ring formed. Assignment of the ring system to the pyrroline group was thus agreed upon\textsuperscript{11}; this also is used as the root name for the compounds. Thus compound [3], trivially named N-phenyl maleimide, would systematically be named 2,5-dioxo-1-N-phenyl-3-pyrroline. If the phenyl group is substituted, then brackets should be employed as described above to properly denote the fact.

N-phenyl maleimide is a brilliant yellow compound displaying needle-like crystals which melt at 90-91 °C. The liquid boils under 12 millimeters of pressure at 162.1 to 163 °C.\textsuperscript{8}
The N-substituted maleimides range in colors from white to red depending on the substituent on the phenyl ring. The melting points of these compounds are in the range of 90 °C to 165 °C. The substituted maleimides are soluble in most polar aprotic solvents such as tetrahydrofuran, dimethylsulfoxide, and dimethylformamide. They are also soluble in some protic solvents like methanol and ethanol. Recrystallization from various solvents such as cyclohexane, toluene, ethanol, and ethyl acetate can be achieved for most of the maleimides. All of the maleimides are highly insoluble in water, which in turn makes a good media for precipitation of the crude form of the maleimides. Sublimation of some of the maleimides can be achieved at temperatures of about 80 °C at reduced pressures, obtainable by standard vacuum equipment.

The nomenclature system used to name the maleimide-based copolymers follows standard IUPAC rules. The two monomers are bracketed and separated by a hyphen. Outside the brackets the term "co" is used to indicate that the polymeric system is heterogenous. For example, the product resulting from
the polymerization of styrene and m-nitro maleimide would be named Poly\{styrene-co-N-[3-nitrophenyl] maleimide\}.

Maleimide copolymers are generally white amorphous solids which do not soften below 400 °C. They are soluble in dimethylformamide, formamide, dimethyl sulfoxide, and pyridine. The copolymers are insoluble in water, the more polar alcohols, benzene, and butyl acetate.¹⁰

D. Spectroscopic Identification of Maleimides

Knowledge of the spectroscopic characterization of maleimides will be of great importance when reviewing the discussion section. The possible production of unwanted isomers as well as cis-trans conformational changes around the olefinic bond of the maleamic acid will be reviewed in depth within the discussion section of this report. The reference spectral assignments will aid in interpreting the collected spectral data and ultimately in determining the presence of unwanted side products.
D1. Infrared Spectroscopy

Maleimides are typically characterizable by infrared spectroscopy because of their multifunctionality. Imido symmetrical and asymmetrical carbonyl stretching frequencies are expected to be observed between the ranges of 1780-1760 cm\(^{-1}\) (weak) and 1720-1700 cm\(^{-1}\) (sharp, strong) respectively\(^{12,13}\). The cis olefinic carbon-hydrogen out-of-plane stretching frequency is expected to be observed at approximately 820 cm\(^{-1}\) strong and sharp in nature due to conjugation with carbonyl groups\(^{14}\). The aromatic carbon-hydrogen out-of-plane bending frequencies are typically observed between 675 cm\(^{-1}\) and 900 cm\(^{-1}\) and are generally strong in nature\(^{15}\). Aromatic carbon-hydrogen stretching bands can generally be observed between 3000 cm\(^{-1}\) and 3100 cm\(^{-1}\)\(^{15}\). The olefinic carbon-carbon stretching vibrations are generally affected by conjugation with aromatic systems and carbonyls\(^{16}\) and thus are observed in the range of 1625 cm\(^{-1}\) to 1650 cm\(^{-1}\).
Applying this information to a reference spectra\(^7\) of N-phenyl maleimide (Figure 1) from Sadtler Research, many of the expected functional group frequencies can be observed. The major absorption frequency in the reference spectra is that of the imido carbonyl asymmetrical stretching band at 1715 cm\(^{-1}\). The symmetrical band can also be observed at approximately 1775 cm\(^{-1}\). The carbon-nitrogen stretching vibrations can be observed at 1600 cm\(^{-1}\). This particular absorption results from the carbon-nitrogen imido ring symmetrical stretching. This absorption peak is a good indicator of the ring closure. The cis olefinic and aromatic out-of-plane carbon-hydrogen stretching frequencies appear at 800 cm\(^{-1}\) and 650 cm\(^{-1}\) respectively. And finally the aromatic carbon-hydrogen stretching frequencies are observed at approximately 3100 cm\(^{-1}\). The information obtained from Figure 1 serves as a good standard spectra to reference all of the maleimides synthesized in this project.

D2. Proton Nuclear Magnetic Resonance (NMR)

The use of proton NMR for structure elucidation is relatively
straight forward for most cyclic imides. Structural similarities between maleimides and maleic anhydride allow one to use maleic anhydride as a point of reference for theoretical predictions of the anticipated spectra. The cis protons of the olefinic carbons are a very good indicator of the cyclic imide. The overall symmetry of maleimides causes each of the olefinic protons to be indistinguishable from one another which suggest that an intense singlet would be observed. The olefinic protons of maleic anyhdrde are in fact observed as a singlet at 7.1 ppm\textsuperscript{18}. This information offers a reasonable approximation, +/- 0.4 ppm, of where the maleimides protons might be observed. The phenyl protons of maleimides are expected to be observed in the usual aromatic region, 7.0-8.0 ppm. Substituents on the phenyl ring are expected to affect the chemical shift of the aromatic protons relative to the type of substituent.

With the aid of computer simulations\textsuperscript{19} a theoretical spectrum of N-(p-methoxyphenyl) maleimide can be obtained to estimate the anticipated experimental spectrum (See Figure2). The actual spectrum of N-(p-methoxyphenyl) maleimide\textsuperscript{20} can be
viewed in Figure 3. As would be expected the olefinic protons are observed at 6.79 ppm. The aromatic protons are obviously shielded due to the p-methoxy group, but are well within the expected frequency range. It should be noted that the computer simulation offers a close approximation to the actual spectrum. This tool will be used as a theoretical foundation for the novel maleimides synthesized by our group.

The olefinic protons were used as a prime indicator of successful dehydration of the maleanilic acid to the maleimide. Proton NMR was used to detect the presence of the non equivalent olefinic protons of the maleanilic acid versus the equivalent olefinic protons of the maleimide. The protons of the former are reported to give two distinct doublets around 6.2-6.9 ppm, whereas the protons of the latter will give a singlet signal around 6.8 ppm. The reference spectrum of n-phenyl maleanilic (Figure 4) acid displays these two doublets 6.3 and 6.5 ppm. This can be compared to the reference spectra of the p-methoxy maleimide (Figure 3) for further comparison.
Figure 2: Computer NMR Simulation of N-(4-Methoxyphenyl) Maleimide
Figure 3: Proton NMR of N-(4-Methoxyphenyl) Maleimide
Figure 4: Proton NMR of N-Phenyl Maleanic Acid

**MALEANILIC ACID**

C₉H₇NO₃ Mol. Wt. 191.19 M. P. 180-190°C

Source: American Cyanamid Company, New York, N. Y.

- Filter bandwidth: 4000 cpm
- Sweep time: 250 sec
- Sweep width: 500 cpm
- Sweep offset: 156 cpm
- Spectrum amp: 80
- Integral amp: 80 (spec. amp. 6.3)

Conc. 60mg/0.5ml Dimethyl sulfoxide-Db

**ASSIGNMENTS**

- a 6.32 or b
- b 6.51 or e
- c 7.22
- d 7.61
- e 7.87
- f 2.52 DMSO-Db
- g

OH is unobserved
D3. Carbon 13 Nuclear Magnetic Resonance

As a further supporting source of spectral evidence, Carbon 13 NMR can be utilized. A distinct difference between the maleanilic acid and the maleimide compounds are carbonyl magnetic equivalences. This difference can be detected by Carbon 13 NMR. Theoretically it would be expected that the carbonyl carbons of the maleimide compounds would be magnetically equivalent due to the symmetry of the maleimide ring, therefore one peak would be observed in the NMR spectra. Conversely, the carbonyl carbons of the maleanilic acid precursor are not magnetically equivalent and thus should give two distinct peaks in the NMR spectra. The imide carbonyl range is reported at 185 ppm-170 ppm\(^{21}\), while the amide carbonyl and the carboxylic carbonyl ranges are reported at 168-175 ppm and 171-179 ppm respectively\(^{22}\). The olefinic carbons are expected to be among the more intense peaks observed in the carbon-13 spectra. Carbons of this nature are generally reported to give peaks in the range of

25
135-145 ppm. The olefinic carbons of maleic anhydride are reported at 136.6 ppm\textsuperscript{22}. This offers a point of reference of where one can expect to observe the olefinic carbons +/- 3 ppm. Matsumoto et. al.\textsuperscript{23} reports the carbonyl carbon peak assignments of N-(m-chlorophenyl) maleimide and N-(p-ethylphenyl) maleimide at 168.3 and 169.4 ppm respectively. The olefinic carbon peak assignments are 134.3 and 134.1 ppm respectively.

E. Characterization of Maleimide Copolymers

E1. Infrared Spectroscopy

The spectra expected for the copolymerization of styrene and N-substituted maleimides should be consistent with that of an overlayed infrared spectrum of styrene and the particular maleimide in question. One should observe a close analogy between the maleimide spectrum and the polymer spectrum. Van Paesschen and Timmerman\textsuperscript{10} reported the overlayed spectra of succinimide and polymaleimide and found close similarities between the two spectra. The absorption peaks of the maleimide
do not shift in wavenumber upon incorporation into the polymer network. The characteristic peaks in the copolymer spectra are expected to be found at 2915-2940 cm\(^{-1}\) (medium intensity,) and 1712 cm\(^{-1}\) (strong intensity) which are the styrene aliphatic carbon-hydrogen bonds and the imide asymmetric carbonyl bonds respectively. An additional carbon-hydrogen aromatic stretch is expected to be observed at approximately 3020 cm\(^{-1}\), due to the aromatic ring of styrene. A 1600 cm\(^{-1}\) peak should also be observed. This can be attributed to the C-N ring stretching.

Tawney et.al.\(^7\) reported the co-polymerization of n-phenyl maleimide with styrene as producing a white powder which softens above 400 °C. The reactivity ratios for this same co-polymer system was found to be 0.02 and 0.05 for n-phenyl maleimide and styrene respectively. Based on the calculated reactivity ratios it was postulated that the monomers would tend to alternate in the copolymer. This same conclusion was also drawn by Van Paesschen and Timmerman.

**E2. Elemental Analysis**

The elemental analysis obtained for the styrene-maleimide
copolymers should consist of a carbon, nitrogen, oxygen, and hydrogen percentage values. The presence of nitrogen, and oxygen would act as a definite indicator of the incorporation of the maleimide into the polymer.

Computational analysis can be performed to calculate the percent composition of the anticipated styrene-maleimide copolymer. This computation involves the calculation of the mole fraction composition of the carbon, nitrogen, oxygen, and hydrogen atoms in the styrene-maleimide copolymer. Calculated values which are close to the empirical values indicate the probability that the polymerization reaction proceeded without the occurrence of undesired side reactions. Values which are not close suggest the formation of side products.
III. EXPERIMENTAL

The experimental section of the report will be devoted solely to the reporting of experimental and spectral data collected. All of the spectral data was compiled into tables and categorized based on the type of analysis being conducted. The infrared and elemental analysis data for a particular compound was reported at the end of each synthetic section for that compound.

Characterization of all compounds was performed using various analytical and spectrophotometric techniques. Thin Layer Chromatography (TLC) was performed using Kodak Silica Gel Chromatography paper using either a benzene-methanol mixture (65%-35%) or a benzene-ethanol solvent system (65%-35%). Infrared spectroscopy was performed using Perkin-Elmer Models 1760 and 1600 FTIR Spectrophotometers. Solids were analyzed in potassium bromide pellets (Aldrich Chemical Co.). The position of absorption peaks are reported in reciprocal centimeters. The abbreviations used to describe the absorption peaks are defined as follows: s=strong, m=medium, w=weak, vw=very weak, b=broad. Nuclear Magnetic Resonance measurements were
performed using a Varian XL 300 Spectrometer. The proton spectra analysed with the Varian were recorded at a frequency of 299.9 MHz and the carbon spectra were recorded at a frequency of 75.4 MHz. Tetramethysilane (TMS) was used as the internal standard. The samples were run in the following deuterated solvents obtained from Aldrich Chemical Company: chloroform, methanol, dimethylsulfoxide. The chemical shifts are reported in ppm from TMS. All corrected chemical shift values are based on the reported deuterated solvent values used to run the samples. The reference chemical shift values of the deuterated solvents were obtained from Spectrometric Identification of Organic Compounds by Silverstein, Bassler, and Morrill.\textsuperscript{24} The abbreviations used to describe the multiplicity of the signals are described as follows: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. All melting points were obtained from a standard melting point apparatus and are uncorrected. Rotovaping of samples was performed using a Buchi 461 waterbath-rotovapor. Elemental analysis of all compounds was performed by Baron Consulting Company, Orange Connecticut. The oxygen content in
the samples was determined by difference calculations. All reagents were ordered from Aldrich Chemical Co. and used as obtained unless otherwise specified.

A. Synthesis of Maleanilic Acid Precursors:

A1. Synthesis and Isolation of 1-N-phenyl-cis
butenoic acid

To a 1000 ml three neck round bottom flask was added 23.371 g (0.238 moles) of crushed maleic anhydride, and 500 ml of toluene. The solution was stirred for 20 minutes until all of the maleic anhydride dissolved into solution. To this solution was added dropwise, 21.68 ml (0.238 moles) of aniline via an addition funnel. The solution was continually stirred during this entire process. After 15 minutes the solution became a slurry and a yellowish-white precipitate was measured. After 30 minutes the solution was vacuum filtered.

Commonly known as N-phenyl maleanilic acid, the melting point of this yellowish-white solid was measured at 201-203 °C. From this 0.24 molar scale reaction was collected 36.13 g (79.41%
crude product yield) of soft powdery solid. Spectral Analysis:
Infrared: Aromatic C-H 3020 (S), Amide Carbonyl 1712(S),
Carboxyl Carbonyl 1599(M);

A2. Synthesis And Isolation of

1-N-[4-chlorophenyl]-cis-butenoic acid

(N-[p-chlorophenyl] maleanilic acid)

The following procedure was typical of the synthetic method
used to synthesize all of the maleanilic acids.

12.23 g (0.0958 moles) of p-chloro aniline was added to 80
mL of diethyl ether. The solution was allowed to stir at room
temperature until most of the p-chloro aniline dissolved into the
ether. To a three neck, 500 mL round bottom flask was added
300 mL of ether and 9.40 g (0.0959 moles) of maleic anhydride.
The solution was allowed to stir at room temperature (25 °C) until
all of the maleic anhydride dissolved into solution. The round
bottom flask was equipped with a thermometer, an addition
funnel, and a condensor. The p-chloro aniline-ether solution was
added to the addition funnel. This solution was slowly dripping
into the stirred solution of maleic anhydride dissolved in ether. All of the undissolved p-chloro aniline was dissolved by an additional 50 mL of ether. Upon addition of three quarters of the p-chloro aniline solution a yellow precipitate was measured. The reaction solution was continously stirred until all of the p-chloro aniline solution was added. The yellow precipitate was collected by vacuum filtration. 18.86g (86.7% crude product yield) was collected and air dried. The measured melting point of the N-phenyl (4-chloro) maleanilic acid was 200-201 °C. Spectral analysis: Proton NMR, Infrared: See Table 1.

**A3. Isolation of**

**1-N-[3-nitrophenyl]-cis butenoic acid**

Commonly known as N-(3-nitrophenyl) maleanilic acid, 27.60g, 0.118 moles (94% crude product yield) of a yellow solid was collected from two percpipatations from the reaction solution. The melting point was measured at 204-206 °C. Spectral analysis: Proton NMR, Infrared: See Table 2.
A4. Isolation of

1-N-[4-methoxyphenyl]-cis butenoic acid

More commonly known as N-(4-methoxyphenyl) maleanilic acid, 36.07 g, 0.164 moles (65.1% crude product yield) of this yellow solid was collected. The measured melting point was 188-190 °C. Spectral analysis: Proton NMR, Infrared: See Table 3.

A5. Isolation of

1-N-[4 nitrophenyl]-cis butenoic acid

Known commonly as N-(4 nitro phenyl) maleanilic acid, this particular species did not precipitate out of solution at room temperature. Rotovaping at 50 °C under vacuum to strip off all of the ether resulted in the collection of a dark yellow solid, 22.845 g 0.097 moles (77.4% crude product yield). It should be noted that 4-nitro aniline (Aldrich Chemical Co.) is only slightly soluble in diethyl ether. The measured melting point of the N-(4 nitro phenyl) maleanilic acid was 202-203 °C. Spectral Analysis: Proton NMR, Infrared: See Table 4.
A6. Isolation of

1-N-[2',3 dimethyl azo benzene]-cis butenoic acid

The synthesis of this novel compound, descriptively named Fast garnet maleanilic acid, was performed following the same procedure as that of all the maleanilic acids. Unlike the other maleanilic acid compounds synthesized, the fast garnet maleanilic acid required further purification before it could be subjected to the next synthetic step. Solubility of the fast garnet into diethyl ether was found to be somewhat less than that of all the other aniline derivatives. Upon slowly adding the somewhat partially dissolved aniline to the stirred maleic anhydride solution, it was measured that it would not stay fully in solution. Once all of the fast garnet-ether solution was added, the solution was quickly vacuum filtered. Slow recrystallization of the product resulted after letting the solution sit at 25 °C. The precipitate, reddish-yellow in color, was collected by vacuum filtration. The precipitate was then redissolved into ether. This was followed by bubbling ammonia gas through the solution for 30 minutes. A yellow precipitate was measured and collected by vacuum
filtration, 24.44g, 0.076 moles (60.3% crude product yield). The melting point of the Fast garnet maleanilic acid was measured at 141-142°C. Spectral analysis: Proton NMR, Infrared: See Table 5.

B. Synthesis of Substituted N-Phenyl Maleimides:

B1. Preparation of 2,5-dioxo-1-phenyl-3-pyrroline

This synthesis follows the procedure reported by Yang and Wang. It is a low temperature, one pot reaction which converts the maleanilic acid to the maleimide.

To a 50 ml 2-neck round bottom flask containing 5 ml of Dimethyl formamide (DMF) was added 3.01 ml (0.033 moles) of aniline. The flask was placed in a 20 °C water bath. The solution was stirred for 5 minutes. 3.45 g (0.0352 moles) of maleic anhydride was crushed and split into three portions. These portions were added in 10 minute intervals to the anilin/DMF solution. A white slurry was measured precipitating out of solution. Once all of the maleic anhydride was added the solution
was allowed to stir for an additional 20 minutes. The temperature of the water bath was bought up to 27 °C. To the reaction flask was added 3.75 ml of acetic anhydride and 0.27 g of sodium acetate. 10 minutes into the reaction, it was measured that the solution turned yellow in color. The reaction was run for a total of two hours.

The maleimide solution was poured into 200 ml of 0 °C water. A yellow precipitate was immediately formed. The solution was vacuum filtered and a yellow solid was obtained. The yellow solid was then recrystallized from 50 ml of warm cyclohexane. Bright yellow needle shaped crystal were formed and collected. 1.842 g (40.8 % yield of product) was collected. The measured melting point of the crystal was 90-92 °C. Spectral Analysis:

Infrared: Imide Carbonyl 1711.8(sym)(S) 1775(asym)(W),
Aromatic C-H 3089(M), Elemental Analysis:

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
<th>Oxygen</th>
<th>Chlorine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated %</td>
<td>69.40</td>
<td>4.10</td>
<td>8.10</td>
<td>18.50</td>
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<tr>
<td>Found %</td>
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<td>4.12</td>
<td>8.15</td>
<td>17.46</td>
<td>---------</td>
</tr>
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</table>
**B2. Preparation of**

**2,5-dioxo-1-[4-chlorophenyl]-3-pyrroline**

To a 500 mL three neck round bottom flask was added 120 mL of acetic anhydride, 7 grams (0.0308 mol) of N-(4-chloro phenyl) maleanilic acid, and 2 grams of sodium acetate (acting as a catalyst). Following the procedure of Cava et. al.\textsuperscript{5}, the solution was heated to 75 °C using a steam bath, while being continuously stirred under nitrogen using a magnetic stirrer. The reaction was heated for 2 hours and cooled down to room temperature. The cooled solution, yellow in color, was poured slowly into 0 °C water at pH 12. A yellow solid slowly precipitated out of solution. The solution was vacuum filtered and the yellow solid was collected. The product was dissolved in ether and extracted with 300 mL of water. The ether was evaporated off and the resulting yellow solid was air dried. The yellow solid was sublimed for 24 hours at 80 °C under vacuum, 2.15 grams (33.6% yield) of bright yellow needles were collected. The melting point of the yellow needles was measured at 117-118 °C. Spectral analysis: Proton NMR, Infrared, Carbon NMR: See Table 7, 8.
Elemental Analysis:

<table>
<thead>
<tr>
<th>Element</th>
<th>Calculated %</th>
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</thead>
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<td>Hydrogen</td>
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<tr>
<td>Nitrogen</td>
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<td>6.76</td>
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<tr>
<td>Oxygen</td>
<td>15.50</td>
<td>15.00</td>
</tr>
<tr>
<td>Chlorine</td>
<td>17.10</td>
<td>17.40</td>
</tr>
</tbody>
</table>

All of the remaining maleimides were prepared by the following procedure. This procedure in a modification of the Cava procedure. Isolation of the various maleimides was accomplished using different techniques. These techniques, along with the spectral data for each compound are discussed separately.

**B4. Preparation of**

**2,5-dioxo-1-[3-nitrophenyl]-3-pyrrole**

A three neck 500 mL round bottom flask was equipped with a drying tube, Soxhlet thimble extractor-condensor, and a thermometer. To the flask was added 250 mL of tetrahydrofuran (THF) and 100 mL of acetic anhydride. To the thimble was added 4.82 grams (0.0204 mol) of N-(3-nitrophenyl) maleanilic acid. The solution of THF and acetic anhydride was boiled (77-79 °C) allowing it to extract N-(3-nitrophenyl) maleanilic acid for 24
After 24 hours all of the N-(3-nitrophenyl) maleanilic acid was totally dissolved into the refluxing solvent system. It was then cooled down to room temperature.

The reaction solution of N-(3-nitrophenyl) maleimide was extracted with 1000 mL of brine. The reaction solution was then rotovaped of all solvent. A thick yellow slurry was observed. 50 mL of ethanol was added to the slurry; which resulted in a clear yellowish-brown solution. The ethanol solution was cooled to 0 °C resulting in the formation of white needle-like crystals. Several batches of the white crystals were collected and dried. 2.63 grams (59% yield) of the white needles were collected altogether. The measured melting point of the product was 123-125 °C.

Spectral analysis: Proton NMR, Infrared, Carbon 13 NMR: See Table 9, 10.

Elemental Analysis:

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
<th>Oxygen</th>
<th>Chlorine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated %</td>
<td>55.10</td>
<td>2.80</td>
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<td>29.40</td>
<td>--------</td>
</tr>
<tr>
<td>Found %</td>
<td>55.22</td>
<td>2.67</td>
<td>12.74</td>
<td>29.37</td>
<td>--------</td>
</tr>
</tbody>
</table>
B5. Isolation of

2,5-dioxo-1-[4-methoxy phenyl]-3-pyrroline

7.00 grams (0.0319 moles) of N-(4-methoxyphenyl) maleanilic acid were subjected to the ring closure reaction procedure reported above. The reaction solution was rotovaped of all the solvent resulting in a yellow oil. The oil was added to 50 mL of ethanol and stirred into 500 mL of 0 °C brine. A brownish-yellow precipitate was measured to recrystallize out of solution. The solid was collected by vacuum filtration. TLC of the solid, to test for purity, confirmed the presence of unreacted N-(4-methoxyphenyl) maleanilic acid. The remaining filtrate was cooled to 10 °C for several hours and a second batch, 0.745g, 0.00373 moles (11.5% yield) of the product was collected. TLC confirmed the absence of unreacted N-(4-methoxy phenyl) maleanilic acid. The measured melting point of the second batch of crystals was 148-149 °C (literature 148-148.5 °C)\textsuperscript{25}. Spectral analysis: Proton NMR, Infrared, Carbon 13 NMR: See Table 11, 12.
Elemental Analysis:

<table>
<thead>
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<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
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<th>Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated %</td>
<td>65.10</td>
<td>4.50</td>
<td>6.90</td>
<td>23.70</td>
</tr>
<tr>
<td>Found %</td>
<td>64.62</td>
<td>4.55</td>
<td>6.92</td>
<td>23.91</td>
</tr>
</tbody>
</table>

**B7. Isolation of**

**2,5-dioxo-1-[4-nitrophenyl]-3-pyrroline**

3.00 g (0.0128 moles) of N-(4-nitrophenyl) maleanilic acid were subjected to the ring closure reaction. All of the solvent was rotovaped off resulting in a yellow oil. The oil was dissolved into 50 mL of n-propanol. The propanol was cooled to 0 °C and left sitting for 24 hours in the freezer. A yellow percpipitate was measured. The solid was collected by vacuum filtration and dried under vacuum. 1.499 grams (53.9% yield) of a golden-flakey solid was collected. The melting point was measured at 160-161 °C (literature 162-165°C)\(^2\). Spectral analysis: Proton NMR, Infrared, Carbon NMR: See Table 13, 14.
Elemental Analysis:

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
<th>Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated %</td>
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<td>2.80</td>
<td>12.90</td>
<td>29.40</td>
</tr>
<tr>
<td>Found %</td>
<td>54.49</td>
<td>2.72</td>
<td>12.63</td>
<td>30.16</td>
</tr>
</tbody>
</table>

**B8. Isolation of**

**2,5-dioxo-1-[2,2'-dimethyl azo benzene]-3-pyrroline**

17 g. (0.0528 moles) of Fast garnet maleanilic acid was subjected to the maleimide formation reaction. The resulting THF solution was extracted with 1000 mL of brine. The washed THF solution was rotovaped down to a red oil. After adding 50 mL of anhydrous ethanol to the oil, and mixing with 200 mL of 0 °C brine, an orange precipitate resulted. The orange precipitate was vacuum filtered and allowed to sit in a vacuum oven at 30 °C for several days. A deep red amorphous solid was measured.

The amorphous solid was dissolved in 50mL of anhydrous ether per 3 grams of product. It should be noted that approximately 5% of the unreacted Fast Garnet maleanilic acid will fall out of the ether because of it’s limited solubility. TLC
confirmed the presence of the desired product with a residual amount of unreacted maleanilic acid. The ether-insoluble maleanilic acid was filtered off and discarded in an effort to sacrifice yield for purity. The filtered ether solution was then subjected to column chromatography. Silica gel (Aldrich Chemical Co.), approximately 7 grams, was slurry packed with cyclohexane/1,4 dioxane (65%/35%) into a 65 mm x 45 mm (dia.) column. The eluting solvent was the same as the solvent system used to pack the column. The solvent containing the product was evaporated down to 20 mL. This was then loaded onto the column. It was measured that there was some overlapping of bands. A dark red band migrated down the column and was collected. Several more bands were subsequently collected from the column. TLC of the aliquots collected from the column suggest that the first two aliquots contain the desired maleimide product. These fractions were combined and eluted through a second column of the same dimensions as described above. As a result of this procedure, two more fractions measured were collected, for which TLC analysis showed a small trace of unreacted maleanilic
acid. The aliquots were combined and rotovaped, resulting in a red oil. The oil was dissolved in hot cyclohexane and left to cool at room temperature. A fine, red, crystalline solid recrystallized out of solution. This was collected by vacuum filtration and dried overnight in a vacuum oven. The measured melting point of the Fast garnet maleimide was 99-100 °C. Spectral analysis: Proton NMR, Infrared, Carbon 13 NMR: See Table 15, 16.

Elemental Analysis:

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Nitrogen</th>
<th>Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated %</td>
<td>70.00</td>
<td>5.00</td>
<td>13.80</td>
<td>10.50</td>
</tr>
<tr>
<td>Found %</td>
<td>69.13</td>
<td>5.02</td>
<td>13.31</td>
<td>12.57</td>
</tr>
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</table>

C. Copolymerization of Maleimides with Styrene

C1. Synthesis of

Poly{styrene-co-N-[4-chlorophenyl] maleimide}

To a 50 mL three neck round bottom flask equipped with a condensor and two glass stoppers was added 1.1 mL (0.0096 moles) styrene, 0.2326g (0.00114 moles) N-[4-chloro phenyl]
maleimide, 15 mL (0.0096 moles) carbon tetrachloride (CCL4), and 0.0315 g (0.000192 moles) of Azobisisobutyronitrile (AIBN). The styrene was initially treated with molecular sieves for a period of 24 hours to purify it of inhibitors. The condensor was equipped with a rubber septa which was inserted an inlet syringe, and an outlet syringe. Argon gas was pumped through the inlet syringe at a low flow rate. The reaction vessel was saturated with the inert gas for 15 minutes. An oil bath was heated and held at a constant temperature of 85 °C. The reaction mixture was allowed to reflux in the oil bath overnight. It was measured after two hours of refluxing that a white cloudy solution resulted. At the completion of the reaction, the solution was cooled to room temperature. The solution was poured into 30 mL of reagent grade methanol and a white, hard, brittle solid precipitated out of solution. This was filtered and dried in a desiccator. Spectral analysis: Infrared: Imide carbonyl 1708 (asym)(S), 1774 (sym)(W), Aromatic C-H 3025 (M), 3046 (M), Styrene C-H2 2912 (M).
Elemental Analysis:

<table>
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<td>3.15</td>
</tr>
</tbody>
</table>

C2. Synthesis of Poly{styrene-co-N-[3-nitrophenyl] maleimide}

The same procedure for polymerization as described above was followed. The solvent system was changed for solubility reasons to 1,2-dichloroethane. 0.2166 g. (0.001067 mol.) of N-[3-nitro phenyl] maleimide, along with 1.1 ml (0.0096 mol.) styrene, and 0.0315 g (0.000192 mol.) of AIBN. The completed reaction solution was poured into 30 mL of methanol and a white powdery solid precipitated out of solution. The product was dried in a vaccume oven overnight. Spectral Analysis: Infrared: Imide carbonyl 1712(asym)(S), 1774(sym)(W), Aromatic C-H 3028(M), 3060(W), Styrene C-H2 2920(M)

Elemental Analysis:

<table>
<thead>
<tr>
<th>Element</th>
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<tbody>
<tr>
<td>Carbon</td>
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<tr>
<td>Hydrogen</td>
<td>5.12</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>6.40</td>
</tr>
<tr>
<td>Oxygen</td>
<td>15.51</td>
</tr>
</tbody>
</table>
C3. Synthesis of

Poly{Styrene-co-N-[2',3 dimethyl azo benzene] maleimide}

The same procedure as described in the polymerization reaction of styrene and N-[3-nitro phenyl] maleimide was followed. The reaction was performed at half the stoichiometric ratio as that of the previous reaction. 0.1605 g. (0.0005335 mol.) of Fast Garnet maleimide, 0.55 mL styrene, and 0.0157 g. AIBN were all refluxed in 10 mL of 1,2- dichloroethane. Upon precipitation of the reaction solvent with methanol, a orange powdery solid was measured. This was filtered and dried.

Spectral analysis: Infrared: Imide carbonyl 1712(asym)(S), 1815(sym)(M), Aromatic C-H 3025(M), Styrene C-H2 2912(S).

Elemental Analysis:

<table>
<thead>
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<th></th>
<th>Carbon</th>
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<th>Oxygen</th>
</tr>
</thead>
<tbody>
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<td>Found %</td>
<td>80.95</td>
<td>6.68</td>
<td>7.05</td>
<td>5.32</td>
</tr>
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</table>
IV. Results

The following tables are a compilation of all the results obtained for the maleanilic acids and maleimide compounds. These tables are composed of the spectral data, specifically the Proton NMR, Infrared, and Carbon 13 NMR, and physical data for all of the synthesized maleanilic acids and maleimides.

The Proton NMR data includes peak assignments, and a description of the peak appearance. A diagram of the compound relative to the spectral information being reported is also included. The type of NMR used along with the deuterated solvent in which the spectra was run is also reported.

The Infrared data includes the absorptions positions in reciprocal centimeters. Also reported was the intensity of the absorption peak.

The tables are numbered sequentially for each compound. The Proton NMR spectral data for each type of maleanilic acid compound (e.g. p-nitro, p-chloro) have been assigned a number and grouped together. The maleimide spectral information (i.e. Proton and Carbon 13 NMR) are also numbered sequentially and grouped together.
TABLE 1: N-(4-ChloroPhenyl) Maleanilic Acid

Proton NMR Data:

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<td>6.42</td>
<td>d</td>
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</tr>
<tr>
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<td>e</td>
<td>2.87</td>
<td>s (broad)</td>
<td>Amide</td>
</tr>
</tbody>
</table>

* 200 Mhz spectra
* Solvent: Acetone
* Spectral peak values adjusted by -0.43 relative to standard peak value of Acetone

Infrared Spectral Data:

<table>
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<tr>
<th>Functionality</th>
<th>Absorption cm⁻¹</th>
<th>Peak Description</th>
</tr>
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<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3076</td>
<td>Medium</td>
</tr>
<tr>
<td>Carboxyl Carbonyl</td>
<td>1702</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide Carbonyl</td>
<td>1635</td>
<td>Medium</td>
</tr>
<tr>
<td>Amide N-H</td>
<td>3291</td>
<td>Weak</td>
</tr>
</tbody>
</table>
TABLE 2: N-(3-NitroPhenyl) Maleanic Acid

Proton NMR Data:

Observed m.p.: 204-206 °C

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>6.42</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>6.72</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>c</td>
<td>8.77</td>
<td>s</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d,f</td>
<td>8.12</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>e</td>
<td>7.72</td>
<td>t</td>
<td>Aromatic</td>
</tr>
<tr>
<td>g</td>
<td>2.87</td>
<td>s (broad)</td>
<td>Amide</td>
</tr>
</tbody>
</table>

* 200 Mhz spectra
* Solvent: Acetone
* Spectral peak values adjusted by - 0.43 relative to standard peak value of Acetone

Infrared Data:

<table>
<thead>
<tr>
<th>Functionality</th>
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<th>Peak Description</th>
</tr>
</thead>
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<td>Aromatic C-H</td>
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</tr>
<tr>
<td>Carboxyl Carbonyl</td>
<td>1713</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide Carbonyl</td>
<td>1595</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide N-H</td>
<td>3276</td>
<td>Medium</td>
</tr>
<tr>
<td>Nitro (asym)</td>
<td>1351</td>
<td>Strong</td>
</tr>
<tr>
<td>Nitro (sym)</td>
<td>1525</td>
<td>Strong</td>
</tr>
</tbody>
</table>
TABLE 3: N-(4-MethoxyPhenyl) Maleanic Acid

Proton NMR Data:

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<tr>
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<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>6.32</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>6.65</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>c</td>
<td>6.91</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>7.57</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>e</td>
<td>4.78</td>
<td>s (broad)</td>
<td>Amide</td>
</tr>
<tr>
<td>f</td>
<td>3.81</td>
<td>s</td>
<td>Methoxy</td>
</tr>
</tbody>
</table>

* 300 Mhz spectra
* Solvent: Chloroform/Methanol

Infrared Data:

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<th>Peak Description</th>
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</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3074</td>
<td>Strong</td>
</tr>
<tr>
<td>Carboxyl Carbonyl</td>
<td>1705</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide Carbonyl</td>
<td>1625</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide N-H</td>
<td>3262</td>
<td>Medium</td>
</tr>
</tbody>
</table>
TABLE 4: N-(4-NitroPhenyl) Maleanilic Acid

Proton NMR Data:

![Chemical Structure]

Observed m.p.: 202-203 °C

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>6.42</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>6.56</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>c</td>
<td>7.81</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>8.16</td>
<td>d</td>
<td>Aromatic</td>
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<tr>
<td>e</td>
<td>10.84</td>
<td>s (broad)</td>
<td>Carboxylic</td>
</tr>
</tbody>
</table>

* 300 Mhz spectra

* Solvent: Dimethylformamide

Infrared Data:

<table>
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<th>Functionality</th>
<th>Absorption (cm⁻¹)</th>
<th>Peak Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3087</td>
<td>Medium</td>
</tr>
<tr>
<td>Carboxyl Carbonyl</td>
<td>1707</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide Carbonyl</td>
<td>1635</td>
<td>Medium</td>
</tr>
<tr>
<td>Amide N-H</td>
<td>3292</td>
<td>Medium</td>
</tr>
<tr>
<td>Nitro (asym)</td>
<td>1338</td>
<td>Strong</td>
</tr>
<tr>
<td>Nitro (sym)</td>
<td>1507</td>
<td>Strong</td>
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</tbody>
</table>
TABLE 5: Fast Garnet Maleanilic Acid

Proton NMR Data:

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Type</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>a</td>
<td>6.04</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>6.41</td>
<td>d</td>
<td>Olefinic</td>
</tr>
<tr>
<td>c</td>
<td>8.02</td>
<td>s</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>7.71</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>e</td>
<td>7.74</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>f</td>
<td>7.57</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>g</td>
<td>7.34</td>
<td>m</td>
<td>Aromatic</td>
</tr>
<tr>
<td>h</td>
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<td>i</td>
<td>7.32</td>
<td>d</td>
<td>Aromatic</td>
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<td>j</td>
<td>2.45</td>
<td>s</td>
<td>Methyl</td>
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<td>k</td>
<td>2.68</td>
<td>s</td>
<td>Methyl</td>
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</tbody>
</table>

* 300 Mhz spectra

* Solvent: Methanol

Infrared Data:

<table>
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<tr>
<th>Functionality</th>
<th>Absorption cm⁻¹</th>
<th>Peak Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3025</td>
<td>Medium</td>
</tr>
<tr>
<td>Carboxyl Carbonyl</td>
<td>1656</td>
<td>Medium</td>
</tr>
<tr>
<td>Amide Carbonyl</td>
<td>1584</td>
<td>Strong</td>
</tr>
<tr>
<td>Amide N-H</td>
<td>3189</td>
<td>Medium</td>
</tr>
<tr>
<td>Aliphatic C-H</td>
<td>2923</td>
<td>Medium</td>
</tr>
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</table>
### Table 6: Physical properties of Maleimides:

<table>
<thead>
<tr>
<th>Maleimide</th>
<th>Melting Point °C</th>
<th>Color</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-phenyl</td>
<td>90-91 *</td>
<td>Yellow</td>
<td>Ace, Eth, ethanol, DMSO, DMF, Meth, THF</td>
</tr>
<tr>
<td></td>
<td>91-92**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Chlorophenyl</td>
<td>117-118 *</td>
<td>Yellow</td>
<td>Ace, Eth, ethanol, DMSO, DMF, Meth, THF</td>
</tr>
<tr>
<td></td>
<td>117-118**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Nitrophenyl</td>
<td>124-125 **</td>
<td>White</td>
<td>Ace, Eth, ethanol, DMSO, DMF, Meth, THF</td>
</tr>
<tr>
<td>4-Methoxyphenyl</td>
<td>148-148.5 *</td>
<td>Yellow</td>
<td>Ace, Eth, ethanol, DMSO, DMF, Meth, THF</td>
</tr>
<tr>
<td></td>
<td>148-149**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Nitrophenyl</td>
<td>162-165 *</td>
<td>Golden</td>
<td>Ace, Eth, DMSO, DMF, THF, n-Prop, THF</td>
</tr>
<tr>
<td></td>
<td>160-161**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast Garnet</td>
<td>99-100 **</td>
<td>Auburn</td>
<td>Ace, Eth, ethanol, DMSO, DMF, Meth, THF</td>
</tr>
<tr>
<td>* Literature²⁵</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>** Observed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 7: N-(4-ChloroPhenyl) Maleimide

Proton NMR Data:

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>6.84</td>
<td>s</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>7.29</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>c</td>
<td>7.42</td>
<td>d</td>
<td>Aromatic</td>
</tr>
</tbody>
</table>

* 300 Mhz spectra
* Solvent: Chloroform

Infrared Data:

<table>
<thead>
<tr>
<th>Functionality</th>
<th>Absorption cm⁻¹</th>
<th>Peak Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3087</td>
<td>Medium</td>
</tr>
<tr>
<td>Imide Carbonyl (asym)</td>
<td>1717</td>
<td>Strong</td>
</tr>
<tr>
<td>Imide Carbonyl (sym)</td>
<td>1774</td>
<td>Weak</td>
</tr>
<tr>
<td>Olefinic C-H</td>
<td>1492</td>
<td>Weak</td>
</tr>
<tr>
<td></td>
<td>3117</td>
<td>Weak</td>
</tr>
</tbody>
</table>
TABLE 8: N-(4-Chlorophenyl) Maleimide

Carbon 13 NMR Data:

![Chemical Structure]

<table>
<thead>
<tr>
<th>Carbon</th>
<th>Peak (ppm)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>134.29</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>169.18</td>
<td>Imide Carbonyl</td>
</tr>
<tr>
<td>c</td>
<td>127.15</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>133.57</td>
<td>Aromatic</td>
</tr>
</tbody>
</table>

Observed m.p.: 117-118 °C  
Literature m.p.: 117-118 °C

* 300 Mhz spectra

* Solvent: Chloroform
TABLE 9: N-(3-NitroPhenyl) Maleimide

Proton NMR Data:

\[
\begin{array}{cccc}
\text{Proton} & \text{Peak (ppm)} & \text{Peak} & \text{Description} \\
\text{a} & 6.98 & s & \text{Olefinic} \\
\text{b} & 7.75 & d & \text{Aromatic} \\
\text{c} & 7.63 & t & \text{Aromatic} \\
\text{d} & 8.18 & d & \text{Aromatic} \\
\text{e} & 8.29 & s & \text{Aromatic} \\
\end{array}
\]

* 300 Mhz spectra
* Solvent: Chloroform

Infrared Data:

<table>
<thead>
<tr>
<th>Functionality</th>
<th>Absorption cm(^{-1})</th>
<th>Peak Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3102</td>
<td>Medium</td>
</tr>
<tr>
<td>Imide Carbonyl (asym)</td>
<td>1713</td>
<td>Strong</td>
</tr>
<tr>
<td>Imide Carbonyl (sym)</td>
<td>1777</td>
<td>Weak</td>
</tr>
<tr>
<td>Carbon-Nitro</td>
<td>795</td>
<td>Medium</td>
</tr>
<tr>
<td>Nitro (sym)</td>
<td>1525</td>
<td>Strong</td>
</tr>
<tr>
<td>Nitro (asym)</td>
<td>1351</td>
<td>Strong</td>
</tr>
</tbody>
</table>
**TABLE 10: N-(3-NitroPhenyl) Maleimide**

Carbon 13 NMR Data:

Observed m.p.: 123-125 °C

<table>
<thead>
<tr>
<th>Carbon</th>
<th>Peak (ppm)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>134.52</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>168.67</td>
<td>Imide Carbonyl</td>
</tr>
<tr>
<td>c</td>
<td>129.98</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>122.33</td>
<td>Aromatic</td>
</tr>
<tr>
<td>e</td>
<td>120.67</td>
<td>Aromatic</td>
</tr>
<tr>
<td>f</td>
<td>131.38</td>
<td>Aromatic</td>
</tr>
</tbody>
</table>

* 300 Mhz spectra

* Solvent: Chloroform
TABLE 11: N-(4-MethoxyPhenyl) Maleimide

Proton NMR Data:

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Peak</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>6.82</td>
<td>s</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>6.96</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>c</td>
<td>7.21</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>3.82</td>
<td>s</td>
<td>Methyl</td>
</tr>
</tbody>
</table>

* 300 Mhz spectra
* Solvent: Chloroform

Infrared Data:

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<th>Functionality</th>
<th>Absorption cm(^{-1})</th>
<th>Peak Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3097</td>
<td>Medium</td>
</tr>
<tr>
<td>Imide Carbonyl (asym)</td>
<td>1707</td>
<td>Strong</td>
</tr>
<tr>
<td>Imide Carbonyl (sym)</td>
<td>1769</td>
<td>Weak</td>
</tr>
<tr>
<td>Olefinic C-H</td>
<td>2953</td>
<td>Weak</td>
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</table>
**TABLE 12: N-(4-MethoxyPhenyl) Maleimide**

Carbon 13 NMR Data:

![Chemical Structure](image)

Observed m.p.: 148-149 °C  
Literature m.p.: 148-148.5 °C

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<tr>
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<th>Peak (ppm)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>134.29</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>169.17</td>
<td>Imide Carbonyl</td>
</tr>
<tr>
<td>c</td>
<td>129.79</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>133.58</td>
<td>Aromatic</td>
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<tr>
<td>e</td>
<td>127.15</td>
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<tr>
<td>f</td>
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<td>Methoxy</td>
</tr>
<tr>
<td>g</td>
<td>159.17</td>
<td>Aromatic</td>
</tr>
</tbody>
</table>

* Solvent: Chloroform
TABLE 13: N-(4-NitroPhenyl) Maleimide

Proton NMR Data:

![Chemical Structure]

Observed m.p.: 160-161 °C  
Literature m.p.: 162-165 °C

<table>
<thead>
<tr>
<th>Proton</th>
<th>Peak (ppm)</th>
<th>Peak</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>7.14</td>
<td>s</td>
<td>Olefinic</td>
</tr>
<tr>
<td>b</td>
<td>7.77</td>
<td>d</td>
<td>Aromatic</td>
</tr>
<tr>
<td>c</td>
<td>8.37</td>
<td>d</td>
<td>Aromatic</td>
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</tbody>
</table>

* 300 Mhz spectra  
* Solvent: Acetone

Infrared Data:

<table>
<thead>
<tr>
<th>Functionality</th>
<th>Absorption cm(^{-1})</th>
<th>Peak</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic C-H</td>
<td>3097</td>
<td>Weak</td>
<td></td>
</tr>
<tr>
<td>Imide Carboxyl (asym)</td>
<td>1717</td>
<td>Strong</td>
<td></td>
</tr>
<tr>
<td>Imide Carboxyl (sym)</td>
<td>1779</td>
<td>Weak</td>
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<tr>
<td>Nitro (asym)</td>
<td>1343</td>
<td>Strong</td>
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</tr>
<tr>
<td>Nitro (sym)</td>
<td>1502</td>
<td>Strong</td>
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</table>
TABLE 14: N-(4-NitroPhenyl) Maleimide

Carbon 13 NMR Data:

![Chemical Structure]

<table>
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<tr>
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<th>Peak (ppm)</th>
<th>Description</th>
</tr>
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<tr>
<td>b</td>
<td>175.86</td>
<td>Imide Carbonyl</td>
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<tr>
<td>c</td>
<td>141.35</td>
<td>Aromatic</td>
</tr>
<tr>
<td>d</td>
<td>130.91</td>
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<td>e</td>
<td>122.90</td>
<td>Aromatic</td>
</tr>
<tr>
<td>f</td>
<td>144.75</td>
<td>Aromatic</td>
</tr>
</tbody>
</table>

* Solvent: Acetone

Observed m.p.: 160-161 °C  
Literature m.p.: 162-165 °C
TABLE 15: Fast Garnet Maleimide

Proton NMR Data:

![Chemical Structure](image)

<table>
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<td>j</td>
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* 300 Mhz spectra
* Solvent: Chloroform

Infrared Data:

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<tr>
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<td>Strong</td>
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<tr>
<td>Imide Carbonyl (sym)</td>
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<td>Aliphatic C-H</td>
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TABLE 16: Fast Garnet Maleimide

Proton NMR Data:

![Chemical Structure]

Observed m.p.: 99-100 °C

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* Solvent: Chloroform
V. DISCUSSION

From numerous attempts to synthesize the various substituted N-phenyl maleimides following the Yang and Wang, and/or Cava et. al. procedures, it seemed that maleimide formation was dependent on the presence of bulky and/or electronically active groups. The formation of unidentified isomers prompted our group to take a closer look at the possibilities of electronic and steric effects which might affect the ring closure reaction. Various aniline derivatives, substituted with chloro, nitro, and methoxy groups in the meta and para positions of the phenyl ring were used to introduce the electronic and/or steric effects desired. It has been observed that the initial ring opening reaction and subsequent formation of the maleanilic acid is not effected by the presence of bulky or electronically active groups. In fact all of the maleanilic acid compounds synthesized to date were obtained in well over 60% yields. On the other hand, the ring closure reaction seemed very dependent on the induction effects of substituents attached to the phenyl ring. This prompted further investigation by our group to explore the influences of
phenyl substituents on ring formation.

\[
\text{[4a]}
\]

**N-Phenyl Maleimide**

The synthesis of the n-phenyl maleimide [4a] was conducted successfully following the Yang and Wang method of low temperature conversion of the maleanilic acid to the maleimide all in a one pot reaction. An overall yield of 32% maleimide was recorded, contrary to the 80% yield reported by Yang and Wang. This yield was calculated on the assumption that there was a 100% conversion of the maleic anhydride and aniline to the maleanilic acid. This of course was an unrealistic assumption. The maleanilic acid had been previously synthesized, under the same conditions as the Yang and Wang method, and isolated as a yellowish-white solid (m.p. 201-203 °C). The yield of this reaction was calculated at 79.4 %. This percentage was used as a correction factor for the probable amount of maleanilic acid formed from the Yang and Wang procedure and thus subsequently converted to the
maleimide. Thus a corrected yield value of 40.8% of N-phenyl maleimide was reported.

![Chemical Structure of N-(p-Chlorophenyl) Maleimide]

**N-(p-Chlorophenyl) Maleimide**

Synthesis of p-chloro maleimide (m.p. 117-118 °C)\(^25\) proved not to be an arduous task. Employing the synthetic methods as described in the experimental section of this report, afforded a good yield (over 90%) of the p-chloro maleanilic acid and a moderate yield of the p-chloromaleimide (34%). This reaction was not a one-pot reaction. The ring closure step was performed in excess acetic anhydride along with the catalyst, sodium acetate. The reaction solution, upon completion was stirred into basic (pH10) 0 °C water, resulting in a yellow emulsion. After several minutes of stirring, the emulsion broke and a yellow solid was collected by vacuum filtration. This solid was recrystallized from ether and dried in a vacuum oven at 65 °C. Surprisingly, yellow needles sublimed on the oven door. Those needles were collected
for characterization. Thin layer Chromatography performed in a 60/40 solvent mixture of cyclohexane/dioxane showed the presence of pure maleimide. Spectroscopic analysis of both the p-chloro maleanilic acid and the p-chloro maleimide was performed. This data can be found in the experimental section of this report. Proton NMR supports the presence of ring closed product with a singlet at 6.8 ppm representing the olefinic hydrogens (3,4) of the symmetrical imide.

The ring closure reaction seemed to go very readily to completion. This conclusion is based on a comparison with the other maleimide formation reactions yet to be discussed. This maleimide isolation was quite easy relative to the isolation of the other maleimides. A possible explanation for this could be the presence of the chlorine atom in the para position and the formation of a salt derivative of the maleimide. Thus enabling the maleimide to be isolated from basic polar solvent, and subsequently sublimed to a purer crystalline form. It also seems that the chlorine atom was not enough of the an electron withdrawing factor to the phenyl ring to deter maleimide
formation thus affording a relatively good yield. This conclusion being based on the lack of electronic distribution around the amide nitrogen of the maleanilic acid due to electron withdrawing effects through the phenyl ring.

\[
\text{N-(3-Nitrophenyl) Maleimide}
\]

The synthesis of the novel compound 3-nitro maleimide [6] was a turning point in our synthetic procedure. After several attempts to synthesis the 3-nitro maleimide following the Cava et. al. method, it was found that while maleanilic acid formation was highly successful, the maleimide formation was not. The procedure of adding the maleimide solution to O\(^\circ\) C water proved to be unsuccessful for recrystallizing the 3-nitro maleimide as a solid. The product would only oil out of the water. The high acidity of the reaction solution, due to the extreme amount of acetic acid produced during the reaction, seemed to hamper the recrystalization of our desired maleimide. It seems that the acidic
environment of the reaction solution is quite preferable to the maleimide species, thus causing our product to oil out of solution. Many techniques such as ether extractions, ether cloud point, and brine washings were employed to break the oil formed from the 3 nitro maleimide. This task proved to be tedious in that the oil was not very soluble in any of the solvents used except tetrahydrofuran (THF). Once the 3-nitro maleimide was found to dissolve in THF it was washed in brine and rotovaped to a thick yellow slurry. An attempt to solidify the slurry was employed by redissolving it in a small amount of THF/Ethanol in a 70/30 ratio. Rotovaping of this solution left the product dissolved in a small volume of ethanol. Approximately 10 milliliters more ethanol was added to the solution. The solution was put in the freezer and after 20 minutes, a batch of fine white needles started to grow out of solution. The solution was left in the freezer for 3 hours, after which the white needles were vacuum filtered from the solvent. The white needles were left to dry and calculated as an overall yield of 36%. This yield was calculated based on the maleanilic acid used to synthesize the maleimide. The melting point of the
needles was measured at 123-124 °C.

Proton NMR avers the formation of our desired maleimide product. A singlet at 6.9 ppm supports the presence of the two equivalent hydrogens of carbon 3 and carbon 4. Carbon-13 NMR shows a singlet at 168 ppm which supports the presence of the imide carbonyl. More supporting data for our N-3-nitrophenyl maleimide is also offered from elemental analysis and infrared spectroscopy. This data can be viewed in the corresponding spectral data tables located in the experimental section of this report.

**Synthetic Procedural Revision**

It seemed that the new method being employed to perform the ring closure reaction worked well. The addition of the maleanilic acid to a refluxing solution of THF with a stoichiometric amount of acetic anhydride was performed using a Soxhlet extractor. It became apparent that the amount of acetic anhydride necessary for the completion of the reaction need not be in extreme excess.

It was found that the use of THF as a refluxing solvent along
with a stoichiometric amount of acetic anhydride worked very nicely as the reaction solvent system. This particular solvent mixture gives a boiling mixture in the range of 78 to 82 °C. This boiling range is a crucial factor in the prevention of potentially isomerizing the maleanilic acid from the cis to the trans conformation which seem to occur when the temperature of the solvent exceeded 100 °C. Subsequent extraction of the reaction solvent with a brine solution aided in the recrystallization of the maleimide.

The maleimide recrystallization proved to be pH dependent, favoring a more basic medium. This was observed during the recrystallization of the maleimides. Several of the maleimides would oil out during the recrystallization step. This oil was broken by the addition of concentrated ammonium hydroxide. This alternative afforded a more suitable environment for isolation of our desired maleimide product (i.e. a substantially less acidic environment). The use of cold ethanol as a recrystallization solvent was tried and appeared to work very well with the majority of our maleimides. It was later observed though, that the
mixing of ethanol with methanol worked better for some of the maleimide recrystallizations.

![Chemical Structure](image)

**N-(4-Nitrophenyl) Maleimide**

Initially in the maleanilic acid synthesis it was found that the 4-nitro aniline did not dissolve very well into the ether solution for the initial ring opening reaction. This caused some concern over the formation of the maleanilic acid. While the solubility of the 4-nitro aniline was increased by heating the ether and dissolving the 4-nitro aniline before adding it to the Maleic anhydride, total solubility could not be achieved. Maleanilic acid conversion was ultimately achieved. Infrared analysis was used to confirm maleanilic acid formation.

The synthesis of 4-nitro maleimide [7] had been attempted by our group several times, each of which failed. Following the now modified procedure of Cava et. al., along with the new
recrystallization techniques, it was found that formation of the 4-nitro maleimide could be achieved.

3.00 grams of p-nitro maleanilic acid was refluxed in the THF/acetic acid solvent solution for 6 hours. The refluxing solution was a dark brown color. The solvent was rotovaped off leaving a thick yellow oil. The oil was dissolved in 40 milliliters of ethanol and put in the freezer to induce crystallization. After 10 hours no crystals were observed. The ethanol was rotovaped away leaving a dark yellow oil. The oil was then dissolved in 20 milliliters of hot propyl alcohol and let cool down to room temperature. The solution was then put in the freezer for 2 hours. A batch of golden colored flakes precipitated out of solution. The flakes were collected and dried. A second batch of flakes later precipitated out of the cold solution. The total weight of the collected crystals was 1.499 grams. This gave a product yield of 49.8 % based on the amount of maleanilic acid used initially. TLC, spectral, and elemental analysis confirm isolation of maleimide.
N-(4-Methoxyphenyl) Maleimide

The synthesis of 4-methoxy maleimide was performed using the new synthetic technique discussed previously. Given the presence of the electron donating group in the para position of the phenyl ring, this particular maleimide was expected to be a greatly favored candidate for successful ring closure of its maleanilic acid precursor. The 4-methoxyphenyl maleanilic acid was refluxed for several hours. The reaction mixture was then brine washed. Isolation of the maleimide product was achieved by mixing the brine washed THF reaction solvent with approximately 50 ml of ethanol. This solution was then rotovaped down to a brownish-yellow solid (m.p. of crude solid 66-68 °C). Infrared analysis showed the presence of the maleimide as well as residual maleanilic acid. Proton NMR of our product showed the formation of maleimide and maleanilic acid. Two doublets at 6.3 ppm and 6.6 ppm were observed. This was conclusive evidence of
the unequivalent olefinic hydrogens of the maleanilic acid. Carbon 13 NMR contained a peak at 167 ppm which is characteristic of a carboxylic acid carbonyl. It became obvious that the degree of ring closure was not high. This came as a surprise to our group, for theoretically the electron donating effect of the p-methoxy group should have enhance the nucleophilicity of the amide nitrogen. 50 milliliters of ethanol was saturated with 2.69 grams of the brownish-yellow solid collected above. The ethanol was placed in the freezer for two days. A batch of yellow fluffy crystals was formed. These crystals were vacuum filtered and let dry. The total weight of the crystals collected was 0.457 grams giving a 11.5% yield of product collected. Spectral and elemental analysis of the solid confirms the presence of the desired maleimide.

Fast Garnet Maleimide

At the beginning of our study it was of great interest to
synthesize and study the polymerization behavior of azo maleimides. Synthesis of a novel azo maleimide monomer was needed to perform the copolymerization reactions. This proved to be an arduous task. Fast garnet maleimide [9] was our target azo maleimide for the synthesis. Given that the Fast garnet aniline could be readily ordered from Aldrich, it seemed like a good place to start. Early synthetic procedures, similar to the ones used in the synthesis of N-phenyl maleimide [3], in which toluene was used as our reaction solvent, were unsuccessful. Several attempts using the Yang and Wang procedure seemed to produce a mixture of the maleanilic acid and the maleimide. Evidence for this was given by Infrared analysis. Separation and isolation of the maleimide product was also unsuccessful because the solubility parameters of both the maleanilic acid and the maleimide are very close. Thus, as the isolation methods, using 0 °C water and subsequent recrystalization from cyclohexane, were employed, emulsions and very crude solids were obtained.

Previous synthetic methods for the maleimide were abandoned and a different synthetic approach was subsequently
explored. Synthesis of the azo maleimide [10] via the diazonium coupling method\(^7\) was attempted. The synthetic strategy was to couple an diazonium salt, derived from aniline, with N-phenyl maleimide [3]. It was reasoned that the nature of the imido bond of N-phenyl maleimide would be electron donating enough to favor a diazonium coupling at the para position of the maleimide. This however proved not to be the case and thus the reactions failed.

\[
\text{[Diagram]}
\]

A literature search on the conditions for and the mechanism of the diazonium coupling reaction was conducted. It was found that the formation of the azo compound is dependant on the formation of an N-azo intermediate followed by isomerization to the C-azo product\(^{27}\). Reaction Scheme \# 4 demonstrates this process. Primary and secondary amines used in the diazonium coupling reactions are subject to competition from neighboring nitrogen species, which might slow down the coupling process, but
do not prevent it. On the other hand, tertiary nitrogen, as in the Reaction Scheme #4:

\[
\begin{array}{c}
\text{N-H} \\
\text{H-N=O} \\
\text{C-Azo Product}
\end{array}
\]

the case of the N-phenyl maleimide, will not work because the N-azo intermediate can not be formed. For this reason the coupling method was abandoned.

The modified Cava procedure discussed previously was
employed as our next method to synthesize compound [9]. This method proved successful to some degree. The Fast Garnet aniline was converted to the maleanilic acid by Cava's method. The maleanilic acid was collected as an auburn colored solid.

An elaborate purification of the maleanilic acid was employed in an attempt to separate out any unreacted aniline from the azo maleanilic acid. The azo maleanilic acid was dissolved into 70 milliliters of THF. Hydrochloric gas was bubbled through the THF/maleanilic acid solution to salt out any unreacted aniline. The solution was added to 0 °C water and a reddish brown solid was isolated. The solid was redissolved in warm ethanol and recrystallized from 0 °C water. This procedure was followed several times in an attempt to purify the maleanilic acid before it was subjected to the ring closure procedure. The maleanilic acid was redissolved in warm ethanol. Water was added to the solution which was then extracted with ether. The ether layer was then mixed with a small amount of ethanol and subsequently rotovaped. An auburn colored solid precipitated once all of the solvent was evaporated using a rotovaporator.
This solid was then subjected to our modified ring closure procedure. 4.052 grams of the Fast Garnet maleanilic acid was measured out and reacted with acetic anhydride. The system was refluxed for approximately thirteen hours.

Recrystallization of the Fast Garnet maleimide was achieved by first washing the THF reaction solution with brine. Next, a small amount of ethanol was added to the solution. The solution was stripped of all the solvent and a red oil was observed. The oil was redissolved in methanol and poured into a cold brine solution. An orange solid precipitated out of solution. This was collected and left to dry. After 24 hours of drying the solid turned dark red in color. Its texture was hard and waxy in appearance. The melting point of the solid was observed at 54-55 °C. Proton and Carbon 13 NMR analysis was performed on this amorphous solid and it was determined that the solid was a mixture of the Fast Garnet maleanilic acid and the maleimide.

Column chromatography was employed in an effort to separate the Fast Garnet maleanilic acid and the maleimide. Several solvent systems were tested using thin layer
chromatography. It was found that a 60/40 mixture of cyclohexane and 1,4, dioxane could be used as an elutant solvent and offered the best separation of the compounds. The amorphous solid was dissolved in a minimum amount of warm cyclohexane and loaded onto a silica gel column. It was observed that as the solid was eluted through the column, three distinct band were formed. Each of these was collected in separate aliquots. Thin layer chromatography was used to analyze the aliquots and it was found that the first two aliquots contained small traces of maleanilic acid, but was predominately the maleimide. Analysis of the third aliquot showed the predominate presence of the maleanilic acid. The first two aliquotes were combined and subjected to yet another column separation. Again, the first two aliquots collected were combined, while the third was discarded.

The two final aliquots collected from column chromatography were dried of all the elutant solvent, leaving a red oil. This oil was subsequently dissolved into a minimum amount of hot cyclohexane. The hexane was set aside and let cool
to room temperature. A bright red solid was observed recrystallizing out of the solvent. This solid was isolated and dried. The weight of the solid was recorded at 0.0837 grams. This afforded a yield of 2.2%. Spectral and elemental analysis supported the isolation of the Fast Garnet maleimide.

It should be noted that in the infrared spectra the symmetric and asymmetric imido carbonyl peaks absorb more down field than the same carbonyl peaks in the other maleimides. The asymmetric and symmetric peaks are observed at 1789 cm\(^{-1}\) and 1805 cm\(^{-1}\) respectively. This shift can be attributed to the high degree of conjugation found in this compound. It can also be speculated that the unusual shift in the asymmetric and symmetric peaks could be attributed to the presence of the isoimide compound. This hypothesis is based on the publication by Rubinstein et. al\(^{30}\). Further discussion on the Rubinstein publication along with the isoimide formation theory can be found in the "Isoimide versus Isomerization" section of the Results and Discussion.
Another unusual observation was made in the NMR spectral data. The chemical shift of the azo maleimide olefinic carbon protons, which are usually observed as a singlet around 6.8 ppm in all of the other maleimide derivatives, was found to occur further down field for the azo maleimide. The chemical shift for these protons was observed at 7.3 ppm. One of the phenyl protons was found to shift more upfield than the other phenyl protons of all the other compounds. This proton signal was observed as a doublet at 6.7 ppm. The Jab coupling constant for this signal was calculated and found to be close to the Jab coupling constant of a phenyl proton. The coupling constant was measured to be 0.0184 hertz. This confirmed that the doublet was indeed a phenyl proton. It should be noted that there was no supporting evidence for the isoimide formation found in the NMR.

The investigation of yet another approach towards the synthesis of an azo maleimide was carried out. The synthesis plan was the reduction of a nitro group to an amine and then subsequent coupling at the amine site. The 3-nitro maleimide [6] discussed earlier was used as our starting molecule. The
reduction was attempted using the method of hydrogenation in the presence of a palladium/carbon catalyst. Compound [8] was dissolved in ethanol where upon the catalyst was added to the solution. The system was run under 60 psi for 24 hours. Once the system was shut down, the catalyst was filtered off. The solution was observed to have a greenish yellow color. Isolation of the product was attempted by pouring the solution into 0 °C water. An oil resulted. The oil was extracted with ether. The ether solvent was evaporated off upon which an oil remained behind. This oil was dissolve in THF and poured in 0 °C water. The product still oiled out of solution. Several hydrogenations were attempted using different polar solvents such as methanol, DMSO, and ethanol/methanol mixtures. From all of these trials, an oil was isolated. Amine salting out methods were employed via bubbling HCl gas through our product. This still did not aid our group in the isolation of the amine in a salt form. Infrared analysis of the oil shows the presence of an amine peak at 3450 cm⁻¹. This gave some means of assessing the success of the hydrogenation.
Isolation of the 3-aminophenyl maleimide [12] was abandoned. Instead the solution collected from the hydrogenation was subjected to the azo coupling procedure. The intent here was to synthesize the Bis-2,5-dioxo-1-3-azo-maleimide [13]. The procedure was modified, though, since the target molecule for diazonium coupling, compound [14], was already dissolved in solution. Once the diazonium salt formation was completed, N-phenyl maleimide was dissolved in THF and added to the diazonium solution. A reddish brown solid precipitated out of solution. This solid was collected and dried overnight. The melting point was observed at 82-83 °C. Infrared analysis of the solid suggest the presence of the amino maleimide only. From this it was concluded that the diazonium coupling failed. The
conditions for successful azo coupling as reported by March\textsuperscript{27} were unfortunately discovered after the coupling reactions were attempted, and thus are referred to in hindsight. Based on the conditions necessary for successful azo coupling, as reported by March\textsuperscript{27}, this agrees with the conditions established by March.

\[
\begin{array}{c}
\text{R}_1 = \text{NO}_2 \\
\text{R}_2 = \text{Cl}, \quad \text{N}=\text{N} \\
\end{array}
\]

\textbf{Copolymerization of Styrene With Several Maleimides}

Copolymerization of 4-chloro, 3-nitro, and Fast garnet maleimide compounds, numbers [5], [7], [9] respectively, with styrene was performed. AIBN was used as the free radical initiator. The reaction was run under argon at 90 °C in carbon tetrachloride for 24 hours. It was observed in the case of the 3-nitro and 4-chloro reactions that after approximately 5 hours, the reaction solution turned from a dark brownish color to a cloudy
-white color and remained this color for the duration of the heating period. The azo reaction solution on the other hand turned from a dark red to a bright orange color. The observed color changes of the reaction solutions was used as the primary indicator of polymerization.

The crude copolymers were collected as a yellow solid in the case of the 3-nitro and 4-chloro compounds. The Fast garnet polymer on the other hand was collected as an orange solid. All three of the polymers precipitated out of the reaction solvent and were collected by vacuum filtration. The occurrence of a precipitate was also used as an indicator of the polymerization.

Isolation of the product was achieved by dissolving each polymer in a minimal amount of 1,2 dichloroethane (approximately 15 milliliters). This solution was then poured into room temperature methanol upon which a white precipitate was immediately observed. The precipitate was vacuum filtered and dried. A white flakey solid was observed for both the 3-nitro and 4-chloro polymers. The azo polymer on the other hand was observed as an orange flakey solid.
All three samples were analyzed by Infrared Spectroscopy. These spectra show the presence of the imido carbonyl peak as well as the aliphatic carbon-hydrogen peaks of the styrene.

The maleimide was observed to be incorporated into the copolymers, as evidenced by the appearance of nitrogen in the elemental analysis of the polymers. Computational analysis was performed using the empirical elemental analysis data as another means of support of successful copolymerization. The mole fraction ratios of carbon, nitrogen, oxygen, and hydrogen for both styrene and the substituted maleimide were calculated relative to the measured percent composition of each element. This data can be reviewed in Table 6 below.

The values calculated in Table 6 represent the maleimide composition of the polymer. The mole fractions of the carbon, nitrogen and hydrogen atoms of the maleimide were calculated. It should be noted that the atom mole fraction values for each type of maleimide are close. This is supported by the low standard deviation values calculated and reported in the table. It is assumed that the maleimide is completely incorporated into
the polymer. This would therefore mean that the percentage of carbon, nitrogen, and hydrogen atoms for each maleimide would be consistent relative to each individual maleimide. The low standard deviations in fact support this consistency. It should be also noted that based on the low standard deviation it can be hypothesized that the co-polymerizations occurred with no undesired side reactions.

**Table 6:** Percent Composition of Maleimide in Copolymer

<table>
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<tr>
<th>Element</th>
<th>p-Nitro</th>
<th>p-Chloro</th>
<th>Fast</th>
<th>Garnet</th>
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<tr>
<td>Carbon</td>
<td>0.34</td>
<td>0.39</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Nitrogen</td>
<td>0.32</td>
<td>0.31</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Hydrogen</td>
<td>0.34</td>
<td>0.32</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Average Value</td>
<td>0.34</td>
<td>0.34</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>0.01</td>
<td>0.05</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

It should also be noted that the calculations suggest approximately 30 percent incorporation of each of the maleimides into the copolymer, which could be interpreted as that of the reactivity ratio of styrene being higher than that of the maleimides. This is indeed the fact, and is supported by VanPaesschen and Timmerman. Remarkable as well, is the consistency with which the maleimide incorporation occur from
one maleimide type to another.

**Electronic Effects On Maleimide Formation**

Synthesis of the various maleimides proved not to be straight forward, high yielding reactions. Reaction conditions, isolation techniques, and other factors seemed to hamper the formation and isolation of the maleimides. As postulated earlier in this report, the electron donating and electron withdrawing groups on the phenyl ring may be contributing some electronic effect throughout the conjugated system which might affect the conversion of the maleanilic acid to the maleimide. As a matter of observation, it can be shown that there may indeed be some correlation between the yield of the maleimides and the electronic effects of the substituents on the phenyl ring. Figure 5 below is a Hammett type plot of percent yield data from the synthesis of the maleanilic acids and maleimides. The plot below shows a direct correlation of the electronic effects of the phenyl substituents on the reactions yields. Note that the N-phenyl compound falls almost dead center of the line, the compounds which contain the electron releasing species fall directly on the line below the N
-phenyl species and the compounds which contain the electron withdrawing species occur off the line and above the N-phenyl species. This observation suggest that there is a possible predictable pattern which might be applicable to similiar compounds. This particular phenomenon requires more data though, and at this can only be sited as observation.

**Figure 5: Plot of Percent Yield Data**

Even more interesting is the fact the m-nitro compound falls very close to the line. This might suggest that pi orbital overlap is very essential for the conductance of any electronic effects.
Isomerization vs. Isoimide Formation

One of the factors speculated as to contributing to the low conversion of the maleanilic acid to the maleimide was the formation of the isomaleimide compound [14]. The first reference to the isomaleimide was reported in the literature by Piutti (1910) [28]. He reported the preparation of

\[ R_1 = \text{NO}_2, \text{H} \]
\[ R_2 = \text{NO}_2, \text{H}, \text{Cl}, \text{OCH}_3, \text{N} = \text{N} \]

\[ \text{N-(4-methoxyphenyl) isomaleimide} \] [15], along with several other derivatives, by acetyl chloride dehydration of the precursor maleanilic acid.
The work of Piutti was followed up by Roderick who could not find evidence to support the presence of the unsymmetrical imide\textsuperscript{25}. Roderick instead showed that the compounds obtained by Piutti were the $\alpha$-chloro-N-(p-alkoxyphenyl)-succinimides [16].

\[
\text{[16]}
\]

Cotter et. al. [1960]\textsuperscript{29} later reported the synthesis of isomaleimide compounds by the dehydration of the corresponding N-substituted maleanilic acid with N,N'-dicyclohexylcarbodiimide, and ethyl chloroformate-triethylamine\textsuperscript{29}. Cotter also found that the isomaleimide was readily isomerized to it's maleimide counterpart in the presence of sodium acetate, or more specifically the acetate ion. The mechanism for this isomerization involves the formation of a mixed anhydride species and is similar to Mechanism 2 shown in the introduction. From this observation, it can be postulated that the isomaleimide may be the primary
dehydration product of the maleanilic acid. This postulate is supported by the kinetic studies performed by Kailani et. al.\textsuperscript{26}. Kailani reported that the rate constants for the imidization of the maleanilic acids were based on both a rapid conversion of the maleanilic acid to the maleimide, and a slower conversion of the maleanilic acid to the isomaleimide and subsequently to the maleimide. Kailani also reported the isolation of the isomide compound just before it's conversion to the maleimide; however, he failed to report any substantial spectral data to support this claim. This fact led to some skepticism as to whether or not Kailani actually was able to isolate the isomaleimide.

Credulous spectral proof of the isolation of the isomaleimide was offered by Rubinstein and Skarbek\textsuperscript{30}. The infrared analysis of the isomaleimides shows twin strong carbonyl absorption in the range of 1778-1790 cm\textsuperscript{-1} and a medium C=N absorption peak in the range of 1600-1650 cm\textsuperscript{-1}. Proton NMR data would show the presence of nonequivalent olefinic protons in the range of 6.3-6.5 ppm. This spectral data also collaborates with that of Cotter et. al. and Hedaya et. al. \textsuperscript{31}. 
The possible formation of the isomaleimide as opposed to the desired maleimide was speculated upon by our group as one of the possible reasons for our low yields and or failed attempts to dehydrate the maleanilic acid to the maleimide.

Upon inspection of the spectral data though, there was no clear indication of the isomaleimide's existence in any of the reaction attempts failed or successful. The infrared spectra of the Fast garnet maleimide offered some indication of the presence of the isoimide. The spectrum displayed unusual shifts for the asymmetric and symmetric imide carbonyl absorption. The peaks, however, do not look like the two individual peaks reported in the literature. The carbonyl peaks do resemble the symmetric and asymmetric peaks as seen in the other maleimide infrared spectra.

Furthermore, it was observed that while some reaction attempts were labeled a failure, there could still be detectable a degree of conversion of the maleanilic acid to the maleimide. Which indicates that if the isomaleimide is an intermediate of the maleimide ring closure reaction it would be difficult to isolate.
Most of the initial attempts were run in the presence of sodium acetate which is probably why the isoimide was never isolated. From this observation it was then speculated by our group that perhaps another factor i.e. isomerization of the olefinic bond was contributing to the failure of some of the reactions.

Bergmann and Schapiro [1942] reported the observation that nitrogen compounds catalyzes the isomerization of maleanilic acid derivatives. It was also observed by our group that the success of the dehydration reaction was temperature dependant. Exceeding the optimal temperature range resulted in a degraded material. An increase in temperature though was not mandatory for the possibility of isomerization to occur.

During one of the attempts to synthesize the maleimide, the temperature of the ring closure reaction was inadvertently allowed to rise to 115 °C. This produced a black tar in which attempts to recrystallize the product from cyclohexane failed. This led our group to believe that higher temperatures promote isomerization of the olefinic ethylene bond in the maleanilic acid species, to form the trans, or fumeric acid, analog. This ultimately
prevented the formation of the desired ring closed product. As a result of this observation it became mandatory that none of the reactions be allowed to exceed 90 °C.

Spectral analysis of the products from failed attempts of the dehydration of the maleanilic acid to the maleimide offered some evidence of the isomerized maleanilic acid to it's fumeric analog. For example, in a failed synthesis of the 4-nitro maleimide [7], the proton NMR showed that we had predominately the maleanilic acid present as the final product. Two doublets peaks at 6.4 ppm and 6.6 ppm are indicative of the two non-equivalent hydrogens on olefinic carbons 3 and 4 (refer back to results section). The distance between the two peaks of each doublet was measured to be approximately 11.94 hertz. Comparing this to the $J_{ab}$ coupling constants for cis and trans olefinic protons suggest that the olefinic protons of the product were in a trans orientation. The 4-nitro maleanilic acid used to originally synthesize the maleimide was analyzed by Proton NMR and a remarkable observation was made. The $J_{ab}$ coupling constant for the same protons was much lower, 9.3 Hz to be exact.
This phenomenon was again observed in the synthesis of the 4-methoxy maleimide[9]. Proton NMR analysis of the maleanilic acid which was collected as the predominate product from a failed attempt to synthesize the maleimide, showed a Jab coupling constant of 17.5 Hz. The Jab coupling constant of the original maleanilic acid was found to be 12.84 Hz.

This data supports the hypothesis that an isomerization of the olefinic carbons could have occurred, resulting in the trans fumeric maleanilic acid. Taking into account that the maleanilic acids are synthesized at room temperature, and based on the observed Jab coupling constants of these compounds, it can be postulated that the these compounds are initially in the cis orientation. However, once these compounds are subjected to the conditions required to produce the maleimide (i.e. high temperatures, solvent effects) isomerization to the trans analog becomes an option for these compounds.
Computer Modeling of Synthesized Compounds

The purpose of this section is to utilize computer modeling as a theoretical tool for the purpose of understanding the conformational patterns of the synthesized maleanilic acids and their subsequent conversion to the respective maleimide. Patterns in structural conformations and energies as a function of the electronically active groups attached to the phenyl ring are explored. This information was used as a theoretical foundation to help understand the most likely thermodynamically favored conformations for these compounds. The data collected from the modeling can be used as a foundation for possible future work, and is thus recommended to be used for such.

The type of computer modeling system used in this study was Computer Aided Chemistry (CaChe) 3-D Molecular Modeling program for the Macintosh computer processing units. This package program contains several programs which work interactively of each other conducting computational analysis of inputed data using an augmented MM2 force field. An example of the computer modeling information gathered for one compound
will be shown here in this section to demonstrate the type of information obtained from the modeling study. The remainder of the modeling diagrams will be filed as unpublished results.

This particular software relies on augmented MM2 calculation which are used to determined the minimal energy conformation for each maleanilic acid, maleimide, and isoimide. Torsional angles between the phenyl carbon and the imide nitrogen are also shown. An example of this information can be viewed in the n-Phenyl maleimide total energy optimized structure diagram on the next page.

Following the conformational diagrams for each maleanilic acid are dihedral energy rotational diagrams. A 2-4-5-9 carbon dihedral rotation for each maleanilic acid was conducted around the 4-5 olefinic carbon-carbon bond. A full rotation of 360° in 5° increments around the 4-5 olefinic was executed. The structural energy for each incremental rotation was calculated and plotted as a function of the rotation. The energy plots generated by the computer were obtained as a function of the atoms, not involved in the rotation, being fixed in space. After each incremental
2,5-dioxo-1-[phenyl]-3-pyrroline
Total Energy of Optimized Structure: -22.9950 kcal/mol
rotation no energetic optimization was computed by the program. The dihedral rotation plots of n-Phenyl maleanilic acid can be viewed on the next page. These plots have been utilized to highlight the highest and lowest energy conformations for each maleanilic acid. The shaded bonds for the cylindrical bond diagrams are representative of pi bonding.

As expected the trans orientation of the maleanilic acid is lower in energy than the cis orientation. The rotational energy diagrams of all the maleanilic acids can be reviewed in Figure 6 below. A trend in the increase of local maxima and minima of each maleanilic acid can be observed.

**Figure 6:**

![Trend of Increasing Delta Energy Barriers For Cis to Trans Conformation](image-url)
N-Phenyl Maleanilic Acid

Total Energy of Optimized Structure: -25.8531 kcal/mol
Rotational Energy Diagram: N-Phenyl Maleanilic Acid

Total Energy of System
22.870 kcal/mol
Rotational Energy Diagram: N-Phenyl Maleanilic Acid

Total Energy of System
9.902 kcal/mol
Rotational Energy Diagrams: N-Phenyl Maleanilic Acid

Total Energy of System
-37.004 kcal/mol
Modeling of the probable isomaleimides for each maleimide gave interesting results. The conformational energies of the structurally optimized isomaleimides were much higher than that of it's maleimide counterpart. This would suggest that the isomaleimide would act as a high energy intermediate.

Shown below are Table 7 and Table 8 which consist of the extracted data from the exhaustive MM2 calculations performed on each compound. This compilation of data was reported individually for each compound accompanied by the optimized molecular structure diagram.

**Table 7:**

Dihedral Rotational Energy Data (Cis versus Trans Conformation)

<table>
<thead>
<tr>
<th>Maleanilic Acid Compound</th>
<th>Cis orientation Energy (kcal/mol)</th>
<th>Trans orientation Energy (kcal/mol)</th>
<th>Delta Energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Phenyl</td>
<td>-22.424</td>
<td>-37.528</td>
<td>-15.104</td>
</tr>
<tr>
<td>p-Chloro</td>
<td>-21.547</td>
<td>-35.783</td>
<td>-14.236</td>
</tr>
<tr>
<td>m-Nitro</td>
<td>-29.03</td>
<td>-33.526</td>
<td>-4.496</td>
</tr>
<tr>
<td>p-Nitro</td>
<td>-24.015</td>
<td>-36.913</td>
<td>-12.898</td>
</tr>
<tr>
<td>Fast Garnet</td>
<td>-5.863</td>
<td>-21.066</td>
<td>-15.203</td>
</tr>
</tbody>
</table>
Table 8:

Compound Optimization Data From Augmented MM2 Calculations

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Phenyl</td>
<td>-25.87</td>
<td>-22.995</td>
<td>-3.016</td>
<td>23.91</td>
</tr>
<tr>
<td>p-Chloro</td>
<td>-30.706</td>
<td>-22.261</td>
<td>-2.412</td>
<td>0</td>
</tr>
<tr>
<td>p-Methoxy</td>
<td>-29.925</td>
<td>-21.751</td>
<td>-1.59</td>
<td>26.83</td>
</tr>
<tr>
<td>p-Nitro</td>
<td>-22.764</td>
<td>-23.29</td>
<td>-3.479</td>
<td>22.95</td>
</tr>
<tr>
<td>Fast Garnet</td>
<td>-12.788</td>
<td>-9.056</td>
<td>-0.895</td>
<td>58.15</td>
</tr>
</tbody>
</table>

Based on the delta energy for each maleanilic acid 180 degree rotation (i.e. isomerization to the trans conformation), one can make several postulations about the potential of a particular maleanilic acid to undergo an actual isomerization. Thus laying the ground work for future investigations.

A comparison of change in energy for maleimide formation to the change in energy for isomerization would afford more insight to the possible mechanisms occurring in the system. The collection of this data would require a thorough kinetics study. This type of study would definitely qualify as a possible future work project as well.

The order of the maleanilic acids for the delta energy trend is surprisingly similar to the order of the substituents found in the
Figure 5 Hammett type plot. This information advocates the relevance of correlating computer modeling data with that of empirical data. Thus justifying the strength of computer modeling data and how it can help formulate new hypothesis about one's research project.
VI. Conclusion

A comprehensive study of the methods employed to synthesize substituted N-phenyl maleimides and the subsequent copolymerization of these compounds with styrene was the purpose of this thesis work. The synthesis of two novel substituted N-phenyl maleimides along with four previously synthesized N-phenyl maleimides was achieved. Three of these maleimides were then copolymerized with styrene.

The synthetic pathway toward substituted N-phenyl maleimides was found to be very inconsistent relative to that of N-phenyl maleimides. It was also observed that the electron withdrawing and donating groups on the phenyl ring of the maleimides of interest seemed to influence the conversion of the maleanilic acid to it's respective maleimide. The transition of the maleanilic acid to the maleimide occurs via a nucleophilic ring closure reaction. The first part of our investigation was to look at whether or not steric and/or electronic effects, of the substituted phenyl ring, enhanced or detered the formation of the maleimide. It was later confirmed that this indeed was the case. A Hammett-
type plot of the percent yield for the maleanilic acid versus the percent yield for the ring closure suggested a correlation between the yields of the two reactions.

It was reported $^{25,26}$ that the ring closure reaction does not follow a direct kinetic pathway. Complete conversion of the maleanilic acid to an isomer referred to as the isoimide was reported to compete with the conversion of the maleanilic acid to the maleimide.

NMR analysis of the maleanilic acid along with computer modeling suggest the occurrence of an isomerization of the maleanilic acid to a fumeric analog. The fumeric analogs of the maleanilic acids were calculated to be lower in structural energy relative to it's respective maleimide and isoimide, thus more favored. It was also observed that the formation of the fumeric analog was temperature dependent.

Thermal isomerization of the maleanilic acid to the fumeric amide acid versus that of the kinetically favored formation of the isoimide are two factor which might be directly involved with the success of the maleimide synthetic reaction. The second part of
our study was to find the proper conditions to eliminate these adverse influences on the maleimide reaction and successfully synthesize all six target maleimides. All six target maleimides were successfully synthesized in modest yields and subsequently characterized.

Copolymerization of several of the substituted maleimides with styrene via free radical polymerization using 2,2'-azobisisobutyronitrile (AIBN) constitutes the third part of our study. This was also successfully accomplished. Each polymer was characterized by elemental analysis.

Characterization of the substituted maleanilic acids, maleimides, and the copolymers was performed using Fourier Transform Infrared (FTIR), Nuclear Magnetic Resonance (NMR), and Elemental Analysis.

Computer aided modeling through the program Computer Aided Chemistry (CaChe™) offered some theoretical foundation to our investigation. The theoretical data collected offered a good foundation for possible future kinetics studies on the maleimide ring closure reaction.
VII. REFERENCES


17. Sadler, Infrared Library, Sadler Research, Ref. Num. 15596 K


19. Beaker Program for the Macintosh system


33. Unpublished results of Victor Vandell
NUCLEAR MAGNETIC RESONANCE SPECTRA
SOLVENT: ACETONE

200 MHz SPECTRA

SPECTRA I: PROTON NMR OF N-(4-CHLOROPHENYL) MALEIMIDE ACID
Spectrum II: Proton NMR of N-(3-Nitophenyl) Malonic Acid

Solute: Acetone

200 MHz spectra
Solvent: Chloroform/Methanol

300 MHz Spectra

Spectra III: Proton NMR of N-(4-Methoxyphenyl) Maleamic Acid
Solvent: Dimethylformamide

300 MHz spectra

![Chemical Structure](image-url)

SPECTRA IV: Proton NMR of N-(4-Nitrophenyl)Malonic Acid
Solvant: MeTHanol

300 MHz Spectra

[Chemical Structure Image]

Spectra V: Proton NMR of 2-Acetyl Napthalene Acid
Spectra VI: Proton NMR N-(4-Chlorophenyl) Melamine

Solvent: Chloroform

300 MHz spectra
Spectra VIII: Carbon-13 NMR of N-(4-Chlorophenyl) Melamine
SPECTRA VIII: Proton NMR of N-(3-Nitrophenoxy) Maleimide

- Solvent: Chloroform

300 MHz spectra
SPECTRA VIII: Carbon-13 NMR of N-(3-Nitrophenoxy) Malonitrile

- 300 MHz spectra
- Solvent: Chloroform
Solvent: Chloroform

300 MHz spectra

Spectra X: Proton NMR (4-Methoxyphenyl) Malonimide
Spec tra XI: Carbon-13 ol N-(4-methoxyphenyl) Mal eimide
SOLVENT: Acetone

Spectra XLI: Carbon-13 NMR of (4-Nitrophenyl) Maleimide
Spectra X: Carbon-13 NMR of 2-Fluoro Carboxamide
Spectral V4: Infrared of Branmalalacetic Acid
Spectra XVL: Infrared of Co-Syirone-Fast Garnet Melamine
Spectra X: Infrared of Co-Isonitrile-4-Nitrophényl Maleimide