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CONVERSION OF AROMATIC AMINES AND N-AROMATIC AMIDES TO O-AROMATIC ESTERS, BIPHENYLS, AROMATIC HALIDES AND ENERGETIC MATERIALS VIA NITROSAMIDE INTERMEDIATES

A Dissertation

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

Doctor of Philosophy

By

RAYMOND R. ROY, JR.
Norman, Oklahoma
2002

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CONVERSION OF AROMATIC AMINES AND N-AROMATIC AMIDES TO O-AROMATIC ESTERS, BIPHENYLS, AROMATIC HALIDES AND ENERGETIC MATERIALS VIA NITROSAMIDE INTERMEDIATES

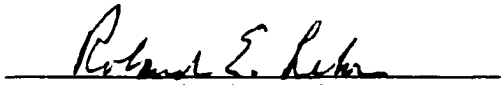
A DISSERTATION APPROVED FOR THE

DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY

BY



Daniel T. Glatzhofer



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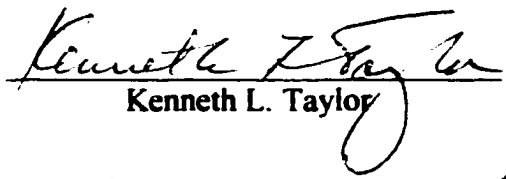

Kenneth L. Taylor



Rudolf J. Wehmschulte



Robert L. White

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Abstract

The conversion of aromatic amines to esters and phenols is a very useful transformation typically carried out using diazonium salt intermediates but the yields and product purity are highly variable. Aliphatic primary amides can be converted to esters *via* the corresponding N-nitrosamides but the reaction is of little utility. Little is known about the analogous reaction of primary amides derived from aromatic amines. It has been discovered that the reaction of aromatic amides with nitrite in a solution of acetic anhydride and acetic acid gives the corresponding esters in good to excellent yields. This reaction is functional group tolerant. Acetanilides, trifluoroacetanilides, and benzanilides gave the corresponding acetates, trifluoroacetates, and benzoates. These esters can be converted to the corresponding phenols easily and quantitatively.

Formation of biphenyls though aromatic nitrosamides have been observed in the past but the nitrosamide either had to be synthesized under harsh conditions, or isolated first. It has been discovered that the introduction of a reactive solvent, methyl methacrylate, into this reaction sequence developed for the formation of esters resulted in polymerization of methyl methacrylate. Changing the reactive solvent to benzene has allowed the formation of biaryls under mild conditions without isolating the aromatic nitrosamide. In some cases, when benzoic acid is added to the reaction, deamination has occurred. In one case, with 1,8-bis(N-acetamido)naphthalene, when benzoic acid was added to the reaction the formation of perylene occurred.

The introduction of halogens into aromatic compounds is an important synthetic procedure. Some of the present methods, in use today, require harsh conditions, provide a mixture of usually ortho or para halogentated products, or provide variable yields

ranging from poor to excellent, depending on the substituent attached to the aromatic ring and/or the conditions the reaction is carried out. It has been discovered that the introduction of a suitable halogen source into the reaction sequence will allow the conversion of the aromatic secondary amides to aromatic halides in moderate to good yields under mild conditions.

These reactions can be carried out directly on aromatic amines (initial *in situ* acetanilide formation) to give aromatic acetates, and halides in good to excellent isolated yields. The mechanism, scope, potential utility of these reaction as well as the use of the nitrosamide as an initiator for polymerization reactions will be discussed in this dissertation.

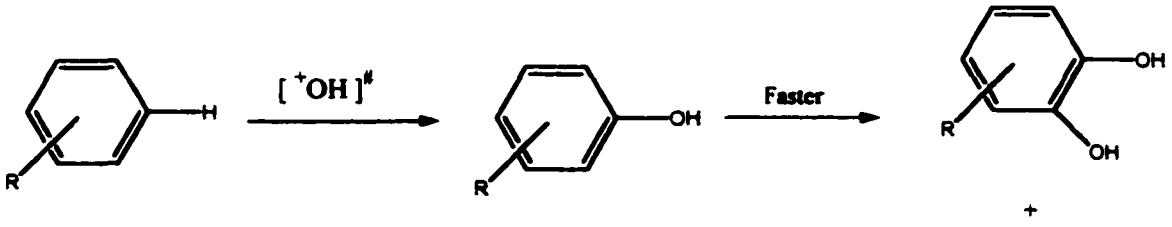
Chapter 1 Introduction & Background

1.1 Synthesizing Esters and Phenols Through Normal Routes

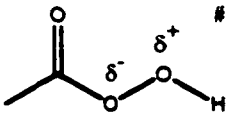
The oxygenation of aromatic rings with various substituents, electron withdrawing as well as electron donating, is of considerable importance as a synthetic transformation. However, the more common methods used to carry out this transformation have problems associated with them. One method for phenol formation is through a direct method.

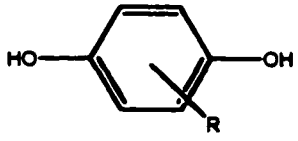
In the direct method (Scheme 1) an electrophilic hydroxyl group is added to the phenyl group through a Friedel-Crafts-type mechanism[1] (Scheme 2).

Scheme1: Direct Method for Making Phenols.



R = Ring Activating Substituent

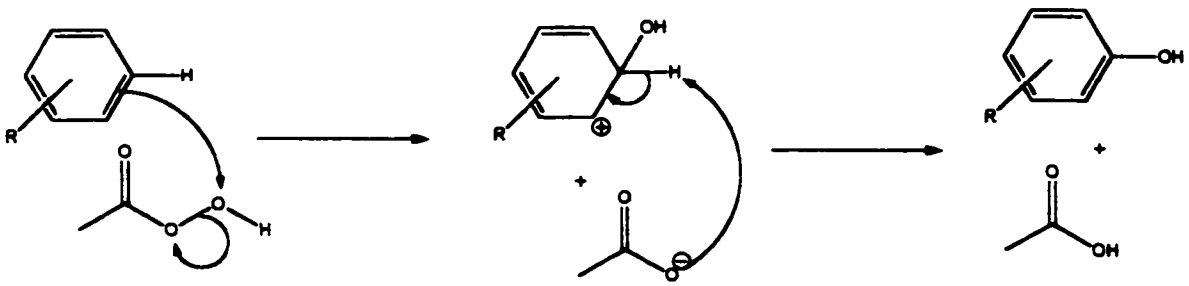




The problem with this method is three-fold. The first is that since the hydroxyl group will activate the aromatic ring, the addition of more than one hydroxyl group becomes favorable.[1] It becomes extremely difficult to just stop at the addition of one hydroxyl group. The second problem will vary with the substituents that are attached to the

aromatic ring . If the group happens to deactivate the ring then the addition of the desired hydroxyl group will be problematic at best. The final problem deals with functional group tolerance. Since peracids are generally used in the direct method, as shown in Scheme 1, if the functional group is intolerant to peracid then this method cannot be employed to make aromatic esters. Since direct methods have their problems, indirect methods have been used to make phenols.

Scheme 2: Mechanism for Direct Phenol Formation Using a Peracid.



R = Ring Activating Substituent

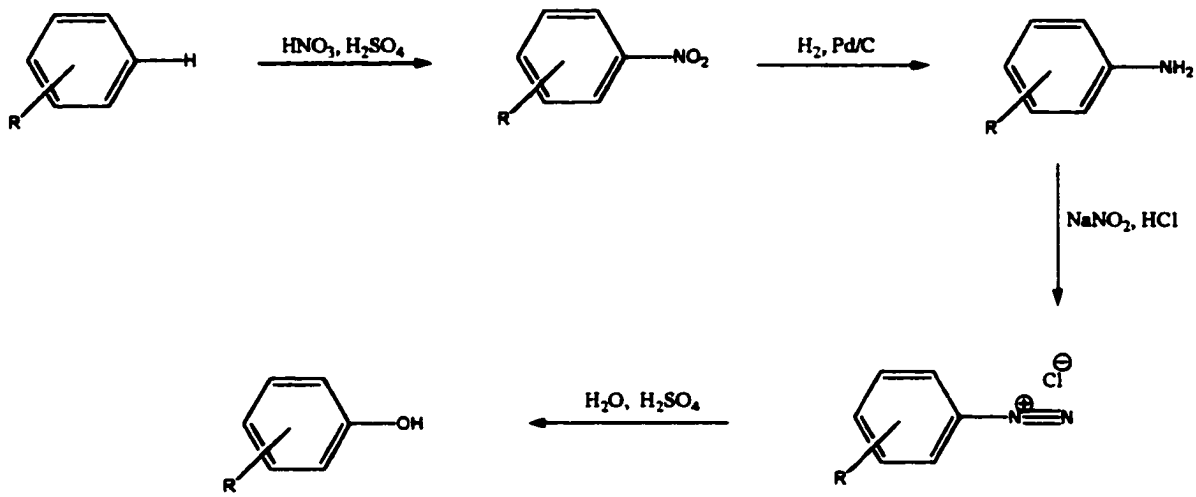
In the indirect method (Scheme 3) the target aromatic system is nitrated and the NO_2 group is reduced to an amino group. The amino group is converted to the diazonium salt. The diazonium salt is then treated with an aqueous solution of sulfuric acid under Sandmeyer reaction conditions to form the phenol.

A brief survey of the literature shows that the decomposition of diazonium salts using this method suffers from high variability in yields depending on the substrate attached to the aromatic ring.[2] Another problem is often the need to isolate the potentially hazardous diazonium salt in order to obtain reasonable yields.[2] This isolation is needed because if nitrous acid is present, under the acidic conditions of the Sandmeyer

reaction, the resulting phenols are often prone to nitrosation or nitration.[2] Phenol coupling to form azo compounds can occur if not under acidic conditions.

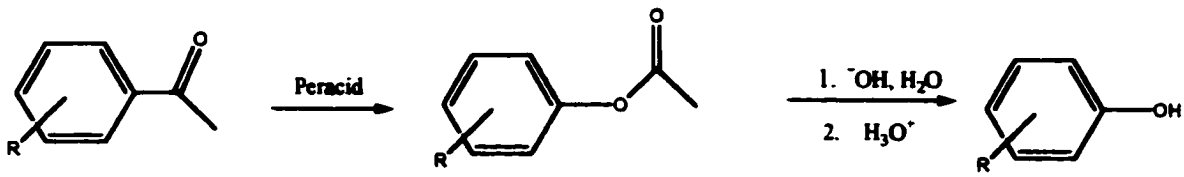
A variety of techniques have been developed in an effort to improve yields,[3,4] however the problem of functional group tolerance still exists with these methods.

Scheme 3: An Indirect Method to Synthesize Phenols.



Another strategy would be the use of aromatic esters to make phenols. Hydrolysis of the esters to make the corresponding phenols is mild and quantitative. An acyl-substituted aromatic compound can be treated under Baeyer-Villiger conditions to form the corresponding ester (Scheme 4). This ester can be easily hydrolyzed or transesterified to the phenol under basic aqueous conditions.[5]

Scheme 4: Synthesis of Phenols Through Esters.

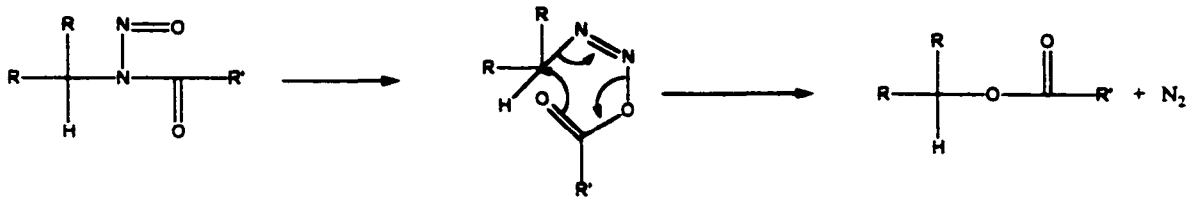


The problem once again is that the yields of the Baeyer-Villiger reaction are highly variable depending on substituents on the ring,[6] along with the fact that the acyl aromatic must be synthesized from other aromatic compounds, adding steps and varying yields. A method is therefore needed to synthesize aromatic esters in high yields from which phenols can be easily derived, and which is substituent tolerant.

1.2 Synthesis of Aliphatic and Benzylic Esters via Nitrosamide Intermediates

Aliphatic nitrosamides were first synthesized by Chancel in 1895.[7] His method for synthesis involved the acidification of an aqueous solution of sodium nitrite and the amide. In 1954, Emil White published his first paper dealing with the synthesis of aliphatic esters through nitrosamide intermediates.[8] The method used for nitrosating amides was treatment with nitrogen tetroxide, by passing N_2O_4 into a carbon tetrachloride solution of the amide in the presence of anhydrous sodium acetate at 0°C.[8] White proposed that the mechanism for the formation of the ester from the nitrosoamide proceeded through a S_Ni reaction,[8] which is shown in Scheme 5.

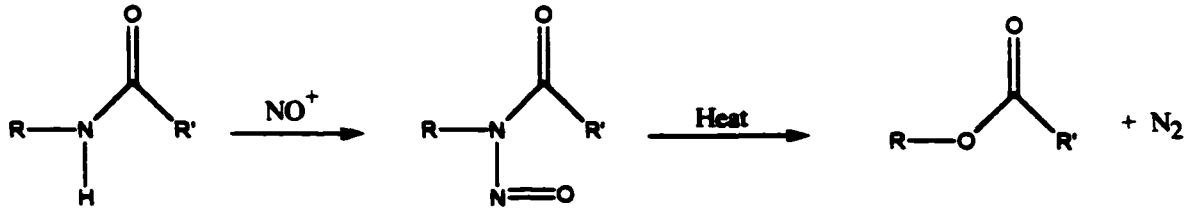
Scheme 5: The Nitrogen Elimination Step Through a Proposed S_Ni Reaction.



R = Aliphatic

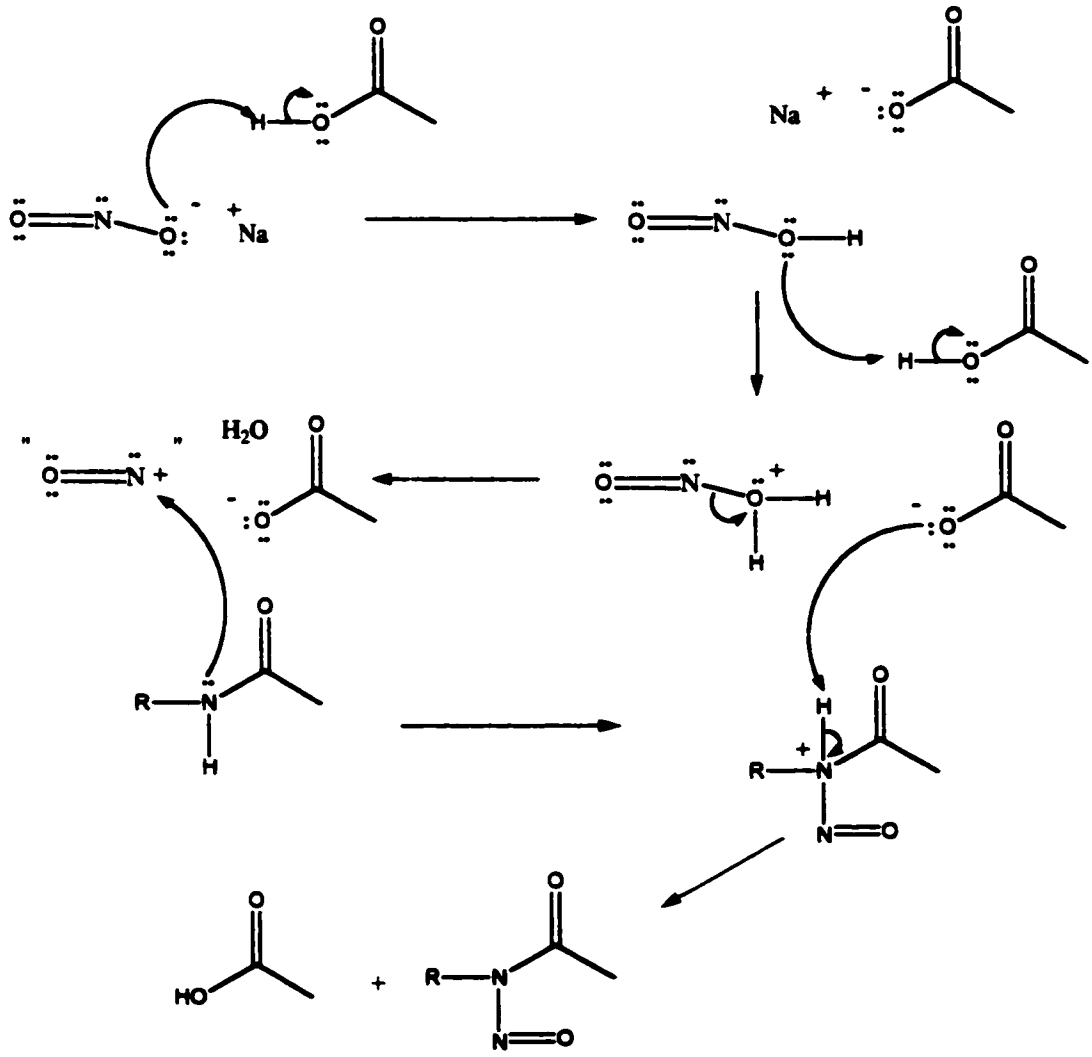
By 1955, White published a method of forming aliphatic nitrosamides through the use of sodium nitrite in a solution of acetic anhydride and acetic acid.[9] The ratio of acetic anhydride to acetic acid was 2 to 1 while the amount of sodium nitrite used was a 20 molar excess to the amide. The nitrosamides were synthesized and then isolated at low temperature. They were then dissolved in an inert solvent and then warmed to give the ester (Scheme 6). The mechanism for the formation of the nitrosamides is shown in Scheme 7.

Scheme 6: Reaction Conditions For The Synthesis of Aliphatic Esters.



R, R' = Alkyl

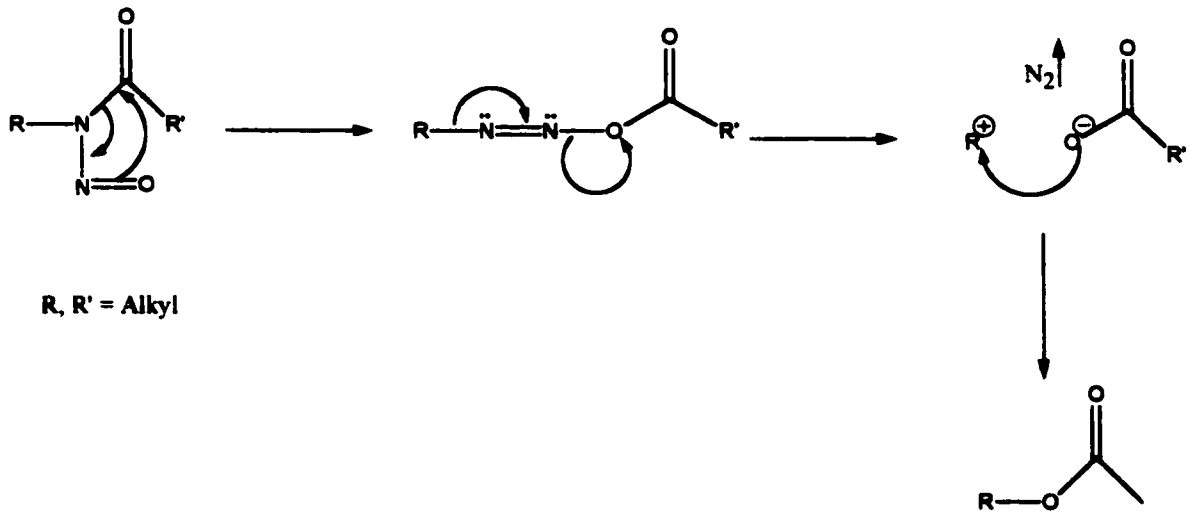
Scheme 7: Mechanism for the Synthesis of Nitrosamides Through the Use of Sodium Nitrite.



It was discovered that there was retention of configuration around optically active sec-butyl nitrosoamides, nitrogen gas was released, and the reaction was likely intermolecular.[10,11] White proposed that instead of a cyclic mechanism the reaction occurred through a carbocation/carbanion mechanism as shown in Scheme 8.[11] The change from his earlier S_Ni occurred because of ^{18}O labeling experiments, where an ^{18}O

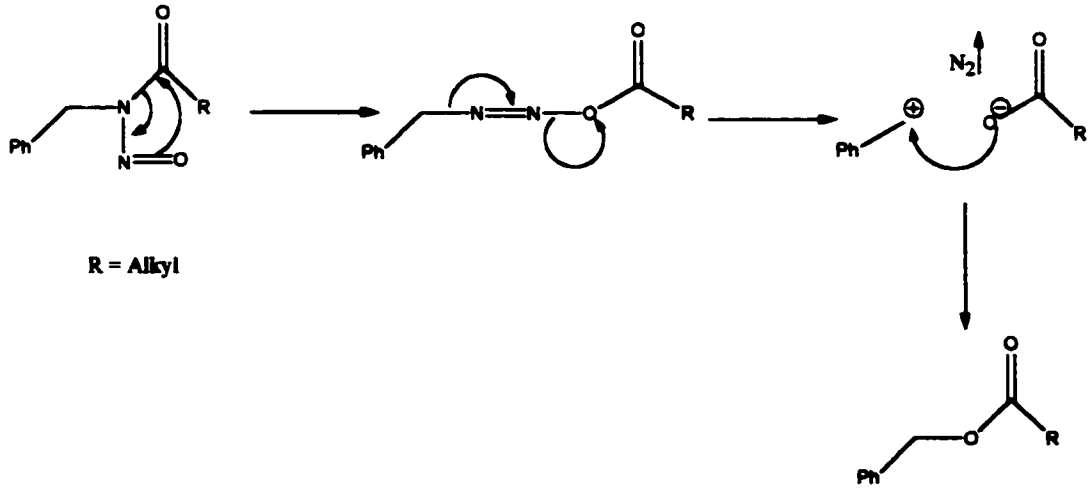
label was placed on the carbonyl oxygen and it was observed that after the reaction the labeled oxygen remained in place.[11]

Scheme 8: Mechanism Proposed by White.



In 1997, Ron Darbeau published work on benzylic esters.[12] In his 1997 work he attempted to trap the benzyl cation that he proposed would form during the mechanism for the formation of benzylic esters that is shown in Scheme 9.

Scheme 9: Mechanism for the Formation of Benzylic Esters.



He used furan in order to trap the benzyl cation that he postulated would form during the decomposition of benzylic nitrosamides. He was looking for the O-benzylfuranonium ion, Figure 1, but did not observe it. Darbeau attributed this to that even at -80° C it is too labile for detection.[12] However, he did detect benzylfuran[12],which demonstrated the formation of the benzyl cation through decomposition of benzylic nitrosamides (Figure 2).

Figure 1: The O-benzylfuranonium Ion.

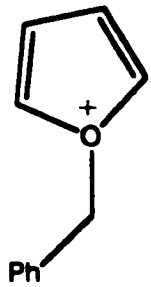
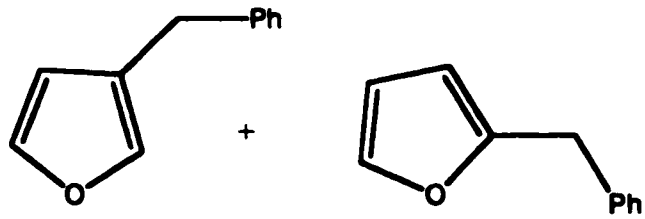


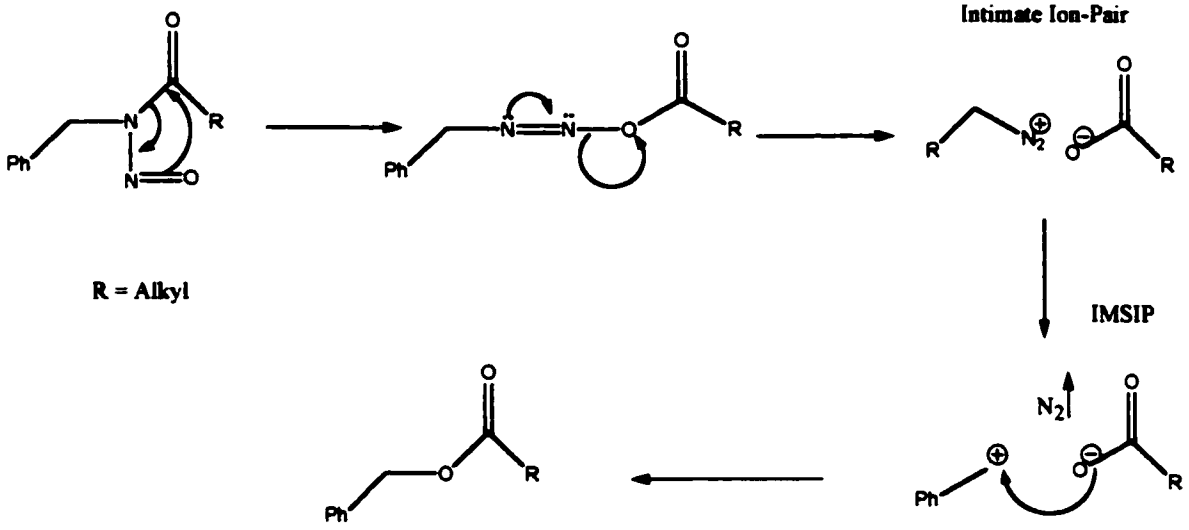
Figure 2: Benzylfuran



Darbeau postulated the idea of formation of an inert-molecule-separated ion pair (IMSIP) in a paper published in 2000.[13] Although not much changed in the reaction mechanism, the ideas of intimate ion pair and IMSIP were now added into the description of the mechanism as shown in Scheme 10. The usefulness of this is the idea that not only aliphatic nitrosamides decomposed into two fragments with loss of nitrogen but that

benzylic nitrosamides also decomposed into two fragments, the benzylic cation and acetyl anion with the loss of nitrogen gas. These fragments can then recombine to form benzylic esters.

Scheme 10: Use of Intimate Ion Pair and IMSIP to Describe the Mechanism.

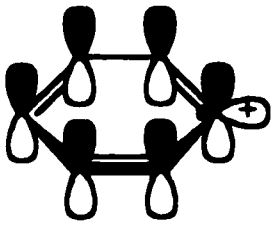


Although the work of White and Darbeau showed that aliphatic and benzylic esters could be formed from amides through nitrosamide intermediates, whenever the starting material was a secondary aromatic amide they were unable to obtain esters from their reactions.[10, 11, 12]

White and Darbeau's proposed mechanism deals with the decomposition of nitrosamides into a carbanion/carbocation pair with the loss of nitrogen gas. Their nitrosamides were either aliphatic or benzylic. With an aromatic nitrosamide this type of decomposition did not work. The apparent reason is that the resulting carbocation formed by a carbocation/anion decomposition would place the positive charge orthogonal to the π system as shown in Figure 3. Therefore, the π system could not provide electron density to this electron deficient center to assist in its stabilization. A positive charge is

also being placed in an sp^2 hybridized orbital. This means that the positive charge is now even closer to the positively charged nucleus than if the charge was placed in an sp^3 hybridized orbital. The formation of this system would be energetically costly, if it could be formed at all.

Figure 3: Location of Positive Charge on an Aromatic System.



However, aromatic nitrosamides have been shown to fragment homolytically so a brief review of aromatic nitrosamide chemistry needs to be provided to indicate possible routes for the conversion of aromatic nitrosamides into aromatic esters.

1.3 A Brief History of Aromatic Nitrosamides.

In 1876, Fischer reported the first synthesis of aromatic nitrosamides.[14] Bamberger discovered, in 1897, that these nitrosamides decomposed in benzene at room temperature to give biphenyls and acetic acid.[15] Work in the 1930's, dealing with decomposition of aromatic nitrosamides, started the development of the concept of the transient existence of radicals in solution.[16] Grieve and Hey's work further advanced this field by suggesting that decomposition of aromatic nitrosamides in benzene, producing biphenyls, arose through a phenyl radical intermediate.[17] How they formed their aromatic

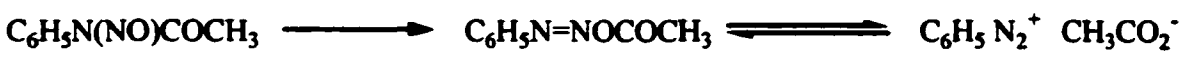
nitrosamides will be further explored in Chapter 3, Section 1. Their work also provided the first evidence that aromatic nitrosamides decomposed homolytically.[17]

In 1951, Huisgen and Horeld suggested that and provided evidence for, the rate determining step in the decomposition of aromatic nitrosamides to form biaryls was the rearrangement of the N-nitrosoacetanilide into the acetoxyazoaromatic complex[18] as shown in Scheme 11. By 1952, it was demonstrated by Huisgen and Nakaten[19] and Hey, Stuart-Webb and Williams,[20] separately, that the rearrangement of the N-nitrosoacetanilide into the acetoxyazoaromatic complex proceeded through a four membered transition state. Suchitzky[21] discovered that arenediazonium acetate ion pairs were present in benzene solutions of substituted N-nitrosoacetanilides as shown in Scheme 12.

Scheme 11: Rate Determining Step for Conversion of N-Nitrosoacetanilide to Biphenyl.[18]



Scheme 12: Formation of Arenediazonium Acetate Ion Pairs.[21]



Freudenberg and Rüchardt then developed a mechanism, Scheme 13, which showed that the key step involved a stable phenyldiazoate radical, Figure 4, which would be capable of abstracting hydrogen from the biphenyl radical, as shown by the # symbol in Scheme 13, forming biphenyl.[22] Rüchard supported this mechanism with the

observation of a long lived ESR signal which was attributed to the phenyldiazoate radical.[23]

Scheme 13: Freudenberg and Rüchardt Mechanism for the Formation of Biphenyl.[22]

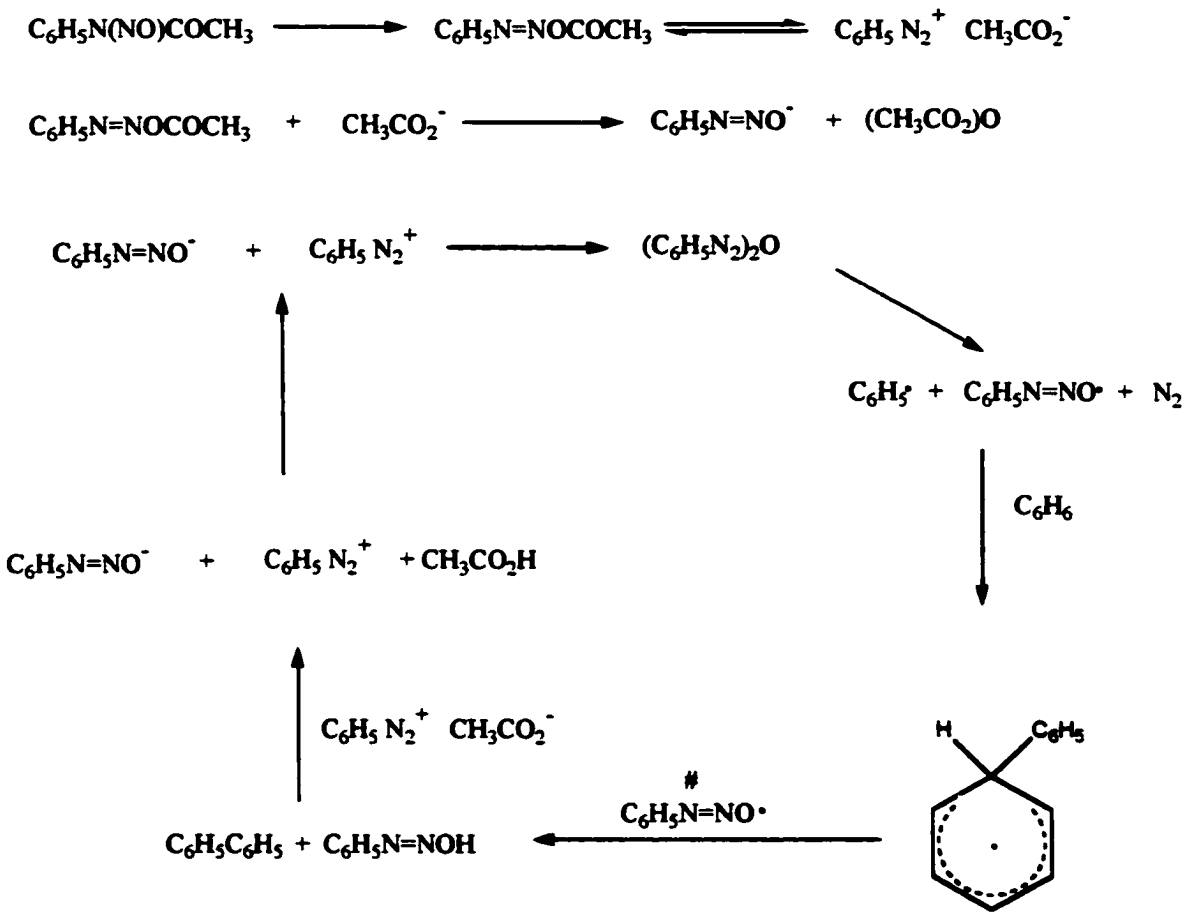
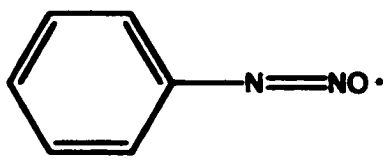
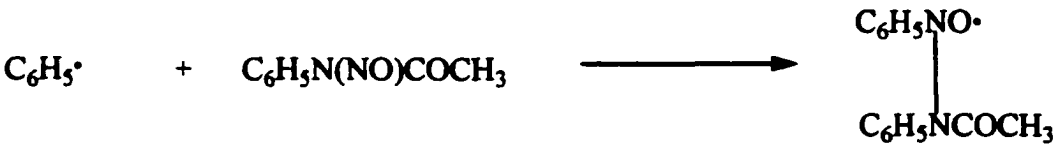


Figure 4: The Phenyldiazoate Radical.



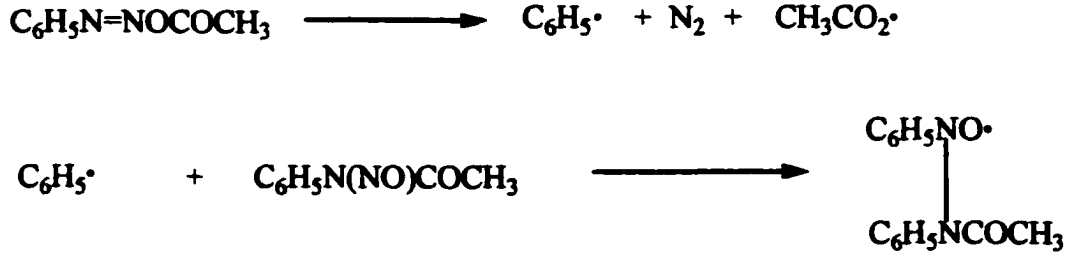
In 1967, Hey and Perkins suggested that Rüchard's ESR signal was not the phenyldiazoate species but that of a (*N*-phenyl-acetamido)phenyl nitroxide produced by the scavenging of a phenyl radical by N-nitrosacetanilide[24] as shown in Scheme 14. This was confirmed by Chalfont and Perkins[25] and other independent syntheses performed by different groups.[26]

Scheme 14: Formation of (*N*-phenyl-acetamido)phenyl nitroxide



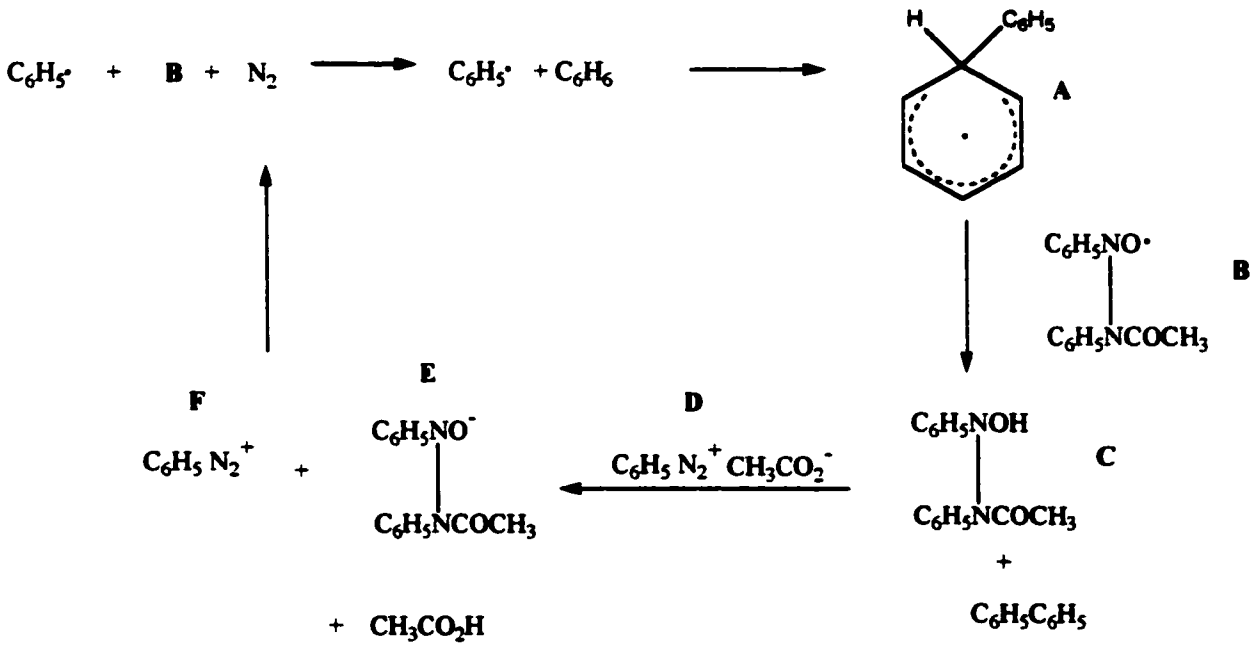
Cadogan, Paton and Thomas provided evidence to show that the ESR signal that was attributed to the (*N*-phenyl-acetamido)phenyl nitroxide species was not present in all solvents and was very weak in solvents having an easily extractable atom forming a stabilized radical.[27] They also found that a second very weak signal existed indicating a new radical existed.[27] They determined that this was an ArN=N· radical.[27] Further studies by Cadogan and Hilbert[26] later developed an initiation process as shown in Scheme 15.

Scheme 15: Initiation Process Developed by Cadogan and Hilbert.[26]



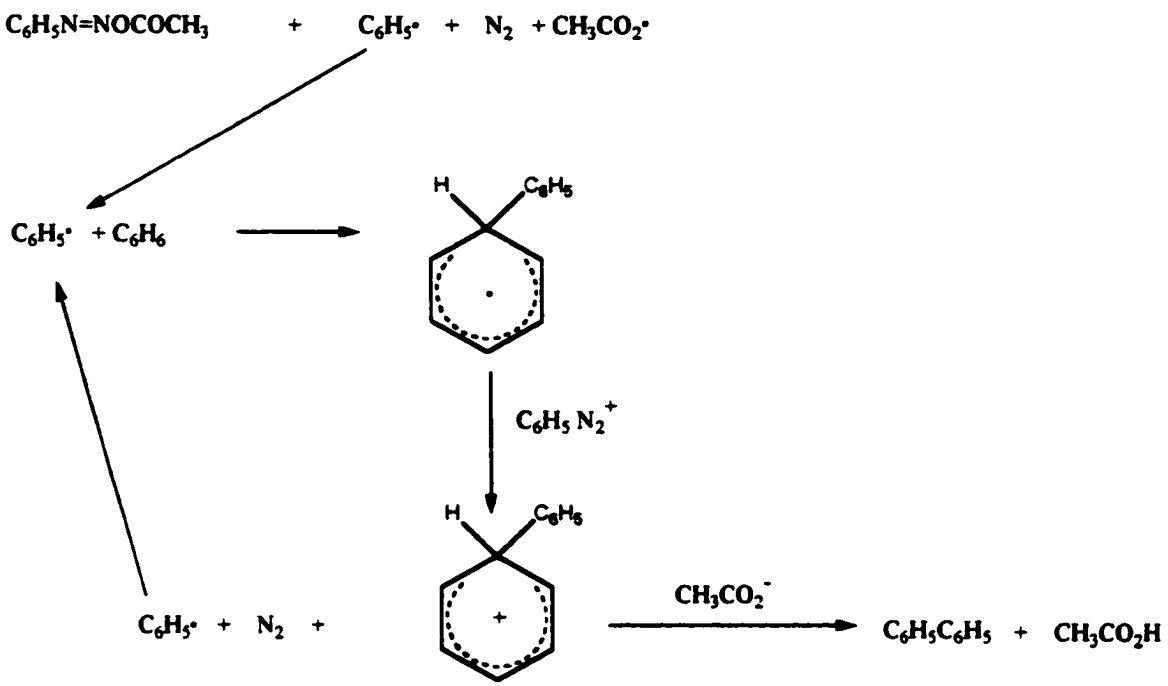
This initiation process then changed the mechanism[26] that is shown in Scheme 16, where the radical species is formed and attacks benzene to form **A**. Then **B** would abstract a hydrogen atom forming **C** and biphenyl. A proton abstraction by **D** then forms acetic acid, **E** and **F**. A redox reaction occurs reforming another phenyl radical and **B**. The process would then continue.

Scheme 16: Cadogan and Hilbert's Modification to the Mechanism.[26]



Cadogan and Hilbert further modified their mechanism, Scheme 17, to show that formation of **B**, from Scheme 16 is not occuring[26] and that the formation of the diazonium cation and subsequent redox reaction forms biphenyl.[26] The important part of this scheme is that it shows that the aromatic nitrosamide can decompose homolytically to form the phenyl and acetoxy radicals. This modification to the mechanism also shows that the phenyl radical can react without the need to be scavenged.

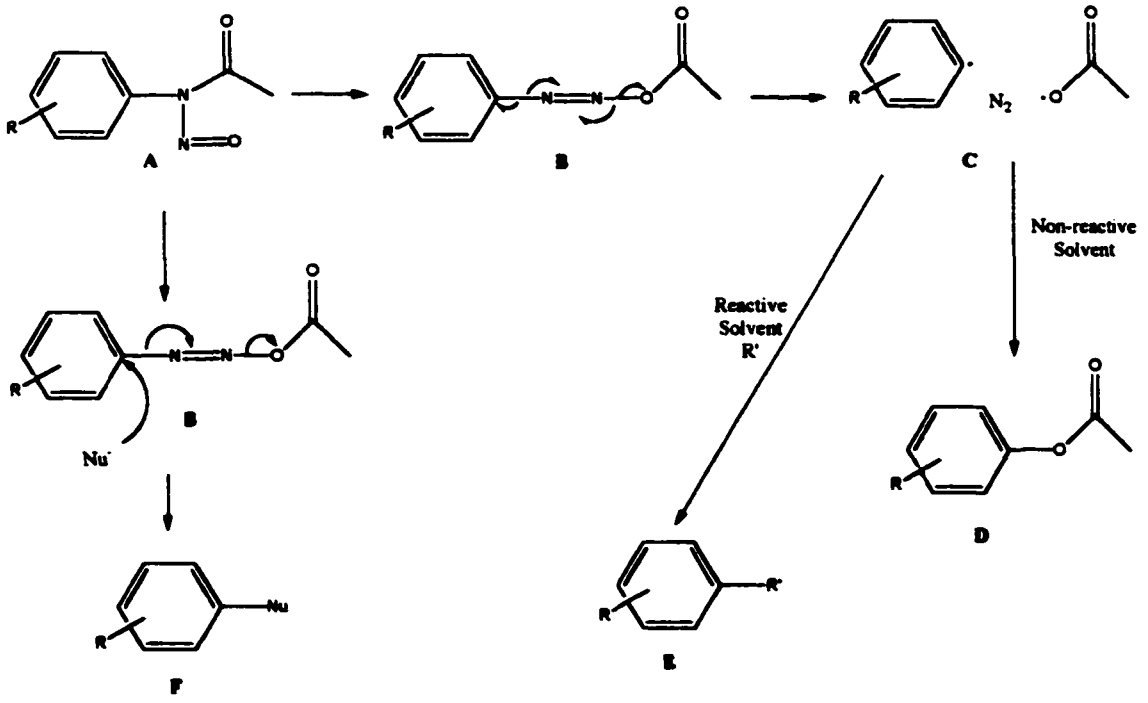
Scheme 17: The Latest Cadogan and Hibbert Modification to the Mechanism.[26]



Even though there is still debate about the mechanism concerning how biphenyls are formed from the decomposition of aromatic nitrosamides in benzene,[26] there is agreement that there is radical decomposition of aromatic nitrosamides forming a phenyl radical species and this can react to form biaryls.[26] However, modification of this reaction by placing it in a non-reactive solvent may result in the formation of esters by allowing the aromatic nitrosamide to decompose forming a phenyl radical and an acetyl radical, which may recombine before the acetyl radical can decarboxylate. Since White and Darbeau's work showed that recombination occurs to form analogous aliphatic and benzylic esters and the mechanistic work discussed earlier showed that aromatic nitrosamides do decompose to the appropriate radical fragments, it appeared reasonable to attempt synthesis of O-aromatic esters from N-aromatic amides. The results of these investigations are discussed in Chapter 2.

In a condensed reaction pathway the aromatic nitrosamide (**A**) will be formed *in situ* and allowed to rearrange to the acetoxyazoaromatic complex (**B**), as shown in Scheme 18. If the acetoxyazoaromatic complex is allowed to decompose in a non-reactive solvent, then the resulting phenyl and acetyl radicals (**C**) will recombine forming an aromatic ester (**D**). If the acetoxyazoaromatic complex is allowed to decompose in a reactive solvent, then the phenyl radical will combine with the solvent forming different products (**E**). Finally, if a nucleophile is introduced before the acetoxyazoaromatic complex decomposes, it may be possible to displace the acetyloxyazo moiety and an aromatic product will be produced with the nucleophile becoming a substituent on the aromatic ring (**F**).

Scheme 18: The Reaction Routes that will be Explored in this Dissertation.



The capture of the intermediate phenyl radicals by reactive solvents will be discussed in Chapters 2, 3 and 4 to achieve polymerization, biaryl formation and halogenations, respectively. The possible nucleophilic displacement of the acetoxyazo moiety by halides to form aromatic halides will be discussed in Chapter 4.

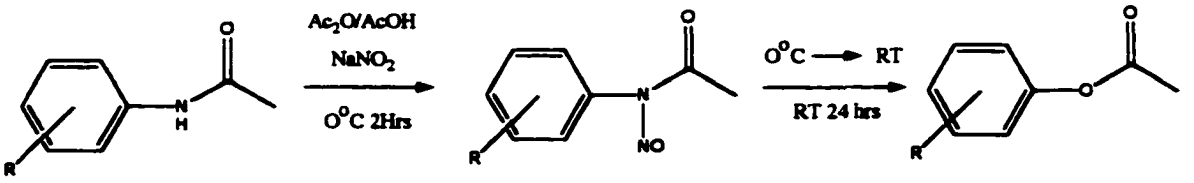
Chapter 2 Conversion of N-Aromatic Amides and Aromatic Amines to O-Aromatic Esters*

2.1 Our Synthetic Approach

In our approach we combined the best of the syntheses of aliphatic and benzylic nitrosamides that were developed from White and Darbeau with the idea of radical decomposition of aromatic nitrosamides as described in Chapter 1. Grieve and Hey's work showed that decomposition of aromatic nitrosamides produces phenyl radical intermediates.[17] Cadogan and Hibbert showed that this decomposition occurs homolytically producing a phenyl radical, nitrogen gas, and an acetyl radical [26] as shown in Scheme 17, Page 15.

The approach that was taken is shown in Scheme 19. Aromatic amides were dissolved in a solution of acetic anhydride and acetic acid and chilled to 0° C, through an ice bath, for approximately thirty minutes. Sodium nitrite was added to form the nitrosamide *in situ*. The nitrosamide was allowed to decompose by warming to room temperature and then remain at room temperature for several hours. If the aromatic nitrosoamide decomposes by a radical mechanism and conditions allow for recombination of radicals to occur, the aromatic esters will form.

Scheme 19: Our Approach to make Aromatic Esters Through Nitrosamide Intermediates.



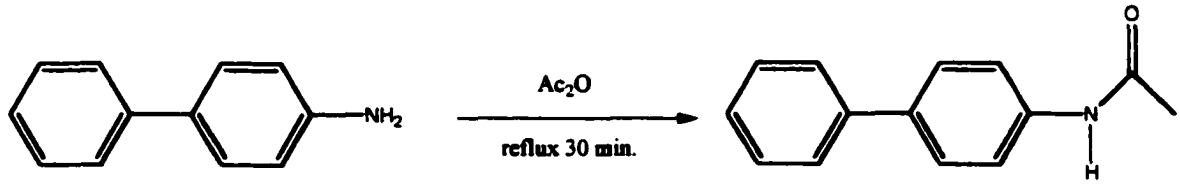
* Some of the material in this chapter is presented in a paper entitled "Conversion of N-Aromatic Amides to O-Aromatic Esters" By D. T. Glatzhofer, R. R. Roy, and K. N. Cossey, *Organic Letters*, Vol.4, No.14, pp 2349-2352.

The use of an acetic anhydride/acetic acid mixture was to provide a non-reactive solvent shell around the nitrosamides. The reason we can say that the solvent shell is non-reactive is because of the inability of the phenyl radical to react with it before recombination with the acetyl radical, forming the aromatic ester. Since the activation energy for radical recombination is low, the ability of the phenyl radical to abstract a proton from the solvent shell is the primary factor which determines how reactive the solvent shell will be. Comparing the bond dissociation energies for the C-H bond to form the phenyl radical is approximately 22kcal/mol[28] while the bond dissociation energy for the O-H bond to form the acetyl radical is approximately 29kcal/mol.[29] This shows that at room temperature there is not enough energy for the phenyl radical to abstract a hydrogen atom from the solvent cage before recombination with the acetyl radical, formed from the homolytic decomposition of the acetoxyazoaromatic complex, can occur. Therefore, under these conditions the solvent cage will be non-reactive.

Upon decomposing to their radical components and the release of nitrogen gas, the radicals should couple together due to the inability to react with the solvent cage. Since electron donating substituents as well as electron withdrawing substituents generally have only a minor effect on radical mechanisms, esters containing both electron withdrawing and electron donating substituents should be easily produced. These esters could later be easily hydrolyzed to their corresponding phenols through standard conditions.[30] These conditions can provide these esters and phenols under milder conditions when compared with usual reactions used to form these compounds, as described in Chapter 1, Section 1.1.

The first synthesis attempted for this dissertation was of N-(4-biphenylyl)acetamide (**2**) (Scheme 20). Commercially obtained 4-aminobiphenyl (**1**) was reacted with acetic anhydride and isolated by pouring the solution into ice/water. The resulting crystals that formed were collected by filtration giving pure **2** in 87% yield.

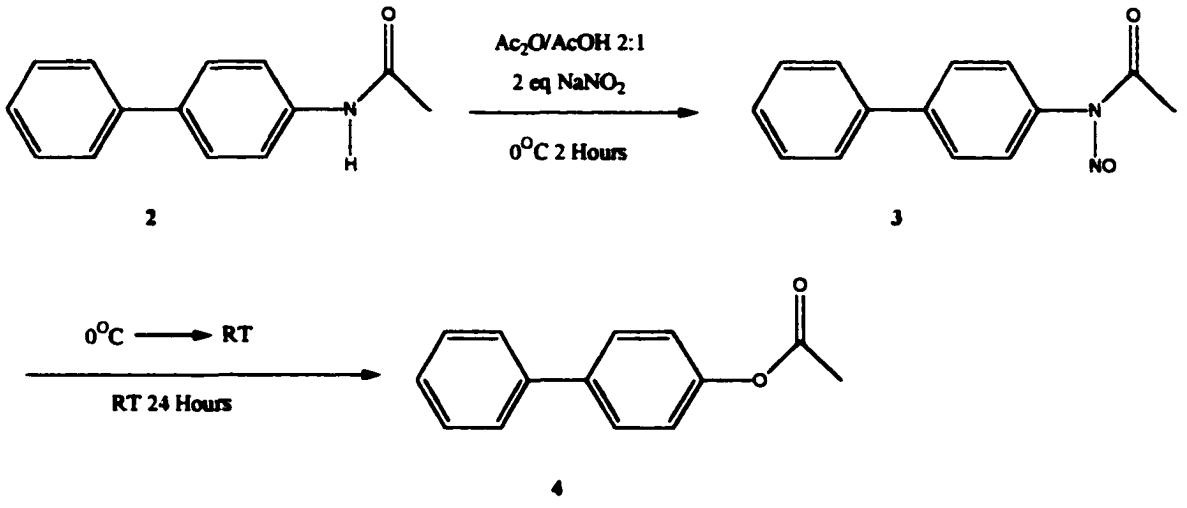
Scheme 20: Synthesis of (N-4-Biphenylyl)acetamide.



1 **2**

The next step of the synthesis was the formation of 4-biphenylyl acetate (**4**) from **2**, shown in Scheme 21, in which **2** was dissolved in a 2 to 1 mixture of acetic anhydride to acetic acid and chilled to 0° C. Two equivalents of sodium nitrite[31] were added to this solution. The mixture changed from a light brown/tan color to a light green color in which a brown gas (NO_2) was evolved. This mixture was kept at 0° C for two additional hours to allow for the formation of N-4-biphenylyl nitrosamide (**3**), *in situ*. The reaction vessel was allowed to warm to room temperature and stay there for an additional 24 hours. A color change from light green to brown was noticed during the equilibration process, with a final dark brown colored solution resulting after the 24-hour period. This mixture was poured into ice/water, the resulting crystals were collected by filtration and purified further by dissolving in ethanol, pouring into ice/water and collecting the resulting crystals by filtration giving pure **4** in 94% yield.

Scheme 21: Synthesis of 4-Biphenylyl acetate from N-(4-Biphenylyl)acetamide.

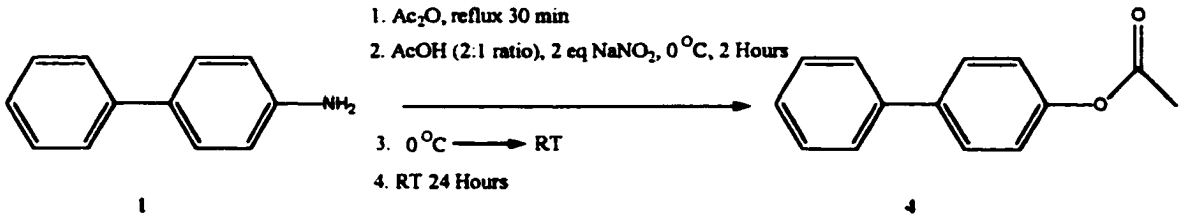


2 3 4

An overall yield of 82% was obtained from this two-pot synthesis. The next synthetic attempt was to combine these steps so a resulting one-pot method could be derived. Although the yield from the two-pot reaction was excellent, if isolation of **2** could be removed, the overall yield of our desired ester should increase.

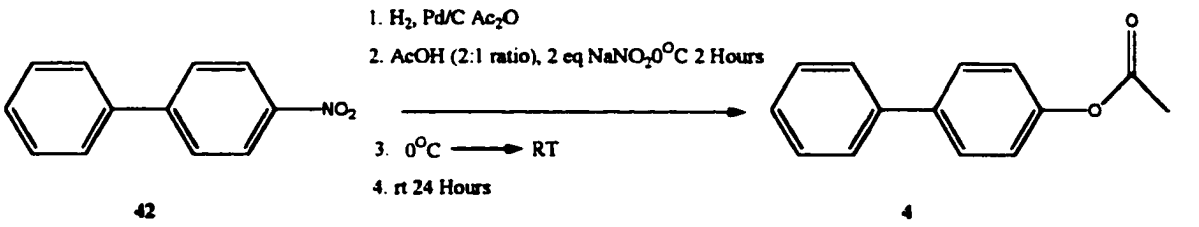
In the one-pot synthetic method, amide **2** was synthesized *in-situ* (Scheme 22) using 4-aminobiphenyl (**1**) as the starting material. The process of synthesizing **2** was the same as described above but instead of isolating it, as soon as the solution cooled down to room temperature, enough acetic acid was added to form a two to one mixture. The rest of the process to synthesize **1** and **4** was as stated above. The isolated yield went from 82% for the two-pot synthesis to 96%.

Scheme 22: One-pot synthetic method for 4-biphenylyl acetate from 4-aminobiphenyl.



Aromatic amines are often generated by catalytic hydrogenation (Pd/C) of aromatic nitro compounds. By carrying out the hydrogenation in acetic anhydride, the amide can be generated *in situ* after reduction.[32] The catalyst can be removed by filtration, the solution cooled, appropriate amounts of acetic acid and sodium nitrite added, and, after reaction and warming to room temperature, the O-aromatic acetate may be generated, as shown in Scheme 23. 4-nitrobiphenyl **(42)** was used as the starting material and was dissolved in acetic anhydride and hydrogenated using 10% palladium on carbon as the catalyst. Amide **2** was thereby synthesized *in-situ* and was not isolated. The palladium on carbon catalyst was removed by filtration and enough acetic acid was added to form a two to one mixture. The rest of the process to synthesize **4** followed the same procedure as described above. This reaction sequence constitutes a two-step, essentially one-pot conversion of aromatic nitro compounds to aromatic acetates. Isolated yield was 97% for the conversion of **42** to **4** through this two-step, one-pot synthetic method.

Scheme 23: One-pot synthetic method for 4-biphenylyl acetate from 4-nitrobiphenyl.



The last reaction sequence constitutes a two-step, essentially one-pot conversion of **42** to **4**. Isolating both 4-aminobiphenyl and N-(4-biphenylyl)acetamide in the reaction sequence before conversion to 4-biphenylyl acetate gave an overall yield of 79%. Isolating the 4-aminobiphenyl but generating the N-(4-biphenyyl)acetamide *in situ* before conversion to 4-biphenylyl acetate gave an overall yield of 87%. However, carrying out the reaction sequence without isolating any of the intermediate compounds gave 4-biphenylyl acetate in 97% yield.

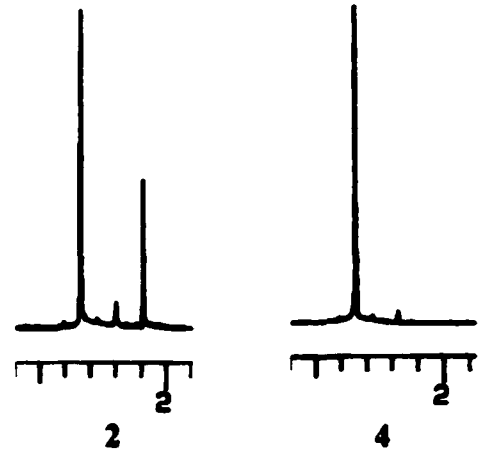
2.2 Use of Mass Spectrometry to Determine the Success of the Reaction

Along with melting points determinations, which were compared to known melting points, mass spectrometry was used to determine if reactions were successful. Generally, ^{1}H-NMR is the major tool used for organic structural characterization. For the ^{1}H-NMR spectrum of **2** a sharp singlet around 2 ppm for the protons on the methyl group near the carbonyl would be expected. There should be a broad singlet near 7.7-7.9 ppm for the amide proton. However, since this proton is fairly acidic, it can rapidly exchange with the solvent used for NMR spectroscopy and may not be observed. There should be a multiplet between 7 and 8 ppm for the aromatic protons on the biphenyl system. For **4** we

would expect a sharp singlet around 2 ppm but further down field of the same peak for the amide. This is because nitrogen was replaced by a more electronegative oxygen. The effect this should have is a greater deshielding of the methyl protons due to the two oxygens being present vs. only one for the amide.

The problem is that ^{1}H-NMR spectra of both compounds were taken, the spectrum for **4** did not show a detectable shift. As shown in Figure 5, the shift was so small that it could be considered just experimental error. Other amide/ester pairs were tested using ^{1}H-NMR spectroscopy with similar results. This left out ^{1}H-NMR spectroscopy as a probe for the determination of success or failure of this reaction.

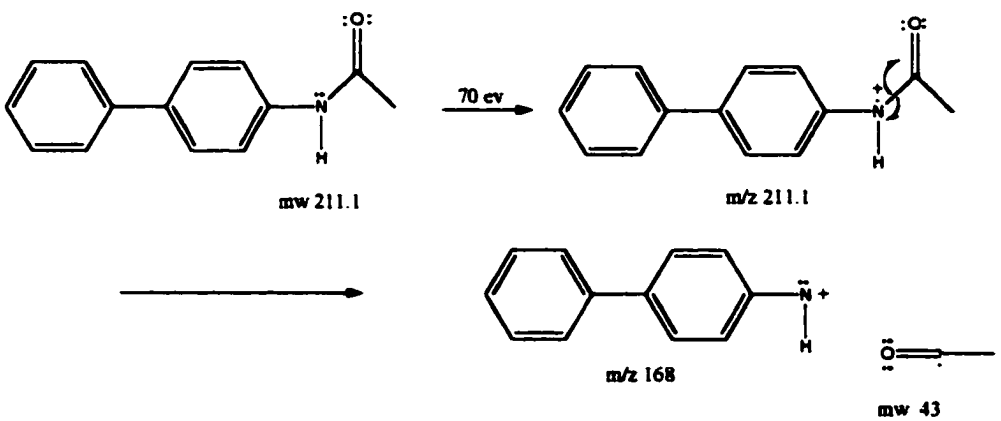
Figure 5: The ^{1}H-NMR Methyl Peaks for the Methyl Protons of **2** and **4**.[33]



Another tool for characterizing these compounds that could be used is Infrared Spectroscopy. A problem with this tool is the absorption peak at the carbonyl region for the ester and the amide is close enough that it would be difficult to discriminate between the two,[34] therefore we would have to use the N-H stretch and bend peaks for the amides.

In the use of Mass Spectrometry (EI) to determine whether the amide was converted to the ester, the differences in molecular weight between the two compounds, and their fragmentation patterns are used. In the conversion of N-(4-biphenylyl)acetamide **(2)** to 4-biphenylyl acetate **(4)**, mass spectra were taken for both of the starting material and the ester. For **2** the spectrum (A.34) shows a M^+ peak (mass peak) at m/z 211.1 The base peak, relative abundance of 100, is at m/z 168.3. This corresponds to the loss of acetyl radical. Scheme 24 shows the fragmentation pathway, which would correlate with this spectrum.

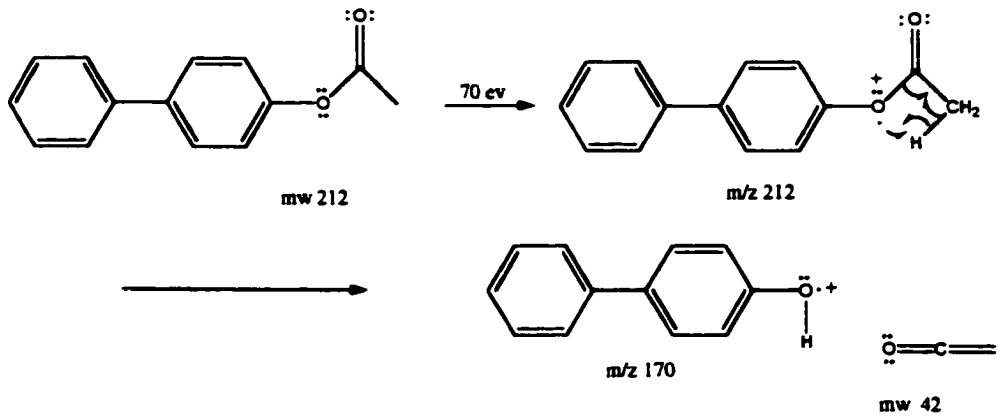
Scheme 24: Fragmentation Pathway of N-(4-biphenylyl)acetamide.



For **4**, (A.1) the spectrum shows a M^+ peak (mass peak) at m/z 212.0. The base peak, relative abundance of 100, is at m/z 170.0. This corresponds to the loss of ketene, molecular weight of 42 as shown in Scheme 25. Mass Spectrometry became the choice of instrumentation to determine the success of the conversion from the starting amides to the esters. This is because, as shown in the fragmentation patterns of **2** and **4**, not only is there a small but definite difference in the M^+ peaks but also in the base peak. The

important fragments of the mass spectra for all the other compounds that were synthesized can be found in the experimental chapter and appendix.

Scheme 25: Fragmentation Pathway of 4-Biphenylyl acetate.



2.3 Summary of Results

The next synthetic attempts involved changing the substituents on the phenyl ring. The reasons for changing the substituents on the phenyl ring were to explore functional group tolerance, to define synthetic utility, and to probe the mechanism of this reaction. These changes included placing electron withdrawing substituents like nitro, cyano, and bromo groups, as well as electron donating substituants like methyl and methoxy groups, on the *para* position of the phenyl ring of the N-arylacetamide (Table 1). All yields were between 81% and 93%. These results show that the reaction is not substantially affected whether the group is electron donating or electron withdrawing. If the reaction were proceeding through some type of a carbocation intermediate, then those esters with electron donating groups, yields should generally give better yields relative to those esters with electron withdrawing groups.

Table 1: Results on Conversion of Aromatic Amides with Electron Withdrawing and Electron Donating Groups to Aromatic Esters.

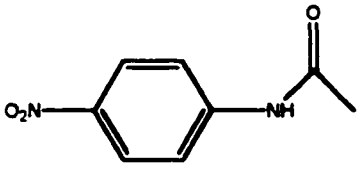
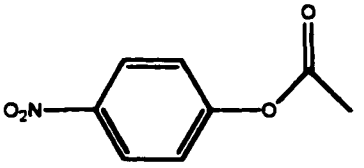
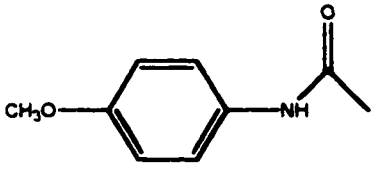
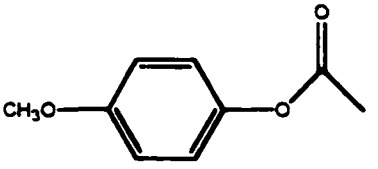
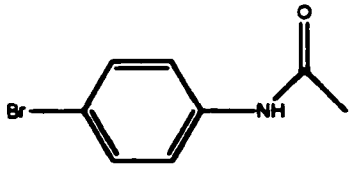
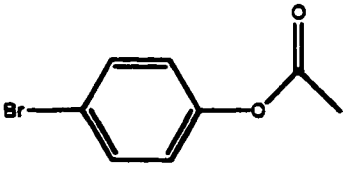
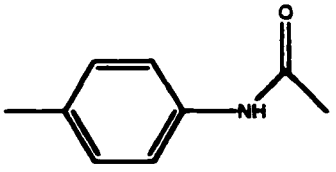
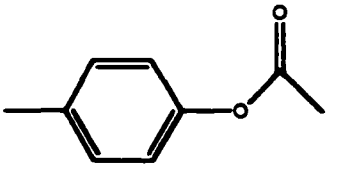
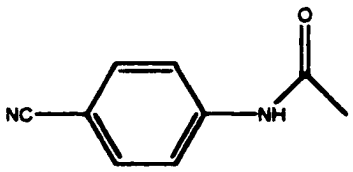
Acetamides	Ester Formed *Percent Yield*
N-(4-Nitrophenyl)acetamide  **5**	4-Nitrophenyl acetate  93% **6**
N-(4-Methoxyphenyl)acetamide  **7**	4-Methoxyphenyl acetate  81% **8**
N-(4-Bromophenyl)acetamide  **9**	4-Bromophenyl acetate  92% **10**
N-(*p*-Tolyl)acetamide  **11**	*p*-Tolyl acetate  82% **12**

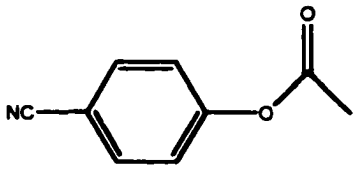
Table 1: Continued.

N-(*p*-Cyanophenyl)acetamide



13

4-Cyanophenyl acetate



88%

14

Going back to Figure 3, Page 10, if an aromatic carbocation is formed, the positive charge would be orthogonal to the π system. If an electron withdrawing group is a substituent on the aromatic ring there would be through resonance, a partial positive charge in the π orbital next to the positive charge which is orthogonal to the π system, destabilizing the system (Figure 6). Because of this we might expect to see relatively poor yields for the compounds with electron withdrawing groups as substituents. For electron donating groups the opposite would be true. If an electron-donating group is a substituent on the aromatic ring there would be through resonance, a partial negative charge in the π orbital next to the positive charge (Figure 7). This, of course, would be stabilizing and one would expect to have relatively high yields. This can be misleading because yields would not actually be affected by electron withdrawing or donating groups but the rates of reaction would be. The fact that the yields would be similar to what is described above is only suggestive. However, at least to a first approximation, the yields can provide a clue toward the possible mechanism that can be occurring.

Figure 6: A resonance structure showing the destabilizing effects due to electron withdrawing groups as substituents.

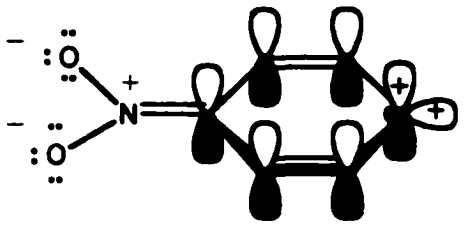
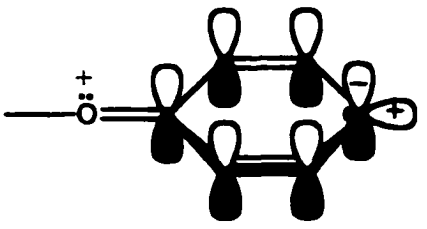


Figure 7: A resonance structure showing the stabilizing effects due to electron donating groups as substituents.

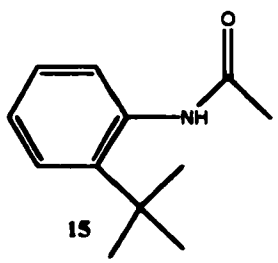
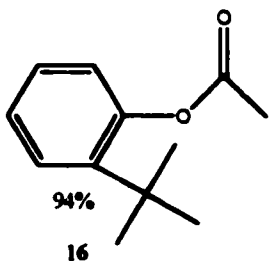
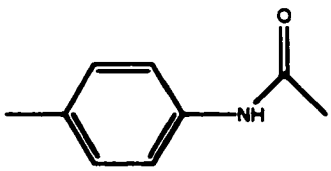
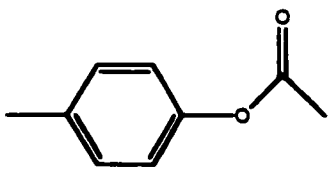
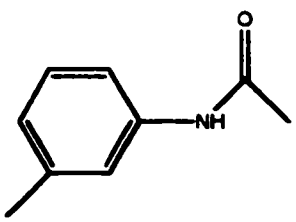
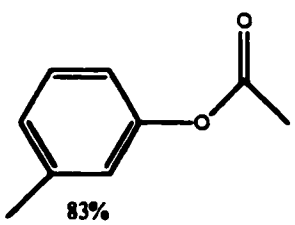


However, for those acetamides that contain electron-withdrawing groups, (**14**, **10** and **6**) as well as those that contain electron donating groups (**12** and **8**), the yields are high. Therefore a type of reaction is occurring that is not substantially affected by electron donating or withdrawing groups, at least with regard to yield during the reaction time frame.

Another series of reactions (Table 2) included changing the position of the substituent from the *para* to the *meta* and *ortho* positions on the phenyl ring and placing bulky substituents on the ring. These changes were made to see if having bulky substituents or substituents in different positions would hinder the reaction. There was no demonstrable effect by having the substituent in the *ortho* or *meta* positions. Having a

bulky *tert*-butyl group in the *ortho* position 16, which is next to the reaction site had no substantial effect on the reaction.

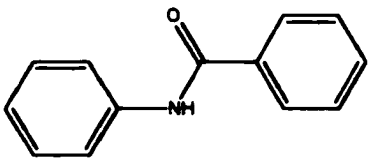
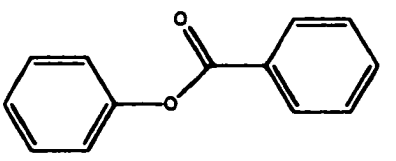
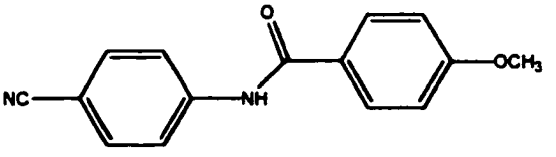
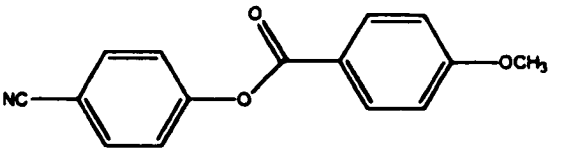
Table 2: Results on Conversion of Aromatic Acetamides, with Bulky Groups and Changing from Para to Ortho to Meta positions, to Aromatic Esters.

Acetamides	**Ester Formed** *Percent Yield*
N-(*o*-*tert*-Butylphenyl)acetamide  **15**	*o*-*tert*-butyl-phenylacetate  **94%** **16**
N-(*p*-Tolyl)acetamide  **11**	*p*-Tolyl acetate  **82%** **12**
N-(*m*-Tolyl)acetamide  **17**	*m*-Tolyl acetate  **83%** **18**

Another series of reactions (Table 3) was designed to see if the reaction involved an exchange with the solvent. Since these reactions are performed in a solvent containing

a 2:1 ratio of acetic anhydride to acetic acid, could there be an acetoxy exchange with the solvent? Changes were made on the acetyl portion of the compound. The methyl group on the acetyl portion was replaced with a phenyl group in **20**. If there is an

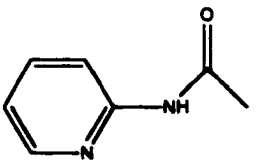
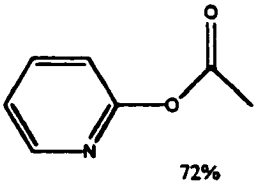
Table 3: Results from Reactions to Test for Solvent Exchange.

Acetamides	**Ester Formed** *Precent Yield*
Benzanilide  **19**	Phenyl Benzoate  91% **20**
N-(4-Cyanophenyl)-4-methoxybenzamide  **21**	4-Cyanophenyl 4-methoxybenzoate  91% **22**

exchange between the amide and the solvent, the benzoyl group should be formally lost and replaced with the acetyl group. A second compound **22**, which has an electron withdrawing cyano group on the aniline portion of the benzamide while having an electron donating group, methoxy group on the benzoate side, was tested. In both cases exchange was not observed and in both instances the yields are still high. These reactions show that solvent exchange is not occurring during the reaction, so the solvent is apparently inert concerning this reaction.

Another reaction was performed to see if it could be successful if there was a hetoroatom in the aromatic ring. The six carbon aromatic ring was replaced with a pyridine moiety which introduced a nitrogen into the aromatic system. N-(2-Pyridyl)acetamide **(23)** was converted to 2-pyridyl acetate **(24)** in 72% yield, as shown in Table 4. This can be hydrolyzed, either through its workup procedure or through further reactions into the 2-pyridinol. Therefore the synthesis of **24** has a potential usefulness to the pharmaceutical industry.

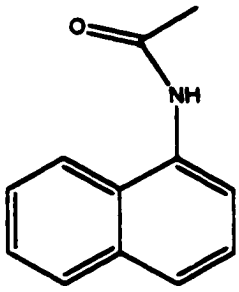
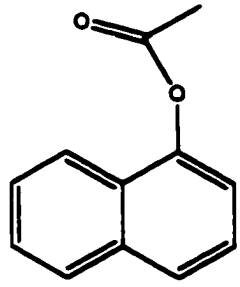
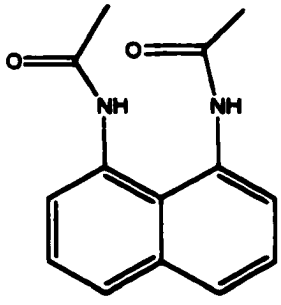
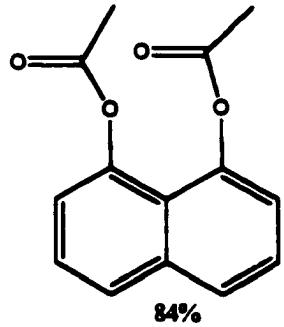
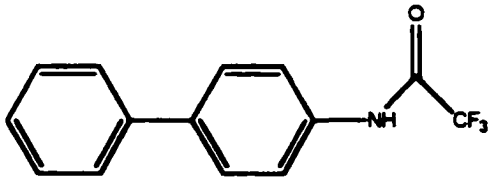
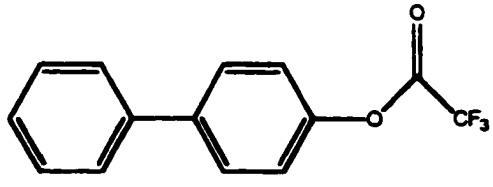
Table 4: Results of a Reaction on a Hetroatom System.

Acetamides	**Ester Formed** *Percent Yield*
N-(2-Pyridyl)acetamide  **23**	2-Pryidyl acetate  72% **24**

A final series of reactions, Table 5 page 3, dealt with the use of N-1-napthyl acetamide **(25)**, 1,8-bis(N-acetamido)naphthalene **(27)**, and N-(4-biphenylyl)trifluoroacetamide **(29)**, which were converted to the corresponding 1-napthyl acetate **(26)**, 1,8-bisacetoxynaphthalene **(28)**, and 4-biphenylyl trifluoroacetate **(30)**. These experiments were designed to determine the effects that the naphthyl system or trifluoromethyl groups could have on this reaction. There were no obvious effects from these changes and all yields were typical. Compound **28** is especially synthetically useful because with hydrolysis it can be converted to the 1,8-dihydroxynaphthalene, which is of

interest as an unusual ligand[35] but such diols are otherwise difficult to access synthetically.

Table 5: Results from Reactions on Napthylene and Fluoroine Systems.

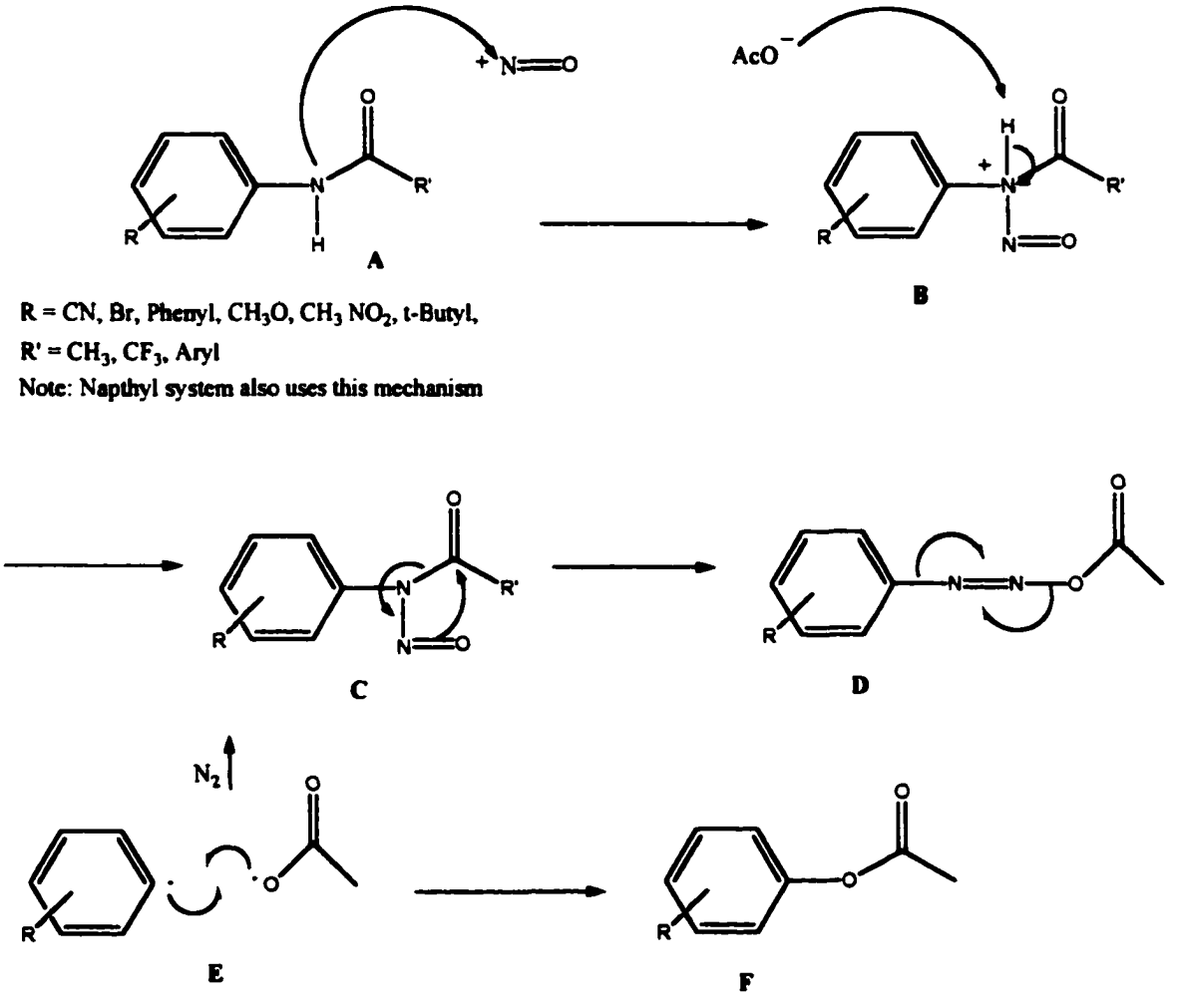
Acetamides	**Ester Formed** *Percent Yield*
N-1-Napthyl acetamide	1-Napthyl acetate
	
25	91% **26**
1,8-bis(N-acetamido)naphthalene	1,8-bisacetoxynaphthalene
	
27	84% **28**
N-(4-Biphenylyl)trifluoroacetamide	4-biphenylyl trifluoroacetate
	
29	94% **30**

2.4 The Proposed Mechanism for this Reaction.

Scheme 26 shows our proposed mechanism for the conversion of aromatic amides to aromatic esters. Starting with the amide **A**, the lone pair on the nitrogen attacks the nitrosonium ion, which was formed *in-situ* from sodium nitrite and acetic acid. This forms the nitrogen tetrahedral intermediate **B**. This intermediate gets deprotonated by the acetyl anion forming the nitrosoamide **C**. This rearranges forming intermediate **D**, which homolytically cleaves forming the radical pair **E** with the loss of nitrogen gas. Huisgen[36] showed that the rate-determining step, during his work on arylation using nitrosoacetanilides is the rearrangement to the aromatic azoacetoxy intermediate **D**. Kinetic studies would have to be performed to determine if this is also the rate determining step in this reaction. The radical pair, which is inside an inert solvent cage, couples together forming our ester **F**.

This mechanism is not new but described in various ways in Chapter 1. **A** through the formation of **D** was described by White and Darbeau in the formation of their allylic and benzylic esters, as described in Chapter 1, Section 2. **A** through **D** was also described by Grieve and Hey as well as Cadogan and Hibbert in the formation of aromatic nitrosamides, as described in Chapter 1, Section 3. Huisgen and Horeld suggested that the conversion of **C** to **D** was the rate determining step as shown in Scheme 11. Grieve and Hey as well as Cadogan and Hibbert described the radical recombination invoked in **E** in their synthesis of their biaryl compounds. This is also supported by work performed by Cadogan and Hibbert as shown in Scheme 15, Page 13. The acetoxyazoaromatic homolytic decomposition is also supported by the reaction in that it is relatively unaffected by both electron donating and electron withdrawing groups.

Scheme 26: Our Proposed Mechanism for Conversion of Aromatic Amides to Aromatic Esters .



Other evidence to support the radical decomposition also includes polymerization work that is described in Section 2.5. A carbocation/anion mechanism is suspect because this would place the positive charge on the aromatic ring orthogonal to the π system thereby allowing no assistance in its stability. If it were to proceed through an anionic/cationic intermediate then electron withdrawing groups should be destabilizing, as described in Section 2.2, and therefore yields might be relatively poor.

The inertness of the solvent was tested by the formation of **20** and **22** in which no exchange with the solvent was shown. The idea that an inert solvent cage surrounds **E** was developed through the lack of any cross-coupling products. Since biaryl products were not observed in either reaction, the aromatic radical must see only the acetyl radical after nitrogen gas escapes, which would explain why no biaryl is produced. These results can only be accomplished through an inert solvent cage. The polymerization work discussed in section 2.5 gives additional evidence concerning the role of the solvent cage by showing a reaction in which the solvent cage is changed to a reactive one.

2.5 Polymerization of Methyl Methacrylate through *p*-Nitrophenylnitrosamide Initiation.

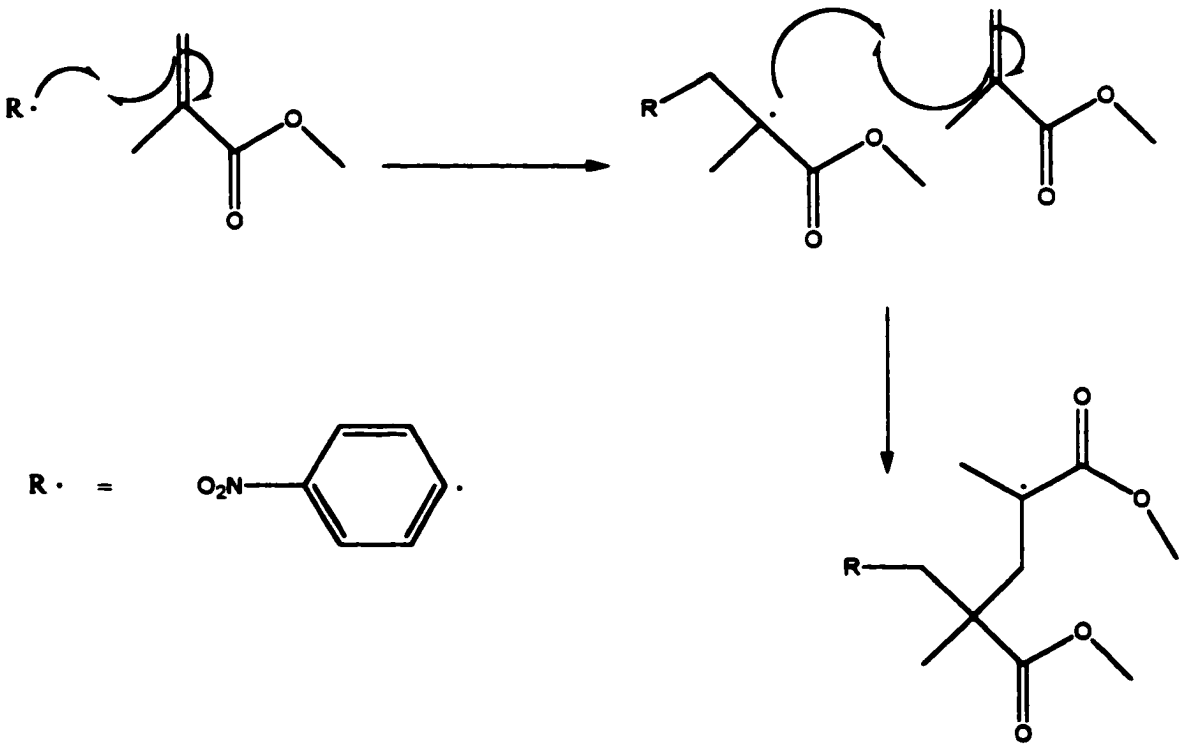
A method was developed to provide further evidence confirming the homolytic cleavage involved in our proposed mechanism. It involved using N-(*p*-nitrophenyl)nitrosamide **31** as the initiator for the polymerization of methyl methacrylate. This system was chosen because of the ability to isolate the nitrosamide as well as other reasons that will be described shortly. In the decomposition of **31**, a *p*-nitrophenyl radical as well as an acetyl radical should be formed. In a solvent containing a mixture of acetic anhydride and acetic acid, the radical pair would form inside an inert solvent cage, coupling together to create ester **6**. However, if this decomposition would take place in a solvent cage that the radicals could react with, the *p*-nitrophenyl radical would be incorporated into the new compound. The reactive solvent that was used was methyl methacrylate.

Methyl methacrylate can be initiated through radical and anionic initiators (Scheme 27). Cationic initiators or acetyl anions cannot initiate polymerization of methyl

methacrylate. Therefore, if methyl methacrylate is used as the solvent for the decomposition of **31** and the *p*-nitrophenyl radical is formed, then it should be incorporated as an end group in the polymer.

p-Nitrotoluene has a lambda max, using UV/Visible spectroscopy, of 274 nm in chloroform .[37] Since polymethylmethacrylate (PMMA) has no absorption near this range, if the *p*-nitrophenyl radical is incorporated into the polymer as end groups, then a lambda max of 274 nm should be observed.

Scheme 27: Polymerization of Methyl Methacrylate Through a Radical Initiator.



N-(*p*-Nitro- nitroso)acetanilide **(31)** was synthesized using previously mentioned methods and isolated by pouring into ice/water and quickly filtering the solid keeping it cold. A blank was also created following the same procedure to synthesize **31** with the

exception that, N-(4-nitrophenyl)acetamide, was not added. A mixture of 1 mL of acetic anhydride and 0.5 mL of acetic acid was used to dissolve 0.1346g of **31** and this was added to a foil covered test tube containing 30 mL of methyl methacrylate, while 1.5 mL of the blank was added to a second foil covered test tube also containing 30 mL of methyl methacrylate. Both test tubes were kept in the dark to prevent any polymerization due to light. After two days the blank showed no sign of polymerization and the solution was clear. However, the test tube containing **31** contained a very viscous, dark brown/reddish solution.

Dissolving this viscous, dark brown/reddish solution into chloroform and adding this to methanol precipitated a white polymer which was collected by filtration. This gave 1.25 grams of polymer. This polymer was purified by dissolving in chloroform, adding this to methanol again and collecting the polymer. The purification steps were performed three times to remove any contaminants that could interfere with UV/Visible spectroscopy.

A solution of *p*-nitrotoluene in chloroform (9g/L, 6.83×10^{-5} moles) was made for two reasons. The first is that since the lambda max of *p*-nitrotoluene is known (274 nm),[37] this solution was used to calibrate the instrument. The second reason is to obtain the experimental molar absorbance number. This number would be used later on in a formula to determine the maximum average molecular weight of the polymer we synthesized. This solution had a lambda max of 255 nm and an absorbance of 0.66. This informed us the instrument recorder was off by 19 nm. The absorbance of 0.66 was plugged into the formula below to obtain the experimental value for molar absorbance.

With A = absorbance l = path length of the cell which was 1 cm and c = concentration

$$\text{Since } A = \xi lc$$

$$\text{Therefore } \xi = A/c$$

$$.66/6.83 \times 10^{-5} = \xi$$

$$\xi = 9650$$

The literature value is 9490,[37] so this is an error of approximately 2%

A solution of the polymer in chloroform (11.16g/L) was made for determination of its maximum molecular weight. This was also tested and had an experimental lambda max of 255nm, corrected to 274 nm. This fit the nitrophenyl end group lambda max. This solution had an absorbance of 0.55. With the absorbance and molar absorbance determined, this information can be placed into the equation shown below in order to determine the polymer's maximum molecular weight.

$$A/\xi = c$$

$$A = .55 \text{ and } \xi = 9651.94$$

$$.55/9651.94 = c$$

$$c = 5.698 \times 10^{-5} \text{ moles}$$

Since we used a polymer solution containing 11.16g/L

$$[.11.16 \text{ g/L}] / [5.698 \times 10^{-5} \text{ moles/L}] = 196010 \text{g/mole}$$

The maximum molecular weight for the polymer was 196,000, in which an assumption was made that that only one p-nitrotoluene end group capped every polymer chain. The reason for stating this would be the maximum weight for the polymer is if the acetoxy or

methyl radical is incorporated into some of the polymer chains as an end group, then the molecular weight of the polymer would be lower. So by making the assumption that p-nitrotoluene is the end group on all the polymer chains we can obtain the maximum molecular weight for the polymer. The polymerization of methyl methacrylate by **31** gives further evidence to support a radical decomposition for our proposed mechanism.

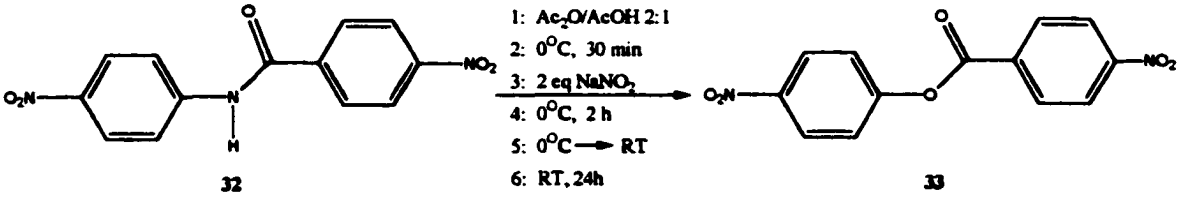
An experiment was conducted to determine if the nitrosamide can polymerize methyl methacrylate without the requirement of isolating the nitrosamide first. *p*-Nitro-N-nitrosacetanilide (**31**) was synthesized using previously mentioned methods, however, it was not isolated. A blank was also created following the same procedure to synthesize **31** with the exception that, N-(4-nitrophenyl)acetamide, was not added. The entire solution containing **31**, 3 mL, was added to a foil covered test tube containing 25 mL of methyl methacrylate while 3 mL of the blank was added to a second foil covered test tube also containing 25 mL of methyl methacrylate. Both test tubes were kept in the dark to prevent any polymerization due to light. After two days the blank showed no sign of polymerization and the solution was clear. However, the tube containing **31** contained a very viscous, dark brown/reddish solution.

Dissolving this viscous, dark brown/reddish solution into chloroform and adding this to methanol precipitated a white polymer which was collected by filtration. This gave 2.27 grams of polymer. The blank was treated in the same fashion but no polymer was detected or recovered. This results show that the nitrosamide does not require isolation for it to be a viable initiator.

2.6 Synthesis of Polynitrophenyl Benzoates as Possible Energetic Materials.

Synthesis of 4-cyanophenyl 4-methoxybenzoate **(22)**, (Table 3, page 31) showed that phenyl benzoates can be constructed that possess an electron donating group in one ring and an electron withdrawing group in the other ring. The next synthetic attempt involved the construction of a phenyl benzoate which contained an electron withdrawing group in each ring. The first attempt involved the conversion of N-(4-nitrophenyl)4-nitrobenzanilide **(32)**, to 4-nitrophenyl 4-nitrobenzoate **(33)**, which is shown in Scheme 28. An overall yield of 81% was obtained from this conversion. This not only gave further evidence for non-exchange with a non-reactive solvent but also showed that this reaction can be conducted with electron withdrawing groups in both structural fragments.

Scheme 28: Conversion of N-(4-Nitrophenyl)4-Nitrobenzanilide to 4-Nitrophenyl 4-nitrobenzoate.



32 33

These results provided the impetus to further investigate by developing polynitro systems based on the phenyl benzoate moiety. The utility of this could result in new carbon, hydrogen, nitrogen, oxygen, (CHNO) energetic materials. In this case one could possibly make a hexanitrophenyl benzoate system as shown in Figure 8. This molecule actually looks like two trinitrotoluene (TNT) molecules (Figure 9) connected by an ester. The benefit of the hexanitrophenyl benzoate system when compared to 2 TNT molecules

would be the extra mole of CO_2, provided by the ester moiety, if it turns out to be an energetic material. Therefore this would be a better energetic material. Another molecular model could be hexanitrostilbene (HNS), Figure 10, which is replacing the ethylene bridge by the ester group. One method of comparing the polynitrophenyl benzoate systems to the trinitrotoluene and hexanitrostilbene is through its oxygen balance.

Figure 8: A Possible Energetic Target, 2,4,6-Trinitrophenyl 2,4,6-Trinitrobenzoate.

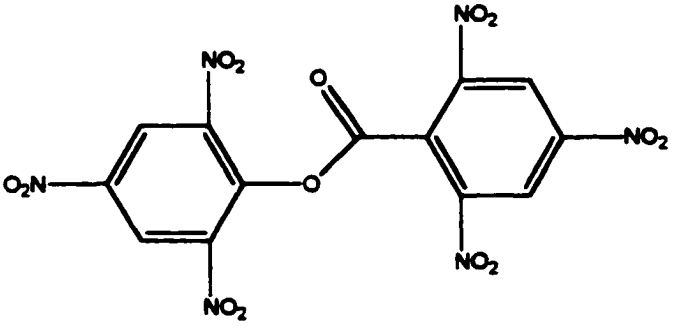


Figure 9: 2,4,6-trinitrotoluene (TNT)

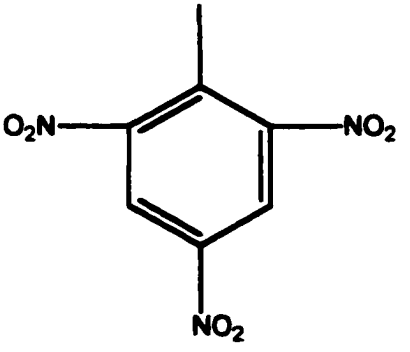
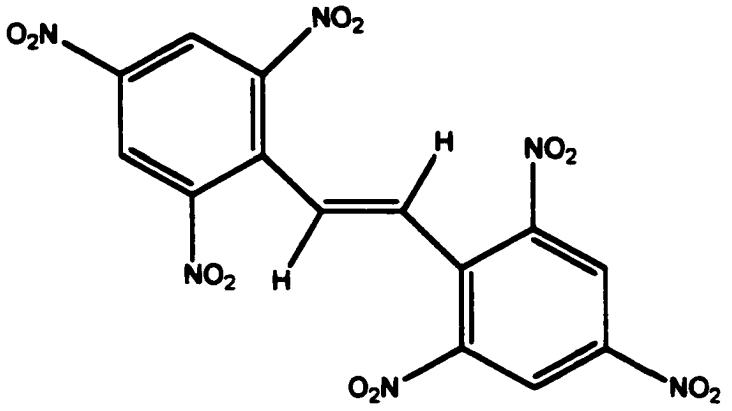


Figure 10: Hexanitrostilbene



To begin to understand what oxygen balance is, an explanation of reaction product hierarchy needs to be provided. In CHNO systems the general formula is expressed as $C_xH_yN_wO_z$,[38] where x, y, w, and z are the number of atoms in the potential explosive or energetic material. When an energetic material, like a propellant, is burning or an explosive detonates the reactant molecule is completely broken down to its individual component atoms.[39] These atoms then recombine to form the final products of the reaction. The reaction hierarchy of products generally follow the rules shown in Table 6.[40]

Table 6: Reaction Hierarchy for Energetic Materials.

1. All the nitrogen forms N_2
2. All the Hydrogen is oxidized to H_2O
3. Any remaining oxygen left after H_2O oxidizes carbon to CO
4. Any remaining oxygen left after CO formation oxidizes CO to CO_2
5. Traces of NO_x (mixed oxides of nitrogen) can be formed in an air explosion/burn.

Using this hierarchy for 4-nitrophenyl 4-nitrobenzoate ($C_{13}H_8N_2O_6$) we end up with the 2 nitrogen atoms to form N_2, 8 hydrogen atoms get oxidized by 4 oxygen atom converting to 4 water molecules. There are 2 oxygen atoms left which will oxidize 2 carbon atoms to 2 CO. No oxygen atoms are left, therefore, there are 11 carbon atoms left and this molecule is extremely oxygen poor. This molecule is therefore a poor candidate for an energetic material. The importance of this is that when an explosive or other energetic material is exactly oxygen balanced, it produces the maximum energy output per unit weight of that material.[41] The relative amount of oxygen, in an explosive or propellant, required to oxidize it completely is expressed quantitatively as oxygen balance. This formula is shown in Figure 11.[42]

Figure 11: Formula for Oxygen Balance.

$$\text{Oxygen Balance\%} = 100[16.00/\text{Molecular Weight}][z - 2x + y/2]$$

Placing 4-nitrophenyl 4-nitrobenzoate into this formula gives the following results.

$$OB\% = [\ 1600/288.0][6-(2 \times 13) + (8/2)]$$

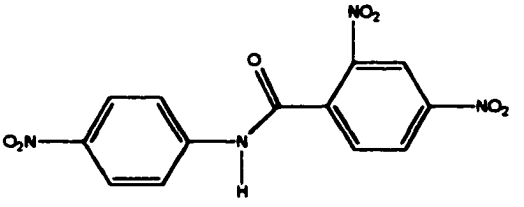
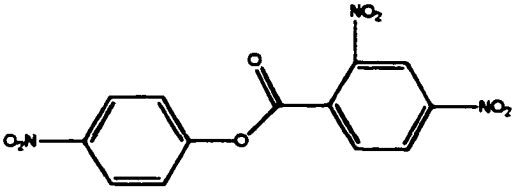
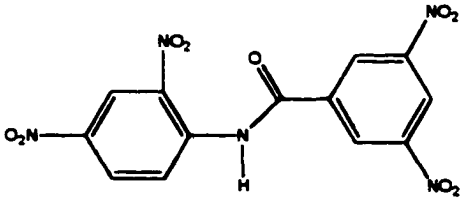
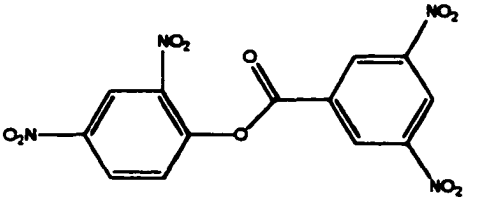
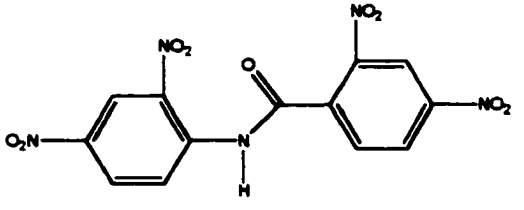
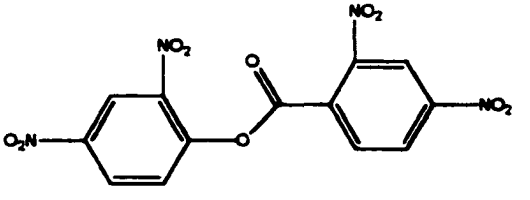
$$OB\% = -89$$

This was not surprising because our reaction hierarchy calculations demonstrated that 11 carbons are left over so this molecule is very under oxidized. Comparatively, TNT, which has one of the lowest oxygen balances and still can explode, has an oxygen balance of –73.97%.[41] So **33** would not be a worthy candidate for an energetic material. The simplest way to boost the oxygen balance would be to add more nitro groups to the compound.

The next target therefore was the formation of 4-nitrophenyl 2,4-dinitrobenzoate **35**, (Table 7) . This compound adds 2 additional oxygen atoms to the chemical formula and more of the carbons can now be oxidized. When 4-nitrophenyl 3,5-dinitrobenzoate's oxygen balance is calculated it, comes out to be a – 69.6%. Although we improved the oxygen balance by about 19.3%, it's now 4.37% above the TNT level.

Comparison of the oxygen balance between a potential energetic material and a known explosive standard, such as the generally used standard TNT, is one method of determining the potential of a possible energetic material. Another, more visual and useful method is through the use of thermal analysis. When a sample of 4-nitrophenyl 3,5-dinitrobenzoate was tested with thermal gravimetric analysis (TGA) methods, the decomposition curve is a shallow curve (A.41). The compound lost 1.44 mg of it's mass over a 52 ° C temperature range. This shows that 4-nitrophenyl 3,5-dinitrobenzoate is a poor candidate for an explosive as a good candidate's decomposition curve would be very sharp, losing a large amount of it's mass in a very short period of time, especially in helium. This is because if you have similar or better results in helium, the energetic material has enough oxygen within it to be able to be used in an oxygen poor atmosphere or in a vacuum environment, ideal for a propellant.

Table 7: Results of this Reaction on Polynitro Systems.

Acetamides	Ester Formed *Precent Yield*
N-(4-Nitrophenyl) 2,4-dinitrobenzamide  34	4-Nitrophenyl 2,4-dinitrobenzoate  73% 35
N-(2,4-Dinitrophenyl) 3,5-dintirobenzamide  36	2,4-Dinitrophenyl 3,5-dinitrobenzoate  77% 37
N-(2,4-Dinitrophenyl) 2,4-dinitrobenzamide  38	2,4-Dinitrophenyl 2,4-dinitrobenzoate  77% 39

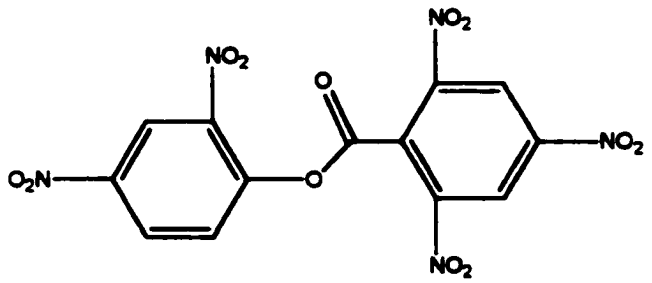
The next target was the formation of 2,4-dinitrophenyl 3,5-dinitrobenzoate (**37**), (Table 7). This compound adds 2 additional oxygen atoms to the chemical formula and the more of the carbons can now start to be oxidized. When **37's** oxygen balance is calculated it comes out to be a – 54.9%. The oxygen balance improved by about 34%

when compared with **33** and it's now about 19.07% above the TNT. When TGAs of **37** were obtained , A.38 in air and A.37 in helium, they show a vast improvement when compared with **35**, showing a decomposition curve that is steeper. The compound lost 51 % of it's mass over a 12 °C range with approximately 28% of residue remaining in air. The compound lost 66 % of it's mass over an 8 °C range with approximately 20% of residue remaining in helium. In an excellent energetic material/explosive there would be a very small amount of residue, ideally less that 10%, because most of its mass would be converted to gas. The results shows that **37** is a becoming a better candidate for an explosive. In may cases the TGA becomes a better analytical tool for analysis of an energetic material because one is dealing with constitutional isomers so the oxygen balance would be the same.

The next target was the formation of 2,4-dinitrophenyl 2,4-dinitrobenzoate (**39**), (Table 7). **39's** oxygen balance would also be a – 54.9%. According to its oxygen balance this compound should behave the same as **37**. TGA analysis shows that this compound has improved when tested in both air (A.39) and helium (A.40). The compound lost 63% of it's mass over a 12 °C range with approximately 26% of residue remaining in air. The compound lost 68 % of it's mass over a 14 °C range with approximately 18% of residue remaining in helium. When **37** is compared with **39, 39** does better in air while, to a first approximation, has similar results in helium. This shows that in many cases comparison of oxygen balance is not enough but one needs to analyze the compound using TGA. In the future, a pentanitro system (Figure 12) and the hexanitro system (Figure 8) need to be synthesized. For the pentanitro system the oxygen balance would be –42% and for the hexanitrosystem it would be –34%. These numbers

are not only better than TNT but for the hexanitrosystem it is 12% better than the hexanitrostilbene model system (oxygen balance of –46%) that was described in the beginning of this section. There are many other factors, other than reaction hierarchy, oxygen balance and it's TGA results, that determine the potential and utility of energetic materials and explosives. These can be found though a more extensive review of the literature. [38-43]

Figure 12: 2,4-dinitrophenyl 2,4,6-trinitrobenzoate.



2.7 Summary of the Ester Reaction

In summary, the method for conversion of N-aromatic secondary amides to O-aromatic esters presented here is inexpensive and convenient, carried out in low environmental impact solvents, using minimal equipment, and not requiring isolation of intermediate N-nitrosamides or diazonium salts. We have scaled-up the reaction without difficulty to effect multi-gram conversions. Yields are uniformly high (although conditions were not optimized) and the reaction can be carried out with a variety of functional groups present in the substrate. The method can be simply modified to be carried out directly on aromatic amines and in some cases can be extended to be carried out on aromatic nitro compounds. Phenols can easily be generated from the resulting

esters and work-up procedures could be easily developed to obtain the phenol without isolating the ester.

We have expanded this reaction to allow for the initiation of polymerization incorporating a UV/Vis active end group (*p*-nitrophenyl) into the polymer. This can be accomplished without isolating the nitrosamide intermediate. We have used this method to form various polynitro systems in reasonable to good yields. While this demonstrates the ability of this method to form esters with electron withdrawing substituants on each phenyl fragment, it also shows that this method can be used as a milder method to form energetic materials. Although the aromatic nitrosamide systems were known since 1876, [14] we are now using this system for the formation of esters, initiation of polymerization, and formation of possible energetic materials under mild and environmentally friendly conditions. In the next chapter it will be shown how the *in situ* nitrosamide formation can be used to form biphenyls.

Chapter 3 *In Situ* Conversion of N-Aromatic Amides to Biphenyls

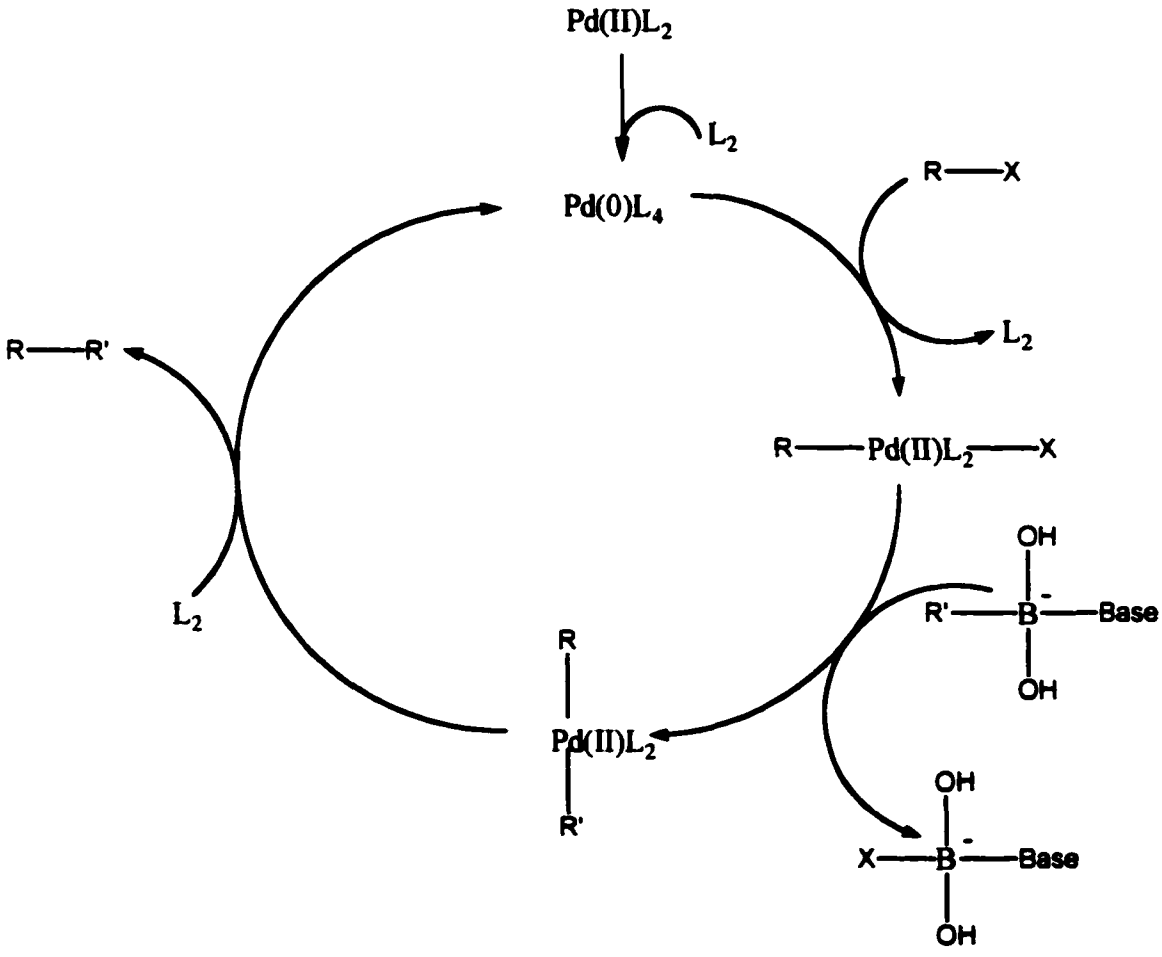
3.1 Introduction and Synthetic Approach

The formation of biphenyls is an important synthetic procedure, especially in the areas of natural product and pharmaceutical synthesis. The most common modern method for the synthesis of biphenyls is through the use of the Suzuki coupling (Scheme 29). This involves the use of an aryl bromide, arylboronic acid and a palladium catalyst to couple them together. Although the Suzuki coupling is generally straightforward, a brief review of the literature shows that the reaction yields can be variable depending on the substituents attached to the aromatic ring.[44,45,46] Another problem is the need to, in some cases, synthesize the arylboronic acid. The common catalysts used in the Suzuki coupling are generally triarylphosphine/Pd complexes,[46] however, these catalysts have an air-sensitivity problems and require special handling. A recent publication by Netherton and Fu reported the use of trialkylphosphonium hydroboronofluorides with palladium catalysts to perform these couplings which are less air-sensitive.[47] A variety of techniques[48,49] have been developed over the recent years in an effort to improve yields. Most notable of these includes a recently published method by Tao and Boykin in which palladium diacetate/2-aryl-2-oxazoline catalysts were used to synthesize various biaryls.[50]

Several decades ago, Grieve and Hey developed a synthesis in which nitrosamides were used to synthesize biphenyls. They synthesized their aromatic nitrosamides by various routes[51] and then allowed them to decompose in benzene to give biaryls. It was shown that both electron donating and electron withdrawing substituents on the anilide

aromatic ring could be used.[52] The mechanism, as discussed in Chapter 1, Scheme 18, is complicated but largely thought to proceed *via* radical intermediates.

Scheme 29: Suzuki Coupling.



However, Grieve and Hey synthesized their nitrosamides under harsh conditions[52] including the use of nitrosyl chloride[53] and concentrated nitric acid.[54] Synthesis of nitrosamides through nitrosation by nitrous fumes[55] presents it own set of problems. Passage of nitrous fumes before nitrosation is complete will cause a reduction in yield as well as a starting material contamination in the product. Continued passage of nitrous

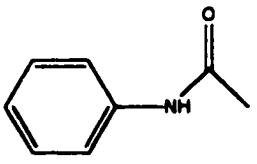
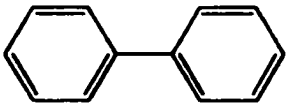
fumes after nitrosation is complete not only reduces the yield but also the product becomes tarry.[56] Unfortunately, there is no simple way to determine when nitrosation is complete.[56] Other methods require the isolation of the aromatic nitrosamide[53] before allowing it to decompose in the aromatic solvent. Isolation of the nitrosamide has three main problems. First, not all aromatic nitrosamides are easily isolable. Second, most aromatic nitrosamides are unstable and decompose rapidly. Third, nitrosamides in general and aromatic nitrosamides most certainly are cancer causing agents[57] requiring special handling methods. Therefore, especially since these nitrosamides are bad actors, a method that can synthesize biaryls without isolation of the aromatic nitrosamide would be very beneficial.

We have shown that introduction of a reactive solvent after formation of the N-nitrosamide but before rearrangement, decomposition, and recombination could occur, would allow for reaction with the solvent (Chapter 2, Section 2.5). A modification of the reaction sequence, through the introduction of excess benzene, after the 2 hour period at 0°C but before allowing to warm up to room temperature could allow for a more mild way of synthesizing biaryls. A byproduct would be the corresponding aromatic esters. These esters can be easily separated from our desired product by conversion to the corresponding water soluble phenolate or through other separation techniques. This would also allow for the synthesis of biaryls without the need to isolate the nitrosamide.

The first synthesis attempted was biphenyl **(41)**. Acetanilide **(40)** was treated as previously described in Chapter 2. After completion of the 2 hour period in the ice bath, a large excess (70 mL) of benzene was added to this solution and the reaction vessel was allowed to warm to room temperature for an additional 24 hours. Deionized water was

added and the benzene layer was separated and the benzene removed under reduced pressure. The resulting brownish crystals were purified by dissolution in benzene and hexane was added until crystals formed. There were collected by filtration to give pure **41** in 60% yield, as shown in Table 8.

Table 8: Results of the Conversion of Acetanilide to Biphenyl

Acetamide	**Biphenyl Formed** *Percent Yield*
Acetanilide 	Biphenyl  60%
40	**41**

3.2 Summary of Results

The next synthetic attempts involved changing the substituent on the phenyl ring of the N-phenyl acetamide while using excess benzene as the reactive aromatic solvent. These changes included using phenyl, nitro, bromo, *o-tert*-butyl and pyrinyl substituents, as shown in Table 9 .

Table 9: Results on Conversion of Various Aromatic Acetamides to Biphenyls using Benzene as the Reactive Solvent.

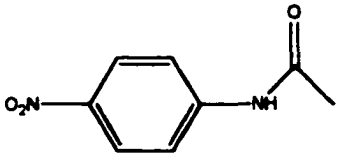
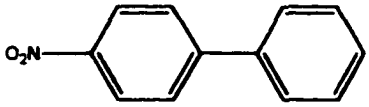
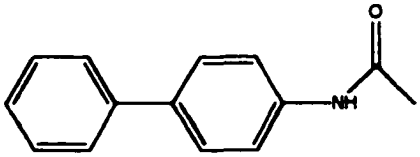
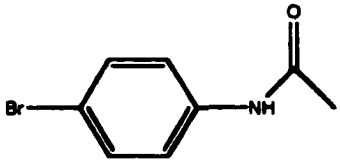
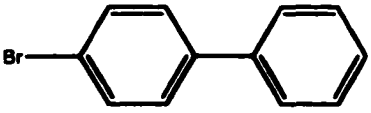
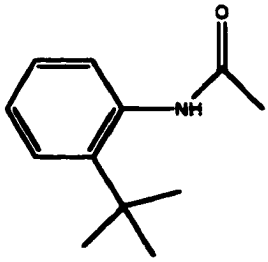
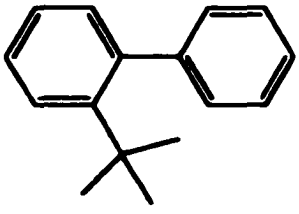
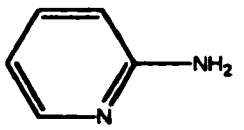
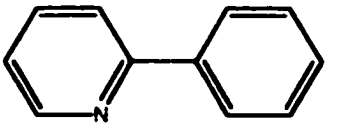
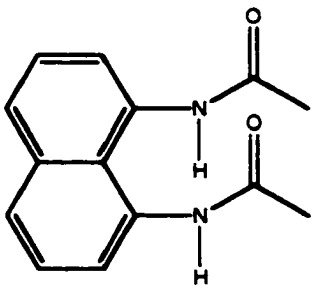
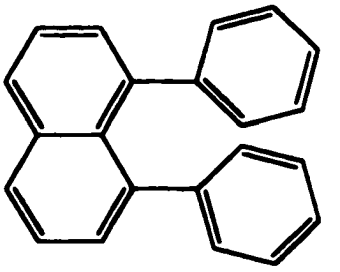
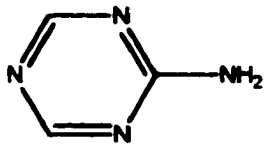
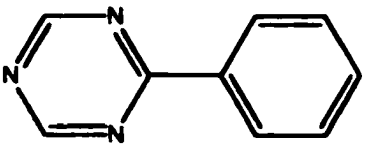
Acetamides	**Biphenyl Formed** *Percent Yield*
N-*4*-Nitrophenyl acetamide  **5**	4-Nitrobiphenyl  81% **42**
N-(4-Biphenylyl)acetamide  **2**	*p*-Terphenyl  62% **43**
N-*p*-Bromophenyl acetamide  **9**	4-Bromobiphenyl  71% **44**
N-*o-tert*-Butylphenyl acetamide  **15**	*o-tert*-Butylbiphenyl  53% **45**

Table 9: Continued.

Acetamide/Amine	Biphenyl Formed *Percent Yield*
2-Aminopyridine  **46**	2-Phenylpyridine  54% **47**
1,8-bis(N-acetamido)naphthalene  **27**	1,8-Diphenylnaphthalene  61% **48**
2-Amino-1,3,5-triazine  **49**	2-Phenyl-1,3,5-triazine  63% **50**

2-Phenylpyridine (**47**), 2-phenyl-1,3,5-triazine (**50**) and 1,8-diphenylnaphthalene (**48**) are notable examples as they are useful in the pharmaceutical industry (**47** and **50**) and as possible ligands and scaffolds for the synthesis of macromolecules (**48**) Although

Grieve and Hey produced biphenyls from aromatic nitrosamides, the remarkable part of the results presented here is the simple *in situ* method. Grieve and Hey used harsher methods, as described in the beginning of this chapter, while our method is mild and proven to be more functional group tolerant. Another benefit is the elimination of the aromatic nitrosamide isolation step. Since we no longer isolate the nitrosamide we eliminate the cancer hazard from this reaction. Bunyan and Hey developed a method for the phenylation of pyridine through electrolysis.[56] In their method, phenylation was accomplished through the use of benzoic acid by electrolysis. Although their final isolated yield was 56%,[56] this was accomplished after electrolysis and extensive purification. This method presented here easily provides a 54% yield under milder conditions, although these conditions were not optimized. Another remarkable result is the synthesis of **48**. Although **48** was synthesized by Clough, Mison and Roberts through direct joining of two nonequivalent aromatic molecules by an organonickel catalyzed Grignard aryl halide coupling reaction at −15 °C gave a 35% yield,[58] synthesizing **48** under these milder conditions, at room temperature, gave a 61% yield.

3.3 Proposed Mechanism for this reaction

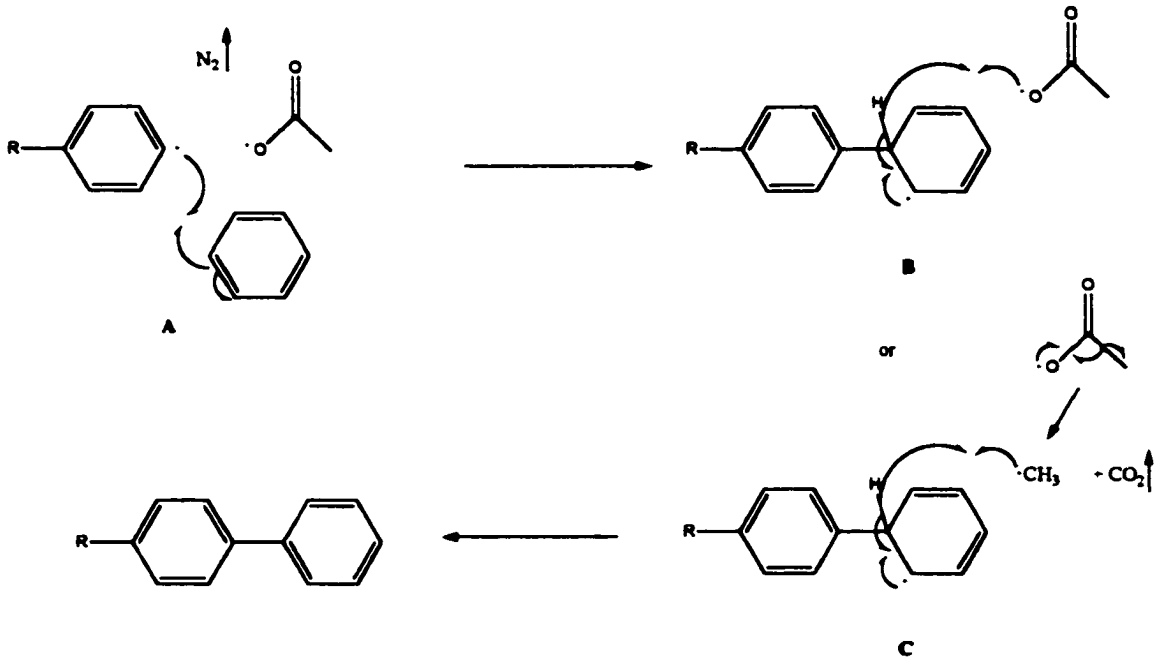
Scheme 30 shows a change in our proposed mechanism as shown in Scheme 25, Page 33. When the radical pair is formed, which is no longer inside an inert solvent cage, the phenyl radical can attack the benzene solvent **A**. The acetoxy radical can remove hydrogen atom **B** creating our product and acetic acid. Another decomposition route for the acetoxy radical **C** would end up creating carbon dioxide and a methyl radical which can then remove a hydrogen atom creating methane.[59] Edwards and Mayo gave evidence

that the acetoxy radical, under these reaction conditions, decomposes to give a methyl radical and carbon dioxide.[60] Kharasch and Gladstone also showed that the acetoxy radical decomposed into methane and carbon dioxide during their research on the decomposition of acetyl peroxide in acetic and chloroacetic acids.[61] However, if the lifetime for the acetoxy radical is long enough, it could end up being the difference between the ΔH for the formation of the O-H bond verses the formation of the C-H bond. During the synthesis of **42** an aliquot of the reaction solution before workup, was subjected to GC/MS analysis. If toluene is present there is evidence to support the decarboxylation of the acetoxy radical. Toluene was detected, as shown in A.49, suggesting at least some decarboxylation of the acetoxy radical. The benzene that was used was also analyzed by GC/MS to determine if it was contaminated with toluene but none was detected. The fact that toluene was formed does not necessarily mean that the acetoxy radical is not abstracting a hydrogen atom forming acetic acid. Both decarboxylation and formation of methane and formation of acetic acid could be taking place at the same time.

One should note that the hydrogen abstraction step may be more complicated than as shown above. Going back to Chapter 1, Section 3 there is great controversy over how this step may actually be occurring. Scheme 17 (located in Chapter 1, Page 15) shows that the formation of the biphenyl could be occurring through a redox reaction in which a the acetyl radical is reduced to the acetyl anion. The phenyl radical is now oxidized to the biphenyl cation. The acetyl anion deprotonates the biphenyl cation completing the reaction and forming acetic acid. While recognizing the importance of the reaction mechanism the simple radical pair model is useful for designing syntheses. The reaction

method used to synthesize aromatic esters from *in situ* formation of aromatic nitrosamides proved, with modification, to be useful in accomplishing an environmentally friendly way of synthesizing biphenyls without the need of isolating the aromatic nitrosamide.

Scheme 30: Proposed Mechanism for Biphenyl(Triphenyl) Formation.

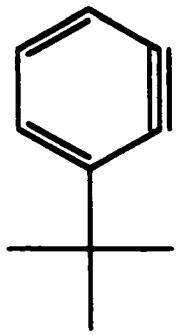


3.4 Why does Isomerization not Occur in these Reactions?

Looking at the results for both the esters and biaryls, as shown so far, the substitution pattern is retained. That is, if one starts with *ortho* or *meta* substitution, ortho or meta substitution, respectively, results. The question about this is why is there a lack of isomerization when these reactions take place. This question arose because in Cadogan's dealing with the *o-tert*-butylphenyl acetamides [26] it was noted that both the ortho and meta isomers were present in the product. This was explained by Cadogan and

others though possible formation of a benzyne type intermediate, as shown in Figure 13.[26]

Figure 13: A Possible Benzyne Intermediate for *o-tert*-Butylphenyl Acetamides



In these reactions, dealing with homolytic aromatic substitution, the only entities that are involved are the radical and the neutral substrate.[26] There is a general assumption that radicals posses little or no dipole moment and therefore there should be no polarizing effects involved in these reactions. Hambling, Hey and Williams conducted a series of experiments dealing with homolytic aromatic substitution.[62] Their results showed that the *p*-nitro-, *p*-chloro, and *p*-methoxyphenyl radicals are slightly polar as shown in Table 10.

Table 10. Dipole Moments for *p*-Nitro, *p*-Chloro, and *p*-Methoxyphenyl Radicals.[62]

Radical	Dipole Moment (D)
p-O_2N-C_6H_4·	-3.98
p-Cl-C_6H_4·	-1.55
p- H_3CO-C_6H_4·	-1.23

It would be expected that the closer the substituent is to the radical center, the stronger the polarizing effect would be due to the increase in the inductive effect.[63] So, to the first approximation, one could say that the reason for the lack of isomerization of the para systems is that for the para position, the polar character of the radical is the smallest while the closer the substituent is to the radical center there is a subsequent enhancement of the polar character of the radical.[64] If this was the case, the explanation does not explain the fact that when the substituent is in the ortho or meta positions, they remain ortho and meta without isomerization.

A better explanation could be that, since the phenyl and acetoxy radicals are surrounded by an non-reactive solvent cage, the two radicals are close enough that after nitrogen leaves the system, recombination is faster that isomerization. In the formation of the biaryls the solvent cage is broken since there is a large excess of benzene, then statistics come into play. It is favorable that the phenyl radical will combine with a molecule of benzene before the radical can rearrange to the other positions within the aromatic molecule. Therefore, the rate of combination with benzene would be faster that isomerization.

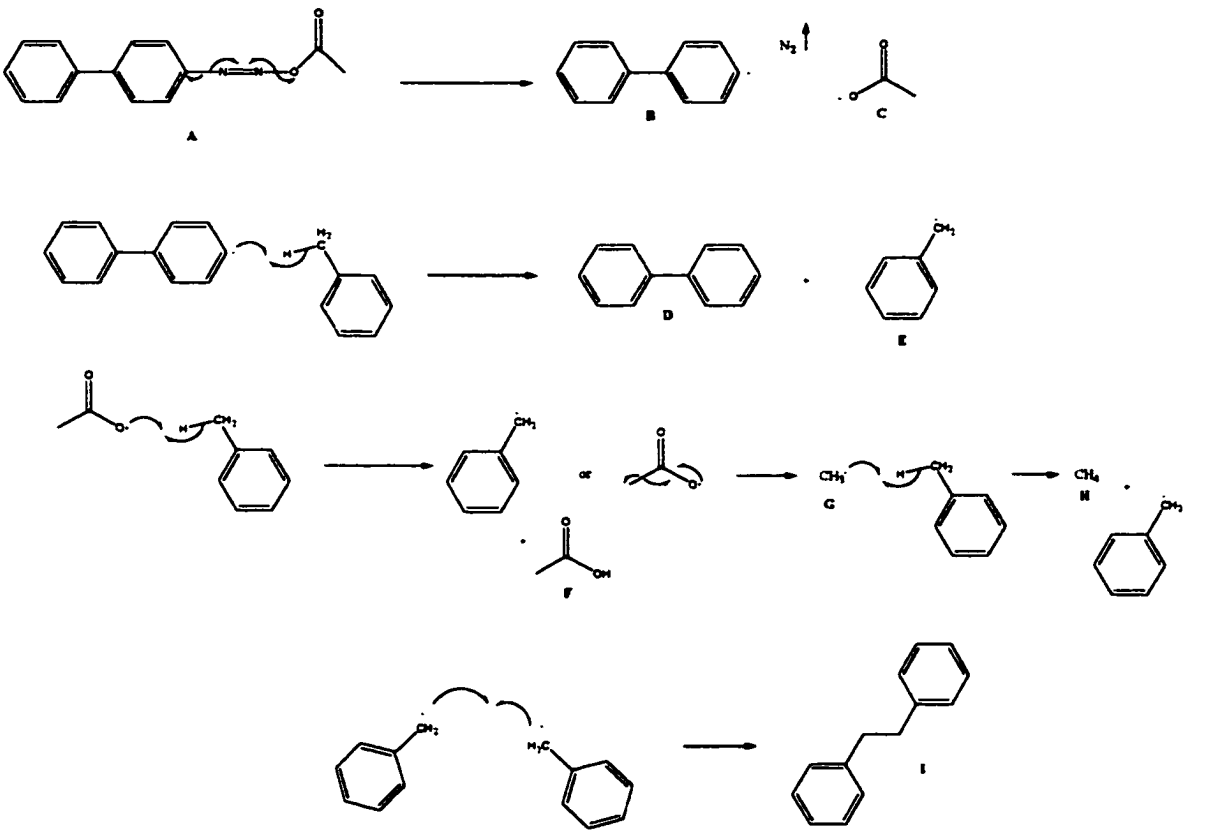
3.5 Using Toluene as a Reactive Solvent.

A synthesis was attempted to determine if another reactive aromatic solvent could be exchanged for benzene. The first attempt involved the use of toluene. N-(4-Biphenylyl)acetamide (2) was treated as described above but excess toluene, instead of benzene was added. The remaining treatment of this solution was as described above and resulted in a tannish white crystals with a melting point of 80 – 90 °C. This wide melting

point was puzzling and a small amount was dissolved in methylene chloride and analyzed using semi-quantitative GC/MS. The major components were 63% bibenzyl, 33% biphenyl, 3% 4-biphenylacetate and 1% other minor products. However, toluated biphenyl toluene products were not detected. This reaction became another stronger bit of evidence to support a homolytic decomposition of the acetoxyazoaromatic complex. This could mainly occur by a radical mechanism as shown in Scheme 31.

When the acetoxyazoaromatic **A** is formed and undergoes homolytic decomposition, the biphenyl radical **B** and the acetoxy radical **C** are formed. The biphenyl radical can then abstract a hydrogen atom from toluene forming biphenyl **D** and a relatively stable benzyl radical **E**. The acetoxy radical can either abstract a hydrogen atom from toluene forming another benzyl radical and acetic acid **F** or decarboxylate forming the methyl radical **G**, followed by radical abstraction to form methane **H** and another benzyl radical. There is also the possibility that these processes occur concurrently. The benzyl radicals can then combine to form bibenzyl **I**. So although this reaction did not work as desired, it did provide another strong bit of evidence toward the radical type mechanism for these reactions. Hey, Molden and Williams also used toluene as a solvent in which they decomposed their isolated aromatic nitrosamides. Their results showed that they obtained a bibenzyl yield of 42% when they decomposed *p*-tolylphenylacetoxynitrosamide and 32.8% bibenzyl when they decomposed *p*-nitrophenylacetoxynitrosamide.[64] A benefit of this reaction is that it shows that synthesizing the aromatic nitrosamides *in situ* does not have an adverse effect toward this reaction. Another aromatic solvent, nitrobenzene was used for an attempt to see if benzene can replaced as the reactive solvent in this reaction.

Scheme 31: A Possible Mechanism for the Formation of Biphenyl and Bibenzyl.

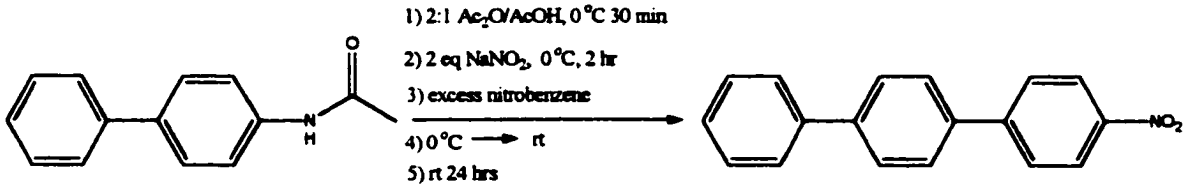


3.6 Using Nitrobenzene as a Reactive Solvent.

In an attempt to find an aromatic solvent other than benzene that could be used in this reaction, nitrobenzene was tried. An immediate benefit, if the reaction proved to be successful is that one can increase the number of aromatic rings by one with the newly attached ring containing a nitro group. The nitro group could then be reduced to the amino group, converted to the amide and then, through this reaction, another aromatic group could be attached, the amide converted to the ester or the phenol though the reaction described in Chapter 2, or conversion to the halide can be accomplished though the reaction described through Chapter 4.

The first attempt used N-(4-biphenylyl)acetamide **(2)**, which was treated as described previously with the exception that after the 2 hour period at 0°C excess nitrobenzene was added. Nitrobenzene was removed though steam distillation (it could also be removed under low pressure), which resulted in 4-nitro-*p*-terphenyl **(51)** in 53% isolated yields, as shown in Scheme 32. Evidence for its successful synthesis was provided by comparing melting point and mass spectrum data (A.51) with known data from the literature.

Scheme 32: Synthesis of 4-Nitro-*p*-terphenyl from N-(4-biphenylyl)acetamide.



2 51

With the success of the first attempt using nitrobenzene as a reactive solvent, a second attempt involved the use of 1,8-bis(N-acetamido)naphthalene **(27)** as the starting material. Treatment was the same as with the N-(4-biphenylyl)acetamide and resulted in the synthesis of 1,8-bis(*p*-nitrophenyl)naphthalene **(52)** in 38% isolated yields, as shown in Scheme 33. Reduction of the nitro groups to the amino groups and repeating the reaction would create a 1,8-bis(4-nitrobiphenyl)naphthalene as shown in Figure 14. This would create a sort of molecular tweezers. Although this has not been attempted yet, this needs to be tried in the future to show expanded synthetic utility for this reaction sequence. With at least preliminary success in using nitrobenzene as a reactive solvent, it

was decided to change the solvent to benzaldehyde, in order to see if the utility of this reaction could be expanded further.

Scheme 33: Synthesis of 1,8 Bis-(*p*-Nitrophenyl)naphthalene.

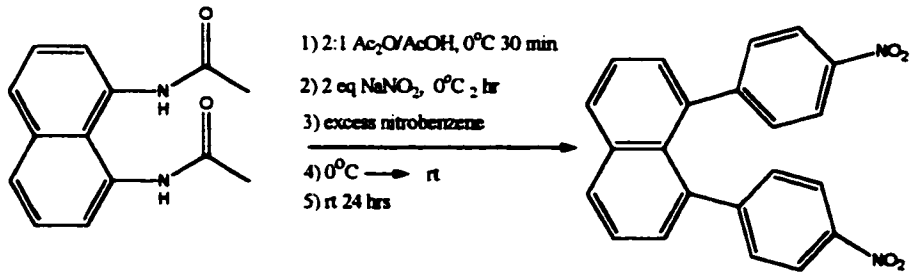
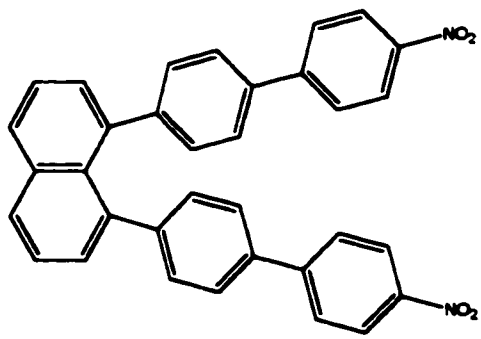


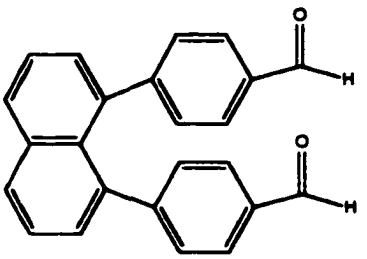
Figure 14: 1,8-Bis(4-nitrobiphenyl)naphthalene.



3.7 Using Benzaldehyde as a Reactive Solvent.

In a further attempt to expand the aromatic solvents that can be used in this reaction, benzaldehyde was used. The first attempt used 1,8-bis(N-acetamido)naphthalene (**27**), which was treated as described previously with the exception that after the 2 hours period at 0°C excess non-distilled benzaldehyde was added. It was hoped that we would synthesize 1,8-bis(4-carboxyphenyl)naphthalene, Figure 15.

Figure 15: 1,8-Bis(4-carboxyphenyl)naphthalene.

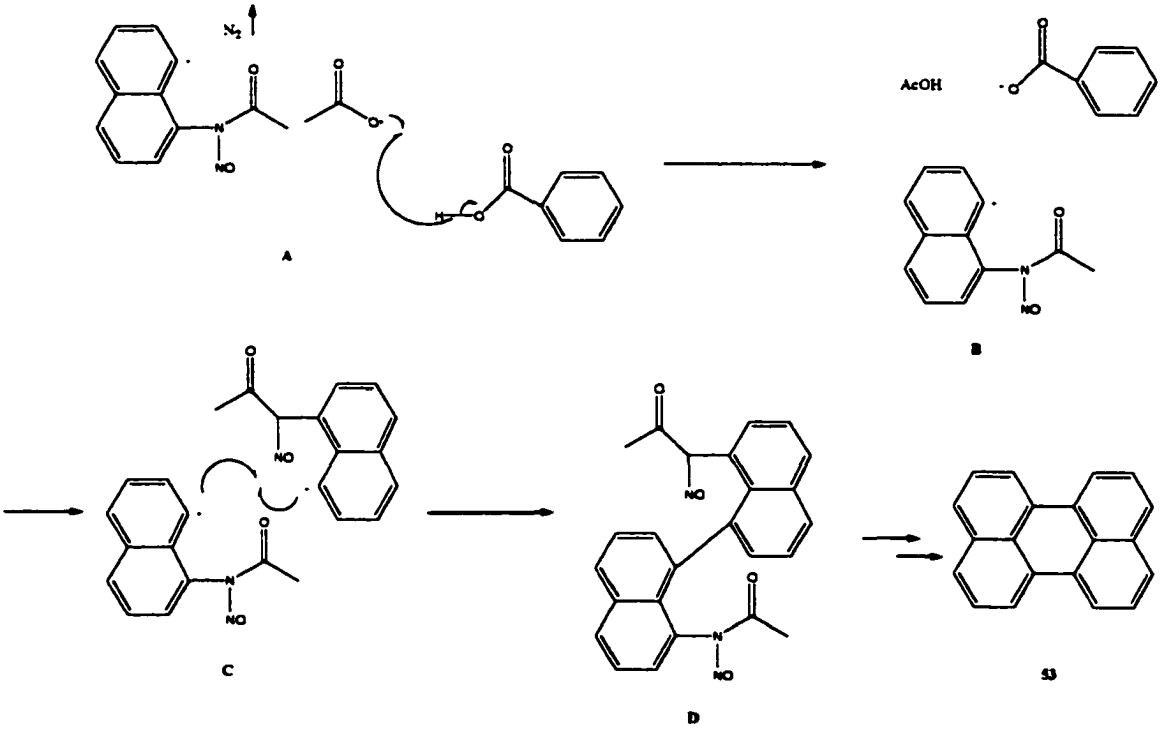


However, after workup, instead of producing the desired 1,8-bis(4-carboxyphenyl)naphthalene, perylene **(53)** was isolated. The perylene was characterized both by mp and ^{1}H-NMR, as shown in A.7, in 65% yield. The experiment was reattempted with similar results. The results were remarkable in that the reaction appeared to be a dimerization of two naphthalene rings. Since benzaldehyde can contain benzoic acid as a contaminant, an aliquot of the benzaldehyde was sent through the GC/MS, and indeed it contained benzoic acid. The reason we did not see this in the perylene product could be that the workup would convert the benzoic acid to sodium benzoate, by deprotonation of benzoic acid by sodium hydroxide, which would remain in the aqueous layer. Since benzoic acid was in the system, it was postulated that benzoic acid could act as some sort of radical scavenger, stabilizing the system long enough to allow the naphthalene rings to get together. This could explain the lack of the ester product **28**. The possible mechanism is shown in Scheme 34.

After the radical intermediates **A** are formed, the acetoxy radical abstracts a proton from the benzoic acid forming a napthyl radical **B**. If **B** is a reasonably stable radical, the coupling of 2 napthyl radicals **C** could occur faster than any attack by the benzoic acid radical or loss of carbon dioxide. Since the napthyl groups are already

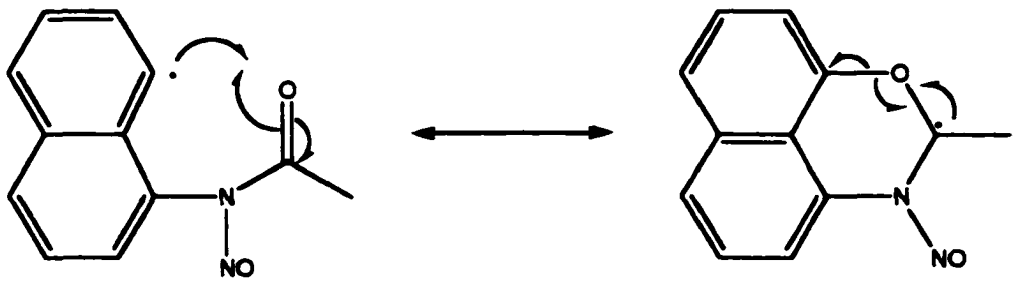
attached (**D**) an intramolecular repeat of this process would allow for the second coupling to occur easily. This would then form perylene (**53**).

Scheme 34: A Possible Mechanism for the Formation of Perylene.



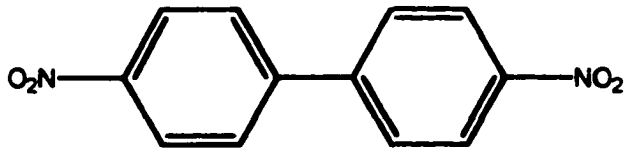
The naphthyl system could be stabilizing the radical long enough for it to find another naphthyl radical. This might be accomplished by anchimeric assistance from the carbonyl system, which is within close proximity to the napthyl radical, forming a 6 membered ring. This may provide some stability to that radical system, as shown in Scheme 35. Once two napthyl radicals couple, the formation of the second radical and subsequent coupling would result in formation of perylene. This theory needs to be further explored. However, the results may demonstrate a possible milder way of forming substituted perylenes.

Scheme 35: A Mechanistic Possibility for the Stability of the Napthyl Radical.



A reaction was set up to use the same non-distilled benzaldehyde but N-(4-nitrophenyl)acetamide (**5**) was used as the acetamide. If this coupling reaction would work 4,4'-dinitrobiphenyl, Figure 15, would be formed. If this dimerization type reaction could be extended beyond the formation of perylene, there would be an easy and mild way of making similar disubstituted biaryls.

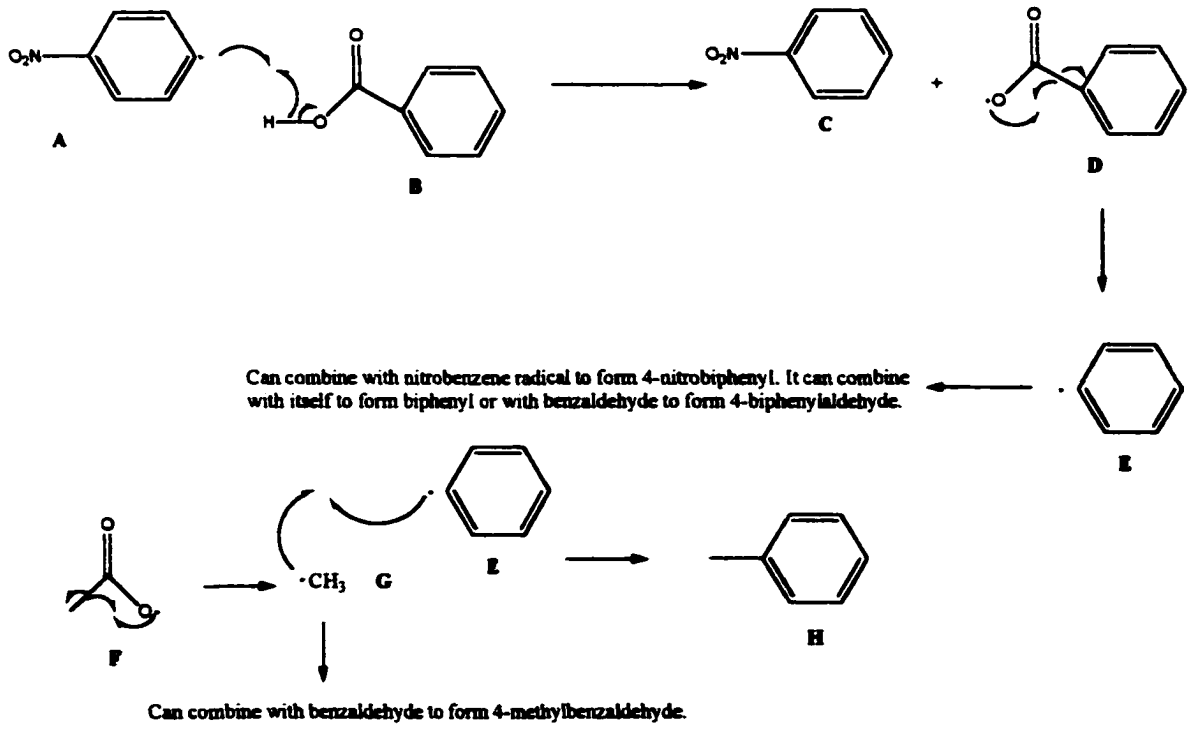
Figure 15: 4,4'-Dinitrobiphenyl



N-4-nitrophenyl acetamide was treated as described previously with the exception that after the 2 hour period at 0°C excess non-distilled benzaldehyde was added. An aliquot of this reaction was analyzed by GC/MS and no evidence of 4,4'-dinitrobiphenyl was present. Instead the majority product in this solution was nitrobenzene, A.48. The rest of the materials in the solution, as shown by GC/MS, were biphenyl, 4-nitrobiphenyl, 2-nitrobiphenyl A.46, p-nitrophenylacetate, benzoic anhydride A.44, 4-biphenylaldehyde A.45, 4-methylbenzaldehyde A.47, and toluene. The products can be explained by the 4-

nitophenyl radical (**A**) abstracting a hydrogen atom from benzoic acid (**B**) forming the benzoic acid radical (**C**) and nitrobenzene (**D**). The benzoic acid radical can then decarboxylate forming a phenyl radical (**E**) explaining the formation of the nitrobiphenyls, biphenyl and the 4-biphenylaldehyde. The acetoxyradical (**F**) can also decarboxylate forming a methyl radical (**G**) and this can recombine with the phenyl radical forming toluene (**H**). The presence of 4-methylbenzaldehyde can be explained through the methyl radical reacting with the benzaldehyde in the system. This is shown in Scheme 36. However, the results of this reaction suggest that the napthyl dimerization reaction is unique and the mechanism is puzzling to understand.

Scheme 36: A Possible Mechanism for the Formation of the Various Nitro Products.



To test the theory that benzoic acid could be involved in this deamination/ donation of a hydrogen atom to the intermediates after the homolytic decomposition of the azoacetoxy intermediate two different experiments were performed. In the first experiment *p*-methoxyphenyl acetamide was reacted under the same conditions used for biaryl formation. After the 2 hours at 0°C, excess benzene and 2 equivalents of benzoic acid were added to the reaction vessel. Upon completion of the 24 hour period at room temperature, an aliquot of the reaction mixture was analyzed by GC/MS. The results showed that the majority products were *p*-methoxyphenyl acetate as well as the *p*-methoxybiphenyl product (A.43), and methoxybenzene (A.42). The first two products would be expected. However, the presence of a large amount of methoxybenzene seems to lend some support toward the benzoic acid deamination/ donation of a hydrogen atom to the intermediates. In a second experiment, p-methoxyphenyl acetamide was treated under conditions shown in chapter 2 for the formation of the ester. After the 2 hours at 0°C, 2 equivalents of benzoic acid were added to the reaction vessel. Upon completion of the 24 hour period at room tempature an aliquot of the reaction mixture was analyzed by GC/MS. The results showed that the majority products were *p*-methoxybiphenyl and methoxybenzene. The p-methoxyphenylacetate product was present but as a minor product. In the first experiment, the results, with exception of the methoxybenzene, could be explained as a normal part of the reaction. The second experimental results can be explained by donation of a hydrogen atom to the methoxyphenyl radical, forming methoxybenzene, and to the acetoxy radical forming acetic acid. The benzoic acid radical then can decarboxylate to form the phenyl radical which can combine with the methoxyphenyl radical forming *p*-methoxybiphenyl. This reaction needs to be further

explored to determine if this is a general trend. If so this deamination reaction with various substituted benzoic acid could result in a mild method for unsymmetrical biaryl formation without the need for a large excess of one aromatic component.

To test to see if 1,8-bis(N-acetamido)naphthalene (**27**) would be deaminated or form perylene (**53**) with benzoic acid without the use of non-distilled benzaldehyde an experiment was set up in which the conditions to make 1,8-napthylene diacetate (**28**) were employed. After the 2 hour period at 0 °C, 2 equivalents of benzoic acid were added to the reaction vessel. Upon completion of the 24 hour period at room temperature work up was performed as described for **28**. The crude material was dissolved in benzene and washed with a 5% NaOH solution until the washings were basic. This was to remove benzoic acid from the crude material. Upon drying perylene was isolated in 65% yield. This further demonstrates that the reaction for the N,N'-(1,8-napthylene)diacetamide (**27**) converting to perylene through the use of benzoic acid is puzzling and will need further study.

3.8 Summary of the Biaryl Reaction

In summary, the method for conversion of N-aromatic secondary amides to biphenyls presented here is inexpensive and convenient, carried out in low environmental impact solvents, using minimal equipment, and not requiring isolation of intermediate N-nitrosamides or diazonium salts. Yields are uniformly moderate to good (although conditions were not optimized) and the reaction can be carried out with a variety of functional groups present in the substrate. This method, when compared to Suzuki coupling, does not require the arylboronic acid nor a palladium catalyst. This allows for

biphenyls to be formed where the arylboronic acid component is not available or difficult to synthesize. It allows for these biaryls to be formed inexpensively where the Suzuki coupling can be economically impractical. This reaction can be expanded to use nitrobenzene, which would allow for biaryls with nitro groups to be synthesized. These nitro groups can then be converted or reduced to allow for different substituents or synthetic designs to be employed to develop even larger molecules. The remarkable result of formation of perylene when 1,8-bis(N-acetamido)naphthalene was used with non-distilled benzaldehyde is still puzzling. This is especially true when N-4-nitrophenyl acetamide and N-4-methoxyphenyl acetamide systems result in deamination and or formation of the biphenyl. These reaction differences need further exploration.

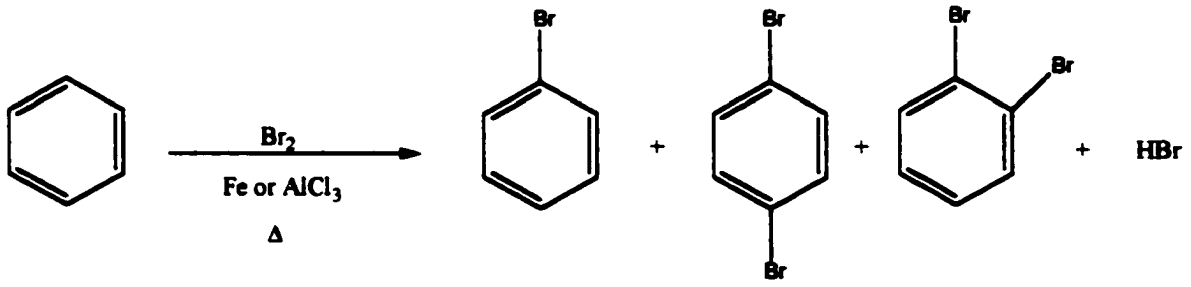
A need developed in one of our laboratories for a sterically hindered aromatic bromide, 1-bromo-2,6-diethylbenzene, for the construction of bulky ligands. This compound also exhibited use as a precursor in the synthesis of a drug used in the treatment of Alzheimer's disease.[65] Literature procedures for the synthesis of 1-bromo-4-*tert*-butyl-2,6-diethylbenzene involved the use of the Sandmeyer reaction and they reported yields of 44%.[66] Repetition in our laboratory gave uniformly unacceptable results (10% yield). Could a modification to the biphenyl reaction, by replacing the reactive solvent with a reactive halide source provide an alternative to the Sandmeyer reaction?

Chapter 4 Conversion of N-Aromatic Amides and Aromatic Amines to Aromatic Halides

4.1 Introduction and Synthetic Approach

Introduction of halogens into aromatic compounds is an important synthetic procedure. The methods of accomplishing aromatic halogenations generally fall into two categories.[67] The first involves aromatic substitution in which molecular halogens or other electrophilic halogen species act as electrophilic reagents.[67] An example of this type of reaction is shown in Scheme 37. Directing effects from substituents on the ring can be problematic and often leads to multiple products that require separation.[67] Unwanted polyhalogenation may occur for some activated aromatic substrates.

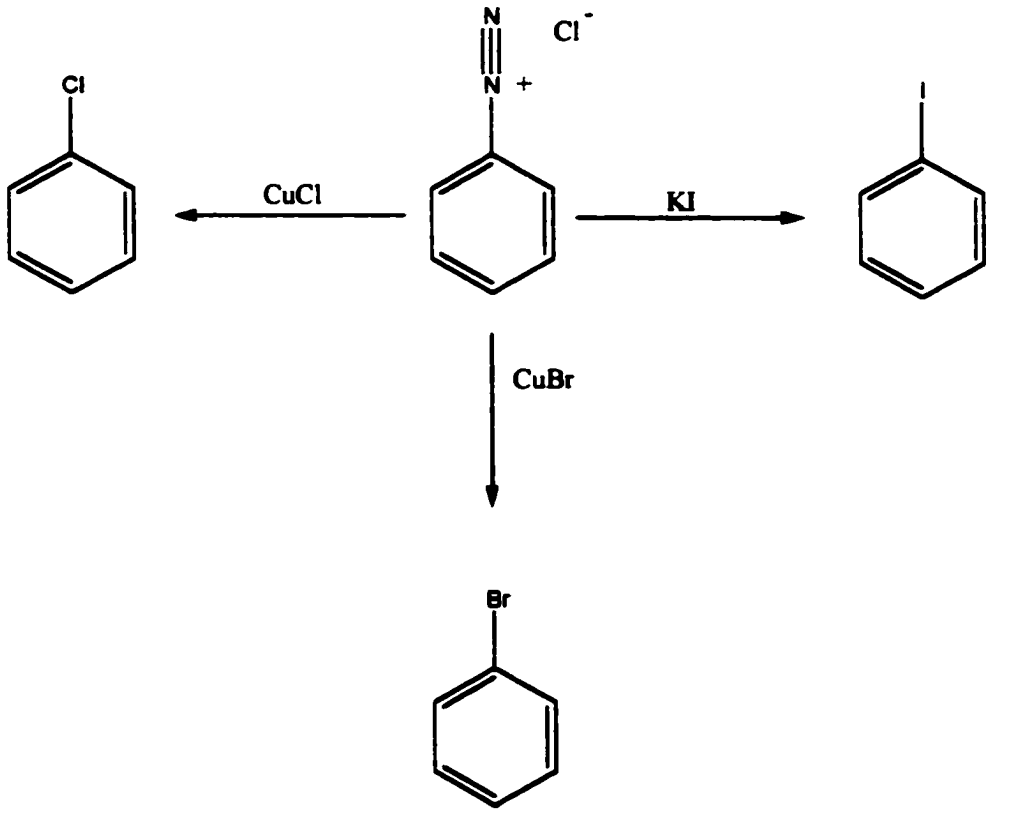
Scheme 37: Electrophilic Aromatic Substitution.



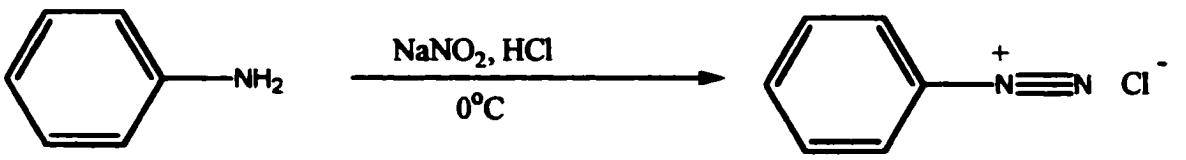
The second method involves aromatic substitution, such as the displacement of dinitrogen in aromatic diazonium salts by nucleophilic halides, also more commonly known as the Sandmeyer reaction[67] (Scheme 38), in which the halide source is often in the form of a copper salt. This method gives highly variable yields of aromatic halides ranging from excellent to none, depending on the other functional groups present. Other problems in the reaction include the formation of the diazonium salt as shown in Scheme

39. Since harsh conditions are employed to form the diazonium salt, the functional groups attached to the ring must be tolerant of the conditions. The reaction sometimes requires isolation of the hazardous diazonium salt and in the case of iodination procedures, explosion hazards have been noted.[67]

Scheme 38: Sandmeyer Reaction.



Scheme 39: Formation of the Diazonium Salt.



A variety of techniques have been developed over the years in an effort to improve safety and yields. These include the use of a combination of lithium bromide and

ceric ammonium nitrate by Roy, Guin, Rana and Maiti[68] for bromination of activated aromatic compounds. The problems are over-halogenation and/or the product being an isomeric mixture which needs further separation to get the desired compound. Barbero, Degani, Dughera and Foci[69] developed a procedure for the preparation of aryl chlorides, bromides and iodides through the use of arenediazonium *o*-benzenedisulfonimides as the electron transfer agent. Problems here include the variability of yields ranging from 3% when the functional group is phenyl to make the aromatic chloride, to 89% when the functional group is *o*-nitrophenyl to make the corresponding bromide, which also requires copper as a catalyst. Obushak, Lyakhovych and Ganushchak[70] developed a procedure for aryl chlorination through the use of arenediazonium tetrachlorocuprates. The problem is not only in the synthesis of these cuprates but also the requirement to isolate them and dissolve them in DMSO to allow for decomposition.

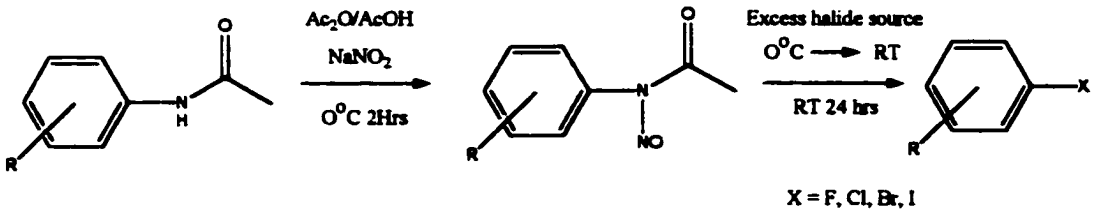
Hey and Peters[71] used nitrosamides to form aryl chlorides by synthesizing these aromatic nitrosamides through techniques described on Chapter 3, Page 49. After isolating these aromatic nitrosamides they then dissolved them in carbon tetrachloride and chloroform with yields from 23% from carbon tetrachloride to 11% from chloroform. A method is therefore needed to synthesize aromatic monohalides which is substituent tolerant, easy to produce, and for which the yields are not so varied between different functional groups.

In our approach for the conversion of 2,6-diethylaniline to 1-bromo-2,6-diethylbenzene, a modification to the reaction sequence for the synthesis of esters from amides was employed. We have shown in Chapter 2 (Section 2.5) and Chapter 3 that if a reactive solvent is added after 2 hours at 0 °C, the intermediates can react with the

solvent to form different products. As stated above, Hey and Peters used nitrosamides to form aryl chlorides by isolating the nitrosamide and allowing it to decompose in carbon tetrachloride. Although their yields were around 23%, these results provided the idea for the use of the reaction sequence developed and shown in Chapter 1 and 2 but with a modification in the reactive "solvent". Instead of using a reactive "solvent", introducing a halide source before warming to room temperature could provide our desired aromatic halide in desirable yields, as shown in Scheme 40.

The mechanism for this reaction could occur through two possible pathways. A first possible pathway, as shown in Scheme 18, Page 16 (**B** to **F**), could occur through attack by the nucleophile to the acetoxyazoaromatic complex forming the sigma complex. The sigma complex then decomposes forming the desired aromatic halide. A second possible pathway, as shown in Scheme 18 (**B** to **E**), involves the homolytic fragmentation of the acetoxyazoaromatic complex forming a phenyl radical intermediate. This intermediate then either abstracts a halogen atom from a halogen source, or combines with a halogen radical forming the desired aromatic halide. These possibilities will be furthered explored in Section 4.4.

Scheme 40: Our Approach to make Aromatic Halides Through Nitrosamide Intermediates

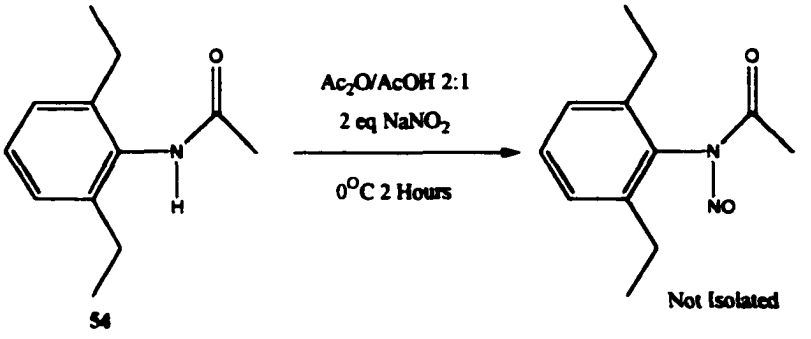


In the first attempt to synthesize 1-bromo-2,6-diethylbenzene (**55**), treatment of 2,6-diethylbenzylamide (**54**) with excess sodium nitrite in 2:1 acetic anhydride/acetic

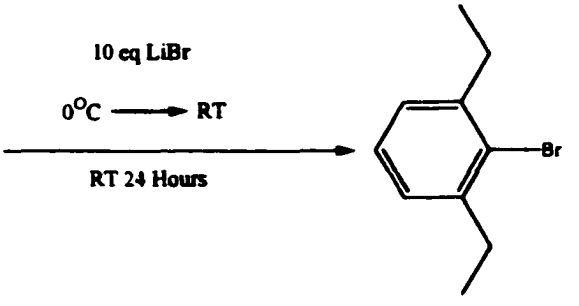
acid at 0°C (to generate the nitrosamide in situ), followed by addition of excess potassium bromide and warming to room temperature provided, after isolation, **55** in yields of 20%. This yield was considered unacceptable. The problem was likely the low solubility of potassium bromide in the 2:1 acetic acid/acetic anhydride, 0.0083g/mL.[72] Therefore, the halide source was switched to lithium bromide. Lithium bromide has a higher solubility, 0.1497g/mL,[73] in the 2:1 acetic anhydride/acetic acid mixture and another attempt was undertaken using this as the bromine source for the reaction. The treatment, as shown in Scheme 41, of **54** was performed as described above but excess potassium bromide was replaced with excess lithium bromide. This proved to be successful and provided, after isolation, **55** in 81% purity and in a yield of 65%. The crude mixture could be further purified through vacuum distillation. This surprising result provided the impetus to investigate the scope and synthetic utility of this transformation.

To determine the feasibility of turning this reaction into a one pot reaction a series of experiments were conducted. The first experiment attempted to convert N-(4-biphenylyl)acetamide (**2**) to 4-bromobiphenyl (**56**). Treatment of **2** with excess sodium nitrite in 2:1 acetic anhydride/acetic acid at 0°C (to generate the nitrosamide in situ), followed by addition of excess lithium bromide and warming to room temperature provided, after isolation, **56**, Scheme 42, in 60% yield.

Scheme 41: Synthesis of 1-bromo-2,6-diethylbenzene from 2,6-diethylbenzylamide



54



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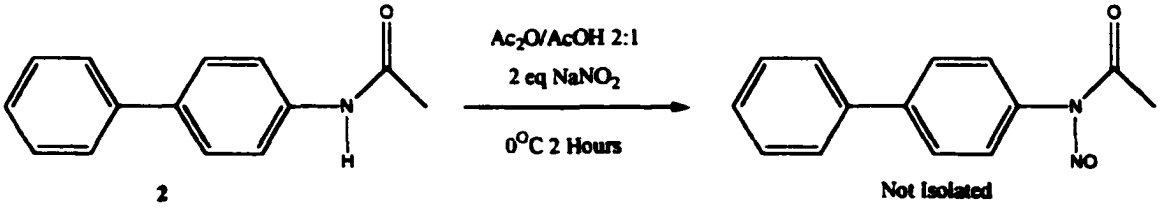
Scheme 42: Synthesis of 4-Bromobiphenyl from N-(4-Biphenylyl)acetamide



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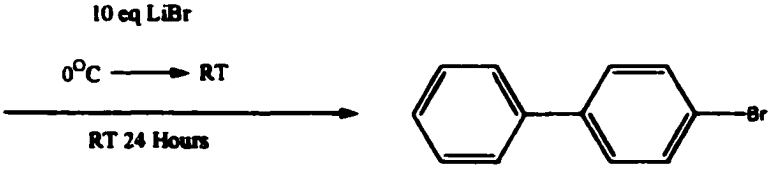
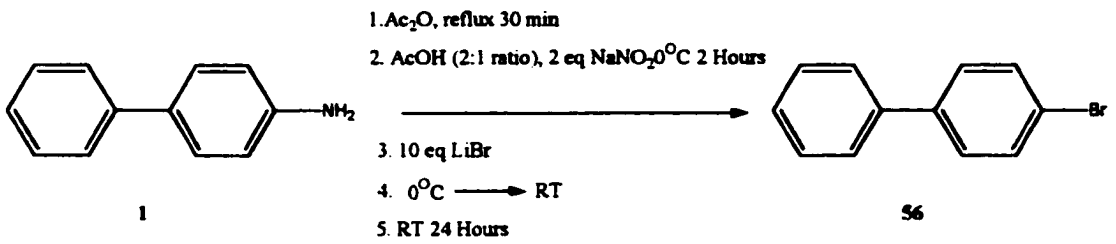


56

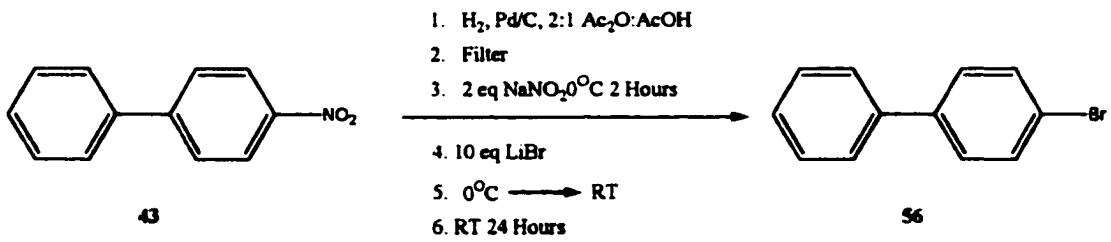
A second experiment involved the in situ generation of **2**, as previously described on page 17. The conversion of 4-aminobiphenyl directly to **56** without isolating **2** , as shown in Scheme 43, resulted in a yield of 65%.

Scheme 43: Synthesis of 4-Bromobiphenyl from 4-Aminobiphenyl.



A third experiment involved what would constitute a two-step, essentially one pot conversion of 4-nitrobiphenyl **43** to **56** without isolating any of the intermediates. The results of converting **43** to **56**, as shown in Scheme 44 resulted in a yield of 67%.

Scheme 44: Synthesis of 4-Bromobiphenyl from 4-Nitrobiphenyl

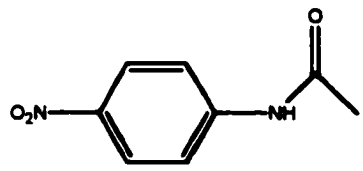
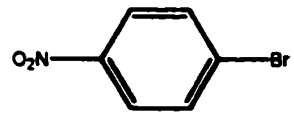
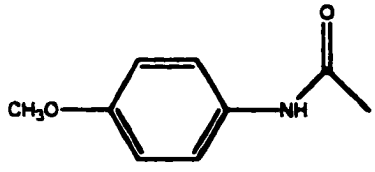
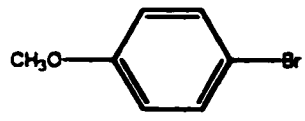


The yield advantage of carrying out this reaction sequence *versus* step-wise synthesis was demonstrated by these experiments. Isolating both 4-aminobiphenyl and 4-acetamidobiphenyl in the reaction sequence before conversion to 4-bromobiphenyl gave an overall yield of 50%. Isolating the 4-aminobiphenyl but generating the 4-acetamidobiphenyl *in situ* before conversion to 4-acetoxybiphenyl gave an overall yield of 59%. However, carrying out the reaction sequence without isolating any of the intermediate compounds gave 4-bromobiphenyl in 67% yield. This advantage was also demonstrated by a similar experiment performed for conversion of 4-nitrobiphenyl to 4-biphenylyl acetate, as shown in Chapter 1, Page 20.

4.2 Summary of Results

The next synthetic attempts involved changing both the substituents on the phenyl ring as well as the halide. The reason for changing the substituents on the phenyl ring was to explore functional group tolerance, to define the synthetic utility of this reaction, and to probe its mechanism. These changes included placing electron withdrawing substituents, like nitro groups, as well as electron donating groups such as methyl and methoxy groups. All these groups were at the para position of the phenyl ring of the arylacetamide and lithium bromide was used as the halide source. The results of these experiments are shown in Table 11.

Table 11: Results of Converting Aromatic Acetamides with Electron Withdrawing and Electron Donating Groups to Aromatic Bromides.

Acetamides	**Aromatic Halide Formed** *Percent Yield*
N-(4-Nitrophenyl)acetamide  **5**	4-Bromonitrobenzene  78% **59**
N-(*p*-Methoxyphenyl)acetamide  **7**	4-Bromoanisole  63% **60**

A series of experiments was conducted to see if changing the halide from bromine to iodine or chlorine would have any effect. In Table 12, the results of using potassium iodide as the iodine source shows that changing the salt from a bromide to an iodide has no adverse effect. The chloride results were interesting. The use of lithium chloride as the chlorine source resulted in low yields for both the nitro as well as the methoxy groups, however, using carbon tetrachloride as a chlorine source produced better yields. These results are shown in Table 13.

Table 12: Results of Converting Aromatic Acetamides with Electron Withdrawing and Electron Donating Groups to Aromatic Iodides.

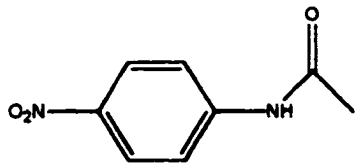
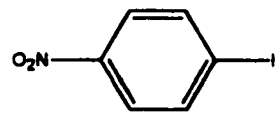
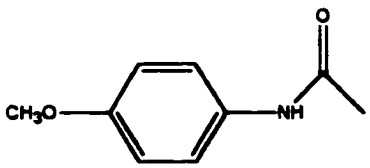
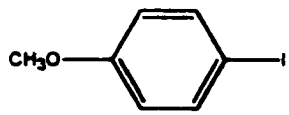
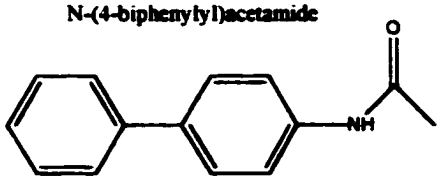
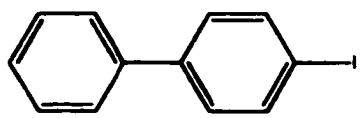
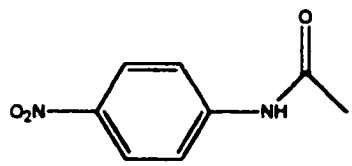
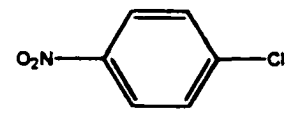
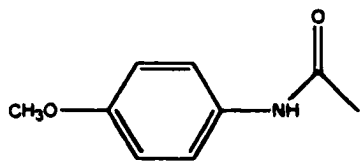
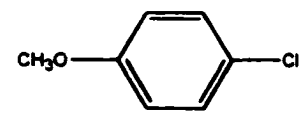
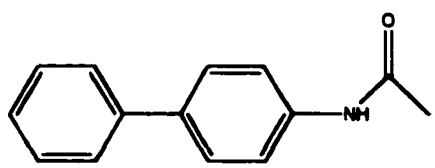
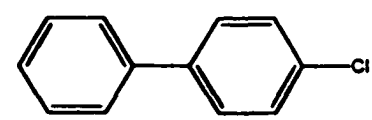
Acetamides	**Aromatic Iodide Formed** *Percent Yield*
N-(4-Nitrophenyl)acetamide  **5**	4-Iodonitrobenzene  68% **61**
N-(*p*-Methoxyphenyl)acetamide  **7**	4-Iodoanisole  63% **62**
N-(4-biphenylyl)acetamide  **2**	4-Iodobiphenyl  63% **57**

Table 13: Results of Converting Aromatic Acetamides with Electron Withdrawing and Electron Donating Groups to Aromatic Chlorides.

Acetamides	Chlorine Source	Aromatic Chloride Formed *Percent Yield*
N-(*p*-Nitrophenyl) acetamide  **5**	**a:** LiCl **b:** CCl_4	4-Chloronitrobenzene  22% 69% **63**
N-(*p*-Methoxyphenyl) acetamide  **7**	**a:** LiCl **b:** CCl_4	*p*-Chloroanisole  5% 65% **64**
N-(4-biphenylyl)acetamide  **7**	**a:** LiCl **b:** CCl_4	4-Chlorobiphenyl  13% 63% **58**

Another series of reactions summarized in Table 14 includes changing the position of the substituent from the para to the meta position to determine if changing the position on the aromatic ring will have any adverse effects on the ring. The results show that for iodine and bromine no adverse effects were seen. The results for chlorine shows

that use of lithium chloride as the chlorine source still resulted in low yields However, using carbon tetrachloride resulted in moderate to good yields.

Table 14: Results of Converting Aromatic Acetamides, Changing from Para to Meta Positions, to Aromatic Halides.

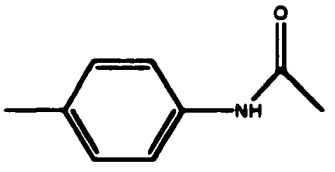
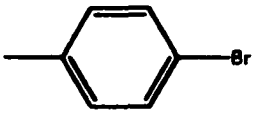
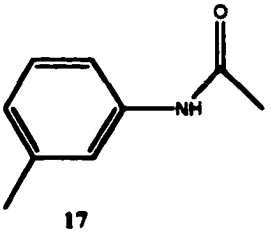
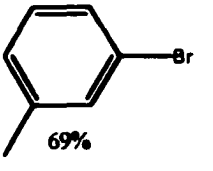
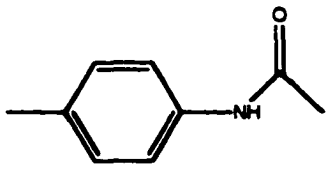
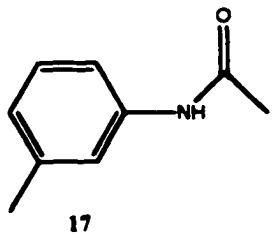
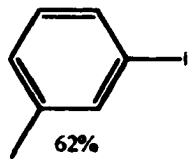
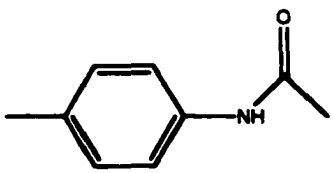
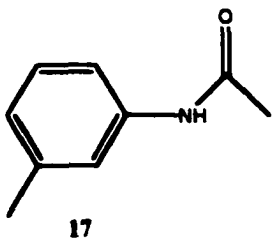
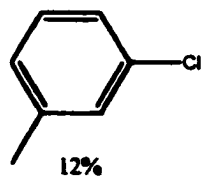
Acetamides	**Aromatic Halide Formed** *Percent Yield*
N-(*p*-Tolyl)acetamide  **9**	*p*-Bromotoluene  61% **65**
N-(*m*-Tolyl)acetamide  **17**	*m*-Bromotoulene  69% **66**

Table 14: Continued

Acetamides		Aromatic Halide Formed *Percent Yield*
N-(*p*-Tolyl)acetamide  **9**		*p*-Iodotoluene  **68%** **67**
N-(*m*-Tolyl)acetamide  **17**		*m*-Iodotoulene  **62%** **68**
N-(*p*-Tolyl)acetamide  **9**	**a**: LiCl **b**: CCl_4	*p*-Chlorotoluene  **13%** **61%** **69**
N-(*m*-Tolyl)acetamide  **17**	**a**: LiCl **b**: CCl_4	*m*-Chlorotoluene  **12%** **64%** **70**

Another series of reactions shown in Table 15 includes placing a bulky substituent on the ortho position to determine if having a substituent on this position on the aromatic ring will have any adverse effects on the reaction. The results show that for iodine and bromine no adverse effects were observed. The results for chlorine again show that use of lithium chloride as the chlorine source resulted in low yields, but, using carbon tetrachloride resulted in moderate to good yields.

Table 15: Results of Converting Aromatic Acetamides, Placing a Bulky Substituent on the Ortho Position, to Aromatic Halides.

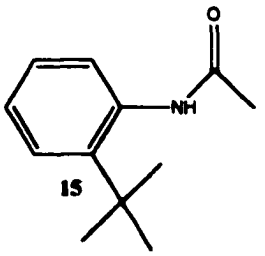
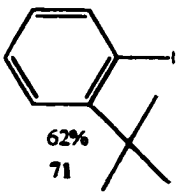
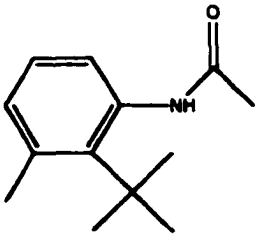
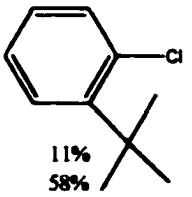
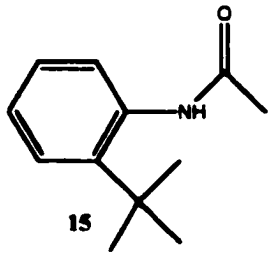
Acetamides		**Aromatic Halide Formed** *Percent Yield*
N-(*o-tert*-Butylphenyl)acetamide  **15**		1-*tert*-butyl-2-iodobenzene  62% **71**
N-(*o-tert*-Butylphenyl)acetamide  **15**	a: LiCl b: CCl_4	1-*tert*-butyl-2-chlorobenzene  11% 58% **72**

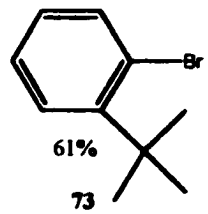
Table 15: Continued.

N-(*o*-*tert*-Butylphenyl)acetamide



15

1-*tert*-butyl-2-bromobenzene



61%

73

In summary, this method for conversion of N-aromatic secondary amides to aromatic halides is inexpensive and convenient. The solvents used are low environmental impact solvents, and if a suitable substitute can be found for carbon tetrachloride the entire system could be considered generally environmentally friendly. Yields are uniformly good to moderate (although conditions were not optimized) and the reaction can be carried out with a variety of functional groups present in the substrate.

4.3 Changes to the Reaction Sequence.

The first set of changes involved the amount of carbon tetrachloride used. This was done for two reasons. As there are environmental problems with the use of carbon tetrachloride, if we can get similar results with less carbon tetrachloride, together with the ability to recover and reuse the carbon tetrachloride, this method may be more useful for wide spread use in research and industry. Secondly, comparison of the results from carbon tetrachloride may lead to the conclusion that carbon tetrachloride is a much better donor than lithium chloride. However, this may not be correct on considering that 10 equivalents of lithium chloride are used compared with 70 mL of carbon tetrachloride

which was approximately 211 equivalents. In the case of the formation of p-chloronitrobenzene it came out to be 321 equivalents. The results form these changes are shown in Table 16.

Table 16: Results from Changes in the Amount of the Chloride Source Used in the conversion of N-4-nitrophenyl acetamide to *p*-Chloronitrobenzene.

Chloride Source	Percent Isolated Yields		
	10 Equivalents	80 Equivalents	321 Equivalents
LiCl	22%	40%	-
CCl_4	8%	62%	69%

We started by lowering the amount of carbon tetrachloride to 6 mL to convert N-4-nitrophenyl acetamide **(5)** to *p*-chloronitrobenzene **(63)**. This turns out to be approximately 80 equivalents of carbon tetrachloride relative to starting material. This resulted in a 62% isolated yield of **63**. Although this is lower than the 69% obtained using 70mL carbon tetrachloride, reduction of 7% in product for using 64 mL less carbon tetrachloride may be considered an excellent trade off, especially if this reaction is used in large scales.

Lowering the amount to 0.75 mL of carbon tetrachloride to convert **5** to **63** turns out to be approximately 10 equivalents of carbon tetrachloride relative to starting material. This resulted in an 8% isolated yield of **63**. When compared to the 22% yield from 10 equivalents of LiCl, 14% less product is being produced. On increasing the LiCl amount to 80 equivalents a comparison with the results from 6 mL (80 equivalents) of carbon tetrachloride could be obtained.

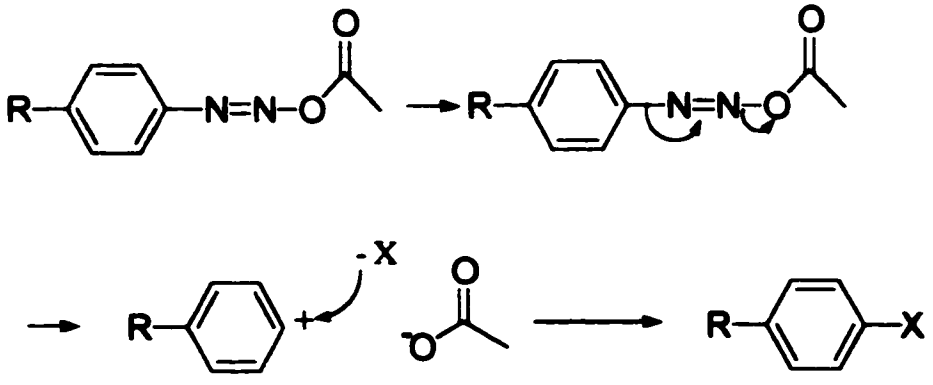
We determined that 0.0981g/mL of LiCl[74] could be dissolved in a 2:1 solution of acetic anhydride to acetic acid. Since at 10 equivalents of LiCl gave 0.0170g/mL and 80 equivalents gave 0.0832g/mL the amount of LiCl was increased to 2.4960 grams to convert **5** to **63** . This turns out to be approximately 80 equivalents of lithium chloride when compared to starting material. This resulted in a 40% isolated yield of **63**. When compared to the 62% we get from 80 equivalents of carbon tetrachloride we are getting 22% less product. These results may give some information about a possible mechanism for this reaction, which will be discussed in the next section.

A series of experiments were carried out to see the effect if changes were made to the halide source or if the halide source is added during the reaction sequence. The first experiment used elemental bromine to replace lithium bromide as the halide source for the synthesis of 1-bromo-2,6-diethylbenzene.[75] The results of the reaction included a multitude of multi-brominated products but 1-bromo-2,6-diethylbenzene was not detected. In another set of experiments, the halide source was added immediately after sodium nitrite addition in order to see if the addition timing was important. When 2,6-diethylphenylacetamide was used as the starting material with lithium bromide as the halide source, the purity of the product dropped from 81% to 76% giving an overall yield of 64% compared to 65% obtained from the standard method. Similar results were obtained when N-(*o-tert*butylphenyl)acetamide was used with carbon tetrachloride as the halide source. The purity of the liquid dropped from 91% to 63% giving an overall yield of 51% compared to 58% obtained from the standard method. These results suggest that the delay in introducing the halide source is important.

4.4 Proposed Mechanism for this Reaction

There are at least three mechanistic possibilities for this reaction. A first possibility is that the azoacetoxyaromatic intermediate can form, undergo heterolytic decomposition forming the aromatic cation followed by halide anion addition. This is shown in Scheme 45. The problems with phenyl cation formation were discussed on pages 10, 28 and 29. The yields for both electron withdrawing groups and electron donating groups are moderate to good. One would expect, as described on pages 28 and 29, that just like for the esters, if a phenyl carbocation formed the electron withdrawing groups would be destabilizing while electron donating groups would be stabilizing. If the heterolytic decomposition with halide addition mechanism were to become a mechanistic probability, the results that both electron withdrawing and donating work relatively well must be explained.

Scheme 45: Hetrolytic Decomposition with Halide Addition Mechanism.



Before moving on to the second and third mechanistic possibility a need to rearrange some of the results in order to show trends within each halide regent would

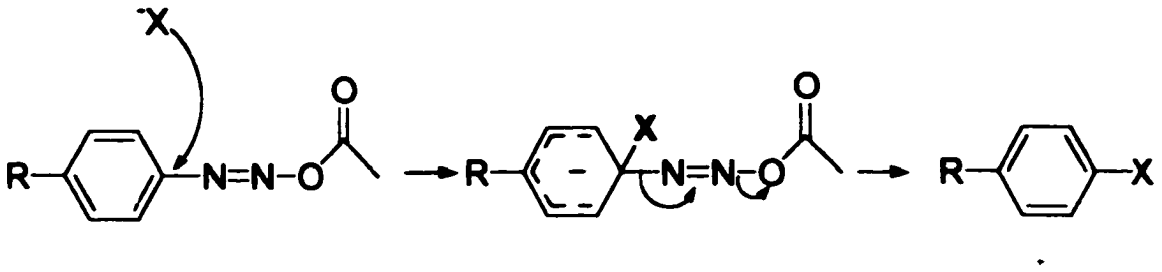
assist in showing how the SN_{AR} and homolytic decomposition could be or could not be the mechanism. The these rearranged results are shown in Table 17.

Table 17: Trends Within the Halogenation Reaction Results.

Example	R Group	Halogen Atom	Halogen Source	Percent Yield
61	NO_2	I	KI	68
63	CH_3O	I	KI	63
57	Ph	I	KI	63
67	*p*-CH_3	I	KI	68
68	*m*-CH_3	I	KI	62
59	NO_2	Br	LiBr	78
60	CH_3O	Br	LiBr	63
56	Ph	Br	LiBr	60
65	*p*-CH_3	Br	LiBr	66
66	*m*-CH_3	Br	LiBr	69
55	2,6-diethyl	Br	LiBr	65
63b	NO_2	Cl	CCl_4	69
64b	CH_3O	Cl	CCl_4	65
58b	Ph	Cl	CCl_4	63
69b	*p*-CH_3	Cl	CCl_4	61
70b	*m*-CH_3	Cl	CCl_4	63
63a	NO_2	Cl	LiCl	22
64a	CH_3O	Cl	LiCl	5
58a	Ph	Cl	LiCl	13
69b	*p*-CH_3	Cl	LiCl	13
70a	*m*-CH_3	Cl	LiCl	12

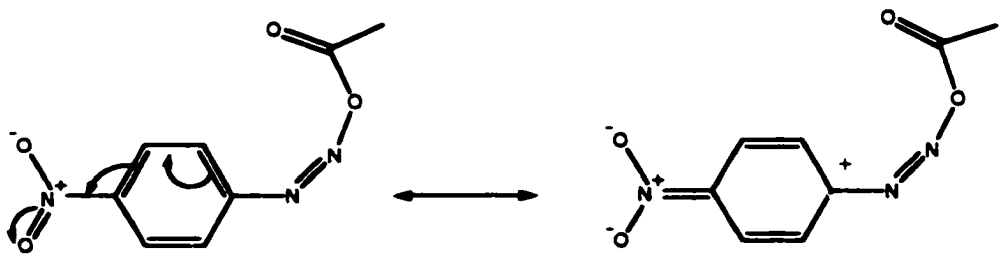
A second mechanistic possibility is the addition of the halide anion to the azoacetoxyaromatic intermediate, forming the sigma complex, followed by homolytic decomposition. This is shown in Scheme 46.

Scheme 46: SN_{AR} Mechanism.



A comparison of the yields between electron withdrawing groups and electron donation groups could suggest whether this could be a mechanistic possibility. This becomes its ground state verses its transition state type of argument. If the substituent on the aromatic ring were an electron withdrawing group, a nitro group for example, a positive charge at would exist at the desired carbon in a resonance form, as shown in Figure 16. Addition of the halide anion to this complex should result, to a first approximation, in yields that are good to reasonable. The results for the nitro substituted systems, as shown in Table 21, for the iodo and bromo systems are between 68 and 78% which are reasonably good. Therefore, the yields for the nitro system generally fit this trend.

Figure 16: Electronic Configuration for a Nitro Group as a Substituent on the Aromatic Ring



If the substituent on the aromatic ring were an electron donating group, a methoxy group for example, a resonance structure with a negative charge at the desired carbon, as shown in Figure 17. Addition of the halide anion to this complex should result, in first approximation, in yields that are relatively poor. The results for the nitro substituted systems, as shown in Table 17, for the iodo and bromo systems are 63% for both systems, which are good yields. Therefore, the yields for the methoxy system do not really fit this trend. However, this could be somewhat misleading because, although the electronic configuration that was described for both the electron withdrawing and donating groups are correct, this is not necessarily the deciding factor. The transition state must be looked at, for this can be the deciding factor. The rate determining step could be the formation of the acetoxyazoaromatic complex as described in Chapter 1, Page 11. However, if the addition of the nucleophile to the acetoxyazoaromatic complex is slower than the rearrangement of the aromatic nitrosamide to the acetoxyazoaromatic complex, then the rate determining step could be the formation of the sigma complex as shown in Figure 18. This complex can work for both electron withdrawing and electron donating groups, although one might expect that an electron withdrawing group could stabilize this complex better so one would expect a complex with electron groups to have slightly better yields. One way to test this, if the SN_{AR} were a mechanistic probability, would be to see if the rate of reaction changed with the use of electron withdrawing verses electron donating groups. If the SN_{AR} were a mechanistic probability, the results, which show that both electron withdrawing and donating resonance works well, needs to be explained.

Figure 17: Electronic Configuration for a Methoxy Group as a Substituent on the Aromatic Ring.

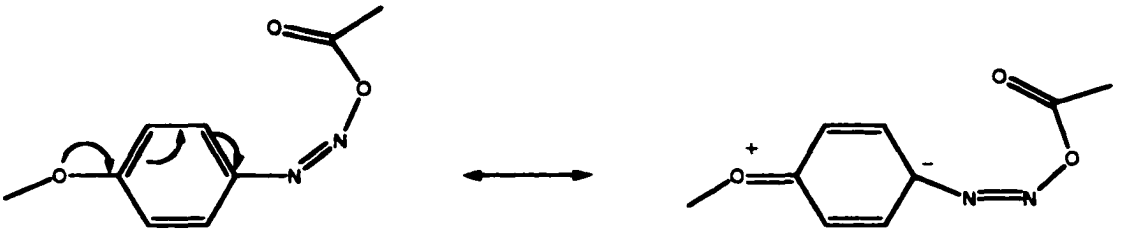
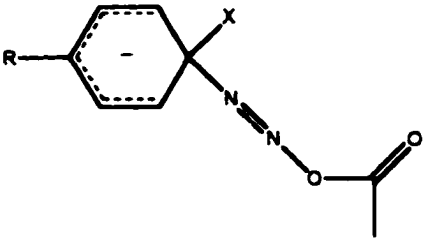
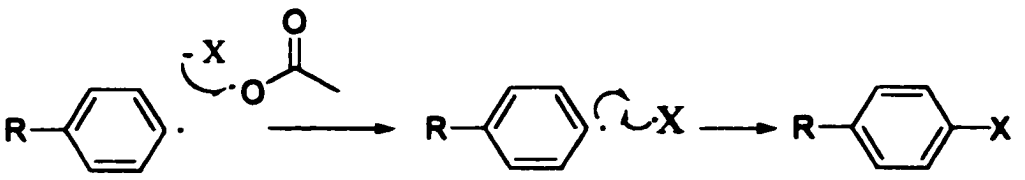


Figure 18: The Sigma Complex



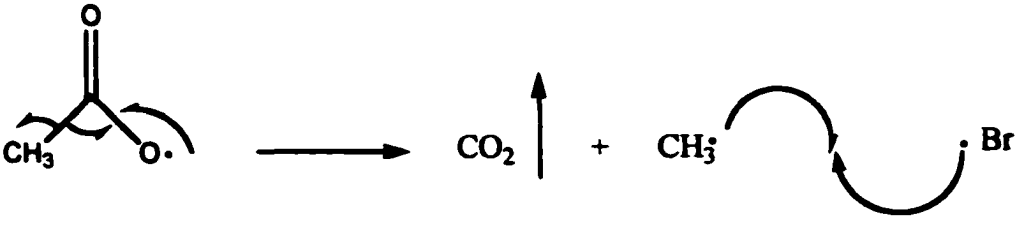
X = I, Br, Cl

A third possibility involves homolytic decomposition of the azoacetoxyaromatic intermediate, forming phenyl and acetoxy radicals, followed by addition of a halide radical to the aromatic ring, either from the halide source directly or oxidized from the halide anion. This is shown in Scheme 47. There would be only a small effect by either electron withdrawing and donating groups. The results for both the nitro substituted systems and the methoxy systems, as shown in Table 17, for the iodo and bromo systems are 63 to 78% yields, which are reasonably good. Therefore, the yields for both the methoxy and the nitro systems, to a first approximation, fit this trend.



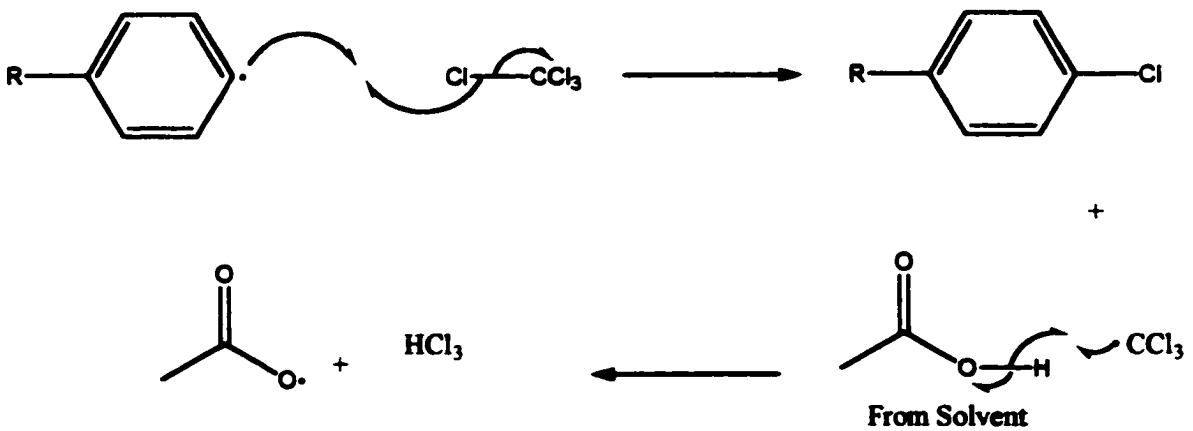
Taking an aliquot of the solution from **59**, before workup, and subjecting it to GC/MS analysis showed the presence of bromomethane, A.24. This could occur from decarboxylation of an acetoxyradical and recombination with a bromine radical as shown in Scheme 48. The bromine radical could be formed from oxidization of the bromide to a bromine radical by the acetoxy radical. Looking back to Chapter 1, Section 3, Cadogan and Hilbert did postulate that the acetoxy radical can oxidize the phenyl radical forming the phenyl cation and acetyl anion. Along with this possible redox reaction the bromine radical could form due to the fact that we are under oxidizing conditions due to the excess sodium nitrite that is being used. It has been noticed that free bromine is formed during this reaction. Since there is a possibility of decarboxylation of the acetoxy anion and recombination with bromine that formed during the reaction can occur, stronger evidence for a radical mechanism was needed.

Scheme 48: A Radical Mechanism for the Formation of Bromomethane.



A stronger piece of evidence for the radical mechanism could be the comparison of the yield using carbon tetrachloride verses lithium chloride as a chlorine source. Yields of the aromatic chlorides, with both electron withdrawing and donating substituents, tend to be better using carbon tetrachloride compared with lithium chloride as the chlorine source. This trend is shown in Table 17 and can be explained by the radical mechanism, which is shown in Scheme 49. If it were to go by radical mechanism the formation of hexachloroethane, by coupling of two trichloromethyl radicals, should be observed. Hexachloroethane was not observed but chloroform was noticed instead. The reason for this is could be that it would be rare to have a high enough concentration of the trichloromethyl radicals[88] for it to be probable that it will combine with another trichloromethyl radical before it has collided productively with acetic acid forming chloroform. Although another reason for not detecting hexachloroethane, or other possible products, could be just that they are formed in such low concentrations that they are below the detection limit of the instrument.

Scheme 49: A Possible Radical Mechanism for the Conversion of the Phenyl Radical to Aromatic Chlorides using Carbon Tetrachloride.



An explanation that lithium chloride did not work so well could be due to the chloride anion is a poor nucleophile under these conditions. This is because the nucleophilic trend in hydrogen bonding solvents, such as those used in these reactions, is $I^- > Br^- > Cl^-$. Therefore, the lithium chloride could work poorly because the chloride anion is just a poorer nucleophile in this solvent system. However, carbon tetrachloride worked well with both electron donating and withdrawing groups as substituants on the aromatic ring. Since carbon tetrachloride almost certainly reacts by a radical mechanism, these results give further support for a radical mechanism. Therefore, it is possible that a dual mechanism is operating depending on the halogenating reagent used. If we use a reagent like carbon tetrachloride the mechanism is likely proceeding through a radical intermediate. If we use nucleophilic reagents, like KI, LiBr and LiCl, the reaction could be forced to proceed by an SN_{AR} mechanism. Further mechanistic studies will be needed to determine the possible mechanism for the formation of aromatic halides through these reaction conditions.

4.5 Summary of the Halide Reaction.

When compared with the Sandmeyer reaction, the need to isolate the diazonium salt and, in some cases, add it to a hot acid solution of the desired cuprous halide[76] has been eliminated. The need to use ceric ammonium nitrate,[77] tetrafluoroborates, tetrachlorocuprates,[78] for more deactivated systems have been removed under these conditions. Finally, the need to create dry conditions[79] for these some of these reactions have been curtailed through this reaction method. In summary, the method for conversion of N-aromatic secondary amides to aromatic halides presented here is inexpensive and

convenient, carried out in low environmental impact solvents, if carbon tetrachloride is replaced with a suitable substitute, using minimal equipment, and not requiring isolation of intermediate N-nitrosamides or diazonium salts. Yields are uniformly good to moderate (although conditions were not optimized) and the reaction can be carried out with a variety of functional groups present in the substrate. The method can be simply modified to be carried out directly on aromatic amines and in some cases can be extended to be carried out on aromatic nitro compounds. While the results presented here are suggestive of a dual SN_{AR}/radical mechanism depending on the halogenation reagent used, further studies will needed to elucidate the exact nature of the mechanisms of these reactions.

Chapter 5 Conclusion and Future Work.

5.1 Conclusion

The research presented in this dissertation concerns the development of successful strategies for the conversion of amides and amines to esters, biphenyls, aromatic halides and energetic materials through N-aromatic nitrosoamide intermediates. This method provides a mild, inexpensive, and environmentally friendly way of synthesizing these types of compounds that is fairly functional group tolerant. Aromatic rings with both electron withdrawing groups and electron donating groups gave esters in excellent yields, while providing biphenyls and aromatic halides in moderate to good yields. It has been shown that the position of the substituent can be changed from *para* to *meta* to *ortho* with no ill effects on the reaction and bulky substituents can be present , even in the ortho position. This reaction method can be performed on N-heterocyclic aromatic amides in excellent yields and phenylated heterocycles in moderate to good yields. These reactions on heteroaromatics are of great interest in the pharmaceutical industry.

It has been demonstrated that N-aromatic nitrosamides likely decompose through a radical mechanism, which can be exploited as a potential low temperature initiator system for polymerization that allows for target end groups to be incorporated into the polymer. It has also been demonstrated that the use benzoic acid in this reaction method has caused deamination. However, when 1,8-bis(N-acetamido)naphthalene was used as the starting material, introduction of benzoic acid formed perylene. If this can be controlled it may be a mild method for deamination and formation of unsymmetrical biaryls and perylene. Finally, this reaction has the possibility for the formation of

energetic materials in a more mild and safer method. Although the 2,4,6-trinitrophenyl 2,4,6-trinitrobenzoate system was not synthesized, the results so far show that this system would hold promise as a potential energetic material and the synthetic route described in this dissertation is an available one.

5.2 Future work

Although there is some evidence to support the homolytic decomposition of the acetoxyazoaromatic intermediate, controversy exists over the mechanisms of these reactions. A perfect example of this is the radical and SN_{AR} mechanistic possibilities for the conversion of N-aromatic amides to aromatic halides. ESR spectroscopy and spin trapping could add more powerful evidence concerning the nature of the reaction intermediates. A reaction could be set up in a ESR tube and allow to go to completion while being analyzed by ESR spectrometry in order to determine if the radical intermediates can be detected.

The reactions discussed in this dissertation need to be further optimized with regard to various parts of the reaction methodology. Experiments need to be performed, through the use of thin layer chromatography to determine the optimum time for each stage of the reaction. For example, in some cases the formation of the ester from the acetoxyazoaromatic complex could be occurring immediately, however, a 24 hour period at room temperature was used to standardize the method.

The formation of aromatic chlorides from aromatic secondary amides with carbon tetrachloride results in reasonable yields. Even though the carbon tetrachloride for these reactions has been used in excess, it can be recovered and reused. However, since there is

a stigma attached to the large scale use of carbon tetrachloride, due to green house effects, ozone layer destroying, and toxicity effects, a different chlorinating solvent needs to be found, if this process is to be used in a large industrial scale.

If a way to easily isolate and purify the nitrosamides could be developed, the rates of decomposition could be readily determined, which means linear free energy relationships could be studied for this reaction. These studies would greatly assist in probing the mechanism of this reaction. This can be accomplished by comparing the log of the reaction rate, [log k], for decomposition of the nitrosamides with different electron withdrawing substituents and electron donating substituents with $\sigma^{\bullet}$ values, determining Hammet Parameters. If it goes through a radical mechanism, then no matter what the electronic effects of the substituants are, withdrawing or donating, the reaction parameters (ρ values) should be small. This information may allow for further development of new reaction possibilities based on the mechanism(s) for these reactions.

Initial results from our use of nitrosamides to induce polymerization, as well as the use of benzene and nitrobenzene demonstrate that if one surrounds the nitrosamide with a reactive solvent cage the radicals can react with the cage as well as with each other. The use of other aromatic solvents, such as chlorobenzene, needs to be further explored as a way of making various substituted biaryls from nitrosamide intermediates without the need of isolating the nitrosamide. If various aromatic solvents can be used it may become an alternative to the Suzuki coupling where making the arylboronic acids or the use of palladium catalysts is impracticable or economically not feasible.

It was shown in Chapter 3, Section 7 that perylene can be formed under these reaction conditions though the addition of benzoic acid after the 2 hours at 0°C step,

when using 1,8-bis(N-acetamido)naphthalene **(27)** as the starting aromatic amide. However, treating other aromatic acetamides with benzoic acid, after the 2 hours at 0°C step, did not result in dimerization but deamination and other products. This reaction needs to be further explored, not only to understand the unique results with the use of **27** as starting material, but also to see if these results be can exploited to allow for the controlled formation of substituted perylenes.

Attempts have been made to use distilled benzaldehyde in this reaction to form 1,8-bis(4-carboxyphenyl)naphthalene with no success. Future attempts should be performed in order to determine if synthesis of this molecule can be conducted using this reaction method. We have demonstrated the ability to produce 1,8-bis(4-nitrophenyl)naphthalene. This reaction was preliminary in nature and should be further performed to optimize the formation of this product. Reduction can be accomplished though standard conditions to form the amide, *in situ*, and this reaction repeated to form 1,8-bis(4-nitrobiphenyl)naphthalene. This compound can then be tested to see if it has the ability to act as molecular tweezers. The 2,4,6-trinitophenyl 2,4,6-trinitrobenzoate system (Figure 8) still needs to be developed and tested to determine its suitability as an energetic material. Finally, attempts have been performed to convert N,N'-(1,8-naphthalyl)diacetamide **(27)** to 1,8-diiodo and 1,8-dibromonaphthalene using this reaction without success. The problem could be the isolation procedures and not with the reaction itself. If the isolation procedures can be worked out and it proves this reaction can work to form these compounds, with optimization, it would be of great interest to pharmaceutical and other industries as building blocks to develop larger macromolecules and drugs.

Chapter 6 Experimental

General Methods.

Unless otherwise noted, all starting materials and reagents were obtained from commercial suppliers and used without further purification. All solvents were used as obtained unless noted. Melting points were obtained using a Mel-Temp® melting point apparatus and were uncorrected. Melting points were correlated with reference melting points that are available in the Dictionary of Organic Coumpounds, 6th edition[80], unless otherwise noted. Mass spectra were obtained using a ThermoFinnigan Polaris GC/MS instrument. All mass spectra obtained for this dissertation were EI, 70 electron volt, unless otherwise noted. For liquid products 4 drops were dissolved in 1 mL methylene chloride for GC/MS injection unless otherwise noted. Purity for liquid products were estimated by semi-quantitative GC/MS. ^{1}H-NMR spectra were obtained by dissolving sample in $DCCl_3$ and spectra were referenced to residual solvent unless otherwise noted, using a Varian Mercury VX 300 MHz NMR spectrometer. ^{1}H-NMR spectra were processed using a SUN workstation equipped with Varian VNMR 6.1c software. All ^{1}H-NMR spectra and Mass spectra were correlated with reference spectra that are available on the SDBS website[81] unless otherwise noted. All UV/Visible spectra for this dissertation were obtained using a Perkin-Elmer Lambda 3 Spectrometer. All thermal gravimetric analysis (TGA) were performed using a Dupont 951 Thermogravimetric Analyzer with Thermal Analysis 2000 software.

N-(4-Biphenylyl)acetamide (2)

4-Aminobiphenyl (0.673 g, 3.19 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride. The mixture was heated to reflux solvent for 30 minutes and allowed to cool to room temperature. The mixture was poured into ice/water. The resulting crystals that formed were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals that were formed were collected by filtration. This procedure gave 0.671 g, 87% isolated yield of **2**: mp 170-172° C; MS *m/z* (%) 211.1(18), 170.7(48), 168.1(100),141.1(3), 115.1(4). Mass spectrum located in A.34.

4-Biphenylyl acetate (4)

N-(4-Biphenylyl)acetamide **(2)** (0.671 g, 3.19 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.455 g, 6.60 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals that formed were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0.6326 g, 94% isolated yield of **4**: mp

87-88° C; MS *m/z* (%) 212(5), 171(12), 170.1(100) 141(15), 115.1(19), 89.1(4). Mass Spectrum located in A.1.

4-Nitrophenyl acetate (6)

N-(4-Nitrophenyl)acetamide (**5**) (0.379 g, 2.10 x 10^{-3} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.292 g, 2.09 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals that formed were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals collected by filtration. This procedure gave 0.352 g, 93% isolated yield of **6**: mp 81-82° C; MS *m/z* (%) M^+ 181(20), 164(5), 138(100), 108(91), 80(37), 65(29). Mass Spectrum located in A.35.

4-Methoxyphenyl acetate (8)

N-(*p*-Methoxyphenyl)acetamide (0.274 g, 1.66 x 10^{-3} moles) (**7**) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.229 g, 3.33 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown

gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.22mL of liquid was obtained at a density of 1.13 which gave 0.224 g, 81% isolated yield of **8:** MS *m/z* (%) 166(35), 123(65), 108(100), 80(32). Mass spectrum located in A.27.

4-Bromophenyl acetate (10)

N-(*p*-Bromophenyl)acetamide (0.271 g, 1.27 x 10^{-3} moles) **(9)** [4-Bromoaniline using synthetic method for **2**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.174g, 2.52 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene

chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and dark brown crystals remained. At room temperature the material clumped together and if held in your hand it would become a brown colored oil. This procedure gave 0.251 g, 81% isolated yield of **10**: mp 21-23° C; MS *m/z* (%) 214.8(50), 212.9(48), 215.9(16), 213(18), 172.9(96), 171(100), 92(20), 65(16). (NIST, C192795)[82] Mass spectrum located in A.32.

p-Tolyl acetate (12)

N-(*p*-Tolyl)acetamide **(11)** (0.327 g, 2.20 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.303g, 4.39 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was then removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated

sodium carbonate solution until acetic anhydride was removed. 0.26 mL of liquid was obtained at a density of 1.047 which gave 0.271 g, 82% isolated yield of **12.** MS *m/z* (%) 150(27), 108.1(100), 107.1(78), 79(20), 77.0(15), 80.1(16). Mass spectrum located in A.2.

4-Cyanophenyl acetate (14)

N-(*p*-Cyanophenyl)acetamide **(13)** (0.274 g, 1.71 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.186g, 2.73 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and orange crystals remained. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals that formed were collected by filtration. This procedure gave 0.240 g, 88% isolated yield of **14**: mp 63-65° C; MS *m/z* (%) 161(24), 162(3), 118(100), 91(14), 63(9). Mass spectrum located in A.28.

o-tert-Butylphenyl acetate (16)

N-(*o-tert*-Butylphenyl)acetamide **(15)** (0.143 g, 7.49 x 10^{-4} moles) [4-*tert*-butylaniline using synthetic method for **2**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.103 g, 1.50 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and light brownish crystals remained. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals that were formed were collected by filtration. At room temperature the material clumped together and if held in your hand it would become a brown colored oil. This procedure gave 0.135 g, 94% isolated yield of **16**: mp 24-27° C; MS *m/z* (%) 192(3), 150.1(59), 135.1(100), 107.1(49), 91(7), 77(5), 65(3).[83] Mass spectrum located in A.3.

m-Tolyl acetate (18)

N-(*m*-Tolyl)acetamide **(17)** (0.721 g, 4.83 x 10^{-3} moles was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid.

The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.667 g, 9.66 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was then removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.26 mL of oil was obtained at a density of 1.05 which gave 0.601 g, 83% isolated yield of **18:** MS *m/z* (%) 149.8(7), 108(100), 107(45), 89(13), 79.0(22), 76.9(31), 50.9(21). (SDBS 2357). Mass spectrum located in A.25.

Benzanilide (19) [84]

Benzoic Acid (1.15g, 9.40 x 10^{-3} moles was placed in a 50 mL round bottom flask with 2 mL of Thionyl Chloride, which was purchased commercially. The solution was heated to solvent reflux for 30 minutes and allowed to cool to room temperature. The flask was cooled to room temperature. Aniline, 2 g in 30 mL of Benzene, was added. The flask was placed in a steam bath for three minuets. Deionized water 2 mL was added. The solution was washed with 2 mL of a 5% HCl solution, followed by 2 mL of 5%

NaOH solution, followed by deionized water, 2 mL. The aqueous layer was removed and the benzene solution was dried using anhydrous sodium sulfate. Solvent was removed under reduced pressure. The resulting crystals that formed were dissolved in ethanol, poured into ice/water, and the resulting crystals that were formed were collected by filtration. This procedure gave 1.645 g, 89% isolated yield of **19**: mp 163-165° C, MS *m/z* (%) 197, 105, 93, 66.

Phenyl Benzoate (20)

Benzanilide **(19)** (0.426g, 2.16 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.298 g, 4.32 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0.132 g, 91% isolated yield of **20**: mp 68-70° C; MS *m/z* (%) 198(16), 105(100), 77(76), 51(29). Mass spectrum located in A.30.

N-(4-Cyanophenyl)-4-methoxybenzamide(21)[84]

p-Anisic acid (1.70 g, 1.20 x 10^{-2}), which was purchased commercially, was placed in a 50 mL round bottom flask with 6 mL of Thionyl Chloride. The solution was heated to solvent reflux for 30 minutes and allowed to cool to room temperature. The flask was cooled to room temperature. *p*-Aminobenzonitrile, 2 g in 30 mL of Benzene, was added. The flask was placed in a steam bath for three minuets. Deionized water was added 2 mL. The solution was washed with 2 mL of a 5% HCl solution, followed by 2 mL of 5% NaOH solution, followed by deionized water, 2 mL. The aqueous layer was removed and the benzene solution was dried using anhydrous sodium sulfate. Solvent was removed under reduced pressure. The resulting crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 2.63 g, 93% isolated yield of **21**: mp 160-162° C,[85] MS *m/z* (%) 251, 152, 135, 107, 77.[80]

4-Cyanophenyl 4-methoxybenzoate (22)

N-(4-Cyanophenyl)-4-methoxybenzamide **(21)** (0.996 g, 3.95 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.546g, 7.90 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown.

The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals collected by filtration. This procedure gave 0.913 g, 91% isolated yield of **22** with a melting point of 60° C. The liquid remained cloudy until 70°C. This matches the literature.[85] MS *m/z* (%) 252.9(2), 153(2), 152(7), 135(100), 107(5), 77(9).[85] Mass Spectrum shown in A.56.

2-Pyridyl acetate (24)

2-Aminopyridene **(23)** (0.215 g, 2.28 x 10^{-3} moles) was placed in a 50 mL round bottom flask and dissolved in 10 mL of acetic anhydride and was heated to reflux and kept at reflux for 30 min and then allowed to cool to room temperature. Acetic acid (5 mL) was added and the flask was cooled to 0° C in an ice bath. Sodium nitrite (0.315 g, 4.56 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the aqueous phase was extracted with (3 x 50 mL) methylene chloride. The organic phase was washed (3 x 100ml) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate

solution until acetic anhydride was removed. 0.265 g of liquid was obtained and the purity, as determined by semi-quantitative GC/MS, was 84%. This gave an isolated yield of 72% of **24:** MS *m/z* (%) 137(3), 95(75), 67(100), 51(11).[86] Mass spectrum located in A.4.

1-Napthyl acetate (26)

N-(1-Napthyl)acetamide **(25)** (0.329 g, 1.78 x 10^{-3} moles) [1-Napthylamine using synthetic method for **2**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.246 g, 3.56 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0.312 g, 91% isolated yield of **26**: mp 47-49° C; MS *m/z* (%) 186(8), 144(14), 143.1(100), 115(14), 116(7), 89(2). Mass spectrum located in A.53.

1,8-bisacetoxynaphthalene (28)

1,8-bis(N-acetamido)naphthalene **(27)** (0.622g, 2.59 x 10^{-3} moles) [1,8-Diaminonaphthalene using synthetic method for **2**] was placed in a 25 mL round bottom

flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.703 g, 1.02 x 10^{-2} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0.523 g, 84% isolated yield of **28**: mp 146-148° C; MS *m/z* (%) 243.9, 182, 158, 130.

N-(4-Biphenylyl)trifluoroacetamide (29)

4-Aminobiphenyl (1.08 g, 6.37 x 10^{-3} moles) was placed in a 50 mL round bottom flask and dissolved in 20 mL of trifluoroacetic anhydride. Upon addition of the trifluoroacetic anhydride the 4-aminobiphenyl turned purple. Caution: trifluoroacetic anhydride reacts violently to water. All purification steps must take place in the hood until you are sure all TFA has been removed. The solvent was heated to reflux for 30 minutes and allowed to cool to room temperature. The flask was placed in an ice bath and purple crystals formed. The resulting crystals collected by filtration. The crystals were washed with deionized water. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 1.63

g, 97% isolated yield of **29:** mp 206-208° C,[87] MS *m/z* (%) 266.1(15), 265.1(100), 271.2(5), 195.2(5), 170.2(7), 168.3(15).[87] Mass spectrum located in A.29.

4-Biphenylyl trifluoroacetate (30)

N-(4-Biphenylyl)trifluoroacetamide **(29)** (0.775 g, 2.92 x 10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic acid and 5 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.402 g, 5.83 x 10^{-2} moles,) was added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.734 g 94% isolated yield of **30:** mp 34-36° C.[87] MS *m/z* (%) 266(6), 170.1(100), 141.1(15), 115.1(13).[87] Mass spectrum located in A.31.

p-Nitro-N-nitrosoacetanilide (31)

[Note: nitrosoamides are carcinogens so care must be used in handling this material.][57] N-(*p*-nitrophenyl)acetamide **(5)** (0.138 g, 7.65 x 10^{-4} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic acid and 5 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.292 g, 2.09 x 10^{-3} moles) was added to this mixture

and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. After the two hours were completed the mixture was dumped into ice and the product filtered out through vacuum filtration with the house vacuum with 0.135g (6.43×10^{-4} moles) of **31** was obtained.

N-(4-Nitrophenyl)4-nitrobenzamide (32) [84]

p-Nitrobenzoic acid (1.85 g, 1.11×10^{-2}), which was purchased commercially, was placed in a 50 mL round bottom flask with 6 mL of Thionyl Chloride. The solvent was heated to reflux for 30 minutes and allowed to cool to room temperature. The flask was cooled to room temperature. *p*-Nitroaniline, 2 g in 30 mL of Benzene, was added. The flask was placed in a steam bath for three minuets. 2 mL of deionized water was added. The solution was washed with 2 mL of a 5% HCl solution, followed by 2 mL of 5% NaOH solution, followed by deionized water, 2 mL. The aqueous layer was removed and the benzene solution was dried using anhydrous sodium sulfate. Solvent was removed under reduced pressure. The resulting crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 3.14 g, 98% isolated yield of **32**: mp 270-273° C;[88] MS *m/z* (%) 287, , 288, 150, 120, 92, 76.[88]

4-Nitrophenyl 4-nitrobenzoate (33)

N-(4-Nitrophenyl)4-nitrobenzamide **(32)** (0.133 g, 4.63×10^{-3} moles) was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of

acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.160 g, 2.32 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0.108 g, 81% isolated yield of **33**: mp 157-159° C;[88] MS *m/z* (%) 288(7), 150.1(100), 120(12), 92.2(22), 76.2(8), 50.2(3).[88] Mass spectrum located in A.58.

2,4-Dinitrophenyl 2,4-dinitrobenzoate (39)

[Note: The material is a probable energetic material and a possible explosive. The synthesis and handling of this material must be undertaken with proper precautions.] N-(2,4-nitrophenyl)2,4-dinitrobenzamide **(38)** (0.055 g, 1.44 x 10^{-4} moles) [2,4-Dinitrobenzoic acid, 2,4-Dinitroaniline using synthetic method for **32**] was placed in a 25 mL round bottom flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.021g, 3.00 x 10^{-4} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The solution reacted rapidly, boiling in the ice bath for approximately 3 min and then turned dark brown. The flask was kept in the ice bath for another 2 hours. The flask was removed from the ice

bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The mixture was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals collected by filtration. This procedure gave 0.044 g, 80% isolated yield of **39**. When mp was attempted the material shot out the capillary tube at 215 °C., therefore, mp could not be taken under normal conditions. MS *m/z* (%) 377.9(5), 168.1(23), 122.1(100), 121(93), 120(15), 108(7), 94.1(25), 92.1(15), 75.1(16), 63.0(26), 51(13). Mass spectrum located in A.54.

Biphenyl (41)

Acetanilide **(40)** (0.326 g, 2.41 x 10^{-3} moles) was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.332 g, 4.82 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and hexane was added until crystals formed. The resulting crystals were collected by filtration. This procedure

gave 0.222 g, 60% isolated yield of **41**: mp 69-71° C, MS *m/z* (%) 155.1(19), 154.1(100), 153.1(34), 152.1(25), 105.1(10), 77.1(6). ^{1}H-NMR, 7.69(4H), 7.46(4H), 7,39(2H). Mass spectrum located in A.5. ^{1}H-NMR spectrum located in A.6.

4-Nitrobiphenyl (42)

N-(4-Nitrophenyl)acetamide **(5)** (0.263 g, 1.46 x 10^{-3} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.252 g, 3.66 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals that were formed were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals that were formed were collected by filtration. This procedure gave 0.633 g, 94% isolated yield of **42**: mp 112-114° C; MS *m/z* (%) 200(14), 199.1(100), 169.1(58), 152.2(63), 141.2(34), 115.2(14). ^{1}H-NMR, 8.21(1H), 7.63(2H), 7.58(2H). 7.40(3H). Mass spectrum is located in A.33. ^{1}H-NMRspectrum is located in A.36.

p-Terphenyl (43)

N-(4-biphenylyl)acetamide **(2)** (0.424 g, 2.01 x 10^{-3} moles) was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.277 g, 4.02x10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and hexane was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.288 g, 62% isolated yield of **43**: mp 211-213° C; MS *m/z* (%) 231.1(20), 230.1(100), 226.1(35), 202.1(15), 189.1(5), 152.1(9), 115.0(11). Mass spectrum located in A.64.

4-Bromobiphenyl (44)

N-(4-Bromophenyl)acetamide **(9)** (0.142 g, 6.67 x 10^{-4} moles) [4-Bromoaniline using synthetic method for **2**] was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.092 g, 1.34 x 10^{-3} moles) was added to this mixture and the vessel

was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional minuets. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in ethanol, poured into ice/water, and the resulting crystals were collected by filtration. This procedure gave 0. 116 g, 75% isolated yield of **44**: mp 90-92.5° C, MS *m/z* (%) 235(13), 233(14), 234(95), 232(100), 154.1(2), 153.1(19), 152.1(44), 151.1(12), 150.1(5), 76.1(8), 75.1(5). Mass spectrum located in A.21.

2-*tert*-Butylbiphenyl (45)

N-(2-*tert*-butylphenyl)acetamide **(15)** (0.194 g, 1.01×10^{-3} moles) [2-*tert*-Butylaniline using synthetic method for **2**] was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.139 g, 2.03×10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and

kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and petroleum ether was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.112 g, 53% isolated yield of **45**: mp 32-34° C; MS *m/z* (%) 210.1(41), 195.1(100), 179.1(15), 167.1(28), 165.1(25), 153.2(9), 89.1(3). Mass spectrum located in A.55.

2-Phenylpyridine (47)

2-Aminopyridine **(23)** (0.324 g, 3.44 x 10^{-3} moles) was placed in a 250 mL round bottom flask and dissolved in 20 mL of acetic anhydride and attached to a condenser. The solution brought it to reflux and kept it at reflux for approximately 30 min. The solution was allowed to cool to room temperature and 10 mL of acetic acid was added. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.475 g, 6.89 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by

reduced pressure. A liquid remained which was dissolved into methylene chloride (100 mL). This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride and then washed with 70 mL of deionized water. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. 0.239 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 72%. This gave 0.287 g, 54% isolated yield of **47:** MS *m/z* (%) 157.1(5), 156.1(63), 155.1(100), 154.2(70). Mass spectrum located in A.10.

1,8-Diphenylnapthylene(48)

1,8-bis(N-acetamido)naphthalene **(27)** (0.284 g, 1.17 x 10^{-3} moles) [1,8-Diaminonaphthalene using synthetic method for **2**] was placed in a 125 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.162 g, 2.35 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath, allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. The mixture was poured into ice/water. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained which was poured into ice/water. The resulting crystals that were formed were collected by

filtration. These crystals were dissolved in benzene and hexane was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.201 g, 61% isolated yield of **48**: mp 149-150.5° C; MS *m/z* (%) 279(5), 247(100), 183.2(34), 182.1(72), 168.1(65), 149.1(35), 92.1(25), 91(76), 65(34). ^{1}H-NMR, 7.28(6H), 7.19(10H).[89] Mass spectrum located in A.9 page 124. ^{1}H-NMR located in A.50.

2-phenyl-1,3,5-triazene (50)

2-Amino-1,3,5-triazine **(49)** (0.315 g, 3.27 x 10^{-3} moles) was placed in a 100 mL round bottom flask and dissolved in 10 mL of acetic anhydride and attached to a condenser. This solution was brought it to reflux and kept it at reflux for approximately 30 min. The solution was allowed to cool to room temperature and added 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.452 g, 6.55 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and hexane was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.409 g, 79% isolated yield of **50**: mp 63-65°

C, [80] MS *m/z* (%) 158.0(25), 157.0(100),154.1(7), 104.0(85), 103.1(20), 77.1(14), 76.0(20), 75.0(8).[90] Mass spectrum is located in A.8.

4-Nitro-p-terphenyl (51)

N-(4-biphenylyl)acetamide **(2)** (0.173 g, 8.21 x 10^{-4} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.113 g, 1.64x10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Benzene (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the benzene layer was separated and the benzene was removed by reduced pressure. A liquid remained was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and petroleum ether was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.120g, 53% isolated yield of **51**: mp 208.5-211° C; MS *m/z* (%) 275.1(100), 276(30), 277(10), 245.2(20), 244.2(8), 228.2(15), 226.2(27), 122.2(25). Mass spectrum located in A.51.

1,8-(4-Nitrophenyl)naphthalene (52)

1,8-bis(N-acetamido)naphthalene **(27)** (0.098 g, 4.06 x 10^{-4} moles) [1,8-Diaminonaphthalene using synthetic method for **2**] was placed in a 125 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.056 g, 8.13 x 10^{-4} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Nitrobenzene (70mL) was added and the flask was kept in the ice bath for 10 additional minuets. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the nitrobenzene layer was separated and the nitrobenzene was removed by reduced pressure steam distillation. The liquid that remained was poured into ice/water. The resulting crystals were collected by filtration. These crystals were dissolved in benzene and petroleum ether was added until crystals formed. The resulting crystals were collected by filtration. This procedure gave 0.057 g, 58% isolated yield of **52**: mp 194-197° C; MS *m/z* (%) 370.1(2), 356.1(10), 355.1(8), 168(25), 122.1(20), 92.1(26), 76.1(42), 75.1(100), 74.1(46), 63.1(67), 51.0(16), 50.2(24). Mass spectrum located in page A.52.

Perylene (53)

1,8-bis(N-acetamido)naphthalene **(27)** (0.293 g, 1.21 x 10^{-3} moles) [1,8-Diaminonaphthalene using synthetic method for **2**] was placed in a 250 mL Erlenmeyer

flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.167 g, 2.42 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Non-distilled benzaldehyde (70 mL) was added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to medium/dark brown. Deionized water (70 mL) was added and the benzaldehyde layer was separated washed three times with saturated sodium bicarbonate (3 x 100 mL) and the benzaldehyde was removed by reduced pressure. The resulting crystals that were formed were dissolved in benzene and petroleum ether was added until crystals formed. The resulting crystals that were formed were collected by filtration.[91] This procedure gave 0.198g, 65% isolated yield of **53**: mp 278-280° C; 1H-NMR, 8.188 (4H), 7.678 (4H), 7.479 (4H). J (8.188, 7.479) = J (7.678, 7.479) = 7.6 HZ. ^{1}H-NMR located spectrum in A.7.

1-Bromo-2,6-diethylbenzene (55)

2,6-Diethylphenylacetamide **(54)** (0.268 g, 1.40 x 10^{-3} moles) [2,6-Diethylaniline using synthetic method for **2**] was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.193g, 2.80 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours.

Lithium bromide (1.22 g, 1.40 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The flask was removed from the ice bath and allowed to equilibrate to room temperature, and kept at room temperature for an additional 24 hours. The solution turned color, from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was then added and the color changed from ruby reddish/light brown to light red. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride and then washed with 70mL of deionized water. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, using the procedure described above, until acetic anhydride was removed. 0.239 g of oil was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 81%. This gave 0.194 g, 65% isolated yield of **55:** MS *m/z* (%) 215(10), 214(91), 213(9), 212(89), 199(71), 197(76), 133.1(100), 117.1(93), 115(74), 105(60), 91.1(44), 77.1(40), 65(12), 51(21). (NIST, C65232577),[82] Mass spectrum located in A.16.

4-Bromobiphenyl (56)

N-(4-Biphenylyl)acetamide **(2)** (0.125 g, 5.91 x 10^{-4} moles) was placed in a 50 mL round bottom flask and dissolved in 10 mL of acetic acid and 5 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.082 g, 1.18 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A

brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Lithium bromide (0.513 g, 5.91 x 10^{-3} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was then removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from ruby reddish/light brown to light red. The mixture was then poured into ice/water. The resulting crystals that were formed were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.083 g, isolated yield 60% of **56:** mp 90-92° C; MS *m/z* (%) 235, 233, 232,234, 154.1 153.1, 152.1, 151.1, 150.1, 76.1, 75.1.

4-Iodobiphenyl (57)

N-(4-Biphenylyl)acetamide **(2)** (0.122g, 5.76 x 10^{-4} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.101 g, 1.47 x 10^{-3} moles,) was added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Potassium iodide (0.956 g, 5.76 x 10^{-3} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was then added and the

color changed from dark brownish red to yellow. The mixture was then poured into ice/water. The resulting crystals that were formed were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.102 g , isolated yield 63% of **57:** mp 113-115° C; MS *m/z* (%) 281(10), 280(100), 154.2(4), 153.2(32), 152.1(59), 151.2(20), 150.1(6), 126.2(5), 102.2(3), 76(5). (NIST, 43808)[86] Mass spectrum located in A.12.

4-Chlorobiphenyl, using lithium chloride (58a)

N-(4-Biphenylyl)acetamide **(2)** (0.207 g, 9.82 x 10^{-4} moles) was placed in a 150 mL Erlenmeyer flask and dissolved in 20mL of acetic acid and 10mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.136 g, 1.96 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Lithium chloride (0.416 g, 9.82 x 10^{-3} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The mixture was then poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.021 g, isolated yield 13% of **58a:** mp of 76-78.5° C. MS *m/z* (%) 190.1, 188.1, 154.1, 153.1, 152.1, 151.1, 76.1

4-Chlorobiphenyl, using carbon tetrachloride (58b)

N-(4-Biphenylyl)acetamide **(2)** (0.198 g, 9.36 x 10^{-4} moles) was placed in a 150 mL Erlenmeyer flask and dissolved in 10 mL of acetic acid and 5 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.129 g, 1.87 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting crystals that were purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.111 g , isolated yield 63% of **58b:** mp 76-78° C; MS *m/z* (%) 190.1(30), 188.1(100), 154.1(4), 153.1(20), 152.1(35), 151.1(10), 76.1(5). Mass spectrum located in A.13.

4-Bromonitrobenzene (59)

N-(4-Nitrophenyl)acetamide **(5)** (0.870 g, 4.83x10^{-3} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 50 mL round bottom flask and dissolved in 20 mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.666 g, 9.66 x 10^{-3} moles,) was then added to this

mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Lithium bromide (4.19 g, 4.83 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was then added and the color changed from ruby reddish/light brown to light red. The mixture was then poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.762 g, isolated yield 78% of **59:** mp 124-127° C; MS *m/z* (%) 204(11), 203(92), 202.1(13), 201(100), 174.2(73), 171.2(87), 186(35), 186(37), 145.3(35), 143(33), 75.3(19). ^{1}H-NMR, 8.107 (d, 2H), 7.692 (d, 2H) J (8.107, 7.692) = 9.1 HZ. Mass spectrum located in A.26. ^{1}H-NMR spectrum located in A.11. [Note: Ac_2O still present as shown in the 2 region].

4-Bromoanisole (60)

N-(*p*-methoxyphenyl)acetamide **(7)** (0.381 g, 2.31 x 10^{-3} moles) was placed in a 250 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.319 g, 4.62 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium bromide (2.01 g, 2.31 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The mixture

was then removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was then added and the color changed from ruby reddish/light brown to light red. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.310 g of oil was obtained with a purity, as determined by semi-quantative GC/MS analysis, of 87%. This gave 0.269 g, 63% isolated yield of **60:** MS *m/z* (%) 187.9(95), 187(7), 186(100), 159(2), 107(50), 79.1(5), 77(30), 62(3), 51(14). Mass spectrum located in A.15.

4-Iodonitrobenzene (61)

N-(4-Nitrophenyl)acetamide **(5)** (0.424 g, 2.35 x 10^{-3} moles) [4-Nitroaniline using synthetic method for **2**]was placed in a 50 mL round bottom flask and dissolved in 10 mL of acetic acid and 5 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.325 g, 4.70 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept

at room temperature for an additional 24 hours. Potassium iodide (3.90 g, 2.35 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from dark brownish red to yellow. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.398 g, 68% isolated yield of **61:** mp 171-173° C; MS *m/z* (%) 249.9(7), 249.0(100), 219.1(39), 191.1(12), 76.1(7). (SDBS, 1116). Mass spectrum located in A.57.

p-Iodoanisole (62)

N-(*p*-Methoxyphenyl)acetamide (**7**) (0.215 g, 1.30 x 10^{-3} moles) was placed in a 250 mL Erlenmeyer flask and dissolved in 20 mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.179 g, 2.60 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Potassium iodide (2.16 g, 1.30 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from dark brownish red to yellow. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol,

pouring into ice/water and filtered. This procedure gave 0.192 g, isolated yield 63% of **62:** mp 50-52° C; mp 50-53° C MS *m/z* (%) 234.1(36), 219.2(100), 75(43), 73.1(53), 58(21), 57(1). Mass spectrum located in A.14.

4-Chloronitrobenzene, using lithium chloride (63a)

N-(4-Nitrophenyl)acetamide (**5**) (0.216 g, 1.20 x 10^{-3} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 250 mL Erlenmeyer flask and dissolved in 20 mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.168 g, 2.40 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Lithium chloride (0.416 g, 9.82 x 10^{-3} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.042 g, isolated yield 22% of **63a:** mp of 82-84° C; MS *m/z* (%) 156.9, 156.9, 141, 127.0(100), 101.1, 99.1, 75.3, 74, 63.1.

4-Chloronitrobenzene, using carbon tetrachloride (63b)

N-(4-Nitrophenyl)acetamide (**5**) (0.393 g, 2.18 x 10^{-3} moles) [4-Nitroaniline using synthetic method for **2**] was placed in a 150 mL Erlenmeyer flask and dissolved in 20 mL

of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.301 g, 4.36 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting crystals were purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.237 g, isolated yield 69% of **63b:** mp of 82-84° C; MS *m/z* (%) 156.9(94), 158.8(32), 141(65), 127.0(100), 101.1(28), 99.1(73), 75.3(75), 74(21), 63.1(11). Mass spectrum located in A.63.

p-Chloroanisole, using lithium chloride (64a)

N-(*p*-Methoxyphenyl)acetamide (**7**) (0.326 g, 1.98 x 10^{-3} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.273 g, 3.92x10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a

brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium chloride (1.68 g, 3.952×10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 50 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish oil remained. The oil was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as describes above, until acetic anhydride was removed. 0.025 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 96%. This gave 0.014 g, 5% isolated yield of **64a:** MS *m/z* (%) 144, 142(100), 127, 107, 99, 73, 63

p-Chloroanisole, using carbon tetrachloride (64b)

N-(*p*-Methoxyphenyl)acetamide (**7**) (0.196 g, 1.19×10^{-3} moles) was placed in a 150 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.164 g, 2.38×10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 min. The mixture was removed

from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The mixture was then removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. Purity, as determined by semi-quantitative GC/MS analysis, was 87%. This gave 0.111 g, 65% isolated yield of **64b:** MS *m/z* (%) 144(27), 142(100), 127(42), 107.1(11), 99(45), 75(17), 73(19), 63(23). Mass spectrum is located in A.61.

p-Bromotoluene (65)

N-(*p*-Tolyl)acetamide **(9)** (0.285 g, 1.91 x 10^{-3} moles) was placed in a 250 mL Erlenmeyer flask and dissolved in 20 mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.264 g, 3.82 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Lithium bromide (4.19 g, 4.83 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was then removed from the ice bath, allowed to equilibrate to room temperature and was kept at room

temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from ruby reddish/light brown to light red. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.216 g, isolated yield 66% of **65**: mp 27-29° C; MS *m/z* (%) 171(40), 169.9(41), 92(10), 91(100), 89.1(17), 65(30). Mass spectrum located in A.62.

m-Bromotoluene (66)

N-(*m*-Tolyl)acetamide **(17)** (0.237 g, 1.59 x 10^{-3} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.220 g, 3.18 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium bromide (1.38 g, 1.59 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from ruby reddish/light brown to light red. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium

sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. The resulting liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. Purity, as determined by semi-quantitative GC/MS analysis, was 94%. This gave 0.189 g, 69% isolated yield of **66:** MS *m/z* (%)172(33), 171(5), 170(40), 91(100), 89.1(20), 65.1(24). Mass spectrum is located in A.18.

p-Iodotoluene (67)

N-(*p*-Tolyl)acetamide (**17**) (0.321 g, 2.15 x 10^{-3} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic acid and 10 mL of acetic acid. This mixture was allowed to cool down to 0° C in an ice bath. Sodium nitrite (0.297 g, 4.31 x 10^{-3} moles,) was then added to this mixture and the vessel was lightly capped. A brown gas (NO_2) was noticed and the solution turned lime green. This mixture was kept in the ice bath for another 2 hours. Potassium iodide (3.57 g, 2.15 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional minuets. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from dark brownish red to yellow. The mixture was poured into ice/water. The resulting crystals were collected by filtration and purified through dissolving in ethanol, pouring into ice/water and filtered. This procedure gave 0.286 g, isolated yield 61% of

67: mp of 34-36° C; MS *m/z* (%) 217.9(100), 127(5), 91.1(55), 83.9(20), 65.0(27). Mass spectrum located in A.19.

m-Iodotoluene (68)

N-(*m*-Tolyl)acetamide **(17)** (0.211 g, 1.41 x 10^{-3} moles), which was purchased commercially, was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.195 g, 2.83 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Potassium iodide (2.33 g, 1.41 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The mixture was then removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was then added and the color changed from dark brownish red to yellow. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. Methylene chloride was dried with anhydrous sodium sulfate. The methylene chloride solution was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.190 g of liquid was obtained with a purity, as determined by

semi-quantitative GC/MS analysis, of 97%. This gave 0.184 g, 60% isolated yield of **68:** MS *m/z* (%) 219(5), 218(100), 91.1(54), 65(26). Mass spectrum located in A.22.

p-Chlorotoluene, using lithium chloride (69a)

N-(*p*-Tolyl)acetamide **(11)** (0.254 g, 1.70×10^{-3} moles), which was purchased commercially, was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.235 g, 3.40×10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium Chloride (0.731 g, 1.72×10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The mixture was then removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.030 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 97%. This gave 0.029 g, 13% isolated yield of **69a:** MS *m/z* (%) 125.9, 127.9, 124.9, 90.8, 88.8, 64.8, 62.8.

p-Chlorotoluene, using carbon tetrachloride (69b)

N-(*p*-Tolyl)acetamide **(11)** (0.205 g, 1.38 x 10^{-3} moles), which was purchased commercially, was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.190 g, 2.75 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 min. The mixture was then removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.109 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 97%. This gave 0.106 g, 61% isolated yield of **69b:** MS *m/z* (%) 125.9(38), 127.9(12), 90.8(100), 124.8(11), 88.8(17), 64.8(15), 62.8(22). Mass spectrum located in A.60.

m-Chlorotoluene, using lithium chloride (70a)

N-(*m*-Tolyl)acetamide **(17)** (0.197 g, 1.32 x 10^{-3} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.182 g, 2.64 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium Chloride (0.559 g, 1.32 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70mL) was added and the aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.019 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 99%. This gave 0.020 g, 12% isolated yield of **70a:** MS *m/z* (%) 126 , 128, 125, 91, 65.1.

m-Chlorotoluene, using carbon tetrachloride (70b)

N-(*m*-Tolyl)acetamide **(17)** (0.217 g, 1.46 x 10^{-3} moles) was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.201 g, 2.91 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 min. The mixture was then removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.117 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 99%. This gave 0.116 g, 63% isolated yield of **70b:** MS *m/z* (%) 126(36), 128(14), 125(7), 91(100), 65.1(14). Mass spectrum located in A.59.

1-*tert*-butyl-2-iodobenzene (71)

N-(*o*-*tert*-Butylphenyl)acetamide **15** (0.215 g, 1.13 x 10^{-3} moles) [2-*tert*-Butylaniline using synthetic method for **2**] was placed in a 125 mL Erlenmeyer flask and dissolved in 20mL of acetic anhydride and 10mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.155 g, 2.25 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Potassium iodide (1.87 g, 1.13 x 10^{-2} moles) was then added and the flask was kept in the ice bath for 10 additional min. The mixture was then removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. The solution turned from lime green to dark brownish red. 70 mL of a saturated sodium thiosulfate solution was then added and the color changed from dark brownish red to yellow. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.202 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 90%. This gave 0.182 g, 62% isolated yield of **71**: MS *m/z* (%) 261(10), 260(100), 245(93), 217(92), 117.1(22), 115.2(12), 91.1(9).[87] Mass spectrum located in A.20.

1-*tert*-butyl-2chlorobenzene, using lithium chloride (72a)

N-(*o*-*tert*-Butylphenyl)acetamide **(15)** (0.215 g, 1.12 x 10^{-3} moles) [2-*tert*-Butylaniline using synthetic method for **2**]was placed in a 125 mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.154 g, 2.23 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium Chloride (0.473 g, 1.11 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution, as described above, until acetic anhydride was removed. 0.024 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 88%. This gave 0.021 g, 11% isolated yield of **72a:** MS *m/z* (%) 168 , 170, 153, 127, 125, 115, 91.1, 77. [87]

1-*tert*-butyl-2-chlorobenzene, using carbon tetrachloride (72b)

N-(*o*-*tert*-Butylphenyl)acetamide **(15)** (0.267 g, 1.38 x 10^{-3} moles) [2-*tert*-Butylaniline using synthetic method for **2**] was placed in a 125 mL Erlenmeyer flask and dissolved in 10 mL of acetic anhydride and 5 mL of acetic acid. The flask was cooled to 0° C in an ice bath. Sodium nitrite (0.190 g, 2.77 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely (NO_2), was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. 70 mL of carbon tetrachloride was added and the flask was kept in the ice bath for an additional 10 minuets. The mixture was removed from the ice bath, allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to whitish in color. Deionized water (70 mL) was added and the carbon tetrachloride was separated from the aqueous layer. This was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride. The carbon tetrachloride was removed under reduced pressure. The resulting liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.150 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 91%. This gave 0.136 g, 58% isolated yield of **72b:** MS *m/z* (%) 170.1(7), 168(25), 153.1(65), 127(35), 125(100), 115.1(17), 91.1(10), 77.1(6).[86] Mass spectrum located in A.17.

o-tert-Butylbromobenzene (73)

N-(*o-tert*-Butylphenyl)acetamide **(15)** (0.144 g, 7.51 x 10^{-4} moles) [2-*tert*-Butylaniline using synthetic method for **2**] was placed in a 125mL Erlenmeyer flask and dissolved in 20 mL of acetic anhydride and 10 mL of acetic acid. The flask was cooled to 0 °C in an ice bath. Sodium nitrite (0.104 g, 1.50 x 10^{-3} moles) was added to this mixture and the vessel was lightly capped. Evolution of a brown gas brown gas, likely NO_2, was noticed and the solution turned lime green. The flask was kept in the ice bath for another 2 hours. Lithium bromide (0.653 g, 7.51 x 10^{-2} moles) was added and the flask was kept in the ice bath for 10 additional min. The mixture was removed from the ice bath and allowed to equilibrate to room temperature and was kept at room temperature for an additional 24 hours. The solution turned from lime green to ruby reddish/light brown. 70 mL of a saturated sodium thiosulfate solution was added and the color changed from ruby reddish/light brown to light red. The aqueous phase was extracted with (3 x 100 mL) methylene chloride. The organic phase was washed (3 x 100 mL) with a saturated sodium carbonate solution to remove any acetic anhydride in the methylene chloride. The methylene chloride solution was dried with anhydrous sodium sulfate. Methylene chloride was removed under reduced pressure and a brownish liquid remained. The liquid was dissolved in methylene chloride and rewashed with a saturated sodium carbonate solution until acetic anhydride was removed. 0.101 g of liquid was obtained with a purity, as determined by semi-quantitative GC/MS analysis, of 97%. This gave 0.098 g, 61% isolated yield of **73:** MS *m/z* (%) 212(50), 214(49), 213(3), 199(85), 197(80), 171(100), 169(96), 117.1(15), 115.1(20), 91.1(11), 77.1(6).[90] Mass spectrum is located in A.23.

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72. 10.0021g of potassium bromide was placed in 30 mL of a 2:1 solution of acetic anhydride and acetic acid. This was kept gently stirring at room temperature for 24 hours. The non-dissolved potassium was filtered though vacuum filtration and allow to dry. 9.7530g remained which meant that 0.2491g of potassium bromide was dissolved. This meant that approximately 0.0083g of potassium bromide can be dissolved per mL of a 2:1 anhydride to acetic acid solution.

73. 10.0079g of lithium bromide was placed in 30 mL of a 2:1 solution of acetic anhydride and acetic acid. This was kept gently stirring at room temperature for 24 hours. The non-dissolved potassium was filtered though vacuum filtration and allow to dry. 5.5156g remained which meant that 4.4923g of lithium bromide was dissolved. This meant that approximately 0.1497g of lithium bromide can be dissolved per mL of a 2:1 anhydride to acetic acid solution.

74. 6.8595g of lithium chloride was placed in 30 mL of a 2:1 solution of acetic anhydride and acetic acid. This was kept gently stirring at room temperature for 24 hours. The non-dissolved potassium was filtered though vacuum filtration and allow to dry. 3.9176g remained which meant that 2.9419g of lithium chloride was dissolved. This meant that approximately 0.0981g of lithium chloride can be

dissolved per mL of a 2:1 anhydride to acetic acid solution.

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91. If residual benzoic acid still remains after normal clean up procedures have been performed, washing with a aqueous NaOH solution will convert the benzoic acid to sodium benzoate and would be removed when the washing is removed.

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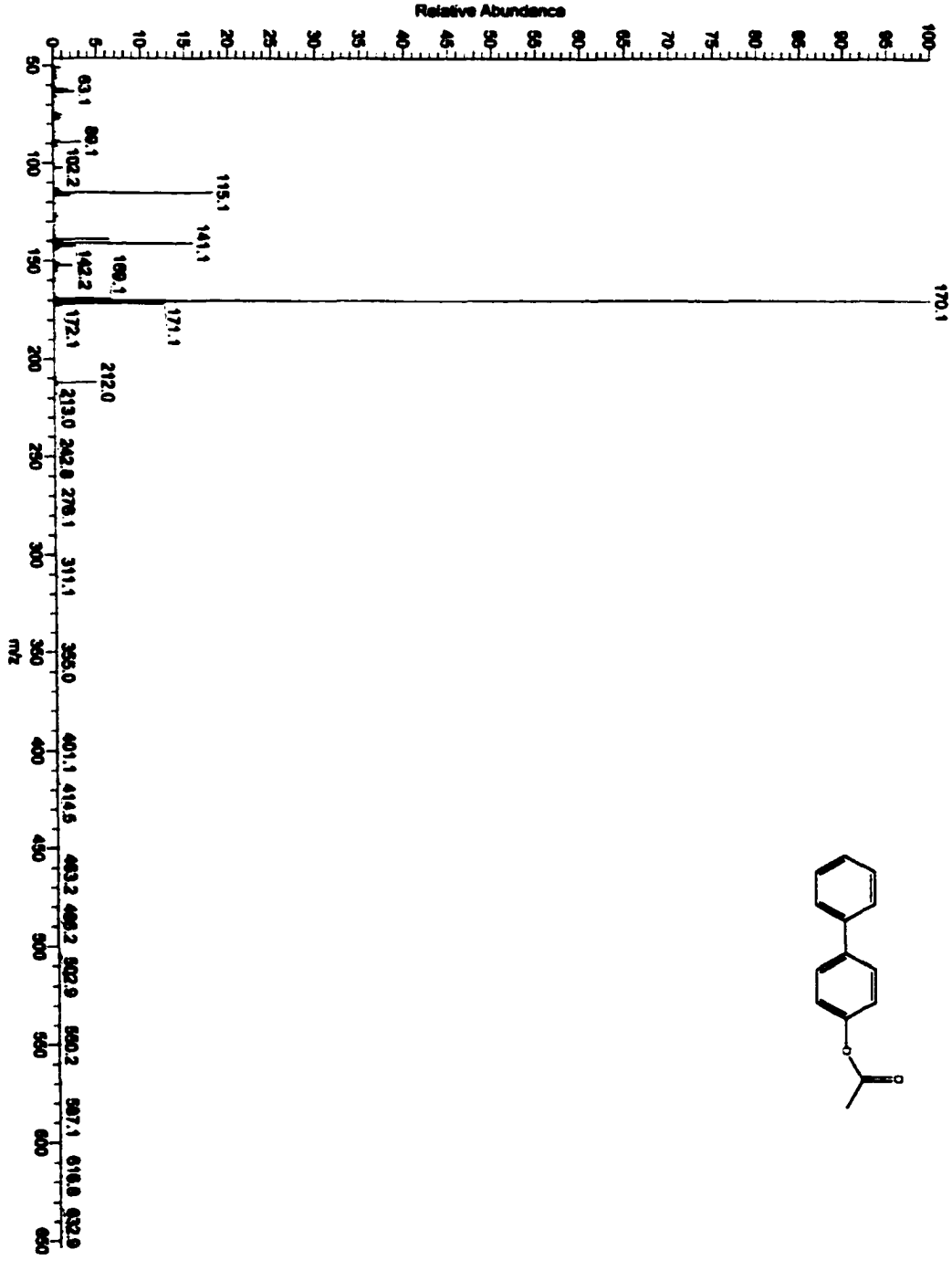
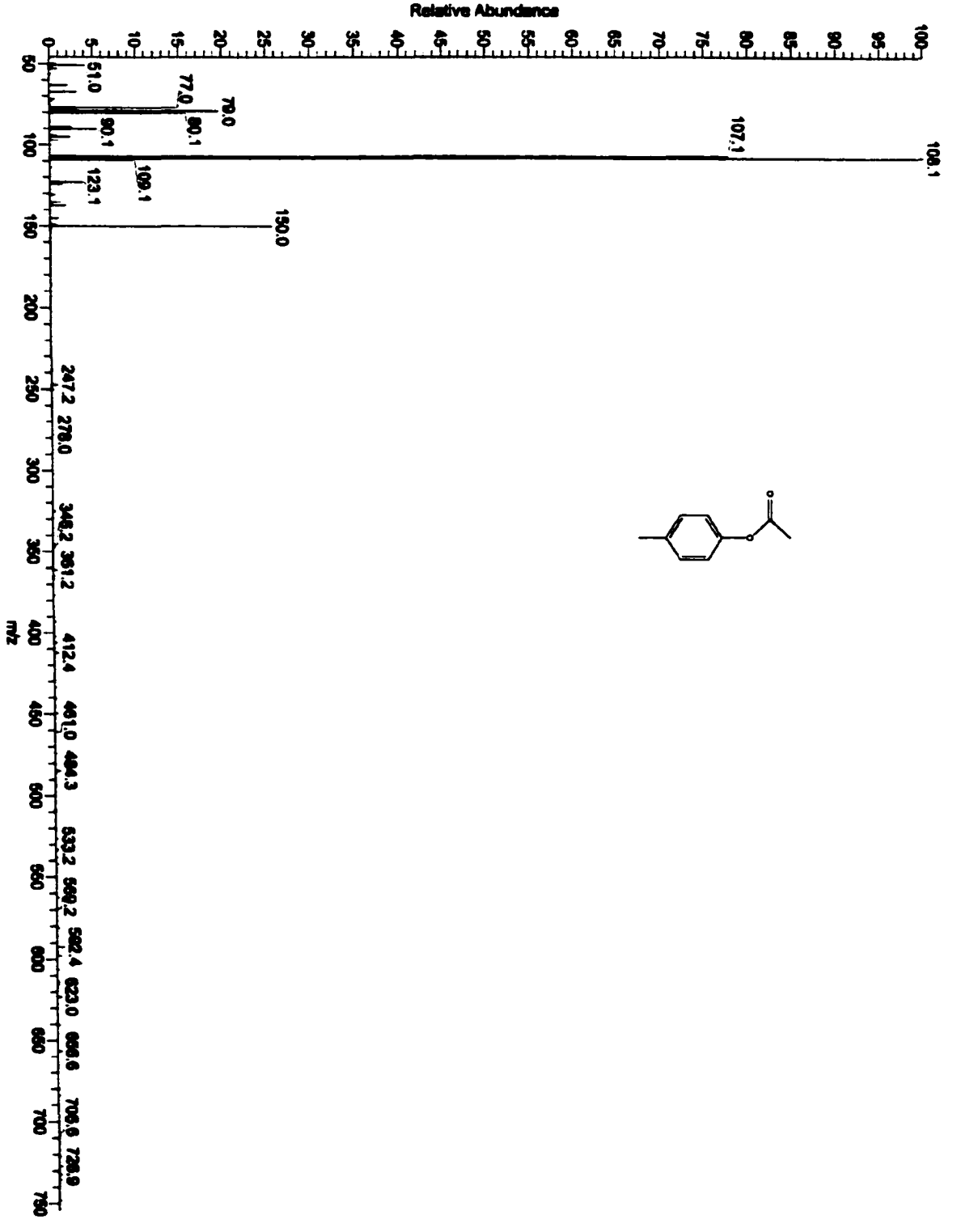
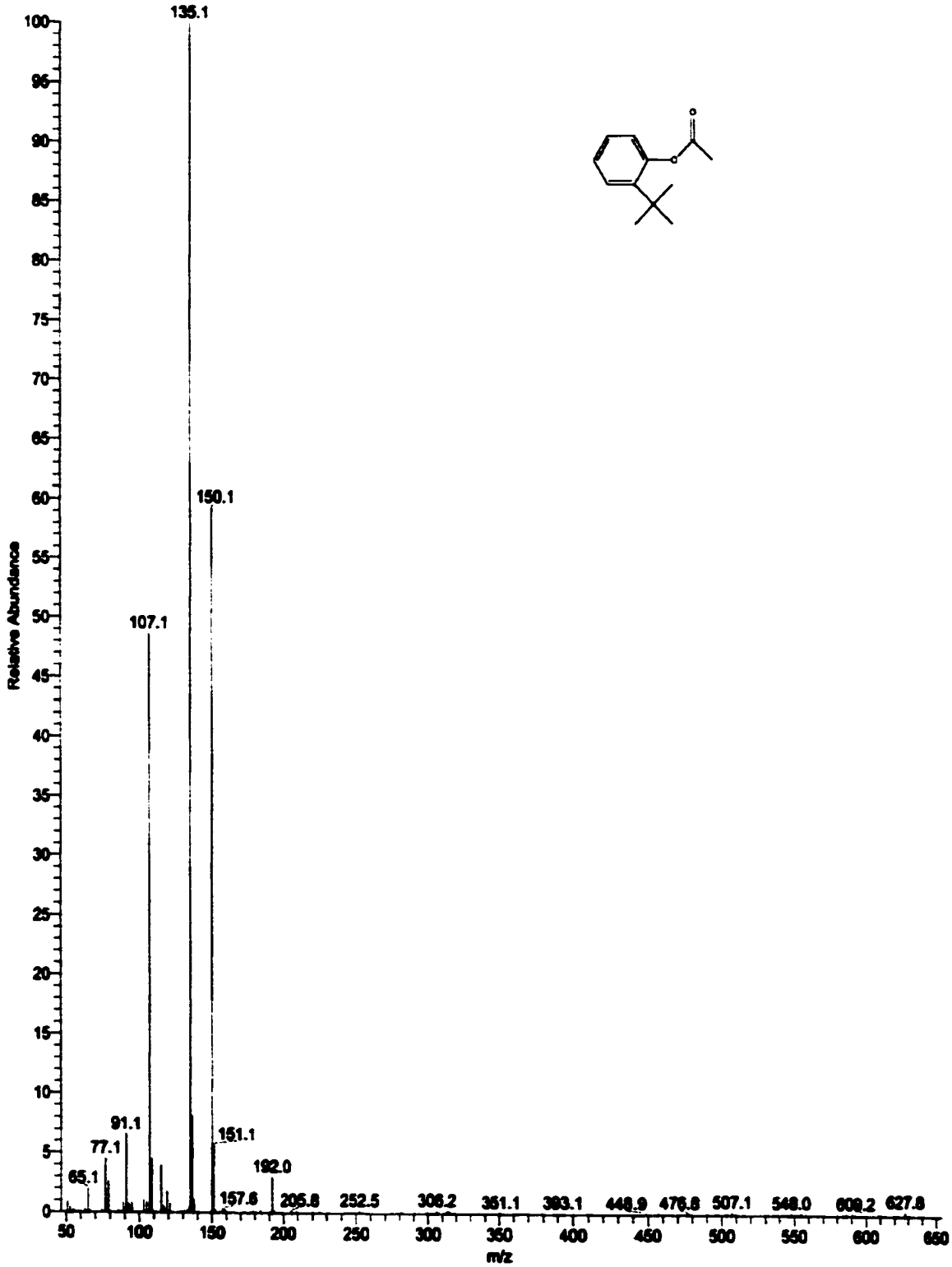


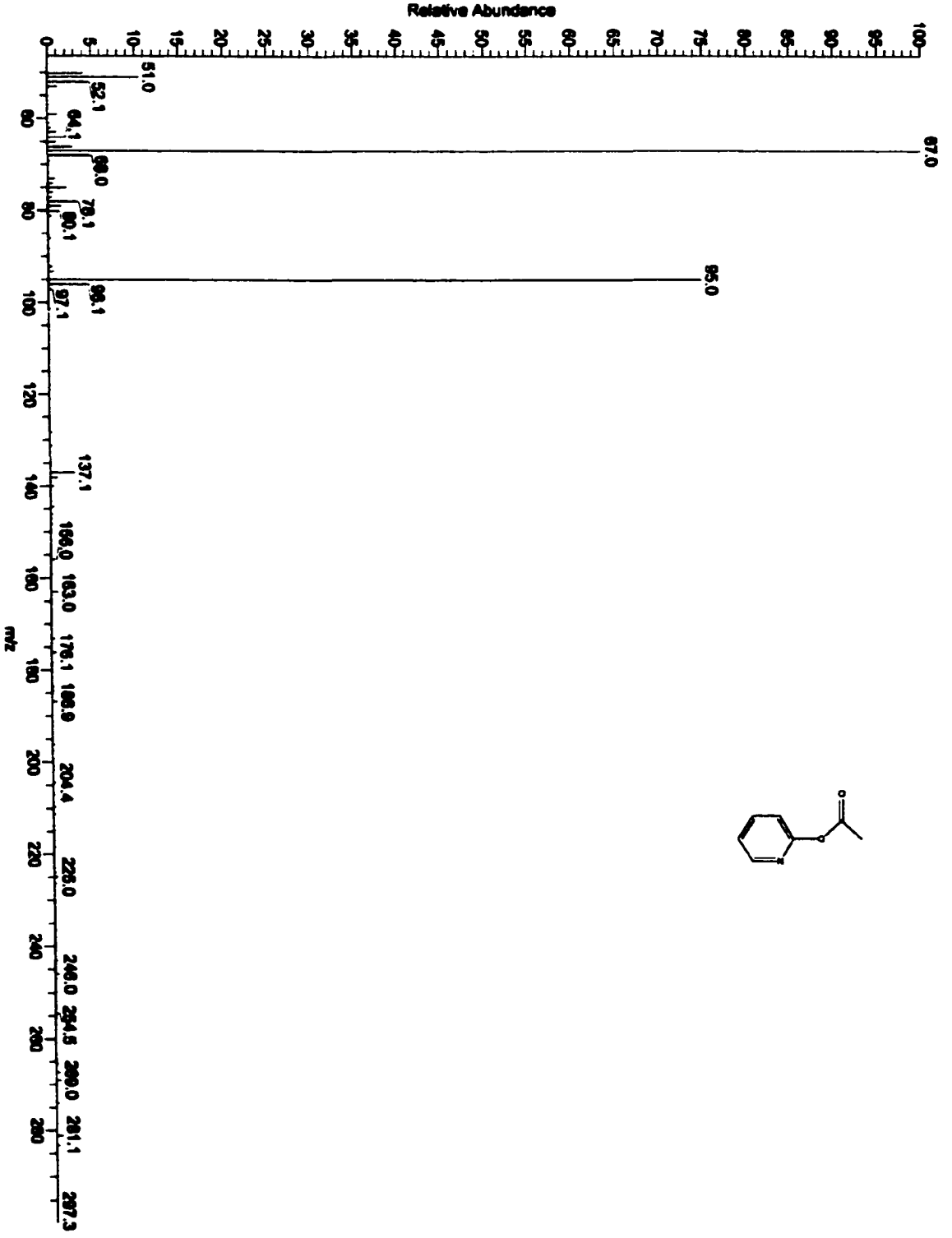
A.2. Mass Spectrum of *p*-Tolyl Acetate



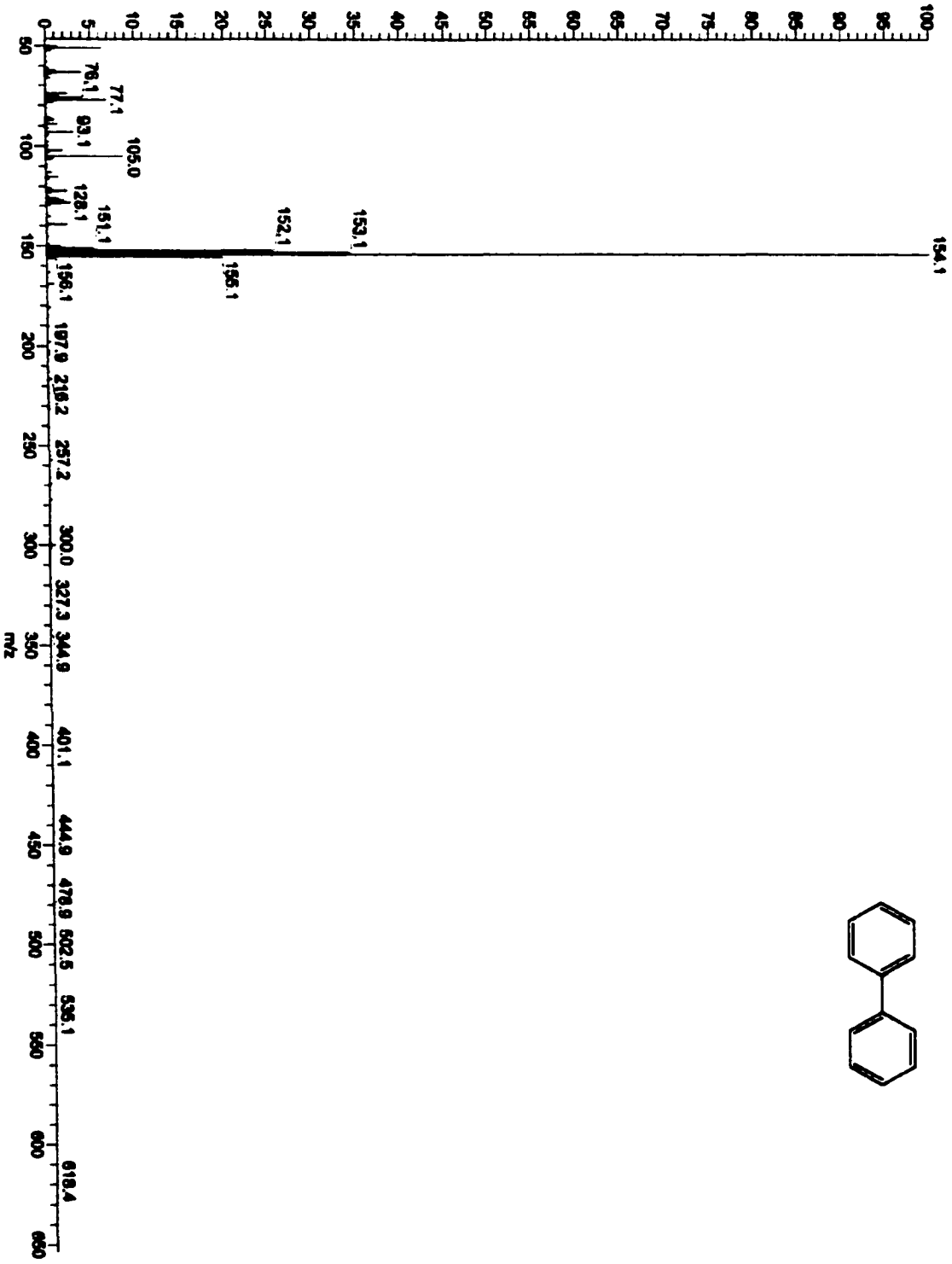
A.3. Mass Spectrum of *o-tert*-Butylphenyl Acetate



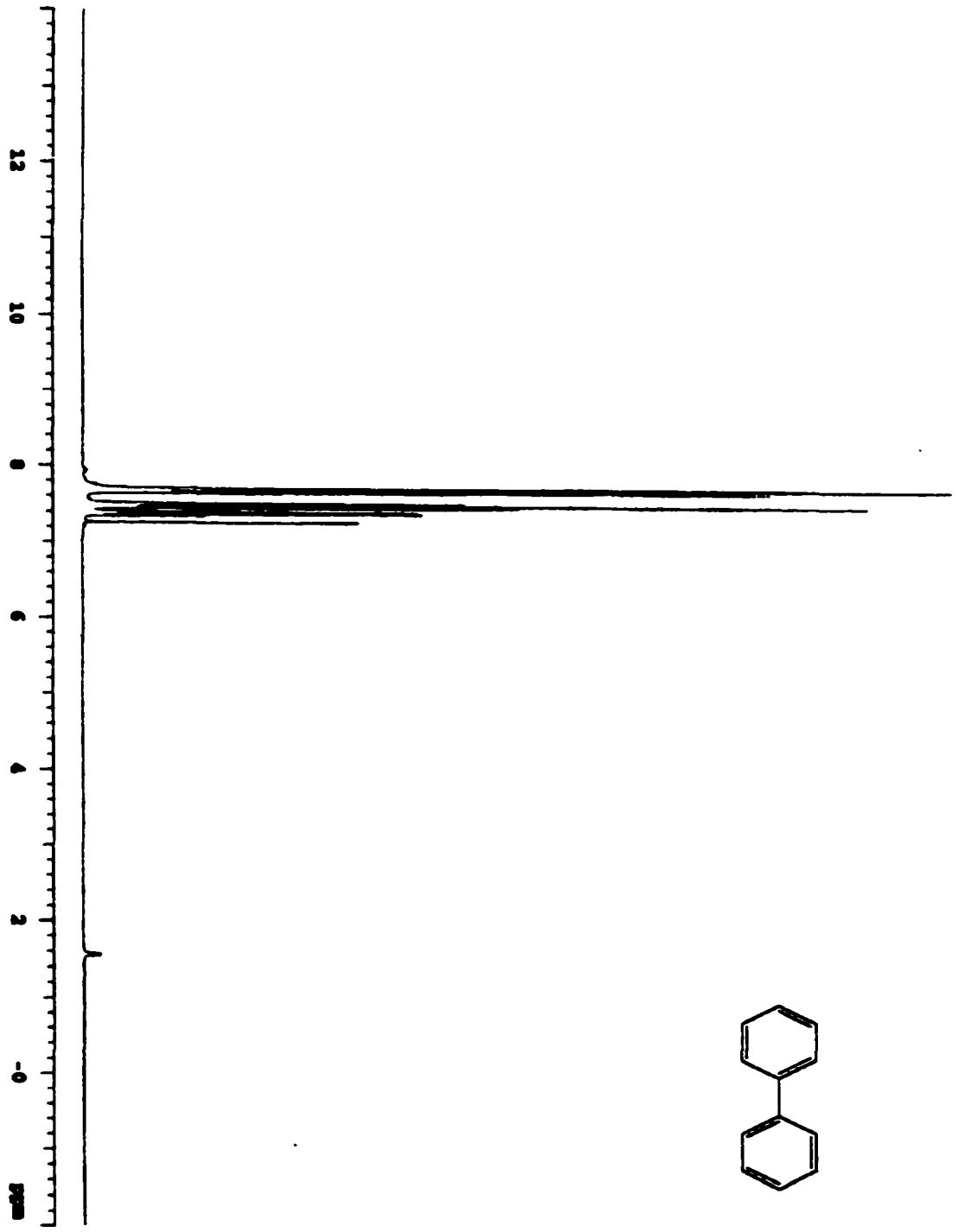
A.4. Mass Spectrum of 2-Pyridyl Acetate



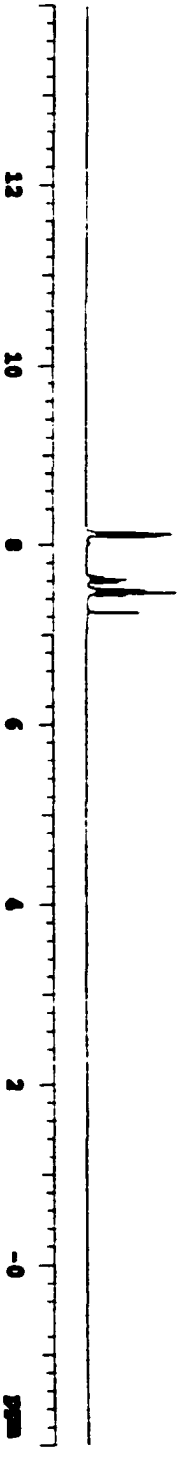
A.5. Mass Spectrum of Biphenyl

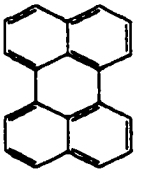


A.6. ^{1}H-NMR Spectrum of Biphenyl

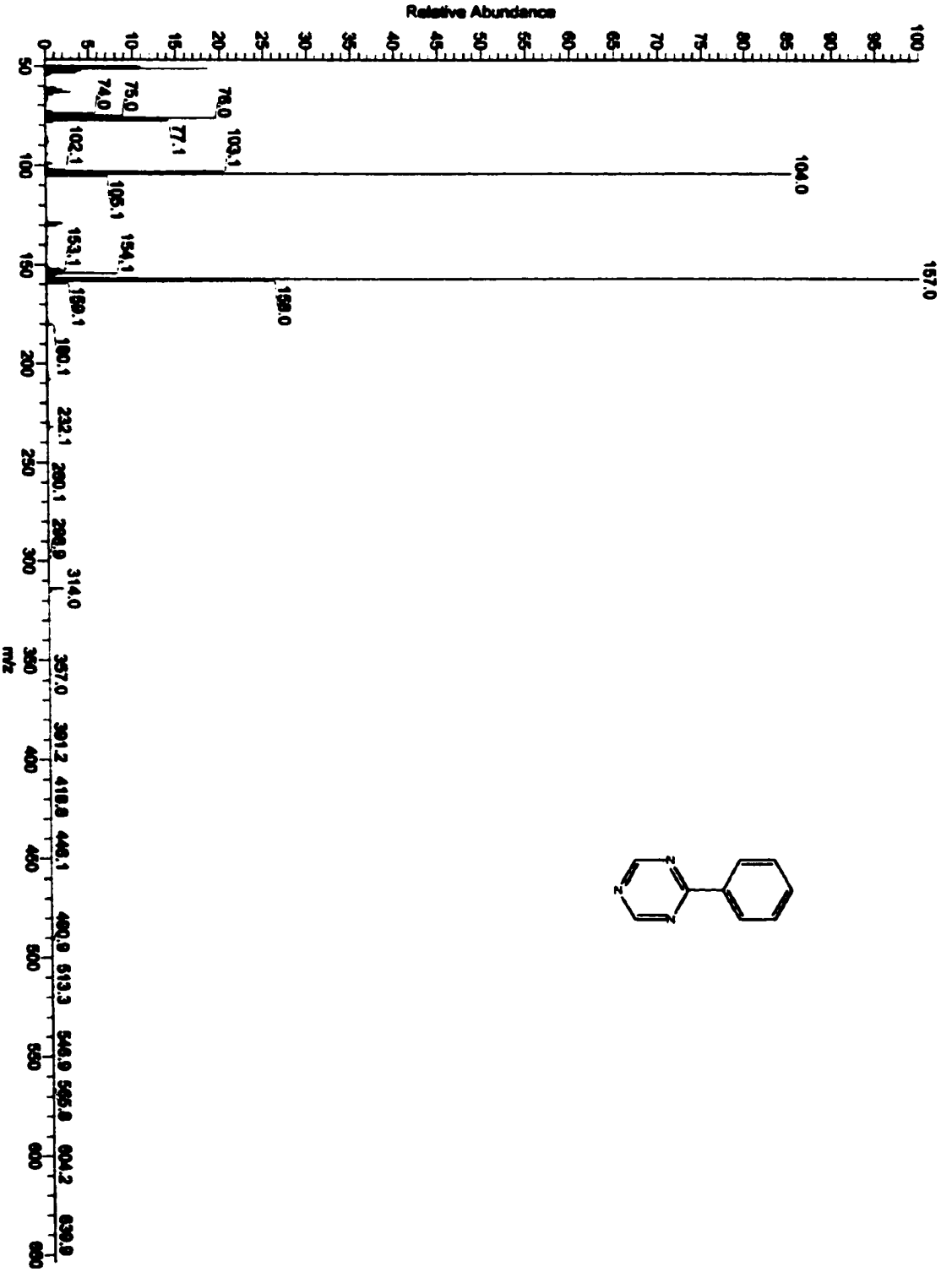


A.7. ^{1}H-NMR Spectrum of Perylene

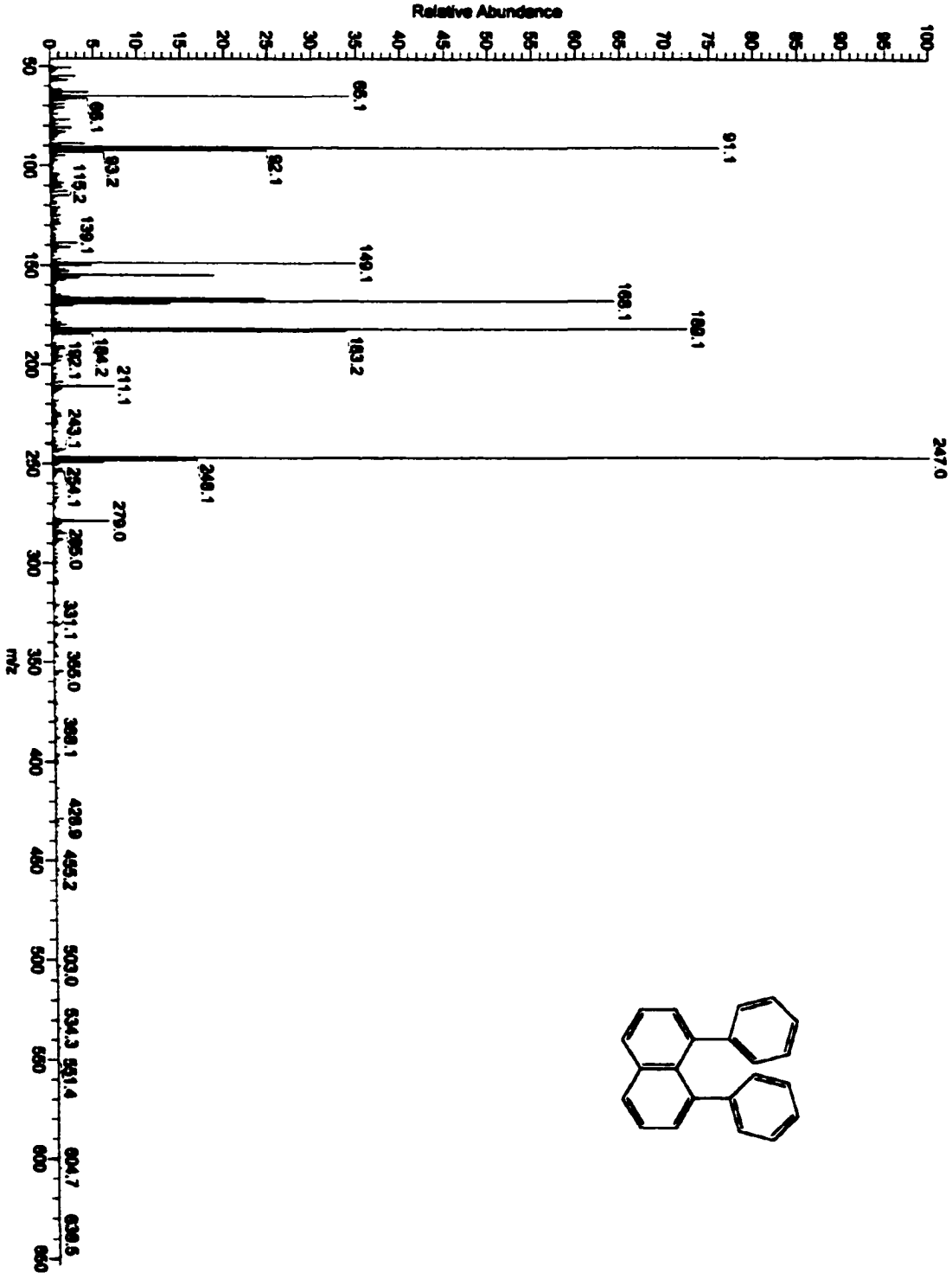




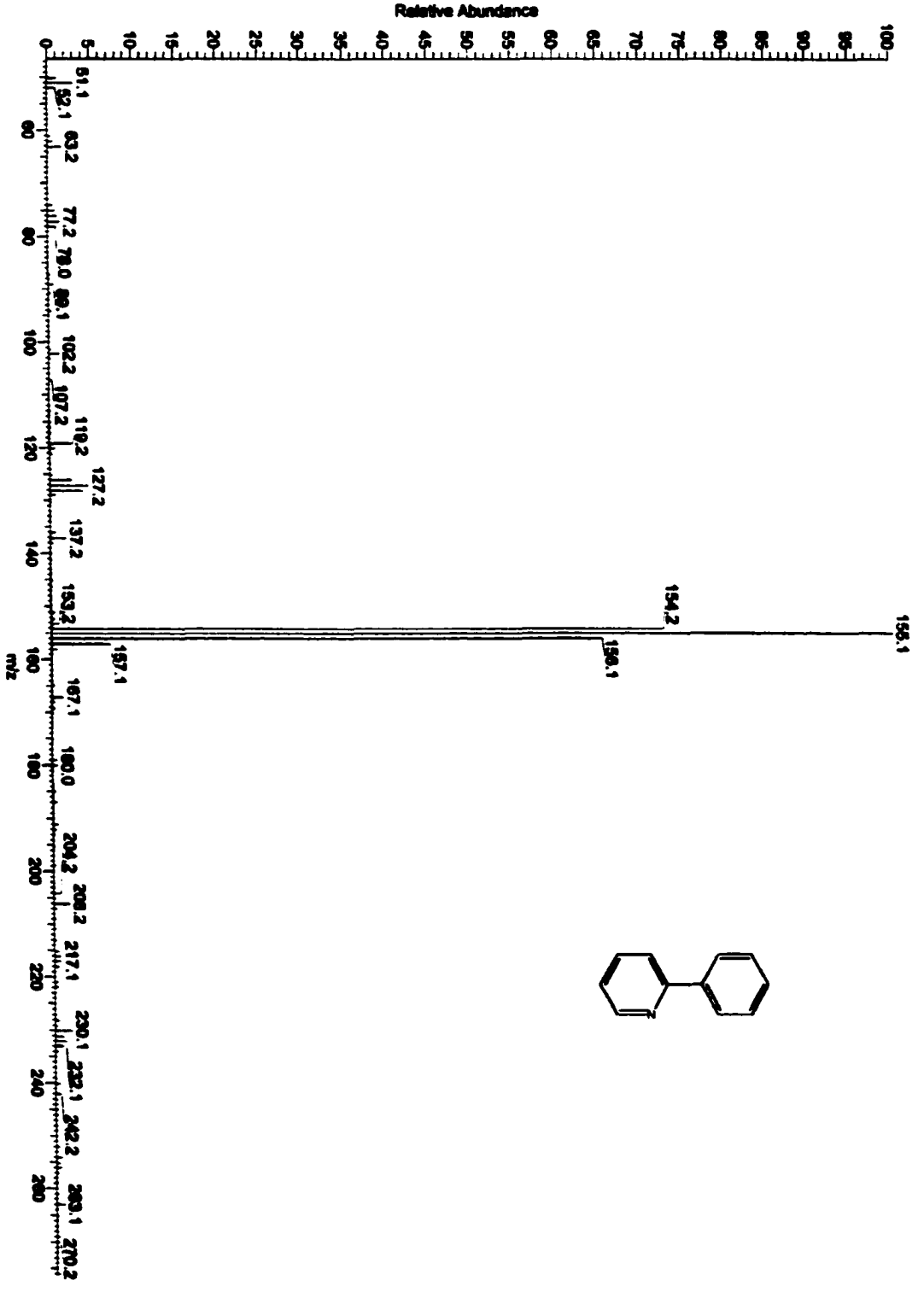
A.8. Mass Spectrum of 2-Phenyl-1,3,5-Triazene



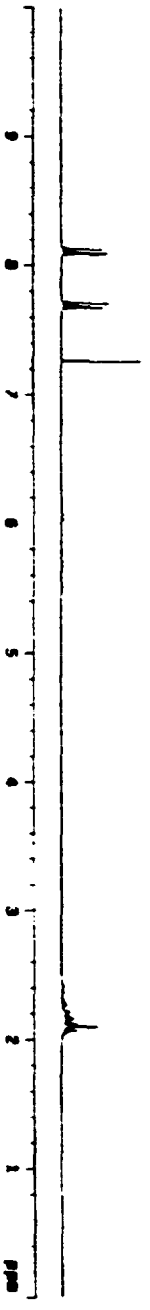
A.9. Mass Spectrum of 1,8-Diphenylnapthylene



A.10. Mass Spectrum of 2-Phenylpyridene

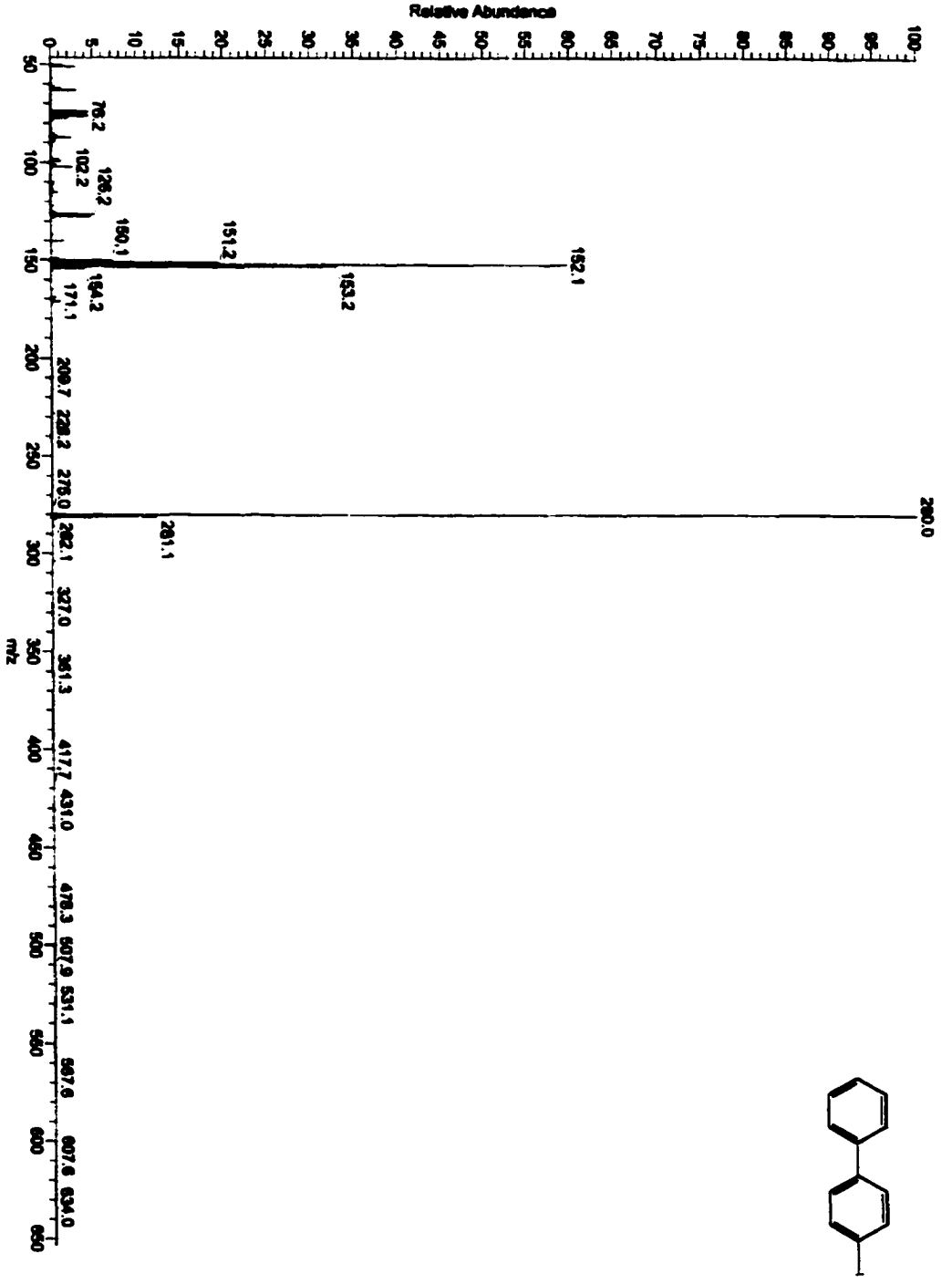


A.11. ^{1}H-NMR Spectrum of 4-Bromonitrobenzene

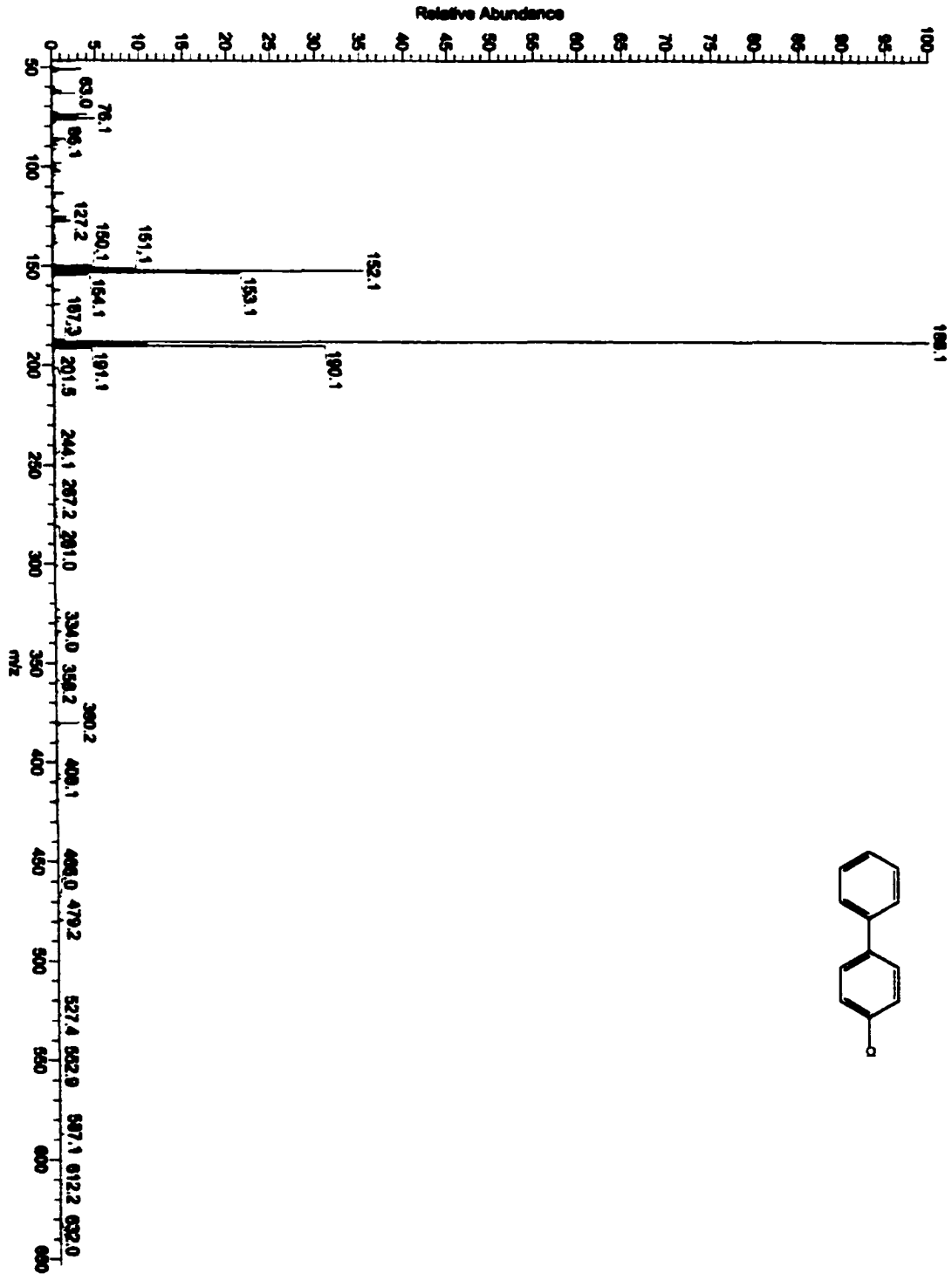




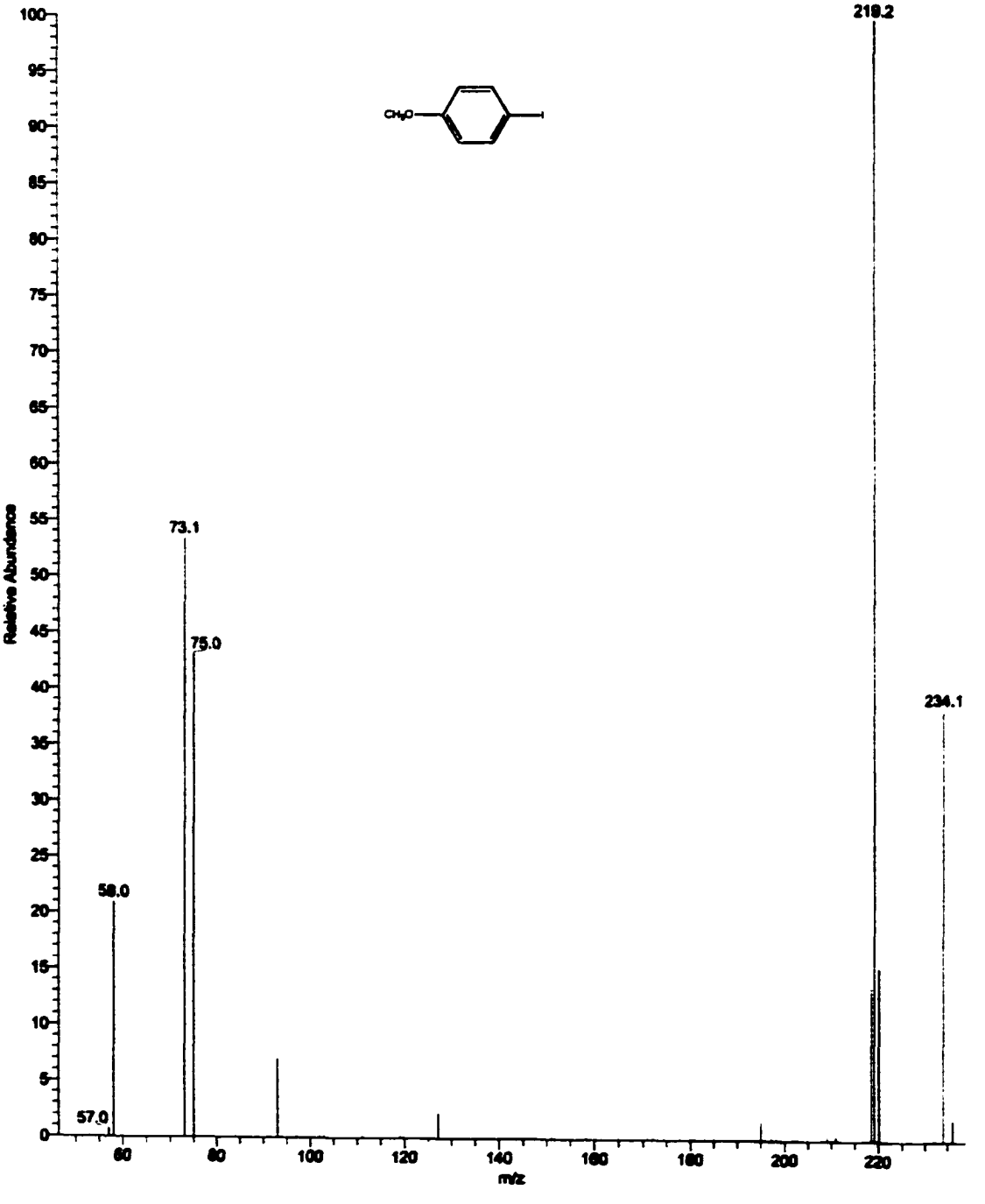
A.12. Mass Spectrum of 4-Iodobiphenyl



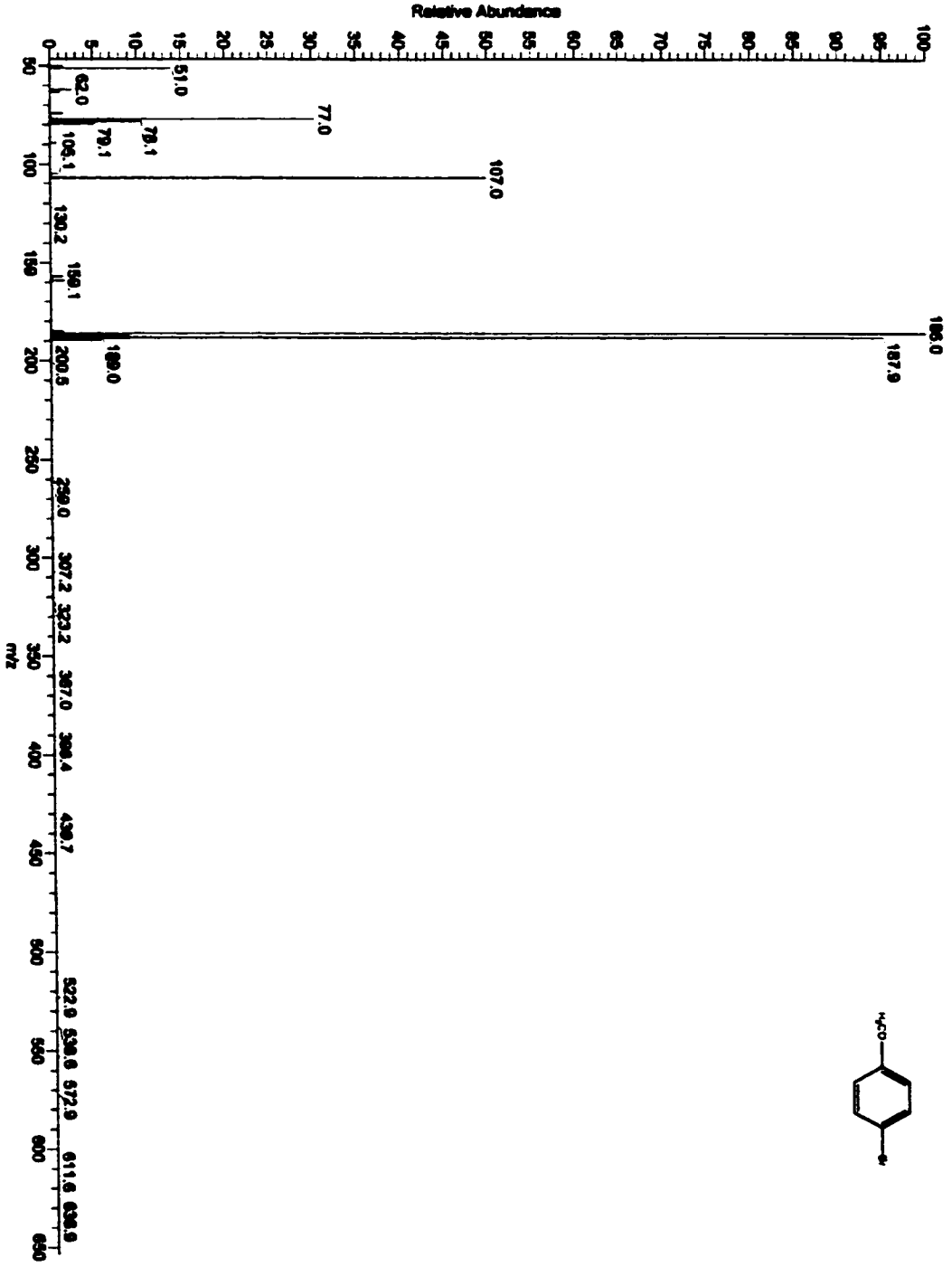
A.13. Mass Spectrum of 4-Chlorobiphenyl



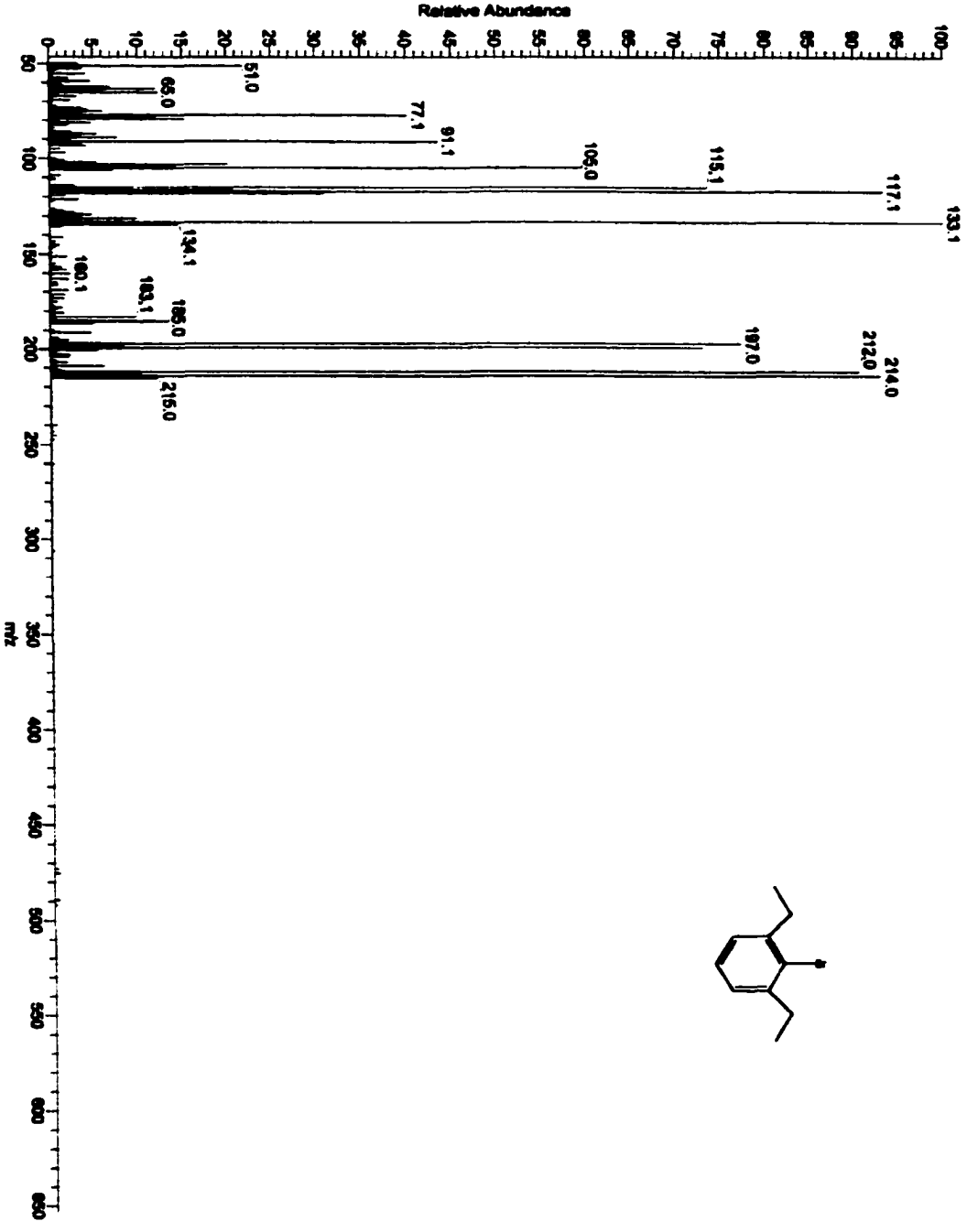
A.14. Mass Spectrum of *p*-Iodoanisole



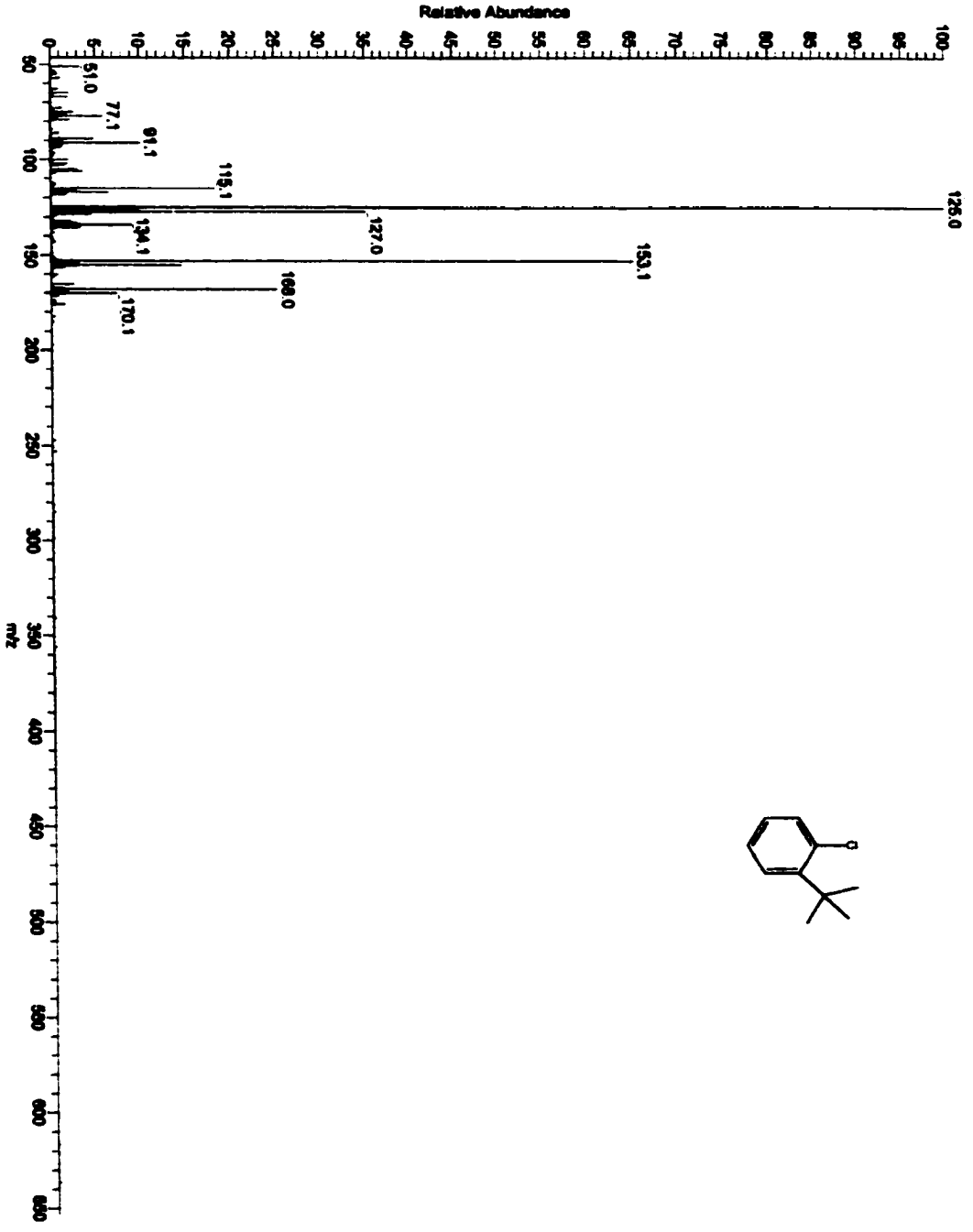
A.15. Mass Spectrum of 4-Bromoanisole



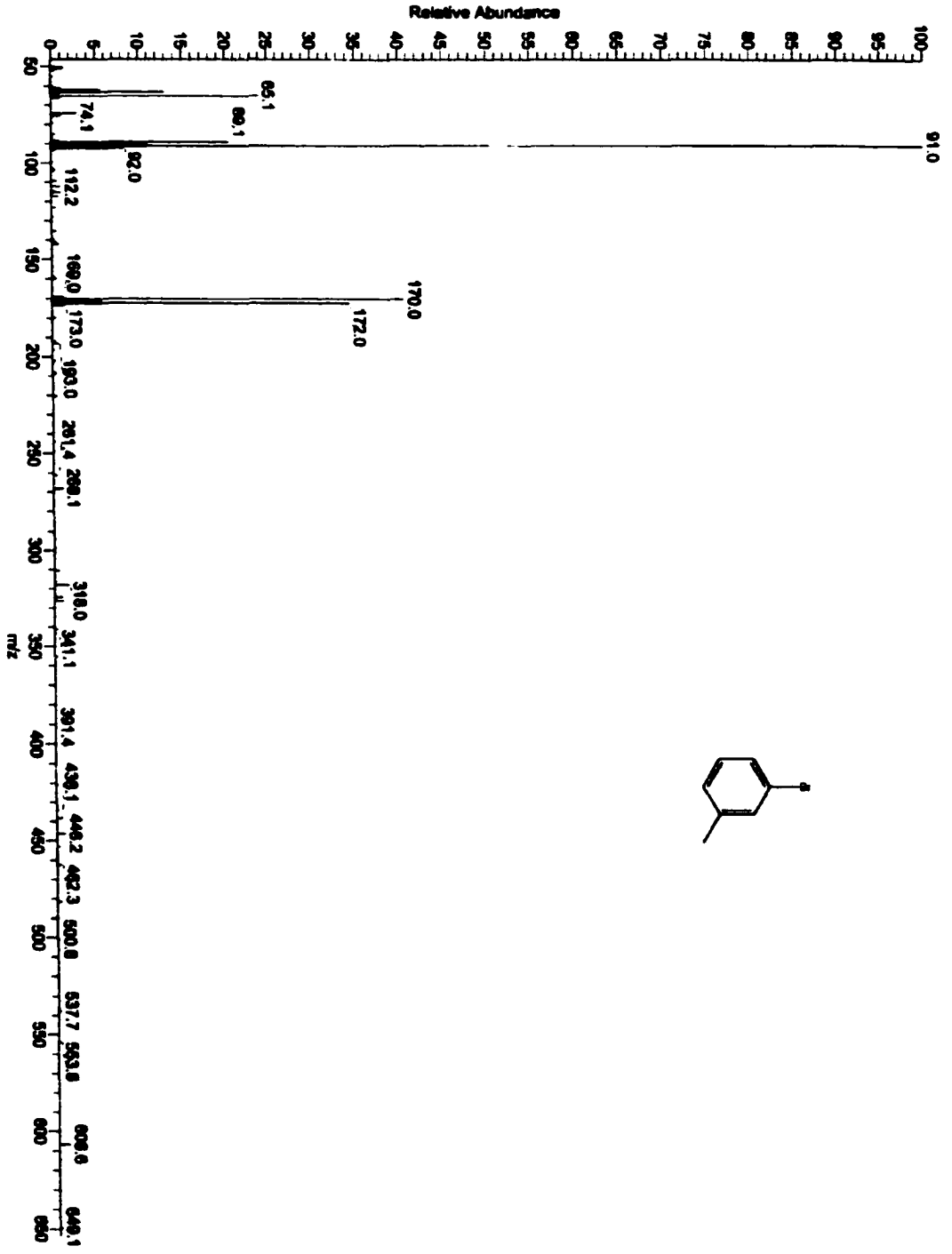
A.16. Mass Spectrum of 1-Bromo-2,6-diethylbenzene



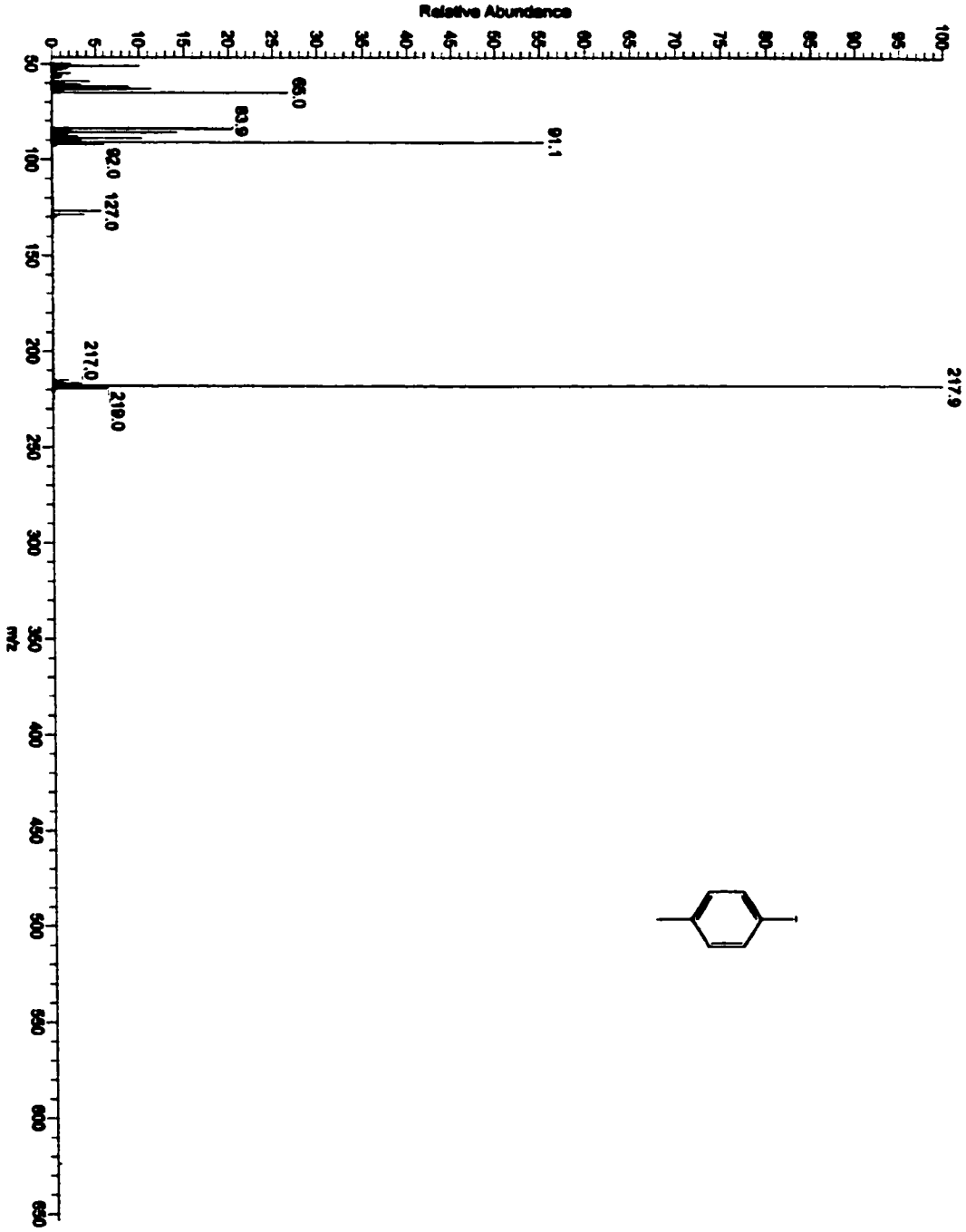
A.17. Mass Spectrum of 1-*tert*-Butyl-2-chlorobenzene



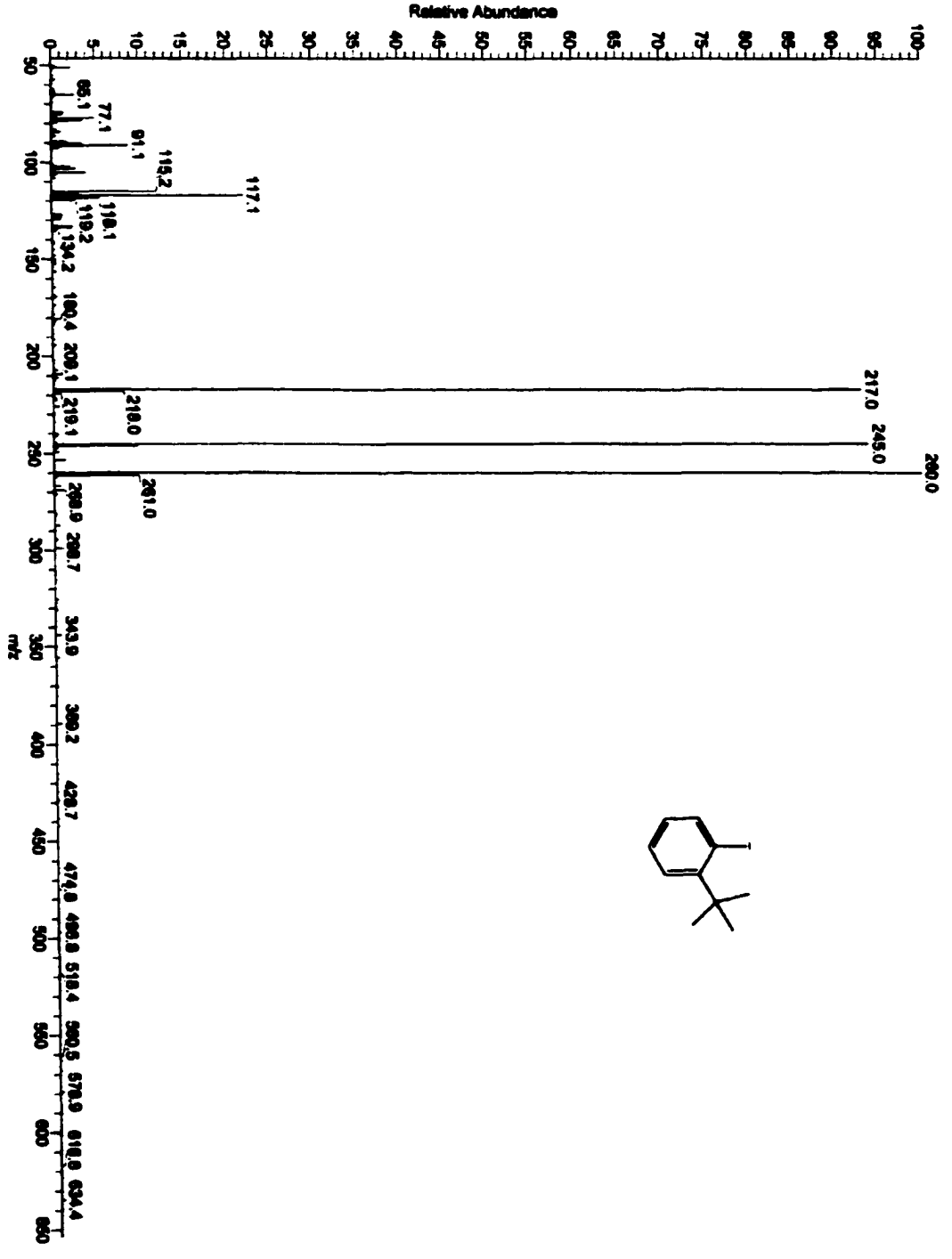
A.18. Mass Spectrum of *m*-Bromotoluene



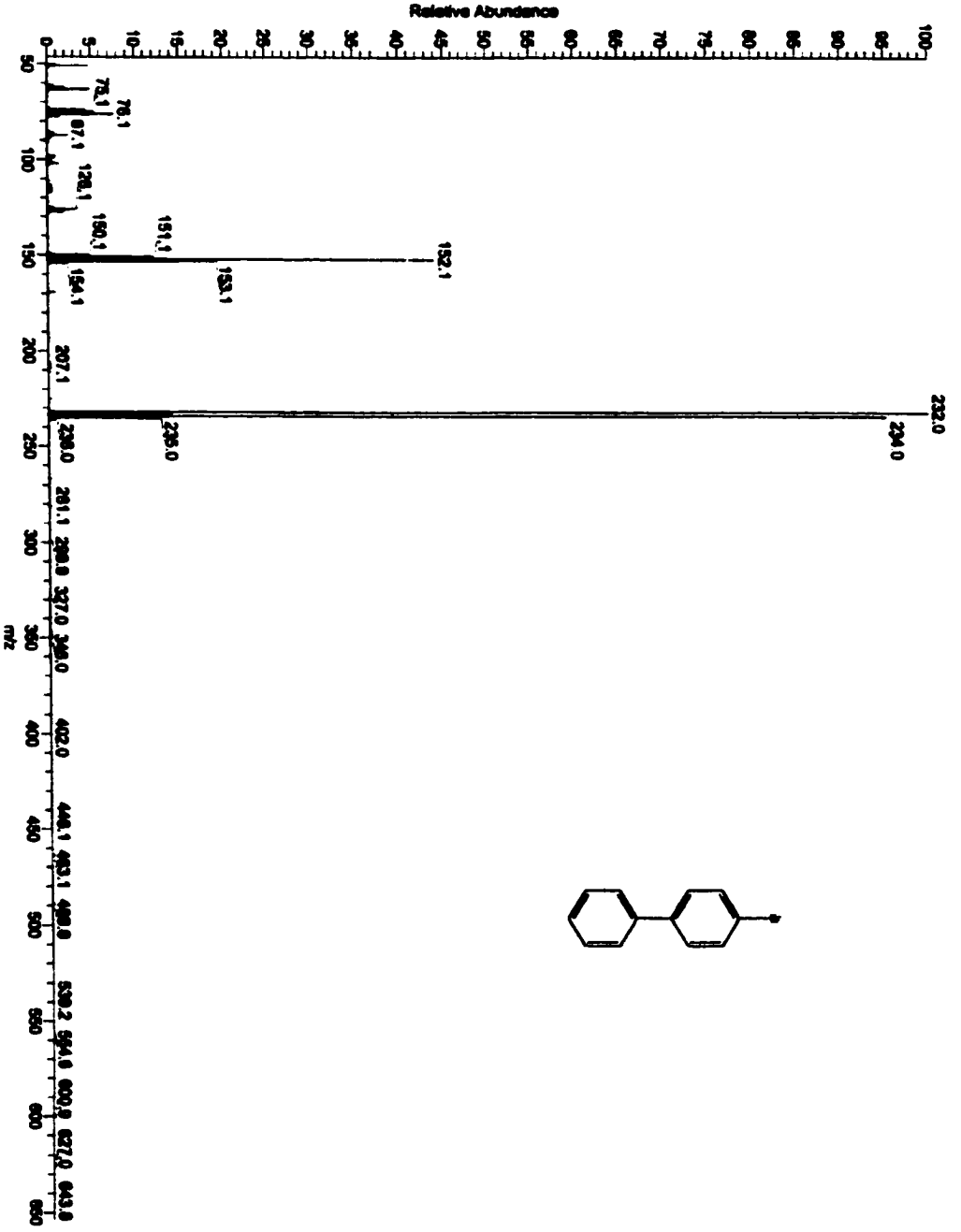
A.19. Mass Spectrum of *p*-Iodotoluene



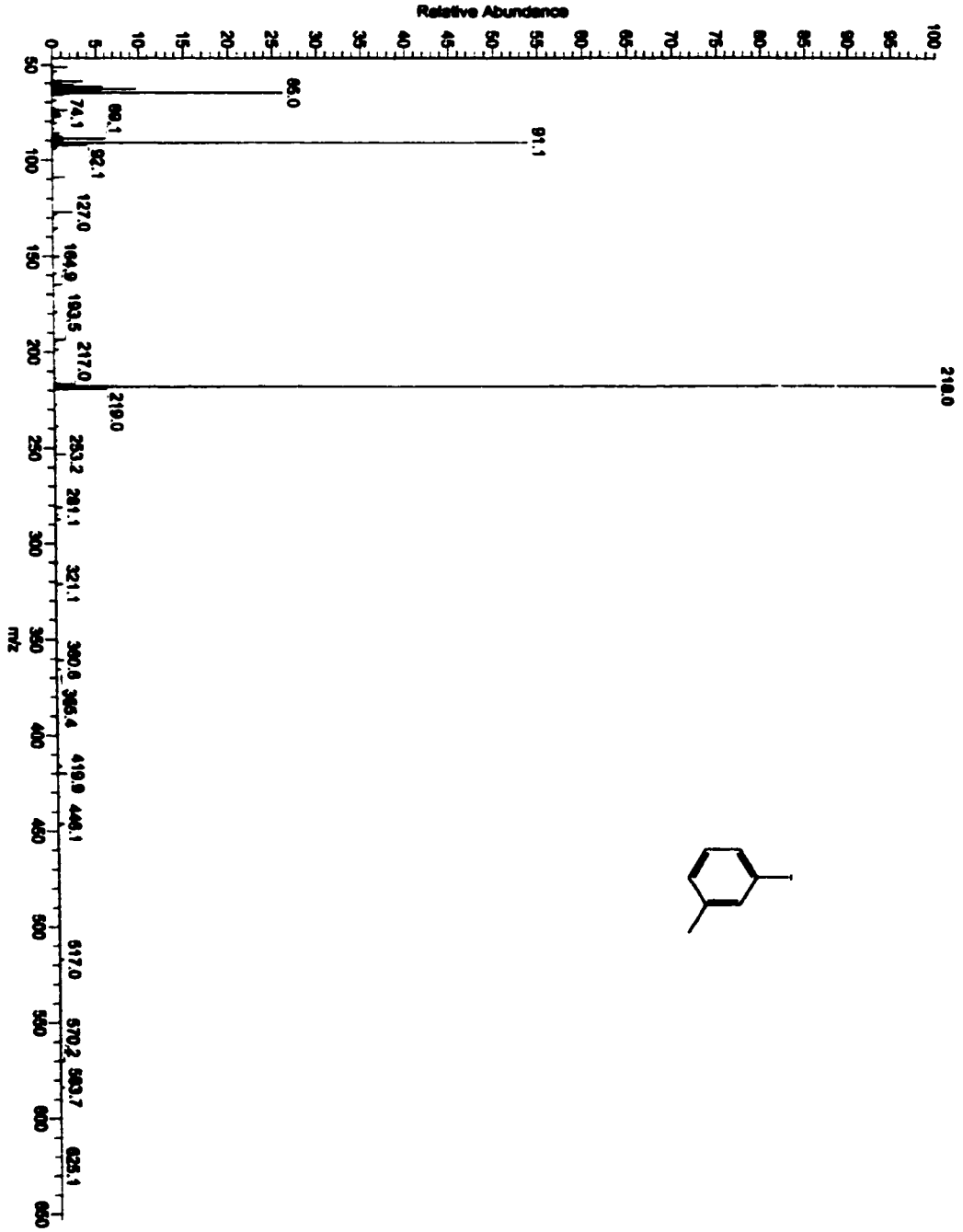
A.20. Mass Spectrum of 1-*tert*-Butyl-2-iodobenzene



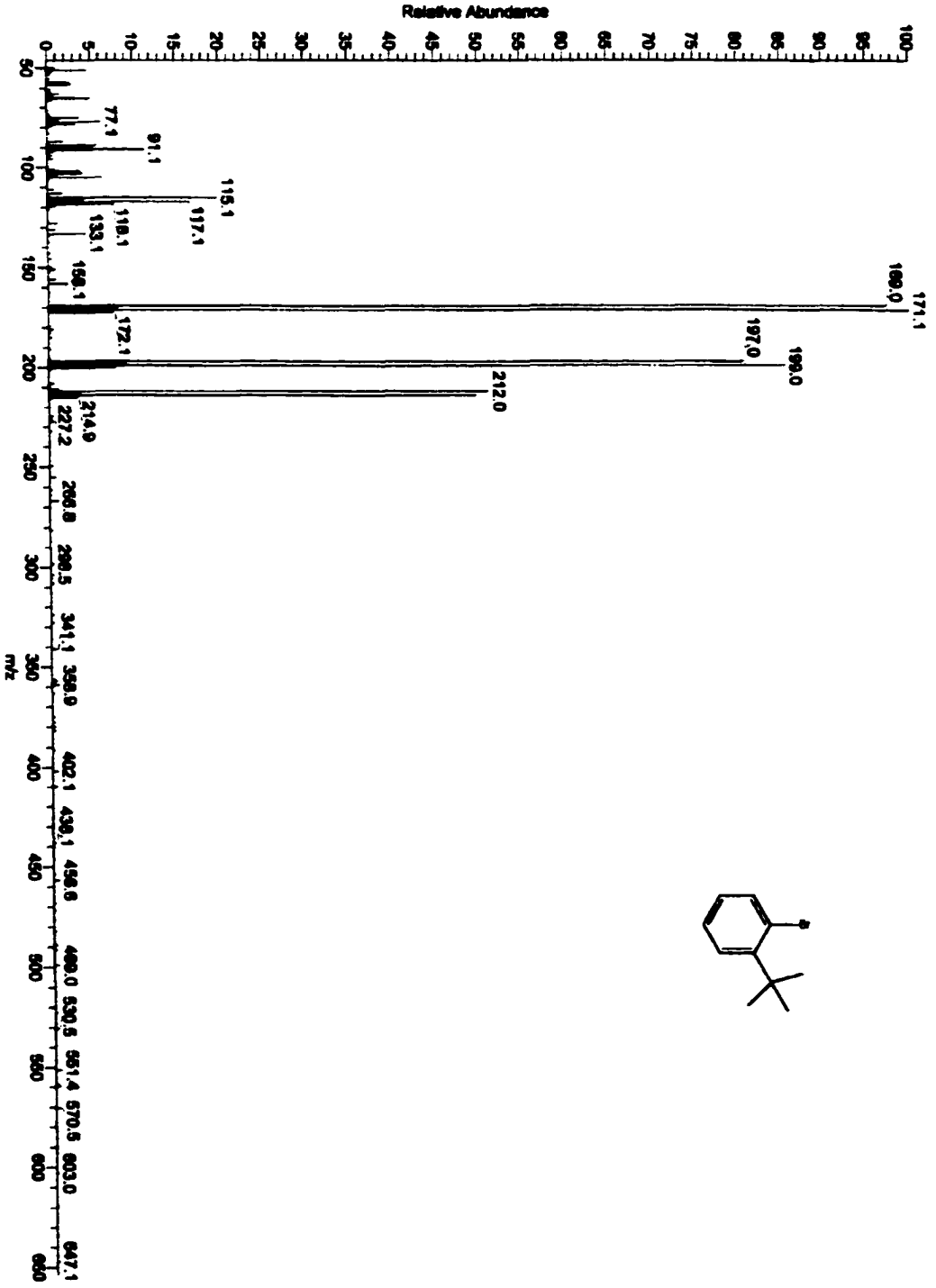
A.21. Mass Spectrum of 4-Bromobiphenyl



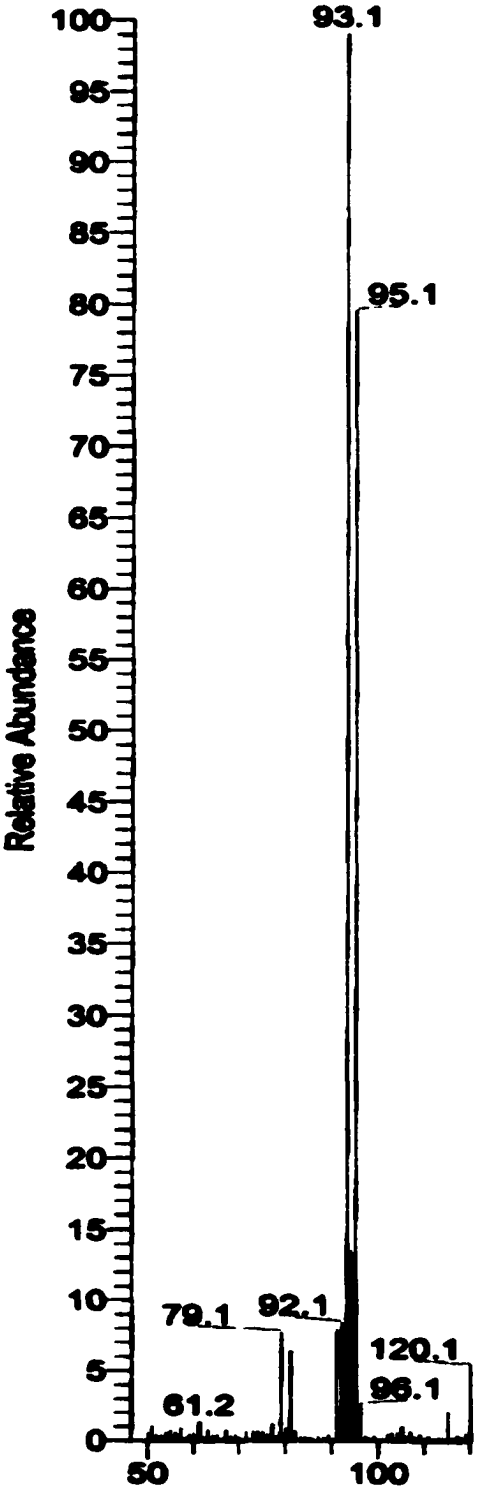
A.22. Mass Spectrum of *m*-Iodotoluene



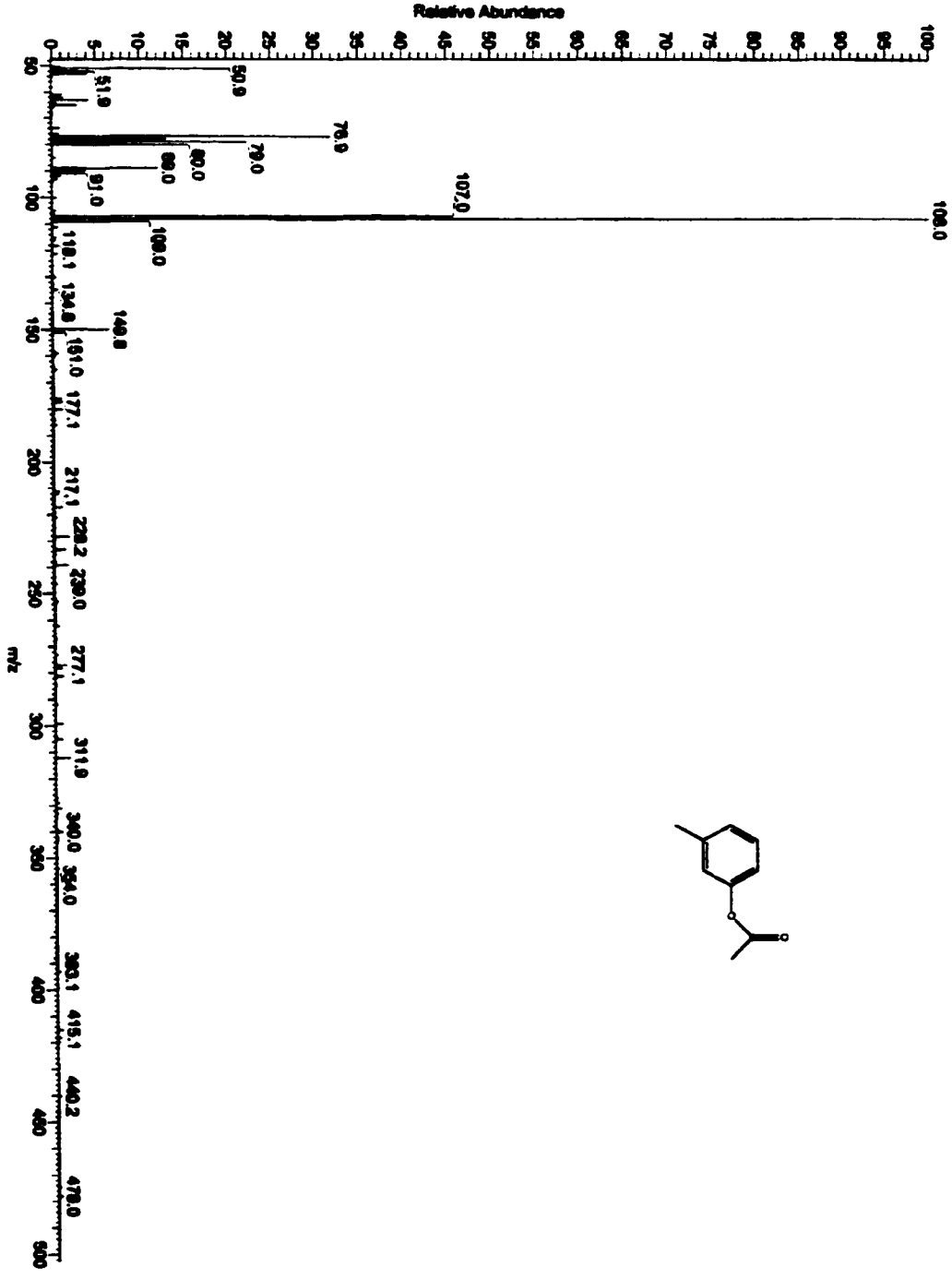
A.23. Mass Spectrum of 1-*tert*-Butyl-2bromobenzene



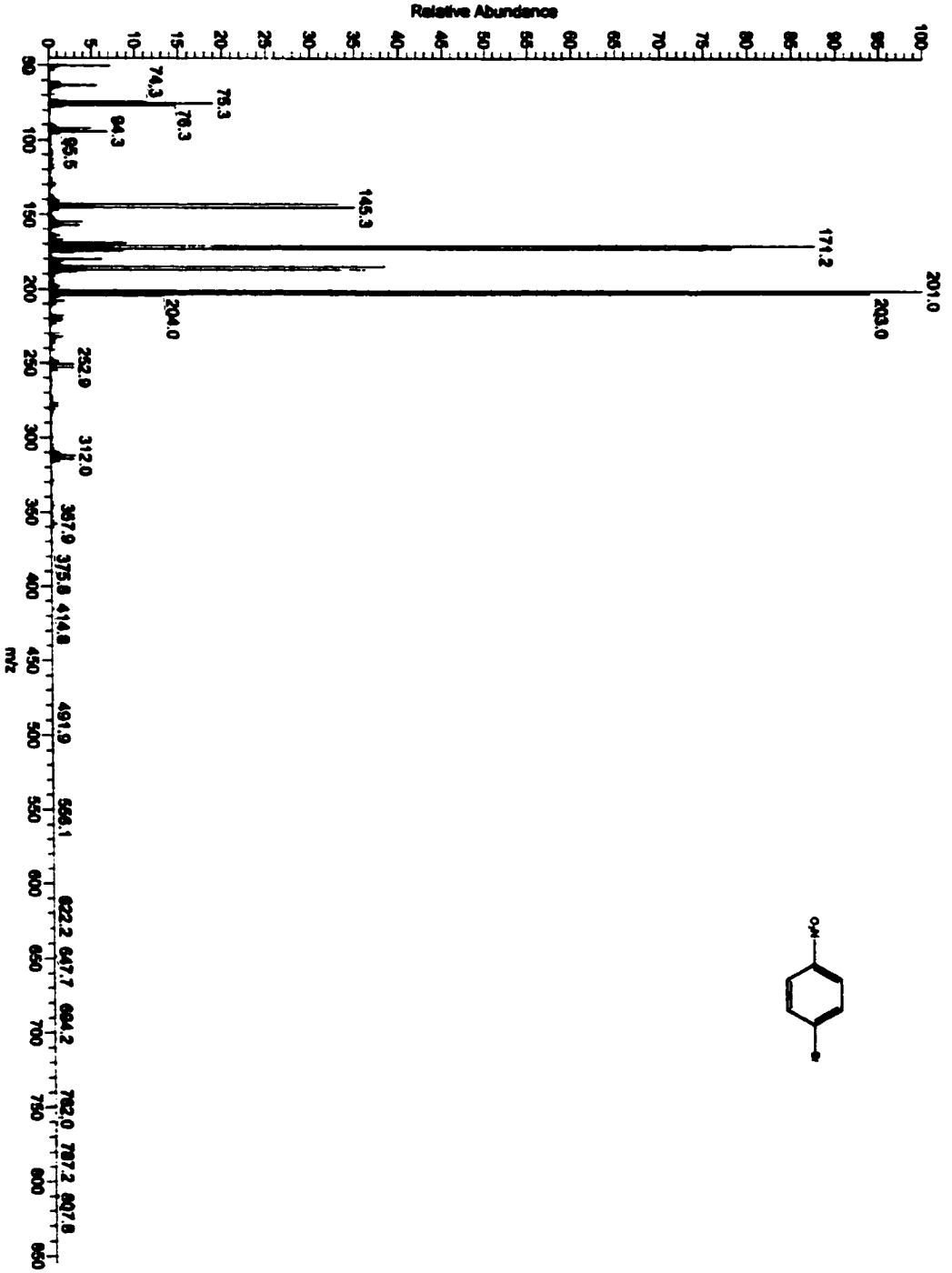
A.24. Mass Spectral Evidence for Bromomethane



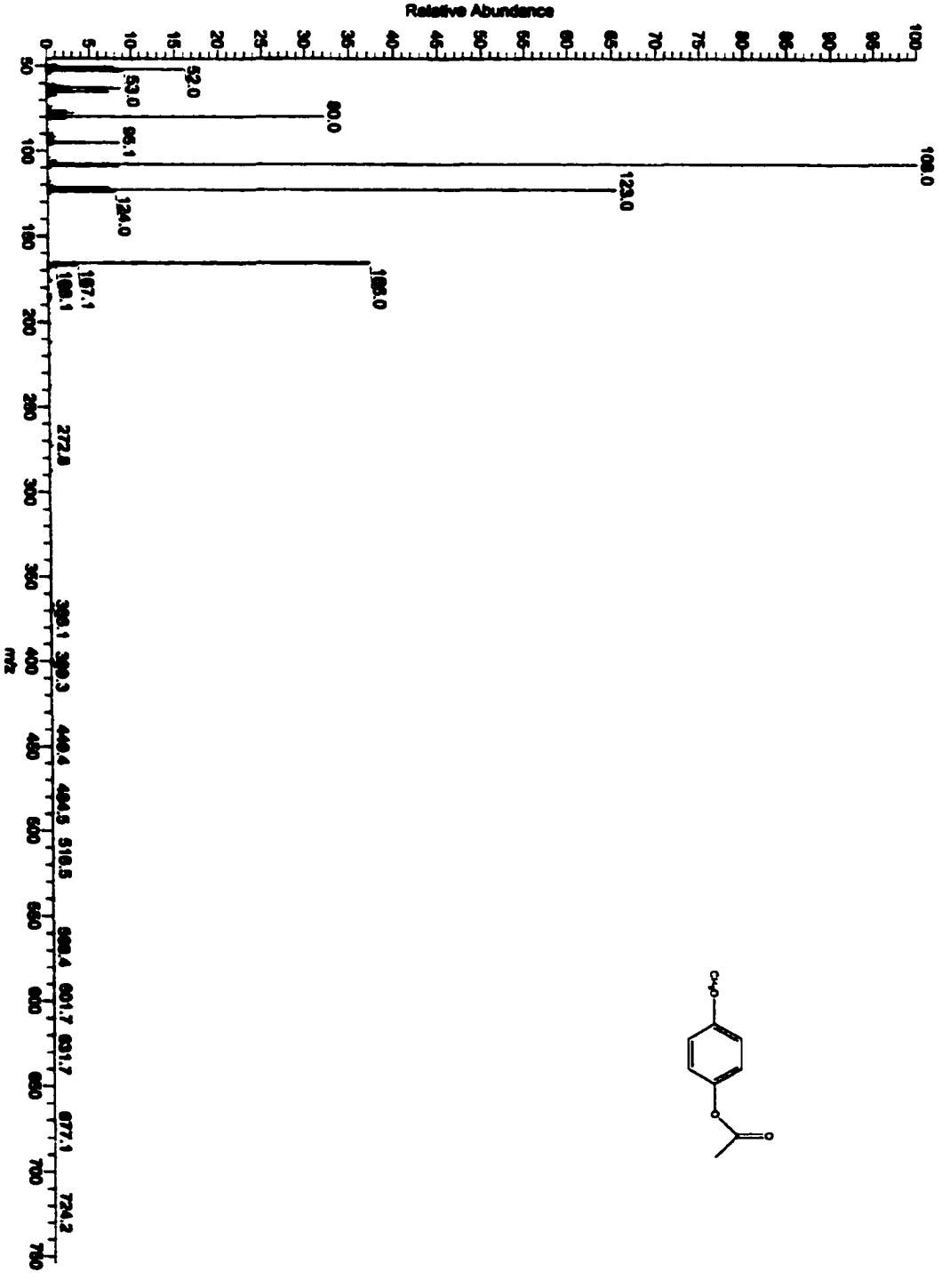
A.25. Mass Spectrum of *m*-Tolyl Acetate



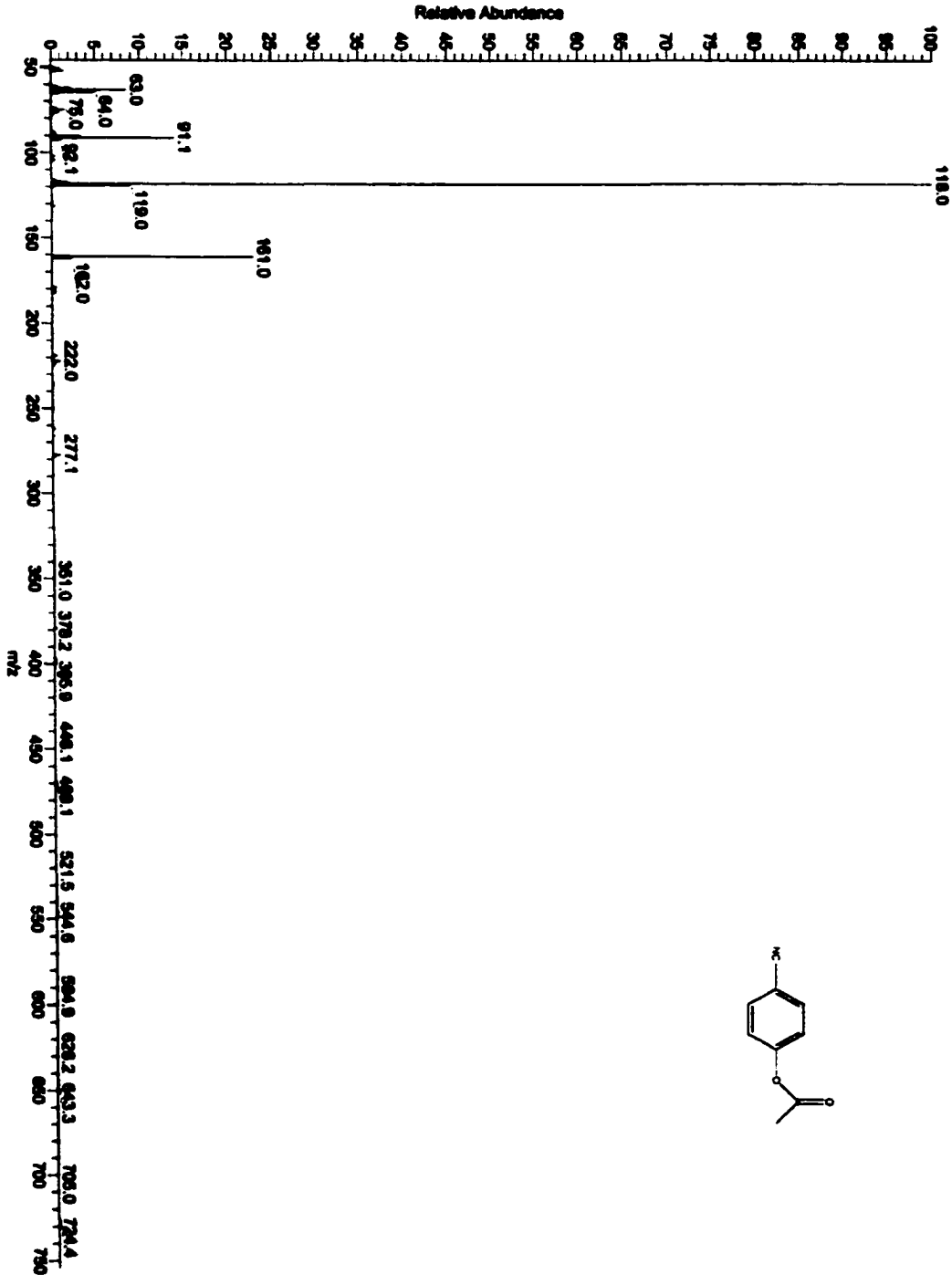
A.26. Mass Spectrum of 4-Bromonitrobenzene



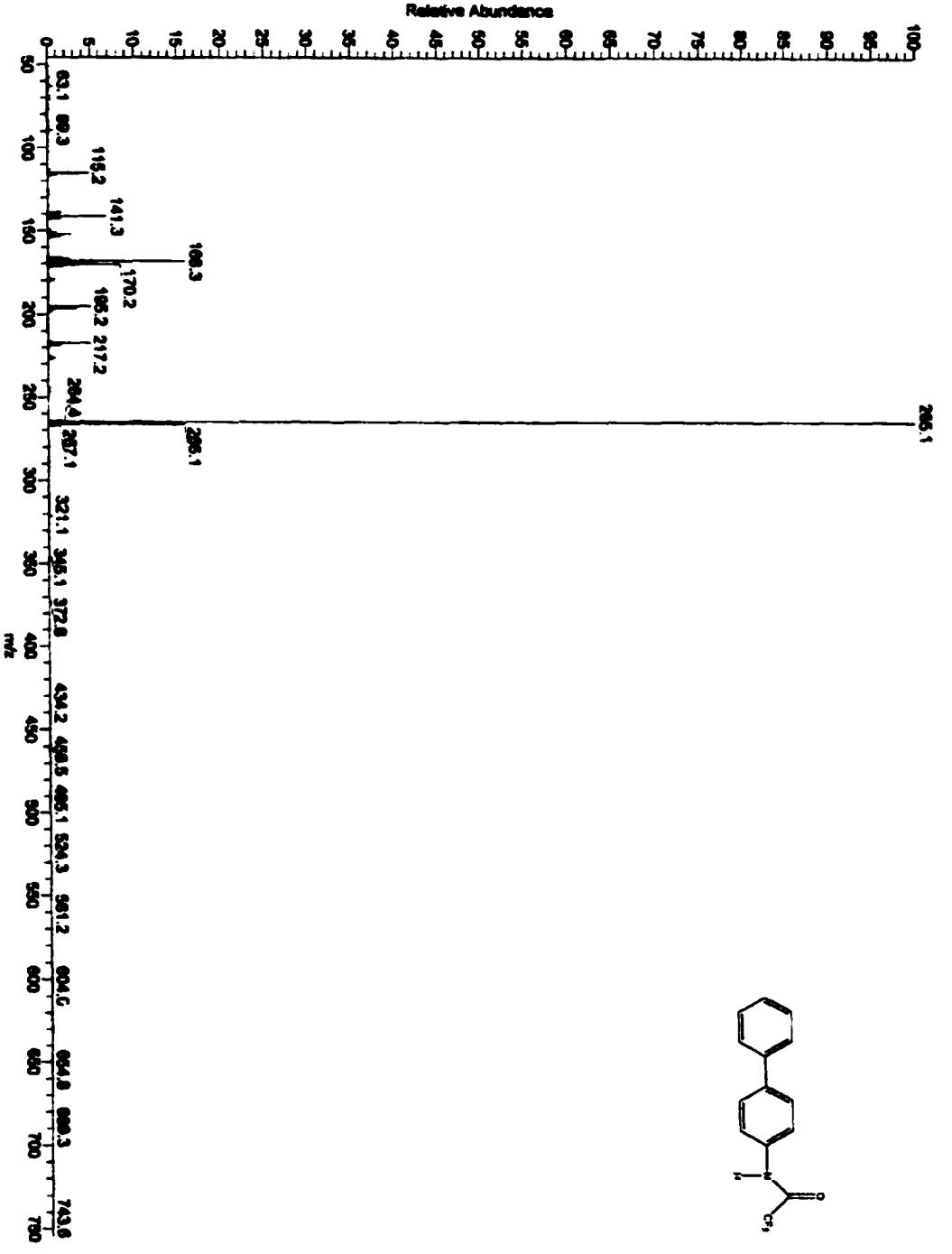
A.27. Mass Spectrum of 4-Methoxyphenyl Acetate



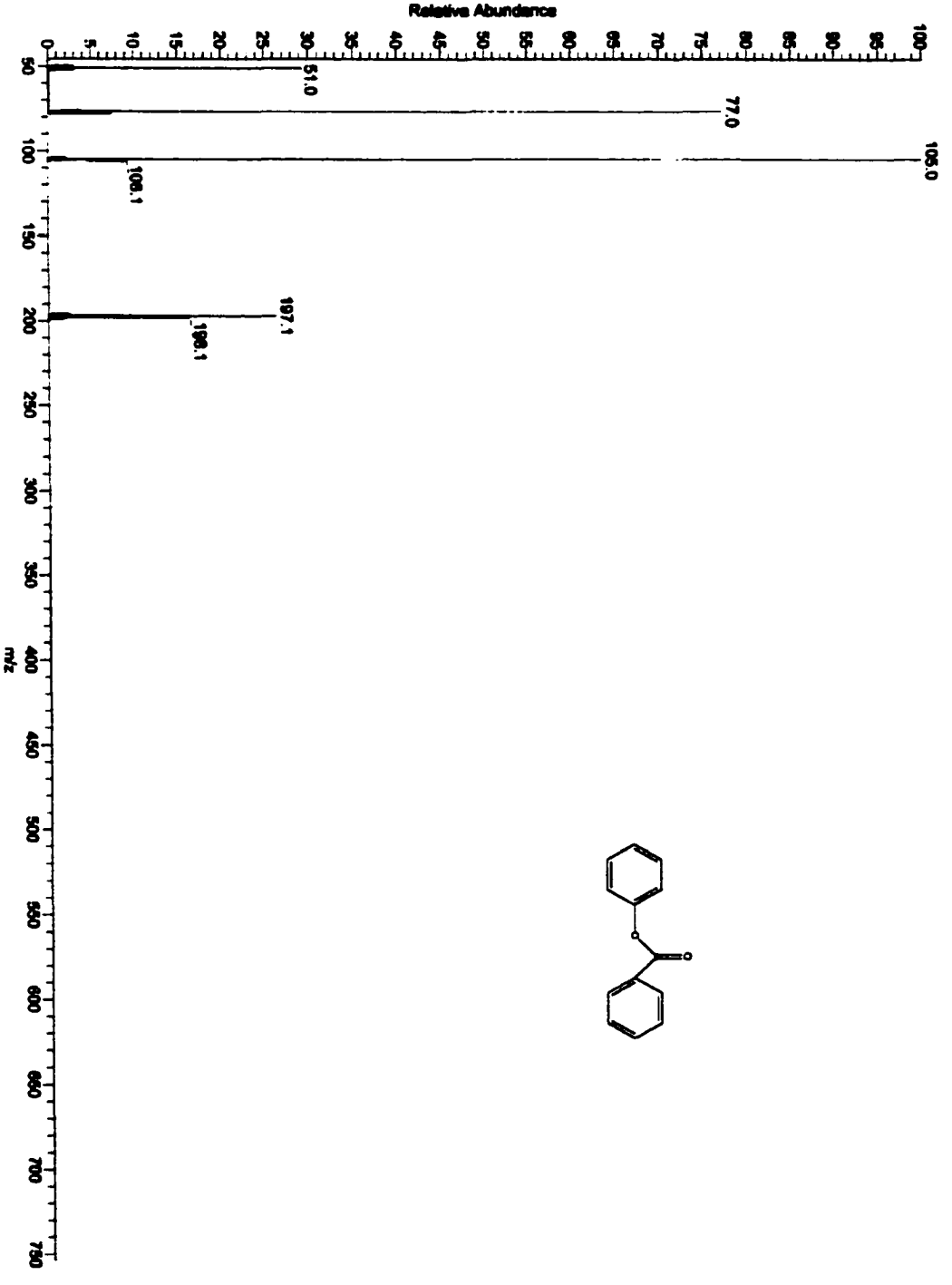
A.28. Mass Spectrum of *p*-Acetoxybenzonitrile



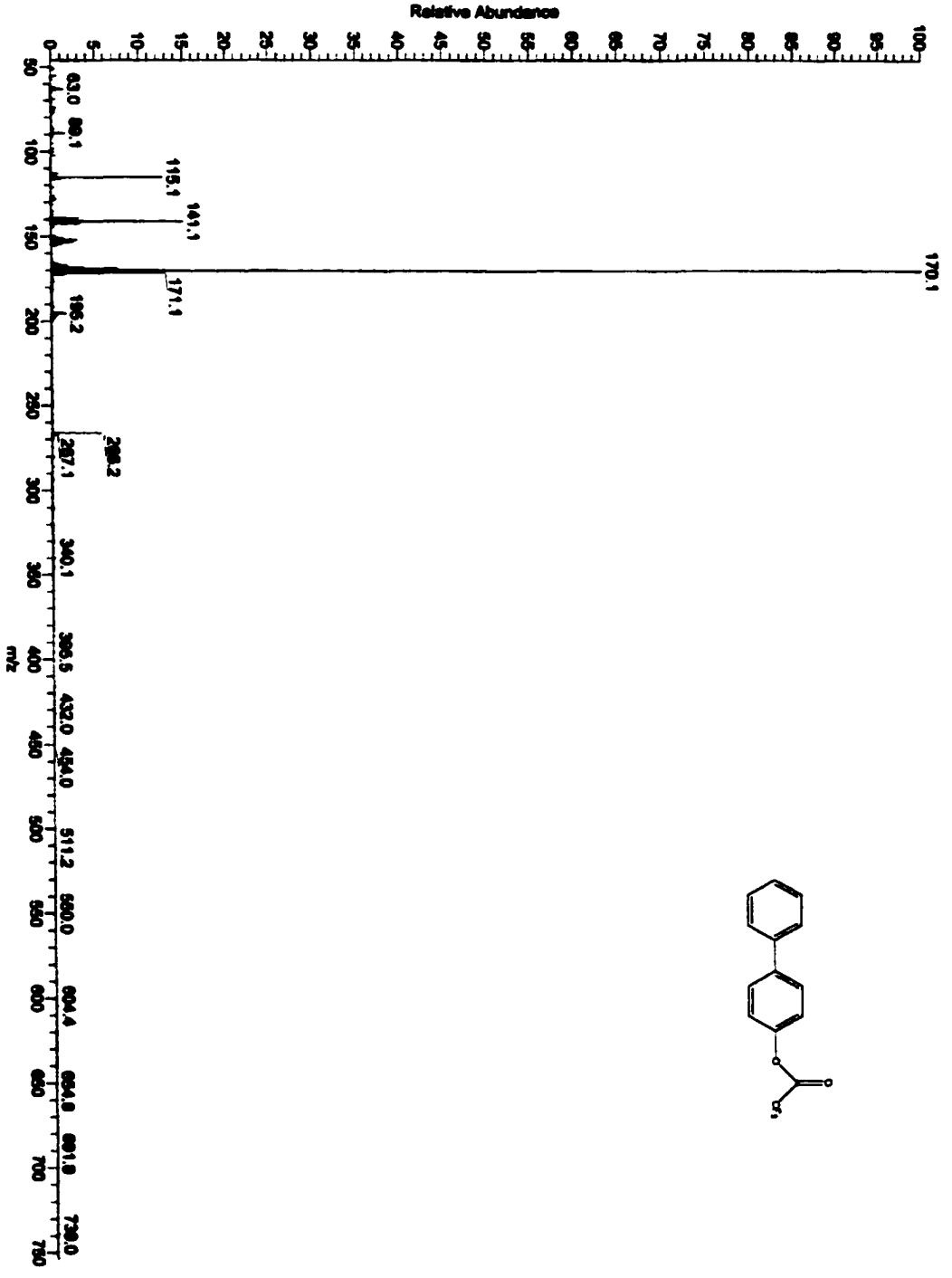
A.29. Mass Spectrum of α,α,α-Trifluoroacetanilide



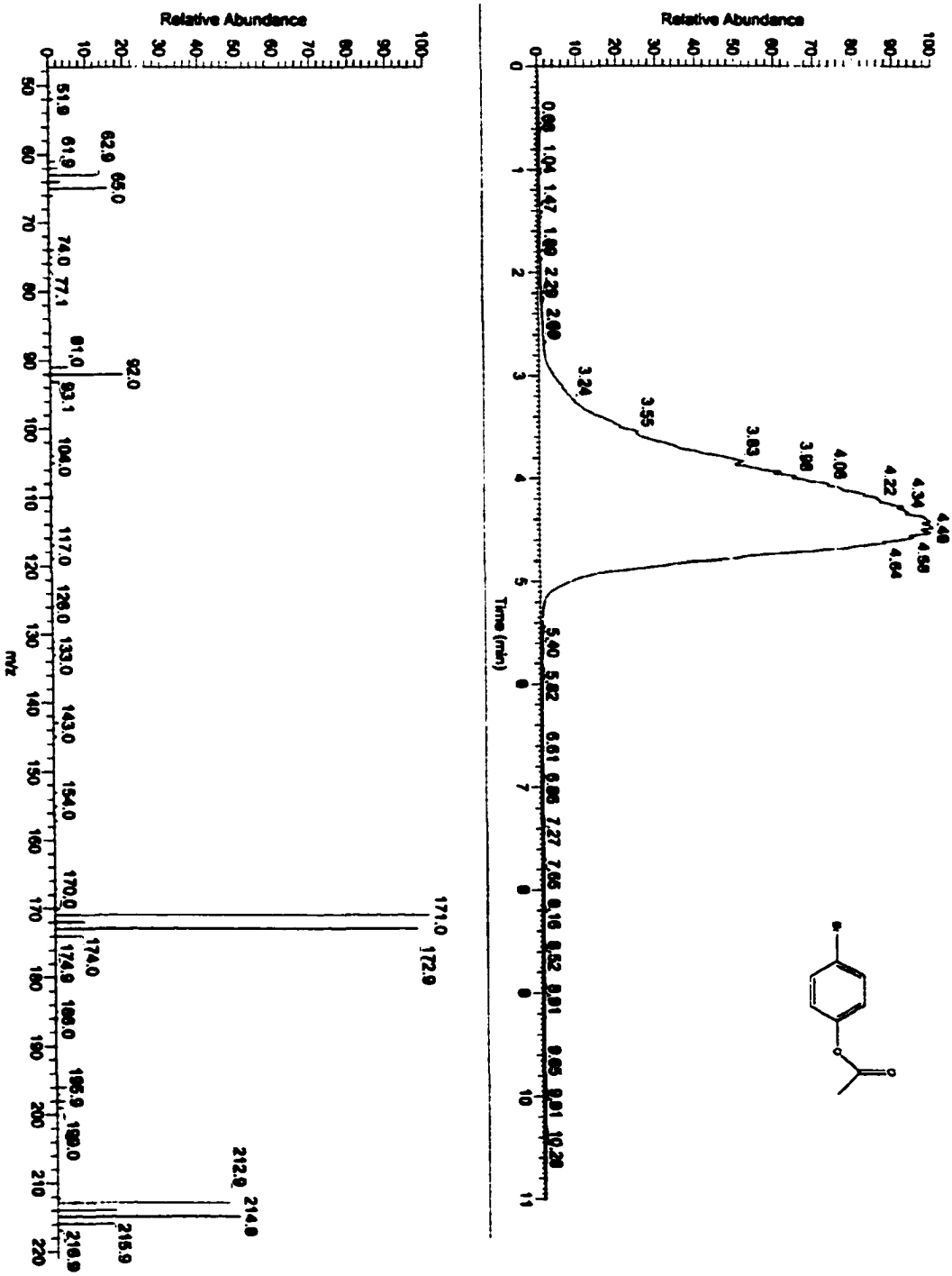
A.30. Mass Spectrum of Phenyl Benzoate



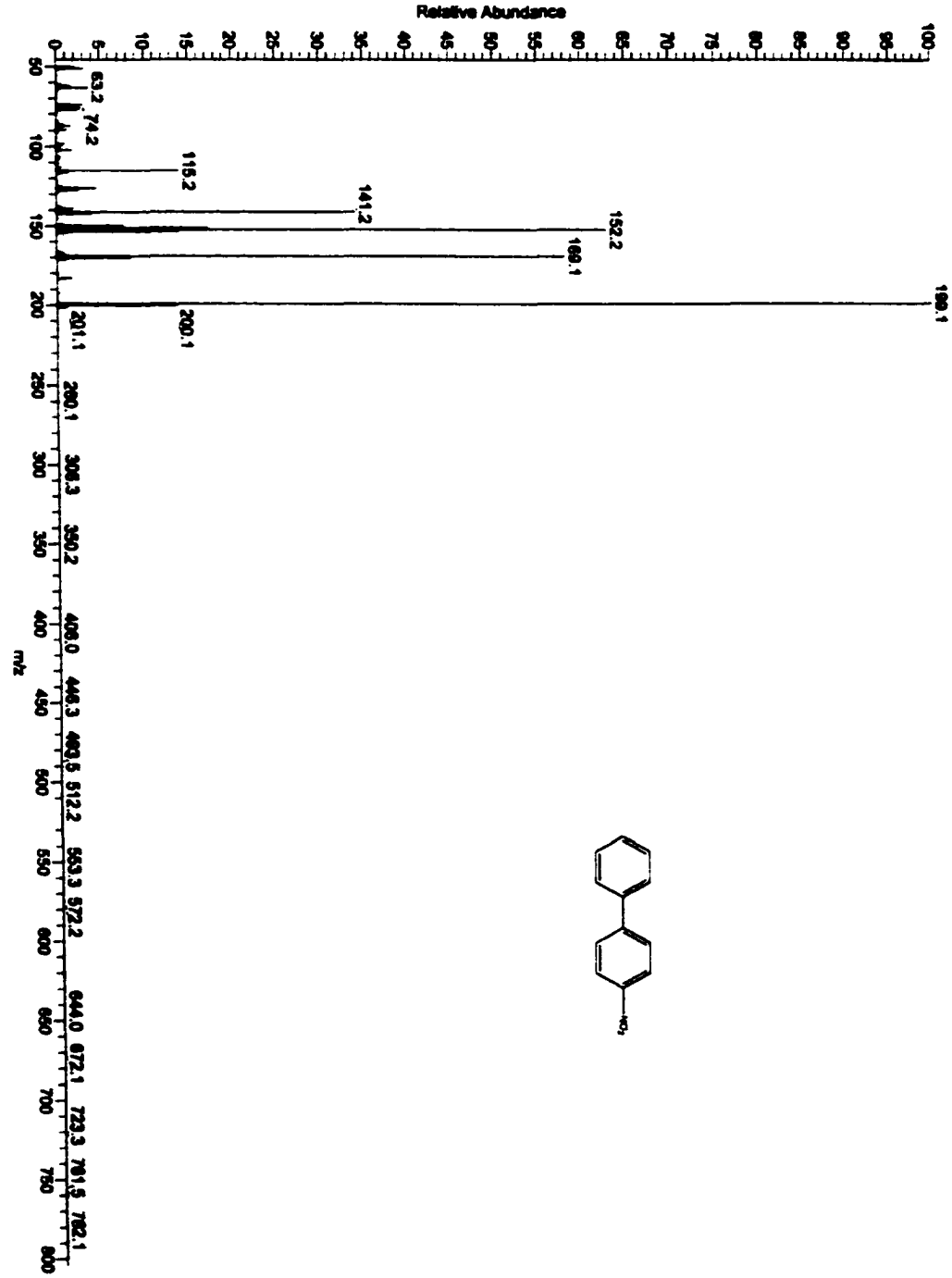
A.31. Mass Spectrum of 4-Biphenylyl Trifluoroacetate



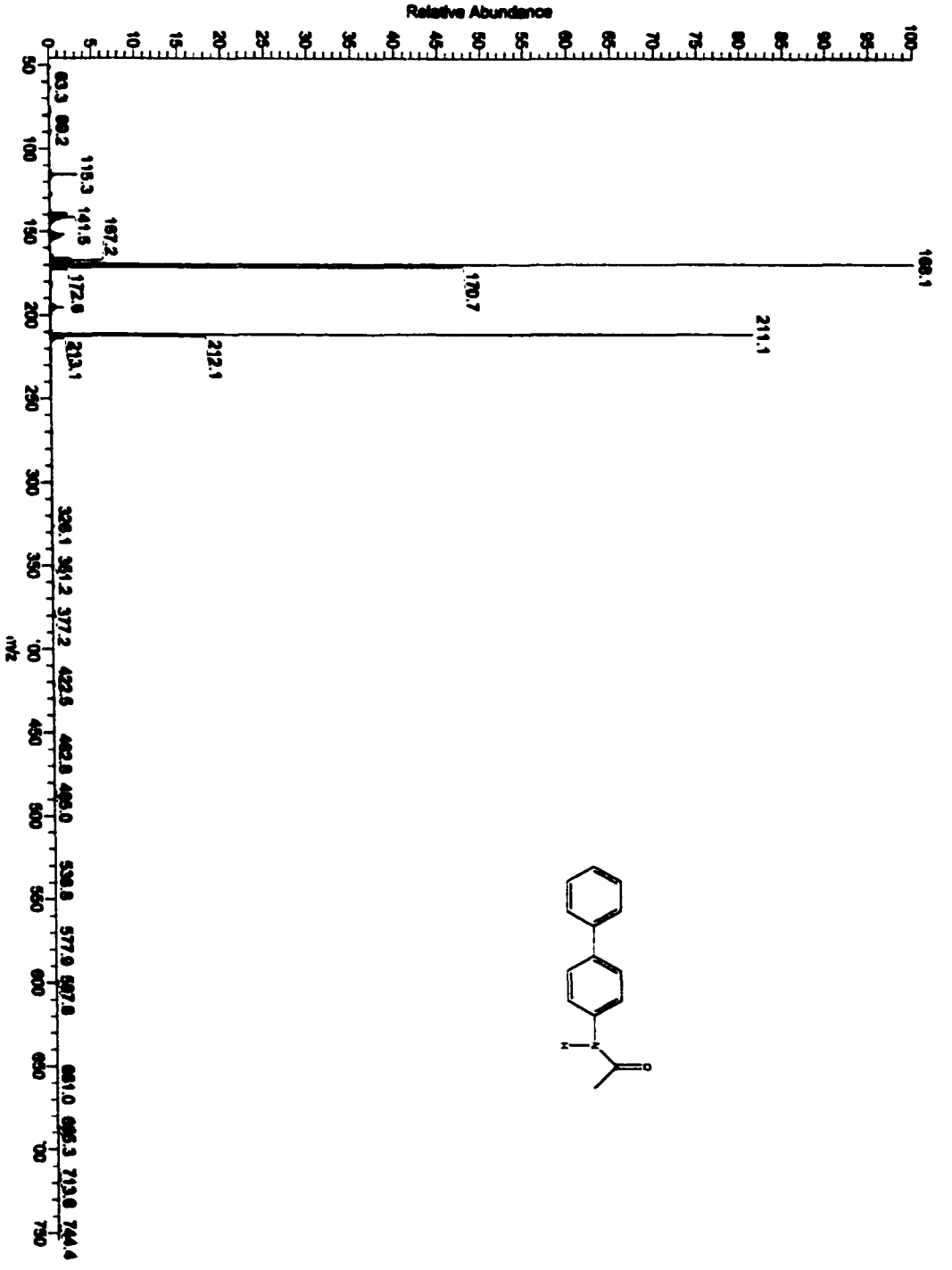
A.32. Mass Spectrum of 4-Bromophenylacetate



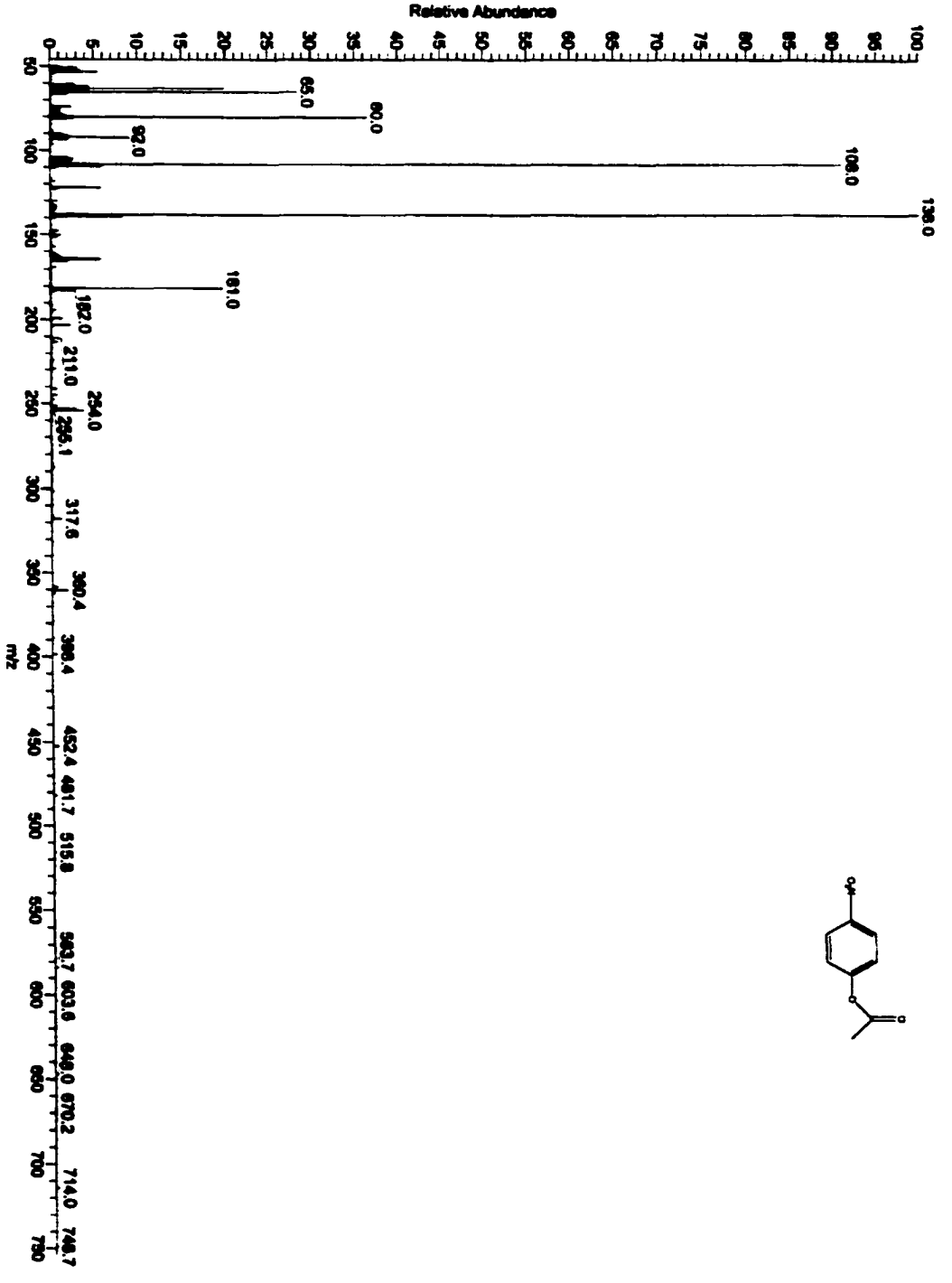
A.33. Mass Spectrum of 4-Nitrobiphenyl



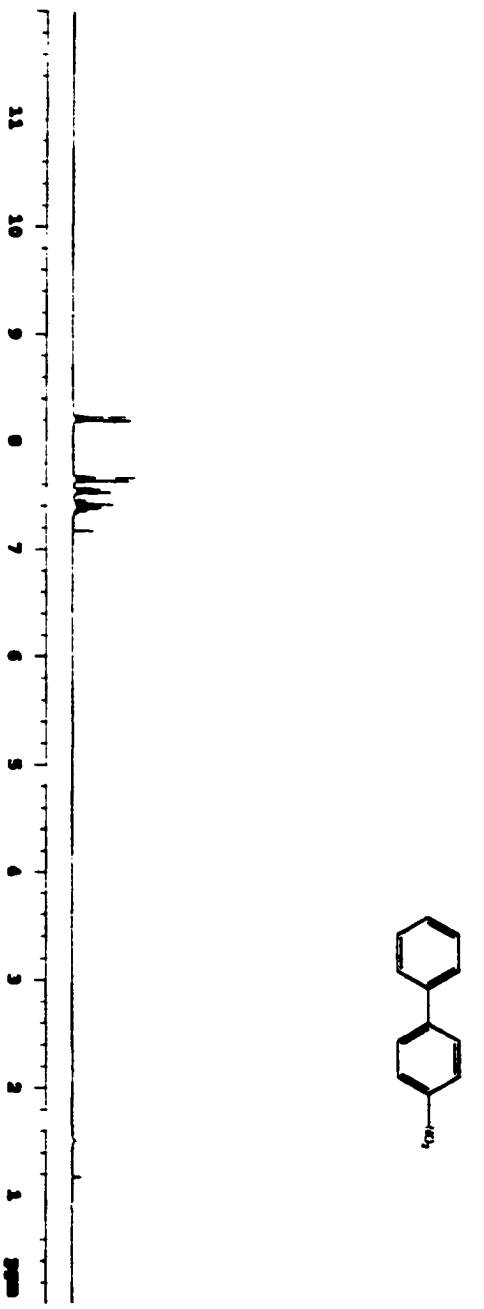
A.34. Mass Spectrum of N-(4-Biphenylyl)acetamide



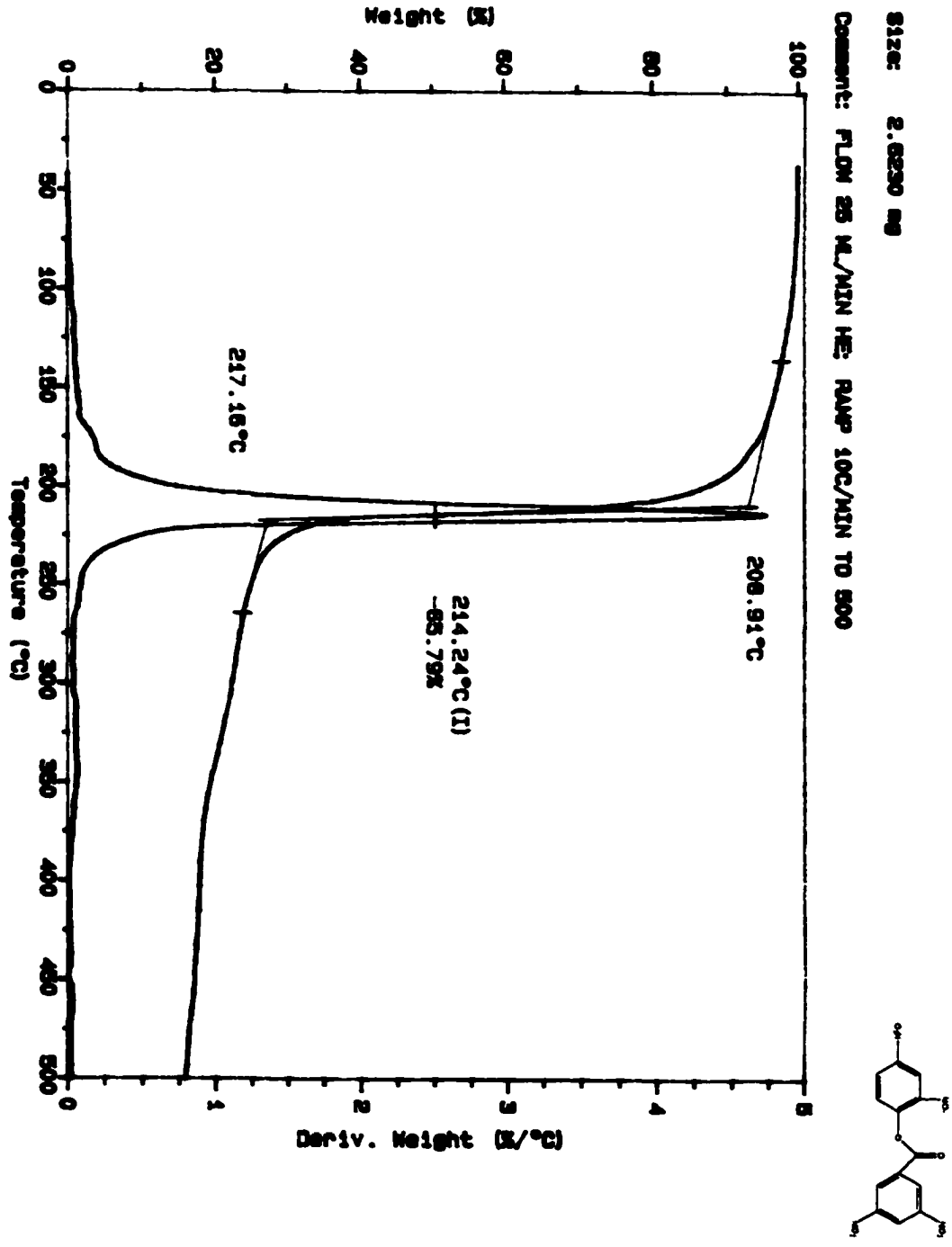
A.35. Mass Spectrum of 4-Nitrophenyl Acetate



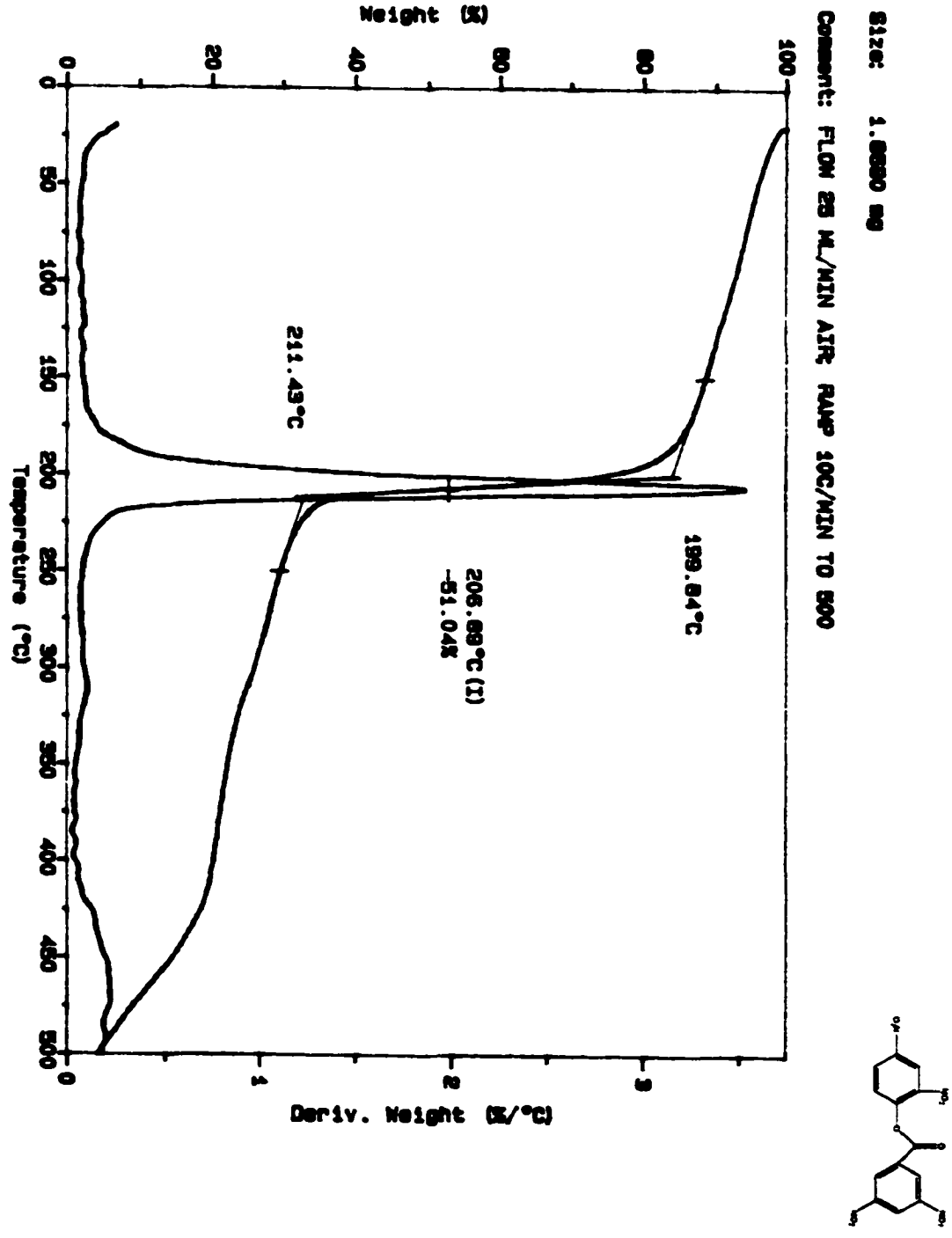
A.36. ^{1}H-NMR of 4-Nitrobiphenyl



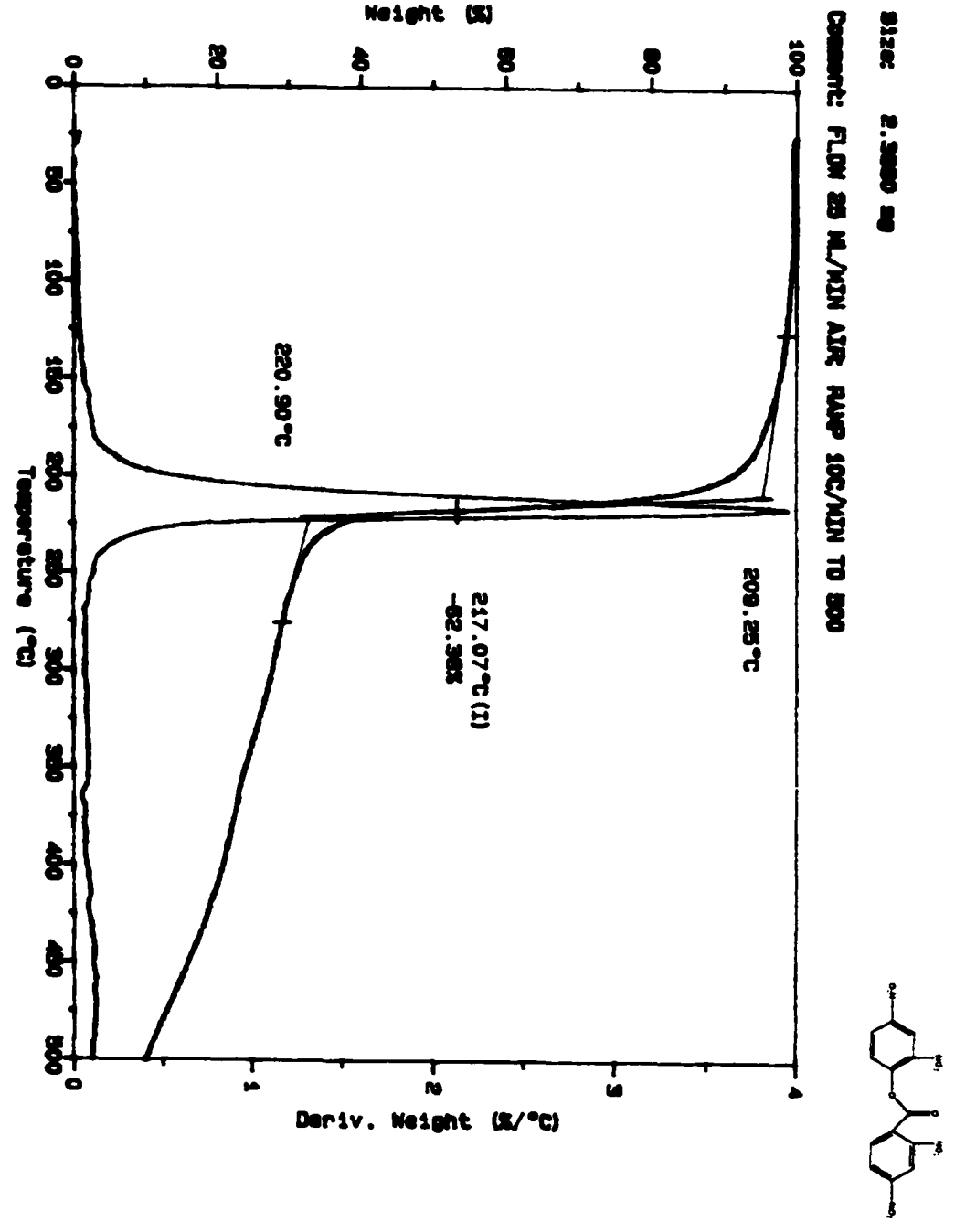
A.37. TGA in Helium of 2,4-Dinitrophenyl 3,5-dinitrobenzoate



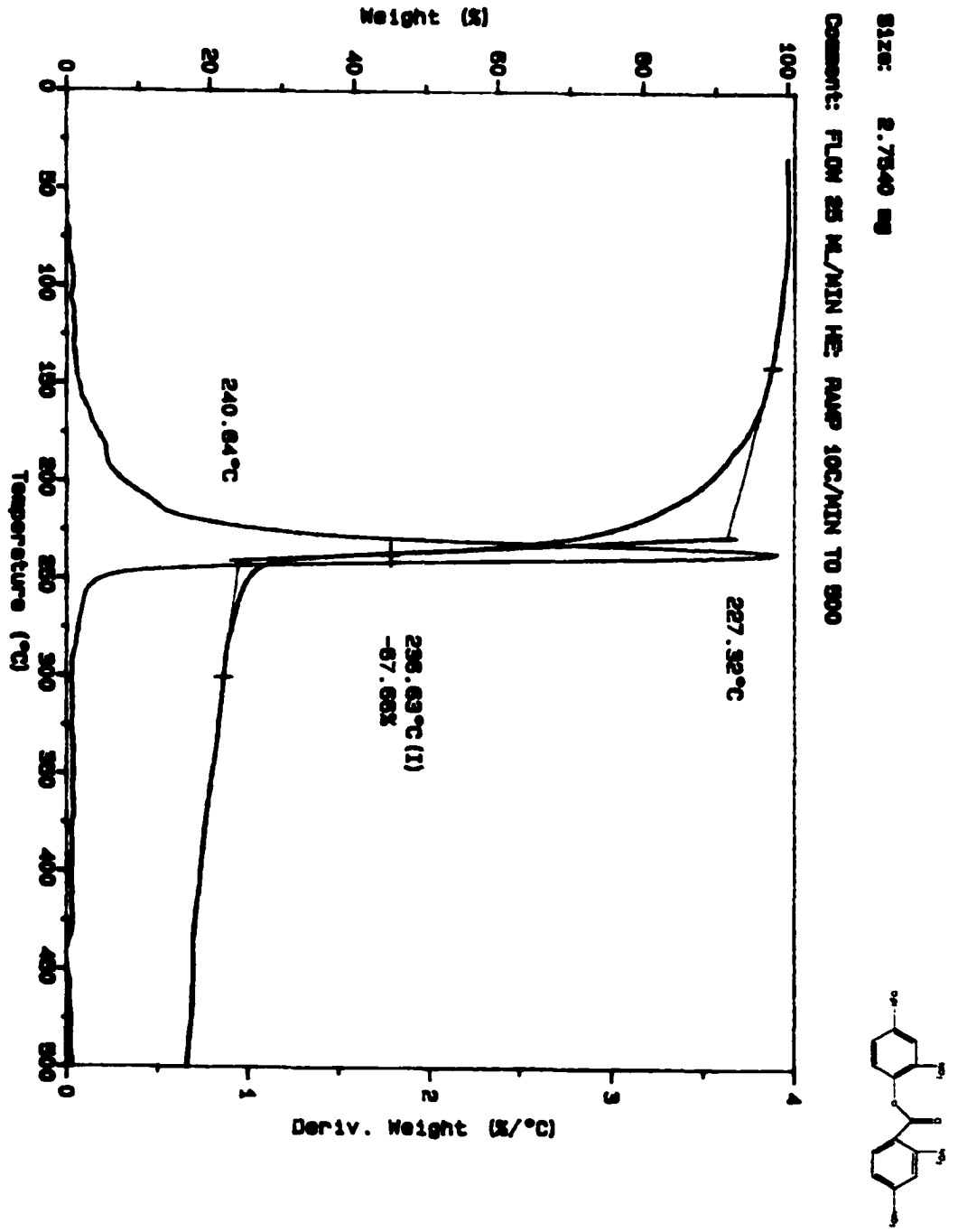
A.38. TGA in Air of 2,4-Dinitronitrophenyl 3,5-dinitrobenzoate



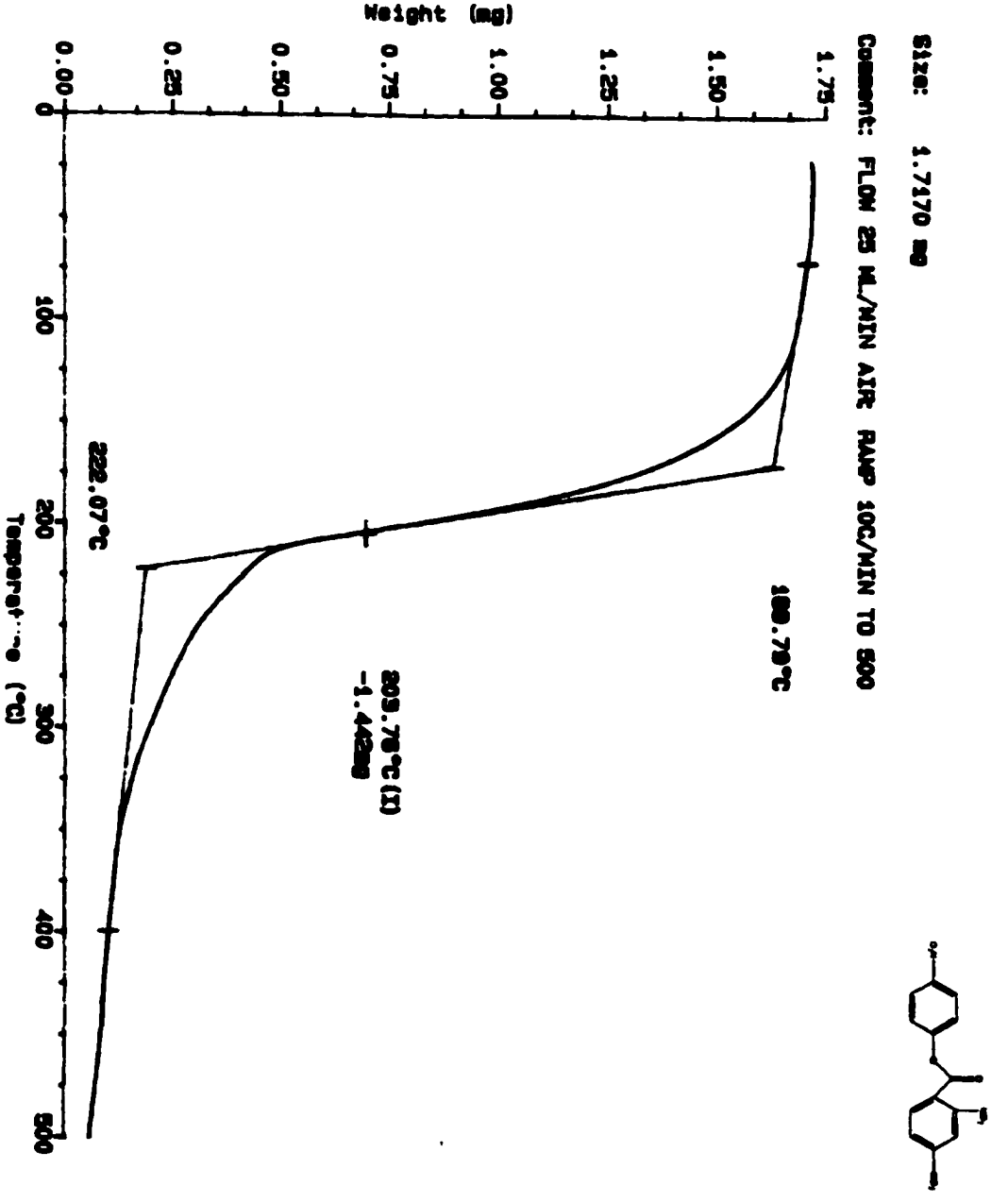
A.39. TGA in Air of 2,4-Dinitrophenyl 2,4-dinitrobenzoate



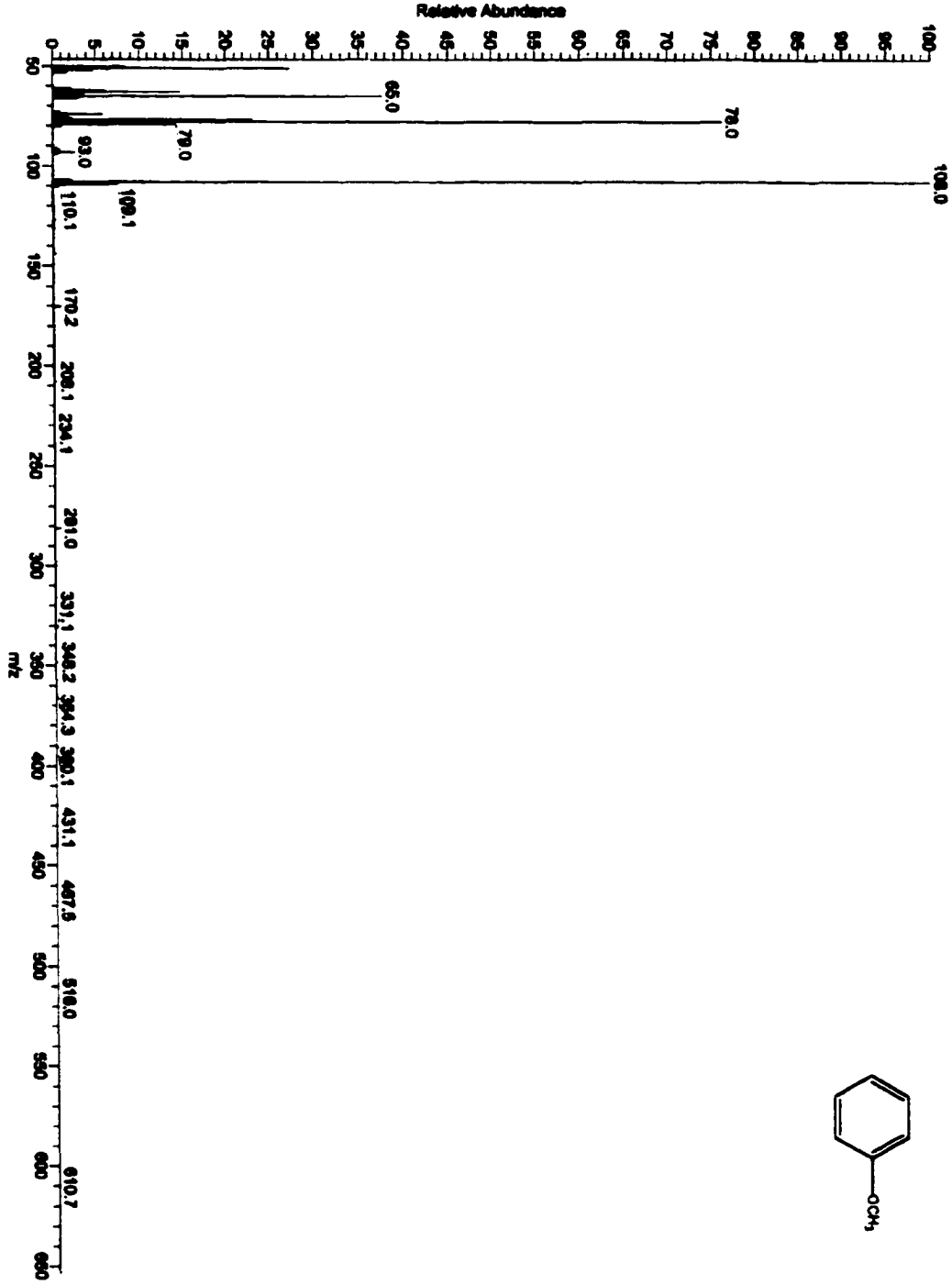
A.40. TGA in Helium of 2,4-Dinitrophenyl 2,4-dinitrobenzoate



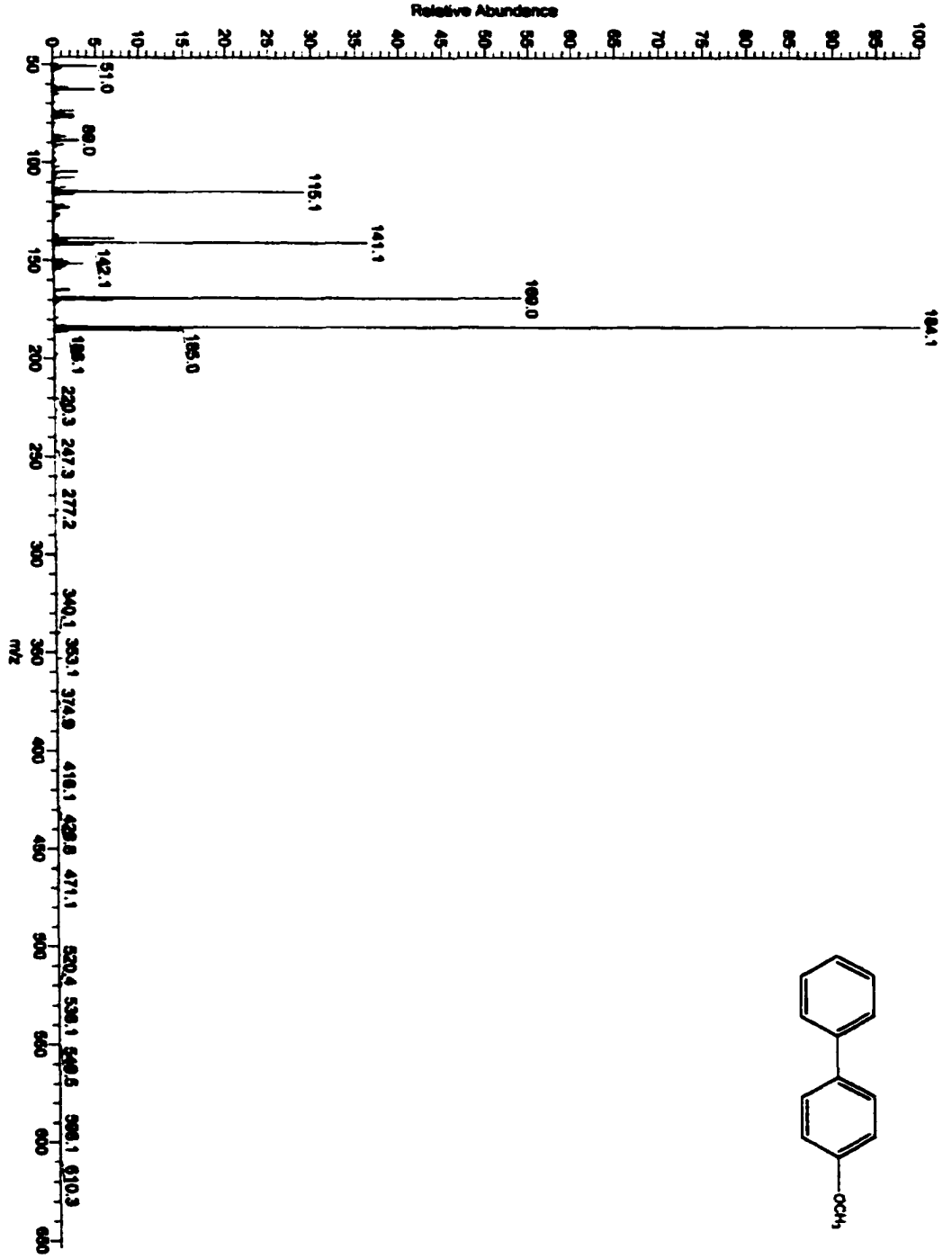
A.41. TGA in Air of 4-Nitrophenyl 2,4-dinitrobenzoate



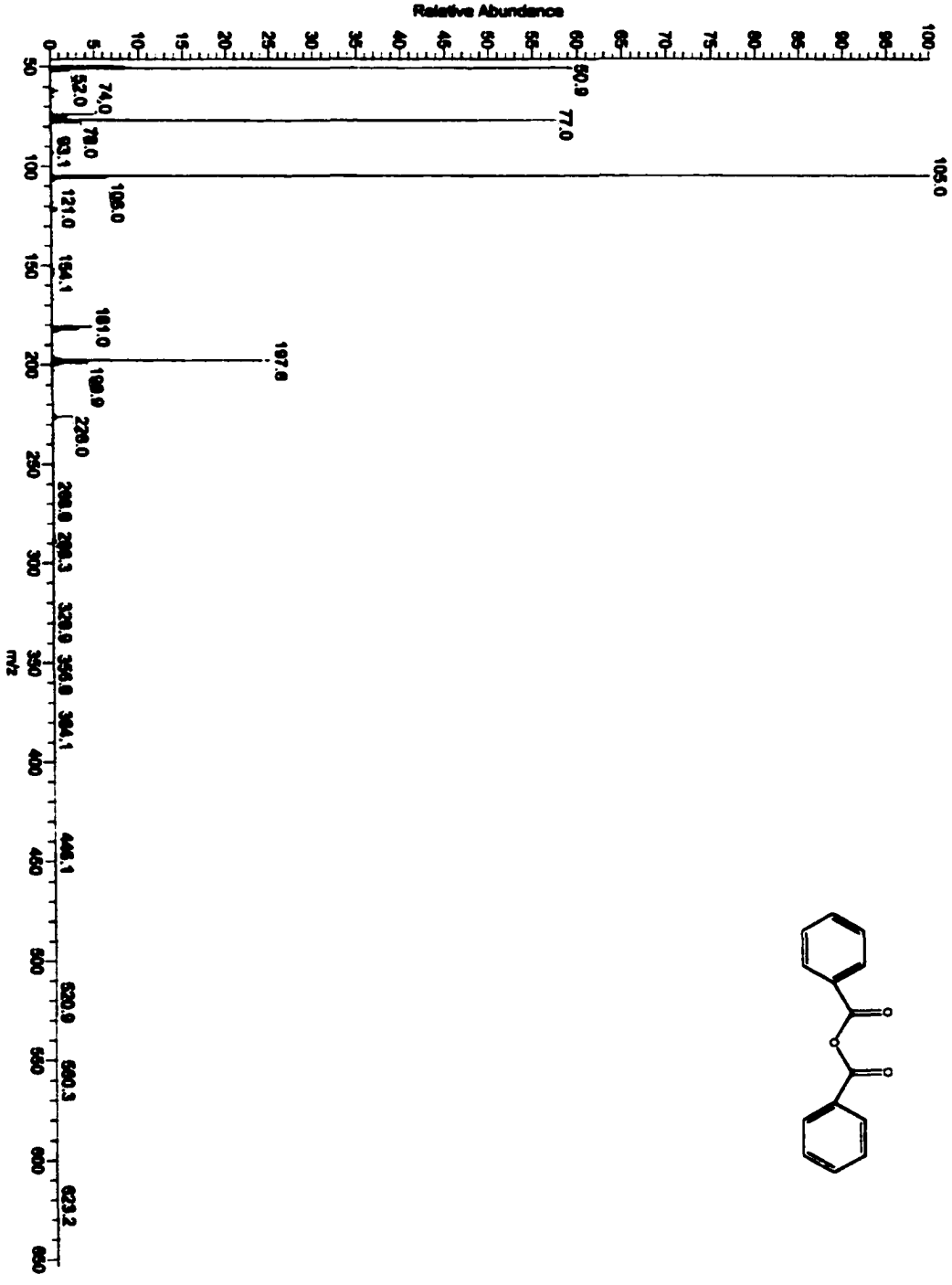
A.42. Mass Spectrum of Methoxybenzene



A.43. Mass Spectrum of *p*-Methoxybiphenyl



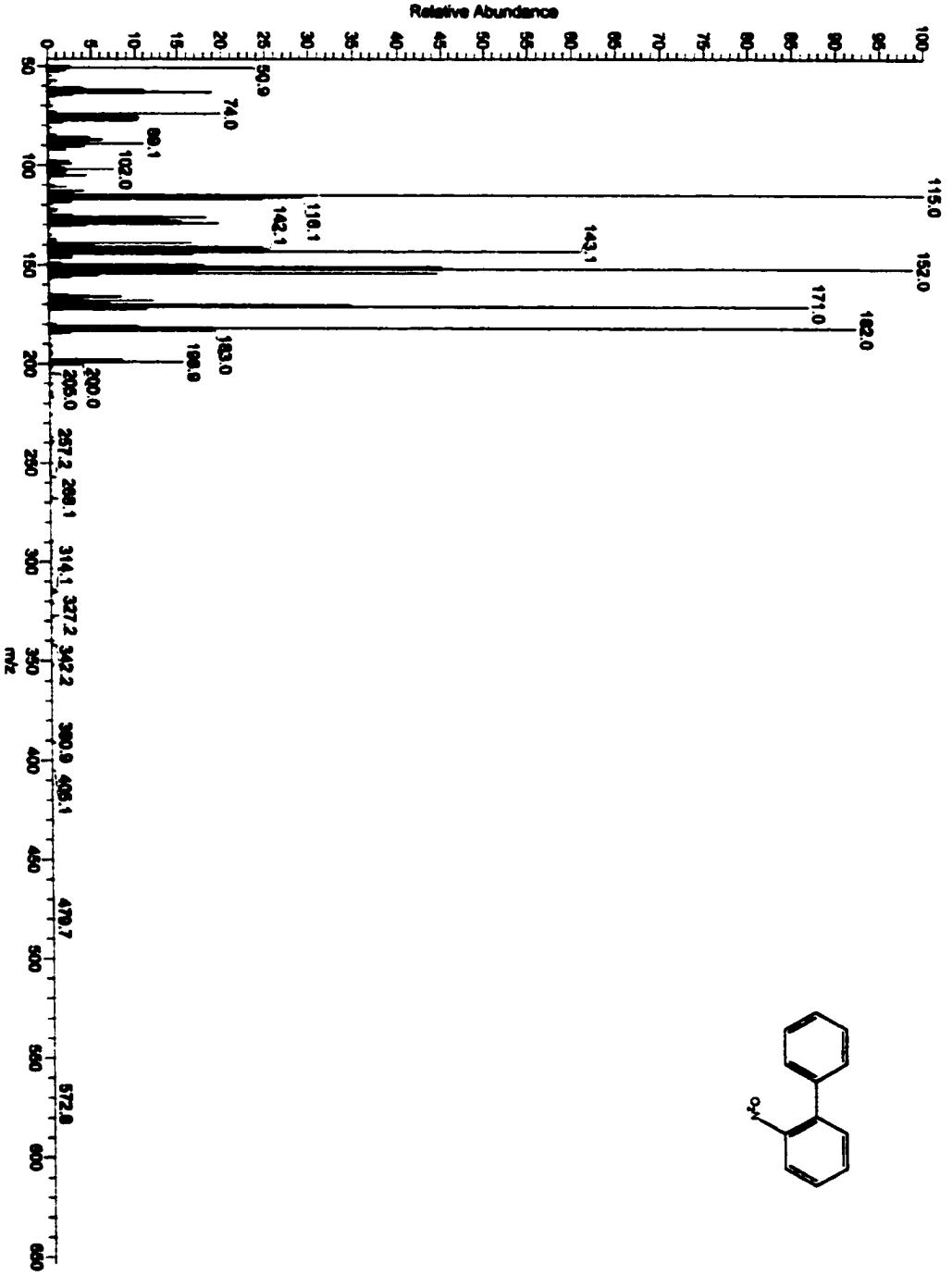
A.44. Mass Spectrum of Benzoic Anhydride



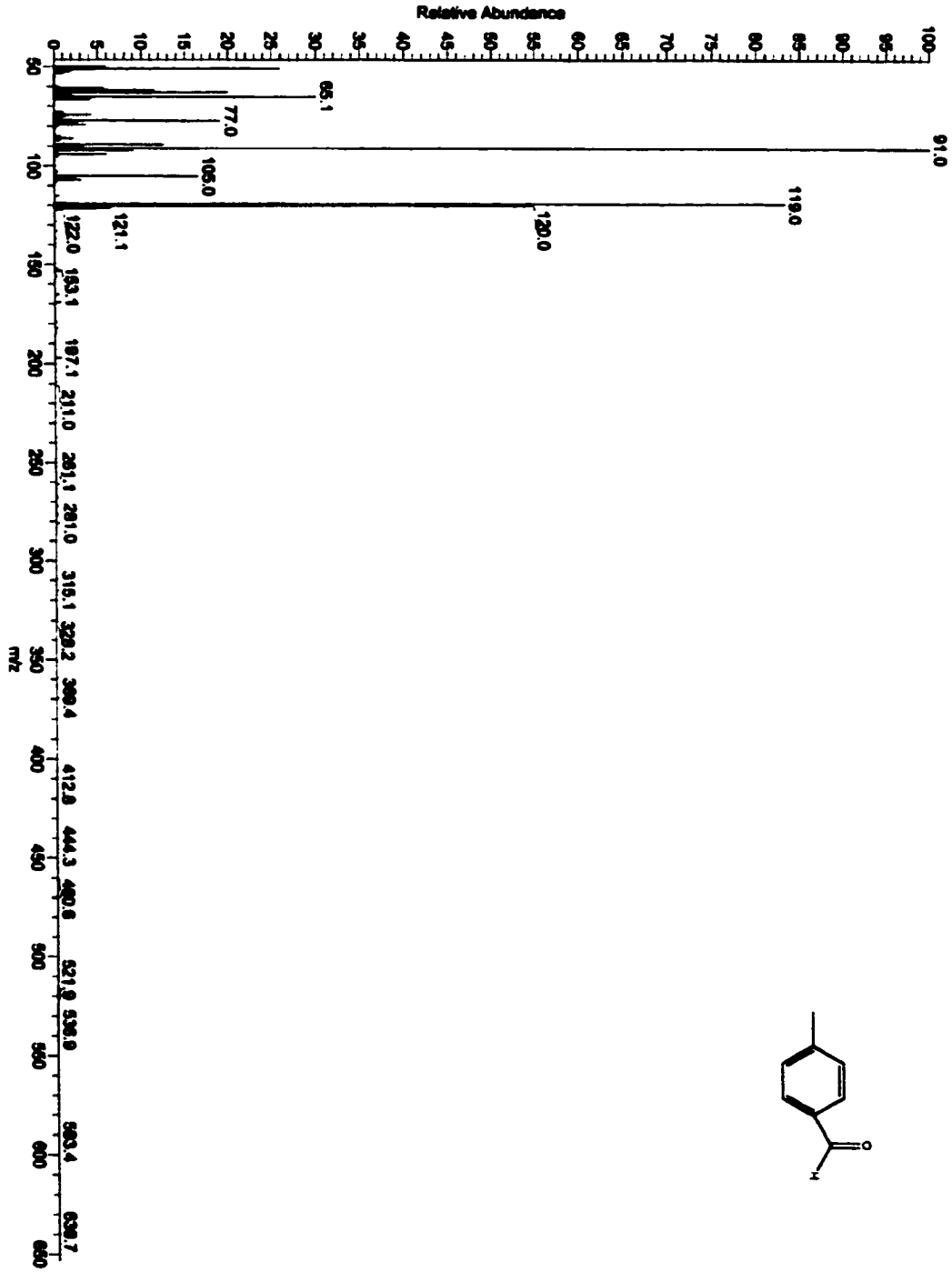
A.45. Mass Spectrum of 4-Biphenylbenzaldehyde



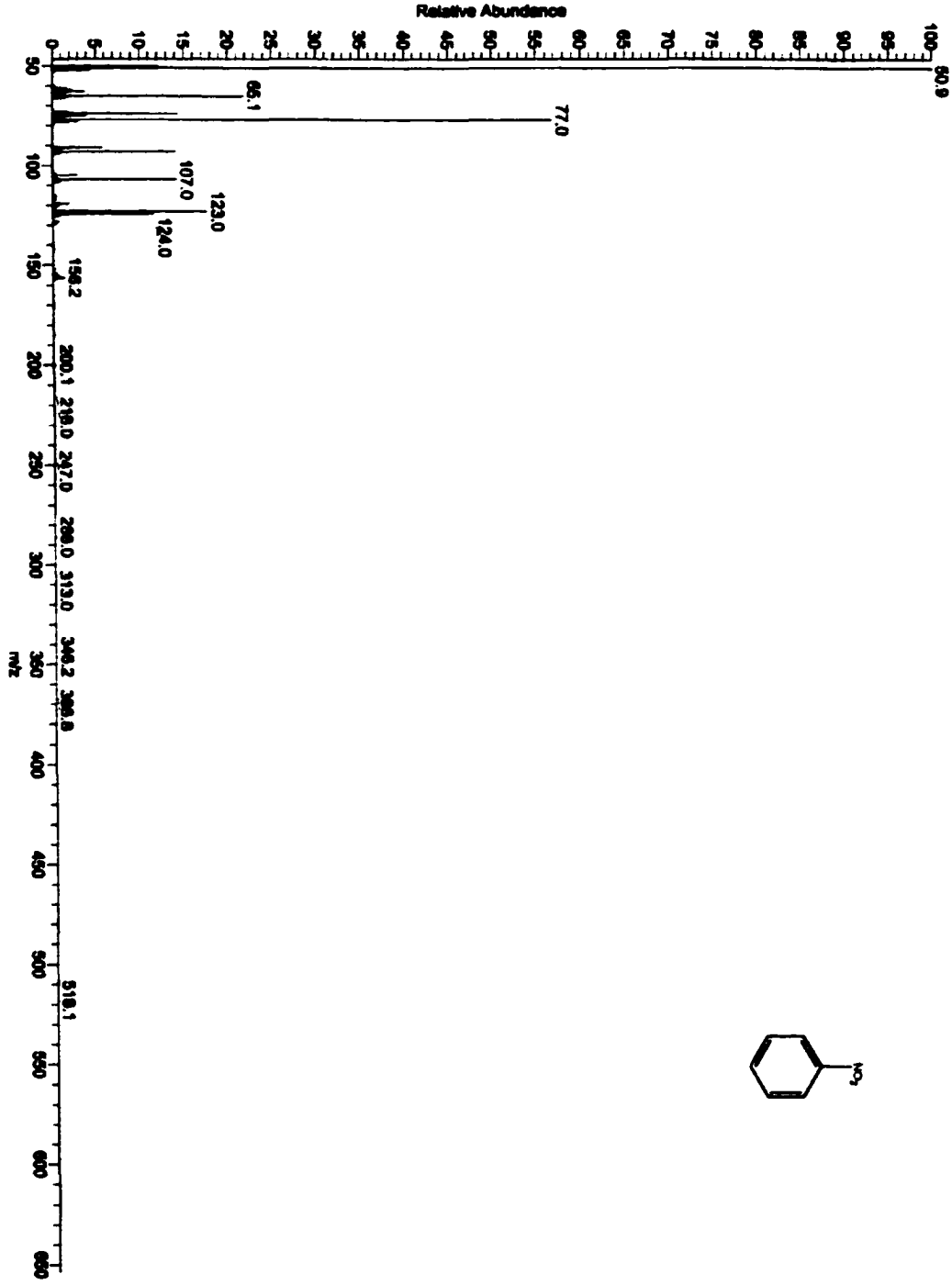
A.46. Mass Spectrum of *o*-Nitrobiphenyl



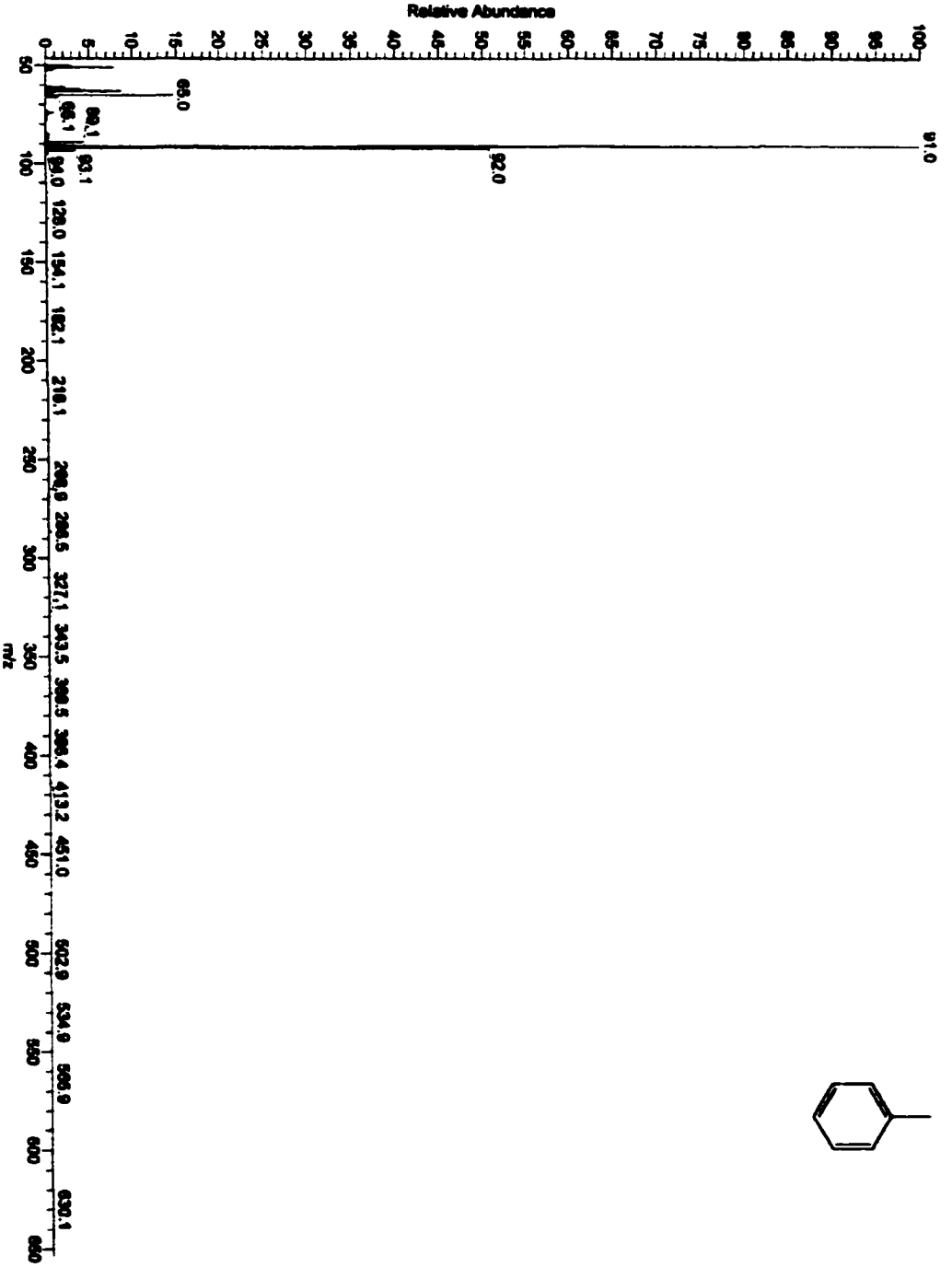
A.47. Mass Spectrum of *p*-Methylbenzaldehyde



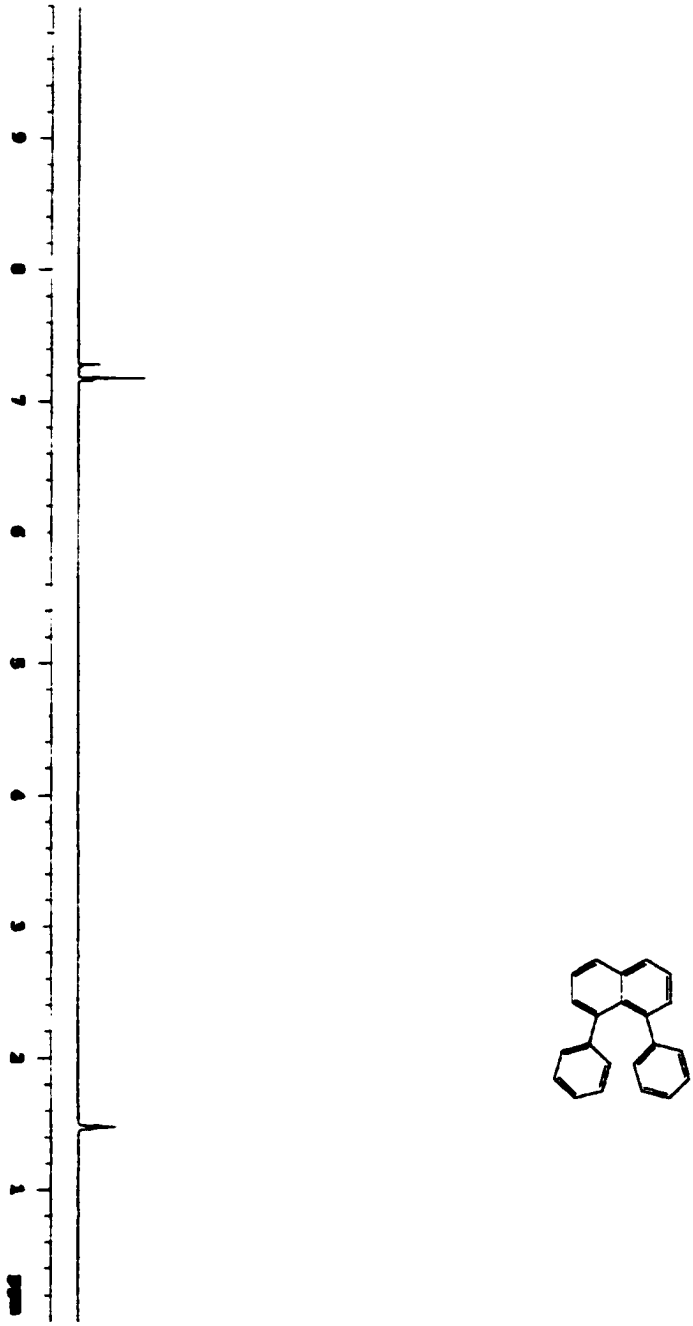
A.48. Mass Spectrum of Nitrobenzene



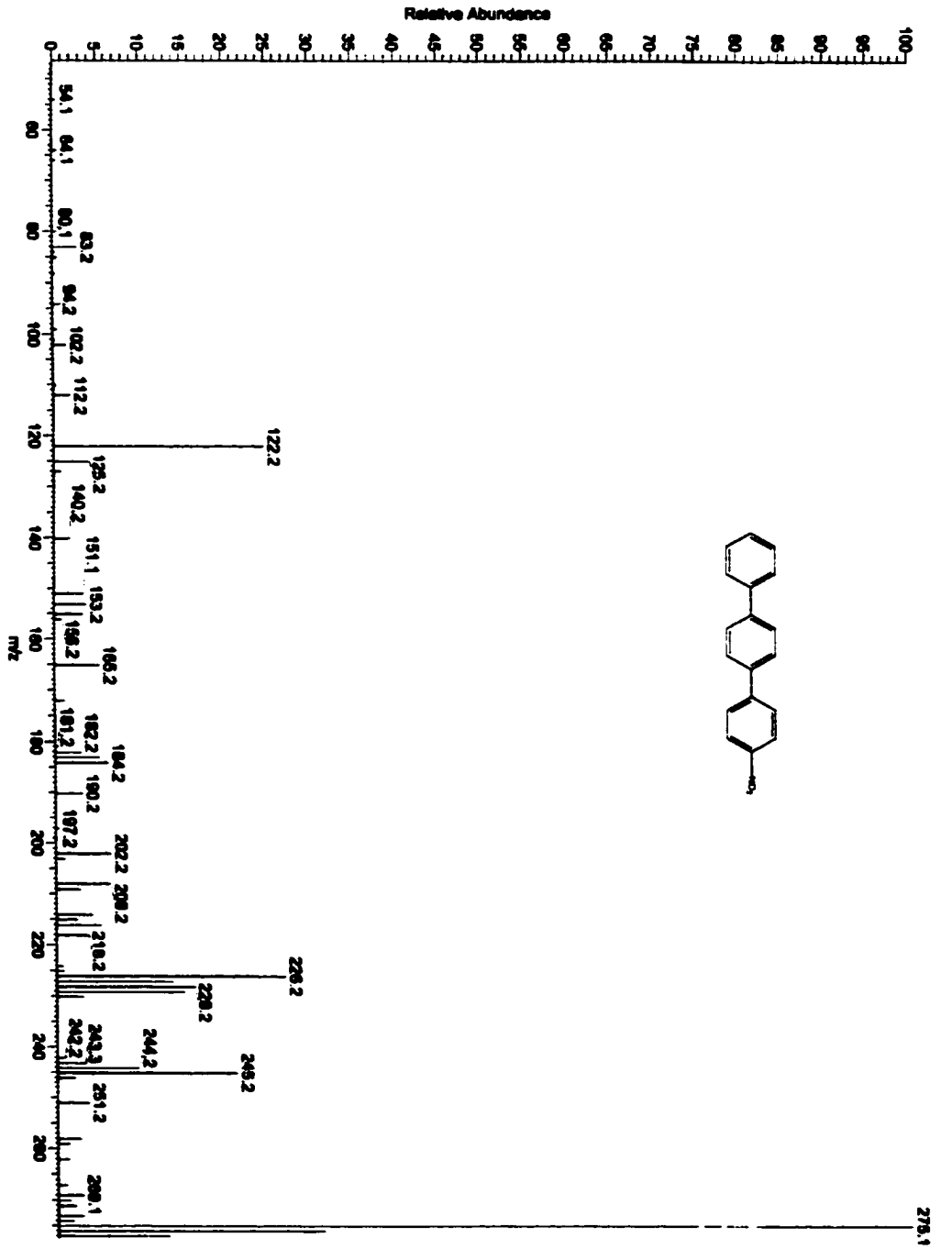
A.49. Mass Spectrum of Toluene



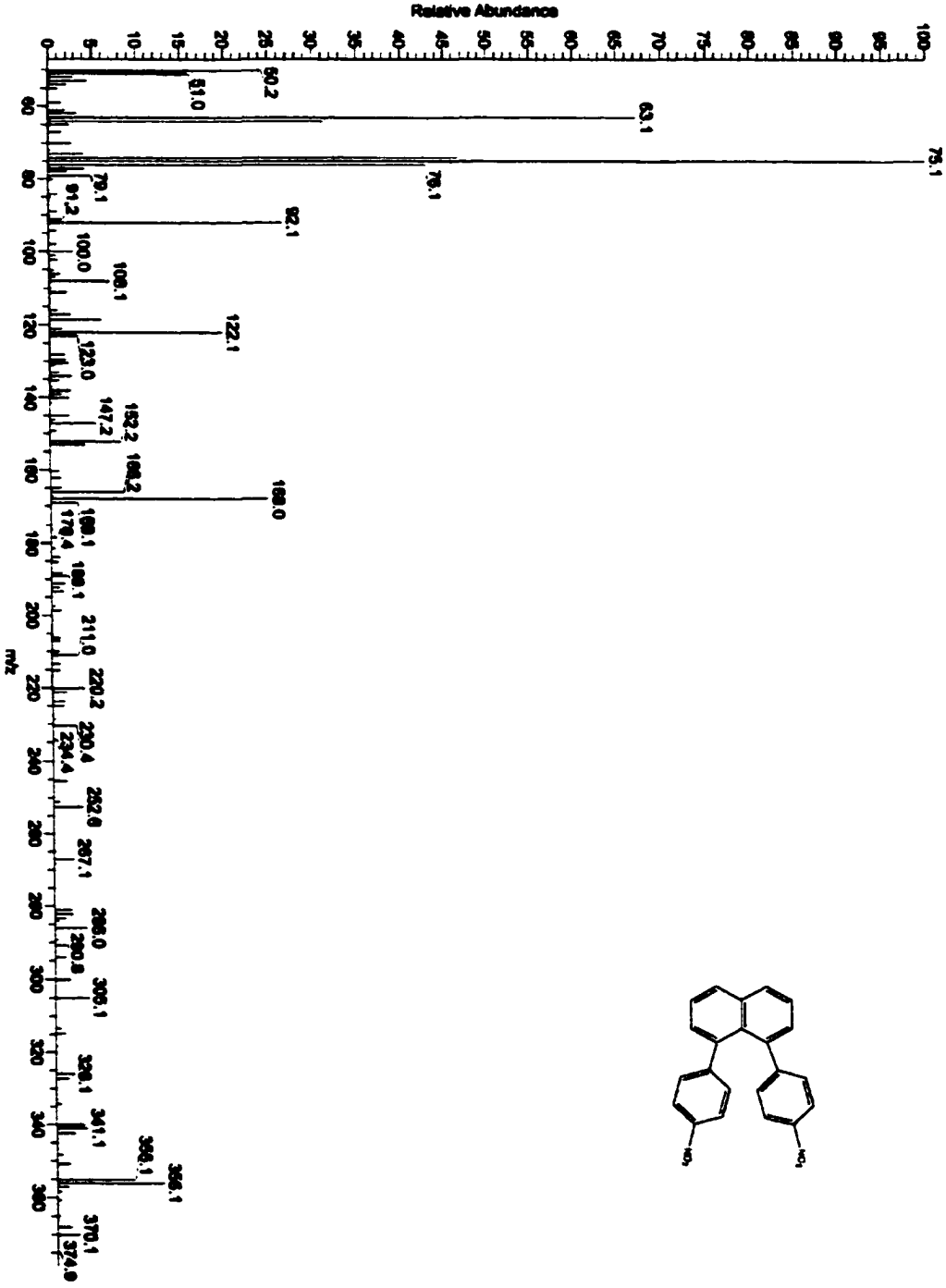
A.50. ^{1}H-NMR Spectrum of 1,8-Diphenylnapthylene



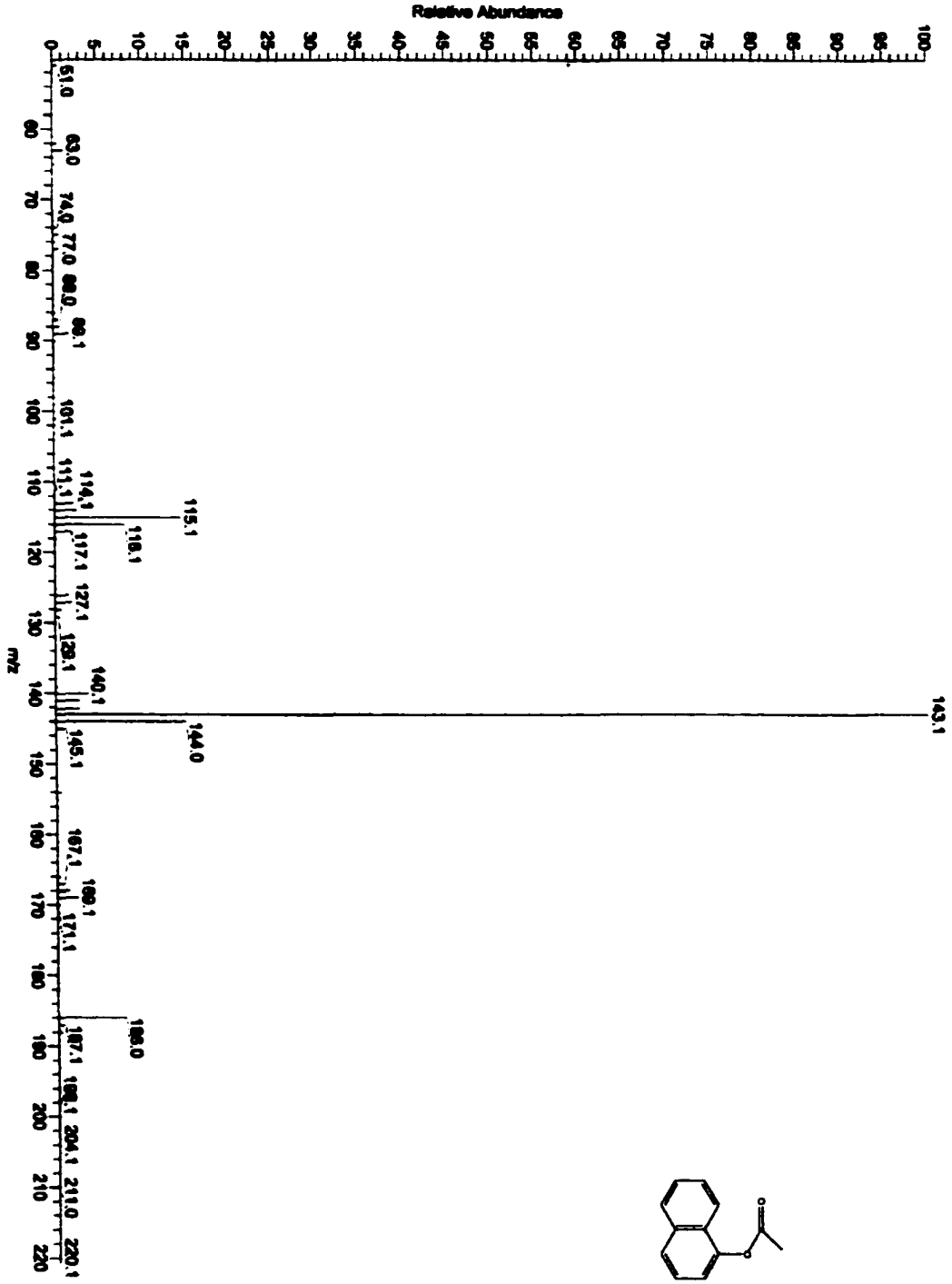
A.51. Mass Spectrum of 4-Nitro-*p*-terphenyl



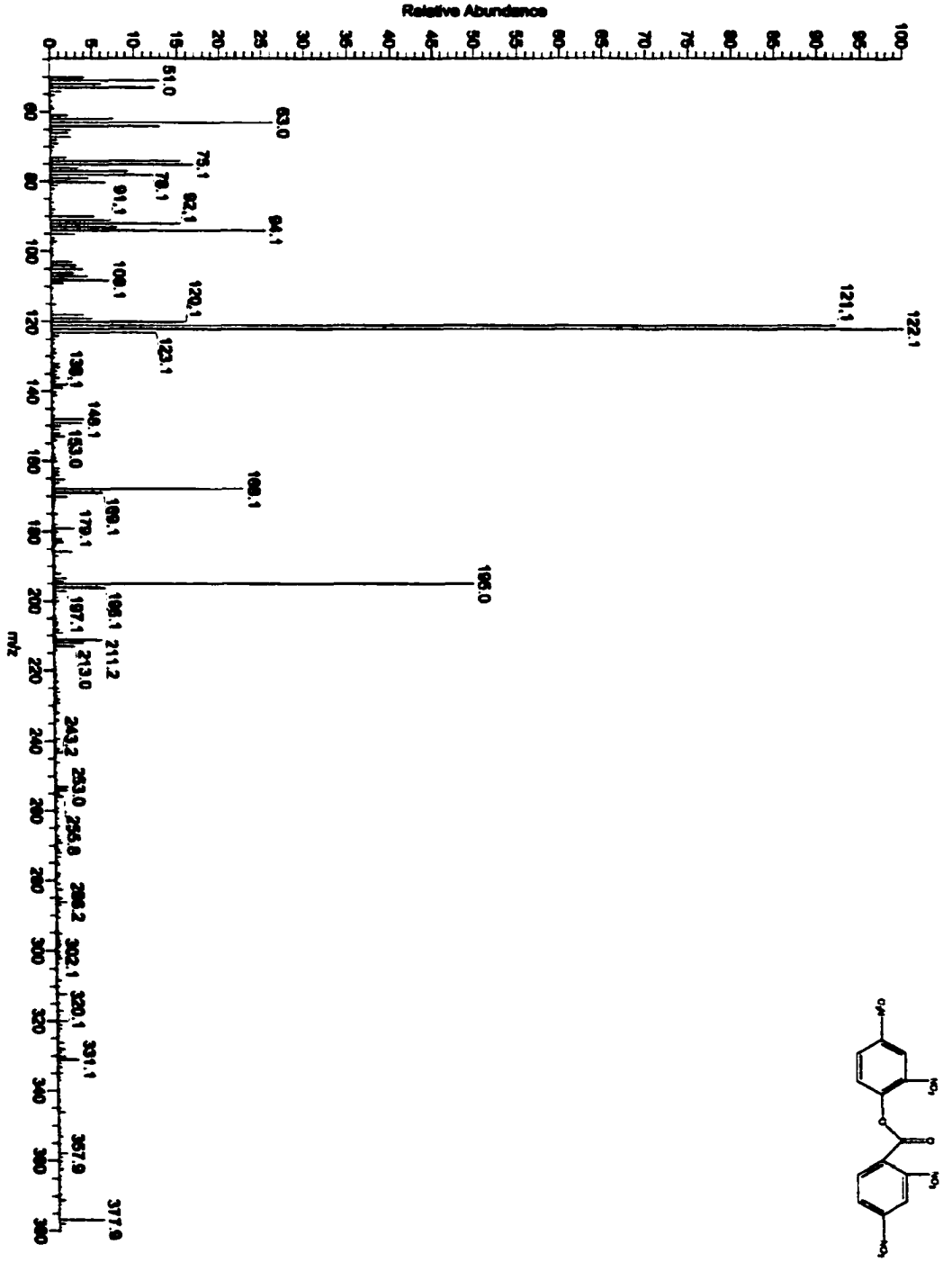
A.52. Mass Spectrum of 1,8-Napthyldi-*p*-nitrobenzene



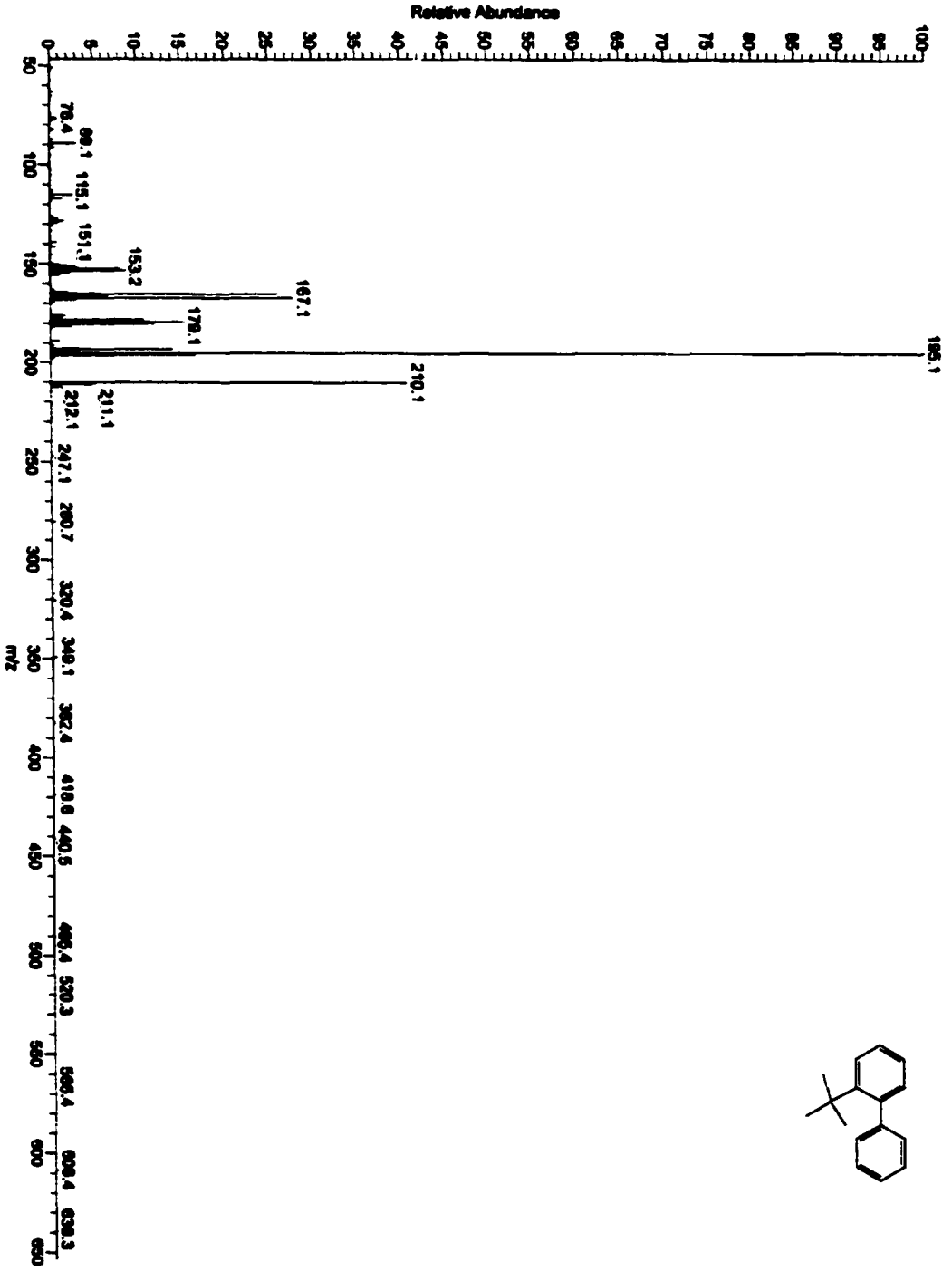
A.53. Mass Spectrum of 1-Napthyl acetate



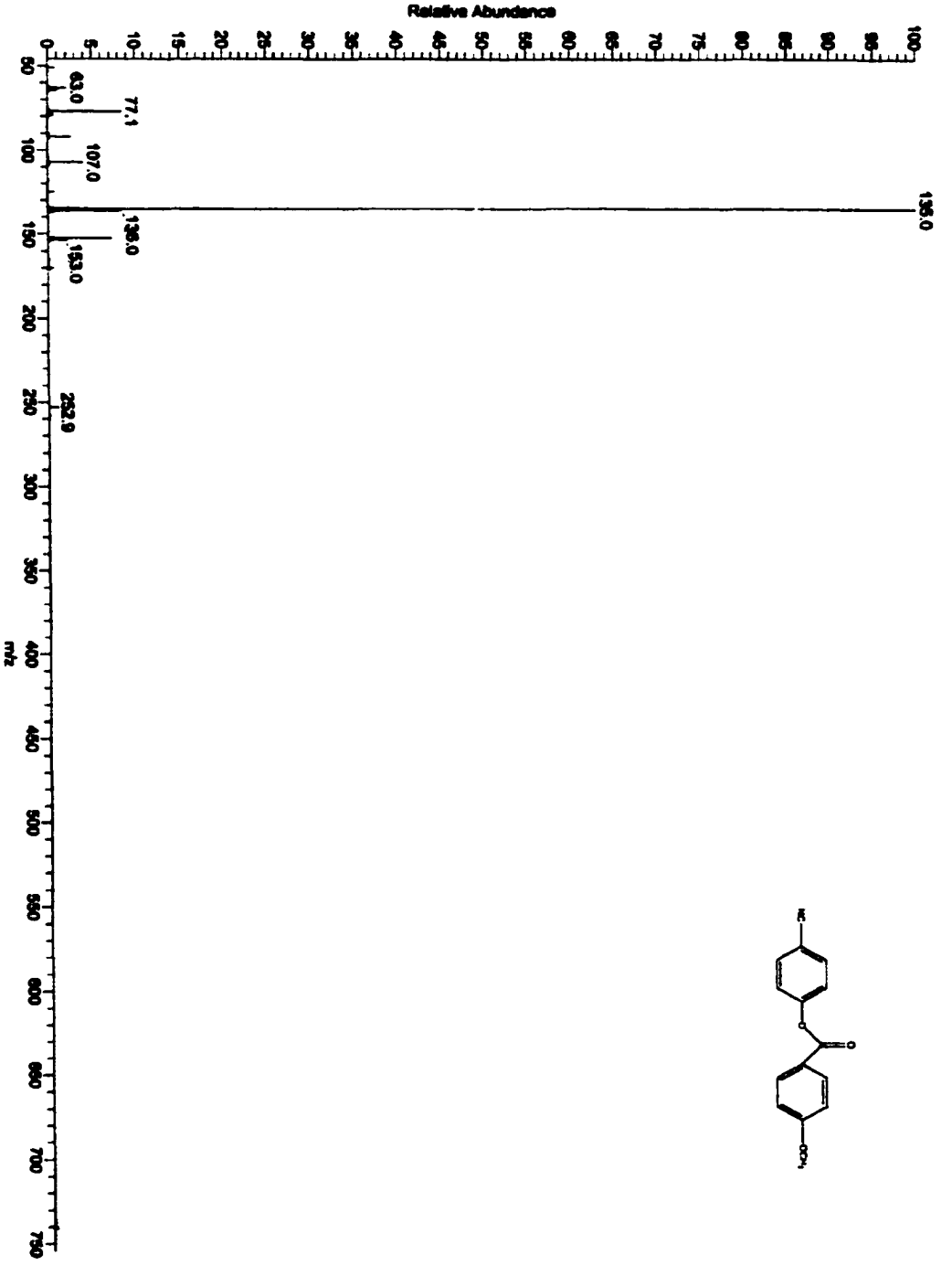
A.54. Mass Spectrum of 2,4-Dinitrophenyl 2,4-dinitrobenzoate



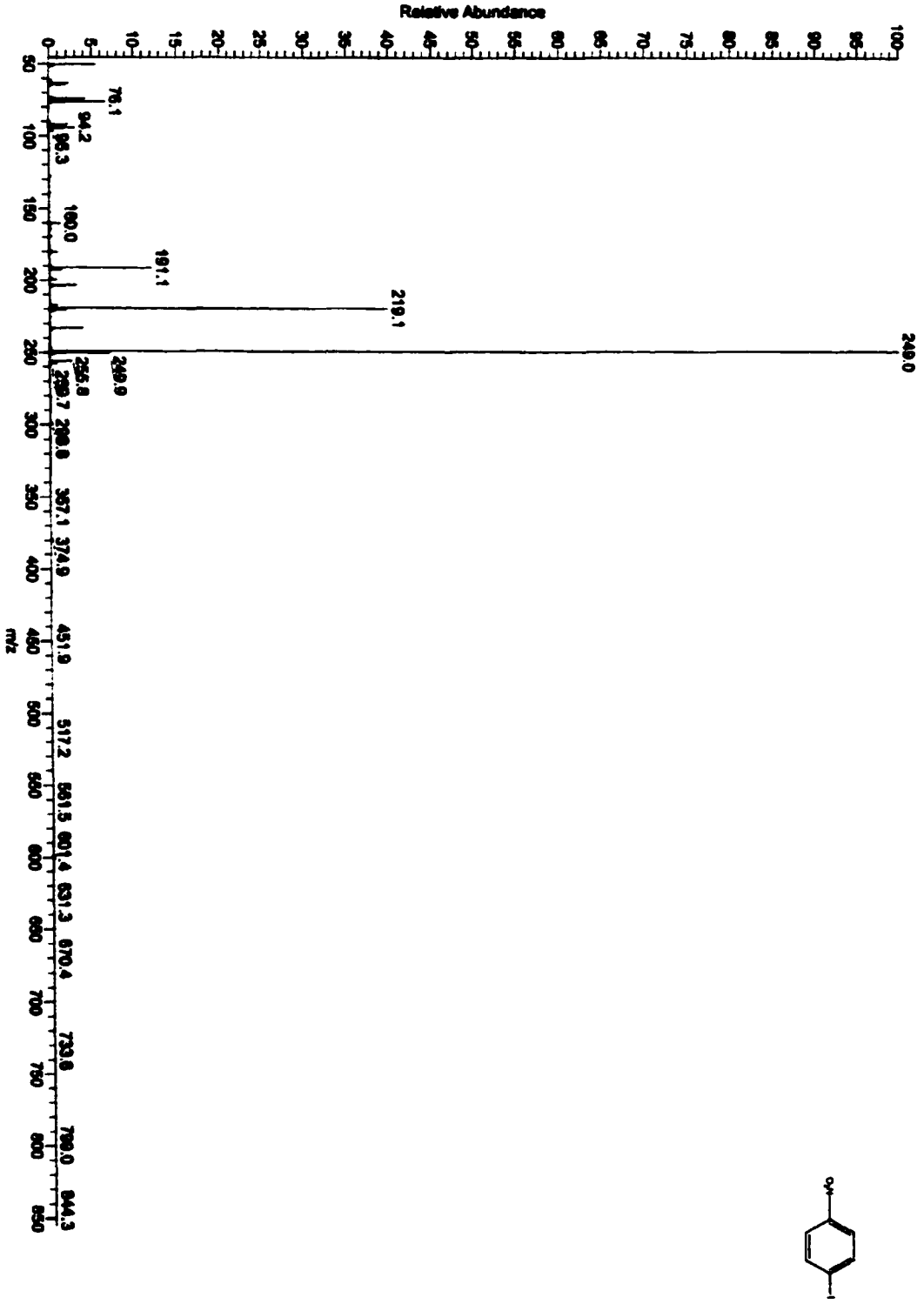
A.55. Mass Spectrum of 2-*tert*-Butylbiphenyl



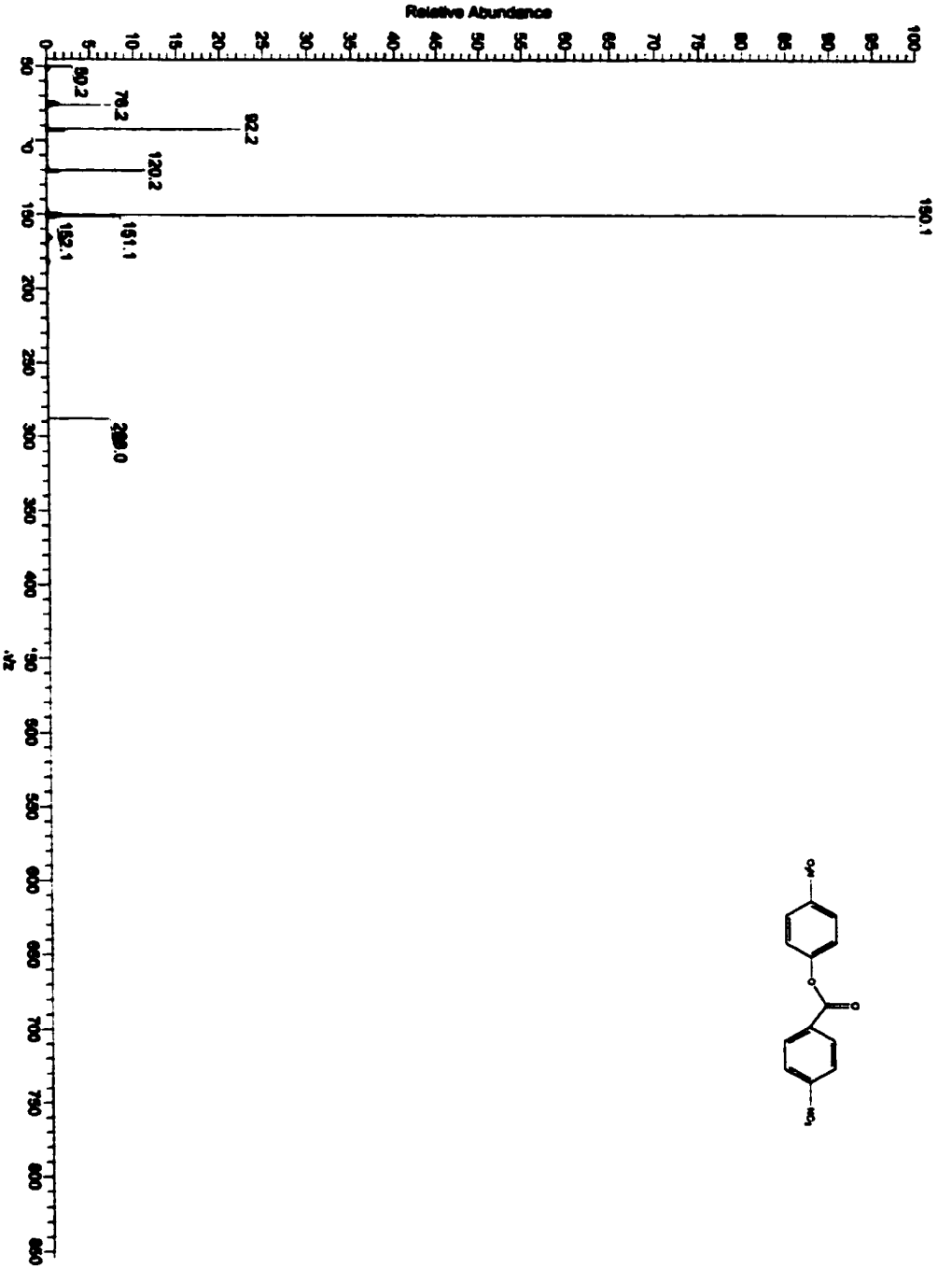
A.56. Mass Spectrum of 4-Cyanophenyl 4-methoxybenzoate



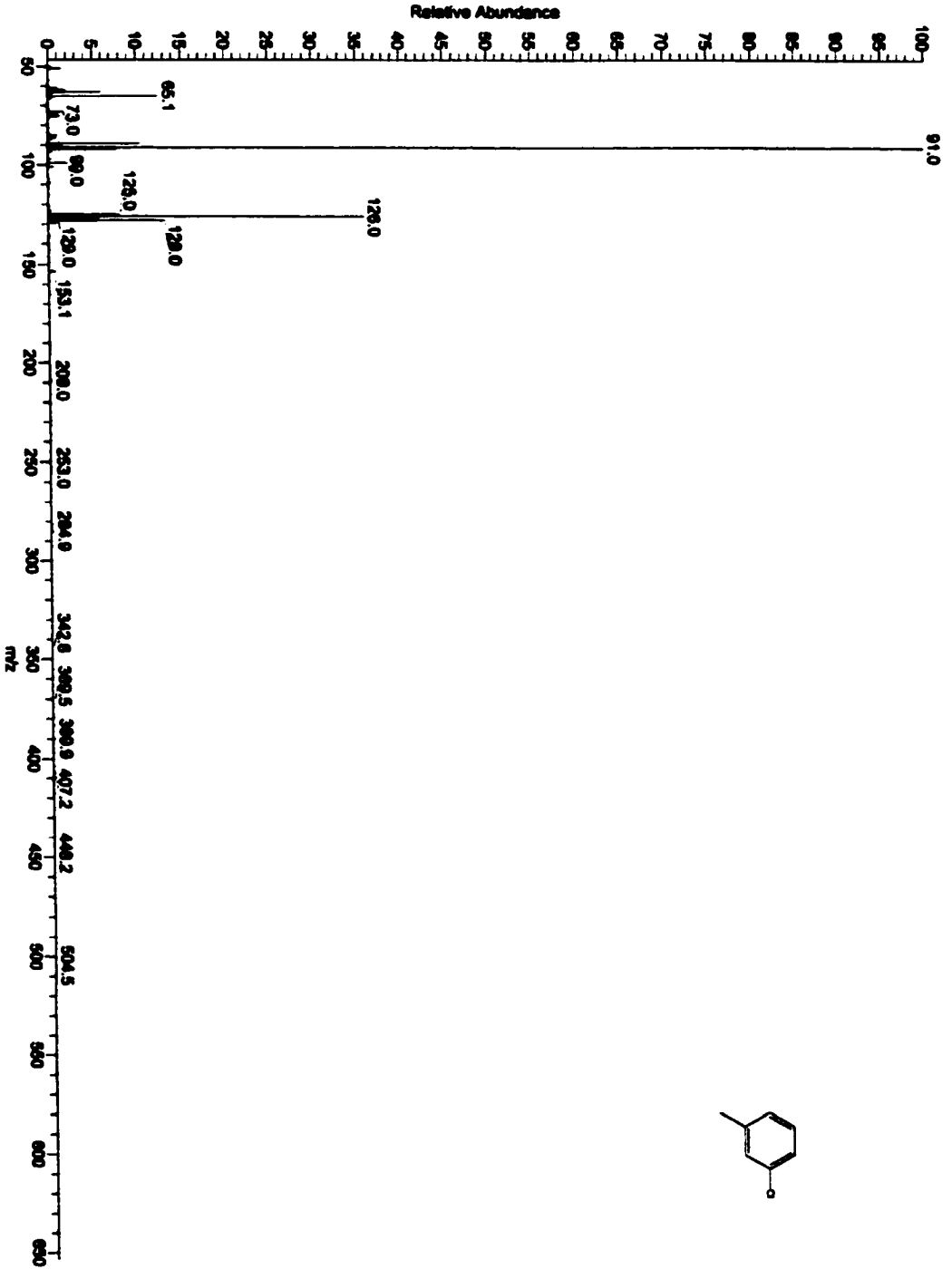
A.57. Mass Spectrum of 4-Iodonitrobenzene



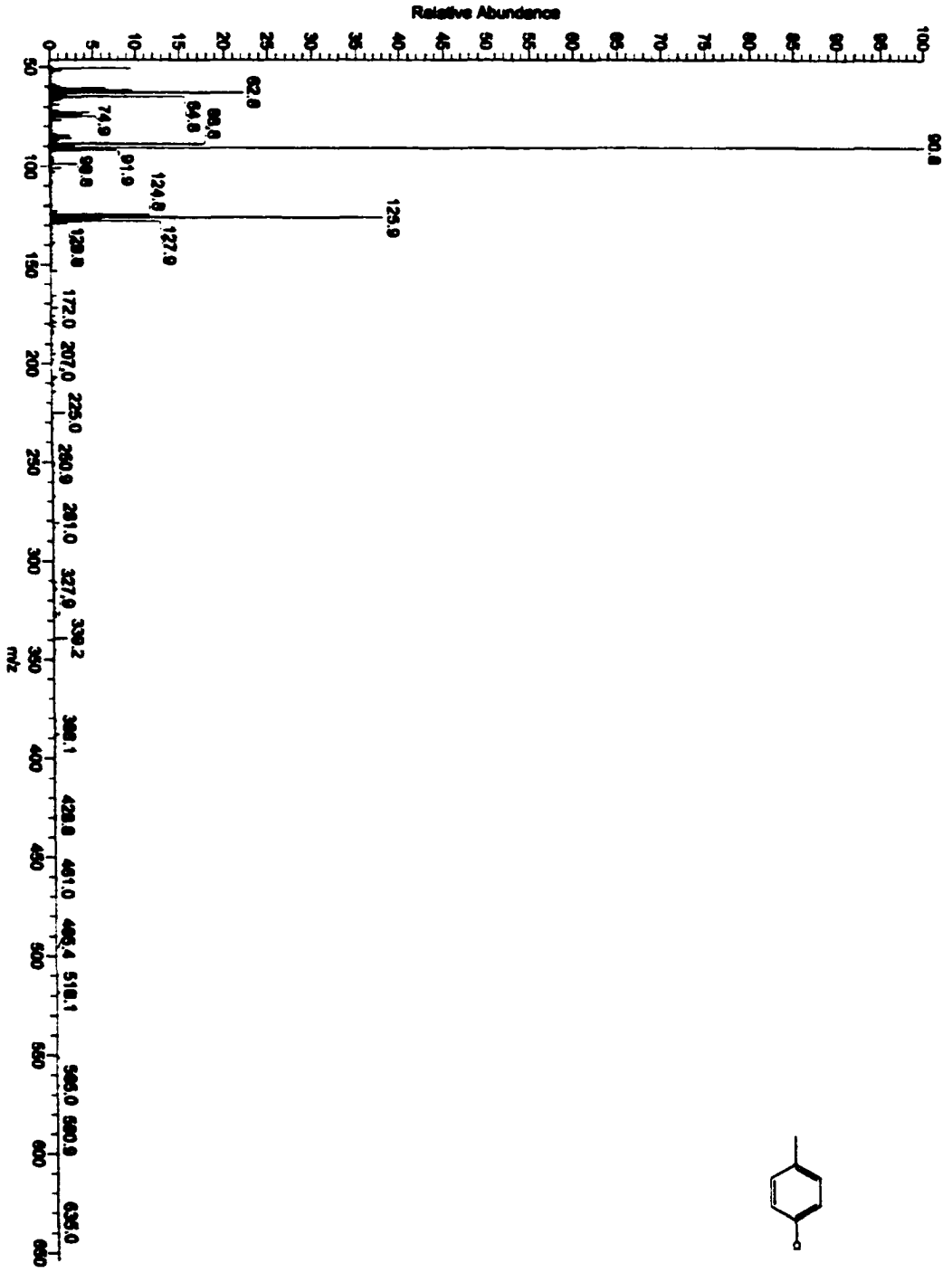
A.58. Mass Spectrum of 4-Nitrophenyl 4-nitrobenzoate



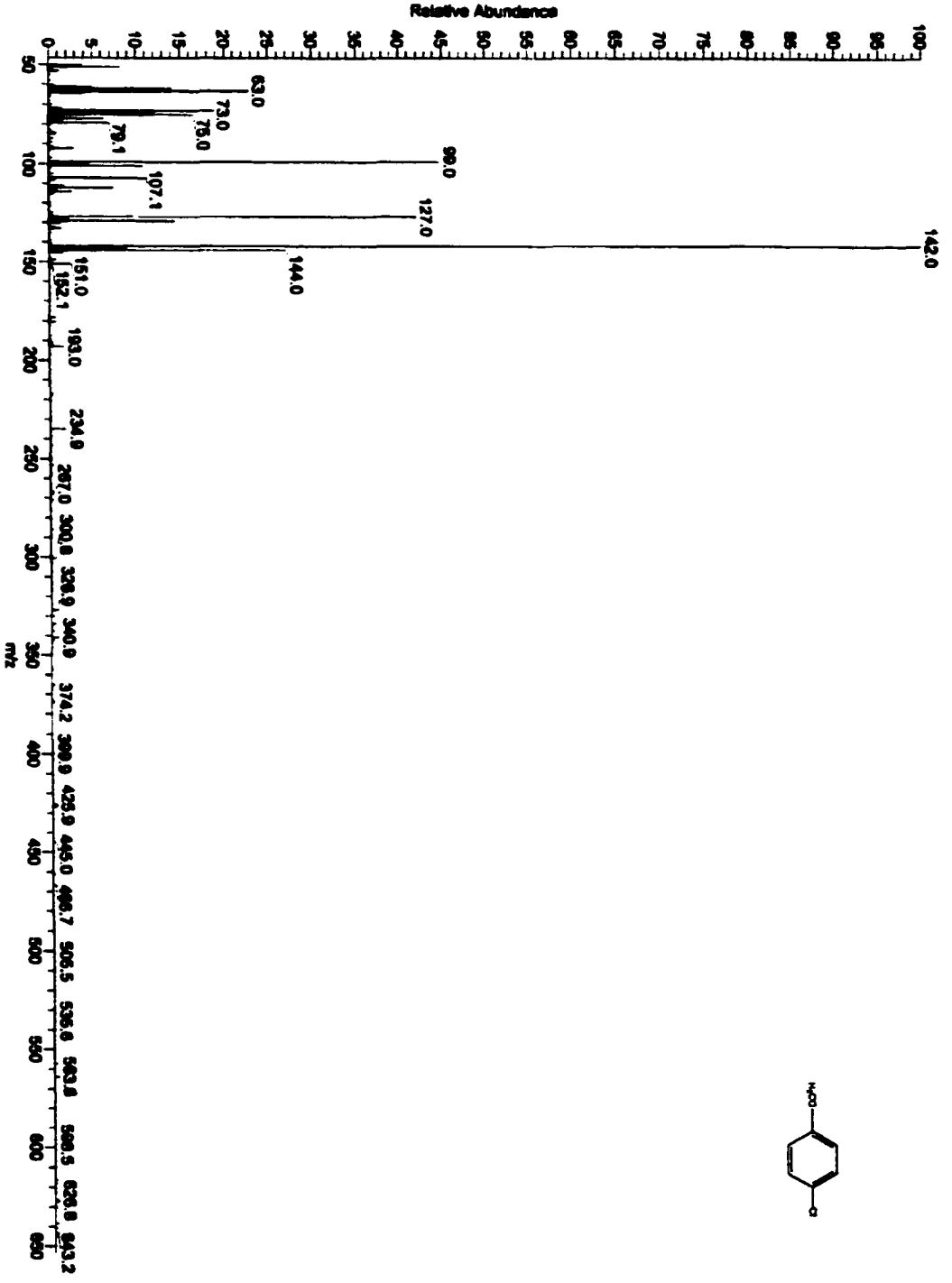
A.59. Mass Spectrum of *m*-Chlorotoulene



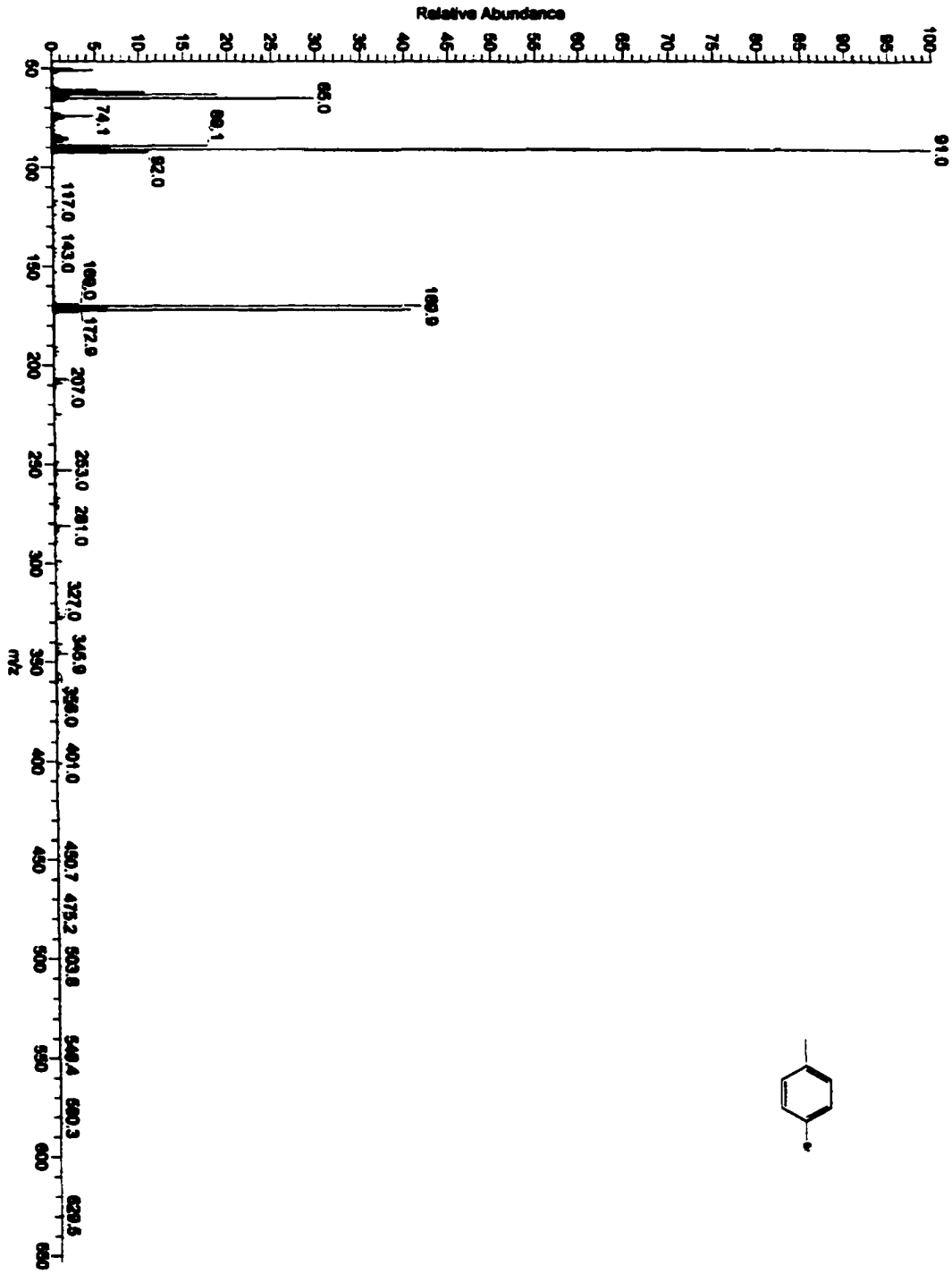
A.60. Mass Spectrum of *p*-Chlorotoulene



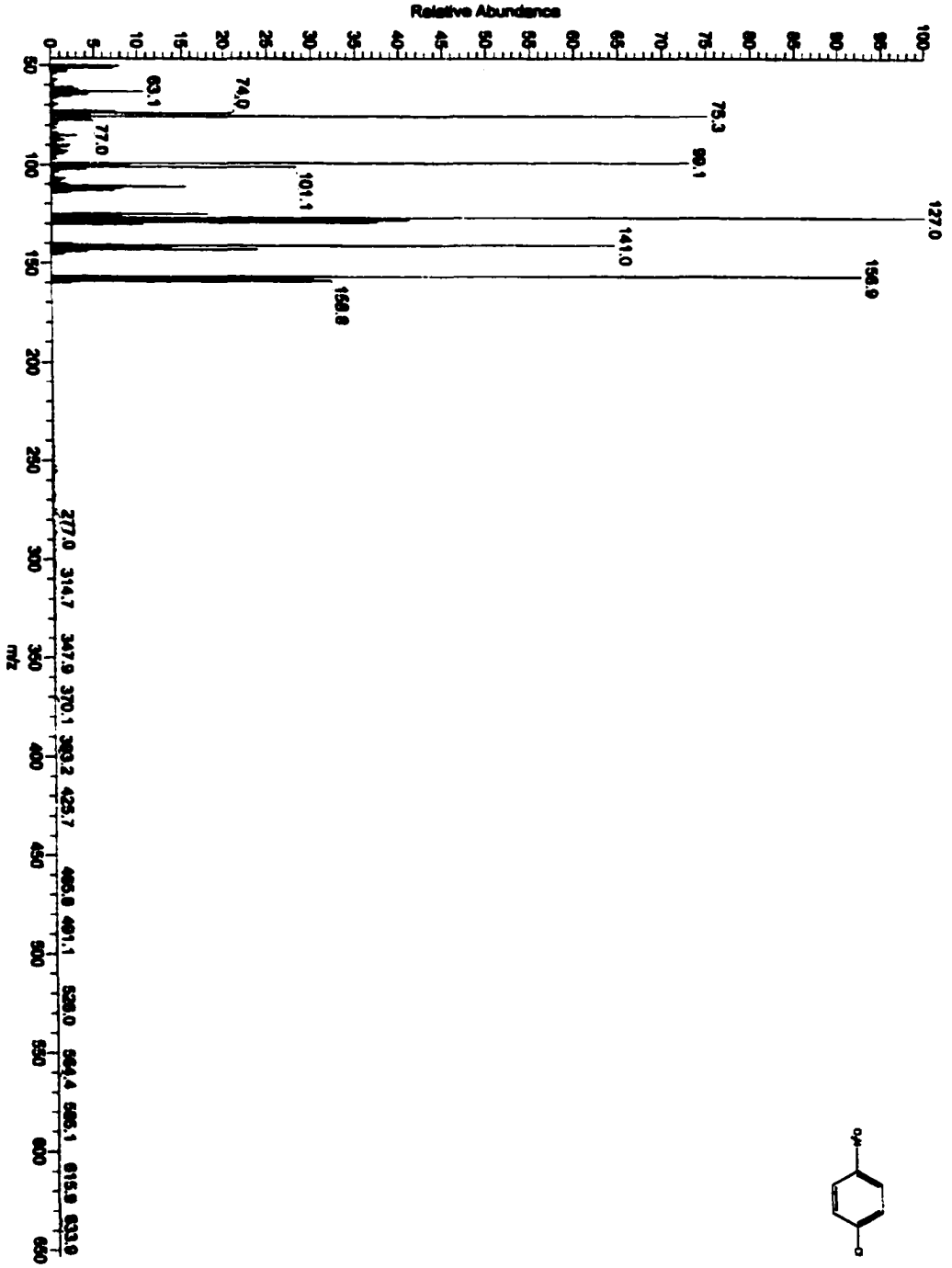
A.61. Mass Spectrum of *p*-Chloroanisole



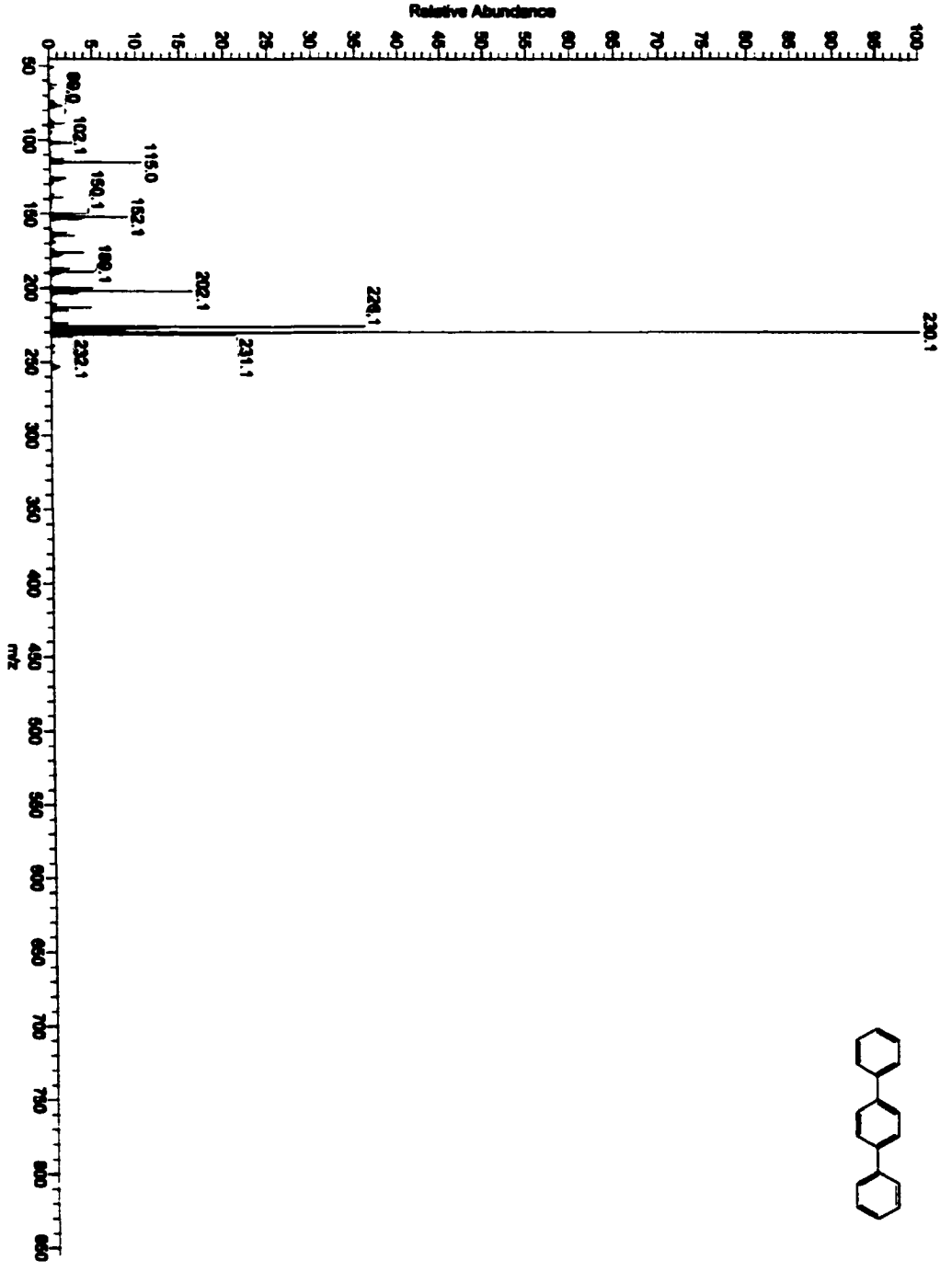
A.62. Mass Spectrum of *p*-Bromotoluene



A.63. Mass Spectrum of *p*-Chloronitrobenzene



A.64. Mass Spectrum of *p*-Terphenyl



A.65. Mass Spectrum of N-(4-Nitrophenyl)4-nitrobenzamide

