PART 1: SYNTHESIS OF STABLE FREE RADICALS AS POTENTIAL ORGANIC METALS. PART 2: SYNTHESIS OF OXYGENATED INDACENE DERIVATIVES. PART 3: REACTIONS OF AROMATIC POLY(N,N-DIMETHYL AMIDES) WITH ELECTROPHILES.

By

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ABSTRACT

PART 1: SYNTHESIS OF STABLE FREE RADICALS AS POTENTIAL ORGANIC METALS. PART 2: SYNTHESIS OF OXYGENATED INDACENE DERIVATIVES. PART 3: REACTIONS OF AROMATIC POLY(N,N-DIMETHYLAMIDES) WITH ELECTROPHILES.

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Part 1: "Organic metals" are organic compounds which conduct electricity. Those which have attracted the most attention are charge transfer salts, like TCNQ-TTF, in which both the donor and acceptor molecules are highly delocalized, planar molecules. Theoretical studies suggest that neutrality and divalency are properties which could be desirable to the design of more effective conductors, perhaps even allowing the development of superconductors.

To this end, several syntheses of diradicals deemed likely to be stable were attempted. These included the diradicals of 2,12-dihydro-6,10-dihydroxy-4H,8H-dibenzo (cd,mn)pyren-2-one (5a), the 4,8,12-trioxa derivative of 5a (5b), 4,7-dihydroxy-1H-phenalen-1-one (4), and several polychloro derivatives of these. The dihydroxy compounds which were successfully prepared (4, 5b) did not give stable diradicals.

Part 2: 1,2,3,5,6,7-Hexahydro-s-indacene-1,2,3,5,6,7-hexone (58), its 4,8-dihydroxy derivative (57), and the quinone of 58 were of interest as electron acceptors in potentially conducting charge transfer salts, as carbon

oxo-acids and oxocarbons and as precursors to the interesting polycyclic aromatic dicyclopentadieno(a,h)-s-indacene. Though the synthesis of none of these compounds was achieved, several interesting pathways were explored.

Part 3: Partly as a result of several reactions explored in part 2, it was of interest to study the reactions of aromatic N,N-dimethylamides with electrophiles. Of particular interest were compounds having two N,N-dimethylamino-carbonyl groups situated ortho to one another on a benzene ring. These were studied to determine whether the groups react independently of each other and, if not, to what extent neighboring group participation occurs. Though other electrophiles were investigated, the major portion of the study was limited to reactions of methyl trifluoromethanesulfonate (MeOTf) and thionyl chloride ($SOCl_2$) because these give straightforward chemical and spectral results. As models, the reactions of these electrophiles with N,N-dimethylbenzamide (153), N,N,N',N'-tetramethyl isophthalamide (156), N,N,N',N'-tetramethyl terephthalamide (157) were also studied. Both 156 and 157 reacted with two equivalents of MeOTf and $SOCl_2$ to give bis(methoxy dimethyliminium) salts and bis(chloro dimethyliminium) salts respectively. N,N,N',N'-dimethyl phthalamide (154) reacts with only one equivalent. NMR spectroscopy shows that the product of 154 with MeOTf displays a small participation by the second amide group, while with $SOCl_2$ this participation is complete, or nearly so.

I hereby dedicate this work to my parents, Norman and Florence, and to my wife, Lynn, and to my future child, who is as yet unnamed.

ACKNOWLEDGMENTS

I am delighted to acknowledge the contributions made by the following people to the completion of this work. First, I thank Professor Eugene LeGoff and the members of his research group for the many discussions and suggestions offered during my years at Michigan State. I am especially grateful to my wife, Lynn, without whom this work, literally, would never have been finished. She served as typist and editor of the many drafts of this dissertation, no easy task. More importantly, she was my motivator, prodding, cajoling and cheering to the very end.

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Part I

SYNTHESIS OF STABLE FREE RADICALS AS POTENTIAL ORGANIC METALS

INTRODUCTION

The vast majority of organic compounds do not conduct electricity to any appreciable extent (10^{-12}-10^{-10}ohm^{-1}cm^{-1}). The very few with considerably higher conductivities have been given the optimistic if not entirely accurate description of "organic metals".

The word "metal" is generally reserved for elements lying to the left of boron, silicon, germanium, antimony and polonium in the periodic table.[1] In this sense the term "organic metal" is a misnomer as no metal atoms are present. In contrast, the class of compounds known as "organometallic" does involve metal atoms, specifically those bonded to a carbon atom in an organic framework.

Alternatively, a metal may be considered to be any substance possessing metallic characteristics, i.e., high electrical conductivity, thermal conductivity, luster and ductility or malleability.[1] In this sense the term "organic metal" is at least partially accurate.

The first organic materials found to have considerable conductivities were radical ion salts of tetracyanoquinodimethane, TCNQ, with various organic electron donors.[2,3] The most studied example of this class of compound is the charge transfer salt of TCNQ with the electron donor tetrathiafulvalene, TTF.

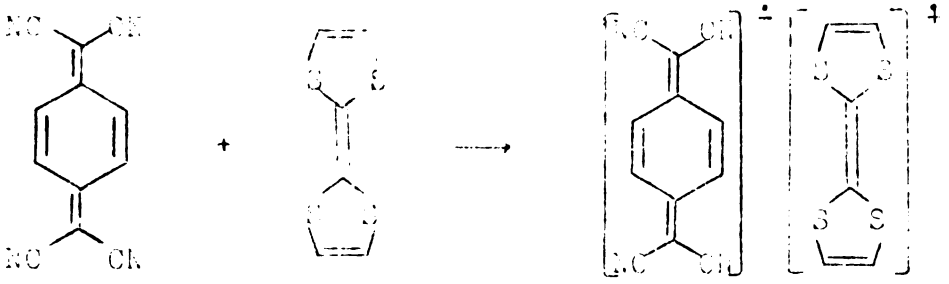


Figure 1. Formation of TCNQ-TTF.

This complex has a room temperature conductivity of $10^2 ohm^{-1} cm^{-1}$, comparable to graphite. For a comparison of the conductivity of TCNQ-TTF with that of other materials see Table 1. The properties of the salt have been detailed by Engler.[4]

Table 1. Conductivity of Selected Materials[5]

Material	$(ohm^{-1}cm^{-1})$
metals	10^4-10^6
TCNQ-TTF	10^2
carbon	10^2
molten organic salts	1
silicon	10^{-4}
alkali TCNQ salts	10^{-4}
most molecular crystals	10^{-14}-10^{-10}
ferrocene	10^{-13}
sulfur	10^{-14}
quartz	10^{-17}
anthracene	10^{-17}

Since the discovery of TTF-TCNQ, several variations have been made in both the donor and acceptor molecules. Changes in the donor molecule[6] have involved replacing the hydrogens in TTF with methyls, polymethylene bridges or benzo rings, and/or replacing the sulfur atoms with selenium. The room temperature conductivities of the compounds with TCNQ range from 10^{-5}ohm^{-1}cm^{-1} to 2×10^{3}ohm^{-1}cm^{-1} for the tetraseleno analog of dicyclopenteno-TTF.[6] Changes in the acceptor has involved adding substituents to the ring of TCNQ,[7] extending the ring system of TCNQ[8] and/or substituting heteroatoms into the ring system of TCNQ[9,10,11]. Unfortunately, those of the above which form charge transfer salts with TTF have room temperature conductivities less than that of TCNQ-TTF.

There are two further properties of TCNQ-TTF and similar compounds which bear mention. First, single crystals of these complexes carry an electric current much more readily along one axis of the crystal than along any other axis. They are thus anisotropic or more specifically, one-dimensional metals.[10] Secondly, the conductivity of TCNQ-TTF increases with decreasing temperature, reaching a maximum at 58°K of over 10^{4}ohm^{-1}cm^{-1}, then falling off sharply at still lower temperatures.[12] This sudden drop-off in conductivity is known as the Peierls transition.[13] It is thought that this transition from conductor to semi-conductor or insulator is

due to distortions in the crystal to lower symmetry.[14]

The maximum value of $10^4 ohm^{-1} cm^{-1}$, approaches the conductivities of certain metals (tin, lead) with conductivities of $5x10^4$-$1x10^5$. This sharp maximum in conductivity[15] at low temperature is reminiscent of the superconductors, metals which in fact lose all resistance at very low temperatures, usually within a few degrees of absolute zero.[15]

Several recently prepared derivatives have proven even more successful and have shed new light on the design of organic metals. These were a series[16] of organic cation radical salts $(TMTSF)_2X$, where TMTSF is tetramethyltetraselenafulvalene (see Figure 2), and X is a symmetrical octahedral anion[16] PF_6^- [16a], AsF_6^- [16b,c], SbF_6^- [16d] and TaF_6^- [16d] or tetrahedral anion[17] BF_4^- and ClO_4^-. The former exhibit superconductivity at moderate hydrostatic pressures of 1.2 GPa in the 0.4-1.5°K region.[16] In these materials high pressure suppresses a metal-to-insulator transition occurring between 10 and 20°K at ambient pressure.[16] In the tetrahedral anion series, $(TMTSF)_2BF_4$ and $(TMTSF)_2ReO_4$ are insulating below 41 and 182°K respectively, while $(TMTSF)_2ClO_4$ remains metallic down to 1.3-1.5°K, where a transition into a superconducting state occurs.[16]

These substances consist of two donor molecules per anion. Thus, formally, only half of the TMTSF molecules are

charged. The structure of the crystal is as might be expected. The planar TMTSF molecules are stacked like pancakes. These stacks are interspersed with lines of anions.[17]

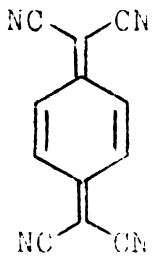
X-ray crystallography of TCNQ-TTF shows separate stacks of TCNQ radical anions and TTF radical cations, with the planar ions in each stack arranged parallel to one another, though not perpendicular to the stack.[18] The distance between molecules in the TCNQ stacks is 3.17A. These very short interplanar distances allow overlap of the pi-clouds and delocalization of the unpaired electrons along the axis of the stack (see Figure 2). Combining conductivity measurements along the various axes of a single crystal with X-ray data shows that the direction of conductivity is parallel to the stacks of TTF and TCNQ ions.

For both practical and theoretical reasons, it is clearly of interest to develop new organic metals.[20] Practical examples include the development of materials which may be superconductors at higher temperatures than are now available. Theoretically, the investigation of such phenomena as the Peierls transition could be aided by the availability of organic metals with higher conductivities.

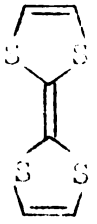
There have been several papers which detail factors important in the design of an organic metal as determined by experimental and theoretical studies.[17,19,20,21] Among these factors are: (1) An unpaired electron.[19] Clearly this is

necessary to allow the motion of individual electrons between molecules. Paired electrons are held in molecular orbitals. This is, of course, why most organic compounds are insulators.

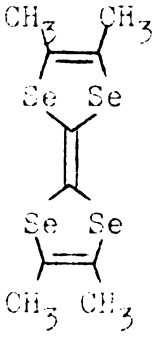
(2) Uniform crystal structure. The conduction band arises



TCNQ



TTF



TMTSF

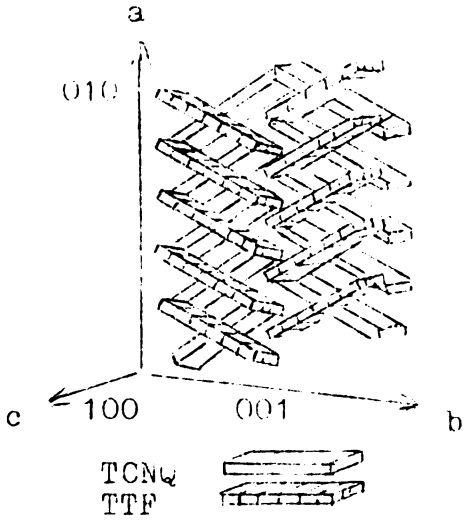


Figure 2. TCNQ, TTF, TMTSF and the crystal structure of TCNQ-TTF.

from a linear combination of the highest occupied molecular orbitals (or conduction orbitals) on each molecule.[19] Crystal defects (as with Peierls distortions) lower symmetry and separate the valence band from the conduction band. The presence of counterions may contribute to Peierls distortions, or at least reduce the symmetry of the crystal. Garito, Heeger and co-workers have suggested,[12,21] in fact, that only one of the two kinds of chains in TTF-TCNQ actually carries a current while the other simply supplies a framework. This is the case in the superconductors $(TMTSF)_{2X}$, and the stack which carries the current is the TTF-like donor, TMTSF, rather than a TCNQ-like acceptor as was earlier thought likely.[20] Clearly if the counterion could be eliminated, symmetry could be increased and, perhaps, defects and distortions decreased. (3) Weak electron-electron repulsion or low ionic fluctuation energy. This is the energy required to transfer an electron from one molecule to the next, as shown in Figure 3 for several types of organic metals. The second type shown in Figure 3, representing incomplete electron transfer from donor to acceptor, would appear to have the lowest ionic fluctuation energy. It has been suggested[22] that complete electron transfer is not only unnecessary, but may actually be detrimental to the stability of the metallic state in organic charge transfer salts. In fact, those salts with highest conductivity contain the

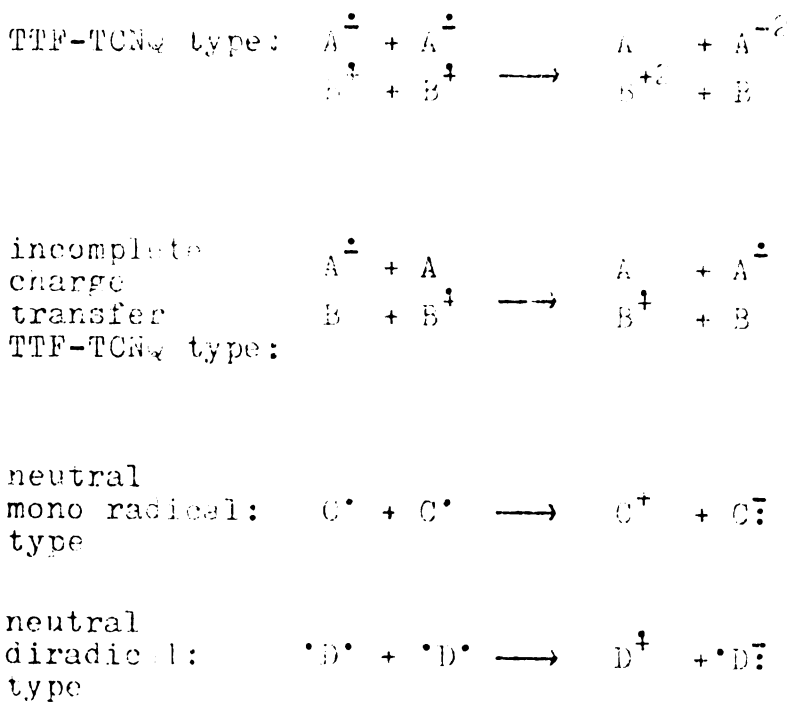


Figure 3. Mechanism of electron transport for several types of organic metals.

species in mixed valence states.[22] This is the case for the $(TMTSF)_2D$ superconductors in which the valence of TMTSF is formally $+\frac{1}{2}$. Thus careful matching of donor and acceptor based on the difference in their oxidation and reduction potentials, respectively, could serve to maximize conductivity. This may explain why some donors only form conducting salts with particular acceptors.[23] (4) Maximum intermolecular transfer integra. The greater the overlap between pi-clouds of adjacent molecules in an organic conductor, the greater the conductivity. This can be achieved in two ways. First, simply decrease the intermolecular distance (Figure 4a). As

the molecules in a given stack of a radical ion salt such as TTF-TCNQ have the same charge, removing the charge would reduce coulombic repulsion and thus decrease intermolecular distance. Secondly, as mentioned earlier, the planes of the TTT and TCNQ radical ions are not perpendicular to the axes of the stacks. Rather they are offset or not directly "above" one another.[24] It is thought that this offset may be due to coulombic attraction to the counterions in adjacent stacks as well as coulombic repulsion between molecules within stacks.[25] Clearly, eliminating the charges could reduce the intermolecular offset and thus increase overlap (Figure 4b).

Based on the above, Haddon[19] proposed that stable neutral radicals, specifically odd-alternant hydrocarbons, could serve

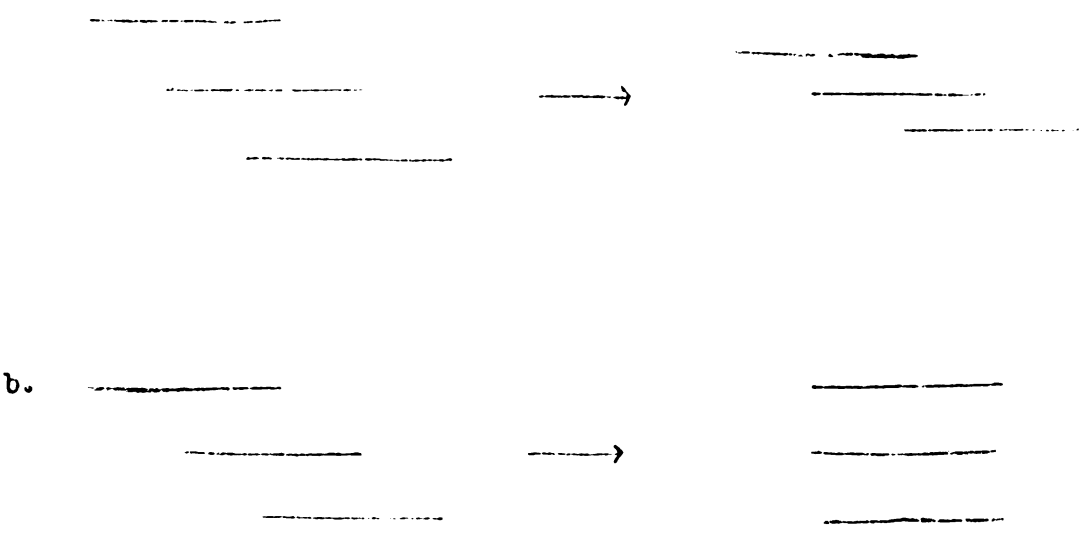
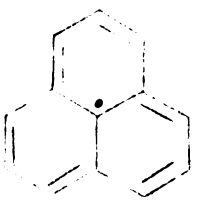


Figure 4. Increasing the intermolecular transfer integral

as models for new organic conductors. Based on calculations (MINDO/3 SCF MO) of geometry, bond order and charge densities, he found the phenalenyl (ply) system to have many of the characteristics (outlined above) considered important in the design of organic metals.

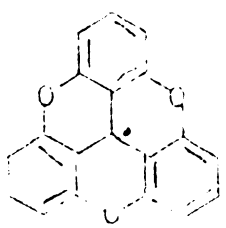


ply

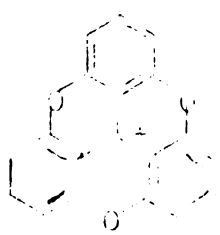
Specifically, it has a delocalized odd electron, no charge, and a planar symmetrical structure. Furthermore, the redox orbital in which the odd electron resides is non-bonding. Calculations show that addition or removal of an electron changes the geometry of the system very little and the energy requirement is equally small. Unfortunately, the phenalenyl radical, though stable in solution undergoes dimerization on attempts to isolate the solid radical.[26]

Haddon[19] also mentions the triphenyl methyl system in passing as an odd-alternant hydrocarbon, but dismissed it out of hand due to its non-planar nature. He apparently did not

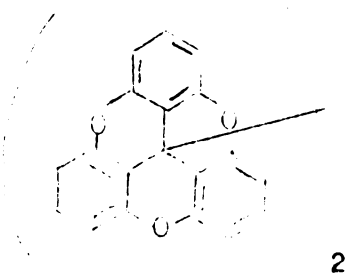
consider a bridged triphenylmethyl such as sesquixanthydryl, 1. The corresponding carbonium ion, 2, was prepared in 1963



1



2



3

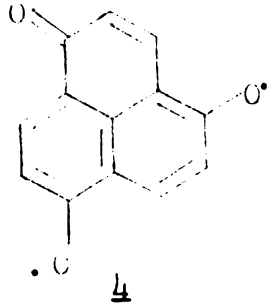
by Martin and Smith.[27] Chromous ion reduction of 2 gave a dimer, probably 3, presumably through the radical 1.[28] Heating the dimer in xylene to 150°C causes dissociation and dissolution enough to allow detection of the radical by ESR.[29] The ESR spectrum of 1 consists of a quartet (J=3.17 gauss) of septets (J=0.89 gauss), arising from the three identical para protons and the six identical meta protons.

Other factors suggested by Garito and Heeger[20] to stabilize the metallic state in organic conductors include nominal divalency to promote mixed valence states, and heteroatoms at points of high spin density in order to stabilize the radical. Thus it was our intention, and the object of my research to extend the idea of planar stable free radicals to include

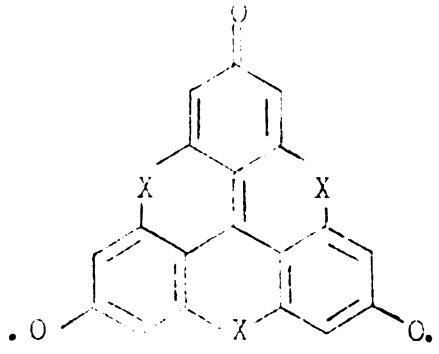
diradicals like 4 and 5.

a:X=CH_2

b:X=O



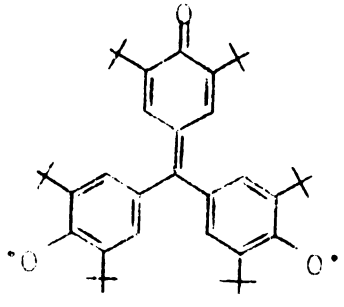
4



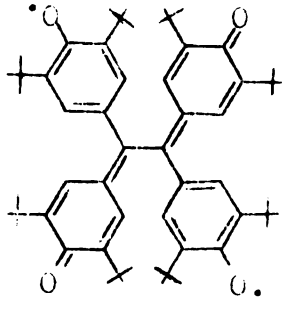
5

These diradicals include the features of the phenalenyl/bridged triarylmethyl systems (planar, symmetrical, delocalized, neutral) and add the features of divalency and heteroatoms at the spin-rich periphery.

That cross-conjugated diradicals of this type can be stable is illustrated by the synthesis in 1960 of 6.[29]



6



7

The triplet ground state for 6 has been studied by ESR spectroscopy,[30] and justified by detailed molecular orbital calculations.[31] A similar diradical, digalvinoxyl, 7, was studied by Chandross; and also shown to be a triplet.[32] Interestingly both 6 and 7 are highly colored with a metallic luster. However, neither is reported to be conducting.

It may well be that much of the stability of 6 and 7 is due to the steric efforts of the bulky t-butyl groups. The same steric effect would be expected to keep the molecules far enough apart in the crystalline state to prevent overlap of the pi-clouds and thus preclude conductivity. In addition it was thought that the rings in 6 and 7 were not coplanar, but rather propeller-like, thus preventing complete delocalization. It was our hope that the planar molecules 4 and 5 would stabilize the diradical enough that the bulky t-butyl groups would be unnecessary.

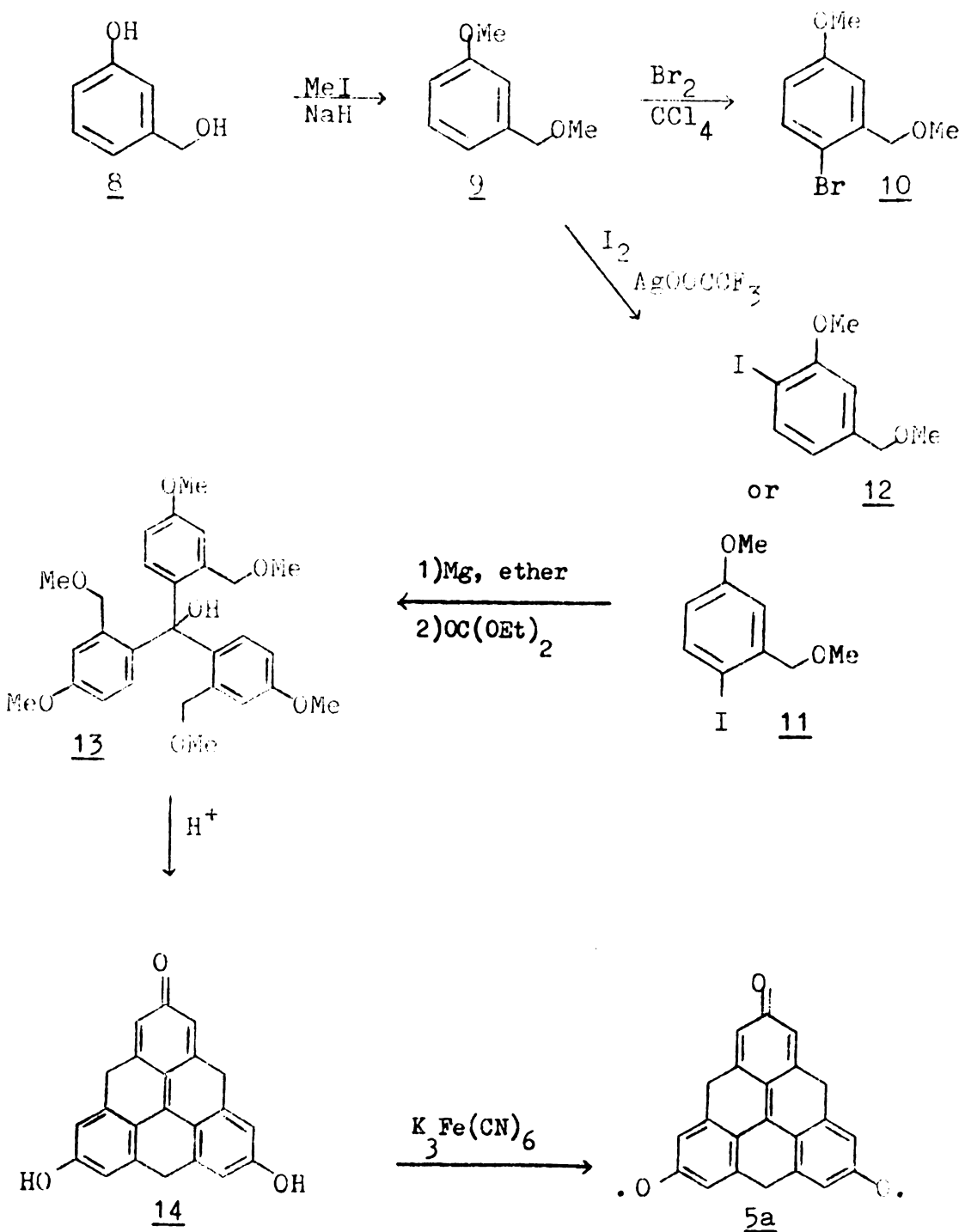


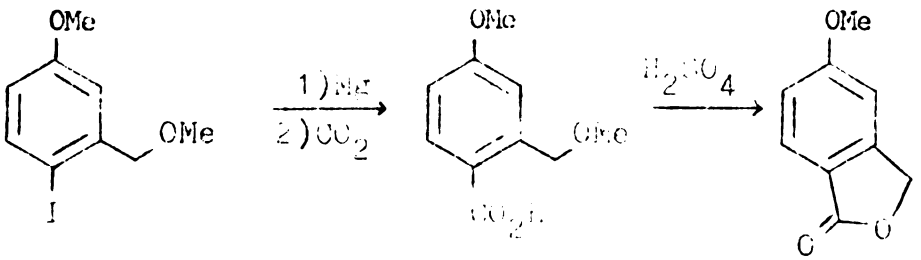
Figure 5. Proposed synthesis of diradical 5a.

RESULTS AND DISCUSSION

The proposed synthesis of diradical 5a is given in Figure 5.

The methylation of 3-hydroxybenzyl alcohol is straightforward and occurs in quantitative yield with sodium hydride and methyl iodide.

The halogenation step is interesting in that the product could be one of two isomers, 11 or 12, ignoring the isomer in which the halogen atom is substituted between the other two substituents. Bromination (Br_2/CCl_4) gives a mixture of isomers, including 4-bromo-3-methoxymethylanisole (10). Iodination (using I_2 and $AgOOCCF_3$) appears to give a single isomer as determined by nmr and TLC. Normal instrumental methods of structure elucidation all fail to distinguish unequivocally between the possible isomers. The pmr spectra, though clearly resolved cannot differentiate between isomers (see Table 2). The structure of 11 was finally determined by the following sequence of reactions.

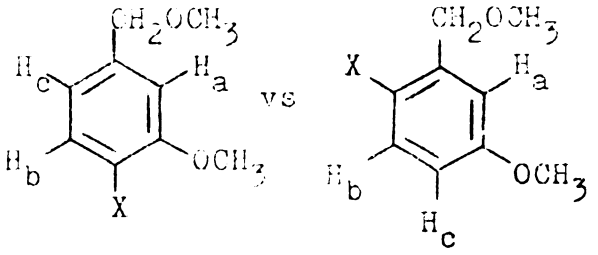


11 15 16

Figure 6. Determination of isomer 11.

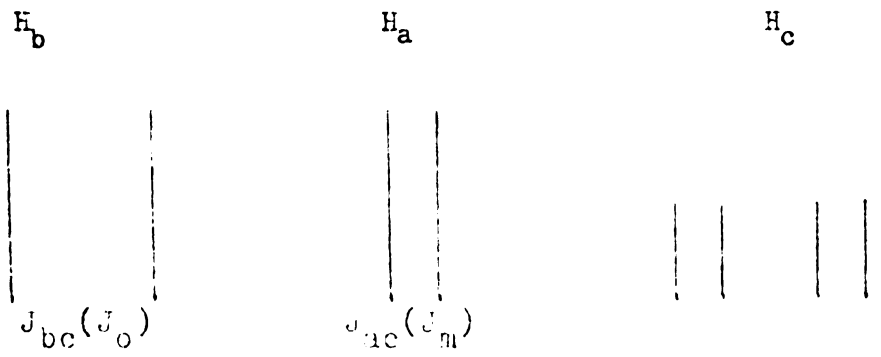
The structure of lactone 16 was proven by mass spec., nmr and IR. Thus the monoiodo compound must be 11, as 12 would not give a δ-lactone in the above reaction sequence. As the nmr spectrum of the isolated monobromo isomer is almost identical to that of 11, it is assumed that it is 10.

Table 2. PMR Chemical Shifts (ppm downfield from TMS)



	X=H	X=Br	X=I	X=COOH
$-CH_2-$	4.25	4.30	4.21	4.79
$BzOCH_3$	3.23	3.34	3.33	3.44
$PhOCH_3$	3.62	3.63	3.63	3.79
H_a		6.90 (J=3Hz)	6.80 (J=3Hz)	7.10 (J=3Hz)
H_b		7.16 (J=8Hz)	7.36 (J=8Hz)	7.93 (J=8Hz)
H_c		6.45 (J=3Hz,8Hz)	6.30 (J=3Hz,8Hz)	6.70 (J=3Hz,8Hz)

Table 2 (cont'd.)



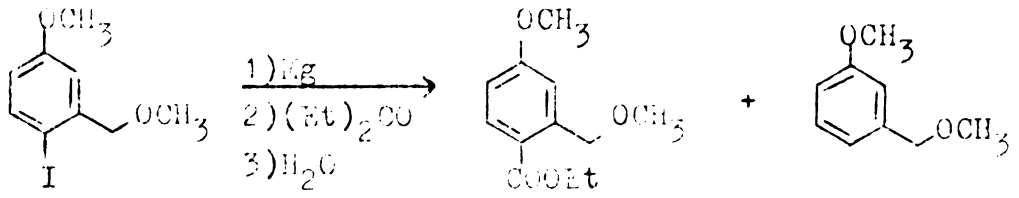
lit[34] values

J_o: 6-10 Hz

J_m: 4-3 Hz

J_p: 0-1 Hz

Treatment of iodide 11 with magnesium followed by diethyl carbonate did not give the desired triaryl methanol, 13. Instead only ethyl 4-methoxy-3-methoxymethylbenzoate, 17 and the diether, 9 were isolated, along with some starting material.



11 17 9

An approach to molecule 5b is shown in Figure 7.

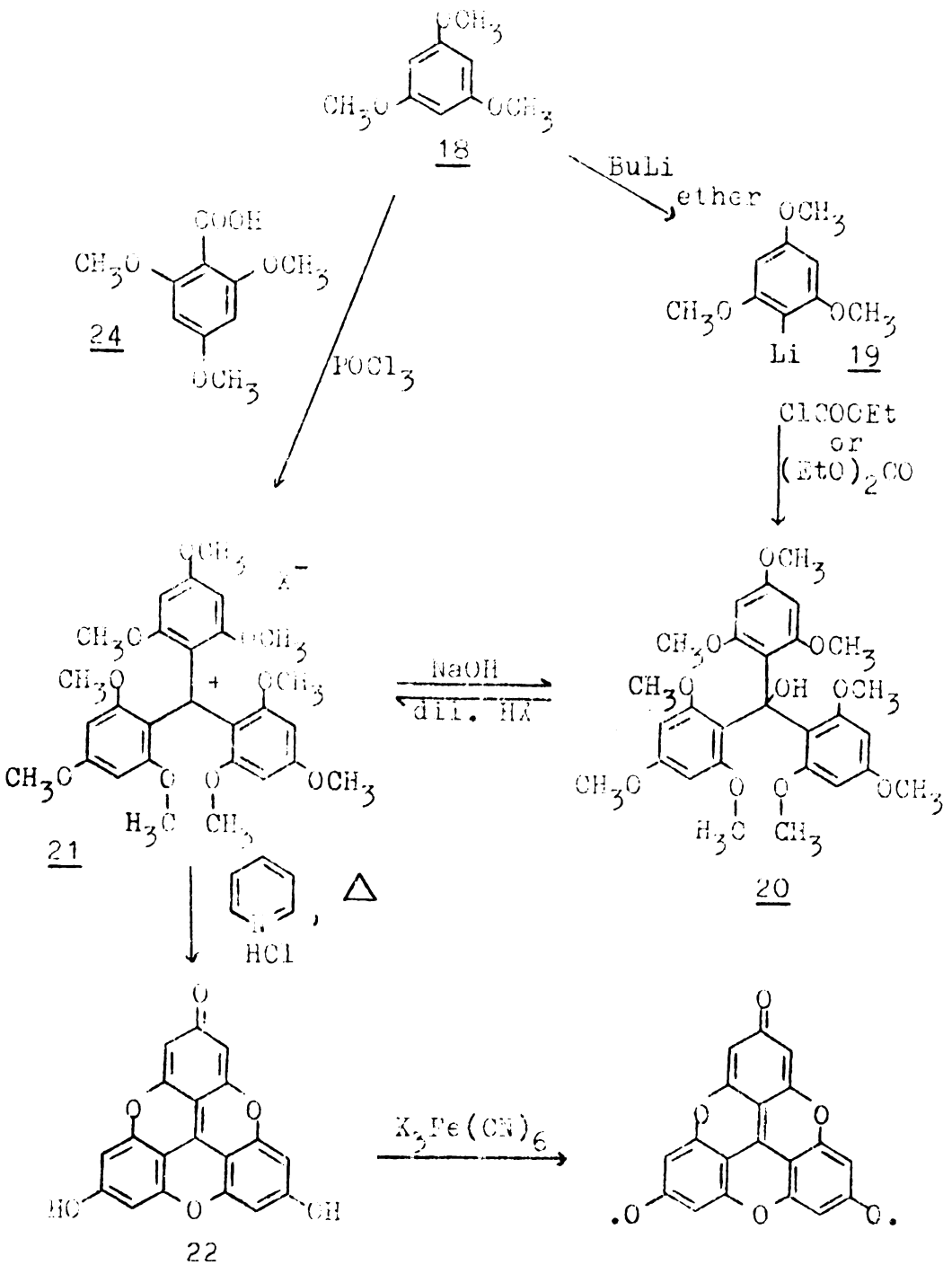


Figure 7. Proposed synthesis of diradical 5b.

Martin and Smith[27] have prepared the bridged triaryl carbonium ion 2 by the reaction of the lithium salt of resorcinol dimethyl ether with diethyl carbonate to give the triaryl methanol, followed by heating with pyridine hydrochloride. It appears, therefore, that the first step of the

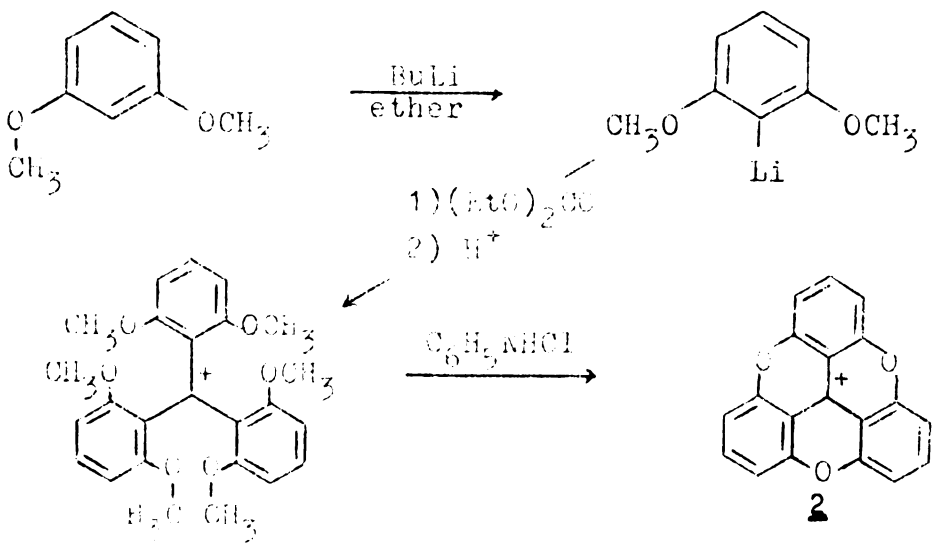


Figure 8. The synthesis of 2 as per Martin and Smith.[27]

sequence shown in Figure 8 should be straightforward. Upon addition of an ether solution of butyllithium to an ether solution of 1,3,5-trimethoxy benzene, a light yellow color results and darkens slowly over a period of time. No precipitate is observed. Upon addition of diethyl carbonate in benzene, the color changes very rapidly to a dark yellow and eventually turns muddy green. The tarry substance obtained is not soluble in water and only slightly soluble in ether.

It is, however, soluble in dilute acid, turning a brilliant deep blue color. The blue material was shown to be the triaryl carbonium ion 21 with the counterion X^- depending on the acid used in the work-up. When dilute hydrochloric acid is used the counterion X^- is chloride. The blue triaryl methyl carbonium ion 21 is analogous and quite similar in its properties to the hexamethoxy triaryl methyl carbonium ion 25 of Martin and Smith[27] (Figure 8).

The blue material can be extracted into chloroform or methylene chloride but is insoluble in benzene. The yield of blue material is only about two percent in this reaction. However, if ethyl chloroformate is used instead of diethyl carbonate yields up to 80% can be obtained.

Reaction of the aryllithium 19 with methyl 2,4,6-trimethoxy benzoate gives the blue material 21 but in poor yield. This ester was prepared from the corresponding acid using sodium carbonate and methyl iodide rather than via the acid chloride, because 2,4,6-trimethoxybenzoic acid readily decarboxylates under acid conditions, as discussed below.

Upon treatment of the blue carbonium ion 21 with hydroxide, it becomes muddy yellow and can be extracted into copious amounts of ether. It is assumed that this material is the triaryl methanol 20.

Using a Grignard reagent instead of the organolithium as outlined above is unsatisfactory for several reasons. First, preparation of the organometallic reagent requires two steps in the case of the Grignard and only one in that of the organolithium. Second, monobromination of trimethoxybenzene is no simple task as di- and tri-bromination tend to occur quite readily. Third, formation of the Grignard is sluggish. Finally, the only products isolable from the reaction of the Grignard reagent with ethyl chloroformate are ethyl 2,4,6-trimethoxy benzoate, 27, and starting material 18.

The same products are obtained on heating 2,4,6-trimethoxybenzoic acid 24, with thionyl chloride followed by evaporation and refluxing in ethanol. The production of 1,3,5-trimethoxybenzene in this reaction is apparently due to acid catalyzed decarboxylation in the thionyl chloride step. The same process occurs in phosphorus oxychloride. The mechanism of this decarboxylation may involve catalysis by traces of proton present in the reaction mixture, aided by the unusual stability of the trimethoxybenzenium ion.

A second approach to the triaryl methyl system (21) involves the phosphorus oxychloride induced condensation of 2,4,6-trimethoxy benzene 18 as shown in Figure 7.

When 2,4,6-trimethoxybenzoic acid is heated with two equivalents of 1,3,5-trimethoxybenzene in phosphorus oxy-

chloride as solvent, the reaction mixture became deeply colored. Work-up involves carefully diluting the reaction mixture with ice, washing with benzene, and extracting the deep blue product into chloroform. Yields range from 5% to 20% and seem to depend strongly on the initial ratio of starting materials used. The only other organic material isolated from the reaction mixture is 1,3,5-trimethoxybenzene, and its quantity accounts for the portion of both starting materials not going to product. Hence, 2,4,6-trimethoxybenzoic acid apparently decarboxylates under the reaction conditions as discussed earlier for reaction with thionyl chloride. The best yield (20%) was obtained when a ratio of 4:1 trimethoxybenzene:trimethoxybenzoic acid was used.

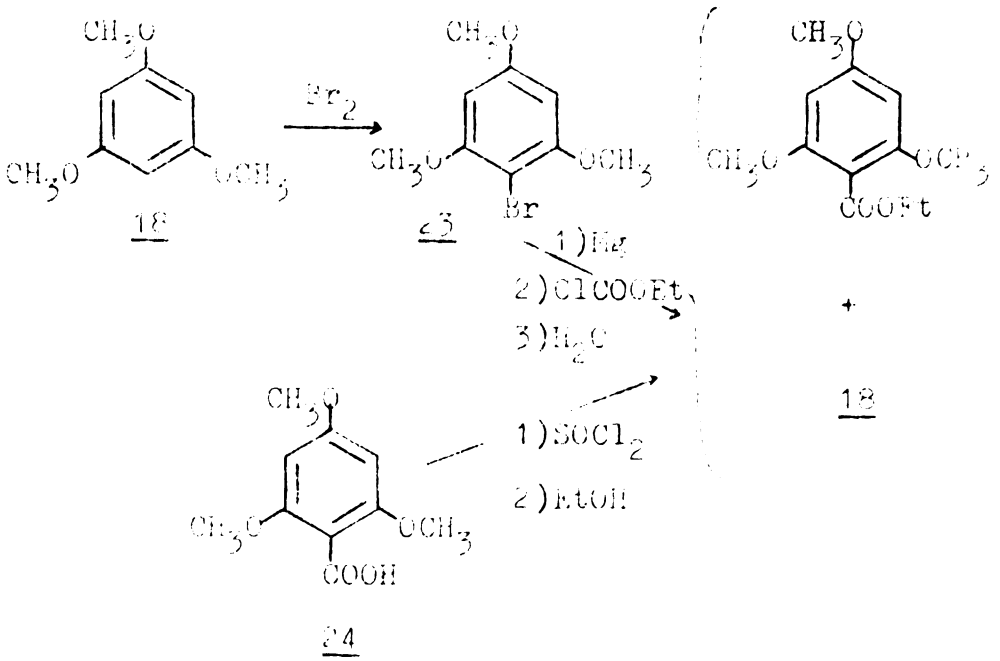


Figure 9. Attempted Grignard synthesis of 21.

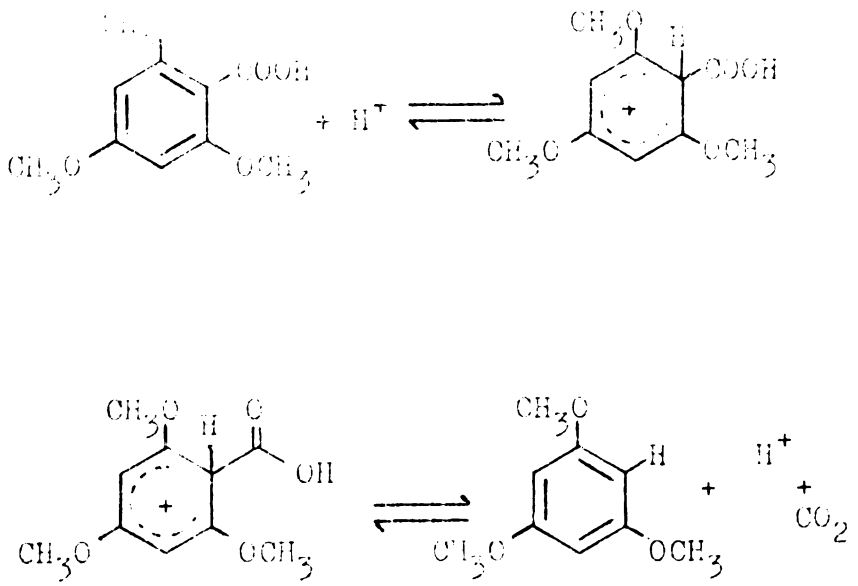


Figure 10. Mechanism of decarboxylation of 24.

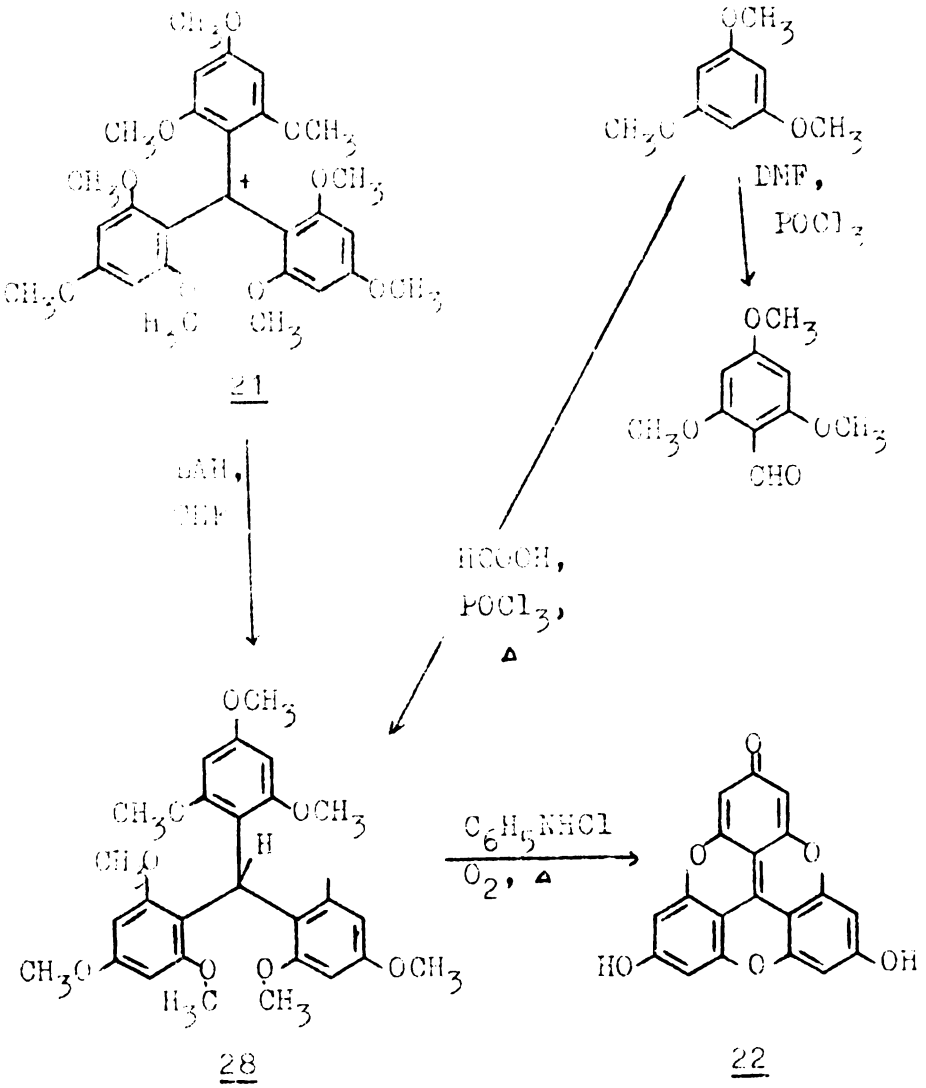
The product is a deep blue-black solid which decomposes at 110°C. The NMR is as expected and the mass spectrum shows a large parent ion at m/e=513, corresponding to the tris(trimethoxyphenyl)methyl carbonium ion.

Reduction of the blue triaryl carbonium ion 21 with lithium aluminum hydride gives the expected triarylmethane 28. This material can also be prepared by adding formic acid to a hot solution of 1,3,5-trimethoxybenzene in phosphorus oxychloride. Large amounts of formic acid are needed as most of it decomposes in phosphorus oxychloride to hydrochloric acid and carbon monoxide. Treatment of 1,3,5-trimethoxybenzene with DMF in $POCl_3$ gives only the Vilsmeier product, 2,4,6-trimethoxybenzaldehyde.

The diphenol 22 was prepared from the carbonium ion 21 by the method of Martin and Smith,[27] that is by fusion in pyridine hydrochloride (prepared by passing hydrogen chloride through a dry solution of pyridine in ether).[35] (See Figure 7). Similar treatment of the triarylmethane 28 with pyridine hydrochloride gives the same product 22. Apparently incidental oxygen in the reaction mixture serves as the oxidizing agent.

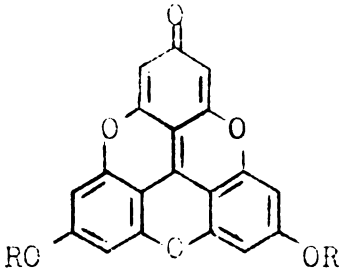
The diphenol 22 is a highly insoluble brick red material whose characterization is difficult. Thus one or more soluble derivatives were necessary.

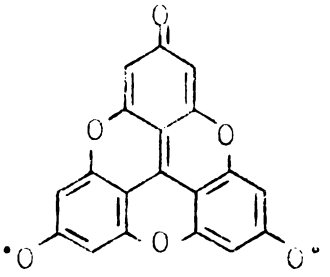
Several attempts to prepare such soluble derivatives of 22 led to the eventual preparation of the diether 30, characterized by nmr (δ0.90,t,6H;δ1.10-1.67,m,24H;δ3.90,t,4H;δ5.97,s, 2H;δ6.25,s,4H) and mass spec. (m/e 556, 444, 332). Furthermore, the diacetate 31 was prepared (acetic anhydride, pyridine)



21 28 22

Figure 11. Preparation of triaryl methane 28.





22 R = H

30 R = n-C_8H_{17}

31 R = $COCH_3$

5b

Figure 12. Sesquixanhydrone-diol and derivatives

and an nmr spectrum of the crude, chloroform-soluble material showed the presence of acetate, but it was not purified.

Oxidation of 22 in an attempt to prepare 5b was carried out in aqueous KOH under N_2 atmosphere using $K_3Fe(CN)_6$. A white solid was obtained in 80% yield which was totally insoluble in all solvents, though the solid turned blue in acidic solvents. The material gave no detectable signal in the mass spectrometer. It was assumed that the radical had polymerized.

One attempt to chlorinate 22 was made using NaOCl. This reaction gave a red solid, but it could not be characterized.

Figure 13 shows the route used to prepare 4,7-dihydroxyphenalenone 36, as well as the diether 37 and the diacetate 38.

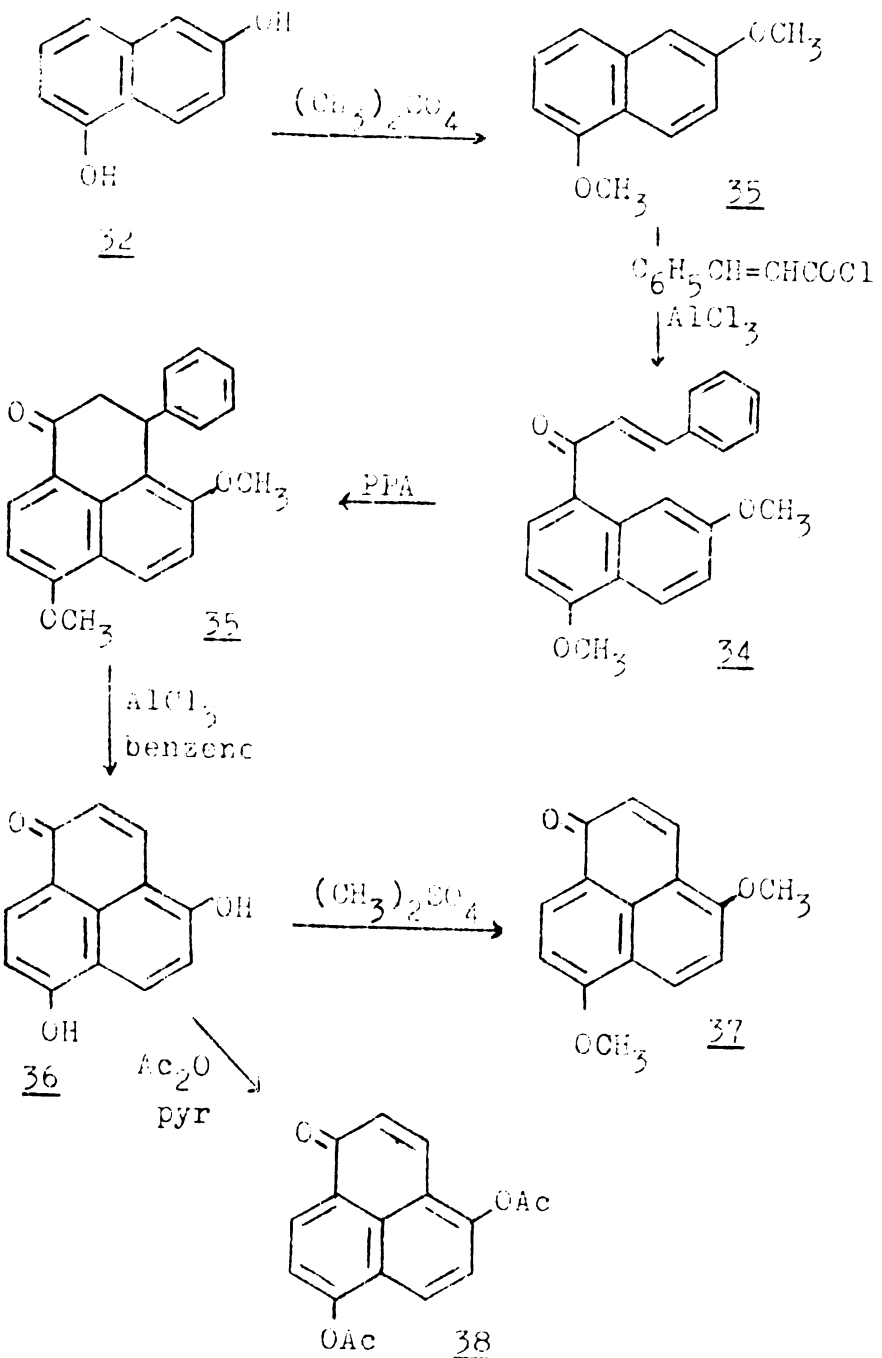


Figure 13. Synthesis of 4,7-dihydroxyphenalone (36) and derivatives.

All but the first step were taken from M. Jarcho.[36]

Methylation of commercial 1,6-dihydroxynaphthalene gave the corresponding diether in 80% yield. Friedel-Crafts acylation with trans-cinnamoyl chloride (generated in situ from trans-cinnamic acid and phosphorus pentachloride) in benzene gave a 71% yield of the single isomer 4-cinnamoyl-1,6-dimethoxynaphthalene. Cyclization occurs in 85% yield in polyphosphoric acid. Treatment of 35 with anhydrous $AlCl_3$ in refluxing benzene results in elimination of the elements of benzene, as well as demethylation, to give a quantitative yield of 36. Methylation of 36 gave only a 30% yield of diether 37. The method given by Jarcho for preparing the diacetate 38 (acetic anhydride, catalytic amount of con. H_2SO_4) failed in my hands, but treatment with acetic anhydride and pyridine gave the diacetate in 70% yield.

At this point an oxidation of 36 was attempted. An oxygen-free solution of $K_3Fe(CN)_6$ in water was added to an oxygen-free solution of 36 in aqueous KOH. The whole system was kept under nitrogen atmosphere. The solution gradually turned from light orange to dark red, which may indicate the formation of a radical or diradical. The material appears to be stable in basic solution, but defies all attempts to isolate it. On introduction of even traces of oxygen, an intractable red solid appears.

Much time was spent in attempts to halogenate 36, 37 and 38. This problem was approached from several angles. The dihydroxy compound 36 was treated with halogen or hypohalite in basic media. The dimethoxy compound 37 was treated with halogen in various organic solvents, and the diacetate with chlorine in acetic acid, with and without added acetate. Because 36 and its halogenated derivatives are insoluble in organic solvents other than pyridine and DMSO, the products of halogenation of 36 were converted to the corresponding diethers or diacetates for purification and characterization. Table 3 lists the reactions carried out and the results of each.

Since we had little success with the direct introduction of three halogen atoms onto the delocalized ring system 36, 37, 38, the feasibility of halogenating intermediate 35 in two or more steps was studied. Figure 14 illustrates the possible pathways. Treatment of 35 with chlorine in benzene at room temperature gave a mixture of 45 or 46 (mp 159-165 dec) and 47 (mp 144-147) in a 60:40 ratio. Note that it is very difficult to distinguish between isomers 45 and 46. The mass spectrum of 47 also showed a small peak at m/e 350 corresponding to 48 or an isomer. The same reaction in the presence of $FeCl_3$ gave mostly tar but a small amount of 45 or 46 was isolated (less than 10%).

Treatment of 35 with 5% aq. NaOCl/methanol in a heterogeneous reaction gave a 60% yield (the remainder being unreacted starting material) of 42. Due to contamination by starting material it was impossible to tell if either or both diastereomers were present.

Reaction of 42 with aluminum trichloride in refluxing benzene gave an insoluble red material which on treatment with acetic anhydride and pyridine gave a 50% yield (from 42) of 50.

Table 3. Halogenation of 36 and derivatives.

Starting material	Conditions	Results
36	1) Br_2, pyridine 2) $(CH_3)_2SO_4$, NaOH	10% yield of mixture of mono-, di-, and tri-bromo diethers by mass spec
36	1) Br_2, aq. NaOH 2) Ac_2O, pyridine	tar
36	1) NaOCl 2) $(CH_3)_2SO_4$, NaOH	insoluble black powder
36	1) NaOCl 2) $C_8H_{17}I$, NaH	insoluble black powder
36	1) NaOCl 2) Ac_2O, pyridine	uncharacterizable oil
37	Br_2, CH_3CO_2H	insoluble black oil
37	Br_2, CH_3CO_2H, CH_3CO_2Na	30% yield of a dibromoether[a] 39
38	Cl_2, CH_3CO_2H, 0°	70% yield of a monochlorodiacetate[b] 40
38	Cl_2, CH_3CO_2H, 70°	insoluble black powder

[a] mp 240.5-242.5, m/e 398

[b] mp 195-197, m/e 330

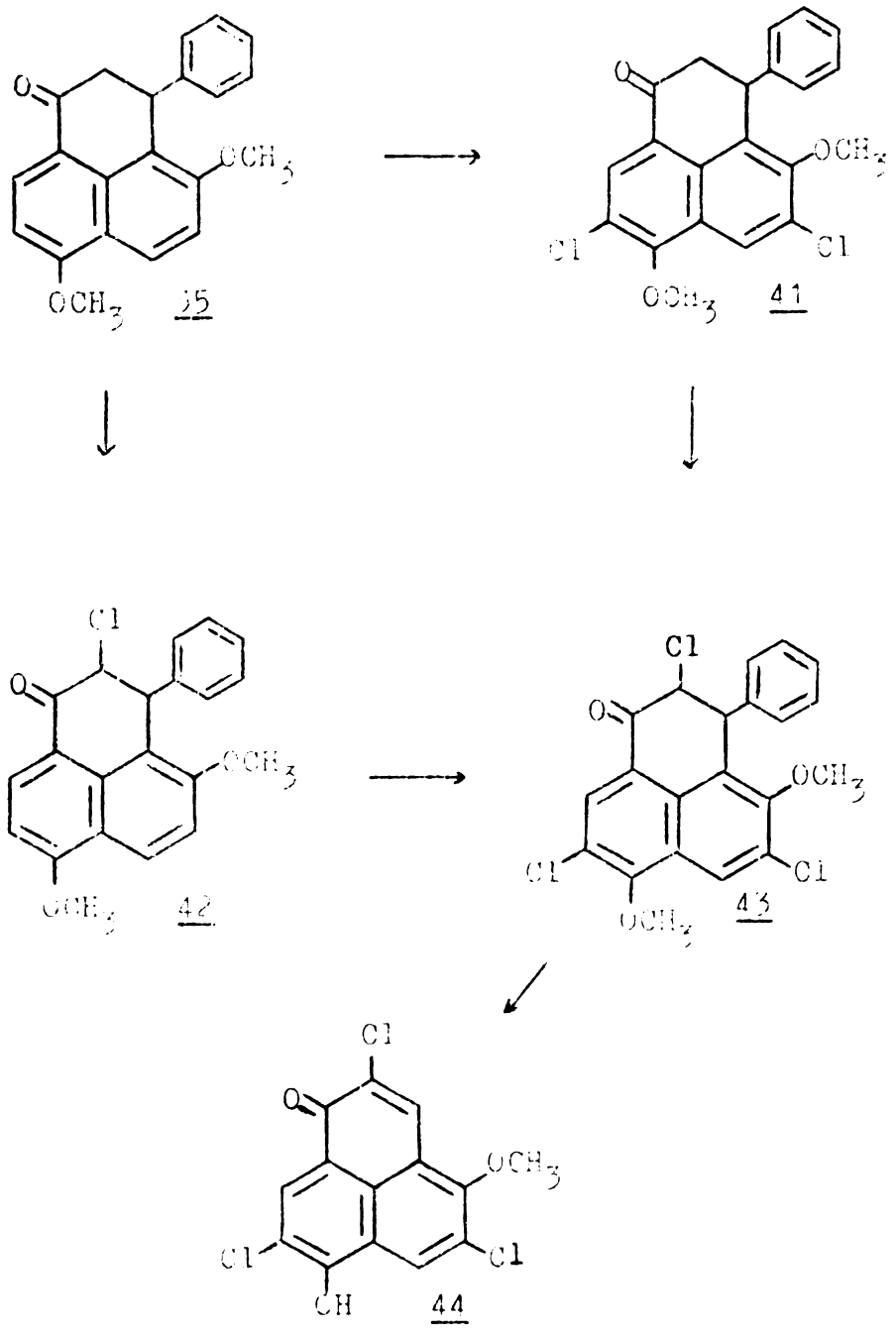


Figure 14. Proposed synthesis of 2,5,8-trichloro-4,7-dihydroxy-1H-phenalen-1-one (44) via 35.

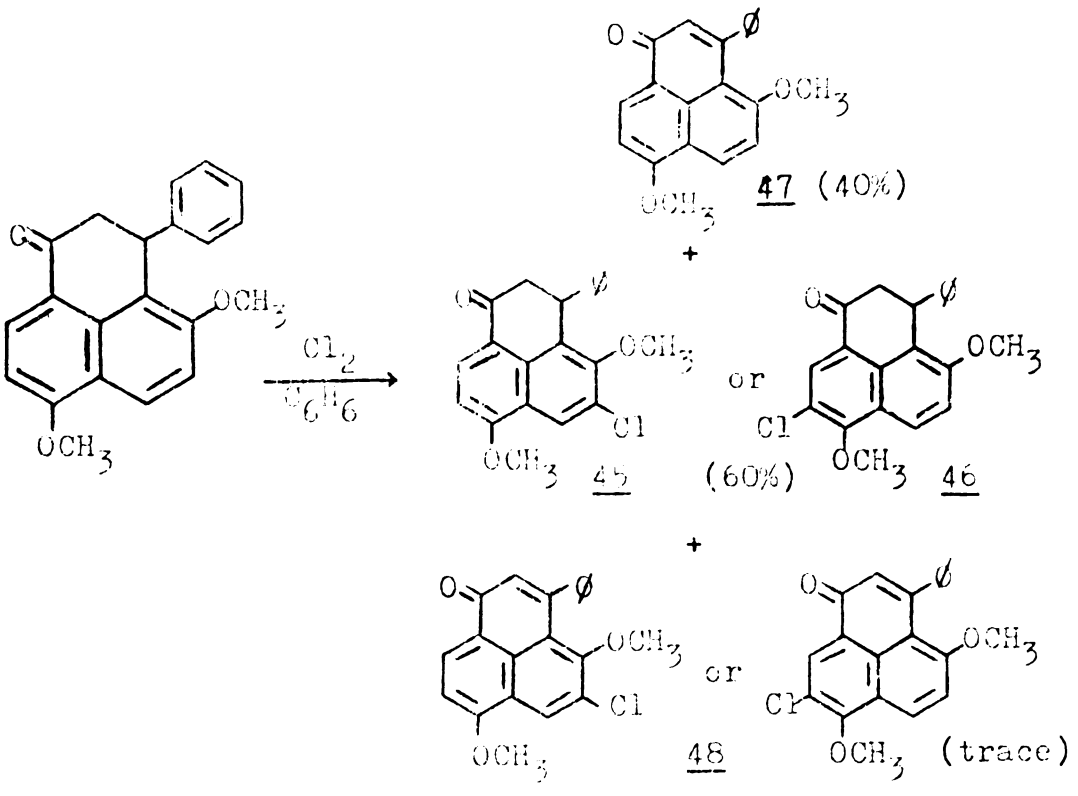


Figure 15. Chlorination of 35 with chlorine in benzene.

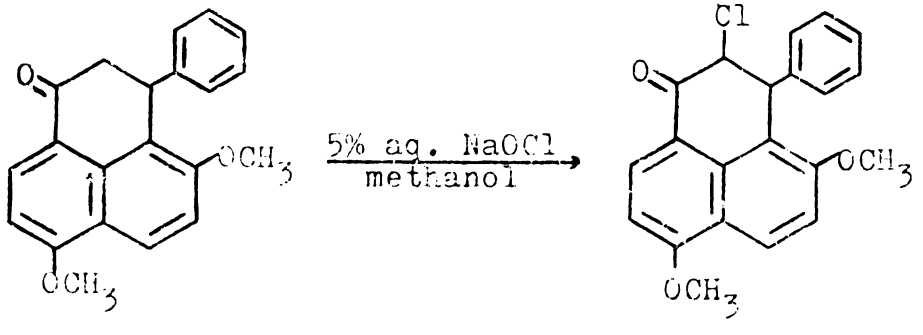


Figure 16. Chlorination of 35 with hypochlorite.

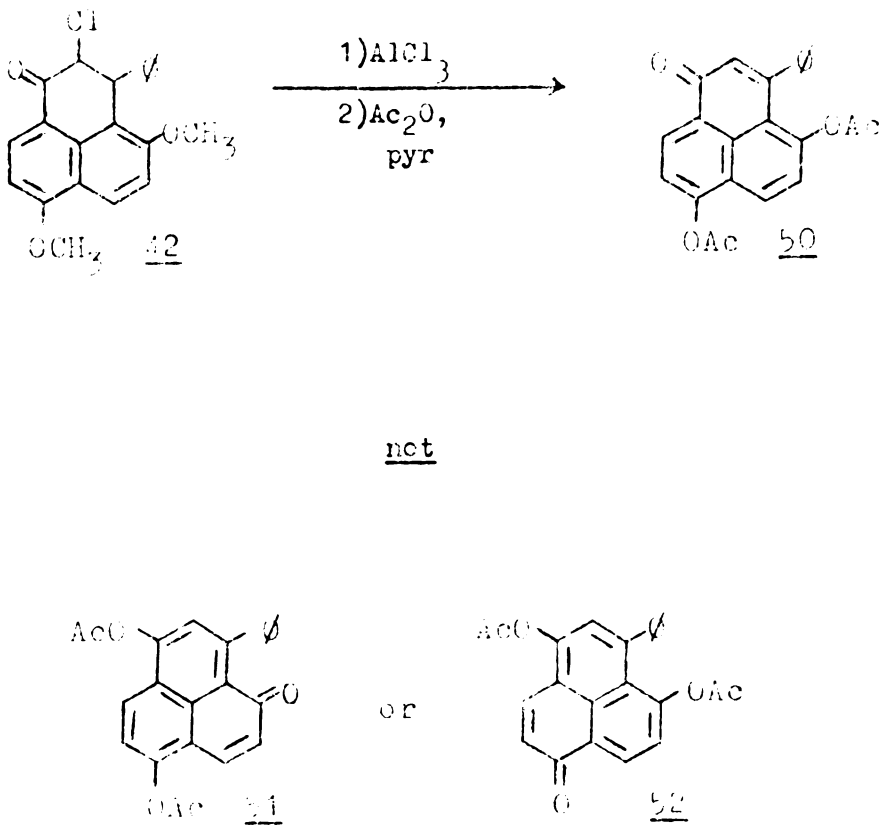


Figure 17. Reaction of 42 with aluminum trichloride.

It is interesting to note that though one might expect to obtain a mixture of isomers 50, 51 and 52, nmr and melting point data indicate the presence of only one isomer, apparently 50. In any case, the elimination of HCl from 42 though not unexpected, is not the desired result.

EXPERIMENTAL

Measurements. Boiling points and melting points were uncorrected. Melting points were determined on a Thomas-Hoover melting point apparatus. ^{1}H NMR spectra were recorded on a Varian T-60 or Bruker 180 NMR spectrometer. ^{13}C NMR spectra were measured with a Varian CFT-20 spectrometer. Both types of NMR spectra were obtained with tetramethylsilane as the internal standard unless otherwise noted. Chemical shifts (δ) in parts per million from the internal standard are given as positive values for downfield shifts in all cases. Infrared spectra were recorded on a Perkin-Elmer Infracord 137 spectrophotometer. Ultraviolet-visible spectra were recorded on a Unicam 800 or Lambda 3. Mass spectra were obtained on a Hitachi RMU-6 mass spectrometer by Mr. Mark Weidner or Mr. Ernest Taylor, to whom I hereby acknowledge my gratitude. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Solvents. Benzene was purified by distillation from sodium metal. Tetrahydrofuran (THF) was dried by distillation from potassium benzophenone ketyl. Anhydrous diethyl ether was prepared via distillation from lithium aluminum hydride. Each of the above distillations was performed under nitrogen.

Anhydrous dimethylsulfoxide (DMSO) was dried over and distilled from calcium hydride at reduced pressure and stored over 4 Å molecular sieves under nitrogen.

3-Methoxymethylanisole(9)[37]. A dried 250 ml, 3-necked round bottom flask equipped with magnetic stirring bar, addition funnel, condenser and drying tube was charged with 2.5 g (20 mmol) of 3-hydroxybenzyl alcohol (Aldrich) dissolved in 100 ml of dry tetrahydrofuran. To the mixture was added 10 ml (5.0 g, 35 mmol) of methyl iodide. The mixture was cooled in an ice bath and, while stirring, 2.4 g (100 mmol) of sodium hydride (previously washed with benzene) was added. The mixture foamed as hydrogen was liberated. After stirring at room temperature for 20 hours, an additional 10 ml of methyl iodide was added.

The excess sodium hydride was destroyed by the careful addition of saturated sodium sulfate. The THF was evaporated and the residue extracted thoroughly with ether. The combined organic phases were dried, filtered and evaporated. Short-path distillation gave 2.63 g (86%) of 3-methoxymethylanisole. Pmr: δ 3.23,s,3H; δ 3.62,s, 3H; δ 4.23,s,2H; δ 6.5-7.2,m,4H.

4-Bromo-3-methoxymethylanisole(10). To a solution of 2.00 g (13.2 mmol) of 3-methoxymethylansiole (9) in 40 ml of carbon tetrachloride was added very slowly and with stirring and cooling, a solution of 2.10 g (13.2 mmol) of bromine in

200 ml of CCl_4. The rate of addition was determined by the decolorization of the bromine. Hydrogen bromide was evolved throughout the reaction. After the addition was complete, stirring was continued for one hour.

The reaction mixture was extracted twice with 30 ml portions of 5% sodium bicarbonate and twice with water, dried ($MgSO_4$), filtered and rotary evaporated. The resulting dark oil contained at least three components, one of which was later shown to be 4-bromo-3-methoxymethylanisole(10). A second spot with a similar rf value may be the other isomer. Chromatography ($CHCl_3$/alumina) gave as the first band (0.9 g, 30%) of a single monobromo isomer. Pmr: δ 3.34,s,3H; δ 3.63,s,3H; δ 4.30,s,2H; δ 5.45,dd(J=3Hz,J=9Hz),1H; δ 6.90,d(J=3Hz),1H; δ 7.16, d(J=8Hz),1H. From the dark oil crystallized a few milligrams of white needles (mp 73.2-73.5°C), assumed from mass spec to be a demethylated analog. Mass spec: m/e 216 (96%), 214 (100%), 185 (12%), 183 (13%), 63 (81%).

4-Iodo-3-methoxymethylanisole(11). Under a nitrogen atmosphere a 200 ml, 3-neck, round bottom flask was equipped with stirring bar, addition funnel and condenser. It was flame dried, charged with 2.80 g (13.0 mmol) of silver(I) trifloro-acetate and redried. To the salt was added 2.00 g (13.0 mmol) of 3-methoxymethylanisole. To the stirred slurry was added through the addition funnel a solution of 3.30 g (0.13

mol) of iodine in 125 ml of chloroform. As the addition proceeded the slurry gradually dissolved and a yellowish precipitate of silver iodide formed. After the addition was complete the mixture was stirred for an additional hour.

The mixture was filtered to remove the AgI, washing with chloroform. The combined chloroform solution was evaporated to give a yellow oil which was distilled under aspirator pressure (bp 158°-160°C). Yield 3.3 g (90%) of colorless oil which on cooling solidified, mp 30-35°C. Pmr: δ 3.33,s,3H; δ 3.63, s,3H; δ 4.21,s,2H; δ 6.30,dd(J=3HZ,8Hz),1H; δ 6.80,d(J=3Hz),1H; δ 7.36,d(J=8Hz),1H.

4-Methoxy-2-methoxymethylbenzoic acid(15). A 100 ml, 3-necked round bottom flask was fitted with stirring bar, two rubber septums and condenser. The apparatus was fitted with a nitrogen atmosphere and flame dried. It was charged with 0.30 g (0.125 mol) of magnesium turnings and redried. Enough dry ether was injected to just cover the magnesium. A portion of a solution of 3.0 g (10.8 mmol) of 4-iodo-3-methoxymethyl-anisole(11) in 20 ml of dry ether was added. When no reaction occurred a few drops of methyl iodide were added. When the mixture warmed slightly and bubbles began to form more of the reaction proceeded. After the addition was complete and the reaction appeared to slow down, the mixture was heated at reflux for several minutes.

Carbon dioxide dried by passage through concentrated sulfuric acid was introduced under the surface of the solution causing masses of white solid to precipitate. When no more white solid formed, the addition was stopped and 30 ml of 5% aqueous sulfuric acid was added slowly to the etherial mixture causing the white solid to dissolve.

The ether layer was removed and the aqueous layer extracted twice more with 15 ml portions of ether. The combined organic layers were extracted three times with 15 ml portions of 10% aqueous sodium hydroxide. The alkaline extracts were combined, made acidic with 5% aqueous hydrochloric acid and extracted again with ether. After drying ($MgSO_4$), filtering and rotary evaporation there was obtained a yellow powder. Recrystallization from water gave 1.1 g (55%) of white needles, mp 152.5-154.5. Pmr: δ3.44,s,3H; δ3.79,s,3H;δ4.79,s,2H; δ6.70, dd(J=3Hz,8Hz),1H; δ 7.10d(J=3Hz),1H; δ 7.93,d(J=8Hz),1H. Mass spec: m/e 196 (14%), 181 (17%), 163 (100%), 149 (3%), 135 (17%).

5-Methoxyphthalide(16). A solution of 100 mg (0.510 mmol) of 4-methoxy-2-methoxymethylbenzoic acid in 10 ml of concentrated sulfuric acid was allowed to stand at room temperature for three days. It was then added dropwise to 100 ml of crushed ice. After melting the aqueous solution was extracted thoroughly with ether. The combined organic extracts were dried ($MgSO_4$), filtered and evaporated to give a dark powder.

Recrystallization from a minimum of water gave white needles, mp 113.0-114.5°C. Yield 47 mg (56%). Mass spec: m/e 164 (72%), 135 (100%), 107 (9%), 92 (11%), 77 (19%); meta stables: 111 (164-135), 85 (135-107). IR: 3025 cm^{-1}(w), 1775(s), 1625, 1505, 1370, 1345, 1275, 1160, 1110, 1060, 1025. Pmr: δ 3.80,s,3H; δ5.78, s,2H; δ6.77, br s,1H; δ7.03,br d(J=8Hz),1H; δ7.67,br d(J=8Hz),1H.

Ethyl 4-methoxy-2-methoxymethylbenzoate(17). The Grignard reagent was prepared from 4-iodo-3-methoxymethylanisole(11) as reported above for the preparation of 15. The quantities of starting materials used were 5.5 g (19 mmol) of 11 and 0.50 g (21 mmol) of magnesium in 50 ml ether. To the Grignard solution was added, through an addition funnel, a solution of 0.93 g (7.0 mmol) of diethyl carbonate in 10 ml of dry ether. After the addition was complete the mixture was stirred at reflux for two hours.

To the cooled mixture was slowly added 30 ml of cold 10% aqueous sulfuric acid. The aqueous layer was separated and extracted with three 50 ml portions of ether. The combined organic extracts were dried ($MgSO_4$), filtered and evaporated to give an oil which on chromatography ($CHCl_3$ on silica) gave in order, 3-methoxymethylanisole(9), 4-iodo-3-methoxymethylanisole(11) and ethyl 4-methoxy-2-methoxymethylbensoate(17). Pmr: δ1.33,t(J=7Hz),3H; δ3.36,s,3H; δ3.80,s,3H; δ4.24,q(J=7Hz). 2H; δ4.80,s,2H; δ6.70,dd(J=3Hz,8Hz),1H; δ 7.83,d(J=8Hz),1H.

Tris(2,4,6-trimethoxyphenyl) carbonium chloride (21) and Tris(2,4,6-trimethoxyphenyl) methanol(20). A 250 ml, 3-necked round bottom flask equipped with septum, condenser, magnetic stirring bar and condenser was charged with a solution of 6.0 ml of 2.2M butyllithium (13 mmol) in 20 ml of dry ether. To this mixture under an atmosphere of nitrogen was added slowly a solution of 2.0 g (12 mmol) of phloroglucinol trimethyl ether (18) in 20 ml of dry ether. The solution was stirred overnight and a solution of 0.47 g (4.0 mmol) of diethyl carbonate in 20 ml dry ether was added slowly. The solution was stirred at room temperature for 12 hours.

To the mixture was added 20 ml of 10% aqueous hydrochloric acid, causing the mixture to turn deep blue. The aqueous layer was separated and the ether layer washed once with 10 ml of 10% HCl to remove the last of the blue color from the ether. The combined aqueous layers were washed five times with 10 ml portions of ether to remove starting material. The blue material stayed in the aqueous layer while the ether extracts remained colorless. The blue material was extracted from the aqueous solution with chloroform. Drying ($MgSO_4$) and filtering the organic solution followed by rotary evaporation gave 0.050 g (2%) of blue-black solid, mp 135-140 dec. When this material is treated with 20 ml of 10% aqueous sodium hydroxide the color is discharged. Extraction with ether followed by drying ($MgSO_4$), filtering and evaporation gave a trace of

material assumed to be 20. Pmr of 21: δ3.57,s,18H; δ3.97,s,9H; δ6.00,s,6H. Mass spec of 21: m/e 513 (62%), 499 (11%), 483 (43%), 346 (100%), 315 (58%). UV/vis of 21: 584 nm, 450 nm, 366 nm, 323.

Method B. Various ratios of 2,4,6-trimethoxybenzoic acid were mixed with 1.0 g of 1,3,5-trimethoxybenzene and dissolved in phosphorus oxychloride. The solution was stirred for 8 hours over a steam bath under a condenser protected by a drying tube. After cooling the solution was poured over crushed ice. The dark aqueous acidic solution was extracted thoroughly with benzene, which removed starting material, as well as a reddish purple material. The blue product stayed in the aqueous layer until extracted into chloroform. Drying ($MgSO_4$), filtering and evaporating gave yields ranging from 6% to 20% of dark blue solid 21. From the benzene layer is obtained mostly 1,3,5-trimethoxybenzene. Anal. Calcd. for $C_{28}H_{33}ClO_9$: C, 61.27; H, 6.06%. Found: C, 59.93; H, 6.15%.

Tris(2,4,6-trimethoxyphenyl)methane(28). A small amount (20 mg) of the blue triarylmethyl material 21 was dissolved in 5 ml of dry THF and added to a slurry of 20 mg (0.53 mmol) of lithium aluminum hydride in 5 ml of dry THF. The blue color was discharged immediately. The excess $LiAlH_4$ was destroyed by adding saturated aqueous sodium sulfate dropwise with stirring in an ice bath. The mixture was filtered and the white solid

washed thoroughly with THF. The organic solution was dried ($MgSO_4$), filtered and evaporated giving a brown oily residue which was crystallized from 95% ethanol. The brownish needles (mp 178-182°C) gave an nmr which suggested the desired triaryl methane, though clearly impure. Pmr: δ 3.40,s,18H; δ 3.70, s,9H; δ 6.00,s,6H; δ 6.17,s,1H. IR: 2920 cm^{-1}, 2810, 1575, 1450, 1400, 1315(w), 1125(st,br), 1050, 945.

Method B. Into a refluxing solution of 2.0 g (12 mmol) of 1,3,5-trimethoxybenzene (18) in 20 ml of phosphorus oxychloride was dripped 20 ml of 80% aqueous formic acid. The resulting reaction is quite vigorous, evolving quantities of gas due to the reaction of $POCl_3$ and water as well as $POCl_3$ and formic acid (giving HCl and CO). After the addition was complete the red solution was diluted carefully with water. The resulting aqueous acid solution contained some solid precipitate. It was extracted thoroughly with benzene. The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and evaporated to give 2.3 g of dark solid residue. Washing with 95% ethanol/chloroform gave 1.2 g (60%) of triaryl methane, mp 205-207°C. Pmr: See above.

2-Bromo-1,3,5-trimethoxybenzene (23). A solution of 3.0 ml (9.0 g, 56 mmol) of bromine in 50 ml of carbon tetrachloride was added dropwise to an ice-bath chilled stirred solution of 10.0 g (60 mmol) of 1,3,5-trimethoxybenzene in 50 ml of CCl_4. After the addition was complete, the solvent was evaporated

and the residue recrystallized from EtOH/H_2O to give 11.6 g (78%) of white needles, mp 92-94.5, lit.[38] 99°C. Pmr: δ 3.75,s, 3H; δ 3.81,s,6H; δ 6.07,s,2H.

Ethyl 2,4,6-trimethoxybenzoate(27). An oven-dried apparatus consisting of a 100 ml, three-necked round bottom flask, condenser, addition funnel, septum and magnetic stirring bar was charged with 0.50 g (21 mmol) of magnesium turnings and redried under nitrogen atmosphere. A portion of a solution of 3.6 g (14.6 mmol) of 2-bromo-1,3,5-trimethoxybenzene in 30 ml of dried tetrahydrofuran was transferred into the reaction flask by syringe. As the reaction did not commence immediately, several drops of 1,2-dichloroethane were added. Soon the mixture began to form small bubbles, to warm slightly and to turn a golden yellow shade. The remainder of the aryl bromide solution was added gradually and the mixture was stirred at room temperature for five hours. After most of the magnesium had been consumed and the solution had become dark brown, a solution of 0.60 ml (0.54 g, 5.0 mmol) of ethyl chloroformate in 15 ml of dry THF was added. The mixture was heated at reflux then stirred at room temperature overnight.

To the reaction mixture was added 50 ml of 20% aqueous hydrochloric acid. The mixture turned a very deep purple. It was extracted several times with 30 ml portions of chloroform until the color was removed from the aqueous layer. The combined organic extracts were washed with brine, dried ($MgSO_4$),

and rotary evaporated to give 2.9 g of a dark oil. Chromatography gave 1.45 g (41%) of ester as indicated by pmr. The rest of the material stayed on the column. Pmr: δ 1.31,t(J=7Hz), 3H; δ 3.69,s,3H; δ 3.74,s,6H; δ 4.27,q(J=7Hz),2H; δ 6.00,s,2H.

Method B. A solution of 2.0 g of 2,4,6-trimethoxybenzoic acid and 15 ml of freshly distilled thionyl chloride was heated at reflux for four hours. The thionyl chloride was removed under reduced pressure. The resulting yellow solid was dissolved in 25 ml of absolute ethanol and the solution was heated at reflux for two hours. Rotary evaporation gave a colorless oil whose pmr spectrum showed it to be a mixture of the desired ester and 1,3,5-trimethoxybenzene.

2,4,6-Trimethoxybenzaldehyde(29). A solution of 3.0 g (18 mmol) of 1,3,5-trimethoxybenzene in 20 ml of phosphorus oxychloride was chilled in an ice bath. With stirring, a solution of 5.0 g (69 mmol) of dimethylformamide in phosphorus oxychloride was added dropwise. After the addition was complete, the solution was allowed to come to room temperature and stirred for three hours.

The solution was poured carefully over 100 ml of crushed ice. The aqueous solution was washed several times with chloroform, neutralized with 20% aqueous sodium hydroxide and allowed to stand overnight. From the solution crystallized 2.9 g (90%) of beautiful white needles, mp 117-119.5°C, lit.[38] 118-120°C. Pmr: δ 3.90,s,9H; δ 6.07,s,2H; δ 10.26,s,1H.

Methyl 2,4,6-trimethoxybenzoate(26). A mixture of 1.0 g (4.75 mmol) of 2,4,6-trimethoxybenzoic acid(24), 2.0 g (14.5 mmol) of potassium carbonate, 2.0 g (14.1 mmol) of methyl iodide and 20 ml of dry acetone was stirred at room temperature for 24 hours. The mixture was then filtered and the acetone evaporated to give 0.97 g (91%) of a white solid. Pmr: δ 3.68, s,3H; δ 3.72,s,6H; δ3.79,s,3H; δ 5.98,s,2H.

Pyridine hydrochloride(33). Hydrogen chloride gas was passed through a solution of 79 g (1.0 mol) of dry pyridine dissolved in 300 ml of dry ether. The white product precipitated. After no more solid formed, the precipitate was filtered and washed thoroughly with ether. Yield 115 g (100%), mp 144-146°C, lit.[35] 143.4. The salt is very hygroscopic, but can be stored indefinitely in a dessicator. Pmr: δ 6.17-7.33,m.

5,9-Dihydroxy-1H-3,7,11-trioxatriangulen-1-one(22). A mixture of 8.60 g (15.7 mmol) of tris(2,4,6-trimethoxyphenyl) carbonium chloride(21) and 30.0 g (261 mmol) of pyridine hydrochloride were sealed in a tube and heated in a 180°C oil bath for six hours. After cooling, the dark fused mass was taken up in water. The brown insoluble solid was washed thoroughly with water, alcohol and chloroform giving 5.1 g (98%) of brown powder, mp300°C. Pmr (CF_3CO_2H): δ 6.7,s. Pmr (D_2O,KOD): δ 5.1,s. UV/vis (KOH/H_2O): 416 nm.

Method B. The same procedure as above starting with

tris(2,4,6-trimethoxyphenyl)methane gave a good yield of the same material.

5,9-Dioctyloxy-1H-3,7,11-trioxatriangulen-1-one(30). A mixture of the brown powder(22) (1.0 g, 3.0 mmol), potassium carbonate (1.2 g, 9.3 mmol) and octyl iodide (2.0 ml, 2.5 g, 10.4 mmol) in 25 ml of dimethylformamide was stirred and heated at reflux for five hours. After cooling, the dark solution was diluted with 100 ml of 5% aqueous sodium hydroxide and extracted with three 30 ml portions of chloroform. The combined organic layers were dried ($MgSO_4$), filtered and evaporated to give a brown solid. Chromatography (CH_3Cl on silica) gave as an intermediate yellow-green fraction 0.5 g (34%) of orange solid, crystallized from acetone/chloroform, mp 247-250°C. Mass spec: m/e 556 (100%), 444 (100%), 332 (49%), 304 (10%). UV/vis: 480, 450, 420(w). Pmr: δ 0.90,br t(J=6Hz), 6H; δ 1.10-2.00,m,24H; δ 3.90,br t(J=7Hz),4H; δ 5.97,s2H; δ 6.25,br s,4H.

Attempted oxidation to diradical 3. A solution of 0.50 g (1.5 mmol) of brown material 19 and 40 ml of 5% aqueous potassium hydroxide was purged of oxygen by refluxing under nitrogen while passing nitrogen through the refluxing solution. To the solution was added an oxygen-purged solution of 1.00 g (3.0 mmol) of potassium ferricyanide in 10 ml of water. The mixture was heated at reflux for five hours, during which the color of the solution lightened considerably, but the visible

spectrum stayed the same (i.e., identical to a spectrum of the starting material dissolved in aqueous potassium hydroxide). Gradually an off-white precipitate formed which was isolated by centrifugation and vaccuum dried. It amounted to 0.40 g (80%), did not melt below 300°C, was insoluble in all solvents including aqueous acid and base, and gave no signal in the mass spectrometer.

1,6-Dimethoxynaphthalene(33). In a 3000ml, three-necked round bottom flask equipped with addition funnel, overhead stirrer and condenser, 100 g (0.625 mmol) of 1,6-dihydroxy-naphthalene was dissolved in 560 ml of 2N aqueous sodium hydroxide. To this was added, with ice bath cooling, 126 g (1.00 mol) of dimethyl sulfate all at once. The ice bath was removed and the exothermic reaction warmed the mixture above room temperature. After the temperature had fallen back to room temperature, an additional 280 ml of 2N sodium hydroxide was added, followed by 60 g (0.47 mol) of dimethyl sulfate. The mixture was stirred for one hour with heating on a steam bath. After cooling to room temperature, the mixture was extracted five times with 75 ml portions of chloroform. The combined chloroform extracts were washed twice with 50 ml portions of 2N sodium hydroxide and once with brine. Drying($MgSO_4$) followed by filtration and evaporation gave 111 g (94%) of a dark oil which eventually solidified. Filtration through a column of silica with chloroform, followed by two

recrystallizations from petroleum ether (bp 60-90°C) gave 94.0 g (80%) of colorless needles. Mp 57.5-59.0°, lit.[39] 60-61°C. Pmr: δ3.78, s,3H; δ3.85,s,3H; δ6.3-6.7,m,1H; δ6.9-7,m,4H; 7.9-9.2,m,1H.

1-Cinnamoyl-4,7-dimethoxynaphthalene[36](34). A 1-liter, 3-necked round bottom flask was fitted with overhead stirrer and condenser with drying tube. It was charged with 55 g (0.37 mol) of trans-cinnamic acid, 70 g (0.37 mol) of 1,6-dimethoxynaphthalene and 500 ml of dry benzene. The solid did not completely dissolve. The mixture was cooled in an ice bath, and 80 g (0.38 mol) of solid phosphorus pentachloride was added by spatula and the mixture was stirred vigorously. After about five minutes the solution had turned light green and there remained clumps of solid. The ice bath was removed and the mixture was stirred at reflux over a steam bath for five minutes until all the solid was dissolved and the solution was dark green. It was again cooled in an ice bath and, while stirring vigorously, 52 g (0.39 mol) of anhydrous aluminum chloride was added in portions. Upon addition of aluminum chloride the mixture immediately turned deep red. After all of the aluminum chloride had been added, the mixture had become semi-solid and difficult to stir. After refluxing for an additional ten minutes, the mixture was cooled to room temperature and a mixture (50:50) of ice and concentrated hydrochloric acid was added slowly. After the hydrolysis

was complete (about 100 ml of aqueous solution had been added) the benzene layer was removed and the aqueous layer extracted twice with 75 ml portions of benzene. The combined organic extracts were washed successively with two 50 ml portions of 10% aqueous hydrochloric acid, 50 ml of 10% aqueous sodium hydroxide and water until neutral. The organic solution was dried ($MgSO_4$), filtered and evaporated to give a dark red oil which slowly solidified. Crystallization from benzene/pet. ether with the use of decolorizing charcoal gave 85 g (71%) of light yellow-green needles, mp 95.5-97,5°C, lit.[36] 96-98°C. Pmr: δ 3.87,s,3H; δ 3.97,s,3H; δ 6.56,d(J=8Hz),1H; δ 6.9-7.5,m,8H; δ 7.78,d(J=8Hz),1H; δ 8.01,d(J=3Hz),1H; δ 8.11,d(J=3Hz),1H.

2,3-Dihydro-4,7-dimethoxy-3-phenyl-1H-phenalen-1-one[36](35). In a one-liter beaker, 66 g (0.21 mol) of 1-cinnamoyl-4,7-dimethoxynaphthalene, 34, was mixed with 300 ml of polyphosphoric acid, and the mixture was heated on a steam bath while stirring the thick, syrupy mixture by hand with a stout glass rod. After stirring and heating for 20 minutes, the brick red mixture had become much easier to stir and essentially homogeneous. As much of the material as possible was poured over 500 ml of crushed ice in another beaker, and that remaining in the reaction beaker was treated with 500 ml of water. Eventually the syrupy insoluble material became hard and lumpy. The water was decanted and, while still hot, was extracted

with 400 ml of benzene. The solid remaining in the two beakers was combined and boiled with 400 ml of benzene. This was decanted and added to the benzene extracts. This process (heat in water, extract with benzene, heat in benzene) was repeated three times, or until all the solid had dissolved. The combined benzene extracts were evaporated to two liters, washed with 500 ml each of water, 5% aqueous sodium hydroxide and water, then dried ($MgSO_4$), filtered and evaporated to give 71 g of orange solid. Two crystallizations from pet. ether/benzene gave 45.2 g (70%) of light yellow needles, mp 169.5-171.5°C, lit.[34] 173-174. Pmr: δ 3.0-3.3,m,2H; δ 3.80,s,3H; δ 3.99,s,3H; δ 4.9-5.1,m,1H; δ 6.67,d(J=8Hz),1H; δ 6.93,br s,5H; δ 6.97, d(J=9Hz),1H; δ 8.10,d(J=8Hz),1H; δ 8.12,d(J=9Hz),1H.

4,7-Dihydroxy-1H-phenalen-1-one[36](36). A two-liter, three-necked round bottom flask was equipped with overhead stirrer, condenser and drying tube and was charged with 45.0 g (0.141 mol) of 2,3-dihydro-4,7-dimethoxy-3-phenyl-1H-phenalen-1-one(35), and 500 ml of dry benzene. To this solution was added, in 10 g portions, 91.0 g (0.681 mol) of anhydrous aluminum chloride. The mixture was stirred at reflux for two hours. After cooling it was poured into iced concentrated hydrochloric acid. The pieces of solid material were rinsed out with water. The solid was broken up as much as possible and separated by filtration. Thorough washing with benzene and water gave an orange silt-like solid which was dissolved

in 350 ml of 5% aqueous sodium hydroxide, washed with benzene and precipitated with acetic acid. Washing with water and vaccuum oven drying gave 29.9 g (100%) of orange solid, mp 300°. Pmr(DMSO): δ 6.87,d(J=8Hz),3H; δ 8.20,d(J=8Hz),3H. Mass spec: m/e 212 (100%), 184 (59%), 155 (22%), 128 (22%), 92 (20%); UV/vis(DMSO); 509 nm, 479, 455, 429, 408, 363.

4,7-Dimethoxy-1H-phenalen-1-one[36](37). In a 50 ml, 3-necked round bottom flask fitted with stirrer and condenser, 2.0 g (9.4 mmol) of 4,7-dihydroxy-1H-phenalen-1-one(36) was dissolved in 17 ml of 1N sodium hydroxide and cooled in an ice bath. To the mixture was added 2.0 ml (21 mmol) of dimethyl sulfate. The mixture was allowed to come to room temperature and stirred until it solidified. An additional 9 ml of 1 N NaOH was added, dissolving the solid, followed by 1.0 ml (10 mmol) of dimethyl sulfate. After stirring for one hour the mixture was heated on a steam bath for 10 minutes. The contents of the flask were poured into methylene chloride and the solid material washed out with 1N NaOH and methylene chloride. The aqueous solution was extracted three times with 20 ml of methylene chloride. The organic phase was dried ($MgSO_4$), filtered and evaporated to give 0.7 g (30%) of yellow solid. Recrystallization from benzene/pet. ether gave yellow needles, mp 173.5-175.5, lit.[36] 176-178°C. Mass spec: m/e 240. Pmr: δ 3.97,s,3H; δ 4.00,s3H; δ 6.50,d(J=10Hz),1H; δ 6.78,

d(J=8Hz),1H; δ 7.01,d(J=9Hz),1H; δ 7.98,d(J=10Hz),1H; δ 8.18,d(J=9 Hz),1H; δ 8.43,d(J=8Hz). UV/vis: 454, 430, 410, 388(sh), 365, 347(sh), 273; lit.[8] 455, 432, 410, 366, 270.

4,7-Diacetoxy-1H-phenalen-1-one[36](38). A mixture of 1.0 g (4.7 mmol) of 4,7-dihydroxy-1H-phenalen-1-one(36), 20 ml of acetic anhydride and 5 ml of pyridine was stirred at room temperature for 18 hours. The solvent was removed at room temperature under reduced pressure. Crystallization of the residue from benzene gave 1.05 g (75%) of golden crystals, mp 177-179°C, lit.[36] 180-182°C. Pmr: δ 2.43,s,3H; δ 2.45,s,3H; δ 6.62, d(J=10Hz),1H; δ 7.28,d(J=9Hz),1H; δ 7.43,d(J=8Hz),1H; δ 7.75,d(J=10Hz),1H; δ 7.97,d(J=9Hz,1H; δ 8.51,d(J=8Hz),1H.

Attempted oxidation to the diradical(4). In the addition funnel of a reaction apparatus which also included a 100 ml, 3-necked round bottom flask and condenser with nitrogen atmosphere, a solution of 1.55 g (4.71 mmol) of potassium ferricyanide in 20 ml of water was purged of oxygen by bubbling nitrogen through the solution. This solution was added to a similarly purged solution of 0.5 g (2.36 mmol) of 4,7-dihydroxy--1H-phenalen-1-one(36) in 5 ml of 5% aqueous sodium hydroxide. The solution turned bright red within a few minutes and the color deepened as time went on. This red material could not be dissolved in water or any organic solvent. On introduction of oxygen, a brown solid precipitated.

5,8-Dibromo-4,7-dimethoxy-1H-phenalen-1-one(39). In a 100 ml round bottom flask equipped with condenser and magnetic stirring bar, a mixture of 0.50 g (2.1 mmol) of 4,7-dimethoxy-1H-phenalen-1-one, 0.82 g (10 mmol) of sodium acetate, 0.32 ml (1.0 g, 6.3 mmol) of bromine and 10 ml of glacial acetic acid were stirred while heating at reflux for one hour. After cooling, the mixture was diluted with 30 ml of water. The resulting solid was filtered out, washed with water, and filtered out, washed with water, and dissolved in methylene chloride. The organic solution was washed with 5% aqueous sodium hydroxide, 1N hydrochloric acid, water and brine. It was dried ($MgSO_4$), filtered and evaporated to give 0.55 g of a dull yellow solid. This was boiled in carbon tetrachloride and the resulting orange solid was filtered out, chromatographed and crystallized from benzene to give 0.13 g of golden needles. From the carbon tetrachloride solution, 0.42 g of needles crystallized. Total yield 0.55 g (66%). MP 240.5-244.5. Mass spec: m/e 400 (49%), 398 (100%), 396 (49%), 357 (13%), 355 (24%0, 353 (12%). UV/vis: 476 nm(sh), 445, 425(sh), 342, 327(sh), 275.

2-Chloro-4,7-diacetoxy-1H-phenalen-1-one(40). A solution of 0.30 g (1.01 mmol) of 4,7-diacetoxy-1H-phenalen-1-one(38) in 25 ml of glacial acetic acid was added dropwise to a solution of 0.2 g (2.8 mmol) of chlorine in 25 ml of glacial acetic acid (prepared by bubbling chlorine gas into a weighed amount

of acetic acid, reweighing, and taking an aliquot to give the desired amount of chlorine). The addition was done at the freezing point of acetic acid (16°C) by freezing the chlorine solution in an ice bath, then adding the diacetate solution with stirring as the acetic acid in the flask melted. The reaction mixture was stirred at room temperature overnight and the solvent was evaporated to give a golden oily liquid which eventually solidified. Recrystallization from ethanol gave 0.21 g (64%) of golden needles, mp 195-197°C. Pmr: δ 2.44, s,6H; δ 7.23,d(J=8Hz),1H; δ 7.42,d(J=8Hz),1H; δ 7.87,s,1H; δ 7.93,d (J=8Hz),1H; δ 8.51,d(J=8Hz),1H. Mass spec: m/e 332 (3%), 330 (5%), 290 (5%), 288 (14%), 248 (34%), 246 (100%).

2-Chloro-2,3-dihydro-4,7-dimethoxy-3-phenyl-1H-phenalen-1-one(42). A mixture of 0.5 g (126 mmol) of 2,3-dihydro-4,7-dimethoxy-3-phenyl-1H-phenalen-1-one(35), 2.4 ml of 5% sodium hypochlorite (0.12 g, 1.65 mmol) was diluted to five ml with methanol. The heterogeneous mixture eventually turned to a gel. After three hours at room temperature, the mixture was dissolved in benzene/water, the organic layer separated, dried (Na_2SO_4) and evaporated to give 0.57 g of yellow solid. Recrystallization from benzene/pet. ether gave 0.54 g of a 60:40 mixture of starting material and product in two crops, the first being mostly product. Analysis was carried out by nmr. Pmr: δ 3.78,s,3H; δ 4.57,d(J=2Hz),1H; δ 4.00,s,3H; δ 5.17.d (J=2Hz),1H; δ 6.6-7.2,m,7H; δ 8.17,d(J=8Hz),2H. Mass spec: m/e 354

(100%), 352 (37%).

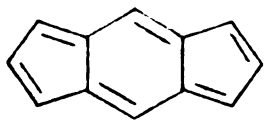
4,7-Diacetoxy-3-phenyl-1H-phenalen-1-one(50). A 5 ml flask fitted with stirrer, condenser and drying tube was charged with a solution of 200 mg of the first crop from above (0.60 mmol) in 4 ml of dry benzene. To the mixture was added all at once 400 mg (3.0 mmol) of anhydrous aluminum chloride. The mixture was heated at reflux for 1½ hours by which time it had become deep red, and allowed to stir at room temperature overnight. A red solid was filtered out and washed with water and benzene. After drying this solid was dissolved in 20 ml of acetic anhydride and 5 ml of pyridine. The solution was stirred for four house at room temperature, then the solvent was rotary evaporated. Recrystallization of the residue from benzene gave 100 mg (47%) of yellow needles, mp 199.5-202°C. Pmr: δ 2.40,s,3H; δ 2.43,s,3H, δ 7.0-8.0,m,9H; δ 8.50,d(J=Hz), 1H. Mass spec: m/e 372 (27%), 330 (30%), 288 (100%), 287 (91%).

Part II

SYNTHESIS OF OXYGENATED INDACENE DERIVATIVES

INTRODUCTION

Indacene, 53, an anti-aromatic, unstable, red liquid was prepared in 1963 by Hafner.[42] It is a "benzo" derivative of pentalene, the anti-aromatic hydrocarbon, 54. Though pentalene itself has resisted synthesis due to its great propensity to dimerize, its 1,3,5-tri-t-butyl derivative[43] and its hexaphenyl derivative[44] have been prepared. Hydrindacene, 55, is the hexahydro derivative of indacene. It was my goal to prepare several oxygenated hydrindacene derivatives, specifically the hexaketone, 56 and its dihydroxy derivative 57 and the octaketone 58.



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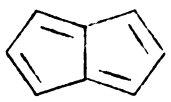

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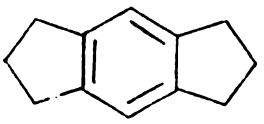

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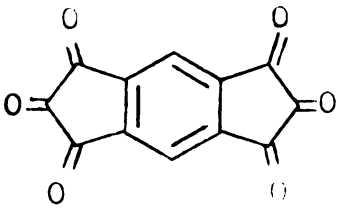

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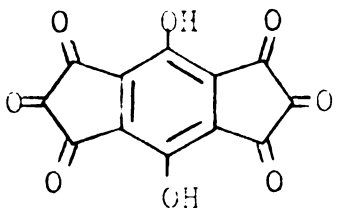

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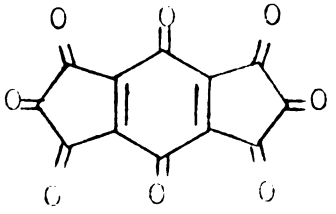

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Figure 18. Indacene and derivatives.

These molecules are interesting in themselves due to their highly electron deficient nature. For example, they could serve as electron acceptors in charge transfer salts. Their small size, coplanarity and highly delocalized nature suggest that the radical anions of 56 and 58 (see Figure 19) might serve as replacements for $TCNQ^{\cdot-}$ in the organic conductor TCNQ-TTF and similar charge transfer salts. The molecules 56 and 57 are also envisioned as precursors to novel polycyclic aromatic compounds. Examples of aromatics which could possibly be synthesized from 56 are 65 and 66 (see Figure 20). The first step is simply a double aldol condensation and will be explored further in the results and discussion section. The second step, though not further explored, was envisioned as a Clemmensen or Wolf-Kishner type reduction to the hydrocarbons 63 and 64. This would be followed by aromatization with a dehydrogenating agent such as chloranil. Though aromatic, the molecules 65 and 66 incorporate two pentalene systems. They thus could be considered benzopentalenes, and could add to the growing body of knowledge about this elusive anti-aromatic system.

Molecules 57 and 58 are of additional interest as each is a member of a class of compounds which has received considerable attention recently, specifically the carbon oxo-acids and the oxo-carbons respectively.[45,46]

Carbon oxo-acids are species containing only carbon, oxygen and oxygen-bound hydrogen. Simple examples are carbonic acid and oxalic acid. The cyclic carbon oxo-acids, squaric acid, 69, croconic acid, 70, and rhodizonic acid, 71,

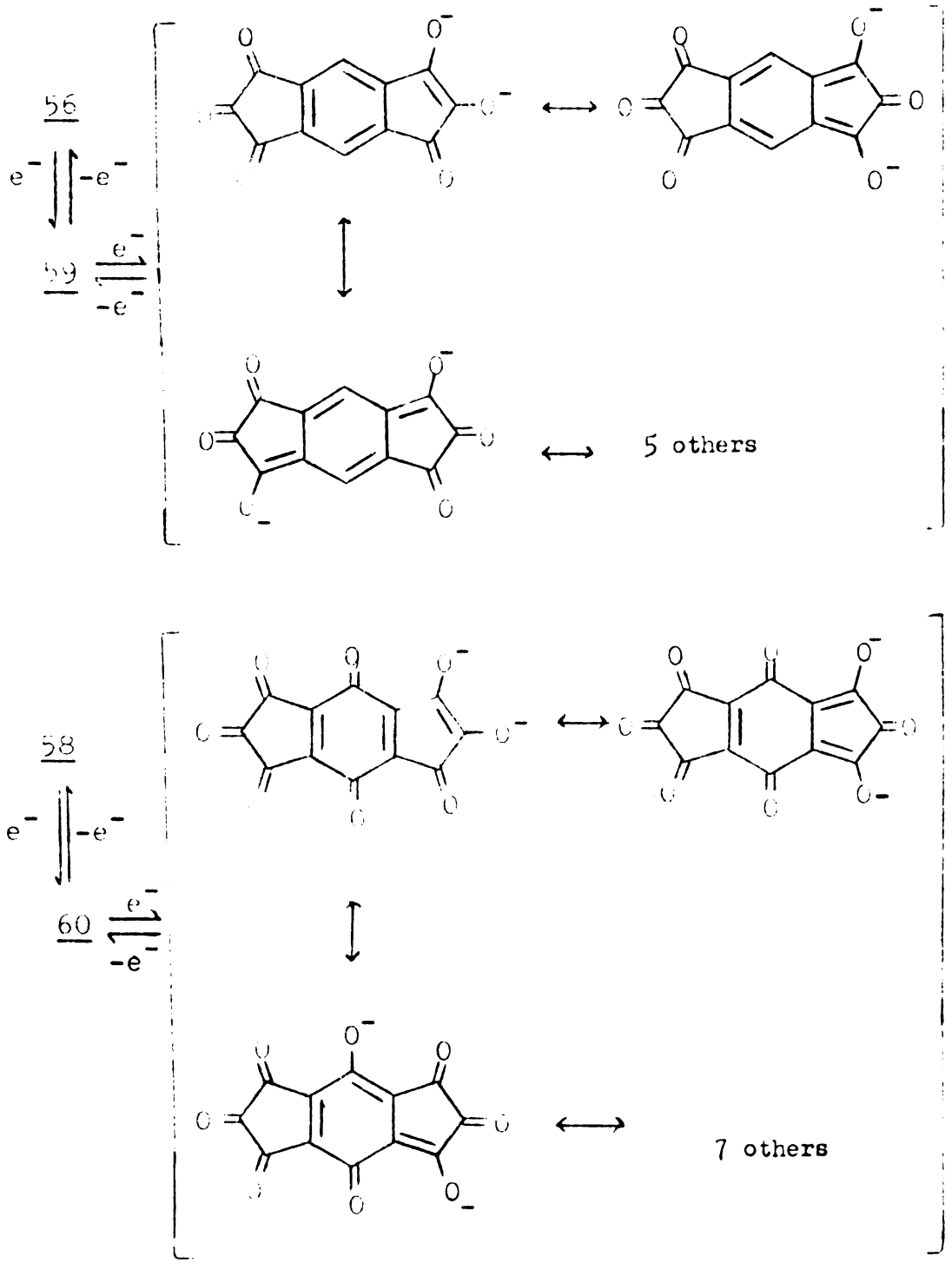


Figure 19. Gain or loss of an electron from radical anions 59 and 60.

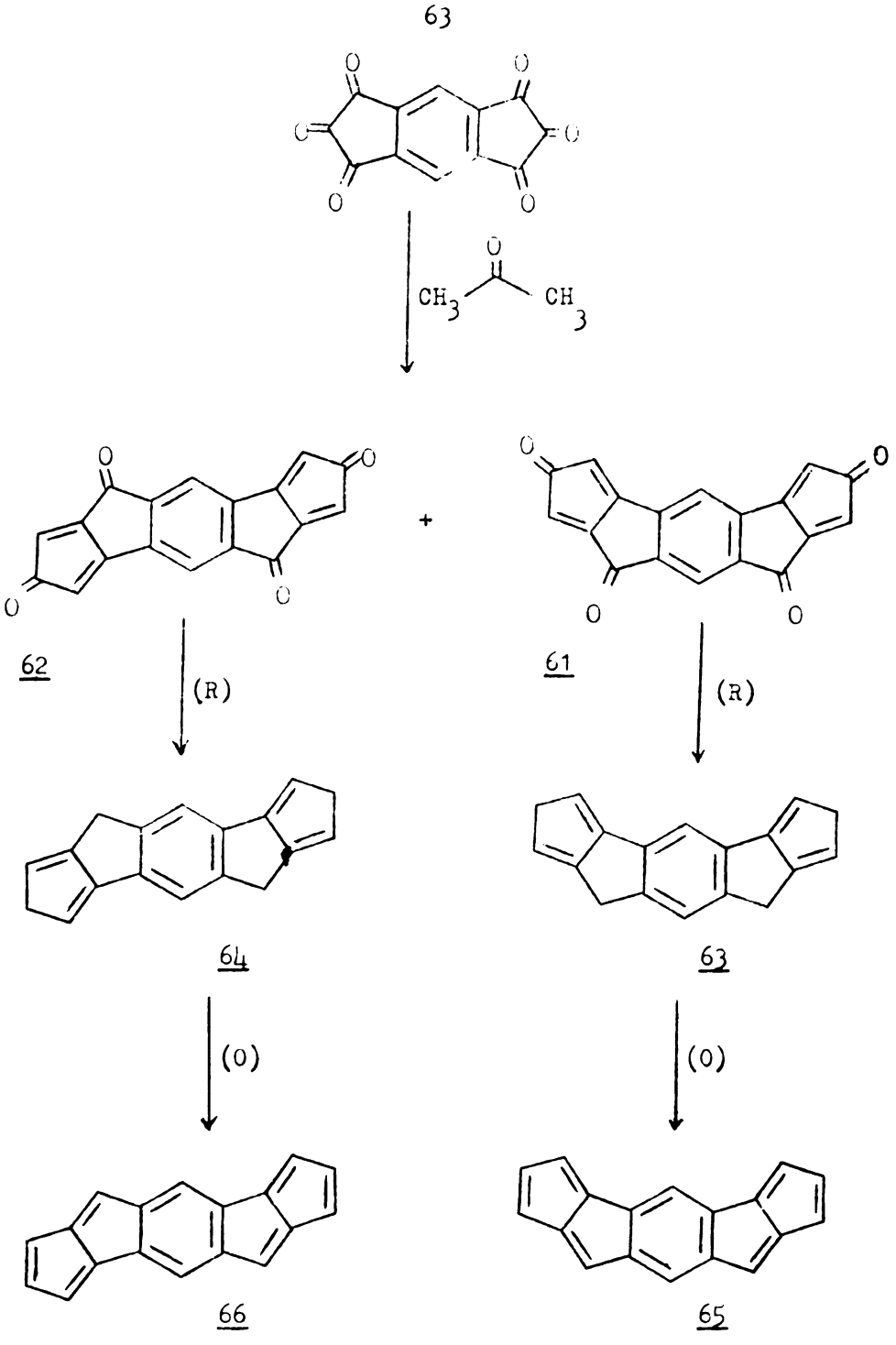


Figure 20. Possible synthesis of aromatics 61 and 62 from hexaketone 56.

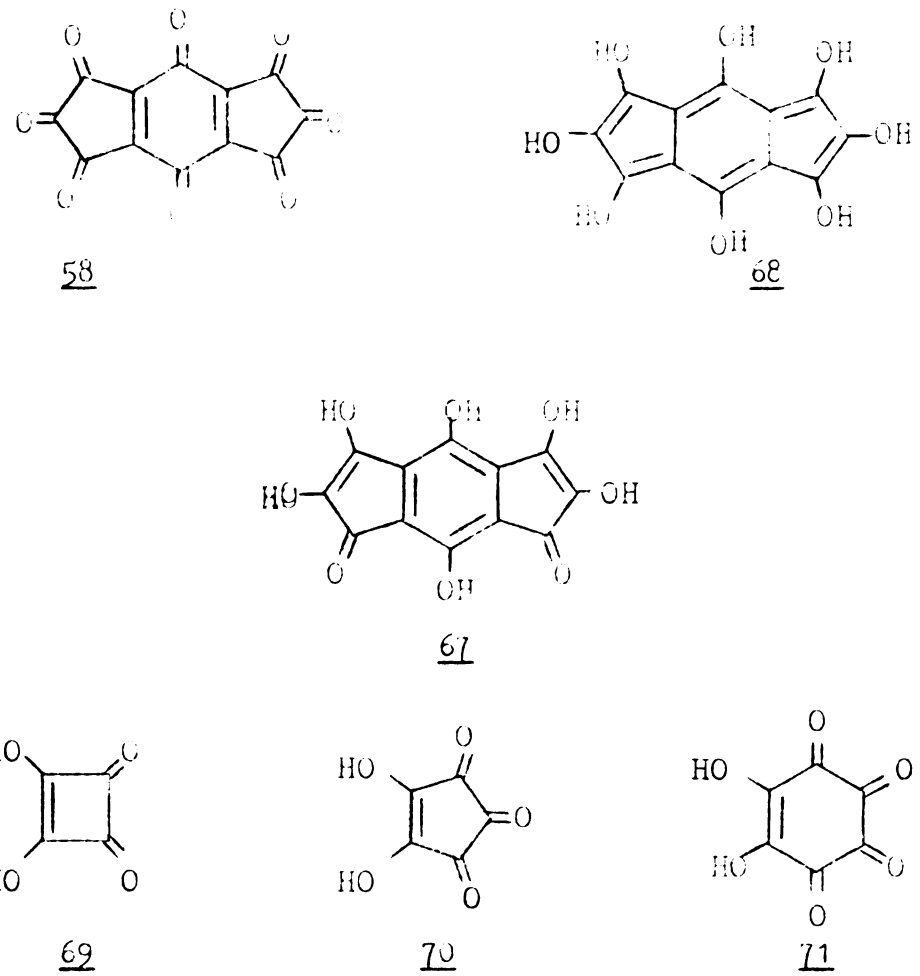


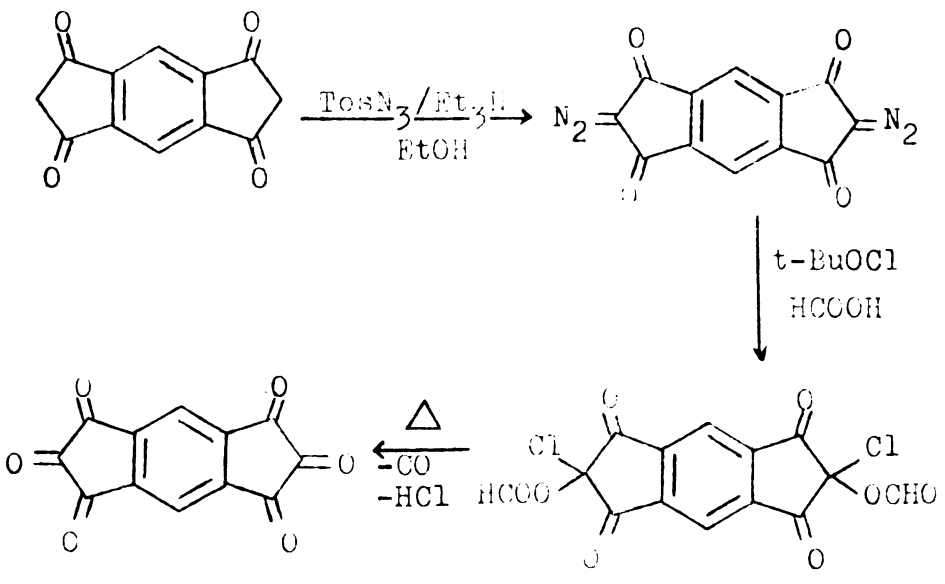
Figure 21. Oxocarbons and carbon oxo-acids.

are strong acids as their mono- and dianions are stabilized by delocalization. In fact, the dianions are delocalized to such an extend that they are considered to be non-benzenoid aromatics.[45,46] The oxo-acids 69, 70, and 71 can be thought of as reduction products of the corresponding oxocarbons cyclobutatetrone, cyclopentapentaone and cyclohexahexaone. Oxacarbons are, of course, compounds containing only oxygen and carbon. The hexaketone-hydroquinone, 57, is one of a series of carbon oxo-acids which includes 67 and octahydroxyindacene, 68, all

reduction products of the oxocarbon 58. For a review of carbon oxo-acids and oxocarbons see References 45 and 46.

RESULTS AND DISCUSSION

After much of the following work was completed, a synthesis of hexaketone 56 was reported.[47] It involves an oxidation of tetraketone 72 (see Figure 22). It was also reported that 56 has a half-wave potential measured on polarographic reduction of 0.15 V (in acetonitrile vs. SCE).[47] This approaches the value of 0.19 V found for tetracyanoquinodimethane.[48] In addition, 56 was found to form a 1:1 complex with pyrene,[47] lending some support to the idea of 56 and similar compounds serving as TCNQ replacements in organic conductors.



56 82

Figure 22. Synthesis of hexaketone 56 by Gleiter and Schanz.[47]

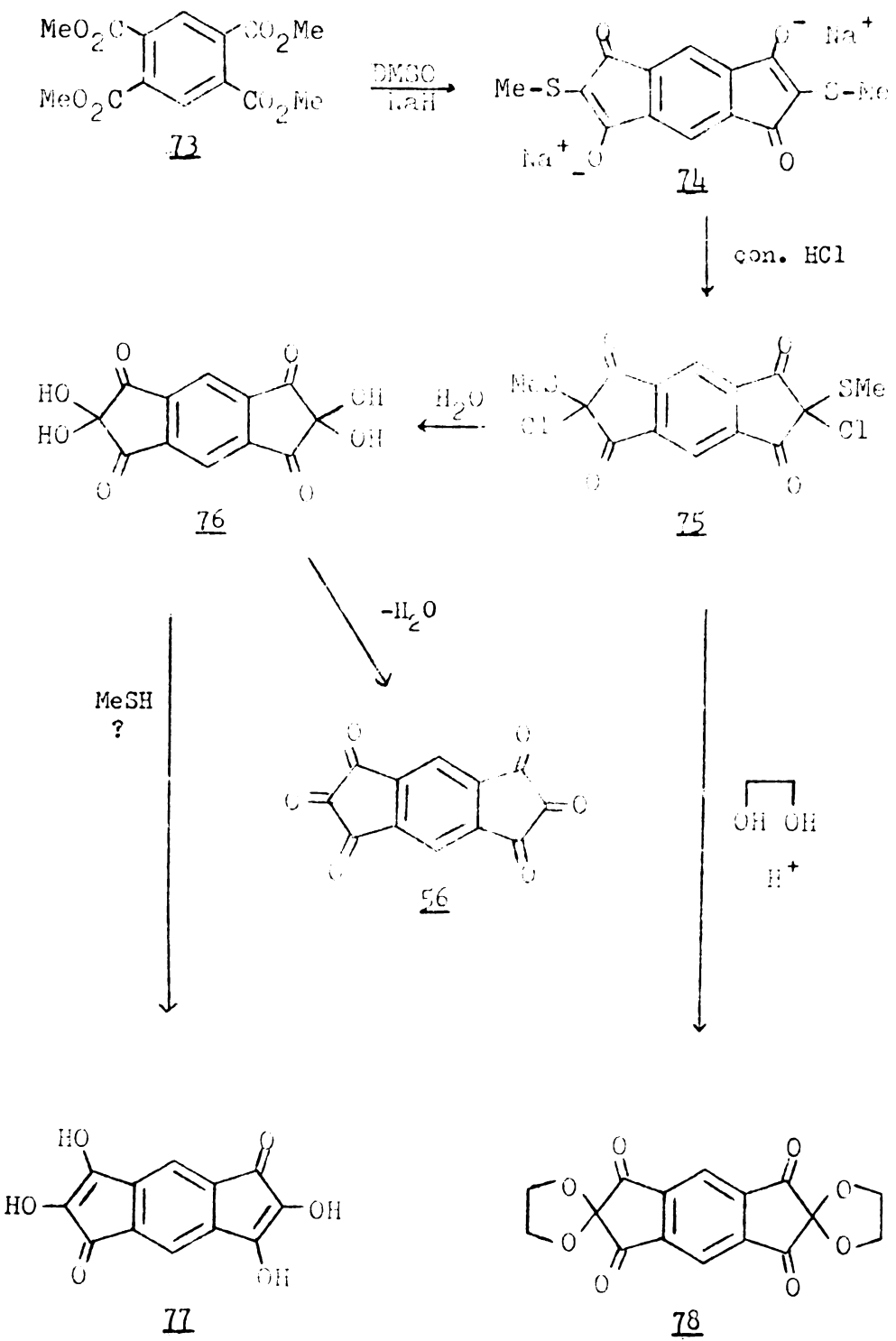


Figure 23. First approach to hexaketone 56

Our first approach to hexaketone 56 is outlined in Figure 23. This synthesis is analogous to a preparation of ninhydrin, 79 (Figure 27), from dimethyl phthalate, as outlined in Fieser and Fieser.[49]

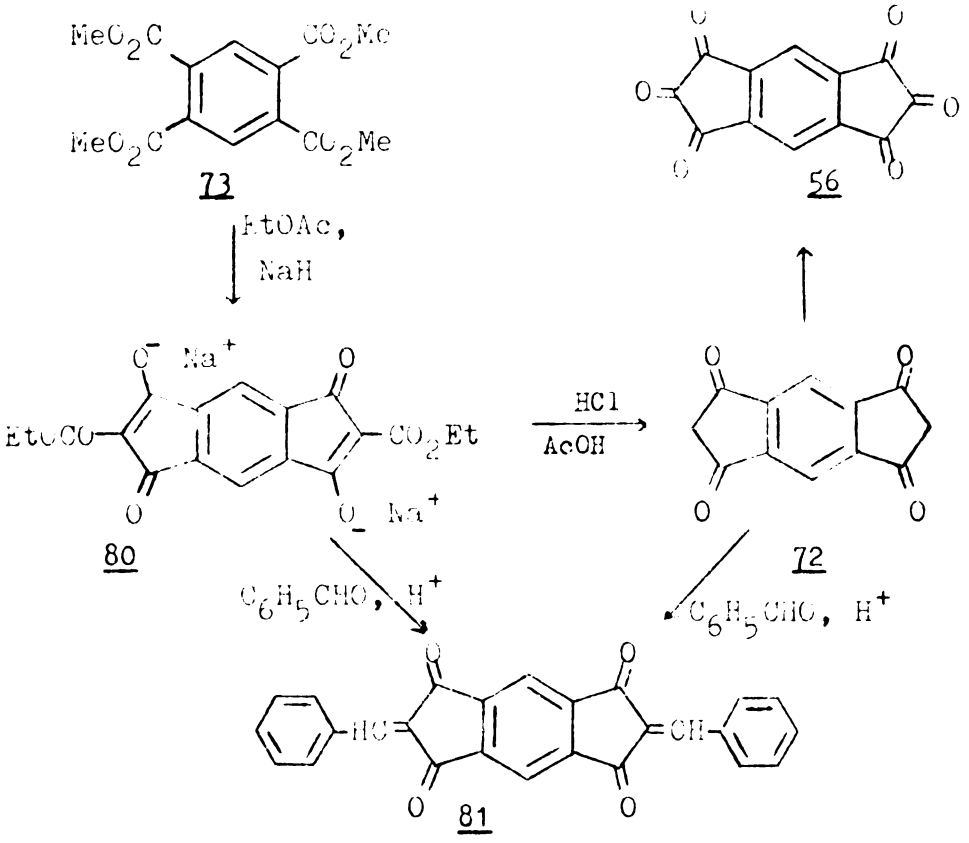


Figure 24. Second approach to hexaketone 56.

Condensation of dimethyl sulfoxide (DMSO) with tetramethyl pyromellitate, 73, gave a dark material, assumed to be the disodium salt 74. Without further purification this material was treated with concentrated hydrochloric acid to give a yellow solid shown to be the tetraketodichlorobis-

(thioether), 75. This interesting reaction, known as the Pummerer rearrangement[50] is an intramolecular redox reaction or, formally, a shift of hydroxide from sulfur to carbon.

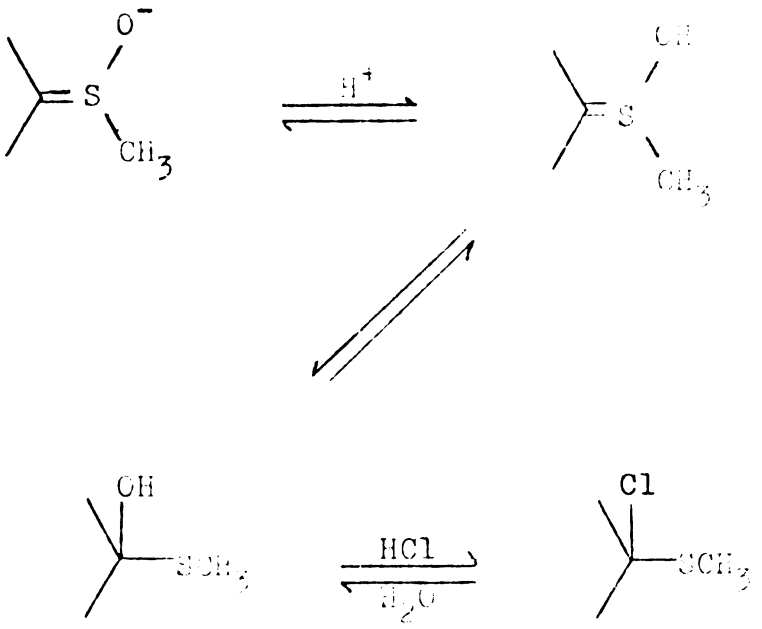


Figure 25. Formal mechanism of Pummerer rearrangement.

The yellow material 75 is apparently readily hydrolized. When it was left exposed to air for any period of time, it darkened and emitted a foul thiol-like odor. Treatment of 75 with water gave a red solid. This material was decolorized with bromine, but always quickly regained its color. All of this suggests that the red material may be a reduced form of the desired hexaketone 56, such as 77. In an attempt to pre-

vent such a reducing process the dichlorobis(methylthio) compound 75 was treated with ethylene glycol and mercury(II) sulfate. It was hoped that the ketal 78 would result. Unfortunately, no product could be isolated from this reaction.

A second approach involves tetraketone 72 as in the scheme of Gleiter and Schanz[47] (see Figure 22). It was prepared by them and by us by the method of Neilands and Vavere.[51] (see Figure 24). Sodium hydride-induced Claisen condensation of ethyl acetate with tetramethyl pyromellitate gave a red solid assumed to be the salt 80. Treatment of this salt with concentrated HCl in glacial acetic acid gave a 50% yield of silvery flakes. This reaction involves protonation of the salt, hydrolysis of the ester and decarboxyaltion of the resulting acid. When the reaction was carried out in the presence of benzaldehyde, aldol condensation gave the bis benzylidene derivative (cis or trans isomers) 81. Similarly, treatment of 72 with benzaldehyde and acid gave 81.

At this point let us pause for a moment for a discussion of solubility aspects of this project. The desired product, 56, or its dihydrate, 76, would be expected to be quite insoluble in organic solvents, but fairly soluble in aqueous solvents. Thus the reaction in which one of these is formed must not involve inorganic by-products which would be difficult to separate from the product. For example, selenium dioxide is a convenient method for conversion of the methylene

group alpha to a carbonyl group.[52] However, it is unsuitable for oxidation of 72 to 56, as separation of products would be difficult. Thus to carry out the conversion of 72 to 56, Gleiter and Schanz pyrolyzed 82 (Figure 22) so that the only by-products were the gases hydrogen chloride and carbon monoxide.

Similarly oxidative cleavage of the bis-benzylidene 81 would give the ketone 56. However, cleavage reactions involving periodate, osmium tetroxide or other inorganic oxides cannot be used for the same reasons as above. Ozonolysis of 81, on the other hand, would not give inseparable by-products and thus would seem to be a reasonable alternative. However, the bis-benzylidene 81 is so insoluble that ozonolysis is not possible.

It was our plan to carry out a multi-step oxidation of 72 to 56 in which the last step involved pyrolytic cleavage of volatile molecules, thus providing the necessity for separation of the product from by-products. This reasoning is, of course, the same as that of Gleiter and Schanz.[47] Our scheme (see Figure 26) was based on a ninhydrin synthesis given in Fieser's undergraduate lab manual.[53] Nitration of the active methylene groups in 72 gave the dinitro compound 83. Bromination gave the dinitrodibromotetraketone 84. Pyrolysis of this compound should give the hexaketone 56. However, heating the material in o-dichlorobenzene (bp 180°C)

gave only a black intractable solid.

One of the key steps in the preparation of the polycyclic aromatics 65 and 66 is condensation of hexaketone 56 with acetone. As a model, ninhydrin 79 was dehydrated (reflux in benzene under a Dean-Stark trap) then treated with acetone and a catalytic amount of toluenesulfonic acid. The only product isolated was 85, as characterized by pmr, IR and mass spec. This is an intermediate along the desired pathway. Dehydration followed by an intramolecular aldol condensation would give 86.

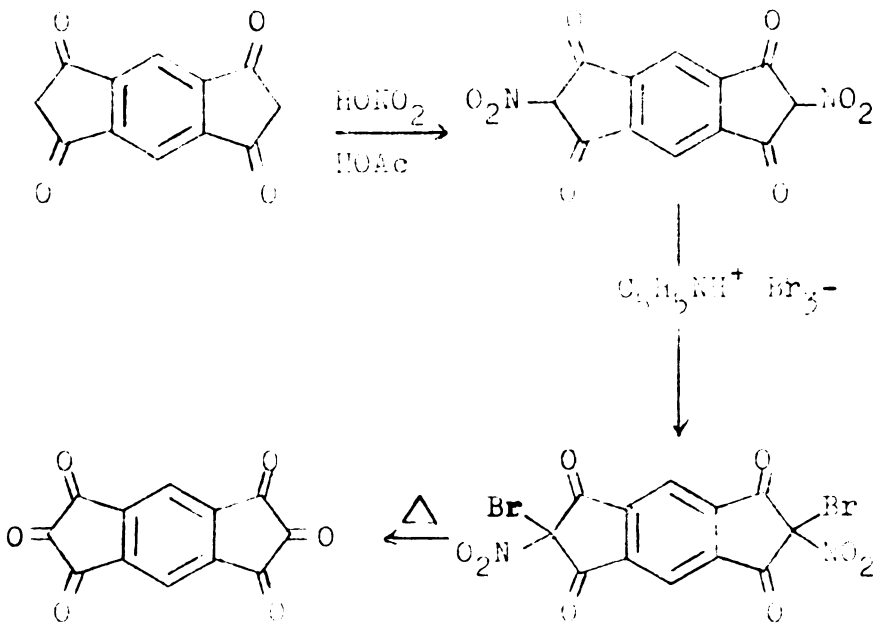


Figure 26. Proposed synthesis of 56 from 72.

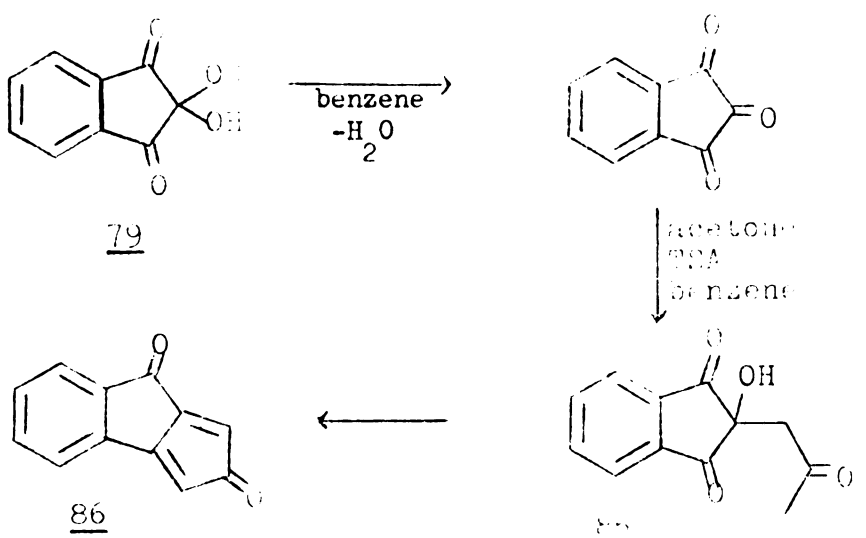


Figure 27. Attempted synthesis of 86 as a model for 62.

A different approach to the oxygenated hydrindacene system 56 involves cyclization of benzene bis-propionic acid derivatives and gives rise not only to the indacene skeleton 56 but also to the as-indacene skeleton of 93 (Figure 28). Cyclizations of the para and meta derivatives were explored, but the ortho derivatives 98 were not, as they can only produce the less desirable as-indacene skeleton. In any case, cyclization of the ortho derivatives should be similar in nature to that of the para derivatives.

Preparation of p-phenylene dipropionic acid derivatives 87- 90 and m-phenylene dipropionic acid derivatives 94 and 95 are outlined in Figures 29 and 30, respectively. Treatment of terephthaladehyde, 100, with malonic acid in refluxing pyridine,[54] followed by esterification of the resulting bis (acrylic acid), 99, gave 1,4-bis-(2-carboethoxyvinyl) benzene, 102 in 75% yield. The same diester was prepared directly from terephthaladehyde by reaction with the Wittig reagent, 103, prepared from ethyl bromoacetate, albeit in lower yield (25%) since separation of the product from triphenylphosphine oxide was difficult. Hydrogenation to the bis(ethyl propionate), 87 and hydrolysis to the bis(propionic acid), 88, both proceeded quantitatively. Similarly, reaction of isophthaldehyde[55] with malonic acid[56] gave the diacrylic acid 106 in 76% yield. Palladium catalyzed hydrogenation in aqueous

ammonia gave a nearly quantitative yield of diacid 94.

Figure 31 shows the results of various attempts to cyclize these derivatives. Warming of diester 87 in polyphosphoric acid followed by hydrolysis gives keto-acid 107

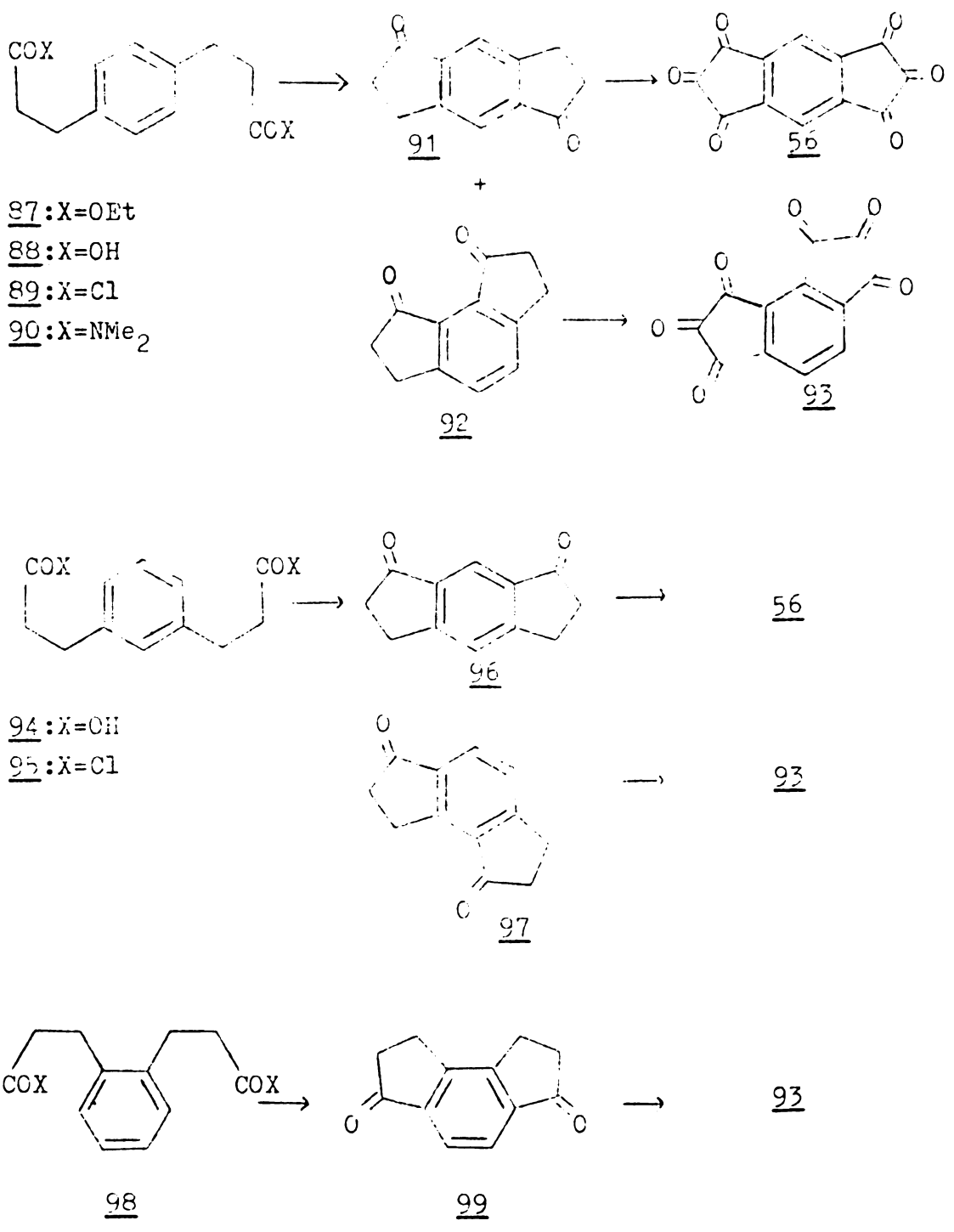


Figure 28. Generalized scheme for preparation of hydrindacene derivatives by cyclization of benzene bispropionic acid derivatives.

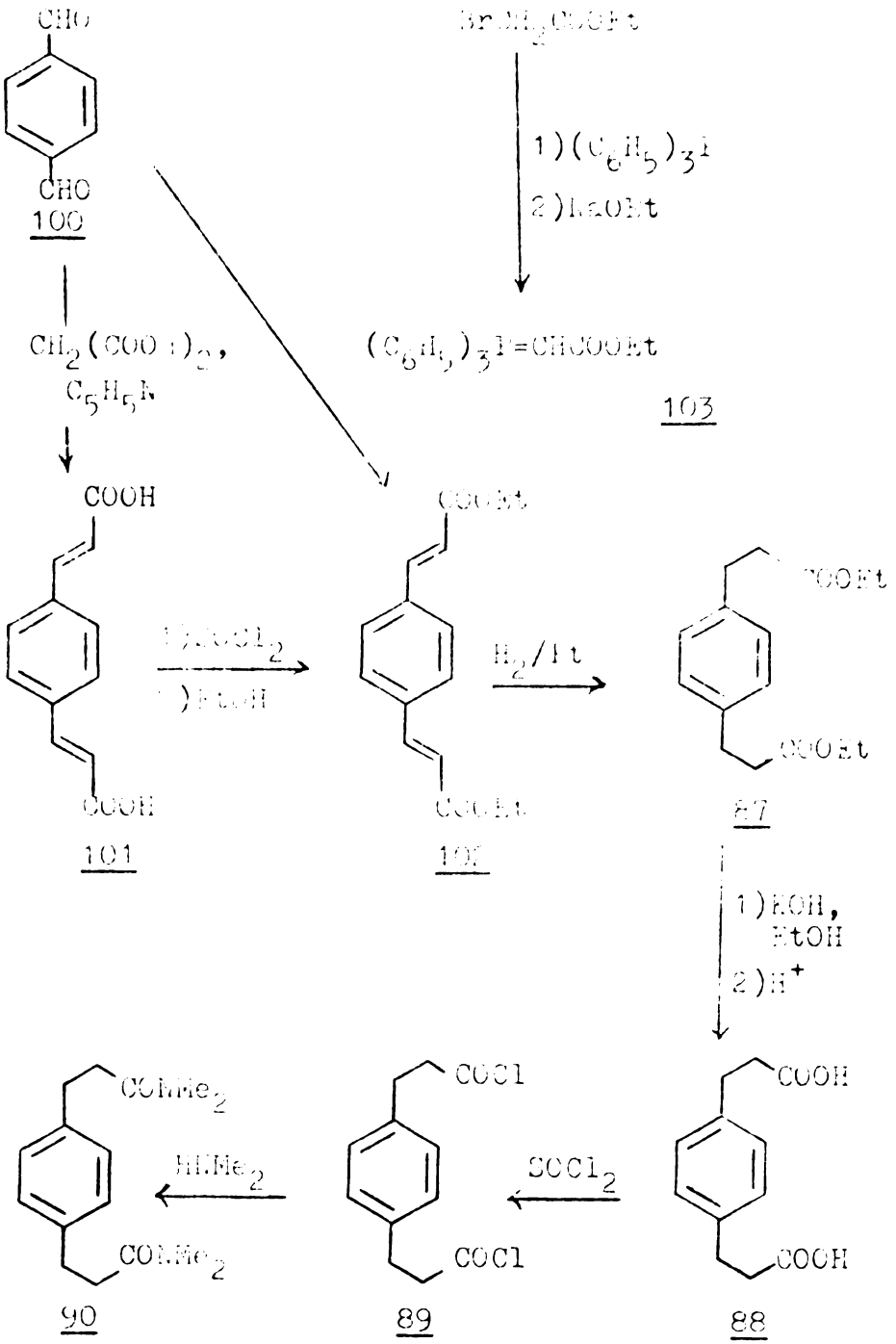


Figure 29. Preparation of p-phenylene dipropionic acid derivatives.

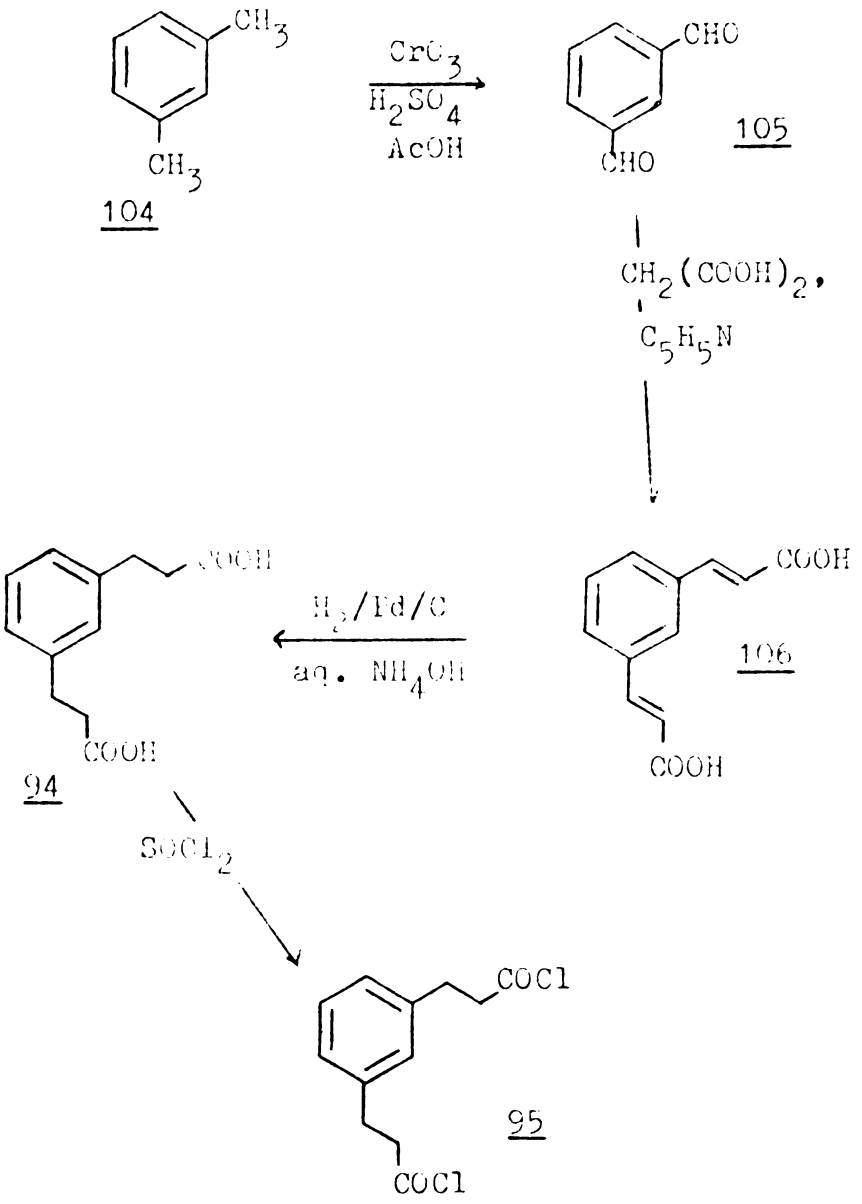
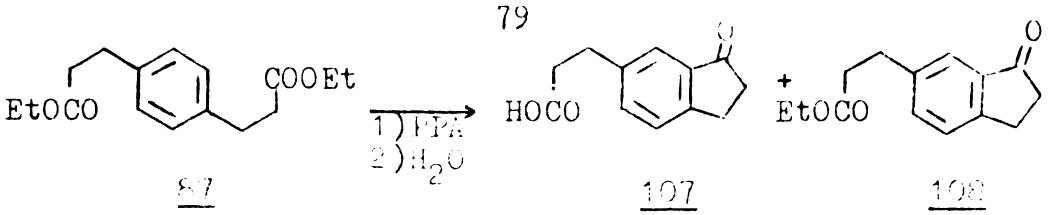
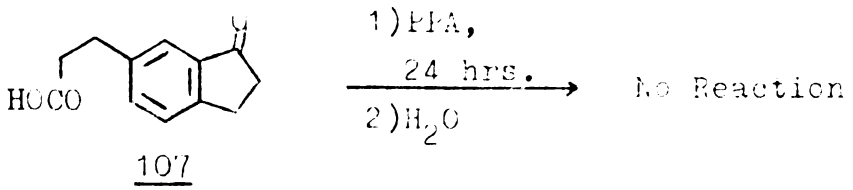


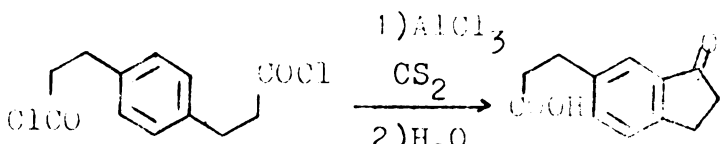
Figure 30. Preparation of m-phenylene propionic acid derivatives.



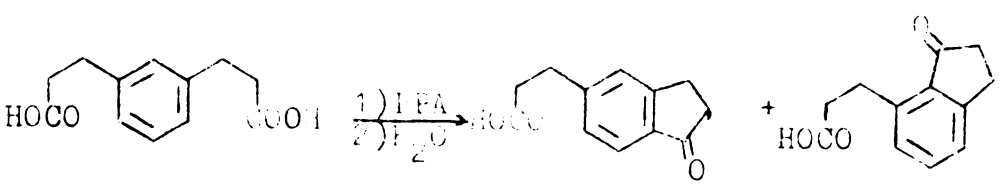
87 107 108



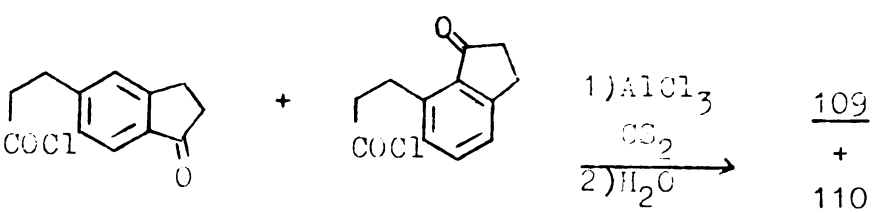
107



89 107



94 109 110



109 + 110

Figure 31. Attempted cyclizations of benzene bis-propionic acid derivatives.

in 91% yield (along with a small amount of keto-ester 108). The product 107 was recovered unchanged after heating in PPA for 24 hours. Treatment of the bis(acid chloride), 89, with aluminum chloride in carbon disulfide gives only the keto-acid 107. Apparently after the first electrophilic substitution, the newly formed ketone carbonyl deactivates the ring to further substitution, especially since the only positions available for the second substitution are ortho and para to the newly formed carbonyl. Thus it was thought that derivatives of 1,3-bis(propionic acids) might lend themselves more readily to double cyclization. However, such was not the case. Warming of diacid 94 with PPA followed by hydrolysis gives a 92% yield of a mixture of keto-acids 109 and 110. This mixture was converted to a mixture of the corresponding acid chlorides 111 and 112 by treatment with thionyl chloride. Treatment of this mixture of acid chlorides with aluminum chloride in carbon disulfide followed by hydrolysis gave only keto acids 109 and 110. Fusion of the same mixture of acid chlorides in a melt of aluminum chloride, sodium chloride and potassium chloride (mp 100°C)[57] gave only unidentified aliphatics.

Later developments in our laboratory showed that failure of our system to undergo a second cyclization is not unusual. In an unrelated project, Dr. L. L. Klein[58] had reason to desire to perform a double cyclization of the dimethoxy-p-phenylenedipropionic acid 113. He found that only one cycliza-

tion would occur even in this system which is considerably more electron-rich than ours, and thus would be expected to undergo electrophilic substitution more readily.

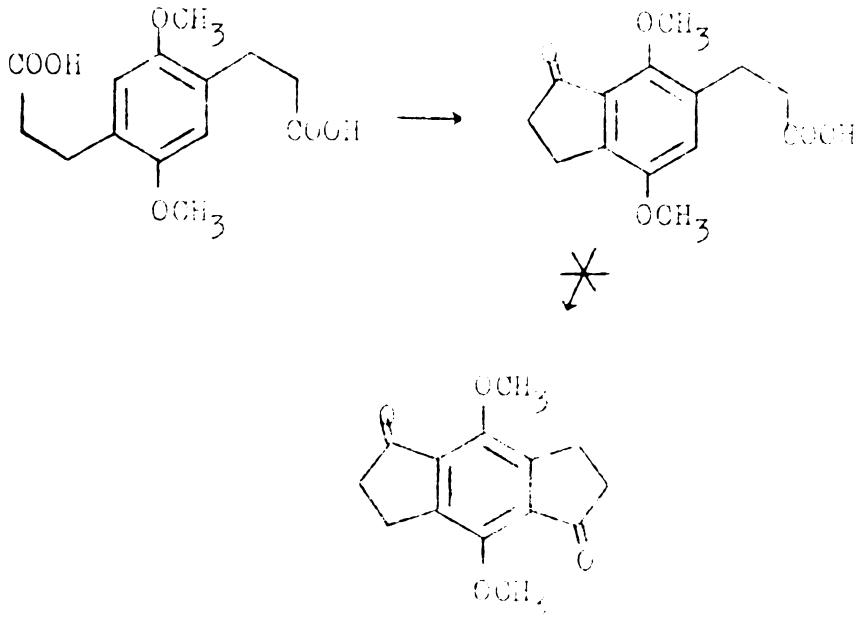


Figure 32. Failure of dimethoxy-p-phenylenedipropionic acid to undergo double cyclization.[58]

One final attempt to cyclize a p-phenylene dipropionic acid derivative was based on the known[59] methylation of N,N-dialkylamides to give N,N-dialkyl methoxyiminium ions using strong methylating agents such as trimethyl oxonium salts of methyl trifluoromethone sulfonate. We considered the possibility that the methylated amide 114 might be a strong enough electrophile to substitute on the aromatic ring. If so, the product (115) would not have a deactivating group

and a second substitution should occur almost as readily as the first. Hydrolysis would then give the desired diketone 21.

Warming of 20 with two equivalents of methyl triflate in chloroform, followed by hydrolysis gave an essentially

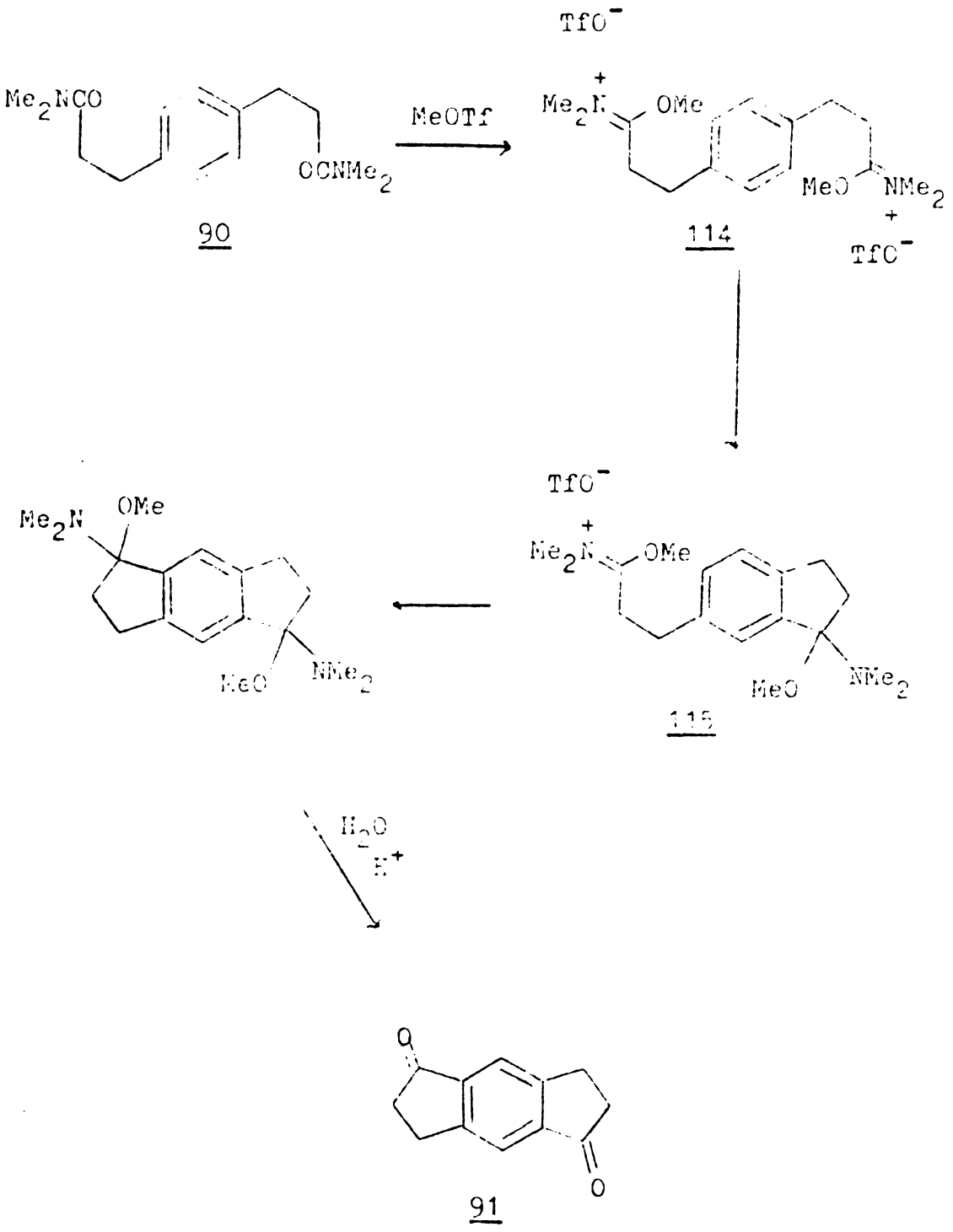
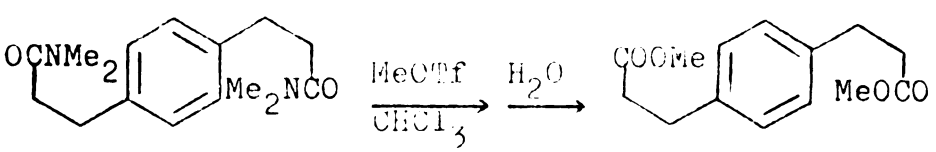


Figure 33. Proposed cyclization of 90 via the O-methylated salt.

quantitative yield of 1,4-bis(2-carbomethoxyethyl)benzene, 116. As esters are the expected product of hydrolysis of O-methylated-N,N-dimethylamide[59], formation of 116 in this reaction indicates that no cyclization occurs, though the salt 114 is formed. Apparently O-methylated-N,N-dimethylamides do not develop sufficiently reactive electrophiles to effect electrophilic aromatic substitution, at least not on unactivated rings.



90 116

Figure 34. Reaction of 90 with methyl triflate.

Another approach to the polyketohydrindacene system involves substitution of a carbonyl equivalent into a tetrasubstituted durene. Tetrakis(bromomethyl) benzene, 118, can be prepared in almost equal yields (50%) by either of two methods. Free-radical bromination of durene,[60] 119, gave a rather impure product. Reducing tetramethyl pyromellitate, 73, with lithium aluminum hydride gave tetrakis(hydroxymethyl)

benzene,[61] 120, which, due to its appreciable water solubility is difficult to separate from the metal hydroxide by-products. Treatment of this 1,2,4,5-tetrakis(hydroxymethyl)benzene with HBr in acetic acid gave a quantitative yield of 1,2,4,5-tetrakis(bromomethyl)benzene, 118.

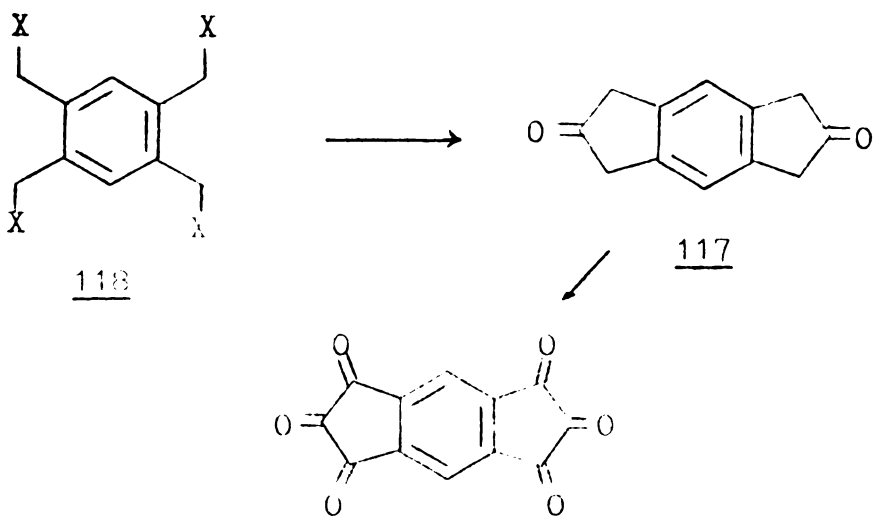
It is reported[62] that treatment of 1,2-bis(bromomethyl) benzene with cobalt octacarbonyl in the presence of lithium chloride gives 2-indanone. However, we found that similar conditions gave no reaction with tetrabromide 118.

Treatment of 118 with malonic ester and sodium ethoxide gave tetraester 121 in 85% yield. Hydrolysis to the tetra-acid 122 was quantitative. The plan was to convert the tetraacyl azide 123, followed by Curtius rearrangement to the isocyanate and hydrolysis to diketone 117[63]. Treatment of tetraacid 122 with thionyl chloride gave a yellow solid which is insoluble in organic solvents. Heating in acetonitrile with activated sodium azide, in a heterogeneous mixture gave, after evaporation of the solvent, a glassy yellow solid, presumably the tetraazide 123. This material was highly insoluble in organic solvents and appeared not to change on short heating in chloroform. Prolonged heating gave only black intractable material. Heating of 123 in ethanol gave a complex mixture of unidentified products.

After the report of the preparation of 56[47], we set aside further work on this system. However, the quinone and

hydroquinone 57 and 58 are significantly different and were deemed worth pursuing. A convenient entry to this system is shown in Figure 36.

Treatment of hydroquinone with aqueous formaldehyde and sodium hydroxide[64] gave a 70% yield of 1,2,4,5-tetrakis(hydrox-



118 117 56

Figure 35. Scheme for the synthesis of 56 by introduction of a carbonyl equivalent into a tetrasubstituted durene.

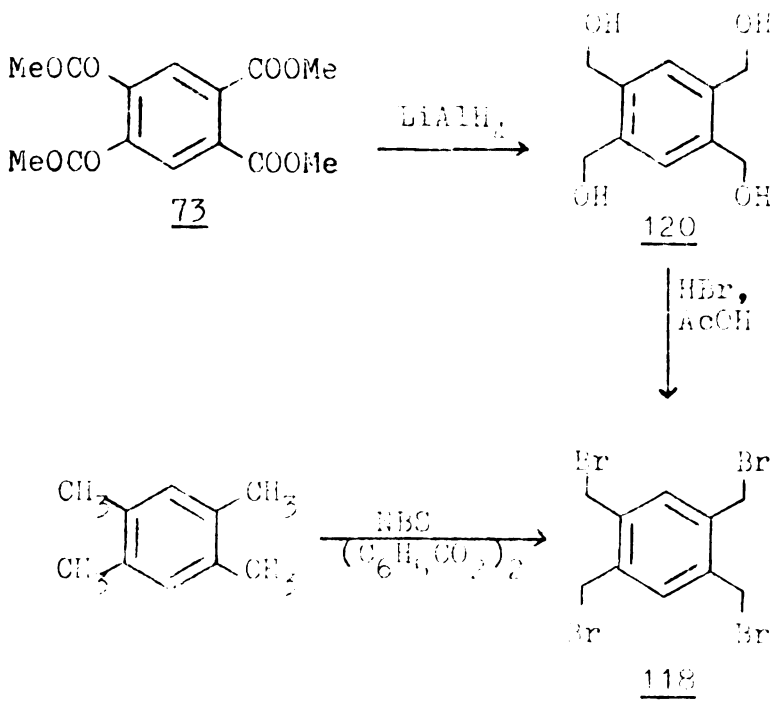


Figure 36. Preparation of 1,2,4,5-tetrakis(bromomethyl)benzene.

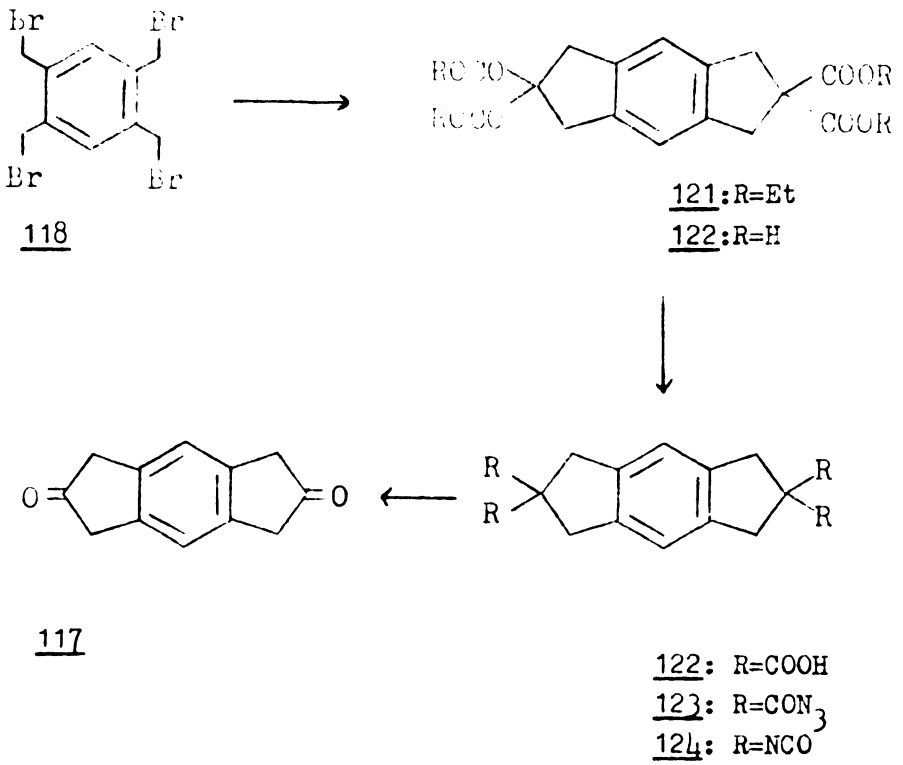


Figure 37. Proposed conversion of tetrabromide 118 to diketone 115 by a malonic ester synthesis.

ymethyl)hydroquinone 125. Treatment of 125 with HBr in acetic acid gave tetrabromide 126. However, this material tends to polymerize or oxidize to intractable material especially in the presence of base, so methylation of 126 was impossible. Thus it was thought to methylate the phenolic hydroxy groups of 125 giving 127, then prepare the tetrakis tosylate 128. (Substituting bromide for the hydroxyl groups in 127 with HBr would cleave the phenolic ethers and give 126). Unfortunately, the only product isolated from several methylation attempts on 125 was a small amount of trimethyl compound 129. It

should be noted that the preparation of 127 was not reported

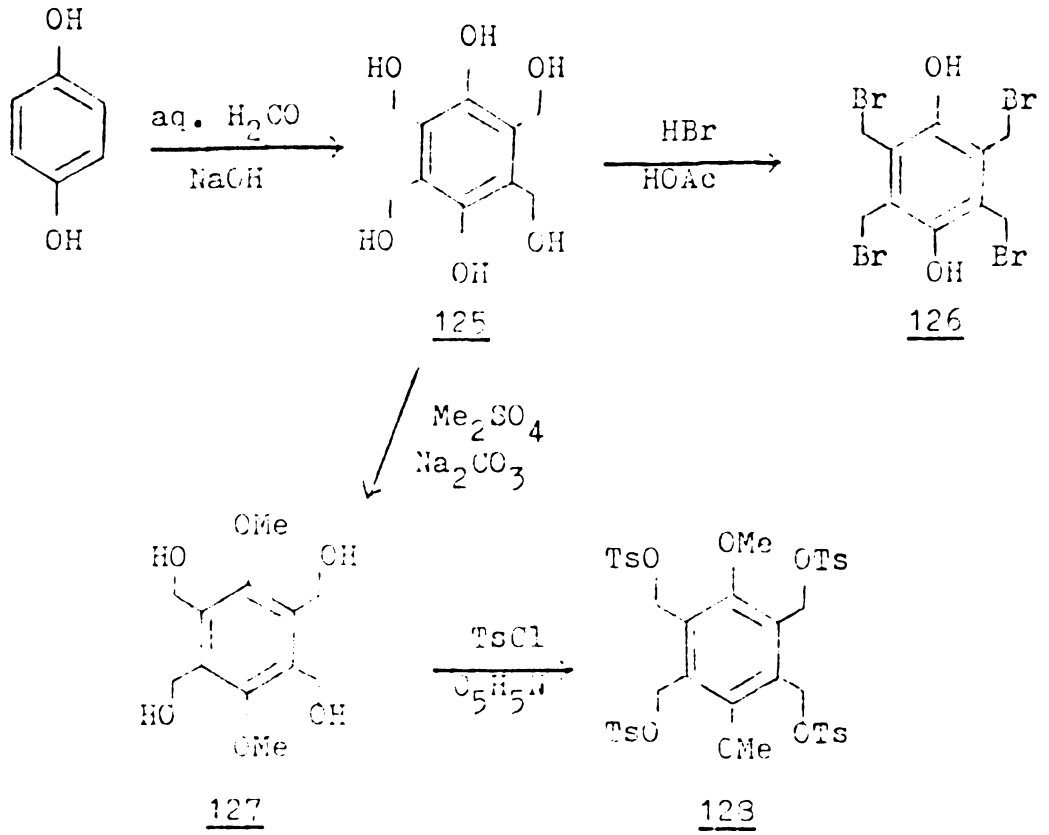
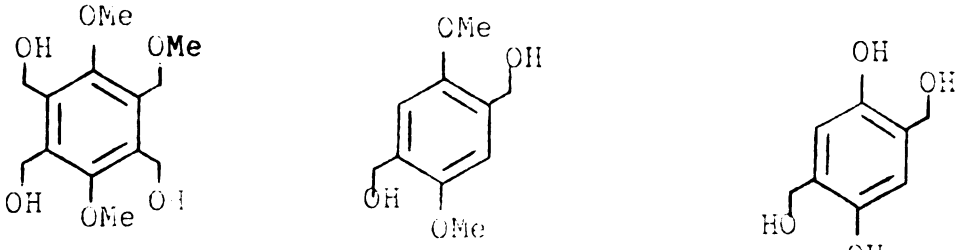


Figure 38. Approach to oxygenated system 57.

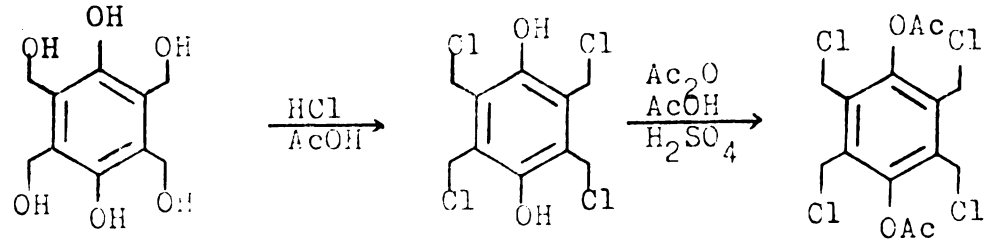
in reference 64 even though the preparation of 130 from 131 was reported, suggesting that there may be a special difficulty in this case. The apparent lack of formation of 127 may in fact simply be a failure to isolate it from aqueous solution, as evidenced by the high water solubility and low organic solubility of the analogous 1,2,4,5-tetrakis(hydroxymethyl)benzene.

When 125 was treated with HCl in acetic acid, followed by acetic anhydride in acetic acid with a catalytic amount of sulfuric acid,[64] there was isolated the tetrachloro diacetate in



129 130 131

Figure 39. Poly(oxymethyl) derivatives of hydroquinone.



125 132 133

Figure 40. Preparation of tetrakis(chloromethyl)hydroquinone diacetate 133.

42% yield. Treatment of 133 with malonic ester and sodium ethoxide led only to an oil which was apparently a mixture of esters.

Another approach to the oxygenated system involves annelation of two three-carbon moieties onto benzoquinone via two Diels-Alder reactions as outlined below. This is based on a paper by Diels and Alder themselves.[65]

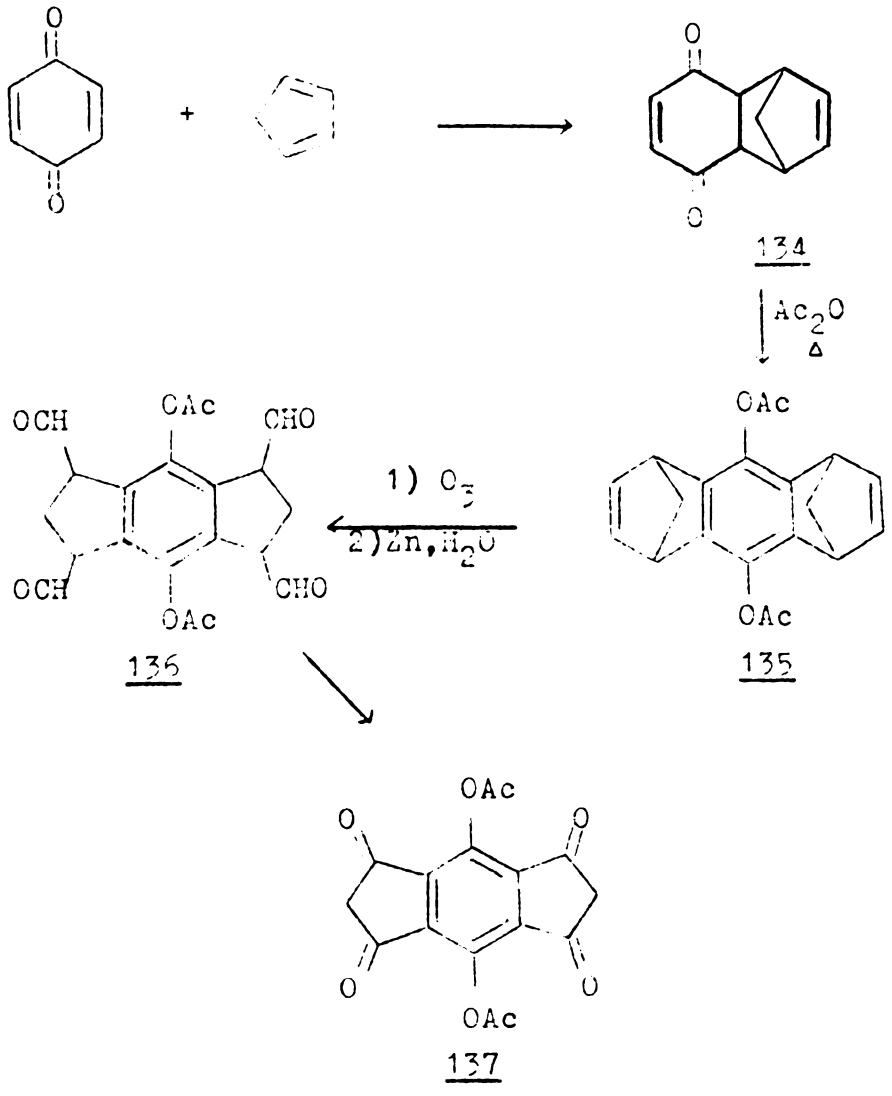
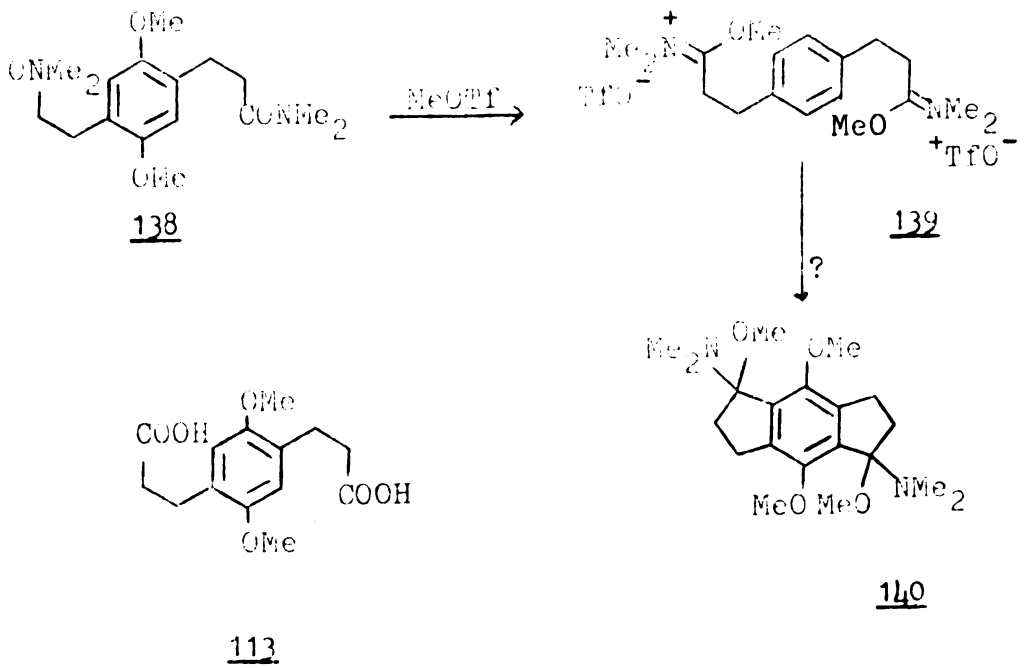


Figure 41. Double Diels-Alder approach to the oxygenated hydrindacene system.

Reaction of benzoquinone with cyclopentadiene (freshly cracked from dicyclopentadiene) gave monoadduct 134. On heating 134 in refluxing acetic anhydride, the diadduct 135 was obtained in 33% overall yield, along with some of the by-product hydroquinone diacetate. Initital attempts at ozonolysis of 135 failed, perhaps due to attack of ozone on the electron-rich aromatic ring. Were the desired tetraaldehyde 136 to be isolated, it could conceivably be converted to tetraketone 137 via any one of a number of multi-step oxidations.

Another approach involves cyclization of some derivatives of the dimethoxy diacid 113. This route is analogous to that explored earlier (Figure 31) for the same system without the aromatic methoxy groups.



138 139 140 113

Figure 42. Proposed cyclization of bis(propionamide) to the hydrindacene skeleton in the dimethoxy system.

As was mentioned earlier, Dr. L. L. Klein[58] explored the cyclization of these derivatives under acidic conditions, and found that after the first cyclization the newly formed ketone carbonyl deactivates the ring to further substitution. In addition, we found (Figure 33) that O-methylated-N,N-dimethyl amides were not powerful enough electrophiles to effect aromatic substitution in the non-functionalized system 114. However, it was of interest to investigate the same reaction starting with 138 in which the aromatic ring should be considerably more active. Again, the rationale behind such a reaction is that, once the first cyclization has occurred, the ring is not deactivated to a second cyclization.

To this end 138 was synthesized via the following route. The bis(chloromethyl) compound 142 was prepared in nearly quantitative yield by the reaction of p-dimethoxybenzene with excess paraformaldehyde and concentrated HCl. It was initially isolated in an attempt to prepare the tetrakis (chloromethyl) diether 141 which, despite all attempts, remained elucive. The malonic ester synthesis and hydrolysis proceeded in 45% and 82% yields respectively giving tetraester 143 and tetraacid 144. The decarboxylation to diacid 113 was carried out in 46% yield by heating 144 to melting (220°C) over a low flame until evolution of gas subsides. The bis-amide 138 was prepared in nearly quantitative yield by reaction

of the acid chloride of acid 113 with aqueous dimethylamine.

Warming of 138 with methyl triflate in chloroform, followed by addition of water gave only the diester 145. In addition

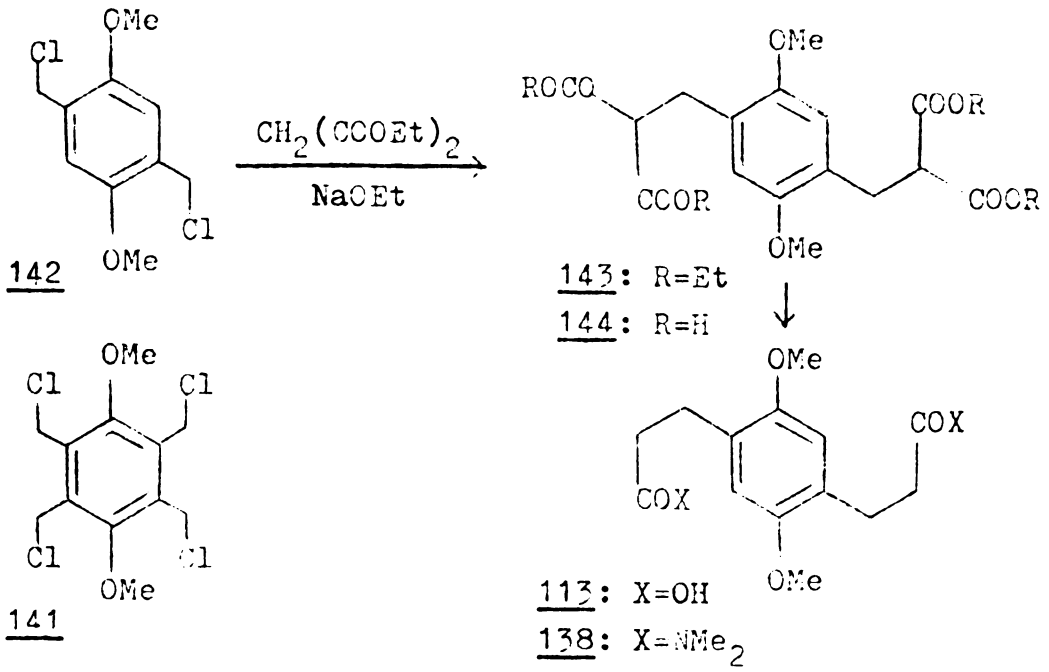


Figure 43. Preparation of dimethoxydiamide 138.

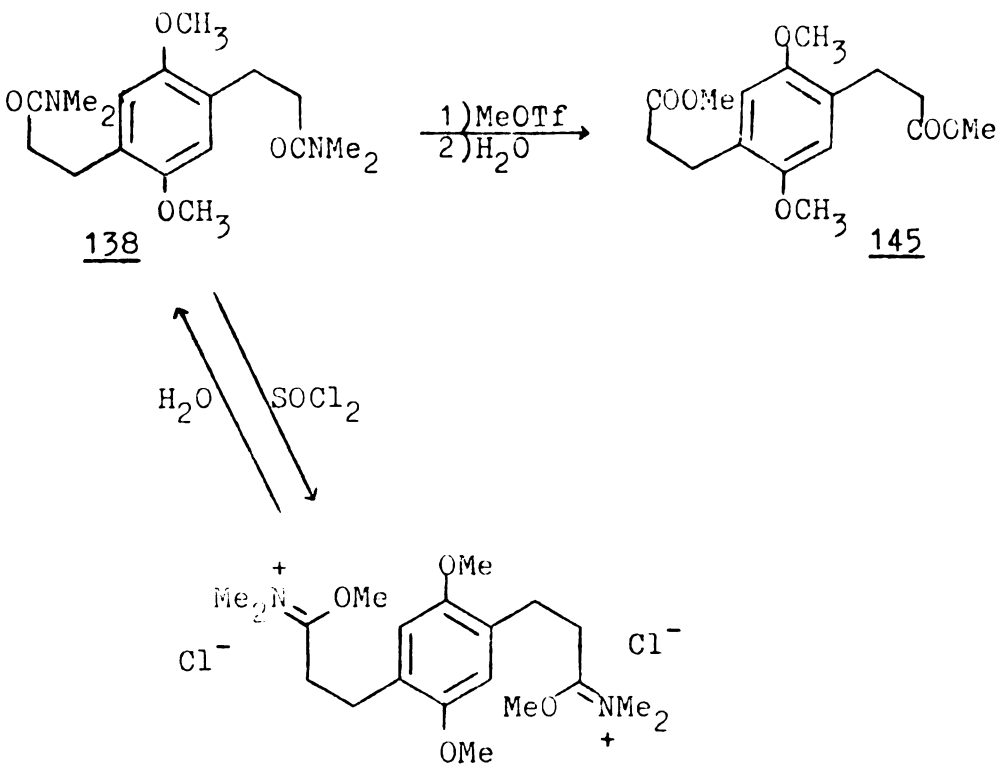


Figure 44. Attempted cyclizations of diamide 138.

the diamide 138 was heated with thionyl chloride to give the bis(chloroiminium) ion 146. Hydrolysis of the residue from evaporation of the thionyl chloride gave a low yield of starting material 138 as the only isolable product.

The failure of these cations to cyclize is predicted by Fodor and Nagubandi.[66] They claim that cyclization of imidium chlorides occurs only through the nitrilium ion, as shown in Figure 45.

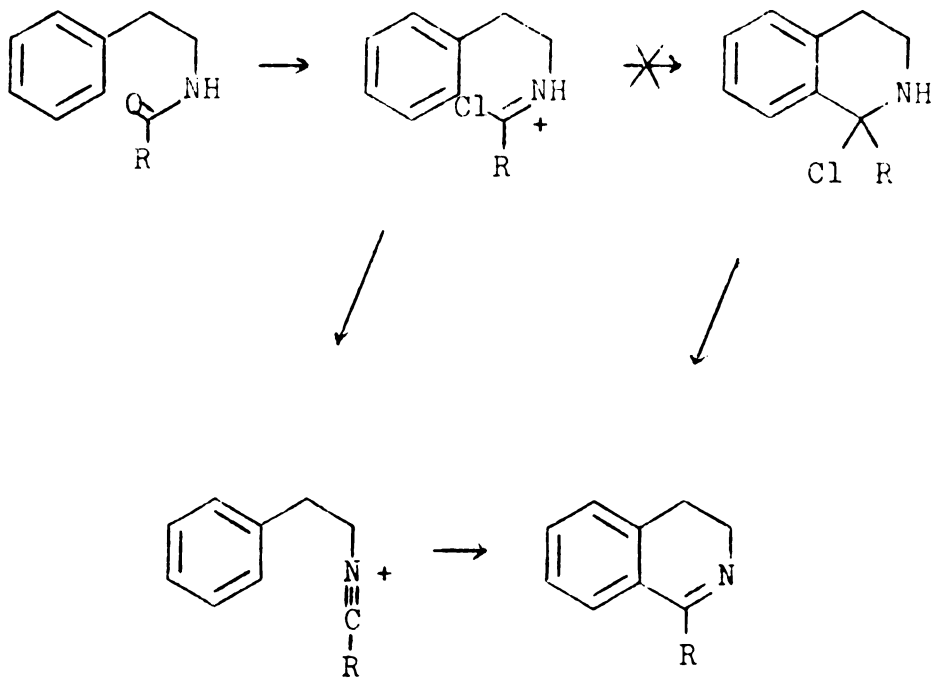


Figure 45. Cyclization of imidium chlorides through nitrilium ions.

As it is not possible to form a nitrilium ion from an N,N-disubstituted amide unless an N-alkyl group is removed, the cyclizations of these amides is not lilely. However, the dinitrile 147, upon alkylation should cyclize once, though a second cyclization is problematical. Nitriles can be alkylated by strong methylating agents such as trimethyloxonium tetrafluoroborate, methyl fluorosulfonate and methyl trifluoromethanesulfonate.[67]

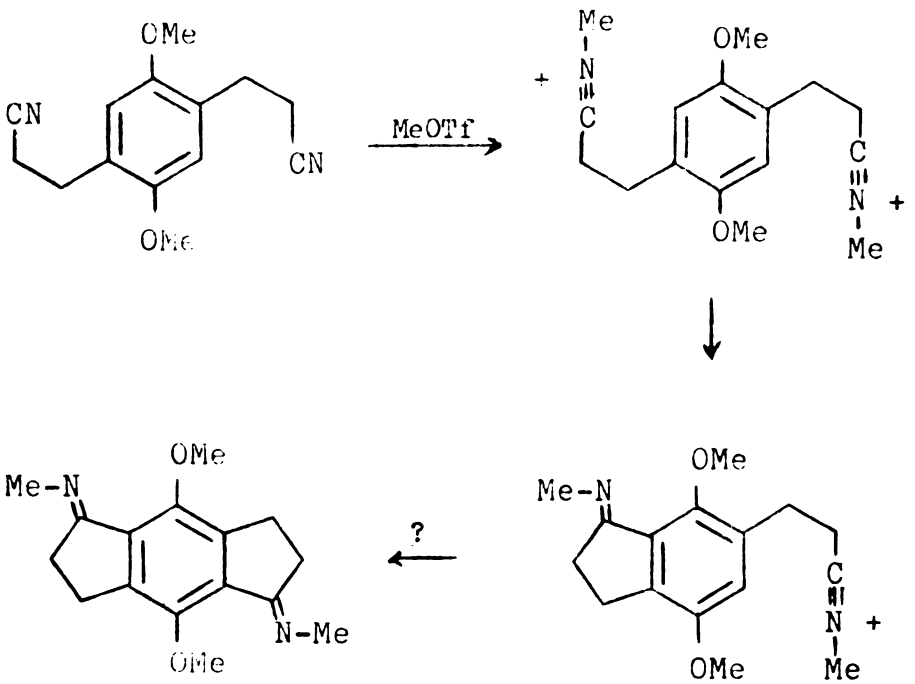
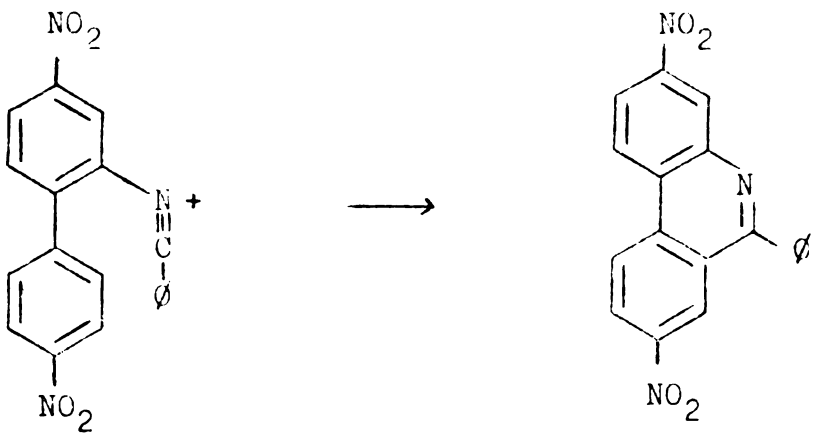


Figure 46. Proposed cyclization of dinitrile 145 through the nitrilium salt.

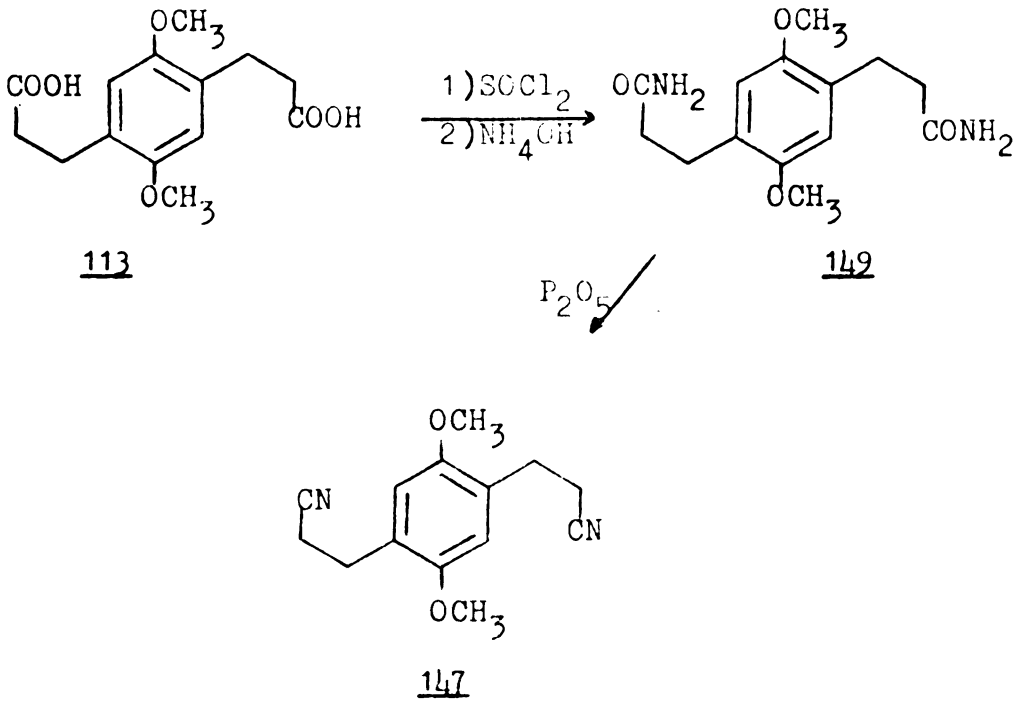
Though the second cyclization may seem unlikely due to the electron withdrawing imino group (perhaps protonated in the reaction mixture), there is precedence for nitrilium ions attacking electron deficient aromatics. For example, the electron deficient nitrilium ion 149 underwent cyclization.[66]

Thus the already prepared diacid 113 was converted to the diamide 149 via the acid chloride. The diamide was converted to the dinitrile by dehydrating with P_2O_5.[69]



149

Figure 47. Electrophilic substitution of a nitrilium salt on an electron deficient aromatic.[66]



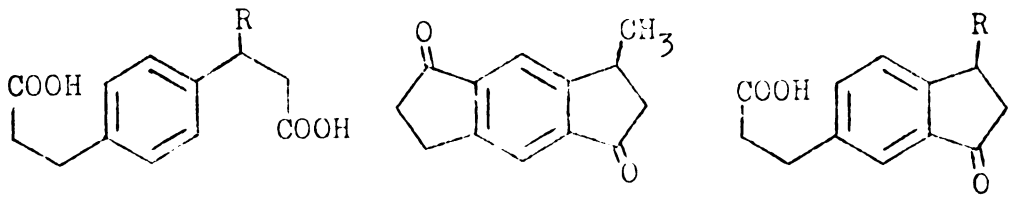
113 149 147

Figure 48. Preparation of dinitrile 147.

Treatment of dinitrile 147 with methyl triflate in carbon tetrachloride gave a complex mixture of products which was partially separated by column chromatography. All of the fractions showed pmr absorbances in the aromatic region. This suggests that, at most, one cyclization had occurred, since double cyclization would require substitution at all six aromatic carbons.

In a related development, it was discovered that some Argentine chemists[70] claimed to have obtained the diketone

151 in 59% yield as the only isolated product of the reaction of diacid 150 with PCl_5 and $AlCl_3$. Although no experimental details were given, it was also stated that, if $SOCl_2$ and $AlCl_3$ were used, there was obtained besides the diketone 151, a 22% yield of the keto acid 152. In my hands, reaction of the diacid 88 in a melt of PCl_5 and $AlCl_3$ gave only a 29% yield of the keto acid 107 along with an intractable tar. Similarly, treatment of the diacid 113 with a melt of PCl_5 and $AlCl_3$ gave no soluble products, perhaps due to cleavage of the ether linkages followed by lactonization, oxidation and/or polymerization.



88: R=H
150: R=CH_3

151

107: R=H
152: R=CH_3

Figure 49. Benzene dipropionic acid and derivatives.

EXPERIMENTAL

Instrumentation, solvents, etc. See experimental section for Part I.

2,6-Bis(methylthio)-2,6-dichloro-1,3,5,7-hydrindacene tetraone (75). A flame dried, 250 ml, 3-necked round bottom flask under a nitrogen atmosphere was equipped with overhead stirrer, addition funnel and condenser. It was charged with 1.5 g (0.063 mol) of sodium hydride. Through the addition funnel was added 40 ml of dry DMSO (distilled from KOH and stored over molecular sieves). After stirring for 15 minutes, a solution of 6.2 g (0.02 mol) of tetramethyl pyromellitate in 40 ml of dry DMSO was added. The mixture was stirred at room temperature for 24 hours. The DMSO was removed under reduced pressure. To the sticky red residue was added 200 ml of 15% aq. hydrochloric acid. The initially homogeneous solution slowly precipitated a yellow solid which was filtered out and washed with water. It was dried in a vaccuum desiccator and recrystallized from benzene. Mp 228-231°C, yield 3.7 g (40%). Mass spec. m/e: 378 (7%), 376 (8%), 374 (10%), 341 (3%), 339 &7%), 317 (8%), 315 (12%), 45 (100%).

2,5-Bis(carboethoxy)-1,3,5,7-hydrindacene tetraone, disodium salt,(80). In a flame dried 250 ml reaction apparatus (flask, condenser, addition funnel, N_2 atmosphere), 4.3 g (0.18 mol) of THF-washed sodium hydride was added to 100 ml

of dry THF. To this mixture was added 10 g (0.032 mol) of tetramethyl pyromellitate (which had been oven dried and stored in a desiccator). The mixture was brought to reflux. A solution of 7.0 g (0.08 mol) of ethyl acetate and 25 ml of THF was added slowly while the reaction mixture continued to reflux. After the addition was complete the reaction mixture was stirred at reflux for 24 hours. After cooling the reaction mixture was rotary evaporated and the brown residue was dispersed in ethanol causing considerable foaming due to the presence of excess sodium hydride. The resulting orange solid was centrifuged out, dispersed in water and recentrifuged. The resulting red solid was dried in vacuo to give 8.2 g (64%) of brick red solid. Mp 300°c.

1,3,5,7-Hydrindacene tetraone(72). 5.0 g (12.4 mmol) of finely divided red salt (80) was dispersed in 50 ml of glacial acetic acid and warmed on a steam bath. A small amount of con. HCl was added by dropper until the red suspension turned light orange. Heating was continued as the mixture darkened, evolved gas and became homogeneous. Within a few minutes a gray precipitate formed. The mixture was cooled in an ice bath then centrifuged. The resulting silvery solid was washed once with acetic acid and once with water then vaccuum dried to give 1.3 g (50%) of solid. This material is quite insoluble in most solvents. It can be sublimed (185°C/1 torr). Mp 300°C. Mass spec. m/e 214 (100%), 186 (12%), 172 (31%),

158 (17%), 144 (27%), 130 (10%), 102(26%). IR: 1750 cm^{-1} (w), 1710 (s), 1345 (m), 1225 (m), 877 (s), 735 (w), 1355 (m).

2,6-Dibenzylidene-1,3,5,7-hydrindacene tetraone(81). The above procedure was followed, except that an excess of benzaldehyde was added before heating. A green-yellow solid is obtained. After washing with acetic acid and drying, it can be recrystallized from anisole. Mp 330-332 dec. Mass spec. m/e: 390 (80%), 389 (100%0, 276 (16%), 194 (42%), 129 (35%), 102 (34%).

2,6-Dinitro-1,3,5,7-hydrindacene tetraone(83). To a mixture of 10 ml acetic anhydride and 15 ml glacial acetic acid was added in one ml portions 5 ml of con. nitric acid. The temperature was kept below 60°C with an ice bath. After the addition was complete the temperature was adjusted to 35° and the mixture was poured over 2.6 g (12.1 mmol) of the gray tetraketone 72. The mixture was warmed to 35° and maintained for twenty minutes by alternate warming and cooling. It was then cooled to 5°C and suction filtered. The dirty yellow solid was rinsed with ether and dried to give 2.70 g (74%).

2,6-Dibromo-2,6-dinitro-1,3,5,7-hydrindacene tetraone(84). In a 50 ml Erlenmeyer flask 2.63 g (8.22 mmol) of freshly prepared[5] pyridinium hydrobromide perbromide and 15 ml acetic acid were heated on a steam bath until all the solid dissolved. It was then poured rapidly into a solution of 2.5 g (8.22 mmol) of dinitrotetraone 83 in 25 ml water. The resulting white

precipitate was suction filtered, dissolved in ether, dried (Na_2SO_4) and evaporated to give 3.0 g (80%) of a white crystalline solid.

Pyrolysis of 84. In a large test tube 3.0 g of the white solid 84 and 10 ml of o-dichlorobenzene (bp 180°C) were heated over a small flame for 3 minutes. The solid blackened and after cooling was intractable.

p-Phenylene bis(3,3'-acrylic acid) (101). A mixture of 15 g (0.112 mol) terephthalaldehyde, 27.0 g (0.260 mol) malonic acid, 42 ml pyridine and a trace of piperdine were heated at 100° for 5 hours. The cooled reaction product was taken up in 300 ml of water and neutralized with 10% aq. HCl. The resulting white solid was filtered, washed with water, suspended in hot acetic acid and suction filtered. Yield 20.0 g (82%). Mp 300°. IR: 1685 cm^{-1}(s), 1630(m), 1330, 1320, 1290, 1230, 985, 950, 830. For lit. values see Ref. 54b.

Diethyl p-phenylene bis(3,3'-acrylate)(102). Method A. To a solution prepared by adding 2.3 g (0.10 mol) of sodium to 30 ml of absolute ethanol was added to a solution of 43 g (0.10 mol) of carboethoxymethyltriphenylphosphonium bromide in 70 ml of absolute ethanol. After the addition was complete the solution was allowed to stand for one hour. To the solution was added 6.7 g (0.05 mol) of terephthaladehyde along with an additional 50 ml of ethanol. The solution was stir-

red for two days at room temperature. The solution was filtered to remove a small amount of sodium bromide, then rotary evaporated. The resulting sticky residue was digested with low boiling ligroin and filtered. This process was repeated several times until the white solid showed no ethyl signals in the nmr. The combined ligroin extracts were rotary evaporated, giving a white semi-solid which is apparently a mixture of the desired product and triphenylphosphine oxide. They can be separated by chromatography on alumina with chloroform.

Method B. A solution of 15 g of p-phenylene bis(3,3'-acrylic acid was heated at reflux with 100 ml of absolute ethanol in 1 ml of concentrated sulfuric acid. After 24 hours the mixture had become homogeneous (the starting diacid is quite insoluble in ethanol). The hot solution was filtered to remove a small amount of insoluble material. Upon cooling, it deposited beautiful white needles. Mp 92-93°; lit.[54a] 95-96°C. Concentration of the mother liquor led to additional product. Total yield 17.2 g (91%). IR: 1717 cm^{-1}, 1640, 1330, 1310, 1290, 1210, 1190, 1030, 1000, 880, 835. Pmr: $1.31, t(J=7Hz), 6H; $4.22, q(J=7Hz), 4H; $6.39, d(J=16Hz), 2H; $7.47, s, 4H; $7.60, d (J=8Hz), 2H.

Diethyl p-phenylene bis(3,3'-propionate)(87). A mixture of 10 g (37 mmol) of diethyl p-phenylene bis(3,3'-acrylate) and 0.1 g of 5% palladium on charcoal in 100 ml of ethanol

was hydrogenated in a Parr hydrogenator at room temperature for 12 hours. Though the starting material was not completely dissolved, the product was. The solution was filtered to remove the catalyst, and the solvent was removed giving 10.1 g (100%) of white solid, mp 69-70°C, lit.[71] 69°. Pmr: δ1.19,t (J=7Hz),6H; δ2.69,m(aa'bb'),8H; δ4.04,q(J=7Hz),4H; δ7.00,s,4H

p-Phenylene bis(3,3'-propionic acid)(88). A solution of 10 g (36 mmol) of diester 85 in 100 ml of ethanol was mixed with a solution of 4.5 g (80 mmol) of potassium hydroxide in 50 ml of water. The mixture was heated at reflux for 15 hours. After cooling, the ethanol was removed by rotary evaporation. The aqueous solution was made acidic with 10% aqueous HCl. The resulting white precipitate was filtered out and washed thoroughly with water. Recrystallization from ethanol gives 7.9 g (99%) of white needles. Mp 225-227°C; lit.[71] 223°C.

Isophthalaldehyde.[55] In a two liter, three necked round bottom flask equipped with overhead stirrer, addition funnel, and thermometer extending to the bottom of the flask were placed 29 ml (25 g, 0.24 mol) of m-xylene, 928 ml (1 kg) acetic anhydride and 382 ml (400 g) of glacial acetic acid. The solution was cooled in an ice bath and 83 ml (150 g) of concentrated sulfuric acid was added through the dropping funnel at such a rate that the temperature stayed between 5 and 10°C. Over a period of 1½ hours, 90 g (0.90 mol) of chromium trioxide was added in small quantities so that the

temperature did not rise above 10°. After the addition was complete, stirring was continued for 3 hours at 5°. The green reaction mixture was poured into two liters of crushed ice and extracted three times with 250 ml portions of chloroform to give two liters of light green solution. It was concentrated to half its volume under 40°, then steam distilled until three liters of distillate were collected. This was extracted with chloroform, which was dried and rotary evaporated to give a yellow oil from which crystallized 4.4 g of white needles. An additional 2.7 g could be obtained from the oil on recrystallization from ethanol/water. Total yield 7.1 g (22%). Mp 85-89°C; lit.[55] 89°. Small amounts of 3-formyl benzoic acid and isophthalic acid could be isolated from the steam distillation still pot.

m-Phenylene bis(3,3'-acrylic acid)[56](106). A mixture of 2.2 g (16.4 mmol) of isophthalaldehyle, 3.4 g (33.0 mmol) of malonic acid and 10 ml of pyridine containing a trace of piperidine was heated at 100°C overnight. After cooling the solution was poured into water and made acidic with 10% aq. HCl. The resulting white solid was filtered out and recrystallized from acetic acid to give 2.9 g (80%) of white solid. Mp 281-284°C; lit.[56] 280°C.

m-Phenylene bis(3,3'-propionic acid)(94). To a mixture of 2.25 g (10.3 mmol) of m-phenylene bis(3,3'-acrylic acid) and 15 ml of water was added enough con. ammonium hydroxide

to dissolve the solid. To this solution was added 0.05 g of 5% Pd on charcoal. The mixture was shaken under hydrogen at room temperature for 1½ hours (until no more hydrogen was taken up). The catalyst was filtered out and the solution was made acidic with 10% HCl. After a moment a flaky white solid began to appear. After an hour this solid was filtered out, washed with water and dried giving 1.9 g (85%). Mp 148-150°C, lit.[56] 146-147°C.

6-(2-Carboxyethyl)-1-indandone(108). Method A. A mixture of 4.5 g (16.2 mmol) of p-diester 85 and 50 ml of polyphosphoric acid was warmed with manual stirring on a steam bath until the mixture became homogeneous and darkened considerably. After cooling, the syrupy mixture was poured into water and stirred until the PPA was completely dissolved. The aqueous solution was extracted thoroughly with chloroform. The organic solution was dried (Na_2SO_4), filtered and evaporated to give a yellow solid. Fractional crystallization (ethanol/water) gave 2.5 g (76%) of 109 (mp 140-142.5°C) and 0.57 g (15%) of oily 108. Nmr of 109: δ2.5-3.3,m,8H; δ7.2-7.75,m,3H Nmr of 108; δ1.19,t(J=3.5Hz),3H; δ2.5-3.2,m,8H; δ4.03,q(J=3.5Hz), 2H; δ6.9-7.7,m,3H.

Method B. A mixture of 3.5 g (15.8 mmol) of p-phenylene bis(3,3'-propionic acid) and 15 ml of thionyl chloride (freshly distilled from quinoline) was heated on a steam bath under reflux. After one hour the solid had dissolved and no further gas was evolved. The mixture was allowed to cool,

and the thionyl chloride was removed under reduced pressure. The resulting yellow solid was dissolved in carbon disulfide, cooled and stirred while 5.0 g (40 mmol) of aluminum chloride was added all at once. A copious quantity of HCl was released and the mixture turned red and lumpy. After standing overnight it was refluxed for an hour. Ice water was added slowly until all the aluminum chloride was hydrolyzed. The mixture was extracted thoroughly with chloroform. The combined extracts were washed with 5% sodium bicarbonate, dried (Na_2SO_4), filtered and evaporated to give a dark solid. This was recrystallized from ethanol/water to give 3.0 g (95%) of 109 (mp 139-142°C). Nmr: see above.

Attempted cyclization of 109 with PPA. Warming of 1.0 g of 109 with 15 ml of polyphosphoric acid overnight under N_2, followed by hydrolysis and work-up as above gave quantitative recovery of starting material.

5-(2-carboxyethyl)-1-indanone(109) and 7-(2-carboxyethyl)-1-indanone(110). A mixture of 1.0 g (4.5 mmol) of m-phenylene bis(3,3'-propionic acid) and 20 ml of polyphosphoric acid was heated for two hours on a steam bath, then allowed to stand overnight. Pouring the mixture into ice-cooled water gave 0.6 g (67%) of white solid (109). Mp 165-166.5°C (lit.[53] 165-166) from acetone. The mother liquor was extracted with chloroform which was dried, filtered and evaporated to give 0.3 g (33%) of a mixture of 109 and 110. Mp 93-100, 140-150°C from

ethanol/water. Nmr of 109: δ2.5-2.9,m,4H; δ2.9-3.5,m,4H; δ 7.32, dd(J=8.75,1.25Hz),1H; δ 7.45,d(J-1.25Hz),1H; δ 7.57,d(J=8.75Hz), 1H. (250 HMz).

1,2,4,5-Tetrakis(hydroxymethyl)benzene(120). The thimble of a dried Soxhlet apparatus under nitrogen was charged with 5.0 g (16.1 mmol) of tetramethyl pyromellitate. A slurry of 5.0 g (132 mmol) of lithium aluminum hydride and 100 ml of ether was boiled in the flask. After all the ester was dissolved and the reaction mixture cooled, the excess LAH was destroyed with saturated ammonium sulfate. After the ether was removed, the white residue was boiled in 200 ml of water. The hot solution was filtered and on cooling deposited 0.6 g (19%) of white needles; mp 192-193°C (lit.[61] 193°C). Concentration of the mother liquor gave an additional 0.9 g (28%).

1,2,4,5-Tetrakis(bromomethyl)benzene(118). Method A. A mixture of 3.1 g (15.6 mmol) of 1,2,4,5-tetrakis(hydroxymethyl)benzene and 100 ml of glacial acetic acid was stirred while gaseous hydrogen bromide was bubbled into the mixture. The temperature increased, the solid slowly dissolved and the solution became greenish. On cooling a light green solid crystallized and was filtered, washed with water and air dried. Yield 6.1 g (85%). Mp 157-159°C recrystallized from acetone. Concentration of the acetic acid solution gave an additional 0.7 g (10%).

Method B. A mixture of 22.8 g (0.170 mol) of finely ground durene, 125 g (0.702 mol) of N-bromosuccinimide, 1.5 g (6.0 mmol) of benzoyl peroxide and 100 ml of carbon tetrachloride was heated at reflux with mechanical stirring. After 30 minutes a vigorous reaction commenced causing considerable foaming. After the reaction appeared to have subsided, the mixture was stirred at reflux for an additional two hours. The hot mixture was filtered and the white solid was rinsed with hot carbon tetrachloride. After standing overnight the combined organic washes had deposited 12.5 g of large plates (mp 139-154°C) Concentration of the mother liquor led to an additional 5.9 g. Crude yield 18.4 g (25%). Crystallization from acetone gave 15 g (mp 148-152; lit.[60] 160°C). Nmr: δ4.40,s,8H; δ7.33,s,2H.

2,2',6,6'-Tetrakis(carboethoxy)hydrindacene(121). Under an N_2 atmosphere,dried 3-necked round bottom flask was equipped with magnetic stirring bar, addition funnel and condenser. Enough ethanol was added to 1.0 g (42 mmol) of sodium metal in 50 ml of dry THF to react with all the sodium. To this solution was added 9.0 g (56 mmol) of diethyl malonate followed as quickly as possible by 6.0 g (13 mmol) of 1,2,4,5-tetrakis (bromomethyl) benzene (prepared by Method A above) and 50 ml THF. The reaction mixture was heated at reflux for ten hours. After cooling most of the solvent was removed by rotary evaporation. Water was added and the waxy white solid was centri-

fuged out. After rinsing with water and drying, it was recrystallized from ethanol, giving in two crops 4.7 g(80%). Mp 159.5-160.5°C. Nmr: δ1.22,t,12H; δ3.44,s,8H; δ4.12,q,8H, δ6.82,s,2H. Mass spec. m/e: 446 (9%), 372 (30%), 298 (110%), 153 (58%).

2,2',6,6'-Tetracarboxyhydrindacene(122). A mixture of 4.0 g (8.96 mmol) of tetraester 120, 4.0 g (72.4 mmol) of potassium hydroxide, 50 ml of water and enough ethanol to dissolve the solid was heated at reflux for 20 hours. After cooling the homogeneous solution was made acidic with 10% HCl. When precipitation of the white solid was complete, it was filtered, washed with acetone and dried to give 2.9 g (95%) of tetraacid 122 (mp320°C). Mass spec. m/e: 246 (39%), 200 (48%), 155 (100%), 44 (92%).

2,3,5,6-Tetrakis(hydroxymethyl)hydroquinone(125). A mixture of 22.0 g (0.20 mol) of hydroquinone and 20 ml of water was purged with N_2 gas. To the mixture was added 80 ml of N_2-purged 10% aqueous sodium hydroxide (0.20 mol). Under nitrigen, 349 g of freshly opened aqueous formaldehyde was slowly added. The homogeneous solution was allowed to stand under nitrogen at room temperature for 3 days. It was acidified with N_2-purged 10% aqueous hydrochloric acid and cooled in an ice bath for several hours. The light brown solid was filtered out, washed thoroughly with water and vaccuum dried to give 32 g (70%) of whitish solid. Mp 200-

210°C in a preheated oil bath, lit.[64] 210-22.

2,3,5,6-Tetrakis(chloromethyl)-1,4-diacetoxybenzene (133). Excess hydrogen chloride was bubbled into a mixture of 10 g (43 mmol) of hexaol 125 and 100 ml of glacial acetic acid. The solution became warm and darkened as the solid dissolved. After standing overnight, the solvent was removed under reduced pressure. To the dark residue was added a solution of 15 ml of acetic anhydride, 2 ml of concentrated sulfuric acid and 100 ml of glacial acetic acid. The solution was stirred overnight, then diluted with water and immediately centrifuged. The light green solid was washed with water and vaccuum dried. Recrystallization from ethyl acetate gave 7.1 g (42%) of the tetrachlorodiacetate. Mp 217.5-220.5°C. Nmr: δ2.41,s,6H; δ4.54,s,8H. Mass spec. m/e: 390 (0.1%), 388 (0.1%), 348 (1%), 346 (3%), 344 (2%), 308 (3%), 306 (12%), 304 (25%), 302 (21%), 43 (100%).

Cyclopentadiene-benzoquinone adduct(134). Cracking of dicyclopentadiene was carried out by heating and distilling the resulting cyclopentadiene through a column of glass helices, bp 40-50°C. To an ice-cooled slurry of 20.3 g (0.172 mol) of benzoquinone in 200 ml of absolute ethanol was added dropwise 11.4 g (0.172 mol) of freshly cracked cyclopentadiene. After the addition was complete the mixture was allowed to warm with stirring until the solution became dark red-brown. The ethanol was distilled off under aspirator pressure. The

dark residue was extracted with hot hexane until the hexane appeared very light yellow. The combined hexane extracts were hot filtered and concentrated. On cooling 16.7 g (53%) of yellow needles formed. Mp 75°C; lit.[65b] 71-73°C. Nmr: δ1.4-1.6,m2H; δ3.05-3.25,m2H; δ3.4-3.5,m2H; δ6.0-6.1,m,2H δ6.45,s,2H. For lit. nmr see Ref. 65b.

1,4,5,8-Dimethano-1,4,5,8-tetrahydro-9,10-diacetocy-anthracene(135). A mixture of cyclopentadiene-benzoquinone adduct (8.5 g, 45.6 mmol) and 45 ml of acetic anhydride was heated at reflux for two hours then allowed to cool in an ice bath. From the solution crystallized 4.8 g (62%) of an orange-white product. It was filtered out, rinsed with ether and recrystallized from ethyl acetate (prisms, mp 222-224°C, lit.[65a] 250°C). The by-product, 1,4-diacetoxybenzene, can be isolated from the acetic anhydride mother liquor. Nmr of 135: δ2.17,m4H; δ2.27,s,6H; δ3.70,m,4H; δ6.33,m,4H. Mass spec. m/e: 322 (46%), 280 (23%), 238 (100%).

2,5-Bis(chloromethyl)-1,4-dimethoxybenzene(142). A mixture of 4.5 g (32.6 mmol) of 1,4-dimethoxybenzene, 25 g (0.83 mol) of paraformaldehyde, 80 ml of concentrated hydrochloric acid and 100 ml of glacial acetic acid was heated on a steam bath for 24 hours. The hot mixture was filtered and after cooling, the mixture was poured over ice, the solid filtered out, washed with water and vacuum dried to give 6.74 g (88%) of yellowish product. Recrystallization from

acetone gave needles, mp 163.5-164.5, lit.[72] 167.5°C. Nmr: δ 3.79,s,6H; δ 4.55,s,4H; δ 6.79,s,2H. Mass spec. m/e:238 (4%), 236 (24%), 234 (38%), 221 (4%, 219 (6%), 201 (32%0, 199 (100%), 134 (41%).

1,4-Dimethoxy-2,5-bis(2,2-dicarboethoxyethyl)benzene(143). In a dried apparatus under nitrogen, 0.7 g (30 mmol) of sodium was dissolved in a minimum of absolute ethanol in 150 ml of dry THF. To the sodium ethoxide was added quickly 4.8 g (30 mmol) of diethyl malonate followed immediately by 3.3 g (14.1 mmol) of 2,5-bis(chloromethyl)-1,4-dimethoxybenzene(142). The reaction mixture was heated at reflux for 20 hours. After cooling, the solvent was evaporated, the residue taken up in water and the resulting yellow solid was filtered and washed with water. After drying, it was recrystallized from petroleum ether to give 3.0 g (45%) of white needles (mp 99.5-100°C). Nmr: δ 1.17,t(J=3Hz),12H; δ 3.08,d(J=4Hz),4H; δ 3.57-3.77, m,2H; δ 3.70,s6H;δ 4.04,q(J=3Hz),8H; δ 6.54,s,2H.

1,4-Dimethoxy-2,5-bis(2,2-dicarboxyethyl)benzene(144). A mixture of 2.9 g (6.0 mmol) of tetraester 143 and 1.4 g (25 mmol) of potassium hydroxide in 10 ml of water was diluted with enough ethanol to dissolve the solid. The mixture was stirred at reflux overnight. After cooling to room temperature the solution was poured into 5% aqueous hydrochloric acid, then stored in the refrigerator overnight. The resulting white solid was filtered out and air dried giving

1.8 g (82%) of off-white powder. An additional 0.4 g (18%) can be obtained by concentrating and chilling the mother liquor. Mp 220°C dec, resulting material mp 189-192°C; lit.[73] 226 and 197-199.5.

1,4-Bis(2-carbomethoxyethyl)benzene(116). To a solution of 0.60 g (2.2 mmol) of N,N,N',N'-tetramethyl-1,4-bis(2-carbamidoethyl)benzene, 90, in 5 ml of chloroform was added 0.50 ml (0.72 g, 4.4 mmol) of methyl trifluoromethanesulfonate. The homogeneous solution was heated at reflux for 3 hours after which time a dark oil had separated. To the mixture was added 5 ml of water and stirring was continued for 2 hours. The organic layer was separated and the aqueous layer extracted twice more with 5 ml portions of methylene chloride. The combined organic layers were dried ($MgSO_4$), filtered and evaporated to give an orange oil which eventually solidified. Recrystallization from methanol gave 0.35 g (64%) of white needles, mp 110-114°C (lit.[74] 115°C). Mass spec. m/e: 250 (32%0, 190 (55%), 176 (38%), 130 (36%), 117(100%). Pmr: δ 2.5-2.9,m,8H; δ 3.60,s6H; δ 7.01,s,4H.

1,4-Dimethoxy-2,5-bis(2-carboxyethyl)benzene(113). In a small round bottom flask topped with an uncooled condenser, 4.0 g (11 mmol) of the bis malonic acid 144 was heated to 240°C in an oil bath and the resulting melt was allowed to stand at 240°C for 15 minutes. After cooling to room temperature, the brown solid was recrystallized from acetonitrile

to give 2.7 g (87%) of white needles, mp 195-197°C (lit.[73] 197-199.5°C). Mass spec. m/e: 282 (100%), 223 (54%). Pmr: δ2.5-2.8,m,8H; δ3.73,s,6H; δ6.73,s,2H.

1,4-Dimethoxy-2,5-bis(2-dimethylaminocarboxylethyl)benzene(138). A solution of 0.9 g (3.2 mmol) of the diacid 113 in 5 ml of thionyl chloride was heated at reflux for 3 hours. The excess thionyl chloride was removed under reduced pressure and the resulting solid was dissolved in 10 ml of methylene chloride and added with stirring to an ice-chilled mixture of 5 ml of 25% aqueous dimethyl amine and 5 ml of methylene chloride. After stirring overnight at room temperature, the organic layer was separated and the aqueous layer was extracted twice more with 10 ml portions of methylene chloride. The combined organic layers were washed with 10 ml portions of 10% NaOH and water, then dried, filtered and evaporated to give 1.0 g (91%) of crude solid. Recrystallization from acetone gives plates, mp 126.5-127°C. Mass spec. m/e: 336 (60%), 177 (67%), 72 (100%). Pmr: δ2.4-2.9,m,8H; δ2.95,s,12H; δ3.71,s,6H; δ6.62,s,2H.

1,4-Dimethoxy-2,5-bis(2-carbamidoethyl)benzene(149). A mixture of 2.70 g of the diacid 113 and 50 ml of thionyl chloride was warmed for 4 hours. The thionyl chloride was removed under vaccuum. The residue was dissolved in toluene, which was in turn removed under reduced pressure. The resulting yellow solid was dissolved in 100 ml of ether and to it

was added slowly with stirring 12 ml of concentrated ammonium hydroxide. A yellow precipitate formed. After 15 minutes the ether was rotary evaporated and the yellow residue was washed with water and suction filtered until dry. Recrystallization from ethanol gave 1.75 g (66%) of yellow powder, mp 225-227°C (turns red on melting), lit.[69] 225-228°C. Mass spec. m/e: 280 (100%), 247 (5%), 235 (22%), 222 (11%), 177 (25%).

1,4-Dimethoxy-2,5-bis(2-cyanoethyl)benzene(147). A mixture of 1.50 g (5.36 mmol) of the diamide 149, 1.0 g (7.07) mmol) of phosphorus pentoxide and 75 ml of mesitylene was heated at reflux for two hours. The hot yellow supernatant was decanted from a black residue. On cooling the mesitylene solution deposited 0.50 g (38%) of yellow leaves (mp 152.5-154.5, lit.[69] 155-156). The mother liquor was concentrated under vaccuum to half volume and chilled to give an additional 0.25 g (19%). Total yield 57% crystallized from ethanol, mp 154-155°C. Pmr: δ2.4-2.9,m,8H; δ3.77,s,6H; δ 6.63,s, 2H. Mass spec. m/e: 244 (8%), 229 (6%), 204 (100%), 189 (12%).

Fusion of 1,4-bis(2-carboxyethyl)benzene(88) in PCl_5/$AlCl_3$. A mixture of 0.90 g of the diacid (4.1 mmol), 2.0 g of phosphorus pentacnloride (10 mmol) and 2.0 g (15 mmol) of aluminum chloride was heated slowly in an oil bath to the melting point and allowed to stand for 15 minutes. After cooling the dark solid mass was treated carefully with water. After the hydrolysis was complete, a quantity of black tar remained. The mixture was extracted thoroughly with methylene

chloride. The organic solution was then dried, filtered and evaporated to give 0.25 g (29%) of a dark oil which by nmr consisted almost exclusively of 6-(2-carboxyethyl)-1-indanone (107).

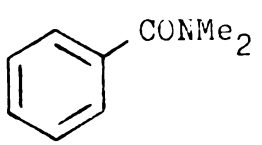
Fusion of 1,4-dimethoxy-2,5-bis(2-carboxyethyl)benzene (113) in $PCl_5/AlCl_3$. The same procedure as above was carried out starting with 1.20 g (4.25 mmol) of the dimethoxy diacid, 3.0 g (15 mmol) of phosphorus pentachloride and 2.0 g (15 mmol) of aluminum trichloride. The resultant methylene chloride extract gave only a trace of unidentifiable material.

Part III

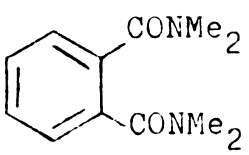
REACTIONS OF AROMATIC POLY(N,N-DIMETHYL AMIDES) WITH ELECTROPHILES

INTRODUCTION

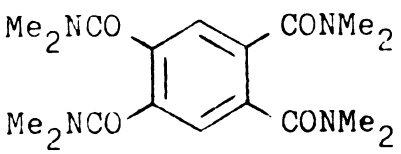
Our investigation of N,N-dimethyl amides 90 and 138 as well as nitrile 147, specifically their reactions with methylating agents and other electrophiles, led us to investigate other examples. Several aromatic poly(N,N-dimethyl)amides have interesting chemical and physical properties. For example, all the amides shown in Figure 50 show appreciable water solubility, but those with amide groups ortho to one another, 154 and 155, are very soluble in water as well as most other organic solvents.



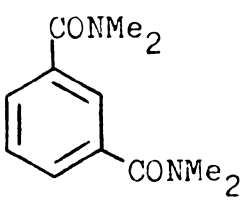
153



154



155



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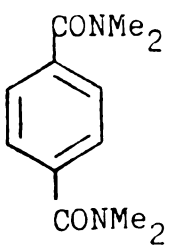


157

Figure 50. Aromatic poly(N,N-dimethyl)amides.

It was of interest to us to explore the reactions of diamide 154 with electrophiles to determine to what extent, if any, the neighboring amide group enters into the reaction of the other. For example, with methylating agents several structures are possible, listed in Figure 51. It was of interest to us to determine which of these, or others, is the correct structure of the salt.

In addition, we desired to investigate the reactions of 154 with chlorine electrophiles such as thionyl chloride, phosphorus oxychloride and oxalyl chloride. The structure of the reaction product could be one of the following or some other. For both types of reaction the salts can be characterized by ^{1}H- and ^{13}C-nmr, as well as by reaction with nucleophiles to give isolable neutral molecules.

The ready availability of amides 153, 156 and 157 makes their use as model systems for the above reactions possible. In addition, reaction of the tetraamide 155 with the above reagents could give insight into the effect of a second identical reaction center in the same molecule.

It was also of interest to investigate the products, if any, of reaction of the salts of 154 with aromatics such as 1,4-dimethoxybenzene and N-methyl pyrrole. It was our intent to determine whether acylation would occur, and, if so, whether one or both amide groups would react.

Also, it was thought that salts of tetraamide 155 could serve as an entry into the polyketo hydrindacene system, explored in Part II of this thesis, by reaction with masked carbonyl anion equivalents such as malonic ester or 1,3-dithiane anions.

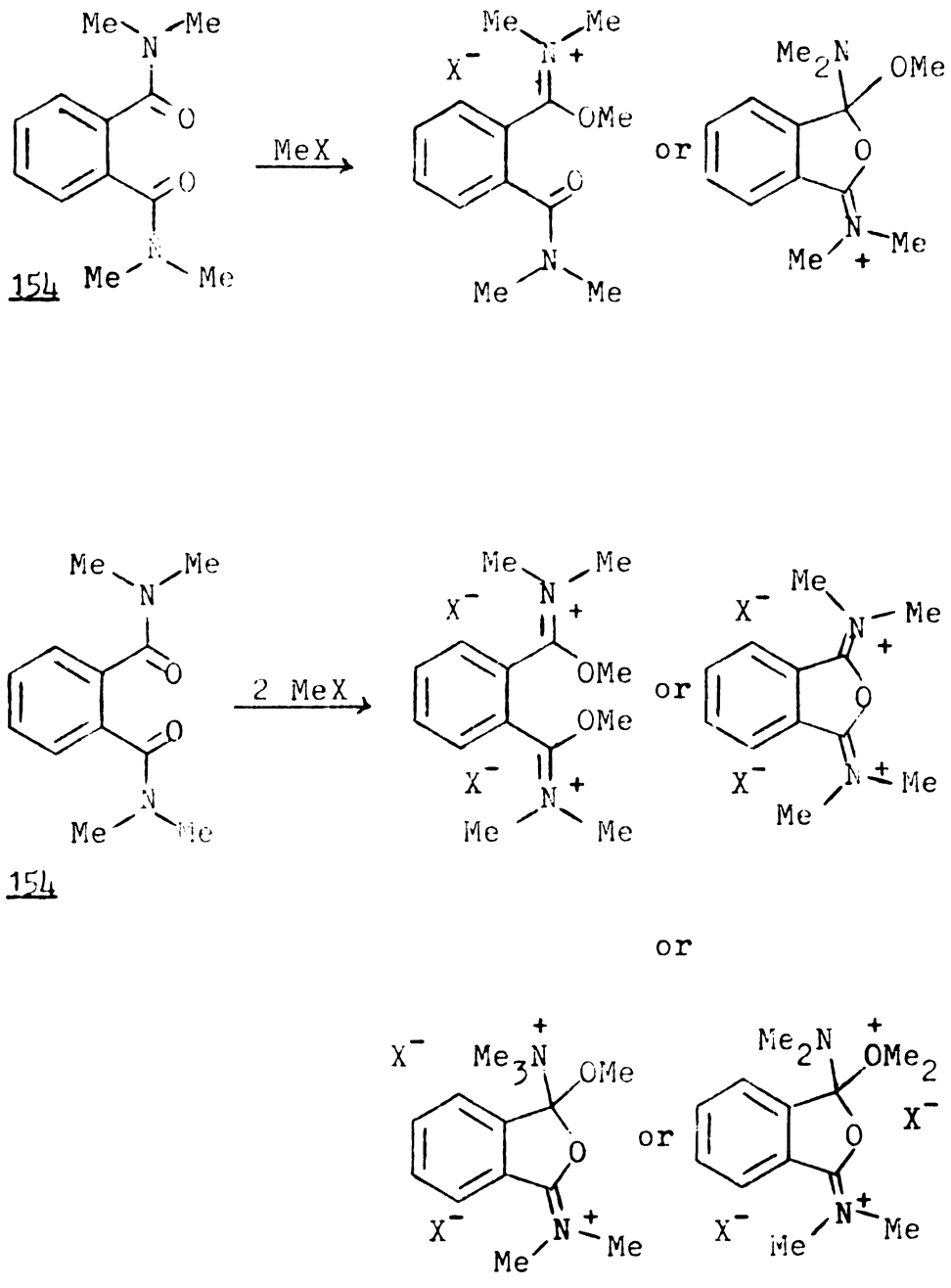


Figure 51. Possible products of methylation of N,N,N',N'-tetramethylphthalamide 154.

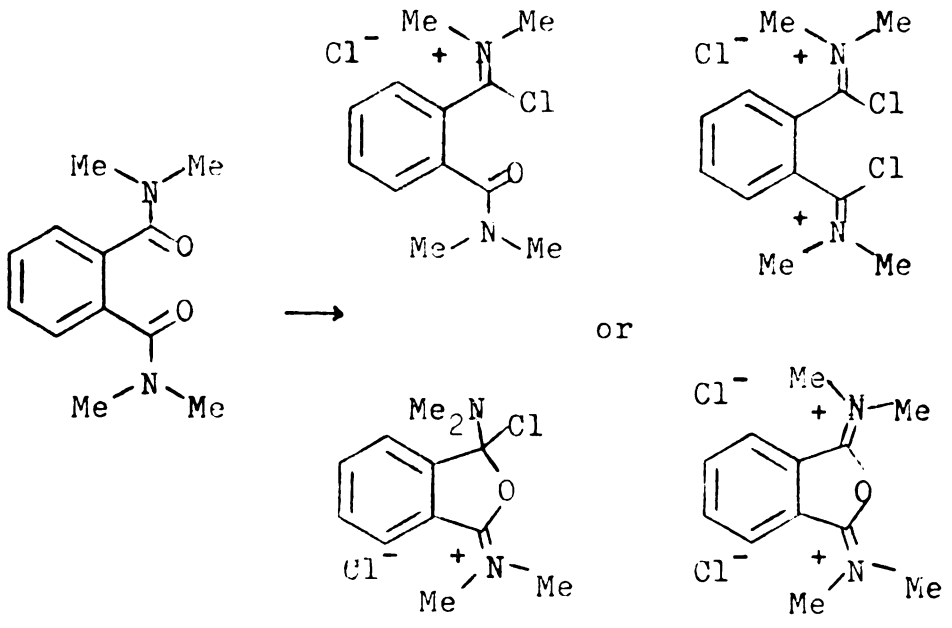


Figure 52. Possible products of reaction of 154 with chlorine electrophiles.

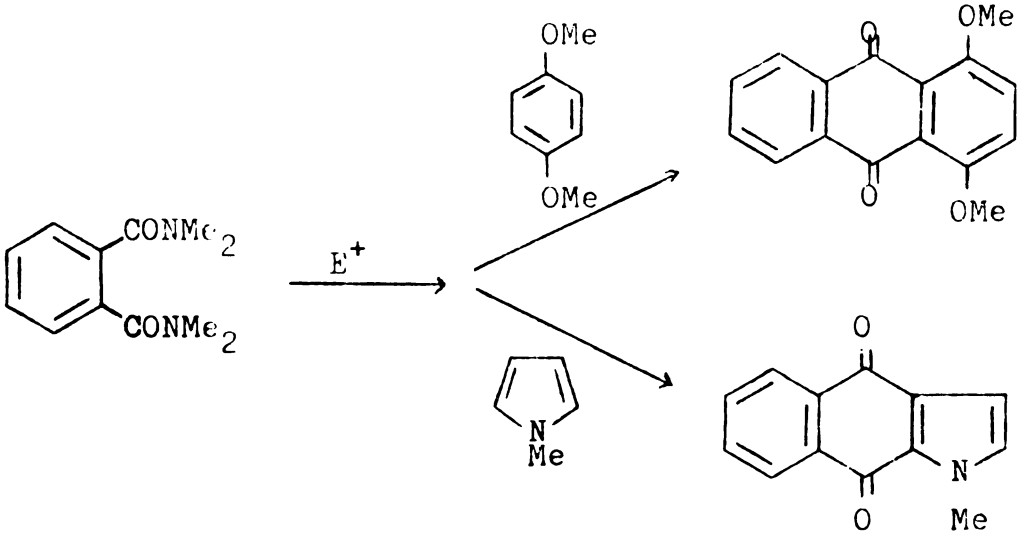


Figure 53. Possible products of reaction of salts of 154 with aromatics.

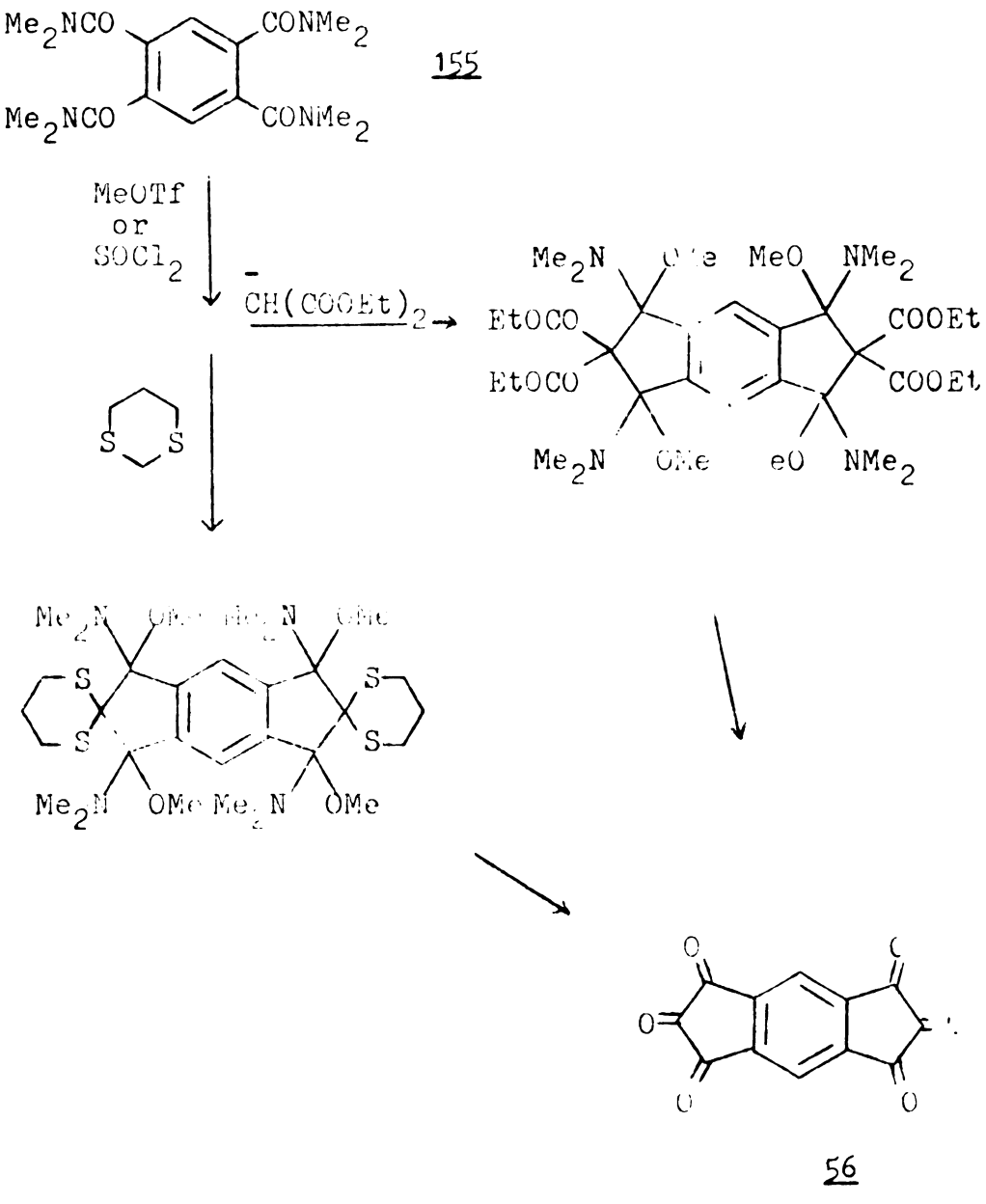


Figure 54. Amide 155 as an entry into the polyketohydrindacene system.

RESULTS AND DISCUSSION

Preparation of the amides. The ortho, meta and para diamides 154, 156 and 157, as well as N,N-dimethyl benzamide 153 were prepared by the reaction of the corresponding acid chlorides with excess 25% aqueous dimethylamine. (As these amides were quite soluble in water it was necessary to extract them from the aqueous reaction mixture with copious quantities of methylene chloride followed by back extracting with a minimum of aqueous sodium hydroxide to remove a small amount of dimethylamine hydrochloride which was inevitably extracted into the organic layer). The tetraamide 155 was prepared in one step, albeit in fairly poor yields (22%) from pyromellitic acid by reaction with dimethylformamide and phosphorus pentoxide.[75] Alternatively, reaction of pyromellitic anhydride with dimethylamine gave a nearly quantitative yield of the diacid-diamide (158). Treatment of this material with thionyl chloride followed by dimethylamine gave the desired tetraamide in 55% yield. This is shown in Figure 55.

Reactions of 154 with electrophiles. The reactions of 154 with various electrophiles, $POCl_3$, $(COCl)_2$, $(CF_3CO)_2O$, $CH_3OSO_2CF_3$ and $(CH_3)_2SO_4$, both neat and in solution were monitored by proton and carbon-13 nmr. The results are given in Table 4.

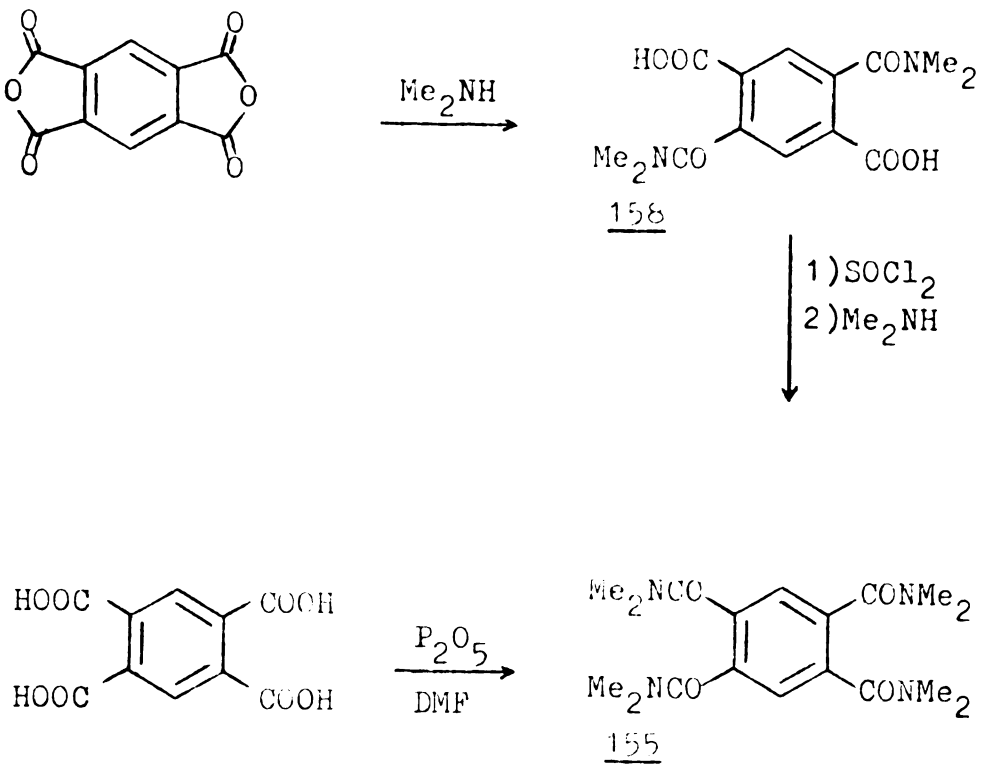


Figure 55. Preparation of 1,2,4,5-tetrakis(N,N-dimethylaminocarbonyl)benzene, 155.

Table 4. Reactions of 154 with electrophiles as monitored by pmr spectroscopy.

Electrophile	Conditions	Solvent	Comments	Spectrum
none	r.t.	$CDCl_3$	homogeneous solution	7.23, aa'bb', 4H 3.00, br s , 6H 2.87, br s , 6H
$POCl_3$	r.t.	$CDCl_3$	yellow crystals appear as set B increases, then redissolve as set C appears 10 min A only 40 min A:B=5:1 4 hr A:B=4:5 18 hr A:B:C=2:5:4 30 hr B:C=1:1 66 hr B:C=1:4	Set A 7.23, aa'bb', 4H 2.92, br s , 12H Set B 7.4-7.9, aa'bb', 4H 3.45, s , 12H Set C 8.2-8.4, m , 1H 7.9-7.6, m , 3H 3.13, br s , 12H
$POCl_3$	r.t.	$POCl_3$	yellow crystals form clogging tube, then redissolve 10 min A:B=11:1 40 min A:B=6:5 5 hr B:C=5:6(very weak signals) 13 days B:C=1:25	see above sets

Table 4 (cont'd.)

Electrophile	Conditions	Solvent	Comments	Spectrum
$POCl_3$	r.t. in $CDCl_3$, 24 hrs, decanted, yellow crystals dissolved in CD_3N at room temp.	CD_3CN	homogeneous solution	2.60, br s 3.03, s 3.70, s 3.90, s 7.4, br s 7.5, s 7.8-8.3, m
$(COCl)_2$	r.t. in $CHCl_3$ 24 hrs, evaporated to dryness, light yellow solid	CD_3CN	small amount of gas evolved white needles form slowly initially: A:B=4:5 then 2:1 and remains constant	Set A 2.53, br s, 12H 7.8, br s, 4H Set B 2.93, s, 12H 7.33, aa'bb', 4H
$(COCl)_2$	"	CF_3COOH	copious amount of gas evolved, homogeneous 90 min A:B:C=2:5:4 later C only	Set A 3.00, br s, 12H 7.31, aa'bb', 4H Set B 3.77, br s, 6H 3.93, br s, 6H 7.6-8.3, m, 4H Set C 2.60, t, 6H 3.57, s, 3H 3.77, s, 3H 7.80, aa'bb', 4H

Table 4 (cont'd.)

Electrophile	Conditions	Solvent	Comments	Spectrum
$(COCl)_2$	$CHCl_3$, heat 24 hrs, evaporate, yellow solid	CD_3CN	no bubbling, white needles form slowly 10 min A:B:C=3:6:2 2 hr 1:5:3 4 hr 1:4:4 1 day 1:1:11 2 days C only	Set A 2.96, s, 12H 7.36, aa'bb', 4H Set B 3.0, br, 12H 7-8, m , 3H 8.3, s, 1H Set C 2.55, br s, 12H 7.90, s , 4H
$(CF_3CO)_2$	r.t.	$(CF_3CO)_2O$	homogeneous	3.36, br s, 6H 3.50, br s, 6H 6.78, aa'bb', 4H
$(CH_3)_2SO_4$	r.t.	$CDCl_3$	homogeneous 10 min-4 days A only 6 days A:B=5:3 8 days 1:1 12 days 1:2	Set A 2.90, br s, 6H 3.01 br s, 6H 6.23 aa'bb', 4H Set B 2.67, m 3.17, br s 3.24, s 3.66, s 7.5-8.0, m

Table 4 (cont'd.)

Electrophile	Conditions	Solvent	Comment	Spectrum
$CH_3OSO_2CF_3$	r.t.	$CDCl_3$	homogeneous	3.23, br s, 9H 3.47, s , 3H 4.03, s , 3H 7.73, aa'bb', 4H

Though no clear pattern emerges from these data (except that these reactions are more complicated than expected), several items can be noted.

1) On treatment with phosphorus oxychloride the pair of signals normally arising from the N-methyl groups coalesces into a singlet. This coalescence may be due to catalysis of C-N bond rotation by traces of proton. In any case this phenomenon was observed with all amides studied in thionyl chloride and phosphorus oxychloride. The reaction with phosphorus oxychloride obviously goes through an insoluble intermediate in which the four methyl groups appear to be identical and the aromatic region symmetrical. The soluble final product is unsymmetrical (note the aromatic region).

2) The product of reaction with oxalyl chloride is apparently hydrolyzed by traces of water in trifluoroacetic acid as dimethyl ammonium ion is apparent in the spectrum. (The same spectrum arises from diamide 15h in TFA.) The product in CD_3CN differs depending on whether or not the reaction mixture is heated, but the main set of peaks is the same in both cases: a broad singlet for the methyls and an apparent singlet for the aromatic protons.

3) The diamide 15h does not react at all with trifluoroacetic anhydride.

4) It reacts only very slowly with dimethyl sulfate and then gives a complex mixture, perhaps due in part to the presence of a small amount of methyl hydrogen sulfate.

5) The diamide appears to add one methyl group immediately (and then remains constant) on reaction with methyl trifluoromethanesulfonate, although the aromatic region appears symmetrical.

Reactions of 154 and related amides with methyl triflate. As the spectrum of 154 with methyl triflate appears to be the most straightforward, the reactions of this electriphile will be taken up first. Later, we will explore the reactions of thionyl chloride and, to a lesser extent, phosphorus oxychloride.

The reactions of aromatic poly(N,N-dimethyl amides) with methylating agents, can be conveniently followed by ^{1}H- and ^{13}C-nmr, as well as by the known hydrolysis of O-alkylated amides to give esters.[76]

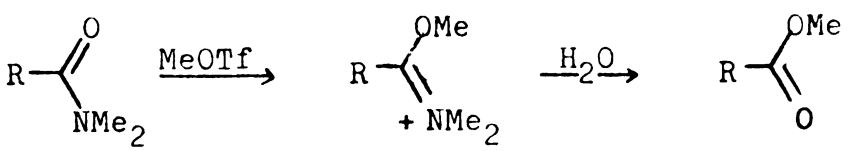
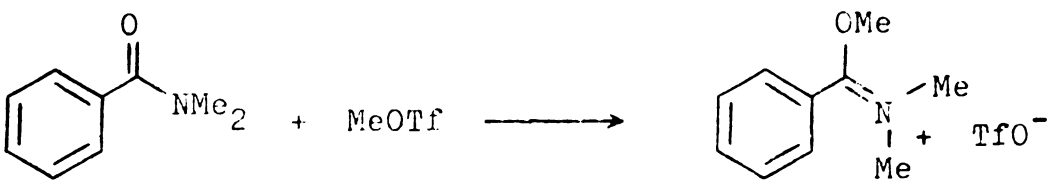


Figure 56. Preparation of esters from amides by alkylation/hydrolysis.

Treatment of N,N-dimethylbenzamide with methyl trifluoromethanesulfonate clearly gives the salt 159 by pmr ($CDCl_3$): δ 7.65, br s,5H(ArH); δ 3.97,s,3H(OMe); δ 3.53,s3H(NMe); δ 3.23,s,3H(NMe); and, by cmr: δ174.6(ArCON); δ133.5, δ130.1, δ127.9, δ124.0(Arom. C's); δ62.6(OMe); δ42.8(NMe); δ39.4(NMe).



159

Figure 57. Reaction of N,N-dimethylbenzamide with methyl triflate.

Treatment of the salt in chloroform with water gives quantitatively methyl benzoate.

In cloroform, N,N,N',N'-tetramethyl isophthalamide reacts very rapidly with excess methyl triflate to give the dimethylated salt 160. This salt immediately oils out of the chloroform solution, but is soluble in acetonitrile, with which it apparently does not react, at least not immediately, as shown by nmr. pmr (CD_3CN): δ 7.92, br, s,4H(Ar-H); δ 3.95,s,3H(OMe); δ 3.43,s3H(NMe); 3.17,s,3H(NMe). cmr: δ 172.7(ArCON); δ133.8, δ132.8, δ128.9, δ 126.1(Arom. C's); δ 63.6(OMe); δ43.2, δ39.7 (NMe). Treatment of the oil in acetonitrile with water gave dimethyl isophthalate.

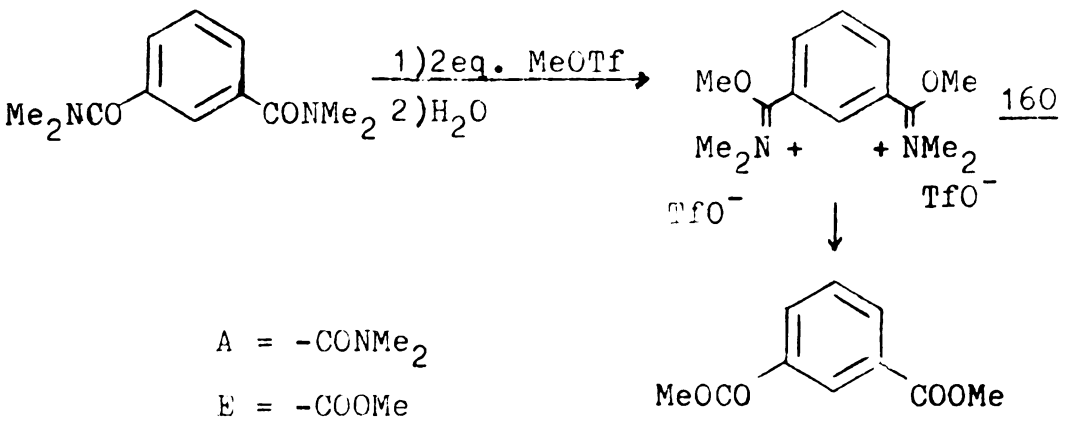


Figure 58. Reaction of 156 with methyl triflate.

N,N,N',N"-tetramethylterephthalamide reacts in chloroform with excess methyl triflate very rapidly and gives crystals which make obtaining an nmr spectrum difficult. An initial spectrum, taken before crystallization becomes heavy, shows (besides the sharp singlet at δ 7.27 and the broad signal at δ 2.98 arising from the starting material) a clear aa'bb' multiplet at δ 7.55 and sharp singlets at δ 3.90, δ 3.47, δ 3.20. Clearly one of the amide functions is becoming methylated. The signal arising from the N-methyl protons on the unaffected amide group are obscured by the corresponding protons in the starting material. Hydrolysis gives a 6:4 mixture of p-carbomethoxy-N,N-dimethylbenzamide and dimethylterephthalate.

Apparently the diamide can be dimethylated but in the reaction mixture rapid crystallization prevents complete reaction.

Similarly, 1,2,4,5-tetrakis(N,N-dimethylaminocarbonyl) benzene reacts rapidly with methyl triflate to give white crystals. Hydrolysis gives a white crystalline compound having the correct molecular ion and pmr for a diester-diamide. The question then arises as to whether the structure of the hydrolysis product is 161, arising from the m-dimethylated tetraamide, or 162 from the p-dimethylated isomer, or a mixture of the two. Careful crystallization from methanol gives

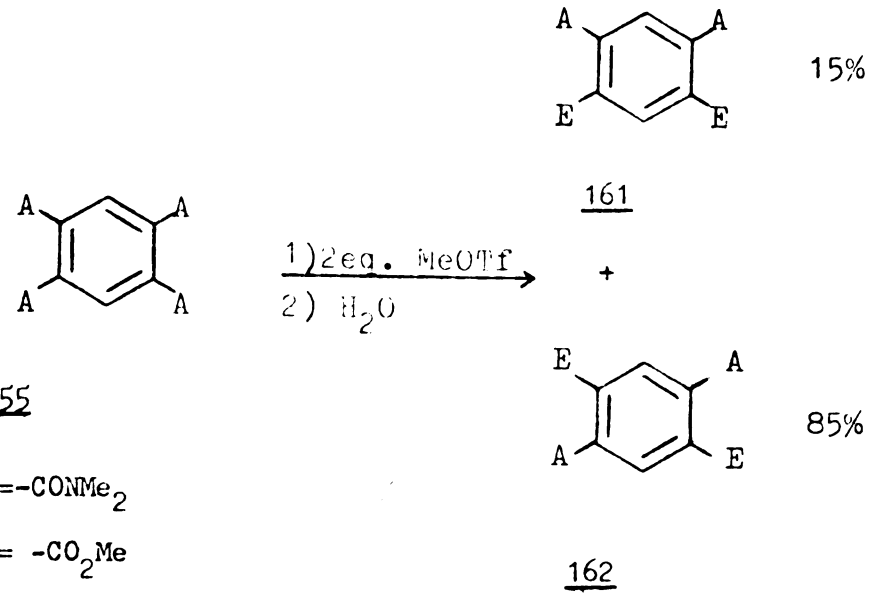


Figure 59. Reaction of tetrakis amide 155 with methyl triflate followed by hydrolysis.

beautiful prisms with a fairly sharp melting point (210.5-213.0°C). The proton nmr ($CDCl_3$) shows sharp singlets at

δ 7.80 (2H), δ 3.83(6H), δ 3.10(6H) and δ 2.77(6H). This material amounts to about half of the isolated product. Based on the unique sharp singlet in the aromatic region, it is assumed that the structure of this material is 162 which has only one kind of aromatic proton. Evaporation of the methanol mother liquor gave a material with a broader melting point range (whose pmr showed it to consist of the above compound 162) and a material shown to have the structure 161 in a ratio of about 3:1, based on the pmr. The structure assignment as 161 is based on the appearance in the pmr of two singlets in the aromatic region as expected for 161 which has two different aromatic protons. The chemical shifts of these two protons are surprisingly different (7.10 ppm and 8.50 ppm). However, they can be confirmed by comparing these chemical shifts with those of the aromatic protons in the meta diamide, N,N,N'N'-tetramethylisophthalamide and in the meta diester, dimethyl isophthalate. In the former all the aromatic protons appear at 7.34 ppm, while in the latter one aromatic proton (assigned by Sadtler[77] as the proton between the ester groups) appears at 8.63 ppm.

A ^{13}C-nmr spectrum of the original product (mp 175-205°C) is consistent with a mixture of the two isomers. It shows two amide carbonyl resonances (δ 168.89 and 168.71, one for each of the isomers. However, there is only one ester carbonyl resonance (δ 164.19) apparently due to coincidental overlap

of the very similar carbons. The ^{13} spectrum also shows seven aromatic resonances. The two isomers have three and four kinds of aromatic carbons, respectively. Thus, 162 outweighs 161 by about 7:1.

This result is surprising since, after the first amide group is methylated, the resultant positive charge is expected to be delocalized into the aromatic ring at the para and ortho positions. Thus, a second methylation of the amide group para to the previously methylated group would appear not to be favored, relative to a methylation on the amide group meta to the previously methylated group. Therefore, it would be predicted that the two methylated groups would be meta to each other rather than primarily para, as was found experimentally.

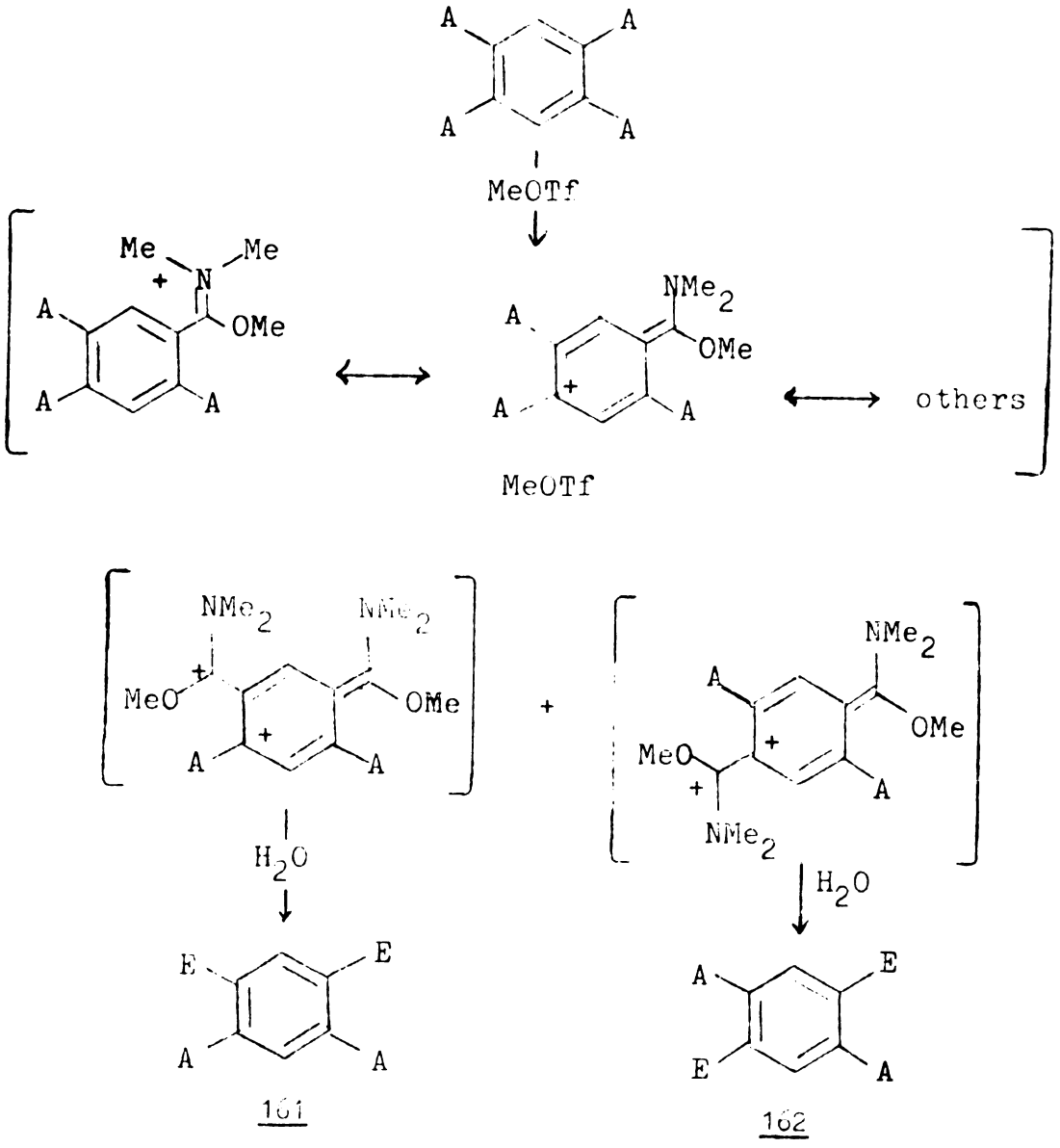
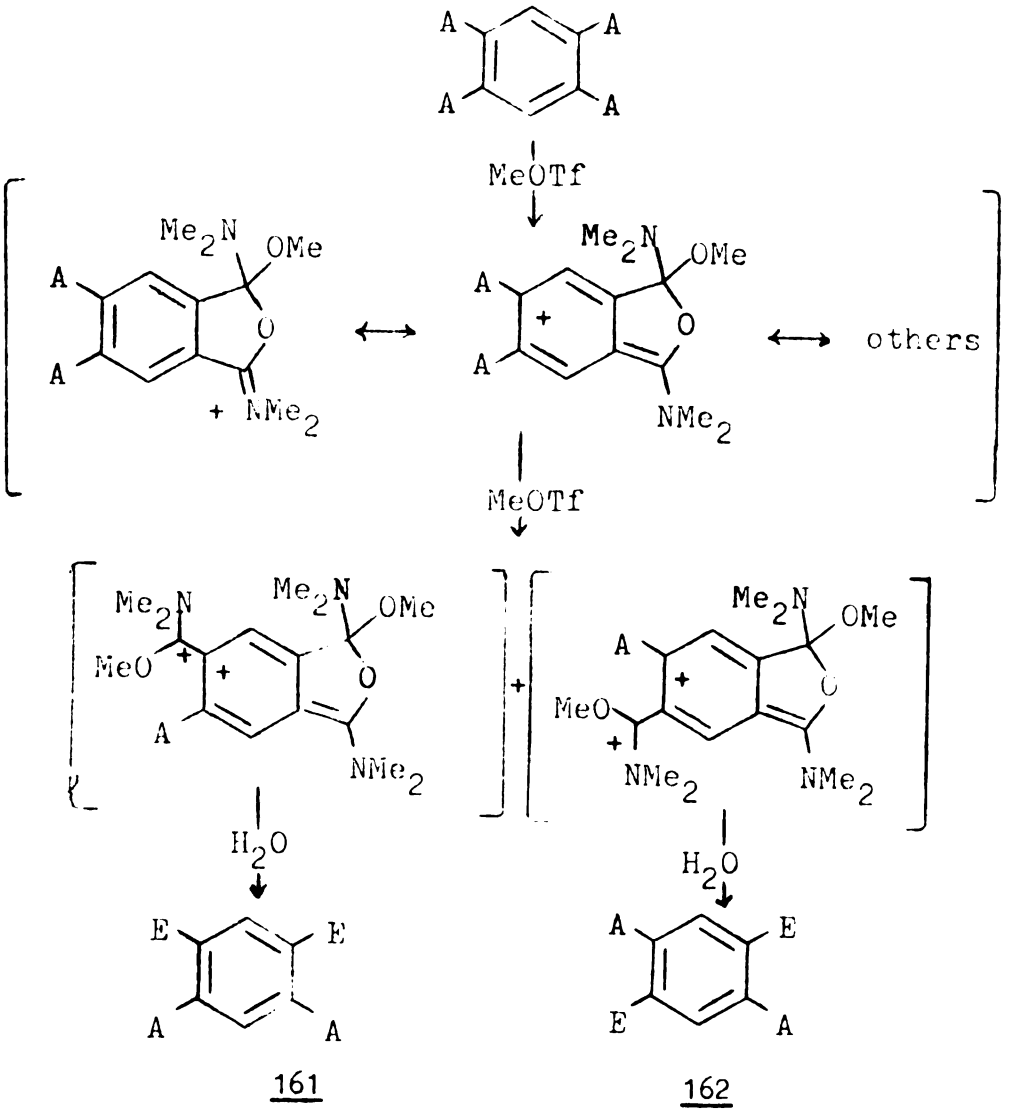


Figure 60. Dimethylation of 155: Mechanism 1.

One possible explanation involves participation by the amide group ortho to the initially methylated group. Should the ortho group participate, the positive charge would be delocalized into the ring at the positions meta and ipso to the initially methylated amide group. Thus, it might be expected that the second methylation would occur at the amide group para to the initially methylated group, as was found experimentally.

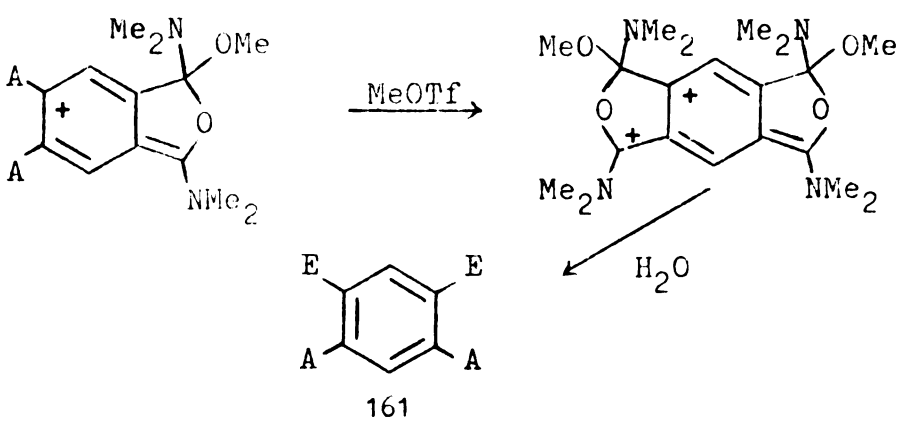


161 162

Figure 61. Dimethylation of 155: Mechanism 2.

Two factors related to this discussion should be noted. First, the idea that the ortho amide group participates in the initially formed cation is supported by the discussion of N,N,N',N'-tetramethylphthalamide found below. It is also supported (though not proved) by the fact that no dimethyl-4,5-bis(N,N-dimethylaminocarbonyl)phthalate was detected. This could be because the ortho group is "protected" by participation with the initially formed cation. On the other hand, it could simply be due to a steric interaction.

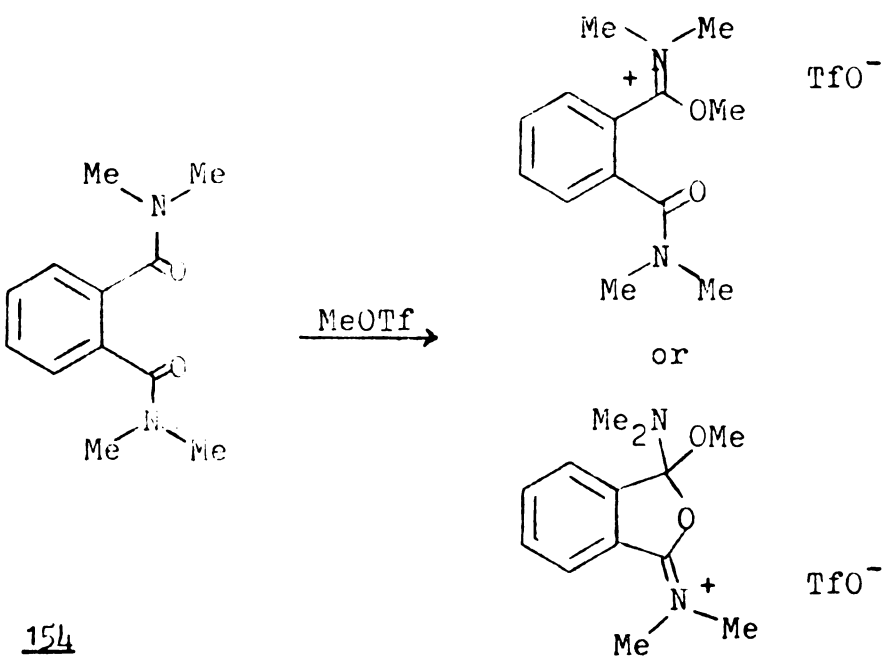
Secondly, it should be noted that the idea of participation by the ortho group in the initial methylation product as an explanation for the product distribution depends upon methylation and neighboring group participation occuring in two separate steps rather than simultaneously. Were the two steps to occur simultaneously, the second methylation would give the wrong isomer.



161

Figure 62. Dimethylation of 155: Mechanism 3.

Of the diamides studied the most interesting is the ortho diamide. Unlike the others, it is only monomethylated, even in the presence of excess methylating agent. The pmr spectra in the presence of 1 equivalent of methyl triflate and in the presence of excess methyl triflate are identical (except for the signal arising from the methylating agent itself): δ 7.75,br s,4H; δ3.97,s,3H; δ3.45,s,3H; δ3.17,br s,9H. ($CDCl_3$). The resonances at δ3.97, δ3.45 and δ3.17 correspond with those arising from other methylated N,N-dimethyl amides studied (see Table 5), thus supporting structure A, Figure 63.



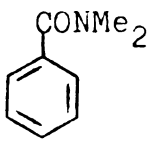
154

Figure 63. Reaction of 154 with methyl triflate.

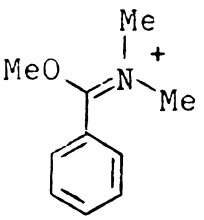
The large signal at δ3.17 does not correspond exactly with the

typical N-methyl signal of N,N-dimethylamides (δ 2.87-3.00) as would be necessary for structure A. This difference will be discussed later. On the other hand, structure B requires a signal at about δ 2.2 for the amino methyl groups,[78] which is not present in the spectrum.

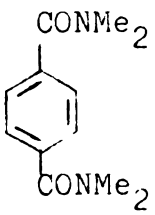
Table 5. Methyl pmr resonances in N,N-dimethyl amides and O-methylated N,N-dimethyl amides.



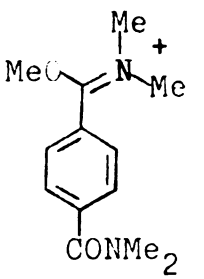
2.97



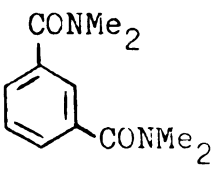
3.97,
3.53,
3.23



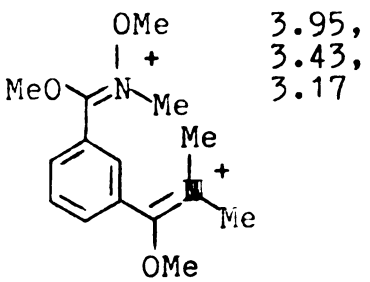
2.98



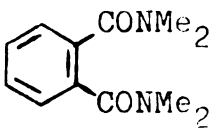
3.90,
3.47,
3.20



3.00



3.95,
3.43,
3.17

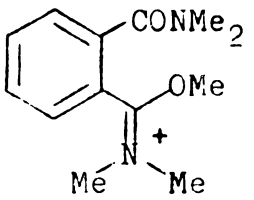


3.00,
2.87

All chemical shifts are in parts per million downfield from internal TMS in $CDCl_3$

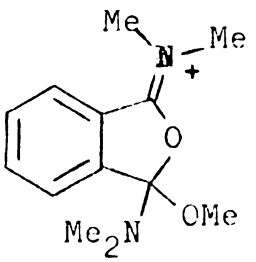
All chemical shifts are in parts per million downfield from internal TMS in CDl_3.

Table 6. Chemical shifts predicted for possible products of methylation of 154.

predicted for 

: 3.94, 3.47, 3.20, 3.00(x2).

found:
3.97, 3.45, 3.17(x3).

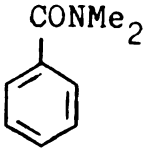
predicted for 

: 3,95, 3.47, 3.2(OMe)[78], 2.2(NMe_2)[78]

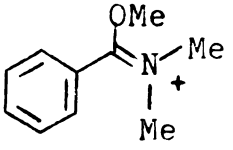
The ^{13}C-nmr spectrum of the methylated N,N,N',N'-tetramethylphthalamide shows two carbonyl resonances (δ 175.2, δ157.1), six aromatic resonances (δ 134.1, δ132.6, δ131.9, δ128.9, δ128.6, δ124.5) and five methyl resonances, one O-methyl (δ 62.4) and four different N-methyls (δ 42.3, δ 39.7, δ 39.1, δ 35.9). The fact that there are two carbonyls

and five methyls corresponds with structure A, but not structure B. The chemical shifts of the carbonyl signals correspond fairly well with one amide and one O-methylated amide, as shown by comparison with the chemical shifts of the carbonyl carbons given below. The slight difference between predicted and actual chemical shifts will be discussed later.

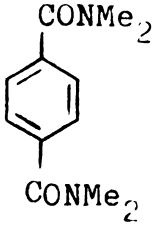
Table 7. ^{13}C chemical shifts of the carbonyl carbons of N,N-dimethyl amides and O-methylated N,N-dimethyl amides.



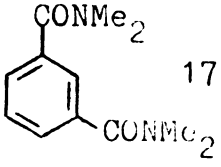
170.8[79]



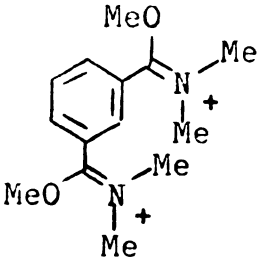
174.6



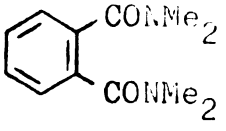
171.0



171.0(CD_3CN)



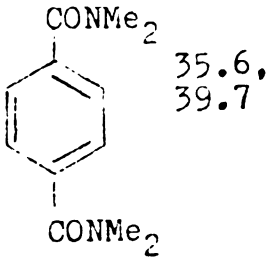
173.8 (CD_3CN)



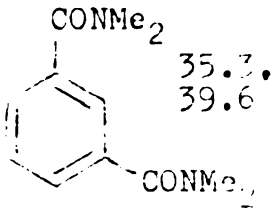
170.5

All chemical shifts are in parts per million downfield from internal TMS in $CDCl_3$ unless otherwise noted.

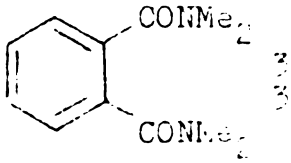
Table 8. Methyl ^{13}C-chemical shifts for amides and O-methylated amides(O-methyl chemical shifts)



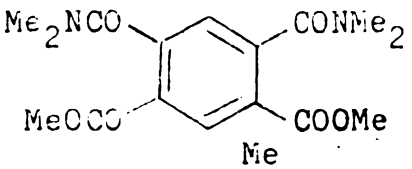
35.6,
39.7



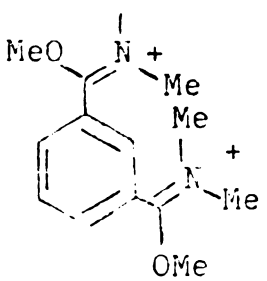
35.3,
39.6



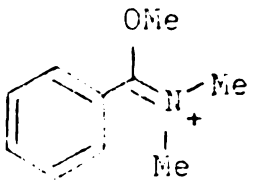
35.0,
39.4



35.1,
38.8,
53.2(OMe)

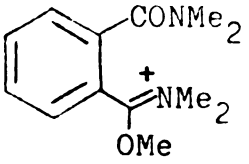
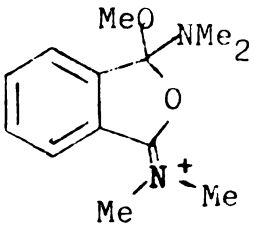


40.0,
43.6,
63.9(OMe)



39.3,
42.8,
62.6(OMe)

Table 9. ^{13}C chemical shifts predicted for possible products of methylation of 154.

predicted for	OMe	^{o}NMe	$^{+}$NMe	^{o}C=O	$^{+}$C=O
	63.3	43.2 39.7	39.4 35.3	171.3	174.2
	60- 65	38- 48	35- 40		
found	62.4	42.3 39.7	39.1 35.9	167.1	175.2

Note that the signals in the range of 35-45 ppm could arise from the N,N-dimethylamino group of structure B (typical chemical shifts of N,N-dimethyl tertiary amines are 38-48 ppm)[80] or from both types of N-methyl groups of structure A (see Table 8 for typical N-methyl chemical shifts).

Thus, from all the evidence it must be concluded that the correct structure for the methylated diamide is structure A. However, several questions must be answered. First, why is the o-diamide only monomethylated while under the same conditions, the m-and p-diamides are dimethylated? Secondly, why do the methyl protons of the unaffected amide function have chemical shifts of 3.17 ppm rather than 3.00 as do other

amide methyl groups? Finally, why are the chemical shifts of the carbonyl carbons (particularly that of the neutral amide) shifted from 171.3 and 174.2 as predicted to 167.1 and 175.2 as found? All of these questions can be answered by invoking a small contribution by structure B, thus involving the second amide group to a considerable extent. This type of neighboring group participation was invoked earlier in the 1,2,4,5-tetrakis amide case.

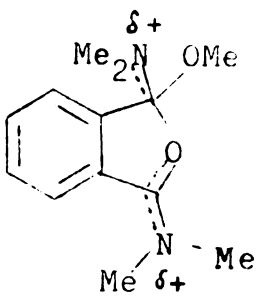


Figure 64. Proposed "hybrid" structure of methylated 154.

Reactions of nitriles with methylating agents. As an analogy to the amides just discussed, and because they are germane to a mechanistic discussion to come later, the reactions of several nitriles with methyl triflate were explored. Neither benzonitrile, nor phthalonitrile react with methyl triflate in chloroform solution, as evidenced by nmr spectra of the reaction mixtures. These show only signals arising from the original nitriles and from methyl triflate. However,

methyl triflate does react with acetonitrile as evidenced by the change in the nmr spectrum of methyl triflate in acetonitrile-d_3. Within seven hours, the methyl singlet at $\delta 4.30$ is replaced by a group of three singlets of equal magnitude (J=1.5Hz) centered at 3.77. The multiplicity of this signal is apparently due to coupling of the methyl protons with the ^{14}N nucleus in the N-methylated acetonitrile.

$$CD_3\text{-}C\equiv N: \quad + \quad MeOTf \quad \longrightarrow \quad CD_3\text{-}C\equiv \overset{+}{N}\text{-}CH_3 \quad \overset{-}{O}Tf$$

Figure 65. Reaction of acetonitrile-d_3 with methyl triflate.

Anticipating an increase in the methylating power of methyl triflate on addition of antimony pentahalides, we investigated the reaction of methyl triflate with antimony pentachloride, and the reactions of that combination of reagents with benzonitrile and phthalonitrile. The pmr spectrum of a mixture of one equivalent each of methyl triflate and antimony pentachloride in chloroform-d is identical to that of methyl triflate alone, suggesting that the alkylating agent is unaffected by antimony pentachloride. Furthermore, when one equivalent of phthalonitrile is added and the homogeneous solution allowed to stand at room temperature for

several minutes, an off-white crystalline solid separates. A pmr spectrum of the mother liquor shows only the singlet due to methyl triflate. Thus, the phthalonitrile is apparently involved in the crystalline solid, but without including the methyl triflate. This suggests formation of an insoluble phthalonitrile-antimony pentachloride complex. Further evidence for such a complex is suggested by hydrolysis. After removal of the supernatant by pipette, the crystals were rinsed with chloroform to remove traces of antimony pentachloride and methyl triflate. Addition of water to the crystals gave a white powdery solid, insoluble in water or chloroform, assumed to be antimony pentoxide (Sb_2O_5). Extraction of the aqueous solution with chloroform gave quantitatively phthalonitrile. This proves that no methylation occurred as hydrolysis of alkylated nitriles is known to give N-methyl amides.

Similarly, treatment of benzonitrile gives a purple solution which soon deposits white crystals. Hydrolysis of the crystalline material gives benzonitrile and antimony pentoxide.

Reactions of poly(N,N-dimethylamides) with thionyl chlorides. The pmr spectra of various polyamides were taken in thionyl chloride as solvent. N,N,N',N'-tetramethylterephthalamide initially shows a singlet at 2.97 arising from the N-methyl signals and a singlet at 7.33 arising from the

aromatic protons. The single methyl signal is due to the coalescence noted earlier. Over a period of about one hour the signal at 7.33 decreases and is replaced by a pair of doublets (J=4Hz) at 7.40 and 7.73. The signal at 2.97 decreases to half its size while singlets at 4.00 and 3.87 increase until together they equal the size of the singlet at 2.97. Clearly, one of the amide groups first reacts to give a chloriminum chloride (or the corresponding chlorosulfite ester).

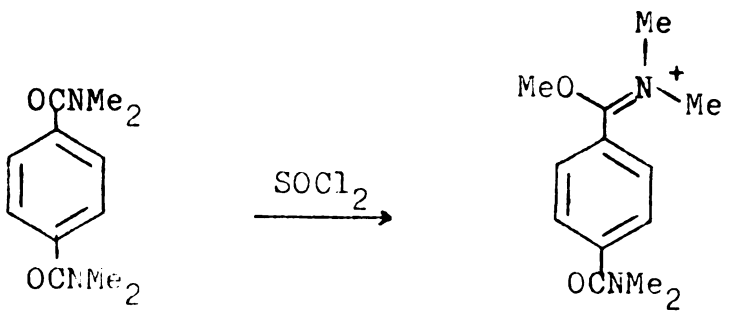
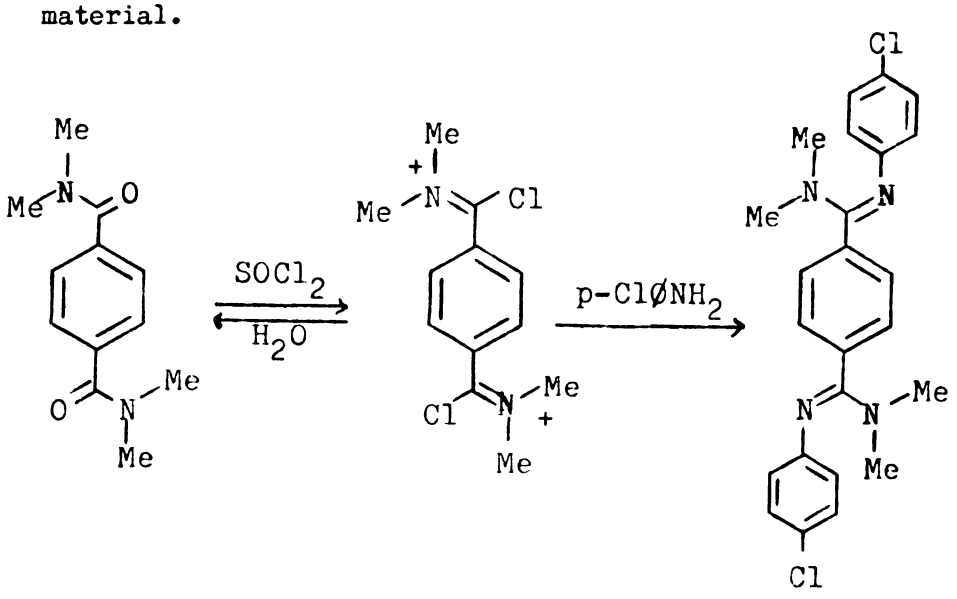


Figure 66. Reaction of 157 with thionyl chloride.

Soon after the complete conversion of the material to the above, the second amide reacts as evidenced by the formation of crystals in the nmr tube, and the appearance of a singlet at 8.07 ppm.

The white crystalline material which separates from the reaction of the bis amide with thionyl chloride is apparently

the bis chloroiminium salt 163. When this material is heated at reflux with a solution of p-chloroaniline in chloroform there is obtained the bis amidine 164. Hydrolysis of the white crystalline salt, 163, gave quantitatively starting material.



157 163 164

Figure 67. Formation of bis-amidine 164.

Similarly, N,N,N',N'-tetramethyl isophthalamide reacts to give the meta bis chloroiminium chloride salt as evidenced by the disappearance of the singlet at δ3.00 and the broad singlet at 7.33 and the appearance of a pair of singlets at 3.07 and 3.87 and a multiplet at 7.2-7.8 ppm.

N,N-dimethylbenzamide reacts in a similar manner, a singlet at 2.97 ppm being replaced by two singlets at δ3.98

and δ3.83 and a singlet at 7.30 being replaced by a multiplet (δ7.4-8.0). However, the reaction is much slower being complete only after two weeks at room temperature. However, prolonged heating of N,N-dimethylbenzamide in thionyl chloride results in 2,4,6-triphenyl triazine, a reaction which will be further discussed later.

As we have seen N,N,N',N'-tetramethylphthalamide does not behave like other amides on reaction with methyl triflate. The same is true on reaction with thionyl chloride. In thionyl chloride as solvent the amide reacts within five minutes to give a material with pmr signals at δ3.63 (two closely spaced singlets) and an aa'bb' multiplet at δ7.83. Within several hours a yellow precipitate forms in the tube making further nmr measurements difficult. However, this material eventually redissolves. The nmr spectrum changes to a very broad methyl signal at 3.07 ppm, two complex aromatic multiplets at δ8.20-8.35 and 7.47-7.93, in a ratio of 1:3, and together amounting to one third (4:12) of the methyl signal. At this point, no further change is noted in the spectrum even after refluxing for three days.

The ^{13}C-nmr spectrum of the reaction product of N,N,N',N'-tetramethylphthalamide with thionyl chloride in deuterochloroform was obtained after formation and redissolution of the yellow solid. The spectrum consists of one carbonyl resonance (167.7 ppm), six aromatic resonances (136.8, 134.2, 133.1,

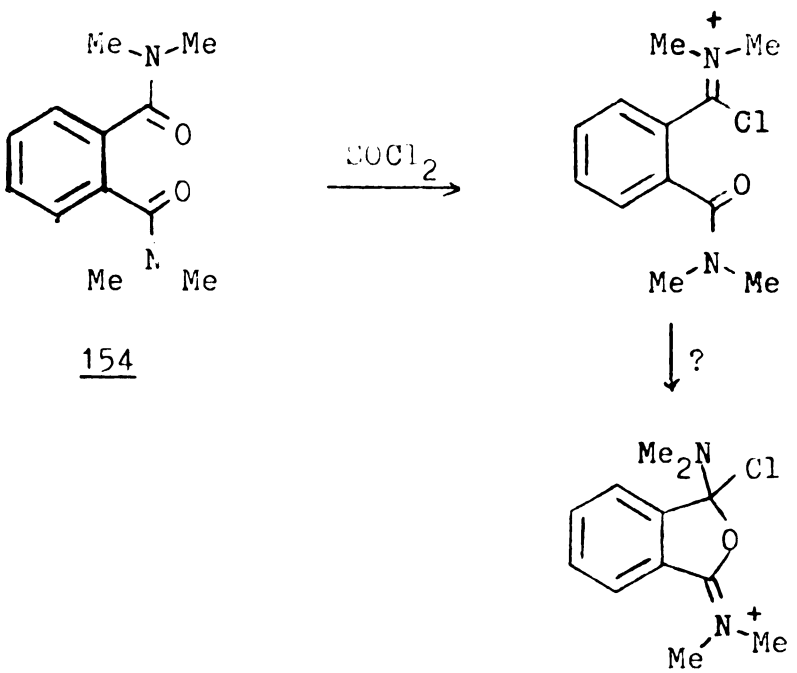
131.1, 130.8, 129.7 ppm) and one large methyl signal (43.7 ppm). The signals at δ129.7 and 131.1 are about half the size of the other four aromatic signals. These apparently arise from the two substituted carbons. When the thionyl chloride is removed and the solid residue is dissolved in water, there is isolated mostly starting material and a small amount of phthalic acid.

A chloroform solution of one equivalent each of the bis amide and thionyl chloride shows no change in its pmr, other than the coalescence of the N-methyl signals. The solution deposits yellow crystals only when a minimum of chloroform is used to dissolve the reagents. At higher concentrations, the mixture remains a homogeneous solution. In any case, the pmr spectrum of the mother liquor remains unchanged. The crystals can be redissolved in greater amounts of chloroform and the pmr spectrum of this solution is identical to that of the mother liquor and to that of the starting materials. Treatment of the yellow crystals with either water or absolute ethanol gives back the starting bis-amide.

This yellow crystalline material apparently is a loose complex of the diamide and thionyl chloride present to a small degree (and hence not apparent in the nmr) in equilibrium with the starting materials. As it is less soluble in chloroform than the starting materials, it is removed from the equilibrium at high concentration, by precipitation from solution.

When N,N,N',N'-tetramethylphthalamide is allowed to react with excess thionyl chloride, the initially formed yellow crystals redissolve, and the reaction is complete as indicated by pmr after 4 days at room temperature or 12 hours at reflux. No further change results from longer reaction times. The product is the same as that from the reaction in thionyl chloride as solvent.

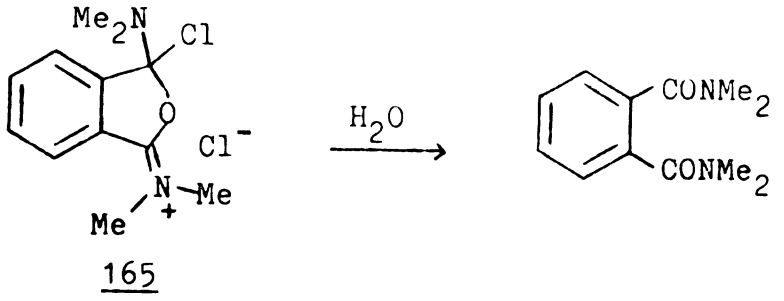
Evaporation of the solvent from this material gives a light yellow residue, 165, which on hydrolysis gives mostly starting material along with a small amount of phthalic acid. This shows that the dimethylamino groups are not cleaved after the reaction with thionyl chloride is complete.



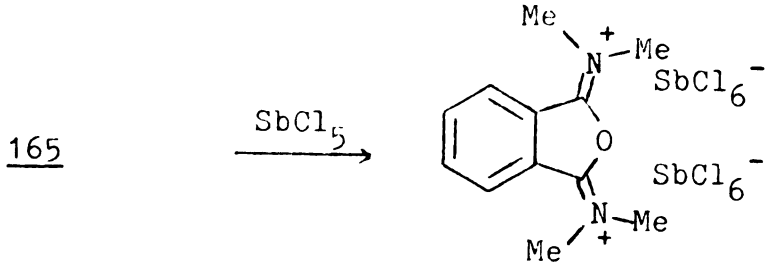
154

Figure 68. Reaction of 154 with thionyl chloride.

When the thionyl chloride product, 165, is treated with antimony pentachloride, in chloroform solution, a green solution is obtained. From this solution soon separates light blue crystals. The supernatant was drawn off and replaced with fresh chloroform. This process was repeated several times, each time waiting for the mixture to come to equilibrium as indicated by no further coloration of the solvent. The individual washings were kept separate. Each successive washing became less green and more blue, suggesting the presence of a yellow chloroform soluble impurity. It is assumed that the blue material has the structure shown in the second reaction in Figure 69.



165



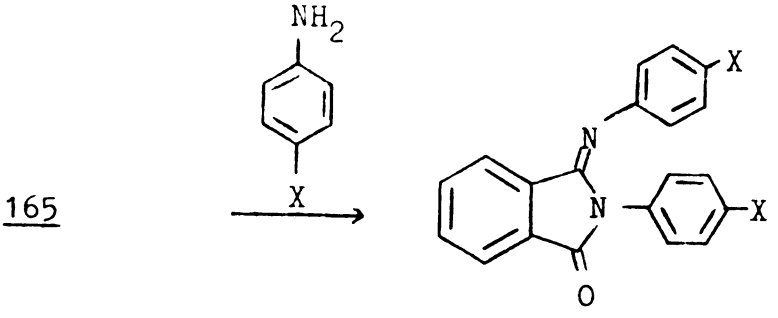


Figure 69. Reactions of thionyl chloride product, 165.

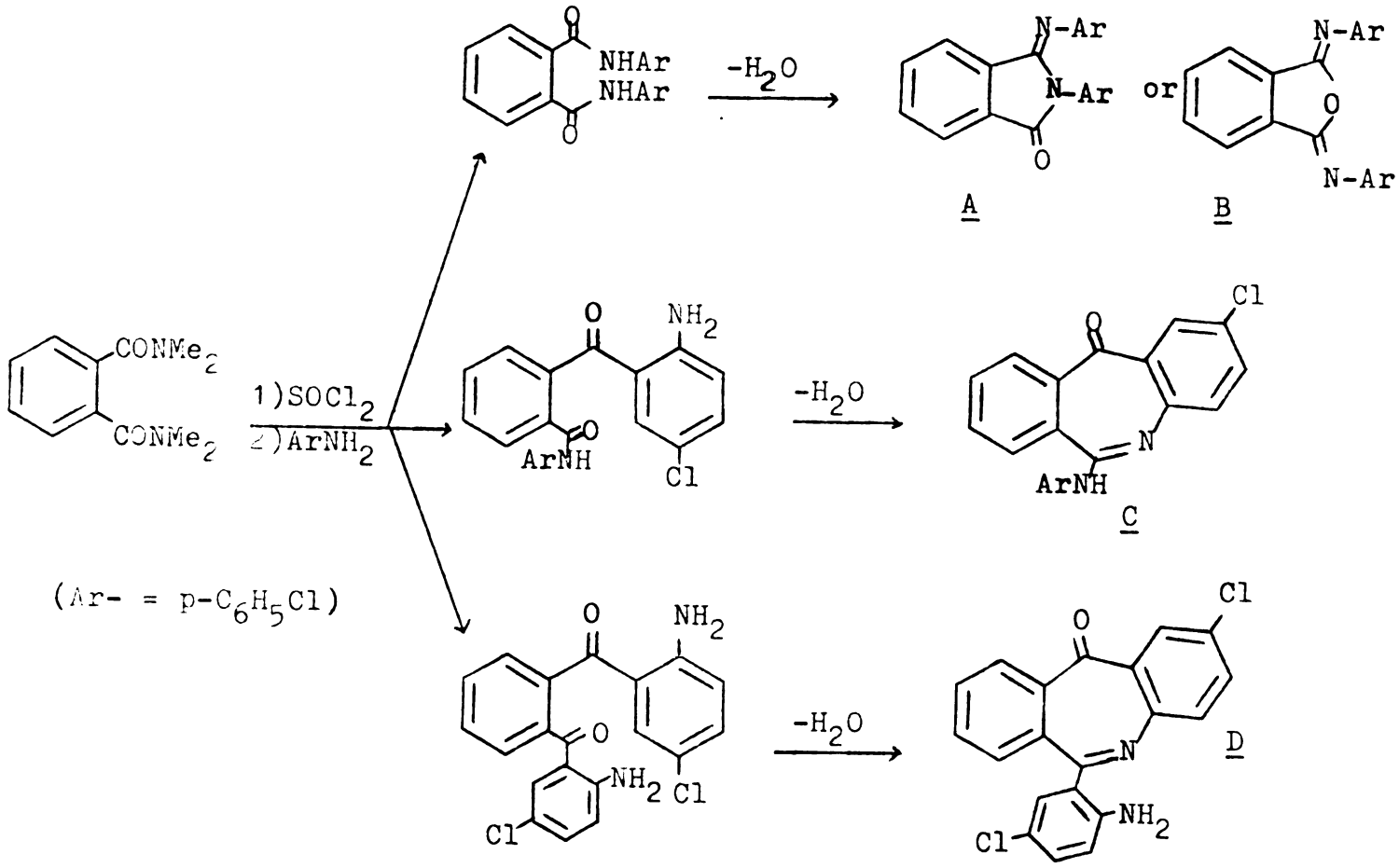


Figure 70. **Possible structures of the product of 165 and p-chloroaniline.**

When the thionyl chloride product 165 was treated with p-chloroaniline, a brilliant yellow material is obtained. Crystallization from petroleum ether gave as beautiful lemon yellow needles a compound which was pure by TLC and melting point (range 1.0°C). It was highly soluble in chloroform, less so in ethanol. It had only aromatic protons as shown by pmr. Thus, it is clear that both dimethylamino groups from the original bis amide were cleaved. The mass spectrum of the yellow material 166 showed the isotope pattern expected for a molecule containing two chlorine atoms. The molecular ion was m/e 366. This corresponds to a molecule obtained by substituting both dimethylamino groups in the original bis amide with p-chloroaniline followed by dehydration. This could arise formally in several ways, depending on whether one assumes N-alkylation, C-alkylation or both.

Structure B would appear to be eliminated based on the unsymmetrical pmr and on the fact that the cmr of the yellow material shows at least 13 and perhaps as many as 16 different aromatic carbons. This ^{13}C evidence also apparently eliminates structure D which would require 18 different aromatic carbons. Thus, it appears that structure A or C is correct for the yellow material. There was some evidence for structure C, which is a substituted 11H-dibenz(b,e)azepin-11-one.

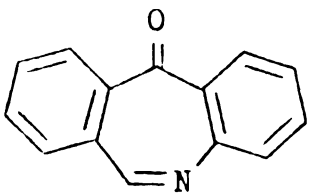


Figure 71. 11H-dibenz(b,e)azepin-11-one.

This basic ring system was characterized in 1972 by Cooke and Russell.[81] It was recrystallized from pet. ether and was described as "yellow". Cooke and Russell give ultraviolet data as λ_{max} (ethanol) 244"nm",312 nm(log E 4.48,3.75). The yellow dichloro compound has a UV maximum at 255 nm and a much smaller one at 305nm. Although Cooke and Russell gave no infrared data, the yellow dichloro compound gave IR data which were not inconsistent with structure C.

On the other hand, there is considerable chemical evidence, as will be shown below, that 166 does not have structure C (orD), but rather structure A.

The N,N,N',N'-tetramethylphthalamide/thionyl chloride, 165, was also treated with p-toluidine to give another bright yellow crystalline material, 167. Its spectral properties are almost identical to those of the dichloro compound. In addition, the pmr has a broad singlet at 2.33 ppm and the cmr has two very closely spaced signals at 20.66 and 20.94 ppm. These resonances correspond to the methyl atoms.

When this yellow tolyl product was heated with excess KOH in aqueous dioxane, a trace of p-toluidine was obtained. The main portion of the product, however, was a white insoluble material, 168, having the same molecular ion as the starting material. In the presence of aqueous acid, this white material dissolves in chloroform from which there is subsequently isolated a white compound crystallized from chilled ethyl acetate/pet. ether (mp 198-198.5) which was shown by chemical ionization mass spectrometry to be mostly N-(p-tolyl)phthalamide (169), MW 237, mp[82] 206°C with small amounts of N,N'-bis(p-tolyl)phthalamide, MW 344, (170) and a compound having molecular weight 326, either the starting material or an isomer.

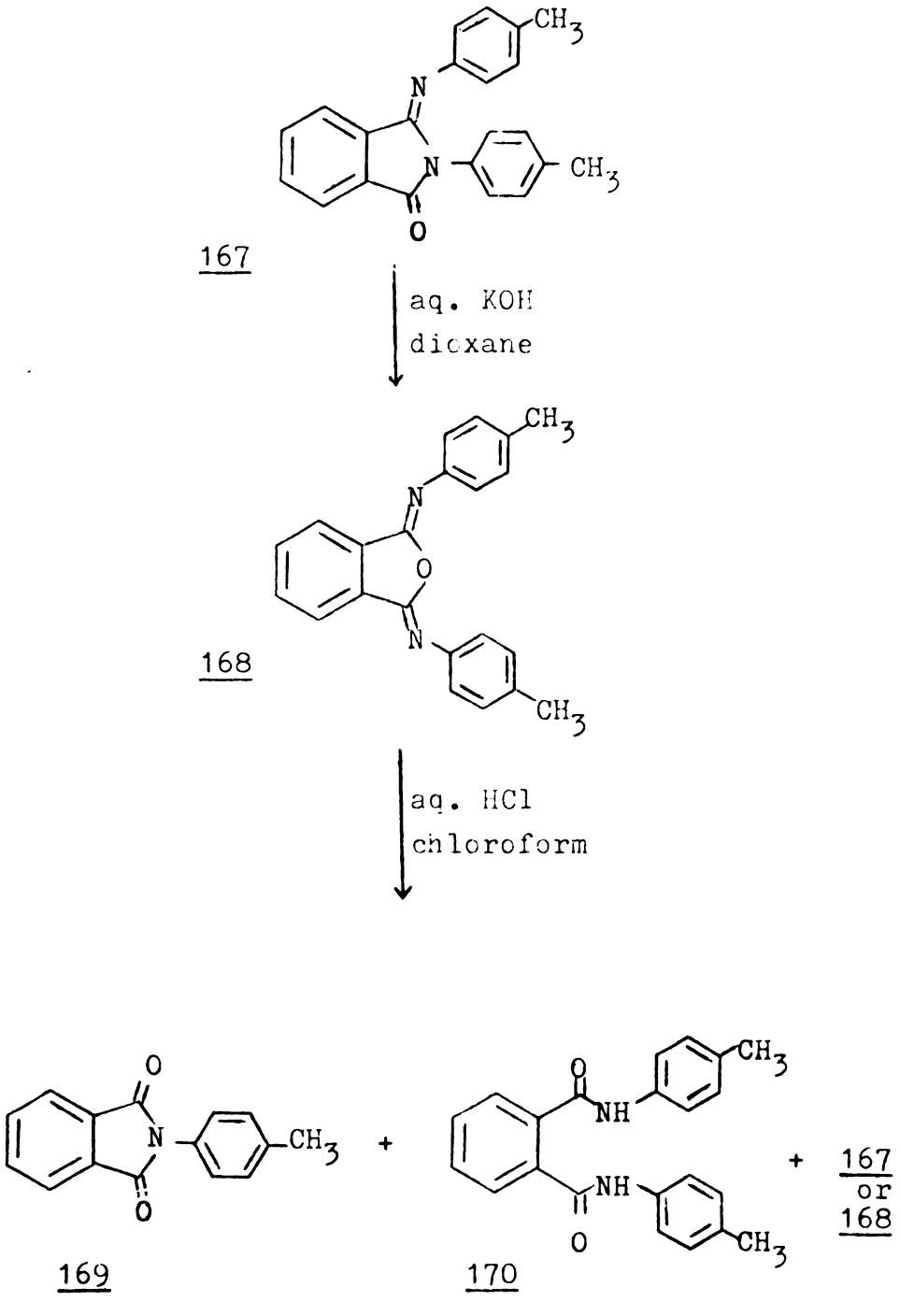
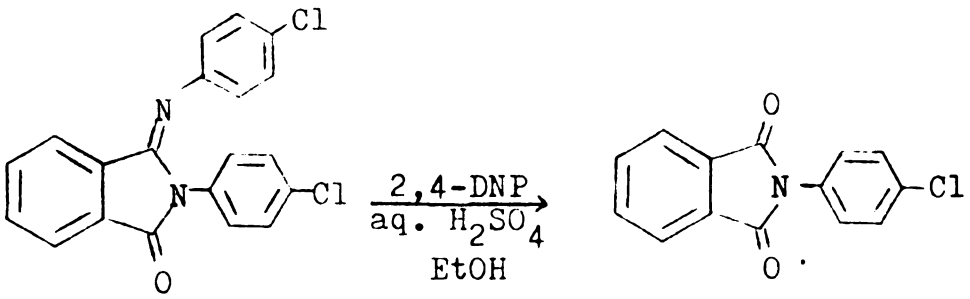


Figure 72. Reactions of yellow 167.

In an attempt to confirm the structure of the p-chloroaniline product as an 11H-dibenz(b,e)azepin-11-one, it was treated with 2,4-dinitrophenylhydrazine in ethanol. There were obtained beautiful orange crystals (mp 193.5-195, lit.[83] 194-195). The mass spectrum and pmr showeed it to be N-(p-chlorophenyl)phthalamide 171. The orange color may apparently arise from a small amount of impurity, specifically 2,4-DNP or a reaction product of 166 with 2,4-DNP, for which some evidence is given below. The formation of this product proves the 11H-dibenz(b,e)azepin-11-one structure is not that of 166 because such a ketone would not be expected to be hydrolyzed.



166 171

Figure 73. Reaction of 166 with 2,4-dinitrophenylhydrazone.

Similar 2,4-DNP treatment of the yellow tolyl compound 167 gave the same type of product, n-(p-tolyl)phthalamide 169.[82] A second compound 172 was detected in the product when it appeared in the mass spectrum at a higher temperature. Its mass is 417 which corresponds to a molecule in which a p-toluidine moiety in the starting material was replaced with a 2,4-DNP moiety.

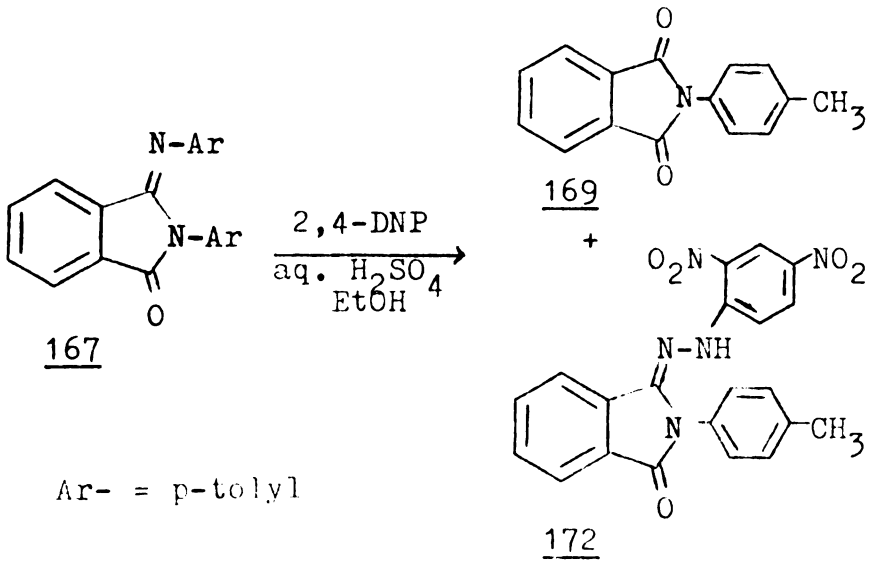


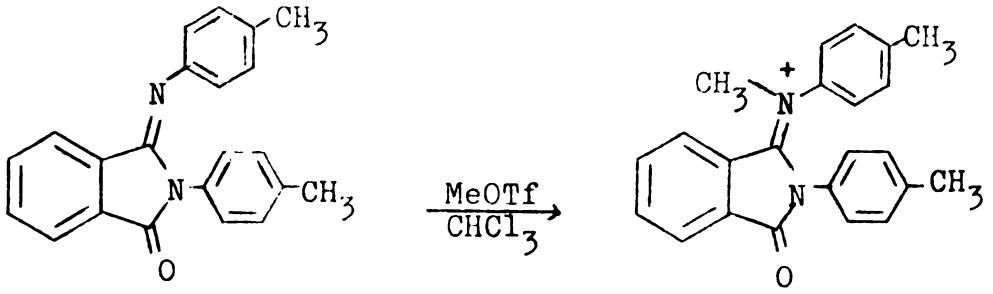
Figure 74. Reaction of 167 with 2,4-dinitrophenylhydrazone.

When the yellow compound was treated with aqueous acidic ethanol in the absence of 2,4-DNP there was obtained N-(p-tolyl)phthalamide 169 characterized by nmr and melting point (199.5-200.5, lit.[82] 206°C). The melting point is low due to a small amount of yellow impurity.

It is clear from these acid catalyzed hydrolyses that the yellow substances 166 and 167 cannot have the 11H-dibenz(b,e) azepin-11-one structure. It seems most likely that the correct structures are as shown in Figures 72-74. One piece of evidence against such a structure is the melting point of 167 reported [84] by Islam et al (207°C). The melting point of our yellow dimethyl compound is 114.5-116°C. The proximity of Islam's melting point to that reported by Porai-Koschiz[82] for N-(p-tolyl)phthalamide 169 (206°C) leads us to believe that Islam may have confused the two compounds. This suspicion is enhanced by Islam's report that the work-up of his compound included treatment with 10% aqueous HCl, a procedure which had been shown[85] (and confirmed by us) to hydrolyze similar compounds to phthalamides. However, Islam reports as microanalytical data numbers which agree with structure 167. A second piece of evidence against structures 166 and 167 is the lack of any recognizable aa'bb' coupling pattern in the pmr. This however, may not be necessary for the proposed structure. For example, the spectra of N-(p-tolyl)phthalaimde 169 and N-(p-chlorophenyl)phthalamide 171 both include singlets for the p-disubstituted aromatic protons. Their chemical shifts are 7.17 and 7.33 ppm, respectively. The yellow ditolyl compound 167 and dichloro compound 166 have broad

singlets at 7.30 and 7.33 ppm, respectively.

A solution of the yellow ditolyl compound 167 in $CDCl_3$ was treated with two equivalents of methyl triflouromethane-sulfonate. One methyl group is added (δ 3.30) and the second equivalent of methyl triflate is unchanged (δ 4.10). The broad singlet (δ 2.33) arising from the aromatic methyl groups in the starting material is replaced by two singlets (δ 2.43 and 2.38). The aromatic region remains relatively unchanged (δ 7.0-7.8, complex multiplet). These data are completely consistent with the proposed structure of the starting material.

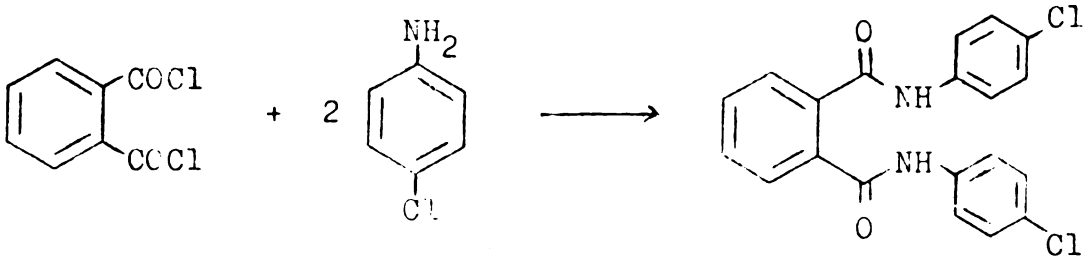


167

Figure 75. Reaction of 167 with methyl triflate.

As a model for 165, (the product of N,N,N',N'-tetramethyl-phthalamide and thionyl chloride) phthaloyl chloride was allowed to react with p-chloroaniline. The white solid obtained (which

was insoluble in organic solvents and in aqueous acid or base) was shown to be N'N'-bis(p-chlorophenyl)phthalamide, 173, as expected. Its melting point was 215-218°C (lit.[83] 213-214°C). The mass spectrum shows a strong peak at m/e 257 which corresponds to N-(p-chlorophenyl) phthalimide, 171. The molecular ion



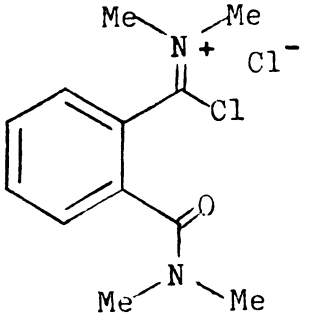
173

Figure 76. Reaction of phthalyl chloride with p-chloroaniline.

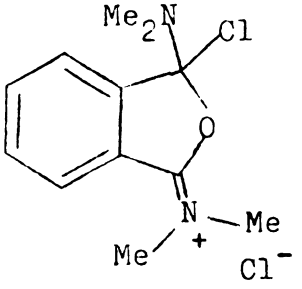
(m/e 384) is a very small peak (1% of the peak at m/e 257). This fact suggests facile fragmentation with loss of p-chloroaniline. The pmr of this material in DMSO-d_6 shows an aa'bb' doublet of doublets centered at 7.45 ppm and a broad singlet at 7.57 ppm in a ratio of 2:1.

Having considered the spectral and chemical evidence, let us now turn to the determination of the structure of the product of

N,N,N',N'-tetramethylphthalamide with thionyl chloride, 165. The nmr data strongly suggest an unsymmetrical molecule. This is not surprising, given the evidence of the analogous reaction with methyl triflate explored earlier. Both hydrolysis and treatment with antimony pentachloride followed by hydrolysis lead to nearly quantitative recovery of N,N,N'N'-tetramethylphthalamide, suggesting that both dimethylamino groups remain bonded to their respective carbons throughout the reactions. Given these results, let us restrict ourselves to consideration of the two structures below (see also Figure 68).



A



B

Figure 77. Possible structures of 165.

Reaction of 165 with anilines to give iminophthalimides 166 and 167 (Figure 69) suggests (but by no means proves) structure B, because B has two electron deficient centers, both of which can

easily undergo nucleophilic attack. To substitute the neutral amide structure of structure A requires protonation or participation by the positive center.

In addition, the fact that yellow crystals form and then redissolve before formation of 165 suggests (but again does not prove) that structure B is the structure of 165 and that A is the structure of the initially formed crystalline material. This suggestion requires a surprisingly slow ring closure from A to B. That this ring closure is slow is supported by the relatively slow second ring closure in the dimethylation of 1,2,4,5-tetrakis(N,N-dimethylaminocarbonyl)benzene 155 with methyl triflate (Figure 61). In addition, when considering the geometry of such a ring closure it becomes obvious that the chloroiminium group must twist out of the plane of the aromatic ring, and thus out of conjugation, to allow nucleophilic attack by the neutral amide oxygen. This clearly raises the energy of activation relative to the level that otherwise might be expected.

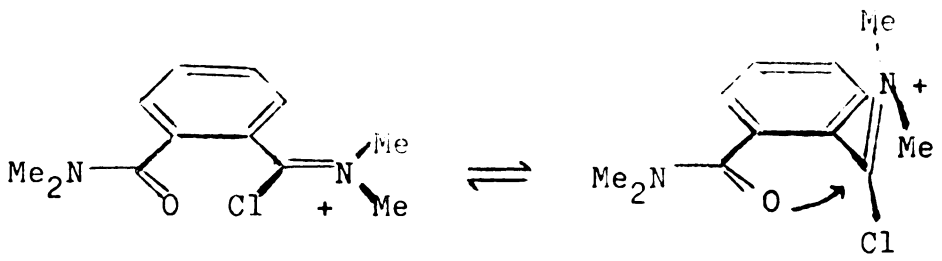


Figure 78. Conformation of ring closure of 165.

Finally, let us compare the reactions of 154 with methyl triflate and with thionyl chloride. The extent of cyclization, that is, the extent of participation by the neighboring amide group, would be expected to be greater in the thionyl chloride case than in the methyl triflate case. In the methoxy iminium case it was shown earlier (figure 64) that there is considerable participation. Therefore, the fact that participation appears to be complete, or nearly so, in the chloro iminium case is not surprising.

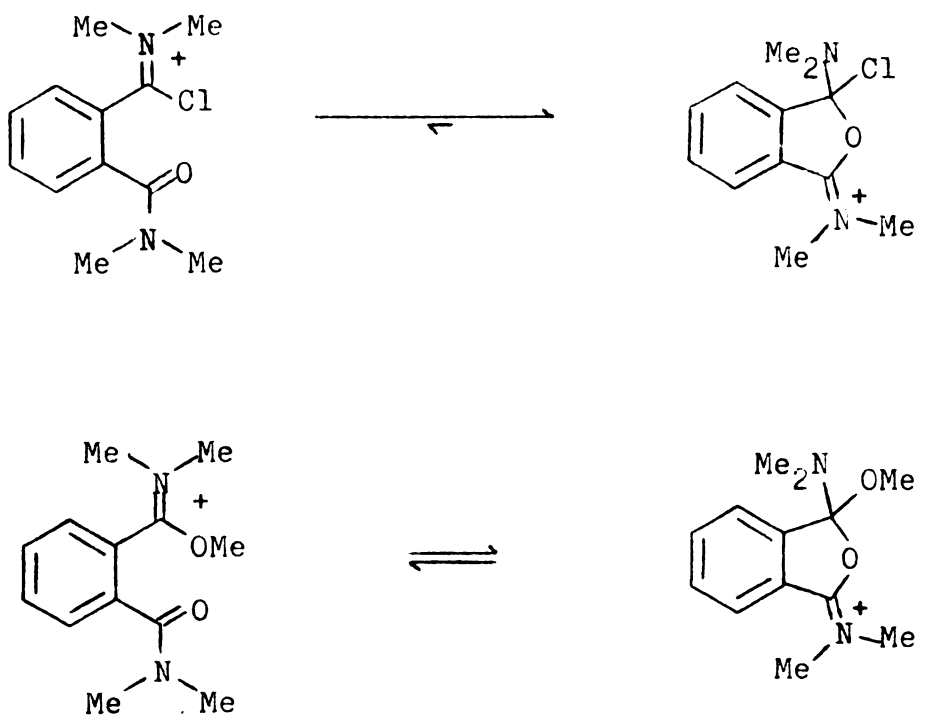


Figure 79. Comparison of the extent of amide group participation in the chloro dimethyliminium ion and in the methoxy dimethyliminium ion.

Addendum. In the course of this work, two unusual, and not unrelated, reactions were discovered. Because these reactions did not directly relate to earlier discussions, but merit some attention in and of themselves, they will be discussed now.

When N,N,N', N'-tetramethylphthalamide, 154, was heated in phosphorus oxychloride there was obtained, along with phthalic acid, a 10% yield of N-methylphthalimide, 174.

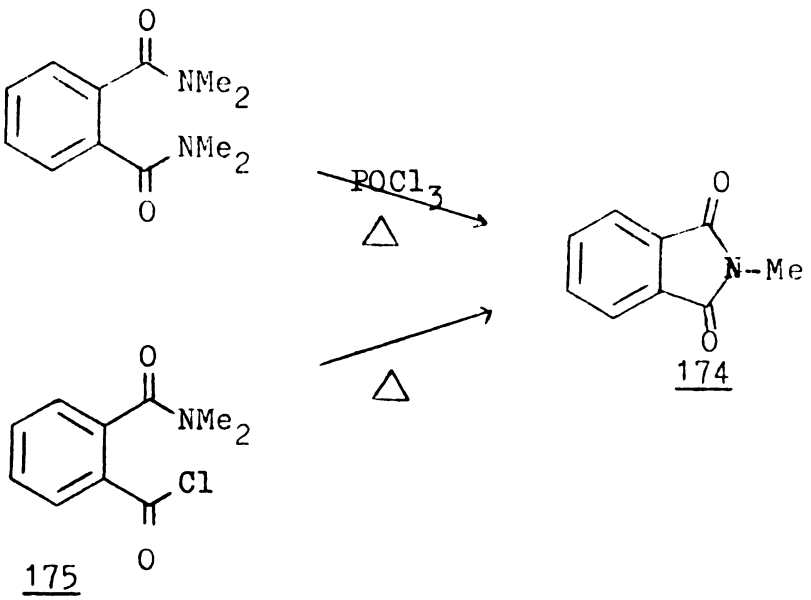


Figure 80. Formation of N-methylphthalimide from N,N,N',N'-tetramethyl phthalamide or N,N-dimethyl phthalamoyl chloride.

Its structure was suggested by mass spec, and pmr (although its pmr was not identical to that given by Sadtler[97]) and confirmed by independent synthesis from potassium phthalimide and methyl iodide.

The formation of N-methylphthalimide in this reaction is somewhat surprising as it involves dealkylation of an amide, a process for which there is little precedent. Some Czech chemists explored the range and limitations of a similar reaction.[86] Pyrolysis of an N,N-dialkyl phthalamoyl chloride gives an N-alkylphthalimide and an alkyl chloride. It is suggested that the mechanisms of these reactions are similar, that is, involving nucleophilic displacement by chloride of an acyl quaternary nitrogen.

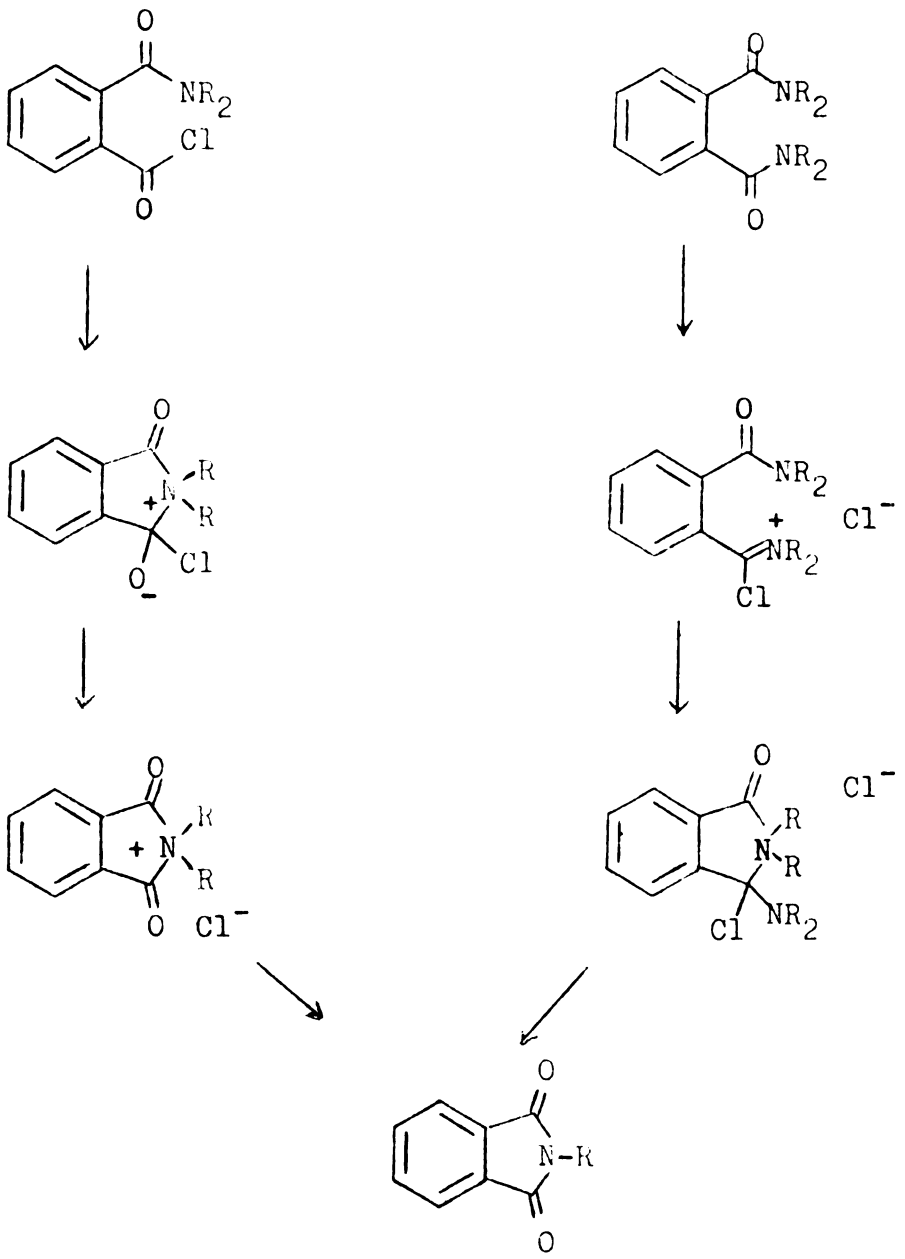


Figure 81. Suggested mechanism of cleavage of per-N-alkyl phthalamide or phthalamoyl chloride.

Note that either of these reactions constitutes a method for cleaving a secondary amine to a primary amine, a process for which there is a surprising paucity of methods. Attempts to increase yield of N-methylphthalimide failed.

A similar reaction occurs when N,N-dimethylbenzamide is heated at reflux in thionyl chloride. From this reaction there was obtained 2,4,6-triphenyl triazine as an insoluble white solid identified by melting point, mass spectrum and solubility properties. As a small amount of benzonitrile was also formed in the reaction as evidenced by the odor, it was hypothesized that the nitrile was an intermediate in the formation of the triphenyl triazine. However, a refluxing solution of benzonitrile in thionyl chloride gave no trace of 2,4,6-triphenyl triazine.

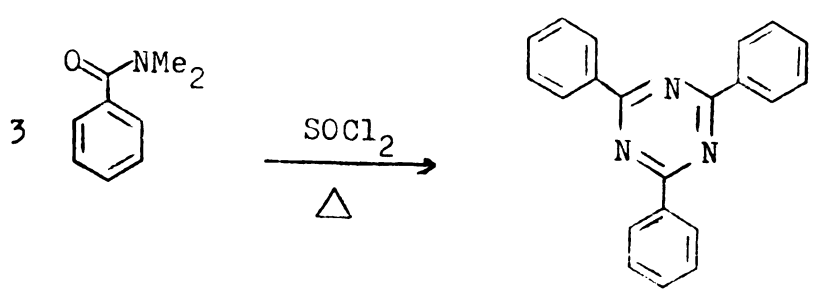


Figure 82. Formation of 2,4,6-triphenyl triazine from N,N-dimethylbenzamide.

It is not difficult to propose a mechanism for this reaction consistent with the available data. Such a mechanism is shown in Figure 83. However, no evidence was obtained which would support this mechanism over others. As was discussed earlier, (Figure 65) the product of acetonitrile and methyl triflate is N-methylacetonitrilium triflate. This salt shows no sign of forming 2,4,6-trimethyltriazine even in the presence of excess acetonitrile as might be expected from a mechanism like that outlined in Figure 83. However, that salt was not heated. Furthermore, this mechanism (Figure 83) includes N-methylbenzonitrilium rather than N-methylacetonitrilium. As was noted earlier, benzonitrile did not react with methyl triflate even at elevated temperatures. Thus, it may be that N-methylbenzonitrilium is less stable and hence more reactive than N-methylacetonitrilium.

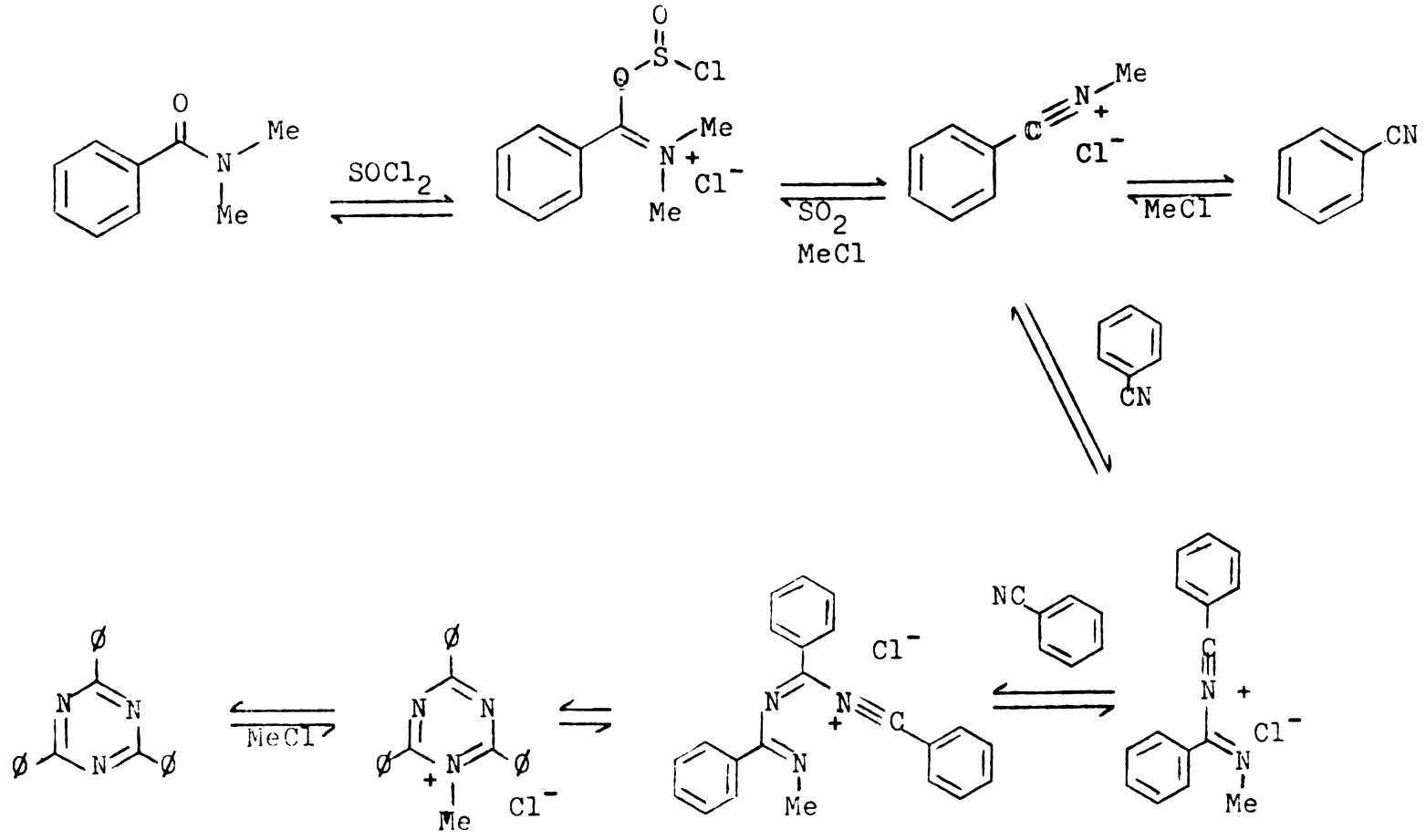


Figure 83. Proposed mechanism for the formation of 2,4,6-triphenyl triazine from N,N-dimethylbenzamide.

EXPERIMENTAL

Instrumentation, solvents, etc. See experimental section for Part 1.

N,N,N',N'-tetramethylphthalamide(154). A solution of 36 ml (50.5 g, 0.25 mol) of phthaloyl chloride in 150 ml of methylene chloride was added to an ice cooled mixture of 250 ml (62 g, 1.4 mol) of 25% aqueous dimethylamine and 50 ml of methylene chloride. The mixture was stirred for one hour. The organic layer was separated and the aqueous layer extracted with two portions of methylene chloride. The combined organic layers were dried (Na_2SO_4), filtered and evaporated to give a white solid which was vacuum dried giving 47.0 g (85%) of off-white solid. Recrystallization from heptane gives beautiful white needles, mp 120-121°C; lit[75b] 122-123°C. Nmr: δ 2.89,br s,6H; δ 302,br s,6H; δ 7.23,m(aa'bb'),4H. Mass spec. m/e: 220 (7%), 219 (21%), 176 (100%), 148 (25%), 133 (50%).

N,N-dimethylbenzamide(153). A solution of 23.2 ml (28.1 g, 0.200 mol) of benzoyl chloride in 100 ml of methylene chloride was added dropwise to an ice-chilled mixture of 100 ml of 25% aqueous dimethylamine (0.55 mol) and 2.5 ml methylene chloride. The mixture was stirred for an hour. The organic layer was removed and the aqueous layer was extracted twice with 50 ml portions of methylene chloride. The combined organic layers were washed once with a small portion of chilled 20% NaOH to remove dimethylamine hydrochloride.

The solution was dried (Na_2SO_4), filtered and evaporated to give a clear colorless liquid. Vacuum distillation gives 25 g (83%) of colorless liquid. Though N,N-dimethylbenzamide is a solid (mp 44-45°C)[95], this colorless liquid has the correct ^1H- and ^{13}C-nmr and behaves normally on reaction with methyl triflate or thionyl chloride. Pmr: δ2.97,br s,6H; δ7.27,s,5H.

N,N,N',N'-tetramethylisophthalamide(156). A solution of 25 g (0.151) mol) of isophthaloyl dichloride in 100 ml of methylene chloride was added dropwise to a chilled mixture of 120 ml of 25% aqueous dimethylamine (30 g, 0.67 mol) and 20 ml of methylene chloride. After the addition was complete, the solution was allowed to warm to room temperature and stirred overnight. The organic layer was separated and the aqueous layer extracted three more times with 50 ml portions of methylene chloride. The combined organic layers were washed once more with 50 ml of chilled 20% aqueous sodium hydroxide, dried ($MgSO_4$), filtered and rotary evaporated to give a white solid. Recrystallization from petroleum ether gives 30.1 g (91%) of white needles, mp 134-135.5; lit.[87] 137-138. Pmr: δ3.03,br s,12H; δ7.36,s,4H. Mass spec. m/e: 220 (25%), 219 (18%), 176 (100%).

N,N,N',N'-tetramethylterephthalamide(157). A mixture of 16.6 g (0.100 mol) of terephthalic acid and 50 ml of freshly distilled (from quinoline and cottonseed oil) thionyl chloride was heated at reflux until the solution became homogeneous (about 24 hours). The thionyl chloride was removed under reduced pressure and the residue taken up in toluene, which was in turn removed under reduced pressure. (This

is to remove the last traces of thionyl chloride, sulfur dioxide and hydrochloric acid.) The residue was dissolved in 50 ml of methylene chloride and added dropwise to a chilled mixture of 100 ml of 25% aqueous dimethylamine and 20 ml methylene chloride. After stirring overnight, the layers were separated and the aqueous layer extracted twice more with 20 ml portions of methylene chloride. The combined organic layers were washed with 20 ml each of 10% NaOH and brine. After drying ($MgSO_4$), filtering and rotary evaporation, a white solid was obtained. Recrystallization from a minimum of DMF gave 15.4 g (70%) of white prisms, mp 192-197; lit. 207-208°C,[75a] 202°C[88]. Mass spec. m/e: 220 (63%), 219 (79%), 176 (100%).

1,4-Dicarboxy-2,5-bis(dimethylaminocarbonyl)benzene(158). To a heterogeneous mixture of 21.8 g of pyromellitic anhydride (0.100 mol) and 100 ml of methylene chloride was added with stirring 80 ml (20 g, 0.44 mol) of 25% aqueous dimethylamine. The mixture was vigorously stirred at room temperature for 5 hours. The organic layer was removed and the aqueous layer washed once with methylene chloride. The basic aqueous solution was acidified with 5% HCl causing the precipitation of a white solid. It was washed thoroughly with water and dried to give 30.0 g (97%) of the diacid-diamide, mp 275. This material was used in the next step without further purification. Mass spec. m/e: 262 (43%), 219 (58%), 174 (100%), 147 (32%).

1,2,4,5-Tetrakis(dimethylaminocarbonyl)benzene(155).

Method A. A mixture of 5.00 g (16.2 mmol) of 2,5-dicarboxy-

1,4-bis(N,N-dimethylaminocarbonyl)benzene and 40 ml of thionyl chloride was stirred at reflux for four hours. The initially heterogeneous colorless mixture became homogeneous and golden yellow in color. After cooling, the excess thionyl chloride was removed under reduced pressure. The light yellow solid residue was suspended in toluene and this was then removed under reduced pressure leaving a white solid. This was taken up in 50 ml of methylene chloride, in which it is partially soluble, and added slowly to an ice-chilled mixture of 25 ml of 25% aqueous dimethylamine (6.25 g, 0.14 mol) and 10 ml of methylene chloride. After the addition was complete, the reaction mixture was stirred overnight at room temperature. The organic layer was separated and the aqueous layer extracted with two more 30 ml portions of methylene chloride. The combined organic layers were washed with 30 ml of 15% NaOH and brine, dried ($MgSO_4$), filtered and evaporated to give 3.2 g (55%) of yellow solid. Recrystallization from acetonitrile gave white prisms, mp 189-193; lit.[75a] 194-196.

Method B. To a mixture of 12.7 g (0.05 mol) of pyromellitic acid and 100 ml of DMF was added 14.2 g (0.10 mol) of phosphorus pentoxide. The temperature rose slightly. The mixture was stirred at reflux for 20 hours. While still hot, the golden yellow solution was decanted from a white sticky solid. This was filtered and air dried to give 3.35 g. Recrystallization from a minimum of DMF gives 3.0 g of prisms, mp 189.5-192.5; lit.[75a] 194-196. An additional 1.0 g can be isolated from the reaction mixture by partial evapor-

ation. Total yield 4.0 g (22%). Pmr: δ2.98,br s,12H; δ3.01,br s, 12H; δ7.13,s,2H. Mass spec. m/e: 366 (5%), 361 (15%), 318 (100%), 317 (24%), 274 (22%), 273 (17%).

Observation of nmr spectra over time. When ^{1}H-nmr spectra were recorded over time (as those in Table 4), the reagents and solvents (if any) were mixed in recorded amounts and at a recorded time in a clean, dry nmr tube. The tube was then sealed. When each spectrum was run, the time was recorded and the time of reaction was recorded. The results of each of these spectra are recorded in Table 4 or in the text. These include reactions of each of the amides studied with excess methyl triflate in chloroform-d, and reactions of each with excess thionyl chloride in chloroform-d. Also included are reactions of N,N,N',N'-tetramethylphthalamide 154 with one equivalent of methyl triflate in $CDCl_3$, with one equivalent of thionyl chloride in $CDCl_3$ and with thionyl chloride as solvent, as well as the reactions of benzonitrile and phthalonitrile with methyl triflate and/or antimony pentachloride in $CDCl_3$. Methyl triflate and thionyl chloride were measured in clean, dry syringes.

Hydrolysis of O-methyl salts of poly(N,N-dimethylaminocarbonyl) benzenes. To a solution of 4.42 mmol of N,N-dimethylbenzamide, the three isomeric N,N,N',N'-tetramethylphthalamides of 1,2,4,5-tetrakis (dimethylaminocarbonyl)benzene in 10 ml of chloroform was added one equivalent per amide group of methyl trifluoromethanesulfonate (i.e., 0.50 ml, 0.72 g, 4.42 mmol for N,N-dimethylbenzamide; 1.00 ml, 14.5 g, 8.82 mmol for N,N,N',N'-tetramethylphthalamide). The

homogeneous solutions were allowed to stand for 24 hours. To each was added 10 ml of water and the mixtures were stirred vigorously for three hours. The organic layers were separated, the aqueous layers extracted twice more with 10 ml portions of methylene chloride. The combined organic layers from each reaction were dried ($MgSO_4$), filtered and evaporated. N,N-dimethylbenzamide gave 0.60 g (100%) of methyl benzoate (not further purified). N,N,N',N'- tetramethylphthalamide gave N,N -dimethyl-2- carbomethoxybenzamide as a colorless oil. Heating the oil under petroleum ether followed by decanting and cooling gave white needles, mp 89-91°C; lit.[89] 91-93°C. Total yield 0.81 g (89%). The salt of N,N,N',N'-tetramethylisophthalamide came out of chloroform solution as a dark oil. Hydrolysis gave 0.80 g (94%) of dimethyl isophthalate, purified by filtration through a short silica gel column with methylene chloride, followed by crystallization from cool petroleum ether. Mp 66-67.5; lit.[90] 67.8-68.3°C.

The salt of N,N,N',N'-tetramethylterephthalamide came out of chloroform solution as white needles. Hydrolysis, followed by work-up gave 0.87 g of white solid which was shown by nmr to be a 58:42 (mole ratio) mixture of monoamide-monoester and diester
This amounts to a quantitative yield of the mixture. The two substances were separated by filtration through a short silica gel column. Methylene chloride eluted the dimethyl terephthalate (mp 136-138°C; lit.[91] 141.0-141.8°C). Ethyl acetate eluted the p-carbomethoxy-N,N-dimethylbenzamide (mp 103.5-105.5; lit.[92] 106-107).

On reaction with methyl triflate the tetracarboxamide 155 also forms white crystals in chloroform solution. Filtration and hydrolysis followed by normal work-up and careful recrystallization from methanol gave white prisms (mp 210.5-213°C) of N,N,N'N'-tetramethyl-2,5-dicarbomethoxy-1,4-benzenedicarboxamide (162). Evaporation of the mother liquor gave a 3:1 mixture (by nmr) of the above p-diamide-diester 162 and N,N,N'N'-tetramethyl-4,6-dicarbomethoxy-1,3-benzenedicarboxamide (161). The overall yield of these compounds was 65% and, as the crystalline 162 accounted for half of the isolated material, the overall ratio of 162:161 is 7:1. N,N-dimethyl-2-carbomethoxybenzamide pmr: δ2.63,s,3H; δ3.09,s,3H; δ3.82,s,3H; δ7.05-7.50,m,3H; δ7.77-7.97,m,1H. Mass spec. m/e: 206 (42%), 176 (12%), 163 (100%). Dimethyl isophthalate pmr: δ3.91,s,6H; δ7.37,t(J=7Hz),1H; δ8.10,dd (J=2Hz,7Hz),2H; δ8.53,t(J=2Hz),1H. N,N-dimethyl-4-carbomethoxybenzamide pmr: δ3.00,br s, 6H; δ3.90,s,3H; δ7.33,d(J=8Hz),2H; δ7.93, d(J=8H),2H. Dimethyl terephthalate pmr: δ3.91,s,6H; δ7.99,s,4H. N,N,N',N'-tetramethyl-2,5-dicarbomethoxy-1,4-benzenedicarboxamide pmr: δ2.77,s,6H; δ3.10,s,6H; δ3.83,s6H; δ7.80,s,2H. N,N,N',N'-tetramethyl-4,6-dicarbomethoxy-1,3-benzenedicarboxamide pmr: δ2.76,s, 6H; δ3.09,s,6H;δ3.84,s6H; δ7.10,s,1H; δ8.50,s,1H. Mass spec of mixture m/e: 336 (13%), 335 (31%), 305 (15%), 292 (100%), 162 (17%).

N,N,N',N'-tetramethyl-1,4-benzene bis(chloroformiminium) dichloride(163). A solution of 2.20 g (10.0 mmol) of N,N,N',N'-tetramethylterephthalamide in 20 ml of freshly distilled thionyl chloride was allowed to stand at room temperature for 24 hours.

The supernatant was decanted from the beautiful white crystals and they were washed several times with chloroform.

Hydrolysis of 163. The white crystals formed in the above reaction were dissolved in 30 ml of water and allowed to stand at room temperature for one hour. The solution was extracted three times with 20 ml portions of chloroform. The combined organic extracts were dried ($MgSO_4$), filtered and evaporated to give 2.00 g (91%) of N,N,N',N'-tetramethylteraphthalamide.

1,4-benzene bis(N,N-dimethyl-N'-(4-chlorophenyl)carboxamidine) (164). The white crystalline material 163 (see above) prepared from 2.20 g (10.0 mmol) of N,N,N',N'-tetramethylterephthalamide was taken up in 25 ml methylene chloride and added to a solution of 5.10 g (40.0 mmol) of p-chloroaniline in 50 ml of methylene chloride. After stirring overnight, a yellow solid had formed. The mixture was chilled in an ice bath and to it was slowly added a chilled solution of 1.6 g (40.0 mmol) of sodium hydroxide in 15 ml of water. The organic layer was separated and the aqueous layer extracted twice more with 20 ml each of methylene chloride. The combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was chromatographed on silica gel. Methylene chloride eluted the excess p-chloroaniline. The bis-amidine was eluted with 10% ethyl acetate/methylene chloride and recrystallized from ethyl acetate, mp 220-221°C. Yield 1.4 g (36%). The yield could probably be improved by further elution of the column with larger proportions of ethyl acetate. Mass spec. m/e: 390, 392, 394. Pmr ($CDCl_3$):

δ6.83,s,4H; δ6.76,d(J=8Hz),4H; δ6.27,d(J=8Hz),4H; δ2.87,s,12H. Anal. calc'd. for $C_{24}H_{24}Cl_2N_4$: C, 65.61%; H, 5.51%. Found C, 65.77%; H, 5.50%.

2-(4-chlorophenyl)-3-(4-chlorophenylimino)-2,3-dihydro-1H-isoindol-1-one(166). A solution of 1.1 g (5.0 mmol) of N,N,N',N'-tetramethylphthalamide in 10 ml of thionyl chloride was allowed to stand at room temperature. The yellow solution deposited crystals which slowly redissolved. After the reaction was complete as monitored by nmr, the thionyl chloride was removed under reduced pressure leaving a solid yellow residue. This was taken up in 10 ml of methylene chloride and added by pipette to a solution of 2.55 g (20.0 mmol) of p-chloroaniline in 15 ml of methylene chloride. A yellow solid immediately began to appear and the reaction mixture warmed slightly. After stirring overnight at room temperature, the mixture was chilled and, with vigorous stirring, enough chilled dilute sodium hydroxide was added to dissolve the solid and make the aqueous layer slightly alkaline. The yellow organic phase was separated and the aqueous phase extracted twice with 10 ml portions of methylene chloride. The combined organic layers were dried ($MgSO_4$), filtered and evaporated to give a yellow residue. Chromatography on silica gel with methylene chloride as the eluting solvent gave an initial yellow band followed closely by the starting p-chloroaniline. The yellow material was recrystallized from petroleum ether to give 1.3 g (72%) of fine yellow needles, mp 148.5-149.5°C. Mass spec. m/e: 366, 368, 377. Pmr: complex multiplet between 6.5

and 8.0 ppm with a large broad singlet at 7.33 ppm. Anal. calc'd. for $C_{20}H_{12}Cl_2N_2O$: C, 65.41%; H, 3.29%. Found: C, 65.32%; H, 3.19%.

N,N'-bis(p-chlorophenyl)phthalamide(173). To a chilled solution of 1.41 ml (2.03 g, 10 mmol) of phthaloyl chloride in 35 ml of methylene chloride was added a solution of 5.10 g (40 mmol) of p-chloroaniline. The mixture was allowed to stir overnight at room temperature. To the mixture, in which some white solid had formed, was added enough dilute aqueous sodium hydroxide to make the organic layer slightly alkaline. As the white solid did not dissolve, it was filtered out, washed with water, ethanol and methylene chloride and dried to give 3.2 g (83%), mp 215-218; lit.[94] 213-214°C. Mass spec. m/e: 384, 257, 127. Pmr (DMSO-d_6): δ7.62,d(J=9Hz),4H; δ7.57,br s, 4H; δ7.28,d(J-9Hz),4H. Anal calc'd. for $C_{20}H_{14}Cl_2N_2O_2$: C, 62.35%; H, 3.66%. Found: C, 62.46%; H, 3.62%.

2,3-dihydro-2-(4-methylphenyl)-3-(4-methylphenylimino)-1H-isoindol-1-one(167). See the above procedure for the preparation of 166. The yellow material was recrystallized from petroleum ether to give an 81% yield of yellow needles, mp 114.5-116. Mass spec. m/e: 326. Pmr: δ6.5-8.0,m,12H; δ2.33, s,6H. Anal. calc'd. for $C_{22}H_{18}N_2O$: C, 80.96%; H, 5.56%. Found: C, 80.65%; H, 5.76%.

1,3-bis(4-methylphenylimino)-1,3-dihydroisobenzofuran(168). A mixture of 0.25 g (0.77 mmol) of the yellow crystalline 167, 0.20 g (2.60 mmol) of potassium hydroxide, five ml of water and enough dioxane to dissolve the solid was heated on a steam bath overnight. After cooling, the resulting white solid was filtered, washed with

boiling ethanol and air dried to give 0.25 g (100%) of white powder, mp 147-148.5°C. Mass spec. m/e: 326 (85%), 325 (100%), 237 (13%), 193 (10%), 192 (13%), 165 (10%).

Acid catalyzed hydrolysis of 168. The white powder from the above reaction (0.20 g, 0.65 mmol) was stirred with a mixture of 5 ml of 5% aqueous hydrochloric acid and 10 ml of chloroform for 30 minutes. The chloroform layer was separated and the aqueous layer extracted with 5 ml of chloroform. The combined chloroform extracts were dried (Na_2SO_4), filtered and evaporated to give a white solid. Crystallization from chilled ethyl acetate/petroleum ether gave white needles, mp 198-198.5°C; lit. for N-(p-tolyl)phthalamide[82], 206°C. Mass spec.(chemical ionization) m/e: 238 (100%), N-p-tolyl) phthalamide+1; m/e: 327 (1.0%, 166 or 168+1; m/e: 345 (0.8%), 173+1.

Acid catalyzed hydrolysis of 167. A small amount of the yellow material was dissolved in 5 ml of ethanol by warming on a steam bath. To the mixture was added 1 ml of 10% aqueous sulfuric acid. The solution was allowed to stand overnight, after which time it had deposited yellow crystals of N-(p-tolyl) phthalamide, mp 199.5-200.5°C; lit.[82] 206°C. Nmr: δ7.70,m(aa'bb'),4H; δ7.20,s,4H; δ2.37, s,3H.

Acid catalyzed hydrolysis of 166. The above procedure gave orange crystals of N-(p-chlorophenyl)phthalamide, mp 199-202°C; lit.[83] 194-195°C. Nmr: δ7.73,m(aa'bb'),4H; δ7.33,s, 4H.

2,4,6-Triphenyl-1,3,5-triazine. A solution of 2.50 g (16.8

mmol) of N,N-dimethylbenzamide in 15 ml of thionyl chloride was heated at reflux for five days. A white solid had formed in the reaction mixture. After cooling, the white solid was filtered out and rinsed successively with chloroform, ethanol and water. It was recrystallized from a large amount of ethanol to give 0.71 g (41%) of white needles, mp 233.2-233.5°C; lit.[93] 234-234.5°C. Mass spec. m/e: 309.

N-methylphthalimide. Method A. N,N,N'N'-tetramethylphthalimide (154) (1.5 g, 6.9 mmol) was dissolved in 20 ml of phosphorus oxychloride and heated at reflux for 6 hours. After cooling, the mixture was poured over enough crushed ice to keep the mixture cold. The aqueous solution was extracted three times with 20 ml portions of methylene chloride. The combined organic layers were dried (Na_2SO_4), filtered and evaporated to give 0.4 g of dark green oily solid. Chromatography (CH_2Cl_2 on silica gel) gave, after a trace of purple material, 0.30 g (30%) of white needles, mp 129-131, lit.[96] 134°C. Pmr (CF_3CO_2H for comparison with lit.[97]): δ 3.15, s,3H; 7.65,m,4H. Note: Sadtler[97] shows a singlet for the aromatic protons. Mass spec.(chemical ionization), m/e: 161 (100%). Mixed mp with independently prepared N-methylphthalamide (Method B) showed no depression.

Method B. In a sealed tube a mixture of 2.0 g (11 mmol) of potassium phthalamide and 10 ml of freshly distilled methyl iodide was heated at 130°C in an oil bath for 10 hours. After cooling, the excess methyl iodide was removed by evaporation and the solid

residue was taken up in 20 ml of water. Extraction with three 20 ml portions of methylene chloride, followed by drying, filtering and evaporation of the organic extracts gave 1.65 g (95%) of yellow solid. Recrystallization from ethanol/water followed by chromatography (CH_2Cl_2 on silica gel) gave off-white crystals, mp 130-131.5° C; lit.[96] 134°C. Pmr: same as above.

LIST OF REFERENCES

63. A. S. Kende, R. G. Greenhouse and John A. Hill, Tetrahedron Lett., 2867 (1979).

64. H. v. Euler, E. Adler and G. J. Gie, Arkiv. Kemi. Min. Geol., 14B (1940); CA 34, 7877 (1940); H. v. Euler, E. Adler, H. Hasselquist and M. Lundin, Arkiv. Kemi. Min. Geol., 18A (1944); CA 38, 3875 (1944).

65. O. Diels and K. Adler, Ber, 62, 2337 (1929); J. A. Landgrebe, "Theory and Practice in the Organic Laboratory," D. C. Heath and Company, Lexington, Mass. (1977), p. 338.

66. G. Fodor and S. Nagubandi, Tetrahedron, 36, 1279 (1980).

67. D. N. Kevill and G. M. L. Lin, Tetrahedron Lett., 949 (1978).

68. H. J. Barber, L. Bretherick, E. M. Eldridge, S. J. Holt and W. R. Wragg, J. Soc. Chem. Ind. (London), 69, 82 (1950); G. T. Morgan and L. P. Walls, J. Chem. Soc., 2447 (1931).

69. D. B. Baird, I. Baxter, D. W. Cameron and W. R. Phillips, J. C. S. Perkin I, 1973, 832.

70. A. U. Rahman and N. M. Rodriguez, C. R. Acad. Sc. Paris C., 270, 230 (1970).

71. H. Pohl, J. Prak., 141, 44 (1934).

72. J. H. Woods and R. E. Gibson, J. Am. Chem. Soc., 71, 393 (1949).

73. J. C. Westfahl and J. L. Gresham, J. Am. Chem. Soc., 76, 1076 (1954).

74. F. S. Kipping, J. Chem. Soc., 53, 39 (1888).

75. (a) H. Schindlbauer, Monat. Chem., 99, 1799 (1968).
(b) H. Schindlbauer and S. Fischer, Synthesis, 634 (1972).

76. H. Perst, "Oxonium Ions in Organic Chemistry", Academic Press, New York, 1971, p. 132.

77. Sadtler NMR # 10550.

78. R. M. Silverstein, G. C. Clayton and T. C. Morrill, "Spectrometric Identification of Organic Compounds, 3rd Ed.", John Wiley and Sons, Inc., New York, 1974, p. 213.

79. G. C. Levy et al., "Carbon-13 Nuclear Magnetic Resonance Spectroscopy, 2nd Ed.", Wiley Interscience, New York, 1980, p. 123.

46. R. West and H. Y. Niu, in J. P. Snyder, "Non-benzenoid Aromatics", I, Academic Press, New York (1969, p. 311; R. West and J. Niu, p. 2441, Wiley (Interscience), New York, 1970; R. West, Isr. J. Chem., in press (1980).

47. R. Gleiter and P. Schanz, Ang. Chem. Int. Ed., 19, 715 (1980).

48. M. E. Peover, Trans. Faraday Soc., 58, 2370 (1962).

49. L. F. Fieser and M. Fieser, Reagents for Organic Synthesis, I, John Wiley and Sons, New York (1967), p. 311; H. D. Becker and G. A. Russell, J. Org. Chem., 28, 1869 (1963).

50. C. R. Johnson and W. G. Phillips, J. Am. Chem. Soc., 91, 682 (1969).

51. O. Neilands and M. Vavere, J. Gen. Chem. USSR, 33, 1032 (1963).

52. See for example T. Yamazaki, T. Oohama, T. Doiuchi and T. Takizawa, Chem. Pharm. Bull., 20, 238 (1972).

53. L. F. Feiser and K. L. Williamson, Organic Experiments, D. C. Heath and Company, Lexington, Mass. (1975), p. 188.

54. (a) P. Ruggli and W. Theilheimer, Helv. Chim. Acta, 24, 899 (1941).
(b) M. Masagawa, F. Suzuki, H. Nakamishi, Y. Suzuki, J. Polym. Sci. B., 6, 293 (1968).

55. Prepared by oxidation of m-xylene with chromic acid. N. W. Johnson and J. L. R. Williams, J. Am. Chem. Soc., 69, 2065 (1947).

56. P. Ruggli and P. Bucheler, Helv. Chim. Acta, 30, 2045 (1947).

57. E. Ota, S. Inoue, M. Horiguchi and S. Otani, Bull. Chim. Soc. Jap., 52, 3400 (1979).

58. Personal communication.

59. H. Perst, "Oxonium Ions in Organic Chemistry", Academic Press, New York, 1971, p. 132.

60. W. Reid and H. Boden, Ber, 89, 2328 (1956).

61. M. H. Hubacher and S. Doernberg, J. Pharm. Sci., 53, 1067 (1964); CA 62, 5250.

62. P. S. Braterman, B. S. Walker and T. H. Robertson, J. C. S. Chem. Comm., 651 (1977).

26. D. H. Reid, Quart. Rev., 19, 274 (1965).

27. J. C. Martin and R. G. Smith, J. Am. Chem. Soc., 86, 2262 (1964).

28. M. J. Sabacky, C. S. Johnson, Jr., R. G. Smith. H. S. Gutkowski and J. C. Martin, J. Am. Chem. Soc., 89, 2054 (1967).

29. E. Muller, A. Moosmayer, A. Rieker and K. Scheffler, Tetrahedron Lett., 3877 (1967).

30. N. C. Yang and A. J. Castro, J. Am. Chem. Soc., 82, 6308 (1960).

31. R. Kreilick, J. Chem. Phys., 43, 308 (1965).

32. D. Kearns and S. Ehrenson, J. Am. Chem. Soc., 84, 739 (1962).

33. E. A. Chondross, J. Am. Chem. Soc., 86, 1263 (1964).

34. R. M. Silverstein, G. C. Bassler and T. C. Morrill, "Spectrometric Identification of Organic Compounds", 3rd Ed., John Wiley and Sons, Inc., New York, 1974, p. 227.

35. M. D. Taylor and L. R. Grant, J. Chem. Ed., 32 (1955).

36. M. Jarcho, J. Am. Chem. Soc., 90, 4644 (1968).

37. B. A. Stoochnoff and N. L. Bentoin, Tetrahedron Lett., 21-24 (1973).

38. E. Holgstrand, Acta Chem. Scand., 18, 1616 (1964).

39. "Aldrich Catalog Handbook of Fine Chemicals", Aldrich Chemical Company, Milwaukee, 1981, p. 927.

40. "Elsevier's Encyclopedia of Organic Chemistry", Series III, Elsevier Publishing Co., New York, 1962, p. 12B.

41. Sadtler pmr 6943.

42. K. Hafner, K. H. Hafner, C. Jonig, M. Kreuder, G. Ploss, G. Schultz, E. Sturm and K. H. Vopel, Ang. Chem. Int. Ed., 2, 123 (1963).

43. K. Hafner and H. Suss, Ang. Chem. Int. Ed., 2, 575 (1973).

44. E. LeGoff, J. Am. Chem. Soc., 84, 3975 (1962).

45. R. West, "Oxocarbons", Academic Press, New York, 1980.

14. D. Adler and H. Brooks, Phys. Rev., 155, 826 (1967).

15. B. T. Matthias, Scientific American, 92 (1957); E. B. Yagubskii and M. L. Khidekel, Russ. Chem. Rev., 41, 1011 (1972).

16. K. Bechgaard, C. S. Jacobsen, K. Mortensen, H. J. Pedersen, N. Thorup, Solid State Commun., 33, 1119 (1980).

(a) D. Jerome, A. Mazaud, M. Ribault, K. Bechgaard, J. Phys. Lett. (Orsay, Fr.), 41, L-95 (1980). M. Ribault. G. Benedek, D. Jerome, K. Bechgaard, J. Phys. Lett. (Orsay, Fr.), 11, L-397 (1980). R. L. Greene, E. M. Engler, Phys. Rev. Lett., 45, 1587 (1980). K. Andres, F. Wudl, D. B. McWhan, G. Thomas, D. Nalewajek, A. L. Stevens, Phys. Rev. Lett., 45, 1449 (1980).
(b) M. Ribault, J. P. Pouget, D. Jerome, K. Bechgaard, J. Phys. Lett. (Orsay, Fr.), in press.
(c) F. Wudl, J. Am. Chem. Soc., 103, 7064 (1981).
(d) S. Parkin, M. Ribault, D. Jerome, K. Bechgaard, J. Phys. C., submitted for publication.

17. K. Bechgaard, K. Carneiro, F. B. Rasmussen, M. Olsen, J. Am. Chem. Soc., 103, 2440 (1981).

18. T. J. Kistenmacher, T. E. Phillips and D. O. Cowan, Acta Cryst., B30, 763 (1974).

19. R. C. Haddon, Aust. J. Chem., 28, 2343 (1975); Nature, 256, 394 (1975).

20. A. F. Garito and A. J. Heeger, Accts. Chem. Res., 7, 232 (1974).

21. A. W. Block, in "Energy and Charge Transfer in Organic Semiconductors", K. Masuda and M. Solver, Eds., Plenum Press, New York, 1974, pp. 159-174; D. B. Tanner, C. S. Jacobsen, A. F. Garito and A. J. Heeger, Phys. Rev. Lett., 32, 1301 (1974; M. J. Cohen, L. B. Coleman, A. F. Garito and A. J. Heeger, Phys. Rev. B., 10, 1298 (1974).

22. J. B. Torrance, Accts. Chem. Res., 12, 79 (1979).

23. R. C. Wheland, J. Amer. Chem. Soc., 98, 3926 (1976).

24. E. Phillips, T. J. Kistenmacher, J. P. Ferraris and D. O. Cowan, J. C. S. Chem. Comm., 471 (1973); F. H. Hervstein in "Perspectives in Structural Chemistry", J. D. Dunitz and J. A. Ibers, Eds., Vol. 4, p. 166, John Wiley, New York, 1971.

25. R. M. Metzger, J. Chem. Phys., 57, 1870, 1876, 2218 (1972).

LIST OF REFERENCES

1. W. L. Masterton and E. J. Slowinski, "Chemical Principles", 4th Ed., W. B. Saunders Co., Philadelphia, 1977, pp.159-160.

2. D. S. Acker and W. R. Hertler, J. Am. Chem. Soc., 84, 3370, 3374 (1962).

3. J. Ferraris, D. O. Cowan, V. Walatka, Jr. and J. H. Perlstein, J. Am. Cham. Soc., 95, 948 (1973).

4. E. M. Engler, Chemtech, 1976, 274

5. "CRC Handbook of Chemistry and Physics, 51st Ed.", Robert Weast, Ed., Chemical Rubber Co., Cleveland (1971).

6. J. H. Perlstein, Angew. Chem. Int. Ed., 8, 519 (1977).

7. R. C. Wheland and E. L. Martin, J. Org. Chem., 40, 3101 (1975); G. Saito and J. P. Ferraris, J. C. S. Chem. Comm., 1027 (1979); J. R. Anderson and O. Jorgenson, J. C. S. Perkin I, 3095 (1979).

8. D. J. Sandman and A. F. Garito, J. Org. Chem., 39, 1165 (1974); A. W. Addison, N. S. Dalal, Y. Hoyano, S. Huizingo and L. Weiler, Can. J. Chem., 55, 4191 (1977); M. Maxfield, D. O. Cowan, A. Bloch, T. O. Poehler, Nouveau J. Chem., 3, 647 (1979).

9. N. F. Haley, J. C. S. Chem. Comm., 1030 (1979); N. F. Haley, J. C. S. Chem. Comm., 207 (1977); F. Wudl, M. L. Kaplan, B. K. Teo and J. Marshall, J. Org. Chem., 42, 1666 (1977).

10. H. J. Keller, "Chemistry and Physics of One-dimensional Metals", Plenum Press, New York, 1977.

11. L. L. Klein, "Studies Toward the Synthesis of Organic Conductors", Ph. D. Thesis, Michigan State University, 1980.

12. I. B. Coleman, M. J. Cohen, D. J. Sandman, F. G. Yamagishi, A. J. Garito, A. F. Heeger, Solid State Comm., 12, 1125 (1973).

13. R. E. Peierls, "Quantum Theory of Solids", Oxford University Press, London, 1955.

80. J. E. Sarnecki, H. L. Suprenant, F. K. Molen and C. N. Reilley, Anal. Chem., 47, 2116 (1975); H. Eggert and C. Djerassi, J. Am. Chem. Soc., 95, 3710 (1973).

81. R. G. Cooke and I. M. Russell, Aust. J. Chem., 25, 2421 (1972).

82. B. A. Porai-Koschiz, Z. Obsc. Chi., 7, 604 (1937).

83. A. F. M. Fahmy, N. F. Aly, and M. O. Orabi, Bull. Chem. Soc. Japan, 51, 2148 (1978).

84. A. M. Islam, I. B. Hannout and A. M. El-Sharief, Ind. J. Chem. Sect. B., 15, 61 (1977).

85. W. E. Parham and C. D. James, J. Org. Chem., 41, 1187 (1976).

86. V. Horak and L. Novotony, Chem. Listy, 46, 357-9 (1952); V. Horak and L. Novotony, Coll. Czech. Chem. Comm., 18, 80 (1953).

87. H. B. Kostenbauder and T. Higuchi, J. Am. Pharm. Assoc., 45, 518 (1956).

88. C. W. Fong and C. R. Hameister, Org. Mass Spec., 13, 711 (1978)

89. C. Mannich and F. Schmitt, Ar, 1928, 78.

90. See Reference 5, p. C-167.

91. See Reference 5, p. C-166.

92. Y. Kigugawa, Chem. Pharm. Bull., 24, 1059 (1976).

93. J. H. Bayer and P. S. Ellis, JCS Perkin I, 1979, 483.

94. R. D. Reynolds, M. J. Zeigker, D. J. Heuck and C. Johnson, J. Chem. Eng. Data, 13, 558 (1968).

95. P. Oxley, M. W. Partridge, T. D. Robson and W. F. Short, J. Chem. Soc., 1946, 763.

96. See Reference 5, p. C-431.

97. Sadtler NMR # 19110.