PRODUCTS OF THE REACTIONS OF CERTAIN 2, 6-DISUBSTITUTED ARYL CHLOROFORMATES WITH SILVER NITRATE

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ABSTRACT

PRODUCTS OF THE REACTIONS OF CERTAIN 2,6-DISUBSTITUTED ARYL CHLOROFORMATES WITH SILVER NITRATE

by Trudie S. Barreras

This investigation primarily involved an examination of the reaction products obtained when several 2,6-disubstituted aryl chloroformates were allowed to react with silver nitrate under various reaction conditions.

The products obtained from the reaction of 2,6-dimethylphenylchloroformate with silver nitrate were 2,6-dimethyl-4-nitrophenol and 3,5,3',5'-tetramethyldiphenoquinone-(4,4'). From the 2,6-diisopropylphenylchloroformate, the analogous 2,6-diisopropyl-4-nitrophenol and 3,5,3',5'-tetraisopropyldiphenoquinone-(4,4') were obtained plus an additional product, a yellow crystalline substance which is not yet conclusively identified, although considerable physical and spectral data were obtained in an effort to elucidate its structure. The 2,3,5,6-tetramethylphenylchloroformate yielded the expected 4-nitrophenol plus 2,3,5,6-tetramethylquinone, but no coupling products were observed.

Variation of reaction conditions, including change of solvent from acetonitrile to nitromethane, seemed to have little effect upon the appearance of the various products, though the relative proportions of each were somewhat influenced. At temperatures below 0°, very little reaction was observed to occur, and no products could be isolated. Variations of temperature in general affected the quantities of the 4-nitrophenol

obtained most significantly.

In addition to this product study an effort was made to determine conditions under which a semi-stable intermediate might be formed and isolated. Also, a possible means of trapping $NO_2^{\oplus}$ was investigated briefly.

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INTRODUCTION

Little had been reported previously in the literature concerning the reactions of aryl chloroformates with silver nitrate. An initial extensive investigation of these reactions was recently undertaken by Matthew J. Zabik of these laboratories, as the research for his doctoral thesis. The present work, reported here, represents further research on the chemistry of aryl chloroformates in an attempt to elucidate in more detail the nature and mechanisms of the unusual rearrangement reactions of these compounds.

As the previous work, in these laboratories, had given some indications that the reaction of an aryl chloroformate with silver nitrate might initially produce a semi-stable intermediate, an attempt was first made to determine the experimental conditions under which such an intermediate might be formed and isolated. This was done with the anticipation of then being able to conduct studies involving isotopic labelling of reactants to elucidate in detail the mechanism of the rearrangement reaction of aryl chloroformates. These efforts were unsuccessful. However, during some of the reactions, the appearance of seemingly anomalous products led to a detailed investigation of properties and structures of these materials which is the central subject matter of the present thesis.

RESULTS AND DISCUSSION

The investigation of the reactions of aryl chloroformates with silver nitrate initiated by Zabik in these laboratories and continued in the present study represents the only investigation to date to attempt to elucidate the nature of these reactions. A major phase of the experimental effort was thus directed to determining what products actually resulted from these reactions and the methods of purification most applicable in each case.

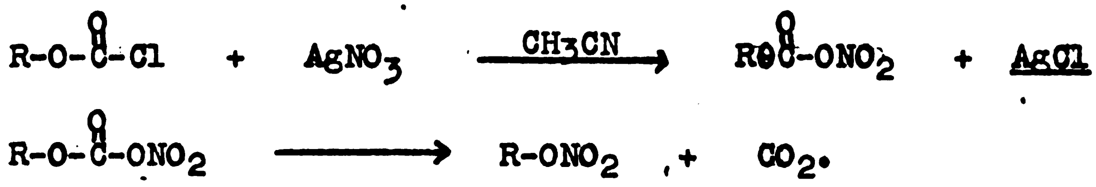
The experiments described in this paper can be placed into five general categories; preparation of the aryl chloroformates, efforts to determine the reaction conditions under which a possible intermediate might be isolated, isolation and investigation of the reaction products, variation of reaction conditions to determine their effects on product formation, and trapping experiments to determine whether ionic species were involved in these reactions.

I. Preparation of Aryl Chloroformates

Since the methods used for the preparation of the various aryl chloroformates used are described at length in the experimental section of this thesis, and are essentially those developed by Zabik and described in his doctoral dissertation, they will not be elaborated on further here. No unusual results were encountered in these reactions, though a nuclear magnetic resonance spectrum determined on the neat 2,6-diisopropylphenylchloroformate for the purpose of comparison with the products actually isolated indicated that the distillation procedure employed for purification may not have successfully eliminated all residual phenol. This may be pertinent since this particular chloroformate gave rise to an additional product apparently not encountered in the analogous reactions of other 2,6-dialkyl phenylchloroformates investigated.

II. Efforts to Determine Conditions Under Which a Possible Intermediate Might Be Formed

Studies of the reactions of alkyl chloroformates with silver nitrate indicated that two distinct steps occurred,



$$\mathrm{R{-}O{-}\overset{\overset{O}{\|}}{C}{-}Cl} + \mathrm{AgNO_3} \xrightarrow{\mathrm{CH_3CN}} \mathrm{RO\overset{\overset{O}{\|}}{C}{-}ONO_2} + \underline{\mathrm{AgCl}}$$

$$\mathrm{R{-}O{-}\overset{\overset{O}{\|}}{C}{-}ONO_2} \longrightarrow \mathrm{R{-}ONO_2} + \mathrm{CO_2}.$$

These steps occurred essentially simultaneously at normal temperatures, but the second step was considerably slower than the first below room temperature (2). It was anticipated that in the case of the aryl chloroformates, presuming that the reactions proceeded via an analogous intermediate, step one might be considerably faster than the second step at low temperatures. If this were the case isotopic labelling studies involving the 2,6-dialkyl phenylchloroformates could have been undertaken to possibly elucidate the mechanism of this rearrangement reaction. Though no exhaustive survey of possible reaction temperatures was conducted, reactions allowed to proceed for times varying from two to five hours at -30° and

-15° involved a minimal precipitation of silver chloride, such precipitation being the only currently available indication of the extent to which the first step had proceeded. It was therefore assumed that virtually none of the indicated intermediate, $ArCOONO_2$, was formed. In any event, it was apparent that extremely long reaction times would be required under these conditions, and it was felt that the technical difficulties of maintaining these low temperatures for such periods would be prohibitive.

One other possibility was considered, however; if an initial step involved the formation of some kind of complex between the silver nitrate and the chloroformate, and if this had been formed extensively in the cold, then perhaps the nitrophenol from this material would still be the predominant product even though another chloroformate was added before the silver chloride precipitated and the reaction proceeded to completion. With this idea in mind, at the conclusion of each reaction time a quantity of a second aryl chloroformate was added to the reaction mixture and the reaction was forced to completion by fairly rapid warming. While no extensive product analysis was undertaken, it was evident that a fairly complex mixture of products resulted in most of the reactions, and no predominance of the product expected from the initially used chloroformate was encountered. Based on these observations efforts to determine experimental conditions conducive to the extensive formation of intermediates were abandoned in order to examine in detail the nature of the complex products actually formed in these reactions of aryl chloroformates with silver nitrate.

It should be noted that in a subsequent series of experiments (Table II) the reaction of 2,6-diisopropylphenylchloroformate conducted for three days in the cold failed to result in the formation of any isolatable products; in fact unreacted silver nitrate was recovered from the reaction mixture at the end of this period. Hence it is evident, especially in the case of the 2,6-disubstituted phenylchloroformates, that attempts to obtain any appreciable reaction at relatively low temperatures would necessitate either some form of catalysis or else exceedingly long reaction periods.

III. Isolation and Investigation of Products

In the course of the preliminary experiments aimed at isolating intermediates as discussed above, it was observed in one case that an unexpected red crystalline material precipitated along with the silver chloride from a reaction involving 2,6-dimethylphenylchloroformate and silver nitrate. This material, while sparingly soluble in many common organic solvents, was recrystallized fairly satisfactorily from benzene or ethanol. This material was identified by quantitative analysis and comparison of the physical properties with the known 3,5,3',5'-tetramethyldiphenoquinone-(4,4'), (3).

An analogous quinone was expected to result from the reaction of the 2,6-diisopropylphenylchloroformate and was indeed isolated.

However, far from being insoluble in the reaction solvent and coprecipitating with the silver chloride, it proved extremely soluble not only in acetonitrile but also in hexane and ethanol. The product composition resulting from this reaction was further complicated by the presence of a third product, a bright yellow crystalline solid which had solubility properties similar to those exhibited by the quinone. Numerous efforts were made to separate these materials by fractional recrystallization, many of which resulted in intimate mixtures of red and yellow crystals of various sizes. In some cases these crystalline products formed in crystals of sufficient size to be partially separable mechanically. This, however, was hardly a practical procedure. In several other cases the reaction products took the form of a dark red colored syrup which was a mixture of the two substances plus other impurities. Eventually a procedure for chromatographing the combined reaction products on a silica gel column was developed which gave a relatively satisfactory separation, even though a certain amount of material appeared to decompose on the column. Unfortunately this technique was developed after most of the work discussed in the experimental section had been concluded and the products had been roughly separated by crystallization procedures. For this reason the actual percentage yields of the specific products obtained from any given reaction can only be approximated. Further, since the structure of the yellow crystalline material must still be considered as not yet fully confirmed, any yield calculations must of necessity depend upon an assumed molecular weight. However, postulating this substance as a dimer of molecular weight approximately 400, it is estimated to be formed in at least a 6-10% yield in all reactions conducted in acetonitrile, at room temperature or above. The 3,5,3',5'-tetraisopropyldiphenoquinone-(4,4') was isolated in a smaller yield under these experimental conditions; the maximum yield of this material obtained being about 5%. The maximum yield of the expected product, 2,6-diisopropyl-4-nitrophenol, was 60%, obtained from a reaction conducted at 55° for a short period of time followed by immediate product isolation. It is interesting to note, however, that the yield of the expected product obtained seemed to vary the most significantly with varying reaction conditions, while the proportions of the other materials appeared to remain fairly constant.

The expected product, 2,6-diisopropyl-4-nitrophenol was identified by its phenolic properties and from the known literature value of its melting point (4). The infrared and nuclear magnetic resonance spectra of this compound were as expected (Fig. 1).

The 3,5,3',5'-tetraisopropyldiphenoquinone-(4,4') isolated in the reactions described above was identified by quantitative analysis and its analogous properties to the previously discussed 3,5,3',5'-tetramethyldiphenoquinone-(4,4'). Spectra were determined and its nuclear magnetic resonance was exactly that anticipated for this structure (Fig. 2).

Both of the products gave n.m.r. spectra typical of symmetrically substituted aromatic compounds. They showed sharp doublets representing the methyl protons on the isopropyl groups, a septet for the tertiary isopropyl proton, and singlets for the aromatic (and phenolic) protons. In view of this fact, it is considered quite significant that the n.m.r. spectrum of the unknown yellow material differed radically from this pattern (Fig. 3). The splitting in the region of the methyl protons, which is clearest and easiest to determine, indicates that there are definitely three non-equivalent types of isopropyl group present in the structure. Further analysis of the spectrum and a determination of the area ratios of each peak indicates that there are two isopropyl groups which are equivalent, and two which differ from these and from eachother. In addition, on the basis of twenty-four methyl protons on the four isopropyl groups, the spectrum accounts for a total of nine others: four isopropyl protons and five in the aromatic region. On the basis of this evidence it is necessary to postulate a dimeric structure of some nature, which is unsymmetrical with respect to both the isopropyl groups and the aromatic hydrogens.

The results of elemental analysis are not as conclusive as had been hoped for, but they strongly support a proposed dimeric structure, with a minimum C:N ratio of 24:1. The molecular weight data is rather inconclusive, but since the compound appears to be unstable above its melting point, all

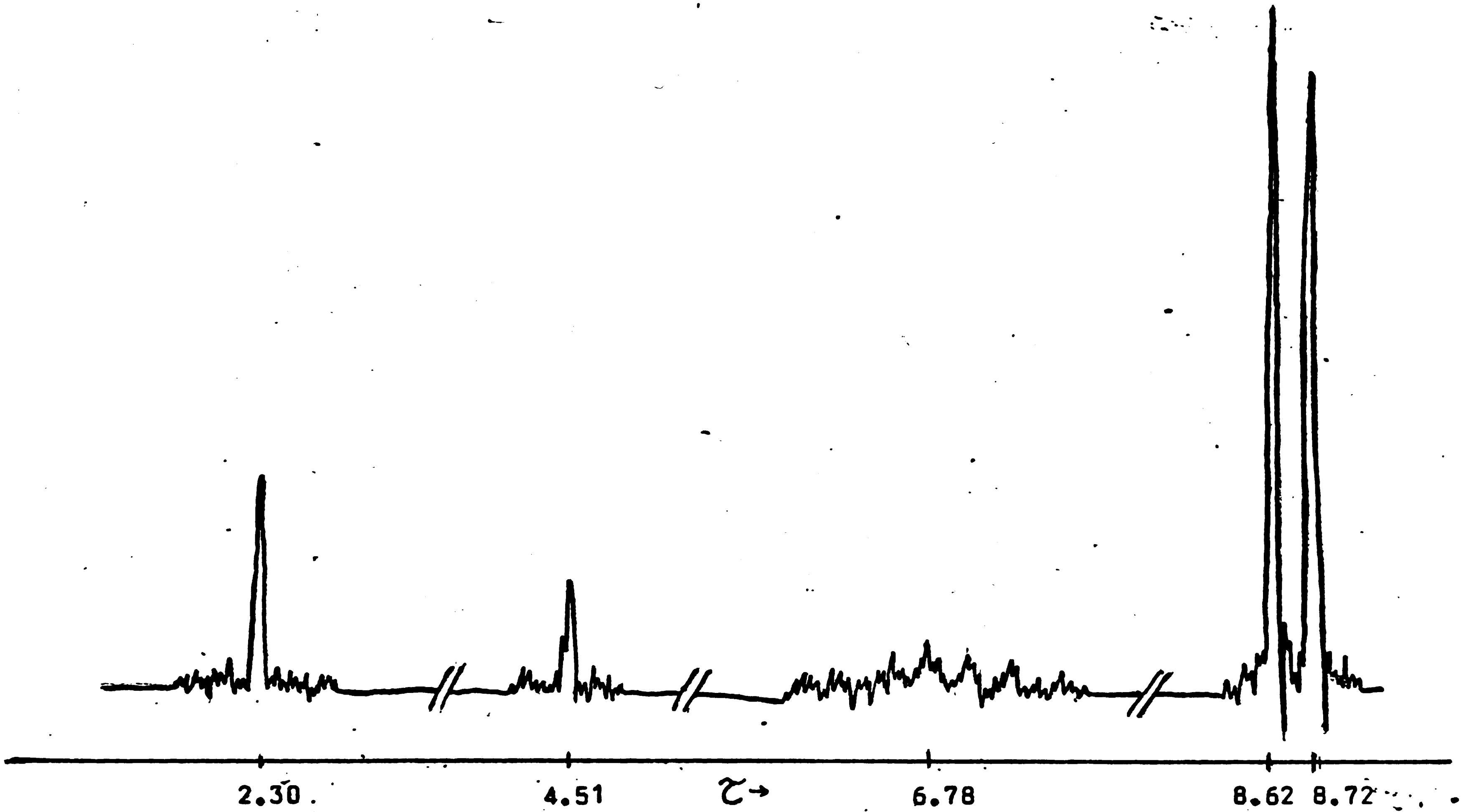


Figure 1. Nuclear Magnetic Resonance Spectrum of 2,6-Diisopropyl-4-nitrophenol

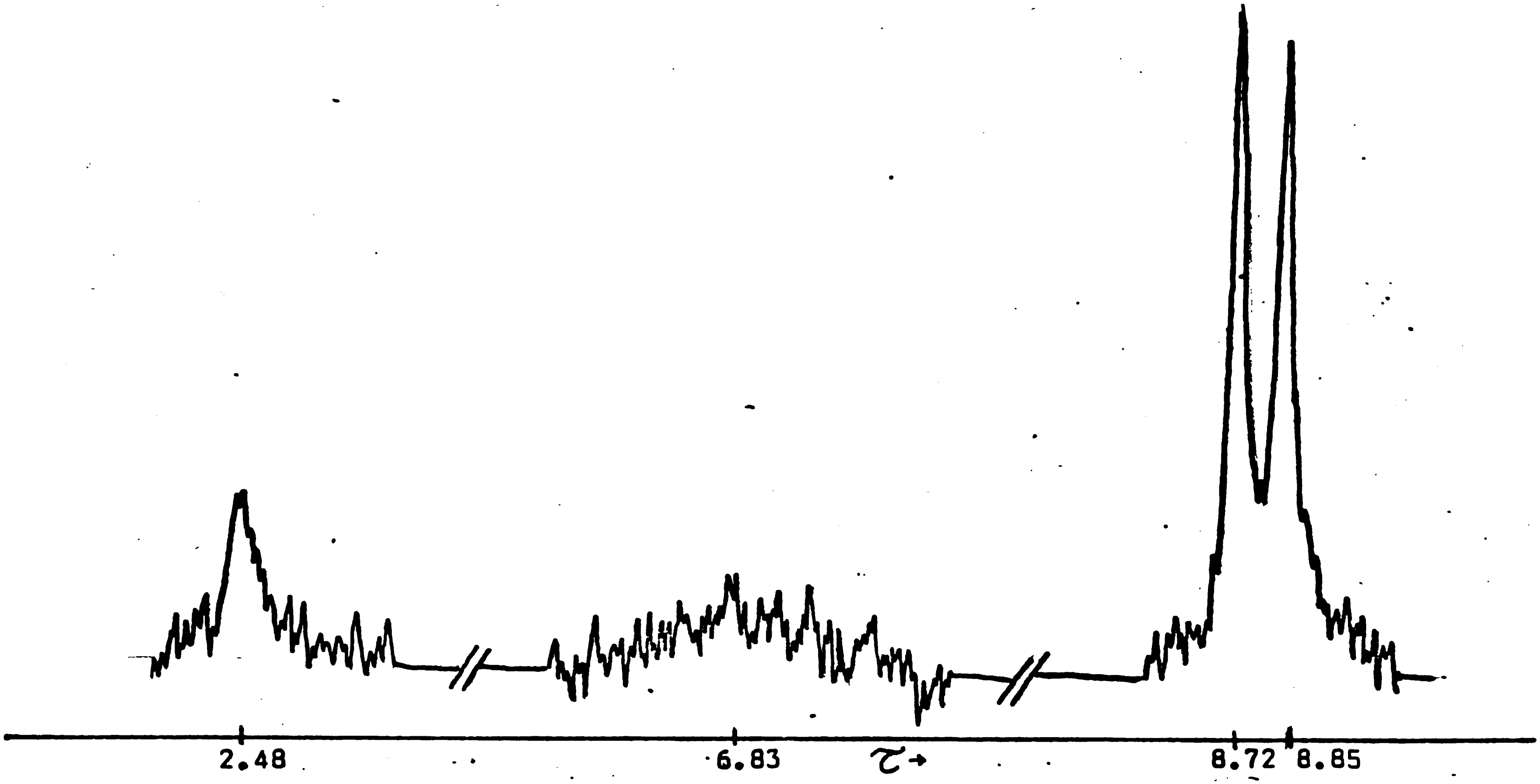


Figure 2. Nuclear Magnetic Resonance Spectrum of 3,5,3',5'-Tetraisopropyldiphenoquinone-(4,4')

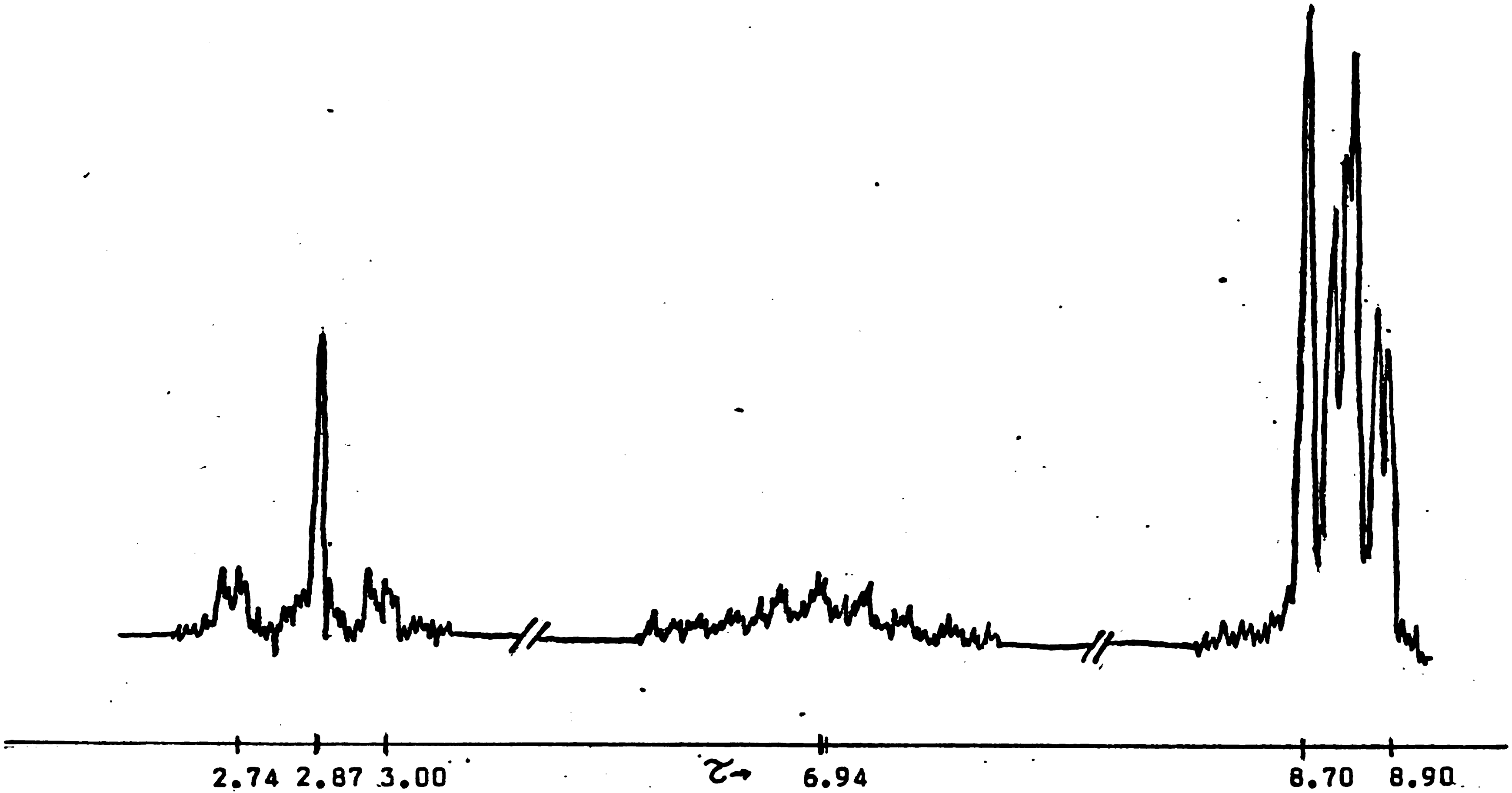
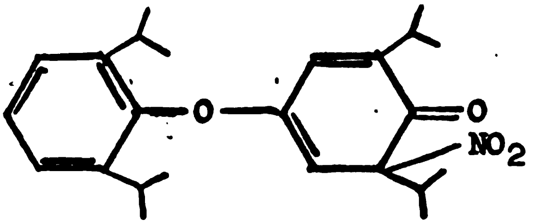


Figure 3. Nuclear Magnetic Resonance Spectrum of Unknown Yellow Material

analytical and instrumental methods involving the use of elevated temperatures would be expected to give questionable results. The osmometric method, which is expected to give a ten percent error, strongly indicates a molecular weight of 400 or above, supporting the dimeric structure.

A structure which reasonably satisfies the above evidence, and particularly the n.m.r. data, is,



Molecular formula $C_{24}H_{33}NO_4$.

It is unfortunate that the unusual and complex nature of this structure makes it difficult to find models for the purpose of comparison of the infrared and ultraviolet spectra. There is an unusual absorption at 1805 cm^{-1} in the carbonyl region of the I.R. spectrum of the material (Fig. 4), a definitive interpretation of which could aid significantly in a clarification of the structure. This absorption is so close to the typical absorption of the chloroformate itself at 1795 cm^{-1} (Fig. 5) that repeated elemental analyses were made to determine that halogen was definitely absent. In any event, it is suggested that if such a carbonyl exists, stearic and polarity effects of the two groups in the β-position might indeed yield unusual spectra.

In the absence of specific chemical evidence, which was not sought as part of the present investigation, other structural possibilities cannot be completely eliminated. Some of

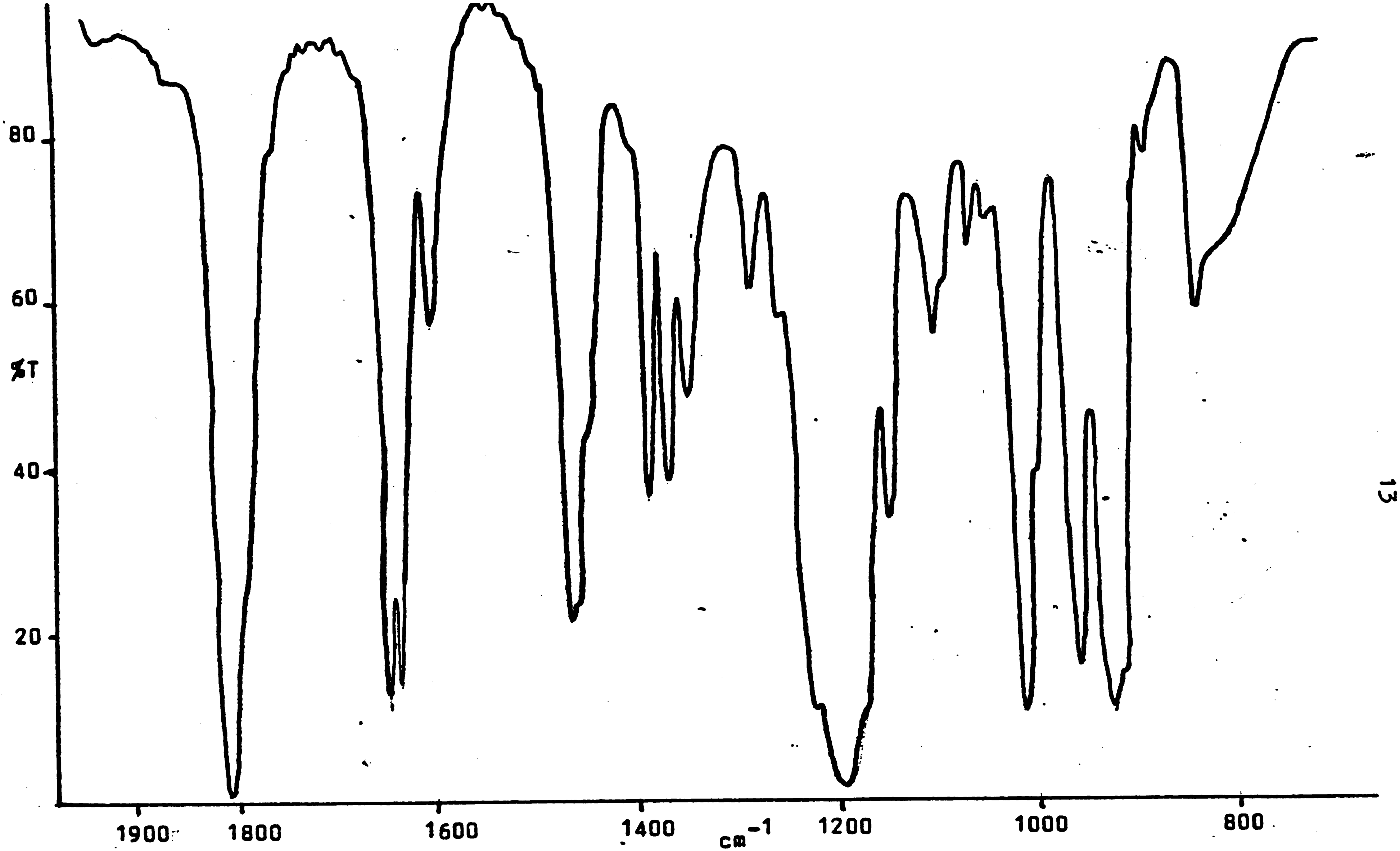


Figure 4. Infrared Spectrum of Unknown Yellow Material

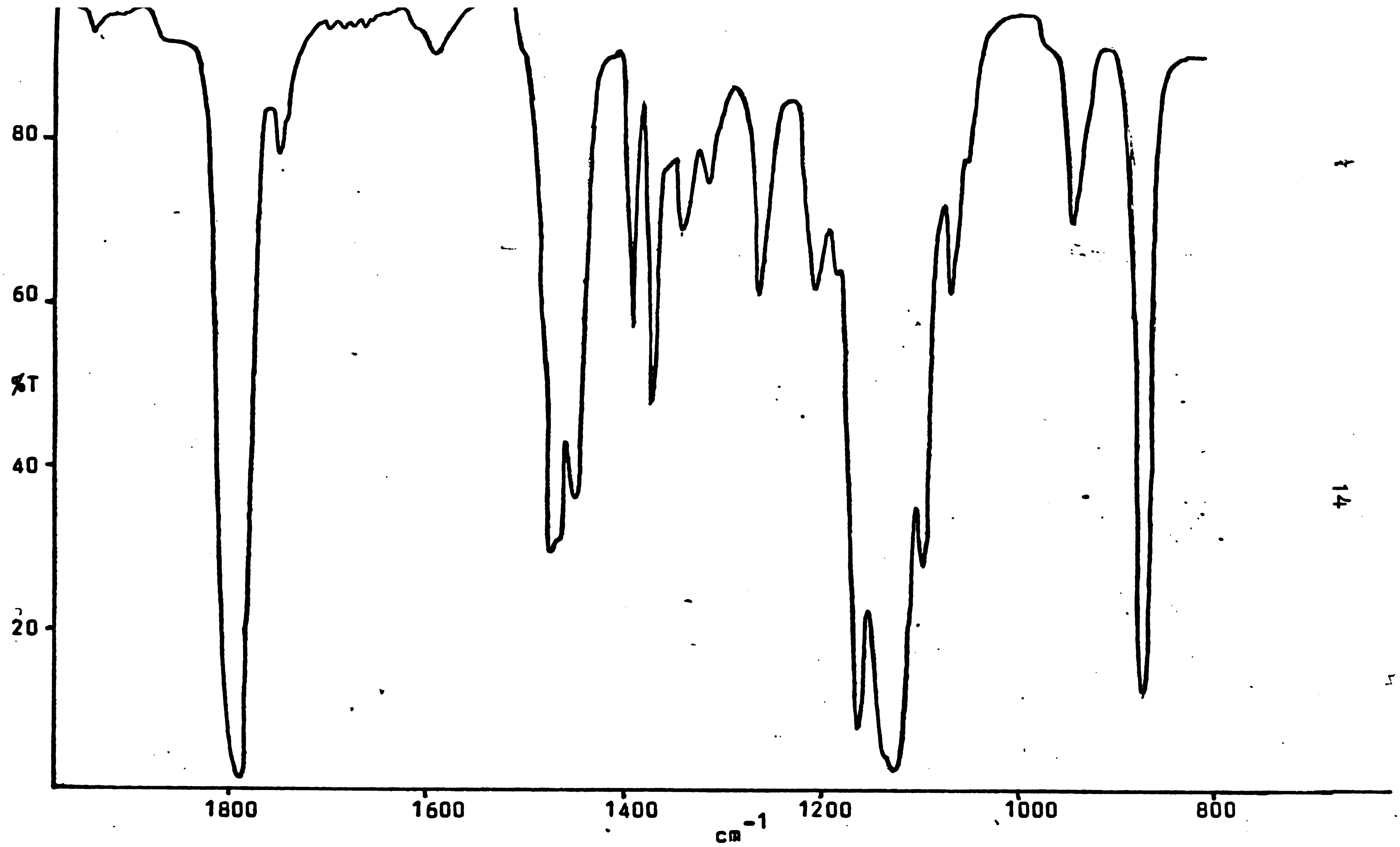
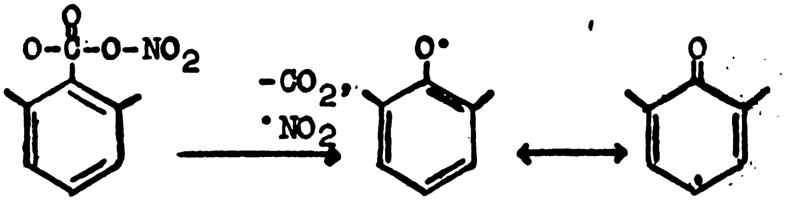


Figure 5. Infrared Spectrum of 2,6-Diisopropylphenylchloroformate

these structures appear to be more satisfactory if only parts of the data are considered. However, the structure proposed above seems at present to be the one best supported by the totality of the evidence and especially by the fairly clearly interpreted n.m.r. spectrum.

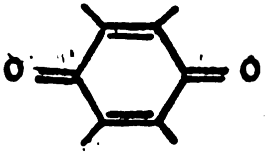
The formation of these unusual compounds in the course of the reactions of the 2,6-dialkyl phenylchloroformates with silver nitrate leads naturally to speculation concerning the mechanism by which they are produced. Although no experiments were undertaken in the course of the present investigation to establish the possibility, it is felt that a homolytic cleavage of the bonds in the hypothesized nitrate ester intermediate, leading to a phenoxide free radical, could be considered,



These radicals are known to be stable and have been demonstrated to couple giving the type of quinone encountered (5). Although in his investigations Zabik failed to find specific evidence of free-radical formation, the major efforts of his study were concerned with rearrangements to the ortho positions. In these cases the probability of a concerted intramolecular rearrangement is greatly enhanced, while the stability of a possible phenoxy radical is decreased. One further indication favoring a possible free radical mechanism is the consistent appearance of oxides of nitrogen being evolved during the course of these reactions.

If a free radical mechanism is assumed to explain the appearance of the quinones, it can probably likewise be used in a modified way to discuss the formation of the third product from the 2,6-diisopropylphenylchloroformate reaction, since this also seems to involve a dimeric structure, suggestive of coupling of some sort.

The appearance of the yellow crystalline unknown in the reaction of the 2,6-diisopropylphenylchloroformate led immediately to speculation as to why a similar product had not been encountered in the case of the previously investigated 2,6-dimethylphenylchloroformate. An immediate possibility seemed to be that the extremely stable crystalline structure of the 3,5,3',5'-tetramethyldiphenoquinone-(4,4'), which rendered it so insoluble in the reaction mixture, might energetically favor this by-product to such an extent that any analogous reaction could not compete. The apparent way to overcome this difficulty was to try to find another compound which closely resembled the 2,6-dimethylphenylchloroformate in properties, but which could not effectively form a diphenoquinone. The obvious choice was durenylchloroformate (2,3,5,6-tetramethylphenylchloroformate). This compound was therefore synthesized and allowed to undergo reaction with silver nitrate under the usual conditions. The only product which was obtained in addition to the expected nitrodurenol was duroquinone,



which may likewise be rationalized in terms of a free radical formation and subsequent oxidation. However, this does not offer the desired experimental evidence in rationalizing the nature of the unknown material obtained from the 2,6-diisopropylphenylchloroformate rearrangement. It should be pointed out, however, that the possibility of the presence of a third product was not absolutely eliminated either in the case of the 2,6-dimethylphenyl- or the 2,3,5,6-tetramethylphenylchloroformate rearrangements. In both situations far less than 100% of the reactant was accounted for in the products, and due to the crystallization procedures generally undertaken for purification, it is possible that a highly soluble third substance might easily have been lost in product isolation, especially if it was present in extremely small quantities.

A fruitful area for future investigation of these reactions would be careful, detailed product analysis to determine the exact amount of each substance obtained under specific reaction conditions. In addition it would be informative to prepare various para-substituted 2,6-dialkyl phenylchloroformates and allow these to react with silver nitrate. To date this has only been attempted with the 2,4,6-trimethylphenylchloroformate, and though the major product from this reaction was identified as 3,5,3',5'-tetramethylstilbenequinone-(4,4'), an extremely complex product mixture was obtained (1). However, since interesting coupling products have been reported from a procedure which generates phenoxide radicals from various

2,4,6-trisubstituted phenols (5), it would be interesting to investigate the extent to which the chloroformate reactions might give analogous products.

IV. Variation of Reaction Conditions to Determine the Effects on Product Formation

It should be noted that at no place in the present study were genuinely "standard" reaction conditions established, nor was an attempt made to systematically change one variable, such as time or temperature, in order to determine the exact effect of an individual change of this sort. However, examination of Tables II and III demonstrates that in reactions conducted at temperatures of 25^{o} or above, and allowed to proceed for times varying upwards from three hours, the same products were always obtained, though in varying quantities. This has already been dealt with in the discussion of yields in Section III above.

Additional variables examined briefly were purity and nature of solvent. Though these results are not conclusive due to the difficulties of product separation already mentioned; examination of entries (1) and (4) in Table II indicates that, other conditions being analogous, using anhydrous, distilled acetonitrile in place of that taken directly from the supplier's container without any purification increases the proportions of the by-products somewhat with respect to the nitrophenol.

Changing the solvent from acetonitrile to nitromethane does not seem to prevent formation of any of the products, though the quantities of each are reversed; the diphenoquinone is obtained in greater than 10% yield from the 2,6-diisopropylphenylchloroformate reaction, while the unknown yellow material is only present to the extent of about 3% and the nitrophenol, while still the major product, was obtained in only a 23% yield. This reaction was catalyzed by the addition of several drops of pyridine, further modifying the conditions.

Finally, it is observed that reactions conducted in the dark except for mixing, occasional momentary checks on progress, and the time necessary for removal of solvent, showed no significant variation of products.

In summary, the major influence on the reaction seems to be temperature; in general, in the case of the 2,6-diisopropylphenylchloroformate reaction, the higher the reaction temperature the greater the total product, mainly representing the expected 2,6-diisopropyl-4-nitrophenol. Within the limits of experimental error, changes of temperature and other variables seem to have relatively little effect of the appearance or quantities of the by-products.

V. Trapping Experiments Attempting to Determine Whether Ionic Species Were Involved

These efforts, which are discussed in detail in the experimental section of this thesis, gave inconclusive results which, in view of more extensive work along the same line by Zabik, did not seem to offer a particularly fruitful area for further investigation.

EXPERIMENTAL

I. Reagents

All reagents were used as obtained from the supplier without additional purification, with the exception of the acetonitrile designated "anhydrous." This was distilled from calcium hydride through a one-foot column packed with glass helices, and the fraction boiling in the range 80.5-81.5° was collected and stored over calcium hydride until use.

II. Preparation of Phenylchloroformates

The chloroformates used in this study were prepared using the general procedure described by Zabik (1).

In the case of 2,6-dimethylphenylchloroformate, 50.0 g. (0.41 mole) of 2,6-dimethylphenol was dissolved in 225 ml. of benzene and placed in a 3-necked round-bottomed flask fitted with an isopropyl alcohol-dry ice condenser, an equilibrating dropping funnel, and a gas inlet tube. All connecting tubing was glass or tygon. A set of traps, one containing a solution of sodium hydroxide in methanol, were connected to the top of the condenser. Approximately 55 ml. of phosgene, previously liquified by passing the gas from a cylinder through a spiral condenser immersed in an isopropyl alcohol-dry ice slush, was added rapidly through the gas inlet tube, which was then replaced by a glass stopper. Then 54.7 g. (0.45 mole) N,N-dimethylaniline was added dropwise to the stirred dialkyl phenol solution via the dropping funnel, while maintaining the reaction mixture at its reflux temperature. Following each addition of a quantity of the base, pronounced color changes in the reaction mixture were observed; in this case from light yellow to deep blue-green. The rate of base addition was regulated so that the color nearly faded to pale yellow between each addition. Immediately following the final addition of the aniline the reaction mixture crystallized to a bright-yellow solid. The reaction mixture was hydrolyzed by cautiously adding 10 ml. of distilled water dropwise. During the hydrolysis gas was vigorously evolved, heating of the mixture was observed, and the solid dissolved to yield a yellow-orange colored solution. This was initially washed with dilute hydrochloric acid, then with dilute sodium hydroxide, and finally with distilled water. The benzene solvent was dried over anhydrous magnesuim sulfate, removed by distillation, and the pure product was isolated by distillation under vacuum. A yield of 45.90 g. (0.25 mole, 60.5% theoretical) of material boiling at 73-76°/3 mm. was collected. Literature value (6), b.p. 71-72°/5.5-6.0 mm.

In a similar preparation of 2,6-diisopropylphenylchloroformate, an immediate solidification of the reaction mixture on adding the last of the N,N-dimethylaniline failed to occur and the reaction mixture was stirred until refluxing had ceased and then it was hydrolyzed, washed and dried as described above. Following removal of the benzene solvent the crude product was distilled to obtain 68.1 g. (0.28 mole, 69% theoretical) of a material boiling at 108-112°/3 mm.

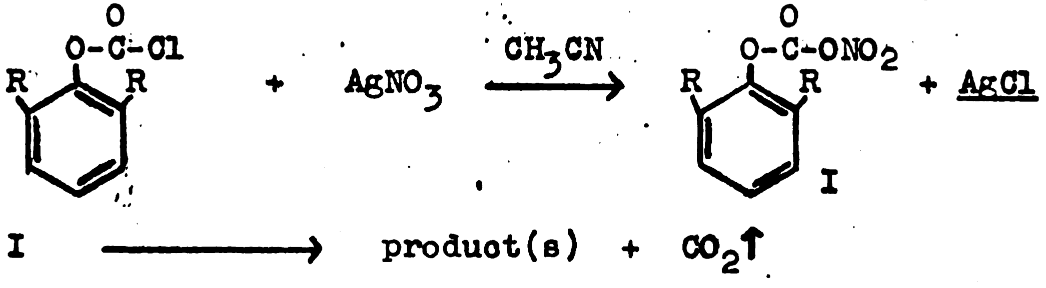
p-Methylphenylchloroformate was similarly prepared and obtained in a 69% yield. Since these chloroformates had been previously synthesized and reported (1), they were used without further analysis or purification.

In the preparation of 2,3,5,6-tetramethylphenylchloroformate, 34 g. (0.22 mole) of the phenol was employed with proportionate amounts of the other reagents. The reaction mixture took on a reddish-brown coloration during the addition of the N,N-dimethylaniline, turning yellow and solidifying following the final addition of organic base as in the case of the 2,6-dimethylphenol. Following washing of the reaction mixture, drying and removal of solvent, the product was found to be a solid. Considerable experimental difficulty in recrystallization of the crude product resulted in a rather poor yield, but a minimum of 15.0 g. of fairly pure material was obtained on recrystallization from benzene. This product, after two additional recrystallizations from benzene, yielded a white flaky material melting at 54-62°.

Anal. Calc'd. for $C_{11}H_{13}O_2Cl$: C, 62.11%; H, 6.14%; Cl, 17.23%
Found: C, 62.10%; H, 6.22%; Cl, 17.25%

III. Preliminary Experiments

In an initial series of experiments involving the reaction of 2,6-dimethylphenylchloroformate with silver nitrate an attempt was made to determine a set of experimental conditions under which the hypothesized intermediate I would form with an appreciable precipitation of silver chloride, but without the rearrangement of the intermediate with the accompanying evolution of carbon dioxide and formation of the final products,



These first reactions were conducted at low temperatures and with the addition of various other reagents. In general the results indicated that the rate of formation of the intermediate at these temperatures was too slow to be of practical experimental value for mechanistic studies.

In a typical experiment, 3.4 g. (0.019 mole) of 2,6-dimethylphenylchloroformate (approximately a two-fold excess) in 75 ml. of acetonitrile were cooled to -30° in a bromobenzene-dry ice bath and mixed. The reaction was allowed to proceed with stirring at this temperature for two hours, but no appreciable clouding of the solution or precipitation of silver chloride was observed. A 1.7 g. (0.011 mole) quantity of phenylchloroformate in 25 ml. acetonitrile was added to the cold reaction mixture and the reaction warmed to room temperature. An immediate cloudiness appeared in the mixture and a few bubbles of gas escaped. Further heating brought a heavy precipitation of silver chloride, and the reaction mixture turned yellow, then brown in color. After removal of the silver chloride by filtration and the solvent by distillation, the product was distilled under vacuum to obtain a mixture of liquid fractions boiling ca. 70-80°/ 4 mm as well as some solid 2,6-dimethyl-4-nitrophenol, m.p. 165-169° after recrystallization from a 4:1 ethanol-water mixture. Literature value (7), m.p. 169-170°. No further separation or identification of products was attempted. Table I gives a schematic representation of the results of a number of these types of experiment.

IV. Investigation of By-Products

The appearance of the red crystalline solid in preliminary experiment four (Table I) led to an effort to determine whether this unexpected product was obtained when the reaction was allowed to proceed in the absence of any interfering reagents as well as in their presence. Two parallel reactions were conducted. In the first, 4.63 g. (0.025 mole) of 2,6-dimethylphenylchloroformate in 50 ml. acetonitrile was mixed at room temperature with an equivalent molar amount (4.25 g.) of silver nitrate in 50 ml. acetonitrile, and the reaction was allowed to proceed with stirring for 72 hours. At this point the solution was light yellow in color and some dark red crystalline material had precipitated along with the silver chloride. The red solid after recrystallization from benzene gave 0.07 g. of a material melting with decomposition in the range 205-225°. The remainder of the reaction mixture was heated to remove the reaction solvent. However, since it was observed that N_2O_4 fumes were being evolved, heating was discontinued and the remainder of

Table I: Results of Preliminary Experiments

Reagents in brackets were mixed at the initiation of the reaction and allowed to react at the given temperature for the recorded time; the observations refer to the reaction mixture prior to the addition of the other designated reagents.

Reagents: I, 2,6-dimethylphenylchloroformate; II, phenylchloroformate; III, phenol. All in ca. 50 ml. acetonitrile solvent.

Product: IV, 2,6-dimethyl-4-nitrophenol .

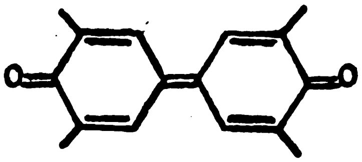
Reagents		Temp. °C	Reaction Time (hrs.)	Products
1.	3.4 g. I 1.7 g. $AgNO_3$ 1.7 g. II	-30	2; Obs: No clouding	IV + liq. mixture, b.p. 70-80°/4 mm.
2.	1.5 g. II 1.7 g. $AgNO_3$ 1.7 g. I	-30	5; Obs: No precipitation	Liq., b.p. 70°/5 mm. oily residue, no solid
3.	1.7 g. I 1.7 g. $AgNO_3$ 1.5 g. II	-15	4; Obs: Slight discoloration and clouding	Liq., b.p. 63-68°/3.5 mm. + IV
4.	1.7 g. I 1.7 g. $AgNO_3$ 1.0 g. III	Rm. temp. (ca. 25) ca. 40	2.5; Obs: precipitation 4; filtered, stored	IV + red crystals + tarry residue

the solvent was removed under vacuum on a rotary evaporator. The residue was crystallized from a 4;1 ethanol-water mixture, and an initial yield of 0.57 g. (0.002 mole, 15% yield) of 2,6-dimethyl-4-nitrophenol melting at 164-167° was obtained.

Simultaneously with the above reaction a second reaction containing the same proportions of chloroformate and silver nitrate, but with an added 2.00 g. (0.021 mole) of phenol, in a slightly more dilute solution (150 ml. acetonitrile) was allowed to proceed. The latter reaction mixture turned brown in color and after 72 hours of reaction a somewhat larger proportion of the red crystalline material (0.10 g.) had precipitated from the solution. Following removal of the reaction solvent by rotary evaporation an oily brown residue was obtained. This was dissolved in ethanol and decolorized with Norite. However, the filtrate remained dark and no solid could be induced to recrystallize from it.

The red crystals were submitted for analysis for carbon, hydrogen and nitrogen.

Anal. found: C, 79.36%; H, 6.80%; N, less than 0.2%. These analytical results yielded, by calculation, the empirical formula C_8H_8O, and suggested the possibility of the dimeric structure,



3,5,3',5'-tetramethyldiphenoquinone-(4,4').

The proposed structure was verified by referrence to Beilstein (3), which contained a description of this compound as a sparingly soluble material which crystallized from solution in the form of dark red colored needles, melting with decomposition in the range 207-217°. Since the solubility in common solvents was low, the only other information obtained on this compound was an infrared spectrum.

V. Products from the Reaction of 2,6-Diisopropylphenylchloroformate

In a similar manner investigation was initiated to determine whether analogous results would occur with other 2,6-dialkyl phenylchloroformates. 2,6-Diisopropylphenylchloroformate was examined using 0.025 mole quantities of the reagents (6.19 g. of 2,6-diisopropylphenylchloroformate and 4.25 g. of silver nitrate) each in 50 ml. of acetonitrile. These reagent solutions were mixed and stirred for six hours at 25° and then set aside at room temperature for an additional 48 hours. At the end of this time no red crystalline material was observed to separate from the reaction mixture. However, the reaction solution had taken on a dark red coloration. The silver chloride was removed by filtration and the reaction solvent removed under reduced pressure in a rotary evaporator. The residue was dissolved in boiling hexane. The hexane solution was allowed to cool and filtered to recover the crystalline product. This material was recrystallized a second time from hexane after decolorization with Norite to obtain 1.5 g. of a pale yellow colored pure material in the form of needles, m.p. 114-116°. Literature value (4) m.p. 2,6-diisopropyl-4-nitrophenol, 112°.

The hexane filtrate from the initial crystallization was dark red in color. Removal of the hexane from this solution left a dark red, semi-solid residue. The residue was treated with 95% ethanol, in which it partially dissolved, leaving a red crystalline solid. The latter was removed by filtration and after further purification yielded material melting at 215-220°.

Concentration of the ethanol solution yielded a quantity of bright yellow colored crystalline material as large rhombic crystals melting at 145-150°. A second recrystallization of this material from ethanol raised its melting point to 152-155°.

The reaction of 2,6-diisopropylphenylchloroformate with silver nitrate described above was repeated under various experimental conditions in an effort to determine the effects these variations had on the products formed. Some difficulty was encountered in separating and analyzing these products, as both by-products, red and yellow, seemed to be very similar in their solubilities. Initial efforts to separate these substances by fractional crystallization were only partially successful. Table II summarizes the results of these experiments. All reactions described in Table II used 6.19 g. (0.025 mole) of 2,6-diisopropylphenylchloroformate, and 4.25 g. (0.025 mole) of silver nitrate. The products are designated I, the expected product, 2,6-diisopropyl-4-nitrophenol; II, the red crystalline solid, identified as 3,5,3',5'-tetraisopropyldiphenoquinone; and II, the yellow material, m.p. 152-155°.

Table II: Reactions of 2,6-Diisopropylphenylchloroformate with Silver Nitrate

	Solvent	Temp. & Rxn. Time	Products
1.	100 ml. CH_3CN	25° 6 hrs. stirring 48 hrs. standing	I: 1.5 g. II: 0.07 g. III: 0.10 g.
2.	100 ml. CH_3CN	-15° mixing 25° w/stirring, 72 hrs.	------------
3.	100 ml. CH_3CN (anhyd.)	0° 5 hrs. w/ stirring; 67 hrs. stored in cold	Unreacted $AgNO_3$, 0.7 g; No organic solid
4.	100 ml. CH_3CN (anhyd.)	25° w/stirring 5 hrs. 43 hrs. standing	I: 0.95 g. II: 0.21 g. III: 0.52 g.
5.	100 ml. CH_3CN (anhyd.)	55° w/stirring 3 hrs. Immediate work-up	I: 3.35 g. II: 0.05 g. III: 0.39 g.
6.	100 ml. CH_3CN	45° w/stirring 48 hrs. in dark 72 hrs. stored in cold	I: 2.58 g. II: 0.10 g. III: 0.30 g.
7.	100 ml. CH_3NO_2	35° w/stirring 28 hrs. 36 hrs. stored in cold	I: 1.28 g. II: 0.51 g. III: 0.15 g.

Comments

Under experiment:

2. Products syrupy, difficult to recrystallize
3. Further precipitation of AgCl during removal of solvent under vacuum
5. Further yield of red and yellow products, but co-crystallized
7. Silver nitrate sparingly soluble in nitromethane; 3 drops pyridine added as a catalyst. Immediate pptn. of AgCl. Darkening of sol'n, sudden evolution of oxides of nitrogen after 5 hrs. rxn. time. Dark red crystals formed on AgCl during storage

VI: Identification of Products from the Reaction of 2,6-Diisopropylphenylchloroformate

Since the expected 2,6-diisopropyl-4-nitrophenol had been previously prepared and reported by Zabik in these laboratories, no further identification of this material other than its melting point was employed, though n.m.r. and I.R. spectra were determined for purposes of comparison.

The red crystalline solid melting at 215-220° was postulated to be the 3,5,3',5'-tetraisopropyldiphenoquinone-(4,4'). A pure sample of this material was submitted for quantitative analysis.

Anal. Calc'd for $C_{24}H_{32}O_2$: C, 81.90%; H, 9.14%

Found: C, 80.96%; H, 9.14%.

The I.R. and n.m.r. spectra were determined to further confirm the structure.

Efforts were made to identify the unknown yellow product melting at 152-155° using various analytical data and instrumental methods. A summary of these data follows.

Yellow Compound from 2,6-Diisopropylphenylchloroformate Reaction

1. Melting point 152-155° (Three recrystallizations from 95% ethanol); some decomposition above melting point, melt becoming dark red. Total decomposition by 250°.
2. Elemental analysis: No chlorine present.
3. Quantitative Analysis: (Found values average of five determinations)

	Found	Ratio x/N	Cald. %, $C_{24}H_{33}NO_4$
C:	73.02%	24.3	72.15%
H:	8.18%	32.5	8.33%
N:	3.50%	1.0	3.57%

Proposed Empirical Formula: $C_{24}H_{33}NO_4$

Calculated Molecular Weight: 399.51

4. Molecular Weight Determinations
   Rast (commercial): 221
   Osmometer: 456
   Mass Spectograph: No mass peaks above 194

5. Infrared Spectrum (Fig. 4)

6. Ultraviolet Spectrum: Low intensity peak; 413 mμ.
   High intensity peak, 283 mμ.

7. Nuclear Magnetic Resonance Spectrum in CCl_4 (Fig. 3)

   A. Considering methyl peaks as three doublets, centered at: τ = 8.87, 8.83, 8.77
   (Individually, τ = 8.90, 8.88, 8.82, 8.79, 8.75, 8.70)

   B. Septet (?) centered at τ = 6.94

   C: In Aromatic: Quartets (?) centered at = 3.00, 2.74
   Singlet τ = 2.87

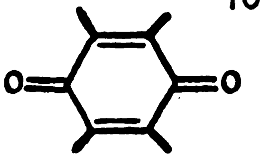
   Ratio A:B:C = 24;4:5

VII. Products from the Rearrangement of 2,3,5,6-Tetramethylphenylchloroformate

In order to investigate the possible formation of other products when the possibility of para coupling was greatly reduced, the 2,3,5,6-tetramethylphenylchloroformate was prepared and allowed to react with silver nitrate. In three separate experiments, conducted under various experimental conditions, two products were obtained. One was the expected 2,3,5,6-tetramethyl-4-nitrophenol, identified by comparison of its properties determined in this work with those reported in the literature. The material recrystallized twice from ethanol melted at 120-124°. Literature value (8), m.p. 123-124°. This compound was verified by carbon, hydrogen and nitrogen analysis.

Anal. Calc'd. for $C_{10}H_{13}NO_3$: C, 61.50%; H, 6.68%; N, 7.29%
Found: C, 61.71%; H, 6.83%; N, 7.35%.

The other product isolated was a bright yellow colored solid which crystallized in the form of needles from ethanol or hexane. The material sublimed above 90° and melted at 110-114°. Quantitative elemental analysis gave the following values, C, 72.88%; H, 7.40%; N, less than 0.3%. Calculation from these analytical results yielded the empirical formula C_5H_6O. A molecular formula $C_{10}H_{12}O_2$, corresponding to the structure



was proposed for the structure of the yellow product. This compound, duroquinone, reported in literature as melting at 111° (9) and having a characteristic infrared absorption at 1640 cm^{-1} (10), (Fig. 6), was in fact verified as the one obtained in the reactions of durenylchloroformate with silver nitrate.

Table III summarizes the several reactions of 2,3,5,6-tetramethylphenylchloroformate and silver nitrate under varying experimental conditions.

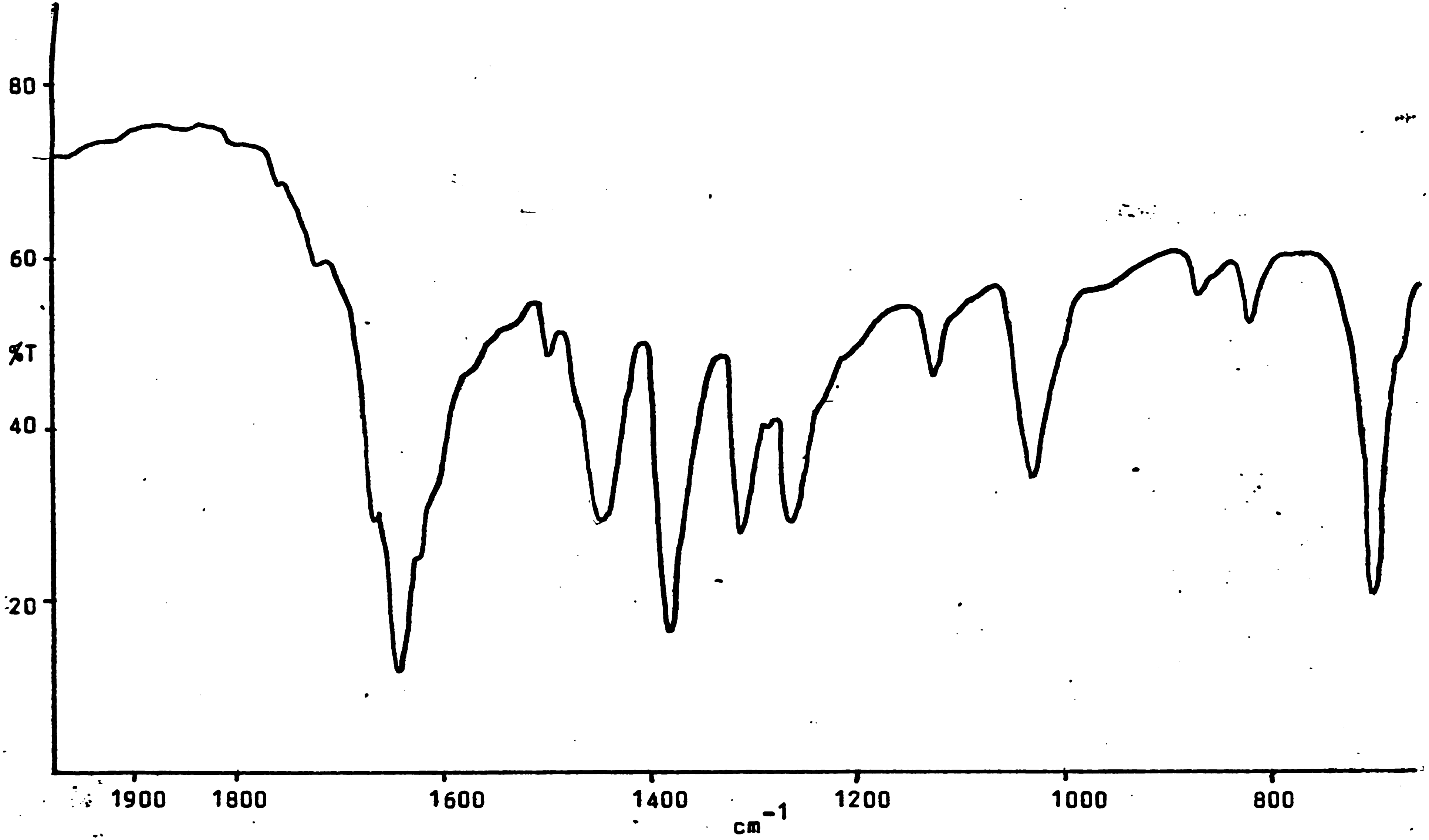


Figure 6. Infrared Spectrum of 2,3,5,6-Tetramethylquinone (Duroquinone)

Table III: Reactions of 2,3,5,6-Tetramethylphenylchloroformate

Compound I, p-NO_2-durenol, Compound II, Duroquinone

Experiments 1 and 2 used 0.025 mole quantities of the chloroformate (5.33 g.) and silver nitrate (4.25 g.) Experiment 3 used half this amount of each reagent.

Reaction Conditions	Products
1. Solvent, 100 ml. CH_3CN. 25° w/stirring 48 hrs. Stored in cold 24 hrs.	I and II
2. Solvent 100 ml. CH_3CN. 45° w/stirring 5 hrs. Stored in cold ca. 60 days.	Mainly II
3. Solvent 60 ml. CH_3CN. 35° w/stirring in the dark 24 hrs. Stored in cold 4 days.	I: 0.27 g. II: 0.11 g.

Note: In experiments 1 and 2 above, numerous separate portions of product were treated with different solvents, sublimed, extracted with base, and so on, in an attempt to find a good separation procedure. Thus no accurate account could be made of the actual quantities of product obtained. However, it is estimated that in (1) the proportions were approximately equal, while in (2) the quinone was definitely the major product. In (3), the residue obtained by removal of the acetonitrile was dissolved in hexane, and compound I recrystallized from solution. The hexane was removed and the residue was treated with dilute sodium hydroxide. That portion which did not dissolve in base was removed and recrystallized from ethanol.

VIII. Trapping Experiment

One additional experiment was undertaken in an effort to determine whether any free $NO_2^{\oplus}$ was formed in the reaction of aryl chloroformates with silver nitrate. This involved the reaction of p-methylphenylchloroformate with silver nitrate in the presence of p-methylanisole. Two parallel reactions, each involving 0.025 mole quantities of the chloroformate and silver nitrate in 100 ml. of acetonitrile were initiated with stirring. To one of these was added 3.05 g. (0.025 mole) of p-methylanisole, and the reactions were allowed to proceed for four hours. The reaction mixtures were then chromatographed in parallel on silica gel slides. Although no conclusive results were obtained, it appeared that both reactions had given rise to a fairly complex series of products, which were nevertheless similar enough that no specific assignment of any given spot as due to a nitro-substituted p-methylanisole could be made.

SUMMARY

1. The diphenoquinone by-products from the reactions of 2,6-dimethyl- and 2,6-diisopropylphenylchloroformate with silver nitrate were isolated and characterized.

2. An additional by-product from the 2,6-diisopropylphenylchloroformate reaction was isolated and studied, though conclusive identification of this material was not accomplished.

3. The previously undescribed 2,3,5,6-tetramethylphenylchloroformate was prepared and characterized. The products of the reaction of this material with silver nitrate were identified as the 2,3,5,6-tetramethyl-4-nitrophenol and the 2,3,5,6-tetramethylquinone.

4. The effects of variation of reaction conditions on the proportions of the various products obtained were considered. It was noted that temperature effects seemed to be the most significant, and that the quantities of the p-nitrophenol product obtained seemed to be the most susceptible to such temperature changes.

5. Means of isolating a possible intermediate, as well as a method for trapping any $NO_2^\oplus$ which might have been produced, were briefly investigated.

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