Synthesis of 2-aryl-tetrahydro-3-methyl-4-H-1,3-thiazine-4-one-1,1-dioxides and chloromrthylation of p-dichloro-benzene

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SYNTHESIS OF 2-ARYL-TETRAHYDRO-3-METHYL-
4-H-1,3-THIAZINE-4-ONE-1,1-DIOXIDES

and

CHLOROMETHYLIATION OF p-DICHLOROBENZENES

by

Robert Dye Downer

Senior Thesis Submitted
in Partial Fulfillment
of the Requirements of Graduation

DEPARTMENT OF CHEMISTRY
UNION COLLEGE
MAY, 1966
This Thesis
Submitted by

Robert W. Orme

to the
Department of Chemistry of Union College
in partial fulfillment of the requirements of the degree of
Bachelor of Science

is approved by

Howard E. Sheffer
IN APPRECIATION

I wish to express my sincere appreciation to Professor Howard Sheffer whose academic guidance has taught me the skills and perseverance necessary for success in scientific investigation, and whose friendship has emphasized the value of the humanistic character: honesty, fairness, and cooperation.

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HISTORICAL BACKGROUND

A. Extensive background material and experimentation on the synthesis of 2-aryl-tetrahydro-3-methyl-4-f-3-1, 3-thiazine-4-one-1, 1-dioxides

\[ \text{Chemical structure} \]

from methyl amine, an aromatic aldehyde and \( \text{B-mercaptobenzenoic} \) acid was reported by Wilson (1). He used meta and para fluorosubstituted benzaldehydes to obtain a final product with fluorine substituted in the 3 and 4 positions of the phenyl radical:

\[ \text{Chemical structures} \]

The synthetic procedure used by this author was supplied in transcript by Dr. Dennis Bailey (2). This is the result of a special study by him to improve Wilson's method. The three basic reactants were the same as in Wilson's (1) work, but the conditions and apparatus were different. The procedure is outlined in Experiment 1, and the apparatus appears in Figure 1.
HISTORICAL BACKGROUND

B. A specific procedure for the chloromethylation of p-dichlorobenzene

\[
\begin{array}{c}
\text{Cl} \\
\text{C} \\
\text{Cl}
\end{array}
\]

was not found in the literature. In Organic Reactions (3) the method of Blanc (for the chloromethylation of benzene) and a modification of it (for the chloromethylation of p-xylene) seemed to offer the most favorable conditions for the desired synthesis.

Other methods were sought for the chloromethylation of p-dichlorobenzene. Stephens et al. (4) in the Journal of the Chemical Society reported the use of paraformaldehyde, concentrated sulfuric acid, and chlorosulfonic acid for synthesizing 5-dichloromethyl ether

\[
\text{ClCH}_2-\text{O-CH}_2\text{Cl}
\]

in yields 95% theoretical. They reacted 0.65 moles of this ether with 0.67 moles of benzene to obtain a 69% (of theoretical) yield of benzyl chloride.

\[
\begin{array}{c}
\text{Cl} \\
\text{C}_\text{H}_2\text{Cl}
\end{array}
\]

Stephens et al. also reported the synthesis of p-chlorobenzylchloride

\[
\begin{array}{c}
\text{Cl} \\
\text{C}_\text{H}_2\text{Cl}
\end{array}
\]
from the reaction of S-dichloromethyl ether and chlorobenzene.

This synthesis was carried out below 25°C and employed 97% sulfuric acid. Stephens also noted the formation of 4,4'-
dichlorodiphenylmethane in nearly theoretical yields at a
temperature of 40°C.

Jean Bolle (5) reported a similar procedure for the
chloromethylation of 1,2,4-trichlorobenzene. Bolles' method
is outlined below and was used in an attempt to chloromethylate
p-dichlorobenzene. The method was later modified and provided
the basis for the success of the synthesis.

1) Cool 8 moles of concentrated sulfuric acid to 0°C
2) Add 1.6 moles of trioxane
3) Add 3.4 moles of chlorosulfonic acid over a 1 hour
interval, keeping the temperature at or near 0°C
4) Add 2.0 moles of 1,2,4-trichlorobenzene over a 5
minute interval
5) Stir: a) 1 hour at 0°C
   b) Overnight at ambient temperatures
   c) 3 hours at 40°C
   d) Cool and pour into ice
6) Wash the organic layer with water and 5% NaHCO₃
7) Dry and distill

Several differences exist between the methods employed by
Stephens, et al. and Bolle. Bolle used trioxane rather than
paraformaldehyde. Also, he did not isolate the S-dichloromethyl
ether, but he controlled temperature much more rigorously.
Bordwell (6) suggested the following as the active agent in chloromethylation:

\[
\left[ \text{CH}_2\text{OH} \right. \quad \leftrightarrow \quad \left. \text{CH}_3\text{OH} \right] \quad \text{ZnCl}_3
\]

Further, he suggested that ZnCl₂ may also catalyse the conversion of the intermediate to the benzyl chloride.

\[
\text{C}_{6}\text{H}_{5} + \text{CH}_2\text{OH} \quad \xrightarrow{H^\text{+}} \quad \text{C}_{6}\text{H}_5\text{CH}_2\text{OH} + H^\text{+}
\]

\[
\text{C}_{6}\text{H}_5\text{CH}_2\text{OH} + \text{Cl}^\text{-} \quad \xrightarrow{H^\text{+} / \text{ZnCl}_2} \quad \text{C}_{6}\text{H}_5\text{CH}_2\text{Cl} + H_2O
\]

Roberts (7) suggests the following as the chloromethylation mechanism:

\[
\text{H}_2\text{C} = \text{O} + \text{HCl} \quad \xrightarrow{\text{ZnCl}_2} \quad \text{CH}_2\text{ClOH} \quad \xrightarrow{\text{H}_2\text{C} = \text{C} - \text{Cl}} \quad \text{CH}_2\text{Cl}
\]

There are two possible mechanisms for chloromethylation.
by Blanc’s method, Nordell’s proposal and Roberts’ mechanism;
neither is definitely proved.

It seems likely, however, that the chloromethyl carbonium ion is the active agent in the method proposed by Stephens, et al. (4). They isolated the ether, and later reacted it in the presence of sulfuric acid with an aromatic ring. In the presence of a proton, a chloromethyl carbonium ion could readily be formed:

\[
\text{Cl-CH}_2-\text{O-CH}_2-\text{Cl} + 3\text{H}^+ \rightarrow 2 \text{Cl-CH}_2^+ + \text{H}_2\text{O}
\]

In Bolle’s procedure, the ether is not isolated, but the reactants are the same.
EXPERIMENTAL RESULTS AND CONCLUSIONS

A. Experiment 1.

Synthesis of 2-((3-fluoro-phenyl)-tetrahydro-3-
methyl-4-0-1, 3-thiazine-4-one-1, 1-dioxide

The procedure for the first two experiments was taken
from Bailey (2):

**Synthesis of 2-aryl-3-methylthiazines**

1) Partly fill a 100 ml x 50 cm crystallization dish
   with ice and water
2) Place 100 ml of benzene in a 150 ml beaker and
   cool in the ice bath
3) Face the whole apparatus, and bubble methyl amine
   into the benzene until 5.4g (0.11 moles) has dis-
   solved in the benzene
4) Place 0.1 moles of the desired benzaldehyde in a
   250 ml round-bottom (1-neck) flask with 50 ml of
   benzene. Insert a magnetic stirrer.
5) Add the cold benzene-methyl amine solution
6) Connect a Dean Stark trap to the neck of the flask
   and fill it with benzene
7) Reflux using a steam bath or heating mantle. Close
   down the reaction when 1.8 ml of water has been
   collected in the Dean Stark trap

\[ \text{CH}_3-\text{NH}_2 + \text{(aryl)CHO} \rightarrow \text{(aryl)CH=N-C}_3\text{H}_3 + \text{H}_2\text{O} \]
8) Cool the solution to touch, and add 0.11 moles of p-mercaptopropionic acid
9) Replace the Dean Stark trap and reflux
10) Shut down the reaction after 1.6 ml of \( \text{H}_2\text{O} \) is collected or after 48 hours, whichever comes first

\[
\begin{align*}
\text{CH}_2 = \text{N} - \text{CH}_3 + \text{HS-CH}_2 - \text{CH}_2 - \text{COON} & \rightarrow \\
\end{align*}
\]

\( + \text{H}_2\text{O} \)

11) Wash the solution: 3 x with 1:3 \( \text{NH}_4\text{OH} \)
2 x with 1:5 HCl
2 x with saturated brine
12) Dry with anhydrous \( \text{Na}_2\text{SO}_4 \)
13) Evaporate filtrate under reduced pressure to remove benzene
14) I.R. at 0.1 \( \mu \)
15) Crystallize if possible using ether or ether-benzene combination.

**Oxidation of 2-aryl-3-methylcystathiones**

1) Dissolve the product (0.1 moles-theoretical) in 140 ml of acetic acid
2) Prepare \( \text{KMnO}_4 \) solution of 31.6g (0.3 moles) in 500 ml of \( \text{H}_2\text{O} \).
3) Cool and stir acetic acid solution to 10\( ^\circ \) - 15\( ^\circ \) C temperature range
4) Add KMnO₄ solution dropwise to maintain temperature range:

![Chemical Reaction Diagram]

5) Continue stirring for 15 minutes and then add 35-40g of KMnO₄ (solid) in small portions over a 5 minute interval.

\[ 2H^+ + 2\text{MnO}_4^- \rightarrow 2\text{MnO}_2 + 3/2 \text{O}_2 + 1 \text{H}_2\text{O} \]

6) Filter off solid product and recrystallize in isopropanol.

7) I.R.:

- 6.05 μm amide
- 7.45 and 8.8 μm sulfone

In this synthesis, the aromatic aldehyde used was 0.11 moles of o-fluoro-benzaldehyde:

![Chemical Structure]

There occurred a slight ammonia-type odor as the benzene with dissolved methyl-amine was poured into the reaction flask; slightly more than 0.11 moles of methyl-amine had originally been dissolved in the benzene. After 1.5 ml of water had been collected during the formation of the Schiff Base (step 7) the reaction was shut down before the expected 1.8 ml of water had been collected; no azetropo was condensing and a clear benzene
layer appeared above the emulsion in the Dean-Stark trap. Also, 1.6 ml of water was collected during step 10. No crystals were present after evaporation. The structure of the expected major reaction product was:

![Chemical structure diagram]

The oxidation of the thioether in the above compound to the dioxide was carried out using 0.30 moles of KMnO₄. A temperature range of 10⁰ - 13⁰ C was maintained during the addition of the permanganate solution. More than 40 g of sodium bisulfite was needed to dissolve the solid manganese dioxide and permit the crystals of the oxidized product to be readily filtered.

The final product

![Chemical structure diagram]

showed the distinctive I.R. peaks at 6.08 μ for the amide, 7.45 μ and 8.6 μ for sulfone. A pure (constant) melting range of 160⁰ - 162⁰ C was recorded. The yield was 36.9% overall and over 30% from the formation of the Schiff Base.

Yield - 6.85 g
% - 36.9 %
M.P. - 160⁰ - 162⁰ C
<table>
<thead>
<tr>
<th>THEORETICAL</th>
<th>MEASURED</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>7.30</td>
</tr>
<tr>
<td>S</td>
<td>12.46</td>
</tr>
<tr>
<td>N</td>
<td>5.48</td>
</tr>
</tbody>
</table>

A 0.4 limit on sulfur necessitated the nitrogen analysis.

**Experiment 2.**

**Synthesis of 2-{2,6-dichloro-phenyl}-tetrahydro-3-methyl-4-3-1, 3-thiazine-4-one-1, 1-dioxide**

The procedure from Experiment 1 was followed precisely:

0.11 moles of 2,6-dichlorobenzaldehyde

![Chemical Structure](image)

was used.

During the formation of the Schiff Base, 1.7 ml of water was collected:

![Chemical Reaction](image)

A greatly reduced volume of water, 0.9 ml (50% of theoretical) was collected during ring closure, formation of the meta-thiansacnone:

![Chemical Structure](image)
After more than 27 hours, the reaction was shut down. While washing the product with \( \text{NH}_4\text{OH} \), a dense emulsion formed. Much of the product was presumed lost, and the experiment was discontinued.

Experiment 3.

Synthesis of 2-(2,5-dichloro-phenyl)-tetrahydro-
3-methyl-4H-1, 3-thiazine-4-one-1, 1-dioxide.

This experiment was a re-run of Experiment 2. More than 1.7 ml of water was collected during formation of the Schiff Base, and only 0.95 ml of water during ring closure.

Sodium chloride was added to the \( \text{NH}_4\text{OH} \) wash to aid in separating the emulsion. The oxidation was followed according to the procedure outlined in Experiment 1; the final product structure was:

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH} \\
\text{Cl} \\
\text{Cl} \\
\text{CH}_2 \\
\text{S} \\
\end{array}
\]

Yield = 7.82 g

% = 30.3 %

S.P. = 220° - 221° C

<table>
<thead>
<tr>
<th>THEORETICAL</th>
<th>MEASURED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>23.01</td>
</tr>
<tr>
<td>S</td>
<td>10.41</td>
</tr>
</tbody>
</table>
(a) Reaction apparatus for synthesis of 2-aryl-tetrahydro-3-methyl-4-H-1,3-thiazine-4-one-1,1-dioxides. Dean-Stark Trap is removed for final oxidation.

(b) Methyl amine is dissolved in cold benzene on a tared balance.
B. Experiment 4.

Chloromethylation of p-dichlorobenzene

Blanc's Method (4) was employed in an attempt to perform the synthesis. Essentially, no reaction occurred, and crystals of p-dichlorobenzene formed in the reflux condenser.

Experiment 5.

Chloromethylation of p-dichlorobenzene

The method suggested by Jean Bolle (5) for the chloromethylation of 1, 2, 4, trichlorobenzene is outlined below. In future experiments it is modified, and modifications are referred to the numbered steps of this outline.

1) Cool 5 moles of concentrated sulfuric acid to 0° C
2) Add 1.8 moles of trioxane
3) Add 5.4 moles of chlorosulfonic acid over a 1 hour period, keeping the temperature at or near 0° C
4) Add 2.0 moles of 1,2,4 trichlorobenzene over a 5 minute interval
5) Stir:  a) 1 hour at 0° C
     b) Overnight at ambient temperatures
     c) 3 hours at 40° C
     d) cool and pour into ice
6) Wash the organic layer with water and 5% NaHCO₃
7) Dry and distill

<table>
<thead>
<tr>
<th>B.P.</th>
<th>148-149</th>
</tr>
</thead>
<tbody>
<tr>
<td>R₂₉</td>
<td>1.5919</td>
</tr>
</tbody>
</table>

In this experiment, p-dichlorobenzene was used in place of 1,2,4 trichlorobenzene and reactants were reduced to 25% of the
above proportions.

During the addition of chlorosulfonic acid, the temperature of the reaction mixture rose to 60 °C, even though it was in an ice bath; the rate of addition was slowed. During step 3(a), the temperature range was 10° - 30° C. In 3(b) the crystals dissolved, and the temperature rose as high as 44° C; a liquid 2-phase system appeared. In step 3(c), the temperature had to be raised to approximately 60° C to attain a liquified, 2-phase system.

The product was distilled over a temperature range of 305° - 311° C; it readily solidified. A constant melting range of 98° - 99° C was determined.

However, the N.M.R. spectrograph showed only 2 peaks which when integrated, showed a ratio of 2 aliphatic hydrogens to 1 aromatic hydrogen. This suggested the disubstitution product:

\[ \text{CH}_2\text{Cl} \]

\[ \text{CH}_2\text{Cl} \]

rather than the mono-substitution product

\[ \text{CH}_2\text{Cl} \]

\[ \text{CH}_2\text{Cl} \]

The aliphatic peak occurred at 4.56 ppm and the aromatic peak at 7.45 ppm.

weight = 16.8 grams

% = 10.3 %
Experiment 6.

Chloromethylation of p-dichlorobenzene

Bolle's procedure from Experiment 5 was used with one modification. Step 5 (c) was omitted, and the reaction was not heated to the suggested temperature of 40° C.

At the end of step 5 (b), a crude, solid mass appeared, and attempts to dissolve it were unsuccessful. The experiment was terminated at this point.

Experiment 7.

Chloromethylation of p-dichlorobenzene

Bolle's procedure was used, using the following ratios of reactants:

- 0.5 moles p-dichlorobenzene
- 0.2 moles trioxane (0.6 moles of formaldehyde)
- 0.75 moles chlorosulfonic acid
- 0.6 moles sulfuric acid

Also, step 3 (c) was omitted.

The reaction product was a viscous, yellow liquid with some small white crystals in it. The crystals showed a spectrograph with N.M.R. identical to that in Experiment 4, indicating the formation of the di-substitution product. However, an N.M.R. on the supernatant liquid showed evidence of the mono-substitution product in approximately 75% purity. The boiling point was 120° C at 19 mm Hg. The amount of product was very small, and no attempt was made to determine the per-cent yield.

Experiment 8.

Chloromethylation of p-dichlorobenzene

Bolle's method was again used; the ratio of reactants was
the same as in Experiment 7. Step 3 (b) was modified so that the reaction was run in a cold water bath overnight. Step 3 (c) was modified to permit two hours at room temperature.

Crystals with a melting point of 93° - 98° were obtained from the crude reaction product, recrystallized from ligroin. The N.M.R. spectrograph showed that the product was the di-substitution product:

Experiment 9.

Chloromethylation of p-dichlorobenzene

Bolle’s method was used with the ratios of reactants as follows: 0.6 moles p-dichlorobenzene
0.187 moles trichloroethylene
0.7 moles sulfuric acid
0.7 moles chlorosulfonic acid

Step 3 (b) was the same as in Experiment 6, overnight in a cold water bath; step 3 (c) was modified to 1 hour at room temperature.

A solid substance (large mass) formed in the reaction vessel.

The N.M.R. spectrograph of the crude product noted that it was mostly p-dichlorobenzene.

Experiment 10.

Chloromethylation of p-dichlorobenzene

Bolle’s method was employed. The ratios of reactants were
the same as in Experiment 9. Step 5 was modified as follows:

a) 2 hours at 0° C
b) cold water bath overnight
c) 2 hours at room temperature

It was noted that during the beginning of the overnight period, the temperature of the bath was slightly warmer (25°-27° C) than the temperature of the tap water (22°-23° C). It was recorded in step 6 that the temperature of the reaction mixture rose from approximately 23° C to a range of 26° - 28° C.

During the washing procedure, the organic layer appeared clear, not yellow as before. The S.M.R. spectrograph of the crude reaction product showed it to contain 40 - 50% 2,6 dichlorobenzyl chloride, the mono substitution product. The remainder was di-phenylmethane. Distillation yielded a pure sample of the mono substitution product:

\[
\begin{align*}
\text{Cl} & \quad \text{Cl} \\
\text{C} & \quad \text{CH}_2\text{Cl} \\
\end{align*}
\]

B.P. 134° - 136° C at 28 mm Hg

\[
\begin{align*}
\text{N}_D & = 1.5735 \\
\text{yield} & = 6.7 \%
\end{align*}
\]
FIGURE 2
Apparatus for chloromethylation of p-dichlorobenzene. The dropping funnel is removed after addition of the chlorosulfonic acid; a cap or plug replaces it.
CONCLUSIONS

A. One significant conclusion which can be drawn from the proposed procedure for synthesis of 2-aryl-tetrahydro-3-methyl-4-β-1,3-thiazine-4-one-1,1-dioxides is that steric factors do not seriously affect the process. The two benzaldehydes used (o-fluoro and 2,6-dichloro) offered some possibilities for steric hindrance, especially the latter. However, in both cases, the yield following ring formation was above 80% as noted from measurements of water production. It seems evident that any steric factors could become significant during ring closure. It should be noted that the o-fluorobenzaldehyde yielded over 80% following ring closure whereas 2,6-dichlorobenzaldehyde yielded less than 60%.

B. The mechanism for the chloromethylation of benzene and substituted benzene compounds is not fully known. Earlier in this paper, Bordwell's proposed mechanism was shown. This mechanism probably is the basis of the Slonc method for chloromethylation of benzene. Stephens, et al. (4) synthesized and isolated 5-dichloromethyl ether; they then reacted this ether with benzene and chlorobenzene to form benzyl chloride and p-chlorobenzylchloride respectively.
The formation of the ether, and the formation of the chloro-
methyl radical may occur in the following manner:

\[
2 \text{H}_2\text{C}=\text{O} + \text{H}^+ \rightarrow \text{HO-CH}_2\text{-O-CH}_2\text{-OH}
\]

\[
\text{HO-CH}_2\text{-O-CH}_2\text{-OH} + 2 \text{HNO}_3 - \text{C}_1 \rightarrow \text{CICH}_2\text{-O-CH}_2\text{Cl} + \text{H}_2\text{SO}_4^+ + \text{H}_2\text{O}
\]

\[
\text{CICH}_2\text{-O-CH}_2\text{Cl} + 2 \text{H}^+ \rightarrow \text{CH}_2\text{Cl} + \text{HO-CH}_2\text{-C}_1
\]

\[
\text{HO-CH}_2\text{-C}_1 + \text{H}^+ \xrightarrow{\text{H}_2\text{SO}_4^-} \text{CH}_2\text{Cl} + \text{H}_2\text{O} + \text{H}_2\text{SO}_4^-
\]

It may not even be necessary for the dihydroxymethyl ether to be
formed, but rather, the following mechanism may occur:

\[
\text{H}_2\text{C}=\text{O} + \text{H}^+ \rightarrow \text{CH}_2\text{OH}
\]

\[
\text{CH}_2\text{OH} + \text{H}_2\text{C}=\text{O} \rightarrow \text{HO-CH}_2\text{-O-CH}_2^+
\]

\[
\text{HO-CH}_2\text{-O-CH}_2^+ + \text{Cl}^- \rightarrow \text{HO-CH}_2\text{-O-CH}_2\text{Cl}
\]

From this product, the other methyl chloride radical is formed
as suggested above, and electrophilic attachment occurs:

\[
\begin{array}{c}
\text{X} \\
\text{Y} \\
\text{Cl}\end{array} + \text{CH}_2\text{Cl} + \text{CH}\xrightarrow{+} \begin{array}{c}
\text{X} \\
\text{Y} \\
\text{Cl}\end{array}
\]

A significant problem encountered during the attempts to
synthesize 2,3 dichlorobenzyl chloride

was the formation of the di-substitution product

by carefully limiting the reactants to a very slight excess (0.05 moles) of formaldehyde, the di-substitution product became such less significant - see Experiment 7. Careful control of temperature was necessary also. However, in the successful synthesis, Experiment 10, a major side reaction involved the formation of the di-phenylmethane derivative:

Stephens, et al. (4) suggested that the di-phenylmethane product may very likely be synthesized at higher temperatures (above 35° - 40° C) and in the presence of large concentration of acid. Stephens reports the presence of 4,4'-dichloro diphenylmethane in the chloromethylation of chlorobenzene. He also noted that longer reaction times tended to form diphenylmethane derivatives.

It should be noted that in the earlier experiments by the author, the large excess of trioxane (formaldehyde), chlorosulfonic acid, and sulfuric acid probably favored the di-
substitution product whereas the length of the reaction time and higher temperatures permitted accounted for the formation of the diphenyl methane derivative.

Virtually no di-substitution product was found in the crude reaction product of Experiment 10. However, some di-phenylmethane derivative was found, and a thick residue remained after distillation of the mono-substitution product. Limiting the time and temperature variables (step 5) more critically may well be the solution for obtaining higher yields of the desired mono-substitution product. After 3 hours in the ice bath, a gradual temperature increase to 22° - 24° C may prove advantageous.

Although it seems unlikely that the dichloromethyl ether is not formed, a mechanism accounting for the direct formation of the chloromethyl radical is suggested below.

\[ \text{H}_2\text{C}=0 + \text{HO-SO}_2\text{-Cl} \rightarrow \text{CH}_2\text{OH} + \text{SO}_2\text{-Cl} \]

\[ \text{CH}_2\text{-OH} + \text{SO}_2\text{-Cl} \rightarrow \text{Cl-CH}_2\text{-OH} + \text{SO}_3 \]

\[ \text{SO}_3 + \text{Cl-CH}_2\text{-OH} \rightarrow \text{Cl-CH}_2\text{Cl} + \text{HSO}_3 \]

Since neither of the chloromethylation products (mono- or di-substituted) appears in the literature, identification of reaction products was dependent largely on the use of N.M.R. spectrographs. Drawn below are the three major compounds obtained in
the experimentation. The "different" hydrogens are designated in red, and denoted by letter.

In the chart below, the peak of that hydrogen is given.

\[
\begin{array}{ccc}
\text{a)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array} \\
\text{b)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array} \\
\text{c)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array} \\
\text{d)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array} \\
\text{e)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array} \\
\text{f)} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{H}_2 \text{C} \\
\text{Cl}
\end{array} & \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{C}_2 \text{H}_2 \text{C} \\
\text{Cl}
\end{array}
\end{array}
\]

\[
\begin{array}{c}
\text{a)} 4.149 \\
\text{b)} 7.34 \\
\text{c)} 7.10 \\
\text{d)} 4.58 \\
\text{e)} 7.45 \\
\text{f)} 4.02
\end{array}
\]
SUMMARY

A method for synthesizing 2-aryl-tetrahydro-3-methyl-4-N-1, 3-thiazine-4-one-1, 1-dioxides which was not sterically affected by the halogen substituents of the phenyl radical was attempted, and it proved successful.

The chloromethylation of p-dichlorobenzene was attempted by conventional means and proved unsuccessful. An alternate method was tried using chlorosulfonic acid, trichloro, and sulfuric acid. The disubstitution product was produced. Limiting the ratio of reactants, and restricting the reaction conditions resulted in the desired end product, 2,5-dichlorobenzoylchloride.
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