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A MECHANISTIC STUDY OF THE REACTIONS OF 4-NITROBENZYL HALIDES WITH SODIUM HYDROXIDE IN AQUEOUS ETHANOL

BY

HOWARD LEVINE

A THESIS

Submitted to the Faculty of the Graduate School of the Creighton University in Partial Fulfillment of the Requirements for the Degree of Master of Arts in the Department of Chemistry

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The author wishes to express his appreciation to Dr. K.H. Takemura for his never ending assistance in the preparation of this thesis and consultation during the course of this investigation. The author also wishes to express his appreciation to Dr. F. Klein for numerous consultations during this period. The author wishes to acknowledge the assistance of Mr. Charles Davenport in obtaining the necessary equipment and supplies and Mr. Stanley Gross who also aided in obtaining special equipment for this research.
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The reaction of 4-nitrobenzyl chloride and sodium hydroxide in ethanol, has been observed to give 4,4'-dinitrostilbene, while 4-nitrobenzyl bromide under similar conditions, gave 4-nitrobenzyl ethyl ether. The purpose of this study was to determine mechanisms for these two reactions, particularly for that leading to the formation of ether.
It has been shown that the product of the reaction of 4-nitrobenzyl chloride with alkali is dependent upon the solvent employed. The reaction gives 4-nitrobenzyl alcohol in water. However in aqueous alcohol, acetone, or dioxane, 4,4'-dinitrostilbene is the principal product.

The formation of 4-nitrobenzyl alcohol from the chloride is generally accepted as proceeding by an SN2 reaction. Several mechanisms, however, have been proposed for the formation of dinitrostilbene I from 4-nitrobenzyl derivative II (Scheme I).

Bergman and Hervey proposed that 4,4'-dinitrostilbene (I) is formed by the dimerization of 4-nitrophenylmethylene (III) (Path A), the latter being produced by elimination of HCl from 4-nitrobenzyl chloride. The intermediacy of a carbene was supported by Hanna. He suggested that the formation of III proceeded in two steps; abstraction of alpha hydrogen by base to give anion IVa, followed by elimination of chloride ion. Hanna's kinetic studies showed a second order rate law, first order in hydroxide and first order in IIa. The second order kinetics is consistent with slow formation of III, which then rapidly dimerized to product.

In the same year, Swain and Thornton proposed another mechanism, involving the carbene intermediate,
SCHEME I

IIa (where x is Cl)
IIb (where x is $S(CH)_{32}$)

$\text{OH}$

IVa (where x is Cl)
IVb (where x is $S(CH)_{32}$)

PATH C

-dX-

PATH A

PATH B

V (where x is Cl)
to account for the formation of I in the reaction of 4-nitrobenzyldimethylsulfonium tosylate (IIb) with hydroxide ion (Path B). His kinetic studies of this reaction also showed a second order rate, first order in hydroxide and in sulfonium ion (IIb). Swain ruled out the dimerization of carbene on the basis of his studies of the sulfur isotope effect.

In, 1929, Hahn proposed that I was formed via the reaction of carbanion IVa with IIa to give intermediate V. The intermediate then went on to form I by loss of HCl (Path C). This mechanism was supported by Hauser who isolated an intermediate analogous to V, in the conversion of benzyl chloride to stilbene with sodium amide in liquid ammonia.

Olivier showed that in an aqueous acetone solvent, with substituted benzyl chlorides in the presence of hydroxide ion, strong electron withdrawing groups have little effect on the rate of the reaction. Hanna observed that 4-nitrobenzyl chloride reacts sixty times faster than benzyl chloride in acetone, which would not be expected if both went via an SN2 mechanism. Hanna also observed in his deuterium exchange studies that the first step in the reaction of 4-nitrobenzyl chloride with base; is a rapid and reversible formation of carbanion
IVa. Hanna therefore concluded that Hahn's mechanism would require the reaction to exhibit third order kinetics, second order in IIIa and first order in hydroxide. This kinetic order is greater than what was observed in Hanna's kinetic studies.

Hine and Shipp both agree that Hanna's kinetic studies show that carbene III is an intermediate in the reaction, but they also point out that no evidence is offered concerning the mechanism by which the methylene is transformed to stilbene I. Pathways A and B are accepted as the two main possibilities for the explanation of this transformation.

In 1970, Ursick obtained 4-nitrobenzyl ethyl ether from the reaction of 4-nitrobenzyl bromide with hydroxide in absolute ethanol. Only trace amounts of stilbene were observed. Several pathways are possible for the formation of ether VI (Scheme II). It was suggested that 4-nitrobenzyl ethyl ether (VI) was formed via a carbene intermediate. Carbenes in alcoholic solvents are known to form ethers by accepting a proton (from the solvent) to give a carbonium ion which then reacts with a molecule of solvent to form the ether (Path A1). Methylenes in alcoholic solvents are also known to form ethers by an insertion mechanism (Path A2).
SCHEME II

PATH A

PATH B (SN 1)

PATH C (SN 2)

3

2

ON-CH Br

2

ON-CH Br

2

ON-CH±

2

(CH₃CH₂OH)

insertion

1

carbon

onium

2

ON-CH OCH CH

2

ON-CH OCH CH

2
Two other pathways (B and C) can account for the formation of ether VI. They both involve nucleophilic substitution reactions; one a unimolecular and the other a bimolecular type of mechanism. Similar mechanisms have been suggested in the literature for the production of benzyl methyl ether from benzyl chloride in methanol with alkali. It was suggested that the mechanism (for the formation of benzyl methyl ether) involved ionization of the benzyl chloride, followed by reaction with methanol and deprotonation by hydroxide ion, or displacement of chloride by methoxide.

Many studies have been undertaken on the effect of solvent, ring substituent, and nucleophile on nucleophilic displacement reactions of substituted benzyl halides. Ko observed in his kinetic studies of substituted benzyl bromides that an ethanol solvent favored the SN2 reaction, whereas water favored the SN1 reaction. He also concluded that the more electron withdrawing the ring substituent (especially in the para position) an SN2 transition state would be more likely. Hyne came to the same conclusion based upon his study of the activation energies of solvolysis reactions of substituted benzyl chlorides. Swain came to the conclusion that the stronger the nucleophile employed, the more an SN2 intermediate would be favored. These studies
suggest that the SN2 reaction (Path C) would be favored with ethanol as the solvent.

A search of the literature revealed that 4-nitrobenzyl ethers (ethyl, phenyl, methyl), have been prepared from 4-nitrobenzyl chloride and alkali in alcohol. No explanation for the formation of ether in these reactions was found. No reference was found to the reaction of 4-nitrobenzyl bromide with base to yield ether VI, other than the work of Ursick.
RESULTS

AND

DISCUSSION
Alpha proton elimination is generally accepted as the first stage in the formation of 4,4'-dinitrostilbene from 4-nitrobenzyl derivatives. The results of reactions of benzyl halides with equimolar amounts of sodium hydroxide in 95% ethyl alcohol, are summarized in Table I. 4-Nitrobenzyl chloride was found to produce 4,4'-dinitrostilbene, in 83% yield. Under the same reaction conditions 4-nitrobenzyl bromide gave only a 6% yield of stilbene I. Since chloride is more electronegative than bromide, the alpha hydrogen in 4-nitrobenzyl chloride would be expected to be more acidic, and consequently more easily abstracted by base. Greater yields of stilbene are therefore observed with the chloride.

The importance of the acidity of the alpha-hydrogen for stilbene formation is further supported by the reaction of benzyl chloride with alcoholic sodium hydroxide. The reaction gave quantitative yields of benzyl ethyl ether. No trace of stilbene was observed. Apparently in the absence of the electron withdrawing nitro group, the benzyllic hydrogen is not sufficiently acidic for reaction with sodium hydroxide in 95% ethyl alcohol.

A search of the literature was undertaken to find reactions in which stilbene is formed from a benzyl bromide with more than one electron withdrawing substituent on the ring. The added withdrawing groups should en-
**TABLE I**

Products of the Reaction of Benzyl Halides \(^a\) with Sodium Hydroxide in 95% Ethanol

<table>
<thead>
<tr>
<th>Halide</th>
<th>4,4'-Dinitrostilbene (% Yield)</th>
<th>Ether</th>
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<tbody>
<tr>
<td>4-nitrobenzyl chloride</td>
<td>88 %</td>
<td>----</td>
</tr>
<tr>
<td>benzyl chloride</td>
<td>----</td>
<td>Quantitative</td>
</tr>
<tr>
<td>4-nitrobenzyl bromide</td>
<td>6 %</td>
<td>88 %</td>
</tr>
<tr>
<td>benzyl bromide</td>
<td>----</td>
<td>Quantitative</td>
</tr>
</tbody>
</table>

**Notes:**
- \(^a\) Equimolar amounts of halide and 0.50 M NaOH in 95% ethyl alcohol. All reactions were run in duplicate.
- \(^b\) Assuming compound indicated is the only product.
- \(^c\) Based upon product isolated and glc analysis.
hance the acidity of the alpha protons which in turn would be expected to favor stilbene production. Reich prepared 2,6,2',6'-tetranitrostilbene in 40% yield from 2,6-dinitrobenzyl bromide and alcoholic potassium hydroxide. 2,4,6,2',4',6'-Hexanitrostilbene was also obtained from 2,4,6-trinitrobenzyl bromide. It seems from these results, that the added nitro groups, compensated for some of the reduced acidity of the alpha protons due to the presence of bromide as compared to the corresponding chloride.

The effect of the strength of the base on stilbene formation, in ethyl alcohol, was investigated. The results of studies employing bases weaker than hydroxide ion are given in Table II. These results are essentially the same as those for the reaction of 4-nitrobenzyl chloride with 95% ethyl alcohol, in the absence of base. Stilbene formation was not observed, except in the case of sodium carbonate which is the strongest of this group of bases. These observations are consonant with the mechanisms proposed for stilbene formation in that the abstraction of alpha hydrogen is required. Bases appreciably weaker than hydroxide ion are ineffective.

It is interesting to note that when n-butyllithium, a base stronger than sodium hydroxide (in tetrahydro-
Reactions of 4-Nitrobenzyl Chloride with Base in 95% Ethanol

<table>
<thead>
<tr>
<th>Base</th>
<th>% Yield</th>
<th>Recovered Starting Material</th>
<th>Product: 4,4'-Dinitrostilbene</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyridine</td>
<td>87 %</td>
<td></td>
<td>----</td>
</tr>
<tr>
<td>collidine</td>
<td>90 %</td>
<td></td>
<td>----</td>
</tr>
<tr>
<td>NaHCO$_3$</td>
<td>92 %</td>
<td></td>
<td>----</td>
</tr>
<tr>
<td>Na$_2$CO</td>
<td>50 %</td>
<td>7.5 %</td>
<td></td>
</tr>
</tbody>
</table>

a. Equimolar amounts of halide and 0.50M Base in 95% ethyl alcohol. All reactions were run in duplicate.
b. Assuming compound indicated is the only product.
c. Listed in order of increasing $K_b$.
d. Insoluble in reaction solvent.
furan) was employed, excellent yields of stilbene were produced from benzyl chloride.

A reaction of equimolar amounts of 4-nitrobenzyl chloride and 4-nitrobenzyl bromide with base in 95% ethanol was undertaken to see if the two halides would behave independently of each other. A 47% yield of I was to be expected if 4-nitrobenzyl chloride alone, were converted to stilbene. The reaction gave a 76% yield of dinitrostilbene I. The increased yield suggests that the formation of stilbene proceeded at least in part by Path C - Schemel, where the bromide served as a substrate for nucleophilic attack by carbanion IVa. This seems plausible because bromide ion is a better leaving group than chloride ion and is also unable to undergo appreciable carbanion formation.

Shipp has proposed a mechanism similar to Path C (Scheme I) for the conversion of 2,4,6-trinitrobenzyl bromide and chloride to the 2,4,6,2',4',6'-hexanitrostilbene. The author, however, accepts the intermediacy of the carbene in the formation of 4,4'-dinitrostilbene from 4-nitrobenzyl chloride (Scheme I: Paths A or B). No explanation is offered for the different pathways for these two reactions (with mono and trinitrobenzyl chloride). Possibly the differences may be due to the electron deficient nature of a carbene. The added
electron withdrawing groups would probably destabilize a carbene and therefore reduce the possibility of its formation.

Traces of 4-nitrostilbene were observed in the reaction of equimolar amounts of benzyl chloride and 4-nitrobenzyl chloride with sodium hydroxide in alcohol. The 4-nitrostilbene is believed to be formed also by the "carbanion-substrate" type of mechanism (Scheme I, Path C). It may be noted that for the most part, the nitrated and unnitrated benzyl halides reacted independently of each other. This seems to suggest that the "carbanion-substrate" mechanism is also not dominant in the reaction of 4-nitrobenzyl chloride with sodium hydroxide in ethanol. This is based on Olivier's work that showed with substituted benzyl chlorides in the presence of hydroxide ion; strong electron withdrawing groups have little effect on the rate of reaction. This also assumes that the difference in solvents does not appreciably effect this system.

The present investigation does not distinguish between the two other suggested mechanisms for stilbene formation (Scheme I: Paths A and B).

In contrast to the behavior of the chloride, 4-nitrobenzyl bromide gave 4-nitrobenzyl ethyl ether in
88% yield with sodium hydroxide in ethyl alcohol. In the absence of base only trace amounts of the ethyl ether are produced. Three mechanisms can be envisioned for the formation of ether (Scheme II), in the presence of base. Path A (via carbene intermediate) is improbable since the absence of stilbene observed in the presence of sodium hydroxide, suggests that the 4-nitrobenzyl bromide does not readily yield the carbanion. Path B, the SN1 reaction, is also unlikely. It requires the formation of a carbonium ion which would be destabilized by the strong electron withdrawing para-nitro group. According to this mechanism the function of the base appears to be that of removal of a proton from the oxonium ion. The reaction was repeated in the presence of other bases, all of which were expected to be effective in the neutralization of the oxonium ion (Table III). Only trace amounts of ether VI were observed. It appears then, that the function of the base in the reaction is not that suggested by Path B.

According to Path C, the function of the base is to transform ethyl alcohol to ethoxide ion. Ether formation is then the result of an SN2 reaction with ethoxide ion as the nucleophile. The reaction of 4-nitrobenzyl bromide with sodium ethoxide in ethanol gave an 83%
### Table III

Reactions of 4-Nitrobenzyl Bromide with Base

<table>
<thead>
<tr>
<th>Base</th>
<th>Recovered Starting Material</th>
<th>Product: 4-nitrobenzyl ethyl ether</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyridine</td>
<td>trace</td>
<td>trace</td>
</tr>
<tr>
<td>collidine</td>
<td>68%</td>
<td>trace</td>
</tr>
<tr>
<td>NaHCO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>85%</td>
<td>trace</td>
</tr>
<tr>
<td>Na CO&lt;sub&gt;2&lt;/sub&gt; CO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>67%</td>
<td>11%</td>
</tr>
</tbody>
</table>

a. Equimolar amounts of halide and 0.5% Base in 95% ethyl alcohol. All reactions were run in duplicate.

b. Assuming compound indicated is the only product.

c. Listed in order of increasing $K_b$. 

b. Assuming compound indicated is the only product.
yield of the ether (VI). The small decrease in ether yield (as compared to the reaction with hydroxide ion) was probably due to the increased production of carbanion in the presence of the stronger base. A slightly higher yield of stilbene I was observed which would be expected if this were the case. Overall, the reaction does not seem to be altered greatly in the presence of ethoxide ion.

It is surprising that hydroxide ion does not act as a nucleophile to give 4-nitrobenzyl alcohol, rather than convert ethanol to ethoxide ion. However, only trace amounts of 4-nitrobenzyl alcohol, from the reaction of 4-nitrobenzyl bromide with sodium hydroxide in ethanol are observed. Calculations based on the Ka's of water and ethanol, and on the concentrations of hydroxide ion and ethanol show that 0.047 moles of hydroxide ions and 0.003 moles of ethoxide ions, are present at the start of this reaction. Although the hydroxide ion concentration is sixteen times greater than that of ethoxide ion, because of the greater nucleophilicity of ethoxide, the reaction proceeds to give ether.

It seems that there are two main reasons for the different reactions observed with 4-nitrobenzyl bromide and 4-nitrobenzyl chloride. The first, is the less acidic alpha hydrogens of the bromide, which prevents appreciable
carbanion formation, and also its better leaving group, which favors nucleophilic substitution to form ether VI instead of stilbene I.
EXPERIMENTAL
All melting points were determined using a Fisher-Johns melting point apparatus, and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 700 Spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained from a Varian T-60 Spectrophotometer.

Gas liquid chromatography (glc) analyses were performed on an Aerograph A-90 P Gas Chromatograph, with a 6 ft. by 0.25 in. column packed with 20% SE 30 on 60/80 acid washed Chromosorb W. At a column temperature of 260°C, retention times observed: 4-nitrobenzyl alcohol (1.60 min.), 4-nitrobenzyl ethyl ether (1.35 min.), benzyl ethyl ether (0.77 min.), ethanol (0.55 min.), and H2O (0.60 min.); at 200°C, 4-nitrobenzyl ethyl ether (4.10 min.) and ethanol (0.60 min.).

Thin layer chromatography (tlc) analyses were carried out on sheets of Eastman Chromagram 6060 silica gel with fluorescent indicator. The developing solvent was a mixture of benzene: petroleum ether: glacial acetic acid (24:8:1 v/v). The following Rf values were observed: 4-nitrobenzyl alcohol (0.26), 4-nitrobenzyl bromide (0.86-0.87), 4-nitrobenzyl chloride (0.89), 4,4'-dinitrostilbene (0.52), 4-nitrobenzyl ethyl ether (0.70), 4,4'-dinitrobenzyl (0.56), benzyl bromide (0.92), benzyl chloride (0.86-0.90), stilbene (0.96), benzyl ethyl ether (0.86-0.87),
benzyl alcohol (0.58-0.60).

Materials:

4-Nitrobenzyl chloride, mp 70-71 ° (Eastman) and 4-nitrobenzyl bromide, mp 97-99 ° (Eastman and K&K) were recrystallized from 95% ethanol. The recrystallized compounds melted at 70.5-71 ° (lit. 71 °) and 98.5-100 ° (lit. 99-100 °), respectively. A.G.S. grade sodium hydroxide (Fisher) and U.S.P. grade 95% ethyl alcohol were used. Unless specified all other reagents were employed without purification.

I- Reactions with Sodium Hydroxide in 95% Ethanol

A. 4-Nitrobenzyl Chloride

To 100 ml of a 0.50M NaOH in 95% ethanol was added 8.60 g (0.050 mol) of 4-nitrobenzyl chloride. The mixture was refluxed under a nitrogen atmosphere, with stirring, for three hours. The reaction mixture, neutral to litmus, was cooled to room temperature. The precipitated solids; dinitrostilbene I and inorganic salts, were filtered, washed with two 10 ml portions of cold ethanol (the filtrate was combined with the mother liquor), followed by two 10 ml portions of cold H O. The solid was then dried to give: 5.94 g (88%), mp 235-295 ° (lit. 232-290 °); ir (KBr) 1610, 1520, 1360, 1115, 980(CH=CH trans), and 870 cm⁻¹ (fig. 1). Concentration of the alcoholic filtrate gave a tarry residue.
Tlc revealed that this consisted of traces of 4,4'-
-dinitrostilbene, 4-nitrobenzyl alcohol, 4-nitrobenzyl
chloride and 4-nitrobenzyl ethyl ether.

B. 4-Nitrobenzyl Bromide

The reaction described in A was repeated with
10.80 g (0.050 mol) of 4-nitrobenzyl bromide. From the
insoluble solids, 0.32 g of I was isolated: mp 235-290 °C.
The alcoholic filtrate was concentrated to give 8.2 g of
an orange oil. Tlc showed that the oil was predominantly
the ethyl ether VI with a trace 4-nitrobenzyl alcohol
and unchanged bromide. Glc analysis indicated the presence
of approximately 8.0 g of ether (88%). The oil crystalized
on standing, mp 22-23 °C (lit. 24 °C); ir (neat) 1100, 1360,
and 1520 cm⁻¹ (fig. 2); nmr (neat) δ 3.2 (3H,t), 3.2 (2H,m),
4.2 (2H,s), and 7.18-7.8 (4H,m), (fig. 10).

C. Benzyl Chloride

The reaction described above was repeated with
6.35 g (0.050 mol) of benzyl chloride. The reaction mix-
ture, neutral to litmus, was cooled to room temperature.
The insoluble solid was removed by filtration (NaCl).
The filtrate was fractionally distilled to give 5.40 g
(80%) of benzyl ethyl ether, bp 186 °C (lit. 186 °C); ir
(neat) 1105 cm⁻¹ (fig. 3), nmr (neat) δ 1.1 (3H,t), 3.32
(2H,m), 4.23 (2H,s) and 7.0 (5H,m), (fig. 11). Glc
analysis of the alcohol distillate showed the presence of benzyl ethyl ether. Based upon the quantity of ether in this distillate and that isolated gave an almost quantitative yield of ether. Note: in all reactions in which benzyl chloride was used as a reagent, it was first redistilled; bp 179 (lit. 179.3).

D. Benzyl Bromide

The results of the reaction of the bromide with ethanolic sodium hydroxide were essentially the same as in the case of the chloride. Note: in all reactions in which benzyl bromide was used as a reagent, it was first redistilled; bp 200 (lit. 201).

II- Solvolysis Reactions

A. 4-Nitrobenzyl Chloride

A solution of 8.60 g (0.050 mol) of 4-nitrobenzyl chloride in 100 ml 95% ethanol was refluxed under nitrogen, with stirring, for three hours. The reaction mixture, acidic to litmus, was concentrated to approximately 30 ml. A solid separated which was filtered and identified as unchanged 4-nitrobenzyl chloride, 8.0 g (93% recovery): mp 70-71; ir(KBr) and nmr(acetone): (fig. 4 and 12).

B. 4-Nitrobenzyl Bromide

The reaction described in A was repeated with 4-
nitrobenzyl bromide. From the reaction mixture 84% of the bromide was recovered unchanged: mp 98;
ir(KBr) and nmr(acetone): (fig. 5 and 13).

C. Benzyl Chloride

The reaction was repeated as in A with 6.35 g (0.050 mol) of benzyl chloride. The reaction mixture, acidic to litmus was fractionally distilled to give unreacted benzyl chloride; 90% recovery, ir (neat), nmr(neat): (fig. 6 and 14).

D. Benzyl Bromide

The reaction was repeated as in C with 8.55 g (0.050 mol) of benzyl bromide. The reaction mixture, acidic to litmus, was fractionally distilled to yield a liquid (bp 200) which was identified as benzyl bromide; 5.99 g (70% recovery), ir(neat), nmr(neat): (fig. 7 and 15). Tlc analysis of the alcoholic distillate showed traces of ethyl benzyl ether and unchanged bromide.

III- Reactions with Sodium Ethoxide in Absolute Ethanol

A. 4-Nitrobenzyl Chloride

To a solution of 1.15 g (0.050 gatm) of sodium metal in 100 ml of absolute ethanol was added 3.60 g (0.050 mol) of 4-nitrobenzyl chloride. The reaction was treated in the same manner as that with sodium hydroxide in ethanol. The reaction mixture, neutral to litmus, gave 5.67 g (84%)
4,4'-dinitrostilbene, mp 235-295 and 0.91 g (10%) of 4-nitrobenzyl ethyl ether, mp 23-24.

B. 4-Nitrobenzyl Bromide

The reaction described in A was repeated with 10.80 g (0.050 mol) of 4-nitrobenzyl bromide. The neutral reaction mixture gave 0.88 g (13%) of 4,4'-dinitrostilbene, mp 235-297 and 7.46 g (32%) of 4-nitrobenzyl ethyl ether, mp 23.

C. Benzyl Chloride

This reaction was run as in A with benzyl chloride. The reaction mixture was filtered free of NaCl and fractionally distilled to give an 88% yield of benzyl ethyl ether, bp 186. Taking into consideration the amount of ether present in the distillate as determined by glc analysis; the overall yield of benzyl ethyl ether was almost quantitative.

D. Benzyl Bromide

The results of the reaction of the bromide with ethoxide ion in ethanol were essentially the same as in the case of the chloride. The reaction of benzyl bromide was repeated with a solution of 1.15 g (0.050 gatm) of sodium metal dissolved in 40 ml of absolute alcohol instead of 100 ml. Upon addition of the benzyl bromide to the ethoxide solution, immediate precipitation of a white solid (NaBr) was observed. The reaction mixture gave 6.26
g (92%) of benzyl ethyl ether, mp 23-24°, the rest was accounted for in the alcohol distillate.

IV- Reactions with Sodium Bicarbonate in 95% Ethanol

A. 4-Nitrobenzyl Chloride

To a mixture of 4.20 g (0.050 mol) of NaHCO₃ in 100 ml of 95% ethanol was added 8.60 g (0.050 mol) of 4-nitrobenzyl chloride. This heterogeneous reaction mixture was refluxed under nitrogen, with stirring, for three hours. The reaction mixture, filtered free of NaHCO₃, was worked up in the usual manner to give: 7.91 g (92% return) of 4-nitrobenzyl chloride, mp 70°. Tlc of the concentrated solvent showed only traces of unreacted chloride.

B. 4-Nitrobenzyl Bromide

The reaction was run as in A with 4-nitrobenzyl bromide. The reaction mixture, neutral to litmus, gave: 9.18 g (85% return) of 4-nitrobenzyl bromide, mp 98.5-99.5°. Tlc of the concentrated solvent showed traces of 4-nitrobenzyl ethyl ether.

V- Reactions with Pyridine in 95% Ethanol

A. 4-Nitrobenzyl Chloride

A solution of 3.96 g (0.050 mol) of redistilled pyridine (Eastman); bp 115° (lit. 115.5°), in 100 ml
of 95% ethanol, was added to 8.63 (0.050 mol) of 4-nitrobenzyl chloride. The reaction was run as in IVA to give 7.48 g (37% return) of 4-nitrobenzyl chloride, mp 70. TLC of the solvent showed only the presence of pyridine and unreacted chloride.

B. 4-Nitrobenzyl Bromide

The reaction was run as in A with 4-nitrobenzyl bromide. The reaction mixture gave a salt, mp 220. The water soluble salt is believed to be 4-nitrobenzyl-pyridine bromide. Only traces of unreacted bromide were discovered through glc analysis of the concentrated solvent.

VI- Reactions with Collidine (2,4,6-trimethylpyridine in 95% Ethanol

A. 4-Nitrobenzyl Chloride

A solution of 2.53 (0.025 mol) of redistilled \textsuperscript{24\textdegree} collidine (Eastman); bp 170-173 (lit. 170-175), in 100 ml of 95% ethanol, was added to 4.30 g (0.025 mol) of 4-nitrobenzyl chloride. The reaction was run as in VA to give 3.87 g (90% recovery) of 4-nitrobenzyl chloride, mp 70-70.5. The filtrate volume was reduced to 1 ml, and tlc analysis showed only traces of 4-nitrobenzyl chloride and collidine.
B. 4-Nitrobenzyl Bromide

The reaction was run as in A with 4-nitrobenzyl bromide. The reaction mixture gave 3.67 g (68% return) of 4-nitrobenzyl bromide, mp 99-100°. Tlc of concentrated solvent showed traces of 4-nitrobenzyl ethyl ether, 4-nitrobenzyl bromide and collidine.

VII- Reactions with Sodium Carbonate in 95% Ethanol

A. 4-Nitrobenzyl Chloride

The reaction was run as in IVA with 0.05 mol of 4-nitrobenzyl chloride and 0.05 mol of Na CO₃. The heterogeneous reaction mixture, neutral to litmus, gave 2.2 g (50% return) of 4-nitrobenzyl chloride, mp 70-71° and .25 g (7.5%) of 4,4'-dinitrostilbene, mp 235-295. Tlc analysis of the solvent showed traces of I and unchanged chloride.

B. 4-Nitrobenzyl Bromide

The reaction was run as in A with 0.05 mol of 4-nitrobenzyl bromide. The reaction mixture gave 3.0 g (55% return) of 4-nitrobenzyl bromide, mp 98-100° and 1 g of an oil which contained a 50/50; v/v mixture of unreacted bromide and 4-nitrobenzyl ethyl ether (by tlc and glc analyses). This would increase the yield of recovered bromide to 67% and give approximately an 11% yield of VI.
VIII- Reactions of Mixtures of Benzyl Halides in 95% Ethanol

A. 4-Nitrobenzyl Chloride - 4-Nitrobenzyl Bromide

A mixture of 100 ml of a 0.5 M solution of NaOtl in ethanol was added to 4.30g (0.025 mol) of 4-nitrobenzyl chloride and 5.40 g (0.025 mol) of 4-nitrobenzyl bromide. The reaction was run as in IA. The reaction mixture gave 5.10 g (76%) of I, mp 229-239° and 1.64 g (18%) of 4-nitrobenzyl ethyl ether, mp 23°. Tlc of the ether showed traces of 4-nitrobenzyl alcohol.

B. Benzyl Chloride - 4-Nitrobenzyl Chloride

The reaction as described in A was run with 0.025 mol of benzyl chloride and 0.025 mol of 4-nitrobenzyl chloride. The reaction mixture gave 2.97 g of a solid with a mp of 220-270° which was chromatographed on a 18 by 1 in. column packed with 80/200 mesh neutral alumina (Brockman Activity 1). The eluant was benzene (2 liters), followed by 50:50 v/v; benzene:chlorform. The separation gave: 4-nitrostilbene (orange crystals), mp 155-169° (lit. 165°); ir (KBr)- fig. 8, cis4,4'-dinitrostilbene (yellow crystals), mp 230-245 (lit. 234°-235°); ir (KBr)- fig.9, and trans 4,4'-dinitrostilbene (light yellow crystals), mp 280-285 (lit. 293°). The pre-
dominant portion of the solid mixture was cis-trans 4,4'-dinitrostilbene (approx. 44% yield). This reaction mixture also gave 3.5 g (33%) of 4-nitrobenzyl ethyl ether. An additional 11% was accounted for in the alcohol distillate by glc analysis.

C. 4-Nitrobenzyl Bromide - Benzyl Bromide

The reaction was run as in A with benzyl bromide and 4-nitrobenzyl bromide. The reaction mixture gave a solid, mp 220-270°C similar to that in reaction B (also believed to contain traces of 4-nitrostilbene-orange crystals). A 2.5% yield was calculated for the 0.17 g on the assumption that cis-trans 4,4'-dinitrostilbene were the predominant species. The reaction mixture also gave an oil which contained almost an equal ratio of benzyl ethyl ether and 4-nitrobenzyl ethyl ether (by glc, tlc, and nmr analyses). Traces of 4-nitrobenzyl alcohol, dinitrobibenzyl and benzyl alcohol were also observed. An 38% yield of ethers was calculated on the basis of equimolar amounts of each ether present.
4-Nitrobenzyl chloride and sodium hydroxide in ethanol, gave an 88% yield of 4,4'-dinitrostilbene (I). The corresponding bromide, benzyl bromide and benzyl chloride all give substantial yields of benzyl ethers. The difference in mechanism with 4-nitrobenzyl chloride is attributed to its more acidic alpha hydrogens as compared to the other benzyl halides. Experimental results seem to favor a mechanism which involves a carbene intermediate (Paths A and B) rather than the one which involves a "carbanion-substrate" reaction (Path C), for the formation of stilbene I. However, this investigation does not give evidence to distinguish which path (A or B) is responsible for stilbene formation.

The formation of ether VI from 4-nitrobenzyl bromide (and the benzyl ethyl ether from the unnitrated benzyl halides) is attributed to an SN2 reaction involving ethoxide ion. It appears that the ethoxide ion is formed from the reaction of ethyl alcohol with hydroxide ion.
Figure 1- ir of: cis and trans 4,4'-dinitrostilbene
Figure 2 - IR of 4-nitrobenzyl ethyl ether
Figure 3- ir of: benzyl ethyl ether
Figure 4- ir of: 4-nitrobenzyl chloride
Figure 5- ir of: 4-nitrobenzyl bromide
Figure 6 - IR of: benzyl chloride
Figure 7 - IR of: benzyl bromide
Figure 8 - ir of: 4-nitrostilbene
Figure 9 - ir of: cis4,4'-dinitrostilbene
Figure 10- nmr of:
4-nitrobenzyl ethyl ether
Figure 11 - nmr of:
benzyl ethyl ether
Figure 12- nmr of:
4-nitrobenzyl chloride
Figure 13 - nmr of:
4-nitrobenzyl bromide
Figure 14 - NMR of benzyl chloride
Figure 15- nmr of:
benzyl bromide
BIBLIOGRAPHY


