THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

NITRATION OF THE BENZENESULFONATE OF 2-HYDROXYBIPHENYL

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

DOCTOR OF PHILOSOPHY

BY

D. PAUL DENNY

Norman, Oklahoma

1957

Downloaded from SHAREOK. Persistent Handle URL: https://hdl.handle.net/11244/226

NITRATION OF THE BENZENESULFONATE OF 2-HYDROXYBIPHENYL

APPROVED BY

J. C. Colbert

J. H. Wender

George W. Murphy

John A. Reeve

Samuel C. Weston

DISSERTATION COMMITTEE

ACKNOWLEDGMENTS

To Dr. J. C. Colbert, who suggested the problem, the author extends his sincere appreciation for kindly direction and encouragement as the research developed; the author is deeply grateful, also, to members of the Faculty of the Department of Chemistry for their patience and helpfulness over a period of several years.

TABLE OF CONTENTS

	Page
LIST OF TABLES	v
LIST OF ILLUSTRATIONS	vi
Chapter	
I. INTRODUCTION AND HISTORY	1
II. DISCUSSION	12
III. PARTIAL REDUCTION	52
IV. EXPERIMENTAL	59
V. SUMMARY	82
BIBLIOGRAPHY	85

LIST OF TABLES

Table		Page
1.	Results of Nitration of 2-Hydroxybiphenyl under Varying Conditions of Acid Strength, Solvent and Reaction Temperatures	17
2.	Weight Summations of Crystallizable Nitrated Ester and Oily Residues from Initial Reaction Mixtures	21
3.	Hydrolysis of the Nitrated Ester from the Benzenesulfonate of Ortho-Hydroxybiphenyl	22
4.	Hydrolysis of Nitrated Esters including Both Isolated Crude Crystals and Yellow-Brown Oil Residue from Five-Gram Samples of Ester	23
5.	Column Yields of Principal Products from Initial Nitration of the Benzenesulfonate of Ortho-Hydroxybiphenyl	35
6.	Color Test for Free Para Position in Substituted Phenols	47
7.	Yields of Assumed 3,4'- and 5,4'-Dinitro-2-Hydroxybiphenyls from Further Nitration of 4'-Nitro-2-Hydroxybiphenyl	48
8.	Yield of Dinitro Derivative from Further Nitration of 2'-Nitro-2-Hydroxybiphenyl with Fuming Nitric Acid in Nitromethane	51

LIST OF ILLUSTRATIONS

Plate		Page
1.	Band Patterns in the Column from Initial Nitration of Benzenesulfonate of 2-Hydroxybiphenyl.....	31
2.	Possible Derivatives from Further Nitration of 4'-Nitro and 2'-Nitro 2-Hydroxybiphenyl.....	40
3.	Band Patterns from the Further Nitration of 4'-Nitro-2-Hydroxybiphenyl.....	45
4.	Band Patterns from Further Nitration of 2-Nitro-2-Hydroxybiphenyl.....	49

NITRATION OF THE BENZENE SULFONATE OF 2-HYDROXYBIPHENYL

CHAPTER I

INTRODUCTION AND HISTORY

Variation in the directive influence of groups through modification of the nature of such groups has often been reported in the literature. Past work has shown that this variation is due to several factors of which those most often mentioned are: a change in electronic effects due to the modifying group; steric effects dependent on molecular weight and structure of the modifying group; the position in the molecule of the unmodified group; the initial orienting power of the unmodified group; the effect of substituents other than the modified substituent in the molecule; and the always present variable factors, the solvent, reagent strength and reaction temperature.

It is well known that the characteristic properties of the various functional groups are altered when attached to radicals possessing widely opposing electron displacement abilities. Thus, the carbonyl group ceases to behave typically when attached to the hydroxyl group, which, itself, becomes more acidic with such attachment. In general, the properties of a group, in the broadest sense, depend qualitatively on the electron-withdrawal or electron-releasing power of attached radicals. This inherent power depends on either an inductive effect characteristic

of functional groups or their capacity to form resonating structures with nearby groups. Resonating structures are possible when such groups as amino and hydroxyl are attached to unsaturated groups.

On the basis of inductive and resonance effects, it has been possible to arrange the functional groups in a series corresponding to their influence, as substituents, upon the reactivity of the benzene ring towards electrophilic substitution. Groups releasing electrons to the ring enhance reactivity (ease of substitution by electrophilic reagents), and groups withdrawing electrons deactivate the ring. The degree of activation or deactivation of the benzene ring by various substituents is firmly established. In addition, the influence upon further substitution in the ring or two or more substituents has been found to be roughly additive.

The influence upon further substitution in the benzene ring of some pairs of substituents has been treated extensively in the literature, but when one of the substituents is the phenyl group, the effects are not as well known. The nitration of biphenyl leads chiefly to 4-nitrobiphenyl, showing the phenyl radical to be ortho, para-directing. Further nitration yields 4-4'-dinitrobiphenyl with lesser amounts of the 2-4'- isomer. Thus, although the nitro group partially deactivates the ring to which it is attached, the substituted ring is still ortho, para-directing. The 4-halobiphenyls react similarly. The influence upon further substitution in the benzene ring of various combinations of two substituents when one is the phenyl group has been studied most extensively, when the other is the hydroxyl group. Such studies have been so complete that possibilities of further substitution, when the phenyl

group is fixed in the benzene ring, can be predicted regardless of the position assigned to the hydroxyl group. This has directed attention to substitution in the unsubstituted benzene ring. The problem has been one of deactivating the ring bearing the hydroxyl group so that an entering group is directed to the attached phenyl group. This has been accomplished by nullifying the activating effect of the hydroxyl group through application of the so-called "ester-block" method in which the hydroxyl group is converted into such groups as acetoxy, benzoyloxy, sulfonyloxy and alkyloxy.

Experimental work in the field dealing with electronic effects attendant upon such modification of the hydroxyl group has shown only the difficulties in establishment of rules governing such effects.

Hill and Hale (1), in 1905, reported that nitration of the methyl ether of 5-nitro-2-hydroxybiphenyl gave 5,4'-dinitro-2-methoxybiphenyl and the latter upon further nitration gave equal amounts of 3,5,4'-trinitro-2-methoxybiphenyl and the 2',4',5-trinitro derivative. Apparently, the blocking action of methoxy, aided by the presence of a deactivating nitro group at the 5-position, is sufficient to throw the first entering nitro group to the 4'-position but is insufficient, once the 4'-position is filled, to withstand the nucleophilic behavior at the 3-position when the second nitro group enters. Also, the electron density at the 2'- and 3-positions seems to be equivalent under these conditions.

In 1937, Hazlet (2) was able to show that bromination of the benzenesulfonate of 4-phenylphenol gave yields of 4'-bromo-4-benzenesulfonylbiphenyl. In 1939, Hazlet, Alliger and Tiede (3) conducted a study to determine if a blocking group, such as the benzoate, hindered substitu-

tion in the substituted ring as does the benzenesulfonate of 4-hydroxybiphenyl. They found substitution to be analogous. They then attempted to correlate known substitution rules with the accumulated experimental evidence. The theories of Hammick and Illingworth (4) were considered and rejected on the grounds that if the hydroxyl group directs ortho (since H is more positive than O) then the benzenesulfonate and phenylacetate groups should direct similarly as both S and C are more positive than O in the linkage.

Latimer and Porter's "residual charge" method for predicting directive influence (5) was examined. Calculations following on the basis of such rules showed that the sulfonyloxy group has the same directive influence as phenolic hydroxyl and that the acyl-linkage has even greater ortho-directive power than hydroxyl. (In biphenyl, the para position is, of course, occupied). Steric hindrance was suggested as the cause of substitution in the unsubstituted ring of biphenyl.

A survey of steric effects, dependent on molecular weight and structure of the modifying group in the substitution of the hydroxybiphenyls, must include mention of the work of Kenyon and Robinson (6). These two workers reported that bromination of 4-acetyl-aminobiphenyl yielded the 3- and the 4'-monobromo derivatives in a 50-30 per cent ratio. Bell and Kenyon (7), pursuing the problem, reported that 4-methoxybiphenyl on nitration gave 3-nitro-4-methoxybiphenyl in 80 per cent yield and 4'-nitro-4-methoxybiphenyl in 15 per cent yield. Nitration of the toluenesulfonate of 4-aminobiphenyl, however, gave mostly the 4'-mononitro derivative.

Raiford and Colbert (8) and Colbert and others (9) had shown that

both halogenation and nitration of 4-phenylphenol proceeded classically with the first substituent entering ortho to the hydroxyl group and the second substituent entering the other ortho position. These facts, coupled with Bell and Kenyon's work, previously mentioned, led Hazlet (2) into an investigation of the possibility that bromination, using a blocking-ester group, would parallel nitration in a general way. Hazlet repeated the work of Kenyon and Robinson, using glacial acetic acid as the solvent rather than chloroform, and got identical results. Thus, bromine enters the 4'-position because of a change in directive influence due to use of a block (the benzenesulfonate) and not because of solvent differences.

In 1939, Hazlet, Alliger and Tiede (3) demonstrated that benzoyloxy directs an entering substituent to the unsubstituted ring in biphenyl. In the same year, Hazlet and Kornberg (10) brominated 4-phenylphenylacetate. They reasoned that Latimer and Porter's calculations showed acetoxy to have the same residual charge as benzoyloxy, and at the same time should exert less steric hindrance. The experimental results were interesting since both ortho positions brominated. The substituted ring was brominated also when 2-phenylphenylacetate was employed.

More evidence for steric hindrance was presented when Hazlet, Hensley and Jass (11) brominated the chloracetic ester of 4-hydroxybiphenyl. In carbon tetrachloride and in 1,1,2-trichlorethane, the bromine entered the 4'-position. In acetic acid, the results were abnormal, only small amounts of the 2,6-dibromo derivative resulting. The latter finding introduced the possibility of solvent effects. In 1943, Hensley and Hazlet (12) found essentially the same effects using the larger bromo-

acetic acid molecule. Hazlet, Stauffer and Hensley (13) reported that the acetate of 4-hydroxybiphenyl gave no products when nitrated under the same conditions as 4-hydroxybiphenyl. When acid strength and reaction temperature were increased, the acetate yielded the 2,6-dinitro derivative. They concluded that the molecular weight of the modifying group appears to influence substitution.

Finally, to round out the ideas on steric hindrance, Holleman (14) states that steric hindrance might affect nitration but not bromination because the nitro group is functionally larger. Hazlet, Stauffer, Hensley and Van Orden (15) say the opposite is true, according to the work of Stanley and Adams (16) who concluded that bromine has a greater effect, sterically, than the nitro group. Finally, Watson (17) remarks that steric effect may be a factor but the answer will not be totally explained geometrically.

The position of hydroxyl in the hydroxybiphenyls before modification apparently plays only a minor role as long as the modifying group is constant in each case. Blakey and Scarborough (18) found that the acetamido group in any of the three positions in the phenolic ring directs an entering nitro group to the 4'-position if the reaction is carried out in a strong mineral acid but, when the acetamido group is at the 2-position and if the solvent is glacial acetic acid, the nitro group enters the substituted ring. These two workers set up rules for substitution in the biphenyl series. The biphenyl linkage was assumed to be such that each phenyl group exerted an ortho, para-directive influence which was less than that of the acetamido group but greater than for chlorine or bromine. Scarborough and Waters (19) reported, in 1927, that while the

free base (4-aminobiphenyl) nitrates in the 3,5-positions, the acetyl derivative directs entering nitro groups to the 3,4'-positions. With 2-acetamidobiphenyl in glacial acetic acid, with the nitrating agent including sulfuric acid, the only product obtained by these same workers (20) was the 4'-mononitro derivative.

There is little evidence regarding the nature of the reagent except that dealing with nitration and halogenation. Kenyon and Robinson (6), working with bromination, and Bell and Kenyon (7), with nitration, showed that substituents in both cases entered like positions. In 1942, Hazlet, Harris and Van Orden (21) nitrated 4-phenylphenylbenzoate and found the reaction strictly paralleled bromination in that the principal product was the 4,-(4-nitrophenyl)-phenylbenzoate.

The effect of substituents other than the modified group will be studied only through examination of the work of Hill and Hale (1). Deactivation of the substituted ring by the 5-nitro derivative of 2-methoxybiphenyl forced the entering nitro group to the unsubstituted ring and both rings were then equally susceptible to further nitration. Apparently, the position taken by an entering substituent in the case of either lightly or heavily substituted biphenyls depends on the degree of activation or deactivation of each phenyl group. This information is standard content in organic chemistry textbooks.

Some mention has been made of solvent effects. Hazlet, Hensley and Jass (11) noted some changes in substitution when acetic acid was the solvent rather than carbon tetrachloride. Solvent effects were checked by Hazlet and Hensley (22), in 1947, by first brominating 4-phenylphenylbenzoate in glacial acetic acid following the method of

Hazlet, Alliger and Tiede (3) and repeating the bromination in carbon tetrachloride. The 4'-nitro derivative was obtained in glacial acetic acid, while, in addition, a small yield of 2-bromo-4(4'-bromophenyl) phenylbenzoate resulted when carbon tetrachloride was the solvent. More recently, the importance of the solvent has been emphasized in nitration of blocked hydroxybiphenyls.

In 1951, Jones and Chapman (23), noting previous reports of exclusive production of 4'-mononitro derivatives of blocked hydroxybiphenyls, investigated the possibility that the 2'-isomer was being overlooked. An excess of fuming nitric acid was employed in the nitration of 4-phenylphenylbenzoate, as well as, the toluenesulfonate and the benzenesulfonate of 4-hydroxybiphenyl. In addition to small yields of the 4'-nitro derivative, a like amount of the 2'-isomer was reported. When the acetate was nitrated, the principal product was the 3,5-dinitro derivative, a result which bears out previous experimental findings showing the small inhibiting effects of the acetyl group. Campbell and Morrill (24) reviewed the work of Jones and Chapman with a view towards increasing production of the 2'-mononitro derivative. Fuming nitric acid in double the volume of acetic anhydride was added dropwise to a creamy suspension of the benzoate in acetaldehyde. The mole ratio of acid to sample was 3.5-1. Yields of the 4'-, 2'-, and 2-nitro derivatives were reported as 45, 45, and 10 per cent respectively. The conclusion drawn from the yields of the 2- and 2'-isomers was that the net reactivity at position 2- is about one fourth that at position 2'- (10-45 per cent) and gives a rough measure of the deactivating influence of benzoyloxy.

English (25) was the first, in the laboratories of the Department

of Chemistry at the University of Oklahoma, to use a blocking group in the nitration of the hydroxybiphenyls. Patterning his experiments after Hazlet (2), he expected a block at the 2-hydroxy position to direct the entering nitro group to the 5-position. Nitration of the benzenesulfonate of 2-hydroxybiphenyl yielded a mononitro product and from this a dibromomononitro derivative was obtained. The latter derivative was not the same as that obtained from the bromination of 5-nitro-2-hydroxybiphenyl. Moreau (26), a year later, showed this compound to be 4'-nitro-2-hydroxybiphenyl melting at 125-126 °C. This melting point is in agreement with that reported by Christiansen and Harris (27) for this compound.

More recently, in connection with nitration of the hydroxybiphenyls in the laboratories at the University of Oklahoma, the chief interest has been directed to 3-hydroxybiphenyl. One of the more difficult problems has been the separation of nitration products. A satisfactory solution to the problem was developed by Fox (29), in 1953, through use of the chromatographic column. The adsorbent used was the synthetic magnesium silicate "Magnesol," a product of the Chlorine Products Division of the Westvaco Food and Machinery Corporation. Differences in acidities and solubilities of the various derivatives cause them to be spread out on the column in colored bands which may be eluted or extruded and extracted depending on their column mobilities.

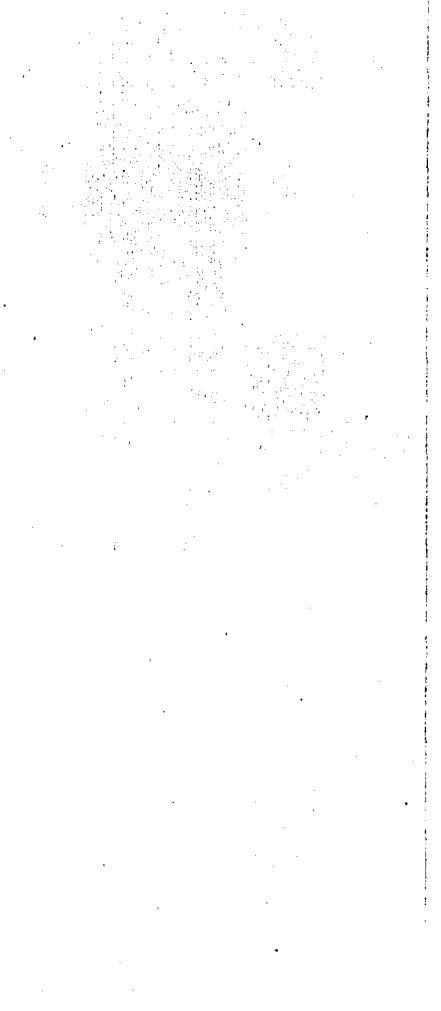
Hanan (29) determined solubilities, both in absolute alcohol and in water and acidities of nitration products in an effort to correlate such properties with order of appearance on the column. The acidities of the nitration products of 3-hydroxybiphenyl were determined by measuring dissociation constants in absolute alcohol.

Once the chromatographic technique was available, subsequent workers were able to show that there is some yield of all possible derivatives regardless of reaction conditions. Individual compounds were found to require unique conditions for maximum yields. Robinson (30), in 1953, prepared several esters of 3-hydroxybiphenyl. The 4'-mononitro derivative was obtained when the benzenesulfonate of 3-hydroxybiphenyl was nitrated and there was some success with the benzoate. Separation was obtained by chromatographic methods. Two derivatives, the 4'-nitro-3-hydroxybiphenyl and 4-nitro-3-hydroxybiphenyl, formed the two principal bands on the column; however, several other bands were discernible, a point which emphasizes the importance of chromatography as a suitable means of separation of such nitration products.

Robinson's report of the large number of bands on the column from a single nitration of a blocked hydroxybiphenyl opened the way for further investigation of the nature of such reactions. Further, there was need for a better understanding of proper nitration agents, solvents and reaction temperatures for maximum yields of mononitro derivatives of the hydroxybiphenyls when the nitro group enters the non-phenolic ring.

The current work was undertaken with the hope that employment of chromatographic separation methods would lead to a broader knowledge of nitration of the hydroxybiphenyls. The choice of starting material fell to 2-hydroxybiphenyl because its employment in the field had not been extensive. The goal for the problem was first, the establishment of optimum reaction conditions for the preparation, by nitration of ester-blocked o-phenylphenol, of 4'-nitro-2-hydroxybiphenyl and second, to investigate the partial reduction of a dinitro derivative of 2-hydroxybi-

phenyl where one nitro group is on the phenolic and one on the non-phenolic ring.



CHAPTER II

DISCUSSION

With o-hydroxybiphenyl selected as the starting material for the present investigation, the choice of an ester block turned upon a study of previous experimental results. Robinson (30) found the benzenesulfonate gave best results in directing entering nitro groups to the non-phenolic ring. Hazlet, Alliger and Tiede (3) claimed the use of the same block constituted a superior method, particularly so over the benzoate. All workers found the acetate hydrolyzed during the reaction, even at low temperatures and using low-strength nitrating agents. Blakey and Scarborough (18) found that even the acetamido group failed to direct entering nitro groups exclusively to the non-phenolic ring.

Nearly all of the work in the field had been confined to nitration of ester-blocked 3- and 4-hydroxybiphenyl. Further, correlation of results proved difficult because of the several solvents employed. In 1937, Hazlet (2) concluded that production of 4'-nitro derivatives from the hydroxybiphenyls depends largely on a steric effect (the larger the blocking group--the greater the yield of the 4'-derivative) and that the solvent effect was small. Such a conclusion is not borne out by the work of Campbell and Morrill (24) whose published results are of interest as regards the solvent. These workers, using acetaldehyde as the solvent,

reported heavy yields of 4'- and 2'-nitro derivatives of the benzoate of 4-hydroxybiphenyl.

The foregoing evidence is based on 3- and 4-hydroxybiphenyls and would not necessarily hold when 2-hydroxybiphenyl is the starting material. With the ortho positions sterically hindered in 4-hydroxybiphenyl by a blocking group and the para position occupied by phenyl, the only positions open are on the non-phenolic ring. The para position should be open for substitution when the hydroxyl group of 2-hydroxybiphenyl is blocked.

There is another consideration when the basic material is 2-hydroxybiphenyl. There may be steric hindrance at the ortho position in the non-phenolic ring when a large blocking group is employed. Fox (28) found no evidence of such hindrance. Bell and Kenyon (7) suggested that free rotation of the two nuclei is possible in lightly substituted biphenyls and when free rotation is inhibited, the two nuclei have a common axis but are not coplanar. Such conclusions are supported by the results of the current investigation inasmuch as yields of the 2'-nitro derivative of ester-blocked 2-hydroxybiphenyl are reported. Incidentally, the work of Jones and Chapman was missed in an early search of the literature and the 2'-nitro derivative, which was thought for some time to be the first such derivative from direct nitration of hydroxybiphenyls reported in the field, became only the first found, specifically, from 2-hydroxybiphenyl.

The decision was made to work with the benzenesulfonate ester, this decision being based on the foregoing discussion of the literature. It is interesting to examine the susceptibility to substitution of each

open position in the phenolic ring of 2-hydroxybiphenyl, keeping in mind the unknown degree of lessening of the normal directive influence of the hydroxyl group by the ester block. Position three is normally substituted in 2-hydroxybiphenyl as is the 5-position. With the ester block, not only is the ortho, para-directive influence of the hydroxyl group lessened at the 3- and 5-positions but there may be steric hindrance at the first of these two positions. The directive influence of the free phenyl ring and the blocked hydroxyl group counteract each other at all open positions. Thus, the position occupied by an entering nitro group in the phenolic ring should be determined by the relative directive strength of the two groups and in the event that the influence of the hydroxyl group is reduced to about that of the phenyl group, perhaps there would be no substitution in the phenolic ring. English (25) reported a mononitro derivative and Moreau showed this product to be the 4'-nitro derivative, when the benzenesulfonate of 2-hydroxybiphenyl was nitrated, i.e., the nitro group did not enter the phenolic ring at the 5-position.

There was little hesitation over the question of nitric acid strength requirements for the nitrating agent. Robinson (30) had tried concentrated nitric acid on the benzenesulfonate of 3-hydroxybiphenyl and recovered only starting material at both reflux and steam bath temperatures with acetic acid as the solvent. Hill and Hale (1) used concentrated nitric acid but only in extreme excess and at boiling nitric acid temperatures on alkyl ethers of 2-hydroxybiphenyls. Robinson's success with the ester-blocked 3-hydroxybiphenyl came with fuming nitric acid. Hazlet and Van Orden (21) used a mixture of concentrated and fuming nitric

acid. In their recent work, Jones and Chapman (23), as well as Campbell and Morrill (24), used fuming nitric acid in quite high mole ratios of acid to phenol esters. For example, Jones and Chapman used a 15-1 mole ratio, acid to the benzoate of 4-hydroxybiphenyl, 11-1 for the toluenesulfonate and 13-1 for the benzenesulfonate.

All nitrations in the current investigation were carried out using fuming nitric acid. Nitric acid as a nitrating agent should not be mentioned without discussion of the solvent employed. An excellent review of the classification of solvents as "slow," "intermediate" and "fast," when used with nitric acid in nitration reactions, is to be found in the report of Frow (31) on his work with such reactions. Benford and Ingold (32) list dioxane and glacial acetic acid as slow, nitromethane and acetaldehyde as intermediate and sulfuric acid as fast solvents in nitration reactions. From the same source comes the concept that the intermediate is the true nitrating agent and the solvent determines the intermediate. Remick (33) selects the acidity of the solvent as the controlling factor--thus, glacial acetic acid is "slow" because of low acidity; nitromethane is of "intermediate" ability because of mixed anhydride formation with nitric acid although of lower acidity than glacial acetic acid.

Until Campbell and Morrill used acetaldehyde as the solvent in the nitration of esters of 4-hydroxybiphenyl with such success, the principal solvent in use for the nitration of the esters of the hydroxybiphenyls was acetic acid. In the current work, glacial acetic acid and nitromethane were compared as solvents for the nitration of the benzenesulfonate of 2-hydroxybiphenyl with the exception of one slight diversion

into the use of concentrated nitric and sulfuric acids which will be presently discussed.

Colbert and his students isolated the benzenesulfonate of 4'-nitro-2-hydroxybiphenyl and found the melting point to be 136 °C prior to the employment of chromatographic separation techniques at the University of Oklahoma. An objective of the current work was the establishment of optimum conditions for production of this nitrated ester. To this end, a series of nitrations were carried out in nitromethane and glacial acetic acid under varying conditions of acid strength and reaction temperature. The results are given in Table 1.

The general procedure involved addition of the fuming nitric acid in an equal volume of reaction solvent, drop by drop, to the dissolved sample. This was followed by a period of reflux on the water bath. The reaction mix was then set aside for twenty hours before stopping the reaction with ice water. The gummy product was isolated by filtration and washed free from acid with water. The product then crystallized from hot alcohol and water in pale yellow prisms melting at 135-137 °C.

Limits, as shown in Table 1, were established for the production of the 4'-mononitro derivative in nitromethane. Below an acid-ester mole ratio of 3-1, the reaction products were unchanged starting materials, and even with a ratio of 6-1, oxidation of the ring system materially reduced the yield. The highest percentage yield resulted from use of a 4-1 ratio.

When glacial acetic acid was the solvent, there appeared to be a definite lower limit, a 6-1 acid-ester mole ratio, below which starting material was largely recovered. An upper limit was not set. Comparable

yields resulted from both 9-1 and 10-1 ratios and even at 12-1 the yield was not materially reduced.

TABLE 1

RESULTS OF NITRATION OF O-HYDROXYBIPHENYL UNDER VARYING CONDITIONS OF ACID STRENGTH, SOLVENT AND REACTION TEMPERATURES[a]

Acid-Ester Mole Ratio	Solvent	Total Solvent ml.	Reaction Temp.	Yield of Mononitro Ester--g.	Percentage Yield
3-1	Nm[b]	4	Room	0.1650	14.41
4-1	Nm	4	Room	0.4800	41.92
6-1	Nm	4	Room	0.3230	28.21
8-1	G. A. A.	4	Room	0.2298	20.07
6-1	G. A. A.	4	Room	0.2980	26.02
8-1	G. A. A.	4	Room	0.4110	35.89
8-1	G. A. A.	4	Reflux	Oxida.	
8-1	G. A. A.	6	Room	0.1304	11.40
9-1[c]	G. A. A.	4	90 °C[c]	0.6080	53.10
9-1[c]	G. A. A.	4	80 °C[c]	0.3000	26.20
9-1	G. A. A.	3	Room	0.5448	47.58
10-1	G. A. A.	4	Room	0.6050	52.05
10-1	G. A. A.	3	Room	0.5636	49.22
10-1	G. A. A.	2	Room	0.3806	33.24
10-1[d]*	G. A. A.	4	90 °C[d]	0.3115	27.25
12-1	G. A. A.	4	Room	0.5616	49.04

[a]All reaction mixtures refluxed on water bath for one and one-half hours after nitration unless otherwise indicated.

[b]Abbreviations: Nm, Nitromethane; G. A. A., Glacial Acetic Acid.

[c]Nitrated at temperature shown and held at this temperature for one and one-fourth hours without any reflux period.

[d]Nitrated at the temperature shown and then refluxed on water bath --Yield of dinitro ester--0.3650 g.--m. pt. 169-170 °C.

Glacial acetic acid was favored as a solvent for the reaction because of consistently higher yields and because the ester was not as sensitive to oxidation in this medium as in nitromethane. Both Matsuzak

(34) and Sonnenfeld (35) found that nitromethane as a solvent resulted in higher yields of mononitro derivatives of phenylphenols, but Fox (36) found glacial acetic acid better than nitromethane for mononitro production and the latter better for dinitro production. The current work involved a phenylphenol ester and the cited references do not necessarily apply. Indeed, as will be pointed out, there is evidence to show that acid strength and temperature rather than solvent are the major controlling factors, with the temperature playing the dominant role. To elaborate, a one gram sample was nitrated in glacial acetic acid using an 8-1 acid-ester mole ratio and the reaction mixture refluxed at the reflux temperature of acetic acid. No nitrated crystallizable products were obtained. Rather, the rings were heavily oxidized at the reflux temperature of acetic acid while at much higher nitric acid strengths on the water bath, the extent of oxidation was not a deterrent.

One unusual product was isolated from the reaction mixture. Its presence was easily noted since it was only moderately soluble in boiling alcohol and crystallized immediately upon cooling. This product melted at 169-170 °C and although it was never identified, analysis showed it contained two or more nitro groups. Moderate amounts of this compound were always present when nitromethane was the solvent and the acid-ester mole ratio exceeded 5-1. At such acid strengths, it never appeared when glacial acetic acid was the solvent. The compound appeared only at a 10-1 acid-ester mole ratio with the reaction temperature held at 90 °C during nitration. This evidence is not strictly in accordance with the observation of Fox (36) but there is a strong resemblance. This particular result is marked by an asterisk in the Table 1.

A point of interest in the results shown in Table 1 lies in the control of reaction temperature. Reactions carried out at either room temperature or at temperature ranges between 80 and 90 °C yield about the same results. The temperature at which the nitrating agent is added does not seem to be a factor as long as a period of reflux on the water bath follows the addition. The results of elevated temperatures have been noted.

Acid strength and temperature are not the only controlling factors in the reaction. The amount of solvent seems to play a part. When one gram of the benzenesulfonate was nitrated in a total of 6 ml. of glacial acetic acid (5 ml. to dissolve the sample and 1 ml. added to the fuming nitric acid as a nitration mix) using an 8-1 acid-ester mole ratio, the yield dropped. Higher yields resulted when the total acetic acid was 3-4 ml. per gram of sample. When the volume of acetic acid was 2 ml. per gram of sample and the fuming nitric acid was undiluted with solvent, the yield again was low with accompanying higher yields of non-crystallizable yellow oil. Such results suggest that the acid strength must be increased as the volume of solvent is increased. This observation was not confirmed but subsequent runs were with 3-4 ml. of acetic acid per gram with the fuming nitric acid always diluted with an equal volume of solvent.

Once the material melting at 136-137 °C is precipitated from alcohol, and is washed with cold alcohol and then with water, a change in color takes place. Some of the very light-yellow crystals take on a pinkish cast which progressively becomes darker until the color is wine-red. When picked from the mass, these colored crystals are found to melt at

84-85 °C. Repeated recrystallization from hot alcohol results in crystals of the 136-137 °C melting point material which do not show this property. Moreau (26) reported the 4'-mononitro-2-hydroxybiphenyl to be dimorphic with the labile form pale yellow needles which changed to yellow plates on standing. Such phenomena were observed in the present investigation. Whether this property carries over to the benzenesulfonate is unknown.

Finally, one may well ask what other products are formed in the reaction in addition to the two compounds discussed. No hint of other products was given by procedural results until column work was begun. However, when the alcoholic filtrate remaining after filtration of the above compounds was evaporated, a light-yellow, oily syrup was obtained. A sample of this material set aside for some months showed no crystallization. Selected samples from several nitrations were weighed. When such weights are added to the weights of crystallizable products there is a close approach in every case to theoretical yields on a mononitro basis. Once column work was begun, it became readily apparent that the yellow oil held several products. Weights of the 4'-mononitro-2-benzenesulfoxybiphenyl and corresponding weights of the accompanying yellow oil are given in Table 2.

The second step in the development of the nitrated phenols was hydrolysis of the ester. A search of the literature on hydrolysis procedures revealed only the use of alcoholic potassium hydroxide as the agent when the blocking group was the benzoate, toluenesulfonate, p-nitrotoluenesulfonate or benzenesulfonate. Scarborough and Waters (21) used a ten per cent alcoholic hydrochloric acid solution with 2-acetamidobiphenyl. Hazlet (2) suspended 1 gram of 4-(4-bromophenyl)-phenylbenzene-

sulfonate in 100 ml. of a ten per cent potassium hydroxide solution (alcohol:water::1:1), and refluxed the reaction mixture for 24 hours. Hydrolysis procedures in the laboratories at the University of Oklahoma were carried out with alcoholic potassium hydroxide. Initially, such an agent was employed in the current work.

The general procedure was the addition of one gram of potassium hydroxide in three ml. of water to the alcohol solution (15 ml. 95 per cent alcohol) of the nitrated products from nitration of a one gram sample of ester. After a reflux period of three hours, the hydrolysate was diluted to 200 ml. and acidified with hydrochloric acid. Exhaustive extraction with chloroform was followed by extraction with five per cent potassium hydroxide. From the alkaline solution, the phenols were recovered by acidification, and then extraction with benzene.

TABLE 2

WEIGHT SUMMATIONS OF CRYSTALLIZABLE NITRATED ESTER AND OILY RESIDUES FROM INITIAL REACTION MIXTURES[a]

Acid-Ester Mole Ratio	Solvent	Weight-Grams of Recovered Crystals	Weight-Grams of Oily Residues	Mononitro Yield[b]
4-1	Nm[c]	0.4801	0.5560	1.0361
6-1	Nm	0.3233	0.3573	0.6806
8-1	G. A. A.	0.4112	0.6282	1.0394
10-1	G. A. A.	0.6055	0.5404	1.1459
12-1	G. A. A.	0.5102	0.6203	1.1305

[a]Results based on one gram samples of the benzenesulfonate of 2-hydroxybiphenyl.

[b]Theoretical Mononitro Yield, 1.1431 g.

[c]Abbreviations: Nm, Nitromethane; G. A. A., Glacial Acetic Acid.

In order to obtain a measure of the effectiveness of this procedure, one gram of the 136-137 °C melting point material was hydrolyzed and the nitrated phenol from its evaporated benzene solution weighed. Results are given in Table 3.

TABLE 3

HYDROLYSIS OF THE NITRATED ESTER FROM THE BENZENESULFONATE OF ORTHO-HYDROXYBIPHENYL

Nitrated Ester	Nitrated Phenols from Hydrolysis (non-column)	Theoretical Yield on Mononitro Basis	Percentage Yield
grams	grams	grams	
1.0	0.3930	0.6056	65.50
1.731	0.6050	1.0483	57.63
1.0	0.4940	0.6056	81.57

In order to obtain cohesiveness, the results of hydrolysis in another instance will be discussed at this point. This involves premature mention of column separation of hydrolysis products, but results only will be given. The alcohol solution of nitrated products from two, 5-gram samples of ester was successively diluted with small portions of water and the resultant crystals and oils collected. No attempt was made to recrystallize nor were the yellow oils extracted with organic solvents. The crude crystalline products, total weight 4.7720 grams, and the yellow oil (unweighed) were separately hydrolyzed with alcoholic potassium hydroxide. The hydrolysates were treated in the above manner and the benzene solutions placed separately on two columns. The total weight of

nitrated products recovered from the columns was 2.1486 grams. This experiment is summarized in Table 4.

TABLE 4

HYDROLYSIS OF NITRATED ESTERS INCLUDING BOTH ISOLATED CRUDE CRYSTALS AND YELLOW-BROWN OIL RESIDUE FROM FIVE-GRAM SAMPLES OF ESTER

Nitrated Ester	Nitrated Phenols from Hydrolysis, Column Yields	Theoretical Yield on Mononitro Basis	Percentage Yield
grams	grams	grams	
4.7720 (crude crystals)	1.8516	2.890	64.07 (hydrolysis)
Yellow Oil (unweighed)	0.2880		
	2.1936		30.85 (over-all)

HYDROLYSIS OF CRUDE CRYSTALS OF NITRATED ESTER WITH POTASSIUM HYDROXIDE IN DIETHYLENE GLYCOL

Nitrated Ester	Nitrated Phenols from Hydrolysis, (non-column)	Theoretical Yield on Mononitro Basis	Percentage Yield
grams	grams	grams	
2.260	0.8920	1.3687	65.17
Yellow Oil (unweighed)	0.0000		

Hydrolysis, using concentrated sulfuric acid, was also tried but

with meager returns. One last method, hydrolysis with potassium hydroxide in diethylene glycol according to the method of Schriner and Fuson (37), was carried out. A sample of the 136-137 °C melting point material was hydrolyzed by this method. The percentage yield given in Table 4 is calculated from the nitrophenol obtained by conventional methods--not from the column. This latter method of hydrolysis apparently gives about the same results as alcoholic potassium hydroxide but is not as convenient. Moreover, some of the yellow oil hydrolyzed by the method gave no yield at all of crystallizable materials, although the characteristic red color of nitrated phenols developed in the alkaline solution. Trace amounts would, of course, show such color.

Satisfactory answers having been reached to the questions growing out of the search for optimum reaction conditions in the maximum production of 4'-mononitro-2-hydroxybiphenyl, the main effort was pointed towards separation of products by chromatographic methods. Separation of nitrated phenylphenols on a column is possible only when some property of the type compounds causes individual compounds to be spread apart. Generally, the convenient properties are solubilities and acidities. One or the other of these factors may control or each may affect the over-all movement of components down the column. The phenols are adsorbed by basic adsorbents such as alumina, silicates, carbonates, oxides and alkaline earth hydroxides. Both solubilities and acidities of the mono, di, and tri-nitrohydroxybiphenyls were compared earlier in the discussion. Extensive differences in either solubilities or acidities will bring separation of components. Relative changes in the order of appearance of components on the column with changes in solvent indicate solubility con-

trol, according to Fox (36), who reviews thoroughly the basic factors in chromatography.

Since nitration of 2-hydroxybiphenyl produces a variety of mono-, di-, and trinitro derivatives, an adsorbent was needed which would permit separation of at least the principal products. A strong adsorbent was necessary to slow the speed of mononitration products (low acidity and high solubility) down the column to the point where retention was of sufficient duration for bands to be separated. Contrarily, the adsorbent had to be of such weakness that the di- and tri-nitro derivatives (low solubility and high acidity) move far enough down the column for individual bands to form and facilitate separation by extrusion.

Magnesol (trade name) is an adsorbent that holds highly soluble-low-acidity type nitrophenols firmly enough to meet, somewhat, the demands of a strong adsorbent and at the same time permits band formation of low-solubility-high-acidity type nitrophenols. This is not to say that Magnesol was ideal for the job at hand. Actually, in the case of nitrated 2-hydroxybiphenyl, the mononitro derivatives moved with such speed that band separation of the first two principal bands required a tightly packed column of inconvenient length while the more highly nitrated ring systems moved so slowly that excessive amounts of eluent were necessary to get band separation. It was only after experiments had ceased that the thought of packing the lower section of the column tightly and the upper half loosely, was entertained. Again, it might be possible to use two mixes of slurry, one made up only of benzene and Magnesol and the other with an added inert diluent such as Cellosolve (trade name), which permits a higher degree of mobility on the column. Unfortunately,

neither was attempted.

It was quickly learned, concerning column capacity, that too much material on a column gave poor band separation but even leading edges of the first band down the column carries along with it appreciable fractions of all components on the column. This is doubtless a mass effect with neither solubilities nor acidities being given opportunity to control like molecules within proper band boundaries. As pointed out by Fox (36), only experience can select proper weight samples for a given column. Specific findings on column size and sample weight will be given presently.

It was found that from those bands with sufficient mobility to warrant elution, the products showed no traces of ion exchange, i.e., there was no decrease in intensity of color in their benzene solutions when dilute hydrochloric acid was added. The products strongly adsorbed always showed a small degree of ion exchange upon extrusion and addition of acid. For some time these colored bands were extracted with 95 per cent alcohol along with small quantities of five per cent hydrochloric acid. It was determined towards the end of this experimental work that extraction with acetone was considerably more efficient. Addition of acid was still necessary.

Band colors were strong enough in all cases so that no artificial light was necessary for detection. The more pronounced colors of the strongly adsorbed di- and tri-nitro derivatives were due, doubtless, to salt formation.

Benzene was the only eluent employed. Fox (36) had reported that added acetic acid would move stubborn bands down the column and suggested that this be done and then stopped, short of elution, with the final

movement being accomplished with wet benzene. This worker also reported that alcohol and acetone had little effect on adsorbed nitrated hydroxybiphenyls; that 95 per cent alcohol deactivated the column and that acetic acid, used to any extent, destroyed the column.

The columns used throughout the experiments were 4.5 x 125 cm. lengths of glass tubing. Each column was supported at the bottom by a 7.5 cm. glass funnel leading into a one-liter Erlenmyer flask. Fashioning of the end of the tube was important. When tapered, there is little tendency for the material to blow out when pressure is applied for packing, but extrusion is more difficult since the central portion of extruded material feeds out ahead of peripheral material. When two bands are close together this feature may prevent clean separation. If the end of the tube is left straight, rather than cupped and tapered, a heavy plug of cotton or glass wool must be inserted in both glass tube and funnel to prevent a blowout. However, a definite advantage lies in the ease of extrusion with the material emerging neatly and exactly as noted on the column.

Columns were packed with a benzene slurry of Magnesol of a consistency such that pouring down the side of the column proceeded smoothly. Generally, the mixing was one volume of Magnesol to 1.15 volumes of benzene. Pouring was halted intermittently while the tube was tapped at the bottom to free air bubbles. After some five minutes of setting to allow a firm base of Magnesol to settle at the bottom, air pressure at the top was slowly built up to ten pounds (gauge). The pressure was held until the clear benzene at the top was one-half cm. in depth. The adsorbent must be level at the top if bands are to move evenly down the column.

This is attainable only if the column is nearly vertical. Inspection and adjustment of the benzene level will insure a satisfactory level of the Magnesol. The sample is introduced slowly down the side of the column where it mixes with the one-half cm. of benzene. Five pounds of pressure is then applied until the liquid level stands again at one-half cm. Then benzene is added slowly down the side of the column until the liquid level is five cm. above the adsorbent and then five pounds of pressure applied. With proper care, the entire sample will now be in place on the adsorbent. The process is completed by carefully adding benzene until direct pouring will not disrupt the surface of the Magnesol at which time the remainder of the tube can be filled rapidly with eluent.

Recovery of the eluent was by distillation with rejection of the cloudy (wet) forerun and passage of the distillate through a 20 cm. column of calcium hydroxide. Nitration products were recovered from the still. Until actual elution of band material, the benzene was not distilled but poured directly into the calcium hydroxide column. A brown, to yellow, color slowly developed in this column with usage. Thus, either there was negligible loss of nitrated products in the benzene distillate or some material moved undetected down the column in eluent that was poured directly over the calcium hydroxide. No attempt was made to isolate such material.

Considerable experimental work was necessary before a satisfactory procedure was established for successful treatment of products coming from the column. As previously mentioned, the final benzene extract of hydrolyzed materials was reduced in volume to 50 ml. and introduced on the column. For some time, in an attempt to purify products from indi-

vidual bands, the residue from distillation of the eluent was washed from the still with a few ml. of benzene and the solvent evaporated. The material was generally impure, containing a slight amount of smelly, yellow oil which did not crystallize on standing. The first crystalline products were obtained from this impure mass by treatment with boiling water and filtration while hot. The yellow oil was completely insoluble in hot water and the nitrated phenylphenols but slightly soluble, necessitating a laborious repetition of the process. This method was later replaced by crystallization from organic solvents in which the objectional oil was soluble.

The nature of this yellow, uncrystallizable oil was never determined. It was carried down the column mostly with the first principal band and to a slight extent in the second band. It formed no band of its own. Eventually, the impurity was eliminated by recrystallization from acetic acid, although the nitrated hydroxybiphenyls (from the first and second bands) are also recoverable upon successive dilutions of their benzene solutions with n-heptane.

The same band pattern always appeared on the column regardless of acid strength or solvent used in the nitration reaction. This pattern is shown in Plate 1. Two thin bands move quickly down the column. The first is light brown in color and the second a light orange. Each of these bands gave materials crystallizable from either benzene or acetic acid after several days. The melting points of both were in the range 49-50 °C. Checked with o-hydroxybiphenyl, both melted on mixing. Due to the slight yield and melting points far removed from known possible nitrated hydroxybiphenyls, no further experiments were performed with them.

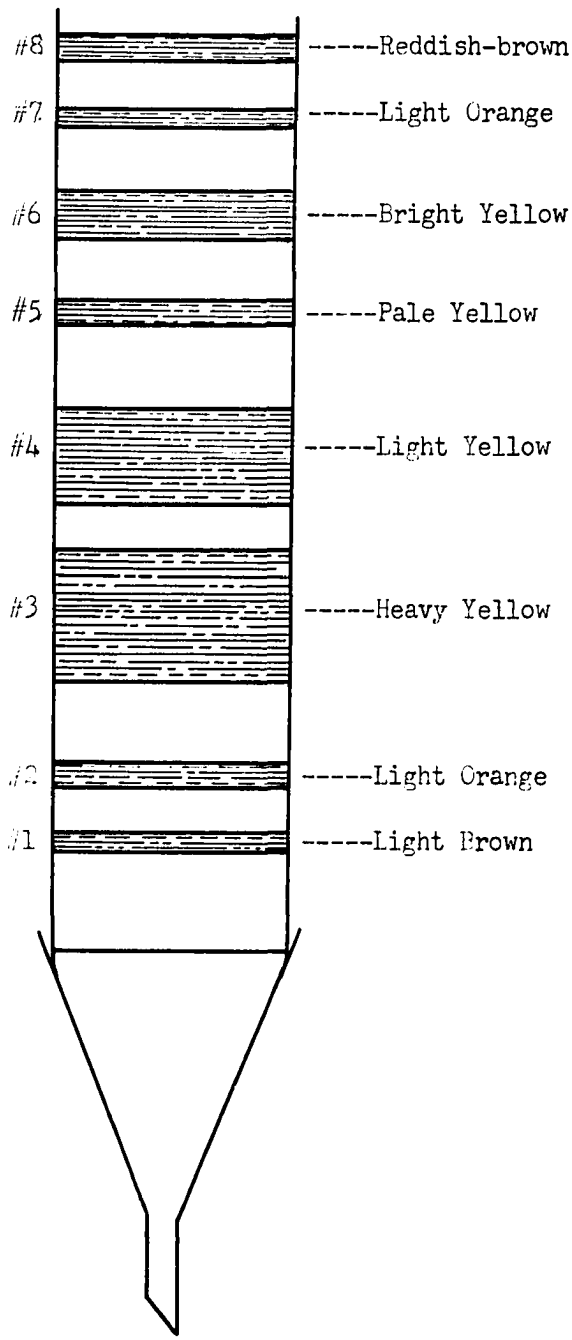
Above these two bands lay the first principal band, (#3 on the pattern) heavy-yellow in color. An interesting phenomenon was observed when the material in this band was crystallized from benzene-n-heptane. Yellow prisms were interspersed with pale yellow needle clusters. When a melting point of the yellow prisms was taken, observation under a microscope showed that the yellow color faded away to leave pale-yellow plates beginning around 100 °C with melting at 122-123 °C. The pale-yellow needles, after powdering, were seen, also, to be plates and these melted in the same range. A mixed melting point showed no depression in the melting point. From both, at 115 °C, a slight amount of material sublimed to long, pointed, clear crystals which melted at 125-126 °C.

Moreau (26) had described such phenomena in his investigation of 4'-nitro-2-hydroxybiphenyl and stated that this compound was dimorphic. Further evidence for such finding was that a weighed amount of the yellow crystals when heated above 100 °C in the oven, lost the yellow color but showed constant weight. Also, either of the two forms when crystallized from boiling water and filtered hot gave pale-yellow rods melting at 125-126 °C and a mixed melting point of the latter with the separate forms showed no depression.

The small amount of material subliming at 115 °C and melting at 125-126 °C could well have been the 5-nitro-2-hydroxybiphenyl which is known to sublime and melt in this range. Analysis of the material from this first principal band showed one nitro group and chromic acid oxidation yielded p, nitrobenzoic acid, thus establishing this compound as 4'-nitro-2-hydroxybiphenyl. The melting point is in agreement with that reported by Christiansen and Harris (27) and by Moreau (26). So, the first

PLATE 1

BAND PATTERNS ON THE COLUMN FROM INITIAL NITRATION OF BENZENESULFONATE OF 2-HYDROXYBIPHENYL



principal band appears to be the 4'-nitro derivative with possibly a slight amount of 5-nitro-2-hydroxybiphenyl. It can then be said that nitration of the benzenesulfonate of 2-hydroxybiphenyl follows the same path as that taken when the starting material is 4-hydroxybiphenyl.

Following close behind the first principal band was one of a lighter yellow (#4 on the pattern) and of considerable width, although, not as extensive as the principal band. It was the last band to be eluted as bands higher on the column moved slowly. The material crystallizes readily from benzene-n-heptane in yellow prisms melting at 139-140 °C but when crystallized from boiling water, the crystals are pale-yellow and melt at 142-144 °C. The solubility in water is slight. Attempts at further purification, in the belief the compound might be the 5,4',2'-trinitro-2-hydroxybiphenyl reported by Hill and Hale (1) which melted at 152 °C, were unsuccessful. Nitrogen analysis showed but one nitro group and chromic acid oxidation led to o-nitrobenzoic acid. Thus, 2'-nitro-2-hydroxybiphenyl was observed for the first time as a product in the direct nitration of 2-hydroxybiphenyl (modified by an ester block). The material sublimes in tiny rhombic crystals beginning at 120 °C when heated slowly up to the melting point and in this form melt at 140-141 °C. Variations in the melting point could well be due to slight amounts of the yellow oil associated with the first principal band. It is quite reasonable that this derivative would be produced along with the 4'-mononitro derivative. It is also quite probably that there would be small amounts of the 4',2',-dinitro- and the 5,-4'-dinitro; the 5,2'-dinitro, and even the 4-mononitro derivatives. However, only the 4'- and 2'- mononitro derivatives were identified from bands on the column re-

sulting from an original ester nitration.

Band number six (Plate 1) gives quite low yields. An accumulation from several columns by extrusion and extraction was crystallized from benzene-n-heptane and showed a melting point of 221-222 °C. Nitrogen analysis indicated two nitro groups. Attempts to obtain a nitro derivative of benzoic acid by chromic acid oxidation were fruitless. It is interesting to note that this band does not appear under extreme reaction conditions. Thus, with an ester-acid ratio of 8-1 and three ml. of nitromethane as solvent, this band is absent and the thin reddish-brown band at the top (#8, Plate 1) of the column is wider. This suggests the material in band number 6 further nitrates to the material in band #8. The melting point of the material agrees closely with the 5,4'-dinitro-2-hydroxybiphenyl reported by Hill and Hale (1).

The yields from several columns of the reddish-brown band at the top were worked up and the material crystallized from chloroform-n-heptane. The crystals were light-yellow and melted over a range of 222-230 °C. Recrystallization narrowed the range to 226-230 °C. Nitrogen analysis indicated a mixture of tri-, and tetra-nitro derivatives. As will be shown later, the 3,5,4'-trinitro derivative forms a reddish-brown band which moves but little when considerable eluent is used. The nitrogen analysis mentioned was 0.65 per cent below theoretical for four nitro groups and 1.59 per cent above theoretical for three nitro groups.

The materials from bands five and seven (see Plate 1) were not further investigated because of negligible yields.

Column efficiency was checked by introducing a weighed amount of crude hydrolyzed products obtained by evaporation of the benzene from the

final extract in the procedure previously described. Only the 4'- and 2'-mononitro derivatives were isolated and weighed. The yield approached quantitative proportions--91.29 per cent. Inasmuch as one gram samples of the sulfonate ester of o- hydroxybiphenyl produced such small yields from the column, a determination of column capacity was made. It was found that separation of the two principal bands could be effected when the ester sample weight was 2.5 grams if the Magnesol column was 50 cm., packed under 10 pounds pressure and elution carried out under five pounds pressure. A stock of the 4'-nitro and 2'-nitro derivatives was obtained by the use of 5 gram samples of the sulfonate ester and division of the final benzene extract equally between two like columns.

The first check on percentage yields through the column was both misleading and informative. A weighed amount of nitrated ester obtained by crystallization from hot alochol solution of reaction products, was hydrolyzed and the nitrated hydroxybiphenyls worked up and placed on the column. The yields were 32.63 per cent of the 4'-mononitro-2-hydroxybiphenyl and 4.29 per cent of the 2'-derivative. This was checked by hydrolysis of the entire alcohol solution (without crystallization as above) from the same weight sample. The yield of the 4'-derivative was 30.06 per cent while the 2'-derivative yield rose to 20.88 per cent. Either the yellow oil in the initial nitration reaction holds the 2'-derivative rather firmly or the 2'-derivative is more soluble in alcohol. Hydrolysis of the entire alcohol solution of initial nitration products is a distinct advantage in the production of 2'-mononitro-2-hydroxybiphenyl. Data for the above are listed in Table 5.

On page 18 there was mention of an initial reaction product

TABLE 5

COLUMN YIELDS OF PRINCIPAL PRODUCTS FROM INITIAL NITRATION OF THE BENZENESULFONATE OF ORTHO-HYDROXYBIPHENYL[a]

Ester Weight grams	Nitrated Ester Wt. grams	Yields 4'-nitro Derivative		2'-nitro Derivative	
5	2.8690 (50.10 % yield on mononitro basis)	1.1308 g.	32.63 %[b]	0.1487 g.	4.29 %[b]
5	Not isolated	1.0415 g.	30.06 %	0.7235 g.	20.88 %

[a]10-1 mole ratio, fuming nitric acid to sample weight; glacial acetic acid solvent; room temperature.

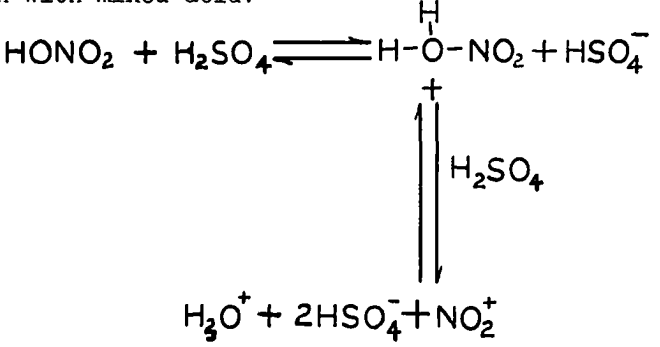
[b]Column yields on o-hydroxybiphenyl basis.

which appeared under certain reaction conditions. This product which melted at 169-170 °C appeared, when the solvent was nitromethane and the acid-ester mole ratio exceeded 5-1. The substance was isolated as a clear crystalline solid difficultly soluble in hot alcohol. At an acid-ester ratio of 8-1 it was the principal product. Since 4'-mononitro-2-hydroxybiphenyl was desired, reaction conditions leading to formation of this unwanted material were avoided. Although this product was not desired some further investigation was made. A quantity of the material was carried through the usual procedures. During hydrolysis the deep, red color characteristic of nitrated phenols developed. When the hydrolysate was acidified, a yellowish-white gelatinous precipitate resulted. This was filtered by suction, washed and dried. The yellow

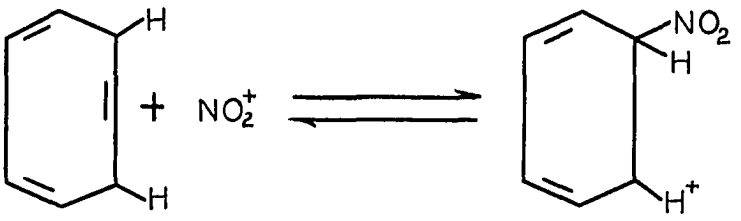
powder resulting was treated with boiling benzene in which it was difficultly soluble. Material not soluble was dried and a melting point taken. At 190-200 °C it sublimed in wavy, iridescent needle clusters melting in the range 214-220 °C. The benzene filtrate produced the same characteristic crystals upon addition of n-heptane. Recrystallization from chloroform-n-heptane produced yellowish crystals melting between 220-227 °C. Nitrogen analysis indicated the presence of two nitro groups. Neither the dinitro compound from band number six (Plate 1.) nor two dinitro compounds prepared later from further nitration of 4'-nitro-2-hydroxybiphenyl proved identical with this material. No further exploratory experiments were carried out on this material.

As yet nothing has been said concerning the use of mixed acid in the nitration of the benzenesulfonate of o-hydroxybiphenyl. Initial efforts with acid-ester ratios of 4-1 and above with varying amounts of concentrated sulfuric acid resulted only in oxidation products--mostly tarry masses. However, when the principles set forth by Alexander (38) were observed, significant yields of the 4'- and 2'- derivatives resulted.

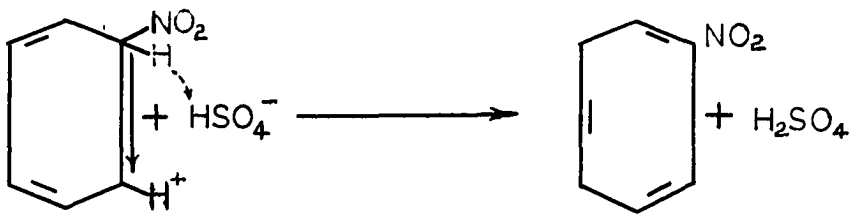
Alexander writes three equations to show the mechanism of nitration with mixed acid:



(1)



(2)



(3)

Equation #2 is the usual one written for nitration reactions. Alexander lists evidence for equations #1 and #3. Equation #3 shows the over-all reaction depends on acceptance of a proton by the bisulfate ion. Thus, addition of water should increase the rate of step #3:

$$H_2O + H_2SO_4 \rightleftharpoons [H_3O]^+ + HSO_4^-$$

Such reaction, however, tends to reverse Step #1. There should be an optimum concentration of water in the sulfuric acid of a nitrating mixture above and below which the rate of nitration should decrease. Alexander's compilation of the literature shows this optimal to be aqueous sulfuric acid of about 90 per cent concentration. It is shown that sulfuric acid acts then, not simply to absorb water formed during the reaction, but to provide an ideal balance between the ionization of nitric acid into the ion (NO_2^+) and the subsequent removal of a proton from an intermediate.

A trial run using nitric-sulfuric acid mole proportions and added water as demanded by the equations was made. The ester was dissolved in glacial acetic acid just sufficient for solution and one ml. of acetic acid added per ml. of nitration mixture. The nitric acid-ester mole ratio was 4-1. Tarry masses resulted. But when the nitric acid-ester mole ratio was lowered to 2-1, the yields from the column of the 4'- and 2'- derivatives, respectively, were 29.91 and 18.61 per cent.

Nitration is accomplished with mixed acid at a greatly decreased nitric acid-ester mole ratio but with somewhat lower yields. Such experimental results are in keeping with the well known strength of mixed acid as a nitrating agent. Reaction conditions are considerably more critical with its use than with fuming nitric acid alone. In the latter case, the acid-ester mole ratio can be varied between fairly wide limits with little change in percentage yields.

The column pattern in this last run was not the same as pictured in Plate 1. Bands number one and two were absent but #3 and #4 were unchanged. Bands #5, #6 and #7 were replaced with a single band, light-orange in color but of little extent. Band #8, the reddish-brown top band, was present and like its counterpart in Plate 1, was quite narrow.

With the 4'-mononitro and 2'-mononitro derivatives prepared, the next step was further nitration of these two compounds to what was hoped would be dinitro derivatives bearing one nitro group on each ring. Plate 2 pictures the route such reactions might take, remembering that reaction conditions are to be milder since the phenolic ring is now unencumbered with a blocking group.

Sonnenfeld (35) established conditions, in 1954, for the nitration

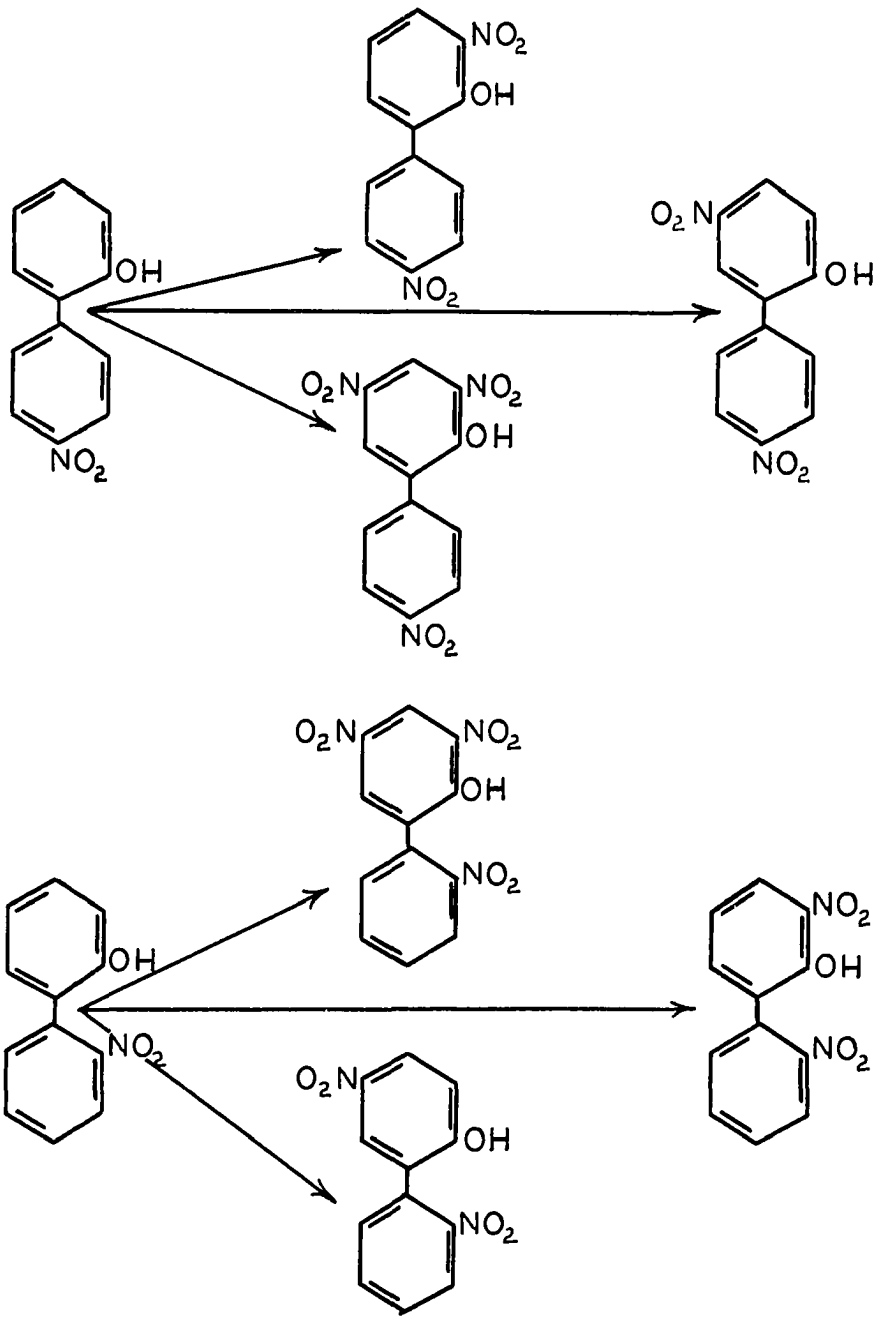
of 2-hydroxybiphenyl. With a mole to mole ratio of nitric acid (calculated amount, fuming or concentrated) to hydroxybiphenyl, he obtained maximum yields of the 3- and 5-mononitro derivatives. With a 4-1 mole ratio acid to sample, the 3,5-dinitro derivative was heavily favored. The problem in the present case was largely the same. With a nitro group deactivating the non-phenolic ring to further substitution except under extreme conditions and with the activating hydroxyl group on the other ring, it is reasonable to predict reaction products such as described by Sonnenfeld.

The 3,5,4'-trinitro derivative was easily prepared and isolated. With a 4-1 mole ratio, fuming or concentrated nitric acid to 4'-mononitro-2-hydroxybiphenyl, the trinitro derivative drops out at room temperature. Without benefit of the column the percentage yield was 71.93. Nitrogen analysis showed three nitro groups and the melting point agreed with that found by Hill and Hale (1) (162-163 °C). Recrystallization was from benzene-n-heptane but better from hot 95 per cent alcohol. The crystals are thin, brownish-yellow needles. On the column the trinitro derivative is reddish-brown, similar in appearance to band #8 on Plate 1. Continuous elution with benzene under five pounds pressure for 12 hours moves the band less than five cm. down the column. One is almost tempted with such evidence to immediately label band number five in Plate 1. a dinitro derivative (since its speed on the column is so much greater than this trinitro derivative). Band #7 lies too close to band #8 to be so labeled.

A close look at Sonnenfeld's (35) results from the nitration of 2-hydroxy- and 4-hydroxybiphenyl shows some interesting facts. His use of a 4-1 mole ratio, nitric acid to biphenylol in dinitro biphenylol pro-

PLATE 2

POSSIBLE DERIVATIVES FROM FURTHER NITRATION OF 4'-NITRO AND 2'-NITRO 2-HYDROXYBIPHENYL



duction, was followed in the experiment described immediately above. His data for mononitrobiphenylol production show that when the solvent is glacial acetic acid and the hydroxybiphenyl-acid ratio is 1-1, mononitro derivatives of both 2- and 4-hydroxybiphenyls heavily predominate. When the reaction temperature is raised to 70 °C from room temperature, the same, almost exclusive, mononitro derivative production is shown for 2-hydroxybiphenyl. (Like data are missing for the 4-hydroxybiphenyl.) But when the biphenylol-nitric acid ratio is raised to 1-2, there is an abrupt shift to heavy dinitro derivative production for both 2- and 4-hydroxybiphenyl.

When the solvent is nitromethane, Sonnenfeld's data differ in part from that for glacial acetic acid. The 1-1 mole ratio, 4-hydroxybiphenyl to nitric acid, parallels the use of glacial acetic acid in that the mononitro derivative is produced almost exclusively. When the acid is doubled, the dinitro derivative increases from 1.2 per cent to 58.3 per cent but there is still 36.8 per cent of the mononitro derivative. At 3-1, acid to sample, the dinitro largely predominates. When the temperature is raised to 70 °C at a 2-1 ratio, acid to sample, the dinitro constitutes the principal yield. At 70 °C the 2-hydroxybiphenyl yields principally the dinitro derivative with a 2-1 mole ratio, acid to sample. It is only at room temperatures that the use of nitromethane apparently favors mononitro derivative production from 2-hydroxybiphenyl as the data show about an equal yield of mono- and dinitro derivatives when the acid-sample mole ratio is as high as 3-1. The results are not wholly conclusive since the reaction time in this last case was one hour compared with two hours for the other experiments.

Since nitration of 4'-mononitro-2-hydroxybiphenyl with the 4-1 acid-sample mole ratio had introduced two nitro groups into the phenolic ring at the anticipated 3-, and 5- positions, employment of a 1-1 ratio should produce the 3,4'- and 5,4'- dinitro derivatives if the rules for mononitro production hold with a nitro group in the 4'- position.

When 4'-nitro-2-hydroxybiphenyl is further nitrated in glacial acetic acid with fuming nitric acid (1-1 mole ratio, acid to sample), the reaction proceeds smoothly at room temperature. There is some precipitation of products during nitration. This is not true when nitromethane is the solvent indicating lower solubility in glacial acetic acid. Treatment is relatively simple. Dilution of the reaction mixture with ice water brings down the products which are extracted with benzene. The benzene solution is dried over sodium sulfate and boiled to dryness several times with n-heptane to remove either glacial acetic acid or nitromethane. The residue is dissolved in benzene and placed on the column.

As a general rule, only mononitro derivatives show mobility on the column. But the first band material from this nitration moves at about the same speed down the column as mononitro derivatives from the initial ester nitration. The band is highly colored--almost red with a slight brownish cast. It gradually stretches out to cover a considerable portion of the column. Although the leading edge is eluted with a moderate amount of benzene, the trailing fraction requires considerable eluent to remove it from the column. A check of this trailing edge showed it to be identical with the leading edge. Yields from successive cuts of this laggard fraction were quite low.

Above this first band, an orange band moved slowly after a like,

slow development. It exhibited much the same phenomena as did the first band in that both above and below the more highly colored central portions of the band were regions where the orange shaded out into a yellow color. A possible explanation is that all molecules starting evenly at the top of the column exert a mass effect among themselves so that the more highly colored central portion represents a high concentration of molecules and the leading and trailing edges of the band represent regions of low concentrations. When the first band was off the column this second band had moved, generally, one-third of the distance. It was extruded and extracted with alcohol. Nitrogen analysis of each of these bands indicated two nitro groups. An immediate attempt was made to identify the second band with the material in band #6, Plate 1, from the ester-nitration reaction but without success.

The material from band one was crystallized from benzene-n-heptane. It melted sharply at 194-195 °C. Crystals were yellow needles with a slight tint of green. Although band number two was extensive on the column, the yield was low. Extrusion and extraction with alcohol, evaporation of the alcohol solution and crystallization from chloroform-n-heptane gave pale-yellow needles, melting at 226-228 °C. This value is above Hill and Hale's (1) report for the 5,4'-dinitro-2-hydroxybiphenyl (224-225 °C). The band pattern for this further nitration of the 4'-nitro-2-hydroxybiphenyl is pictured in Plate 3.

Where eight bands were discernible on the column from the initial reaction, only four were observed in this further nitration. The third band was narrow, brown-orange in color and moved but slightly. Finally, at the top of the column and almost stationary, was the usual reddish-

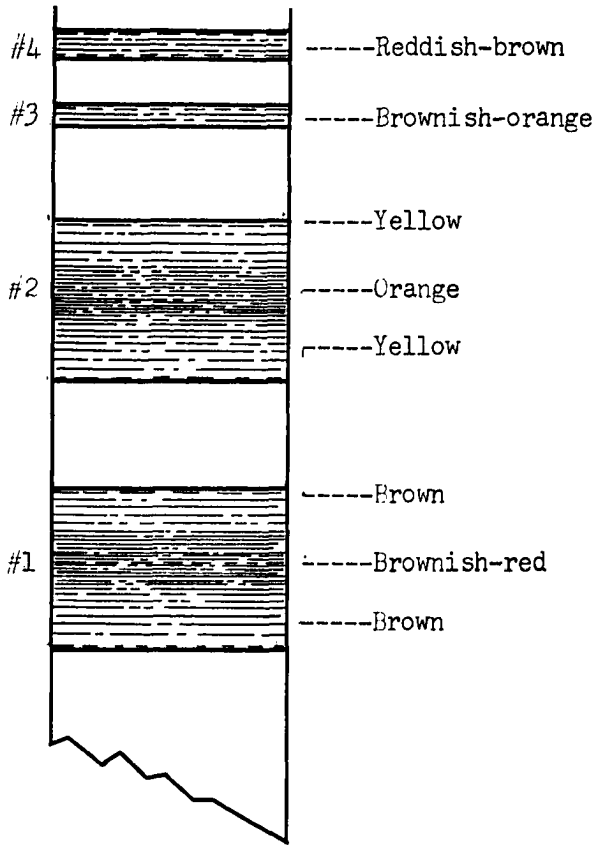
brown narrow band indicative of tri- and tetranitro derivatives. Both the materials from bands one and two were oxidized with chromic acid to para-nitrobenzoic acid. The crystals melting at 194-195 °C pass easily to the identifiable 3,5,4'-trinitro-2-hydroxybiphenyl when treated in glacial acetic acid with fuming nitric acid using a 4-1 mole ratio of nitric acid to sample (considered as a dinitro compound). The material from band number two also proceeds to the 3,5,4'-trinitro derivative under like conditions except that a 30-minute reflux period is necessary (water bath).

Thus it may be assumed that one of these two products is the 3,4'- and the other the 5,4'-dinitro derivative. Two facts are the basis for a choice: One, the mobility of the first band material on the column suggests that this is the 3,4'- derivative with a hydrogen bridge between the hydroxy group at the 2- position and the nitro group at position three responsible for reduced acidity and consequent column mobility; two, the slow speed of the second band material on the column, typical of a dinitro derivative, coupled with the close agreement of the melting point with that reported by Hill and Hale (1) for the 5,4'- derivative, indicates this second band material is the 5,4'- derivative. In addition, the latter is only moderately soluble in warm benzene (soluble in boiling benzene) as was reported by Hill and Hale (1). These two products with one nitro group on each ring were the beginning compounds in an attempt to selectively reduce the one and not the other nitro group with sodium polysulfide. This will be discussed presently.

A recently developed method for distinguishing substituted phenols was employed in an attempt to shed further light on the structure

PLATE 3

BAND PATTERNS FROM THE FURTHER NITRATION OF 4'-NITRO-2-HYDROXYBIPHENYL[a]



[a]Acid-Sample mole ratio: 1-1

Solvent: G. A. A. or Nitromethane

of these two compounds. Soloway and Santoro (39) found that phenols are readily oxidized to colored products in ammoniacal solution by persulfate ion in the presence of a catalytic amount of silver ion. Derivatives having a free para position are distinguished from others in yielding blue or green dyes. Tests on 65 phenols showed that those derivatives (with few exceptions) which had unsubstituted para positions and did not contain strong electronegative groups such as nitro or cyano, gave a blue or green color while other derivatives gave yellow or amber colors or were unoxidized. The test was made on all derivatives prepared thus far as well as on samples of 3- and 5-mononitro-2-hydroxybiphenyl obtained at the University of Oklahoma. The developed colors are shown in Table 6. With nitro groups present, positive tests were not anticipated nor did they develop. It will be noticed, however, that the 3, 4'- and 3,4'-(dinitro) derivatives are of similar shades of amber. This probably has little significance since the 2'- derivative is a dark amber.

Table 7 lists yields of the assumed 3,4'- and 5,4'-dinitro-2-hydroxybiphenyls.

Fox (28) reacted concentrated nitric acid with his 2'-nitro-2-hydroxybiphenyl using a 3-1 mole ratio, acid to sample. After a one-hour reflux period the reaction mixture was diluted with water. Yellow crystals melting at 123 ^{o}C were recovered from alcohol. This was the extent of the literature covering the nitration of the 2'-mononitro derivative when its further nitration was undertaken. Samples of the 2'- derivative were nitrated using a 4-1 mole ratio, acid to sample, in glacial acetic acid and a 1-1 mole ratio in nitromethane. The general procedure of dilution with ice water, filtration of the precipitate, benzene extraction

TABLE 6

COLOR TEST FOR FREE PARA POSITION
IN SUBSTITUTED PHENOLS[a]

Compound	Color	Scale
3-nitro-2-hydroxybiphenyl	light amber	(1)
5-nitro-2-hydroxybiphenyl	dark amber	(2)
4'-nitro-2-hydroxybiphenyl	light amber	(1-2)
2'-nitro-2-hydroxybiphenyl	deep amber	(4)
3,4'-dinitrohydroxybiphenyl	light amber	(1)
5,4'-dinitrohydroxybiphenyl	deep amber	(4)
3,5,4'-trinitrohydroxybiphenyl	dark amber	(2-3)

[a]Color scale in ascending depth of amber shade: 1, 2, 3, 4, 5, 6.

followed by extraction with five per cent sodium hydroxide solution, acidification and further extraction with benzene was followed. Solvents were removed by boiling to dryness several times with n-heptane. The final benzene extracts placed on the column produced bands pictured in Plate 4.

No matching bands, either on a color basis or on a basis of mobility, were observed. Evidently the 2'- derivative is more difficult to nitrate than the 4'-nitro derivative since the light-orange, fast-moving principal band associated with the 1-1 mole ratio in nitromethane yielded starting material. The material from the slow-moving, lemon colored band was difficultly soluble in benzene but moderately soluble in hot benzene. The crystals, from either benzene-n-heptane or from alcohol,

TABLE 7

YIELDS OF ASSUMED 3,4'- AND 5,4'-DINITRO-2-HYDROXYBIPHENYLS FROM FURTHER NITRATION OF 4'-NITRO-2-HYDROXYBIPHENYL

Sample Weight in mg.	Acid-Sample Mole Ratio	Solvent	Conc. Nitric Acid	Yields 3,4'-nitro Wt-mg	Per cent	5,4'-nitro Wt-mg	Per cent
500	1-1	G. A. A.	fum.	191	31.59	72.5	11.99
250	1-1	Nm.	fum.	81	26.79	52.0	17.20
250	1-1	Nm.	conc.	Insignificant			
250	2-1	Nm.	conc.	116.5	38.54	Not Recovered	

YIELD OF 3,5,4'-TRINITRO-2-HYDROXYBIPHENYL FROM FURTHER NITRATION OF 4'-NITRO-2-HYDROXYBIPHENYL

Sample Weight in g.	Acid-Sample Mole Ratio	Solvent	Conc. Nitric Acid	Trinitro Yield Grams	Per cent
2.2392	4-1	G. A. A.	fum.	2.2846	71.93

were pale-yellow needles. A material which failed to dissolve in the initial benzene treatment was identical with the compound isolated from this band. The band moved far enough down the column to allow convenient separation (from bands above and below) by extrusion. The melting point, 228-229 °C, lies quite close to that of one of the two products from further nitration of the 4'-nitro-2-hydroxybiphenyl (226-228 °C). A mixed melting point with the latter melted over the range--200-210 °C. No nitrogen analysis or oxidation with chromic acid was carried out on this material. Since only a mole ratio of 1-1, acid to sample, was

PLATE 4

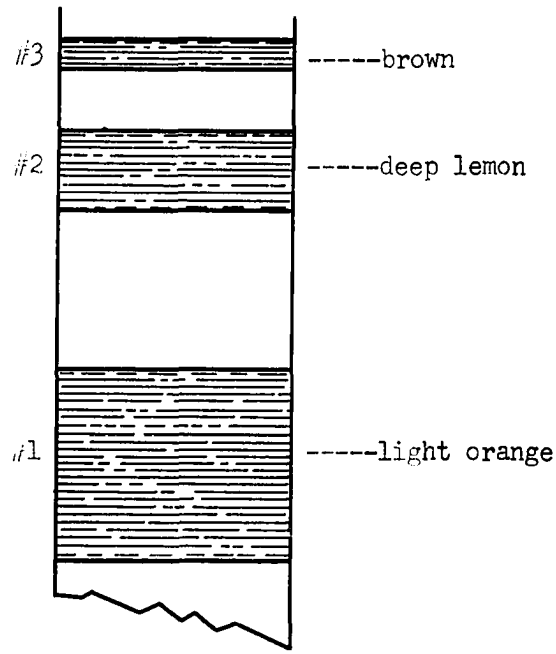
BAND PATTERNS FROM FURTHER NITRATION OF
2'-NITRO-2-HYDROXYBIPHENYL

(a)

1-1 mole ratio,

acid to sample,

in nitromethane



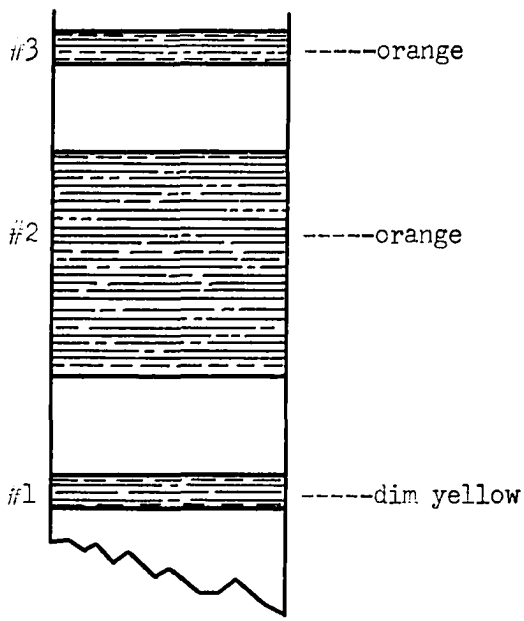
(b)

4-1 mole ratio,

acid to sample,

in glacial acetic

acid



employed, and in view of the results from a 4-1 mole ratio (in glacial acetic acid) to be discussed, the material was assumed to be either the 3,2'- or 5,2' dinitro derivative.

A glance at the band pattern (Plate 4) on the column containing the materials from the reaction employing a 4-1 mole ratio, acid to sample, and glacial acetic acid as the solvent shows only one principal band. No starting material was recovered. The material from the principal band after extrusion, extraction and crystallization from benzene-n-heptane appeared as yellow needles melting at 152-153 °C. Nitrogen analysis showed three nitro groups and oxidation with chromic acid produced o-nitrobenzoic acid. Thus, the compound appears to be the 3,5,2'-trinitro-2-hydroxybiphenyl.

Hill and Hale (1) reported a trinitro derivative of o-hydroxybiphenyl melting at 152-153 °C. This compound was obtained in equal quantities with their 3,5,4'-trinitro-2-hydroxybiphenyl when the 5-nitro-2-methoxybiphenyl was treated with concentrated nitric acid to the extent of twenty times by weight of the sample. It was reported as the 5,2',4'-trinitro derivative.

Only the principal bands were examined in these experiments with 2'-nitro-2-hydroxybiphenyl. Thus, the product obtained by Fox (28), melting at 123 °C (see page 46), may have been overlooked. As a check, Fox's experiment with a 3-1 mole ratio, concentrated nitric acid to sample, was followed exactly (in acetic acid) and the final benzene extract placed on the column. Aside from a narrow band at the top of the column assumed to be oxidation products or polynitro derivatives, only one principal band appeared. It matched the band produced on the column

when the mole ratio was 4-1 and proved to be the crystals melting at 152-153 °C. Table 8 shows yields from the further nitration of the 2'-nitro-2-hydroxybiphenyl.

TABLE 8

YIELD OF DINITRO DERIVATIVE FROM FURTHER NITRATION OF 2'-NITRO-2-HYDROXYBIPHENYL WITH FUMING NITRIC ACID IN NITROMETHANE

Sample in mg.	Acid-Sample Mole Ratio	Column Recovery in mg.	Non-Column Recovery in mg.	Total mg.	Percentage Yield
250	1-1	69.5 band #2	21 (same as band #2)	90.5	40.95
		59.5 (starting material)			

YIELD OF TRINITRO DERIVATIVE FROM FURTHER NITRATION OF 2'-NITRO-2-HYDROXYBIPHENYL WITH FUMING NITRIC ACID IN GLACIAL ACETIC ACID

Weight Sample	Acid-Sample Mole Ratio	Column Recovery	Total Recovery	Percentage Yield
250 mg.	4-1	170 mg. band #2	170 mg.	48.02

CHAPTER III

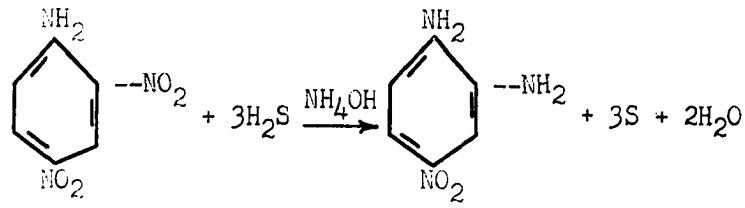
PARTIAL REDUCTION

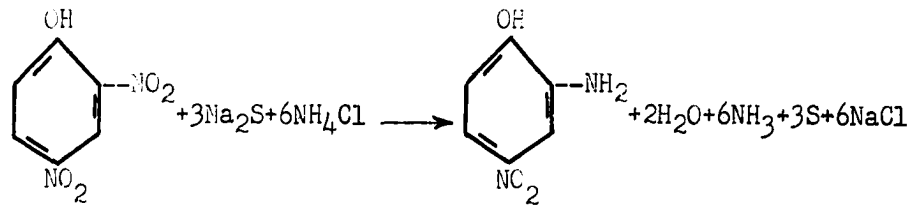
As outlined at the beginning of this thesis, a secondary objective of the problem was the investigation of partial reduction of dinitro derivatives of 2-hydroxybiphenyl where one nitro group is on the phenolic and the other on the non-phenolic ring. Although the problem here is concerned with partial reduction of two nitro groups when a third substituent is present, viz., hydroxyl, a survey of the general problem of partial reduction is both informative and interesting.

The first partial reduction in the biphenyl series was reported by Schultz (40) who used hydrogen sulfide to reduce 4,4'-dinitrobiphenyl to 4-nitro-4'-aminobiphenyl. Important in the present study, since it formed the basis for successful partial reduction experiments carried out at the University of Oklahoma by Ward (41), was the work of Guglialmelli and Franco (42) in 1929. These two workers used sodium sulfide and sulfur in aqueous media to partially reduce the 4,4'-dinitrobiphenyl.

Meanwhile, experiments in partial reduction of dinitrophenyl compounds when a third substituent is present were beginning to appear in the literature. A method by Griffin and Peterson (43) for partial reduction of 2,4-dinitroaniline was published in 1941. Hydrogen sulfide was passed into an alcoholic solution of the dinitroaniline in the pres-

ence of concentrated ammonium hydroxide. The hydrochloride of the amino product was formed and ammonia used to precipitate the reduction product. Hartman and Silloway (44), in 1945, used sodium sulfide and ammonium chloride to prepare a like derivative from 2,4-dinitrophenol, the first instance of partial reduction (aside from Ward's work) where the third substituent was the phenolic hydroxyl group. The reactions for these experiments are as follows:





In the above experiments and in Ward's (41) method now to be described, it is seen that the only partial reduction products reported have been those in which the nitro group ortho to the third substituent has been reduced. Later experiments, to be described presently, proved that reaction conditions can be set up to obtain the isomer of such derivative.

Ward, working in the laboratories at the University of Oklahoma, experimented with the partial reduction of 3,5-dinitro-2-hydroxyphenyl. Several methods were tried but only the method of Guglialmelli and Franco (42) and Maccarelli and Gatti (45) proved successful. The dinitro com-

pound was suspended in water and a fused sodium sulfide-sulfur solution added slowly with stirring while the reaction mixture was held at the boiling point on a sand bath. The sodium salt of the monoamino-mononitrophenol formed and the free phenol, obtained by acidification with hydrochloric acid, was the 3-amino-5-nitro-2-hydroxybiphenyl. Ward concluded that a third substituent has little directive influence unless such group be the phenolic hydroxyl. Later experiments in the field show Ward's conclusion as to the phenolic hydroxyl group to be true only in that such directive group marks a limit in a series of alkyloxy-dinitrophenols. These experiments are surveyed below.

Blanksma and van der Weyden (46), in 1940, using Brand's (47) method (sodium disulfide in alcoholic medium) for partial reduction, partially reduced several alkyloxy-2,4-dinitrobenzenes and reported only the 2-amino-4-nitro derivatives. Thus far in the field it was accepted that the nitro group ortho to the third substituent (phenolic hydroxyl, amino and now alkyloxy) was preferentially reduced.

However, in 1946, Verkade, van Dijk and Meerburg (48) were able to report both isomers. These workers treated 1-alkyloxy-2,4-dinitrobenzene in corresponding alcoholic medium with sodium disulfide. With 1-methoxy-2,4-dinitrobenzene the 2-amino derivative was obtained in a 4-1 ratio to the 4-amino derivative. The method of separation was the addition of ammonia, drop by drop, to a solution of the sulfates of the two derivatives, or to clarify, the solubility of the 2-amino derivative was less than that of the 4-amino derivative in the corresponding dilute acid. When n-propoxy was employed the production ratio was 1.5-1, the 2-amino to the 4-amino derivative. The series was extended to the

aryloxy- compounds with like results. Verkade et al then partially reduced 1-hydroxy-2,4-dinitrobenzene and reported separation of the 2- and 4-aminomononitrophenols in the ratio of 7-1. From this yield they concluded that the phenolic hydroxyl group is the final term in the descending series of alkyloxy groups with the yield of the 2-amino derivative increasing as the ether group becomes smaller. (Recall the 1-methoxy group produced a 4-1 ratio and propoxy a 1.5-ratio.) Such conclusion bears out that of Ward, that the phenolic hydroxyl group shows considerable directive influence in the ease of reduction of ortho nitro groups.

A comparison of Ward's method and that of the above workers is interesting. Ward used an excess of sulfur in preparing the sodium disulfide while Verkade et al used a mole to mole ratio of sodium sulfide and sulfur. The latter used a 12 per cent excess of reducing agent and Ward used 100 per cent excess. Both prepared the sodium salt, Ward, in aqueous suspension and Verkade et al in 96 per cent alcohol along with the calculated amount of 1 N. sodium hydroxide to form the sodium salt of the dinitrophenol. This was done so that the disulfide would not decompose in the presence of the strongly acid starting material. Neglect in taking such precaution was responsible, according to Verkade et al, for van der Weyden's poor yield--even of the 2-amino isomer. Ward removed free sulfur and unchanged starting material by filtration of the hot reaction mixture and obtained the sodium salt by concentration and cooling. Verkade et al neutralized with the calculated amount of 1 N. hydrochloric acid, extracted with ether, distilled the ether and boiled the residue with 2 N. hydrochloric acid to form the hydrochloride. Advantage was then taken of the difference in basicity of the two isomers by adding

three-fourths of the alkali necessary for neutralization of the hydrochloride. This brought down 2-amino-4-nitrophenol. Further addition of one-eighth of the calculated amount of alkali produced a mixture of the two isomers and addition of the final one-eighth portion of alkali resulted in precipitation of 4-amino-2-nitrophenol. If Ward's final product contained both isomers, it is possible that their different solubilities in aqueous alcohol enabled isolation of the 2-amino derivative reported since he crystallized three times from alcohol-water. Nitrogen analysis would, of course, show only mononitromonoamino percentages. It is noteworthy that the melting point of his crystalline product was 125-129.5 °C.

In the present investigation the two principal products obtained by further nitration of 4'-nitro-2-hydroxybiphenyl, viz., the crystalline products melting at 194-195 °C and 226-228 °C, were the starting materials in the attempt at partial reduction. Each was known to contain two nitro groups. Further, it was known that each ring contained one nitro group. It was assumed that one of the compounds had a nitro group in the 3-position, adjacent to the phenolic hydroxyl group and that the other compound had a nitro group in the 5- position.

As a check on the observation of Verkade et al that Blanksma and van der Heyden had failed to neutralize the acidic starting material, the first attempt at partial reduction was made in alcoholic medium without added alkali. Starting material was a sample of the prepared 3,5,4'-trinitro-2-hydroxybiphenyl. Sodium disulfide was prepared by fusing the hydrate (9 aqueous) of sodium sulfide and sulfur mole to mole. The disulfide was added in small portions to the alcohol solution of the sample

at reflux temperature with stirring. The disulfide was added in a mole to mole ratio--reagent to sample. After a two-hour reaction period the alcohol was removed under vacuum and the residue diluted with water. Extraction with benzene followed by distillation of the benzene left a residue which proved to be an almost quantitative yield of starting material.

The dinitrophenol melting at 194-195 °C was then used as a starting material. The procedure of Verkade et al was followed using a 12 per cent excess of sodium disulfide. After a two-hour reaction period at reflux temperature, the mix was neutralized with hydrochloric acid and extracted with ether. The ether was evaporated and the residue boiled with 2 N. hydrochloric acid. Filtration of the hot solution produced only starting material. A second attempt using a 30 per cent excess of sodium disulfide ended once more with recovery of starting material. The dinitro compound melting at 226-228 °C was put through the same procedure and this experiment, too, met with failure. Filtrates remaining after the recovery of starting materials were neutralized and samples checked for amines by the carbylamine reaction. All such tests were negative. The reaction which went easily with 2,4-dinitrophenol failed, in this instance, when the nitro groups are on separate rings.

It should be pointed out that Verkade and Witjens (49), in 1946, were able to partially reduce 1-ethoxy-2,6-dinitrobenzene in benzene solution with hydrogen at 55 °C in the presence of platinum oxide to the 2-amino-6-nitro derivative but the reaction failed when alcohol was the medium and also failed when sodium disulfide was employed with alcohol as the medium.

Attempts to partially reduce the two dinitrohydroxybiphenyls met

with some degree of success when the reaction was tried in aqueous media. Most of the starting material was recovered by filtration of the hot reaction mixture. However, the filtrate was red in color and was treated as though it contained a partial reduction product. In moderately strong acid solution the color disappeared and reappeared in alkaline solution. In very dilute acid solution a brown, flocculent precipitate came down. This was accomplished by addition of sodium hydroxide drop by drop to the moderately strong acid solution. Maximum precipitation occurred just on the acid side.

The dark-brown precipitate was dried under vacuum in a desiccator. The yield was insignificant. The substance was amorphous and failed to give the characteristic odour of iso-cyanides under the carbylamine reaction despite its behavior as an aminophenol. Deamination was not attempted. Exhaustion of starting-materials stocks and lack of time precluded further experimentation.

CHAPTER IV

EXPERIMENTAL

Preparation of the Benzenesulfonate of 2-Hydroxybiphenyl

Twenty-five grams (0.147 mole) of 2-hydroxybiphenyl, m. p. 56-57 °C, were dissolved in 75 ml. of pyridine and 20 ml. of benzenesulfonyl chloride (6.6 per cent excess) was added to the pyridine solution with the temperature held below 10 °C. After standing for one hour, the reaction mixture was heated on the water bath for an additional hour. Overnight, long needle crystals of the benzenesulfonate separated and were collected on the filter. The mother liquor was poured over 200 grams of crushed ice and a further yield of the ester was removed by filtration. Recrystallization from 95 per cent alcohol gave 40.5 grams. (88.90 per cent yield.) The melting point was 66-67 °C.

Nitration of the Benzenesulfonate of 2-Hydroxybiphenyl

One gram (0.0032 mole) of the ester was dissolved in 2 ml. of warm glacial acetic acid. A nitration mixture made up of one and one-fourth ml. of fuming nitric acid (sp. gr. 1.49-1.5) (0.0289 mole) and an equal volume of glacial acetic acid was added dropwise with shaking to the solution at room temperature. There was no evident rise in temperature. The reaction mixture was heated on the water bath for one and one-

half hours during which the color became a reddish-brown. The mixture was poured into 50 ml. of ice water after standing for 20 hours. There was an immediate precipitation of a gummy white mass which took on a pinkish cast upon standing. The mass was washed free of acid on the filter with distilled water and the last traces of acid were removed by washing with a five per cent sodium bicarbonate solution followed by further washing with water. The gummy mass was dissolved in 15 ml. of hot 95 per cent alcohol and distilled water was added until a faint cloudiness persisted. A few drops of alcohol were added and the solution was cooled. In one to two hours a mass of whitish-yellow crystals precipitated. These crystals were collected on the filter (1), the filtrate reheated and water added dropwise until cloudiness persisted. A few drops of alcohol were added and the solution was cooled. A further yield of crystals were collected on the filter and added to (1). No further yield of crystals was obtained from the alcoholic filtrate. Upon evaporation of the alcohol a yellowish-brown oil remained. This oil was found as a residue in all nitrations. Samples set aside for three months failed to crystallize. The crystal mass (1) was washed with cold dilute alcohol followed by water and dried in the desiccator. The total yield was 0.5448 g. On a mononitro basis this is 47.58 per cent. A slight pink color appeared on standing. However, after two recrystallizations from hot 95 per cent alcohol, the pink color was no longer observed. After drying the whitish-yellow crystals melted at 136-137 °C.

Nitration of the Benzenesulfonate of 2-Hydroxybiphenyl under Varying Reaction Conditions

One gram of the ester was dissolved in three ml. of nitromethane and a nitration mixture made up of 0.56 ml. of fuming nitric acid (0.0129 mole) and one ml. of nitromethane was added dropwise with shaking to the ester solution at room temperature. The procedure already described for use of acetic acid as the solvent was followed. The yield of nitrated ester melting at 136-137 °C was 0.48 g. or 41.9 %. This was the highest yield obtained when nitromethane was used as the solvent with the mole ratio of acid to ester varied between the limits 3-1 and 6-1. When the mole ratio, acid to ester, was 8-1 (1.13 ml. fuming nitric acid per gram sample), the product consisted of prismatic crystals melting at 169-170 °C.

One gram of the ester was dissolved in five ml. of glacial acetic acid and nitrated with a mixture made up of 1.13 ml. (0.026 mole) of fuming nitric acid and one ml. of glacial acetic acid at room temperature. The procedure followed that carried out when acetic acid was the solvent as above. The yield of nitrated ester was 0.13 g. or 11.4 %.

One gram of ester was dissolved in three ml. of glacial acetic acid and nitrated with 1.13 ml. (0.026 mole) of fuming nitric acid mixed with one ml. of glacial acetic acid. The previously described procedure was changed in that a reflux period of one and one-half hours at the reflux temperature of acetic acid was used rather than reflux on the water bath. The nitrated ester melting at 136-137 °C obtained in some previous runs was not obtained. Three crystal fractions were precipitated from hot dilute alcohol. One of these fractions melted at 57-58 °C (I); another at 118-119 °C (II) and the third at 183-184 °C (III). Neither

(I) nor (II) contained N or S when the resultant solutions from sodium-fusion were tested for these elements. (I) was not 2-hydroxybiphenyl nor its benzenesulfonate and (II) was not benzoic acid. (III) contained S but no N. All, apparently, were oxidation products.

Two, one gram samples of the ester dissolved separately in three ml. of glacial acetic acid were nitrated with 1.25 ml. (0.0289 mole) of fuming nitric acid mixed with one ml. of glacial acetic acid. One sample was nitrated at 90 °C and the other at 80 °C. The two reaction mixtures were then held at these respective temperatures (oil bath) for one and one-fourth hours without any period of heating on the water bath. Employing the general procedure outlined above, the sample nitrated at 90 °C produced a 53.1 per cent yield of the nitrated ester melting at 136-137 °C (0.608 g.). The 80 °C product yield was 0.30 g. (26.2 per cent).

One gram of the ester was dissolved in three ml. of glacial acetic acid and nitrated with 1.41 ml. of fuming nitric acid (0.032 mole) mixed with one ml. of glacial acetic acid at 90 °C. A one and one-half hour period of heating on the water bath followed. Using the general procedure, already described, 0.3115 grams of the nitrated ester melting at 136-137 °C was obtained (27.25 per cent). In addition 0.365 g. of the clear prismatic crystals melting at 169-170 °C were isolated.

Hydrolysis of the Nitrated Ester Melting at 136-137 °C

One gram of the nitrated ester was dissolved in 15 ml. of 95 per cent alcohol and one gram of KOH in three ml. of distilled water was added to the alcoholic solution. There was immediate reaction and a dark red color characteristic of alkali salts of nitrated phenols, indicative

in this instance of some degree of hydrolysis at room temperature, appeared. The hydrolysis mixture was refluxed for three hours and then poured into 50 ml. of distilled water. The wine-red solution was acidified with hydrochloric acid to the colorless end point and extracted with 15 ml. portions of chloroform until only a faint yellow color was shown by the chloroform. The solution was further extracted with 15 ml. portions of a five per cent KOH solution until only a faint yellow color was shown by the last portion of alkali. The alkali solution was acidified with HCl and the slightly acidic solution was exhaustively extracted with 15 ml. portions of benzene. The benzene solution was reduced in volume to 25 ml. (hot plate) and washed twice with five ml. portions of cold water to which two drops of dilute HCl had been added. Two washings with cold water followed. The benzene solution was then dried over anhydrous sodium sulfate, 10 ml. of n-heptane added, and evaporated to dryness on the hot plate. The weight of nitrated phenols was 0.393 g. which represents a 65.5 % yield on a mononitro basis.

Using the identical procedure above, a second, one gram sample of the nitrated sulfonate ester gave 0.494 grams of nitrated phenols. This represents a yield of 81.57 per cent.

Hydrolysis of the Nitrated Ester Melting at 136-137 °C and of the Yellow Oil Residue from the Alcoholic Solution of the Nitrated Ester

The crude yield, 4.772 g., of the nitrated ester melting at 136-137 °C from two, five gram samples of the sulfonate ester was dissolved in 75 ml. of 95 per cent alcohol and hydrolyzed, using the above procedure. The final benzene extract was dried, similarly, over anhydrous

sodium sulfate and made up to 50 ml. The solution was divided equally and placed on two columns. Band numbers three and four (see Plate 1) were eluted and the materials were recovered from the benzene still. Band number six was extruded and extracted with 95 per cent alcohol made slightly acidic with dilute HCl. The alcohol was distilled under vacuum (water pump); the residue was taken up in hot benzene and the solution filtered hot. After cooling, the filtrate was washed twice with water and then dried over anhydrous sodium sulfate. The benzene solution was then reduced on the hot plate to five ml. and three ml. of n-heptane was added. Cooling produced a yield of yellow plates. The materials from bands three and four recovered from the benzene still were crystallized from their benzene solutions with n-heptane. Total yield from the 4.772 grams of nitrated sulfonate was 1.8516 g. of nitrated phenols. This represents a 64.07 % yield on a mononitro basis. The yellow oil residue from the alcoholic solution of the nitrated sulfonate ester (unweighed) was similarly hydrolyzed and the nitrated phenols were worked up and placed on the column. The material from the first and only principal band was eluted and recovered from the benzene still. The solution of nitrated phenol was reduced in volume to 10 ml. and five ml. of n-heptane added. Cooling produced yellow prisms (I). Further addition of n-heptane (2 ml.) to the heated filtrate and cooling resulted in an additional yield (II). (I) and (II) were recrystallized from hot benzene and n-heptane. The total yield was 0.29 g. Added to the 1.85 g. above, the over-all yield was 2.14 g. which represents an over-all percentage yield of 30.8 on a mononitro basis.

Hydrolysis of the Nitrated Ester in Diethylene Glycol

Two and twenty-six hundredths grams of the crude crystalline products recovered from the alcoholic solution of initial nitration products of the sulfonate ester were added to a solution of KOH in diethylene glycol contained in a glass stoppered Erlenmyer flask. (Three grams of KOH were dissolved in 15 ml. of diethylene glycol and warmed gently to effect solution. A thermometer was used for stirring and the temperature was held below 130 °C. The warm solution was poured into 35 ml. of diethylene glycol in a glass stoppered bottle and allowed to cool.) The ester was mixed with the reagent by a rotary motion of the flask. With the stopper in place the mixture was heated on the oil bath to 70-80 °C. This temperature was reached in about three minutes and a whirling motion of the flask was maintained throughout the heating. The flask was then removed from the oil bath and shaken vigorously. With the stopper removed, the mixture was heated at 120-130 °C for ten minutes. The flask and contents were cooled below 90 °C and 150 ml. of distilled water was added. The color was similar to the wine-red color noted in hydrolysis with alcoholic KOH. The mixture was neutralized to a slightly acidic end point (colorless) with dilute HCl. The procedure from this point followed the usual routine extraction with chloroform followed by extraction with five per cent KOH solution, acidification with HCl and final extraction with benzene. The benzene solution was dried over anhydrous sodium sulfate and the benzene was removed on the hot plate. The yield of nitrated phenols was 0.89 g. which represents a yield of 65.17 % on a mononitro basis.

A sample of the yellow oil recovered from the alcoholic solution of initial nitration products of the sulfonate ester was carried through

the above procedure. No products were recovered from the final benzene extract.

Treatment of Nitrated Phenols Recovered from the Column

Two and one-half grams (0.008 mole) of the sulfonate ester dissolved in 7.5 ml. of glacial acetic acid were nitrated at room temperature with a nitrating mixture made up of 3.4 ml. of fuming nitric acid (sp. gr. 1.49-1.5) (0.078 mole). The reaction mixture was heated on the water bath for one and one-half hours and set aside for 20 hours at which time the reaction was stopped by addition of 125 ml. of ice water. The gummy mass was washed free of acid on the filter and the last traces of acid were removed by washing with a five per cent solution of sodium bicarbonate followed by further washing with water. The mass was dissolved in 50 ml. of hot 95 per cent alcohol and hydrolyzed with two and one-half g. of KOH in 7.5 ml. of water. The hydrolysis mixture was refluxed for three hours and 125 ml. of water added to the deep red mixture. The nitrated phenols were worked up as previously described and the dried, final benzene extract was reduced in volume to 25 ml. and placed on the column. (The column was filled to a depth of 50 cm. with adsorbent after packing as described on pages 28 and 34). Benzene (thiophene free) was passed through the column under five pounds pressure. The bands observed on the column (see Plate 1) gradually separated from the dark yellow mass at the top. Eluted materials from separate bands were recovered from the residue in the benzene still after distillation of the benzene.

Band Numbers 1 and 2

Band numbers one and two moved rapidly down the column. Number

one was light brown in color and number two was a light orange. Crystallization of each was observed from the yellowish-syrup residue from either of their benzene or acetic acid solutions following several days standing. The yield of clear, prismatic crystals was negligible. The melting point of each following removal of occluded liquid with filter paper and drying over calcium chloride in the desiccator was in the range 49-50 °C. Both samples melted at room temperature when mixed with 2-hydroxybiphenyl.

Band Number 3

The material from band number three which was of a pronounced yellow color was recovered from the residue in the benzene still. Crystallization from benzene-n-heptane gave a mixture of yellow prisms and pale yellow needle clusters. Decantation and dilution of the mother liquor with n-heptane produced a second crop of crystals. Evaporation of the solvents left a slight amount of yellow oil of unpleasant odor. Both crystal forms carried the same odor which disappeared after two recrystallizations from benzene-n-heptane. Yield of the yellow crystals was 0.52 g. On a mononitro basis this represents an over-all 30.0 % yield. The yellow oil impurity was also eliminated by crystallization from 50 per cent acetic acid followed by recrystallization from benzene-n-heptane. Both crystal forms melted at 122-123 °C. The yellow prisms lost their color when heated above 100 °C leaving pale-yellow plates. The yellow needle clusters on powdering were observed as plates. A mixed melting point of the two forms showed no depression, and both crystal forms were slightly soluble in boiling water. A slight cooling of such solutions produced pale-yellow rods which, after drying, melted at 125-126 °C. A

mixed melting point of these rods from each crystal form gave 125-126 °C. Both crystal forms upon heating showed a slight amount of sublimation resulting in almost colorless needles melting at 125-126 °C.

Two and one-tenth grams (0.020 mole) of chromic acid in 10 ml. of 65 per cent acetic acid were added to 0.27 g. of the yellow prisms in four ml. of glacial acetic acid. Addition was dropwise from a dropping funnel in a 3-necked flask equipped with stirrer. When addition was completed, the flask was heated to a gentle reflux for one and one-half hours and a 40 per cent formaldehyde solution was added dropwise to the reaction mixture until noticeable reaction ceased. A further 0.5 ml. of formaldehyde was added to insure reduction of the excess chromic acid. The mixture was cooled to room temperature and an equal volume of concentrated HCl was added. The mixture was then extracted with four 10 ml. portions of ether and the ether extract was washed twice with 10 ml. portions of dilute HCl followed by two washings with 10 ml. portions of ice water. Evaporation of the ether gave 0.11 g. of crude p-nitrobenzoic acid, melting at 236 °C. A sample of the yellow prisms and needle clusters weighing 4.33 mg. on nitrogen analysis (Dumas) gave 0.265 ml. of nitrogen at 731.5 mm Hg and 37.5 °C. Calculated for $C_{12}H_9O_3N$: Nitrogen--6.51 %; found: Nitrogen--6.36 %.

Band Number 4

The material in band number four required roughly twice the volume of eluent as for band three material. Recovery was carried out as for the material in band three. Recrystallization from benzene-n-heptane (or from chloroform-n-heptane) gave fairly large, dark-yellow crystal

prisms melting at 139-141 °C. Recrystallization from boiling water (in which solubility was slight) gave crystals lighter in color and melting at 142-144 °C. The dark-yellow crystals sublime around 120 °C to small, well formed, prisms, light-yellow in color and melting in this form at 140-141 °C. Yield of the yellow crystals was 0.36 g. On a mononitro basis this represents a yield of 20.9 per cent based upon o-hydroxybiphenyl. Chromic acid oxidation, carried out as above, produced o-nitrobenzoic acid crystals melting at 147-148 °C. The weight was not determined. A sample of the yellow crystals weighing 8.53 mg. gave 0.542 ml. of nitrogen gas at 732 mm Hg and 35.8 °C. Calculated for $C_{12}H_9O_3N$: Nitrogen--6.51 %; found: Nitrogen--6.68 %.

Band Number 6

The material in band number 6 moved 7-8 cm. down the column in the time required for complete elution of band number four. The color is a bright yellow. Recovery was by extrusion and extraction with 95 per cent alcohol to which a few ml. of dilute HCl had been added. The alcohol was removed by distillation under vacuum (water pump) to a volume of 25 ml. and then 100 ml. of water were added. The precipitated nitrated phenol was extracted with three 20 ml. portions of benzene and the benzene extract was dried in the usual manner. Crystallization from benzene-n-heptane produced pale-yellow, shiny crystal plates melting at 221-222 °C. A sample weighing 5.7 mg. gave 0.59 ml. nitrogen gas at 632.6 mm Hg and 34.25 °C. Calculated for $C_{12}H_8O_5N_2$: Nitrogen--10.77 %; found: Nitrogen --10.94 %.

Band Number 8

An accumulation of the material in band eight from several columns was worked up as previously described (extrusion and extraction) and crystallized from chloroform-n-heptane as light-yellow prismatic crystals melting in the range 222-230 °C. Recrystallization narrowed the range to 226-230 °C. A sample weighing 4.79 mg. gave 0.708 ml. of nitrogen gas at 731.3 mm Hg and 37.5 °C. Calculated for $C_{12}H_7O_7N_3$: Nitrogen--13.76 %; for $C_{12}H_6O_9N_4$: Nitrogen--16.0 %; found: Nitrogen--15.35 %.

Production of Unknown Dinitro Compound Formed in Initial Ester Nitration under Extreme Reaction Conditions

Five grams (0.016 mole) of the sulfonate ester were dissolved in 10 ml. of nitromethane and nitrated at 90 °C with five and one-half ml. of fuming nitric acid (0.13 mole) in five ml. of nitromethane. The reaction mixture was refluxed on the water bath for one and one-half hours and then poured into 150 ml. of ice water after standing for 20 hours. The whitish, gummy mass was collected on the filter and washed free of acid with water. The mass was dissolved in 100 ml. of boiling 95 per cent alcohol and the solution was cooled. Clear, small, prismatic crystals formed within a few minutes. A second crop of crystals was not sought. The crystals were collected on the filter and washed at room temperature with 95 per cent alcohol followed by washing with water. After being dried, the crystals melted at 169-170 °C. The crystals were hydrolyzed in the usual manner with alcoholic KOH. The characteristic red color of nitrated phenols was evident. Acidification of the hydrolysate (diluted to 200 ml. with water) with HCl brought down a gelatinous, whitish-yellow precipitate. This was collected on the filter (water

pump) as tiny, yellow crystals (I). The filtrate was extracted with chloroform in three portions of 25 ml. each. The chloroform solution was extracted with five per cent KOH in three portions of 25 ml. each. The alkaline solution was acidified with HCl and extracted with three 25 ml. portions of benzene. The benzene solution (yellow) was reduced in volume to 10 ml. on the hot plate and addition of an equal volume of n-heptane brought down, on cooling, a small quantity of tiny, yellow crystals (II). These were collected on the filter and dried in the desiccator over calcium chloride. (I) was treated with 50 ml. of boiling benzene for several minutes and filtered hot. The yellow crystals on the filter (III) were dried in the desiccator over calcium chloride. The filtrate was reduced in volume to 15 ml. and 10 ml. of n-heptane was added. Yellow crystals (IV) formed within a short time. (II), (III) and (IV) all undergo a change in state above 185 °C and melt in the range 214-220 °C. The crystal form above 185 °C is iridescent, star-shaped clusters. (II), (III) and (IV) are readily soluble in chloroform and form pale-yellow prismatic crystals on dilution with n-heptane. The melting point of these rises to the range 220-227 °C. A sample weighing 7.2 mg. produced 0.72 ml. nitrogen gas at 731 mm Hg and 34.2 °C. Calculated for $C_{12}H_8O_5N_2$: Nitrogen--10.77 %; found: Nitrogen--10.51 %.

Nitration of the Sulfonate Ester Using Mixed Acid

Two grams (0.0065 mole) of the sulfonate ester were dissolved in six ml. of glacial acetic acid and treated at room temperature with a nitrating mixture made up as follows: 1.4 ml. of concentrated (95 per cent) sulfuric acid (0.026 mole) were added to 0.6 ml. of fuming nitric acid

(0.013 mole) and 0.1 ml. of distilled water. Two ml. of glacial acetic acid were added to the mixed acids and the mixture was added dropwise with shaking to the dissolved ester. The temperature rose 3-4 °C during addition of the nitrating agent. A one and one-half hour reflux period on the water bath followed. The usual procedure of hydrolysis and column recovery of nitrated phenols was followed. The first two bands on the column were the 4'-nitro and 2'-nitro derivatives, respectively. Two more bands were visible; one, a light-orange, narrow band, which moved quite slowly, and the other, the usual reddish-brown band at the top of the column. Yield of the 4'-nitro derivative was 0.415 g. (29.91 per cent) and that of the 2'-nitro derivative, 0.258 g. (18.61 per cent).

Preparation of the 3,5,4'-Trinitro Derivative of 2-Hydroxybiphenyl

A sample of 4'-nitro-2-hydroxybiphenyl weighing 2.239 g. (0.01 mole) was dissolved in 15 ml. of glacial acetic acid and treated dropwise, with stirring, at room temperature with 1.8 ml. (0.042 mole) of fuming nitric acid in two ml. of glacial acetic acid. Precipitation was observed over the period of addition of the nitrating agent. The temperature was held at 25 °C by cooling with tap water. The reaction mixture was allowed to stand for two hours after addition of the nitrating agent. The precipitate (I) was collected on the filter and washed three times with distilled water followed by washing with a five per cent sodium bicarbonate solution and then washed twice more with water. The filtrate was heated and distilled water added drop by drop until a faint cloudiness persisted. Two drops of dilute acetic acid were added to dispel the cloudiness and the solution was cooled. A further precipitate of yellow

crystals was collected on the filter and added to (I). The crystal mass was then taken up in 15 ml. of benzene and 10 ml. of n-heptane and the solvents were evaporated to a volume of three ml. on the hot plate. This treatment was repeated and the crystal mass then dissolved in 15 ml. of benzene followed by drying over anhydrous sodium sulfate. Crystallization was effected by addition of 10 ml. of n-heptane. The crystals were thin, brownish-yellow needles. The yield, 2.285 g. (m. p. 162-163 °C) was 71.93 %. Crystallization was also effected from hot, dilute alcohol. Chromic acid oxidation produced p-nitrobenzoic acid by the procedure previously employed. A sample weighing 5.74 mg. produced 0.75 ml. of nitrogen at 732.6 mm Hg and 34.25 °C. Calculated for $C_{12}H_7O_7N_3$: Nitrogen--13.76 %; found: Nitrogen--13.76 %.

Further Nitration of 4'-Nitro-2-Hydroxybiphenyl in Glacial Acetic Acid Using 1-1 Mole Ratio, Fuming Nitric Acid to Sample

One-half gram (0.0023 mole) of 4'-nitro-2-hydroxybiphenyl was dissolved in seven ml. of glacial acetic acid and nitrated at room temperature with one ml. of a nitration mixture made up of one ml. of fuming nitric acid and nine ml. of glacial acetic acid. The dark colored reaction mixture was set aside for two hours and then poured over 50 ml. of ice water. The yellow precipitate (I) was washed on the filter with cold dilute acetic acid and then three times with water. The filtrate was extracted twice with 15 ml. portions of benzene. (I) was added to the benzene extracts and warmed to effect solution. Fifteen ml. of n-heptane were added and the solution evaporated to near-dryness on the hot plate. The mass was again taken up in benzene and the treatment with n-heptane was repeated. The yellow crystals were dissolved in 25 ml. of benzene,

the solution was dried over anhydrous sodium sulfate and the dried solution was placed on the column. Four bands were discernible. The first two, only, were recovered, number one by elution and number two by extrusion and extraction. The material from band number one was recovered in the usual manner from the benzene still and crystallized readily from benzene-n-heptane as yellow needles with a slight greenish cast, m. p. 194-195 °C.

The yield was 0.19 g., a 31.59 per cent yield on a dinitro basis. After extrusion and alcohol extraction, the material from band number two was crystallized from chloroform-n-heptane as shiny plates of pale-yellow color, m. p. 226-228 °C (II). The yield was 0.073 g., a 11.99 per cent yield on a dinitro basis. A sample of (I) was oxidized with chromic acid employing the usual procedure and a sample of the end product, when mixed with p-nitrobenzoic acid and heated, showed no significant lowering of the m. p. of the latter. A sample of (I) weighing 7.2 mg. produced 0.74 ml. of nitrogen gas at 731.6 mm Hg and 36.3 °C. Calculated for $C_{12}H_8O_5N_2$: Nitrogen--10.77 %; found: Nitrogen--10.73 %. A sample of (II) was oxidized with chromic acid to a product which, when mixed with p-nitrobenzoic acid and heated, showed no lowering of the m. p. of the latter. A sample of (II) weighing 4.08 mg. produced 0.41 ml. of nitrogen gas at 732.5 mm Hg and 34.8 °C. Calculated for $C_{12}H_8O_5N_2$: Nitrogen--10.77 %; found: Nitrogen--10.56 %. A sample of (I) weighing 0.208 g. was dissolved in 10 ml. of glacial acetic acid and nitrated at room temperature with one ml. (0.0032 mole) of a nitrating mixture made up of 1.3 ml. of fuming nitric acid (sp. gr., 1.5) and 8.7 ml. of glacial acetic acid. The mixture was set aside for two hours and then poured into 25 ml.

of ice water. The yellow precipitate was collected on the filter, washed free of acid with water and taken up in benzene. The benzene solution was taken to dryness twice with added n-heptane and the mass was redissolved in 15 ml. of benzene. Addition of an equal volume of n-heptane precipitated brown-yellow needles (III) which, after purification by recrystallization, melted at 162-163 °C. A mixed melting point with 3,5,4'-trinitro-2-hydroxybiphenyl, previously prepared, showed no depression of the melting point of the latter. A sample of (II) weighing 0.1864 g. was dissolved in 10 ml. of glacial acetic acid and nitrated at room temperature with one ml. of the nitrating agent used with (I) above. The reaction mixture was refluxed on the water bath for thirty minutes. The product (IV) was worked up in the same manner as above for (I). The purified product melted in the range 161-163 °C. There was no significant lowering of the melting point of previously prepared 3,5,4'-trinitro-2-hydroxybiphenyl when mixed with (IV).

Further Nitration of 4'-Nitro-2-Hydroxybiphenyl in Nitromethane Using Fuming Nitric Acid

A sample of the prepared 4'-mononitro derivative of 2-hydroxybiphenyl weighing 0.25 g (0.0012 mole) was dissolved in five ml. of nitromethane and nitrated with one ml. of a nitration mixture made up of 0.5 ml. of fuming nitric acid (sp. gr., 1.5) and 9.5 ml. of nitromethane. The reaction mixture was set aside for two hours and then poured over 25 ml. of ice water. The procedure paralleled in all respects that followed when acetic acid was used as the solvent. The same bands developed on the column. The yield of the dinitro derivative melting at 194-195 °C was 0.081 g. (26.79 per cent yield) and that of the dinitro derivative

melting at 226-228 °C was 0.052 g., a yield of 17.20 per cent.

Further Nitration of 4'-Nitro-2-Hydroxybiphenyl in Nitromethane Using Concentrated Nitric Acid

A sample of 4'-nitro-2-hydroxybiphenyl weighing 0.25 g. (0.0012 mole) was dissolved in five ml. of nitromethane and nitrated at room temperature with one ml. of a nitration mixture made up of 0.75 ml. of concentrated nitric acid (sp. gr., 1.42) and 9.25 ml. of nitromethane. The same procedure was employed as that used for nitration when acetic acid was used as the solvent. Two bands developed on the column. Number one, when recovered, yielded less than five mg. of a yellow crystal which crystallized from benzene-n-heptane and decomposed above 225 °C. Band number two was reddish-brown and hung at the top of the column. The quantity of nitrating mixture was then doubled (2 ml.) and the reaction mixture refluxed for 30 minutes with the sample weight 0.25 g. as before. Band patterns from this treatment were similar to those observed when fuming nitric acid was used as the nitrating agent. The yield of the dinitro derivative from the column was 0.117 g. m. p. 194-195 °C. The percentage yield was 38.54. The yield of the second dinitro derivative was lost during extrusion.

Further Nitration of 2'-Nitro-2-Hydroxybiphenyl in Nitromethane with an Acid-Sample Mole Ratio of 1-1

A sample of the prepared 2'-nitro derivative of 2-hydroxybiphenyl weighing 0.25 g. (0.0012 mole) was dissolved in five ml. of nitromethane and one ml. of nitration mixture (0.0012 mole nitric acid) added dropwise at room temperature. The nitrating mixture was made up with 0.5 ml. of fuming nitric acid (sp. gr., 1.5) and 9.5 ml. of nitromethane. There was

immediate darkening of the reaction mixture along with a moderate increase in temperature. The reaction mixture was set aside for two hours and then poured into 25 ml. of ice water. The precipitated mass was washed free of acid in the usual way and taken up in 25 ml. of hot benzene. A fraction (I) failed to dissolve and was recovered on the filter. The filtrate was extracted three times with 10 ml. portions of benzene and the extract was added to (I) in hot benzene solution. The benzene solution was boiled to near-dryness twice with 10 ml. portions of n-heptane, taken up in 25 ml. of benzene and dried over anhydrous sodium sulfate before being placed on the column. The first band, light-orange in color, was eluted. The product, recovered from the benzene still, was starting material and weighed 0.06 g. The material in band number two, deep-lemon in color, was extruded and extracted with 95 per cent alcohol. Crystallization was from hot benzene-n-heptane in pale-yellow, fernlike leaflets (II). The yield was 0.07 g. Fraction (I) was dissolved in 25 ml. of boiling benzene and 10 ml. of n-heptane added to the hot solution. The material crystallized as light-yellow needles which, when heated, underwent a change of state above 200 °C, forming pale-yellow rectangular plates, m. p. 228-229 °C. The yield was 0.02 g. Fraction (II), from the column, when heated, showed the same change of state to rectangular plates, m. p. 228-229 °C. A sample of (I) and (II), when mixed and heated, melted in the range 226-229 °C. The total weight of (I) and (II), 0.09 g., represents a percentage yield of 40.95.

Further Nitration of 2'-Nitro-2-Hydroxybiphenyl in Glacial Acetic Acid with an Acid-Sample Mole Ratio of 4-1

A sample of the prepared 2'-nitro derivative of 2-hydroxybiphenyl

weighing 0.25 g. (0.0012 mole) was dissolved in five ml. of glacial acetic acid and nitrated with four ml. of the nitrating mixture prepared in the preceding experiment. (0.0047 mole nitric acid.) The reaction mixture darkened at once and a precipitate came down during the latter part of the addition period. The product was worked up as usual and placed on the column. There was no insoluble fraction in benzene. Three bands developed on the column. Number one was narrow, dim-yellow in color and moved, under moderate elution with benzene, with sufficient speed to enable extrusion of band number two, the principal band, orange in color, without overlapping. The material crystallized readily from benzene-n-heptane as yellow needles, m. p. 152-153 °C. The weight was 0.17 g., a yield of 48.02 per cent. A sample of the crystals was oxidized with chromic acid to a product which melted in the range of ortho-nitrobenzoic acid. A sample mixed with the latter compound melted at 146-147 °C. A sample of the yellow needles weighing 6.95 mg. produced 0.905 ml. of nitrogen gas at 727.8 mm Hg and 34.8 °C. Calculated for $C_{12}H_7O_7N_3$: Nitrogen--13.77 %; found: Nitrogen--13.60 %.

Attempted Reduction of Tri- and Dinitro Derivatives of 4'-Nitro-2-Hydroxybiphenyl

A sample of the prepared 3,5,4'-trinitro-2-hydroxybiphenyl weighing 0.75 g. was dissolved in 15 ml. of 95 per cent alcohol and transferred to a 200 ml., 3-necked flask equipped with stirrer. The flask was placed on the water bath. A reducing solution of sodium disulfide was prepared by fusing 0.198 g. of sodium sulfide with 9 moles of water of crystallization and 0.08 g. of sulfur. The reducing solution was added slowly to the alcohol solution of the nitrated biphenyl from a

cylindrical dropping funnel inserted into one neck of the flask. The temperature was held at the boiling point of water during the addition and for three hours after addition. The contents of the flask were transferred to a small distilling flask and the alcohol removed under vacuum (water pump). The residue was acidified with a few drops of dilute hydrochloric acid and shaken with 25 ml. of benzene. The benzene solution was washed twice with cold water and dried over anhydrous sodium sulfate. The dried solution was reduced in volume to 10 ml. on the hot plate and 10 ml. of n-heptane added. A precipitate of brownish-yellow crystals proved to be starting material.

A sample of the dinitro derivative, melting at 195 °C, weighing 0.5 g. was dissolved in five ml. of 95 per cent alcohol. To the alcohol solution, 1.92 ml. of 1 N. sodium hydroxide solution was added. The alkaline solution was dark red. Reduction was attempted as before by slow addition to the reaction mixture, in a 3-necked flask, of a fused solution of 0.516 g. of sodium sulfide with 9 moles of water of crystallization and 0.069 g. of sulfur (12 per cent excess). The contents of the flask were filtered hot after stirring for three hours at the temperature of boiling water. A small amount of solid on the filter was free sulfur. The filtrate was taken to dryness under vacuum and 25 ml. of water added to the residue. Neutralization of the dark-red solution with dilute HCl resulted in precipitation of yellow crystals. Extraction with ether removed the precipitate. The ether was evaporated and the residue boiled with 2 N. HCl. The suspension was cooled and the yellow crystals collected on the filter. The weight of starting material recovered was 0.47 g. The filtrate was neutralized with sodium hydroxide and tested for amines by

the carbylamine reaction. There was no odor of isocyanides.

A sample of the above dinitro compound weighing 0.146 g. was carried through the above procedure using a 30 per cent excess of sodium disulfide (175 mg. sodium sulfide with 9 moles of water of crystallization and 23 mg. of sulfur). The recovery of starting material was almost quantitative.

Attempted Reduction of the Dinitro Derivative of 4'-Nitro-2-Hydroxybiphenyl in Aqueous Suspension with Sodium Disulfide

A sample of the dinitro derivative of 4'-nitro-2-hydroxybiphenyl, melting at 194-195 °C, weighing 0.21 g. was suspended in 25 ml. of water in the reaction flask and a fused solution of red sodium disulfide, made up with 0.185 g. of sodium sulfide with 9 moles of water of crystallization and 0.1 g. of sulfur added slowly at the temperature of boiling water. The temperature was held at this point with stirring for three hours and the reaction mixture then filtered hot. The red-colored filtrate was set aside (I). The material on the filter was dissolved in 15 ml. of five per cent sodium hydroxide and filtered through an asbestos mat (water pump). The filtrate was acidified and extracted with benzene. The dried (anhydrous sodium sulfate) benzene solution was reduced in volume to five ml. (hot plate) and five ml. of n-heptane added. Precipitated crystals proved to be starting material. A total of 0.183 g. was recovered. The filtrate (I) was made strongly acidic with HCl and a five per cent sodium hydroxide solution slowly added. Close to the neutral point, a brown flocculent precipitate came down. With the solution still faintly acidic, the mass was collected on the filter. The substance was a brown amorphous solid. Samples dissolved in dilute alkali gave no

characteristic odors with chloroform under conditions for the carbylamine reaction. The yield was insignificant. A sample of the dinitro derivative melting at 226-228 °C was carried through the above procedure with similar results.

CHAPTER V

SUMMARY

The 4'- and 2'-mononitro derivatives of the benzenesulfonate of 2-hydroxybiphenyl were obtained when the ester, in either glacial acetic acid or in nitromethane, was treated with fuming nitric acid.

Glacial acetic acid is favored as the solvent because the nitric acid-sulfonate ester mole ratio is not critical within fairly wide limits (8-1 to 12-1), while nitromethane, when used as the solvent, requires careful control of the nitric acid-ester mole ratio. Oxidation products, as well as higher nitration products, were observed in the reaction when nitromethane was used as the solvent.

Temperature is an important factor in the reaction. At room temperature, the reaction does not proceed, while at steam bath temperatures, maximum yields of both the 4'- and 2'-nitro derivatives were obtained. Above steam bath temperatures, an increase in oxidation products was observed and at the reflux temperature of glacial acetic acid, oxidation products further increase.

A comparison of yields of the 2' and 4' isomers (ca. 21 % and 32 % respectively), lends some support to theories that the respective rings in heavily substituted biphenyls have a common axis but are not coplanar. At the same time, the lower yield of the 2' isomer is indicative

of some degree of steric hindrance at that position. The para position in the substituted ring of the benzenesulfonate of 2-hydroxybiphenyl is open for substitution but the 5-nitro derivative was not identified among the nitration products. This fact, coupled with observed 2' and 4'-nitro derivative production, emphasized previous findings that substitution in the system depends upon the degree of activation or deactivation of the respective rings. Moderate yields of both the 4' and 2'-nitro derivatives were observed when mixed acid was employed as the nitrating agent.

Nitrated ester products were hydrolyzed with alcoholic KOH. Maximum percentage yields for this step were 65 % to 70 %. Hydrolysis in diethylene glycol solution gave lower yields and was inconvenient.

Chromatographic methods were used to separate the nitrophenols. Columns were packed with "Magnesol" (trade name), a synthetic magnesium silicate. The nitrophenols were spread out as colored bands in this adsorbent in the same order, generally, as their corresponding acidities and/or solubilities in the eluent, benzene. Specifications have been given for maximum operating efficiency of these columns. Their employment made possible the finding and isolation of the 2'-mononitro derivative, as yet unreported as a direct nitration product of 2-hydroxybiphenyl esters. It has been shown that the adsorbent used, while not ideal, satisfactorily meets requirements for the fairly strong adsorbent demanded by the mixture of low and high-acidity type nitrophenol products.

Proof of structure of the two mononitro derivatives rests on chromic acid oxidation to their corresponding nitrobenzoic acids and conventional nitrogen analysis.

Treatment of 4'-nitro-2-hydroxybiphenyl with fuming nitric acid

led to the 3,5,4'-trinitro derivative when either glacial acetic acid or nitromethane was used as the solvent and when the nitric acid-phenol mole ratio was 4-1. When the mole ratio was 1-1, two dinitro derivatives were separable in the column. Both of these dinitro derivatives gave 3,5,4'-trinitro-2-hydroxybiphenyl upon further nitration using a nitric acid-phenol mole ratio of 4-1. Thus, one of the dinitro derivatives is the 3,4'- and the other the 5,4'-dinitro-2-hydroxybiphenyl.

Treatment of 2'-nitro-2-hydroxybiphenyl with fuming nitric acid resulted in a trinitro phenol, assumed to be the 3,5,2'-trinitro derivative, when glacial acetic acid was used as the solvent and the nitric acid-phenol mole ratio was 4-1. When the nitric acid-phenol mole ratio was lowered to 1-1, only one band of appreciable width was observed in the column. Nitrogen analysis of this material indicated a dinitro structure.

A description of band patterns in the column has been given for each nitration reaction which was investigated. Only the principal nitration products which gave bands of appreciable width in the column were reported in this investigation. The presence of many narrow bands, indicative of negligible yields, unreported here, suggests that all possible nitration products were obtained and that much work remains to be done in the solution of the general problem of nitration of hydroxybiphenyls.

Partial reduction of dinitro derivatives of 2-hydroxybiphenyls where each ring contains one nitro group, was not accomplished. Sodium disulfide in both alcoholic and aqueous media was employed in the attempts at partial reduction. Negative results indicate that this part of the work must be considered as a preliminary investigation.

BIBLIOGRAPHY

(1) Hill, H. B., and Hale, W. J., Am. Chem. J., 33, 1-21 (1905).

(2) Hazlet, S. E., J. Am. Chem. Soc., 59, 1087 (1937).

(3) Hazlet, S. E., Alliger, Glen, and Tiede, Ralph, J. Am. Chem. Soc., 61, 1447 (1939).

(4) Hammick, D. L., and Illingworth, W. S., J. Chem. Soc., 133, 2358 (1930).

(5) Latimer, W. M., and Porter, C. W., J. Am. Chem. Soc., 52, 206 (1930).

(6) Kenyon, Joseph, and Robinson, P. H., J. Chem. Soc., 129, 3050 (1926).

(7) Bell, Frank, and Kenyon, Joseph, J. Chem. Soc., 129, 3044 (1926).

(8) Raiford, L. C., and Colbert, J. C., J. Am. Chem. Soc., 47, 1457 (1925).

(9) Colbert, J. C., and others, J. Am. Chem. Soc., 56, 202, 2128 (1934).

(10) Hazlet, S. E., and Kornberg, H. A., J. Am. Chem. Soc., 61, 3037 (1939).

(11) Hazlet, S. E., Hensley, L. C., and Jass, Herman, J. Am. Chem. Soc., 64, 2449 (1942).

(12) Hensley, L. C., and Hazlet, S. E., J. Am. Chem. Soc., 65, 987 (1943).

(13) Hazlet, S. E., Stauffer, D. A., and Hensley, L. C., J. Am. Chem. Soc., 66, 1245 (1944).

(14) Holleman, A. F., Chem. Rev., 1, 217 (1924).

(15) Hazlet, S. E., Stauffer, D. A., Hensley, L. C., and Van Orden, H. O., J. Am. Chem. Soc., 64, 2505 (1942).

(16) Stanley, W. M. and Adams, Roger, J. Am. Chem. Soc., 52, 1200 (1930).

(17) Watson, H. B., "Modern Theories in Organic Chemistry," 2nd ed., Oxford, The Clarendon Press, 1941, p. 246.

(18) Blakey, William, and Scarborough, H. A., J. Chem. Soc., 130, 3000 (1927).

(19) Scarborough, H. A., and Waters, W. A., J. Chem. Soc., 130, 1133 (1927).

(20) Ibid., p. 89.

(21) Hazlet, S. E., Harris, J. M., and Van Orden, H. O., J. Am. Chem. Soc., 63, 1890 (1941).

(22) Hazlet, S. E., and Hensley, L. C., J. Am. Chem. Soc., 69, 708 (1947).

(23) Jones, Brynmor, and Chapman, Frank, J. Chem. Soc., 155, 1829-32 (1952).

(24) Campbell, I. G. M., and Morrill, D. J., J. Soc. Chem. and Ind., 72, 1229 (1953).

(25) English, S. G., "Bromo and Nitro Derivatives of 2-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1940.

(26) Moreau, J. M., "Bromination of 5-nitro-2-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1941.

(27) Christiansen, W. G., and Harris, S. E., J. Am. Pharm. Asso., 22, 723 (1933).

(28) Fox, D. W., "Properties of 2-hydroxy-2-nitrobiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1951.

(29) Hanan, J. A., "The Dissociation Constants and Solubilities of Nitro Derivatives of 2- and 4-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1954.

(30) Robinson, C. F., "Nitration of the Esters of 3-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1953.

(31) Frow, F. R., "The Mononitration of Ortho-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1949.

(32) Benford, G. A., and Ingold, C. K., J. Chem. Soc., 141, 954 (1938).

(33) Remick, A. E., "Electronic Interpretations of Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, 1949.

(34) Matsuzak, C. A., "Preparation and Characterization of 3-hydroxy-2-nitrobiphenyl and 3-hydroxy-6-nitrobiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1953.

(35) Sonnenfeld, R. J., "Concentration-Solvent Studies in the Nitration of 2- and 4-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1954.

(36) Fox, D. W., "Studies of the Nitration of 3-hydroxybiphenyl," Ph. D. dissertation, University of Oklahoma, 1953.

(37) Shriner, R. L., and Fuson, R. C., "The Identification of Organic Compounds," 3d ed., John Wiley and Sons, Inc., New York, 1948, p. 133.

(38) Alexander, E. R., "Ionic Organic Reactions," John Wiley and Sons, Inc., New York, 1950, p. 250.

(39) Soloway, Saul, and Santoro, Angelo, Anal. Chem., 27, 798 (1955).

(40) Schultz, von Gustave, Ann. 174, 222 (1874).

(41) Ward, W. H., "The Reduction of 3,5-dinitro-2-hydroxybiphenyl," Master's thesis, Department of Chemistry, University of Oklahoma, 1943.

(42) Guglialmelli, L., and Franco, M. R., Anales Asoc. quim. Argentina 17, 340-51 (1929).

(43) Griffin, K. P., and Peterson, W. D., Org. Syn., 21, 20 (1941).

(44) Hartman, W. W., and Silloway, H. L., Org. Syn., 25, 5 (1945).

(45) Mascarelli, L., and Gatti, D., C. A., 24, 2454 (1929).

(46) Blanksma, J. J., and van der Weyden, W. M., Rec. trav. Chim., 59, 629 (1940).

(47) Brand, K., J. prakt. Chem., 74, 449-72 (1906).

(48) Verkade, P. E., van Dijk, C. P., and Meerburg, W., Rec. trav. Chim., 65, 346 (1946).

(49) Verkade, P. E., and Witjens, P. H., Rec. trav. Chim., 65, 371 (1946).