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SOME COMPARISONS OF DIBENZOFURAN AND DIBENZOTHIOPHENE TYPES

by

Donald Levern Esmay

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Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

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TABLE OF CONTENTS

INTRODUCTION

Dibenzofuran (I) was first used in these laboratories in attempts to prepare certain furan derivatives by oxidative degradation.[1] Although dibenzofuran and some of its derivatives were found to be resistant to attack, an interest in the chemistry of dibenzofuran had been aroused which resulted in the initiation of numerous studies[2,3,4,5,6,7,8,9] directed toward bringing order to the confusing and incomplete literature on dibenzofurans. The early recognition that a reduced dibenzofuran nucleus forms part of the skeletal structure of morphine[10] resulted in extensive experiments for the purpose of preparing derivatives of dibenzofuran which might be of

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[1] H. Oatfield, Unpublished Masters Thesis, Iowa State College, 1933.

[2] D. M. Hayes, Unpublished Masters Thesis, Iowa State College, 1934.

[3] M. W. Van Ess, Doctoral Dissertation, Iowa State College, 1936.

[4] P. R. Van Ess, Doctoral Dissertation, Iowa State College, 1936.

[5] L. C. Cheney, Doctoral Dissertation, Iowa State College, 1938.

[6] J. Swislowsky, Doctoral Dissertation, Iowa State College, 1939.

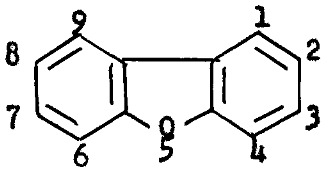
[7] H. B. Willis, Doctoral Dissertation, Iowa State College, 1943.

[8] J. R. Thirtle, Doctoral Dissertation, Iowa State College, 1943.

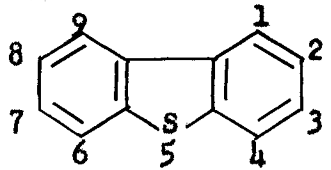
[9] J. A. Hogg, Doctoral Dissertation, Iowa State College, 1944.

[10] J. M. Gulland and R. Robinson, Mem. Proc. Manchester Lit. Phil. Soc., 69, 79 (1925) /C. A., 20, 765 (1926)/.

value as analgesics.[11,12,13,14,15,16] The wartime interest in antimalarials suggested the preparation and testing of a number of dibenzofuran derivatives patterned after the known active synthetic types.[17] This latter work was also extended to include a few selected derivatives of dibenzothiophene (II).



(I)



(II)

In connection with studies on various metalation reactions which were being carried out at that time,[18] some of the initial investigations on the chemistry of dibenzofuran and its derivatives were centered on reactions with organometallic compounds.[19,20] The observation that *n*-butyllithium unexpectedly metalated dibenzofuran

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[11] W. G. Bywater, Doctoral Dissertation, Iowa State College, 1934.

[12] W. H. Kirkpatrick, Doctoral Dissertation, Iowa State College, 1935.

[13] E. W. Smith, Doctoral Dissertation, Iowa State College, 1936.

[14] C. W. Bradley, Doctoral Dissertation, Iowa State College, 1937.

[15] P. T. Parker, Doctoral Dissertation, Iowa State College, 1937.

[16] F. A. Yoeman, Doctoral Dissertation, Iowa State College, 1944.

[17] S. Avakian, Doctoral Dissertation, Iowa State College, 1944.

[18] For a comprehensive review of the early metalation studies, see H. Gilman and R. V. Young, *J. Org. Chem.*, *1*, 315 (1936).

[19] H. Gilman and R. V. Young, *J. Am. Chem. Soc.*, *56*, 1415 (1934).

[20] H. Gilman and R. V. Young, *ibid.*, *57*, 1121 (1935).

in the 4-position, _ortho_ to the ether linkage, gave impetus to numerous metalation experiments on dibenzofuran derivatives and related types[21] which culminated in formation of the rule:*

> All aromatic polynuclear compounds possessing either ether or tetiary amino substituents can be metalated with ease by _organoalkali_ compounds, and, in every case, the entering alkali metal will replace a nuclear hydrogen _ortho_ to those substituents.

Two notable exceptions were observed when attempts were made to extend this rule to cover analagous sulfur-containing compounds. Phenylcalcium iodide metalated dibenzothiophene in the 3-position[22] (_meta_ to the sulfide linkage), and n-butyllithium metalated methyl phenyl sulfide laterally to give phenylmercaptoacetic acid on carbonation.[23]

After a measure of order had been brought to the basis chemistry of dibenzofuran, a natural step further was to the investigation of the sulfur analog dibenzothiophene.[24] Nitration of dibenzothiophene had only recently been established[25] as giving a 2-substituted derivative in contrast to the known formation of

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*See reference 5, p. 113.

[21] H. Gilman, L. C. Cheney and H. B. Willis, _ibid._, _61_, 951 (1939).

[22] H. Gilman, A. L. Jacoby and H. A. Pacevitz, _J. Org. Chem._, _3_, 120 (1938).

[23] H. Gilman and F. J. Webb, _J. Am. Chem. Soc._, _62_, 987 (1940).

[24] A. L. Jacoby, Doctoral Dissertation, Iowa State College, 1938.

[25] C. Courtot, _Compt. rend._, _198_, 2260 (1934).

3-nitrodibenzofuran in a similar nitration of dibenzofuran.[26] This discrepancy, coupled with the already mentioned anomalous metalation of dibenzothiophene by phenylcalcium iodide, made even the most fundamental reaction studies on dibenzothiophene of interest for comparative purposes.[16,24,27] Additional interest in dibenzothiophene was provided by the observation that replacement of oxygen by sulfur in certain organic compounds may produce desirable characteristics in their physiological properties, and also by the possibility of greatly increasing the number of interesting compounds by oxidation of the sulfides to sulfoxides or sulfones. The latter types are of particular interest since the *meta*-directing influence of the sulfoxide or sulfone group is in contrast to the *ortho*-directing influence of the sulfide linkage, and thus greatly adds to the possibility of preparing selected derivatives by direct substitution.

Direct comparison of the relative orienting effects of oxygen and sulfur was the objective of some initial studies on the chemistry of phenoxathiin (III).[28] From the results obtained, the greater influence of oxygen over sulfur was generally observed. Further confirmation of these results was obtained by a comparison of the

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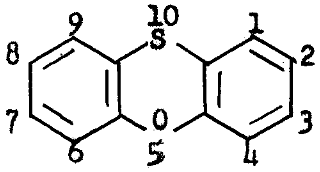
[26] N. M. Cullinane, *J. Chem. Soc.*, 2267 (1930).

[27] J. F. Nobis, Doctoral Dissertation, Iowa State College, 1948.

[28] H. Gilman, M. W. Van Ess, H. B. Willis and C. G. Stuckwisch, *J. Am. Chem. Soc.*, *62*, 2606 (1940).

reactivities of thianthrene (IV) and dibenzo-p-dioxin (V) in a few selected reactions.[29]



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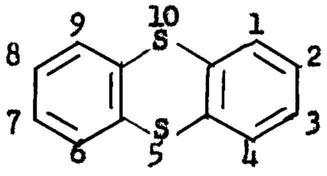

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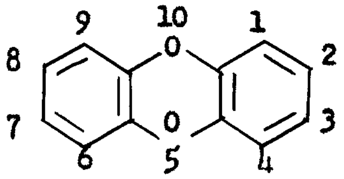
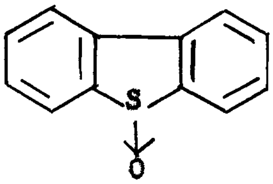


(V)

The work embodied in this thesis was undertaken with the objectives of correlating and extending the knowledge of the orientations in dibenzofuran and dibenzothiophene derivatives and related types. In keeping with the interest in compounds of possible pharmacological use, many of the investigations were designed with the additional purpose in mind of preparing compounds for physiological testing. Particular attention was centered on the preparation and study of derivatives of dibenzothiophene, dibenzothiophene-5-oxide (VI) and dibenzothiophene-5-dioxide (VII).



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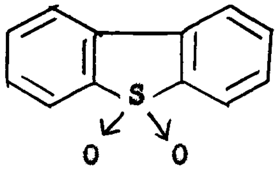

(VII)

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[29] H. Gilman and C. G. Stuckwisch, ibid., 65, 1461 (1943).

HISTORICAL

The purpose of the literature survey to be discussed in the following pages is to summarize and correlate the available information and data which are pertinent to the experimental work carried out during the course of this study. The discussion is limited to a consideration of the five heterocycles: dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-*p*-dioxin.

Throughout the course of this investigation frequent recourse was made to the appropriate sections of the books on heterocycles by Morton[30] and Elderfield,[31] to the phenoxathiin review article by Deasy,[32] and to the chapter on organometallic compounds by Gilman.[33] The naming and the numbering of all compounds have been made to conform with the current *Chemical Abstracts* usage.

The final portion of the literature survey consists of a table which is an extension of the compilation of known derivatives of dibenzothiophene made earlier by Nobis,[27] and a complete bibliography of the published work on dibenzothiophene. The literature was covered thoroughly through 1950, and as completely as possible through

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[30] A. A. Morton, "The Chemistry of Heterocyclic Compounds", McGraw-Hill Book Company, Inc., New York, N. Y., 1946.

[31] R. C. Elderfield, "Heterocyclic Compounds", John Wiley and Sons, Inc., New York, N. Y., 1951, Vol. 2.

[32] C. L. Deasy, *Chem. Rev.*, *32*, 173 (1943).

[33] H. Gilman, "Organic Chemistry", 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, Vol. 1, p. 489.

September, 1951.

Metalation Reactions

The metalation* reaction with a number of polynuclear heterocycles has proved to be a valuable method for the introduction of functional groups into positions not available by other direct substitution reactions. The present review has been restricted to a summary and some comparisons of the various metalation reactions which have been accomplished with dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin.

The metalation of dibenzofuran and its derivatives has been studied more extensively than that of any of the other four heterocycles or their derivatives under consideration. The results of the various metalation reactions of dibenzofuran and its derivatives have been thoroughly reviewed by previous workers in these laboratories[5,6,7,11,12,34,35] thus making leading references to the published literature conveniently available. Consequently, only a brief summary of the more illustrative metalation reactions of dibenzofuran will be given.

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*A term proposed[19] for those substitution reactions which involve the replacement of hydrogen by a metal to give a true organometallic compound.

[34] R. L. Bebb, Doctoral Dissertation, Iowa State College, 1938.

[35] F. J. Webb, Doctoral Dissertation, Iowa State College, 1941.

Direct monometalation of dibenzofuran has been shown to take place in the 4-position whether the metalating agent is a metal,[19] a heavy metal salt like mercuric acetate[19] or thallic chloride,[36] an organo-alkali compound,[19,20] or an organo-metallic compound such as diethylstrontium[37] or diethylbarium.[38] One apparent anomaly is the metalation of dibenzofuran with ethylaluminum iodides $[(C_2H_5)_2AlI + C_2H_5AlI_2]$ or aluminum iodide itself to yield, subsequent to carbonation, 2-dibenzofurancarboxylic acid.[39] However, no acid product was isolated on carbonating the mixture from the reaction of dibenzofuran with triethylaluminum. These results were interpreted as indicating that possibly metalation with the aluminum halide is the initial step involved in a Friedel-Crafts type of reaction. The explanation of the observation that direct arsonation of dibenzofuran gives a 2-substituted product[40] may lie in the fact that a substantial though catalytic amount of aluminum chloride was employed.

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[36] H. Gilman and R. K. Abbott, J. Am. Chem. Soc., 65, 122 (1943).

[37] H. Gilman, R. N. Meals, G. J. O'Donnell and L. A. Woods, ibid., 65, 268 (1943).

[38] H. Gilman, A. H. Haubein, G. J. O'Donnell and L. A. Woods, ibid., 67, 922 (1945).

[39] H. Gilman and A. H. Haubein, ibid., 67, 1033 (1945).

[40] W. C. Davies and C. W. Othen, J. Chem. Soc., 1236 (1936).

Metalation of 2-methoxydibenzofuran with n-butyllithium[34,41] results in substitution in both the 1- and 3-positions, while metalation of 2-hydroxydibenzofuran gives only 2-hydroxy-1-dibenzofuryllithium.[42] The reaction of 4-methoxydibenzofuran with n-butyllithium[5,21] or n-butylsodium[20,21] gives on carbonation about equal amounts of 4-methoxy-6-dibenzofurancarboxylic acid and 4-methoxy-3-dibenzofurancarboxylic acid, whereas a similar reaction with 4-hydroxydibenzofuran yields only 4-hydroxy-6-dibenzofurancarboxylic acid.[42] 4-Methyldibenzofuran was metalated by n-butylsodium to give, subsequent to carbonation, 6-methyl-4-dibenzofurancarboxylic acid.[20]

The initial reaction of 2-bromodibenzofuran with n-butyllithium[21] did not form the expected 2-dibenzofuryllithium by halogen-metal interconversion but yielded 2-bromo-4-dibenzofuryllithium instead. It was shown later,[43] however, that by treating 2-bromodibenzofuran with n-butyllithium for only a short period of time, excellent yields of the 2-dibenzofuryllithium could be obtained. On the other hand, the reaction of 2, 8-dibromodibenzofuran with n-butyllithium gave only 2,8-dibenzofurandicarboxylic acid on carbonation,[44] although replacement

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[41] H. Gilman and R. L. Bebb, J. Am. Chem. Soc., 61, 109 (1939).

[42] H. Gilman, H. B. Willis, T. H. Cook, F. J. Webb and R. N. Meals, ibid., 62, 667 (1940).

[43] H. Gilman, W. Langham and H. B. Willis, ibid., 62, 346 (1940).

[44] H. Gilman, H. B. Willis and J. Swislowsky, ibid., 61, 1371 (1939).

of the n-butyllithium with phenylcalcium iodide was found[45] to give dimetalation with 2,8-dibromo-4,6-dibenzofurandicarboxylic acid being the only product isolated. The reaction of 2,8-dibromodibenzofuran with benzylsodium or phenylsodium, however, gave only acidic gums which could not be purified or identified.[45]

The dimetalation of 2,8-dibromodibenzofuran with phenylcalcium iodide is particularly interesting since the parent dibenzofuran is dimetalated in appreciable yields only with the more reactive organosodium or organopotassium compounds.[20] n-Butyllithium reacts with dibenzofuran in ether solution to give 4-dibenzofuryllithium almost exclusively, although there is one brief report[**] that a small amount of dimetalation occurred when the reaction mixture was refluxed for periods of four to five hours.

The reaction of dibenzofuran with lithium is noteworthy in that only ring-rupture was observed instead of the expected reduction or metalation.[14] When refluxing dioxane was used as the reaction medium, a 78% yield of o-hydroxybiphenyl was obtained after twelve hours of stirring. The same reaction proceeded at a much slower rate in diethyl ether with a 60% yield of the o-hydroxybiphenyl being obtained after a 36-hour period of shaking in a Schlenk tube.

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[45] R. E. Dickey, Unpublished Studies.

[**] See reference 34, p. 40.

Metalation studies on dibenzothiophene have not been as extensive as those on the closely related dibenzofuran, largely because, with a few notable exceptions, dibenzothiophene and dibenzofuran and their derivatives have been found to react analagously with organometallic reagents. The following survey has been made as complete as possible in order to bring together in one place the results of all the metalation reactions that have been carried out with dibenzothiophene and its derivatives and thereby compile and supplement the scattered reviews which have been made by others.[5,24,27,34,35,46] The reaction of dibenzothiophene with n-butyllithium has been shown to yield 4-dibenzothienyllithium in a manner strictly analagous to dibenzofuran.[28,41,47,48,49,50,51,52,53,54] Monometalation in the 4-position was observed also with phenyllithium,[47] α-naphthyllithium,[47]

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[46] H. A. Pacevitz, Doctoral Dissertation, Iowa State College, 1940.

[47] H. Gilman and A. L. Jacoby, J. Org. Chem., 3, 108 (1938).

[48] R. L. Bebb, Iowa State Coll. J. Sci., 13, 41 (1938).

[49] A. L. Jacoby, ibid., 13, 70 (1938).

[50] H. Gilman, F. W. Moore and O. Baine, J. Am. Chem. Soc., 63, 2479 (1941).

[51] H. Gilman and C. G. Stuckwisch, ibid., 67, 877 (1945).

[52] H. Gilman and J. F. Nobis, ibid., 67, 1479 (1945).

[53] H. Gilman and S. Avakian, ibid., 68, 1514 (1946).

[54] K. E. Lentz, Unpublished Masters Thesis, Iowa State College, 1949.

n-amylsodium,[41] phenylsodium,[41] diethylstrontium,[37] diethylcalcium,[38] and diethylbarium.[38] No reaction occurred between dibenzothiophene and p-anisyllithium[47] or triphenylmethylsodium.[41]

The possibility of selective nuclear metalation of aromatic compounds in general by the proper choice of organometallic reagents was again demonstrated when it was established[22] that the reaction of dibenzothiophene with phenylcalcium iodide gave after carbonation 3-dibenzothiophenecarboxylic acid. This result was unexpected and in direct contrast to the corresponding metalation of dibenzofuran which yields 4-dibenzofurancarboxylic acid after carbonation.[55]

In an attempt to extend the work of Haubein[39] on the metalation of dibenzofuran with aluminum halides to dibenzothiophene, Nobis[27,56] heated dibenzothiophene with aluminum chloride, bromide and iodide in sealed tubes under a variety of conditions. No acid was obtained on carbonation of the reaction mixtures.

No mercurial derivative could be isolated when mercuric acetate was allowed to react with dibenzothiophene in boiling alcohol.[24,47] However, mercuration appeared to be effected when the calculated quantity of mercuric acetate was slowly added to a melt of dibenzothiophene at 140-145° since acetic acid distilled from the mixture.

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[55] H. Gilman, R. H. Kirby, M. Lichterwalter and R. V. Young, Rec. trav. chim., 55, 79 (1936).

[56] H. Gilman and J. F. Nobis, J. Am. Chem. Soc., 71, 274 (1949).

The compound isolated could not be purified and was believed to be dibenzothienylmercuric acetate contaminated with a dimercurial product, because analysis showed a mercury content about 2% too high for a mono-derivative.

The only attempted metalation of a nuclearly substituted derivative of dibenzothiophene was made by Pacevitz.[46] He reacted 2-bromodibenzothiophene with n-butyllithium in an effort to determine whether metalation or halogen-metal interconversion would predominate. Only 2-dibenzothiophenecarboxylic acid was isolated after carbonation thus indicating that halogen-metal interconversion occurred exclusively.

The first successful nuclear metalation of a sulfoxide was accomplished by treating dibenzothiophene-5-oxide with n-butyllithium at -10°.[57] The acid obtained on carbonation was established as being 4-dibenzothiophenecarboxylic acid, thereby showing that reduction of the sulfoxide group occurred along with the nuclear metalation. The reduction probably was to be expected since ethylmagnesium bromide was found[58] to effectively reduce dibenzothiophene-5-oxide to dibenzothiophene, although phenylmagnesium bromide showed no reaction.

Initial attempts to metalate dibenzothiophene-5-dioxide with n-butyllithium yielded only acidic gums after carbonation.[59] The

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[57] H. Gilman and D. L. Esmay, ibid., 73, in press (1951).

[58] C. Courtot and C. Pomonis, Compt. rend., 182, 893 (1926).

[59] H. Gilman and F. J. Webb, J. Am. Chem. Soc., 71, 4062 (1949).

use of reduced temperatures (-20° to -30°) was found[60] to effectively control the reaction and permit satisfactory metalation. If only one equivalent of n-butyllithium was used, carbonation gave 4-carboxydibenzothiophene-5-dioxide. The use of two equivalents of the metalating agent gave mostly 4,6-dicarboxydibenzothiophene-5-dioxide along with some 4-carboxydibenzothiophene-5-dioxide, while three or more equivalents gave 4,6-dicarboxydibenzothiophene-5-dioxide entirely. No other successful attempt at dimetalation of dibenzothiophene or any of its derivatives including the oxides has been reported.

On comparing the various metalation reactions of dibenzofuran and dibenzothiophene, it is immediately apparent that dibenzofuran must be more susceptible to reaction with organometallic compounds than is dibenzothiophene. A few reasons are as follows: (1) dibenzofuran was readily dimetalated with n-butylsodium while n-amylsodium gave only monometalation of dibenzothiophene, (2) aluminum iodide metalated dibenzofuran but showed no reaction with dibenzothiophene, (3) dibenzofuran was readily mercurated, whereas mercuration of dibenzothiophene was largely unsuccessful, and (4) the reaction of 2-bromodibenzothiophene with n-butyllithium results only in halogen-metal interconversion while the same reaction with 2-bromodibenzofuran may proceed further to give nuclear metalation. Similar observations by others led to an attempt to determine the relative activities of

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[60] This Thesis, p. 95.

dibenzofuran and dibenzothiophene toward metalation. Dibenzofuran was established as being the more reactive by three different procedures.[28] First, only 4-dibenzofurancarboxylic acid was isolated from a competitive metalation of a mixture of dibenzofuran and dibenzothiophene with n-butyllithium followed by carbonation. Second, preformed 4-dibenzothienyllithium metalated dibenzofuran, whereas preformed 4-dibenzofuryllithium did not metalate dibenzothiophene. Third, separate metalations showed dibenzofuran to be metalated more readily than dibenzothiophene. The comparisons were later extended to include the related nitrogen-containing heterocycle N-ethylcarbazole.[51] The results established that the relative rates of metalation of these three compounds by n-butyllithium were:

dibenzofuran > dibenzothiophene > N-ethylcarbazole

The metalation of phenoxathiin by n-butyllithium in the nuclear position ortho to oxygen[28] further established the greater influence of oxygen over sulfur in directing the course of substitution. Additional studies again demonstrated the ability of phenylcalcium iodide to behave anomalously in metalation reactions. The acid obtained on refluxing phenoxathiin with phenylcalcium iodide in ether followed by carbonation was found to be different from the acid obtained by a similar reaction with n-butyllithium. Although the melting points of the two acids were in agreement, a mixed melt~~h~~ing point showed a depression. It was reported later[61] that a dibasic acid which was isolated

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[61] S. Avakian, Unpublished Studies. See reference ~~31~~ 35, p. 36.

in small amounts from a metalation of phenoxathiin with n-butyllithium by the previously mentioned procedure[28] was identical with the acid from the phenylcalcium iodide reaction since a mixed melting point showed no depression. No definite conclusion can be made on the basis of the meager data available.

A fifteen-minute period of reaction between 2-bromophenoxathiin and n-butyllithium was found[28] to give sufficient 2-phenoxathiinyllithium to yield 63.7% of pure 2-phenoxathiincarboxylic acid on carbonation. No report could be found of the use of a longer reaction period in order to determine whether a two-stage metalation might occur as was the case with the related 2-bromodibenzofuran.

Further evidence that oxygen-containing heterocycles are more easily metalated than the corresponding sulfur-containing compounds was obtained by a comparison of thianthrene and dibenzo-p-dioxin.[29] Treatment of the sulfur compound with n-butyllithium gave largely monometalation ortho to the hetero atom together with a small amount of dimetalation. The oxygen compound, however, gave only 1,9-dimetalation under the same conditions and consequently must be more readily substituted. No other metalation studies of thianthrene or dibenzo-p-dioxin or their derivatives, including the oxides of thianthrene, have been reported.

Oxidation Reactions

The oxidation reactions which we were concerned with for purposes of comparison were those involving oxidation of a heterocyclic sulfide to a sulfoxide or sulfone. Consequently, the following discussion is limited to dibenzothiophene, phenoxathiin, and thianthrene and their derivatives and does not include dibenzofuran or dibenzo-p-dioxin or their derivatives.

Dibenzothiophene-5-oxide has been prepared by oxidation of dibenzothiophene with nitric acid,[58,62,63,64] chromic acid,[65] 30% aqueous hydrogen peroxide,[64,65,66,67] chlorine,[68] and iodosobenzene.[69] Hydrogen peroxide or chlorine, both under carefully controlled conditions, appear to be the reagents of choice; both give good yields

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[62] C. Courtot, L. Nicolas and T. H. Liang, Compt. rend., 186, 1624 (1928).

[63] N. M. Cullinane, C. G. Davies and G. I. Davies, J. Chem. Soc., 1435 (1936).

[64] F. Muth and B. Putzer, PB L 63936, Enlargement Print of Frames 1004-1010 of FIAT Microfilm Reel C 60, PB 17657, March, 1933. 7p. Photo. Ger. 5, p. 568a, #7, May 16, 1947.

[65] M. Chaix, Bull. soc. chim. France, 53, 700 (1933).

[66] A. H. Schlesinger and D. T. Mowry, J. Am. Chem. Soc., 73, 2614 (1951)

[67] H. Gilman and D. L. Esmay, ibid., 74, in press (1952).

[68] R. K. Brown, R. G. Christiansen and R. B. Sandin, ibid., 70, 1748 (1948).

[69] R. K. Brown, N. A. Nelson and J. C. Wood, ibid., 74, in press (1952).

of easily purified sulfoxide. With nitric acid, the competing reaction of nuclear nitration occurs appreciably, while with chromic acid and iodosobenzene, the meager reports concerning their use makes a satisfactory comparison impossible.

Chromic acid[22,66,70,71] and 30% aqueous hydrogen peroxide[52,64,65,67,72] have both been used successfully to prepare dibenzothiophene-5-dioxide from dibenzothiophene. Although Schlesinger and Mowry[66] report that they were unable to obtain the dioxide by hydrogen peroxide oxidation, other workers have found the method eminently satisfactory. It should be pointed out that two different groups of workers[65,67] concluded that the oxidation of dibenzothiophene to dibenzothiophene-5-dioxide with hydrogen peroxide was a stepwise process since the monoxide could be obtained intermediately with proper choice of reaction time and conditions.

The number of known derivatives of dibenzothiophene-5-oxide is relatively few, whereas there are a large number of derivatives of dibenzothiophene-5-dioxide reported in the literature.[73] Many of the latter were prepared indirectly, although in both cases direct oxidation appears feasible with any derivative which does not contain

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[70] J. Stenhouse, Ann., 156, 332 (1870).

[71] C. Graebe, ibid., 174, 185 (1874).

[72] G. A. Martin, Iowa State Coll. J. Sci., 21, 38 (1946).

[73] See reference 27, p. 25 and This Thesis, p. 54.

an easily oxidized or a strongly negative functional group. The report of Neumoyer and Amstutz[74] that 2,8-diacetaminodibenzothiophene could not be oxidized to the dioxide was later shown to be in error[27,56] since the sulfone could be obtained quite readily using either hydrogen peroxide or sodium hypochlorite as the oxidizing agent. Brown, Nelson and Wood[69] were unable to prepare 2-nitrodibenzothiophene-5-dioxide, 2,8-dinitrodibenzothiophene-5-oxide, or 2,8-dinitrodibenzothiophene-5-dioxide by direct oxidation. They attributed the failures to the ability of the nitro group to effectively withdraw electrons from the remainder of the molecule and thus decrease the ability of the sulfur atom to coordinate with atoms of oxygen. This postulate is supported by the work of Bordwell and Albisetti[75] who found that a nitro group in the 3-position of thianaphthene effectively prevented sulfone formation.

The preparation of phenoxathiin-10-oxide has been carried out using a mixture of concentrated nitric acid (d.1.45) and glacial acetic acid (no nuclear nitration reported),[76] or a glacial acetic acid solution of phenoxathiin and 30% aqueous hydrogen peroxide, either in

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[74] C. R. Neumoyer and E. D. Amstutz, J. Am. Chem. Soc., 69, 1920 (1947).

[75] F. G. Bordwell and C. J. Albisetti, ibid., 70, 1955 (1948).

[76] M. Tomita and T. Ikeda, J. Pharm. Soc. Japan, 58, 780 (in German, 231) (1938).

slight excess[77] or in excess under carefully controlled conditions.[67] Also, when phenoxathiin was dissolved in cold concentrated sulfuric acid and allowed to stand for three hours, one-half of it was converted to the monoxide.[77] The reaction apparently is reversible since phenoxathiin could be isolated in yields up to 35% on treating phenoxathiin-10-oxide in the same manner.

Phenoxathiin-10-dioxide was obtained by reacting phenoxathiin[78] or phenoxathiin-10-oxide[76] with chromic acid or by treating a glacial acetic acid solution of phenoxathiin with hydrogen peroxide.[67,77] Various derivatives of phenoxathiin have been satisfactorily oxidized to either the monoxide or the dioxide by following procedures similar to those above. In contrast to the unsuccessful attempts to prepare 2,8-dinitrodibenzothiophene-5-dioxide, 3,7-dinitrophenoxathiin was readily oxidized to the sulfone.[79] Mauthner[76] was able to successfully prepare 2,4-dinitrophenoxathiin-10-dioxide also.

The oxidation of thianthrene has been studied quite extensively, and all five of the possible oxides have been prepared. Thianthrene-5-oxide has been prepared by oxidation of thianthrene with dilute nitric acid (d. 1.2) in glacial acetic acid solution (no nuclear

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[77] H. D. K. Drew, J. Chem. Soc., 511 (1928).

[78] F. Mauthner, Ber., 39, 1340 (1906).

[79] E. D. Amstutz, J. Am. Chem. Soc., 72, 3420 (1950).

nitration reported),[80] with an equivalent amount of chlorine (in benzene solution with subsequent hydrolysis),[80] or with peracetic acid.[81] Two of the three possible isomeric 5,10-dioxides of thianthrene were obtained by oxidation of thianthrene with excess chlorine,[82] with hot, dilute nitric acid (d. 1.2),[83] or with peracetic acid,[81] or by oxidation of thianthrene-5-oxide with excess chlorine. Oxidation of thianthrene with chlorine in hot aqueous acetic acid yielded thianthrene-5,5-dioxide,[80] while the 5,5,10-trioxide was prepared by oxidation with concentrated nitric acid (d. 1.4) of either the 5-oxide, the 5,10-dioxide, or the 5,5-dioxide.[80] Reaction of thianthrene[84] or thianthrene-5,10-dioxide[82] with chromic acid, or of thianthrene[85] or thianthrene-5,5-dioxide[80] with hydrogen peroxide (30%) gave thianthrene-5,5,10,10-tetraoxide. Interesting oxidations of a number of derivatives of thianthrene have been carried out following procedures used to obtain the desired oxide of thianthrene itself. Again in contrast to dibenzothiophene, the tetraoxides, as well as other oxides,

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[80] K. Fries and W. Vogt, Ann., 381, 312 (1911).

[81] J. Böeseken and A. T. H. van der Meulen, Rec. trav. chim., 55, 925 (1936).

[82] K. Fries and W. Vogt, Ber., 44, 756 (1911).

[83] H. Baw, G. M. Bennett and P. Dearns, J. Chem. Soc., 680 (1934).

[84] V. V. Kozlov, E. P. Fruktova and D. M. Shemyakina, J. Gen. Chem. (U.S.S.R.), 10, 1077 (1940) [C. A., 35, 4028 (1941)].

[85] G. A. Martin, Doctoral Dissertation, Iowa State College, 1945.

of 2-nitrothianthrene[86] and 2-methyl-8-nitrothianthrene[87] have been prepared. In fact, a survey of the literature reveals no case in which an attempt at oxidation of a derivative of phenoxathiin or thianthrene was considered unsuccessful due to the nature of the compound being oxidized. It should be mentioned, also, that no report of a successful attempt at nuclear nitration of phenoxathiin or thianthrene has yet been made (see Nitration Reactions section of the Historical portion of this thesis).

Halogenation Reactions

Dibenzofuran is the only one of the five heterocycles being considered (dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin) which undergoes the usual halogenation reactions in a completely normal and expected manner. A comprehensive review of the halogenation of dibenzofuran was made by Willis.[7] Later studies have served only to broaden the generalizations already worked out.[9,17,88] Briefly, direct chlorination, bromination, and iodination of dibenzofuran gives the corresponding 2-monosubstituted or 2,8-disubstituted dibenzofurans in good yields. If an acetamino or hydroxy group is already present in the dibenzofuran molecule, monohalogenation occurs in the

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[86] S. Krishna, J. Chem. Soc., 123, 156 (1923).

[87] S. Krishna, ibid., 123, 2786 (1923).

[88] Buu-Hoi and R. Royer, Rec. trav. chim., 67, 175 (1948).

same nucleus, whereas carboxy, nitro, carbomethoxy, and other halogen groups give heteronuclear substitution.

Unfortunately, there is no report in the literature of any attempt at direct halogenation of dibenzo-p-dioxin. The prediction would certainly be reasonable, though, that monohalogenation would yield a 2-derivative while disubstitution would give either the 2,7- or 2,8-dihalo compound, or a mixture of both (see Nitration Reactions section of Historical portion of this thesis).

The reaction of any of the three sulfur-containing heterocycles, dibenzothiophene, phenoxathiin, or thianthrene, with free halogens in a non-aqueous solvent presents the possibility of coordination of the halogen molecule with the sulfur atom to form a di- or tetra-halide addition product. The reaction of bromine with some sulfides takes place so readily that it has been used[89] as a quantitative method for their determination. With aryl sulfides, reaction with halogens usually must be carried out below 0° in order to suppress the competing reaction of nuclear halogenation.[90] In general, reaction of the sulfide dihalides with water yields the corresponding sulfoxide.

Dibenzothiophene and its unoxidized derivatives ordinarily undergo nuclear halogenation in a manner analagous to that of

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[89] J. R. Sampey, K. H. Slagle and E. E. Reid, J. Am. Chem. Soc., 54, 3401 (1932).

[90] R. Connor in H. Gilman, "Organic Chemistry", 2nd ed., John Wiley & Sons, Inc., New York, N. Y., 1943, Vol. 1, p. 858.

dibenzofuran.[17,24,27,47,54] The reaction of dibenzothiophene at 0-5° with exactly one mole of chlorine, however, has been shown[68] to yield the sulfide dichloride which was readily hydrolyzed to dibenzothiophene-5-oxide in 77% yield. As there is no reference in the literature to the direct nuclear chlorination of dibenzothiophene, a complete comparison cannot be made.

Bromination of dibenzothiophene-5-dioxide was found to yield 3,7-dibromodibenzothiophene-5-dioxide.[63] 3-Bromodibenzothiophene-5-dioxide has been prepared indirectly.[91] No direct halogenation of dibenzothiophene-5-oxide has been reported.

Bromination of phenoxathiin has been shown to yield either 2-bromophenoxathiin[28,92] or 2,8-dibromophenoxathiin.[92] The direct chlorination of phenoxathiin apparently yields a chlorophenoxathiin in which the chlorine atom is not in the 2-position as would be expected from the results of direct bromination. The product obtained by direct chlorination[93] melts at 81-82° and forms a 10-dioxide melting at 178-179°, whereas the 2-chlorophenoxathiin prepared by heating p-chlorophenyl phenyl ether with sulfur and aluminum chloride[93,94]

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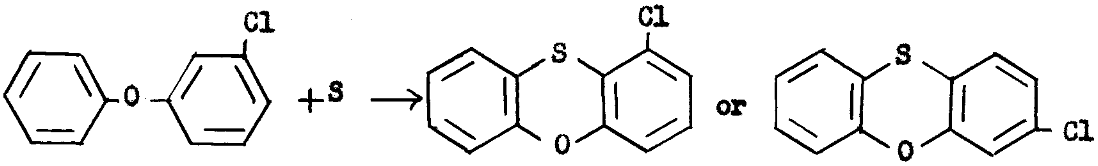
[91] G. Illuminati, J. F. Nobis and H. Gilman, _J. Am. Chem. Soc._, _73_, in press (1951).

[92] C. M. Suter, J. P. McKenzie and C. E. Maxwell, _ibid._, _58_, 717 (1936).

[93] C. M. Suter and F. O. Green, _ibid._, _59_, 2578 (1937).

[94] German Patent 234,743 [_C. A._, _5_, 2912 (1911)].

melts at 88-89° and forms a 10-dioxide melting at 158-159°. The same 2-chlorophenoxathiin-10-dioxide was also obtained by the action of aqueous alkali on 5-chloro-2-hydroxy-2'-nitrodiphenyl sulfone.[95] The 4-chlorophenoxathiin has been prepared from o-chlorophenyl phenyl ether[93] and indirectly from 4-aminophenoxathiin.[28] It was found to be an oil, b.p. 192-193°/7 mm., which on oxidation with hydrogen peroxide gave the 4-chlorophenoxathiin-10-dioxide; m.p. 148-149°. A compound assumed to be the 3-chlorophenoxathiin was prepared by heating m-chlorophenyl phenyl ether with sulfur and aluminum chloride[93]; m.p. 59-60° and m.p. dioxide 152-153°. However, the compound could also be the 1-derivative, depending upon the route taken for ring closure.



Assuming the compound formed to be the 3-chlorophenoxathiin, then the product of direct chlorination must be the 1-chlorophenoxathiin. The reverse, however, is certainly possible. If the former is true, then the following Table I can be set up:

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[95] B. A. Kent and S. Smiles, J. Chem. Soc., 422 (1934).

Table I

Melting Points of the Chlorophenoxathiins

Parent compound	Sulfide m.p.	Sulfone m.p.
1-Chlorophenoxathiin	81-82	178-179
2-Chlorophenoxathiin	88-89	158-159
3-Chlorophenoxathiin	59-60	152-153
4-Chlorophenoxathiin	oil	148-149

If the melting points for the supposed 1- and 3-derivates are reversed, we obtain Table II:

Table II

Melting Points of the Chlorophenoxathiins

Parent compound	Sulfide m.p.	Sulfone m.p.
1-Chlorophenoxathiin	59-60	152-153
2-Chlorophenoxathiin	88-89	158-159
3-Chlorophenoxathiin	81-82	178-179
4-Chlorophenoxathiin	oil	148-149

Nobis[27] has shown that, in general, the melting points of derivatives of either dibenzofuran or dibenzothiophene follow the order $1<2<3>4$. Extending this relationship to phenoxathiin we see that the order could be $1<2<3>4$ or $4<3<2>1$, depending on whether we start ortho to the oxygen or the sulfur. Assuming the order to be $1<2<3>4$, we observe that only the melting points of the 10-dioxides of Table II are correct. Using the order $4<3<2>1$, the melting points of the sulfides of both Table I and Table II fit satisfactorily, but the melting points of the 10-dioxides are in correct order in neither table. The successive decrease (or increase) of the melting points of the 10-dioxides of Table I is inconsistent with either order.

Since the relationships shown in Table II are satisfactory for the melting points of the sulfides in the $4<3<2>1$ order and for the melting points of the sulfones in the $1<2<3>4$ order, the positions thus assigned are perhaps correct. The product obtained from direct chlorination would thus be 3-chlorophenoxathiin. In either case, however, the direct chlorination of phenoxathiin apparently occurs <u>meta</u> to the oxygen bridge and <u>ortho</u> or <u>para</u> to the sulfur bridge contrary to the known greater orienting influence of oxygen over sulfur in other substitution reactions. The results of direct iodination of phenoxathiin would certainly be of interest for comparative purposes, as would the results of direct halogenation of any kind of phenoxathiin-10-oxide or -10-dioxide. In addition, a search of the literature reveals that halogenation, with subsequent hydrolysis, has not been used to prepare either phenoxathiin-10-oxide or the 10-dioxide.

Fries and Vogt[80] have shown that treatment of thianthrene with chlorine in benzene, with subsequent hydrolysis, yields thianthrene-5-oxide, which, on further treatment with chlorine, gives thianthrene-5,10-dioxide; that when chlorine is added to a hot aqueous acetic acid solution of thianthrene, thianthrene-5,10-dioxide is obtained; and that passage of the theoretical amount of chlorine into a chloroform solution of thianthrene results in nuclear chlorination to produce either 2-chlorothianthrene or 2,8-dichlorothianthrene. The same workers also found[82] that thianthrene-5,10-dioxide could be prepared directly from thianthrene by treatment with chlorine in benzene solution followed by hydrolysis. The only other reported halogenation of thianthrene is contained in a patent,[96] the abstract of which records that treatment of thianthrene with bromine in nitrobenzene gives a dibromothianthrene. No experimental details or structure proof are included in the abstract. Various derivatives have been found[86,97,98] to undergo similar nuclear halogenation or dihalide formation.

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[96] Swiss Patent 236,231 [C. A., 43, 869 (1949)]

[97] K. Fries and E. Engelbertz, Ann., 407, 194 (1915).

[98] K. Fries, H. Koch and H. Stukenbrock, ibid., 468, 162 (1929).

Nitration Reactions

The use of nitric acid for the introduction of the nitro group, $-NO_2$, into organic compounds has been known for over one hundred years and is one of the most useful reactions of organic chemistry.[99] The nitric acid used may be either dilute, concentrated, or fuming, may be either hot or cold, and may be employed either alone or in conjuction with some other reagent. The most commonly used nitrating agent is a mixture of concentrated or fuming nitric acid and concentrated sulfuric acid.

In the aromatic series, the ease of nitration depends upon the nature of the group or groups that are already attached to the aromatic nucleus. In general, groups that direct ortho-para facilitate the entry of the nitro group (except the halogens which appear to have little effect on the ease of nitration), whereas meta-directing groups decrease the susceptibility of the ring to nitration. In most cases, however, the groups that may be present initially are limited to those that are strongly resistant to oxidation since nitric acid is a good oxidizing agent, particularly when hot and concentrated.

The nitrations of dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin present some interesting anomalies with exceptions to the above generalizations being almost the rule.

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[99] For leading references and a brief discussion of the more important methods of nitration, see T. W. J. Taylor and W. Baker, "Sidgwick's The Organic Chemistry of Nitrogen", Oxford University Press, London, England, 1937, p. 227.

Dibenzofuran undergoes the usual substitution reactions of halogenation, sulfonation, and acylation[100] in satisfactory yields with the entering group taking the expected 2-position (para to the oxygen bridge). Nitration, however, unexpectedly occurs in the 3-position[7,26,101,102] in yields as high as 80% with only very small amounts of the 2-nitro isomer being isolated.[7,101] On dinitration, the second nitro group enters the position para to the oxygen linkage to give 2,7-dinitrodibenzofuran as the major product. This is in keeping with other disubstitution reactions (except metalation) in which the second group enters the 2-or8-position.*

Tomita[103] found that when dibenzo-p-dioxin was treated with nitric acid (d. 1.45) in acetic acid solution while cooling with ice, large amounts of 2-nitrodibenzo-p-dioxin were obtained along with traces of the 2,7-dinitro derivative, while similar treatment at room temperature gave large amounts of the 2,7-dinitro compound with traces of the 2,8-isomer and of 2,3,8-trinitrodibenzo-p-dioxin being isolated. Gentle warming of the dibenzo-p-dioxin with nitric acid (d. 1.38) without the use of acetic acid gave a mixture of the two dinitro

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[100] See reference 7 for leading references.

[101] H. Gilman, W. G. Bywater and P. T. Parker, J. Am. Chem. Soc., 57, 885 (1935).

[102] W. Borsche and B. Schacke, Ber., 56, 2498 (1923).

*For a theoretical discussion of the anomalous nitration of dibenzofuran, with leading references, see reference 27, p. 89.

[103] M. Tomita, J. Pharm. Soc. Japan, 55, 1060 (1935) [C. A., 31, 6661 (1937)].

derivatives, while warming with stronger nitric acid (d. 1.45) yielded only the trinitro compound. Further nitration of the mononitro product gave a mixture of both dinitro compounds and the trinitro derivative, while similar treatment of both dinitro compounds gave the same trinitro derivative. Since in all cases the nitro group entered a position <u>para</u> to one of the oxygen bridges and <u>meta</u> to the other, it is impossible to determine whether the nitration was normal or abnormal. The above work is interesting, nevertheless, in that it demonstrates how the degree of nitration can be controlled by varying the strength of the nitric acid as well as the reaction conditions of solvent and temperature.

Dibenzothiophene, in contrast to dibenzofuran, has been found to nitrate normally in the 2-position.[27,56,58,63] The yields are poor (40% or less), however, since the nuclear nitration reaction must compete with the reaction involving the oxidation of the sulfide linkage to the sulfoxide form. The use of dilute nitric acid and a glacial acetic acid solution at room temperature gives chiefly the sulfoxide, while warming and the use of stronger nitric acid increases the yield of 2-nitrodibenzothiophene and decreases the yield of dibenzothiophene-5-oxide. Nitration of the mono-nitro compound proceeds normally to give 2,8-dinitrodibenzothiophene in low yields.[27,56,58] Dinitration of dibenzothiophene reportedly[58] gave a 45% yield of the 2,8-dinitro derivative, although later workers[27,56] were unable to repeat the preparation.

In accord with the general meta-directing properties of the sulfoxide and sulfone groups, nitration of dibenzothiophene-5-oxide[64,68,69] and dibenzothiophene-5-dioxide[22,63,68] yields the 3- or 3,7-substituted derivatives. The recently reported[69] selective reduction of the monoxide derivatives to either the nitro- or dinitro-sulfide or the amino-or diamino-sulfide is of considerable importance since it indirectly makes available in good yields derivatives of dibenzothiophene substituted in the 3- or 3,7-positions.*

No report has yet been made of a successful direct nitration of either phenoxathiin or thianthrene. In all cases, reaction of either heterocycle with nitric acid has yielded only sulfoxide or sulfone derivatives. When phenoxathiin is treated with a mixture of concentrated nitric acid (d. 1.45) and glacial acetic acid at 30-40°, phenoxathiin-10-oxide is obtained 93% yield.[76] On heating with concentrated nitric acid (d. 1.4) in glacial acetic acid for three hours on a water-bath, 2-nitrophenoxathiin (prepared by ring closure) is converted to the dioxide.[104] Treatment of 1 g. of 1,3-(or possibly

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*The only other direct method reported is by the phenylcalcium iodide metalation of dibenzothiophene (see Metalation Reactions section of Historical portion of this thesis). Synthetic use of this metalation method is severely limited by the poor yields obtained. The amination rearrangement of a 4-halodibenzothiophene on treatment with sodamide in liquid ammonia to give 3-aminodibenzothiophene[52] is the only other method of obtaining a 3-derivative by direct substitution.

[104] S. Krishna, J. Chem. Soc., 123, 2783 (1923).

2,4-) dinitrophenoxathiin (prepared by intermolecular condensation) with warm, dilute nitric acid (d. 1.2) gave 0.8 g. of the corresponding monoxide.[105]

The reaction of nitric acid with thianthrene presents an even more interesting and more complex picture. Fries and Vogt[78] treated thianthrene with dilute nitric acid (d. 1.2) in warm glacial acetic acid and obtained thianthrene-5-oxide. They also found that a similar reaction of thianthrene-5-oxide, 5,5-dioxide, or 5,10-dioxide with concentrated nitric acid (d. 1.4) gave thianthrene-5,5,10-trioxide. The treatment of thianthrene with warm, dilute nitric acid (d. 1.2) was reported by Krafft and Lyons[106] and by Baw, Bennett and Dearns[83] to give a mixture of the α- and β-isomers of thianthrene-5,10-dioxide. Tomita and Ikeda[76] used concentrated nitric acid to obtain thianthrene-5,5,10,10-tetroxide. Thus all of the possible oxides of thianthrene have been prepared by the use of nitric acid except the 5,5-dioxide, and in no case was any nuclear nitration reported. It should be mentioned that 2-nitro-,[86] 2,7-dichloro-,[83] 2,7-dimethyl-,[83,107] 2,7-dimethoxy-,[83,97] and 2,3,7,8-tetramethoxythianthrene[98] reacted with nitric acid in much the same fashion at the parent thianthrene. In view of the recent successful nitration of dibenzothiophene-5-oxide,[68,69]

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[105] F. Mauthner, Ber., 38, 1411 (1905).

[106] F. Krafft and R. E. Lyons, ibid., 29, 435 (1896).

[107] K. Fries and W. Volk, ibid., 42, 1170 (1909).

the absence of nitrated products in the above reactions is somewhat surprising. The failure of nuclear nitration to occur, however, does emphasize the influence that functional groups already present in the molecule may have upon the facility with which compounds can be nitrated.

Condensation Reactions

Condensations in the presence of aluminum chloride

The use of anhydrous aluminum chloride as a catalyst in various organic reactions has been adequately reviewed elsewhere,[108] and only those reactions of immediate interest will be discussed here. In addition, only selected references of major importance are included.

In connection with the heterocyclic types under consideration in this work, condensations in the presence of aluminum chloride have been carried out to prepare the parent compound or simple derivatives either by intramolecular or intermolecular condensations. The dehydration of 2,2'-dihydroxydiphenyl by aluminum chloride is reported[109] to give quantitative yields of dibenzofuran. The most satisfactory method yet developed for the preparation of dibenzothiophene is by the reaction of biphenyl with sulfur in the presence of aluminum chloride.

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[108] C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry", Reinhold Publishing Corporation, New York, N. Y., 1941.

[109] L. E. Hinkel, E. E. Ayling and J. H. Beynon, _J. Chem. Soc._, 778 (1937).

Yields of 80%[110] and 65-70%[45] have been obtained. The use of this procedure for the preparation of derivatives of dibenzothiophene has not been successful in all cases[24]; for example, p-bromodiphenyl yields only a small amount of dibenzothiophene and a large amount of insoluble, resinous material.

Phenoxathiin reportedly has been prepared in yields greater than 80% by the reaction of diphenyl ether with sulfur in the presence of aluminum chloride.[111] A number of alkyl and halogen derivatives of phenoxathiin have been prepared by analagous reactions.[32] The reaction of diphenyl sulfide or diphenyl disulfide with sulfur in the presence of aluminum chloride was found to give 95-100% yields of thianthrene, provided that the proper ratio of reactants was used.[112] Aluminum chloride has also been used as a catalyst for the preparation of thianthrene from benzene and sulfur dichloride[80] or sulfur monochloride.[84] The only thianthrene derivative prepared in this manner was a dimethyl derivative obtained when toluene was substituted for the benzene.[106] The use of aluminum chloride for the preparation of dibenzo-p-dioxin or its derivatives by condensation reactions has not been reported.

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[110] German Patent 579,917 [C. A., 28, 1053 (1934)].

[111] For leading references, see C. M. Suter and C. E. Maxwell in R. C. Fuson, "Organic Syntheses", John Wiley and Sons, Inc., New York, N. Y., 1938, Vol. 18, p. 64.

[112] G. Dougherty and P. D. Hammond, J. Am. Chem. Soc., 57, 117 (1935).

Friedel-Crafts type reactions, chiefly acylation types, have been carried out successfully with dibenzofuran,[5,9,113,114,115,116,117,118,119] dibenzothiophene,[47,120,121,122] phenoxathiin,[92,123,124,125] thianthrene,[125,126,127]

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[113] P. Galewsky, *Ann.*, *264*, 187 (1891).

[114] W. Borsche and W. Bothe, *Ber.*, *41*, 1940 (1908).

[115] R. Stümmer, *Monatsh.*, *28*, 411 (1907).

[116] U. S. Patent 2,033,542 [*C. A.*, *30*, 3124 (1936)].

[117] H. Gilman, P. T. Parker, J. C. Bailie and G. E. Brown, *J. Am. Chem. Soc.*, *61*, 2836 (1939).

[118] E. Mosettig and R. A. Robinson, *ibid.*, *57*, 2186 (1935).

[119] W. H. Kirkpatrick and P. T. Parker, *ibid.*, *57*, 1123 (1935).

[120] A. Bürger, W. B. Wartman and R. E. Lutz, *ibid.*, *60*, 2628 (1938).

[121] A. Burger and H. W. Bryant, *J. Org. Chem.*, *4*, 119 (1939).

[122] N. M. Cullinane, A. G. Rees and C. A. J. Plummer, *J. Chem. Soc.*, 151 (1939).

[123] M. Tomita, *J. Pharm. Soc. Japan*, *58*, 510 (in German, 136) (1938) [*C. A.*, *32*, 7467 (1938)].

[124] R. G. Flowers and L. W. Flowers, *J. Am. Chem. Soc.*, *71*, 3102 (1949).

[125] U. S. Patent 2,480,220 [*C. A.*, *44*, 1142 (1950)]

[126] R. Scholl and C. Seer, *Ber.*, *44*, 1233 (1911).

[127] M. Tomita, *J. Pharm. Soc. Japan*, *58*, 517 (in German, 139) (1938) [*C. A.*, *32*, 7463 (1938)].

and dibenzo-p-dioxin.[128,129,130,131] The acetylation of dibenzothiophene reflects admirably the difficulties often encountered in carrying out Friedel-Crafts type reactions. Gilman and Jacoby report the preparation of 2-acetyl dibenzothiophene in 70% yield by the reaction of acetyl chloride with dibenzothiophene in the presence of aluminum chloride. Burger, Wartman and Lutz[120] and Burger and Bryant[121] were unable to duplicate the 70% yield of 2-acetyldibenzothiophene and obtained in each of many runs a mixture of ketones from which the 2-isomer could be isolated in only 25% yields. The other ketone was later[121] shown to be 4-acetyldibenzothiophene. In contrast to the work of both of the above groups, Cullinane, Rees and Plummer[122] were unable to obtain a mono-acetyl derivative of dibenzothiophene even though various conditions were tried. Later, Nobis[27,56] was able to repeat the work of Gilman and Jacoby obtaining a 78% crude and a 41% pure yield of 2-acetyldibenzothiophene, while Cason[132] realized only a 56% crude yield and about 25% pure.

In condensation reactions in the presence of aluminum chloride which involve the evolution of hydrogen chloride, the degree of

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[128] M. Tomita, ibid., 54, 891 (1934) [C. A., 31, 103 (1937)].

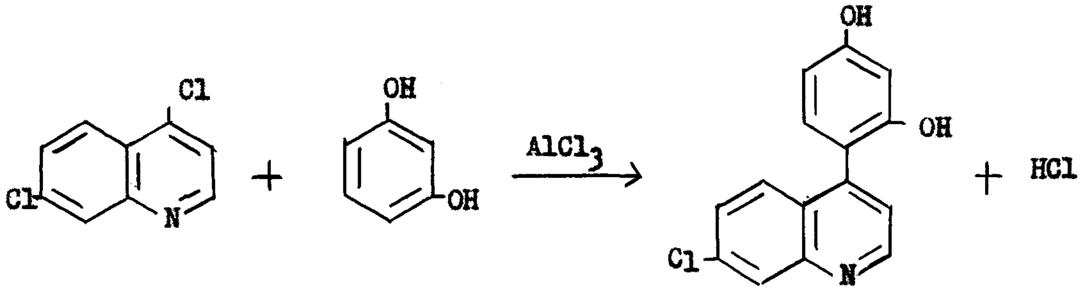
[129] M. Tomita, ibid., 56, 906 (1936) [C. A., 31, 3484 (1937)].

[130] M. Tomita, ibid., 58, 498 (1938) [C. A., 32, 7463 (1938)].

[131] German Patent 668,875 [C. A., 33, 5006 (1939)].

[132] L. F. Cason, Doctoral Dissertation, Iowa State College, 1948.

reactivity depends greatly upon the kind of group or groups present in the molecule donating the hydrogen atom and upon the type of nucleus to which the halogen is attached.[108] The effects are much the same as those observed in other reactions which involve substitution of an aromatic nucleus. In general, positive groups facilitate and negative groups inhibit substitution by the replacement of a hydrogen atom. While most halogen atoms attached to an alkyl or cycloalkyl carbon are readily replaced, halogens attached to aromatic nuclei enter into Friedel-Crafts type reactions only if situated in "active" positions. An excellent example of the combination of the above two requisites is found in the recent work of Illuminati and Gilman[133] in which resorcinol and 4-chlororesorcinol, each of which contains two strongly positive hydroxyl groups, were condensed in the presence of aluminum chloride with various heterocycles containing "active" halogens such as 2-chloroquinoline, 4,7-dichloroquinoline, and 2-chlorobenzothiazole. In line with the



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[133] G. Illuminati and H. Gilman, J. Am. Chem. Soc., 74, in press (1952). This paper contains leading references to earlier examples of condensations of this type.

general deactivating influence of halogen substituents towards further substitution of aromatic rings, the reactivity of 4-chlororesorcinol was found to be less than that of resorcinol. These experiments indicate that, with proper activation of the components involved, Friedel-Crafts types of reactions can be satisfactorily carried out with only aromatic (or heterocyclic) systems being involved.

Condensations of phenols with aldehydes

The condensation of phenols with aldehydes in the presence of basic or acidic catalysts has found extensive use both for the preparation of phenolic resins and for the preparation of the intermediate phenolic benzyl alcohols and phenolic diarylmethanes. Excellent reviews have been published elsewhere.[134,135,136,137] The following reactions serve to illustrate the stepwise nature of the condensations:

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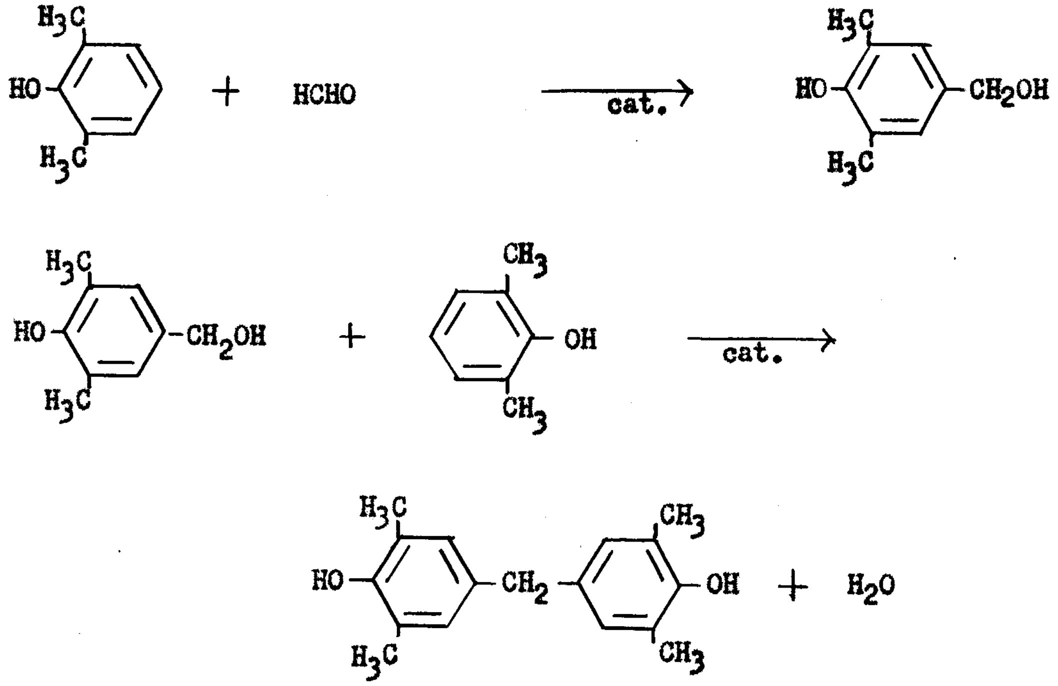
[134] L. H. Baekeland and H. L. Bender, Ind. Eng. Chem., 17, 225 (1925).

[135] F. S. Granger, ibid., 24, 442 (1932).

[136] F. S. Granger, ibid., 29, 1305 (1937).

[137] T. S. Carswell, "Phenoplasts", Interscience Publishers, Inc., New York, N. Y., 1947.



Both acids and bases have been used to catalyze the reaction. Bases are generally to be preferred for the preparation of the alcohol or diarylmethane derivatives because the reaction is more easily controlled, i.e., the final resinification step proceeds more slowly.

The excellent antiseptic properties exhibited by phenols in general[138] have long been known. Hexachlorophene, 2,2'-dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane, is an example of a polyhydroxydiarylmethane which has recently achieved considerable importance as a useful bactericide.[139] The incorporation of a

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[138] For a comprehensive review of the relation between the structure and bactericidal action of phenols, see C. M. Suter, Chem. Rev., 28, 269 (1941).

[139] M. John, J. Am. Pharm. Assoc. Prac. Pharm. Ed., 10, 488 (1949).

heterocyclic nucleus as the aryl portion of the molecule in various polyhydroxydiarylmethanes would certainly be of interest since
dibenzofuran,[140,141,142,143,144]
dibenzothiophene,[143,145,146,147,148,149]
phenoxathiin[143,144,150,151,152,153,154] and thianthrene,[143]

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[140] N. B. Eddy, J. Pharmacol. Exp. Therap., 58, 159 (1936).

[141] N. M. Phatak and C. D. Leake, ibid., 58, 155 (1936).

[142] U. S. Patent 2,191,860 /C. A., 34, 4528 (1940)7.

[143] L. E. Smith and R. Melvin, J. Econ. Entomol., 36, 475 (1943).

[144] J. P. Linduska, F. A. Morton and W. C. McDuffie, ibid., 41, 43(1948).

[145] D. E. Fink and L. E. Smith, ibid., 29, 804 (1936).

[146] L. E. Smith, E. H. Siegler and F. Munger, ibid., 31, 322 (1938).

[147] R. C. Buchland and W. V. King, U. S. Dep. Agr., Bur. Entomol. Plant Quarantine, E-585, 15 pp., 1943.

[148] J. E. Dudley, T. E. Bronson and F. H. Harris, ibid., E-651, 10 pp., 1945.

[149] H. F. Cross and F. M. Snyder, Soap Sanit. Chemicals, /27 25, 135 (1949).

[150] L. E. Smith, Ind. Eng. Chem., 34, 499 (1942).

[151] T. Irie, Bull. Inst. Phys. Chem. Research (Tokyo), 20, 150 (1941) /C. A., 36, 2881 (1942)7.

[152] L. E. Smith, U. S. Dep. Agr., Bur. Entomol. Plant Quarantine, E-580, 4 pp., 1942.

[153] H. S. Telford, J. Econ. Entomol., 38, 573 (1945).

[154] F. M. Snyder and F. A. Morton, ibid., 39, 385 (1946).

and dibenzo-*p*-dioxin[143,155] and certain of their derivatives have been shown to possess the power to kill various organisms. However, no diarylmethane derivatives of any of the five heterocycles have been reported in the literature.

Condensations with organometallic compounds

The synthetic possibilities of the reaction of an organometallic compound with a halide to obtain coupling of the two organic radicals were demonstrated and reviewed recently.[156] Satisfactory yields were reported in most of the cases studied. For example, an 83% yield of 1-*n*-butylnaphthalene was obtained from the reaction of 1-bromonaphthalene with *n*-butyllithium. The treatment of Grignard type reagents with cupric chloride to yield *bis*-type coupled products was found feasible a number of years ago[157] and was later[158] studied extensively and found applicable with a large variety of RMgX types where R may be R'S-, R'_2N-, or R'-CH=CH-, but not R'O-, in addition to the more usual saturated hydrocarbon radical.

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[155] M. Okada and S. Fuse, *Japan. J. Med. Sci. IV. Pharmacol. Trans.*, *9*, 9 (1936) [*C. A.*, *31*, 8021 (1937)].

[156] C. G. Brannen, Doctoral Dissertation, Iowa State College, 1951.

[157] J. Krizewsky and E. E. Turner, *J. Chem. Soc.*, *115*, 559 (1919).

[158] H. Gilman and H. H. Parker, *J. Am. Chem. Soc.*, *46*, 2823 (1924).

In view of the above results, it was not too surprising to find that bi-dibenzofuryl derivatives have been isolated as by-products from reactions involving the corresponding organometallic compounds. Bi-(6-methoxy-4-dibenzofuryl) was isolated from the oxidation of the reaction mixture obtained by treating 4-methoxydibenzofuran with n-butyllithium, and bi-(4-dibenzofuryl) was found present after a similar oxidation of 4-dibenzofuryllithium.[21] Bi-(2-dibenzofuryl) was obtained in 1.5% yield from the reaction of 2-dibenzofurylmagnesium bromide with ethylene oxide which gave 2-β-hydroxyethyldibenzofuran as the main product.[7,159] The above three bi-derivatives, along with bi-(3-dibenzofuryl), were also prepared satisfactorily by coupling of the corresponding magnesium bromide derivatives in the presence of cupric chloride.

No record of similarly coupled derivatives of dibenzothiophene, phenoxathiin, thianthrene, or dibenzo-p-dioxin could be found.

Rearrangement Reactions

The Hofmann reaction has found extensive use for the conversion of various amides to the corresponding amines containing one less carbon atom by treatment with bromine (or chlorine) and alkali.[160]

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[159] H. B. Willis, Iowa State Coll. J. Sci., 18, 98 (1943).

[160] E. S. Wallis and J. F. Lane in R. Adams, "Organic Reactions", John Wiley and Sons, Inc., New York, N. Y., 1946, Vol. 3, p. 267.

In general, the reaction is applicable to the preparation of amines from amides of aliphatic, aromatic, arylaliphatic, and heterocyclic carboxylic acids. Wallis and Lane[160] state, "Little use has been made of the [Hofmann] reaction in the degradation of amides containing a five-membered heterocyclic ring attached to the carbonyl group". The few examples that they do list are concerned with derivatives of pyrollidine, piperidine, pyridine and quinoline. No mention is made either in the tables or in the text of Hofmann reactions involving compounds in which the carbonyl group is attached to the benzene ring of a fused-ring heterocycle. A few such examples are known; the most pertinent of which are listed below.

In 1934, Bywater reported the use of the Hofmann reaction for the preparation of 4-aminodibenzofuran in 33.2% yield.[11,119] By modifying the usual procedure for the Hofmann reaction somewhat, yields of 4-aminodibenzofuran as high as 56.7% have been obtained.[4,6,12,161] These yields of 4-aminodibenzofuran compare very favorably with those of 16.5% obtained by fusion of 4-hydroxydibenzofuran with ammonium chloride in the presence of zinc chloride,[11] of 45% by the Bucherer reaction,[6] of 31% by amination of 4-bromodibenzofuran with sodamide in liquid ammonia,[14] of 17%[14] and 50-60%[161] by heating 4-bromodibenzofuran with ammonium hydroxide and cuprous bromide at 190-200° (bomb method), and of 78.4% (based on the amount of dibenzofuran actually used, with

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[161] H. Gilman and P. R. Van Ess, J. Am. Chem. Soc., 61, 1365 (1939).

72% of the starting dibenzofuran being recovered) by the reaction of 4-dibenzofuryllithium with α-methylhydroxylamine.[7]

4-Aminophenoxathiin has been prepared from 4-phenoxathiincarboxylic acid amide by means of the Hofmann reaction in 34% yield,[28] and by the reaction of α-methylhydroxylamine with 4-phenoxathiinyllithium in 70.6% yield (based on the amount of α-methylhydroxylamine used with 57 g. of an initial 84 g. of phenoxathiin being recovered).[28]

The use of the Hofmann reaction has recently[54,67] been extended to include the preparation of 4-aminodibenzothiophene from 4-dibenzothiophenecarboxylic acid amide. The yields varied from 23%[54] to 48.0%.[67] The 4-aminodibenzothiophene had been previously prepared in 25% and 35% yields by the use of the Bucherer Reaction and the amination with ammonium hydroxide and cuprous bromide in a steel bomb, respectively,[24,47,49] and in 64% yield by the reaction of 4-dibenzothienyllithium with α-methylhydroxylamine[53] (the yield being based on the amount of α-methylhydroxylamine used with 30 g. of an initial 78 g. of dibenzothiophene being recovered). The yields of 4-aminodibenzothiophene obtained by the Hofmann reaction are thus at least equal to those obtained by other procedures.

No report could be found of the use of the Hofmann reaction for the preparation of any amine derivatives of thianthrene or dibenzo-*p*-dioxin. In view of the success that attended the above cited uses of the Hofmann reaction with similar heterocycles, no difficulties should be encountered in extending the reaction to the carboxylic acid amides of thianthrene and dibenzo-*p*-dioxin.

On comparing the above discussed preparations using the Hofmann reaction, the yields of 4-aminodibenzofuran are the highest with those for 4-aminodibenzothiophene and 4-aminophenoxathiin being about equal to each other and some 20% less than the yield of 4-aminodibenzofuran. It would be interesting to be able to include thianthrene and dibenzo-*p*-dioxin derivatives in the comparisons.

Reduction Reactions

The literature concerning reactions that may be considered as reducing in type is obviously too voluminous to permit any extensive review. Even if the field is limited only to reduction reactions carried out in the presence of an added catalyst, the wealth of material available precludes any attempt at a comprehensive coverage. Consequently, it was deemed advisable to limit the present survey to those phases of catalytic reduction directly related to the problems investigated during the course of this work.

Reductions with Raney nickel

In twenty-four years since M. Raney patented a process for the activation of nickel by alloying with aluminum and then dissolving out the aluminum with sodium hydroxide,[162] Raney nickel has become one of

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[162] U. S. Patent 1,628,190 [*C. A.*, *21*, 2116 (1927)].

our most valuable catalysts,[163,164] particularly in hydrogenation reactions. As early as 1938[165] it was pointed out that the hydrogen adsorbed by the Raney nickel during its preparation made possible the hydrogenation of a large number of compounds without the use of any additional hydrogen. Of particular interest was the report made the following year[166] that on agitating Raney nickel with various sulfur containing compounds in aqueous or alcoholic solutions, the sulfur was removed as nickel sulfide.

$$CH_2SHCH_2SH + 2Ni \longrightarrow CH_3CH_3 + 2NiS$$

This work was later extended[167] to include a larger number of representative organic sulfur compounds, and it was reported that benzene containing thiophene and methylthiophene gave a negative test with sulfuric acid and isatin after treatment with Raney nickel. It should be noted, however, that in studies on the removal of prepared sulfur compounds from petroleum by use of a nickel catalyst,

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[163] S. Berkman, J. C. Morrell and G. Egloff, "Catalysis", Reinhold Publishing Corporation, New York, N. Y., 1940.

[164] H. W. Lohse, "Catalytic Chemistry", Chemical Publishing Co., Inc., Brooklyn, N. Y., 1945.

[165] J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim. France*, *5*, 1699 (1938).

[166] J. Bougault, E. Cattelain and P. Chabrier, *Compt. rend.*, *208*, 657 (1939).

[167] J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim. France*, *7*, 781 (1940).

Elgin[168,169] found it necessary to add hydrogen in order to remove thiophene.

In 1943 Mozingo and co-workers[170] reported the use of Raney nickel for the hydrogenolysis, in the absence of added hydrogen, of a number of sulfur compounds. Of particular interest was the isolation of benzene in 65 to 75% yields when diphenyl sulfide, diphenyl sulfoxide, and diphenyl sulfone were subjected to the hydrogenolysis since the series includes two compounds which contain oxidized sulfur.

Wolfrom and Karabinos[171] were the first to apply the Raney nickel desulfurization technique to the preparation of 1- and 2-desoxy sugar alcohols.* It was found that the preparation of the required mercaptal of the desired sugar was readily accomplished, and that the subsequent desulfurization could be effected in acceptable, and often excellent, yields. Later workers[172,173,174] have refined the

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[168] J. C. Elgin, G. H. Wilder and H. S. Taylor, Ind. Eng. Chem., 22, 1284 (1930).

[169] J. C. Elgin, ibid., 22, 1290 (1930).

[170] R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, J. Am. Chem. Soc., 65, 1013 (1943).

[171] M. L. Wolfrom and J. V. Karabinos, ibid., 66, 909 (1944).

[172] G. N. Bollenback and L. A. Underkofler, ibid., 72, 741 (1950).

[173] N. K. Richtmyer and C. S. Hudson, ibid., 72, 3880 (1950).

[174] E. Zissis, N. K. Richtmyer and C. S. Hudson, ibid., 72, 3882 (1950).

*For a recent review of Raney nickel desulfurization, see J. F. W. McOmie, Ann. Repts. on Progress Chem. (Chem. Soc. London), 45, 198 (1948).

technique and extended the number of compounds desulfurized successfully. It should be mentioned that the desulfurization of thioacetals has not been confined to sugar derivatives, but has been shown to be applicable also as a means of reducing α- and β-ketoesters.[175] For example, ethyl acetoacetate was converted to ethyl butyrate in 74% yield by first forming the thioacetal then desulfurizing with Raney nickel.

The first authentic report of the elimination of sulfur from a thiophene by nickel was made by Blicke and Sheets in 1948.[176] The structures of two isomeric thianaphtheneacetic acids were established by the reductive desulfurization technique since γ-phenylbutyric acid was obtained in good yield from thianaphthene-2-acetic acid, while the thianaphthene-3-acetic acid was converted into β-phenylbutyric acid. In subsequent studies[177] it was found that when thianaphthene, several substituted thianaphthenes, dibenzothiophene, and a few derivatives of thiophene were treated with Raney nickel, the nuclear sulfur atom was replaced by hydrogen, and a simple benzene derivative which contained a saturated side chain was formed. Under their experimental conditions dibenzothiophene was desulfurized to give a 97.5% yield of biphenyl. They concluded that the process seemed to represent a simple procedure for the determination of the

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[175] M. S. Newman and H. M. Walborsky, <u>ibid</u>., <u>72</u>, 4296 (1950).

[176] F. F. Blicke and D. G. Sheets, <u>ibid</u>., <u>70</u>, 3768 (1948).

[177] F. F. Blicke and D. G. Sheets, <u>ibid</u>., <u>71</u>, 4010 (1949).

structures of derivatives of the several heterocycles.

No literature report could be found on the use of the reductive desulfurization technique with Raney nickel for the purpose of cleaving the hetero ring of phenoxathiin, thianthrene, or their derivatives.

Reductive dehalogenation reactions

The removal of a halogen atom, or the substitution of another group for a halogen atom is a common operation in experimental organic chemistry. Excellent reviews[178,179,180,181] of the laboratory methods for dehalogenation make unnecessary any attempt at a critical survey here.

The term "reductive debromination" was recently used[182] to describe the reaction in which a bromine atom was replaced by a hydrogen atom. In general, the replacement of any halogen atom by a hydrogen atom may be called "reductive dehalogenation", and the following brief survey includes selected references to reactions of

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[178] Lassar-Cohn, "Arbeitsmethoden für Organisch-chemische Laboratorien", Verlag von Leopold Voss, Leipzig, Germany, 1923, Vol. 2, p. 364.

[179] R. Stoermer in J. Houben, "Die Methoden der Organischen Chemie", Verlag Georg Thieme, Leipzig, Germany, 1925, Vol. 2, p. 355.

[180] R. Kempf, *ibid*., 1930, Vol. 3, p. 1215.

[181] W. Theilheimer, "Synthetische Methoden der Organischen Chemie", Kargel AG. Verlag, Basel, Switzerland, 1946 *et al*., in all volumes under the symbol HC⇑Hal.

[182] H. Gilman, D. L. Esmay and R. K. Ingham, *J*. *Am*. *Chem*. *Soc*., *73*, 470 (1951).

this type with special attention being placed upon those carried out in alkaline media in the presence of a metal catalyst.

Some of the agents used to effect reductive dehalogenation are: zinc dust with water, alcohol, acid, or alkali; iron with water, acid, or alkali; copper with aqueous alcohol; magnesium (via the Grignard reagent) and water; aluminum chloride with alkali or silver oxide; various metal couples or amalgams with water or alcohol; hydrazine with potassium hydroxide solution; aniline derivatives; and hydrogen over metal catalysts such as platinum, palladium, and nickel. Most of the examples cited involve the use of a catalyst and hydrogen. Although the hydrogen may be added as such, it is quite commonly obtained by oxidation of a hydrogen donor present in the reaction mixture. That a source of hydrogen is necessary can be deduced from the work of Ullman and Bielecki[183] who found that when picryl chloride was treated with copper in toluene, only hexanitrobiphenyl was isolated, whereas later workers[184] showed that treatment of the same chloride with copper in ethanol solution gave trinithrobenzene.

One of the early examples of reductive dehalogenation was the reaction of carbon tetrabromide and carbontetraiodide with potassium ethylate to give bromoform and iodoform, respectively. The replaced

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[183] F. Ullman and J. Bielecki, Ber., 34, 2177 (1901).

[184] German Patent 234,726 [Chem. Zentr., 82, 1767 (1911)].

bromide or iodide ion was recovered as the potassium salt, and acetaldehyde was also isolated. Later work along this same line[185,186] showed that the ease with which a halogen atom could be replaced depended not only upon the halogen atom present, but also upon the type of other substituents attached to the molecule being dehalogenated. The groups most effective for the facilitation of the reaction were found to be those which contained a double bond, *e.g.*, (in order of increasing effectiveness) $=C=C=$, $=COOAlkyl$, $=C=O$, and $-NO_2$. A novel modification of these general ideas was made recently[187] when it was reported that copper powder in molten benzoic acid could be used to reductively dehalogenate picryl chloride, 2,4-dinitrochlorobenzene, and *o*-, *m*-, and *p*-chloronitrobenzene. Although no experimental proof was offered, Smith[187] postulated that the hydrogen needed came from the carboxyl goup of the benzoic acid.

Sodium and amyl alcohol were used to accomplish reductive dehalogenation in the phenazine series,[188] but the use of higher molecular weight alcohols in such reactions appears to have been very

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[185] E. Schmidt, W. von Knilling and A. Ascherl, *Ber.*, *59*, 1876 (1926).

[186] N. V. Sidgwick, "The Chemical Elements and Their Compounds", Oxford University Press, London, England, 1950, Vol. 2, p. 1189.

[187] W. T. Smith, *J. Am. Chem. Soc.*, *71*, 2855 (1949).

[188] H. Wieland, *Ber.*, *41*, 3478 (1908).

limited. Water, methyl alcohol, and ethyl alcohol are the most often used when an hydroxyl containing compound is to be used as the hydrogen source. The ease with which reductive dehalogenation was accomplished when high-boiling (240-290°) glycols were used as the reaction medium[182] suggests that the substitution of such glycols for the lower-boiling alcohols might prove beneficial.

Derivatives of Dibenzothiophene

Tables III, IV, and V are an extension of the compilation of known derivatives of dibenzothiophene prepared in 1948 by Nobis.[27] In the tables are entered all dibenzothiophene derivatives with the appropriate references which were not included in the earlier work. Also, entries have been made for additional references found to various compounds already listed in Nobis' table. No attempt was made to include in the survey fused ring or reduced ring derivatives of dibenzothiophene. The literature was covered thoroughly through 1950 and as completely as possible through September, 1951.

Table III

Derivatives of Dibenzothiophene

Name of Compound	M.P.	Reference
MONOSUBSTITUTED DIBENZOTHIOPHENES		
2-Acetaminodibenzothiophene	181-3	(49,53,58,189)
3-Acetaminodibenzothiophene	199-200	(68,190)
4-Acetaminodibenzothiophene	198	(49)
2-Acetoxydibenzothiophene	114	(64)
2-Acetyldibenzothiophene	111-2	(27,49,124) (132,191)
2-Acetyldibenzothiophene oxime	161-4	(56)
2-Aminodibenzothiophene	132	(27,53,56) (64,121)
3-Aminodibenzothiophene	121.5-22	(64,68,91)
4-Aminodibenzothiophene	110	(49,54,192)
Benzyl 2-dibenzothienyl ketone	100	(88)
2-Bromodibenzothiophene	127	(46,88,91,121)

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[189] E. Eagle and A. J. Carlson, J. Pharmacol. Exp. Therap., 99, 450 (1950).

[190] E. C. Miller, J. A. Miller, R. B. Sandin and R. K. Brown, Cancer Research, 9, 504 (1949).

[191] U. S. Patent 2,499,186 [C. A., 44, 5393 (1950)].

[192] This Thesis.

Table III (Continued)

Name of Compound	M.P.	Reference
3-Bromodibenzothiophene	100	(27,91)
4-Bromodibenzothiophene	83-4	(47,192)
n-Butyl 4-dibenzothienyl ketone	116-7	(192)
4-Carbomethoxydibenzothiophene	95	(27,37,49,52) (121)
2-Decanoyldibenzothiophene	49	(193)
2-Decyldibenzothiophene	b.p., 289-90/ 18 mm.	(194)
o-(2-Dibenzothenoyl)benzoic acid	120-5	(49)
β-(2-Dibenzothenoyl)propionic acid	160.5-61	(49)
γ-(2-Dibenzothienyl)butyric acid	131	(49)
4-Dibenzothienyl diazomethyl ketone	161-2	(195)
1-(2-Dibenzothienyl)-3-(p-dimethylaminophenyl)-2-propene-1-one	163-4	(196)
2-(2-Dibenzothienyl)-1,2-diphenylethylene	150°	(88)
4-Dibenzothienyllithium	——	(53,54,192)

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[193] Buu-Hoï, P. Cagniant and R. Royer, Rec. trav. chim., 68, 473 (1949).

[194] Ng. Ph. Buu-Hoï and R. Royer, ibid., 69, 861 (1950).

[195] H. Gilman and S. Avakian, J. Am. Chem. Soc., 68, 2104 (1946).

[196] H. Gilman and L. F. Cason, ibid., 72, 3469 (1950).

Table III (Continued)

Name of Compound	M.P.	Reference
2-(2-Dibenzothienyl)-2-methylcinchoninic acid	312	(197)
2-(2-Dibenzothienyl)-2-methylquinoline	149	(197)
2-Dibenzothienyl β-phenyl-β-(3-acetamido-4-methoxyphenylsulfonyl)ethyl ketone	175-7	(196)
1-(2-Dibenzothienyl)-3-phenyl-2-propene-1-one	154-5	(132,196)
2-Dibenzothienyl β-phenyl-β-(p-tolylsulfonyl)ethyl ketone	180-2	(196)
2-Dibenzothienyl o-tolyl ketone	——	(198)
4-Dibenzothiopheneacetic acid	161.5-2.5	(195)
4-Dibenzothiopheneacetamide	205-6	(195)
4-Dibenzothiophenecarboxamide	250-1	(54,67,192)
2-Dibenzothiophenecarboxylic acid	255	(46,199)
3-Dibenzothiophenecarboxylic acid	300-5	(47,192)
4-Dibenzothiophenecarboxylic acid	261-2	(37,50,54,57) (67,192,195)
4-Dibenzothiophenecarboxylic acid chloride	159-160	(54,192,195)

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[197] Buu-Hoï and P. Cagniant, Bull. soc. chim. France, 123 (1946).

[198] French Patent 614,959 [Chem. Zentr., 100, 797 (1929)].

[199] R. R. Burtner and G. Lehman, J. Am. Chem. Soc., 62, 527 (1940).

Table III (Continued)

Name of Compound	M.P.	Reference
2-Dibenzothiophenesulfonic acid	172	(25)
2-Dibenzothiophenesulfonyl chloride	141	(120)
Ethyl o-2-dibenzothenoylbenzoate	105-6	(47,49)
2-Heptanoyldibenzothiophene	65	(193,197)
2-Heptyldibenzothiophene	b.p.,258/ 18 mm.	(194)
2-Hydroxydibenzothiophene	156	(27,64,200) (201,202,203)
4-Hydroxydibenzothiophene	167	(49,54)
2-(α-Hydroxyethyl)dibenzothiophene	61-2	(124,191)
2-Methoxydibenzothiophene	170	(64)
4-Methoxydibenzothiophene	123	(49,53)
2-Myristoyldibenzothiophene	63	(193)
2-Nitrodibenzothiophene	65	(47,56,64)
3-Nitrodibenzothiophene	153-4	(69)
2-Octanoyldibenzothiophene	78	(193)
2-Octyldibenzothiophene	b.p.,280-5/ 20 mm.	(194)

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[200] German Patent 591,213 [C. A., 28, 2366 (1934)].

[201] German Patent 593,506 [C. A., 28, 3422 (1934)].

[202] U. S. Patent 1,997,744 [C. A., 29, 3853 (1935)].

[203] U. S. Patent 2,479,513 [C. A., 43, 9432 (1949)].

Table III (Continued)

Name of Compound	M.P.	Reference
2-Phenylacetyldibenzothiophene	100	(88)
2-Phenylacetyldibenzothiophene oxime	149	(88)
2-Phenylacetyldibenzothiophene semicarbazone	205-6	(88)
3-Phenyl-2-(2-dibenzothienyl)cinchoninic acid	245	(88)
3-Phenyl-2-(2-dibenzothienyl)quinoline	206	(88)
x-Phenyldibenzothiophene	—	(71)
2-(α-Phenylstyrl)dibenzothiophene	150	(88)
2-Propionyldibenzothiophene	72-72.5	(197)
2-Succinyldibenzothiophene	158-9	(47)
2-Tetradecyldibenzothiophene	52-3	(194)
2-Trimethylsilyldibenzothiophene	48.2-49.2	(91)
3-Trimethylsilyldibenzothiophene	103.5-4.5	(91)
4-Trimethylsilyldibenzothiophene	b.p.,135-7/ 0.8 mm.	(204)
4-Triphenylsilyldibenzothiophene	193-4	(27,204)
DISUBSTITUTED DIBENZOTHIOPHENES		
3-Amino-4-methoxydibenzothiophene	132-3	(53)

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[204] H. Gilman and J. Nobis, J. Am. Chem. Soc., 72, 2629 (1950).

Table III (Continued)

Name of Compound	M.P.	Reference
1-Bromo-4-acetaminodibenzothiophene	254	(49)
1-Chloro-4-hydroxydibenzothiophene	195-6	(54)
2-Decyl-8-propionyldibenzothiophene	b.p.,315-20/ 15 mm.	(194)
2,8-Diacetaminodibenzothiophene	304-5.5	(56)
2,8-Diacetyldibenzothiophene	208-9	(56,122,191)
2,8-Diacetyldibenzothiophene oxime	272	(56)
2,8-Diaminodibenzothiophene	199.5-201.5	(56)
3,7-Diaminodibenzothiophene	169-70	(69)
2,8-Dibromodibenzothiophene	229	(182,192,203)
1,4-Dihydrodibenzothiophene	76	(24,47,49)
1,4-Dihydrodibenzothiophene picrate	105	(24,47,49)
1,4-Dihydro-1,4-dibenzothiophenequinone	80-5	(205)
2,8-Dihydroxydibenzothiophene	278-9	(203)
2,8-Dimethyldibenzothiophene	287-8	(206)
2,8-Dinitrodibenzothiophene	324-5	(56)
3,7-Dinitrodibenzothiophene	354-6	(69)

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[205] O. Hinsberg, Ber., 56, 2008 (1923).

[206] K. Fuchs and P. Gross, ibid., 63, 1009 (1930).

Table III (Continued)

Name of Compound	M.P.	Reference
8-Ethoxy-2-acetamidodibenzothiophene	195.5-6.5	(207)
8-Ethoxy-2-aminodibenzothiophene	109-10	(207)
8-Ethoxy-2-nitrodibenzothiophene	209.5-210.5	(207)
2-Hydroxy-3-dibenzothiophenecarboxylic acid	283	(64,208)
2-Octyl-8-acetyldibenzothiophene	——	(194)
2-Octyl-8-propionyldibenzothiophene	——	(194)
2,8-Tetraacetaminodibenzothiophene	——	(74)
<u>TRISUBSTITUTED</u> <u>DIBENZOTHIOPHENES</u>		
8-Ethoxy-4-iodo-2-aminodibenzothiophene	148.5-9.5	(207)
8-Ethoxy-4-iodo-2-nitrodibenzothiophene	222	(207)
<u>TETRASUBSTITUTED</u> <u>DIBENZOTHIOPHENES</u>		
1,2,3,4-Tetrahydrodibenzothiophene	b.p.,180/ 3.3 mm.	(209)

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[207] P. Block, <u>J. Am. Chem. Soc.</u>, <u>72</u>, 5643 (1950).

[208] German Patent 607,381 [<u>C. A.</u>, <u>29</u>, 1997 (1935)].

[209] Buu-Hoï and P. Cagniant, <u>Ber.</u>, <u>76</u>, 1269 (1943).

Table III (Continued)

Name of Compound	M.P.	Reference
1-Keto-1,2,3,4-tetrahydrodibenzothiophene	109	(209)
1-Keto-1,2,3,4-tetrahydrodibenzothiophene oxime	170	(209,210)
1-Keto-1,2,3,4-tetrahydrodibenzothiophene semicarbazone	263 d.	(209)

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[210] P. Cagniant, Bull. soc. chim. France, 382 (1949).

Table IV

Derivatives of Dibenzothiophene-5-oxide

Name of Compound	M.P.	Reference
Dibenzothiophene-5-oxide	188-88.5	(57,62,64,65) (66,67,68,69,) (192)
MONOSUBSTITUTED DIBENZOTHIOPHENE-5-OXIDES		
3-Acetaminodibenzothiophene-5-oxide	265-7	(68,190)
x-Aminodibenzothiophene-5-oxide	252-3	(64)
3-Aminodibenzothiophene-5-oxide	208-9	(68)
2-Bromodibenzothiophene-5-oxide	171-2	(64,211)
2-Hydroxydibenzothiophene-5-oxide	147	(64,200,201)
3-Nitrodibenzothiophene-5-oxide	209.5-210.5	(64,68)
DISUBSTITUTED DIBENZOTHIOPHENE-5-OXIDES		
3,7-Dinitrodibenzothiophene-5-oxide	267-8	(69)
2-Hydroxy-3-carboxydibenzothiophene-5-oxide	258	(201)
TETRASUBSTITUTED DIBENZOTHIOPHENE-5-OXIDES		
2,8-Dibromo-3,7-dinitrodibenzothiophene-5-oxide	312-3	(192)

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[211] C. Courtot and F. Rochebouet, *ibid.*, *4*, 1972 (1937).

Table V

Derivatives of Dibenzothiophene-5-dioxide

Name of Compound	M.P.	Reference
Dibenzothiophene-5-dioxide	235	(47,49,59,64) (65,66,67,70) (71,72,75,122) (192,212,213) (214,215,216) (217,218)
MONOSUBSTITUTED DIBENZOTHIOPHENE-5-DIOXIDES		
2-Acetaminodibenzothiophene-5-dioxide	273-4	(69)
3-Acetaminodibenzothiophene-5-dioxide	325-7	(68)
2-Aminodibenzothiophene-5-dioxide	278-80	(27,56,64,69)
2-Bromodibenzothiophene-5-dioxide	266-7	(47,64,211)
3-Bromodibenzothiophene-5-dioxide	224-5	(91)
4-Bromodibenzothiophene-5-dioxide	202-3	(192)

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[212] F. G. Bordwell and W. H. McKellin, J. Am. Chem. Soc., 73, 2251 (1951).

[213] R. R. Brown and co-workers, ibid., 73, 465 (1951).

[214] C. Courtot and Motamedi, Compt. rend., 199, 531 (1934).

[215] C. Courtot and C. C. Lin, Bull. soc. chim. France, 49, 1047 (1931).

[216] N. M. Cullinane, N. M. E. Morgan and C. A. J. Plummer, Rec. trav. chim., 56, 627 (1937).

[217] P. Griess and C. Duisberg, Ber., 22, 2467 (1889).

[218] O. Kruber, ibid., 53, 1566 (1920).

Table V (Continued)

Name of Compound	M.P.	Reference
4-Carbomethoxydibenzothiophene-5-dioxide	----	(4)
4-Carboxydibenzothiophene-5-dioxide	338-9	(192)
2-Chlorodibenzothiophene-5-dioxide	249	(211)
4-Dibenzothiophenecarboxamide-5-dioxide	236-8	(67,192)
2-Hydroxydibenzothiophene-5-dioxide	264	(64,200,201) (219)
2-Iododibenzothiophene-5-dioxide	----	(211)
4-Methoxydibenzothiophene-5-dioxide	191-2	(27,56)
2-Nitrodibenzothiophene-5-dioxide	258	(56,64,69)
3-Nitrodibenzothiophene-5-dioxide	265-6	(68)
2-Trimethylsilyldibenzothiophene-5-dioxide	164-5	(133)
3-Trimethylsilyldibenzothiophene-5-dioxide	170.8-1.8	(133)
4-Trimethylsilyldibenzothiophene-5-dioxide	146-7	(27,204)
4-Triphenylsilyldibenzothiophene-5-dioxide	212-3	(27,204)
DISUBSTITUTED DIBENZOTHIOPHENE-5-DIOXIDES		
2-Amino-8-(2-pyridylamino)dibenzothiophene-5-dioxide	----	(220)

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[219] German Patent 606,350 [C. A., 29, 1434 (1935)].

[220] U. S. Patent 2,529,860 [C. A., 45, 2984 (1951)].

Table V (Continued)

Name of Compound	M.P.	Reference
2,8-Diacetaminodibenzothiophene-5-dioxide	356-7	(56)
3,7-Diacetaminodibenzothiophene-5-dioxide	382-3	(215,221)
2,8-Diaminodibenzothiophene-5-dioxide	329-31	(56,220)
3,7-Diaminodibenzothiophene-5-dioxide	327	(69,215,217) (221,222)
3,7-Dibenzoaminodibenzothiophene-5-dioxide	384-5	(215,221)
2,4-Dibromodibenzothiophene-5-dioxide	----	(211)
2,8-Dibromodibenzothiophene-5-dioxide	361-2	(192,220,223)
2,8-Dicarboxydibenzothiophene-5-dioxide	400	(122)
4,6-Dicarboxydibenzothiophene-5-dioxide	394-5	(192)
2,4-Dichlorodibenzothiophene-5-dioxide	----	(211)
3,7-Dichlorodibenzothiophene-5-dioxide	295-6	(224,225a)
3,7-Dinitrodibenzothiophene-5-dioxide	290	(69)
8-Ethoxy-2-acetaminodibenzothiophene-5-dioxide	313	(207)

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[221] C. Courtot and R. Evain, Bull. soc. chim. France, 49, 527 (1931).

[222] C. Courtot and R. Evain, ibid., 49, 1555 (1931).

[223] C. Courtot and C. Chaix, Compt. rend., 192, 1667 (1931).

[224] C. Courtot and R. Evain, Bull. soc. chim. France, 55, 881 (1936).

[225a] German Patent 230,409 [Chem. Zentr., 82, 440 (1911)].

Table V (Continued)

Name of Compound	M.P.	Reference
2-Hydroxy-3-carboxydibenzothiophene-5-dioxide	284	(64,201)
x-Nitro-4-trimethylsilyldibenzothiophene-5-dioxide	223-4	(27,204)
Sodium 2,8-diaminodibenzothiophene-5-dioxide *bis*(formaldehydsulfoxylate)	267.5-8.5	(220)
TRISUBSTITUTED DIBENZOTHIOPHENE-5-DIOXIDES		
8-Ethoxy-4-iodo-2-acetaminodibenzothiophene-5-dioxide	289	(207)
8-Ethoxy-4-iodo-2-nitrodibenzothiophene-5-dioxide	300	(207)
3,7-Diamino-x-sulfonyldibenzothiophene-5-dioxide	——	(217)
TETRASUBSTITUTED DIBENZOTHIOPHENE-5-DIOXIDES		
3,7-Dibromo-2,8-dibenzothiophenedisulfonic acid 5-dioxide	——	(215)
x,x-Diamino-x,x-dibenzothiophenedisulfonic acid 5-dioxide	——	(225b)

[225b] M. Deribere, *Tiba*, *15*, 349 (1937) [*C. A.*, *32*, 1602 (1938)].

Table V (Continued)

Name of Compound	M.P.	Reference
3,7-Diamino-1,9-dimethyldibenzothiophene-5-dioxide	——	(217)
3,7-Diamino-x,x-disulfonyldibenzothiophene-5-dioxide	——	(217)
<u>PENTASUBSTITUTED</u> <u>DIBENZOTHIOPHENE-5-DIOXIDES</u>		
3,7-Diamino-x,x,x-trisulfonyldibenzothiophene-5-dioxide	——	(217)
<u>HEXASUBSTITUTED</u> <u>DIBENZOTHIOPHENE-5-DIOXIDES</u>		
3,7-Diamino-x,x,x,x-tetrasulfonyldibenzothiophene-5-dioxide	——	(217)

Bibliography of Dibenzothiophene

The bibliography of dibenzothiophene represents an attempt to present in one place all of the literature references concerning the chemistry of dibenzothiophene. For the convenience of later workers the entries have been made alphabetically in respect to the last names of the authors. The literature was covered thoroughly through 1950 and as completely as possible through September, 1951.

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EXPERIMENTAL

Metalation Reactions

General procedure

The customary precautions required for the satisfactory preparation of organometallic compounds were observed in the metalation reactions described below. All glassware was dried overnight in the oven at 110°, assembled while still warm, and flushed out with a rapid stream of dry, oxygen-free nitrogen for at least one-half hour before the reaction was started. The ether was allowed to stand in contact with fresh sodium for at least two days before usage. The metalations were carried out in a three-necked, round-bottomed flask of proper size equipped with a motor stirrer, reflux condenser, and dropping funnel. If the reaction temperature was below 0°, a specially constructed 4-necked flask was used so that a thermometer could be introduced into the reaction mixture.

Unless otherwise noted, the procedure of Gilman and co-workers[226] was followed, with minor modification, for the preparations of *n*-butyllithium and *n*-propyllithium. Block lithium (instead of the recommended lithium wire) was pounded to a thickness of less than 1.0 mm., rinsed with ether, and cut into pieces about 0.5 cm. square which

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[226] H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, *J. Am. Chem. Soc.*, *71*, 1499 (1949).

were allowed to fall directly into the reaction flask. It was found more convenient and much quicker to add the solution of butyl bromide rather rapidly while controlling the temperature by raising or lowering an acetone-Dry Ice bath which contained excess Dry Ice. In this way, the time required for the addition of a solution of 0.5 mole of butyl bromide could be reduced from about 30 minutes to less than 10 minutes. It is necessary, however, to stir the mixture for at least one hour after addition of the butyl bromide is complete in order to obtain the maximum yield.

The metalation reactions were carried out by adding the solution of n-butyllithium to a solution or suspension of the reagent to be metalated. Unless otherwise stated, carbonation was effected by pouring the reaction mixture or solution jetwise onto a slush of ether and Dry Ice. After all of the carbon dioxide had evaporated, hydrolysis was effected by adding about an equal volume of water and shaking vigorously. If an insoluble material remained suspended between the ether and water layers, it was found advisable to filter the mixture before attempting to separate the layers. The ether layer was separated and washed at least twice with water or dilute sodium hydroxide. The combined water layer was then washed at least once with ether, warmed on a steam-bath in the hood to remove dissolved ether, filtered hot, cooled in an ice-bath, and acidified with 6 N hydrochloric acid. The combined ether layer was dried over sodium sulfate before removing the solvent by distillation from a steam-bath.

Dibenzothiophene

Metalation with lithium in ether (attempted).

Run I. To a stirred suspension of 18.4 g. (0.1 mole) of dibenzothiophene in 150 ml. of ether was added 1.73 g. (0.25 g. atom) of lithium. While stirring at room temperature, Color Test I[227] was negative at the end of 16, 24, and 40 hours. Since a large amount of the dibenzothiophene had crystallized at the sides of the flask above the solution, refluxing was started. Color Test I results were still negative at the end of a total of 48, 64, 72, 88, 96, 112, and 120 hours. The reaction mixture was then cooled and filtered first through a plug of glass wool then through a fluted filter. Removal of the ether solvent resulted in the recovery of 16.8 g (91.3%) of pure dibenzothiophene; m.p. and mixed m.p. 98-99°.

Run II. In this experiment the stirred mixture was brought to reflux immediately, and maintained at this temperature for 36 hours. Color Test I[227] was negative throughout except at the end of 22 hours when a moderately positive test was obtained. At the end of 24 hours, however, it was necessary to replace some of the ether which had escaped, after which Color Test I was negative. The reaction was terminated by carbonation in the usual manner. No acidic material was isolated from the alkaline layer. Removal of the solvent from the dried

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[227] H. Gilman and F. Schulze, ibid., 47, 2002 (1925).

ether layer resulted in a 95.1% recovery of dibenzothiophene; m.p. and mixed m.p. 98-99°.

Metalation with lithium in dioxane.

Run I. A mixture of 0.1 mole of dibenzothiophene (18.4 g.) which had been well-desiccated over sulfuric acid, 0.22 g. atom (1.5 g.) of lithium, and 200 ml. of purified and sodium-dried dioxane was refluxed and stirred vigorously for 12 hours. The reaction flask was closed with a calcium chloride tube. Most of the lithium had disappeared by the end of 8 hours. After cooling overnight a few particles of unreacted lithium were removed mechanically, and the mixture was carefully hydrolyzed with a water-dioxane mixture. Most of the solvent was removed by distillation under a water-pump vacuum. About 100 ml. of water was added to the remaining mixture of liquid and solid, and the whole was acidified with 6 N hydrochloric acid. A very strong odor of hydrogen sulfide was immediately observed. Extraction with ether removed the brown color and some solid material from the water layer. The solvent was removed from the dried ether layer leaving a brown liquid which solidified after being transferred to a distilling flask. Vacuum distillation gave a small first fraction which melted at 67-70°, a second fraction which melted at 55-60°, and a third fraction which melted at 84-93°. The first fraction was digested with 5% sodium hydroxide, then cooled and filtered. The residue was 0.4 g. of nearly pure diphenyl; m.p. 68-69.5° and mixed m.p. with authentic diphenyl (m.p. 69-70°) 69-70°. The second and third fractions were combined, digested with 5% sodium hydroxide, and finally distilled with steam until a total of 300 ml. of distillate had been collected. The combined distillate was extracted with three 75-ml. portions of ether. Removal of the solvent from the dried ether layer gave 4.3 g. of nearly pure diphenyl melting at 67-68.5°; identified by the method of mixed melting points. Filtration of the still-pot residue from the steam distillation yielded 2.7 g. of material melting at 65-85° which was recrystallized from diluted ethanol to give 2.4 g. of pure dibenzothiophene; m.p. and mixed m.p. 98-99°. Digestion of the still-pot residue from the vacuum distillation with ethanol, filtration while hot, dilution of the filtrate hot just to turbidity, cooling, and filtration yielded 3.7 g. of pure dibenzothiophene; m.p. and mixed m.p. 98-99°. The total yield of diphenyl was 30.5%, and the total recovery of dibenzothiophene was 33.2%.

Run II. The same amounts of reagents and conditions of reaction were used in this experiment as in Run I, except that the reaction was conducted under an atmosphere of nitrogen. Color Test I[227] was negative at the end of 4, 8, and 12 hours. After stirring and refluxing for 12 hours the mixture was carbonated as usual. The carbon dioxide-free material was cautiously hydrolyzed with a water-dioxane mixture, transferred to a distillation flask, treated with excess 10% sodium hydroxide, and the bulk of the solvent removed under a water-pump vacuum. The remaining residue was made strongly alkaline with 3 N sodium hydroxide, then extracted with three 150-ml. portions of ether. The alkaline solution was warmed on the steam-bath, filtered hot, cooled in an ice-bath, and acidified with 6 N hydrochloric acid. A strong odor of hydrogen sulfide was observed. Filtration gave 3.4 g. (18.3%) of o-mercaptodiphenyl melting at 38-40°. The material was dissolved in 100 ml. of ether, and the resulting solution was extracted first with 8% sodium bicarbonate then with 10% sodium hydroxide. After warming on the steam-bath, the alkaline solutions were separately filtered hot, cooled in an ice-bath, and acidified. From the bicarbonate layer there was obtained only a very small amount of tan gummy material. From the hydroxide solution there was isolated 3.0 g. (16.1%) of pure o-mercaptodiphenyl melting at 40-41°. The infrared spectrum[228] of this compound exhibited absorption at 3.9 μ, characteristic for the mercapto group. Interfering bands covered up the principal bands indicating 1,2-substitution of the benzene ring. Absorption was absent in the regions which indicate 1,3- and 1,4-substitution.

Anal. Calcd. for $C_{12}H_{10}S$: S, 17.21. Found: S, 17.12, 17.05.

Removal of the solvent from the dried ether layer yielded 13.3 g. of liquid which solidified on standing; m.p. 55-70°. The material was steam distilled until about 350 ml. of distillate had been collected. The distillate and still-pot residue were each extracted

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[228] The author is grateful to Dr. Velmer A. Fassel and Mr. Marvin Margosches for their infrared absorption measurements.

with three 125-ml. portions of ether. The combined ether layers were separately dried and the solvent removed. From the distillate there was obtained 3.3 g. (21.4%) of diphenyl melting at 66-68° which gave a mixed melting point with pure diphenyl (m.p. 69-70°) of 67-69°. From the still-pot residue there was obtained a brown gummy material that was recrystallized from ethanol (Norite) to give 3.1 g. of dibenzothiophene; m.p. 96-98°. Reduction in the volume of the filtrate, then progressive dilution with water gave 2.2 g., 1.6 g., and 2.1 g. fractions of less pure dibenzothiophene melting at 92-95°, and 88-94°, respectively. None of the fractions gave a depression in the melting point when mixed with dibenzothiophene. The total recovery of dibenzothiophene was 9.0 g. (48.8%). Based on the amount of dibenzothiophene which actually reacted, the yield of <u>o</u>-mercaptodiphenyl was 35.8%, and the yield of diphenyl was 41.8%.

<u>Metalation with n-propyllithium.</u>

<u>Run I</u>. Three grams (0.432 g. atom) of lithium in 100 ml. of ether were reacted with 18.5 g. (0.15 mole) of <u>n</u>-propyl bromide in 50 ml. of ether in the usual manner to give 155 ml. of a 0.777 M solution of <u>n</u>-propyllithium (0.1205 mole; 80.3% yield).

To a stirred suspension of 18.4 g. (0.1 mole) of dibenzothiophene in 175 ml. of ether was added the 0.1205 mole of <u>n</u>-propyllithium prepared above. The solution was stirred and refluxed gently for 24 hours. Aliquots of 75 ml. each were removed and carbonated by pouring jetwise onto Dry Ice at the end of 6, 13, and 18 hours, with the remaining 50 ml. being carbonated at the end of 24 hours. Hydrolysis and acidification were effected as usual to give four products melting at 236-245°, 238-256°, 237-247°, and 242-244° and weighing 2.45 g., 4.3 g., 4.35 g., and 2.1 g., respectively, after drying in the oven at 100° for 3-4 hours. Repeated recrystallizations raised the melting points of the four products to 252-253°. The pure fractions were identified as 4-dibenzothiophenecarboxylic acid (total crude yield of 58.2%) by the method of mixed melting points. From the various ether layers there was isolated a total of 4.9 g. of unreacted dibenzothiophene (26.8% recovery). Based on the amount of dibenzothiophene which actually reacted, the yield of acid was 79.6%.

Run II. To a solution of 12.2 g. (0.065 mole) of dibenzothiophene in 125 ml. of ether was added 160 ml. of a 0.613 M solution of *n*-propyllithium (prepared as above; 0.098 mole). The solution was stirred and refluxed for 12 hours, during which time Color Test I[227] and Color Test II[229] were both given and remained positive, although the latter became progressively weaker. The solution was carbonated, hydrolyzed, and acidified as in Run I. Filtration gave 11.2 g. (75.2%) of dry crude acid melting at 239-247°. Recrystallization from methanol yielded 7.2 g. (48.4%) of pure

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[229] H. Gilman and J. Swiss, *J. Am. Chem. Soc.*, *62*, 1847 (1940).

4-dibenzothiophenecarboxylic acid; m.p. and mixed m.p. 252-253°. From the ether layer there was obtained 1.4 g. (11.5% recovery) of slightly impure dibenzothiophene melting at 88-92°. Based on the amount of dibenzothiophene which actually reacted, the yields of acid were 84.9% crude and 54.7% pure.

Metalation with n-butyllithium.

Preparation of 4-dibenzothiophenecarboxylic acid and the sodium salt. Several preparations of 4-dibenzothiophenecarboxylic acid were made by following the directions given by Gilman and Jacoby.[47] The crude yields ranged from 75-85% while the pure yields ran from 40-50%.

The sodium salt of 4-dibenzothiophenecarboxylic acid was readily prepared by refluxing the acid with 4% sodium hydroxide, filtering the solution hot, and cooling in air. Filtration yielded fine, white needles melting with decomposition at 320-325°. Ignition of a small sample of the sodium salt showed that the compound decomposed with little apparent burning leaving an infusible residue.

Isolation of a by-product, n-butyl 4-dibenzothienyl ketone. An ether- and alkali-insoluble material was usually isolated during the preparation of 4-dibenzothiophenecarboxylic acid. This by-product was identified[230] as n-butyl 4-dibenzothienyl ketone by comparison of its properties with those of a sample of authentic material.

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[230] H. Gilman and D. L. Esmay, ibid., 74, in press (1952).

Metalation at a reduced temperature.

Run I. A solution of 4.6 g. (0.025 mole) of dibenzothiophene in 200 ml. of ether was cooled to -10° and a total of 25 ml. of a 1.367 M ether solution of n-butyllithium (1.4 equivalents; prepared in 84.0% yield in the usual way) was added in predetermined portions. Color Test I[227] was positive throughout. Color Test II[229] was negative until 0.8 equivalents of n-butyllithium had been added but did not remain positive on prolonged stirring until after 1.4 equivalents of the organometallic compound had been run in. After stirring at -10° ± 5° for 2.75 hours carbonation, hydrolysis, and acidification were carried out in the usual way. Although the acidified water layer possessed a strong odor of valeric acid, no precipitate appeared even on prolonged standing. Removal of the solvent from the dried ether layer and recrystallization of the resulting residue from diluted ethanol gave 4.0 g. (86.4% recovery) of pure dibenzothiophene; m.p. and mixed m.p. 98-99°.

Run II. The procedure and amounts of reagents were the same as in Run I except that a 1.318 M ether solution of n-butyllithium was used and that the total reaction time was 7 hours. Carbonation, hydrolysis, and acidification as above again gave no solid acid. From the ether layer there was recovered 4.1 g. (89.3%) of the starting dibenzothiophene.

Run III. This run was identical with Run II except that 0.5 g. (0.0025 mole) of dibenzothiophene-5-oxide was added to the initial reaction mixture, and a 1.285 M ether solution of n-butyllithium (prepared in the customary manner in 79.6% yield) was used. Only a trace of acid was isolated, and 91.3% of the starting dibenzothiophene was recovered.

Run IV. For this run, 0.6 g. (0.0025 mole) of dibenzothiophene-5-dioxide was added to the initial reaction mixture and a 1.234 M ether solution of n-butyllithium (prepared in 81.4% yield in the usual way) was used. Less than 0.1 g. of acid melting at 378-381° was obtained and the dibenzothiophene recovered represented 89.1% of the starting material.

Preparation of 4-bromodibenzothiophene. To a stirred solution of 27.6 g. (0.15 mole) of dibenzothiophene in 250 ml. of ether was added 140 ml. of a 1.317 M ether solution of n-butyllithium (0.184 mole; prepared as usual in 83.1% yield). After stirring and refluxing for 20 hours Color Test II[229] was only weakly positive. The temperature of the solution was then maintained below 5° by means of an ice-bath while 24.0 g. (0.15 mole) of bromine was admitted by entraining in a slow stream of nitrogen. Bromine vapor was plainly visible going into the reaction flask, but at no time was there evidence of bromine vapor above the reaction mixture. A silver nitrate test for escaping hydrogen bromide was negative. After addition of the bromine was completed (4.5 hours) the mixture was hydrolyzed by pouring into about an equal volume of water. Separation of the ether and water layers was easily effected, after which the aqueous layer was washed well with ether and the combined ether layer was washed first with sodium bisulfite solution then with water. Removal of the solvent from the dried ether layer left an oily residue which was crystallized from ethanol to yield 13.3 g. (33.6%) of crude 4-bromodibenzothiophene melting at 70-73°. The material was purified by a laborious process of fractional crystallization from ethanol and diluted ethanol. Digestion with Norite was necessary to remove a persistent yellow color. The total pure yield was 8.4 g. (21.3%) melting at 83-84°. The infrared spectrum[228] showed absorption bands at 13.35μ and 13.5μ, characteristic of 1,2,3- and 1,2-substitution of the benzene rings, respectively. The presence of the latter band indicates substitution in only one of the benzene rings.

Anal. Calcd. for $C_{12}H_7SBr$: Br, 30.4. Found: Br, 29.9, 30.2.

Dimetalation with n-butyllithium (attempted). An ether solution of 0.33 mole of n-butyllithium (prepared in the usual manner in 78.8% yield) was added rapidly over a period of 15 minutes to a stirred suspension of 27.6 g. (0.15 mole) of dibenzothiophene in 450 ml. of ether. Color Test II[229] was positive at the end of 11, 14, 19, and 24 hours of stirring and refluxing, but negative after a total of 36 hours. Color Test I[227] was positive throughout. Carbonation, hydrolysis and acidification were effected as usual giving 31.1 g. (90.9%) of crude 4-dibenzothiophenecarboxylic acid melting at 237-245°. The crude product was extracted overnight in a Soxhlet extractor with 600 ml. of methanol. From the cooled methanol solution there was filtered 12.1 g. (35.4%) of exceptionally pure 4-dibenzothiophenecarboxylic acid melting at 255-255.5°; identified by the method of mixed melting points. Two reductions in the volume of the filtrate gave 7.6 g. (22.2%) and 5.7 g. (16.7%) of less pure acid melting at 250-252° and 244-250°, respectively. Removal of the solvent from the dried ether layer gave only a small amount of gummy material which melted at 172-185° after crystallization from ethanol. No attempt was made to identify the product.

Dimetalation with n-butylsodium (attempted).

Run I. The directions followed in this experiment were those given by Gilman and Young[20] for the preparation of 4,6-dibenzofurandicarboxylic acid in over 70% yields.

To a solution of 5.9 g. (0.032 mole) of dibenzothiophene in 75 ml. of ether was added 1.84 g. (0.08 g. atom) of sodium and 10.0 g. (0.032 mole) of di-n-butylmercury. The stirred mixture was warmed slightly to start the reaction, then allowed to proceed at room temperature until the vigorous reaction had subsided (one hour). The color changed through brown to black. After refluxing for 4 hours the mixture was carbonated as usual. Filtration of the carbon dioxide-free material gave a dark-grey powder containing black clumps of material. Since adding a small portion of the solid cautiously to 500 ml. of water showed the creation of considerable fire hazard, the residue was added slowly to 100 ml. of ethanol, and after all reaction had ceased, the resulting mixture was filtered and the residue safely added to the water. The ether filtrate was extracted once with dilute sodium hydroxide, and the alkaline layer was added to the water layer above. The solvent was removed from the ethanol filtrate, and the resulting residue was dissolved in water and added to the water layer above. The combined water layer was warmed on the steam bath, filtered hot, evaporated on a steam-plate until the volume was about 450 ml., filtered hot, cooled in an ice bath, and acidified with 6 N hydrochloric acid. A few flakes of black solid were filtered off which melted at 205-212°. The amount of product was insufficient for purification or identification. Removal of the solvent from the dried ether layer gave 5.6 g. (94.8% recovery) of pure dibenzothiophene; m.p. and mixed m.p. 99-100°.

Run II. The same amounts of reagents were used as in Run I except that the ether was replaced with 75 ml. of benzene. The mixture was warmed slightly to initiate the reaction, then allowed to stir at room temperature for 6 hours. The color changed through brown to black. The mixture was then refluxed for 18 hours and carbonated as usual. Filtration of the carbon dioxide-free mixture gave a black, powdery material which was safely added in small portions to 500 ml. of water. The mixture was slowly brought to boiling and filtered hot. The cooled filtrate was extracted with ether, warmed on the steam bath, filtered hot, cooled in an ice bath, and acidified with 6 N hydrochloric acid. Filtration yielded 0.6 g. of dark brown material melting at 241-253°. the product was dissolved in 100 ml. of methanol, and the resulting solution was digested with Norite and filtered hot. From the cooled solution there was obtained a few light-tan flakes; m.p. 335-340°. The amount was too small for purification or identification and no other high melting fractions could be isolated. Removal of the solvent from the dried ether-benzene layer gave 5.3 g. of slightly impure dibenzothiophene (89.7% recovery); m.p. 93-95° and mixed m.p. 96-98°. Recrystallization from ethanol yielded 4.7 g. (80.0% recovery) of pure dibenzothiophene; m.p. and mixed m.p. 98-99°.

Dimetalation with benzylsodium (attempted). The procedure used in this experiment was a modification of that given by Avakian[17] for the preparation of 4,6-diiododibenzofuran via the intermediate 4,6-dibenzofuryldisodium which in turn was prepared by the metalation of dibenzofuran with benzylsodium in toluene.

In accordance with the procefures of Avakian[17] and Pacevitz[46] phenylsodium was prepared by placing a mixture of 120 ml. of toluene, 11.5 g. (0.5 g. atom) of sodium shot,* and 22.5 g. (0.2 mole) of chlorobenzene in 500 ml. 4-necked flask equipped with a condenser, stirrer, nitrogen inlet, and thermometer. A small crystal of iodine was added to the stirred mixture as a catalyst. About 25 minutes after the addition the temperature began to rise and by appropriate cooling with an acetone-Dry Ice bath was maintained between 38° and 43° during the entire reaction period of 4 hours. When the temperature began to fall, a suspension of 18.4 g. (0.1 mole) of dibenzothiophene in 80 ml. of toluene was added all at once, and the temperature was raised to 100-105° by means of an oil-bath. The black reaction mixture was stirred at this temperature for 11 hours, then carbonated by pouring jetwise onto a toluene-Dry Ice slurry. Unreacted sodium in the carbon

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*The sodium shot was that supplied by the Pierce Chemical Co., Rockford, Ill.. It was stored under xylene and was 1-2 mm. in diameter. The shot was washed twice with toluene before using.

dioxide-free mixture was destroyed by the cautious dropwise addition of water. Water was added until the volume of the aqueous layer was about one-third that of the toluene. The layers were separated, and the toluene solution was washed three times with 100-ml. portions of water. The combined water layer was extracted once with ether, warmed on the steam-bath, filtered hot, cooled in an ice-bath, and acidified with 6 N hydrochloric acid. A small amount of dark brown gummy material was filtered off and digested with 175 ml. of ethanol. The solution was filtered hot and cooled in air. From the cooled mixture there was isolated a very small amount of black powder melting indefinitely at 330-350°. No other high melting acid fraction was obtained. Removal of the solvent from the combined ether-toluene layer gave 16.1 g. (87.4% recovery) of nearly pure dibenzothiophene; m.p. 95-97° and mixed m.p. 96-98°. Recrystallization from diluted ethanol yielded 15.6 g. (84.8% recovery) of pure dibenzothiophene; m.p. and mixed m.p. 98-99°.

Metalation with phenylcalcium iodide.

Preparation of 3-dibenzothiophenecarboxylic acid. The procedure followed in the preparation of the phenylcalcium iodide was that used by Mr. John Morton in his most successful run. The clean glassware was dried overnight in the oven, then assembled while still warm and flushed out with dry nitrogen overnight. Into the 1 l., 3-necked flask, equipped with a motor stirrer, condenser and dropping funnel, was placed

40 g. (1.0 g. atom) of calcium,* a few crystals of iodine, and 100 ml. of dry ether. About 20 ml. of a solution of 102 g. (0.5 mole) of iodobenzene (Eastman Kodak White Label; distilled just prior to use) in 400 ml. of dry ether was run into the flask. After stirring at room temperature for about five minutes, the iodine color in the mixture began to fade, and at the end of about 12 minutes the solution was nearly colorless, a slight cloudiness had developed in the solution, and spontaneous refluxing had begun. The remainder of the solution of iodobenzene was then added slowly at such a rate that spontaneous, gentle refluxing was maintained. The total time of addition was two hours and twenty minutes. During this time the solution had gradually become reddish-brown and had slowly become filled with a finely divided precipitate. The mixture was stirred for an additional 1.5 hours, during 45 minutes of which spontaneous refluxing continued. Stirring was then discontinued and the mixture was allowed to settle for six hours. The clear, dark red-brown supernatant liquid was siphoned off under nitrogen pressure to give 425 ml. of a 0.874 M solution of phenylcalcium iodide. The molarity was determined by adding 2 ml. samples to excess acid and back-titrating with standard base. The yield was 74.4%.

In accordance with the procedure used by Jacoby[22,24] the above-prepared 0.372 mole of phenylcalcium iodide was run into a stirred solution of 27.6 g. (0.15 mole) of dibenzothiophene in 250 ml. of ether.

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*Kindly provided by Dr. A. Daane.

The resulting solution was stirred and refluxed for eight hours, stirred at room temperature overnight (14 hours), refluxed for four more hours, and finally carbonated in the usual manner. Hydrolysis and acidification of the alkaline layer were carried out as usual. The voluminous precipitate obtained from the acidified solution was digested with 500 ml. of hot water. Filtration yielded a black gum which was recrystallized from methanol to yield about 0.1 g. of almost white product melting at 305-308° plus three fractions of very impure material weighing a total of 1.9 g. A mixed melting point of the pure fraction with authentic material was not depressed. From the cooled water filtrate there was obtained 30.7 g. (67.6%) of benzoic acid; m.p. and mixed m.p. 120-121°. From the reaction mixture ether layer there was isolated 24.5 g. (88.7% recovery) of dibenzothiophene; identified by m.p. and mixed m.p.

Preparation of 3-bromodibenzothiophene (attempted). Following the procedure described above, a 0.829 M ether solution of phenylcalcium iodide (450 ml.; 0.373 mole) was obtained in 74.7% yield.

The solution of organometallic compound was rapidly run into a stirred solution of 27.6 g. (0.15 mole) of dibenzothiophene in 250 ml. of ether. The mixture was refluxed for 13 hours, stirred at room temperature for 11 hours, refluxed for an additional 4 hours, and finally cooled in an ice-bath. To the cooled solution of 3-dibenzothienylcalcium iodide was admitted a slow stream of bromine vapor obtained by bubbling nitrogen through 40 g. (0.15 mole) of bromine. Bromine vapor was plainly visible going into the reaction flask, but at no time was there evidence of bromine vapor above the reaction mixture. A silver nitrate test for escaping hydrogen bromide was negative. After addition of the bromine was completed (6 hours) the mixture was hydrolyzed by pouring into about an equal volume of water. Considerable inorganic material (ignition test) was filtered off and the ether and aqueous layers were separated. The aqueous layer was washed well with ether, and the combined ether layer was washed once with bisulfite solution. Removal of the solvent from the dried ether layer left a mixture of solid and liquid which was distilled <u>in vacuo</u> to give three liquid fractions (tentatively identified as either bromobenzene or iodobenzene) and one solid fraction which was recrystallized from diluted ethanol to give 15.6 g. (56.5% recovery) of dibenzothiop~~ehen~~hene; m.p. and mixed m.p. 98-99°. Extraction of the still-pot residue with ethanol yielded small amount of nearly black material melting at 210-214° which was recrystallized from <u>n</u>-butanol to give about 0.1 g. of 2,8-dibromdibenzothiophene; m.p. and mixed m.p. 220-221°.

Dibenzothiophene derivatives and related compounds

Metalation of dibenzothiophene-5-dioxide with n-butyllithium.

Run I. To a suspension of 21.6 g. (0.1 mole) of dibenzothiophene-5-dioxide in 100 ml. of ether was added 91.8 ml. of a 1.308 M ether solution of n-butyllithium (0.12 mole; prepared as usual in 78.4% yield) at such a rate that the vigorously exothermic reaction caused only gentle refluxing (40 minutes). A bright red color developed immediately and gradually darkened during the reaction. The mixture had become homogeneous by the time all of the n-butyllithium had been added. The mixture was stirred and refluxed gently for one hour, at which time Color Test I[227] was positive and II[229] negative, then carbonated and hydrolyzed as usual. A total of 6.7 g. of gummy solid was filtered from the hydrolyzed reaction mixture before the layers could be separated satisfactorily. No attempt was made to identify the material. Acidification of the aqueous layer gave an acidic gum which could not be made to crystallize. No purification was achieved by steam distillation, super-heated steam distillation, or vacuum sublimation. Removal of the solvent from the dried ether layer gave only a small amount of syrupy material which was not identified.

Run II. A suspension of 5.8 g. (0.025 mole) of dibenzothiophene-5-dioxide in 250 ml. of ether was cooled to -10° in an acetone-Dry-Ice bath. To this cooled solution was added predetermined portions of a 1.20 M ether solution of n-butyllithium (0.09 mole total) at such a rate that the temperature did not rise above -10°. Color Test I[227] was positive throughout, while Color Test II[229] was negative after a total of 1.2, 1.8, 2.4 and 3.6 equivalents of n-butyllithium had been run in. After a total reaction time of 3.5 hours the solution was carbonated and worked up as usual. The product obtained by acidification of the aqueous layer was very gummy. It was dissolved in 50 ml. of hot 4% sodium hydroxide, filtered hot, cooled, and acidified. Filtration gave 0.3 g. of white, shiny product which melted at 385-388° with decomposition. The compound was insoluble in alcohol, water, benzene, and glacial acetic acid. A neutral equivalent was obtained with difficulty by dissolving a sample of the acid in excess hot standard sodium hydroxide, then back-titrating the excess base with standard acid. A value of 272 was obtained which is in agreement with the calculated value of 272 for a dicarboxydibenzothiophene. Removal of the solvent from the ether layer gave only a small amount of pleasant-smelling liquid which was not identified.

In order to obtain further data concerning the isolated acid, an attempt was made to oxidize the compound. To a refluxing suspension of a small amount of the acid in 15 ml. of glacial acetic acid was added 5 ml. of 30% aqueous hydrogen peroxide. An additional 5 ml. of peroxide was added after a 30-minute reflux period, and after refluxing an additional one hour, the mixture was allowed to stand overnight. Filtration yielded only a small amount of very white material which melted sharply at 394-395°. A mixed melting point with the starting acid (m.p. 385-388°) was 386-390°. It was concluded that no oxidation had occurred.

Run III. A total of 84.0 ml. of a 1.242 M ether solution of 0.105 mole (4.2 equivalents) of n-butyllithium (prepared in the customary manner in 84.4% yield) was added in predetermined portions to a stirred suspension of 5.8 g. (0.025 mole) of dibenzothiophene-5-dioxide in 250 ml. of ether. The temperature of the reaction mixture was maintained at -65° to -70° by cooling in an acetone-Dry Ice bath. Color Test I[227] was positive throughout while Color Test II[229] did not remain positive on prolonged stirring until after 3.0 equivalents of the organometallic compound had been run in. A pink color slowly developed which had turned to a bright red by the end of a total reaction time of 9.0 hours. The mixture was then carbonated and hydrolyzed as usual. It was necessary to filter off considerable suspended solid before the aqueous and ether layers could be separated satisfactorily. The solid was identified as 2.9 g. (50.0% recovery) of pure dibenzothiophene-5-dioxide; m.p. and mixed m.p. 234-235°. Removal of the solvent from the dried ether layer gave an additional 1.7 g. (29.3%) of recovered dioxide melting at 234-235°. The total recovery of starting material was 79.3%. Acidification of the alkaline solution gave less than 0.1 g. of white, finely divided product melting at 332-334° with prior softening at 325-330°. Although the product was not purified, it was tentatively identified as 4-carboxydibenzothiophene-5-dioxide since a mixed melting point with authentic material (m.p. 337-338°) was 333-336°.

Run IV. The procedure for this run was the same as in Run III except that the temperature of the reaction mixture was maintained at -20° to -25° throughout and that a 1.175 M ether solution of *n*-butyllithium was used. A total of 3.0 equivalents of organometallic compound was added. Color Test I[227] was positive throughout while Color Test II[229] did not remain positive on prolonged stirring until all three equivalents had been run in. After a total reaction time of 11 hours the very dark red homogeneous solution was carbonated and hydrolyzed in the usual way. Acidification of the alkaline layer caused the precipitation of a very gummy acid which was filtered off and dissolved in hot 4% sodium hydroxide. On cooling the alkaline solution, a flaky, white material appeared. Filtration yielded 0.8 g. (10.1% yield of a disodium salt of a dicarboxydibenzothiophene-5-dioxide) of white material which on ignition was found to decompose without melting. The product was soluble in water. Tests showed that phenolphthalein and methyl red were unsatisfactory indicators for titration of the disodium salt with standard acid, but that methyl orange and thymol blue were apparently satisfactory. A 0.1655 g. sample of the acid material was dissolved in 30 ml. of water and titrated with 0.1963 N sulfuric acid, using thymol blue as the indicator. Since the free acid precipitated during the titration, it was necessary to filter the solution before the end-point was reached then finish the titration. A total of 5.36 ml. of acid was required (after subtracting a blank). The resulting neutral equivalent of 315 is in very good agreement with the value of 316 calculated for a dicarboxydibenzothiophene. Acidification of the alkaline filtrate from the disodium salt yielded 0.7 g. (10.3% yield of 4,6-dicarboxydibenzothiophene-5-dioxide) of white, finely divided product melting at 390-391°. The total yield of product was 20.4%. A completely satisfactory neutral equivalent was finally obtained by using a hot ethanol solution of the acid.

Anal. Calcd. for $C_{14}H_8O_6S$: S, 10.5; neut. equiv., 304. Found: S, 10.5, 10.4; neut. equiv., 308.

These analyses thus indicate a dicarboxydibenzothiophene-5-dioxide. The infrared spectrum[228] of the acid showed absorption at 5.92μ, 8.65μ, and 13.1μ, characteristic of the carbonyl group, the sulfone group, and 1,2,3-substitution of a benzene ring, respectively. The absence of a band between 13μ and 14μ, characteristic of 1,2-substitution, indicates substitution in both benzene rings. The absorption band commonly observed for the sulfoxide group was also absent. The infrared spectrum of the disodium salt of the acid showed absorption at 6.2μ, 8.7μ, and 12.87μ, characteristic of the carbonyl group, the sulfone group, and 1,2,3-substitution of the benzene ring, respectively. The bands indicating 1,2-substitution and the presence of the sulfoxide group again were absent.

Run V. To a stirred suspension of 10.8 g. (0.05 mole) of dibenzothiophene-5-dioxide in 400 ml. of ether cooled to -30° was added 40.9 ml. of a 1.221 M ether solution of n-butyllithium (0.05 mole; 1.0 equivalent). The mixture was stirred at -20° to -25° for 6 hours during which Color Test I[227] was positive, Color Test II[229] was negative, and the solution gradually became deep red in color. Carbonation and hydrolysis were effected as usual. It was necessary to filter off considerable ether- and alkali-insoluble material before the layers could be satisfactorily separated. Filtration of the acidified water layer yielded 10.3 g. (slightly wet) of white product melting at 295-305°. Recrystallization from methanol gave 2.8 g. (21.5%) of 4-carboxydibenzothiophene-5-dioxide melting at 328-331°. Recrystallization from dioxane gave 2.3 g. of pure material (17.7%); m.p. and mixed m.p. 338-339°. Removal of the solvent from the dried ether layer gave, after recrystallization from glacial acetic acid, 2.2 g. (20.4% recovery) of dibenzothiophene-5-dioxide melting at 231-232°; identified by the method of mixed melting points. The yields of acid based on the amount of dibenzothiophene-5-dioxide actually used were 27.0% crude and 22.3% pure.

Run VI. This run was the same in all respects as Run V except that 2.0 equivalents of n-butyllithium were used. Carbonation, hydrolysis, and acidification were carried out as usual. Filtration of the acidified alkaline layer gave 7.8 g. (slightly wet) of product melting at 330-334°. Two digestions with methanol left 1.9 g. of residue melting at 378-384° which was recrystallized from dioxane to give 0.6 g. of white product (4.0% yield of 4,6-dicarboxydibenzothiophene-5-dioxide); m.p. and mixed m.p. with the product from Run IV 391-392°. From the methanol filtrates there was isolated 2.6 g. (20.1%) of pure 4-carboxydibenzothiophene-5-dioxide; m.p. and mixed m.p. 337-338°. Removal of the solvent from the dried ether layer left only a small amount of pleasant-smelling oil.

Metalation of diphenyl sulfoxide with n-butyllithium. The several metalations of diphenyl sulfoxide with n-butyllithium were carried out in the same general manner. The following procedure was used unless otherwise noted. The desired amount of an ether solution of n-butyllithium (prepared in the usual way) was added slowly to a stirred solution of 5 g. (0.025 mole) of diphenyl sulfoxide in 250 ml. of ether at such a rate that the temperature did not rise above -70° (internal). The temperature was controlled by means of an acetone-Dry Ice bath. Color tests on the initial run showed Color Test I[227] to be positive throughout while Color Test II[229] did not become positive until three equivalents of the organometallic compound had been run in. The solution became very turbid on adding the first few ml. of n-butyllithium. Further addition of the organometallic compound caused a pink color to appear that changed to deep red by the time 1.0 equivalent had been added. On adding more n-butyllithium, the red color disappeared, and by the time 2.0 equivalents had been added the solution was light amber (and clear). Carbonation, hydrolysis, separation of layers, and acidification of the aqueous layer were carried out as usual. If no solid appeared, the acid solution was extracted with ether, and the resulting ether solution was extracted first with 8% sodium bicarbonate, then with 10% sodium hydroxide. The resulting alkaline solutions were acidified, and if no precipitation occurred, separately extracted with ether. Removal of the solvent from the dried ether layers yielded acid residues. The yields of benzoic acid which are given are based upon a reaction which produces one molecule of benzoic acid for each molecule of diphenyl sulfoxide used up.

Run I. In this run the temperature was maintained at -20° to -25°, 3.5 equivalents of a 1.282 M ether solution of n-butyllithium were used, and the total reaction time was five hours. No product was obtained from the ether layer from the sodium hydroxide extraction. The ether layer from the bicarbonate extraction yielded about 1 ml. of liquid with a pungent odor. Most of the material was used in unsuccessful attempts to cause the precipitation of a solid. Removal of the solvent from the reaction mixture ether layer left about 2 ml. of a pleasant-smelling liquid that was not identified.

Run II. Three equivalents of n-butyllithium (1.347 M ether solution), a temperature range of -35° to -30°, and a total reaction time of 5.75 hours were used. No residue was recovered from the ether layer from the sodium hydroxide solution. The ether layer from the bicarbonate extraction gave about 8 ml. of a liquid smelling strongly of valeric acid. Crystallization was finally effected by first cooling in an acetone-Dry Ice bath until a glassy solid had formed, then allowing to warm slowly with stirring. It was found necessary to cover the filter paper of a Buchner funnel with Dry Ice in order to carry out a satisfactory filtration. If this precaution was not observed, most of the precipitate redissolved. Filtration by this procedure gave 0.9 g.

(28.8%) of crude benzoic acid melting at 115-119°. Recrystallization from water gave 0.3 g. (9.6%) pure acid; m.p. and mixed m.p. 122-123°. The remaining acidic liquid was distilled to give as a first fraction 1.6 g. of liquid which had a micro-boiling point of 167°, n_D^{20} 1.4310. Although the index of refraction is about 0.15 too low for thiophenol, the b.p. is quite close. Two unsuccessful attempts were made to prepare the 2,4-dinitrophenyl phenyl sulfide derivative of thiophenol by the method of Bost, Turner and Norton.[231] The second fraction of distillate was an additional 0.8 g. (25.6%) of benzoic acid. The total crude yield of benzoic acid was 54.4%. Removal of the solvent from the ether layer from the reaction mixture gave about 2 ml. of a pleasant-smelling liquid which was not identified.

Run III. Using 2.2 equivalents of n-butyllithium and the same procedure as in Run II, there was obtained about 5 ml. of an acidic liquid from which was isolated 1.3 g. of crude benzoic acid (42.0%) melting at 110-115°. Recrystallization from water gave 0.5 g. (16.1%) of pure acid; m.p. and mixed m.p. 122-123°. The acidic liquid filtrate was vacuum distilled to give two liquid fractions of 1.2 g. distilling at 60-70°/35 mm. (n_D^{20}1.4288) and 0.8 g. distilling at 85-100°/35 mm. (n_D^{20} 1.4648) and a solid fraction of 0.8 g. distilling at 160-165°/35 mm. which was recrystallized from water to give 0.3 g.

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[231] R. W. Bost, J. O. Turner and R. D. Norton, J. Am. Chem. Soc., 54, 1985 (1932).

(9.7%) of pure benzoic acid. The total crude yield of benzoic acid was 67.8%. Removal of the solvent from the reaction mixture ether layer left about 1 ml. of a pleasant-smelling liquid which was not identified.

Run IV. The conditions for this run were the same as in Run III except that a temperature of -70° to -75° was used. The total reaction time was three hours. About 6 ml. of an acidic liquid was obtained from which was isolated 0.8 g. (25.8%) of crude benzoic acid (9.7% pure). Initial vacuum distillation with a short-path column gave a liquid fraction distilling below 120°/35 mm. and 0.5 g (16.1%) of nearly pure benzoic acid. The total crude yield of benzoic acid was 41.9%. Micro distillation of the liquid fraction gave two fractions distilling at 170-174° which weighed 1.0 g. (n_D^{20} 1.4250) and three fractions distilling at 175° which weighed 0.7 g. (n_D^{20} 1.4985). Attempts to prepare a p-toluide[232] derivative of each fraction were unsuccessful. Removal of the solvent from the reaction mixture ether layer gave about 1 ml. of an unidentified pleasant-smelling liquid.

Run V. In this run 0.5 equivalents of a 1.073 M ether solution of n-butyllithium was used, a temperature range of -30° to -25° was maintained, and the total reaction time was four hours. About 1 ml. of an acidic liquid was obtained from which no solid could be made to precipitate. Vacuum distillation likewise yielded no solid.

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[232] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds", John Wiley and Sons, Inc., New York, N. Y., 1940, p. 132.

Micro vacuum distillation gave four small fractions with indexes of refraction of 1.4613, 1.4510, 1.4600, and 1.4648. Identification was not completed. From the ether layer of the reaction mixture there was isolated 2.8 g. (54% recovery) of diphenyl sulfoxide.

Run VI. Two equivalents of a 1.418 M ether solution of n-butyllithium were used in this run at -70° to -75°. The total reaction time was six minutes. Acidification of the alkaline layer gave 1.6 g. of pure benzoic acid (51.6%); m.p. and mixed m.p. 122-123°. The usual ether extraction, followed by extraction with bicarbonate and hydroxide of the resulting ether solution, acidification of the alkaline solutions, and ether extractions gave about 6 ml. of acidic liquid from which an additional 0.3 g. of nearly pure benzoic acid melting at 119-121° was isolated (9.7%). A second cold filtration gave 0.3 g. more of benzoic acid (9.7%); m.p. 117-120°. An initial vacuum distillation gave 1.3 g. of liquid boiling below 100°/25 mm. and 0.3 g. of benzoic acid melting at 119-121° (9.7%). The total crude yield of benzoic acid was 80.7%. Micro vacuum distillation of the remaining acidic liquid gave as the main product five fractions boiling at 86-89°/20 mm. which had a total weight of 0.3 g. and whose indexes of refraction varied from 1.4192 to 1.4202. An attempt to prepare a p-toluide derivative[232] yielded a few crystals of material which, after two recrystallizations from diluted ethanol, melted at 98-99°. The above physical constants do not correspond to those for any of the normally expected products. Removal of the solvent from the reaction mixture ether layer left a small amount of pleasant-smelling liquid which was not identified.

Run VII. One equivalent of a 1.418 M ether solution of n-butyllithium was used in this run which was carried out at -70° to -75° for two hours. About 3 ml. of an acidic liquid was isolated from which was obtained 0.3 g. (9.7%) of benzoic acid. The remaining acidic liquid was micro vacuum distilled to give five liquid fractions whose boiling points varied from 92 to 120°/20 mm. and whose indexes of refraction varied from 1.4410 to 1.4826. From the reaction mixture ether layer there was isolated 0.8 g. (16.0% recovery) of diphenyl sulfoxide; m.p. and mixed m.p. 70-71°.

Run VIII. This run was identical with Run VII except that the reaction mixture was carbonated as soon as the one equivalent of organometallic had been added. From the acidic liquid there was isolated a total of 1.4 g. (45.1%) of pure benzoic acid. Micro vacuum distillation of the remaining liquid gave five unidentified fractions whose boiling points were from 75° to 95°/18 mm. and whose indexes of refraction ranged from 1.4250 to 1.4545. From the reaction mixture ether layer there was recovered 2.4 g. (48%) of the starting diphenyl sulfoxide.

Run IX. In this run 20 g. (0.10 mole) of diphenyl sulfoxide in 600 ml. of ether was used with 2.0 equivalents of a 1.256 M ether solution of n-butyllithium at -70° to -75° and with a total reaction time of 25 minutes. From the acidic liquid there was obtained 2.9 g. (23.4%) of nearly pure benzoic acid melting at 120-121.5°. Vacuum distillation of the remaining liquid gave four fractions whose boiling points varied from 85° to 105°/10 to 15 mm. and whose indexes of refraction ranged from 1.4195 to 1.4390, a fifth fraction boiling at 110° to 125°/10 to 15 mm. with an index of refraction of 1.4608 and a final solid fraction of 1.0 g. (8.1%) of benzoic acid. The liquid fractions could not be identified. The total crude yield of benzoic acid was 31.5%. Removal of the solvent from the reaction mixture ether layer left about 5 ml. of pleasant-smelling liquid which was micro distilled. The major portion of product passed over at 80-85°; n_D^{20} 1.4851. These physical constants do not correspond to those of any of the normally expected products.

Metalation of diphenyl sulfone with n-butyllithium. The general procedure followed in the metalations of diphenyl sulfone with n-butyllithium differed only in minor detail from that employed in the corresponding metalations of diphenyl sulfoxide. Eleven grams (0.05 mole) of diphenyl sulfone suspended in 500 ml. of ether was treated with the desired amount of n-butyllithium at -25° to -30° unless otherwise noted. Color Test I[227] was positive throughout, but Color Test II[229] did not remain positive on prolonged stirring until 3.0 equivalents of the organometallic compound had been run in. The mixture became yellow-orange in color during the addition of the first equivalent of n-butyllithium, orange-red during the addition of the second equivalent, and a deep red by the time three or more equivalents had been admitted. Carbonation, hydrolysis, separation of layers, acidification of the aqueous solution, extraction of the acid solution with ether, and removal of the solvent from the dried ether layer were carried out in the customary manner. The acid residue was purified by recrystallization if a solid, or distillation if a liquid. Identification of the solid acids was accomplished by the method of mixed melting points.

Run I. One equivalent of n-butyllithium wasused in this run, and the total reaction time was 1.5 hours. The crude acid weighed 6.3 g. (48.2% yield of o-carboxydiphenyl sulfone) and melted at 132-138°. Digestion with benzene and filtration while hot left a small amount of insoluble residue which was recrystallized from glacial acetic acid diluted with xylene to give 0.2 g. of nearly pure o,o'-dicarboxydiphenyl sulfone melting at 217-218.5°. From the benzene filtrate there was isolated 5.4 g. (41.2%) of nearly pure o-carboxydiphenyl sulfone melting at 145-146.5°; identified by the method of mixed melting points. Further recrystallizations raised the melting point to 146-147°. Removal of the solvent from the reaction mixture ether layer gave 2.4 g. (21.8% recovery) of slightly impure diphenyl sulfone; m.p. 124-125.5°. Based on the amount of sulfone actually used, the yield of acid was 52.5%.

Run II. This run was made with two equivalents of n-butyllithium and a total reaction period of 4.5 hours. Nine grams (58.2%) of very crude o,o'-dicarboxydiphenyl sulfone was isolated which melted at 165-174°. Digestion with benzene and filtration while hot left 7.5 g. of product melting at 200-210°. Three recrystallizations from glacial acetic acid yielded 4.0 g. (25.9%) of pure dicarboxy material; m.p. and mixed m.p. 221-222°. Infrared absorption measurements[228] on this compound gave bands at 5.77μ and 5.9μ, 8.73μ, and 13.17μ and 13.9μ, characteristic of the carbonyl group, sulfone group, and 1,2-substitution of the benzene rings, respectively.

Anal. Calcd. for $C_{14}H_{10}O_6S$: neut. equiv., 306.3; S, 10.48. Found: neut. equiv., 308.6, 313.2, 308.4, 307.4; S, 10.54, 10.57.

From the benzene filtrate there was isolated 1.2 g. (9.2%) of o-carboxydiphenyl sulfone melting at 141-143°. Recrystallization from benzene gave 0.7 g. (5.3%) of pure material; m.p. and mixed m.p. 146-147°. No starting material was recovered.

Run III. A total of 3.0 equivalents of n-butyllithium was used, with a total reaction time of 3.0 hours. In the same manner as in Run II there was obtained 0.9 g. (7.6%) of a monocarboxy sulfone melting at 143-145° and 4.6 g. (30.1%) of a dicarboxy sulfone melting at 220-221°. One-tenth of a gram of very crude unreacted diphenyl sulfone was recovered.

Run IV. For this experiment, 4.0 equivalents of n-butyllithium were added and 3.5 hours were used for the reaction. The acidic material isolated was a mixture of liquid and solid. Filtration gave 3.9 g. (25.5%) of o,o'-dicarboxydiphenyl sulfone melting at 216-219° which was recrystallized from glacial acetic acid to yield 3.3 g. (21.6%) of pure product; m.p. and mixed m.p. 220-221°. The acidic filtrate (n_D^{20} 1.3460) weighed 0.7 g. and on the basis of its odor and index of refraction was probably a mixture of valeric acid and water. From the reaction mixture ether layer there was isolated 0.4 g. of unidentified material melting at 175-185°.

Run V. This experiment was identical with Run IV except that the temperature was maintained at -70° to -75° throughout and that the total reaction time was 5.0 hours. Valeric acid (identified by odor and b.p.) was isolated in 56.8% yield, and *o*-carboxydiphenyl sulfone was obtained in 7.7% yield. An additional very small amount of acidic material melting above 200° was also isolated. From the reaction mixture ether layer there was recovered 21.8% of the starting material.

Dibenzofuran and derivatives

Metalation of dibenzofuran.

Metalation with lithium.

Run I. The experimental procedure given by Bradley[14] was followed for this reaction. One-tenth of a mole (16.8 g.) of dibenzofuran which had been well-desiccated over sulfuric acid, 0.22 g. atom (1.5 g.) of lithium, and 200 ml. of purified and sodium-dried dioxane was heated to slow reflux and rapid stirring was maintained. The reaction mixture turned brick red immediately. After stirring and refluxing for 12 hours, the mixture was filtered hot through a plug of glass wool to remove a few particles of unreacted lithium. The cooled solution was hydrolyzed by carefully adding a water-dioxane mixture, then most of the solvent was removed by distillation under a water-pump vacuum. The still-pot residue was acidified with 3 N hydrochloric acid and extracted with ether. Removal of the solvent from the dried ether layer gave a residual oil which was vacuum distilled to yield a total of 12.9 g. (77.2%) of o-hydroxydiphenyl; m.p. 54-56° and mixed m.p. with authentic material (m.p. 57-58°) 55-57°.

Run II. This reaction was carried out in a manner identical to Run I except that an atmosphere of nitrogen was used. The results were essentially the same.

Run III. This experiment was the same as Run II except that the reaction was terminated by carbonation in the usual manner. Color Test I[227] was negative throughout. Hydrolysis and removal of most of the dioxane solvent were carried out as above. The remaining residue was treated with 200 ml. of 1% sodium hydroxide, then extracted with three 150-ml. portions of ether. The combined ether layer was washed twice with 100-ml. portions of 4% sodium hydroxide. Removal of the solvent from the dried ether layer yielded 11.1 g. (65.2% of slightly impure o-hydroxydiphenyl melting at 53-55° which gave a mixed melting point with authentic material (m.p. 57-58°) of 55-57°. The combined alkaline layer was warmed on a steam-bath, filtered hot, cooled in an ice-bath, and acidified with 6 N hydrochloric acid. Filtration gave 2.6 g. (15.3%) of nearly pure o-hydroxydiphenyl; m.p. and mixed m.p. 56-57°. The total yield of o-hydroxydiphenyl was 80.5%.

Run IV. This run was the same as Run III except that the dioxane was replaced with 200 ml. of ether and the total reaction time was 22 hours. Color Test I[227] was positive at the end of 8, 18, and 22 hours. An additional 150 ml. of ether was added at the end of 18 hours to replace the solvent which had been carried off in the slow stream of nitrogen. Carbonation, hydrolysis, and isolation of products were carried out as in Run III. From the alkaline solution there was obtained 12.6 g. (64.3%) of impure 3,4-benzocoumarin (the lactone of 2'-hydroxy-2-diphenylcarboxylic acid) melting at 80-86°. The product was recrystallized from 150 ml. of ethanol (Norite) to yield 3.2 g. (16.3%) of white needles; m.p. and mixed m.p. 95-96°.[233] Reduction in the volume of the filtrate gave 3.3 g. (16.9%) of pure product melting at 95-96°. Dilution of the filtrate while hot with hot water, cooling, and filtration yielded 2.7 g. (13.8%) of nearly pure material; m.p. 93-95°. The total yield of pure and nearly pure 3,4-benzocoumarin was 47.0%. Removal of the solvent from the dried ether layer from the reaction mixture gave 2.5 g. (14.9% recovery) of dibenzofuran melting at 78-81°; identified by the method of mixed melting points. The yield of 3,4-benzocoumarin based on the amount of dibenzofuran which actually reacted was 75.7% crude and 55.2% pure and nearly pure.

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[233] An authentic sample of 3,4-benzocoumarin was prepared in 18.7% yield by the procedure of R. S. Cahn, *J. Chem. Soc.*, 1400 (1933). Cahn reports a m.p. of 94-95° and yields of 20-22%.

Preparation of 4-hydroxydibenzofuran by metalation with n-butyllithium. The procedure followed in this preparation was essentially that given by Cheney[5] and by Hogg.[9] To a stirred suspension of 121 g. (0.714 mole) of dibenzofuran in 300 ml. of ether was added 550 ml. of a 1.29 M ether solution of *n*-butyllithium (0.714 mole; prepared in the usual way). The solution was stirred and refluxed for 18 hours, then cooled to -2° in an ice-salt bath. The temperature was maintained below -5° while 0.714 mole of *n*-butylmagnesium bromide was added and the resulting solution was stirred for 1.5 hours. The cooling was continued while oxygen was swept over the surface of the stirred solution until a Color Test I[227] was negative (10 hours). The resulting mixture was hydrolyzed with iced 6 N hydrochloric acid and the layers were separated. The water layer was washed several times with ether, and the combined ether layer was extracted with 5% sodium hydroxide until no turbidity developed in an acidified portion. The alkaline solution was digested with Norite, filtered hot, and cooled in an ice-bath. Acidification and filtration yielded 59.8 g. (45.2%) of pure 4-hydroxydibenzofuran; m.p. and mixed m.p. 99-100°. Removal of the solvent from the dried ether layer yielded 25.5 g. of recovered dibenzofuran (21.4%); m.p. and mixed m.p. 83-84°. The yield of 4-hydroxydibenzofuran based on the amount of dibenzofuran which actually reacted was 57.5%.

Metalation of 2,8-dichlorodibenzofuran with n-butyllithium (attempted). To a stirred suspension of 14.2 g. (0.06 mole) of 2,8-dichlorodibenzofuran in 100 ml. of ether was added 0.06 mole of n-butyllithium in 65 ml. of ether (prepared in the usual manner) at such a rate that a spontaneous gentle reflux was maintained. After an additional one hour of refluxing over a hot-plate a Color Test II[229] was negative and Color Test I[227] was positive. Carbonation, hydrolysis, separation of layers, and acidification of the water layer were effected in the usual manner. Filtration yielded a small amount of light brown material which melted indefinitely between 175° and 205°. The product was not identified. Due to the accidental breaking of the flask containing the ether layer, no starting material was recovered.

Phenoxathiin and derivatives

Metalation of phenoxathiin.

Metalation with n-butyllithium. One-tenth of a mole of n-butylithium in 72 ml. of ether (prepared in the customary manner in 77.8% yield) was added rapidly to a stirred suspension of 20.0 g. (0.1 mole) of phenoxathiin in 50 ml. of ether. After stirring and refluxing for 24 hours, the mixture was cooled in an ice-salt bath.

Preparation of 4-hydroxyphenoxathiin. One-tenth mole of n-butylmagnesium bromide was added to the cooled mixture prepared above at such a rate that the temperature did not rise above -2°. The resulting mixture was stirred and cooled for one hour, then oxygen was swept over the surface until a Color Test I[227] was negative (12 hours). Hydrolysis was carried out with iced 6 N hydrochloric acid. The acid layer was extracted well with ether and the resulting combined ether layer was extracted with 5% sodium hydroxide until an acidified sample gave no precipitate. Acidification of the combined alkaline solution and filtration gave 10.1 g. (46.7%) of light tan product melting at 85-91°. Repeated recrystallizations from methanol and petroleum ether (b.p. 77-115°) raised the melting point to 98-99° and gave a final pure yield of 3.5 g. (15.5%).

Anal. Calcd. for $C_{12}H_8O_2S$: S, 14.83. Found: S, 14.75, 14.97.

Removal of the solvent from the reaction mixture ether layer left only a small amount of pleasant-smelling liquid.

Metalation of phenoxathiin-10-oxide with n-butyllithium. A suspension of 5.4 g. (0.025 mole) of phenoxathiin-10-oxide in 250 ml. of ether was cooled to -30°, and 74 ml. of a 1.345 M ether solution of n-butyllithium (4.0 equivalents; prepared in the usual way in 87.5% yield) was added in predetermined portions. Color Test I[227] was positive throughout the reaction period, but Color Test II[229] did not remain positive on prolonged stirring until 3.5 equivalents of the n-butyllithium had been run in. After a total reaction time of 3.0 hours, the light amber solution was carbonated in the usual manner. Hydrolysis, separation of layers, acidification of the water layer, and filtration were carried out as usual to give 4.6 g. of a light yellow product which melted at 185-206°. Repeated recrystallizations from 50%

acetic acid raised the melting point to 223-224°. The material was not identified. Removal of the solvent from the reaction mixture ether layer yielded only a small amount of pleasant-smelling liquid.

Thianthrene

Metalation with n-butyllithium. The procedure followed in this metalation was essentially that given by Gilman and Stuckwisch.[29] To a stirred suspension of 21.6 g. (0.1 mole) of thianthrene in 50 ml. of ether was rapidly added 92 ml. of a 1.198 M ether solution of n-butyllithium (0.11 mole; prepared in the customary manner in 75.8% yield). Color Test[227] was positive, and Color Test II[229] was negative after the mixture had been stirred and refluxed for 22 hours.

Preparation of 1-hydroxythianthrene. The solution of 1-thianthrenyllithium prepared above was cooled to -2° by means of an ice-salt bath, 0.1 mole of n-butylmagnesium bromide was slowly added, and the resulting mixture was cooled and stirred for one hour. While maintaining the internal temperature below -2°, oxygen was swept over the surface of the reaction mixture until Color Test I[227] became negative (11.0 hours). The mixture was hydrolyzed with iced hydrochloric acid, the layers were separated, the acid layer was washed well with ether, and the combined ether layer was extracted with 5% sodium hydroxide until no precipitate appeared when a test portion was acidified. Acidification of the combined alkaline layer and filtration gave 5.0 g. (21.6%) of 1-hydroxythianthrene melting at 74-82°. The product was found to be soluble in methanol, ethanol, hot dioxane, hot butanol, and hot carbon tetrachloride, but insoluble in water and Skelly D. Numerous tests showed that satisfactory crystallization could be obtained only from Skelly D. Repeated recrystallizations from Skelly D raised the melting point to 117-118°. The pure yield was 0.4 g. (1.7%).

Anal. Calcd for $C_{12}H_8OS_2$: S, 27.60. Found: S, 27.62, 27.71.

Removal of the solvent from the reaction mixture ether layer yielded 6.8 g. of unreacted thianthrene (31.5% recovery) melting at 151-153°. Based on the amount of thianthrene actually used up, the crude yield of 1-hydroxythianthrene was 31.5% and the pure yield was 2.5%.

Preparation of phenyllithium in dioxane

To a stirred suspension of 1.4 g. (0.2 g. atom) of lithium in 50 ml. of dioxane was added 10 ml. of a solution of 15.7 g. (0.1 mole) of bromobenzene in 50 ml. of dioxane. Within 5 minutes a slight turbidity developed and the mixture became warm. A Color Test I[227] was strongly positive. The remainder of the bromobenzene solution was added at an even rate over a period of 15 minutes. The mixture became quite warm, but did not reflux. A Color Test I was again strongly positive. After stirring and refluxing for one hour the mixture was carbonated as usual when a color test was found to be negative. The carbon dioxide-free material was hydrolyzed with a small amount of water, and most of the solvent was removed by distillation under a water-pump vacuum. No attempt was made to isolate possible cleavage products from the distillate. To the residue was added 100 ml. of 2% sodium hydroxide. After shaking vigorously, the mixture was extracted with three 75-ml. portions of ether. The combined ether layer was washed once with 50 ml. of 1% sodium hydroxide, dried, and the solvent removed by distillation. The residue remaining was insufficient for recovery. The combined alkaline layer was warmed on a steam-bath, filtered hot, cooled in an ice-bath, and acidified with 6 N hydrochloric acid. No turbidity developed, no solid precipitated, and the solution had no definite odor.

Reaction of dioxane with n-butyllithium

To 50 ml. of an ether solution of *n*-butyllithium (about 1.0 M) was added 25 ml. of dioxane. A white precipitate formed immediately, and the solution refluxed spontaneously for about 5 minutes. A Color Test[227] was positive at the end of 0.1, 0.5, 1.0, 2.0, 3.0, and 5.0 hours, but negative after stirring overnight at room temperature (15 hours total).

Oxidation Reactions

Oxidation of dibenzothiophene

The following are descriptions of typical preparations in which the procedure used was such as to give optimum yields of the desired dibenzothiophene-5-oxide or -dioxide. The results obtained by using various other conditions have been reported elsewhere.[67]

Preparation of dibenzothiophene-5-oxide. Into a 250-ml. three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer were placed 20.0 g. (0.109 mole) of dibenzothiophene, 75 ml. of glacial acetic acid, and 62 ml. (0.60 mole) of 30% aqueous hydrogen peroxide. The stirred mixture was warmed to 106° (reflux temperature of the mixture) and heated at this temperature until the mixture became homogeneous (4 min.). A hot plate placed about one-half inch below the reaction flask and turned to "high" heat was used. Stirring and heating were immediately discontinued, and the reaction flask was cooled in a cold water bath until refluxing ceased. The condenser, stirrer, and thermometer were removed, and the solution was poured into 200 ml. of water contained in a 600-ml. beaker and stirred with a stirring rod. The reaction flask was rinsed once with a few ml. of glacial acetic acid. The mixture was stirred while the beaker was cooled in a bath of running tap water until room temperature was approached (5 min.). The white solid was filtered off with suction and washed three times with water. The air-dried crude product weighed 20.9 g. (95.7%) and melted at 174-180°. The material was dissolved in the minimum amount of refluxing benzene (300 ml.). The resulting solution was filtered while hot through a steam or hot water heated funnel. As considerable precipitate appeared in the filtrate, it was again refluxed to solution and allowed to cool slowly to room temperature. Best results were obtained if the hot-plate was simply turned off and the solution left suspended above it until cool. Filtration gave 17.2 g. (78.8%) of white platelets of essentially pure dibenzothiophene-5-oxide which melted at 186-187°. Reduction in the volume of the filtrate to about 75 ml. (by distillation) yielded 3.3 g. (15.1%) of less pure material; m.p. 181-183°. The identity of both fractions was established by the method of mixed melting points.

Preparation of dibenzothiophene-5-dioxide. Into a 250-ml. three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer were placed 20.0 g. (0.109 mole) of dibenzothiopehen, 75 ml. of glacial acetic acid, and 62 ml. (0.60 mole) of 30% aqueous hydrogen peroxide. The stirred mixture was warmed to 106° (reflux temperature of the mixture) and heated at this temperature for one hour. The mixture became homogeneous in 4 min., and a copius precipitate appeared at the end of 12 min.. Stirring and heating were then discontinued, and the mixture was allowed to stand overnight at room temperature. The long white needles were filtered off with suction and washed three times with glacial acetic acid. The pure dibenzothiophene-5-dioxide weighed 22.6 g. (97.2%); m.p. and mixed m.p. 232-233°.

In another experiment the mixture was refluxed for a total of thirty minutes, then poured into 200 ml. of water contained in a 600-ml. beaker and stirred with a stirring rod. The white solid was filtered off with suction and washed three times with water. The air-dried crude product weighed 23.3 g. (99.2%) and melted at 228-230°. The material was dissolved in the minimum amount of glacial acetic acid (200 ml.). The resulting solution was filtered while hot through a steam- or hot water-heated funnel. As considerable precipitate appeared in the filtrate, it was again refluxed to solution, and allowed to cool to room temperature. Best results were obtained if the hot-plate was simply turned off and the solution left suspended above it until cool. Filtration yielded 19.5 g. (81.8%) of pure dibenzothiophene-5-dioxide; m.p. and mixed m.p. 232-233°. Dilution of the hot filtrate with an equal volume of hot water followed by cooling and filtration gave an additional 2.1 g. (8.9%) of pure product; m.p. and mixed m.p. 232-233°.

Oxidation of phenoxathiin

The following are descriptions of typical preparations in which the procedure used was such as to give optimum yields of the desired phenoxathiin-10-oxide or -dioxide. The results obtained by using various other conditions have been reported elsewhere.[67]

Preparation of phenoxathiin-10-oxide.

Method I. A stirred mixture of 20 g. (0.10 mole) of phenoxathiin and 75 ml. of glacial acetic acid was heated to 100° (the mixture became homogeneous between 80° and 90°). To the hot solution was added 62 ml. (0.60 mole) of 30% aqueous hydrogen peroxide, and heating was continued until the temperature reached 106° and the solution was refluxing vigorously. The stirring and heating were then immediately stopped, the flask was cooled slightly, and the solution was poured into 250 ml. of water contained in a 600-ml. beaker and stirred with a stirring rod. After cooling to near room temperature in a cold water bath, the white solid was filtered off and washed three times with water. The crude material weighed 21.4 g. (99.0%) and melted at 132-140°. Recrystallization from 100 ml. of benzene gave a first crop of 12.6 g. (58.3%) of pure phenoxathiin-10-oxide; m.p. and mixed m.p. 152-153°. Reduction in the volume of the filtrate to 25 ml. by distillation gave 1.6 g. (7.4%) of less pure material melting at 146-150°. Dilution of the hot filtrate with an equal volume of Skelly D, followed by cooling and filtration yielded 6.6 g. (30.5%) of impure product which melted at 118-129°.

Method II. A mixture of 10.0 g. (0.05 mole) of phenoxathiin and 250 ml. of absolute ethanol contained in a 500-ml. erlenmeyer flask equipped with a reflux condenser was brought to reflux on a steam-bath and 30 ml. of 30% aqueous hydrogen peroxide was added. After refluxing for three hours, an additional 20 ml. of peroxide was added, refluxing was continued for 9 hours more, and the solution was allowed to stand overnight at room temperature. The volume of the solution was reduced to about 75 ml. by distillation and the remaining solution was diluted hot just to turbidity with hot water. Cooling and filtration yielded 10.8 g. (98.1%) of pure phenoxathiin-10-oxide; m.p. and mixed m.p. 152-153°.

Preparation of phenoxathiin-10-dioxide. Into a 250-ml. three-necked flask equipped with a stirrer, a reflux condenser and a thermometer were placed 20.0 g. (0.10 mole) of phenoxathiin, 75 ml. of glacial acetic acid, and 62 ml. (0.60 mole) of 30% aqueous hydrogen peroxide. The stirred mixture was warmed to 106° (reflux temperature of the solution) and heated at this temperature for one hour. The mixture became homogeneous between 80° and 90° and remained so for the entire period of heating. Stirring and heating were then discontinued and the solution was allowed to stand overnight at room temperature. Filtration gave 20.0 g. (86.2%) of long white needles of pure phenoxathiin-10-dioxide; m.p. and mixed m.p. 147-148°. Dilution of the hot filtrate with hot water, followed by cooling and filtration gave an additional 2.5 g. (10.8%) of nearly pure material melting at 146-147°. Recrystallization from glacial acetic acid gave a pure compound.

It was found that the reaction mixture could be poured into 250 ml. of water at the end of 30 minutes of reflux to give a product of equal yield but of somewhat lower purity than that obtained by the above process. One recrystallization from glacial acetic acid, however, produced a pure product.

Oxidation of 4-bromodibenzothiophene

To a refluxing solution of 1.3 g. (0.005 mole) of 4-bromodibenzothiophene in 50 ml. of glacial acetic acid was added 2 ml. of 30% aqueous hydrogen peroxide. The color of the solution gradually became yellow then brown. After refluxing for one hour an additional 2 ml. of peroxide was added and refluxing was continued one hour more. Filtration of the cooled mixture yielded 0.3 g. of white needles melting at

202-203°. Reduction in the volume of the filtrate gave 0.5 g. of brownish granular material melting at 201-202.5°. The total yield of 4-bromodibenzothiophene-5-dioxide was 0.8 g. (53.3%). The infrared spectrum[228] of the compound showed bands at 8.6μ, 13.16μ, and 13.3μ, characteristic of the sulfone group, 1,2-substitution and 1,2,3-substitution, respectively. Bands indicating the presence of a sulfoxide group were absent.

Anal. Calcd. for $C_{12}H_7O_2SBr$: Br, 27.1. Found: Br, 26.9, 27.1.

Oxidation of 2,8-dibromodibenzothiophene

A stirred suspension of 27.4 g. (0.08 mole) of 2,8-dibromodibenzothiophene in 350 ml. of glacial acetic acid was heated to just below reflux temperature without obtaining complete solution. To the hot suspension was added 40 ml. (0.32 mole) of 30% aqueous hydrogen peroxide. The mixture was then stirred and refluxed for 1.5 hours during which the suspended material became very finely divided and much heavier. An additional 20 ml. (0.16 mole) of peroxide was then added, and stirring and refluxing were continued for 1.5 hours more. The mixture was cooled and the white product filtered off and dried in air. The slightly impure 2,8-dibromodibenzothiophene-5-dioxide weighed 28.5 g. (95.3%) and melted at 357-360°. The product was digested one hour with boiling dioxane and then cooled slowly in air. Filtration yielded 26.5 g. (88.6%) of white finely divided, pure dioxide; m.p. 360-361°. This yield of pure product is higher than any reported in the literature (see Discussion section of this thesis). The infrared spectrum[228] showed absorption bands at 8.59μ and 2.1μ and 12.5μ, characteristic of the sulfone group and 1,2,4-substitution, respectively.

Oxidation of 4-dibenzothiophenecarboxylic acid

A stirred suspension of 4.6 g. (0.02 mole) of 4-dibenzothiophenecarboxylic acid in 100 ml. of glacial acetic acid was heated to reflux without effecting complete solution. Ten ml. of 30% aqueous hydrogen peroxide was added to the hot mixture, and stirring and refluxing were continued. The mixture became homogeneous by the end of 8 min., and a precipitate began to form at the end of 15 min. After a total of one hour of stirring and refluxing, an additional 10 ml. of peroxide was added, and the reaction was allowed to proceed one hour longer. The mixture was cooled over-night, then filtered to yield 5.1 g. (98.1%) of finely divided, shiny crystalline material melting at 334-337°. The compound was insoluble in hot methanol, glacial acetic acid, and acetone, and only a slightly soluble in hot dioxane. Digestion with 100 ml. of acetone and filtration while hot left 4.9 g. of insoluble pure 4-carboxydibenzothiophene-5-dioxide; m.p. 337-338°. The melting point of a small sample was not raised on recrystallizing from dioxane. The infrared spectrum[228] of this acid showed absorption at 5.81μ, 8.68μ, 13.05μ, and 13.9μ, characteristic of the carbonyl group, the sulfone group, 1,2,3-substitution, and 1,2-substitution of the benzene ring, respectively.

Oxidation of 4-dibenzothiophenecarboxamide

To a stirred and refluxing solution of 7.0 g. (0.0308 mole) of 4-dibenzothiophenecarboxamide in 200 ml. of glacial acetic acid was added 10 ml. of 30% aqueous hydrogen peroxide. After 1.5 hours of stirring an additional 10 ml. of peroxide was added, and the reaction was allowed to continue one hour more. The volume of the solution was then reduced to about 100 ml. by distillation. From the cooled mixture there was filtered 6.2 g. (77.5%) of 4-dibenzothiopehecarboxamide-5-dioxide melting at 236-238°. Dilution of the filtrate with water yielded an additional 1.8 g. (22.5%) of impure material; m.p. 223-228°. Recrystallization of the first fraction from glacial acetic acid failed to raise the melting point. The infrared spectrum[228] showed absorption at 8.62μ, 12.98μ, and 13.15μ, characteristic of the sulfone group, 1,2,3-, and 1,2-substitution, respectively. Bands characteristic of the amide group were present at 2.98μ, 3.2μ, 6.17μ, and 6.37μ. Bands indicating the presence of a sulfoxide group were absent.

Anal. Calcd. for $C_{13}H_9O_3NS$: S, 12.37. Found: S, 12.21, 11.96.

Oxidation of o,o'-dicarboxydiphenyl sulfide

Preparation of o,o'-dicarboxydiphenyl sulfoxide.

Peroxide oxidation. A mixture of 1.4 g. (0.005 mole) of o,o'-dicarboxydiphenyl sulfide and 25 ml. of ethanol was refluxed on a steam bath until solution was complete. To the hot solution was added two ml. of 30% aqueous hydrogen peroxide. After refluxing for 3.0 hours an additional one ml. of peroxide was added, and refluxing was continued for 3.0 hours more. An equal volume of hot water was added slowly to the hot solution and heating was discontinued. Filtration of the cooled mixture gave 1.0 g. (71.4%) of pure o,o'-dicarbosydiphenyl sulfoxide melting at 310-311°.

Permanganate oxidation. The following procedure is essentially that used by Mayer[234] for the reported preparation of o,o'-dicarboxydiphenyl sulfone (see sulfone preparation below, and also, Discussion section of this thesis). One gram (0.0036 mole) of o,o'-dicarboxydiphenyl sulfide was dissolved in a very slight excess of 2% sodium hydroxide, and the resulting solution was diluted to 50 ml. with water. A warm solution of 0.8 g. (0.005 mole) of potassium permanganate in 100 ml. of water was added, and the resulting solution was warmed overnight in a steam bath. The precipitated manganese dioxide was filtered off to leave a clear, colorless solution. The filtrate was acidified with a solution of sodium bisulfite to which had been added

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[234] F. Mayer, Ber., 43, 584 (1910).

excess 6 N hydrochloric acid. No solid product was obtained until the volume of the solution was reduced to about 25 ml. Filtration gave 0.8 g. of brown flakes which melted at 215-229°. Repeated recrystallizations from glacial acetic acid diluted with xylene resulted in a total yield of pure *o,o*'-dicarboxydiphenyl sulfoxide of 38.1%; m.p. 312-313°. An extensive search of the various filtrates did not reveal presence of any other compound.

Preparation of o,o'-dicarboxydiphenyl sulfone.

Peroxide oxidation of o,o'-dicarboxydiphenyl sulfide. A mixture of about 1.0 g. of *o,o*'-dicarboxydiphenyl sulfide and 15 ml. of glacial acetic acid was refluxed to give complete solution of the sulfide. To the slightly cooled solution was added 3 ml. of 30% aqueous hydrogen peroxide. After refluxing for 30 min., an additional 1.0 ml. of peroxide was added, refluxing was continued for 30 min. longer, and the solution was allowed to stand overnight at room temperature. No product was obtained until the volume of the solution had been reduced to about 1 ml. The crystals were dissolved in 5 ml. of glacial acetic acid and the resulting solution was digested with Norite, filtered hot, and cooled. Filtration yielded 0.3 g. of small rectangular plates which melted at 220-221°.

Permanganate oxidation of o,o'-dicarboxydiphenyl sulfide. The following procedure is essentially that reported by Mayer[234] (see, however, the preparation of *o,o*'-dicarboxydiphenyl sulfoxide described above). One gram (0.0036 mole) of *o,o*'-dicarboxydiphenyl sulfide was dissolved in a very slight excess of 2% sodium hydroxide and the solution was back-titrated with 3 N hydrochloric acid until the precipitated acid just redissolved. A warm solution of 0.9 g. (0.006 mole) of potassium permanganate in 100 ml. of water was added, and the resulting solution was warmed overnight on a steam bath. The precipitated manganese dioxide was filtered off giving a clear permanganate colored filtrate. A solution of sodium bisulfite which had been made strongly acid with 6 N hydrochloric acid was added until the filtrate was colorless and acid in reaction. The solution was evaporated to a volume of about 25 ml., filtered hot, and cooled in air. Filtration yielded 0.7 g. (63.6%) of impure material melting at 216-219°. One recrystallization from glacial acetic acid diluted with an equal volume of xylene gave 0.4 g. (36.4%) of pure _o,o_'-dicarboxydiphenyl sulfone melting sharply at 220-221°. The melting point reported by Mayer was 137°.

A check run using the above procedure gave essentially identical results.

Peroxide oxidation of o,o'dicarboxydiphenyl sulfoxide. To a solution of about 0.1 g. of _o,o_'-dicarboxydiphenyl sulfoxide in 5 ml. of glacial acetic acid was added one ml. of 30% aqueous hydrogen peroxide. After standing for 48 hours the solvent was removed under a water-pump vacuum by distillation from a steam bath. The residue was recrystallized from glacial acetic acid diluted with an equal volume of xylene to give nearly 0.1 g. of product melting at 212-215°. Two recrystallizations from the same solvent pair raised the melting point to 220-221°. A mixed melting point with the sulfone prepared by permanganate oxidation was not depressed.

Oxidation of o-carboxydiphenyl sulfide

About 0.1 g. of o-carboxydiphenyl sulfide (o-phenylmercaptobenzoic acid[41]) was dissolved in 5 ml. of glacial acetic acid. One ml. of 30% aqueous hydrogen peroxide was added, and the solution was allowed to stand at room temperature for 48 hours. The solvent was removed under a water-pump vacuum by warming on a steam bath. The remaining residue was recrystallized from 5 ml. of benzene to give nearly 0.1 g. of o-carboxydiphenyl sulfone (o-benzenesulfonylbenzoic acid[235]) which melted at 139-142°. Two recrystallizations from benzene raised the melting point to 146-147°. The reported[235] melting point is 143-144°.

Halogenation Reactions

Monochlorination of 4-hydroxydibenzofuran

To a solution of 9.2 g. (0.05 mole) of 4-hydroxydibenzofuran and 0.1 g. of iodine in 200 ml. of chloroform contained in a 500-ml. flask equipped with a motor stirrer, a dropping funnel, and a reflux condenser closed with a calcium chloride tube was added dropwise a solution of 6.8 g. (0.05 mole) of sulfuryl chloride in 50 ml. of chloroform (15 min.).

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[235] W. E. Truce and M. F. Amos, J. Am. Chem. Soc., 73, 3013 (1951).

The color of the solution gradually changed during the addition of the sulfuryl chloride from a deep red to a light amber. After stirring at room temperature for 45 minutes the solution was allowed to stand overnight (red color returned), then refluxed 1.5 hours. The solvent was removed by distillation leaving a pink solid which was dissolved in 35 ml. of boiling methanol. The solution was digested with Norite, filtered hot, diluted hot with hot water to strong turbidity, and cooled in air. Filtration yielded 8.3 g. (85.3%) of 1-chloro-4-hydroxydibenzofuran melting at 85-105°. Purification was effected by a laborious scheme of systematic fractional recrystallization[156] from carbon tetrachloride which involved over fifty steps. A total of 1.5 g. (11.8%) of pure product was obtained which melted at 154-155°. The infrared spectrum[228] showed absorption bands at 3.0μ and 13.5μ, characteristic of the hydroxyl group and 1,2-substitution in the benzene ring, respectively. The presence of the latter group indicated substitution in only one benzene ring.

Anal. Calcd. for $C_{12}H_7O_2Cl$: Cl, 16.2. Found: Cl, 16.3, 16.2.

Dichlorination of 4-hydroxydibenzofuran

A solution of 8.6 ml. (0.10 mole) of sulfuryl chloride in 50 ml. of chloroform was added dropwise over a period of 30 minutes to a stirred solution of 9.2 g. (0.05 mole) of 4-hydroxydibenzofuran in 200 ml. of chloroform. The reaction flask was closed with a drying tube. The solution was stirred at room temperature for 3 hours, then refluxed for 1.5 hours (until there was no further evidence of hydrogen chloride being evolved). After the solvent was removed by distillation, the remaining grey residue was taken up in the minimum amount of refluxing carbon tetrachloride (250 ml.), and the resulting solution was digested with Norite, filtered hot through a heated funnel, and allowed to cool slowly. The copius precipitate of white needles was filtered off yielding 6.6 g. (52.0%) of product melting at 158-159.5°. One recrystallization from carbon tetrachloride gave 4.6 g. (36.2%) of pure 1,3-dichloro-4-hydroxydibenzofuran; m.p. 160-161°. The infrared spectrum[228] showed absorption bands at 3.15μ and 13.4μ, characteristic of the hydroxyl group and 1,2-substitution of a benzene ring, respectively. The presence of the latter band indicates substitution in only one benzene ring.

Anal. Calcd. for $C_{12}H_7O_2Cl_2$: Cl, 27.8. Found: Cl, 27.5, 27.8.

Chlorination of 1-chloro-4-hydroxydibenzofuran

To a solution of 0.22 g. (0.001 mole) of the monochloro-4-hydroxydibenzofuran in 4 ml. of chloroform was added with stirring 1.1 ml. of a solution of 0.5 ml. of sulfuryl chloride in 6 ml. of chloroform, i.e., 0.085 ml. (0.0015 mole) of sulfuryl chloride. The resulting solution was stirred at room temperature for 1.5 hours, then just below reflux temperature for 1.5 hours. After removing the solvent by distillation under a water-pump vacuum the residue was taken up in the minimum amount (5 ml.) of boiling carbon tetrachloride. From the cooled mixture there was obtained 0.15 g. (60.0% yield) of pure 1,3-dichloro-4-hydroxydibenzofuran; m.p. and mixed m.p. with the 1,3-dichloro-4-hydroxydibenzofuran 160-161°. An additional 0.08 g. of impure material was obtained from the filtrate (32.0%) which melted at 157-158.5°. The total yield of product was 92.0%.

Chlorination of dibenzofuran

Preparation of 2,8-dichlorodibenzofuran by chlorination with sulfuryl chloride (attempted).

Run I. To the light amber solution of 84.0 g. (0.5 mole) of dibenzofuran in 250 ml. of chloroform was added with stirring and heating a solution of 85 ml. (1.05 mole) of sulfuryl chloride in 100 ml. of chloroform. The solution was refluxed until the evolution of hydrogen chloride had ceased (3.5 hours). The solvent was removed by distillation and the resulting light tan residue was recrystallized from dilute methanol to give 82.4 g. (98.0%) of dibenzofuran; m.p. 78-80° and mixed m.p. 79-80.5°.

Run II. This run was made in the same manner as Run I except that 2.5 g. of anhydrous aluminum chloride was added to the solution of dibenzofuran prior to the addition of the sulfuryl chloride. There was recovered 78.1 g. (93.0%) of the starting dibenzofuran.

Run III. The chloroform used in Run II was replaced with carbon tetrachloride, otherwise the conditions were the same. Considerable tarry material was formed that resisted attempts at purification, and 71.4% of the initial amount of dibenzofuran was recovered.

Preparation of 2,8-dichlorodibenzofuran by chlorination with chlorine. The procedure previously used in this laboratory[236] for the preparation of 2,8-dichlorodibenzofuran was followed except that a few crystals of iodine were added to the reaction mixture and that the product was recrystallized only from chloroform. The yield of pure material melting at 184-185° was 22.7%.

Preparation of 2,8-dibromodibenzothiophene

The following procedure is a modification of that reported by Neumoyer and Amstutz[74] for the preparation of 2,8-dibromodibenzothiophene. To a suspension of 0.4 mole (73.6 g.) of dibenzothiophene and 1.0 g. of iron powder in 250 ml. of carbon tetrachloride was added dropwise 0.90 mole (143.6 g.; 48.0 ml.) of bromine over a period of 30 minutes. The solution was stirred at room temperature for 4 hours, during which time a heavy precipitate began to form, then allowed to stand overnight without stirring, and finally stirred and refluxed for an additional 4 hours. Filtration of the cooled mixture gave 104.9 g. (76.6%) of crude 2,8-dibromodibenzothiophene melting at 204-211°. One recrystallization from toluene yielded 62.1 g. (45.4%) of product; m.p. 217-220°. A second recrystallization gave 60.4 g. (44.2%) of pure 2,8-dibromodibenzothiophene which melted at 225-226°. The best yield previously reported[74] was 40% of somewhat impure material melting at

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[236] H. Gilman, G. E. Brown, W. G. Bywater and W. H. Kirkpatrick, J. Am. Chem. Soc., 56, 2473 (1934).

225-228°. The infrared spectrum[228] showed absorption at 12.5μ indicating 1,2,4-substitution of a benzene ring. The absence of bands characteristic of 1,2-substitution indicated that both benzene rings were substituted.

Nitration Reactions

Nitration of 2,8-dibromodibenzothiophene

Run I. To a stirred suspension of 6.8 g. (0.02 mole) of 2,8-dibromodibenzothiophene in 75 ml. of glacial acetic acid was added dropwise 4 ml. of fuming nitric acid (d. 1.4-1.5). As there was no evidence of reaction, the mixture was slowly warmed to 100° over a period of 1.5 hours and heated at 100-105° for an additional 0.5 hours. The contents of the reaction flask were then poured into 300 ml. of water. Filtration of the cooled mixture yielded 6.9 g. of light yellow product melting at 223-231°. Recrystallization from glacial acetic acid gave 5.5 g. of recovered pure 2,8-dibromodibenzothiophene (80.4%); m.p. and mixed m.p. 223-224°. Reductions in the volume of the filtrate yielded 1.0 g. of material melting indefinitely in the range 250-262°. Repeated recrystallizations from glacial acetic acid failed to raise the melting point above 263-268°.

Run II. A lumpy mixture of 6.8 g. (0.02 mole) of 2,8-dibromodibenzothiophene and 10 ml. of concentrated sulfuric acid was cooled under the tap while the solution of 5 ml. of concentrated nitric acid in 5 ml. of sulfuric acid was added. The solids rapidly dissolved and the temperature rose to 90° before the reaction was brought under control by cooling under the tap. After the vigorous reaction had subsided, the solution was heated on a steam bath for 20 minutes with stirring. A precipitate rapidly formed. When precipitation had ceased, the mixture was poured onto cracked ice and filtered to give 8.9 g. of light yellow product melting at 281-287°. Recrystallization from glacial acetic acid gave 4.4 g. (48.9%) of crude dinitro-2,8-dibromodibenzothiophene-5-oxide melting at 294-302°. Four digestions with acetone left a residue that melted at 301-304°. This product was recrystallized from glacial acetic acid to yield 2.1 g. (23.3%) of short yellow needles; m.p. 312-313°. The infrared spectrum[228] showed absorption at 9.7μ and 11.5μ, characteristic of the sulfoxide group and of a tetrasubstituted benzene ring, respectively. Bands indicating the presence of a sulfone group were absent. The absence of bands characteristic of 1,2-substitution indicated that both benzene rings were substituted.

Anal. Calcd. for $C_{12}H_4O_5N_2Br_2S$: Br, 35.7. Found: Br, 36.0, 35.6, 35.6, 35.4.

The analytical values found for bromine are thus in good agreement with the theoretical value for a dinitro-2,8-dibromodibenzothiophene-5-oxide.

Run III. In this run the procedure used by Yamashiro[237] for the mononitration of 2,8-dibromodibenzofuran was followed. Seventeen ml. of concentrated nitric acid (d. 1.42) was added to 6.8 g. (0.02 mole) of 2,8-dibromodibenzothiophene. The resulting mixture was slowly warmed to 50° and heated at this temperature for one hour. After pouring onto crushed ice filtration yielded 8.2 g. of yellow product; m.p. 220-233°. Recrystallization from glacial acetic acid gave 4.4 g. of recovered 2,8-dibromodibenzothiophene (64.2%). Repeated digestions with acetone of the material obtained from the glacial acetic acid filtrate did not give a pure product, and subsequent recrystallizations from dilute acetic acid failed to raise the melting point above 263-270°.

Run IV. This run was carried out in the same manner as Run III except that 80 ml. of fuming nitric acid (d. 1.52) was used. The crude product weighed 8.4 g. and melted at 278-299°. Four recrystallizations from glacial acetic acid gave 2.2 g. (24.4%) of pure 3,7-dinitro-2,8-dibromodibenzothiophene-5-oxide; m.p. and mixed m.p. 312-313°.

Run V. The same procedure was used as in Run IV except that a better grade of fuming nitric acid (Baker-Adams, C.P.) was used. The yield of crude product melting at 283-292° was 7.8 g. (86.7%), and two recrystallizations from glacial acetic acid gave 5.0 g. (55.6%) of pure

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[237] S. Yamashiro, Bull. Chem. Soc. Japan, 17, 76 (1942) [C. A., 41, 4487 (1947)].

3,7-dinitro-2,8-dibromodibenzothiophene-5-oxide; m.p. and mixed m.p. 312-313°. The results of this run were checked.

Nitration of 2,8-dibromodibenzothiophene-5-dioxide (attempted)

Run I. To a stirred suspension of 7.5 g. (0.02 mole of 2,8-dibromodibenzothiophene-5-dioxide in 75 ml. of glacial acetic acid was added dropwise 4 ml. of fuming nitric acid (d. 1.4-1.5). The stirred mixture was slowly warmed to 100° over a period of one hour and heated at 100-105° for one hour more. After pouring into water and cooling, filtration gave 7.5 g. (100% recovery) of pure 2,8-dibromodibenzothiophene-5-dioxide; m.p. and mixed m.p. 361-362°.

Run II. A mixture of 7.5 g. (0.02 mole) of a 2,8-dibromodibenzothiophene-5-dioxide and 10 ml. of concentrated sulfuric acid was cooled under the tap, and 5 ml. of concentrated nitric acid in 5 ml. of concentrated sulfuric acid was added. The temperature spontaneously rose to 55°. When the temperature began to fall the mixture was warmed on the steam-bath for 15 minutes, then poured onto cracked ice. Filtration yielded a very light yellow material which melted and decomposed at 322-331°. Recrystallizations from glacial acetic acid, diluted dioxane, toluene, and acetone failed to give a pure product. One very small fraction of material was obtained which melted at 331-333° and gave a mixed melting point with starting material (m.p. 360-361°) of 323-327°. No pure compound was isolated or identified.

Condensation Reactions

Preparation of 4,4'-bidibenzothienyl (attempted).

Run I. n-Butyllithium (0.175 mole in 160 ml. of ether) was prepared in the usual manner and added rather rapidly (12 min.) to a stirred solution of 26.6 g. (0.144 mole) of dibenzothiophene in 200 ml. of ether.[47,52] After refluxing for 20 hours, the mixture was allowed to come to room temperature. To the cool, stirred solution of 4-dibenzothienyllithium was added in small portions through a Liebig type condenser 25.6 g. (0.19 mole) of anhydrous cupric chloride. The reaction flask was immersed occasionally in an ice-bath in order to dissipate the heat generated by the reaction. The solution gradually turned from light amber to nearly black. After the addition of the cupric chloride had been completed and the vigorous reaction had subsided, the solution was stirred and refluxed until a Color Test I[227] was negative (2 hr.). The mixture was decomposed by pouring onto ice, and the water layer was made strongly acid with concentrated hydrochloric acid. The layers were separated, and the ether layer was extracted with dilute hydrochloric acid until the absence of a green color in the acid layer showed that all of the cupric chloride had been removed. A large amount of insoluble material that remained suspended at the bottom of the ether layer was filtered off, air-dried, and found to melt at 154-159° and to weigh 11.1 g. Numerous solubility tests were run on this material with only ethanol, acetone, and glacial acetic acid showing promise of being satisfactory. Ethanol and acetone were found to be unsatisfactory when larger runs were made. The use of glacial acetic acid appeared to be satisfactory, but after three recrystallizations the product still melted over a three degree range of 180-183° with prior shrinking. Three additional recrystallizations from the same solvent did not change the melting point. In addition, steam distillation and Soxhlet extraction with Skelly D failed to improve the purity of the product. Removal of the solvent from the dried (sodium sulfate) ether layer yielded a gum from which 1.5 g. of solid was obtained by crystallization from ethanol; m.p. 143-149°. This solid fraction also could not be purified by recrystallization.

Run II. This experiment was essentially the same as Run I. An ether solution of 0.0924 mole of n-butyllithium was used to metalate 17 g. (0.0924 mole) of dibenzothiophene. Addition of the cupric chloride (13.7 g.; 0.1016 mole), refluxing (45 min.), and hydrolysis were carried out as above. Very little solid remained suspended in the ether layer. The layers were separated, and the water layer was washed twice with 150-ml. portions of ether. The combined ether layer was washed with water, 10% sodium carbonate solution, and again with water, dried over sodium sulfate, and freed of solvent by distillation from a steam-bath. The crude material weighed 6.4 g. and melted at 142-152°. As in Run I recrystallization from glacial acetic acid failed to give a pure product.

Run III. This run was a duplicate of Run II in all respects. Attempts were made to purify the crude product by prolonged Soxhlet extraction with Skelly D, by steam distillation, and by vacuum sublimation. Although the last method of treatment did yield a small amount of sublimed dibenzothiophene, the main product showed no improvement in the melting point.

Condensation of 2,8-dibromodibenzothiophene-5-dioxide with resorcinol (attempted)

The procedure followed in the attempted condensation was essentially that used by Illuminati and Gilman[133] for the reaction of resorcinol with various heterocycles containing "active" halogen atoms. In a 250-ml. flask equipped with a stirrer, thermometer, and a calcium chloride tube was placed 7.5 g. (0.02 mole) of 2,8-dibromodibenzothiophene-5-dioxide, 2.2 g. (0.02 mole) of resorcinol, and 10 ml. of quinoline. Complete solution was not obtained even on stirring, heating to 100°, and adding 10 ml. more of quinoline. The mixture was cooled in a tap-water bath and 3.0 g. (0.022 mole) of anhydrous aluminum chloride was added in small portions over a period of 10 minutes. There was no noticeable evolution of heat on removing the cooling bath, and no change in the dark amber color could be observed. The reaction flask was slowly warmed to 145° and heated at 145-150° for 12 hours. The mixture gradually became homogeneous and dark red, then very viscous and filled with a fine precipitate. Heating and stirring were discontinued at the end of 12 hours, and the mixture was allowed to stand overnight. The solid was broken up and removed mechanically after extraction with boiling ethanol, water, and acid had failed. The dark red material was treated with hot 10% sodium hydroxide. Filtration while hot yielded an orange solid that melted at 250-260°. Treatment with dilute acetic acid again yielded the red material. Recrystallization from dioxane resulted in the recovery of 6.7 g. (89.4%) of 2,8-dibromodibenzothiophene-5-dioxide; m.p. and mixed m.p. 360-361°.

Condensation of 3,7-dinitro-2,8-dibromodibenzothiophene-5-oxide with resorcinol (attempted)

To a stirred mixture of 9.0 g. (0.02 mole) of 3,7-dinitro-2,8-dibromodibenzothiophene-5-oxide, 2.2 g. (0.02 mole) of resorcinol, and 20 ml. of quinoline was added in small portions 3.0 g. (0.022 mole) of anhydrous aluminum chloride while cooling in a tap-water bath. The cooling bath was then removed, and the mixture was slowly warmed to 145° and heated at 145-150° for 12 hours. To the cooled mixture was added 50 ml. of 1 N hydrochloric acid and 25 ml. of ethanol. On heating to about 60° the solid melted and a two-phase liquid suspension was formed. The suspension was poured into about 500 ml. of water, and the resulting mixture was acidified with 6 N hydrochloric acid. Filtration yielded a dark brown, finely divided product which was stirred with 400 ml. of 8% sodium hydroxide then filtered. Only inorganic, aluminum-containing material was isolated from the alkaline filtrate on acidification. The residue from the sodium hydroxide extraction weighed 6.5 g. and melted at 175-200°. One recrystallization from dilute acetic acid raised the melting point to 245-260°, but subsequent recrystallizations from the same solvent gave no further improvement. The product was then tested with ethanol, dilute ethanol, dioxane, dilute dioxane, benzene, and toluene without finding a satisfactory medium for recrystallization.

Condensation of 4-hydroxydibenzofuran with formaldehyde (attempted)

Condensations of 2-hydroxy-1,3-dimethylbenzene with formaldehyde by the method of Auwers[238] using an alkaline medium and by the method of Abel[239] using an acid medium were successfully carried out in preliminary experiments. The yields of 5,5'-di-(2-hydroxy-1,3-dimehylphenyl)methane were about the same (70% crude; 50% pure), but the product from the experiment using an alkaline solution was the more easily purified.

Run I. To a warm solution of 9.2 g. (0.05 mole) of 4-hydroxydibenzofuran in 36 ml. of water containing 4.0 g. of sodium hydroxide was added 3.8 g. of 40% aqueous formaldehyde (0.05 mole). After warming on the steam bath for 3.5 hours, the dark red solution was cooled slightly and acidified with 6 N hydrochloric acid. A dark green oil

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[238] K. Auwers, Ber., 40, 2524 (1907).

[239] J. Abel, ibid., 25, 3477 (1892).

precipitated which could not be made to crystallize and was separated by decanting off the aqueous layer. The green residue was dissolved in 100 ml. of boiling methanol. The resulting solution was filtered hot giving a filtrate that was deep red to transmitted light and green to reflected light. The hot solution was diluted just to turbidity with hot water and cooled in air. A dark green gum again separated which could not be made to crystallize and which could not be satisfactorily crystallized from dioxane, carbon tetrachloride, Skelly D, or glacial acetic acid. A check run gave essentially the same results.

Run II. A warm solution of 9.2 g. (0.05 mole) of 4-hydroxydibenzofuran in 150 ml. of 50% acetic acid was shaken thoroughly with 3.8 g. of 40% aqueous formaldehyde (0.05 mole), then allowed to cool overnight. The nearly white, granular product (which began to form in about 15 minutes after addition of the formaldehyde) was filtered off and found to weigh 4.5 g. and to melt indefinitely at 185-195°. Progressive dilutions of the filtrate with water yielded 2.6 g. of material melting at 100-160°, 0.9 g. melting at 101-102°, and 0.4 g. melting at 101-102°. The last two fractions were identified as unreacted 4-hydroxydibenzofuran (14.1% recovery) by the method of mixed melting points. The initial product could not be purified by recrystallization from methanol, dilute methanol, or glacial acetic acid. Solution in dilute alkali followed by reprecipitation by acid similarly did not improve the melting point.

Run III. This experiment was carried out in the same manner as Run II except that 250 ml. of 50% acetic acid was used, the solution was allowed to cool before adding the formaldehyde solution, and the reaction mixture was allowed to stand three days at room temperature. Filtration yielded 2.3 g. of a light tan, fluffy product which melted indefinitely at 200-225° and could not be purified either by recrystallization or by reprecipitation from an alkaline solution. Progressive dilution of the acetic acid filtrate gave a total of 3.6 g. (37.9% recovery) of 4-hydroxydibenzofuran; m.p. and mixed m.p. 101-102°.

Preparation of o,o'-dicarboxydiphenyl sulfide

This preparation was made in essential accordance with the procedure used by Bebb[34] for the preparation of an authentic sample of o-carboxydiphenyl sulfide. To a filtered solution of 2.8 g. (0.05 mole) of potassium hydroxide in 75 ml. of ethanol was added a filtered solution of 7.8 g. (0.05 mole) of o-chlorobenzoic acid in 25 ml. of ethanol. After reducing the volume to about 25 ml. the hot solution was added to a warm mixture of the disodium salt of thiosalicylic acid and ethanol prepared by adding a solution of 7.7 g. (0.05 mole) of thiosalicylic acid in 75 ml. of ethanol to a solution of 2.3 g. (0.1 g. atom) of sodium in 50 ml. of ethanol. The solvent was removed by evaporation under a water-pump vacuum while warming slightly to remove the last traces. The residue was warmed to 120°, a pinch of copper bronze was stirred in, and heating was continued under an air condenser until the temperature reached 250°. The mixture remained solid throughout, and after heating at 250° for 5 minutes, it was cooled and digested with 100 ml. of 10% sodium hydroxide. The nearly black solution was digested with Norite, filtered hot, cooled, and carefully neutralized with 6 N hydrochloric acid. Filtration yielded a slightly yellow product which melted at 218-223°. The slightly wet material was recrystallized from glacial acetic acid to give 10.3 g. (75.1%) of nearly pure o,o'-dicarboxydiphenyl sulfide melting at 228-231°. Further recrystallizations raised the melting point to 233-234°.

Anal. Calcd. for $C_{14}H_{10}O_4S$: neut. equiv., 274.3; S, 11.7. Found: neut. equiv., 275.0; S, 11.4, 11.7.

Initial attempts to prepare o,o'-dicarboxydiphenyl sulfide by the method of Mayer[234] (two runs), by the method of Hinsberg[240] (two runs), and following the general directions of Reinhalt[241] (one run) and of Hunter[242,243] (one run) were unsuccessful.

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[240] O. Hinsberg, ibid., 43, 1877 (1910).

[241] F. E. Reinhalt, J. Franklin Inst., 249, 248 (1950).

[242] B. A. Hunter, Doctoral Dissertation, Iowa State College, 1941.

[243] B. A. Hunter, Iowa State Coll. J. Sci., 15, 215 (1941).

Rearrangement Reactions

Preparation of 4-dibenzothiophenecarboxylic acid amide

Sixteen grams (0.07 mole) of 4-dibenzothiophenecarboxylic acid[47] were converted to the 4-dibenzothiophenecarboxylic acid chloride[195] by dissolving in 26 ml. of freshly distilled thionyl chloride and refluxing for one hour. After removal of the excess thionyl chloride by distillation, the crude acid chloride was allowed to stand overnight with 200 ml. of concentrated ammonium hydroxide. Filtration yielded 15.5 g. (98.4%) of crude amide melting at 240-242°. Two recrystallizations from dioxane gave 8.0 g. (50.8%) of pure 4-dibenzothiophenecarboxylic acid amide; m.p. 250-251°. The infrared spectrum[228] showed absorption at 13.2μ and 13.36μ, characteristic of 1,2,3- and 1,2-substitution. Bands at 3.03μ, 3.2μ, 6.03μ, and 6.2μ were those normally shown for the amide group.

Anal. Calcd. for $C_{13}H_9ONS$: S, 14.07. Found: S, 13.81.

Preparation of 4-aminodibenzothiophene by the Hofmann reaction

This preparation was made in essential accordance with the procedure used for the preparation of 4-aminophenoxathiin by the Hofmann reaction.[28] A solution of 4.3 g. (0.027 mole) of bromine and 5.3 g. (0.132 mole) of sodium hydroxide in 45 ml. of water was added to a suspension of 5.0 g. (0.022 mole) of 4-dibenzothiophenecarboxylic acid amide in 45 ml. of dioxane and 30 ml. of 10% sodium carbonate. The solution was heated on the water bath for 12 hours, then cooled and extracted with ether. The crude amine hydrochloride was precipitated by passing hydrogen chloride into the dried ether extract. Filtration gave 3.5 g. (67.4%) of crude 4-aminodibenzothiophene hydrochloride melting at 243-248°. This product was suspended in 500 ml. of dilute (1:10) ammonium hydroxide and allowed to stand overnight. The yield of crude 4-aminodibenzothiophene melting at 103-106° was 4.4 g. (63.9%). One recrystallization from dilute methanol gave 2.1 g. (48.0%) of pure amine; m.p. 109-110°. A mixed melting point with an authentic specimen[47,53] was not depressed. The yield of 4-aminodibenzothiophene obtained in this experiment is higher than that obtained by any other method (see Historical and Discussion sections of this thesis).

Reduction Reactions

Cleavage reactions with Raney nickel

The cleavage reactions described below were carried out in accordance with the procedure reported by Blicke and Sheets[177] for the reaction of dibenzothiophene with Raney nickel to yield diphenyl. The Raney nickel was activated by the procedure of Mozingo,[244] using the slight modifications suggested by Mozingo and co-workers[170], and incorporating ideas presented by Covert and Adkins.[245]

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[244] R. Mozingo, "Organic Syntheses", 21, 15 (1941).

[245] L. W. Covert and H. Adkins, J. Am. Chem. Soc., 54, 4116 (1932).

Cleavage of 2-bromodibenzothiophene.

Run I. A mixture of 1.3 g. (0.005 mole) of 2-bromodibenzothiophene, about 18 g. of freshly prepared Raney nickel, and 250 ml. of ethanol was refluxed for 0.5 hour, cooled, and filtered. Reduction in the volume of the filtrate, followed by dilution while hot with hot water to turbidity yielded 0.6 g. of material melting at 85-97°. The only pure material isolated and identified was 0.3 g. of unreacted 2-bromodibenzothiophene obtained by recrystallization from ethanol; m. p. and mixed m.p. 121-122°.

Run II. In this run an oil was obtained instead of a solid as in Run I. After attempts to induce solidification failed, the oil was removed by extraction with ether, recovered, and vacuum distilled to yield a small amount of liquid which could not be identified.

Run III. The product from this experiment was an oily emulsion obtained on vacuum distillation of the catalyst-free reaction mixture. On standing overnight in the refrigerator, the emulsion partially solidified. Filtration yielded 0.3 g. of white, shiny flakes melting at 67-70° and a very small amount of liquid which was not identified. Recrystallization of the solid from dilute ethanol yielded 0.25 g. (31.2%) of pure diphenyl; m.p. and mixed m.p. 70-71°.

Cleavage of dibenzothiophene-5-oxide (attempted). No identified product was obtained from the reaction of Raney nickel with dibenzothiophene-5-oxide. The small amount of oil that was isolated could not be crystallized or sublimed. A sample of the purest fraction had an index of refraction of 1.5286. This value does not correspond to that of any of the normally expected products.

Cleavage of dibenzothiophene-5-dioxide (attempted). The reaction of Raney nickel with dibenzothiophene-5-dioxide also yielded only a small amount of an unidentified oil.

Cleavage of dibenzothiophene (attempted). Two unsuccessful attempts were made to repeat the work of Blicke and Sheets.[177] Although their directions were followed as exactly as possible, no diphenyl was isolated in either run. The failure to obtain positive results may possibly have been due to the difficulties encountered in preparing Raney nickel of constant activity (see Discussion section of this thesis.)

Reductive debromination reactions

Reductive debromination of 2,8-dibromodibenzothiophene. The mole ratios of reactants used in this experiment were the same as those employed by Swislowski[6] in his preparation of 2,8-dihydroxydibenzofuran, and the same general procedure was followed except that an attempt was made to replace the steel bomb with a high-boiling solvent. Eighty ml. of triethylene glycol, 8.6 g. of 2,8-dibromodibenzothiophene, 12.4 g. of sodium hydroxide pellets, 1.9 g. of copper bronze, 8.1 g. of copper turnings, and 2.5 g. of cupric sulfate pentahydrate were placed in a 250-ml. two-necked flask equipped with an air condenser and a motor stirrer. The mixture was slowly warmed with stirring until the metal bath temperature was 165°. A period of two hours was then required to raise the bath temperature from 165° to 205° due to vigorous frothing of the reaction mixture. The reaction mixture was finally slowly warmed to reflux and heated at 245-250° for 12 hours. The cooled reaction mixture was vacuum distilled at 115-120°/0.7 mm. (175-180° external temperature) until the distillate remained clear on cooling. Filtration of the distillate yielded 1.1 g. of dibenzothiophene melting at 96-98°; identified by the method of mixed melting points. Dilution of the filtrate with water yielded an additional 1.4 g. of less pure material melting at 89-94°. The total yield of crude dibenzothiophene was 54.3%. Recrystallization from diluted ethanol yielded 1.6 g. (34.8%) of pure dibenzothiophene; m.p. and mixed m.p. 98-99°. The still-pot residue was boiled with water and the resulting mixture was filtered, cooled, and extracted with ether. An additional 0.1 g. of impure dibenzothiophene was isolated from the ether solution. Acidification of the water layer gave a gummy material that could not be crystallized or purified.

Reductive debromination of 2,8-dibromodibenzofuran.

Run I. A stirred mixture of 8.2 g. (0.025 mole) of 2,8-dibromodibenzofuran, 12.4 g. of sodium hydroxide pellets, 1.9 g. of copper bronze, 8.1 g. of copper turnings, 2.5 g. of hydrated copper sulfate, and 80 ml. of dimethoxytetraglycol was refluxed (220-230° bath temperature) for 12 hours. Vacuum distillation gave about 35 ml. of clear distillate at 108°/0.5 mm. which was diluted with water and filtered to yield 1.4 g. of white, flaky crystals; m.p. 78-80°. The product was established as being nearly pure dibenzofuran (33.3%) by a mixed melting point of 82-83° with known dibenzofuran (m.p. 83-83.5°). The residue remaining in the reaction flask was vacuum distilled three more times after adding additional dimethoxytetraglycol between each distillation. Dilution of the distillates with water yielded three fractions of less pure dibenzofuran which melted at 78-81°, 72-77°, and 76-79°, respectively, and which weighed a total of 0.8 g.. The total yield of crude dibenzofuran was 52.3%. Treatment of the still-pot residue as in the dibenzothiophene debromination experiment above yielded only gums which could not be identified.

Run II. This experiment was carried out in exactly the same manner as Run I except that the copper and copper sulfate catalysts were omitted. Only a small amount of impure dibenzofuran was isolated from the distillate of the initial vacuum distillation. Treatment of the residue remaining in the reaction flask as above yielded a very small amount of impure dibenzofuran and a small amount of ethanol insoluble material melting above 300° which could not be identified.

DISCUSSION

Metalation Reactions

The "direct" metalation reaction, i.e., the replacement of hydrogen by an elemental metal, is obviously the simplest method of preparing a selected organometallic compound.* Unfortunately, the successful preparation of heterocyclic organometallic compounds by this "direct" method is more the exception than the rule. It is usually necessary to resort to hydrogen-metal or halogen-metal interconversion reactions with more reactive organometallic compounds.

The only reported successful "direct" metalation of dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, or dibenzo-p-dioxin was the reaction of dibenzofuran with sodium-potassium alloy to yield 4-dibenzofurylpotassium.[19] Treatment of dibenzofuran with sodium in ethanol[246] and of dibenzothiophene with sodium[47] in liquid ammonia leads to reduction of the benzenoid ring. Consequently, the report by Bradley[14] that the reaction of dibenzofuran with lithium in dioxane or ether gave good yields of o-hydroxybiphenyl was of considerable interest and suggested further experiments to determine the scope of the reaction,

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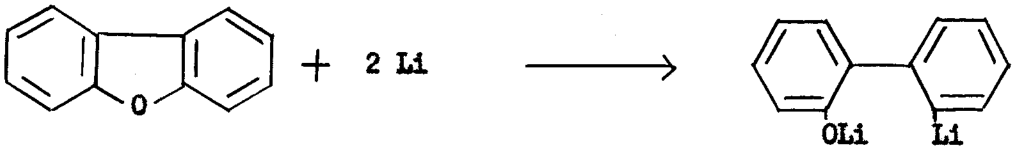
*The reaction of an organic halide with the free metal is, of course, equally facile, but usually involves preliminary preparation of the requisite halogen compound.

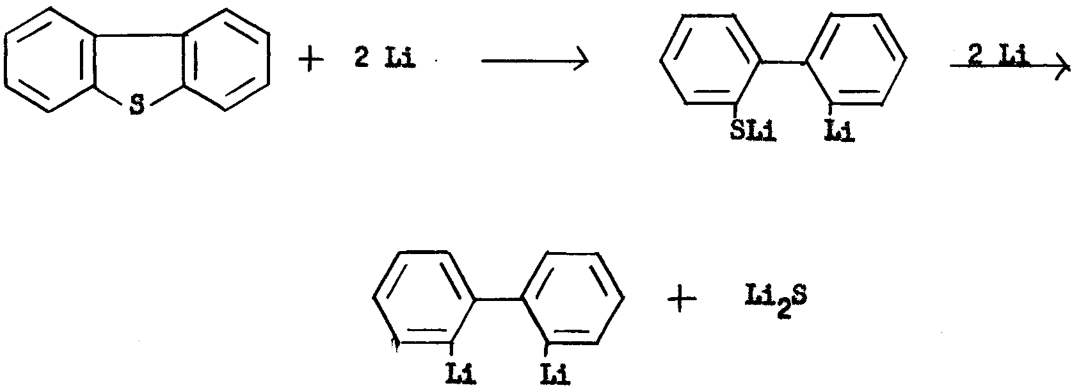
[246] H. Gilman, E. W. Smith and L. C. Cheney, J. Am. Chem. Soc., 57, 2095 (1935).

both in respect to its use as a means of structure proof of derivatives of dibenzofuran, and to its extension to other related heterocycles.

The experimental results obtained by Bradley were satisfactorily duplicated for the cleavage of dibenzofuran with lithium in dioxane using an atmosphere of either dry air or of nitrogen and terminating the reaction by hydrolysis. The most logical reaction mechanism would involve the cleavage of an oxygen-carbon bond to form an oxygen-lithium bond and a carbon-lithium bond. This explanation appeared to be in jeopardy when it was observed that at no time was Color Test I[227] positive and that no carboxylic acid product could be isolated when the dioxane reaction mixture was carbonated.



The only product that could be isolated when dibenzothiophene was treated with lithium in dioxane and the reaction mixture hydrolyzed was a small amount of diphenyl. When the reaction was terminated by carbonation, however, diphenyl and o-mercaptodiphenyl were isolated in about equal amounts. A two-step cleavage reaction was thus indicated. As with dibenzofuran, though, Color Test I[227] was negative throughout, and no carboxylic acid product could be isolated from the carbonated dioxane reaction mixture.



The reaction of lithium with dibenzofuran in ether was carried out by Bradley by using a sealed tube and mechanical shaking at room temperature. It appeared of interest to determine what reaction, if any, would occur at the reflux temperature of ether at atmospheric pressure. Somewhat unexpectedly, in view of the above results, Color Test I[227] was positive throughout the reaction, and carbonation of the reaction mixture resulted in a good yield of 3,4-benzocoumarin (the lactone of 2'-hydroxy-2-diphenylcarboxylic acid). On the basis of these results, the above two reaction mechanisms are thought to be satisfactory, although no cleavage could be obtained with lithium and dibenzothiophene in ether.

In connection with the failure to obtain a positive Color Test I[227] and to isolate any carboxylic acid on carbonation from the reaction of dibenzofuran with lithium in dioxane, the following previously reported observations are of interest. Bebb[34] found that when n-butyllithium was prepared in dioxane and then reacted with dibenzothiophene, the color test gradually became weaker, no acid was obtained on carbonation, and 90% of the starting dibenzothiophene was recovered. In addition, he was unable to isolate any cleavage products from the dioxane fraction. As part of a general study on the cleavage of ethers by organolithium compounds, Haubein[247] added dioxane to a petroleum ether solution (0.6 M) of n-butyllithium and observed that heat was evolved and that Color Test I[227] became negative in 55 minutes. If the reaction was carried out while cooling in an ice-bath, one hour was required for the color test to become negative. No attempt to isolate cleavage products was reported. All of the above results can be explained by assuming that the organolithium compound was used up in cleavage of dioxane. In the lithium cleavage reactions in dioxane carried out during this work, the temperature of refluxing dioxane was used. On the basis of the results reported by Haubein[247], rapid cleavage under these relatively drastic conditions would be expected. This was substantiated when it was found that phenyllithium prepared in dioxane gave a negative Color Test I[227] after one hour of stirring at reflux temperature, whereas over 5 hours were required for the reaction of dioxane with n-butyllithium in ether to go to completion at room temperature. That no phenyllithium remained in the first reaction was demonstrated when no benzoic acid

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[247] A. H. Haubein, Doctoral Dissertation, Iowa State College, 1942.

could be isolated after carbonation. On the basis of these observations, it was concluded that the cleavage of dibenzofuran (and of dibenzothiophene) by lithium in refluxing dioxane probably yields an intermediate compound containing a carbon-metal linkage which is immediately destroyed through reaction with the dioxane.

It should be mentioned that the cleavage of dibenzofuran with lithium in diethyl ether followed by carbonation is probably the method of choice for the preparation of 3,4-benzocoumarin. Cahn[233] reported that the condensation of phenol with the diazonium sulfate of anthranilic acid gave yields of 3,4-benzocoumarin only slightly over 20%, but that even these relatively low yields were better than those that could be obtained by any of the other procedures tried. The yield of 47.0% obtained during the present investigation from the lithium cleavage of dibenzofuran is consequently over twice as high as any previously reported.

Time did not permit a thorough evaluation of the possibilities for the proof of structure of heterocycles by cleavage of the carbon-hetero atom linkage with lithium. Should the process be found to be quite general, a very useful synthetic and analytical tool would be available. The method has two distinct advantages over the Raney nickel cleavage procedure (see Historical section of this thesis). First, the reaction is much easier and simpler to carry out with lithium since it does not involve an initial activation of the metal. It was the author's experience that the activation of the Raney nickel was a very critical part of the cleavage reactions carried out with that metal.

Second, it seems reasonable that the hydrogen present in the Raney nickel catalyst might react with certain functional groups which would be stable towards lithium. Further experimental work is certainly indicated.

Monometalation of the heterocycles under consideration has usually been accomplished most satisfactorily with n-butyllithium. With dibenzothiophene the pure yields run below 50% when the reaction is carried out in diethyl ether. The superiority of n-propyllithium over n-butyllithium in certain related reactions[248] lead to the initiation of experiments for the purpose of comparing the relative efficiency of the two organometallic compounds for the metalation of dibenzothiophene. An initial experiment using n-propyllithium in which aliquots of the ether solution were carbonated at regular intervals indicated that a reflux time of 12 hours gave the highest yields of 4-dibenzothiophenecarboxylic acid. A second experiment in which the entire reaction mixture was carbonated after 12 hours of refluxing confirmed this conclusion. The 75% crude yield and 48% pure yield of 4-dibenzothiophenecarboxylic acid with n-propyllithium as the metalating agent are higher than any the author was able to isolate in the corresponding reaction with n-butyllithium. In addition, washing of the crude acid with water gave a much purer product from the n-propyllithium reaction due to the greater solubility of the butyric acid over valeric acid.

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[248] B. F. Hofferth, Doctoral Dissertation, Iowa State College, 1950.

Dimetalation with n-butyllithium has been observed in reactions with phenoxathiin,[61] thianthrene,[29] and dibenzo-p-dioxin.[29] Only one brief report (see Historical section of this thesis) of the isolation of a dimetalated product from the reaction of dibenzofuran and n-butyllithium has been made. It was found during the present work that treatment of dibenzothiophene with 3.3 equivalents of n-butyllithium for a prolonged period of time led only to an excellent yield of the monometalated derivative. This result was to be expected since it has been demonstrated that the metalation of dibenzofuran is relatively much easier than that of dibenzothiophene (see Historical section of this thesis). Quite unexpected, however, was the failure to isolate dimetalated products from the reactions of dibenzothiophene with n-butylsodium and benzylsodium, since the corresponding reactions with dibenzofuran give good yields of 4,6-disubstituted products. Smaller yields of the disubstituted dibenzothiophenes would not have been surprising, but the apparently complete absence of dimetalation could not be explained.*

The selective metalation of dibenzothiophene in the 3-position presents the possibility of preparing 3-substituted derivatives via the organometallic compound. Treatment of the intermediate 3-dibenzothienylcalcium iodide with bromine, however, did not yield any of the desired 3-bromodibenzothiophene. Instead, only nuclear bromination of non-metalated dibenzothiophene occurred to yield a very small amount of

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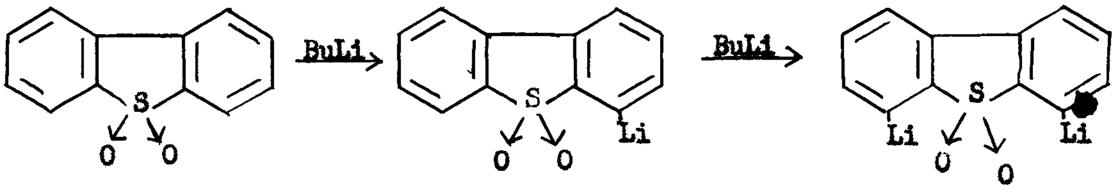
*Further attempts to dimetalate dibenzothiophene by means of metalating agents more active than n-butylsodium and benzylsodium are currently being carried out by Mr. John Morton.

2,8-dibromodibenzothiophene. The metalation procedure was checked by the author and by Mr. John Morton by satisfactory repetitions of Jacoby's preparation of the 3-dibenzothiophenecarboxylic acid, and the bromination technique was checked by the author by a parallel preparation of 4-bromodibenzothiophene by the reaction of bromine with 4-dibenzothienyllithium. The latter experiment was also undertaken in order to determine the unpublished physical constants of the previously prepared 4-bromodibenzothiophene.[47]

The literature concerning the reactions of sulfides, sulfoxides, and sulfones with metals and organometallic compounds was thoroughly reviewed by Webb.[35] As part of a general study of such reactions, he treated dibenzothiophene-5-dioxide and diphenyl sulfone with n-butyllithium at room temperature, but was unable to isolate any pure products after carbonation.

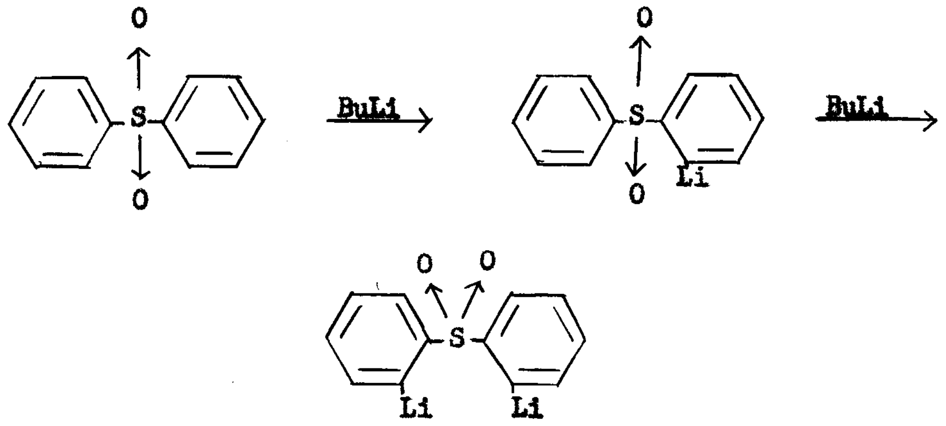
The successful metalation of dibenzothiophene-5-oxide with n-butyllithium which was accomplished by using reduced temperatures, has been reported elsewhere.[57] Application of this technique to the metalation of dibenzothiophene-5-dioxide similarly gave after carbonation acid products which could be purified. The progress of the reaction was followed in the initial experiments by the use of color tests. Color Test I[227] was found to be positive throughout the reaction, but Color Test II[229] did not remain positive on prolonged stirring until at least 3.0 equivalents of n-butyllithium had been added. The acid product from these experiments was identified as 4,6-dicarboxydibenzothiophene-5-dioxide. It was then observed that the use of only 1.0 equivalent of the organometallic compound yielded on carbonation 4-carboxydibenzothiophene-5-dioxide, thus indicating that the metalation proceeded in a step-wise fashion as follows:



These experiments also again demonstrate the greater stability of the sulfone group over the sulfoxide group since the reaction of n-butyllithium with dibenzothiophene-5-oxide resulted in reduction of the sulfoxide group to the sulfide along with the observed metalation.

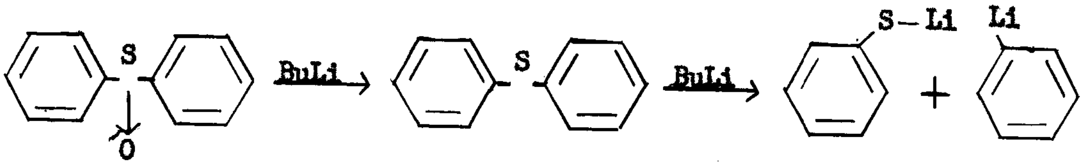
It should be noted that, while an authentic sample of 4,6-dicarboxydibenzothiophene-5-dioxide could not be prepared, the structure assigned to the product obtained by the reaction of two or more equivalents of n-butyllithium with dibenzothiophene-5-dioxide with subsequent carbonation is undoubtedly correct. This conclusion was reached by consideration of the results of the analyses for the percentage of sulfur and the neutral equivalent, by observing that the infrared spectrum[228] indicates the presence of a sulfone group and 1,2,3-substitution in both benzene rings, by noting that the same reaction using only one equivalent of n-butyllithium definitely yields 4-carboxydibenzothiophene-5-dioxide, and by analogy with the corresponding metalation reactions with diphenyl sulfone which were found to yield *o*-carboxydiphenyl sulfone and *o,o'*-dicarboxydiphenyl sulfone on carbonation.

The technique of metalation at lowered temperatures was next extended satisfactorily to the reaction of diphenyl sulfone with *n*-butyllithium. The course of the reaction was again followed by color tests. As was to be expected from the observations discussed above for dibenzothiophene-5-dioxide, Color Test II[229] did not remain positive on prolonged stirring until at least 3.0 equivalents of the organometallic compound had been added, although Color Test I[227] was positive throughout. Under these conditions carbonation likewise yielded a dicarboxy sulfone, *o,o'*dicarboxydiphenyl sulfone. While this work was in progress, Truce and Amos[235] reported the reaction of diphenyl sulfone with about one equivalent of n-butyllithium to yield on carbonation *o*-carboxydiphenyl sulfone (*o*-benzenesulfonylbenzoic acid). A check of their results using reduced temperature conditions was then satisfactorily carried out. These results indicated that the metalation of diphenyl sulfone also proceeds step-wise:

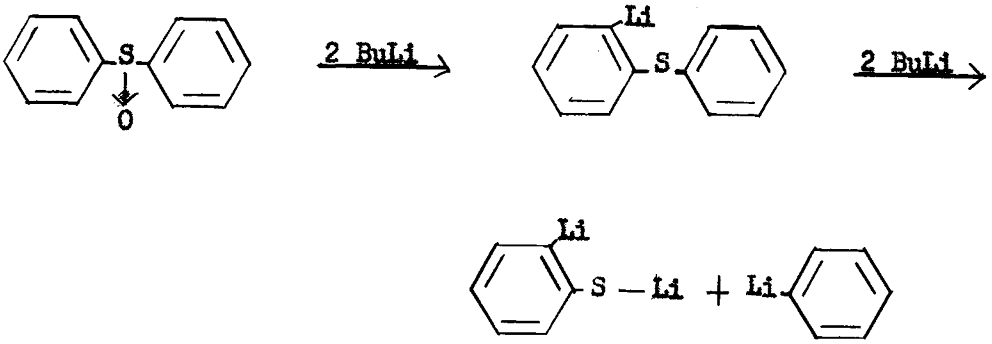


In order to prove the structure of the o,o'-dicarboxydiphenyl sulfone, an authentic sample of the compound was prepared. The melting point (220-1°) of the compound obtained by the author, however, did not agree with the recorded value[234] of 137°, although the melting points of the sulfide and sulfoxide were in agreement. The first attempt to check the experimental procedure of Mayer yielded only the sulfoxide, possibly because the permanganate solution used was too alkaline. In two subsequent experiments in which a neutral solution was used, the only compound isolated melted at 220-221° and gave no depression in the melting point when mixed with a sample of the material obtained by peroxide oxidation of the sulfide in glacial acetic acid. In addition the same product was obtained on oxidizing the sulfoxide with peroxide in glacial acetic acid. The analytical values for the per cent of sulfur and for the neutral equivalent found for the material melting at 220-221° also were in agreement with those calculated for o,o'-dicarboxydiphenyl sulfone. Further evidence for the correctness of this structure was obtained by infra-red absorption measurements which indicated only 1,2-substitution of the benzene ring and the presence of a sulfone group. Consequently, the melting point reported by Mayer[234] is believed to be in error. The fact that o,o'-dicarboxydiphenyl sulfoxide melts higher than either the corresponding sulfide or sulfone whereas the sulfone has the lowest melting point of the three compounds is noteworthy, since the melting point of the sulfide, sulfoxide, and sulfone generally increase in that order in any particular series.

To date attempts to extend the reduced-temperature metalation technique to diphenyl sulfoxide have not been completely successful. By analogy with the reaction of dibenzothiophene-5-oxide with n-butyllithiu, reduction of the diphenyl sulfoxide to diphenyl sulfide with concurrent or subsequent metalation to yield o-phenylmercaptobenzoic acid on carbonation was expected. However, the isolation of benzoic acid in appreciable yields on carbonating the reaction mixture of n-butyllithium and diphenyl sulfoxide indicates that a cleavage reaction of some sort is involved. In view of the fact that diphenyl sulfide itself was cleaved to some extent by n-butyllithium,[34] a reasonable series of reactions would be



Although the search for thiophenol was both extensive and intensive, none was isolated. Similarly, no thiosalicylic acid was isolated which might have been formed by the following sequence of reactions:



Apparently the reaction is much more complicated, and time did not permit further attempts at identification of the bicarbonate soluble acidic liquid which was always obtained along with the benzoic acid. The neutral liquid that was repeatedly isolated from the ether layer of the reaction mixture likewise could not be identified.

In connection with the general problem of the relative orienting influences of ortho-para and meta directing groups, it seemed of interest to extend the metalation reaction with n-butyllithium to phenoxathiin-10-oxide. The reaction of phenoxathiin itself with n-butyllithium yields 4-phenoxathiinyllithium, i.e., metalation occurs in the 4-position. As pointed out elsewhere,[57] the reaction of dibenzothiophene-5-oxide with n-butyllithium is strongly exothermic, whereas the same reaction with dibenzothiophene proceeds at room temperature with no noticeable evolution of heat. On this basis the assumption might be made that the coordination of the lithium cation with the oxygen of the sulfoxide group is a much more energetic reaction than is the corresponding coordination with the sulfide linkage. The reaction of dibenzofuran with n-butyllithium is similar to the reaction with dibenzothiophene in that no heat is evolved. Consequently it is conceivable that in phenoxathiin-10-oxide the sulfoxide group might exert the greater directive influence in metalation reactions by virtue of its apparent ability to undergo the initial coordination more readily than the hetero oxygen or sulfur atoms. The product isolated from the one metalation of phenoxathiin-10-oxide with n-butyllithium that was carried out was not identified, but monometalation in the 4-position was definitely ruled out on the basis of the melting point since the acid isolated melted at 223-224°, whereas 4-phenoxathiincarboxylic acid melts at 168-169°.[28] The reaction is presently being investigated further by Mr. T. Reid. A corresponding metalation of phenoxathiin-10-dioxide would certainly be worthwhile.

4-Hydroxydibenzofuran has reportedly[21] been prepared in yields varying from 45% to 52%. Under essentially the same conditions, only 33%[47] and 21%[54] yields of 4-hydroxydibenzothiophene were obtained. These results again reflect the relative greater ease of metalation of dibenzofuran over dibenzothiophene. In order to further extend the comparison, 1-hydroxythianthrene and 4-hydroxyphenoxathiin were prepared in 2.5% and 15.5%, respectively, after first satisfactorily checking the experimental procedure by the preparation of 4-hydroxydibenzofuran in 45% yield. The higher yield of 4-hydroxyphenoxathiin over 1-hydroxythianthrene was the expected result.

As mentioned earlier (see Historical section of this thesis) the reaction of _n_-butyllithium with 2-bromodibenzofuran may proceed in one of two ways to form either 2-dibenzofurancarboxylic acid or 2-bromo-4-dibenzofurancarboxylic acid. 2,8-Dibromodibenzofuran, however, undergoes only halogen-metal interconversion with _n_-butyllithium. It would be of interest to know whether or not the same reactions occur with the analagous chloro-and iodo-substituted derivatives. An initial experiment with 2,8-dichlorodibenzofuran and _n_-butyllithium was carried out, but no clear-cut results could be obtained. The author feels that perhaps the use of slightly different reaction conditions might have given positive results but a lack of time prevented further investigation.

Oxidation Reactions

As discussed elsewhere[67] (see, also, Historical section of this thesis) phenoxathiin was found to be oxidized with greater ease than was dibenzothiophene. During the course of the comparative studies which were carried out by the author reaction conditions that gave optimum yields of dibenzothiophene-5-oxide and 5-dioxide and phenoxathiin-10-oxide and -10-dioxide were developed. Hydrogen peroxide (30% aqueous solution) in glacial acetic acid was found to be the reagent of choice for the preparation of the dioxides. The same oxidizing agent was found to work equally well for the preparation of 4-bromodibenzothiophene-5-dioxide, 2,8-dibromodibenzothiophene-5-dioxide, 4-carboxydibenzothiophene-5-dioxide, and 4-dibenzothiophenecarboxamide-5-dioxide.

The use of 30% aqueous hydrogen peroxide in refluxing ethanol solution proved to be a convenient method for the preparation of the sulfoxides of phenoxathiin and o,o'-dicarboxydiphenyl sulfide. Good yields were obtained in both cases with products being obtained that were completely free of the sulfone derivatives.

Halogenation Reactions

The bromination of 4-hydroxydibenzofuran was reported[161] to result in a 35% yield of 1-bromo-4-hydroxydibenzofuran. Since Avakian[17,53] was able to obtain 2-acetamino-3-chlorodibenzothiophene in 87% yield by the chlorination of 2-acetamindibenzothiophene with sulfuryl chloride, and Lentz[54] was able to similarly prepare a monochloro-4-hydroxydibenzothiophene, it seemed of interest to extend the sulfuryl chloride chlorination procedure[249] to 4-hydroxydibenzofuran. It was found that by proper variation of the reaction conditions either a monochloro- or a dichloro-4-hydroxydibenzofuran could be obtained in yields at least equal to those obtained in bromination. The monochloro-4-hydroxydibenzofuran was assumed to be 1-chloro-4-hydroxydibenzofuran by analogy with the bromination product. Similarly, the dichloro derivative is considered to be 1,3-dichloro-4-hydroxydibenzofuran since nitration of 1-bromo-4-methoxydibenzofuran has been shown to yield 1-bromo-3-nitro-4-methoxydibenzofuran[117] and since the infra-red spectrum indicated substitution in only one of the benzene rings. That one of the chlorine atoms of the dichloro derivative is in the same position as the chlorine atom in the monochloro compound was established by chlorination of the monochloro material to a dichloro product which did not depress the melting point when mixed with a sample of the dichloro compound prepared by direct chlorination of 4-hydroxydibenzofuran.

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[249] For a comprehensive review of the chlorination of organic compounds with sulfuryl chloride see H. C. Brown, Ind. Eng. Chem., 36, 785 (1944).

Attempts to extend the sulfuryl chloride chlorination technique to the chlorination of dibenzofuran itself met with little success. When it was found that the only pure compound that could be isolated was recovered starting material, recourse was made to the previously reported[236] procedure for the preparation of the desired 2,8-dichlorodibenzofuran by direct chlorination.

Although the preparation of 2,8-dibromodibenzothiophene has been reported by several workers[27] (see, also, Table III), only Neumoyer and Amstutz[74] record any yields and specific reaction conditions. They state that direct bromination in carbon disulfide solution gave a 40% yield of material which melted at 225-228° after recrystallization from acetic anhydride, while the use of a glacial acetic acid solution resulted in a 24% yield of product melting at 226-228.5°. No catalyst was used in either preparation. Modification of the above procedures through the use of iron powder as a catalyst and of carbon tetrachloride as the solvent yielded 76.6% of crude product melting at 204-211°. Recrystallizations from toluene gave a pure yield of 44.2%; m.p. 225-226° (uncorrected).

Nitration Reactions

The labilizing influence of the nitro group on a substituent group or atom in the ortho or para positionis awell-known and much-used phenomonen of the chemistry of aromatic nitro compounds. With this fact in mind, attempts were made to nitrate 2,8-dibromodibenzothiophene and

2,8-dibromodibenzothiophene-5-dioxide. It was hoped that the resulting nitro-bromo derivative would possess a bromine atom sufficiently "active" to enter into a Friedel-Crafts type of reaction (see section on Condensation Reactions).

The successful nitration of 2,8-dibromodibenzothiophene was accomplished only after resorting to the rather drastic conditions of treating the dry starting material with warm, fuming nitric acid. In accordance with the known action of nitric acid on sulfur-containing heterocycles (see Historical section of this thesis) the isolation of a monoxide derivative was not unexpected. The nitro groups most probably could have entered into the 1,3-, 1,7-, 1,9-, or 3,7-positions. The first three possibilities were ruled out on general considerations of the nitration reactions of dibenzofuran and dibenzothiophene derivates. The product was thus tentatively established as being 2,8-dibromo-3,7-dinitrodibenzothiophene-5-oxide. The presence of a sulfoxide group was confirmed by infra-red absorption measurements.[228]

Although dibenzothiophene-5-dioxide[22,63,68] canbe satisfactorily nitrated, all attempts to nitrate 2,8-dibromodibenzothiophene-5-dioxide were unsuccessful. Perhaps this should not have been surprising since both the two bromine atoms and the sulfone group deactivate the molecule towards further substitution.

Condensation Reactions

In an effort to extend the previously mentioned (see Historical section of this thesis) reaction of resorcinol with heterocycles containing "active" halogens to derivatives of dibenzothiophene, 2,8-dibromodibenzothiophene-5-dioxide was treated with resorcinol in quinoline in the presence of aluminum chloride. The hope that the meta-directing sulfone group had labilized the bromine atoms sufficiently for them to enter into the condensation reaction, however, was not realized. When the same experiment was carried out with 2,8-dibromo-3,7-dinitrodibenzothiophene-5-oxide, reaction of some sort apparently occurred, but the product obtained could not be purified. This result was not too unexpected since Friedel-Crafts type reactions usually cannot be successfully carried out with compounds containing nitro groups.[108]

The lack of success which attended efforts to condense 4-hydroxydibenzofuran with formaldehyde cannot be readily explained. Since the para-position and one ortho-position are unsubstituted in 4-hydroxydibenzofuran, and since the procedures tried had been checked by the preparation of known compounds, the preparation of 1,1'-(or 3,3'-)-di-(4-hydroxydibenzofuryl)methane should have proceeded quite readily. That some reaction occurred was evidenced by the isolation of crude materials which melted at temperatures above the melting point of the starting material. However, the reaction was certainly not clear-cut since the crude products could not be purified.

It was reported recently[156,250] that the hydrocarbon perylene had been isolated from several mixtures involving 1-naphthyllithium and 1-naphthylmagnesium bromide. Evidence was presented which supported a reaction mechanism involving the cyclodehydrogenation by lithium metal of 1,1'-binaphthyl rather than a free radical mechanism. If the former supposition is correct, then one might expect other similarly constituted bi-radicals to undergo analagous cyclodehydrogenations by means of lithium metal. In considering the extension of this hypothesis to dibenzofuran and dibenzothiophene derivatives, the most logical choices for initial experiments appeared to be either 1,1'- or 4,4'-bidibenzofuryl or -bidibenzothienyl. The ready availability of the 4-position in both dibenzofuran and dibenzothiophene through metalation with organolithium compounds, and the difficulties inherent in any procedure leading to 1-substitution in either heterocycle, indicated that the starting material of choice should be the one condensed <u>ortho</u> to the hetero atom.

Attempts were consequently made to prepare 4,4'-bidibenzothienyl by the reaction of 4-dibenzothienyllithium with anhydrous cupric chloride. Thisprocedure is a modification of the method used earlier in these laboratories for the preparation of bidibenzofuryls (see Historical section of this thesis). Although a crude product was obtained which probably contained some of the desired condensed compound, attempts

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[250] H. Gilman and C. G. Brannen, J. Am. Chem. Soc., 71, 657 (1949).

at purification were unsuccessful. For this reason the cyclodehydrogenation was not attempted, and time did not permit further experiments directed toward the preparation of the intermediate biaryl.

Rearrangement Reactions

As pointed out previously (see Historical section of this thesis) the 48% yield of 4-aminodibenzothiophene obtained by use of the Hofmann reaction with 4-dibenzothiophenecarboxylic acid amide is equal to or better than the yields of the same compound prepared by other procedures. A discussion of the possibility of oxidation of the nuclear sulfur by the hypochlorite solution present while the Hofmann reaction is being carried out has been given elsewhere.[67] The conclusion was reached that the oxidizing conditions were not sufficiently strong in this case, since the unoxidized 4-aminodibenzothiophene was the only compound isolated.

Reduction Reactions

The reported reductive desulfurization of dibenzothiophene[177] with Raney nickel appeared to offer a convenient method for the determination of the structures of derivatives of dibenzothiophene. Orienting experiments with 2-bromodibenzothiophene, dibenzothiophene-5-oxide, dibenzothiophene-5-dioxide, and dibenzothiophene, however, soon indicated that one or more phases of the reaction must be quite critical. In only one of the three runs which were made with 2-bromodibenzothiophene, was any cleavage product isolated, and since reductive debromination had also occurred to give diphenyl instead of the hoped-for m-bromodiphenyl, further variations in the experimental conditions were not tried. Attempts to isolate and identify cleavage products from the reaction of Raney nickel with dibenzothiophene-5-oxide and dibenzothiophene-5-dioxide proved fruitless, as did also attempts to repeat the work reported by Blicke and Sheets[177] on the cleavage of dibenzothiophene. From observations made during the course of these experiments, the author believes that the most critical step of the cleavage reaction is the preparation of the Raney nickel. It was found very difficult to prepare Raney nickel of constant reactivity, and consequently it was difficult to duplicate the results of any one cleavage reaction. As pointed out above (see Metalation section of Discussion portion of this thesis), the use of lithium metal in refluxing dioxane solution appears to be a simpler and more reproducible method for the cleavage of dibenzothiophene derivatives as a means of structure proof.

Initial attempts to carry out alkali fusions of bromodibenzofurans and bromodibenzothiophenes in the presence of high-boiling glycol solvents were previously reported[182] as yielding only debrominated products. A discussion of the mechanism and scope of this "reductive debromination" reaction was given at that time. Since the presence of an hydroxyl group in the glycol solvent molecule was thought to make possible the observed reduction reaction, subsequent experiments (see Experimental section of this thesis) were carried out using dimethoxytetraglycol as the high-boiling solvent. However, only dibenzofuran was isolated from the attempted alkali fusion of 2,8-dibromodibenzofuran in dimethoxytetraglycol. Since the manufacturer's[*] specifications indicated that the hydroxyl content of the dimethoxytetraglycol was well below that needed for the reductive debromination, the initial step of the reduction reaction must have been different from that which occured when glycols were involved. In all probability the sodium hydroxide first cleaved the glycol ether to give the sodium alcoholate, which was then oxidized in the same manner as proposed earlier.[182]

No further attempts to carry out the alkali fusion reaction were made, although the use of a high-boiling ether that is more stable to cleavage by alkali than dimethoxytetraglycol might have been proven successful.

Suggestions for Further Research

A critical survey of the Historical section of this thesis reveals that many of the comparisons of the reactions of dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin were severely limited by a lack of experimental data. In numerous places throughout the preceding sections brief mention has been made of various experiments that would be of interest for comparative purposes. The following material

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[*] Carbide and Carbon Chemicals Corporation, 30 East 42nd Street, New York 17, N. Y..

is an attempt to present in one place the several ideas for experiments to be carried out which seemed of particular interest to the author.

The successful cleavage of dibenzofuran and dibenzothiophene with lithium in dioxane and of dibenzofuran in diethyl ether (see pp. 78 and 110 of this thesis) suggests that the following experiments should be tried:

1. React lithium with other heterocyclic compounds such as carbazole, phenoxathiin, phenothiazine, phenoxazine, benzofuran, benzothiophene, and indole. The results of experiments presently being carried out by Mr. R. K. Ingham on the reaction of lithium with phenothiazine derivatives and by Mr. T. Reid on the reaction of lithium with phenoxathiin will be of interest.

2. React lithium with dibenzothiophene-5-oxide and -5-dioxide, phenoxathiin-10-oxide and -10-dioxide, andphenothiazine-5-oxide and -5-dioxide.

3. Extend the lithium cleavage reaction to derivatives of dibenzofuran, dibenzothiophene, and any of the other heterocycles mentioned in 1 and 2 which give easily identifiable products in order to investigate the scope of the reaction as a method of structure proof. The possibility of secondary reactions such as the replacement of a halogen atom by lithium should be kept in mind. A methyl derivative would probably be the compound of choice for initial experiments.

4. Terminate by carbonation as well as hydrolysis those reactions which give a positive Color Test I[227].

5. Terminate by oxidation with molecular oxygen in the presence of an equivalent amount of n-butylmagnesium bromide those reactions which are found to yield carboxylic acids on carbonation. Both the carbonation and oxidation procedures present the possibility of introducing water-solubilizing groups into the molecule.

6. React lithium with a compound such as triphenyl-4-dibenzofuryltin in dioxane or ether. Should cleavage occur, an excellent method for introducing water-solubilizing groups into tetra-aryl tin compounds would be available. The corresponding reaction might be extended to the trialkyl-dibenzofuryltin derivatives. Reactions of this type could be tried with other organometallic compounds and organosilicon derivatives.

7. React lithium with dibenzothiophene in an ether solution which boils higher than diethyl ether. Di-n-butyl ether should be tried. Use of the higher temperature might possibly lead to a cleavage reaction which produced an organometallic compound susceptible to carbonation.

8. React lithium with dibenzothiophene in liquid ammonia and compare with the analagous reaction with sodium which leads to reduction of the benzenoid ring.

9. React calcium with dibenzofuran in dioxane or ether as a means of comparing the relative reactivities of lithium and calcium.

As mentioned in the Historical section (see p. 9 of this thesis), the reaction of 2-bromodibenzofuran with n-butyllithium yields on carbonation 2-dibenzofurancarboxylic acid if the reaction period is short, or 2-bormo-4-dibenzofurancarboxylic acid if the reaction time is relatively long. The reactions of n-butyllithium with 2-bromodibenzothiophene and 2-bromophenoxathiin were observed to give only halogen-metal interconversion, but in both cases the reaction time was relatively short. It would certainly be of interest to carry out the last two reactions for longer periods of time. A reaction time of 20 to 24 hours should be sufficient. In addition, reactions in which the chloro- or iodo-derivates were substituted for the bromo-compounds should be run. Also, the reaction of n-butyllithium with any 2-positioned halogen derivative of thianthrene or dibenzo-p-dioxin would be of interest.

The reaction of n-butyllithium with 2,8-dibromodibenzofuran to give halogen-metal interconverion, coupled with the reaction of phenylcalcium iodide with the same halogen compound to yield on carbonation 2,8-dibromo-4,6-dicarboxydibenzofuran (see p. 9 of this thesis) offers a method of selectively introducing carboxylic acid groupings which should be extended to the analagous halogen derivatives of dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin. In addition, analagous reactions in which the dichloro and diiodo derivatives are used in place of the 2,8-dibromo compound should be investigated.

The reaction of n-butyllithium with methoxy derivatives of dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin should be studied to determine the relative influences of the hetero elements present. Of particular interest would be a reaction of

4-methoxydibenzothiophene and butyllithium, since the oxygen with its stronger directing influence might direct the metalation exclusively to the 3-position, rather than allow the formation of equal amounts of the 4- and 6-metalated isomers as happens with dibenzofuran (see p. 9 of this thesis).

In view of the apparently anamolous behavior of phenylcalcium iodide in reactions with dibenzothiophene and phenoxathiin, similar reactions should be carried out with thianthrene and dibenzo-p-dioxin. In this connection, work on the identification of the product obtained from the reaction of phenylcalcium iodide with phenoxathiin should be completed (see p. 15 of this thesis).

Since dibenzofuran was readily mercurated, and since it was found very difficult, if not impossible, to mercurate dibenzothiophene (see p. 12 of this thesis), the mercuration of phenoxathiin should be carried out for comparative purposes. Similarly, mercuration of thianthrene and dibenzo-p-dioxin should be attempted.

The inordinate resistance to dimetalation exhibited by dibenzothiophene (see p. 87 of this thesis), in contrast to the ease of dimetalation of dibenzofuran, suggests that a complete comparison should be made. From the comparative viewpoint it would be of interest to run under identical conditions attempted dimetalations of the five heterocycles being considered.

The successful metalations of dibenzothiophene-5-oxide and dibenzothiophene-5-dioxide with n-butyllithium at reduced temperatures firmly establish the possibility of metalating sulfoxides and sulfones (see p. 13 of this thesis). The results of the metalation reactions currently being carried out on phenoxathiin-10-oxide by Mr. T. Reid and on 10-ethylphenothiazine-5-oxide by Mr. R. D. Nelson will be of considerable interest. Metalations of the corresponding dioxides also should be carried out. Reactions of any of the oxides of thianthrene with n-butyllithium should be run. Of particular interest would be the tri- and tetra-oxides of thianthrene since they offer the possibility of yielding tri- and tetra-metalated products. The above reactions also offer the possibility of comparing the relative directing influence towards metalation reactions of the heterocyclic oxygen, sulfur, and nitrogen atoms, the sulfoxide group, and the sulfone group.

As reported elsewhere (see p. 84 of this thesis), n-butyl 4-dibenzothienyl ketone was isolated after carbonation of the reaction mixture of dibenzothiophene and n-butyllithium. A reaction should be tried in which dibenzothiophene is treated with a large excess of n-butyllithium for a nominal period of time followed by carbonation to determine if a good yield of the unsymmetrical ketone can be obtained.

Direct nitration and other direct substitution reactions should be carried out on phenoxathiin-10-oxide, phenoxathiin-10-dioxide, and any of the oxides of thianthrene as a possible means of introducing substituent groups into positions not otherwise available by direct methods.

In view of the reported failure to prepare oxides of 2,8-dinitrodibenzothiophene and the dioxide of 2-nitrodibenzothiophene (see p. 19

of this thesis), attempts to prepare the oxides of other derivatives containing strongly negative groups should be made. The results of attempts presently being made by Mr. Gene Wilder to oxidize 2,8-dicyanodibenzothiophene will be of much interest.

For purposes of comparison the following halogenation reactions should be attempted:

1. Nuclear chlorination and iodination of dibenzothiophene, dibenzothiophene-5-oxide, and dibenzothiophene-5-dioxide.
2. Nuclear bromination of dibenzothiophene-5-oxide.
3. Chlorination or bromination of dibenzothiophene with excess chlorine or bromine to determine if nuclear halogenation as well as oxidation to the monoxide might be accomplished.
4. Dichlorination or mono- or di-iodination of phenoxathiin.
5. Preparation of phenoxathiin-10-oxide by halogenation.
6. Bromination or iodination of thianthrene.
7. Halogenation of any oxide of thianthrene.
8. Halogenation of dibenzo-p-dioxin.
9. Halogenation of a monoxide of phenoxathiin or thianthrene to determine if the oxygen or sulfur atoms (ortho-para-directing groups) exert a stronger orienting influence than the sulfoxide group (a meta-directing group).
10. Halogenation of thianthrene-5,5,10-trioxide to determine the relative directing influence of the sulfoxide and sulfone groups.
11. Halogenations of 4-hydroxyphenoxathiin and 1-hydroxythianthrene.

Nuclear nitration of phenoxathiin should be attempted. By analogy with the nitrations of dibenzofuran and dibenzothiophene (see p. 29 of this thesis) mononitration should yield 3-nitrophenoxathiin (provided oxidation of the sulfide linkage could be depressed), but dinitration would be more unpredictable since both the oxygen- and sulfur-containing compounds direct the second nitro group into the position _para_ to the hetero element. Nitration reactions should also be carried out on thianthrene.

In order to make a complete comparison possible, the Hofmann reaction should be carried out with 1-thianthrenecarboxylic acid amide and with 1-dibenzo-_p_-dioxincarboxylic acid amide (see p. 43 of this thesis).

An attempt to prepare bi-(4-dibenzothienyl) should be made using 4-dibenzothienylmagnesium bromide and cupric chloride. If the _bis_ compound could be obtained, then an attempted cyclodehydrogenation with lithium could be carried out (see p. 172 of this experiment).

An experiment designed to condense 2-hydroxydibenzofuran with formaldehyde would be of interest, and possibly more successful than the corresponding reaction with 4-hydroxydibenzofuran (see p. 143 of this thesis) since the 2-isomer has two _ortho_ positions available for reaction.

SUMMARY

A survey of the literature was made for the purpose of comparing the metalation, oxidation, halogenation, nitration, and selected condensation, rearrangement, and reduction reactions which have been carried out with dibenzofuran, dibenzothiophene, phenoxathiin, thianthrene, and dibenzo-p-dioxin.

The reaction of lithium with dibenzofuran and dibenzothiophene in dioxane and ether solutions was investigated. Cleavage rather than metalation occurred.

The metalation of diphenyl sulfone and dibenzothiophene-5-dioxide with n-butyllithium was successfully accomplished using temperatures of -20° to -30°.

Attempts to dimetalate dibenzothiophene with n-butyllithium, n-butylsodium, and benzylsodium were unsuccessful.

4-Hydroxyphenoxathiin and 1-hydroxythianthrene were prepared by treating the corresponding organolithium compound with oxygen in the presence of a molar equivalent of n-butylmagnesium bromide.

Hydrogen peroxide was established as being a satisfactory reagent for the oxidative preparation of dibenzothiophene-5-oxide and -5-dioxide, phenoxathiin-10-oxide and -10-dioxide, 4-bromodibenzothiophene-5-dioxide, 2,8-dibromodibenzothiophene-5-dioxide, 4-carboxydibenzothiophene-5-dioxide, 4-dibenzothiophenecarboxamide-5-dioxide, and o,o'-dicarboxydiphenyl sulfoxide and sulfone.

4-Hydroxydibenzofuran was successfully chlorinated with sulfuryl chloride to yield either 1-chloro-4-hydroxydibenzofuran or 1,3-dichloro-4-hydroxydibenzofuran.

2,8-Dibromodibenzothiophene was prepared by an improved procedure and nitrated satisfactorily to yield 2,8-dibromo-3,7-dinitrodibenzothiophene-5-oxide.

Attempts to condense 4-hydroxydibenzofuran with formaldehyde in both basic and acidic media failed. A similar lack of success attended efforts to condense 2,8-dibromodibenzothiophene-5-dioxide and 2,8-dibromo-3,7-dinitrodibenzothiophene-5-oxide with resorcinol in the presence of aluminum chloride.

4-Dibenzothiophenecarboxamide was found to undergo the usual rearrangement of the Hofmann reaction to give 4-aminodibenzothiophene in satisfactory yield.

The reductive desulfurization of dibenzothiophene derivatives with Raney nickel as a means of structure proof was found to be unsatisfactory when applied to 2-bromodibenzothiophene, dibenzothiophene-5-oxide, and dibenzothiophene-5-dioxide.

Alkali fusion of 2,8-dibromodibenzofuran when carried out in refluxing dimethoxytetraglycol gave only reductive debromination.

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