DERIVATIVES OF 1,4-NAPHTHOQUINONE

AND 1,4-ANTHRAQUINONE

APPROVED:

Price Truitt
Major Professor

Carl T. York
Minor Professor

T. L. Carrico
Director of the Department
of Chemistry

Robert B. Toulouse
Dean of the Graduate School

DERIVATIVES OF 1,4-NAPHTHOQUINONE AND 1,4-ANTHRAQUINONE

THESIS

Presented to the Graduate Council of the
North Texas State College in Partial
Fulfillment of the Requirements

For the Degree of

MASTER OF SCIENCE

By

Peter Aboytes, B.S.

Denton, Texas

August, 1959

TABLE OF CONTENTS

CHAPTER I

INTRODUCTION

The use of quinones and their derivatives, in particular those of 1,4-naphthoquinone and 1,4-anthraquinone as metabolites and antimetabolites, has become quite important in recent years. Dam (8), Almquist (1), Fieser (11), and Doisey (10) discovered and proved the structure of the antihemorrhagic vitamins K_1 and K_2. These were found to be 3-substituted derivatives of 2-methyl-1,4-naphthoquinone.

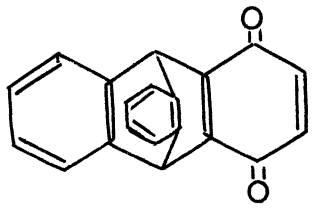
It was found that these physiological properties exhibited by the K vitamins were also exhibited by other substituted 1,4-naphthoquinones. Phthiocol (2) (2-methyl-3-hydroxy-1,4-naphthoquinone), the tubercle bacillus, and menadione (2-methyl-1,4-naphthoquinone) were found to be approximately as potent as vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone).

Other physiological properties of the substituted 1,4-naphthoquinones have been observed. Hydrolapachol (2-isopentyl-3-hydroxy-1,4-naphthoquinone) and some related compounds were prepared by Fieser et al. (12) and were found to possess antimalarial activity. Compounds which possess significant activity were from a group listed as 3-alkyl or 3-aryl derivatives of 2-hydroxy-1,4-naphthoquinone or closely related samples (12).

J. C. Calandra and Earnest C. Adams, Jr. (6) prepared four types of derivatives of 2-chloro-1,4-naphthoquinone. It was found that 1,4-naphthoquinones are useful inhibitors of acid formation by oral bacteria from carbohydrates.

Bactericidal and bacteriostatic activity has been exhibited by several 1,4-naphthoquinones. Buu-Hoi (5) reported that certain arylamine derivatives are capable of inhibiting the tubercle bacillus, and Zetterberg (18) reported quantitative measurements on naphthoquinone inhibition of the growth of tubercle bacillus. Activity has been exhibited against strains of Brucella and Salmonella (9) by 2-methyl-1,4-naphthoquinone and against Mycobacterium tuberculosis (15) by tetrasodium-2-methyl-1,4-naphthoquinone diphosphoric ester and related compounds.

Clar (7) prepared the adduct from anthracene and p-benzoquinone to obtain 9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone.



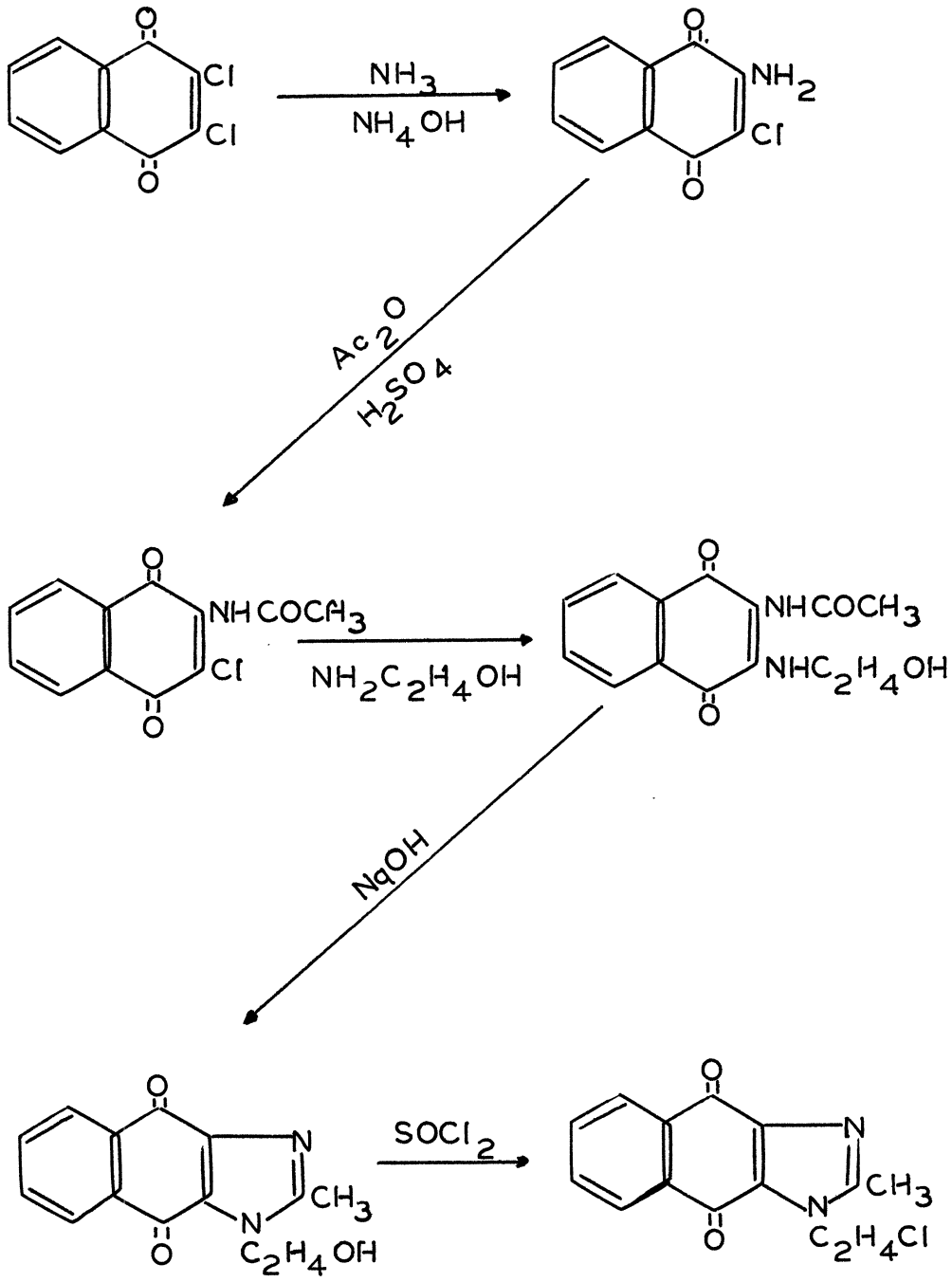
Mullins (16) chlorinated 9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone giving 2,3-dichloro-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone. Upon reacting the chlorinated compound with pyridine, Mullins obtained 1-(1,4,9,10-tetrahydro-3-hydroxy-1,4-dioxo-9,10-o-benzenoanthracene-2-yl) pyrdinium inner salt. This compound was found by Parke-Davis and Company to be active against the tubercle bacillus.

Benzimidazole and 5(6)-aminobenzimidazole were found to exhibit bacteriostatic action which could be reversed by the addition of guanine or adenine (17).

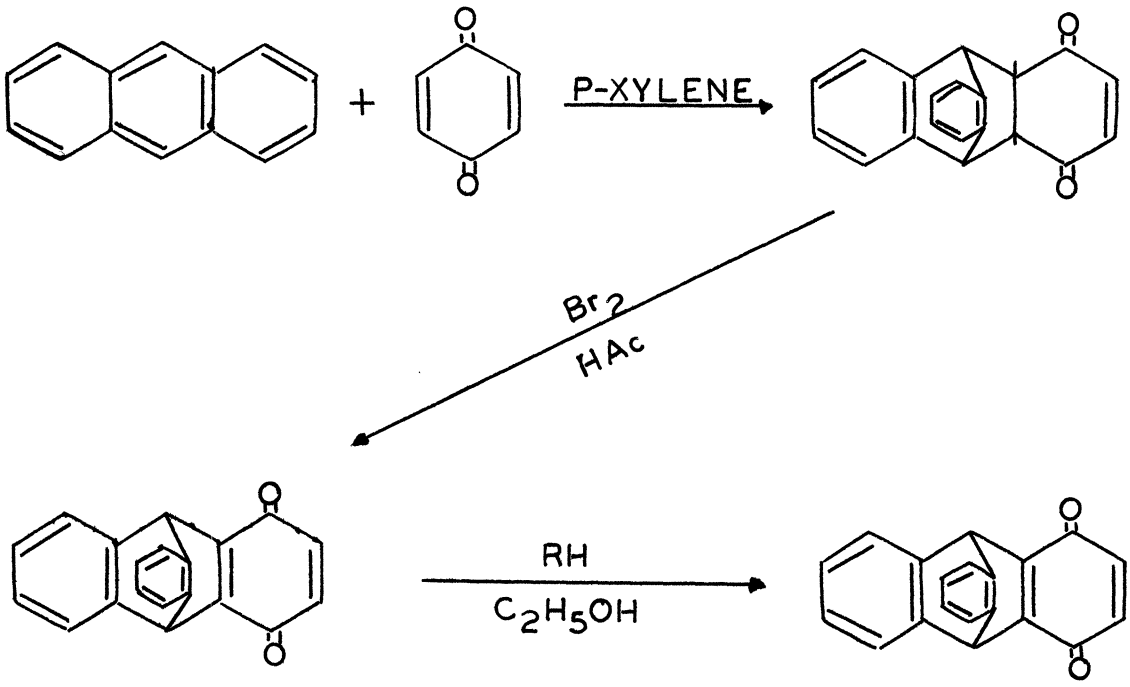
The above reports suggest the synthesis of certain substituted 1,4-naphthoquinones and 1,4-anthraquinones for possible physiological activity.

The method used for the preparation of the imidazole is essentially the one used by Hoover and Day (14) which is an adaption of a method first reported by Fries and Billig (13).

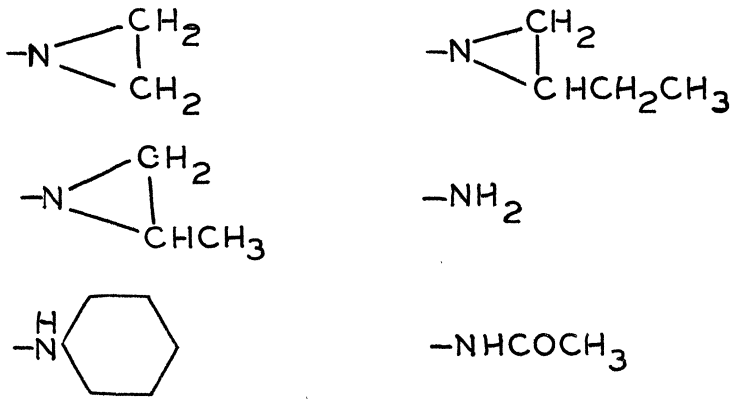
The method involves several steps starting with 2,3-dichloro-1,4-naphthoquinone which is commercially available under the name phygon.


Cl
Cl
O
O
NH3
NH4OH
NH2
Cl
O
O
Ac2O
H2SO4
NHCOCH3
Cl
O
O
NH2C2H4OH
NHCOCH3
NHC2H4OH
O
O
NaOH
N
CH3
N
C2H4OH
O
O
SOCl2
N
CH3
N
C2H4Cl
O
O

The procedure used for the preparation of the anthracene and p-benzoquinone adduct was the one followed by Clar (7). A modification in the initial step as used by Bartlett, Ryan, and Cohen was adopted.



WHERE R=



BIBLIOGRAPHY

CHAPTER I

1. Almquist, H.J., and Mecchi, E., "Properties of the Antihemorrhagic Vitamin (Vitamin K)," Journal of Biological Chemistry, CXXV (1938), 681.

2. Anderson, R.J., and Newman, M.S., "The Chemistry of the Lipids of Tubercle Bacilli," Journal of Biological Chemistry, CI (1933), 773-9.

3. Ansbacher, S., and Fernholtz, E., "Simple Compounds with Vitamin K Activity," Journal of the American Chemical Society, LXI (1939), 1924.

4. Bartlett, Paul D., Ryan, M. Josephine, Cohen, Saul G., "Triptycene (9,10-O-Benzenoanthracene)," Journal of the American Chemical Society, LXIV (1942), 2650-2651.

5. Buu-Hoi, Bull. Soc. Chim., 11578-84 (1944); cited in "The Preparation of Amine Derivatives of 2-Chloro-1,4-Naphthoquinone," Journal of the American Chemical Society, LXXII (1950), 4804.

6. Calandra, J.C., and Adams, E.C., "The Preparation of Amine Derivatives of 2-Chloro-1,4-Naphthoquinone," Journal of the American Chemical Society, LXXII (1950), 4804.

7. Clar, E., "Uber die Konstitution des Anthracens (Zur Kenntis mehrkernigen aromatischen Kohlenwasserstoffe und ihrer Abkommlinge, IX. Mitteil)," Berichte der deutschen chemischen Gesellschaft, LXIV (1931), 1671.

8. Dam, H., and Shonheyder, "The Requirement for Vitamin K of Some Different Species of Animals," Biochemical Journal, XXXI (1937), 22.

9. Del Vecchio, G., Carratu, C., Napoli, A., and Argenziano, R., "Antibiotic Action of Quinones," Boll. soc. ital. biol. sper., XXIV (1948), 1167-8; cited in Chemical Abstracts, XLIV (1950), 2071.

10. Doisey, E.A., and others, "The Isolation of Vitamins K_1 and K_2," Journal of the American Chemical Society, LXI (1939), 1295.

11. Fieser, L.F., "Synthesis of 2-Methyl-3-Phytyl-1,4-Naphthoquinone," Journal of the American Chemical Society, LXI (1939), 2559.

12. Fieser, L.F., and others, "Naphthoquinone Antimalarials," Journal of the American Chemical Society, LXX (1948), 3151.

13. Fries, K., and Billig, K., "Uber Abkommlinge des Diamino-2,3-Naphthochinons-1.4," Berichte der deutschen chemischen Gesellschaft, LVIII (1925), 1128.

14. Hoover, John R.E., and Day, Allan R., "The Preparation of Some Imidazole Derivatives of 1,4-Naphthoquinone," Journal of the American Chemical Society, LXXVI (1954), 4148-4152.

15. Kimler, A., "The In Vitro Effect of Analogs of Vitamin K on Mycobacterium Tuberculosis Var. Hominis, Strain H37Rv," Journal of Bacteriology, LX (1950), 469-72.

16. Mulline, Charles, unpublished research papers, Department of Chemistry, North Texas State College, Denton, Texas, 1955.

17. Wooley, D.W., "Some Biological Effects Produced by Benzimidazole and Their Reversal by Purines," Journal of Biological Chemistry, (1944) CLII, 225.

18. Zetterburg, "Effects on tubercle bacilli of bacteriostatics, respiration inhibitors and bactericules," Acta Path Microbiol. Scand. Suppl., LXXXII (1949), 1-151; cited in Chemical Abstracts, XLIII (1949), 7545.

CHAPTER II

EXPERIMENTAL

2-AMINO-3-CHLORO-1,4-NAPHTHOQUINONE

In the preparation of this compound the procedure followed was the same as the one reported by Hoover and Day (1). Two hundred and twenty-five grams of 2,3-dichloro-1,4-naphthoquinone was placed in a five-liter three-necked flask. Three liters of ethanol and 150 ml. of ammonium hydroxide were added. A mechanical stirrer was employed. The mixture was refluxed for two hours over a steam bath while ammonia gas was passed through the solution. The hot solution was then treated with decolorizing carbon and filtered. The product was washed with water and dried at 110 C.; yield, 76 per cent; melting point, 195 C.

2-ACETAMIDO-3-CHLORO-1,4-NAPHTHOQUINONE

Twenty-five grams of 2-amino-3-chloro-1,4-naphthoquinone were placed in a beaker containing 30 ml. of acetic anhydride. One half milliliter of concentrated H_2SO_4 was added dropwise to catalyze the reaction. The mixture was then heated slightly while stirring until the orange color changed to a pale yellow color. The mixture was filtered and washed with water to remove the H_2SO_4 and acetic anhydride. The product was recrystallized from ethanol and dried at 110 C.; yield, 50 per cent; melting point, 219 C.

2-ACETAMIDO-3-(2-HYDROXYETHYLAMINO)-1,4-NAPHTHOQUINONE

Six grams of 2-acetamido-3-chloro-1,4-naphthoquinone were placed in a flask containing 50 ml. of ethanol and 2.5 ml. of ethanol amine. The mixture was gently refluxed for 30 minutes. A brick red product was obtained. The product was recrystallized from ethanol and dried at 110 C.; yield, 80 per cent; melting point, 174-176 C.

Anal. Calcd. for $C_{14}H_{17}O_4N_2$: N, 10.4.

Found: N, 9.34.

1-(2-HYDROXYETHYL)-2-METHYLNAPHTHIMIDAZOLE-4,9-DIONE

Three grams of 2-acetamido-3-ethanol-1,4-naphthoquinone were added to 100 ml. of ethanol. The mixture was heated and then 10 ml. of 2N sodium hydroxide was added. The mixture was heated for twenty minutes and then poured into 300 ml. of water containing 10 ml. of 2N hydrochloric acid. A yellow precipitate was obtained. The product was recrystallized from ethanol and dried at 110 C.; yield, 80 per cent; melting point, 298 C.

Anal. Calcd. for $C_{14}H_{12}O_4N_2$: N, 10.89.

Found: N, 10.54.

1-(2-CHLORETHYL)-2-METHYLNAPHTHIMIDAZOLE-4,9-DIONE

One gram of 1-(2-hydroxyethyl)-methylnaphthimidazole was placed in a beaker containing 50 ml. of thionyl chloride. A watch glass was put over the beaker and the mixture was left to stand over night. Forty ml. of benzene were added and the resulting mixture was put on a steam bath to remove the benzene and thionyl chloride. The yellow orange crystalline product obtained was dried at 110 C.; yield, 85 per cent; melting point, 177-78 C.

Anal. Calcd. for $C_{14}H_{11}O_2N_2Cl$: N, 10.39; Cl, 8.05.

Found: N, 10.35; Cl, 8.08.

ANTHRACENE-P-BENZOQUINONE ADDUCT

The procedure used was a modification of the Clar (2) method as employed by Bartlett, Ryan, and Cohen (1). Sixty-five grams of anthracene twice recrystallized from xylene and 44 grams of reagent grade quinone were heated and refluxed in 390 cc. of xylene for two hours. The solid was collected on filter paper and washed with hot water to remove quinone and quinhydrone. The product was recrystallized from acetic acid. Seventy grams of pale yellow drystals were obtained. The product was dried at 110 C.; yield, 80 per cent; melting point, yellow at 207 C, red at 210 C., and carbonized at higher temperatures.

2,3-DIBROMO-9,10-ENDO-O-PHENYLENE-9,10-DIHYDRO-1,4-ANTHRAQUINONE

Twenty grams of the anthracene-p-benzoquinone adduct were placed in a 500 ml. flask containing 54 grams of bromine in 300 ml. of glacial acetic acid. The resulting mixture was then refluxed for 15 minutes. Forty grams of sodium acetate were added and refluxing was continued for 45 minutes. The bright yellow orange precipitate was washed with water to remove the bromine and glacial acetic acid. The melting point of the product was 294-297 C. After recrystallization from xylene the orange red crystals obtained have a melting point of 322-323 C.

An alternate method is the route followed by Clar (2). Five grams of the anthracene-p-benzoquinone adduct are placed in a flask containing 100 ml. of glacial acetic acid. The resulting mixture is heated to boiling. To this hot mixture was added dropwise a solution of bromine in glacial acetic acid until an excess was indicated by the red color of the bromine. The crystals formed were red orange and the melting point was 322-323 C. Clar (2) reported a melting point of 320-325 C. after recrystallization from xylene. In both cases the product was dried at 110 C.

2-ETHYLENEIMIDO-3-BROMO-9,10-ENDO-O-PHENYLENE-9,10-DIHYDRO-1,4-ANTHRAQUINONE

Two grams of 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone were placed in a flask containing 175 ml. of absolute ethanol. The solution was heated on a water bath and 2 ml. of ethyleneimine were added. Upon the addition of the ethyleneimine the solution turned a red color. The resulting mixture was heated over a water bath for 45 minutes. The hot solution was filtered and the resulting filtrate upon cooling gave maroon or dark purple crystals. The product was dried at 110 C.; yield, 60 per cent; melting point, 227-8 C.

Anal. Calcd. for: $C_{22}H_{14}O_2NBr$: N, 3.47; Br, 19.8.

Found: 3.43; Br, 19.72.

2-METHYLETHYLENEIMIDO-3-BROMO-9,10-ENDO-O-PHENYLENE 9,10-DIHYDRO-1,4-NAPHTHOQUINONE

Two grams of 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone were placed in a flask containing 175 ml. of absolute ethanol. The solution was heated on a water bath and 2 ml. of 2-methylethyleneimine were added. Upon addition of the amine the mixture turned a red color. The resulting mixture was heated over a water bath for 45 minutes. The hot solution was filtered and the resulting filtrate upon cooling gave maroon crystals. The color of these crystals was lighter than that of the ethyleneimine derivative. The product was dried at 110 C.; yield, 65 per cent; melting point, 239 C.

Anal. Calcd. for $C_{25}H_{16}O_2NBr$: N, 3.36; Br, 19.11.

Found: N, 3.08; Br, 18.99.

2-ETHYLETHYLENEIMIDO-3-BROMO-9,10-ENDO-O-PHENYLENE 9,10-DIHYDRO-1,4-ANTHRAQUINONE

Two grams of 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone were placed in a flask containing 175 ml. of absolute ethanol. The solution was heated on a steam bath and 2 ml. of 2-ethylethyleneimine were added. Upon addition of the amine the solution turned red. The resulting mixture was heated over a water bath for 45 minutes. The hot solution was filtered and the resulting precipitate upon cooling gave dark maroon crystals. The product was dried at 110 C.; yield, 60 per cent; melting point, 225 C.

Anal. Calcd. for $C_{24}H_{18}O_2NBr$: N, 3.24; Br, 18.5.

Found: N, 3.29; Br, 18.4.

2-AMINO-3-BROMO-9,10-ENDO-o-PHENYLENE 9,10-DIHYDRO-1,4-ANTHRAQUINONE

Four grams of 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone were placed in a flask containing 75 ml. of absolute ethanol. Ammonia gas was bubbled through the solution for one hour. The solution turned reddish brown in color and finally a dark purple. The product was filtered giving dark brown crystals. The product was recrystallized from ether and dried at 110 C.; yield, 75 per cent; melting point, 298 C.

Anal. Calcd. for $C_{20}H_{12}O_2NBr$: N, 3.71; Br, 21.20.

Found: N, 3.81; Br, 20.89.

2-ACETAMIDO-3-BROMO-9,10-ENDO-O-PHENYLENE 9,10-DIHYDRO-1,4-ANTHRAQUINONE

One gram of 2-amino-3-bromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone was placed in a 50 ml. beaker. Sufficient acetic anhydride to cover the quinone was added. Four drops of sulfuric acid were then added and the mixture was thoroughly stirred with a glass rod until the color changed to a light brown. The resulting mixture was then diluted by placing the contents in a beaker containing 50 ml. of water. The filtered product was recrystallized from ethanol and dried at 110 C.; yield, 60 per cent; melting point, 169 C.

Anal. Calcd. for $C_{22}H_{14}O_3NBr$: N, 3.34; Br, 18.25.

Found: N, 3.33; Br, 18.41.

2-N-CYCLO-HEXYLAMINO-3-BROMO-9,10-ENDO-O-PHENYLENE 9,10-DIHYDRO-1,4-ANTHRAQUINONE

One gram of 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone was placed in a flask containing 175 ml. of ethanol. The mixture was heated over a water bath and one ml. of N-hexylamine was added. The color slowly changed during refluxing to a dark purple color. The mixture was filtered after one hour of refluxing and the product obtained was recrystallized from ether. Five tenths of a gram of dark purple crystals were obtained. The product was dried at 110 C.; melting point, 159 C.

Anal. Calcd. for $C_{26}H_{17}O_2NBr$: N, 3.09; Br, 17.50.

Found: N, 3.20; Br, 17.52.

BIBLIOGRAPHY

CHAPTER II

1. Bartlett, Paul D, Ryan, M. Josephine, and Cohen, Saul G., "Triptycene (9,10-o-benzenoanthracene)," Journal of the American Chemical Society, LXIV (1942), 2650-2651.

2. Clar, E., "Uber die Konstitution des Anthracens (Zur Kenntis mehrkernigen aromatischen Kohlenwasserstoffe und ihrer Abkommlinge, IX. Mitteil), " Berichte der deutschen chemischen Gesellschaft, LXIV (1931), 1686-87.

3. Hoover, J.R.E., and Day, A.R., "Preparation of Some Imidazole Derivatives of 1,4-Naphthoquinone," Journal of the American Chemical Society, LXX (1954), 4148-4151.

CHAPTER III

DISCUSSION

The purpose of this investigation was the synthesis of some 1,4-naphthoquinones and 1,4-anthraquinones. It has been shown that some of these substituted quinones exhibit physiological properties. The effect of the different substituent groups on the compounds prepared in this investigation are to be studied.

The method employed for the synthesis of the imidazole was the same as that followed by Hoover and Day (3). It was found that the conversion to the corresponding imidazole was readily accomplished by warming in alcohol containing 15 per cent of 2N sodium hydroxide.

It was then desired to replace the hydroxyl group of the substituted imidazole with a chlorine molecule. The best method found was to react the substituted imidazole with thionyl chloride alone in the cold. After standing for ten hours, benzene was added and the resulting mixture was heated over a steam bath until the benzene and excess thionyl chloride were evaporated off. Recrystallization was from alcohol.

In the preparation of the anthracene and p-benzoquinone adduct the method followed was the same as that employed by

Bartlett, Ryan, and Cohen (1). This method was found to give the highest yield and also the greatest degree of purity.

In the preparation of the 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone the method employed by MacLaughlin (4) gave a compound which darkened at 270 C. and melted at 291 C. Upon recrystallization the yield of the pure dibromo compound obtained was too low to be of practical use. An alternate method and the one which was used in this investigation was the one used by Clar (2). This consisted of dissolving the anthracene-p-benzoquinone adduct in glacial acetic acid, heating the mixture to boiling, and then adding dropwise a solution of bromine in glacial acetic acid. The bromine was added until an excess was indicated by the bromine color. Red orange crystals were precipitated even in the hot solution. These red orange crystals were found to have a melting point of 322-323 C. Clar (2) reported a melting point range of 320-325 C. for the dibromo compound recrystallized from xylene. The method of Clar was found to be superior to the one used by MacLaughlin (4).

In the preparation of the substituted 1,4-anthraquinones from the 2,3-dibromo-9,10-endo-o-phenylene-9,10-dihydro-1,4-anthraquinone and the various reactants used in this investigation, the solvent used in each case was ethanol. Recrystallization was from ethanol and from diethyl ether.

The analysis for nitrogen was determined by the micro Dumas method. In the halogen analysis the micro "Parr Peroxide Bomb" was used for the combustion of the halogen compound to the sodium halide. The halogen content was then determined volumetrically using the "Mohr method."

BIBLIOGRAPHY

CHAPTER III

1. Bartlett, Paul D., Ryan, M. Josephine, and Cohen, Saul G., "Triptycene (9,10-o-Benzenoanthracene)," Journal of the American Chemical Society, LXIV (1942), 2650-2651.

2. Clar, E., "Über die Konstitution des Anthracens (Zur Kenntis mehrkernigen aromatischen Kohlenwasserstoffe und ihrer Abkommlinge, IX. Mitteil)," Berichte der deutschen chemischen Gesellschaft, LXIV (1931), 1686-87.

3. Hoover, J.R.E., and Day, A.R., "Preparation of Some Imidazole Derivatives of 1,4-Naphthoquinone," Journal of the American Chemical Society, LXXVI (1954), 4148-4151.

4. Maclaughlin, Edward P., "Pyridinium Derivatives of 1,4-Naphthoquinone," unpublished master's thesis, Department of Chemistry, North Texas State College, Denton, Texas, 1956.

BIBLIOGRAPHY

Articles

Almquist, H.J., and Mecchi, E., "Properties of the Anti-hemorrhagic Vitamin (Vitamin K)," Journal of Biological Chemistry, CXXV (1936), 681.

Anderson, R.J., and Newman, M.S., "The Chemistry of the Lipids of Tubercle Bacilli," Journal of Biological Chemistry, CI (1933), 773-9.

Ansbacher, S., and Fernholtz, E., "Simple Compounds with Vitamin K Activity," Journal of the American Chemical Society, LXI (1939), 1924.

Bartlett, Paul D., Ryan, M. Josephine, and Cohen, Saul G., "Triptycene (9,10-O-Benzenoanthracene)," Journal of the American Chemical Society, LXIV (1942), 2650-2651.

Buu-Hoi, Bull. Soc. Chim., 11578-84 (1944); cited in "The Preparation of Amine Derivatives of 2-Chloro-1,4-Naphthoquinone," The Journal of the American Chemical Society, LXXII (1950), 4804.

Calandra, J.C., and Adams, E.C., "The Preparation of Amine Derivatives of 2-Chloro-1,4-Naphthoquinone," Journal of the American Chemical Society, LXXII (1950), 4804.

Clar, E., "Uber die Konstitution des Anthracens (Zur) Kenntis mehrkernigen aromatischen Kohlenwasserstoffe und ihrer Abkommlinge, IX. Mitteil)," Berichte der deutschen chemischen Gesellschaft, LXIV (1931), 1671.

Dam, H., and Shonheyder, "The Requirement for Vitamin K of Some Different Species of Animals," Biochemical Journal, XXXI (1937), 22.

Del Vecchio, G., Carratu, C., Napoli, A., and Argenziano, R., "Antibiotic Action of Quinones," Boll. soc. ital. biol. sper., XXIV (1950), 2071.

Doisey, E.A., and others, "The Isolation of Vitamins K_1 and K_2," Journal of the American Chemical Society, LXI (1939), 1295.

Fieser, L.F., "Synthesis of 2-Methyl-3-Phytyl-1,4-Naphthoquinone," Journal of the American Chemical Society, LXI (1939), 2559.

Fieser, L.F., and others, "Naphthoquinone Antimalarials," Journal of the American Chemical Society, LXX (1948), 3151.

Fries, K., and Billig, K., "Uber Abkommlinge des Diamino-2,3-Naphthochinons-1.4," Berichte der deutschen chemischen Gesellschaft, LVIII (1925), 1128.

Hoover, John R.E., and Day, Allan R., "The Preparation of Some Imidazole Derivatives of 1,4-Naphthoquinone," Journal of the American Chemical Society, LXXVI (1954), 4148-4152.

Kimler, A., "The In Vitro Effect of Analogs of Vitamin K on Mycobacterium Tuberculosis Var. Hominis, Strain H37Rv," Journal of Bacteriology, LX (1950), 469-72.

Wooley, D.W., "Some Biological Effects Produced by Benzimidazole and Their Reversal by Pyrines," Journal of Biological Chemistry, (1944), 152, 225.

Zetterburg, "Effects on Tubercle Bacilli of Bacteriostatics, Respiration Inhibitors and Bactericules," Acta Path Microbiol. Scand. Suppl., LXXXII (1949), 1-151; cited in Chemical Abstracts, XLIII (1949), 7545.

Unpublished Materials

MacLaughlin, Edward Phillip, "Pyridinium Derivatives of 1,4-Naphthoquinone," unpublished master's thesis, Department of Chemistry, North Texas State College, Denton, Texas, 1956.

Mullins, Charles; unpublished research papers, Department of Chemistry, North Texas State College, Denton, Texas, 1955.