THE SYNTHESIS OF 9,10-DIMETHYL-1,2-BENZ-3,4-ANTHRAQUINONE

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By

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The author wishes to express his appreciation to Dr. Melvin S. Newman for suggesting this problem and for his interest and guidance during the course of its development.

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FIELD OF STUDY

Major Field: Organic Chemistry

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INTRODUCTION

The objective of the present investigation was the synthesis of 9,10-dimethyl-1,2-benz-3,4-anthraquinone. Of the twenty-five quinones possible in the 9,10-dimethyl-1,2-benzanthracene system the compound mentioned above was chosen because the 3,4- bond region seems to be associated with carcinogenity in the 1,2-benzanthracene system.[1] The theories of hydrocarbon carcinogenesis are as yet inadequate;[2] so it

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(1) J.A. Miller and E.C. Miller, Cancer Res., 23 (2) (Pt. 1), 229 (1963).

(2) N.H. Cromwell, Am. Scientist, 53, 213 (1965).

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would be unrealistic to discuss the possible role of 9,10-dimethyl-1,2-benz-3,4-anthraquinone in carcinogenesis. For the interested reader several books[3,4,5,6] have been written recently which review the

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(3) D.B. Clayson, "Chemical Carcinogenesis," Little, Brown and Company, Boston (1962).

(4) G.M. Badger, "The Chemical Basis of Carcinogenic Activity," C. Thomas, Springfield, Illinois (1962).

(5) I. Hieger, "Carcinogenesis," Academic Press, London, New York (1961).

(6) G.E.W. Wolstenholme and Maeve O'Connor, "Carcinogenesis Mechanisms of Actions," A. Ciba Foundation Symposium, Little, Brown and Company, Boston (1961).

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numerous theories and hypotheses. There is, however, the possibility that 9,10-dimethyl-1,2-benzanthracene is metabolized to a quinone or hydroquinone which could then act as an inhibitor or a promoting agent. The validity of this particular hypothesis would be established by biological testing. The title compound has been submitted for testing to three[7] research groups.

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(7) J. Miller, McArdale Laboratory, Madison, Wisconsin; C. Huggins, Ben May Cancer Laboratory, Chicago, Illinois; E. Boyland, Chester Beatty Research Institute, London, England.

In any case the information derived from biological testing would increase in value as more of these twenty-five quinones were synthesized. The original objective was to synthesize as many of these quinones as possible. However, the difficulty encountered in the synthesis of the title compound curtailed these efforts.

RESULTS AND DISCUSSION

I. Preparation and reactions of 3-methoxy-9,10-dimethyl-1,2-benzanthracene, VI

A generalized procedure for the preparation of a quinone starts with a phenol or phenolic ether. The phenol or its ether may be oxidized directly to a quinone. Alternatively, the phenol may be converted, through the azo derivative (coupling), into the corresponding amino derivative, and this intermediate oxidized in acid solution.

The methyl ether, VI, was prepared in hopes that one of these general methods might be successful. The preparation of VI was basically the one described[1] and is outlined in Figure 1.

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(1) W.M. Smith, Jr., E.F. Pratt and H.J. Croech, J. Am. Chem. Soc., 73, 319 (1951).

The synthesis of quinones by oxidation of phenolic ethers was demonstrated by Ruzicka.[2] Phenanthraquinone and 1,7-dimethyl-phenanthraquinone were prepared by chromic acid oxidation of their

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(2) L. Ruzicka and H. Woldmann, Helv. Chim. Acta., 15, 907 (1932).

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respective 9-methyl ethers.[2] These two examples were also encouraging due to the similar nature of the 3,4-benzanthracene and the

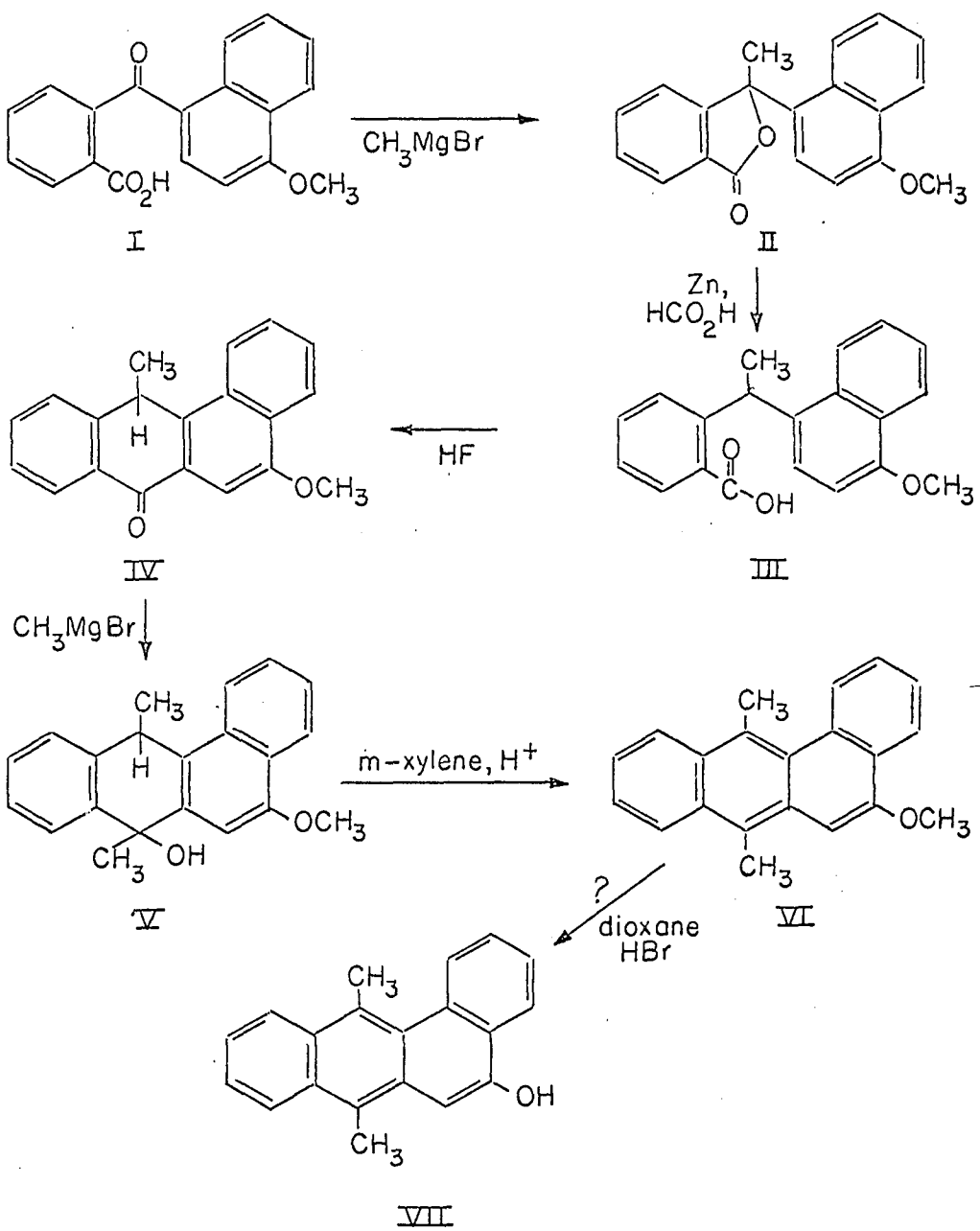

Figure 1

PREPARATION OF 3-METHOXY-9,10-DIMETHYL-1,2-BENZANTHRACENE

9,10-phenanthrene bonds. However, chromic acid oxidation of VI failed to yield any identifiable products. The multiplicity of products and their similar chromatographic mobilities prevented isolation and characterization. Similar results, i.e. decomposition and/or complex reaction mixtures, were obtained with acidic permanganate, alkaline peroxide, peracetic acid, trifluoroperacetic acid and selenium dioxide.

The methyl ether, VI, was evidently more sensitive to vigorous oxidation than the phenanthrene ethers. In order to use more selective and more gentle oxidants, several attempts were made to prepare VII by cleavage of the methyl ether, VI. There was one reported[1] cleavage of VI which was accomplished with hydrobromic acid in dioxane. The supposed phenol, VII, was not isolated in this case but was converted to the corresponding amine by a Bucherer reaction.[1] Several attempts were made to prepare the phenol, VII, with a number of other cleavage agents (Table 1) in addition to the one described.[1] These attempts were unsuccessful; only green oils were obtained which could not be purified by crystallization, chromatography or sublimation. The attempts to isolate an ester derivative of the "phenol, VII" were also unsuccessful. With standard techniques of acetylation or benzoylation there resulted complex reaction mixtures. Once again the similar chromatographic mobilities of the components prevented isolation and characterization.

Even though a phenol could not be isolated, several attempts were made to oxidize the crude reaction mixtures. The primary

oxidant, studied was Fremy's salt, potassium nitrosodisulfonate. This stable free radical had been used by Teuber[3,4,5,6] to convert a wide

(3) H.J. Teuber and G. Jellinek, Ber., 85, 95 (1952).

(4) H.J. Teuber and W. Rau, Ibid., 86, 1036 (1953).

(5) H.J. Teuber and N. Gotz, Ibid., 87, 1239 (1954).

(6) H.J. Teuber and H. Limdner, Ibid., 92, 932 (1959).

range of phenols into quinones. In this case Fremy's salt did not oxidize the supposed phenol, VII, to the title compound. The crude reaction mixtures as evidenced by thin layer chromatography (t.l.c.) contained four components and showed only a very weak carbonyl absorption at 1660 cm^{-1}.

Since Fremy's salt was not an effective oxidant, several attempts were madeto oxidize the crude cleavage product of VI with chromic acid, trifluoroperacetic acid or chromium trioxide-pyridine. Workup of these reactions afforded only a small recovery of phenolic material and a major amount of tar.

As stated earlier a quinone may be prepared by direct oxidation or by oxidation of the corresponding amino-phenol. Since the direct oxidation of VI or of the reported[1] VII had failed, an attempt was made to prepare and oxidize the 4-amino derivative of "VII." The 3,4 quinone of 1,2-benzanthracene was first prepared[7] in this manner,

(7) L.F. Fieser and E. Dietz, J. Am. Chem. Soc., 51, 3141 (1930).

i.e. by oxidation of the 4-amino derivative of 3-hydroxy-1,2-benzanthracene with chromic acid.

The crude cleavage product from VI yielded a red dyestuff when coupled with p-nitrophenyldiazonium sulfate in acetic acid,[7] but this vat was a mixture of coupled products as evidenced by t.l.c. Since the components could not be separated the mixture was reduced with stannous chloride in dioxane. The resulting mixture of aminophenol hydrochlorides was treated with: chromic acid; potassium permanganate-acetic acid; peracetic acid or ferric chloride. Each of these oxidants effected severe decomposition into dark resinous oils.

II. Synthesis and reactions of 3,4-dimethoxy-9,10-dimethyl-1,2-benzanthracene, XIV

The unpromising results described in the preceding section necessitated a different approach. It seemed more feasible to synthesize a benzanthracene derivative which contained oxygen functions at positions 3 and 4 rather than attempting to oxidize (directly or indirectly), VI. The oxygen functions must withstand the conditions of a multistep synthesis and be ultimately convertable into a 1,2-diketone (quinone). Thus the diether, XIV, was synthesized as outlined in Figure 2. The methyl ethers were acceptable protective groups but could not be cleaved successfully. Thus the synthesis of the title compound was not achieved.

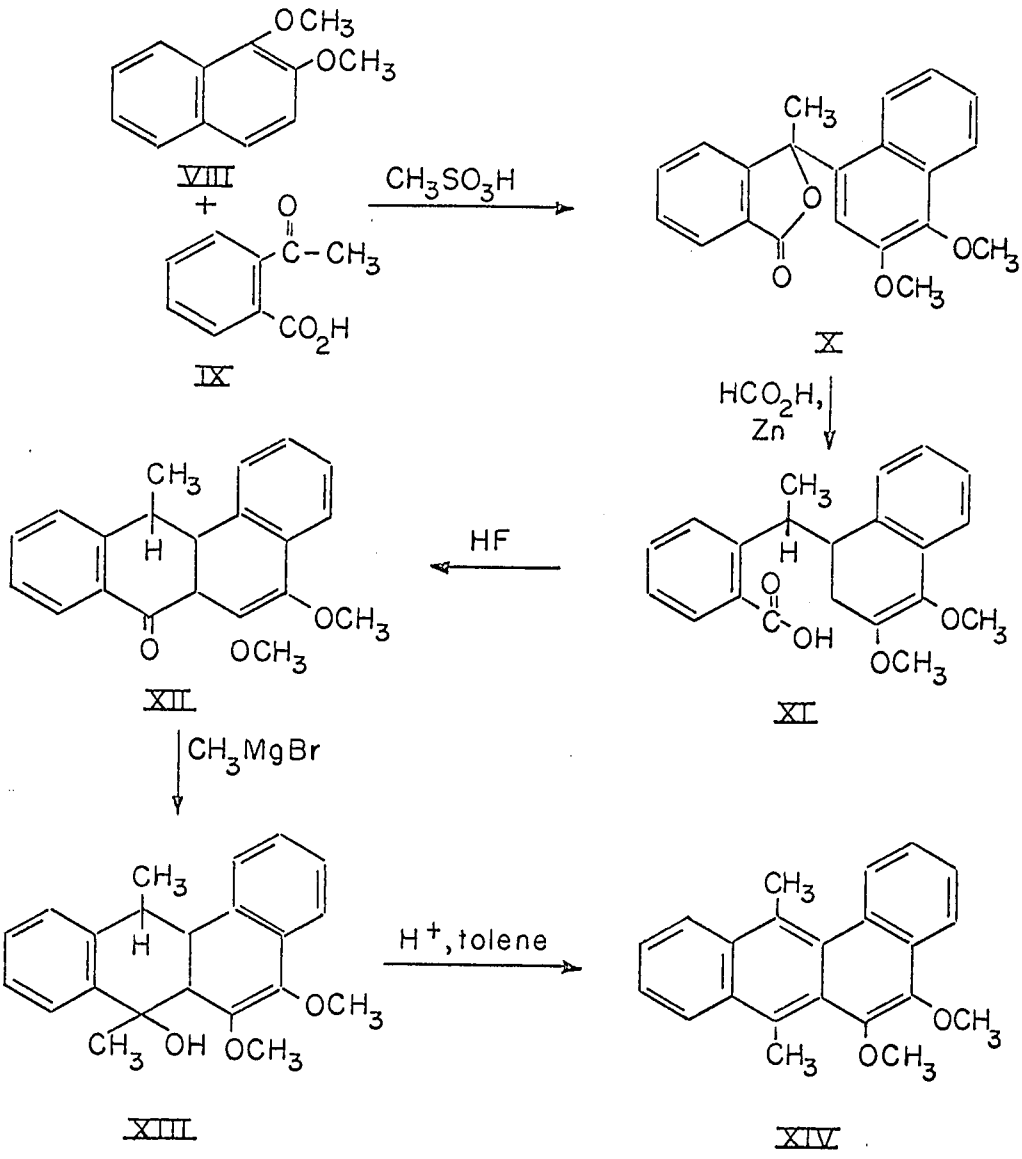

Figure 2

SYNTHESIS OF 3,4-DIMETHOXY-9,10-DIMETHYL-1,2-BENZANTHRACENE

Nevertheless, the synthesis of XIV is worthy of note, particularly in the first step. This reaction is the first reported Friedel-Craft's condensation of o-acetobenzoic acid, IX, and is also the first such condensation effected with methanesulfonic acid.

This reaction was modeled after analagous condensations of phthaldehydic acid which has been reacted with phenols, phenolic ethers[8,9,10] and alkylated benzenes[11] in sulfuric acid to form substituted phthalides.

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(8) A. Bistrzycki and G.J. Oehlert, Ber., 27, 2632 (1894).

(9) A. Bistrzycki and D.W. Yssel de Schepper, Ber., 31, 2790 (1898).

(10) M.M. Brobaker and R. Adams, J. Am. Chem. Soc., 49, 2279 (1927).

(11) V.W. Floutz, J. Org. Chem., 25, 643 (1960).

The infrared spectrum[12] of phthaldehydic acid indicates that it exists primarily in the hydroxy-lactone form which could be

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(12) D.D. Wheeler, D.C. Young and D.S. Erley, J. Org. Chem., 22, 547 (1957).

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converted directly into a cyclic carbonium ion in strong acid by protonation and elimination of water. There is good reason to expect such a mechanism since 2-benzoyl-1-naphthoic acid forms a

cyclic carbonium ion in concentrated sulfuric acid.[13] If this mechanism is operative there would be good reason to expect o-acetobenzoic acid, IX, to undergo analogous condensations since it also exists in the hydroxy-lactone form.[14,15] Whether or not this mechanism

(13) M.S. Newman, J. Am. Chem. Soc., 64, 2324 (1942).

(14) J.F. Grove and H.A. Willis, J. Chem. Soc., 877 (1951).

(15) D.S. Erley et al., Chem. and Ind. (London, 1915 (1964).

was operative was not established. However, IX did condense with 1,2-dimethoxynaphthalene, VIII, in 90% methanesulfonic acid to yield a phthalide in 50% yield.

There was strong but not unequivocal evidence that this phthalide had the structure indicated by X. The phthalide nature of X was evident from the infrared and n.m.r. spectra. However, the point of attachment of the phthalide group was inferred from precedent and from the structure of XIV. Since the structure of the diether, XIV, was established by an unequivocal synthesis which is presented in the next section, the complete evidence and arguments for the structures of X, XI, XII, XIII and XIV will be presented at that time. For the sake of convenience, we will consider these structures as established.

As mentioned earlier, methanesulfonic acid has not been reported in the synthesis of phthalides by Friedel-Craft's

condensation. In the synthesis of XIV and in the synthesis of 3-ethoxy-9,10-dimethyl-1,2-benzanthracene[16] this acid was far superior

(16) N. Venkateswaran, Post-doctoral fellow, The Ohio State University, 1964-1965.

to sulfuric. The problems of sulfonation and oxidation which occur with sulfuric were eliminated and demethylation was markedly reduced. O-acetobenzoic acid, IX, did condense with VIII in 80% sulfuric acid at room temperature to give X, but only in trace amounts.

The reaction sequence leading from X to XIV was analogous to the sequence used in preparation of 3-methoxy-9,10-dimethyl-1,2-benzanthracene, VI.[1] Reduction of X with zinc-formic acid[17] afforded

(17) R.L. Letsinger, J.D. Jamison and A.S. Hussey, J. Org. Chem., 26, 97 (1961).

a quantitative yield of acid, XI. This acid was cyclized with anhydrous hydrofluoric acid to the benzanthrane, XII, which was reacted with methylmagnesium bromide. The resulting alcohol, XIII, was dehydrated to the diether, XIV. The overall yield of 3,4-dimethoxy-9,10-dimethyl-1,2-benzanthracene, XIV, from XI was 55%.

The diether, XIV, was not a suitable intermediate for the synthesis of 9,10-dimethyl-1,2-benz-3,4-anthraquinone as it could not be converted into the necessary hydroquinone. Several cleaving agents

(Table 2) were tried without success. In each case complex reaction mixtures resulted which could not be separated or oxidized to the desired quinone.

III. Synthesis of 9,10-dimethyl-1,2-benz-3,4-anthraquinone, XVII, and other reactions of 3,4-dihydroxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XVI

Since the diether, XIV, was shown not to be a suitable intermediate for the synthesis of quinone, XVII, a different starting material was required. A successful synthesis of XVII was thus worked out by oxidation of the dihydrodiol, XVI,[18] as described below.

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(18) J.W. Cook and R. Schoental, J. Chem. Soc., 170 (1948).

There was good precedent for this oxidation since cis-3,4-dihydroxy-3,4-dihydro-1,2-benzanthracene had been oxidized to the corresponding quinone with chromic acid.[19] It was difficult, however, to find an appropriate oxidant. There were even two previous reports[20,21] of unsuccessful attempts to oxidize XVI to the quinone,

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(19) C.J. Collins, J.G. Burr, Jr., and D.N. Hess, J. Am. Chem. Soc., 73, 5176 (1951).

(20) H.I. Hadler and A.C. Kryger, J. Org. Chem., 25, 1896 (1960).

(21) E. Boyland and P. Sims, Biochem. J., 95, 780 (1965).

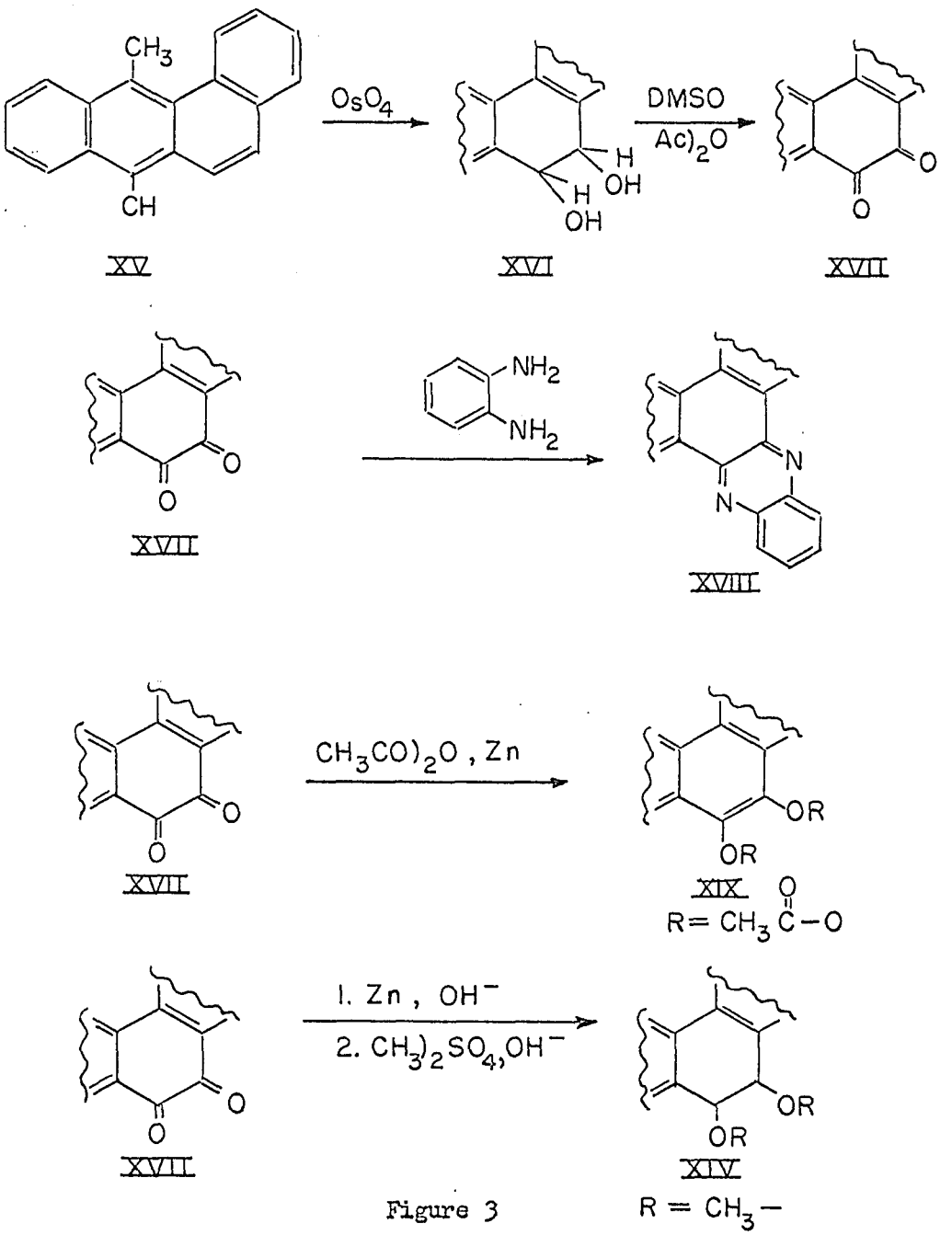
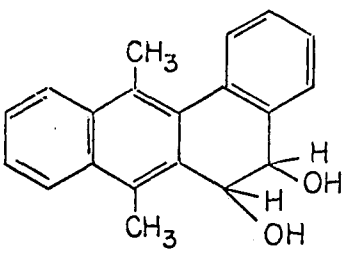
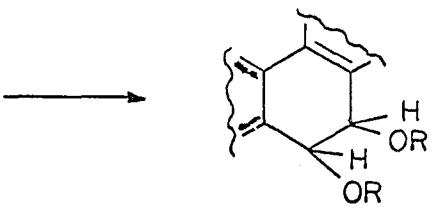


Figure 3

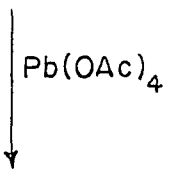
SYNTHESIS AND REACTIONS OF 9,10-DIMETHYL-1,2-BENZ-3,4-ANTHRAQUINONE

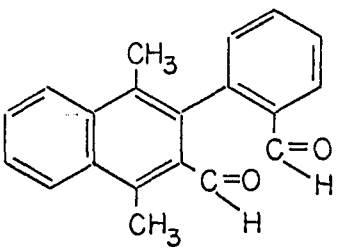




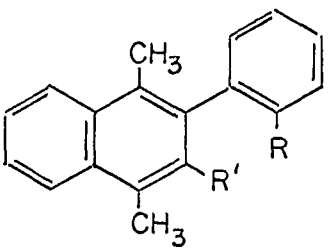
XX a $R = CH_3CH_2^-$

XX b $R = CH_3-\overset{\overset{O}{\|}}{C}-$





XXI



XXII , $R=R'= -CH=N-OH$

XXIII , $R=R'= -C\equiv N$

XXIV , $R=-CO_2H$, $R'=-\overset{\overset{O}{\|}}{C}-NH_2$

XXV , $R=R'= -\underset{\underset{O}{\|}}{C}-OCH_3$

Figure 4

SYNTHESIS OF 1,4-DIMETHYL-2-PHENYLNAPHTHALENE-3,2'-DICARBOXYLIC ACID, DIMETHYL ESTER

XVII. Since chromic acid was not an effective oxidant[20] several other oxidants were tested with equally unpromising results. Those oxidizing agents studied were: chromium trioxide-pyridine; chromium trioxide-t-butanol; unbuffered potassium permanganate-t-butanol-water; cyclohexanane-aluminum isopropoxide; manganese dioxide in chloroform; silver oxide in ether; silver benzoate in benzene and ruthenum tetroxide[22] in carbon tetrachloride. In each case except

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(22) At the suggestion of Professor D.H. Horton, The Ohio State University, 1966.

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that of manganese dioxide, some oxidation occurred but no identifiable products could be isolated from the reaction mixtures.

The oxidation of XVI to XVII was finally achieved with dimethyl sulfoxide (DMSO)-acetic anhydride[23] in 47% yield. This method was tried at the suggestion of a fellow student[24] who noted that this

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(23) J.D. Albright and L. Goldman, J. Am. Chem. Soc., 87, 4214 (1965).

(24) Mr. J.B. Hughes, M.Sc., The Ohio State University, 1966.

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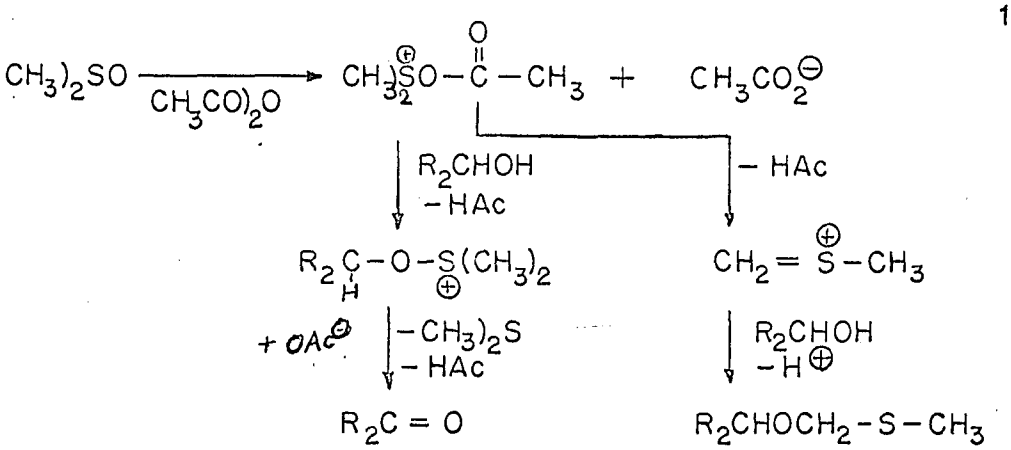
particular oxidizing system was very effective for converting secondary alcohols into ketones.[23] The oxidation proceeds via sulfoxonium salt intermediates as illustrated below for a general case.



It should be noted that the initial sulfoxonium intermediate may also react with a secondary alcohol by Path B to give methylthiomethyl ethers. This side reaction and partial oxidation probably accounts for the low yield of XVII.

The quinone, XVII, formed the quinoxaline derivative, XVIII, and the diacetate, XIV. The quinoxaline derivative, XVIII, is quite relevant to the structure proof of XVII which will be considered shortly. This is the first reported case of a 1,2-diketone synthesis by means of a DMSO type oxidation, and it is also the first case of a quinone synthesis by means of this type of oxidation.

By nature of the synthesis, the structure of the quinone, XVII, would be determined by the structure of XVI. Since osmium tetroxide reacts with ethylenic double bonds to produce only cis-1,2-glycols,[25,26]

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(25) R. Criegee, Ann., 522, 75 (1936).

(26) R. Criegee, B. Marchand and H. Wannowiss, Ann., 550, 99 (1942).

the product derived from the reaction of XV with osmium tetroxide must be a cis-vicinal glycol. That this glycol has the structure, XVI, is indicated by two sets of reactions.

In one set of reactions the aforementioned glycol was dehydrated to a phenol and this phenol was converted to the corresponding methyl ether by reaction with dimethy sulfate and base.[18] This ether was shown to be VI in two ways. The ether, VI, produced by dehydration and methylation had the same infrared spectra as that of VI prepared by the sequence outlined in Figure 1.[1] The melting point of the ether produced by dehydration and methylation was undepressed when mixed with an authentic sample of VI.[1] The structure of the ether, VI, produced by the ring building sequence (Fig. 1), is unequivocal since the structure of the intermediate keto-acid, I, was well established.[7] For a vicinal glycol of 9,10-dimethyl-1,2-benzanthracene, XV, to be converted to VI by the two step sequence of dehydration and methylation, one of the hydroxyls in the glycol must have been at position 3. The possibility of the other hydroxyl being at position 2 is quite remote since osmium tetroxide reacts at the 9,10-position in phenanthrene to produce cis-9,10-dihydroxy-9,10-dihydrophenanthrene.[25]

In the second case, the glycol produced by the reaction of osmium tetroxide with XV was cleaved to a dialdehyde, XXI.[19] The n.m.r. spectra of this cleavage product clearly indicated a dialdehyde by the presence of two sharp one proton singlets at 0.2

and -0.1 τ respectively.[27] This fact definitely eliminates a 2,3-dihydrodiol since its cleavage product would be a keto-aldehyde.

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(27) N.S. Bhacca and D.H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden Day, Inc., San Francisco, 1964, p. 76.

The complexity of the aromatic region in the n.m.r. spectra of the dialdehyde, XXI, prevented a complete structural proof by this method alone. However, the dialdehyde was converted by an unambiguous sequence[20] (reduction to a dialcohol; conversion to the corresponding dibromide and ring closure with phenyl lithium) to a dihydro-9,10-dimethyl-1,2-benzanthracene. The ultraviolet spectrum of this dihydro compound had the same curve shape as that of 6,7-dihydro-20-methylcholanthrene[28] and showed a slight blue shift of 6 mu (average)

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(28) L.F. Fieser and E.B. Hershberg, J. Am. Chem. Soc., 60, 940 (1938).

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relative to the dihydrocholanthrene. The slight hypsochromic shift would be expected from loss of an alkyl substitute.[28] For the dihydrobenzanthracene and the dihydrocholanthrene to show such very similar spectra they must possess the same chromophoric group, i.e. 2-phenylnaphthalene. The ultraviolet spectrum of 2-phenylnaphthalene does show a curve which is quite similar to 6,7-dihydro-20-methylcholanthrene[28] and consequently to 3,4-dihydro-9,10-dimethyl-1,2-benzanthracene.[20] The identification of the chromophore which is

also the same in the dihydrodiol, XVI,[20] and the sequence of reactions leading to the 3,4-dihydro compound can be explained only on the basis of 3,4-dihydroxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XVI.

Since the structure of XVI is well supported by the data and arguments given above, the quinone, XVII (diketone), must have the indicated structure. The ortho nature of the ketonic groupings in XVII was definitely shown by the formation of the quinoxaline derivative, XVIII.

Thus, the quinone XVII was a suitable intermediate for an independent and unequivocal synthesis of XIV. A reductive methylation of XVII with alkaline zinc and dimethyl sulfate afforded XIV in 14% yield. Comparison of the physical constants of the diether derived by reductive methylation with that derived by the ring building sequence showed them to be identical. They had the same n.m.r., ultraviolet and infrared spectra, possessed the same chromagraphic mobility and formed identical 2,4,5,7-tetranitrofluorenone (TENF)[29] derivatives. The spectral data were consistent with the structural assignment.

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(29) M.S. Newman and B. Lutz, J. Am. Chem. Soc., 78, 2469 (1956).

Although the reductive methylation of XVII establishes the structure of the diether, XIV, it does not establish the structure

of the intermediates (X, XI, XII, XIII). This follows from the observation that the diether, XIV, could be derived from a 2-naphtyl phthalide as well as from the indicated phthalide, X, by the reaction sequence. However, the formation of a 2-naphthyl phthalide is very unlikely since the reported condensations[30,31] of 1,2-dimethoxy naphthalene, VIII, have occurred at the four position.

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(30) S. Rajagopalar, J. Ind. Chem. Soc., 17, 567 (1940).

(31) T. Bisanz, Roczniki Chem., 30, 111 (1956).

The saturated diether, XXa, and the saturated diacetate, XXb,[18] (Fig. 4) were prepared as possible intermediates for the synthesis of 3,4-dihydroxy-9,10-dimethyl-1,2-benzanthracene. If either XVIa or XVIb could be aromatized a gentle cleavage or hydrolysis would afford the hydroquinone. Since the quinone XVII was prepared by an alternate route, this procedure was not developed. The diether XXa and the diacetate XXb[18] were prepared by standard techniques in 84 and 64% respective yields.

The dimethyl ester, XXV, was synthesized to see whether XVII could be prepared by a ring closure with sodium. This method[32] has been used successfully in the preparation of substituted phenanthraquinones.[33] The diester, XXV, was reacted with dispersed sodium

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(32) G. Wittig and H. Zimmerman, Ber., 86, 629 (1953).

(33) H.A. Karnes, Ph.D. Dissertation, The Ohio State University, 1965, p. 43.

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at several different temperatures (Table 3). In no case was XXV converted to XVII.

The diester, XXV, was prepared by the sequence illustrated in Figure 4. Lead tetraacetate cleavage of XVI afforded the dialdehyde, XXI, in 81% yield. This cleavage is of itself quite interesting since the cis-3,4-dihydrodiol of benzanthracene itself is not cleaved by lead tetraacetate.[19] The three compounds, XXII, XXIII and XXIV, were prepared as described[20] in 86, 75 and 87% respective yields. The diester, XXV, was prepared in 48% overall yield by treatment of XXIV with nitrous acid and then esterification of the resulting acid with diazomethane. A previous attempt[20] to hydrolyze the acid-amide, XXIV , with polyphosphoric acid was unsuccessful. In this case there was obtained a neutral substance which appeared to be 1,4-dimethyl-2,3-benz-9-fluorenane.[20]

The structure of XXV is established by the method of synthesis. This follows from the establishment of the structure of the dihydrodiol, XVI, which was discussed earlier.

EXPERIMENTAL

I. Generalizations

1. All melting points were uncorrected. Those melting points followed by (m) were taken on a Fisher-Johns Melting Point Apparatus. The remaining melting points were obtained with capillary tubes in a Thomas-Hoover Melting Point Apparatus.

2. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

3. Infrared spectra were obtained with a Perkin-Elmer Infracord Spectrophotometer and ultraviolet spectra were obtained with a B and L Spectronic 505 Spectrophotometer.

4. Nuclear magnetic resonance spectra (n.m.r.) spectra were obtained with a Varian Model A-60 spectrometer at 60 Mc with tetramethylsilane as an internal reference. In reporting n.m.r. spectra, peaks are described by (a, b, c) where a refers to the number of protons represented by the peak; b refers to the peak multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet); and c gives the peak assignment.

5. Micro thin layer chromatographic analyses (t.l.c.) were run on microscope slides sprayed with Silica Gel G and activated by baking one hour at 110°.

6. Alcoa F-20 grade chromatographic alumina and Davidson 923 grade silica gel were used for column chromatography unless otherwise stated.

7. The phrase "treated in the usual manner" means that the organic solvent layer was washed successively with water, saturated sodium chloride solution, filtered through anhydrous magnesium sulfate and the solvent distilled under reduced pressure.

II. 3-Methoxy-9,10-dimethyl-1,2-benzanthracene, VI

2-(4-Methoxy-1-naphthoyl)benzoic acid, I. -- In a 2 l. flask equipped with a high torque stirrer, solid addition funnel and gas outlet tube were placed 100.0 g. (0.63 mole) of 1-methoxynapthalene, 100.0 g. (0.68 mole) of phthalic anhydride and 525 ml. of purified tetrachloroethane. The resulting slurry was cooled to 10° with ice-water and 190 g. (1.42 mole) of anhydrous aluminum chloride was added during one-hour so that the temperature was maintained below 20°. The resulting mixture was stirred at room temperature for 12 hours and then allowed to stand 12 hours without stirring. The dark addition product was then decomposed with ice and hydrochloric acid and the solvent removed by steam distillation. After cooling the liquid was decanted from the granular grey residue which was dissolved in the requisite amount of hot sodium carbonate solution. The resulting solution was steam distilled a second time and filtered hot through

Hyflo Super-cel,[1] cooled, and neutralized with dilute hydrochloric acid. The resulting white floculent solid was collected, washed well with water and dried at 100° to yield 175.5 g. (90.5%) of I, m.p. 198.0-199° (m) (lit. m.p. 193-194°).[2]

(1) Hyflo Super-cel is an inert cellulose filtering acid.

(2) R. Scholl, C. Seer and A. Zinke, Monatsh., 41, 598 (1920).

3-Methyl-3-(4-methoxy-1-naphthyl)-phthalide, II. -- In a 2 l. flask equipped with stirrer, drying tube, addition funnel and reflux condenser were placed 60.0 g. (0.20 mole) of I, 400 ml. of dry benzene and 1.2 l. of dry ether. To the cooled suspension was added 170 ml. of 2.5 M methylmagnesium bromide during one hour. The cooling bath was then removed and the mixture refluxed with stirring for 24 hours. During this period the reaction mixture became homogenous and changed from an initial light yellow to deep brown. The complex then decomposed with cold dilute hydrochloric acid, the layers separated and the aqueous layer extracted repeatedly with 1:1 ether-benzene. The combined non-aqueous layers were washed well with dilute sodium carbonate solution and then treated in the usual manner to yield 47.9 g. (80.3%) of crude II as a pale yellow oil. Crystallization from absolute ethanol-Skellysolve B afforded 20.7 g. (34.6%) of light yellow crystalline II, m.p. 139.0-140° (lit. m.p. 139.8-140.5°).[3]

(3) W.M. Smith, Jr., E.F. Pratt and H.J. Creech, J. Am. Chem. Soc., 73, 319 (1951).

The remaining 45.7% was recovered from the mother liquor as a pale yellow oil which showed an infrared spectrum identical to that of crystalline I. This non-crystalline material was used as such in the next step.

2-(α-4-methoxy-1-naphthylethyl)benzoic acid, III. -- A mixture of 10.00 g. (0.033 mole) of crystalline II, 150 ml. of 90% formic acid, 20.00 g. of zinc dust and 20 ml. of water was refluxed 10 hours with vigorous stirring. After dilution with 1 l. of water the solids were collected and extracted with approximately 1 l. of 6 N sodium hydroxide solution. After filtration the colorless solution was acidified with dilute hydrochloric acid to yield 9.87 g. (98.4%) of white III (lit. yield 98%),[3] m.p. 196-198° (m) (lit. m.p. 197.3-198.1).[3] The crude phthalide, II, was reduced in the same manner. From 67.8 g. of crude II there was obtained 59.7 g. (88.0%) of III, m.p. 196-198 (m).

3-Methoxy-9-methyl-10-keto-9,10-dihydro-1,2-benzanthracene, IV. -- Compound IV was prepared as described[3] by cyclization of III with anhydrous hydrofluoric acid. From 57.6 g. (0.19 mole) of III there was obtained 52.4 g. (96.7%) of crude IV. Since previous attempts[3] to recrystallize IV were unsuccessful, crude IV was used in the next step.

3-Methoxy-9,10-dimethyl-1,2-benzanthracene, VI. -- A solution of 224 g. (0.78 mole) of crude IV in 600 ml. of dry toluene and

600 ml. of dry dioxane was added during one hour to a stirred solution of 2 moles of methylmagnesium bromide in 1 l. of ether. The color changed from a light brown to a deep brown after a 12 hour reflux. The complex was then decomposed with cold dilute sulfuric acid, the layers separated and the aqueous layer extracted repeatedly with 1:1 ether-benzene. The combined non-aqueous layers were treated in the usual manner and the resulting brown oil taken up in 2.5 l. of xylene. A trace of sulfuric acid was added to the solution which was then refluxed for 7 hours in a system equipped with a water separator. The cooled reaction mixture was reduced to 1/3 of its original volume in vacuo and treated with a hot alcoholic solution of 250 g. of picric acid. The resulting black crystalline complex was recrystallized twice from ethanol and decomposed with an aqueous solution of diethanolamine to yield 153.4 g. (69.1% from IV) of pale yellow VI, m.p. 128-129° (m) (lit. m.p. 129.9-130.9°).[3]

The methyl ether, VI, was also prepared as described[4] by dehydration of XVI and methylation with base and dimethyl sulfate.

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(4) J.W. Cook and R. Schoental, J. Chem. Soc., 170 (1948).

The ether, VI, prepared by this method had the same infrared spectrum as that of VI prepared as described.[1] The melting point of VI produced by dehydration and methylation was undepressed when mixed with VI prepared by the sequence described.[1]

Cleavages of 3-methoxy-9,10-dimethyl-1,2-benzanthracene, VI. -- On treatment of VI with hydrobromic acid in dioxane[3] at reflux a green oil containing four components (t.l.c.) in addition to some unreacted VI was obtained. The other cleaving agents listed in Table 1 gave similar results. As stated in the discussion the supposed phenol, VII, could not be isolated, converted to an ester or oxidized to any identifiable products.

TABLE 1

ATTEMPTED DEMETHYLATIONS OF 3-METHOXY-9,10-DIMETHYL-1,2-BENZANTHRACENE

Acid	Solvent	Conditions
HBr (47%)	Acetic acid	Reflux under nitrogen 1-2 hours
HBr (anhydrous)	Acetic acid	Same
HI (47%)	Acetic acid	Same
BBr_3[5]	Methylene chloride	Stir 12 hours; initial temperature: -78°; final temperature: 27°

[5]J.F. W. McOmie and M.L. Watts, Chem. and Ind. (London), 1658 (1963).

III. 3,4-Dimethoxy-9,10-dimethyl-1,2-benzanthracene, XIV

o-Acetobenzoic acid, IX.[6] -- A mixture of 527 g. (3.56 mole) of crystalline phthalic anhydride, 440 g. of malonic acid and 350 ml. of

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(6) Essentially the method of H.L. Yale, J. Am. Chem. Soc., 69, 1547 (1947).

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malonic acid and 350 ml. of reagent grade pyridine was heated on a steam bath for 5 hours. Carbon dioxide was evolved during the entire heating period. The clear yellow solution was then added to 3 l. of water and filtered free of unreacted phthalic anhydride. The resulting solution was treated with 350 ml. of concentrated hydrochloric acid, continuously extracted with ether for 10 hours, and with benzene for 8 hours. The combined extracts were treated in the usual manner and the resulting white solid recrystallized from benzene to yield 254 g. (43.6%) (lit. yield 48.5%)[6] of white crystalline IX, m.p. 120-121° (m) (lit. m.p. 114-115°).[6]

1,2-Dimethoxynaphthalene, VIII.

1-Amino-2-naphthol hydrochloride. -- This intermediate was prepared as described[7] on a 3 molar scale and the moist product was carried into the next reaction.

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(7) L.F. Fieser, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1943, Coll. Vol. II, p. 35.

1,2-Naphthoquinone. -- This intermediate was prepared by oxidation of 1-amino-2-naphthol hydrochloride as described[8] with a six-fold scale increase.

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(8) Ibid., p. 430.

1,2-Naphthalenediol. -- The moist 1,2-naphthoquinone from above was dispersed in 2.5 l. of water at 40° and treated with 917 g. of reagent sodium hydrosulfite. The suspension became quite fluid and the red color rapidly faded to a pale yellow. The yellow suspension was heated just to the boiling point during 45 minutes and then cooled to 10°. The resulting solid was collected and dried under reduced pressure to yield 377 g. (78.3% from 2-naphthol) of crude 1,2-naphthalenediol.

This preparation was carried out several times with yields ranging from 40 to 78% overall. Since this diol causes severe skin burns both in solution and in the solid form, no attempt was made at purification.

1,2-Dimethoxynaphthalene, VIII. -- In a 5 l. flask equipped with stirrer, take-off condenser, addition funnel and nitrogen inlet tube was placed 2.5 l. of absolute ethanol. A solution of 5.2 mole of sodium ethoxide was prepared by the portion-wise addition of 120 g. of freshly cut sodium. A solution of 377 g. of crude 1,2-naphthalenediol in 700 ml. of absolute ethanol was added to the warm solution

during 15 minutes. After 30 minutes 681 g. (5.4 mole) of dimethyl sulfate was added during 45 minutes. The reaction mixture was then stirred at gentle reflux under nitrogen for 18 hours. A white voluminous solid began precipitating from the solution after 2 hours and continued during the entire reflux period: approximately 2 l. of ethanol was then distilled and replaced with water. The resulting mixture was extracted repeatedly with 1:1 ether-benzene and the combined extracts treated in the usual manner. The resulting brown oil was vacuum distilled to yield 255 g. (57.5%) of light yellow VIII, b.p. 150-165° at 4 mm. (lit. b.p. 278-280°).[9] This crude material

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(9) A. Bezdzik and P. Friedlaender, Monatsh., 30, 283 (1909).

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contained two components in addition to VIII as evidenced by micro t.l.c. These two components were removed by passing a hexane solution of the crude material through 1000 g. of alumina. Concentration of the eluant yielded 220 g. (50.7%) of pure colorless liquid VII. The picrate which was formed in and recrystallized from ethanol had a melting point of 95.5-96.5° (lit. m.p. 97°).[9]

3-Methyl-3-(3,4-dimethoxy-1-naphthyl) phthalide, X.[10] -- In a 50 ml. flask were placed 40 ml. of commercial 90% methane-sulfonic

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(10) Procedure analogous to that of V.W. Floutz, J. Org. Chem., 25, 643 (1960).

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acid and 10.40 g. (0.063 mole) of o-acetobenzoic acid, IX. The resulting mixture was warmed on a steam bath until all the acid, IX, had dissolved, cooled to room temperature and treated with 11.70 g. (0.063 mole) of VIII. After stirring for 12 hours in a closed container the mixture was diluted with 800 ml. of water. The resulting mixture was extracted repeatedly with small portions of 1:1 ether-toluene and the combined non-aqueous layers washed well with water and then with 10% sodium hydroxide solution.[11] The organic phase

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(11) The acidic components thus removed were not identified.

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which now contained only the neutral material was treated in the usual manner to afford 14.10 g. (66.7%) of crude X. The crude product was recrystallized from toluene-petroleum ether (65-110°) and then from ether-petroleum ether (30-60°) to yield 10.34 g. (49.7%) of white crystalline X, m.p. 127.5-128.0°.

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.4; H, 5.4

Found: C, 75.4; H, 5.3

Infrared spectrum: (KBr) 5.71 u, 1751 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

218.1 (4.525); 234.1 (4.760); 287.3 (3.869); 297.3 (3.833); 329.3 (3.480) and 336.3 (3.468).

N.m.r. spectrum (τ units):

7.8 (3s, Ar_2-C^{CH_3}-O); 6.2 (3s, CH_3-O-Ar); 6.0 (3s, CH_3-O-Ar), and 2.1 (9m, Ar).

2-(α-3,4-Dimethoxy-1-naphthylethyl) benzoic acid, XI. -- A mixture of 6.00 g. (0.018 mole) of X, 90 ml. of 90% formic acid, 12.00 g. of zinc dust and 12 ml. of water was refluxed 12 hours with stirring. After dilution with 1 l. of water the solids were collected and extracted with 1 l. of 2% potassium hydroxide solution. After filtration, acidification with dilute hydrochloric acid afforded a quantitative yield of colorless XI, m.p. 154-156° (m). Recrystallization from toluene-petroleum ether (65-110°) gave a melting point of 152.0-154.0°.

Anal. Calcd. for $C_{21}H_{20}O_4$: C, 75.0; H, 6.0; O, 19.0

Found: C, 74.9; H, 6.0; O, 19.7

Infrared spectrum: (KBr) 5.89 u, 1689 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

217.5 (4.555); 235.5 (4.777); 289.7 (3.904); 298.7 (3.877); 331.7 (3.548) and 337.7 (3.542).

N.m.r. spectrum (τ units):

8.3 (4m, Ar_2-$CHCH_3$); 6.0 (6s, CH_3OAr); 2.7 (6m, Ar) and 1.9 (2m, Ar).

3,4-Dimethoxy-9-methyl-10-keto-9,10-dihydro-1,2-benzanthracene, XII. -- To 6.38 g. (0.019 mole) of acid, XI, m.p. 154-156° (m) in a 500 ml. polyethylene bottle was added 100 ml. of anhydrous hydrogen fluoride. The red solution was allowed to stand 20 minutes with occasional swirling and then cautiously added to a large quantity of finely chopped ice. The resulting brown sand was collected and

dissolved in ether. This solution was washed well with 10% potassium hydroxide solution[11] and then treated in the usual manner to afford XII as a brown oil. This oil was used as such in the next reaction.

3,4-Dimethoxy-9,10-dimethyl-1,2-benzanthracene, XIV. -- A solution of crude anthrone, XII, from above in 125 ml. of dry toluene was added dropwise during 10 minutes to a stirred solution of 0.046 mole of methylmagnesium bromide in 100 ml. of dry ether. After stirring at room temperature for 12 hours the complex was decomposed with cold dilute hydrochloric acid. The layers were separated and the aqueous layer extracted several times with 1:1 ether-benzene. The combined non-aqueous layers were washed with 10% potassium hydroxide solution[11] and then treated in the usual manner to yield benzylic alcohol, XIII, as a yellow oil.

This oil was dissolved in 100 ml. of toluene containing a trace of p-toluenesulfonic acid and refluxed for 1.5 hours in a system equipped with a water separator. The solution was cooled and the solvent removed in vacuo to afford a yellow oil which was dissolved in 4:1 petroleum ether-toluene and placed on a silica gel column. After washing the column with petroleum ether-toluene and toluene a light yellow oil was eluted with 10% methanol-toluene in 87.8% yield (from acid XI). This yellow oil was recrystallized twice from hexane-toluene (100:1) at -80° to yield 3.30 g. (55.0% from acid XI) of yellow crystalline XIV, m.p. 51.8-52.5°.

The 2,4,5,7-tetranitrofluorenone (TENF)[12] was formed in and recrystallized from ethanol-toluene, m.p. 190.0-190.5°.

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(12) M.S. Newman and B. Lutz, J. Am. Chem. Soc., 78, 2469 (1956).

Anal. Calcd. for $C_{22}H_{20}O_2$: C, 83.5; H, 6.4; O, 10.1

Found: C, 83.7; H, 6.4; O, 9.8

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

218.7 (4.512); 228.3 (4.533); 249.2 (4.219); 271.1 (4.589); 283.3 (4.521); 294.7 (4.705) and 306.1 (4.731).

N.m.r. spectrum (τ units):

6.8 (6s, Ar-CH_3); 6.2 (3s, CH_3-O-Ar); 5.9 (3s, CH_3-O-Ar); 2.4 (4m, Ar) and 1.7 (4m, Ar).

A wide variety of acidic and alkaline demethylating agents were reacted with XIV as shown in Table 2. In each of the eleven cases listed, the results were approximately the same, i.e. the di-ether, XIV, was decomposed into dark resinous oils from which no identifiable products could be isolated.

When these oils were oxidized with silver oxide-magnesium sulfate in ether, lead dioxide-magnesium sulfate-ether or chloranil in benzene, only black tars were obtained.

TABLE 2

ATTEMPTED CLEAVAGES OF 3,4-DIMETHOXY-9,10-DIMETHYL-1,2-BENZANTHRACENE

Cleavage Agent	Conditions
Pyridine hydrochloride	Heat a 10:1 weight mixture of pyridine hydrochloride:XXIV at 220° for 12 minutes.
Hydriodic acid (47%)-acetic acid	Heat at reflux for 4 hours under nitrogen.
Hydrobromic acid (47%)-acetic acid	Same conditions.
Phosphorus oxychloride-pyridine	Reflux 10 hours under nitrogen.
Phosphonium iodide-acetic acid	Reflux 10 hours under nitrogen.
Aluminum chloride-toluene	Reflux 1.5 hours under nitrogen.
Aluminum chloride-xylene	Reflux 10 hours under nitrogen.
Zinc-chloride-chlorobenzene	Reflux 1 1/3 hours under nitrogen.
BBr_3-methylene chloride[5]	Closed system -78° to room temperature over 12 hours.
Sodium hydroxide	Fusion.
Potassium-p-cymene[13]	Reflux 3 hours under nitrogen.

(13) P. Schorigin, Ber., 56, 176 (1923).

IV. 3,4-Dihydroxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XVI

o-1-Naphthoylbenzoic acid. -- In a 2 l. flask equipped with a high torque stirrer, solid addition funnel and gas outlet tube were placed 129.0 g. (1.05 mole) of naphthalene, 149.0 g. (1.05 mole) of phthalic anhydride and 600 ml. of reagent grade o-dichlorobenzene. The resulting slurry was cooled to 0° and 350 g. (3.6 mole) of anhydrous aluminum chloride was added during one hour so that the temperature was maintained below 10°. The mixture was then allowed to attain room temperature with stirring during 12 hours. The dark addition product was decomposed with ice and hydrochloric acid and the solvent removed by steam distillation. After cooling, the liquid was decanted from the granular grey solid which was dissolved in the requisite amount of hot potassium carbonate solution. The resulting solution was steam distilled a second time, filtered hot through Hyflo Super-cel,[1] cooled and neutralized with dilute hydrochloric acid. The resulting white floculent solid was collected, washed well with water and dried at 100° to yield 263 g. (94.8%) of o-1-naphthoylbenzoic acid, m.p. 165-168° (m) (lit. m.p. 170-172°; lit. yield 97.5%).[14]

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(14) P.H. Groggins and P. Newton, Ind. Eng. Chem., 22, 157 (1930).

1,2-Benz-9,10-anthraquinone. -- This compound was prepared as described[15] by cyclization of o-1-naphthoylbenzoic acid with benzoyl chloride in 87.5% yield (lit. yield, 81%).[15]

(15) G.M. Badger and J.W. Cook, J. Chem. Soc., 802 (1939).

9-Methyl-10-iodomethyl-1,2-benzanthracene. -- In a 1 l. flask equipped with magnetic stirrer and dry ice condenser were placed 10.00 g. (0.038 mole) of benzanthraquinone, 5.0 g. (0.21 mole) of magnesium, 25 ml. of methyl iodide, 50 ml. of dry benzene and 50 ml. of dry ether.[16] The initial vigorous reaction subsided after 20 minutes and

(16) Essentially the method of G.M. Badger and R.S. Pearce, J. Chem. Soc., 2311 (1950).

the solution became deep brown. After one hour of stirring at room temperature the brown solution was cooled to 0° and added carefully to a cooled solution of 40 ml. of 48% hydriodic acid in 100 ml. of anhydrous methanol. A light yellow solid began to precipitate when approximately three-quarters of Grignard complex had been added. This mixture was then treated with 250 ml. of glacial acetic acid and allowed to stand 45 minutes at 5°. The resulting yellow orange solid was collected and air dried in the dark to yield 10.00 g. (70%) of 9-methyl-10-iodomethyl-1,2-benzanthracene (lit. yield, 70%).[17]

(17) R.B. Sandin and L.F. Fieser, J. Am. Chem. Soc., 62, 3098 (1940).

This compound has no melting point. When heated it begins to decompose at 96° (m) (reported decomposition at 99°).[17]

9,10-Dimethyl-1,2-benzanthracene, XV. -- A slurry of 13.95 g. (0.038 mole) of 9-methyl-10-iodomethyl-1,2-benzanthracene in 300 ml. of dioxane containing 30 ml. of concentrated hydrochloric acid was added to a warm stirred solution of 90.0 g. of stannous chloride dihydrate in 500 ml. dioxane and 250 ml. of concentrated hydrochloric acid. The stirred solution was brought to reflux over a 40 minute period and refluxed 10 minutes; the cooled pale yellow solution was added to 3 l. of water and allowed to coagulate overnight. The faintly colored solid was collected and recrystallized from ethanol-benzene to yield 7.47 g. (76.2%) of light yellow XV, m.p. 125.5-126.0° (m) (lit. m.p. 122-123°).[17] The yield reported in the literature[17] for crude material was 99%. This crude yield was reproduced but in no case was that of recrystallized material above 76.2%.

3,4-Dihydroxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XVI. -- The dihydrodiol, XVI, was prepared as described[18] by hydroxylation of XV with osmium tetroxide on a 0.066 mole scale. A 72.4%

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(18) H.I. Hadler and A.C. Kryger, J. Org. Chem., 25, 1896 (1960).

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yield of XVI, m.p. 172.5-173.5° was obtained. The reported yield and melting point[18] were 78% and 172.5-173.5° respectively.

3,4-Diethoxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XXa. -- To a stirred solution of 0.5 g. (0.021 mole) of sodium hydride in 50 ml. of dry tetrahydrofuran under nitrogen was added a solution of 0.50 g. (0.0017 mole) of XVI in 50 ml. of dry tetrahydrofuran. After stirring for 40 minutes, 15 ml. of ethyl bromide was added to the brown solution. The mixture was stirred in a closed flask for 2 days at which time the color was a deep yellow. After dilution with 200 ml. of water the solid was collected, dissolved in 1:1 ether-benzene and treated in the usual manner. The resulting yellow solid was recrystallized once from toluene-petroleum ether (65-110°) and sublimed to yield 0.50 g. (83.7%) of XXa, m.p. 122.8-125.0°.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.2; H, 7.6

Found: C, 83.4; H, 7.8

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

213.1 (4.546); 220.5 (4.590); 252.7 (4.498); 260.5 (4.643); 269.4 (4.664) and 299.3 (4.147).

N.m.r. spectrum (τ units):

9.1 (3q, CH_3-); 8.6 (3t, CH_3-); 7.2 (3s, CH_3-Ar); 7.1 (3s, CH_3-Ar); 6.3 (4m, -CH_2-); 5.5 (1d $J \cong 4$ cps, Ar-CH); 5.1 (1d $J \cong 4$ cps, Ar-CH); 2.8 (6m, Ar); 2.0 (2m, Ar).

3,4-Diacetoxy-3,4-dihydro-9,10-dimethyl-1,2-benzanthracene, XXb. -- To a stirred cooled solution of 0.50 g. (0.0017 mole) of XVI in 10 ml. of dry pyridine was added 8 ml. of acetic anhydride. The reaction mixture was stirred at room temperature for 12 hours and

then added to 200 ml. of water. The resulting solid was collected, recrystallized from ethanol and sublimed to yield 0.41 g. (63.8%) of white XXb, m.p. 148.0-149.0 (lit. m.p. 153-153.5°).[4]

Anal. Calcd. for $C_{24}H_{22}O_2$: C, 77.0; H, 5.9

Found: C, 77.0; H, 6.1

Infrared spectrum: (KBr) 5.69 u, 1757 cm^{-1} and

5.76 u, 1736 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

213.5 (4.597); 223.7 (4.626); 251.1 (4.588); 259.1 (4.754); 269.1 (4.876); 294.1 (4.158) and 305.1 (4.201).

N.m.r. spectrum (τ units):

8.2 (3s, CH_3-C(=O)-O); 7.8 (3s, CH_3-C(=O)-O); 7.3 6s, Ar-CH_3); 3.8 (1d, $J \cong 4$ cps, Ar-CH); 3.2 (1d, $J \cong 4$ cps, Ar-CH); 2.5 (6m, Ar) and 1.8 (2m, Ar).

V. 9,10-Dimethyl-1,2-benz-3,4-anthraquinone, XVII, and its derivatives

To a stirred solution of 10.00 g. (0.034 mole) of XVI in 250 ml. of dimethyl sulfoxide at room temperature was added 100 ml. of acetic anhydride. The solution became pale yellow after one hour, light red after 3 hours and deepened to a dark red after 46 hours. At this time the solution was diluted with 500 ml. of water and repeatedly extracted with 200 ml. portions of 4:1 hexane-benzene. The organic layers were combined, washed well with water and then treated in the usual manner. The resulting red oil was crystallized twice from

acetone to yield 4.34 g. (46.9%) of crystalline XVII, m.p. 152.0-153.0°.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 83.9; H, 4.9; O, 11.2

Found: C, 83.9; H, 4.9; O, 11.0

Infrared spectrum: (CH_2Cl_2) 5.94 u, 1684 cm^{-1}; 6.27 u, 1595 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$) 216.1 (4.556);

249.4 (4.508); 270.1 (4.587); 280.5 (4.629) and 304.1 (4.216).

N.m.r. spectrum (τ units):

7.2 (3s, Ar-CH_3); 7.1 (3s, Ar-CH_3); 2.4 (6m, Ar); 1.9 (2m, Ar).

The quinoxaline derivative, XVIII, was formed by warming a solution of 0.08 g. (0.0003 mole) of XVII, and 0.03 g. of o-phenylenediamine in 5 ml. of glacial acetic acid. The resulting yellow solid was recrystallized three times from toluene-petroleum ether (65-110°) to yield 0.04 g. (40.1%) of XVIII, m.p. 170.5-172.5°.

Anal. Calcd. for $C_{26}H_{18}N_2$: C, 87.1; H, 5.1; N, 7.8

Found: C, 87.1; H, 5.2; N, 7.8

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

272.7 (4.404); 281.8 (4.657); 290.9 (4.692) and 347.6 (4.028).

3,4-Diacetoxy-9,10-dimethyl-1,2-benzanthracene, XIX. -- A mixture of 0.30 g. (0.001 mole) of XVII, 0.30 g. of zinc dust, 0.30 g. of freshly fused sodium acetate and 10 ml. of acetic anhydride was refluxed 10 minutes, treated with 10 ml. of glacial acetic acid and then refluxed for one hour. The cooled solution was decanted into 200 ml. of water and the resulting yellow solid collected by filtration. The yellow solid was crystallized twice from ethanol to yield 0.24 g. (61.5%) of yellow crystalline XIX, m.p. 196.0-197.5°.

Anal. Calcd. for $C_{24}H_{20}O_4$: C, 77.4; H, 5.4; O, 17.2

Found: C, 77.3; H, 5.4; O, 17.3

Infrared spectrum: (KBr) 5.68 u, 1761 cm^{-1} and

6.12 u, 1634 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

216.5 (4.444); 224.5 (4.478); 237.5 (5.336); 269.5 (4.589); 280.5 (4.612); 290.3 (4.821) and 301.7 (4.839).

N.m.r. spectrum (τ units):

7.6 (3s, CH_3-C(=O)-O); 7.5 (3s, CH_3-C(=O)-O); 6.9 (3s, Ar-CH_3); 6.7 (3s, Ar-CH_3); 2.5 (6m, Ar) and 1.8 (2m, Ar).

3,4-Dimethoxy-9,10-dimethyl-1,2-benzanthracene, XIV. -- In a 50 ml. flask equipped with magnetic stirrer, addition funnel, reflux condenser and nitrogen inlet tube were placed 0.20 g. (0.007 mole) of XVII, 0.20 g. of zinc dust and 50 ml. of 95% ethanol. After the system had been flushed with nitrogen, 10 ml. of 20% potassium hydroxide solution was added. The mixture immediately became dark brown. After 15 minutes reflux the mixture was cooled to 0° and treated successively with 10 ml. of dimethyl sulfate and 20 ml. of 20% potassium hydroxide solution. The cooling bath was then removed and the mixture heated to a gentle reflux. At this time the solution was a pale yellow. After 15 minutes the mixture was again cooled to 0° and treated successively with 10 ml. of dimethyl sulfate and 20 ml. of 20% potassium hydroxide solution. The cooling bath was again removed and the mixture heated to reflux. After 25 minutes

the mixture was added to 1 l. of water and extracted three times with 100 ml. portions of 1:1 benzene-hexane. The combined organic layers were washed once with dilute hydrochloric acid and then treated in the usual manner to afford 0.22 g. of a light yellow oil which showed 7 components on micro t.l.c. One component had the same mobility as that of the diether, XIV, from the sequence illustrated in Figure 2. This component was isolated by preparative t.l.c. on silica gel with 1:1 benzene-hexane (volume) as the eluant in 13.8% yield. As mentioned previously, this compound was identified as XIV by a comparison of the spectral properties and by the formation of a TENF[12] derivative.

VI. 3-(o-Carboxyphenyl)-1,4-dimethyl-2-naphthoic acid, dimethyl ester, XXV

3-(o-Formylphenyl)-1,4-dimethyl-2-naphthaldehyde, XXI. -- To a solution of 17.63 g. (0.061) of XVI in 500 ml. of benzene was added 27.0 g. (0.61 mole) of lead tetraacetate[19] in small portions during

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(19) Freshly prepared and supplied by G. Fredric Smith and Co., Columbus, Ohio.

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10 minutes. After stirring for 75 minutes at room temperature the mixture was filtered through Hyflo Super-cel.[1] The resulting solution was washed successively with water and dilute sodium bicarbonate solution and then treated in the usual manner to afford crude XXI as a pale yellow solid. The crude XXI was recrystallized from

toluene-Skellysolve F to yield 14.1 g. (80.8%) of crystalline XXI, m.p. 133.0-134.5°. Repeated recrystallization of a small sample raised the melting point to 137.0-137.5° (lit. m.p. 136.3-138.0°).[18] The reported[18] crude yield of XXI was quantitative. As cited earlier, XXI was first prepared[18] by sodium metaperiodate cleavage.

N.m.r. spectrum (units):

7.7 (3s, CH_3-Ar); 7.0 (3s, CH_3-Ar); 2.3 (8m, Ar);

0.2 (1s, -CHO) and -0.1 (1s, -CHO).

3-(o-Formylphenyl)-1,4-dimethyl-2-naphthaldehyde dioxime, XXII. -- The dioxime, XXII, was prepared by reaction of XXI with hydroxylamine as described[18] in 74.9% yield (lit. yield, 92%).[18]

3-(o-Cyanophenyl)-1,4-dimethyl-2-cyanonaphthalene, XXIII. -- The dinitrile, XXIII, was prepared as described[18] by dehydration of XXII in 74.9% yield (lit. yield, 92%).[18]

3-(o-Amidophenyl)-1,4-dimethyl-2-naphthoic acid, XXIV. -- The acid-amide was prepared by basic hydrolysis of XXIII as described[18] in 83.3% yield. The reported yield[18] was quantitative for crude XXIV.

3-(o-Carboxyphenyl)-1,4-dimethyl-2-naphthoic acid, XXV. -- A solution of 5.40 g. (0.017 mole) of XXIV, m.p. 220-223° in 130 ml. of dioxane containing 4 ml. of concentrated sulfuric acid was cooled to 0° with stirring and treated with 7 ml. of isoamyl nitrite. The mixture was stirred at 0° for 45 minutes, treated with 3 ml. of water and then warmed on a water bath until gas evolution had ceased.

The resulting dark brown solution was concentrated to 25 ml. at room temperature under reduced pressure, and this solution added to 250 ml. of water. The resulting solution was extracted several times with 1:1 ether-benzene and the combined organic layers treated in the usual manner to yield a brown oil which contained a significant amount of unreacted XXIV, as indicated by the infrared spectrum.

This brown oil was dissolved in 200 ml. of glacial acetic acid containing 4 ml. of concentrated sulfuric acid. The solution was cooled to 20° and 4.0 g. of sodium nitrite was added during 15 minutes. After stirring an additional 45 minutes the mixture was treated with 10 ml of water and then warmed on a water bath until gas evolution had ceased. After cooling, the mixture was diluted with 2 l. of water and extracted several times with 1:1 ether-toluene. The combined extracts were washed once with 10% potassium bicarbonate solution and treated in the usual manner to afford a heavy brown oil which was dissolved in 200 ml. of ether and treated with 0.07 mole of diazomethane.[20] After standing at room temperature for 2 hours

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(20) J.A. Moore and D.E. Reed, "Organic Synthesis," John Wiley and Sons, Inc., New York, 1961, Vol. 41, p. 16.

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the ether was distilled under reduced pressure to afford 5.4 g. of a brown oil. The colored impurities were removed by passing an ethyl acetate solution of the crude material through 100 g. of alumina. The resulting pale yellow oil was crystallized three times from

ether-hexane to yield 2.84 g. (48.2% from XXIV) of colorless crystalline XXV, m.p. 110.0-110.5°.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.8; H, 5.8

Found: C, 75.8; H, 5.6

Infrared spectrum: (KBr) 5.79 u, 1727 cm^{-1}

Ultraviolet spectrum: $\lambda_{max}^{Et\ OH}$ mu ($\log_{10}E$)

232.7 (4.841); 289.9 (3.805); 302.9 (3.678) and 327.9 (3.146).

N.m.r. spectrum (τ units):

7.6 (3s, CH_3-Ar); 7.3 (3s, CH_3-Ar); 6.6 (3s, CH_3-O-C-); 6.4 (3s, CH_3-O-C-); 2.5 (6m, Ar) and 1.9 (2m, Ar).

Several attempts were made (Table 3) to prepare XVII by a ring closure of XXV with sodium. A solution of the diester, XXV, in carefully dried solvent was added to excess of sodium which had been dispersed in the same solvent. When the indicated length of time had elapsed, the cooled reaction mixture was treated with a slight excess of methanol and then water. The non-aqueous layer was separated, washed with 10% potassium hydroxide solution[11] and treated in the usual manner to afford a yellow oil. In each of the six cases enumerated, this oil contained four components. These four components were isolated by preparative t.l.c. on silica gel with benzene as the eluant. The infrared spectra of these components showed no quinone absorption and since none of the components could be crystallized, the method was not studied further.

TABLE 3

ATTEMPTED RING CLOSURE OF 3-(o-CARBOXYLPHENYL)-1,4-DIMETHYL-2-NAPHTHOIC ACID, DIMETHYL ESTER

Solvent	Reaction Conditions
Toluene	$3\frac{1}{2}$ hours at 80°
Toluene-benzene	30 minutes at 102°
Toluene	15 minutes at reflux (110°)
Xylene	10 minutes at reflux (137°)
Xylene	55 minutes at reflux (137°)
p-Cymene	15 minutes at reflux (176°)