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Synthetic Studies on Anthracyclinones. VI.[1] The Friedel-Crafts Condensation between 3-Methoxyphthalic Anhydride and α-Naphthol Derivatives

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The Friedel-Crafts condensation of 3-methoxyphthalic anhydride (IV) gave predominantly 3-methoxy-2-aroylbenzoic acid types. On employment of anhydrous aluminum chloride as a condensing agent, this tendency was exclusive. The Grignard reaction of IV also gave a similar result. The boron trioxide catalyzed condensation of 3-hydroxyphthalic anhydride (IVa), on the contrary, gave exclusively 2-hydroxy-6-aroylbenzoic acid types. The structures of the isomeric aroylbenzoic acid derivatives were established by conversion of them into hydroxynaphthacenequinones.

In connection with the synthetic studies on anthracyclinones[3] and related compounds, such as bisanhydroaklavinone (I),[4] bisanhydro-ε-rhodomycinone (II)[5] and bisanhydrodaunomycinone (III),[6] it was necessary for the present authors to investigate the behaviour of 3-methoxyphthalic anhydride (IV)[7] in the Friedel-Crafts condensation.

The Friedel-Crafts condensations of unsymmetrically substituted phthalic anhydrides were extensively studied,[8,9] and there has been concluded that 3-substituted phthalic anhydrides condense predominantly at the hindered carbonyl group with the exception of 3-methyl[9f,h] and 3-bromo[8] derivatives, the former of which condenses comparably at both carbonyl groups and the latter exclusively at the unhindered one. The behaviour of IV, however, has not yet been studied hitherto.[10]

Recently, Brockmann, *et al.*[11] reported the condensation of 3-hydroxyphthalic anhydride (IVa) with α-naphthol, who, however, obtained only a mixture of two isomeric keto acids and employed it for subsequent reactions without separation or characterization of the isomers.

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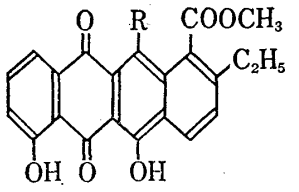
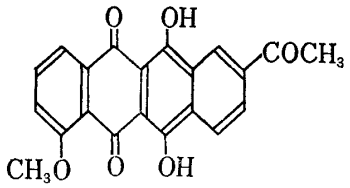
1) The previous paper entitled "Synthetic Studies on η-Pyrromycinone. V." [Z. Horii, T. Momose, and Y. Tamura, *Chem. Pharm. Bull.* (Tokyo), **13**, 797 (1965)] forms Part V of this series.
2) Location: *Toneyama, Toyonaka, Osaka-fu.*
3) The term "anthracyclinone" is based on that proposed by H. Brockmann [H. Brockmann, *Fortschr. Chem. Org. Naturstoffe*, **21**, 121 (1963)].
4) W.D. Ollis, J.J. Gordon, L.M. Jackman, and I.O. Sutherland, *Tetrahedron Letters*, **1960**, 28.
5) H. Brockmann and H. Brockmann, Jr., *Chem. Ber.*, **94**, 2681 (1961).
6) F. Arcamone, G. Franceschi, P. Orezzi, and G. Cassinelli, *J. Am. Chem. Soc.*, **86**, 5334 (1964).
7) E.D. Amstutz, E.A. Fehnel, and C.R. Neumoyer, *J. Am. Chem. Soc.*, **68**, 349 (1946).
8) H.N. Stephens, *J. Am. Chem. Soc.*, **43**, 1950 (1921).
9) *a*) L.F. Fieser and M.S. Newman, *J. Am. Chem. Soc.*, **58**, 2376 (1936); *b*) M.S. Newman, *ibid.*, **59**, 1003 (1937); *c*) M.S. Newman and M. Orchin, *ibid.*, **60**, 586 (1938); *d*) M.S. Newman, *ibid.*, **60**, 1368 (1938); *e*) M.S. Newman and M. Orchin, *ibid.*, **61**, 244 (1939); *f*) M.S. Newman and C.D. McCleary, *ibid.*, **63**, 1542 (1941); *g*) M.S. Newman and B.T. Lord, *ibid.*, **66**, 733 (1944), and Reference 7 therein; *h*) M.S. Newman and C.W. Muth, *ibid.*, **72**, 5191 (1950); *i*) M.S. Newman and P.G. Scheurer, *ibid.*, **78**, 5004 (1956); *j*) M.S. Newman and E.D. Wiseman, *J. Org. Chem.*, **26**, 3208 (1961); *k*) H. Brockmann and H. Brockmann, Jr., *Naturwissenschaften*, **50**, 519 (1963).
10) The condensation of IV with α-naphthol and subsequent cyclisation of the product were reported by Weizmann, *et al.* (W.H. Bently, A. Friedl, F. Thomas, and C. Weizmann, *J. Chem. Soc.*, **1907**, 411) without either isolation of pure isomers or characterization of the product.
11) *a*) H. Brockmann and R. Zunker, *Tetrahedron Letters*, **1966**, 45; *b*) H. Brockmann, R. Zunker, and H. Brockmann, Jr., *Ann.*, **696**, 145 (1966).

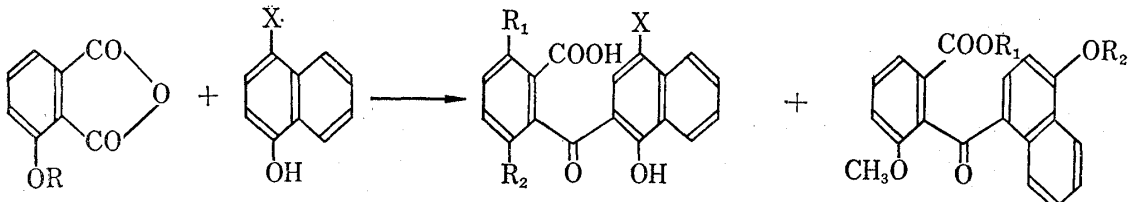
This paper describes the exploratory experiments concerning estimation of the relative amounts of isomeric 2-naphthoylbenzoic acids formed when IV reacts with α-naphthol derivatives in the Friedel-Crafts condensation, and refers to the structural proof of the isomers by conversion of them into the corresponding hydroxynaphthacenequinones.



I : R=H
II : R=OH



III

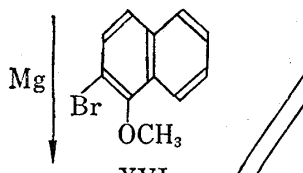


IV : R=CH_3
IVa : R=H

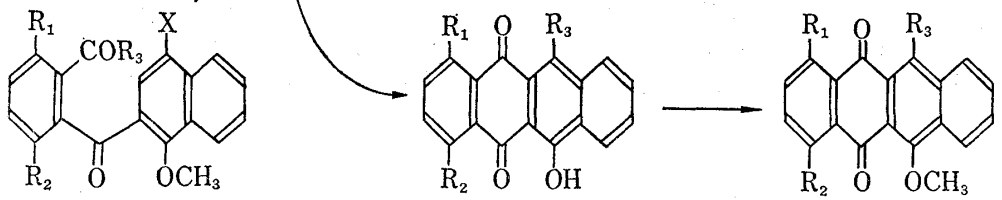
(X=H or Br)

V : R_1=X=H, R_2=OCH_3
Va : R_1=X=H, R_2=OH
VI : R_2=X=H, R_1=OCH_3
VIa : R_2=X=H, R_1=OH
XII : R_1=H, X=Br, R_2=OCH_3
XIII : R_2=H, X=Br, R_1=OCH_3
XIIIa : R_2=H, X=Br, R_1=OH

VII : R_1=R_2=H
X : R_1=R_2=CH_3
XI : R_1=H, R_2=CH_3



XVI



VIII : R_1=X=H, R_2=R_3=OCH_3
IX : R_2=X=H, R_1=R_3=OCH_3
XIV : R_1=H, R_2=R_3=OCH_3, X=Br
XV : R_2=H, R_1=R_3=OCH_3, X=Br
XVII : R_1=X=H, R_2=OCH_3, R_3=OH
XVIII : R_2=X=H, R_1=OCH_3, R_3=OH

XIX : R_1=R_3=H, R_2=OCH_3
XX : R_2=R_3=H, R_1=OH
XXI : R_1=R_3=H, R_2=OH
XXII : R_1=H, R_2=R_3=OH

XXIII : R_1=R_3=H, R_2=OCH_3
XXIV : R_2=R_3=H, R_1=OCH_3

Chart 1

Compound IV was prepared by diazotization of 3-aminophthalic acid hydrochloride[12] and subsequent methylation of the resulting hydroxy-anhydride (IVa) with diazomethane.[7] These procedures are convenient for a large scale preparation.

In order to obtain authentic samples of isomeric 2-naphthoylbenzoic acid derivatives, the present authors began with reinvestigation of the condensation between IVa and α-naphthol by Brockmann's procedure[11b] in which boron trioxide was employed as a condensing agent. 3-Hydroxy-2-(1-hydroxy-2-naphthoyl)benzoic acid (Va) and 2-hydroxy-6-(1-hydroxy-2-naphthoyl)benzoic acid (VIa) could be isolated by differential extraction in the

12) C.H. Wang, R. Isensee, A.M. Griffith, and B.E. Christensen, *J. Am. Chem. Soc.*, **69**, 1909 (1947).

yields of 3.7% and 46.5%,[13] respectively. Methylations of Va and VIa with methyl iodide and potassium carbonate gave their permethylates (VIII) and (IX), respectively. Bromination (XIIIa) of VIa and subsequent methylation with methyl iodide and potassium carbonate gave the permethylate (XV).

Condensation of IV with α-naphthol in boiling acetylene tetrachloride in the presence of anhydrous aluminum chloride gave three products, which were analysed by gas-liquid chromatography (GLC)[14] (Fig. 1) after methylation of the acid mixture with methyl iodide in acetone in the presence of anhydrous potassium carbonate. They appeared as well-resolved three peaks in the chromatogram. One of the products, 3-methoxy-2-(1-hydroxy-2-naphthoyl)benzoic acid (V), was isolated in the form of crystalline sodium salt from the acid mixture by extraction with saturated sodium carbonate solution, and its permethylate (VIII, methyl ether methyl ester of V) was identical with the component of the least retention time in the GLC of the permethylate of the acid mixture. Demethylation of V with boron tribromide gave Va. The isomer of V, 2-methoxy-6-(1-hydroxy-2-naphthoyl)benzoic acid (VI), or its permethylate (IX) could not be isolated, but the latter was detected as the second peak in the chromatogram and identified with the authentic specimen by GLC analysis of the permethylated mixture. The third product, 4-acylated naphthol (VII),[15] was isolated in the form of the permethylate (X) from the permethylated acid mixture by crystallization from ether. Compound X appeared as the last peak in the GLC analysis. The calculated yields of V, VI and VII are 37.3%, 2.5% and 6.5%, respectively.

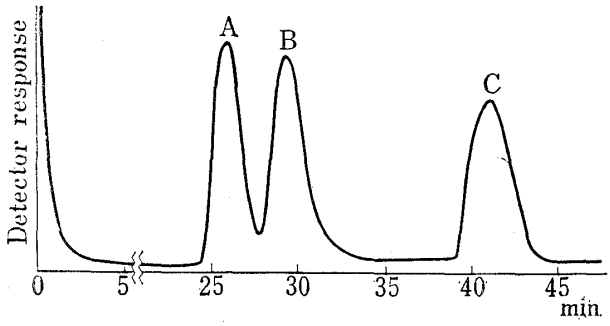


Fig. 1. Separation of Permethylates of Isomeric Naphthoylbenzoic Acid Derivatives (weight ratio=1).

A: methyl 3-methoxy-2-(1-methoxy-2-naphthoyl)benzoate (VIII)
B: methyl 2-methoxy-6-(1-methoxy-2-naphthoyl)benzoate (IX)
C: methyl 3-methoxy-2-(4-methoxy-1-naphthoyl)benzoate (X)

In the experiment employing boron trioxide as a condensing agent at 180°, condensation products were major V and minor VI, and no 4-acylated naphthalene derivative (VII) was

13) Predominance of the product resulting from condensation at the hindered carbonyl group of IVa would be ascribed to a less favorable cleavage of 2-CO-O-linkage due to intramolecular hydrogen bonding between phenolic hydroxyl and a hindered carbonyl group of IVa as illustrated below.

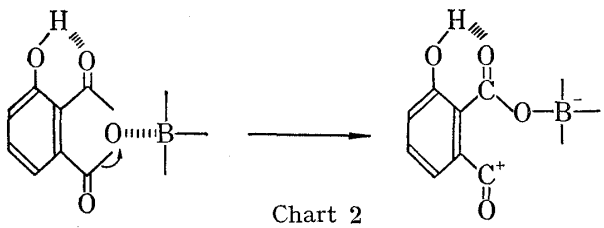


Chart 2

14) Analysis was carried out by employing Perkin-Elmer 800 Gas Chromatograph on SE-52 column (Column size, 1/8 in×6 ft. Column packing, 1.5% SE-52 on 60—80 mesh Chromosorb W. Flow rate (N_2), 35 ml per min. Column temperature, 214°. Injection port temperature, 290°).

15) The NMR spectrum of X quite resembles in its pattern to that of 4-methoxy-1-naphthaldehyde in the 0—2τ region and exhibits a doublet of multiplets centered at 0.66τ, which is ascribable to an α-naphthalene proton deshielded by peri carbonyl group. Methyl 2-(1-naphthoyl)benzoate (a) (1.01 τ) and 1-(2-methoxybenzoyl)naphthalene (b) (1.40 τ) also demonstrate the peri carbonyl effect while α-benzonaphthone (c) (1.89 τ) exhibits no signal below 1.8 τ region. The carbonyl group of (c) cannot lie in the plane of naphthalene ring. However, phenyl α-naphthyl ketones in which the carbonyl group is sterically hindered by *ortho* substituents on the benzene ring, exhibit deshielding of peri protons. That the shift (0.66 τ) in X is much larger than that in (a) may be interpreted by assuming structure X in which the carbonyl group is located between both methoxyl and methoxycarbonyl groups on the benzene nucleus. The NMR studies on this subject will appear in near future from this laboratory.

obtained. The minor isomer (VI) could not be isolated as a genuine product, but could in the form of the permethylate (IX). Demethylation of IX by heating under reflux for a long time with 20% aqueous potassium hydroxide gave VI quantitatively.[16] The calculated yields of V and VI were 24.5% and 15.3%, respectively.

The character of Lewis acid employed as a condensing agent greatly influenced the relative ratio of V and VI as above. In the case of aluminum chloride which is bulky and has high acidity, cleavage of anhydride linkage is rather rapid and intermediate structure (A) would be much more favorable than (B). On the other hand, boron trioxide is less bulky and less acidic, and cleavage of anhydride linkage would be slow. Consequently, condensations at each carbonyl group are considered to be rather comparable.

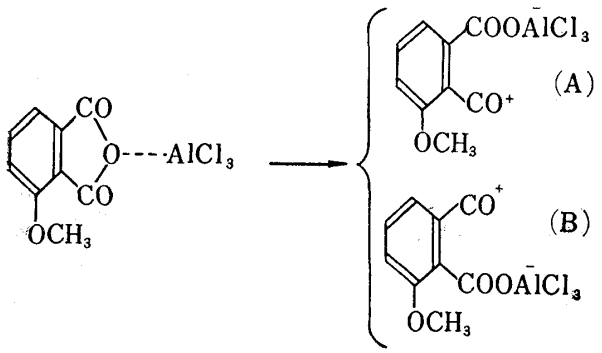


Chart 4

Condensation of IV with 4-bromo-1-naphthol[17] was carried out similarly in the presence of aluminum chloride, and the calculated yields of 3-methoxy-2-(1-hydroxy-4-bromo-2-naphthoyl)-benzoic acid (XII) and its isomer (XIII) were 61% and 8%, respectively.

The compound XII was correlated to V as follows. Methylation of XII with methyl iodide and potassium carbonate gave the permethylate (XIV), which was hydrogenated in methanol in the presence of potassium hydroxide and subsequently methylated[18] to give VIII. In addition, bromination of V with bromine in chloroform gave XII quantitatively. The minor isomer (XIII) could not be isolated, but was identified in the form of the permethylate (XV) by GLC analysis with an authentic specimen prepared above.

It has been observed[9a-i,19,20] that 3-substituted phthalic anhydride condenses with Grignard reagent preferentially at the unhindered carbonyl group.[21] In expectation to

16) A short time alkaline hydrolysis of VIII or IX in aqueous alcohol was accompanied by partial demethylation, and the resulting methoxy acid was contaminated with the hydroxy acid (V or VI), while hydrolysis of X gave only the methoxy acid (XI). That the demethylation takes place in naphthyl ether and not in phenyl ether is detected by coloration in $FeCl_3$-test (in ethanol): 2-acylphenol, blue; 2-acyl-α-naphthol, green. In the cleavage of naphthyl ether linkage in an alkaline medium under a mild condition may be posturated a participation of such an intermediate structure (i) as illustrated below, which would be difficult to participate in phenyl ether.

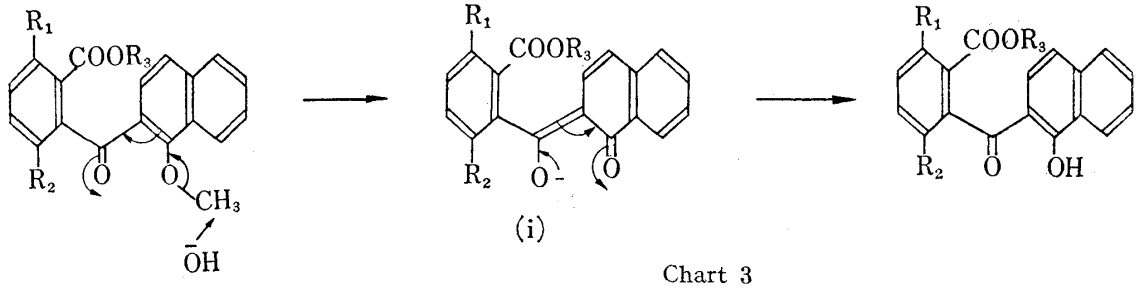


Chart 3

17) W. Militzer, *J. Am. Chem. Soc.*, **60**, 256 (1938).
18) Hydrogenation product from XIV was a mixture of V and the methoxy acid (XVII) owing to partial demethylation. Thus the identification was carried out by comparison of the permethylate.
19) M.S. Newman and P.H. Wise, *J. Am. Chem. Soc.*, **63**, 2109 (1941).
20) R. Goncalves, M.R. Kegelman, and E.V. Brown, *J. Org. Chem.*, **17**, 705 (1952).
21) The normal reaction between a carboxylic anhydride and a Grignard reagent takes place by addition at a carbonyl group. Thus, in the case of 4-substituted phthalic anhydride,[20,23] the inductive effect of the substituents mainly affect the relative amounts of the isomeric products, while it is not true in the case of hindered 3-substituted derivatives.

obtain isomers of a reverse proportion to that in the Friedel–Crafts condensation, IV was condensed with the Grignard reagent prepared from 2–bromo–1–methoxynaphthalene(XVI)[22] to give a mixture of the two isomeric keto acids, which was methylated with methyl iodide in acetone in the presence of potassium carbonate and analysed by GLC. The calculated yields of VIII and IX were 64% and 23%, respectively, and seem unusual as compared with those expected from the hitherto reported examples. Predominance of the product resulted from the condensation at the hindered carbonyl group would probably be ascribed to an extreme tendency to cleave at 2–CO–O– linkage[24] due to delocalization of the unshared electron pairs on oxygen of the methoxyl group.

Separation of the isomers through alumina column using benzene as eluent gave no satisfactory result, but a short time hydrolysis[16] of the mixture in boiling aqueous alcoholic alkali and subsequent chromatography through silica gel–chloroform system gave pure 3–methoxy–2–(1–methoxy–2–naphthoyl)benzoic acid (XVII) and its isomer (XVIII). Demethylation of XVII and XVIII by heating under reflux for a long time with 20% aqueous potassium hydroxide gave V and VI, respectively, in quantitative yields.

Cyclization of V with sulfuric acid containing boric acid gave the monohydroxynaphthacenequinone (XIX), while VI afforded the dihydroxyquinone (XX)[25] on cyclization accompanied by simultaneous demethylation.[26] However, an attempt to cyclize VIa to XX was fruitless.

That the infrared spectrum of XX exhibits no non–chelated quinone carbonyl band[27] and that those of both XIX and its demethylated product (XXI)[28] exhibit those bands at 1665 cm^{-1} and 1666 cm^{-1}, respectively, provide an unequivocal structural proof to both V and VI.

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22) Compound XVI was reported by Cassebaum (H. Cassebaum, *Chem. Ber.*, **90**, 1537 (1957)), who prepared 2–bromo–1–naphthol (XVIa) by bromination of α–naphthol and methylated it with diazomethane. The present authors prepared XVIa according to both Cassebaum's and Heesing's method (A. Heesing, *Chem. Ber.*, **96**, 2176 (1963)) and methylated it with methyl iodide and potassium carbonate.

23) R. Melby, R. Crawford, D. McGreer, and R.B. Sardin, *J. Am. Chem. Soc.*, **78**, 3816 (1956).

24) It has been posturated[9g] that, when Grignard reagents react with phthalic anhydride types, the mechanism involves reaction both by addition to the carbonyl group and metathetical reaction by cleavage of the carbon–oxygen single bond, and that in hindered phthalic anhydrides the successful competition of the metathetical reaction with the addition reaction is responsible for the ratio of the isomeric products.

25) The ultraviolet and visible absorption of XX was provided by Professor W.D. Ollis in his private communication. Brockmann, *et al.*[11b] recently reported the separation of XX from the cyclization product of a mixture of Va and VIa.

26) A methoxyl group located at peri position to non–chelated quinone carbonyl group was selectively cleaved on cyclization as illustrated below. *cf.* Z. Horii, T. Momose, and Y. Tamura, *Chem. Pharm. Bull.* (Tokyo), **13**, 737 (1965).

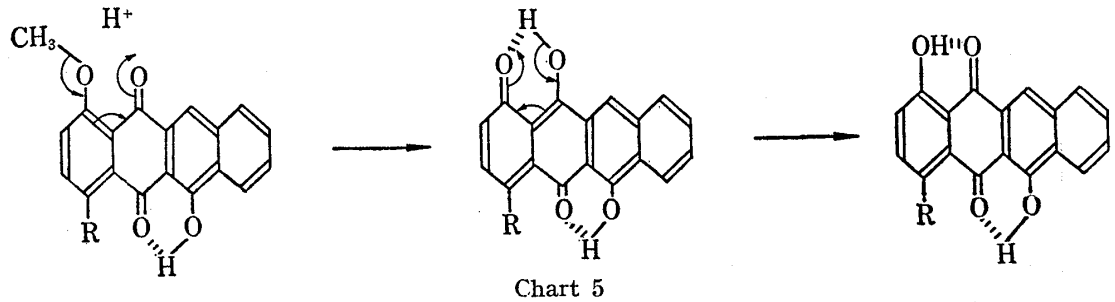

Chart 5

27) *cf.* Z. Horii, T. Momose, M. Naruse, and Y. Tamura, *Chem. Pharm. Bull.* (Tokyo), **10**, 1013 (1962); Z. Horii, T. Momose, and Y. Tamura, *ibid.*, **13**, 740, 797 (1965).

28) Compound XXI was reported by Brockmann, *et al.*[9k] who prepared it *via* the Friedel–Crafts reaction of 3–nitrophthalic anhydride with α–naphthol, subsequent reduction to the amino compound and cyclization of the latter.

Cyclization of XIIIa gave 1,6,11-trihydroxynaphthacenequinone (XXII)[29] as a result of both simultaneous exchange of bromo group with hydroxyl group and demethylation.

The characteristic spectral features of the isomeric hydroxyquinones (XX and XXI) and their methyl ethers (XXIII and XXIV) were shown in Figs. 2 and 3. There is no extinct difference enough to differentiate both isomers between the spectra of methyl ethers. Spectra of the hydroxyquinones, however, are quite distinguishable.

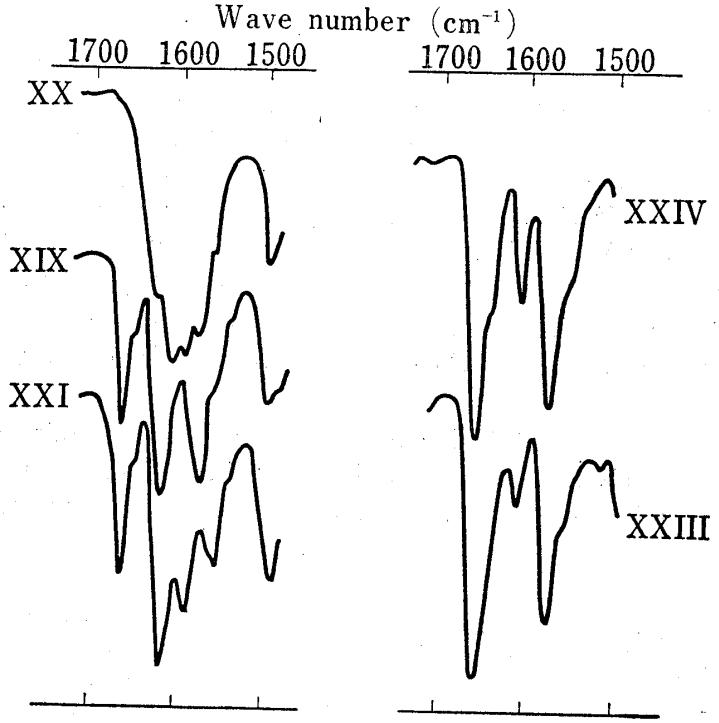

Fig. 2. Infrared Spectra of Hydroxynaphthacenequinones and Their Methyl Ethers (in KBr disk)

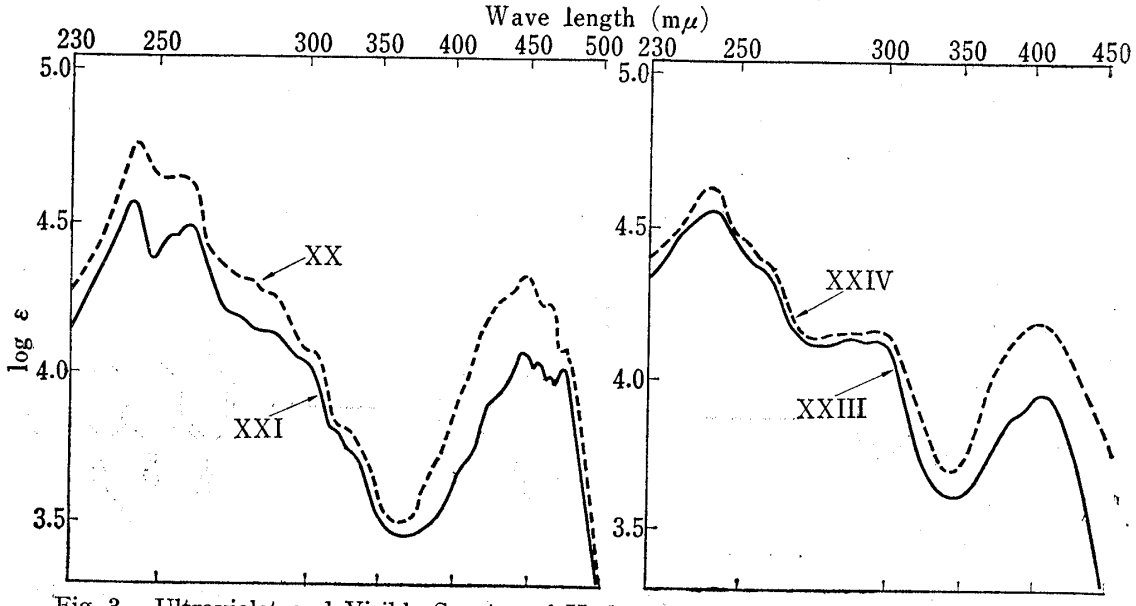

Fig. 3. Ultraviolet and Visible Spectra of Hydroxynaphthacenequinones (in *n*-hexane) and Their Methyl Ethers (in 95% EtOH).

29) H. Brockmann and W. Müller, *Chem. Ber.*, **92**, 1164 (1959).

Experimental[30]

3-Hydroxyphthalic Anhydride (IVa)[31]——To an ice-cooled and stirred solution of 450 g (2 moles) of $SnCl_2 \cdot 2H_2O$ in 600 ml of conc. HCl was added 123 g (0.6 moles) of 3-nitrophthalic anhydride[33] at 0° in one portion. The ice bath was removed and the mixture was allowed to warm up to 80° under stirring and maintained at this temperature for 20 min. The resulting clear solution was cooled to 0°, and the deposited pale yellow needles of 3-aminophthalic acid hydrochloride[12] were collected by suction and suspended[34] in 600 ml of conc. HCl. A solution of 40 g (0.58 mole) of $NaNO_2$ in 150 ml of H_2O was then added to the suspension in 1.5 hr, the temperature being maintained at 5—7°. After an additional 1 hr's stirring at 4—5°, the deposited pale yellow crystals were collected by filtration and added in small portions to 1.7 liter of boiling H_2O. The resulting orange yellow solution was cooled to 0° and filtered to remove deposited 3-chlorobenzoic acid (11.5 g, 11%). The filtrate was evaporated to dryness under reduced pressure, and the resulting solid was extracted with boiling ether (100 ml×2). The ethereal extract was evaporated and the resulting residue was refluxed with 100 ml of toluene. The solvent was evaporated and the residue was reextracted with boiling ether (50ml×2). The ethereal extract gave 4.4 g (5%) of 3-hydroxybenzoic acid on evaporation of the solvent. From the ether-insoluble solid was obtained 32.3 g (30.9%) of IVa as pale yellow crystals, mp 195—196° (lit.[32], mp 199—200°), by recrystallization from benzene. By treatment of IVa with CH_2N_2 in ether was obtained the methyl ether (IV), mp 161—162° from C_6H_6 (lit.,[7] mp 155—158° from toluene; lit.,[35] mp 160—161° from toluene), quantitatively.

Friedel-Crafts Condensation between IVa and α-Naphthol employing Boron Trioxide [3-Hydroxy-2-(1-hydroxy-2-naphthoyl)benzoic Acid (Va) and 2-Hydroxy-6-(1-hydroxy-2-naphthoyl)benzoic Acid (VIa)]——A mixture of IVa (8.2 g, 0.05 mole), α-naphthol (7.2 g, 0.05 mole) and B_2O_3 (17.4 g, 0.25 mole) was heated to melt with stirring. The temperature was elevated up to 190° during 20 min and maintained at 190° for 30 min. The cooled mass was digested with hot H_2O and resulting black tarry material was taken in AcOEt. The AcOEt layer was washed with H_2O and exhaustively shaken with 2% Na_2CO_3. The alkaline layer was saturated with NaCl and extracted with AcOEt (50 ml×3). The AcOEt layer was washed with satd. NaCl, dried over anhyd. Na_2SO_4 and evaporated to give 5.8 g of a yellowish brown solid, which was recrystallized from 50 ml of benzene to 7.5 g of yellow crystals. Recrystallization from MeOH–H_2O gave 7.18 g (46.5%) of VIa as yellow short prisms, mp 114—116°. *Anal.* Calcd. for $C_{18}H_{12}O_5$: C, 70.13; H, 3.92. Found: C, 70.04; H, 3.88. IR ν_{max}^{KBr} cm^{-1}: 1656, 1628 (C=O), 1602, 1570 (arom.).

The NaCl saturated alkaline layer, after AcOEt extraction, was acidified with conc. HCl and extracted with AcOEt. The AcOEt layer was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 3.4 g of a dark brown viscous oil, which gave 1.5 g of slightly yellow crystals on crystallization from 50 ml of benzene. The crystals were washed with 50 ml of hot H_2O in order to remove 3-hydroxybenzoic acid and 3-hydroxyphthalic acid, and undissolved crystals were washed with ether. The ethereal layer was evaporated to give a yellow glassy solid, which gave 0.57 g (3.7%) of Va, as yellow short prisms, mp 204—207°. Recrystallization from MeOH–H_2O caused a melting point depression to 137—192° by holding crystalline H_2O, which could be removed only after drying at 110° for 12 hr. *Anal.* Calcd. for $C_{18}H_{12}O_5$: C, 70.13: H, 3.92. Found: C, 69.87; H, 3.97. IR ν_{max}^{KBr} cm^{-1}: 1712, 1631 (C=O), 1603, 1569 (arom.).

Methyl 3-Methoxy-2-(1-methoxy-2-naphthoyl)benzoate (VIII) (Permethylate of Va)——A mixture of Va (200 mg), MeI (5 g), anhyd. K_2CO_3 (5 g) and dry Me_2CO (15 ml) was refluxed for 10 hr. The solvent was removed, and the residue was extracted with $CHCl_3$ (10 ml×3). The extract was filtered and evaporated to give 250 mg of residue, which gave 195 mg of VIII as colorless crystals, mp 120—122°, after purification by column chromatography using alumina–benzene system. An analytical sample was prepared by two recrystallizations from MeOH. *Anal.* Calcd. for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 72.41; H, 5.30. IR ν_{max}^{KBr} cm^{-1}: 1711, 1668 (C=O), 1620, 1595, 1584, 1564 (arom.).

Methyl 2-Methoxy-6-(1-methoxy-2-naphthoyl)benzoate (IX) (Permethylate of VIa)——The acid (VIa) was methylated similarly to that for VIII to give IX in a quantitative yield. Colorless needles (from

30) All melting points are uncorrected.

31) E.L. Eliel, *et al.*[32] prepared IVa from 3-nitrophthalic anhydride *via* the catalytic reduction and subsequent diazotization of the resulting amino-anhydride in the total yield of 54—70%. Their procedures are somewhat laborious and the total yield was not always reproducible when checked by the present authors. On the other hand, E.D. Amstutz, *et al.*,[7] prepared IVa through diazotization of 3-aminophthalic acid hydrochloride without a sufficient separation of IVa from 3-hydroxybenzoic acid and detailed description of diazotization experiment. The present procedure is very simple and suitable for a large scale preparation.

32) E.L. Eliel, A.W. Burgstahler, D.E. Rivard, and L. Haefele, *J. Am. Chem. Soc.*, **77**, 5092 (1955).

33) B.H. Nicolet and J.A. Bender, *Org. Syn.*, Coll. Vol. I, 410 (1948).

34) 3-Aminophthalic acid hydrochloride is quite soluble in cold water while sparingly in conc. hydrochloric acid.

35) W.H. Bently, R. Robinson, and C. Weizmann, *J. Chem. Soc.*, **1907**, 104.

MeOH), mp 114—116°. *Anal.* Calcd. for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.99; H, 4.96. IR ν_{max}^{KBr} cm^{-1}: 1736, 1657 (C=O), 1623, 1585, 1575, 1567 (arom.).

2-Methoxy-6-(1-hydroxy-2-naphthoyl)benzoic Acid (VI)——A mixture of IX (170 mg), KOH (5 g), H_2O (6 ml) and MeOH (15 ml) was refluxed for 32 hr, and then MeOH was evaporated. The mixture was diluted with 30 ml of H_2O and acidified with conc. HCl to give 160 mg of yellow micro-needles, mp 183—186°, which were recrystallized from MeOH to 120 mg of VI. Yellow needles, mp 189—190°. *Anal.* Calcd. for $C_{19}H_{14}O_5$: C, 70.80; H, 4.38. Found: C, 71.13; H, 4.46. IR ν_{max}^{KBr} cm^{-1}: 1689 (C=O), 1628 (C=O, shoulder of arom.), 1607, 1587, 1567 (arom.).

2-Hydroxy-6-(4-bromo-1-hydroxy-2-naphthoyl)benzoic Acid (XIIIa)——To an ice-cooled and stirred solution of VIa (1.0 g, 0.00325 mole) in $CHCl_3$ (50 ml) was added a solution of Br_2 (0.5 g, 0.00313 mole) in $CHCl_3$ (20 ml) over a period of 1 hr. After an additional 1 hr's stirring at room temperature, the mixture was cooled in an ice bath, and the deposited crystals were collected. Yield: 1.1 g. Yellow prisms (from MeOH), mp 247—249°. *Anal.* Calcd. for $C_{18}H_{11}O_5Br$: C, 55.83; H, 2.86. Found: C, 56.15; H, 2.85. IR ν_{max}^{KBr} cm^{-1}: 1657 (C=O), 1623 (C=O, shoulder of arom.), 1612, 1601 (arom.).

Methyl 2-Methoxy-6-(4-bromo-1-methoxy-2-naphthoyl)benzoate (XV)——A mixture of XIIIa (500 mg), K_2CO_3 (10 g), MeI (10 g) and Me_2CO (20 ml) was refluxed for 19.5 hr and treated similarly to that for VIII. A glass (560 mg) was obtained, and crystallized from MeOH to 490 mg of colorless crystals, mp 136—138°. One more recrystallization from MeOH gave 390 mg of XV as colorless long prisms, mp 137—139°. *Anal.* Calcd. for $C_{21}H_{17}O_5Br$: C, 58.75; H, 3.99. Found: C, 58.85; H, 3.96. IR ν_{max}^{KBr} cm^{-1}: 1737, 1646 (C=O), 1613, 1582, 1564 (arom.).

Friedel-Crafts Condensation between IV and *α*-naphthol employing Aluminum Chloride [3-Methoxy-2-(1-hydroxy-2-naphthoyl)benzoic Acid (V) and Methyl 3-Methoxy-2-(4-methoxy-1-naphthoyl)benzoate (X)]——A mixture of IV (11.1 g, 0.062 mole), *α*-naphthol (16.4 g, 0.14 mole) and anhyd. $CHCl_2CHCl_2$ (200 ml) was heated up to 140° until a clear solution was obtained, and then cooled to room temperature. To this was added 13.3 g (0.1 mole) of pulverized anhyd. $AlCl_3$ in one portion, and the temperature was elevated up to 130° by gradual heating. A clear solution which resulted at 90° solidified at 120°. After 30 mins' heating at 130° (bath temperature 150—155°), the mixture was poured onto cracked ice, and the dark solid was crushed and treated with conc. HCl and AcOEt one after the other to destroy the complex. The whole mixture was extracted with AcOEt (400 ml×3). The extract was washed with H_2O and shaken repeatedly with satd. Na_2CO_3 until the last alkaline layer afforded no precipitate on acidification. From the earlier part of the alkaline extracts deposited greenish yellow precipitates of Na salt of V on standing, which were collected, washed with satd. NaCl and AcOEt, and then dried. The Na salt was dissolved in H_2O and the solution was filtered and acidified to give 6.2 g of pale yellow precipitates, mp 223—232°, recrystallization of which from MeOH gave 6.0 g of V as greenish yellow prisms, mp 230—232°. The sample holds MeOH even after 24 hrs' drying at 60°. $FeCl_3$-Test: dark green in EtOH. *Anal.* Calcd. for $C_{19}H_{14}O_5 \cdot \frac{1}{5}CH_4O$: C, 70.15; H, 4.54. Found: C, 70.10; H, 4.59. IR ν_{max}^{KBr} cm^{-1}: 1689 (C=O), 1631 (C=O, shoulder of arom.), 1615 (arom.), 1582 (arom.).

The alkaline extract, after removing solid Na salt of V, was shaken twice with AcOEt, filtered, acidified with conc. HCl and extracted with AcOEt (100 ml×3). The extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to yield 3.4 g of a solid, which was methylated by 10 hrs' refluxing with MeI (20 g) and anhyd. K_2CO_3 (14 g) in dry Me_2CO (40 ml) to give 3.5 g of a pale brown solid. Analysis of this permethylate by GLC[14] gave three peaks[36] with areas of 23:7:19 in the sequence of increasing retention time. In the mixed experiment, the first peak was identical with that of the permethylate (VIII) of V, and the second with that of the isomer (IX) of VIII. After a column chromatography through an alumina–benzene system, the permethylate of the acid mixture was dissolved in 15 ml of ether. On standing at room temperature, 0.32 g of X separated from the solution as colorless needles, mp 143—144°. The analytical sample was prepared by one recrystallization from MeOH. *Anal.* Calcd. for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 72.21; H, 5.44. IR ν_{max}^{KBr} cm^{-1}: 1716 (C=O), 1650 (C=O), 1616, 1587, 1577 (arom.). NMR (τ) (in CCl_4): 0.66 (1H, doublet of multiplets, 8-proton of 1-acylnaphthalene).

The peak of this sample in GLC was identical with the last peak of the three mentioned above. The ethereal mother liquor, after removing X, gave 50 mg of VIII as colorless clustered crystals, which were identified with the sample obtained in the above experiment. The yields of V, VI and VII, calculated from GLC analysis, were 37.3%, 2.5% and 6.5%, respectively.

Demethylation of V——A solution of V (100 mg) in dry CH_2Cl_2 (20 ml) was cooled to −60°, and to this was added a cooled solution of BBr_3 (3.1 g) in dry CH_2Cl_2 (5 ml) at −60° in one portion. The resulting deep red clear solution was stood at room temperature for 1 hr, then poured onto cracked ice and extracted

36) The sample was dissolved in acetone into 1 w/v% solution, and 2 μl of the latter was injected. In the model experiment, a sample consisting of equal amount (weight ratio=1) of pure VIII, IX and X gave, within a 1—3 μl injection, a chromatogram with three peaks of equal peak area as illustrated in Fig. 1. It was confirmed that the ratio of peak area well agreed with weight ratio (IX/VIII or X/VIII). Retention time observed: 25.9 min for VIII, 29.3 min for IX and 41.1 min for X.

with 50 ml of AcOEt. The AcOEt layer was washed with satd. $NaHCO_3$ (20 ml × 3), and the alkaline layer was shaken with $CHCl_3$ (10 ml × 2), filtered through wet filter paper, acidified with conc. HCl and extracted with AcOEt. The AcOEt layer was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 80 mg of a yellow glass, which was crystallized from benzene to give 63 mg of Va as yellow crystals, mp 204—207°. This sample was identified with the authentic sample obtained above by IR comparison (KBr).

3-Methoxy-2-(4-methoxy-1-naphthoyl)benzoic Acid (XI)——A mixture of X (150 mg), KOH (1 g), EtOH (5 ml) and H_2O (10 ml) was refluxed for 4 hr. Ethanol was removed by evaporation, and the resulting clear solution was acidified to give 140 mg of colorless precipitates, which were recrystallized from Me_2CO–H_2O to 100 mg of XI. Colorless microneedles, mp 259—261°. *Anal.* Calcd. for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80. Found: C, 71.59; H, 4.78. IR ν_{max}^{KBr} cm^{-1}: 1706 (C=O), 1623, 1615, 1575 (arom.). The spectrum suggests for XI to have a lactol structure.

Friedel-Crafts Condensation between IV and α-Naphthol employing Boron Trioxide——A mixture of IV (5.9 g, 0.033 mole), α-naphthol (4.8 g, 0.033 mole) and B_2O_3 (11.6 g, 0.166 mole) was heated to melt with stirring. The temperature was elevated up to 180° during 30 min and maintained at 180° for 30 min. The cooled mass was digested with hot H_2O, and extracted with AcOEt (50 ml × 2). The extract was washed with H_2O and shaken exhaustively with satd. Na_2CO_3. The alkaline layer afforded, on saturation with NaCl, Na salt of V as greenish yellow crystals, which were dissolved in H_2O, filtered and acidified with conc. HCl to give 0.85 g of V as pale yellow precipitates. From the alkaline mother liquor, after removing the Na salt, was obtained, on acidification with conc. HCl and subsequent extraction with AcOEt, 0.8 g of a solid which was proved to be 3-methoxyphthalic acid containing a trace of V from GLC analysis of its permethylate.

The organic layer, after the exhaustive shaking with satd. alkali as mentioned above, was shaken twice with 1% Na_2CO_3 and then thrice with H_2O. The 1% Na_2CO_3 and H_2O washings were combined and acidified with conc. HCl to give 2.4 g of a solid, which was recrystallized from 30 ml of benzene to give 1.78 g of pure V as the first crop and 0.65 g of crystals as the second crop on evaporation of solvent. The second crop was proved to be a mixture of V and VI (1:3) from GLC analysis of its permethylate.

The organic layer, after shaking with satd. and 1% Na_2CO_3, was dried over anhyd. Na_2SO_4 and evaporated to give 6.1 g of a dark solid, which was recrystallized from 50 ml of benzene to give 1.82 g of a pale yellow crystalline powder. This could not be purified further, but was methylated with MeI and K_2CO_3 to its permethylate, which was proved to be identical with IX by GLC analysis and was crystallized on trituration with ether to give 1.3 g of IX.

Calculated total yields of V and VI were 24.5% and 15.3%, respectively.

Friedel-Crafts Condensation between IV and 4-Bromo-1-naphthol employing Aluminum Chloride [3-Methoxy-2-(4-bromo-1-hydroxy-2-naphthoyl)benzoic Acid (XII) and Its Permethylate (XIV)]——The condensation between IV (6.5 g, 0.036 mole) and 4-bromo-1-naphthol (8 g, 0.036 mole) was carried out, in a similar manner to that for the condensation between IV and α-naphthol, in boiling $CHCl_2CHCl_2$ (200 ml) in the presence of anhyd. $AlCl_3$ (5.3 g). Through a purification of the product *via* the Na salt was obtained 2.0 g of XII as yellow plates (benzene), mp 215—127°. *Anal.* Calcd. for $C_{19}H_{13}O_5Br \cdot \frac{2}{3}C_6H_6$: C, 60.94; H, 3.78. Found: C, 60.66; H, 3.84. IR ν_{max}^{KBr} cm^{-1}: 1689 (C=O), 1623 (C=O, shoulder of arom.), 1618, 1595, 1583, 1570 (arom.).

An acidic mixture (7.0 g, a brown solid) obtained *via* acidification of the satd. Na_2CO_3 extract and subsequent extraction was methylated (6.9 g of the permethylate) in the usual manner and then subjected to GLC analysis, in which two peaks[37] were observed in the ratio of 8:1 in the sequence of increasing retention time. The permethylated acid mixture (3.0 g) was subjected to column chromatography using alumina–benzene system, giving 2.1 g of XIV as colorless prisms (iso-PrOH), mp 129—130°. *Anal.* Calcd. for $C_{21}H_{17}O_5Br$: C, 58.76; H, 3.99. Found: C, 58.86; H, 4.11. IR ν_{max}^{KBr} cm^{-1}: 1712, 1645 (C=O), 1613, 1585, 1563 (arom.).

The first peak in GLC was identical with that of XIV, which was also prepared from XII by methylating with MeI, anhyd. K_2CO_3 in boiling Me_2CO in an almost quantitative yield.

Although a compound affording the second peak could not be isolated, it was proved to be XV, the permethylate of XIII, by GLC analysis.

The calculated yields of XII and its isomer (XIII) from GLC analysis were 53.5% and 5.0%, respectively.

Bromination of V——To an ice-cooled and stirred solution of V (1.0 g) in $CHCl_3$ (50 ml) was added a solution of Br_2 (0.5 g) in $CHCl_3$ (20 ml) over a period of 50 min. After the addition was complete, the mixture was stirred at room temperature for an additional 1 hr and then cooled in an ice bath. The deposited precipitates were collected, washed with $CHCl_3$ and then H_2O and dried to give 1.2 g of XII as yellow crystals, mp 215—217°, which was identified with the sample obtained above by IR (KBr) comparison.

Hydrogenolysis of XIV——A mixture of XIV (200 mg), KOH (3 g), H_2O (10 ml) and EtOH (40 ml) was shaken under H_2 in the presence of Raney nickel (1 g) at room temperature. During 10 hrs' shaking was

37) These peaks were accompanied by three peaks of both extremely short retention times and negligibly small molar ratio, which were assumed to be derived from phthalic acid moiety.

consumed 20 ml of H_2. After removing EtOH by evaporation, the mixture was diluted with 40 ml of H_2O and acidified with conc. HCl to give 150 mg of yellowish green crystals[18] (a negative Beilstein test; $FeCl_3$-test: green), which were methylated. with MeI (2 g) and anhyd. K_2CO_3 (2 g) in dry Me_2CO (10 ml) under 20 hrs' refluxing, and chromatographed through alumina–benzene system. Colorless crystals (70 mg) were obtained and identified with the sample of VIII by IR spectral comparison (KBr).

2-Bromo-1-methoxynaphthalene (XVI)[22]——A mixture of 2-bromo-1-naphthol[22] (20 g), MeI (100 g), anhyd. K_2CO_3 (50 g) and dry Me_2CO (200 ml) was refluxed for 20 hr, and then inorganic salt was separated by filtration and washed with $CHCl_3$ (100 ml×2) by refluxing. The Me_2CO layer was evaporated and the residue was combined with the $CHCl_3$ washing and filtered. Evaporation of the solvent gave 21 g of a crystalline solid. Vacuum distillation of the product gave 19 g of a colorless oil (bp 127° (0.8 mmHg)) which solidified on standing. mp 47° (lit.[22]), bp 170—173° (15 mmHg), mp 59—60°). *Anal.* Calcd. for $C_{11}H_9OBr$: C, 55.72; H, 3.83. Found: C, 56.01; H, 4.00.

Grignard Condensation between IV and XVI [3-Methoxy-2-(1-methoxy-2-naphthoyl)benzoic Acid (XVII) and 2-Methoxy-6-(1-methoxy-2-naphthoyl)benzoic Acid (XVIII)]——A mixture of Mg turnings (3.1 g, 0.13 mole), EtBr (2 drops) and anhyd. ether (12 ml) was stirred under N_2 until reaction started, and then to this was added a mixture of XVI (15 g, 0.063 mole), EtBr (6.9 g, 0.063 mole), anhyd. ether (50 ml) and anhyd. benzene (25 ml) at a rate to maintain reflux with stirring. The mixture was refluxed for 20 min after the addition was complete, during which time 50 ml of anhyd. benzene was added slowly. A solution of IV (25 g, 0.14 mole) in anhyd. benzene (400 ml) was added rapidly to the Grignard reagent with stirring at room temperature, and then refluxing and stirring were continued for 6 hr. The mixture was cooled, decomposed with dil. HCl, and the organic layer was washed with H_2O and then shaken with saturated. Na_2CO_3 (100 ml×5). The alkaline layer was shaken twice with benzene, acidified with conc. HCl and extracted with AcOEt (50 ml×3). The extract was washed with H_2O, dried over anhyd. Na_2SO_4 and evaporated to give 27 g of a brown solid, which was methylated with MeI (70 g) and anhyd. K_2CO_3 (60 g) in dry Me_2CO (100 ml) by 20 hrs' refluxing to give 26 g of a brown paste. After removing a fraction (6.5 g) of low boiling point (bp 120—130° (5 mmHg)) by vacuum distillation, the remaining fraction (19.5 g) was analysed by GLC, giving two peaks[38] in the ratio of 19:7 in the sequence of increasing retention time. In mixed experiment, the first peak was identical with that of VIII, and the second with that of IX. The calculated yields of XVII and XVIII were 64% and 23%, respectively. The methylated mixture (3.7 g) employed above for GLC analysis was hydrolyzed by 3 hrs' heating in a solution consisting of NaOH (2 g), H_2O (5 ml) and EtOH (20 ml), giving 3.4 g of an acid mixture as a brownish glass, which was chromatographed through silica gel–$CHCl_3$ system. From the earlier fraction of eluate was obtained 0.5 g of XVIII as slightly yellow needles (MeOH), mp 238°, and from the later 2.5 g of XVII as colorless plates (MeOH), mp 206—209°. *Anal.* Calcd. for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80. Found (XVII): C, 71.40; H, 5.14. Found (XVIII): C, 71.59; H, 5.17. IR ν_{max}^{KBr} cm^{-1}: (XVII): 1686, 1650 (C=O), 1621, 1597, 1585, 1565 (arom.). (XVIII): 1701, 1658 (C=O), 1616, 1596, 1580, 1572 (arom.).

Methylation of XVII——A mixture of XVII (200 mg), MeI (5 g), anhyd. K_2CO_3 (5 g) and dry Me_2CO (15 ml) was refluxed for 10 hr, and then treated in a similar manner to that for VIII to give 180 mg of VIII, which was identified with the authentic sample obtained above by IR comparison (KBr).

Demethylation of XVIII——A mixture of XVIII (500 mg), KOH (5 g) and H_2O (20 ml) was refluxed for 30 hr, and then diluted with 30 ml of H_2O. After removing MeOH by evaporation, the solution was acidified with conc. HCl to give 450 mg of precipitates, mp 183—187°. Recrystallization from MeOH gave 400 mg of VI, which was identified with the authentic sample obtained above by IR comparison (KBr).

1-Methoxy-11-hydroxynaphthacenequinone (XIX)——A mixture of H_3BO_3 (4 g) and H_2SO_4 (40 ml) was heated until a clear solution resulted, and then cooled. To this was added 750 mg of V, and the mixture was heated with stirring at 120—130° for 10 min, during which time initial dark brown color of the mixture turned into dark green. The mixture was poured onto 300 g of cracked ice to give orange red precipitates, which were collected, washed with H_2O, then with satd. $NaHCO_3$ and again with H_2O to neutral to lithmus and dried. The crude quinone (230 mg) was sublimed at 210—220°/2 mmHg to give 210 mg of XIX as orange needles (toluene), mp 263—266°. *Anal.* Calcd. for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97. Found: C, 74.61; H, 3.74. IR ν_{max}^{KBr} cm^{-1}: 1665 (C=O), 1616, 1595, 1580 (arom.).

1,6-Dihydroxynaphthacenequinone[25] (XX)——To a solution of H_3BO_3 (4 g) in H_2SO_4 (40 ml) was added VI (400 mg) at room temperature. The mixture was heated with stirring at 120—130° for 5 min, then poured onto 300 g of cracked ice and extracted with AcOEt (100 ml×3). The extract was washed once with H_2O, twice with satd. $NaHCO_3$ and again twice with H_2O, then dried over anhyd. Na_2SO_4 and evaporated. The resulting orange red residue was extracted with benzene by refluxing, and the benzene layer was filtered and evaporated to give 200 mg of orange brown solid. Sublimation at 200—210°/2 mmHg gave 160 mg of a sublimate, mp 245—249°, which was recrystallized twice from benzene to give 100 mg of XX as orange red needles, mp 270—271°. *Anal.* Calcd. for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47. Found: C, 74.14; H,

38) Although three peaks of extremely short retention time (within 2 min) appeared in the chromatogram, the molar ratio of them to the main peaks of a longer retention time (above 20 min) was negligibly small.

3.35. IR ν_{max}^{KBr} cm^{-1}: 1631 (C=O, shoulder), 1613, 1603, 1587, 1563 (arom.). UV $\lambda_{max}^{n\text{-hexane}}$ $m\mu$ (ε): 243 (58900), 262 (44900), 277 (21700), 305 (18200) (ref. 25; 243, 261—262, 279). $\lambda_{max}^{n\text{-hexane}}$ $m\mu$ (ε):437 (17300), 448 (22200), 464 (17200), 475 (15600) (ref. 25; 449—450, 467, 478).

1,11-Dihydroxynaphthacenequinone (XXI)——A cooled solution of XIX (50 mg) in dry CH_2Cl_2 (20 ml) was mixed, at −60°, with a cooled solution of BBr_3 (3.8 g) in dry CH_2Cl_2 (2 ml), and the mixture was allowed to warm up to room temperature and then stand for 2 hr, and poured into a mixture of craked ice and saturated $NaHCO_3$. The mixture was extracted with $CHCl_3$, and the extract was dried over anhyd. Na_2SO_4 and evaporated. The residual solid was sublimed at 210—220°/2 mmHg to give 36 mg of a sublimate, mp 278—280°. Recrystallization from toluene gave 30 mg of XX as orange needles, mp 281—283° (lit.,[9k] mp 276—278°). *Anal.* Calcd. for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47. Found: C, 74.56; H, 3.53. IR ν_{max}^{KBr} cm^{-1}: 1666 (C=O), 1617, 1595, 1567, 1542 (arom.) (lit.,[9k] ν_{max}^{KBr} cm^{-1}: 1670, 1615). UV $\lambda_{max}^{n\text{-hexane}}$ $m\mu$ (ε): 241.5 (37000), 255 (29000), 261 (31600), 275(16000), 302 (11000) (lit.,[9k] $\lambda_{max}^{cyclohexane}$ $m\mu$: 256, 300). $\lambda_{max}^{n\text{-hexane}}$ $m\mu$ (ε): 438 (10100), 447 (12000), 445 (11000), 463 (9900), 475 (10000), 485 (5200) (lit.,[9k] $\lambda_{max}^{cyclohexane}$ $m\mu$: 443).

1,6,11-Trihydroxynaphthacenequinone (XXII)——To a solution of H_3BO_3 (2 g) in H_2SO_4 (20 ml) was added XII (0.5 g) at room temperature. The mixture was heated with stirring at 135—138° for 10 min, during which time initial dark brown color of the mixture turned into dark green, then into cobalt blue and finally into purple. The mixture was poured onto 200 g of cracked ice, and the resulting deep red precipitates were collected and washed with H_2O, then with satd. $NaHCO_3$ and again with H_2O, and dried to give 350 mg of a dark red solid. Sublimation at 200—210°/2 mmHg gave 320 mg of a sublimate, mp 270—280°, which was recrystallized twice from toluene to give 200 mg of XXII as deep red needles, mp 296—298° (lit.,[29] above 300°). *Anal.* Calcd. for $C_{18}H_{10}O_5$: C, 70.59; H, 3.29. Found: C, 70.72; H, 3.25. IR ν_{max}^{KBr} cm^{-1}: 1630 (C=O, shoulder of arom.), 1585, 1563, 1542 (arom.).

1,11-Dimethoxynaphthacenequinone (XXIII)——A mixture of XIX (90 mg), anhyd. K_2CO_3 (10 g), MeI (10 g) and dry Me_2CO (30 ml) was refluxed for 27 hr, and treated in the usual manner to give 90 mg of XXIII as yellow needles (Me_2CO), mp 203—204°. *Anal.* Calcd. for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.56; H, 4.53. IR ν_{max}^{KBr} cm^{-1}: 1663 (C=O), 1615, 1585, 1564 (arom.). UV $\lambda_{max}^{95\%\ EtOH}$ $m\mu$ (ε): 139 (36500), 296 (13800). $\lambda_{max}^{95\%\ EtOH}$ $m\mu$ (ε): 405 (9100).

1,6-Dimethoxynaphthacenequinone (XXIV)——A mixture of XX (80 mg), anhyd. K_2CO_3 (10 g), MeI (5 ml), dry benzene (10 ml) and dry Me_2CO (20 ml) was refluxed for 38 hr, and treated in the usual manner. The product was purified through alumina-benzene system to give 74 mg of the crude quinone, mp 195—222°, Two recrystallization from benzene gave 65 mg of XXIV as yellow needles, mp 225—227°. *Anal.* Calcd. for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.65; H, 4.34. IR ν_{max}^{KBr} cm^{-1}: 1664 (C=O), 1614, 1586, 1561 (arom.). UV $\lambda_{max}^{95\%\ EtOH}$ $m\mu$ (ε): 240 (32600), 297 (14400). $\lambda_{max}^{95\%\ EtOH}$ $m\mu$ (ε): 405 (15600).