1959

Base-catalyzed reactions of 1-methyl-2-naphthol and its derivatives

Raymond David Youssefyeh
Iowa State University

Recommended Citation

Youssefyeh, Raymond David, "Base-catalyzed reactions of 1-methyl-2-naphthol and its derivatives " (1959). *Retrospective Theses and Dissertations*. 2191.
https://lib.dr.iastate.edu/rtd/2191

BASE-CATALYZED REACTIONS OF 1-METHYL-2-NAPHTHOL AND ITS DERIVATIVES

by

Raymond David Youssefyeh

A Dissertation submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
Of Science and Technology
Ames, Iowa
1959

TABLE OF CONTENTS

INTRODUCTION

The introduction of angular methyl groups in polycyclic ring systems has been of considerable interest in recent years because of the general interest in the synthesis of naturally occurring terpenes and steroids.

The purpose of the present research concerned, firstly, the study of C-alkylation of α-substituted β-naphthols by different alkyl halides, secondly, an inspection of the reactions of the resulting halomethylcyclohexadienones with various bases, and, thirdly, a novel synthesis of a hydrophenanthrone, which could be a useful intermediate in the total synthesis of the tricarbocyclic diterpenes.

HISTORICAL

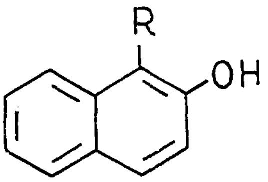
Alkylation of Phenols

There are three customary procedures for preparing alkyl phenyl ethers: the inter reaction of dialkyl sulfates with aqueous solutions of phenol salts, similar reactions of alkyl halides (1), and the reaction of phenols with halides in the presence of potassium carbonate in acetone or alcohol (2, 3). The yields of the ethers depend upon several factors. It has been shown that the yields of O-alkylation products increase, and hence C-alkylation substances decrease, as the halogen atoms of the reagents become less reactive (4), as the polarity of the solvent increases (5, 6), as the ionizability of the halides increases (2, 3), and as the phenols become less acidic (7, 8).

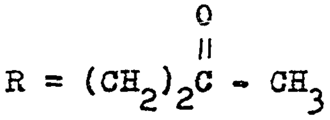
Recently, Kornblum and Lurie (8) have reported the alkylation of sodium and potassium salts of phenols with allyl and benzyl halides in a variety of solvents. It was demonstrated that quantitative yields of O-alkylation products were obtained in homogeneous reactions carried out in polar solvents, while C- and O-alkylation resulted when similar reactions were carried out in heterogeneous manner.

The base-catalyzed reaction of methyl vinyl ketone and

β-chloroethyl methyl ketone with 2-naphthol (I) was reported by Robinson (9, 10). Potassium ethoxide was used as the catalyst, and 1-(γ-ketobutyl-)2-naphthol(II) proved to be the product in the first case. Hardman (11), found that acrylonitrile could be condensed with 2-naphthol (I) in benzene in the presence of sodium hydroxide to give 1-(β-cyanoethyl-)2-naphthol(III).

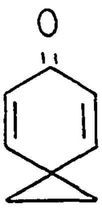


I R = H

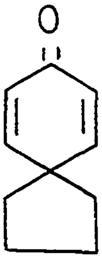
II

$R = (CH_2)_2\overset{\overset{O}{\parallel}}{C} - CH_3$

III $R = (CH_2)_2CN$

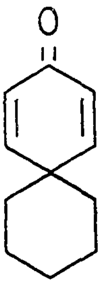
Winstein and Baird (12, 13) have reported the synthesis of 4,4-dimethylene- and 4,4-tetramethylene-2,5-cyclohexadienone, IV and V respectively, by means of intramolecular alkylation. In a similar manner, Dreiding (14) prepared 4,4-hexamethylene-2,5-cyclohexadienone (VI).



IV

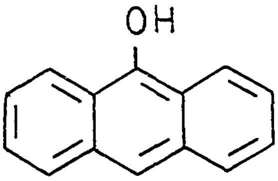


V

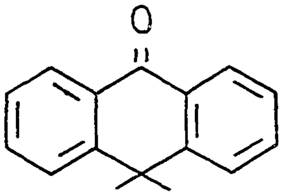


VI

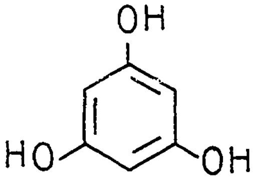
Certain polynuclear phenols have been reported to undergo alkylation at a nuclear position as well as at oxygen. For example, the sodium salt of anthranol (VII) has been reported (15) to react with methyl iodide in ethanol to yield 9,9-dimethyl anthranone (VIII). Polyhydric phenols, such as phloroglucinol (IX), have been found to undergo alkylation, the position of which was dependent on the order of mixing of the reagents (16, 17, 18).



VII

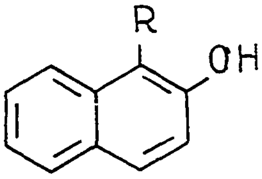


VIII



IX

Zagorevsky has reported (19, 20) that a solution of sodium -naphthoxide reacts with benzyl bromide to give the C-alkylated product X in 22% yield. Similarly, when p-nitrobenzyl bromide reacted with a solution of lithium 2-naphthoxide, XI was formed in 14% yield.

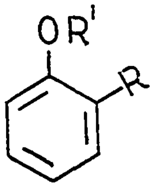


X R = $C_6 H_5$-CH_2

XI R = P-NO_2-C_6H_5-CH_2

Claissen (5, 6) discovered that the sodium salts of phenols, in non-polar solvents, such as benzene or toluene, react with very reactive alkyl halides such as allyl or benzyl halides to give C-alkylation products preponderantly.

Since the Claissen rearrangement gives nuclear substituted phenols, it was suggested that perhaps the substituted phenols prepared in this manner resulted from the rearrangement of ether intermediates. However, Claissen (21) observed that phenol XII resulted when the reaction between phenol and 1-bromo-2-butene was carried out in a solution of potassium carbonate and acetone, when followed by the rearrangement of the intermediate ether XIII, while phenol XIV was obtained when sodium phenoxide in benzene was treated with 1-bromo-2-butene. These reaction products negated intermediacy of ethers in the second reaction.

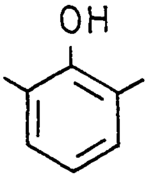


XII $R' = H$,
$R = CH_3\text{-}CH\text{-}CH = CH_2$

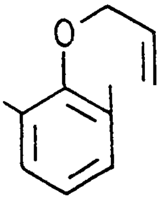
XIII $R' = CH_2\text{-}CH = CH\text{-}CH_3$
$R = H$

XIV $R' = H$
$R = CH_2\text{-}CH = CH\text{-}CH_3$

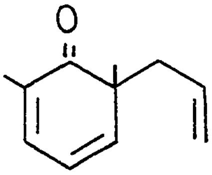
The demonstration by Claissen (5, 6) that sodium salts of phenols undergo alkylation in an ortho position when treated with allyl or benzyl halides has been extended recently by Curtin (22, 23, 24, 25) to substituted phenols. For example, 2,6-dimethyl phenol (XV) and allyl bromide yielded ether XVI and ketone XVII.



XV

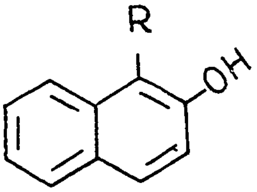


XVI



XVII

The preparation of 1-benzyl-2-naphthol (XVIII) from the sodium salt of 2-naphthol in toluene has been reported by Claissen (6) in 60-70% yield. Dodson and Webb (26) have synthesized 1-allyl-2-naphthol (XIX) under the same condition in 40% yield, using sodium salt of 2-naphthol (1) and allyl bromide. The same authors (27) prepared phenol XX by treating the sodium salt of 2-naphthol (1) with 1,3-dichloro-2-butene.

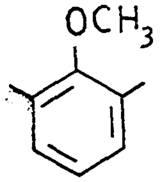


XVIII $R = C_6H_5 - CH_2$

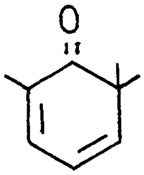
XIX $R = CH_2 - CH = CH_2$

XX $R = CH_2 - CH = \underset{\substack{| \\ Cl}}{C} - CH_3$

It has been reported recently (28, 29, 30) that the lithium salts of substituted phenols react with methyl iodide in toluene to form cyclohexadienones. For example, 2,6-dimethyl phenol (XV) and methyl iodide produced not only the expected 2,6-dimethylanisole (XXI), but also 2,6,6-trimethyl-2,4-cyclohexadienone (XXII) in 22% yield.



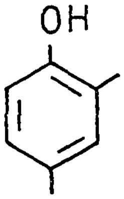
XXI



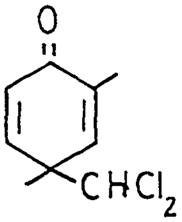
XXII

The "Abnormal" Reimer-Tiemann Reaction Products

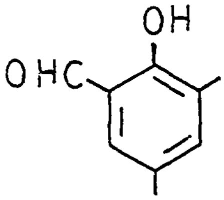
The Reimer-Tiemann reaction (31) has been a standard method of synthesis of phenolic aldehydes. Ortho and para alkyl substituted phenols yield both phenolic aldehydes and dichloro-methylcyclohexadienones on treatment with chloroform and aqueous base. For example, von Auwers (32, 33, 34) showed that 2,4-dimethyl phenol (XXIII) gave some "abnormal" product XXIV along with the expected aldehyde XXV. The ratio of the "normal" to "abnormal" product in similar reactions varied with the structure of the phenol.



XXIII

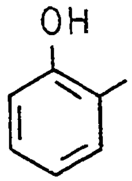


XXIV

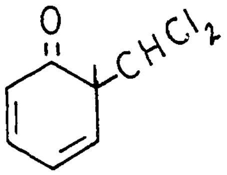


XXV

At first, the experimental evidence indicated that only phenols with para substituents gave "abnormal" products. However, it was found later (35) that ortho substituted phenols would yield them also. In the case of ortho cresol (XXVI) an 8% yield of 2-methyl-2-dichloromethyl-1-keto-1,2-dihydrobenzene (XXVII) was obtained.



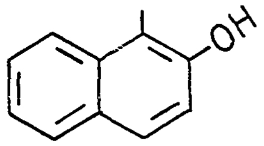
XXVI



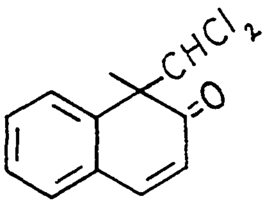
XXVII

Von Auwers (36) also discovered that bromoform reacts with the substituted phenols in the same manner as chloroform to give dibromomethylcyclohexadienones, but iodoform gave only small yields of "abnormal" products.

Dodson and Webb (27) have reported the synthesis of 1-dichloromethyl-1-methyl-2(IH)-naphthalenone (XXIX) from 1-methyl-2-naphthol (XXVIII) and chloroform.

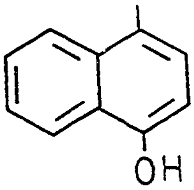


XXVIII

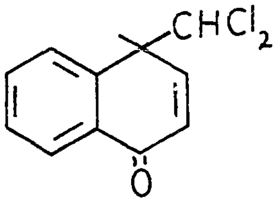


XXIX

The dichloromethylnaphthalenone XXXI has been isolated by Fuson and Miller (37) as a product of the Reimer-Tiemann reaction on 4-methyl-1-naphthol (XXX).

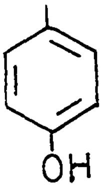


XXX

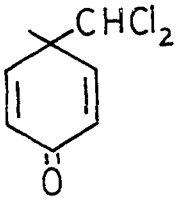


XXXI

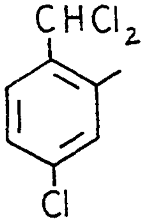
Von Auwers carried out a series of reactions on his "abnormal" products. For example, their reduction by zinc and acetic acid gave the starting phenols and dichloromethane (34). The reaction of the cyclohexadienone XXXIII, obtained from para cresol XXXII, with phosphorous pentachloride led to XXXIV (38, 39), which on further reaction gave the known 2-methyl-4-chlorobenzoic acid XXXV.



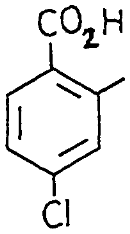
XXXII



XXXIII

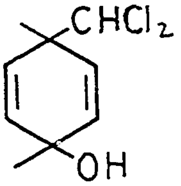


XXXIV

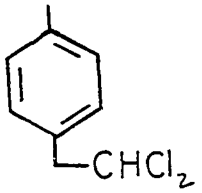


XXXV

The methylation of cyclohexadienone XXXIII with methyl magnesium iodide has been reported (38) to yield the hydroxycyclohexadiene XXXVI, which was rearranged to 1-(2',2'-dichloroethyl-)4-methylbenzene (XXXVII).

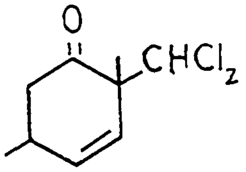


XXXVI

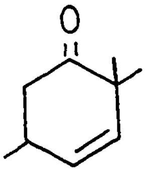


XXXVII

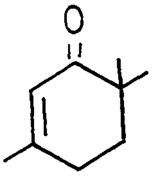
Von Auwers and Hessenland (40) utilized the cyclohexadienone XXVII for conversion to several interesting monocylic compounds. On its treatment with methyl magnesium iodide followed by acid treatment, substance XXVII led to the ketone XXXVIII, which on reduction with zinc in acetic acid gave β , γ -pulenenone (XXXIX). The acid treatment of XXXIX yielded α , β -pulenenone (XL) which on sodium-alcohol reduction led to pulenol (XLI). The chromic acid oxidation of pulenol gave pulenone (XLII).



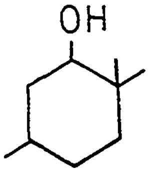
XXXVIII



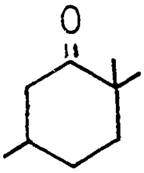
XXXIX



XL

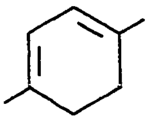


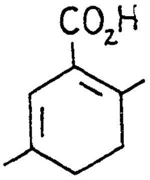
XLI



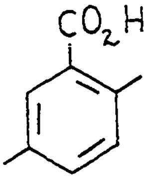
XLII

Hydrolysis of the XXXVIII with alcoholic potassium hydroxide led to a mixture of neutral and acidic products, which were shown to be 1,4-dimethyl-1,3-cyclohexadiene (XLIII), by oxidation to acetonyl acetone, 2,5-dimethyl-3,4-dihydrobenzoic acid (XLIV), which could be converted to 2,5-dimethylbenzoic acid (XLV); and 2,5-dimethyl-6-chlorocyclohexene-1-carboxylic acid (XLVI), which was converted to both XLIV and XLV (40).

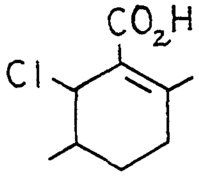

XLIII



XLIV

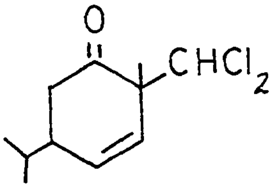


XLV

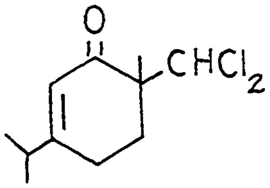


XLVI

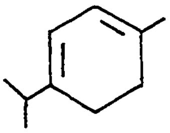
In a similar manner, α -terpinene (XLIX) was synthesized by von Auwers and Heyden (41) by the following reactions. The ketone XXVII was treated with isopropyl magnesium iodide to yield XLVII, which upon acid treatment led to the cyclohexenone XLVIII. Base treatment of this product gave the known α -terpinene (XLIX).



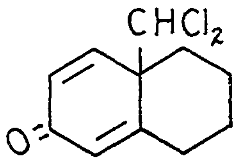
XLVII



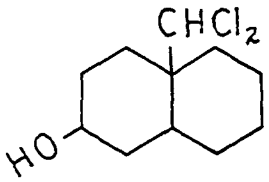
XLVIII


XLIX

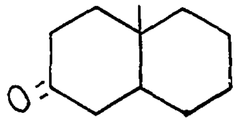
Woodward (42) made use of the Reimer-Tiemann reaction to synthesize 10-methyl-2-decalone (LII). This was accomplished by the reduction of the dichloromethyl ketone L to the dichloromethyl alcohol LI, followed by hydrogenolysis of the chlorine atoms and chromic acid oxidation of the alcohol to the methyldecalone LII.



L

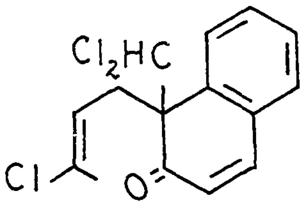


LI

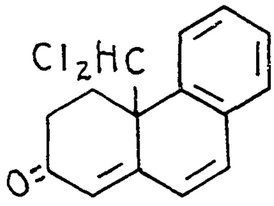


LII

The introduction of a potential angular methyl group in the form of a dichloromethyl group by means of the Reimer-Tiemann reaction was reported by Dodson and Webb (26), who attempted to synthesize 4,α -(dichloromethyl-)4,4a-dihydro-2 (3H)-phenanthrone (LIV). The ketone LIII was obtained from the naphthol XX, but the hydrolysis and cyclization of LIII to LIV was not successful.

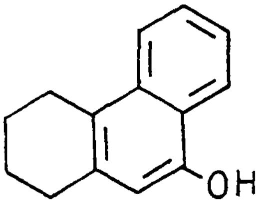


LIII

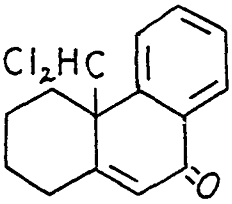


LIV

For similar reasons, Gibson (43) synthesized the dichloromethyl ketone LVI from the phenol LV.



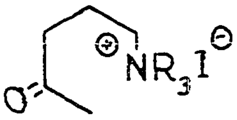
LV



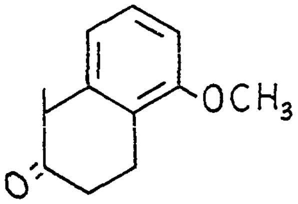
LVI

Synthesis of Hydrophenanthrones with Angular Methyl Groups

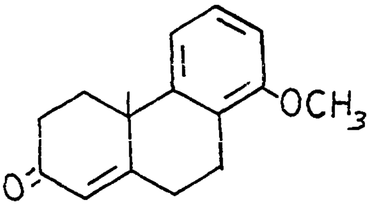
Robinson and Cornforth (44) in 1946 synthesized the methoxyphenanthrone LIX by adding 4-diethylamino-2-butanone methiodide (LVII) to 1-methyl-5-methoxy-2-tetralone (LVIII).



LVII

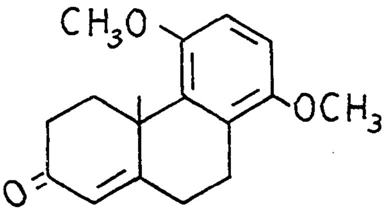


LVIII

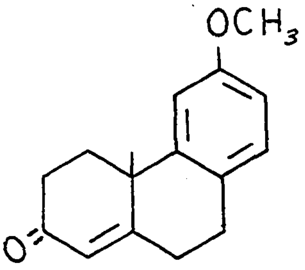


LIX

In a similar manner, Grob and Junt (45) prepared 4a-methyl-5,8-dimethoxy-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (KX), and Stork (46, 47) synthesized the methoxyketone LXI.

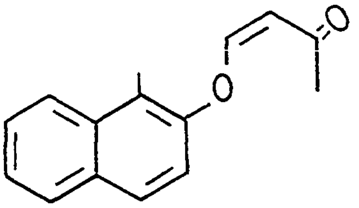


LX

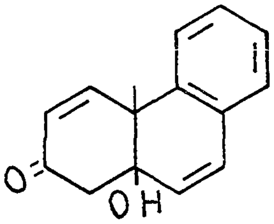


LXI

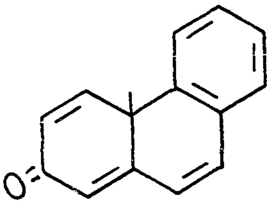
Wenkert and Stevens (48, 49) have reported the synthesis of a tricarbocyclic ketone by two different methods. Firstly, by treating methyl ethynyl ketone with 1-methyl-2-naphthol in the presence of potassium t-butoxide catalyst. Three products were obtained, LXII, LXIII and LXIV. Hydrogenation of the unsaturated ketol LXIII yielded its tetrahydroderivative LXV, which on dehydration, gave the unsaturated ketone LXVI. Secondly, the Michael addition of ethyl acetoacetate to the naphthalenone XXXI led to LXVII. The acid catalyzed hydrolysis of LXVII followed by reduction gave the saturated ketone LXVIII, which upon treatment with sodium triphenylmethyl yielded the hydrophenanthrone LXIX.



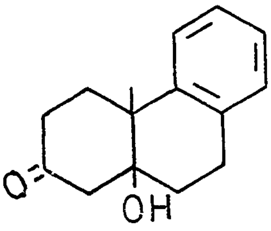
LXII



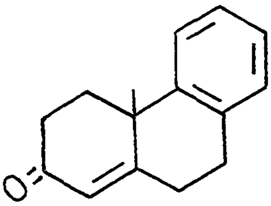
LXIII



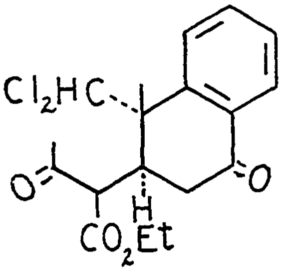
LXIV



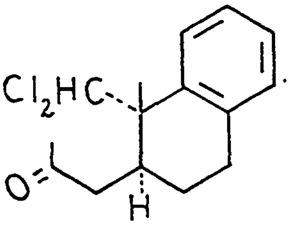
LXV



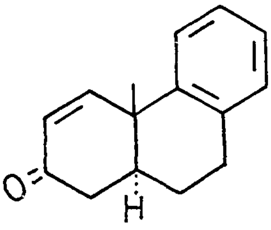
LXVI



LXVII



LXVIII



LXIX

DISCUSSION

One of the purposes of this research was the synthesis of a hydrophenanthrone from β-naphthol. To accomplish this goal, it became of importance to study alkylation reactions with simple reagents, and then to attempt the more complicated project.

It was implied by Claissen (6) and has been accepted generally that C-alkylation of unsubstituted monohydroxylic phenol salts was peculiar to benzylic and allylic halides. However, it has been reported recently (28, 29, 30) that the salts of substituted phenols also react with methyl iodide without solvent, or in toluene, to form the corresponding cyclohexadienones.

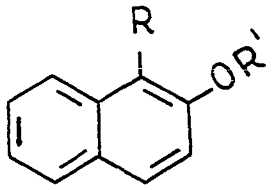
It has been shown that β-naphthoxide ion is a good nucleophile. For example, β-naphthoxide ion can be C-alkylated in solution whereas phenoxide ion can not (19).

It therefore seemed possible that the sodium salt of β-naphthol suspended in toluene, should also undergo C-alkylation in good yield. Such proved to be the case. The sodium salt of β-naphthol, suspended in toluene, was refluxed with methyl iodide for 12 hours. After work-up neutral and acidic fractions were obtained. The neutral fraction was chromatographed over alumina. Elution with petroleum ether led to a 25% yield of a mixture of ethers, probably methyl β-naphthyl ether (LXX) and methyl 1-methyl-2-naphthyl ether (LXXI). The ultraviolet spectrum of this mixture was similar to that of the starting material, having ultraviolet maxima at 230 mμ (ϵ 91,400) and 272 mμ (ϵ 7,800) and infrared absorption bands at 6.20 μ and 6.30μ . The reason for assuming "a mixture" was the fact that repeated crystallization of this material failed to narrow its wide melting point range. Elution with 20:1 petroleum ether-benzene gave an 8% yield of 1,1-dimethyl-2(1H)naphthalenone (LXXII), identified by its hydrogenation to the known 1,1-dimethyl-2-tetralone (LXXIII) (50).

Some difficulties were experienced in obtaining 1-methyl-2-naphthol (XXVIII) in a pure state, since the unreacted 2-naphthol was hard to remove. To obtain the pure product, the acidic fraction was chromatographed over alumina and the first portion of the chromatographed substances was crystallized from hexane, m.p. 108-110.

At the time this research began, 1-methyl-2-naphthol (XXVIII) was prepared by another procedure. The method of Adams and Levine (51) was used to prepare 2-hydroxy-1-naphthaldehyde (LXXIV). The reduction of this aldehyde by zinc in acetic acid led to the desired compound. The same compound has been obtained by Fries and Hubner (52) by reduction of bis-(2-hydroxy-1-naphthyl-)methylene (LXXV).

However, at the present time the direct methylation of the sodium salt of 2-naphthol is by far the best method for the preparation of 1-methyl-2-naphthol (XXVIII), since it is only a one-step reaction and easier to execute.



LXX $R' = CH_3$, $R = H$

LXXI $R' = R = CH_3$

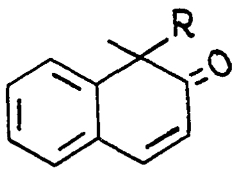
LXXXV $R' = CO(CH_2)_2CH_3$, $R = H$

LXXXVII $R' =$ n-Bu, $R = CH_3$

LXXXVIII $R' = CH_3$, $R =$ n-Bu

XCII $R' = CH_3$, $R=(CH_2)_2CH(OH)CH_3$

CVII $R' = CH_3$, $R = (CH_2)_2\ CO\ CH_3$



LXXII $R = CH_3$

LXXVIII $R = CH_2I$

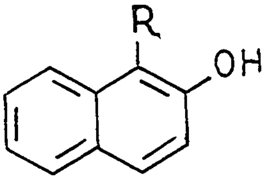
LXXX $R = CH_2Cl$

LXXXVI $R =$ n-Bu

XCI $R = (CH_2)_2CH(OH)CH_3$

XCV $R = (CH_2)_2CO\ CH_3$

CII $R = (CH_2)_2CH(OAc)CH_3$



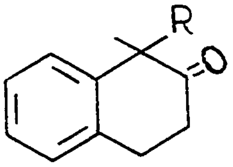
LXXIV $R = CHO$

LXXXII $R = (CH_2)_2CO\ CH_3$

LXXXIII $R = n\text{-}Bu$

LXXXIV $R = CO(CH_2)_2CH_3$

XC $R = (CH_2)_2CH(OH)CH_3$



LXXIII $R = CH_3$

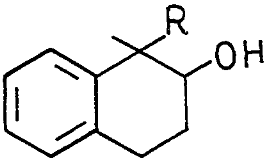
LXXVII $R = CH\ Cl_2$

LXXXI $R = CH_2Cl$

XCIV $R = (CH_2)_2CO\ CH_3$

C $R = (CH_2)_2CH(OH)CH_3$

CIII $R = (CH_2)_2CH(OAc)CH_3$



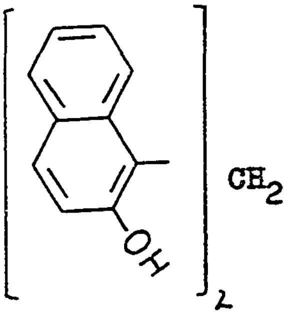
LXXVI $R = CH\ Cl_2$

XCVIII $R = (CH_2)_2Co\ CH_3$

CIV $R = (CH_2)_2CH(OAc)CH_3$

CVI $R = (CH_2)_2CH(OH)CH_3$

LXXV



Since 1-methyl-2-naphthol (XXVIII) has shown to be a strong nucleophile, as exhibited in its ready formation of a naphthalenone in the "abnormal" Reimer-Tiemann reaction (27), the Michael reaction (48, 49) and the halogenation reaction (53), it was thought advisable to choose this compound for further alkylation reaction studies.

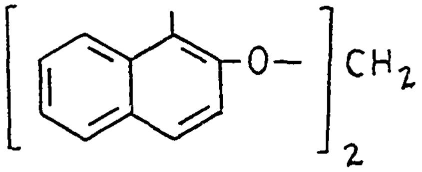
When the sodium salt of XXVIII wad refluxed in methyl iodide for four hours, there was obtained an 88% yield of the 1,1-dimethyl-2(1H)-naphthalenone (LXXII), which was identified by its catalytic hydrogenation to the known ketone LXXIII (50), and a 4% yield of the known methyl 1-methyl-2-naphthyl ether (LXXI) (52).

In a similar manner, chloroform was added to the sodium salt of XXVIII and the resulting mixture was refluxed for four hours, which led to a 60% yield of the known dichloromethylnaphthalenone XXIX, m.p. 64-65° (27). Hydrogenation of the product gave a 27% yield of the alcohol LXXVI, which was identified by elemental analysis and the presence of an alcoholic O-H band at 2.8μ, and a 65% yield of the known 1-methyl-1-dichloromethyl-2-tetralone (LXXVII) (26, 27).

Refluxing of a mixture of the sodium salt of XXVIII and methylene iodide for four hours, gave a 29% yield of 1-methyl-1-iodimethyl-2(1H)naphthalenone (LXXVIII) and 3% of bis(1-methyl-2-naphthyl)methylene ether (LXXIX), m.p. 146-147°. Attempts to prepare a carbonyl derivative of the compound

LXXVIII was unsuccessful. However, the ultraviolet spectrum of this compound was typical of a naphthalenone chromophore, exhibiting ultraviolet maxima at 232 mμ (ϵ 30,000) and 310 mμ (ϵ 7,450). The infrared absorption bands at 6.05 and 6.21 were consistent with the presence of a conjugated carbonyl group in the substance.

Assignment of the structure of the ether LXXIX was based on its ultraviolet spectrum, which exhibited maxima at 222 mμ (ϵ 35,300), 234 mμ (ϵ 54,000) and 280 mμ (ϵ 4,750), the presence of unsaturation bands at 6.20 μ and 6.30 μ in its infrared spectrum, and its ready acid hydrolysis to 1-methyl-2-naphthol.



LXXIX

Since no reaction occurred when the sodium salt of XXVIII was refluxed with methlene chloride for four hours, this reaction had to be carried out in a sealed tube. The mixture in the sealed tube was heated at 100° for eight hours. After work-up a 32% yield of 1-methyl-1-chloromethyl-2(1H)naphthalenone (LXXX) and a 10% of the ether LXXIX, m.p. 146-147°, were obtained.

While the liquid LXXX was not exposed to elemental analysis, its ultraviolet spectrum was a typical of a naphthalenone chromophore, and its infrared spectrum indicated the presence of a conjugated carbonyl group. Its red 2,4-dinitrophenylhydrazone was prepared, m.p. 184-185°. The catalytic hydrogenation of LXXX led to LXXXI, which exhibited an infrared absorption band at 5.82 μ due to the saturated carbonyl group.

It is interesting to note that the results obtained from these reactions had two important features. The high carbon-oxygen product ratio followed expectations. Neglecting the possible solubility difference of the salt of 1-methyl-2-naphthol in dichloromethane and chloroform, the yields of C-alkylated products would be expected to be highest in the first solvent, if both reactions had proceeded by similar mechanism. However, in spite of the higher temperature and pressure applied in the latter case, the opposite results were observed. This fact suggests, in concert with interpretations of previously reported reactions of various nucleophiles with halomethanes (54, 55), that the above substitution processes proceeded by concerted displacement of chloride in case of dichloromethane, but not in case of chloroform. In the latter solvent dichlorocarbene may be a reaction intermediate (55).

The addition of methyl vinyl ketone to 2-naphthol was carried out by a slight modification of the Robinson procedure (56). The Wolff-Kishner reduction of the product, 1-(γ-Keto-butyl-)2-naphthol (LXXXII), resulted in 1-(n-butyl-)2-naphthol (LXXXIII), m.p. 79-80°. This same compound had been synthesized previously (57) by Clemmensen reduction of 1-(α-ketobutyl-)2-naphthol (LXXXIV), which in turn has been obtained from the Fries rearrangement of 2-naphthyl butyrate (LXXXV).

N-butylation of the dry sodium salt of XXVIII gave a 2:1 ratio of the products LXXXVI and LXXXVII, respectively. Both of these compounds were identified from their ultraviolet and infrared spectra, which exhibited naphthalenone and β-naphthol chromophores, respectively. The elemental analysis of the 2,4-dinitrophenylhydrazone derivative of the naphthalenone LXXXVI was in accord with a $C_{21}H_{22}O_4N_4$ formula, m.p. 125-126°.

Under similar conditions the methylation of 1-(n-butyl-) 2-naphthoxide ion in methyl iodide yielded a 2:1 ratio of C/O alkylated products, LXXXVI and the known LXXXVIII (57), respectively. The infrared and ultraviolet spectra of this naphthalenone and the ketone LXXXVI were identical. Also the melting point of a mixture of the 2,4-dinitrophenyl hydrazone of this material and that of the ketone LXXXVI (m.p. 125-126°) was undepressed.

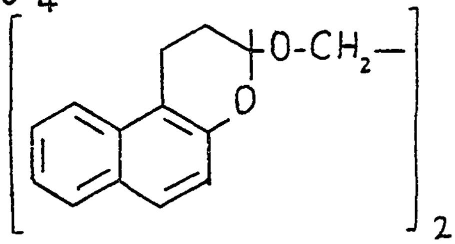
Neglecting the solubility difference of the sodium salt of 1.0 g. of 1-methyl-2-naphthol (XXVIII) and 1-n-butyl-2-naphthol (LXXXIII) in 30 ml. of methyl iodide, it would be expected that the amount of O-alkylated products obtained in each case be identical. However, a more appreciable quantity of the O-alkylated product was obtained in the second case (30% yield) than in the first case (4% yield). This may illustrate the importance of steric factors in the alkylation of phenol salts. The same conclusion can be drawn in the case of the n-butylation of 1-methyl 2-naphthoxide ion which again afforded a high yield (29%) of the O-alkylated product. These results were similar to those observed by Curtin (28, 29, 30) and Kornblum (8) in the alkylation of the substituted phenoxide salts.

Since it had now been shown that alkylation of 1-substituted 2-naphthols would give a good yield of C-alkylated products, it was thought of interest to apply this one-step method of introduction of a methyl group to the synthesis of the hydrophenanthrone LXVI. This was especially necessary, since the overall yield in a previous synthesis had been low.

Since the reactions with the model compounds had proceeded as expected, the methylation of 1-(γ -ketobutyl-)2-naphthol (LXXXII) was carried out under the same conditions. However, it led to a complicated mixture of products, which will be discussed subsequently. Therefore, it was decided to mask the side-chain carbonyl group.

Ketalation of 1-(γ -ketobutyl-)2-naphthol (LXXXII) with ethylene glycol yielded a mixture of products from which compound LXXXIX was isolated, m.p. 200-201°.

The evidence for assignment of structure LXXXIX rests on the fact that its ultraviolet spectrum indicated maxima at 232 mμ (ε 69,200) and 280 mμ (ε 5,030) and its infrared spectrum showed absorption band at 6.20 μ and 6.30 μ due to carbon-carbon unsaturation. Elemental analyses were in accord with a $C_{30}H_{30}O_4$ formulation.

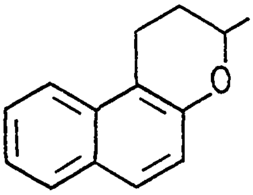


LXXXIX

Failure to find the ketalation as a good masking procedure for the side chain carbonyl group resulted in the preparation of the known (58) 1-(γ -hydroxybutyl-)2-naphthol (XC) and investigation of its reaction with methyl iodide. As a consequence compound XC was prepared by lithium aluminum hydride reduction of the ketone LXXXII.

Treatment of the sodium salt of XC with methyl iodide led to a 55% yield of 1-methyl-1-(γ -hydroxybutyl-)2(1H) naphthalenone (XCI) and 24% yield of methyl 1-(γ -hydroxybutyl-) naphthyl ether (XCII). The presence of an alcoholic O H band at 2.8 μ and 2.9 μ and a conjugated carbonyl band at 6.07 μ in the infrared spectrum, and the appearance of maxima in the former's ultraviolet spectrum at 232 mμ (ε 62,000) and 300 mμ (ε 8,150) revealed its structure as that of a C-alkylation product. Elemental analysis of its 3,5-dinitrobenzoate was in accord with a $C_{22}H_{20}O_7N_2$ formulation.

The identity of the hydroxyether XCII was assured from its characteristic ultraviolet spectrum with maxima at 232 mμ (ε 109,000) and 282 mμ (ε 11,100) and its infrared spectrum with absorption bands at 2.84 μ due to an O H group and at 6.20 μ and 6.32 μ corresponding to carbon-carbon unsaturation. Further proof of the structure of this substance was gained by its ready conversion on acid treatment to a mixture of the starting naphthol XC and the known ether XCIII (58).



XCIII

The hydroxyketone XCI was the crucial intermediate, which by a combination of oxidation and reduction steps was expected to lead to the diketone XCIV. Both sequences of these steps were studied. In view of the non-stereospecific introduction of the potential angular methyl group, a reaction which created a second asymetric center, XCI was a liquid mixture of two racemates. Since both were expected to be convertible to the desired diketone XCIV, no attempt of separation was made.

Chromic acid oxidation of XCI in acetic acid solution yielded liquid 1-methyl-1-(γ-ketobutyl-)2(1H)naphthalenone (XCV). The absence of bands in the 2.8-3μ region, and the appearance of bands at 5.81μ, 6.03μ and 6.18μ in its infrared spectrum were the basis for the assignment of this structure. Its orange mono-2,4-dinitrophenylhydrazone, m.p. 155-156°, exhibited no infrared peak for a saturated carbonyl group, but did reveal a conjugated carbonyl band at 6.03μ, C=N band at 6.18μ and C=C band at 6.25μ. Its elemental analysis was in accord with a $C_{21}H_{20}O_5N_4$ formula.

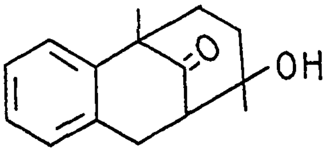
Hydrogenation of XCV over palladium-charcoal led to a mixture of products. Chromatography of this mixture led to three substances, an ether, a ketonic compound and a ketolic material.

The first substance, m.p. 50-56°, was not identified. There was no indication of absorption bands in the 2.8-3μ and 5-6μ region, while the broad band at 9μ suggested an ether linkage. Thus, its infrared spectrum its tetralin chromaphore as revealed by its ultraviolet spectrum, suggested it to be a product of over-reduction.

A similar tetralin chromophore and a 5.83μ infrared band appeared to make the second compound the desired

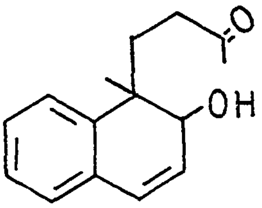
1-methyl-1-(γ -ketobutyl-)2-tetralone (XCIV). Its orange bis-2,4-dinitrophenylhydrazone revealed an elemental analysis in accord with $C_{27}H_{26}O_8N_8$, m.p. 181-182°.

The structure of the ketolic compound obtained in 40% yield was established to be the aldol product of the diketone XCIV, since the same compound was obtained by a mild base treatment of the diketone XCIV, m.p. 147-149°. The infrared spectrum of this compound also exhibited OH bands at 2.79 μ and 2.91 μ and carbonyl band at 5.83 μ . Its non-identity with a previously described ketol LXV (48) indicated that it was either the C-5 epimer of LXV or one of the two epimers of XCVI.



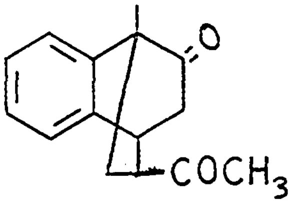
XCVI

The fact that the XCIV could be shown to be unreactive toward catalytic hydrogenation constituted the first indication of the susceptibility of the keto group in the naphthalenones to hydrogenation. Thus, two possible pathways of hydrogenation existed: XC to XCVII to XCVIII and XC to XCIV.



XCVII

While acquired by different means, the diketone XCV could be considered as being the product of the Michael reaction between 1-methyl-2-naphthol (XXVIII) and methyl vinyl ketone, a reaction which has been studied in detail by Wenkert and Stevens (48). Whereas two diketones of structure XCIX had been the actual reaction products, compound XCV had been considered a vital reaction intermediate. As a consequence, the behavior of XCV toward alkaline reagents became of interest.



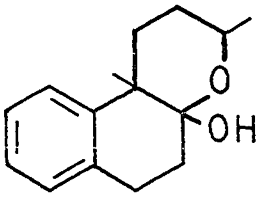
XCIX

Treatment of XCV with sodium methoxide and ethoxide led exclusively to the *retro*-Michael product XXVIII. However, the reaction of the same compound with potassium *tert*-butoxide gave both the *retro*-Michael product XXVIII and the known internal Michael product XCIX (48). Compound XCIX had identical infrared and ultraviolet spectra, melting point and mixed melting point as an authentic sample.

The results of these base treatments indicated that the previously observed low yield of XCIX may be a consequence of competitive high rates of the <u>retro</u>-Michael process of XCV and the formation of methyl vinyl ketone polymer.

When the hydroxyketone XCI, dissolved in ethanol, was exposed to catalytic hydrogenation over palladium-charcoal, there was obtained a mixture of products, containing a small amount of the desired ketone C. The oily substance, left after filtration of the catalyst and evaporation of the solvent, exhibited an infrared spectrum of high intensity C-H bands and a low intensity C=O band. Chromic acid oxidation of the mixture led to a liquid from which the desired ketone XCIV was isolated in only 65% yield and was shown to be identical with XCIV described above.

The unusual low intensity of the carbonyl absorption band as compared to other bands in the infrared spectrum of the reduction mixture of the hydroxyketone XCI was suspected to be due not only to over-reduction but perhaps also to the presence of the expected ketone C partly in hemiketal form CI. In order to differentiate between these two possibilities, an attempt was made to prepare 1-methyl-1-(γ-acetoxybutyl-)2(1H) naphthalenone (CII) to inspect its behavior toward catalytic hydrogenation, and to examine the carbonyl band in the infrared spectrum of the hydrolyzed product.

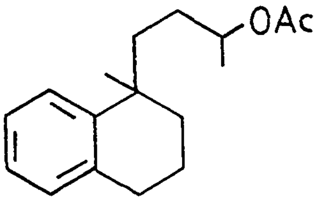


CI

Acetylation of the liquid mixture of epimeric ketols XCI yielded CII which exhibited infrared absorption bands at 5.80 μ , 6.05 μ and 6.22 μ .

Catalytic hydrogenation of CII in ethanol over palladium charcoal gave a mixture of products, which could be separated by chromatography into three distinctly different fractions. Examination of their ultraviolet spectra showed all to have tetralin chromophores. Inspection of the infrared spectrum of the first compound revealed two carbonyl bands at 5.78 μ (ester) and 5.82 μ (ketone), characteristic of the structure of the desired ketoacetate CIII. The second compound appeared to be the hydroxyacetate CIV with hydroxyl absorption at 2.8 μ and a carbonyl band at 5.77 μ . The third compound seemed to be CV whose spectrum showed an absorption band at 5.78 μ .

The problem of over-hydrogenation led to two difficulties: firstly, low yields of the desired products were obtained,



CV

secondly, separation of the mixture of products was very difficult and time-consuming.

In order to overcome the erratic nature of the hydrogenation reaction, another procedure had yet to be found to lead to an efficient conversion of hydroxyketone XCI to diketone XCIV. The most efficient method for this transformation was found to be a chemical reduction.

The reduction of the hydroxyketone XCI by lithium in liquid ammonia converted the ketone to a mixture of diols XVI, which was identified by the absence of a carbonyl band and the presence of an intense and wide hydroxy band at 2.8-3μ in its infrared spectrum. The chromic acid oxidation of the diols CVI led to an 82% overall yield of the known diketone XCIV.

At this point, interpretation of the results of the methylation of the sodium salt of 1-(γ-ketobutyl-)2-naphthol (LXXXII) became feasible. While the stoichiometry of the reaction could not be ascertained because of the intimate mixture of the reaction products, the structure of most of the latter was unravelled.

Chromatography of the mixture over alumina and elution with petroleum ether gave a solid, which after crystallization from hexane was shown to be methyl 1-methyl-2-naphthyl ether LXXI, m.p. 37-38°. Elution with 10:1 petroleum ether-benzene gave methyl 1-(γ-ketobutyl-)2-naphthyl ether CVII, m.p. 54°. This same compound was prepared from the reaction of the sodium salt of 1-(γ-ketobutyl)2-naphthol (LXXXII) in methanol and methyl iodide, m.p. 54°, and showed identical infrared and ultraviolet spectra with those of the keto-ether CVII. Further elution with the same mixture of solvents led to the previously described diketone XCV. Finally, elution with benzene gave a mixture of phenolic compounds, which were separated by crystallization from petroleum ether-carbon tetrachloride followed by sublimation of the residue remaining upon removal of the solvent and were shown to be 1-methyl-2-naphthol (XXVIII) and starting material LXXXII.

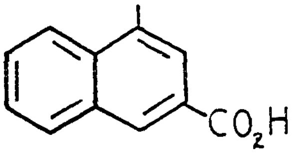
It is interesting to note that beside the expected C- and O-alkylated products and the starting material, 1-methyl-2-naphthol (XXVIII) and its methyl ether LXXI were also identified as further products. It would appear that the retro-Michael process on XCV, discussed above, is even prevalent during formation of the diketone by methylation, and probably is induced by various naphthoxides acting as bases.

Finally, the tricyclic ketone LXVI was obtained by refluxing the diketone XCIV with a methanolic solution of sodium methoxide for four hours. A 70% yield of the product; m.p. 89-90°, was realized. Mixed m.p. with an authentic sample (m.p. 89-90°) was 89-90. Its infrared and ultraviolet spectra were identical with those of an authentic sample.

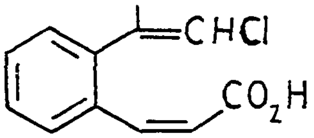
Along with the studies discussed thus far, the chemistry of the naphthalenone XXIX was investigated. It had been noted briefly by Dodson and Webb (27) and Wenkert and Stevens (49) that this compound was sensitive to base treatment. As a consequence it became of interest to study its chemical behavior and that of its dihydro product LXXVII in various bases. Some time after the initiation of these studies a private communication by Dodson disclosed the results of a similar but less involved investigation in his laboratory (26). Dodson and Webb found that potassium hydroxide treatment of ketone XXIX led to 1-methyl-2-naphthol, 1-methyl-3-naphthoic acid (CVIII), m.p. 203-205, which had been previously prepared by Darzens (59) and <u>o</u>-(α-methyl-β-chlorovinyl-) <u>cis</u>-cinnamic acid (CIX), m.p. 113-114. The acid CIX was identified by its oxidation to phthalic acid (CX), its reduction to <u>o</u>-(α-methyl-β-chlorovinyl-) hydrocinnamic acid CXI, and the latter's oxidation to <u>o</u>-carboxyhydrocinnamic acid CXII.

Dodson and Webb (26) also discovered that the reaction of the ketone LXXVII with sodium hydroxide solution led to

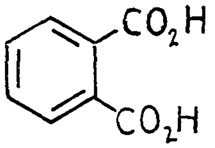
1-methyl-3,4-dihydro-3-naphthoic acid CXIII, m.p. 94.5-95°. Confirmation of its structure was obtained by its sulfur dehydrogenation to the known 1-methyl-3-naphthoic acid (CVIII).



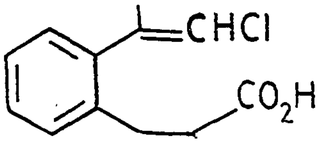
CVIII



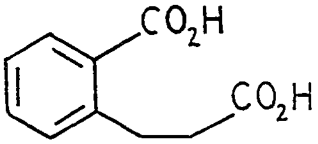
CIX



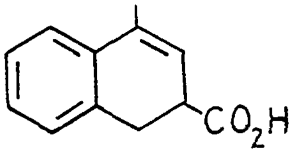
CX



CXI



CXII

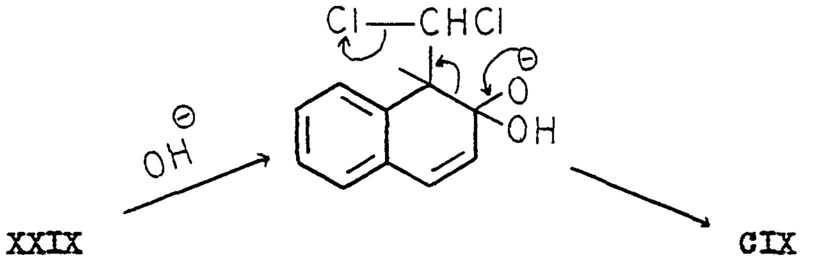


CXIII

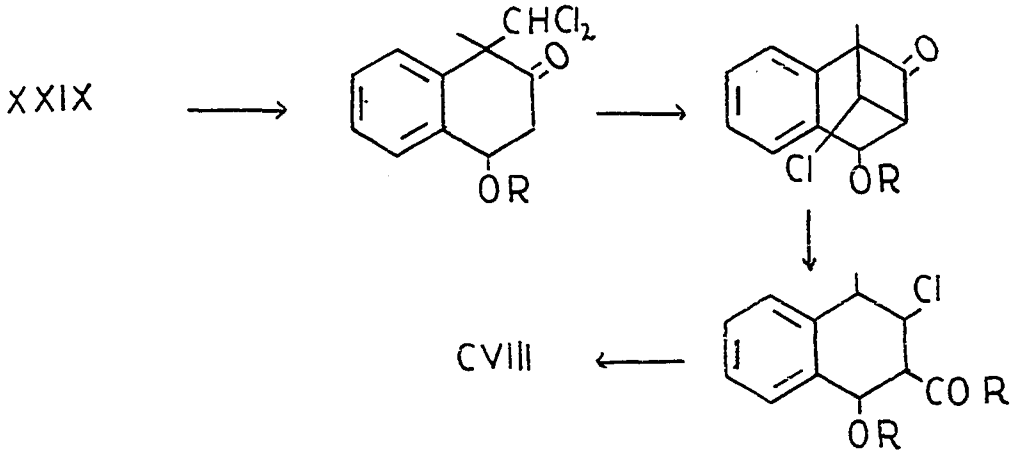
Refluxing of the ketone XXIX with 20% potassium hydroxide for 24 hours, led to neutral, phenolic and acidic fractions. The neutral fraction (40%) was shown to be the starting ketone XXIX. Chromatography of the phenolic fraction on a Celite-silicic acid column and elution with 20:1 petroleum ether-ether gave an 18% yield of 1-methyl-2-naphthol, m.p. 107-109°. Separation of the acidic fraction on Celite-silicic acid led to three substances. The first substance was identified as *o*-(α-methyl-β-chlorovinyl-)*cis*-cinnamic acid (20%), m.p. 113-114°, which exhibited an ultra-violet absorption maximum at 260 mμ (ε 8,800). The second compound was shown to be 1-methyl-3-naphthoic acid (2%), m.p. 203-205°, by its ultraviolet absorption maxima at 238 mμ (ε 56,400) and 284 mμ (ε 8,289). The third substance, m.p. 205-210°, which revealed a broad carboxy OH band at 2.8-3.15 μ and a carbonyl band at 5.85 μ and an ultraviolet absorption maximum at 260 mμ, was not identified.

Work-up of the reaction mixture from a seven hour reflux of the ketone XXIX with potassium hydroxide in ethanol-water led to an unidentified neutral substance, which was resistant toward acid or base treatment, 18% of starting ketone XXIX, 4% of 1-methyl-2-naphthol, 9% of <u>o</u>-(α-methyl-β-chlorovinyl-) <u>cis</u>-cinnamic acid (CIX) and 36% of 1-methyl-3-naphthoic acid (CVIII).

There is only one possible reaction path from the ketone XXIX to the acid CIX, which is illustrated in the sequence below.



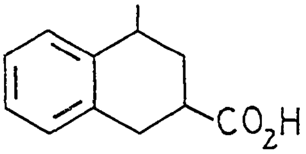
There are two possible pathways for the formation of 1-methyl-3-naphthoic acid. One path involves the transformation of acid CIX to CVIII. This was shown not to be the case, when base treatment of CIX under identical reaction conditions led to recovered starting material in 90% yield. A second possible pathway is illustrated in the following sequence.



Neopentyl halides are known to undergo bimolecular nucleophilic displacement with difficulty (60). The method of synthesis of the abnormal Reimer-Tiemann product verifies this fact. However, Wenkert and Stevens (49, see Historical Section) have demonstrated that internal chloride ion displacement can occur under certain circumstances.

As expected, path b was favored over path a, when the reaction was carried out in aqueous ethanol solution. In the latter medium ethoxide ion would be expected to compete, perhaps favorably, with hydroxide as active reagent. Because of its greater bulk, but also its higher nucleophilicity, it would be prone to attack the carbonyl carbon more slowly but its β -carbon more rapidly than hydroxide ion.

As the next investigation, ketone LXXVII was submitted to several base treatments. A solution of the ketone LXXVII and sodium hydroxide in ethanol water was refluxed for eight hours under nitrogen, whereupon neutral and acidic fractions were separated. The neutral fraction was shown to consist of the starting ketone LXXVII. Repeated crystallizations of the acidic fraction led to 1-methyl-3-naphthoic acid (CVIII), m. p. 202-204°, and 1-methyl-3,4-dihydro-3-naphthoic acid (CXIII), m.p. 94-95°. The acid CXIII exhibited an ultraviolet maximum at 260 mμ (ε 10,200). Its catalytic hydrogenation over palladium-charcoal yielded the known 1-methyl-1,2,3,4-tetrahydro-3-naphthoic acid (CXIV) (58), m.p. 124-125°. The acid CXIV was recovered when its ester was equilibrated and hydrolyzed with sodium hydroxide.



CXIV

The reaction of the ketone LXXVII and sodium methoxide in methanol under nitrogen led to a neutral fraction, which exhibited infrared absorption peaks at 5.6μ and 5.85μ , probably due to the carbonyl groups of a cyclobutanone and starting ketone, respectively.

Crystallization of the acidic fraction yielded one crystalline acid, which was identified as 1-methyl-3-naphthoic acid (CVIII), m.p. 203-205°. The remainder of the mixture of the acids was separated as their methyl esters, obtained by esterification with diazomethane and chromatographed over alumina. Elution with petroleum ether gave first methyl ester of 1-methyl-3,4-dihydro-3-naphthoic acid and then methyl 1-methyl-3-naphthoate (59). The first ester showed an ultraviolet absorption maximum at 260 mμ (ϵ 9,980), while the second ester exhibited maxima at 240 mμ (ϵ 52,000) and 285 mμ (ϵ 8,130).

A t-butanol solution of the ketone LXXVII and potassium t-butoxide was stirred at room temperature for 24 hours under nitrogen. The acidic products consisted only 1-methyl-3,4-dihydro-3-naphthoic acid (CXIII), m.p. 91-92°. The neutral products again exhibited 5.6μ and 5.85μ infrared peaks.

Attempts to separate the latter products by chromatography were unsuccessful, since the eluted material still consisted of a mixture whose 5.6μ peak, however, had decreased in intensity. This mixture was stirred in a t-butoxide solution for another 24 hours. The yield of neutral products as compared to acidic substances now was low and the former again revealed 5.6μ absorption peaks.

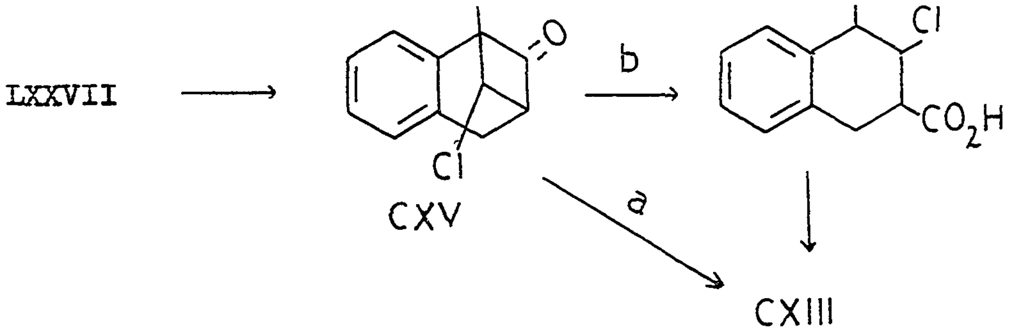
In regard to the base-catalyzed reaction of the ketone LXXVIII several factors must be considered. Firstly, there was no indication of the presence of the acid CXI, which would have been expected to form, had a path similar to sequence a been followed.

Secondly, the formation of acids in the alkoxide runs must have been due to the presence of water in the media despite the use of dry alcohols and protection of the reaction mixtures from atmospheric moisture. In the case of the methoxide run, the origin of the acidic products may lie in a direct displacement of methoxide ion on the methoxy carbon atom of the intermediate methyl esters.

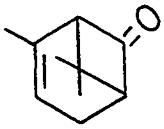
Thirdly, the formation of 1-methyl-3-naphthoic acid (CVII) is unusual, since this product is in a higher oxidation state than expected. To gain more insight into this oxidation, both the acid CXIII and its methyl ester were refluxed in sodium methoxide-methanol under nitrogen. In the first case only starting acid CXIII was isolated. In the second case, involving a reflux time of only four hours instead of the usual eight hours, a mixture of the esters of the acids CVIII and CXIII and a 45% yield of 1-methyl-3-naphthoic acid (CVIII), m.p. 195-198° were obtained.

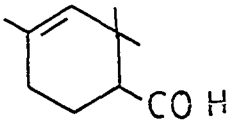
These results indicate that 1-methyl-3-naphthoic acid was obtained from the methyl ester of the acid CXIII, but not from the acid itself. Thus the rate of oxidation of ester of the acid CXIII is higher than its rate of hydrolysis. The absence of the acid CVIII in the reaction products of the <u>t</u>-butoxide run indicated that the oxidation of ester of the acid CXIII must be accomplished by oxidants in the methanolic and ethanolic media rather than air.

From the observations made above the reaction path from the ketone LXXVII to the acid CXIII may be postulated as illustrated in the sequence below.



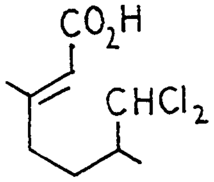
At least two analogies seem to favor path b. It has been shown (61, 62) that a reaction of chlorine-less chrysanthenone (CXVI) with base led to the acid CXVII. This indicates that a chlorine atom is not necessary for the opening of a cyclobutanone ring.


CXVI



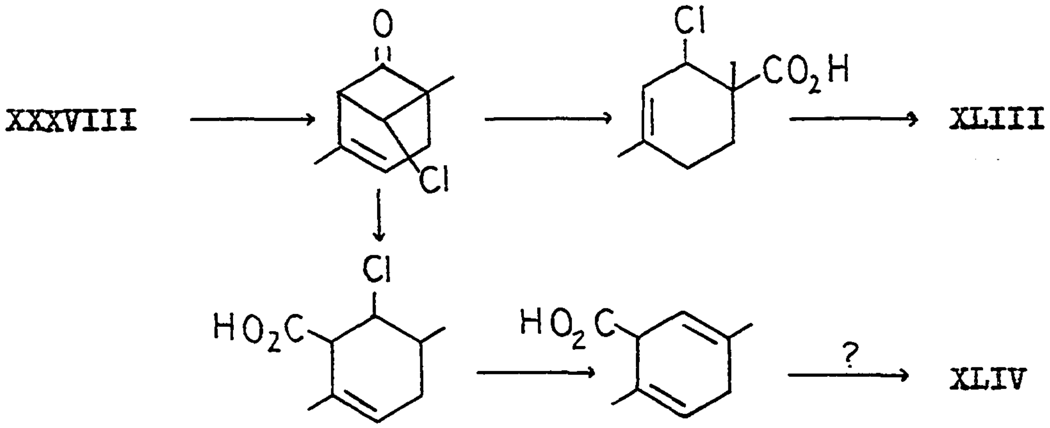
CXVII

The mechanism of the basic hydrolysis and rearrangement of XXXVIII to XLVI was suggested by von Auwers to involve a ring opening to the intermediate CXVIII, followed by a ring closure to the product XLVI.



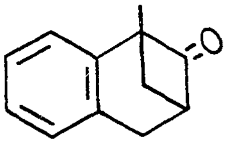
CXVIII

Since a base-catalyzed cyclization of CXVIII has no mechanistic precedents, the following alternate reaction paths need to be postulated.



It is interesting to note that the isolation of the intermediate chloroacid XLVI favors the aforementioned path b, and again demonstrates that the chlorine atom is not involved in the ring-opening step.

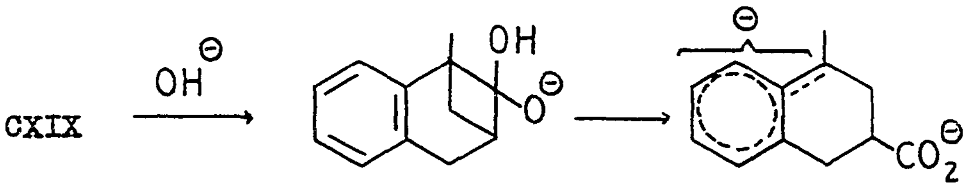
As a further check on path b it became of interest to investigate the behavior of cyclobutanone CXIX toward base.



CXIX

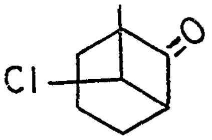
As a consequence a mixture of the ketone LXXXI and t-butoxide in t-butanol was stirred for eight hours. Two fractions were isolated, one of which was unseparable, but exhibited infrared absorption bands at 5.6μ and 5.85μ probably due to the C=0 of the ketones CXIX and LXXXI, respectively. However, 1-methyl-1,2,3,4-tetrahydro-3-naphthoic acid (CXIV), m.p. 124-125°, was obtained from the second fraction. This compound indicated ultraviolet absorption maxima at 266 mμ (ε 532) and 273 mμ (ε 548), characteristic of a tetralin chromophore. Its mixed melting point with an authentic sample was undepressed.

It is noteworthy that in all present cases the opening of the cyclobutanone rings occurs toward the most stable anion, e.g.:

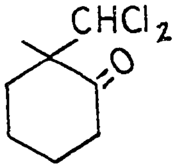


Since the instability of the preceding cyclobutanones had prevented their isolation, the synthesis of another ketone was sought. It was decided to construct CXX.

The procedure of von Auwers (35) was used to prepare the ketone XXVII, m.p. 33°, which on hydrogenation over palladium-charcoal led to the known ketone CXXI, m.p. 33-34° (63).



CXX



CXXI

The acidic mixture obtained from the reaction of the ketone CXXI with t-butoxide in t-butanol was not investigated. The infrared spectrum of the neutral fraction indicated a band of strong intensity at 5.6μ and a weak band at 5.85μ. The mixture was converted to a single semicarbazone in 83% yield.

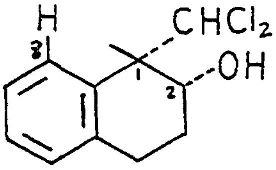
Hydrolysis of the semicarbazone of CXX in aqueous levulinic acid solution, in analogy with a procedure which has been studied recently in detail by DePuy and Ponder (64), led to the ketone CXX, which now exhibited only one carbonyl band at 5.6μ. Its semicarbazone was crystallized from methanol-water, m.p. 218-220°. Thus, finally a pure cyclobutanone had been trapped. It appears that CXX is more stable than its aromatic analogues.

In view of the isolation of some alcohol LXXVI in the reduction of XXIX to LXXVII, the structure of the alcoholic sideproduct became of interest.

Since the dichloromethyl naphthalenone XXIX must have a planar or nearly planar structure, addition of hydrogen to this system should occur predominantly on the side of the methyl group. The dichloromethyl moiety would be expected to offer considerably more steric hindrance than the methyl group to the approach of the hydrogenation catalyst. Isolation of only one product tended to support this point.

The reduction of the tetralone LXXVII with lithium aluminum hydride and with lithium aluminum tri-t-butoxy hydride led to a high yield of the same tetralol.

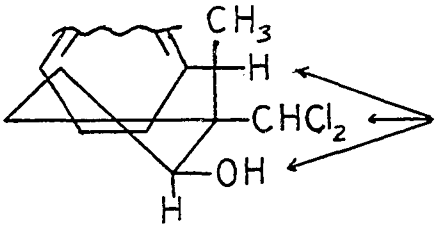
These results were in agreement with the hydrogenation data, since the hydride attack, especially in the case of the bulky tri-_t_-butoxy hydride, would be expected also to occur from the less hindered methyl side of LXXVII. As a consequence, the alcohol can be assigned structure CXXII.



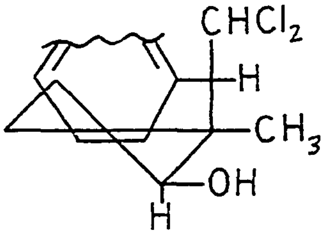
CXXII

When the alcohol LXXVI was equilibrated with aluminum isopropoxide, it was recovered unchanged in 69% yield. This would seem to indicate that the hydroxyl group prefers a *cis* orientation with respect to the bulky dichloromethyl function, rather than the usual *trans* relationship.

Inspection of a molecular model of such a system reveals that there is considerably more non-bonded interaction in compound LXXVI between the quasi-equatorialy oriented dichloromethyl group at C-1, the hydrogen atom at C-8 and the equatorial hydroxyl group at C-2 (CXXIII), than in its C-1 epimer CXXIV. Such a *peri* effect, leading to a more stable *cis* relationship between two vicinal bulky substituents, was also observed by Wenkert and Jackson (65).



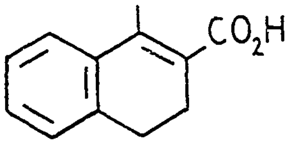
CXXIII



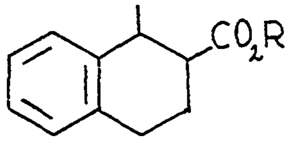
CXXIV

In connection with the previously discussed isolation of the dihydronaphthoic acid CXIII its isomer came under scrutiny.

1-Methyl-3,4-dihydro-2-naphthoic acid (CXXV) was prepared by the von Auwers (66) procedure. It was reduced by catalytic hydrogenation to the known 1-methyl-1,2,3,4-tetrahydro-2-naphthoic acid (CXXVI), m.p. 84-85° (66).



CXXV

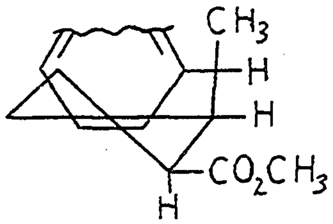


CXXVI R = H

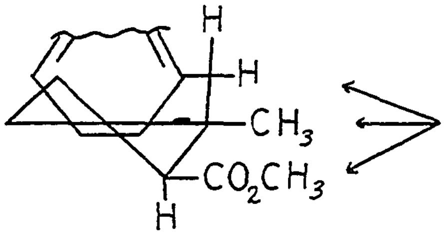
CXXVII R = CH_3

When the saturated acid was esterified with diazomethane, and its ester CXXVII was equilibrated and hydrolyzed with base, it was recovered unchanged. If the C-2 carbomethoxyl were in the thermodynamically unstable orientation, the base catalyzed equilibrium of such an oriented ester function would isomerize it to the most stable conformation.

Since the acid must be a cis substituted tetralin, having been obtained through a catalytic hydrogenation process, the equilibration result implies a greater stability in the cis (CXXVIII) than the trans (CXXIX) system. Thus, this represents another example of the peri effect.



CXXVIII



CXXIX

SPECTRA

Ultraviolet spectra were run in 95% ethanol using a Beckman model D U quartz spectrophotometer. Infrared absorption spectra were recorded using a Baird Double Beam infrared spectrophotometer and Perkin-Elmer Infracord spectrophotometer.

Figure 1. Ultraviolet spectra

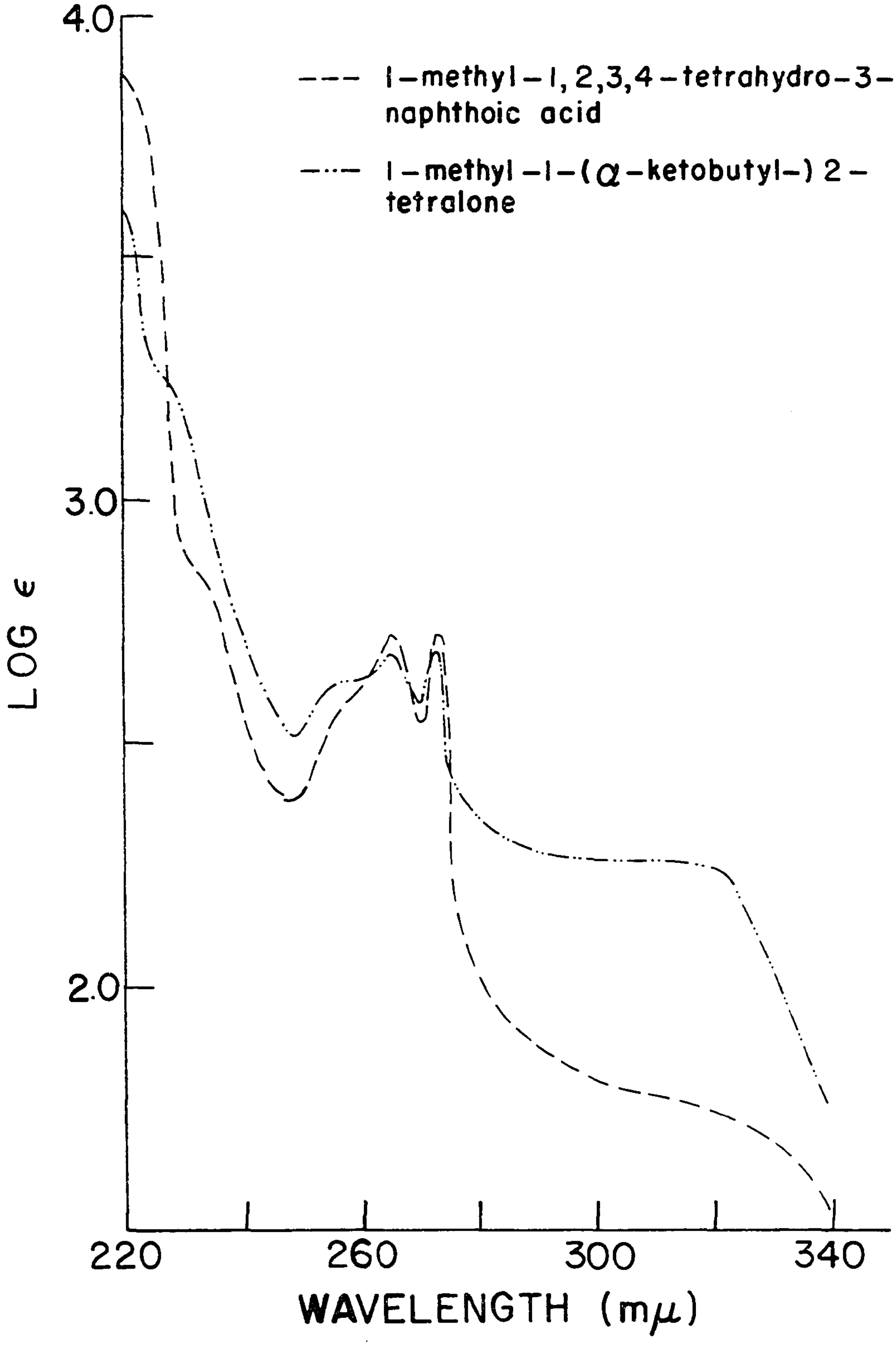

4.0
3.0
2.0
LOG ε
220
260
300
340
WAVELENGTH (mμ)
--- 1-methyl-1,2,3,4-tetrahydro-3-naphthoic acid
-··- 1-methyl-1-(α-ketobutyl-) 2-tetralone

Figure 2. Ultraviolet spectra

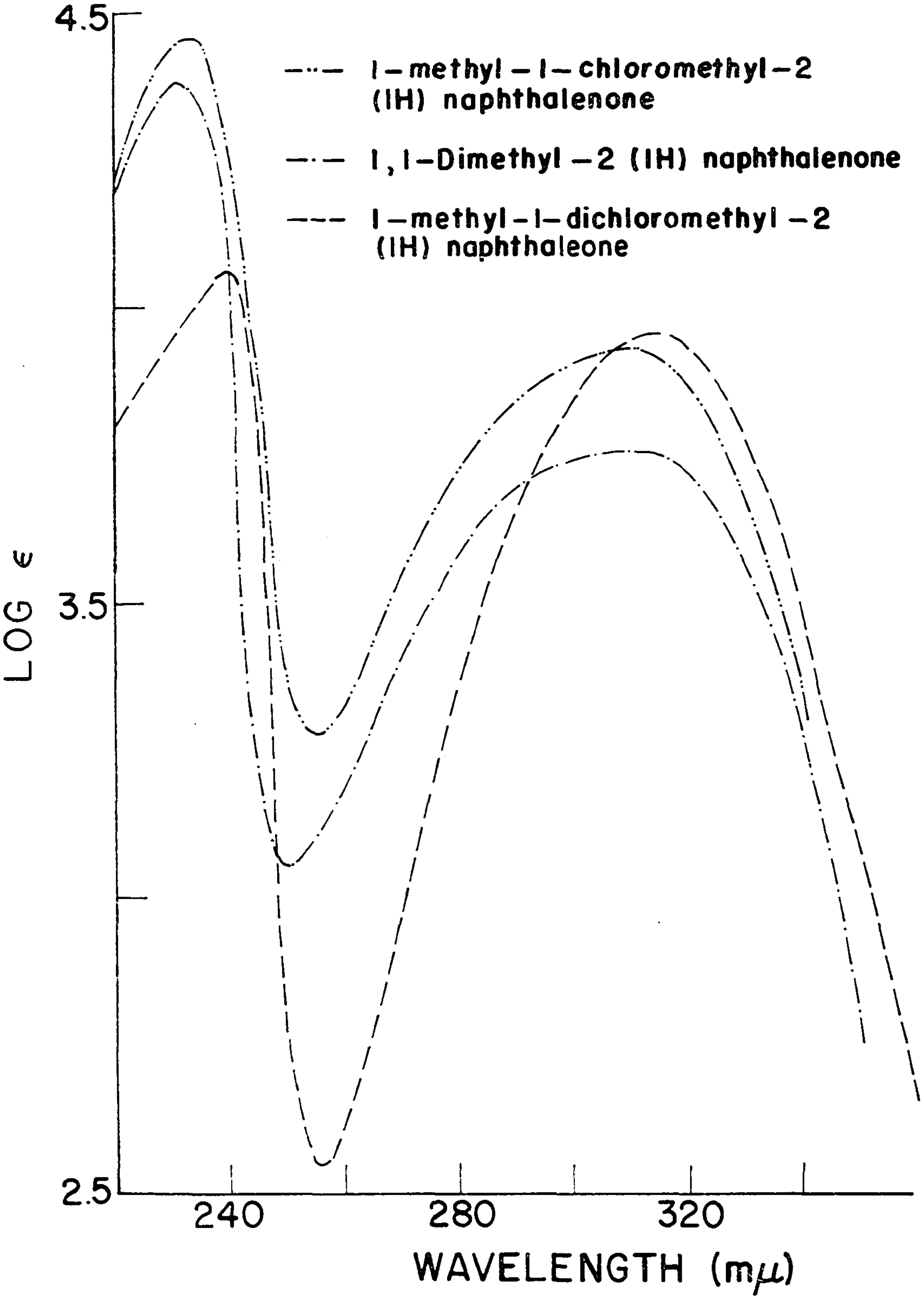

—··— 1-methyl-1-chloromethyl-2 (1H) naphthalenone
—·— 1,1-Dimethyl-2 (1H) naphthalenone
——— 1-methyl-1-dichloromethyl-2 (1H) naphthaleone
4.5
3.5
2.5
LOG ε
240
280
320
WAVELENGTH (mμ)

Figure 3. Ultraviolet spectra

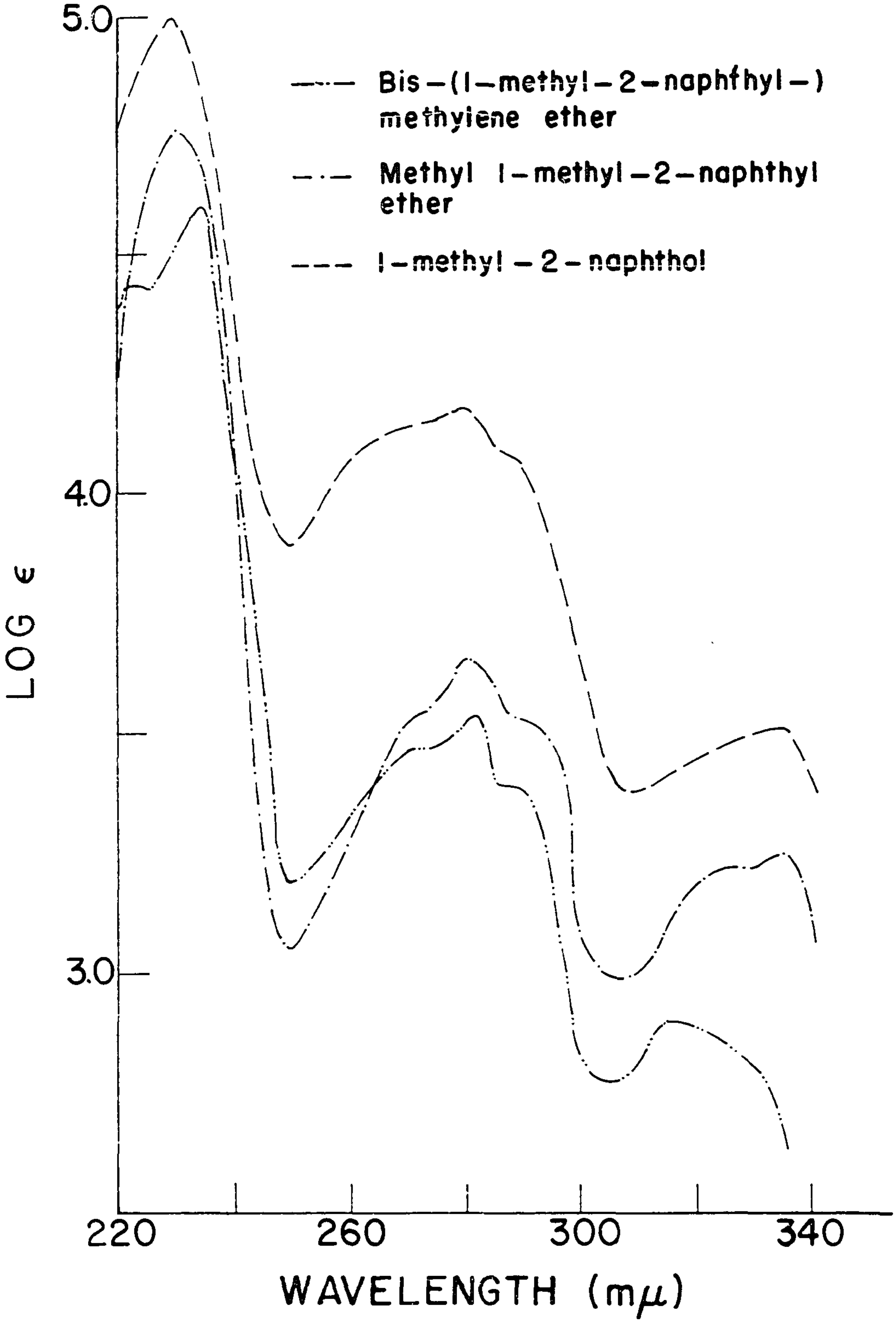

Bis-(1-methyl-2-naphthyl-) methylene ether
Methyl 1-methyl-2-naphthyl ether
1-methyl-2-naphthol
5.0
4.0
3.0
LOG ε
220
260
300
340
WAVELENGTH (mμ)

Figure 4. Ultraviolet spectra

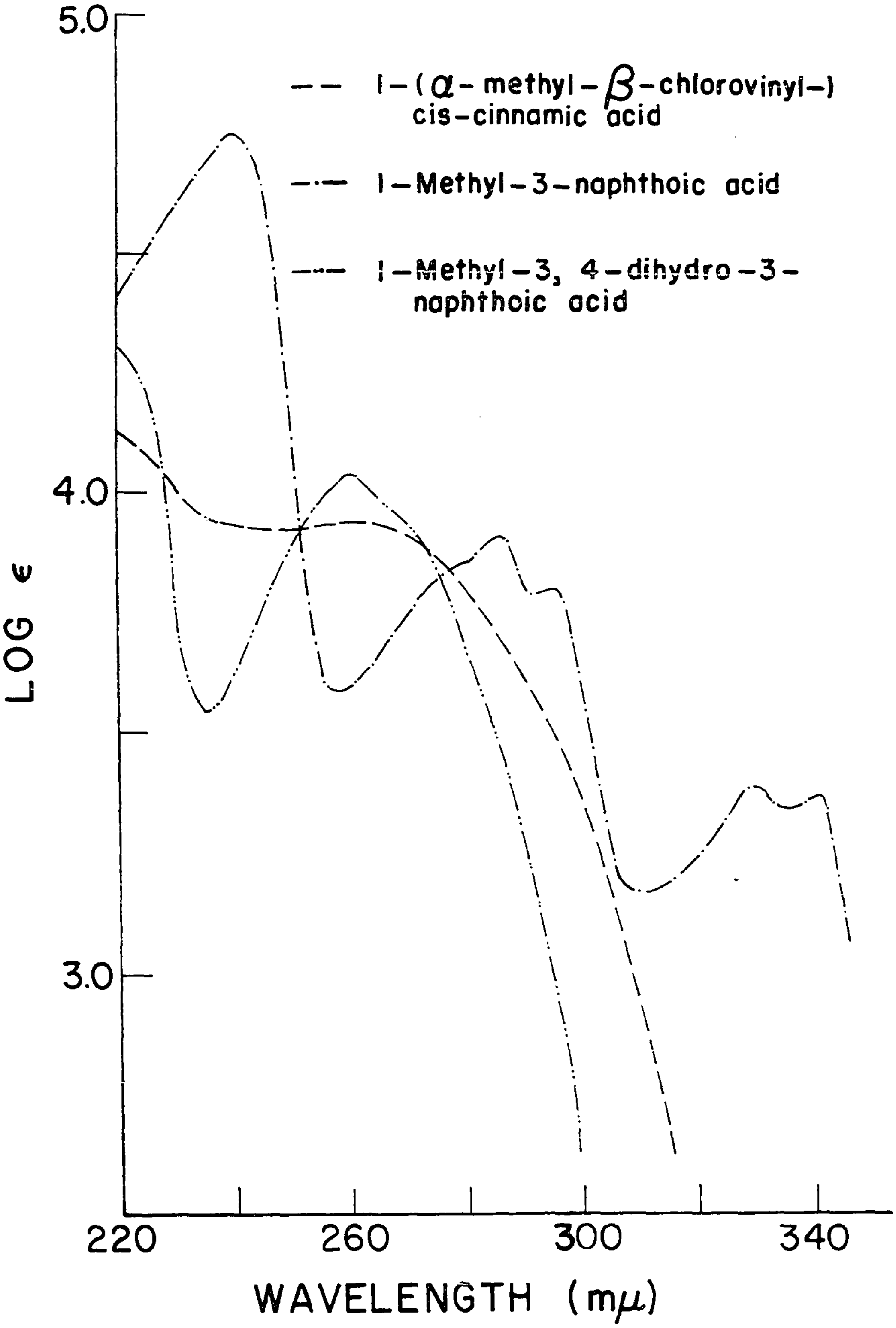
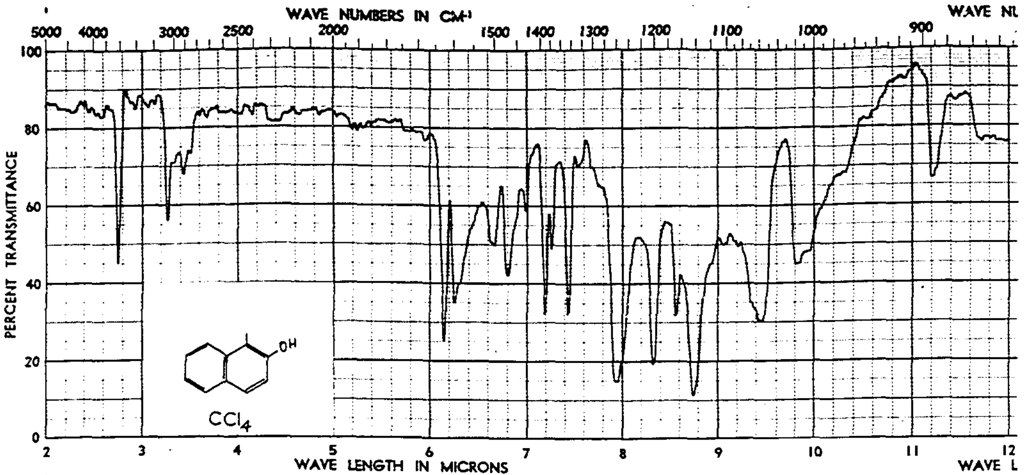
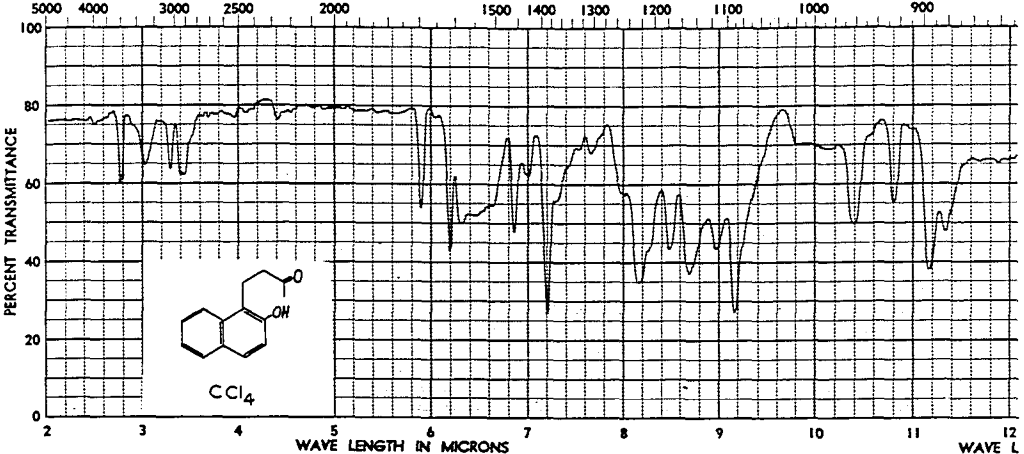

5.0
4.0
3.0
LOG ε
220
260
300
340
WAVELENGTH (mμ)
1-(α-methyl-β-chlorovinyl-) cis-cinnamic acid
1-Methyl-3-naphthoic acid
1-Methyl-3, 4-dihydro-3-naphthoic acid

Figure 5. Infrared spectra


WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
0 20 40 60 80 100
OH
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L


WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
0 20 40 60 80 100
O
OH
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L

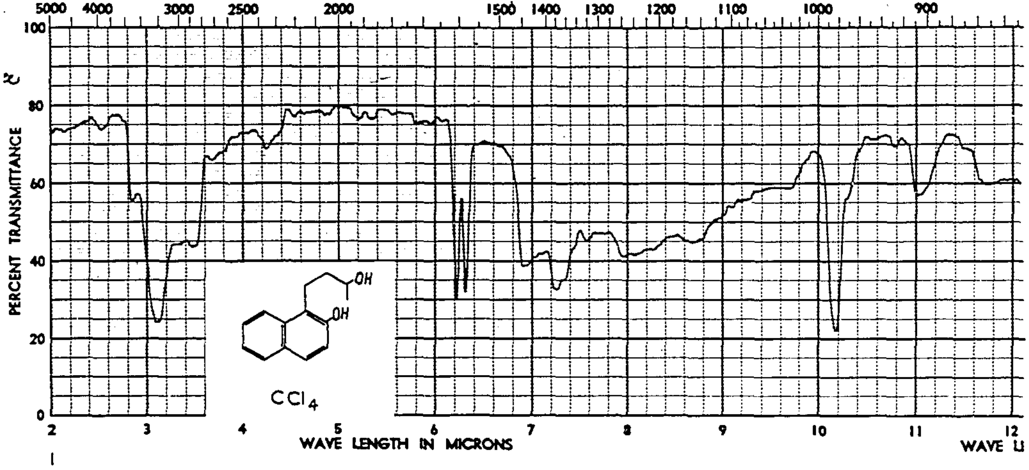
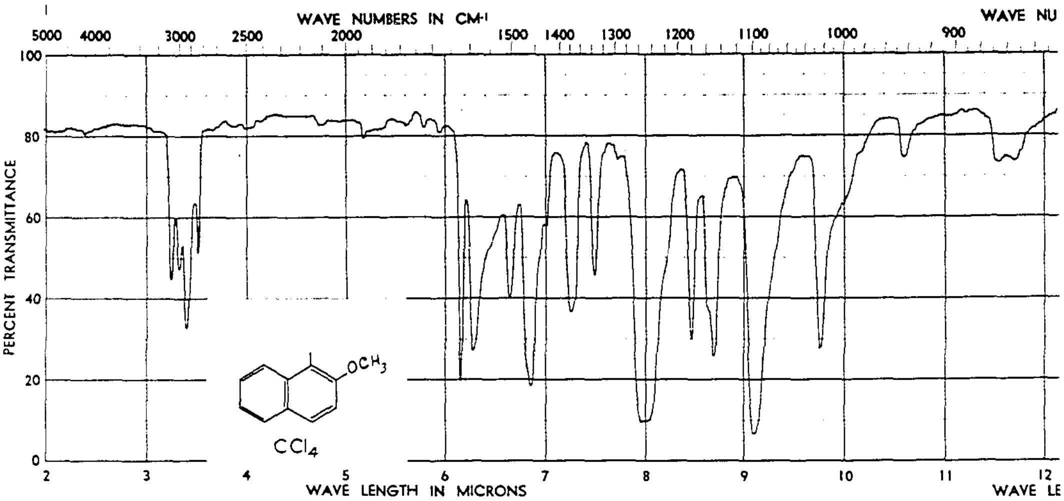
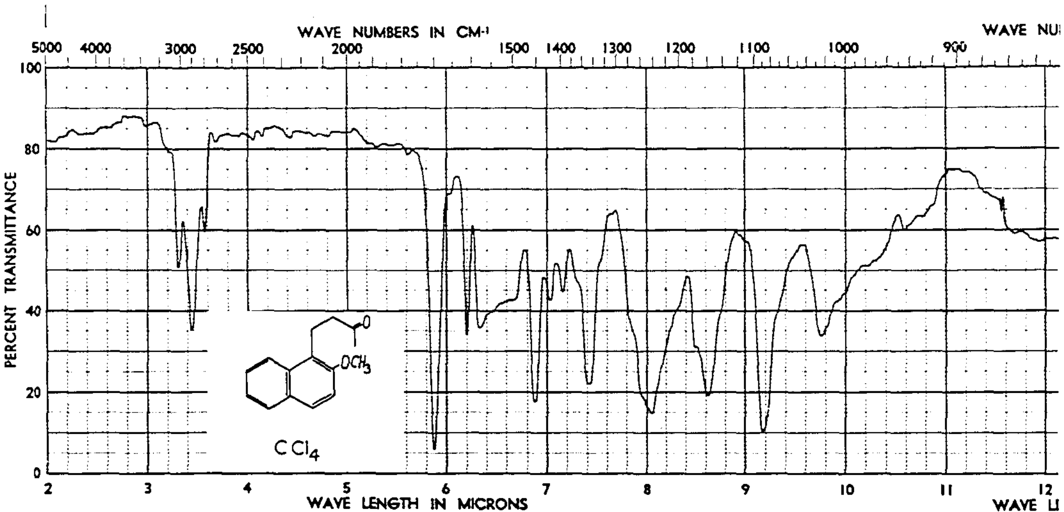

WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
0 20 40 60 80 100
OH
OH
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L

Figure 6. Infrared spectra


WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
OCH3
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE


WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
O
OCH3
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE

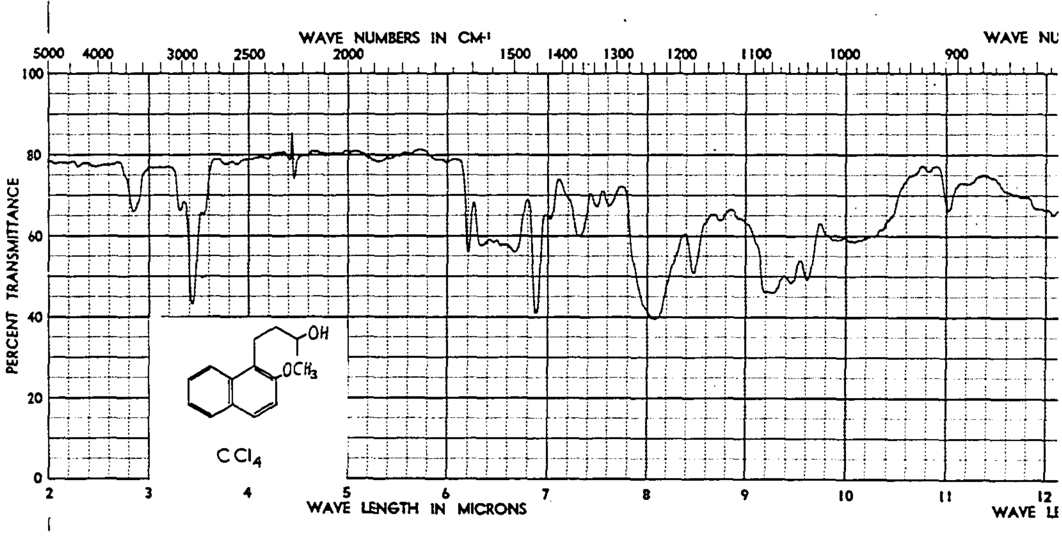
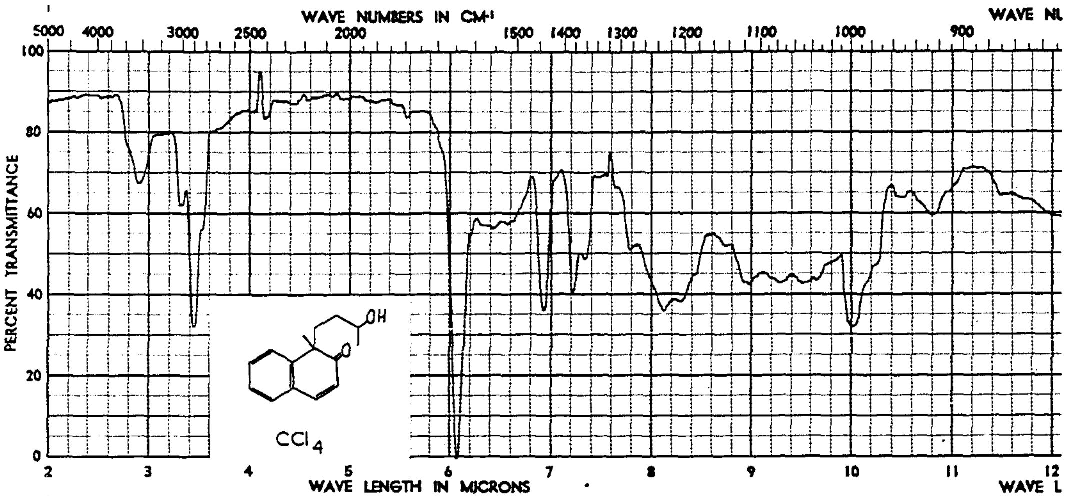
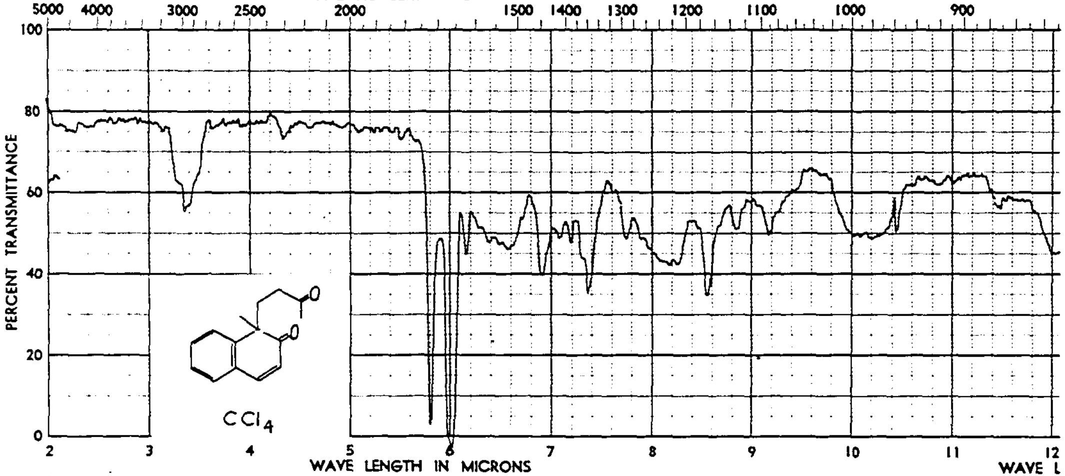

WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
OH
OCH3
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE

Figure 7. Infrared spectra


WAVE NUMBERS IN CM⁻¹
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
OH
O
CCl4


WAVE NUMBERS IN CM⁻¹
WAVE NI
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
O
O
CCl4

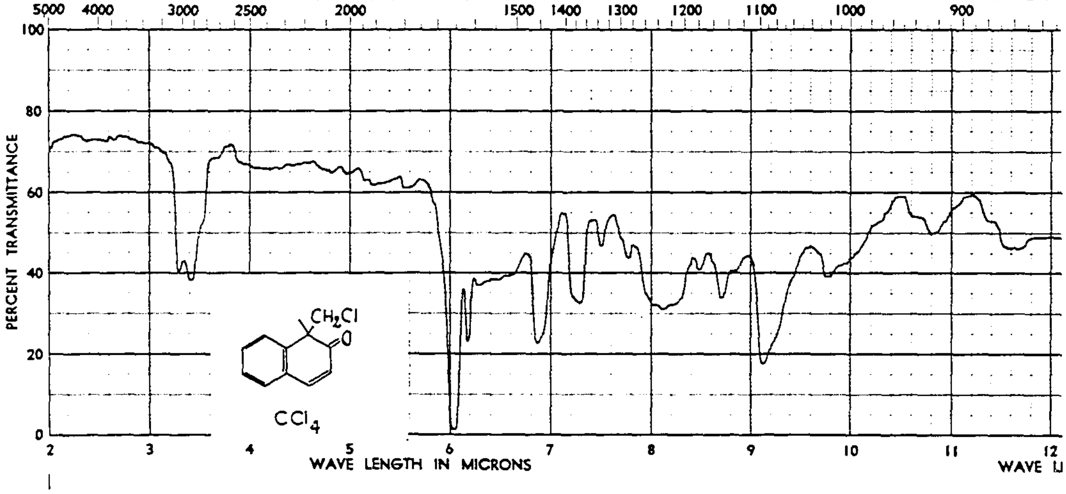
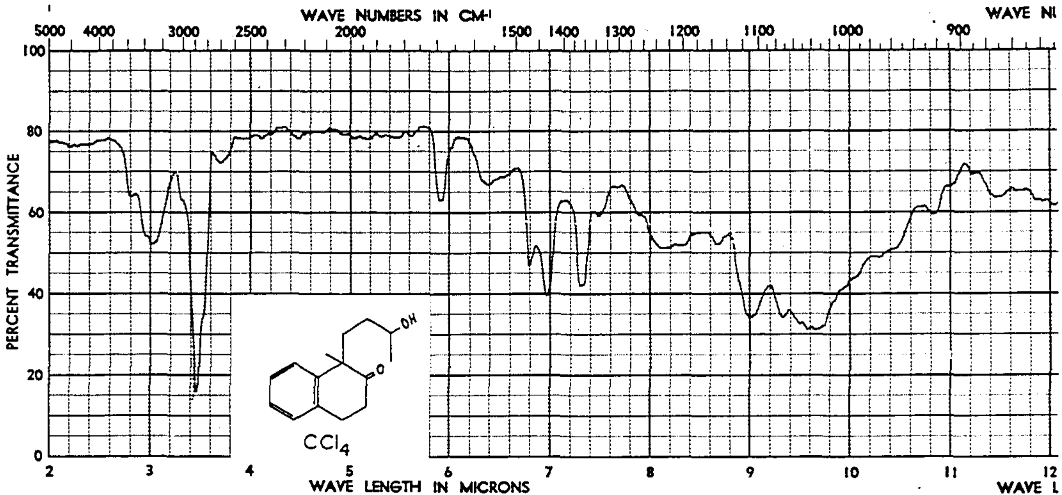
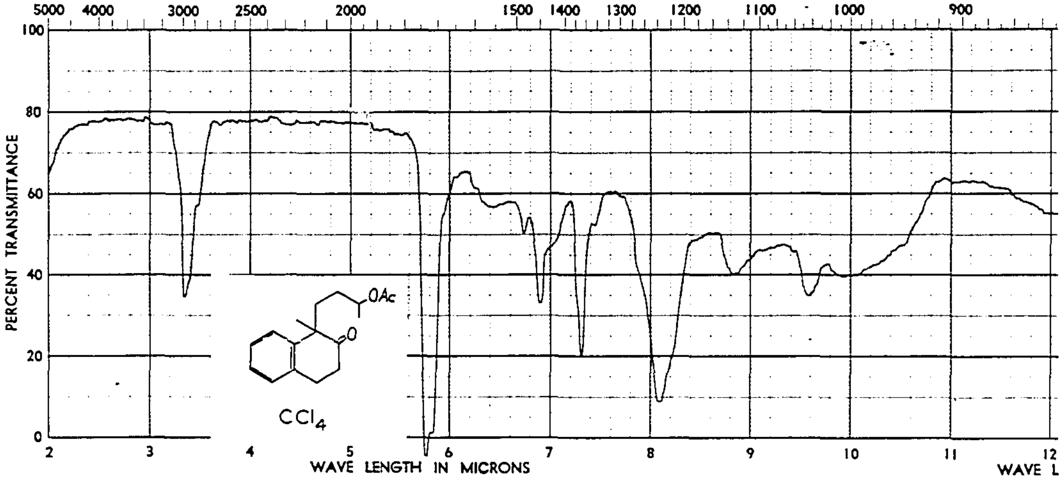

WAVE NUMBERS IN CM⁻¹
WAVE NI
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
CH2Cl
O
CCl4

Figure 8. Infrared spectra


WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
100 80 60 40 20 0
OH
O
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L


WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
100 80 60 40 20 0
OAc
O
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L

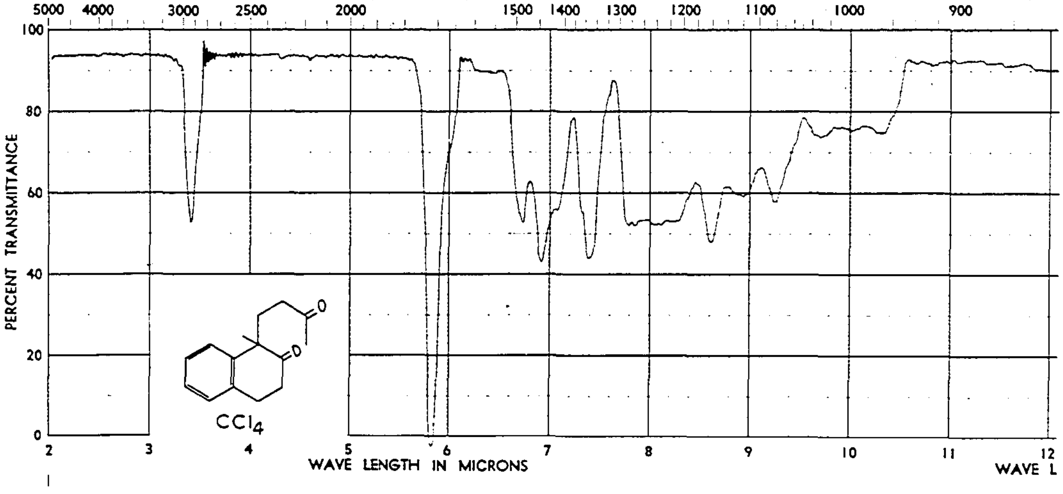
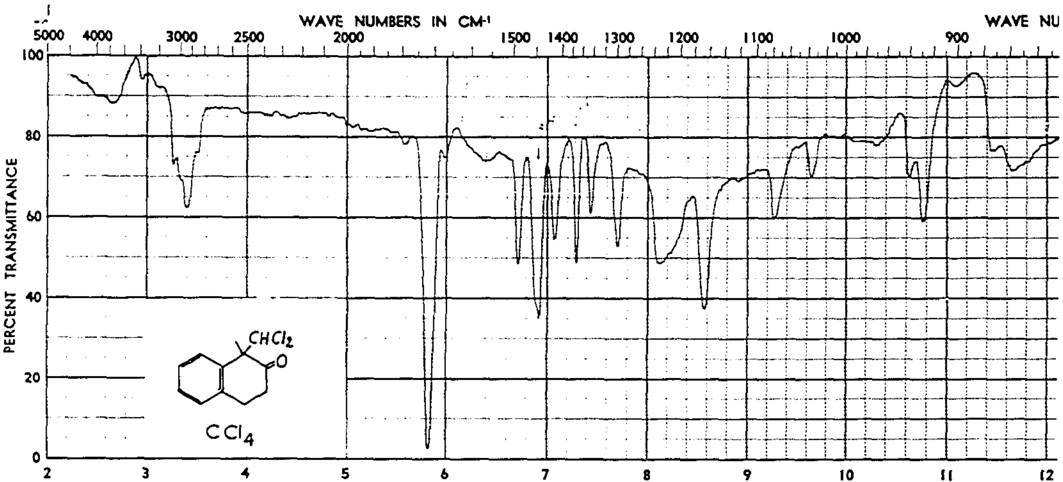
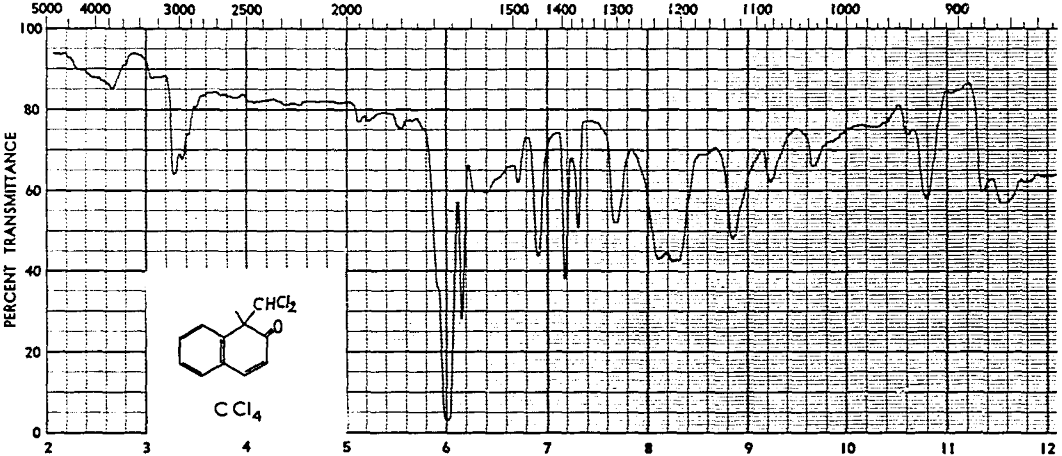

WAVE NUMBERS IN CM-1
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
PERCENT TRANSMITTANCE
100 80 60 40 20 0
O
O
CCl4
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L

Figure 9. Infrared spectra


WAVE NUMBERS IN CM-1
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
CHCl2
O
CCl4


WAVE NUMBERS IN CM-1
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
CHCl2
O
CCl4

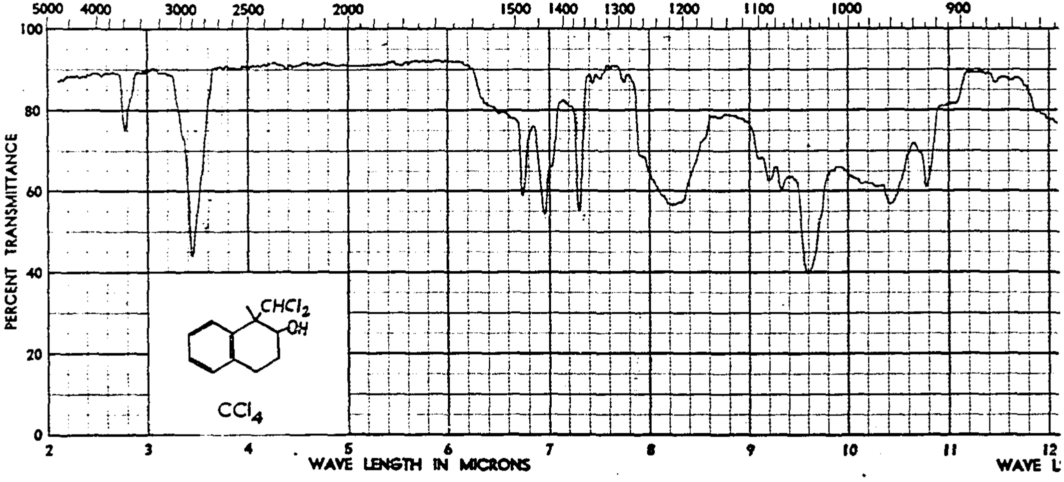
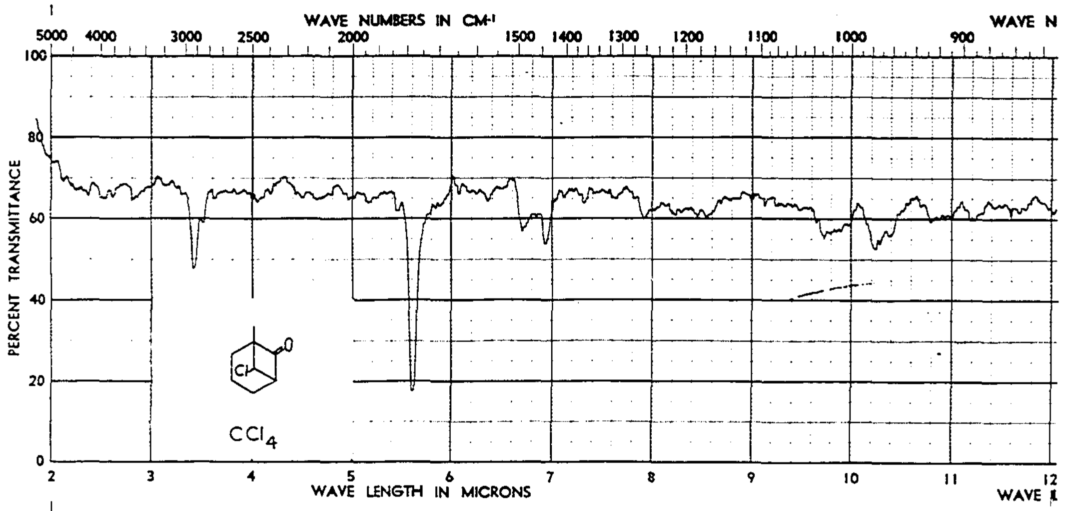
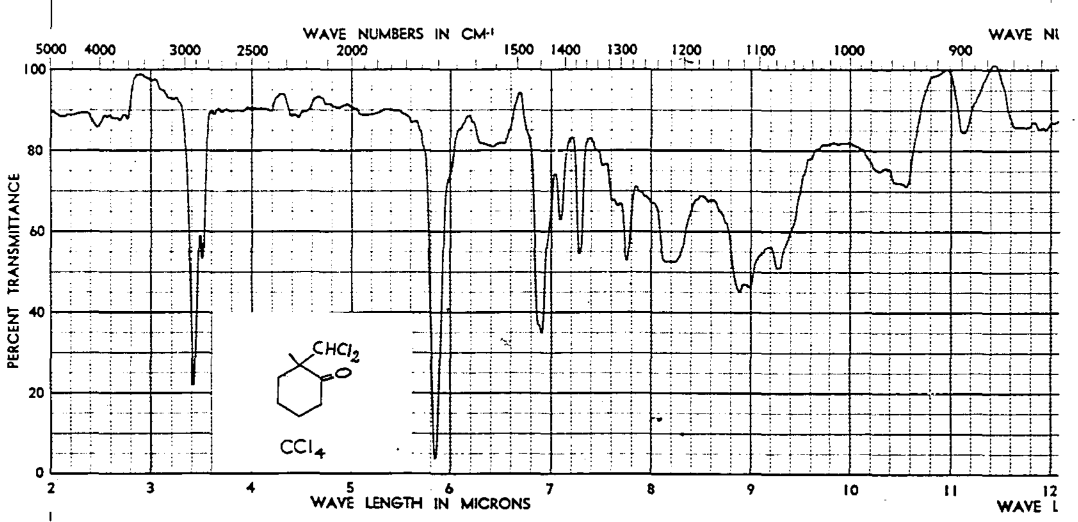

WAVE NUMBERS IN CM-1
WAVE NI
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L
CHCl2
OH
CCl4

Figure 10. Infrared spectra


WAVE NUMBERS IN CM⁻¹
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE N
100 80 60 40 20 0
PERCENT TRANSMITTANCE
Cl
O
CCl₄
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L


WAVE NUMBERS IN CM⁻¹
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
WAVE NU
100 80 60 40 20 0
PERCENT TRANSMITTANCE
CHCl₂
O
CCl₄
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE L

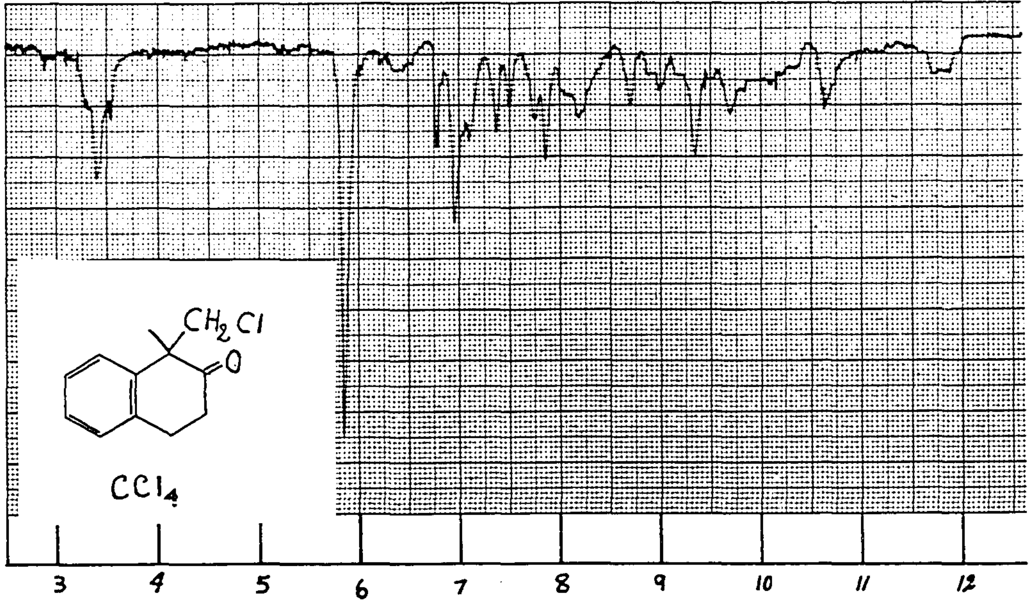
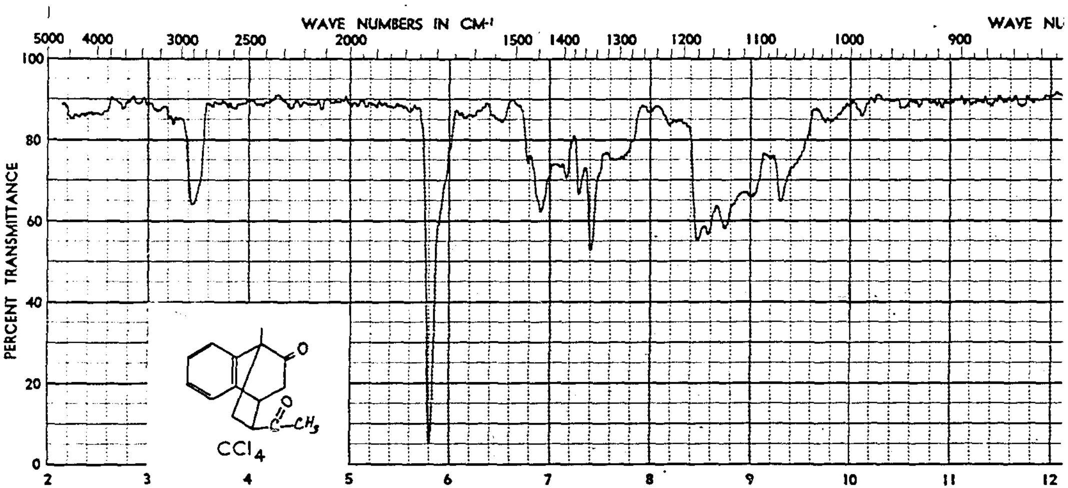
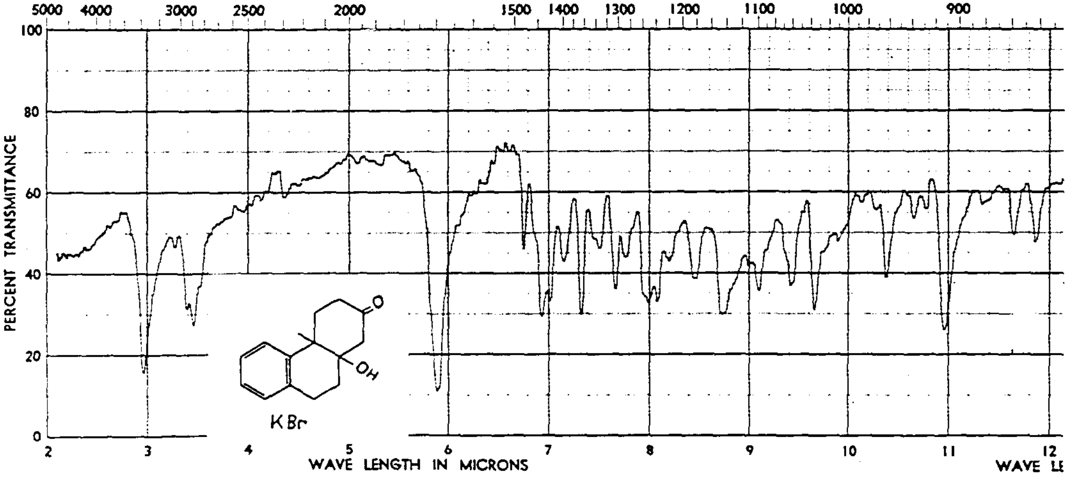

CH₂Cl
O
CCl₄
3 4 5 6 7 8 9 10 11 12

Figure 11. Infrared spectra


WAVE NUMBERS IN CM⁻¹
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
CCl4
O
C—CH3


WAVE NUMBERS IN CM⁻¹
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
KBr
O
OH

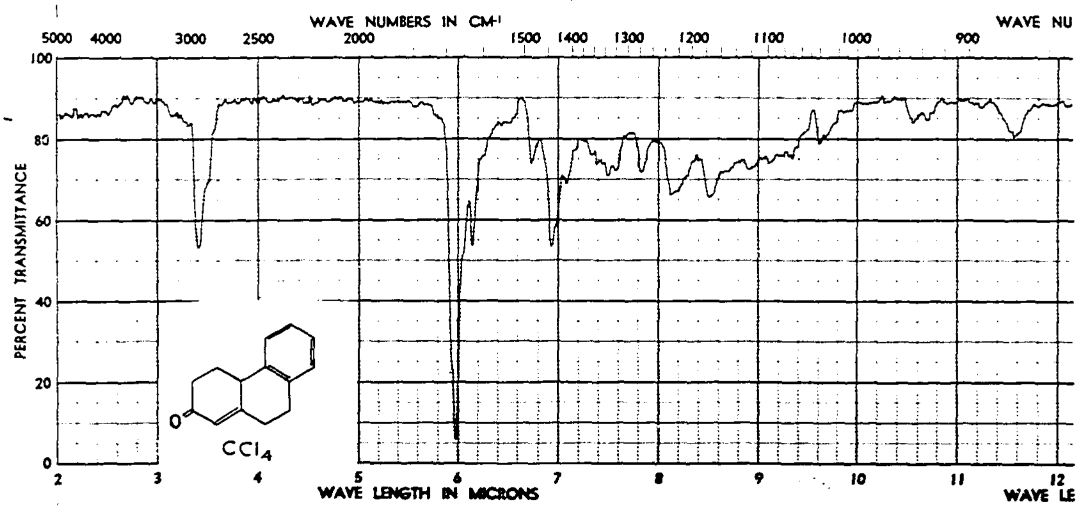
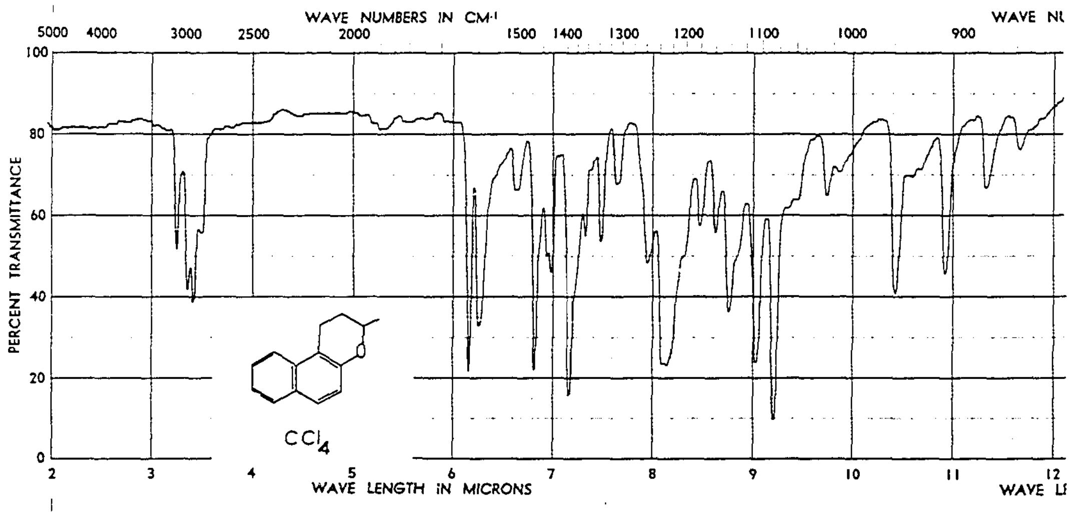
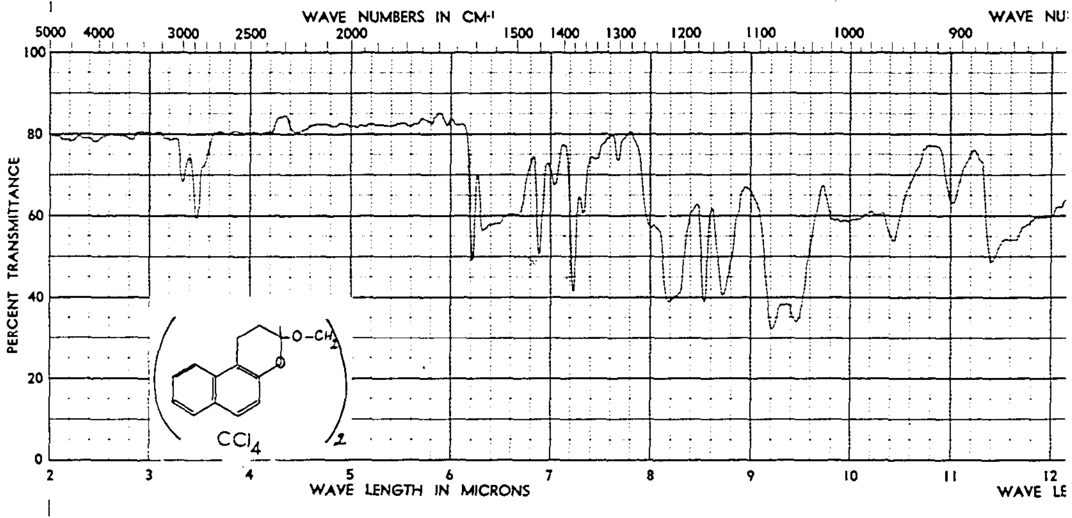

WAVE NUMBERS IN CM⁻¹
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
100 80 60 40 20 0
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
CCl4
O

Figure 12. Infrared spectra


WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE


WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
O-CH2
2
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE

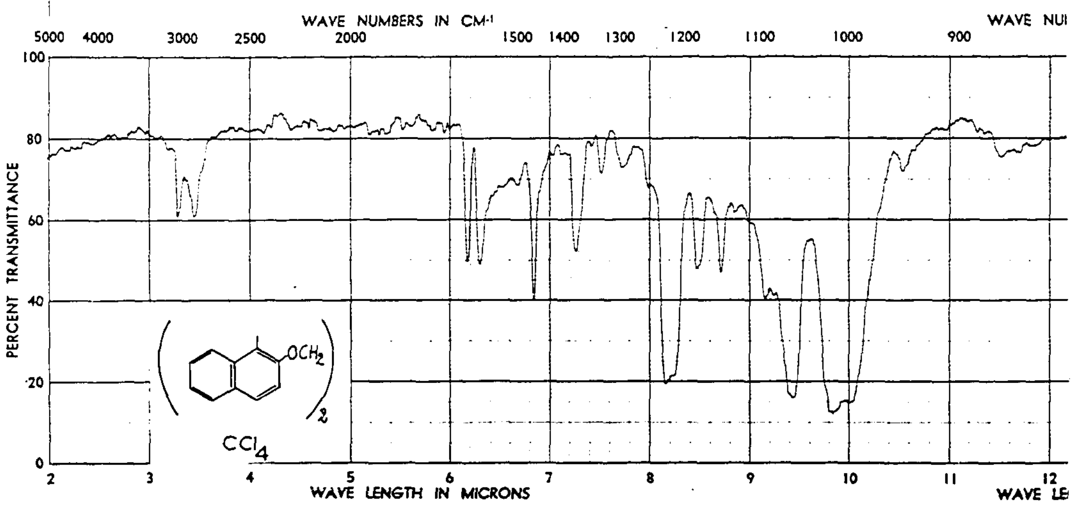
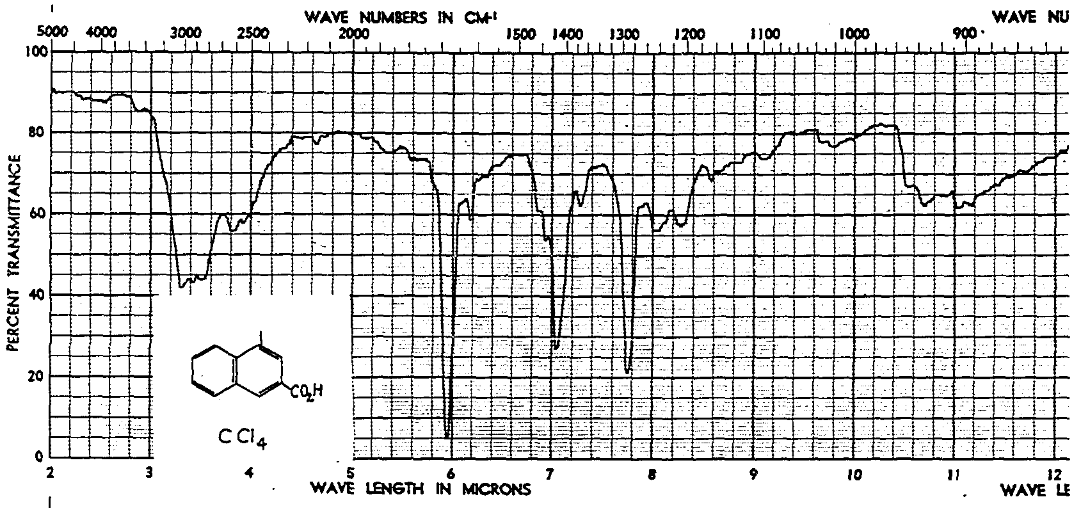
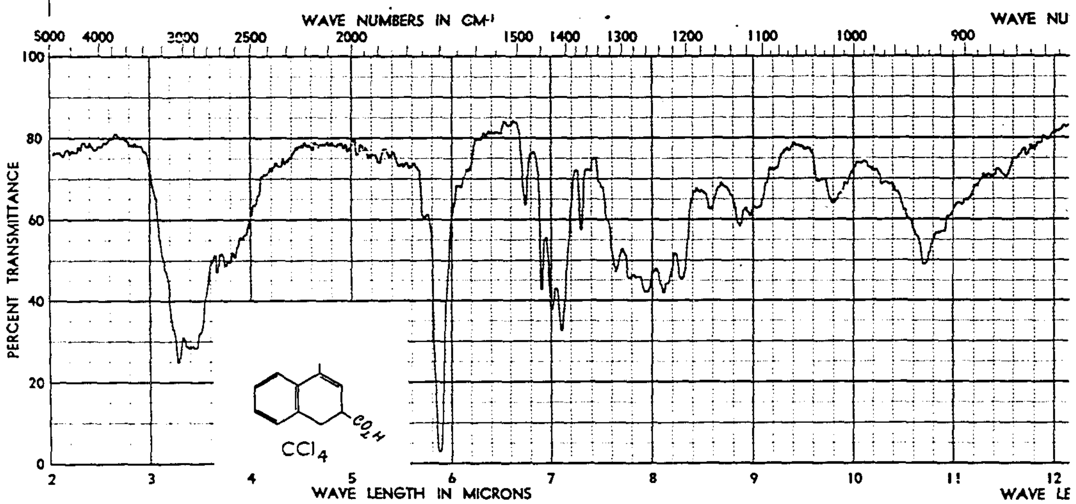

WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
WAVE NU
PERCENT TRANSMITTANCE
100
80
60
40
20
0
OCH2
2
CCl4
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE

Figure 13. Infrared spectra


WAVE NUMBERS IN CM-1
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
0 20 40 60 80 100
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
CO_2H
CCl_4


WAVE NUMBERS IN CM-1
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
0 20 40 60 80 100
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
CO_2H
CCl_4

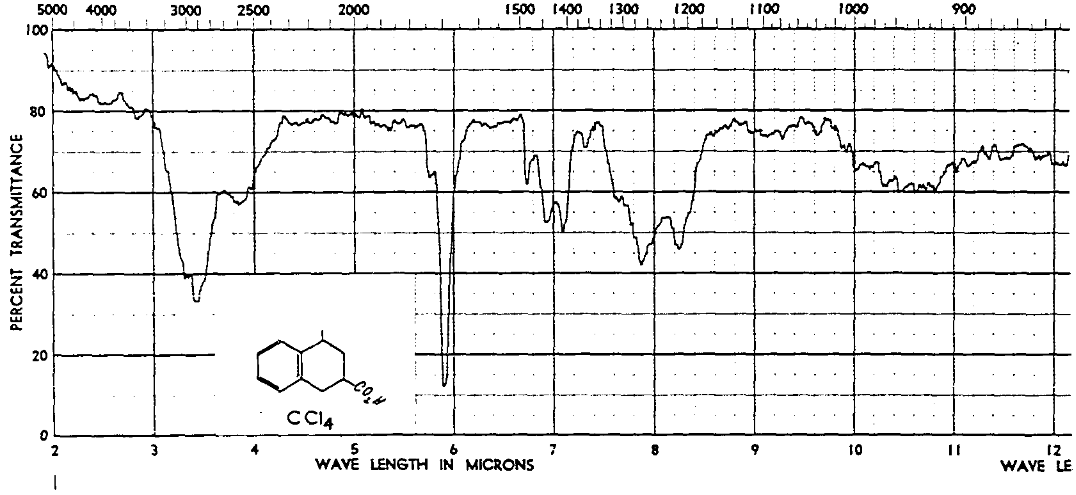
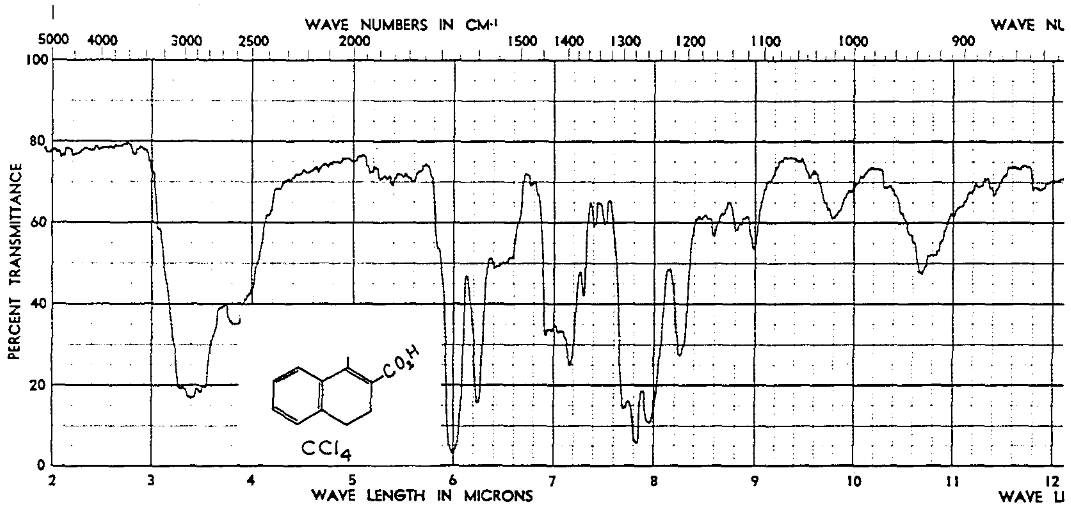
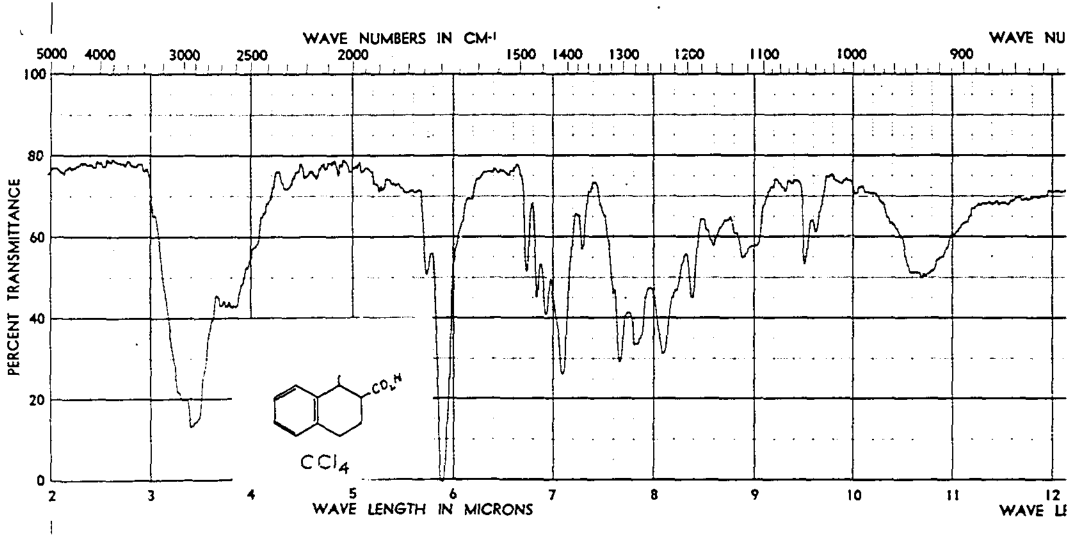
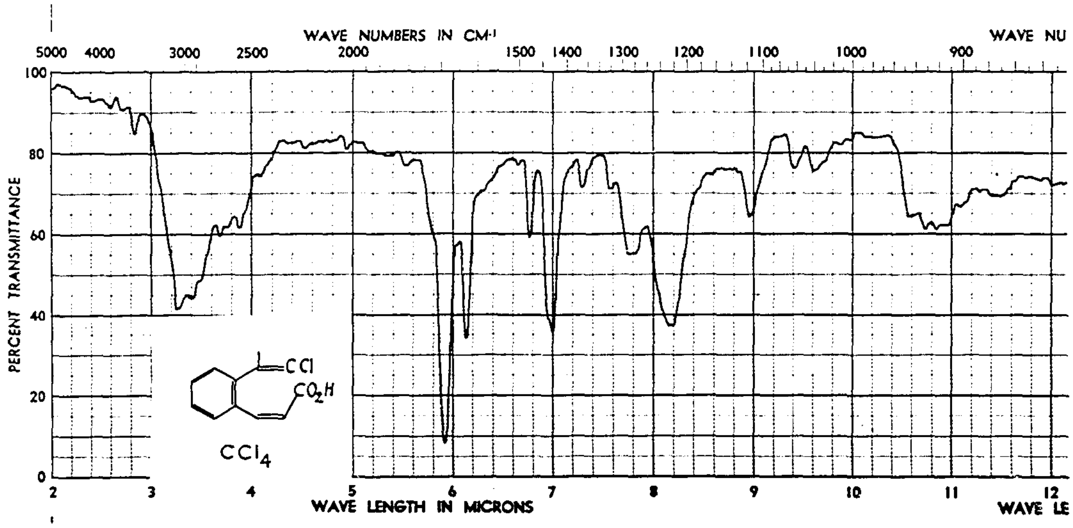

WAVE NUMBERS IN CM-1
WAVE NU
5000 4000 3000 2500 2000 1500 1400 1300 1200 1100 1000 900
PERCENT TRANSMITTANCE
0 20 40 60 80 100
2 3 4 5 6 7 8 9 10 11 12
WAVE LENGTH IN MICRONS
WAVE LE
CO_2H
CCl_4

Figure 14. Infrared spectra


WAVE NUMBERS IN CM-1
WAVE NU
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
PERCENT TRANSMITTANCE
100
80
60
40
20
0
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LI
CO2H
CCl4


WAVE NUMBERS IN CM-1
WAVE NU
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
PERCENT TRANSMITTANCE
100
80
60
40
20
0
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE
CO2H
CCl4


WAVE NUMBERS IN CM-1
WAVE NU
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
PERCENT TRANSMITTANCE
100
80
60
40
20
0
2
3
4
5
6
7
8
9
10
11
12
WAVE LENGTH IN MICRONS
WAVE LE
CCl
CO2H
CCl4

EXPERIMENTAL

All melting points and boiling points are uncorrected. The term petroleum ether refers to the petroleum fraction of b.p. 60-70°. Ultraviolet spectra were measured in 95% ethanol solution with a Beckman model DU quartz spectrophotometer. Micro-analyses were carried out by the Strauss and Weiler Microanalytical Laboratory, Oxford, England, and by the Midwest Microlab, Inc., Indianapolis, Indiana.

Absorbents for Chromatography

Activated alumina, 80-280 mesh, was allowed to stand with ethyl acetate for 24 hours, then washed with water and methanol, and dried at 100° for 24 hours.

The Celite-silicic acid adsorbent was prepared by mixing equal weights of Celite and 100 mesh silicic acid.

1-Methyl-2-Naphthol (XXIX)

Method A

The method of Adams and Levine (51) was used to prepare 2-hydroxy-1-naphthaldehyde. This was reduced by the following procedure.

Amalgamated zinc was prepared by adding 200 g. of 20 mesh zinc to a mixture of 8 g. of mercuric chloride and a solution of 5 ml. of concentrated hydrochloric acid in 200 ml. of water. The mixture was stirred at room temperature for a half hour, after which the water solution was decanted, and the amalgamated zinc was washed three times with 100 ml. of water. Glacial acetic acid, 150 ml. and 15 g. of 2-hydroxy-1-naphthaldehyde was added to the amalgamated zinc, and the resulting mixture was refluxed for eight hours. The cooled mixture was diluted with water, a precipitate formed which was filtered and washed with 400 ml. of water. The crude residue, 11 g., m.p. 100-105° was crystallized from hexane. It now melted at 110-111°.

Method B

A methanolic solution of 10 g. of 2-naphthol and sodium methoxide, 1.6 g. of sodium in 30 ml. of methanol, was evaporated to dryness under vacuum. After addition of 10 ml. of methanol, the distillation to dryness was repeated. Freshly distilled methyl iodide (20 ml.) and dry toluene (50 ml.) was added to the salt and the mixture was refluxed for 18 hours. The cooled mixture was diluted with water extracted with toluene. Organic extract was washed with water, dried with anhydrous magnesium sulfate, and evaporated to give a crude material which was chromatographed over alumina. Elution with petroleum ether gave 2.57 g. (25%) of a mixture of methyl 2-naphthyl ether (LXX) and methyl 1-methyl-2-naphthyl ether (LXXI), m.p. 50-55°, crystallized from hexane, m.p. 62-66°. Elution with 20:1 petroleum ether-benzene gave 0.78 g. (8%) of the naphthalenone LXXII, which was identified by its hydrogenation to the known tetralone LXXIII.

The aqueous basic solution was acidified with 1N hydrochloric acid and extracted with ether. The ether extract was dried over magnesium sulfate, evaporated, and the solid residue was chromatographed over alumina. Elution with petroleum ether led to two fractions. Crystallization of the first fraction from hexane gave 2.52 g. of 1-methyl-2-naphthol, m.p. 108-110°. The second fraction melting at 110-118° was assumed to be a mixture of the starting material, m.p. 122°, and 1-methyl-2-naphthol, m.p. 110°.

Dry Sodium Salt of 1-Methyl-2-Naphthol

To 10 ml. of methanol in which 0.14 g. of sodium had been dissolved, there was added 1.0 g. of 1-methyl-2-naphthol. The mixture was evaporated to dryness under vacuum, 10 ml. of benzene was added, and the distillation to dryness repeated.

Methylation of 1-Methyl-2-Naphthol

Freshly distilled methyl iodide (30 ml.) was added to the salt of 1 g. of 1-methyl-2-naphthol, prepared as described above, and the mixture was refluxed for four hours. Upon cooling, 30 ml. of water was added and the mixture extracted with two 25 ml. portions of chloroform. Drying over magnesium sulfate and vacuum removal of the solvent gave a residue which was chromatographed over alumina. Elution with petroleum ether yielded 12 mg. of an impure unidientified solid, m.p. 267-270°. Further elution with petroleum ether gave 40 mg. (4%) of methyl 1-methyl-2-naphthyl ether, melting at 38-39° after crystallization from petroleum ether. Finally, elution with 5:1 petroleum ether-benzene produced 0.94 g. (88%) of oily 1,1-dimethyl-2(1H)-naphthalenone (LXXII).

Ultraviolet spectrum

λ max. 230 mμ (ϵ 24,000) and 310 mμ (ϵ 5,640);
λmin. 255 mμ (ϵ 1,300).

The red 2,4-dinitrophenylhydrazone was crystallized from ethanol-ethyl acetate, m.p. 230-231°.

Anal.

Calcd. for $C_{18}H_{16}O_4N_4$: C, 61.37; H, 4.58; N, 15.90.

Found: C, 61.20; H, 4.61; N, 16.17.

Hydrogenation of 1,1-Dimethyl-2(1H)Naphthalenone (LXXII)

A mixture of 0.50 g. of the compound LXXII dissolved in 60 ml. of ethanol was hydrogenated over 0.05 g. of 5% palladium on carbon at room temperature and atmospheric pressure until hydrogen uptake ceased. After filtration of the catalyst and vacuum removal of the solvent, 0.42 g. of a residue was obtained, which was chromatographed over alumina. Elution with petroleum ether gave 0.31 g. (62%) of oily 1,1-dimethyl-2-tetralone (LXXIII).

The 2,4-dinitrophenylhydrazone was crystallized from ethanol, m.p. 130-140°.

1-Methyl-1-Dichloromethyl-2(1H)-Naphthalenone (XXIX)

Method A

The procedure of Dodson and Webb was used to prepared 1-methyl-1-dichloromethyl-2(1H)-naphthalenone (XXIX), m.p. 64-65°.

Method B

The sodium salt of 1.00 g. of 1-methyl-2-naphthol was prepared as described above. Distilled chloroform (30 ml.) was added and the mixture was refluxed for four hours. After dilution with water, the mixture was extracted with chloroform. The chloroform layer was dried over magnesium sulfate and evaporated to dryness under vacuum. The crude residue was chromatographed over alumina. Elution with petroleum ether gave first 10 mg. of an unidentified substance, m.p. 220-235°, and then 0.90 g. (60%) of 1-methyl-1-dichloromethyl-2(1H)-naphthalenone (XXIX) which was crystallized from chloroform-petroleum ether, m.p. 64-65°.

Hydrogenation of 1-Methyl-1-Dichloromethyl-2(1H)-Naphthalenone (XXIX)

A solution of 2.0 g. of the naphthalenone XXIX in 20 ml. of ethanol was hydrogenated over 100 mg. of palladium-charcoal at room temperature and atmospheric pressure. The catalyst was removed by filtration, the solution was heated on the steam bath under vacuum to remove the solvent, and the oily residue was chromatographed over alumina. Elution with petroleum ether led to 1.30 g. (65%) of the tetralone LXXVII, m.p. 67-70°, which was crystallized from chloroform-petroleum ether, m.p. 72-73°. Elution with 3:1 petroleum ether-benzene led to 0.55 g. (27%) of 1-methyl-1-dichloromethyl-2-tetralol (LXXVI), m.p. 68-70°. Crystallization of the compound from chloroform-petroleum ether raised the m.p. to 75-76°.

Anal.

Calc. for $C_{12}H_{14}OCl_2$: C, 58.8; H, 5.77; Cl, 28.95.
Found: C, 58.6; H, 5.74; Cl, 29.10.

1-Methyl-1-Iodomethyl-2(1H)-Naphthalenone (LXXVIII)

To the sodium salt of 1-methyl-2-naphthol, prepared from 1.0 g. of 1-methyl-2-naphthol as described above, there was added 30 ml. of freshly distilled methylene iodide and the mixture was refluxed for four hours. Upon cooling, 30 ml. of water was added and the mixture extracted with two 25 ml. portions of chloroform. Drying over magnesium sulfate and vacuum removal of the solvent gave a residue which was chromatographed over alumina. Elution with petroleum ether and crystallization of the eluate from ether gave 30 mg. (3%) of bis-(1-methyl-2-naphthoxy-)methane (LXXV), m.p. 146-47°.

Ultraviolet spectrum

λ max. 222 mμ (ϵ 35,300), 234 mμ (ϵ 54,000) and 280 mμ (ϵ 4,750), λ shoulder 270 mμ (ϵ 2,900) and 290 mμ (ϵ 2,440), λ min. 225 mμ (ϵ 35,200) 250 mμ (ϵ 2,480) and 305 mμ (ϵ 1,080).

Anal.

Calcd. for $C_{23}H_{20}O_2$: C, 84.12; H, 6.12. Found: C, 84.27; H, 5.84.

Further elution with 5:1 petroleum ether-benzene gave 0.55 g. (29%) of 1-methyl-1-iodomethyl-2(1H)-naphthalenone (LXXVIII) as an oil.

Ultraviolet spectrum

λ max. 232 mμ (ϵ 30,000) and 310 mμ (ϵ 7,450), λ min. 255 mμ (ϵ 2,250).

1-Methyl-1-Chloromethyl-2(1H)-Naphthalenone (LXXX)

Methylene chloride, 20 ml. was added to the sodium salt of 1-methyl-2-naphthol, prepared from 1.0 g. of 1-methyl-2-naphthol as described above, in a pyrex tube which was sealed and heated at 100° for eight hours. The mixture was diluted with water and extracted with chloroform. The organic layer was dried and the solvent removed, 0.85 g. of a crude substance was obtained which was chromatographed over alumina. Elution with petroleum ether gave 0.10 g. (10%) of crystalline bis-(1-methyl-2-naphthoxy-)methane (LXXV), m.p. 146-147° after crystallization from ether. Elution with 5:1 petroleum ether-benzene yielded 0.42 g. (32%) of 1-methyl-1-chloromethyl-2(1H)-naphthalenone (LXXX) as an oil.

Ultraviolet spectrum

λmax. 232 mμ (ϵ 30,400) and 310 mμ (ϵ 8,540), λ min. 255 mμ (ϵ 2,160).

Its 2,4-dinitrophenylhydrazone was crystallized from ethanol-ethyl acetate, m.p. 184-85°.

Hydrogenation of 1-Methyl-1-Chloromethyl-2(1H)-Naphthalenone (LXXX)

A solution of 400 mg. of the ketone LXXX in 20 ml. of ethanol was hydrogenated over 20 mg. of palladium-charcoal at room temperature and atmospheric pressure. After filtration and removal of the solvent, this oily residue was chromatographed over alumina. Elution with petroleum ether gave 230 mg. of the tetralone LXXXI.

Its 2,4 dinitrophenylhydrazone was crystallized from ethanol-ethyl acetate, m.p. 177-178°.

Hydrolysis of bis-(1-Methyl-2-Naphthoxy-)Methane (LXXV)

A mixture of 50 mg. of LXXV in 15 ml. of 95% ethanol and 5 ml. of 2N hydrochloric acid was heated for 15 minutes and left standing for 24 hours at room temperature. After extraction with ether, drying of the extract, and vacuum removal of the solvent, the crude product, 35 mg. was chromatographed over alumina. Elution with 5:1 petroleum ether-benzene yielded 20 mg. of 1-methyl-2-naphthol, m.p. 106-108°.

n-Butylation of 1-Methyl-2-Naphthol

The sodium salt of 1.0 g. of 1-methyl-2-naphthol was prepared as described above, 30 ml. of n-butyl iodide was added, and the mixture was refluxed for four hours. After dilution with water, extraction with chloroform, drying of the organic extract, and vacuum removal of the solvent, the crude product was chromatographed on alumina. Elution with petroleum ether yielded 0.36 g. (29%) of an oil which became crystalline on standing, m.p. 33-36°. Crystallization from petroleum ether gave n-butyl 1-methyl-2-naphthyl ether (LXXXVII), m.p. 35-36°.

<u>Ultraviolet spectra</u>

λ max. 232 $m\mu$ (ϵ 65,300) and 282 $m\mu$ (ϵ 5,500), λ shoulder 272 $m\mu$ (ϵ 4,430) and 292 $m\mu$ (ϵ 4,360), λ min. 252 $m\mu$ (ϵ 2,220) and 305 $m\mu$ (ϵ 1,430).

<u>Anal</u>.

Calcd. for $C_{15}H_{N}O$: C, 84.07; H, 8.47. Found: C, 84.13; H, 8.62.

Elution with 5:1 petroleum ether-benzene yielded 0.65 g.

(50%) of 1-methyl-1-(n-butyl-)2(1H)-naphthalenone (LXXXVI) as an oil.

The red 2,4-dinitrophenylhydrazone was crystallized from ethanol, m.p. 125-126°.

Anal.

Calcd. for $C_{21}H_{22}O_4N$: C, 63.94; H, 5.62; N, 14.21.
Found: C, 63.64; H, 5.73; N, 14.4.

Addition of Methyl Vinyl Ketone to β-Naphthol

1-(γ-ketobutyl-)2-naphthol (LXXXII) was prepared by a slight modification of the Robinson procedure. Freshly distilled methyl vinyl ketone (16.5 g.) was added dropwise and under nitrogen to a stirred, ice-cold ethanolic solution of 30.0 g. of β-naphthol and potassium ethoxide, prepared from 7.5 g. of potassium and 100 ml. of ethanol, and the solution was concentrated under vacuum, acidified with 1 N hydrochloric acid, diluted with 200 ml. of water and extracted with ether. The extract was dried over anhydrous magnesium sulfate and the solvent was removed. Two crystallizations of the residue from 80% ethanol yielded 32.5 g. (72%) of 1-(γ-ketobutyl-)2-naphthol melting at 88-89°.

1-(n-Butyl)-2-Naphthol (LXXXIII)

A mixture of 1.00 g. of 1-(γ-ketobutyl-)2-naphthol (LXXXII), 4 g. of potassium hydroxide, 6 ml. of 95% hydrazine and 20 ml. of ethylene glycol was refluxed for one hour. The mixture then was heated for two hours without reflux condenser to remove excess hydrazine. The cooled mixture was diluted with water, acidified with 2N hydrochloric acid and extracted with ether. Drying of the extract over magnesium sulfate and removal of the solvent gave 0.92 g. (99%) of solid, which on crystallization from petroleum ether-chloroform gave 1-(n-butyl-)2-naphthol, m.p. 79-81°.

Methylation of 1-(n-butyl)-2-naphthol (LXXXIII)

A mixture of the sodium salt of 1.00 g. of 1-(n-butyl-) 2-naphthol and 30 ml. of freshly distilled methyl iodide was refluxed for four hours. After the usual work-up the crude product was chromatographed over alumina. Elution with petroleum ether yielded 0.32 g. (30%) of oily methyl 1-(n-butyl-)2-naphthyl ether (LXXXVIII).

Ultraviolet spectrum

λ max. 232 mμ (ε 70,500) and 282 mμ (ε 6,160), λ shoulder 272 mμ (ε 4,640) and 295 mμ (ε 5,310), λ min. 252 mμ (ε 2,320) and 305 mμ (ε 1,740).

Elution with 5:1 petroleum ether-benzene gave 0.63 g. (59%) of oily 1-methyl-1-(n-butyl-)2(1H)-naphthalenone (LXXXVI). The infrared and ultraviolet spectra of this material and the ketone (LXXXVI) above were identical. Also the mixed m.p. of the 2,4-dinitrophenylhydrazone of this material and that of the ketone (LXXXVI) (m.p. 125-126°) was not depressed.

Methyl 1-(γ-Ketobutyl-)2-Naphthyl Ether (CVII)

A mixture of 200 mg. of 1-(δ-ketobutyl-)2-naphthol (LXXXII) sodium methoxide, prepared by the dissolution of 20 mg. of sodium in 15 ml. of methanol, and 10 ml. of methyl iodide was refluxed for two hours. The cooled mixture was diluted with water and extracted with ether. The extract was washed with water, dried over magnesium sulfate and evaporated. The residue, 135 mg. (59%), was crystallized from hexane, yielding crystalline ether (CVII), m.p. 54°.

<u>Ultraviolet spectrum</u>

λmax. 232 mμ (ε 100,500) and 280 mμ (ε 9,600) shoulder 270 mμ (ε 7,650) and 295 mμ (ε 7,960), λ min. 252 mμ (ε 4,550) and 305 mμ (ε 2,440).

Anal.

Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.93; H, 6.90.

Methylation of 1-(γ-Ketobutyl-)2-Naphthol (LXXXII)

The sodium salt of 2.00 g. of the compound LXXXII was prepared as described for 1-methyl-2-naphthol, 30 ml. of methyl iodide was added, and the mixture was refluxed for four hours. After extraction with chloroform and subsequent identical workup with the cases described above, the resulting residue was chromatographed over alumina. Elution with petroleum ether gave a solid, which on crystallization from hexane proved to be methyl 1-methyl-2-naphthyl ether (LXXI), m.p. and mixed m.p. with authentic sample (m.p. 37-38°) were 37-38°. The spectra of the two ethers were identical. Elution with 10:1 petroleum ether-benzene gave another solid, which after crystallization from hexane could be shown to be methyl 1-(γ-ketobutyl-)2-naphthyl ether (CVII), m.p. and mixed m.p. with authentic sample (m.p. 54°) were 54°. The spectra of the two ethers were also identical. Further elution with the same solvent mixtures yielding oily ketonic material, which included 1-methyl-1-(γ-ketobutyl-)2(1H)-naphthalenone (XCV), as indicated by its infrared spectrum. Finally, elution with benzene afforded the phenolic products. Crystallization of this phenolic mixture from petroleum ether-carbon tetrachloride gave the starting material, m.p. and mixed m.p. with authentic sample (m.p. 88-89°) were 86-89°. Evaporation of the mother liquor and sublimation of the residue yielded another solid, which on crystallization from the same solvent mixture could be identified by m.p., mixed m.p. and infrared spectrum as 1-methyl-2-naphthol, m.p. 109-110°.

Ketalation of 1-(γ-Ketobutyl-)2-Naphthol (LXXXII)

A mixture of 2.0 g. of 1-(γ-ketobutyl-)2-naphthol, 75 mg. of p-toluenesulfonic acid monohydrate, 16 ml. of ethylene glycol and 90 ml. of tuluene was distilled slowly for six hours. The volume of the mixture was kept constant by the addition of fresh toluene every half hour. The mixture was washed with saturated sodium bicarbonate solution and then with water, was dried over magnesium sulfate, after which it was heated under vacuum to remove the solvent. Crystallization of the oily residue from methanol gave a solid which was chromatographed over alumina. Elution with petroleum ether gave 1.40 g. (33%) of the ether LXXXIX which was crystallized from methanol, m.p. 200-201°.

Ultraviolet spectrum

λmax. 232 mμ (ϵ 69,200), 280 mμ (ϵ 5,030), λ min. 250 mμ (ϵ 4,880), 300 mμ (ϵ 1,980).

Reduction of 1-(γ-Ketobutyl-)2-Naphthol (LXXXII)

A solution of 2.00 g. of 1-(γ-ketobutyl-)2-naphthol (LXXXII) in 30 ml. of tetrahydrofuran was added slowly to a mixture of 3.5 g. of lithium aluminum hydride and 30 ml. of tetrahydrofurom. The mixture was stirred for three hours under nitrogen, ethyl acetate added to decompose the excess hydride, and the mixture acidified with 1N hydrochloric acid. The aqueous layer was extracted with ether, and the combined organic solution washed with water, until the washings were neutral to litmus. Drying of the organic extracts over magnesium sulfate and removal of the solvent led to 1.92 g. (94%) of a solid material which on crystallization from ether gave 1-(γ-hydroxybutyl-)2-naphthol (XC), m.p. 136-37°.

Anal.

Calcd. for $C_{14}H_{16}O_2$: C, 77.74; H, 7.43. Found: C, 77.75; H, 7.46.

Methylation of 1-(γ-Hydroxybutyl-)2-Naphthol (XC)

The sodium salt of 1.0 g. of 1-(γ-hydroxybutyl-)2-naphthol (XC) was prepared as described for the preparation of sodium salt of 1-methyl-2-naphthol, 30 ml. of methyl iodide was added, and the mixture was refluxed for four hours. The mixture was extracted with chloroform, and the combined organic layer was dried over magnesium sulfate, and evaporated to remove the solvent. The crude oily residue was chromatographed over alumina. Elution with 1:1 petroleum ether-benzene gave a solid, which on crystallization from petroleum ether-carbon tetrachloride yielded 0.25 g. (23%) of methyl 1-(δ-hydroxybutyl-)2-naphthyl ether (XCII), m.p. 61-62°.

Ultraviolet spectrum

λmax. 232 mμ (ϵ 109,000) and 282 mμ (ϵ 11,100), λ shoulder 270 mμ (ϵ 8,830) and 295 mμ (ϵ 8,900), λ min. 252 mμ (ϵ 4,150) and 305 mμ (ϵ 2,940).

Anal.

Calcd. for $C_{15}H_{18}O$: C, 78.23; H, 7.88. Found: C, 78.53; H, 7.99.

Elution with benzene gave 0.58 g. (54%) of 1-methyl-(-hydroxybutyl-)2(1H)-naphthalenone (XCI) as an oil.

Ultraviolet spectrum

λ max. 232 mμ (ϵ 62,000) and 300 mμ (ϵ 8,150), λ min. 252 mμ (ϵ 1,490).

Its 3,5-dinitrobenzoate was crystallized from carbon tetrachloride, m.p. 138-139°.

Anal.

Calcd. for $C_{22}H_{20}O_7N_2$: C, 62.26; H, 4.75. Found: C, 62.18; H, 4.82.

Reduction of 1-Methyl-1-(γ-Hydroxybutyl-)2(1H)-Naphthalenone (XCI)

A solution of 0.40 g. of the hydroxyketone (XCI) in 30 ml. of ethanol was hydrogenated over 0.04 of 10% palladium on carbon at room temperature and atmospheric pressure until hydrogen uptake ceased. The mixture was filtered and evaporated. The remaining 0.38 g. of an oil was used for oxidation without further purification.

Oxidation of 1-Methyl-1-(γ-Hydroxybutyl-)2-Tetralone (C)

A chromic acid solution containing 50 mg. of chromic oxide dissolved in 0.2 ml. of water and 3 ml. of acetic acid was added to a solution of 100 mg. of the hydroxyketone (C) in 3 ml. of glacial acetic acid. The resulting mixture was allowed to stand at room temperature for three hours. The mixture then was diluted with water and extracted with ether. The extract was washed with 2% sodium hydroxide solution and then with water, dried over magnesium sulfate, and the solvent evaporated. The crude product was chromatographed over alumina. Elution with 10:1 petroleum ether-benzene gave 65 mg. (65%) of the diketone (XCIV) as an oil.

Ultraviolet specta

λ max. 265 mμ (ε 472) and 272 mμ (ε 480), λ min. 248 mμ (ε 322) and 270 mμ (ε 374).

The bis-2,4-dinitrophenylhydrazone was crystallized from ethanol, m.p. 181-182°.

Anal.

Calcd. for $C_{27}H_{26}O_8N_8$: C, 54.92; H, 4.43. Found: C, 55.36; H, 4.39.

2-Methyl-5:6-Benzchroman (XCIII)

A mixture of 200 mg. of methyl 1-(γ -hydroxybutyl-)2-naphthyl ether (XCII) and 0.5 ml. of concentrated hydrochloric acid in 30 ml. of 60% aqueous ethanol was refluxed for three hours. The mixture was extracted with ether, the extract washed with water, dried over magnesium sulfate, and the solvent evaporated. Alumina chromatography of the crude residue and elution with petroleum ether gave 82 mg. (42%) of 2-methyl-5:6-benzchroman (XCIII), which was crystallized from hexane, m.p. 90-91°.

Ultraviolet spectrum

λ max. 234 mμ (ϵ 60,000) and 280 mμ (ϵ 4,680), λ shoulder 270 mμ (ϵ 4,130) and 290 mμ (ϵ 3,770), λ min. 250 mμ (ϵ 2,440) and 300 mμ (ϵ 992).

Elution with benzene first gave a solid, which after crystallization from carbon tetrachloride proved to be starting material (45 mg., 22%) and secondly another solid, which on crystallization from ether yielded 12 mg. (6%) of 1-(γ-hydroxybutyl-)2-naphthol (XC), m.p. 135-137°. This material was in all respects identical with the authentic material.

Acetylation of 1-(γ-Hydroxybutyl-)2(1H)-Naphthalenone (XCI)

A solution of 100 mg. of XCI in 3 ml. of acetic anhydride and 1 ml. of pyridine was left standing in the refrigerator for 12 hours. After dilution with water, the mixture was extracted with ether and the extract washed with dilute hydrochloric acid, sodium carbonate solution and water. The extract then was dried over magnesium sulfate, the solvent evaporated and the residue chromatographed over alumina. Elution with 5:1 petroleum ether-benzene gave 92 mg. (77%) of oily 1-methyl-1-(γ-acetoxybutyl-)2(1H)-naphthalenone (CII).

Reduction of 1-Methyl-1-(γ-Acetoxybutyl-)2(1H)-Naphthalenone (CII)

The ketoacetate (CII), 90 mg. dissolved in 20 ml. of ethanol was hydrogenated over 0.01 g. of 5% palladium on carbon at room temperature and atmospheric pressure until hydrogen uptake ceased. The crude material obtained, after removal of the solvent, was chromatographed over alumina. Elution with petroleum ether gave 10 mg. (11%) of CV.

Ultraviolet spectrum

λmax. 258 mμ (ϵ 1,110), λmin. 248 mμ (ϵ 1,050).

Elution with 10:1 petroleum ether-benzene gave 47 mg. (52%) of oily 1-methyl-1-(γ-acetoxybutyl-)2-tetralone (CIII).

Ultraviolet spectrum

λmax. 266 mμ (ϵ 925) and 272 mμ (ϵ 900), λmin. 248 mμ (ϵ 535) and 270 mμ (ϵ 725).

Finally, elution with benzene afforded 22 mg. (24%) of an oil which may be hydroxyacetate CIV.

Ultraviolet spectrum

λmax. 265 mμ (ϵ 960) and 272 mμ (ϵ 950), λmin. 250 mμ (ϵ 696) and 270 mμ (ϵ 795).

Hydrolysis of 1-Methol-1-(γ-Acetoxybutyl-)2-Tetralone (CIII)

A mixture of 100 mg. of the ketoacetate CIII in 20 ml. of methanol and 2 ml. of saturated sodium carbonate solution was refluxed for three hours. The mixture was made acidic with acetic acid, evaporated to dryness and the residue extracted with ether. The extract was washed with water, dried over magnesium sulfate and evaporated under vacuum. The remaining colorless oil, 78 mg. (95%), exhibited an infrared spectrum possessing the characteristics of the hemiketal CI.

Reduction of 1-Methyl-1-(γ-Hydroxybutyl-)2(1H)-Naphthalone (XCI)

A solution of 120 mg. of the compound XCI in 10 ml. of dry ethanol and 50 ml. of liquid ammonia was stirred while 500 mg. of lithium wire was added over a 15 minute period during which the solution became deep blue in color and gradually again colorless. Ether (20 ml.) was added slowly and the ammonia evaporated by warming the flask in a water bath. Water (150 ml.) was added and the aqueous layer extracted with ether. The combined extracts were washed with saturated brine solution, dried over magnesium sulfate and evaporated to dryness. The resulting oily diol mixture was used for oxidation without further purification.

Oxidation of the Lithium Reduction of XCI

All of the product obtained from lithium reduction of 120 mg. of the compound XCI was dissolved in 8 ml. of glacial acetic acid and was added to a mixture of 150 mg. of chromium trioxide dissolved in 0.8 ml. of water and 8 ml. of acetic acid. After the work-up as described above, 99 mg. (82% overall) of spectrally pure diketone XCIV was obtained.

Oxidation of 1-methyl-1-(γ-Hydroxybutyl-)2(1H)-Naphthalenone (XCI)

The hydroxyketone XCI (500 mg.) in 13 ml. of glacial acetic acid was added to a solution of 250 mg. of chromic acid in 1 ml. of water and 13 ml. of acetic acid, and the mixture was allowed to stand at room temperature for three hours. After the usual work-up and chromatography of the crude product over alumina, 0.41 g. of the diketone XCV was obtained from the 5:1 petroleum ether-benzene eluate.

Its mono-2,4-dinitrophenylhydrazone was crystallized from ethanol-ethyl acetate, m.p. 155-156°.

Anal.

Calcd. for $C_{21}H_{20}O_5N_4$: C, 61.76; H, 4.94; N, 13.72. Found: C, 61.61; H, 5.27; N, 13.72.

Reaction of 1-Methyl-1-(γ-Ketobutyl-)2(1H)-Naphthalenone (XCX) with Base

Depending on the catalyst and solvent used, different products or mixtures of products were obtained.

Sodium ethoxide

A sodium ethoxide solution, 10 mg. of sodium in 20 ml. of dry ethanol, containing 50 mg. of the diketone XCX, was kept at room temperature for eight hours. The solution then was acidified with acetic acid, concentrated to a reduced volume, diluted with water and extracted with ether. The extract was dried over magnesium sulfate, the solvent was evaporated, and the residue was chromatographed over alumina. Elution with 1:1 petroleum ether-ether gave 30 mg. (85%) of 1-methyl-2-naphthol, m.p. and mixed m.p. 109-110°. It exhibited the identical infrared spectrum as an authentic sample.

Sodium methoxide

The same product, 1-methyl-2-naphthol, was obtained when the compound XCX was treated with a methanolic solution of sodium methoxide.

Potassium t-butoxide

To a solution of 10 mg. of potassium in 5 ml. of *t*-butanol there was added 100 mg. of the diketone (XCX), dissolved in 5 ml. of *t*-butanol, and the mixture was kept at room temperature for ten hours. The mixture was diluted with water, neutralized with acetic acid and extracted with ether. The organic extract was washed with water, dried over anhydrous magnesium sulfate and evaporated to dryness. Alumina chromatography of the oily residue and elution with 20:1 petroleum ether-ether led to 25 mg. of an oil. Elution with 10:1 petroleum ether-ether yielded 55 mg. (78%) of 1-methyl-2-naphthol, as identified by m.p. and infrared and ultraviolet spectra. Rechromatography of the oily eluate, obtained above, on 50:50 Celite-silicic acid and elution with 10:1 petroleum ether-ether gave 8 mg. (8%) of diketone XCIX, m.p. 105-107°. It revealed an identical infrared spectrum with that of an authentic specimen. Elution with 5:1 petroleum ether-ether gave 10 mg. of an unidentified solid, m.p. 176-179° after crystallization from petroleum ether-carbon tetrachloride.

Reduction of 1-Methyl-1-(γ -Ketobutyl-)2(1H)-Naphthalenone (XCV)

Hydrogenation of 50 mg. of the diketone XCV, dissolved in 25 ml. of ethanol, over 10 mg. of 5% palladium-charcoal at room temperature and atmospheric pressure, followed by filtration and removal of the solvent, led to an oily mixture which was chromatographed over alumina. Elution with petroleum ether gave 15 mg. of an unidentified solid, whose m.p. was 50-56° after crystallization from petroleum ether. It did not reveal OH or C=O bands in the infrared spectrum.

Ultraviolet spectra

λmax. 265 mμ (ϵ 482) and 272 mμ (ϵ 480), λmin. 248 mμ (ϵ 322) and 270 mμ (ϵ 374).

Elution with 10:1 petroleum ether-benzene gave 8 mg. (8%) of 1-methyl-1-(γ -ketobutyl-)2-tetralone (XCIV) as an oil; spectra identical with those of authentic material.

Finally, elution with benzene led to 20 mg. (40%) of the ketol LXV or XCVI, crystallized from hexane-carbon tetrachloride, m.p. 147-149°; identified from its infrared spectrum.

Anal.

Calcd. for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88. Found: C, 78.39; H, 8.34.

Reaction of 1-Methyl-1-(γ -Ketobutyl-)2-Tetralone (XCIV) with Base

Different reaction conditions led to a variety of products.

Low-temperature

A sodium methoxide solution, 10 mg. of sodium dissolved in 15 ml. of dry methanol, containing 25 mg. of 1-methyl-1-(γ-ketobutyl-)2-tetralone (XCIV) was kept in the refrigerator for 10 hours. After dilution with water, the mixture was extracted with ether. The combined organic layer was dried over magnesium sulfate, the solvent was evaporated, and the remaining oily residue was chromatographed over 1:1 Celite-silicic acid. Elution with 10:1 petroleum ether-ether yielded 12 mg. (48%) of a solid, m.p. 140-143°, crystallization from hexane-carbon tetrachloride gave the ketol LXV or XCVI, m.p. 147-149°; identical spectra with those of the above sample.

High-temperature

To a solution of 50 mg. of sodium in 20 ml. of methanol there was added 100 mg. of the diketone XCIV dissolved in 10 ml. of methanol. The mixture was refluxed for four hours, it then was acidified with acetic acid, the solvent removed under vacuum, and the remaining oil dissolved in ether. The ether solution was washed with water, dried over magnesium sulfate, and evaporated to dryness. The crude residue, 76 mg., was chromatographed over alumina. Elution with 5:1 petroleum ether-benzene led to 65 mg. (70%) of the tricyclic ketone LXVI, which was crystallized from hexane, m.p. 89-90°. The melting point was undepressed when admixed with authentic material. It revealed identical spectra with those of an authentic sample.

Reactions of 1-Methyl-1-Dichloromethyl-2(1H)-Naphthalenone (XXIX) with Bases

Potassium hydroxide in water

To a solution of 15 g. of potassium hydroxide in 75 ml. of water, there was added 5 g. of 1-methyl-1-dichloromethyl-2(1H)-naphthalenone (XXIX), and the resulting mixture was refluxed for 24 hours. The solution was then extracted with ether several times, until the last ether extract was colorless. The ether layer was dried over magnesium sulfate.

Upon evaporation of the solvent, 2.01 g. (50%) of crude starting material was obtained, which was crystallized from chloroform, m.p. 64-65°. The aqueous solution was acidified with 1N hydrochloric acid, extracted with ether. The ether extract, in turn, was washed with water and extracted with a saturated solution of sodium bicarbonate. The organic layer was washed with water, dried over magnesium sulfate leaving a residue, which was chromatographed and evaporated over Celite-silicic acid. Elution with 20% petroleum ether-ether led to 0.62 g. (18%) of 1-methyl-2-naphthol, m.p. 107-109° after purification from hexane. The sodium bicarbonate solution was acidified with 1N hydrochloric acid and extracted with ether. The crude solid material, remaining after removal of the solvent, was chromatographed over Celite-silicic acid. Elution with 20:1 petroleum ether-ether led to 0.84 g. (20%) of 1-(α-methyl-β-chlorovinyl-)cis-cinnamic acid (CIX), m.p. 110-112°, which was crystallized from methanol-water, m.p. 113-114°.

Ultraviolet spectrum

λ max. 260 mμ (ϵ 8,800), λ min. 245 mμ (ϵ 8,400).

Further elution with 20:1 petroleum ether-ether gave 0.07 g. (2%) of 1-methyl-3-naphthoic acid (CVIII), m.p. 199-203°, crystallized from methanol-water, m.p. 203-205°.

Its methyl ester was crystallized from hexane, m.p.

39-40°.

Ultraviolet spectrum

max. 238 mμ (ε 56,400) and 284 mμ (ε 8,280), λ min. 255 mμ (ε 3,900).

Finally, elution with 10:1 petroleum ether-ether led to an acid which upon repeated crystallization from ethanol-water melted at 205-210°.

Potassium hydroxide in ethanol-water

1-methyl-1-dichloromethyl-2(1H)-naphthalenone (3.0 g.) was added to a solution of 30 ml. of ethanol, 4 g. of potassium hydroxide and 15 ml. of H_2O, and the resulting mixture was refluxed for seven hours. After work-up as described above, three fractions, neutral, phenolic and acidic, were obtained.

The neutral fraction was dissolved in hexane and chromatographed over alumina. Elution with petroleum ether gave 1.55 g. of the starting ketone XXIX, which was crystallized from chloroform, m.p. 62-64°. Further elution with 30:1 petroleum ether-ether gave 0.05 g. of a solid, which was crystallized from hexane, m.p. 55°. The structure of this compound was not investigated.

Chromatography of the phenolic residue over Celite-silicic acid and elution with 20:1 petroleum ether-ether gave

0.081 g. (4%) of 1-methyl-2-naphthol, m.p. 107-109°.

The crude acidic fraction was crystallized twice from methanol-water, giving 0.85 g. (36%) of 1-methyl-3-naphthoic acid, m.p. 202-204°. The residue, remaining after removal of the solvent, was esterified with an ether solution of Ca. 0.5 g. of diazomethane and chromatographed over alumina. Elution with petroleum ether led to two fractions, which were hydrolyzed back to the corresponding acids by refluxing a solution of esters, 0.5 g. of potassium hydroxide, 10 ml. of ethanol and 2 ml. of water for two hours. The first fraction melting at 110-116° was crystallized a few times from hexane leading to 0.08 g. (4%) of 1-methyl-3-naphthoic acid, m.p. 195-198°, and 0.22 g. (9%) 1-(α-methyl-β-chlorovinyl-)cis-cinnamic acid, m.p. 110-112°. The second acid fraction was crystallized from cyclohexane, m.p. 205-209°. Its structure was not investigated.

Reaction of 1-Methyl-1-Dichloromethyl-2-Tetralone (LXXVII) with Base

Sodium hydroxide in ethanol-water

To a solution of 20 ml. of 20% sodium hydroxide there was added 3 g. of the ketone LXXVII dissolved in 25 ml. of ethanol, and the reaction mixture was refluxed under nitrogen for eight hours. The solution was concentrated under vacuum, diluted with water and extracted with ether. The ether extract was washed with water, dried over magnesium sulfate and evaporated, leaving 0.30 g. of the starting ketone LXXVII. The aqueous solution was acidified with 1N hydrochloric acid and extracted with ether. After drying and removal of the solvent, solid material was obtained, which was extracted with hexane. The residue, 0.65 g., was crystallized twice with methanol-water, leading to 1-methyl-3-naphthoic acid, m.p. 202-204°. The hexane solution was evaporated and the remaining 1.15 g. solid material was crystallized a few times from cyclohexane-hexane, which led to 1-methyl-3,4-dihydro-3-naphthoic acid CXIII, m.p. 94-95°.

<u>Ultraviolet spectrum</u>. λ max. 260 mμ (ϵ 10,200), λ min. 235 mμ (ϵ 3,580).

Hydrogenation of 1-Methyl-3,4-Dihydro-3-Naphthoic Acid (CXIII)

A solution of 100 mg. of the acid CXIII in 20 ml. of ethanol was hydrogenated over palladium-charcoal. After work-up as described above, 94 mg. (94%) of 1-methyl-1,2,3,4-tetrahydro-3-naphthoic acid (CXIV) was obtained, m.p. 124-125°.

Ultraviolet spectrum

λ max. 266 mμ (ϵ 532) and 273 mμ (ϵ 548), λ min. 248 mμ (ϵ 242) and 270 mμ (ϵ 333).

Anal.

Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.94; H, 7.42.

Sodium methoxide in methanol

A mixture of 2 g. of the ketone LXXVII, 0.2 g. of sodium in 40 ml. of methanol was refluxed under a nitrogen atmosphere for eight hours. After work-up as described above, neutral and acidic fractions were isolated. The neutral fraction exhibited infrared absorption bands at 5.6 and 5.85 due to the starting ketone LXXVII and the ketone CXV.

The acidic fraction was crystallized from hexane; 0.86 g. (55%) of 1-methyl-3-naphthoic acid (CVIII), m.p. 196-198°, was obtained. Further crystallization from methanol-water raised the m.p. to 203-205°.

The hexane extract was evaporated, leading to 0.21 g. of solid material, m.p. 108-116°, which was esterified with an ether solution of *ca.* 0.1 g. of diazomethane and chromatographed over alumina. Elution with petroleum ether gave 0.16 g. (10%) of pure methyl ester of 1-methyl-3,4-dihydro-3-naphthoic acid (CXIII). Further elution with petroleum ether yielded 0.02 g. (1%) of methyl ester of 1-methyl-3-naphthoic acid, which was crystallized from hexane, m.p. 38-40°.

Potassium t-butoxide in t-butanol

To a solution of 0.2 g. of potassium in 30 ml. of *t*-butanol, there was added 1.5 g. of the ketone LXXVII, and the reaction mixture was stirred at room temperature under a nitrogen atmosphere for 24 hours. The reaction mixture was diluted with water and extracted with ether. Drying and removal of the solvent led to an oily substance which was chromatographed over alumina. Elution with petroleum ether gave 0.86 g. of a mixture of the starting ketone LXXVII, and the ketone CXV, which on repeated chromatography over alumina could not be separated, but partly decomposed.

The aqueous solution was acidified with 1N hydrochloric acid and extracted with ether. The extract was dried over magnesium sulfate and evaporated to leave 0.32 g. (27%) of 1-methyl-3,4-dihydro-3-naphthoic acid (CXIII), m.p. 89-90°, which was crystallized from hexane, m.p. 91-92°.

Reaction of 1-Methyl-3,4-Dihydro-3-Naphthoic Acid (CXIII) with Base

A mixture of 200 mg. of the acid CXIII, 10 mg. of sodium in 15 ml. of methanol was refluxed for eight hours. The solution was acidified with 1N hydrochloric acid and extracted with ether. Removal of the solvent led to 192 mg. (96%) of 1-methyl-3,4-dihydro-3-naphthoic acid, m.p. 87-90°, which was crystallized from hexane, m.p. 91-93°.

Reaction of the Methyl Ester of 1-Methyl-3,4-Dihydro-3-Naphthoic Acid with Base

To a solution of 250 mg. of the acid CXIII in 10 ml. of ether there was added ether solution of ca. 0.3 g. of diazomethane. After allowing the solution to stand for 30 minutes, the ether and the excess diazomethane were removed. The resulting liquid was identified as the methyl ester of the acid CXIII by its infrared spectrum; no OH bands in the 2.8 to 3.1 μ region.

Ultraviolet spectrum

λmax. 260 mμ (ε 9,950), λmin. 235 mμ (ε 3,500).

The ester formed was added to a solution of 1.0 mg. of sodium in 15 ml. of methanol, and the mixture was refluxed under a nitrogen atmosphere for four hours. It was then diluted with water and extracted with ether. The ether extract was dried over magnesium sulfate and evaporated, leaving 95 mg. of a mixture of methyl esters of the acid CVIII and CXIII, which was identified as such by its ultraviolet spectrum.

The aqueous solution was acidified with 1N hydrochloric acid and extracted with ether. Removal of the solvent, after drying with magnesium sulfate, led to 112 mg. (45%) of

1-methyl-3-naphthoic acid whose crystallization from carbon tetrachloride-hexane gave m.p. 185-189°. Further crystallization from methanol-water raised the melting point to 195-198°.

Reaction of 1-Methyl-1-Chloromethyl-2-Tetralone (LXXXI) with Base

A mixture of 200 mg. of the ketone LXXXI in 10 ml. of t-butanol was added to a solution of 60 mg. of potassium in 20 ml. of t-butanol. The resulting mixture was stirred under nitrogen atmosphere for eight hours, after which it was concentrated to a reduced volume, diluted with water and extracted with ether. The extract was dried over magnesium sulfate, and the solvent was evaporated. A liquid substance (94 mg.) was obtained, which was shown to be a mixture of the starting material LXXXI and the ketone CXIX by its infrared spectrum.

The basic aqueous solution was acidified with acetic acid and extracted with ether. The organic layer was washed with water, dried over magnesium sulfate, and evaporated. Sublimation of the crude product (67 mg., 37%) led to an acid, m.p. 105-109°, which after two crystallizations from hexane was shown to be 1-methyl-1,2,3,4-tetrahydro-3-naphthoic acid (CXIV), m.p. 123-125°.

6-Methyl-6-Dichloromethyl-2,4-Cyclohexadienone (XXVII)

The procedure of von Auwers (35) was used to prepare the ketone XXVII, m.p. 32-33°.

Reduction of the Ketone XXVII

A solution of 2.65 g. of the ketone XXVII in 50 ml. ethanol was hydrogenated over 100 mg. of palladium-charcoal at room temperature and atmospheric pressure. After removal of catalyst and solvent, the oily residue was dissolved in petroleum ether and chromatographed over alumina. Elution with petroleum ether led to 2.18 g. of the known ketone CXX (63) m.p. 28-30°, which was crystallized from hexane m.p. 33-35°.

Its semicarbazone was crystallized from methanol-water, m.p. 195-196°.

Reaction of 2-Methyl-2-Dichloromethylcyclohexanone (CXXI) with Base

To a solution of 0.3 g. of potassium in 50 ml. of *t*-butanol there was added 1.3 g. of the ketone CXXI, and the mixture was stirred under nitrogen for 24 hours. The solution was concentrated under vacuum, diluted with water and extracted with ether. The extract was dried over magnesium sulfate and evaporated to dryness. This operation led to 0.82 g. of a mixture of CXX and CXXI.

The basic solution was acidified with 1N hydrochloric acid and extracted with ether. After drying of the extract over magnesium sulfate and removal of the solvent, 0.24 g. of an oily substance was obtained, the structure of which was not investigated.

Semicarbazone of the Ketone CXX

To a solution of 200 mg. of semicarbazide hydrochloride in 1 ml. of water there was added 145 mg. of the ketone CXX, 10 drops of pyridine and sufficient methanol to form a homogeneous solution. The reaction mixture was left on the steambath until crystalline semicarbazone of the ketone CXX precipitated. The solid substance was then filtered and crystallized from carbon tetrachloride. There was obtained 162 mg. (83%) of the desired semicarbazone, m.p. 219-222°. Further crystallization from methanol-water raised the melting point to 225-226°.

Hydrolysis of the Semicarbazone of the Ketone (CXX)

A solution of 50 mg. of the semicarbazone of the ketone CXX, 2 ml. of levulinic acid and 1 drop of 2N hydrochloric acid was left in the refrigerator with occasional shaking for

36 hours. The reaction mixture was then diluted with water and extracted with ether. The organic extract was washed with water, saturated solution of sodium bicarbonate and water again. The solution was dried, the solvent was removed, and the liquid substance (24 mg.) (65%) remaining was shown to be pure ketone CXX by its infrared spectrum.

Its semicarbazone was crystallized from methanol-water, m.p. 218-220°.

1-Methyl-3,4-Dihydro-2-Naphthoic Acid (CXXV)

The method of von Auwers was used to prepared 1-methyl-3,4-dihydro-2-naphthoic acid (CXXV), m.p. 129-130° (66).

<u>Ultraviolet spectrum</u>

λ max. 225 mμ (ϵ 15,400) and 282 mμ (ϵ 13,300), λ min. 240 mμ (ϵ 2,420).

Reduction of the Acid CXXV

A solution of 1.25 g. of the acid CXXV in 30 ml. of ethanol was hydrogenated over 100 mg. of palladium-charcoal at atmospheric pressure. After filtration and removal of the solvent, 1.18 g. (95%) of 1-methyl-1,2,3,4-tetrahydro-2-naphthoic acid (CXXVI) was isolated, which was crystallized from cyclohexane, m.p. 84-85°.

Ultraviolet spectrum

λ max. 265 mμ (ϵ 564) and 272 mμ (ϵ 515), λ min. 250 mμ (ϵ 310) and 270 mμ (ϵ 400).

Anal.

Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.83; H, 7.29.

Methyl 1-Methyl-1,2,3,4-Tetrahydro-2-Naphthoic (CXXVII)

To a solution of 1.0 g. of the acid CXXVI in 15 ml. of ether there was added an ether solution of ca. 0.5 g. of diazomethane. After allowing the resulting mixture to stand for 30 minutes, the ether and excess diazomethane were removed by evaporation under reduced pressure at room temperature. The resulting liquid ester CXXVII (1.02 g., 95%) showed no OH bands in the infrared spectrum.

Reaction of the Ester CXXVII with Base

To a solution of 0.15 g. of sodium in 25 ml. of methanol there was added 1.0 g. of the ester CXXVII dissolved in 10 ml. of methanol, and the mixture was refluxed for two hours. Water (5 ml.) was then added and the solution was refluxed for another two hours. The aqueous solution was acidified with 1N hydrochloric acid and extracted with ether. The ether layer was dried and evaporated, leaving 0.91 g. of a solid substance, m.p. 80-85°, which was crystallized from hexane, m.p. 83-85°. A mixed melting point of this acid and the acid CXXVI (m.p. 84-85°) was 83-85°.

Reduction of 1-Methyl-1-Dichloromethyl-2-Tetralone (LXXVII)

Method A

Lithium aluminum hydride (200 mg.) in 10 ml. of ether was placed in a flask equipped with a magnetic stirrer, condenser and separatory funnel. Anhydrous tert-butyl alcohol (1.5 ml.) was added slowly through the separatory funnel. The solvent was removed under vacuum, the solid residue was dissolved in 10 ml. diglyme, to which 200 mg. of the compound in 5 ml. of diglyme was added slowly. The resulting mixture was stirred for two hours. After extraction with ether, the organic layer was dried over $MgSO_4$ and evaporated, leading to 185 mg. (93%) of a solid material, m.p. 70-73°, which was crystallized from hexane, m.p. 73-74°. Mixed melting point with an authentic sample of LXXVI (m.p. 75-76°) was 73-75°.

Method B

A solution of 0.5 g. of the ketone LXXVII in 10 ml. of tetrahydrofuran was added to a stirred solution of 0.5 g. of lithium aluminum hydride in 10 ml. of tetrahydrofuran. The resulting mixture was stirred for two hours. The excess lithium aluminum hydride was reacted with ethyl acetate, the basic solution was acidified with 1N hydrochloric acid and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated to remove the solvent. The solid residue was dissolved in petroleum ether and chromatographed over alumina. Elution with 5:1 petroleum ether-benzene gave 0.42 g. (82%) of the alcohol II, m.p. 71-75°, which was crystallized from hexane, m.p. 75°. No depression in its melting point was observed when it was mixed with an authentic sample.

Equilibration of the Alcohol LXXVI

To 25 ml. of dry isopropyl alcohol there were added 1.00 g. of the alcohol LXXVI, 0.9 g. of aluminum isopropoxide and 3 drops of acetone, and the resulting mixture was refluxed for 90 hours. At the end of the reflux period 50 ml. of water along with sufficient 1N hydrochloric acid to neutralize the solution was added, and the mixture was extracted with ether. The ether extract was washed with water and saturated sodium chloride solution, dried over magnesium sulfate, and evaporated. Solid material (0.69 g., 69%) was obtained, m.p. 70-74°, which was crystallized from hexane, m.p. 73-75°. Mixed m.p. with an authentic sample was 73-75°.

SUMMARY

The reactions of the salts of 1-substituted-2-naphthols with alkyl halides are illustrated, and structures of the products proposed.

A new synthetic route to a hydrophenanthrone is presented, which takes advantage of the ease of C-methylation of 1-substituted-2-naphthol salts.

The reactions of 1-methyl-1-dichloromethyl-2(1H)-naphthalenone and its dihydro compound with various bases are investigated, and structures of the reaction products and mechanisms for their formation are presented.

LITERATURE CITED

1. G. S. Hiers and F. D. Hager, Anisole, in Organic Synthesis, Collective Vol. 1, pp. 58-60. John Wiley and Sons, Inc., New York, N. Y. 1948.

2. L. Claissen, *Ber.*, *45*, 3157 (1912)

3. L. Claissen and O. Eisleb, *Ann.*, *401*, 21 (1913)

4. L. I. Smith, H. E. Ungnade, W. M. Lauer and R. M. Leekley, *J. Am. Chem. Soc.*, *61*, 3059 (1925)

5. L. Claissen, *Z. Angew. Chem.*, *36*, 478 (1923)

6. L. Claissen, F. Kremers, F. Roth and E. Tietze, *Ann.*, *442*, 210 (1925)

7. G. S. Misra and R. S. Asthana, *ibid.*, *609*, 240 (1957)

8. N. Kornblum and A. P. Lurie, American Chemical Society, Abstracts of Papers, 14N (1958)

9. S. A. Miller and R. Robinson, *J. Chem. Soc.*, 1535 (1934)

10. F. J. McQuillin and R. Robinson, *ibid.*, 586 (1941)

11. A. F. Hardman, *J. Am. Chem. Soc.*, *70*, 2119 (1948)

12. S. Winstein and R. Baird, *J. Am. Chem. Soc.*, *79*, 757 (1957)

13. S. Winstein and R. Baird, *ibid.*, *79*, 4238 (1957)

14. A. S. Dreiding, *Helv. Chim. Acta.*, *40*, 1812 (1957)

15. K. H. Meyer and H. Schlosser, *Ann.*, *420*, 126 (1920)

16. J. Herzig and F. Wenzel, Monatsh., *27*, 781 (1906)

17. A. Spitzer, *ibid.*, *11*, 287 (1890)

18. A. C. Jain and T. R. Seshadri, *Proc. Indiana Acad. Sci.*, *42A*, 279 (1955)

19. V. A. Zagorevsky, *J. Gen. Chem.* (U.S.S.R.), *27*, 3055 (1957)

20. V. A. Zagorevsky, *ibid.*, *28*, 488 (1958)

21. L. Claissen and E. Tietze, *Ber.*, *59*, 2344 (1926)

22. D. Y. Curtin and R. J. Crawford, *Chem. and Ind.*, 313 (1936)

23. D. Y. Curtin and R. J. Crawford, *J. Am. Chem. Soc.*, *79*, 3156 (1957)

24. D. Y. Curtin, R. J. Crawford and M. Wilhelm, *ibid.*, *80*, 1391 (1958)

25. D. Y. Curtin and M. Wilhelm, *J. Org. Chem.*, *23*, 9 (1958)

26. R. M. Dodson and W. Webb, University of Minnesota, private communication, 1957.

27. R. M. Dodson and W. Webb, *J. Am. Chem. Soc.*, *73*, 2767 (1951)

28. D. Y. Curtin and R. R. Fraser, *Chem. and Ind.*, 1358 (1957)

29. T. L. Brown, D. Y. Curtin and R. R. Fraser, *J. Am. Chem. Soc.*, *80*, 4339 (1958)

30. D. Y. Curtin and R. R. Fraser, *ibid.*, *80*, 6016 (1958)

31. K. Reimer and F. Tiemann, *Ber.*, *9*, 824 (1876)

32. K. Auwers, *ibid.*, *17*, 2976 (1884)

33. K. Auwers, *ibid.*, *32*, 3598 (1899)

34. K. Auwers and F. Winternitz, *ibid.*, *35*, 465 (1902)

35. K. Auwers and G. Keil, *ibid.*, *35*, 4207 (1902)

36. K. Auwers, *ibid.*, *18*, 2655 (1885)

37. R. C. Fuson and T. Miller, *J. Org. Chem.*, *17*, 316 (1952)

38. K. Auwers and G. Keil, *Ber.*, *36*, 3902 (1903)

39. K. Auwers and G. Keil, *ibid.*, *38*, 1693 (1905)

40. K. Auwers and M. Hessenland, *ibid.*, *41*, 1790 (1908)

41. K. Auwers and F. von der Heyden, *ibid.*, *42*, 2404 (1909)

42. R. B. Woodward, *J. Am. Chem. Soc.*, *62*, 1208 (1940)

43. M. S. Gibson, *Experientia*, *7*, 176 (1951)

44. J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 676 (1946)

45. C. A. Grob and W. Junt, *Helv. Chim. Acta.*, *31*, 1691 (1948)

46. G. Stork and J. W. Schulenbeg, *J. Am. Chem. Soc.*, *78*, 250 (1956)

47. G. Stork, J. J. E. Loewenthal and P. C. Mukharji, *ibid.*, *78*, 501 (1956)

48. E. Wenkert and T. E. Stevens, *ibid.*, *78*, 2318 (1956)

49. E. Wenkert and T. E. Stevens, *ibid.*, *78*, 5627 (1956)

50. M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson and E. A. Bowler, *ibid.*, *72*, 3704 (1950)

51. R. Adams and J. Levine, *ibid.*, *45*, 2375 (1923)

52. K. Fries and E. Hubner, *Ber.*, *39*, 435 (1906)

53. K. Fries and E. Hemplemann, *Ber.*, *41*, 2614 (1908)

54. P. Petrenko-Kritshenko and V. Opotsky, *Ber.*, *59B*, 2131 (1926)

55. J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956.

56. S. A. Miller and R. Robinson, *J. Chem. Soc.*, 1535 (1934)

57. K. Ch. Gulati, S. R. Seth and Venkataraman, *J. Prakt. Chem.*, *137*, 47 (1933)

58. F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 588 (1941)

59. G. Darzens, *Compt. Rend.*, *183*, 749 (1926)

60. C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953

61. M. Kotake and H. Nonaka, *Ann.*, *607*, 153 (1957)

62. E. P. Blantchard, Jr., *Chem. and Ind.*, 293 (1958)

63. K. Auwers and E. Lange, *Ann.*, *401*, 317 (1913)

64. C. H. DePuy and B. W. Ponder, Levulinic Acid as a Reagent for the Hydrolysis of Oximes and 2,4-Dinitrophenylhydrazones, to be published in *J. Am. Chem. Soc.*, [*ca.* 1959] .

65. E. Wenkert and B. Jackson, *J. Am. Chem. Soc.*, *80*, 211 (1958)

66. K. Auwers and K. Moller, *J. Prakt. Chem.*, *109*, 124 124 (1925)

ACKNOWLEDGEMENT

The author is indebted to Dr. Ernest Wenkert for suggesting this problem and for guidance during the course of the investigation.

He wishes to thank the National Science Foundation, Ciba Pharmaceutical Products, Inc. and Proctor and Gamble Co. for their financial support.

Special thanks are due the Institute for Atomic Research, Iowa State College, for the use of the Baird instrument.