Oxidation of 4-Acetoxy-2,6-dimethylphenol (4) with Lead Dioxide.—A solution of 600 mg of **4** in 10 ml of glacial acetic acid was heated with 700 mg of lead dioxide until a pale yellow homogeneous solution was obtained. Vpc analysis showed essentially quantitative conversion into 2,6-dimethylbenzoquinone.

Acknowledgments.—The authors wish to thank Dr. Hans-Dieter Becker for a gift of nickel peroxide and Dr. John B. Bush, Jr., for a gift of manganese dioxide.

The Synthesis of 2-Methyl-3-vinyl-1,4-naphthoquinones[1]

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Chlorobiumquinone, previously isolated from *Chlorobium thiosulfatophilum* and characterized as a 2-methyl-3-vinylmultiprenyl-1,4-naphthoquinone, is unique among natural multiprenylquinones in being a vinyl- rather than an allylquinone. Various approaches to the synthesis of 2-methyl-3-vinyl-1,4-naphthoquinones have been studied, and two general syntheses have been developed, both constructing the substituted vinyl side chain *via* the Wittig reaction. A primary requirement for both methods was a protecting protocol for the 1,4-oxygen functions which would be inert to the ylide yet would allow generation of the quinone without destruction of the vinyl group. Such functionality was provided by the 1-pivalate ester–4-methyl ether. These groups do not react with the ylide, and removal of the ester with lithium aluminum hydride and oxidation of the 1-hydroxy-4-methoxy compound with ferric chloride gave quinone while leaving the vinyl side chain intact. One synthesis proceeded *via* 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate which was converted into its triphenylphosphonium salt and thence to vinyl derivative by generation of the naphthalenic ylide and reaction with a carbonyl component. The other synthesis utilized the 3-naphthaldehyde, prepared from the chloromethyl compound and potassium 2-propanenitronate, in reaction with the appropriate ylide. To avoid isomers, some secondary ylides were prepared by alkylation of primary ylides. The relative advantages and disadvantages of both methods are considered. The separate, isomeric vinyl compounds were obtained, and *cis* and *trans* stereochemical assignments were made by relating their nmr absorptions to those of unambiguous synthetic models. Various vinyl substitution patterns can be easily distinguished from the ultraviolet absorption of the resulting 2-methyl-3-vinyl-1,4-naphthoquinones.

We have reported the isolation and structure determination of chlorobiumquinone (I), a novel 2-methyl-3-vinylmultiprenylnaphthoquinone isolated from the anaerobic, photosynthetic sulfur bacterium, *Chlorobium thiosulfatophilum*, strain PM.[5,6] Chlorobiumquinone is unique[7] among the menaquinones, ubiquinones, and plastoquinones found in nature in that it has a double bond conjugated with the ring moiety and the side chain contains one carbon less than the multiples of five found in all other natural multiprenylquinones. Hence, chlorobiumquinone may be visualized as menaquinone-7 (II),[8] which also occurs in *C. thiosulfatophilum*, minus the 1′-methylene, rather than as a double-bond isomer.

Our interest in the chemistry of chlorobiumquinone, especially as it relates to a possible role for the quinone in photosynthesis and oxidative phosphorylation in *C. thiosulfatophilum*[9] and the fact that vinylquinones are a little studied class of compounds (except for their use in polymerizations) have led us to develop general methods for the synthesis of vinylnaphthoquinones, which is the subject of this paper.

The syntheses reported in the literature have been designed for the preparation of vinylhydroquinone diesters or diethers with vinyl moieties bearing no substitutents, the object being the preparation of monomers from which a redox polymer might be obtained.[10]

Most of the vinylhydroquinones and vinylhydroquinone derivatives have been prepared by (1) synthesis and decarboxylation of a 2,5-dihydroxy cinnamic acid, (2) reduction of the ketone moiety of an acetylhydroquinone diacetate and dehydration of the resulting alcohol, or (3) metalation or formation of the Grignard reagent of a hydroquinone diether followed by reaction with ethylene oxide or acetaldehyde and dehydration of the resulting alcohol. The reverse of 3, formation of the diether of a 2,5-dihydroxybenzaldehyde followed by reaction with methyllithium or a Grignard reagent, is also known. In only one case did the vinyl group contain a substituent and that was an α-methyl group.[11]

Several 2-hydroxy-3-(1-alkenyl)-1,4-naphthoquinones (IV) have been prepared by heating 2-hydroxy-1,4-naphthoquinone (III) with a variety of straight-chain, aliphatic aldehydes and hydrochloric acid in acetic acid.[12] Under these conditions 1,4-naphthoquinones (V) do not yield (1-alkenyl)-1,4-naphthoquinones (VI) but give instead pigments of the anthocyanidin type,[13] VII. By moderating the conditions, however, 2-methyl-1,4-naphthoquinone (VIII) was successfully condensed with acetaldehyde and hydrogen bromide to afford 2-methyl-3-(1-bromoethyl)-1,4-naphthoquinone

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(2) National Institutes of Health Predoctoral Fellow.

(3) Facultad de Farmacia y Bioquimica, Universidad de Buenos Aires, Buenos Aires, Argentina.

(4) National Science Foundation Undergraduate Research Participant.

(5) B. Frydman and H. Rapoport, *J. Amer. Chem. Soc.*, **85**, 823 (1963); menaquinone-7 also was isolated.

(6) R. Powls and E. R. Redfearn [*Biochem. J.*, **102**, 3c (1967)] also have isolated chlorobiumquinone and menaquinone-7 from *C. thiosulfatophilum*.

(7) A quinone detected spectrophotometrically in *Sarcina lutea* also may be of this type: D. H. L. Bishop, K. P. Pandya, and H. K. King, *ibid.*, **83**, 606 (1962).

(8) IUPAC–IUB Commission on Biochemical Nomenclature Tentative Rules, *Arch. Biochem. Biophys.*, **118**, 505 (1967).

(9) I. Chmielewska [*Biochem. Biophys. Acta*, **39**, 170 (1960)] has postulated the intermediacy of a vinylquinone in the mechanism of the quinone's role in oxidative phosphorylation.

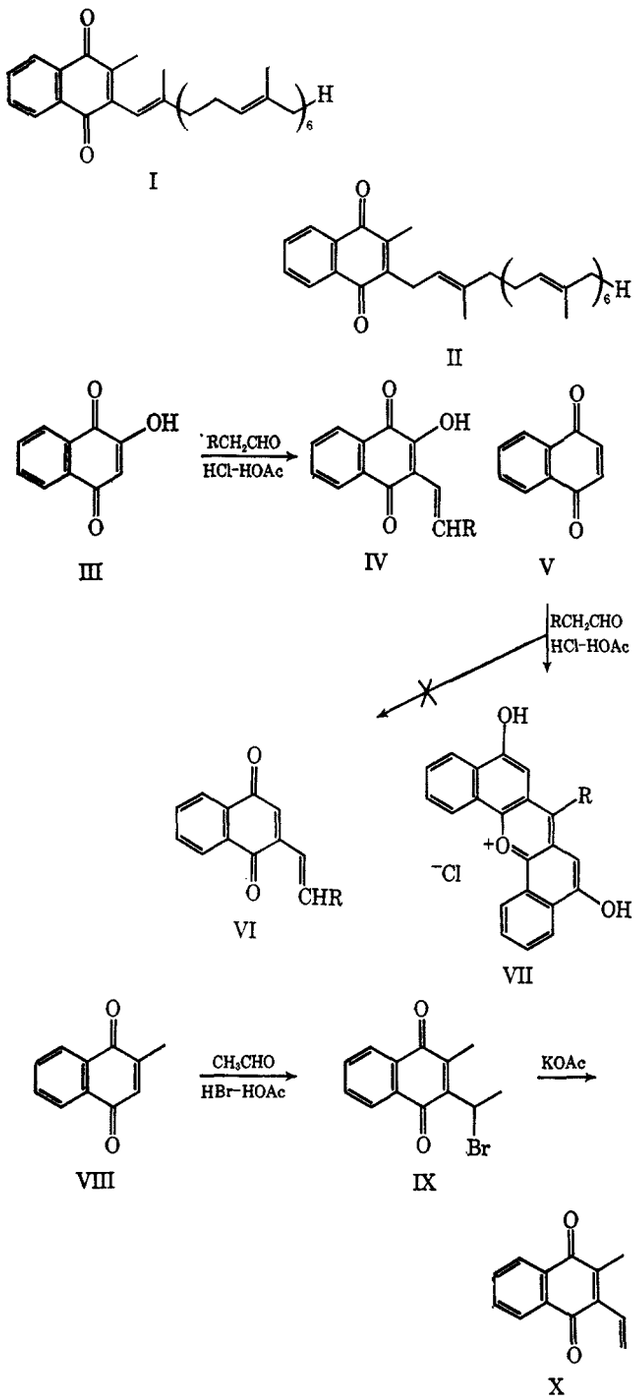
(10) For a review of the synthesis of vinylhydroquinones, see H. C. Cassidy and K. A. Kun, "Polymer Reviews," Vol. 11, Interscience Publishers, New York, N. Y., 1965, Chapter 2.

(11) J. M. Bruce and P. Knowles, *J. Chem. Soc., C*, 1627 (1966).

(12) S. C. Hooker, *J. Amer. Chem. Soc.*, **58**, 1163, 1168 (1936).

(13) M. Fieser and L. F. Fieser, *ibid.*, **63**, 1572 (1941).

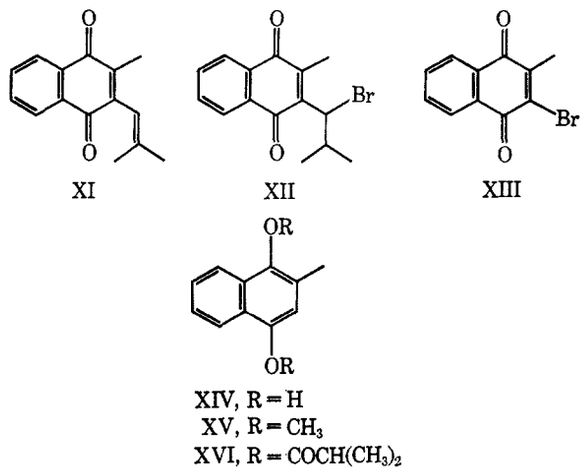
SCHEME I



(IX) which was dehydrohalogenated to 2-methyl-3-vinyl-1,4-naphthoquinone (X).[14] See Scheme I.

While some of these methods are not applicable to the preparation of β,β-dialkylvinylnaphthoquinones of the chlorobiumquinone type, others held promise, and suitable modifications were studied, as well as new methods.

Direct Introduction of the Vinyl Side Chain.—We first investigated those reactions which would allow direct introduction of a vinyl side chain or of a vinyl side chain precursor. Our initial goal was the synthesis of 2-methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI) which contains many of the features present in I. Following the method used for the preparation of 2-methyl-3-vinyl-1,4-naphthoquinone (X), isobutyraldehyde was condensed with 2-methyl-1,4-naphthoquinone (VIII), but no 2-methyl-3-(1-bromo-2-methylpropyl)-1,4-naphthoquinone (XII) could be isolated. The only product was a small amount of 2-methyl-3-bromo-1,4-naphthoquinone (XIII).[15]



A second approach which was investigated for the direct introduction of the entire vinyl side chain was alkenylation with an α,β-unsaturated diacyl peroxide. The preparation of 2-methyl-3-(1-hexadecenyl)-1,4-naphthoquinone by this method has been reported;[16] however, parallel reactions with other α,β-unsaturated acyl peroxides were reported to fail.[16,17] We carried out the reaction with β,β-dimethylacryloyl peroxide and 2-methyl-1,4-naphthoquinone (VIII). No alkenylation product was obtained and only starting quinone was recovered.

Our third approach was to introduce the vinyl side chain precursor by preparing the acyl derivative which could then be reduced and dehydrated. This was first attempted by acylating 1,4-dimethoxy-2-methylnaphthalene[18] (XV) with isobutyryl chloride and aluminum chloride. Acylation occurred, as indicated by the nmr signals for one isobutyryl group, but it had entered the unsubstituted ring since the C-3 proton signal was undiminished. Fries rearrangement of 2-methyl-1,4-naphthalenediol diisobutyrate (XVI) also failed.

Building the Vinyl Side Chain on a Substituted Naphthohydroquinone.—Inability to introduce the vinyl side chain directly led us to approach the synthesis by first inserting a functionalized carbon at C-3 and then building the vinyl side chain on this carbon. As a model, the 2-aminoethyl compound XIX was prepared, since success in eliminations with this compound could be translated to secondary and tertiary amines for the corresponding substituted vinyl derivatives. The 2-aminoethyl compound XIX was prepared from 3-chloromethyl-1,4-dimethoxy-2-methylnaphthalene (XVII) by treatment with aqueous sodium cyanide to give the nitrile XVIII followed by lithium

(14) G. Manecke and W. Storck, *Ber.*, **94**, 300 (1961).

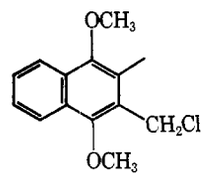
(15) R. H. Thomson [*J. Chem. Soc.*, 1196 (1953)] has reported that formaldehyde, acetaldehyde, and benzaldehyde react with 2-methyl-1,4-naphthoquinone to give 3-(1-chloroalkyl) derivatives whereas propionaldehyde, 2-naphthaldehyde, and 2-formylthiophene instead gave only traces of 2-methyl-3-chloro-1,4-naphthoquinone.

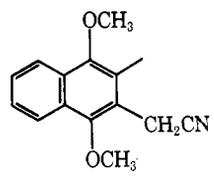
(16) L. F. Fieser and A. E. Oxford, *J. Amer. Chem. Soc.*, **64**, 2060 (1942); L. F. Fieser, U. S. Patent 2,398,418 (1946).

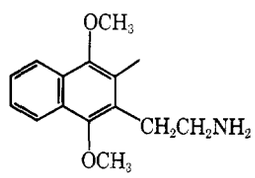
(17) L. F. Fieser, M. T. Leffler, and coworkers, *J. Amer. Chem. Soc.*, **70**, 3175, 3195 (1948).

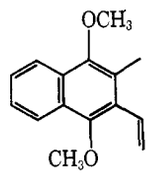
(18) S. Ansbacher, E. Fernholz, and M. A. Dolliver, *ibid.*, **62**, 155 (1940).

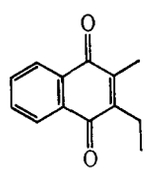
aluminum hydride reduction to amine XIX. Exhaustive methylation to the quaternary methiodide followed by heating in alkali gave a good yield of 1,4-dimethoxy-2-methyl-3-vinylnaphthalene (XX). However, ether


XVII


XVIII


XIX


XX

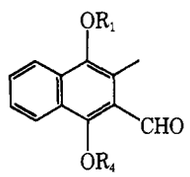

XXI

cleavage with acidic reagents[19] proceeded in very poor yield and subsequent oxidation gave the vinylquinone X in only 10% yield from dimethoxy compound XX. Significant by-products in this reaction were 2-methyl-1,4-naphthalenediol (XIV) and the ethylquinone XXI, which may be considered as a tautomer of the intermediate 2-methyl-3-vinyl-1,4-naphthohydroquinone. Loss of the entire vinyl side chain in such ether-cleaving reactions has been observed previously[19] with benzohydroquinones; however, conversion into the ethylquinone has not been heretofore reported.

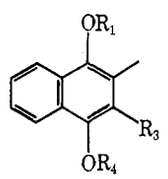
Although this Hofmann elimination approach was abandoned because of its complexity and the poor yield in the ether cleavage step, it clearly established that a protecting protocol other than methylation–demethylation had to be developed for a successful, general synthesis of vinylquinones.

Synthesis of Vinyl Side Chain Using Wittig Reaction.—The failures and limitations of the various methods considered above directed our attention to the use of the Wittig reaction. This method has been used to prepare a number of vinyl-1,4-dimethoxybenzenes,[19,20] but conversion into the corresponding quinones was thwarted at the ether cleavage stage. Thus the problem became one of finding protecting groups compatible with the Wittig reagent and removable without destruction of the vinyl side chain. Approaches both through the naphthaldehyde and the naphthalenic ylide were explored in detail.

A. *Via* the Naphthaldehyde.—Three protected derivatives of 1,4-dihydroxy-2-methyl-3-naphthaldehyde (XXIIa)[21] were prepared and tested for their efficacy in the Wittig reaction and for ease in subsequent conversion into quinone. These were the diacetate XXIIc, the 4-methyl ether 1-acetate XXIId, and the 4-methyl ether 1-pivalate XXIIe. Acetylation of the dihydroxyaldehyde XXIIa by heating with acetic anhydride and either sulfuric acid or sodium acetate or pyridine led to excellent yields of the tetraacetate XXIII. Although treatment with methanol–HCl or



XXIIa, $R_1 = H$; $R_4 = H$
b, $R_1 = CH_3CO$; $R_4 = H$
c, $R_1 = CH_3CO$; $R_4 = CH_3CO$
d, $R_1 = CH_3CO$; $R_4 = CH_3$
e, $R_1 = (CH_3)_3CCO$; $R_4 = CH_3$



XXIII, $R_1 = CH_3CO$; $R_4 = CH_3CO$; $R_3 = CH(OCOCH_3)_2$
XXIV, $R_1 = CH_3CO$; $R_4 = H$; $R_3 = H$
XXV, $R_1 = CH_3CO$; $R_4 = CH_3$; $R_3 = H$
XXVI, $R_1 = CH_3CO$; $R_4 = CH_3$; $R_3 = CH_2Cl$
XXVII, $R_1 = H$; $R_4 = CH_3$; $R_3 = H$
XXVIII, $R_1 = (CH_3)_3CCO$; $R_4 = CH_3$; $R_3 = H$
XXIX, $R_1 = (CH_3)_3CCO$; $R_4 = CH_3$; $R_3 = CH_2Cl$

acetic acid did convert this tetraacetate into diacetate XXIIc, the product always contained the difficultly removed 1-acetoxy compound XXIIb. A superior preparation of the pure aldehyde diacetate XXIIc directly from dihydroxy aldehyde XXIIa was then found using milder acetylation conditions.

To prepare the 4-methoxyaldehyde acetate XXIId, 2-methyl-1,4-naphthalenediol 1-acetate (XXIV)[22] was methylated with dimethyl sulfate. The 1-hydroxy-4-methoxy-2-methyl-1-naphthol acetate (XXV) formed was always accompanied by some of the dimethoxy compound (XV). This troublesome side product could be removed by treatment with Claisen alkali which hydrolyzed the ester and removed the resulting 4-methoxy-2-methyl-1-naphthol (XXVII) as its salt; reacetylation gave XXV. This separation was avoided by direct conversion of 2-methyl-1,4-naphthalenediol into the same 4-monomethyl ether XXVII in practically quantitative yield using methanol and hydrogen chloride.[23] Conversion of XXV into the aldehyde then followed by chloromethylation to XXVI and transformation of the chloromethyl to an aldehyde group using 2-nitropropane and potassium *t*-butoxide in *t*-butyl alcohol. These conditions reduced deacetylation to <20%, but reacetylation was still necessary for a good yield of the 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde acetate (XXIId).

Esterification of the 4-monomethyl ether XXVII with pivalic acid in trifluoroacetic anhydride[24] gave the pivalate ester XXVIII. Because of limited solubility, chloromethylation was carried out using formalin–acetic acid saturated with hydrogen chloride, and the

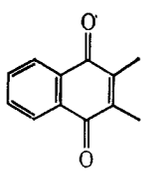
(19) L. I. Smith and J. J. Baldwin, *J. Org. Chem.*, **27**, 1770 (1962).
(20) M. Hashimoto, K. Uno, and H. G. Cassidy, *J. Polym. Sci., Part A-1*, **5**, 993 (1967).
(21) L. I. Smith and I. M. Webster, *J. Amer. Chem. Soc.*, **59**, 662 (1937).
(22) B. R. Baker, T. H. Davies, L. McElroy, and G. H. Carlson, *ibid.*, **64**, 1096 (1942); B. R. Baker and G. H. Carlson, *ibid.*, **64**, 2657 (1942).
(23) Patterned after the procedure M. Tishler, L. F. Fieser, and N. L. Wendler [*ibid.*, **62**, 1982 (1940)] used to prepare the monoethyl ether.
(24) R. C. Parish and L. M. Stock, *J. Org. Chem.*, **30**, 927 (1965).

chloromethyl derivative XXIX was converted into 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate XXIIe with potassium 2-propanenitronate in the usual way.

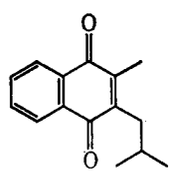
Construction of the vinyl side chain was now undertaken first with the diacetate aldehyde XXIIc by adding to its suspension in tetrahydrofuran 1 equiv of the ylide, isopropylidenetriphenylphosphorane, and refluxing the mixture for several hours. Analysis of aliquots by nmr indicated a substantial loss of acetyl groups while the aldehydic proton signal remained. To simplify product analysis, lithium aluminum hydride was added at the conclusion of the reaction (indicated by the disappearance of the ylide) to remove all ester groups and reduce any remaining aldehyde, which surprisingly was converted into a methyl rather than a hydroxymethyl group. The hydroquinones were then oxidized with silver oxide, and the mixture of quinones was analyzed by glpc.

Three quinones, 2,3-dimethyl-1,4-naphthoquinone (XXX), 2-methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI), and 2-methyl-3-isobutyl-1,4-naphthoquinone (XXXI), were obtained in the ratio of 4:1:2. When the ratio of ylide to naphthaldehyde XXIIc was increased to 3:1, the product ratio now changed to 2:3:5 for dimethyl-, 2-methyl-1-propenyl-, and isobutylquinones. An authentic sample of the isobutylquinone (XXXI) was prepared by the reaction of 2-methyl-1,4-naphthoquinone (VIII) and diisovaleryl peroxide.

The source of the isobutylquinone XXXI is not clear. Using a mixture of methylene chloride and tetrahydrofuran, in which the starting diacetate aldehyde XXXIIc is completely soluble or carrying out the reaction at 0° caused no change in the product ratio. Also, the action of lithium aluminum hydride on the vinylquinone XI or on the corresponding vinylhydroquinone diacetate under the conditions of the isolation procedure followed by silver oxide oxidation gave only recovered vinylquinone XI and no isobutylquinone XXXI. However, lithium aluminum hydride must be involved in some way in its formation, since treatment of the reaction mixture with Claisen alkali and then silver oxide gave the vinylquinone XI in 60% yield and no isobutylquinone XXXI.



XXX

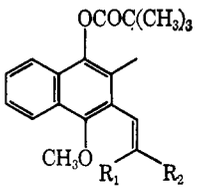


XXXI

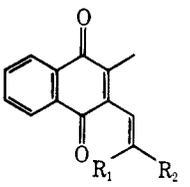
As a method for synthesizing vinylquinones, this procedure may be useful when the ylide is readily available since the diacetate aldehyde XXIIc is easily obtained. However, the reaction of one or both of the ester groups with the Wittig reagent, necessitating the use of at least 3 equiv of ylide, makes this procedure prohibitively expensive with difficultly available ylides.

On the assumption that the 4-acetoxy group might be the major source of the ester–ylide reaction, the same procedure was applied to XXIId in which the 4-methoxy group has replaced the acetoxy, but the results were essentially the same. Clearly, a much more hindered ester was required, and we turned to the 1-pivaloyloxy-4-methoxyaldehyde XXIIe.

When XXIIe was treated with isopropylidenetriphenylphosphorane, reaction occurred rapidly and practically quantitatively to give the corresponding 4-methoxy-2-methyl-3-(2-methyl-1-propenyl)-1-naphthol pivalate (XXXIIa). The pivaloyl group was removed with lithium aluminum hydride, and the intermediate naphthol was oxidized to the vinylquinone XI in 88% over-all yield from aldehyde XXIIe. Again, this procedure applied to XXIIe and *n*-butylidenetriphenylphosphorane gave a *cis–trans* mixture (the stereochemistry of these compounds is treated in detail in a later section) of the vinylquinone XXXIIIa in good yield. Clearly, an excellent protecting pattern—1-pivaloyloxy-4-methoxy—had been found which allows synthesis of vinylquinones in high yield with respect to naphthaldehyde and ylide.



XXXIIa, $R_1 = R_2 = CH_3$
b, $R_1 = H$; $R_2 = CH_2CH_2CH_3$
c, $R_1 = CH_3$; $R_2 = CH_2CH_2CH_3$
d, $R_1 = R_2 = CH_2CH_3$
e, $R_1 = H$; $R_2 = C_6H_5$
f, $R_1 = CH_3$; $R_2 = n\text{-}C_6H_{13}$
g, $R_1 = CH_3$; $R_2 = CH_2(CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2)_3H$



XXXIIIa, $R_1, R_2 = H, CH_2CH_2CH_3$
b, $R_1, R_2 = CH_3, CH_2CH_2CH_3$
c, $R_1, R_2 = H, C_6H_5$
d, $R_1, R_2 = CH_3, n\text{-}C_6H_{13}$
e, $R_1, R_2 = CH_3, CH_2(CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2)_3H$

To extend the scope of this synthesis, we next investigated its application to unsymmetrical secondary ylides, since this would be needed for the synthesis of chlorobiumquinone (I) and presumably other natural vinylquinones. For this purpose, a secondary alkyltriphenylphosphonium halide would be needed. Six such compounds have been reported in the literature, prepared by heating triphenylphosphine and the halide, neat. Two of these (cyclopentyl,[25] and cyclohexyl[25,26]) offer no complications, since only one salt can be formed; the obtention of isomers is possible with the others (isopropyl,[27] 2-butyl,[26,28] 2-octyl,[28] and α-phenylethyl[26]).

(25) A. Moercker, *Org. Reactions*, **14**, 270 (1965).
(26) H. J. Bestmann and O. Kratzer, *Ber.*, **96**, 1899 (1963).
(27) (a) U. H. M. Fagerlund and D. R. Idler, *J. Amer. Chem. Soc.*, **79**, 6473 (1957); (b) G. Wittig and D. Wittenberg, *Ann.*, **606**, 1 (1957).
(28) C. F. Hauser, T. W. Brooks, M. L. Miles, M. A. Raymond, and G. B. Butler, *J. Org. Chem.*, **28**, 372 (1963).

We pursued the synthesis of 2-pentyltriphenylphosphonium bromide by heating triphenylphosphine and pure 2-bromopentane,[29] and the best yield of phosphonium salt was obtained with excess phosphine at 170° in a sealed tube for 48 hr. However, glpc showed the recovered bromopentane to be a 2:1 mixture of 2- and 3-bromopentanes, and this was true also for lower temperature and shorter time reactions where conversion into salt was less.

This result strongly suggested that the phosphonium salt was also a mixture, and this was established as the case by conversion into ylide and reaction with the 1-pivaloyloxy-4-methoxyaldehyde XXIIe as above. The product was a mixture of *cis*- and *trans*-2-methyl-1-pentenylhydroquinones XXXIIc and 2-ethyl-1-butenylhydroquinone XXXIId. Again, when the triphenylphosphonium salt of 6,10,14-trimethyl-2-pentadecyl bromide[30] was used similarly and the reaction carried through to quinone, at least four products were isolated by tlc, and none was the vinylquinone which would have resulted from unrearranged bromide.

This formation of rearranged bromide undoubtedly occurs by elimination and readdition of hydrogen bromide. For example, when 2-bromopentane was heated at 170° for 24 hr, a 1:9 mixture of 3- and 2-bromopentanes was obtained; in the presence of 10 mol % triphenylphosphine or pentylphosphonium salt, the isomer ratio became 1:2. In both cases, hydrogen bromide and olefin also were formed. Similar observations obtained with 2-bromooctane, but in no case was any primary bromide or its phosphonium salt formed. The phosphonium salt, once formed, appears to be stable to these conditions since the triphenylphosphonium salts of 3- and 2-bromopentanes, heated with 2-bromooctane, gave only octenes and bromooctanes.

Attempts to prepare phosphonium salts under milder, nonrearranging conditions failed. The same results were obtained with 2-iodopentane at 130°, and the 2-pentyl tosylate gave entirely olefin and no phosphonium salt. Clearly, this direct formation of phosphonium salts from secondary halides is useful only when no other secondary or tertiary isomers are possible.

An alternative route to 2-alkylphosphonium salts is available by alkylation of the *n*-alkylidenephosphorane. This can be quite successfully accomplished with iodomethane with which we alkylated *n*-butylidenetriphenylphosphorane to pure 2-pentyltriphenylphosphonium iodide;[31] we also prepared other secondary phosphonium salts in this way. The only drawback to this method might be residual primary salt which was not converted into ylide and which would lead to a difficultly removed impurity; however, care in the stoichiometry should eliminate this possibility.

Alkylation with other than iodomethane leads to mixtures because of dehydrohalogenation of the haloalkane. Formation of the tertiary salt by transylidation followed by alkylation of the secondary ylide is also a possibility.[32] In tetrahydrofuran at 25°, alkylation

$$RCH{=}P(C_6H_5)_3 \xrightarrow{R'X}$$

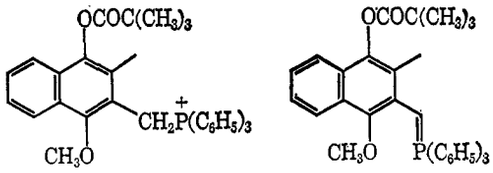
$$RCH\overset{R'}{\underset{|}{}}\overset{+}{P}(C_6H_5)_3,\quad RCH_2\overset{+}{P}(C_6H_5)_3,\quad RC\overset{R'}{\underset{R'}{}}\overset{+}{P}(C_6H_5)_3,$$

of ethylidenetriphenylphosphorane with either 1-bromopropane or 1-bromobutane led to 80% the secondary and 20% the regenerated primary phosphonium salt; no tertiary salt was formed. The distribution between secondary and primary could be easily determined by the ratio of the α-methinyl proton peak at about δ 5 to the α-methylene proton absorption at about δ 4. Although this method results in a mixture,[33,34] it may have useful applications where the alkylating group is large, making for a ready separation of the salts or the subsequent products.

In summary, the preparation of vinylnaphthoquinones *via* 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate (XXIIe) and an alkylidenetriphenylphosphorane is an excellent method. No difficulties are encountered when the alkylidene group is primary or secondary, if no isomeric secondary structures are possible for the latter. Other pure secondary ylides may be prepared if the branching group is methyl, *via* alkylation with iodomethane. However, for larger branching group mixtures are encountered.

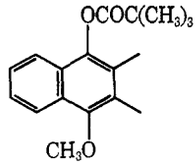
B. *Via* the Naphthalenic Ylide.—Because of the slight limitation in scope of potential side chains and the fact that in many cases the corresponding aldehyde or ketone would be readily available, the alternate approach using the naphthalenic ylide was investigated. Treatment of 4-methoxy-2-methyl-3-chloromethyl-1-naphthol pivalate (XXIX) with triphenylphosphine in refluxing benzene gave the naphthylmethyl salt XXXIV in quantitative yield. The naphthalenic ylide XXXV was generated by adding butyllithium to a suspension of this salt in toluene, and the addition of benzaldehyde caused immediate reaction at room temperature; an essentially quantitative yield of the styrylnaphthalene XXXIIe was isolated.

With 2-octanone and ylide XXXV reaction was much slower. The course of the reaction could be followed by titration of aliquots with standard benzaldehyde solutions to disappearance of the orange–red ylide color; 72 hr at 110° was required for complete consumption of ylid. The reaction product consisted of the desired



XXXIV

XXXV



XXXVI

(29) J. Cason and J. S. Correia, *J. Org. Chem.*, **26**, 3645 (1961).

(30) Prepared from 6,10,14-trimethyl-2-pentadecanone [S. J. DiMari, C. D. Snyder, and H. Rapoport, *Biochemistry*, **7**, 2301 (1968)] by reduction to the alcohol and conversion into the bromide *via* the tosylate.

(31) H. J. Bestmann and F. Seng, *Tetrahedron*, **21**, 1373 (1965).

(32) S. Tripett, *Advan. Org. Chem.*, **1**, 83 (1960); D. Seyferth and G. Singh *J. Amer. Chem. Soc.*, **87**, 4156 (1965).

(33) H. J. Bestmann and E. Kranz, *Angew. Chem.*, **79**, 95 (1967).

(34) The recent alkylation of α-lithiophosphonic acid bisamides may offer some advantage: E. J. Corey and G. T. Kwiatkowski, *J. Amer. Chem. Soc.*, **88**, 5652 (1967).

2-methyl-1-octenylnaphthohydroquinone XXXIIf in about 30% yield, but the 2,3-dimethyl compound XXXVI was isolated as well.

This undoubtedly results from aldol-type condensation of the less reactive ketone, catalyzed by ylide and liberating water or hydroxide ion, which in turn reacts with ylide to give the dimethyl compound XXXVI and triphenylphosphine oxide.[35] To test this interpretation, 2-octanone-d_5-1,1,1,3,3 was prepared[36] and used in the condensation with naphthalenic ylide XXXV. The 2,3-dimethyl compound XXXVI now obtained contained about 70% deuterium in the C-3 methyl, as would be anticipated if two atoms of deuterium were incorporated from the ketone.

With 6,10,14-trimethyl-2-pentadecanone, a 21% yield of the vinyl compound XXXIIg was obtained, and again the 2,3-dimethyl compound XXXVI was formed. The amount of the latter compound fluctuated in the various condensations, but it could not be eliminated. Apparently, it will always be formed to some extent when less reactive ketones, which can self-condense, are used. Although this leads to a decreased yield, no vinylhydroquinone by-products are formed, and the naphthalenic ylide procedure is a good method for synthesizing the vinyl side chain when the carbonyl component is available.

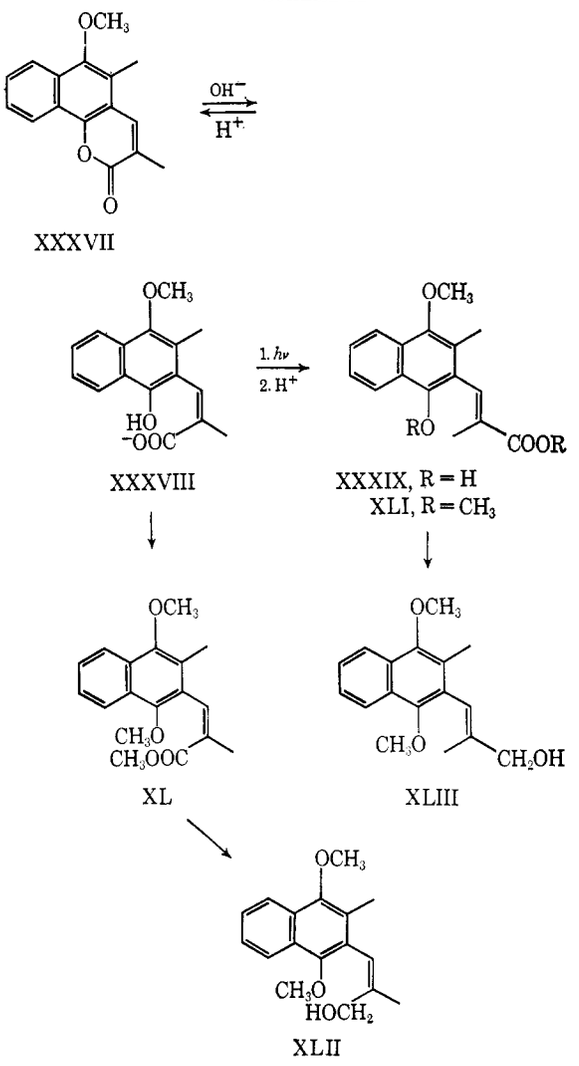
Stereochemistry.—In all of the syntheses described above where *cis* and *trans* isomers are possible, both isomers were indeed found and definitive stereochemistry was assigned on the basis of nmr spectra.

For the β-monosubstituted compound, 1-pentenylhydroquinone XXXIIb, stereochemical assignment relied on the splitting constants for the vinyl protons. By glpc, the synthetic olefinic product was separated into two fractions in the ratio 2:3, the first of which in the vinyl proton region of the nmr shows an AB quartet, J = 11 Hz, with the doublet due to the β-vinyl proton split into triplets, J = 7 Hz, by the adjacent methylene. The second fraction had a similar pattern with J = 17 Hz. From these values and by comparison with the spectra of *cis*- and *trans*-isoeugenos,[37] the isomer (J = 11 Hz) eluted first is assigned the *cis* configuration and the isomer (J = 17 Hz) eluted second the *trans*. In addition, the signals due to the *n*-propyl group are shifted upfield to lower δ values in the *cis* isomer relative to the *trans*, as would be expected if the *cis*-alkyl group is shielded by being held in the π-electron cloud of the aromatic ring.

Since the stereochemical assignments for the β,β-dialkylvinyl compounds would rest solely on the interaction with the aromatic nucleus, an unassailable isomeric pair was needed as models. These were derived from the coumarin XXXVII with its fixed, *trans*-vinyl methyl. Ring opening with alkali led to the salt XXXVIII which on acidification quantitatively recyclized to the coumarin. However, if this salt was irradiated with a low-pressure mercury lamp,[38] nmr analysis revealed the appearance of a second vinyl methyl group which grew to 70% of the total. This represents the *trans* acid XXXIX which can be isolated by acidification whereas the *cis* acid immediately reverts into coumarin. Therefore, a pure sample of each isomer can be readily obtained.

These isomerically pure acids (salts), XXXVIII and XXXIX, were then methylated under mild conditions,[39] a single, pure isomer of the 1,4-dimethoxy methyl ester (XL and XLI) being obtained in each case thus establishing stereochemical integrity. The methyl ester XL contains a *trans*-methyl group which appears at δ 2.15, whereas the methyl ester XLI contains a *cis*-methyl appearing at δ 1.8. Each isomer was reduced to the corresponding allylic alcohol (XLII and XLIII) and the *trans*-methyl signal in XLII appears at δ 2.08 while the *cis*-methyl signal in XLIII is at δ 1.58. Thus shielding by the aromatic ring current for the *cis*-methyl is established in each case, $\Delta\delta_{trans-cis}$ being 0.35 for the methyl esters and 0.50 for the allylic alcohols. See Scheme II.

SCHEME II



The 2-methyl-1-propenylhydroquinone XXXIIa shows two vinyl methyl signals, one at δ 1.95 (*trans* to ring) and the other at δ 1.55 (*cis* to the ring) ($\Delta\delta_{trans-cis}$

(35) G. Wittig, W. Böll, and K. Krück [*Ann.*, **95**, 2514 (1962)] have observed similar behavior in the condensation of cyclopentanone with methoxymethylenetriphenylphosphorane.

(36) Following the procedure of A. C. Cope and D. M. Gale, *J. Amer. Chem. Soc.*, **85**, 3747 (1963).

(37) H. Rottendorf, S. Sternhell, and J. R. Wilmshurst, *Aust. J. Chem.*, **18**, 1759 (1965); G. P. Newsoroff and S. Sternhell, *ibid.*, **19**, 1667 (1966).

(38) F. A. Haskins and H. J. Gorz, *Arch. Biochem. Biophys.*, **81**, 204 (1959).

(39) R. Kuhn and H. Trischmann, *Ber.*, **94**, 2258 (1961).

0.40), completely consistent with the above correlation. In the other vinylhydroquinone compounds (XXXIIc and f) the isomers were separated by glpc, and in each instance the isomer eluted first has a vinyl methyl signal at δ 1.95 and therefore is the *cis* isomer (*trans* methyl). The second fraction has its vinyl methyl at δ 1.55 and thus is the *trans* isomer. Signals due to the other β-alkyl groups show similar shifts.

The 3-styrylhydroquinone XXXIIe is tentatively assigned *trans* stereochemistry by analogy with the stilbenes where the vinyl protons appear as singlets at δ 6.55 and 7.10 for the *cis* and *trans* isomers, respectively. In XXXIIe all vinyl and aromatic absorption falls in a multiplet from δ 7.1 to 7.8; however, there is a sharp singlet at δ 7.15 which is presumably due to the *trans* vinyl protons. The remaining vinylhydroquinone (2,6,10,14-tetramethyl-1-pentadecenyl-) XXXIIg, was separated into isomers at the quinone stage.

Preparation and Properties of the Vinylnaphthoquinones.—In every case, the pivaloyl group was removed by reductive cleavage with lithium aluminum hydride to the hydroquinone 4-monomethyl ethers. A single isomer was obtained each time, and the nmr spectra were essentially unchanged except that the pivalate signal was absent, showing maintenance of stereochemistry during this removal. Oxidation to the quinones was then easily accomplished with ferric chloride in aqueous acetonitrile or ethanol–ether, as required for solubility.

The nmr spectra of the vinylquinones are similar to those of the pivalate esters and hydroquinone monomethyl ethers from which they were derived, showing the same distinctive vinyl methyl resonances which allow stereochemical assignment and show that no isomerization had occurred in the conversion. The *cis*- and *trans*-2,6,10,14-tetramethyl-1-pentadecenylvinylquinones XXXIIIe were separated by tlc at this stage and assigned stereochemistry on the same nmr basis.

In their uv absorption all the vinylnaphthoquinones are similar; however there are sufficient differences to allow all of the various substitution patterns to be distinguished. All types (unsubstituted, β-mono-, and β,β-disubstituted) have their most intense absorption around 250 nm. The unsubstituted and β-monosubstituted compounds then have a lesser peak at ~280 nm and a still weaker maximum at 330 nm. The *trans*-β-monosubstituted compound shows the longest wavelength absorption of the group with another peak at 365 nm, probably the result of substitution which still allows coplanarity and full conjugation between vinyl and naphthoquinone chromophores. In the β,β-disubstituted compounds (*cis* and *trans* isomers identical) the 280-nm peak is shifted hipsochromically to a shoulder at 264 nm, this effect probably being the result of decreased planarity between the naphthoquinone and the β,β-disubstituted vinyl group. The four types of uv absorptions are shown in Figure 1.

In their mass spectra, both the *cis*- and *trans*-2-methyl-1-pentenylvinylnaphthoquinones (XXXIIIb) give identical fragmentation patterns. The molecular ion, *m/e* 254, is also the base peak. Other strong peaks are at *m/e* 239 (M − 15), 225 (M − 29), and 211 (M − 43), probably arising from loss of alkyl groups from the vinyl side chain.

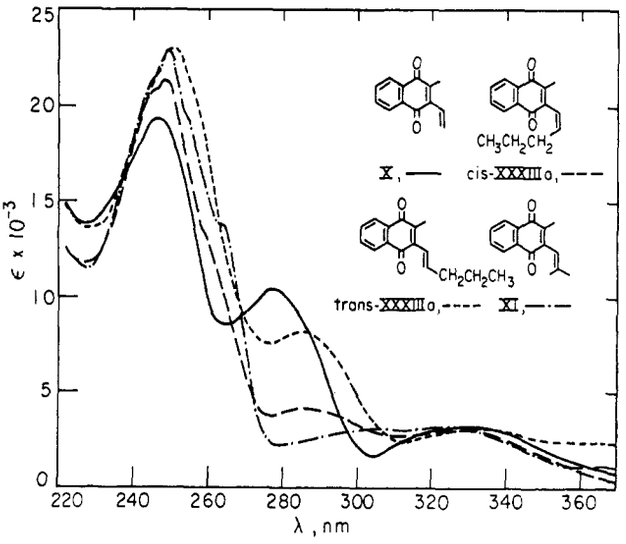


Figure 1.—Ultraviolet absorption spectra of 2-methyl-3-vinyl-1,4-naphthoquinone (X), *cis*-2-methyl-3-(1-pentenyl)-1,4-naphthoquinone (*cis* XXXIIIa), *trans*-2-methyl-3-(1-pentenyl)-1,4-naphthoquinone (*trans* XXXIIIa), and 2-methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI) in isooctane.

Experimental Section[40]

2-Methyl-3-vinyl-1,4-naphthoquinone (X) was prepared by heating 3-(1-bromoethyl)-2-methyl-1,4-naphthoquinone (IX) with sodium acetate in glacial acetic acid to 120–125° as previously described:[14] mp 79.5–80.5° (lit.[14] mp 81–82°); λ_{max} 330 nm (ϵ 3300), 278 (10,400), 246 (19,400); nmr (CCl_4) δ 5.57 (d, J = 2 Hz), 5.7 (t, J = 2 Hz), 6.0 (d, J = 2 Hz) ArC=CH_2; 6.45 (d, J = 11 Hz), 6.74 (d, J = 11 Hz) ArCH=C.

β,β-Dimethylacryloyl Peroxide.—A solution of 2.4 g of β,β-dimethylacryloyl chloride, bp 60–61° (30 mm) [lit.[41] bp 59–61° (30 mm)], dissolved in 8 ml of ether was converted into β,β-dimethylacryloyl peroxide in 50% yield following the general procedure for the preparation of diacyl peroxides.[17]

2-Methyl-1,4-naphthalenediol Diisobutyrate (XVI).—Boron trifluoride was bubbled through a suspension of 5 g of 2-methyl-1,4-naphthalenediol (XIV) in 30 ml of isobutyric acid cooled in an ice bath. When the internal temperature reached 80° (several minutes) and the hydroquinone dissolved, the solution was poured onto crushed ice and allowed to stand overnight at 0°. The upper aqueous layer was decanted, and the remaining oil crystallized on addition of ethanol. Recrystallization from ethanol gave 4 g (44%) of 2-methyl-1,4-naphthalenediol diisobutyrate (XVI), mp 75° (lit.[18] mp 73–74°).

3-Cyanomethyl-1,4-dimethoxy-2-methylnaphthalene (XVIII).—To a solution of 2.2 g (33 mmol) of potassium cyanide in 8 ml of water was added 5.5 g (22 mmol) of 3-chloromethyl-1,4-dimethoxy-2-methylnaphthalene (XVII)[42] dissolved in 27 ml of 95% ethanol. The solution was heated on a steam bath for 45 min; the ethanol was evaporated; and the residue was diluted fivefold with water and allowed to stand at 0°. The resulting

(40) All melting points are corrected; microanalyses were performed by the Microchemical Laboratory, University of California at Berkeley; uv spectra were obtained in isooctane unless otherwise noted on a Cary 14 spectrophotometer; nmr spectra were obtained on a A-60 Varian Associates instrument in deuteriochloroform unless otherwise stated with internal TMS, δ 0; all evaporations were *in vacuo* using a rotary evaporator, and all reactions were carried out in a nitrogen atmosphere. Glpc analyses were performed on a 5 ft × 1/4 in. column, 5 or 10% SE-30 on acid-washed, DMCS-treated (60–80 mesh) Chromosorb P, at 200–250° and a flow rate of 60–100 ml of He/min. Preparative work was performed on a 8 ft × 3/8 in. column, 10% SE-30 on acid-washed, DMCS-treated (60–80 mesh) Chromosorb P, at 200–250° and a flow rate of 200 ml of He/min. Glpc analysis of alkyl halides and olefins was carried out on a 10 ft × 1/4 in. column, 10 or 20% polypropylene glycol on (60–80 mesh) Chromosorb P, at 60–100° and a flow rate of 60 ml of He/min. Some exploratory experiments were performed by J. H. Supple and O. Muscio, to whom we are grateful.

(41) L. I. Smith and V. A. Engelhardt, *J. Amer. Chem. Soc.*, **71**, 2671 (1949).

(42) L. I. Smith, S. Wawzonek, and H. C. Miller, *J. Org. Chem.*, **6**, 229 (1941).

crystals were filtered, washed with water, dried, and recrystallized from petroleum ether to give 4 g (75%) of 3-cyanomethyl-1,4-dimethoxy-2-methylnaphthalene (XVIII), mp 105°.

Anal. Calcd for $C_{15}H_{15}O_2N$: C, 74.7; N, 5.8. Found: C, 74.4; N, 5.8.

3-(2-Aminoethyl)-1,4-dimethoxy-2-methylnaphthalene (XIX).—A solution of 4 g (17 mmol) of 3-cyanomethyl-1,4-dimethoxy-2-methylnaphthalene (XVIII) in 60 ml of ether was added slowly to a stirred suspension of 4 g (0.105 mol) of lithium aluminum hydride in 60 ml of ether. Stirring was continued an additional 15 min, and excess hydride was destroyed with ice followed by 200 ml of a 25% solution of sodium bitartrate in water. The solution was extracted three times with 200-ml portions of ether, and the combined ether extracts were washed with 1.5 *N* hydrochloric acid. After being made alkaline with 30% aqueous sodium hydroxide, the acid washes were extracted with ether, and the combined ether phase was washed free of alkali, dried, and evaporated to give 2.9 g (72% yield) of 3-(2-aminoethyl)-1,4-dimethoxy-2-methylnaphthalene (XIX).

The hydrochloride was recrystallized from absolute ethanol, mp 270°.

Anal. Calcd for $C_{15}H_{20}O_2NCl$: N, 5.0. Found: N, 4.9.

1,4-Dimethoxy-3-(2-dimethylaminoethyl)-2-methylnaphthalene Methiodide.—A solution of 5.3 g (21 mmol) of 3-(2-aminoethyl)-1,4-dimethoxy-2-methylnaphthalene (XIX) in 300 ml of absolute ethanol containing 25 ml of iodomethane and 24 g of anhydrous potassium carbonate was refluxed for 6 hr, 25 ml of iodomethane was added, and the solution was refluxed for 24 hr. Then 25 ml of iodomethane and 24 g of anhydrous potassium carbonate were added, and the solution was refluxed for 24 hr. The resulting suspension was evaporated, the residue was dissolved in water and cooled to 0°, and the crystals which formed were removed. Recrystallization from ethanol gave 3.7 g (43%) of 1,4-dimethoxy-3-(2-dimethylaminoethyl)-2-methylnaphthalene methiodide, mp 265°.

Anal. Calcd for $C_{18}H_{26}O_2NI$: C, 52.1; H, 6.3; N, 3.4; I, 30.6. Found: C, 52.0; H, 6.3; N, 3.2; I, 30.3.

1,4-Dimethoxy-2-methyl-3-vinylnaphthalene (XX).—A solution of 3.7 g of 1,4-dimethoxy-3-(2-dimethylaminoethyl)-2-methylnaphthalene methiodide in 490 ml of ethanol and 300 ml of 30% aqueous potassium hydroxide was refluxed for 2 hr. The ethanol was evaporated; the remaining solution was extracted with ether; and the ether extracts were washed with water, dried, and evaporated. The residue was crystallized from methanol to give 1.3 g (62% yield) of 1,4-dimethoxy-2-methyl-3-vinylnaphthalene (XX): mp 42°; $\lambda_{max}^{C_2H_5OH}$ 290–295 nm (sh), 243 (ϵ 58,000); nmr (CS_2) δ 5.5 (d, J = 3 Hz), 5.67 (t, J = 3 Hz) 5.95 (d, J = 3 Hz) ArC=CH_2; 6.75 (d, J = 11 Hz), 7.05 (d, J = 11 Hz) ArCH=C.

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.9; H, 7.1. Found: C, 78.9; H, 7.2.

3-Ethyl-2-methyl-1,4-naphthoquinone (XXI) and 2-Methyl-3-vinyl-1,4-naphthoquinone (X).—A mixture of 200 mg (0.9 mmol) of 1,4-dimethoxy-2-methyl-3-vinylnaphthalene (XX) and 1.2 g (10.5 mmol) of pyridine hydrochloride was heated at 220° for 8 min, after which it was cooled, diluted with 5 ml of water, and extracted with ether. The ether extract was dried and evaporated, and the residue was dissolved in 20 ml of ether; 1 g of anhydrous sodium sulfate and 1 g of silver oxide were added, and the mixture was shaken in the dark for 30 min, filtered, and the ether evaporated. Chromatography on Decalso and elution with isooctane gave (fraction 1) 30 mg (15% yield) of starting material and (fractions 2–5) 20 mg (14%) of impure 3-ethyl-2-methyl-1,4-naphthoquinone (XXI): mp 72–73° after crystallization from methanol (lit.[43] mp 72–72.6°); λ_{max} 327 nm (ϵ 3100), 268 (17,000), 259 (16,900), 248 (18,600), 243 (23,600). Fractions 5–7 gave on evaporation 30 mg which was crystallized from acetone giving 15 mg (10%) of 2-methyl-3-vinyl-1,4-naphthoquinone (X).

1,4-Dimethoxy-2-methyl-3-naphthaldehyde.—To a solution of 10.2 g (0.45 g-atom) of sodium dissolved in 300 ml of anhydrous ethanol was added 54 ml (0.6 mol) of 2-nitropropane followed by a solution of 7.5 g (0.03 mol) of 3-chloromethyl-1,4-dimethoxy-2-methylnaphthalene (XVII) in 600 ml of absolute ether. After 24 hr at 25° the solvent was evaporated; the residue was dissolved in water and extracted with ether; the ether extract was washed, dried, and evaporated; and the residue was crystallized from ethanol giving 3 g (43%) of 1,4-dimethoxy-2-methyl-3-naphthaldehyde: mp 92–93°; $\lambda_{max}^{C_2H_5OH}$ 285–292 nm (sh), 258 (ϵ 43,000); nmr (CS_2) δ 3.85 (s, OCH_3), 4.0 (s, OCH_3), 10.7 (s, ArCHO).

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 72.8; H, 6.2.

1,4-Dihydroxy-2-methyl-3-naphthaldehyde (XXIIa) was prepared by treatment of 2-methyl-1,4-naphthalenediol (XIV) with zinc cyanide and hydrogen chloride in ether as previously described:[21] mp 159.5–161° (lit.[21] mp 158–160°).

1,4-Dihydroxy-2-methyl-3-naphthaldehyde 1-Acetate (XXIIb).—A suspension of 9.6 g (33.6 mmol) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde diacetate (XXIIc) in 70 ml of 50% aqueous acetic acid was refluxed for 90 min to give a clear yellow solution. Cooling gave 7.4 g (90% yield) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde 1-acetate (XXIIb), mp 126–127°.

Anal. Calcd for $C_{14}H_{12}O_4$: C, 68.8; H, 5.0. Found: C, 68.9; H, 5.3.

1,4-Dihydroxy-2-methyl-3-naphthaldehyde Tetraacetate (XXIII).—A suspension of 1.4 g of 1,4-dihydroxy-2-methyl-3-naphthaldehyde (XXIIa) in 4 ml of pyridine–acetic anhydride (1:1) was heated at reflux for 30 min. The solution was poured into water and extracted with chloroform which was washed, dried, and evaporated. The crystalline residue was recrystallized twice from methanol to give 1 g (23%) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde tetraacetate (XXIII), mp 169–171°.[44]

Anal. Calcd for $C_{20}H_{20}O_8$: C, 61.9; H, 5.2. Found: C, 61.8; H, 5.0.

1,4-Dihydroxy-2-methyl-3-naphthaldehyde Diacetate (XXIIc).—A solution of 13.5 g (67 mmol) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde (XXIIa) in 10 ml of pyridine and 12 ml of acetic anhydride was stirred at 25° for 1 hr. The precipitate which formed was removed, washed with water, and dissolveed in methylene chloride. Evaporation of the dried methylene chloride and crystallization of the residue twice from chloroform–petroleum ether gave 12.7 g (65%) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde diacetate (XXIIc): mp 202–204°;[45] nmr δ 2.45–2.52 (s, s, s, 2 $ArOCOCH_3$, $ArCH_3$), 10.5 (s, ArCHO).

Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.1; H, 4.9. Found: C, 66.8; H, 4.9.

2-Methyl-1,4-naphthalenediol 1-acetate (XXIV) was prepared by selective hydrolysis of 2-methyl-1,4-naphthalenediol diacetate[46] in methanolic ammonia in the manner described:[22] mp 124–125° (lit.[22] mp 124.5–125.8°).

4-Methoxy-2-methyl-1-naphthol (XXVII). A. O^4 Methylation of (XIV).—A solution of 50 g of 2-methyl-1,4-naphthalenediol (XIV), dissolved in 500 ml of methanol containing 20 g of hydrogen chloride, was stirred at room temperature for 24 hr. Threefold dilution with water caused the product to precipitate as a mass of fine needles. The mixture was extracted with ether, washed, dried, and evaporated giving 50 g (98%) of 4-methoxy-2-methyl-1-naphthol (XXVII), mp 101–102.5° (lit.[22] mp 101–103°). Glpc showed the product to be >95% pure, the chief impurity being 1–2% 1,4-dimethoxy-2-methylnaphthalene (XV).

B. Methylation of XXIV and Hydrolysis to XXVII.—A suspension of 50 g (0.23 mol) of 2-methyl-1,4-naphthalenediol 1-acetate (XXIV) in 246 g (1.95 mol) of dimethyl sulfate was cooled at 0° and stirred vigorously as a solution of 193 g (3.5 mol) of potassium hydroxide in 200 ml of water was added dropwise over 90 min. Toward the end of the reaction the oily organic layer solidified, and it was removed, washed, and dried to give 50 g of solid. By glpc it consisted of 80–85% 4-methoxy-2-methyl-1-naphthol acetate (XXV) and 10–15% 1,4-dimethoxy-2-methylnaphthalene (XV).

The solid was dissolved in 500 ml of pentane and cooled to 0°, Claisen' salkali (200 ml) was added slowly with stirring, and the two-phase system was allowed to warm to room temperature. Repeated washing with pentane removed all the 1,4-dimethoxy-2-methylnaphthalene (XV). Cooling to 0° and neutralizing by dropwise addition of concentrated hydrochloric acid followed by extraction with ether which was washed, dried, and evaporated gave 30 g (70% yield) of 4-methoxy-2-methyl-1-naphthol (XXVII), mp 102–103°.

(43) L. F. Fieser and F. C. Chang, *J. Amer. Chem. Soc.*, **64**, 2043 (1942).

(44) J. Madinaveitia [*Rev. Acad. Cienc* (Madrid), **31**, 617 (1934)] reports an unspecified acetate derivative of 1,4-dihydroxy-2-methyl-3-naphthaldehyde with mp 168°.

(45) G. Carrara and G. Bonacci [*Gazz. Chem. Ital.*, **73**, 225 (1943)] report mp 154–155° for the aldehyde diacetate. We have found the following melting points in this series: aldehyde, 159–161°; O^4-monoacetate, 126–127°; diacetate, 202–204°; and tetraacetate, 169–171°.

(46) R. J. Anderson and M. S. Newman, *J. Biol. Chem.*, **103**, 405 (1933).

4-Methoxy-2-methyl-1-naphthol Acetate (XXV).—A mixture of 40 g of 4-methoxy-2-methyl-1-naphthol (XXVII) and 5 g of anhydrous sodium acetate was suspended in 80 ml of acetic anhydride and heated to 100° for 1 hr. The hot solution was then poured onto crushed ice, and the resulting solid was washed, dried, and crystallized from methanol to give 46 g (95%) of 4-methoxy-2-methyl-1-naphthol acetate (XXV): mp 68.5–70° (lit.[22] mp 67–68°); nmr δ 2.22, 2.32 (s, s, $ArCH_3$, $ArOCOCH_3$), 3.8 (s, $ArOCH_3$), 6.5 (s, C-3), 7.3–7.8 (m, C-5, -6, -7), 8.05–8.3 (m, C-8).

3-Chloromethyl-4-methoxy-2-methyl-1-naphthol Acetate (XXVI).—A suspension of 4.6 g (20 mmol) of 4-methoxy-2-methyl-1-naphthol acetate (XXV) in 15 ml of 36% formalin and 20 ml of concentrated hydrochoric acid was stirred in an ice bath, and hydrogen chloride was bubbled through at a rate such that the internal temperature did not rise above 10°. After 1 hr, the ice bath was removed, and hydrogen chloride addition was continued for 12 hr. The mixtue was poured onto ice, and the resulting solid was dried and crystallized twice from ether–hexane to give 3.6 g (65%) of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol acetate (XXVI), mp 103–103.5°.

Anal. Calcd for $C_{15}H_{15}ClO_3$: C, 64.7; H, 5.4; Cl, 12.6. Found: C, 64.7; H, 5.2; Cl, 13.0.

1-Hydroxy-4-methoxy-2-methyl-3-naphthaldehyde acetate (XXIId) was prepared from the corresponding chloromethyl compound XXVI, using the 2-nitropropane procedure described in the preparation of 1,4-dimethoxy-2-methyl-3-naphthaldehyde, except that potassium *t*-butoxide in *t*-butyl alcohol was used and the reaction was conducted at 35°. The partially deacetylated naphthol aldehyde was acetylated in acetic anhydride–pyridine and an 82% yield of 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde acetate (XXIId) was obtained: mp 99–100°.

Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.7; H, 5.5. Found: C, 69.4; H, 5.4.

4-Methoxy-2-methyl-1-naphthol Pivalate (XXVIII).—A solution of 13.5 g (0.13 mol) of pivalic acid in 84 g (0.40 mol) of trifluoroacetic anhydride was added to 25 g (0.13 mmol) of 4-methoxy-2-methyl-1-naphthol (XXVII). After 4 hr at room temperature, benzene was added, and the solution was poured into ice water and extracted with benzene which was washed with 10% aqueous sodium hydroxide and then with water. Evaporation of the benzene and crystallization of the residue from hexane gave 29 g (80% yield) of 4-methoxy-2-methyl-1-naphthol pivalate (XXVIII), mp 90.5–91°.

Anal. Calcd for $C_{17}H_{20}O_3$: C, 75.0; H, 7.4. Found: C, 75.1; H, 7.3.

3-Chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXIX) was prepared by chloromethylation of the naphthol pivalate XXVIII in the same manner as described for the chloromethyl acetate XXVI at 40° in acetic acid–HCl instead of aqeuous HCl. A 90% yield of chloromethyl compound was obtained: mp 92–93° from cyclohexane.

Anal. Calcd for $C_{18}H_{21}ClO_3$: C, 67.4; H, 6.6; Cl, 11.1. Found: C, 67.0; H, 6.7; Cl, 11.1.

1-Hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate (XXIIe) was prepared from the chloromethyl compound and 2-nitropropane as described for the corresponding acetate XXIId. The naphthaldehyde pivalate was obtained in 97% yield: mp 81–82° after sublimation at 80° (6 μ).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 72.0; H, 6.7. Found: C, 71.9; H, 6.9.

Reaction of 1,4-Dihydroxy-2-methyl-3-naphthaldehyde Diacetate (XXIIc) with Isopropylidenetriphenylphosphorane.—Butyllithium in hexane (3.0 ml, 1.6 *N*) was added to a suspension of 1.87 g (4.85 mmol) of isopropyltriphenylphosphonium bromide[28a] in 20 ml of tetrahydrofuran. The ylide solution was stirred 90 min; 13 ml (2.5 mmol) was removed and added dropwise to a suspension of 0.7 g (2.45 mmol) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde diacetate (XXIIc) in 20 ml of tetrahydrofuran; the solution was refluxed 3.5 hr; 0.3 g (8.0 mmol) of lithium aluminum hydride was added; and the mixture was refluxed an additional 3 hr. It was cooled to 0°; wet ether was added followed by saturated aqueous ammonium chloride; the ether phase was removed; the aqueous phase was extracted with several portions of ether; and the combined extracts were washed and dried. Silver oxide was then added to the ether, and the suspension was stirred for 30 min, filtered, and evaporated to give a mixture of quinones. Glpc analysis showed three peaks at 12.6, 24.2, and 29 min in the ratio of 4:2:1 based on peak areas. The assignments based on uv, nmr, tlc, and glpc comparison with authentic samples are 12.6 min ≡ 2,3-dimethyl-1,4-naphthoquinone (XXX), 24.2 min ≡ 3-isobutyl-2-methyl-1,4-naphthoquinone (XXXI), and 29 min ≡ 2-methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI).

3-Isobutyl-2-methyl-1,4-naphthoquinone (XXXI) was prepared as described for similar compounds.[17] This material has been reported[16] as melting at 123°. However, we find it to be a clear yellow oil, molecularly distilling at 60° (5 μ): nmr (CCl_4) δ 0.92 (d, Ar—C—$CH(CH_3)$—CH_3), 2.5 (d, Ar—CH_2—CH<); mass spectrum *m/e* 228 (M^+).

Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.9; H, 7.1. Found: C, 78.8; H, 6.9.

2-Methyl-3-(2-methyl-1-propenyl)-1,4-naphthalenediol Diacetate.—Zinc dust (2 g) and pyridine (1 ml) were added to a solution of 2 g of 2-methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI) dissolved in 20 ml of acetic anhydride, which was stirred 20 min at 0° and then at room temperature for 24 hr. Acetic acid (20 ml) was added; the mixture was heated to reflux and filtered; the precipitate was washed with hot acetic acid; and the combined filtrates poured onto crushed ice. The product solidified and was crystallized from ethanol–water to give 1.95 g (70% yield) of 2-methyl-2-(2-methyl-1-propenyl)-1,4-naphthalenediol diacetate: mp 161–161.5°; nmr δ 1.54 (d, J = 1 Hz, *cis* ArC=C—CH_3), 1.9 (d, J = 2 Hz, *trans* ArC=C—CH_3), 6.0 (b, ArCH=).

Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.0; H, 6.4. Found: C, 72.8; H, 6.2.

4-Methoxy-2-methyl-3-(2-methyl-1-propenyl)-1-naphthol Pivalate (XXXIIa).—Butyllithium (4.6 ml, 1.3 *N*, 6 mmol) was added dropwise to a stirred suspension of 2.32 g (6 mmol) of isopropyltriphenylphosphonium bromide in 20 ml of tetrahydrofuran, and after 2 hr this solution was added dropwise to 1.5 g (5 mmol) of 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate (XXIIe) in 6 ml of tetrahydrofuran. The solution was stirred for 1 hr and evaporated. Then the residue was chromatographed on silica gel, eluting with benzene, to give 1.5 g (92% yield) of 4-methoxy-2-methyl-3-(2-methyl-1-propenyl)-1-naphthol pivalate (XXXIIa), pure by tlc and glpc: nmr (CCl_4) δ 1.55 (d, J = 1 Hz, *cis* ArC=C—CH_3), 1.95 (d, J = 1 Hz, *trans* ArC=C—CH_3), 6.2 (b, ArCH=).

***cis*- and *trans*-4-methoxy-2-methyl-3-(1-pentenyl)-1-naphthol pivalates (XXXIIb)** were prepared from *n*-butyltriphenylphosphonium bromide[47] and 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate (XXIIe) in the same manner as described for the preparation of 4-methoxy-2-methyl-3-(2-methyl-1-propenyl)-1-naphthol pivalate (XXXIIa). A mixture of 1.55 g (88% yield) was obtained of *cis*- and *trans*-4-methoxy-2-methyl-3-(1-pentenyl)-1-naphthol pivalates. The *cis* and *trans* isomers were present in a ratio of 2:3 and were separated by glpc: R_T *cis* 35 min, *trans* 55 min.

cis **XXXIIb**: nmr (CCl_4) δ 0.83 (t, J = 7 Hz, CH_2CH_3), 5.72 (t, J = 7 Hz), 5.9 (t, J = 7 Hz), *trans* ArC=C—H, 6.38 (d, J = 11 Hz, ArCH=C).

trans **XXXIIb**: nmr (CCl_4) δ 0.95 (t, J = 7 Hz, CH_2CH_3); 5.92 (t, J = 5 Hz), 6.2 (t, J = 5 Hz) *cis* ArC=CH—; 6.45 (d, J = 17 Hz, ArCH=C).

***cis*- and *trans*-4-methoxy-2-methyl-3-(2-methyl-1-pentenyl)-1-naphthol pivalates (XXXIIc)** were prepared from 2-pentyltriphenylphosphonium iodide and 1-hydroxy-4-methoxy-2-methyl-3-naphthaldehyde pivalate (XXIIe) in the same manner as described for 4-methoxy-2-methyl-3-(2-methyl-1-propenyl)-1-naphthol pivalate (XXXIIa). A mixture of 1.6 g (85% yield) was obtained of *cis*- and *trans*-4-methoxy-2-methyl-3-(2-methyl-1-pentenyl)-1-naphthol pivalates. The *cis* and *trans* isomers were present in a ratio of 1:1 and were separated by glpc: R_T *cis* 30 min, *trans* 42 min.

cis **XXXIIc**: nmr (CCl_4) δ 0.78 (t, J = 7 Hz, CH_2CH_3), 1.95 (d, J = 1 Hz, *trans* ArC=C—CH_3), 6.15 (b, ArCH=C).

trans **XXXIIc**: nmr (CCl_4) δ 1.0 (t, J = 7 Hz, CH_2CH_3), 1.55 (d, J = 1 Hz, *cis* ArC=C—CH_3) 6.15 (b, ArCH=C).

2- and 3-Pentyltriphenylphosphonium Bromides.—A mixture of 20 g (76 mmol) of triphenylphosphine and 11.5 g (76 mmol) of 2-bromopentane[29] was sealed in a glass tube in a nitrogen atmosphere and heated at 170° for 48 hr. The tube was cooled to room temperature; the contents were dissolved in ethanol and decolorized with carbon; and the salt was precipitated by addition of ether. Solution in ethanol and reprecipitation by

(47) R. Mechoulam and F. Sondheimer, *J. Amer. Chem. Soc.*, **80**, 4386 (1958).

addition of ether gave 18 g (57%) of a mixture of 2- and 3-pentyltriphenylphosphonium bromides: mp 208–211°; nmr δ 0.75–2.0 (t, J = 6 Hz, CH_3–C-5), 1.6 (d, J = 7 Hz, ⩾P⁺—C-(CH_3)<, m, ⩾P—C—CH_2—), 4.7–5.25 (b, ⩾P—CH<), 7.65–8.3 (m, Ph_3P^+—).

Anal. Calcd for $C_{23}H_{26}BrP$: C, 66.8; H, 6.3. Found: C, 66.3; H, 6.3.

Glpc analysis of the unreacted bromopentane showed two distinct peaks (R_T 60 and 64 min) in the ratio of 2:1, shown to be 2- and 3-bromopentanes.

2-Pentyltriphenylphosphonium Iodide.—Butyllithium in hexane (18.5 ml, 1.6 N, 0.3 mol) was added dropwise to a suspension of 12 g (30 mmol) of n-butyltriphenylphosphonium bromide in 90 ml of tetrahydrofuran. The solution was stirred for 2 hr, and then the clear red supernatant was added dropwise to a solution of 0.85 g (60 mmol) of iodomethane in 10 ml of tetrahydrofuran. Reaction was immediate, and a white solid precipitated from solution. The solvent was evaporated after stirring for 1 hr, and the residue was purified by solution in ethanol and precipitation with ether to give 7.5 g (53%) of 2-pentyltriphenylphosphonium ioidide: mp 172–173° (lit.[31] mp 172°); nmr δ 0.8–2.0 (t, J = 6 Hz, 5-CH_3; two d, J = 7 Hz, —P⁺CHCH_3, —P⁺—C—CH_2CH_2), 4.6–5.05 (b, —P⁺—CH), 7.65–8.2 (m, Ph_3P^+—).

Alkylation of Ethylidenetriphenylphosphorane with n-Bromobutane.—Butyllithium (6.3 ml, 10 mmol, 1.6 N) in hexane was added dropwise to a suspension of 3.71 g (10 mmol) of ethyltriphenylphosphonium bromide[27b] suspended in 20 ml of tetrahydrofuran. The mixture was stirred 1 hr; the suspended salts were added to settle; and the clear orange-red supernatant was added to a solution of 3 ml of n-bromobutane in 10 ml of tetrahydrofuran. Complete loss of ylide color required 3 hr as a white precipitate formed. The mixture was evaporated to dryness; the residue was dissolved in chloroform, filtered, and again evaporated to dryness; and the residue was triturated with ether to give a white solid. Comparison of the nmr signals due to the α-methylene protons of ethyltriphenylphosphonium bromide at δ 3.5–4.0 and the α-methinyl proton of 2-pentyltriphenylphosphonium bromide at δ 4.6–5.2 indicated that the product was 20% ethyl salt and 80% 2-pentyl salt.

Triphenylphosphonium salt of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXXIV) was prepared from triphenylphosphine and 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXIX) in refluxing benzene, giving 9 g (77% yield) of the triphenylphosphonium salt of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate, mp 185–186° (d).

Anal. Calcd for $C_{36}H_{36}ClO_3P$: C, 74.2; H, 6.2; Cl, 6.1. Found: C, 74.0; H, 6.4; Cl, 6.0.

4-Methoxy-2-methyl-3-(2-styryl)-1-naphthol Pivalate (XXXIIe).—To a suspension of 2.9 g (5 mmol) of triphenylphosphonium salt of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXXIV) in 15 ml of toluene stirred under nitrogen was added butyllithium (3.3 ml, 1.5 N, 5 mmol) in hexane. The resulting orange-red solution was stirred for 1 hr and 0.5 ml (5 mmol) of benzaldehyde was added. After 1 hr, the solvent was evaporated, and the residue was chromatographed on silica gel, eluting with benzene, to give 1.7 (90% yield) of 4-methoxy-2-methyl-3-(2-styryl)-1-naphthol pivalate pure by tlc: nmr (CCl_4) δ 7.1–7.75 (11 H, m, C-5, -6, -7, -8, Ar—CH=CH—Ph).

***cis*- and *trans*-4-Methoxy-2-methyl-3-(2-methyl-1-octenyl)-1-naphthol Pivalates (XXXIIf).**—To a suspension of 8.74 g (15 mmol) of triphenylphosphonium salt of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXXIV) in 50 ml of toluene was added 8.5 ml (1.6 N, 13.5 mmol) of butyllithium in hexane. The resulting orange-red solution was stirred 1 hr at 25° and then was centrifuged. To the clear supernatant 1.54 g (12 mmol) of 2-octanone was added and the solution was heated at reflux for 72 hr. The solvent was evaporated, and the residue was chromatographed on silica gel, eluting with benzene–hexane (1:1). Initial fractions contained 800 mg (3.05 mmol) of triphenylphosphine and intermediate fractions contained 1.45 g (3.6 mmol, 30% yield) of a mixture of *cis*- and *trans*-4-methoxy-2-methyl-3-(2-methyl-1-octenyl)-1-naphthol pivalates in a ratio of 35:65. The isomers were separated by glpc: R_T *cis* 65 min, *trans* 113 min.

***cis* XXXIIf**: nmr (CCl_4) δ 0.78 (t, J = 5 Hz, ArC=C($C)_5$-CH_3), 1.95 (d, J = 1 Hz, *trans* ArC=C—C—CH_3), 6.15 (b, ArCH=).

***trans* XXXIIf**: nmr (CCl_4) δ 0.95 (t, J = 5 Hz, ArC=C($C)_5$-CH_3), 1.55 (d, J = 1 Hz, *cis* ArC=C—CH_3), 6.2 (b, ArCH=).

The last fractions contained 700 mg (2.5 mmol) of 2,3-dimethyl-4-methoxy-1-naphthol pivalate (XXXVI) pure by tlc and glpc: nmr (CCl_4) δ 2.15 (s, 2-ArCH_3), 2.32 (s, 3-ArCH_3).

2-Octanone-1,1,1,3,3-d_5.—A solution of 500 mg of anhydrous potassium carbonate in 25 ml of deuterium oxide and 12 ml of 2-octanone were refluxed for 24 hr; the organic phase was then removed; and fresh K_2CO_3–D_2O was added to it. Three such exchanges were carried out after which the organic layer was distilled to give 10 ml of 2-octanone-1,1,1,3,3,d_5, bp 170–171.5°. The signals present in the nmr spectrum of 2-octanone at δ 2.05 (s, CH_3CO—) and 2.38 (t, J = 6 Hz, —$COCH_2$—) were absent.

***cis*- and *trans*-4-Methoxy-2-methyl-3-(2,6,10,14-tetramethyl-1-pentadecenyl)-1-naphthol Pivalates (XXXIIg).**—The triphenylphosphonium salt of 3-chloromethyl-4-methoxy-2-methyl-1-naphthol pivalate (XXXIV) was converted into ylide and then treated with 6,10,14-trimethyl-2-pentadecanone as previously described. The solution was refluxed for 72 hr; the solvent was evaporated; and the residue was chromatographed on silica gel, eluting with benzene–hexane (1:1). Triphenylphosphine was eluted first. Intermediate fractions contained a 21% yield of a mixture of *cis*- and *trans*-4-methoxy-2-methyl-3-(2,6,10,14-tetramethyl-1-pentadecenyl)-1-naphthol pivalates: nmr (CCl_4) δ 1.56 (*cis* ArC=C—CH_3), 1.95 (*trans* ArC=C—CH_3), 6.15–6.28 (b, ArCH=).

The last fraction contained a small amount of 2,3-dimethyl-4-methoxy-1-naphthol pivalate (XXXVI), pure by glpc and tlc.

1,4-Dihydroxy-α,2-dimethyl-3-naphthaleneacrylic Acid δ-Lactone 1-Propionate.—A suspension of 500 mg (2.5 mmol) of 1,4-dihydroxy-2-methyl-3-naphthaldehyde (XXIIa) and 275 mg (3 mmol) of sodium propionate in 1 g (7.5 mmol) of propionic anhydride was heated at 195° (bath temperature) for 8 hr; the solution was cooled; water was added; and the the solid organic phase was removed, ground, and washed with water. Crystallization from absolute ethanol gave 470 mg (63% yield) of 1,4-dihydroxy-α,2-dimethyl-3-naphthaleneacrylic acid δ-lactone 1-propionate: mp 184.5–185.5°; nmr δ 2.2 (d, ArC=CCH_3).

Anal. Calcd for $C_{18}H_{16}O_4$: C, 73.0; H, 5.4. Found: C, 73.0; H, 5.4.

1,4-Dihydroxy-α,2-dimethyl-3-naphthaleneacrylic Acid δ-Lactone.—A suspension of 7.5 g (25 mmol) of 1,4-dihydroxy-α,2-dimethyl-3-naphthaleneacrylic acid δ-lactone 1-propionate in 125 ml of absolute ethanol containing 3 g of sodium was refluxed for 2 hr; the solution was then cooled in an ice bath, diluted with water, neutralized with concentrated hydrochloric acid, and evaporated. The residue was washed with water to give 1,4-dihydroxy-α,2-dimethyl-3-naphthaleneacrylic acid δ-lactone: mp 224–227°; nmr (DMSO) δ 2.12 (d, ArC=CCH_3).

α,2-Dimethyl-4-hydroxy-1-methoxy-3-naphthaleneacrylic Acid δ-Lactone (XXXVII).—To a suspension of the crude 1,4-dihydroxy-α,2-dimethyl-3-naphthaleneacrylic acid δ-lactone in 19.5 g (155 mmol) of dimethyl sulfate was added dropwise over 30 min a solution of 13.0 g (233 mmol) of potassium hydroxide in 30 ml of water. The solid was removed, washed with water, and dried to give 4.0 g (63% yield) of α,2-dimethyl-4-hydroxy-1-methoxy-3-naphthaleneacrylic acid δ-lactone: mp 163–164.5° after crystallization from absolute ethanol; nmr δ 2.15 (d, ArC=CCH_3), 3.8 (s, ArOCH_3).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.6; H, 5.5. Found: C, 75.3; H, 5.5.

***trans*-4-Hydroxy-1-methoxy-α,2-dimethyl-3-naphthaleneacrylic Acid (XXXIX).**—A solution of 3 g (12 mmol) of α,2-dimethyl-4-hydroxy-1-methoxy-3-naphthaleneacrylic acid δ-lactone (XXXVII) in 250 ml of 3 N methanolic potassium hydroxide was irridiated for 48 hr with a low-pressure mercury lamp with a Vycor filter. The contents were then diluted with water, cooled in an ice bath, neutralized with concentrated hydrochloric acid, and extracted with ether. The residue from the combined, washed, dried, and evaporated ether extracts was taken up in ether and washed with 1% aqueous sodium bicarbonate. The combined bicarbonate washes were extracted with ether, and the combined ether extracts were washed with water and evaporated, leaving a residue which was sublimed at 100° (20 μ) to give 500 mg (16%) of recovered lactone XXXVII.

The combined bicarbonate extracts were acidified with hydrochloric acid and extracted with ether. Evaporation of the combined ether extracts left a residue which was chromatographed on silica gel, eluting with ether–hexane (1:1). The fractions containing the acid were pooled and evaporated. Crystallization from chloroform gave 400 mg (12.5% conversion) of *trans*-α,2-dimethyl-4-hydroxy-1-methoxy-3-naphthaleneacrylic acid

(XXXIX): mp 140° dec (very sensitive to rate of heating); nmr (DMSO) δ 1.72 (d, ArC=CCH$_3$).

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.6; H, 5.9. Found: C, 70.5; H, 5.4.

Methyl *cis*-1,4-Dimethoxy-α,2-dimethyl-3-naphthaleneacrylate (XL).—A solution of 508 mg (2 mmol) of 4-hydroxy-α,2-dimethyl-1-methoxy-3-naphthaleneacrylic acid δ-lactone (XXXVII) and 2.3 g (16 mmol) of iodomethane in 7 ml of N,N-dimethylformamide was stirred with 2 g (6.3 mmol) of barium hydroxide octahydrate for 50 hr at 25°. Volatiles were then evaporated, and the remainder was diluted with water and extracted with ether. The combined ether layers were washed and evaporated to give a yellow oil which was purified by preparative glpc on 10% SE-30 to yield 580 mg (96% yield) of methyl *cis*-1,4-dimethoxy-α,2-dimethyl-3-naphthaleneacrylate: nmr δ 2.15 (d, J = 2 Hz, ArC=CCH$_3$), 6.75 (b, ArCH=).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 72.0; H, 6.7. Found: C, 72.2; H, 6.9.

Methyl *trans*-1,4-Dimethoxy-α,2-dimethyl-3-naphthaleneacrylate (XLI).—The *trans*-methyl ester was prepared exactly as described for the *cis*-methyl ester above. Purification by preparative glpc on 10% SE-30 gave a 63% yield of methyl *trans*-1,4-dimethoxy-α,2-dimethyl-3-naphthaleneacrylate: mp 45–46°; nmr δ 1.8 (d, J = 2 Hz, ArC=CCH$_3$), 7.62 (b, ArCH=).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 72.0; H, 6.7. Found: C, 71.7; H, 6.8.

***cis*-1,4-Dimethoxy-2-methyl-3-(2-methyl-1-propen-3-ol)naphthalene (XLII).**—A solution of 100 mg (0.33 mmol) of methyl *cis*-1,4-dimethoxy-α,2-dimethyl-3-naphthaleneacrylate (XL) dissolved in 20 ml of ether was added slowly to a solution of 100 mg (2.5 mmol) of lithium aluminum hydride in 15 ml of ether maintained at −15°. After addition was complete, the solution was stirred 1 hr at −15° and then treated with wet ether followed by saturated aqueous ammonium chloride. Extraction with ether which was then washed and evaporated left an oil, purified by preparative tlc on Kiesel gel G (eluting with ether–hexane, 1:1) and sublimed at 60° (20 μ) to give *cis*-1,4-dimethoxy-2-methyl-3-(2-methyl-1-propen-3-ol)naphthalene: mp 69–70°; nmr δ 2.08 (d, J = 1 Hz, ArC=CCH$_3$), 3.8 (s, ArOCH$_3$, =CCH$_2$O), 6.15 (b, ArCH=).

Anal. Calcd for $C_{17}H_{20}O_3$: C, 75.0; H, 7.4. Found: C, 74.6; H, 7.5.

***trans*-1,4-Dimethoxy-2-methyl-3-(2-methyl-1-propen-2-ol)naphthalene (XLIII).**—Prepared from 100 mg (0.33 mmol) of methyl *trans*-1,4-dimethoxy-α,2-dimethyl-3-naphthaleneacrylate (XLI) exactly as described for the *cis* isomer. Purification by tlc (Kiesel gel G, eluting with ether–hexane, 2:1) and sublimation at 75° (20 μ) gave *trans*-1,4-dimethyl-2-methyl-3-(2-methyl-1-propen-2-ol)naphthalene: mp 49–50°; nmr δ 1.58 (d, ArC=CH$_3$), 4.25 (b, =C—CH$_2$O), 6.45 (b, ArCH=).

Anal. Calcd for $C_{17}H_{20}O_3$: C, 75.0; H, 7.4. Found: C, 74.7; H, 7.1.

Conversion of Pivalate Esters into Quinones. A. Removal of Pivaloyl Group.—A solution of 1 mmol of the 4-methoxy-1-naphthol pivalate in 5 ml of ether was added dropwise to 145 mg (3.5 mmol) of lithium aluminum hydride in 5 ml of ether. After being refluxed for 1 hr, the solution was cooled to 0°; wet ether followed by saturated aqueous ammonium chloride was added; the ether layer was removed; and the aqueous phase was extracted several times with ether. Evaporation of the combined, washed, and dried ether extracts left the 4-methoxy-1-naphthol.

B. Oxidation of the 4-Methoxy-1-naphthol to Quinone.—A solution of 680 mg (2.5 mmol) of ferric chloride hexahydrate in 40 ml of 50% aqueous acetonitrile was added to a solution of 1 mmol of the 4-methoxy-1-naphthol in 40 ml of 50% aqueous acetonitrile. The solution was stirred for 15 min, diluted with two volumes of water, and extracted several times with ether. Evaporation of the combined, washed, and dried ether extracts left the quinone.

This procedure was used for the 4-methoxy-1-naphthols with shorter chains, soluble in the 50% aqueous acetonitrile. For the longer chain methoxynaphthols, insoluble in this medium, an ether–ethanol mixture (1:1) was used as solvent, and 30% aqueous ferric chloride was added.

The following quinones were prepared by the above procedure.

2-Methyl-3-(2-methyl-1-propenyl)-1,4-naphthoquinone (XI): 88% yield from pivalate ester; mp 42–43° after chromatography on silica gel, eluting with benzene–hexane (1:1), and crystallization from methanol at −20°; λ_{max} 315 nm (broad) (ϵ 3300), 264 (sh), (14,000), 249 (23,000); nmr δ 1.58 (d, J = 1 Hz, *cis* ArC=CCH$_3$), 1.98 (d, J = 1 Hz, *trans* ArC=CCH$_3$), 6.08 (b, CH=C).

Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.6; H, 6.2. Found: C, 79.6; H, 6.1.

***cis*-2-Methyl-3-(2-methyl-1-pentenyl)-1,4-naphthoquinone (XXXIIIb):** 50% yield from pivalate ester; mp 79–80° after chromatography on silica, eluting with hexane–ether (19:1), and sublimation at 50° (10 μ); λ_{max} 315 nm (broad) (ϵ 3200), 265 (sh) (13,000), 249 (23,000); nmr (CCl$_4$) δ 0.8 (t, J = 7 Hz, —CH$_2$CH$_3$), 1.95 (d, J = 2 Hz, *trans* ArC=CCH$_3$), 5.85 (b, ArCH=); mass spectrum m/e 254 (M$^+$), 239, 225, 221.

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.3; H, 7.1. Found: C, 80.2; H, 7.3.

***trans*-2-Methyl-3-(2-methyl-1-pentenyl)-1,4-naphthoquinone (XXXIIIb):** 60% yield from pivalate ester; mp 64.5–66° after sublimation at 50° (10 μ); λ_{max} 315 nm (broad) (ϵ 3150), 265 (sh) (13,500), 249 (23,000); nmr (CCl$_4$) δ 1.0 (t, J = 7 Hz, —CH$_2$CH$_3$), 1.55 (d, J = 1 Hz, *cis* ArC=CCH$_3$), 5.95 (b, ArCH=); mass spectrum m/e 254 (M$^+$), 239, 225, 221.

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.3; H, 7.1. Found: C, 79.8; H, 7.1.

***cis*-4-Methoxy-2-methyl-3-(1-pentenyl)-1-naphthol** was oxidized to quinone which was chromatographed on silica gel, eluting with ether–hexane. The quinone so obtained contained 10% of the *trans* isomer (R_F *cis* 0.28, *trans* 0.34 on tlc, Kiesel gel G, 15% butyl ether in hexane) which was removed by crystallization from methanol. Pure ***cis*-2-methyl-3-(1-pentenyl)-1,4-naphthoquinone (XXXIIIa)** had mp 68.5–69°; λ_{max} 330 nm (ϵ 3000), 285 (4400), 250 (21,200); nmr (CCl$_4$ δ 0.86 (t, J = 6 Hz, —CH$_2$CH$_3$), 5.65 (t, J = 5 Hz), 5.85 (t, J = 5 Hz) ArC=CH; 6.1 (d, J = 10 Hz, ArCH=).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7. Found: C, 80.0; H, 6.8.

***trans*-2-Methyl-3-(1-pentenyl)-1,4-naphthoquinone (XXXIIIa),** purified by tlc (Kiesel gel G, benzene), remained an oil: λ_{max} 365 nm (ϵ 2300), 330 (3150), 285 (8150), 250 (23,000); nmr (CCl$_4$) δ 1.0 (t, J = 7 Hz, —CH$_2$CH$_3$), 6.3 (s, ArCH=), 6.35 (t, J = 6 Hz, ArC=CH).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7. Found: C, 80.0; H, 6.8.

2-Methyl-3-(2-styryl)-1,4-naphthoquinone (XXXIIIc) crystallized from methanol and had mp 97–98°; λ_{max} 400 nm (ϵ 8150), 280 (24,200).

Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.2; H, 5.2. Found: C, 83.3; H, 5.4.

***cis*-2-Methyl-3-(2-methyl-1-octenyl)-1,4-naphthoquinone (XXXIIId):** oil; λ_{max} 315 nm (broad) (ϵ 3200), 265 (sh) (13,500), 249 (22,400); nmr (CCl$_4$) δ 0.75 (t, J = 5 Hz, —CH$_2$CH$_3$), 1.9 (d, J = 1 Hz, *trans* ArC=CCH$_3$), 5.88 (b, ArCH=).

Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.0; H, 8.2. Found: C, 81.2; H, 8.0.

***trans*-2-Methyl-3-(2-methyl-1-octenyl)-1,4-naphthoquinone (XXXIIId):** oil; λ_{max} 315 nm (broad) (ϵ 3150), 265 (sh) (13,500), 249 (23,000); nmr (CCl$_4$) δ 0.92 (t, J = 5 Hz, —CH$_2$CH$_3$), 1.55 (d, J = 1 Hz, *cis* ArC=CCH$_3$), 5.95 (b, ArCH=).

Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.0; H, 8.2. Found: C, 81.4; H, 8.1.

2-Methyl-3-(2,6,10,14-tetramethyl-1-pentadecenyl)-1,4-naphthoquinone (XXXIIIe) was obtained as an oily *cis–trans* mixture which was separated by tlc on Kiesel gel G, developing with butyl ether–hexane, 1:12 (R_F *cis* 0.84, *trans* 0.92).

***cis* XXXIIIe:** λ_{max} 315 nm (broad) (ϵ 3300), 263 (sh) (14,100), 248 (23,100); nmr (CCl$_4$) δ 1.95 (d, J = 1 Hz, *trans* ArC=CCH$_3$), 5.87 (b, ArCH=).

Anal. Calcd for $C_{30}H_{44}O_2$: C, 82.5; H, 10.2 Found: C, 81.9; H, 10.1.

***trans* XXXIIIe:** λ_{max} 315 nm (broad) (ϵ 3300), 263 (sh) (13,600), 248 (23,100); nmr (CCl$_4$) δ 1.55 (d, J = 1 Hz, *cis* ArC=CCH$_3$), 6.0 (b, ArCH=).

Anal. Calcd for $C_{30}H_{44}O_2$: C, 82.5; H, 10.2. Found: C, 82.1; H, 10.0.

Registry No.—X, 5571-10-8; XI, 17827-37-1; XVIII, 17838-73-2; XIX HCl, 17827-38-2; 1,4-dimethoxy-3-(2-dimethylaminoethyl)-2-methylnaphthalene methiodide, 17827-57-5; XX, 17827-39-3; 1,4-dimethoxy-2-methyl-3-naphthaldehyde, 17827-40-6; XXIIb,

17827-41-7; XXIIc, 17827-42-8; XXIIa, 17827-43-9; XXIId, 17827-44-0; XXIIe, 17827-45-1; XXIII, 17827-56-4; XXVI, 17827-46-2; XXVIII, 17827-47-3; XXIX, 17827-48-4; XXXI, 2397-62-8; 2-methyl-2-(2-methyl-1-propenyl)-1,4-naphthalenediol diacetate, 17827-58-6; XXXIIa, 17827-59-7; XXXIIb (*cis*), 17831-10-6; XXXIIb (*trans*), 17831-11-7; XXXIIc (*cis*), 17831-12-8; XXXIIc (*trans*), 17831-13-9; 2-pentyltriphenylphosphonium bromide, 17827-53-1; 3-pentyltriphenylphosphonium bromide, 7333-53-1; XXXIIe, 17827-51-9; XXXIIf (*cis*), 17831-25-3; XXXIIf (*trans*), 17831-15-1; 2-octanone-1,1,1,3,3-d_5, 17827-52-0; XXXIIg (*cis*), 17831-26-4; XXXIIg (*trans*), 17831-27-5; 1,4-dihydroxy-α,2-dimethyl-3-naphthaleneacrylic acid δ-lactone 1-propionate, 17838-75-4; 1,4-dihydroxy-α,2-naphthaleneacrylic acid δ-lactone, 17838-76-5; XXXIIIa (*cis*), 17831-16-2; XXXIIIa (*trans*), 17831-17-3; XXXIIIb (*cis*), 17831-18-4; XXXIIIb (*trans*), 17831-19-5; XXXIIIc, 17827-50-8; XXXIIId (*cis*), 17831-09-3; XXXIIId (*trans*), 17831-08-2; XXXIIIe (*cis*), 17838-74-3; XXXIIIe (*trans*), 17831-14-0; XXXIV chloride, 17866-64-7; XXXVII, 17827-55-3; XXXIX, 17831-20-8; XL, 17831-21-9; XLI, 17831-22-0; XLII, 17831-24-2; XLIII, 17831-23-1

N-Alkyl Substituents as Competition Reaction Sites in the α Alkylation of Tertiary Amines[1a]

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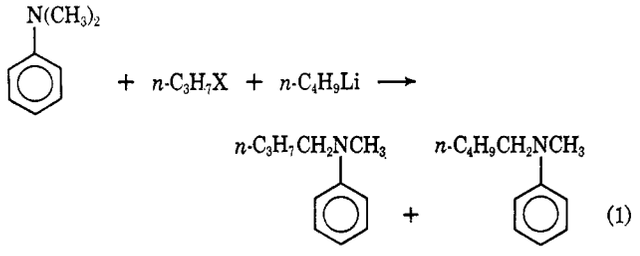
The direct α butylation of tertiary amines with *n*-butyllithium and 1-iodobutane was investigated by inter- and intramolecular competition reactions. Structure changes at the α position in the reacting amine were used as the competition variables. The intermolecular competition of N,N-dimethylaniline with N,N-diethylaniline, N-methyldiphenylamine, N-methyl-N-ethylaniline, triethylamine, or triethylenediamine showed that reactivity per α hydrogen was significantly greater for methyl than for ethyl groups. This effect of alkyl structure was much greater than the conjugative or resonance effects caused by increasing or decreasing the number of aromatic rings attached to nitrogen. Intramolecular competition in N-methyl-N-ethylaniline and in N-methyl-N-(2-butyl)aniline extended the reactivity order to methyl > ethyl > *sec*-butyl or primary > secondary > tertiary. The quantitative alkyl reactivity ratios closely parallel hydrocarbon acidities and σ^* values for cumulative inductive effects. A model is therefore suggested for the reaction transition state which is compatible with previous α alkylation results and with two other simultaneously occurring reactions, halogen–metal interchange and Wurtz coupling.

The direct α-carbon alkylation of tertiary amines takes place when these amines are used as solvents for the reaction of organolithium reagents with alkyl or aryl halides[2] (eq 1). Either the bromo- or iodoalkanes



(1)

will participate in the reaction, but the former are less reactive while the latter also undergo extensive halogen–metal interchange.[3]

Trialkylamines[4] as well as N-alkylanilines[2,3,5] can undergo substitution. However, the reaction is limited to an α-alkyl position as demonstrated with triethylamine[4] and N,N-diethylaniline.[5]

These observations seemed to be in agreement with a simple mechanism involving metalation of the amine at an α-alkyl site followed by a "Wurtz" coupling with the available halide. Metalation studies of both N,N-dimethylaniline[6] and triethylamine[4] failed to confirm such a pathway, although the aniline reactivity was in reasonable agreement with hydrogen–deuterium exchange data.[7] A second route for product formation, amine quaternization with a subsequent Stevens rearrangement, was also eliminated in these same studies.

Although the reaction is described as a *direct* α alkylation because of the initial lack of a cogent mechanism, it seemed desirable to attempt to clarify this situation. Since steric effects and the relative reactivity of alkyl groups are closely related in many cases to the type of species involved as intermediates or in transition states, we have investigated the competition of α reaction sites in direct alkylation of tertiary amines. In order to ascertain comparability of steric factors as well as group reactivity, both inter- and intramolecular competition reactions were considered.

Results

The direct α-substitution reaction of tertiary amines was carried out on compounds or mixtures of compounds in which two nonequivalent positions were available for competitive alkylation. *n*-Butyllithium and 1-iodobutane were used so that the alkyl group

(1) (a) Presented in part before the Division of Organic Chemistry, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, Abstracts S161; A. R. Lepley and W. A. Khan, *Chem. Commun.*, 1198 (1967). This work was supported by U. S. Public Health Grants GM-09136 and GM-13987 from the National Institute of General Medical Sciences. (b) Department of Chemistry, Marshall University, Huntington, W. Va. (c) Department of Chemistry, Queen's University of Belfast, Belfast 9, Northern Ireland.

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