



8-1972

The Dimetalation and Subsequent Functionalization of 1,3-Dimethylnaphthalene by Means of Amylsodium in the Presence of Certain Tertiary Amines

Atilla Tuncay

Follow this and additional works at: https://scholarworks.wmich.edu/masters_theses



Recommended Citation

Tuncay, Atilla, "The Dimetalation and Subsequent Functionalization of 1,3-Dimethylnaphthalene by Means of Amylsodium in the Presence of Certain Tertiary Amines" (1972). *Master's Theses*. 4370.

https://scholarworks.wmich.edu/masters_theses/4370

This Masters Thesis-Open Access is brought to you for free and open access by the Graduate College at ScholarWorks at WMU. It has been accepted for inclusion in Master's Theses by an authorized administrator of ScholarWorks at WMU. For more information, please contact wmu-scholarworks@wmich.edu.



THE DIMETALATION AND SUBSEQUENT
FUNCTIONALIZATION OF 1,3-DIMETHYLNAPHTHALENE
BY MEANS OF AMYLSODIUM IN THE
PRESENCE OF CERTAIN TERTIARY AMINES

by

Atila Tuncay

A Thesis
Submitted to the
Faculty of The Graduate College
in partial fulfillment
of the
Degree of Master of Arts

Western Michigan University
Kalamazoo, Michigan
August 1972

ACKNOWLEDGEMENTS

I am deeply indebted to my research advisor, Dr. George B. Trimitsis for his untiring assistance and understanding during the course of this work. I am also grateful to Dr. Don C. Iffland and Dr. Dean W. Cooke for their help.

The financial benefits of teaching assistantships from the Chemistry Department are being recognized with gratitude.

A special thank you is also given to my wife for her moral support.

Atilla Tuncay

TABLE OF CONTENTS

	PAGE
I. INTRODUCTION	1
II. HISTORICAL	3
A. The Preparation of Organosodium Compounds	4
B. Metalation of Alkylbenzenes	6
C. Metalation of Alkyl ⁿ naphthalenes and Related Polynuclear Hydrocarbons	13
D. The Catalytic Effect of Certain Alkoxides and Tertiary Amines in Metalations with Organosodium Reagents	17
III. RESULTS AND DISCUSSION	19
A. The Metalation and Subsequent Functionalization of 1,3-Dimethylnaphthalene	19
B. The Mechanism of the Catalytic Effect of N,N,N',N'-Tetramethylethylenediamine on Metalations with <u>n</u> -Amylsodium	25
C. Attempted Selective Monoalkylation of 1,3-Dimethylnaphthalene Dianion <u>14</u> at the 3-Position	28
IV. EXPERIMENTAL	34
A. General	34
B. The Metalation and Subsequent Functionalization of 1,3-Dimethylnaphthalene	35
C. Attempted Selective Monoalkylation of 1,3- Dimethylnaphthalene Dianion <u>14</u> at the 3-Position . . .	43
V. SUMMARY	44
VI. BIBLIOGRAPHY	45
VII. VITA	47

LIST OF FIGURES

	PAGE
Figure 1. <u>n</u> -Amylsodium-TMEDA Coordination Complex . . .	26

I. INTRODUCTION

It is well known that the hydrogen atoms of a methyl group directly attached to an aromatic system are sufficiently acidic to be abstracted by suitable bases to generate the corresponding α -anion.^{1,2} These monoanions have frequently served as suitable intermediates for the formation of a large variety of α -condensation products in good to excellent yields.² On the other hand, attempts to obtain α, α' -dianions from various dimethylaromatic systems have met with limited success.² Due to the lack of sufficiently strong bases, dimetalation products were obtained only in poor yields even at high temperatures and prolonged reaction times, and their use in synthetic transformations has been very limited.

The purpose of the present investigation was to develop new and efficient methods capable of transforming dimethylarenes into their α, α' -dianions under mild conditions and short reaction times, and to investigate the suitability of such dianions in various synthetic transformations.

More specifically, the present study sought to develop a new basic system capable of transforming 1,3-dimethylnaphthalene into its α, α' -dianion and to examine the reactions of this dianion with a variety of electrophilic reagents such as alkyl halides, ketones, and carbon dioxide.

1,3-Dimethylnaphthalene was specifically chosen for this study because of its relative ease of preparation, and because of the expectation that its behavior would be representative of a large

variety of other mononuclear and polynuclear aromatic hydrocarbons.

II. HISTORICAL

Although the hydrogen atoms of a methyl group directly attached to an aromatic ring are much more acidic than those of a simple alkane¹, their acidity is still quite low and only very strong bases can be used for their abstraction. Traditionally, organosodium compounds and to a much less extent organopotassium compounds have been used as bases². Organolithium reagents are not sufficiently strong bases to ionize the α -hydrogen atoms of alkylarenes to any great extent.^A

In the following sections, a concise literature review of the methods used for the chain metalation and subsequent functionalization of certain mono and dimethylaromatic systems, will be presented.

^AAlthough organolithium reagents alone are not sufficiently strong bases to ionize the α -hydrogen atoms of alkylarenes, certain tertiary amines greatly enhance their basicity and under such conditions α -lithiation of alkylarenes proceeds in high yield. See for example, Historical p 18 and Discussion p 23.

A. The Preparation of Organosodium Compounds

In the past most organosodium^A compounds needed for metalation reactions were prepared from the corresponding organomercury compounds and metallic sodium in a hydrocarbon solvent².



Direct treatment of alkyl halides with metallic sodium invariably lead to Wurtz coupling.



Morton³ in 1939, showed that with the aid of a vertically creased flask (Morton flask), high speed stirring and efficient control of the reaction temperature, Wurtz coupling can be almost totally eliminated and organosodium compounds may be conveniently prepared in high yield (70-80%) by the direct action of the appropriate halide with metallic sodium.

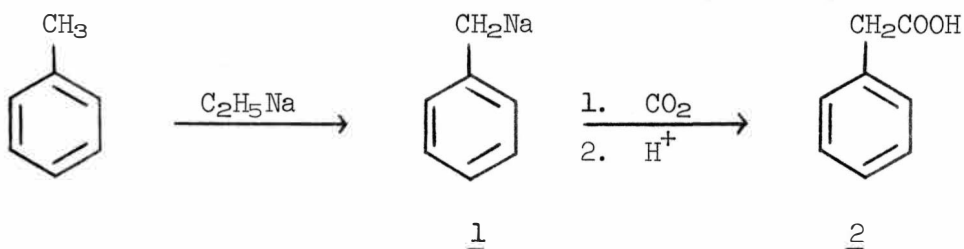
Although it is generally agreed that not all organosodium compounds are of equal reactivity, the marked difference in behavior among the various organosodium reagents is far from being well understood². Of the various organosodium compounds available, n-amylsodium

^AAlthough organosodium compounds are considered largely ionic, the extent of ionic character varies with the structure of the anion. In order to avoid representing such compounds of different reactivity by the possibly misleading designation R^-Na^+ , charges have been omitted throughout the present manuscript for reasons of simplicity.

has been most extensively used in metalation reactions², since this reagent was found to be considerably more reactive than the lower chain alkylsodium compounds, and approximately as reactive as the longer chain organosodium reagents.

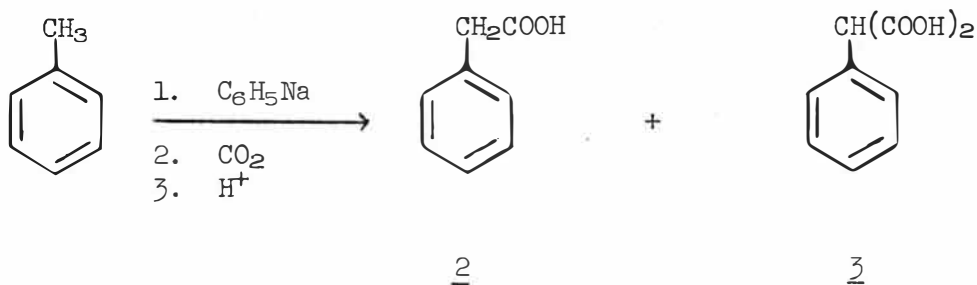
B. Metalation of Alkylbenzenes

The α -metalation of the simplest alkylbenzene, toluene, to give the benzyl anion 1, was first reported by Schorigin⁴ in 1908. He



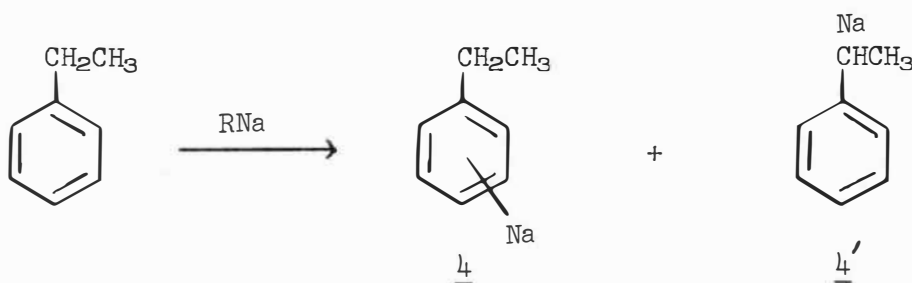
used ethylsodium as the base and obtained 14% metalation as determined by subsequent carbonation of the reaction mixture to afford the expected phenylacetic acid (2). In subsequent years a large number of other organosodium bases were used in the metalation of toluene, and yields of up to 77% were obtained⁵.

Nobis⁶ reported that metalation of toluene with phenylsodium followed by carbonation produced not only phenylacetic acid (2) but also phenylmalonic acid (3).



Nobis also found that by carefully controlling the reaction conditions either of the two acids could be formed with the virtual exclusion of the other. Thus, when the reaction was performed in the presence of a large excess of carbon dioxide only phenylacetic acid (2) was produced, while carbonation with a limited amount of CO_2 resulted in the formation of phenylmalonic acid (3).

The metalation of ethylbenzene was investigated by a number of workers^{4,7} and its behavior was found to be somewhat different from that of toluene. Thus, ethylbenzene was found to undergo α -metalation with more difficulty than toluene^{7b}, but more importantly ethylbenzene was found to undergo a certain amount of nuclear metalation^{7a,b} as well.

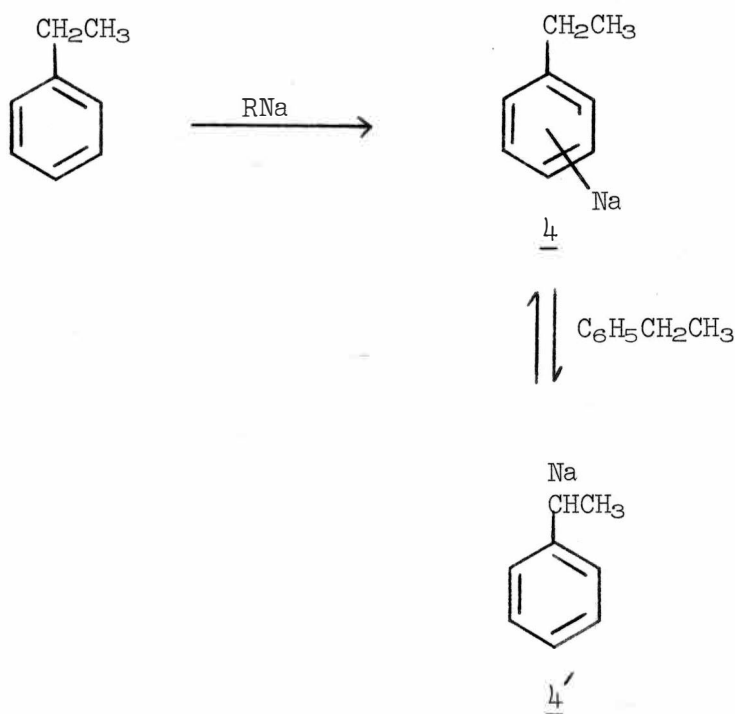


The inertness of ethylbenzene toward metalation as compared to toluene has been attributed to the electron releasing properties of the additional methyl group^{7b}, and to the fact that the α -hydrogen atoms in ethylbenzene are more sterically hindered^{7b} than in toluene.

The extent of α -metalation compared to nuclear metalation was shown to be critically dependent on the reaction time^{7a}. Short reaction periods favored nuclear metalation, while prolonged reaction time resulted in predominant α -metalation. Benkeser^{7a} and his group

attributed these results to a competition between thermodynamic and kinetic factors. Thus, the metalation of ethylbenzene was visualized as proceeding by way of a kinetically controlled first step, where a nuclear hydrogen atom was abstracted by the base to form anion 4, followed by a second step involving the rearrangement of this anion to the thermodynamically more stable benzyl anion 4' (Scheme I).

Scheme I

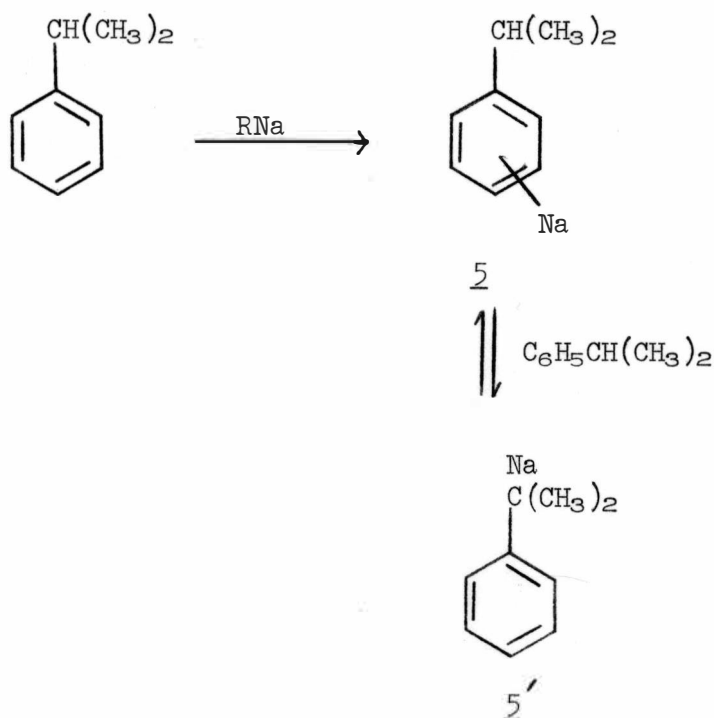


A number of contradicting reports have appeared in the literature concerning the mode of metalation of isopropylbenzene. Thus, while Morton⁸ and Bryce-Smith^{7b} in separate investigations found that treatment of isopropylbenzene with n-amylsodium afforded almost exclusively ring metalation products, Gilman⁹ and his group claimed

that metalation of isopropylbenzene with ethylsodium produced 40% of α -cumylsodium (5').

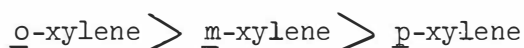
In a comprehensive study published in 1960, Benkeser and his coworkers, showed that the metalation of isopropylbenzene proceeds through a mechanism (Scheme II) quite similar to that proposed for the metalation of ethylbenzene, except that the rearrangement of anion 5 to the more thermodynamically stable anion 5' is much slower in the case of isopropylbenzene than in the case of ethylbenzene.

Scheme II

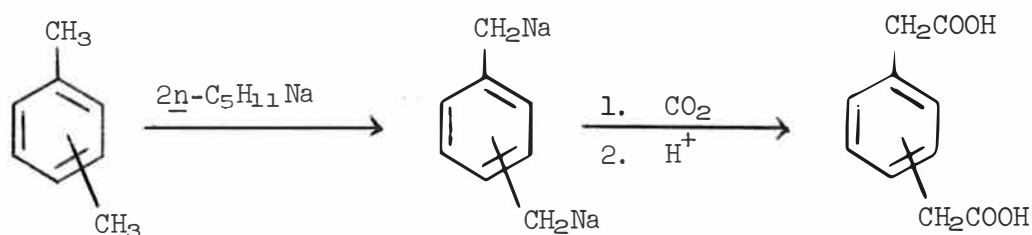


A somewhat different, and possibly more accurate mechanism for the metalation of alkylbenzenes has been recently proposed by Broadus¹⁰. Thus, while Benkeser's mechanism depicts initial attack as occurring

The above reactivity sequence for the α -monometalation of the xylenes is somewhat unexpected, especially in view of recent kinetic studies¹¹ indicating that the acidity of the α -hydrogen atoms of the three isomeric xylenes decreases in the order,

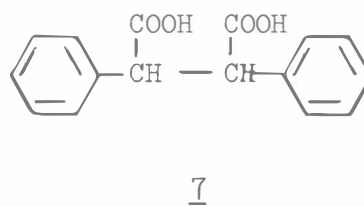
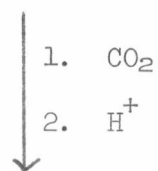
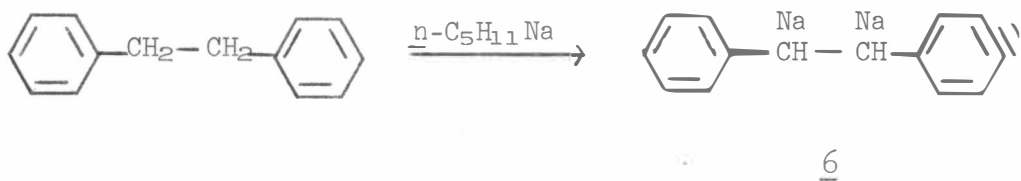


Morton^{5e} demonstrated that the xylenes can also be α,α' -dimetalated in low yield by heating with two equivalents of n-amylsodium in octane for three hours. Upon carbonation the disodium intermediates afforded



the expected phenylene diacetic acids, in 36, 37, and 19% yields, for the para, meta, and ortho isomers, respectively.

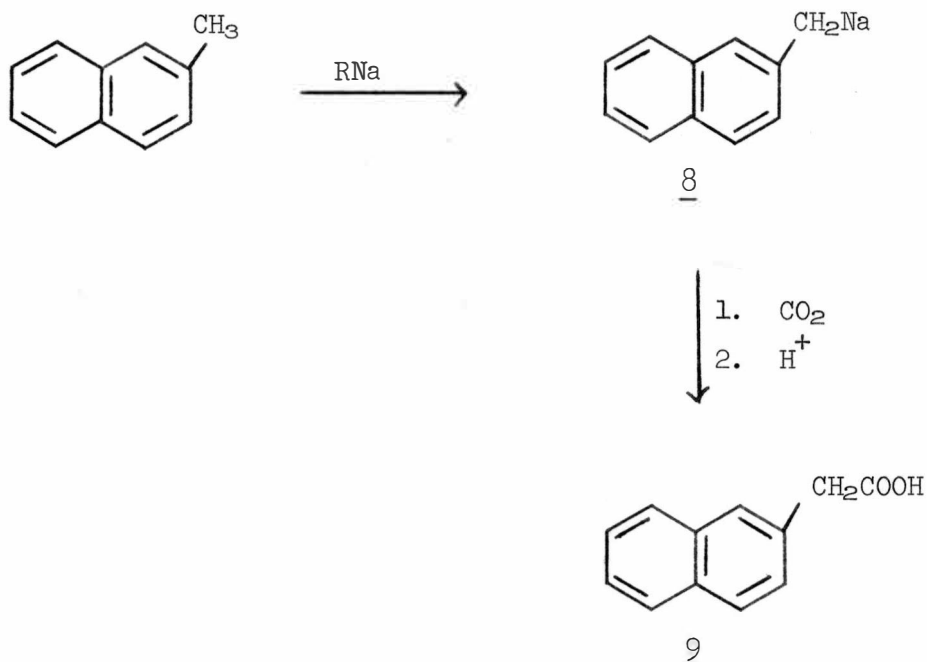
Unlike the xylenes, bibenzyl^{7c} could be easily dimetalated with n-amylsodium in high yield as ascertained by carbonation of the reaction mixture to give α,β -diphenylsuccinic acid (7) in 70% yield.



C. Metalation of Alkyl-naphthalenes and Related Polynuclear Hydrocarbons

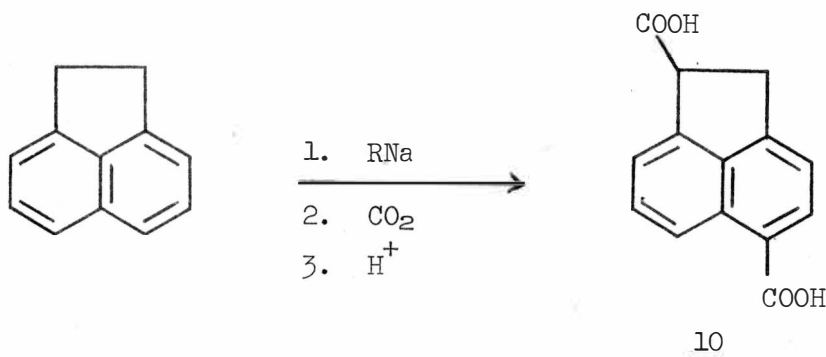
Only sporadic reports have appeared in the literature concerning the metalation of alkyl-naphthalenes and related polynuclear hydrocarbons. Based on these limited reports it appears that just as in the case of alkylbenzenes, metalation of alkyl substituted polynuclear hydrocarbons again occurs preferentially at the α -position and that the yields of the metalated products vary considerably depending upon the particular substrate and base used.

The α -metalation of 2-methylnaphthalene was first reported by Gilman⁹ in 1940, who used phenylsodium and *n*-butylsodium as the metalating agents, but the yields (based on carbonation) were very poor. In later years Morton^{7c} was able to obtain monosodium salt 8,



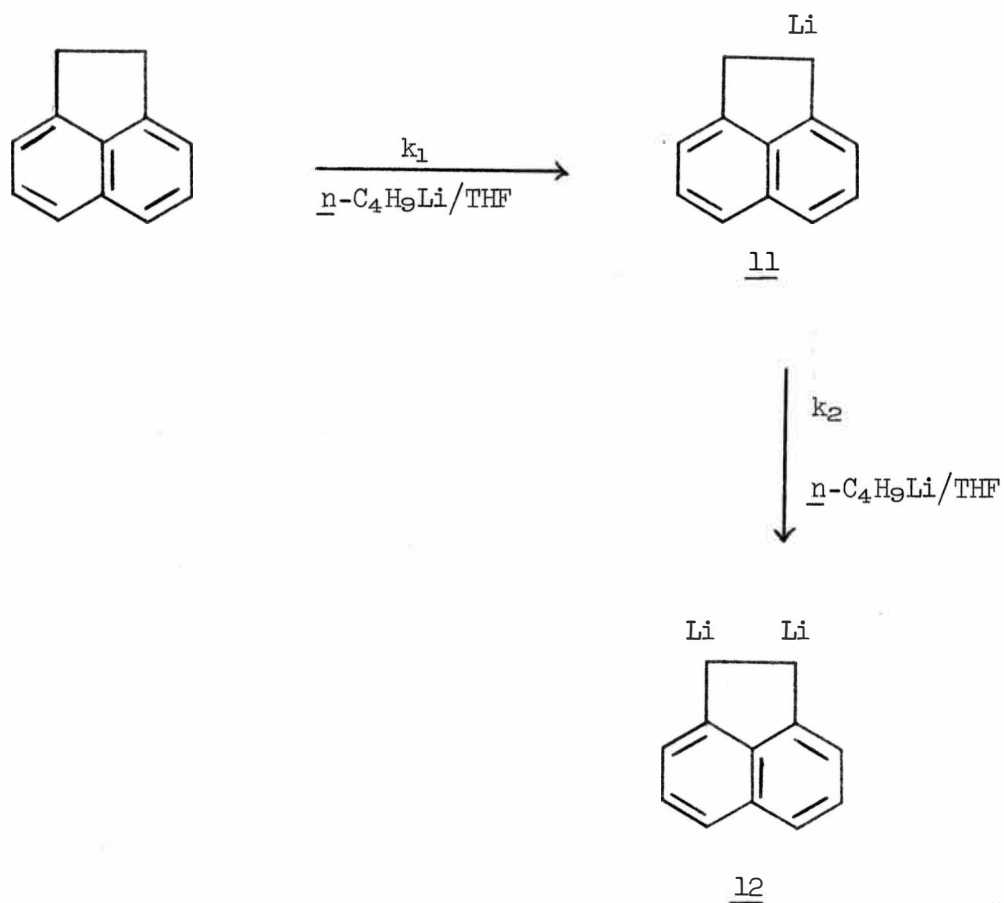
in much better yields by employing n-amylsodium as the metalating agent. Similarly, Ziegler¹² and his coworkers showed that metalation of 2-methylnaphthalene and 1-methylnaphthalene could be accomplished by heating with α -phenylisopropylpotassium for 22-48 hours.

Interestingly, when acenaphthene was allowed to react with n-amylsodium and the reaction mixture was carbonated, 1,5-acenaphthene-dicarboxylic acid (10) was produced, indicating that both lateral and nuclear metalation had occurred¹³. Very recently, Freedman¹⁴ and his

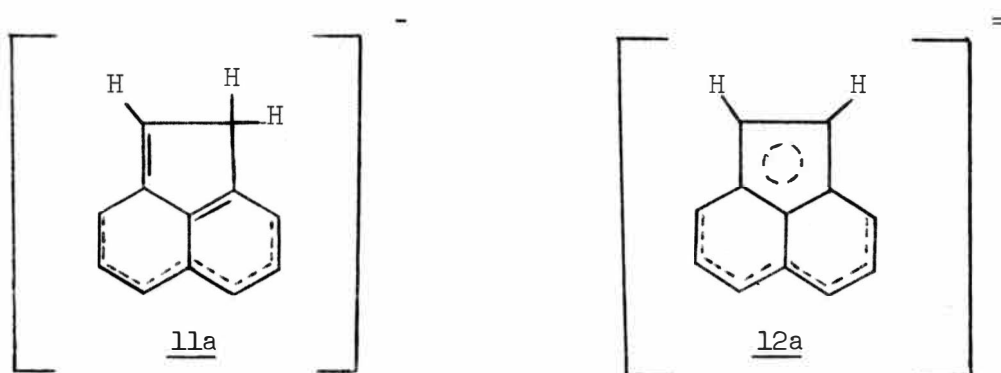


group undertook a careful reinvestigation of the metalation of acenaphthene and certain most unusual results were uncovered. Thus, it was found that acenaphthene was so prone to forming a dianion that dimetalation could be accomplished even with certain organolithium reagents, such as n-butyllithium under exceedingly mild reaction conditions. Even more remarkable, however, was the finding that the rate of dianion formation was faster than the rate of monoanion formation (Scheme IV, $k_2 > k_1$).

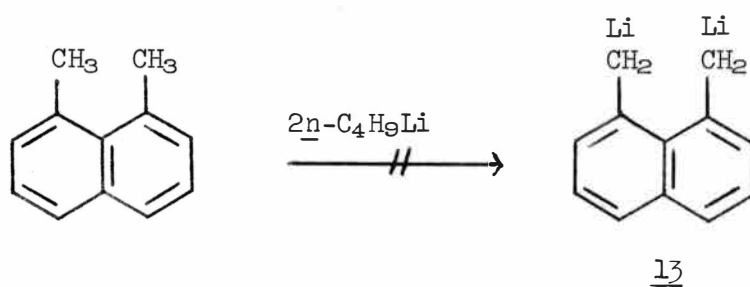
Scheme IV



The enhanced acidity of the protons in the monoanion 11 compared to those in acenaphthene was attributed to the cyclopentadienoid character of the monoanion via charge delocalization, as illustrated in 11a. Proton abstraction from 11a produced dianion 12, whose cyclopentadienide character (structure 12a) apparently makes it unusually stable.

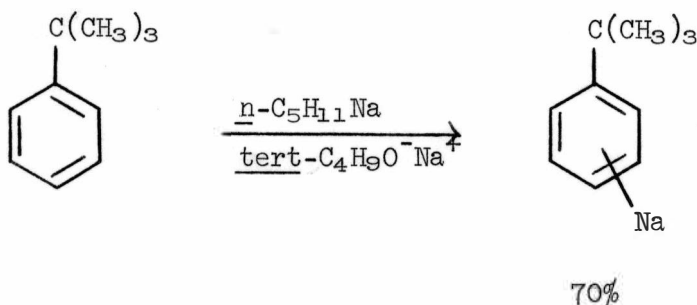


Unlike acenaphthene, attempts to convert 1,8-dimethylnaphthalene to its dianion 13, by means of n-butyllithium were unsuccessful¹⁵.

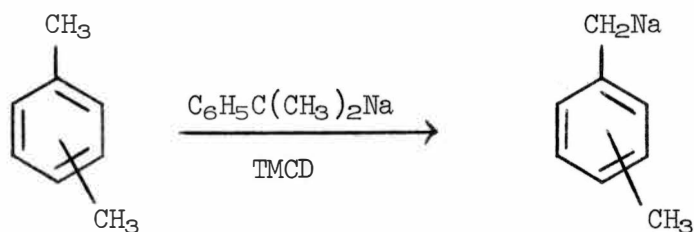


D. The Catalytic Effect of Certain Alkoxides and Tertiary Amines in Metalations with Organosodium Reagents

Morton¹⁶ and his coworkers in the 1950's and more recently Benkeser¹⁷ and his group have observed that certain metal alkoxides can exert a profound catalytic effect on metalation reactions involving organosodium compounds. For example, while treatment of tert-butylbenzene^{16a,17} with n-amylsodium for 20 hours at room temperature resulted in a 15-20% ring metalation, addition of sodium tert-butoxide to the reaction mixture raised the yield of metalation to 70%.



Similarly, it was recently reported that certain polyamines can also act as catalysts in organosodium metalations¹⁸. Thus, it was found that N,N,N',N'-tetramethyl-1,2-cyclohexanediamine (TMCD) could catalyze the metalation of xylenes by means of α -cumylsodium in cumene.

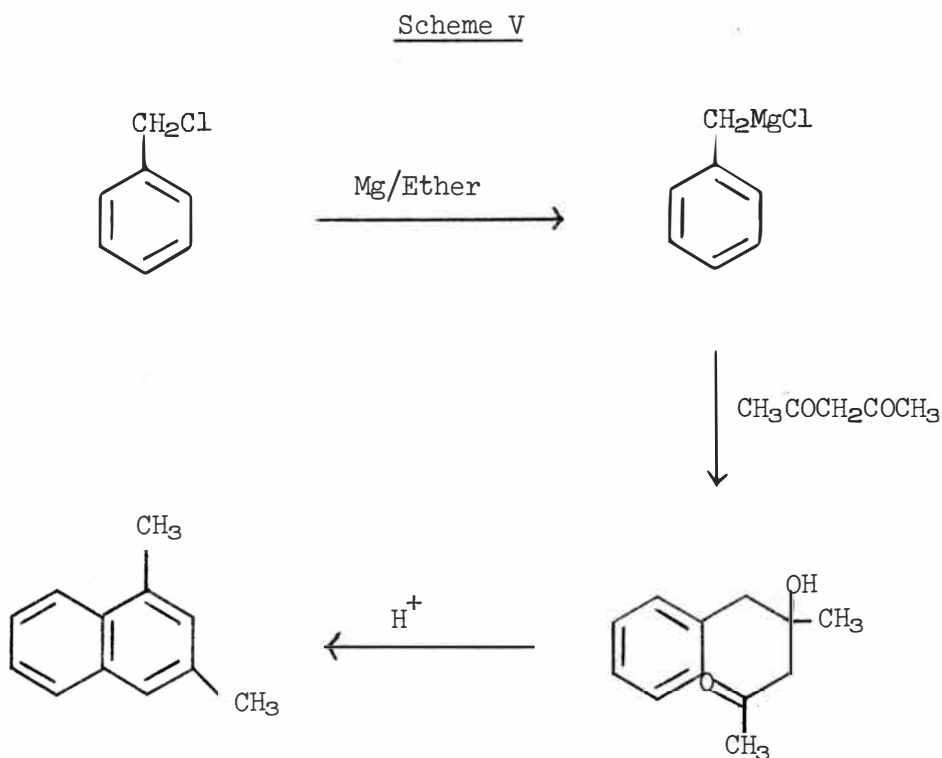


Metalations by means of organolithium reagents have also been shown to be catalyzed by certain tertiary amines¹⁹, such as N,N,N',N'-tetramethylethylenediamine (TMEDA), 1,4-diazabicyclo[2.2.2]octane (DABCO) and sparteine. For example, while toluene is not easily metalated by n-butyllithium alone²⁰, it is attacked quantitatively by n-butyllithium-TMEDA²¹, and in at least 85% yield by n-butyllithium-DABCO^{19a}.

III. RESULTS AND DISCUSSION

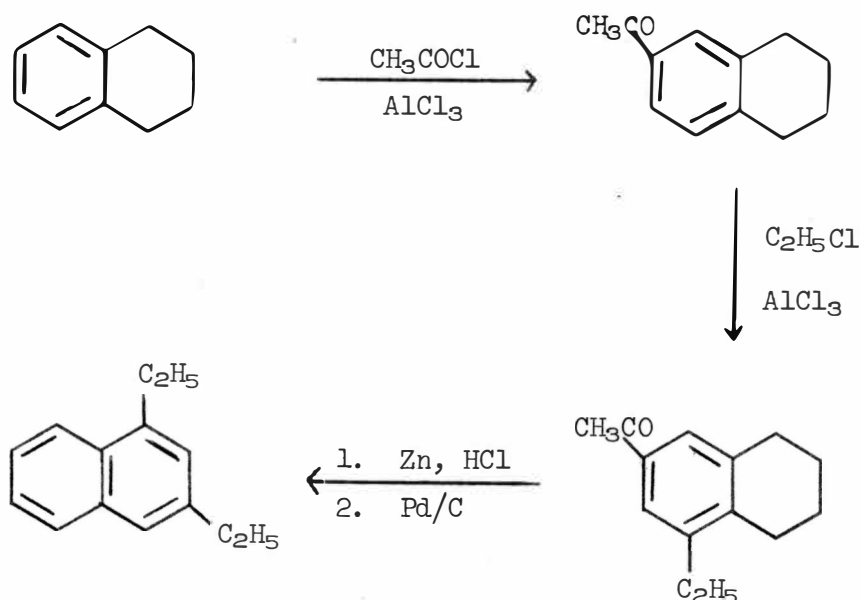
A. The Metalation and Subsequent Functionalization of 1,3-Dimethylnaphthalene

In the past, 1,3-dialkylnaphthalenes have been prepared via highly specific, multi-step synthetic routes, with rather low overall yields. For example, while 1,3-dimethylnaphthalene²² was prepared by the acid catalyzed cyclization of 4-hydroxy-4-methyl-5-phenyl-2-pentanone (Scheme V), in an overall yield of 15-60%, its homologue,



1,3-diethylnaphthalene²³ was synthesized by an entirely different route, as shown in Scheme VI.

Scheme VI

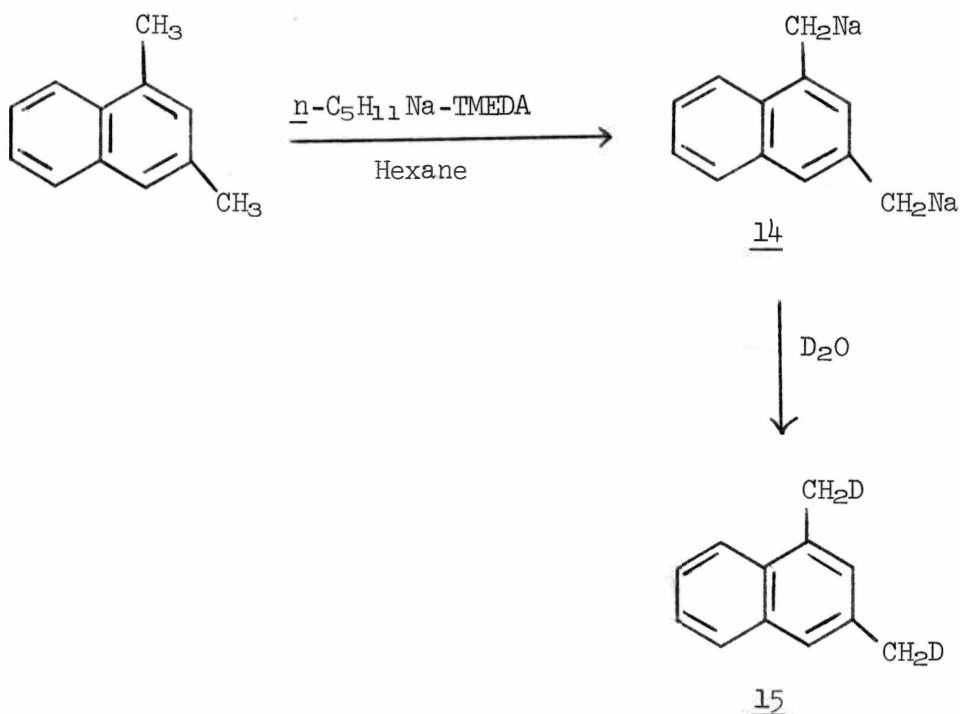


It thus becomes quite clear that the task of preparing a series of homologous 1,3-dialkylnaphthalenes could be tedious and time consuming.

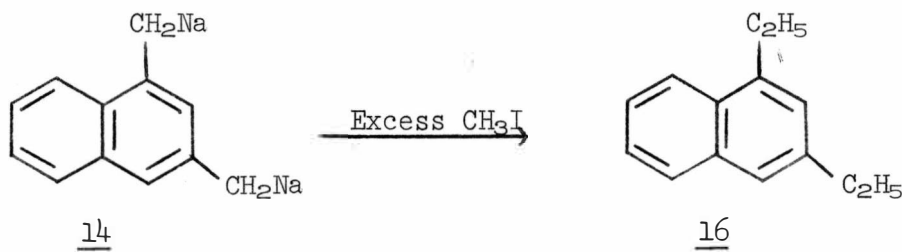
It occurred to us that a more direct route to such dialkylnaphthalenes would be to convert the lowest member of the series, i.e., 1,3-dimethylnaphthalene, to its α, α' -dianion, and subsequently allow this highly reactive intermediate to react with suitably chosen alkyl halides. As mentioned earlier the α -hydrogens of alkylarenes are only weakly acidic and therefore an exceedingly strong base would be required for the conversion of 1,3-dimethylnaphthalene to its α, α' -dianion. During the course of the present investigation it was found that *n*-amylsodium in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) as a catalyst could

convert 1,3-dimethylnaphthalene to the desired dianion in virtually quantitative yield, and that this intermediate could be successfully used not only in the formation of higher 1,3-dialkylnaphthalenes but also for a variety of other 1,3-disubstituted naphthalenes. In a typical experiment, 1,3-dimethylnaphthalene was added at -15° to slightly over 2 equivalents of a freshly prepared mixture of *n*-amylsodium-TMEDA in hexane and the reaction mixture was allowed to warm slowly to room temperature. Reaction occurred quite rapidly to give the insoluble brick-red 1,3-dimethylnaphthalene dianion 14 (Scheme VII) in quantitative yield, as evidenced by quenching the reaction mixture with deuterium oxide followed by nmr analysis of the deuterated product 15.

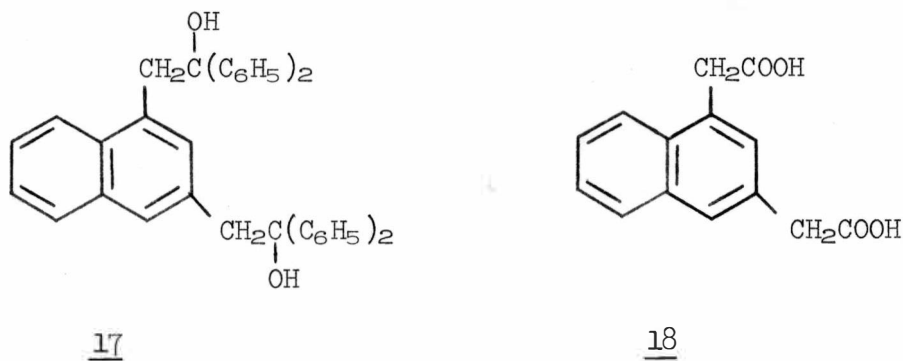
Scheme VII



The 1,3-dimethylnaphthalene dianion 14 was found to react quite readily at room temperature with alkyl halides to give higher 1,3-dialkyl naphthalenes in excellent yields. For example, reaction with excess methyl iodide converted dianion 14 almost exclusively to 1,3-diethylnaphthalene²⁴ (16), as shown by vapor phase chromatographic (vpc) analysis of the crude reaction mixture. Only trace amounts of a second component, most likely the monoalkylation product could be detected, and no starting material was recovered.



Dianion 14 was also found to be an excellent intermediate for the synthesis of a number of other 1,3-disubstituted naphthalenes. Thus, treatment of 14 with two equivalents of benzophenone gave the new carbonyl addition product 17, in 50% yield. The identity



of diol 17 was supported by C,H analysis and by its nmr and ir spectra (see Experimental). In particular, the nmr spectrum of 17 exhibited absorptions for two methylene groups at 3.83 and 3.49 ppm, as well as absorptions for two hydroxyl hydrogens at 5.48 and 5.39 ppm. As expected the ir spectrum of 17 displayed strong -OH absorption at 3540 cm^{-1} . Finally, dianion 14 was treated with excess solid carbon dioxide to afford the new dicarboxylic acid 18 in 74% yield. Structural assignment of product 18 was based on C,H analysis and on spectral data. Thus, the nmr spectrum of 18 showed appropriate singlets for the two methylene groups at 4.05 and 3.76 ppm, while its ir spectrum displayed the expected absorptions at 3000 (OH) and at 1700 cm^{-1} (COOH).

It is particularly important to note that when 1,3-dimethylnaphthalene was treated with n-amylsodium in the absence of TMEDA followed by deuteration only one deuterium atom was incorporated in the 1,3-dimethylnaphthalene molecule, indicating that no dianion formation had occurred.

The possibility of catalyzing n-amylsodium metalations with substances other than TMEDA was next investigated. In the past few years a number of tertiary amines other than TMEDA have been shown to have pronounced catalytic effects on metalations with organolithium reagents¹⁹. Of these amines, 1,3-diazabicyclo[2.2.2]octane (DABCO) has been used most extensively, since its catalytic effect was shown to be almost as high as that of TMEDA¹⁹. Interestingly, we found that DABCO had no catalytic effect on metalations with n-amylsodium in hexane. Thus, treatment of 1,3-dimethylnaphthalene

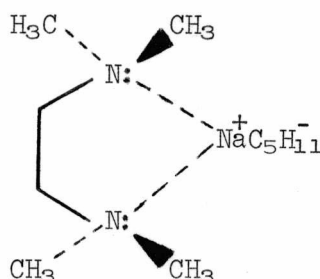
with n-amylsodium in the presence of DABCO under conditions similar to those employed in metalations with n-amylsodium-TMEDA, followed by addition of excess ethyl iodide afforded largely unreacted starting material, indicating that only limited metalation had taken place under these conditions.

The improved yields of metalation of tert-butylbenzene with n-amylsodium in the presence of sodium tert-butoxide^{16,17} prompted us to investigate whether this alkoxide could also serve as a catalyst in the dimetalation of 1,3-dimethylnaphthalene. However, when 1,3-dimethylnaphthalene was subjected to treatment with n-amylsodium in the presence of sodium tert-butoxide, a mixture of products resulted, including an appreciable amount of starting material, clearly showing that no appreciable dimetalation had occurred.

B. The Mechanism of the Catalytic Effect of
N,N,N',N'-Tetramethylethylenediamine on
Metalations with n-Amylsodium

The results described in the previous section clearly indicate that unlike DABCO and sodium tert-butoxide, TMEDA is an exceedingly effective catalyst in metalations of weak carbon acids by means of n-amylsodium. In order for this catalytic effect to be understood, the physical state of n-amylsodium in hydrocarbon solvents needs to be examined. Although extensive studies are not available in the literature it is generally believed that n-amylsodium, generated from n-amyl chloride and sodium metal in hydrocarbon solvents is extremely insoluble in this medium and exists as a highly associated species^{17,25}. Together with sodium chloride, formed as a by-product during the reaction, n-amylsodium molecules form large aggregates with only a small percentage of the molecules being on the surface. Metalations are thus considered to be heterogeneous reactions occurring almost entirely on the surface of the aggregates^{17,25}. As the surface of these aggregates becomes coated by the metalation products, the metalating ability of n-amylsodium ceases and the reaction stops prematurely.

Conceivably TMEDA can catalyze metalations with organosodium reagents in at least two different ways. First it can coordinate with the sodium ion (Figure 1) and in doing so it can cause the large n-amylsodium aggregates to disintegrate into smaller particles, thereby providing a much larger surface area for the reaction to occur. That a peptizing action does indeed occur when TMEDA is



19

Figure 1. n-Amylsodium-TMEDA Coordination Complex

added to the organosodium reagent is quite evident, since an n-amylsodium slurry in hexane appears as a true solution upon addition of TMEDA. It should be pointed out, however, that high speed centrifugation of the reaction mixture afforded a dark blue precipitate and a clear supernatant layer, thereby clearly indicating that the effect of TMEDA was to peptize rather than to solubilize the n-amylsodium aggregates in the hydrocarbon solvent.

In addition to its peptizing action TMEDA may also catalyze metalation with n-amylsodium in another way. Complex formation between the sodium and TMEDA will undoubtedly help diffuse the polarizing power of the metal ion thus weakening the carbon-sodium bond. As a result, the carbanion will become more basic and therefore more reactive. Similar theories have been proposed in order to explain the catalytic effect of TMEDA and other tertiary amines on metalation reactions with organolithium reagents.¹⁹

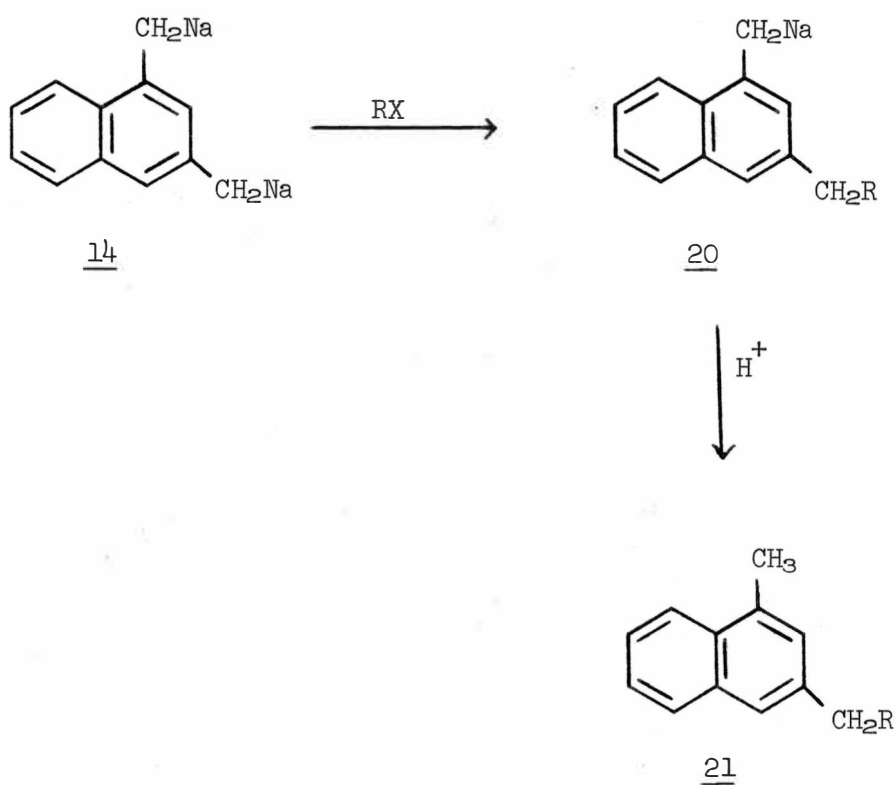
The inability of DABCO to catalyze metalations with n-amylsodium

is quite interesting especially since this diamine has been found to be almost as effective in catalyzing metalations with alkyllithium reagents as TMEDA (see Historical, p 18). The inability of DABCO to catalyze metalations with n-amylsodium is most likely due to the fact that unlike TMEDA this diamine cannot act as a bidentate ligand. Its coordinating power is therefore much lower than that of TMEDA, and its ability to disintegrate the tightly packed organosodium aggregates is considerably weaker. Although organolithium reagents also exist in a polymeric form²⁶ in hydrocarbon solvents, these compounds are much less ionic than organosodium compounds and the monomer units are held much less tightly in the aggregates. Consequently even monodentate ligands such as DABCO and triethylamine have been found to be capable of disrupting the polymeric alkyllithium species^{19b} thereby catalyzing metalations by means of these reagents.

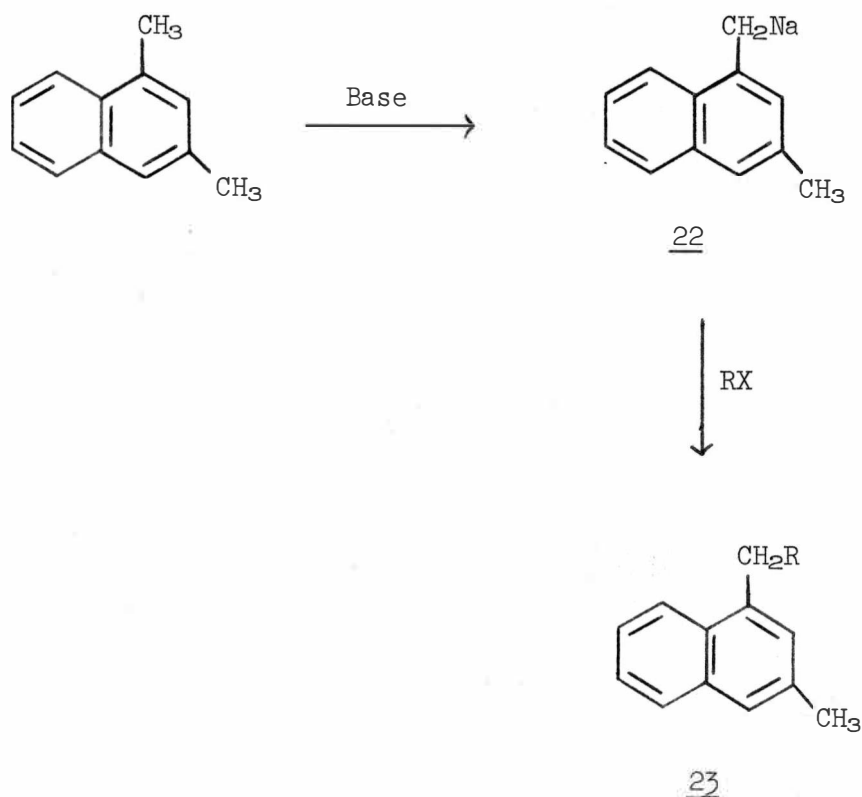
C. Attempted Selective Monoalkylation of
1,3-Dimethylnaphthalene Dianion 14 at the 3-Position

In the preceding sections the reactions of 1,3-dimethylnaphthalene dianion 14 with two or more equivalents of an electrophilic reagent were discussed. In all cases high yields of α,α' -dicondensation products were obtained. We next wished to investigate the reaction of dianion 14 with only one equivalent of an electrophilic reagent. Specifically, we were interested in determining whether reactions will occur selectively at only one of the two reactive sites of the dianion intermediate, or whether mixtures of products would result.

Base-catalyzed hydrogen-deuterium exchange studies by Streitwieser^{27a,b} and by others^{27c} have shown that the hydrogen atoms of the 1-methyl group of 1,3-dimethylnaphthalene are approximately ten times more acidic than the hydrogen atoms of the 3-methyl group. On the basis of these results it may be expected that reaction of 1,3-dimethylnaphthalene dianion 14 with one equivalent of an electrophilic reagent might proceed exclusively at the 3-methylene site since this position should be the most nucleophilic of the two (Scheme VIII).

Scheme VIII

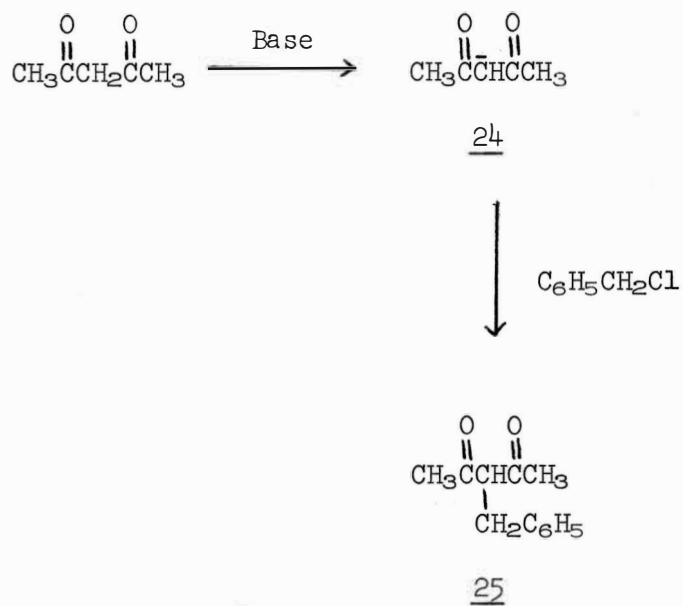
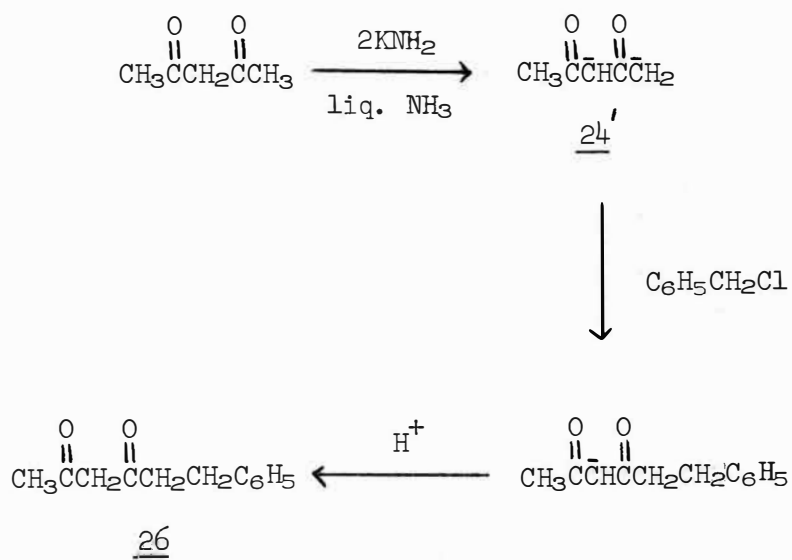
It is of particular interest to note that the monoalkylation product 21 obtained via the above sequence would be precisely the opposite of that obtained when 1,3-dimethylnaphthalene is converted to its monoanion and subsequently alkylated (Scheme IX).

Scheme IX

In the latter case proton abstraction and subsequent alkylation would be expected to occur at the more acidic 1-position rather than at the 3-position, thereby producing monoalkylation product 23.

Preferential condensations at the most nucleophilic site of a dianion have been previously observed by Hauser and Harris^{28a} and more recently by others^{28b} in the case of certain β -diketones and related systems. For example, while acetylacetone monoanion²⁹ 24 underwent alkylation at its α -methylene group, (Scheme X) to afford monoalkylation product 25, monoalkylation of its dianion^{28a} 24' occurred exclusively at its terminal methylene site (Scheme XI) to produce the

entirely different product, 26.

Scheme XScheme XI

In order to determine if 1,3-dimethylnaphthalene dianion 14 would indeed react selectively in the presence of a limited amount of an electrophile, the above intermediate was prepared as described earlier and subsequently treated with one equivalent of ethyl iodide for two hours at room temperature. Vpc analysis of the crude reaction mixture revealed the presence of three new products (1.0:1.2:1.6 ratio) in addition to a substantial amount of starting material. Although no rigorous attempt was made toward the identification of the new reaction products it is quite evident that preferential alkylation at the 3-methylene position did not occur. Similar results were obtained even when the alkylation reaction was performed at -10° .

The failure of the alkylation reaction to take place selectively at the 3-position is most likely due to the lack of sufficient difference between the nucleophilicity of the 1- and 3-methylene sites of dianion 14.

IV. EXPERIMENTAL

A. General

Melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes.

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Gas chromatograms were run on a Varian Aerograph, series 2700 gas chromatograph equipped with a thermal conductivity detector, and using helium as a carrier gas. A 5' x 1/4" SE-30 on Varaport 30 column was used. The compositions of mixtures were determined directly from ratios of the measured areas of individual peaks.

Infrared spectra were taken on a Beckman IR-8 infrared spectrophotometer with the sample incorporated in a potassium bromide pellet.

Nuclear magnetic resonance (nmr) spectra were obtained on a Varian Associates A-60 spectrometer. Chemical shifts, relative to tetramethylsilane, were measured to the center of a singlet or multiplet.

Unless otherwise specified, chemicals were commercial reagent grade, and were used without further purification.

All organosodium reactions were carried out under nitrogen and in a 250 ml Morton flask equipped with a high-speed stirrer (Lab-Line Instruments, Melrose Park, Illinois).

B. The Metalation and Subsequent Functionalization
of 1,3-Dimethylnaphthalene

Preparation of starting material

1,3-Dimethylnaphthalene was prepared essentially by the method of Canonne, et al.,²² with certain slight modifications as described below. (See Scheme V.)

A 2-l. three-necked round-bottom flask was charged with 36.0 g (1.5 moles) of magnesium turnings and 800 ml of dry ethyl ether. A solution of 190 g (1.5 moles) of benzyl chloride in 200 ml of dry ethyl ether was added dropwise at room temperature over a period of 1 hr and stirring was continued until all of the magnesium had been consumed. 2,4-Pentanedione (50.0 g, 0.5 mole) in 200 ml of ether was introduced over a period of 2 hr and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then poured gradually into 2 l. of a stirred, ice-cold, saturated solution of aqueous ammonium chloride. The ether layer was separated, dried over anhydrous magnesium sulfate, filtered, and evaporated by means of a rotary evaporator under reduced pressure. The residue was added to a solution of 100 g of Girard's reagent T in 200 ml of methanol, 2 g of Amberlite 50 resin was added as catalyst, and the solution was heated for 1 hr under reflux on the steam bath. Most of the solvent was then removed under reduced pressure. The cold residue was treated with 500 ml of water, and the suspension was filtered on a Buchner funnel with the aid of Celite. The clear filtrate was extracted three times with 200 ml of petroleum ether,

bp 30-60°. The aqueous layer was then treated with 50 ml of 36% formalin solution and extracted in a continuous extractor for 72 hr with petroleum ether, bp 30-60°. The ether extract was washed with 25 ml of water and freed of solvent on the rotary evaporator under reduced pressure. Low-boiling ketones, such as phenylacetone, and unsaturated ketones were removed from the crude hydroxy ketone by stirring the mixture at 45° overnight under reduced pressure (0.2-0.3 mm). Under these conditions nearly all of the by-products passed over into a trap cooled in dry ice. The yield of 4-hydroxy-4-methyl-5-phenyl-2-pentanone was 32 g (30% of the theoretical amount).

A solution of 20 g (0.1 mole) of 4-hydroxy-4-methyl-5-phenyl-2-pentanone (prepared as described above) in a mixture of 100 ml of glacial acetic and 100 ml of 48% hydrobromic acid was heated for 2 hr on the steam bath, with occasional shaking. Soon after the solution reached 65-70°, it became turbid and separated into two layers. The cooled reaction mixture was extracted with 300 ml of petroleum ether (bp 30-60°). The extract was washed first with water and then with dilute aqueous sodium bicarbonate, and dried over anhydrous magnesium sulfate. The filtered solution was freed of solvent on the flash evaporator and the residue was purified by bulb-to-bulb distillation (56-58°, 0.15 mm). There was obtained 10.0 g (64%) of pure 1,3-dimethylnaphthalene; nmr (CCl_4) δ 7.40 (m, 6H, aromatic), 2.48 (s, 3H, CH_3), and 2.32 ppm (s, 3H, CH_3).

Preparation of sodium dispersion

Sodium dispersions were prepared by stirring molten sodium metal

at high speed (12,000-15,000 rpm) in a hydrocarbon solvent³⁰. In a typical experiment 1.38 g (0.06 mole) of sodium metal was introduced into a 250 ml three-necked Morton flask containing 80 ml of dry octane and equipped with a high-speed stirrer, a reflux condenser connected to a nitrogen tank through a T-tube, and a heating mantle. The octane-sodium mixture was refluxed for 10 min; heating was discontinued and the molten sodium was stirred at high speed (12,000-15,000 rpm) for 2 min. The mixture was then allowed to cool to room temperature, and most of the octane was syringed out through a septum. The fine sodium dispersion was washed three times with 20 ml portions of dry hexane, and employed as described below.

Preparation of n-amylsodium

n-Amylsodium was prepared by the slow addition of n-amyl chloride to a sodium dispersion at low temperature and high-speed stirring³⁰. In a typical experiment 0.06 mole of finely dispersed sodium, prepared as described above, was covered with 80 ml of hexane in a 250 ml Morton flask and cooled to -15°. High-speed stirring was started and 3.21 g (0.03 mole) of n-amyl chloride was added dropwise over a period of 50 min. The dark blue reaction mixture was stirred for an additional 30 min at -15°, and then used as described below. A 75-80% yield was assumed in all of the n-amylsodium preparations³⁰.

Dimetalation of 1,3-dimethylnaphthalene with n-amylsodium in the presence of TMEDA

To a stirred (12,000-15,000 rpm) suspension of n-amylsodium

prepared from 0.03 mole of n-amylchloride and 0.06 mole of sodium dispersion in 80 ml of anhydrous hexane was added at -15° , over a period of 8 min, a solution of 1.56 g (0.01 mole) of 1,3-dimethylnaphthalene and 2.32 g (0.02 mole) of TMEDA in 15 ml of dry hexane. The cold bath was then removed and the reaction mixture was allowed to warm slowly to room temperature. Dimetalation was completed by stirring for 2 additional hr at room temperature and the resulting brick-red 1,3-dimethylnaphthalene dianion 14 was employed as described below.

Deuteration of dianion 14

A suspension of dianion 14 (0.01 mole) in hexane was prepared as described above and subsequently quenched with 10 ml of deuterium oxide. Water (50 ml) was then added to the reaction mixture, the layers were separated, and the organic layer was dried over anhydrous magnesium sulfate and freed of most of the solvent under reduced pressure to give 1,3-dimethylnaphthalene- d_2 (15), as shown by quantitative nmr analysis; nmr (CCl_4) δ 7.40 (m, 6H, aromatic), 2.50 (s, 2H, CH_2), and 2.32 ppm (s, 2H, CH_2).

Alkylation of dianion 14 with methyl iodide

To a stirred suspension of 0.01 mole of 14 in 80 ml of hexane at -15° , was added 5.67 g (0.04 mole) of methyl iodide over a period of 8-10 min. The cold bath was then removed and the reaction mixture was allowed to stir (10,000 rpm) for 45 min at room temperature. Water (50 ml) was then added, the layers were separated, and the

organic layer was dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Gas chromatographic analysis of the residue revealed the presence of two components in a ratio of 19:1. The predominant component was shown to be 1,3-diethylnaphthalene (16), picrate 99-100°, (lit.²⁴ mp 100.5°). No attempt was made to identify the minor component.

Condensation of dianion 14 with benzophenone

To a stirred suspension of 0.01 mole of dianion 14 in 80 ml of hexane at room temperature was added dropwise a solution of 4.55 g (0.025 mole) of benzophenone in 50 ml of dry hexane. After 58 min of stirring (10,000 rpm) at room temperature 50 ml of water were added. The resulting yellow solid was collected by filtration, washed with water, and dried to afford 2.60 g (50%) of crude diol 17, mp 176-181°. Several recrystallizations of the crude product from ethanol-water raised the mp to 192-193°; ir 3540 cm^{-1} (OH); nmr (DMSO- d_6) δ 7.33 (m, 26H, aromatic), 5.48 (s, 1H, CH_2COH), 5.39 (s, 1H, CH_2COH), 3.83 (s, 2H, CH_2COH), and 3.49 ppm (s, 2H, CH_2COH).

Anal. Calcd for $\text{C}_{38}\text{H}_{32}\text{O}_2$: C, 87.69; H, 6.16. Found: C, 87.61; H, 6.26.

Carbonation of dianion 14 with excess solid carbon dioxide

A suspension of 0.02 mole of dianion 14 in hexane was prepared in the usual manner, and then syringed onto a large excess of moisture free, solid carbon dioxide. The resulting slurry was allowed to stand overnight at room temperature; 300 ml of water was then introduced

with stirring, the layers were separated, the aqueous layer was washed twice with 50 ml portions of hexane and twice with 50 ml portions of ethyl acetate and acidified with 12N HCl. Upon cooling the acidic solution afforded a yellow-white precipitate which was collected by filtration and dried to give 3.62 g (74%) of crude 1,3-naphthalenediacetic acid (18), mp 215-217°, and 224-225° after several recrystallizations from ethyl acetate-petroleum ether (bp 30-60°); ir 3000 (OH), and 1700 cm^{-1} (C = O); nmr ($\text{DMSO}-d_6$) δ 7.65 (m, 6H, aromatic), 4.05 (s, 2H, CH_2COOH), and 3.76 ppm (s, 2H, CH_2COOH).

Anal. Calcd for $\text{C}_{14}\text{H}_{12}\text{O}_4$: C, 68.85; H, 4.91. Found: C, 69.03; H, 4.78.

Effect of TMEDA on the solubility of n-amylsodium in hexane

n-Amylsodium was prepared in the usual manner from 0.03 mole of n-amyl chloride and 0.06 mole of sodium dispersion in 80 ml of dry hexane. Approximately one half of the reaction mixture was transferred into a centrifuge tube and centrifuged for 5 min at 1500 rpm. A clear supernatant layer and a blue precipitate resulted. The remaining one half of the reaction mixture was treated with 0.01 mole of TMEDA before it was centrifuged. Upon centrifugation this portion of the reaction mixture also afforded a clear supernatant liquid and a dark blue precipitate.

Effect of TMEDA on the solubility of 1,3-dimethylnaphthalene dianion 14 in hexane

In this experiment 0.0078 mole of dianion 14 was prepared in 80

ml of dry hexane as described earlier. A portion (30 ml) of the reaction mixture was transferred into a centrifuge tube and centrifuged for approximately 5 min at 1500 rpm. A red precipitate and yellowish, but otherwise clear supernatant layer resulted.

Metalation of 1,3-dimethylnaphthalene with n-amylsodium in the absence of a catalyst

To a stirred (12,000-15,000 rpm) suspension of n-amylsodium prepared from 0.03 mole of n-amyl chloride and 0.06 mole of sodium dispersion in 80 ml of anhydrous pentane was added at -15° , 1.56 g (0.01 mole) of 1,3-dimethylnaphthalene over a period of 5 min, and stirring was continued for 2 hr at room temperature. The reaction mixture was then quenched with 5 ml of deuterium oxide and processed in the usual manner to give 1,3-dimethylnaphthalene- d_1 as shown by quantitative nmr analysis; nmr (CCl_4) δ 7.40 (m, 6H, aromatic), 2.55 (s, 2.6H, CH_3), and 2.36 ppm (s, 2.4H, CH_3).

Metalation of 1,3-dimethylnaphthalene with n-amylsodium in the presence of sodium tert-butoxide followed by alkylation with ethyl iodide

To a suspension of n-amylsodium prepared from 0.04 mole (4.24 g) of n-amyl chloride and 0.09 mole (2.07 g) of sodium dispersion in 80 ml of dry hexane was added 0.02 mole (1.92 g) of sodium tert-butoxide and the reaction mixture was allowed to stir for 15 min before 1.56 g (0.01 mole) of 1,3-dimethylnaphthalene was introduced. Stirring was then continued for an additional 4 hr after which 6.24 g (0.04 mole) of ethyl iodide was added. After 2 hr of stirring at room temperature, 50 ml of water were added, and the reaction was

processed as described earlier. Gas chromatographic analysis of the crude reaction mixture revealed the presence of starting material (identified by comparison of its retention time with an authentic sample) and three new products, in the ratio of 5.1:1.0:2.5:7.0. No attempt was made to identify the new reaction products.

Metalation of 1,3-dimethylnaphthalene with n-amylsodium in the presence of DABCO followed by alkylation with ethyl iodide

n-Amylsodium was prepared from 0.03 mole of n-amyl chloride and 0.06 mole of sodium dispersion in the usual manner. DABCO, 2.24 g (0.02 mole) was then added to the reaction mixture followed by 0.01 mole of 1,3-dimethylnaphthalene. The reaction mixture was stirred for 2 hr, 0.04 mole of ethyl iodide was added and stirring was continued for 45 min. The reaction was then processed as previously described and the residue analyzed by means of gas chromatography. Starting material and three new products could be detected in a ratio of 1.0:1.3:2.3:1.3. No attempt was made to identify the new products.

C. Attempted Selective Monoalkylation of
1,3-Dimethylnaphthalene Dianion 14 at the 3-Position

Reaction of dianion 14 with one equivalent of ethyl iodide

To a stirred suspension of 0.01 mole of 1,3-dimethylnaphthalene dianion 14 in 80 ml of dry hexane was added 1.56 g (0.01 mole) of ethyl iodide, the reaction mixture was stirred for 45 min at room temperature, and was subsequently processed in the usual manner. Analysis of the crude reaction mixture by gas chromatography revealed the presence of starting material and three additional new products in a 2.0:1.0:1.2:1.6 ratio. No attempt was made to identify any of the new products.

In another experiment 1,3-dimethylnaphthalene dianion 14 (0.01 mole) was treated with ethyl iodide (0.01 mole) for 1 hr but the temperature was kept at -10° . The reaction mixture was processed as usual to afford essentially the same mixture of products as above.

V. SUMMARY

1,3-Dimethylnaphthalene was quantitatively converted to its α,α' -dianion 14 by means of *n*-amylsodium in the presence of TMEDA as a catalyst. The reaction was performed at room temperature and completed within 2 hrs. Dianion 14 was found to react quite readily with excess methyl iodide and solid carbon dioxide to give 1,3-diethylnaphthalene (16), and 1,3-naphthalenediacetic acid (18) in excellent yield. Similarly, treatment of dianion 14 with 2 equivalents of benzophenone afforded 1,3-di(2,2-diphenyl-2-hydroxy)ethylnaphthalene (17) in good yield. Under the above conditions, *n*-amylsodium in the presence of sodium *tert*-butoxide, or DABCO effected only partial dimetalation of 1,3-dimethylnaphthalene, while *n*-amylsodium alone effected no dimetalation at all.

The catalytic effect of TMEDA was attributed to its ability to disperse the large *n*-amylsodium aggregates into smaller particles thereby providing a larger surface area for the metalation reaction to occur.

Attempts to selectively monoalkylate 1,3-dimethylnaphthalene dianion 14 at its most nucleophilic β -position were not successful, most likely due to the lack of sufficient difference between the nucleophilicity of the 1- and 3-methylene sites of dianion.

VI. BIBLIOGRAPHY

1. D.J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York, N.Y., 1965.
2. R.A. Benkeser, D.J. Foster, D.M. Sauve and J.F. Nobis, Chem. Rev., 57, 867 (1957).
3. A.A. Morton, Ind. Eng. Chem. Anal. Ed., 11, 170 (1939).
4. P. Schorigin, Ber., 41, 2723 (1908).
5. (a) A.A. Morton and I. Hechenbleikner, J. Amer. Chem. Soc., 58, 1024 (1936); (b) A.A. Morton, F. Fallwell, Jr., and L. Palmer, ibid., 60, 1426 (1938); (c) A.A. Morton, J.B. Davidson and R.J. Best, ibid., 64, 2239 (1942); (d) H.A. Pacevitz, Iowa State Coll. J. Sci., 16, 117 (1941); (e) A.A. Morton, E.L. Little, Jr., and W.O. Strong, Jr., J. Amer. Chem. Soc., 65, 1339 (1943).
6. J.F. Nobis and L.F. Moormeier, Ind. Eng. Chem., 46, 539 (1954).
7. (a) R.A. Benkeser, A.E. Trevillyan and J. Hooz, J. Amer. Chem. Soc., 84, 4971 (1962); (b) D. Bryce-Smith, J. Chem. Soc., 1079 (1954); (c) A.A. Morton and E.L. Little, J. Amer. Chem. Soc., 71, 487 (1949).
8. A.A. Morton, J.T. Massengale and M.L. Brown, ibid., 67, 1620 (1945).
9. H. Gilman, H. Pacevitz and O. Baine, ibid., 62, 1514 (1940).
10. C.D. Broaddus, ibid., 88, 4174 (1966).
11. J.E. Hofmann, R.J. Muller and A. Schriesheim, ibid., 85, 3002 (1963); see also (a) A. Streiwieser, Jr. and D.E. VanSickle, ibid., 84, 249 (1962); (b) A. Streitwieser, Jr. and H.F. Koch, ibid., 86, 404 (1964).
12. K. Ziegler and H. Dislich, Chem. Ber., 90, 1107 (1957).
13. A.A. Morton, J.T. Massengale and G.M. Richardson, J. Amer. Chem. Soc., 62, 126 (1940).
14. L.D. Kershner, J.M. Gaidis and H.H. Freedman, ibid., 94, 985 (1972).
15. See footnote 6, ref. 14.

16. (a) A.A. Morton, C.E. Claff, Jr. and F.W. Collins, J. Org. Chem., 20, 428 (1955); (b) A.A. Morton and A.E. Brachman, J. Amer. Chem. Soc., 73, 4363 (1951); (c) A.A. Morton, Ind. Eng. Chem., 42, 1488 (1950).
17. R.A. Benkeser, T.F. Crimmins and W. Tong, J. Amer. Chem. Soc., 90, 4366 (1968).
18. Report appearing in Chem. Eng. News, 49 (24), 31 (1971).
19. (a) G.G. Eberhardt and W.A. Butte, J. Org. Chem., 29, 2928 (1964); (b) C.G. Screttas and J.F. Eastham, J. Amer. Chem. Soc., 87, 3276 (1965).
20. H. Gilman and B.J. Gaj, J. Org. Chem., 28, 1725 (1963).
21. (a) A.W. Langer, Jr., Trans. N.Y. Acad. Sci., 27, 741 (1965); (b) A.W. Langer, Jr., Polymer Preprints, Vol. 7, No. 1, American Chemical Society Division of Polymer Chemistry, Jan. 1966, p. 132.
22. P. Canonne, P. Holm and L.C. Leitch, Can. J. Chem., 45, 2151 (1967).
23. G. Baddeley and W. Pickles, J. Chem. Soc., 2855 (1957).
24. R.T. Arnold and R.A. Barnes, J. Amer. Chem. Soc., 66, 960 (1944).
25. A.A. Morton, "Solid Organoalkali Metal Reagents", Gordon and Breach Science Publishers, Inc., New York, N.Y., 1964, pp. 5-6.
26. T.L. Brown, Advan. Organomet. Chem., 3, 365 (1965).
27. (a) A. Streitwieser, Jr. and W.C. Langworthy, J. Amer. Chem. Soc., 85, 1757 (1963); (b) A. Streitwieser, Jr., W.C. Langworthy and J.I. Brauman, ibid., 85, 1761 (1963); (c) M.J.S. Dewar and C.C. Thompson, Jr., ibid., 87, 4414 (1965).
28. (a) C.R. Hauser and T.M. Harris, J. Amer. Chem. Soc., 80, 6360 (1958); (b) J.F. Wolfe, G.B. Trimitsis and D.R. Morris, J. Org. Chem., 34, 3263 (1969).
29. G.T. Morgan and C.J.A. Taylor, J. Chem. Soc., 127, 797 (1925).
30. M. Schlosser in "Newer Methods of Preparative Organic Chemistry", W. Foerst, Ed., Academic Press, 1968, Vol. V, p. 299.

VII. VITA

Name: Atilla Tuncay

Born: May 4, 1948, Istanbul, Turkey

Education:

Primary school: 23rd District Primary School, Istanbul, Turkey, 1959.

High school: Kabatas Lycée, Istanbul, Turkey, 1965.

College: Robert College Language Preparatory School, Istanbul, Turkey, 1966.

College: Robert College, Istanbul, Turkey, B.S. in Chemistry, 1970

College: Western Michigan University, Kalamazoo, Michigan, U.S.A., Candidate for M.A. degree, 1972.

Honorary and Professional Societies:

American Chemical Society

Positions: Teaching assistant, Western Michigan University, 1970-72.

Publications: "Metalations of Dimethylarenes with Organosodium Reagents. The Catalytic Effect of Certain Tertiary Amines" (with G.B. Trimitsis), J. Amer. Chem. Soc., 94, 2152 (1972).