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Synthesis of anthrone derivatives

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SYNTHESIS OF ANTHRONE DERIVATIVES

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San Jose State University

In Partial Fulfillment

of the Requirements for the Degree

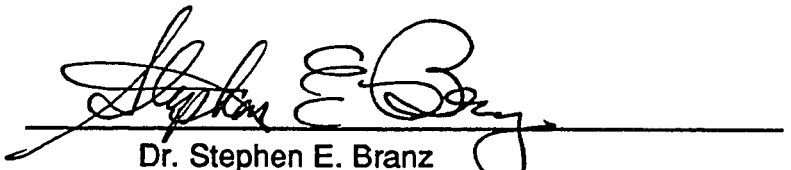
Master of Science

By

Kate Li-Jie Jin

December, 1989

APPROVED FOR THE DEPARTMENT OF CHEMISTRY



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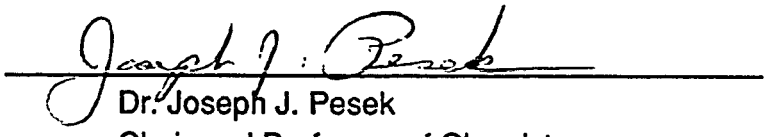
Associate Professor of Chemistry



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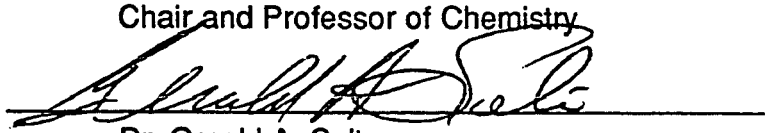

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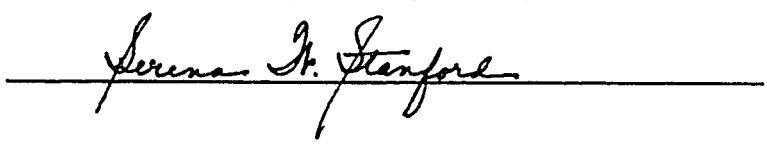

ABSTRACT

SYNTHESIS OF ANTHRONE DERIVATIVES

by Kate Li-Jie Jin

Based on stereoelectronic considerations, a 1,7/1,2 hydride shift sequence has been proposed as an alternative to the 1,6-hydride shift currently accepted as the explanation for the base-catalyzed conversion of prephenic acid to *para*-hydroxyphenyllactic acid. To distinguish between these two mechanisms, a series synthetic analogs of prephenic acid are needed. This thesis describes new approaches and improvements in the existing synthetic methodology leading to anthrone derivatives - the synthetic analogs of prephenic acid. We developed a new method for the preparation of 10-bromoanthrones, and successfully reduced a hindered 10,10-disubstituted anthrone using Super-hydride. Also, we demonstrated that the direct synthesis of cyanoanthrone from bromoanthrone is not possible; an unanticipated dimer is formed instead. Efforts directed toward the synthesis of 10-substituted and 10,10-disubstituted anthrones using Michael additions and intermolecular radical addition reactions were unsuccessful; further work is needed on these two new routes.

Acknowledgements

I would like to take this opportunity to thank my research advisor Professor Stephen E. Branz, for his guidance and help throughout this project. I deeply thank my colleagues at Syntex for all the support and help they gave me. I thank the NIH for their partial financial support for my research through the Minority Biochemistry Research Support (MBRS) program. Furthermore, I would also like to thank all my friends; without their encouragement I would not have succeeded.

I would like to express my most special thanks to my parents for all the hard work they did for their children.

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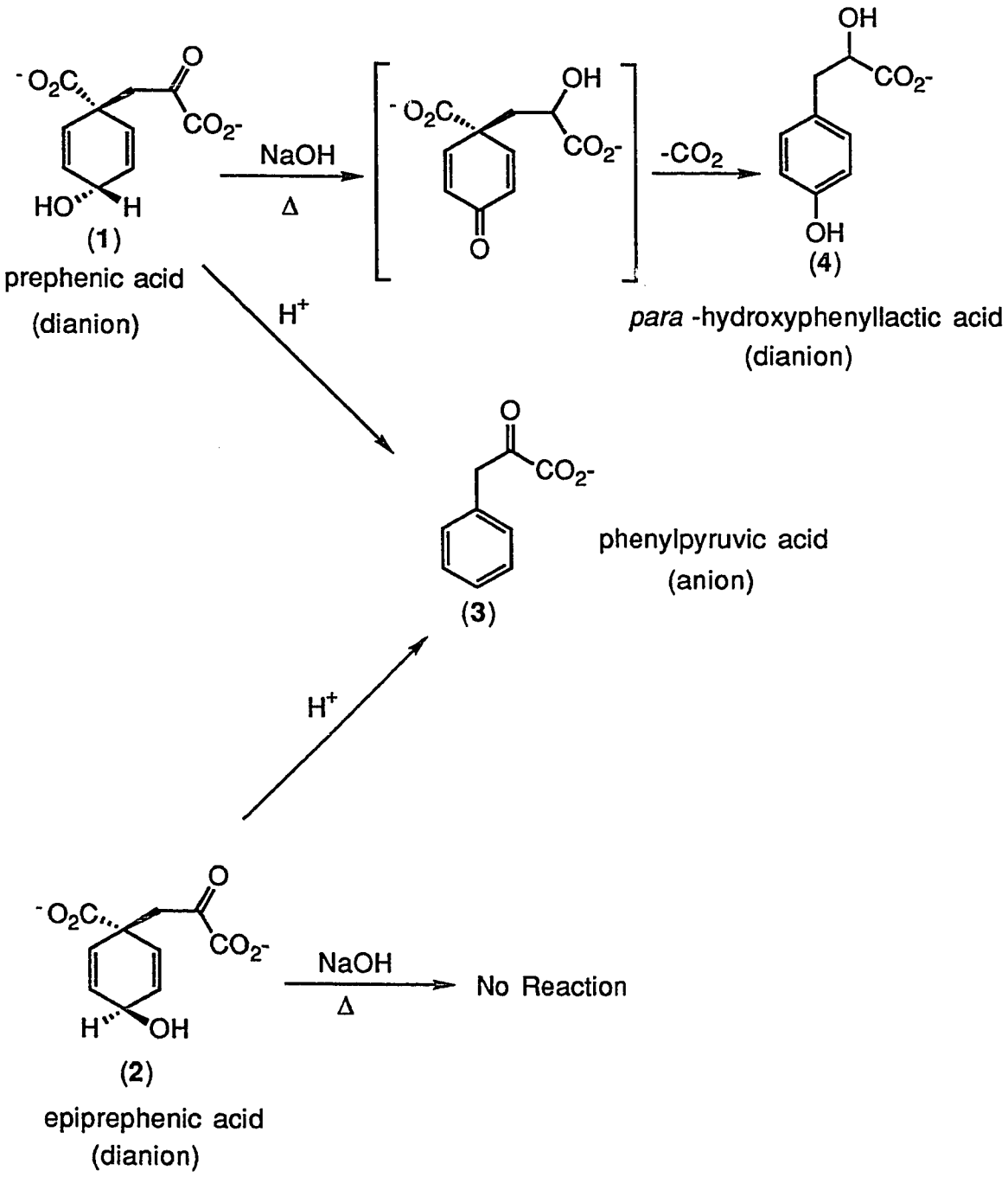
Introduction

Prephenic acid (**1**) is a key intermediate in the shikimic acid pathway. It is a biosynthetic precursor of the essential aromatic amino acids - phenylalanine and tyrosine.[1] It serves as a vital connecting link between the "aliphatic" and "aromatic" domains.[2] Due to its importance in cellular metabolism, prephenic acid has been the object of substantial research attention. Its structure has been determined [3] and the total synthesis was reported by Danishefsky and coworkers in 1979.[2]

The essential chemistry of prephenic acid (**1**) is summarized in Scheme I. In acid, both prephenic acid and its epimer (**2**) convert to phenylpyruvic acid (**3**). In base, the naturally occurring prephenic acid diastereomer converts to *para*-hydroxyphenyllactic acid (**4**), whereas its epimer undergoes no reaction. Since this redox conversion only works on the naturally occurring epimer, it is presumed that the hydride transfer is intramolecular.[2] Several mechanistic explanations have been proposed for this hydride transfer.[4,5] The currently accepted explanation, a one step 1,6-hydride shift followed by loss of carbon

Scheme I

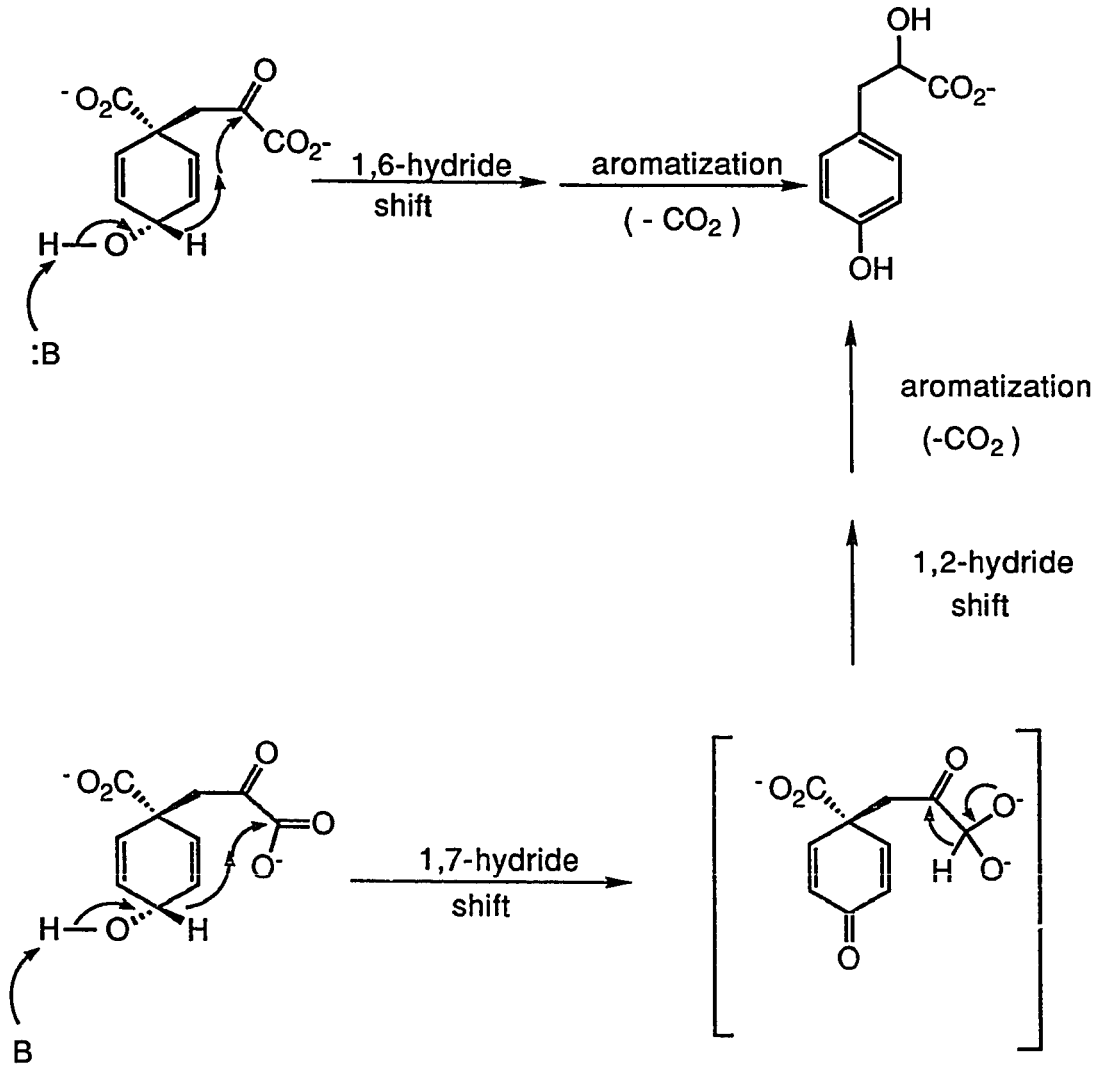

(1)
prephenic acid
(dianion)
NaOH
Δ
-CO2
(4)
para -hydroxyphenyllactic acid
(dianion)
H+
(3)
phenylpyruvic acid
(anion)
H+
(2)
epiprephenic acid
(dianion)
NaOH
Δ
No Reaction

dioxide and aromatization, was first presented by Plieninger in early 1960's.[5]

We think that this mechanism is unlikely and still open to further experimentation. Our alternative proposal is a 1,7/1,2-hydride shift sequence followed by a decarboxylation and an aromatization (Scheme II). We base our proposal on several arguments. First, the hydride trajectory for the reaction with the carboxylate carbonyl is much more favorable than that for the ketone. This conclusion is based on a number of studies on stereoelectronic effects.[6] These studies indicate that there is a well-defined minimum energy pathway for the approach of a nucleophile to a carbonyl carbon. By examining Drieding models and a computer model, we found that the distance from the transferring hydride to the ketone carbonyl is quite far away as compared with the distance from the transferring hydride to the carboxylate carbonyl. Furthermore, the approach angle to the carboxylate was much closer to tetrahedral. We propose testing the validity of our hypothesis by comparing the two mechanisms - the 1,6- *vs.* the 1,7/1,2-hydride shifts.

Since the two pathways are indistinguishable by kinetic studies or isotopic labeling, we plan to distinguish between them by using a series of synthetic

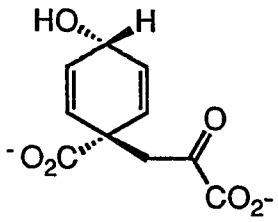
Scheme II


OH
CO2-
O
-O2C
CO2-
1,6-hydride
shift
aromatization
(- CO2)
OH
H
O
H
:B
aromatization
(-CO2)
1,2-hydride
shift
-O2C
O
O
O-
1,7-hydride
shift
O-
H
O-
B
O

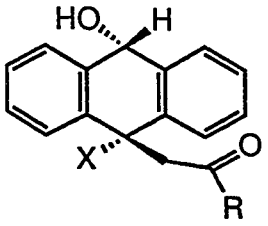
analogs which share all of the essential steric and electronic features of prephenic acid. The 9,10-dihydroanthracene system was chosen for our model compounds (Figure 1) because it is accurately models the conformational mobility of the dihydrobenzenoid structure of prephenic acid, yet is synthetically more accessible than the monocyclic system. The two fused rings permit more vigorous reaction conditions during synthesis by "protecting" the double bounds of the cyclohexadiene as fused phenyl rings. Scheme III shows a retrosynthetic approach to the key intermediate (**9**) from which the model compounds may be obtained by elaboration of the allylic side chain.

The synthesis of a series of analogs of prephenic acid is the long range goal of this research project. Two masters students, Jessica A. Carr and Rekha P. Bansal, have previously worked on this project. They made tremendous progress, including the synthesis of a series of 10,10-disubstituted anthrones,[7] and the mechanistic investigation of the rearrangement reactions of 9-anthryl ethers.[7,8] My research has focused primarily on improving the existing synthetic methodology but also included some new progress toward the long range goal of preparing model compounds for our mechanistic investigation.

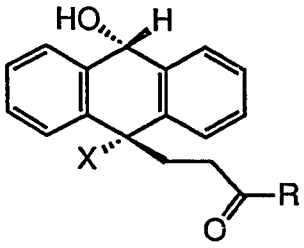
Figure 1



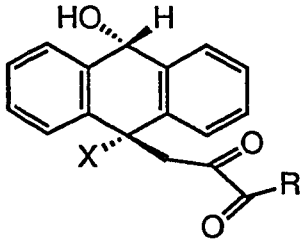
prephenic acid



model I



model II

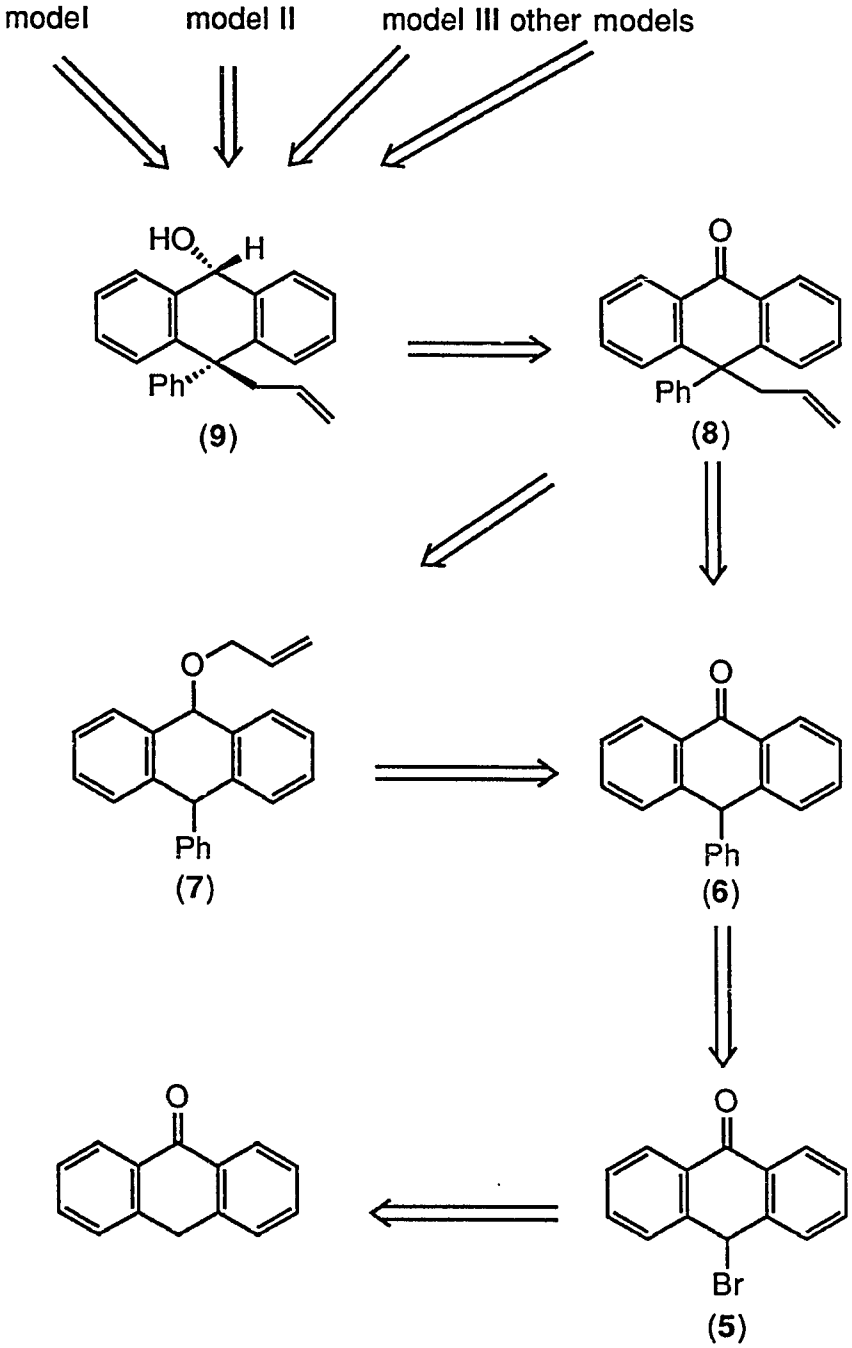


model III

X = Ph, CO_2^-, CN.

R = H, CH_3, Ph.

Scheme III


model
model II
model III other models
HO
H
Ph
(9)
O
Ph
(8)
O
Ph
(7)
O
Ph
(6)
O
O
Br
(5)

The synthesis of bromoanthrone (**5**) is the very first step in our synthetic scheme. The yield and quality of the product resulting from this step have a significant influence on the next steps in the synthesis. Our original method was based on the procedure reported by Barnett, Cook, and Mattews.[9] Using N-bromo-succinimide (NBS) as the halogenation reagent , we were able to improve the yield and quality of bromoanthrone and also extend the method to the bromination of phenylanthrone. The most recent literature reference for the preparation of 10-bromo-10-phenylanthrone (**11**) is by Liebermann, Giawe, and Lindenbaum in 1904.[10] They passed dry HBr gas into a benzene solution of hydroxyphenylanthrone and obtained a colorless needles of 10-bromo-10-phenylanthrone. Interestingly, attempted bromination of phenylanthrone gave hydroxyphenylanthrone (**10**) as the final product and not bromophenylanthrone as expected. The mass spectrum of crude reaction mixture shows that the bromophenylanthrone does formed and is stable prior to purification. It appears that the bromophenylanthrone hydrolyzed in the following workup process. Separation of the product remains as a problem for the bromination of phenylanthrone with NBS.

Reduction of the carbonyl of anthrone is another key point in our model

derivatives using 9-borabicyclo [3.3.1] nonane (9-BBN)[2] and lithium aluminum hydride (LAH)[11] gave primarily recovered starting material. In order to successfully reduce 10-allyl-10-phenylanthrone, I used Superhydride (lithium triethylborohydride), the strongest S_N2 hydride source and a very powerful reducing agent for carbonyl compounds. The reaction works very well, and It shows that the Superhydride is a suitable reducing reagent for our compounds.

A modified Friedel-Crafts alkylation using amalgamated aluminum wire and mercuric chloride has been used to prepare a series of alkylbenzenes.[12] However, this mild method of generating alumium chloride *in situ* did not work as a catalyst for the reaction of bromoanthrone and benzene. According to Barnett, Needham and Powell,[13] the carbonyl deactivates the 10-position of anthrone by destablizing any (partial) positive charge at that site. This deactivation is also evident in the attempted preparation of 10-cyanoanthrone from bromoanthrone and potassium cyanide.

10-Cyanoanthrone could lead to a parallel set of model compounds. 10-Cyanoanthrone has been prepared in several different ways,[14] but never by the direct reaction of cyanide with bromoanthrone. We attempted to prepare of 10-cyanoanthrone from bromoanthrone and cyanide. The reaction gave an

unexpected compound, 10-(10-anthronyl)-10-bromoanthrone (**12**) which is, in fact, an intermediate in the preparation of the thermochromic compound, bianthryl (**13**)[15]. We have demonstrated that in this reaction, cyanide acts as a mild base instead of a nucleophile, so that the direct synthesis of cyano-anthrone from bromoanthrone and cyanide does not work. We think that it is the carbonyl carbon's electron withdraw effect which increased the acidity of 10-position hydrogen, result the formation of 10-(10-anthronyl)-10-bromoanthrone.

In the development of general strategies for the synthesis of desired model compounds, one tactic is to overcome the deactivating effect of the carbonyl group of anthrone. We attempted to protect the carbonyl as its dimethyl ketal. A unexpected compound, 10-methoxy-10-phenylanthrone (**14**) formed from the reaction of 10-hydroxy-10-phenylanthrone and trimethyl orthoformate.

For each of these reactions, detailed discussions of both mechanisms and experimental details are given in the following sections. We believe that the significance of our research extends far beyond this specific problem. There is an increased awareness amongst organic chemists that not just electronic effects, but also stereoelectronic effects play an important part in determining if a reaction can occur readily or not. We hope that our research will help to resolve the more general problems of intramolecular hydride shifts.

Results and Discussion

In pursuing the goal of model compound synthesis, I started improving the existing synthetic methodology. As mentioned in the Introduction, the synthesis of bromoanthrone is the first step in our synthetic sequence (Scheme III), the yield and quality of the product resulting from this step have significant influence in our whole synthetic scheme. The original method for bromoanthrone synthesis[9] called for the addition of liquid bromine to suspension of anthrone in carbon disulfide. This resulted in the precipitation of bromoanthrone. Bromination of organic molecules can be carried out with several other reagents besides molecular bromine. N-bromosuccinimide (NBS) has been used quite extensively as brominating reagent to carry out radical halogenation reactions. Accordingly, we tried a radical reaction using NBS. By trying different solvents, we found that both benzene and carbon tetrachloride (CCL_4) are suitable. The NBS/benzene reaction mixture remains homogeneous. The starting material and product, as well as the by-product, succinimide, are all soluble in benzene, and the crude yield increased to 91%. The original Br_2/CS_2 procedure gave an 86% yield of a crude product which, unlike that from the NBS procedure, required further purification before use. The crude product of

NBS/benzene method was a nice yellow precipitate having much better purity and suitable for use in the next step of the synthesis. Recrystallization from a mixture of chloroform and hexane gave yellow crystals in 51% yield.[16]

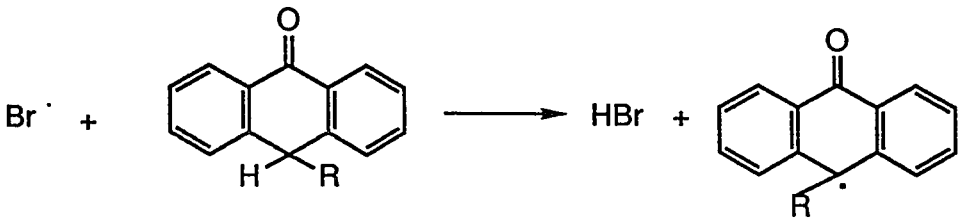
We are further pursuing the use of the NBS/benzene method in the synthesis of bromophenylanthrone. Bromophenylanthrone is the desired starting material in our proposed radical reaction to make 10,10-disubstituted model compounds. A mass spectrum showed a characteristic bromine pattern at 366 and 368, which corresponds to an $[M+NH_4]^{+\cdot}$ peak (MW 348 +18) of bromophenyl-anthrone. However, following the aqueous workup, we isolated 10-hydroxy-10-phenylanthrone[13] instead 10-bromo-10-phenylanthrone. (Aqueous base is necessary to wash out unreacted byproduct succinimide.) In an attempt to avoid contact with water, we tried to separate the product by column chromatography. Unfortunately, this method failed too. The silica gel used must have enough adsorbed surface water to hydrolyze our compound. Perhaps a less active chromatographic support, such as fluorosil, should be used in the future. Another alternative would be fractional crystallization. The only literature method for the preparation of bromophenylanthrone[10] is to pass dry HBr gas into a benzene solution of hydroxyphenylanthrone; in a

nonaqueous workup, colorless needles of bromophenylanthrone were precipitated by the addition of ligroin. The bromide is soluble in cold benzene, ethanol, or ether, and has a mp of 145-147 °C. Scheme IV shows the mechanism of the NBS bromination of anthrone and phenylanthrone.

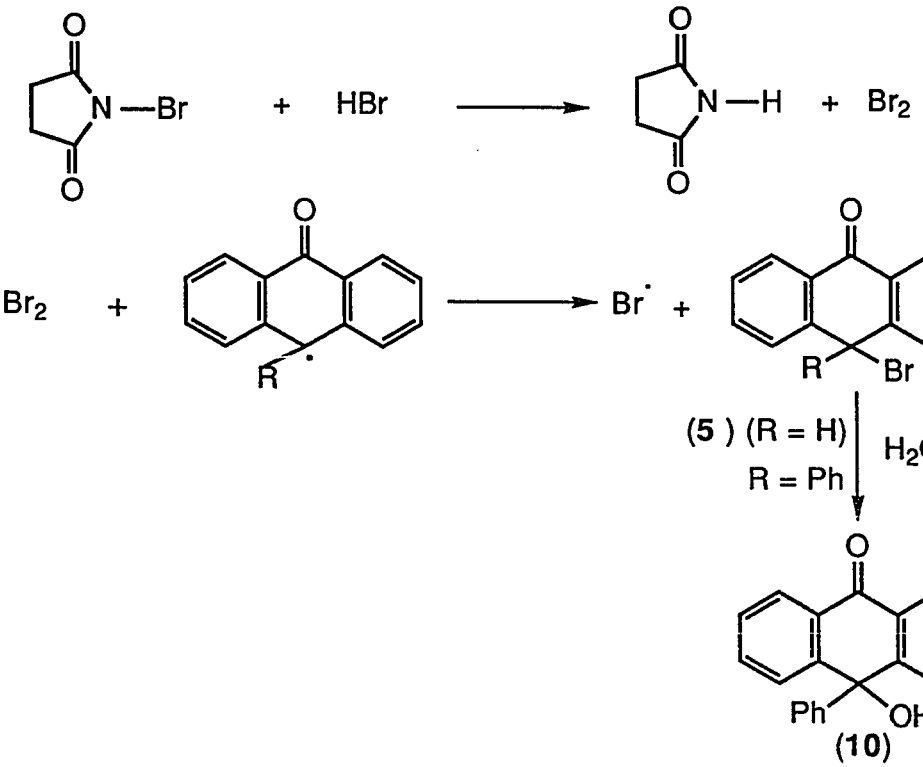
The most important goal of my work was to obtain the correct stereoisomer of 10,10-disubstituted-9-hydroxyanthrone, from which, our model compounds may be prepared and we might ultimately determine the mechanism of the hydride transfer in the prephenic acid rearrangement. 9-Borabicyclo [3.3] nonane (9-BBN)[2] and lithium aluminum hydride (LAH)[11] were both examined in some detail. Neither reagent worked for the reduction of 10-allyl-10-phenylanthrone. Weak TLC evidence in the case of LAH prompted us to try Superhydride (lithium triethylborohydride, $LiEt_3BH$) as the reducing agent. This more poweful reducing agent was successful, leading to a 3:1 mixture of diastereomeric alcohols (**9**) (Scheme V). We have not yet made stereochemical assignments fo the major and minor isomers, but an NOE (nuclear Overhauser effect) experiment should solve this analytical problem for us. We anticipate that even more hindered trialkylborohydrides (e.g. "Selectride") should increase the stereoselectivity of this reaction.

Scheme IV

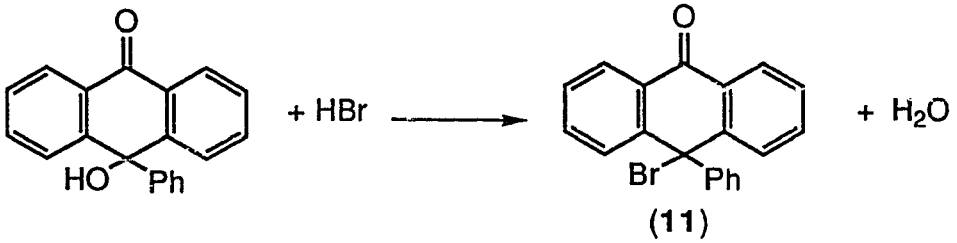
Initiation:



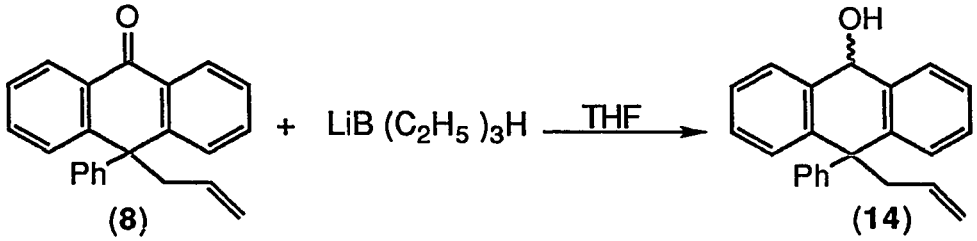
Propagation:



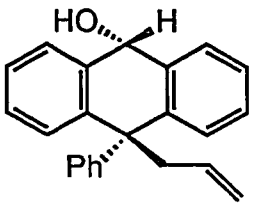
Literature method[10]



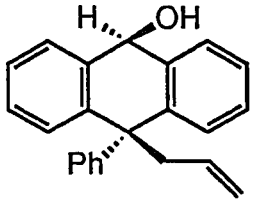
Scheme V



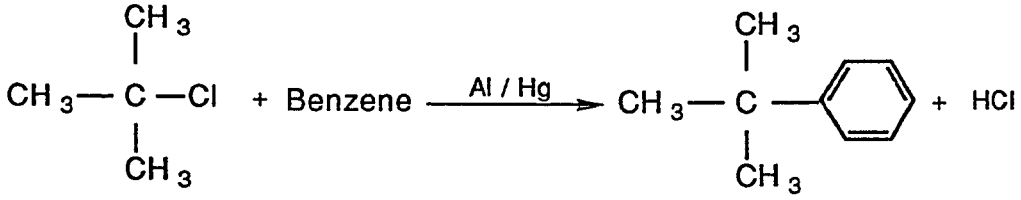
two diastereoisomers (ratio 1:3)

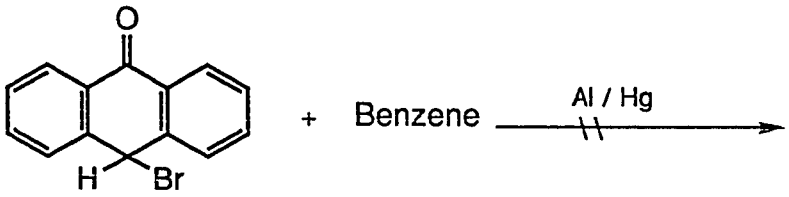


(major ?)



Scheme VI





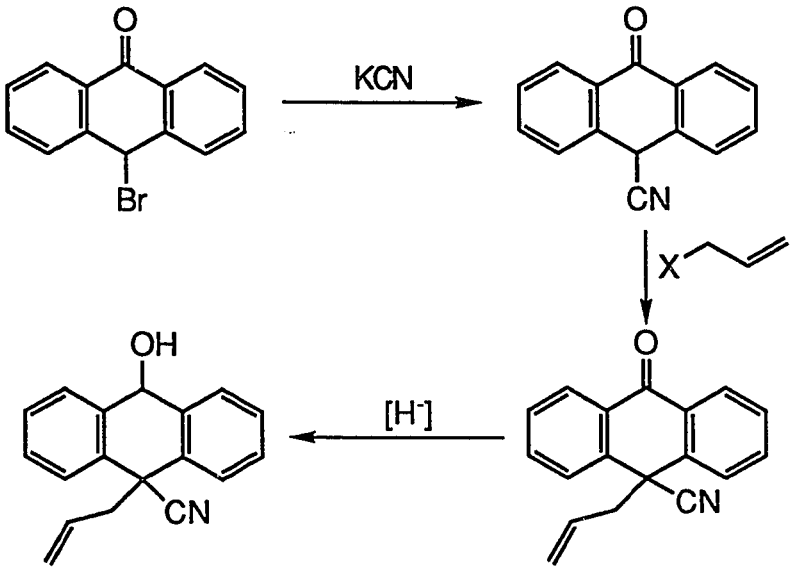
Friedel-Crafts alkylation using aluminum chloride ($ALCl_3$) is a common synthetic method. A modified Friedel-Crafts alkylation using amalgamated aluminum wire and mercuric chloride generates aluminum chloride *in situ* and has many advantages over $AlCl_3$ method.[12] It has been reported that a series of alkyl-benzenes can be prepared via Friedel-Crafts procedure using this catalyst.[17] I tried this modified Friedel-Crafts alkylation in an attempt to prepare phenyl-anthrone from bromoanthrone and benzene. Unfortunately, no reaction occurred. A second attempt using silver nitrate ($AgNO_3$) in addition to the aluminum amalgam also failed. I was able to repeat the literature reaction, the alkylation of benzene with t-butyl chloride under the same conditions. Therefore we have demonstrated that bromoanthrone is deactivated relative to t-butyl chloride, and the aluminum amalgam will not serve as catalyst for our reaction (Scheme VI). We also found literature evidence for the deactivating effect of the anthrone carbonyl.[13b] The phenylanthrone cation is less stable than a trityl cation; the corresponding phenylanthrone cation might be difficult to form because the electrophilic carbonyl carbon atom destabilizes the developing positive charge of the cation. By extension to our experiment, in which a phenyl group is formally replaced by a hydrogen atom, bromodiphenyl-methane should easily form a very stable cation, whereas the formation of an

anthrone cation from bromoanthrone will be less favorable.

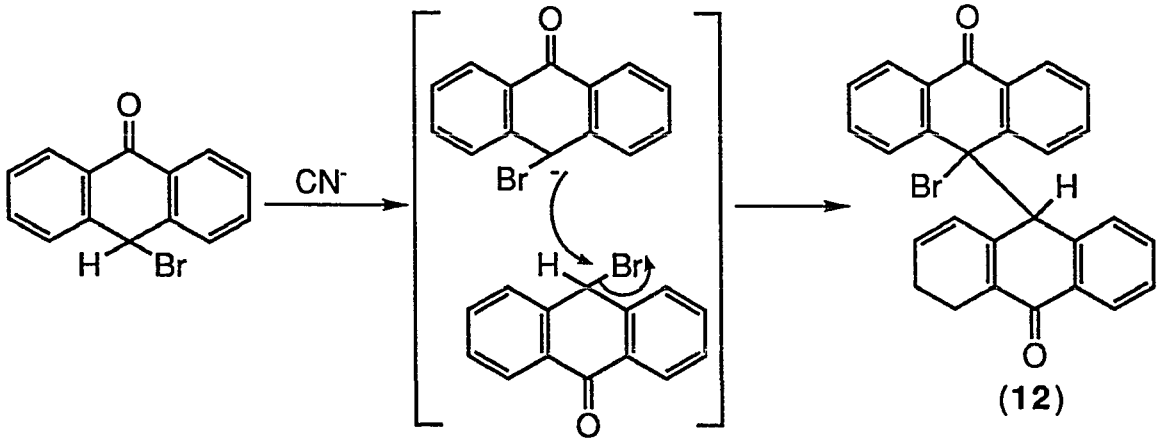
10-Cyanoanthrone is a starting material in a parallel route to make model compounds in our synthetic scheme. Reduction will give a cyanoalcohol, the branch point for this series of model compounds (Scheme VII). There are several different literature methods for the preparation of 10-cyanoanthrone,[14] but none used the direct reaction of cyanide with bromoanthrone. I tried to synthesize 10-cyanoanthrone directly from bromoanthrone and potassium cyanide. Instead of the anticipated product, a yellow precipitate was formed. It was shown by NMR; MS and elemental analysis to be 10-(10-anthronyl)-10-bromoanthrone (**12**) (MW 464, $C_{28}H_{17}BrO_2$)[18] as shown in Scheme VIII. Variations on this procedure, including the addition of silver nitrate ($AgNO_3$) and the reverse addition of the reagents gave the same product. We postulate that cyanide ion deprotonated bromoanthrone, and that this anion attacked the remaining bromoanthrone to give 10-(10-anthronyl)-10-bromoanthrone as the final product.

Based on above experimental results, protection of the anthrone carbonyl group will be required for the preparation of model compounds in our research. Our plan is to protect the carbonyl group as a ketal, carry out the desired reactions,

Scheme VII



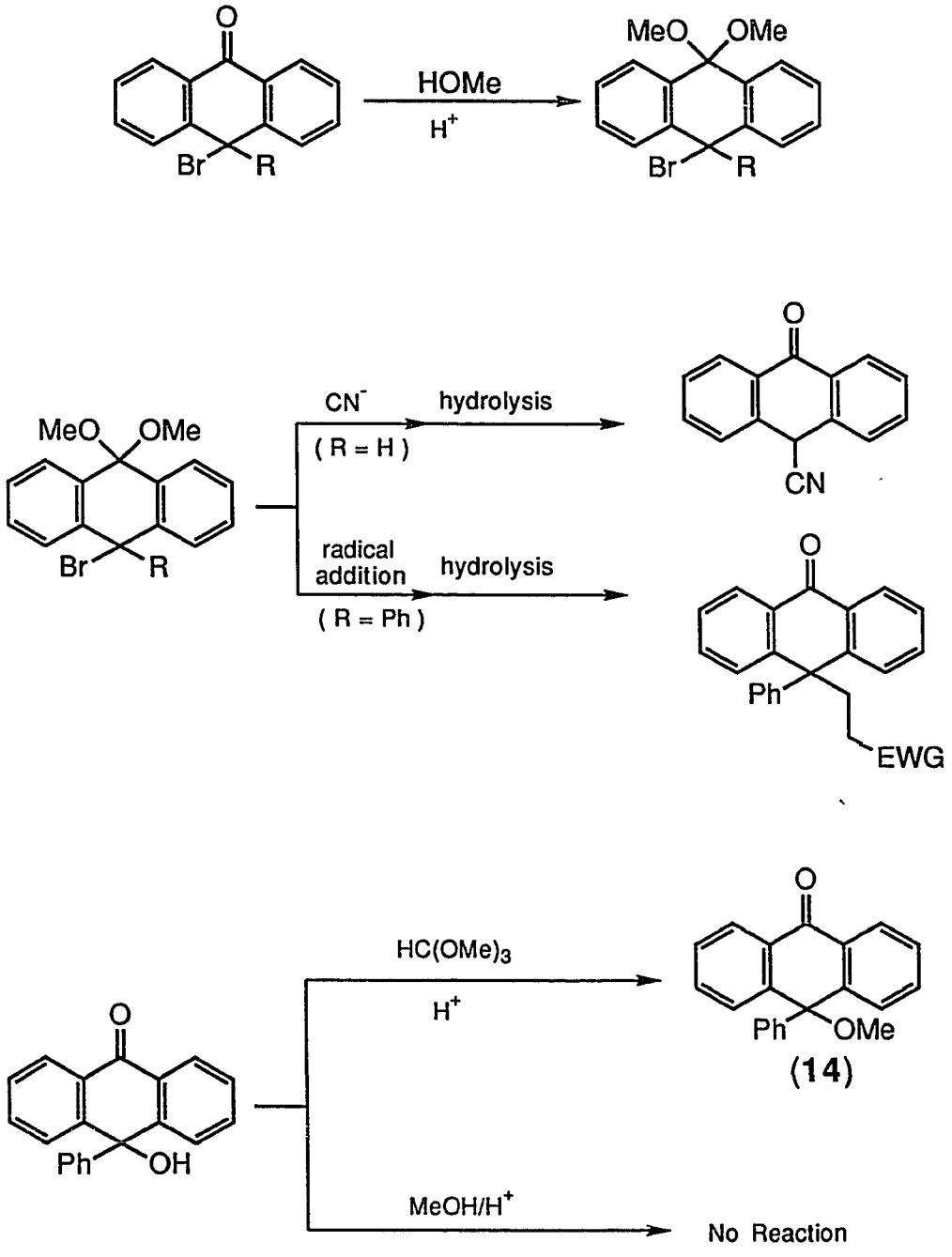
Scheme VIII



then regenerate the carbonyl by hydrolysis of the ketal (SchemeIX). Bromoanthrone and hydroxyphenylanthrone (HPA) were allowed to react in separate runs, with trimethyl orthoformate (TMOF), methanol, acetic acid or acetic anhydride. Concentrated sulfuric acid was used as a catalyst in each of these reactions. Only in the case of HPA and TMOF was a characterizable product formed. The analytical data show that the new compound is 10-methoxy-10-phenyl anthrone (**14**). We have not speculated about the mechanism of this transformation.

Both radical reactions and Michael additions have been attempted in search for new, more direct routes to prepare 10-substituted and 10, 10- disubstituted anthrones. In unpublished result, Rickborn and Koerner[19] have shown that under basic conditions, certain Michael acceptors with anthrone will react either by conjugate addition or by a Diels - Alder reaction. Using triethylamine as a catalyst, they could form a bicyclic compound from anthrone and ethyl acrylate. With another eqivalent of ethyl acrylate and two equivalent methoxide, the initial product was converted into a 10,10-disubstituted anthrone. Using two equivalents sodium methoxide and ethyl acrylate as solvent, the same final product was obtained[19] (Scheme X). We anticipated that under basic condition,

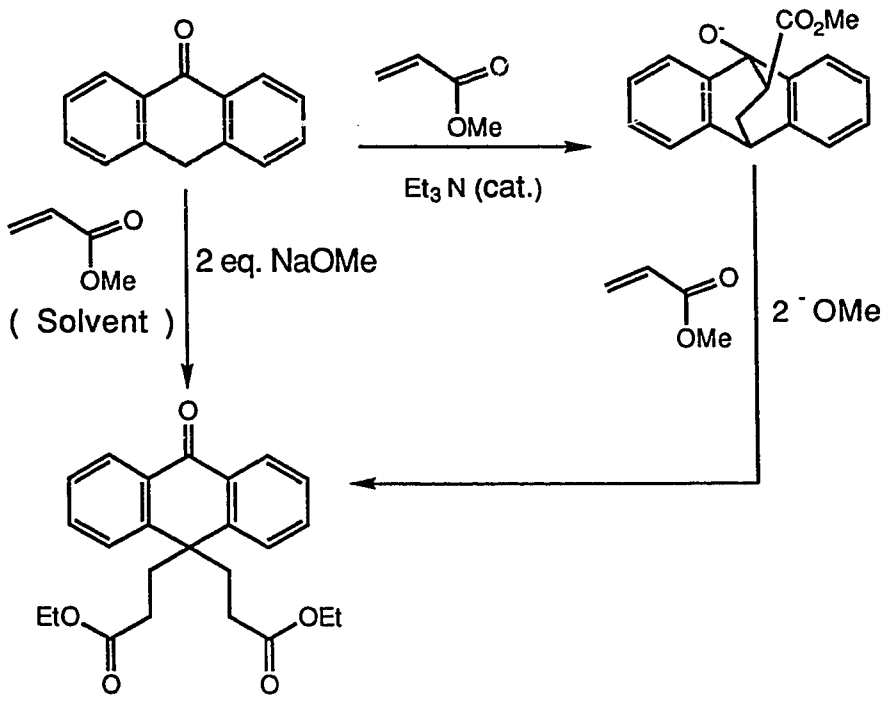
Scheme IX


O
Br
R
HOMe
H+
MeO
OMe
Br
R
MeO
OMe
Br
R
CN-
hydrolysis
(R = H)
O
CN
radical
addition
hydrolysis
(R = Ph)
O
Ph
EWG
O
Ph
OH
HC(OMe)3
H+
O
Ph
OMe
(14)
MeOH/H+
No Reaction

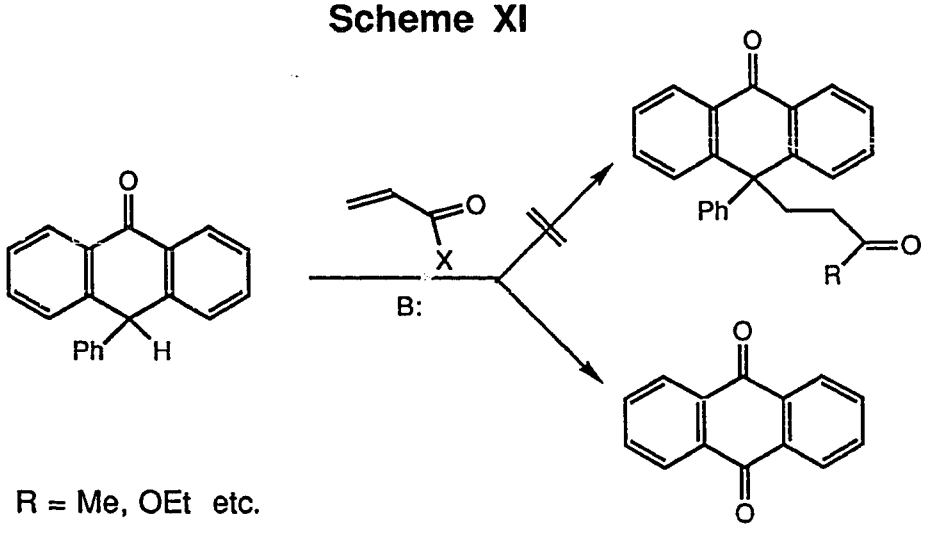
phenylanthrone will react similarly with α, β-unsaturated carbonyl compounds, such as methyl vinyl ketone and ethyl acrylate (Scheme XII). If successful, this will lead directly to 10,10 disubstituted anthrones. Our preliminary attempts, using chloroform as a solvent and triethylamine as catalyst, gave anthraquinone as the only characterizable product. The formation of the phenylanthrone anion was confirmed by reaction with methyl iodide. (The NMR spectrum showed both O-methyl and C-methyl peaks; the TLC was consistent.) Further effort on this approach is warranted for the future.

Radical reactions are synthetically useful. They often allow syntheses of compounds which would be very difficult using more traditional procedures. They are also compatible with many different functional groups. We designed some intermolecular radical reactions of bromophenylanthrone which would produce 10,10-disubstituted anthrones. Bromophenylanthrone should be a good precursor for the phenylanthrone radical. (Tri-n-butyltin hydride ($[CH_3(CH_2)_3]_3SnH$), the most commonly used "chain carrier," and 2, 2'-azobis (2-methyl propionitrile) (AIBN), which is a radical initiator, along with appropriate radical acceptors complete the chain reaction as illustrated in Scheme X.) Bromophenylanthrone is easily hydrolyzed but this route is also very promising.

Scheme X



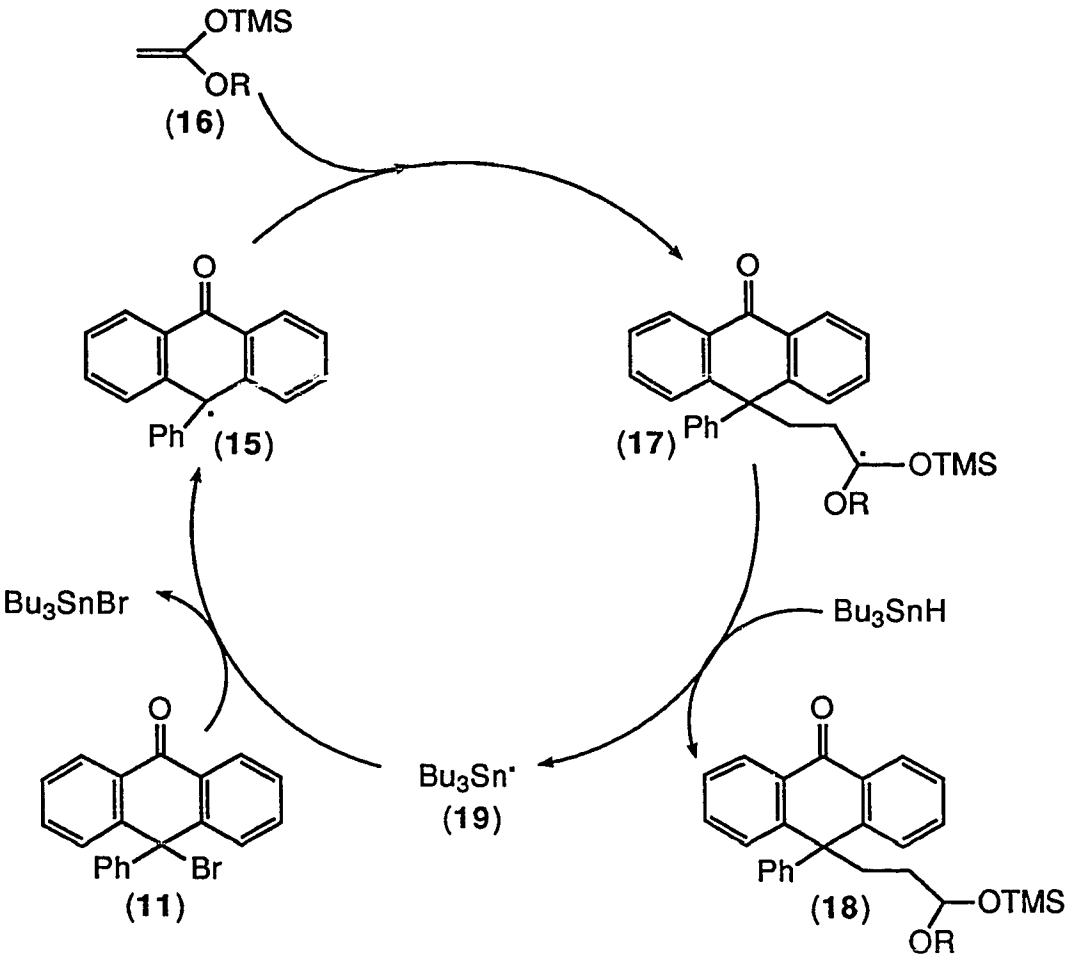
Scheme XI



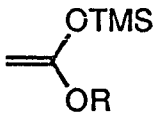
R = Me, OEt etc.

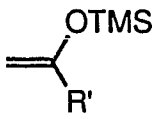
B: = Et_3N; NaOEt

Scheme XII



typical receptors





TMS = trimethylsilyl

R' = H, CN, etc.

R = H, Me, t-Butyl, etc.

Conclusion

In summary, we have discovered a cleaner, easier method for the bromination of anthrone. We have prepared 10-hydroxy-10-phenylanthrone and 10-methoxy-10-phenylanthrone by new routes. Finally, we successfully reduced a hindered 10,10-disubstituted anthrone to the corresponding alcohol. These compounds have been identified and fully characterized. My work has shown that certain "reasonable" reactions are not possible, for instance, the direct synthesis cyanoanthrone from bromoanthrone and potassium cyanide.

Future work includes improving the separation of bromophenylanthrone in the NBS method. Superhydride reduction should be extended to a wide variety of 10,10-disubstituted anthrones. Preparation of 10,10-disubstituted anthrones by both radical reactions and Michael addition reactions should be thoroughly investigated as these methods have great promise. Some of the reactions in this category have been tried in my research. Unfortunately, there are no positive results yet but in most cases the reactions are still very promising and deserve further experimentation. These reactions will be the focus of future

work in our research group.

One of the new approaches in my research was the preparation of 10,10-disubstituted anthrone through either radical reaction or Michael addition, both which of are very promising.[19,20] The Michael additions have been discussed in the Resultls and Discussion section; the radical route will be discussed below.

The radical reaction we are planning to carry out is a chain reaction between radicals and non-radicals. Since the radical character is not destroyed during the reactions, one can work with catalytic amounts of radical initiator. Obviously, the concentration of the non-radicals can be easily controlled. In general, in order to build a chain reaction, two conditions must be obeyed: the selectivities of the radicals involved in the chain have to differ from each other, and the reactions between radicals and non-radicals must be faster than radical combination reactions.[20] For instance, in our chain reaction (Scheme XII), phenlyanthrone radical **15** reacts with ketene acetal **16** in the presence of tributyltin hydride to give product **18**. In order to keep the cycle running, alkyl radical **15** must *selectively* attack ketene acetal **16** to form adduct radical **17**. Trapping of **17** with tributyltinhydride yields product **18** and regenerates

tributyltin radical **19**. These reactions must be faster than all other possible reactions of radicals **15**, **17**, and **19**; otherwise, this chain reaction will break down and this method will not be synthetically useful.

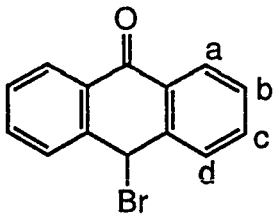
It is known that electron-poor radicals prefer to add to electron-rich alkenes (and that electron-rich radicals prefer electron-poor alkenes).[20] The phenylanthrone radical is an electron poor radical; accordingly, we need electron-rich radical acceptors in order to run the chain reaction successfully. We chose acetone trimethylsilyl enol ether (*or* silane, trimethyl[(1-methyletheny)oxy]-)[21] and O-*t*-butyl-O-(*t*-butyl-dimethylsilyl) ketene acetal [22] as the first targets, because they not only have the structural features needed for our model compounds, but also because they are known compounds. Ketene acetals are more electron-donating than acetone trimethylsilyl enol ethers but present a greater synthetic challenge. An even better radical acceptor, a tin ketene acetal (**20**), was suggested by Janet Grissom.[23] It is even more electron-rich than a silyl ketene acetal, because tin is more electropositive then silicon. More importantly, each cycle automatically liberates tributyltin radical and gives a desired model compound. There is one fewer radical in this chain reaction so there will be fewer selectivity problems.

Experimental Section

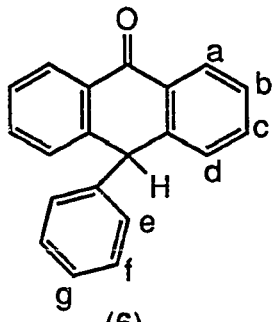
General Procedures: Reactions were routinely run under a nitrogen atmosphere with magnetic stirring. Melting points were determined with an Electrothermal capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 710B Infrared Spectrophotometer. Band positions are reported in reciprocal centimeters (cm^{-1}). ^{1}H-NMR spectra were recorded on either a Bruker 300 or a Bruker AM500 NMR spectrometer. ^{13}C-NMR were recorded at 125 MHz on a Bruker AM500 NMR spectrometer. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane. Mass spectra were run on Finnigan Mat 8230. Elemental analyses were performed by Chemical Analytical Services, UC Berkeley, California, and Syntex Research.

Bromoanthrone (5). Anthrone (1.9 g; 10.0 mmol) and N-bromosuccinimide (NBS) (1.96 g; 11.0 mmol) were dissolved in benzene (150 mL). The homogeneous solution was irradiated with a 60W lamp and stirred for 3 hours, then the reaction solution was washed successively with $NaHCO_3$ (2x100 mL), H_2O (2x100 mL), and satd. NaCl (2x100 mL). After drying over $MgSO_4$, the

solution was concentrated *in vacuo* to give a brownish yellow solid (2.48 g, 91%), mp 139-145 °C (dec). (lit.[24]. mp 148 °C), it suitable for further reaction. An analytical sample was recrystallized from a mixture of chloroform and hexane to give yellow crystals (1.39 g; 50% yield): mp 122 °C (dec); IR (nujol) 1655, 1595 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.64 (s, 1H,), 7.52 (t, 2H, J =7.5 Hz, H_b), 7.64 (t, 2H, J =7.5 Hz, H_c), 7.72 (d, 2H, J =7.5 Hz, H_d), 8.27 (d, 2H, J =7.5 Hz, H_a); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 43.75 (d), 127.87 (d), 129.22 (d), 130.11 (d), 131.12 (s), 133.57 (d), 141.00 (s), 182.96 (s); MS (EI, relative intensity), m/z 271 ((M-H), 20), 193 (100); MS (CI,relative intensity), 307 ((M+N_2H_7), 24), 290 ((M+NH_4), 44), 273 ((M+H), 15).



(5)



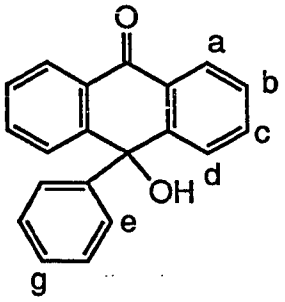
(6)

10-Phenylanthrone (6). This compound was prepared by the method of Carr[7]. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.42 (s, 1H), 7.11 (d, 2H, J =8.0 Hz, H_d), 7.20 (t, J =7.5 Hz, H_g), 7.24 -7.30 (m, 4H), 7.42 (t, 2H, J =7.5 Hz, H_c), 7.49 (dt, 2H, J =7.5 Hz, J =1Hz, H_b), 8.39 (dd, 2H, J =7.5 Hz, J =1 Hz, H_a). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 48.44 (d), 126.92 (d), 127.16 (d), 127.29 (d), 128.86 (d), 129.03

(d), 129.66 (d), 131.14 (s), 133.16 (d), 144.14 (s), 144.40 (s), 184.38 (s).

10-Hydroxy-10-phenylanthrone(10). Phenylanthrone (1.35 g; 5 mmol) and NBS (0.979 g; 5.5 mmol) were dissolved in benzene (100 mL). The homogeneous solution was irradiated with a 60W lamp and stirred overnight. The solution was treated successively with satd. $Na_2S_2O_3$ (2x100 mL, to remove excess NBS), Na_2CO_3 (2x100 mL, to remove succinimide), H_2O (2x100 mL), and satd. NaCl (2x100 mL). After drying with $MgSO_4$, the solution was concentrated *in vacuo* (without any heating) until it reached one-fifth of its original volume. The brownish white precipitate which separated from the deep brown mother liquor had crude mp 212-214 °C. Recrystallization from a mixture of chloroform and hexane gave white crystals (35.5%): mp 218 °C (lit.[23] mp 213-214°C); IR (KBr) 1650, 1600 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.14 (tt,1H, J_{ortho}=7.5 Hz, J_{meta}=1.0 Hz, H_g), 7.22 (t, 2H, J_{ortho}=7.5 Hz, Hf), 7.35 (dd, 2H, J_{ef} =8.0 Hz, J_{eg}=1.0 Hz,H_e), 7.42 (dt, 2H, J_{ortho}=7.5 Hz, J_{bd}=1.0Hz, H_b), 7.56 (dt, 2H, J_{ortho}=7.5 Hz, J_{ac}=1.5Hz, H_c), 7.62 (dd, 2H, J_{cd}=8.0 Hz, J_{bd}=1.0 Hz, H_d), 8.25 (dd, 2H, J_{ab}=8.0 Hz, J_{ac}=1.5Hz, H_a); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 73.10 (s), 125.43 (d), 126.86 (d), 126.93 (d), 128.24 (d), 128.38 (d), 129.80 (s), 134.12 (d), 145.93 (s), 147.73 (s), 183.74 (s); MS (EI, relative intensity), m/z 286 (M^+, 68), 268 (20), 209 (100); MS (CI, relative intensity) 304 (($M+NH_4$), 16),

287((M+H), 16), 269 (100).



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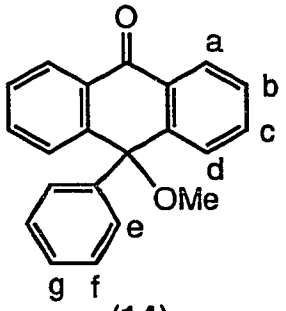
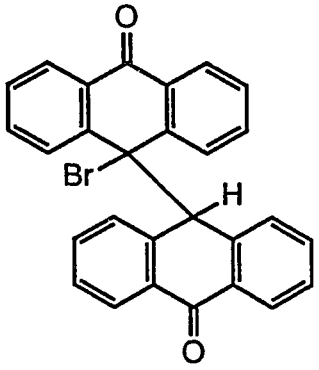


(14)

10-Methoxy-10-phenylanthrone (14). 10-hydroxy-10-phenylanthrone (75 mg; 0.26 mmol) was dissolved into methanol (50 mL). Trimethyl orthofomate (747 mg; 0.69mL; 0.26 mmol) was added to the solution by syringe; a catalytic amount of conc. H_2SO_4 (4 drops) was added. The solution was refluxed overnight under N_2, then quenched with sat. $NaHCO_3$ (30 mL) and extracted with ether (3x20 mL). The combined organic layers were dried over $MgSO_4$, and the solution was concentrated *in vacuo.* Recrystallization from hexane and ethyl acetate gave white crystals (40 mg, 50.9%): mp 168-170 °C; IR (nujol) 1600, 1590 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.01 (s, 3H), 7.12 (t.1H, J=6.0 Hz, H_g), 7.20 (t, 2H, J=7.5 Hz, $2H_f$), 7.32 (d, 2H, J=8.5 Hz, $2H_e$), 7.46 (t, 2H, J=7.5 Hz, $2H_b$), 7.50 (d, 2H, J=7.7 Hz, $2H_d$), 7.57 (t, 2H, J=7.5 Hz, $2H_c$), 8.35 (d, 2H, J=7.7 Hz,$2H_a$). ^{13}C NMR (125 MHz,$CDCL_3$) δ 51.67 (q, OCH_3), 78.62 (s), 125.64 (d), 126.66 (d), 127.03 (d), 128.16 (d), 128.22 (d), 128.56 (d), 131.89 (s), 134.03 (d), 144.95 (s), 146.31 (s), 183.56 (s). MS (EI, relative intensity), m/z 300

(M^+, 22), 269 (100), 223 (36). Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.97, H, 5.37. Found: C, 83.63, H, 5.39.

10-(10-Anthronyl)-10-bromoanthrone (12). Bromoanthrone (2.05 g; 7.5 mmol) was dissolved in methanol (30 mL). When potassium cyanide (0.54 g; 8.25 mmol) was added to the refluxing solution, there was an immediate change from colorless to yellow followed by precipitation of a yellow solid. The reaction mixture was refluxed under N_2 for 2 hr, then cooled to room temperature. The yellow precipitate which separated was identified as 10-(10-anthronyl)-10-bromoanthrone (1.40 g; 40%); mp 165 °C (with decomposition). The yellow precipitate was recrystallized from a mixture of chloroform and hexane (60% for the recrystallization): m.p 176 °C (dec); IR (KBr) 1670,1600 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.01 (s,1H), 6.97 (br s, 2H), 7.27 (t, 2H,J= 7.3 Hz), 7.37 (t, 2H, J= 7.4 Hz), 7.47 (t, 2H,J=7.5 Hz), 7.50 (t, 2H, J= 6.7 Hz), 7.54 (br s, 2H), 7.75 (d, 2H, J=7.6 Hz), 7.91 (d, 2H, J= 8.0 Hz); ^{13}C-NMR (125 MHz, $CDCL_3$) δ 61.15 (d), 70.88 (s), 125.85 (d), 126.13 (d), 128.46 (d), 129.16 (d), 130.61 (two overlapping doublets, double intensity), 131.56 (s), 132.17 (d), 132.76 (d), 134.99 (s), 137.40 (s), 141.31 (s), 180.97 (s), 182.85 (s). MS (CI, relative intensity,%) m/z 482 ($M+NH_4$, 60). Anal. Calcd for $C_{28}H_{17}O_1Br_1$: C,72.47; H, 3.69. Found: C, 71.80; H, 3.75.



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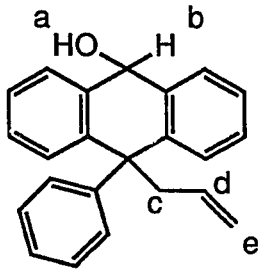
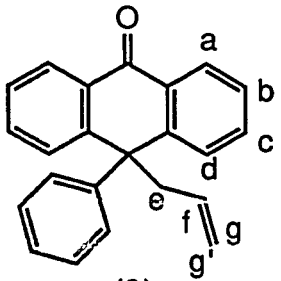


(9)

10-Allyl-9-hydroxy-10-phenyl-9,10-dihydroanthracene (9). 10-Allyl-10-phenylanthrone (0.72 g, 2.3 mmol) was dissolved in dry THF (100 mL) under N_2 at RT. Lithium triethylborohydride (13.8 mL of a 1 M solution in THF, 13.8 mmol) was added to the solution slowly by syringe. The solution was pale yellow and TLC showed a new spot at lower R_f (1:9 ethyl acetate/hexane). The reaction solution was kept at a gentle reflux for 2 h, then cooled to RT and quenched with water (50 mL). Following extraction with ether (3x50 mL), the combined organic extracts were washed with satd. NaCl (2x50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give a yellow oil. IR (KBr) 3337, 1620, 1575 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ 2.1 (d, J =10 Hz, H_a from major isomer, exchangeable with D_2O), 2.2 (d, J = 10 Hz, H_a from minor isomer, exchangeable with D_2O), 3.1 (d, J=7 Hz, H_c from minor isomer), 3.2 (d, J = 7 Hz, H_c from major isomer), 4.5-5.0 (m, H_e), 5.1-5.6 (m, H_d), 5,65 (d, J = 10, H_b from two isomers), 5.69 (d, J = 10, H_b from minor isomer), 6.9-8.1 (m, 13H).

10-Allyl-10-phenylanthrone (8). Alkylation of 10-phenylanthrone with allyl bromide followed by rearrangement of the crude O/C alkylation mixture was carried out by the procedure of Carr.[7] IR (KBr) 1660, 1663, 1601 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.26 (d, 2H, J =7.1 Hz, H_e), 4.49 (d, 1H, J =16.9 Hz, $H_{g'}$), 4.62 (d, 1H, J =10.2 Hz, H_g), 4.49 (m, 1H, H_f), 7.05 (d, 2H, J =7.9 Hz, H_d), 7.28 (m, 5H, phenyl), 7.37 (t, 2H, J =7.5 Hz, H_b or H_c), 7.46 (t, 2H, J =7.5 Hz, H_b or H_c), 8.34 (d, 2H, J =7.8 Hz, H_a); MS (EI, relative intensity), m/z 310 (M,8), 269 [(M - allyl, 100]; MS(CI, relative intensity) 328 [(M+NH4), 84]311[(M+H), 100].



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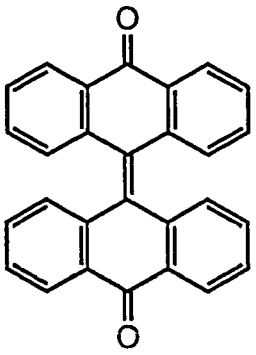

(13)

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