SYNTHESIS OF SOME DERIVATIVES OF 7-PHENYLBENZ[a]ANTHRACENE AND 9-PHENYLANTHRACENE

by

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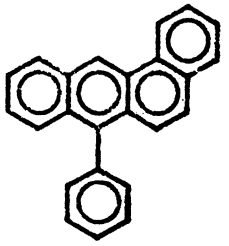
INTRODUCTION

Since 1929, when the first known chemically pure carcinogen, dibenz[a,h]anthracene, was reported,[1] a large number of polycyclic aromatic hydrocarbons and derivatives have been synthesized and tested for their physiological activity. Characteristically, many of these compounds were found to be carcinogenic.[2] Of the more than 450 compounds which had been found to be carcinogenic up to 1953, more than 200 were polycyclic hydrocarbons, their derivatives and analogues.[2] Thus far, attempts to correlate chemical structure and physiological activity of such compounds have been met with only limited success.[2]

In contrast to the many polycyclic hydrocarbons found to be carcinogenic, a few polycyclic hydrocarbons and derivatives have been synthesized which possess anti-tumor activity. For example, in these laboratories the three compounds, 7-phenylbenz[a]anthracene (1),[3] 4-(7-benz[a]anthracenyl)benzamide (2),[4] and 7-(2-carboxyphenyl)benz[a]-anthracene (3),[5] were synthesized and found to possess anti-tumor activity. In the case of the amido compound 2, significant anti-tumor



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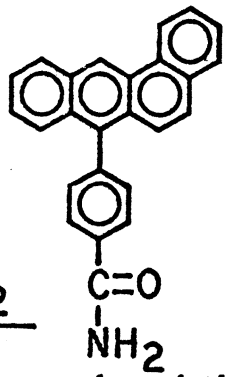

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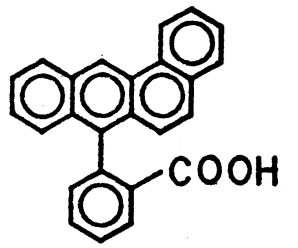


3

activity was apparently observed, and the compound was prepared in large quantity by Merck Sharpe and Dohme and is currently being subjected to extensive testing at the Cancer Chemotherapy National Service Center.[6]

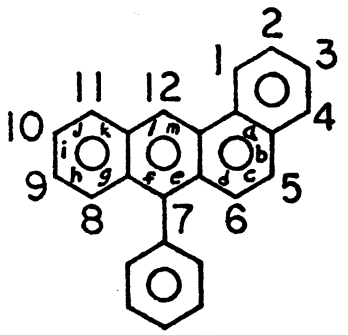
Interestingly, whereas these three derivatives of benz[a]anthracene display anti-tumor activity, benz[a]anthracene displays weak carcinogenic activity.[7] Apparently, the presence of a phenyl substituent at the 7-position of benz[a]anthracene alters the physiological activity of the benz[a]anthracene group. Also, the presence of an amido functional group substituted at the para position of the phenyl ring apparently greatly enhances the anti-tumor activity of the 7-phenylbenz[a]anthracene group.

In the light of these observations, it would appear to be of some significance to explore possible methods by which a variety of other nitrogen containing compounds analogous to 4-(7-benz[a]anthracenyl)-benzamide (2) might be prepared. Such compounds might not only display significant anti-tumor activity, but also might lead to useful deductions in regard to efforts to correlate chemical structure and physiological activity of polycyclic compounds.

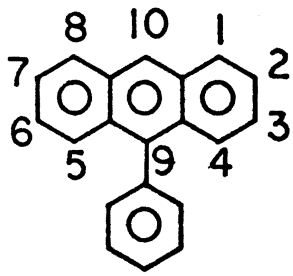
With the present methods available for preparing 7-substituted benz[a]anthracenes, as well as 9-substituted anthracenes, functional groups which are reactive with organo metallic reagents or inorganic acids must be introduced into the compounds only after the polycyclic ring systems have been synthesized. In view of this and the previous observations, this dissertation discusses the preparation, from appropriate polycyclic carboxylic acids, of some nitrogen containing derivatives of 7-phenylbenz[a]anthracene and 9-phenylanthracene.

NOMENCLATURE

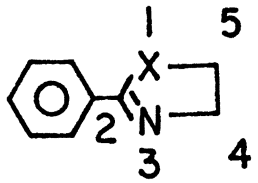
The nomenclature used throughout this dissertation is consistent with the recommendations presented in the J. Am. Chem. Soc., 82, 5545 (1960). The following numbered systems will serve as a guide to the compounds encountered in this dissertation.



7-phenylbenz[a]anthracene



9-phenylanthracene

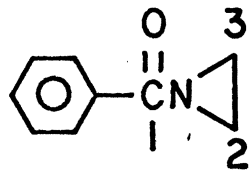


X = O, S, or NH

2-phenyloxazoline (X = O)

2-phenylthiazoline (X = S)

2-phenylimidazoline (X = NH)



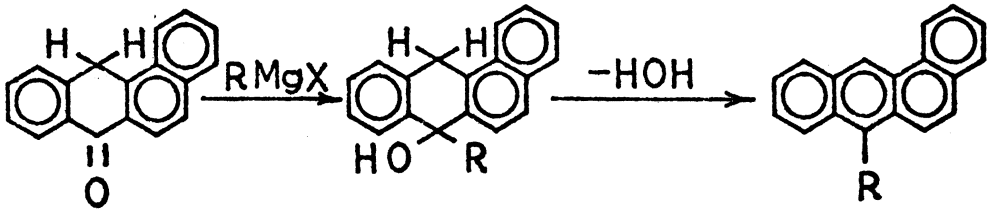
benzaziridamide

or 1-benzoyl aziridine

HISTORICAL

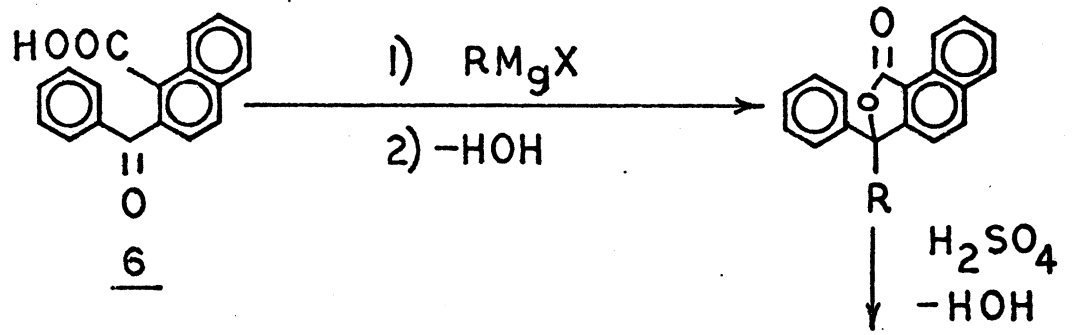
A. 7-Substituted Benz[a]anthracenes and 9-Substituted Anthracenes.*

Basically, 7-substituted benz[a]anthracenes (5) have been prepared by four methods, while 9-substituted anthracenes (9) have been prepared by three methods. Until 1940, 7-substituted benz[a]anthracenes (5) were prepared primarily by either reacting Grignard reagents with 1,2-benz-10-anthrone (4) and dehydrating the resulting carbinols to hydrocarbons 5,[8-12] or by reacting excess Grignard reagents with 2-benzoyl-



4 5

R = alkyl



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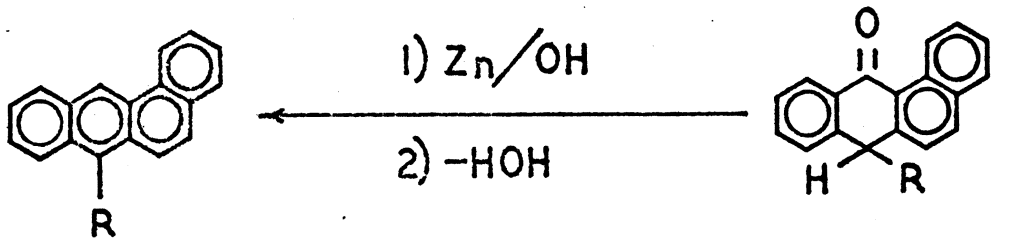


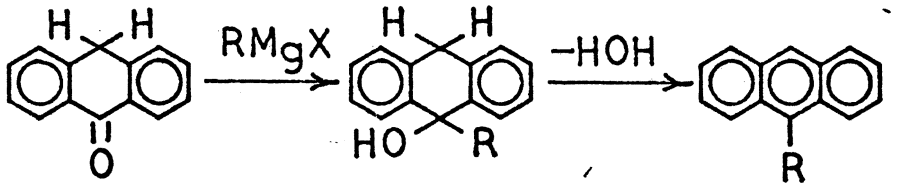
5 7

R = alkyl

*Substituted with alkyl or aryl groups.

1-naphthoic acid (6) and cyclizing the resultant acids or lactones to the corresponding anthrones (7) which were then reduced and dehydrated to hydrocarbons 5.[13]

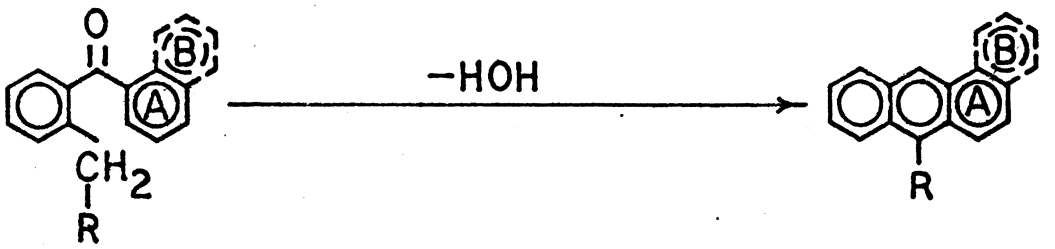
9-Substituted anthracenes (9) were prepared during this time primarily in a manner similar to the first method, in which Grignard reagents were reacted with anthrone (8), and the resulting carbinols were then dehydrated.[14]



8 9

R = alkyl, aryl

Compounds 5 and 9 were also prepared by the Elbs reaction,[20] although to only a limited extent. Pyrolytic cyclodehydration of ketones of the nature 12 and 13 generally have resulted in low yields of compounds 5 and 9.[21]



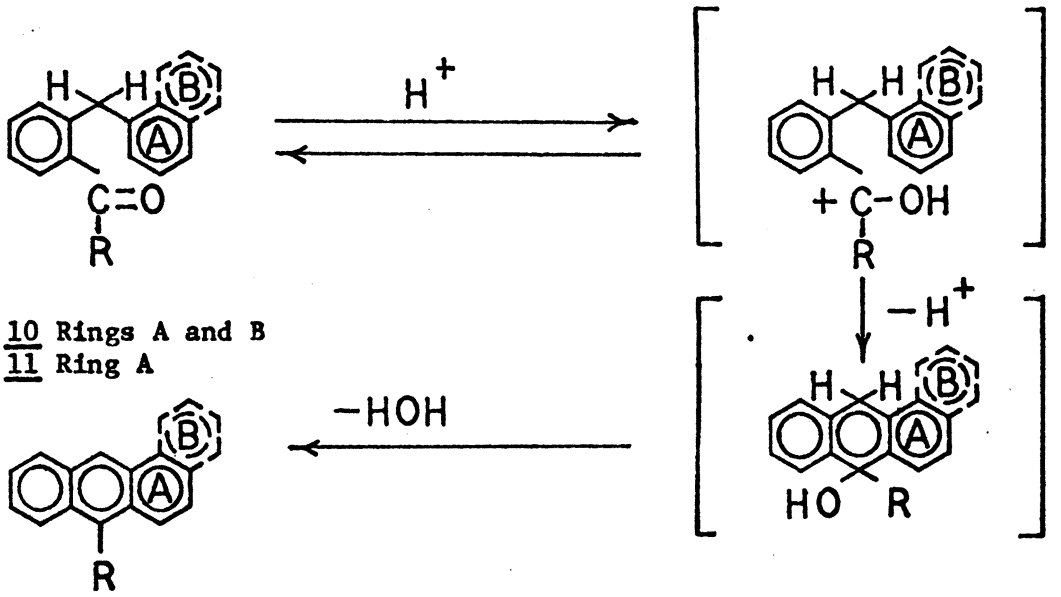
12 Rings A and B
13 Ring A

5 Rings A and B
9 Ring A

R = alkyl, aryl

But since 1940 7-substituted benz[a]anthracenes (5) and 9-substituted anthracenes (9) have been prepared primarily by the Bradsher reaction,[15,16]

in which 2-(1-naphthylmethyl)phenyl ketones (10) and 2-benzylphenyl ketones (11) have been cyclodehydrated with acid catalysts into compounds 5 and 9, respectively. Generally, these reactions have been accomplished with hydrobromic acid in glacial acetic acid solvent, although other solvents and acid catalysts have been used in certain cases.[17,18,21]



10 Rings A and B
11 Ring A

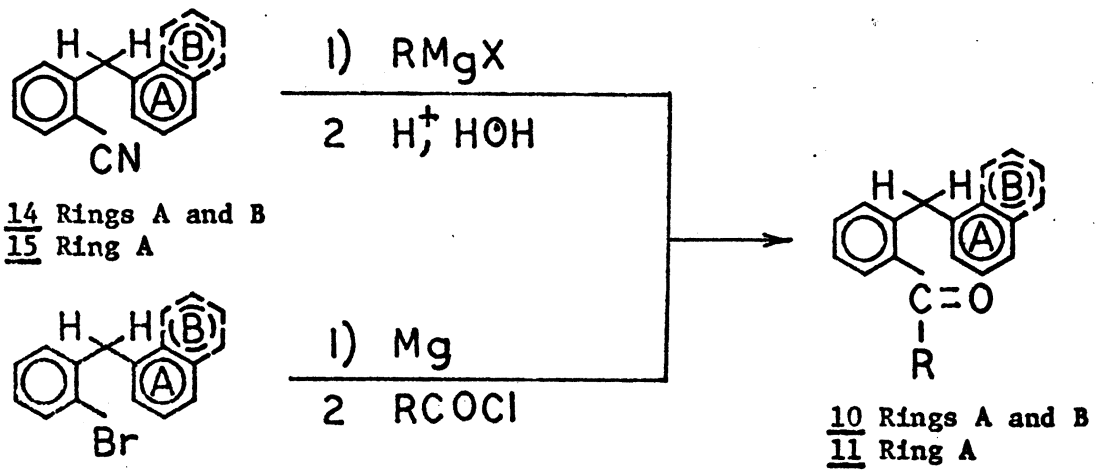
5 Rings A and B
9 Ring A

R = alkyl, aryl

The Bradsher reaction was first observed by Bergman[22] in 1939, developed by Bradsher[15,23,24] in the early 1940's, and has since been studied mechanistically[25-33] and used extensively by Vingiello and coworkers in these laboratories for the preparation of compounds 5[3,5,17,19,34-45] and 9.[28,29,35,38,46-49]

The synthetic value of the Bradsher reaction has been demonstrated by the relatively high yields of cyclized product obtained -- in most cases better than 50% -- and by the ease, in general, of preparing the necessary ketone intermediates. The ketone intermediates necessary for

preparing compounds 5 and 9 have been prepared by two methods. One method has involved the reaction of Grignard reagents with 2-(1-naphthylmethyl)cyanobenzene (14)[23] and 2-cyanodiphenylmethane (15),[15] respectively, followed by hydrolysis of the intermediate ketimines to give ketones 10 and 11. The other method has involved the reaction of acid chlorides with the Grignard reagents formed from 2-(1-naphthylmethyl)bromobenzene (16)[39,50] and 2-bromodiphenylmethane (17),[51] respectively.



14 Rings A and B
15 Ring A

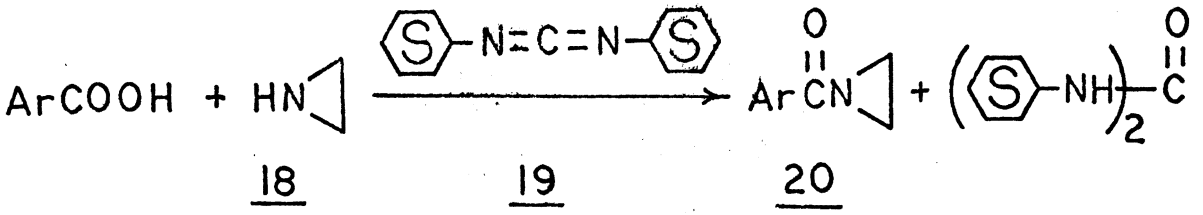
16 Rings A and B
17 Ring A

10 Rings A and B
11 Ring A

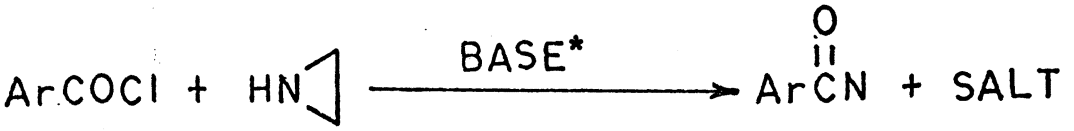
R = alkyl, aryl

B. 1-Aroylaziridines.

A literature survey shows that the numerous 1-aroylaziridines (20) reported have been prepared primarily by methods which have been used for the preparation of other N-substituted amides. Two methods of particular interest in connection with this thesis involve the preparation of such compounds 20 from carboxylic acids and acid chlorides, i.e., reacting aziridine (18) with carboxylic acids in the presence of dicyclohexylcarbodiimide (19) and with acid chlorides in the presence of a base.



18 19 20



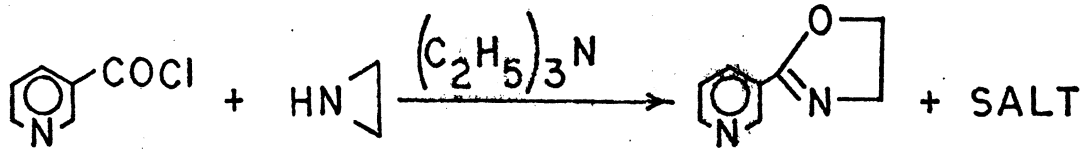
20

Ar = aryl**, *Base = NaOH or $(C_2H_5)_3N$

The majority of 1-aroylaziridines (20) have been prepared from acid chlorides, but unlike in the preparation of other amides from acid chlorides, excess aziridine (18) cannot be used to serve as a base since it tends to polymerize in the presence of mineral acids.[52] Sodium hydroxide or triethylamine[53] have commonly been used as bases for this type of reaction.

The other method, involving the use of carboxylic acids, has not been used extensively, but it does provide an alternative if other methods fail or are not practical. Ross,[54] for example, prepared N-nicotinoyl aziridine (21) in 74% yield by this method after the reaction of an acid chloride with aziridine and triethylamine in ether gave only oxazoline 22.

**Throughout this thesis, Ar = aryl.



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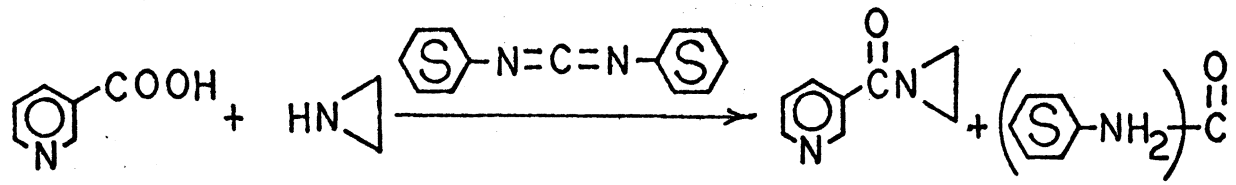
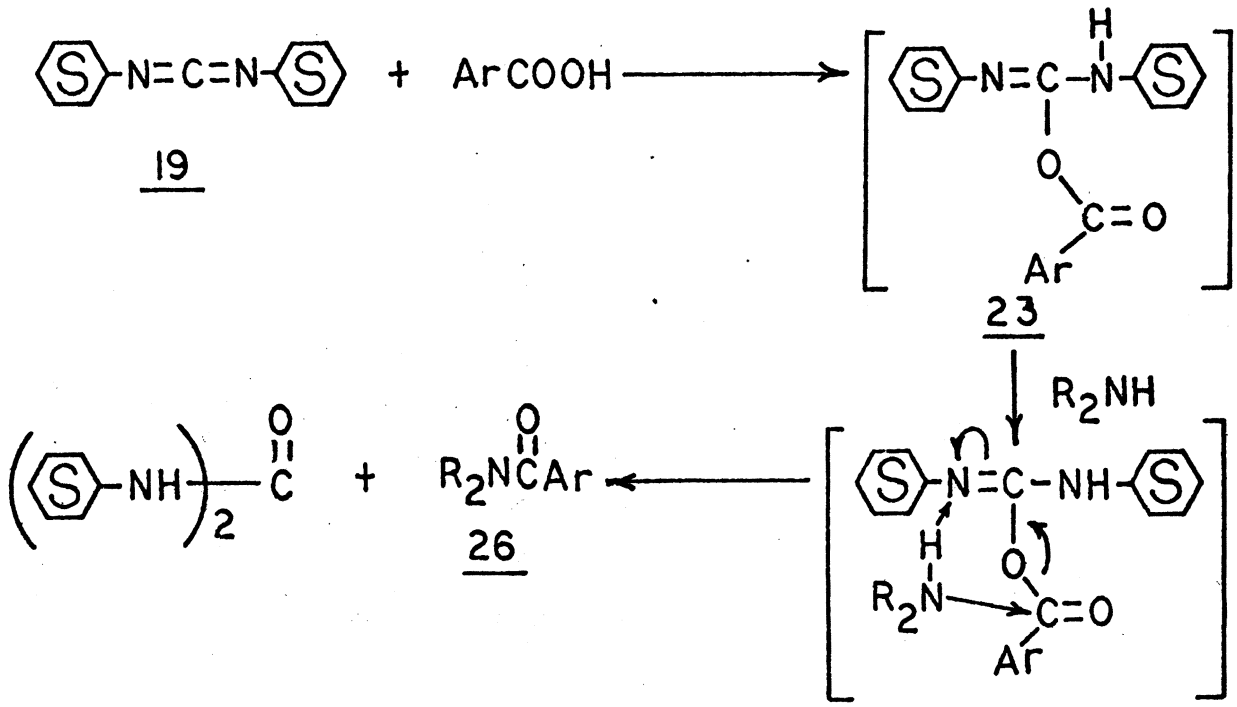


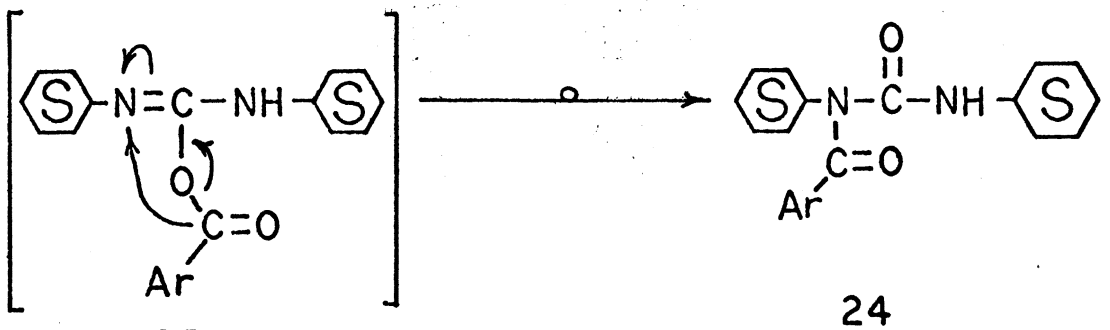
19 21

Sheehan,[55,56] in 1955, first reported this type of reaction for the preparation of amide bonds, in which amines are reacted directly with carboxylic acids in the presence of a carbodiimide, usually 19. To date the reaction has been used primarily for the preparation of peptides from amino acids, although some simple amides have been prepared by this method.[57]

Mechanistically, the reactions are considered to occur by the



19 23 26



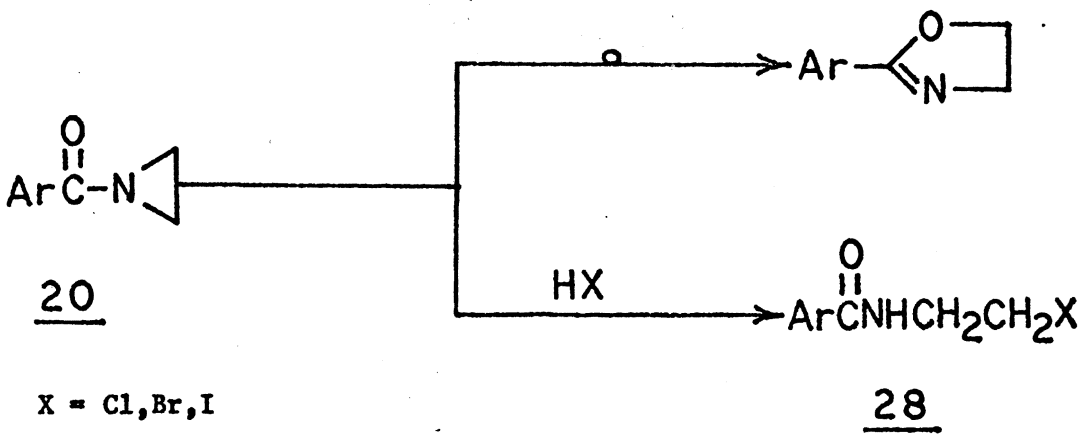
23 24

initial formation of an intermediate O-acyl-urea (23), which may then either react with the amine to form amide 26 or form an N-acyl-urea (24) side product by intramolecular rearrangement.[57,58,59] Generally, the reactions have been carried out at room temperature or lower to reduce the possibility for side product formation.[54,57]

Characteristically, 1-aroylaziridines are chemically reactive, and reactions have been reported involving isomerizations to 2-oxazolines,[60] N-allylamides,[61] α-benzamidobenzalacetophenones,[62] and oxazepines;[63] dimerization to piperazines;[64] cleavages with ammonium sulfide,[65] hydrohalic acids (Cl,Br,I),[66] organic acids,[67] alcohols,[67] and primary and secondary amines[68] to form N-substituted amides; reductions to N-substituted amides;[67] as well as some isolated reactions particular to specific compounds.[69] Of particular interest in this work are those reactions involving the formation of 2-oxazolines (27) and N-(2-haloethyl)amides (28) (Cl,Br,I).

Pettit[66] has noted that 1-aroylaziridines (20) in chloroform solutions are rapidly cleaved at room temperature to N-(2-haloethyl)amides (28) when anhydrous hydrogen halides (HCl,HBr,HI) are bubbled through the solutions. 1-Aroylaziridines are also readily cleaved with aqueous

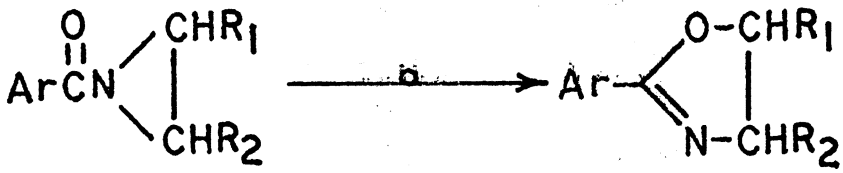
hydrohalic acids, but the resulting N-(2-haloethyl)amides are susceptible to hydrolysis reactions in the aqueous mediums. These reactions are commented upon in the next section.



Heine[60] has noted that 1-aroylaziridines (20) have been isomerized to 2-oxazolines (27) with heat, acids, aluminum chloride, as well as nucleophilic catalysts, such as iodide and thiocyanate ions. The use of nucleophilic catalysts to form 2-oxazolines from 1-aroylaziridines was first reported by Heine[70] in 1959, and since then this method appears to have become a basic method for preparing 2-oxazolines. The first three methods have never been used to any degree for preparing 2-oxazolines and appear to serve primarily to illustrate the general reactivity of 1-aroylaziridines.

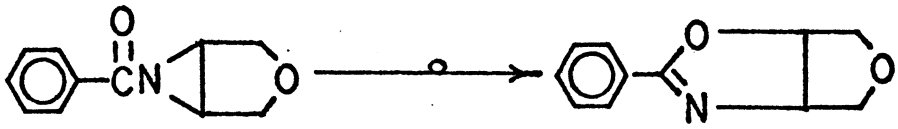
1-Aroylaziridines are relatively unstable to heat, and several different isomerization products have been reported where the type of product formed has been found to depend in a great part upon the substituents attached to the carbon atoms of the aziridine ring. To date only unsubstituted 1-aroylaziridines (20),[65,71,72] 1-aroyl-2,3-diarylaziridines (29),[62] and a few 1-aroylaziridines fused to another ring

system (example, 30)[73,74] have been thermally isomerized to 2-oxazolines (27).



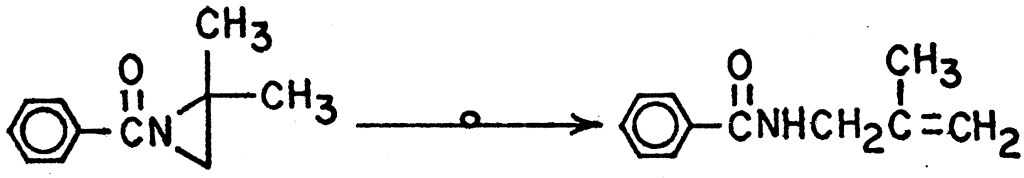
20 $R_1 = R_2 = H$

29 $R_1 = R_2 = C_6H_5$

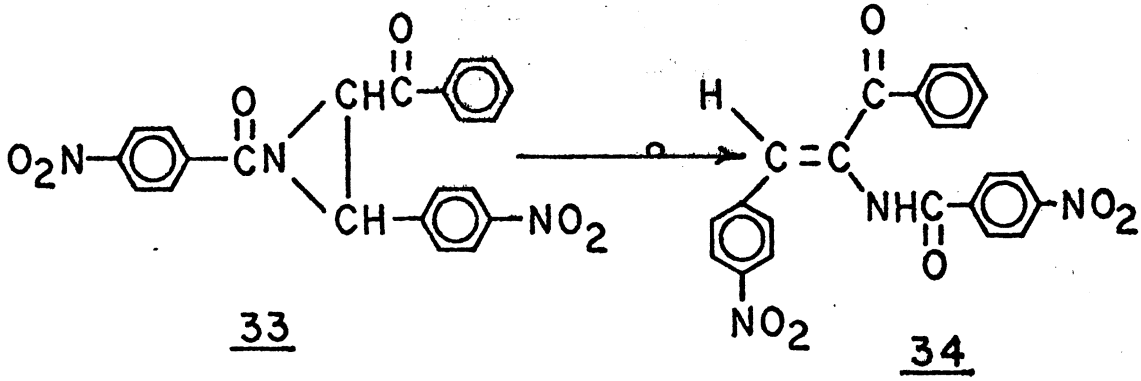


30

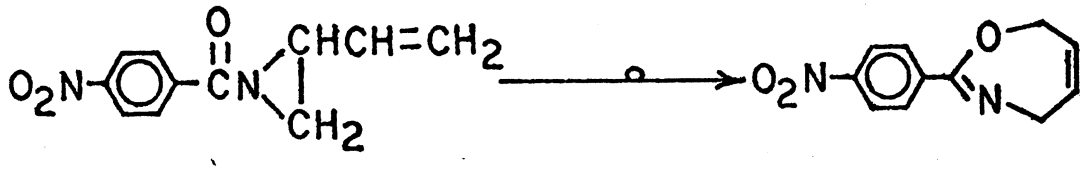
Pyrolysis of other substituted 1-aroylaziridines have resulted in the formation of a variety of products. Thus, the 1-aroyl-2,2-dialkylaziridine 31 was pyrolyzed into the N-allylamide 32, the 1,3-diaroyl-2-alkylaziridine 33 was pyrolyzed into the α-benzamidobenzalacetophenone 34,[62] while the 1-aroyl-2-vinylaziridine 35 was pyrolyzed into the oxazepine 36.[63]



31 32

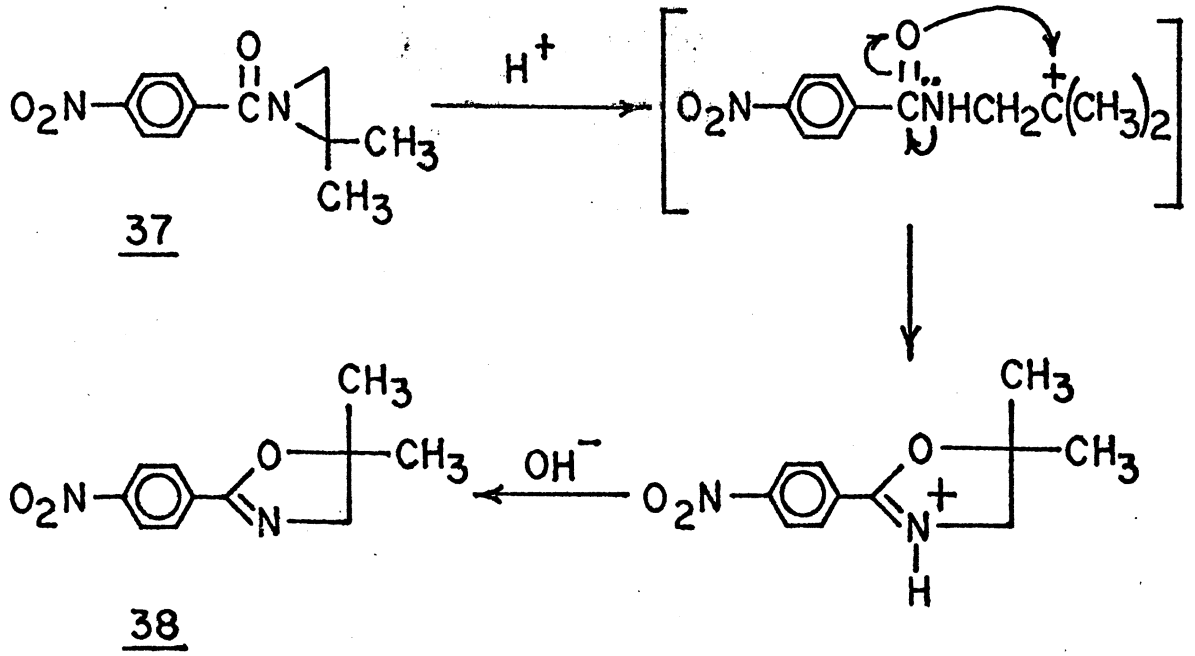


33 34



35 36

1-Aroylaziridines are also reactive towards acids and have been isomerized in high yields to 2-oxazolines with concentrated sulfuric acid,[70] N-bromoethylamine hydrobromide,[76] and with aluminum chloride.[76] Heine,[70] for example, isomerized the 1-aroylaziridine 37 to the 2-oxazoline 38 in 97% yield with concentrated sulfuric acid. Such acid catalyzed reactions are considered to occur by a first step protonation of the amido nitrogen, followed by ring opening to the more stable carbonium ion, and subsequent O-alkylation to form a 2-oxazolinum ion which is then neutralized to form the 2-oxazoline.[70]

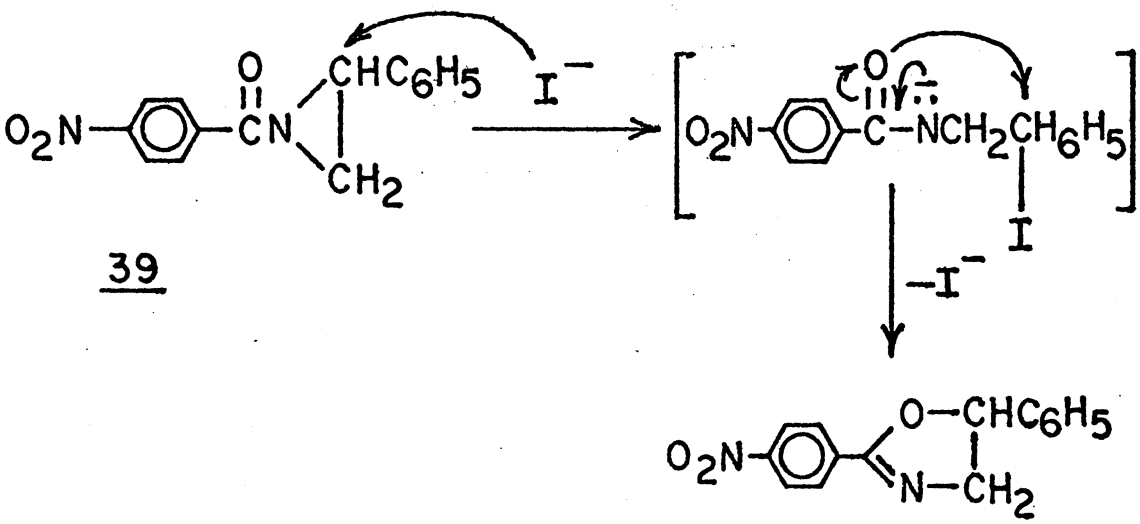


37

38

But since 1959, 2-oxazolines have been prepared from 1-aroylaziridines primarily by the use of nucleophilic catalysts. Thiocyanate ions,[70] as well as tetra-n-butylammonium iodide,[77] and tributylamine[68] have been used in a few cases, but most such reactions have been reported with iodide ion as the nucleophilic catalyst. Mechanistically, Heine[62] studied the isomerization of a number of substituted 1-aroylaziridines, including the isomerization of 39 to the 2-oxazoline 40, and concluded that such reactions occur by a first step nucleophilic attack by the iodide ion on the more positive aziridinyl carbon atom (except in cases where steric influence overrides electronic influence) to form a N-(2-iodoethyl)benzamido ion with subsequent O-alkylation to the 2-oxazoline and displacement and regeneration of the iodide ion. In agreement with the observed experimental results, this mechanism predicts correctly that such isomerizations should occur with retention of configuration, since an inversion of configuration takes place when the aziridine ring

is opened by the nucleophile and another inversion takes place when the intermediate N-(2-iodoethyl)benzamido ion cyclizes.[62]

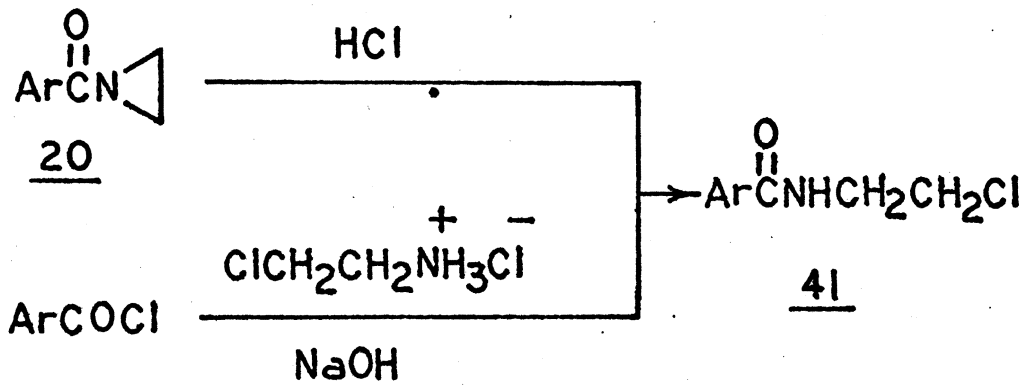


39

40

C. N-(2-Chloroethyl)amides and N,N-Bis(2-Chloroethyl)amides.

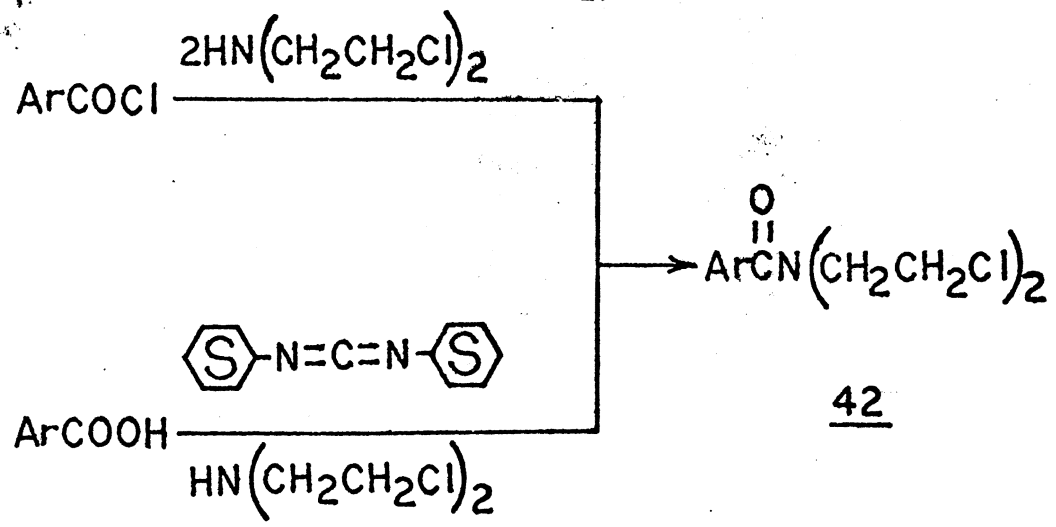
Basically, N-(2-chloroethyl)amides (41) and N,N-bis(2-chloroethyl)-amides (42) have each been prepared by two methods. N-(2-Chloroethyl)-amides (41) have been prepared by the reaction of hydrochloric acid with 1-aroylaziridines (20)[66] and by the reaction of 2-chloroethylamine hydrochloride with acid chlorides.[78] N,N-Bis(2-chloroethyl)amides (42) have



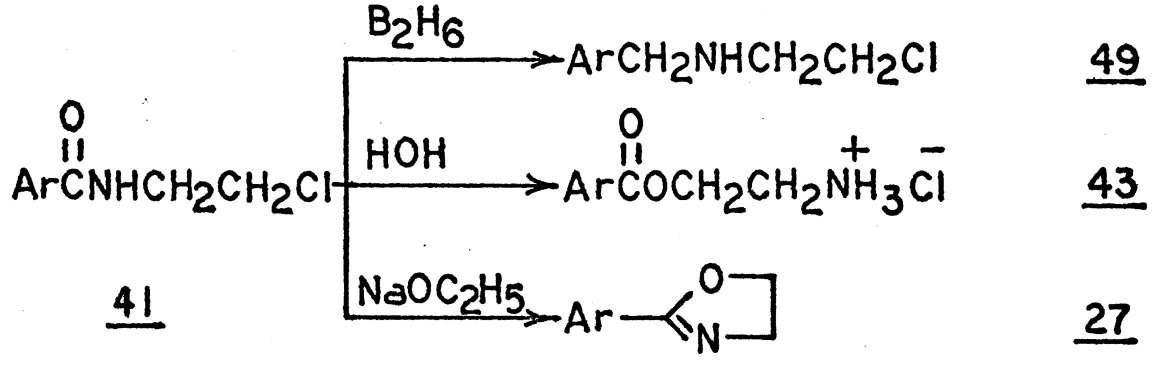
20

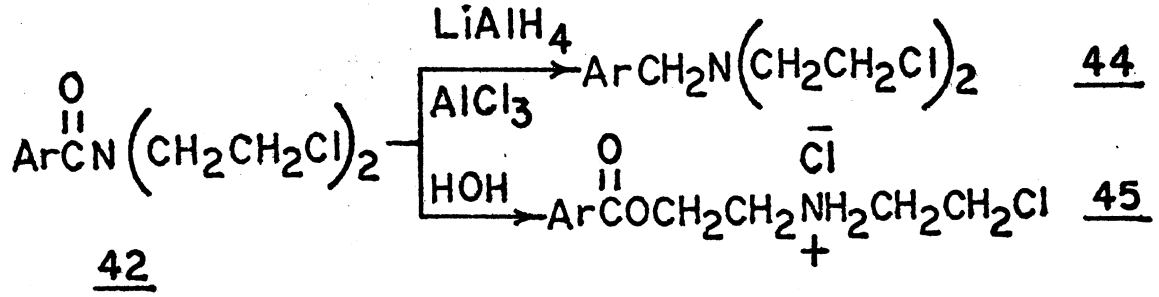
41

been prepared by the Sheehan method from carboxylic acids[79] and by the reaction of N,N-bis(2-chloroethyl)amine with acid chlorides.[80,81,82]



Three types of reactions which amides 41 undergo and two types of reactions which amides 42 undergo have been reported.

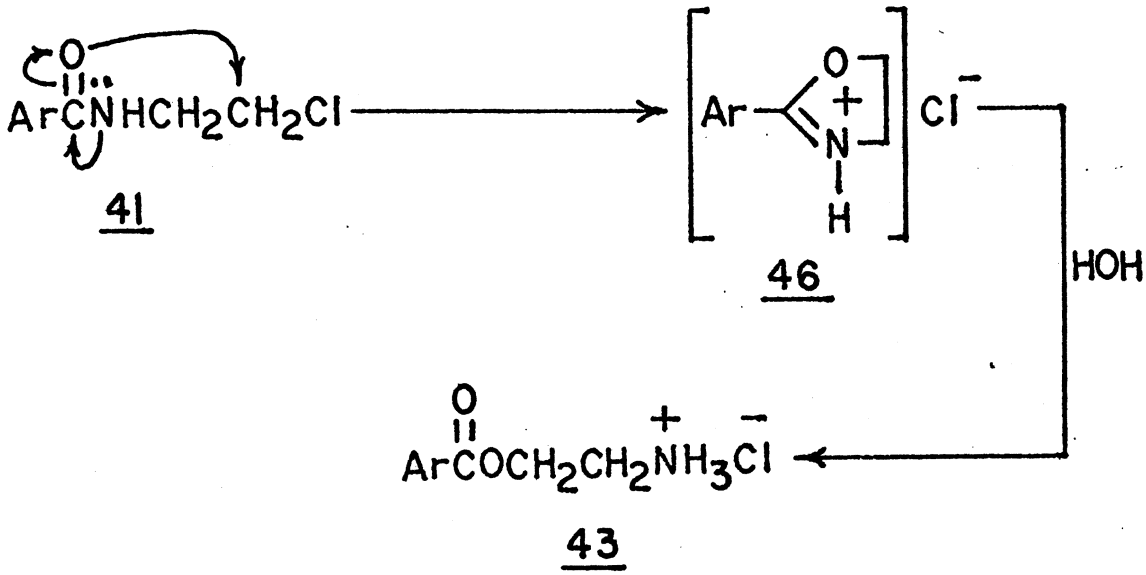




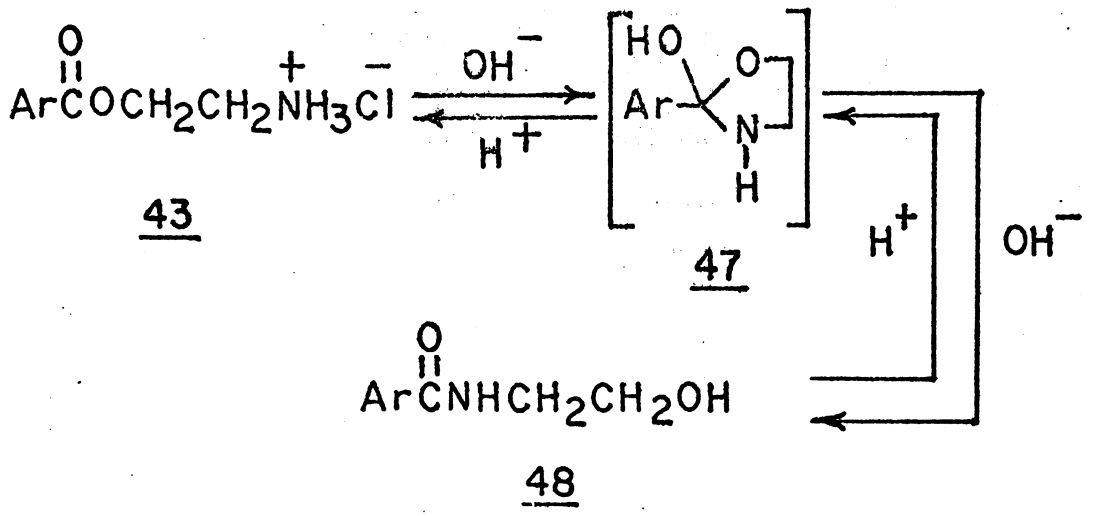
Following reports of the successful reduction of various amides to amines by diborane, Pettit,[66] in 1967, reported the successful reduction of some N-(2-chloroethyl)amides to N-(2-chloroethyl)amines (49). N,N-Bis(2-chloroethyl)amides (42) have not been reportedly reduced with

diborane but have been reduced to N,N-bis(2-chloroethyl)amines (44) with the mixed reagent, lithium aluminum hydride-aluminum chloride,[80,83] and, in one case, with lithium aluminum hydride.[84]

In general, N-(2-chloroethyl)amides (41) have been found to be somewhat unstable to water and have been converted in essentially quantitative yields to 2-aminoethyl ester hydrochloride salts (43) by prolonged contact with aqueous solutions at room temperature or by short term heating in aqueous solutions.[66,85] Mechanistically, such reactions have been depicted as occurring by an initial rate determining step involving the formation of an oxazolinum ion 46 followed by rapid hydrolysis of the imine bond to form salts 43.[86]

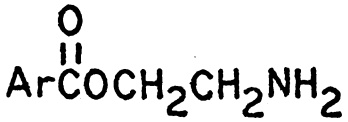


Whereas salts 43 have been found to be stable and can be isolated, attempts to isolate the free amines by addition of base have invariably resulted in rapid rearrangement of salts 43 into N-(2-hydroxyethyl)-amides (48).[87,88,89] This type of rearrangement (commonly referred to as an acyl shift or migration since the acyl group "shifts" bonding from

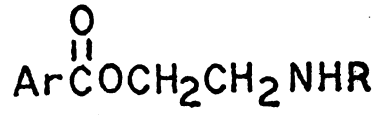


43 47 48

the oxygen to the nitrogen atom)[80,90] has been found to be characteristic for primary and secondary amines with the groupings:[88,91]

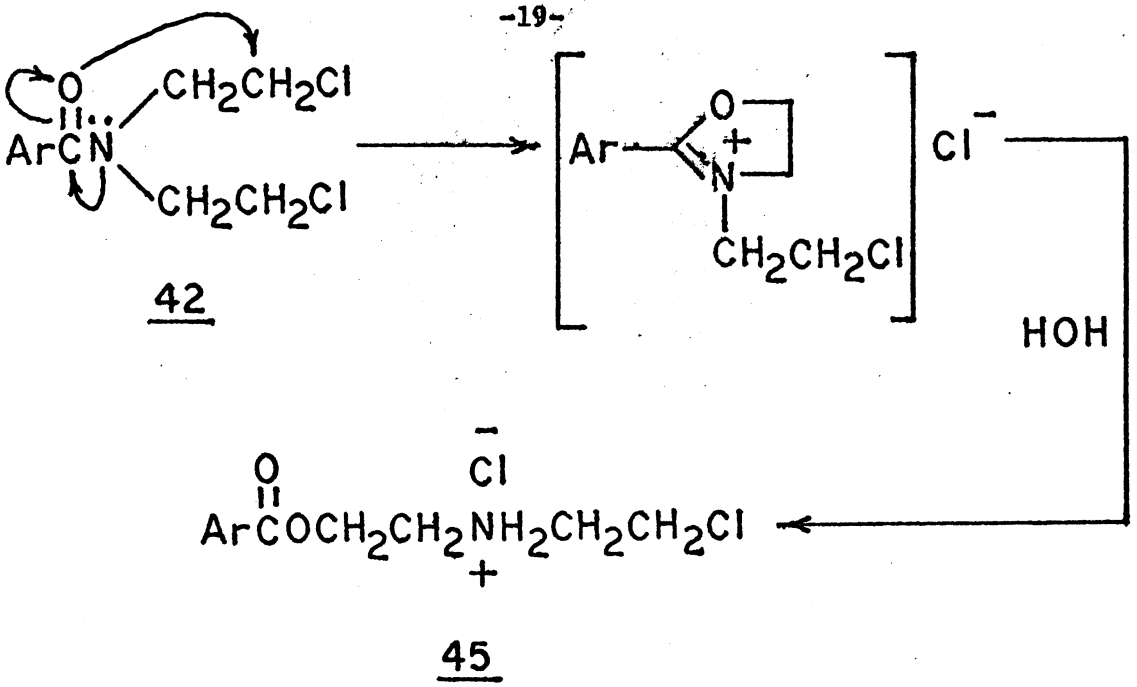


R = $-CH_3$, $-C_2H_5$



Additionally, Kanao,[92] in 1928, showed that alcohols 48 could be converted back to amine salts 43 with strong acids. Mechanistically, Phillips and Baltzly[89] suggested that both rearrangements (43 ⇌ 48) occur through an intermediate of the nature 47.

Like N-(2-chloroethyl)amides (41), N,N-bis(2-chloroethyl)amides (42) are also unstable to water, only more so, and reportedly are readily hydrolyzed in aqueous solutions to 2-(2'-chloroethylamine)ethyl ester hydrochloride salts (45).[79,80,93] Ross and Wilson[93] suggested a mechanism for this type of reaction which is similar to that suggested for the conversion of N-(2-chloroethyl)amides (41) to amine salts 43.



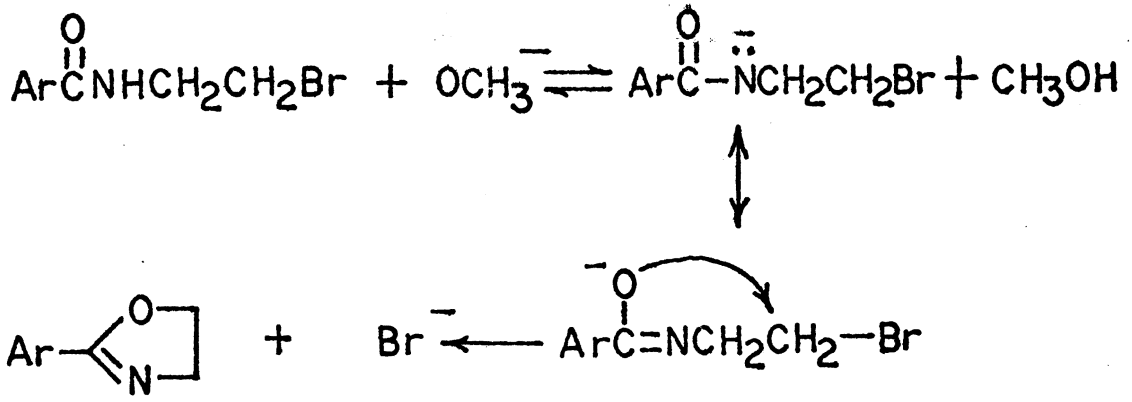
42

45

Gabriel, in 1890, was the first to report the preparation of 2-oxazolines (27) from N-(2-haloethyl)amides (28) (Cl,Br,I) via base induced intramolecular substitution reactions.[94] This type of reaction has since been used as a basic method for preparing 2-oxazolines.[90] With strong bases, such as sodium hydroxide or sodium methoxide, the reactions have been found to occur rapidly and in essentially quantitative yields. With weak bases, such as sodium acetate, the reactions have been found to occur more slowly but again in essentially quantitative yields.

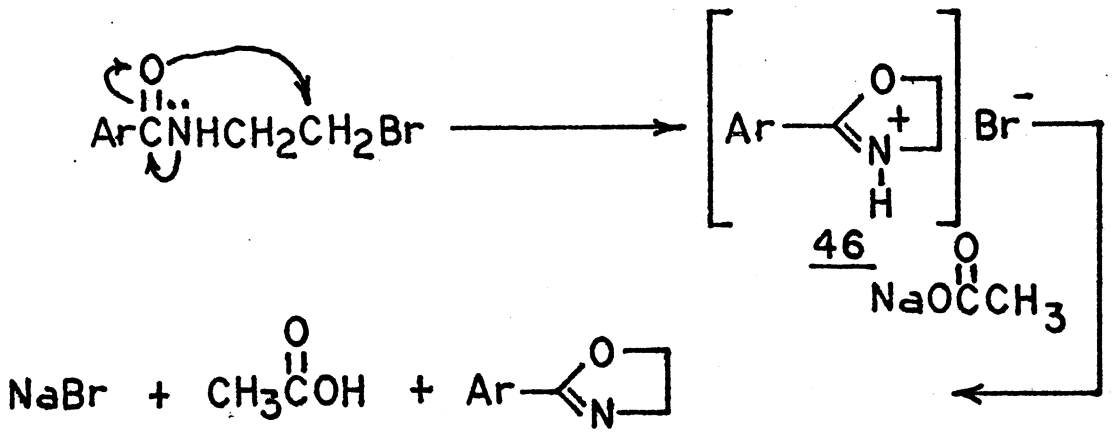
Heine,[86] in 1956, suggested mechanisms to account for the different reaction rates, after kinetic studies with some N-(2-bromoethyl)benzamides demonstrated that with the strong base, sodium methoxide, the reactions were second order, while with the weak base, sodium acetate, the reactions were first order. With the strong base, he concluded that the reactions occurred by an initial rate determining step, whereby a rapid reversible proton exchange took place between the base and the

benzamide to form a benzamido ion, followed by a subsequent displacement of bromide ion by the negatively charged oxygen of the benzamido ion and the formation of the 2-oxazoline (27). With the weak base, he concluded



27

that the initial rate determining step involved a nucleophilic displacement of bromide ion by the benzamide group to form an oxazolinium ion 46, followed by rapid neutralization with the sodium acetate to form the 2-oxazoline (27).



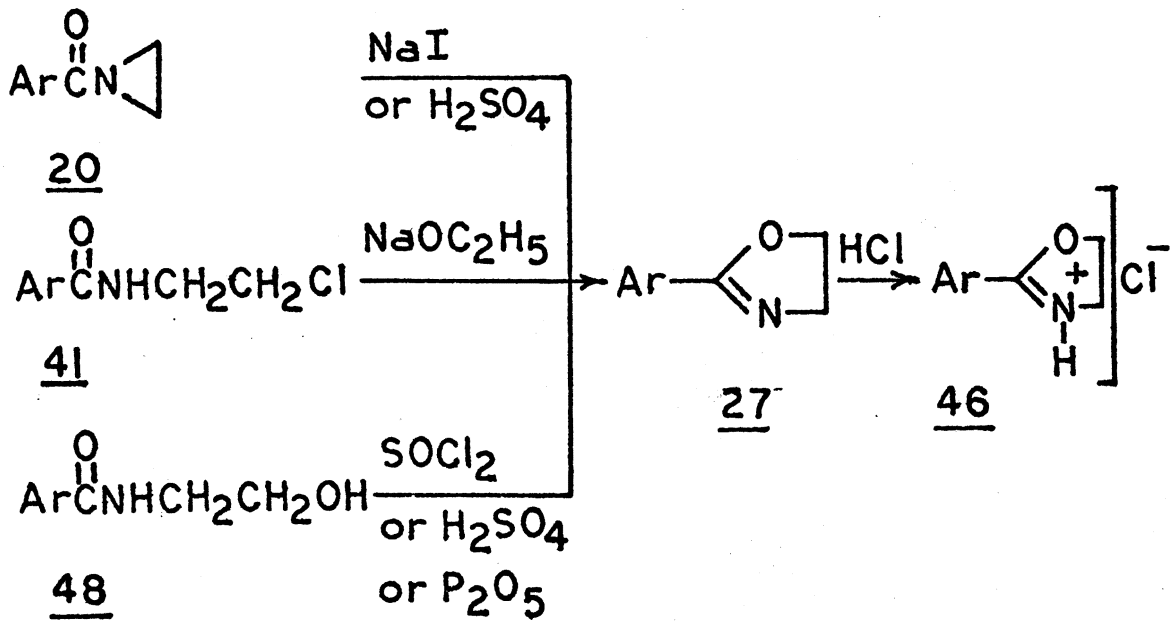
27

Winstein,[95] in a paper published prior to Heine's kinetic study, had already suggested the role of the benzamide group in the formation of 2-oxazolines.

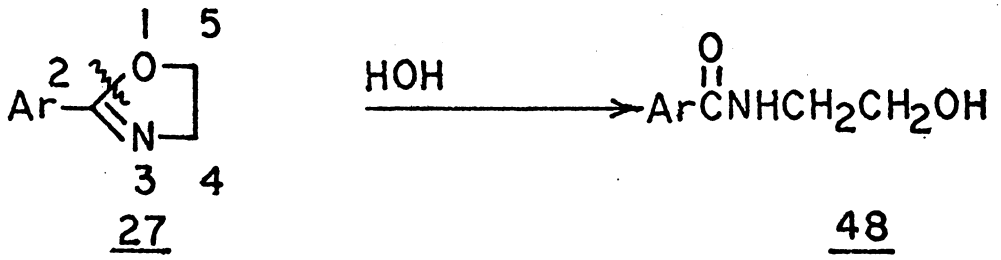
D. 2-Oxazolines, 2-Thiazolines, and 2-Imidazolines.

A portion of this thesis is devoted to the preparation, from derivatives of carboxylic acids, of some polycyclic compounds containing the functional groups, 2-oxazoline (27), 2-thiazoline (47), 2-imidazoline (48), and their hydrochloride salts. Although it is beyond the scope of this thesis to present a complete review of the chemistry of these functional groups, comments on the preparation, from acid derivatives, and the stability of these functional groups are in order.

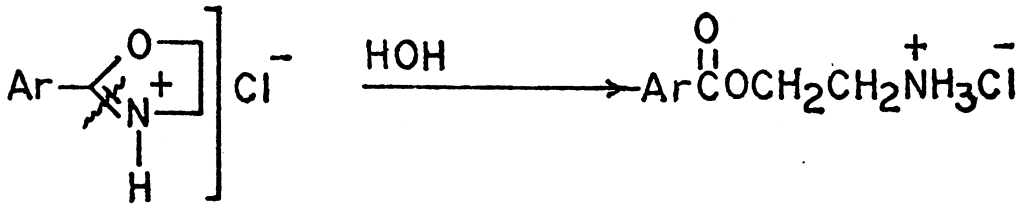
2-Oxazolines (27) have been prepared from 1-aroylaziridines (20) with nucleophilic catalysts and with acids,[60] from N-(2-chloroethyl)-amides (41) with bases,[90] and from N-(2-hydroxyethyl)amides (48) with dehydrating agents such as thionyl chloride, sulfuric acid, and phosphorus pentoxide.[90] With the exception of 2-phenyloxazoline, 2-oxazolines (27) are reported to generally form stable hydrochloride salts (46).[90]



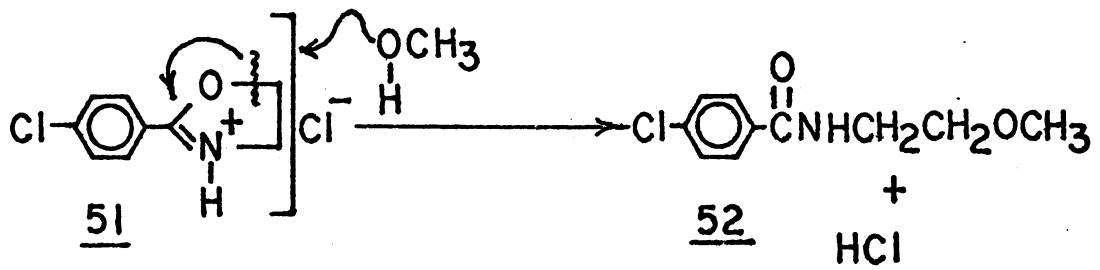
Both 2-oxazolines (27) and 2-oxazoline hydrochlorides (46) are chemically reactive, since an oxazoline ring is susceptible to ring cleavage at three different positions: the 2-3 carbon-nitrogen bond, the 5-1 carbon-oxygen bond, and the 2-1 carbon-oxygen bond.[65,77,96]



27 48



46 43

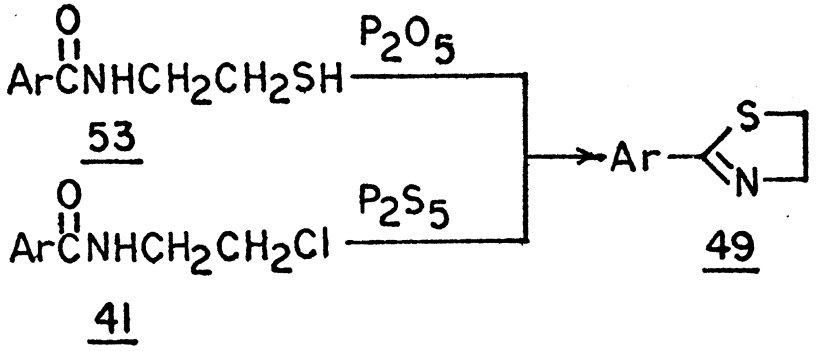


51 52

For example, although relatively stable towards water, 2-oxazolines (27) are converted to N-(2-hydroxyethyl)amides (48) by prolonged heating in aqueous solutions, while 2-oxazoline hydrochlorides (46) are very sensitive to water and are readily hydrolyzed to amine salts 43 when warmed in aqueous solutions.[65,90,96] Also, for example, Heine[86] reported that the hydrochloride salt 51 was converted to the N-(2-methoxyethyl)amide 52 in 18% yield after prolonged contact with anhydrous methanol at room temperature. The latter reaction was considered to occur by the

cleavage of the 5-1 carbon-oxygen bond. Other reagents which are reported to induce 5-1 bond cleavage in 2-oxazolines have been summarized by Tomalia.[77]

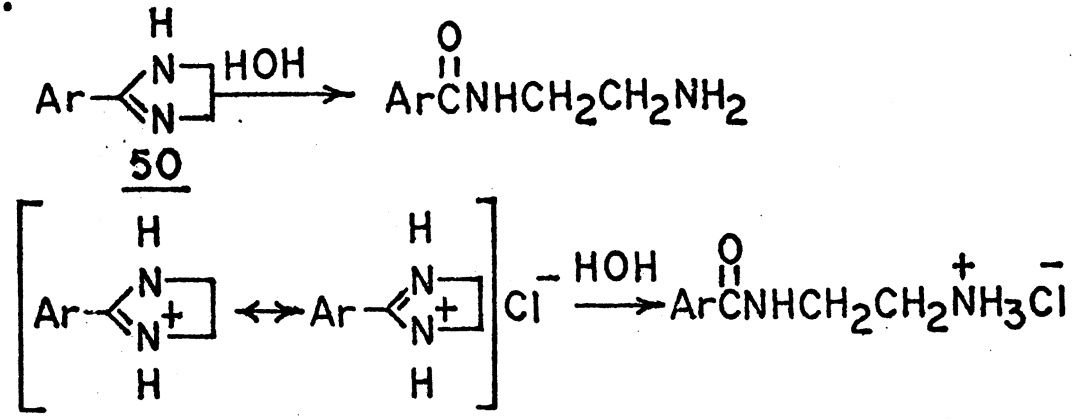
2-Thiazolines (49) have been prepared from N-(2-thiolethyl)amides (53) with phosphorus pentoxide and from N-(2-chloroethyl)amides (41) with phosphorus pentasulfide.[97]



53 41 49

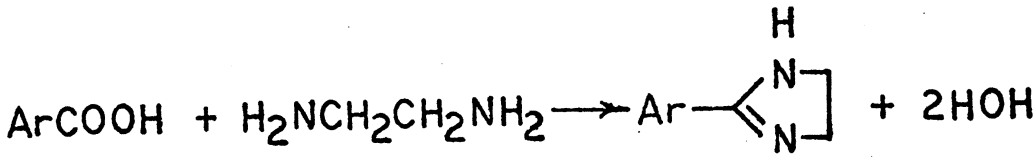
Unlike 2-oxazolines, hydrochloride salt derivatives of 2-thiazolines are reported to be generally unstable and difficult to isolate in pure form.[97] Similar to 2-oxazolines, 2-thiazolines are hydrolyzed by prolonged heating in aqueous solutions.[97]

A variety of methods for preparing 2-imidazolines (50) are available, although the most obvious methods involve reacting ethylenediamine either directly with carboxylic acids or with their nitrile derivatives.[98]

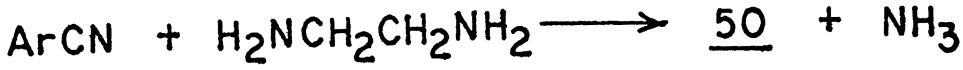


50 54

Like 2-oxazolines, 2-imidazolines (50) form stable hydrochloride salts 54.[98] Both 2-imidazolines (50) and 2-imidazoline hydrochlorides (54) are hydrolyzed to amides on prolonged heating in aqueous solutions.[98] However, salts 54 are more resistant to hydrolysis than are 2-imidazolines (50), since the salts are stabilized by resonance.



50



DISCUSSION OF RESULTS

A. Preparation of Carboxylic Acids.

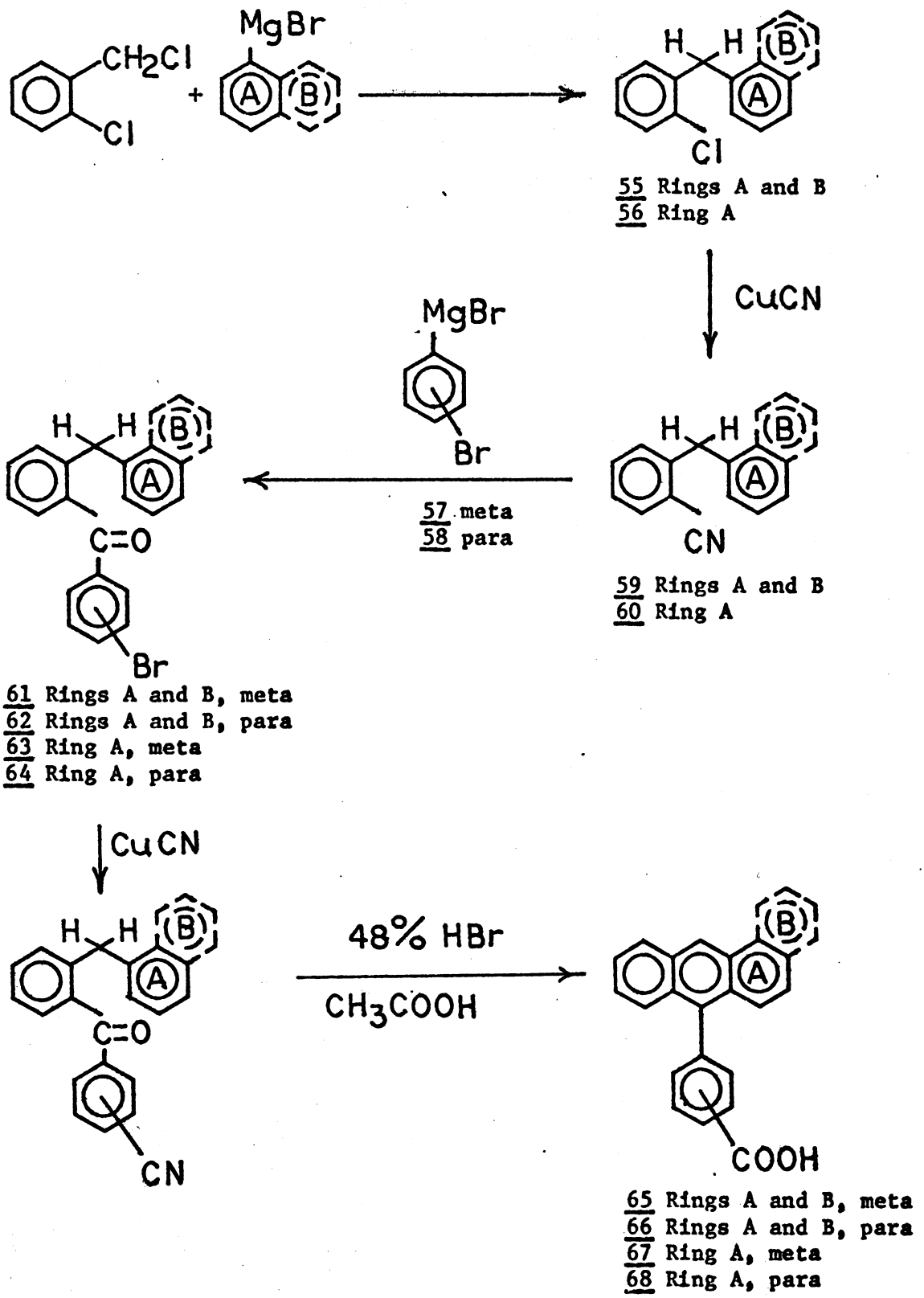
The four carboxylic acids, 7-(3- and 4-carboxyphenyl)benz[a]-anthracenes (65 and 66) and 9-(3- and 4-carboxyphenyl)anthracenes (65 and 68), were prepared by the five step procedure illustrated in Chart 1, and the results are summarized in Table 1. This method, with the exception of the first step, had been successfully used previously to prepare small quantities of 65,[100] 66,[17] and 68.[51]

Of the several procedures available for the preparation of 2-chlorodiphenylmethane (56)[22,23,47] and 2-(1-naphthylmethyl)chloro-benzene (55),[23] the Grignard coupling reaction developed in these laboratories was considered to be the most suitable.[101,102] By this method, 55 was prepared in 50% yield and 56 in 61% yield by the cross condensation of commercially available o,α-dichlorotoluene with 1-naphthylmagnesium bromide and phenylmagnesium bromide, respectively.

The Rosenmund-von Braun reaction[103,104,105] has been generally used in these laboratories for the preparation of cyano derivatives of aryl compounds. 2-Cyanodiphenylmethane (60) was prepared in 75% yield and 2-(1-naphthylmethyl)cyanobenzene (59) in 78% yield by refluxing the chloro compounds 56 and 55, respectively, with cuprous cyanide and catalytic amounts of cupric sulfate in N-methyl-2-pyrrolidone solvent.

The four bromo ketones, 2-(1-naphthylmethyl)-3'- and 4'-bromo-benzophenones (61 and 62) and 2-benzyl-3'- and 4'-bromobenzophenones (63 and 64), were prepared by the method Stevens[17] had used to prepare ketones. Ketone 61 was prepared in 54% yield and 62 in 50% yield by coupling 2-(1-naphthylmethyl)cyanobenzene (59) with m-bromophenyl-magnesium bromide (57) and p-bromophenylmagnesium bromide (58),

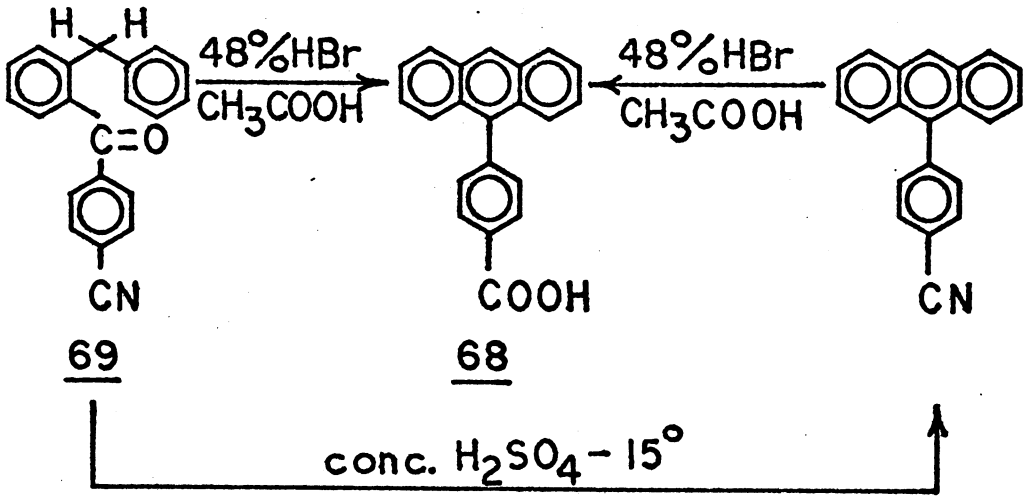
CHART 1


MgBr
CH2Cl
Cl
A
B
H
H
B
A
Cl
55 Rings A and B
56 Ring A
CuCN
MgBr
Br
57 meta
58 para
H
H
B
A
CN
59 Rings A and B
60 Ring A
H
H
B
A
C=O
Br
61 Rings A and B, meta
62 Rings A and B, para
63 Ring A, meta
64 Ring A, para
CuCN
H
H
B
A
C=O
CN
48% HBr
CH3COOH
B
A
COOH
65 Rings A and B, meta
66 Rings A and B, para
67 Ring A, meta
68 Ring A, para

respectively. The intermediate ketimines formed in these reactions were not isolated but were hydrolyzed directly to the ketones with 25% sulfuric acid. Similarly, ketone 63 was prepared in 62% yield and 64 in 71% yield by coupling 2-cyanodiphenylmethane (60) with the Grignard reagents 57 and 58, respectively. The ketones were crudely purified by vacuum distillations and converted to cyano ketones without further purification.

The cyano ketones were prepared from the bromo ketones by Rosenmund-von Braun type reactions. The resultant cyano ketones were viscous black oils, which were slow to crystallize from ethanol, cumbersome to distill, and were thus converted directly to the respective carboxylic acids without purification.

Two different procedures are available for converting the cyano ketones into polynuclear carboxylic acids. Bradsher and Vingiello[51]



69 68

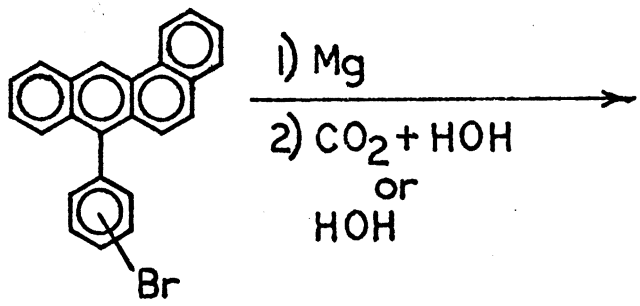
demonstrated that cyano ketone 69 could be converted to carboxylic acid 68 in higher yield by a one step aromatic cyclodehydration-hydrolysis reaction than by a two step process involving first the preparation and isolation of the aromatic nitrile, followed by hydrolysis of the nitrile to the carboxylic acid.

The four carboxylic acids 65, 66, 67, and 68 were prepared in yields of 60%, 50%, 64%, and 65%, respectively, from precursor cyano ketones by one step aromatic cyclodehydration-hydrolysis reactions with 48% hydrobromic acid in glacial acetic acid solvent. The carboxylic acids precipitated from the solutions during the reactions and were isolated by vacuum filtrations and purified by recrystallizations from toluene-tetrahydrofuran.

An alternate method for preparing these carboxylic acids would involve carbonating the Grignard reagents formed from bromo compounds analogous to 7-(4-bromophenyl)benz[a]anthracene (70). This method would eliminate the need for preparing the cyano ketones, the preparations of which involve laborious extraction procedures. However, carbonation and hydrolysis reactions with the Grignard reagents formed from 70, as well as 7-(3-bromophenyl)benz[a]anthracene (71), clearly demonstrate that this procedure is not a satisfactory method for preparing the carboxylic acids.

The bromo compounds 70 and 71 were prepared from the bromo ketones 62 and 61, respectively, by methods previously reported[17,19] and were purified by chromatography through an acid alumina substrate with 20% chloroform-hexane as eluant. The resultant white solids were dried and reacted with equimolar amounts of magnesium in refluxing anhydrous tetrahydrofuran. The reactions were initiated only after small amounts of methyl iodide were added, and after several hours of reflux, 70 and 71 appeared to be reacting readily with the magnesium giving reddish black and bluish black solutions, respectively. After several more hours of reflux individual Grignard reagent solutions of 70 and 71 were hydrolyzed to 7-phenylbenz[a]anthracene (1) in 42% and 37% yields,

respectively, but were carbonated to the carboxylic acids 66 and 65 in yields of only 25% and 22%, respectively, by pouring the Grignard reagent solutions over a slurry of tetrahydrofuran and powdered carbon dioxide. Similar results were obtained when carbon dioxide gas was bubbled through the Grignard reagent solutions.



70, para
71, meta

1 R=H
66 R=COOH, para
65 R=COOH, meta

Several previous attempts in these laboratories to prepare the Grignard reagent of 7-(4-bromophenyl)benz[a]anthracene (70) had been unsuccessful.[19,100,106,107,108] The desire to prepare this reagent had stemmed from the fact that 1 has shown anti-tumor activity,[6] and that the Grignard reagent could be used to prepare a variety of 7-(4-substituted phenyl)benz[a]anthracene compounds which could be studied for potential anti-tumor activity. The above hydrolysis data indicates that the Grignard reagent of 70 can be formed in sufficient amounts to be of synthetic value when alternate methods for preparing the 7-(4-substituted phenyl)benz[a]anthracenes are not available. However, while this study was in progress, Menon[109] clearly demonstrated that these compounds could be prepared in higher yields by using the lithium reagent of 70. He showed that the lithium reagent of 70 could be formed more rapidly and in greater yield than the Grignard reagent.

Table 1

Physical Data for Bromo Ketones and Carboxylic Acids

Comp.	Yield %	M.p. °C	B.p. °C (mm.)	Formula	% Calcd. C	% Calcd. H	% Found C	% Found H
61	54		225-238 (0.3)[a]	$C_{24}H_{17}BrO$				
62	50		230-245 (0.4)[b]	$C_{24}H_{17}BrO$				
63	62		190-195 (0.3)[c]	$C_{20}H_{15}BrO$				
64	71		195-197 (0.5)[d]	$C_{20}H_{15}BrO$				
65	60	274-276[e]		$C_{25}H_{16}O_2$	86.18	4.64	86.01	4.59
66	50	280-283[f]		$C_{25}H_{16}O_2$				
67	64	300-302		$C_{21}H_{14}O_2$	84.53	4.74	84.31	4.61
68	65	259-262[g]		$C_{21}H_{14}O_2$				

[a]Reported M.p. 105-106°.[19] [b]Reported M.p. 106-107°, B.p. 275-278° (2 mm.).[17] [c]Ketone not analytically purified. [d]Reported M.p. 83-84.5°, B.p. 210-220° (1 mm.).[51] [e]Reported M.p.. 253-254°.[100] [f]Reported M.p. 298-300°.[17] [g]Reported M.p. 262-264°.[51]

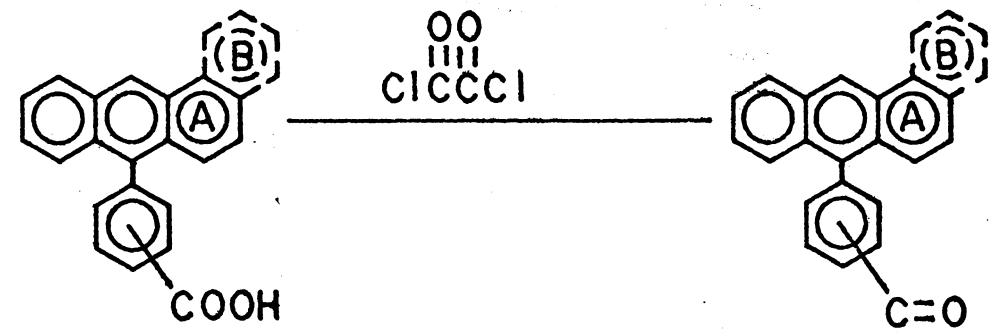
B. Preparation of 1-Aroylaziridines.

The two different methods used to prepare the four 1-aroylaziridines, 3- and 4-(7-benz[a]anthracenyl)benzaziridamides (76 and 77) and 3- and 4-(9-anthracenyl)benzaziridamides (78 and 79), are illustrated in Chart 2, and the results are summarized in Table 2.

A literature survey shows that 1-aroylaziridines have generally been prepared by coupling acid chlorides with aziridine in the presence of a base, usually either sodium hydroxide or triethylamine.[53] By this method, with triethylamine as base, the two para compounds 77 and 79 were prepared as solids in 75% and 73% yields, respectively, while the two meta compounds 76 and 78 were obtained as impure oils in approximately 78% and 76% yields, respectively. The acid chloride reagents necessary for these reactions were prepared in essentially quantitative yields by reacting the four carboxylic acids 65, 66, 67 and 68 with oxalyl chloride in benzene, and all four of the acid chlorides were isolated as greenish yellow solids.* Without purification the respective acid chlorides were then reacted with excess aziridine and triethylamine in benzene at room temperature. After the reactions were complete the precipitated triethylamine hydrochloride was removed by filtration, and the four 1-aroylaziridines were purified by chromatography through silica gel

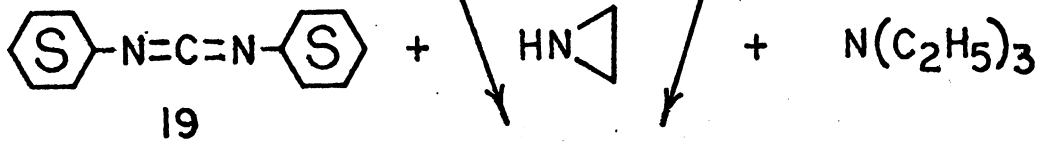
* Oxalyl chloride was superior to thionyl chloride for preparing the acid chlorides in relatively pure and high yields. With thionyl chloride the acid chlorides were obtained as oils, which contained impurities that were difficult to remove. The 1-aroylaziridines prepared from these acid chlorides also were found to contain these impurities, particularily the two anthracene compounds. For example, the meta compound, 3-(9-anthracenyl)benzaziridamide (78'), was obtained as a solid which contained impurities that were not removed even after three chromatography procedures through silica gel, four treatments with charcoal, and seven recrystallizations from ethyl acetate (see 78', Table 2). No such purification problems were encountered when the four acid chlorides were prepared with oxalyl chloride.

CHART 2

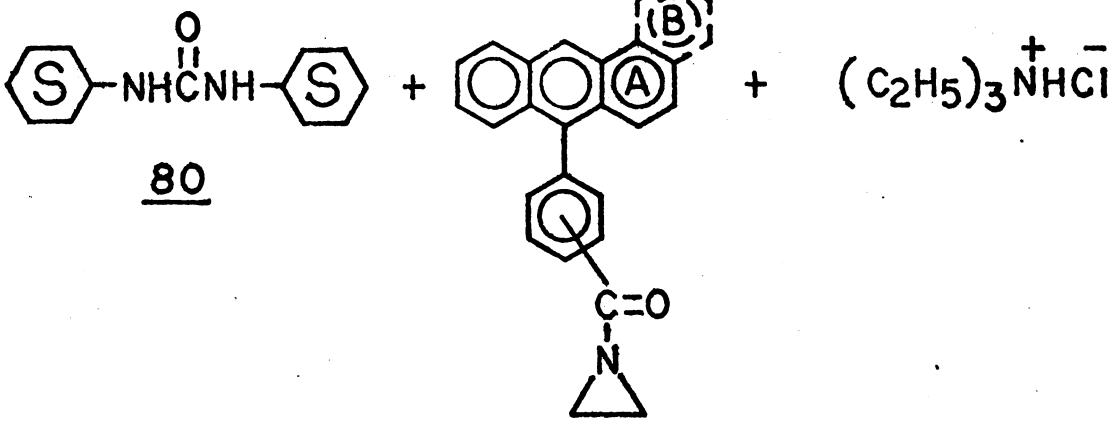


65 Rings A and B, meta
66 Rings A and B, para
67 Ring A, meta
68 Ring A, para

72 Rings A and B, meta
73 Rings A and B, para
74 Ring A, meta
75 Ring A, para



19



80

76 Rings A and B, meta
77 Rings A and B, para
78 Ring A, meta
79 Ring A, para

substrate with benzene as eluant. The two para compounds 77 and 79 were further purified by recrystallization from ethyl acetate, while the two meta compounds 76 and 78 were again obtained as oils which could not be precipitated from ethyl acetate, as well as a variety of other solvents.

Another possible method for preparing 1-aroylaziridines involves reacting carboxylic acids directly with aziridine, in the presence of dicyclohexylcarbodiimide (19).[54] This method was also used to prepare the four compounds 76, 77, 78 and 79, and somewhat surprisingly, the four compounds were prepared in essentially the same high yields as were obtained by the former method (see Table 2). The reactions were carried out by simply stirring at room temperature for several hours a mixture of the respective carboxylic acids with equimolar amounts of aziridine and dicyclohexylcarbodiimide (19) in anhydrous tetrahydrofuran. Within minutes after the reactants were mixed the by-product, dicyclohexylurea (80), began to precipitate from solution. After the reactions were complete, the majority of the dicyclohexylurea was removed by vacuum filtration, and the 1-aroylaziridines were purified by chromatography and recrystallization procedures similar to those used in the first method. The two meta compounds 76 and 78 were again obtained as oils which could not be crystallized.

According to the mechanism proposed by Sheehan[57] and others[58,59] for reactions of this type, formation of N-acylureas may occur. Such side products were not observed in these reactions, although they may well have formed to some extent and were removed by the chromatography procedure. In any event, based on the shorter reaction route, simplicity of reaction conditions, and high yields of products obtained, this latter method would appear to be the more efficient synthetic procedure

for preparing the four 1-aroylaziridines 76, 77, 78 and 79.

Characterization of these four 1-aroylaziridines was based on the synthetic routes used, elemental analysis in the case of 77 and 79, and by ir and nmr spectra. The presence of the aziridinyl amide functional group in each of the compounds was evident from the spectra. The nmr spectra showed the four equivalent aliphatic protons as a singlet centered at 1.22 ppm (δ).* The ir spectra showed the aliphatic carbon-hydrogen stretching frequencies in the region 3000-2800 cm^{-1} and the carbonyl stretching frequency at 1690 cm^{-1}. The carbonyl stretching frequency represents a shift from the 1680-1630 cm^{-1} range generally observed for tertiary amides.[110] The shift is found to be characteristic for aziridinyl amides and, according to Brown,[111] suggests that there is little conjugation within such amide groups as contrasted with the usual tertiary amide.

*All nmr chemical shifts reported in this thesis are expressed in ppm (δ) values.

Table 2

Physical Data for 1-Aroylaziridines

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	% Calcd. H	% Calcd. N	% Found C	% Found H	% Found N	% Found S
76	78[a,c], 72[b,c]		$C_{27}H_{19}NO$							
77	75[a], 70[b,e]	204-205.5	$C_{27}H_{19}NO$	86.83	5.14	3.75	86.98	5.20	3.83	
78	76[a,c], 71[b,c]		$C_{23}H_{17}NO$							
78'	79[d]	146-147	$C_{23}H_{17}NO$	85.41	5.31	4.33	77.43	3.14	3.67	1.04
79	73[a], 68[b]	175-176	$C_{23}H_{17}NO$	85.31	5.31	4.33	85.34	5.21	4.15	

[a]From acid chlorides. [b]From carboxylic acids. [c]Isolated as oils which were not crystallized or analytically purified. [d]From acid chloride prepared with thionyl chloride. [e]Reported M.p. 187-189°.[44]

C. Preparations and Reactions of N-(2-Substituted ethyl)amides.

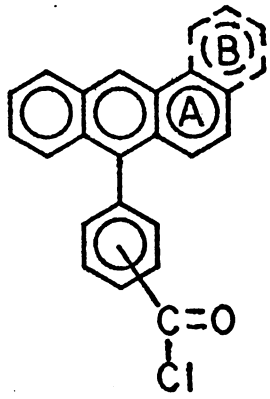
1. Preparation of N-(2-Chloroethyl)amides

The two methods used to prepare the four N-(2-chloroethyl)amides, 3- and 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamides (81 and 82) and 3- and 4-(9-anthracenyl)-N-(2-chloroethyl)benzamides (83 and 84), are illustrated in Chart 3, and the results are summarized in Table 3.

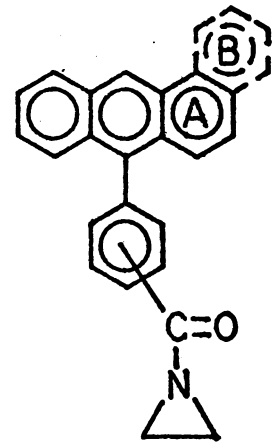
Pettit[66] recently showed that aziridine rings in 1-aroylaziridines are readily cleaved by anhydrous hydrogen halides (Cl,Br,I) to form N-(2-haloethyl)amides. The four amides 81, 82, 83 and 84 were prepared by this method in yields of 71%, 90%, 78% and 89%, respectively, by bubbling anhydrous hydrogen chloride through chloroform solutions at room temperature containing the 1-aroylaziridines 76, 77, 78 and 79, respectively. The two para amides 82 and 84 were purified by recrystallization from benzene, while the more soluble meta amides 81 and 83 were recrystallized from ethyl acetate. The lower yields of the two meta amides 81 and 83 probably resulted because of impurities in the two meta 1-aroylaziridine reagents 76 and 78 which were oils and difficult to purify.

The two meta amides, as well as the para amides, were prepared more efficiently by reacting the acid chlorides 72, 73, 74 and 75 with equimolar amounts of 2-chloroethylamine hydrochloride and excess sodium hydroxide in water-benzene at 0°. All four amides readily precipitated from the solutions as the reactions progressed and were isolated by filtration and purified by recrystallization procedures similar to the first method. By this method the two meta amides 81 and 83 were prepared in 86% and 84% yields and the two para amides 82 and 84 in 83% and 85% yields, respectively.

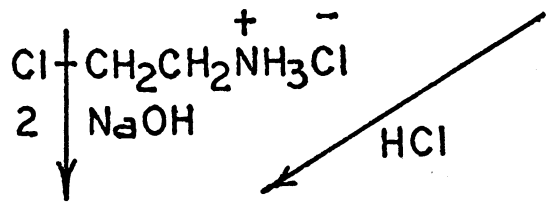
CHART 3

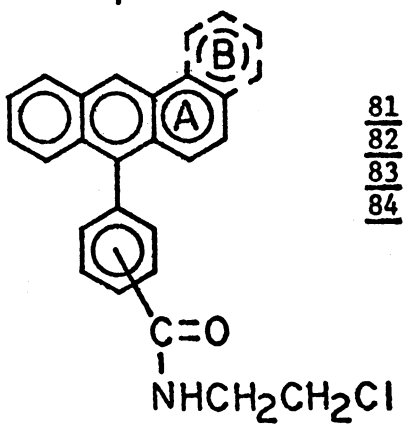


72 Rings A and B, meta
73 Rings A and B, para
74 Ring A, meta
75 Ring A, para

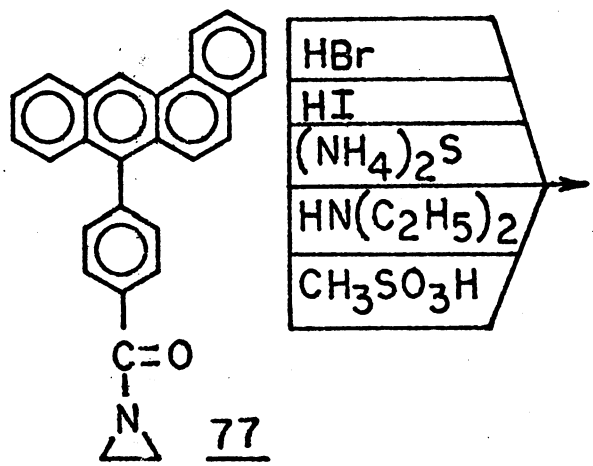


76 Rings A and B, meta
77 Rings A and B, para
78 Ring A, meta
79 Ring A, para





81 Rings A and B, meta
82 Rings A and B, para
83 Ring A, meta
84 Ring A, para



77

R
85 — Br
86 — I
87 — SH
88 — $N(C_2H_5)_2$
89 — OSO_2CH_3

2. Preparation of 4-(7-Benz[a]anthracenyl)-N-(2-substituted ethyl) benzamides

Several 4-(7-benz[a]anthracenyl)-N-(2-substituted ethyl)benzamide compounds were prepared from 4-(7-benz[a]anthracenyl)benzaziridamide (77) by cleavage of the aziridine ring with various acids. These reactions are illustrated in Chart 3, and the results are summarized in Table 3.

4-(7-Benz[a]anthracenyl)-N-(2-bromoethyl)benzamide (85) was prepared in 87% yield by bubbling anhydrous hydrogen bromide through a chloroform solution containing 77 at room temperature and was purified by recrystallization from benzene.

4-(7-Benz[a]anthracenyl)-N-(2-iodoethyl)benzamide (86) was prepared in 73% yield by stirring a mixture of 77 in benzene with aqueous 45% hydriodic acid and was purified by recrystallization from ethyl acetate.

Using the procedure of Goldberg and Kelly,[65] 4-(7-benz[a]anthracenyl)-N-(2-thiolethyl)benzamide (87) was prepared in 43% yield by the reaction of 77 in tetrahydrofuran with 45% aqueous ammonium sulfide at room temperature and was purified by recrystallization from dimethylsulfoxide-ethanol. The amide 87 was prepared in only 23% yield when hydrogen sulfide gas was bubbled through a chloroform solution containing 77.

Thyrum and Day[68] recently showed that a variety of primary and secondary amines can cleave the aziridine ring in 1-aroylaziridines. 4-(7-Benz[a]anthracenyl)-N-(2-diethylaminoethyl)benzamide (88) was prepared in 76% yield by refluxing 77 with excess diethylamine in benzene and was purified by recrystallization from ethyl acetate.

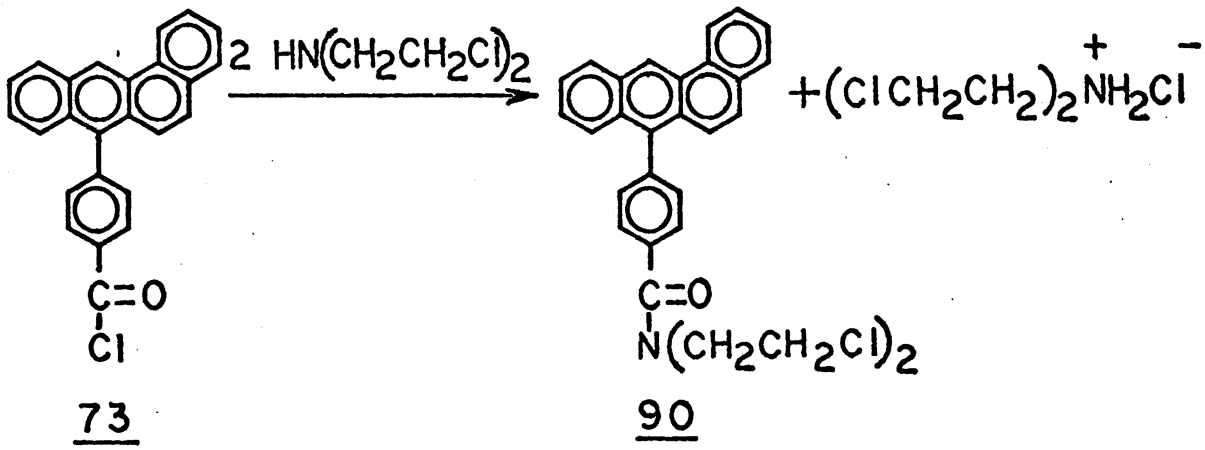
4-(7-Benz[a]anthracenyl)-N-(2-methylsulfonylethyl)benzamide (89) was prepared in 74% yield by stirring in benzene at room temperature equimolar

amounts of 77 and methanesulfonic acid and was purified by recrystallization from toluene-95% ethanol.

3. Reactions of 4-(7-Benz[a]anthracenyl)-N-(2-chloroethyl)-benzamide (82) and 4-(7-Benz[a]anthracenyl)-N,N-bis(2-chloroethyl)-benzamide (90)

The reactions of 82 and 90 with diborane and with water are illustrated in Chart 4, and the results are summarized in Table 4.

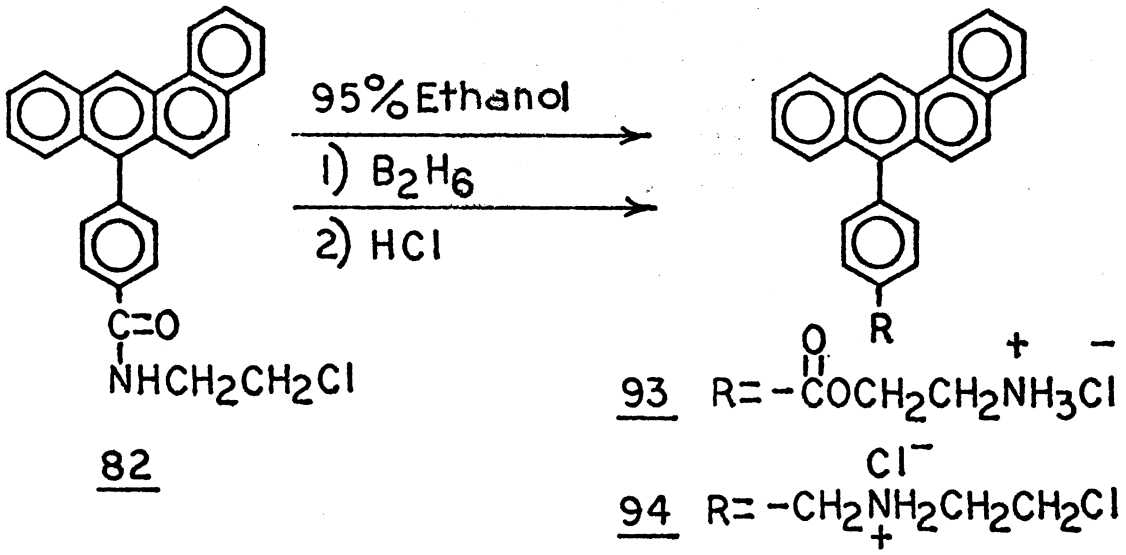
The N,N-bis(2-chloroethyl)amide 90 was prepared as a viscous oil in 78% yield when acid chloride 73 was reacted with excess N,N-bis(2-chloroethyl)amine in anhydrous benzene at room temperature. The precipitated N,N-bis(2-chloroethyl)amine hydrochloride was easily removed by filtration, and attempts to crystallize the isolated oily product 90 from a variety of anhydrous solvents were unsuccessful.

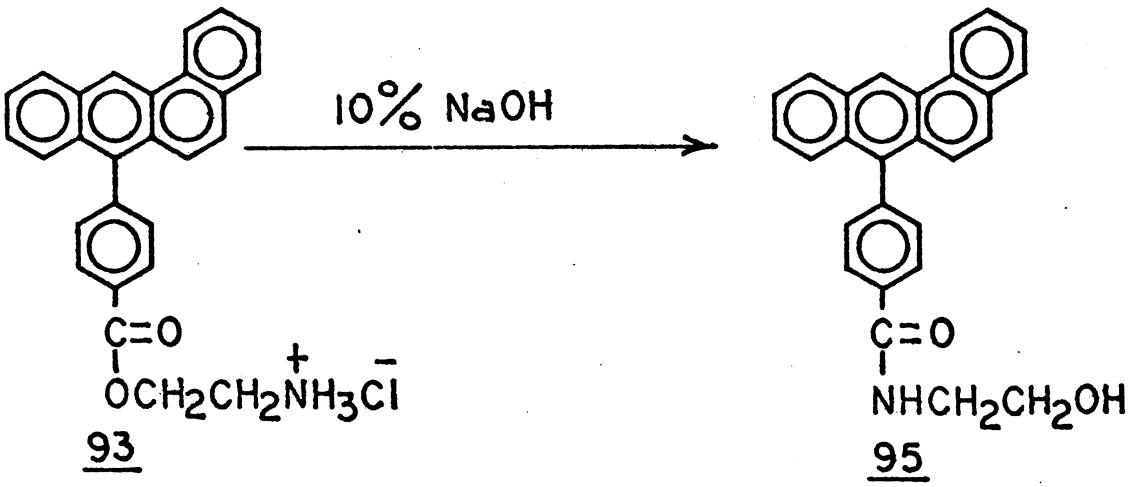


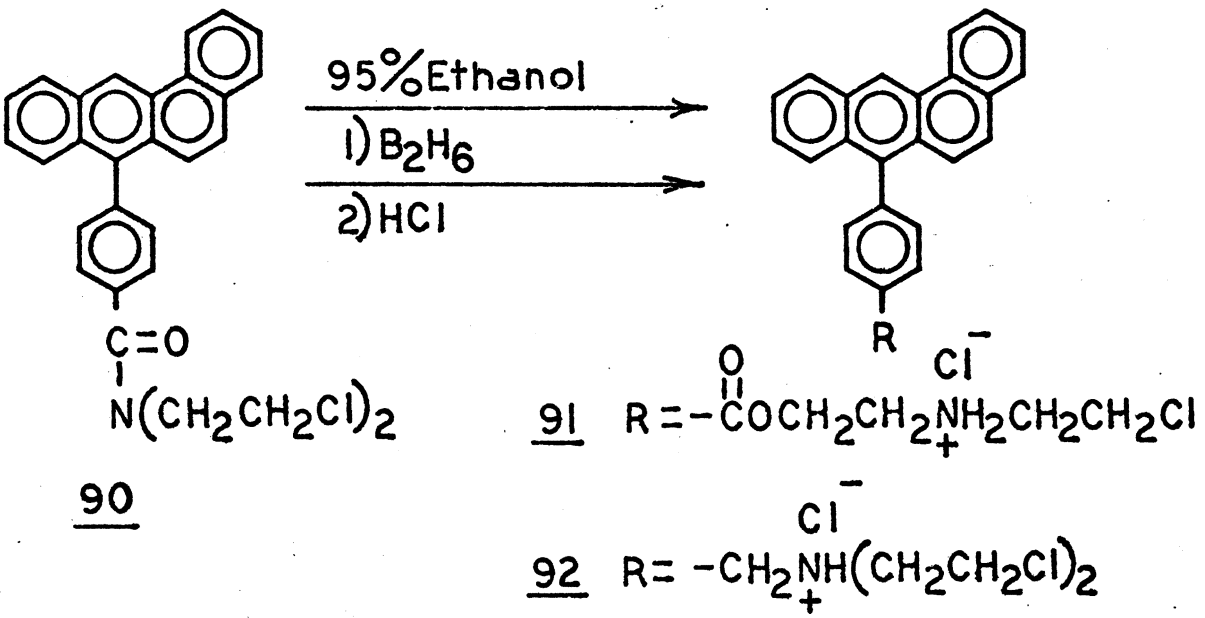
73 90

Both 82 and 90 underwent reactions with water which are characteristic of compounds containing an N-(2-chloroethyl)amide[66,85] or N,N-bis-(2-chloroethyl)amide[70,80,93] functional group (see p. 16). Refluxing 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide (90) in 95%

CHART 4


95% Ethanol
1) B_2H_6
2) HCl
C=O
$NHCH_2CH_2Cl$
82
R
O
$+$ $-$
93 $R=-COCH_2CH_2NH_3Cl$
Cl^-
94 $R=-CH_2\overset{+}{N}H_2CH_2CH_2Cl$


10% NaOH
C=O
$O\overset{+}{C}H_2CH_2NH_3Cl^-$
93
C=O
$NHCH_2CH_2OH$
95


95% Ethanol
1) B_2H_6
2) HCl
C=O
$N(CH_2CH_2Cl)_2$
90
R
Cl^-
O
91 $R=-COCH_2CH_2\overset{+}{N}H_2CH_2CH_2Cl$
Cl^-
92 $R=-CH_2\overset{+}{N}H(CH_2CH_2Cl)_2$

ethanol-tetrahydrofuran (2-1) for four hours resulted in a 84% transformation to 2-(2'-chloroethylamino)ethyl-4-(7-benz[a]anthracenyl)-benzoate hydrochloride (91). Refluxing 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (82) in 95% ethanol for four hours resulted in a 91% transformation to 2-aminoethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride (93).

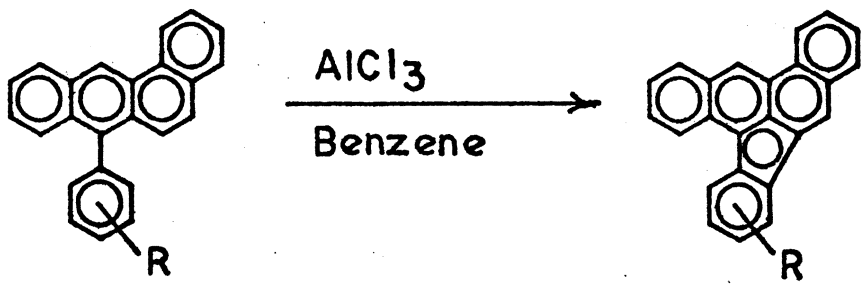
Interestingly, neutralization of salt 93 with 10% sodium hydroxide resulted in the formation of 4-(7-benz[a]anthracenyl)-N-(2-hydroxyethyl)-benzamide (95) in 63% yield. This type of rearrangement has been reported to be characteristic of compounds containing the 2-aminoethyl ester hydrochloride functional group (see p. 18).[87,88,89]

Pettit[66] recently showed that diborane is an excellent reagent for reducing N-(2-chloroethyl)amides to nitrogen mustards. Both amides 82 and 90 were reduced to nitrogen mustards by reacting the respective amides with commercially available 1M diborane in tetrahydrofuran at room temperature. Both nitrogen mustards were isolated as viscous oils which resisted crystallization from a variety of polar and non-polar solvents, and the oils were thus converted to hydrochloride salts. 4-(7-Benz[a]anthracenyl)-N-(2-chloroethyl)benzylamine hydrochloride (94) was isolated in 71% yield and 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzylamine hydrochloride (92) in 66% yield by adding ethyl ether solutions saturated with hydrogen chloride to tetrahydrofuran solutions containing the nitrogen mustards. The salts were purified by recrystallization from 95% ethanol-ethyl acetate.

Diborane proved to be a good reagent for reducing the two polynuclear amides to nitrogen mustards. Other reagents that have been reportedly used to reduce N-(2-chloroethyl)amides to nitrogen mustards

are lithium aluminum hydride[84] and the mixed reagent, lithium aluminum hydride-aluminum chloride.[80,83] Lithium aluminum hydride, alone, has not been used extensively for reductions of this type because of the possibility for reduction of the carbon-chlorine bonds.[83,112] The mixed reagent, lithium aluminum hydride-aluminum chloride, however, has been commonly used for reducing N-(2-chloroethyl)amides to nitrogen mustards. No attempts were made to reduce the two polynuclear amides 82 and 90 to nitrogen mustards with this latter mixed reagent.

Interestingly though, this mixed reagent would probably not have been suitable for preparing the pure polynuclear nitrogen mustards in high yields because of the potential reactivity of the 7-phenylbenz[a]-anthracenyl moieties towards aluminum chloride. In these laboratories, Menon[108] and Youssef[113] showed that 7-phenylbenz[a]anthracenes are converted readily to fluoranthenes when refluxed with excess aluminum chloride in benzene.



R = CH_3

4. Characterization of Amides and Derivatives

The preceding amides and derivatives are new compounds, with the exception of 92,[44] and their structures were assigned on the basis of the synthetic routes used, elemental analysis, and ir and nmr spectra.

(a) $-\overset{O}{\overset{\|}{C}}NHCH_2CH_2X$ (b) $-\overset{O}{\overset{\|}{C}}NHCH_2CH_2SH$

X = Cl, Br, I

(a) The ethylene protons of functional group (a) in amides 81, 82, 83, 84, 85 and 86 appeared in an A_2B_2 system with the difference in chemical shifts near zero. The four protons appeared as a slightly jagged singlet centered at 1.99 ppm. The carbonyl stretching frequency for each of the amides appeared at 1635 cm^{-1}, characteristic of secondary amides.[110]

(b) The ethylene protons of functional group (b) in amide 87 appeared in an A_2B_2 system as two broad multiplet bands centered at 1.75 ppm and 2.09 ppm, while the sulfhydryl proton appeared as a singlet at 1.37 ppm. The carbonyl stretching frequency for the secondary amide appeared at 1645 cm^{-1}. The sulfur-hydrogen stretching frequency, characteristically weak and in the region 2600-2500 cm^{-1},[110] was not detectable.

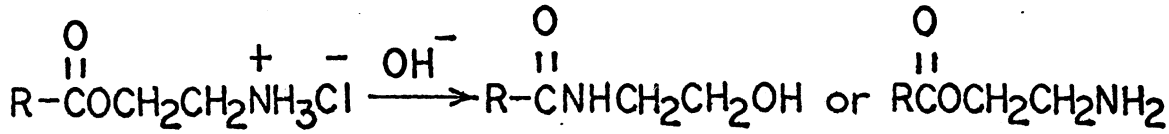
(c) $-\overset{O}{\overset{\|}{C}}NH-CH_2-CH_2-N(CH_2-CH_3)(CH_2-CH_3)$ (d) $-\overset{O}{\overset{\|}{C}}NHCH_2CH_2OSO_2CH_3$

A_2 M_2 M_2 X_3 M_2 X_3

(c) The protons of the functional group (c) in amide 88 appeared in an $A_2M_6X_6$ system. The methylene protons (A_2) appeared as a quartet at 1.96 ppm, the methylene protons (M_6) appeared as a quartet at 1.44 ppm, while the terminal methyl protons (X_6) appeared as a triplet at 0.59

ppm. The carbonyl stretching frequency for the secondary amide appeared at 1625 cm^{-1}.

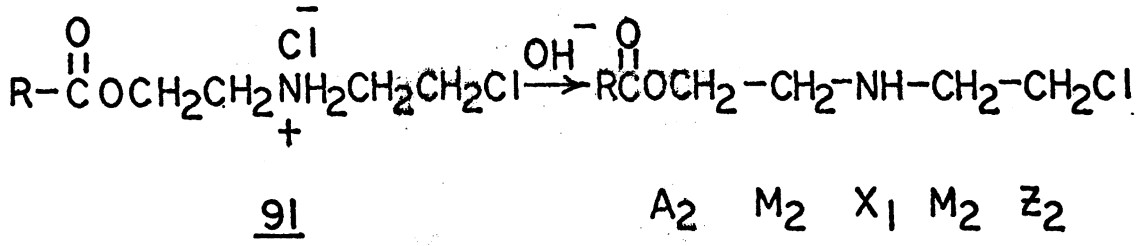
(d) The protons of the functional group (d) in amide 89 appeared in three bands. The ethylene protons appeared in two broad multiplet bands at 2.56 ppm and 1.90 ppm, while the terminal methyl protons appeared as a singlet at 1.40 ppm. The carbonyl stretching frequency occurred at 1720 cm^{-1}, while broad intense absorptions appearing in the region 1300-1100 cm^{-1} were attributed in part to O = S = O and S - O stretching modes.



93 95

R = 4-(7-benz[a]anthracenyl)phenyl-

Neutralization of amine salt 93 with aqueous sodium hydroxide could have formed either the primary amine or alcohol 95. The presence of the N-(2-hydroxyethyl)amide functional group was confirmed by ir and nmr spectra. The nmr spectrum showed a band at 1.42 ppm which integrated for one proton and was attributed to the hydroxy proton, while the ethylene protons appeared in a single multiplet band at 2.05 ppm. The carbonyl stretching frequency for the secondary amide occurred at 1625 cm^{-1}, while the O - H stretching frequency was obliterated due to moisture in the KBr pellet. Amine salt 93 was too insoluble for a suitable nmr, but the ir spectrum showed the ester carbonyl stretching frequency at 1720 cm^{-1} and strong broad absorption in the region 3070-2850 cm^{-1}, characteristic for salts of primary amines.[110]



91 $A_2\ M_2\ X_1\ M_2\ Z_2$

R = 4-(7-benz[a]anthracenyl)phenyl-

(f) Similar to 93, amine salt 91 was characterized by ester carbonyl absorption at 1734 cm^{-1}, and the strong broad absorption in the region 2900-2600 cm^{-1} was attributed to symmetrical and asymmetrical stretching in the $-\overset{+}{N}H_2-$ group. The protons of the neutralized salt appeared in four bands as an $A_2M_4X_1Z_2$ system. The terminal methylene protons (A_2, Z_2) appeared as triplets at 2.43 ppm and 1.95 ppm, the middle methylene protons (M_4) as a triplet at 1.61 ppm, while the secondary amino proton (X_1) appeared as a singlet at 1.07 ppm.

Table 3

Physical Data for N-(2-substituted)ethyl amides

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	H	N	X[c]	% Found C	H	N	X[c]
81	71[a], 86[b]	135-138	$C_{27}H_{20}ClNO$	79.10	4.93	3.42	8.65(Cl)	79.21	5.01	3.24	8.52(Cl)
82	90[a], 83[b]	203-208	$C_{27}H_{20}ClNO$	79.10	4.93	3.42	8.65(Cl)	78.82	4.82	3.48	8.89(Cl)
83	78[a], 84[b]	167-169	$C_{23}H_{18}ClNO$	76.76	5.05	3.89	9.85(Cl)	76.87	5.09	3.81	9.68(Cl)
84	89[a], 85[b]	203-208	$C_{23}H_{18}ClNO$	76.76	5.05	3.89	9.85(Cl)	77.04	5.23	3.66	9.98(Cl)
85	87	203-208	$C_{27}H_{20}BrNO$	71.36	4.45	3.08	17.59(Br)	71.50	4.38	3.27	17.88(Br)
86	73	196-198	$C_{27}H_{20}NIO$	64.69	4.03	2.79	25.31(I)	64.45	3.80	2.51	24.04(I)
87	43	304-306	$C_{27}H_{21}NOS$	79.53	5.24	3.44	7.86(S)	79.03	5.15	3.53	8.37(S)
88	76	164-166	$C_{31}H_{30}N_2O$	83.36	6.78	6.27		83.52	6.85	6.00	
89	74	236-238	$C_{28}H_{23}NO_4S$	71.61	4.95	2.98	6.83(S)	71.68	5.07	2.94	6.54(S)

[a]From 1-aroylaziridines. [b]From acid chlorides. [c]X = Cl, Br, I or S.

Table 4

Physical Data for Amine Salts and Nitrogen Mustard Salts

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	H	N	Cl	% Found C	H	N	Cl
91	84	209-211	$C_{29}H_{25}Cl_2NO_2$	71.01	5.15	2.86	14.46	71.26	5.09	2.60	14.69
92	63	273-276[a]	$C_{29}H_{26}Cl_3N$	70.37	5.31	2.83	21.49	69.77	5.15	2.74	22.29
93	91	197-200	$C_{27}H_{22}ClNO_2$	78.71	5.39	3.40	8.61	78.58	5.58	3.23	8.35
94	71	259-262	$C_{27}H_{23}Cl_2N$	74.99	5.37	3.24	16.40	75.63	5.19	3.41	15.99
95	66	218-220	$C_{27}H_{21}NO_2$	82.82	5.42	3.58		82.80	5.45	3.69	

[a]Reported M.p. 164-165°.[44]

D. Preparation of 2-Oxazolines.

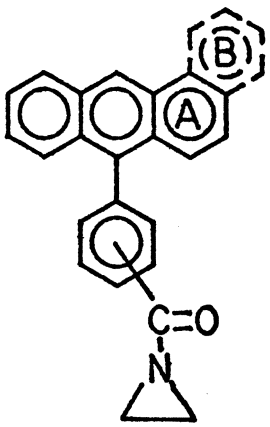
The two methods used to prepare the four 2-oxazolines, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-oxazolines (96 and 97) and 3- and 4-(9-anthracenyl)phenyl-2-oxazolines (98 and 99), are illustrated in Chart 5, and the results are summarized in Table 5.

The 2-oxazolines were prepared in fair yields from N-(2-chloroethyl)-amides via base induced intramolecular substitution reactions.

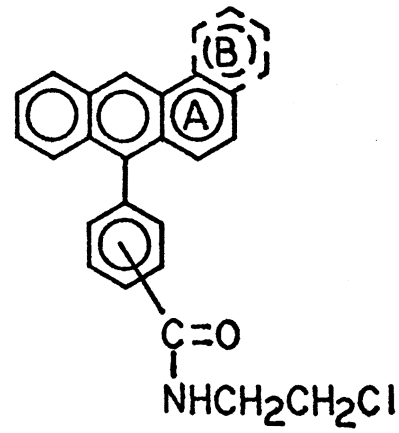
The four 2-oxazolines 96, 97, 98 and 99 were prepared in 46%, 53%, 52% and 55% yields, respectively, by reacting the N-(2-chloroethyl)-amides 81, 82, 83 and 84 with excess sodium ethoxide in absolute ethanol-tetrahydrofuran solutions. The major problem with this procedure was that the amides were too insoluble to give homogenous reactions. The amides were very insoluble in absolute ethanol, but were made more soluble by the addition of anhydrous tetrahydrofuran.

The 2-oxazolines were prepared in higher yields and more efficiently from 1-aroylaziridines by isomerization reactions catalyzed by sodium iodide. The four compounds 96, 97, 98 and 99 were prepared in 73%, 84%, 70% and 86% yields, respectively, by refluxing the 1-aroylaziridines 76, 77, 78 and 79 with a five molar excess of sodium iodide in tetrahydrofuran with vigorous stirring for at least 24 hours. These reactions were also heterogeneous in nature, the sodium iodide being insoluble, and the vigorous stirring with the excess sodium iodide for prolonged reaction times was necessary to insure completness of the reactions. It should be noted that refluxing the 1-aroylaziridines in the absence of sodium iodide resulted in essentially no isomerization products being formed. The four 2-oxazolines were easily purified by recrystallizations from chloroform-95% ethanol.

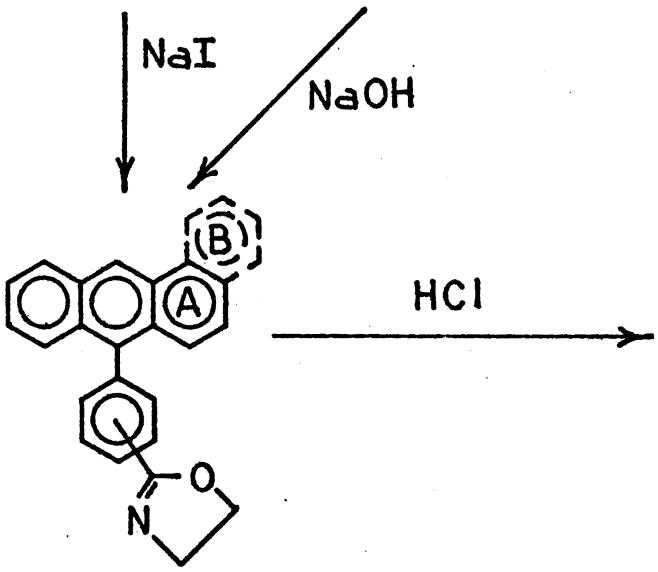
CHART 5



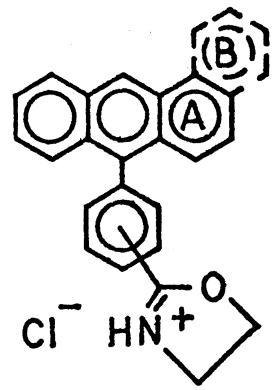
76 Rings A and B, meta
77 Rings A and B, para
78 Ring A, meta
79 Ring A, para



81 Rings A and B, meta
82 Rings A and B, para
83 Ring A, meta
84 Ring A, para



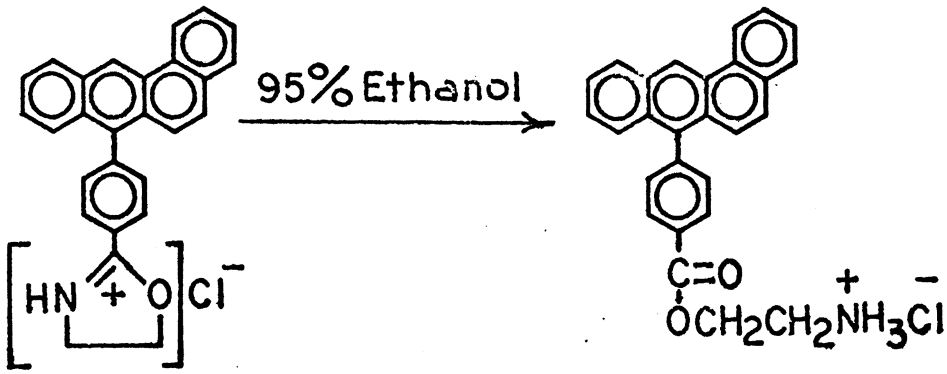
96 Rings A and B, meta
97 Rings A and B, para
98 Ring A, meta
99 Ring A, para



100 Rings A and B, meta
101 Rings A and B, para
102 Ring A, meta
103 Ring A, para

Under anhydrous conditions high molecular weight 2-oxazolines have been reported to form stable hydrochloride salts.[90] The four hydrochloride salts, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-oxazoline hydrochlorides (100 and 101) and 3- and 4-(9-anthracenyl)phenyl-2-oxazoline hydrochlorides (102 and 103), were prepared in 75-85% yields by the addition of ethyl ether solutions saturated with anhydrous hydrogen chloride to anhydrous tetrahydrofuran solutions containing the four 2-oxazolines 96, 97, 98 and 99. The salts were purified by recrystallizations from ethyl acetate-absolute ethanol.

That the salts were unstable towards water was demonstrated with 101 which was converted quantitatively to amine salt 93 after being refluxed in 95% ethanol for approximately 20 minutes.



101 93

The four 2-oxazolines were further characterized by ir and nmr spectra. Absorption bands at 1652 cm^{-1} and 1210 cm^{-1} were attributed to imine and ether stretching modes respectively. The ethylene protons appeared as two closely spaced triplets centered at 2.22 ppm and 2.45 ppm.

Table 5

Physical Data for 2-Oxazolines and Hydrochloride Salts

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	H	N	Cl	% Found C	H	N	Cl
96	46[a], 73[b]	188-189	$C_{27}H_{19}NO$	86.83	5.14	3.75		87.07	5.00	3.58	
97	53[a], 84[b]	223-224	$C_{27}H_{19}NO$	86.83	5.14	3.75		86.92	5.23	3.58	
98	52[a], 70[b]	159-161	$C_{23}H_{17}NO$	85.41	5.31	4.33		85.54	5.14	4.14	
99	55[a], 86[b]	274-275	$C_{23}H_{17}NO$	85.41	5.31	4.33		85.35	5.24	4.28	
100	73	197-199	$C_{27}H_{20}ClNO$	79.10	4.93	3.42	8.65	79.27	5.11	3.35	8.81
101	84	203-205	$C_{27}H_{20}ClNO$	79.10	4.93	3.42	8.65	79.31	4.68	3.23	8.79
102	70	152-154	$C_{23}H_{18}ClNO$	76.76	5.05	3.89	9.85	76.82	5.07	3.74	9.61
103	86	199-201	$C_{23}H_{18}ClNO$	76.76	5.05	3.89	9.85	76.83	5.10	3.99	10.05

[a]From N-(2-chloroethyl)amides. [b]From 1-aroylaziridines.

E. Preparation of 2-Thiazolines.

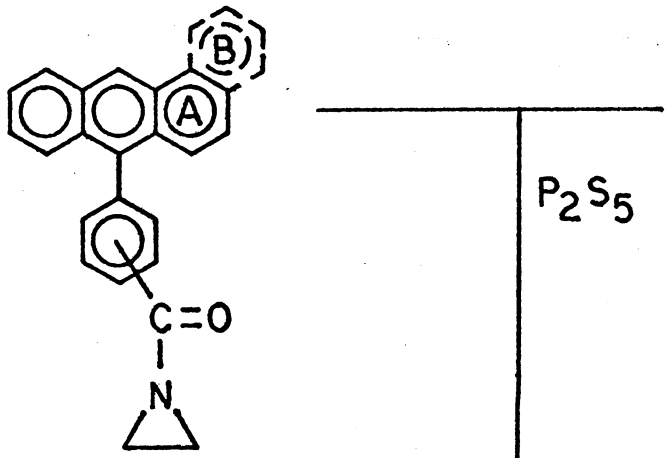
The two methods used to prepare the four 2-thiazolines, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-thiazolines (104 and 105) and 3- and 4-(9-anthracenyl)phenyl-2-thiazolines (106 and 107), are illustrated in Chart 6, and the results are summarized in Table 6.

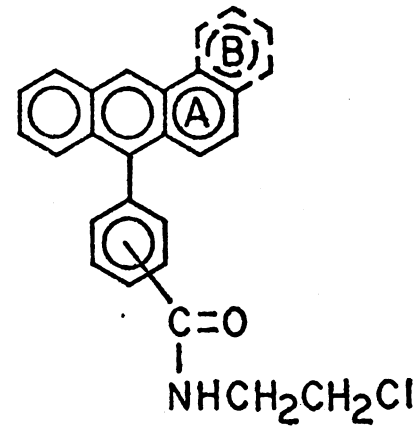
The four compounds 104, 105, 106 and 107 were prepared in excellent yields of 76%, 76%, 80% and 88%, respectively, by refluxing in toluene the four N-(2-chloroethyl)amides 81, 82, 83 and 84 with excess phosphorus pentasulfide. The compounds were purified by chromatography through silica gel substrate with benzene as eluant and recrystallizations from benzene-ethanol.

The four compounds were also prepared in good yields by reacting phosphorus pentasulfide with 1-aroylaziridines, a method for preparing 2-thiazolines apparently not previously reported. The compounds 104, 105, 106 and 107 were prepared in 70-80% yields by refluxing the four 1-aroylaziridines 76, 77, 78 and 79 with excess phosphorus pentasulfide in toluene for short periods of time.

The reactions occurred rapidly, and the 2-thiazolines were formed from the 1-aroylaziridines either by a one step concerted type mechanism or by the formation of 1-thioylaziridine moieties which rapidly isomerized to the 2-thiazoline moieties under the conditions of the reactions. No evidence for the presence of the 1-thioylaziridine moiety was obtained when the reaction times for the preparation of 105 were varied from two hours down to one-half hour in one-half hour intervals, and the reaction products separated by chromatography through silica gel substrate with benzene as eluant.

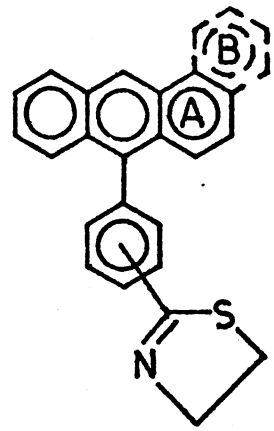
CHART 6



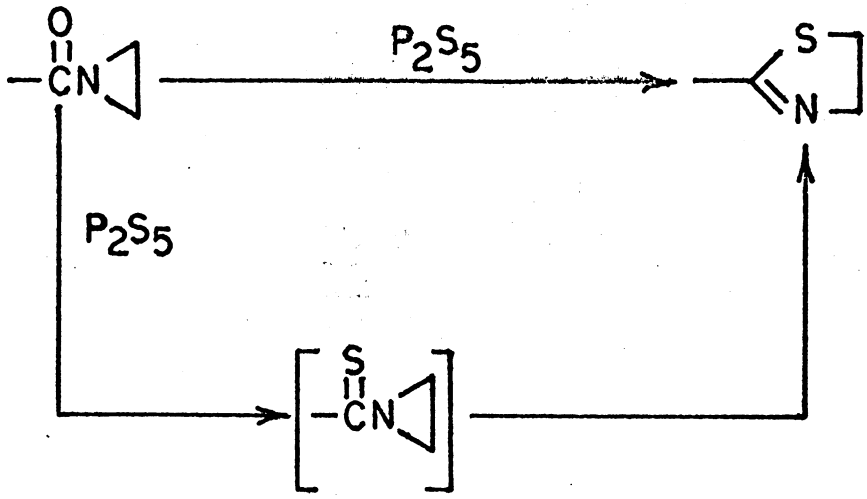


76 Rings A and B, meta
77 Rings A and B, para
78 Ring A, meta
79 Ring A, para

81 Rings A and B, meta
82 Rings A and B, para
83 Ring A, meta
84 Ring A, para



104 Rings A and B, meta
105 Rings A and B, para
106 Ring A, meta
107 Ring A, para



The four 2-thiazolines were characterized by elemental analysis and by ir and nmr spectra. The ethylene protons appeared as two triplets centered at 2.42 ppm and 1.82 ppm. Absorption at 1605 cm^{-1} was attributed to imine stretching modes.

Table 6

Physical Data for 2-Thiazolines

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	H	N	S	% Found C	H	N	S
104	76[a], 71[b]	173-174	$C_{27}H_{19}NS$	83.24	4.93	3.59	8.23	83.37	4.97	3.58	8.07
105	76[a], 75[b]	211-213	$C_{27}H_{19}NS$	83.24	4.93	3.59	8.23	83.06	4.90	3.56	8.22
106	80[a], 70[b]	126-128	$C_{23}H_{17}NS$	81.37	5.06	4.13	9.45	81.37	5.09	3.89	9.37
107	88[a], 77[b]	215-217	$C_{23}H_{17}NS$	81.37	5.06	4.13	9.45	81.25	4.83	4.13	9.26

[a]From N-(2-chloroethyl)amides. [b]From 1-aroylaziridines.

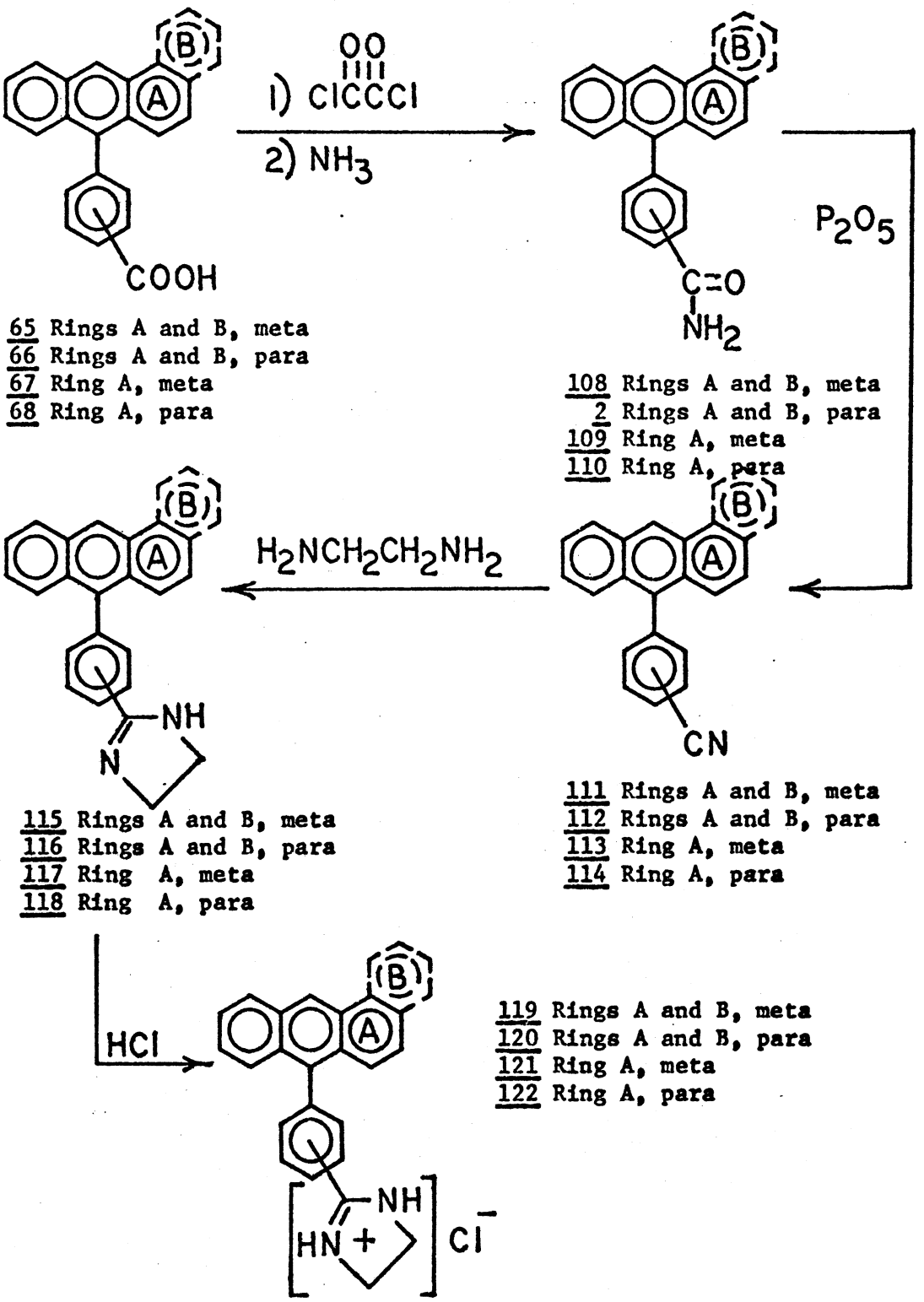
F. Preparation of 2-Imidazolines.

The four 2-imidazolines, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-imidazolines (115 and 116) and 3- and 4-(9-anthracenyl)phenyl-2-imidazolines (117 and 118), were prepared by the four step procedure illustrated in Chart 7, and the results are summarized in Tables 7 and 8. Starting with carboxylic acid reagents, the methods most commonly used to prepare 2-imidazolines involve the reaction of ethylenediamine either with the carboxylic acids directly or with cyano derivatives of the acids. While direct reaction with carboxylic acids invariably give low yields of 2-imidazoline products, reaction of ethylenediamine with cyano compounds reportedly give excellent yields of 2-imidazolines.[97] The four 2-imidazolines 115, 116, 117 and 118 were prepared by this latter method. The necessary cyano reagents were prepared from amides by dehydration reactions with phosphorus pentoxide, while the amides, in turn, were prepared from carboxylic acids *via* acid chloride intermediates.

The four amides, 3- and 4-(7-benz[a]anthracenyl)benzamides (108 and 2) and 3- and 4-(9-anthracenyl)benzamides (109 and 110), were prepared in yields of 87%, 89%, 95% and 86%, respectively, by the reaction of acid chlorides 72, 73, 74 and 75 with liquid ammonia in tetrahydrofuran at room temperature. The amides were purified by recrystallizations from 95% ethanol.

The four cyano compounds, 3- and 4-(7-benz[a]anthracenyl)cyanobenzenes (111 and 112) and 3- and 4-(9-anthracenyl)cyanobenzenes (113 and 114), were prepared in yields of 67%, 64%, 61% and 68%, respectively, by the reaction of the four amides 108, 2, 109 and 110 with excess phosphorus pentoxide in refluxing toluene. This method was found to be

CHART 7



65 Rings A and B, meta
66 Rings A and B, para
67 Ring A, meta
68 Ring A, para

108 Rings A and B, meta
2 Rings A and B, para
109 Ring A, meta
110 Ring A, para

111 Rings A and B, meta
112 Rings A and B, para
113 Ring A, meta
114 Ring A, para

115 Rings A and B, meta
116 Rings A and B, para
117 Ring A, meta
118 Ring A, para

119 Rings A and B, meta
120 Rings A and B, para
121 Ring A, meta
122 Ring A, para

a better synthetic procedure for preparing the cyano compounds in reasonable quantities than the method which involved the cyclodehydration of cyano ketones with concentrated sulfuric acid at low temperatures (see p.27). The four cyano compounds were purified by chromatography through silica gel substrate with benzene as eluant and recrystallization procedures.

The four 2-imidazolines 115, 116, 117 and 118 were prepared in yields of 75%, 84%, 71% and 85%, respectively, by refluxing cyano compounds 111, 112, 113 and 114 in anhydrous ethylenediamine for short periods of time. The four compounds were purified by recrystallizations from ethanol.

2-Imidazolines reportedly form hydrochloride salts which are stabilized by resonance.[99] The four hydrochloride salts, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-imidazoline hydrochlorides (119 and 120) and 3- and 4-(9-anthracenyl)phenyl-2-imidazoline hydrochlorides (121 and 122), were prepared in 75-85% yields by the addition of ethyl ether solutions saturated with anhydrous hydrogen chloride to anhydrous tetrahydrofuran solutions containing the four 2-imidazolines 115, 116, 117 and 118, respectively.

The four 2-imidazolines were further characterized by ir and nmr spectra. The ethylene protons appeared in an A_2B_2 system with the difference in chemical shifts approaching zero. The ethylene protons appeared as a singlet at 2.00 ppm, while the amino proton appeared as a broad band centered at 3.1 ppm. Absorption at 1610 cm^{-1} was attributed to the imine stretching modes.

Table 7

Physical Data for Amides and Nitriles

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	% Calcd. H	% Calcd. N	% Found C	% Found H	% Found N
108	87	135-137	$C_{25}H_{17}NO$	86.42	4.94	4.03	86.22	4.98	4.25
2	89	298-300[a]	$C_{25}H_{17}NO$						
109	95	199-200	$C_{21}H_{15}NO$	84.81	5.09	4.71	84.98	5.24	4.68
110	86	270-271	$C_{21}H_{15}NO$	84.81	5.09	4.71	84.98	5.09	4.90
111	67	153-155	$C_{25}H_{15}N$	91.15	4.59	4.25	91.25	4.76	4.02
112	64	196-198[b]	$C_{25}H_{15}N$						
113	61	129-130	$C_{21}H_{13}N$	90.28	4.70	5.02	90.49	4.73	5.13
114	68	134-135[c]	$C_{21}H_{13}N$						

[a]Reported M.p. 299-300°.[108] [b]Reported M.p. 197-198°.[17] [c]Reported M.p. 125-126°.[51]

Table 8

Physical Data for 2-Imidazolines and Hydrochloride Salts

Compd.	Yield %	M.p. °C	Formula	% Calcd. C	H	N	Cl	% Found C	H	N	Cl
115	76	227-229	$C_{27}H_{20}N_2$	87.05	5.42	7.52		86.91	5.42	7.35	
116	84	221.5-223	$C_{27}H_{20}N_2$	87.05	5.42	7.52		87.20	5.38	7.47	
117	71	241-242	$C_{23}H_{18}N_2$	85.67	5.64	8.69		85.91	5.86	8.43	
118	85	309 decomp.	$C_{23}H_{18}N_2$	85.67	5.64	8.69		85.54	5.77	8.65	
119	75	291-294	$C_{27}H_{21}ClN_2$	79.29	5.19	6.85	8.67	79.37	5.28	6.64	8.87
120	81	325 decomp.	$C_{27}H_{21}ClN_2$	79.29	5.19	6.85	8.67	79.35	5.34	6.75	8.74
121	77	314 decomp.	$C_{23}H_{19}ClN_2$	76.97	5.35	7.81	9.88	76.69	5.42	7.54	10.18
122	85	333 decomp.	$C_{23}H_{19}ClN_2$	76.97	5.35	7.81	9.88	77.13	5.30	7.83	10.10

G. Comments on Spectra.

Each of the new compounds prepared in this work contained either an anthracenyl or a benz[a]anthracenyl functional group, and the presence of one of these functional groups in each of the compounds was evident from an examination of their ir, nmr, and uv spectra.

Polycyclic aromatic hydrocarbons show characteristic absorption in three regions of the infrared spectrum.[110] The aromatic C-H stretching and the C-C skeletal vibrations occur at 3100-3000 cm^{-1} and 1600-1400 cm^{-1} respectively, while the C-H out of plane bending vibrations occur in the region 900-675 cm^{-1}.[110] Since all of the new compounds showed characteristic absorption in these three regions -- particularly the 900-675 cm^{-1} region -- these absorption bands were not of any particular value in identifying the individual compounds.

In the nmr spectra the aromatic protons of the new compounds appeared as multiplets of bands in the region 5.3-3.9 ppm. While of no value in identifying the individual compounds, these multiplets of bands were characteristically different for the benz[a]anthracene and anthracene compounds such that the two types of compounds were easily distinguishable (see examples in Appendix).

The ultraviolet absorption patterns for the new compounds were similar to the spectral absorption patterns generally observed for 7-substituted benz[a]anthracenes and 9-substituted anthracenes.* Apparently, any absorptions by the hetero chromophoric functional groups present in the various compounds were blanketed by the broad intense absorption maxima exhibited by the 7-phenylbenz[a]anthracenyl and

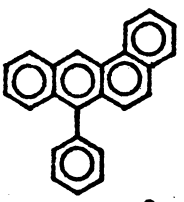
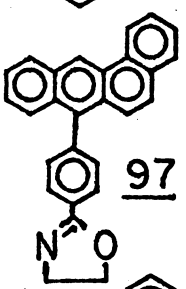
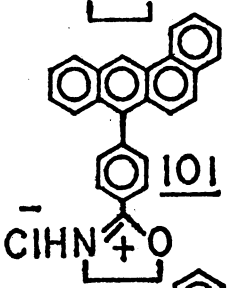
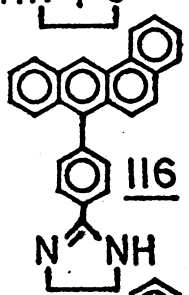
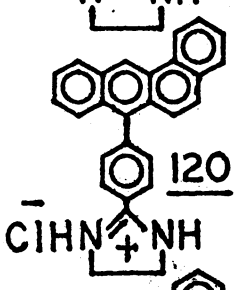
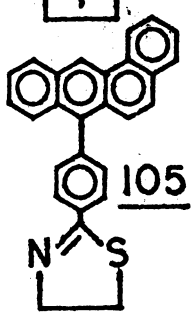
*For recent examples, refer to Ph.D. Theses in this Department by P. D. Henson and R. L. Kornmann.

9-phenylanthracenyl portions of the compounds. As examples, the absorption maxima for some benz[a]anthracenes are listed for comparative purposes in Table 9, while the absorption maxima for each of the new compounds are given in the Experimental Section.

Table 9

Absorption Maxima for Some Benz[a]anthracenes

λ_{max} in mu

	365	352	292	281	271	260	222
 97	367	352	292	281	271	258	220
 101	364	351	292	281	271	257	223
 116	368	351	291	280	270	255	220
 120	365	350	292	281	271	258	220
 105	366	353	292	281	271	258	222

EXPERIMENTAL

A. General

1. The melting points of all compounds melting below 300° were taken on a Fisher-Johns melting point block and are uncorrected; those melting above 300° were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. Boiling points are uncorrected.

2. Analysis marked (*) were performed by Galbraith Laboratories, Knoxville, Tennessee and those marked (**) by M-H-W Laboratories, Garden City, Michigan. All unmarked analysis were obtained on an F&M Scientific Corporation, Model 185, C, H, and N analyzer in this department. The majority of the compounds synthesized in this work were not analyzed correctly with the C, H and N analyzer but were correctly analyzed at the other laboratories.

3. The infrared spectra were recorded on a Beckman IR-5 infrared spectrophotometer or a Perkin-Elmer Model 621 spectrophotometer. The spectra were obtained using 10-20% chloroform solutions or potassium bromide disks.

4. The nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrophotometer. The spectra were obtained using 10% $CDCl_3$ or deuterated DMSO solutions with tetramethylsilane (TMS) as an internal standard.

5. The ultraviolet spectra were recorded on a Beckman DK-2A ratio recording spectrophotometer. Ethanol (95%) was used as the solvent.

6. The chromatography columns were 1 1/2" in diameter and 11" in length. The columns were wet packed with either Fisher's acid alumina, Brockman Activity I, 80-200 mesh, or Baker's Silica gel, powder,

"Suitable for Chromatographic Use", with benzene. The acid alumina columns were eluted with either 5% or 20% chloroform-hexane; all the silica gel columns were eluted with benzene.

B. Preparation of Carboxylic Acids.

2-(1-Naphthylmethyl)chlorobenzene (55)

A Grignard reagent was prepared by the rapid addition of 207 g. (1.0 mole) of 1-bromonaphthalene in 600 ml. of anhydrous ethyl ether to 24.3 g. (1.0 mole) of magnesium turnings contained in a 2-liter, 3-necked, round-bottomed flask that was immersed in a water bath. The flask was equipped with a mechanical stirrer, take-off condenser, dropping funnel, and dry nitrogen atmosphere. After the addition was complete, the mixture was refluxed one hour, the ether was then replaced with 400 ml. of dry benzene, and when the reflux temperature reached 55°, 129 g. (0.80 mole) of o,α-dichlorotoluene in 300 ml. of benzene was added over a period of one hour. The reaction mixture was heated at reflux temperature for 12 hours, allowed to cool to room temperature, and the complex was decomposed with 300 ml. of 10% hydrochloric acid solution while cooling the reaction flask in an ice bath. The benzene layer was separated, washed three times with 300 ml. portions of water, and dried over sodium sulfate. The dried solution was filtered, concentrated and distilled under reduced pressure. The product was collected as an impure yellow viscous oil at 180-188° (0.7 mm.), [Lit.[23] 189-192° (2.0 mm.)]. Some α,α'-binaphthyl impurity codistilled with the product. The distillate was dissolved in 75 ml. of acetone, cooled overnight, the precipitated α,α'-binaphthyl was removed by vacuum filtration, and concentration of the filtrate gave the product as a yellow viscous oil; yield 101 g. (50%).

2-Chlorodiphenylmethane (56)

A Grignard reagent was prepared by the rapid addition of 157 g. (1.0 mole) of bromobenzene in 600 ml. of dry ethyl ether to 24.3 g. (1.0 mole) of magnesium turnings contained in a 2-liter, 3-necked, round-bottomed flask that was immersed in a water bath. The flask was equipped with a mechanical stirrer, take-off condenser, dropping funnel, and dry nitrogen atmosphere. After the addition was complete, the mixture was refluxed one hour, the ether was replaced with 400 ml. of dry benzene, and when the reflux temperature reached 55°, 129 g. (0.8 mole) of o,α-dichlorotoluene was added over a period of one hour. The reaction mixture was heated at reflux temperature for 10 hours, allowed to cool, and the complex was decomposed with 300 ml. of 10% hydrochloric acid solution while cooling the reaction flask in an ice bath. The benzene layer was separated, washed twice with 300 ml. portions of water, and dried over sodium sulfate. The dried solution was filtered, concentrated and distilled under reduced pressure. The product was collected as a water clear oil at 135-142° (5 mm.) [Lit.[15] 138-142° (5 mm.)]; yield 124 g. (61%).

2-(1-Naphthylmethyl)cyanobenzene (59)

A mixture of 253 g. (1.0 mole) of 2-(1-naphthylmethyl)chlorobenzene (55), 134 g. (1.5 mole) of cuprous cyanide and a few crystals of anhydrous cupric sulfate in 600 ml. of freshly distilled N-methyl-2-pyrrolidone was vigorously refluxed for 48 hours in a 2-liter, 3-necked, round-bottomed flask equipped with a mechanical stirrer and a water condenser. The resultant black solution was cooled to 100° and transferred to a 5-liter, 3-necked, round-bottomed flask equipped with water

condenser, mechanical stirrer and dropping funnel. A solution of 368 g. (7.5 mole) of sodium cyanide in 1500 ml. of water was slowly added (exothermic initially), and the mixture was stirred at 100° for one hour as the complex was decomposed. The mixture was poured into two 2-liter separatory funnels, 300 ml. of benzene was added to each, the mixtures were shaken carefully while warm and left overnight as the water and benzene layers slowly separated. An ultraviolet lamp was used to distinguish the benzene and water layers. The benzene layers were separated, the water layers were extracted twice more with 100 ml. portions of benzene, the benzene layers were combined, washed three times with 200 ml. portions of water, and dried over sodium sulfate. The dried solution was filtered, concentrated, and distilled under reduced pressure. The product was collected as a viscous yellow oil at 175-180° (0.5 mm.) [Lit.[23] 216-217° (3.0 mm.)]. The oil was dissolved in 75 ml. of acetone and cooled overnight. Any α,α'-binaphthyl which was not removed during the purification of 2-(1-naphthylmethyl)chlorobenzene (55) and which codistilled with the product was precipitated and removed by filtration. Concentration of the filtrate gave the product as a viscous yellow oil; yield 190 g. (78%).

2-Cyanodiphenylmethane (60)

A mixture of 203 g. (1.0 mole) of 2-chlorodiphenylmethane (56), 134 g. (1.5 mole) of cuprous cyanide and a few crystals of anhydrous cupric sulfate in 500 ml. of freshly distilled N-methyl-2-pyrrolidone was vigorously refluxed for 48 hours in a 2-liter, 3-necked, round-bottomed flask equipped with a mechanical stirrer and a water condenser. The resultant black solution was cooled to 100° and transferred to a

5-liter, 3-necked, round-bottomed flask equipped with water condenser, mechanical stirrer and dropping funnel. A solution of 368 g. (7.5 mole) of sodium cyanide in 1500 ml. of water was slowly added (exothermic initially), and the mixture was stirred at 100° for one hour as the complex was decomposed. The mixture was poured into two 2-liter separatory funnels, 300 ml. of benzene was added to each, the mixtures were shaken carefully while warm and left overnight as the water and benzene layers slowly separated. An ultraviolet lamp was used to distinguish the benzene and water layers. The benzene layers were separated, the water layers were extracted twice more with 100 ml. portions of benzene, the benzene layers were combined, washed three times with 150 ml. portions of water and dried over sodium sulfate. The dried solution was filtered, concentrated, and distilled under reduced pressure. The product was collected as a light yellow oil at 160-165° (5 mm.) [Lit.[15] 160-164° (4 mm.)]; yield 212 g. (75%).

2-(1-Naphthylmethyl)-4'-bromobenzophenone (62)

A Grignard reagent was formed by the addition of 176.9 g. (0.75 mole) of p-dibromobenzene in 600 ml. of dry ethyl ether (solid is soluble in warm ethyl ether) to 18.2 g. (0.75 mole) of magnesium turnings contained in a 2-liter, 3-necked, round-bottomed flask that was immersed in a water bath. The flask was equipped with a mechanical stirrer, take-off condenser, dropping funnel and dry nitrogen atmosphere. After the addition was complete the solution was refluxed one hour as all the magnesium appeared to react. The ether was replaced with 400 ml. of dry benzene, and when the reflux temperature reached 50°, 121.5 g. (0.5 mole) of 2-(1-naphthylmethyl)cyanobenzene (59) in

100 ml. of dry benzene was added over a one-half hour period. The solution was refluxed for 14 hours, cooled in an ice bath, and 443 ml. of 25% sulfuric acid solution was slowly added (very exothermic initially). The resultant mixture was refluxed for 48 hours, cooled to room temperature, and transferred to a 2-liter separatory funnel. The benzene layer was separated, washed with 200 ml. of water, 200 ml. of 10% sodium bicarbonate solution, then twice more with 200 ml. portions of water, and dried over sodium sulfate. The dried solution was filtered, concentrated, and distilled under reduced pressure using a short-neck distilling head tightly insulated with glass wool. The product was obtained as an impure pale greenish yellow viscous oil at 230-245° (0.4 mm.) [Lit.[17] 275-278° (2 mm.)]; yield 100 g. (50%). This product was used in subsequent reactions with good results without further purification.

2-(1-Naphthylmethyl)-3'-bromobenzophenone (61)

This ketone was prepared analogously to 62. A Grignard reagent was formed by the addition of 118 g. (0.5 mole) of m-dibromobenzene in 500 ml. of dry ethyl ether to 12.2 g. (0.5 mole) of magnesium turnings contained in a 2-liter, 3-necked, round-bottomed flask that was immersed in a water bath. The solution was refluxed one hour, the ether was replaced with 400 ml. of dry benzene, and when the reflux temperature reached 55°, 121.5 g. (0.5 mole) of 2-(1-naphthylmethyl)cyanobenzene (60) in 100 ml. of dry benzene was added over a one-half hour period and the solution was refluxed for 12 hours. The solution was then cooled in an ice bath, 443 ml. of 25% sulfuric acid solution was slowly added (very exothermic initially), and the resultant mixture was

refluxed 48 hours. The mixture was then cooled to room temperature, the benzene layer was separated and washed successively with 100 ml. of water, 100 ml. of 10% sodium bicarbonate solution, twice with 100 ml. portions of water, and the benzene layer was separated and dried over sodium sulfate. The dried solution was filtered, concentrated, and distilled under reduced pressure. The product was collected as an impure viscous greenish yellow oil at 225-238° (0.3 mm.); yield 110 g. (54%). The majority of the ketone was employed with good results in subsequent reactions without further purification. A portion of the oily ketone was crystallized three times from benzene-95% ethanol (7:3) to give white crystals, m.p. 100-103° [Lit.[19] m.p. 105-106°].

2-Benzyl-4'-bromobenzophenone (64)

This ketone was prepared analogously to 62. A Grignard reagent was formed with 176.9 g. (0.75 mole) of p-dibromobenzene and 18.2 g. (0.75 mole) of magnesium turnings in 600 ml. of dry ethyl ether. After the reaction was complete the ether was replaced with 400 ml. of dry benzene, and when the reflux temperature reached 50°, 97 g. (0.5 mole) of 2-cyanodiphenylmethane (60) in 100 ml. of dry benzene was added over a one-half hour period. The solution was refluxed for 12 hours, cooled in an ice bath, and 443 ml. of 25% sulfuric acid solution was slowly added (very exothermic initially). The resultant mixture was refluxed 48 hours, cooled to room temperature, the benzene layer was separated, washed successively with 200 ml. of water, 200 ml. of 10% sodium bicarbonate solution, then twice more with 100 ml. portions of water and dried over sodium sulfate. The dried solution was

filtered, concentrated, and distilled under reduced pressure. The product was collected as an impure reddish brown oil at 195-197° (0.5 mm.) [Lit.[51] 210-220° (1 mm.)]; yield 126 g. (71%). The product was used in subsequent reactions with good results without further purification.

2-Benzyl-3'-bromobenzophenone (63)

This ketone was prepared analogously to 61. A Grignard reagent was formed with 118 g. (0.5 mole) of m-dibromobenzene and 12.2 g. (0.5 mole) of magnesium turnings in 500 ml. of dry ether. After the reaction was complete the ether was replaced with 400 ml. of dry benzene, the reflux temperature was allowed to reach 55°, and 97 g. (0.5 mole) of 2-cyanodiphenylmethane (60) in 100 ml. of dry benzene was added over a one-half hour period. The solution was refluxed for 12 hours, cooled in an ice bath, and 443 ml. of 25% sulfuric acid solution was slowly added (very exothermic initially). The resultant mixture was refluxed 48 hours, cooled to room temperature, the benzene layer was separated, washed successively with 200 ml. of water, 200 ml. of 10% sodium bicarbonate solution, then twice more with 100 ml. portions of water and dried over sodium sulfate. The dried solution was filtered, concentrated, and distilled under reduced pressure. The product was collected as a greenish yellow oil at 190-195° (0.3 mm.); yield 109 g. (62%). No attempt was made to prepare an analytically pure sample for elemental analysis. The product was used in subsequent reactions with good results without further purification.

2-(1-Naphthylmethyl)-3'-cyanobenzophenone
2-(1-Naphthylmethyl)-4'-cyanobenzophenone
2-Benzyl-3'-cyanobenzophenone
2-Benzyl-4'-cyanobenzophenone

These four cyano ketones were prepared from the bromo ketones 61, 62, 63 and 64, respectively, by the same procedure. A mixture of 0.5 mole of bromo ketone, 90 g. (1.0 mole) of cuprous cyanide and a few crystals of anhydrous cupric sulfate in 700 ml. of freshly distilled N-methyl-2-pyrrolidone was refluxed vigorously for 48 hours in a 2-liter, 3-necked, round-bottomed flask with mechanical stirring. After the reaction was complete, the solution was cooled to 100°, transferred to a 5-liter flask equipped with a mechanical stirrer, 245 g. (5 mole) of sodium cyanide in 1000 ml. of water was added slowly, and the resultant mixture was stirred at approximately 100° for one hour. The mixture was then transferred to two 2-liter separatory funnels and each was extracted while warm with 200 ml. of benzene. The benzene layers were separated (U.V. lamp helped distinguish the layers), the aqueous layers were extracted twice more with 100 ml. portions of benzene, the benzene layers were combined and dried over sodium sulfate. The dried solution was filtered and concentrated to give the product as a viscous black oil (an oil was obtained in each case). The oils were isolated in 85-95% crude yields and, in each case, the products were used in subsequent reactions without any purification.

7-(4-Carboxyphenyl)benz[a]anthracene (66)

To a solution containing 104 g. (0.3 mole) of 2-(1-naphthylmethyl)-4'-cyanobenzene dissolved in 2000 ml. of refluxing glacial acetic acid in a 5-liter flask with magnetic stirring was added dropwise 500 ml. of

48% hydrobromic acid over a two hour period. The resultant solution was refluxed for 24 hours, cooled to room temperature, and the precipitated product was isolated by vacuum filtration. The product was washed with water until the washings were neutral to litmus and dried at 80° (10 mm.) in a vacuum oven for five hours. The product was obtained as light brownish white powdery solid after one crystallization from toluene-tetrahydrofuran (8:2); m.p. 280-283°; yield 52 g. (50%). This material was dried again and was used with excellent results in subsequent reactions without any further purification. A portion was recrystallized five times from toluene-tetrahydrofuran (8:2); m.p. 297-299° [Lit.[17] 298-300°].

7-(3-Carboxyphenyl)benz[a]anthracene (65)

To a solution containing 74 g. (0.21 mole) of 2-(1-naphthylmethyl)-3'-cyanobenzene dissolved in 1480 ml. of refluxing glacial acetic acid contained in a 5-liter flask with magnetic stirring was added dropwise 400 ml. of 48% hydrobromic acid over a two hour period. The resultant solution was refluxed for 30 hours, cooled to room temperature, and the precipitated product was isolated by vacuum filtration. The product was washed with water until the washings were neutral to litmus and then dried at 94° (10 mm.) in a vacuum oven for seven hours. The product was obtained as light brown crystals after one crystallization from toluene-tetrahydrofuran (8:2); m.p. 267-271°; yield 45 g. (60%). This material was dried again and was used with good results in subsequent reactions without any further purification. A portion was further purified by four recrystallizations from toluene-tetrahydrofuran (8:2) and one treatment with charcoal: m.p. 274-275° [Lit.[100] 253-254°].

Anal. Calcd. for $C_{25}H_{16}O_2$: C, 86.18; H, 4.64.
Found: C, 86.01; H, 4.59.

9-(4-Carboxyphenyl)anthracene (68)

To a solution containing 75 g. (0.25 mole) of 2-benzyl-4'-cyanobenzophenone dissolved in 1500 ml. of glacial acetic acid contained in a 5-liter flask with magnetic stirring was added dropwise 500 ml. of 48% hydrobromic acid over a two hour period. The resultant solution was refluxed for 30 hours, cooled to room temperature, and the precipitated product was isolated by vacuum filtration. The product was washed with water until the washings were neutral to litmus and dried at 75° (10 mm.) for eight hours. The product was obtained as yellow needle crystals after one crystallization from toluene-tetrahydrofuran (7:3); m.p. 259-262°; yield 48 g. (65%). This material was dried and used in subsequent reactions without further purification. A portion was recrystallized twice from toluene-tetrahydrofuran (7:3); m.p. 262-264° [Lit.[51] 262-264°].

9-(3-Carboxyphenyl)anthracene (67)

To a solution containing 89 g. (0.3 mole) of 2-benzyl-3'-cyanobenzophenone dissolved in 1800 ml. of glacial acetic acid contained in a 5-liter flask equipped with a magnetic stirrer was added dropwise 800 ml. of 48% hydrobromic acid over a three hour period. The resultant solution was refluxed for 30 hours, cooled to room temperature, and the precipitated product was isolated by vacuum filtration. The product was washed with water until the washings were neutral to litmus and dried at 85° (10 mm.) for 10 hours. The product was obtained as light

brown crystals after one crystallization from toluene-tetrahydrofuran (7:3); m.p. 294-297°; yield 47 g. (64%). This material was dried and used in subsequent reactions without further purification. A portion was purified by four recrystallizations from toluene-tetrahydrofuran (7:3) and one treatment with charcoal to give the product as light yellowish white crystals; m.p. 300-302°.

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 84.46; H, 4.74.

Found: C, 84.31; H, 4.61.

7-(4-Bromophenyl)benz[a]anthracene (70)

To a solution containing 30 g. (0.074 mole) of 2-(1-naphthylmethyl)-4'-bromobenzophenone (62) dissolved in 900 ml. of glacial acetic acid contained in a 2-liter flask equipped with a magnetic stirrer was added dropwise 300 ml. of 48% hydrobromic acid over a two hour period. The resultant solution was refluxed for 24 hours, cooled to room temperature, and the slightly viscous product which precipitated was isolated by vacuum filtration. The product was dissolved in 200 ml. of benzene and washed successively with 100 ml. of 10% sodium bicarbonate, twice with 100 ml. portions of water, and the benzene solution was separated and dried over sodium sulfate. The dried solution was filtered, concentrated, and the resultant yellow solid was chromatographed in 5 gram portions through acid alumina columns. Each portion was dissolved in 25 ml. of benzene, placed on a column, and eluted with 20% chloroform-hexane (350 ml.). The eluted solutions were combined and concentrated to give a white crystalline solid. The solid was recrystallized once from benzene-95% ethanol (8:2) and dried at 35° (0.5 mm.) for five hours. The product was obtained as white crystals; m.p. 163-

164° [Lit.[17] 163-164°]; yield 21.5 g. (75%).

7-(3-Bromophenyl)benz[a]anthracene (71)

To a solution containing 30 g. (0.074 mole) of 2-(1-naphthylmethyl)-3'-bromobenzophenone (61) dissolved in 900 ml. of glacial acetic acid contained in a 2-liter flask equipped with a magnetic stirrer was added dropwise 300 ml. of 48% hydrobromic acid over a two hour period. The resultant solution was refluxed for 30 hours, cooled to room temperature, and the product was present as an oil. The solvent was removed by vacuum distillation to give a reddish brown viscous oil which was dissolved in 300 ml. of benzene, washed successively with 100 ml. of 10% sodium bicarbonate solution, twice with 100 ml. portions of water, and the benzene solution was separated and dried over sodium sulfate. The dried solution was filtered and concentrated to give a viscous oil. The oil was dissolved in 100 ml. of benzene and passed in four portions through acid alumina columns with 20% chloroform-hexane (400 ml. per portion) as the eluting solvent. The eluted solutions were combined and concentrated to give a light yellow oil. The oil slowly crystallized from benzene-95% ethanol (9:1) to give the product as a white powdery solid which was dried at 35° (0.3 mm.) for five hours; m.p. 128-130° [Lit.[19] 129.5-131°]; yield 19 g. (69%).

Formation of Grignard Reagent with 7-(4-Bromophenyl)benz[a]-anthracene; Carbonation and Hydrolysis Reactions

A mixture of 5 g. (0.013 mole) of 7-(4-bromophenyl)benz[a]anthracene (70) and 0.32 g. (0.013 mole) of magnesium turnings in 25 ml. of anhydrous tetrahydrofuran (dried 24 hours over lithium aluminum hydride) contained in a 50 ml. 3-necked flask with vigorous mechanical stirring

and dry nitrogen atmosphere, was refluxed for two hours with no visible sign of reaction. One drop of methyl iodide was added and, after one hour of reflux, a reaction was visible. After seven hours reflux the resultant reddish black solution (no magnesium turnings visible) was poured over a slurry of 100 ml. of anhydrous tetrahydrofuran and 20 g. of powdered carbon dioxide with vigorous stirring. After two hours 100 ml. of water saturated with sodium chloride was added, the tetrahydrofuran layer was separated and concentrated to give a brown oil. The oil was dissolved in 20 ml. of toluene, cooled overnight, and the precipitated 7-(4-carboxyphenyl)benz[a]anthracene (66) was isolated by vacuum filtration; m.p. 280-283°; yield 1 g. (26%). A second Grignard reagent was prepared similar to the first one, carbon dioxide was bubbled through the solution for one hour, the mixture was then poured into 100 ml. of water saturated with sodium chloride, stirred one-half hour, and the tetrahydrofuran layer was separated and concentrated to give a brown oil. The oil was dissolved in toluene, cooled overnight, and the precipitated carboxylic acid 66 was isolated by vacuum filtration; m.p. 281-284°; yield 1.5 g. (29%). A third Grignard reagent was prepared similar to the first one and was poured into 100 ml. of water saturated with sodium chloride. The tetrahydrofuran layer was separated and concentrated to give a yellow oil. The oil was dissolved in 20 ml. of benzene and passed through an acid alumina column with 5% chloroform-hexane (300 ml.) as eluant. Removal of the solvent from the first fraction isolated from the column gave a clear yellow oil. The oil was crystallized from benzene-95% ethanol (9:1) and identified by mixture m.p. and ir spectra as 7-phenylbenz[a]anthracene, m.p. 180-183° [Lit.[18] 183-184°]; yield 1.5 g. (42%).

Formation of Grignard Reagent from 7-(3-Bromophenyl)benz[a]-anthracene; Carbonation and Hydrolysis Reactions

A Grignard reagent was prepared from 5 g. (0.013 mole) of 7-(3-bromophenyl)benz[a]anthracene (71), 0.32 g. (0.013 mole) of magnesium turnings and one drop of methyl iodide in 25 ml. of anhydrous tetrahydrofuran by the same procedure used to prepare the Grignard reagent of 7-(4-bromophenyl)benz[a]anthracene (70). The resultant bluish black Grignard reagent solution was poured into a slurry of 100 ml. of anhydrous tetrahydrofuran and 20 g. of powdered carbon dioxide. After two hours stirring, 100 ml. of water saturated with sodium chloride was added, the tetrahydrofuran layer was separated, concentrated, and the resultant brown oil was taken up in 20 ml. of toluene and cooled overnight. The precipitated 7-(3-carboxyphenyl)benz[a]anthracene (65) was isolated by vacuum filtration, m.p. 270-274°; yield 1 g. (22%). A second Grignard reagent solution was hydrolyzed by pouring the solution into 100 ml. of water saturated with sodium chloride. The tetrahydrofuran layer was removed, concentrated, and the resultant yellow oil was purified by chromatography through acid alumina with 5% chloroform-hexane (300 ml.) as eluant, similar to the preceding procedure. The resultant oil isolated from the first fraction removed from the column was crystallized from benzene-95% ethanol (9:1) and identified by mixture m.p. and ir spectra as 7-phenylbenz[a]anthracene, m.p. 180-183°; yield 1.4 g. (37%).

C. Preparation of Acid Chlorides.

1. The acid chloride derivatives of the carboxylic acids 65, 66, 67 and 68 were prepared by refluxing the acids in benzene (200-400 ml.) for six hours with a 10 molar excess of thionyl chloride. The acid

chlorides were isolated as oils, except for the acid chloride, 4-(9-anthracenyl)benzoyl chloride, which was isolated as a green solid, m.p. 287-298°. All four acid chlorides contained impurities, however, that were difficult to remove. The four acid chlorides were prepared as solids and in purer form using oxalyl chloride instead of thionyl chloride.

2. The four acid chlorides, 3- and 4-(7-benz[a]anthracenyl)benzoyl chlorides (72 and 73) and 3- and 4-(9-anthracenyl)benzoyl chlorides (74 and 75), used in this work were prepared with oxalyl chloride. The acid chlorides were prepared by refluxing the carboxylic acids (65, 66, 67 and 68) with one molar excess of oxalyl chloride in 300-500 ml. of dry benzene for a minimum of ten hours. After concentrating the benzene solution, any unreacted oxalyl chloride remaining was removed azeotropically by the addition of 100 ml. of chloroform to the acid chloride and removing the solvent under reduced pressure. This was done three times. The two para acid chlorides 73 and 75 were isolated as yellowish green solids, m.p.'s 180-185° and 213-218°, when the solutions were concentrated, while the two meta acid chlorides 72 and 74 precipitated on standing overnight; m.p.'s 137-143° and 120-125°. The four acid chlorides were used in subsequent reactions without further purification.

D. Preparation of 1-Aroylaziridines.

The four 1-aroylaziridines 76, 77, 78 and 79 were each prepared by two methods. The 1-aroylaziridines were prepared from acid chlorides and from carboxylic acids.

1. A mixture of 0.027 mole of acid chloride (72, 73, 74 or 75),

1.4 g. (0.033 mole) of aziridine, and 3.3 g. (0.033 mole) of triethylamine in 400 ml. of dry benzene was magnetically stirred for three hours as the temperature was allowed to rise from an initial 0° to room temperature. The precipitated triethylamine hydrochloride was removed by vacuum filtration, the filtrate concentrated, and the resultant solid or oil was dissolved in 60 ml. of benzene, placed in two 30 ml. portions onto silica gel columns, and eluted with benzene (300 ml.). The eluted solutions were combined and concentrated to give the products.

2. A mixture of 0.057 mole of carboxylic acid (65, 66, 67 or 68), 11.7 g. (0.0057 mole) of dicyclohexylcarbodiimide, and 2.5 g. (0.057 mole) of aziridine in 450 ml. of anhydrous tetrahydrofuran was magnetically stirred at room temperature for five hours. The precipitated dicyclohexylurea was removed by vacuum filtration, the filtrate was concentrated to give a viscous oil (an oil was obtained in all four cases). The oil was dissolved in 100 ml. of benzene and passed in four parts through silica gel columns with benzene (300 ml.) as eluant. Concentration of the combined eluted solutions gave the product.

4-(7-Benz[a]anthracenyl)benzaziridamide (77)

1. Compound 77 was isolated by the first method as a light yellow crystalline solid, m.p. 175-180°; yield 7.5 g. (75%). This crude material was used with excellent results in subsequent reactions. An analytical sample was prepared by four recrystallizations of the crude product from ethyl acetate, and the product was obtained as light yellow crystals, m.p. 204-205° [Lit.[44] 187-189°].

Anal. Calcd. for $C_{27}H_{19}NO$: C, 86.83; H, 5.14; N, 3.75.

Found: C, 86.98; H, 5.20; N (*) 3.83.

nmr($CDCl_3$): multiplet 4.8-3.7 ppm (15 protons); singlet 1.2 ppm (4 protons).

ir(20% $CHCl_3$): 3050, 2950, 1690, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 390, 368, 352, 292, 281, 270, 258 mu.

2. Compound 77 was obtained by the second method as a clear viscous oil which readily crystallized when 25 ml. of ethyl acetate was added. The precipitated product was isolated as light yellow crystals, m.p. 173-180°; yield 15 g. (70%). This material was used in subsequent reactions without further purification. A portion was purified by four recrystallizations from ethyl acetate, and the product was isolated as light yellow crystals, m.p. 204-205°.

3-(7-Benz[a]anthracenyl)benzaziridamide (76)

1. Compound 76 was isolated by the first method as a light yellow viscous oil which could not be crystallized from a variety of solvents, including ethyl acetate, absolute ethanol, and benzene-hexane. This crude oil was used with good results in subsequent reactions. The yield of the crude oily product was 8 g. (78%).

nmr($CDCl_3$): multiplet 4.8-3.7 ppm (15 protons): singlet 1.2 ppm (4 protons).

ir(20% $CDCl_3$): 3050, 3940, 1690, multiplet 990-700 cm^{-1}.

uv(95% ethanol): 390, 368, 352, 280, 270, 258 mu.

2. Compound 76 was obtained by the second method as a clear viscous oil which could not be crystallized from a variety of solvents, including ethyl acetate, absolute ethanol, and benzene-hexane. The yield of the crude oily product was 15.5 g. (72%), and the oil was used with good

results in subsequent reactions without further purification.

4-(9-Anthracenyl)benzaziridamide (79)

1. Compound 79 was isolated by the first method as greenish yellow crystals, m.p. 173-178°; yield 6.4 g. (73%). This crude material was used in subsequent reactions without further purification. A portion was purified for analysis by four recrystallizations from chloroform-absolute ethanol (3:7), and the product was obtained as bright greenish yellow crystals, m.p. 185-186°.

Anal. Calcd. for $C_{23}H_{17}NO$: C, 85.41; H, 5.31; N, 4.33.

Found: C, 85.34; H, 5.21; N, 4.15.

nmr($CDCl_3$): multiplet 4.4-3.4 ppm (13 protons); singlet 1.2 ppm (4 protons).

ir(20% $CHCl_3$): 3050, 2940, 1690, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 365, 348, 255 (broad) mu.

2. Compound 79 was obtained by the second method as a clear viscous oil which readily crystallized when 25 ml. of ethyl acetate was added, and the product was obtained as bright greenish yellow crystals, m.p. 165-169°; yield 12.6 g. (68%). This material was used with good results in subsequent reactions without further purification. A portion was recrystallized four times from chloroform-absolute ethanol (3:7), m.p. 184-186°.

3-(9-Anthracenyl)benzaziridamide (78)

1. Compound 78 was isolated by the first method as a light yellow viscous oil which could not be crystallized from a variety of solvents, including ethyl acetate, absolute ethanol, and benzene-hexane. This crude oil was used with good results in subsequent reactions. The yield

of the crude oil was 7 g. (76%).

nmr($CDCl_3$): multiplet 4.4-3.7 ppm (13 protons); singlet 1.2 ppm (4 protons).

ir(20% $CHCl_3$): 3050, 2950, 1690, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 385, 365, 348, 255 (broad) mu.

2. Compound 78 was isolated by the second method as a clear viscous oil which could not be crystallized from benzene-hexane, absolute ethanol, or ethyl acetate. The oil was used in subsequent reactions without further purification. The crude yield was 13 g. (71%).

3-(9-Anthracenyl)benzaziridamide (78')

The reaction of 0.027 mole of acid chloride 74 (prepared with thionyl chloride), 1.4 g. (0.033 mole) of aziridine and 3.3 g. (0.033 mole) triethylamine in benzene by the same procedure used in the first method gave here a yellow solid, m.p. 140-143°. The compound was purified by three chromatography procedures through silica gel, with benzene as eluant (250 ml.), seven recrystallizations from ethyl acetate, and four treatments with charcoal. The product still contained impurities and was isolated as yellow needles, m.p. 146-147°; yield 6.5 g. (79%).

Anal. Calcd. for $C_{23}H_{17}NO$: C, 85.41; H, 5.31; N, 4.33.

Found (**): C, 77.43; H, 3.14; N, 3.67; S, 1.04.

Nmr, ir, and uv spectra for 78' were similar to 78 except for a slight distortion of the aromatic region in the nmr spectrum.

In the case of 76, 77, and 79 the same products were obtained using acid chlorides prepared with thionyl chloride as with oxalyl chloride. The products, however, were much more difficult to purify, requiring at least two treatments with charcoal in addition to chromatography through

silica gel (250 ml. of benzene as eluant) and recrystallization procedures.

E. Preparation of Amides and Derivatives.

The four N-(2-chloroethyl)amides 81, 82, 83 and 84 were each prepared from 1-aroylaziridines and from acid chlorides.

1. Anhydrous hydrogen chloride was bubbled vigorously through a solution of 0.0083 mole of 1-aroylaziridine (76, 77, 78 or 79) in 100 ml. of chloroform at room temperature for one-fourth hour. The solution was then transferred to a separatory funnel, washed successively with 100 ml. of water, 100 ml. of 10% sodium bicarbonate solution, twice with 100 ml. portions of water, and the chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered, concentrated, and the product was isolated as a solid (a solid was isolated in all four cases).

2. A solution of 0.042 mole of acid chloride (72, 73, 74 or 75) in 300 ml. of benzene was added over a one-fourth hour period to a mixture of 6.1 g. (0.053 mole) of 2-chloroethylamine hydrochloride and 5.2 g. (0.13 mole) of sodium hydroxide in 100 ml. of benzene and 200 ml. of water contained in a flask immersed in an ice bath at 0°. The mixture was magnetically stirred at 0° for three hours, the product was removed by filtration (the product precipitated during the reaction in all four cases) and dried at 50° (10 mm.) for five hours.

4-(7-Benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (82)

1. Compound 82 was obtained by the first method as a white solid, purified by four recrystallizations from benzene, and the product was

isolated as a white powdery solid, m.p. 203-208°; yield 3 g. (90%).

Anal. Calcd. for $C_{27}H_{20}ClNO$: C, 79.10; H, 4.93; N, 3.42; Cl, 8.65.
Found: C, 78.82; H, 4.82; N, 3.48; Cl, 8.89.

nmr(DMSO): multiplet 5.1-4.1 ppm (15 protons); slightly jagged singlet at 2.0 ppm (4 protons).

ir(KBr): 3050, 2950, 1635, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 391, 368, 352, 292, 281, 271, 258 mu.

2. Compound 82 was obtained by the second method, after drying, as a white solid that was purified by one recrystallization from benzene and was obtained as a white solid, m.p. 200-204°; yield 14.3 g. (83%). This material was dried at 50° (10 mm.) for five hours and used in subsequent reactions without further purification.

3-(7-Benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (81)

1. Compound 81 was obtained by the first method as a brown crystalline solid, purified by five recrystallizations from ethyl acetate, and the product was obtained as white nugget crystals, m.p. 135-138°; yield 2.4 g. (71%).

Anal. Calcd. for $C_{27}H_{20}ClNO$: C, 79.10; H, 4.83; N, 3.42; Cl, 8.65.
Found (*): C, 79.21; H, 5.01; N, 3.24; Cl, 8.52.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); slightly jagged singlet 1.99 ppm (4 protons).

ir(KBr): 3050, 2950, 1633, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 370, 353, 291, 281, 258 mu.

2. Compound 81 was obtained by the second method, after drying, as white crystalline solid which was recrystallized once from ethyl acetate, dried at 35° (10 mm.) for six hours, and used in subsequent reactions

without further purification; m.p. 133-135°; yield 14.7 g. (86%).

4-(9-Anthracenyl)-N-(2-chloroethyl)benzamide (84)

1. Compound 84 was obtained by the first method as a yellow solid, purified by four recrystallizations from benzene, and the product was isolated as light yellow scaly crystals, m.p. 203-206°; yield 2.5 g. (89%).

Anal. Calcd. for $C_{23}H_{18}ClNO$: C, 76.76; H, 5.05; N, 3.89; Cl, 9.85.
Found: C, 77.04; H, 5.23; N, 3.66; Cl (*) 9.98.

nmr(DMSO): multiplet 4.65-3.95 ppm (13 protons); slightly jagged singlet 2.0 ppm (4 protons).

ir(KBr): 3050, 2948, 1635, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 382, 363, 348, 254 (broad) mu.

2. Compound 84 was obtained by the second method, after drying, as a yellow solid, which was recrystallized once from benzene, dried at 45° (10 mm.) for four hours, and used in subsequent reactions without further purification; m.p. 203-206°; yield 13 g. (85%).

3-(9-Anthracenyl)-N-(2-chloroethyl)benzamide (83)

1. Compound 83 was obtained by the first method as a brown solid, purified by five recrystallizations from ethyl acetate, and the product was isolated as yellow needles, m.p. 167-169°; yield 2.2 g. (78%).

Anal. Calcd. for $C_{23}H_{18}ClNO$: C, 76.76; H, 5.05; N, 3.89; Cl, 9.85.
Found (**): C, 76.87; H, 5.09; N, 3.81; Cl, 9.68.

nmr($CDCl_3$): multiplet 4.65-3.95 ppm (13 protons); slightly jagged singlet 2.0 ppm (4 protons).

ir(KBr): 3049, 2950, 1633, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 383, 363, 348, 254 (broad) mu.

2. Compound 83 was obtained by the second method, after drying, as yellow solid which was recrystallized once from ethyl acetate, dried at 50° (10 mm.) for four hours, and used in subsequent reactions without further purification; m.p. 166-169°; yield 12.6 g. (84%).

4-(7-Benz[a]anthracenyl)-N-(2-bromoethyl)benzamide (85)

Anhydrous hydrogen bromide was bubbled vigorously through a solution of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) in 50 ml. of chloroform at room temperature for one-fourth hour. The solution was then transferred to a separatory funnel, washed successively with 50 ml. of water, 50 ml. of 10% sodium bicarbonate solution, twice with 50 ml. portions of water, and the chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered, concentrated, and the resultant white solid was recrystallized five times from benzene. The product was obtained as white powdery solid, m.p. 203-208°; yield 3.2 g. (87%).

Anal. Calcd. for $C_{27}H_{20}BrNO$: C, 71.36; H, 4.45; N, 3.08; Br, 17.59.
Found (*): C, 71.50; H, 4.38; N, 3.27; Br, 17.88.

nmr(DMSO): multiplet 5.1-4.1 ppm (15 protons); slightly jagged singlet 1.99 ppm (4 protons).

ir(KBr): 3050, 2950, 1634, multiplet 900-700 cm^{-1}.

uv(95% ethanol); 392, 368, 352, 292, 271, 258 mu.

4-(7-Benz[a]anthracenyl)-N-(2-iodoethyl)benzamide (86)

A mixture of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) in 50 ml. of benzene and 10 ml. of 45% aqueous hydriodic acid was magnetically stirred at 0° for one-fourth hour. The

benzene layer was separated and diluted with benzene to a volume of 100 ml. The benzene layer was washed successively with 50 ml. of water, 50 ml. of 10% sodium bicarbonate solution, twice with 50 ml. portions of water, and the benzene layer was separated and dried over sodium sulfate. The dried solution was filtered after one-fourth hour, concentrated, and the resultant viscous solid was recrystallized five times from ethyl acetate solution. The product was isolated as light yellow powdery solid, m.p. 196-198°; yield 3 g. (73%).

Anal. Calcd. for $C_{27}H_{20}INO$: C, 64.69; H, 4.03; N, 2.79; I, 25.31.
Found (**): C, 64.45; H, 3.80; N, 2.51; I, 24.04.

nmr(DMSO): multiplet 5.1-4.1 ppm (15 protons); slightly jagged singlet 2.0 ppm (4 protons).

ir(KBr): 3050, 2950, 1634, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 391, 368, 354, 292, 282, 272, 258 mu.

4-(7-Benz[a]anthracenyl)-N-(2-thiolethyl)benzamide (87)

A mixture of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) in 100 ml. of tetrahydrofuran and 50 ml. of 45% aqueous ammonium sulfide was magnetically stirred at room temperature for 12 hours. The mixture was transferred to a separatory funnel, the aqueous layer was saturated with sodium chloride, the tetrahydrofuran layer was separated and washed successively with 50 ml. of water, 50 ml. of 10% sodium bicarbonate solution and twice with 50 ml. portions of water (each water washing was saturated with sodium chloride). The tetrahydrofuran layer was separated, dried over sodium sulfate one-fourth hour, filtered and concentrated to give a viscous pale reddish-brown oil. The oil was dissolved in 50 ml. of ethyl acetate, cooled overnight,

and the precipitated product was isolated by vacuum filtration. The product -- now insoluble in benzene, ethyl acetate, chloroform, or tetrahydrofuran -- was recrystallized five times from dimethylsulfoxide-absolute ethanol (6:4). The product was isolated as a light yellow powdery solid, m.p. 304-306°; yield 1.2 g. (43%). (Yield based on weight of product after one crystallization from dimethylsulfoxide-absolute ethanol.)

Anal. Calcd. for $C_{27}H_{21}NOS$: C, 79.53; H, 5.24; N, 3.44; S, 7.86.
Found (**): C, 79.03; H, 5.15; N, 3.53; S, 8.27.

nmr(DMSO): multiplet 5.2-4.1 ppm (15 protons); broad bands centered at 1.75 ppm (2 protons) and 2.09 ppm (2 protons); singlet at 1.37 ppm (1 proton).

ir(KBr): 3050, 2920, 1645, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 393, 368, 351, 292, 282, 272, 258 mu.

4-(7-Benz[a]anthracenyl-N-(2-diethylaminoethyl)benzamide (88)

A mixture of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) and 1.2 g. (0.016 mole) of diethylamine in 50 ml. of benzene was refluxed for 12 hours, the solution was concentrated, and the resultant viscous oil was crystallized from ethyl acetate. The product was recrystallized four times from ethyl acetate and isolated as white feathery needles, m.p. 164-166°; yield 2.7 g. (76%).

Anal. Calcd. for $C_{31}H_{30}NO_2$: C, 83.36; H, 6.78; N, 6.27.
Found (**): C, 83.52; H, 6.85; N, 6.00.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); quartets centered at 1.96 ppm (2 protons) and 1.44 ppm (6 protons); triplet centered at 0.59 ppm (6 protons).

ir(KBr): 3050, 2960, 1625, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 368, 352, 292, 282, 272, 258 mu.

4-(7-Benz[a]anthracenyl)-N-(2-methylsulfonylethyl)benzamide (89)

A mixture of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) and 1.5 g. (0.016 mole) of methanesulfonic acid in 75 ml. of benzene was magnetically stirred at room temperature for three hours, the solution was concentrated, and the resultant yellow solid was taken up in 25 ml. of ethyl acetate and vacuum filtered. The solid was vacuum washed with 100 ml. of ethyl ether in 10 ml. portions. The solid was then recrystallized five times from toluene-95% ethanol (7:3), and the product was obtained as white powdery solid, m.p. 236-238°; yield 2.8 g. (74%).

Anal. Calcd. for $C_{28}H_{23}NO_4S$: C, 71.61; H, 4.95; N, 2.98; S, 6.83.
Found (**): C, 71.68; H, 5.07; N, 2.94; S, 6.54.

nmr(DMSO): multiplet 5.2-4.1 ppm (15 protons); broad bands centered at 2.56 ppm (2 protons) and 1.90 ppm (2 protons); singlet at 1.40 ppm (3 protons).

ir(KBr): 3050, 2950, 1720, 1260, 1190, 1100, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 366, 351, 293, 283, 271, 258 mu.

4-(7-Benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide (90)

To 6.3 g. (0.06 mole) of N,N-bis(2-chloroethyl)amine hydrochloride dissolved in 50 ml. of water and contained in a separatory funnel was added 100 ml. of 10% sodium hydroxide solution. After the solution was shaken for several minutes, the aqueous layer was extracted three times with 75 ml. portions of benzene, and the benzene layers were combined

and dried two hours over sodium sulfate. The dried solution -- containing the neutralized N,N-bis(2-chloroethyl)amine -- was filtered and added to a solution of 10 g. (0.027 mole) of 4-(7-benz[a]anthracenyl)-benzoyl chloride (73) in 100 ml. of dry benzene. The solution was magnetically stirred at room temperature in a closed flask for three hours. The precipitated N,N-bis(2-chloroethyl)amine hydrochloride was removed by vacuum filtration, and the filtrate was concentrated to give a clear viscous oil. Attempts to precipitate the product from dry benzene-hexane, ethyl acetate, and methylene chloride were unsuccessful. The product was used in subsequent reactions without purification.

2-(2'-Chloroethylamino)ethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride (91)

3 g. (0.0064 mole) of 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide (90) oil was refluxed in a solution of 100 ml. of 95% ethanol and 50 ml. of tetrahydrofuran for five hours. The solution was concentrated to give a greenish yellow oil which crystallized from 95% ethanol-ethyl acetate (3:7). The solid was recrystallized four more times from 95% ethanol-ethyl acetate (3:7), and the product was isolated as white crystals, m.p. 209-211°; yield 2.5 g. (84%).

Anal. Calcd. for $C_{29}H_{25}Cl_2NO_2$: C, 71.01; H, 5.15; N, 2.86; Cl, 14.46.

Found (**): C, 71.26; H, 5.09; N, 2.60; Cl, 14.69.

One gram of the salt was added to 50 ml. of 10% sodium hydroxide solution and stirred for one-half hour until all the solid disappeared. The mixture was transferred to a separatory funnel and extracted twice with 25 ml. portions of benzene, and the benzene layers were combined and dried over sodium sulfate. The dried solution was filtered and concentrated to give the free amine as a clear viscous oil. An nmr spectrum of this oil was obtained.

nmr, neutralized salt ($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); three triplets centered at 2.43 ppm (2 protons), 1.95 ppm (2 protons), and 1.61 ppm (4 protons); singlet at 1.07 ppm (1 proton).

ir, with salt (KBr): 3050, 2950, 2750-2650 (broad), 1734, multiplet 900-700 cm^{-1}.

uv, with salt (95% ethanol): 392, 364, 349, 292, 282, 272, 258 mu.

2-Aminoethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride (93)

3 g. (0.0073 mole) of 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)-benzamide (82) was refluxed in 100 ml. of 95% ethanol. The solid completely disappeared after four hours reflux, and the solution was then concentrated to give a white solid, m.p. 190-195°. The solid was recrystallized five times from absolute ethanol-ethyl acetate (3:7), and the product was isolated as white crystals, m.p. 197-200°; yield 2.9 g. (91%).

Anal. Calcd. for $C_{27}H_{22}ClNO_2$: C, 78.71; H, 5.39; N, 3.40; Cl, 8.61.
Found (**): C, 78.58; H, 5.58; N, 3.23; Cl, 8.35.

ir(KBr): 3050-2850 (broad), 1720, multiplet 900-700 cm^{-1}.

4-(7-Benz[a]anthracenyl)-N-(2-hydroxyethyl)benzamide (95)

2.5 g. (0.0058 mole) of 2-aminoethyl-4-(7-benz[a]anthracenyl)-benzoate hydrochloride (93) was added to a mixture of 50 ml. of chloroform and 50 ml. of 10% sodium hydroxide solution, and the mixture was stirred at room temperature for one hour as the solid slowly disappeared. The chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered and concentrated to give a

viscous oil which was taken up in 25 ml. of ethyl acetate and cooled overnight. The precipitated product was isolated by vacuum filtration and recrystallized four times from ethyl acetate. The product was obtained as light yellowish white plate crystals, m.p. 217-219°; yield 1.6 g. (66%).

Anal. Calcd. for $C_{27}H_{21}NO_2$: C, 82.83; H, 5.42; N, 3.58.

Found (**): C, 82.80; H, 5.45; N, 3.69.

nmr(DMSO): multiplet 5.3-4.1 ppm (15 protons); multiplet band centered at 2.05 ppm (4 protons); singlet at 1.42 ppm (1 proton).

ir(KBr): 3050, 2930, 1625, multiplet 900-700 cm^{-1}.

4-(7-Benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzylamine hydrochloride (92)

To 4 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide (90) oil in 100 ml. of anhydrous tetrahydrofuran was added 24 ml. of 1M diborane in tetrahydrofuran, and the solution was stirred in a closed flask for 12 hours at room temperature and then refluxed for one hour. The tetrahydrofuran solution was poured slowly into 100 ml. of 10% sodium hydroxide solution saturated with sodium chloride and stirred for one-half hour (the reaction flask was immersed in an ice bath). The mixture was transferred to a separatory funnel, the tetrahydrofuran layer was separated, the water layer was washed twice with 25 ml. portions of tetrahydrofuran, the tetrahydrofuran layers were combined, washed successively with 50 ml. of water, 50 ml. of 10% sodium bicarbonate, twice with 50 ml. portions of water, and the tetrahydrofuran layer was separated and dried over sodium sulfate. The dried solution was

filtered and concentrated to give a clear viscous oil which did not crystallize from benzene-hexane, ethyl acetate or 95% ethanol. The oil was dissolved in 75 ml. of tetrahydrofuran and to it was added 25 ml. of ethyl ether saturated with hydrogen chloride. The mixture was concentrated, and the resultant viscous solid was recrystallized five times from 95% ethanol-ethyl acetate (7:3), and the product was obtained as white crystals, m.p. 273-276° [Lit.[44] m.p. 162-164°]; yield 2.5 g. (63%).

Anal. Calcd. for $C_{29}H_{26}Cl_3N$: C, 70.37; H, 5.31; N, 2.83; Cl, 21.49.

Found (**): C, 69.77; H, 5.15; N, 2.74; Cl, 22.29.

ir(KBr): 3000-2700 (broad); multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 365, 353, 292, 282, 269, 272, 258 mu.

4-(7-Benz[a]anthracenyl)-N-(2-chloroethyl)benzylamine hydrochloride (94)

To 4 g. (0.0097 mole) of 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)-benzamide (82) in 400 ml. of anhydrous tetrahydrofuran was added 29 ml. of 1M diborane in tetrahydrofuran, and the solution was stirred in a closed flask for 14 hours at room temperature and then refluxed for two hours. The tetrahydrofuran solution was poured slowly into 100 ml. of 10% sodium hydroxide solution saturated with sodium chloride and contained in a flask immersed in an ice bath. The mixture was stirred one-half hour and then transferred to a separatory funnel. The tetrahydrofuran layer was separated, the water layer was washed twice with 25 ml. portions of tetrahydrofuran, the tetrahydrofuran layers were combined and washed successively with 50 ml. of water, 50 ml. of 10% sodium bicarbonate solution, twice with 50 ml. portions of water, and the tetrahydrofuran layer was separated and dried over sodium sulfate. (The water

washings were saturated with sodium chloride.) The dried solution was filtered and concentrated to give a clear viscous oil. The oil was dissolved in 100 ml. of tetrahydrofuran and to this was added 50 ml. of ethyl ether saturated with hydrogen chloride. The mixture was concentrated, the resultant white solid was recrystallized five times from 95% ethanol-ethyl acetate (8:2), and the product was obtained as white crystals, m.p. 259-262°; yield 3 g. (71%).

Anal. Calcd. for $C_{27}H_{23}Cl_2N$: C, 74.99; H, 5.37; N, 3.24; Cl, 16.40.
Found (**): C, 75.63; H, 5.19; N, 3.41; Cl, 15.99.

ir(KBr): 3050-2650 (broad); multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 368, 352, 292, 271, 258 mu.

F. Preparation of 2-Oxazolines and Hydrochloride Salts.

4-(7-Benz[a]anthracenyl)phenyl-2-oxazoline (97)

1. A mixture of 8.2 g. (0.022 mole) of 4-(7-benz[a]anthracenyl)-benzaziridamide (77) and 20 g. (0.13 mole) of powdered sodium iodide in 200 ml. of tetrahydrofuran was refluxed for 24 hours with vigorous mechanical stirring. The solution was then concentrated, the residue was dissolved by the addition of 100 ml. of chloroform and 100 ml. of water, and the chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered and concentrated to give a viscous oil. The oil readily crystallized when 50 ml. of 95% ethanol was added. The solid was recrystallized four times from benzene-95% ethanol (1:1), and the product was obtained as white flaky crystals, m.p. 223-224°; yield 7.5 g. (84%).

Anal. Calcd. for: $C_{27}H_{19}NO$: C, 86.83; H, 5.14; N, 3.75.

Found: C, 86.92; H, 5.23; N, 3.58.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); two triplet centered at 2.2 ppm (2 protons) and 2.4 ppm (2 protons).

ir($CHCl_3$): 3050, 2920, 1652, 1210, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 391, 367, 352, 292, 281, 271, 258 mu.

2. Metallic sodium [0.6 g. (0.028 mole)] was added to 25 ml. of absolute ethanol. After the sodium had reacted 2.3 g. (0.0056 mole) of 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (82) was added, and the mixture was heated to reflux. Tetrahydrofuran (50 ml.) was added to make the amide more soluble. The mixture was refluxed four hours, cooled to room temperature, 50 ml. of 95% ethanol was added, the mixture was stirred for one-fourth hour and concentrated to give a mixture of viscous oil and solid. The mixture was dissolved in 30 ml. of benzene and passed through a silica gel column with benzene (300 ml.) as eluant. Concentration of the eluted benzene gave a viscous oil which crystallized upon the addition of 70 ml. of 95% ethanol, m.p. 218-222°; yield 1.1 g. (53%).

3-(7-Benz[a]anthracenyl)phenyl-2-oxazoline (96)

1. A mixture of 8.2 g. (0.022 mole) of 3-(7-benz[a]anthracenyl)-benzaziridamide (76) and 20 g. (0.13 mole) of powdered sodium iodide in 200 ml. of tetrahydrofuran was refluxed for 27 hours with vigorous mechanical stirring. The solution was then concentrated, the residue was dissolved by the addition of 100 ml. of chloroform and 100 ml. of water, and the chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered and concentrated to give a viscous oil. The oil slowly crystallized when 50 ml. of 95% ethanol was added. The solid was purified by three recrystallizations from benzene-95% ethanol

(7:3) and one treatment with charcoal. The product was obtained as white crystals, m.p. 188-189°; yield 6 g. (73%).

Anal. Calcd. for $C_{27}H_{19}NO$: C, 86.83; H, 5.14; N, 3.75.

Found (**): C, 87.07; H, 5.00; N, 3.58.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); two triplets centered at 2.2 ppm (2 protons) and 2.4 ppm (2 protons).

ir($CHCl_3$): 3050, 2940, 1652, 1210, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 392, 366, 352, 292, 282, 272, 258 mu.

2. Metallic sodium (0.6 g. (0.028 mole)) was added to 25 ml. of absolute ethanol. After the sodium had reacted 2.3 g. (0.0056 mole) of 3-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (81) was added, and the mixture was refluxed four hours, cooled to room temperature, 50 ml. of 95% ethanol was added and the mixture was stirred for one-fourth hour and concentrated to give a viscous oil. The oil was dissolved in 25 ml. of benzene and passed through a silica gel column with benzene (300 ml.) as eluant. Concentration of the eluted benzene gave a viscous oil which slowly crystallized after the addition of 25 ml. of ethyl acetate and 25 ml. of absolute ethanol, m.p. 183-186°; yield 0.9 g. (46%).

4-(9-Anthracenyl)phenyl-2-oxazoline (99)

1. A mixture of 9.17 g. (0.03 mole) of 4-(9-anthracenyl)benzaziridamide (79) and 22 g. (0.15 mole) of powdered sodium iodide in 200 ml. of tetrahydrofuran was refluxed for 24 hours with vigorous mechanical stirring. The solution was then concentrated, the residue was dissolved by the addition of 150 ml. of chloroform and 75 ml. of water, and the chloroform layer was separated and dried over sodium sulfate. The

dried solution was filtered and concentrated to give a light green viscous oil which readily crystallized when 50 ml. of 95% ethanol was added. The solid was recrystallized four times from chloroform-95% ethanol (4:6), and the product was isolated as greenish yellow needles, m.p. 274-275°; yield 8.4 g. (86%).

Anal. Calcd. for $C_{23}H_{17}NO$: C, 85.41; H, 5.31; N, 4.33.

Found: C, 85.35; H, 5.24; N, 4.28.

nmr($CDCl_3$): multiplet 4.6-4.0 ppm (13 protons); two triplets centered at 2.44 ppm (2 protons) and 2.22 ppm (2 protons).

ir($CHCl_3$): 3050, 2920, 1620, 1210, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 385, 365, 347, 264 (broad) mu.

2. Metallic sodium [0.6 g. (0.028 mole)] was added to 25 ml. of absolute ethanol. After the sodium had reacted 2 g. (0.0056 mole) of 4-(9-anthracenyl)-N-(2-chloroethyl)benzamide (84) was added, and the mixture was heated to reflux. Anhydrous tetrahydrofuran (60 ml.) was added to make the amide more soluble. The mixture was refluxed four hours, cooled to room temperature, 50 ml. of 95% ethanol was added, the mixture was stirred for one-fourth hour and concentrated to give a mixture of viscous oil and solid. The mixture was dissolved in 25 ml. of benzene and passed through a silica gel column with benzene (300 ml.) as eluant. Concentration of the eluted benzene gave a viscous oil which crystallized upon the addition of 50 ml. of 95% ethanol, m.p. 269-272°; yield 0.95 g. (55%).

3-(9-Anthracenyl)phenyl-2-oxazoline (98)

1. A mixture of 10 g. (0.031 mole) of 3-(9-anthracenyl)benzaziridamide (78) and 22 g. (0.15 mole) of powdered sodium iodide in 260

ml. of tetrahydrofuran was refluxed for 24 hours with vigorous mechanical stirring. The solution was then concentrated, the residue was dissolved by the addition of 150 ml. of chloroform and 100 ml. of water, and the chloroform layer was separated and dried over sodium sulfate. The dried solution was filtered and concentrated to give a pale brown oil which crystallized on standing. The solid was purified by four recrystallizations from tetrahydrofuran-95% ethanol (7:3) and one treatment with charcoal, and the product was isolated as light yellowish white needles, m.p. 159-161°; yield 7.1 g. (70%).

Anal. Calcd. for $C_{23}H_{17}NO$: C, 85.41; H, 5.31; N, 4.33.

Found: C, 85.54; H, 5.14; N, 4.14.

nmr($CDCl_3$): multiplet 4.6-4.0 ppm (13 protons); two triplets centered at 2.4 ppm (2 protons) and 2.2 ppm (protons).

ir($CHCl_3$): 3050, 2920, 1652, 1210, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 385, 365, 347, 254 (broad) mu.

2. Metallic sodium [0.6 g. (0.028 mole)] was added to 25 ml. of absolute ethanol. After the sodium had reacted 2 g. (0.0065 mole) of 3-(9-anthracenyl)-N-(2-chloroethyl)benzamide (83) was added, and the mixture was heated to reflux. Anhydrous tetrahydrofuran (50 ml.) was added to make the amide more soluble. The mixture was refluxed four hours, cooled to room temperature, 50 ml. of 95% ethanol was added, the mixture was stirred for one-fourth hour and concentrated to give a mixture of viscous oil and solid. The mixture was dissolved in 25 ml. of benzene and passed through a silica gel column with benzene (300 ml.) as eluant. Concentration of the eluted benzene gave a viscous oil which crystallized upon the addition of 30 ml. of 95% ethanol, m.p. 155-158°; yield 0.95 g. (52%).

4-(7-Benz[a]anthracenyl)phenyl-2-oxazoline hydrochloride (101)

To 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)phenyl-2-oxazoline (97) in 150 ml. of tetrahydrofuran at room temperature was added 60 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred one-fourth hour, concentrated, the resultant white solid was recrystallized four times from absolute ethanol, and the product was isolated as white powdery crystals, m.p. 203-205°; yield 2.8 g. (84%).

Anal. Calcd. for $C_{27}H_{20}ClNO$: C, 79.10; H, 4.93; N, 3.42; Cl, 8.65.
Found (**): C, 79.31; H, 4.68; N, 3.23; Cl, 8.79.

ir(KBr): 3050, 1640, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 389, 364, 351, 292, 281, 271, 257 mu.

3-(7-Benz[a]anthracenyl)phenyl-2-oxazoline hydrochloride (100)

To 3 g. (0.008 mole) of 3-(7-benz[a]anthracenyl)phenyl-2-oxazoline (96) in 75 ml. of tetrahydrofuran at room temperature was added 50 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred one-fourth hour, concentrated, and the resultant oil slowly crystallized from ethyl ether-ethyl acetate (1:1) after cooling overnight. The resultant white solid was recrystallized four times from ethyl acetate-absolute ethanol-ethyl ether (2:7:1), and the product was isolated as white powdery solid, m.p. 197-199°; yield 2.5 g. (73%).

Anal. Calcd. for $C_{27}H_{20}ClNO$: C, 79.10; H, 4.93; N, 3.42; Cl, 8.65.
Found (**): C, 79.27; H, 5.11; N, 3.35; Cl, 8.81.

ir(KBr): 3050, 2960, 1650, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 388, 367, 349, 292, 281, 271, 258 mu.

4-(9-Anthracenyl)phenyl-2-oxazoline hydrochloride (103)

To 3 g. (0.009 mole) 4-(9-anthracenyl)phenyl-2-oxazoline (99) in 150 ml. tetrahydrofuran at room temperature was added 60 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred one-fourth hour, concentrated, and the resultant light green oil was crystallized when 50 ml. of ethyl acetate was added. The solid was recrystallized four times from absolute ethanol, and the product was isolated as light yellow feathery crystals, m.p. 199-201°; yield 2.8 g. (86%).

Anal. Calcd. for $C_{23}H_{18}ClNO$: C, 76.76; H, 5.05; N, 3.89; Cl, 9.85.
Found (**): C, 76.83; H, 5.10; N, 3.99; Cl, 10.05.

ir(KBr): 3050, 2960, 1640, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 364, 347, 352 (broad) mu.

3-(9-Anthracenyl)phenyl-2-oxazoline hydrochloride (102)

To 2.5 g. (0.0077 mole) of 3-(9-anthracenyl)phenyl-2-oxazoline (98) in 150 ml. of warm tetrahydrofuran was added 25 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred one-fourth hour, concentrated, and the resultant yellow oil was recrystallized four times from absolute ethanol, and the product was isolated as greenish yellow nugget crystals, m.p. 152-154°; yield 1.8 g. (70%).

Anal. Calcd. for $C_{23}H_{18}ClNO$: C, 76.76; H, 5.05; N, 3.89; Cl, 9.85.
Found (**): C, 76.82; H, 5.07; N, 3.74; Cl, 9.61.

ir(KBr): 3050, 1630, 1640, multiplet 900-700 cm^{-1}.

uv(95%) ethanol): 384, 364, 347, 352 (broad) mu.

G. Preparation of 2-Thiazolines.

4-(7-Benz[a]anthracenyl)phenyl-2-thiazoline (105)

1. To 7 g. (0.017 mole) of 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (82) dissolved in 700 ml. of refluxing anhydrous toluene, contained in a 1-liter flask equipped with a mechanical stirrer, was added 7.6 g. (0.034 mole) of phosphorus pentasulfide, and the resultant mixture was refluxed five hours. After one-half hour the bottom of the flask was coated with viscous red oil. After five hours reflux the mixture was cooled to room temperature, the solvent was decanted from the red oil and concentrated to give a yellow solid. The yellow solid was dissolved in 200 ml. of tetrahydrofuran-200 ml. of 10% sodium hydroxide, the solution was poured back into the reaction flask, and the mixture was stirred one hour at room temperature as the red oil was completely decomposed. The mixture was transferred to a 2-liter separatory funnel, the tetrahydrofuran layer was separated, and the aqueous layer was saturated with sodium chloride and extracted twice with 50 ml. portions of tetrahydrofuran. The tetrahydrofuran layers were combined and washed successively with 100 ml. of water, 100 ml. of 10% sodium bicarbonate solution, and twice more with 100 ml. portions of water (the water washings were saturated with sodium chloride). The tetrahydrofuran solution was dried over sodium sulfate, filtered, and concentrated to give a yellow viscous oil. The oil was dissolved in 50 ml. of benzene and passed in two 25 ml. portions through silica gel columns with benzene as eluting (500 ml.) solvent. The eluted benzene solutions were combined, concentrated, the resultant white solid was recrystallized four times from chloroform-absolute ethanol (7:3), and the

product was isolated as white needles, m.p. 211-213°; yield 5 g. (76%).

Anal. Calcd. for $C_{27}H_{19}NS$: C, 83.24; H, 4.93; N, 3.59; S, 8.23.

Found (**): C, 83.06; H, 4.90; N, 3.56; S, 8.22.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); two triplets centered at 2.45 ppm (2 protons) and 1.85 ppm (2 protons).

ir(KBr): 3050, 2940, 2850, 1605, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 391, 366, 353, 292, 281, 271, 258 mu.

2. In a 500 ml. flask equipped with a mechanical stirrer, a mixture of 3 g. (0.008 mole) of 4-(7-benz[a]anthracenyl)benzaziridamide (77) and 3.6 g. (0.016 mole) of phosphorus pentasulfide in 100 ml. of toluene was refluxed for three hours (after one-fourth hour the bottom of the reaction flask was coated with a viscous red oil). After three hours of reflux, the mixture was cooled to room temperature, the solvent was decanted from the red oil and concentrated to give a yellow solid. The solid was dissolved in 100 ml.of tetrahydrofuran-100 ml. of 10% sodium hydroxide, this solution was poured back into the reaction flask, and the mixture was stirred at room temperature for one hour as the red oil was decomposed. The mixture was transferred to a separatory funnel, the tetrahydrofuran layer was separated, the aqueous layer was saturated with sodium chloride and twice extracted with 50 ml. portions of tetrahydrofuran. The tetrahydrofuran layers were combined, washed successively with 75 ml. of water, 75 ml. of 10% sodium bicarbonate, twice with 75 ml. portions of water, and the tetrahydrofuran layer was dried over sodium sulfate. The dried solution was filtered, concentrated, and the resultant pale red oil was dissolved in 25 ml. of benzene and passed through a silica gel column with benzene (500 ml.)

as the eluting solvent. The eluted benzene was concentrated, the resultant white solid was recrystallized twice from chloroform-absolute ethanol (7:3), and the product was isolated as white needles, m.p. 210-212°.

3-(7-Benz[a]anthracenyl)phenyl-2-thiazoline (104)

1. A mixture of 7 g. (0.017 mole) of 3-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (81) and 7.5 g. (0.034 mole) of phosphorus pentasulfide in 400 ml. of toluene was refluxed for five hours (a viscous red oil coated the bottom of the reaction flask after one-half hour). The mixture was cooled to room temperature and worked up by the same procedure used to prepare 105 (part 1.). The isolated tetrahydrofuran solution was dried over sodium sulfate, then filtered and concentrated to give a viscous yellow oil. The oil was dissolved in 50 ml. of benzene and passed in two 25 ml. portions through silica gel columns with benzene (500 ml.) as the eluting agent. Concentration of the eluted benzene gave a light yellow transparent oil which slowly crystallized from benzene-95% ethanol (7:3). The solid was recrystallized four times from benzene-95% ethanol (8:2), and the product was isolated as white spherical crystals, m.p. 173-174°; yield 4.7 g. (76%).

Anal. Calcd. for $C_{27}H_{19}NS$: C, 83.24; H, 4.93; N, 3.59; S, 8.23.
Found (**): C, 83.37; H, 4.97; N, 3.58; S, 8.07.

nmr($CDCl_3$): multiplet 5.0-4.0 ppm (15 protons); two triplets centered at 1.4 ppm (2 protons) and 1.8 ppm (2 protons).

ir(KBr): 3050, 2940, 2850, 1650, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 382, 365, 353, 292, 281, 271, 258 mu.

2. A mixture of 3 g. (0.008 mole) of 3-(7-benz[a]anthracenyl)-

benzaziridamide (76) and 3.6 g. (0.016 mole) of phosphorus pentasulfide in 100 ml. of toluene was refluxed for three hours (a viscous red oil coated the bottom of the reaction flask after one-fourth hour). The mixture was cooled to room temperature and worked up by the same procedure used for the preparation of 105 (part 2.). The isolated tetrahydrofuran layer was dried over sodium sulfate, filtered, concentrated, and the resultant red oil was passed through silica gel with benzene (500 ml.) as the eluting agent. The eluted benzene was concentrated, and the isolated oil slowly crystallized from benzene-95% ethanol (7:3) as white spherical crystals, m.p. 171-174°; yield 2.2 g. (71%).

4-(9-Anthracenyl)phenyl-2-thiazoline (107)

1. A mixture of 5.8 g. (0.016 mole) of 4-(9-anthracenyl)-N-(2-chloroethyl)benzamide (84) and 7.1 g. (0.032 mole) of phosphorus pentasulfide in 600 ml. of toluene, contained in a 1-liter flask equipped with a mechanical stirrer, was refluxed for five hours (a viscous red oil coated the bottom of the reaction flask after one-fourth hour). The mixture was cooled to room temperature and worked up by the same procedure used in the preparation of 105 (part 1.). The isolated tetrahydrofuran solution was dried over sodium sulfate, filtered, concentrated, and the resultant yellow solid was dissolved in 75 ml. of benzene and passed in two equal portions through silica gel columns with benzene (500 ml.) as the eluting agent. Concentration of the eluted benzene gave a light greenish yellow solid which was recrystallized three times from chloroform-95% ethanol (8:2), and the product was isolated as light greenish yellow plate crystals, m.p. 215-217°; yield 4.8 g. (88%).

Anal. Calcd. for $C_{23}H_{17}NS$: C, 81.37; H, 5.06; N, 4.13; S, 9.45.

Found (**): C, 81.25; H, 4.83; N, 4.13; S, 9.26.

nmr($CDCl_3$): multiplet 4.6-4.0 ppm (13 protons); two triplets centered at 2.5 ppm (2 protons) and 1.9 ppm (2 protons).

ir(KBr): 3050, 2940, 2850, 1605, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 365, 347, 254 (broad) mu.

2. A mixture of 3 g. (0.009 mole) of 4-(9-anthracenyl)benzaziridamide (79) and 3.9 g. (0.018 mole) of phosphorus pentasulfide in 100 ml. of toluene was mechanically stirred and refluxed for three hours (a viscous red oil coated the surface of the reaction flask after one-fourth hour). The mixture was then cooled to room temperature and worked up by the same procedure used in the preparation of 105 (part 2.). The isolated tetrahydrofuran solution was dried over sodium sulfate, filtered, concentrated, the yellow solid isolated was dissolved in 30 ml. of benzene and passed through a silica gel column with benzene (500 ml.) as the eluting agent. The eluted benzene was concentrated, the resultant greenish yellow solid was recrystallized once from chloroform-95% ethanol (7:3), m.p. 212-214°; yield 2.4 g. (77%).

3-(9-Anthracenyl)phenyl-2-thiazoline (106)

1. To 7 g. (0.021 mole) of 3-(9-anthracenyl)-N-(2-chloroethyl)-benzamide (83) dissolved in 300 ml. of refluxing toluene, contained in a 1-liter flask equipped with a mechanical stirrer was added 9.3 g. (0.042 mole) of phosphorus pentasulfide, and the resultant mixture was refluxed for five hours (a viscous red oil coated the bottom of the reaction flask after one-fourth hour). The mixture was then cooled to room temperature and worked up by the same procedure used in the

preparation of 105 (part 2.). The isolated tetrahydrofuran solution was dried over sodium sulfate, filtered, concentrated, and the resultant red oil was dissolved in 50 ml. of benzene and passed in two portions through silica gel columns with benzene (500 ml.) as the eluting agent. The eluted benzene was concentrated, and the resultant yellow oil slowly crystallized from absolute ethanol. The solid was recrystallized four times from absolute ethanol, and the product was isolated as light yellow needles, m.p. 126-128°; yield 5.8 g. (80%).

Anal. Calcd. for $C_{23}H_{17}NS$: C, 81.37; H, 5.06; N, 4.13; S, 9.45.

Found (**): C, 81.37; H, 5.09; N, 3.89; S, 9.37.

nmr($CDCl_3$): multiplet 4.6-4.0 ppm (13 protons); two triplets centered at 2.45 ppm (2 protons) and 1.85 ppm (2 protons).

ir(KBr): 3050, 2930, 2840, 1600, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 382, 364, 346, 255 (broad) mu.

2. A mixture of 3 g. (0.009 mole) of 3-(9-anthracenyl)benzaziridamide (78) and 4 g. (0.018 mole) of phosphorus pentasulfide in 100 ml. of toluene was mechanically stirred and refluxed for three hours (a viscous red oil coated the bottom of the reaction flask after one-fourth hour). The mixture was cooled to room temperature and worked up by the same procedure used for the preparation of 105 (part 2.). The isolated tetrahydrofuran layer was dried over sodium sulfate, filtered, concentrated, and the resultant red oil was passed through silica gel with benzene (500 ml.) as the eluting agent. The eluted benzene was concentrated, and the isolated yellow oil slowly crystallized from absolute ethanol as light yellow needles, m.p. 119-123°.

H. Preparation of 2-Imidazolines and Hydrochloride Salts.

4-(7-Benz[a]anthracenyl)benzamide (2)

The acid chloride reagent 73 which was prepared from 12 g. (0.034 mole) of 7-(4-carboxyphenyl)benz[a]anthracene (66) (see Experimental, Section C.) was dissolved in 400 ml. of tetrahydrofuran, a small quantity of liquid ammonia was added, and the mixture was magnetically stirred as the excess liquid ammonia was allowed to evaporate. The tetrahydrofuran mixture was concentrated, the resultant viscous solid was taken up in 75 ml. of 95% ethanol and vacuum filtered. The solid was vacuum washed thoroughly with water (300 ml.), dried in a vacuum oven at 50° (10 mm.) for five hours, and the product was isolated as white powdery solid, m.p. 292-297°; yield 10.4 g. (89%). This product was used without further purification in a subsequent reaction to prepare the cyano compound 112. A portion of the amide was recrystallized twice from chloroform-95% ethanol (7:3), and the product was isolated as white crystals, m.p. 298-300° [Lit.[108] 298-300°].

3-(7-Benz[a]anthracenyl)benzamide (108)

The acid chloride reagent 72 which was prepared from 15 g. (0.04 mole) of 7-(3-carboxyphenyl)benz[a]anthracene (65) (see Experimental, Section C.) was dissolved in 350 ml. of tetrahydrofuran, a small quantity of liquid ammonia was added, and the mixture was magnetically stirred at room temperature as the excess liquid ammonia was allowed to evaporate. The tetrahydrofuran mixture was concentrated, the resultant viscous solid was taken up in cold 95% ethanol (75 ml.) and vacuum filtered. The solid was then thoroughly vacuum washed with water (200 ml.), dried in a vacuum oven at 50° (10 mm.) for six hours,

and the product was isolated as light brown crystals, m.p. 132-135°; yield 12.1 g. (87%). This product was used without further purification in a subsequent reaction to prepare the cyano compound 111. A portion of the amide was purified by four recrystallizations from 95% ethanol and one treatment with charcoal, and the product was isolated as white crystals, m.p. 135-137°.

Anal. Calcd. for $C_{25}H_{17}NO$: C, 86.42; H, 4.94; N, 4.03.
Found (**): C, 86.22; H, 4.98; N, 4.25.

ir(KBr): 3050, 2970, 1660, multiplet 900-700 cm^{-1}.

4-(9-Anthracenyl)benzamide (110)

The acid chloride reagent 75 which was prepared from 13 g. (0.04 mole) of 9-(4-carboxyphenyl)anthracene (68) (see Experimental, Section C.) was dissolved in 650 ml. of tetrahydrofuran, a small quantity of liquid ammonia was added, and the mixture was magnetically stirred at room temperature as the excess liquid ammonia was allowed to evaporate. The tetrahydrofuran mixture was concentrated, the resultant viscous solid was taken up in cold 95% ethanol (75 ml.) and vacuum filtered. The solid was then thoroughly vacuum washed with water (300 ml.), dried in a vacuum oven at 55° (10 mm.) for six hours, and the product was isolated as light yellow solid, m.p. 267-270°; yield 10 g. (86%). This product was used without further purification in a subsequent reaction to prepare the cyano compound 114. A portion of the amide was purified by four recrystallizations from tetrahydrofuran-95% ethanol (7:3), and the product was isolated as white needles, m.p. 270-271°.

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.81; H, 5.09; N, 4.71.

Found (**): C, 84.98; H, 5.09; N, 4.90.

3-(9-Anthracenyl)benzamide (109)

The acid chloride 74 which was prepared from 15 g. (0.05 mole) of 9-(3-carboxyphenyl)anthracene (67) (see Experimental, Section C.) was dissolved in 400 ml. of tetrahydrofuran, a small quantity of liquid ammonia was added, and the mixture was magnetically stirred at room temperature as the excess liquid ammonia was allowed to evaporate. The tetrahydrofuran mixture was concentrated, the resultant viscous solid was taken up in cold 95% ethanol (75 ml.) and vacuum filtered. The solid was then thoroughly vacuum washed with water (300 ml.), dried at 35° (0.3 mm.) for 20 hours, and the product was isolated as greenish yellow transparent needles, m.p. 90-94°. This product apparently is a semistable ethanolate or hydrate. The solid was redried over toluene at 110° (0.3 mm.) for eight hours, and the product was used without further purification in a subsequent reaction to prepare the cyano compound 113. A portion of the amide was purified by four recrystallizations from 95% ethanol, and the product was isolated as opaque greenish yellow needles, m.p. 199-200°.

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.81; H, 5.09; N, 4.71.

Found (**): C, 84.98; H, 5.24; N, 4.68.

ir(KBr): 3050, 1660, multiplet 900-700 cm^{-1}.

4-(7-Benz[a]anthracenyl)cyanobenzene (112)

To a solution of 9 g. (0.025 mole) of 4-(7-benz[a]anthracenyl)-benzamide (2) in 900 ml. of refluxing toluene, contained in a 2-liter flask equipped with a mechanical stirrer, was added 18 g. (0.13 mole)

of phosphorus pentoxide, and the resultant mixture was refluxed for 24 hours. After one hour the bottom of the flask became coated with viscous gray oil. After 24 hours of reflux the mixture was cooled to room temperature, and the solvent was decanted from the oil and concentrated to give a viscous solid. The viscous solid was dissolved in 100 ml. of tetrahydrofuran-100 ml. of 10% sodium hydroxide, and this solution was poured back into the reaction flask which was immersed in an ice bath. The resultant mixture was stirred at room temperature for one hour as all the gray oil was decomposed. The solution was then transferred to a separatory funnel, the tetrahydrofuran layer was separated, the aqueous layer was saturated with sodium chloride and extracted twice with 50 ml. portions of tetrahydrofuran, the tetrahydrofuran layers were combined and washed successively with 100 ml. of water, 100 ml. of 10% sodium bicarbonate, and twice with 100 ml. portions of water. The tetrahydrofuran layer was separated and dried over sodium sulfate, and the dried solution was filtered and concentrated to give a viscous oil. The oil was dissolved in 50 ml. of ethyl acetate and cooled overnight. Some unreacted amide 2 (1.5 g.) was removed by vacuum filtration, the filtrate was concentrated, and the resultant oil was dissolved in 30 ml. of benzene and passed through a silica gel column with benzene (300 ml.) as the eluting agent. Concentration of the eluted benzene gave an oil which readily crystallized when 25 ml. of 95% ethanol was added. The solid was recrystallized once from 95% ethanol, and the product was isolated as white crystals, m.p. 196-198° [Lit.[17] 196-198°]; yield 5.3 g. (64%).

3-(7-Benz[a]anthracenyl)cyanobenzene (111)

To a solution of 9 g. (0.025 mole) of 3-(7-benz[a]anthracenyl)-benzamide (108) in 900 ml. of refluxing toluene, contained in a 2-liter flask equipped with a mechanical stirrer, was added 18 g. (0.13 mole) of phosphorus pentoxide, and the resultant mixture was refluxed for 24 hours. After one hour the bottom of the flask became coated with viscous gray oil. After 24 hours of reflux the mixture was cooled to room temperature and the reaction was worked up by the same procedure used in the preparation of 112. The isolated tetrahydrofuran layer was dried over sodium sulfate, filtered, concentrated, and the resultant oil was dissolved in 50 ml. of benzene and passed in two portions through silica gel columns with benzene (300 ml.) as the eluting agent. The eluted benzene was concentrated and the resultant oil slowly crystallized from benzene-heptane (1:3). The solid was recrystallized four times from benzene-heptane (1:3), and the product was isolated as white powdery solid, m.p. 153-155°; yield 5.6 g. (67%).

Anal. Calcd. for $C_{25}H_{15}N$: C, 91.15; H, 4.59; N, 4.25.

Found (**): C, 91.25; H, 4.76; N, 4.02.

4-(9-Anthracenyl)cyanobenzene (114)

To a solution of 9 g. (0.03 mole) of 4-(9-anthracenyl)benzamide (110) in 1000 ml. of refluxing toluene, contained in a 2-liter flask equipped with a mechanical stirrer, was added 17 g. (0.12 mole) of phosphorus pentoxide, and the resultant mixture was refluxed for 18 hours. After one hour the bottom of the flask became coated with viscous brownish red oil. After 18 hours of reflux the mixture was cooled to room temperature, and the reaction was worked up by the same

procedure used in the preparation of 112. The isolated tetrahydrofuran layer was dried over sodium sulfate, filtered, concentrated, and the resultant viscous solid was dissolved in 25 ml. of ethyl acetate and cooled overnight. Some unreacted amide 110 (1.6 g.) precipitated and was isolated by vacuum filtration, the filtrate was concentrated, and the resultant oil was dissolved in 50 ml. of benzene and passed in two 25 ml. portions through silica gel with benzene (300 ml.) as the eluting agent. The eluted benzene was concentrated, the resultant oil readily crystallized when 25 ml. of 95% ethanol was added. The solid was recrystallized once from 95% ethanol, and the product was isolated as greenish yellow needles, m.p. 134-135° [Lit.[51] 125-126°]; yield 5.6 g. (68%).

3-(9-Anthracenyl)cyanobenzene (113)

To a solution of 10 g. (0.033 mole) of 3-(9-anthracenyl)benzamide (109) in 600 ml. of refluxing toluene, contained in a 2-liter flask equipped with a mechanical stirrer, was added 18.4 g. (0.13 mole) of phosphorus pentoxide, and the resultant mixture was refluxed for 18 hours. After one hour the bottom of the flask became coated with pale red oil. After 18 hours of reflux the mixture was cooled to room temperature, and the reaction was worked up by the same procedure used in the preparation of 112. The isolated tetrahydrofuran layer was dried over sodium sulfate, filtered, concentrated, and the resultant viscous oil was dissolved in 50 ml. of benzene and passed in two 25 ml. portions through silica gel columns with benzene (300 ml.) as the eluting agent. The eluted benzene was concentrated, and the resultant oil slowly crystallized from chloroform-95% ethanol (1:4) solution. The

solid was recrystallized four times from chloroform-95% ethanol (1:4) and the product was isolated as greenish yellow plate crystals, m.p. 129-130°; yield 5.6 g. (61%).

Anal. Calcd. for $C_{21}H_{13}N$: C, 90.28; H, 4.70; N, 5.02.
Found (**): C, 90.49; H, 4.73; N, 5.13.

4-(7-Benz[a]anthracenyl)phenyl-2-imidazoline (116)

4-(7-Benz[a]anthracenyl)cyanobenzene (112) [4 g. (0.012 mole)] was refluxed in 30 ml. of ethylenediamine for five hours. The product precipitated from the solution as the reaction progressed. After the reaction was complete, the mixture was cooled overnight, the solid was isolated by vacuum filtration and washed with 100 ml. of water, and the product was dried at 35° (0.3 mm.) for four hours. The solid was then recrystallized five times from chloroform-ethyl acetate (1:1), and the product was isolated as light yellow scaly crystals, m.p. 221.5-223°; yield 3.7 g. (84%).

Anal. Calcd. for $C_{27}H_{20}N_2$: C, 87.05; H, 5.42; N, 7.52.
Found (**): C, 87.20; H, 5.38; N, 7.47.
ir(KBr): 3050, 2930, 2860, 1610, multiplet 900-700 cm^{-1}.
uv(95% ethanol): 389, 368, 351, 291, 280, 270, 255 mu.

3-(7-Benz[a]anthracenyl)phenyl-2-imidazoline (115)

3-(7-Benz[a]anthracenyl)cyanobenzene (111) [5 g. (0.015 mole)] was refluxed in 50 ml. of anhydrous ethylenediamine for five hours. The resultant solution was cooled overnight without any precipitation. The solvent was then removed under reduced pressure to give a brown viscous oil which readily crystallized when 25 ml. of methanol was added. The

mixture was vacuum filtered, and the solid was washed with 100 ml. of water. The washed solid was dried at 35° (0.3 mm.) for five hours, purified by four recrystallizations from 95% ethanol-ethyl acetate (1:9) and one treatment with charcoal, and the product was isolated as white crystals, m.p. 227-229°; yield 4.1 g. (76%).

Anal. Calcd. for $C_{27}H_{20}N_2$: C, 87.05; H, 5.42; N, 7.52.
Found (**): C, 86.91; H, 5.42; N, 7.35.

nmr(DMSO): multiplet 5.25-4.0 ppm (15 protons); broad band centered at 3.1 ppm (1 proton); singlet at 2.0 ppm (4 protons).

ir(KBr): 3050, 2930, 2860, 1600, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 389, 365, 350, 291, 281, 271, 257 mu.

4-(9-Anthracenyl)phenyl-2-imidazoline (118)

4-(9-Anthracenyl)cyanobenzene (114) [5 g. (0.018 mole)] was refluxed in 40 ml. of anhydrous ethylenediamine for six hours. The product precipitated as the reaction progressed. The mixture was cooled overnight, vacuum filtered, and the product was washed with 100 ml. of water. The solid was dried at 35° (0.3 mm.) for five hours and recrystallized five times from 95% ethanol-chloroform (7:3). The product was isolated as light yellow needles, m.p. 309° decom.; yield 4.8 g. (85%).

Anal. Calcd. for $C_{23}H_{18}N_2$: C, 85.67; H, 5.64; N, 8.69.
Found (**): C, 85.54; H, 5.77; N, 8.65.

ir(KBr): 3050, 2970, 2930, 2860, 1610, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 386, 367, 353, 254 (broad) mu.

3-(9-Anthracenyl)phenyl-2-imidazoline (117)

3-(9-Anthracenyl)cyanobenzene (113) [5 g. (0.018 mole)] was refluxed in 50 ml. of anhydrous ethylenediamine for five hours. After the reaction was complete, the solution was cooled overnight but the product did not precipitate. The solvent was then removed under reduced pressure to give a viscous brown solid. The solid was taken up in 25 ml. of 95% ethanol and vacuum filtered. The solid was washed with 100 ml. of water, dried five hours at 35° (0.3 mm.) and purified by four recrystallizations from chloroform-95% ethanol (3:4) and one treatment with charcoal. The product was collected as light yellow crystals, m.p. 241-242°; yield 4.2 g. (71%).

Anal. Calcd. for $C_{23}H_{18}N_2$: C, 85.67; H, 5.64; N, 8.69.

Found (**): C, 85.91; H, 5.86, N, 8.43.

nmr($CDCl_3$): multiplet 4.7-4.0 ppm (13 protons); broad band centered at 2.5 ppm (1 proton); singlet at 2.0 ppm (4 protons).

ir(KBr): 3050, 2920, 2860, 1610, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 365, 347, 253 (broad) mu.

4-(7-Benz[a]anthracenyl)phenyl-2-imidazoline hydrochloride (120)

To 2.5 g. (0.067 mole) of 4-(7-benz[a]anthracenyl)phenyl-2-imidazoline (116) dissolved in 100 ml. of hot tetrahydrofuran was added 50 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was magnetically stirred at room temperature for one-fourth hour, and then concentrated to give a white solid. The solid was recrystallized five times from absolute ethanol-ethyl acetate (8:2), and the product was isolated as white powdery solid, m.p. 325° decomp.; yield 2.2 g. (81%).

Anal. Calcd. for $C_{27}H_{21}ClN_2$: C, 79.29; H, 5.19; N, 6.85; Cl, 8.67.
Found (**): C, 79.35; H, 5.34; N, 6.75; Cl, 8.74.
ir(KBr): 3050, 2960-2880 (broad), 1610 multiplet 900-700 cm^{-1}.
uv(95% ethanol): 389, 365, 350, 292, 281, 271, 259 mu.

3-(7-Benz[a]anthracenyl)phenyl-2-imidazoline hydrochloride (119)

To 3 g. (0.008 mole) of 3-(7-benz[a]anthracenyl)phenyl-2-imidazoline (115) dissolved in 100 ml. of tetrahydrofuran at room temperature was added 60 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred at room temperature for one-fourth hour and then concentrated to give an oil. The oil was dissolved in 25 ml. of warm absolute ethanol and crystallized when 50 ml. of ethyl acetate was added. The solid was recrystallized five times from absolute ethanol, and the product was isolated as white flakey crystals, m.p. 291-294°; yield 2.5 g. (75%).

Anal. Calcd. for $C_{27}H_{21}ClN_2$: C, 79.29; H, 5.19; N, 6.85; Cl, 8.67.
Found (**): C, 79.37; H, 5.28; N, 6.64; Cl, 8.87.
ir(KBr): 3050, 2970-2850 (broad), 1610, multiplet 900-700 cm^{-1}.
uv(95% ethanol): 390, 366, 351, 290, 280, 270, 256 mu.

4-(9-Anthracenyl)phenyl-2-imidazoline hydrochloride (122)

To 2.6 g. (0.008 mole) of 4-(9-anthracenyl)phenyl-2-imidazoline (118) dissolved in a warm solution of 275 ml. of chloroform and 100 ml. of absolute ethanol was added 50 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred one-fourth hour as the temperature approached room temperature and then concentrated to give a greenish yellow solid. The solid was recrystallized five times

from absolute ethanol-chloroform (3:1), and the product was isolated as light greenish yellow needles, m.p. 333° decomp.; yield 2.4 g. (85%).

Anal. Calcd. for $C_{23}H_{19}ClN_2$: C, 76.97; H, 5.35; N, 7.81; Cl, 9.88.
Found (**): C, 77.13; H, 5.30; N, 7.83; Cl, 10.10.

ir(KBr): 3050, 2970-2930 (broad), 1610, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 365, 349, 251 (broad) mu.

3-(9-Antrhacenyl)phenyl-2-imidazoline hydrochloride (121)

To 3 g. (0.009 mole) of 3-(9-anthracenyl)phenyl-2-imidazoline (117) dissolved in 100 ml. of tetrahydrofuran at room temperature was added 50 ml. of ethyl ether saturated with anhydrous hydrogen chloride. The mixture was stirred at room temperature for one-fourth hour and then concentrated to give a viscous solid. The solid was recrystallized five times from absolute ethanol-ethyl acetate (3:1), and the product was isolated as light greenish yellow crystals, m.p. 314° decomp.; yield 2.5 g. (77%).

Anal. Calcd. for $C_{23}H_{19}ClN_2$: C, 76.97; H, 5.35; N, 7.81; Cl, 9.88.
Found (**): C, 76.69; H, 5.42; N, 7.54; Cl, 10.18.

ir(KBr): 3050-2850 (broad), 1610, multiplet 900-700 cm^{-1}.

uv(95% ethanol): 384, 364, 347, 253 (broad) mu.

SUMMARY

The four carboxylic acids, 7-(3- and 4-carboxyphenyl)benz[a]-anthracenes (65 and 66) and 9-(3- and 4-carboxyphenyl)anthracenes (67 and 68), were prepared by known five step procedures in sufficient quantities to serve as starting materials in some subsequent reactions. The two acids 65 and 67 were not previously reported.

The two compounds, 7-(3- and 4-bromophenyl)benz[a]anthracenes (70 and 71) were prepared by known procedures. Contrary to the results of several previous investigators, both compounds were found to react with magnesium and form reactive Grignard reagents. While hydrolysis reactions indicated that the Grignard reagents were formed in at least 35-45% yields, carbonation reactions, however, resulted in the formation of the carboxylic acids 66 and 65 in only 20-25% yields.

Oxalyl chloride was found to be superior to thionyl chloride for preparing the acid chloride derivatives of the four carboxylic acids 65, 66, 67 and 68. With thionyl chloride the acid chlorides were invariably obtained as oils which contained impurities that were difficult to remove. With oxalyl chloride all four acid chlorides were obtained as solids which did not contain such impurities.

The four compounds, 3- and 4-(7-benz[a]anthracenyl)benzaziridamides (76 and 77) and 3- and 4-(9-anthracenyl)benzaziridamides (78 and 79), were each prepared by two methods. One method involved reacting an acid chloride (72, 73, 74 or 75) with aziridine and triethylamine in benzene at 0°, while the other method involved reacting a carboxylic acid (65, 66, 67 or 68) directly with aziridine and dicyclohexylcarbodiimide in tetrahydrofuran at room temperature. The two para

compounds 77 and 79 were obtained as solids, while by both methods the two meta compounds 76 and 78 were isolated as oils which could not be crystallized. The latter method was considered to be the better synthetic procedure for preparing all four compounds.

The four compounds, 3- and 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamides (81 and 82) and 3- and 4-(9-anthracenyl)-N-(2-chloroethyl)benzamides (83 and 84), were each prepared by two methods. One method involved reacting an acid chloride (72, 73, 74 or 75) with 2-chloroethylamine hydrochloride and sodium hydroxide in benzene-water at 0°, while the other method involved reacting a 1-aroylaziridine (76, 77, 78 or 79) with anhydrous hydrogen chloride in chloroform at room temperature. The former method was considered to be a better synthetic procedure.

Five compounds were prepared from 4-(7-benz[a]anthracenyl)benzaziridamide (77) by reactions in which the aziridine ring was cleaved by the reagents hydrogen bromide, 45% aqueous hydrogen iodide, diethylamine, 45% aqueous ammonium sulfide, and methanesulfonic acid. By this procedure the following five compounds were prepared in yields of 40-80%: 4-(7-benz[a]anthracenyl)-N-(2-bromoethyl)benzamide (85), 4-(7-benz[a]anthracenyl)-N-(2-iodoethyl)benzamide (86), 4-(7-benz[a]-anthracenyl)-N-(2-diethylaminoethyl)benzamide (88), 4-(7-benz[a]-anthracenyl)-N-(2-thiolethyl)benzamide (87), and 4-(7-benz[a]-anthracenyl)-N-(2-methylsulfonylethyl)benzamide (89). With the exception of the preparation of 87, the reactions occurred readily at room temperature.

4-(7-Benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide (90) was obtained as an oil from the reaction of 4-(7-benz[a]anthracenyl)-

benzoyl chloride (73) with N,N-bis(2-chloroethyl)amine. Both 90 and 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide (82) underwent reactions with water and with diborane which are characteristic for compounds containing the functional groups, N,N-bis(2-chloroethyl)-benzamide or N-(2-chloroethyl)benzamide. The amides 90 and 82 were refluxed in 95% ethanol for short periods of time and were transformed to 2-(2'-chloroethylamino)ethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride (91) and 2-aminoethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride (93), respectively. The amides 90 and 82 were reduced with diborane to nitrogen mustards that were isolated as oils and were converted to the hydrochloride salts, 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzylamine hydrochloride (92) and 4-(7-benz[a]-anthracenyl)-N-(2-chloroethyl)benzyylamine hydrochloride (94), respectively.

The four compounds, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-oxazolines (96 and 97) and 3- and 4-(9-anthracenyl)phenyl-2-oxazolines (98 and 99) were each prepared by two methods. One method involved reacting a N-(2-chloroethyl)amide (81, 82, 83 or 84) with sodium ethoxide, while the other method involved isomerizing a 1-aroyl-aziridine (76, 77, 78 or 79) with sodium iodide catalyst. The latter method was found to be the better synthetic procedure. The following four hydrochloride salt derivatives were prepared by reacting the 2-oxazolines (96, 97, 98 and 99) with anhydrous hydrogen chloride in tetrahydrofuran-ethyl ether solvent: 3- and 4-(7-benz[a]anthracenyl)-phenyl-2-oxazoline hydrochlorides (100 and 101) and 3- and 4-(9-anthracenyl)phenyl-2-oxazoline hydrochlorides (102 and 103).

The four compounds, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-thiazolines (104 and 105) and 3- and 4-(9-anthracenyl)phenyl-2-thiazolines (106 and 107), were each prepared by two different methods. One method involved reacting a N-(2-chloroethyl)amide (81, 82, 83 or 84) with phosphorus pentasulfide in refluxing toluene, while the other method involved reacting a 1-aroylaziridine (76, 77, 78 or 79) with phosphorus pentasulfide in refluxing toluene. The former method was considered to be the better synthetic procedure. The latter type reaction, however, appears to be a new method for preparing 2-thiazolines, not previously reported.

The four amides, 3- and 4-(7-benz[a]anthracenyl)benzamides (108 and 2) and 3- and 4-(9-anthracenyl)benzamides (109 and 110), were prepared by the reactions of acid chlorides with ammonia.

The four cyano compounds, 3- and 4-(7-benz[a]anthracenyl)cyanobenzenes (111 and 112) and 3- and 4-(9-anthracenyl)cyanobenzenes (113 and 114) were prepared by reacting the amides, 108, 2, 109 and 110, with phosphorus pentoxide in refluxing toluene.

The four 2-imidazolines, 3- and 4-(7-benz[a]anthracenyl)phenyl-2-imidazolines (115 and 116) and 3- and 4-(9-anthracenyl)phenyl-2-imidazolines (117 and 118), were prepared by refluxing the cyano compounds 111, 112, 113 and 114 in ethylenediamine. The following four hydrochloride salt derivatives were prepared by reacting the four 2-imidazolines with anhydrous hydrogen chloride in tetrahydrofuran-ethyl ether: 3- and 4-(7-benz[a]anthracenyl)phenyl-2-imidazoline hydrochlorides (119 and 120) and 3- and 4-(9-anthracenyl)phenyl-2-imidazoline hydrochlorides (121 and 122.

In all, 43 new compounds were prepared. The compounds were characterized by elemental analysis, ir, uv, and where possible, by nmr spectroscopy.

APPENDIX

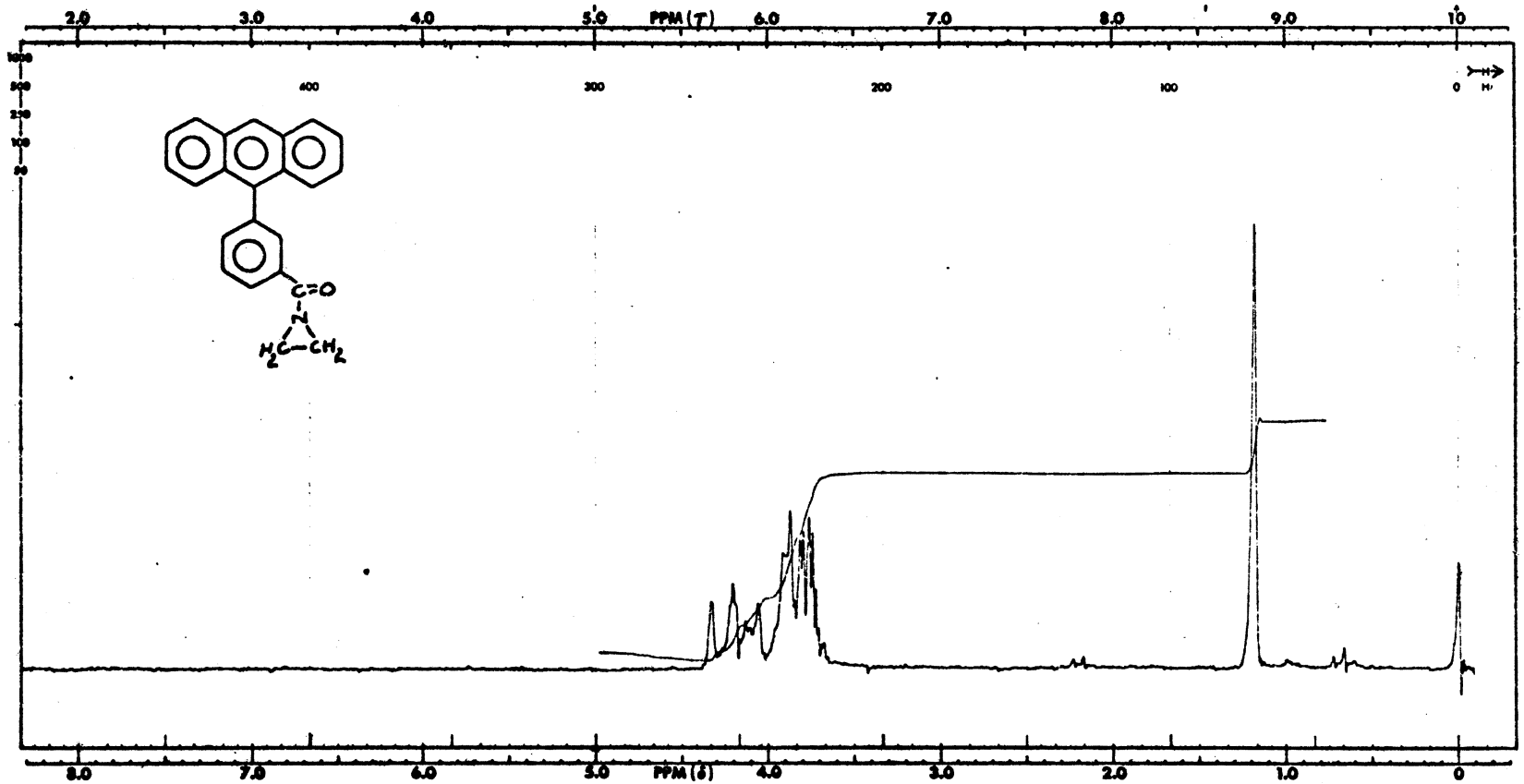


Figure 1: 3-(9-Anthracenyl)benzaziridamide in $CDCl_3$ with TMS (1000 cps)

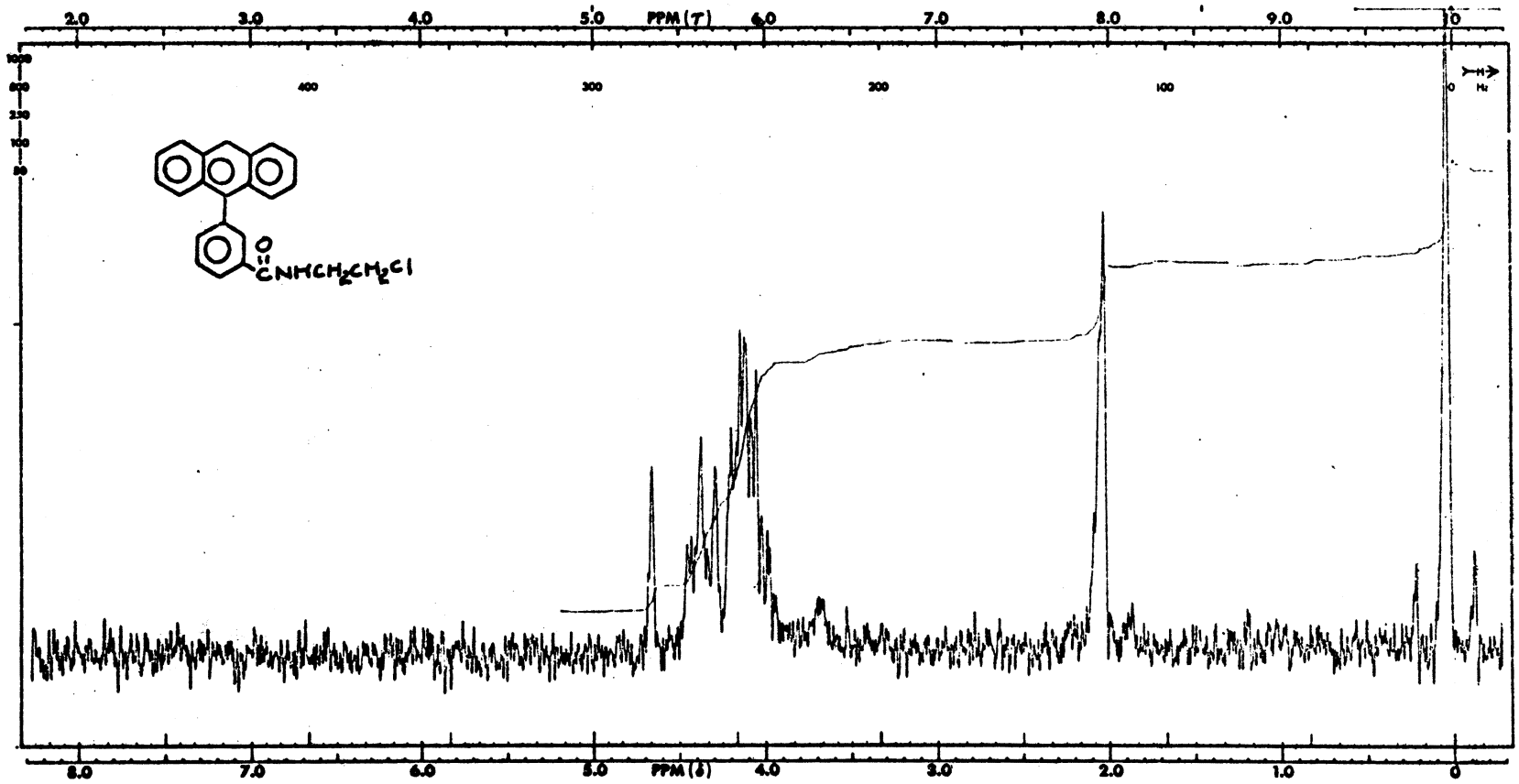


Figure 2: 3-(9-Anthracenyl)-N-(2-chloroethyl)benzamide in $CDCl_3$ with TMS (1000 cps)

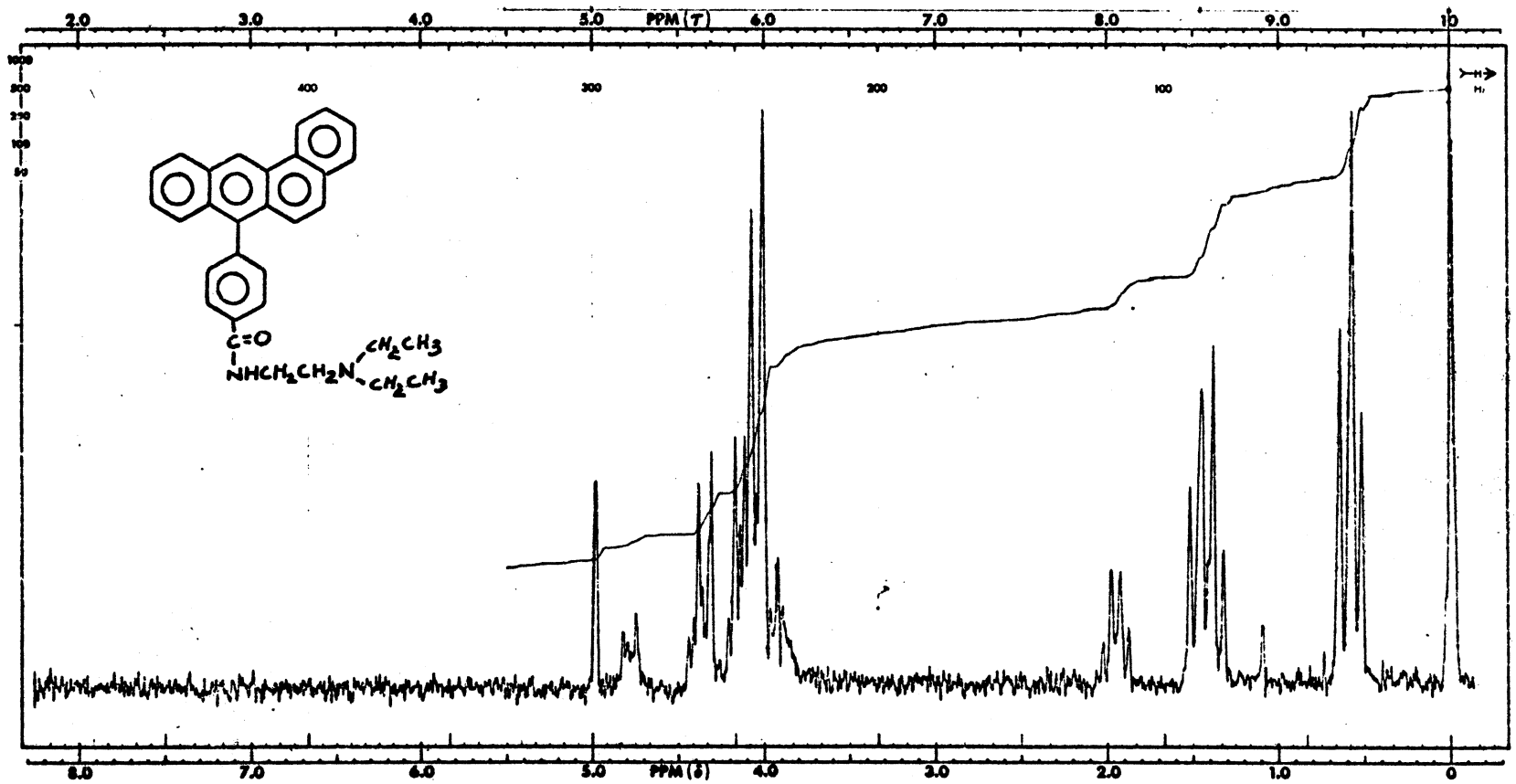


Figure 3: 4-(7-Benz[a]anthracenyl)-N-(2-diethylaminoethyl)benzamide in $CDCl_3$ with TMS (1000 cps)

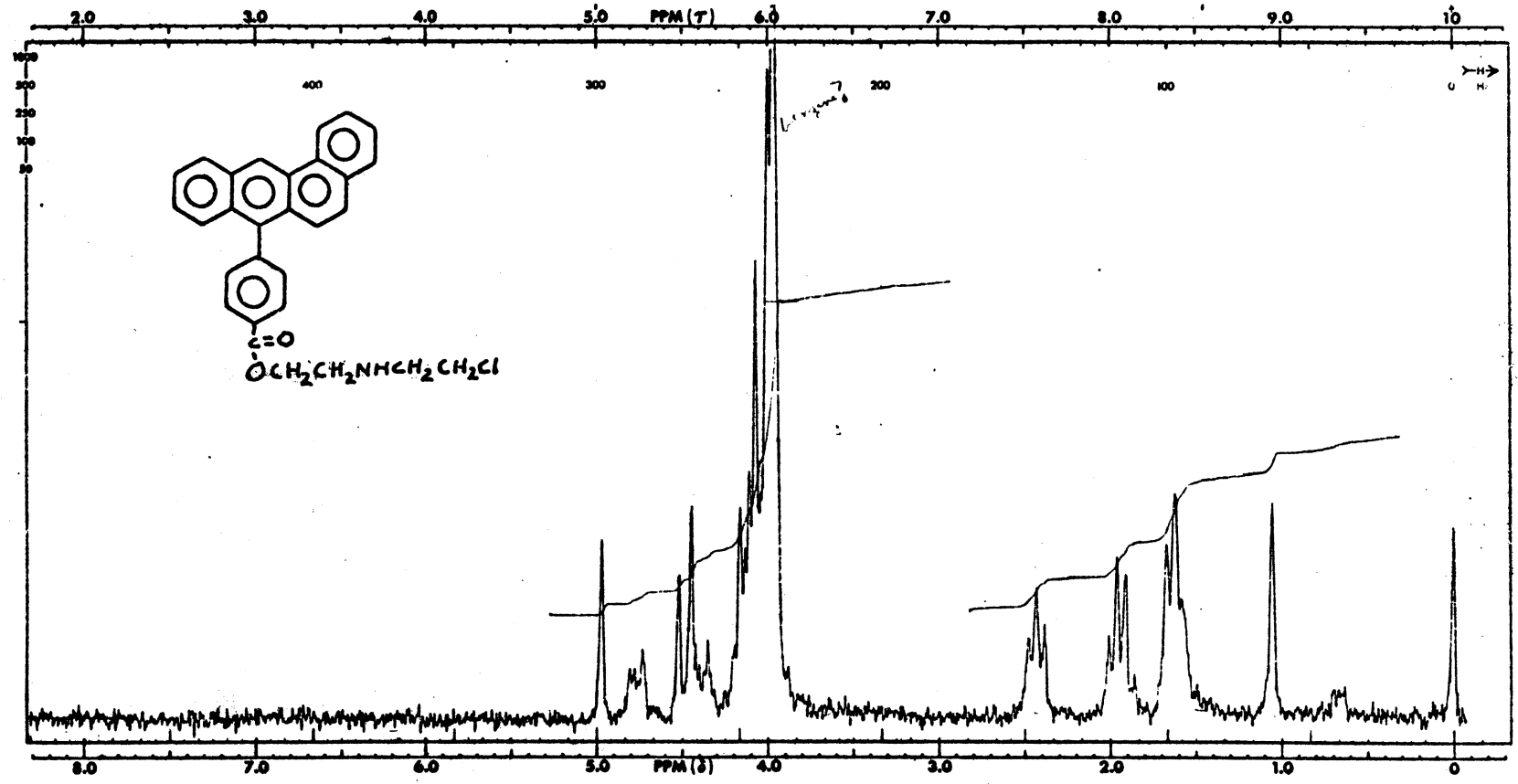


Figure 4: 2-(2'-Chloroethylamino)ethyl-4-(7-benz[a]anthracenyl)benzoate in $CDCl_3$ with TMS (1000 cps)

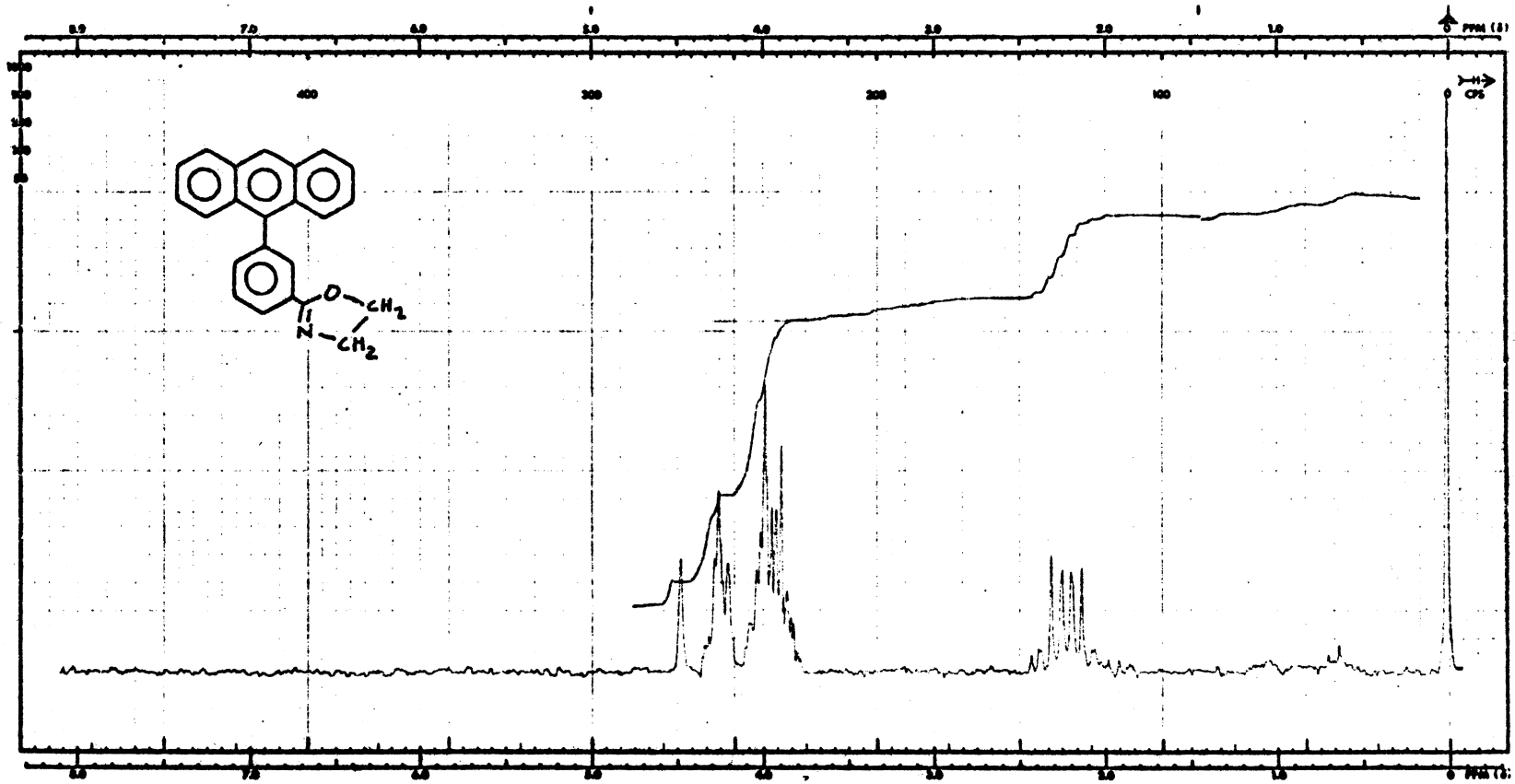


Figure 5: 3-(9-Anthracenyl)phenyl-2-oxazoline in $CDCl_3$ with TMS (1000 cps)

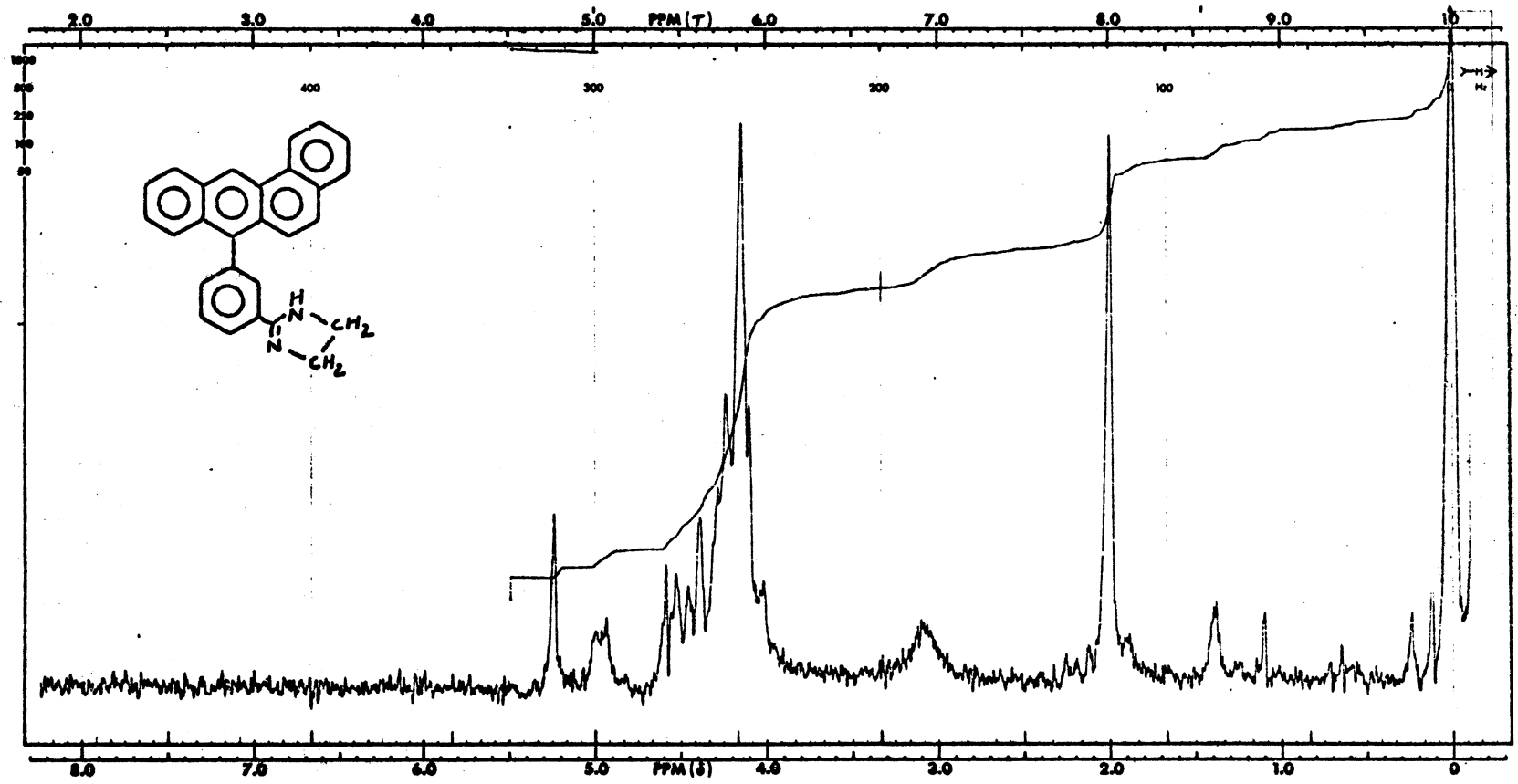


Figure 6: 3-(7-Benz[a]anthracenyl)phenyl-2-imidazoline in DMSO with TMS (1000 cps)

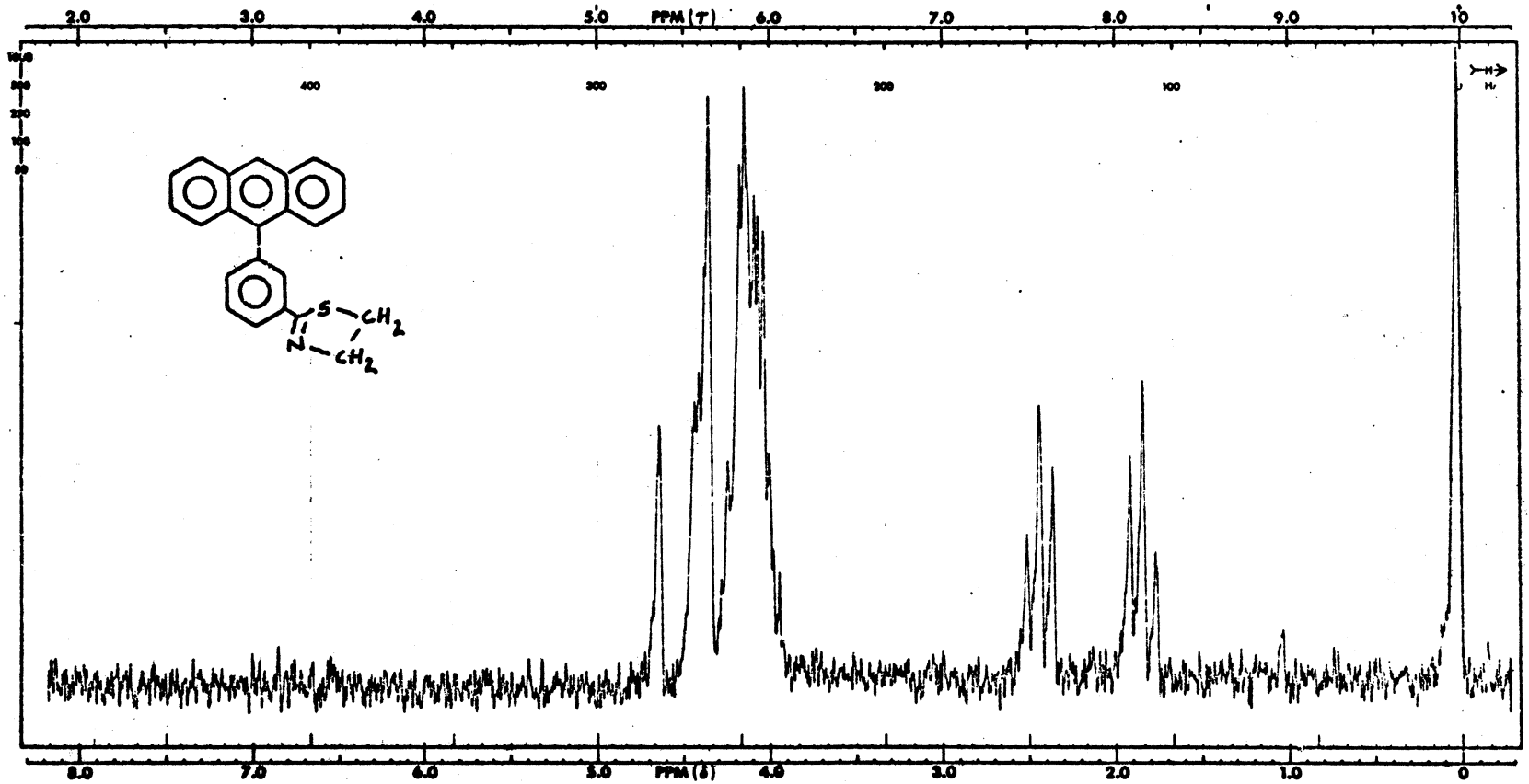


Figure 7: 3-(9-Anthracenyl)phenyl-2-thiazoline in $CDCl_3$ with TMS (1000 cps)

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SYNTHESIS OF SOME DERIVATIVES OF 7-PHENYLBENZ[a]ANTHRACENE AND 9-PHENYLANTHRACENE

by

Morris P. Rorer

Abstract

In view of recent evidence which has indicated that the compound, 4-(7-benz[a]anthracenyl)benzamide, possesses anti-tumor activity, an investigation was undertaken to synthesize a variety of nitrogen containing compounds analogous to 4-(7-benz[a]anthracenyl)benzamide.

The four carboxylic acids, 7-(3- and 4-carboxyphenyl)benz[a]-anthracenes and 9-(3- and 4-carboxyphenyl)anthracenes, were prepared by a published procedure. These four carboxylic acids, as well as their acid chloride and nitrile derivatives, served as starting material for the synthesis of each of the new compounds prepared during this investigation.

A portion of this investigation was concerned with the synthesis of compounds of the nature, 7-(3- and 4-substituted phenyl)benz[a]-anthracenes and 9-(3-and 4-substituted phenyl)anthracenes, in which the following functional groups were substituted at the meta or para positions in each of the four types of compounds: aziridinyl amide, N-(2-chloroethyl)amide, 2-oxazoline and 2-oxazoline hydrochloride salt, 2-thiazoline, and 2-imidazoline and 2-imidazoline hydrochloride salt.

Another portion of this work concerned the preparation of five compounds of the nature 4-(7-benz[a]anthracenyl)-N-(2-substituted ethyl)-benzamide, in which the following functional groups were substituted at the 2- position: -Br, -I, $-N(CH_2CH_3)_2$, $-OSO_2CH_3$, and -SH. Each of

these compounds was prepared from 4-(7-benz[a]anthracenyl)benzaziridamide, in which the aziridine ring was cleaved by the respective reagents, hydrogen bromide, 45% aqueous hydriodic acid, diethylamine, methane-sulfonic acid, and 45% aqueous ammonium sulfide.

Finally, 4-(7-benz[a]anthracenyl)-N,N-bis(2-chloroethyl)benzamide was prepared and hydrolyzed in 95% ethanol to 2-(2'-chloroethylamino)-ethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride. The amide was also reduced with diborane to a nitrogen mustard which was isolated as a hydrochloride salt. Similarly, 4-(7-benz[a]anthracenyl)-N-(2-chloroethyl)benzamide was hydrolyzed in 95% ethanol to 2-aminoethyl-4-(7-benz[a]anthracenyl)benzoate hydrochloride and was reduced with diborane to a one-armed nitrogen mustard which was isolated as a hydrochloride salt.

In all, 43 new compounds were prepared. The compounds were characterized by elemental analysis, ir, uv, and where possible, by nmr spectroscopy.